Electronic Supplementary Material (ESI) for Dalton Transactions.

Development of bioactive 2-substituted benzimidazole derivatives by using MnO_x/HT nanocomposite catalyst

Loveneesh Kumar[a], Nishant Verma[a], Ravi Tomar[a,c], Hitesh Sehrawat[a], Rupesh Kumar[a,b],Ramesh Chandra[a,d,e*]

[a] Drug Discovery & Development Laboratory,
Department of Chemistry,
University of Delhi,
Delhi 110007, India.
Email: acbrdu@hotmail.com, rchandra@chemistry.du.ac.in, rameshchandragroup@gmail.com, director@inms.du.ac.in

[b] Department of Chemistry,
Kirori Mal College,
University of Delhi,
Delhi 110007, India.
Email: Chembio005@yahoo.co.in

[c] Department of Chemistry,
Faculty of Science,
SGT University,
Gurugram,
Haryana-122505, India.

[d] Dr. B. R. Ambedkar, Centre for Biomedical Research (ACBR),
University of Delhi,
Delhi 110007, India.

[e] Institute of Nanomedical Sciences (INMS),
University of Delhi,
Delhi 110007, India.

Material and Instruments

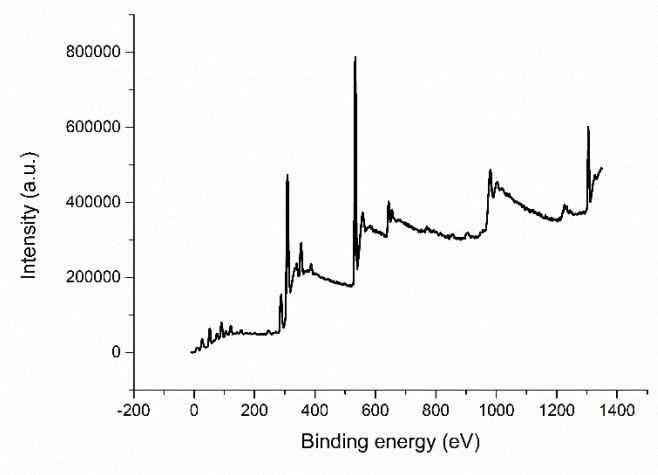
All the starting materials were procured from Thomas Baker (Mumbai, India), Alfa Aesar (England) and Spectrochem (Mumbai, India) and used without any purification. NMR spectroscopy was performed on JEOL (400 MHz, JNM-EXCP 400) spectrometer using $CDCl_3$ and DMSO-d_6 as NMR solvent obtained from eurisotop. The reactions were followed using silica gel 60F254 TLC (Thin layer chromatography) plates (Merck, Darstadt, Germany). Purification of synthesised substrate derivatives were done using 100-200 mesh (Merck, Mumbai, India) silica gel-based column chromatography. PHI 5000 Versa Probe II model having monochromatic Al K_α 945 radiation as the X-ray source was used for XPS (X-ray photoelectron spectroscopy) which was supplied by ULVAC-PHI Inc., Japan. To study morphology and qualitative analysis of the nanocomposite was performed on Scanning Electron Microscope (JEOL Japan, JSM 6610LV). Zetasizer Nano ZS90 (Malvern Instruments Ltd., UK), equipped with He-Ne (4 mW, 632.8 nm) was used for DLS (Dynamic Light Scattering) analysis. TEM (Transmission Electron Microscopy) analysis was performed on LaB_6/Tungsten filaments emitter-based JEM-1400 Transmission Electron Microscope. Thermal stability of synthesized materials was performed on TGA/DA instrument (Perkin Elmer, pyrisdiamond TGA/DA). XRD analysis was done on a Bruker Discover D8 with Cu Kα radiation (3 kW). Gas chromatography studies were performed with a PerkinElmer Clarus 580 equipped with RTX-5SIL-MS column. Atomic Absorption spectroscopic studies were performed on Varian 220FS Atomic Absorption Spectrophotometer. HRMS studies was done on Agilent G6530AA with ESI and APCI source.

Reaction Procedure

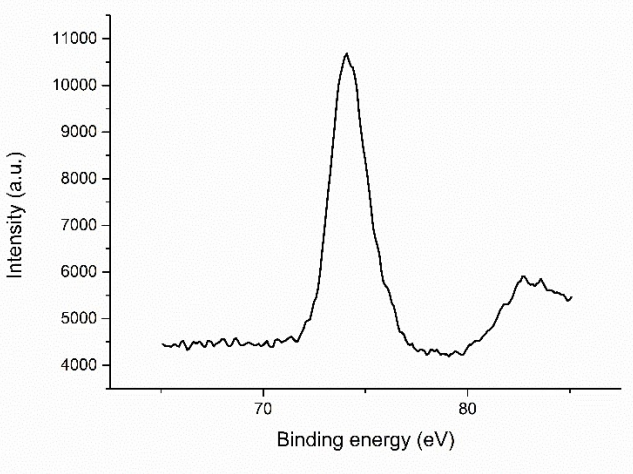
A 10 ml round bottom flask was charged with substrate *o*-phenylenediamine (1 mmol), aldehyde (1 mmol), Solvent ethanol: water (50:50) 1 ml, and catalyst 20 mg. Then, the reaction mixture was stirred at room temperature for 1 hr. The reaction was monitored by TLC. After the reaction was completed, the resulting solution was extracted with EtOAc and dried over anhydrous Na_2SO_4. Following that, it was filtered to remove the catalyst, concentrated in vacuo, and Gas chromatography (GC) was done. If the GC graph indicated the presence of aldehyde or *o*-phenylenediamine in the reaction mixture then it was purified by column chromatography using hexane/ethyl acetate as eluent to afford the corresponding pure products. Otherwise, the reaction mixture is simply recrystallized using ethanol to get the pure product. The purity of the synthesised compound was confirmed by High resolution mass spectrometry (HRMS).

(Note: For Gas chromatography, the reaction mixture was analysed after workup and dried. AR Grade Methanol was taken as a solvent for the preparation of GC solutions).

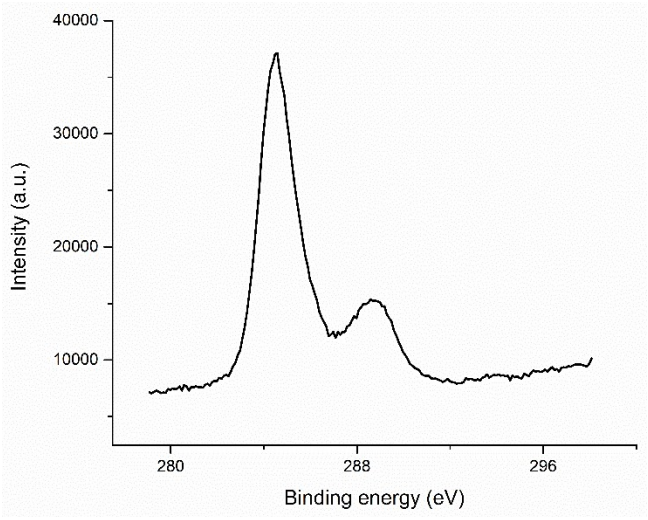
XPS full range plot of MnO_x/HT nanocomposite catalyst



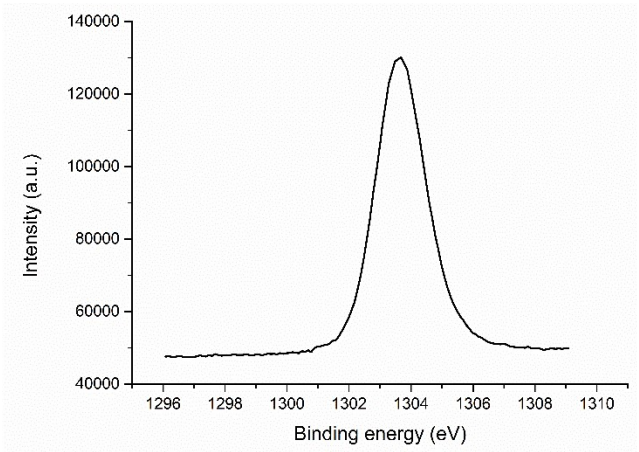
Narrow Scan XPS Plot of Al



Narrow Scan XPS Plot of Carbon



Narrow Scan XPS Plot of Magnesium



Calculation for metal loading:

Metal loading = $\frac{Concentration\ of\ metal\ (ppm)\ X\ Volume\ of\ extract\ (Litre)}{Weight\ of\ solid\ sample\ taken\ for\ extraction\ (grams)}$ =

Calculation for mol% of catalyst:

Mol % of catalyst used = $\frac{no.\ of\ moles\ of\ catalyst\ used}{(no.\ of\ moles\ of\ catalyst\ used + no.\ of\ moles\ of\ limiting\ reagent)}$ X 100

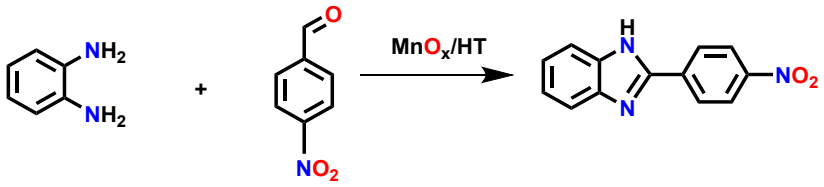
Calculation for TON:

$$\text{TON} = \frac{\%\ Conversion}{mmoles\ of\ catalysts}$$

Calculation for TOF:

$$\text{TOF} = \frac{TON}{Times\ of\ reaction\ (h)}$$

Calculation for Green Matrix:



M.W.	108.14 g/mol	151.12 g/mol	239.234 g/mol
Mmol	1.0	1.0	0.96
Amount	108 mg	151 mg	229 mg

E-factor:

The ideal value of E-factor is zero.

E-factor = [total mass of raw materials - the total mass of product]/ mass of product.

E-factor of i = [(108 + 151)-229]/229

= 0.13

Process mass intensity (PMI):

PMI= ∑ (mass of stoichiometric reactants)/[mass of product]

= (108+ 151)/229

= 1.13.

Reaction mass efficiency (RME):

RME = [mass of product /∑ (mass of stoichiometric reactants)] × 100

= [229 /(108+ 151)] × 100

= 88.41 %

Carbon efficiency (CE):

CE denotes the percentage of carbon in the reactants that remains in the product.

CE= [Amount of carbon in product/ Total carbon present in reactants] x 100

= [no. of moles of product x no. of carbons in product / (moles of a x carbons in 1 + moles of y carbons in 2)] x 100

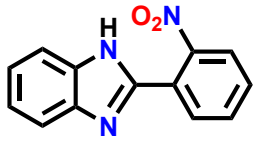
= [0.96 x 13 / (1.0 x 7 + 1.0 x 6)] x 100

= [12.48 / (7 + 6)] x 100

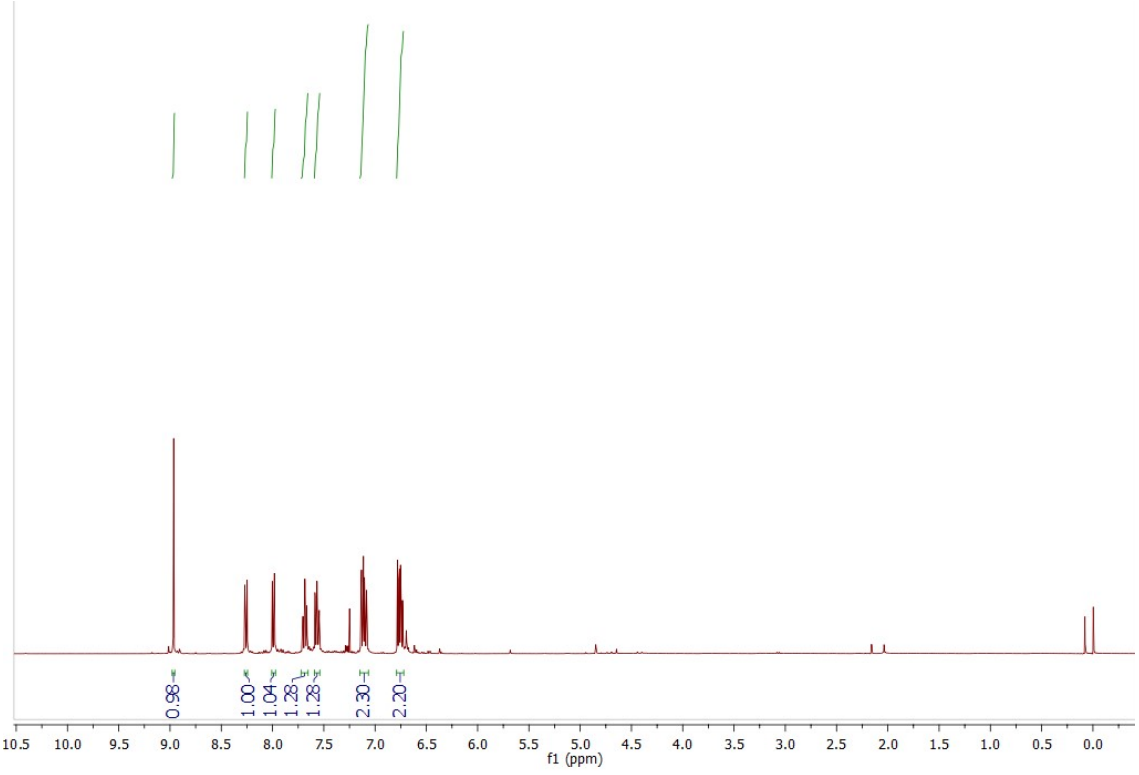
= 96%

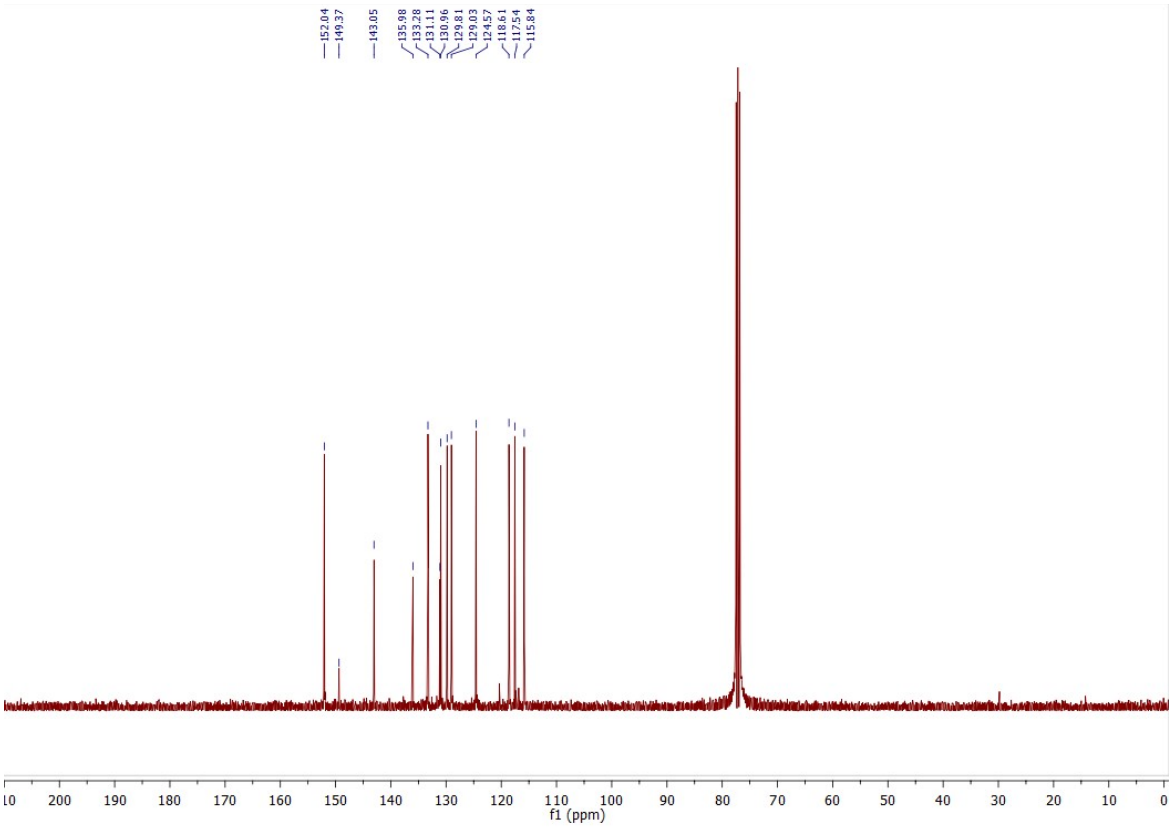
NMR data of Selective Compounds:

(4a) 2-(2-nitrophenyl)-1H-benzo[d]imidazole

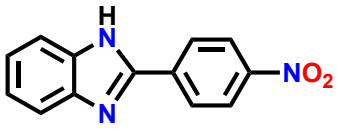


NMR (400 MHz, $CDCl_3$) δ (ppm) 8.97 (d, J = 4.5 Hz, 1H), 8.27 – 8.24 (m, 1H), 8.01 – 7.97 (m,1H), 7.72 – 7.65 (m, 1H), 7.59 – 7.54 (m, 1H), 7.15 – 7.07 (m, 2H), 6.79 – 6.72 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.04, 149.37, 143.05, 135.98, 133.28, 131.03, 129.81, 129.03, 124.57, 118.61, 117.54, 115.84.

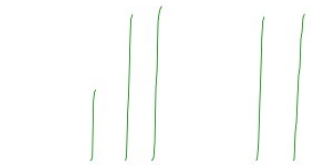


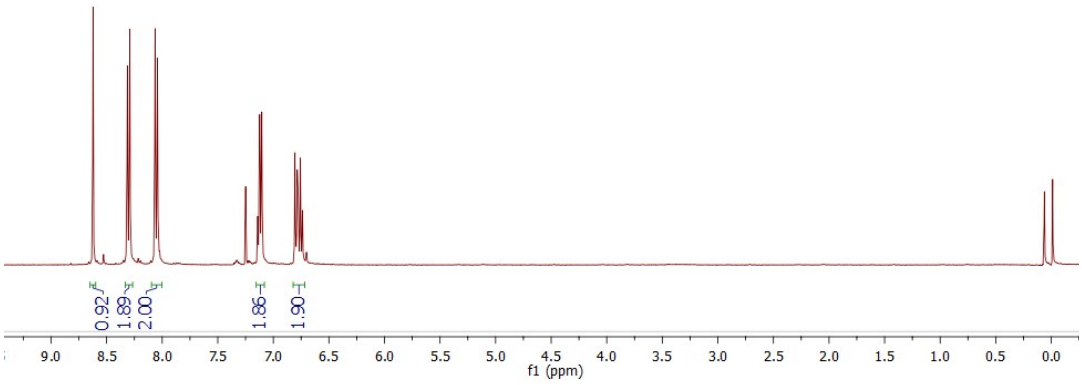


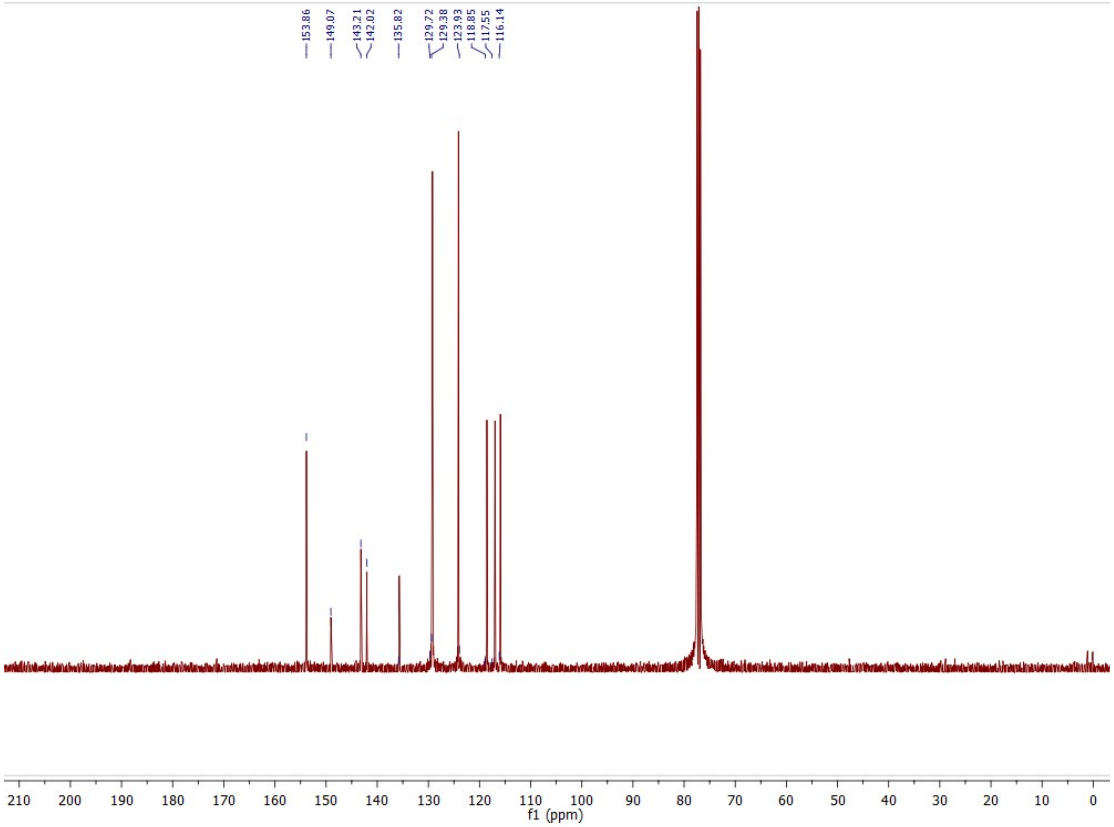
(4c) 2-(4-nitrophenyl)-1H-benzo[d]imidazole



NMR (400 MHz) δ 8.62 (s, 1H), 8.30 (d, J = 8.6 Hz, 2H), 8.04 (t, J = 8.3 Hz, 2H), 7.15 – 7.08 (m, 2H), 6.82 – 6.72 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.86 (s), 149.07 (s), 143.21 (s), 142.02 (s), 135.82 (s), 129.72 (s), 129.38 (s), 123.93 (s), 118.85 (s), 117.55 (s), 116.14 (s).




0.92
1.89
2.00
1.86
1.90
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


153.86
149.07
143.21
142.02
135.82
129.72
129.38
123.93
118.85
117.55
116.14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

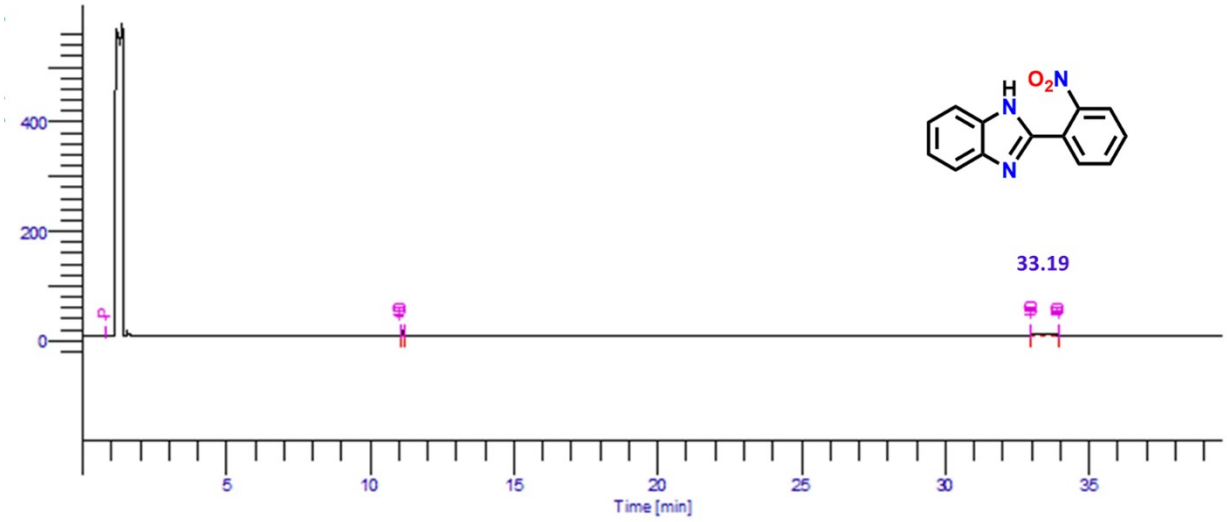
Gas Chromatograms for the Organic Products

Gas chromatograms for various organic products with the method used:

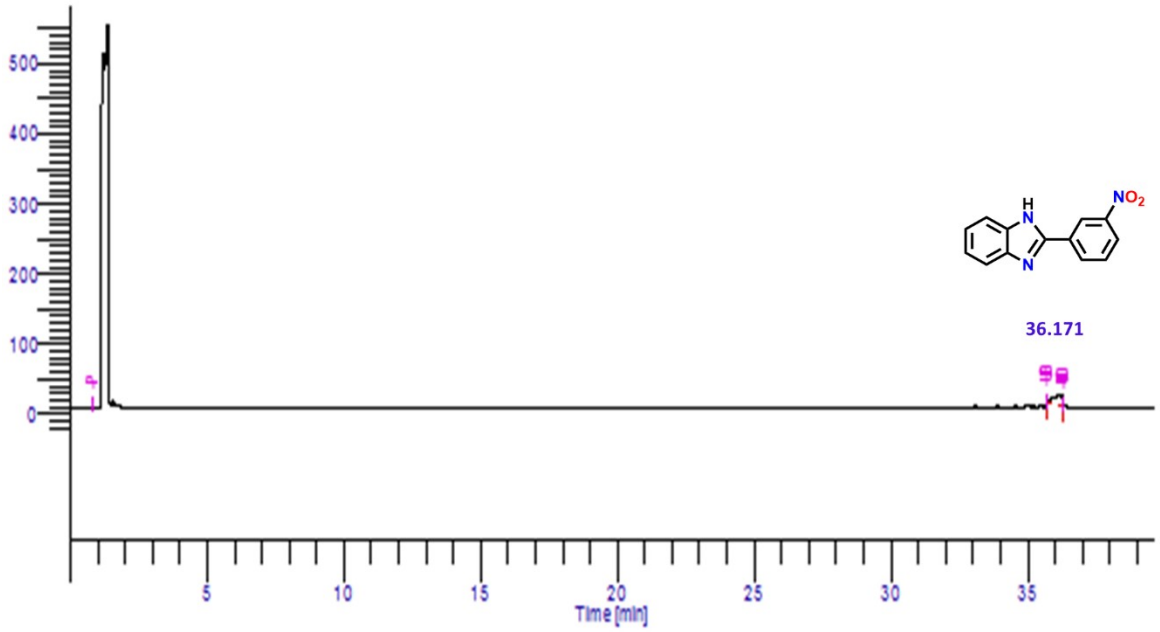
Method: Column information Elite-5, L = 30 m, ID: 0.25 mm, injector temperature 50 °C, column flow rate 1.13 mL/min, column temperature 50 – 180°C, temperature program 10 °C/min, detector temperature 250 °C.

Methanol is used as the solvent.

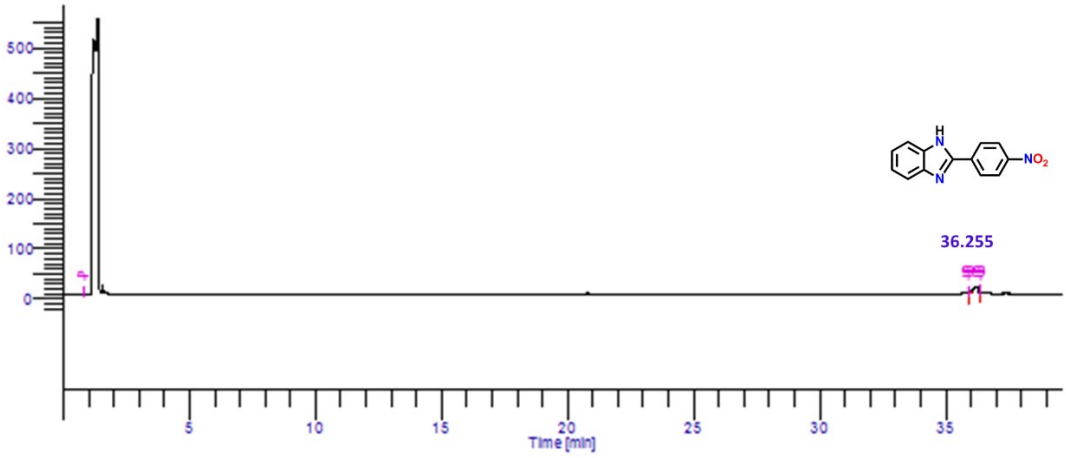
(4a) 2-(2-nitrophenyl)-1H-benzo[d]imidazole



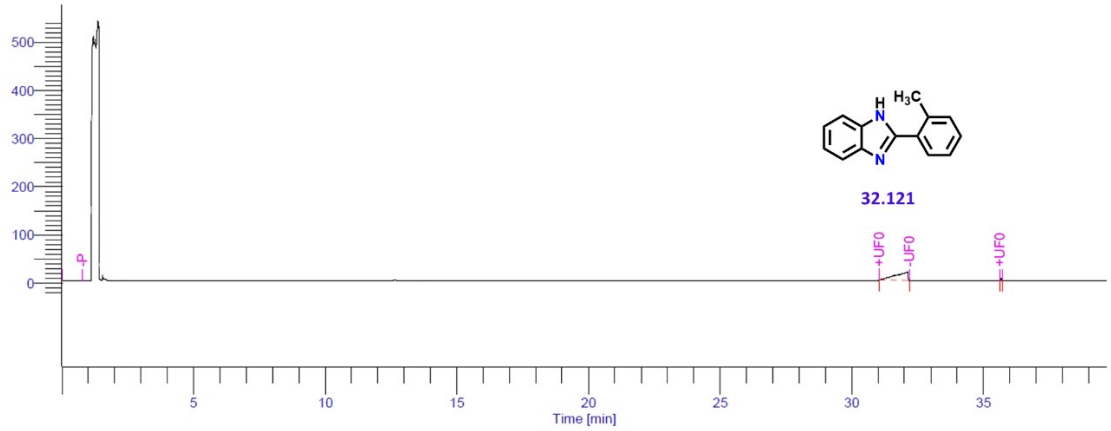
(4b) 2-(3-nitrophenyl)-1H-benzo[d]imidazole



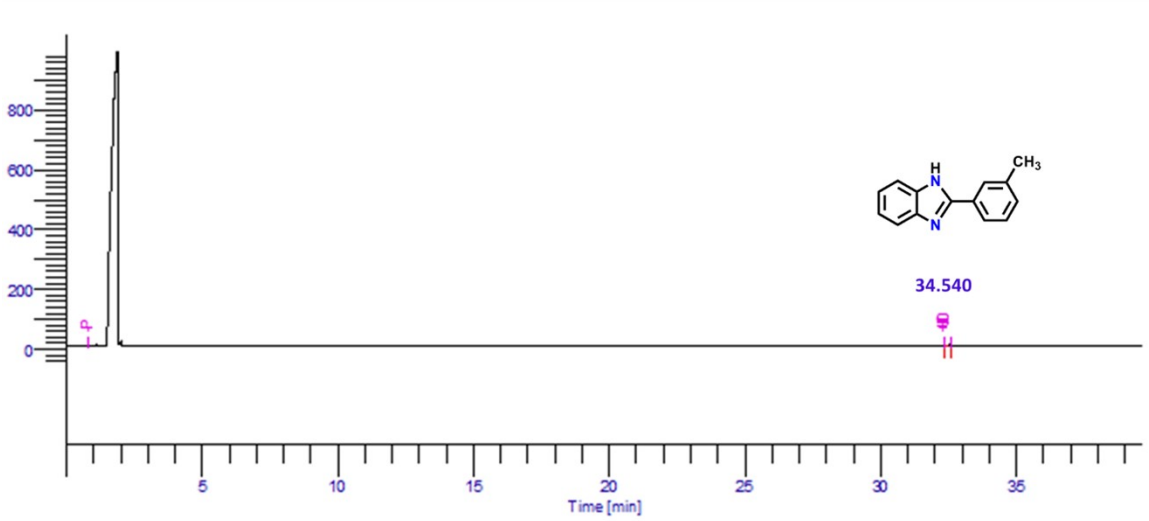
(4c) 2-(4-nitrophenyl)-1H-benzo[d]imidazole



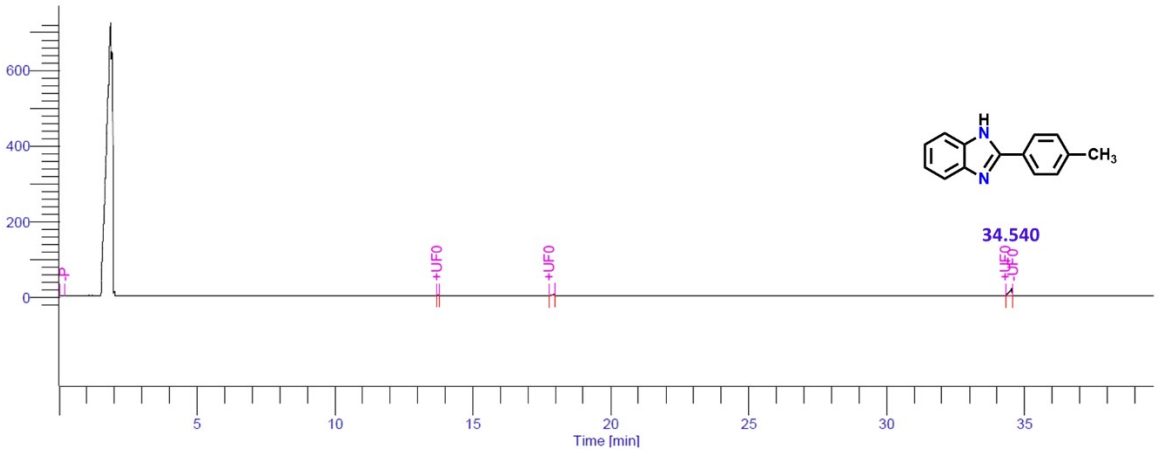
(4d) 2-(o-tolyl)-1H-benzo[d]imidazole



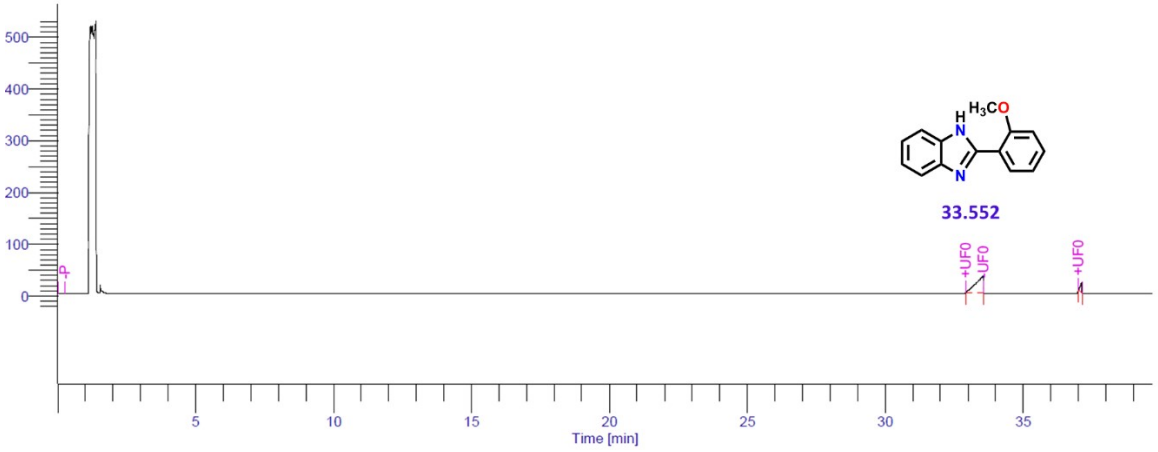
(4e) 2-(m-tolyl)-1H-benzo[d]imidazole



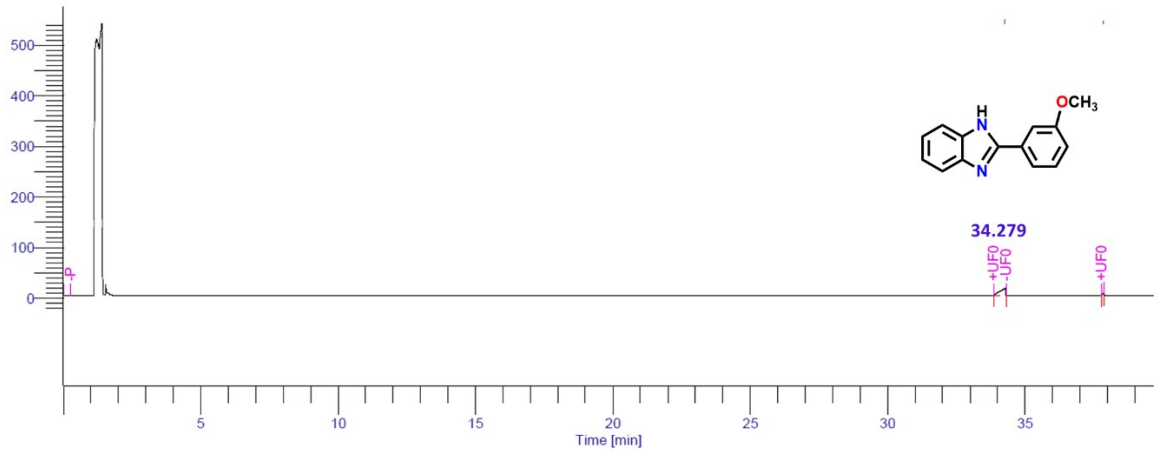
(4f) 2-(p-tolyl)-1H-benzo[d]imidazole



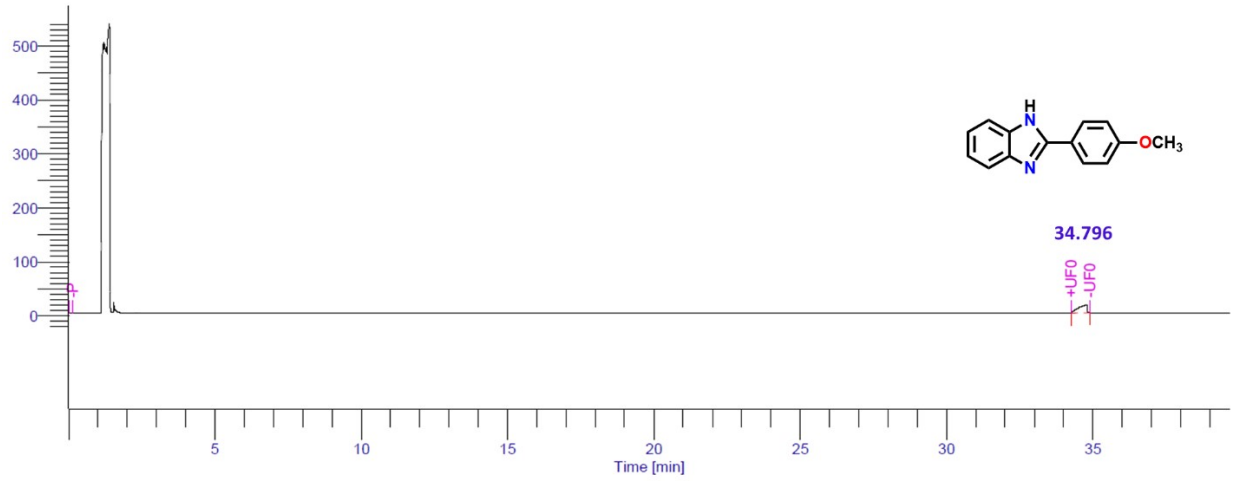
(4g) 2-(2-methoxyphenyl)-1H-benzo[d]imidazole



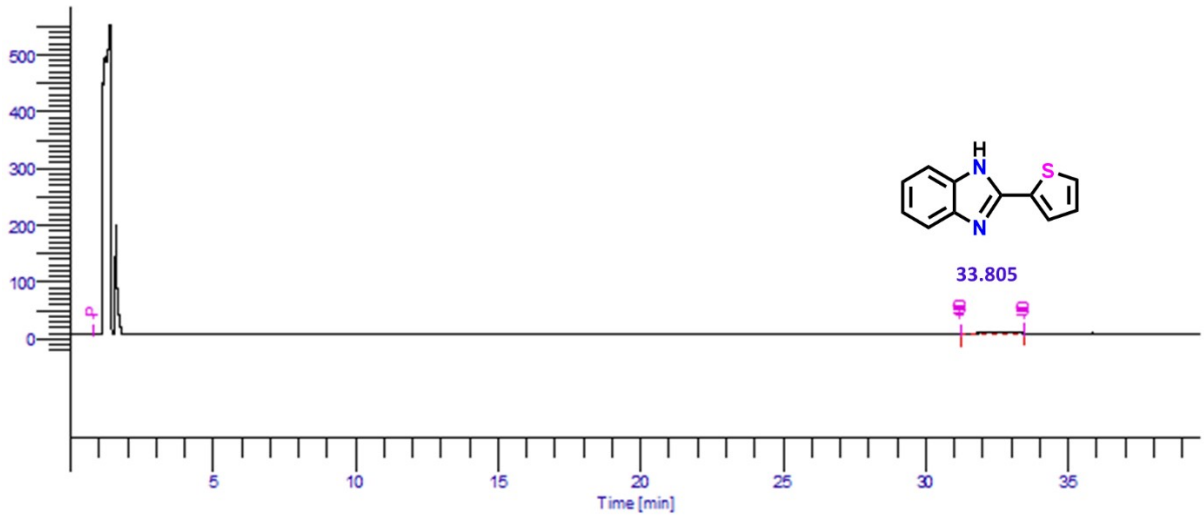
(4h) 2-(3-methoxyphenyl)-1H-benzo[d]imidazole



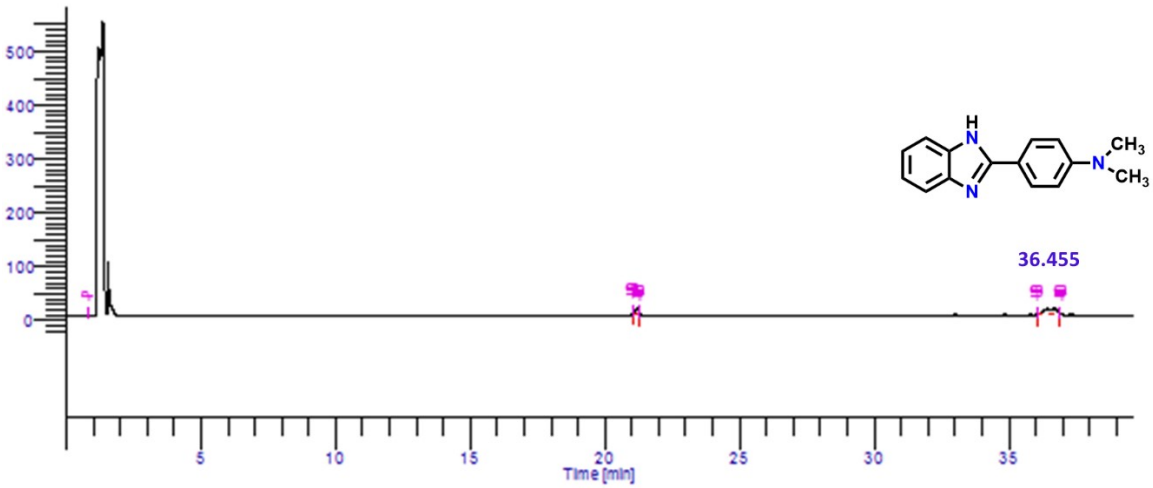
(4i) 2-(4-methoxyphenyl)-1H-benzo[d]imidazole



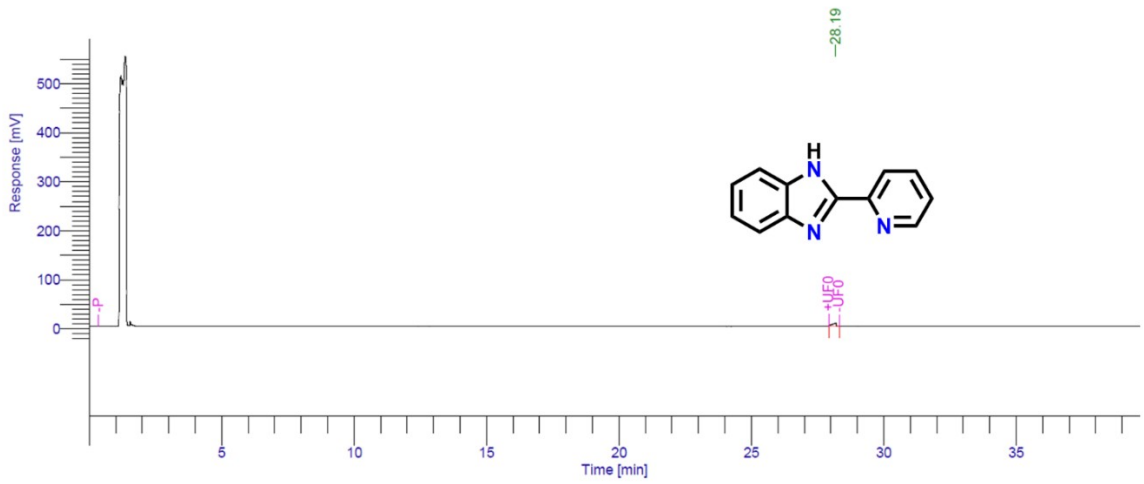
(4j) 2-(thiophen-2-yl)-1H-benzo[d]imidazole



(4k) 4-(1H-benzo[d]imidazol-2-yl)-N,N-dimethylaniline



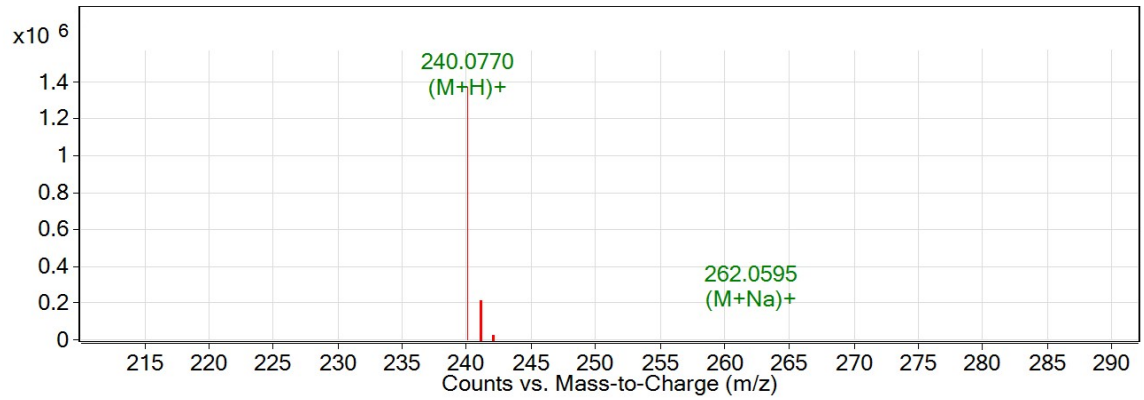
(4l) 2-(pyridin-2-yl)-1H-benzo[d]imidazole



HRMS data for the Organic Products

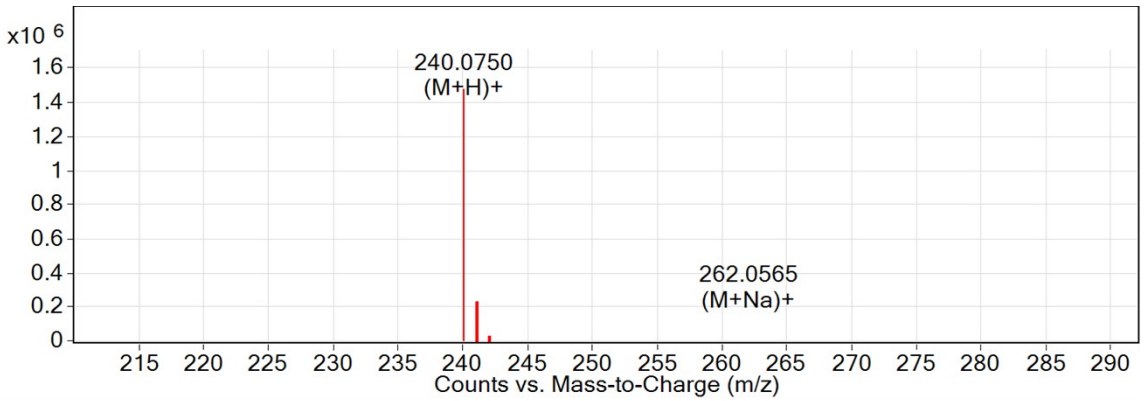
(4a) 2-(2-nitrophenyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{13}H_9N_3O_2$ $[M+H]^+$: 240.07 found $[M+H]^+$: 240.0770.



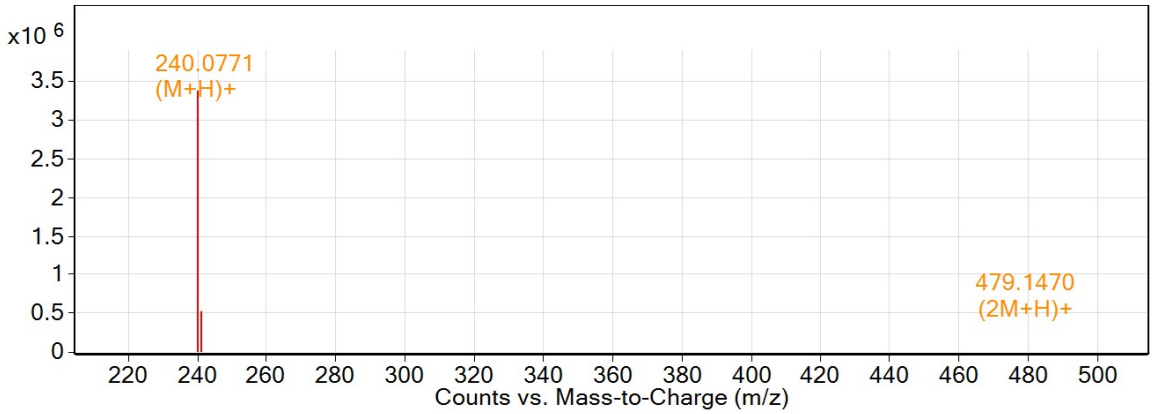
(4b) 2-(3-nitrophenyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{13}H_9N_3O_2$ $[M+H]^+$: 240.07 found $[M+H]^+$: 240.0750.



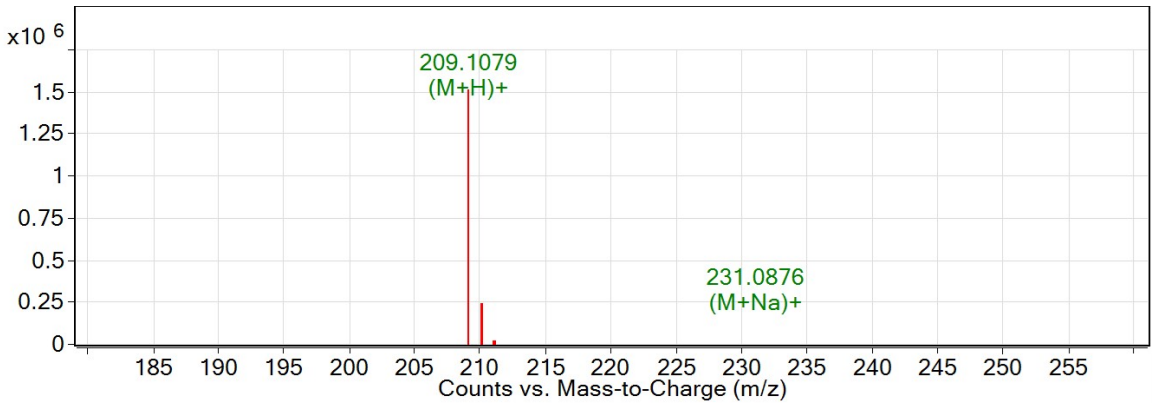
(4c) 2-(4-nitrophenyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{13}H_9N_3O_2$ $[M+H]^+$: 240.07 found $[M+H]^+$: 240.0771.



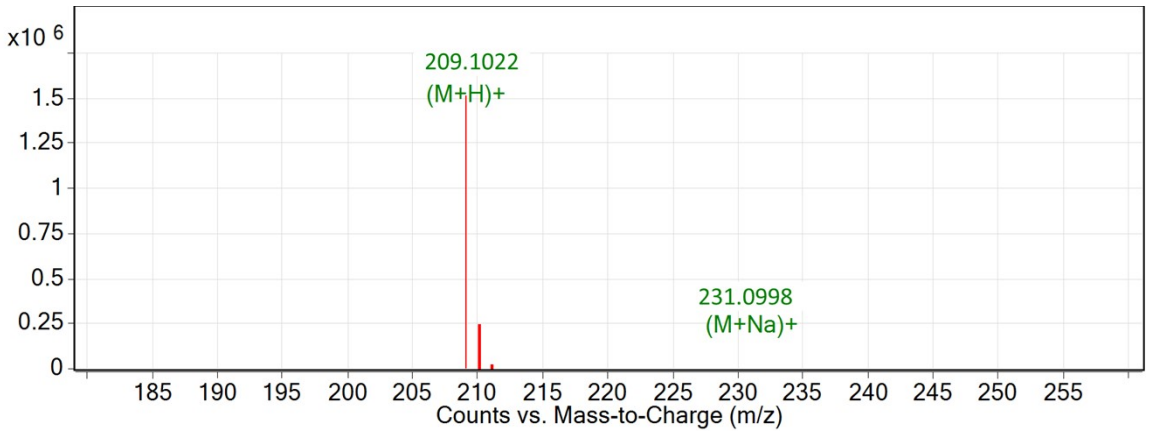
(4d) 2-(o-tolyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{14}H_{12}N_2$ $[M+H]^+$: 209.10 found $[M+H]^+$: 209.1079.



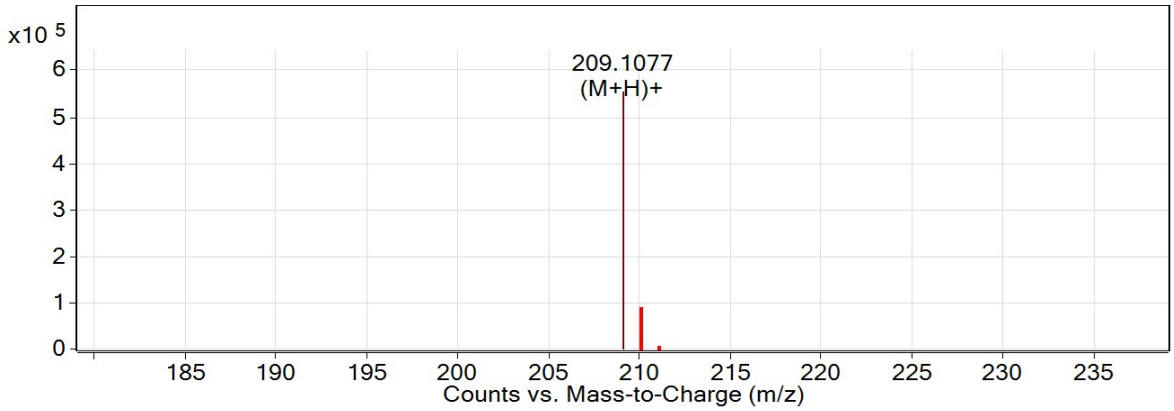
(4e) 2-(m-tolyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{14}H_{12}N_2$ $[M+H]^+$: 209.10 found $[M+H]^+$: 209.1022.



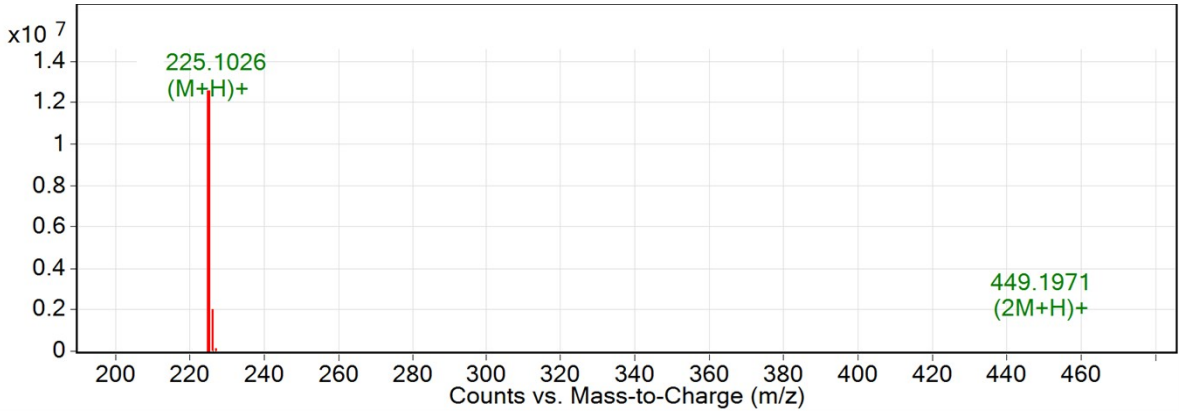
(4f) 2-(p-tolyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{14}H_{12}N_2$ $[M+H]^+$: 209.10 found $[M+H]^+$: 209.1077.



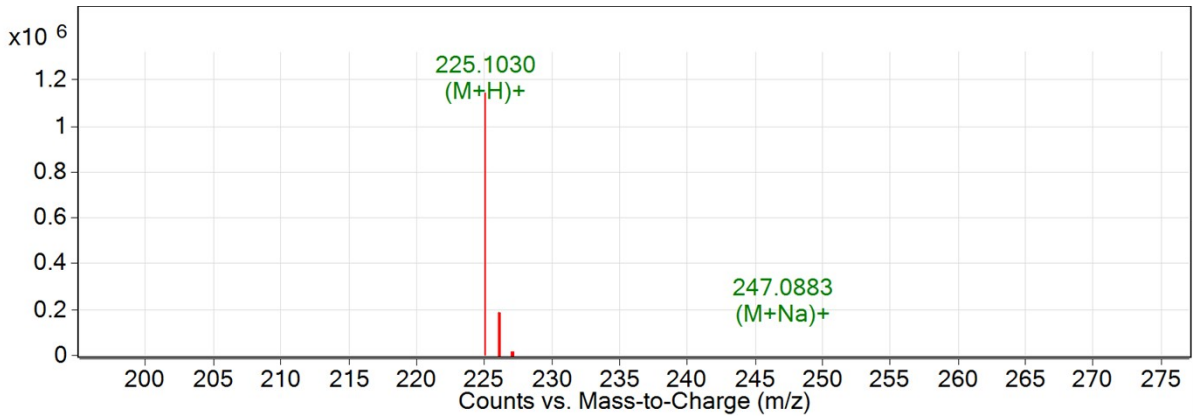
(4g) 2-(2-methoxyphenyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{14}H_{12}N_2O$ $[M+H]^+$: 225.10 found $[M+H]^+$: 225.1026.



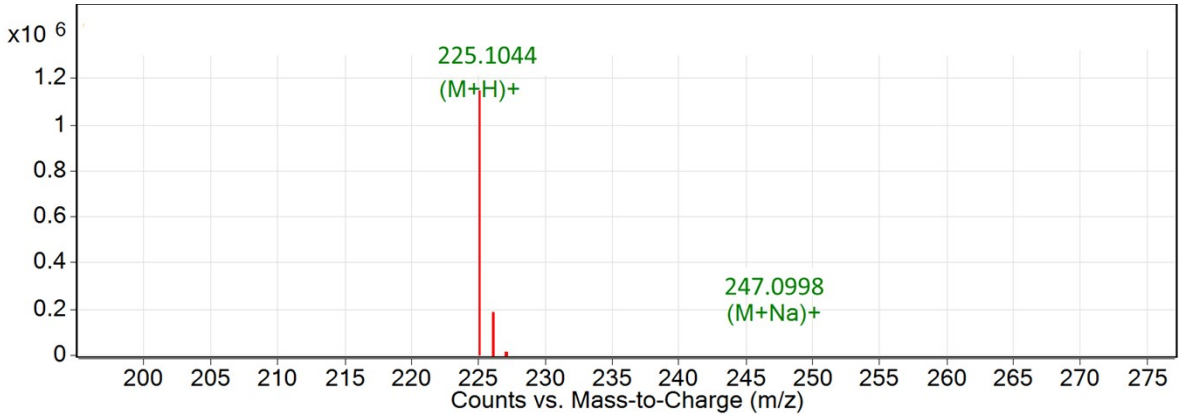
(4h) 2-(3-methoxyphenyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{14}H_{12}N_2O$ $[M+H]^+$: 225.10 found $[M+H]^+$: 225.1030.



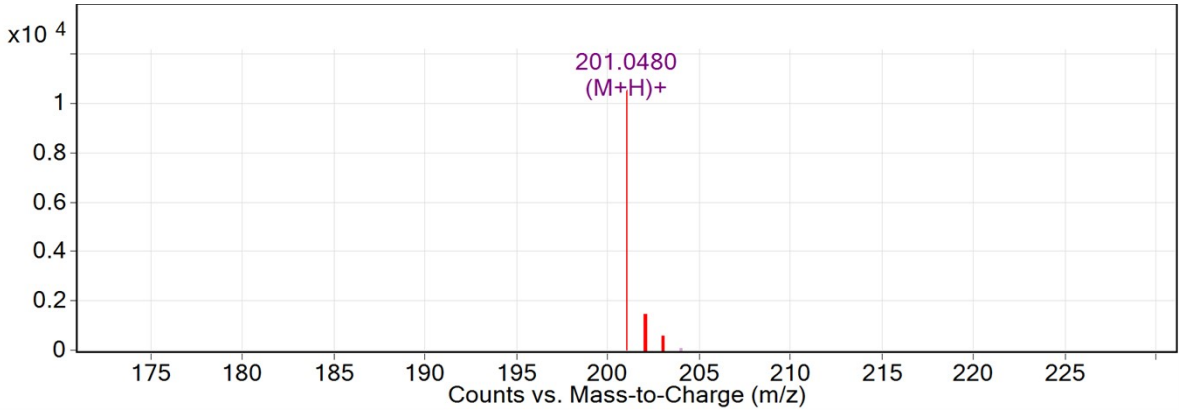
(4i) 2-(4-methoxyphenyl)-1H-benzo[d]imidazole

HRMS calculated for $C_{14}H_{12}N_2O$ $[M+H]^+$: 225.10 found $[M+H]^+$: 225.1044.



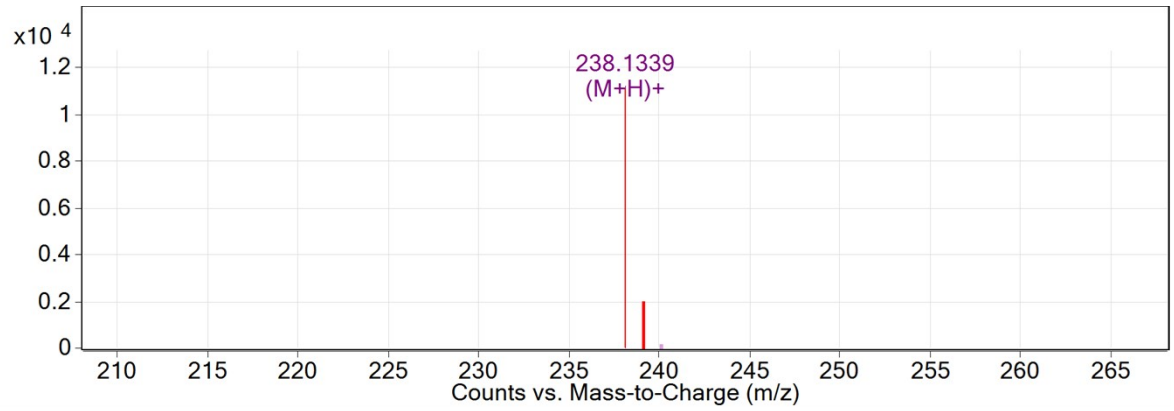
(4j) 2-(thiophen-2-yl)-1H-benzo[d]imidazole

HRMS calculated for $C_{11}H_8N_2S$ $[M+H]^+$: 201.04 found $[M+H]^+$: 201.0480.



(4k) 4-(1H-benzo[d]imidazol-2-yl)-N,N-dimethylaniline

HRMS calculated for $C_{15}H_{15}N_3$ $[M+H]^+$: 238.13 found $[M+H]^+$: 238.1339.



(4l) 2-(pyridin-2-yl)-1H-benzo[d]imidazole

HRMS calculated for $C_{12}H_9N_3$ $[M+H]^+$: 196.08 found $[M+H]^+$: 196.0865.