Electronic Supplementary Material (ESI) for RSC Medicinal Chemistry.


# Nanoscale, automated, high throughput synthesis and screening for the accelerated discovery of protein modifiers

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# 1. General materials and methods

All the reagents and solvents were purchased from Sigma-Aldrich, AK Scientific, Fluorochem, Abcr GmbH, Acros and were used without further purification. All isocyanides were prepared in house by either performing the Ugi,[1] Hoffman[2] or our recently described Leukart-Wallach reductive amination procedure (Fig. S1).[3]

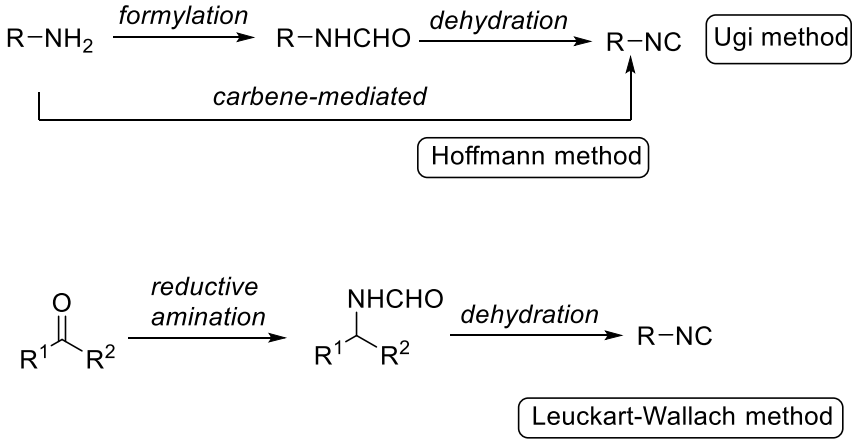



**Fig. S1.** Isocyanide syntheses.

Thin layer chromatography was performed on Millipore precoated silica gel plates (0.20 mm thick, particle size 25 µm). Nuclear magnetic resonance spectra were recorded on a Bruker Avance 500 spectrometers {$^{1}$H NMR (500 MHz), $^{13}$C NMR (126 MHz)}. Chemical shifts for $^{1}$H NMR were reported as *δ* values and coupling constants were in hertz (Hz). The following abbreviations were used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, dd = double of doublets, m = multiplet. Chemical shifts for $^{13}$C NMR were reported in ppm relative to the solvent peak. Flash chromatography was performed on a Reveleris® X2 Flash Chromatography, using Grace® Reveleris Silica flash cartridges (12 grams). Mass spectra were measured on a Waters Investigator Supercritical Fluid Chromatograph with a 3100 MS Detector (ESI) using a solvent system of methanol and $CO_2$ on a Viridis silica gel column (4.6 x 250 mm, 5 µm particle size) or Viridis 2-ethyl pyridine column (4.6 x 250 mm, 5 µm particle size). High resolution mass spectra were recorded using a LTQ-Orbitrap-XL (Thermo) at a resolution of 60000@m/z400.

# 2. Nanomole-scale chemical reactions

## 2.1. General materials

Stock solutions were prepared in glass flat bottom vials (Screening devices, Catalog#: 9920-812FBT, 2.0 mL (Topas) Plate) and they were kept at -20 °C.

Nanomole-scale chemistry was performed using Echo qualified 384-well polypropylene microplate (Labcyte, Catalog#: PP-0200, clear, flat bottom) according to the producers' manual.

384-Well source and destination plates were sealed by a sealing tape (Thermo Scientific, Catalog#: 232701, polyolefin acrylate) and were kept at -20 °C.

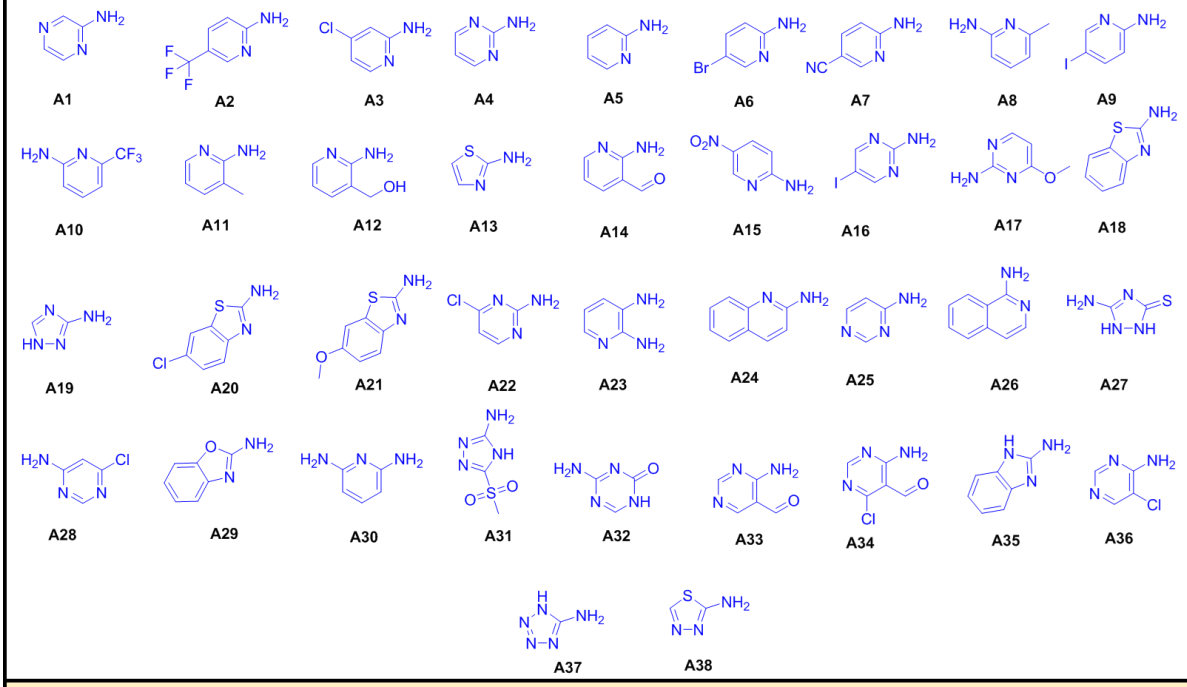
## 2.2. Instrumentation

The Echo 555 liquid handler (Labcyte) was used in order to transfer nL droplets of starting materials from the 384-well source plate to the 384-well destination plate.

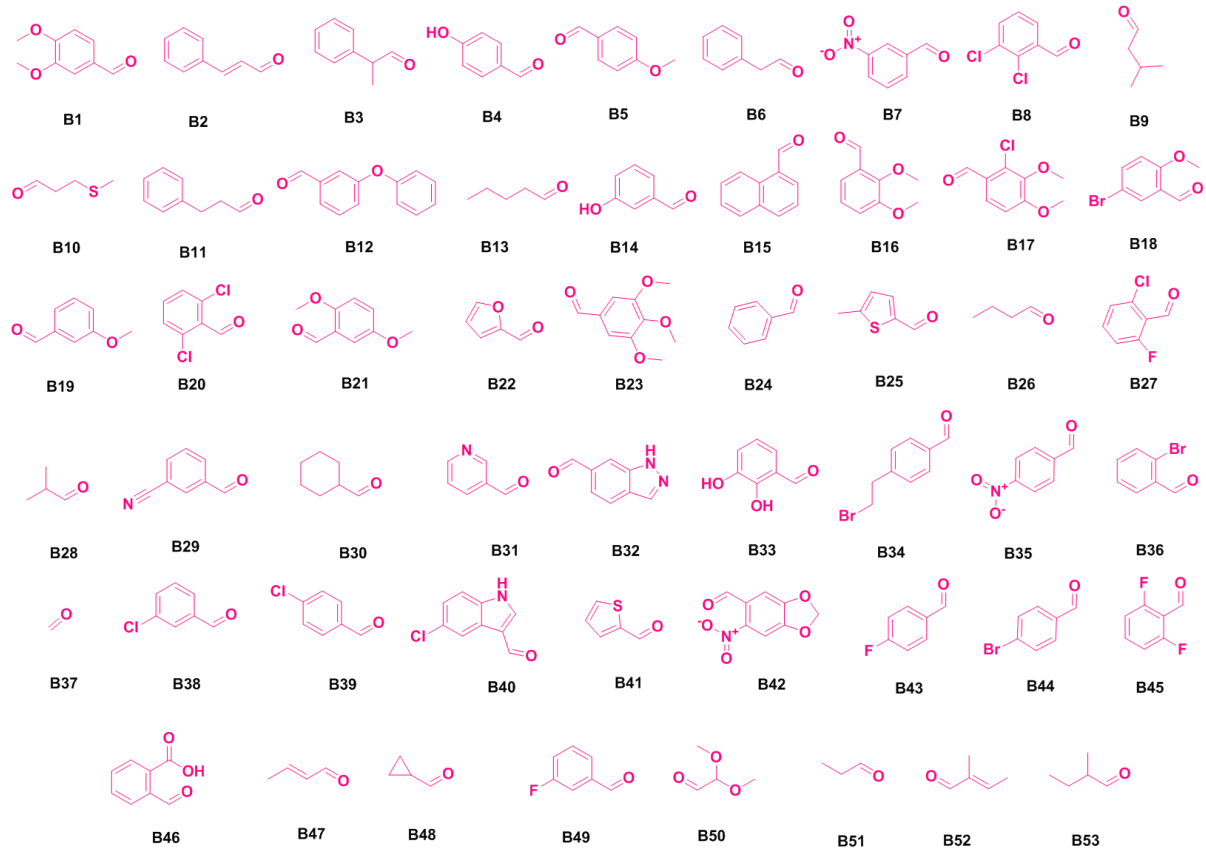
## 2.3. Nanomole-scale automated chemistry

### 2.3.1. Structures of building blocks

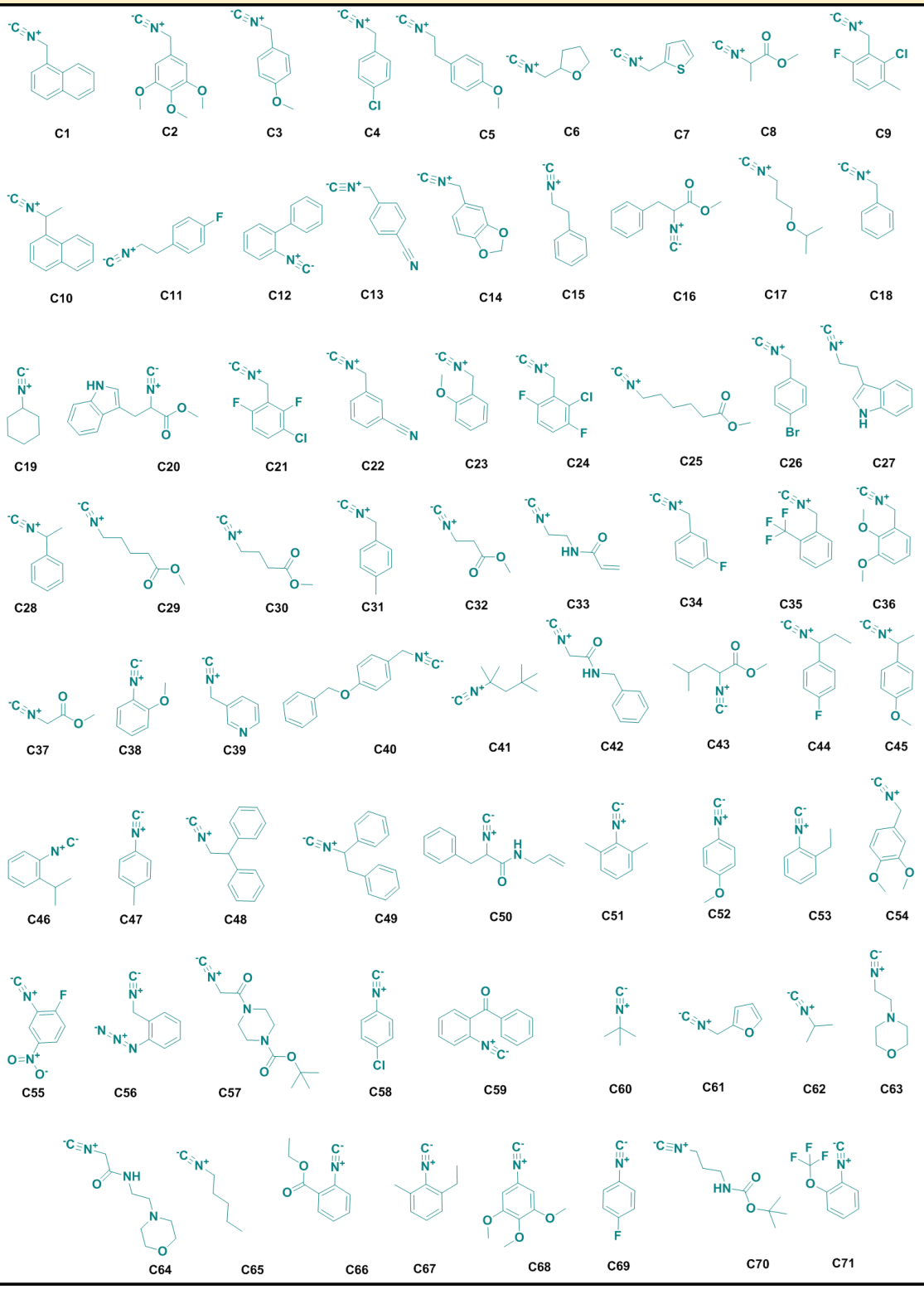
**Amidines**




**Aldehydes**



## Isocyanides



### 2.3.2.Stock solution preparation

Stock solutions of amidines (**A1, A2, A4-A7, A9-A14, A18, A19, A21, A23-A26, A29-A32, A35, A37, A38**) were prepared as 0.5 M in ethylene glycol. Due to the insolubility of some amidines in ethylene glycol, their stock solutions were instead prepared as 0.5 M: **A3** in ethylene glycol/2-methoxyethanol (1:2); **A8, A17, A20, A27, A28** in 2-methoxyethanol. Due to the insolubility of some of the amidines in 0.5 M 2-methoxyethanol, their stock solutions were diluted to 0.25 M (**A15, A33, A34**) and 0.16 M (**A16, A22, A36**), respectively.

Stock solutions of aldehydes (**B4, B5, B9, B10, B13, B18, B19, B22, B24-B26, B28, B30, B31, B37, B38, B41, B45, B48, B49, B51, B53**) were prepared as 0.5 M in ethylene glycol. Due to insolubility of some aldehydes and ketones in ethylene glycol, their stock solutions were instead prepared as 0.5 M: **B3, B11, B12, B27, B29, B36, B44, B46, B47, B50,** in ethylene glycol/2-methoxyethanol (2:1); **B1, B2, B6, B8, B14, B15, B16, B21, B43, B52** in ethylene glycol/2-methoxyethanol (1:1); **B7, B23, B34** in ethylene glycol/2-methoxyethanol (1:2); **B17, B20, B32, B33, B35, B39, B40, B42** in 2-methoxyethanol.

Stock solutions of isocyanides (**C3-C8, C11, C15, C17-C19, C25, C27, C29-C34, C37-C39, C41, C43-C47, C52, C53, C57, C60-C67, C69-C71**) were prepared as 0.5 M in ethylene glycol. Due to the insolubility of some isocyanides (**C1, C2, C9, C10, C12-C14, C16, C20-C24, C26, C28, C35, C36, C40, C42, C48-C51, C54-C56, C58, C59, C68**) in ethylene glycol, their stock solutions were instead prepared as 0.5 M in 2-methoxyethanol.

Stock solutions of $Sc(OTf)_3$ was prepared as 0.5 M in ethylene glycol.

### 2.3.3.Nano scale synthesis

The stock solutions were dispensed to a 384-well source plate using Eppendorf multi-channel pipettes. The Echo 555 was used to transfer the starting materials into the corresponding well in the destination plate.

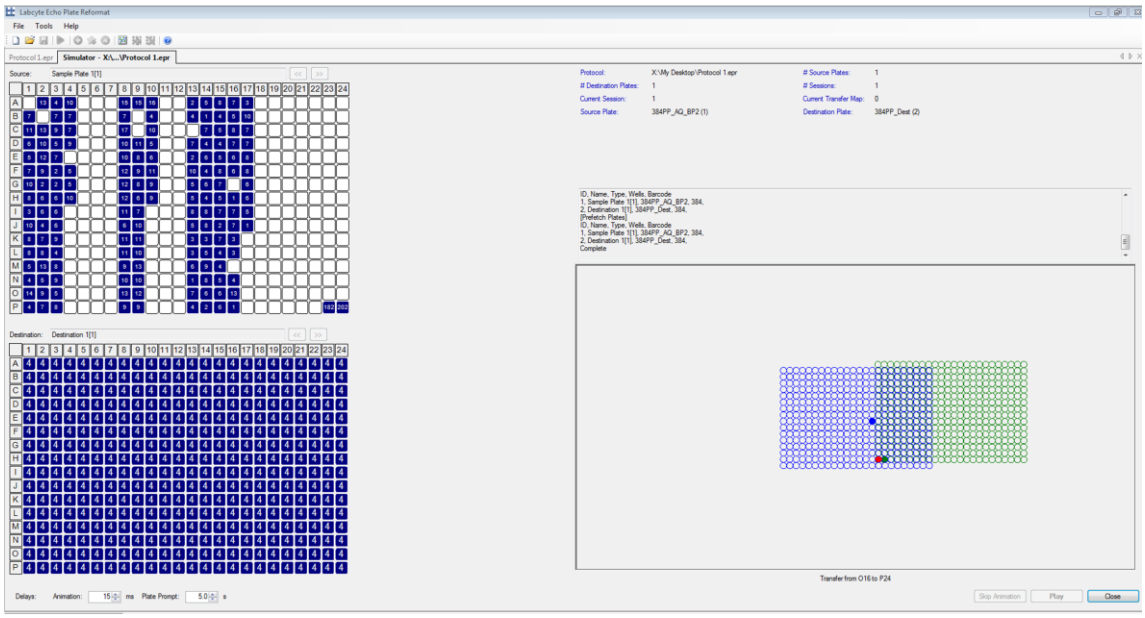
For GBB-3CR reaction, amidines (1 eq, 1000 nL), aldehydes (1 eq, 1000 nL), $Sc(OTf)_3$ (10 mol%, 100 nL) and isocyanides (1 eq, 1000 nL) were transferred into the corresponding well in the destination plate, respectively. In case of diluted amidines with 0.25 M and 0.16 M concentration, 2000 nL and 3000 nL were transferred, respectively.

### 2.3.4.Pick list preparation

Labcyte Echo plate reformat software using custom mapping mode with the run protocol as defined by a pick list was used (Fig. S2A).

In order to generate a random library of products (N=1536), a modified version of our previously reported program RandReactor was used.[4] The smiles files of the starting materials with the corresponding location in the source plate and mrv file of reaction were the input of the RandReactor program. The smiles file of the randomly generated products with their corresponding locations in the source and destination plate were the output of the RandReactor program. The smiles file was converted to a csv file which was the required format for Labcyte Echo plate reformat software (Fig. S2B). The structures of the products are shown in Fig. S3.

**A**



**B**

| | A | B | C | D | E | F | G | H | I | J |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Source Plate Name | Source Well | Destination Plate Name | Destination well | Transfer Volume | | | | | |
| 2 | Sample Plate 1 | G9 | Destination 1 | A1 | 1000 | | | | | |
| 3 | Sample Plate 1 | G1 | Destination 1 | A1 | 1000 | | | | | |
| 4 | Sample Plate 1 | O9 | Destination 1 | A2 | 2000 | | | | | |
| 5 | Sample Plate 1 | D4 | Destination 1 | A2 | 1000 | | | | | |
| 6 | Sample Plate 1 | F9 | Destination 1 | A3 | 1000 | | | | | |
| 7 | Sample Plate 1 | L2 | Destination 1 | A3 | 1000 | | | | | |
| 8 | Sample Plate 1 | O8 | Destination 1 | A4 | 1000 | | | | | |
| 9 | Sample Plate 1 | F2 | Destination 1 | A4 | 1000 | | | | | |
| 10 | Sample Plate 1 | F8 | Destination 1 | A5 | 1000 | | | | | |
| 11 | Sample Plate 1 | F2 | Destination 1 | A5 | 1000 | | | | | |
| 12 | Sample Plate 1 | E10 | Destination 1 | A6 | 1000 | | | | | |
| 13 | Sample Plate 1 | C2 | Destination 1 | A6 | 1000 | | | | | |
| 14 | Sample Plate 1 | C10 | Destination 1 | A7 | 1000 | | | | | |
| 15 | Sample Plate 1 | I2 | Destination 1 | A7 | 1000 | | | | | |
| 16 | Sample Plate 1 | E8 | Destination 1 | A8 | 1000 | | | | | |
| 17 | Sample Plate 1 | A2 | Destination 1 | A8 | 1000 | | | | | |
| 18 | Sample Plate 1 | O8 | Destination 1 | A9 | 1000 | | | | | |
| 19 | Sample Plate 1 | M2 | Destination 1 | A9 | 1000 | | | | | |
| 20 | Sample Plate 1 | K9 | Destination 1 | A10 | 1000 | | | | | |
| 21 | Sample Plate 1 | O1 | Destination 1 | A10 | 1000 | | | | | |
| 22 | Sample Plate 1 | M9 | Destination 1 | A11 | 2000 | | | | | |
| 23 | Sample Plate 1 | J3 | Destination 1 | A11 | 1000 | | | | | |
| 24 | Sample Plate 1 | D10 | Destination 1 | A12 | 1000 | | | | | |

**Fig. S2.** (**A**) Labcyte Echo plate reformat software, showing on top the source plate and below the destination plate II; (**B**) Picklist in csv format required for Labcyte Echo plate reformat software.

**Destination plate I**

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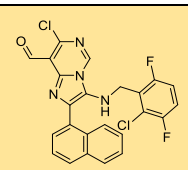
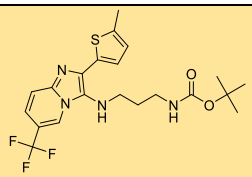
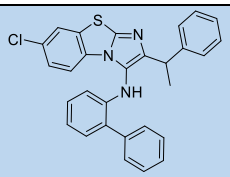
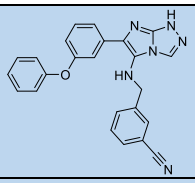
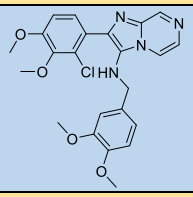
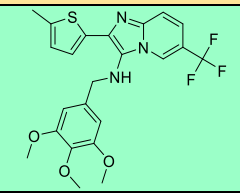
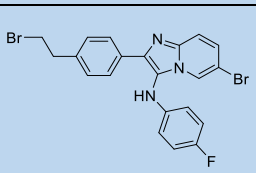
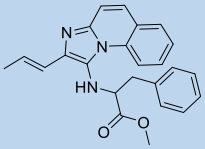
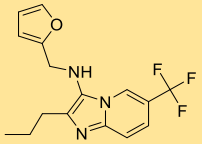
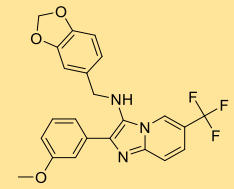
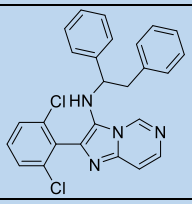
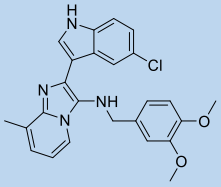
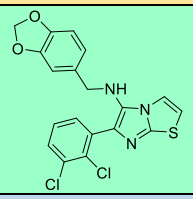
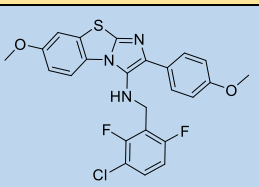
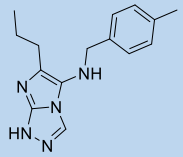
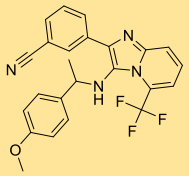
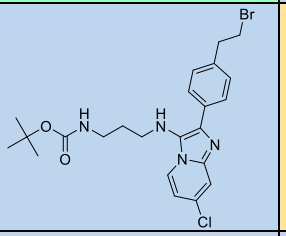
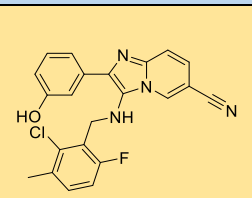
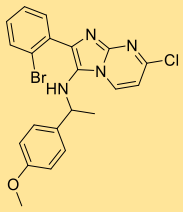
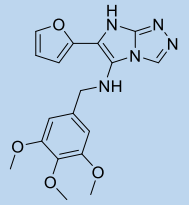
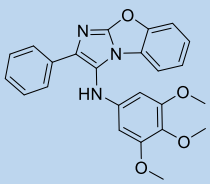
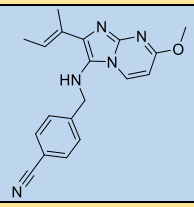
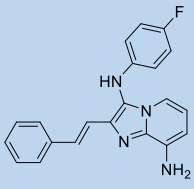
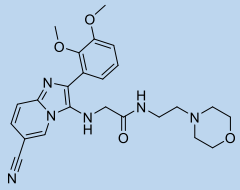
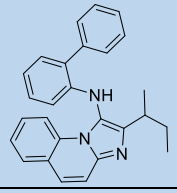
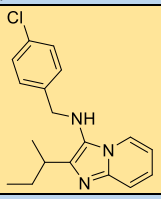
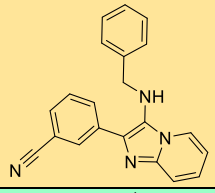
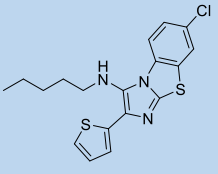
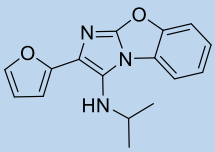
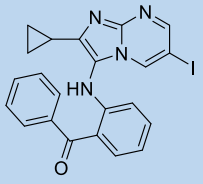
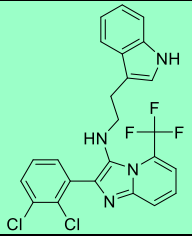
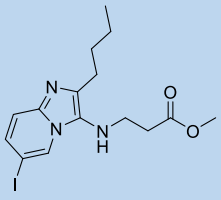
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |
| 7 |  |  |  |  |
| 8 |  |  |  |  |

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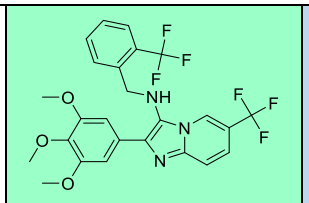
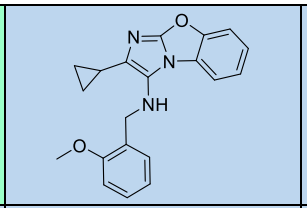
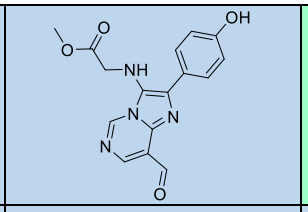
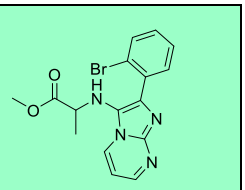
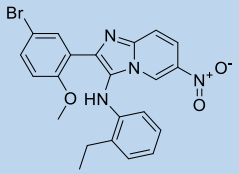
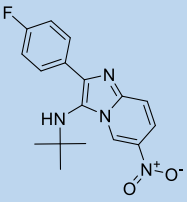
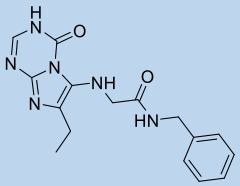
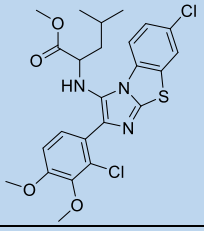
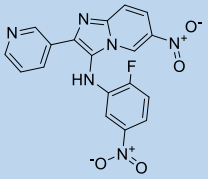
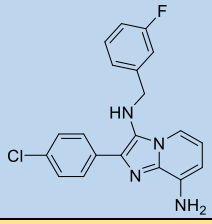
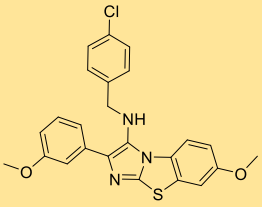
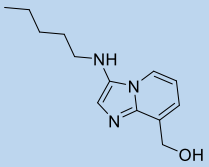
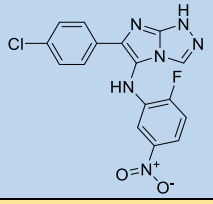
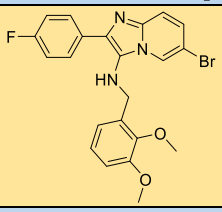
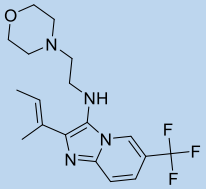
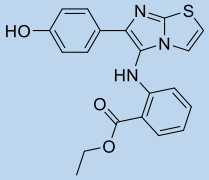
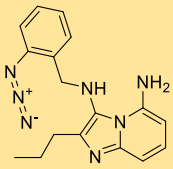
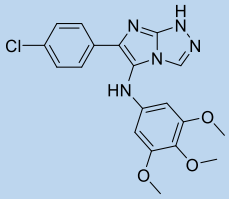
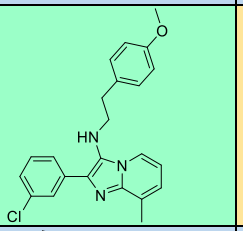
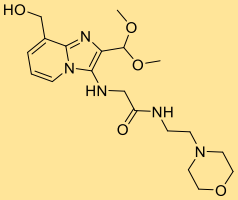
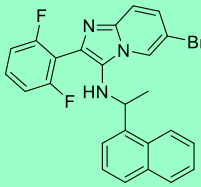
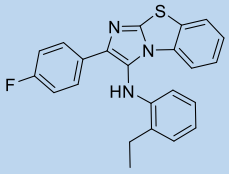
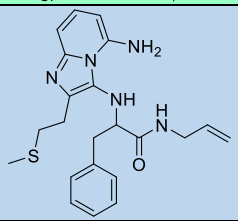
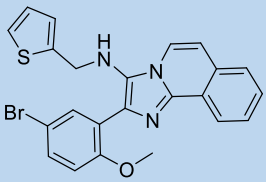
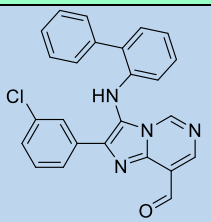
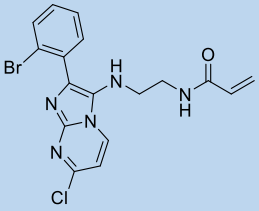
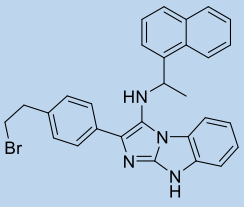
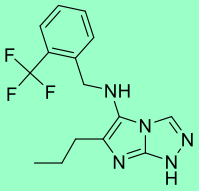
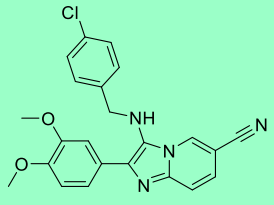
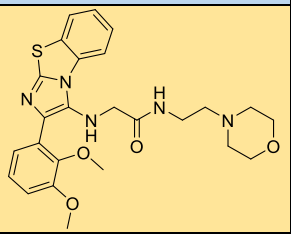
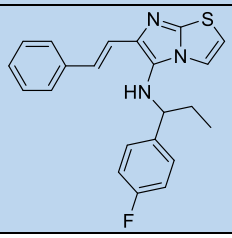
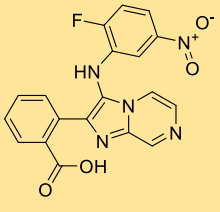
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |

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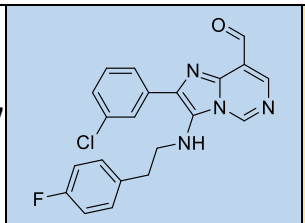
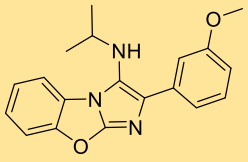
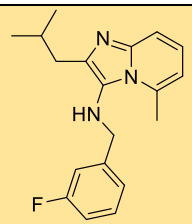
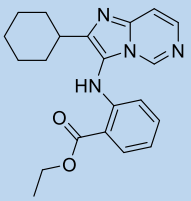
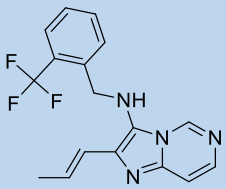
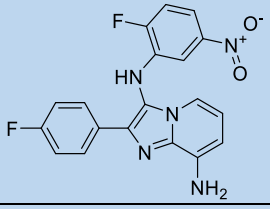
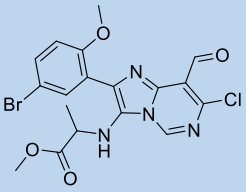
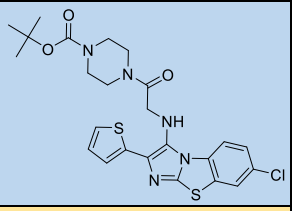
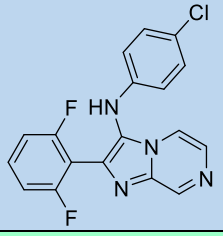
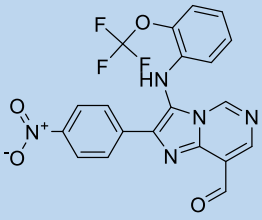
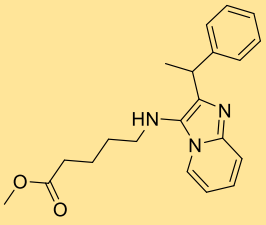
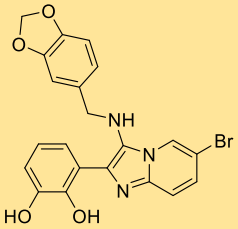
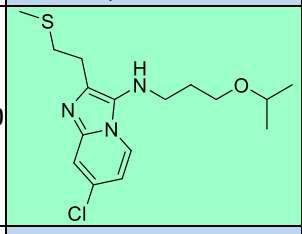
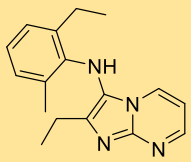
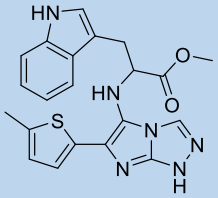
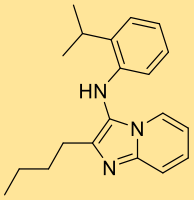
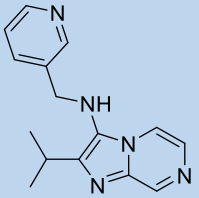
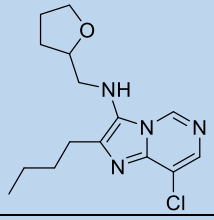
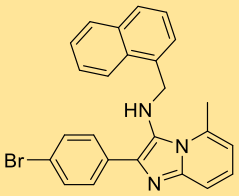
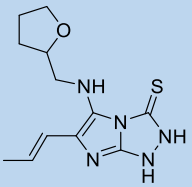
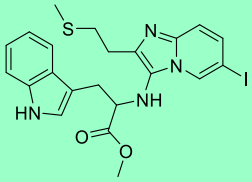
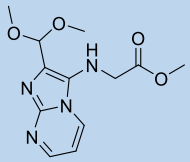
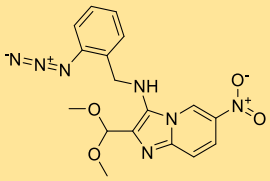
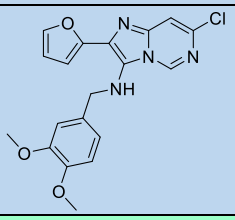
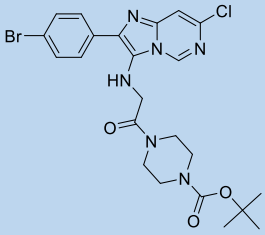
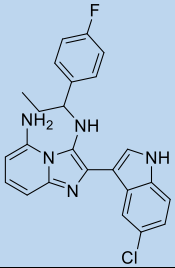
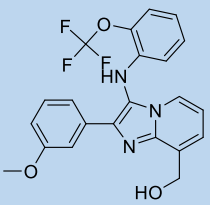
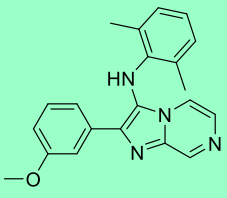
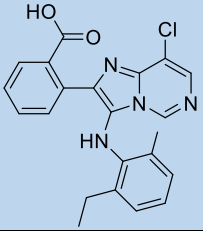
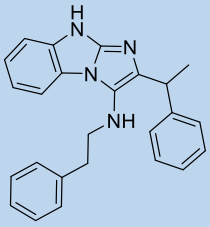
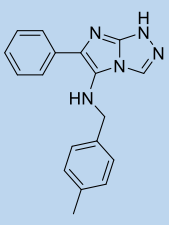
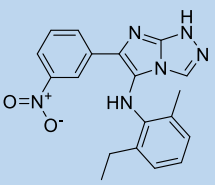
| 17 |  |  |  |  |
| 18 |  |  |  |  |
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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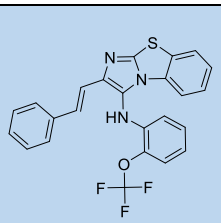
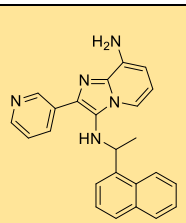
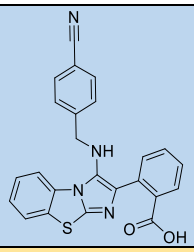
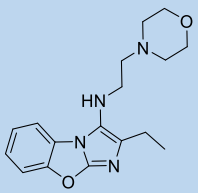
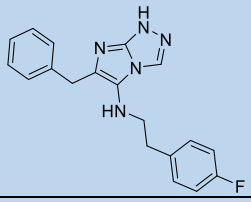
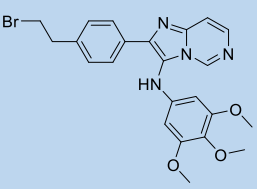
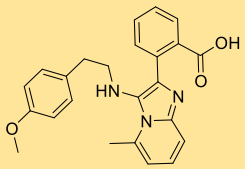
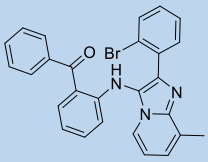
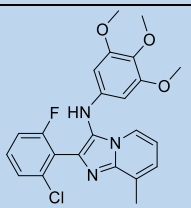
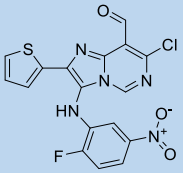
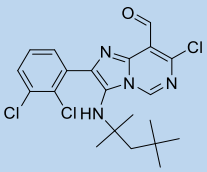
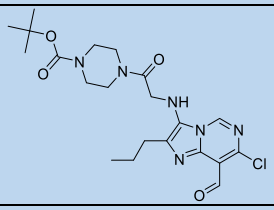
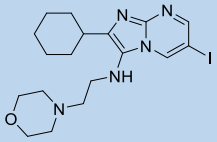
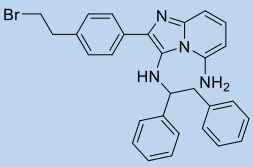
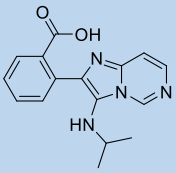
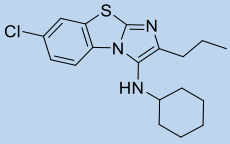
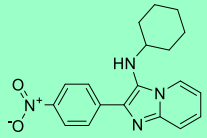
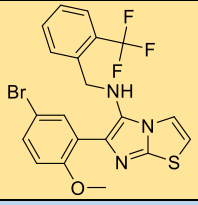
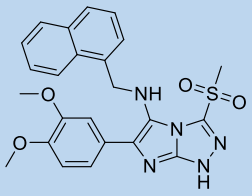
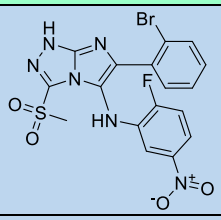
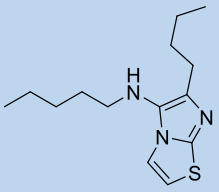
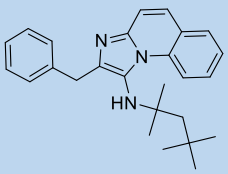
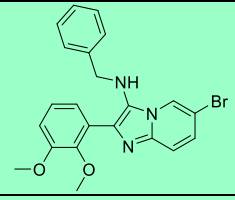
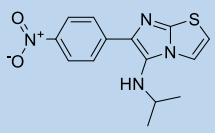
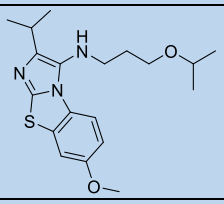
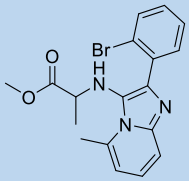
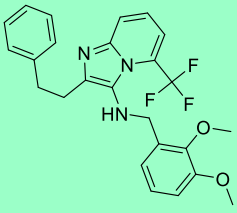
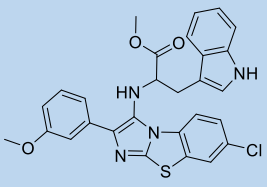
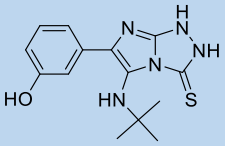
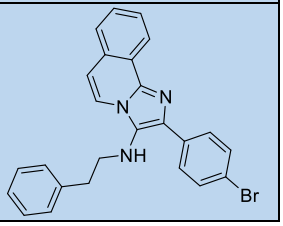
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |
| 7 |  |  |  |  |
| 8 |  |  |  |  |

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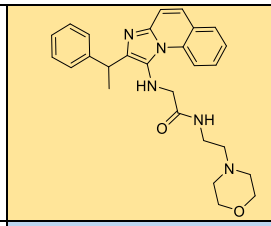
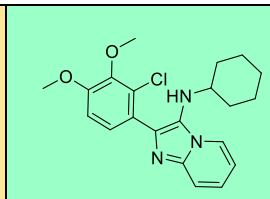
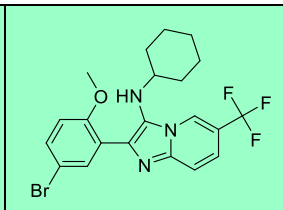
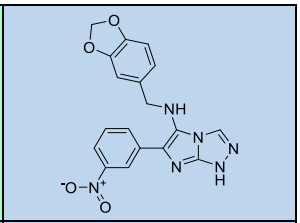
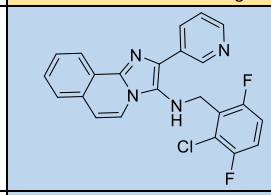
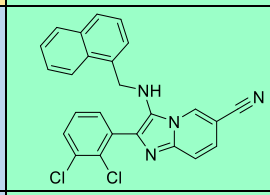
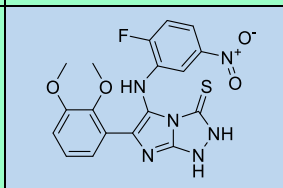
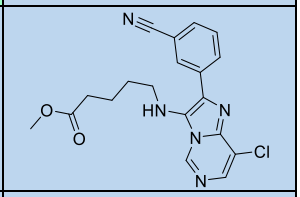
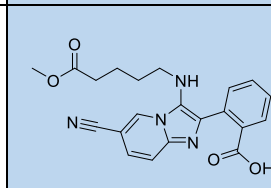
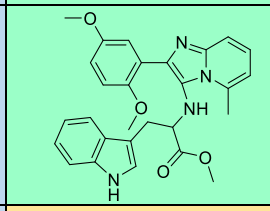
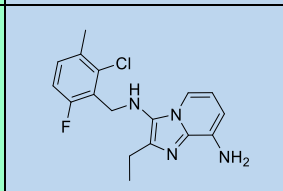
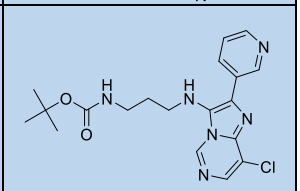
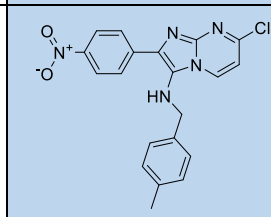
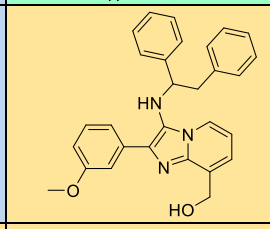
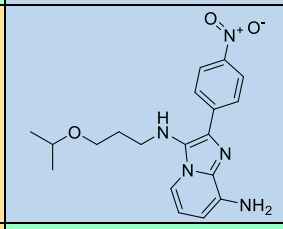
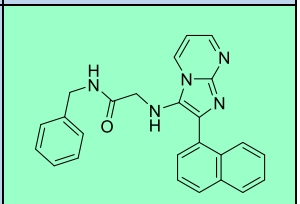
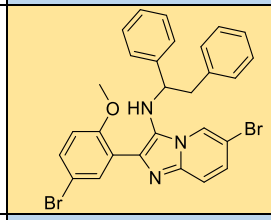
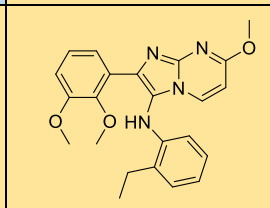
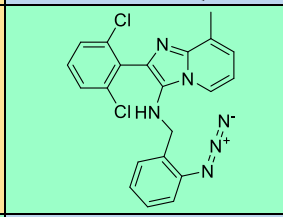
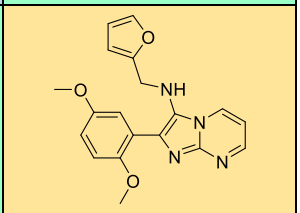
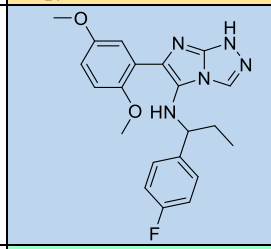
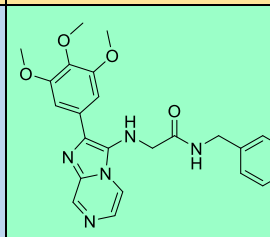
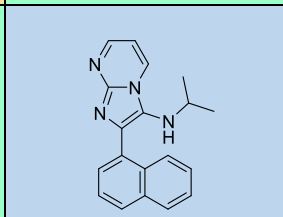
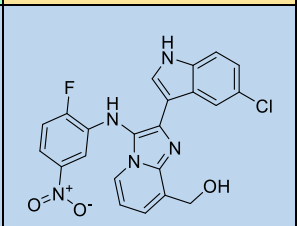
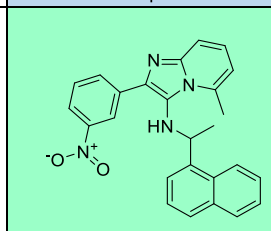
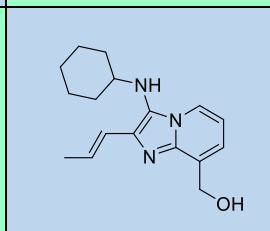
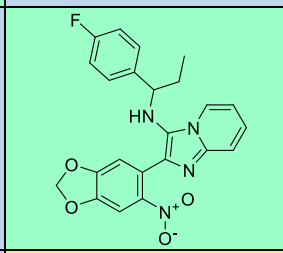
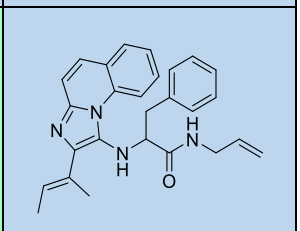
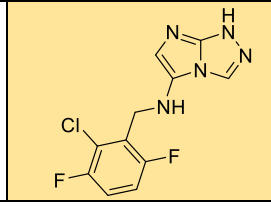
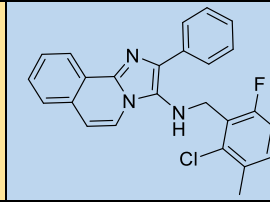
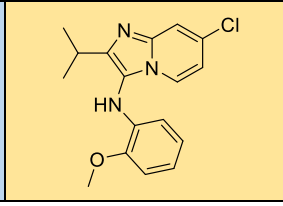
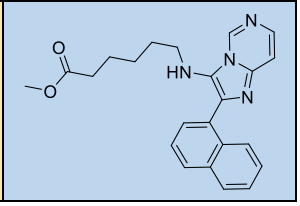
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |

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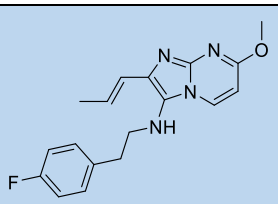
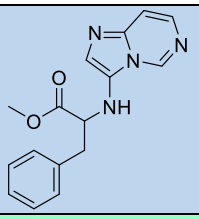
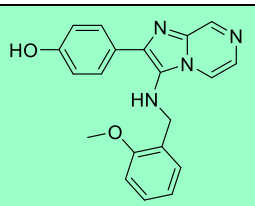
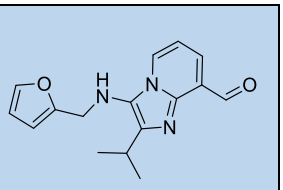
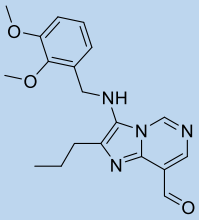
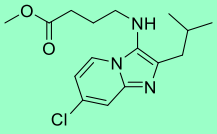
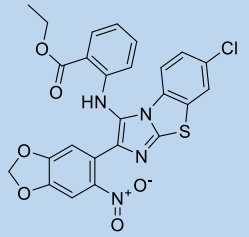
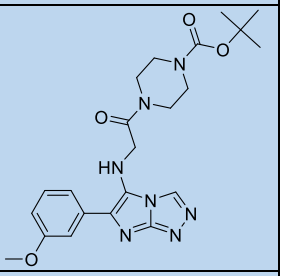
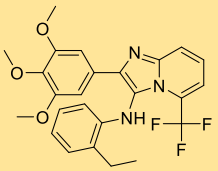
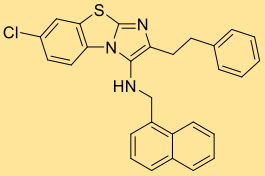
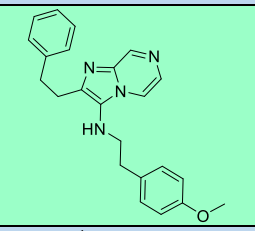
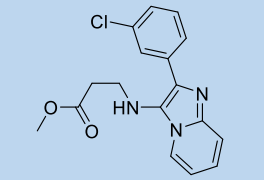
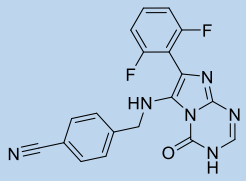
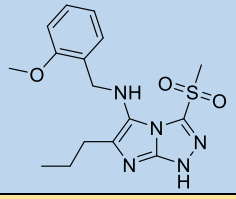
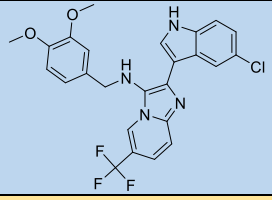
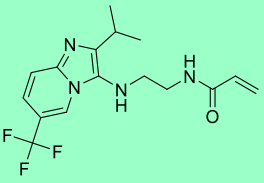
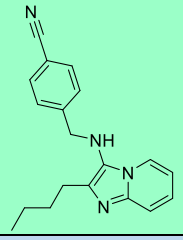
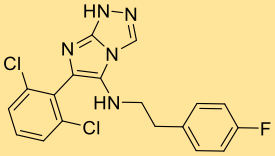
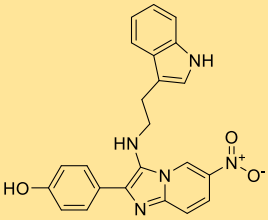
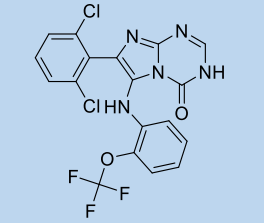
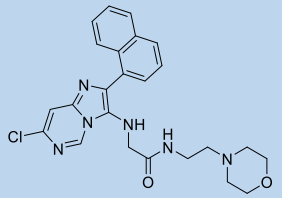
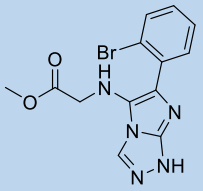
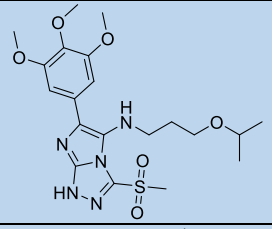
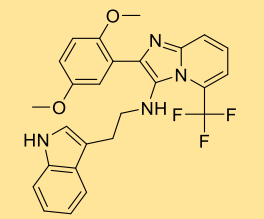
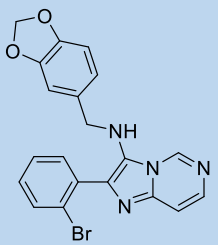
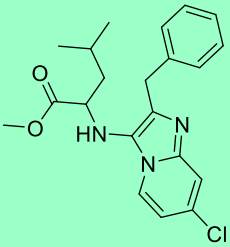
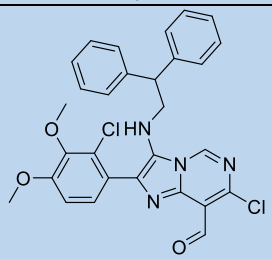
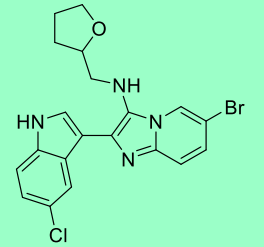
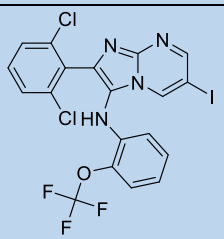
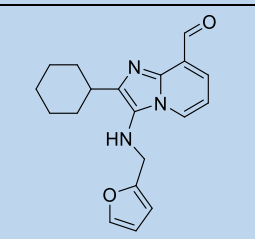
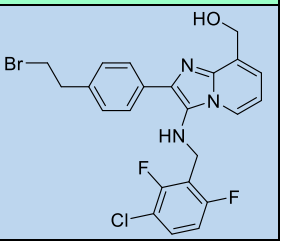
| 17 |  |  |  |  |
| 18 |  |  |  |  |
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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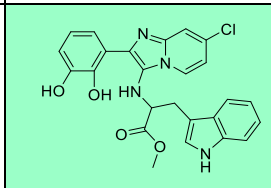
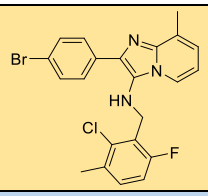
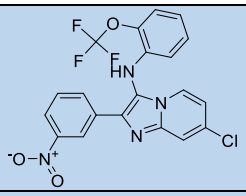
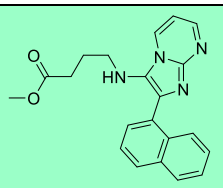
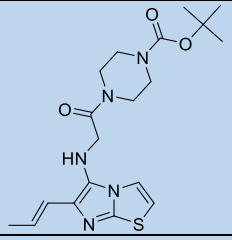
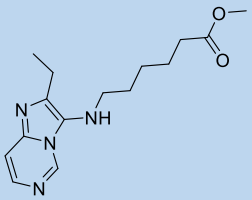
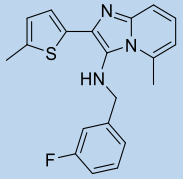
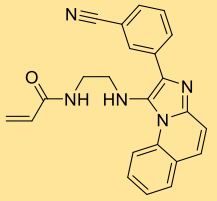
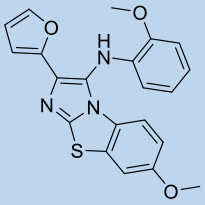
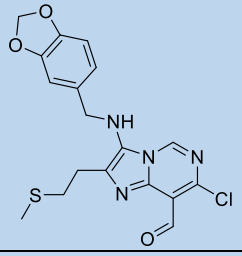
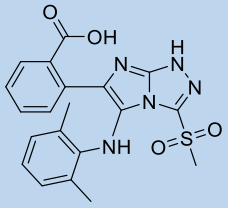
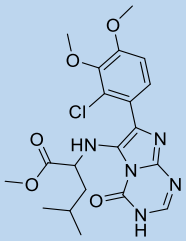
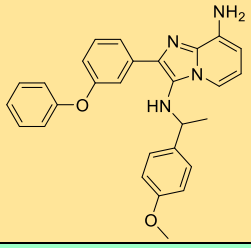
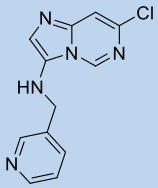
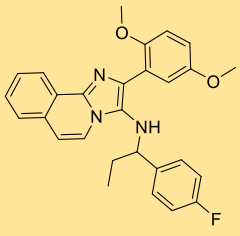
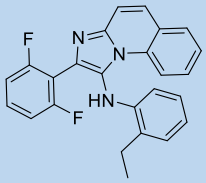
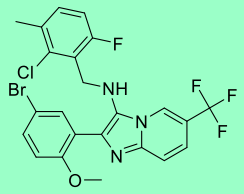
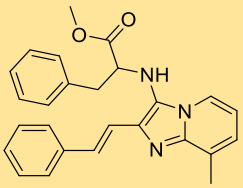
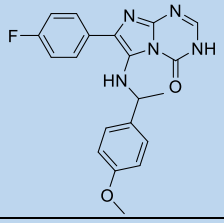
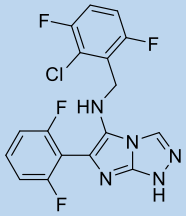
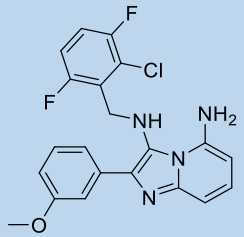
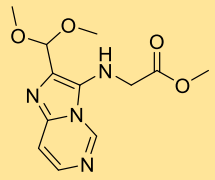
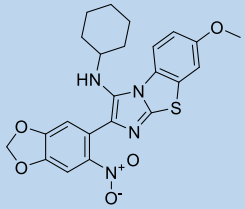
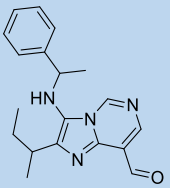
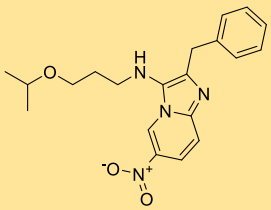
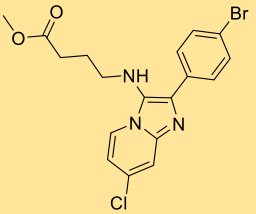
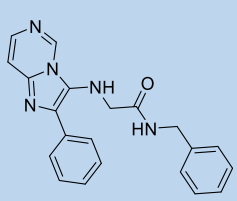
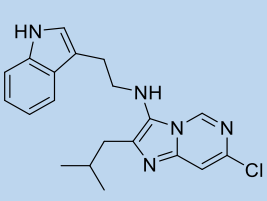
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |
| 7 |  |  |  |  |

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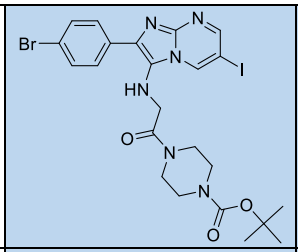
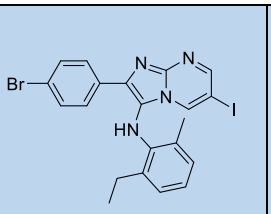
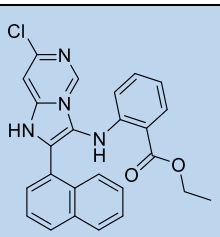
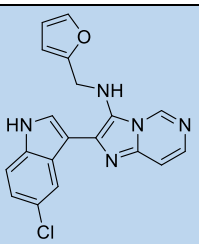
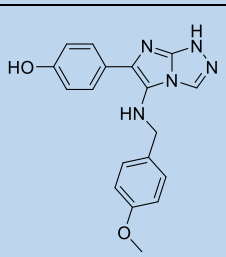
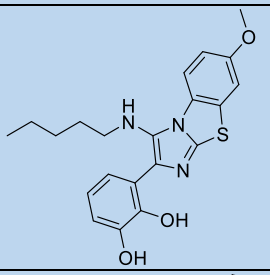
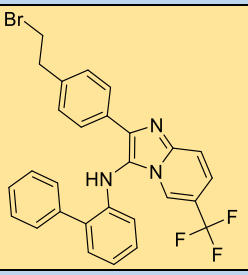
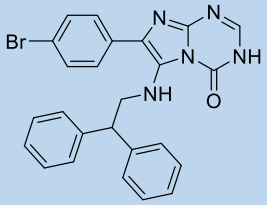
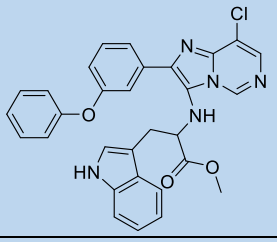
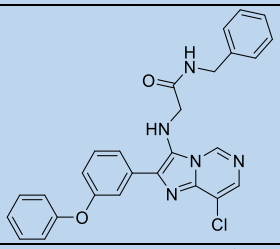
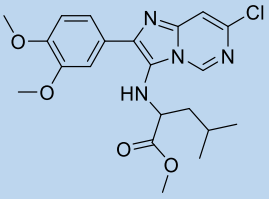
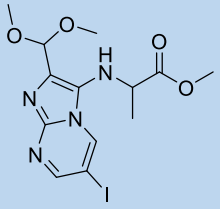
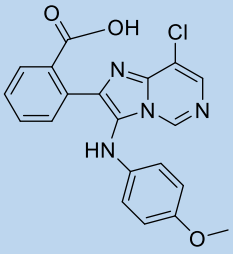
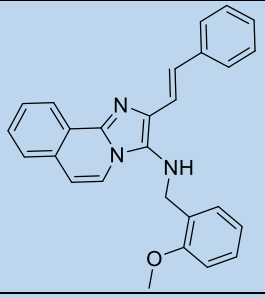
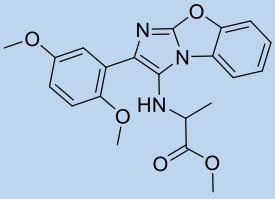
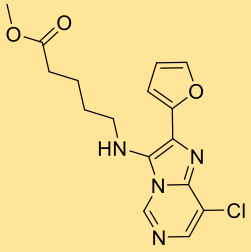
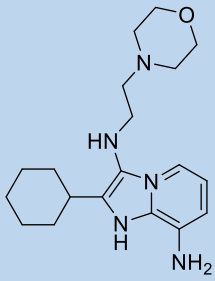
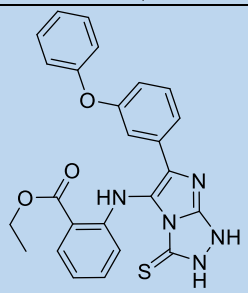
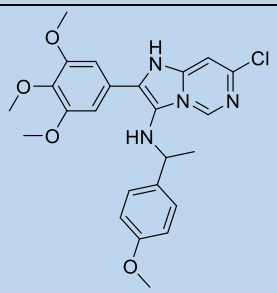
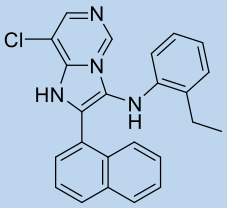
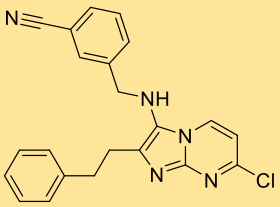
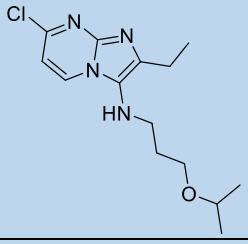
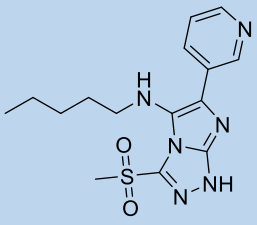
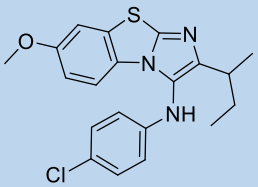
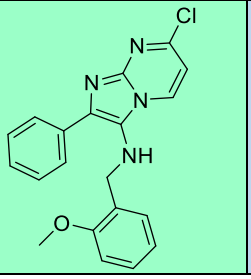
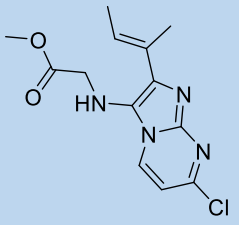
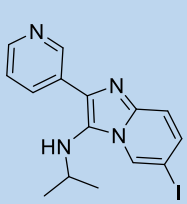
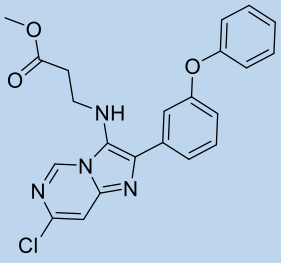
| **8** |  |  |  |  |
| **9** |  |  |  |  |
| **10** |  |  |  |  |
| **11** |  |  |  |  |
| **12** |  |  |  |  |
| **13** |  |  |  |  |
| **14** |  |  |  |  |

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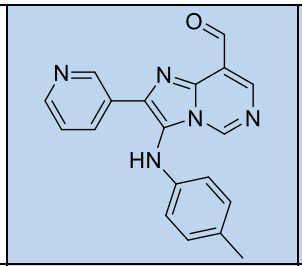
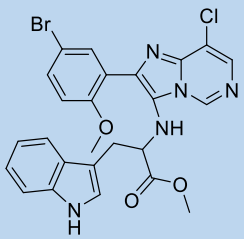
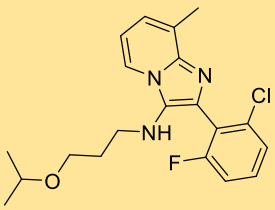
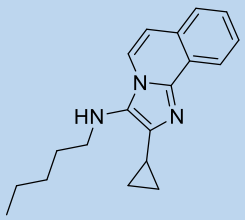
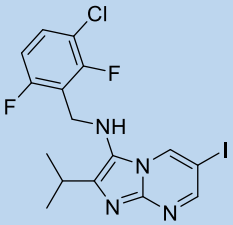
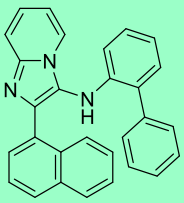
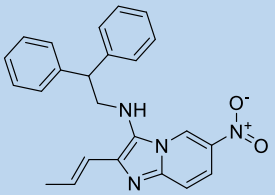
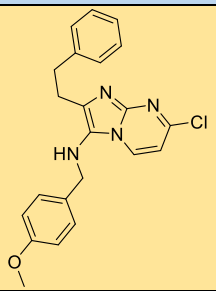
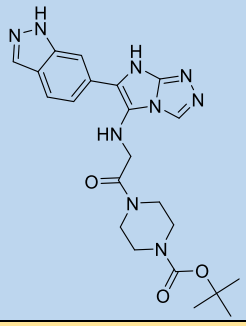
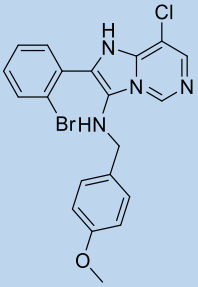
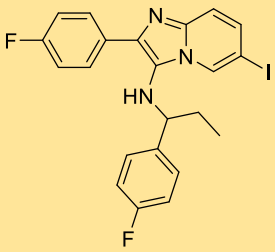
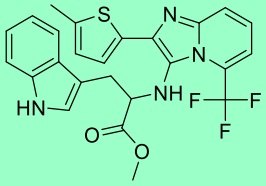
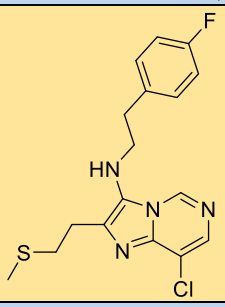
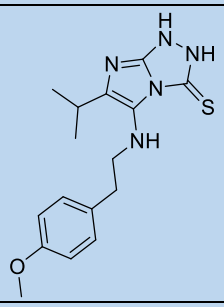
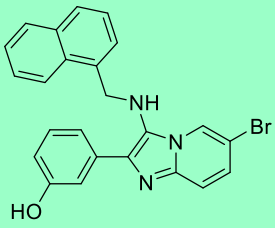
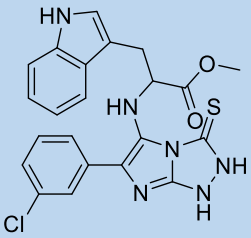
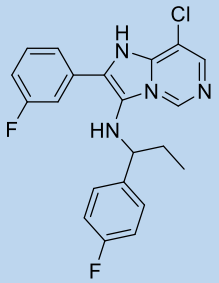
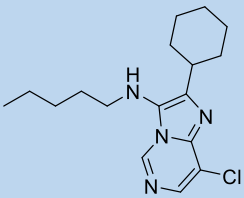
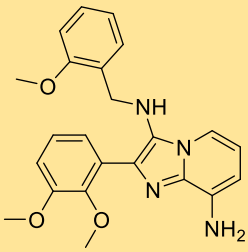
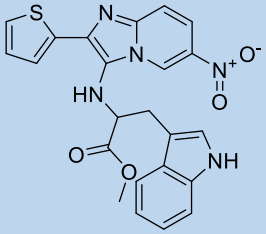
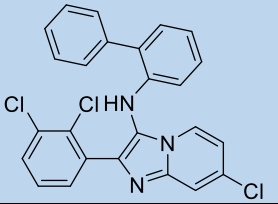
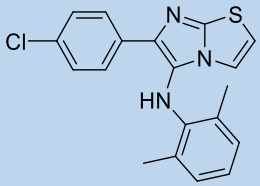
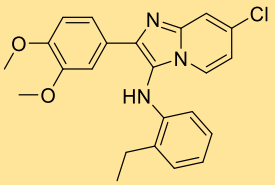
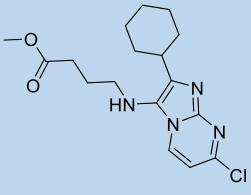
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |
| 19 |  |  |  |  |
| 20 |  |  |  |  |

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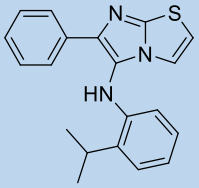
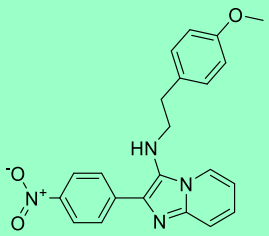
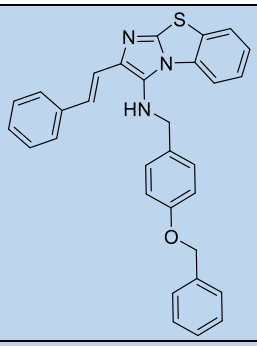
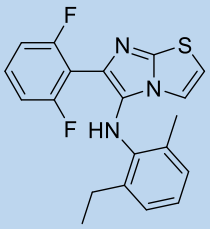
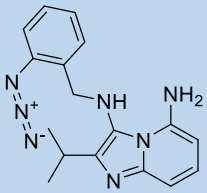
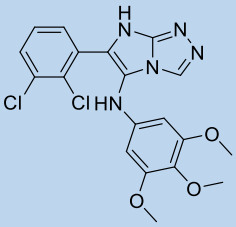
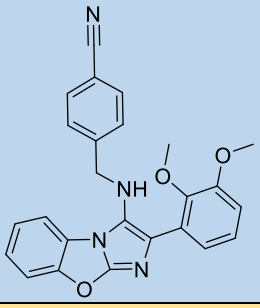
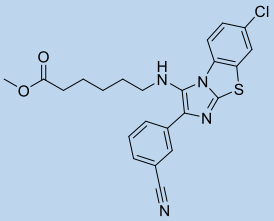
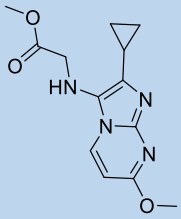
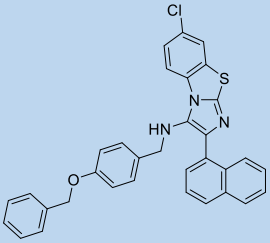
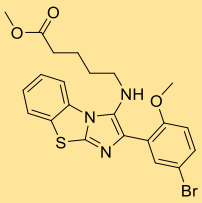
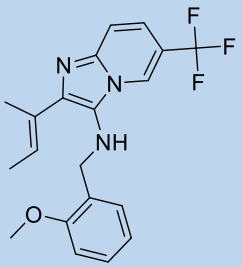
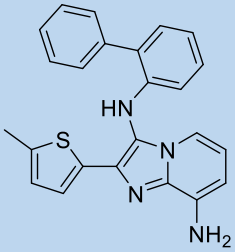
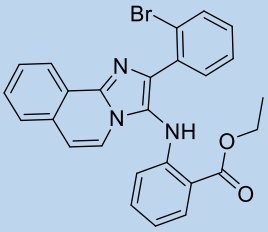
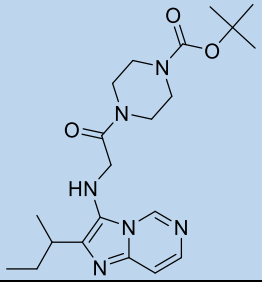
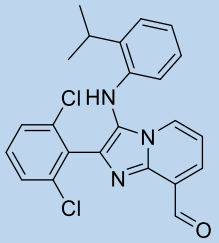
| **21** |  |  |  |  |
| **22** |  |  |  |  |
| **23** |  |  |  |  |
| **24** |  |  |  |  |

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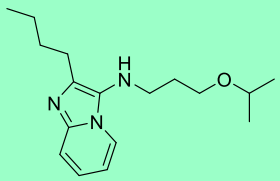
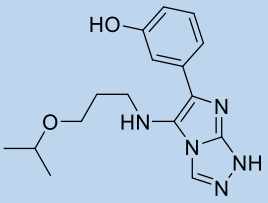
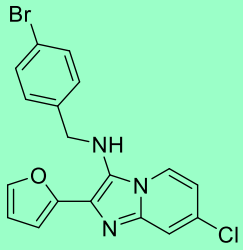
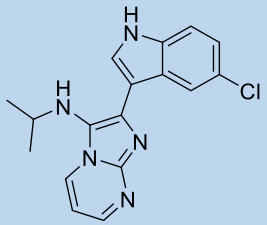
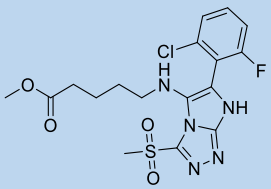
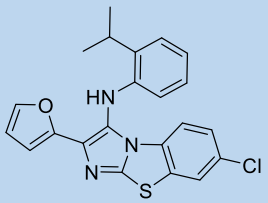
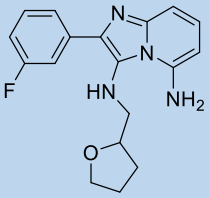
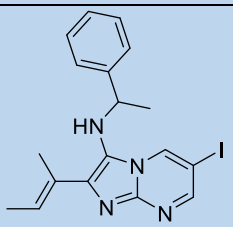
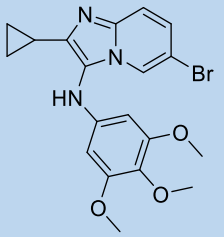
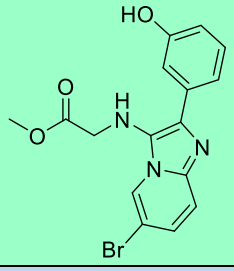
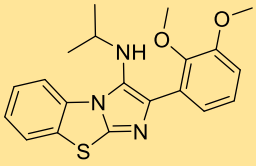
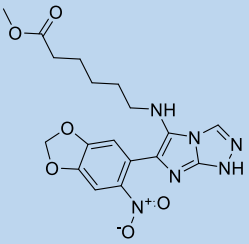
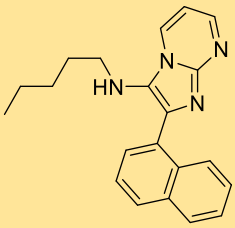
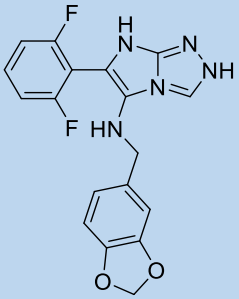
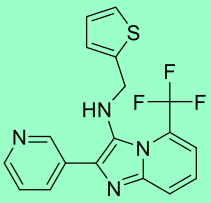
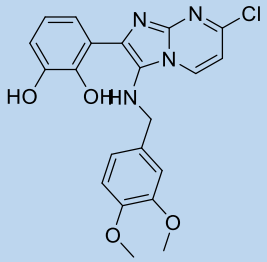
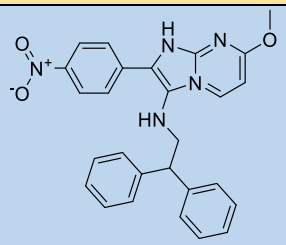
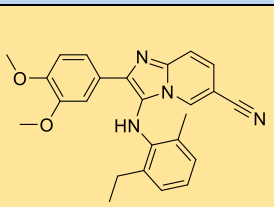
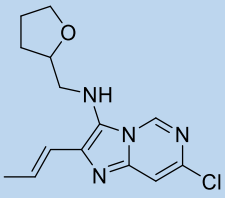
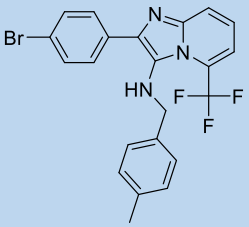
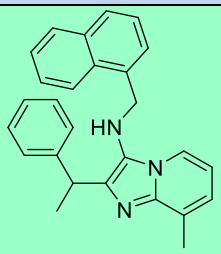
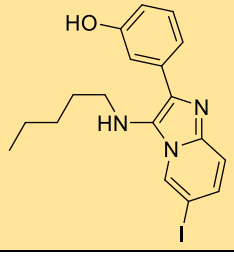
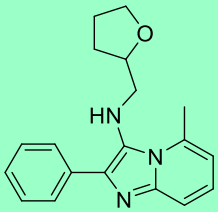
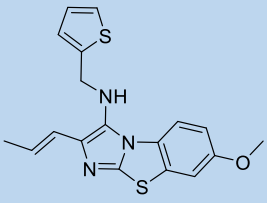
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |

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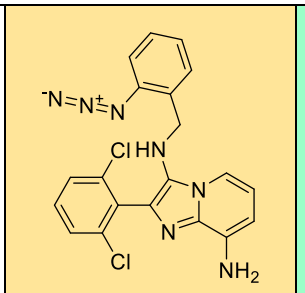
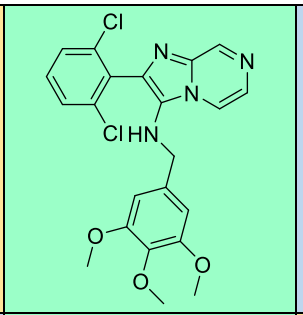
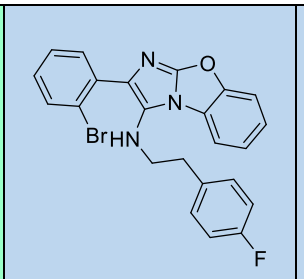
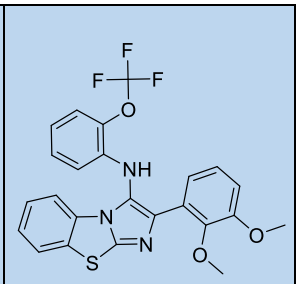
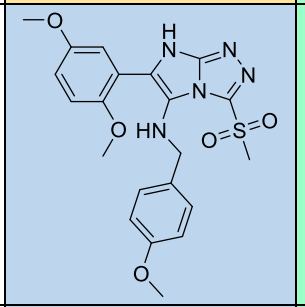
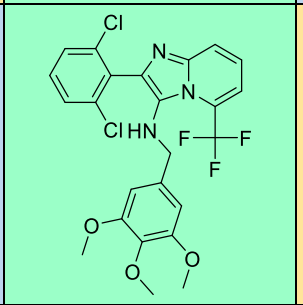
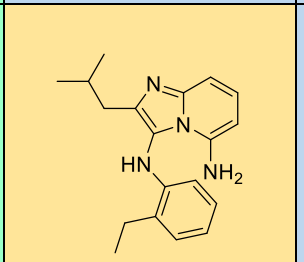
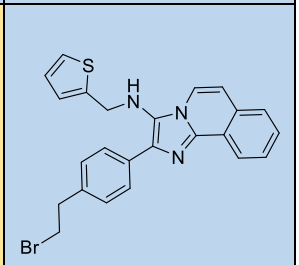
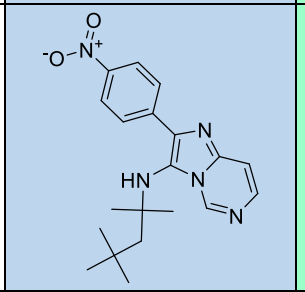
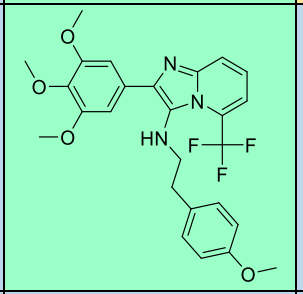
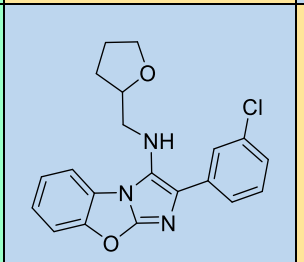
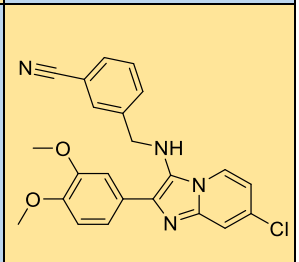
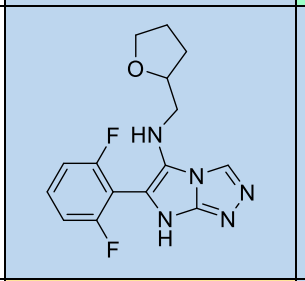
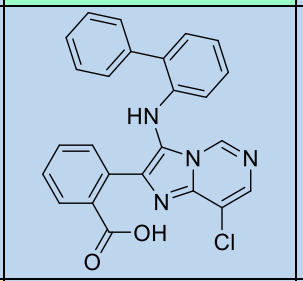
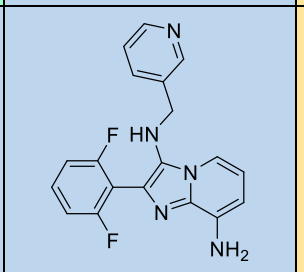
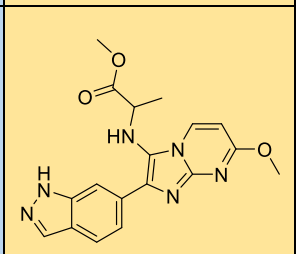
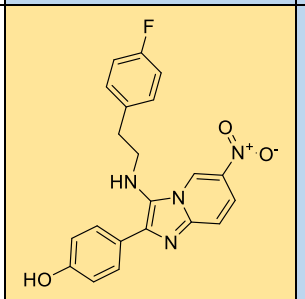
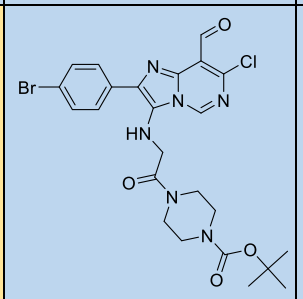
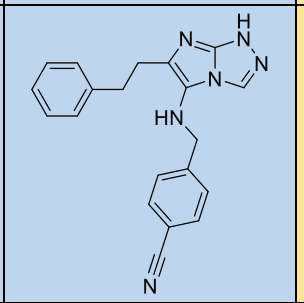
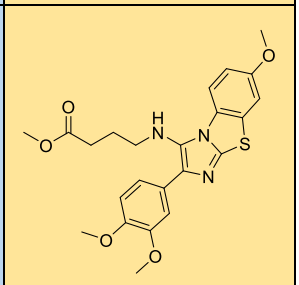
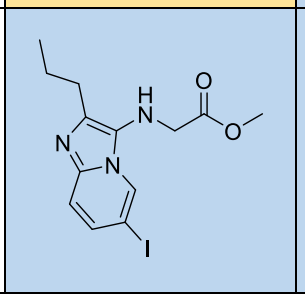
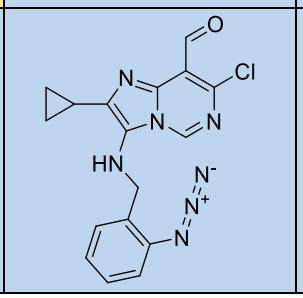
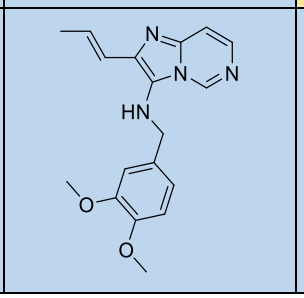
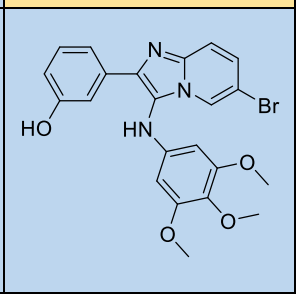
| 7 |  |  |  |  |
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |

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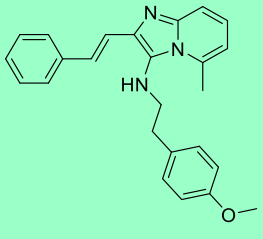
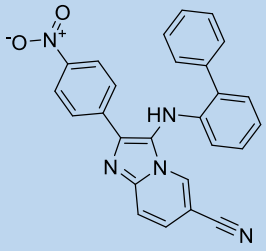
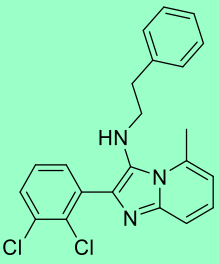
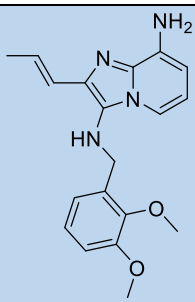
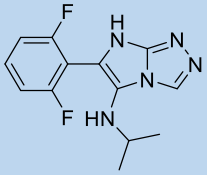
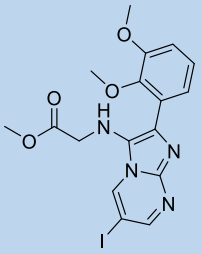
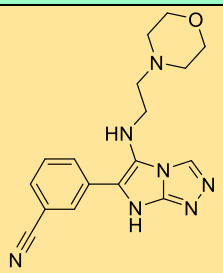
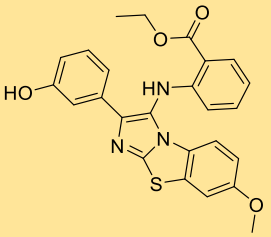
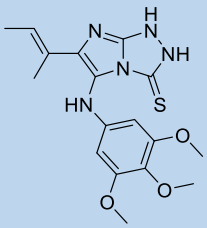
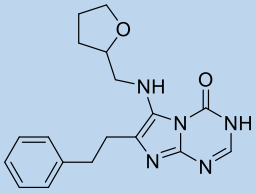
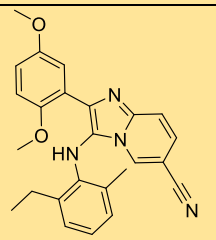
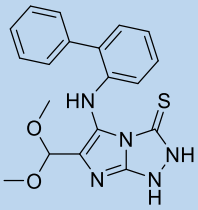
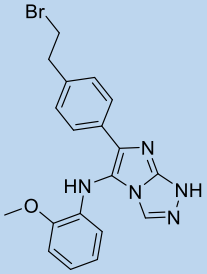
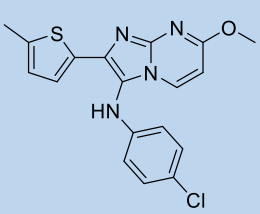
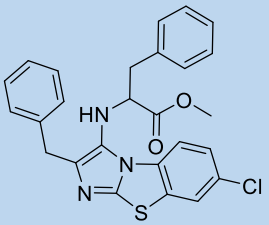
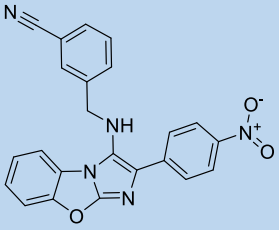
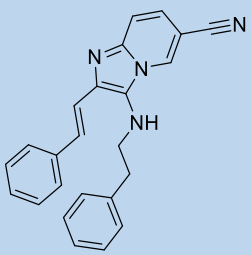
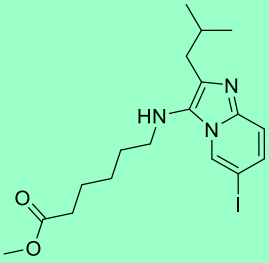
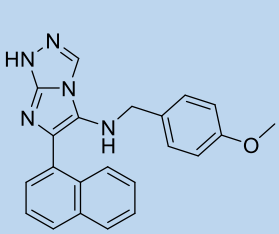
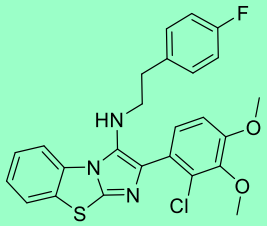
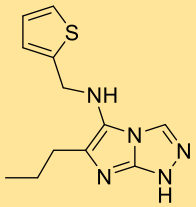
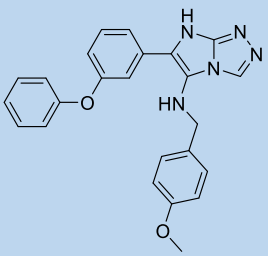
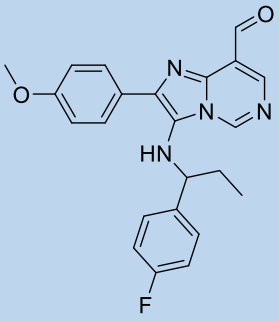
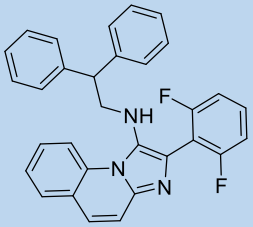
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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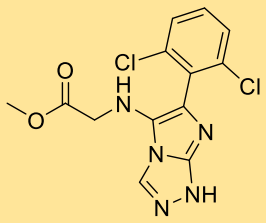
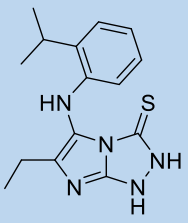
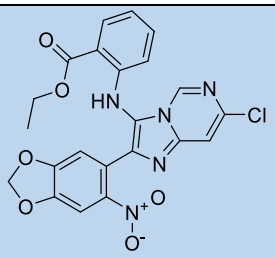
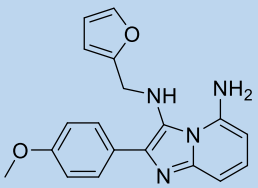
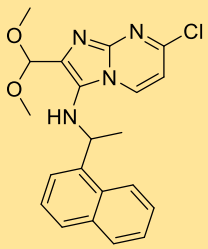
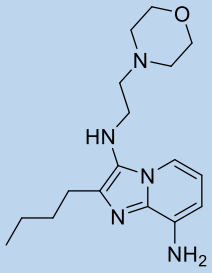
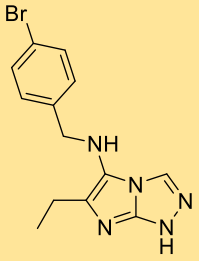
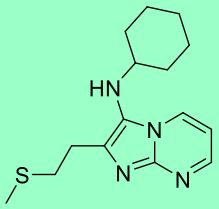
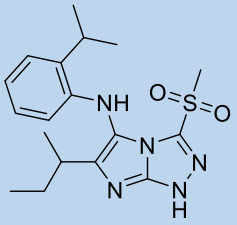
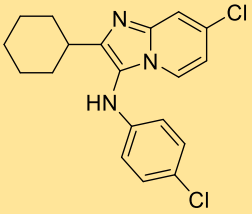
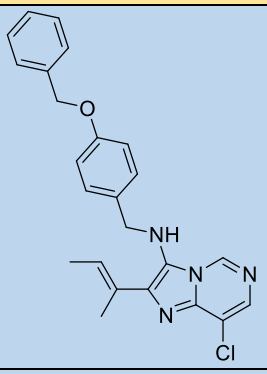
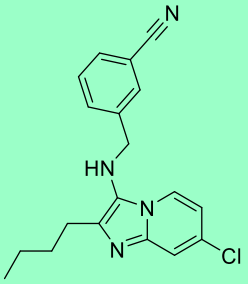
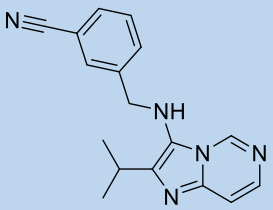
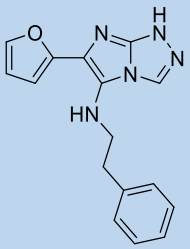
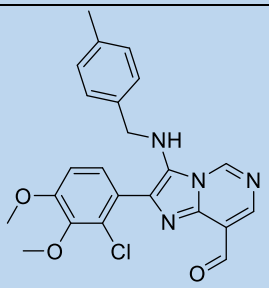
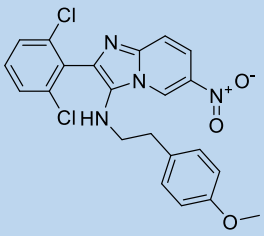
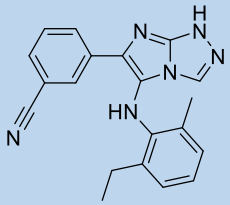
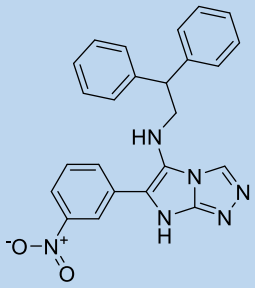
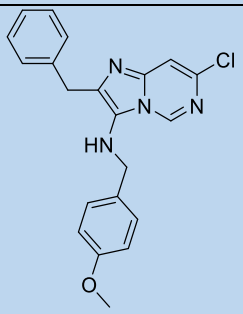
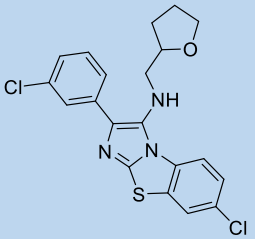
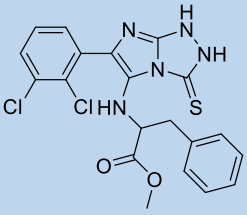
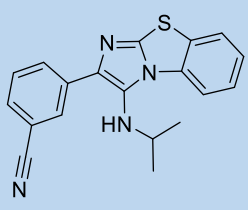
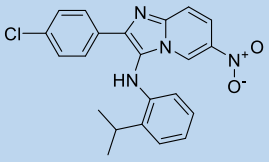
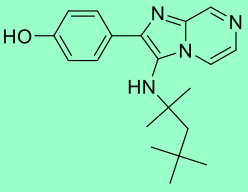
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

**Destination plate II**

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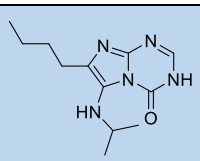
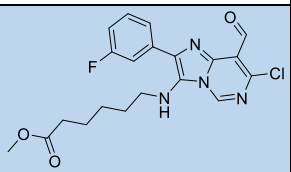
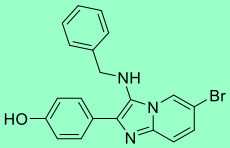
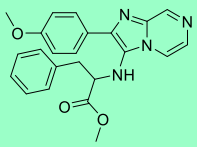
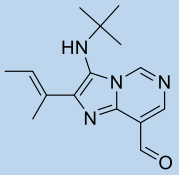
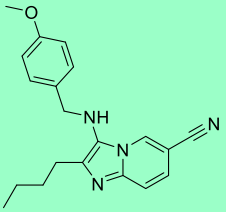
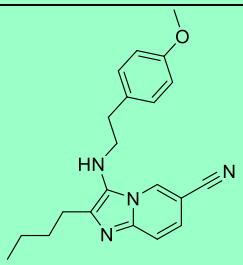
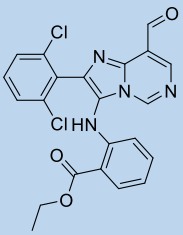
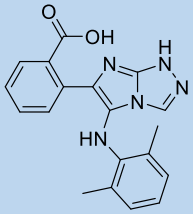
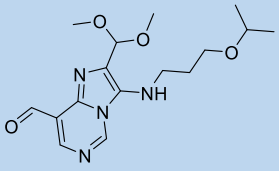
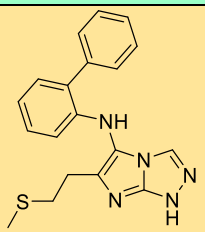
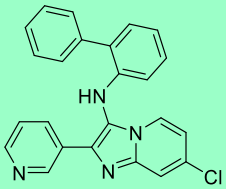
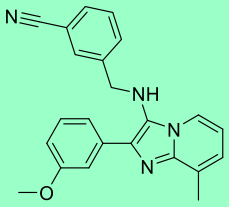
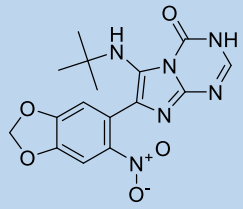
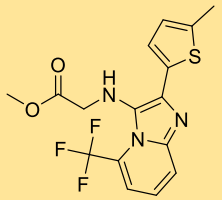
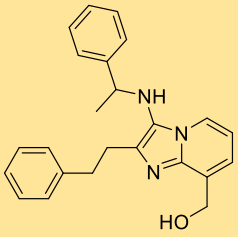
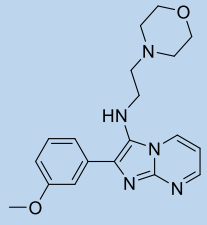
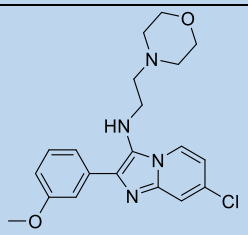
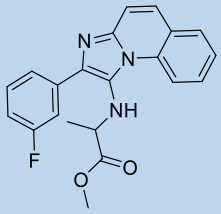
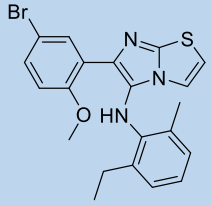
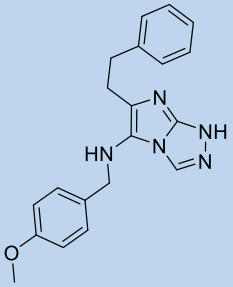
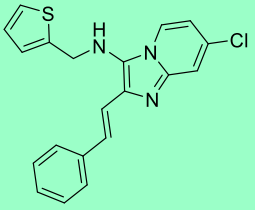
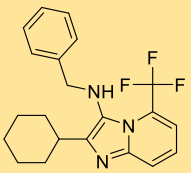
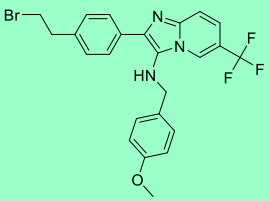
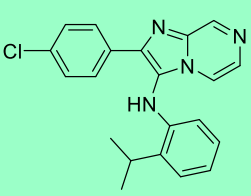
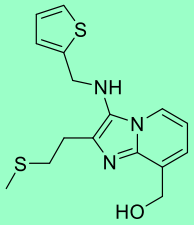
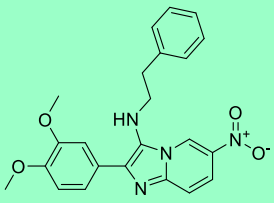
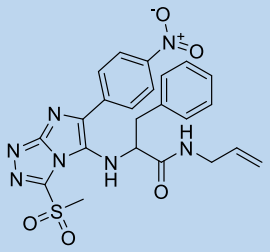
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |
| 7 |  |  |  |  |

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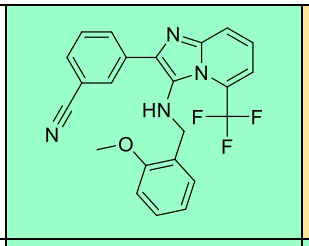
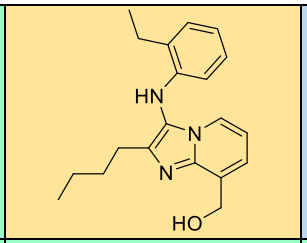
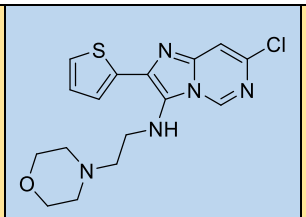
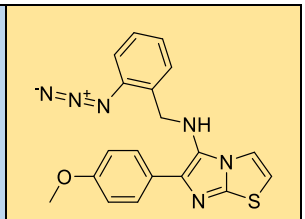
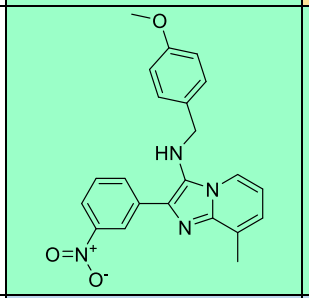
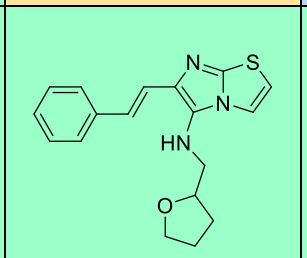
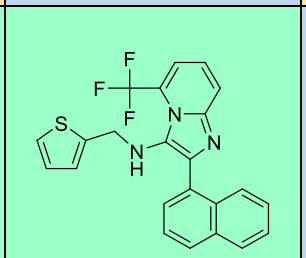
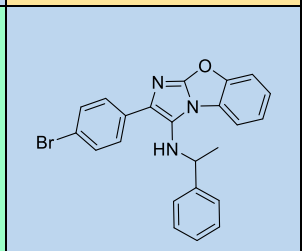
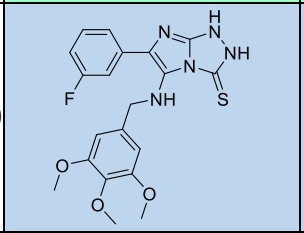
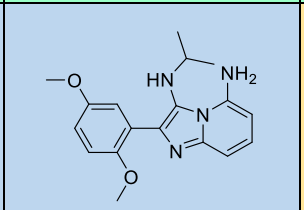
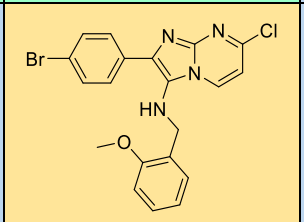
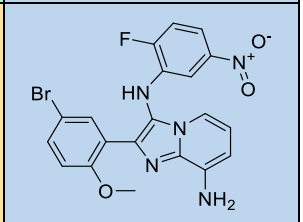
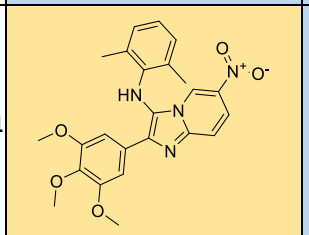
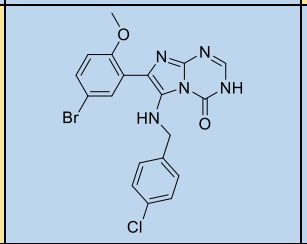
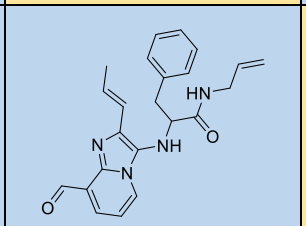
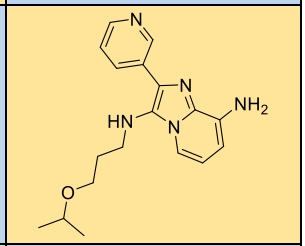
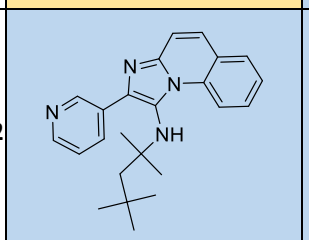
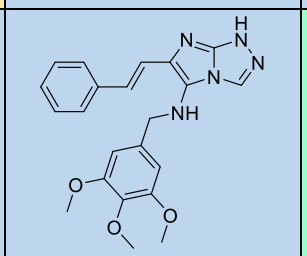
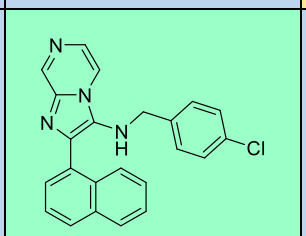
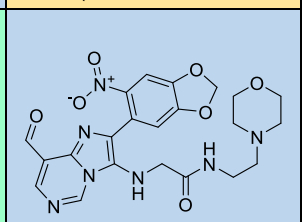
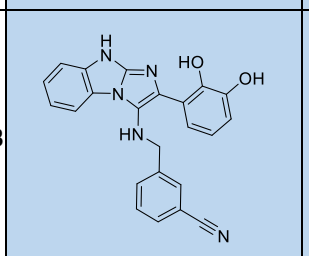
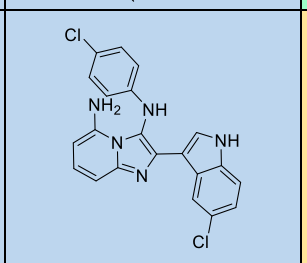
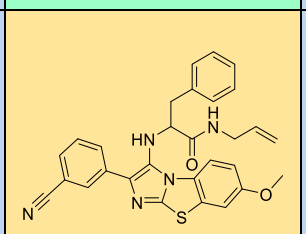
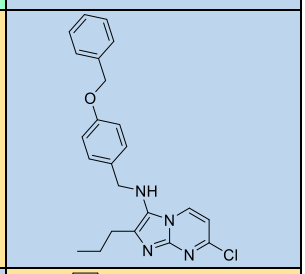
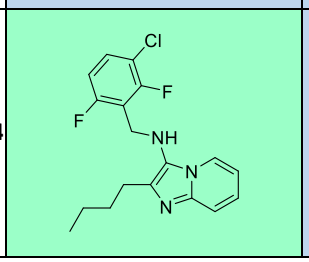
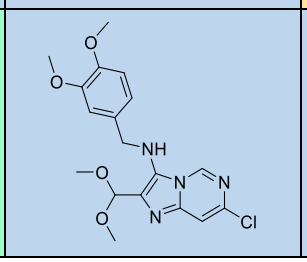
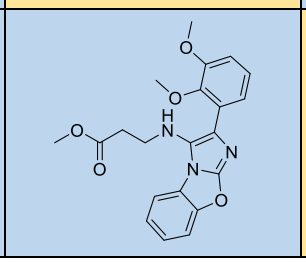
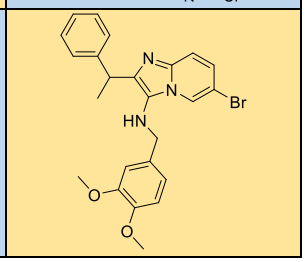
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |
| 13 |  |  |  |  |
| 14 |  |  |  |  |

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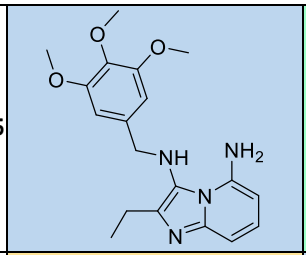
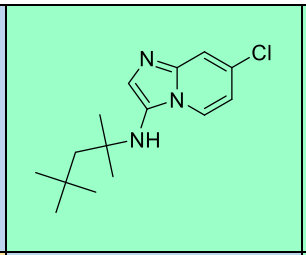
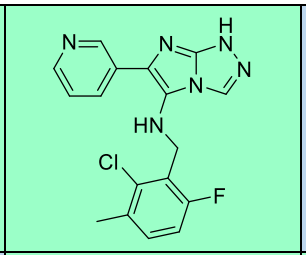
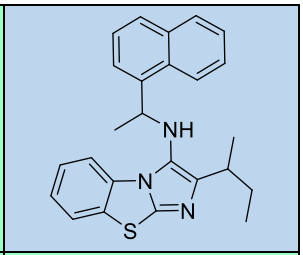
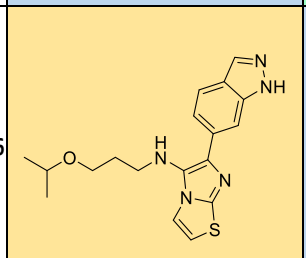
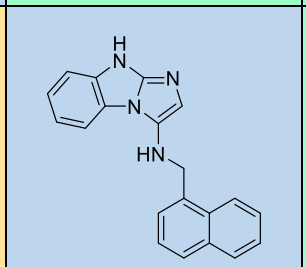
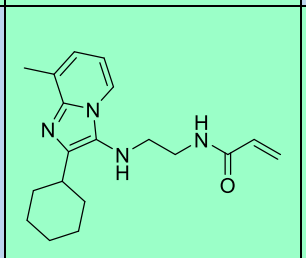
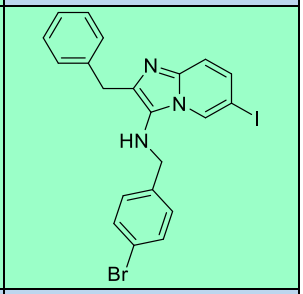
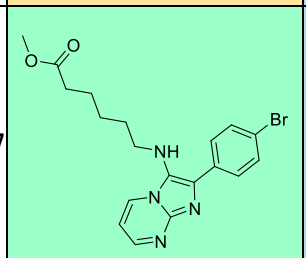
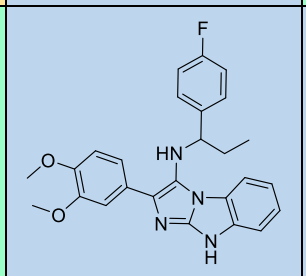
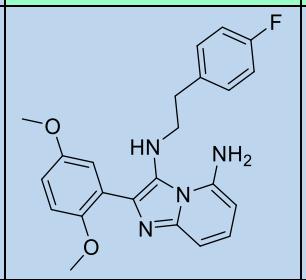
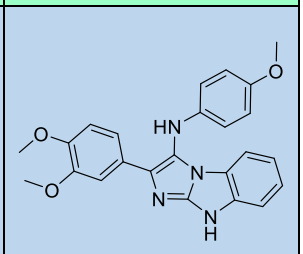
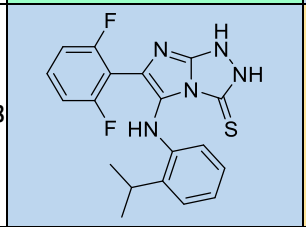
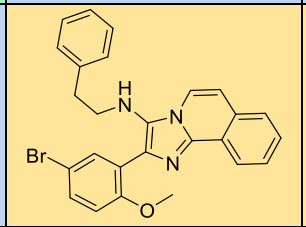
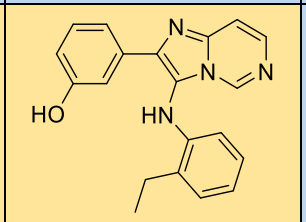
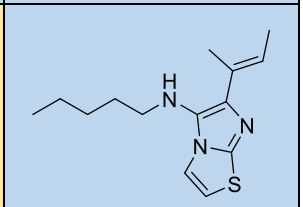
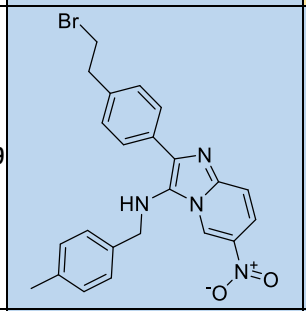
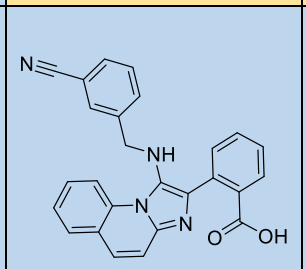
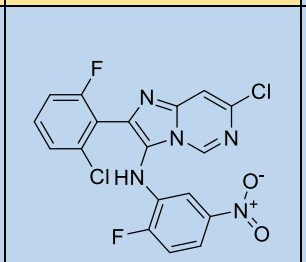
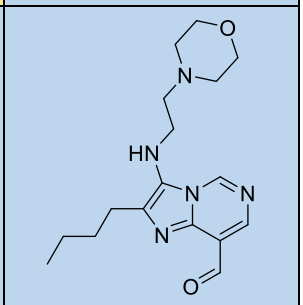
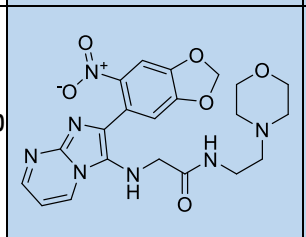
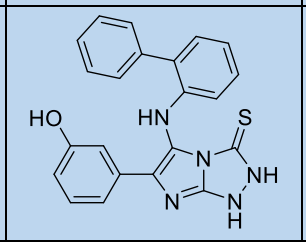
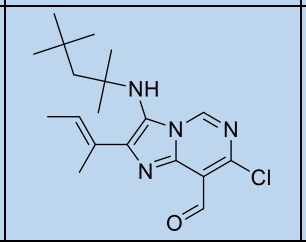
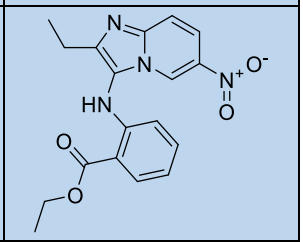
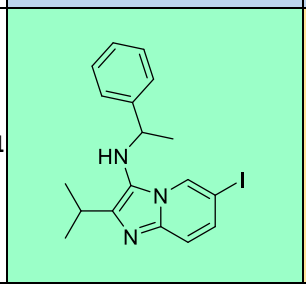
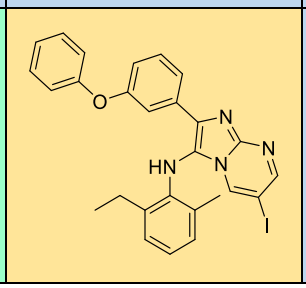
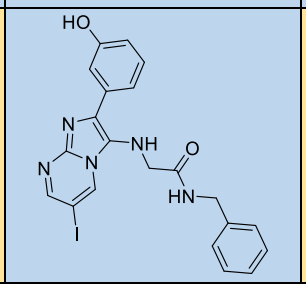
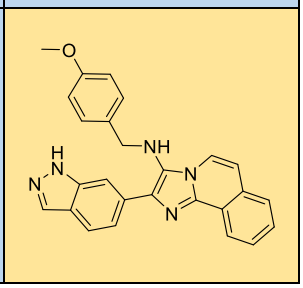
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |

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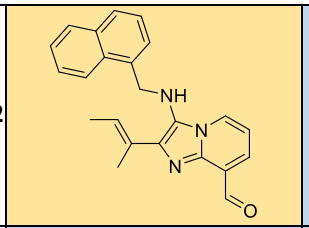
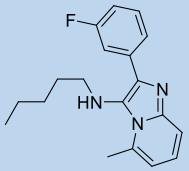
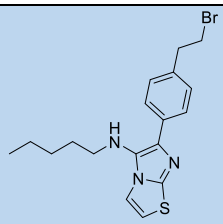
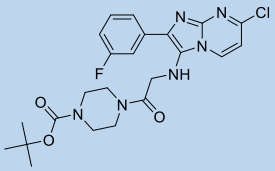
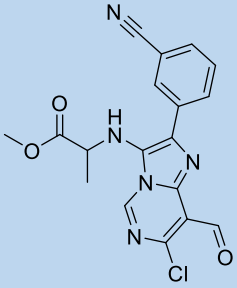
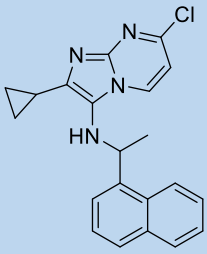
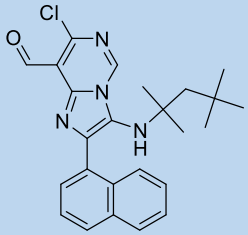
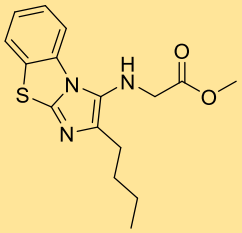
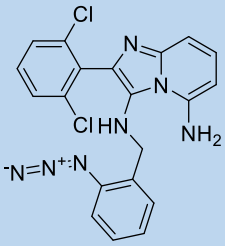
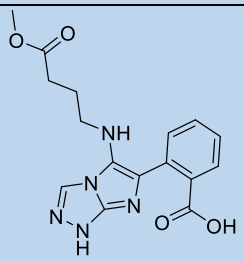
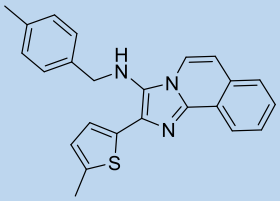
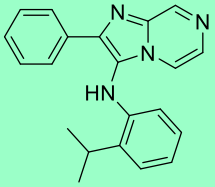
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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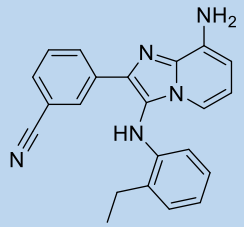
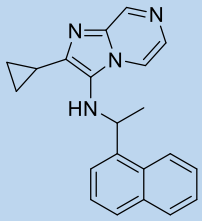
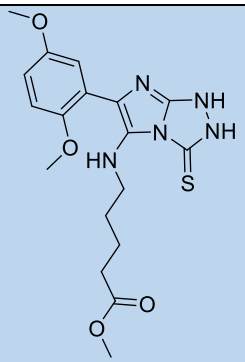
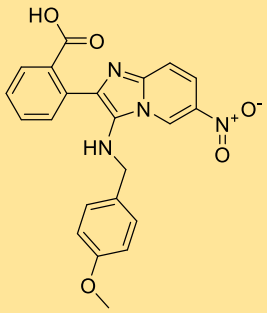
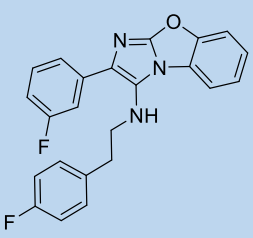
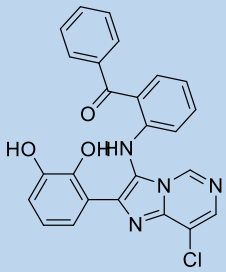
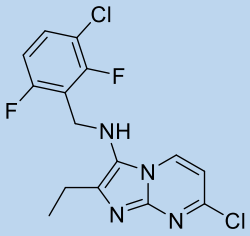
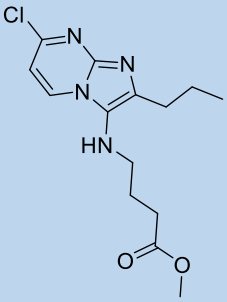
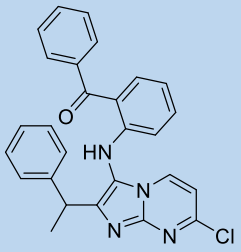
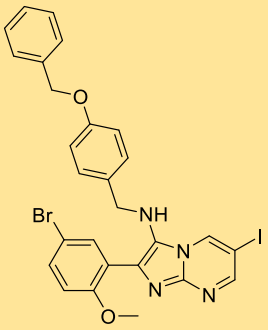
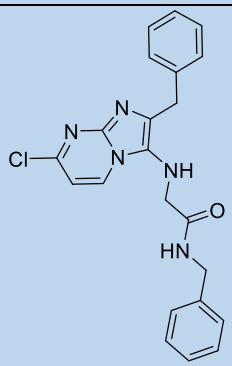
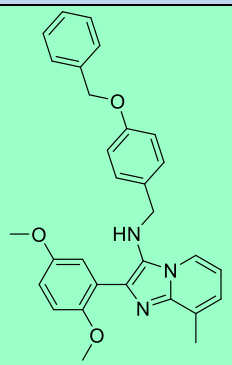
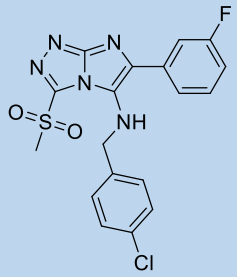
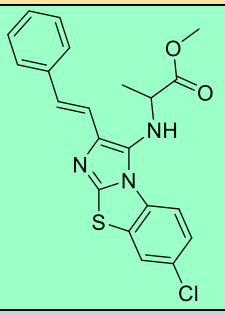
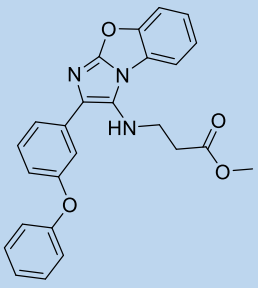
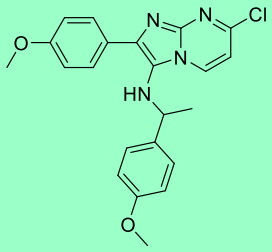
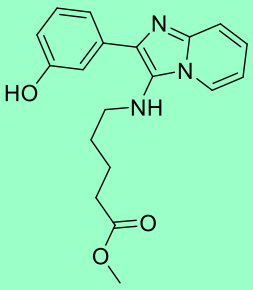
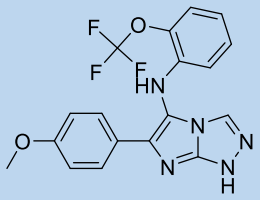
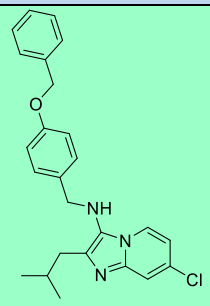
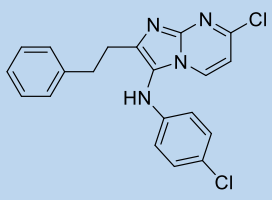
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |

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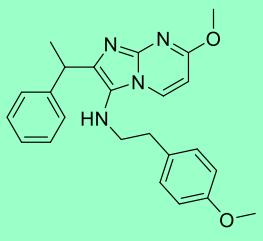
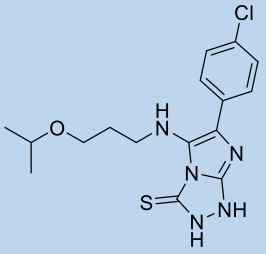
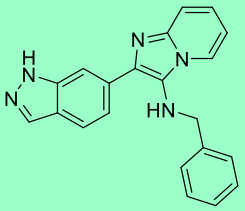
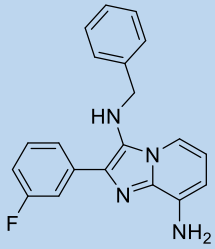
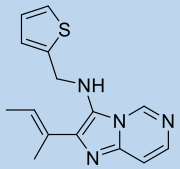
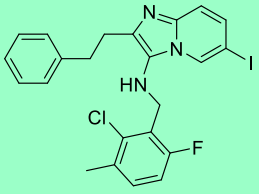
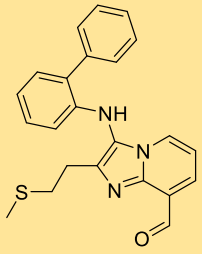
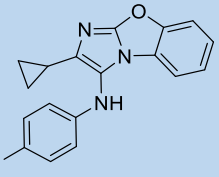
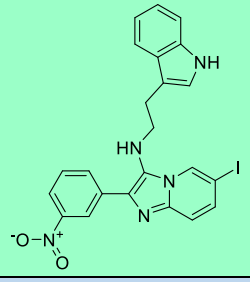
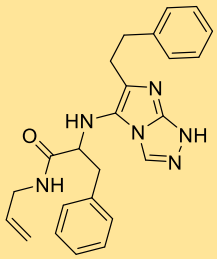
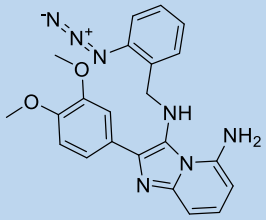
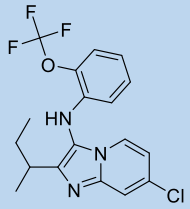
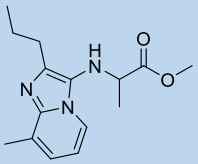
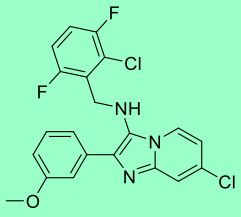
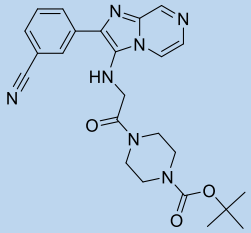
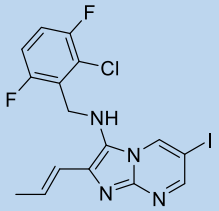
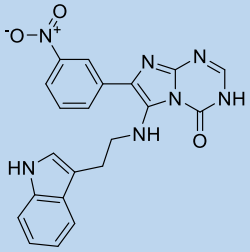
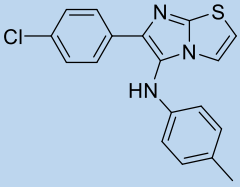
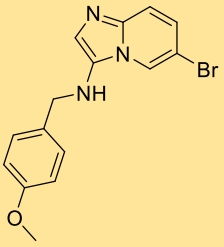
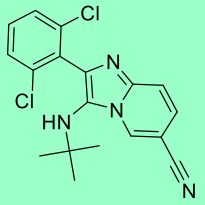
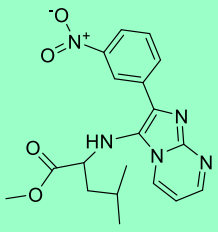
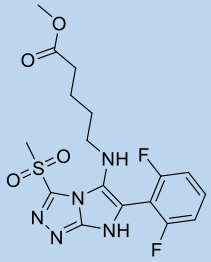
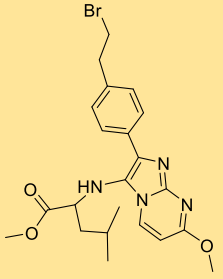
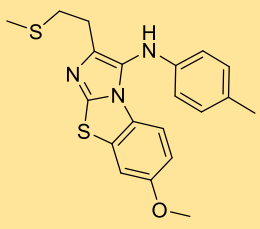
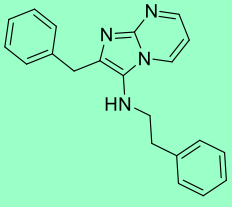
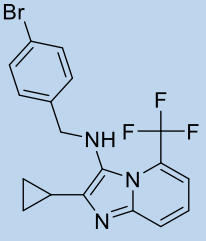
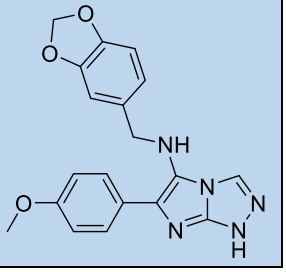
| 6 |  |  |  |  |
| 7 |  |  |  |  |
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |

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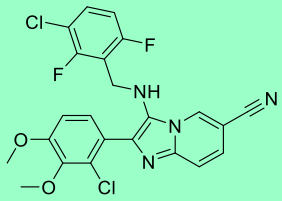
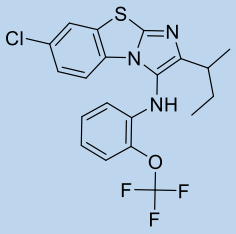
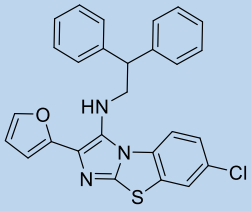
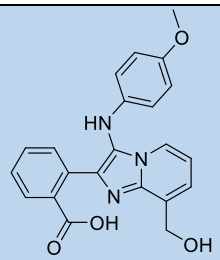
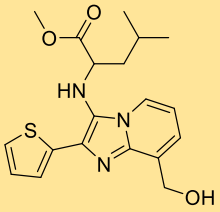
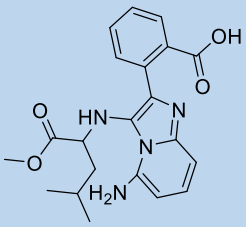
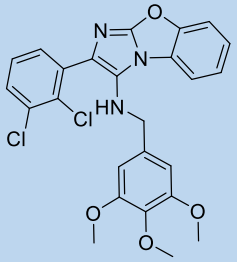
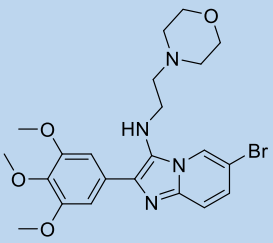
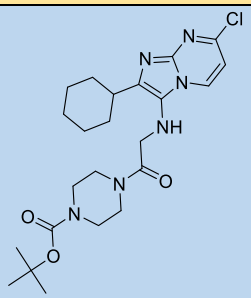
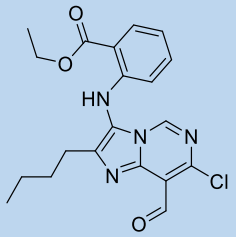
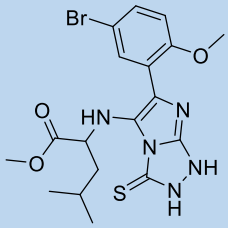
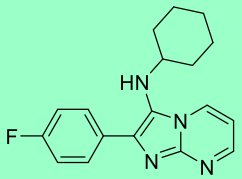
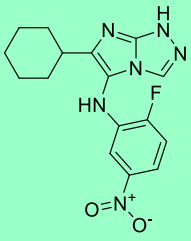
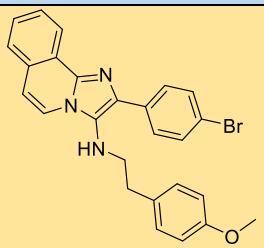
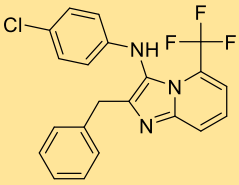
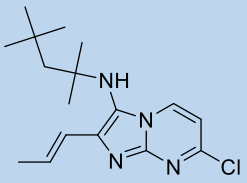
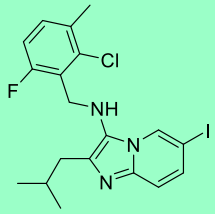
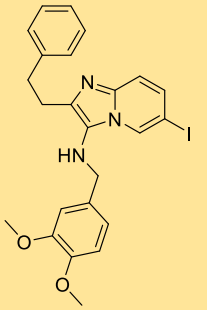
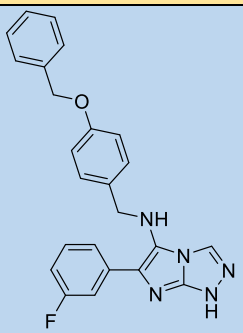
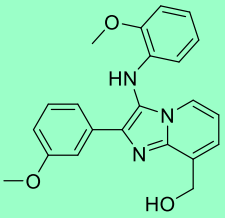
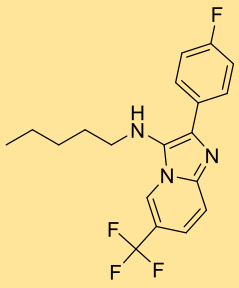
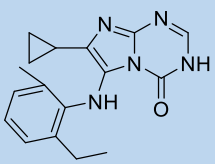
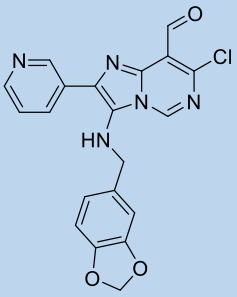
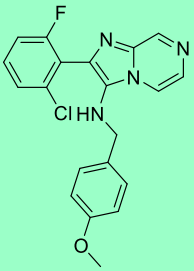
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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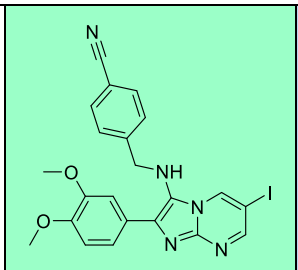
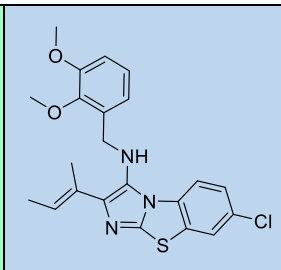
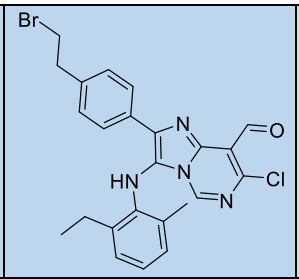
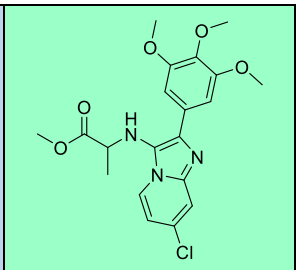
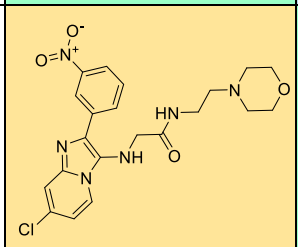
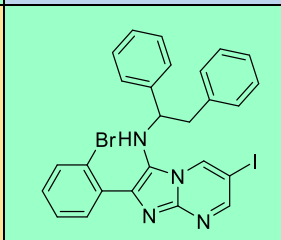
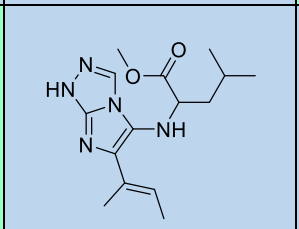
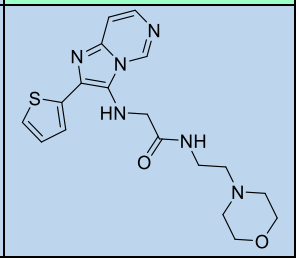
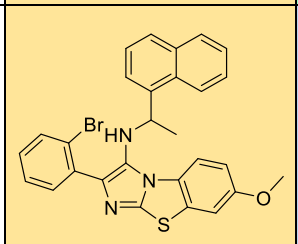
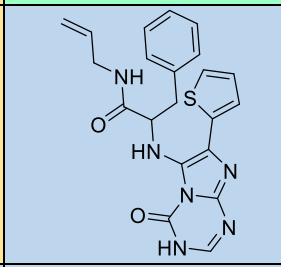
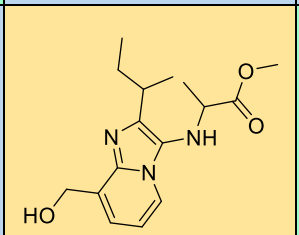
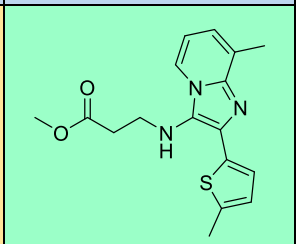
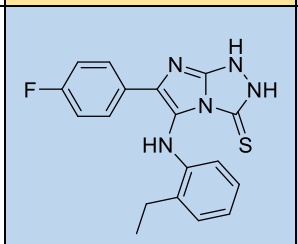
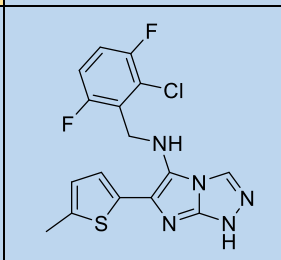
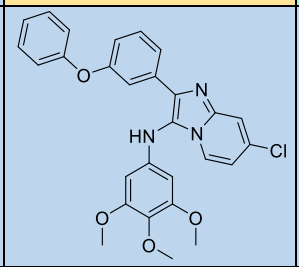
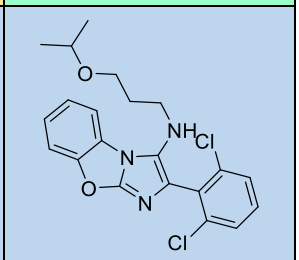
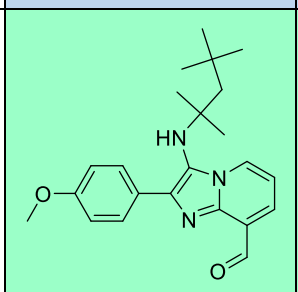
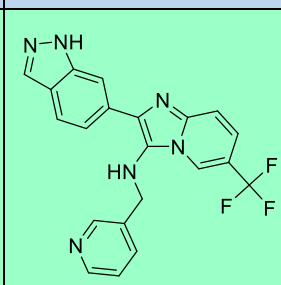
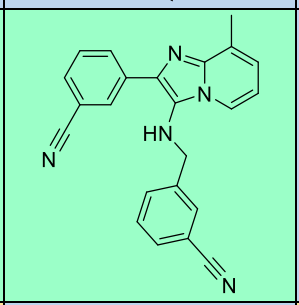
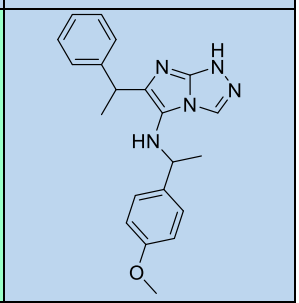
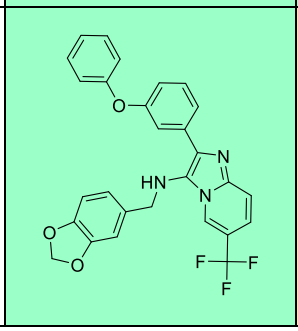
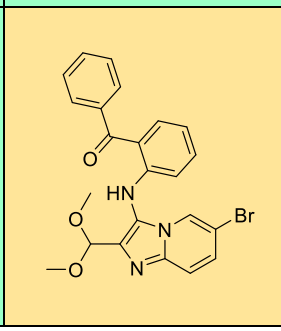
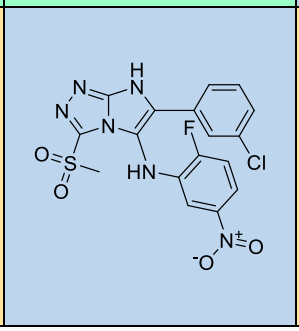
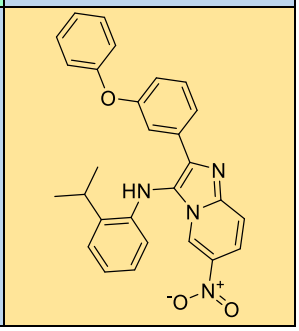
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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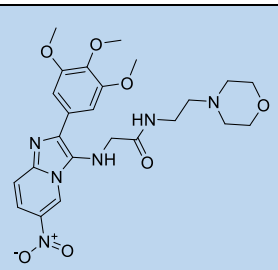
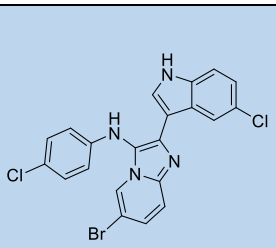
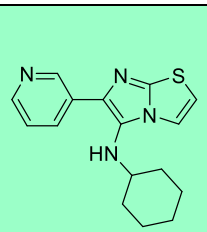
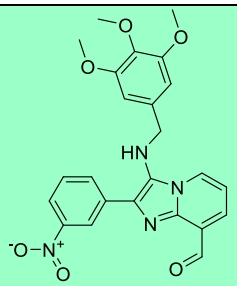
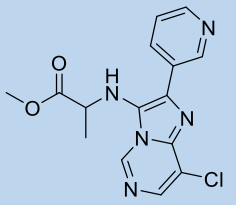
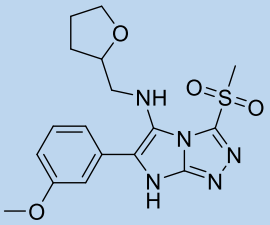
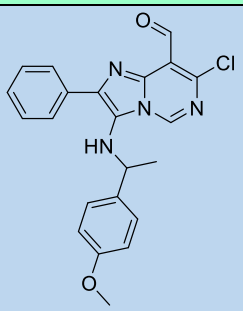
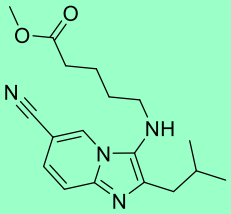
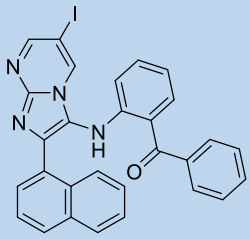
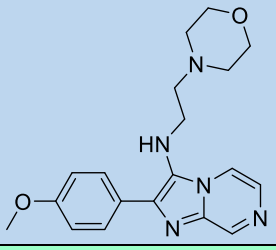
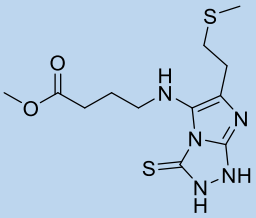
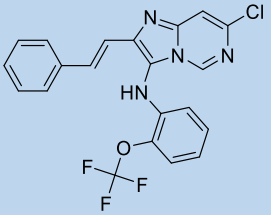
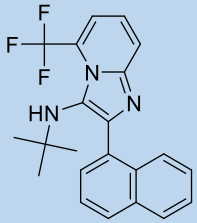
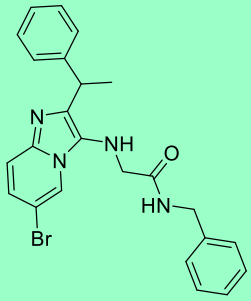
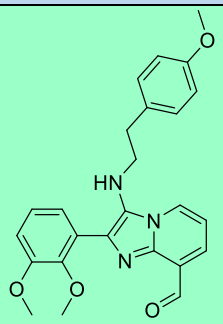
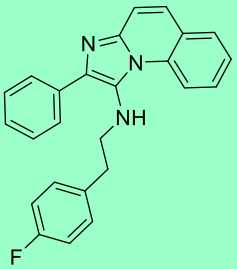
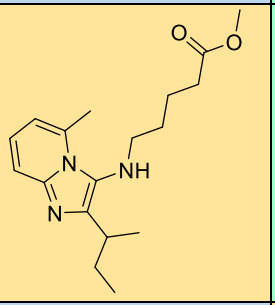
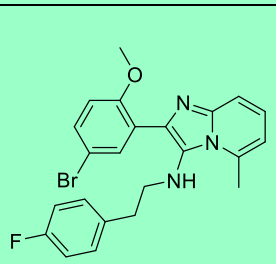
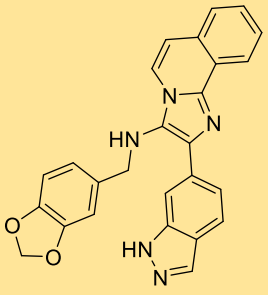
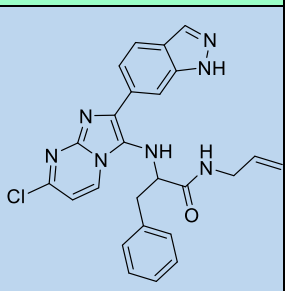
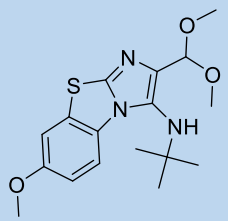
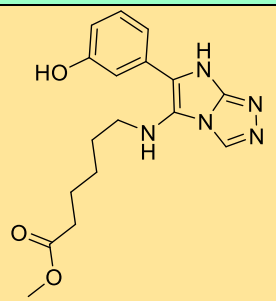
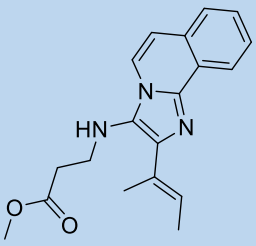
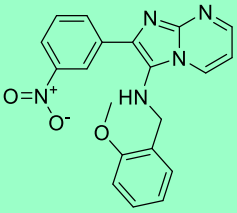
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |

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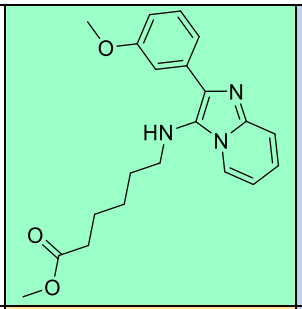
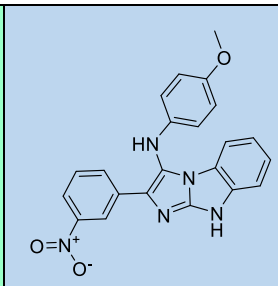
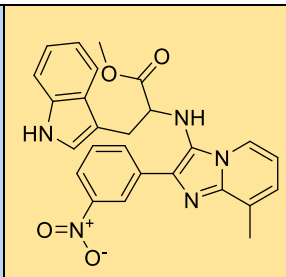
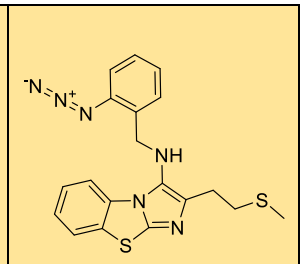
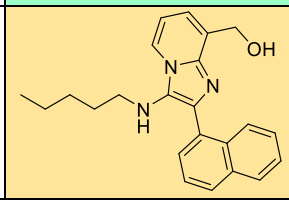
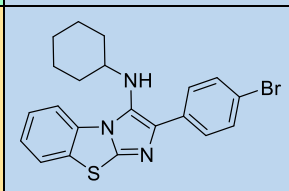
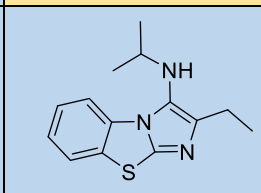
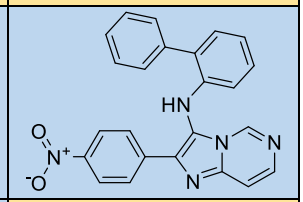
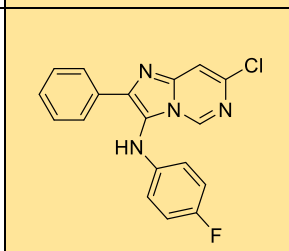
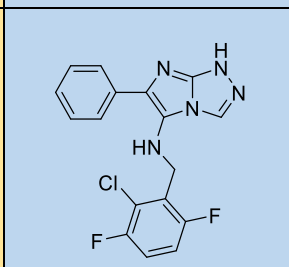
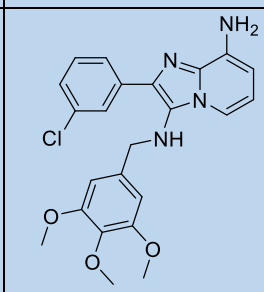
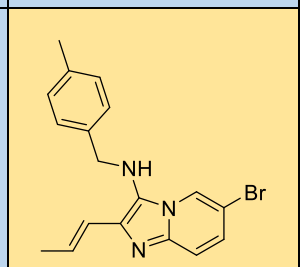
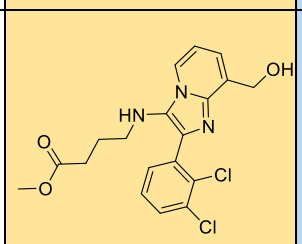
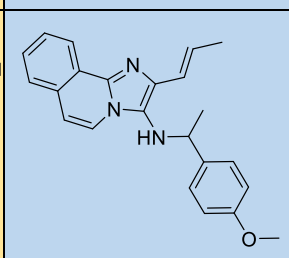
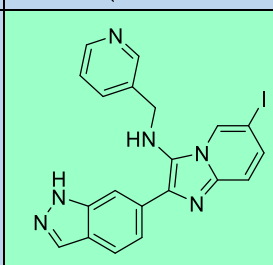
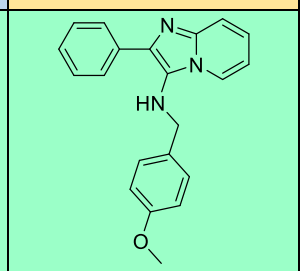
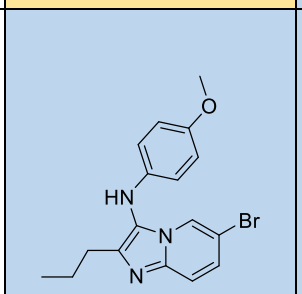
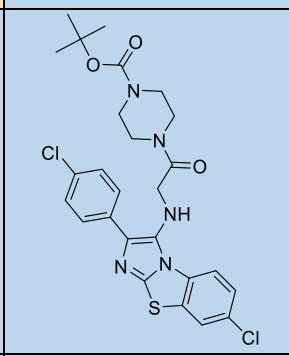
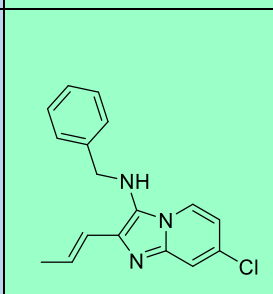
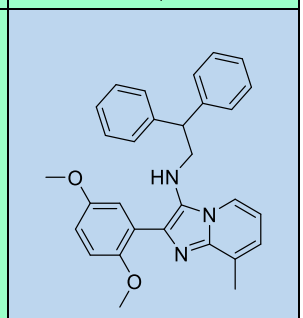
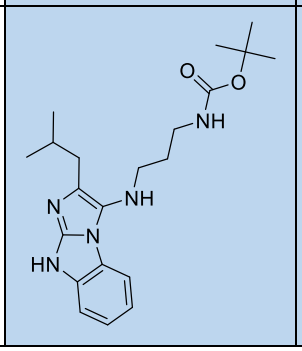
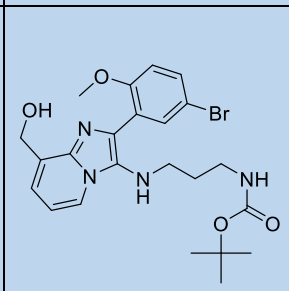
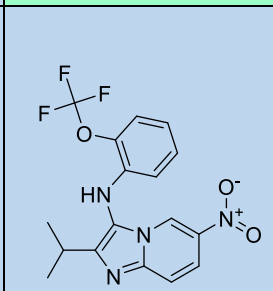
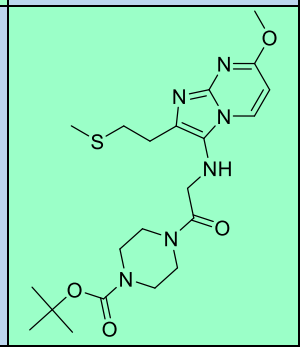
| **7** |  |  |  |  |
| **8** |  |  |  |  |
| **9** |  |  |  |  |
| **10** |  |  |  |  |
| **11** |  |  |  |  |
| **12** |  |  |  |  |

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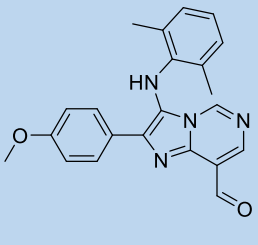
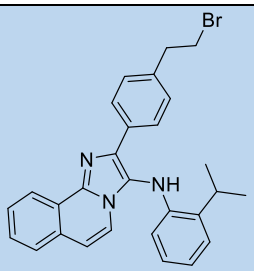
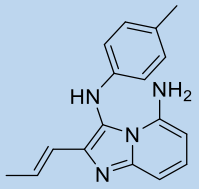
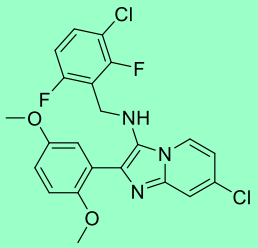
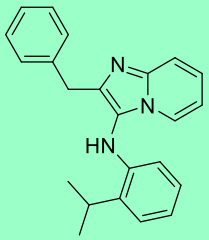
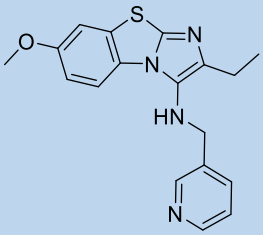
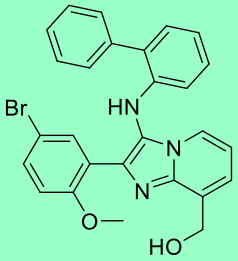
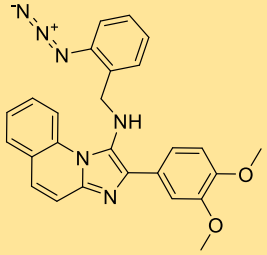
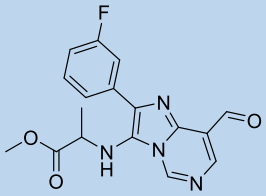
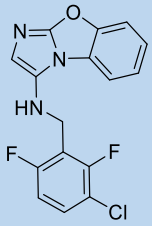
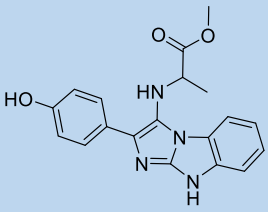
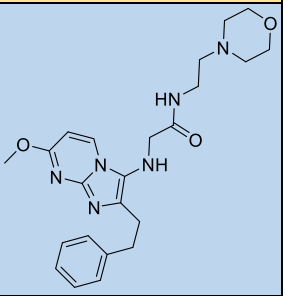
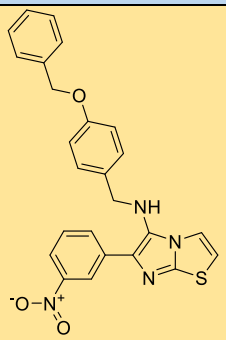
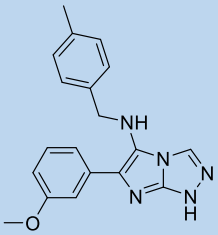
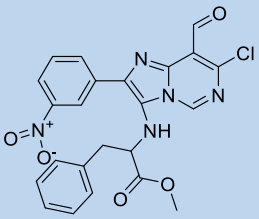
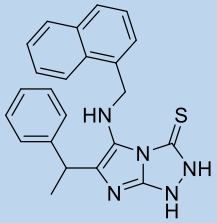
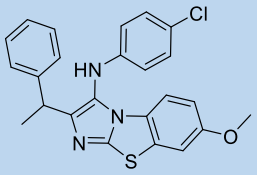
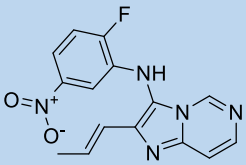
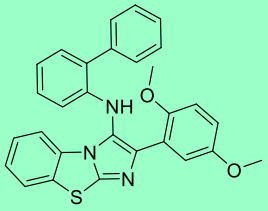
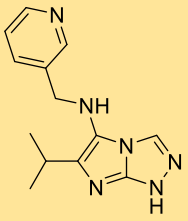
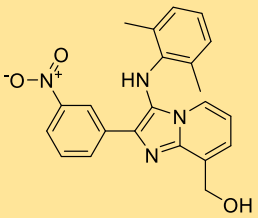
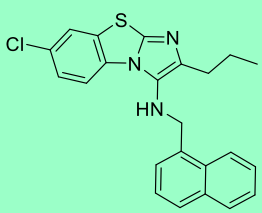
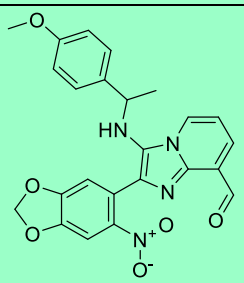
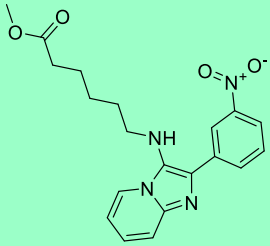
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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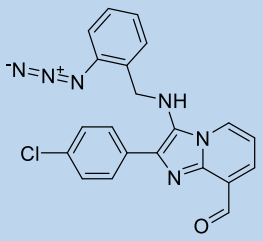
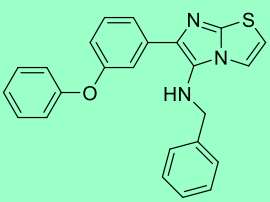
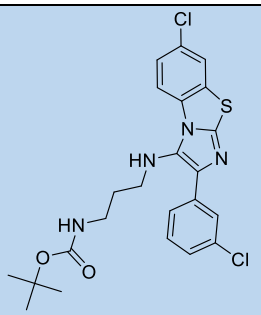
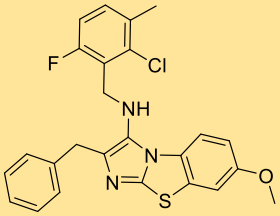
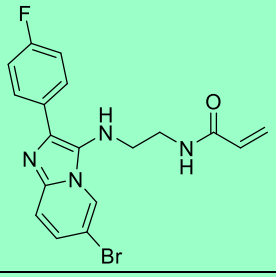
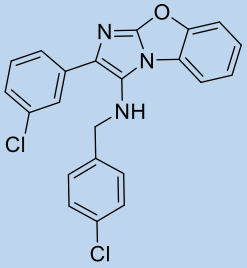
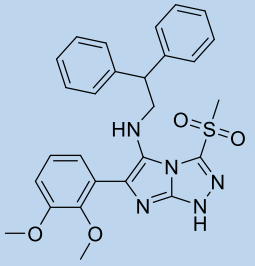
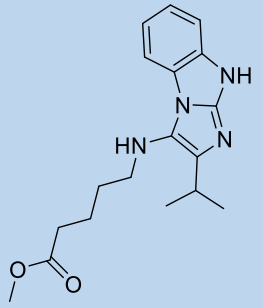
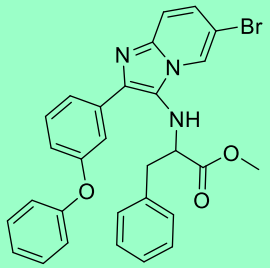
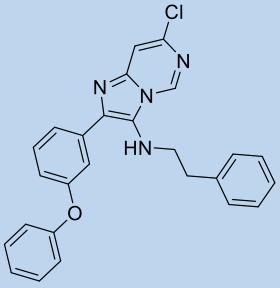
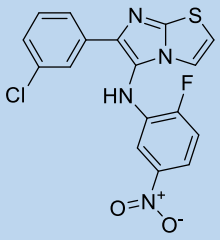
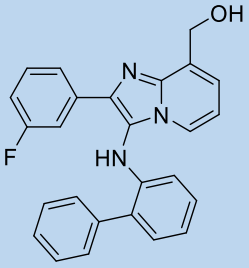
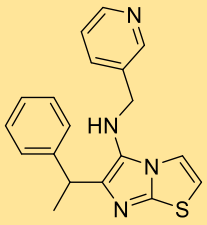
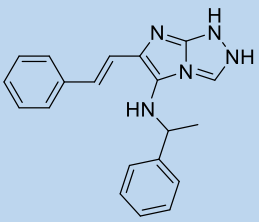
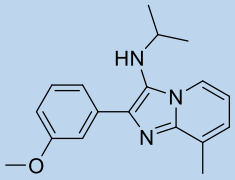
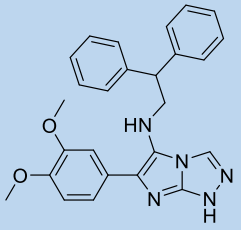
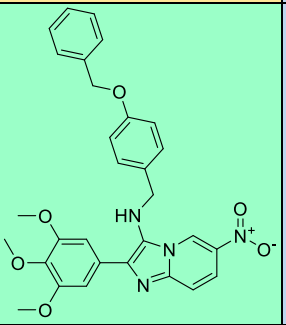
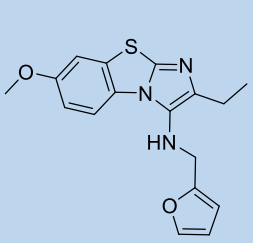
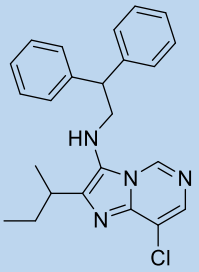
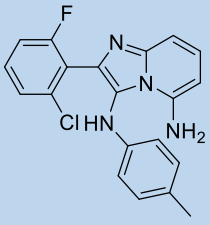
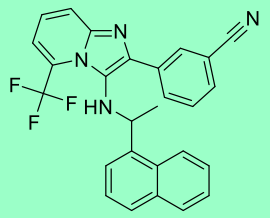
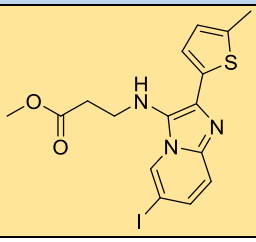
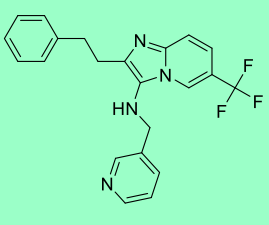
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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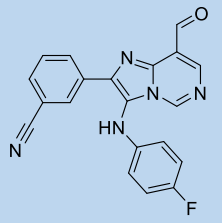
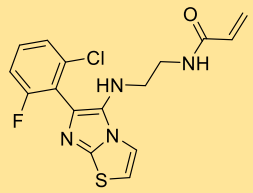
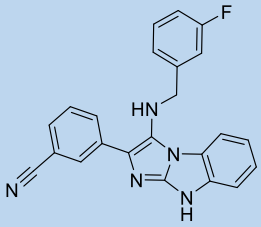
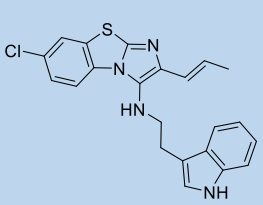
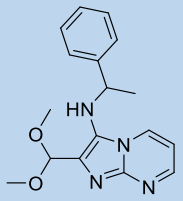
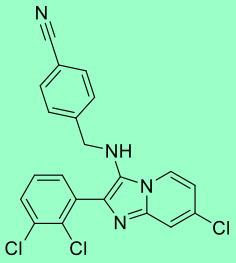
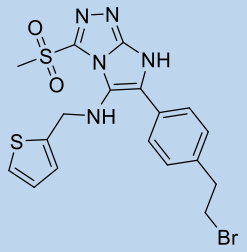
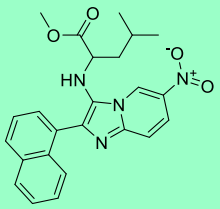
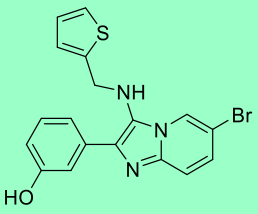
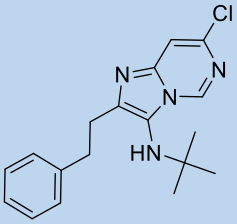
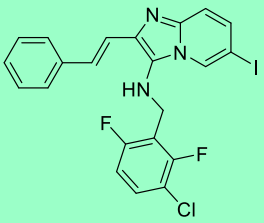
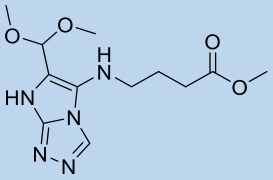
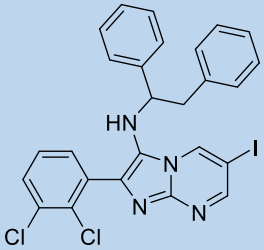
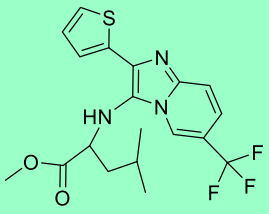
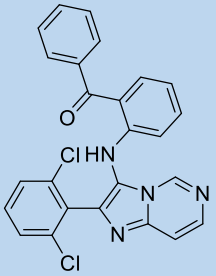
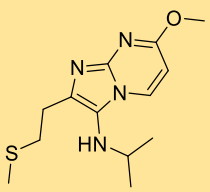
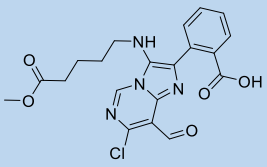
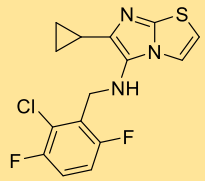
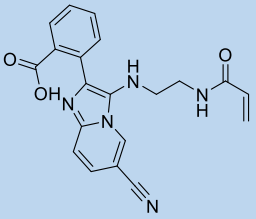
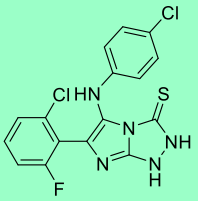
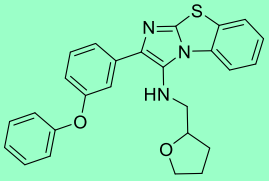
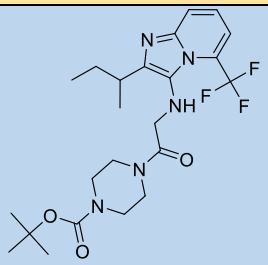
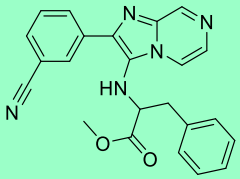
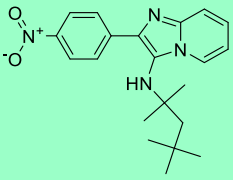
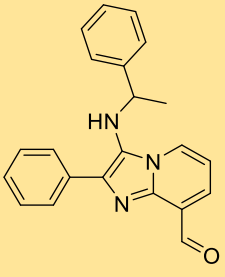
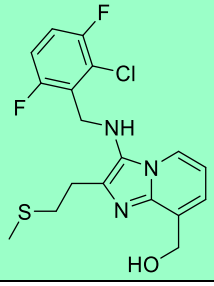
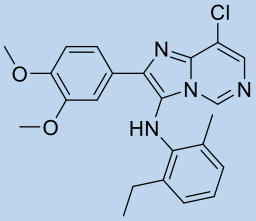
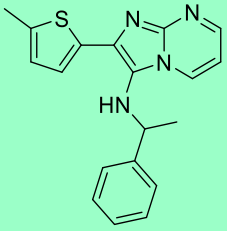
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |
| 7 |  |  |  |  |

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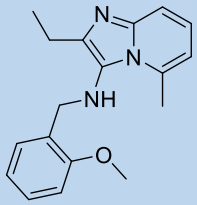
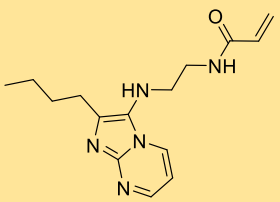
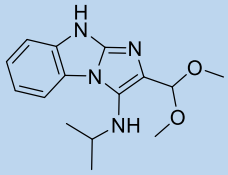
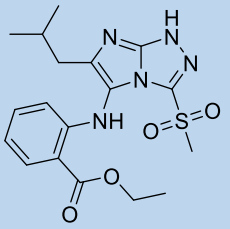
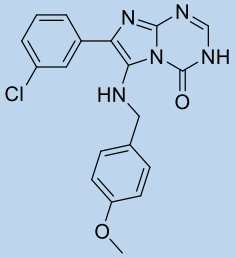
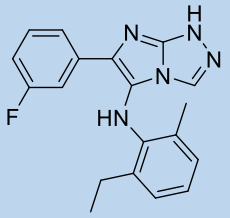
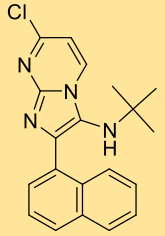
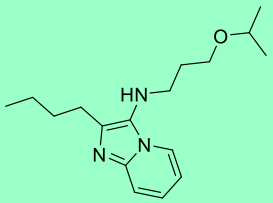
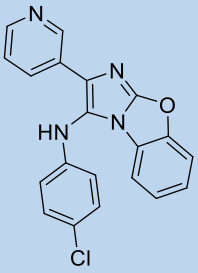
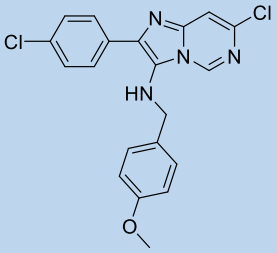
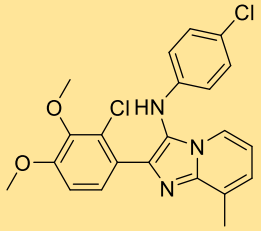
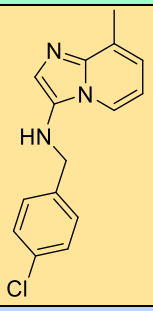
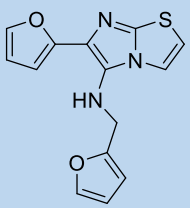
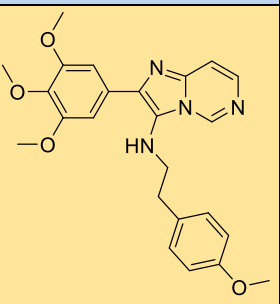
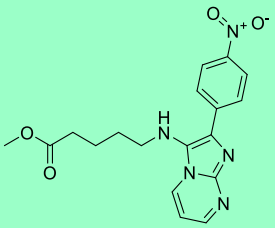
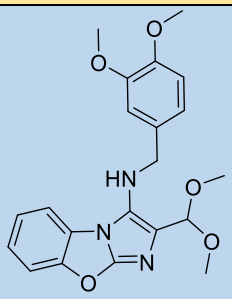
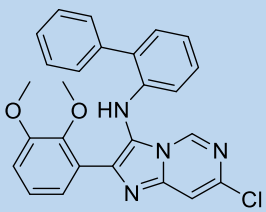
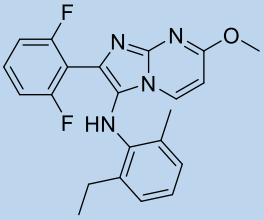
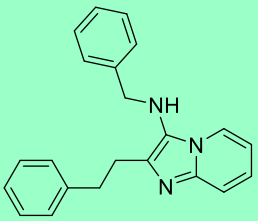
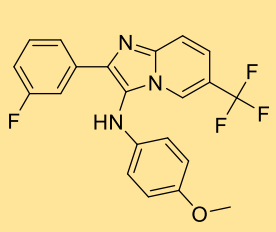
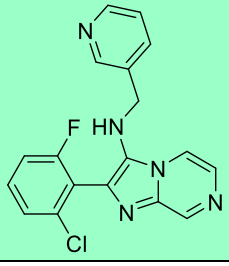
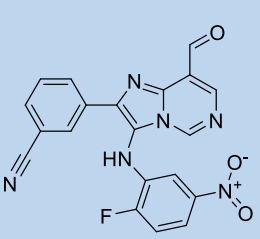
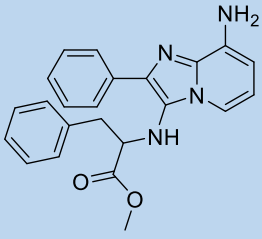
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |
| 13 |  |  |  |  |

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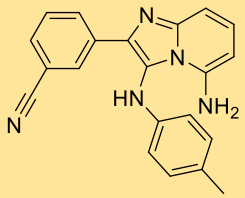
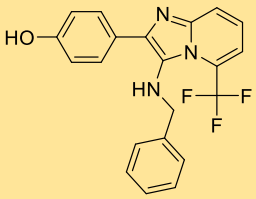
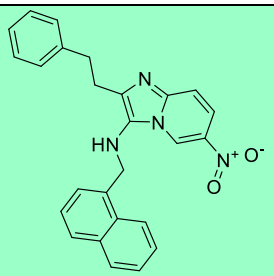
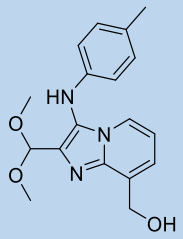
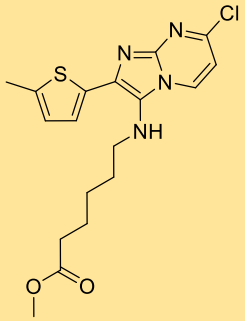
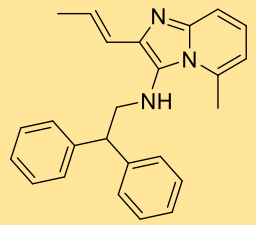
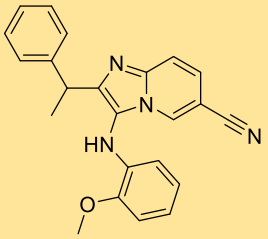
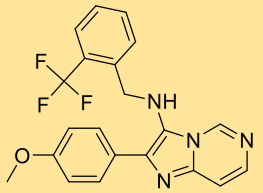
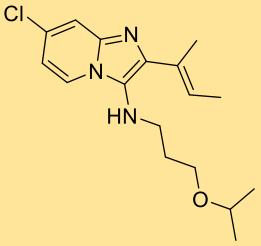
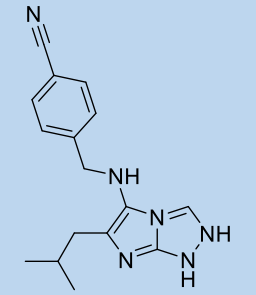
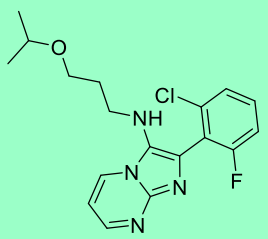
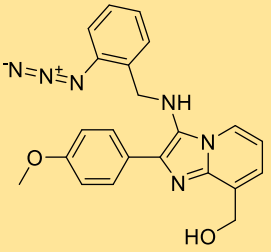
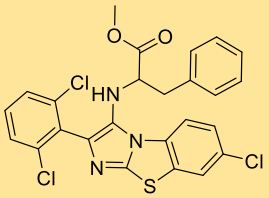
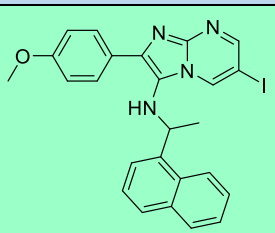
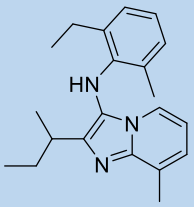
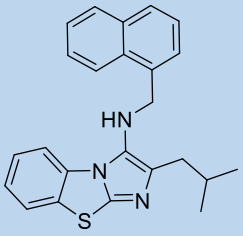
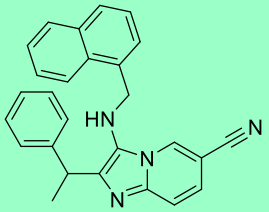
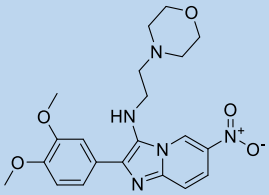
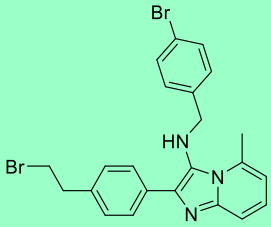
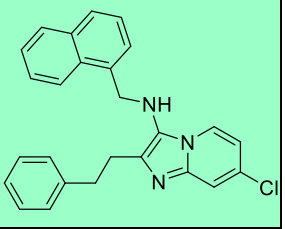
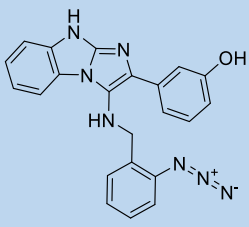
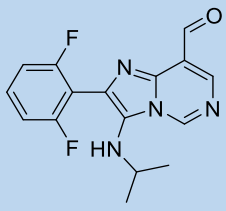
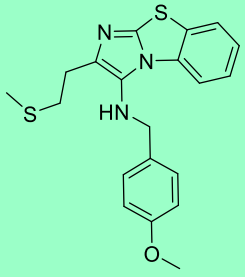
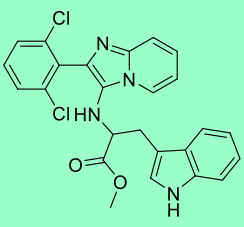
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |
| 19 |  |  |  |  |

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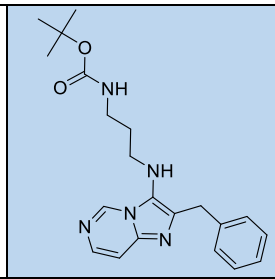
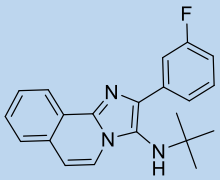
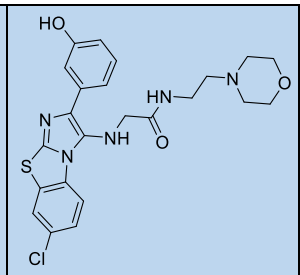
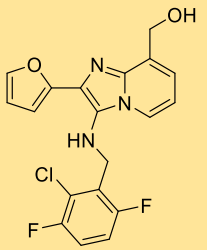
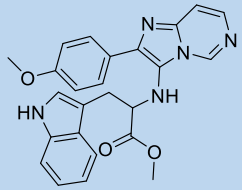
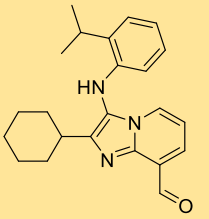
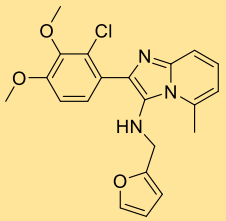
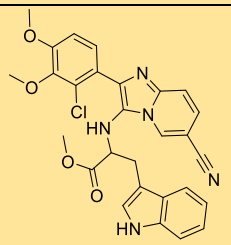
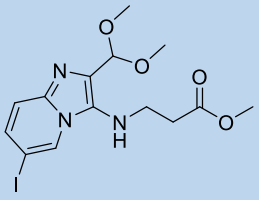
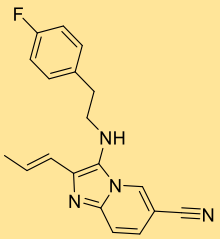
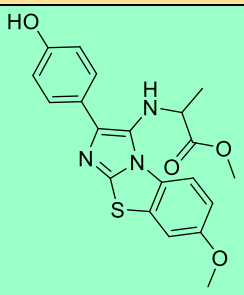
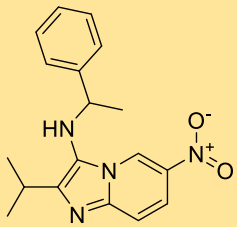
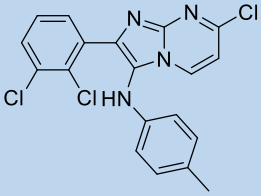
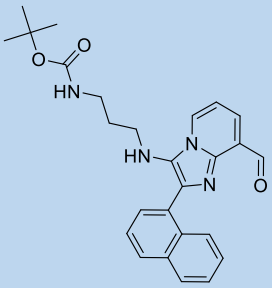
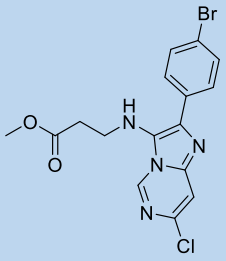
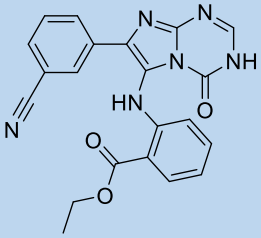
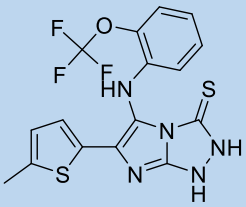
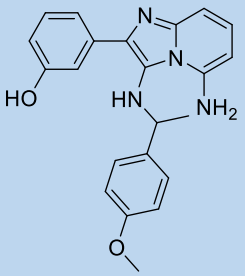
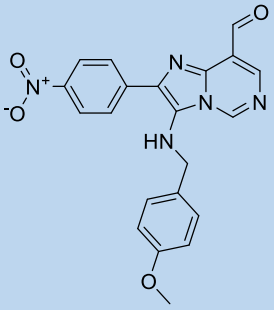
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

**Destination plate III**

| | A | B | C | D |
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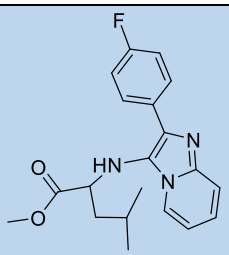
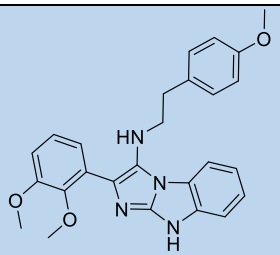
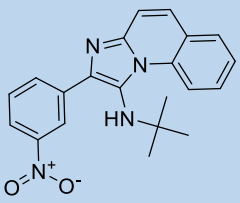
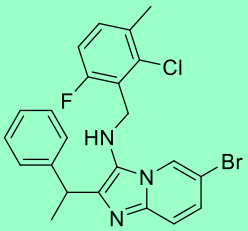
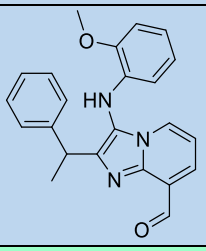
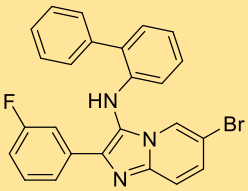
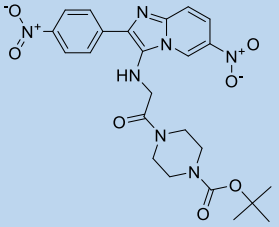
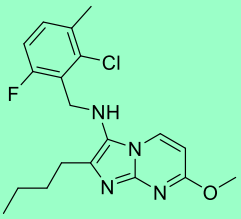
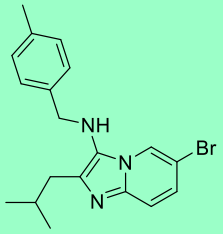
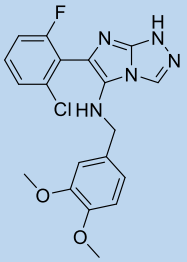
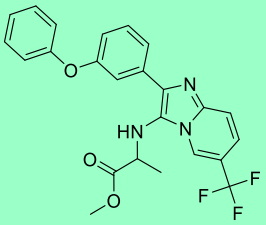
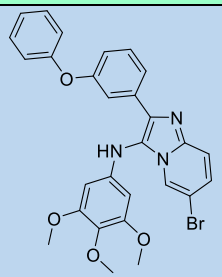
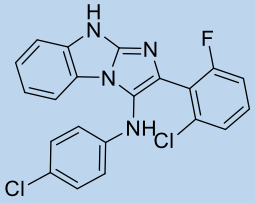
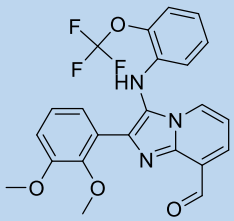
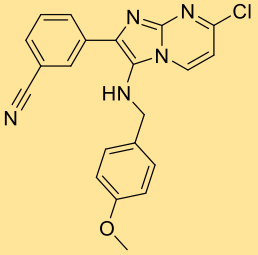
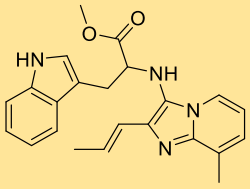
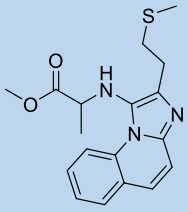
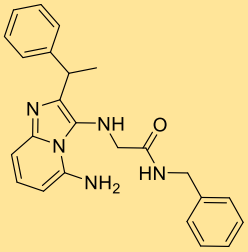
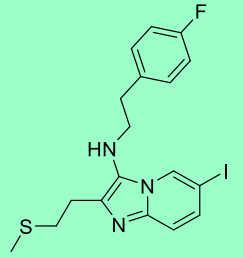
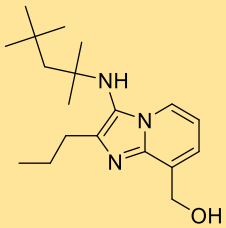
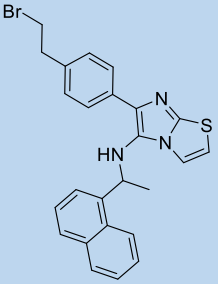
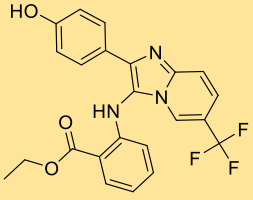
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |

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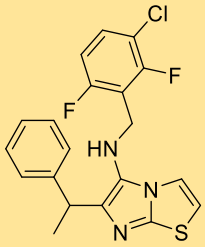
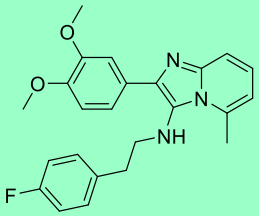
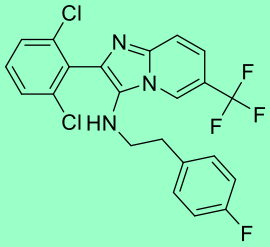
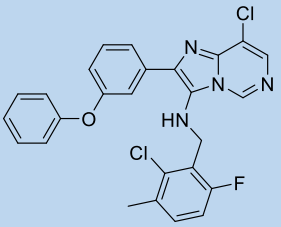
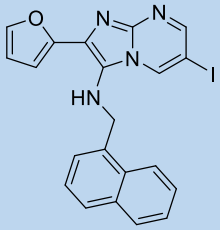
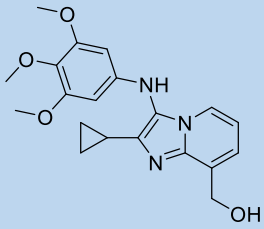
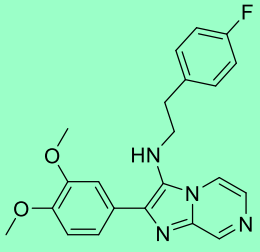
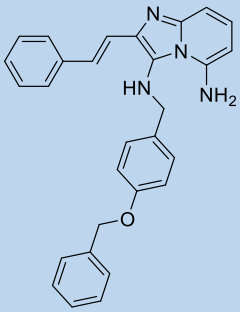
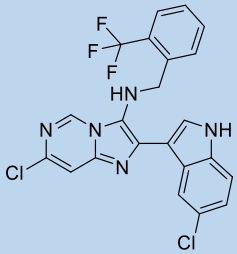
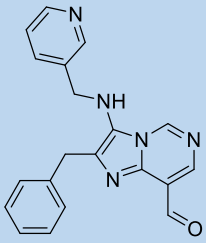
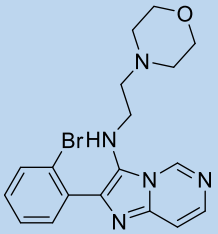
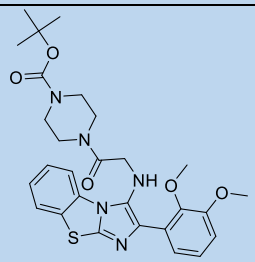
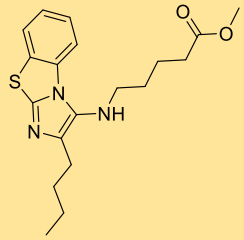
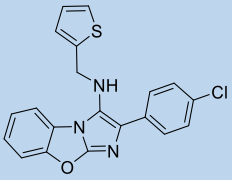
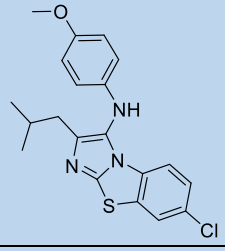
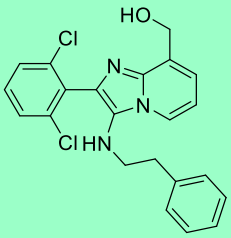
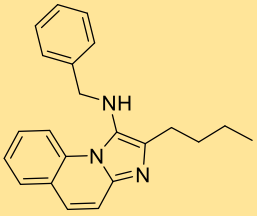
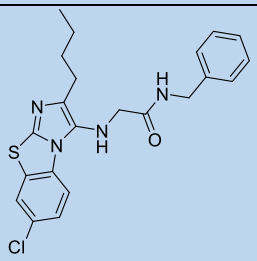
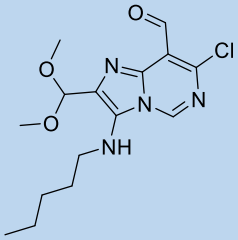
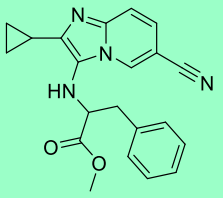
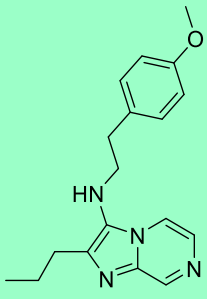
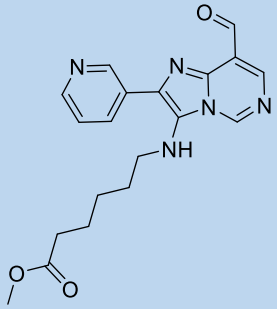
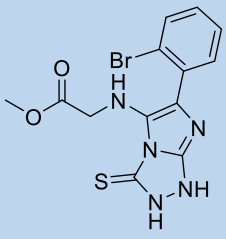
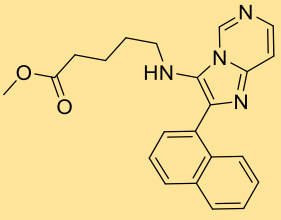
| 7 |  |  |  |  |
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |

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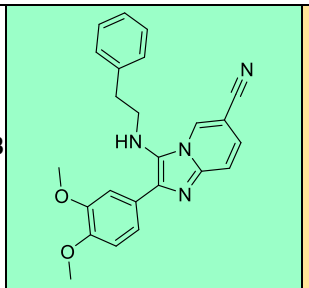
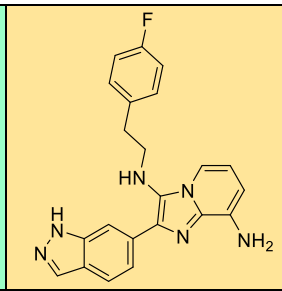
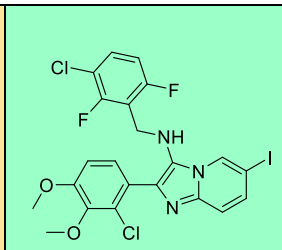
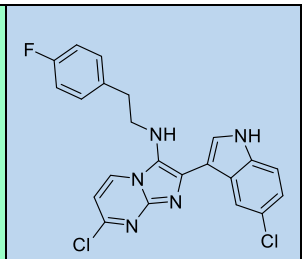
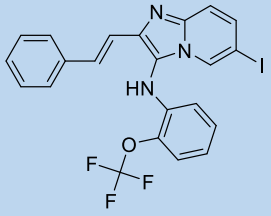
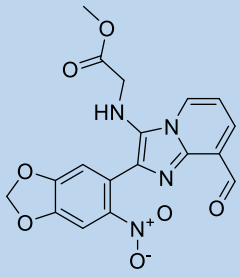
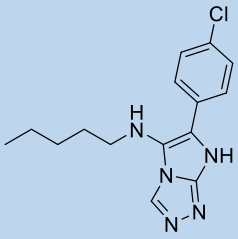
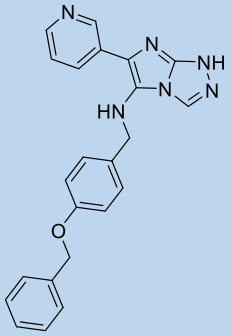
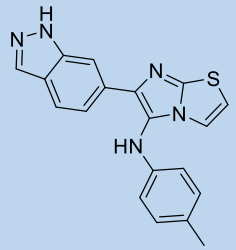
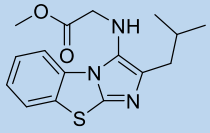
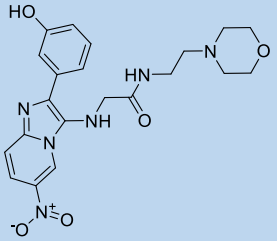
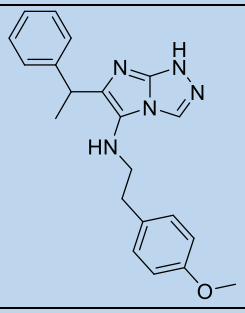
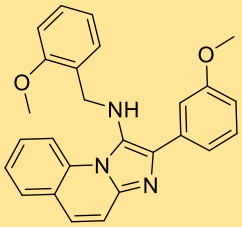
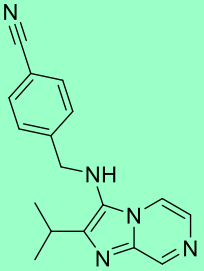
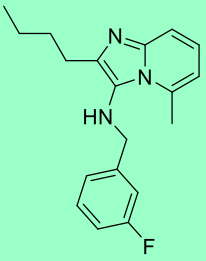
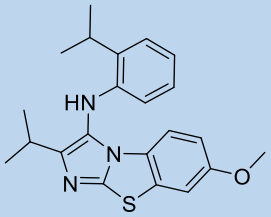
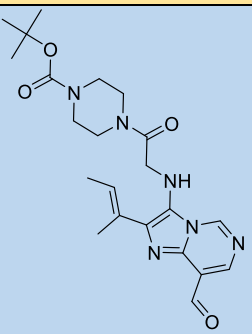
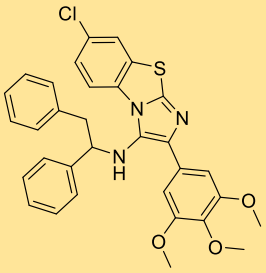
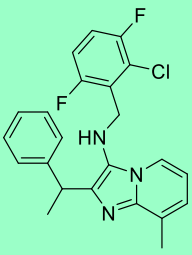
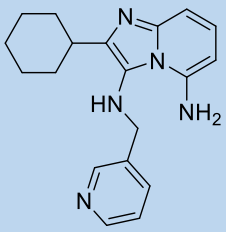
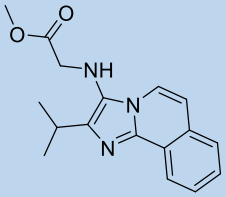
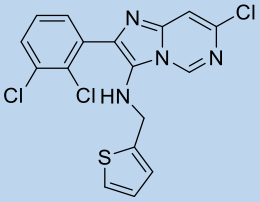
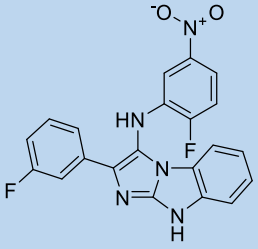
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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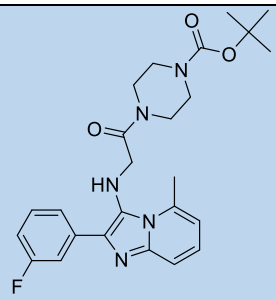
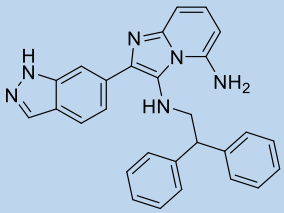
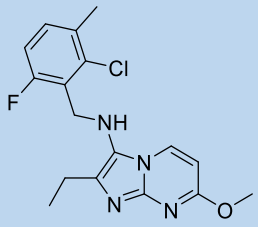
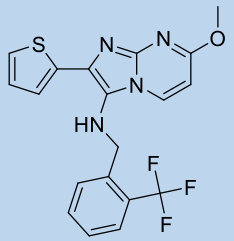
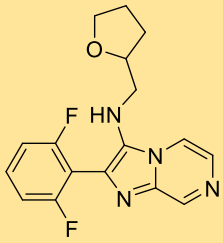
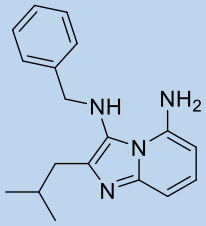
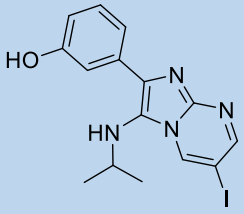
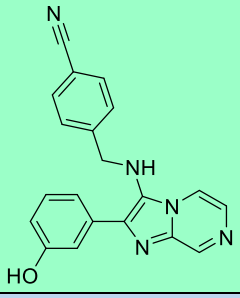
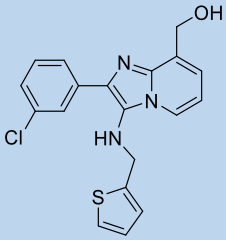
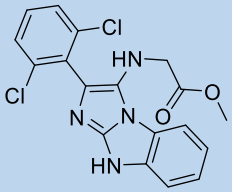
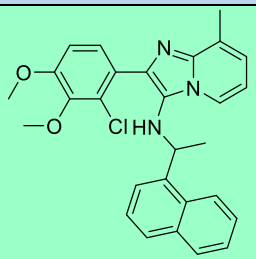
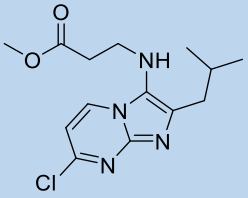
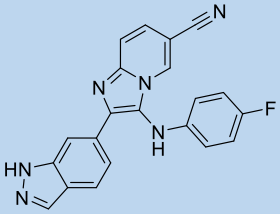
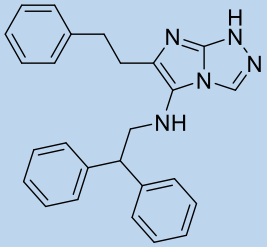
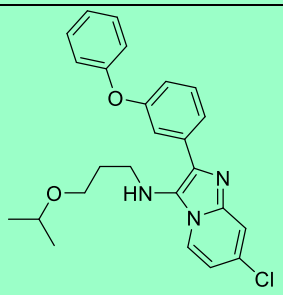
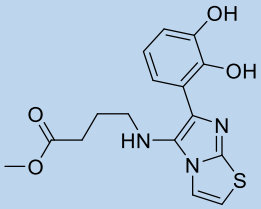
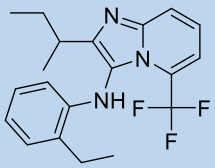
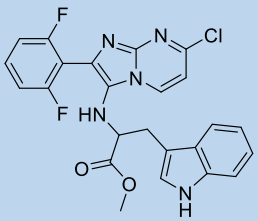
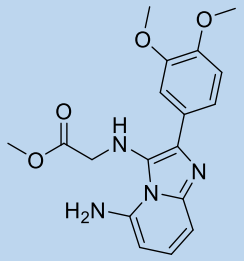
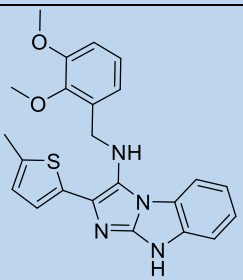
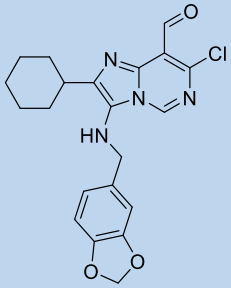
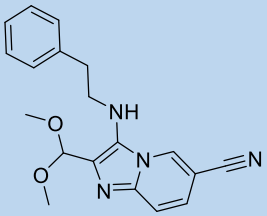
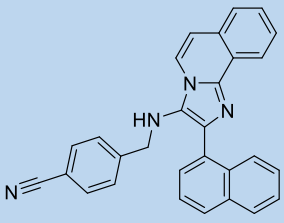
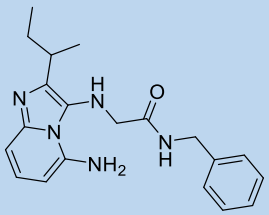
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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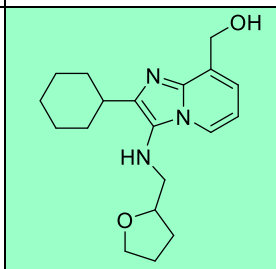
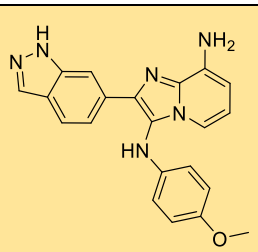
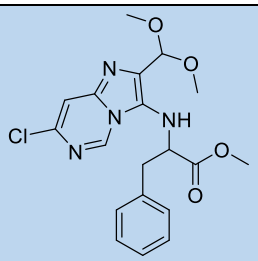
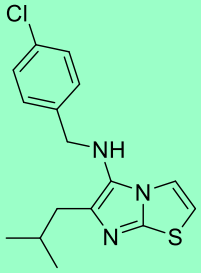
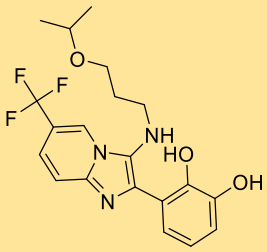
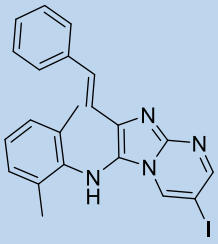
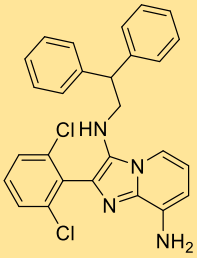
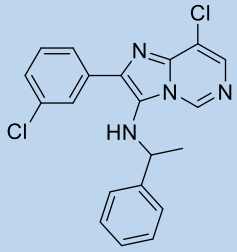
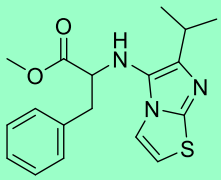
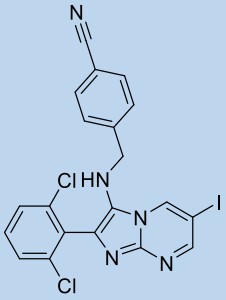
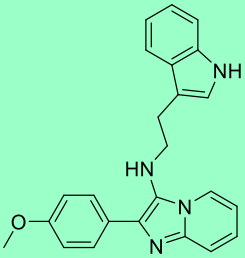
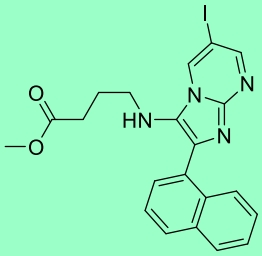
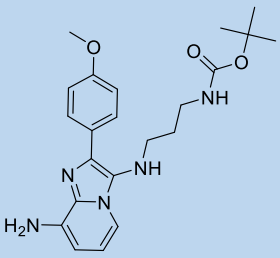
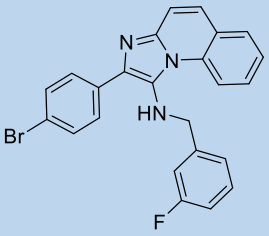
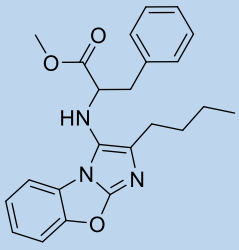
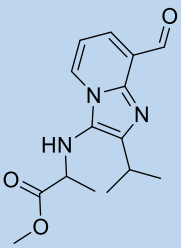
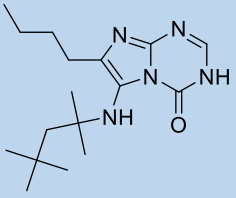
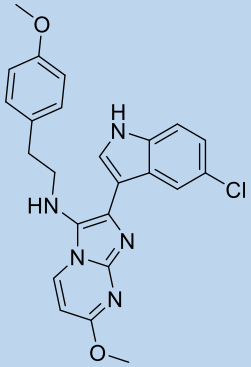
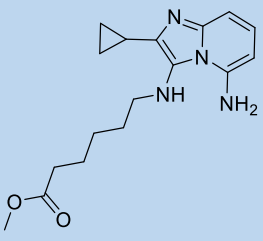
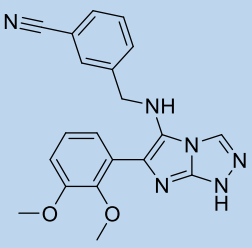
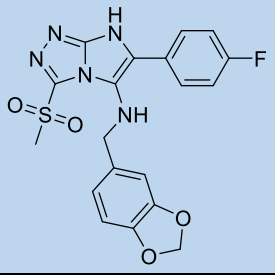
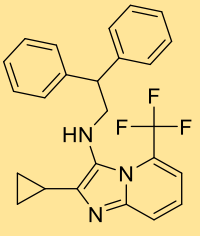
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |

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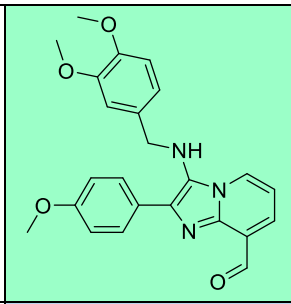
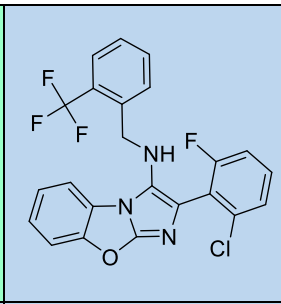
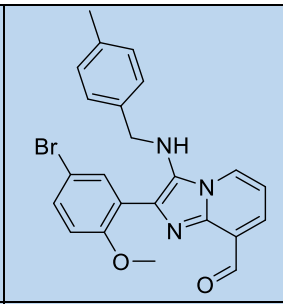
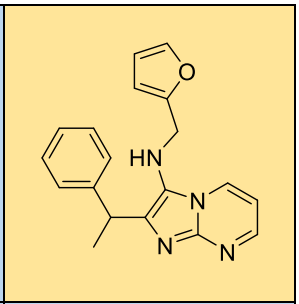
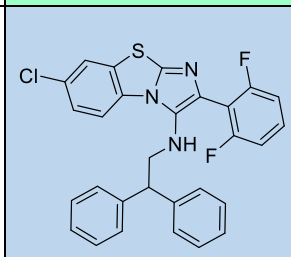
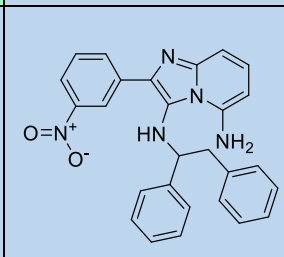
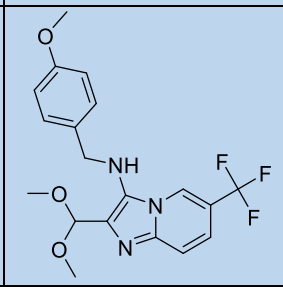
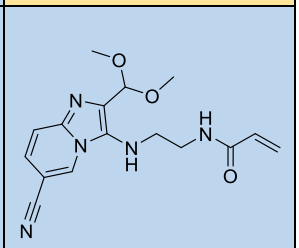
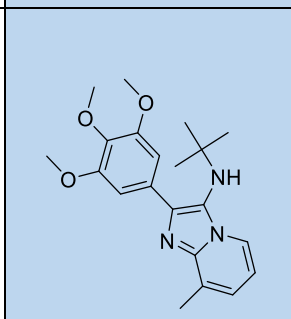
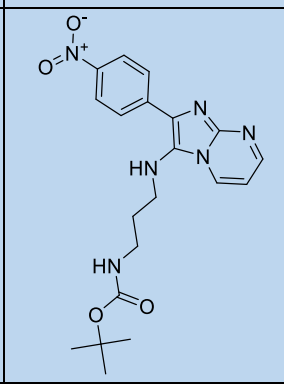
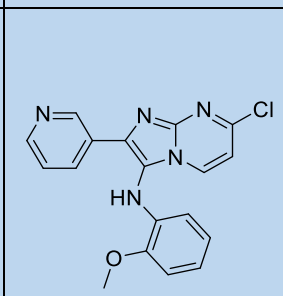
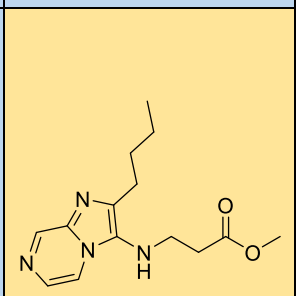
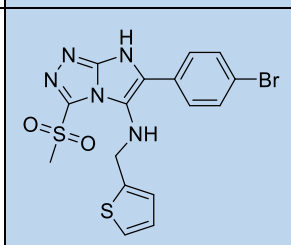
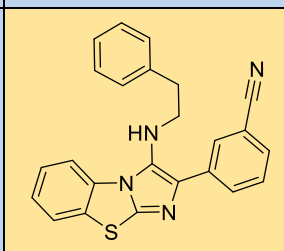
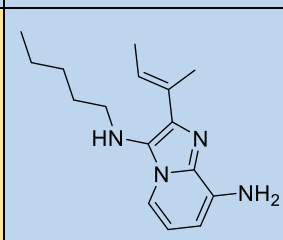
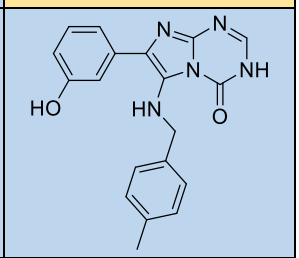
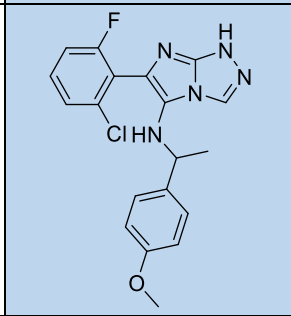
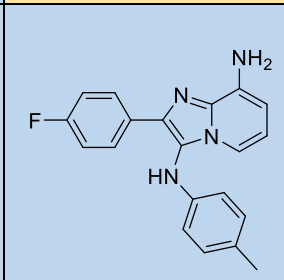
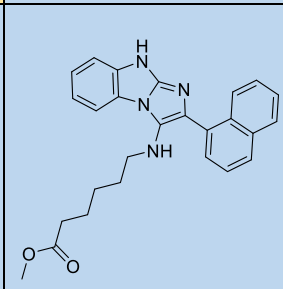
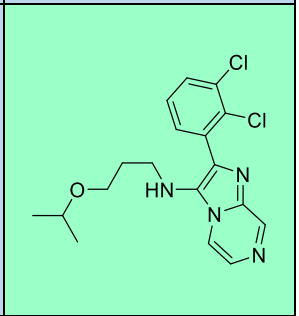
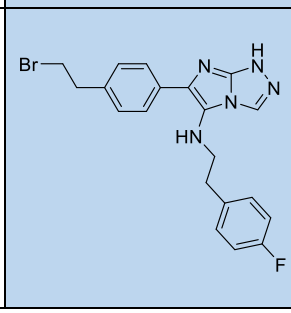
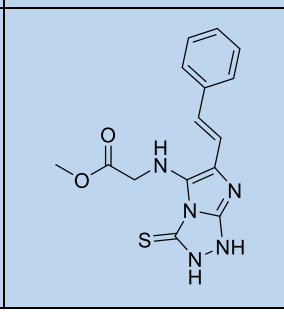
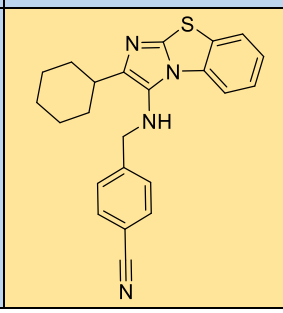
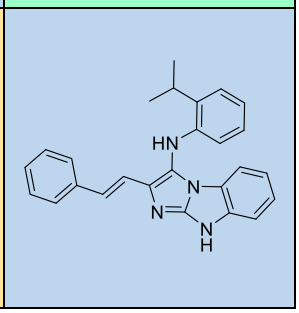
| **7** |  |  |  |  |
| **8** |  |  |  |  |
| **9** |  |  |  |  |
| **10** |  |  |  |  |
| **11** |  |  |  |  |
| **12** |  |  |  |  |

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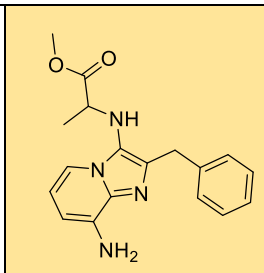
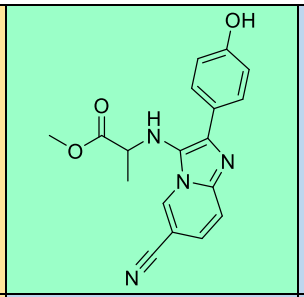
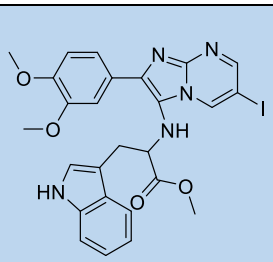
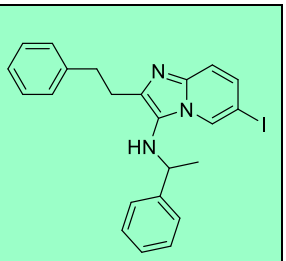
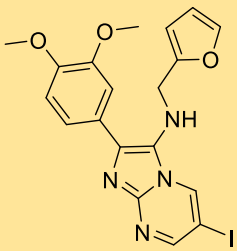
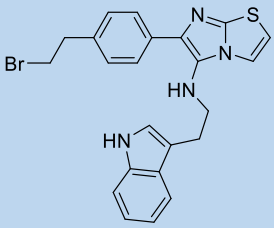
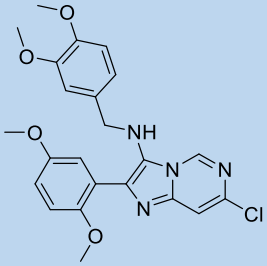
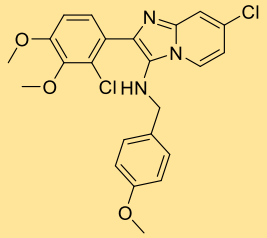
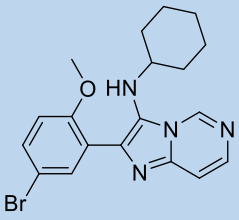
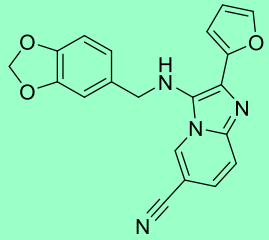
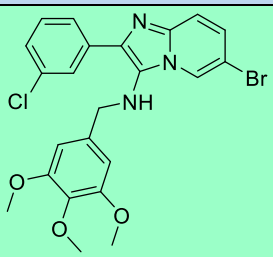
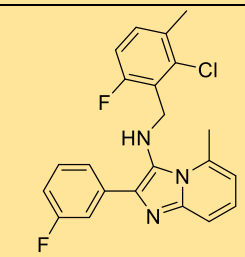
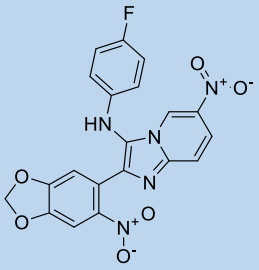
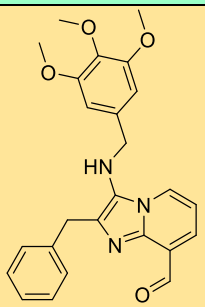
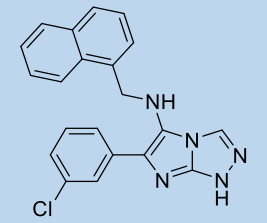
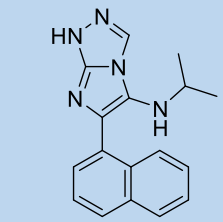
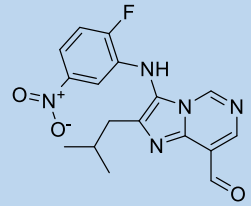
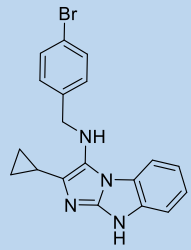
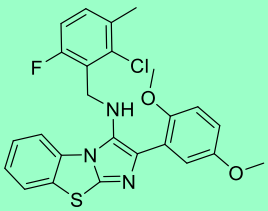
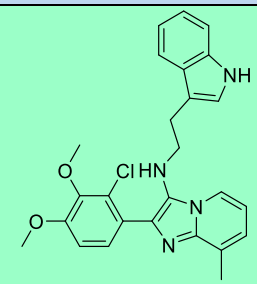
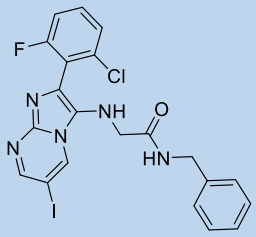
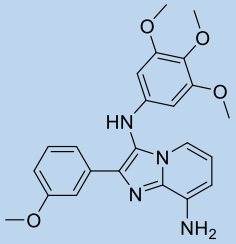
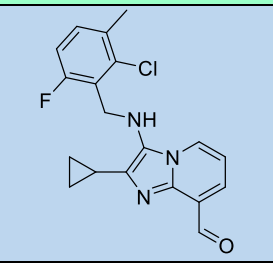
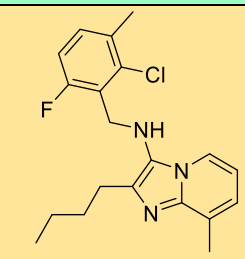
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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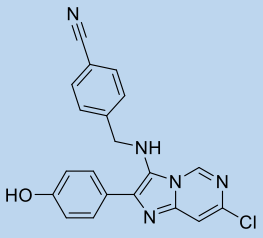
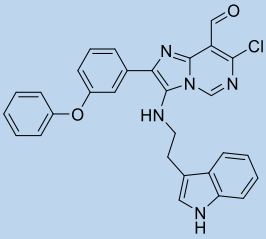
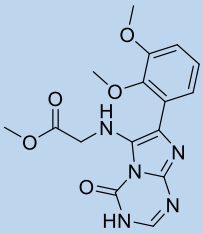
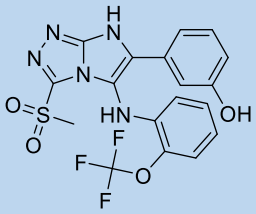
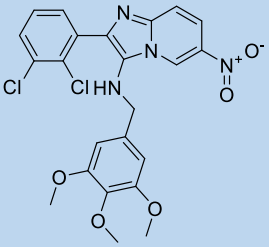
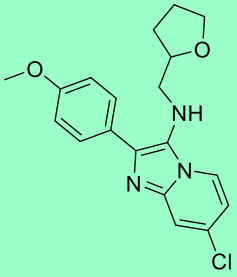
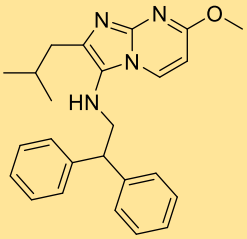
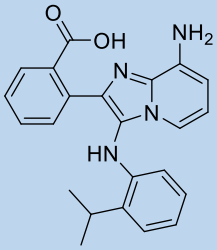
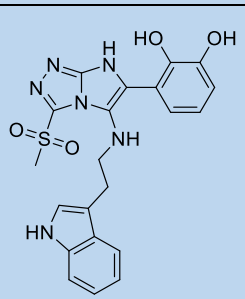
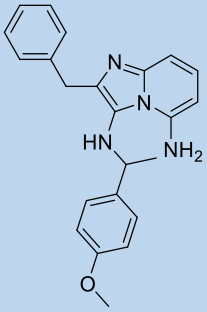
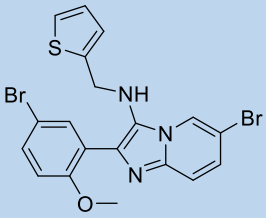
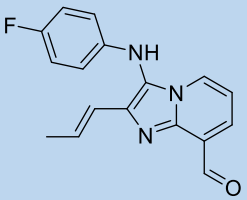
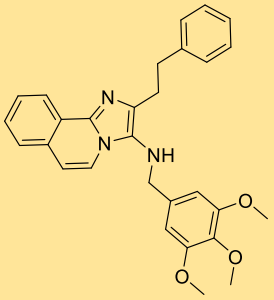
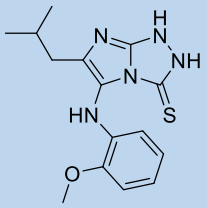
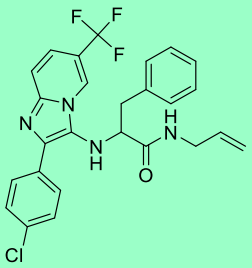
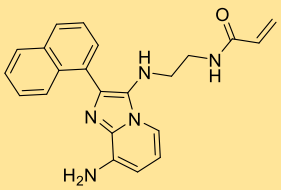
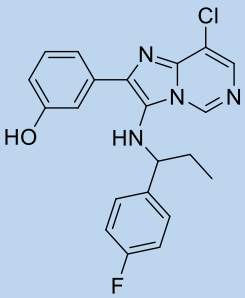
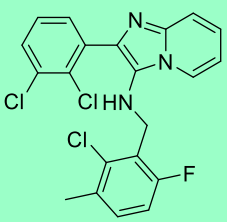
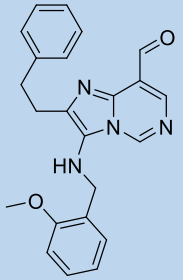
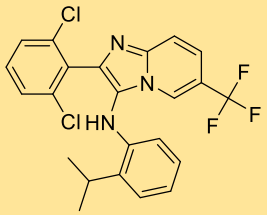
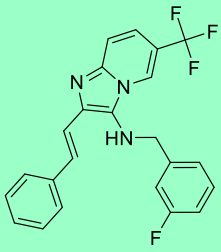
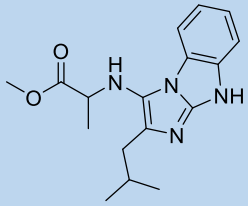
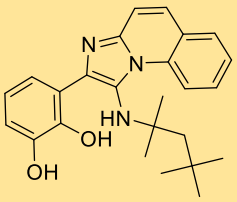
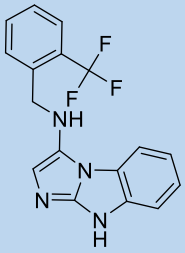
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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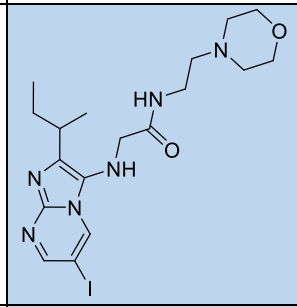
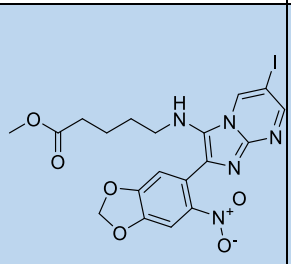
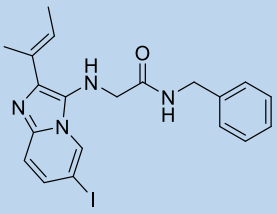
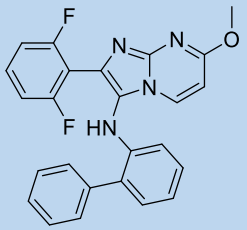
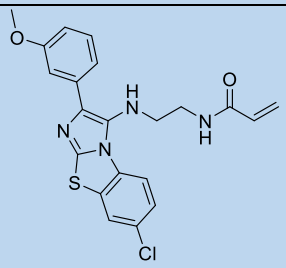
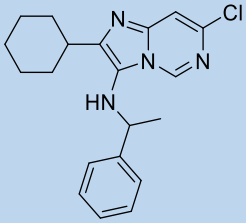
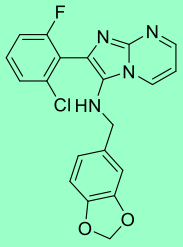
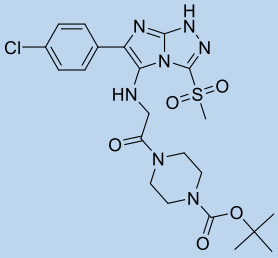
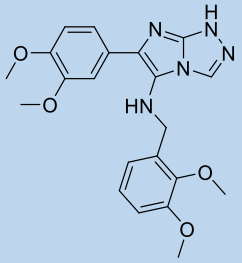
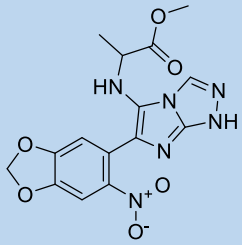
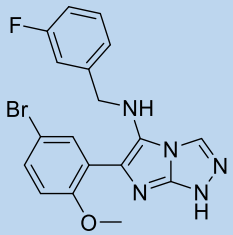
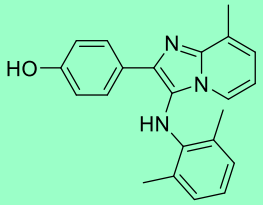
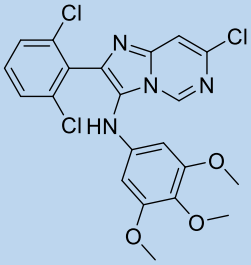
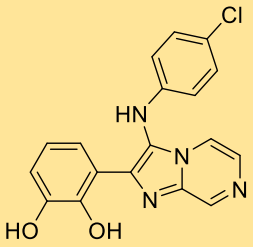
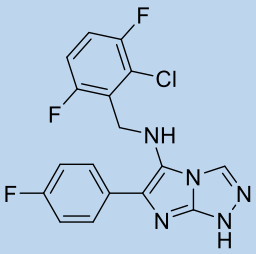
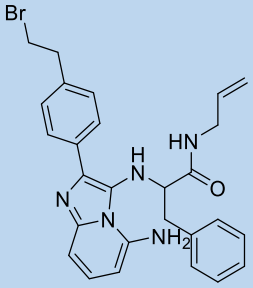
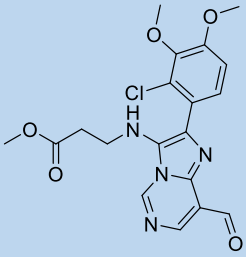
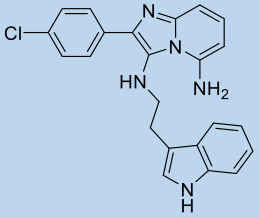
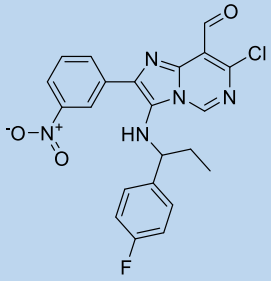
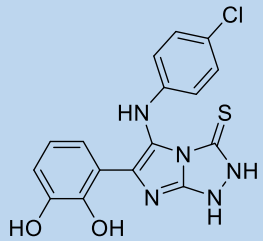
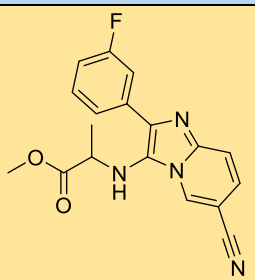
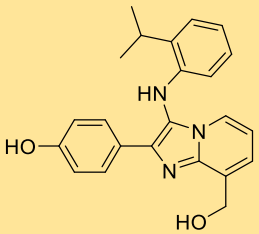
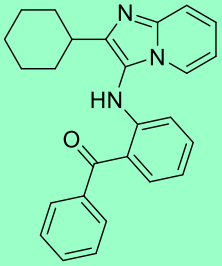
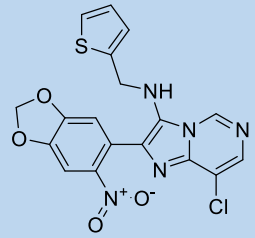
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |

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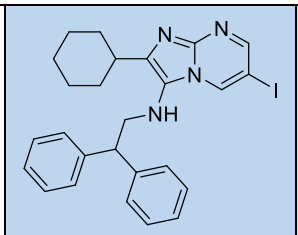
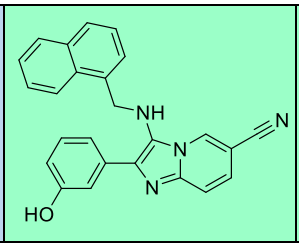
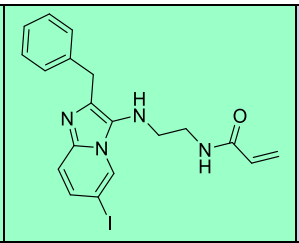
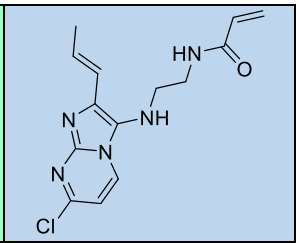
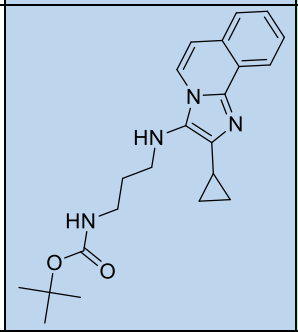
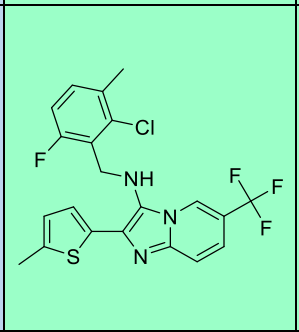
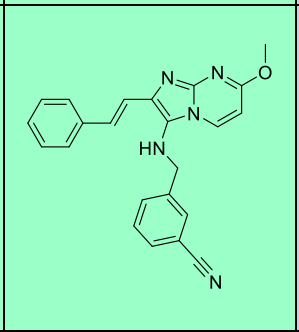
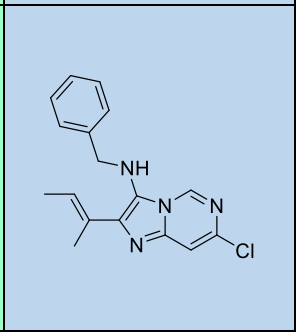
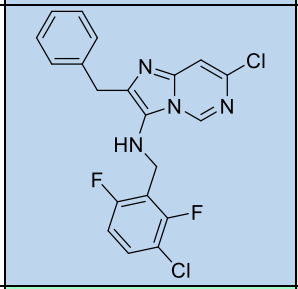
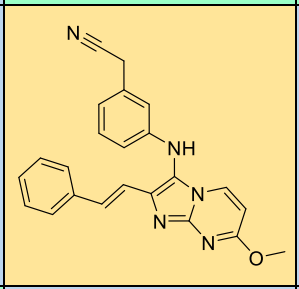
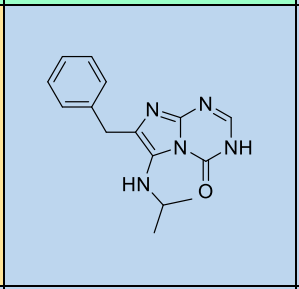
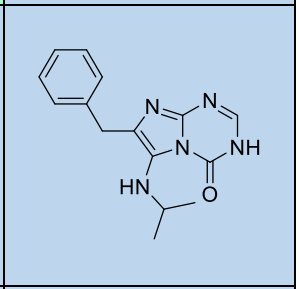
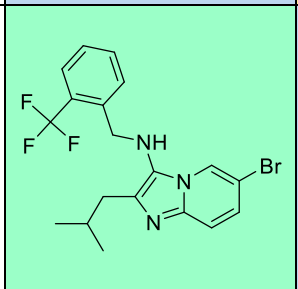
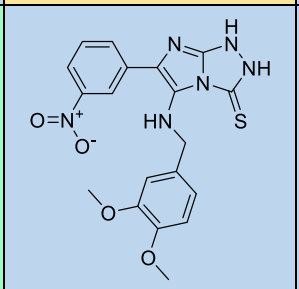
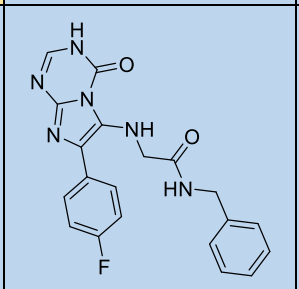
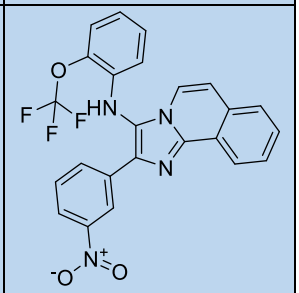
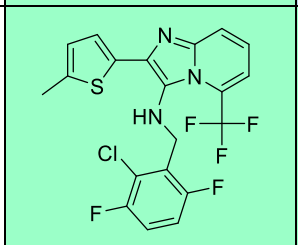
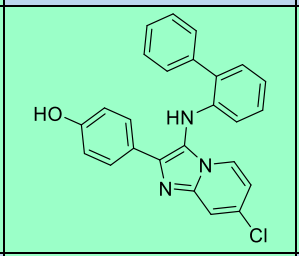
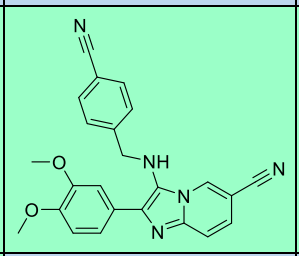
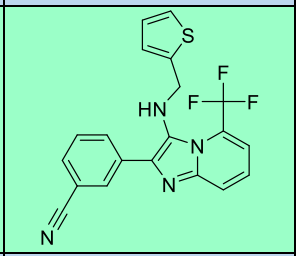
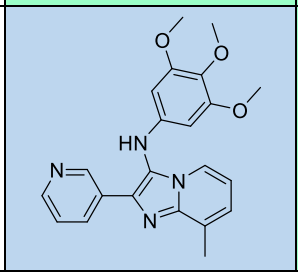
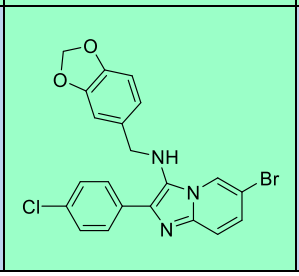
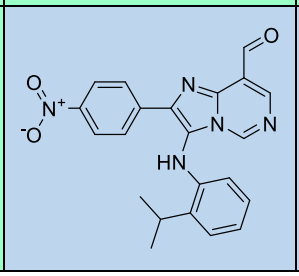
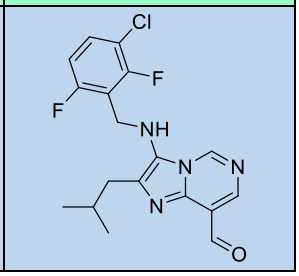
| **7** |  |  |  |  |
| **8** |  |  |  |  |
| **9** |  |  |  |  |
| **10** |  |  |  |  |
| **11** |  |  |  |  |
| **12** |  |  |  |  |

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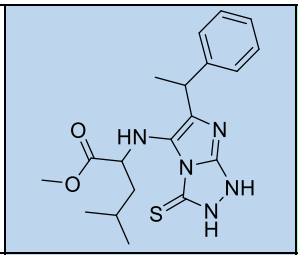
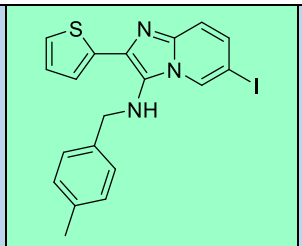
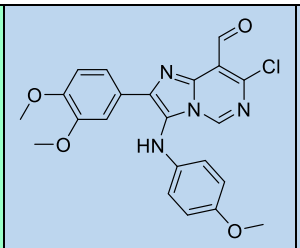
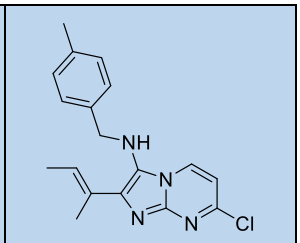
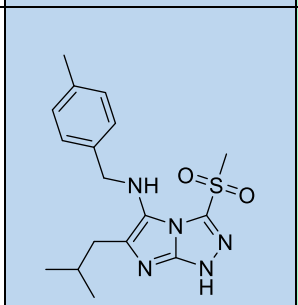
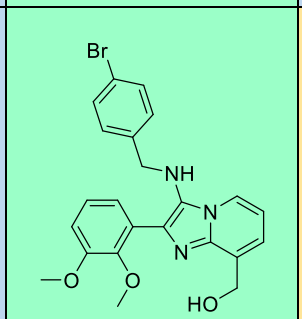
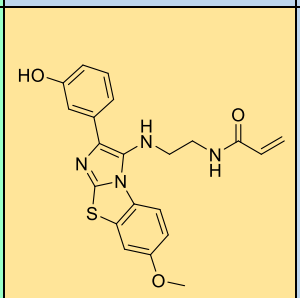
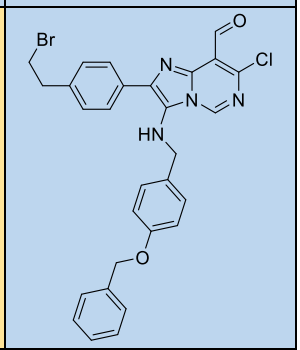
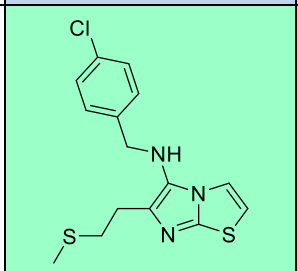
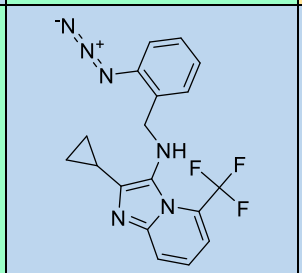
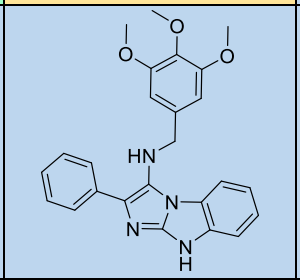
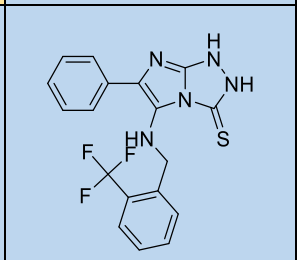
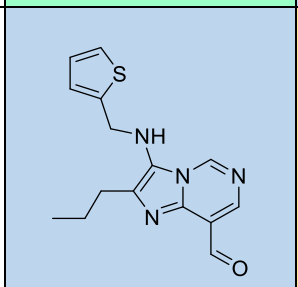
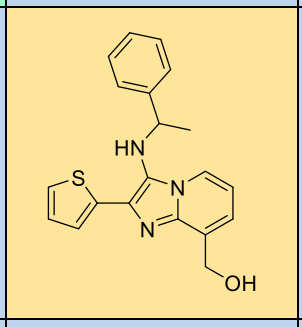
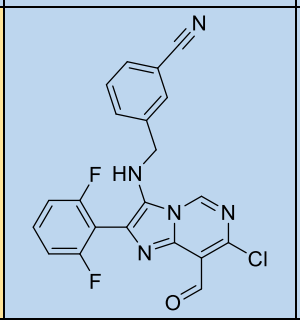
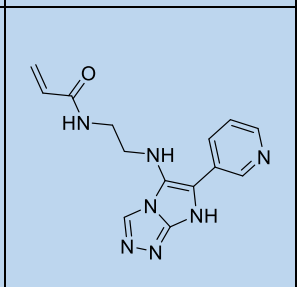
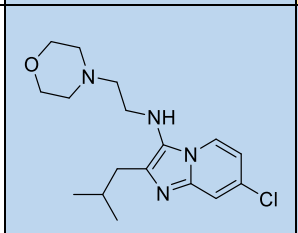
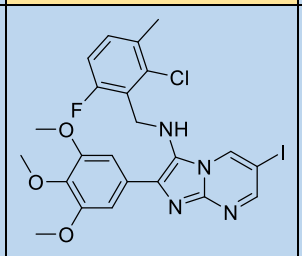
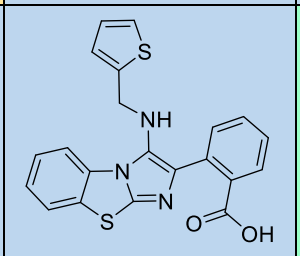
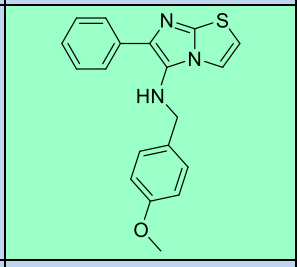
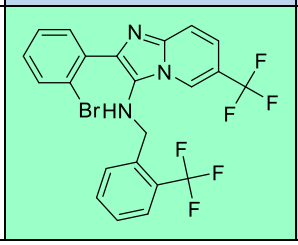
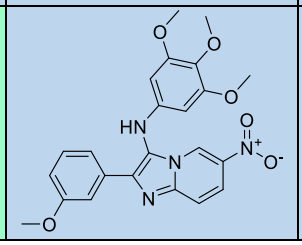
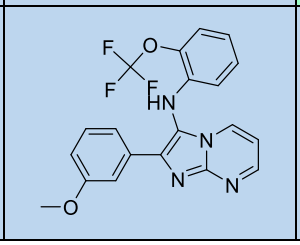
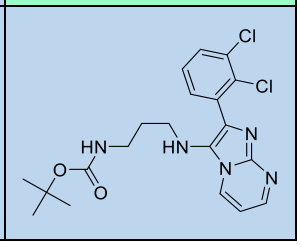
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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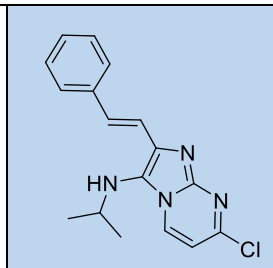
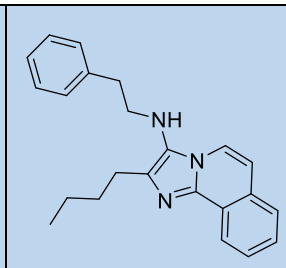
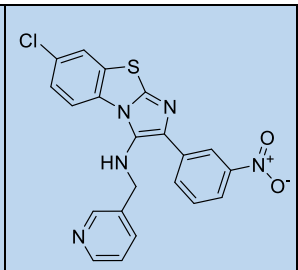
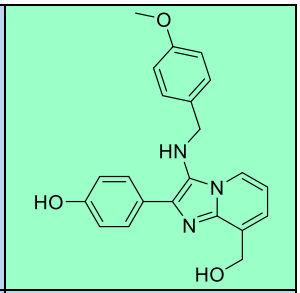
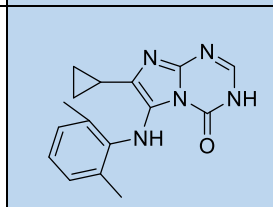
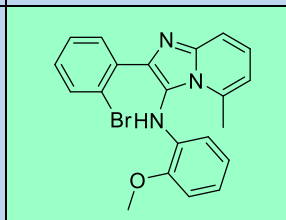
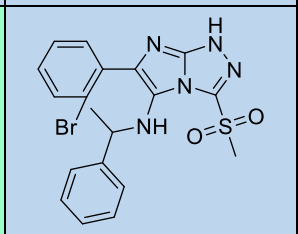
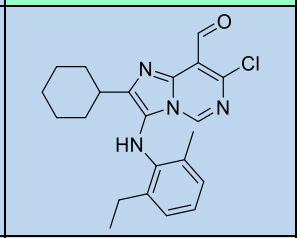
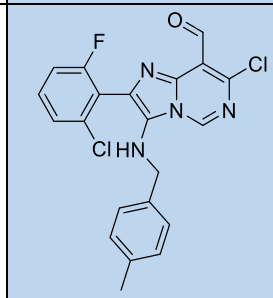
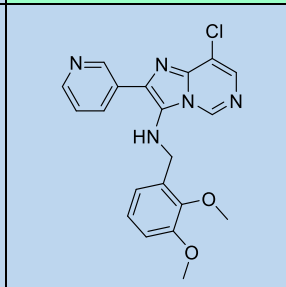
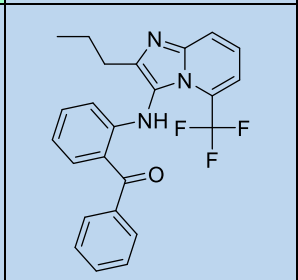
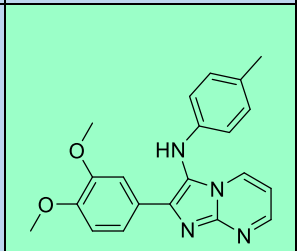
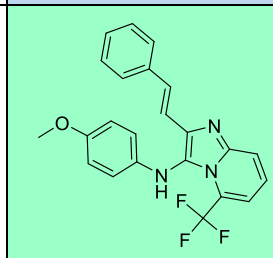
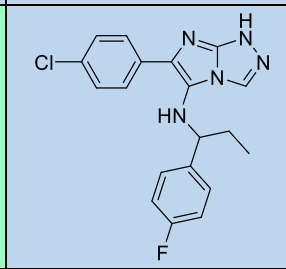
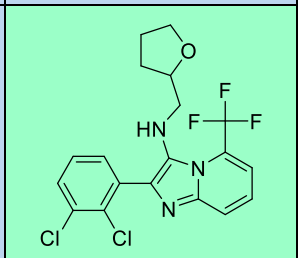
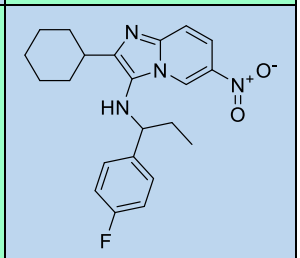
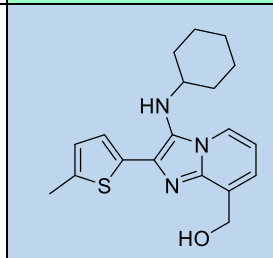
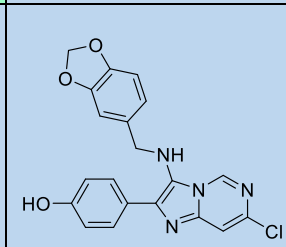
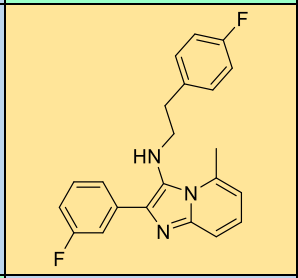
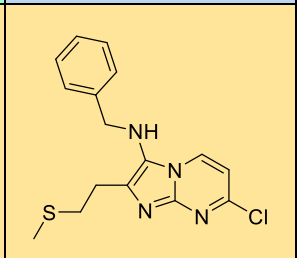
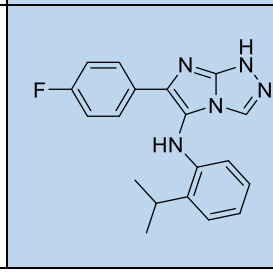
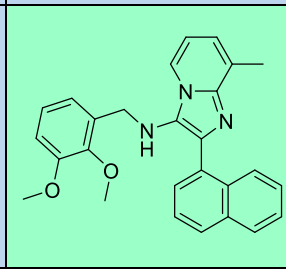
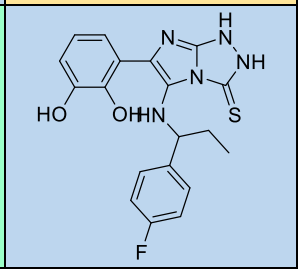
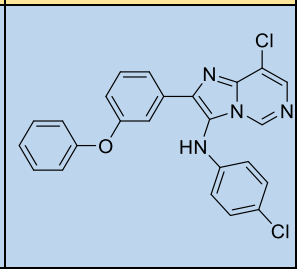
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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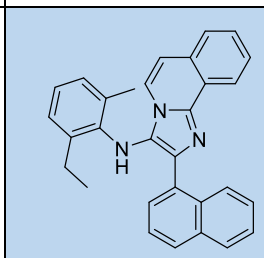
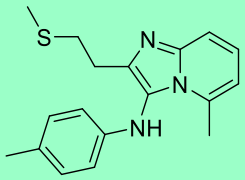
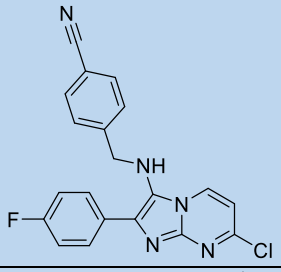
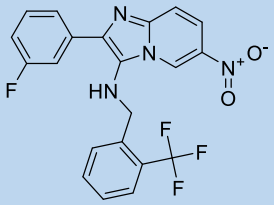
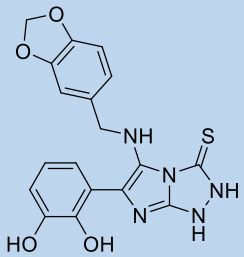
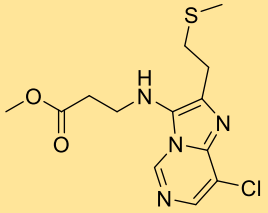
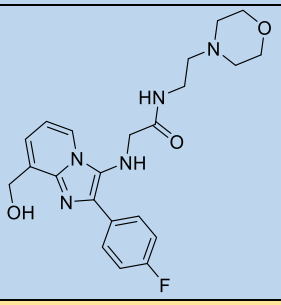
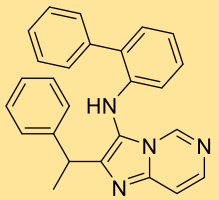
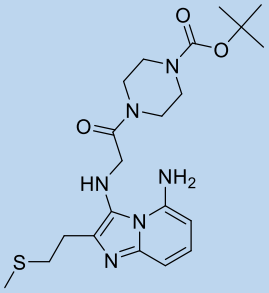
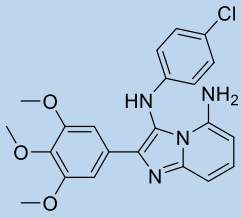
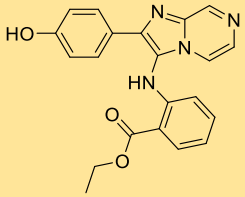
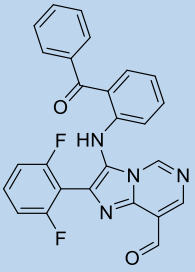
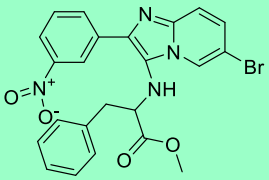
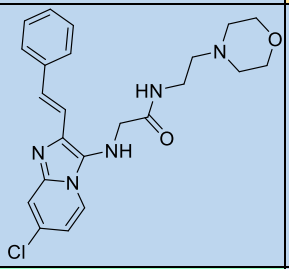
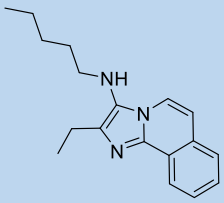
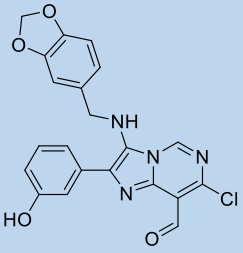
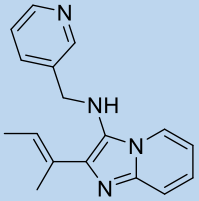
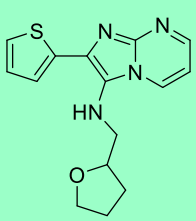
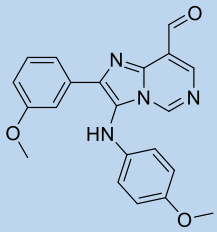
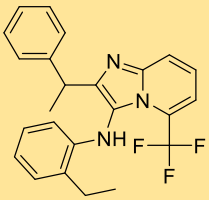
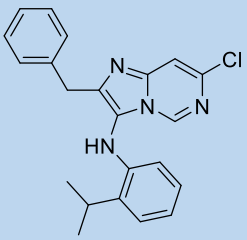
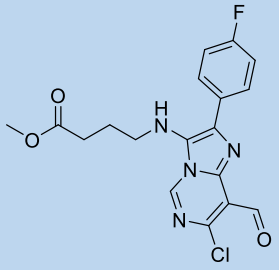
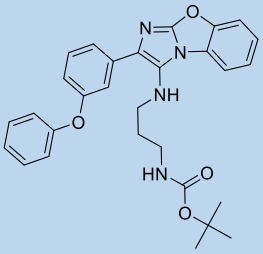
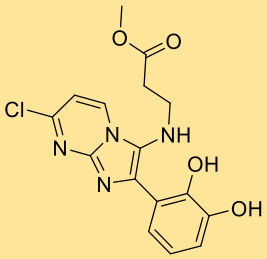
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |

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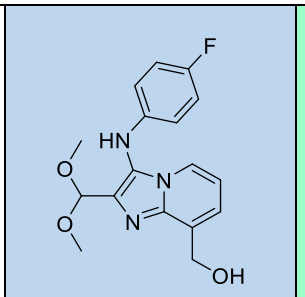
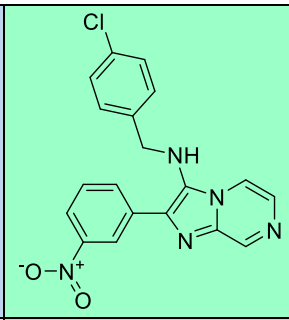
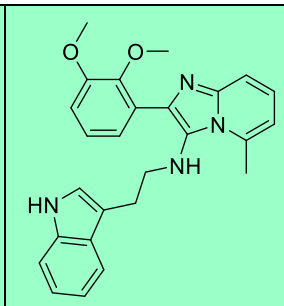
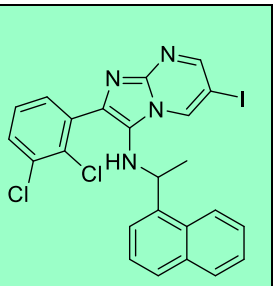
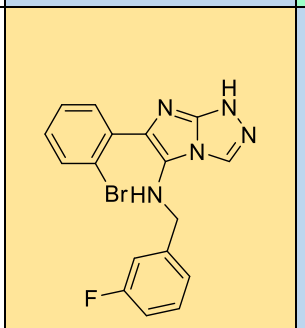
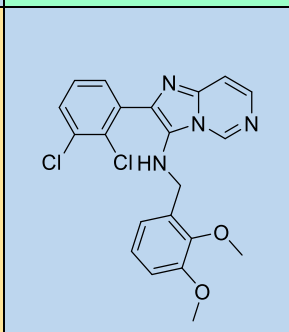
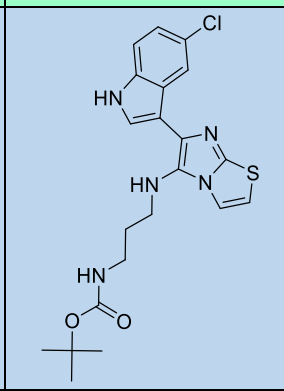
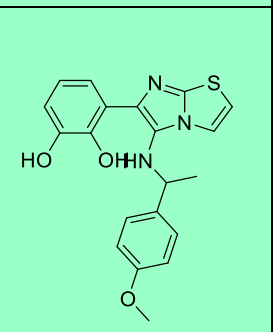
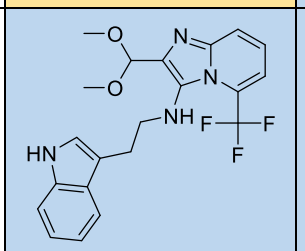
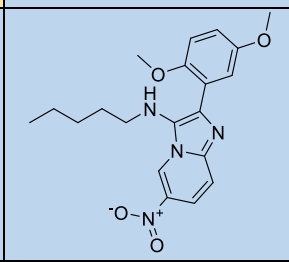
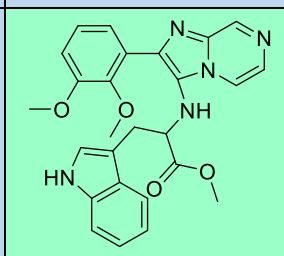
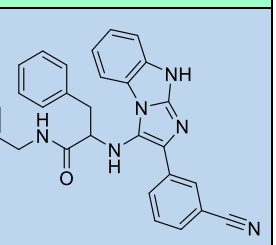
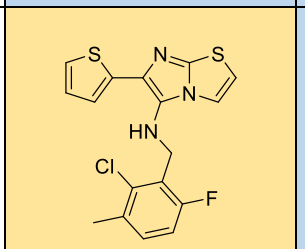
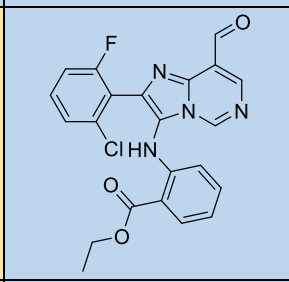
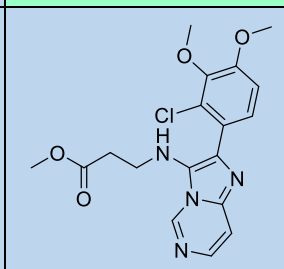
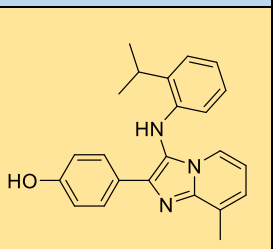
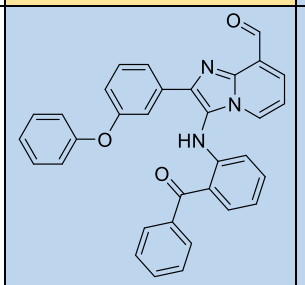
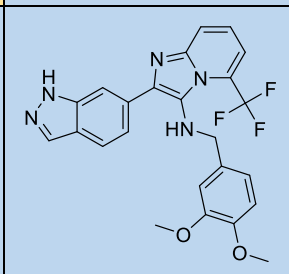
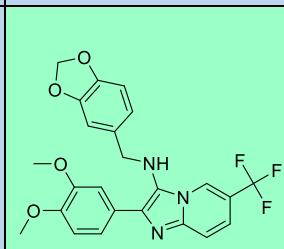
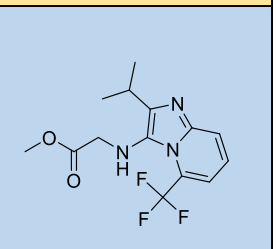
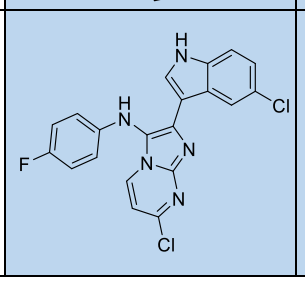
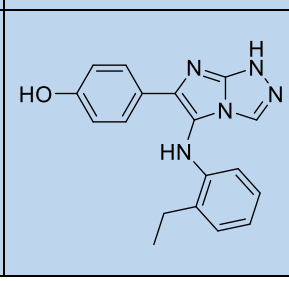
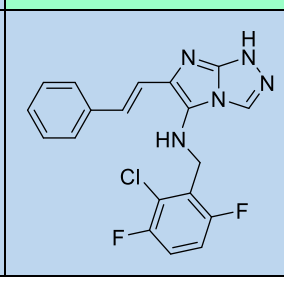
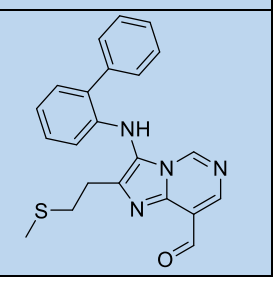
| 7 |  |  |  |  |
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |

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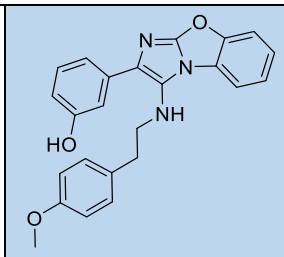
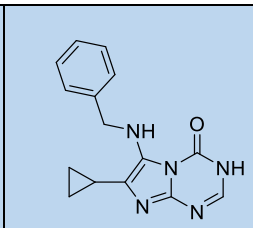
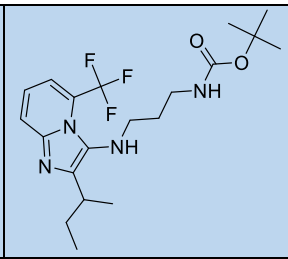
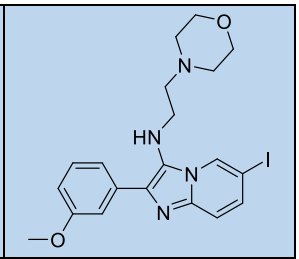
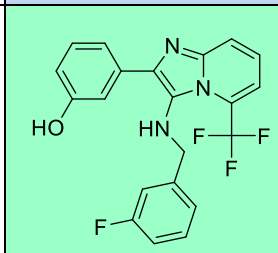
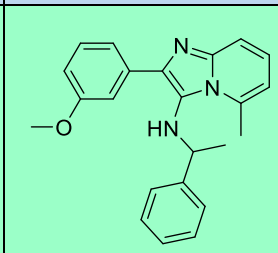
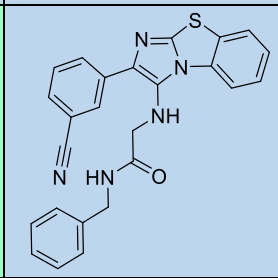
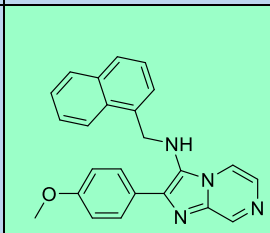
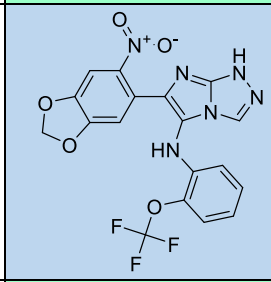
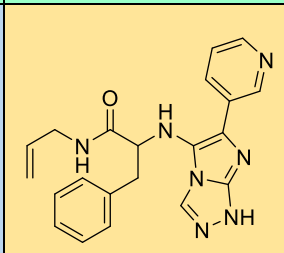
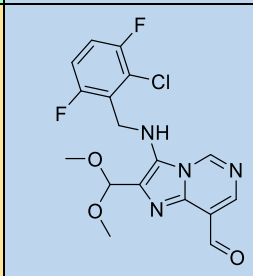
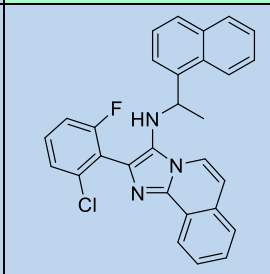
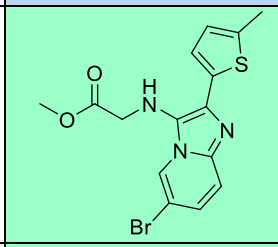
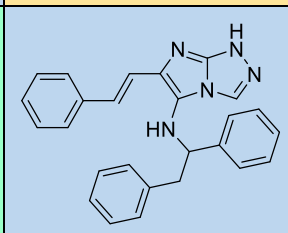
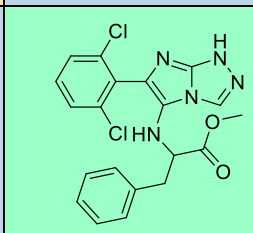
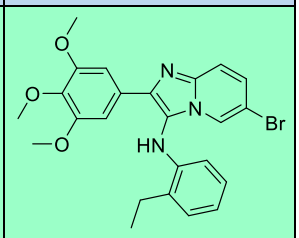
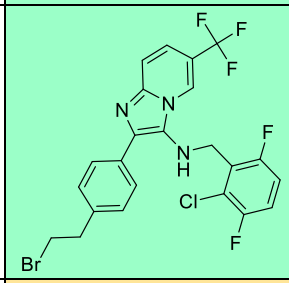
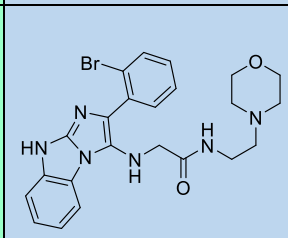
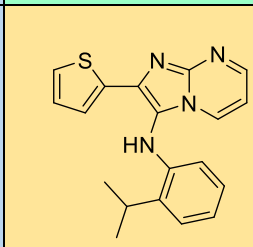
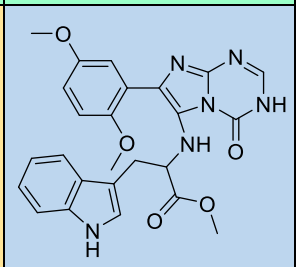
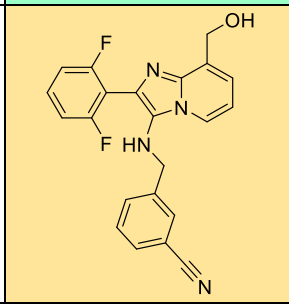
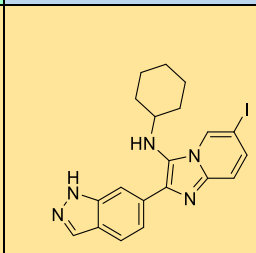
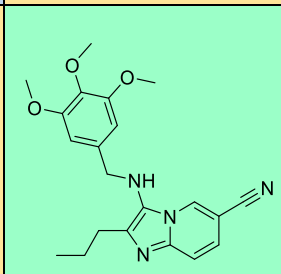
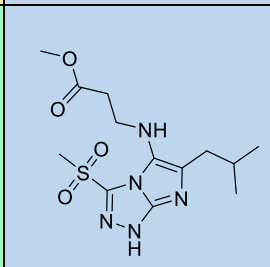
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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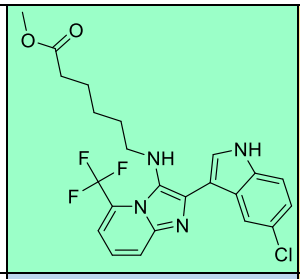
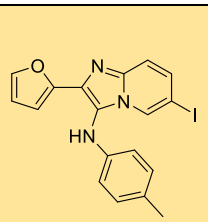
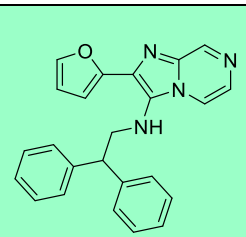
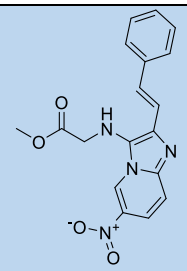
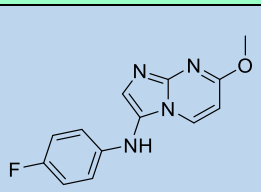
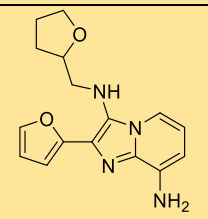
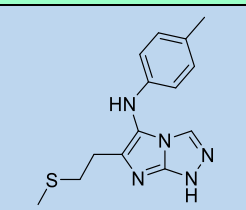
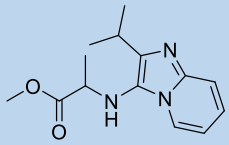
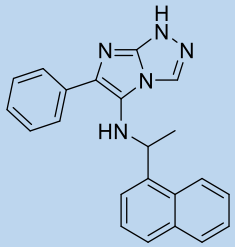
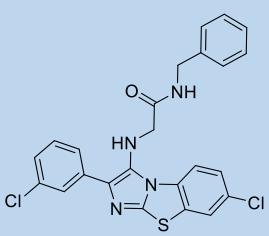
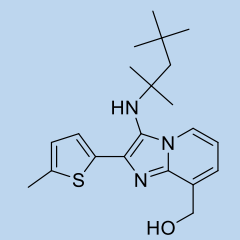
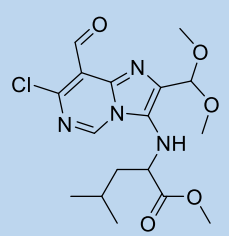
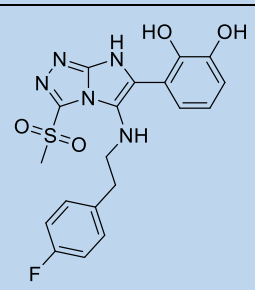
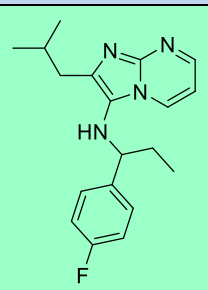
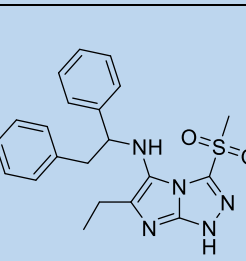
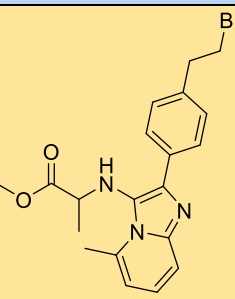
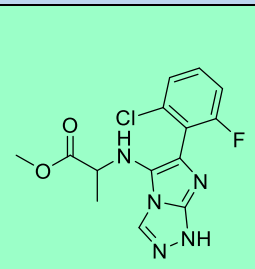
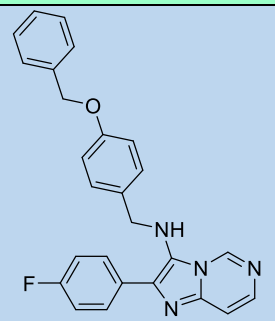
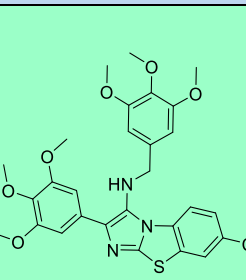
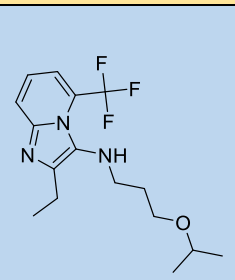
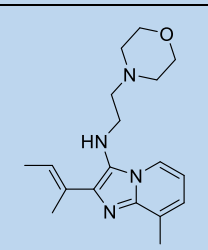
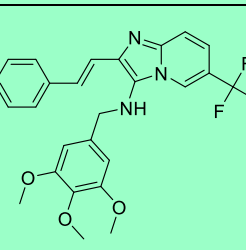
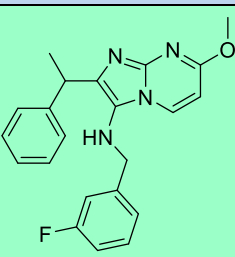
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

**Destination plate IV**

| | A | B | C | D |
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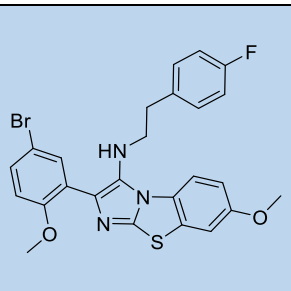
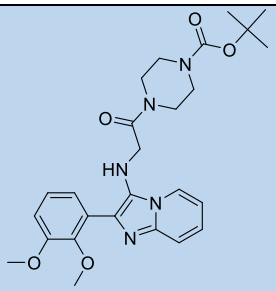
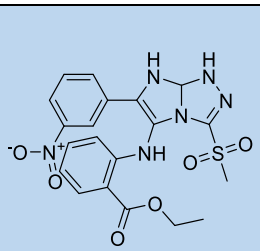
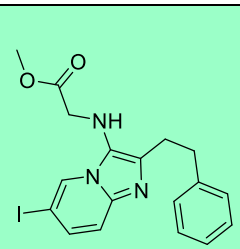
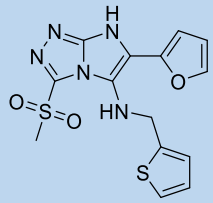
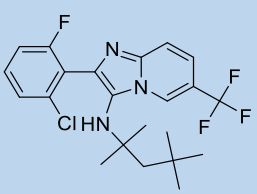
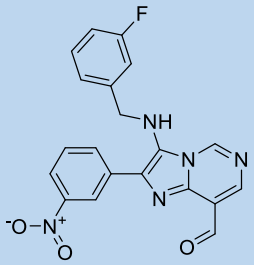
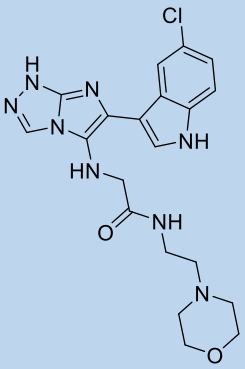
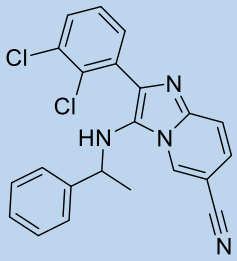
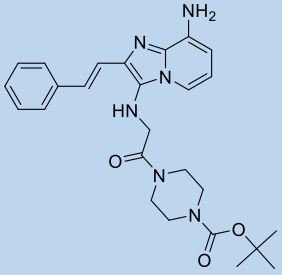
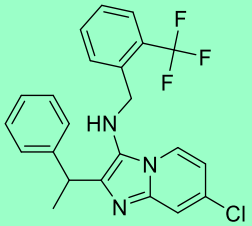
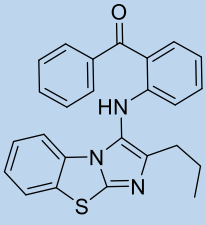
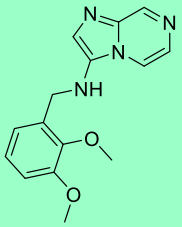
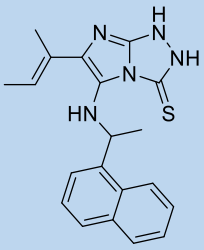
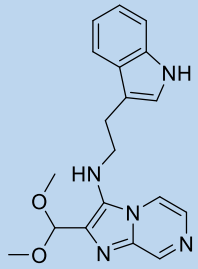
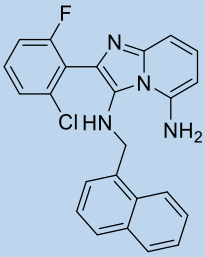
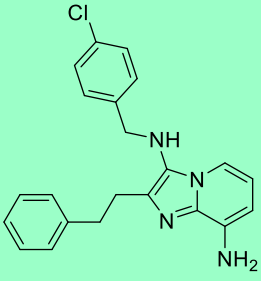
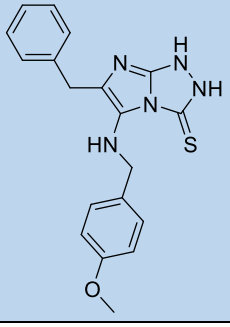
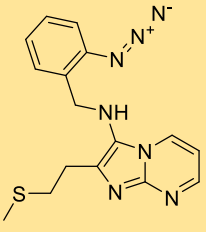
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |

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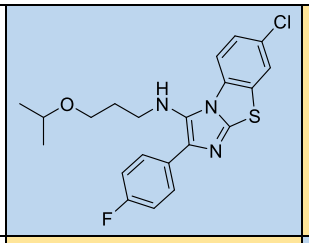
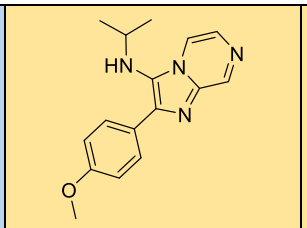
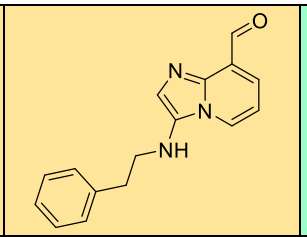
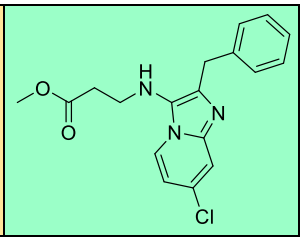
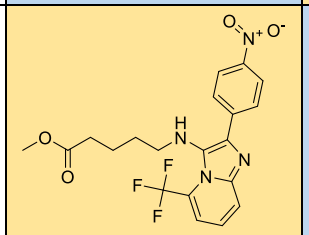
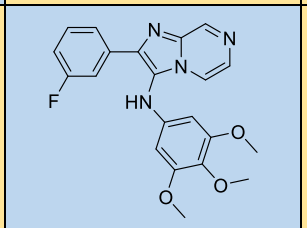
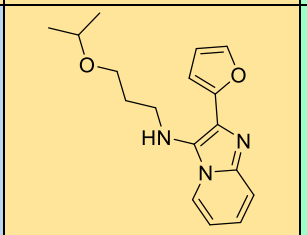
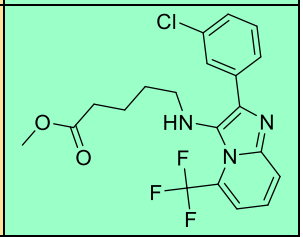
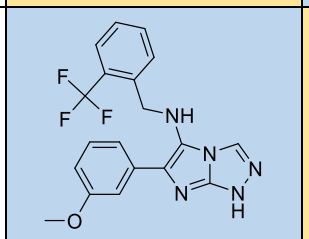
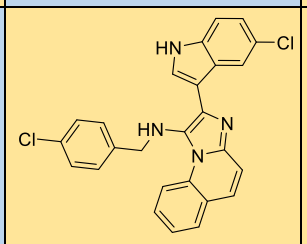
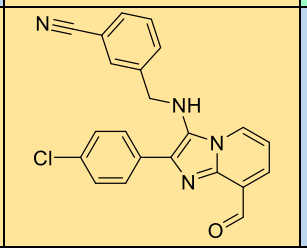
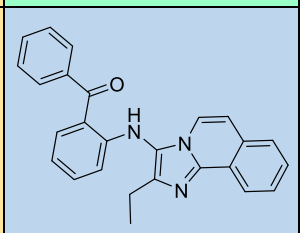
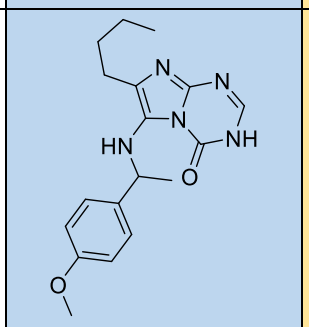
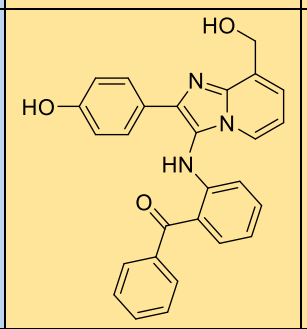
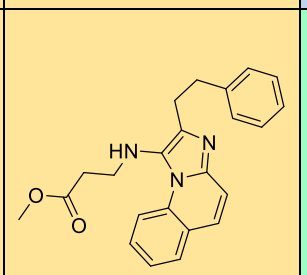
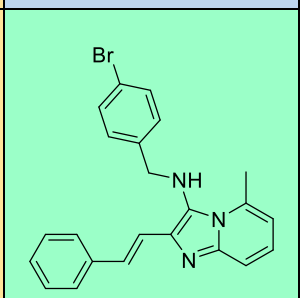
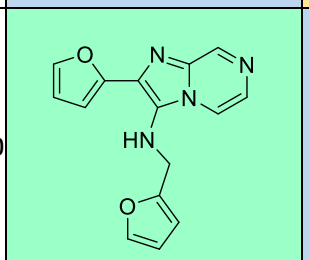
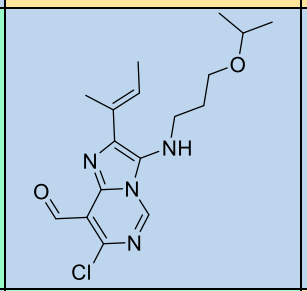
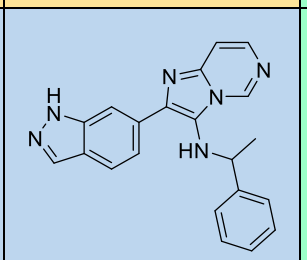
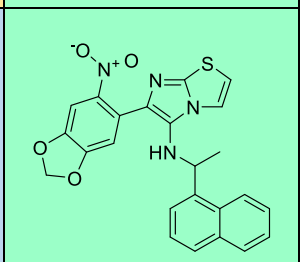
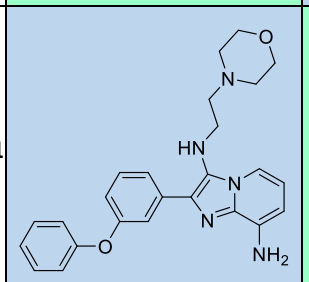
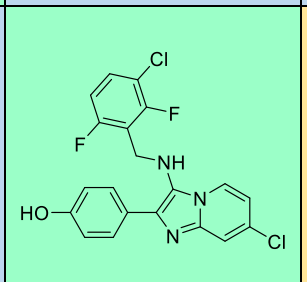
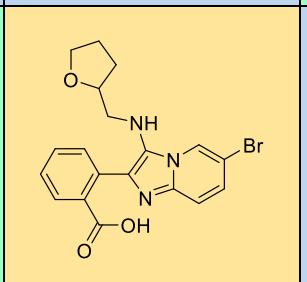
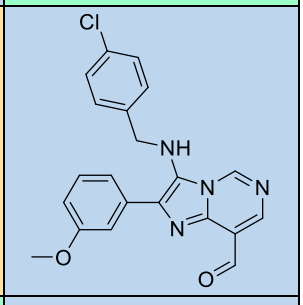
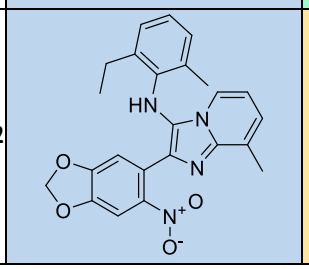
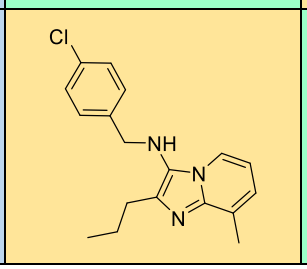
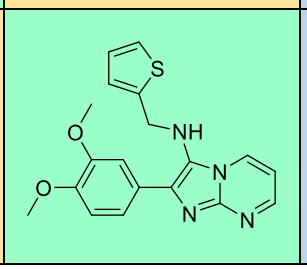
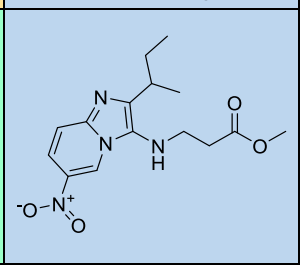
| 6 |  |  |  |  |
| 7 |  |  |  |  |
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |

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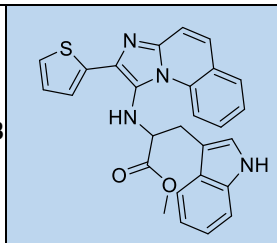
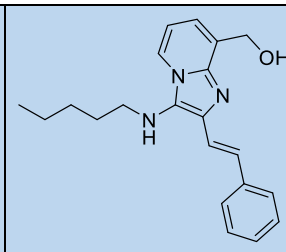
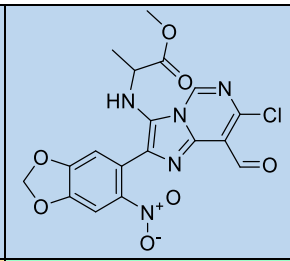
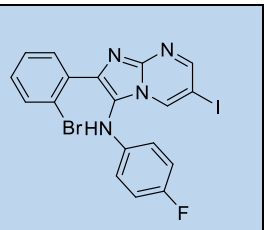
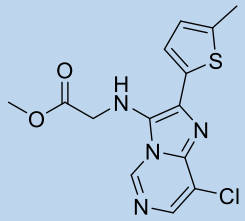
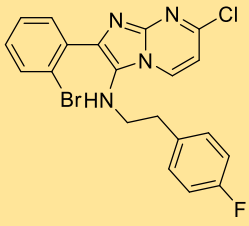
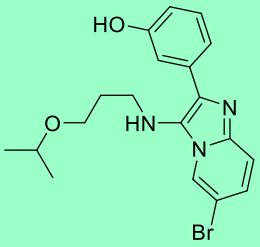
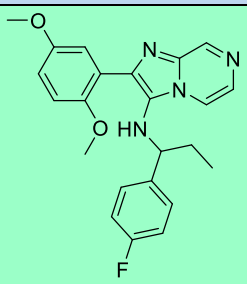
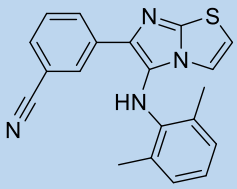
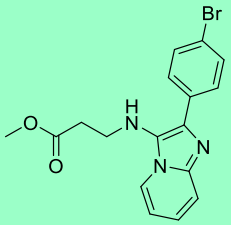
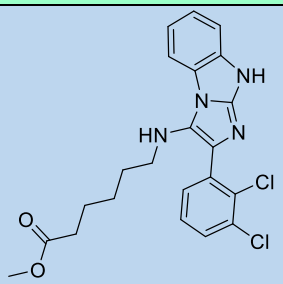
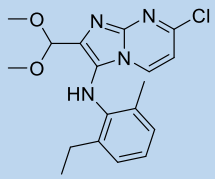
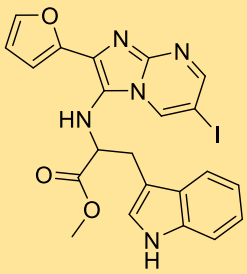
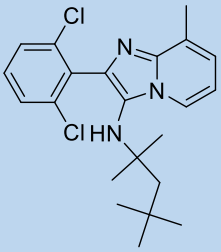
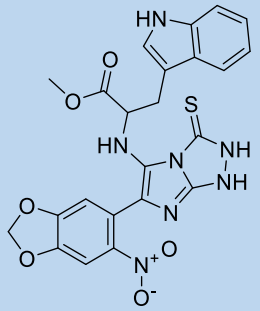
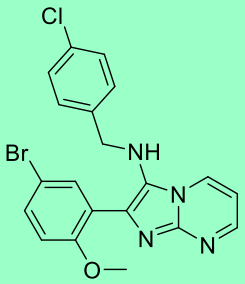
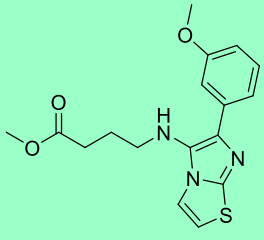
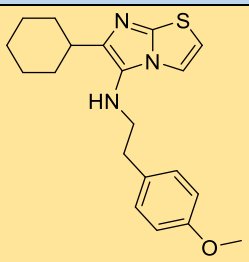
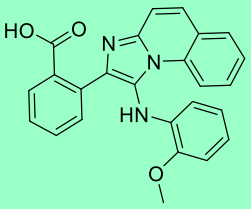
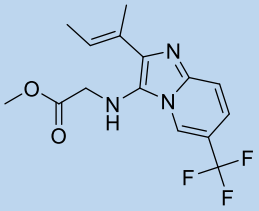
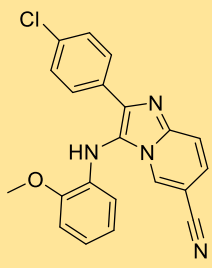
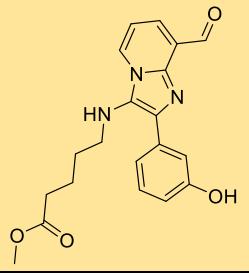
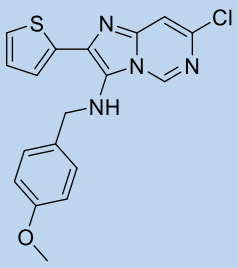
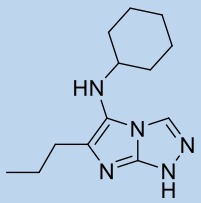
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

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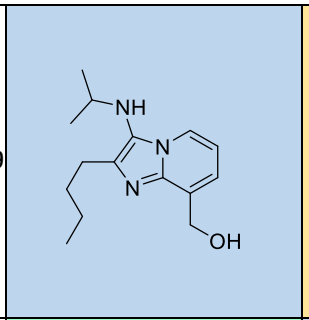
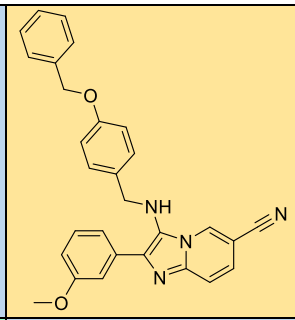
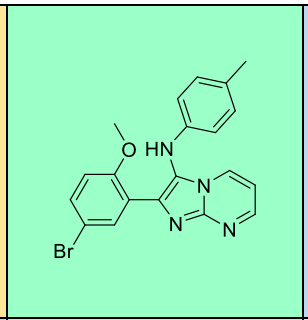
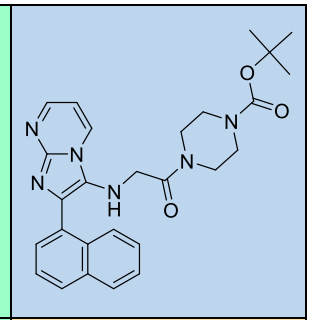
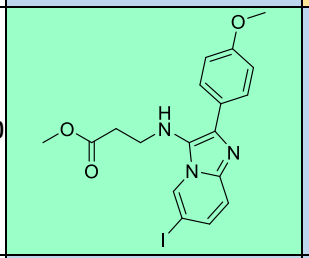
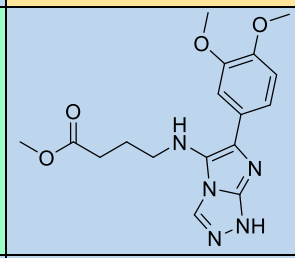
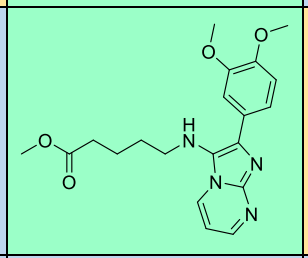
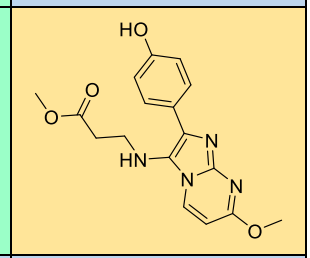
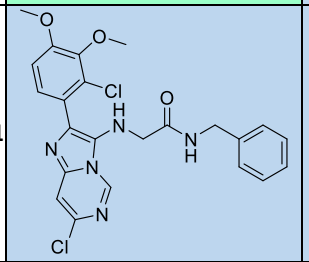
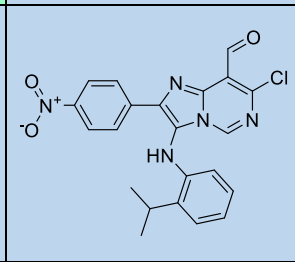
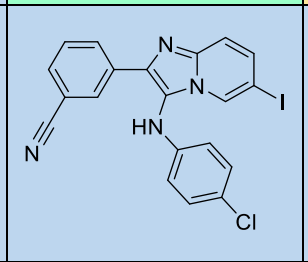
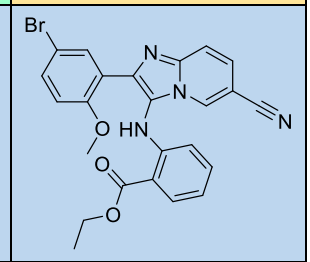
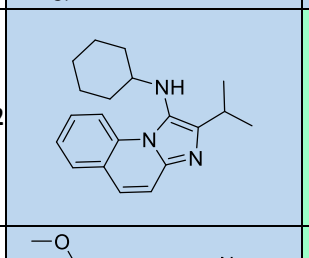
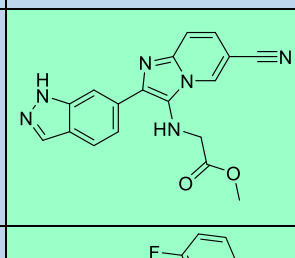
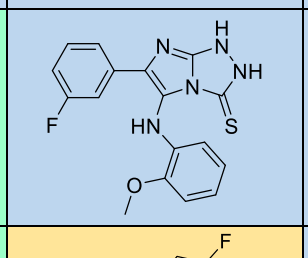
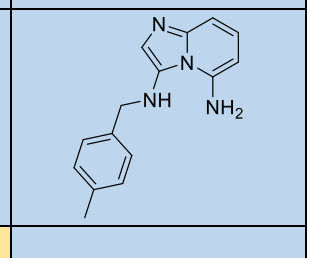
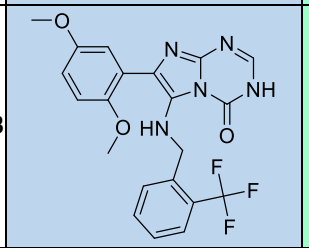
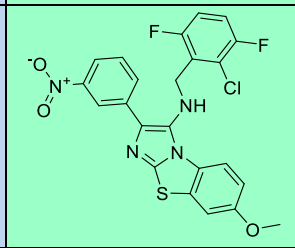
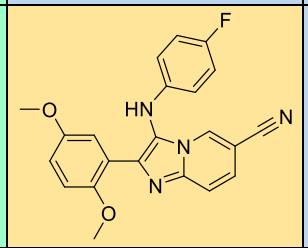
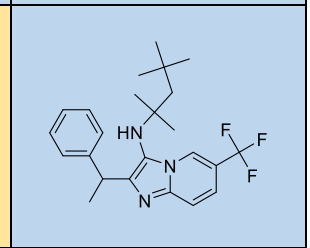
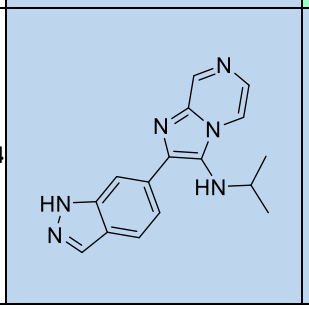
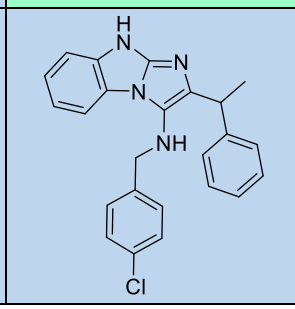
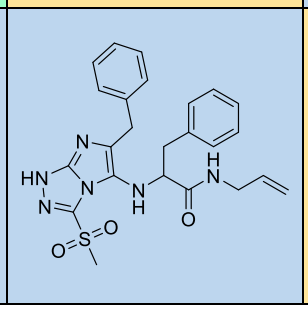
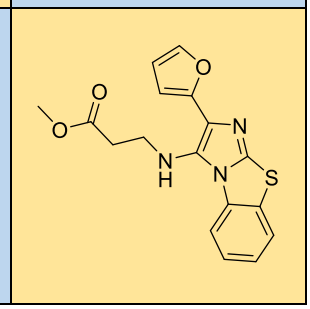
| 19 |  |  |  |  |
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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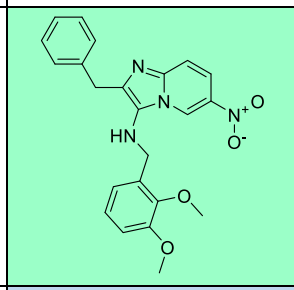
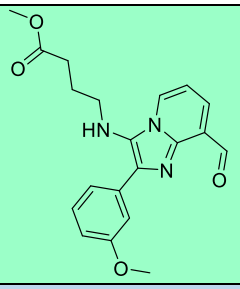
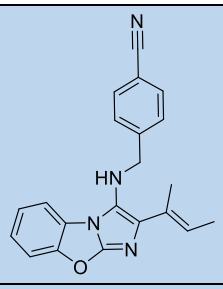
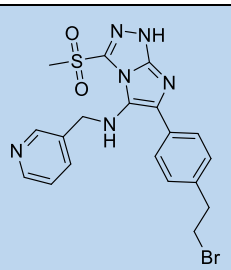
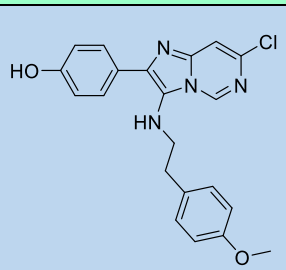
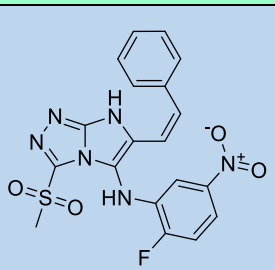
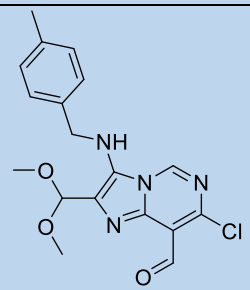
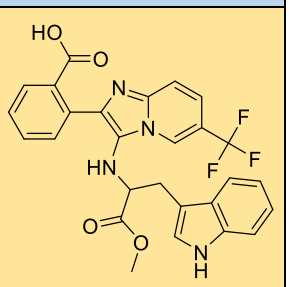
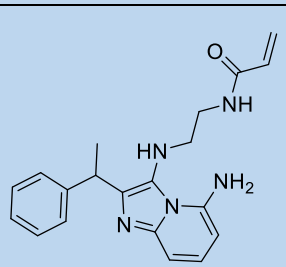
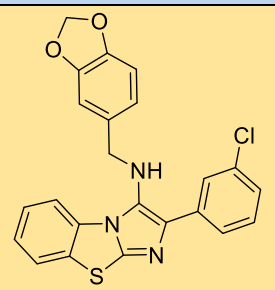
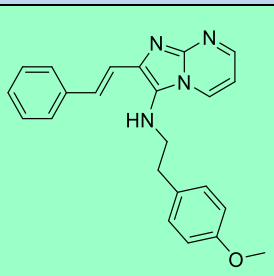
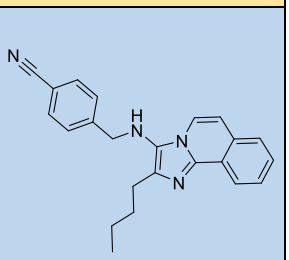
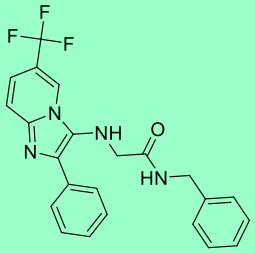
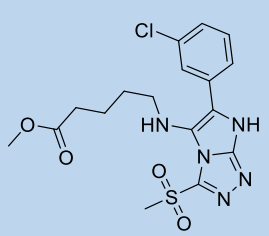
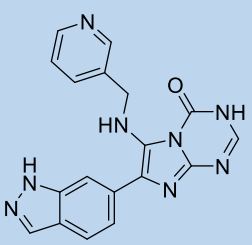
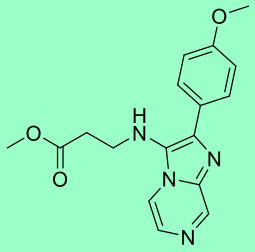
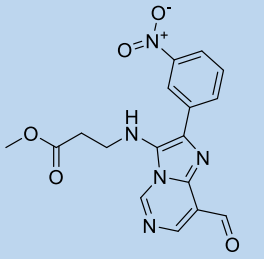
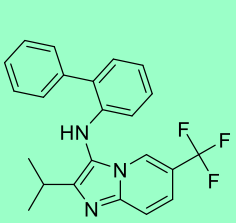
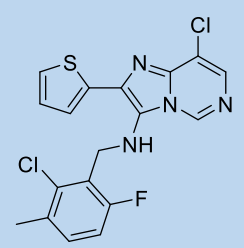
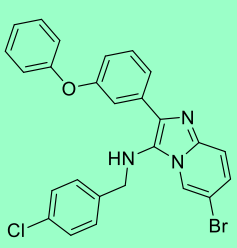
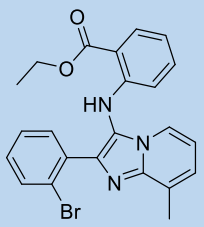
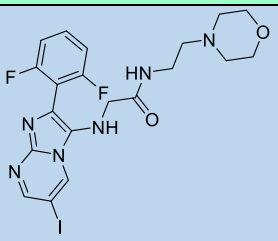
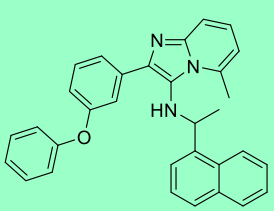
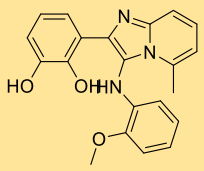
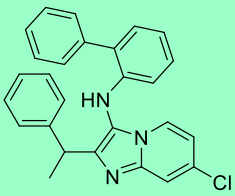
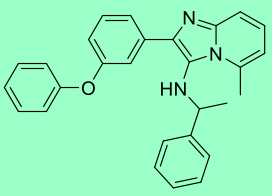
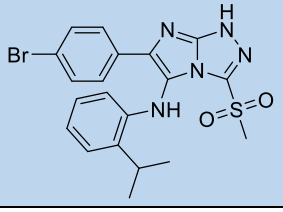
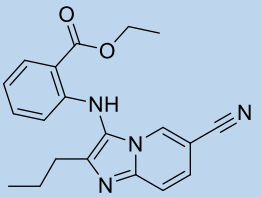
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |
| 7 |  |  |  |  |

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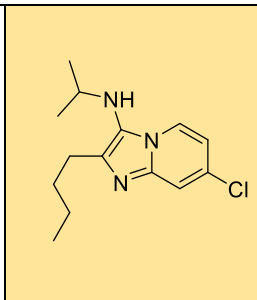
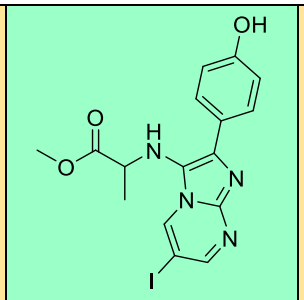
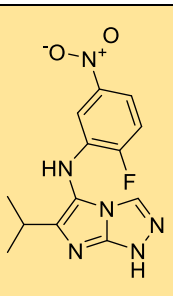
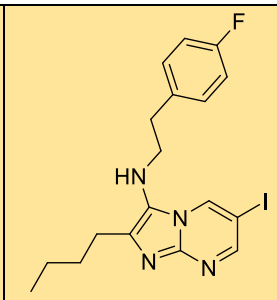
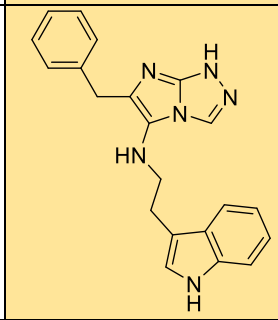
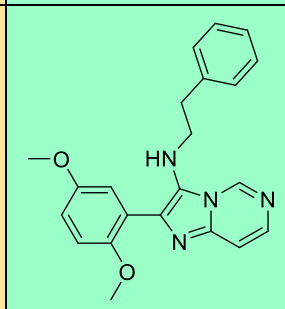
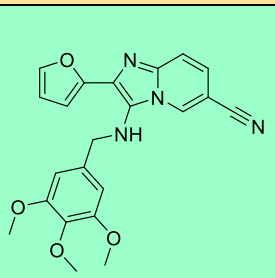
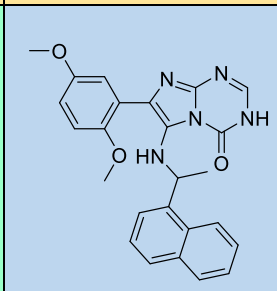
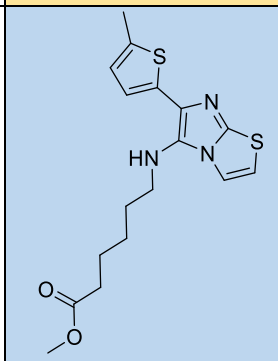
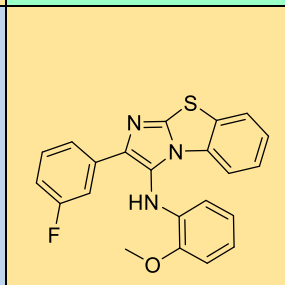
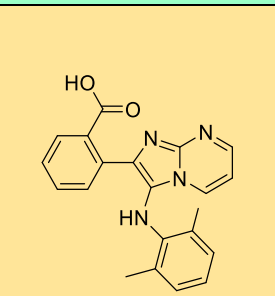
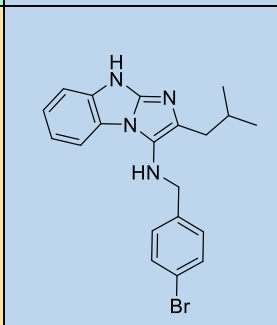
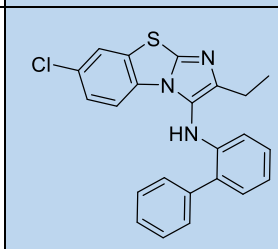
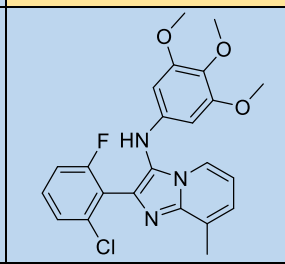
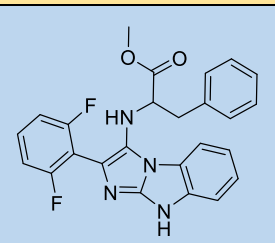
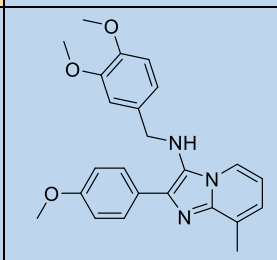
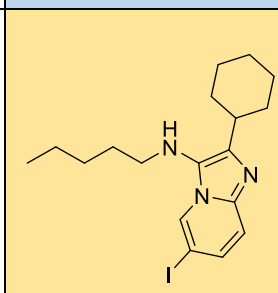
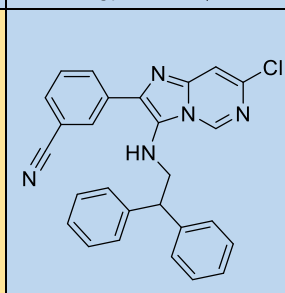
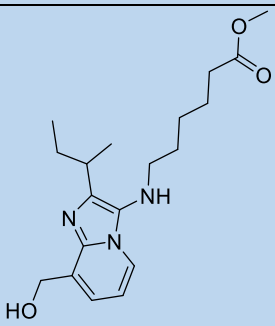
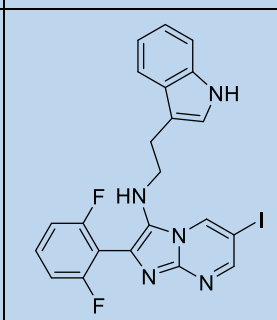
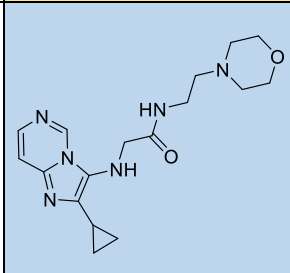
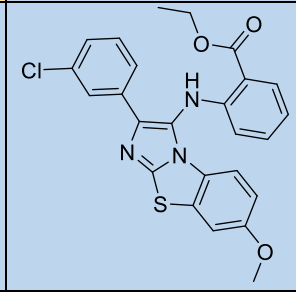
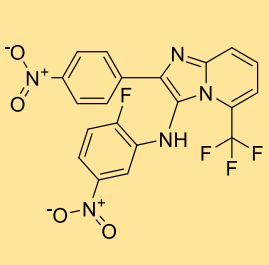
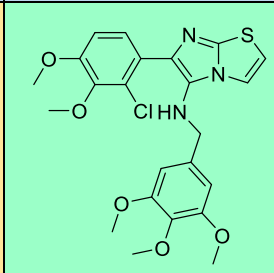
| 8 |  |  |  |  |
| 9 |  |  |  |  |
| 10 |  |  |  |  |
| 11 |  |  |  |  |
| 12 |  |  |  |  |
| 13 |  |  |  |  |

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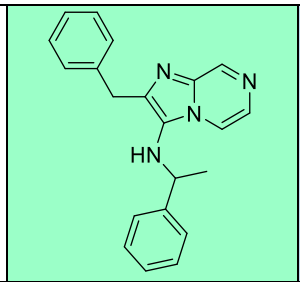
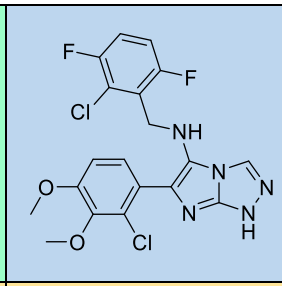
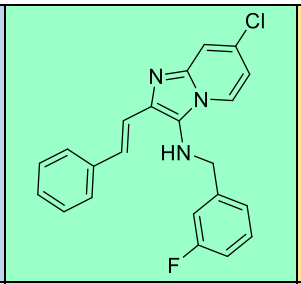
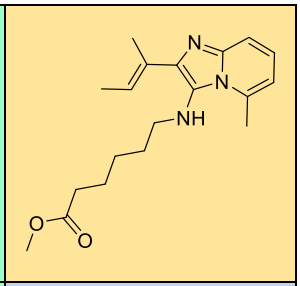
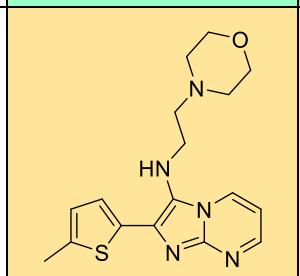
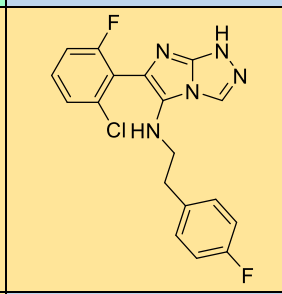
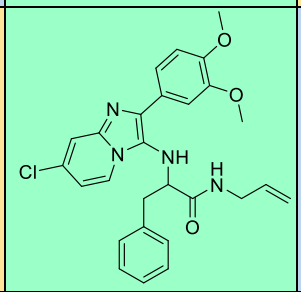
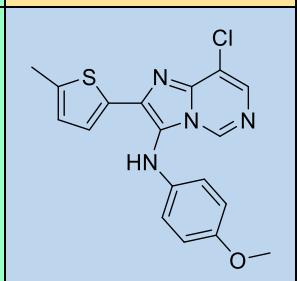
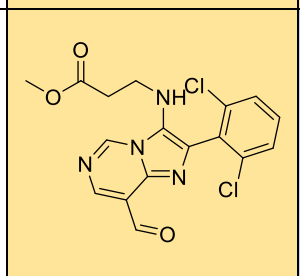
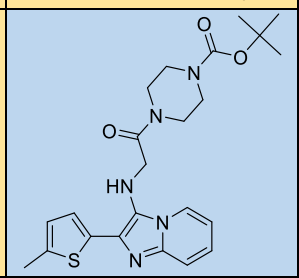
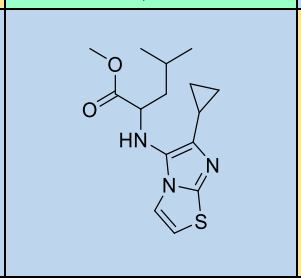
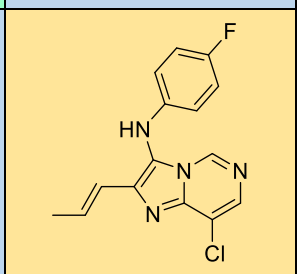
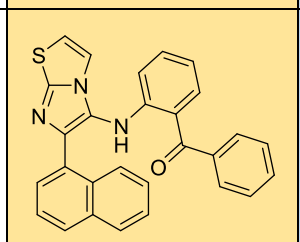
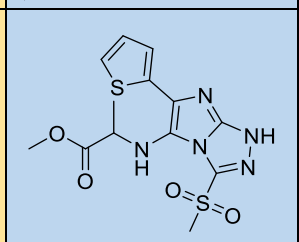
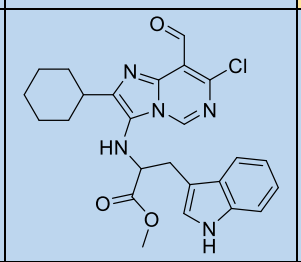
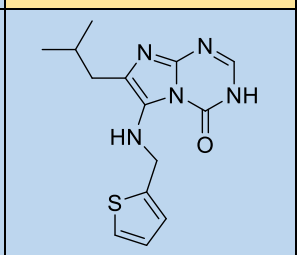
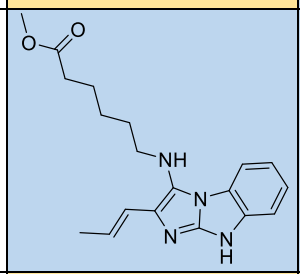
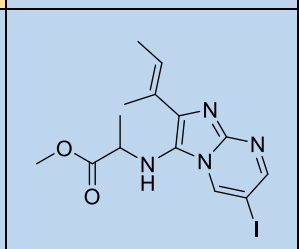
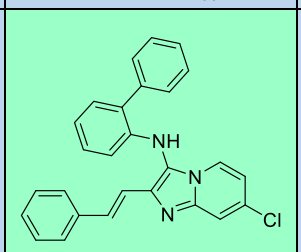
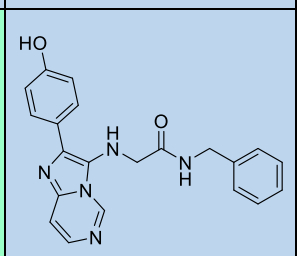
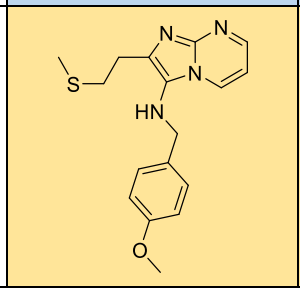
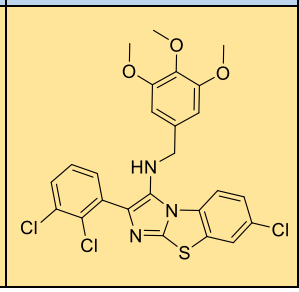
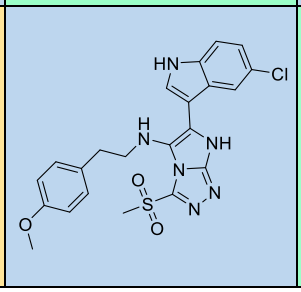
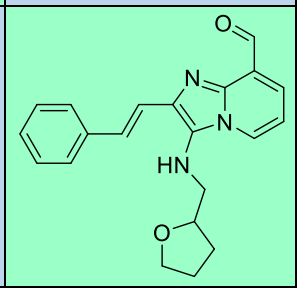
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |
| 19 |  |  |  |  |

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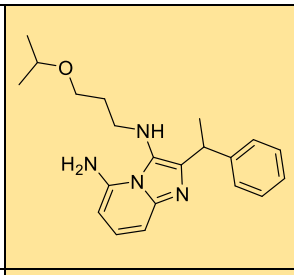
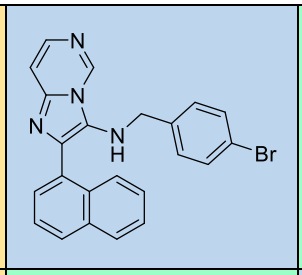
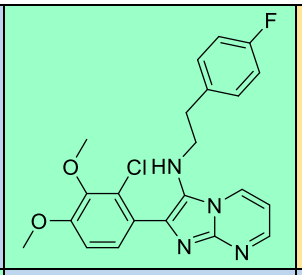
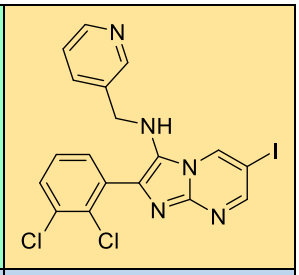
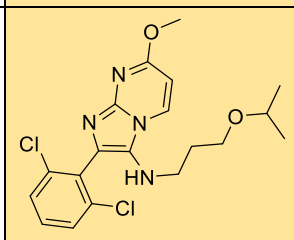
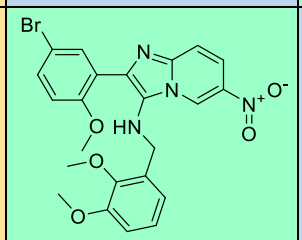
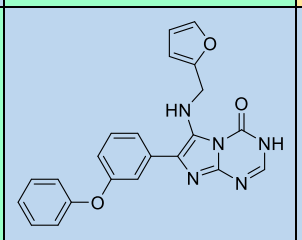
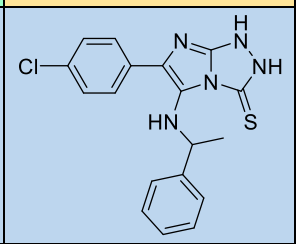
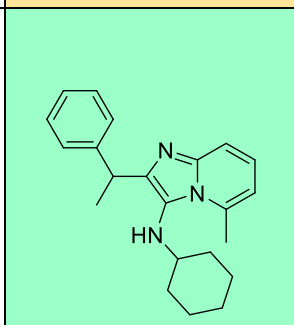
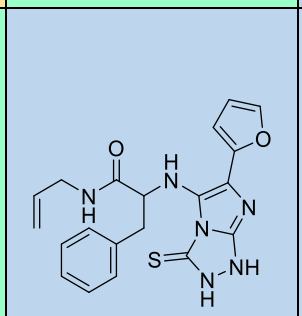
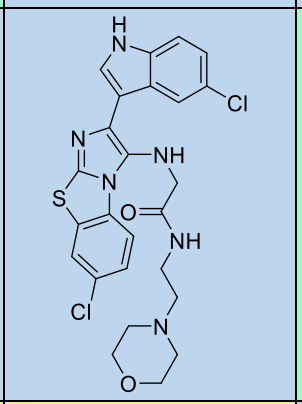
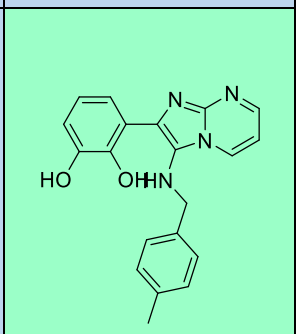
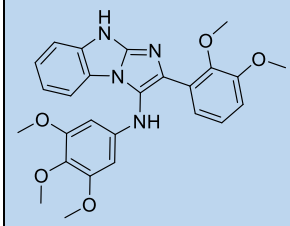
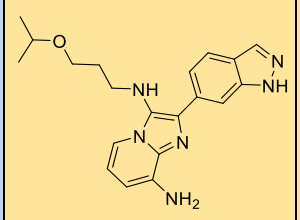
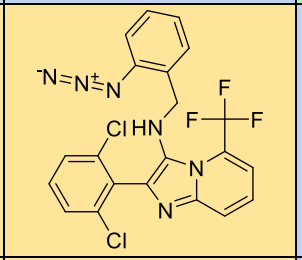
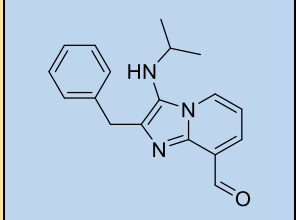
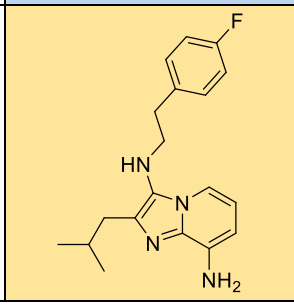
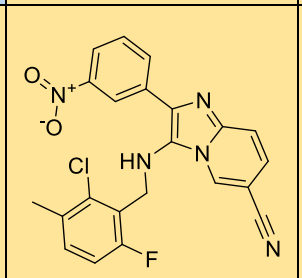
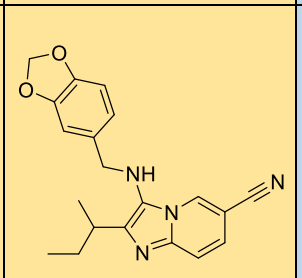
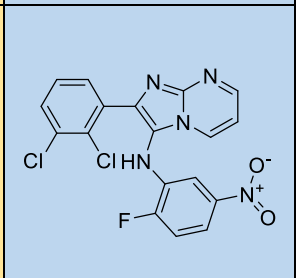
| **20** |  |  |  |  |
| **21** |  |  |  |  |
| **22** |  |  |  |  |
| **23** |  |  |  |  |
| **24** |  |  |  |  |

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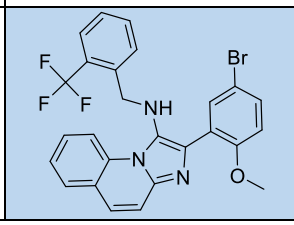
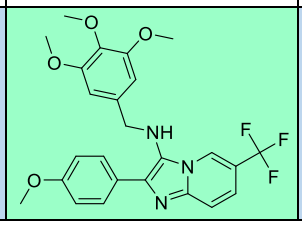
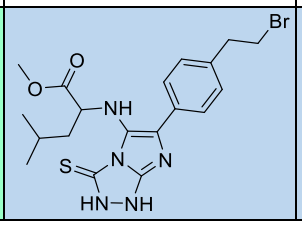
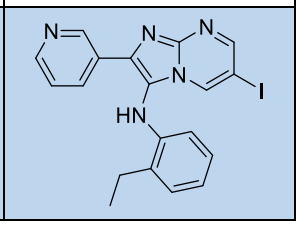
| **1** |  |  |  |  |

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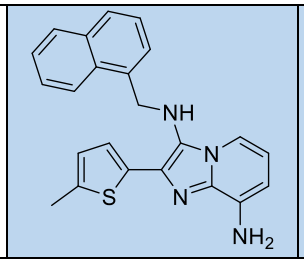
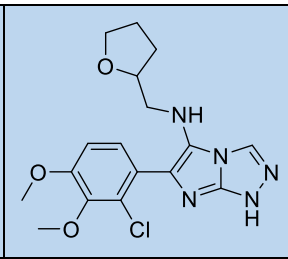
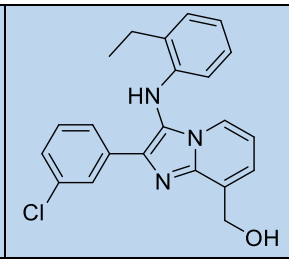
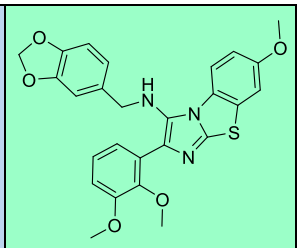
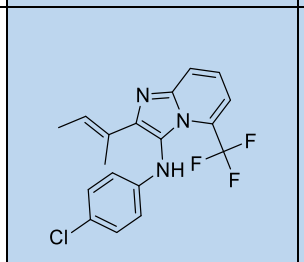
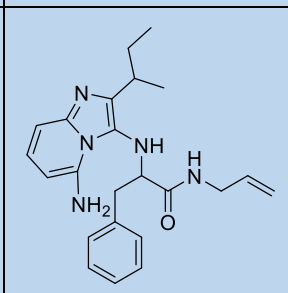
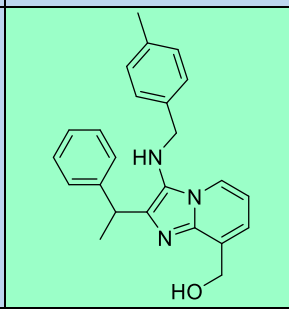
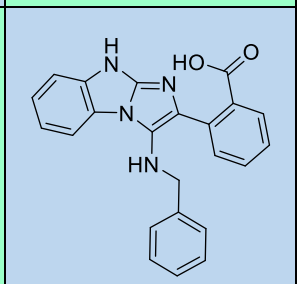
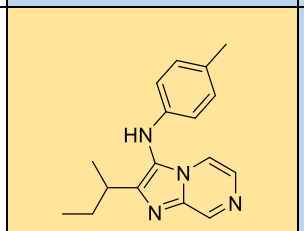
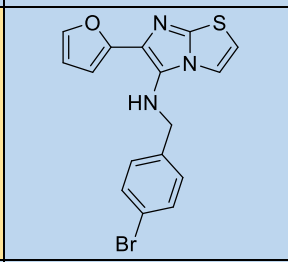
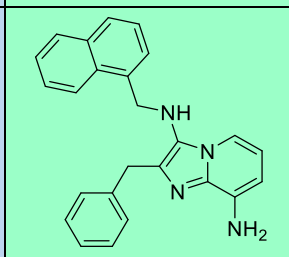
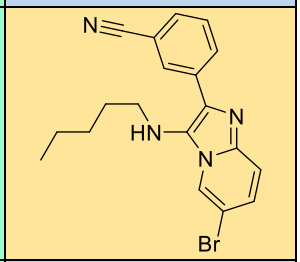
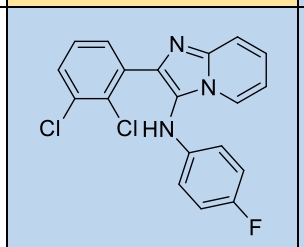
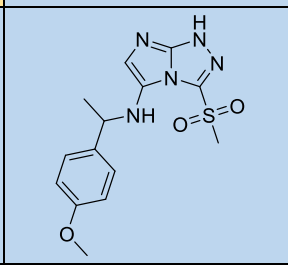
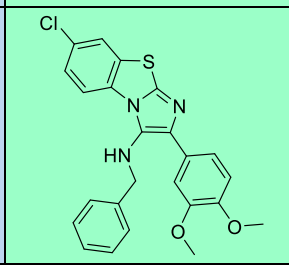
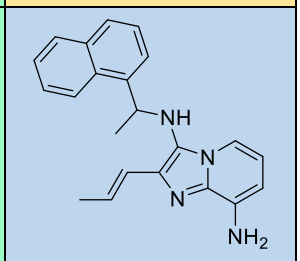
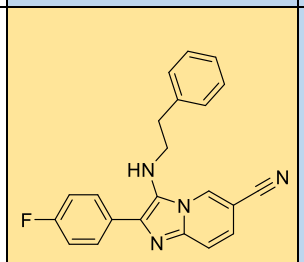
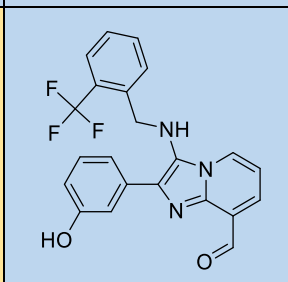
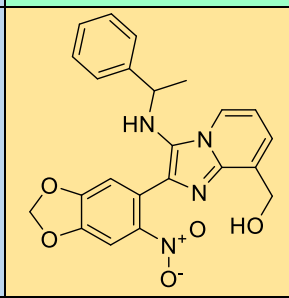
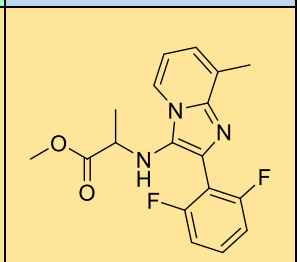
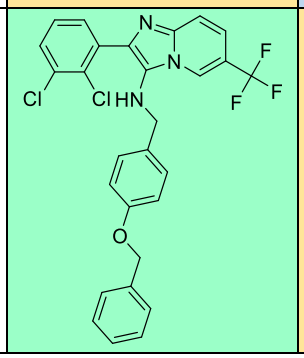
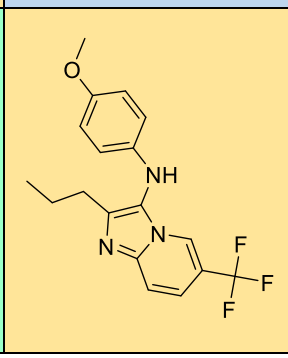
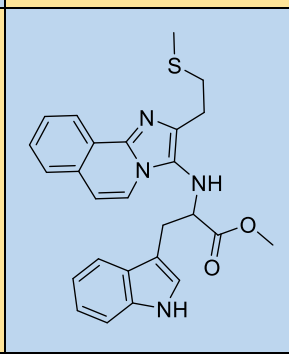
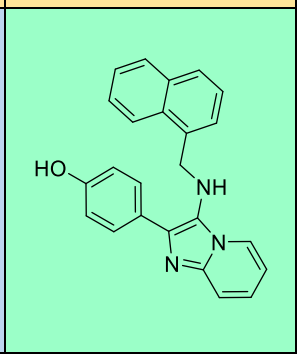
| **2** |  |  |  |  |
| **3** |  |  |  |  |
| **4** |  |  |  |  |
| **5** |  |  |  |  |
| **6** |  |  |  |  |
| **7** |  |  |  |  |

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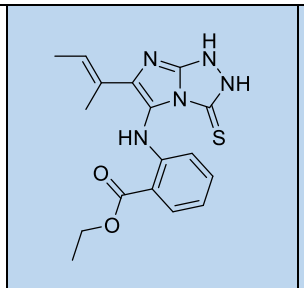
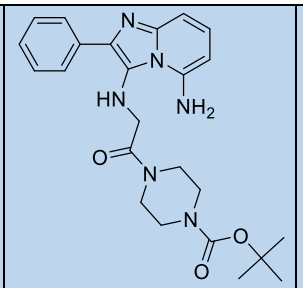
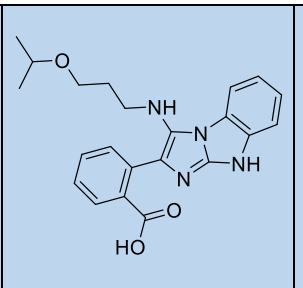
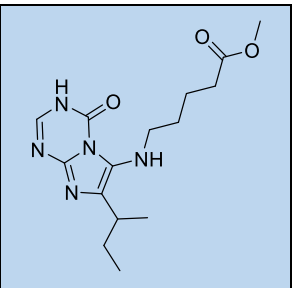
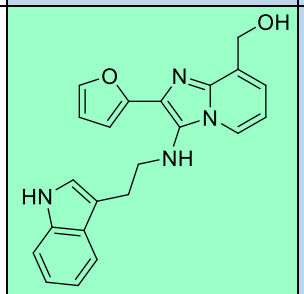
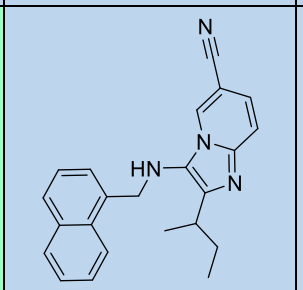
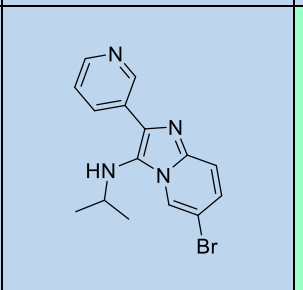
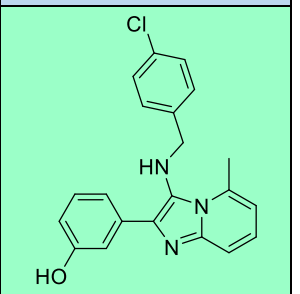
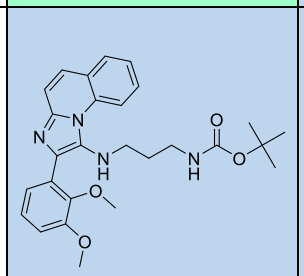
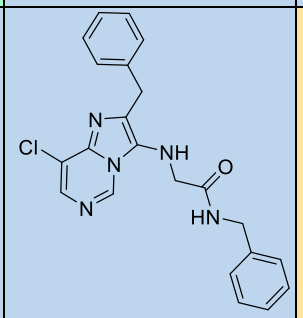
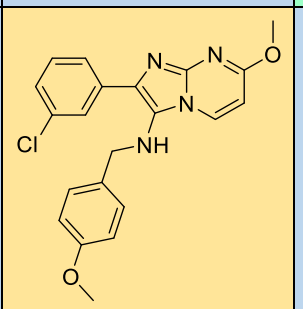
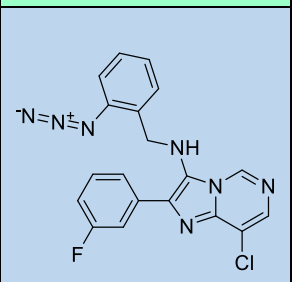
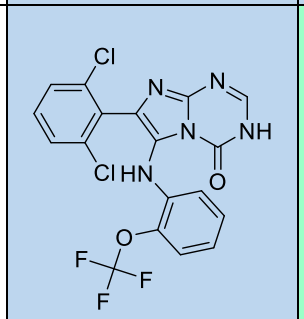
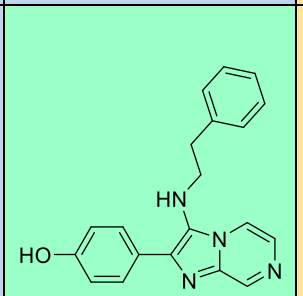
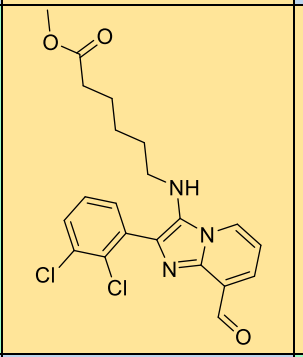
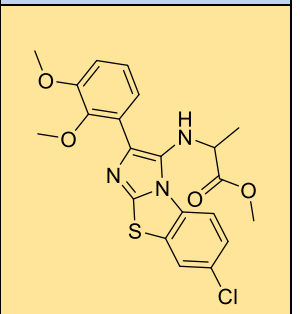
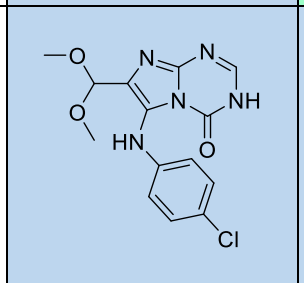
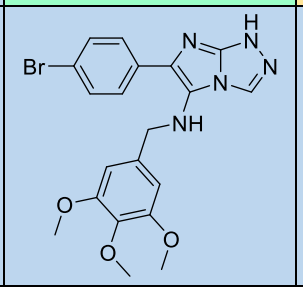
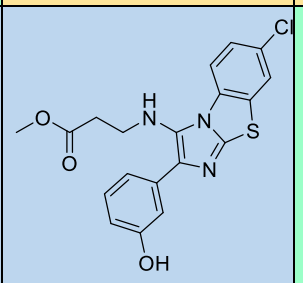
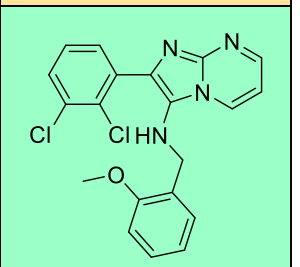
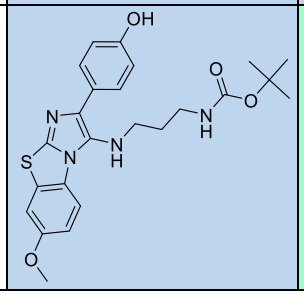
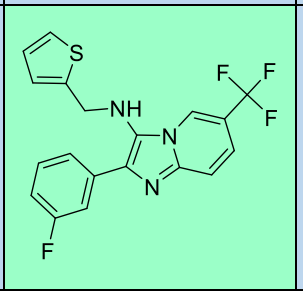
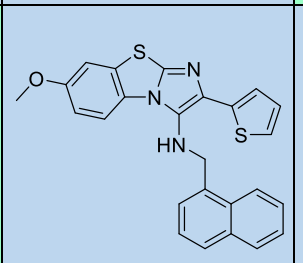
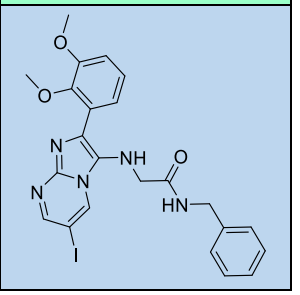
| **8** |  |  |  |  |
| **9** |  |  |  |  |
| **10** |  |  |  |  |
| **11** |  |  |  |  |
| **12** |  |  |  |  |
| **13** |  |  |  |  |

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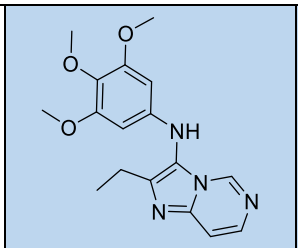
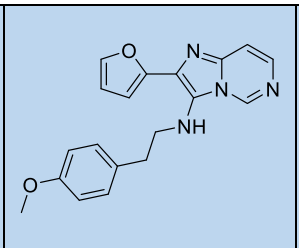
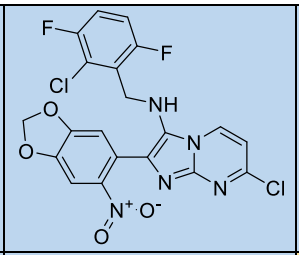
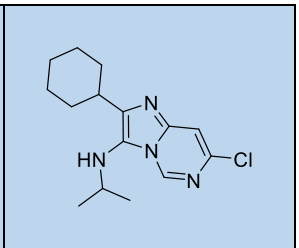
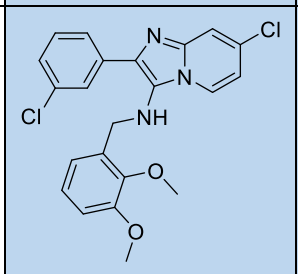
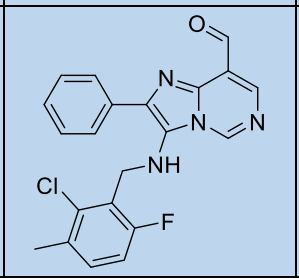
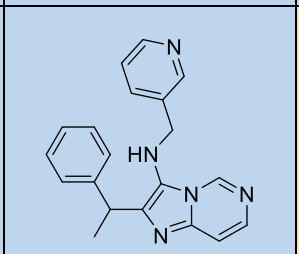
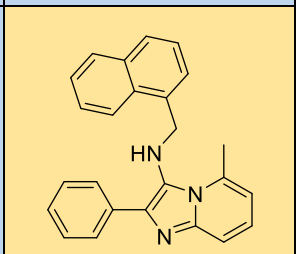
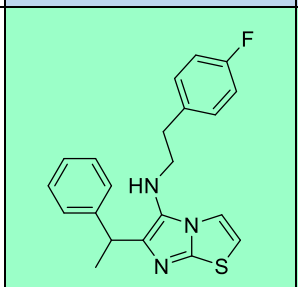
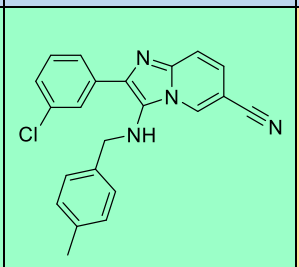
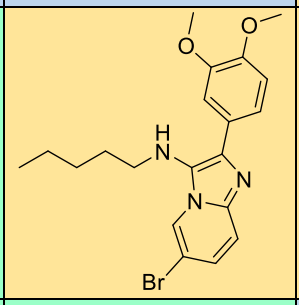
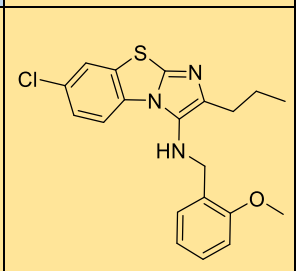
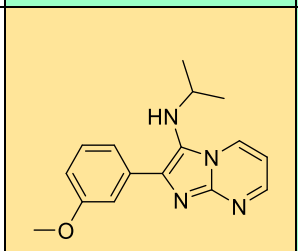
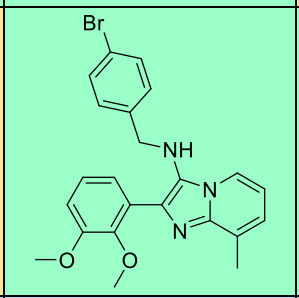
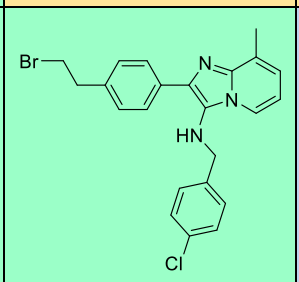
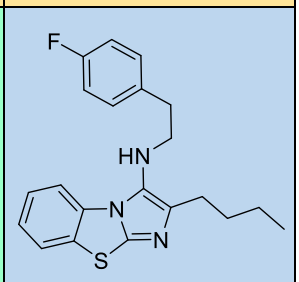
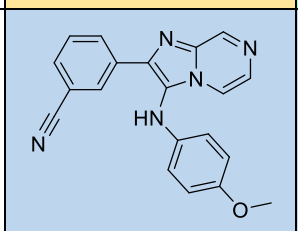
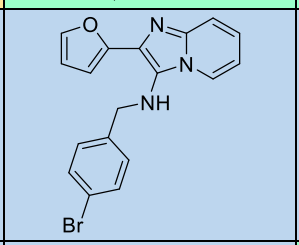
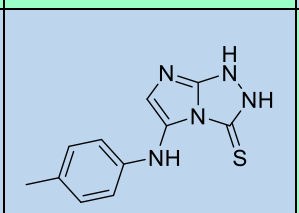
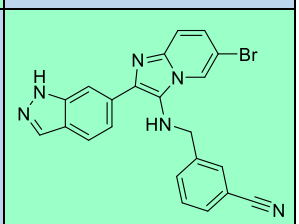
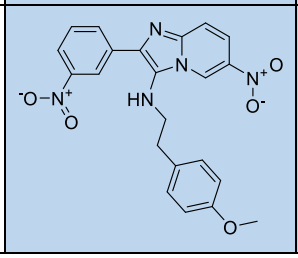
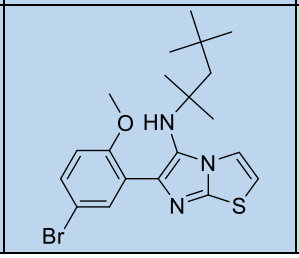
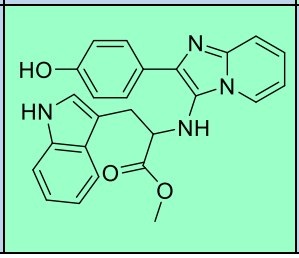
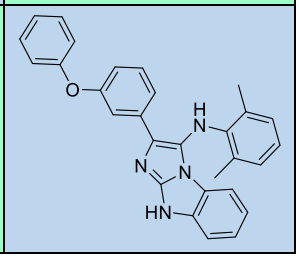
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |
| 19 |  |  |  |  |

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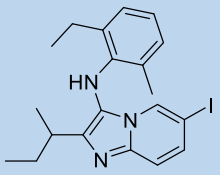
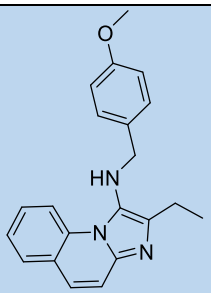
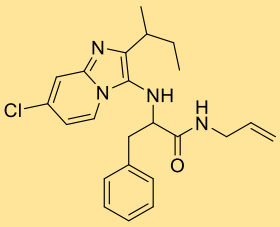
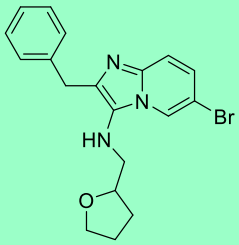
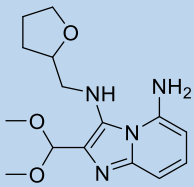
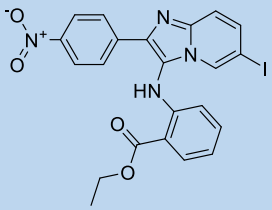
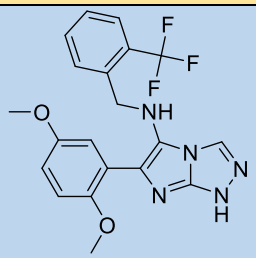
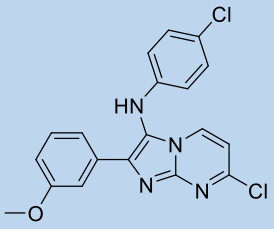
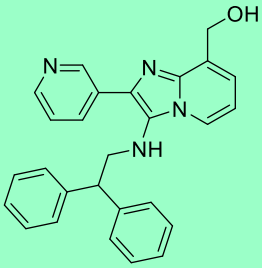
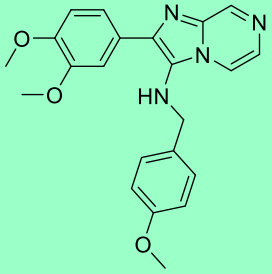
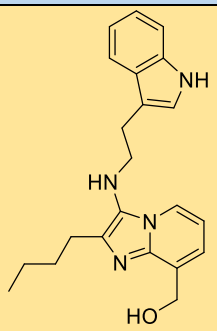
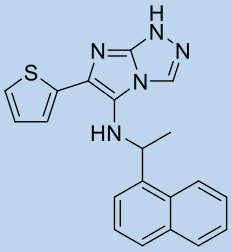
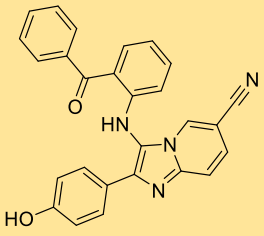
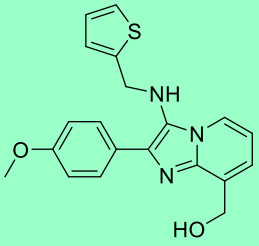
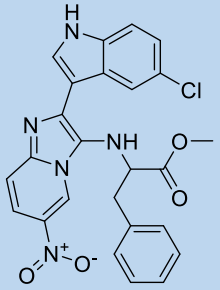
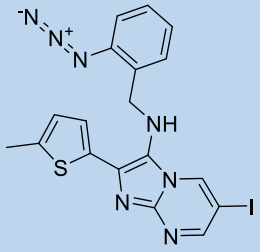
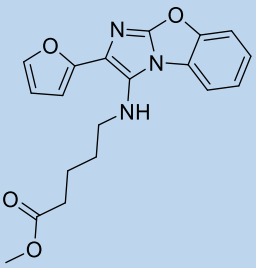
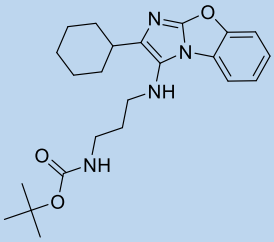
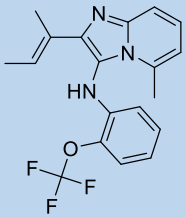
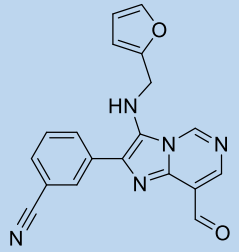
| 20 |  |  |  |  |
| 21 |  |  |  |  |
| 22 |  |  |  |  |
| 23 |  |  |  |  |
| 24 |  |  |  |  |

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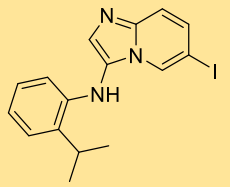
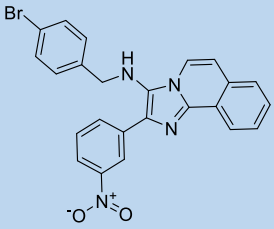
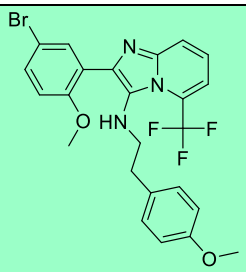
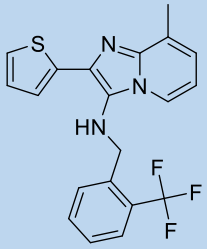
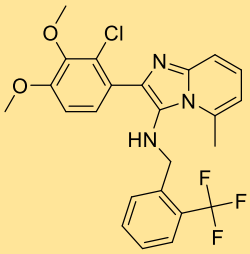
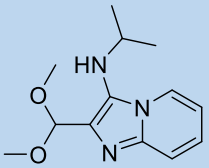
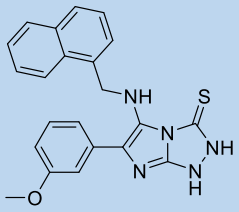
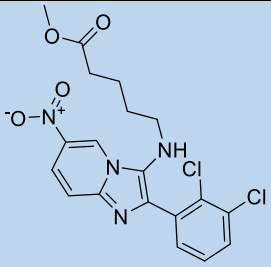
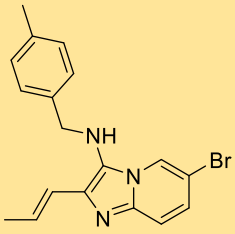
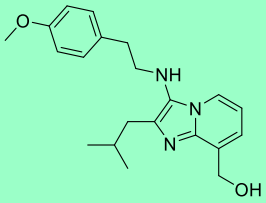
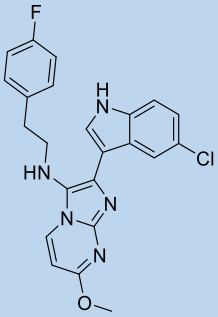
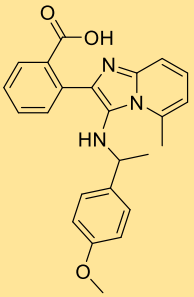
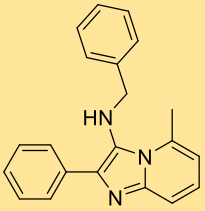
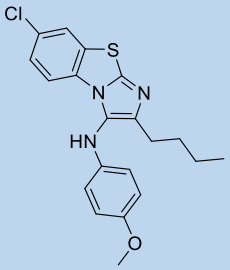
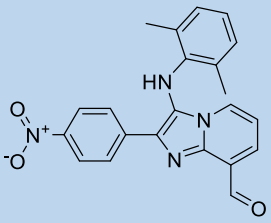
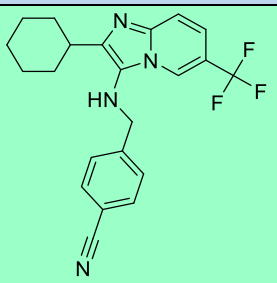
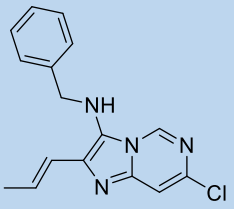
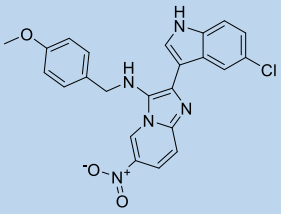
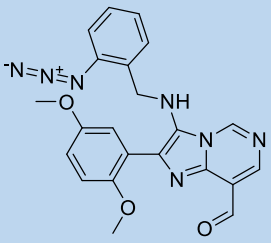
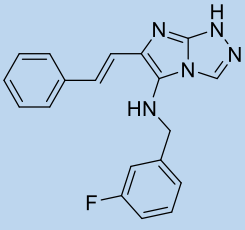
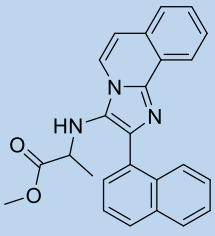
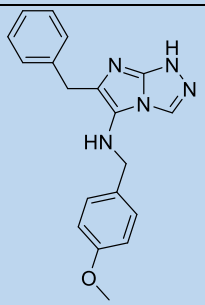
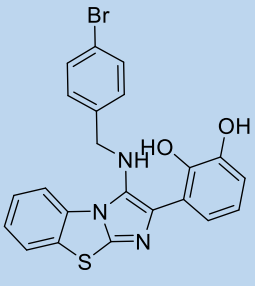
| 1 |  |  |  |  |
| 2 |  |  |  |  |
| 3 |  |  |  |  |
| 4 |  |  |  |  |
| 5 |  |  |  |  |
| 6 |  |  |  |  |

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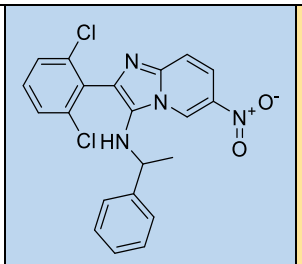
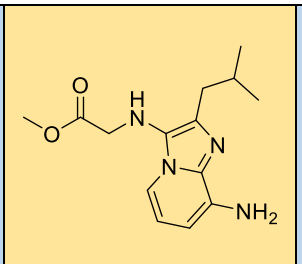
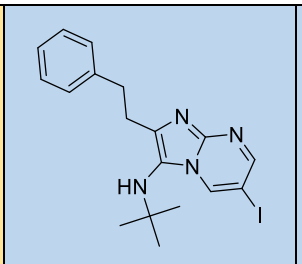
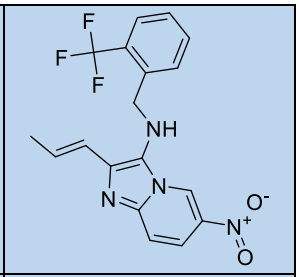
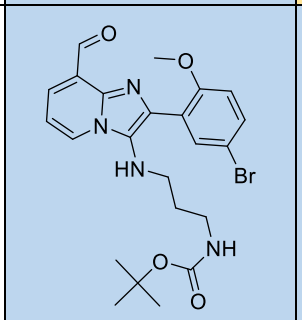
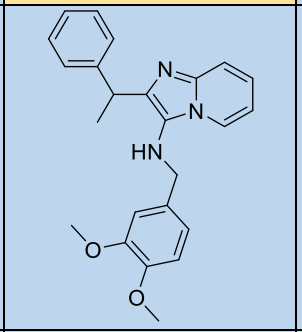
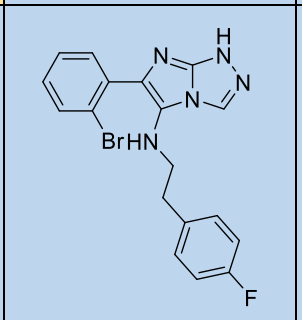
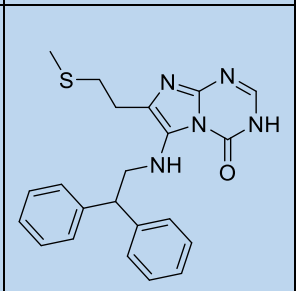
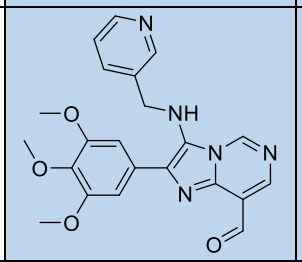
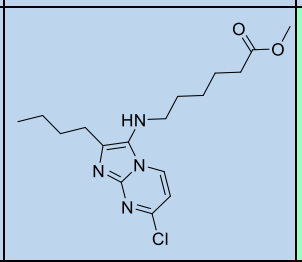
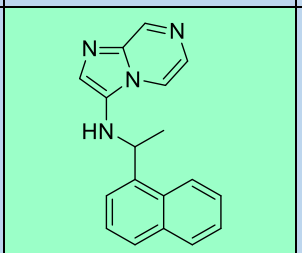
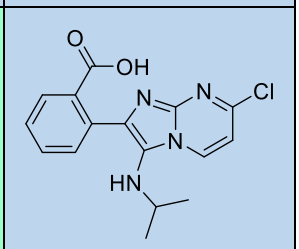
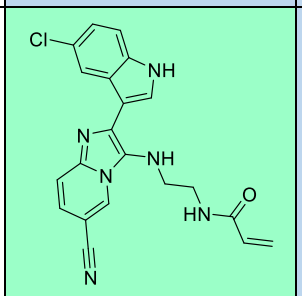
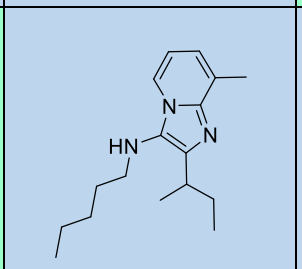
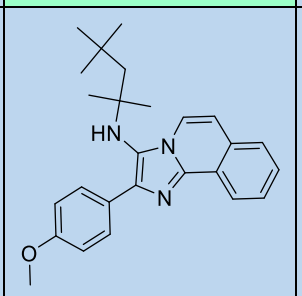
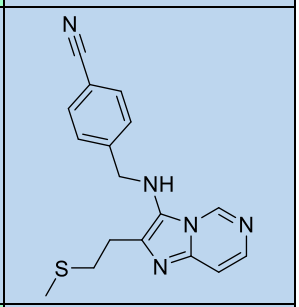
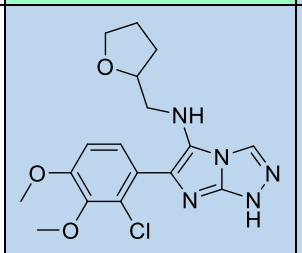
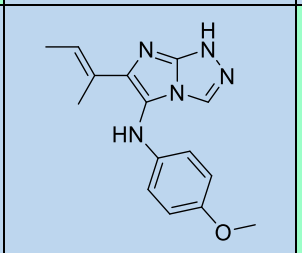
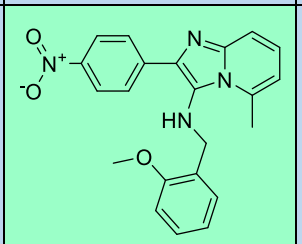
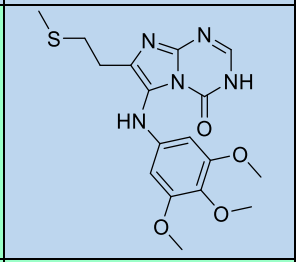
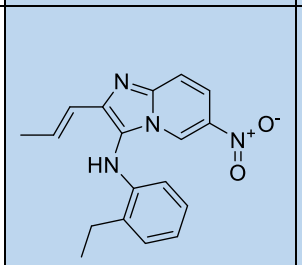
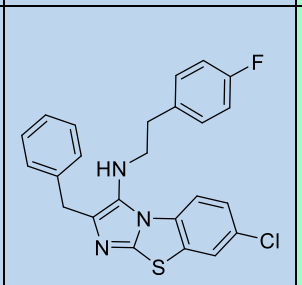
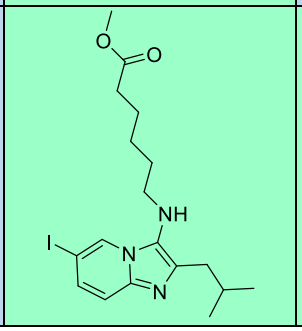
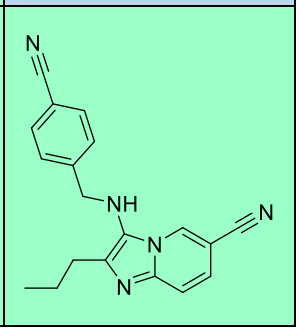
| **7** |  |  |  |  |
| **8** |  |  |  |  |
| **9** |  |  |  |  |
| **10** |  |  |  |  |
| **11** |  |  |  |  |
| **12** |  |  |  |  |

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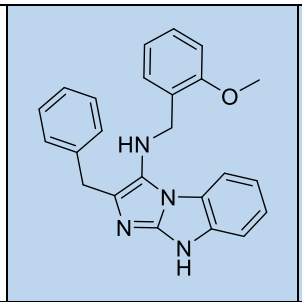
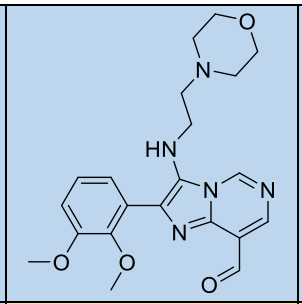
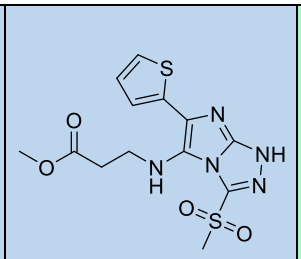
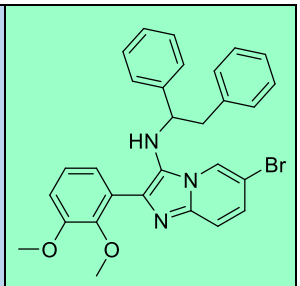
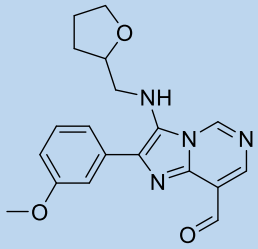
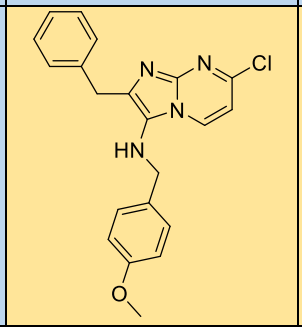
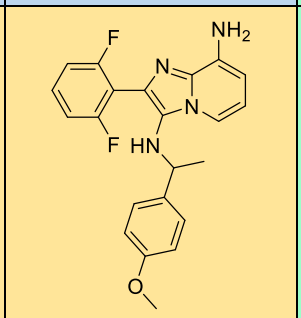
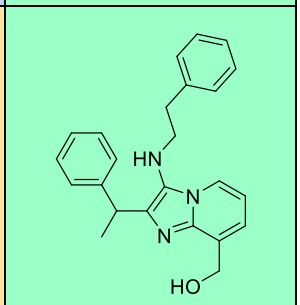
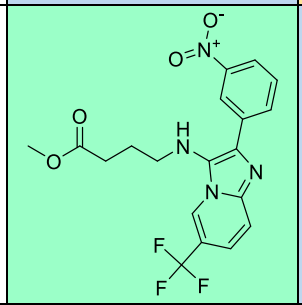
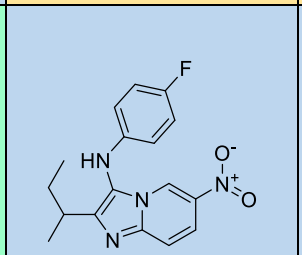
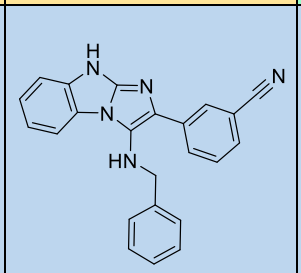
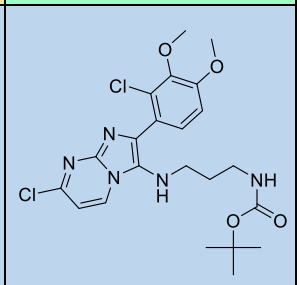
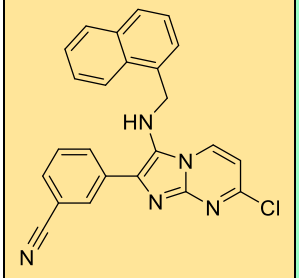
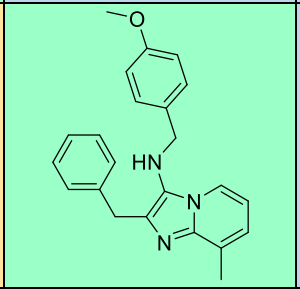
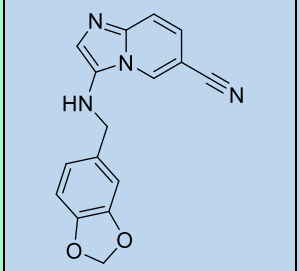
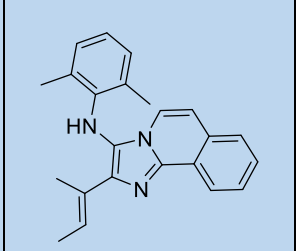
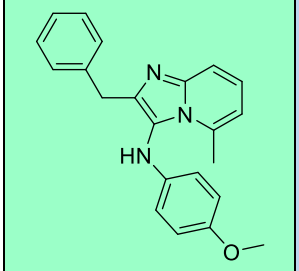
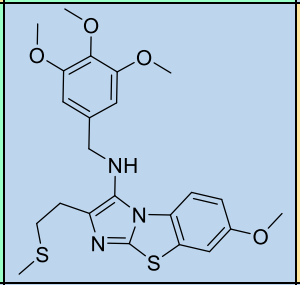
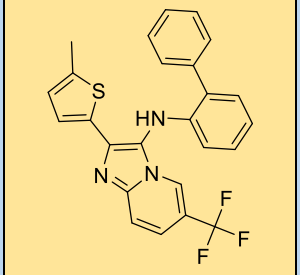
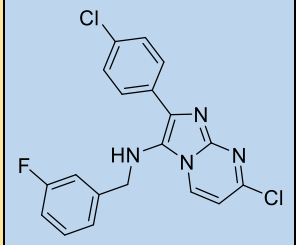
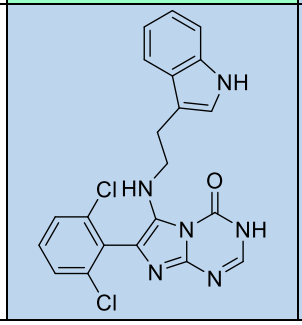
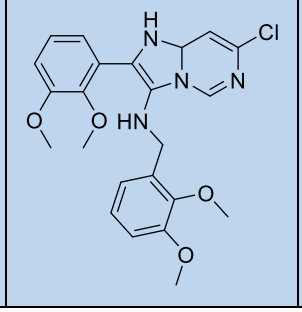
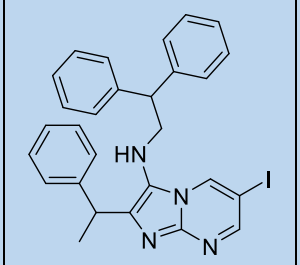
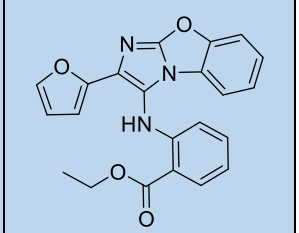
| 13 |  |  |  |  |
| 14 |  |  |  |  |
| 15 |  |  |  |  |
| 16 |  |  |  |  |
| 17 |  |  |  |  |
| 18 |  |  |  |  |

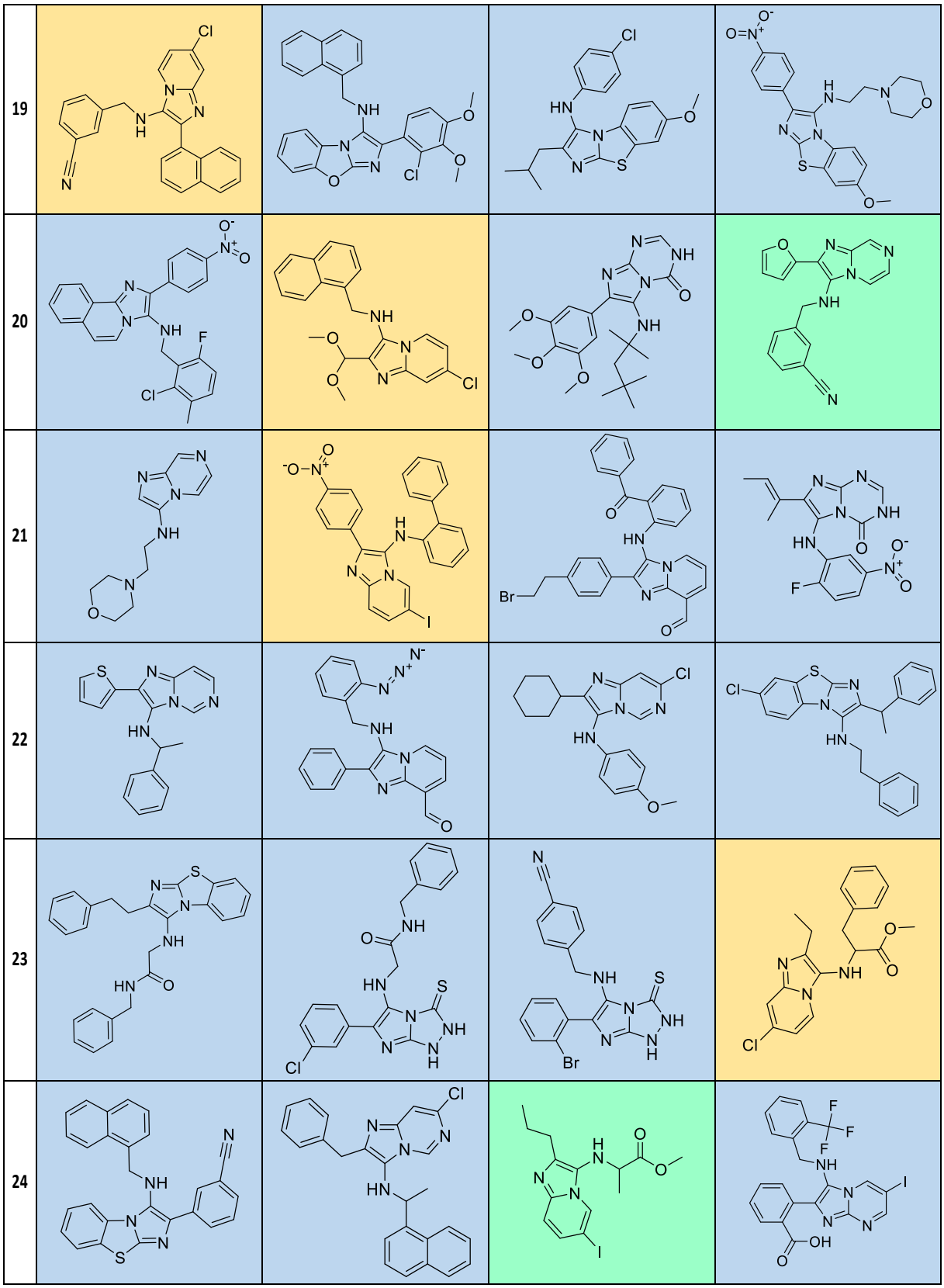



**Fig. S3.** Heat plots with product structures, green for major product formation □, yellow for medium product formation □ and blue for no product formation□ .

## 2.4. Quality control (QC)

The analytics of all wells were performed by SFC-UV-MS. Mass spectra were measured on a Waters Investigator Supercritical Fluid Chromatograph with a 3100 MS Detector ($ESI^+$) via flow injection analysis (FIA) and MassLynx software.

Conditions: eluent composition: MeOH, 2% $H_2O$, 0.1% formic acid; run time: 2 min; flow rate: 1 mL/min.

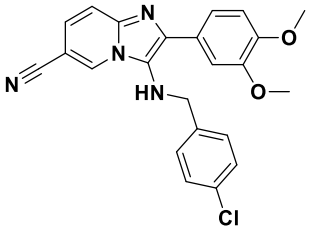
Each well of the destination plate was diluted with 100 µL ethylene glycol and then the chromatographic analysis was done by SFC-MS using an autosampler. A right-click and drag operation of the total ion current (TIC) spectrum generated a mass chromatogram for the selected range. If the peak corresponding to M+H or M+Na or M+K was the major peak, the well received a green designation and otherwise yellow. If the peak of M+H or M+Na or M+K was absent, the well received a blue designation.

The SFC analytic of one well took ~2 min, resulting in an overall measuring time for the 1536 wells of around 52 h.

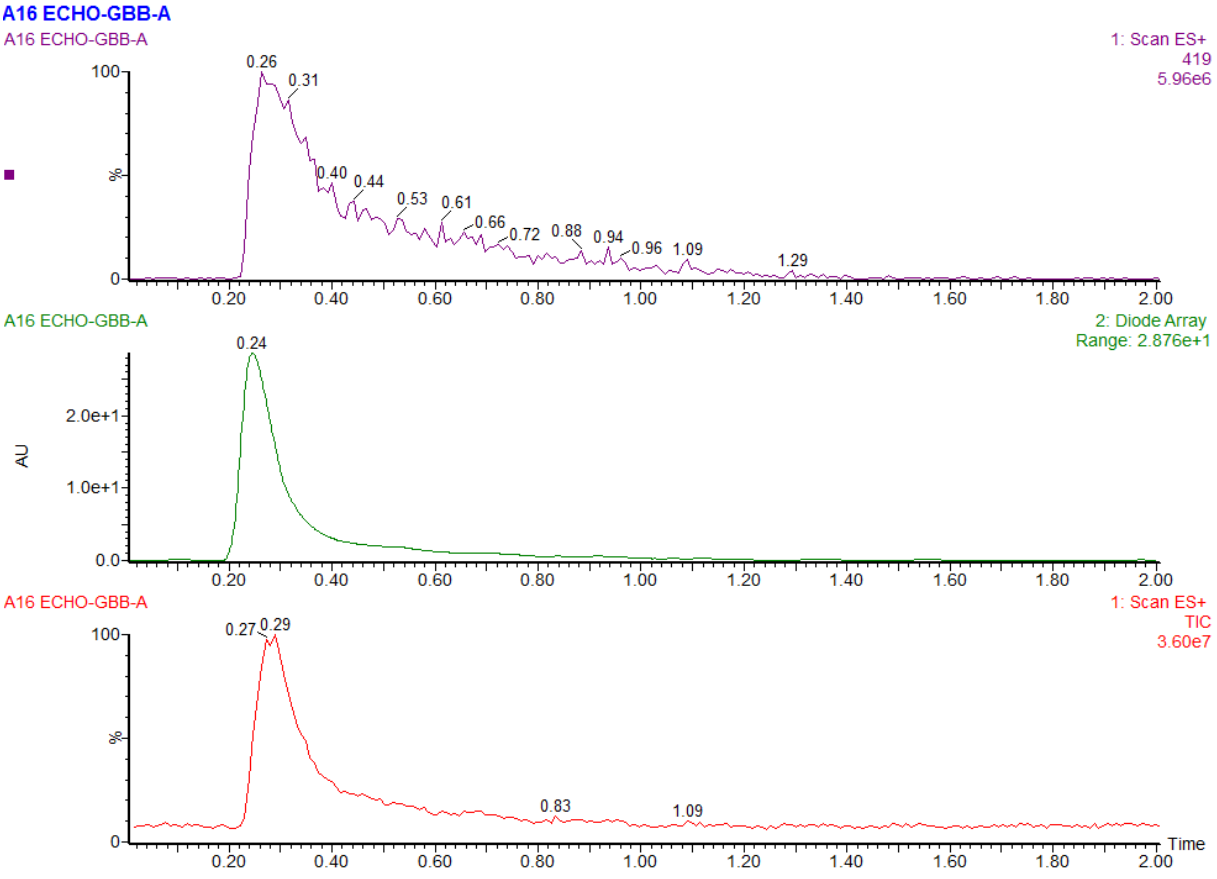
## Examples of SFC-MS analytics directly out of 384-well plate

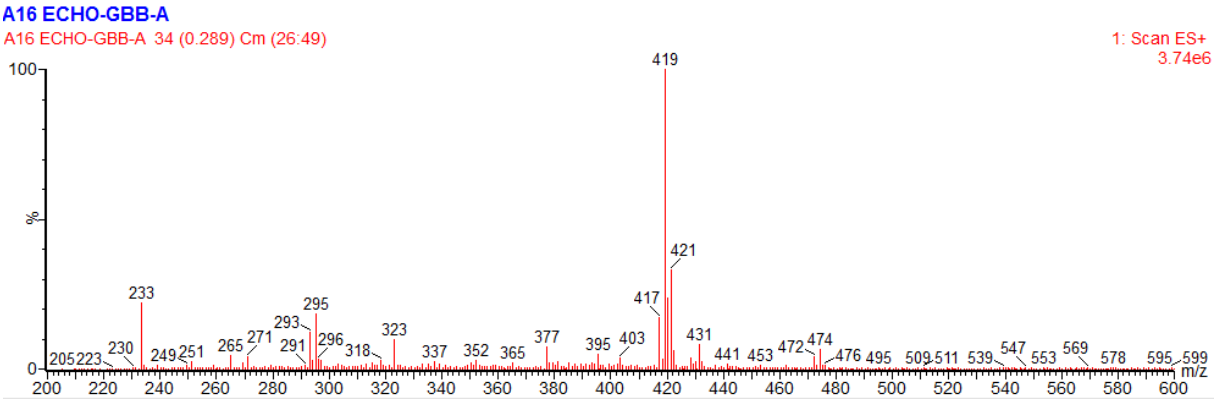
**Destination plate I**

**A16 (Green)**

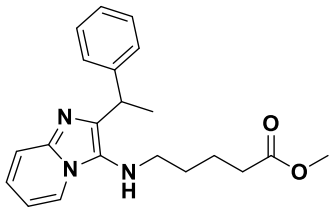



**Exact Mass: 418,12**



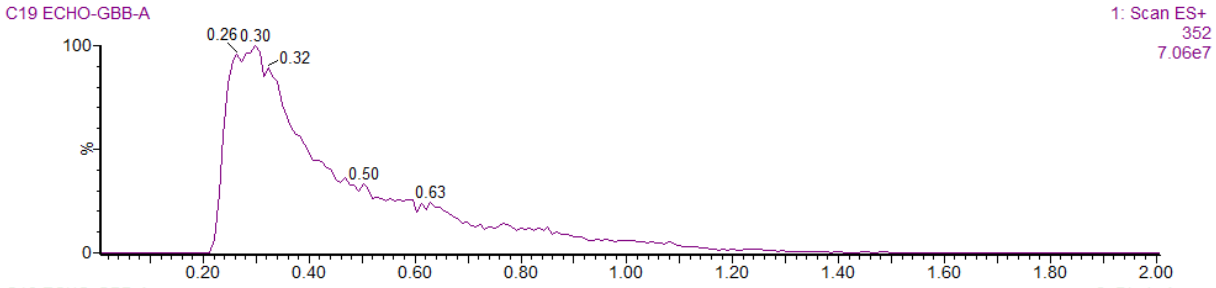



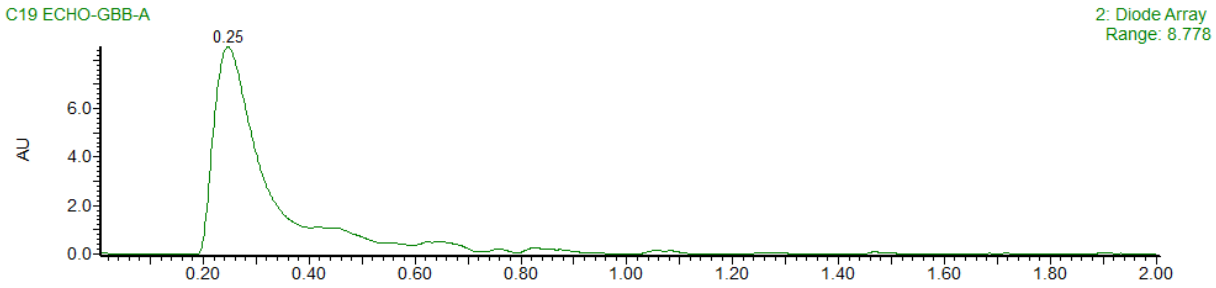
## C19 (Green)

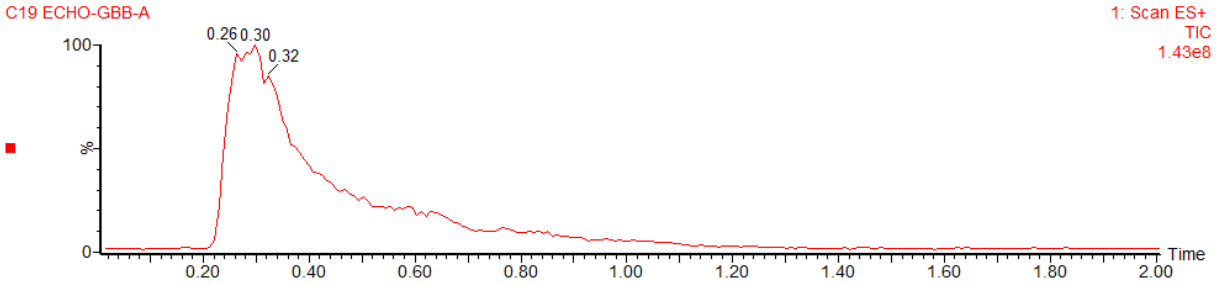



**Exact Mass: 351,19**

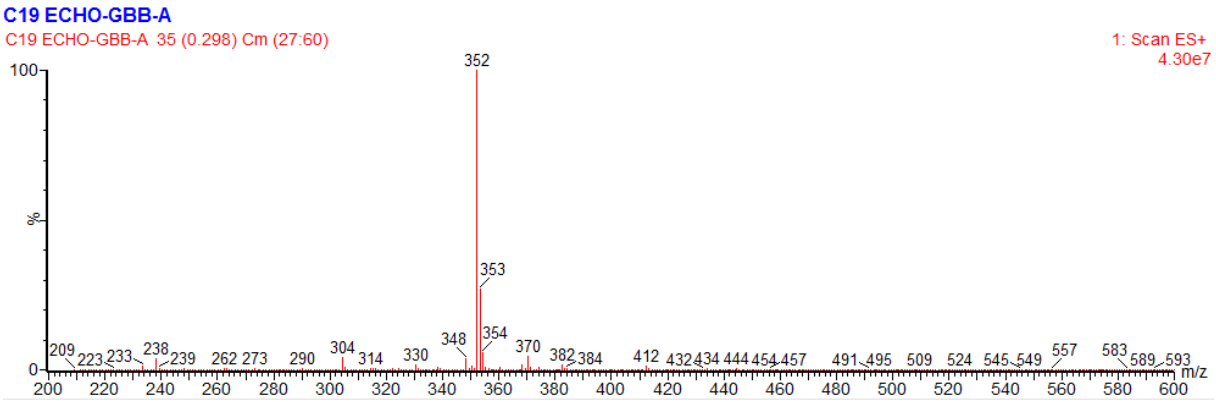
**C19 ECHO-GBB-A**



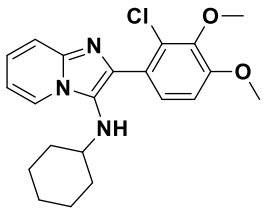



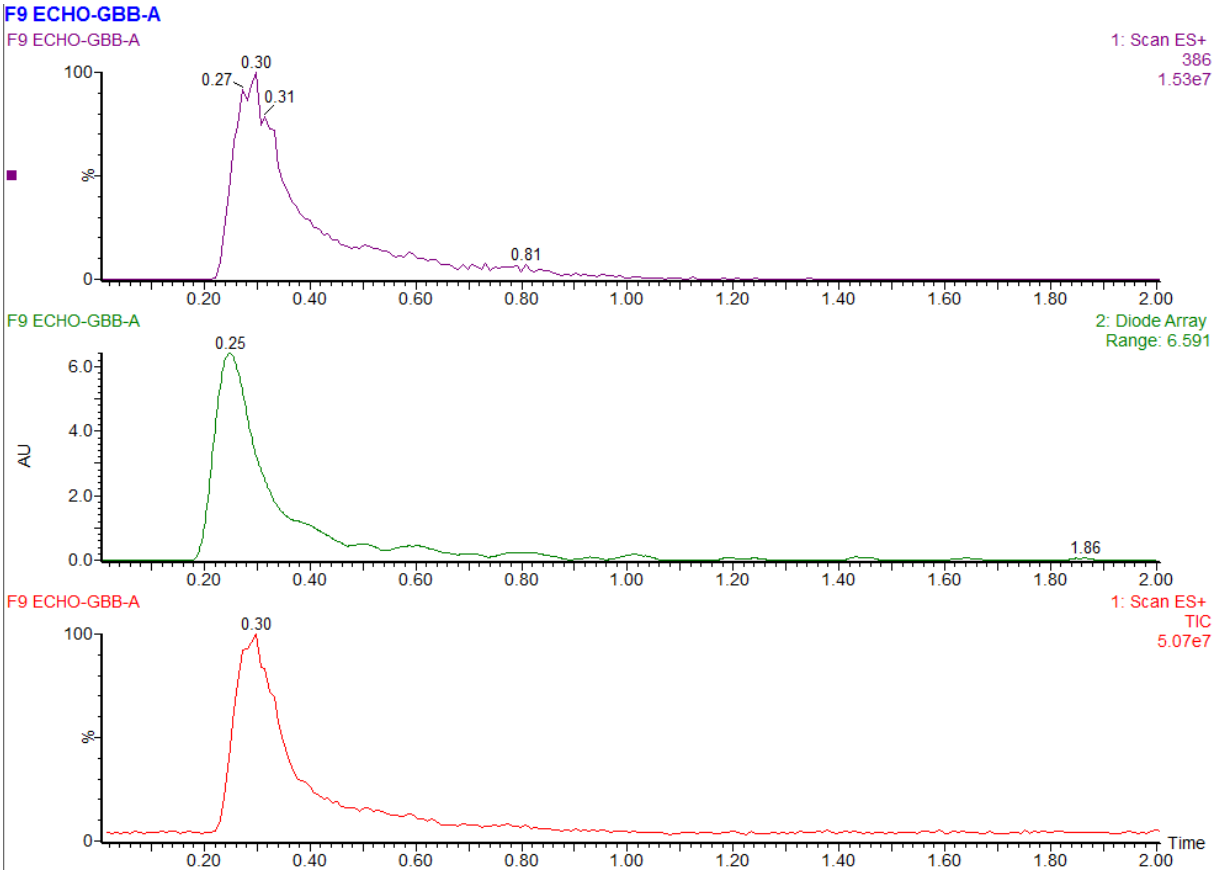

**C19 ECHO-GBB-A**

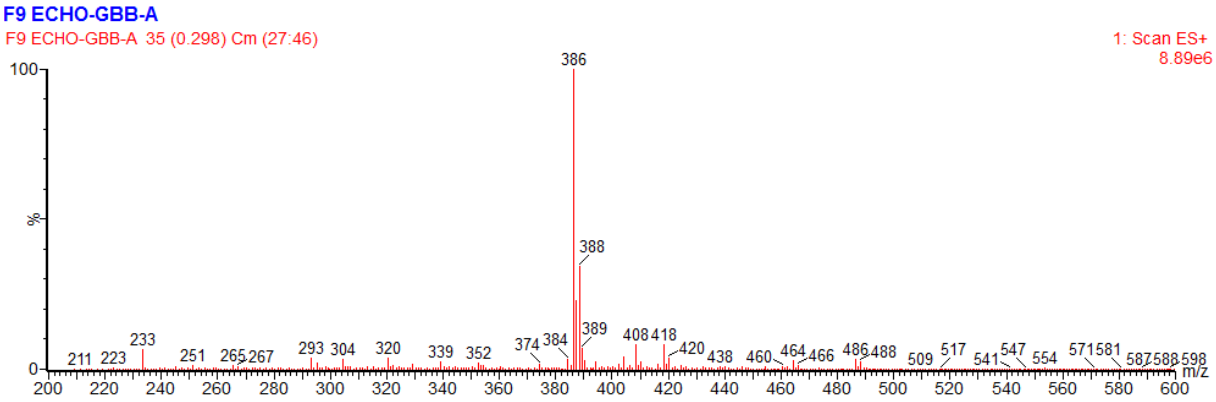


**F9 (Green)**

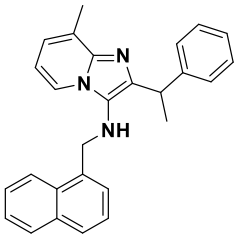



**Exact Mass: 385,16**

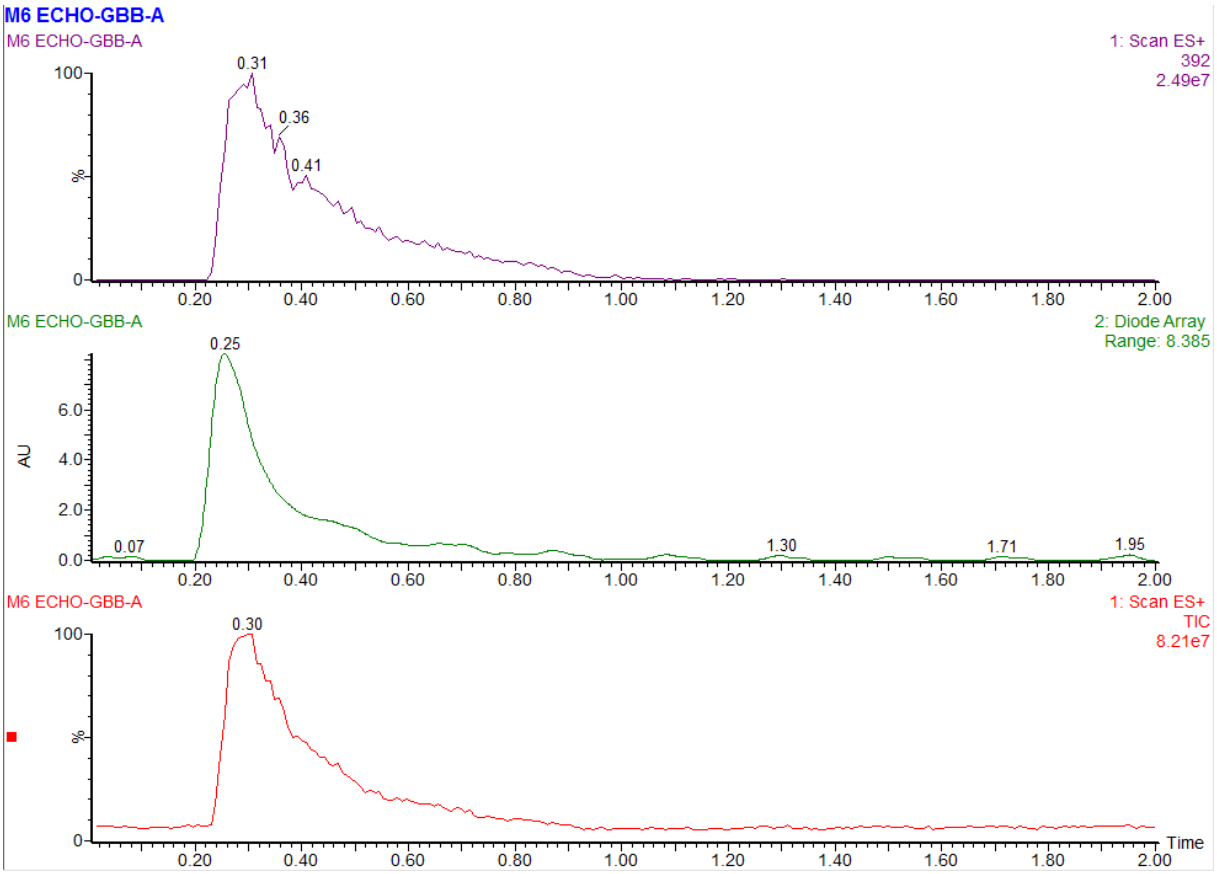


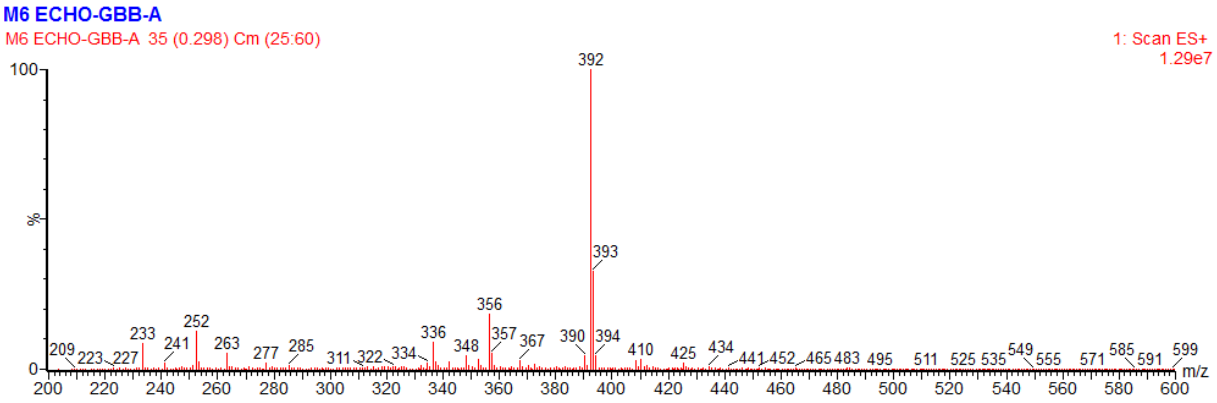



**M6 (Green)**

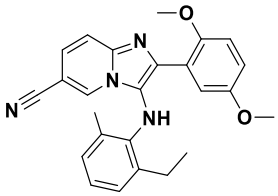



**Exact Mass: 391,20**

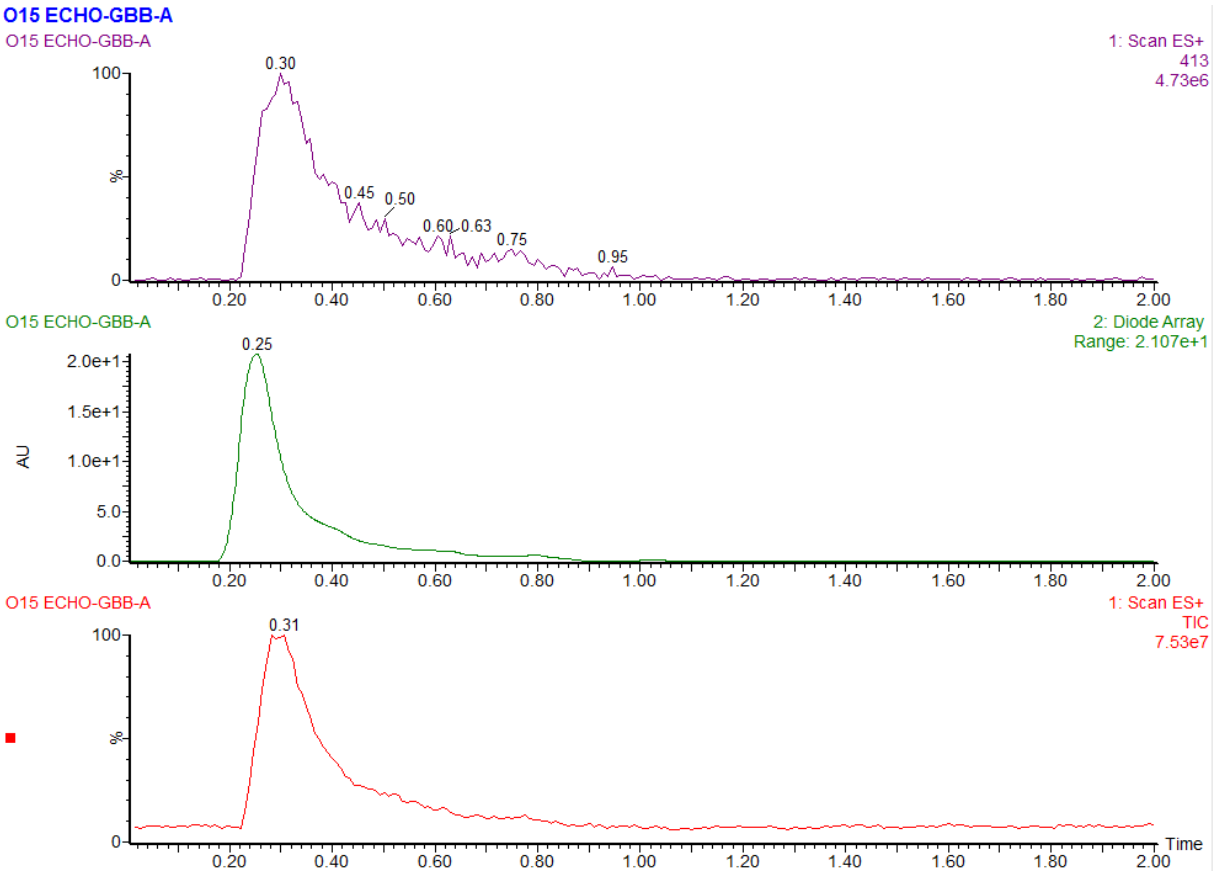


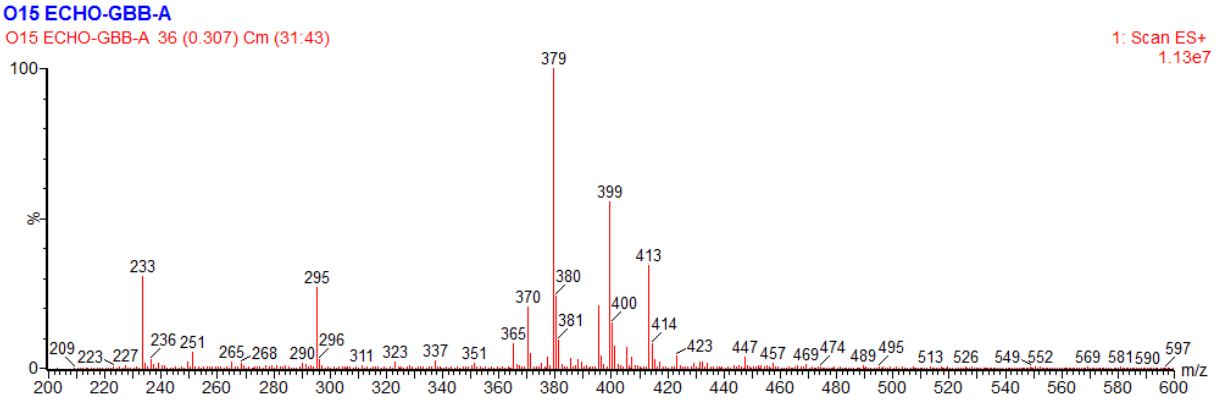



## O15 (Yellow)



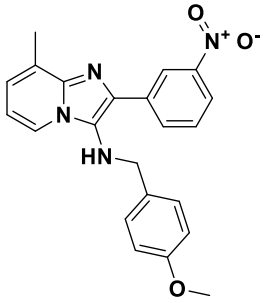
**Exact Mass: 412,19**



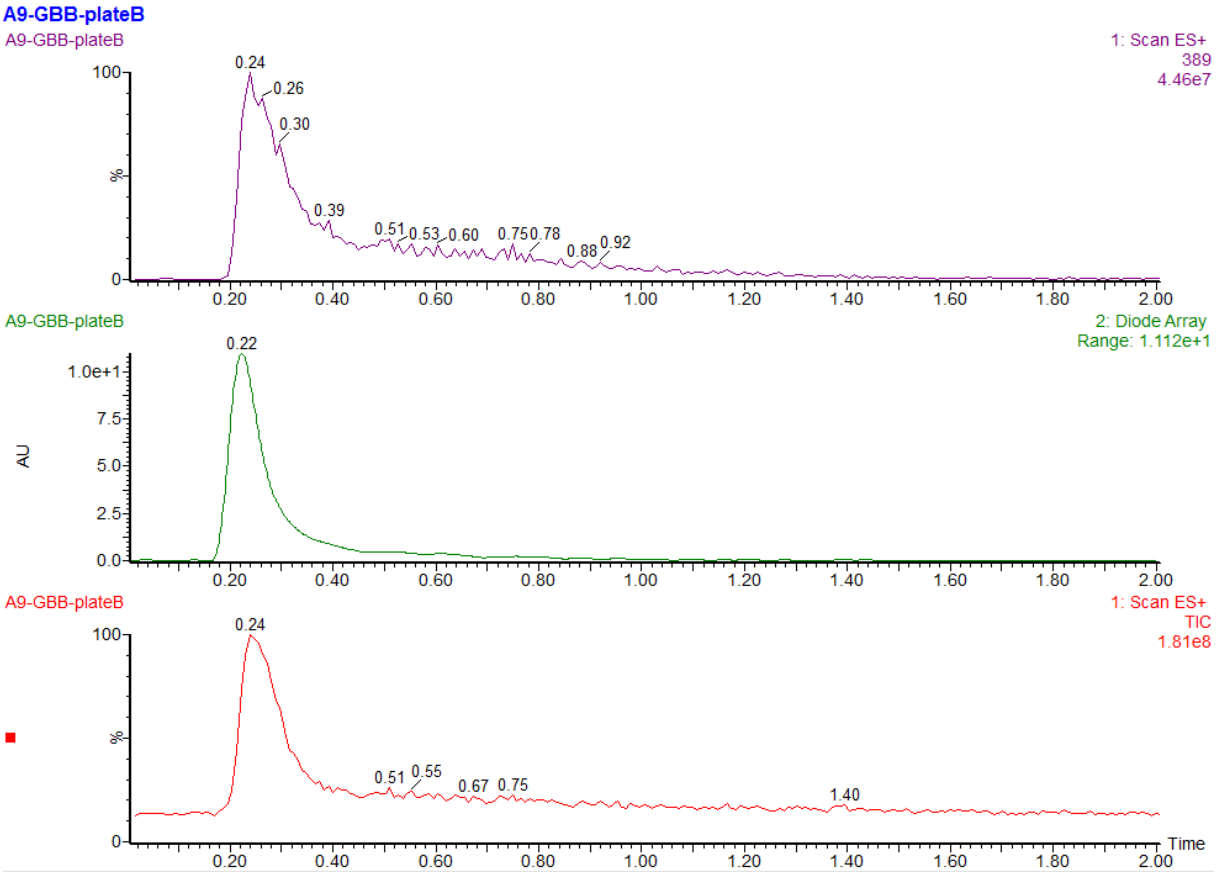



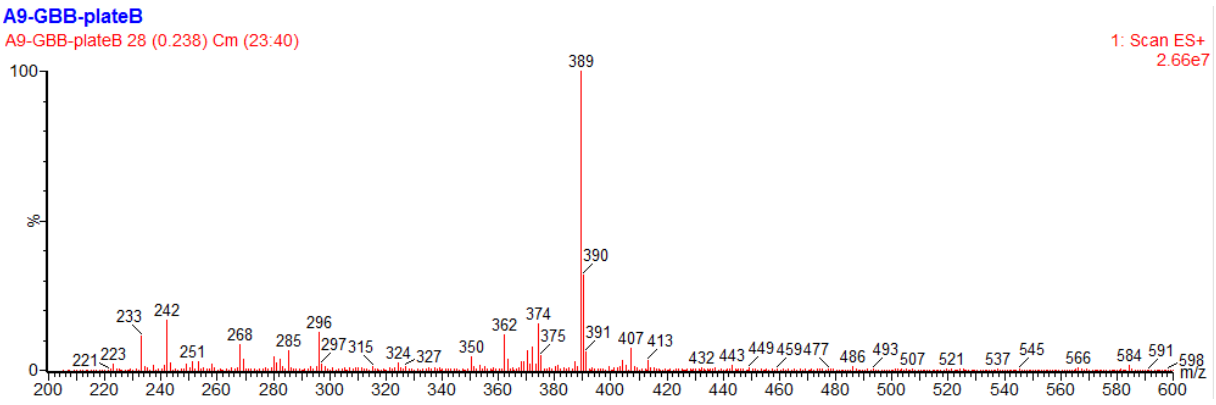
**Destination plate II**

**A9 (Green)**

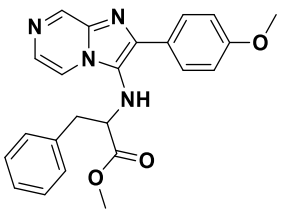



**Exact Mass: 388,15**

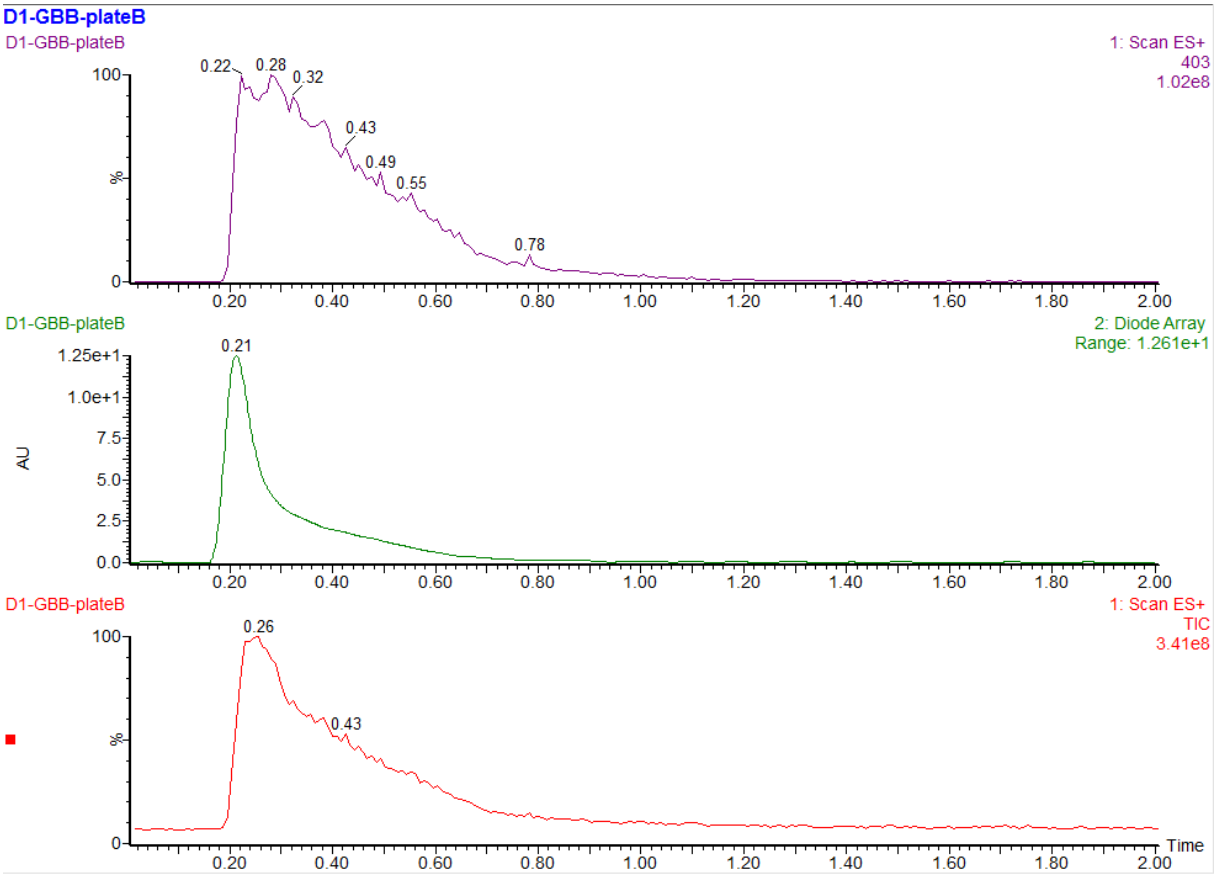


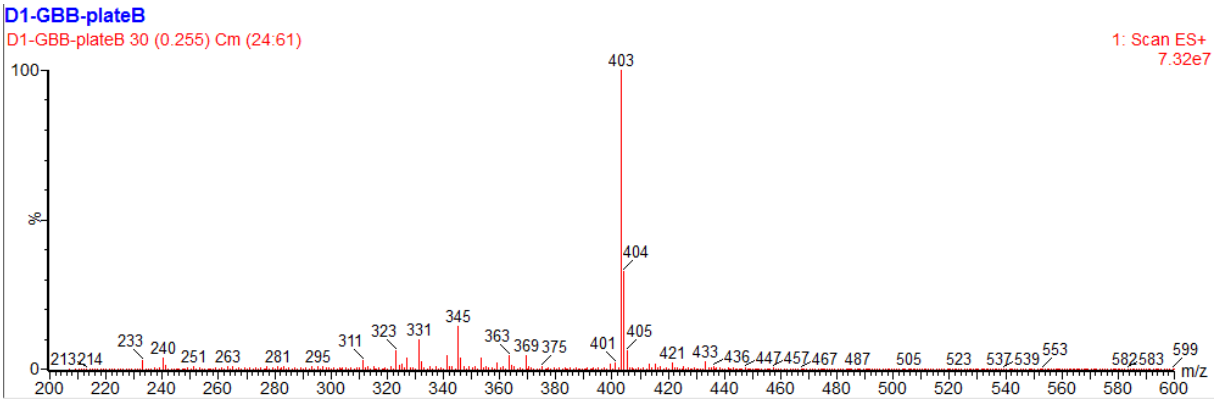



**D1 (Green)**

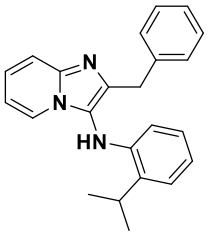



**Exact Mass: 402,17**

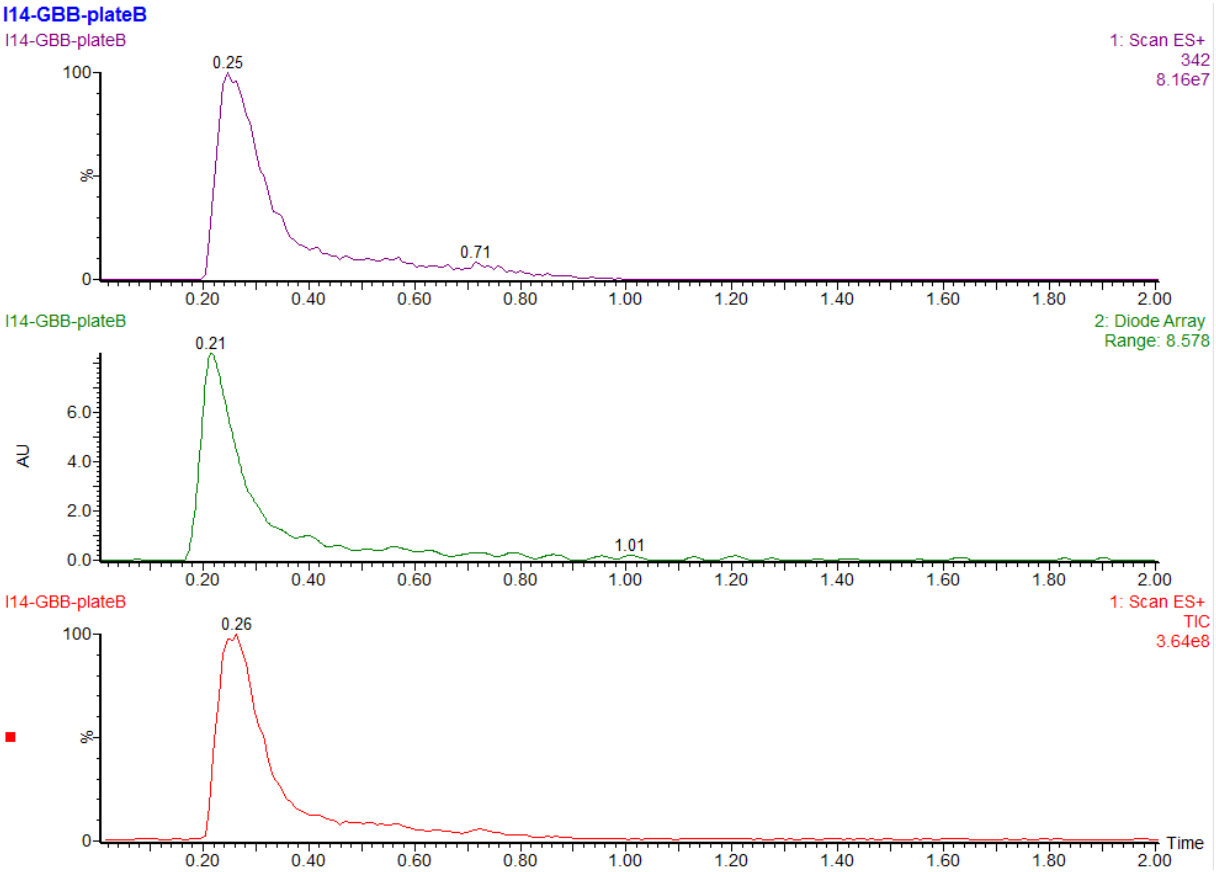


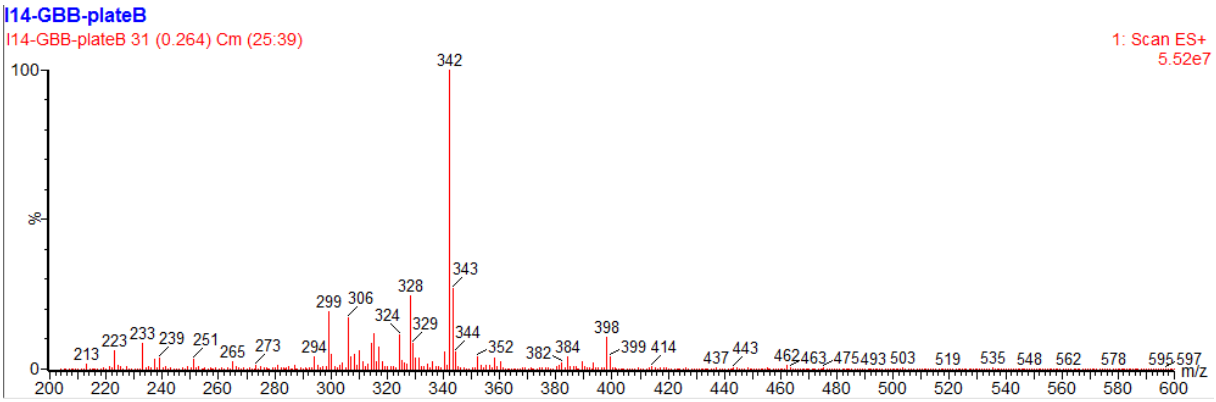



## I14 (Green)

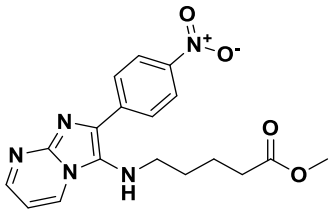



**Exact Mass: 341,19**

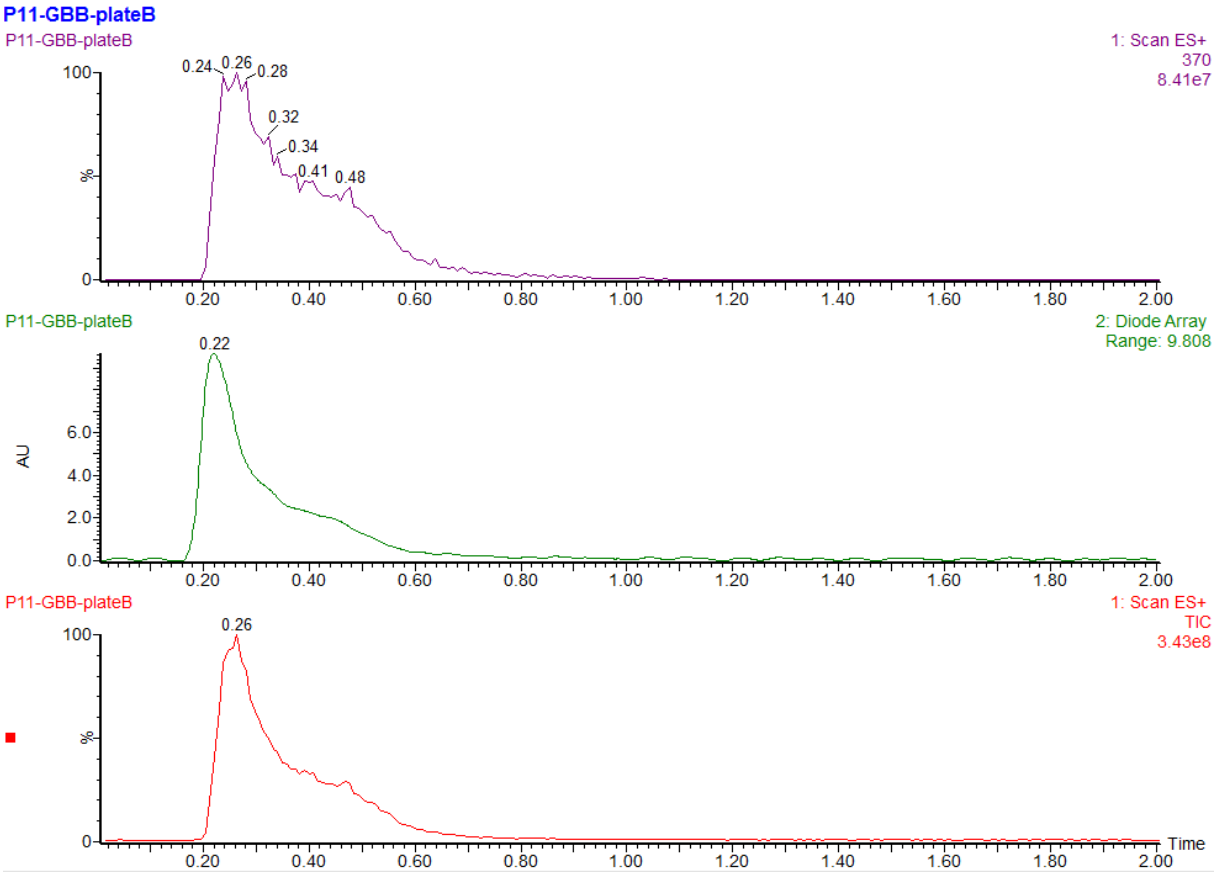


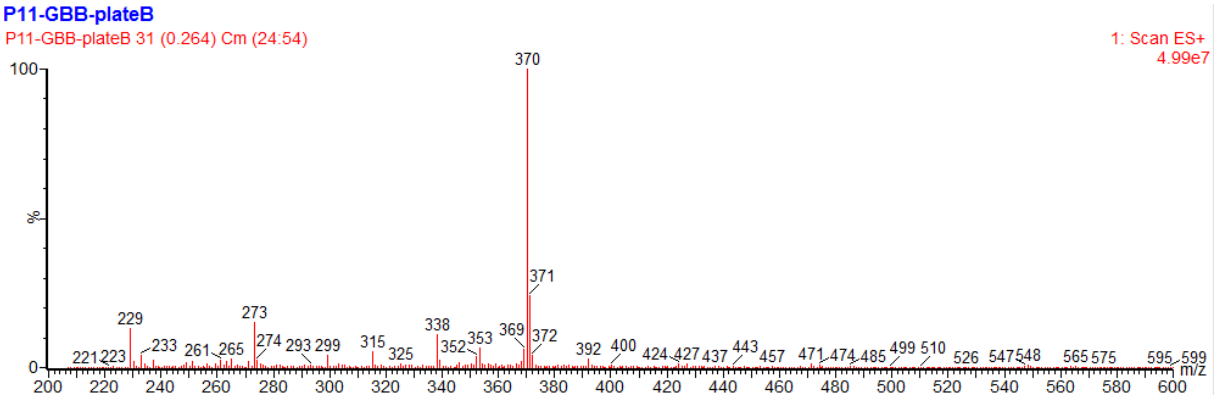



**P11 (Green)**

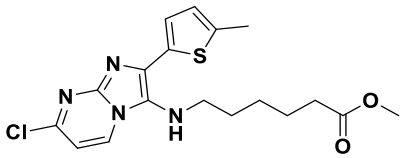


**Exact Mass: 369,14**

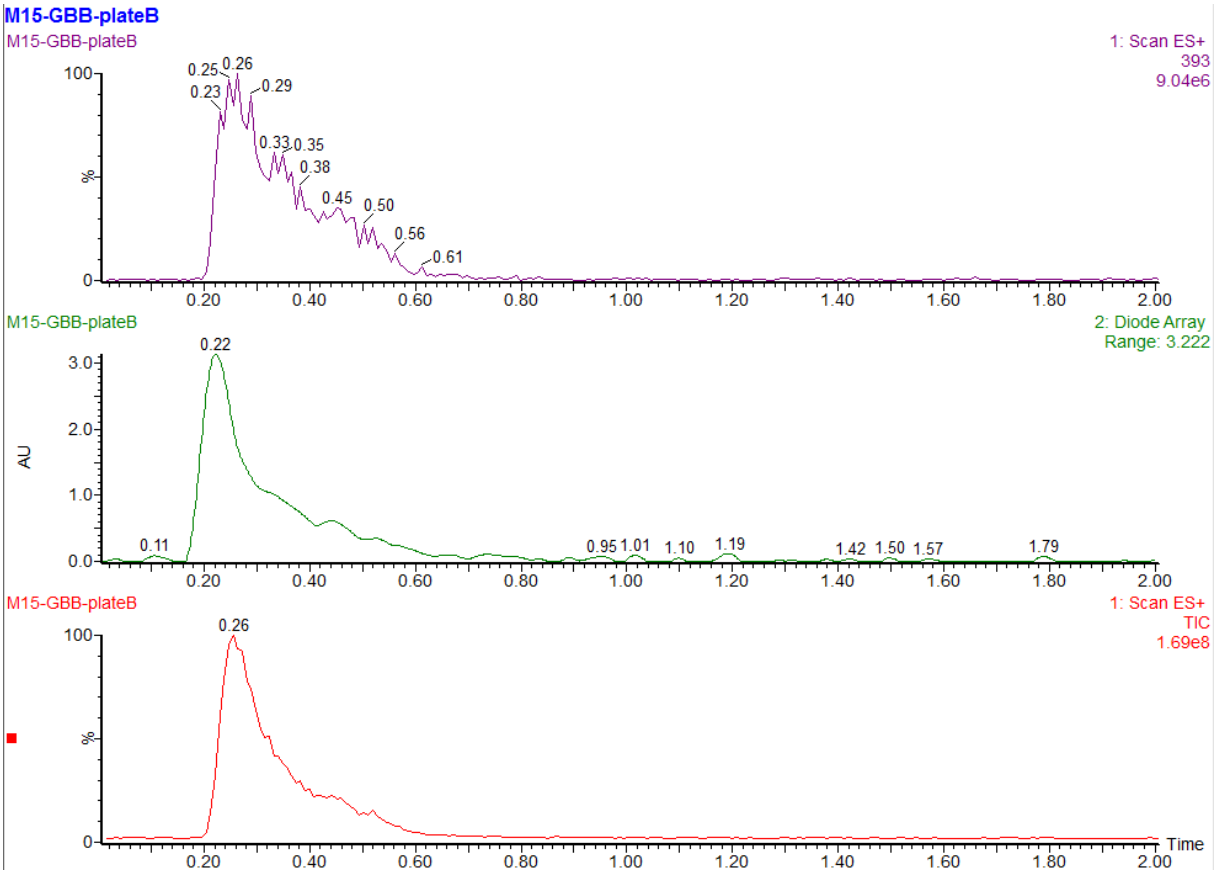


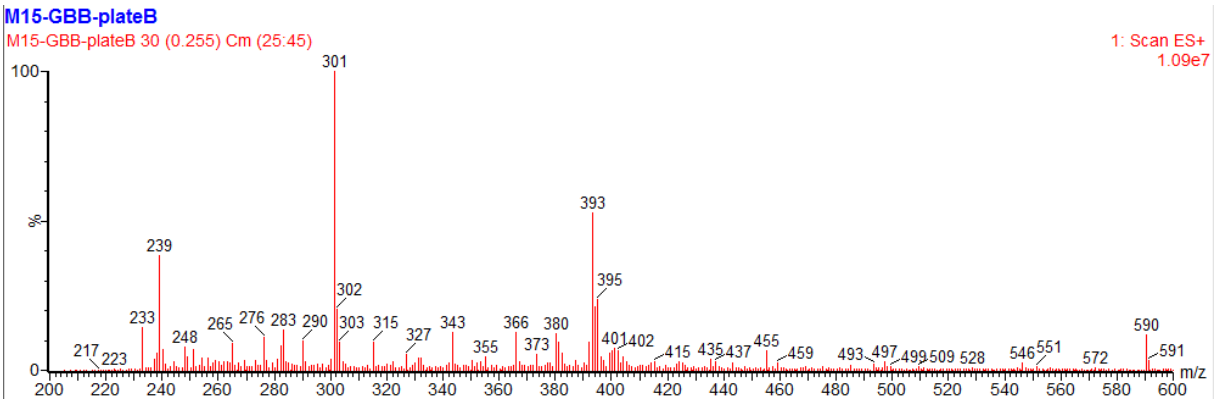



**M15 (Yellow)**



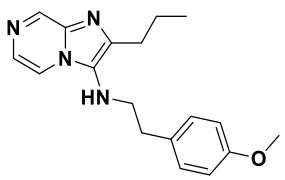

**Exact Mass: 392,11**



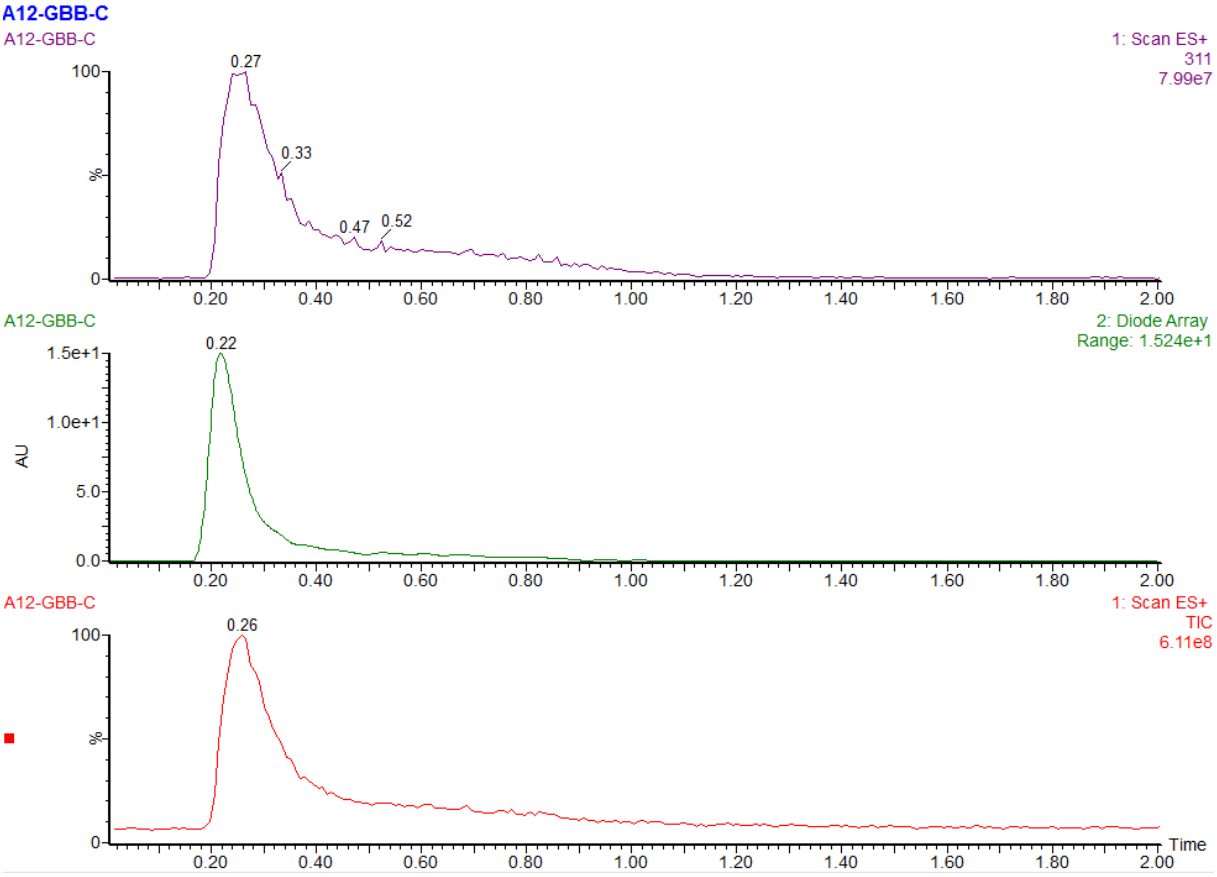



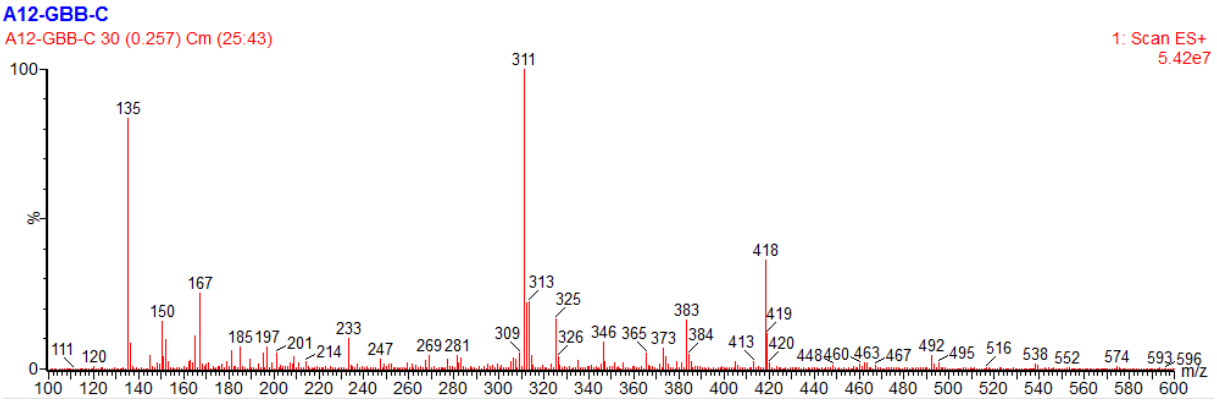
**Destination plate III**

**A12 (Green)**

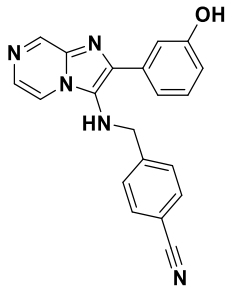



**Exact Mass: 310,18**

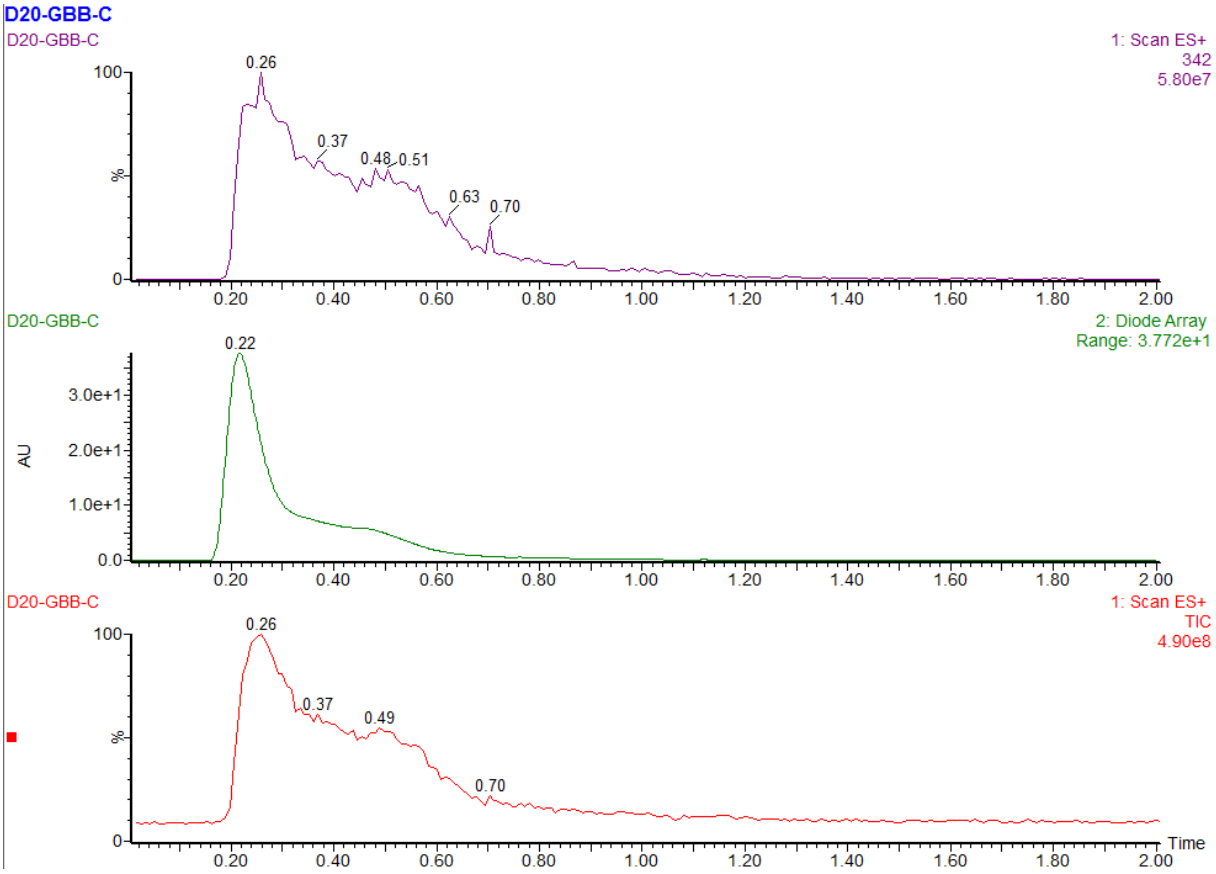


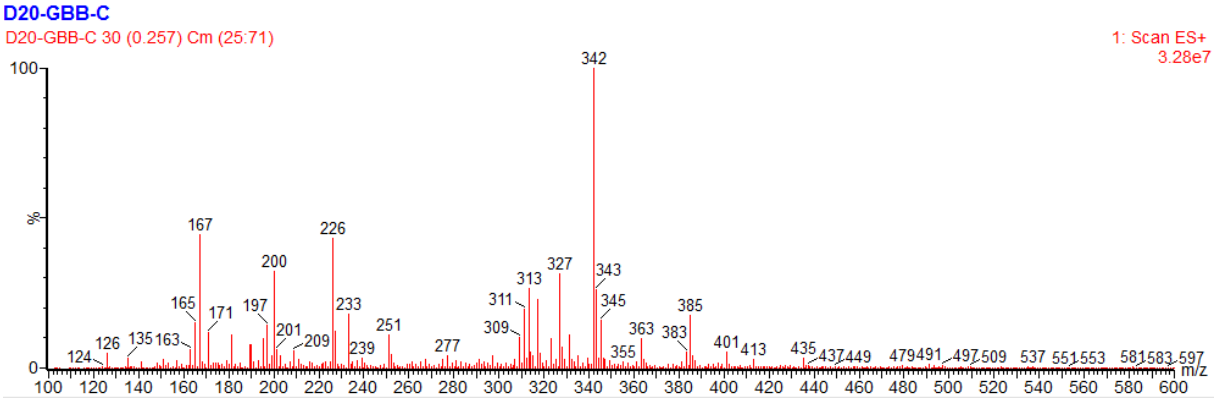



**D20 (Green)**

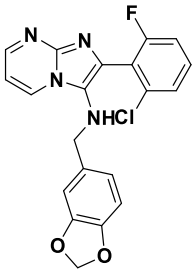



**Exact Mass: 341,13**

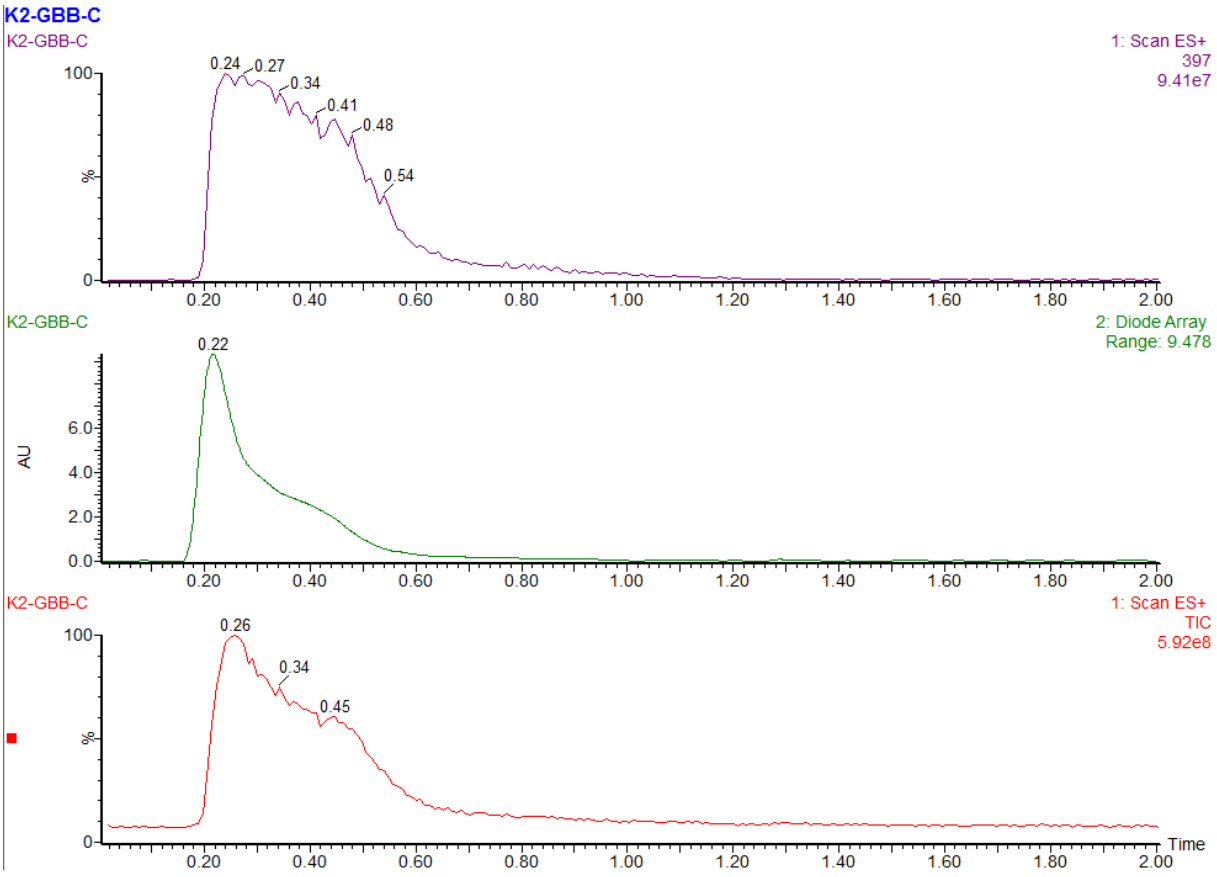


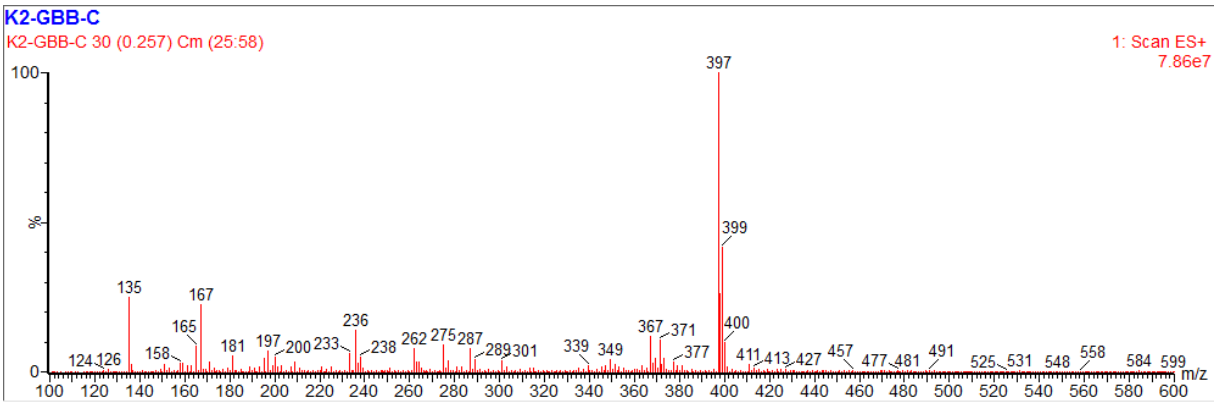



**K2 (Green)**

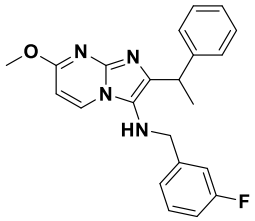



**Exact Mass: 396,08**

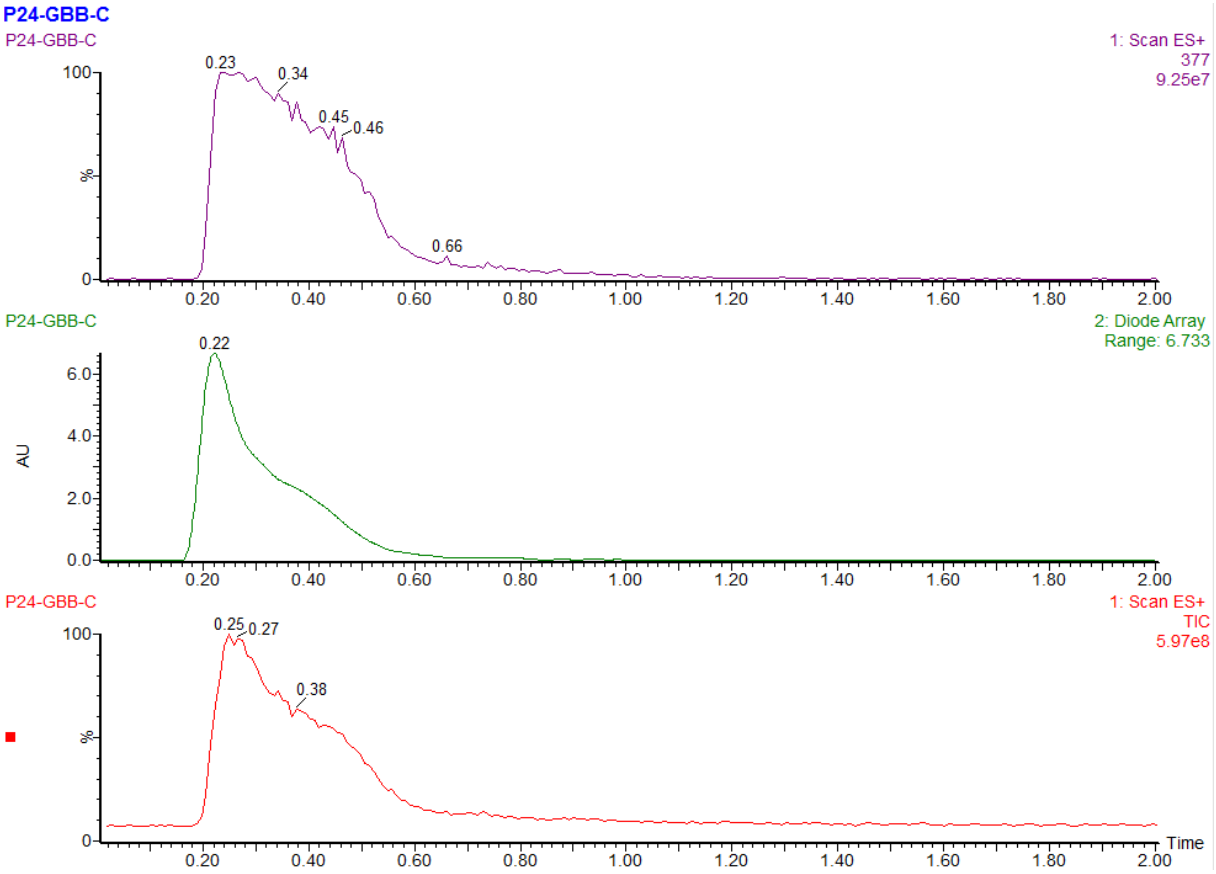


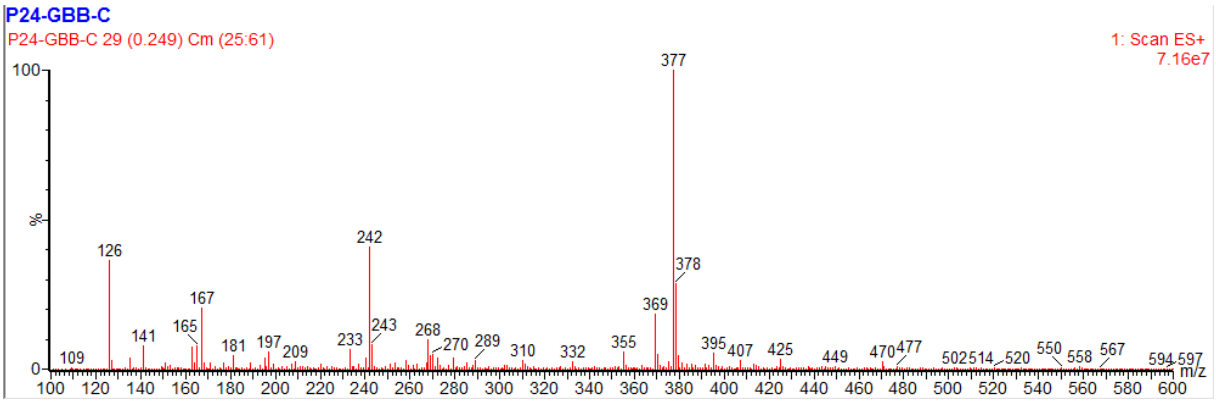



## P24 (Green)

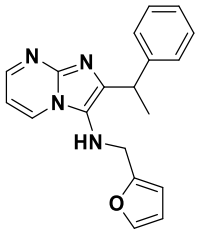



**Exact Mass: 376,17**

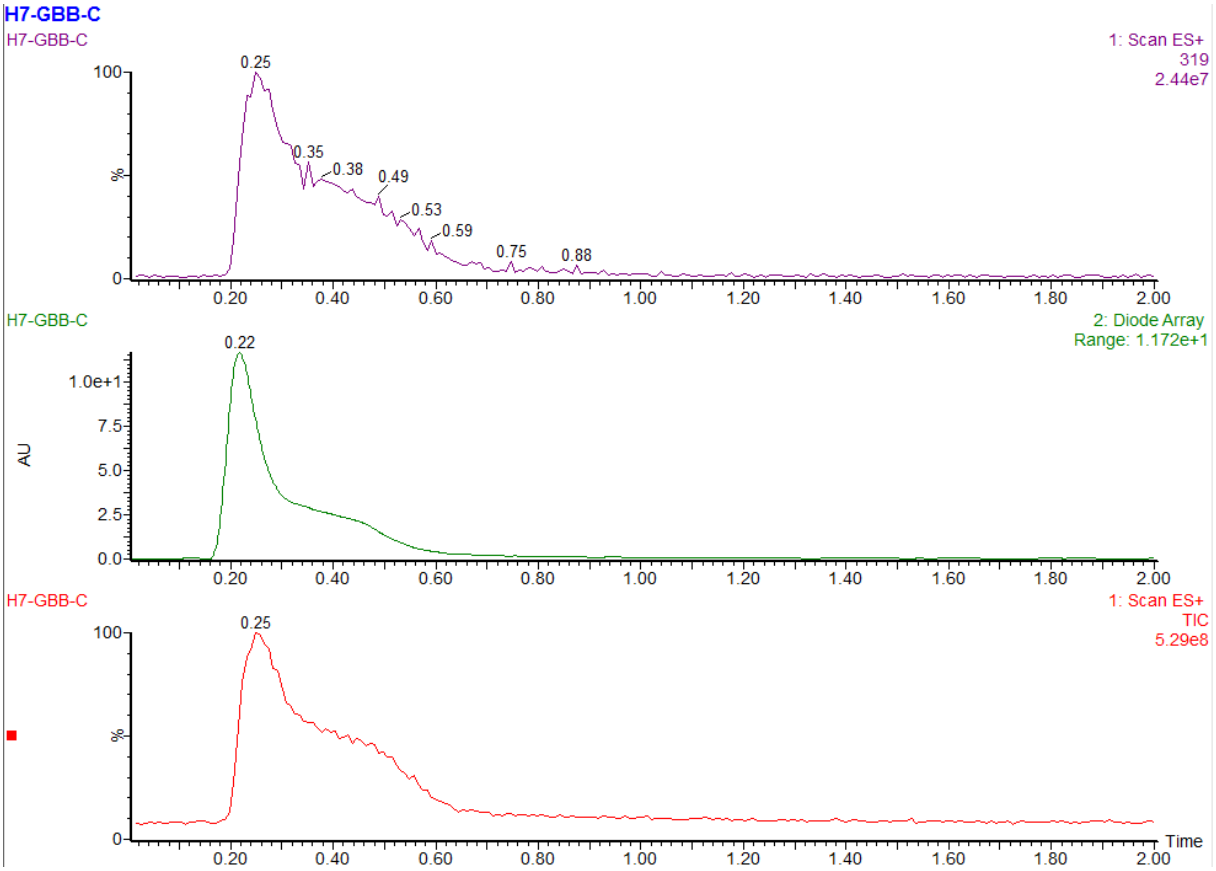


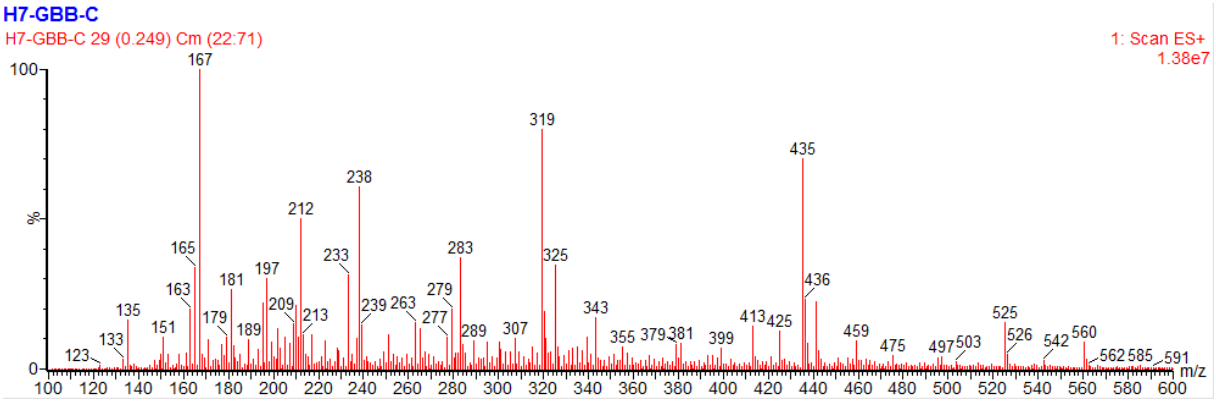



## H7 (Yellow)



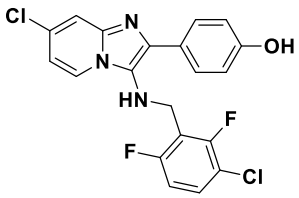

**Exact Mass: 318,15**



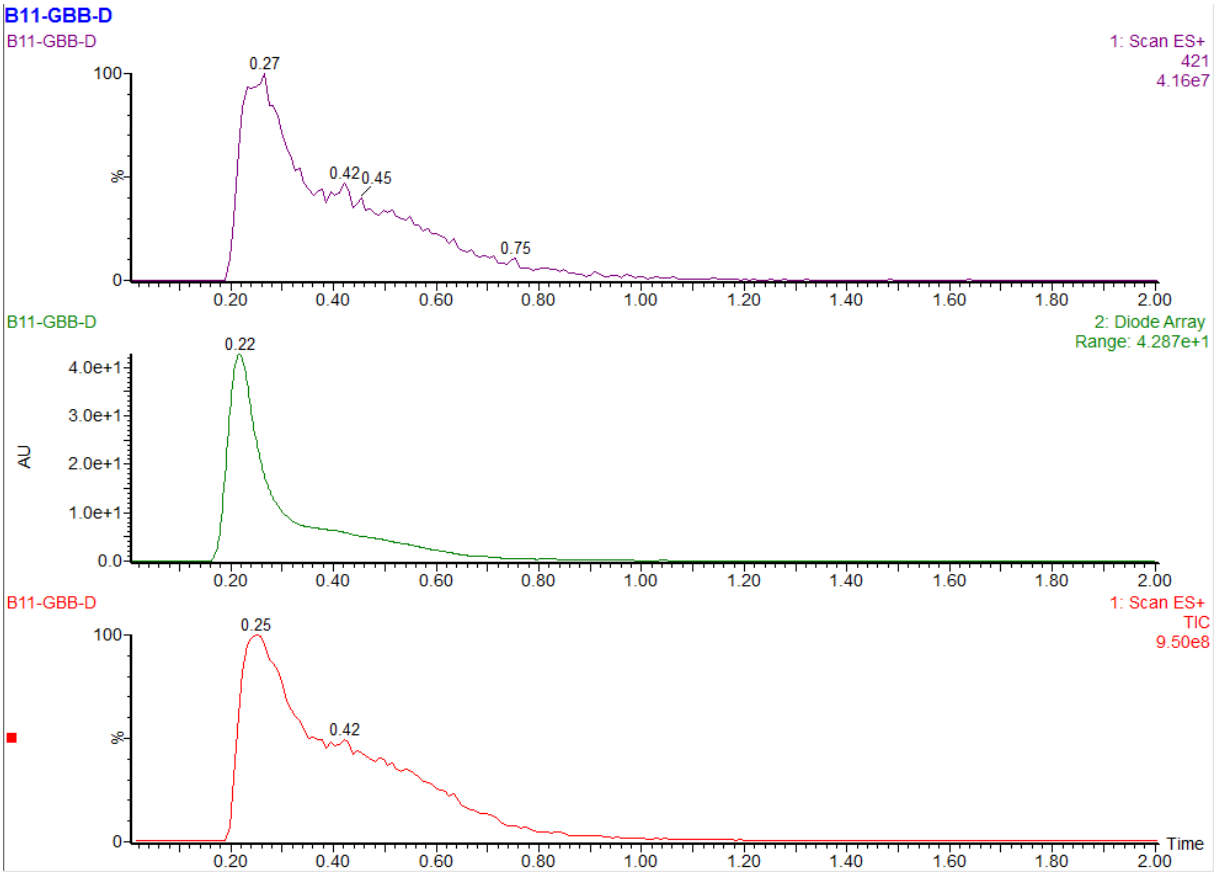



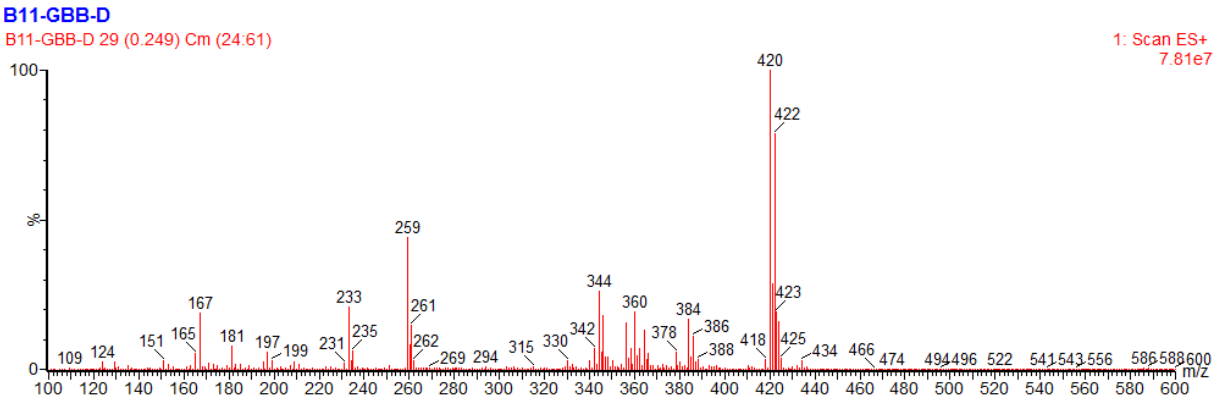
**Destination plate IV**

**B11 (Green)**

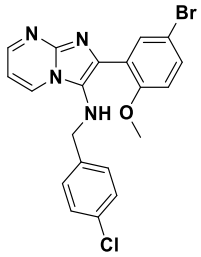



**Exact Mass: 419,04**

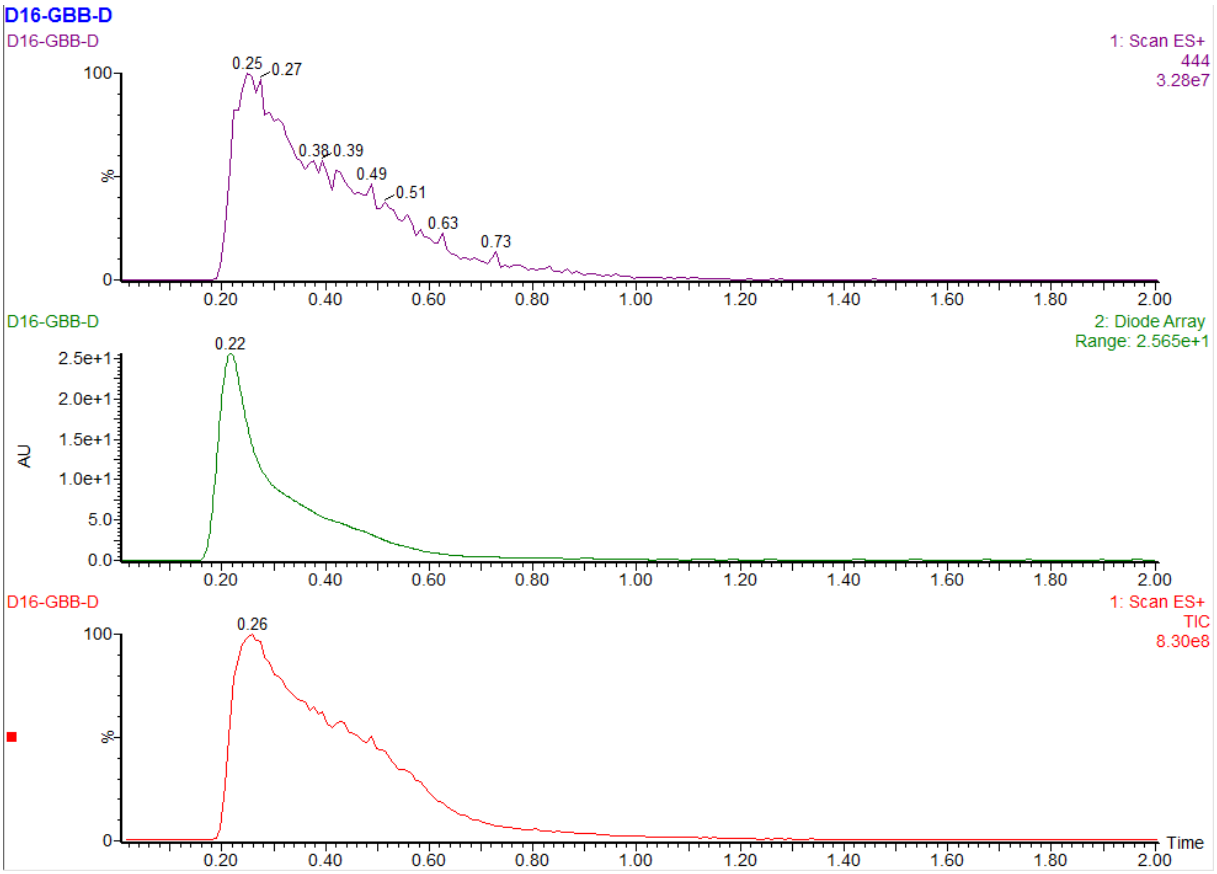


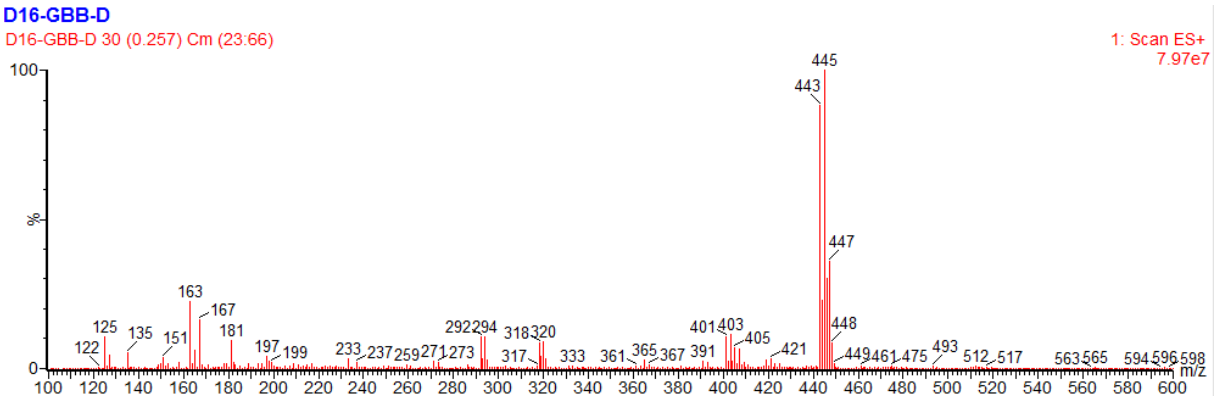



**D16 (Green)**

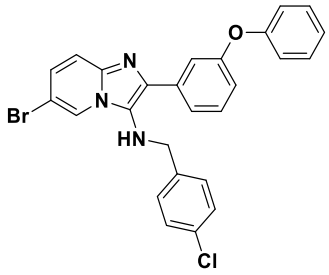



**Exact Mass: 442,02**

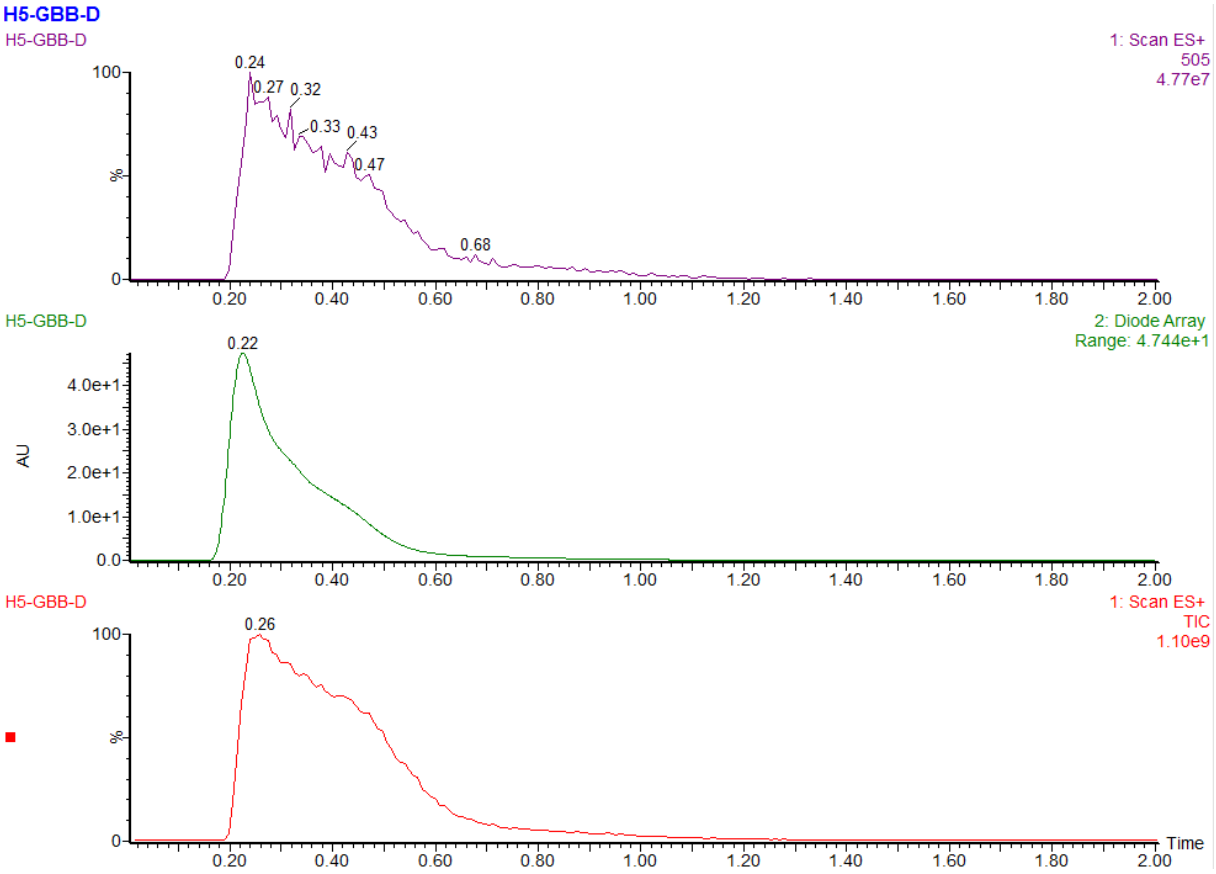


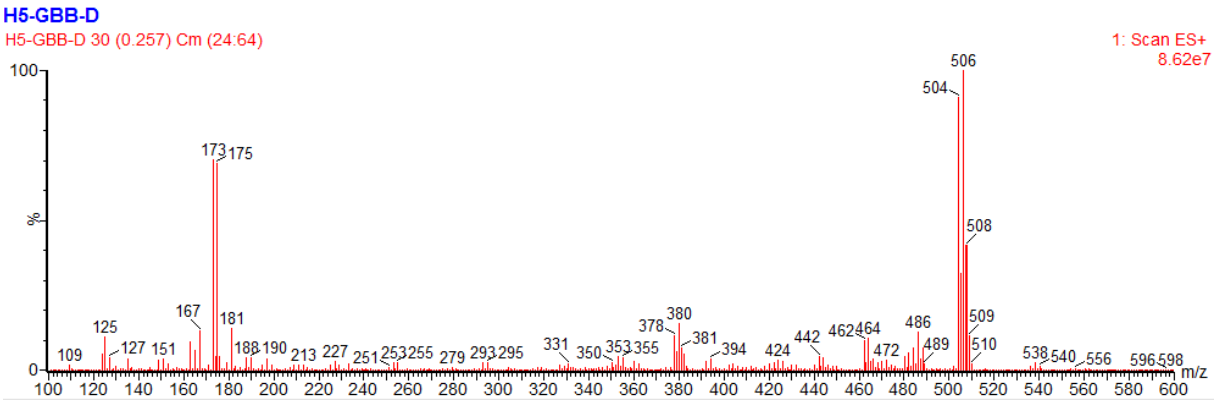



## H5 (Green)

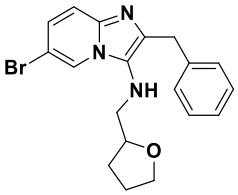



**Exact Mass: 503,04**

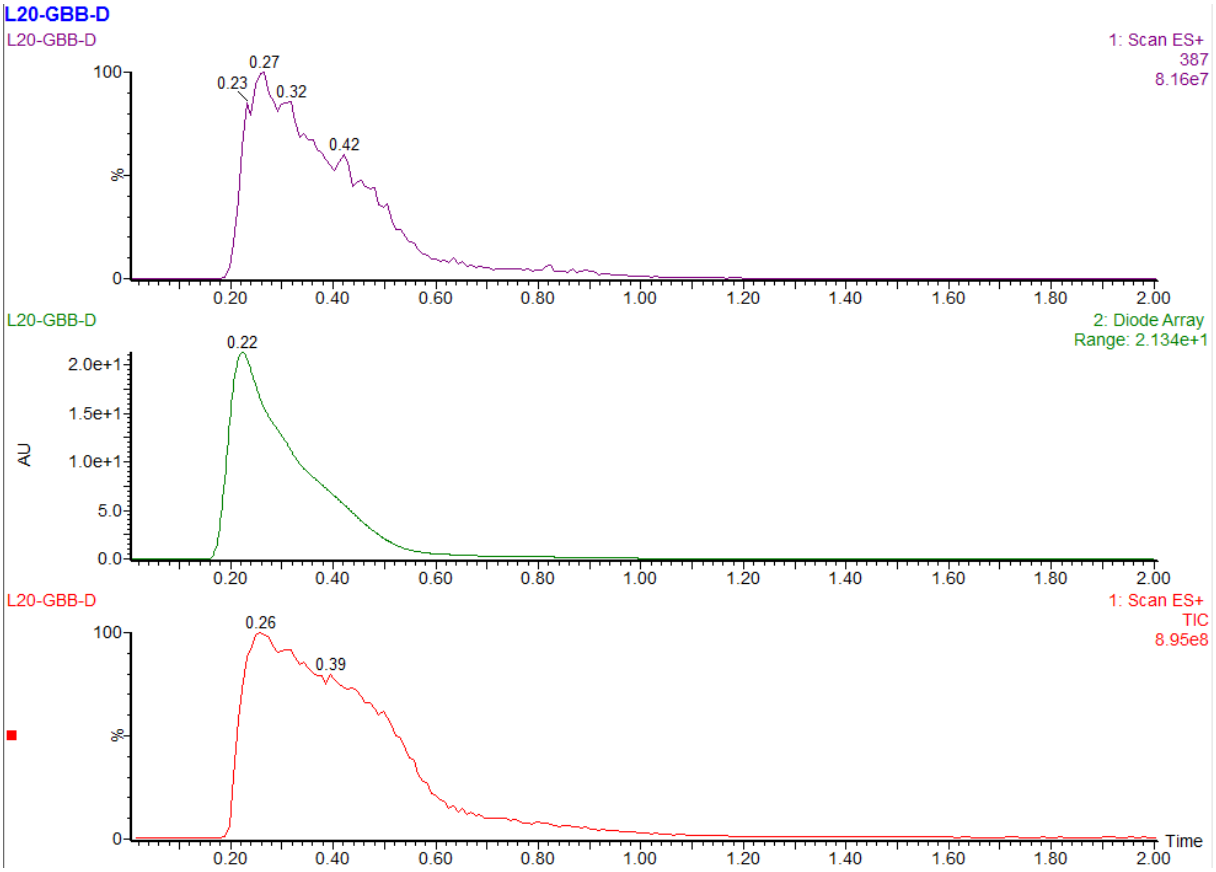


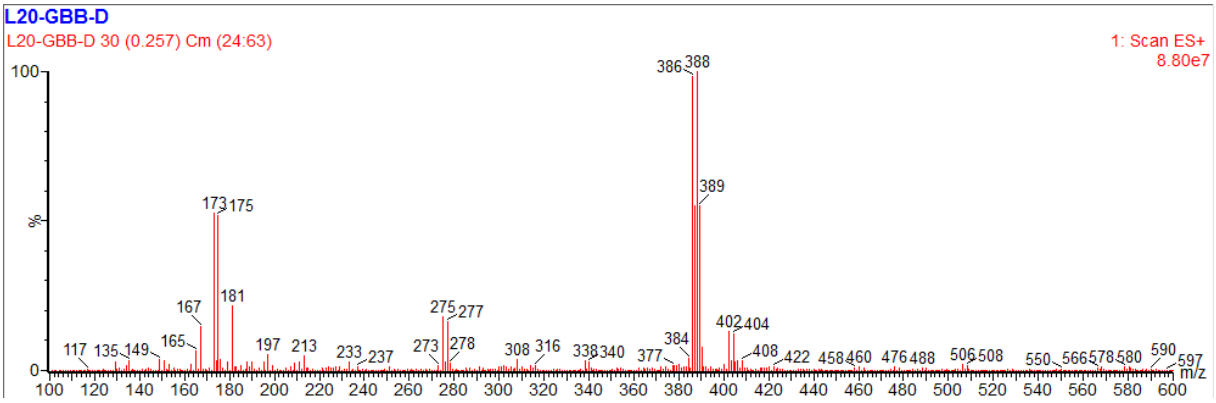



**L20 (Green)**

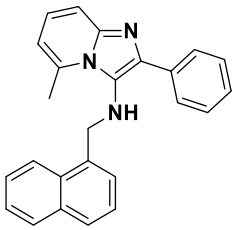



**Exact Mass: 385,08**

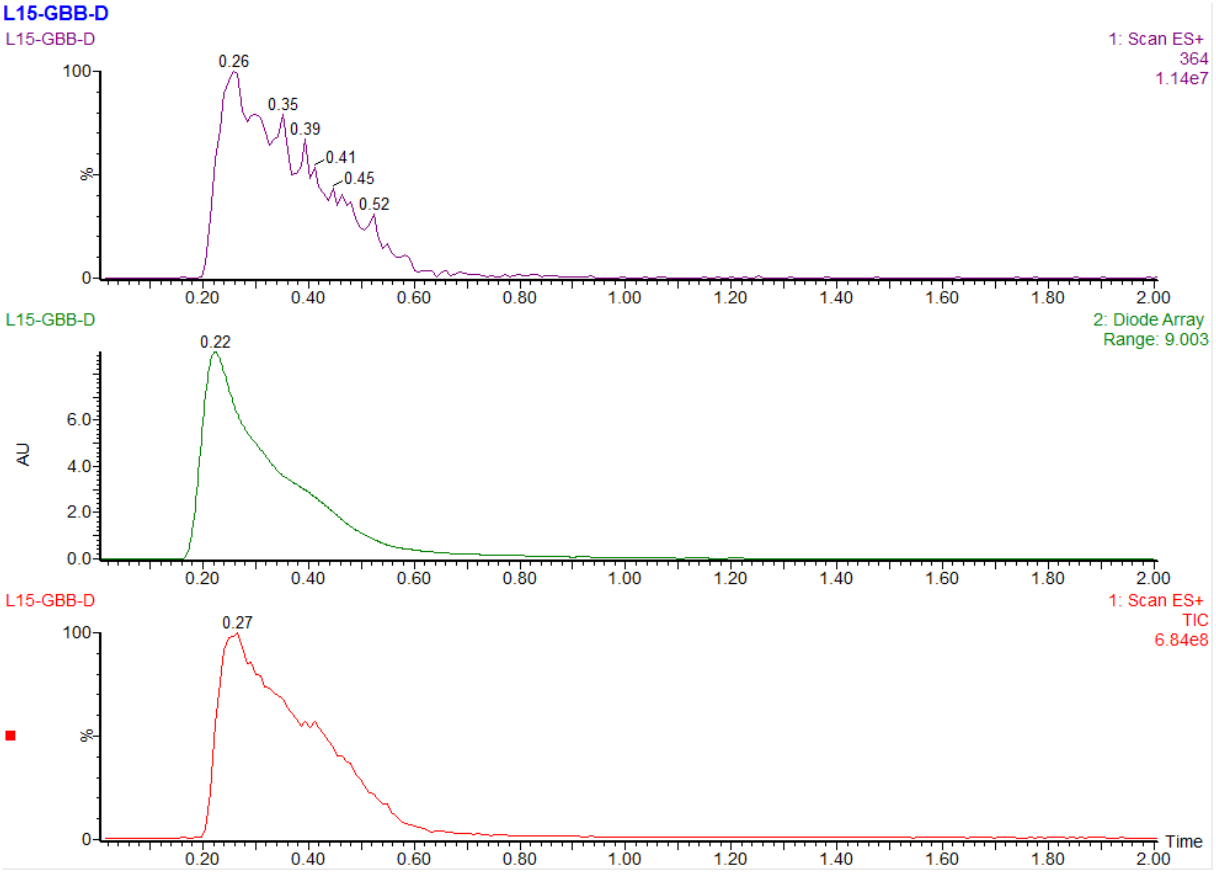


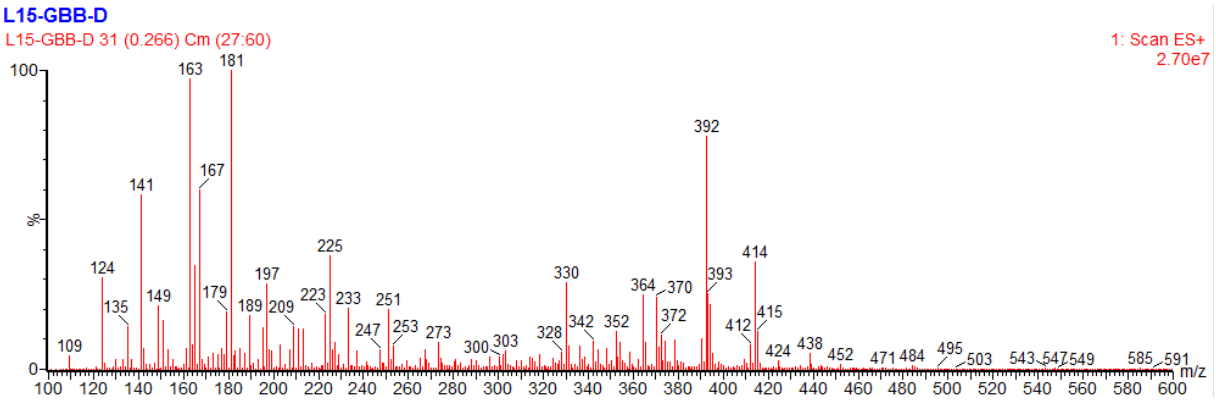



**L15 (Yellow)**



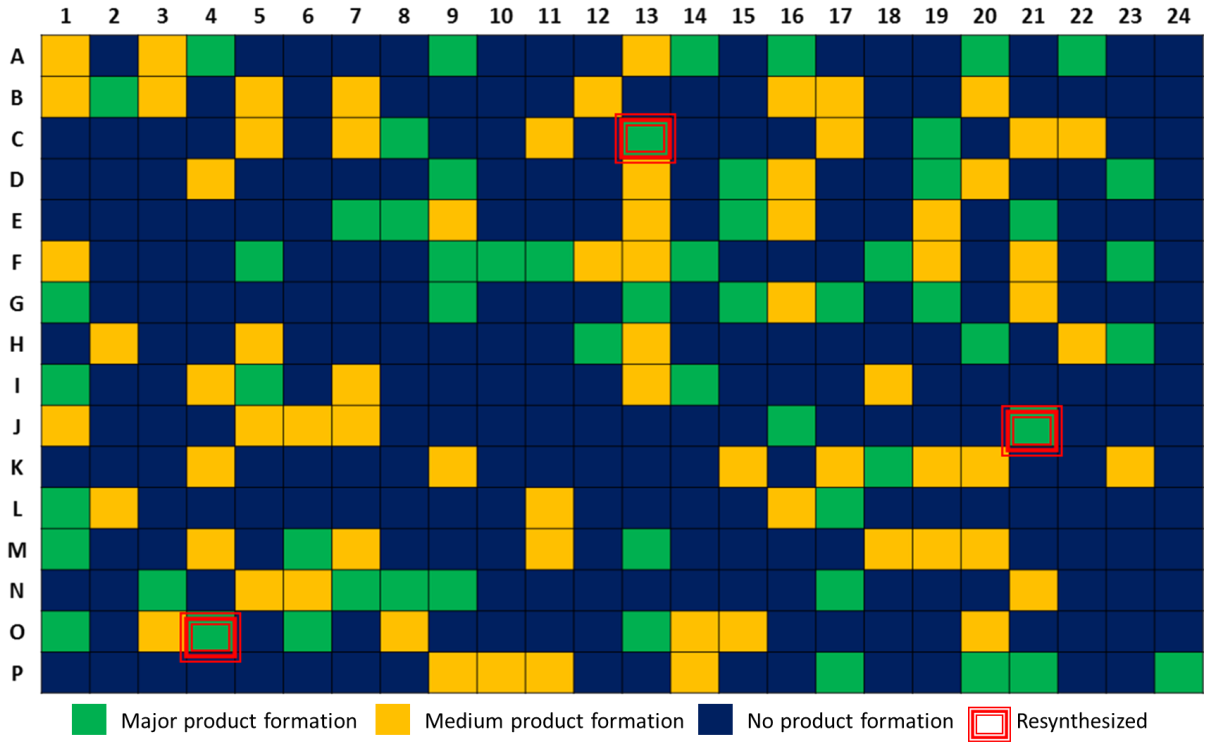

**Exact Mass: 363,17**



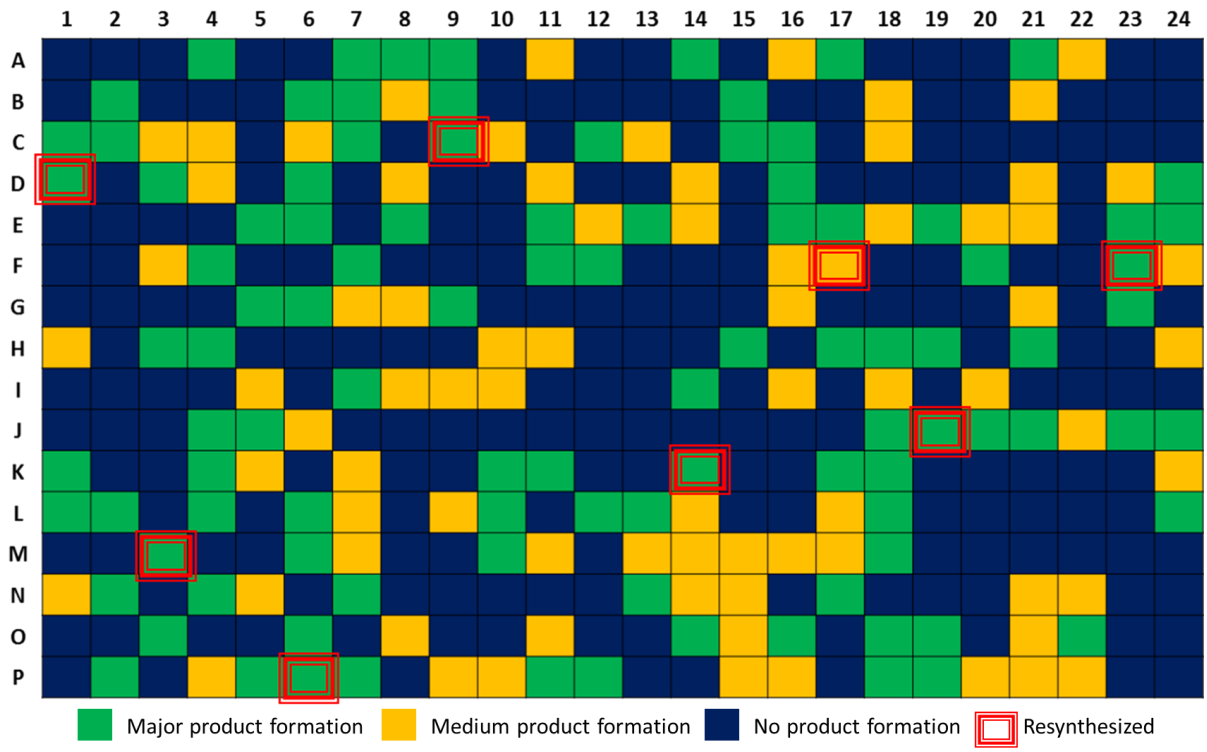



# 3. Heat plots

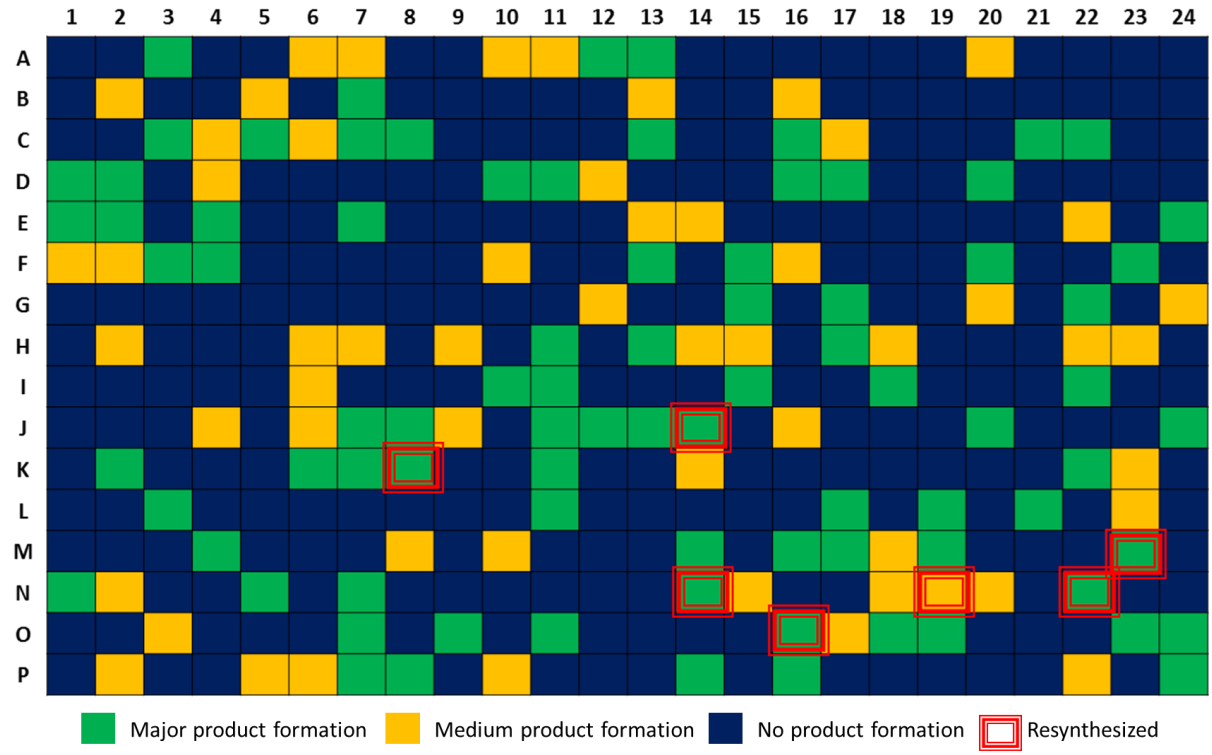
### Destination plate I



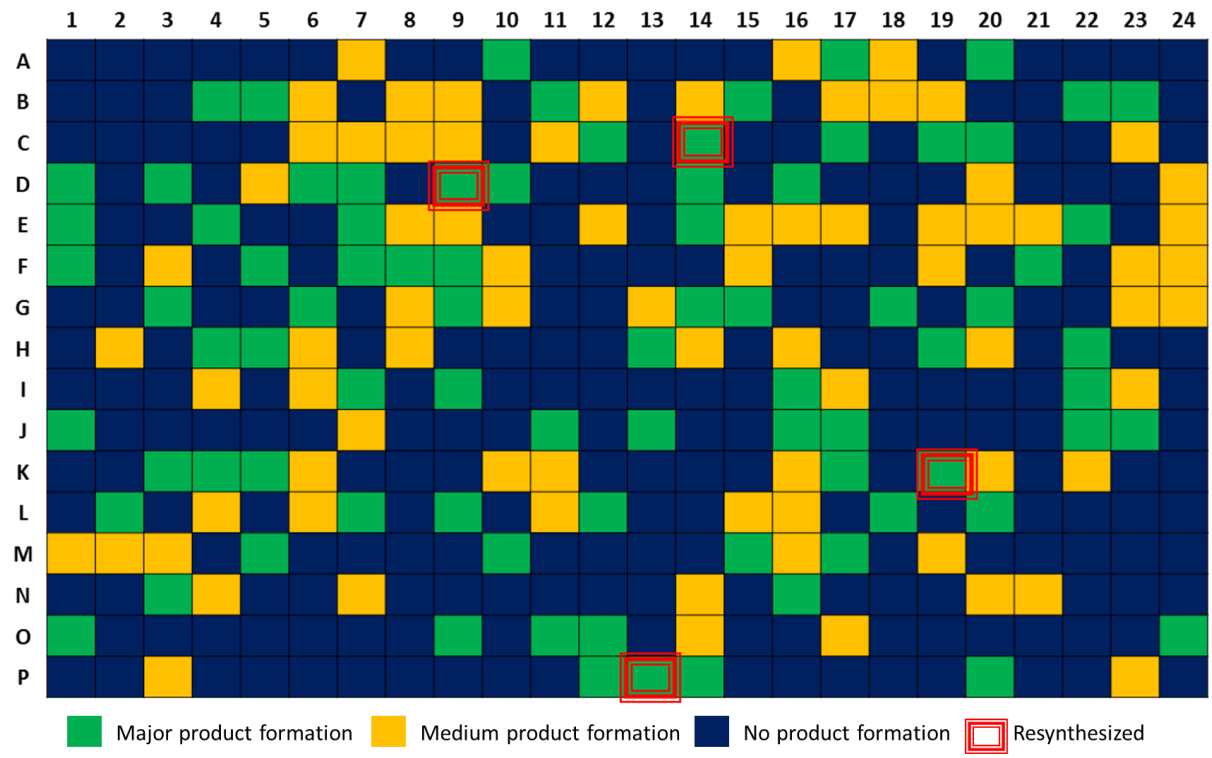

### Destination plate II



**Destination plate III**




**Destination plate IV**



## 4. Statistical reaction analysis

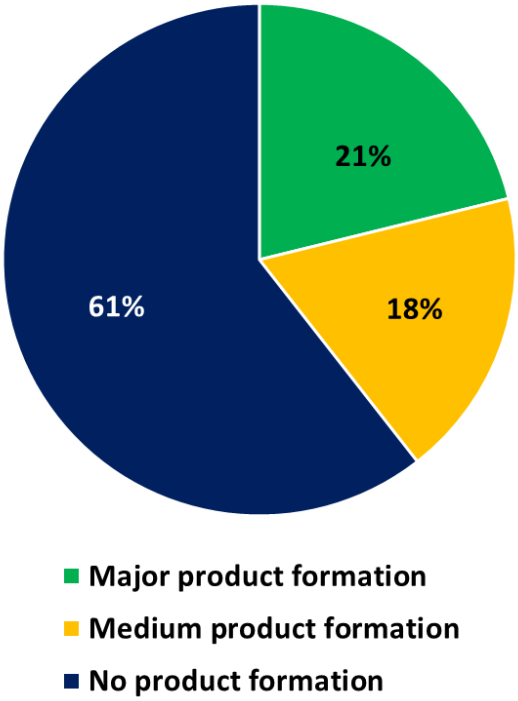



**Fig. S4**. QC results of 1536 wells.

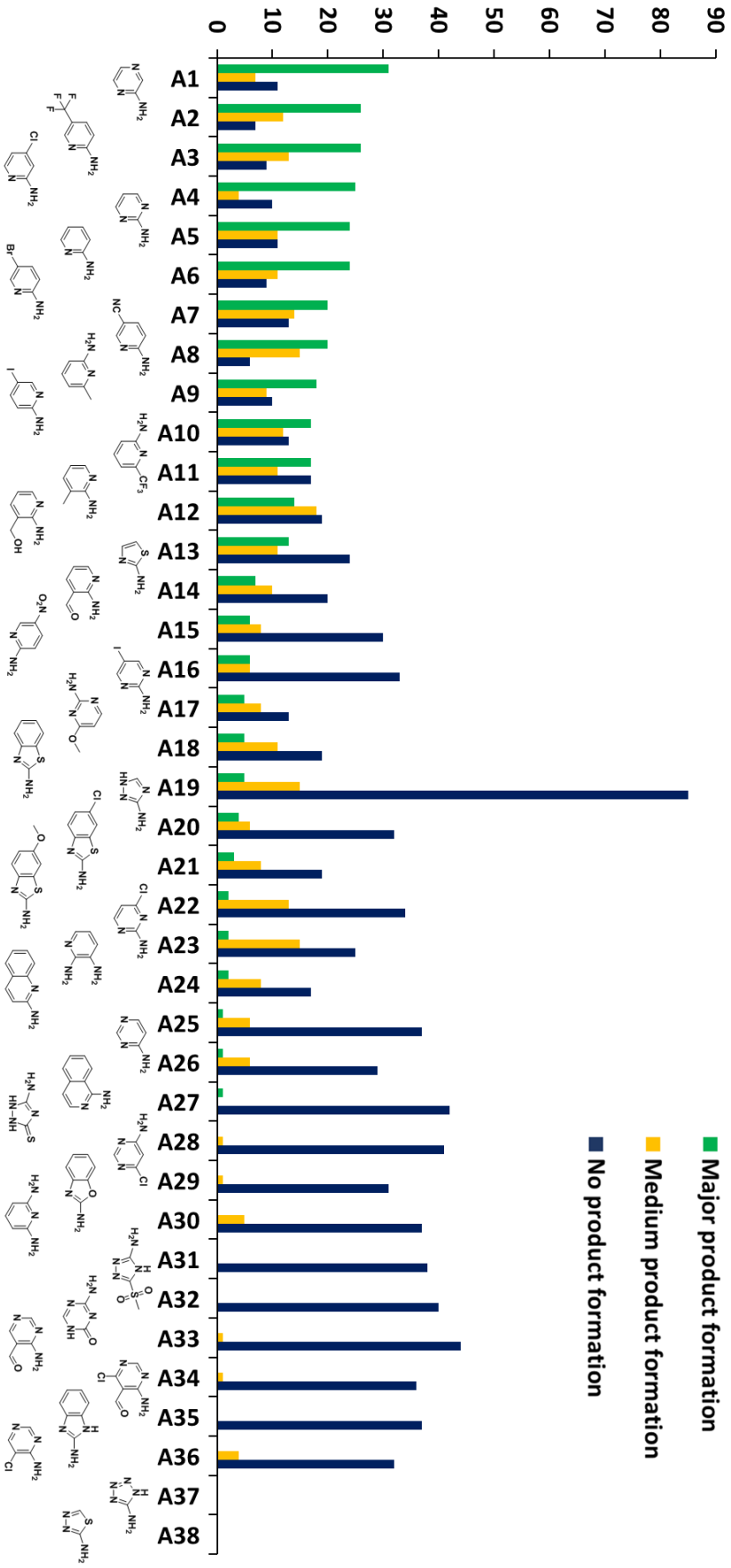



**Fig. S5**. Performance of amidines.

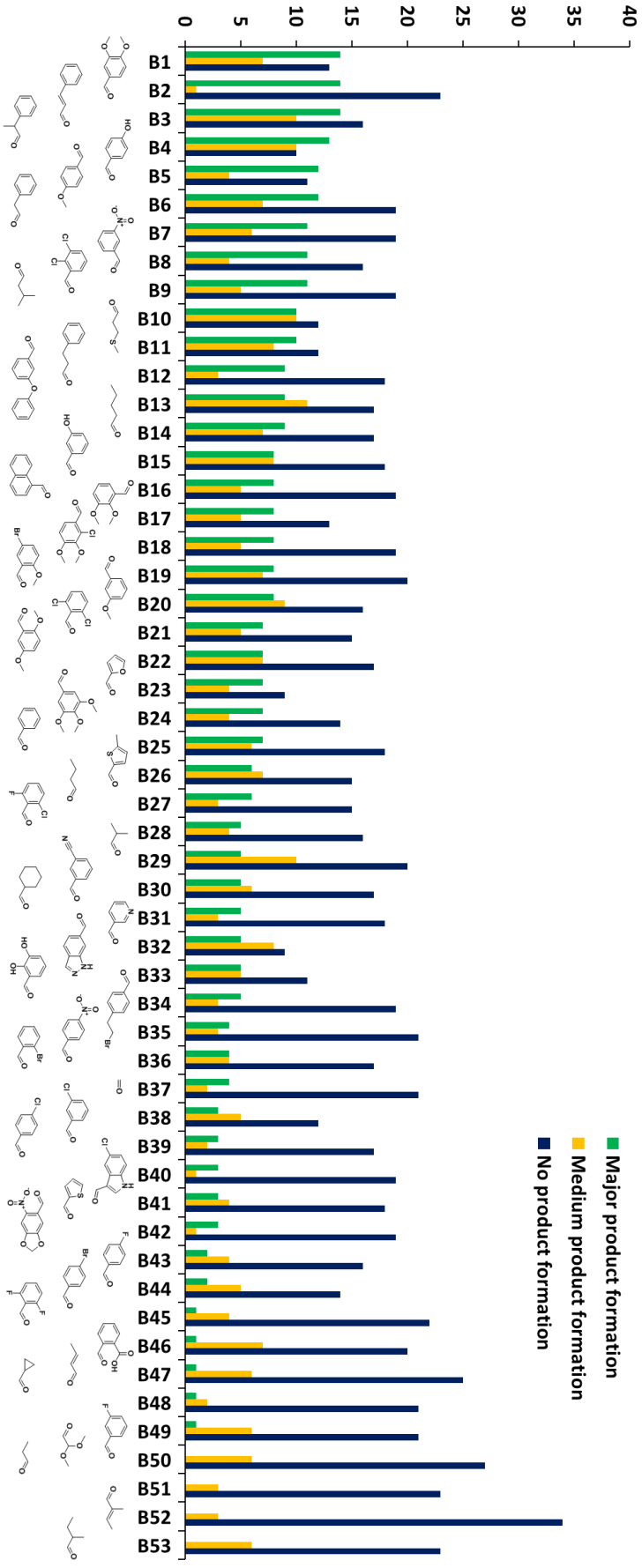



**Fig. S6**. Performance of aldehydes.

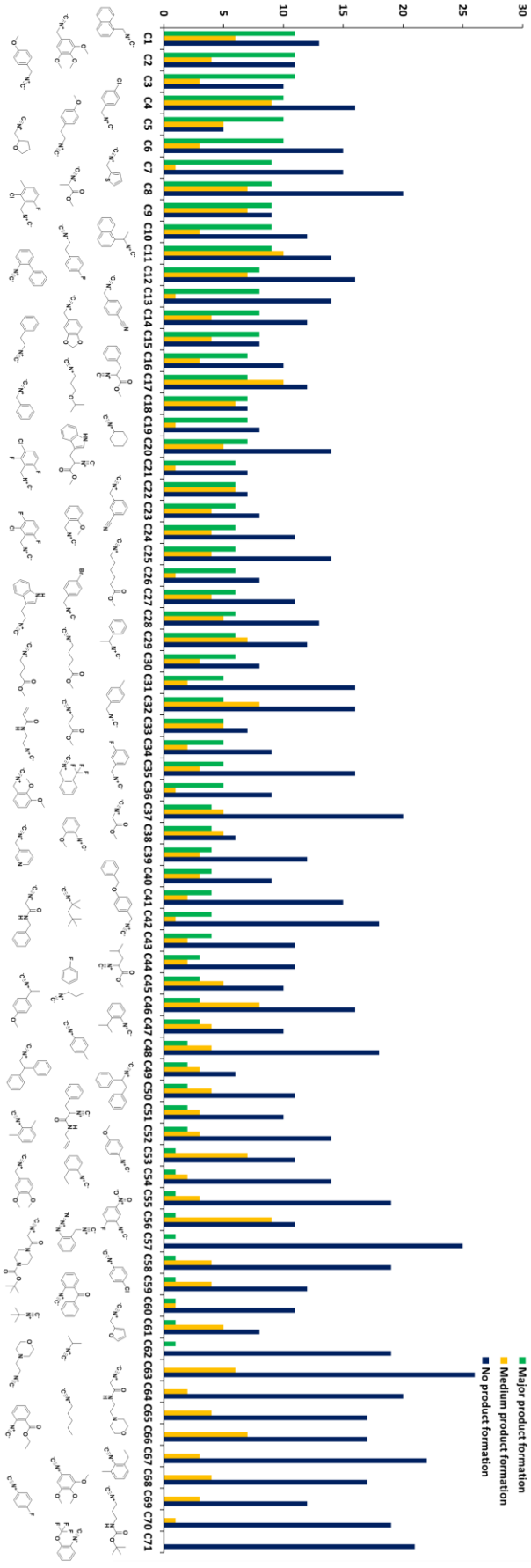


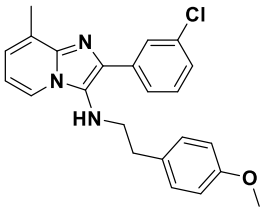

**Fig. S7**. Performance of isocyanides.

# 5. Synthetic procedure and analytical data

To a stirred solution of the corresponding aldehyde (1.0 mmol) in MeOH (1 mL), the amidine (1.0 mmol), the isocyanide (1.0 mmol) and catalytic amount of $Sc(OTf)_3$ (10 mol%) were added. The reaction mixture was stirred overnight at rt. Afterwards, the solvent was evaporated and the crude product was purified with column chromatography on silica gel affording the targeted compounds.

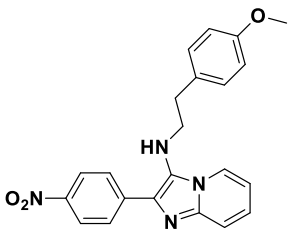
## Destination plate I

**2-(3-chlorophenyl)-N-(4-methoxyphenethyl)-8-methylimidazo[1,2-a]pyridin-3-amine (C13)**



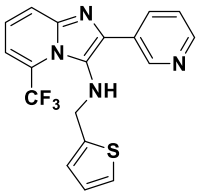

Yellow oil (299 mg, 76% yield); $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.70 – 7.65 (m, 1H), 7.58 (d, *J* = 6.8 Hz, 1H), 7.23 – 7.16 (m, 2H), 7.10 – 7.05 (m, 2H), 6.87 – 6.79 (m, 3H), 6.57 (t, *J* = 6.8 Hz, 1H), 3.75 (s, 3H), 3.22 – 3.13 (m, 2H), 3.13 – 3.03 (m, 1H), 2.77 (t, *J* = 6.7 Hz, 2H), 2.57 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 158.2, 141.7, 136.3, 134.3, 133.6, 130.7, 129.6, 129.5, 127.1, 126.9, 126.8, 126.4, 124.7, 122.7, 120.0, 113.9, 111.6, 55.1, 49.0, 35.7, 16.4; HRMS (ESI) m/z calculated for $C_{23}H_{22}ClN_3O$ $[M+H]^+$: 392.1524; found $[M+H]^+$: 392.1519.

**N-(4-methoxyphenethyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (J21)**




Orange oil (202 mg, 52% yield); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H), 8.02 (d, *J* = 8.8 Hz, 2H), 7.80 (d, *J* = 6.8 Hz, 1H), 7.53 (d, *J* = 9.1 Hz, 1H), 7.22 – 7.13 (m, 3H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.77 (t, *J* = 6.7 Hz, 1H), 3.85 (s, 3H), 3.30 (dd, *J* = 6.4 Hz, 2H), 3.15 (t, *J* = 6.2 Hz, 1H), 2.91 (t, *J* = 6.4 Hz, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 158.6, 146.4, 141.9, 140.8, 133.2, 130.5, 129.9, 127.6, 126.9, 124.8, 123.9, 122.4, 117.9, 114.3, 112.3, 55.3, 49.1, 35.6; HRMS (ESI) m/z calculated for $C_{22}H_{20}N_4O_3$ $[M+H]^+$: 389.1608; found $[M+H]^+$: 389.1608.

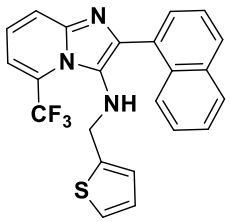
**2-(pyridin-3-yl)-N-(thiophen-2-ylmethyl)-5-(trifluoromethyl)imidazo[1,2-a]pyridin-3-amine (O4)**




Yellow solid (202 mg, 54% yield), M.P.= 156 – 157 °C; $^1$H NMR (500 MHz, $CDCl_3$) δ 9.50 – 9.34 (m, 1H), 8.69 – 8.52 (m, 1H), 8.46 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.78 (d, *J* = 8.9 Hz, 1H), 7.48 – 7.33 (m, 2H), 7.25 – 7.11 (m, 2H), 6.98 – 6.82 (m, 2H), 4.21 (d, J = 5.4 Hz, 2H), 3.51 (d, J = 5.4 Hz, 1H); δ $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.9, 148.6, 142.8, 140.4, 136.7, 134.5, 129.6, 127.4, 126.7, 126.3, 125.4, 124.8 (q, *J* = 35.3 Hz), 123.4, 122.5, , 121.9, 120.9 (q, *J* = 271.6 Hz),114.6 (q, *J* = 6.0 Hz), 47.0; HRMS (ESI) m/z calculated for $C_{18}H_{13}F_3N_4S$ $[M+H]^+$: 375.0886; found $[M+H]^+$: 375.0883.

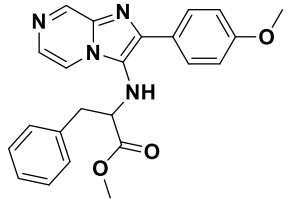
## Destination plate II

**2-(naphthalen-1-yl)-N-(thiophen-2-ylmethyl)-5-(trifluoromethyl)imidazo[1,2-a]pyridin-3-amine (C9)**



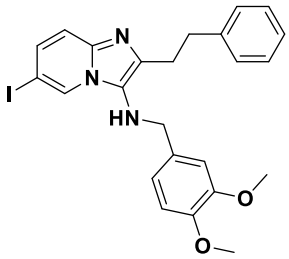

Yellow oil (313 mg, 74% yield); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.1 Hz, 1H), 7.97 – 7.91 (m, 2H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.74 (dd, *J* = 7.1, 1.3 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.54 – 7.45 (m, 2H), 7.40 (d, *J* = 7.1 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.04 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.72 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.45 (d, *J* = 2.7 Hz, 1H), 3.84 (d, *J* = 5.5 Hz, 2H), 3.27 (t, *J* = 5.5 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 142.3, 141.2, 139.9, 133.8, 131.7, 131.2, 129.0, 128.5, 128.4, 128.1, 126.6, 126.3, 125.9, 125.8, 125.7, 125.3, 125.0, 122.3, 121.3, 120.96 (q, *J* = 271.5 Hz), 114.40 (q, *J* = 6.3 Hz), 47.3; HRMS (ESI) m/z calculated for $C_{23}H_{16}F_3N_3S$ $[M+H]^+$: 424.1090; found $[M+H]^+$: 424.1091.

**methyl (2-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-3-yl)phenylalaninate (D1)**



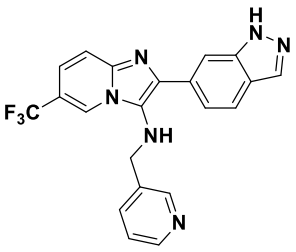
Yellow oil (241 mg, 60% yield); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.78 – 7.70 (m, 4H), 7.36 – 7.27 (m, 3H), 7.21 – 7.14 (m, 2H), 6.97 – 6.88 (m, 2H), 3.98 – 3.92 (m, 1H), 3.86 (s, 3H), 3.80 – 3.73 (m, 1H), 3.52 (s, 3H), 3.15 (dd, *J* = 13.7, 4.9 Hz, 1H), 2.99 (dd, *J* = 13.7, 8.5 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.7, 159.2, 142.4, 138.2, 136.3, 136.2, 129.1, 128.4, 128.4, 126.9, 125.4, 124.4, 115.5, 113.8, 60.7, 55.0, 51.9, 39.4; HRMS (ESI) m/z calculated for $C_{18}H_{14}IN_3O$ $[M+H]^+$: 403.1765; found $[M+H]^+$: 403.1774.

**N-(3,4-dimethoxybenzyl)-6-iodo-2-phenethylimidazo[1,2-a]pyridin-3-amine (F17)**



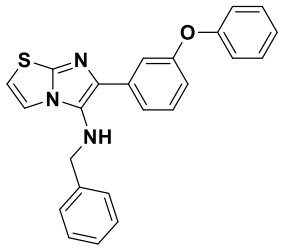
Light yellow solid (220 mg, 43% yield), M.P.= 124 – 125 °C; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.26 – 7.14 (m, 5H), 7.12 – 7.06 (m, 2H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.67 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.61 (d, *J* = 2.0 Hz, 1H), 3.87 (s, 3H), 3.80 (s, 3H), 3.78 (s, 2H), 3.00 (t, *J* = 7.5 Hz, 2H), 2.87 (t, *J* = 7.5 Hz, 2H), 2.74 (s, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 149.0, 148.6, 141.9, 139.9, 138.8, 131.7, 130.9, 128.5, 128.4, 127.6, 126.0, 125.8, 120.6, 117.9, 111.4, 111.1, 74.0, 55.9, 52.9, 35.6, 29.5.; HRMS (ESI) m/z calculated for $C_{24}H_{24}IN_3O_2$ $[M+H]^+$: 514.0986; found $[M+H]^+$: 514.0985.

**2-(1H-indazol-6-yl)-N-(pyridin-3-ylmethyl)-6-(trifluoromethyl)imidazo[1,2-a]pyridin-3-amine (F23)**



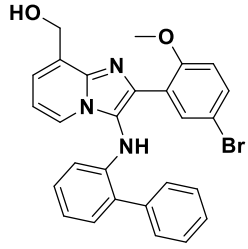
White solid (130 mg, 32% yield), M.P.= 236 – 238 °C; $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 13.16 (s, 1H), 8.57 (s, 1H), 8.42 – 8.34 (m, 3H), 8.09 (d, *J* = 1.4 Hz, 1H), 8.05 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.34 (dd, *J* = 9.3, 1.7 Hz, 1H), 7.23 (dd, *J* = 7.9, 4.7 Hz, 1H), 5.76 (t, *J* = 6.2 Hz, 1H), 4.17 (d, *J* = 6.2 Hz, 2H); $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 149.4 (d, *J* = 13.3 Hz), 148.4 (d, *J* = 13.5 Hz), 140.4, 140.0, 136.1, 135.9 (d, *J* = 24.3 Hz), 134.9, 133.4, 131.5, 127.8, 124.0 (d, *J* = 270.4 Hz), 123.3, 122.6, 122.2, 120.5, 119.6, 119.1, 117.7 (d, *J* = 24.9 Hz), 113.9 (d, *J* = 33.5 Hz), 107.8 (d, *J* = 12.8 Hz), 48.8; HRMS (ESI) m/z calculated for $C_{21}H_{15}F_3N_6$ $[M+H]^+$: 409.1383; found $[M+H]^+$: 409.1382.

**N-benzyl-6-(3-phenoxyphenyl)imidazo[2,1-b]thiazol-5-amine (J19)**



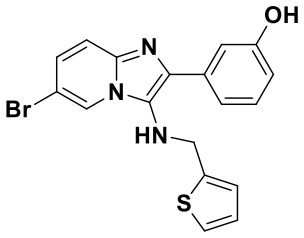
Yellow oil (120 mg, 30% yield); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 2.0 Hz, 1H), 7.41 – 7.19 (m, 8H), 7.12 – 7.00 (m, 3H), 6.95 – 6.89 (m, 2H), 6.60 (d, *J* = 4.5 Hz, 1H), 4.11 (s, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.4, 157.4, 145.1, 139.0, 136.3, 136.1, 129.9, 129.7, 128.7, 128.2, 128.1, 127.6, 123.1, 121.1, 118.8, 117.4, 116.7, 116.5, 111.8, 53.3.; HRMS (ESI) m/z calculated for $C_{24}H_{19}N_3OS$ $[M+H]^+$: 398.1322; found $[M+H]^+$: 398.1319.

**(3-([1,1'-biphenyl]-2-ylamino)-2-(5-bromo-2-methoxyphenyl)imidazo[1,2-a]pyridin-8-yl)methanol (K14)**



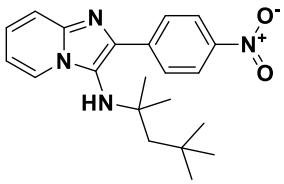
White solid (462 mg, 92% yield), M.P.= 217 – 218 °C; $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ δ 7.90 (d, *J* = 6.8 Hz, 1H), 7.73 (d, *J* = 2.6 Hz, 1H), 7.62 – 7.50 (m, 4H), 7.48 – 7.39 (m, 2H), 7.34 (d, *J* = 6.8 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 7.06 – 6.95 (m, 2H), 6.92 (d, *J* = 9.0 Hz, 1H), 6.81 (t, *J* = 7.3 Hz, 1H), 6.67 (s, 1H), 5.84 (d, *J* = 8.1 Hz, 1H), 5.43 (t, *J* = 5.7 Hz, 1H), 4.92 (d, *J* = 5.7 Hz, 2H), 3.21 (s, 3H); $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 155.0, 141.6, 140.1, 138.6, 133.2, 133.0, 132.2, 131.4, 131.2, 130.5, 129.3, 128.9, 128.6, 127.9, 127.4, 125.1, 121.8, 121.6, 121.4, 120.2, 119.2, 113.6, 112.1, 58.2, 55.2; HRMS (ESI) m/z calculated for $C_{27}H_{22}BrN_3O_2$ $[M+H]^+$: 500.0968; found $[M+H]^+$: 500.0963.

**3-(6-bromo-3-((thiophen-2-ylmethyl)amino)imidazo[1,2-a]pyridin-2-yl)phenol (M3)**



Yellow solid (260 mg, 65% yield), M.P.= 199 – 201 °C; $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 9.45 (s, 1H), 8.30 (s, 1H), 7.67 – 7.60 (m, 2H), 7.41 (d, $J$ = 9.4 Hz, 1H), 7.36 (d, $J$ = 5.0 Hz, 1H), 7.28 – 7.16 (m, 2H), 6.93 – 6.86 (m, 1H), 6.85 (s, 1H), 6.76 – 6.68 (m, 1H), 5.56 (t, $J$ = 6.2 Hz, 1H), 4.29 (d, $J$ = 6.2 Hz, 2H); $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 157.5, 142.8, 138.6, 135.3, 135.0, 129.4, 126.8, 126.6, 126.4, 125.9, 125.5, 123.1, 117.8, 117.4, 114.4, 113.5, 105.3, 45.6; HRMS (ESI) m/z calculated for $C_{18}H_{14}BrN_3OS$ $[M+H]^+$: 400.0114; found $[M+H]^+$: 400.0110.

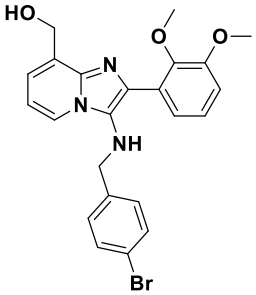
**2-(4-nitrophenyl)-N-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-a]pyridin-3-amine (P6)**



Orange solid (236 mg, 64% yield), M.P.= 159 – 161 °C; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.32 – 8.26 (m, 2H), 8.23 – 8.17 (m, 3H), 7.55 (d, $J$ = 9.0 Hz, 1H), 7.23 – 7.16 (m, 1H), 6.83 (t, $J$ = 6.8 Hz, 1H), 3.15 (s, 1H), 1.63 (s, 2H), 1.06 (s, 9H), 0.99 (s, 6H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 146.7, 142.5, 142.2, 137.4, 128.6, 124.9, 124.5, 123.5, 123.4, 117.7, 111.9, 61.1, 57.2, 31.8, 31.8, 29.1; HRMS (ESI) m/z calculated for $C_{21}H_{26}N_4O_2$ $[M+H]^+$: 367.2129; found $[M+H]^+$: 367.2123.

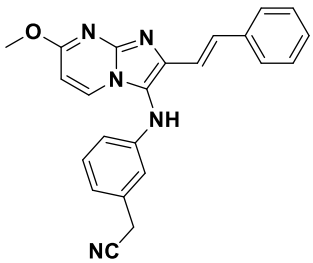
## Destination plate III

**(3-((4-bromobenzyl)amino)-2-(2,3-dimethoxyphenyl)imidazo[1,2-a]pyridin-8-yl) methanol (J14)**



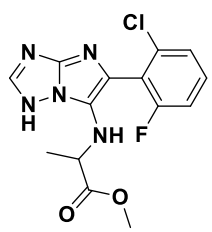
Light yellow solid (371 mg, 80% yield), M.P.= 71 – 72 °C; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, $J$ = 6.8 Hz, 1H), 7.22 (dd, $J$ = 7.9, 1.5 Hz, 1H), 7.17 – 7.09 (m, 3H), 7.04 (d, $J$ = 6.8 Hz, 1H), 6.91 (dd, $J$ = 8.1, 1.5 Hz, 1H), 6.85 (m, 2H), 6.79 (t, $J$ = 6.8 Hz, 1H), 5.04 (s, 2H), 4.81 (t, $J$ = 7.0 Hz, 1H), 4.57 (s, 1H), 3.93 (s, 3H), 3.88 (d, $J$ = 7.0 Hz, 2H), 3.58 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 152.4, 145.2, 140.7, 137.9, 131.8, 131.0, 129.5, 129.4, 128.0, 127.5, 124.8, 123.1, 121.4, 121.1, 120.8, 111.7, 111.3, 62.1, 61.3, 55.8, 51.4.; HRMS (ESI) m/z calculated for $C_{23}H_{22}BrN_3O_3$ $[M+H]^+$: 468.0917; found $[M+H]^+$: 468.0915.

**(E)-2-(3-((7-methoxy-2-styrylimidazo[1,2-a]pyrimidin-3-yl)amino)phenyl)acetonitrile (K8)**



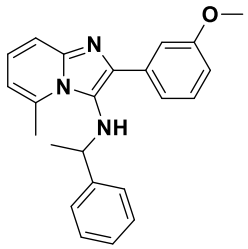
Yellow solid (160 mg, 42% yield), M.P.= 185 – 186 °C; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, $J$ = 7.3 Hz, 1H), 7.68 (s, 1H), 7.58 – 7.50 (m, 2H), 7.48 – 7.43 (m, 1H), 7.43 – 7.31 (m, 5H), 7.26 – 7.21 (m, 1H), 6.76 (d, $J$ = 15.8 Hz, 1H), 6.28 (d, $J$ = 7.3 Hz, 1H), 4.20 (d, $J$ = 5.8 Hz, 2H), 4.01 (s, 3H), 3.59 (t, $J$ = 6.1 Hz, 1H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 163.3, 144.8, 140.6, 137.2, 135.3, 132.8, 131.7, 131.4, 131.2, 130.2, 129.4, 128.6, 127.6, 126.4, 123.9, 118.5, 117.0, 112.7, 100.2, 54.3, 53.0; HRMS (ESI) m/z calculated for $C_{23}H_{19}N_5O$ $[M+H]^+$: 382.1662; found $[M+H]^+$: 382.1659.

**methyl (5-(2-chloro-6-fluorophenyl)-1H-imidazo[1,2-b][1,2,4]triazol-6-yl)alaninate (M23)**



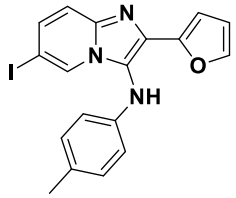
Yellow oil (172 mg, 51% yield); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.47 – 7.29 (m, 2H), 7.15 (t, $J$ = 8.4 Hz, 1H), 4.49 – 4.24 (m, 1H), 4.01 (d, $J$ = 9.3 Hz, 1H), 3.59 (s, 3H), 1.39 (d, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.3, 161.1 (d, $J$ = 250.9 Hz), 152.6, 148.2, 135.9 (d, $J$ = 3.0 Hz), 131.2 (d, $J$ = 9.6 Hz), 125.8 (d, $J$ = 3.4 Hz), 124.2, 117.3 (d, $J$ = 18.1 Hz), 114.5 (d, $J$ = 22.7 Hz), 107.5, 53.6, 52.1, 19.0; HRMS (ESI) m/z calculated for $C_{14}H_{13}ClFN_5O_2$ $[M+H]^+$: 338.0815; found $[M+H]^+$: 338.0811.

**2-(3-methoxyphenyl)-5-methyl-N-(1-phenylethyl)imidazo[1,2-a]pyridin-3-amine (N14)**



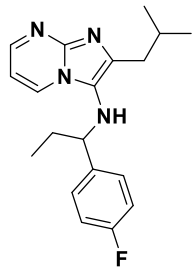
Yellow oil (230 mg, 64% yield); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 2H), 7.39 (d, *J* = 8.9 Hz, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 7.23 – 7.09 (m, 5H), 7.00 – 6.91 (m, 1H), 6.86 (dd, *J* = 7.9, 2.2 Hz, 1H), 6.37 (d, *J* = 6.7 Hz, 1H), 4.12 (q, *J* = 6.6 Hz, 1H), 3.82 (s, 3H), 3.50 (s, 1H), 2.90 (s, 3H), 1.13 (d, *J* = 6.6 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 159.5, 143.7, 143.0, 139.1, 136.3, 135.9, 129.1, 128.3, 127.2, 126.5, 126.4, 124.2, 120.0, 115.4, 113.6, 113.5, 112.6, 58.5, 55.1, 21.7, 20.5; HRMS (ESI) m/z calculated for $C_{23}H_{23}N_3O$ $[M+H]^+$: 358.1914; found $[M+H]^+$: 358.1910.

**2-(furan-2-yl)-6-iodo-N-(p-tolyl)imidazo[1,2-a]pyridin-3-amine (N19)**



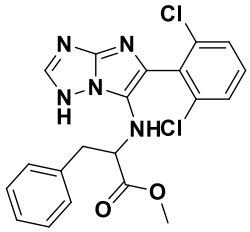
White solid (178 mg, 60% yield), M.P. > 300 °C; $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ δ 8.15 (s, 1H), 7.98 (s, 1H), 7.75 – 7.69 (m, 1H), 7.51 – 7.41 (m, 2H), 6.94 (d, *J* = 8.2 Hz, 2H), 6.64 (d, *J* = 3.3 Hz, 1H), 6.57 – 6.51 (m, 1H), 6.40 (d, *J* = 8.2 Hz, 2H), 2.16 (s, 3H); $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 147.9, 143.0, 142.8, 140.4, 132.5, 130.9, 129.9, 129.8, 127.3, 127.3, 118.8, 118.5, 113.1, 111.7, 108.3, 76.5, 20.1; HRMS (ESI) m/z calculated for $C_{18}H_{14}IN_3O$ $[M+H]^+$: 416.0254; found $[M+H]^+$: 416.0252.

**N-(1-(4-fluorophenyl)propyl)-2-isobutylimidazo[1,2-a]pyrimidin-3-amine (N22)**



Yellow oil (190 mg, 58% yield); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.43 – 8.27 (m, 1H), 8.16 (dd, *J* = 6.7, 2.1 Hz, 1H), 7.32 – 7.16 (m, 2H), 7.06 – 6.85 (m, 2H), 6.67 (dd, *J* = 6.8, 4.1 Hz, 1H), 3.92 (t, *J* = 5.8 Hz, 1H), 3.44 (s, 1H), 2.57 – 2.44 (m, 2H), 2.28 – 2.14 (m, 1H), 2.01 – 1.87 (m, 1H), 1.87 – 1.73 (m, 1H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 161.9 (d, *J* = 245.9 Hz), 147.9, 144.3, 141.6, 138.5 (d, *J* = 3.2 Hz), 129.6, 128.64 (d, *J* = 8.0 Hz), 123.4, 115.1 (d, *J* = 21.2 Hz), 107.2, 64.7, 36.2, 29.4, 28.3, 22.5, 10.7; HRMS (ESI) m/z calculated for $C_{19}H_{23}FN_4$ [M+H]+: 327.1980; found [M+H]+: 327.1977.

**methyl (5-(2,6-dichlorophenyl)-1H-imidazo[1,2-b][1,2,4]triazol-6-yl)phenylalaninate (O16)**

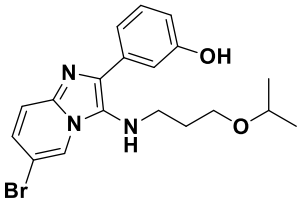


Yellow oil (123 mg, 25% yield); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.39 (m, 2H), 7.39 – 7.28 (m, 2H), 7.23 – 7.11 (m, 3H), 7.11 – 6.94 (m, 2H), 4.55 – 4.39 (m, 1H), 3.96 (d, *J* = 9.0 Hz, 1H), 3.51 (s, 3H), 3.15 – 2.92 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.0, 152.3, 147.7, 137.5, 137.2, 135.9, 131.2, 129.1, 128.3, 128.2, 127.5, 126.7, 123.4, 111.0, 59.1, 51.9, 39.3; HRMS (ESI) m/z calculated for $C_{20}H_{17}Cl_2N_5O_2$ $[M+H]^+$: 430.0832; found $[M+H]^+$: 430.0830.

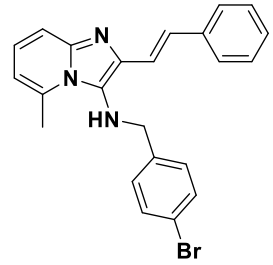
## Destination plate IV

**3-(6-bromo-3-((3-isopropoxypropyl)amino)imidazo[1,2-a]pyridin-2-yl)phenol (C14)**

Light yellow solid (350 mg, 87% yield), M.P.= 131 – 133 °C; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.73 (s, 1H), 7.45 (d, *J* = 9.5 Hz, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 7.32 – 7.23 (m, 1H), 7.16 (d, *J* = 9.5 Hz, 1H), 6.82 (d, *J* = 7.9 Hz, 1H), 3.83 – 3.49 (m, 4H), 3.12 (d, *J* = 5.9 Hz, 2H), 1.89 – 1.78 (m, 2H), 1.20 (d, *J* = 6.1 Hz, 6H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 157.5, 139.6, 135.8, 134.4, 129.8, 127.5, 127.0, 122.6, 118.1, 117.7, 115.5, 114.9, 106.9, 71.9, 66.4, 46.3, 30.3, 22.1; HRMS (ESI) m/z calculated for $C_{19}H_{22}BrN_3O_2$ $[M+H]^+$: 404.0968; found $[M+H]^+$: 404.0965.

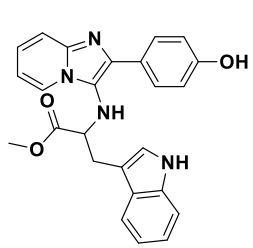


**(E)-N-(4-bromobenzyl)-5-methyl-2-styrylimidazo[1,2-a]pyridin-3-amine (D9)**



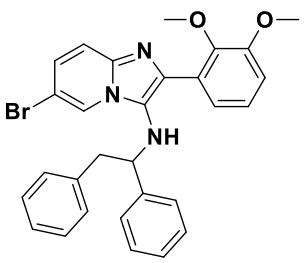
Light yellow solid (372 mg, 89% yield), M.P.= 234 – 235 °C; $^{1}$H NMR (500 MHz, DMSO-$d_6$) δ 7.55 (d, $J$ = 8.3 Hz, 2H), 7.43 – 7.32 (m, 8H), 7.30 – 7.25 (m, 1H), 7.23 (d, $J$ = 16.2 Hz, 1H), 6.86 – 6.75 (m, 2H), 5.35 (t, $J$ = 6.5 Hz, 1H), 4.13 (d, $J$ = 6.5 Hz, 2H), 2.97 (s, 3H); $^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 141.3, 138.8, 137.8, 136.6, 131.2, 130.8, 130.3, 129.0, 128.8, 127.8, 126.3, 122.0, 120.4, 119.4, 117.0, 114.7, 112.7, 54.4, 18.8; HRMS (ESI) m/z calculated for $C_{23}H_{20}BrN_3$ $[M+H]^+$: 418.0913; found $[M+H]^+$: 418.0911.

**methyl (2-(4-hydroxyphenyl)imidazo[1,2-a]pyridin-3-yl)tryptophanate (K19)**



Yellow solid (389 mg, 91% yield), M.P.= 131 – 132 °C; $^{1}$H NMR (500 MHz, MeOD-$d_4$) δ 7.92 (d, $J$ = 6.8 Hz, 1H), 7.45 (d, $J$ = 8.6 Hz, 2H), 7.29 – 7.16 (m, 3H), 7.15 – 7.03 (m, 1H), 7.03 – 6.91 (m, 2H), 6.84 (t, $J$ = 7.5 Hz, 1H), 6.67 – 6.52 (m, 3H), 3.83 (dd, $J$ = 8.2, 5.9 Hz, 1H), 3.26 (s, 3H), 3.19 – 2.97 (m, 2H); $^{13}$C NMR (126 MHz, MeOD-$d_4$) δ 175.5, 159.6, 139.3, 138.0, 131.0, 130.8, 129.9, 128.3, 125.9, 125.8, 124.9, 122.6, 121.1, 119.9, 119.1, 116.8, 115.4, 113.5, 112.3, 110.8, 61.3, 52.5, 30.4; HRMS (ESI) m/z calculated for $C_{25}H_{22}N_4O_3$ $[M+H]^+$: 427.1765; found $[M+H]^+$: 427.1761.

**6-bromo-2-(2,3-dimethoxyphenyl)-N-(1,2-diphenylethyl)imidazo[1,2-a]pyridin-3-amine (P13)**

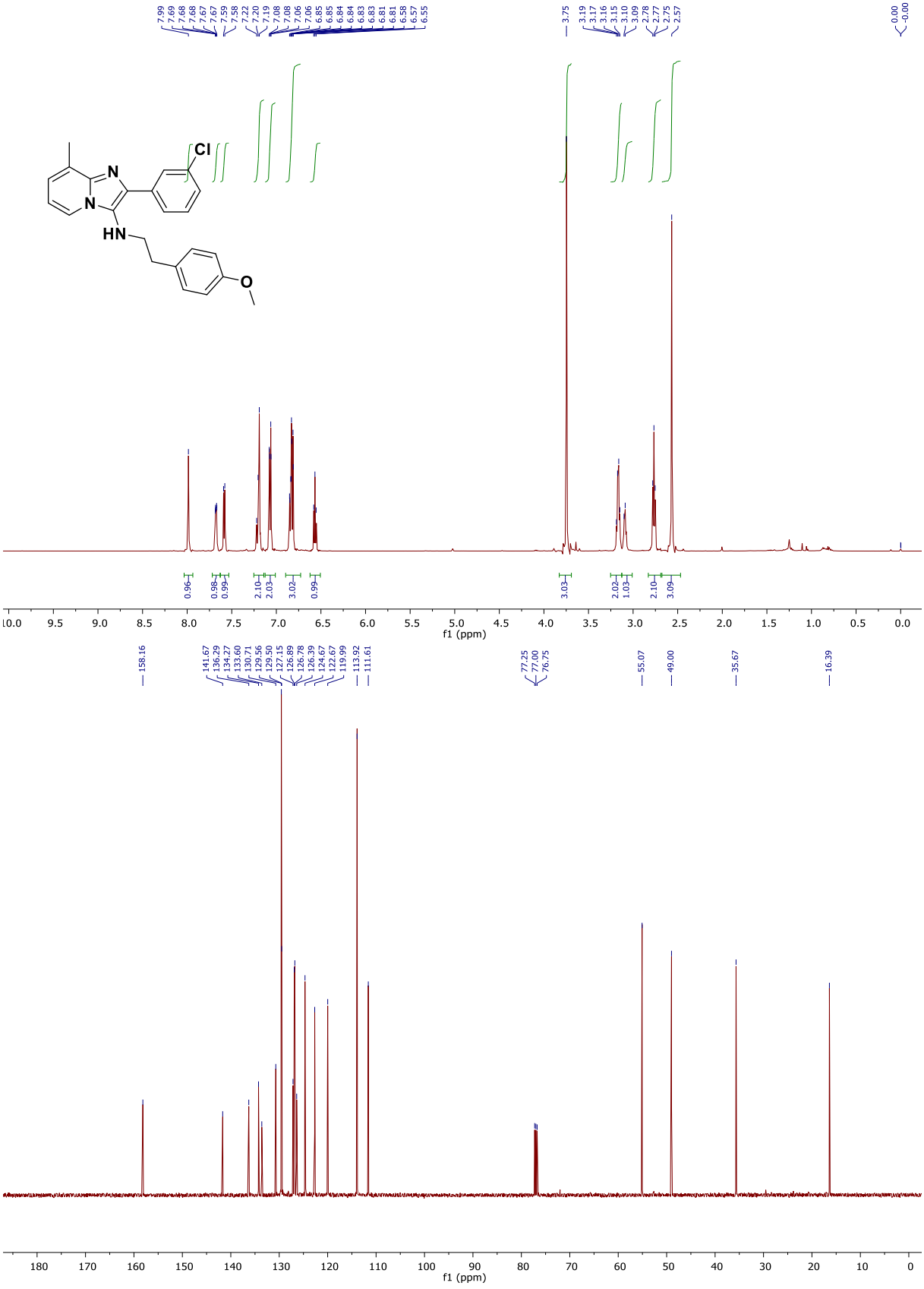


Yellow oil (303 mg, 57% yield); $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 1H), 7.35 – 7.26 (m, 4H), 7.19 (d, $J$ = 7.0 Hz, 2H), 7.10 – 6.97 (m, 3H), 6.96 – 6.86 (m, 5H), 6.83 (dd, $J$ = 7.9, 1.7 Hz, 1H), 4.77 (d, $J$ = 9.6 Hz, 1H), 3.94 (s, 3H), 3.88 – 3.79 (m, 1H), 3.53 (s, 3H), 3.13 – 2.96 (m, 2H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 152.3, 145.4, 142.5, 140.0, 139.2, 134.0, 129.4, 128.4, 128.3, 127.8, 127.2, 127.1, 126.6, 126.5, 126.4, 124.6, 123.0, 122.8, 117.8, 111.3, 106.2, 64.4, 61.3, 55.8, 43.3; HRMS (ESI) m/z calculated for $C_{29}H_{26}BrN_3O_2$ $[M+H]^+$: 528.1281; found $[M+H]^+$: 528.1282.

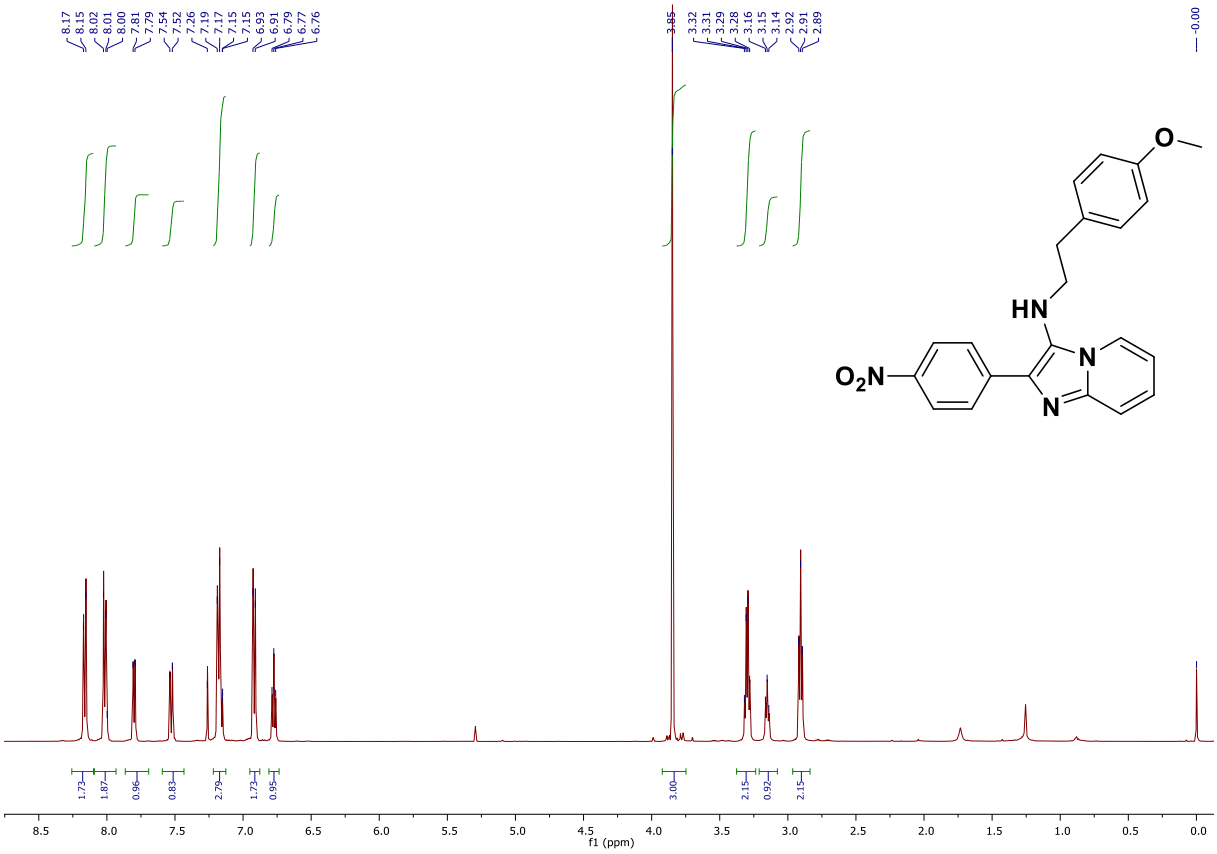
## $^{1}H$ and $^{13}C$ NMR spectra

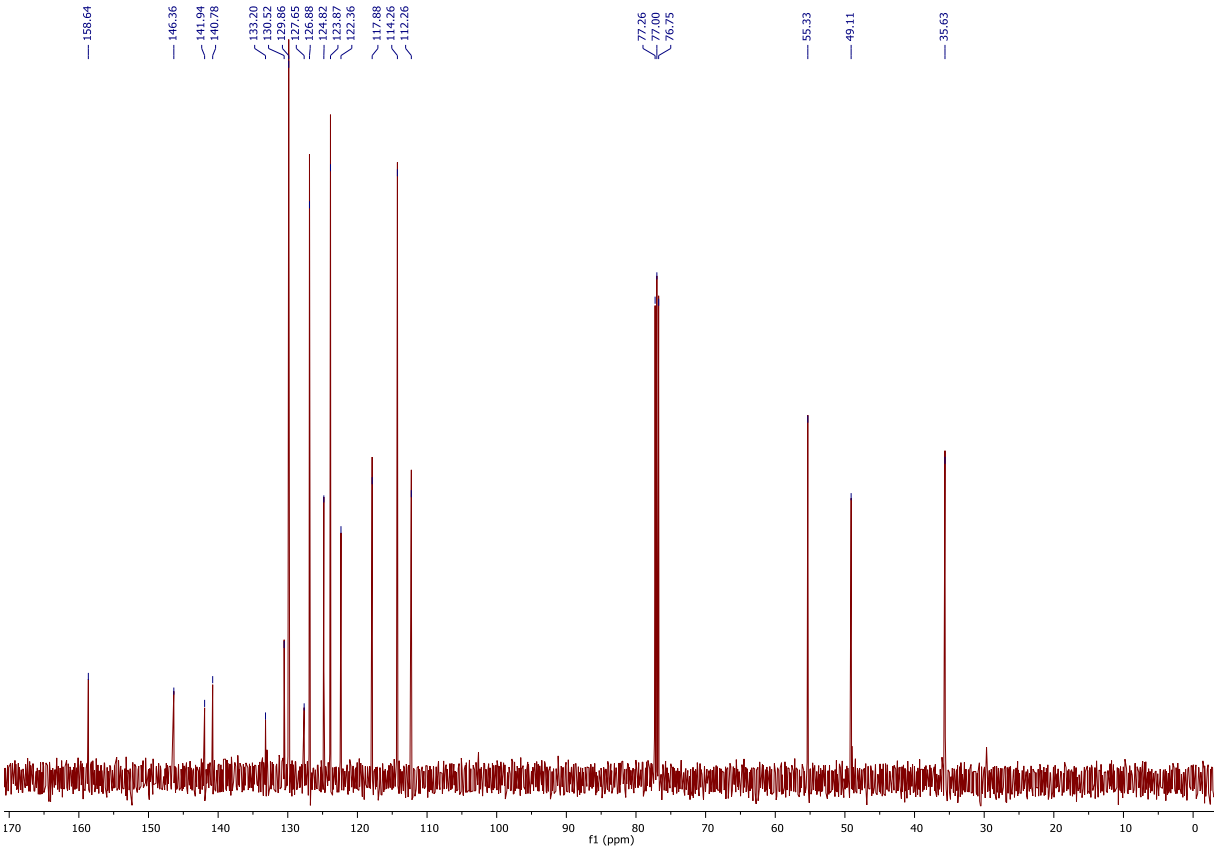
### Destination plate I

### 2-(3-chlorophenyl)-N-(4-methoxyphenethyl)-8-methylimidazo[1,2-a]pyridin-3-amine (C13)

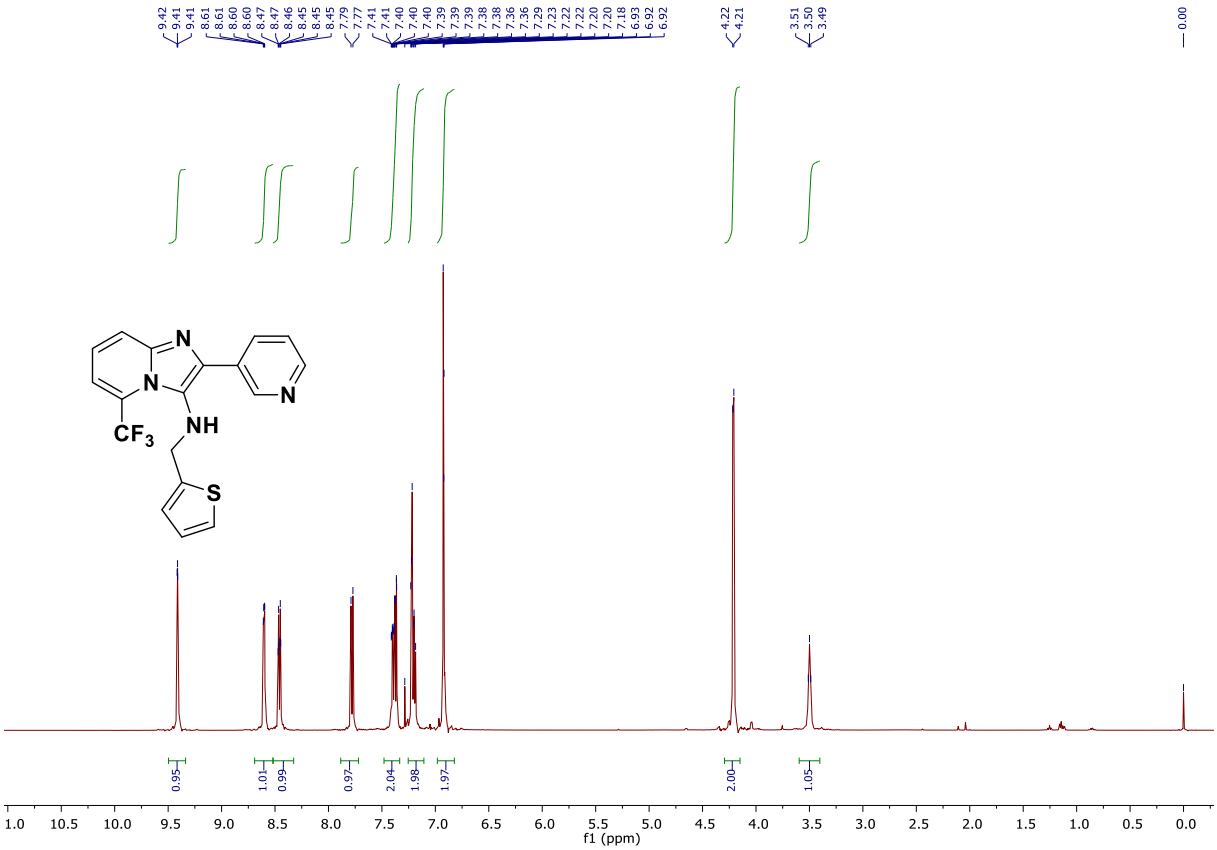


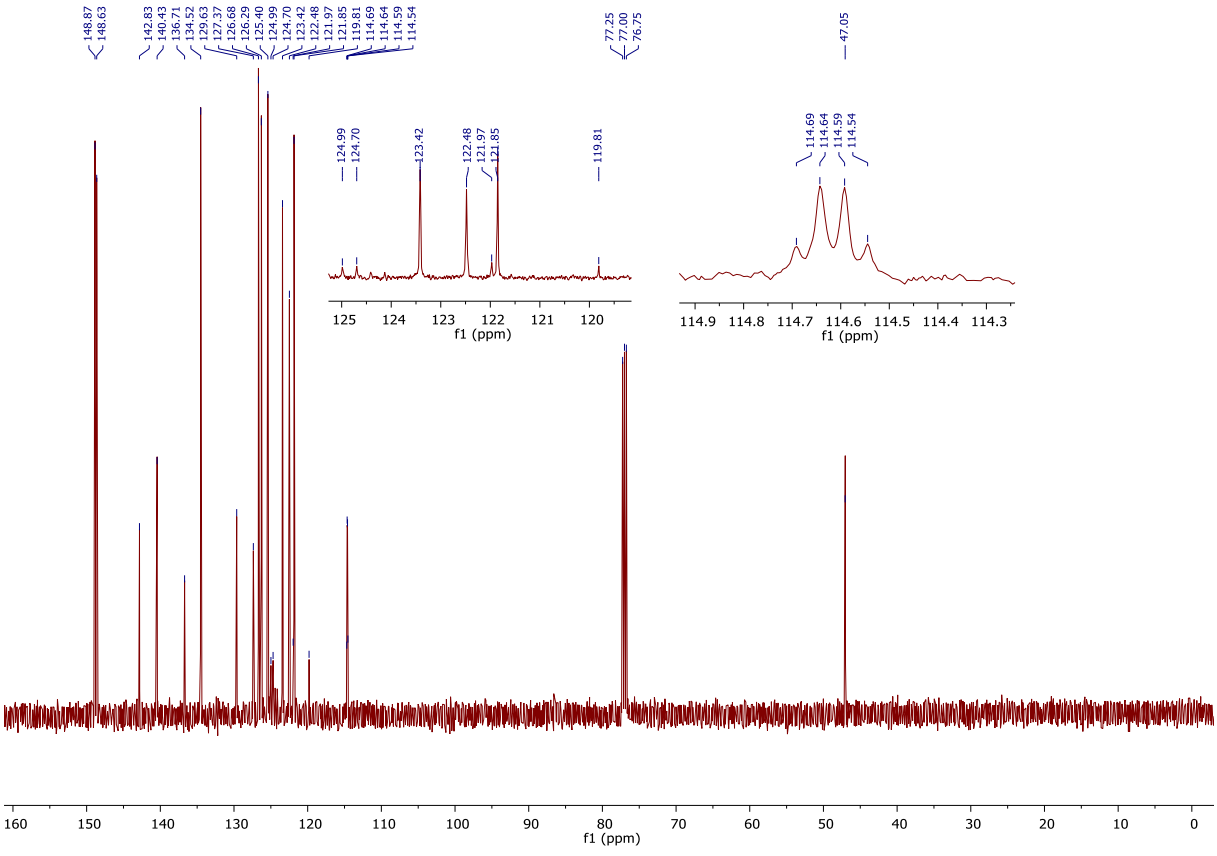
**N-(4-methoxyphenethyl)-2-(4-nitrophenyl)imidazo[1,2-a]pyridin-3-amine (J21)**



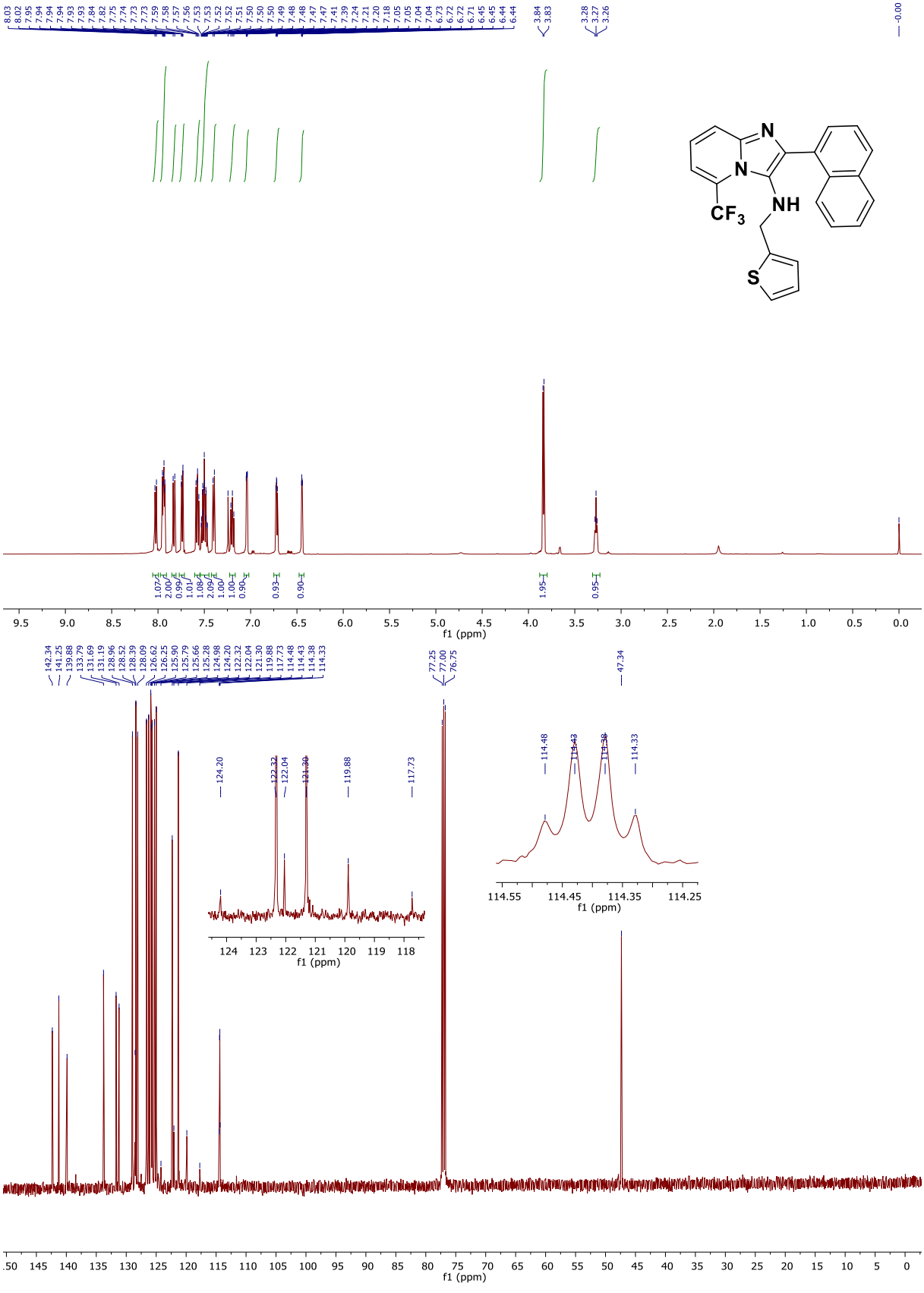
## 2-(pyridin-3-yl)-N-(thiophen-2-ylmethyl)-5-(trifluoromethyl)imidazo[1,2-a]pyridin-3-amine (O4)



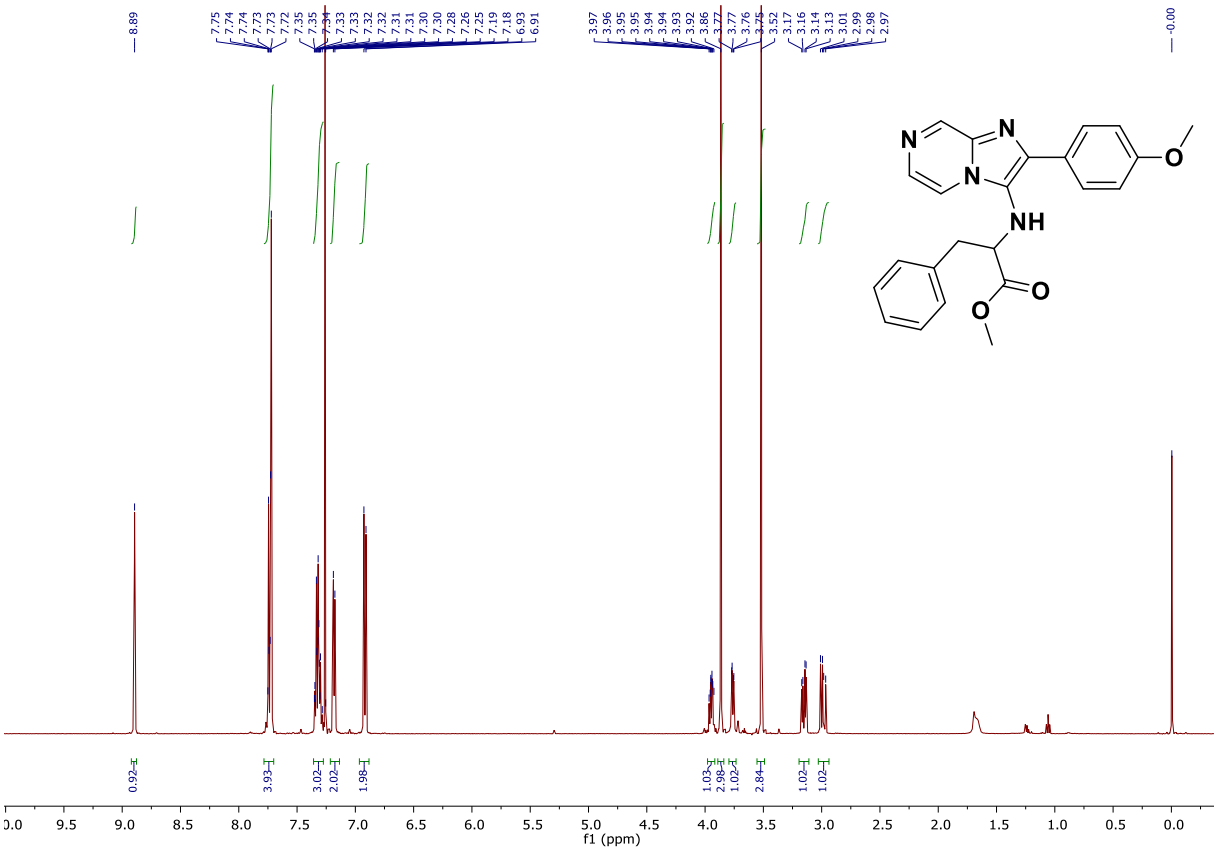



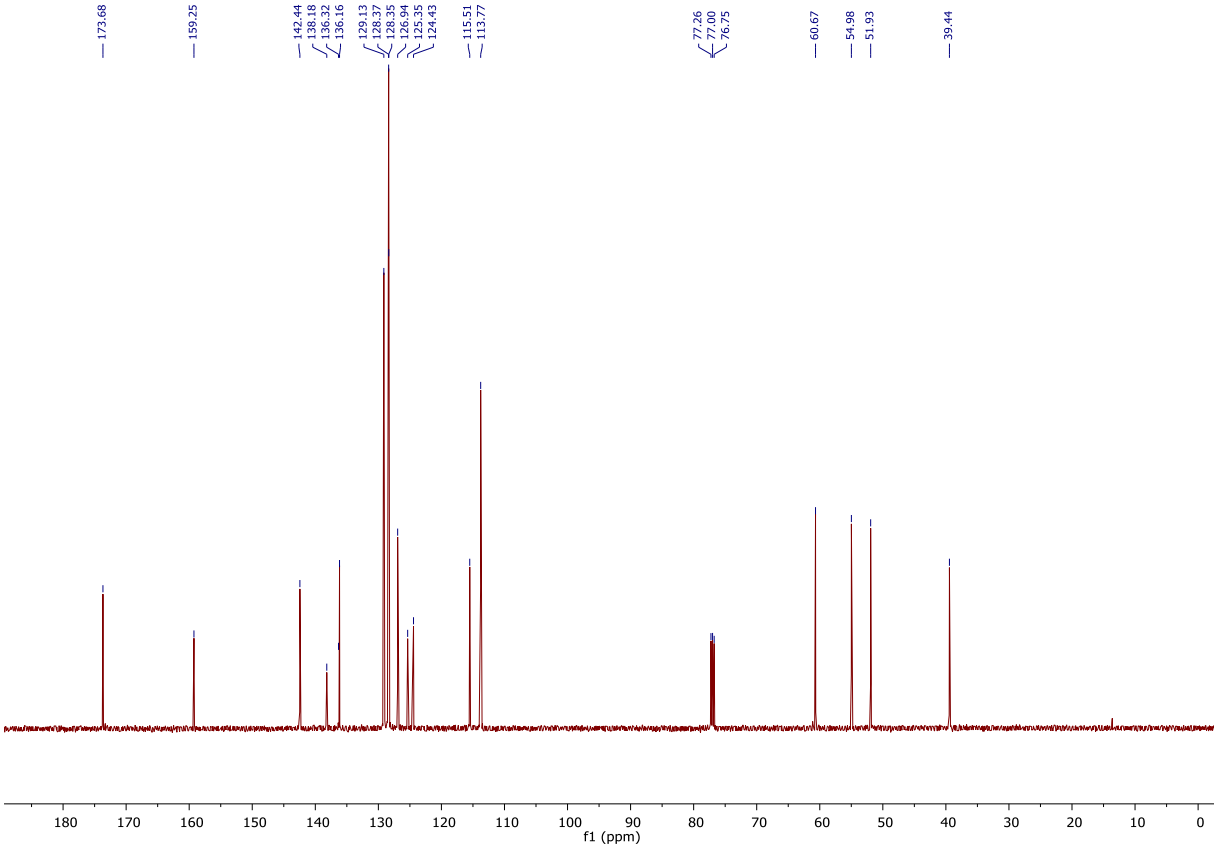
## Destination plate II

## 2-(naphthalen-1-yl)-N-(thiophen-2-ylmethyl)-5-(trifluoromethyl)imidazo[1,2-a]pyridin-3-amine (C9)

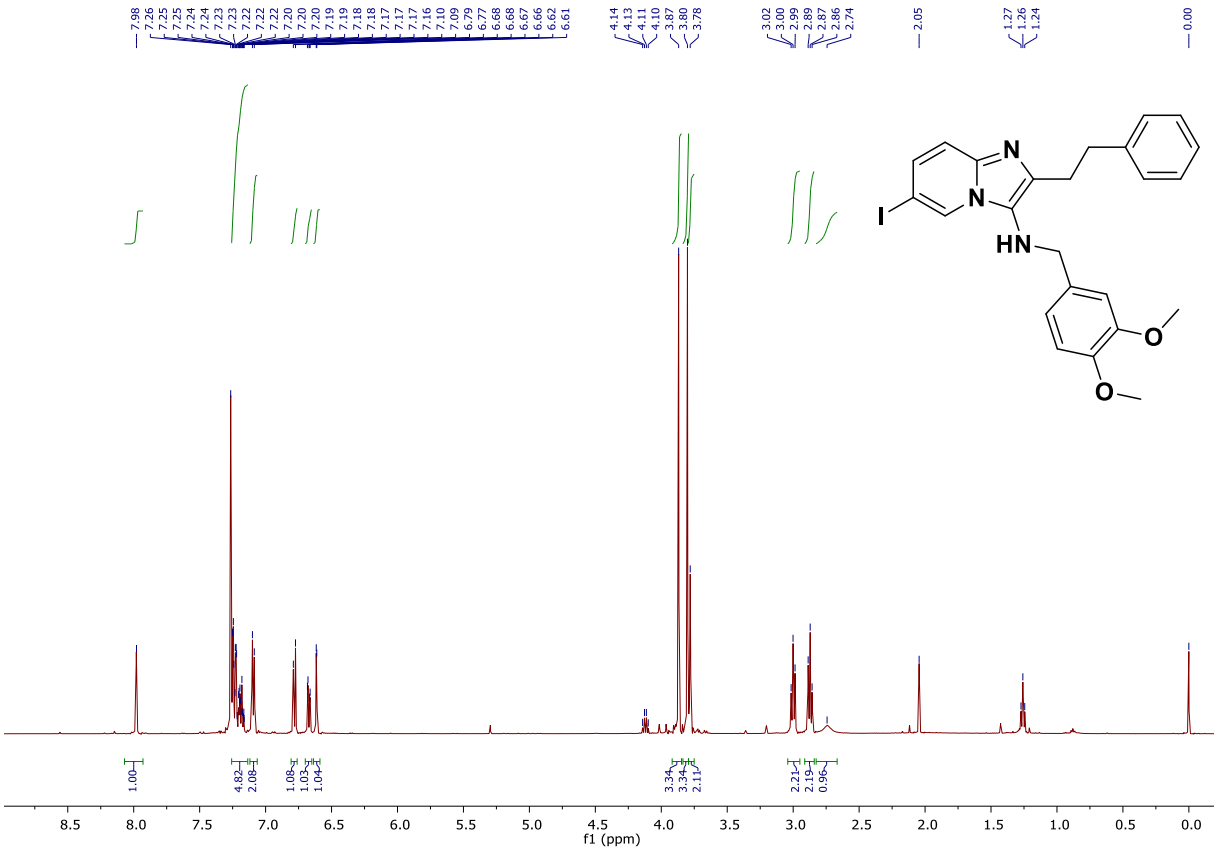


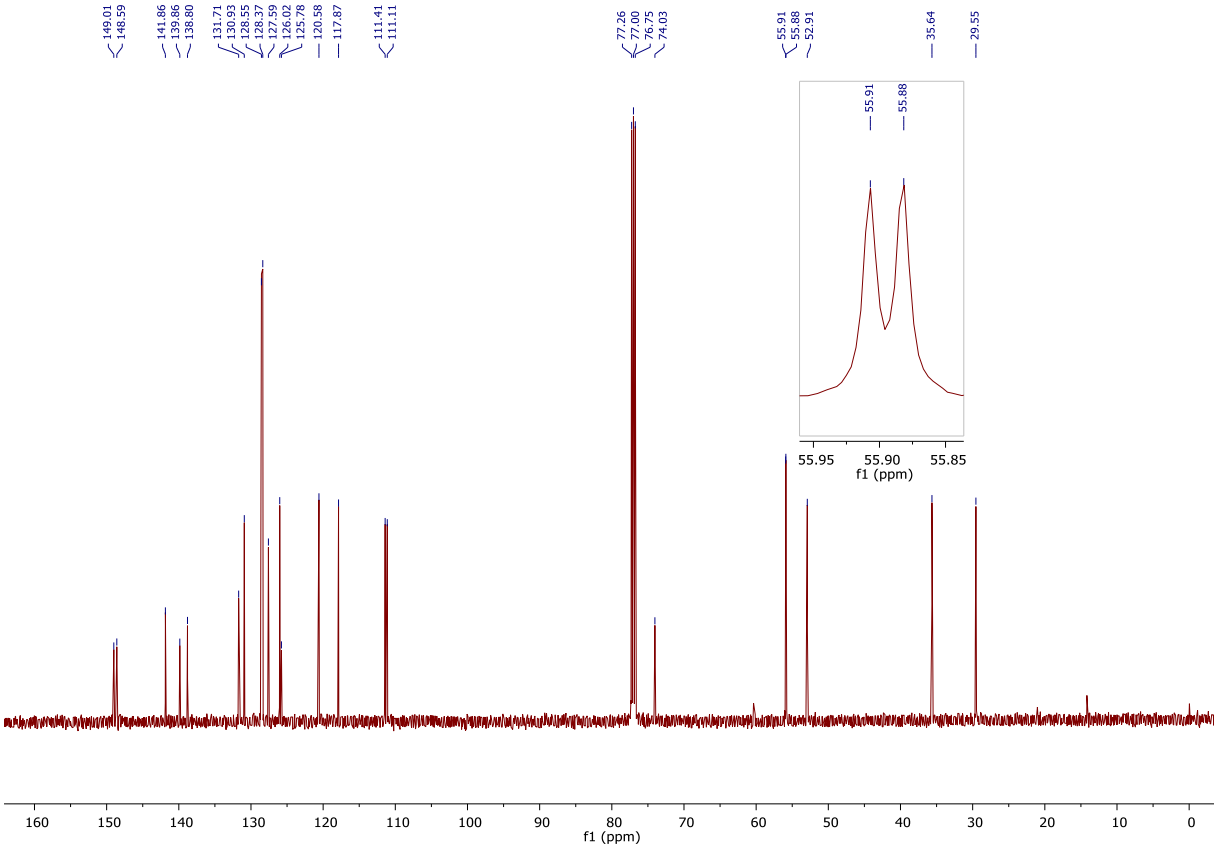
**methyl (2-(4-methoxyphenyl)imidazo[1,2-a]pyrazin-3-yl)phenylalaninate (D1)**



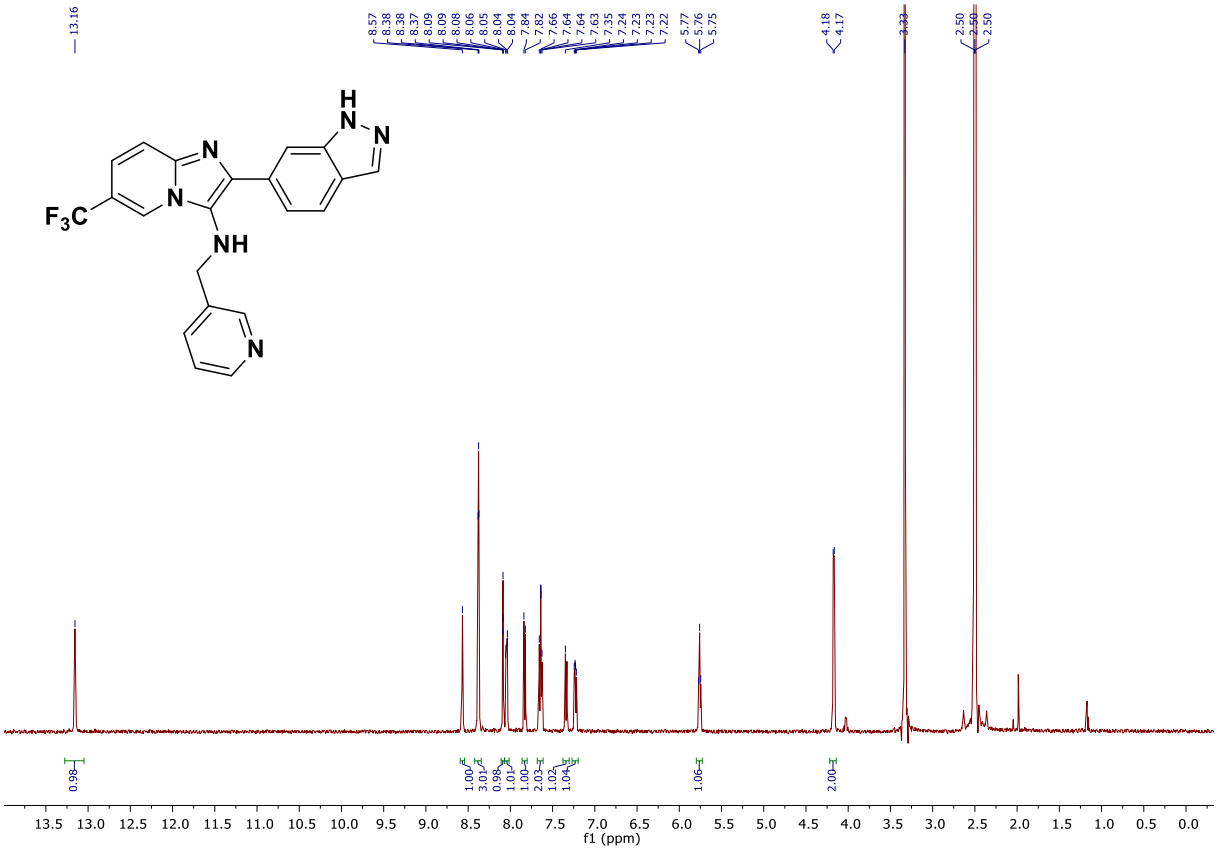



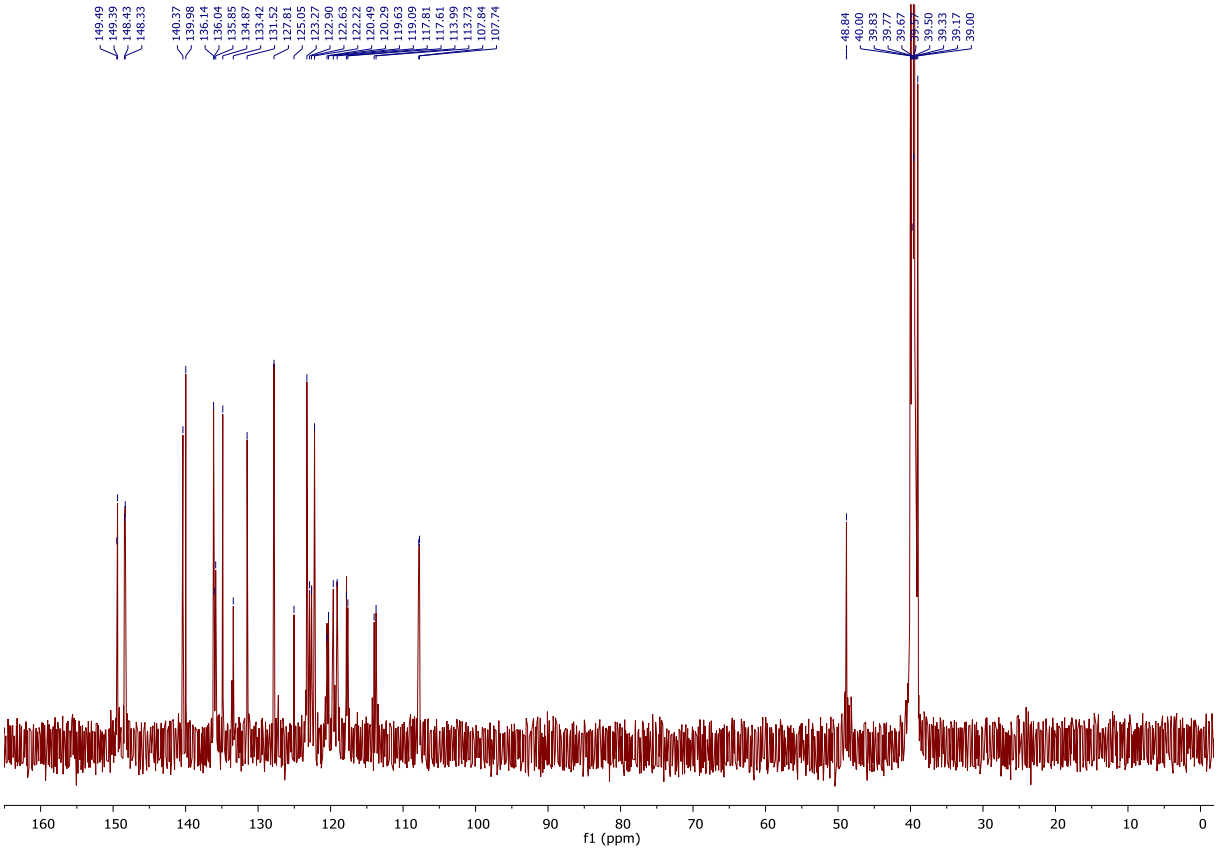
## N-(3,4-dimethoxybenzyl)-6-iodo-2-phenethylimidazo[1,2-a]pyridin-3-amine (F17)



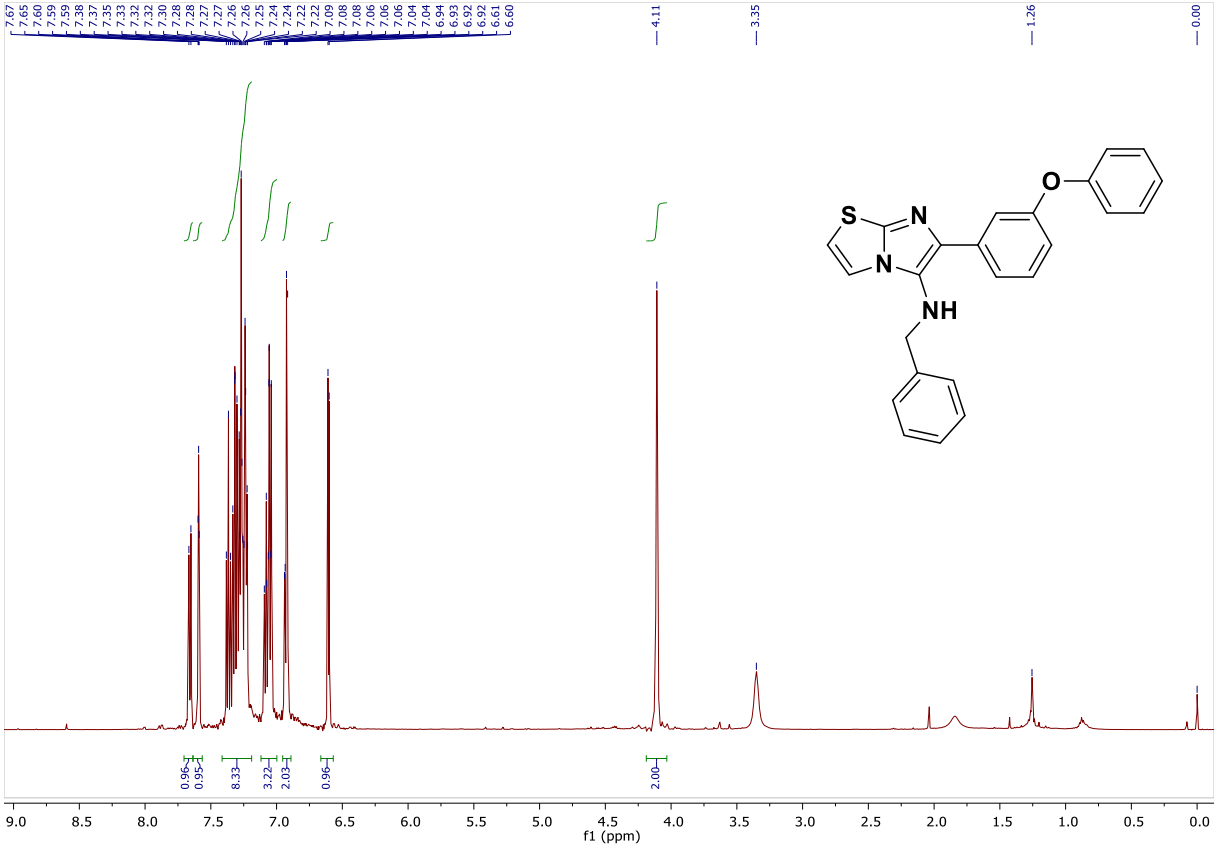



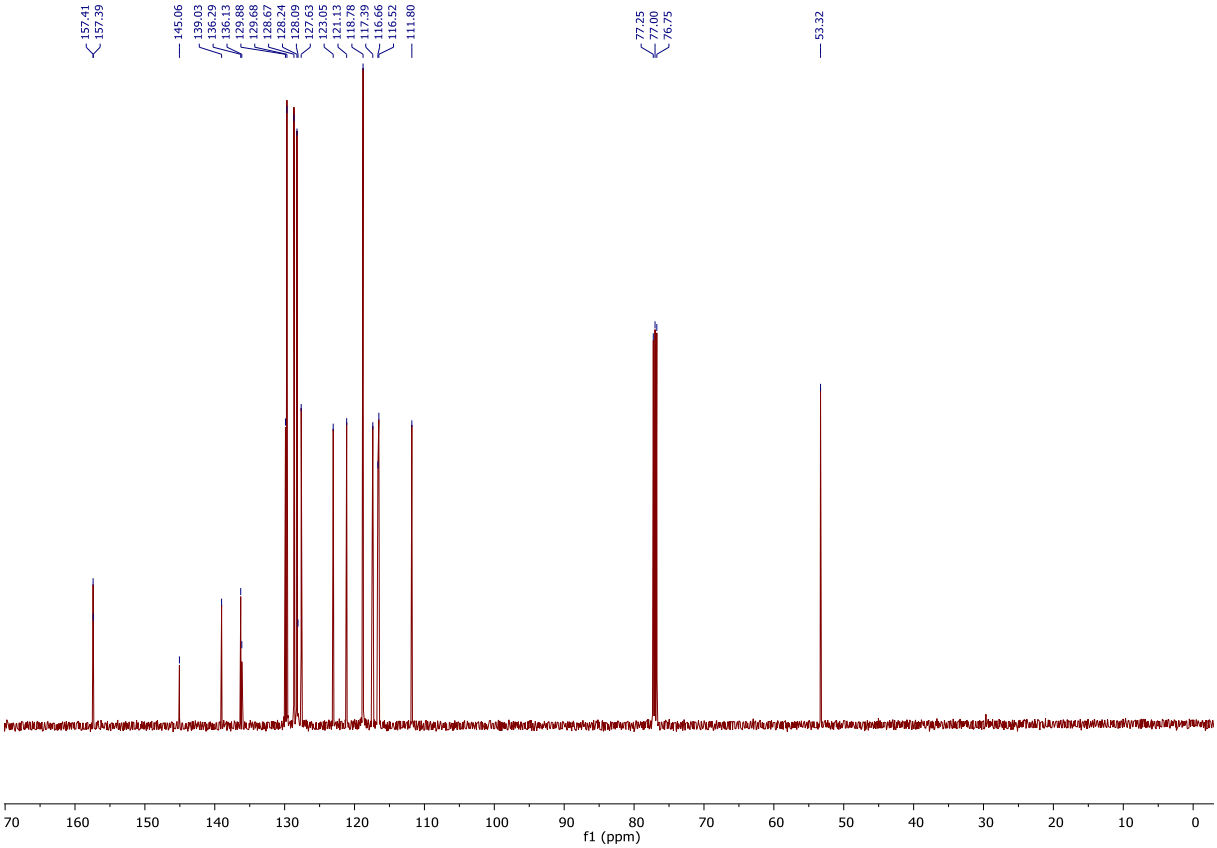
## 2-(1H-indazol-6-yl)-N-(pyridin-3-ylmethyl)-6-(trifluoromethyl)imidazo[1,2-a]pyridin-3-amine (F23)



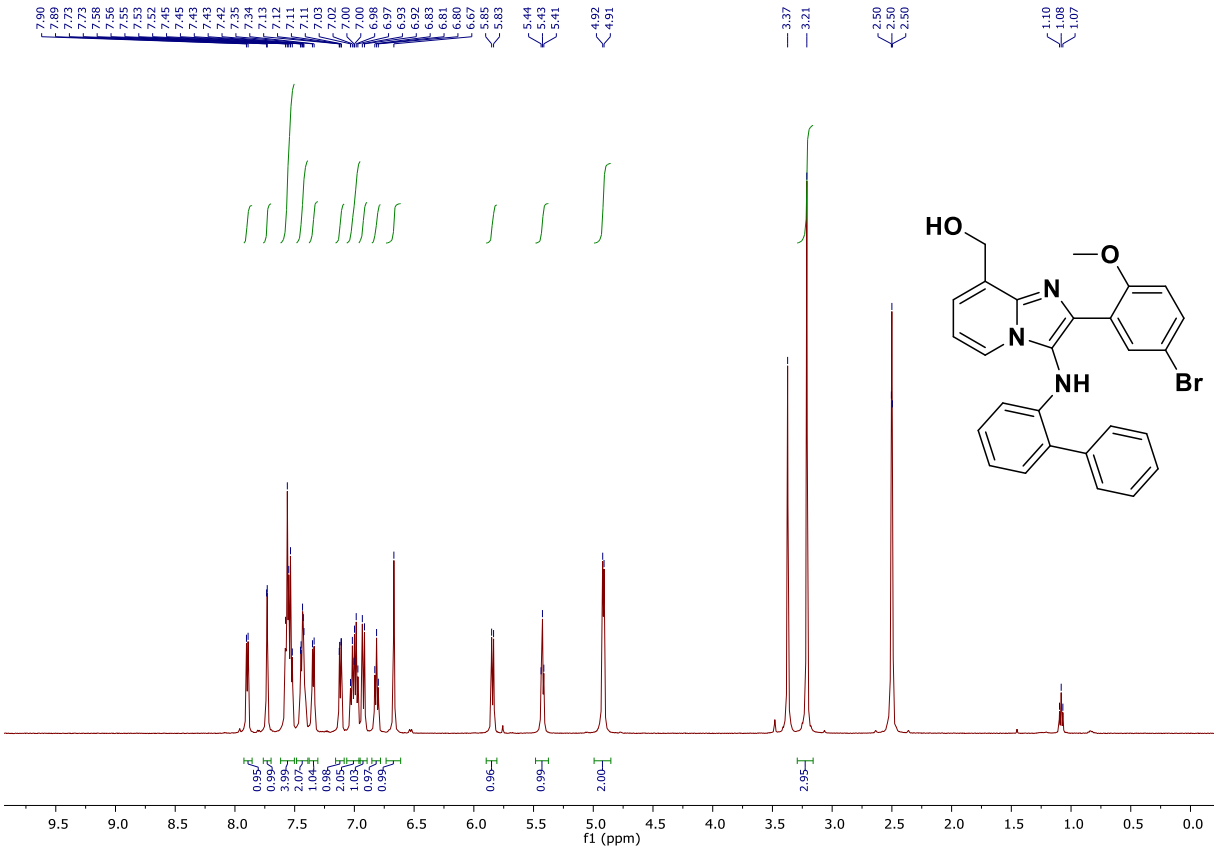



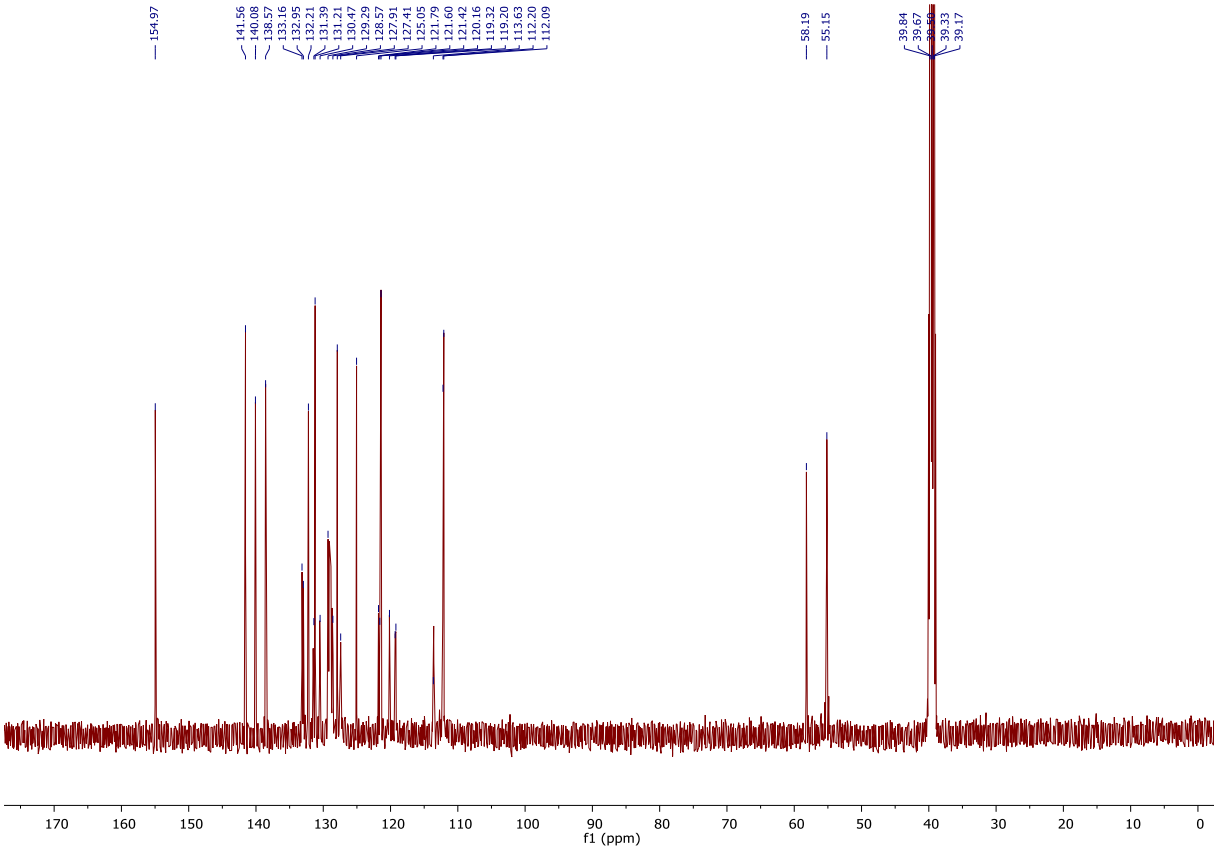
## N-benzyl-6-(3-phenoxyphenyl)imidazo[2,1-b]thiazol-5-amine (J19)



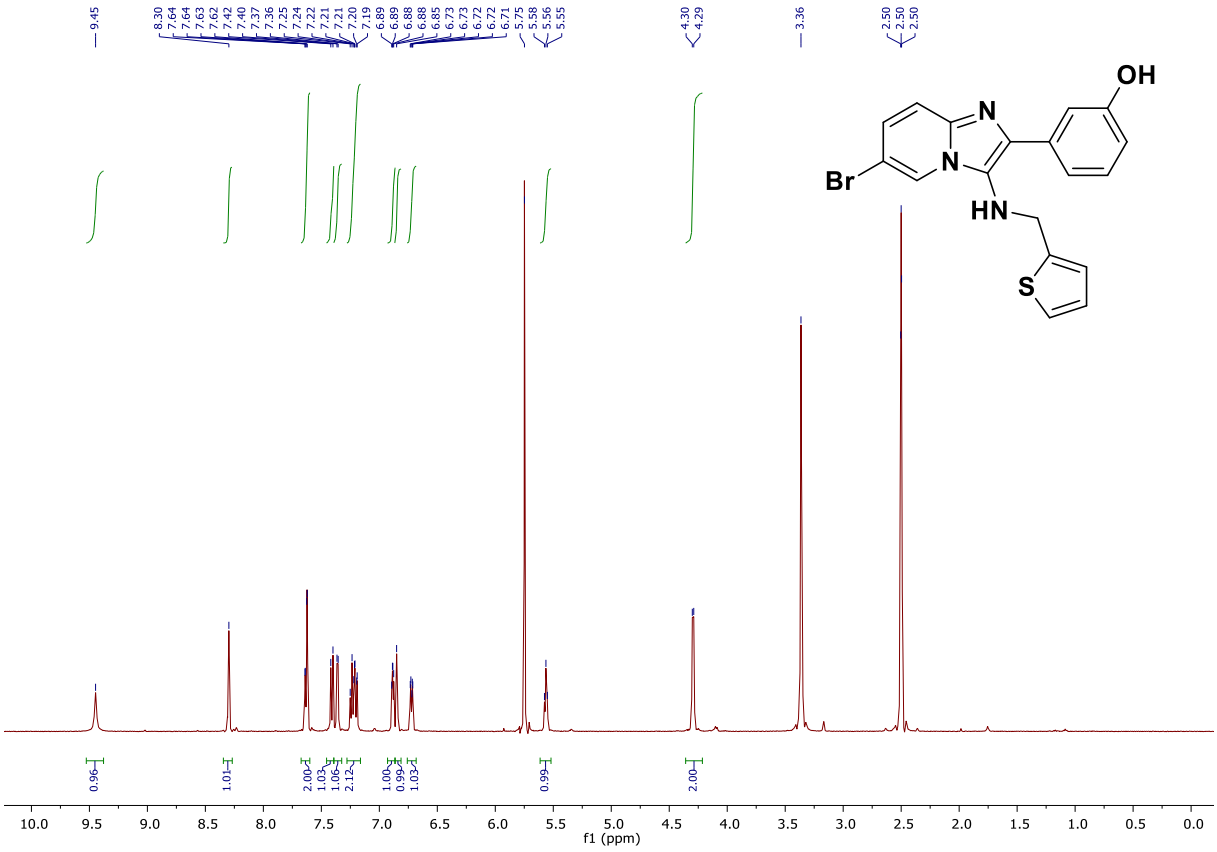



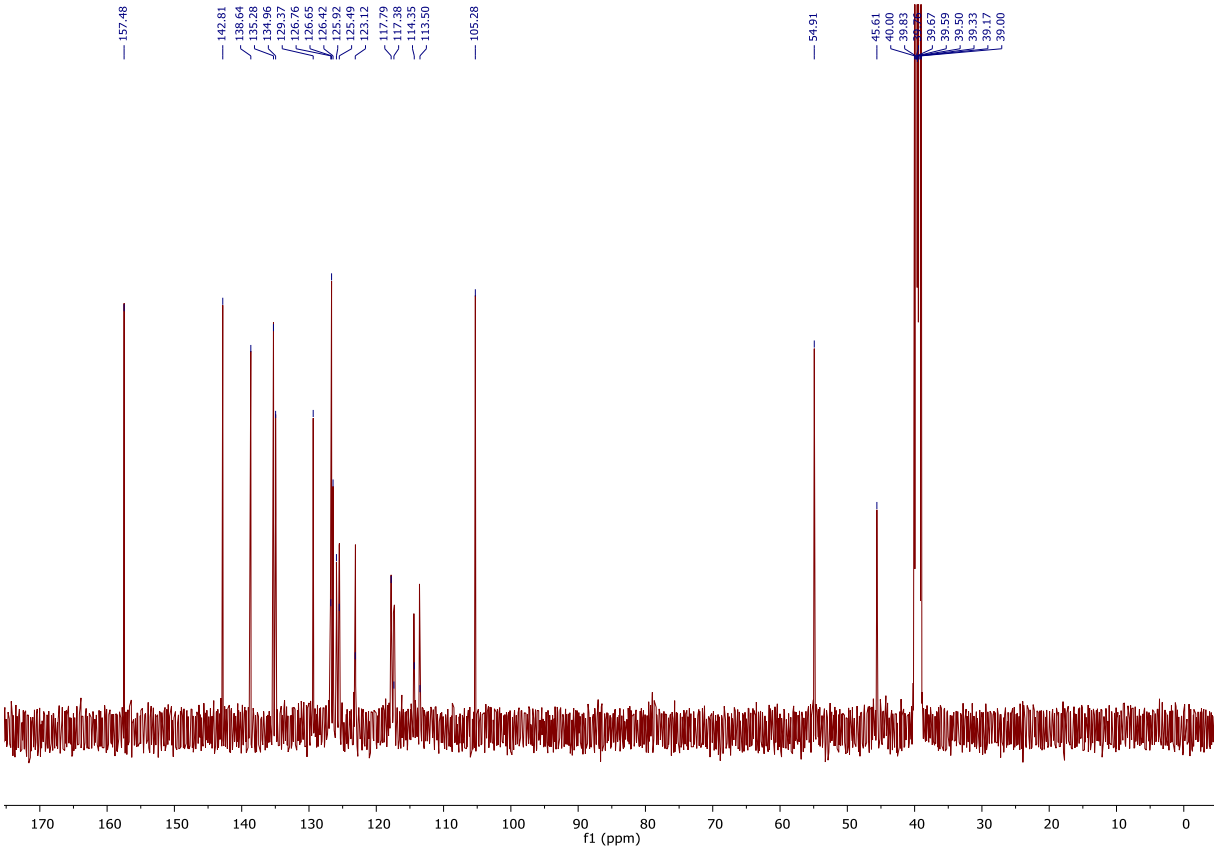
**(3-([1,1'-biphenyl]-2-ylamino)-2-(5-bromo-2-methoxyphenyl)imidazo[1,2-a]pyridin-8-yl)methanol (K14)**



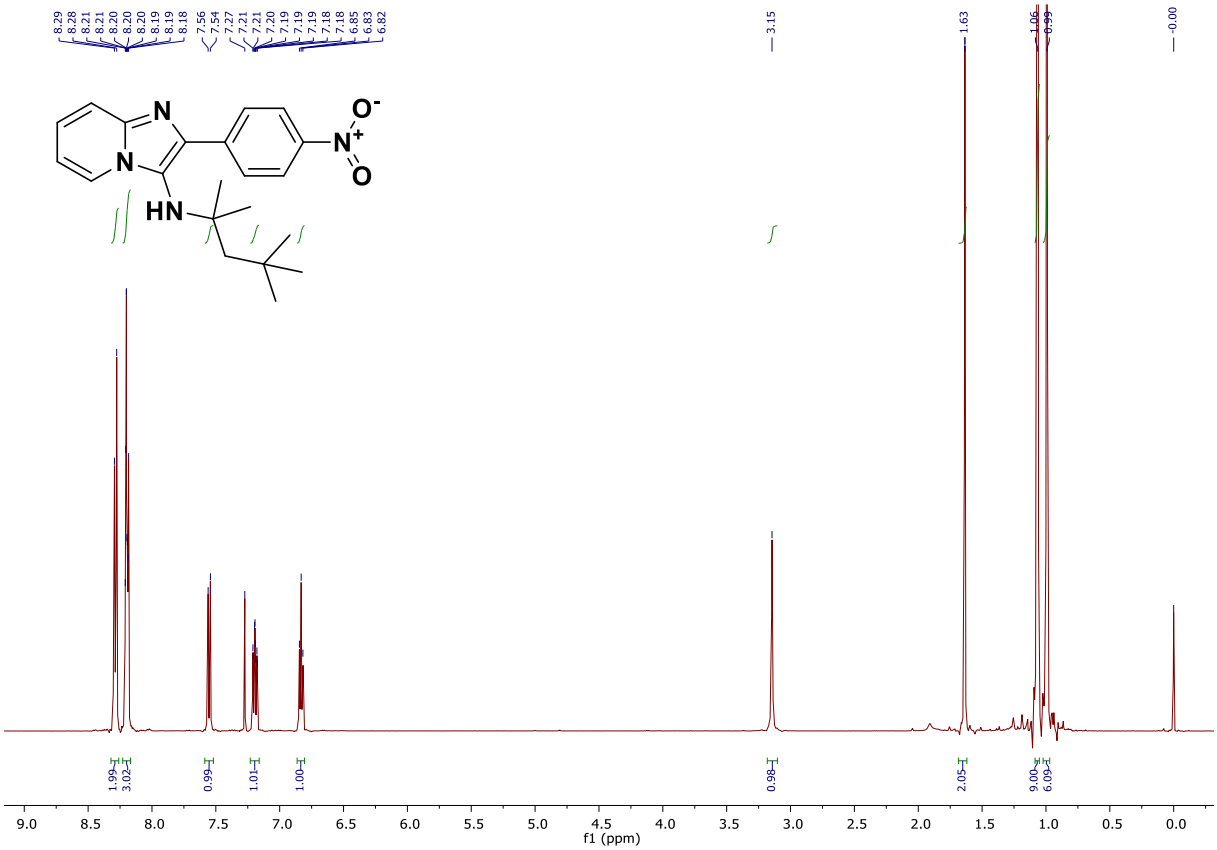



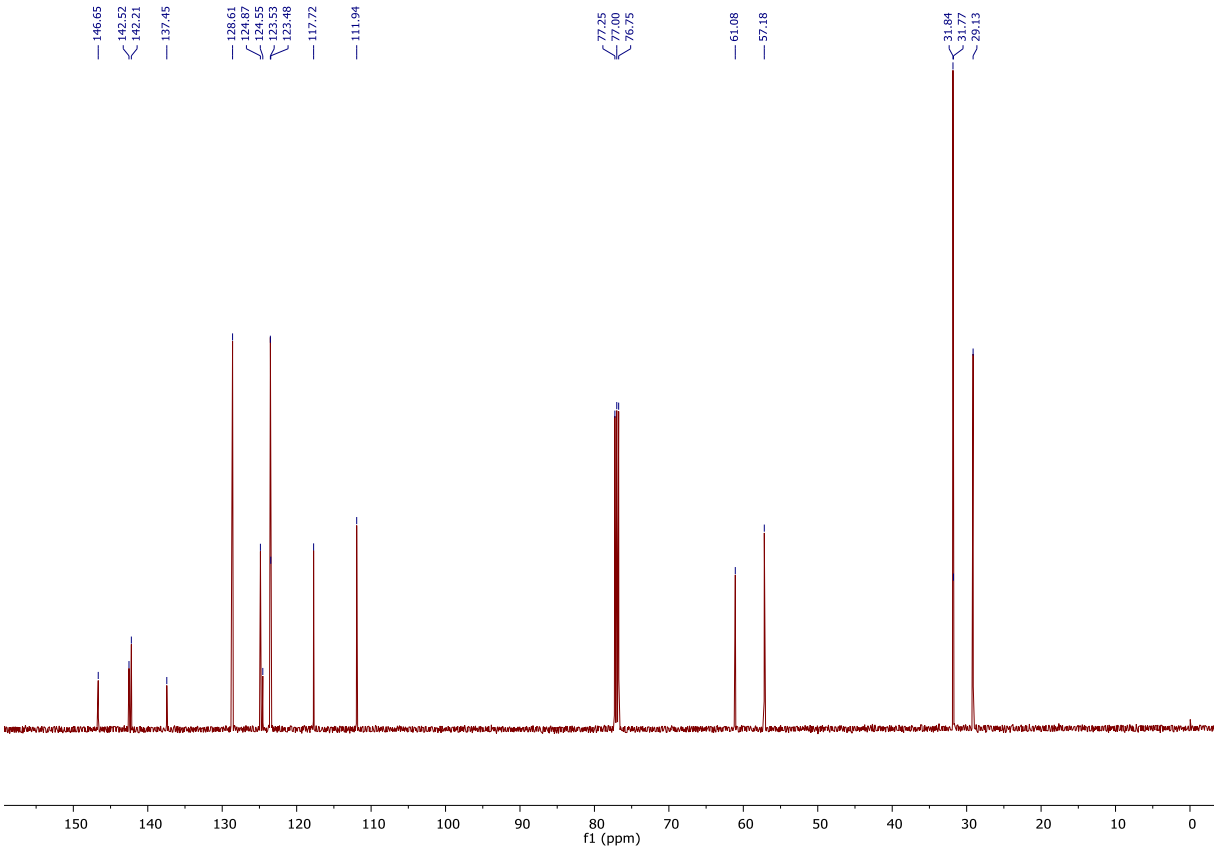
**3-(6-bromo-3-((thiophen-2-ylmethyl)amino)imidazo[1,2-a]pyridin-2-yl)phenol (M3)**



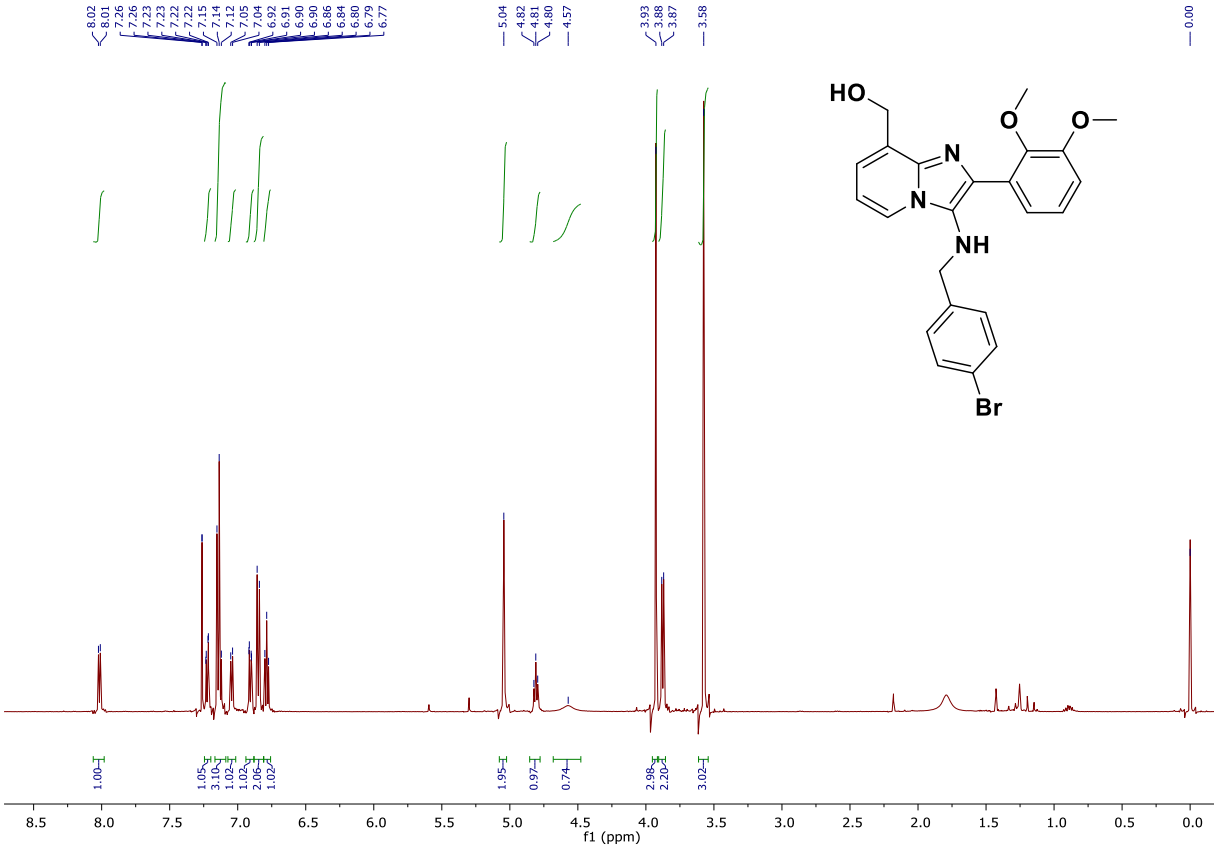
## 2-(4-nitrophenyl)-N-(2,4,4-trimethylpentan-2-yl)imidazo[1,2-a]pyridin-3-amine (P6)

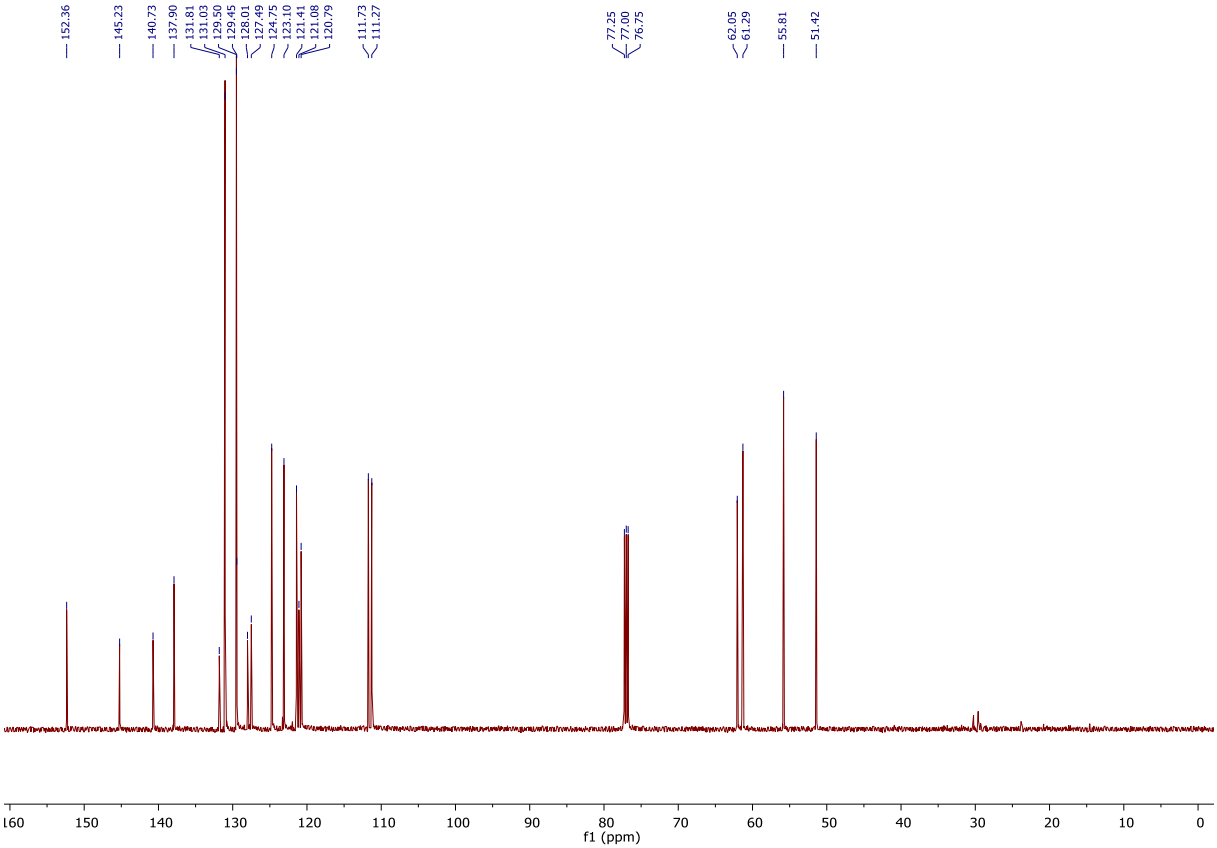


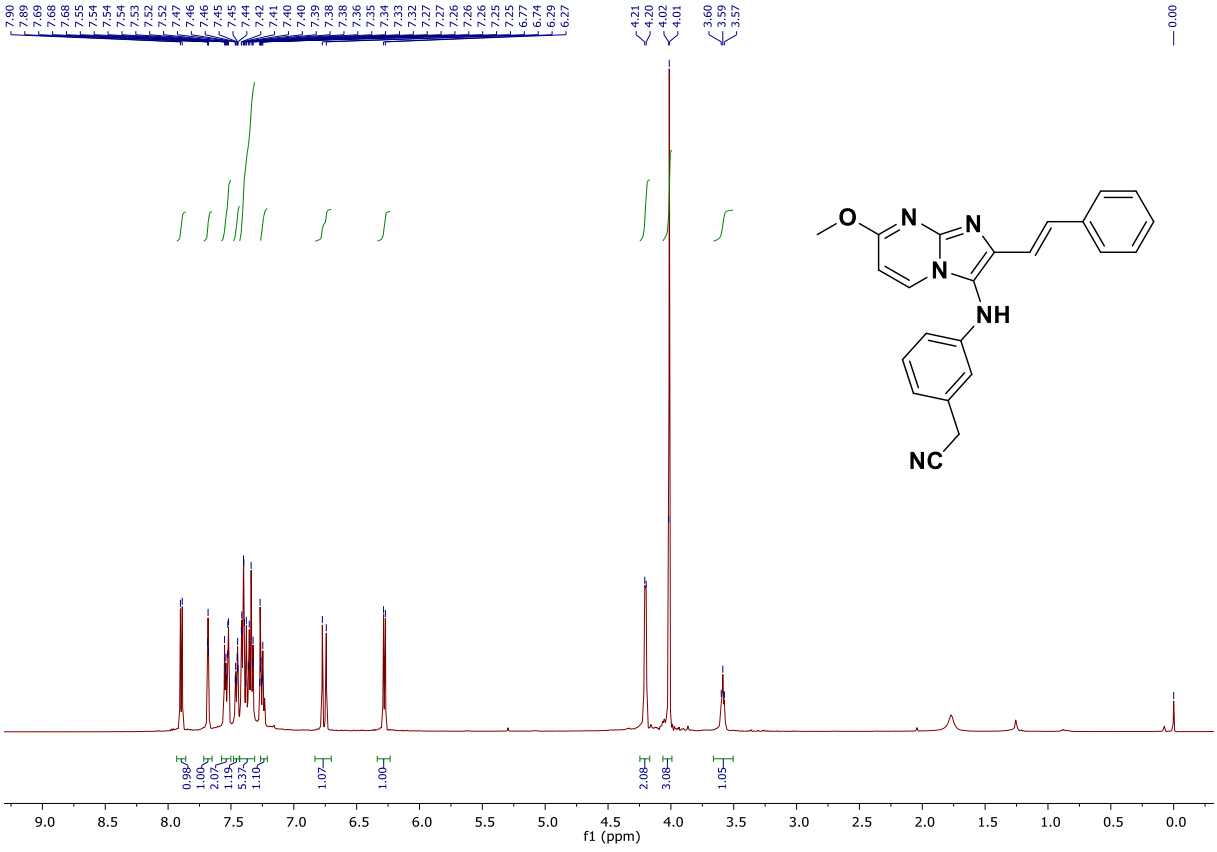
## Destination plate III

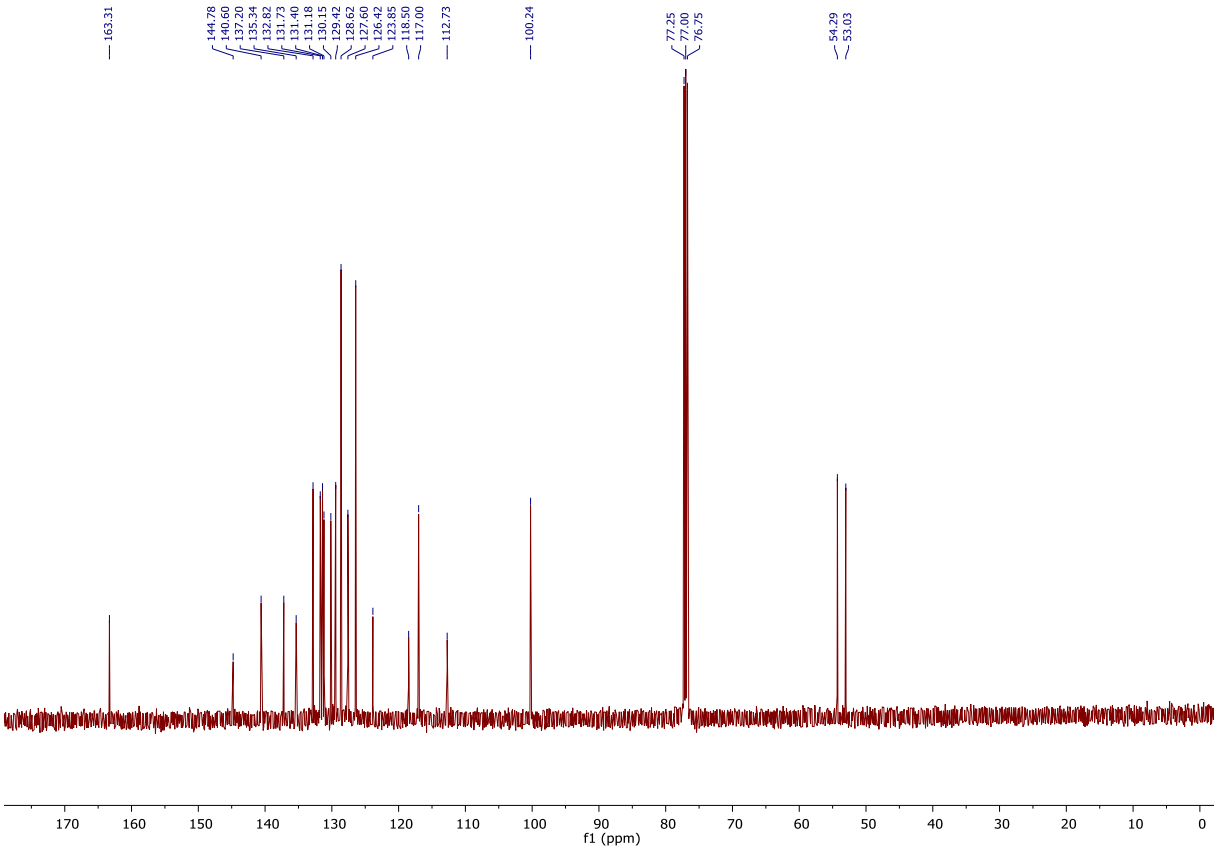
## (3-((4-bromobenzyl)amino)-2-(2,3-dimethoxyphenyl)imidazo[1,2-a]pyridin-8-yl) methanol (J14)



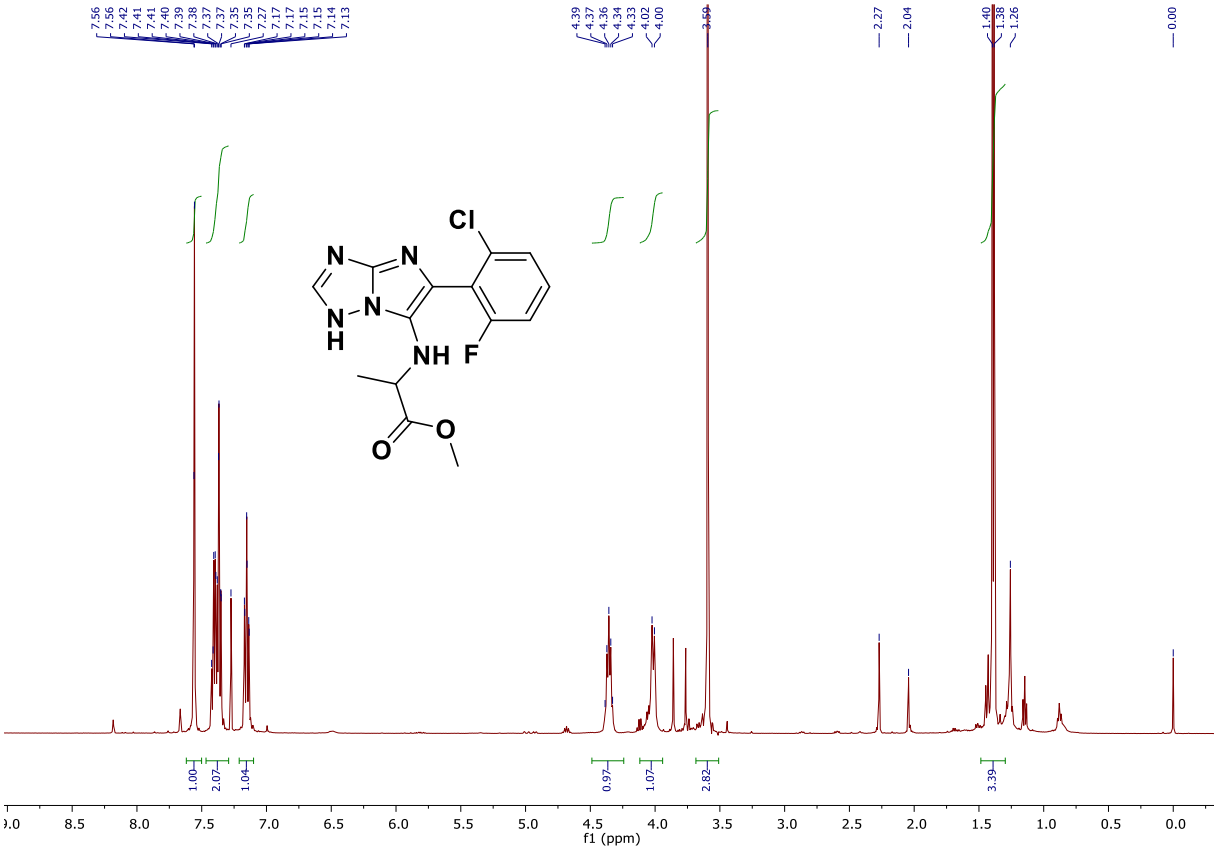



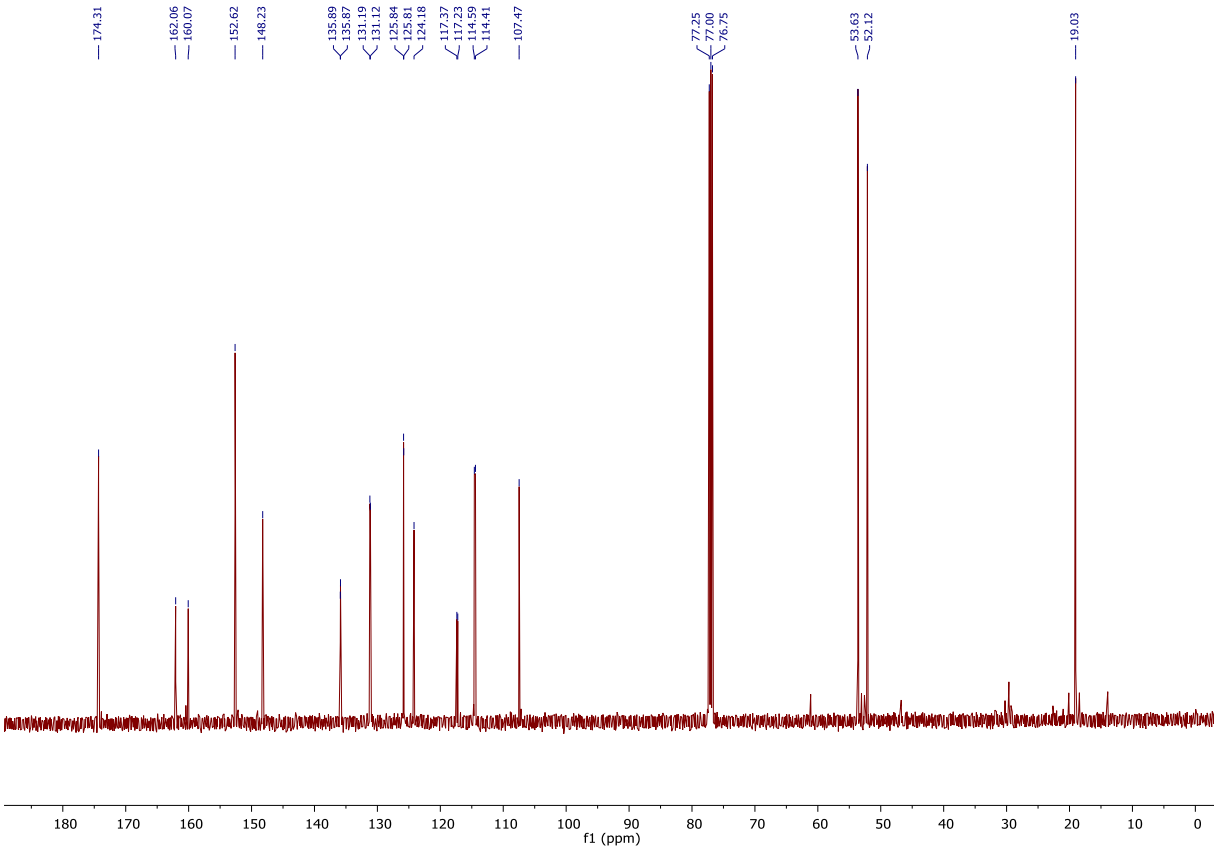
**(E)-2-(3-((7-methoxy-2-styrylimidazo[1,2-a]pyrimidin-3-yl)amino)phenyl)acetonitrile (K8)**



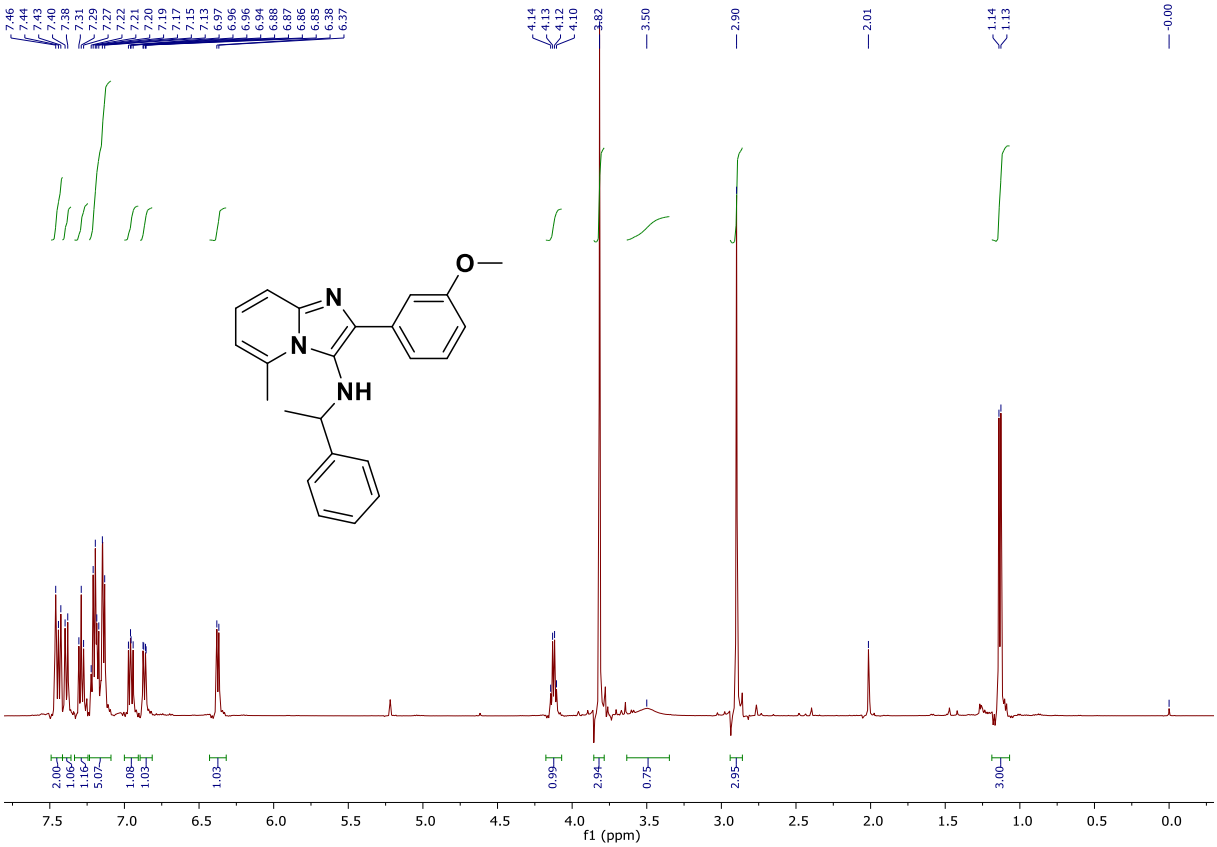



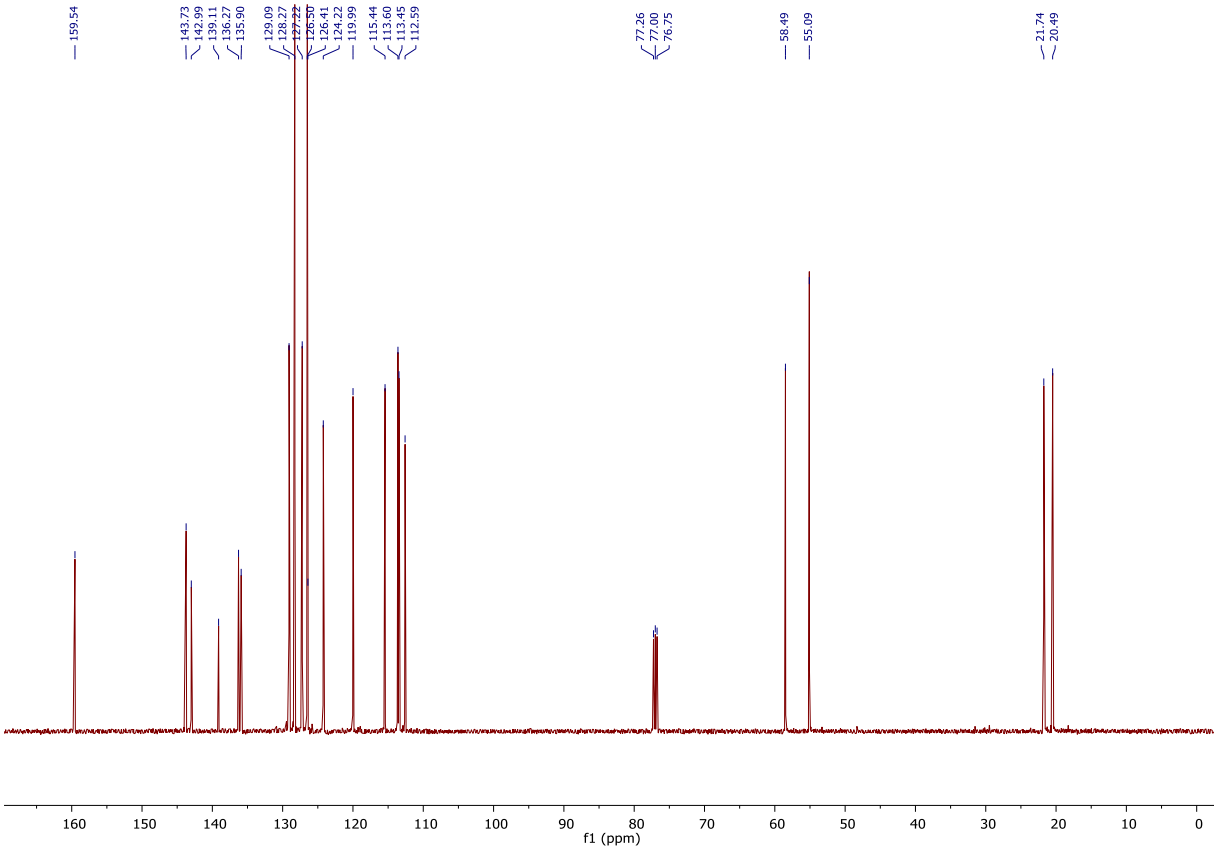
**methyl (5-(2-chloro-6-fluorophenyl)-1H-imidazo[1,2-b][1,2,4]triazol-6-yl)alaninate (M23)**



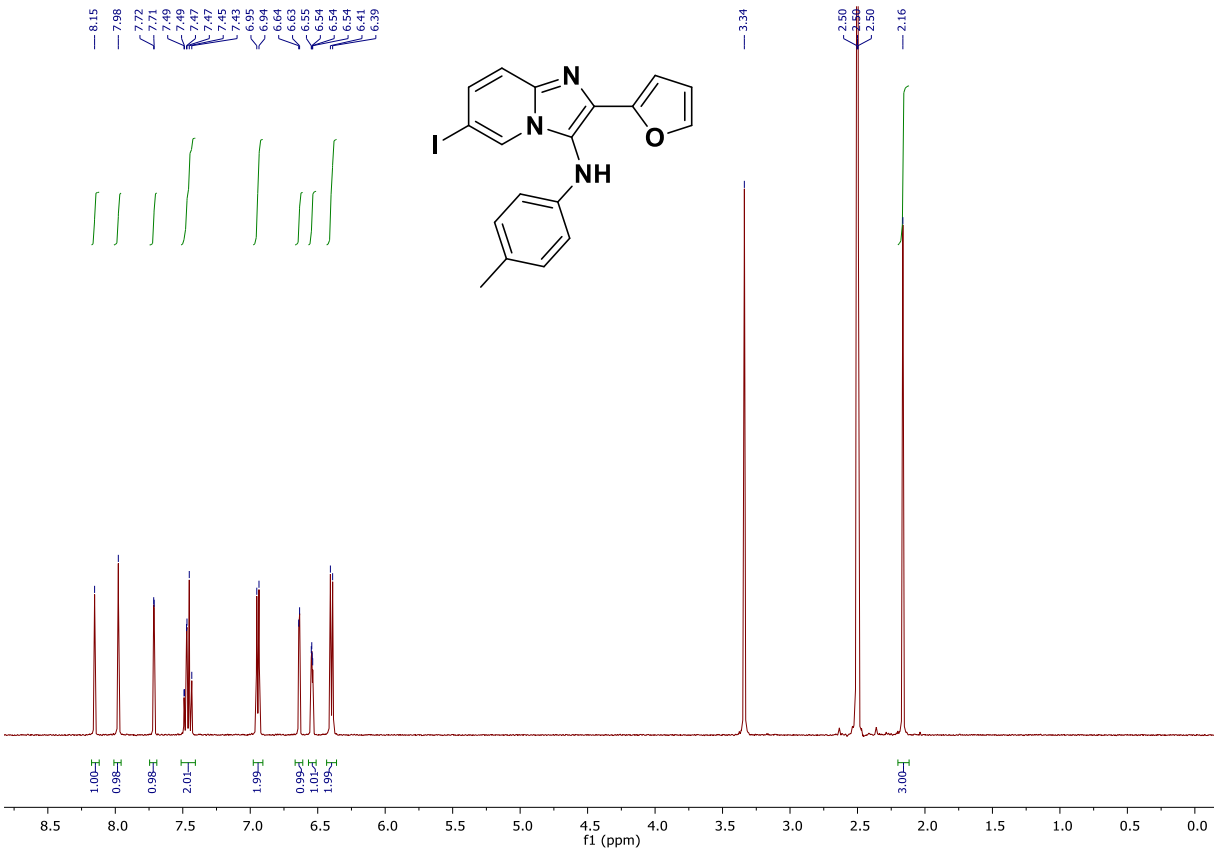



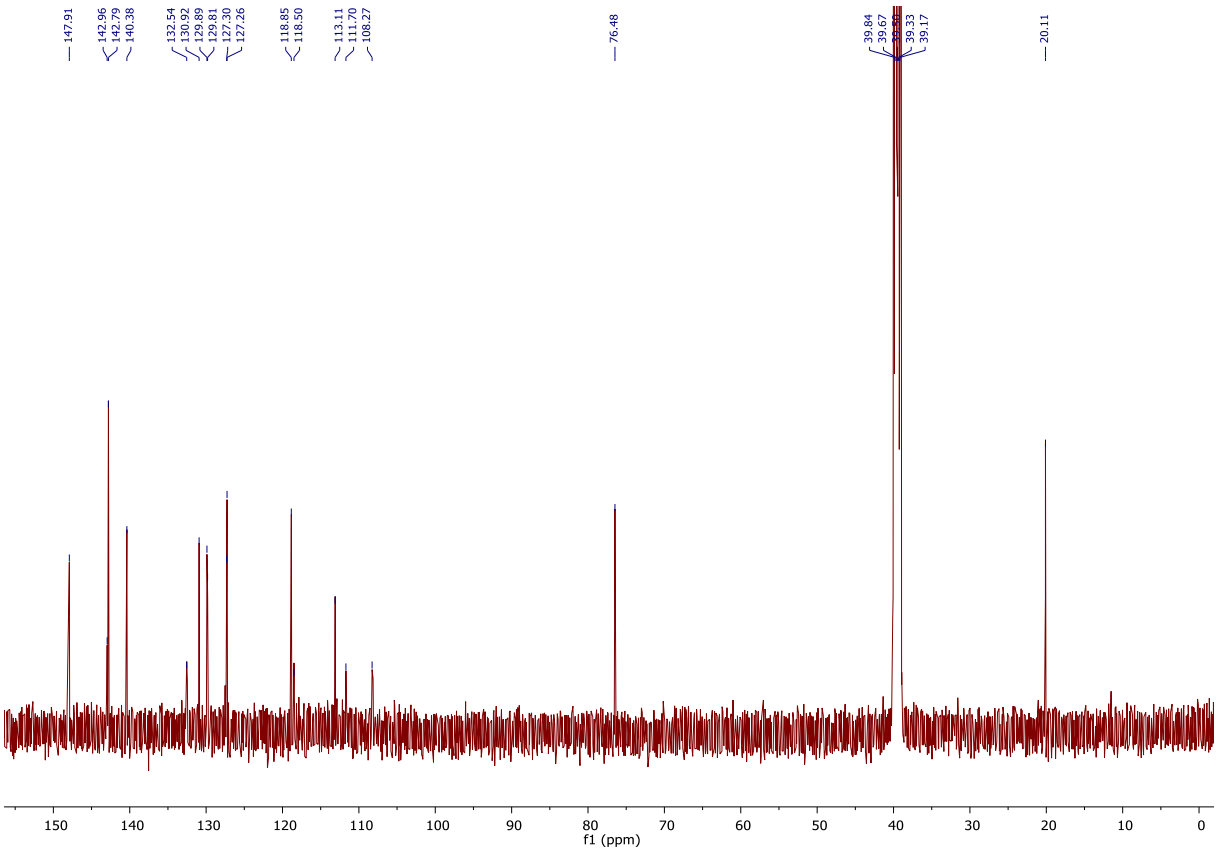
## 2-(3-methoxyphenyl)-5-methyl-N-(1-phenylethyl)imidazo[1,2-a]pyridin-3-amine (N14)



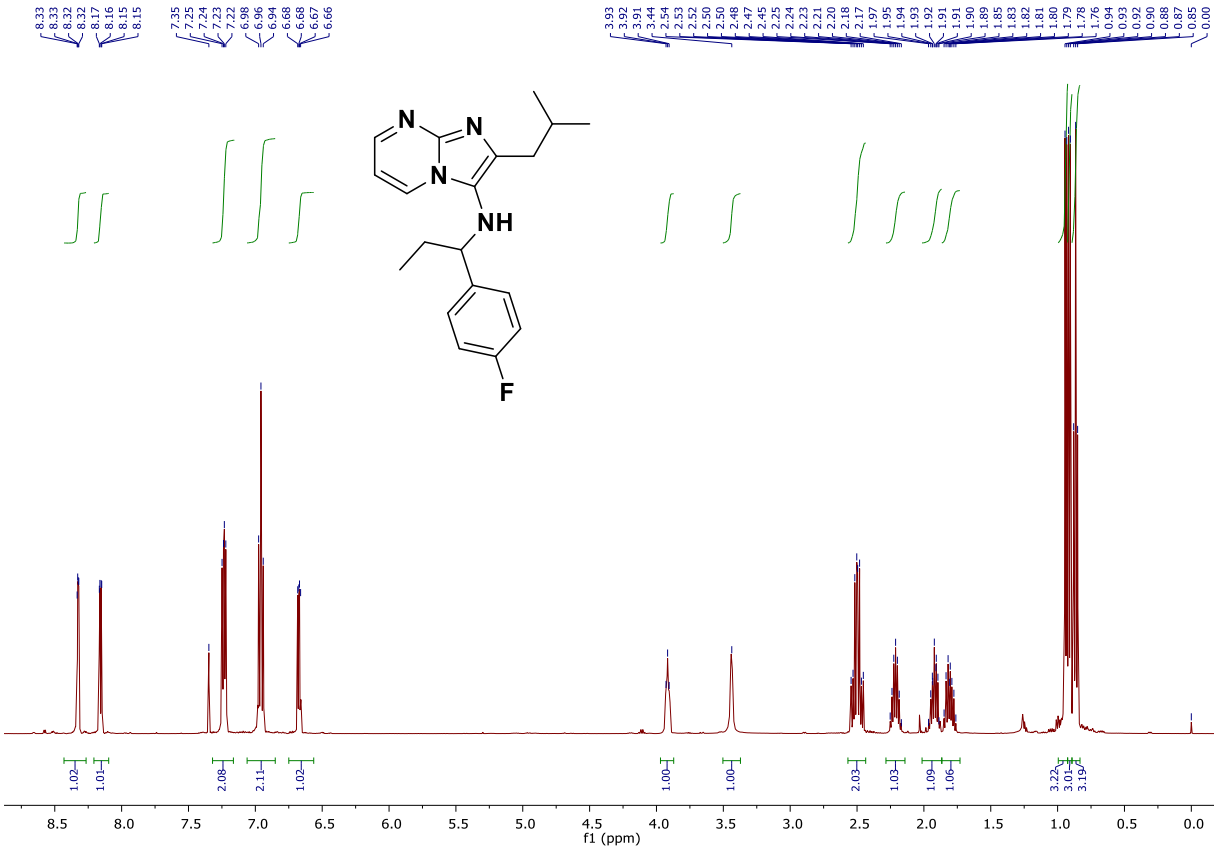



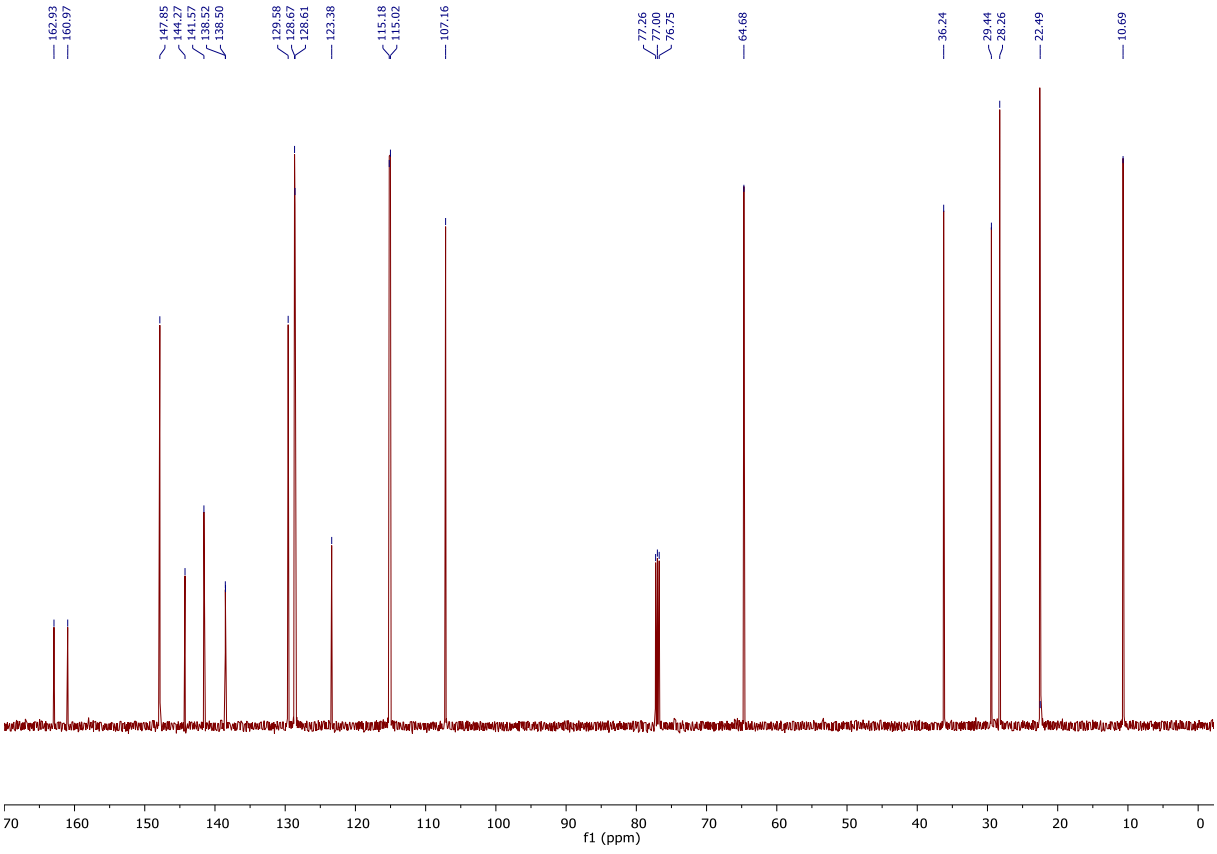
## 2-(furan-2-yl)-6-iodo-N-(p-tolyl)imidazo[1,2-a]pyridin-3-amine (N19)



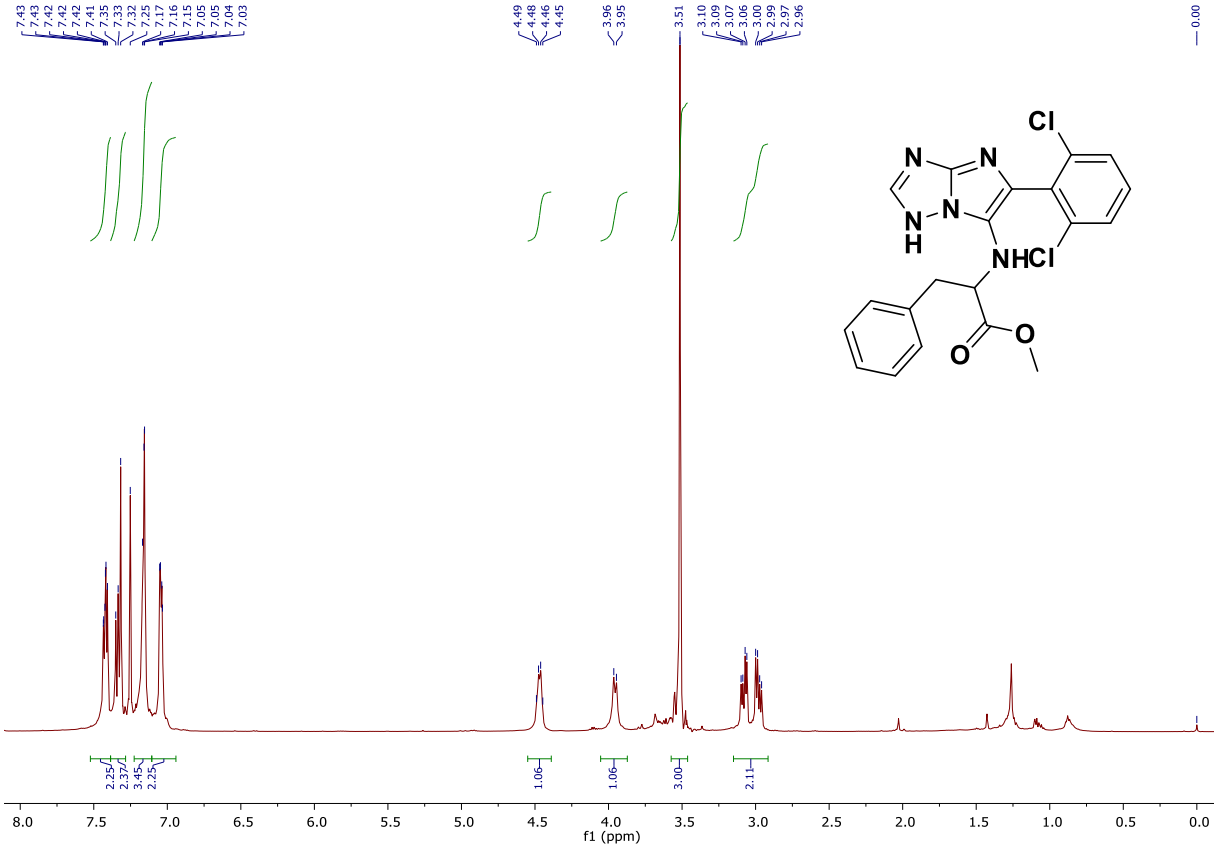



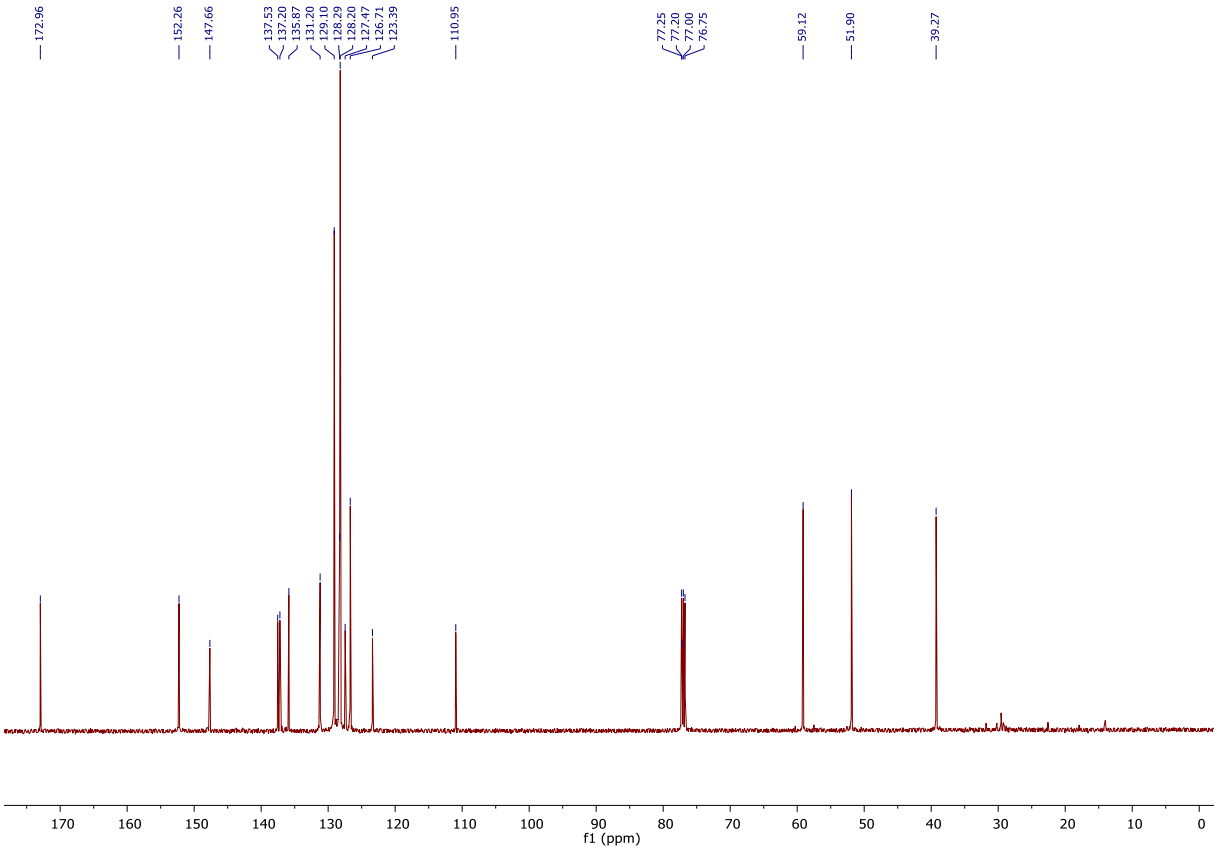
## N-(1-(4-fluorophenyl)propyl)-2-isobutylimidazo[1,2-a]pyrimidin-3-amine (N22)



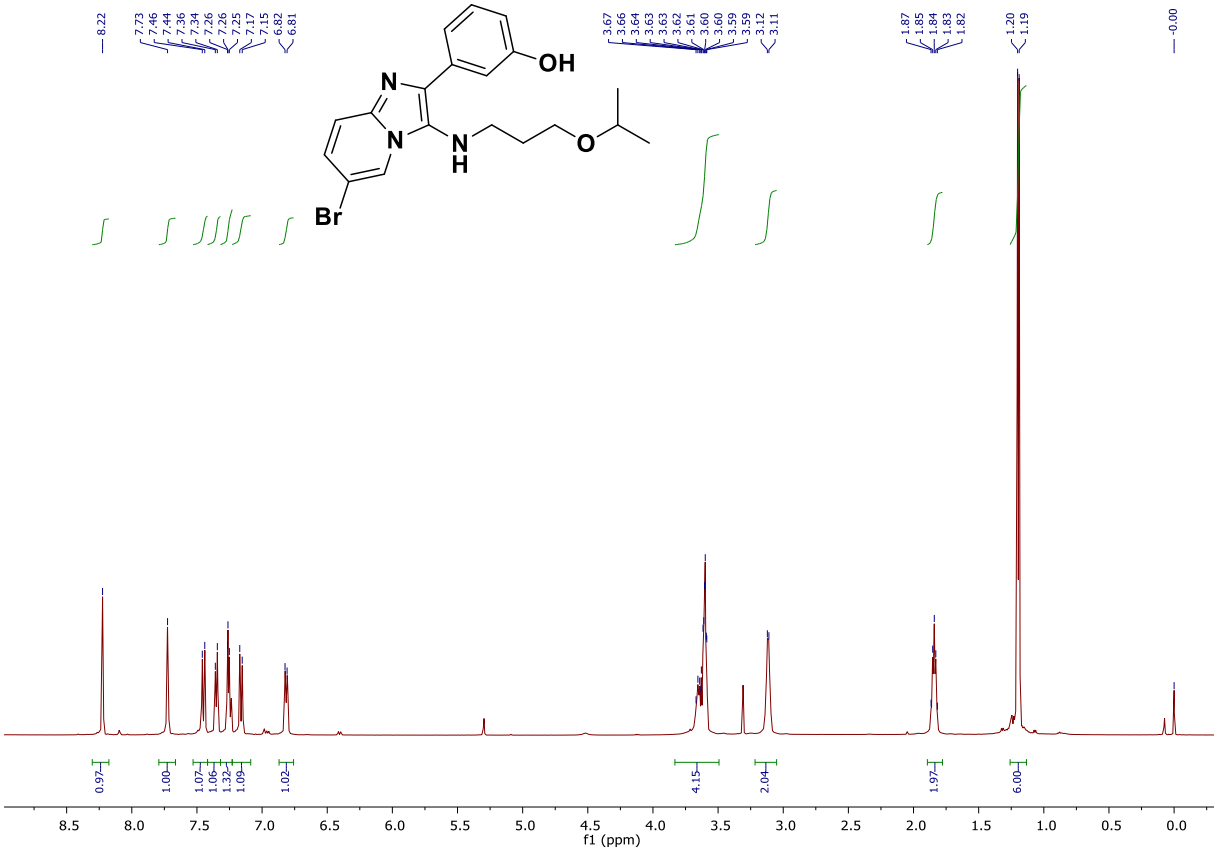
**methyl (5-(2,6-dichlorophenyl)-1H-imidazo[1,2-b][1,2,4]triazol-6-yl)phenylalaninate (O16)**

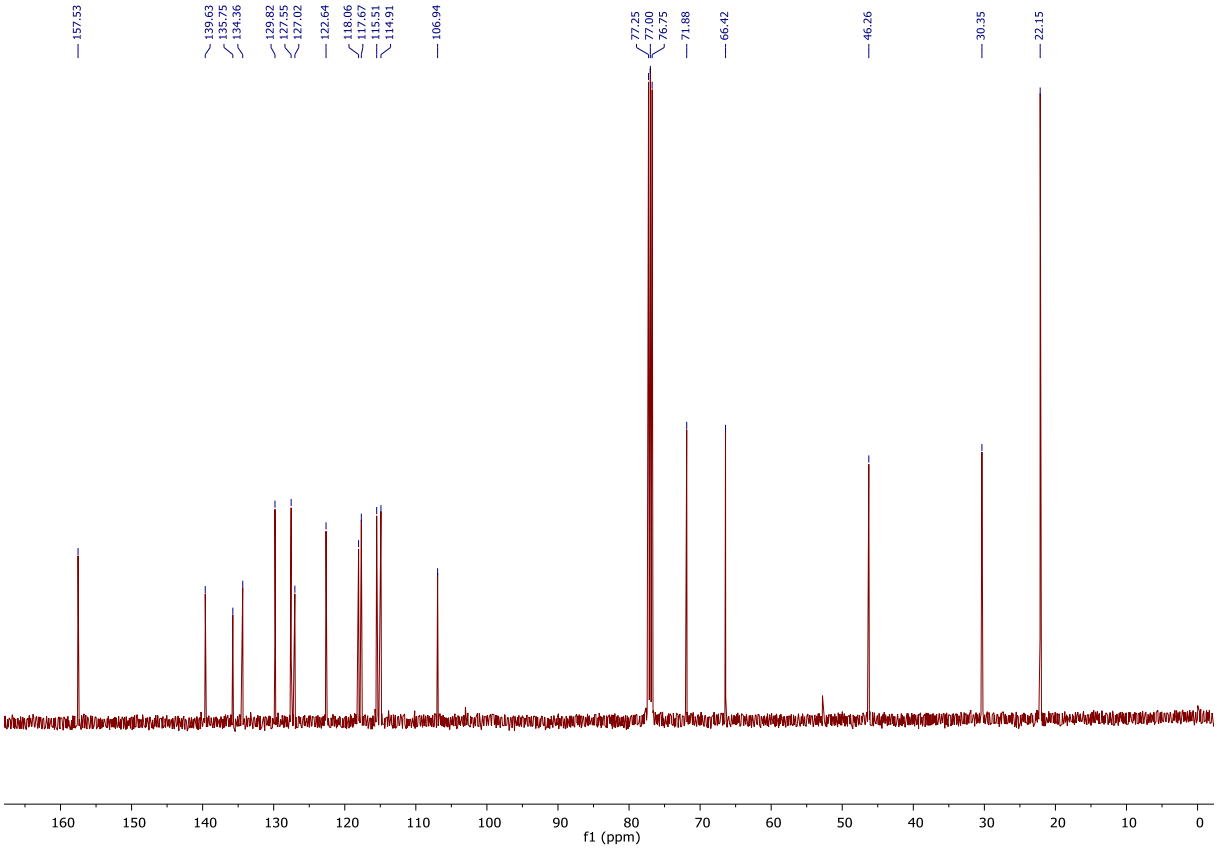


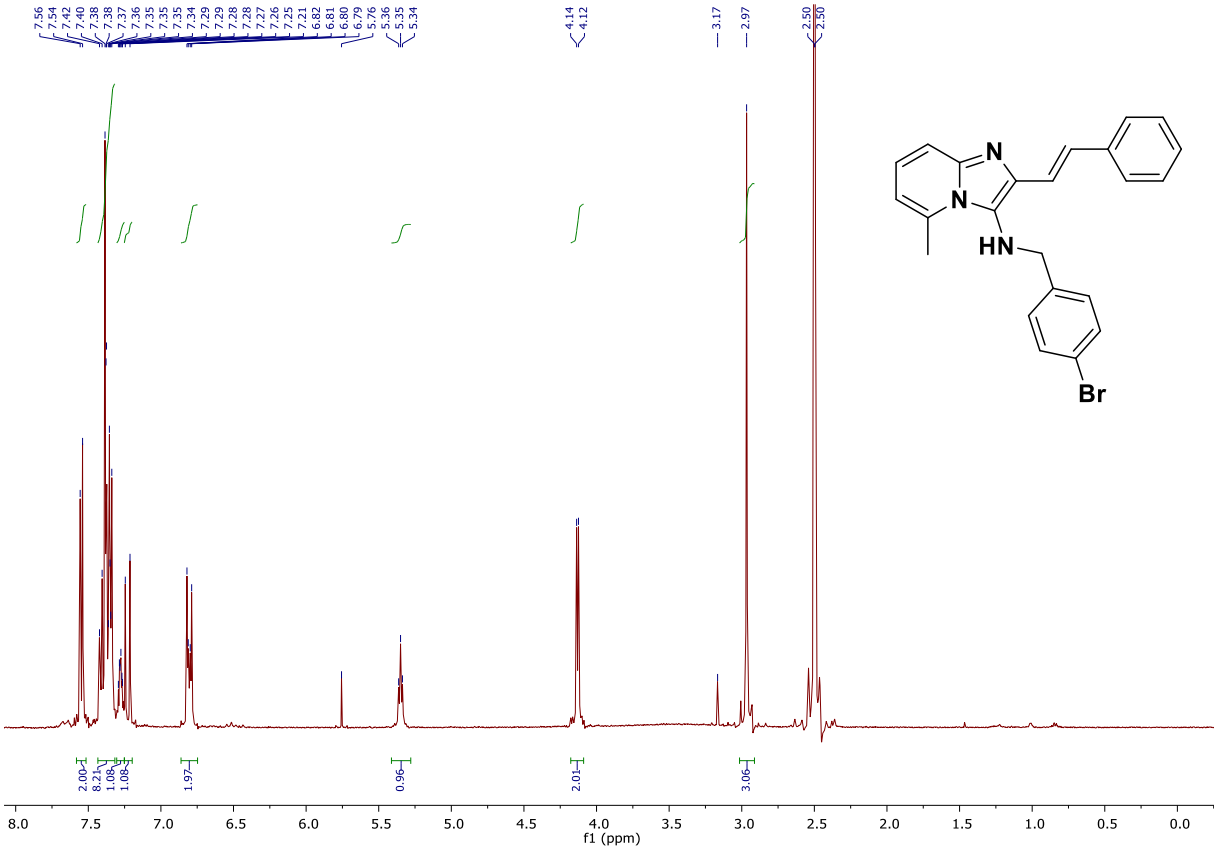
## Destination plate IV

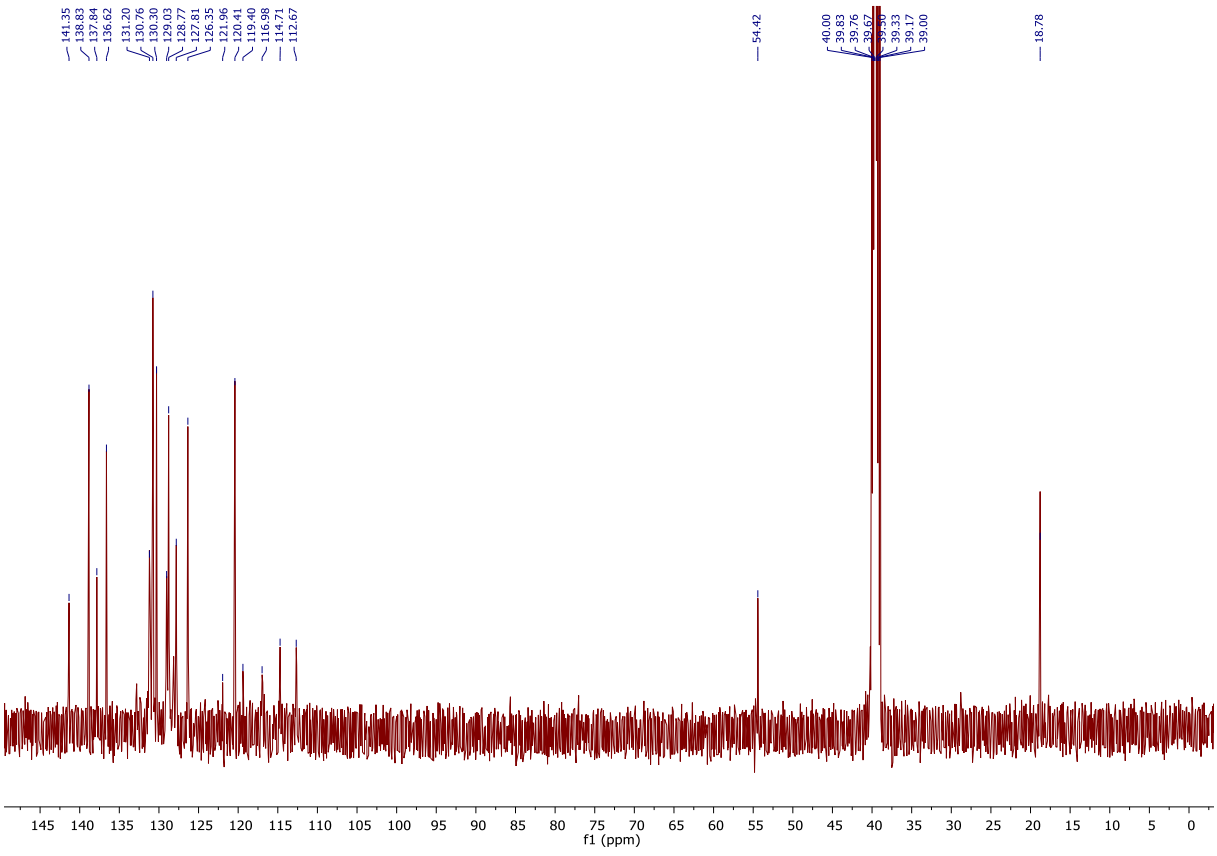
## 3-(6-bromo-3-((3-isopropoxypropyl)amino)imidazo[1,2-a]pyridin-2-yl)phenol (C14)



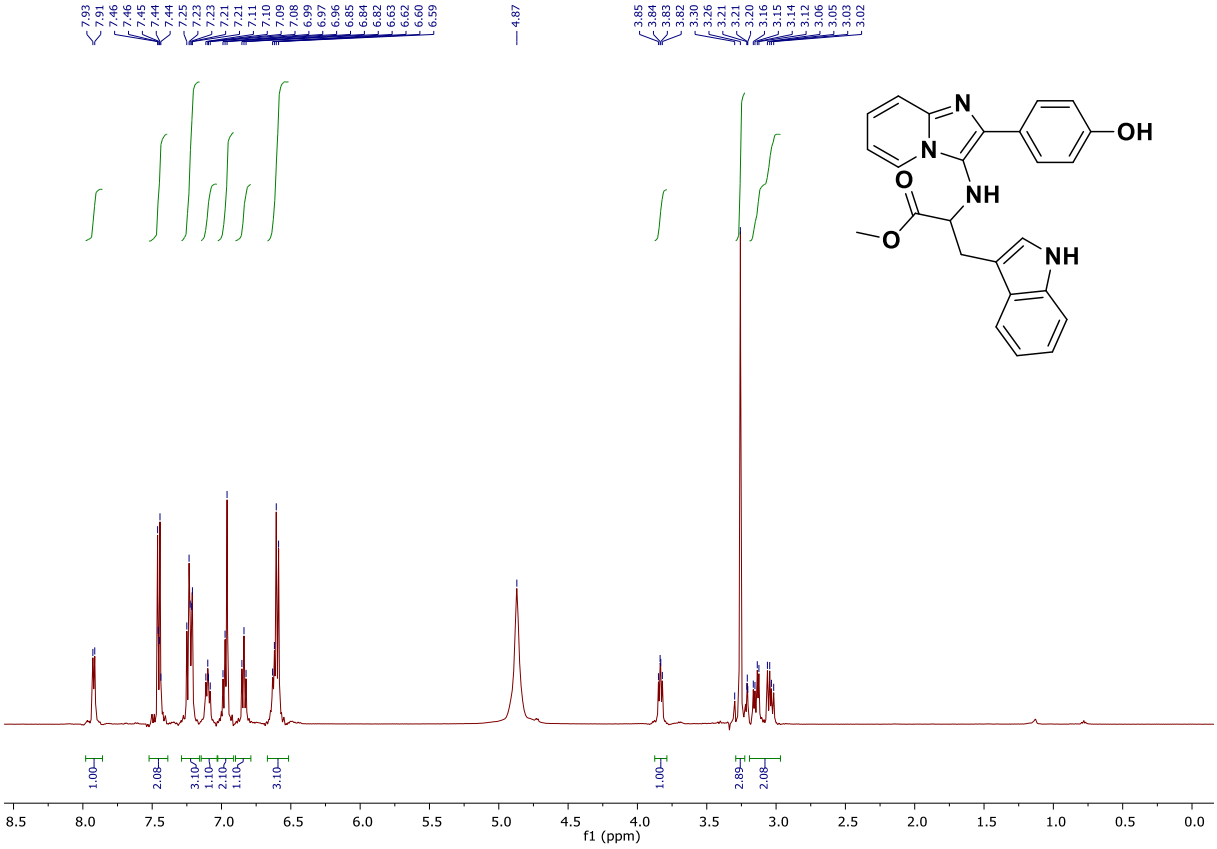



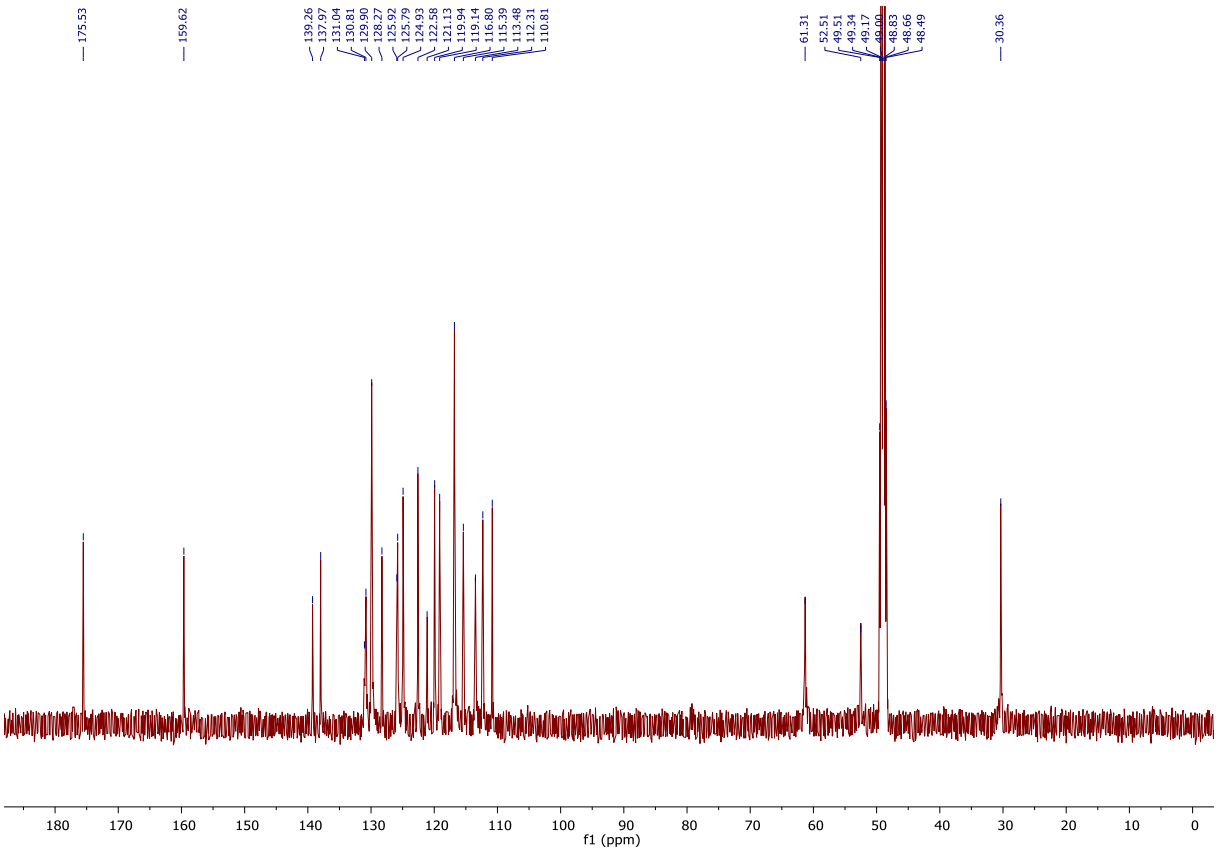
## (E)-N-(4-bromobenzyl)-5-methyl-2-styrylimidazo[1,2-a]pyridin-3-amine (D9)



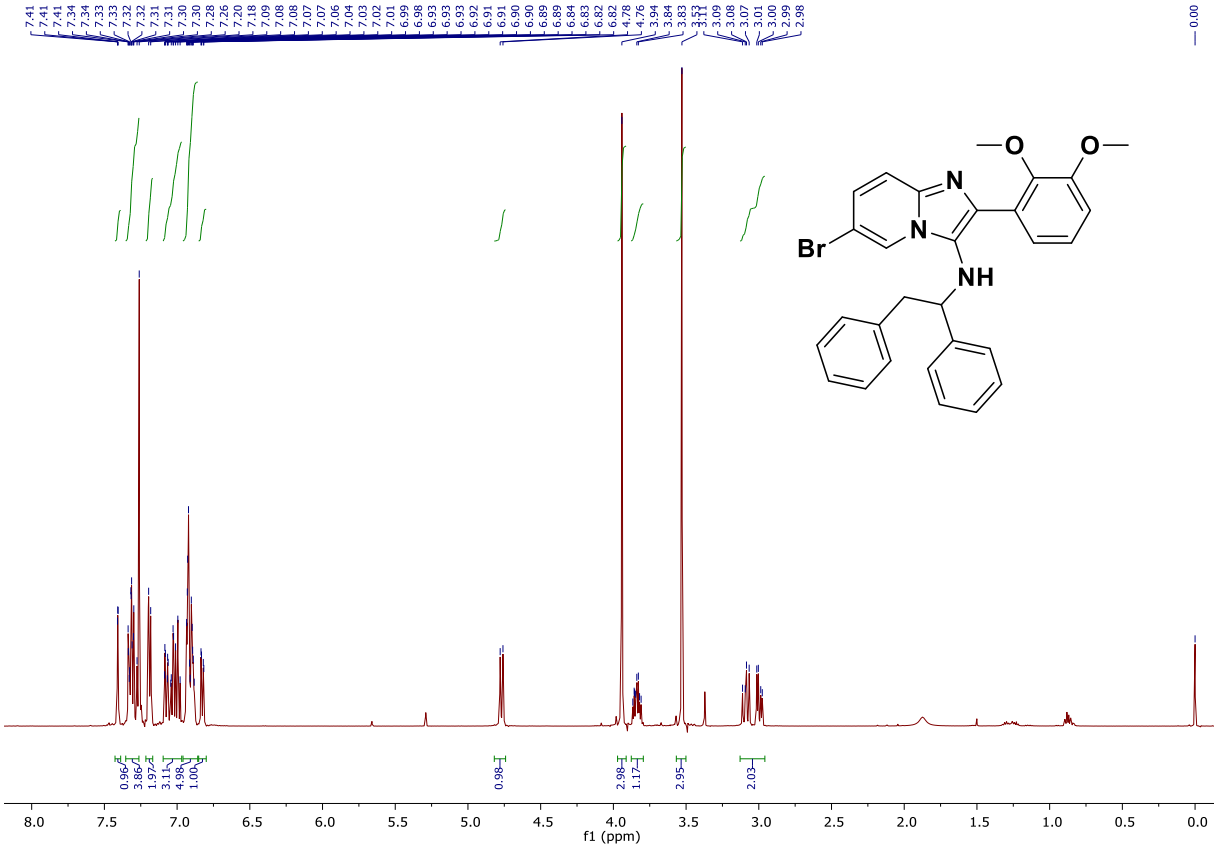



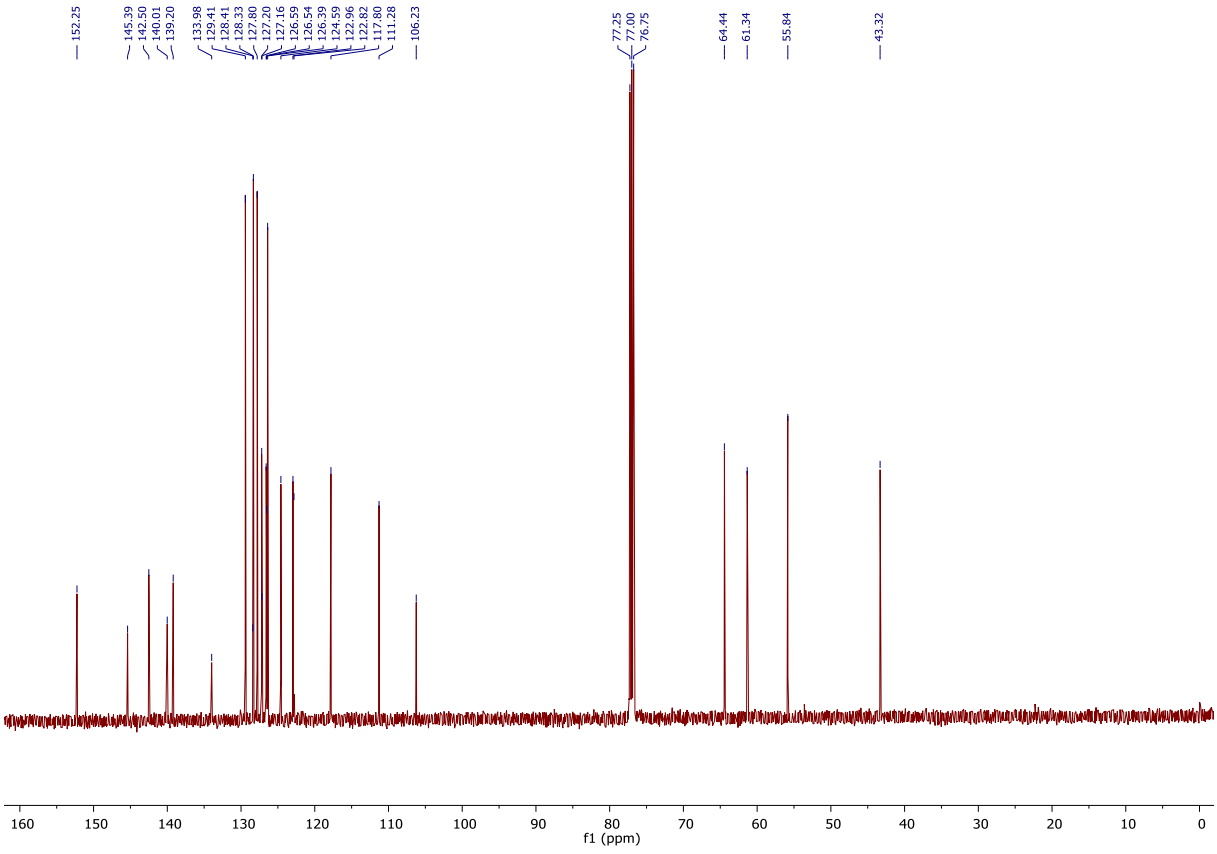
## methyl (2-(4-hydroxyphenyl)imidazo[1,2-a]pyridin-3-yl)tryptophanate (K19)



## 6-bromo-2-(2,3-dimethoxyphenyl)-N-(1,2-diphenylethyl)imidazo[1,2-a]pyridin-3-amine (P13)



## 6. Protein expression and purification

To facilitate protein crystallization, we genetically truncated the full length human Menin (residues 1-610) by deleting an unstructured loop(residues 460-519), and a flexible tail at C terminal(residues 585-610). Menin gene was subcloned into the pETM11 vector (EMBL), which encodes a TEV cleavage site after the N-terminal His6 tag, by HindIII and NcoI restriction sites. The recombinant gene was expressed in *E. coli* BL21(DE3), and cultured in Terrific Broth medium at 37 °C to an $O.D._{600}$ of 1.0-1.2. After induction for 16h with 0.4 mM IPTG(Isopropyl β-D-1-thiogalactopyranoside) at 18 °C , the cells were collected by centrifugation and pellets were resuspended in lysis buffer(50 mM Tris-HCl, pH 8.0; 200 mM NaCl; 20 mM imidazole; 5% glycerol; 3 mM 2-mercaptoethanol), followed by sonication. The debris were then removed by ultracentrifugation(18,000 g for 60 min at 4°C), resultant supernatant was load onto a HisTrap FF column (GE Healthcare). The main Menin protein peak started to appear at an imidazole concentration around 180 mM, and fractions were pooled together for dialysis to get rid of the high imidazole. TEV protease was then added to remove the His6-TEV tag. After 7 h digestion, Menin protein was further purified by gel-filtration using a HiLoad 16/60 Superdex 75 column (GE Healthcare) equilibrated with buffer A (20 mM Tris-HCl, pH 8.0; 200 mM NaCl; 1 mM TCEP). The purified protein was concentrated to 20 mg/mL and stored at -80 °C for later use.

## 7. Crystallization

Menin was crystallized by sitting-drop vapour diffusion with a concentration of 20 mg/mL at 4 °C. An initial screening through the JCSG *plus* and PACT *premier* (Molecular Dimensions) commercial kits were applied, and small needle-like crystals formed after 3 weeks in the well contains 100 mM Bis-Tris propane, pH 7.5, 200 mM KSCN, 20% (w/v) PEG 3350. Further optimization showed replacing PEG3350 by PEG8000 at 16% (w/v) can create bigger crystals. The crystal was soaked into mother liquor containing 5% DMSO with a final ligand concentration of 5 mM, after 2h, 4h or overnight incubation, crystals were transferred to the mother liquor mixed with 20% (v/v) ethylene glycol and flash-frozen in liquid nitrogen for later data collection (Table S1). The PDB ID is 6S2K.

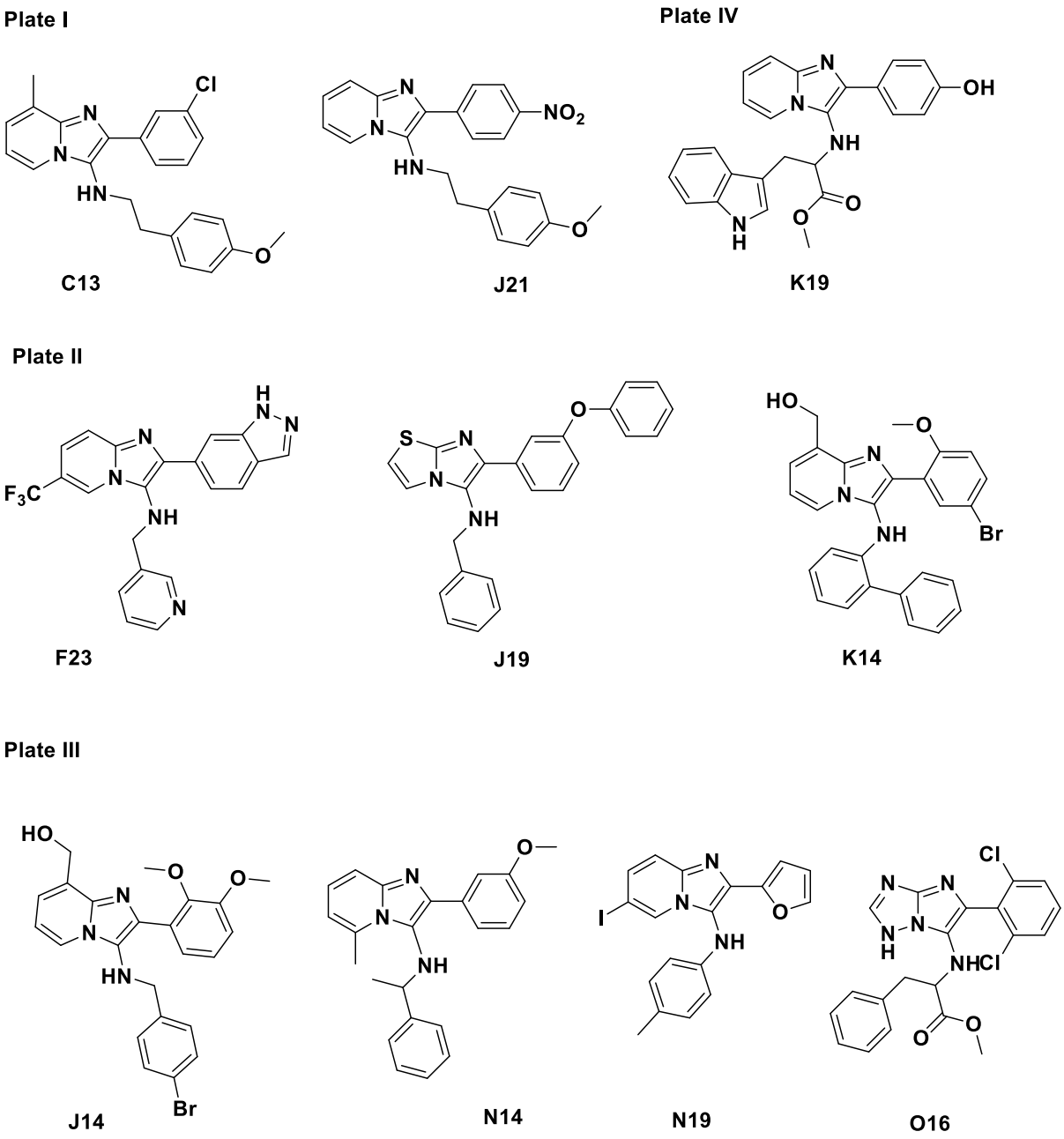
**Table S1.** Data collection and refinement statistics.

| | **Menin with Plate I - J21** |
|---|---|
| **Wavelength** | 1.0 Å(12.398 keV) |
| **Resolution range** | 47.04 - 3.10 (3.459 - 3.10) |
| **Space group** | P 21 21 21 |
| **Unit cell** | 84.399 101.31 126.842 90 90 90 |
| **Total reflections** | 73438(3296) |
| **Unique reflections** | 19448(1567) |
| **Multiplicity** | 3.78 |
| **Completeness (%)** | 94.89 (97.51) |
| **Mean I/sigma(I)** | 1.96 |
| **Wilson B-factor** | 36.66 |
| **R-merge** | 21.2 |

| | |
|---|---|
| **R-meas** | 27.3 |
| **R-pim** | 17.9 |
| **CC1/2** | 0.97 |
| **Reflections used in refinement** | 15515 (1567) |
| **Reflections used for R-free** | 752 (71) |
| **R-work** | 0.4518 (0.3953) |
| **R-free** | 0.4583 (0.3935) |
| **Number of non-hydrogen atoms** | 3763 |
| **Macromolecules** | 3734 |
| **Ligands** | 29 |
| **Protein residues** | 471 |
| **RMS(bonds)** | 0.014 |
| **RMS(angles)** | 1.87 |
| **Ramachandran favored (%)** | 87.64 |
| **Ramachandran allowed (%)** | 11.06 |
| **Ramachandran outliers (%)** | 1.30 |
| **Rotamer outliers (%)** | 3.56 |
| **Clashscore** | 10.35 |
| **Average B-factor** | 29.47 |
| **Macromolecules** | 29.41 |
| **Ligands** | 37.54 |

## 8. DSF screening assay

For the ligand stock preparation of DSF (differential scanning fluorimetry) screening assay, the GBB reaction mixtures inside the 384 well plates were mixed properly with 10 µL DMSO as an initial stock. 1 µL condensed stock was further diluted 25 times with DMSO to get a rough ligand concentration of 2 mM, considering an ideal yield (100%) for the GBB reactions. Purified Menin 2.5 mL in buffer A at the concentration of 0.2 mg/ml was carefully mixed with 1µL Sypro-Orange dye at rt until solution get homogeneous. Then in a 96-well plate, 2.5 µL diluted ligand was mixed with 22.5 µL dye labeled Menin, the plate was then slowly heated up from 20 °C to 80 °C in 30 min via a Q-PCR equipment (Bio-Rad CFX96™ Real-Time System). Fluorescence changes were monitored and recorded, hits that increased Menin Tm by 0.5 °C compared to the control were selected as positive ligands. By DSF screening of 1536 wells, 10 hits were found which were then resynthesized in mmol scale and purified to be measured by MST (Scheme S1).




**Scheme S1.** Structure of the hits from DSF screening.

## 9. MST binding assay

The purified compounds tested in the microscale thermophoresis (MST) assay were prepared in DMSO to acquire a 100 mM ligand stocks initially, for the binding test, stock was further diluted by mixing 1 µL compound with 49 µL PBS-T (0.05% Tween 20) to have a 2 mM ligand stock as the starting point. The serial dilution began with transferring 10 µL ligand of 2 mM in tube 1, and then followed a two-fold serial dilution procedure from tube 2 until 16 by mixing with PBS-T buffer. Menin protein with His tag before TEV digestion was purified and diluted to 200 nM in PBS-T(0.05% Tween 20) buffer, 100 µL protein was then mixed with 100 µL Red-tris-NTA Dye (NanoTemper) solution which prediluted to 100 nM, the mixture was incubated at room temperature for 30 min, after another 15 min centrifugation at 140,000g, the labeled protein was ready to use. Adding 10 µL labeled protein to the PCR tubes from 1 to 16, mixing properly before the standard treated capillaries (NT.115, NanoTemper) withdrew it. All the 16 capillaries were load into MST (Monolith NT.115 Labelled), and the $K_d$ values between protein and ligands were

calculated based on the MST traces in a ligand concentration range from 1 mM to 30 nM. Finally, out of 10 hits found by DSF, 3 hits were validated by MST binding assay (Fig. S8).

**Plate I - C13** $K_d$ = 9.3 ± 0.2 µM

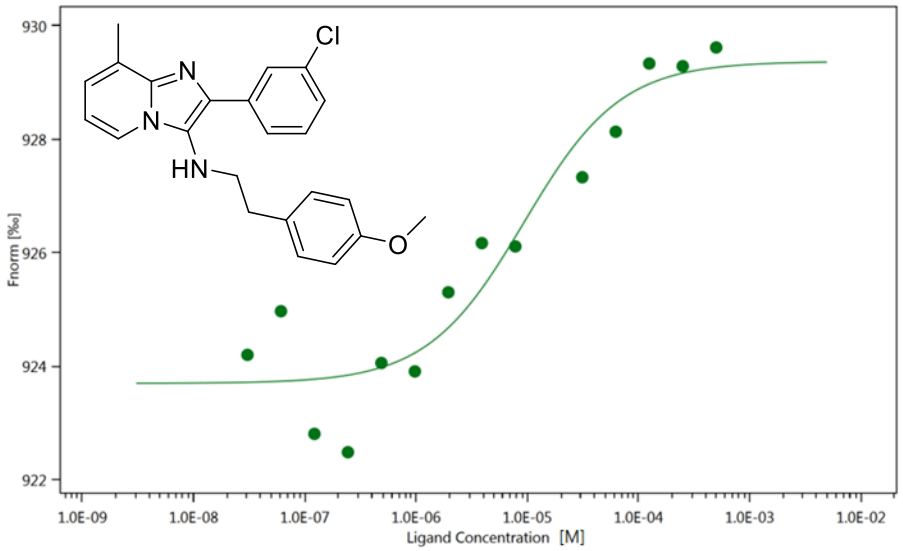



**Plate I - J21** $K_d$ = 2.8 ± 0.1 µM

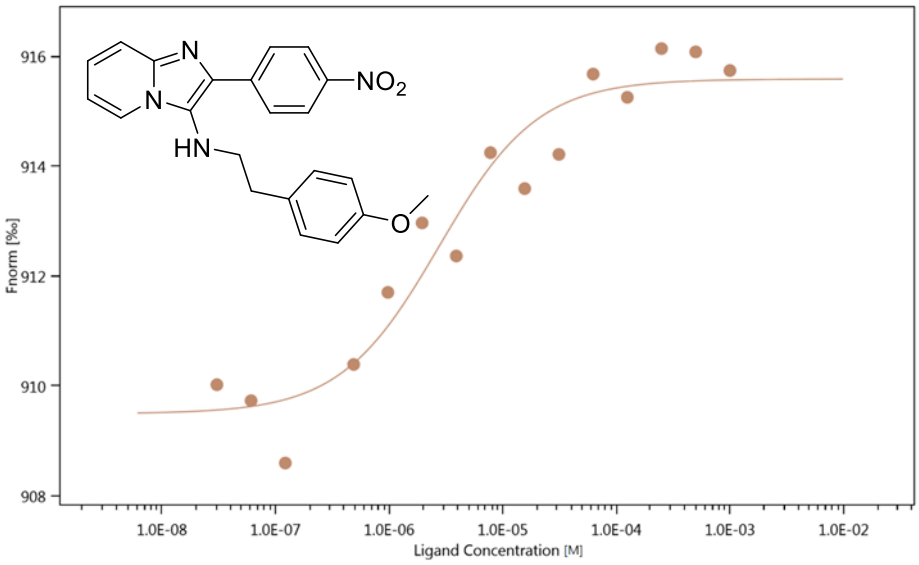


**Plate III - O16** $K_d$ = 156.5 ± 2.5 µM

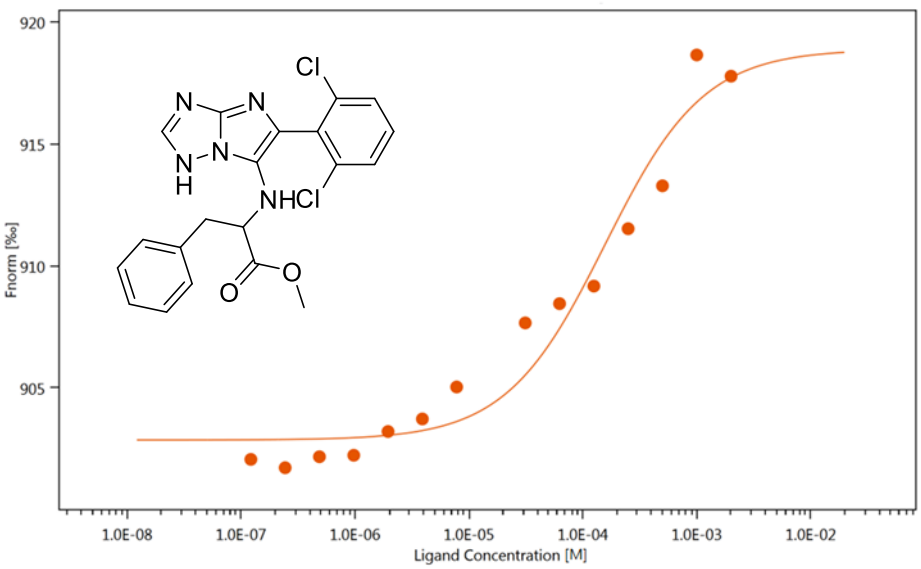



**Fig. S8.** MST validated compounds.

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