Supporting Information

Asymmetric synthesis of Cyclic β-Amino Carbonyl Derivatives by a Formal [3+2] Photocycloaddition

Leonardo Mollari, Miguel A. Valle-Amores, Ana M. Martínez-Gualda, Leyre Marzo, Alberto Fraile,* José Aleman*

Contents

1. General considerations S-2
2. General procedures S-3
3. Preparation of starting materials S-5
4. Screening of the reaction conditions S-8
5. Synthesis of compounds **3** S-9
6. Synthetic playground information S-17
7. UV-visible absorption spectra S-19
8. Quantum Yield determination S-19
9. NMR spectra section S-22
10. X-ray information S-39
11. SFC chromatograms for quiral compunds S-41
12. References S-54

1. General considerations.

The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a *Bruker Avance 300 MHz spectrometer* running at 300 MHz for ^{1}H and 75 MHz for ^{13}C or on a *Bruker DRX-500 spectrometer* running at 500 MHz for ^{1}H, 126 MHz for ^{13}C and 471 MHz for ^{19}F coupled mode, respectively. The chemical shifts (δ) are reported relative to the tetramethylsilane signal at 0 ppm or relative to the residual signal of the solvent ($CDCl_3$ at 7.26 ppm or $C_2D_2Cl_4$ at 5.91 ppm), while for ^{13}C-NMR are given in ppm relative to the residual signal of solvent ($CDCl_3$ at 77.16 ppm or $C_2D_2Cl_4$ at 74.2 ppm) ^{13}C NMR spectra were acquired on a broadband decoupled mode. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; dd, doublet of doublets; ddd, doublet of doublet of doublets; t, triplet; dt, doublet of triplets; td, triplet of doublets; tt, triplet of triplets; q, quartet; dq, doublet of quartets; p, pentuplet; m, multiplet; br, broad signal. The following abbreviations are used to indicate the solvents: Cy, Cyclohexane; DCM, dichloromethane, EtOH, Ethanol; EtOAc, Ethyl acetate; MeOH, Methanol; THF, Tetrahydrofuran.

Optical rotations were measured on an Anton Paar NCP 100 Polarimeter at room temperature and and $[\alpha]^{20}_{D}$ values are given in $deg \cdot mL \cdot g^{-1} \cdot dm^{-1}$; concentration *c* is listed in $g \cdot (100\ mL)^{-1}$.

Enantiomeric excess was determined on an *SFC Agilent Technologies 1260 Infinity Series* instrument equipped with a UV-VIS detector, employing *Daicel Chiralpak* IA, IB-3, IC, ID, and IG-3 columns as chiral stationary phase. The exact conditions for the analyses are specified in each case.

High-Resolution Mass Spectra (HRMS) were obtained on an *Agilent Technologies 6120 Quadrupole LC/MS* coupled with an *SFC Agilent technologies 1260 Infinity Series* instrument for the ESI-MS (Electrospray Ionization). *MassWorks* software version 4.0.0.0 (*Cerno Bioscience*) was used for the formula identification. *MassWorks* is an MS calibration software which calibrates isotope profiles to achieve high mass accuracy and enables elemental composition determination on conventional mass spectrometers of unit mass resolution allowing highly accurate comparisons between calibrated and theoretical spectra.[1]

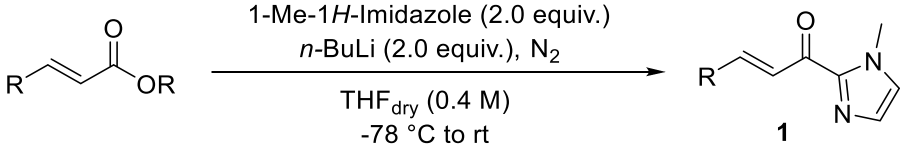
Commercial grade reagents and solvent were purchased from *Sigma-Aldrich*, *Alfa Aesar*, *Fluorochem*, *TCI Chemicals* and used without further purifications while anhydrous solvents were taken from a SPS solvent dispenser.

Analytical TLC was performed using pre-coated aluminium-backed plates (*Merck TLC Silicagel* 60 F_{254}) and visualized by ultraviolet irradiation. Chromatographic purification of products was accomplished using flash column chromatography (FC) on *Merck* Geduran® Si 60 silica gel (40 – 63 µm). *Celite® 512 medium* (*Sigma-Aldrich*) was used for filtration. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

The stereogenic-at-metal Lewis's acid catalysts Δ/λ-Rh were synthesized according to published reports.[2]

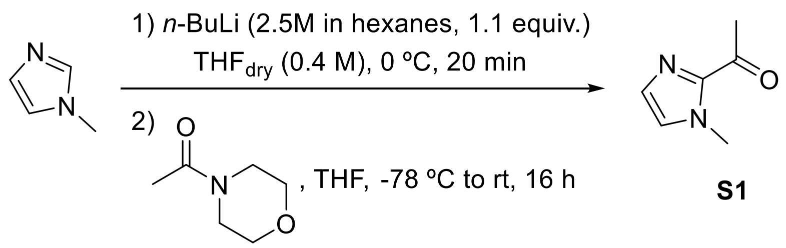
2. General Procedures.

2.1. *General Procedure **GP1** for the synthesis of the Michael acceptor derivatives from the corresponding ester.*



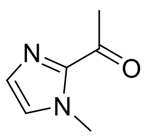
Following a modified procedure described by Evans et al.:[3] To a solution of 1-methyl-1*H*-Imidazole (2.0 equiv.) in dry THF (0.4 M) at -78 °C was added *n*-BuLi (2.5M in Hexanes, 2.0 equiv.) dropwise. The reaction was stirred at -78 °C for 30 min, then stirred at room temperatre for another 30 min. The corresponding α,β-unsaturated ester (1 equiv. in THF) was added dropwise to the flask after the reaction was cooled back down to -78 °C. The reaction was allowed to slowly warm to room temperature and stirred overnight. The reaction was quenched with NH_4Cl sat. solution and extracted with EtOAc. The orgainc layers were washed with brine, and the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was further purified by flash column chromatography on silica gel (Cy / EtOAC) to provide the 2-acylimidazoles **1a**, **1b**, **1f**, **1g**, and **1h**.

*2.1.2. General Procedure **GP2** for the synthesis of Michael acceptor derivatives through aldolic reaction.[4]*



Step 1: To a solution of 1-methyl-1*H*-imidazole (9.3 mL, 80 mmol, 1.0 equiv.) in dry THF (50 mL) was added *n*-BuLi (2.5 M in hexanes, 35.2 mL, 88 mmol, 1.1 equiv.) dropwise at 0 °C. The reaction mixture was stirred for 20 min and was then transferred via cannula to a solution of 4-acetylmorpholine in dry THF (50 mL) at –78 °C. The resulting mixture was allowed to warm to rt and stirred for a further 16 h. The reaction was then quenched by addition of a 3M aqueous solution of HCl (3.3 mL), diluted with additional water and extracted with EtOAc (3 x 100 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by flash column chromatography over silica gel (Cy / EtOAc = 1 : 1) afforded the desired product **S1** as a colourless oil (7.4 g, 59 mmol, 74%).

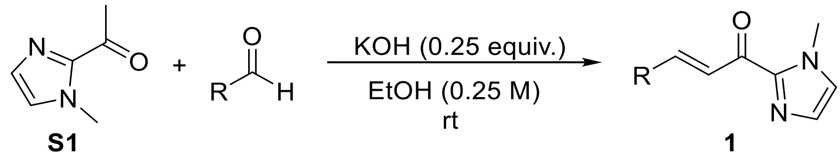
1-(1-methyl-1H-imidazol-2-yl)ethan-1-one (S1).



S1

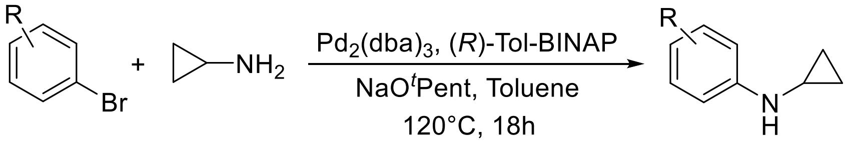
Spectroscopic data were consistent with the literature data for this compound.[5]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.11 (brs, 1H), 7.00 (brs, 1H), 3.98 (s, 3H), 2.64 (s, 3H).
^{13}C-NMR (75 MHz, $CDCl_3$): δ 190.5, 143.1, 128.9, 126.8, 36.1, 27.1.



Step 2. To a round bottom flask, 2-acetyl-1-methyl-1*H*-imidazole (**S1**) (1 equiv.) and EtOH (0.25 M) were added. After stirring 10 minutes, the desired aldehyde (1 equiv.) and a catalytic amount of KOH (0.25 equiv.) were added. The solution was stirred until reaction completion monitored by TLC. The solvent was evaporated, and the obtained residue was dissolved in $CHCl_3$ and washed with NH_4Cl sat. solution. The aqueous phase was extracted three times with $CHCl_3$ and the combined organic layers were dried over $MgSO_4$. The crude was further purified by flash column chromatography on silica gel.

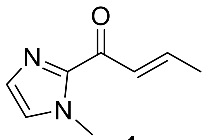
2.2. General Procedure **GP3** for the synthesis of *N*-unsubstitued imines.[6]



Following a modified procedure,[7] an oven-dried microwave vial was charged with $Pd_2(dba)_3$ (1 mol%), (*R*)-Tol-BINAP (3 mol%) and NaO^{t}Pent (1.5 equiv.). Then, toluene (0.5 M), cyclopropylamine (2.0 equiv.) and the aromatic bromide (1 equiv.) were added via syringe to the vial, and it was heated at 120 °C for 18 h. The reaction mixture was then cooled to room temperature, diluted with Et_2O, and filtered through a small pad of Celita®. The filtrate was evaporated under reduced pressure, and the obtained crude residue was subjected to column chromatography with the indicated solvents in each case.

3. Preparation of the starting materials.

(*E*)-1-(1-methyl-1*H*-imidazol-2-yl)but-2-en-1-one (**1a**).

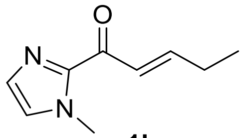


1a

Following the general procedure **GP1**, from (*E*)-methyl but-2-enoate, compound **1a** was obtained in as an orange oil after purification by flash column chromatography (Cy : EtOAc = 80 : 20). Spectroscopic data were consistent with the literature data for this compound.[3]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.40 (dq, *J* = 15.5, 1.6 Hz, 1H), 7.17 – 7.05 (m, 2H), 7.03 (s, 1H), 4.03 (s, 3H), 1.98 (dd, *J* = 6.9, 1.6 Hz, 3H).

(*E*)-1-(1-methyl-1*H*-imidazol-2-yl)pent-2-en-1-one (**1b**).

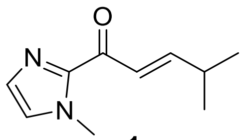


1b

Following the general procedure **GP1**, from (*E*)-methyl pent-2-enoate, compound **1b** was obtained as an orange oil after purification by flash column chromatography (Cy : EtOAc = 80 : 20). Spectroscopic data were consistent with the literature data for this compound.[3]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.39 (dt, *J* = 15.7, 1.6 Hz, 1H), 7.23 – 7.12 (m, 2H), 7.03 (s, 1H), 4.04 (s, 3H), 2.39 – 2.29 (m, 2H), 1.13 (t, *J* = 7.4 Hz, 3H).

(*E*)-4-methyl-1-(1-methyl-1*H*-imidazol-2-yl)pent-2-en-1-one (**1c**).

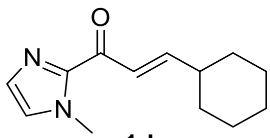


1c

Following the general procedure **GP2**, from isobutyraldehyde, compound **1c** was obtained as an orange oil after purification by flash column chromatography (Cy : EtOAc = 85 : 15). Spectroscopic data were consistent with the literature data for this compound.[3]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.35 (dd, *J* = 15.7, 1.4 Hz, 1H), 7.16 (s, 1H), 7.09 (dd, *J* = 15.7, 6.7 Hz, 1H), 7.03 (s, 1H), 4.03 (s, 3H), 2.57 – 2.50 (m, 1H), 1.12 (d, *J* = 6.8 Hz, 6H).

(*E*)-3-cyclohexyl-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (**1d**).

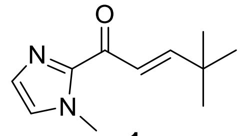


1d

Following the general procedure **GP2**, from cyclohexylaldehyde, compound **1d** was obtained as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 55 : 45). Spectroscopic data were consistent with the literature data for this compound.[8]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.35 (dd, *J* = 15.8, 1.4 Hz, 1H), 7.16 (s, 1H), 7.06 (dd, *J* = 15.8, 6.8 Hz, 1H), 7.02 (s, 1H), 4.03 (s, 3H), 2.13 – 2.19 (m, 1H), 1.88 – 1.79 (m, 2H), 1.79 – 1.72 (m, 2H), 1.68 – 1.76 (m, 1H), 1.38 – 1.13 (m, 5H).

(*E*)-4,4-dimethyl-1-(1-methyl-1*H*-imidazol-2-yl)pent-2-en-1-one (**1e**).

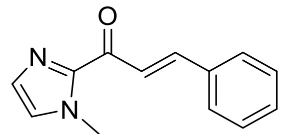


1e

Following the general procedure **GP2**, from pivaldehyde, compound **1e** was obtained as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 85 : 15). Spectroscopic data were consistent with the literature data for this compound.[9]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.33 (d, *J* = 15.8 Hz, 1H), 7.18 (s, 1H), 7.12 (d, *J* = 15.8 Hz, 1H), 7.04 (brs, 1H), 4.05 (s, 3H), 1.15 (s, 9H).

(E)-1-(1-methyl-1*H*-imidazol-2-yl)-3-phenylprop-2-en-1-one (**1f**).

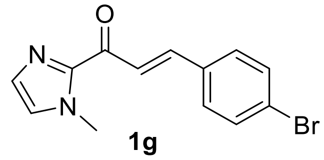


1f

Following the general procedure **GP1**, from ethyl *trans*-cinnamate, compound **1f** was obtained as a a white solid after purification by flash column chromatography (Cy : EtOAc = 85 : 15). Spectroscopic data were consistent with the literature data for this compound.[4]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.08 (d, *J* = 16.0 Hz, 1H), 7.83 (d, *J* = 16.0 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.44 – 7.36 (m, 3H), 7.22 (d, *J* = 0.9 Hz, 1H), 7.08 (d, *J* = 0.9 Hz, 1H), 4.10 (s, 3H).

(*E*)-3-(4-bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (**1g**).

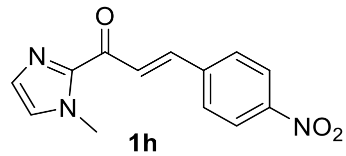


1g

Following the general procedure **GP1**, from ethyl *trans*-4-bromocinnamate, compound **1g** was obtained as a white solid after purification by flash column chromatography (Cy : EtOAc = 85 : 15). Spectroscopic data were consistent with the literature data for this compound.[4]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.06 (d, *J* = 16.0 Hz, 1H), 7.74 (d, *J* = 16.0 Hz, 1H), 7.57 – 7.52 (m, 4H), 7.22 (d, *J* = 1.0 Hz, 1H), 7.09 (d, *J* = 0.9 Hz, 1H), 4.10 (s, 3H).

(*E*)-1-(1-methyl-1*H*-imidazol-2-yl)-3-(4-nitrophenyl)prop-2-en-1-one (**1h**).

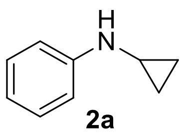


1h

Following the general procedure **GP1**, from ethyl *trans*-4-nitrocinnamate, compound **1h** was obtained as a yellow solid after purification by flash column chromatography (Cy : EtOAc = 55 : 45). Spectroscopic data were consistent with the literature data for this compound.[10]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.7 Hz, 2H), 8.19 (d, *J* = 16.1 Hz, 1H), 7.85 – 7.78 (m, 3H), 7.26 – 7.23 (m, 1H), 7.15 – 7.11 (m, 1H), 4.11 (s, 3H).

***N*-cyclopropylaniline** (**2a**).

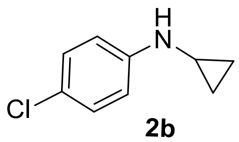


2a

Following the general procedure **GP3**, from bromobenzene, compound **2a** was obtained as a colorless oil after purification by flash column chromatography (Cy : EtOAc = 95 : 5) and further vacuum distillated. Spectroscopic data were consistent with the literature data for this compound.[6]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.24 – 7.15 (m, 2H), 6.84 – 6.77 (m, 2H), 6.77 – 6.70 (m, 1H), 4.21 (brs, 1H, NH), 2.43 (tt, *J* = 6.7, 3.6 Hz, 1H), 0.77 – 0.70 (m, 2H), 0.56 – 0.49 (m, 2H).

4-Chloro-*N*-cyclopropylaniline (**2b**).

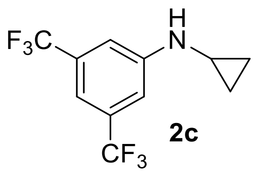


2b

Following the general procedure **GP3**, from 1-bromo-4-chlorobenzene, compound **2b** was obtained as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 95 : 5) and further vacuum distillated. Spectroscopic data were consistent with the literature data for this compound.[6]

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.13 (d, *J* = 8.9 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 4.61 (brs, 1H), 2.47 – 2.36 (m, 1H), 0.78 – 0.70 (m, 2H), 0.57 – 0.49 (m, 2H).

***N*-Cyclopropyl-3,5-bis(trifluoromethyl)aniline** (**2c**).

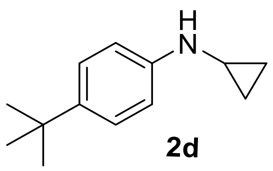


2c

Following the general procedure **GP3**, from 1-bromo-3,5-bis(trifluoromethyl)benzene, compound **2c** was obtained as a light-red oil after purification by flash column chromatography (Cy : EtOAc = 95 : 5) and further vacuum distillated. Spectroscopic data were consistent with the literature data for this compound.[6]

^{1}H-NMR (300 MHz, $CDCl_3$): *δ* 7.19 – 7.15 (m, 1H), 7.12 – 7.09 (m, 2H), 2.48 (tt, *J* = 6.7, 3.6 Hz, 1H), 0.88 – 0.80 (m, 2H), 0.59 – 0.52 (m, 2H).

4-(*tert*-Butyl)-*N*-cyclopropylaniline (**2d**).



2d

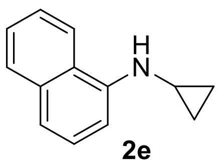
Following the general procedure **GP3**, from 1-bromo-4-(*tert*-butyl)benzene, compound **2d** was obtained as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 95 : 5) and further vacuum distillated.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.21 and 6.74 (AA'BB' system, 4H); 2.39 (tt, *J* = 6.6, 3.6 Hz, 1H), 1.28 (s, 9H), 0.82 – 0.58 (m, 2H), 0.53 – 0.44 (m, 2H).

^{13}C-NMR (76 MHz, $CDCl_3$): δ 146.4, 140.6, 126.0 (2C), 113.0 (2C), 34.0, 31.7 (3C), 25.5, 7.5 (2C).

HRMS (ESI): Calculated for $C_{13}H_{19}N$ $[M + H]^+$: 190.1517, found 190.1515.

***N*-Cyclopropylnaphthalen-1-amine** (**2e**).



2e

Following the general procedure **GP3**, from 1-bromonapthalene, compound **2e** was obtained as a green-blue oil after purification by flash column chromatography (Cy : EtOAc = 95 : 5). Spectroscopic data were consistent with the literature data for this compound.[6]

^{1}H-NMR (300 MHz, $CDCl_3$): *δ* 7.83 – 7.77 (m, 1H), 7.76 – 7.70 (m, 1H), 7.49 – 7.37 (m, 3H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.08 (dd, *J* = 7.6, 1.1 Hz, 1H), 4.89 (brs, 1H), 2.59 (tt, *J* = 6.8, 3.6 Hz, 1H), 0.90 – 0.81 (m, 2H), 0.69 – 0.62 (m, 2H).

4. Screening of the reaction conditions.

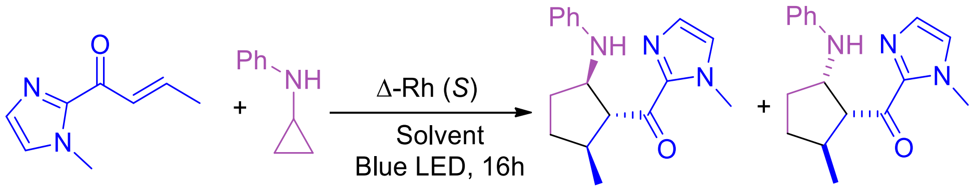


Table S1. Full screening of the reaction conditions.

Entry	*Ratio (1a:2a)*	*Δ-Rh (mol%)*	*PC*	*hv*	*Solvent*	*Conversion[c] [dr][d]*	*Yield [ee][e]*
1	1:2	2	None	Yes	MeCN (0.2M)	100% [1.3:1]	37% [79%]
2	1:2	2	CBz (2%)	Yes	MeCN (0.2M)	100% [1.1:1]	33% [75%]
3	1:2	None	None	Yes	MeCN (0.2M)	16% [1:5]	-
4	1:2	2	None	no	MeCN (0.2M)	0%	-
5	1:2	5	None	Yes	MeCN (0.2M)	100% [2:1]	40% [91%]
6	1:2	5	None	Yes	MeCN (0.33M)	100% [3:1]	47% [92%]
7	1:2	5	None	Yes	MeCN (0.5M)	100% [2.5:1]	43% [92%]
8	1:3	5	None	Yes	MeCN (0.33M)	100% [3.2:1]	25% [91%]
9	3:1	5	None	Yes	MeCN (0.33M)	0%	-
10[a]	1:2	5	None	Yes	MeCN (0.33M)	100% [2:1]	31% [93%]
11[b]	1:2	5	None	Yes	MeCN (0.2M)	100% [2.3:1]	35% [93%]
12	1:2	5	None	Yes	MeOH (0.33M)	0%	-
13	1:2	5	None	Yes	CH_2Cl_2 (0.33M)	100% [2.5:1]	43% [91%]
14	1:2	5	None	Yes	Toluene (0.33M)	100% [2.5:1]	38% [92%]
15	**1:2**	**5**	**None**	**Yes**	**Acetone (0.33M)**	**100% [3.3:1]**	**50% [93%]**
16	1:2	8	None	Yes	Acetone (0.33M)	100% [3.5:1]	53% [94%]

[a] The reaction was performed at 0 °C. [b] The reaction was performed at 45 °C. [c] Determinated by ^{1}H-RMN. [d] Ratio **3aa** : **3'aa**. [e] Value for the major diastereoisomer **3aa**.

5. Synthesis of compounds 3.

5.1. *Photoreactor Setup.*

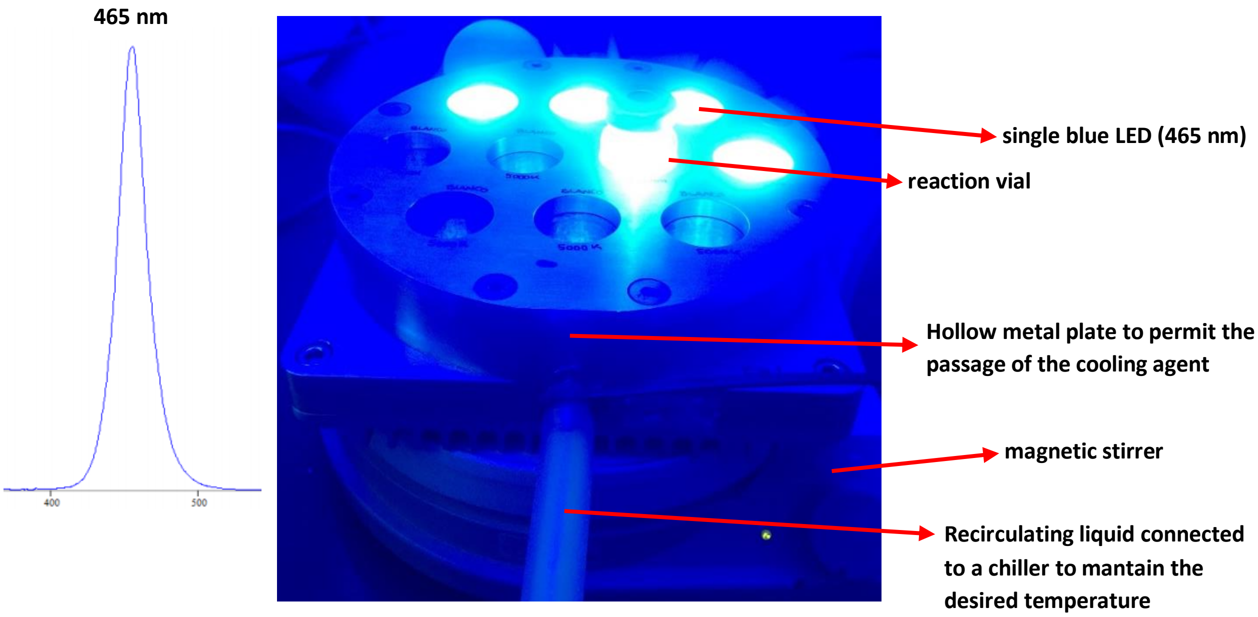
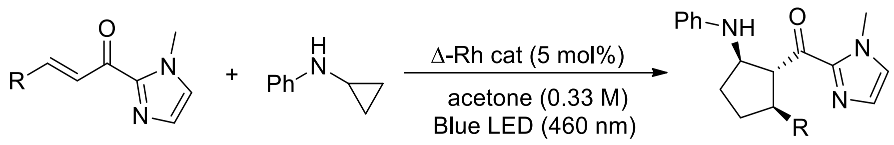


Figure S1: Photoreactor setup

5.2. *General procedure A for the Michael acceptor scope.*

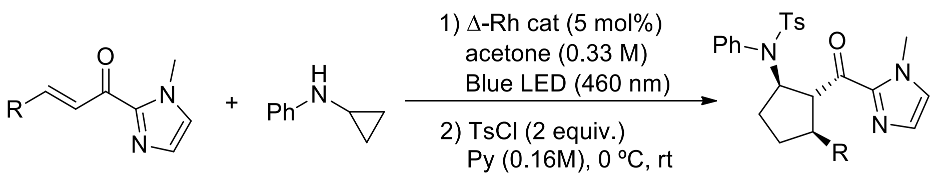
5.2.1. GPA 1: Procedure for alkylic residues (R = alkyl).



1a-e **2a** **3aa-3ea**

An oven-dried 6 mL vial equipped with a magnetic stirring bar was charged with the Michael acceptor **1a-e** (0.05 mmol), *N*-cyclopropylaniline (**2a**) (2.0 equiv.), and Δ-Rh cat. (5 mol%). Then, 150 µL of acetone was added. The vial was closed with a PTFE/rubber septum. The reaction mixture was irradiated and stirred in the photoreactor setup at 465 nm for 2 hours. After the reaction was complete, the solvent was eliminated under reduced pressure and the residue was further purified by flash column chromatography to afford the corresponding products **3aa-3ea.**

5.2.2. GPA 2: Procedure for aromatic residues (R = Aryl).



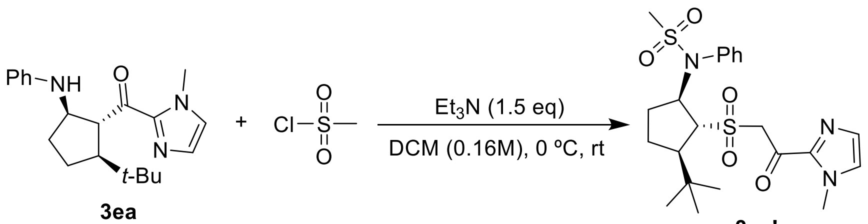
1f-h **2a** **3fa-3ha**

An oven-dried 6 mL vial equipped with a magnetic stirring bar was charged with the Michael acceptor **1f-h** (0.05 mmol), *N*-cyclopropylaniline (**2a**) (2.0 equiv.) and Δ-Rh cat. (5 mol%). Then, 150 µL of acetone was added. The vial was closed with a PTFE/rubber septum. Then, the reaction was irradiated and stirred in the photoreactor setup at 465 nm for 2 hours. After the reaction was complete, the solvent was evaporated under reduced pressure.

To the crude mixture, obtained before, was added pyridine and the mixture was stirred for 10 min at 0 °C. Then, 4-toluenesulfonyl chloride was added dropwise and further stirred at rt for 2h. After completion of the reaction, ice water was added and extracted with CH_2Cl_2. The organic layer was separated, dried over $MgSO_4$ and vacumed. The residue was purified by flash column chromatography to afford the desired product.

Tosylation reaction was required to separate complex diasteroisomers mixture **3fa-3ha**.

5.2.3. GPA 3: Mesylation procedure.

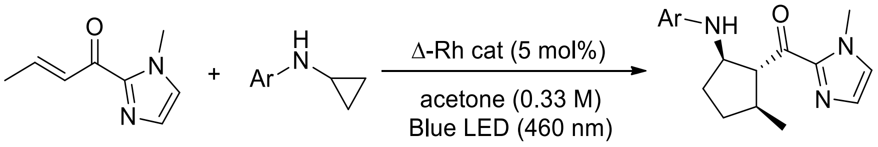


3ea **3ea'**

Triethylamine was added to a solution of **3ea** in dicloromethane and stirred at 0 °C for 10 min. Then, methanesulfonyl chloride (2 equiv.) was added dropwise at that temperature. The reaction was allowed to warm up to room temperature and the reaction was stirred until completion by TLC (Cy : AcOEt = 80 :20). After completion of the reaction, ice water was added and extracted with CH_2Cl_2. The organic layers were dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by flash column chromatography (Cy : AcOEt = 80 :20) to afford the desired product **3ea´**.

Mesylation was needed to determine the enantiomeric excess of **3ea**.

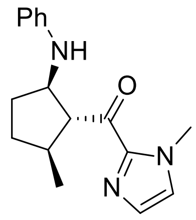
5.3. General procedure B for the imine scope (GPB).



1a **2b-e** **3ab-3ae**

An oven-dried 6 mL vial equipped with a magnetic stirring bar was charged with (*E*)-1-(1-methyl-1*H*-imidazol-2-yl)but-2-en-1-one (**1a**) (0.05 mmol), the desired *N*-cyclopropylarylamine **2b-e** (2.0 equiv.) and Δ-Rh cat. (5 mol%). Then, 0.15 mL of acetone were added, the vial was closed with PTFE/rubber septum, and the reaction was irradiated and stirred in the photoreactor setup at 465 nm for 2h. After the reaction was complete, the solvent was evaporated under reduced pressure and the residue was further purified by flash column chromatography to afford the corresponding products **3ab-3ae**.

(1-Methyl-1*H*-imidazol-2-yl)((1*R*,2*S*,5*R*)-2-methyl-5-(phenylamino)cyclopentyl)methanone (3aa).



3aa

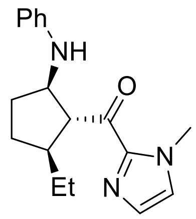
Following the general procedure **GPA 1**, from Michael aceptor **1a** (7.5mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3aa** was obtained (7.1 mg, 50% yield) as a yellow solid after purification by flash column chromatography (Hex : Et_2O = 80 : 20). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* IC column: CO_2/MeOH isocratic 95:5 in 15 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 5.28 min, τ_{major} = 4.83 min (94% *ee*). $[\alpha]^{20}_{D}$ = – 108.0 (c = 0.56, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.16 (s, 1H), 7.09 (t, *J* = 7.8 Hz, 2H), 7.00 (s, 1H), 6.71 – 6.47 (m, 3H), 3.96 (s, 3H), 3.89 – 3.69 (m, 2H), 2.58 – 2.44 (m, 1H), 2.34 – 2.18 (m, 1H), 2.06 – 1.92 (m, 1H), 1.82 – 1.66 (m, 1H), 1.65 – 1.47 (m, 1H), 1.06 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (76 MHz, $CDCl_3$): δ 193.7, 144.3 (2C), 129.3, 129.2 (2C), 127.5, 117.6, 113.9 (2C), 61.7, 60.7, 36.8, 36.4, 33.3, 32.6, 19.4.

HRMS (ESI): Calculated for $C_{17}H_{21}N_3O$ $[M + H]^+$: 284.1685, found 284.1689.

((1*R*,2*S*,5*R*)-2-Ethyl-5-(phenylamino)cyclopentyl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ba).



3ba

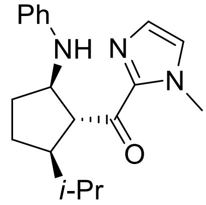
Following the general procedure **GPA 1**, from Michael aceptor **1b** (8.2 mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3ba** was obtained (7.4 mg, 50% yield) as a yellow solid after purification by flash column chromatography (Hex : Et_2O = 80 : 20). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* IC column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 3.19 min, τ_{major} = 2.96 min (86% *ee*). $[\alpha]^{20}_{D}$ = – 115.8 (c = 0.12, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.16 (s, 1H), 7.07 (t, *J* = 7.8 Hz, 2H), 6.99 (s, 1H), 6.60 (t, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 2H), 5.02 (brs, 1H), 3.94 (s, 3H), 3.89 – 3.74 (m, 2H), 2.46 – 2.38 (m, 1H), 2.30 – 2.25 (m, 1H), 2.10 – 1.96 (m, 1H), 1.75 – 1.67 (m, 1H), 1.61 – 1.47 (m, 2H), 1.41 – 1.29 (m, 1H), 0.86 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 194.0, 144.2 (2C), 129.3 (2C), 129.1, 127.5, 117.4, 113.7 (2C), 60.9, 60.1, 43.5, 36.3, 33.3, 29.6, 28.0, 12.8.

HRMS (ESI): Calculated for $C_{18}H_{23}N_3O$ $[M + H]^+$: 298.1841, found 298.1844.

((1*R*,2*R*,5*R*)-2-Isopropyl-5-(phenylamino)cyclopentyl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ca).



3ca

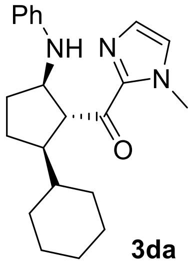
Following the general procedure **GPA 1**, from Michael aceptor **1c** (8.9 mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3ca** was obtained (8.3 mg, 53% yield) as a yellow solid after purification by flash column chromatography (Hex : Et_2O = 80 : 20). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* IG-3 column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{major} 3.21 min, τ_{minor} = 3.93 min (89% *ee*). $[\alpha]^{20}_{D}$ = – 119.4 (c = 0.39, $CHCl_3$)

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.15 (d, *J* = 0.8 Hz, 1H), 7.06 (t, *J* = 7.9 Hz, 2H), 6.97 (s, 1H), 6.59 (t, *J* = 7.5 Hz, 1H), 6.48 (d, *J* = 6.7 Hz, 2H), 4.00 – 3.95 (m, 1H), 3.92 (s, 3H), 3.82 – 3.73 (m, 1H), 2.48 – 2.34 (m, 1H), 2.32 – 2.20 (m, 1H), 2.03 – 1.88 (m, 1H), 1.63 – 1.57 (m, 3H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 194.1, 147.8, 143.9, 128.9, 128.7 (2C), 127.1, 116.7, 112.9 (2C), 61.1, 57.6, 47.7, 35.9, 33.4, 32.2, 26.9, 21.4, 20.0.

HRMS (ESI): Calculated for $C_{19}H_{25}N_3O$ $[M + H]^+$: 312,1998 found 312.1996.

((1*R*,2*R*,5*R*)-2-Cyclohexyl-5-(phenylamino)cyclopentyl)(1-methyl-1*H*-imidazol-2-yl)methanone (3da).



3da

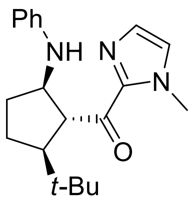
Following the general procedure **GPA 1**, from Michael aceptor **1d** (11 mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3da** was obtained (7.6 mg, 43% yield) as a yellow solid after purification by flash column chromatography (Hex : Et_2O = 80 : 20). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* IG-3 column: CO_2/MeOH gradient fom 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{major} = 4.09 min, τ_{minor} = 3.38 min (89% *ee*). $[\alpha]^{20}_D$ = – 126.1 (c = 0.48, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.15 (d, *J* = 0.8, 1H), 7.05 (dd, *J* = 8.5, 7.4 Hz, 2H), 6.97 (brs, 1H), 6.58 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.50 – 6.42 (m, 2H), 4.93 (brs, 1H), 4.03 – 3.88 (m, 1H), 3.91 (s, 3H), 3.78 – 3.63 (m, 1H), 2.50 – 2.34 (m, 1H), 2.32 – 2.18 (m, 1H), 2.07 – 1.89 (m, 1H), 1.86 – 1.41 (m, 6H), 1.37 – 1.02 (m, 5H), 1.02 – 0.79 (m, 2H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 194.2, 150.6, 143.0, 129.3, 129.1 (2C), 127.5, 117.0, 113.3 (2C), 61.4, 57.8, 46.9, 42.9, 36.4, 33.8, 32.4, 31.2, 27.6, 26.7, 26.6, 26.5.

HRMS (ESI): Calculated for $C_{22}H_{29}N_3O$ $[M + H]^+$: 352.2311, found 352.2313.

((1*R*,2*S*,5*R*)-2-(*tert*-Butyl)-5-(phenylamino)cyclopentyl)(1-methyl-1H-imidazol-2-yl)methanone (3ea).



3ea

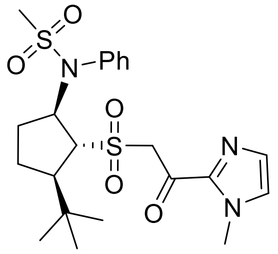
Following the general procedure **GPA 1**, from Michael aceptor **1e** (9.6 mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3ea** was obtained (6.4 mg, 39% yield) as a yellow solid after purification by flash column chromatography (Hex : Et_2O = 80 : 20). The enantiomeric excess was determined from mesilated compounds **3ea´**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.16 (d, *J* = 1.0 Hz, 1H), 7.05 (dd, *J* = 8.6, 7.3 Hz, 2H), 6.96 (d, *J* = 1.0 Hz, 1H), 6.57 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.46 (dd, *J* = 8.6, 1.1 Hz, 2H), 4.09 (t, *J* = 9.3 Hz, 1H), 3.90 (s, 3H), 3.82 – 3.68 (m, 1H), 2.56 (td, *J* = 9.7, 6.8 Hz, 1H), 2.36 – 2.20 (m, 1H), 1.97 – 1.78 (m, 1H), 1.79 – 1.62 (m, 1H), 1.53 (dq, *J* = 12.3, 8.8 Hz, 1H), 0.84 (s, 9H).

^{13}C-NMR (76 MHz, $CDCl_3$): δ 194.7, 147.8, 144.1, 129.2, 129.1 (2C), 127.4, 117.2, 113.4 (2C), 62.3, 55.3, 51.0, 36.4, 34.3, 33.2, 27.8 (3C), 25.2.

HRMS (ESI): Calculated for $C_{20}H_{27}N_3O$ $[M + H]^+$: 326.2154, found 326.2159.

***N*-((1*R*,2*R*,3*R*)-3-(*tert*-butyl)-2-((2-(1-methyl-1*H*-imidazol-2-yl)-2-oxoethyl)sulfonyl)cyclopentyl)-*N*-phenylmethanesulfonamide (3ea')**



3ea'

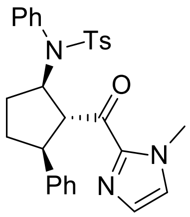
Following the general procedure **GPA 3**, from compound **3ea**, compound **3ea'** was obtained. The enantiomeric excess was determined by SFC on a *Diacel Chiralpak* IG-3 column: CO_2/MeOH gradient fom 95:5 to 60:40 in 8 min, flow rate 3 mL/min, τ_{major} = 4.43 min, τ_{minor} = 4.15 min (95% *ee*). $[\alpha]^{20}_{D}$ = – 96.1 (c = 0.43, $CHCl_3$).

^{1}H-NMR (500 MHz, CDCl3) δ 7.72 (d, *J* = 7.4 Hz, 2H), 7.52 – 7.43 (m, 3H), 7.29 (d, *J* = 0.9 Hz, 1H), 7.12 (d, *J* = 0.9 Hz, 1H), 4.76 (td, *J* = 9.2, 7.1 Hz, 1H), 4.37 – 4.29 (m, 2H), 4.15 (d, *J* = 15.0 Hz, 1H), 4.05 (s, 3H), 3.09 (s, 3H), 2.40 (td, *J* = 9.4, 5.6 Hz, 1H), 2.12 – 2.02 (m, 1H), 1.78 – 1.69 (m, 1H), 1.43 – 1.32 (m, 2H), 0.68 (s, 9H).

^{13}C-NMR 13C NMR (75 MHz, $C_2D_2Cl_4$, 353 K) δ 195.6, 144.2, 134.9, 132.9 (2C), 129.85, 129.47 (2C), 129.5, 128.0, 70.1, 67.9, 53.6, 53.1, 42.6 (3C), 36.3 (3C), 33.3, 32.2, 27.7, 25.4.

HRMS (ESI): Calculated for $C_{22}H_{31}N_3O_5S_2$ $[M + H]^+$: 481.1705, found 481.1933.

4-Methyl-*N*-((1*R*,2*R*,3*S*)-2-(1-methyl-1*H*-imidazole-2-carbonyl)-3-phenylcyclopentyl)-*N*-phenylbenzene sulfonamide (3fa).



3fa

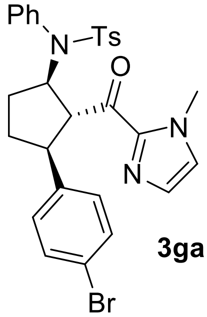
Following the general procedure **GPA 2**, from Michael aceptor **1f** (10.6 mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3fa** was obtained (12.5 mg, 50% yield) as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 80 : 20). The enantiomeric excess was determined by SFC on a *Diacel Chiralpak* ID column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 3.91 min, τ_{major} = 4.40 min (94 % *ee*). $[\alpha]^{20}_{D}$ = – 93.1 (c = 0.34, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.38 (m, 5H), 7.16 – 6.95 (m, 9H), 5.22 – 5.05 (m, 1H), 4.53 (dd, *J* = 10.3, 9.1 Hz, 1H), 3.92 (s, 3H), 3.64 – 3.47 (m, 1H), 2.36 (s, 3H), 2.21 – 1.97 (m, 2H), 1.93 – 1.75 (m, 1H), 1.55 – 1.36 (m, 1H).

^{13}C-NMR (76 MHz, $CDCl_3$): δ 193.8, 143.9, 142.9, 142.8, 138.1, 135.8, 133.1 (2C), 129.3, 129.2 (4C), 129.0, 128.4 (2C), 127.6 (2C), 127.3, 127.2 (2C), 126.4, 65.0, 57.4, 48.6, 36.2, 32.7, 30.1, 21.6.

HRMS (ESI): Calculated for $C_{29}H_{29}N_3O_3S$ $[M + H]^+$: 500.1930, found 500.1933.

***N*-((1*R*,2*R*,3*S*)-3-(4-Bromophenyl)-2-(1-methyl-1*H*-imidazole-2-carbonyl)cyclopentyl)-4-methyl-*N*-phenylbenzenesulfonamide (3ga).**



3ga

Following the general procedure **GPA 2**, from Michael aceptor **1g** (14.6 mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3ga** was obtained (11 mg, 38% yield) as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 85 : 15). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{major} = 4.89 min, τ_{minor} = 4.42 min (91% *ee*). $[\alpha]^{20}_{D}$ = – 77.6 (c = 0.46, $CHCl_3$).

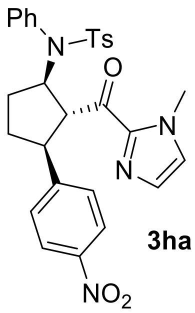
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.2 Hz, 2H), 7.40 (s, 5H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 7.11 (s, 1H), 7.00 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.11 (q, *J* = 8.3

Hz, 1H), 4.49 (t, *J* = 9.6 Hz, 1H), 3.93 (s, 3H), 3.49 (q, *J* = 9.1 Hz, 1H), 2.36 (s, 3H), 2.16 – 1.94 (m, 2H), 1.93 – 1.74 (m, 1H), 1.45 – 1.31 (m, 1H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 193.5, 143.8, 142.9, 141.9, 138.0, 135.7, 133.1 (2C), 131.5 (2C), 129.4, 129.3 (2C), 129.2 (2C), 129.04, 128.99 (2C), 127.6 (2C), 127.5, 120.1, 64.8, 57.3, 48.0, 36.2, 32.6, 30.0, 21.6.

HRMS (ESI): Calculated for $C_{29}H_{28}BrN_3O_3S$ [M + H]$^+$: 578.1035, found 578.1038.

4-Methyl-*N*-((1*R*,2*R*,3*S*)-2-(1-methyl-1*H*-imidazole-2-carbonyl)-3-(4-nitrophenyl)cyclopentyl)-*N*-phenyl benzenesulfonamide (3ha).



3ha

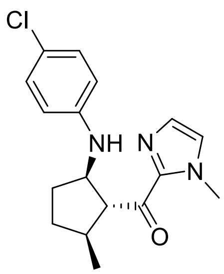
Following the general procedure **GPA 2**, from Michael aceptor **1h** (12.9 mg, 0.05 mmol) and amine **2a** (13.3 mg, 0.1 mmol), compound **3ha** was obtained (9.8 mg, 36% yield) as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 85 : 15). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* ID column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.90 min, τ_{major} = 5.37 min (93% *ee*). $[\alpha]^{20}_D$ = – 52.7 (c = 0.64, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.44 – 7.33 (m, 5H), 7.18 – 7.09 (m, 5H), 7.02 (s, 1H), 5.15 (q, *J* = 8.4 Hz, 1H), 4.56 (t, *J* = 9.5 Hz, 1H), 3.95 (s, 3H), 3.69 – 3.56 (m, 1H), 2.37 (s, 3H), 2.20 – 2.03 (m, 2H), 1.93 – 1.79 (m, 1H), 1.53 – 1.40 (m, 1H).

^{13}C-NMR (76 MHz, CDCl3): δ 192.9, 150.8, 146.7, 143.7, 143.0, 137.9, 135.7, 133.1 (2C), 129.6, 129.35 (2C), 129.31 (2C), 129.2, 128.1 (2C), 127.73, 127.65 (2C), 123.8 (2C), 64.7, 57.2, 48.3, 36.2, 32.4, 30.2, 21.6.

HRMS (ESI): Calculated for $C_{29}H_{28}N_4O_5S$ [M + H]$^+$: 545.1780, found 545.1783.

((1*R*,2*R*,5*S*)-2-((4-Chlorophenyl)amino)-5-methylcyclopentyl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ab)



3ab

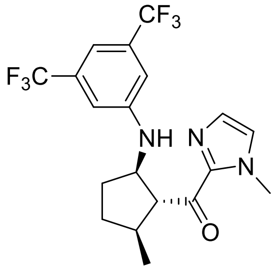
Following the general procedure **GPB**, from Michael aceptor **1a** (7.5mg, 0.05 mmol) and amine **2b** (16.7 mg, 0.1 mmol), compound **3ab** was obtained (6.7 mg, 42% yield) as a yellow solid after purification by flash column chromatography (Cy : EtOAc = 60 : 40). The enantiomeric excess was determined, by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 5.02 min, τ_{major} = 4.71 min (92% *ee*). $[\alpha]^{20}_D$ = – 94.9 (c = 0.29, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.15 (d, *J* = 1.0 Hz, 1H), 7.06 – 6.97 (m, 3H), 6.44 (d, *J* = 8.5 Hz, 2H), 3.96 (s, 3H), 3.85 – 3.63 (m, 2H), 2.49 (tt, *J* = 9.7, 6.8 Hz, 1H), 2.31 – 2.16 (m, 1H), 2.07 – 1.91 (m, 1H), 1.78 – 1.62 (m, 1H), 1.61 – 1.45 (m, 1H), 1.05 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 193.5, 146.5, 144.2, 129.3, 128.9 (2C), 127.6, 122.2, 114.9 (2C), 61.7, 60.7, 36.9, 36.4, 33.2, 32.5, 19.4.

HRMS (ESI): Calculated for $C_{17}H_{20}ClN_3O$ [M + H]$^+$: 318.1295, found 318.1295.

((1*R*,2*R*,5*S*)-2-((3,5-bis(Trifluoromethyl)phenyl)amino)-5-methylcyclopentyl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ac).



3ac

Following the general procedure **GPB**, from Michael aceptor **1a** (7.5mg, 0.05 mmol) and amine **2c** (26.9 mg, 0.1 mmol) compound **3ac** was obtained (7 mg, 33% yield) as a yellow oil after purification by flash column chromatography (Cy : EtOAc = 90 : 10). The enantiomeric excess was determined, after mesilation, by SFC on a *Daicel Chiralpak* IB-3 column: CO_2/MeOH gradient from 95:5 to 70:30 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{major} = 0.93 min, τ_{minor} = 1.06 min (80% *ee*). $[\alpha]^{20}_D$ = – 111.3 (c = 0.41, $CHCl_3$).

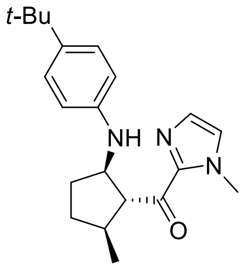
^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.18 (s, 1H), 7.04 (s, 1H), 7.02 (s, 1H), 6.79 (s, 2H), 5.76 (brs, 1H), 3.98 (s, 3H), 3.89 – 3.70 (m, 2H), 2.61 – 2.47 (m, 1H), 2.41 – 2.25 (m, 1H), 2.11 – 1.97 (m, 1H), 1.77 – 1.63 (m, 1H), 1.61 – 1.46 (m, 1H), 1.06 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 193.0, 148.8, 143.9, 132.3 (q, *J* = 32.6 Hz, 2C), 129.2, 127.8, 123.7 (q, *J* = 272.5 Hz, 2C), 112.3 (q, *J* = 4.4 Hz, 2C), 109.8 (p, *J* = 4.2 Hz), 61.5, 59.8, 36.8, 36.5, 33.0, 32.3, 19.3.

^{19}F NMR (471 MHz, $CDCl_3$) δ – 63.15.

HRMS (ESI): Calculated for $C_{19}H_{19}F_6N_3O$ $[M + H]^+$: 420.1432, found 420.1437.

((1*R*,2*R*,5*S*)-2-((4-(*tert*-Butyl)phenyl)amino)-5-methylcyclopentyl)(1-methyl-1*H*-imidazol-2-yl)methanone (3ad).



3ad

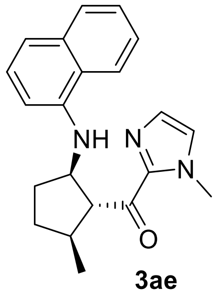
Following the general procedure **GPB**, from Michael aceptor **1a** (7.5mg, 0.05 mmol) and amine **2d** (18.9 mg, 0.1 mmol), compound **3ad** was obtained (10.8 mg, 33% yield) as an orange solid after purification by flash column chromatography (Cy : EtOAc = 60 : 40). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* IA column: CO_2/MeOH gradient from 95 : 5 to 60 : 40 in 8 min, flow rate 2 mL/min, λ = 210 nm, τ_{minor} = 4.35 min, τ_{major} = 4.69 min (87% *ee*). $[\alpha]^{20}_D$ = – 235 (c = 0.04, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.15 (d, *J* = 1.0 Hz, 1H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 1.0 Hz, 1H), 6.49 (d, *J* = 8.3 Hz, 2H), 3.94 (s, 3H), 3.87 – 3.67 (m, 2H), 2.51 (tt, *J* = 9.8, 6.8 Hz, 1H), 2.25 (dq, *J* = 12.8, 7.9 Hz, 1H), 2.04 – 1.91 (m, 1H), 1.81 – 1.66 (m, 1H), 1.63 – 1.48 (m, 1H), 1.23 (s, 9H), 1.05 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (76 MHz, $CDCl_3$): δ 193.9, 146.0, 144.4, 139.8, 129.3, 127.4, 125.9 (2C), 113.1 (2C), 61.8, 60.6, 36.8, 36.4, 33.9, 33.8, 32.6, 31.7 (3C), 19.4.

HRMS (ESI): Calculated for $C_{21}H_{29}N_3O$ $[M + H]^+$: 340.2311, found 340.2312.

(1-Methyl-1*H*-imidazol-2-yl)((1*R*,2*S*,5*R*)-2-methyl-5-(naphthalen-1-ylamino)cyclopentyl)methanone (3ae).



3ae

Following the general procedure **GPB**, from Michael aceptor **1a** (7.5mg, 0.05 mmol) and amine **2e** (18.3 mg, 0.1 mmol), compound **3ae** was obtained (8.4 mg, 50% yield) as a red-orange oil after purification by flash column chromatography (Cy : EtOAc = 50 : 50). The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* IC column: CO_2/MeOH gradient from 95 : 5 to 60 : 40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{minor} = 4.03 min, τ_{major} = 3.91 min (83% *ee*). $[\alpha]^{20}_{D}$ = – 267.9 (c = 0.08, $CHCl_3$).

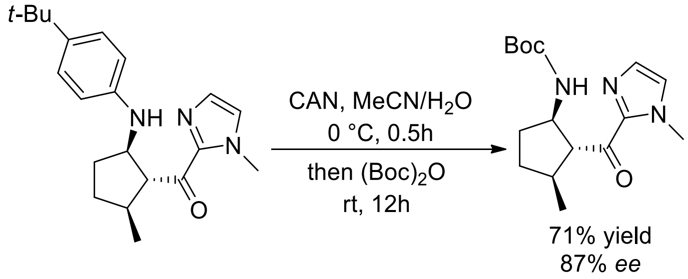
^{1}H-NMR (300 MHz, $CDCl_3$): 1H NMR (300 MHz, DMSO) δ 8.13 – 8.00 (m, 1H), 7.77 – 7.67 (m, 1H), 7.45 – 7.38 (m, 2H), 7.29 – 7.22 (m, 1H), 7.19 (d, *J* = 1.0 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.96 (d, *J* = 1.0 Hz, 1H), 6.40 (d, *J* = 7.5 Hz, 1H), 3.96 (s, 3H), 3.89 – 3.79 (m, 1H), 2.73 – 2.54 (m, 1H), 2.51 – 2.33 (m, 1H), 2.04 (dtd, *J* = 11.5, 7.4, 3.6 Hz, 1H), 1.83 (ddt, J = 13.0, 9.0, 4.5 Hz, 1H), 1.71 – 1.51 (m, 2H), 1.10 (d, *J* = 6.5 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 193.3, 144.3, 143.9, 134.4, 129.4, 128.5, 127.6, 126.6, 125.7, 124.4, 123.8, 121.2, 116.8, 104.7, 61.6, 60.1, 36.3, 36.1, 33.5, 32.9, 19.1.

HRMS (ESI): Calculated for $C_{21}H_{23}N_3O$ $[M + H]^+$: 334.1841, found 334.1844.

6. Synthetic playground information.

a) Oxidation with CAN



3ad **4ad**

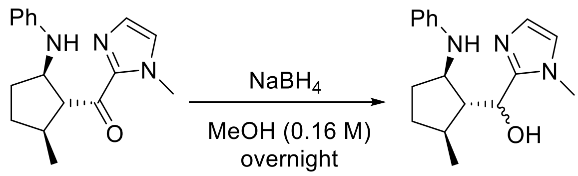
To a solution of ceric ammonium nitrate (CAN) (69 mg, 0.125 mmol, 2.50 equiv) in H_2O (0.5 mL) was added a solution of **3ad** (17 mg, 0.05 mmol, 1.00 equiv) in MeCN (0.5 mL) dropwise slowly at 0 °C. After being stirred for 30 min, $(Boc)_2O$ (80 µL, 0.35 mmol, 7.00 equiv) was added and the reaction mixture was stirred for 12 h at room temperature. The resulting reddish-brown solution was diluted with water, neutralized with $NaHCO_3$ saturated solution, and extracted with EtOAc twice. The combined organic extracts were dried over Na_2SO_4 and filtered. After concentration, the residue was purified by column chromatography on silica gel (Cy : EtOAc = 65 : 35) to give **4ad** (11 mg, 0.036 mmol, 71% yield) as a yellow solid. The enantiomeric excess was determined by SFC on a *Daicel Chiralpak* IC column: CO_2/MeOH gradient from 95:5 to 60:40 in 8 min, flow rate 3 mL/min, λ = 210 nm, τ_{major} = 2.46 min, τ_{minor} = 2.69 min (87% *ee*). $[\alpha]^{20}_D$ = – 61.3 (c = 0.13, $CHCl_3$).

^{1}H-NMR 1H NMR (300 MHz, $CDCl_3$, 323 K) δ 7.14 (s, 1H), 7.01 (s, 1H), 4.10 – 3.94 (m, 3H), 4.03 (s, 3H), 3.69 (t, *J* = 9.4 Hz, 1H), 2.54 – 2.39 (m, 1H), 2.31 – 2.15 (m, 1H), 2.03 – 1.88 (m, 1H), 1.74 – 1.54 (m, 1H), 1.53 – 1.36 (m, 1H), 1.28 (s, 9H), 1.04 (d, *J* = 6.7 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 193.5, 155.6, 144.2, 128.7, 127.1, 79.0, 61.4, 57.5, 37.2, 36.4, 32.6, 31.6, 28.3 (3C), 19.7.

HRMS (ESI): Calculated for $C_{16}H_{25}N_3O_3$ $[M + H]^+$: 308.1896, found 308.1899.

b) Reduction with $NaBH_4$



3aa **5aa**

91% yield
1.3:1 dr

To a solution of **3aa** (14.5 mg, 0.05 mmol, 1 equiv) in MeOH (0.3 mL) was added portionwise $NaBH_4$ (5 mg, 0.125 mmol, 2.5 equiv) and the mixture was stirred at room temperature for 1.5h under N_2. After reaction completion, the solution was diluted with water, neutralized with $NaHCO_3$ saturated solution, and extracted with EtOAc twice, filtered, dried over $MgSO_4$ and vacuumed. The product **5aa** was obtained (12.8 mg, 0.045 mmol, 91% yield) as a light-yellow solid with a diasteromeric ratio of (1.3:1) without further purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21 – 7.07 (m, 4H, major+minor), 6.93 (dd, *J* = 6.0, 1.2 Hz, 2H, major), 6.83 – 6.51 (m, 8H, major+minor), 5.46 – 5.29 (m, 1H, minor), 4.87 (t, *J* = 6.5 Hz, 1H, major), 3.87 – 3.74 (m, 2H, major+minor), 3.70 (s, 3H, major), 3.54 (s, 3H, minor), 2.26 – 1.95 (m, 7H, major+minor), 1.95 – 1.76 (m, 4H, major+minor), 1.69 – 1.47 (m, 3H, major+minor), 0.85 (d, *J* = 6.6 Hz, 3H, minor), 0.73 (d, *J* = 6.0 Hz, 3H, major).

^{13}C-NMR (76 MHz, $CDCl_3$): δ 149.7, 149.0, 147.9, 147.3, 129.3 (2C), 129.2 (2C), 124.3, 123.6, 121.8, 121.6, 118.6, 117.4, 114.9 (2C), 113.5 (2C), 68.7, 67.9, 59.7, 58.9, 58.2, 58.1, 35.7, 34.5, 33.9, 32.8, 32.6, 32.2, 31.8, 27.0, 21.7, 19.7.

HRMS (ESI): Calculated for $C_{17}H_{23}N_3O$ $[M + H]^+$: 286.1841, found 286.1843.

7. UV-Vis Absorption spectra.

The absorption spectra of acetone solutions of **1a**, **2a**, Δ-Rh complex initial, and the complex Rh-I at the concentration of the reaction was measured using a quartz cuvette with 0,1 cm of optical pathway (Figure S2).

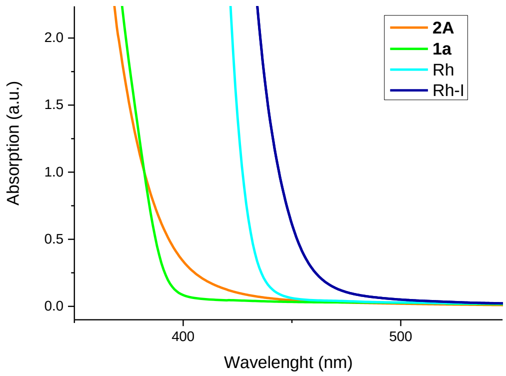


Figure S2. Absorption spectra of **1a**, **2A**, Rh complex and Rh-I complex in acetone.

8. Quantum Yield determination.

A solution of ferrioxalate was chosen as actinometer following the procedure described by the IUPAC (subcommittee on photochemistry).[11] The procedure is based on the decomposition under irradiation of ferric ions to ferrous ions which are complexed by 1,10-phenanthroline. This photochemical transformation has a known quantum yield and the complexation of Fe^{2+} with 1,10-phenanthroline can be monitored by UV-Visible absorption since its extinction coefficient at 510 nm is known (ε =11100 M^{-1} cm^{-1}). Therefore, the moles transformed can be related with the moles of photons absorbed by the equation [eq. 1].

$$\Phi = \frac{mol\ transformed}{photons\ absorbed} \qquad [eq.\ 1]$$

The complete procedure should be done under a red safe-light environment. At 465 nm ferroxilate has a Φ = 0.85.[12] 0.006, 0.012, or 0.15 M solutions of $K_3[Fe(C_2O_4)_3]\ 3H_2O$ can be used for actinometry. In this case, we chose a concentration of 0.15 M. The solutions were prepared and stored in a dark laboratory:

1. Potassium ferrioxalate solution (0.15 M): 368.4 mg of $K_3[Fe(C_2O_4)_3]\ 3H_2O$ (commercially available) and 26.6 µL of H_2SO_4 were added into a 5 mL volumetric flask and filled to the mark with Milli-Q water.

2. Phenanthroline solution (0.15 M): 1.35 g of 1,10-phenantroline monohydrate were added to 50 mL volumetric flask and filled to the mark with MilliQ water.

3. Buffer solution: 4.94 g of NaOAc and 1 mL of H_2SO_4 were added to 100 mL volumetric flask and filled to the mark with MilliQ water.

4. Model reaction solution: An oven-dried 6 mL vial equipped with a magnetic stirring bar was charged with the Michael acceptor **1a** (0.05 mmol), *N*-cyclopropylaniline (**2a**) (2.0 equiv.) and Δ-Rh cat. (5 mol%). Then, 150 µL of acetone were added. The vial was closed with PTFE/rubber septum. The reaction was irradiated and stirred in the photoreactor setup under 465 nm LED irradiation (22.0216 W/m^2 intensity; approximate distance was 2 cm from the vial) at 20 °C.

Actinometry procedure: Due to the reactor setup (see Figure S1), the simultaneous irradiation of both the actinometer solution and model reaction is not feasible. However, the stability of the irradiation light was checked through radiometer measurements (from spectro-radiometer equipment Stellarnet model Blue-Wave UV-NB50). Therefore, we assumed that consecutive measurements of both actinometer and model reaction are comparable. In addition, using the same spectrometer, the LED source spectrum was measured, detecting a maximum wavelength of emission of 465 nm (see Figure S1).

2 mL of Potassium ferrioxalate solution (0.15 M) were introduced into the photoreactor under dark conditions while being stirred. Then, the LED was switched on. Every 5 s the light was switched off and a 0.1 mL aliquot was taken. To each aliquot, 2 mL of buffer solution and 0.5 mL of 1,10-phenanthroline 0.15 M were added and the final volume was raised to 10 mL with MilliQ water. Then 83 µL of this solution were diluted to 5 mL with MilliQ water. As a blank sample, a solution was prepared with 0.1 mL of potassium ferrioxalate solution (0.15 M) before irradiation, 2 mL of buffer solution and 0.5 mL of 1,10-phenanthroline 0.15 M in a 10 mL of volumetric flask filled with water until the mark, and 83 µL of this solution were diluted to 5 mL with MilliQ water. The absorbance spectrum of each sample was monitored at 510 nm. The absorbance to each time was related with the photochemically produced Fe^{2+} ions across the Lambert-Beer Law (eq 2), where V_1 is the irradiated volume (noting that the initial volume is 2 mL but it changes as the aliquots are taken); V_2 is the aliquot volume (0.1 mL), V_3 is the final volume after addition of 1,10-phenanthroline and buffer (10 mL). b is referred to the optical pathway (1 cm), ΔA (510 nm) is the difference in absorbance between the irradiated solution and the blank sample, ε (510 nm) is the extinction coefficient of the complex formed by Fe(II) and 1,10-phenanthroline (ca. 11100 M^{-1} cm^{-1}).

$$moles\ of\ Fe^{2+} = \frac{V_1 \cdot V_3 \cdot \Delta A_{(510\ nm)}}{10^3 \cdot V_2 \cdot b \cdot \varepsilon_{(510\ nm)}} \qquad \text{[eq. 2]}$$

The moles of Fe^{2+} formed (x) are plotted as a function of time (t) (Figure S3).

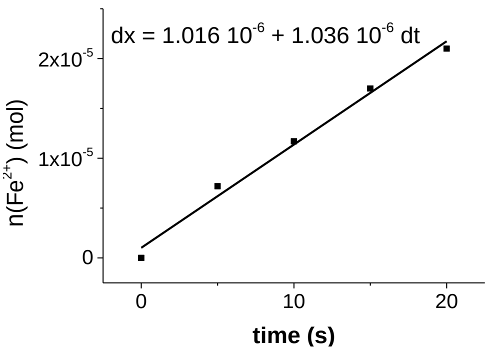


Figure S3. Actinometer.

The slope of this line (dx/dt) was correlated to the moles of incident photons by unit of time ($q^0_{n,p}$) using the following [eq.3]:

$$q^0_{n,p} = \frac{dx/dt}{\Phi_{(\lambda)} \cdot [1 - 10^{-A(\lambda)}]} \qquad \text{[eq. 3]}$$

Where $\Phi_{(\lambda)}$ is the quantum yield of the actinometer reaction at the irradiated wavelength, in this case being 0.85 at 465 nm for 0.15 M dilution[12] and $A_{(\lambda)}$ is the absorbance of the actinometer solution (ferrioxalate) at the irradiated wavelength (465 nm). The absorbance at 465 nm was measured with an Agilent 8453 UV-visible Spectroscopy System using a quartz cuvette with 1 cm of optical pathway.

Therefore, the moles of incident photons by unit of time ($q^0_{n,p}$) was determined as 1.036 10^{-5} einstein s^{-1}.

The kinetics of the reaction under study were done as follows: the photoreactor (blue LEDs) was switched on and the reaction mixture was stirred. At 12, 24, 36 and 48 minutes an aliquot of 0.05 mL were taken from the reaction mixture under a positive flow of nitrogen, the solvent evaporated under reduced pressure, and the crude diluted with 0.4 mL of $CDCl_3$. Thus, the conversion of the reaction at the different indicated time was determined by ^{1}H-NMR. Knowing the initial molar concentration, the determination of the moles of photo-converted product is possible.

Plotting the moles of product versus the irradiation time (Figure S4), the slope *dx*/*dt* can be related with the quantum yield across the [eq.3] being equal to time ($q^0_{n,p}$) $\Phi_{(\lambda)}$·[1-10-$A_{(\lambda)}$]. Therefore, the quantum yield at the wavelength of irradiation Φ (465 nm) can be calculated once A (465 nm) is determined. To measure A (465 nm), a model reaction solution was added to a 1 mm optical pathway cuvette and the UV-Visible spectrum was recorded obtaining an absorbance of 0.95.

Therefore, the quantum yield for the reaction is: Φ = 0.031 = 3.1%.

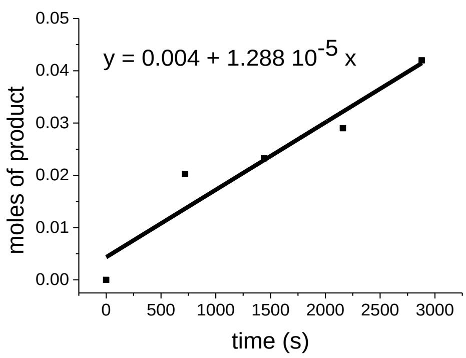


Figure S4. Kinetic of the reaction.

9. NMR Spectra section.

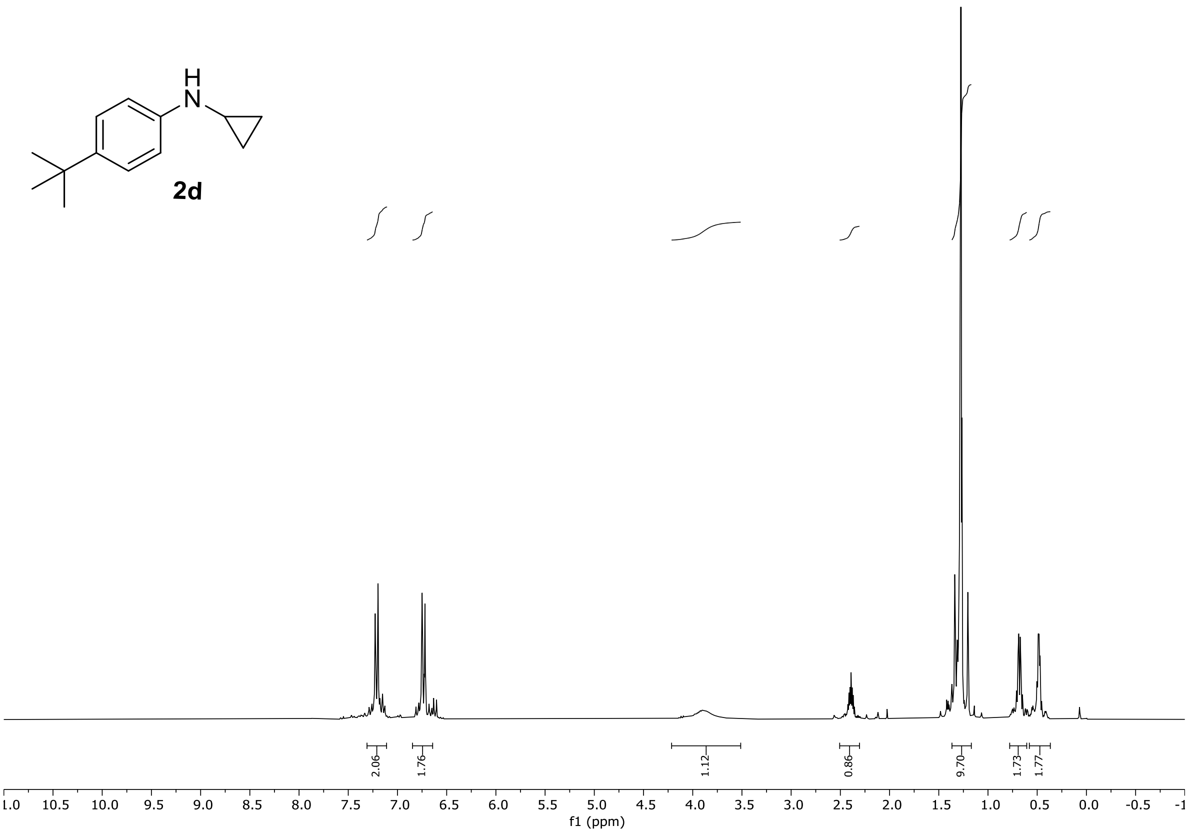


Figure S5. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **2d.**

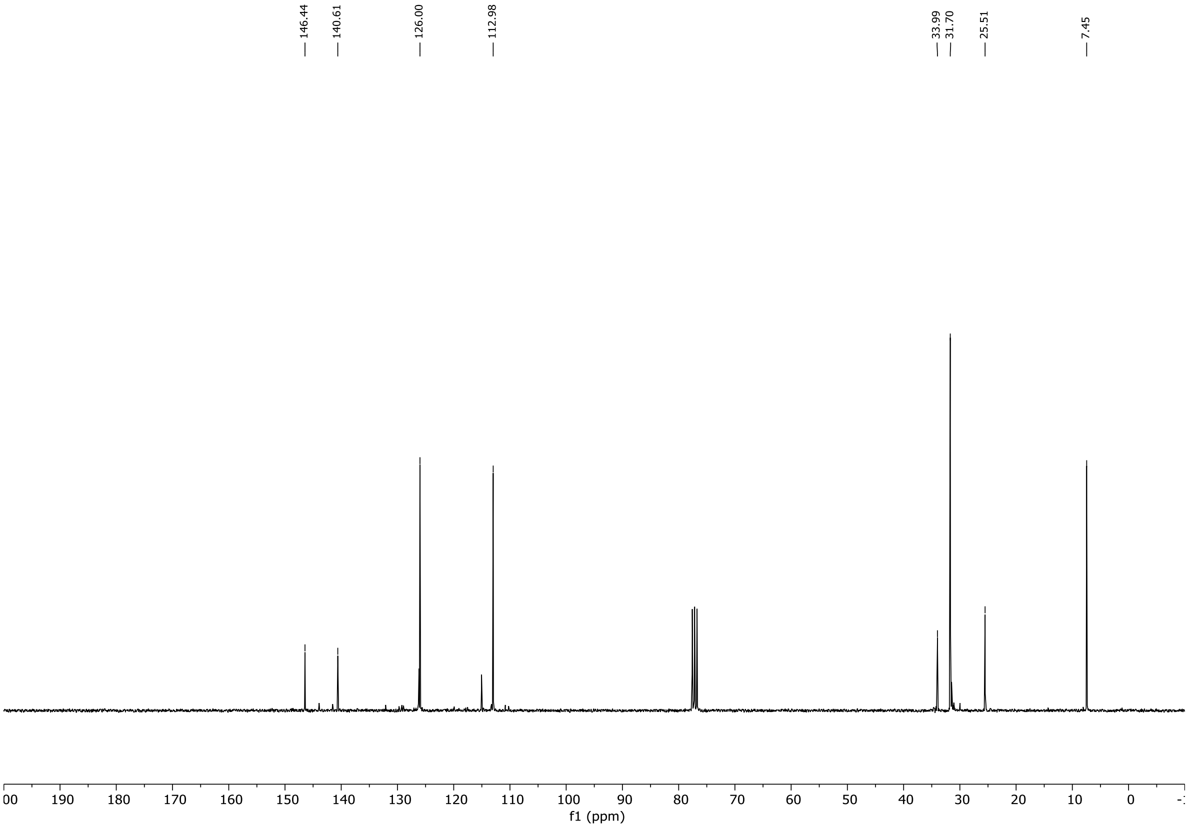
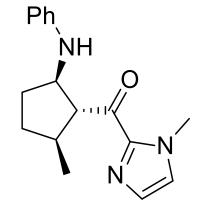


Figure S6. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **2d.**



3aa

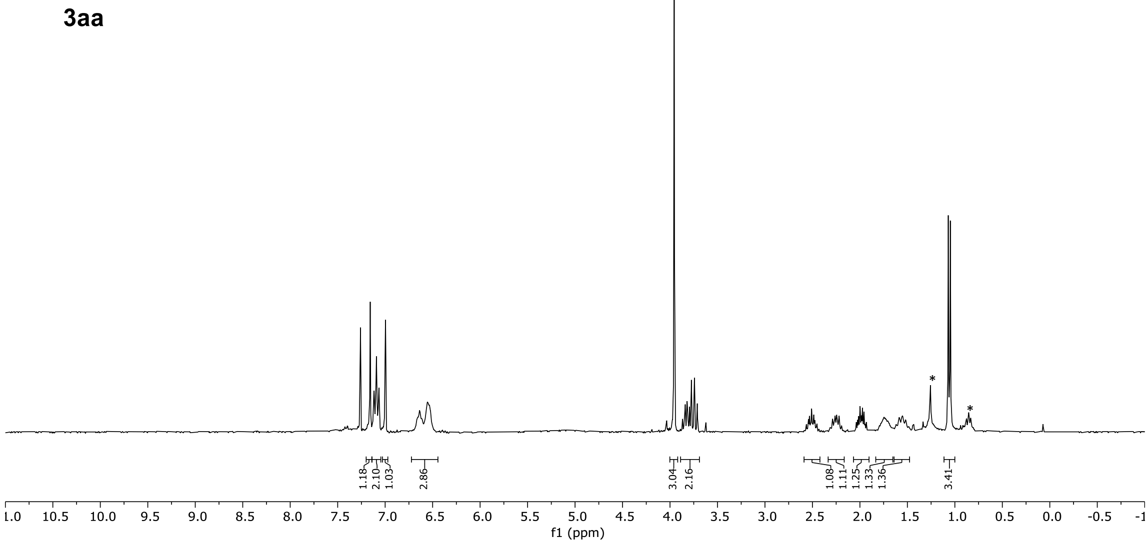


Figure S7. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3aa.** (*Grease peaks)

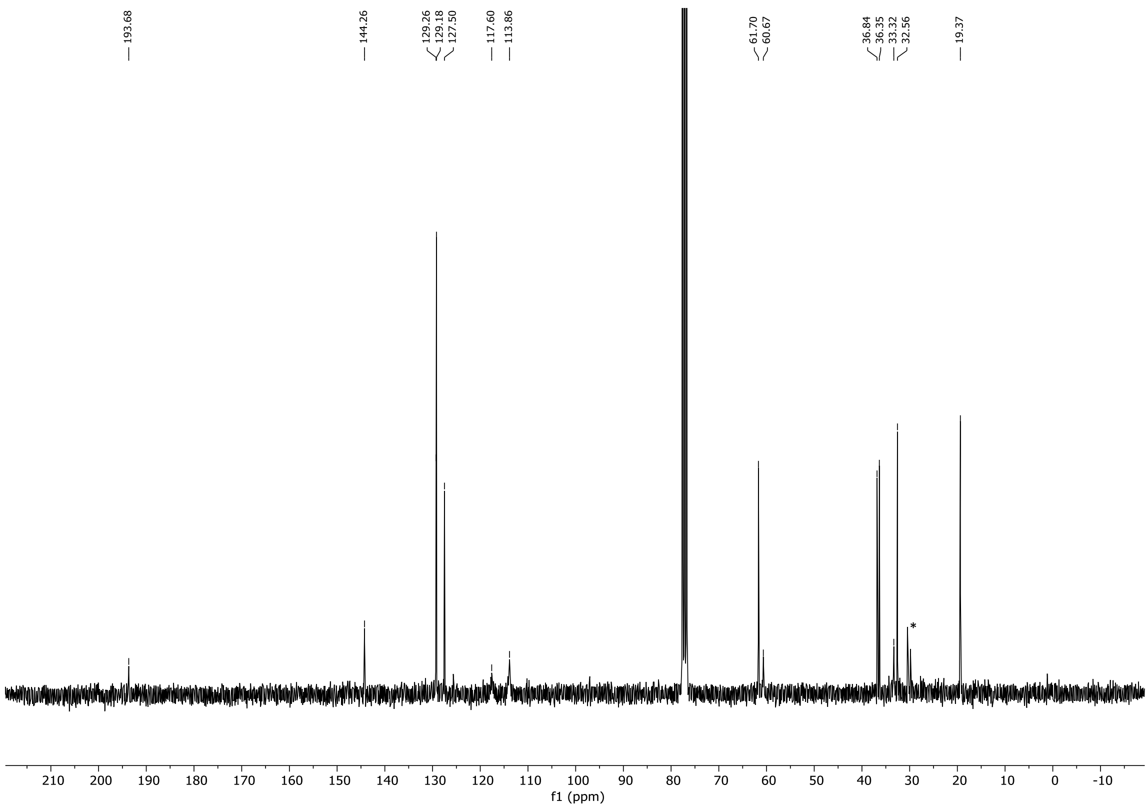
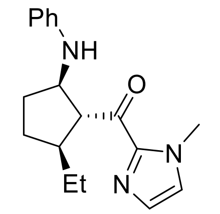


Figure S8. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3aa**. (*Grease peak)



3ba

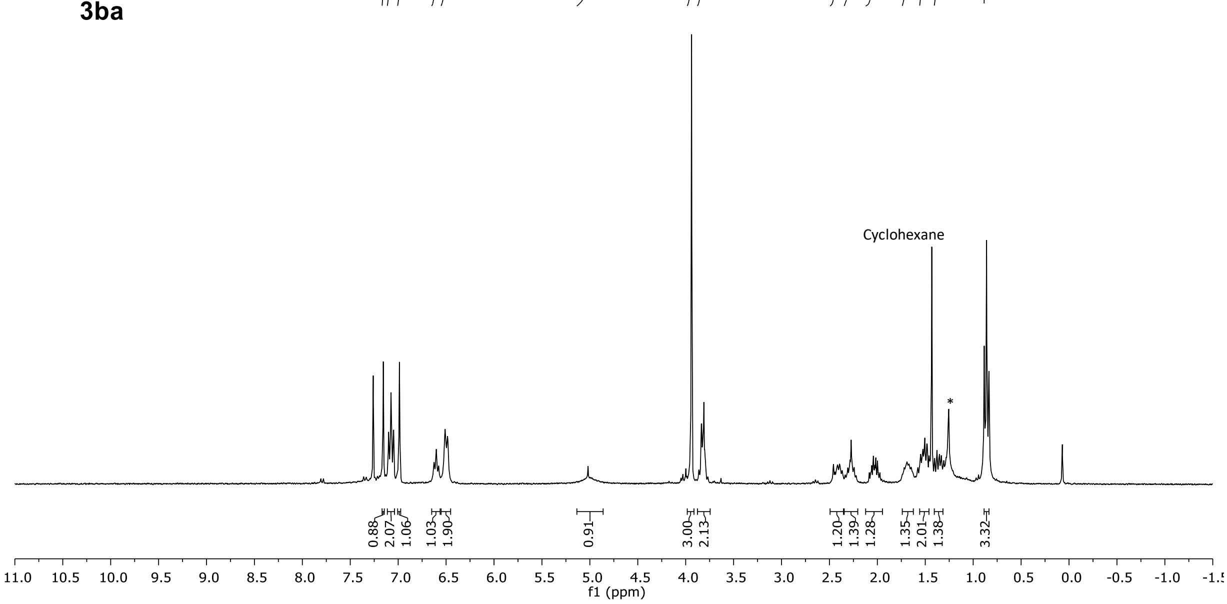


Figure S9. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ba** (*Grease peak).

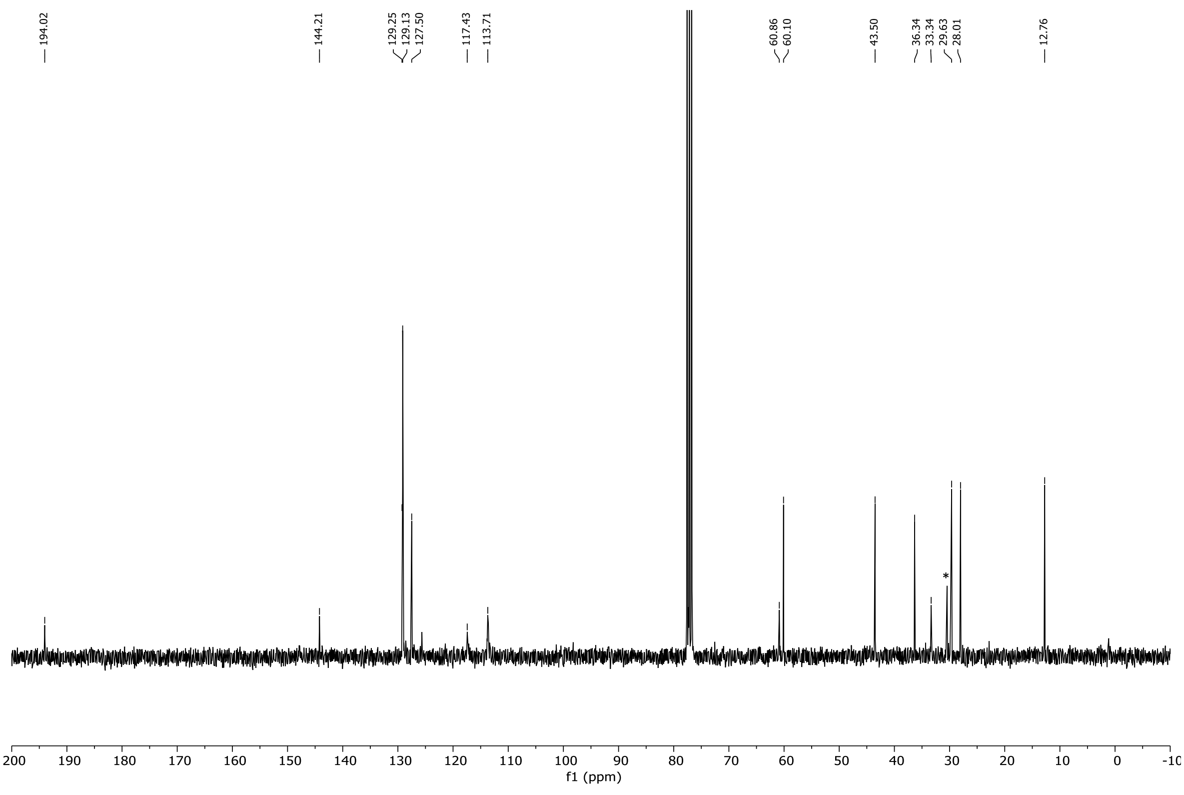


Figure S10. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ba** (*Grease peak).

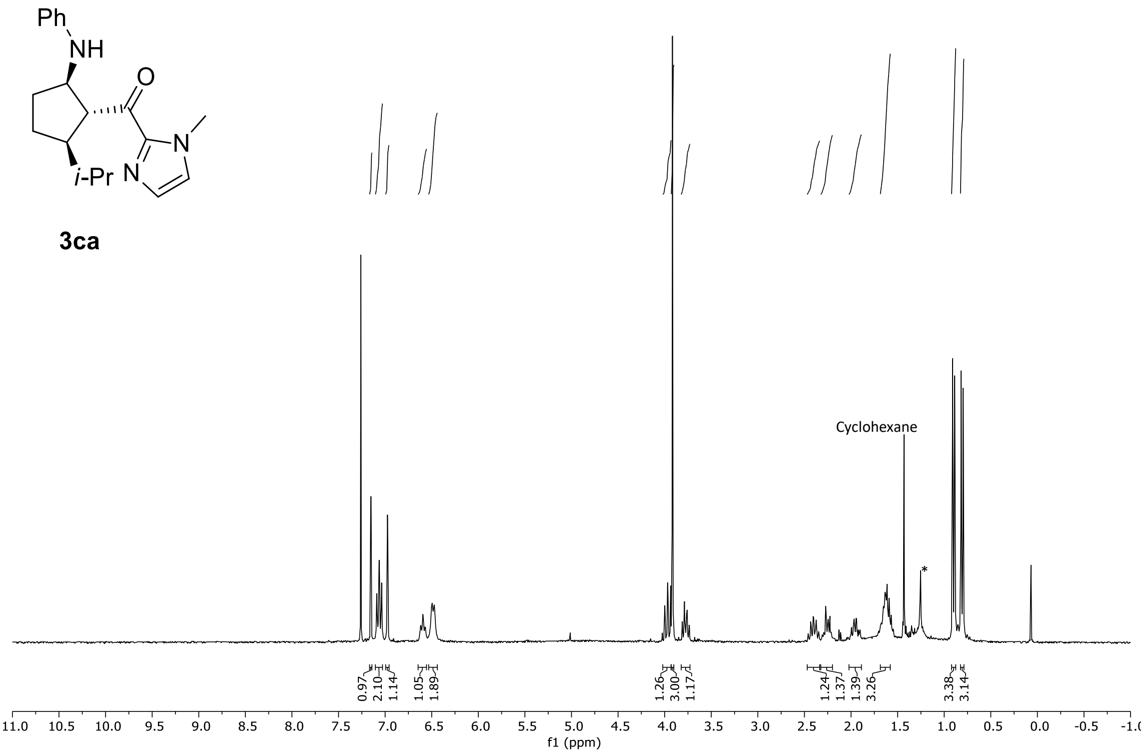


Figure S11. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ca** (*Grease peak).

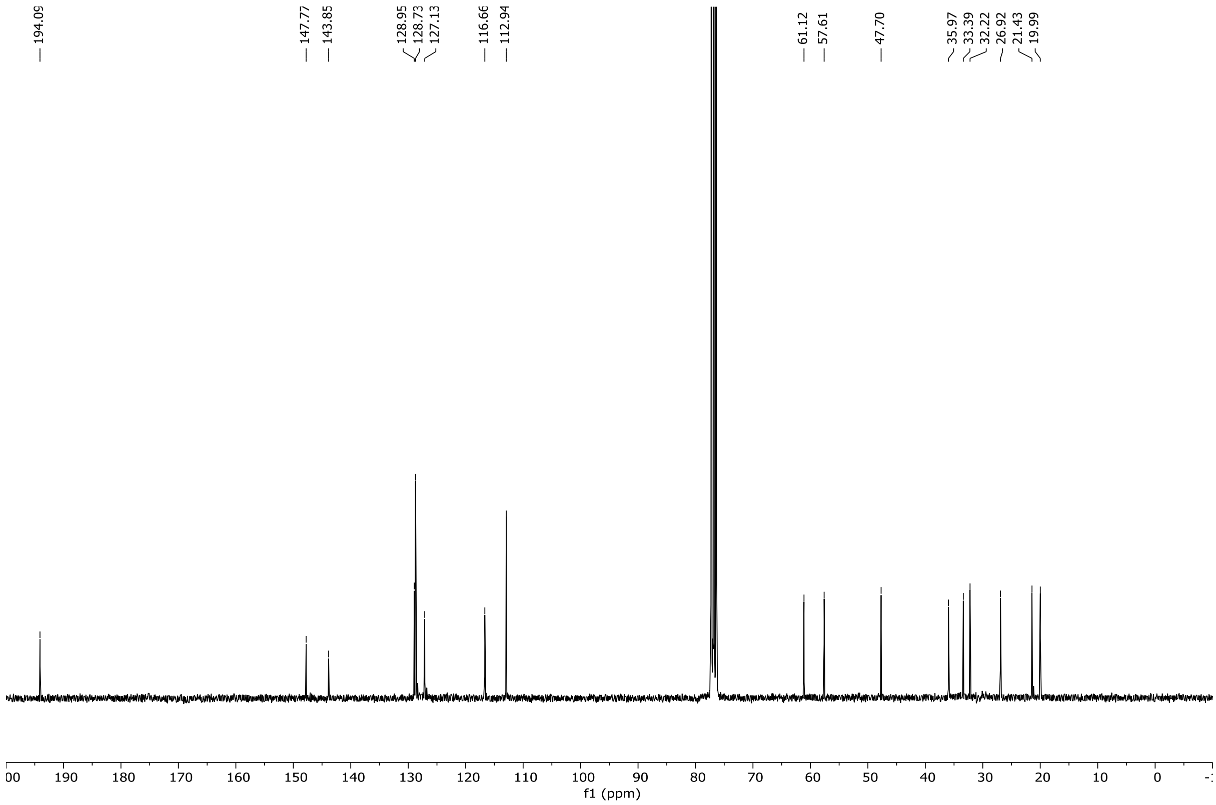


Figure S12. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ca.**

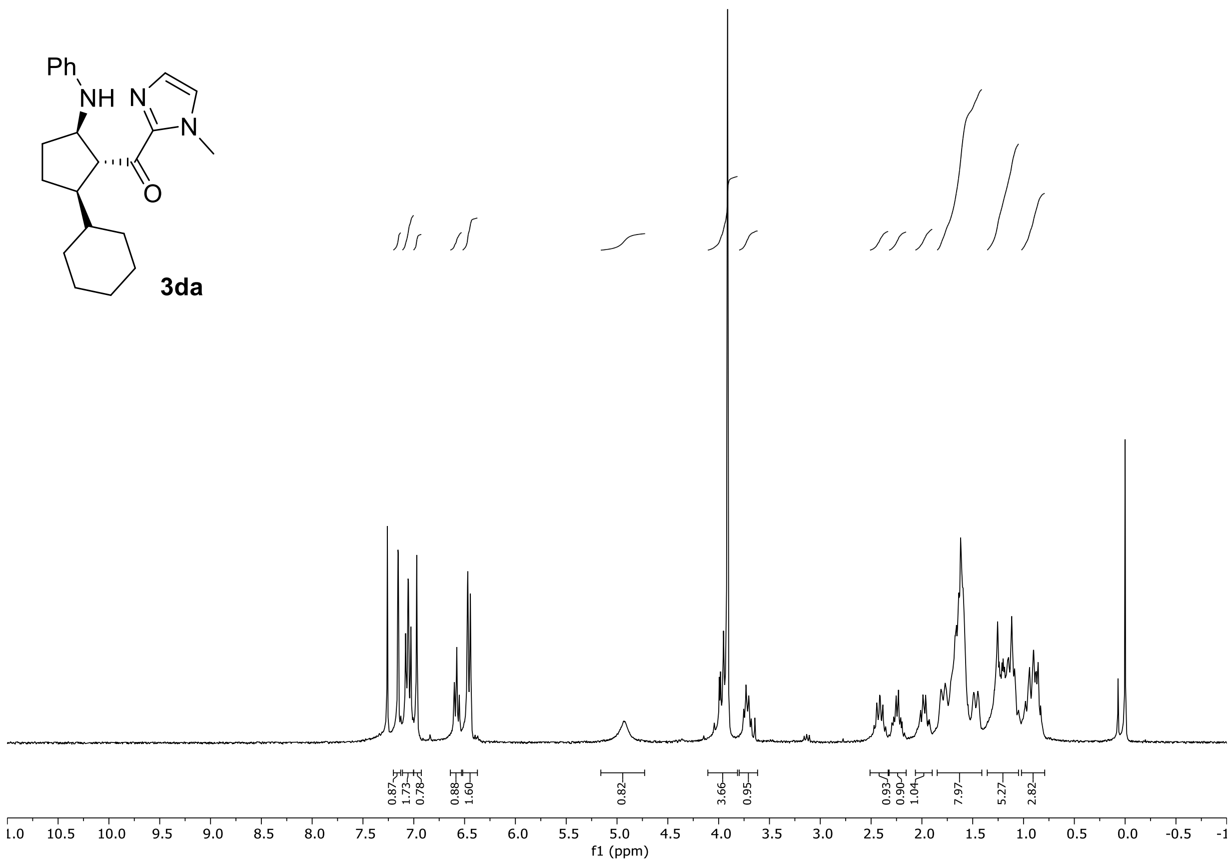


Figure S13. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3da.**

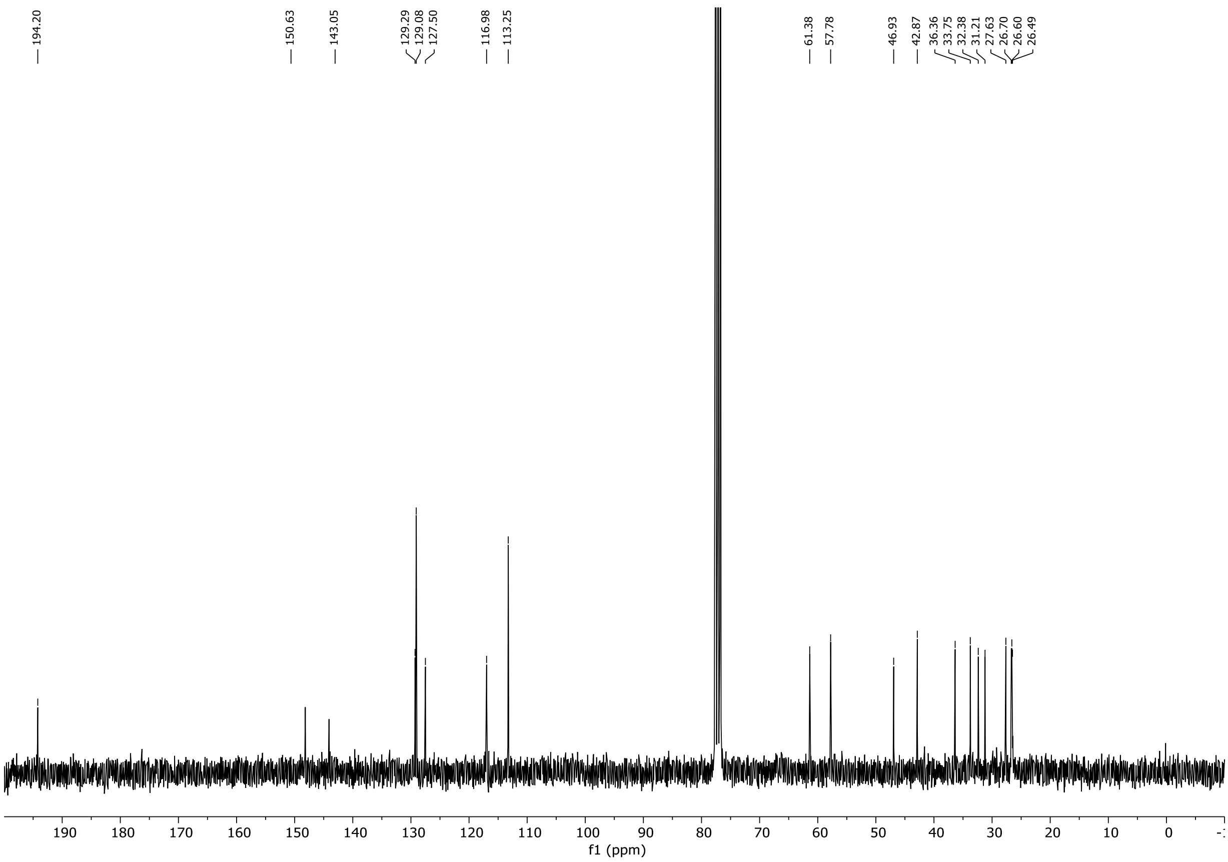


Figure S14. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3da.**

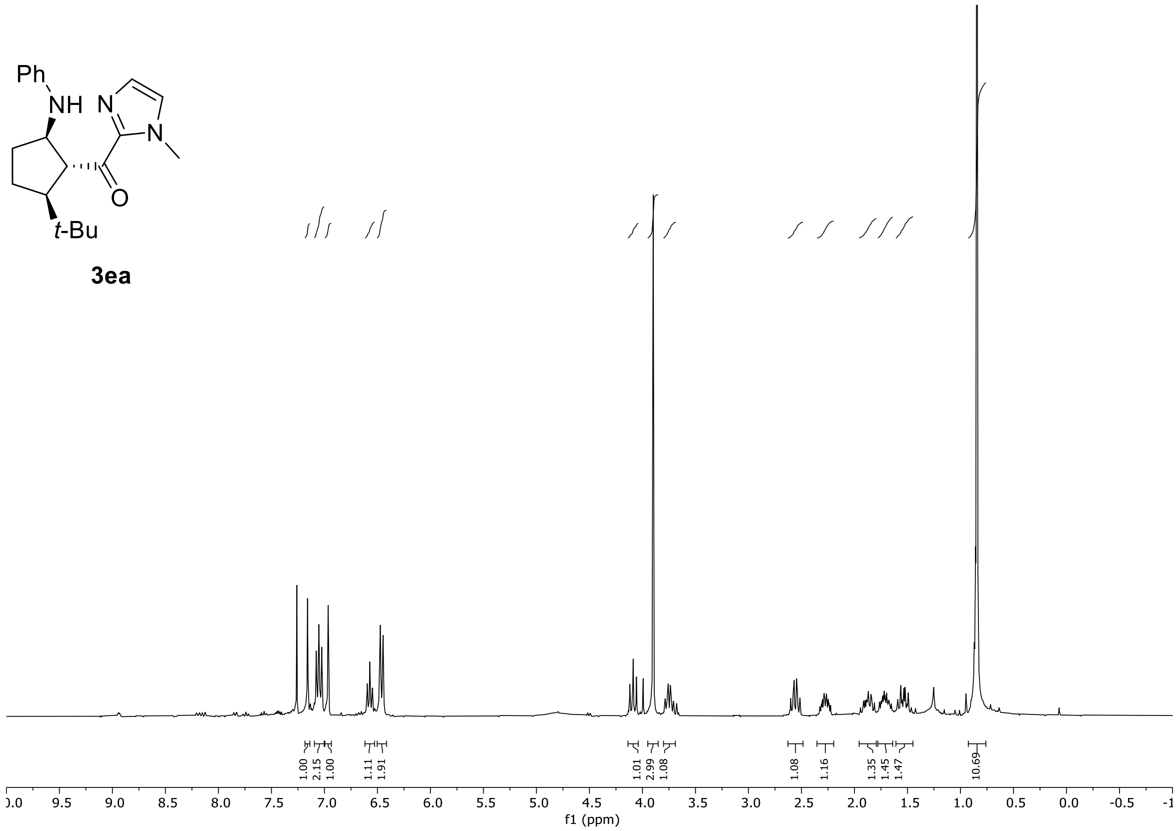


Figure S15. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ea.**

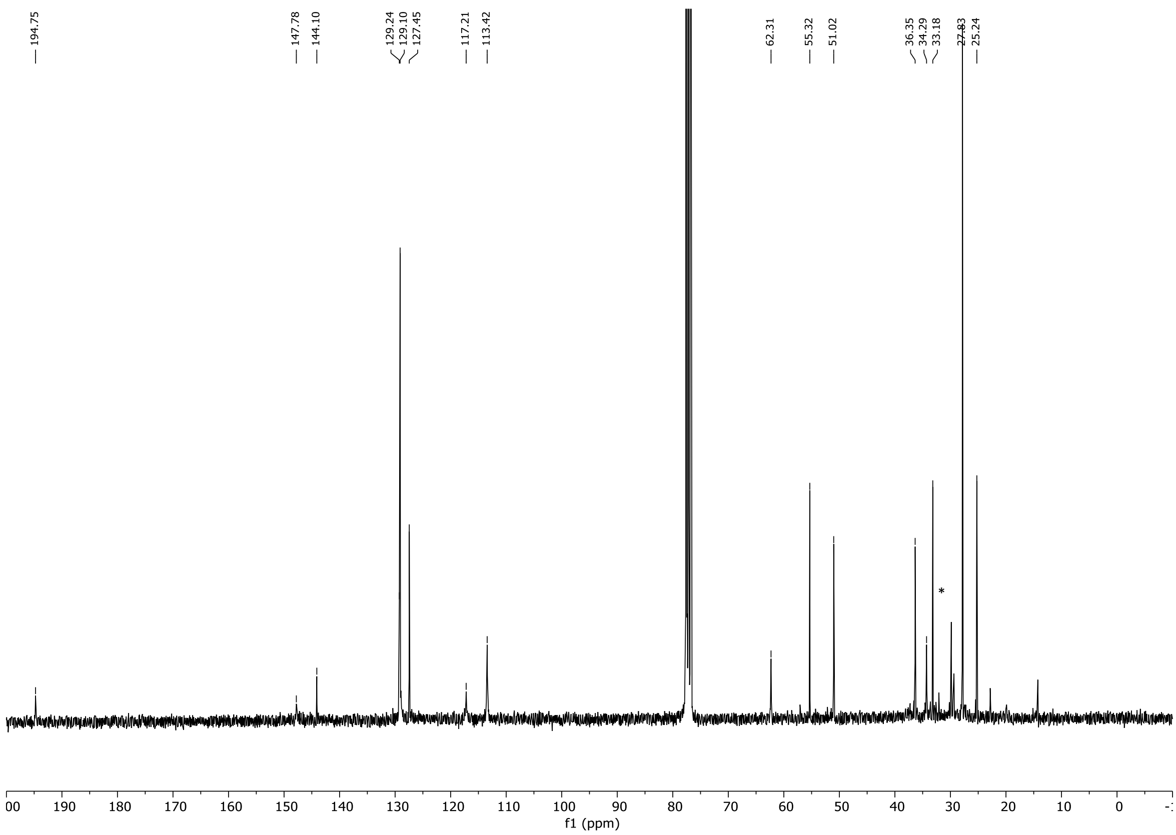


Figure S16. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ea** (*Grease peak).

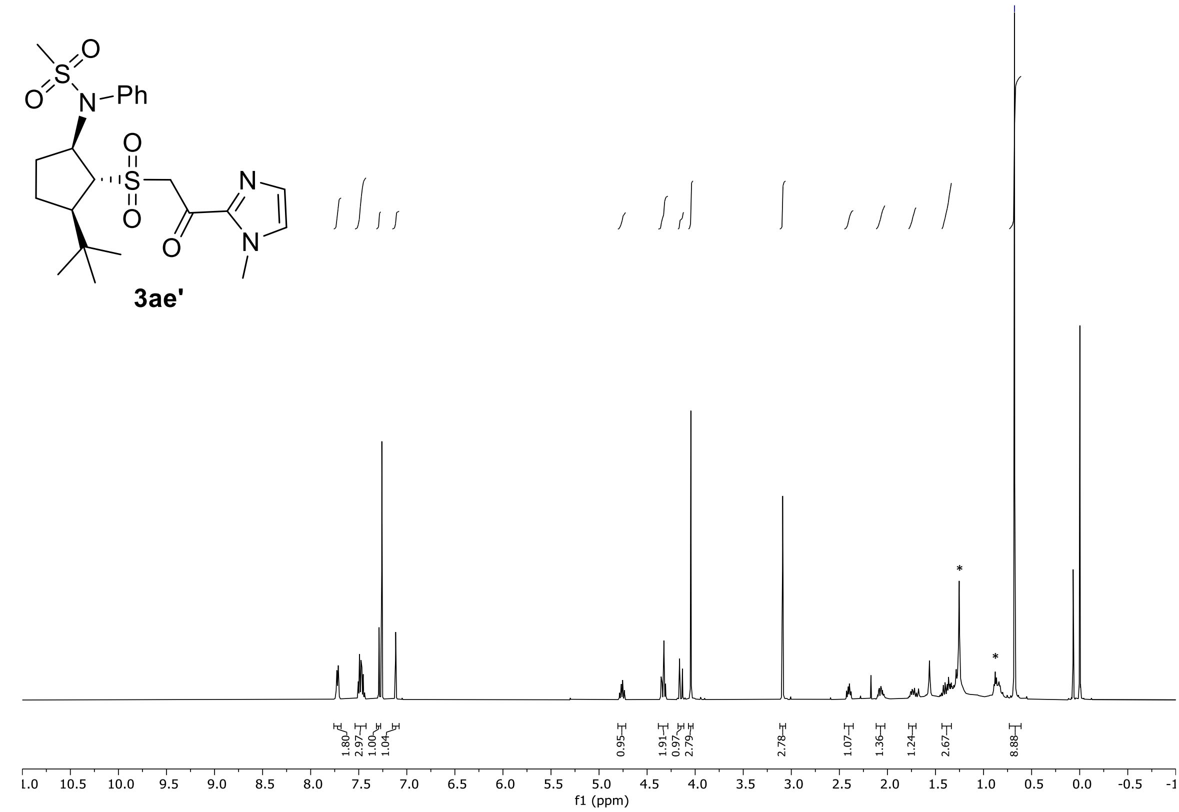


Figure S17. ^{1}H NMR spectrum (500 MHz, 298K, $CDCl_3$) of **3ea´** (*Grease peaks).

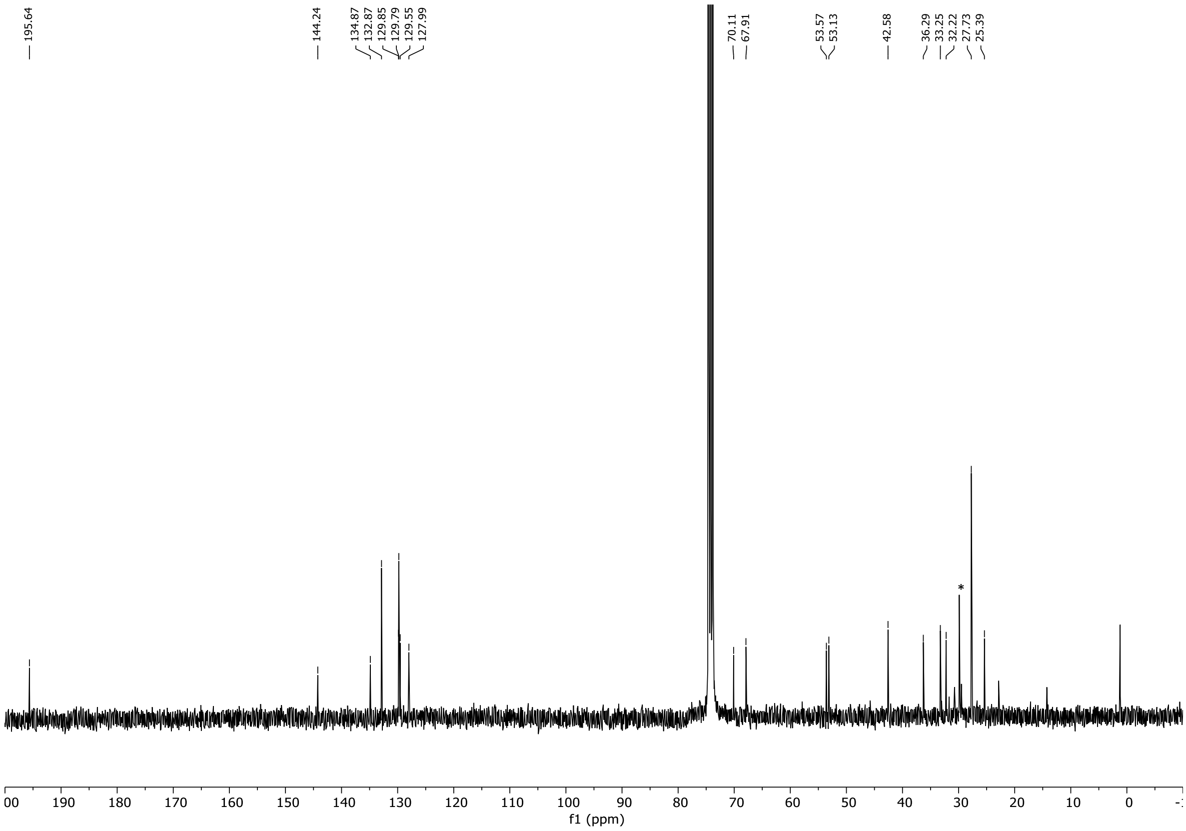
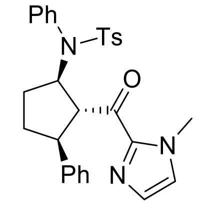


Figure S18. ^{13}C NMR spectrum (75 MHz, 353K, $C_2D_2Cl_4$) of **3ea´** (*Grease peak).



3fa

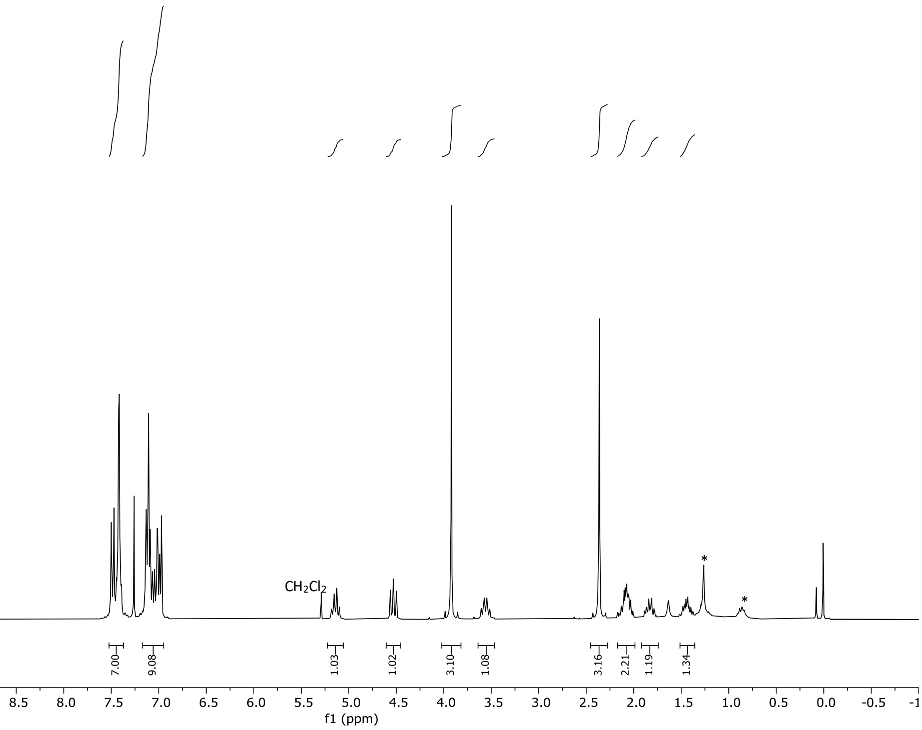


Figure S19. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3fa** (*Grease peaks).

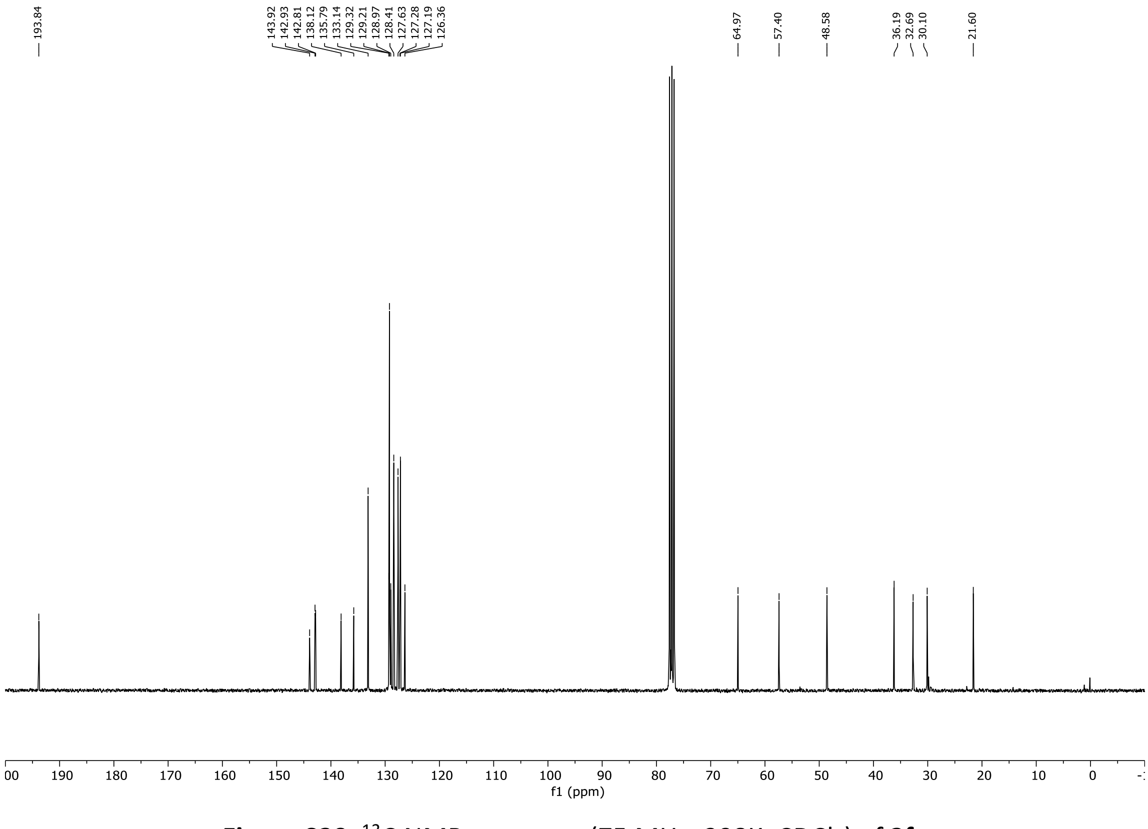


Figure S20. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3fa**.

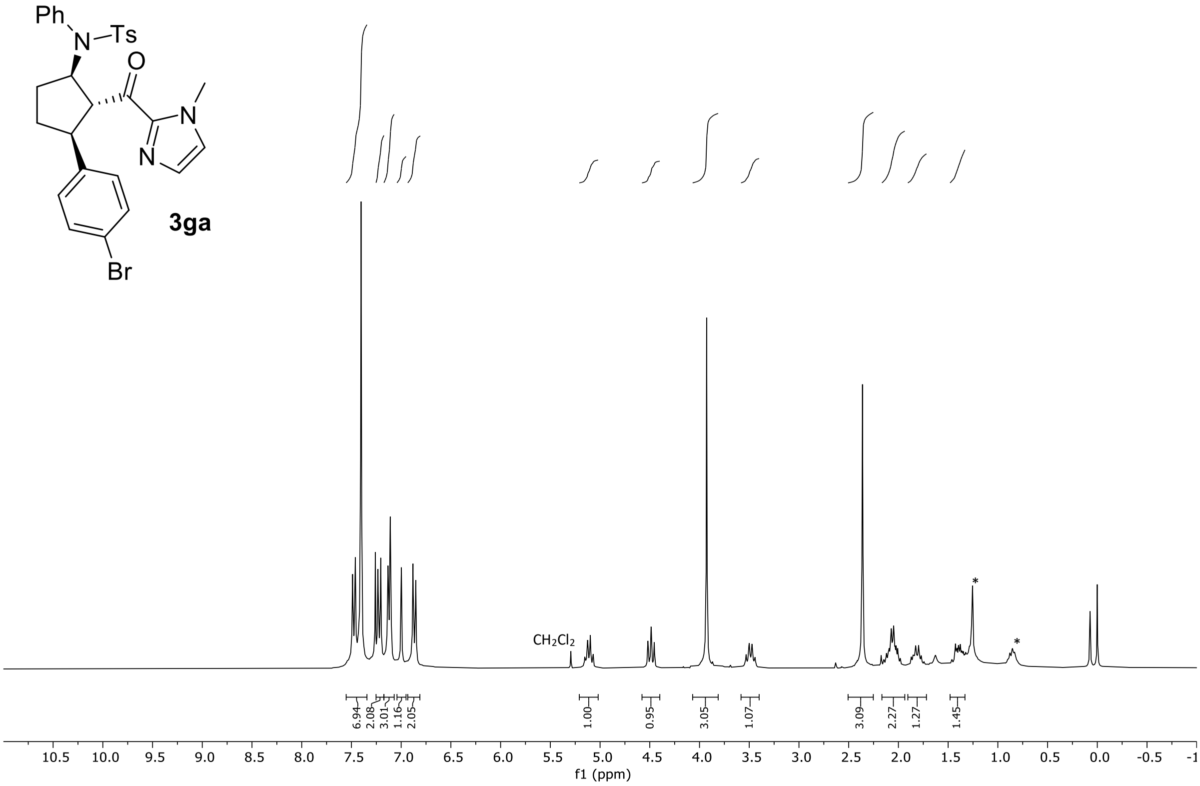


Figure S21. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ga** (*Grease peaks).

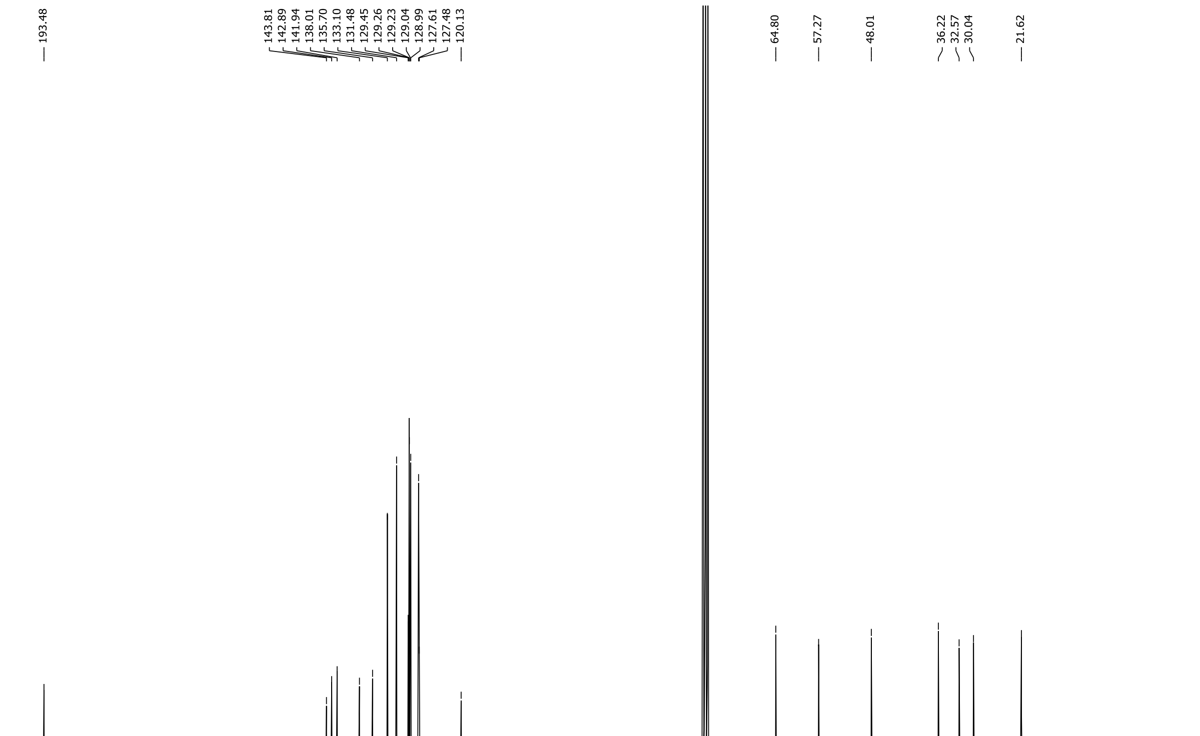
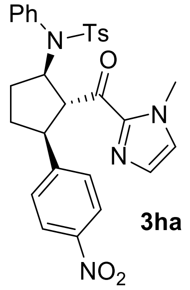


Figure S22. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ga.**



3ha

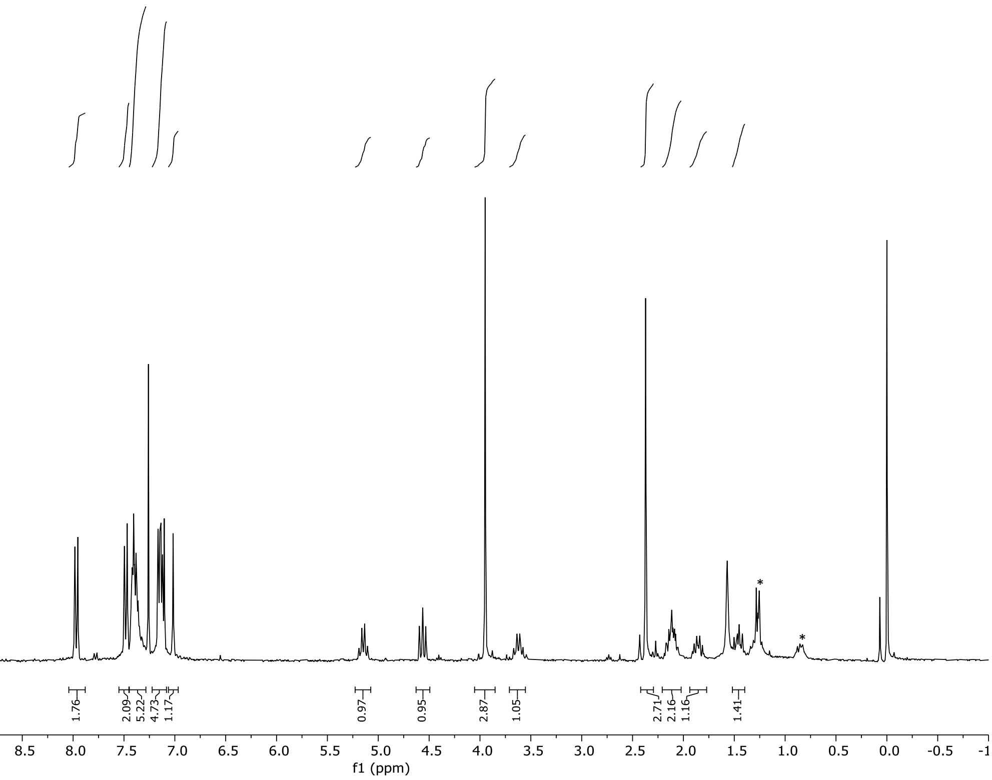


Figure S23. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ha** (Grease peaks).

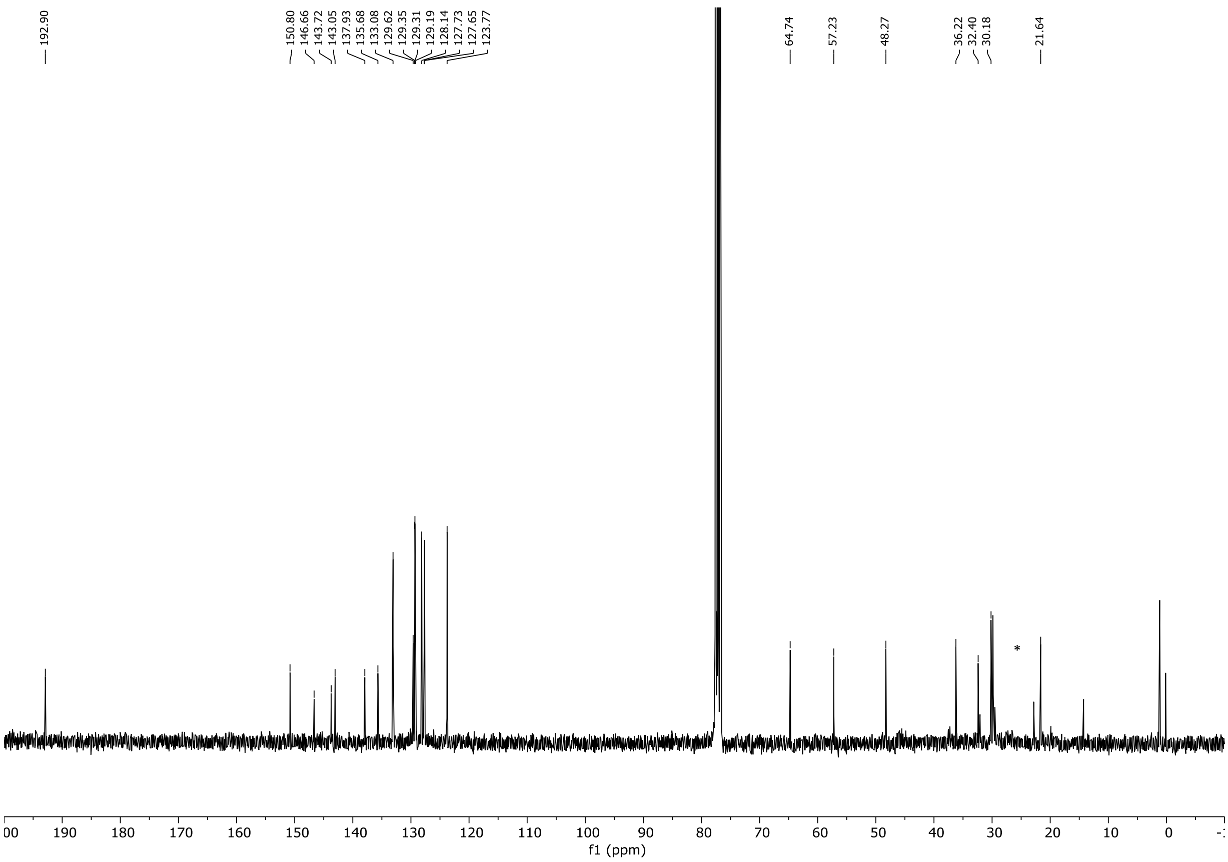


Figure S24. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ha** (Grease peak).

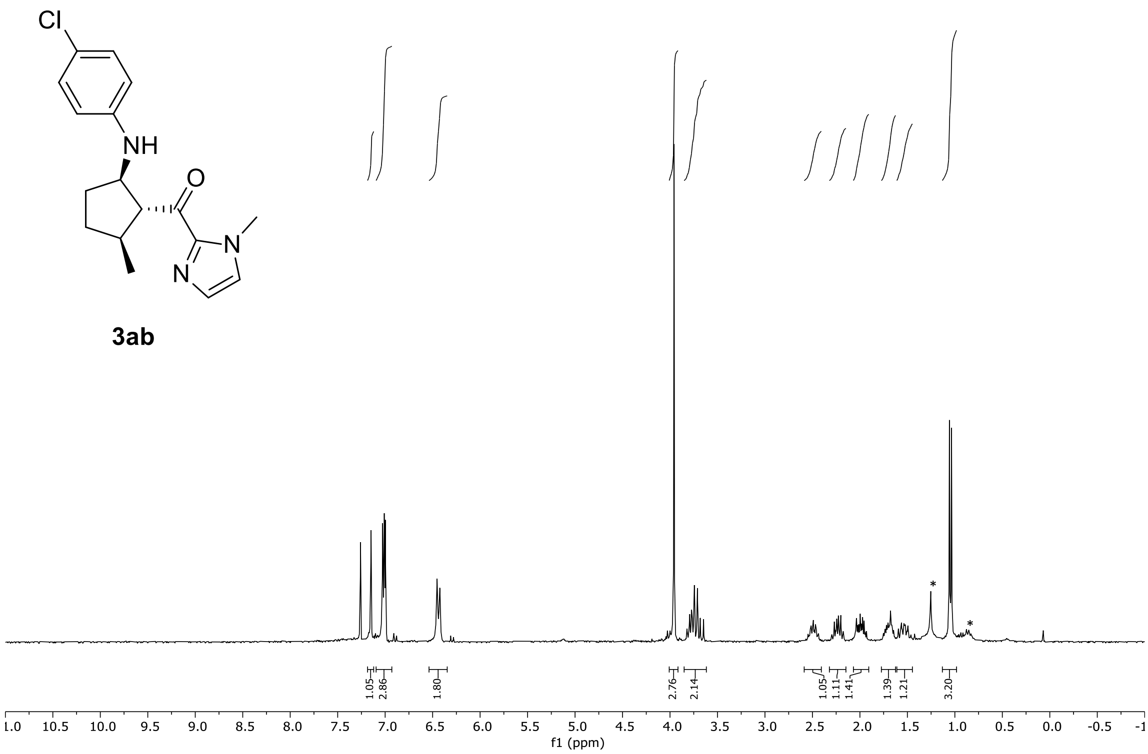


Figure S25. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ab** (Grease peaks).

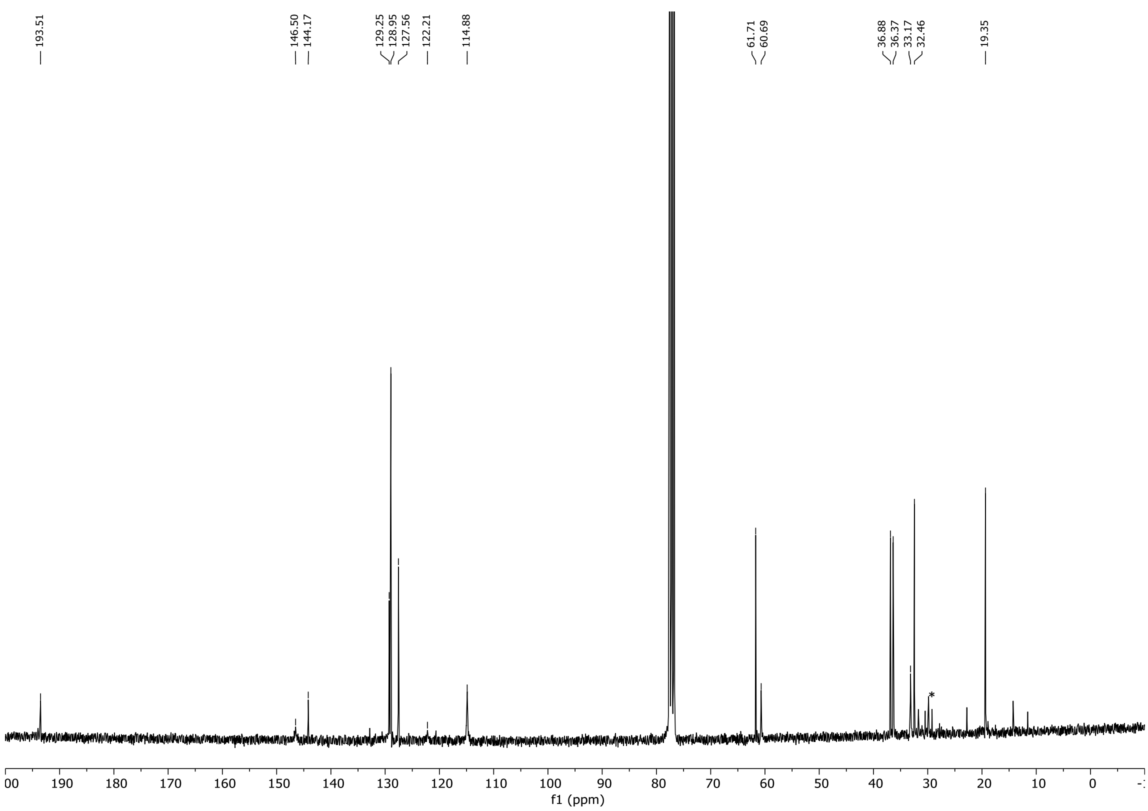
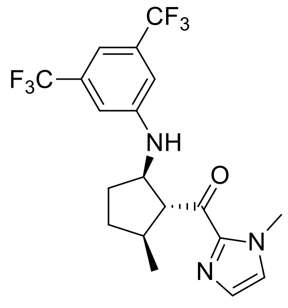


Figure S26. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ab** (Grease peak).



3ac

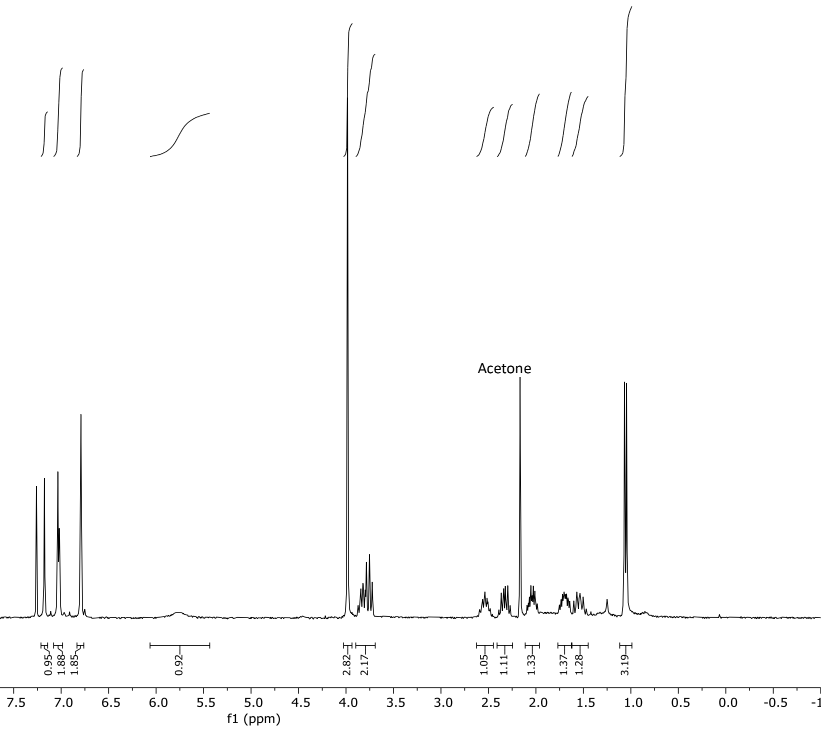


Figure S27. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ac.**

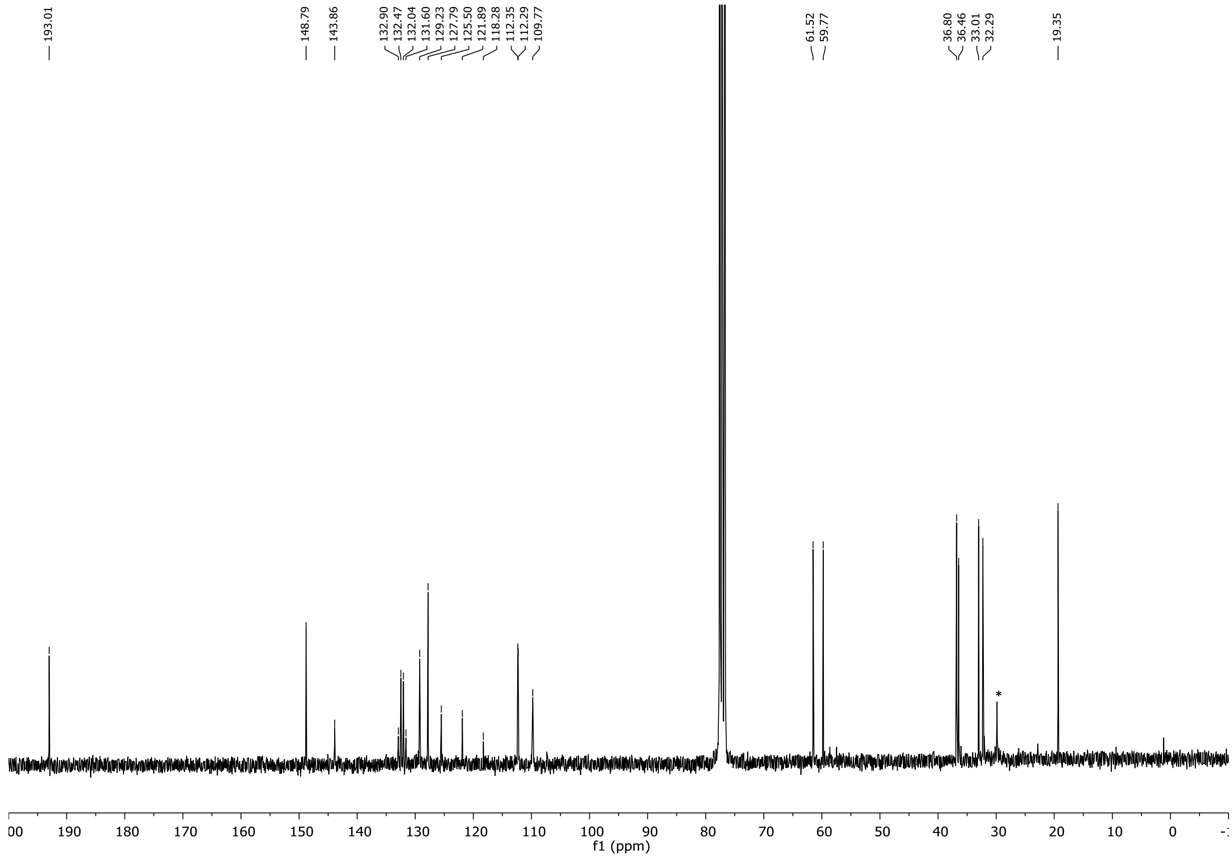


Figure S28. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ac** (Grease peak).

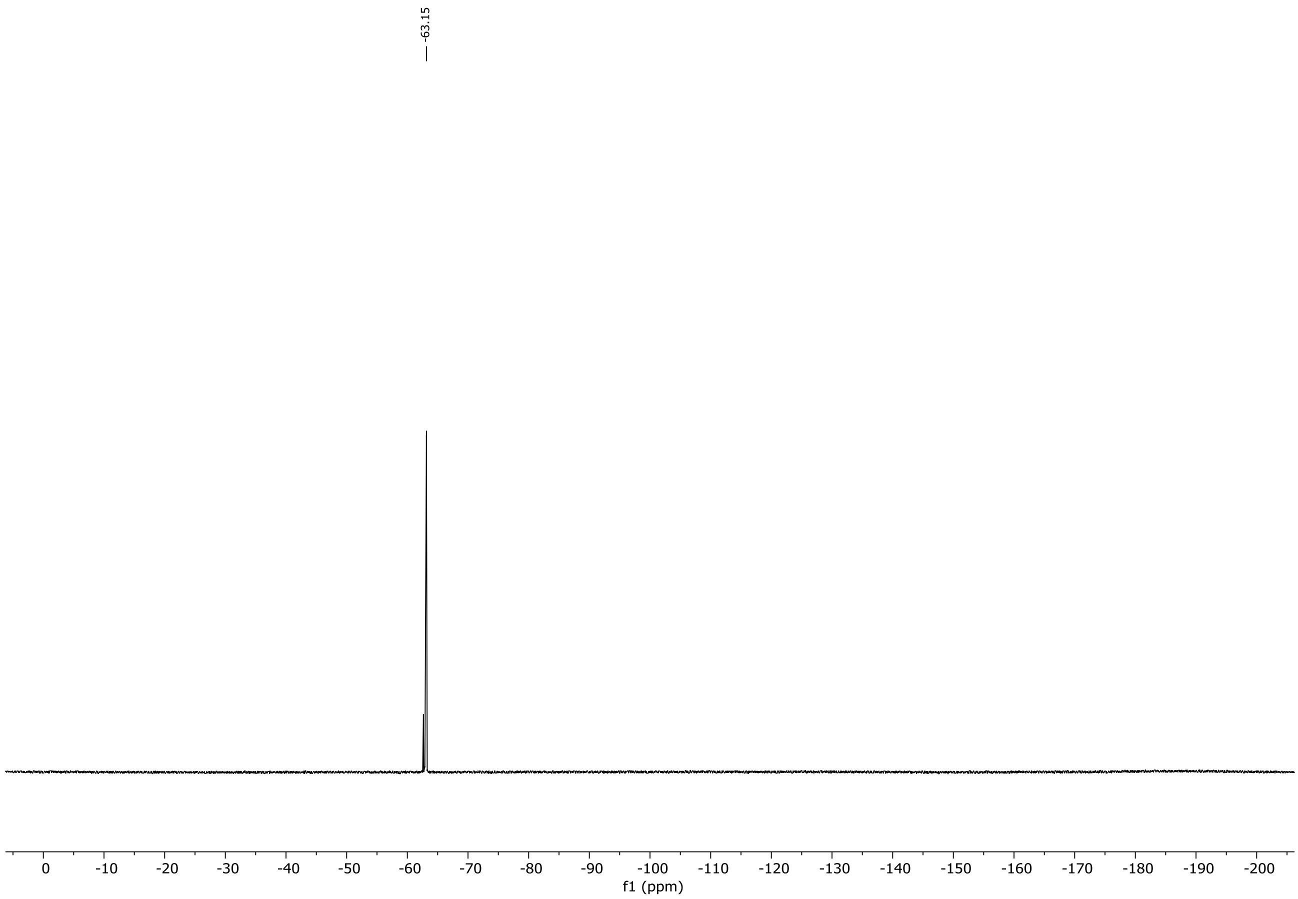
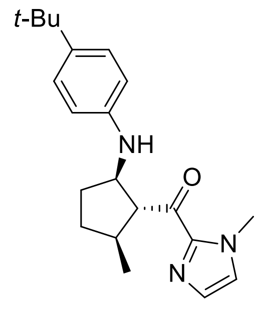


Figure S29. ^{19}F NMR spectrum (471 MHz, 298K, $CDCl_3$) of **3ac.**



3ad

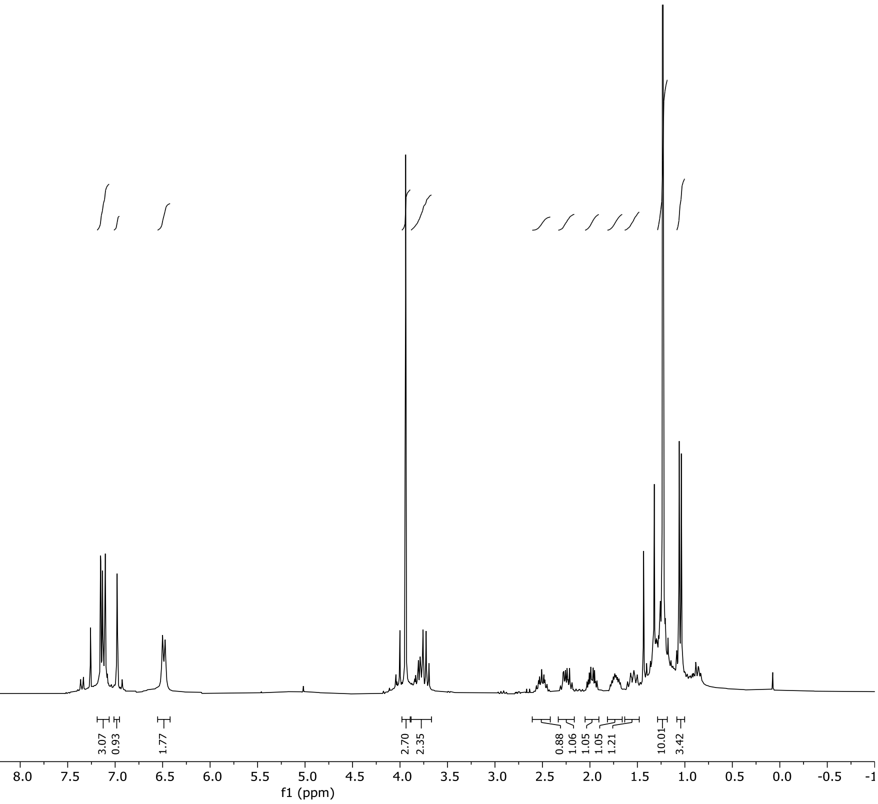


Figure S30. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ad.**

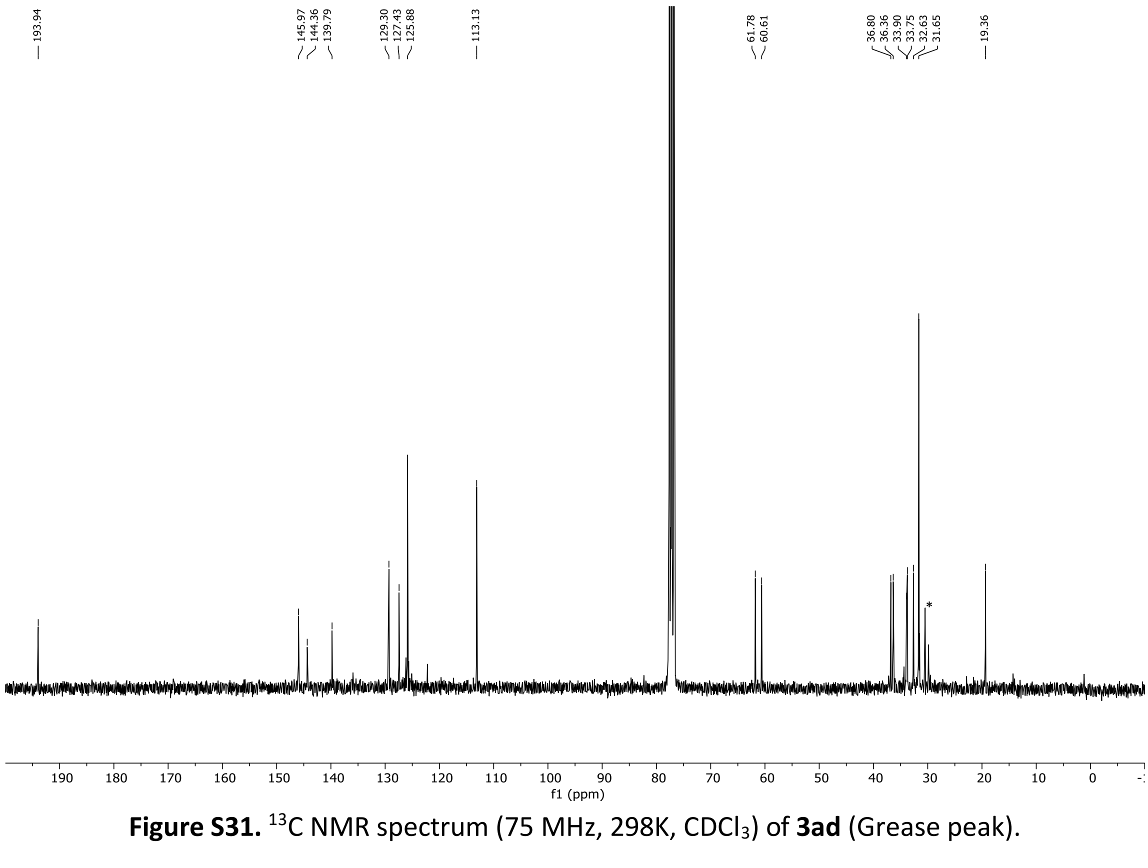
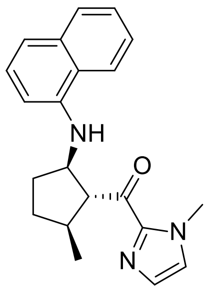


Figure S31. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ad** (Grease peak).



3ae

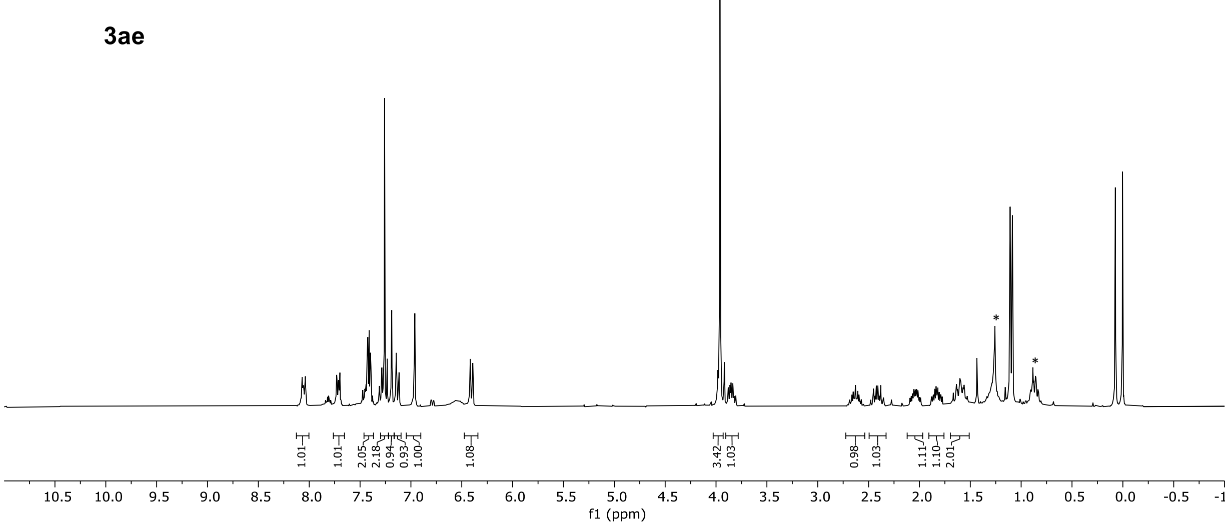


Figure S32. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **3ae** (Grease peaks).

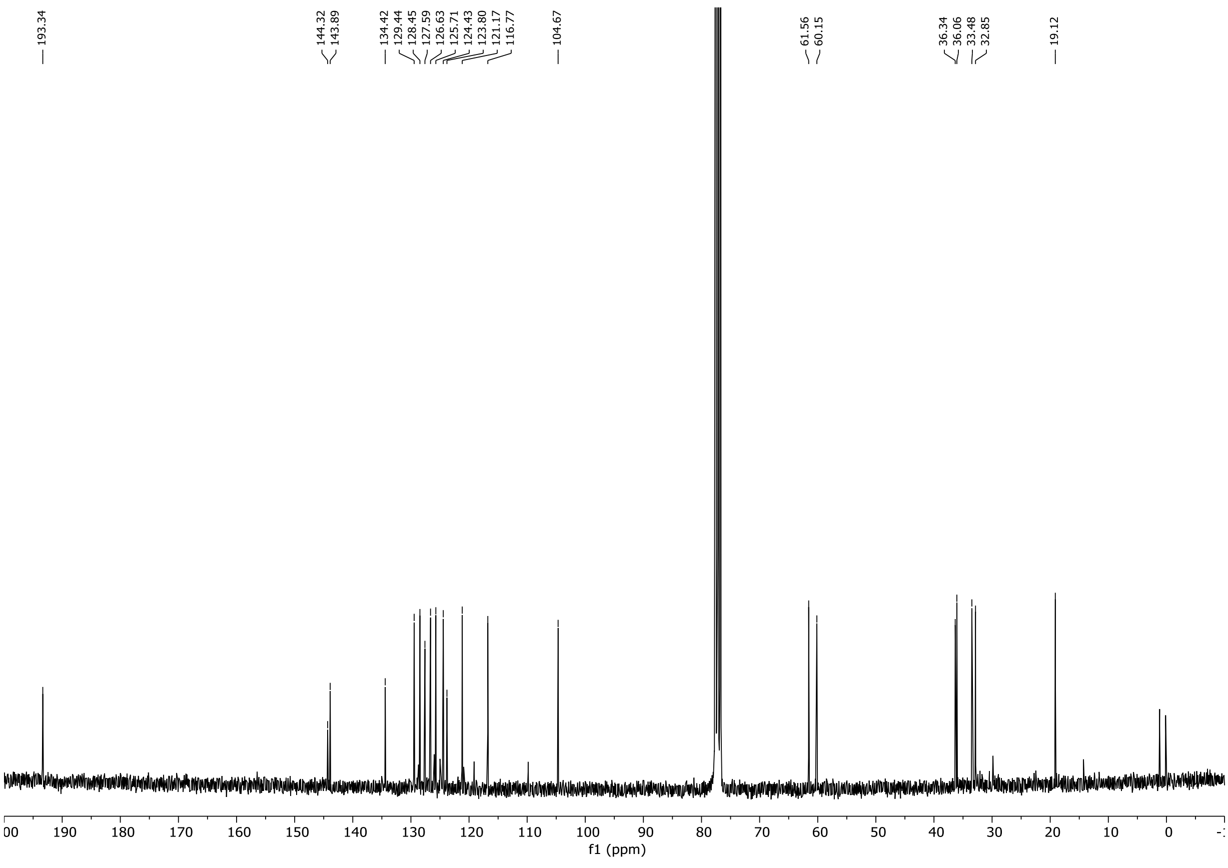


Figure S33. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **3ae.**

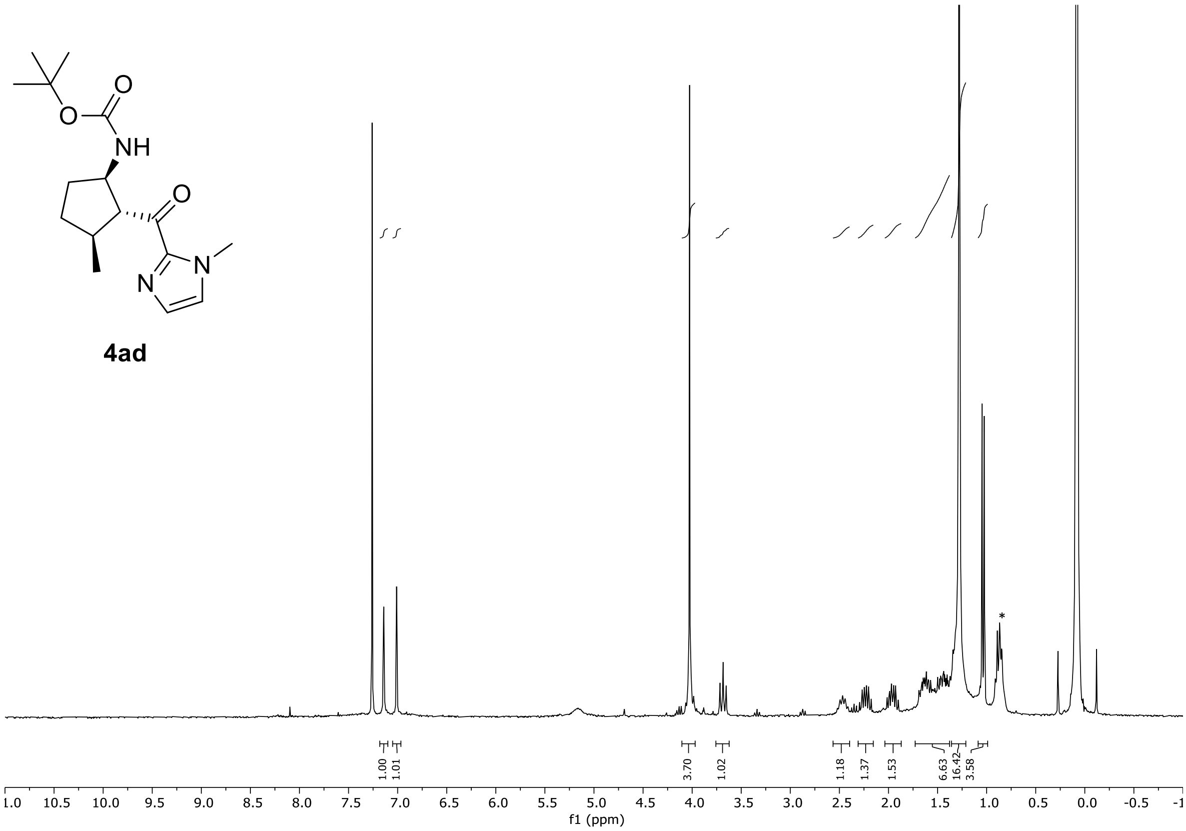


Figure S34. ^{1}H NMR spectrum (300 MHz, 323K, $CDCl_3$) of **4ad** (Grease peak).

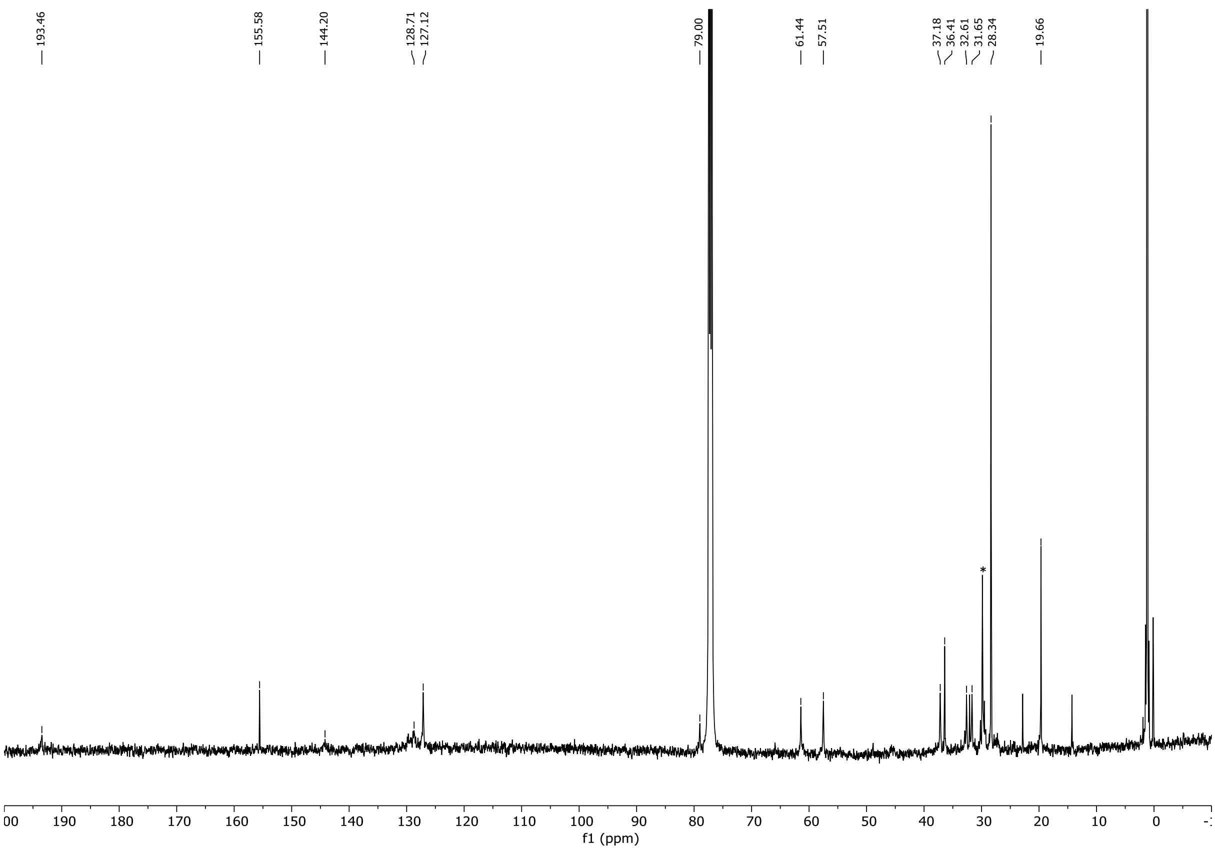
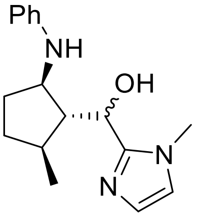


Figure S35. ^{13}C NMR spectrum (126 MHz, 298K, $CDCl_3$) of **4ad** (Grease peak).



5aa

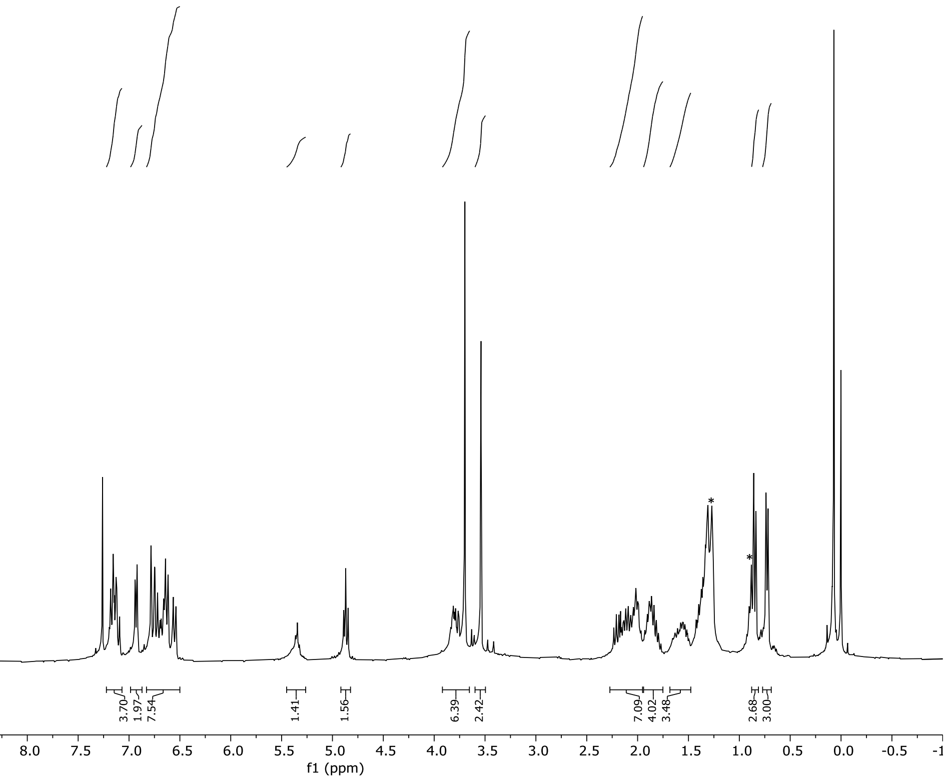


Figure S36. ^{1}H NMR spectrum (300 MHz, 298K, $CDCl_3$) of **5aa** (Grease peaks).

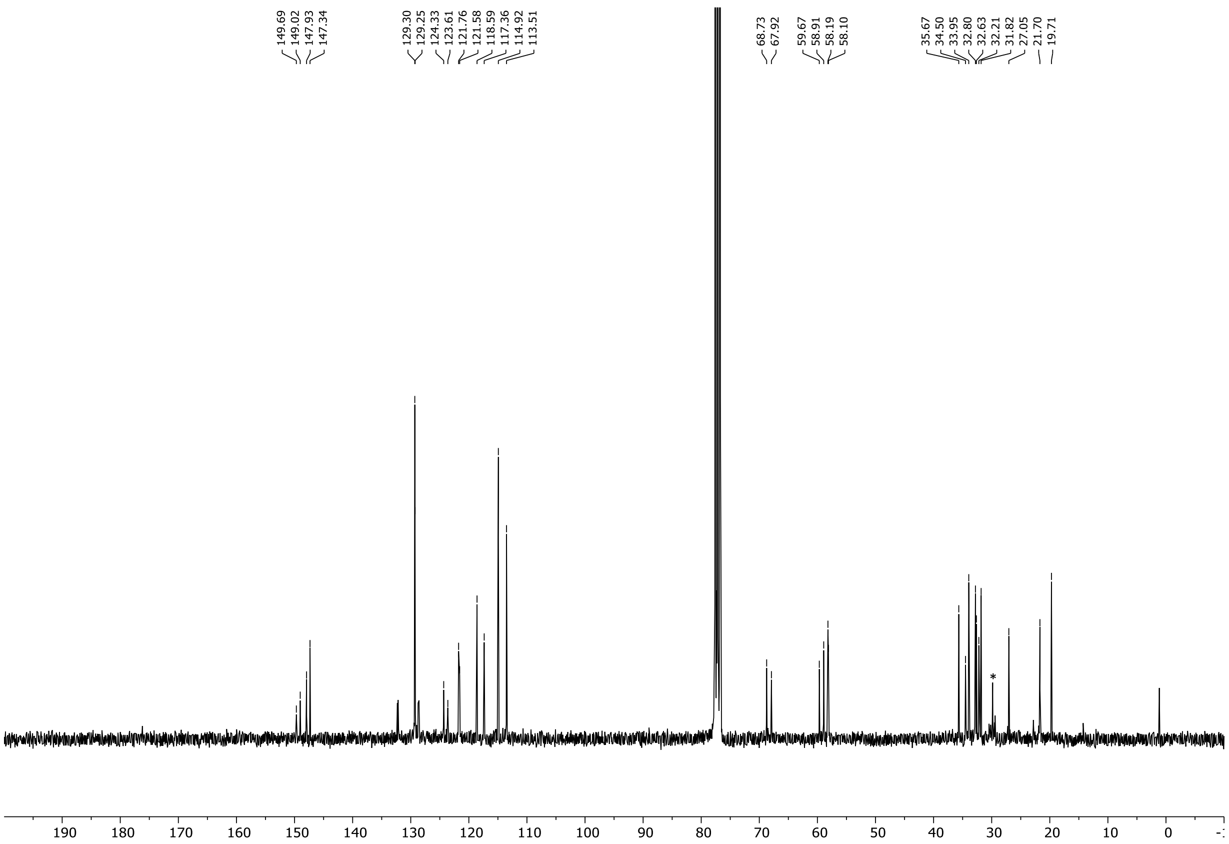


Figure S37. ^{13}C NMR spectrum (75 MHz, 298K, $CDCl_3$) of **5aa** (Grease peak).

10. X-ray information.

10.1. Compound **3ab**:

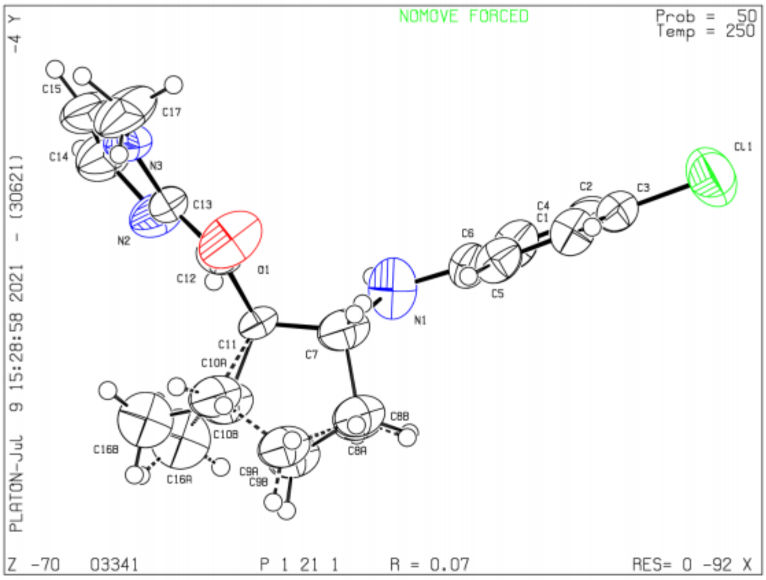


Figure S38. X-Ray structure of **3ab**.

Bond precision: C-C = 0.0126 A Wavelength=0.71073

Cell:	a=7.262(6)	b=10.514(6)	c=11.343(8)
	alpha=90	beta=97.63(3)	gamma=90
Temperature:	250 K		

	Calculated	Reported
Volume	858.4(11)	858.4(11)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C17 H19.44 Cl N3 O, 0.557(H)	?
Sum formula	C17 H20 Cl N3 O	C17 H20 Cl N3 O
Mr	317.81	317.81
Dx,g cm-3	1.230	1.230
Z	2	2
Mu (mm-1)	0.228	0.228
F000	336.0	336.0
F000'	336.41	
h,k,lmax	8,12,13	8,12,13
Nref	3152[1669]	2999
Tmin,Tmax	0.962,0.979	0.780,0.980
Tmin'	0.948	

Correction method= # Reported T Limits: Tmin=0.780 Tmax=0.980
AbsCorr = MULTI-SCAN

Data completeness= 1.80/0.95 Theta(max)= 25.310

R(reflections)= 0.0700(1433) wR2(reflections)= 0.1939(2999)

S = 1.009 Npar= 199

10.2. Compound **3´aa:**

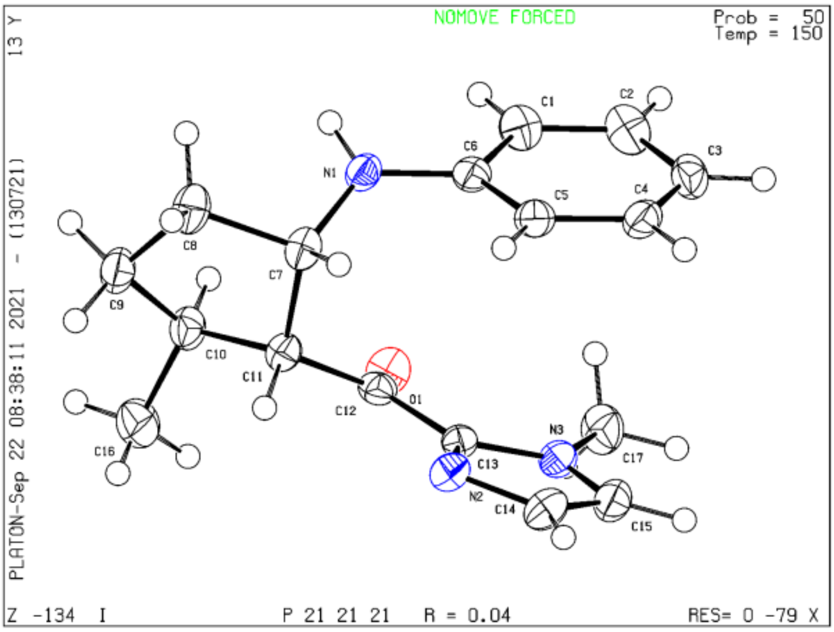
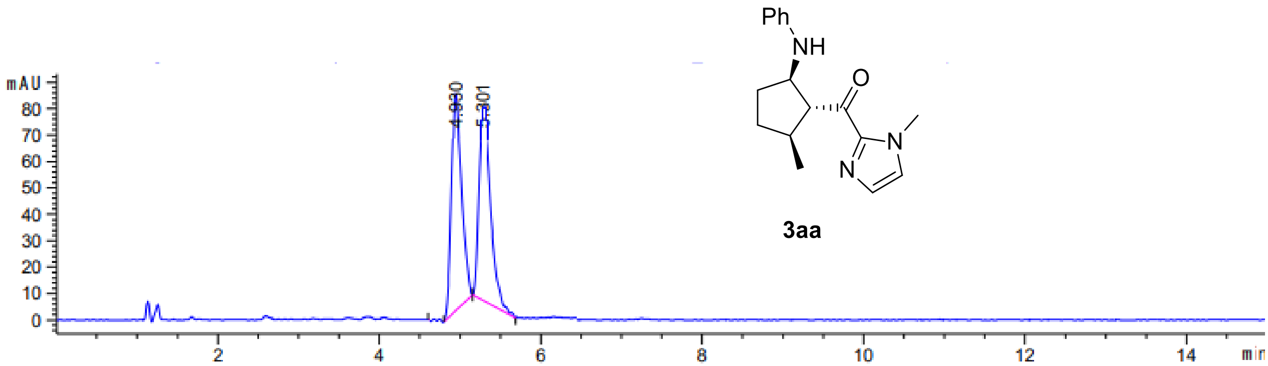


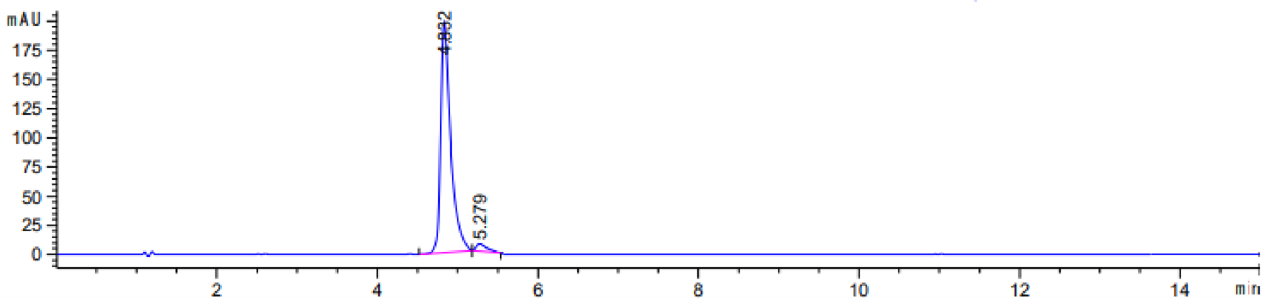
Figure S39. X-Ray structure of **3´aa**.

```
Bond precision:    C-C = 0.0030 A          Wavelength=0.71073

Cell:               a=10.0084(5)     b=11.0369(6)      c=13.3690(7)
                    alpha=90         beta=90           gamma=90
Temperature:        150 K

                  Calculated                  Reported
Volume            1476.76(13)                 1476.76(13)
Space group       P 21 21 21                  P 21 21 21
Hall group        P 2ac 2ab                   P 2ac 2ab
Moiety formula    C17 H21 N3 O                ?
Sum formula       C17 H21 N3 O                C17 H21 N3 O
Mr                283.37                      283.37
Dx,g cm-3         1.275                       1.275
Z                 4                           4
Mu (mm-1)         0.081                       0.081
F000              608.0                       608.0
F000'             608.21
h,k,lmax          12,13,16                    12,13,16
Nref              3068[ 1765]                 3055
Tmin,Tmax         0.994,0.996                 0.700,0.750
Tmin'             0.986

Correction method= # Reported T Limits: Tmin=0.700 Tmax=0.750
AbsCorr = MULTI-SCAN

Data completeness= 1.73/1.00        Theta(max)= 26.510

                                                    wR2(reflections)=
R(reflections)= 0.0357( 2691)                       0.0902( 3055)

S = 1.033                  Npar= 192
```

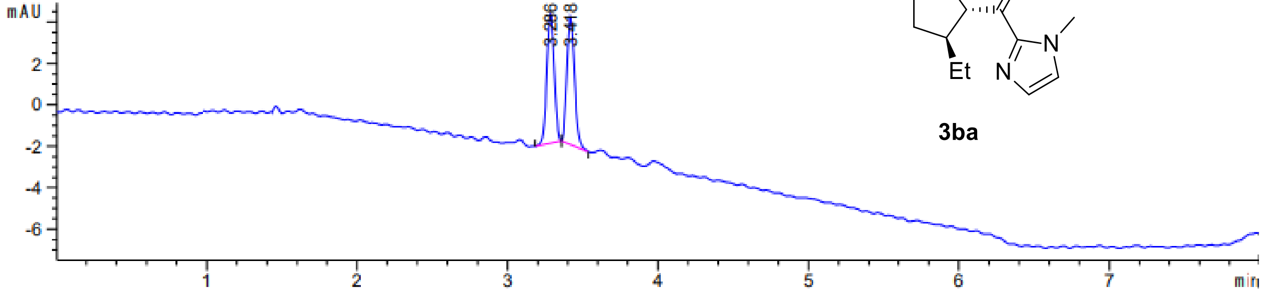
11. SFC chromatograms for quiral compounds.

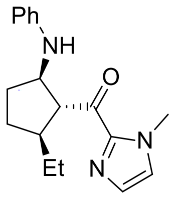



```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]         [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.930 BB    0.1171  835.37225   95.96170   50.2540
   2   5.301 BB    0.1111  826.92657   88.23700   49.7460
```



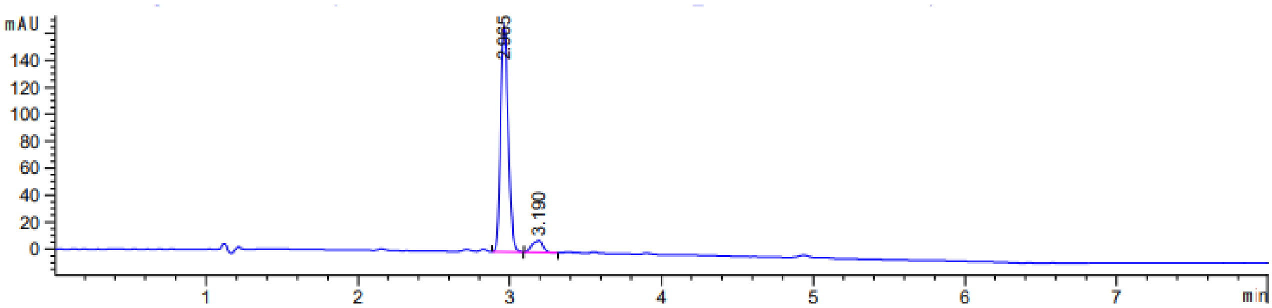

```
Peak RetTime Type  Width      Area       Height      Area
  #   [min]         [min]   [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.832 BB    0.1267 1702.33911  197.21123   96.8261
   2   5.279 BB    0.1367   55.80078    6.09888    3.1739
```



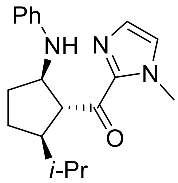


3ba

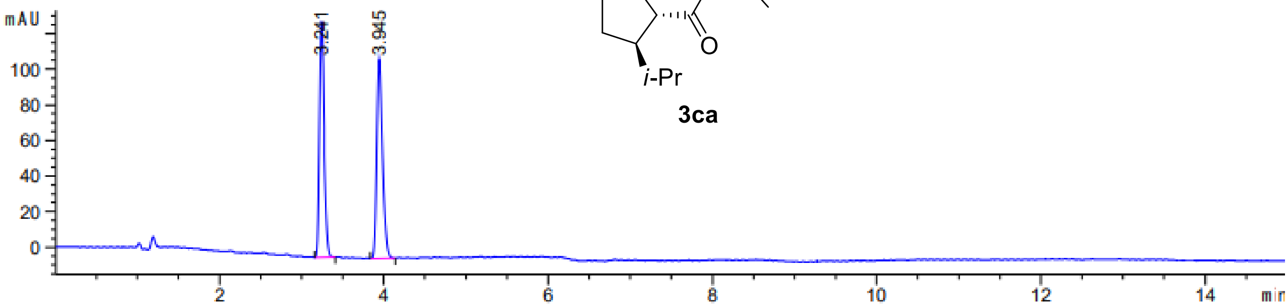
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.286	BB	0.0538	21.31854	6.24705	49.7119
2	3.418	BB	0.0551	21.56563	6.12449	50.2881



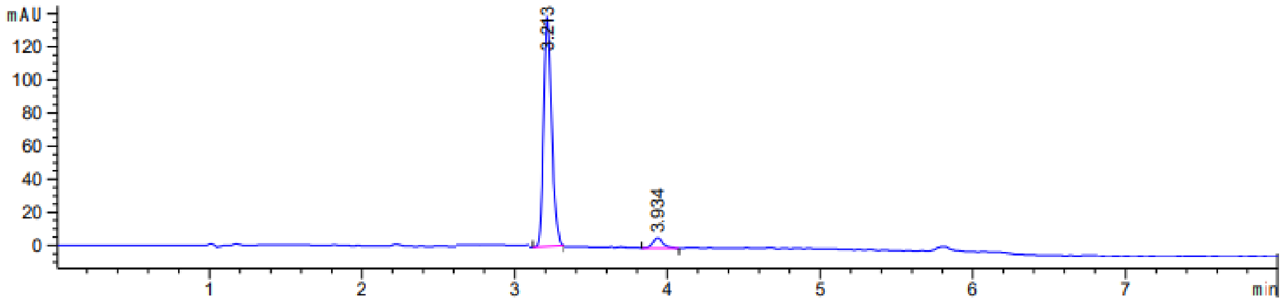
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.965	BB	0.0544	578.78571	167.03435	93.0155
2	3.190	BB	0.0852	43.46056	8.55874	6.9845



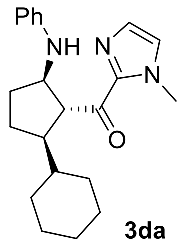
3ca



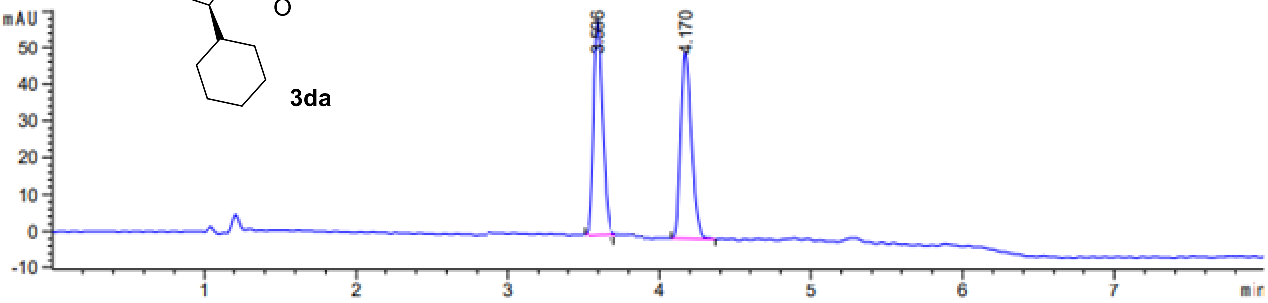
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.241	BB	0.0602	527.76666	133.34747	49.5550
2	3.945	BB	0.0741	537.24548	111.69067	50.4450



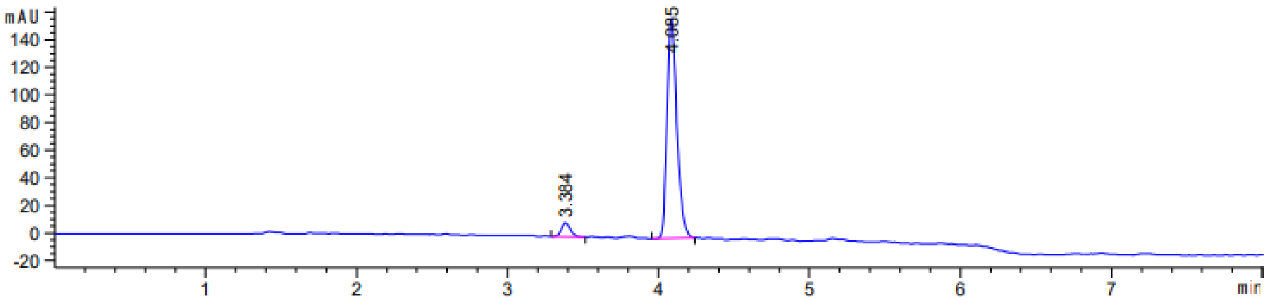
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.213	BB	0.0577	520.73596	139.08580	94.6337
2	3.934	BB	0.0717	29.52910	6.18665	5.3663



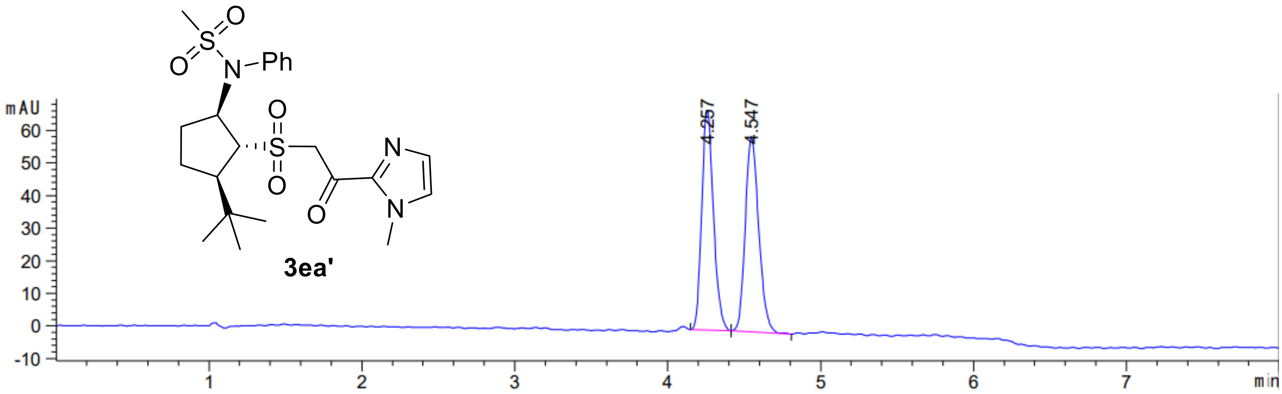
3da



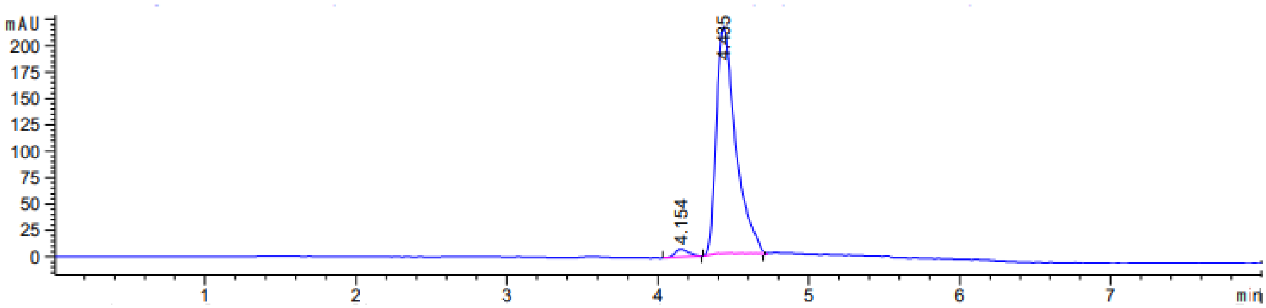
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.596	BB	0.0673	246.80251	58.36287	49.6173
2	4.170	BB	0.0759	250.60988	50.50155	50.3827



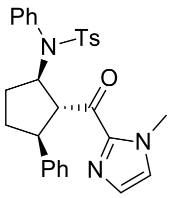
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.384	BB	0.0638	41.96161	10.24793	5.5163
2	4.085	BB	0.0685	718.72052	159.65935	94.4837



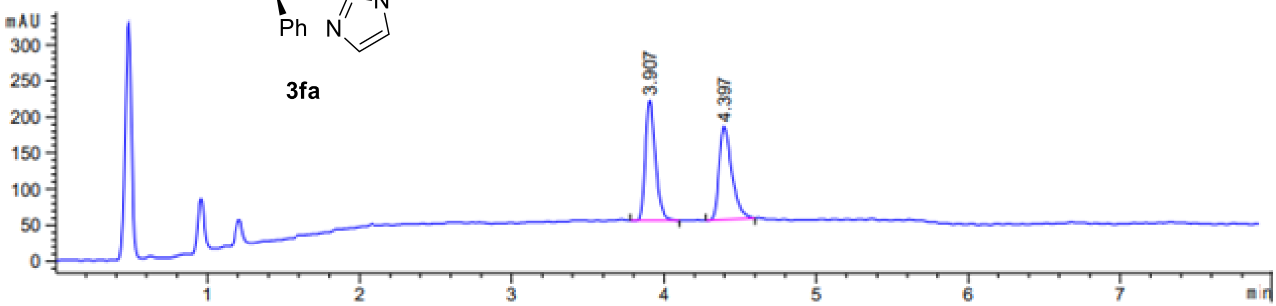
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.257	BB	0.0820	360.07736	67.76046	49.4671
2	4.547	BB	0.0937	367.83615	59.81936	50.5329



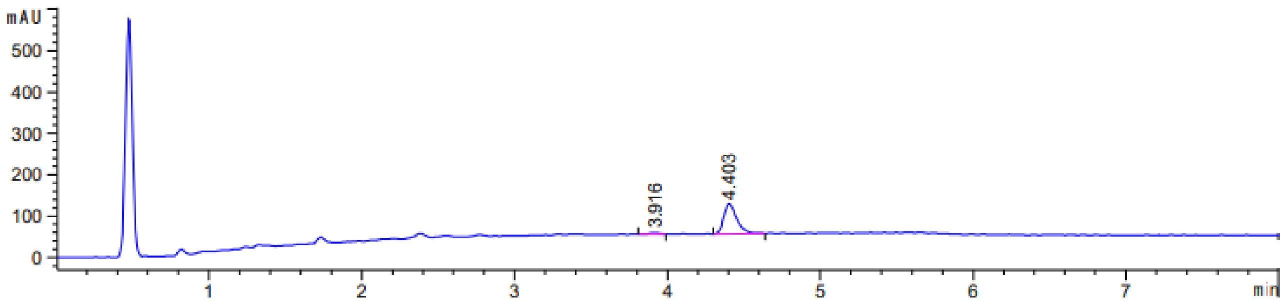
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.154	BB	0.0954	47.42971	7.53824	2.5072
2	4.435	BB	0.1266	1844.32458	213.86523	97.4928



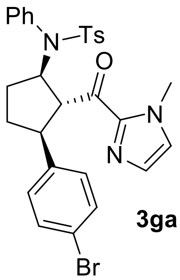
3fa



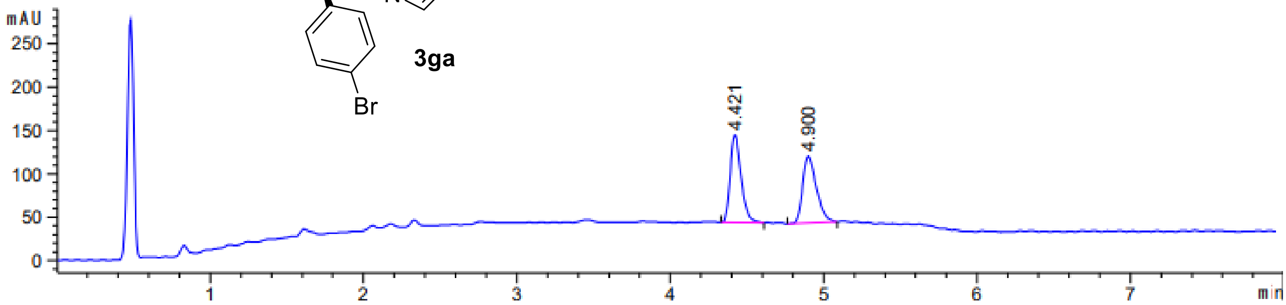
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.907	BB	0.0692	761.30396	166.82169	50.2383
2	4.397	BB	0.0901	754.08105	129.10774	49.7617



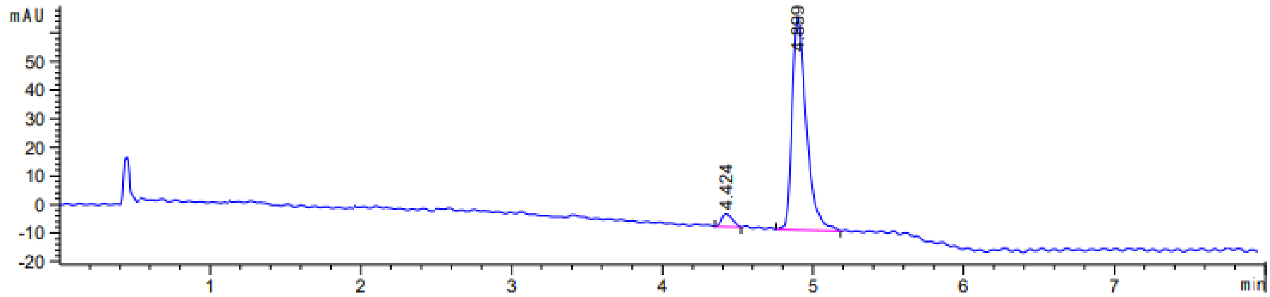
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.916	BB	0.0691	13.75164	3.13907	3.1394
2	4.403	BB	0.0887	424.27618	72.01147	96.8606



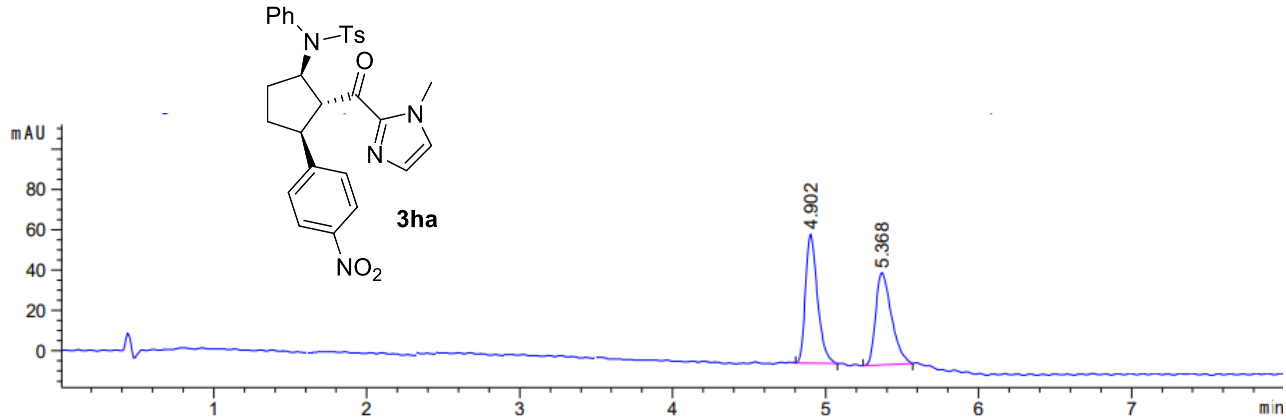
3ga



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.421	BB	0.0735	500.13043	101.55972	50.9747
2	4.900	BB	0.0942	481.00406	77.67348	49.0253

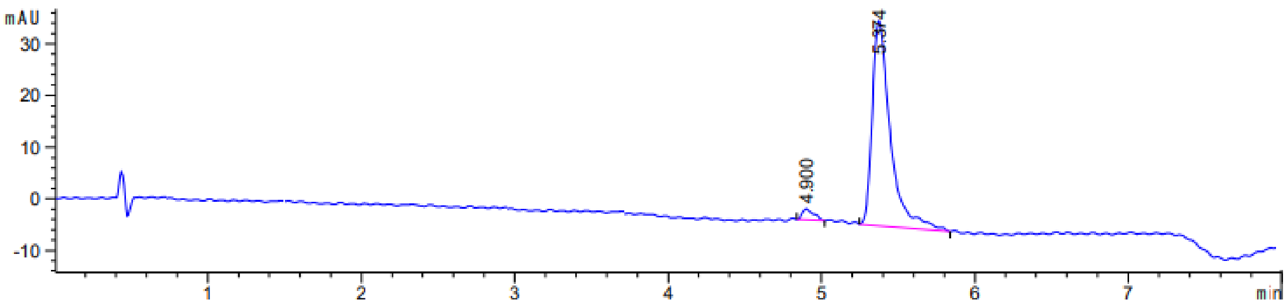


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.424	BB	0.0807	22.42240	4.45740	4.3962
2	4.899	BB	0.0982	487.61829	74.65633	95.6038

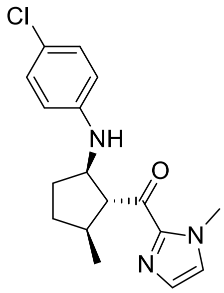


3ha

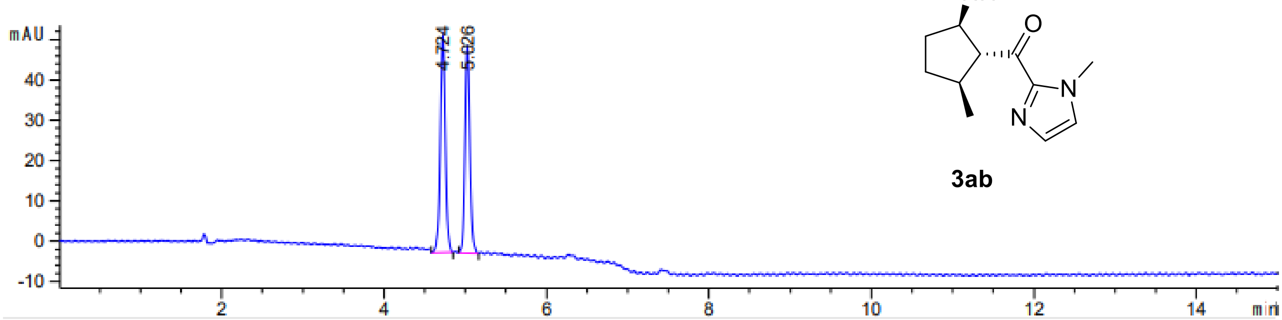
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.902	BB	0.0834	348.15546	64.05414	51.4364
2	5.368	BB	0.1080	328.71075	45.67255	48.5636



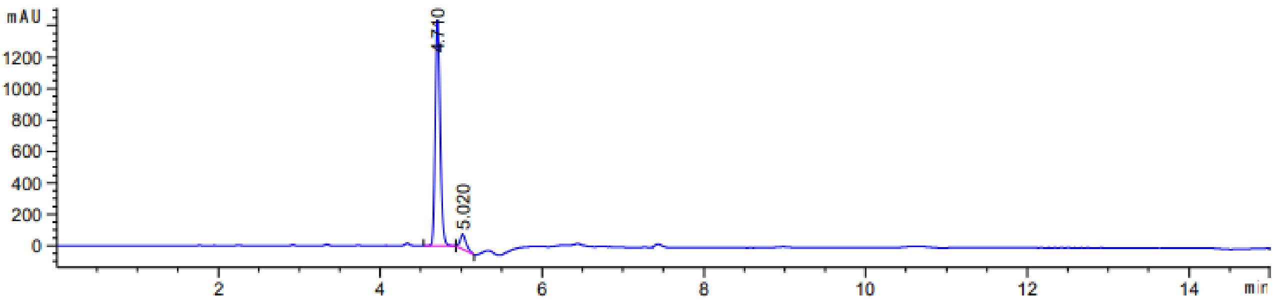
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.900	BB	0.0767	11.30044	2.17204	3.3581
2	5.374	BB	0.1216	325.21017	39.67083	96.6419



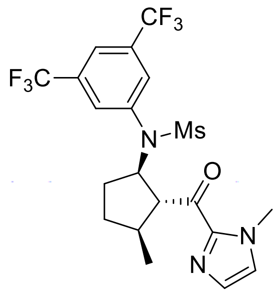
3ab



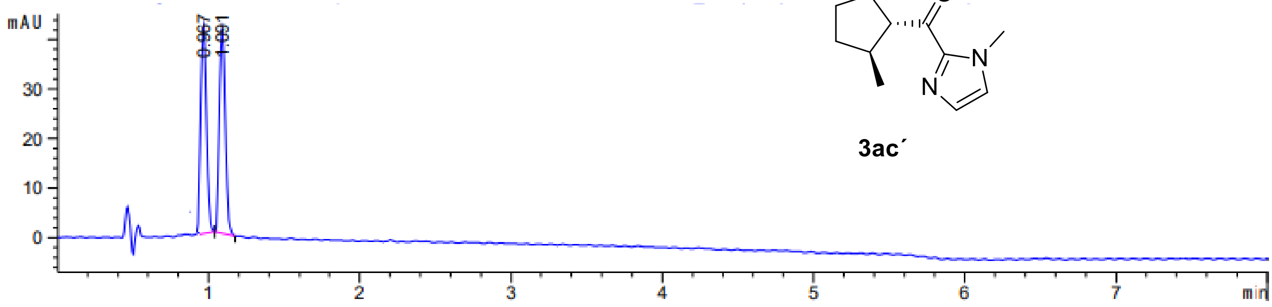
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.724	BB	0.0625	223.08469	53.62494	51.2709
2	5.026	BB	0.0620	212.02527	51.56154	48.7291



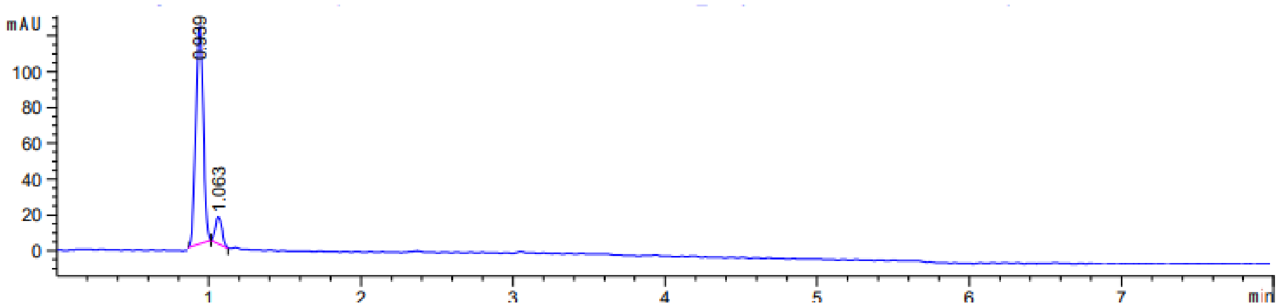
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.710	BB	0.0615	5857.86719	1437.29187	96.0767
2	5.020	BB	0.0768	497.19684	95.35513	3.9233



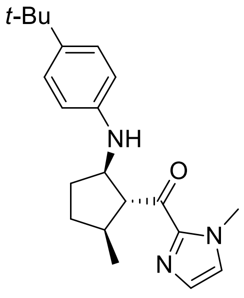
3ac´



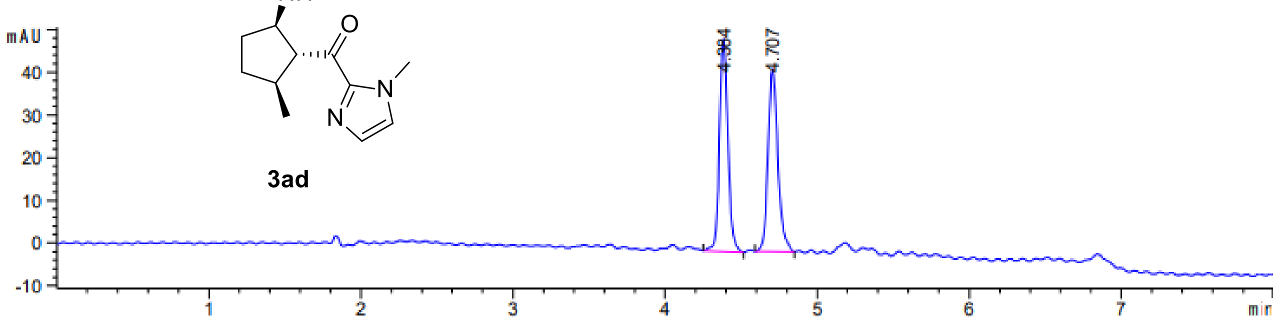
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.967	BB	0.0438	115.42554	42.37280	50.2617
2	1.091	BB	0.0441	114.22376	41.55993	49.7383



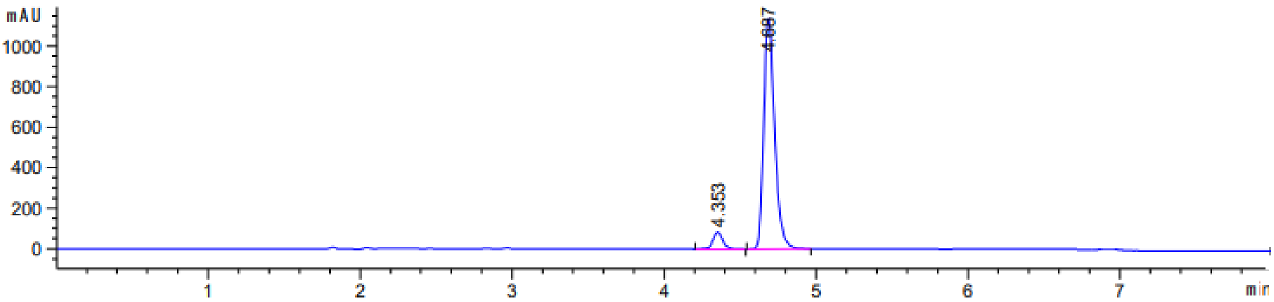
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.939	BB	0.0536	412.09918	121.47387	90.1237
2	1.063	BB	0.0493	45.16010	14.91525	9.8763



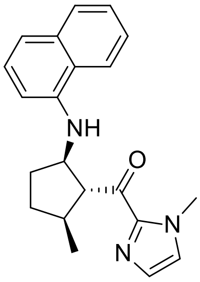
3ad



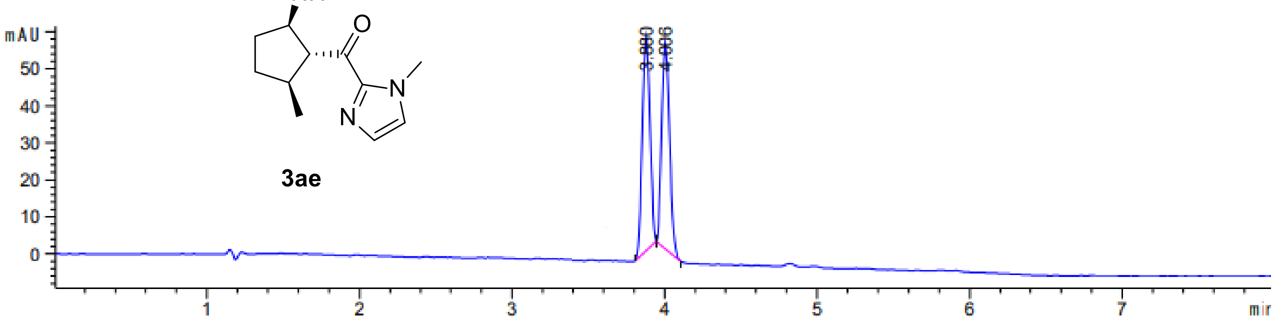
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.384	BB	0.0608	192.14474	50.08756	50.0587
2	4.707	BB	0.0686	191.69391	42.49160	49.9413



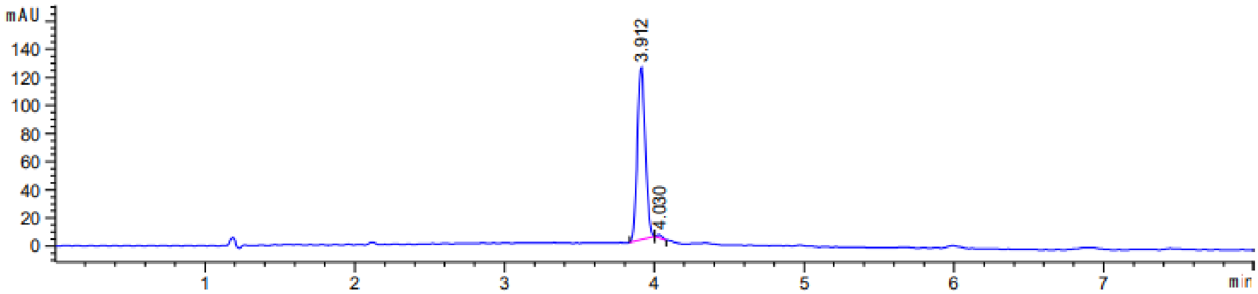
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.353	BB	0.0690	381.86783	84.04269	6.3364
2	4.687	BB	0.0737	5644.70410	1142.19763	93.6636



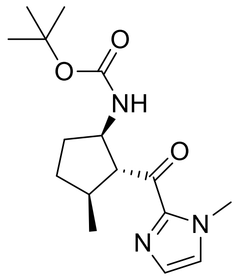
3ae



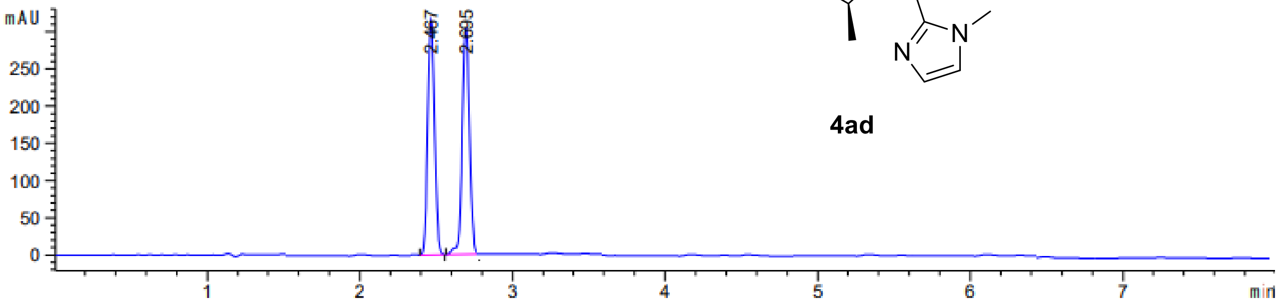
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.880	BB	0.0546	199.85112	57.39271	50.1431
2	4.006	BB	0.0558	198.71025	55.43157	49.8569



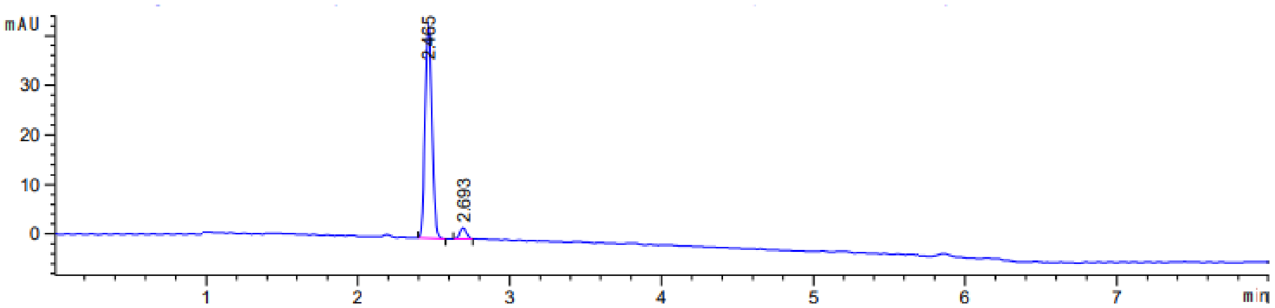
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.912	BB	0.0593	512.65790	122.77338	91.7595
2	4.030	BB	0.0399	46.03962	2.25090	8.2405



4ad



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.467	BB	0.0502	980.26660	315.78687	49.2318
2	2.695	BB	0.0505	1010.85876	306.51648	50.7682



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.465	BB	0.0506	133.83217	42.61705	93.3666
2	2.693	BB	0.0478	6.83212	2.22869	6.4363

12. References.

1. Y. Wang, M. Gu, *Anal. Chem.* **2010**, *82*, 7055-7062; b) Y. Wang, *Methods for Operating MS Instrument Systems*, United States Patent No. 6,983,213, **2006**; c) N. Ochiai, K. Sasamoto, K. MacNamara, *Journal of Chromatography A* **2012**, *1270*, 296-304; d) H. -P. Ho, R. -Y. Lee, C. -Y. Chen, S.- R. Wang, Z. -G. Li, M. -R. Lee, *Rapid Commun. Mass Spectrom.* **2011**, *25*, 25-32.
2. a) J. Ma, X. Shen, K. Harmsa, E. Meggers, *Dalton Trans.* **2016**, *45*, 8320-8323; b) J. Ma, X. Zhang, X. Huang, S. Luo, E. Meggers, *Nat. Protoc.* **2018**, *13*, 605-632.
3. D. A. Evans, K. R. Fandrick, H. -J. Song, *J. Am. Chem. Soc.* **2005**, *127*, 8942-8943.
4. M. C. Myers, A. R. Bharadwaj, B. C. Milgram, K. A. Scheidt, *J. Am. Chem. Soc.* **2005**, *127*, 14675-14680.
5. M. Zhang, T. Zhang, D. Zhang, W. Hu, *Adv. Synth. Catal*. **2020**, 362, 4662-4667.
6. B. Muriel, A. Gagnebin, J. Waser, *Chem. Sci*., **2019,** 10, 10716-10722.
7. S. Maity, M. Zhu, R. S. Shinabery, N. Zheng, *Angew. Chem. Int. Ed.* **2012**, *51*, 222-226.
8. A. J. Boersma, B. L. Feringa, G. Roelfes, *Org. Lett.* **2007**, *9*, 3647-3650.
9. E. L. Tyson, E. P. Farney, T. P. Yoon, *Org. Lett.* **2012**, *14*, 1110-1113.
10. C. Allais, F. Liéby-Muller, T. Constantieux, J. Rodriguez, *Adv. Synth. Catal.* **2012**, *354*, 2537-2544.
11. H. J. Kuhn, S. E. Braslavsky, R. Schmidt, *Pure Appl. Chem*. **2004**, *76*, 2105-2146.
12. S. Hamai, F. Hirayama, *J. Phys. Chem.* **1983**, *87*, 83-89.