Electronic Supporting Information

Bovine Serum Albumin: An Efficient and Green Biocatalyst for the One-Pot, Three-Component Synthesis of Valuable Imidazole *N*-oxides in H_2O-EtOH Medium

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General Information

All commercially available reagents, such as aldehydes, amines, monoximes, ammonium acetate, and hydroxylamine hydrochloride, were used without further purification. The aldehydes and amines were purchased from several companies, which are Acros, Sigma-Aldrich, and Thomas and Baker Merck. Ammonium acetate and benzil were purchased from Loba Chemie. Hydroxylamine hydrochloride was purchased from Research-Lab Fine Chem Industries. 2,3-Butanedione monoxime was Hyma Synthesis Private Limited (Formerly Avra Synthesis Pvt. Ltd.). Ethanol was purchased from Changshu Hongsheng Fine Chemical Co., Ltd. Methanol and sodium hydroxide were purchased from Sisco Research Laboratories Pvt. Ltd. (SRL). Incubator Shaker was purchased from Riviera Glass Pvt. Ltd. The glasswares used for work were dried in the oven and cooled.

Methods

^{1}H (300 MHz) spectra and ^{13}C (75 MHz) nuclear magnetic resonance (NMR) spectra were recorded on a *Bruker Avance* 300 spectrometer. Chemical shifts (δ) are provided in ppm unit, and tetramethylsilane (TMS, δ 0.00 ppm) was used as reference. Infrared (IR) spectra were recorded on a *Schimadzu* FTIR-8300 spectrometer in the 4000 – 400 cm^{-1} region as in KBr pellets or neat, or solution. The given unit of absorption is cm^{-1} (wave numbers). MICROMASS QUATTRO II triple quadruple mass spectrometer was used for the electron-spray mass spectra. The FAB MS analyses were taken on a Jeol SX 102/Da-600 mass spectrometer, Argon/Xenon (6 kV, 10mA) was used as the FAB gas in Data System. The accelerating voltage was 10 kV, and the spectra were taken at room temperature.

Synthesis

General Procedure for the Synthesis of α-Benzil Monoxime (3b)

The previously reported approach was followed to produce α-benzil monoxime (**3b**)[1]. Benzil (1 equiv., 100 mmol, 21g) was ground to a thin paste by adding a little bit of ethanol, followed by the addition of a concentrated aqueous solution of hydroxylamine hydrochloride (1.25 equiv., 125 mmol, 8.75 g). After that, an ice bath was used to cool down the reaction mixture to -5 ◦C, and stirred, followed by the dropwise addition of 20% aqueous solution of sodium hydroxide (3 equiv., 300 mol, 12 g) to the stirring reaction mixture. The process was handled attentively to maintain the temperature of the process below 0 ◦C. After 90 minutes, water was added to dilute the mixture and filtered to remove the unreacted benzil. Next, acetic acid was added to the filtrate to acidify the solution and allowed to rest for 30 minutes to acquire the

crude pinkish α-benzil monoxime. Then, the product was collected in 60% aqueous ethanol, and the recrystallized product was obtained (16.3 g, 72.44%, m.p. 142 ◦C).

General Procedure for the Synthesis of Imidazole *N*-oxides

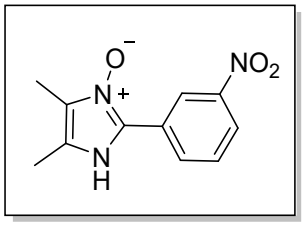
In a 50 mL round-bottom flask, monoxime (**3a** or **3b**) (1.0 mmol, 1.0 equiv.), aromatic aldehydes (1.0 mmol, 1.0 equiv.), and ammonium acetate, or hydroxylamine hydrochloride, or amines (1.0 mmol, 1.0 equiv.) were taken in the presence of 50 mg BSA in 5 mL of a mixture of deionized water-ethanol solvents in a 4:6 ratio. The mixture was put in the incubator shaker and was shaken at 60 °C for 5 hrs. After that, the reaction mixture was cooled down to room temperature. If needed, maybe 1-2 mL of ethanol can be added to fully precipitate the catalyst BSA. Then, the solvent mixture was filtered, and the organic part was collected as filtrate, and BSA was collected as residue in filter paper. After that, the solvent was removed under vacuum and washed with 1-2 mL ethyl acetate to obtain imidazole *N*-oxides. Then, the imidazole *N*-oxide was recrystallized in ethanol.

General Procedure for the Gram-scale Synthesis of Imidazole *N*-oxide (4aa)

In a 100 mL round-bottom flask, 15 mmol of 2,3-butanedione monoxime (1.0 equiv., 1.5 g), 15 mmol of 3-nitrobenzaldehyde (1.0 equiv., 2.3 g), and 15 mmol of ammonium acetate (1.0 equiv., 1.2 g) were taken in 30 mL of solvent mixture of ethanol and deionized water in a 6:4 ratio, in the presence of 750 mg of BSA. The reaction mixture was shaken in the incubator shaker at 60 °C for 5 hrs. After that, the reaction mixture was cooled down to room temperature. Then the reaction mixture was filtered and concentrated under vacuum. The filtrate was collected, and after some time, the crystals started to precipitate, and pure corresponding imidazole *N*-oxide **4aa** was obtained. After washing the imidazole *N*-oxide in ethyl acetate, the yield was calculated.

Characterization Data of the Products

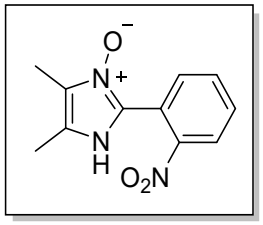
2-(3-Nitrophenyl)-4,5-dimethyl Imidazole 3-oxide [4aa][2]:



M.P.: 172-174 °C, ***[1]HNMR (400 MHz, DMSO):*** δ 12.76 (s, 1H); δ 8.77 (s, 1H); δ 8.23 (d, 1H); δ 8.10 (d, 1H); δ 7.61 (d, 1H); δ 2.02 (6H); ***[13]CNMR (100 MHz, DMSO):*** 148.02, 134.68, 132.62, 131.18, 129.55, 128.08, 124.47, 120.60, 119.33, 22.12,

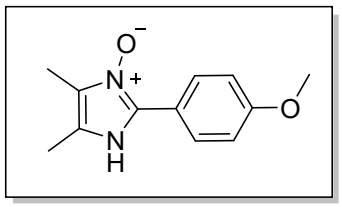
13.37, 8.04. ***IR (KBr, cm^{-1}):*** 3390 (N-H), 3076 (Ar C-H), 2732 (Al C-H), 1646 (C=C), 1523 (C=N), 1347, 1230, 1071 cm^{-1}. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{11}N_3O_3$):*** 234.0674 $[M+H]^+$, Calculated: 234.0873.

2-(2-Nitrophenyl)-4,5-dimethyl Imidazole 3-oxide [4ab]:



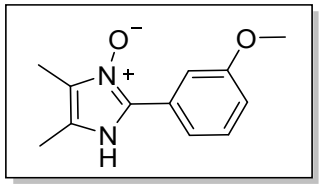
M.P.: 125-127 °C, ***^{1}HNMR (300 MHz, DMSO):*** δ 11.750 (s, 1H); δ 7.950 (d, 1H); δ 7.756 (dd, 1H), δ 7.680 (d, 1H), δ 7.623 (dd, 1H), δ 2.05 (s, 3H); δ 2.01 (s, 3H); ***^{13}CNMR (100 MHz, DMSO):*** 148.49, 133.30, 131.71, 129.92, 124.69, 123.17, 13.01, 7.74. ***IR (KBr, cm^{-1}):*** 3390 (N-H), 3050 (Ar C-H), 2921 (Al C-H), 1611 (C=C), 1508 (C=N), 1366, 1205, 1096. ***HRMS* (ESI/Q-TOF) *m/z found for ($C_{11}H_{12}N_2O$):*** 234.0822 $[M+H]^+$, Calculated: 234.0873.

2-(4-Methoxy phenyl)-4,5-dimethyl Imidazole 3-oxide [4ac][2]:



M.P.: 138-140 °C, ***^{1}HNMR (300 MHz, DMSO):*** δ 8.35 (d, 2H); δ 6.96 (d, 2H); δ 3.77 (s, 1H); δ 2.05 (s, 4H); δ 1.79 (s, 2H): ***^{13}CNMR (75 MHz, DMSO):*** 172.91, 158.64, 135.60, 127.14, 124.40, 122.75, 121.49, 113.55, 11.80, 7.32. ***IR (KBr, cm^{-1}):*** 3409 (N-H), 3152 (Ar C-H), 2921 (Al C-H), 1614 (C=C), 1507 (C=N), 1384, 1262, 1031. ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_2$):*** 219.0931 $[M+H]^+$, Calculated: 219.1129.

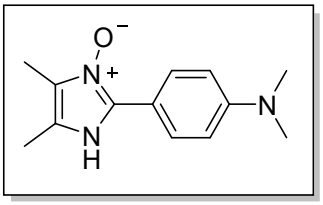
2-(3-Methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4ad]:



M.P.: 118-120 °C, ***^{1}HNMR (300 MHz, DMSO):*** δ 10.05 (s, 1H); δ 7.65-7.60 (m, 2H); δ 7.287 (dd, 1H); δ 6.885 (d, 1H); δ 3.76 (s, 3H); δ 2.05 (s, 3H); δ 2.00 (s, 3H); ***^{13}CNMR (75 MHz, DMSO):*** 159.02; 134.19; 129.41; 128.90; 124.31; 123.96; 117.83;

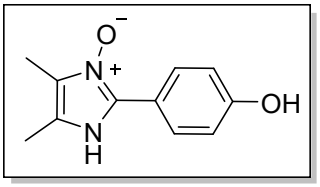
113.61; 110.69; 54.97; 11.03; 7.19. ***IR (KBr, cm^{-1}):*** 3418 (N-H), 3076 (Ar C-H), 1603 (C=C), 1559 (C=N), 1404, 1238, 1108, 1034. ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_2$):*** 219.0932 $[M+H]^+$, Calculated: 219.1129.

2-(4-*N,N*-dimethylphenyl)-4,5-dimethyl Imidazole 3-oxide [4ae][2]:



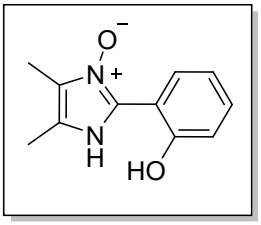
M.P.: 233-235 ^oC, ***^{1}HNMR (400 MHz, DMSO):*** δ 7.98 (d, 2H); δ 7.24 (d, 2H); δ 2.94 (s, 6H); δ 2.08(s, 3H); δ 2.05 (s, 3H); ***^{13}CNMR (75 MHz, DMSO):*** 150.54; 135.29; 127.73; 124.27; 119.69; 112.32; 111.38; 40.03; 9.56; 7.13. ***IR (KBr, cm^{-1}):*** 3390(N-H), 3050 (Ar C-H), 2921 (Al C-H), 1611 (C=C), 1508 (C=N), 1366, 1205, 1096 cm^{-1}; ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_2$):*** 232.1209 $[M+H]^+$, Calculated: 232.1444.

2-(4-Hydroxy phenyl)-4,5-dimethyl Imidazole 3-oxide [4af][2]:



M.P.: >260 ^oC, ***^{1}HNMR (300 MHz, DMSO):*** δ 7.89 (d, 2H); δ 6.77 (d, 2H); δ 2.03 (s, 3H); δ 1.98 (s, 3H): ***^{13}CNMR (75 MHz, DMSO):*** 157.18; 135.49; 127.21; 123.50; 122.66; 119.36; 114.92; 11.52; 7.28. **IR (KBr):** 3409 (N-H), 3059 (Ar C-H), 2923 (Al C-H), 1654, 1614 (C=C), 1512 (C=N), 1380, 1286, 1095 cm^{-1}. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{12}N_2O_2$):*** 205.0810 $[M+H]^+$, Calculated: 205.0972.

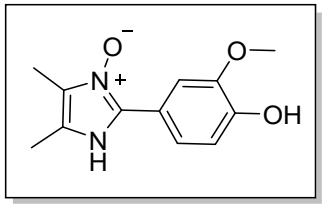
2-(2-Hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4ag]:



M.P.: 233-235 ^oC, ***^{1}HNMR (300 MHz, DMSO):*** δ 7.52 (d, 1H); δ 7.26 (t, 1H); δ 6.88 (d, 2H); δ 2.15 (s, 3H); δ 2.06 (s, 3H); δ 1.77 (s, 1H); ***^{13}CNMR (75 MHz, DMSO):*** 157.39; 134.28; 130.67; 127.37; 123.24; 123.10; 119.02; 118.21; 114.19; 10.16; 7.03. ***IR (KBr,***

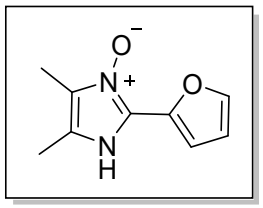
cm^{-1}): 3400(N-H), 3047 (Ar C-H), 2904 (Al C-H), 1649, 1602 (C=C), 1496(C=N), 1305, 1269, 1154, 1087. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{12}N_2O_2$):*** 205.0908 $[M+H]^+$, Calculated: 205.0972.

2-(4-Hydroxy-3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4ah]:



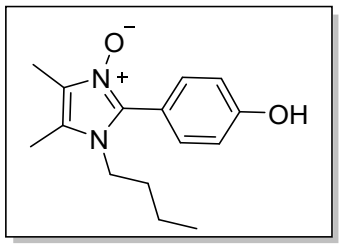
M.P.: 258-259 ^oC, ***^{1}HNMR (400 MHz, DMSO):*** δ 7.73 (s, 1H); δ 7.57 (d, 1H); δ 6.77 (d, 1H); δ 3.73 (s, 3H); δ 2.04 (s, 3H); 1.99 (s, 3H); ***^{13}CNMR (100 MHz, DMSO):*** 147.72; 147.30; 136.07; 123.90; 123.36; 120.19; 119.32; 115.63; 110.47; 55.83; 22.98; 11.97; 7.88. ***IR (KBr, cm^{-1}):*** 3418 (N-H), 3057 (Ar C-H), 2923 (Al C-H), 1648 (C=C), 1507 (C=N), 1438, 1279, 1038. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{12}N_2O_2$):*** 235.0868 $[M+H]^+$, Calculated: 235.1077.

2-(2-Furyl)-4,5-dimethyl Imidazole 3-oxide [4ai]:



M.P.: 95-97 ^oC, ***^{1}HNMR (400 MHz, DMSO):*** δ 7.690 (dd, 1H); δ 6.845 (d, 1H); δ 6.552 (dd, 1H); δ 2.03 (s, 3H); δ 2.00 (s, 3H); ***^{13}CNMR (100 MHz, DMSO):*** 142.85, 142.42, 130.07, 125.60, 122.91, 111.53, 108.02, 11.83, 7.10. ***IR (KBr, cm^{-1}):*** 3466 (N-H), 3085 (Ar C-H), 1559 (C=C), 1528 (C=N), 1400, 1280, 1005. ***HRMS (ESI/Q-TOF) m/z found for ($C_9H_{10}N_2O_2$):*** 179.0783 $[M+H]^+$, Calculated: 179.0815.

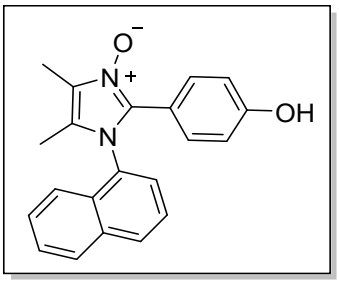
1-Butyl-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4aj][2]:



M.P.: 128-130 ^oC, ***^{1}HNMR (400 MHz, DMSO):*** δ 2.51 (s, 3H); δ 2.22 (s, 3H); δ 1.31-1.39 (m, 2H); δ 1.09 (t, 2H); δ 1.05-1.20 (m, 2H); δ 0.73 (t, 3H); ***^{13}CNMR***

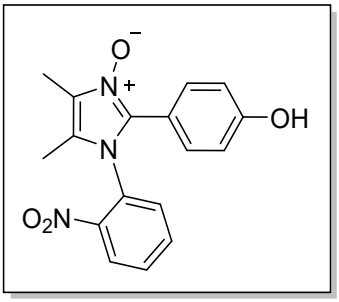
(75 MHz, DMSO): 131.20; 124.16; 119.84; 115.35; 31.59; 18.91; 13.20; 8.53; 7.39. ***IR (KBr, cm^{-1}):*** 3047 (Ar C-H), 2958 (Al C-H), 1602(C=C), 1544(C=N), 1454, 1340, 1282, 1168, 839. ***m/z found for ($C_{15}H_{20}N_2O_2$):*** 260.15 $[M+H]^+$.

1-Napthyl-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4ak][2]:



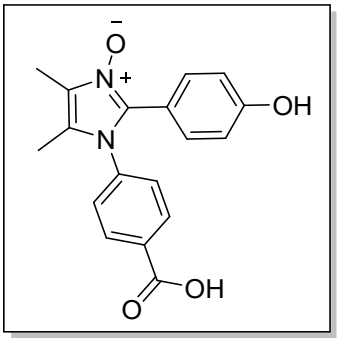
M.P.: 232-235 °C, ***^{1}HNMR (300 MHz, DMSO):*** δ 6.62 - δ 7.95 (m, 11H); δ 2.00 (t, 6H); ***^{13}CNMR (75 MHz, DMSO):*** 158.50, 138.24, 136.16, 134.25, 131.35, 128.90, 126.50, 126.34, 124.39, 120.25, 116.25, 109.36, 10.87, 5.62. ***IR (KBr, cm^{-1}):*** 3058(Ar C-H), 2925 (Al C-H),7 (C=C), 1560 (C=N), 1510, 1454, 1388, 1245, 1170, 839. ***m/z found for $C_{21}H_{18}N_2O_2$):*** 330.14 $[M+H]^+$.

1-(2-Nitrophenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4al][2]:



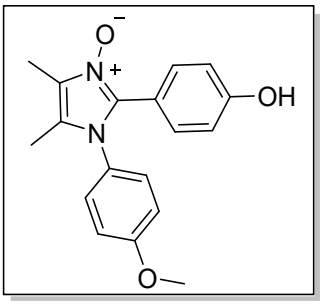
M.P.: 272-273 °C, ***^{1}HNMR (300 MHz, $CDCl_3$):*** δ 8.12 (d, 1H); δ 7.88 (d, 1H); δ 7.59 (d, 2H); δ 7.49 (d, 2H); δ 7.26 (d, 2H); δ 7.02 (d, 2H); δ 4.83 (s, 1H); δ 2.00 (t, 6H); ***^{13}CNMR (75 MHz, $CDCl_3$):*** 159.79, 148.08, 1144.33, 134.40, 132.18, 131.09, 130.01, 129.92, 129.34, 129.19, 128.53, 128.38, 128.30, 127.36, 127.05, 123.49, 122.89, 114.76, 55.51, 10.87, 5.62. ***IR (KBr, cm^{-1}):*** 3200(Ar C-H), 2929 (Al C-H), 1593 (C=C), 1510 (C=N), 1438, 1350, 1259, 1172, 1105, 837. ***m/z found for ($C_{17}H_{15}N_3O_4$):*** 325.32 $[M+H]^+$.

1-(4-Carboxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl-1*H*-imidazole 3-oxide [4am]:



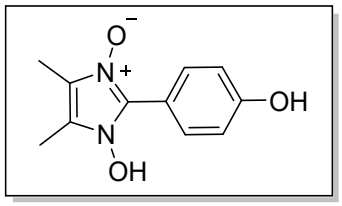
M.P.: 210-213 °C, ***[1]HNMR (400 MHz, DMSO):*** 7.61 (d, 1H); 7.38 (d, 1H); 6.92-7.01 (m, 4H), 6.79 (d, 1H); 6.77 (d, 1H); 2.25 (s, 6H); ***[13]CNMR (100 MHz, DMSO):*** 160.92, 148.33, 135.37, 134.63, 131.92, 128.35, 124.36, 122.13, 120.06, 116.92, 116.09, 116.02, 110.70, 101.22, 7.68. ***IR (KBr, cm^{-1}):*** 3219, 2808, 1685, 1605, 1440, 1377, 1280, 1172, 1010, 837. ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_2$):*** 325.0860 $[M+H]^+$, Calculated: 325.1183.

1-(4-Methoxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4an][2]:



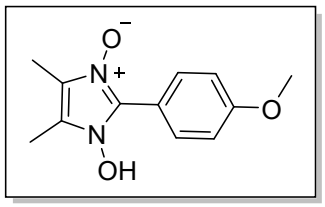
M.P.: 205-207 °C, ***[1]HNMR (400 MHz, DMSO):*** δ 10.13 (s, 1H); δ 8.46 (s, 1H); δ 7.75 (d, 2H); δ 7.22 (d, 2H); δ 6.95 (d, 2H); δ 6.88 (d, 2H); δ 3.76 (s, 3H); ***[13]CNMR (100 MHz, DMSO):*** 160.82; 158.42; 157.88; 145.20; 130.80; 128.19; 122.56; 116.08, 114.81, 55.72. ***IR (KBr, cm^{-1}):*** 3170 (Ar C-H), 2929 (Al C-H), 1608(C=C), 1512(C=N), 1461, 1251, 1172, 1031, 833. ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_2$):*** 311.1120 $[M+H]^+$, Calculated: 311.1391.

1-Hydroxy-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4ao][2]:



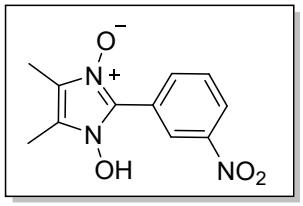
M.P.: 165-168 °C, ***[1]HNMR (300 MHz, DMSO):*** δ 7.86 (d, 2H); δ 7.04 (d, 2H); δ 2.27 (s, 6H); δ 2.19 (s, 1H); ***[13]CNMR (75 MHz, DMSO):*** 160.83; 135.26; 131.83; 122.09; 116.06; 110.68; 7.64. ***IR (KBr, cm^{-1}):*** 3400, 3000 (Ar C-H), 2671 (Al C-H), 1611, 1560 (C=C), 1446 (C=N), 1385, 1252, 1178, 1087, 1000, 837 cm^{-1}. ***m/z found for ($C_{11}H_{12}N_2O_3$):*** 220.0 $[M+H]^+$.

1-Hydroxy-2-(4-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4ap][2]:



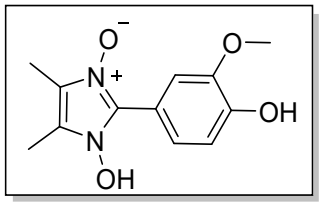
M.P.: 196-198 °C, ***[1]HNMR (300 MHz, DMSO):*** δ 8.12 (d, 2H); δ 6.93 (d, 2H); δ 3.78 (s, 3H), δ 1.83 (s, 6H): ***[13]CNMR (75 MHz, DMSO):*** 159.10; 129.10; 119.11; 113.21; 55.49; 7.41. ***IR (KBr, cm^{-1}):*** 3418, 3003 (Ar C-H), 2929 (Al C-H), 1610, 1541 (C=C), 1444 (C=N), 1380, 1296, 1256, 1182, 1026, 837 cm^{-1}. ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_3$):*** 235.0985 $[M+H]^+$, Calculated: 235.1078.

1-Hydroxy-2-(3-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide [4aq][2]:



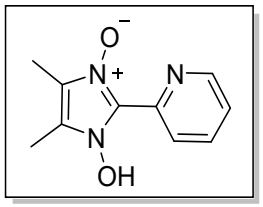
M.P.: 209-211 °C, ***[1]HNMR (300 MHz, DMSO):*** δ 9.22 (s, 1H); δ 8.72 (d, 1H); δ 8.05 (d, 1H); δ 7.58 (t, 1H); δ 1.91; ***[13]CNMR (75 MHz, DMSO):*** 148.13, 135.79, 131.75, 131.13, 126.37, 124.38, 123.41, 122.13, 7.57. ***IR (KBr, cm^{-1}):*** 3428, 3088 (Ar C-H), 2927 (Al C-H), 2580, 1634, 1530(C=C), 1435(C=N), 1355, 1284, 1248, 812 cm^{-1}. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{11}N_3O_4$):*** 250.0640 $[M+H]^+$, Calculated: 250.0823.

1-Hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide [4ar]:



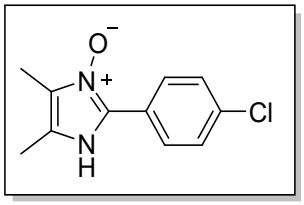
M.P.: 201-203 °C, ***[1]HNMR (400 MHz, DMSO):*** δ 7.67 (s, 1H); δ 7.44 (d, 1H); δ 7.01 (d, 2H); δ 3.80 (s, 3H); δ 2.24 (s, 6H). ***[13]CNMR (100 MHz, DMSO):*** 150.31, 147.95, 135.40, 128.84, 122.18, 115.97, 114.27, 110.27, 55.61, 7.66. ***IR (KBr, cm^{-1}):*** 3390, 3076 (Ar C-H), 2928 (Al C-H), 1636, 1596 (C=C), 1493 (C=N), 1388, 1279, 1205, 1177, 1031, 856 cm^{-1}. ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_2$):*** 251.0796 $[M+H]^+$, Calculated: 251.1027.

1-Hydroxy-2-(2-pyridyl)-4, 5-dimethyl Imidazole 3-oxide [4as]:



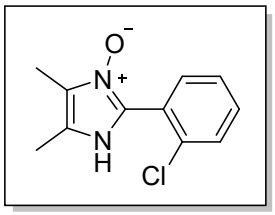
Hygroscopic, ***[1]HNMR (400 MHz, DMSO):*** δ 11.38 (s, 1H); δ 8.80 (d, 1H); δ 8.39 (t, 1H); δ 8.13 (t, 1H); δ 7.83 (d, 1H); δ 1.88; ***[13]CNMR (100 MHz, DMSO):*** 153.46, 151.75, 150.39, 147.75, 144.42, 138.22, 126.71, 126.48, 123.43, 123.21, 112.17, 9.81, 7.69. ***IR (KBr, cm^{-1}):*** 3400, 3085 (Ar C-H), 2667 (Al C-H), 1621, 1578 (C=C), 1456 (C=N), 1404, 1287, 1194, 1158, 1088, 998, 779 cm^{-1}. ***HRMS (ESI/Q-TOF) m/z found for ($C_{12}H_{14}N_2O_2$):*** 206.0701 $[M+H]^+$, Calculated: 206.0925.

2-(4-chlorophenyl)-4,5-dimethyl-1*H*-imidazole 3-oxide (4at):



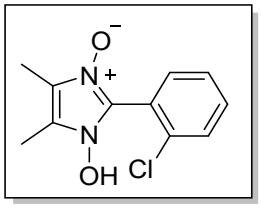
[1]HNMR (400 MHz, DMSO): δ 7.98 (d, 2H); δ 7.42 (d, 2H); δ 2.02 (s, 3H); δ 2.00 (s, 3H); ***[13]CNMR (100 MHz, DMSO):*** 134.63; 132.62; 131.56; 129.02; 128.77; 127.43; 127.21; 125.76; 124.39; 12.04; 7.71. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{11}ClN_2O$):*** 223.0543 $[M+H]^+$, Calculated: 223.0633.

2-(2-chlorophenyl)-4,5-dimethyl-1*H*-imidazole 3-oxide (4au):



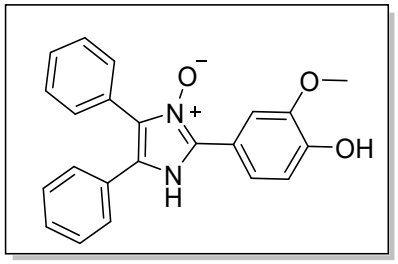
[1]HNMR (400 MHz, DMSO): δ 12.13 (s, 1H), δ 7.54 (d, 1H), δ 7.40-7.40 (m, 1H), δ 7.35 (d, 2H), δ 2.04 (s, 3H); δ 1.09 (s, 3H); ***[13]CNMR (100 MHz, DMSO):*** 134.10, 132.93, 132.23, 130.35, 129.48, 126.41, 123.75, 122.97, 10.22, 6.82. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{11}ClN_2O$):*** 223.0560 $[M+H]^+$, Calculated: 223.0633.

2-(2-chlorophenyl)-1-hydroxy-4,5-dimethyl-1*H*-imidazole 3-oxide (4av):



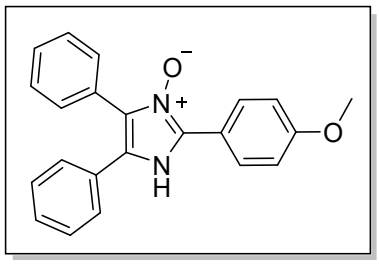
[1]HNMR (400 MHz, DMSO): δ 7.69 (s, 1H); δ 6.845 (d, 2H); δ 6.555 (d, 1H); δ 2.03 (s, 3H); δ 2.00 (s, 3H); ***[13]CNMR (100 MHz, DMSO):*** 142.13; 142.41; 130.12; 125.68; 122.85; 111.53; 107.96; 11.89; 7.12. ***HRMS (ESI/Q-TOF) m/z found for ($C_{11}H_{11}ClN_2O_2$):*** 239.0550 $[M+H]^+$, Calculated: 239.0582.

2-(4-Hydroxy-3-methoxyphenyl)-4,5-diphenyl Imidazole 3-oxide [4ba][2]:



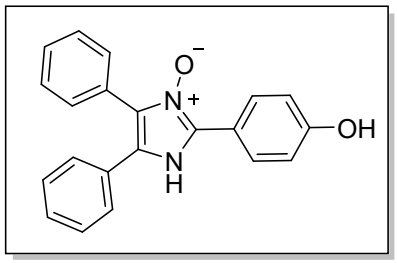
M.P.: 197-199 °C, ***[1]HNMR (400 MHz, DMSO):*** δ 7.79 (s, 1H); δ 7.61 (d, 1H), δ 7.20-7.52 (m, 8H); δ 7.13 (d, 2H); δ 6.81 (s, 1H); δ 3.77 (s, 3H); ***[13]CNMR (100 MHz, DMSO):*** 147.56, 147.08, 141.08, 136.11, 131.94, 130.71, 128.84, 127.91, 126.79, 126.26, 122.11, 120.54, 111.62, 111.61, 55.94, 22.18. ***IR (KBr, cm^{-1}):*** 3494 (N-H), 3050 (Ar C-H), 2939 (Al C-H), 1600 (C=C), 1496 (C=N), 1267, 1226, 1029. ***m/z found for ($C_{22}H_{18}N_2O_3$):*** 358.1 $[M+H]^+$.

2-(4-Methoxyphenyl)-4,5-diphenyl Imidazole 3-oxide [4bb][2]:



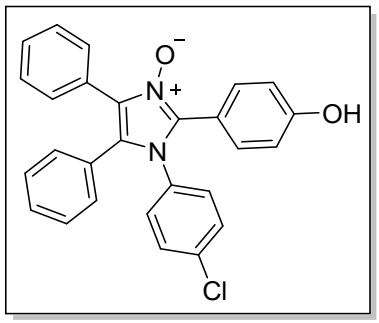
M.P.: 95-96 °C, ***[1]HNMR (300 MHz, DMSO):*** δ 9.11 (s, 1H); δ 7.20-7.53 (m, 10H); δ 7.06; δ 6.78; δ 6.32; δ 6.19; δ 5.54; 3.09 (s, 3H); ***[13]CNMR (75 MHz, DMSO):*** 158.93, 145.07, 127.95, 126.73, 126.22, 122.61, 113.61, 54.72. ***IR (KBr, cm^{-1}):*** 3419 (N-H), 3057 (Ar C-H), 2829 (Al C-H), 1608 (C=C), 1494 (C=N), 1298, 1253, 1028, 835, 696. ***m/z found for ($C_{22}H_{18}N_2O_2$):*** 342.4 $[M+H]^+$.

2-(4-Hydroxyphenyl)-4, 5-diphenyl Imidazole 3-oxide [4bc][2]:



M.P.: 230-233 °C, ***[1]HNMR (400 MHz, DMSO):*** δ 8.01 (d, 1H); δ 7.99 δ 7.32-7.51 (m, 4H); δ 7.23 (1 H); δ 7.14 (d, 1H); δ 6.81 (d, 1H); ***[13]CNMR (100 MHz, DMSO):*** 157.97, 141.23, 136.11, 131.93, 130.75, 130.71, 128.84, 128.67, 128.45, 128.14, 127.94, 127.83, 126.72, 126.23, 121.62, 115.45. ***IR (KBr, cm^{-1}):*** 3409 (N-H), 3045 (Ar C-H), 2790 (Al C-H), 1610 (C=C), 1492 (C=N), 1285, 1173, 836, 696. ***m/z found for ($C_{21}H_{16}N_2O_2$):*** 328.1 $[M+H]^+$.

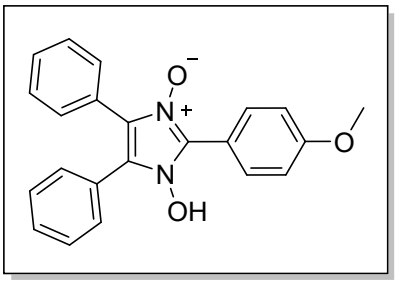
1-(4-Chlorophenyl)-2-(4-hydroxyphenyl)-4,5-diphenyl Imidazole 3-oxide [4bd][2]:



M.P.: 182-184 °C, ***[1]HNMR (400 MHz, DMSO):*** δ 10.24 (s, 1H); δ 8.45 (s, 2H); δ 7.77 (d, 4H); δ 7.42 (d, 4H); δ 7.21 (d, 4H); δ 6.89 (d, 4H); ***[13]CNMR (100 MHz, DMSO):*** 161.39; 161.25; 151.24; 132.01; 131.72; 131.31; 130.08; 129.97; 129.57;

129.51; 128.88; 128.24; 127.69; 123.18; 116.17. ***IR (KBr, cm^{-1}):*** 3057 (Ar C-H), 2885 (Al C-H), 1602, 1573 (C=C), 1485 (C=N), 1442, 1388, 1284, 1161, 1101, 1008, 902, 835. ***m/z found for ($C_{27}H_{19}N_2O_2Cl$):*** 438.7 $[M+H]^+$.

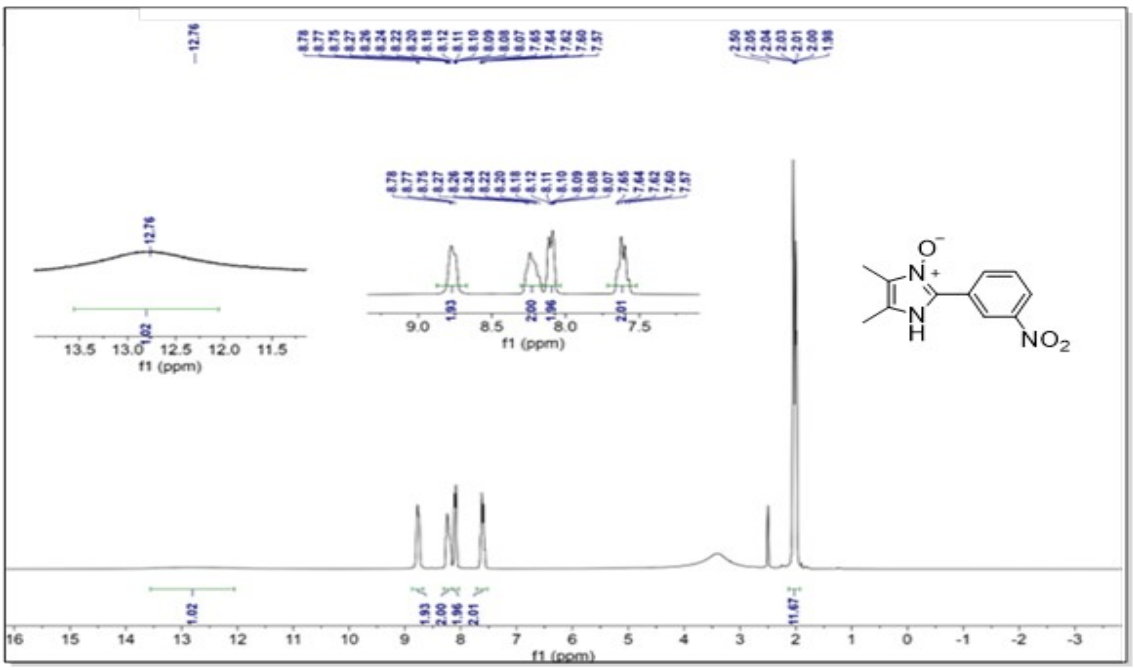
1-Hydroxy-2-(4-methoxyphenyl)-4,5-diphenyl Imidazole 3-oxide [4be][2]:



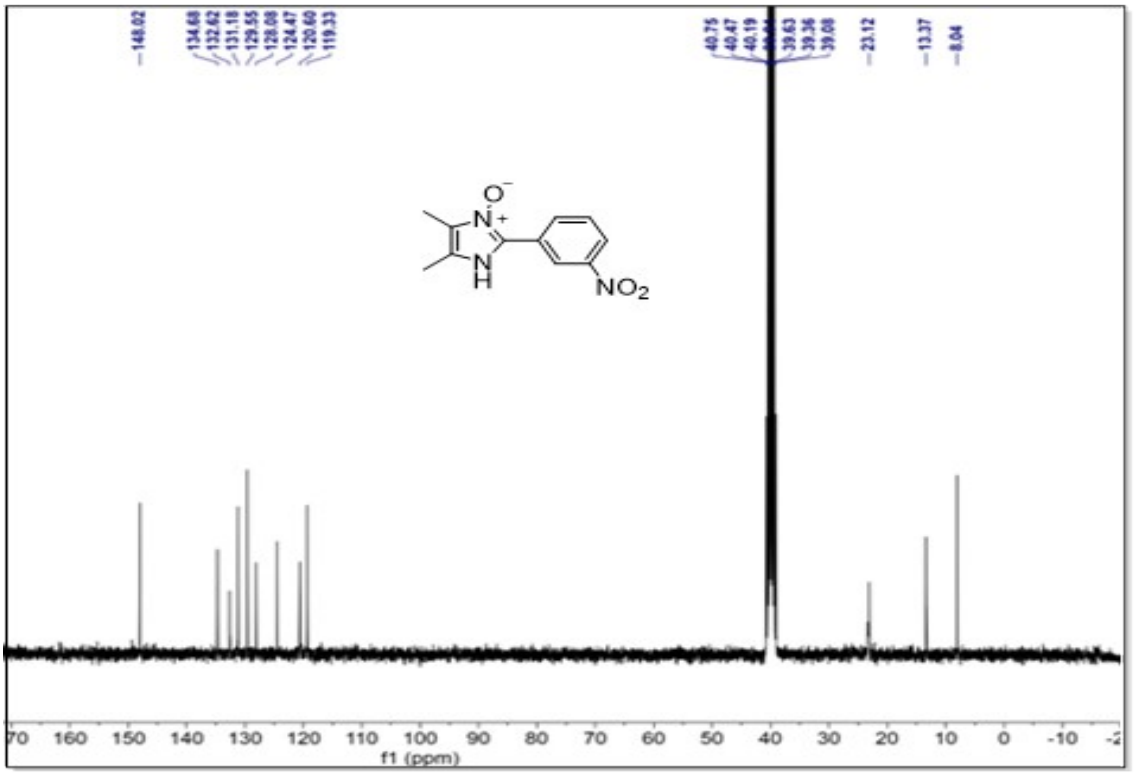
M.P. 233-235 ^oC, ***^{1}HNMR (400 MHz, DMSO):*** δ 8.77; δ 7.51 (2H); δ 7.16- δ 7.29 (m, 10H); δ 6.93 (2H); 3.53 (s, 3H); ***^{13}CNMR (100 MHz, DMSO):*** 159.13; 130.87; 129.54; 128.96; 128.56; 127.97; 127.81; 127.69; 126.55; 114.36; 55.48. ***IR (KBr, cm^{-1}):*** 3431, 3055 (Ar C-H), 2835 (Al C-H), 1608, 1575 (C=C), 1488 (C=N), 1442, 1394, 1301, 1255, 1087, 1029 cm^{-1}. ***m/z found for ($C_{22}H_{18}N_2O_3$):*** 358.3 $[M+H]^+$.

Spectral Data of ^{1}H-NMR and ^{13}C-NMR

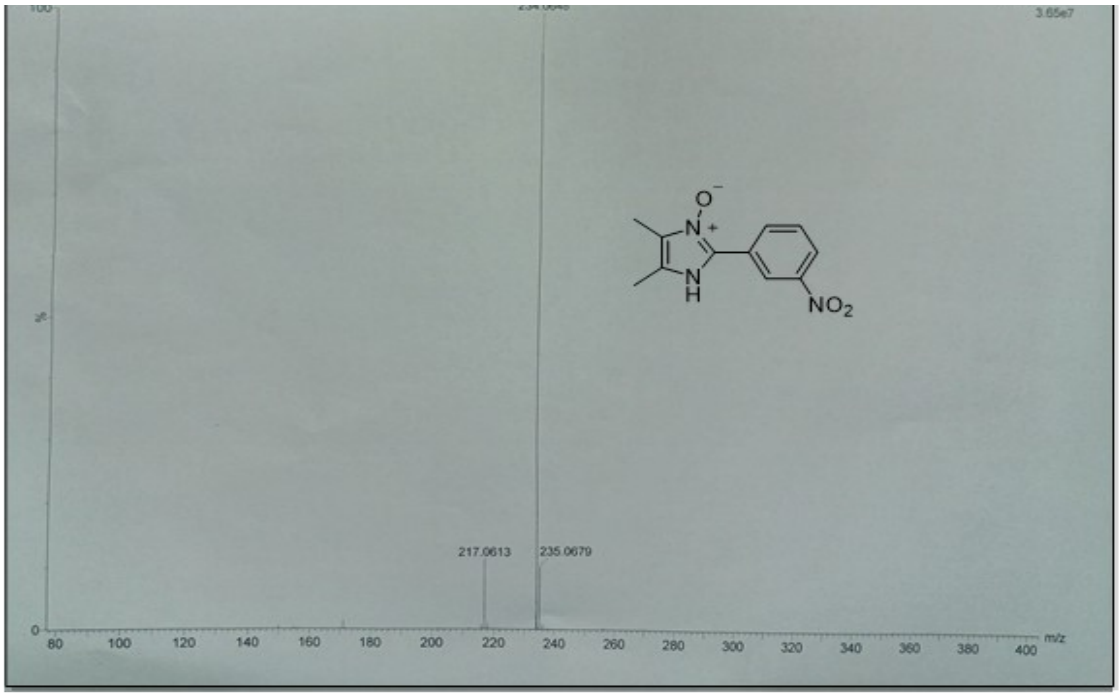
^{1}HNMR - 2-(3-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4aa)



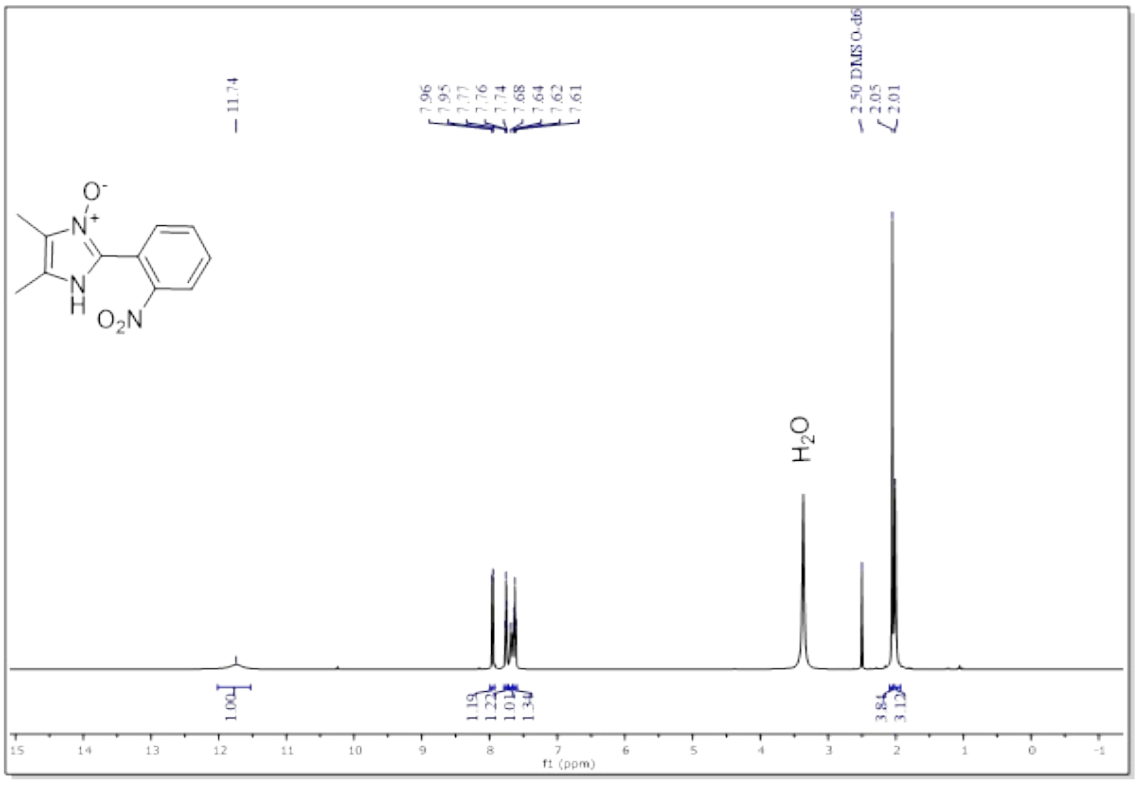
^{13}CNMR - 2-(3-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4aa)



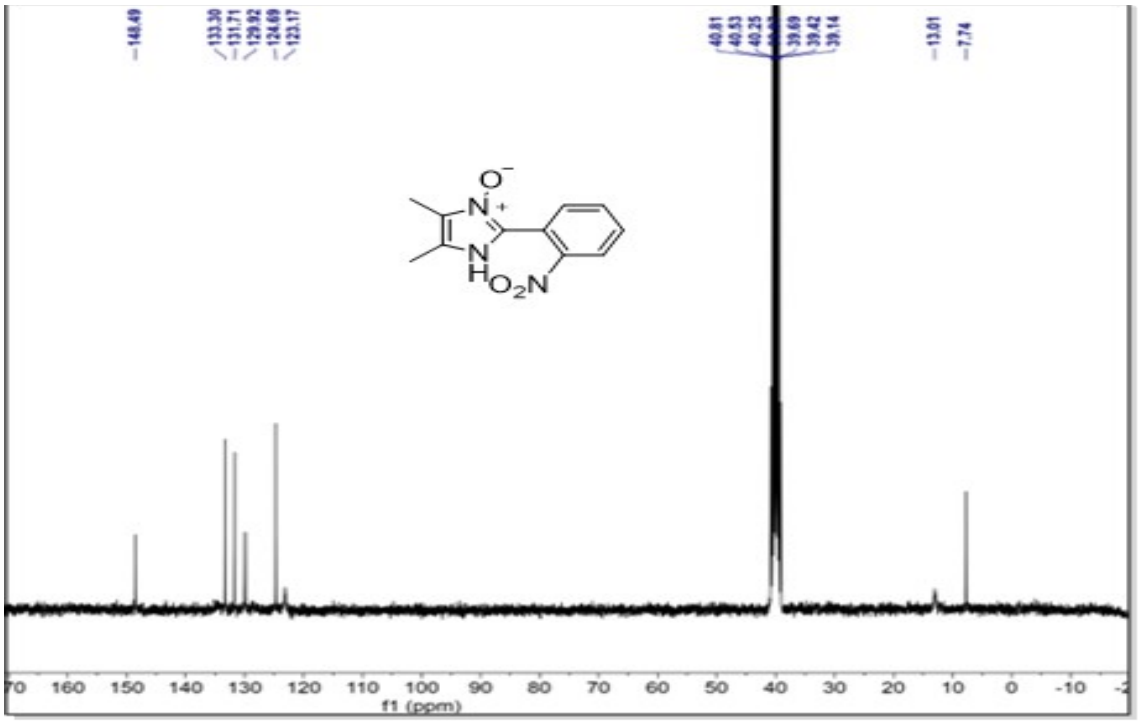
HRMS - 2-(3-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4aa)



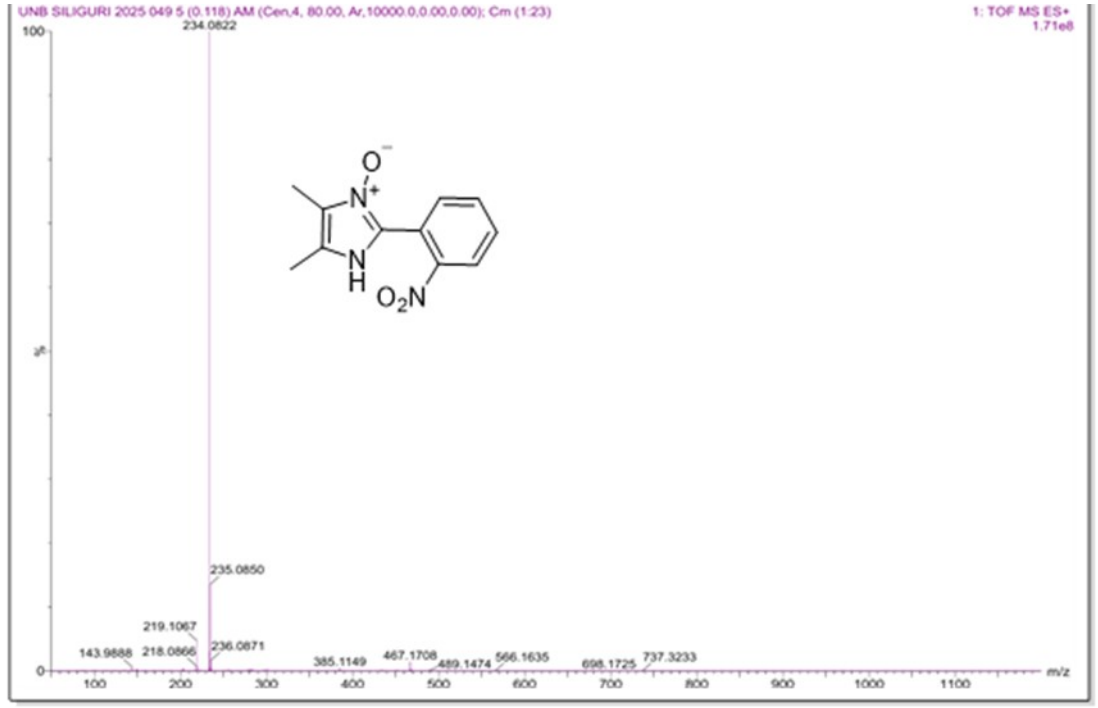
[1]HNMR - 2-(2-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4ab)



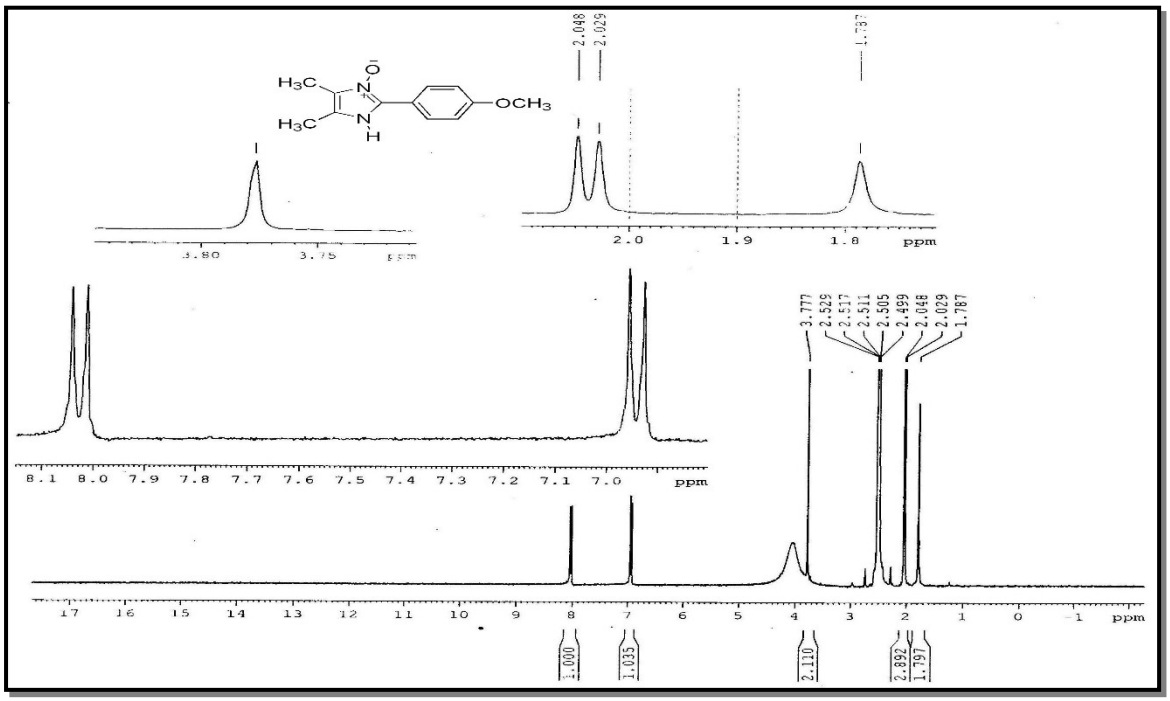
[13]CNMR - 2-(2-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4ab)



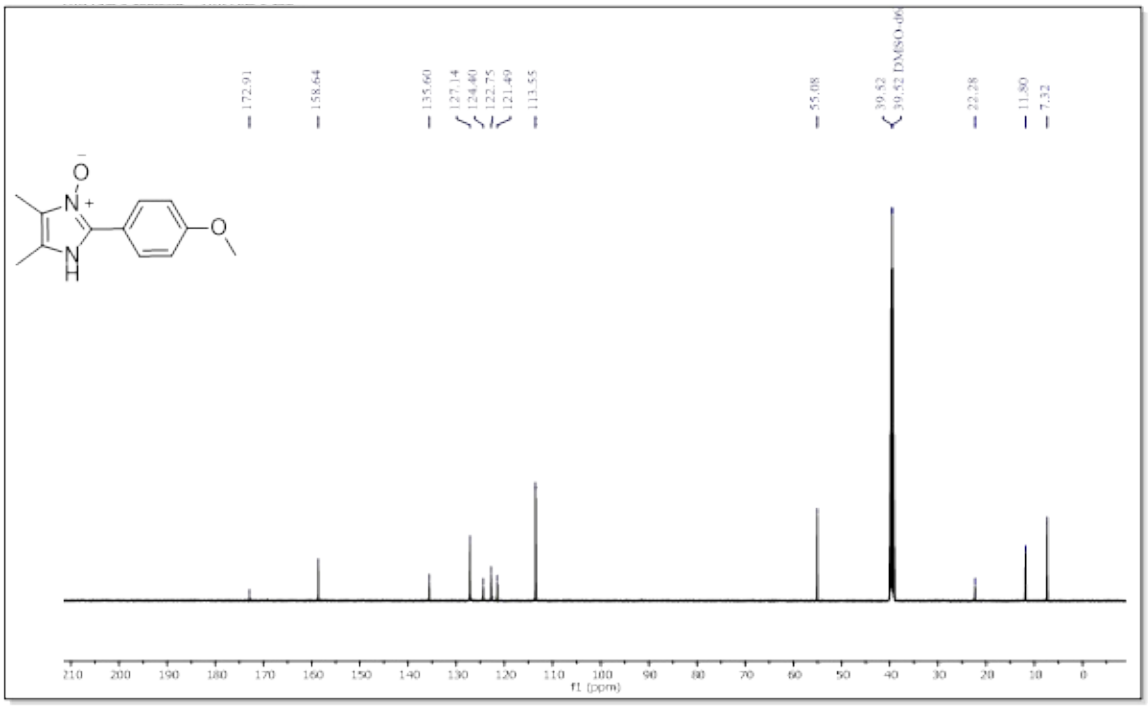
HRMS - 2-(2-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4ab)



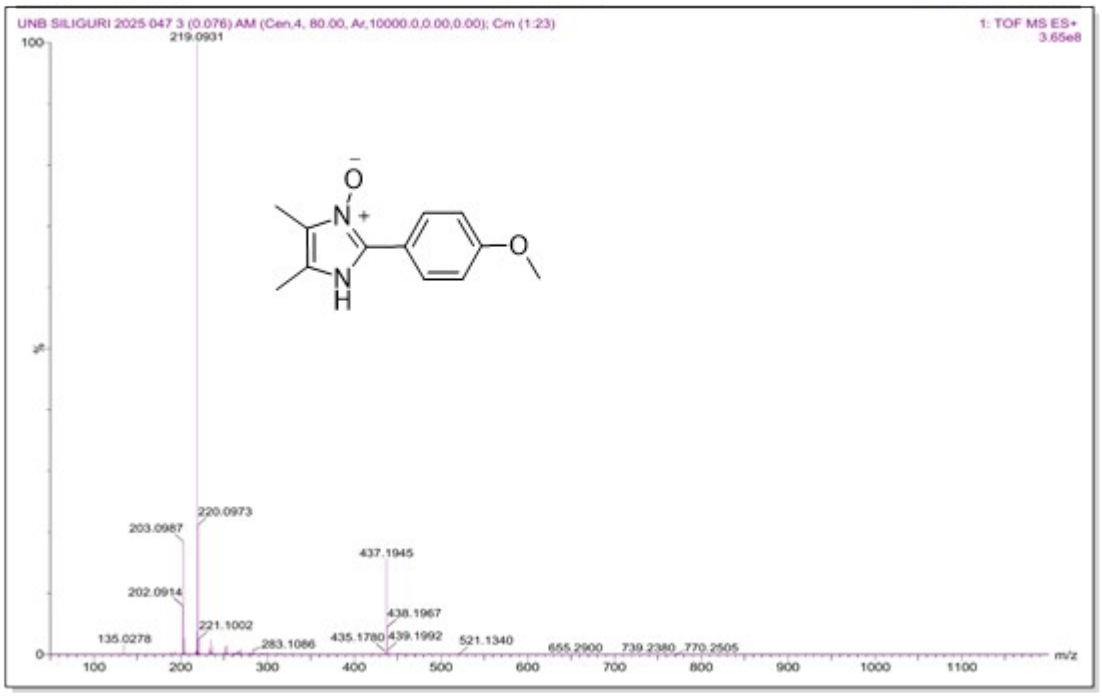
[1]HNMR - 2-(4-methoxy phenyl)-4,5-dimethyl Imidazole 3-oxide (4ac)



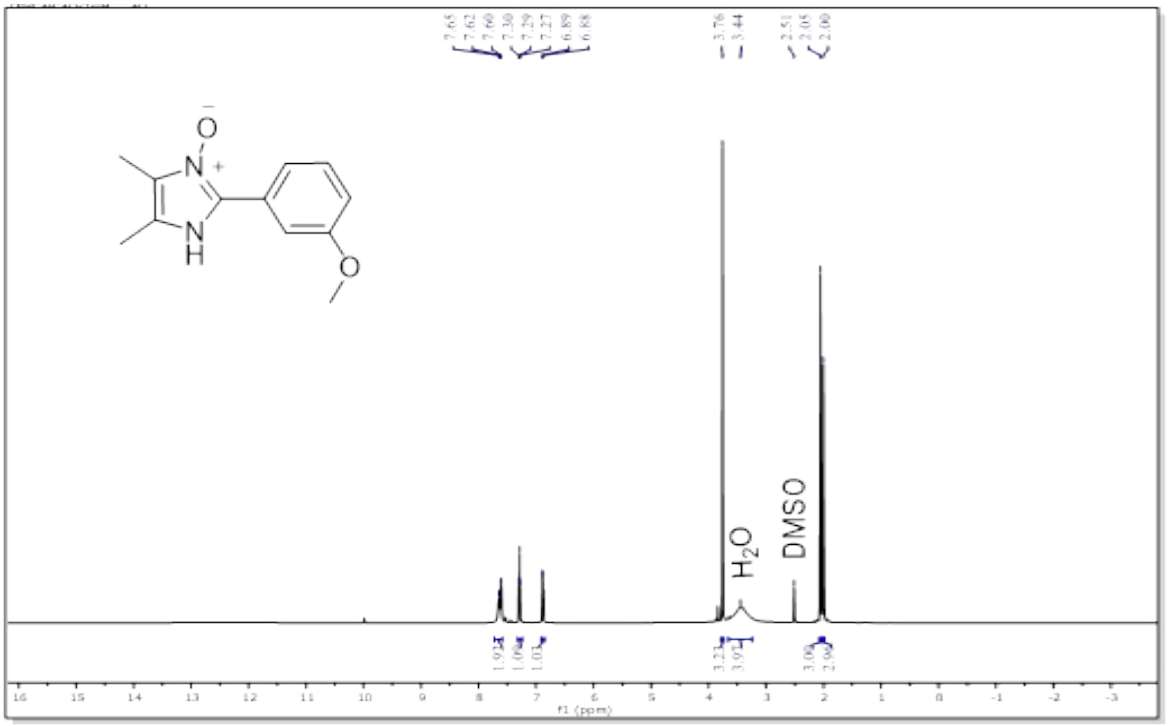
[13]CNMR - 2-(4-methoxy phenyl)-4,5-dimethyl Imidazole 3-oxide (4ac)



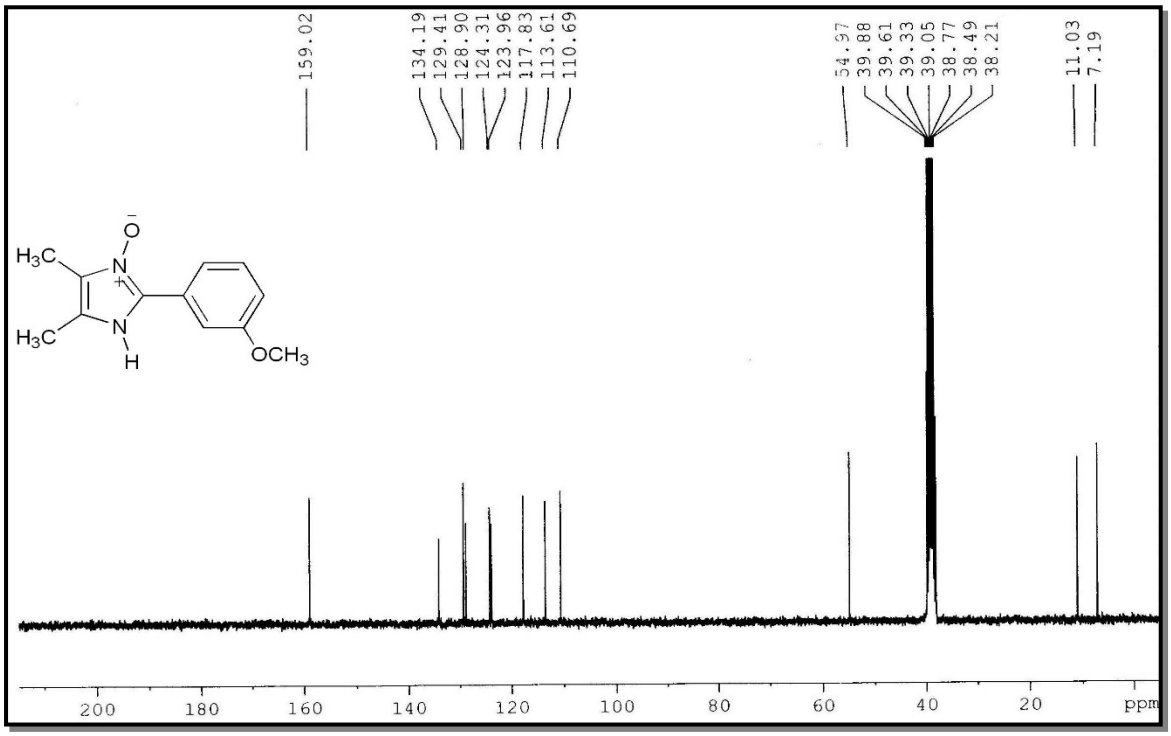
HRMS - 2-(4-methoxy phenyl)-4,5-dimethyl Imidazole 3-oxide (4ac)



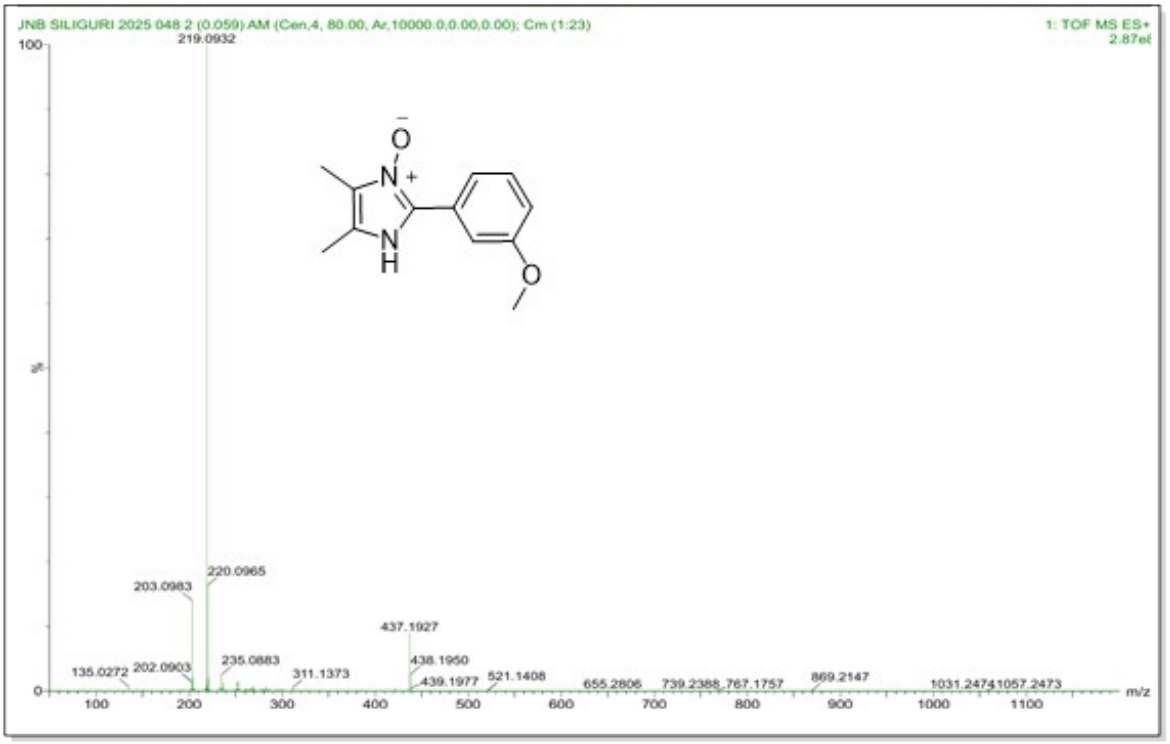
[1]HNMR - 2-(3-methoxyphenyl)-4, 5-dimethyl Imidazole 3-oxide (4ad)



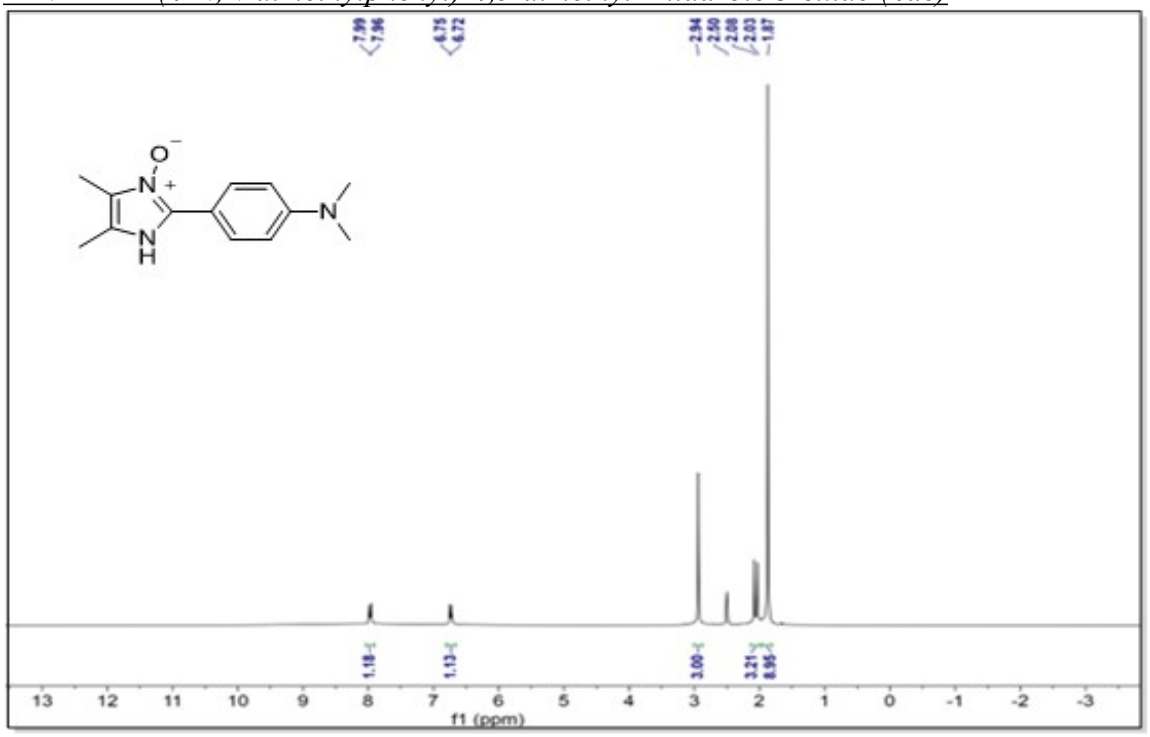
[13]CNMR - 2-(3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ad)



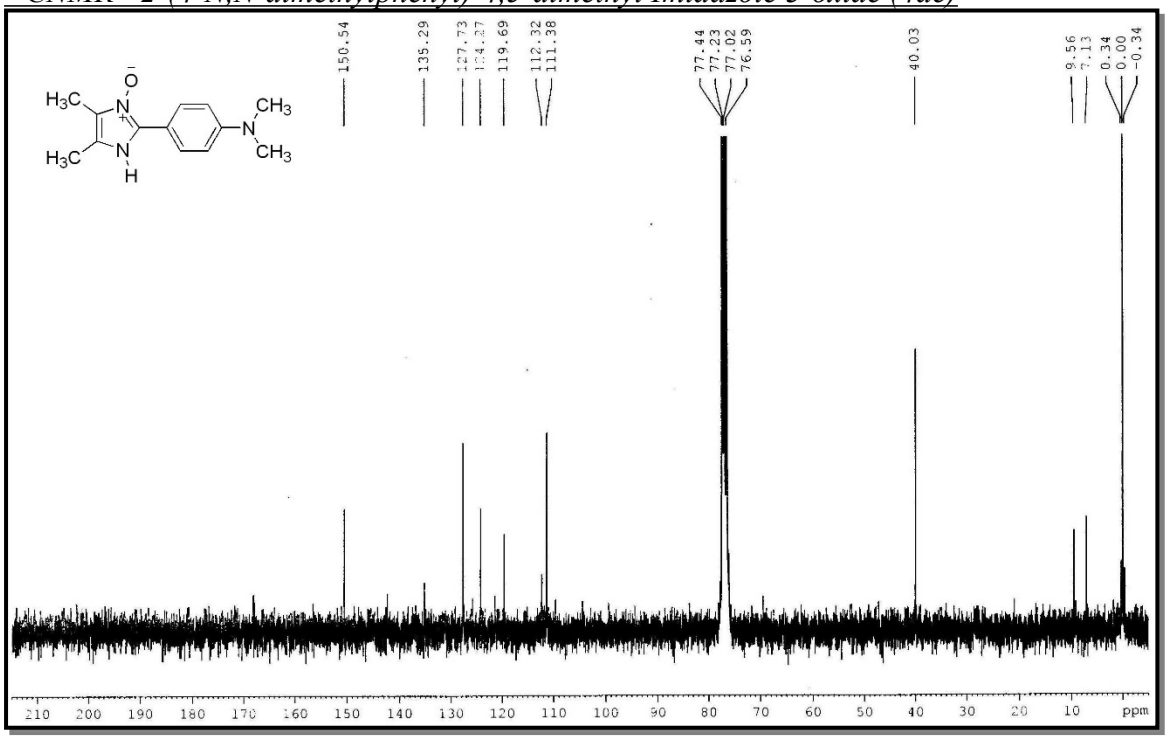
HRMS - 2-(3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ad)



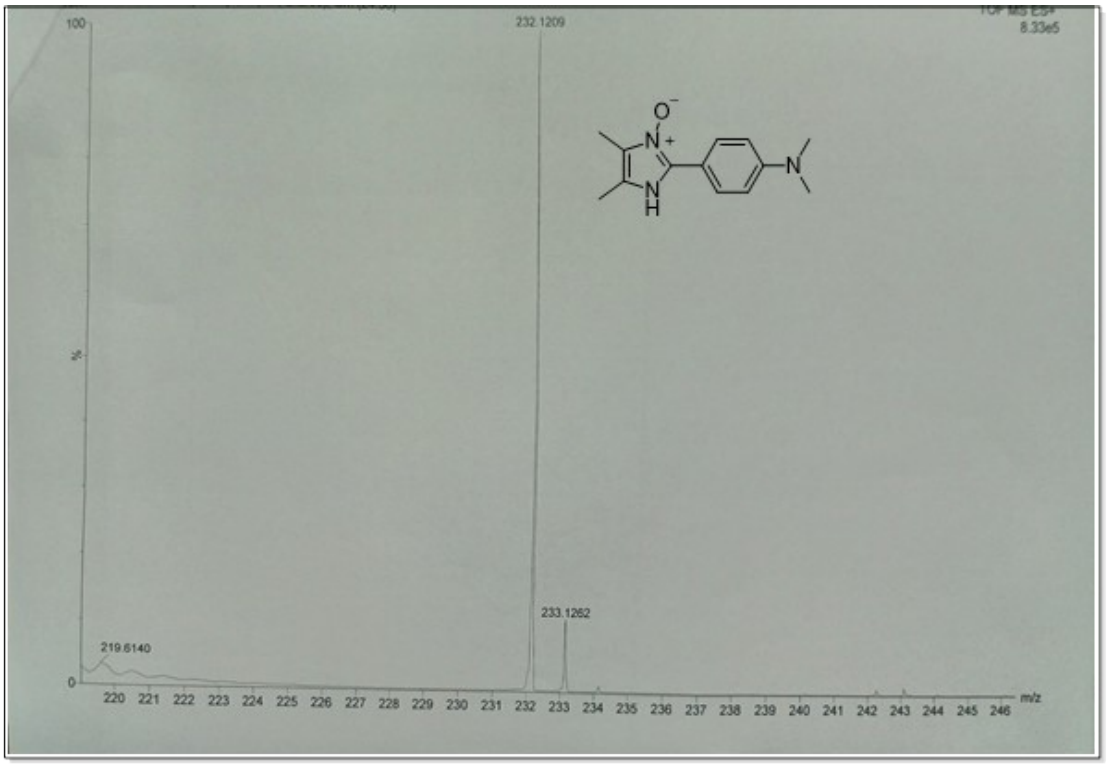
[1]HNMR - 2-(4-N,N-dimethylphenyl)-4,5-dimethyl Imidazole 3-oxide (4ae)



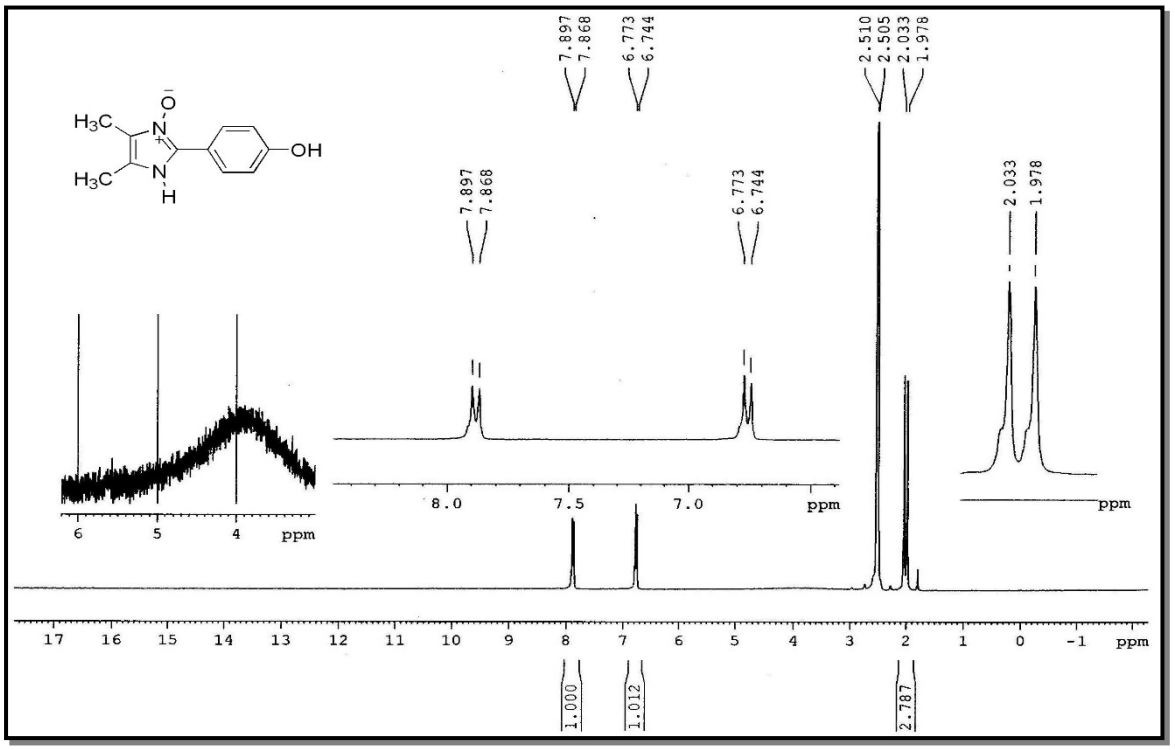
[13]CNMR - 2-(4-N,N-dimethylphenyl)-4,5-dimethyl Imidazole 3-oxide (4ae)



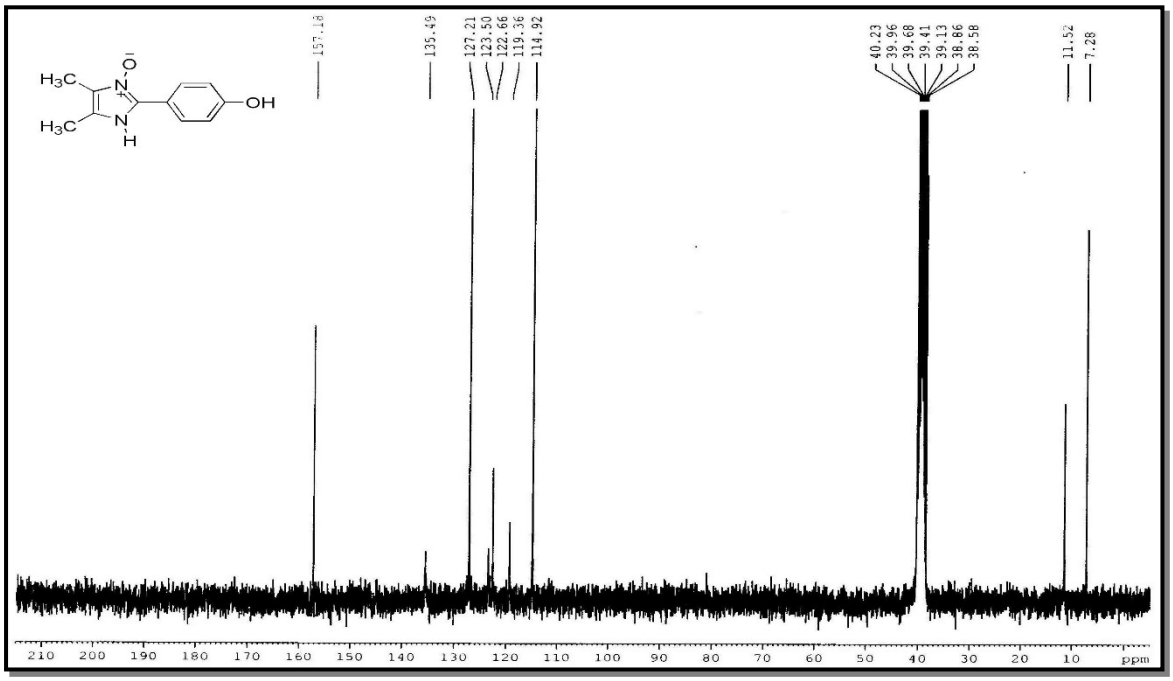
HRMS - 2-(4-N,N-dimethylphenyl)-4,5-dimethyl Imidazole 3-oxide (4ae)



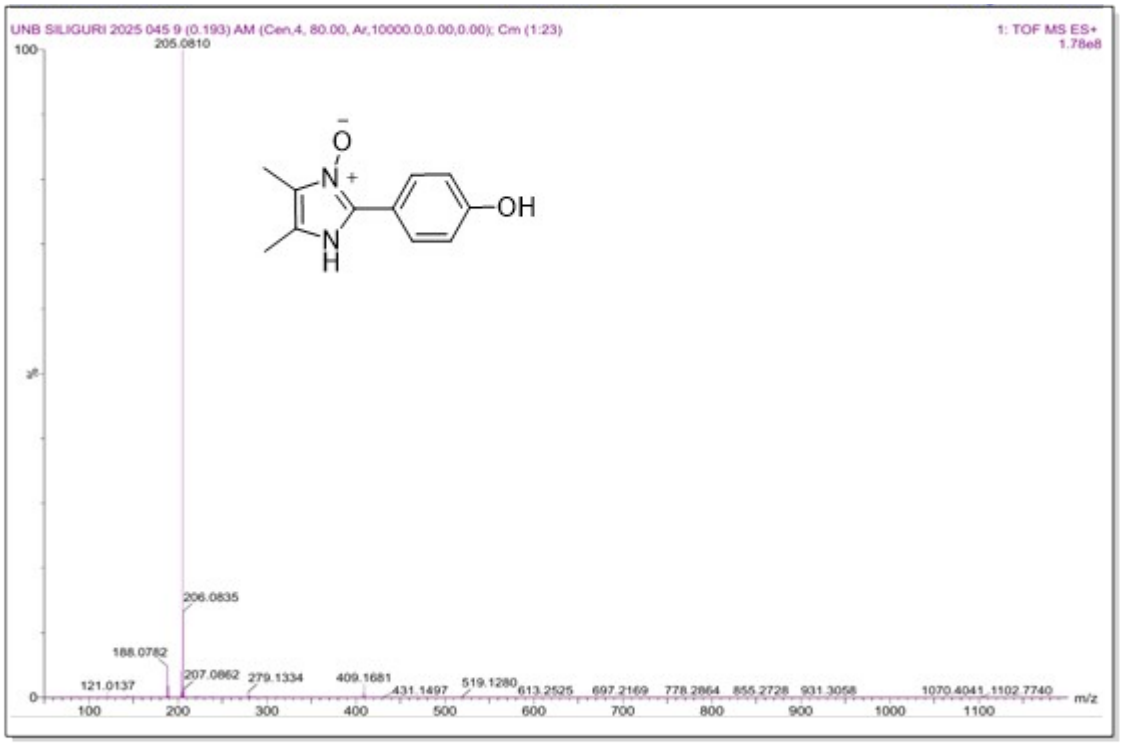
[1]HNMR - 2-(4-hydroxy phenyl)-4,5-dimethyl Imidazole 3-oxide (4af)



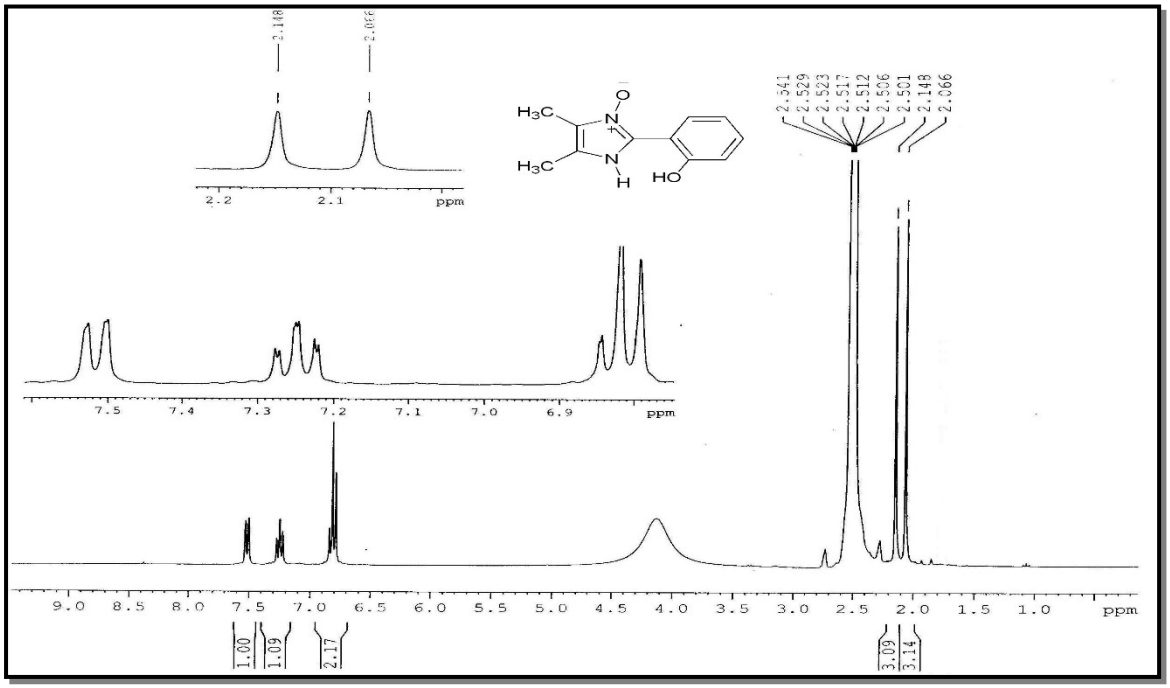
[13]CNMR - 2-(4-hydroxy phenyl)-4,5-dimethyl Imidazole 3-oxide (4af)



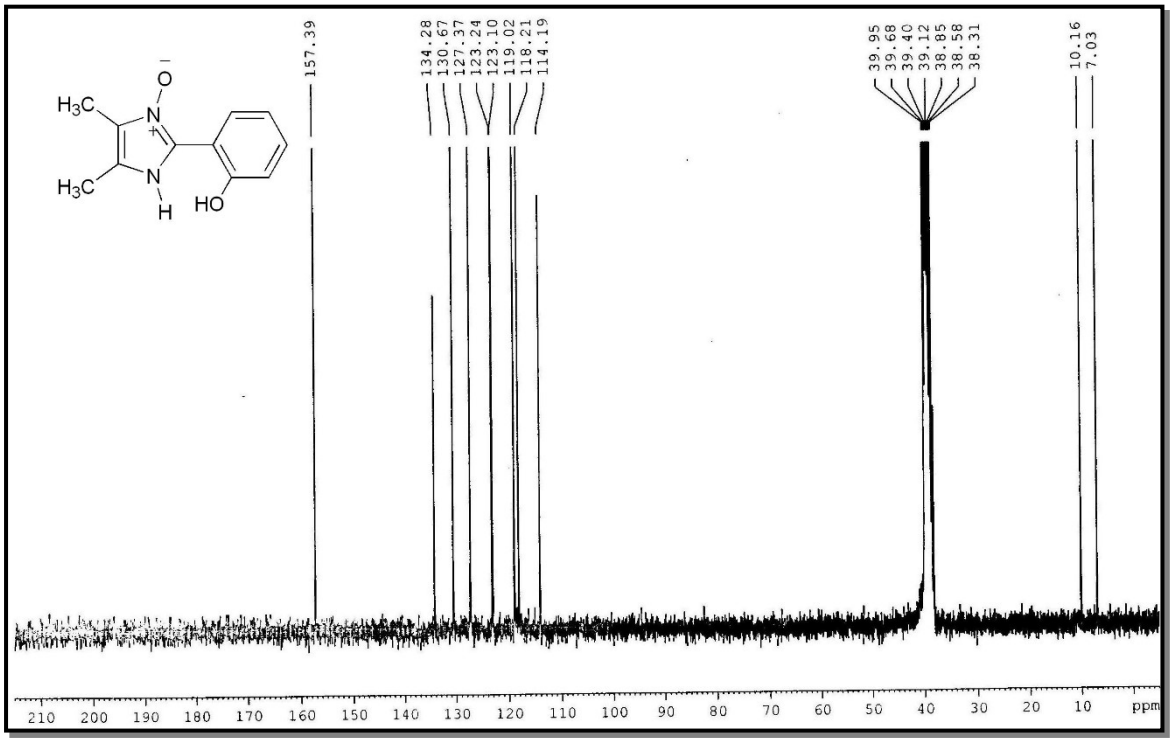
HRMS - 2-(4-hydroxy phenyl)-4,5-dimethyl Imidazole 3-oxide (4af)



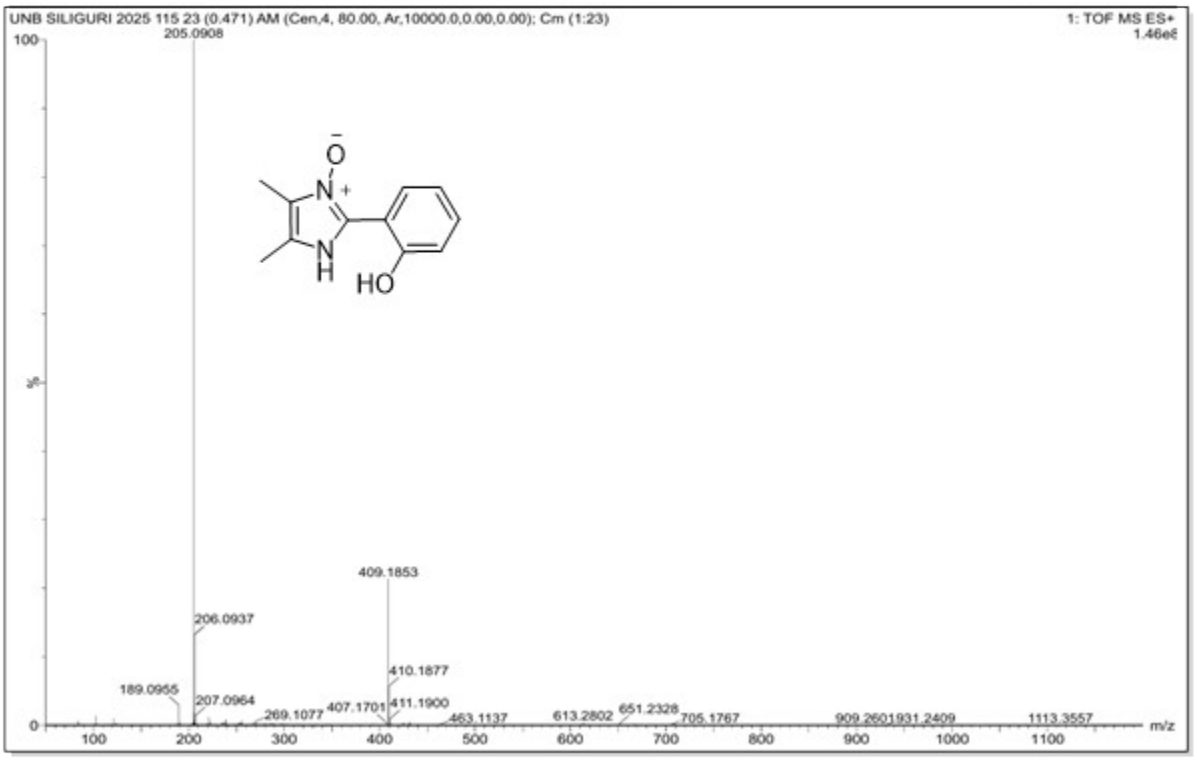
[1]HNMR - 2-(2-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ag)



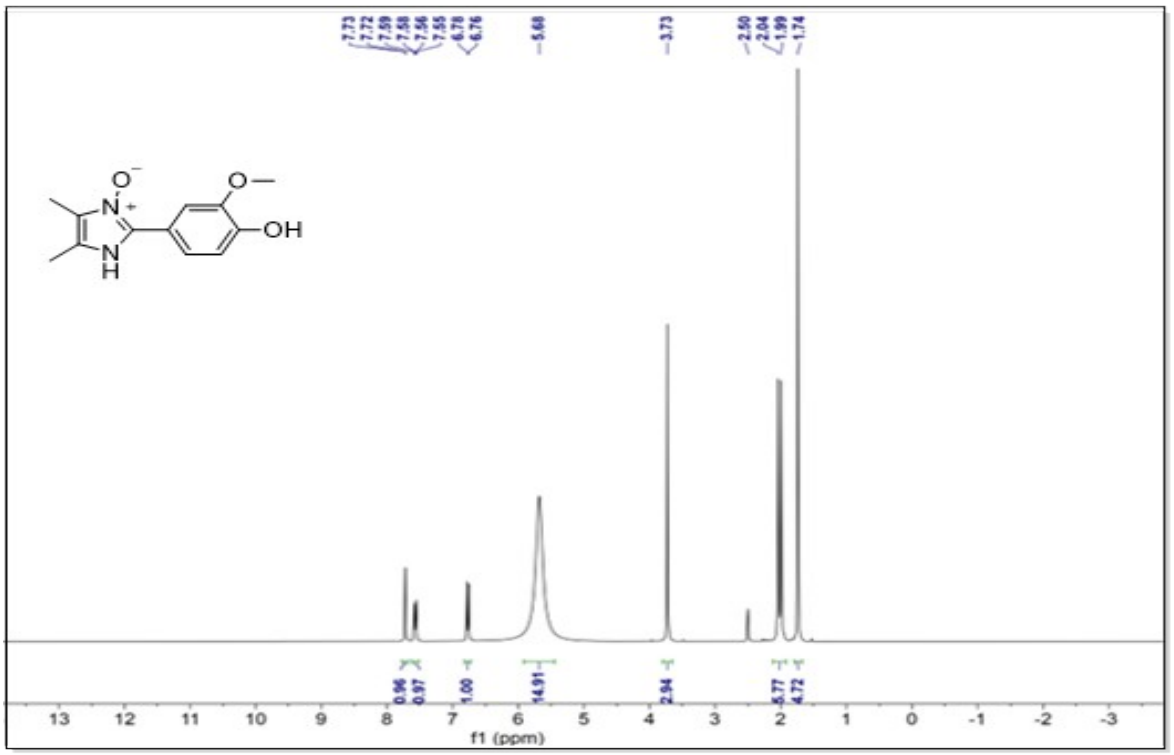
[13]CNMR - 2-(2-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ag)



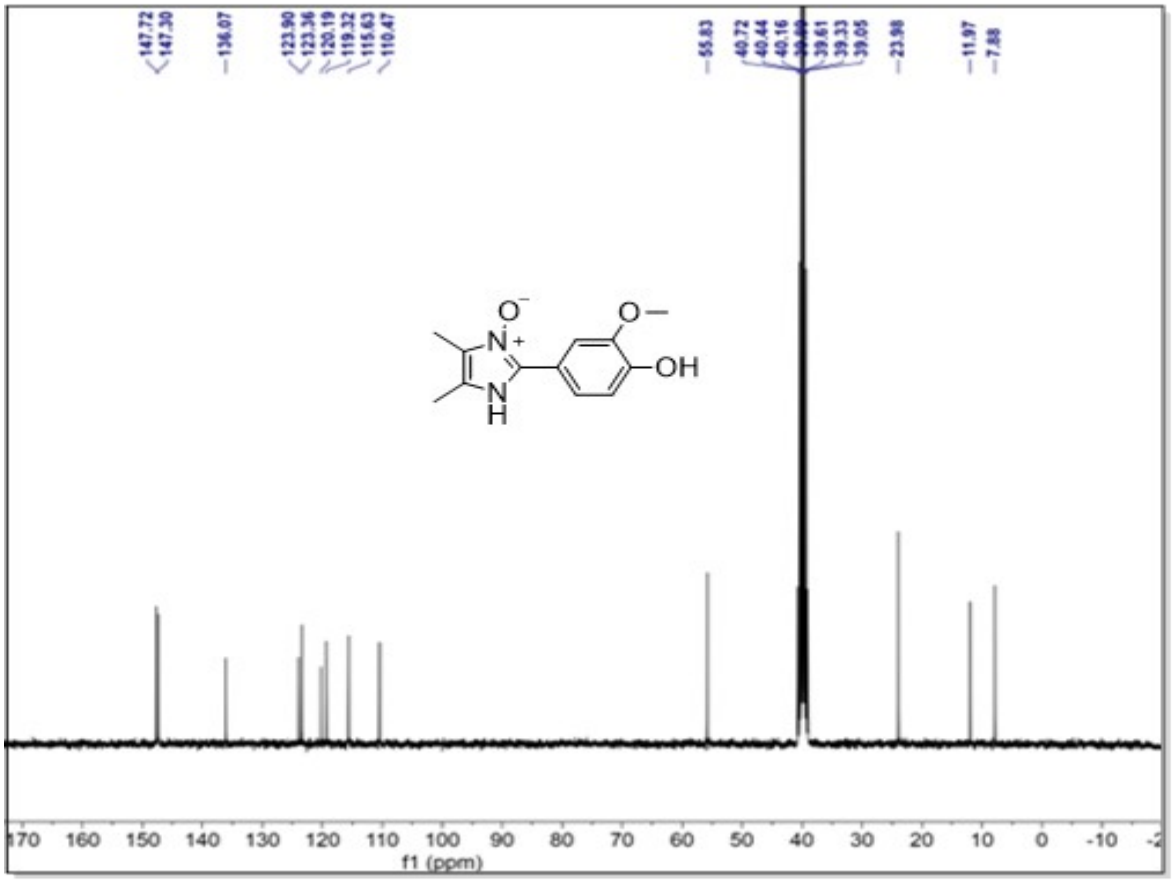
HRMS - 2-(2-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ag)



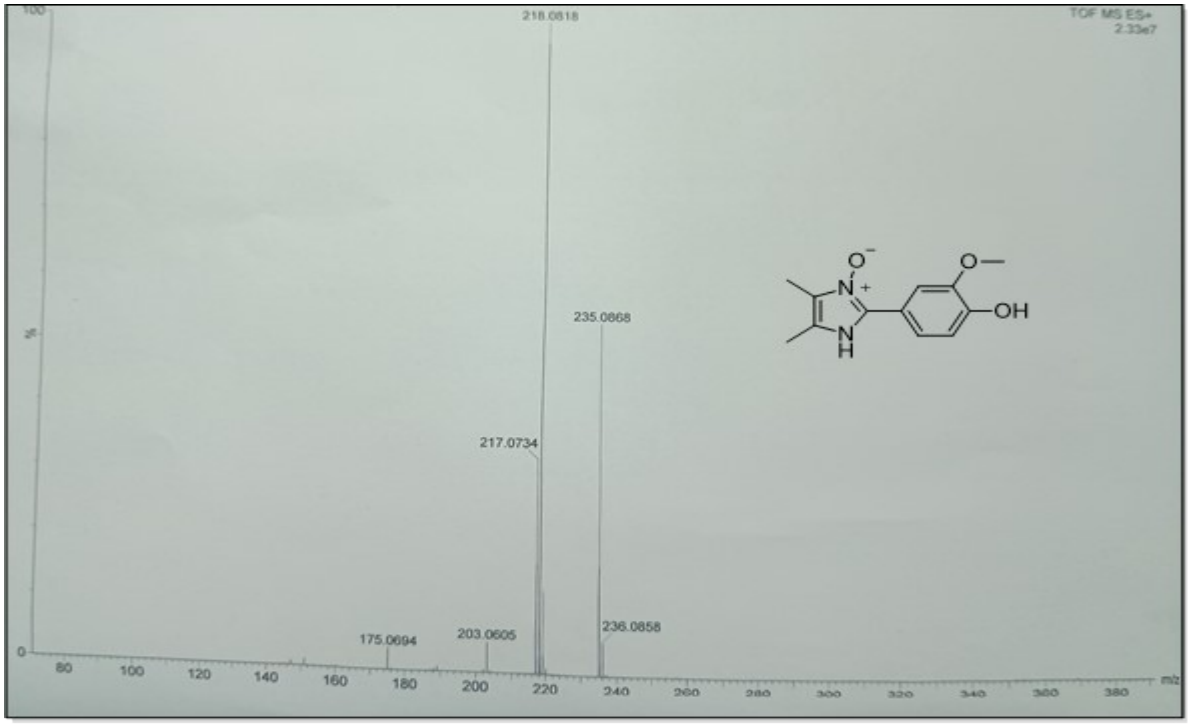
[1]HNMR - 2-(4-hydroxy -3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ah)



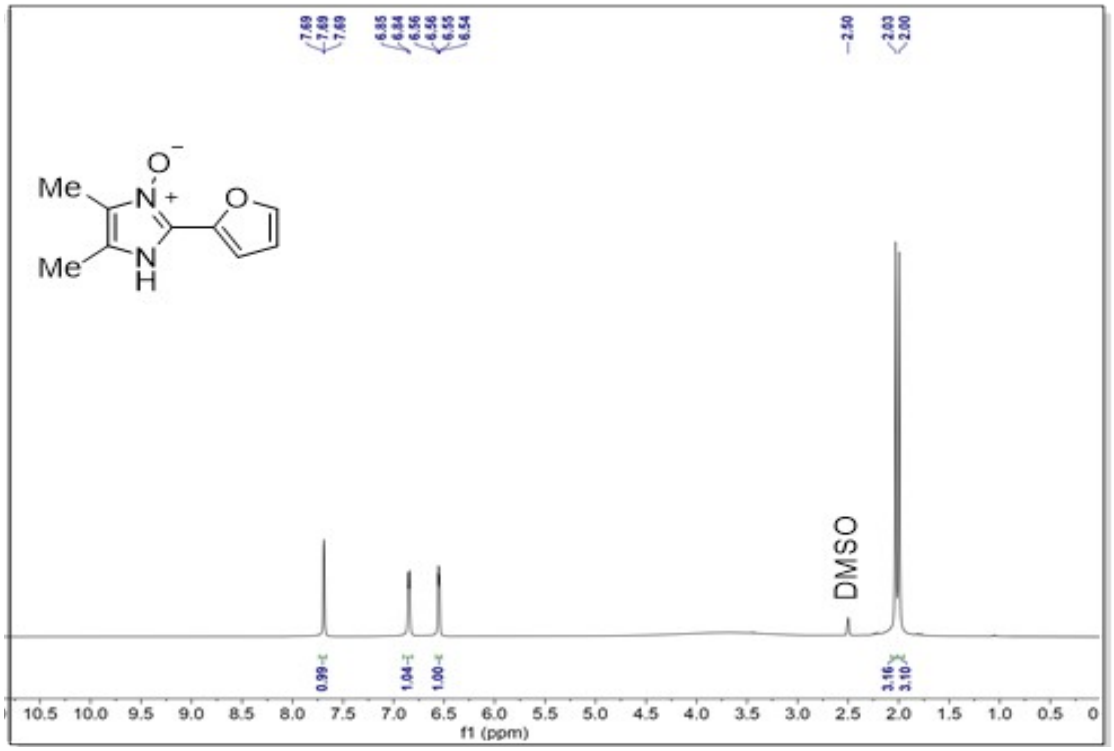
[13]CNMR - 2-(4-hydroxy -3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ah)



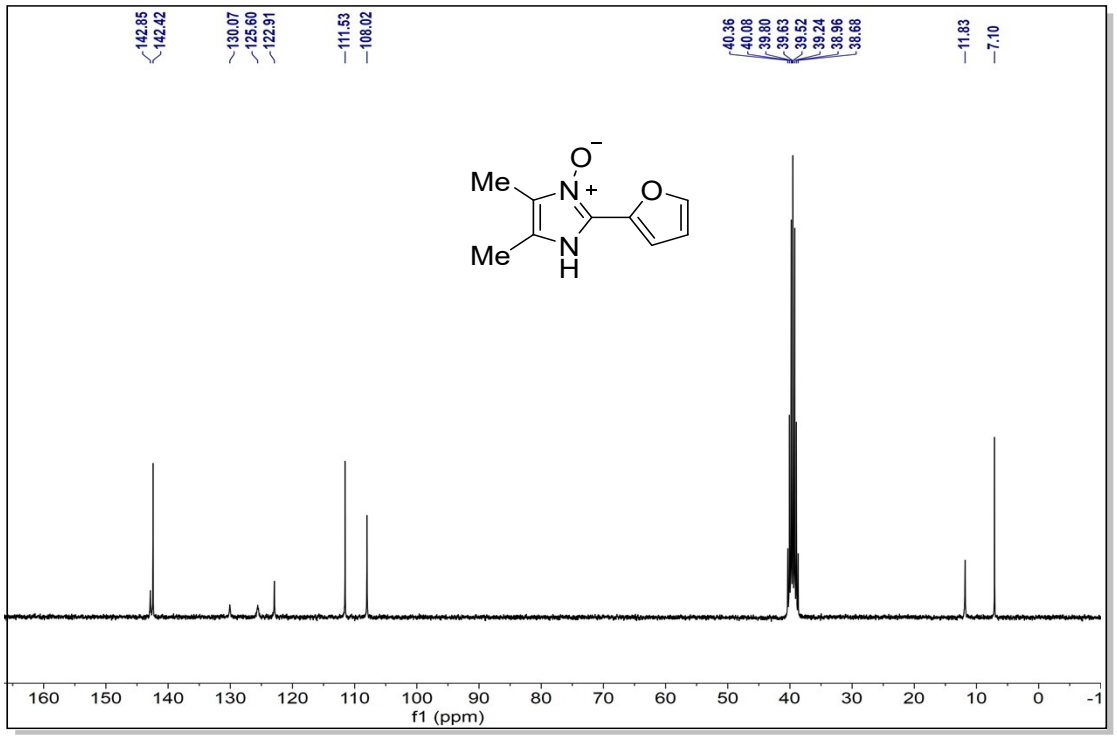
HRMS -2-(4-hydroxy -3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ah)



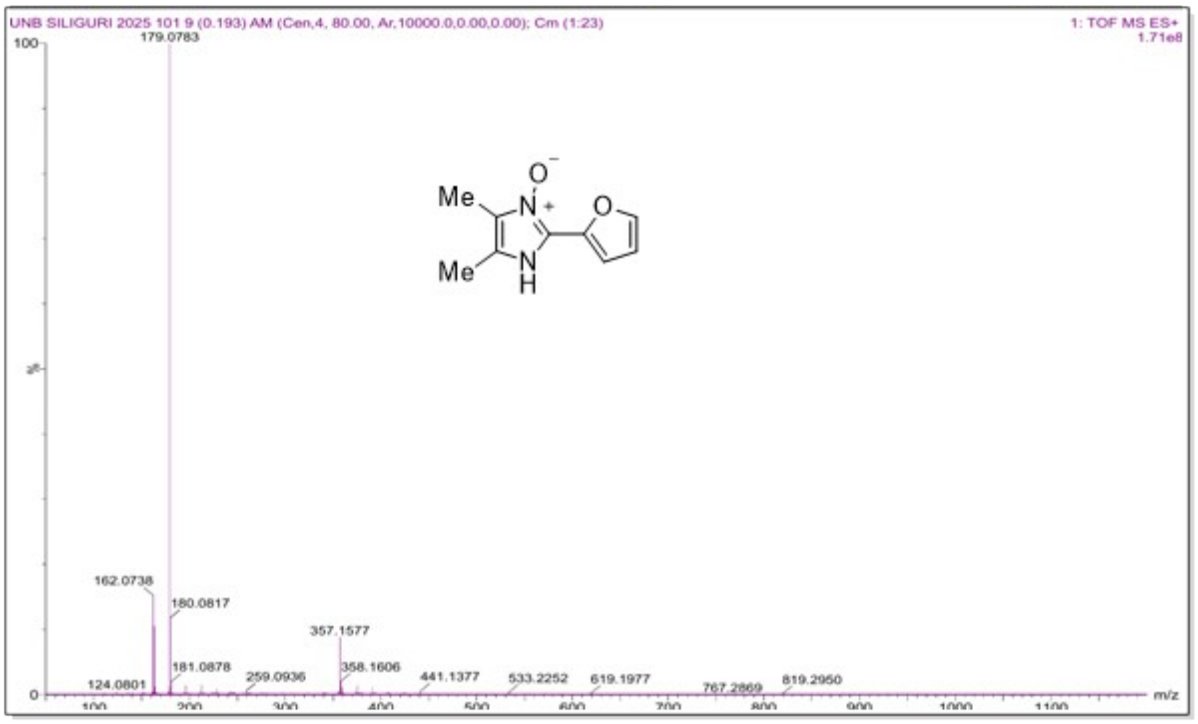
[1]HNMR - 2-(2-furyl)-4,5-dimethyl Imidazole 3-oxide (4ai)



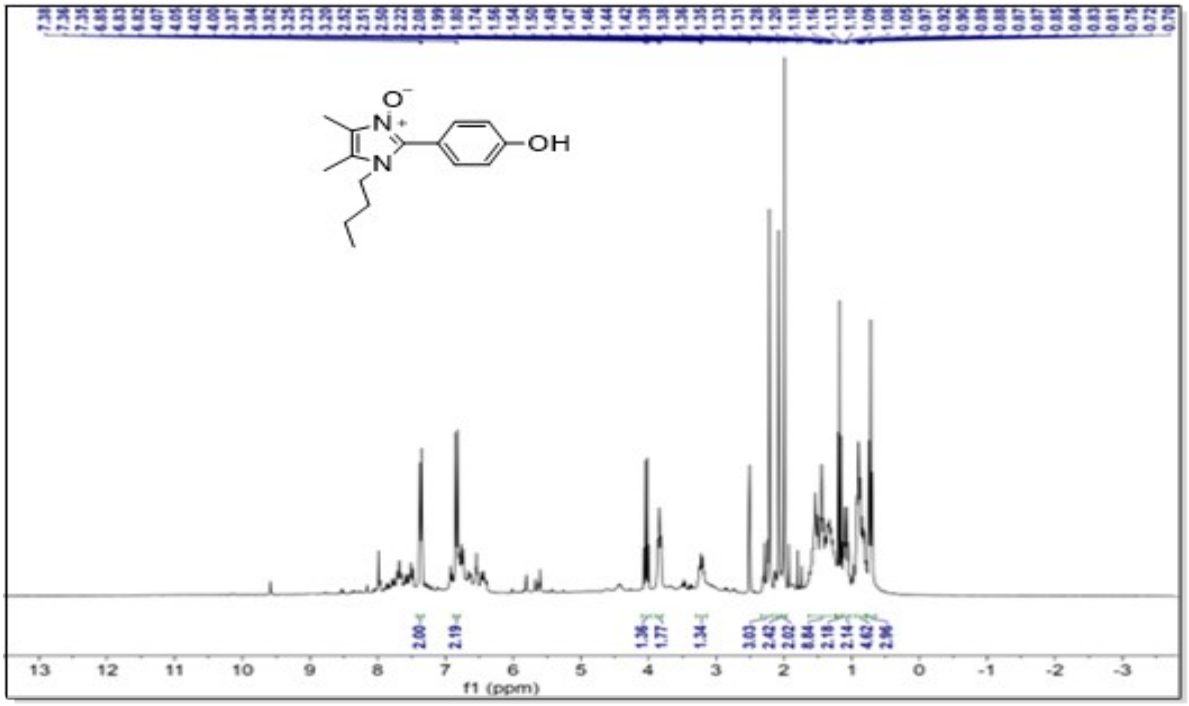
[13]CNMR - 2-(2-furyl)-4,5-dimethyl Imidazole 3-oxide (4ai)



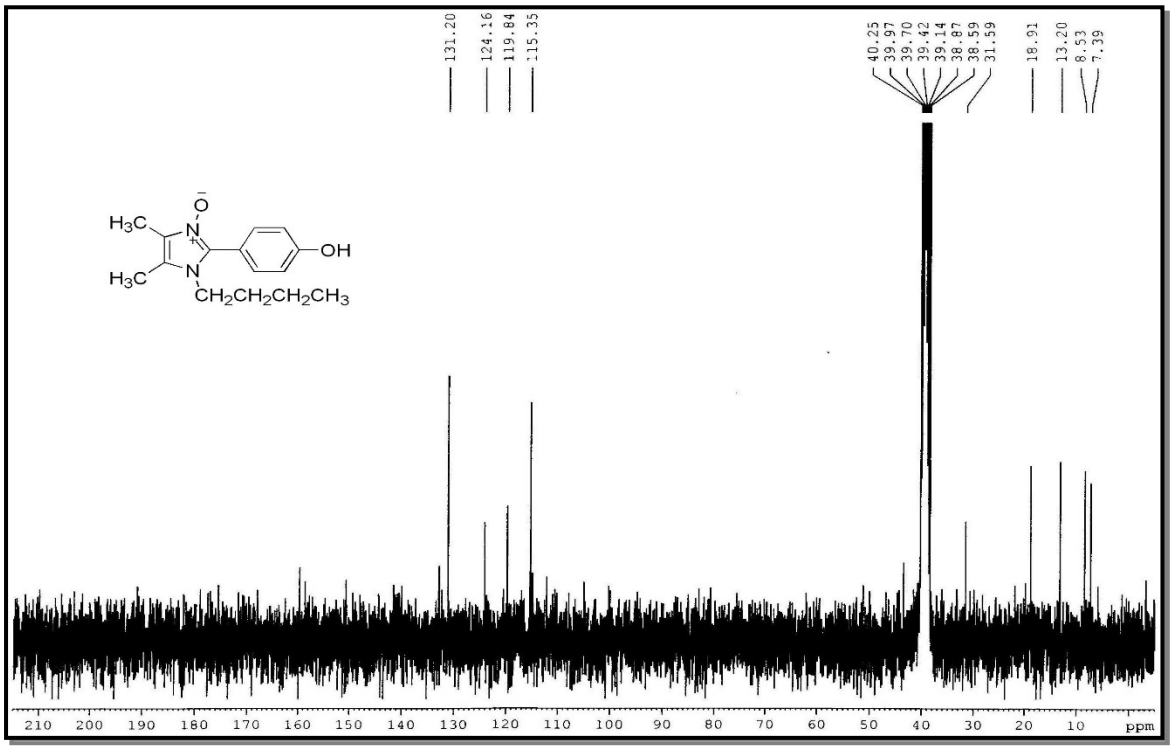
HRMS - 2-(2-furyl)-4,5-dimethyl Imidazole 3-oxide (4ai)



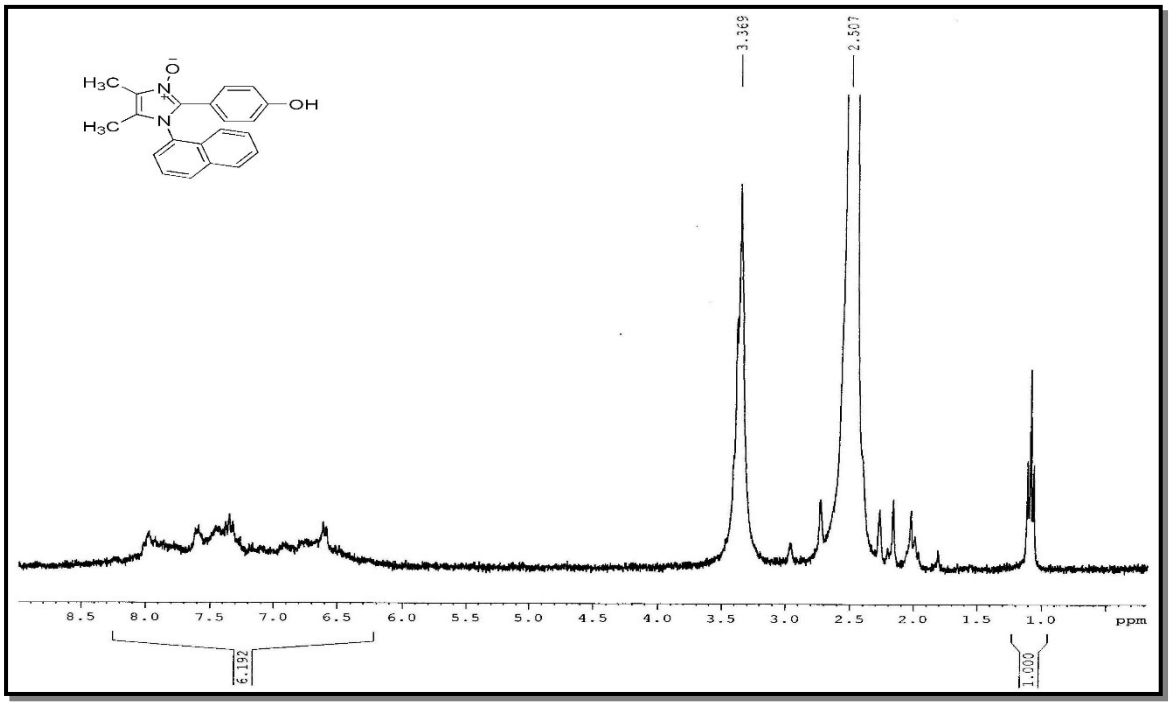
[1]HNMR - n-butyl-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4aj)



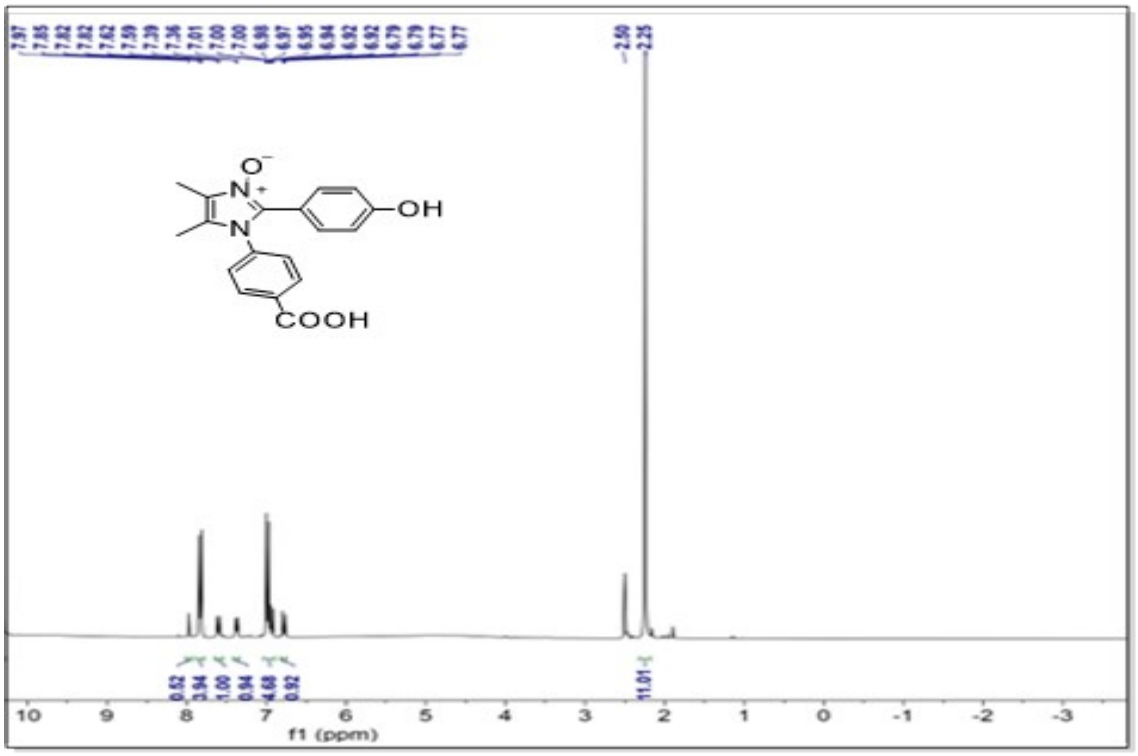
[13]CNMR - n-butyl-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4aj)



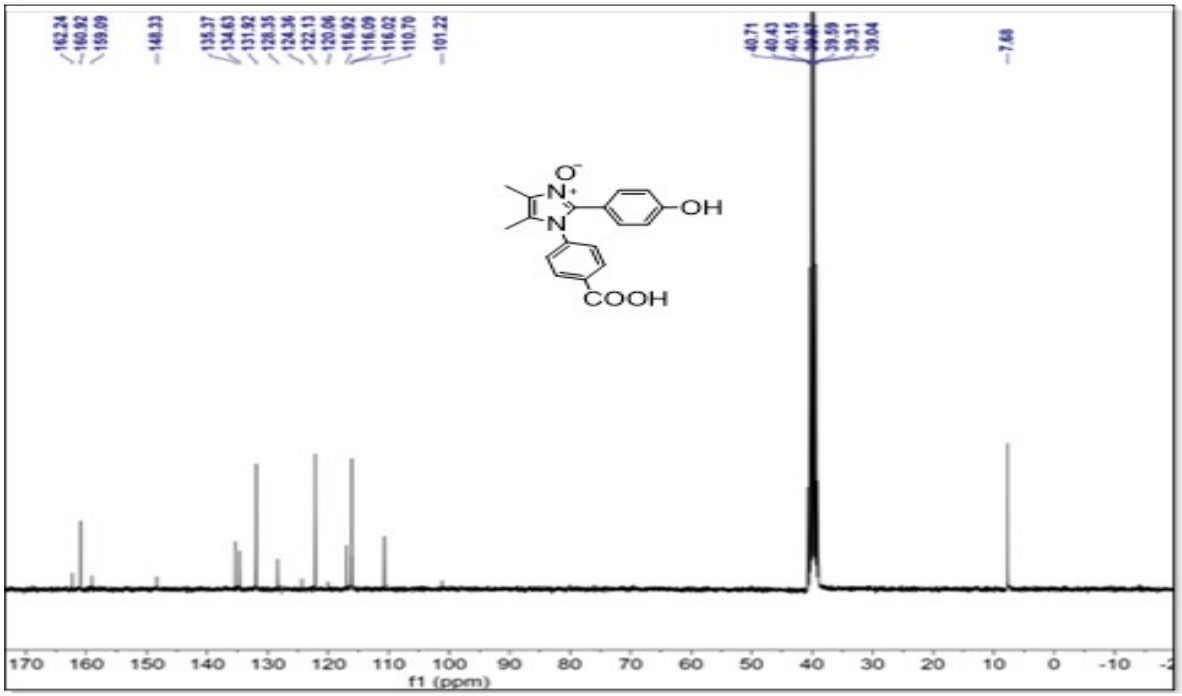
[1]HNMR - n-napthyl-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ak)



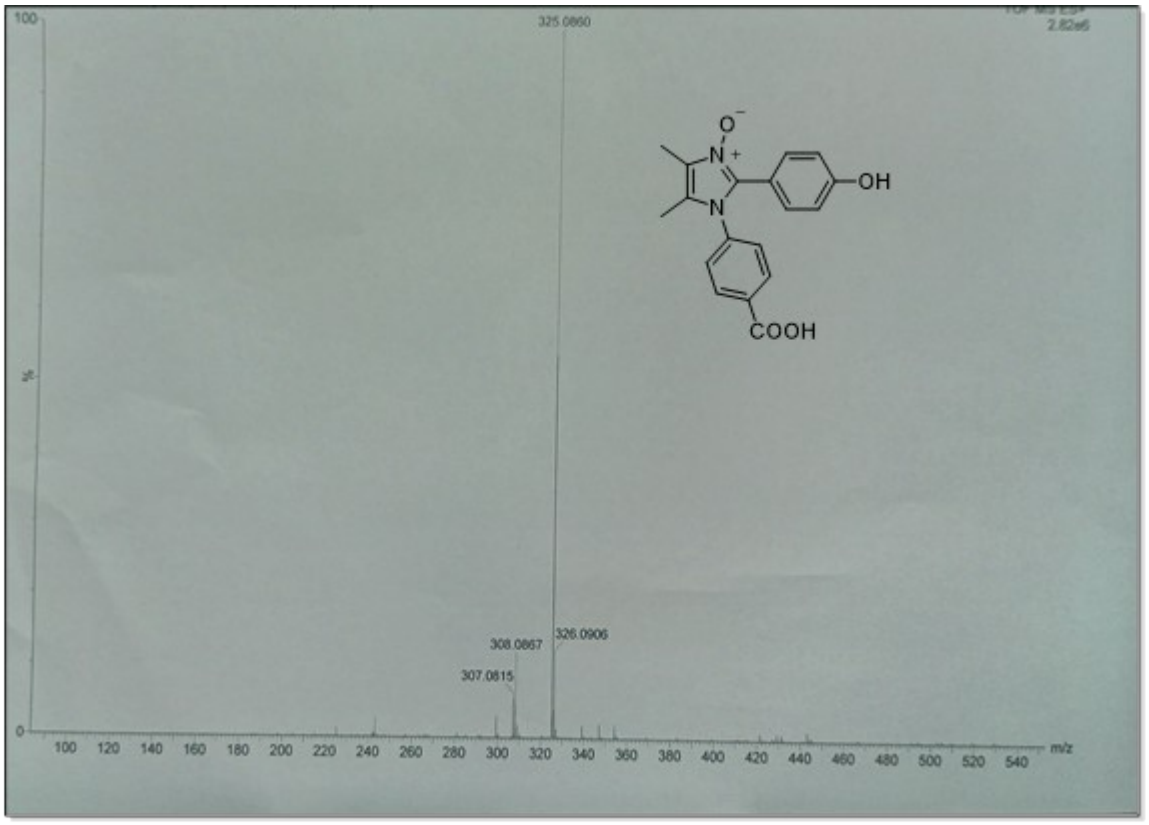
[1]HNMR - 1-(4-carboxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl-1H-imidazole 3-oxide (4am)



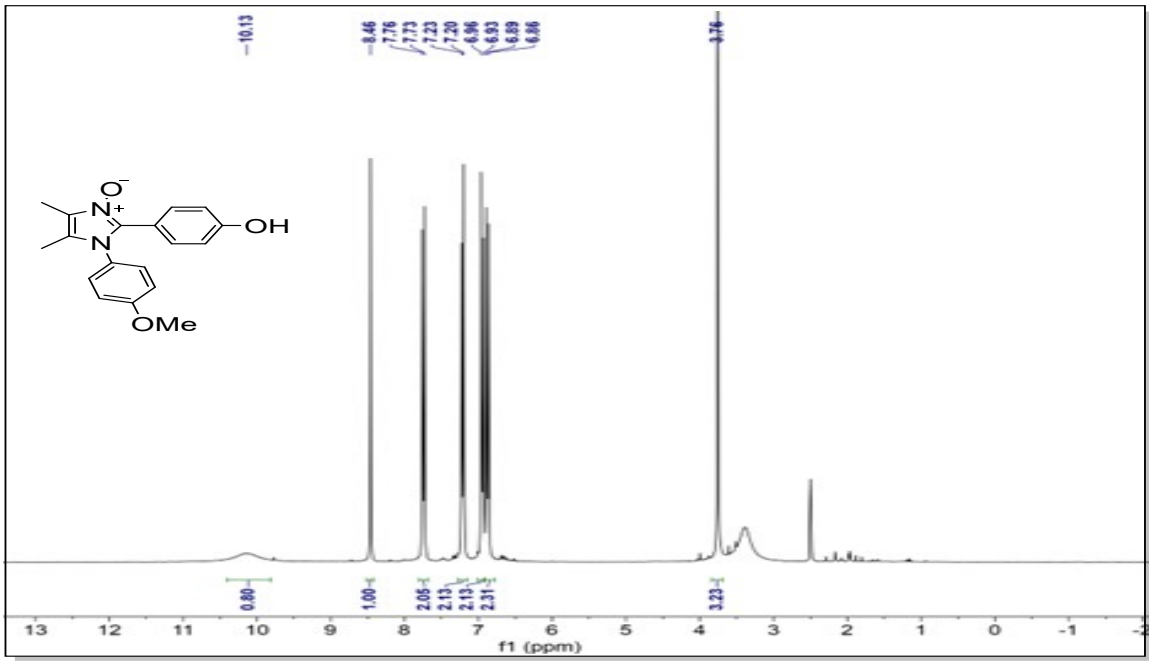
[13]CNMR - 1-(4-carboxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl-1H-imidazole 3-oxide (4am)



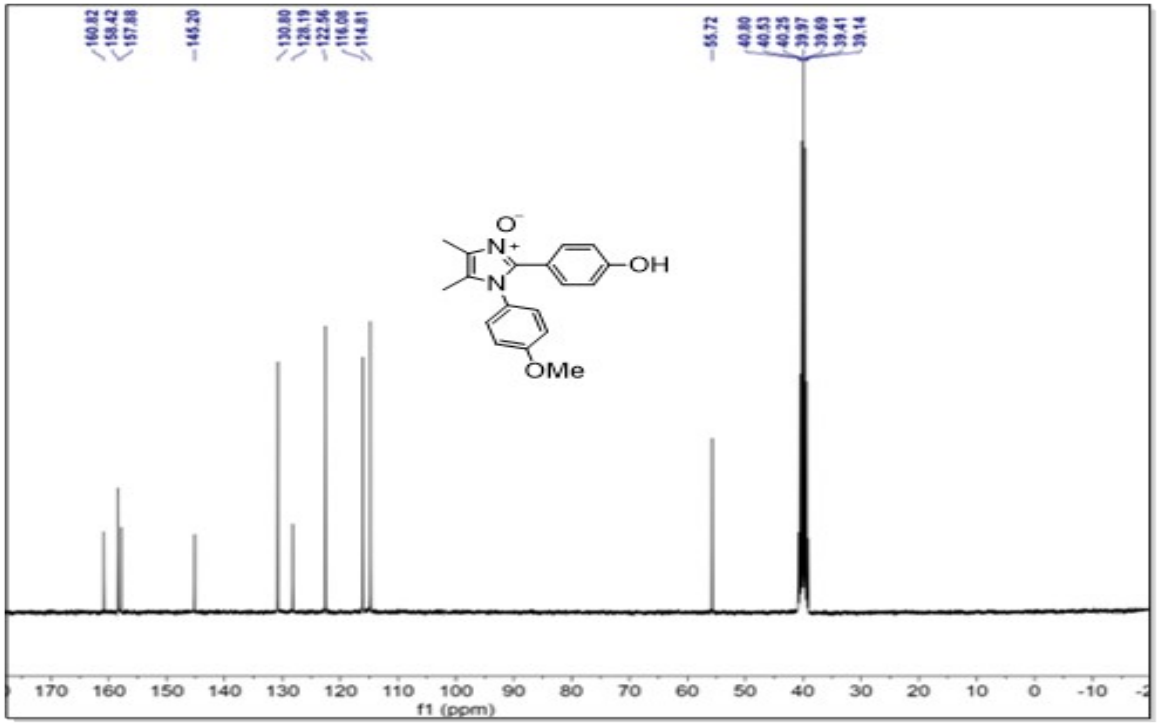
HRMS -1-(4-carboxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl-1H-imidazole 3-oxide (4am)



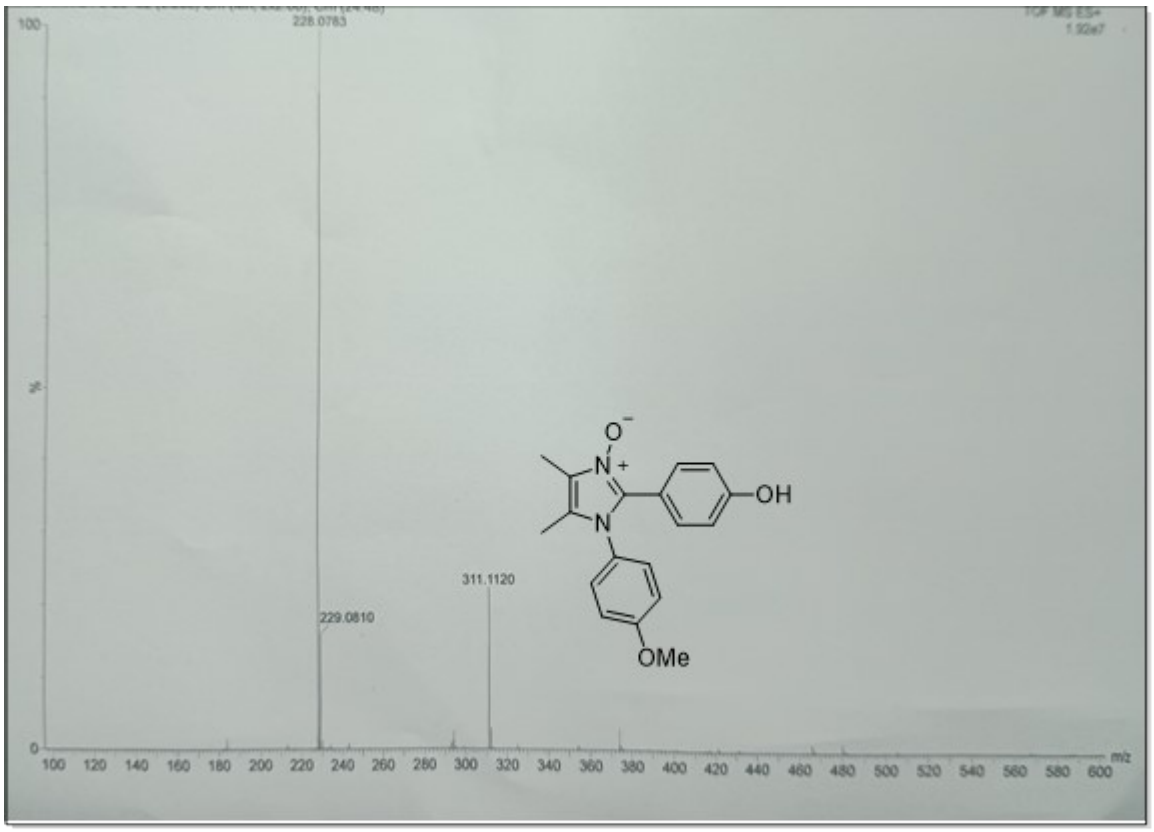
[1]HNMR - N-(4-methoxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4an)



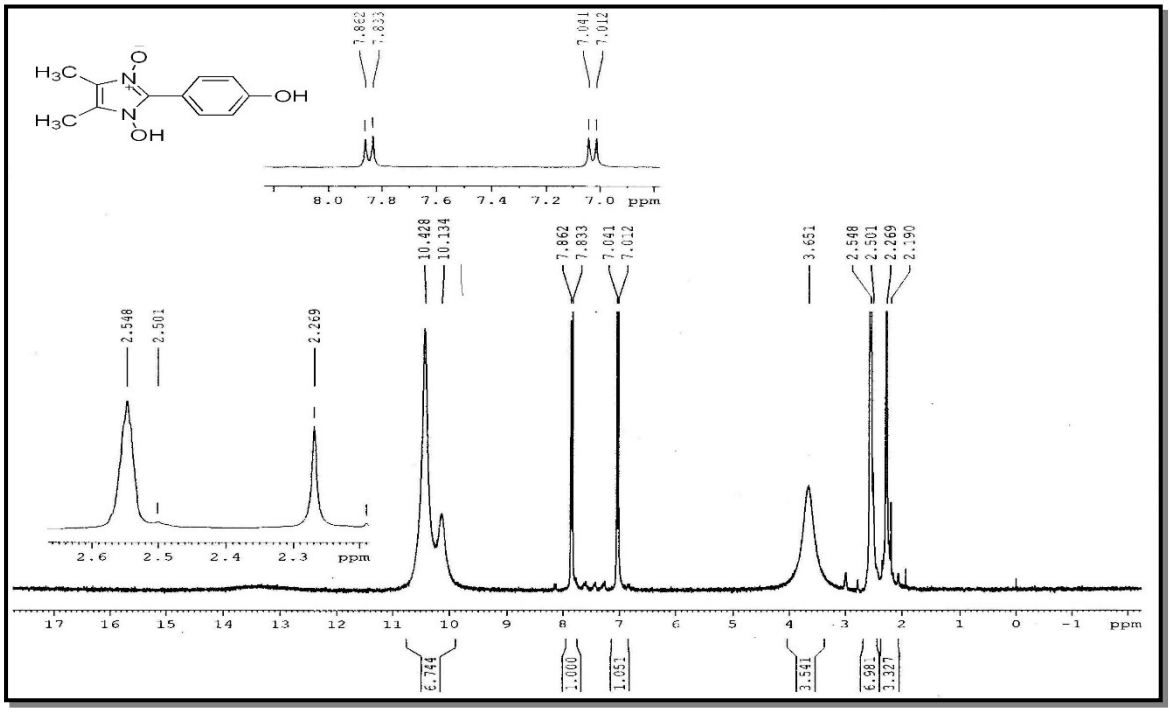
[13]CNMR - N-(4-methoxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4an)



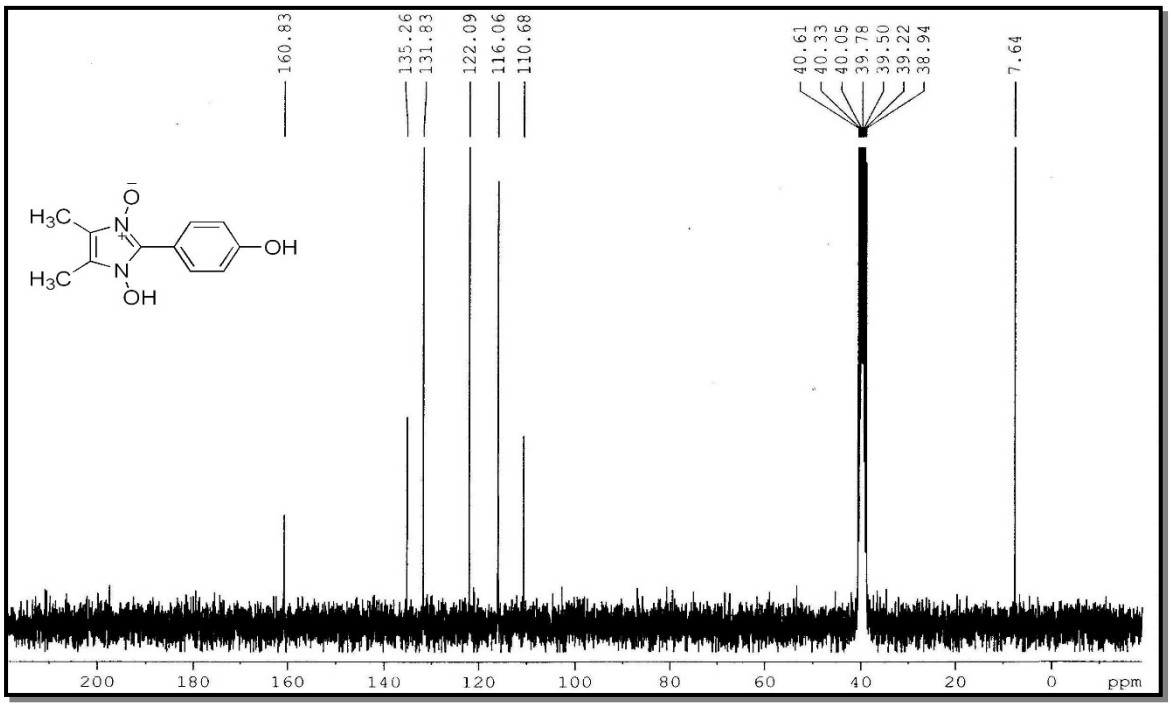
HRMS - N-(4-methoxyphenyl)-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4an)



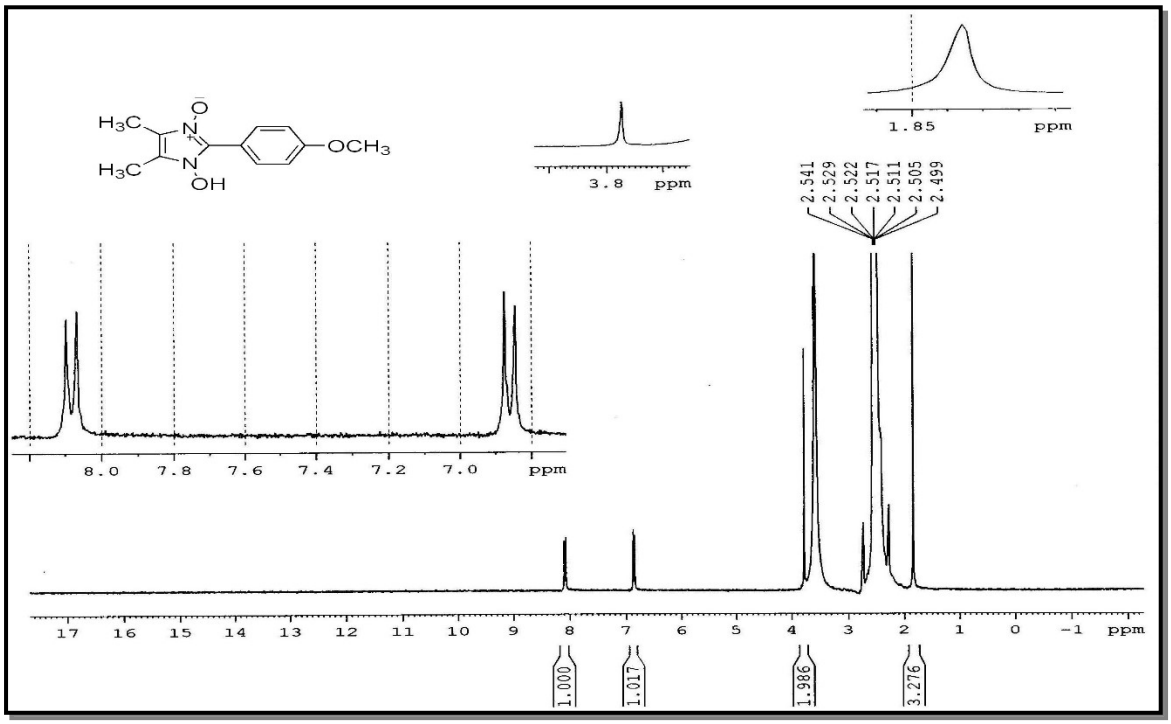
[1]HNMR - 1-hydroxy-2-(4-hydroxyphenyl)-4, 5-dimethyl Imidazole 3-oxide (4ao)



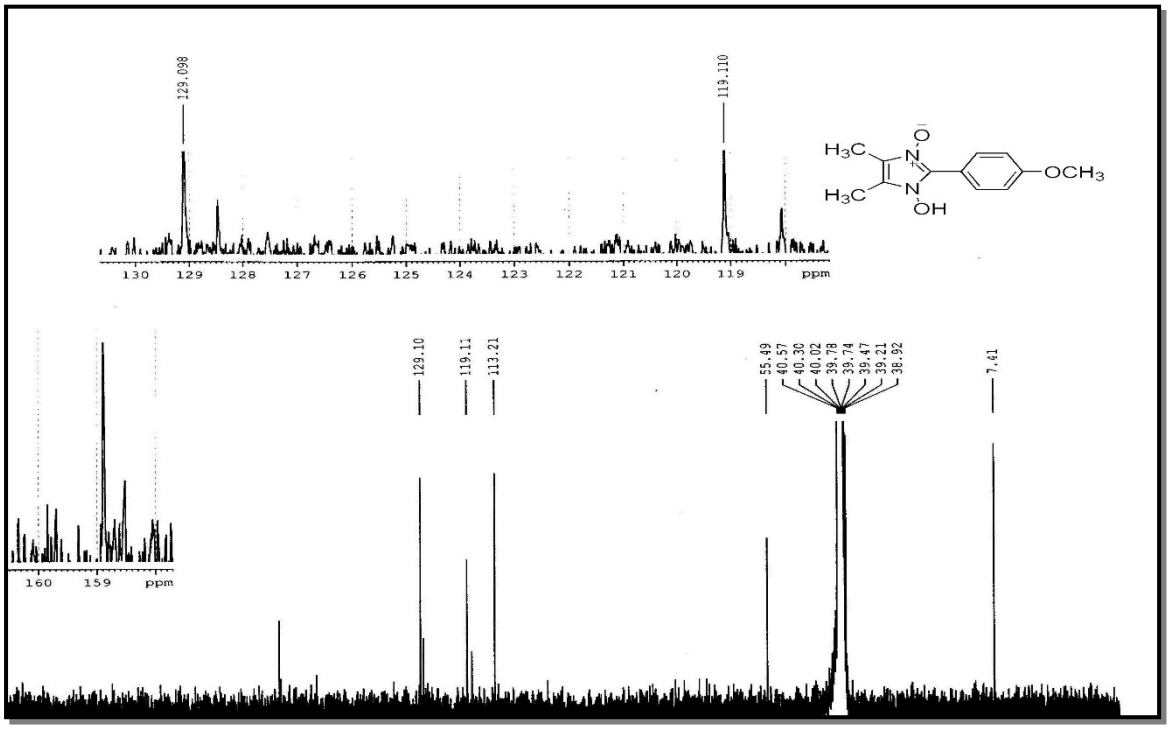
[13]CNMR - 1-hydroxy-2-(4-hydroxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ao)



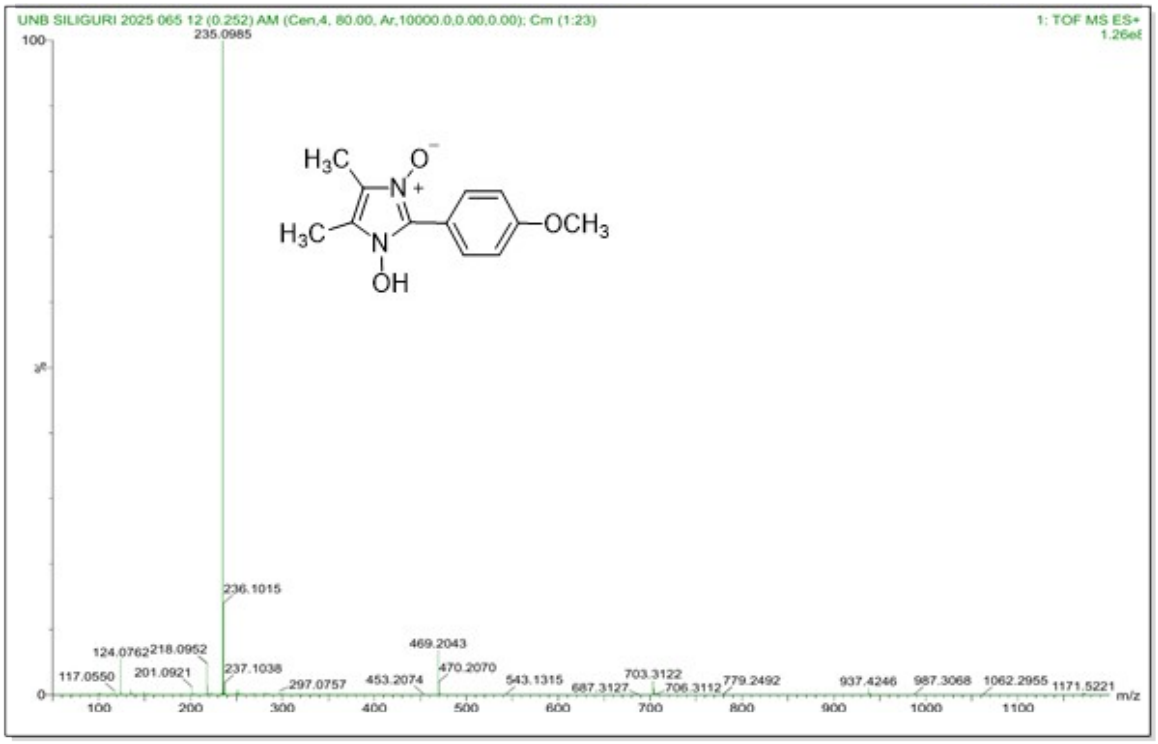
[1]HNMR - 1-hydroxy-2-(4-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ap)



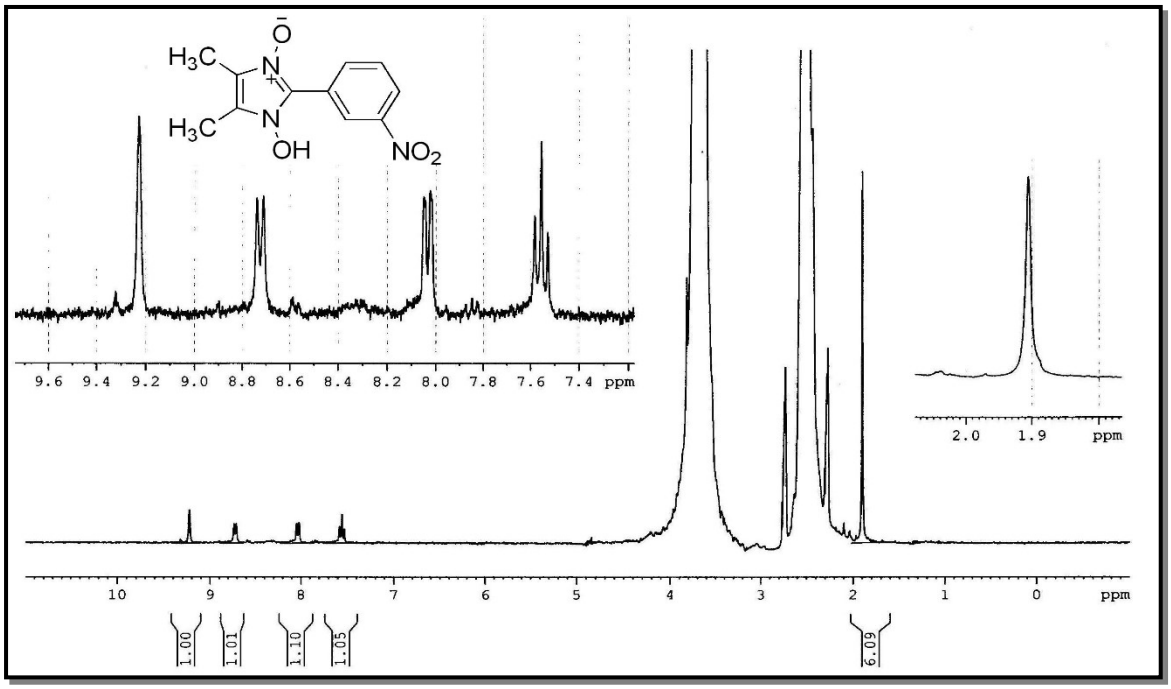
[13]CNMR - 1-hydroxy-2-(4-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ap)



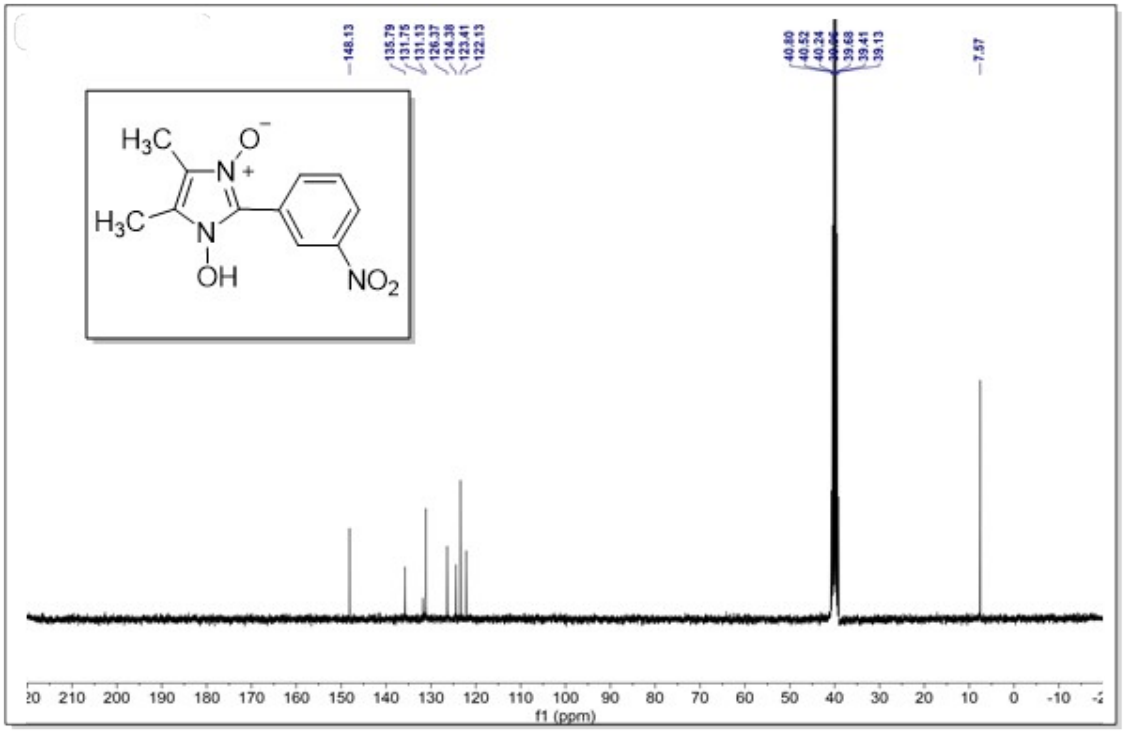
HRMS - 1-hydroxy-2-(4-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ap)



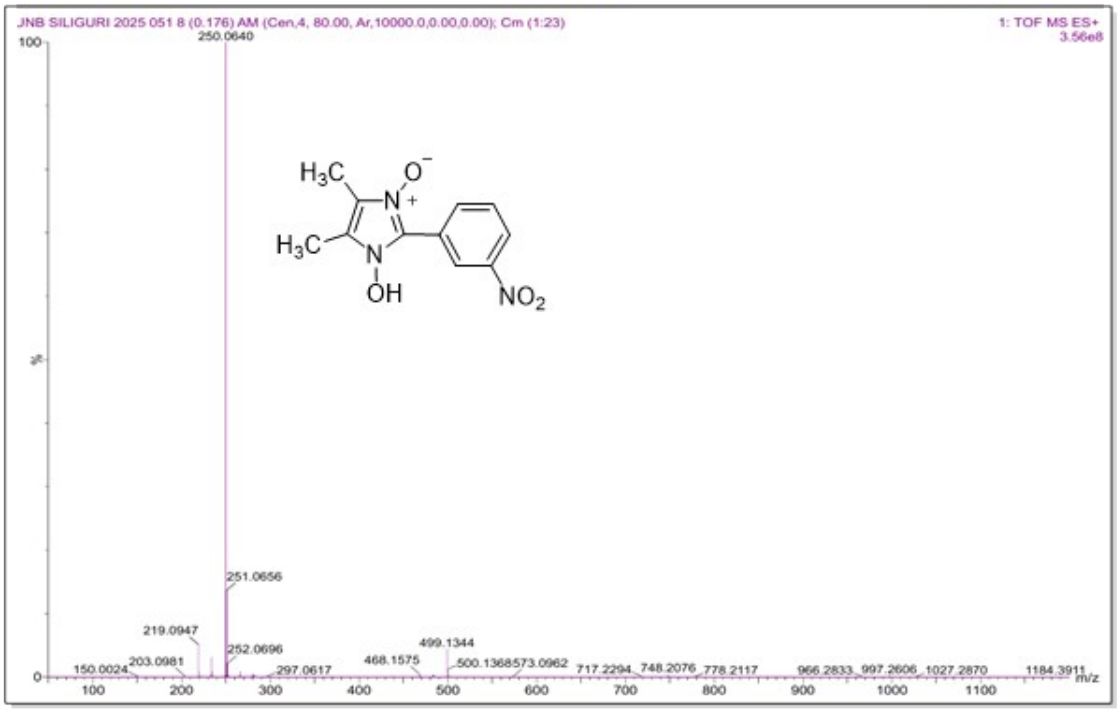
[1]HNMR - 1-hydroxy-2-(3-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4aq)



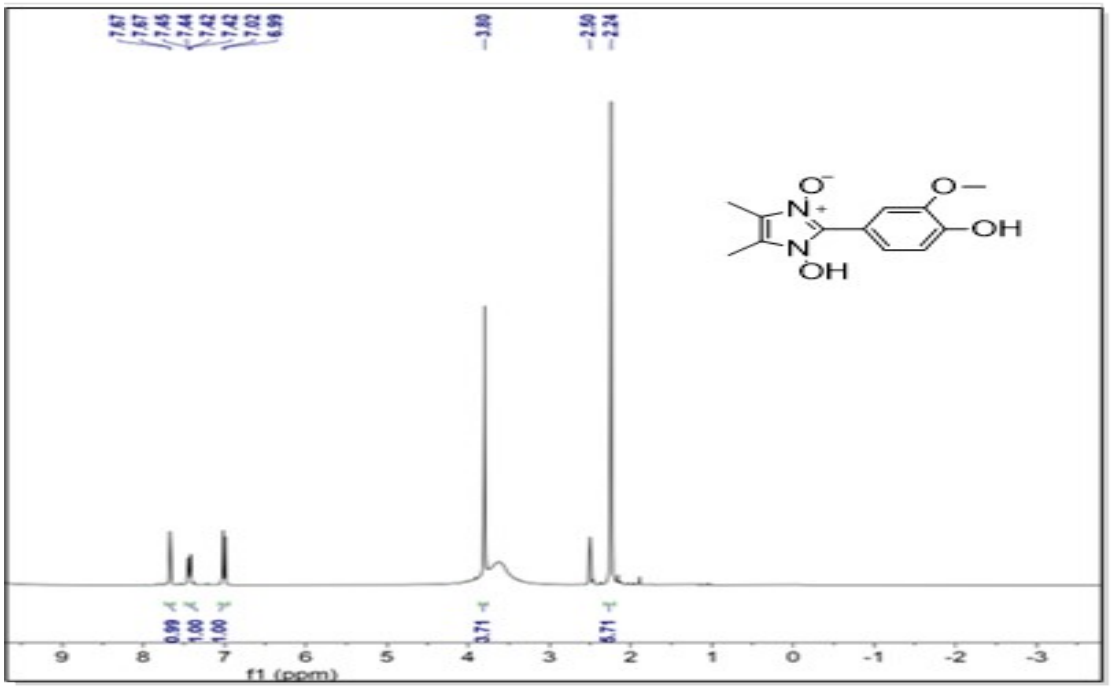
[13]CNMR - 1-hydroxy-2-(3-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4aq)



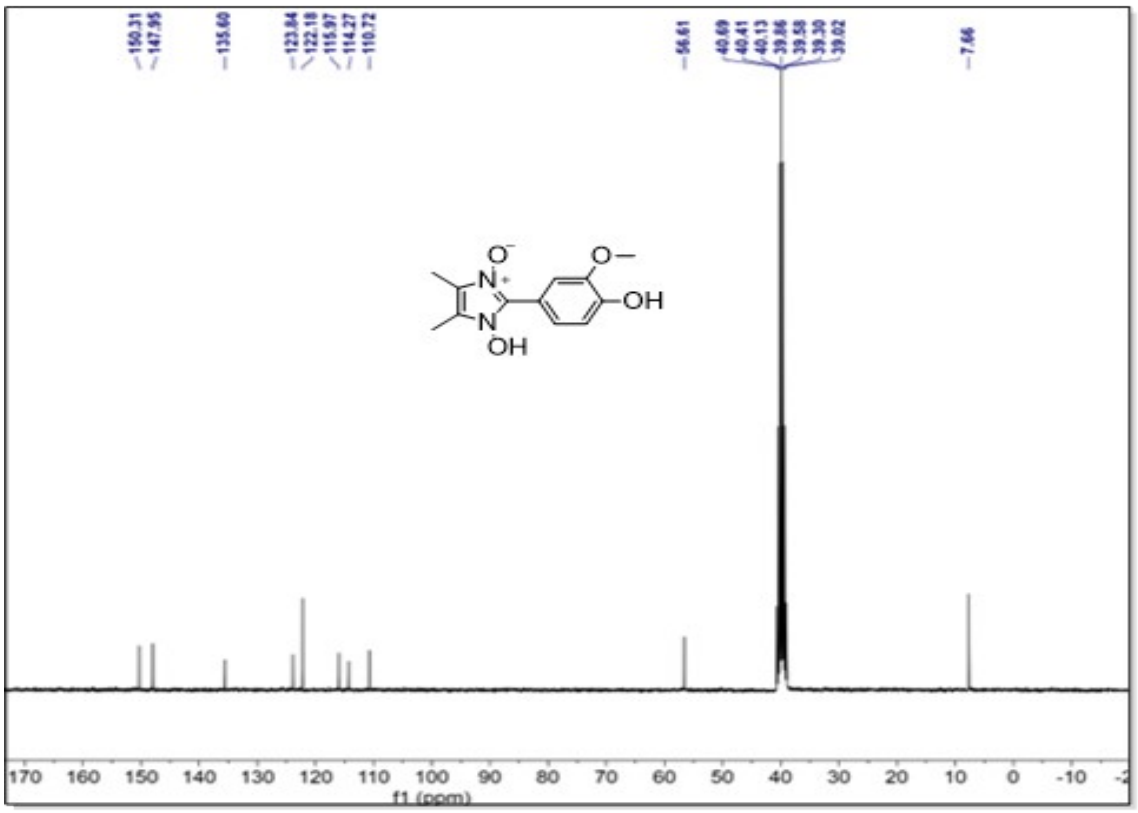
HRMS - 1-hydroxy-2-(3-nitrophenyl)-4,5-dimethyl Imidazole 3-oxide (4aq)



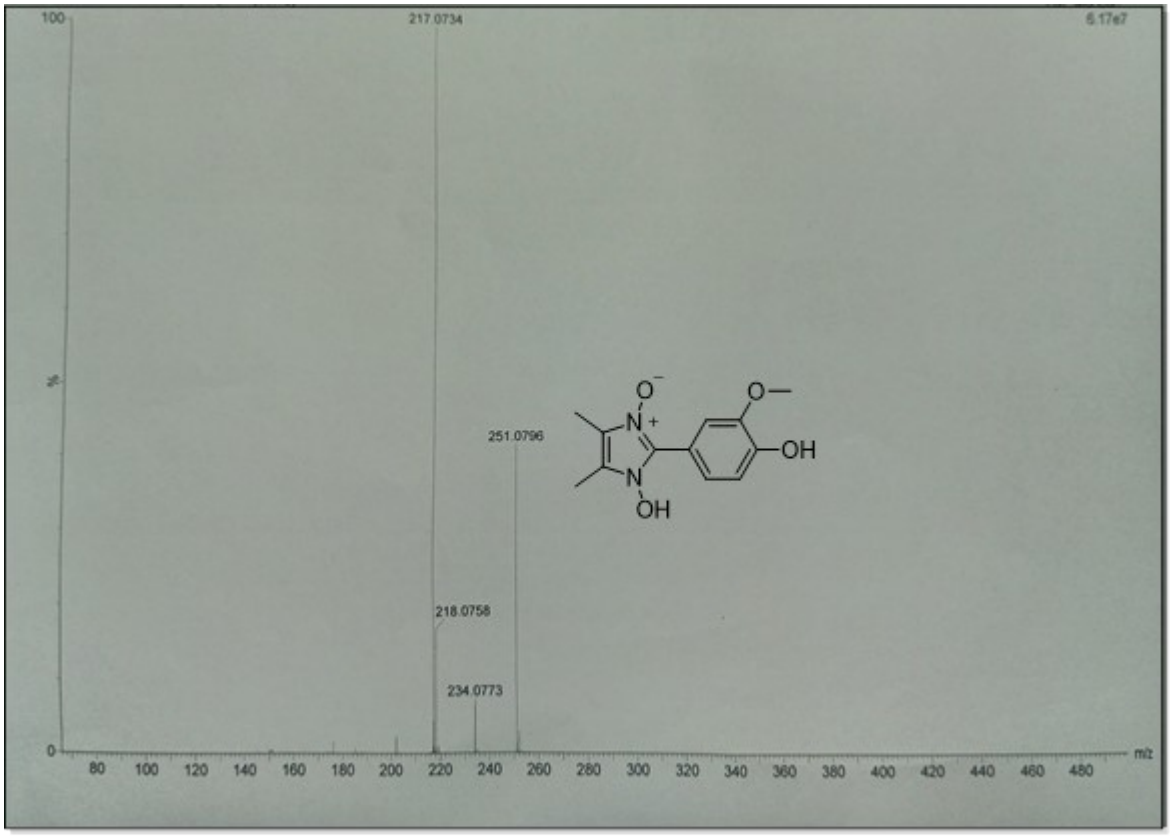
[1]HNMR - 1-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ar)



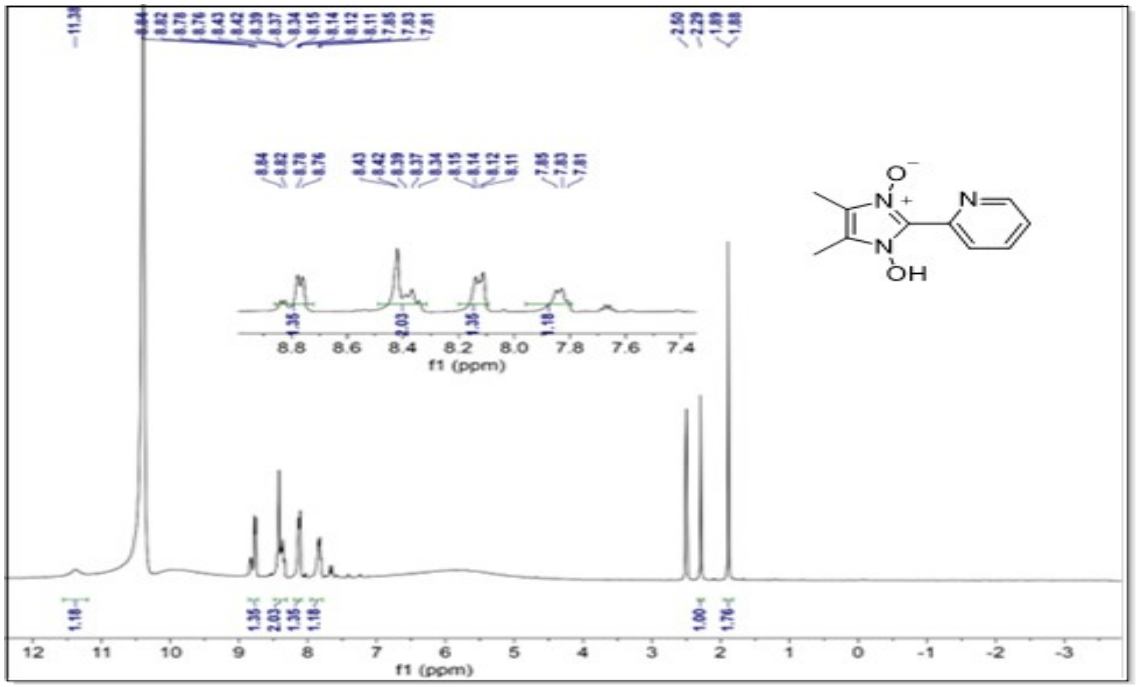
[13]CNMR - 1-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ar)



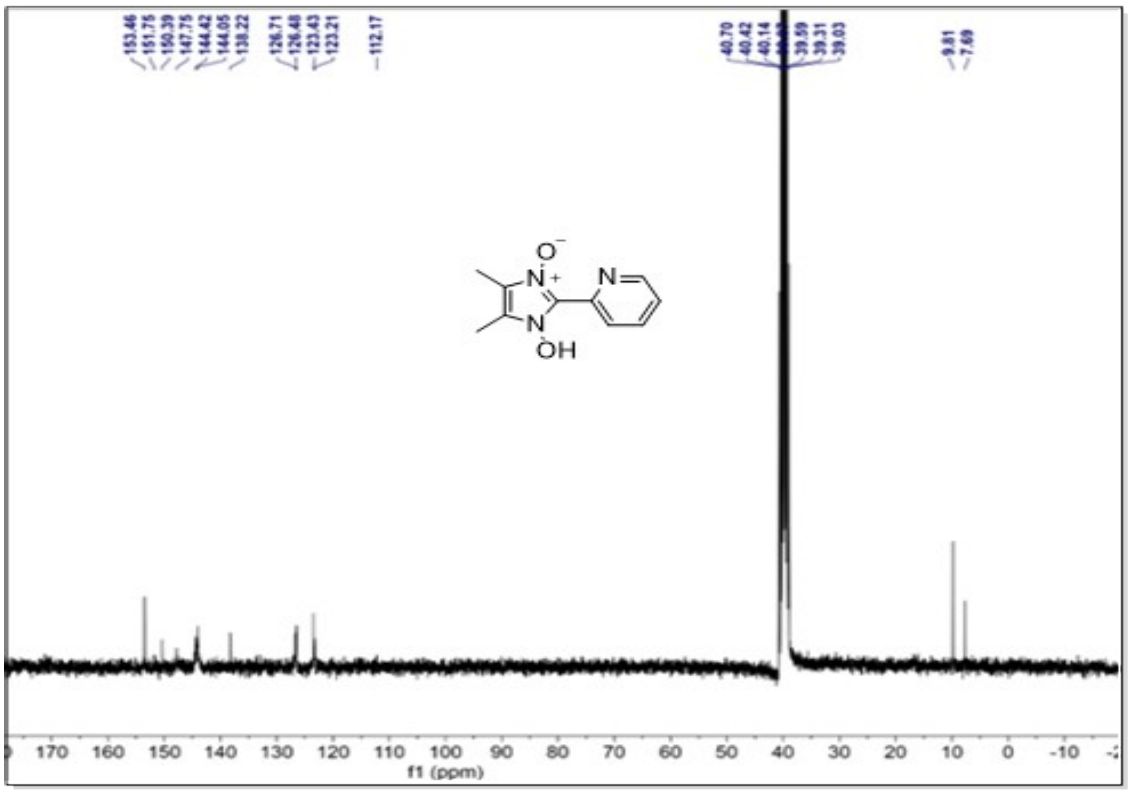
HRMS - 1-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4,5-dimethyl Imidazole 3-oxide (4ar)



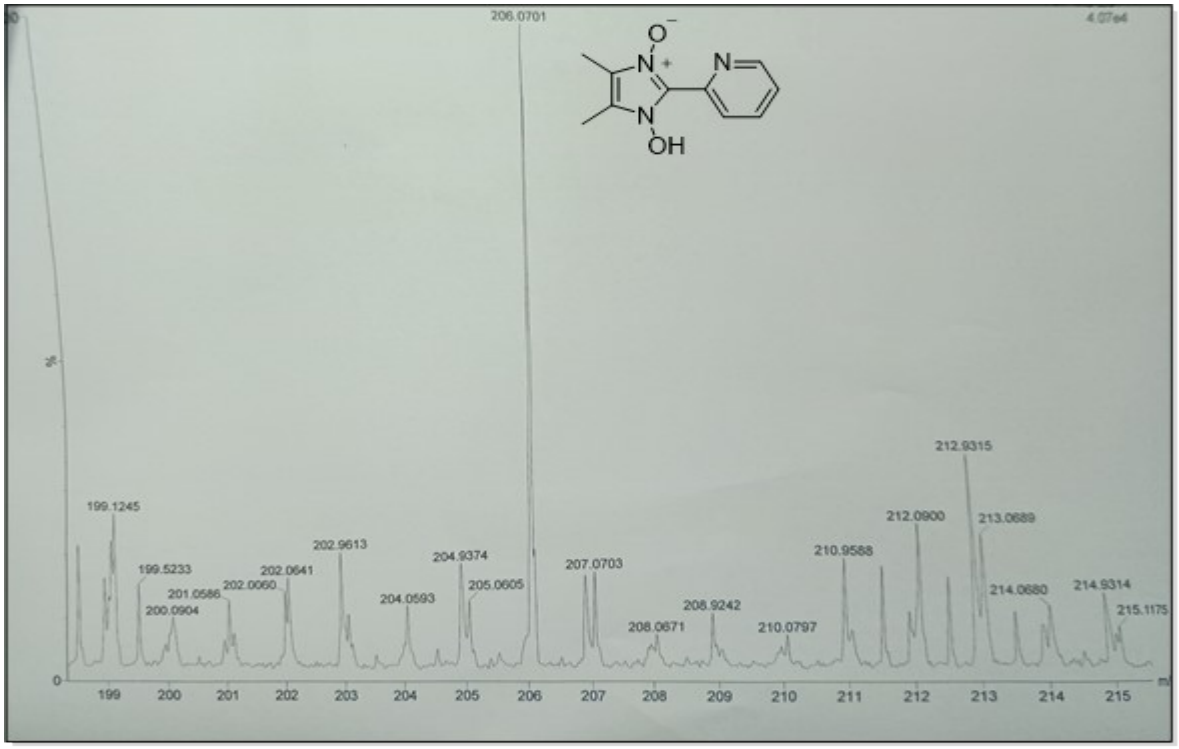
[1]HNMR - 1-hydroxy-2-(2-pyridyl)-4,5-dimethyl Imidazole 3-oxide (4as)



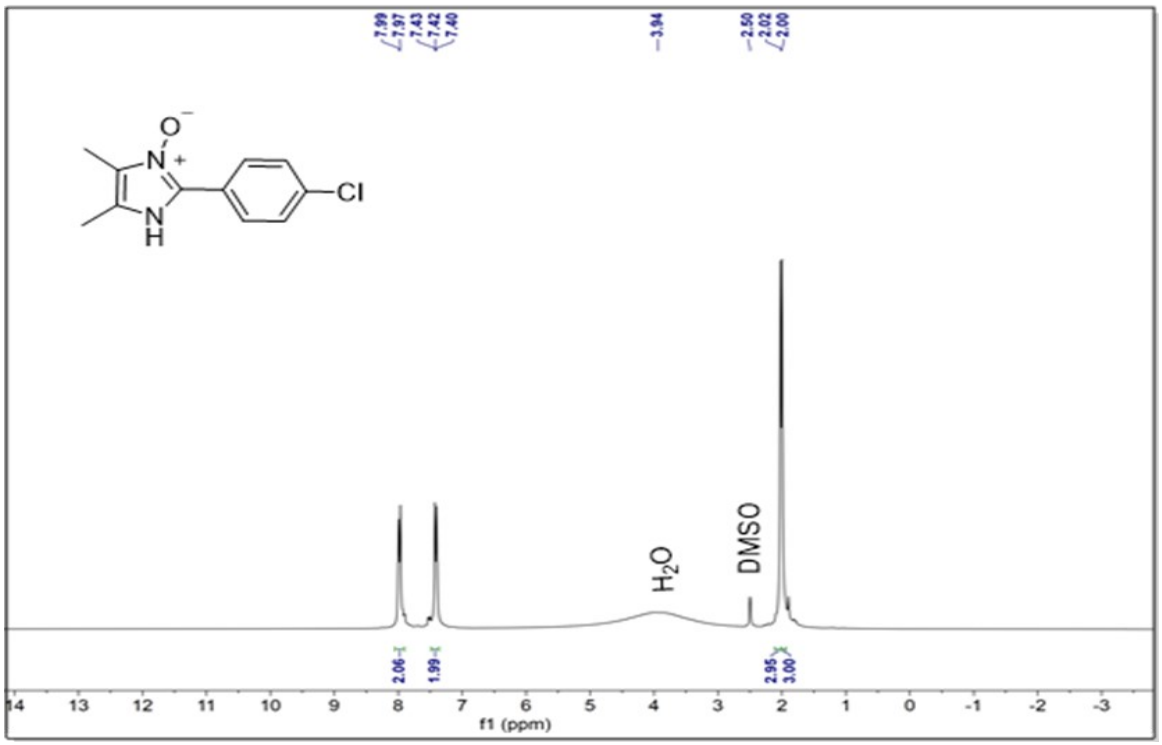
[13]CNMR - 1-hydroxy-2-(2-pyridyl)-4,5-dimethyl Imidazole 3-oxide (4as)



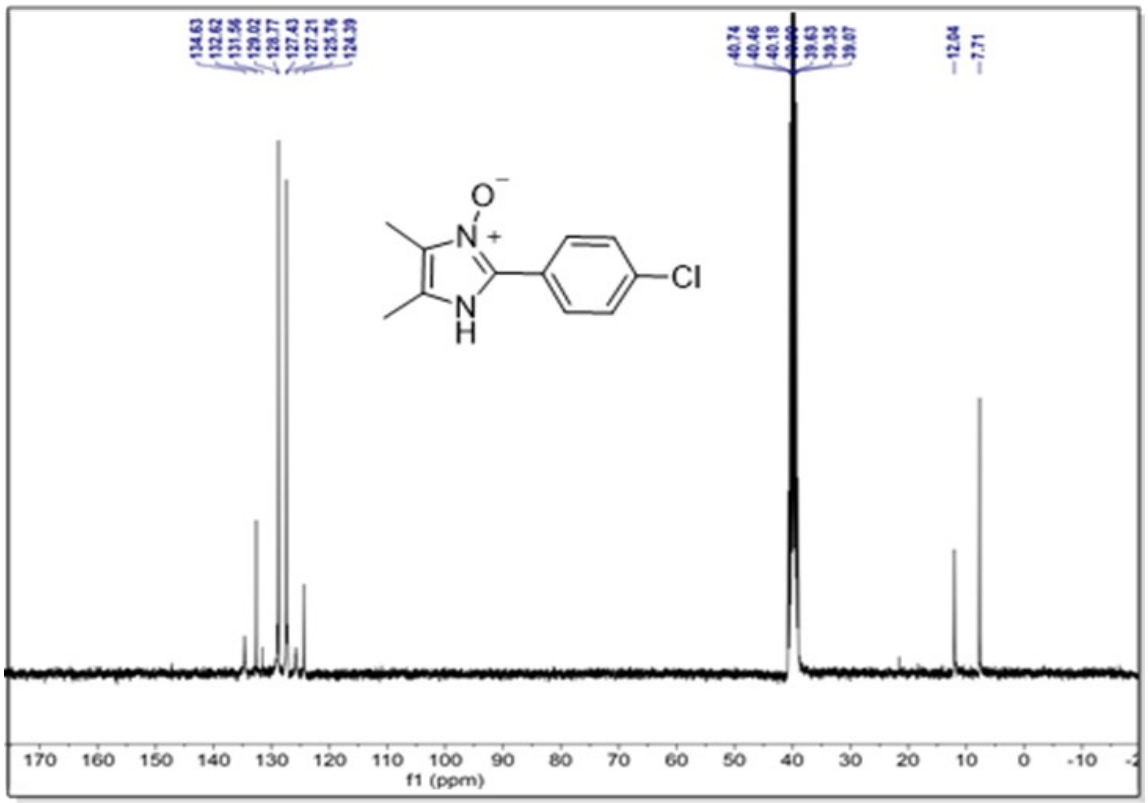
HRMS -1-hydroxy-2-(2-pyridyl)-4,5-dimethyl Imidazole 3-oxide (4as)



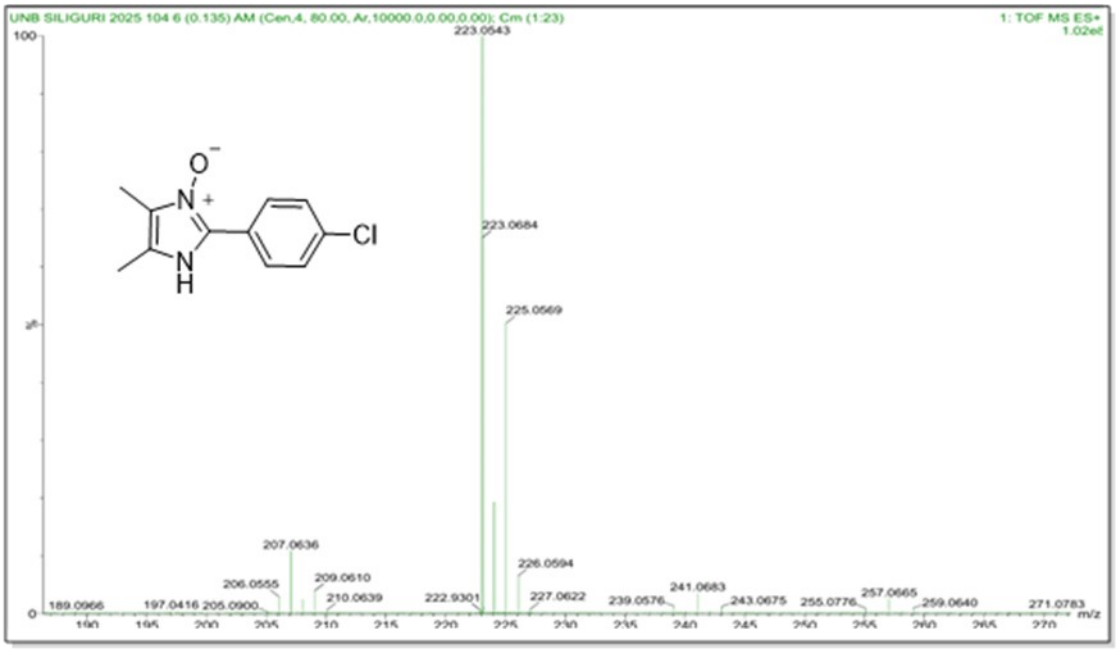
[1]HNMR - 2-(4-chlorophenyl)-4,5-dimethyl-1H-imidazole 3-oxide (4at)



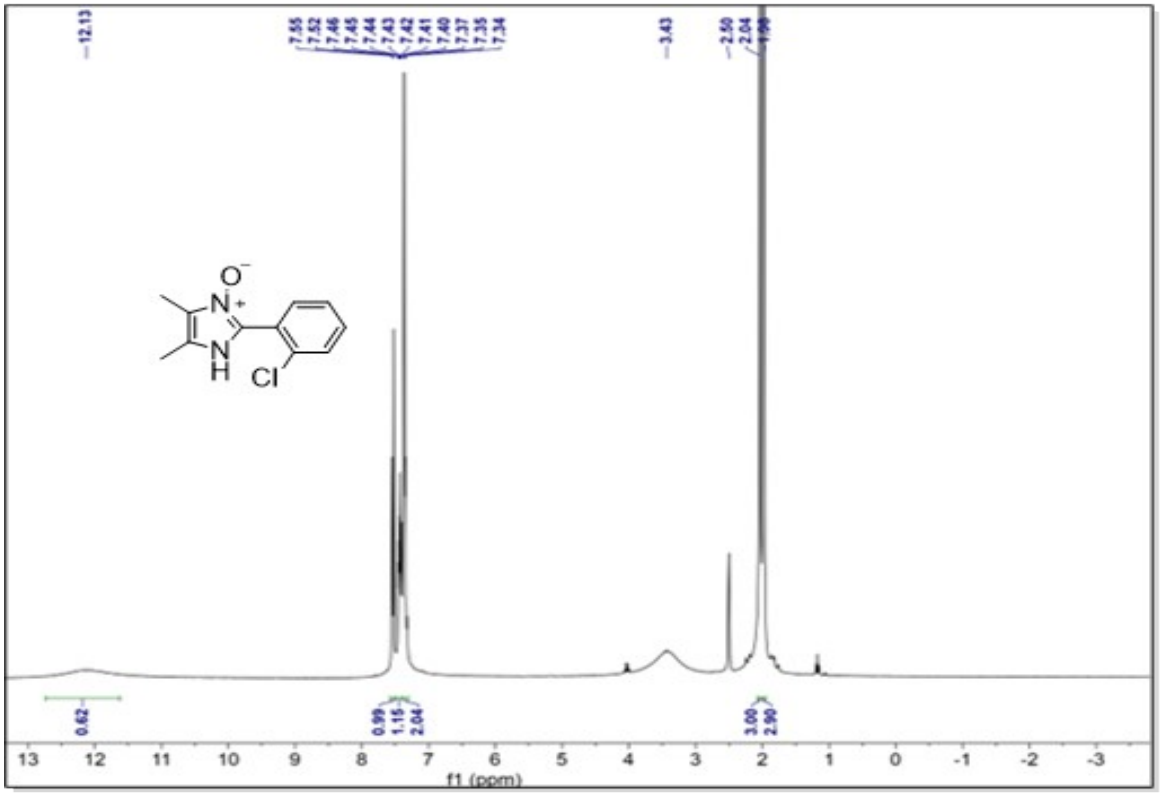
[13]CNMR - 2-(4-chlorophenyl)-4,5-dimethyl-1H-imidazole 3-oxide (4at)



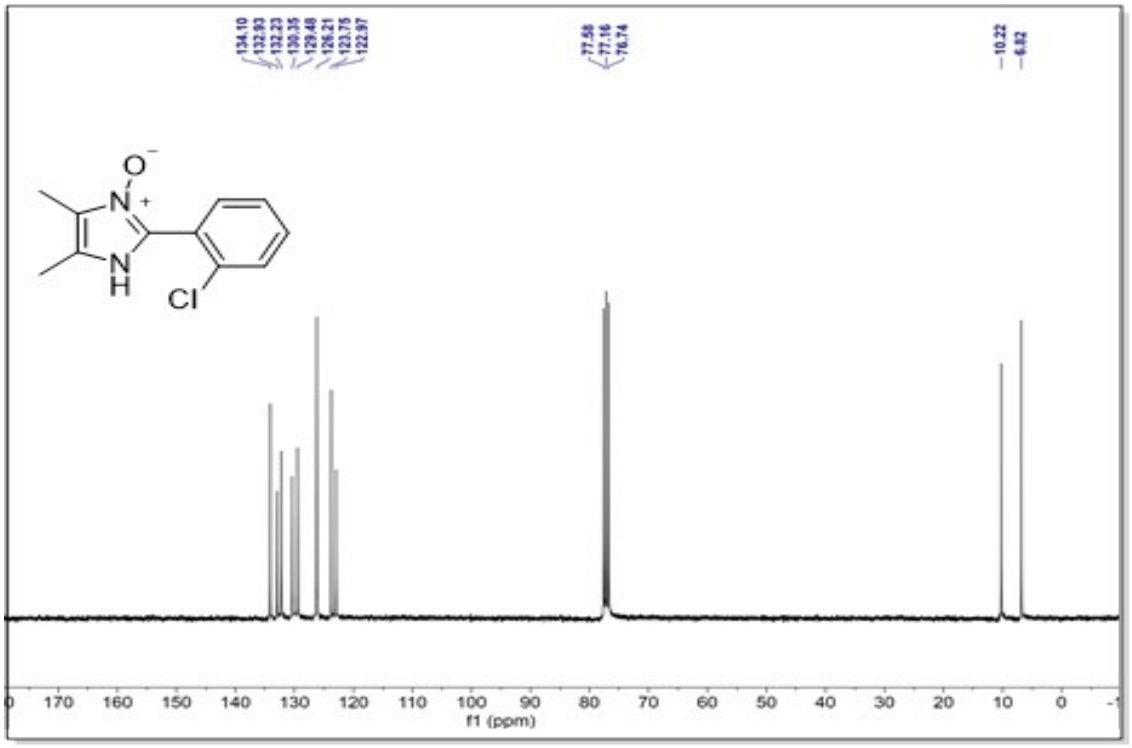
HRMS - 2-(4-chlorophenyl)-4,5-dimethyl-1H-imidazole 3-oxide (4at)



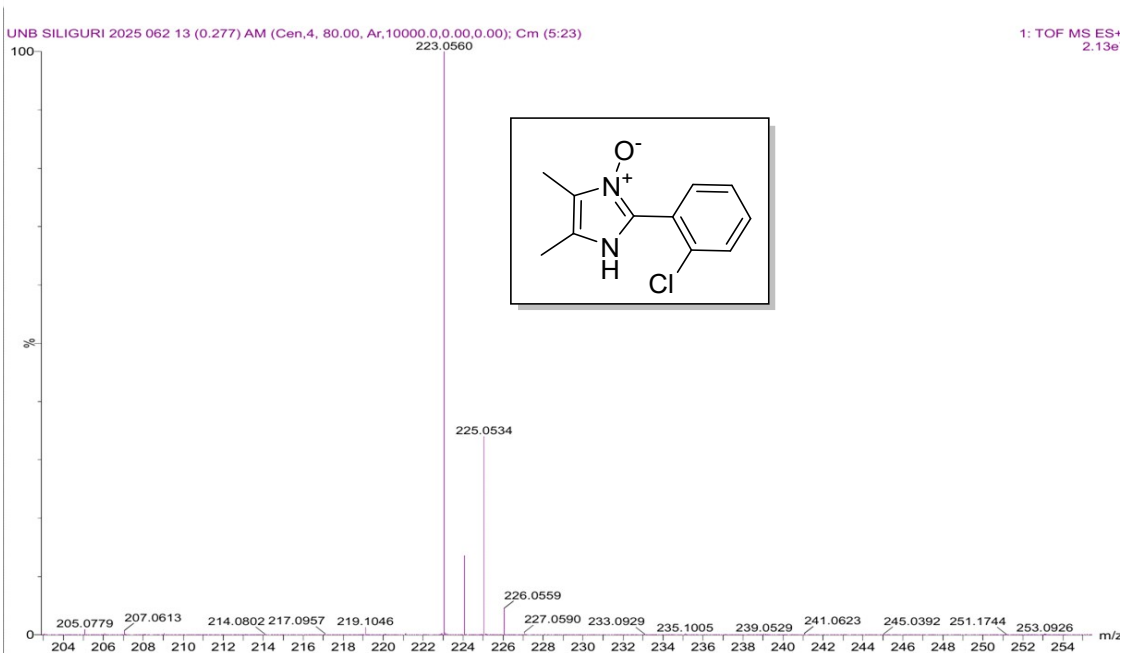
[1]HNMR - 2-(2-chlorophenyl)-1-hydroxy-4,5-dimethyl-1H-imidazole 3-oxide (4au)



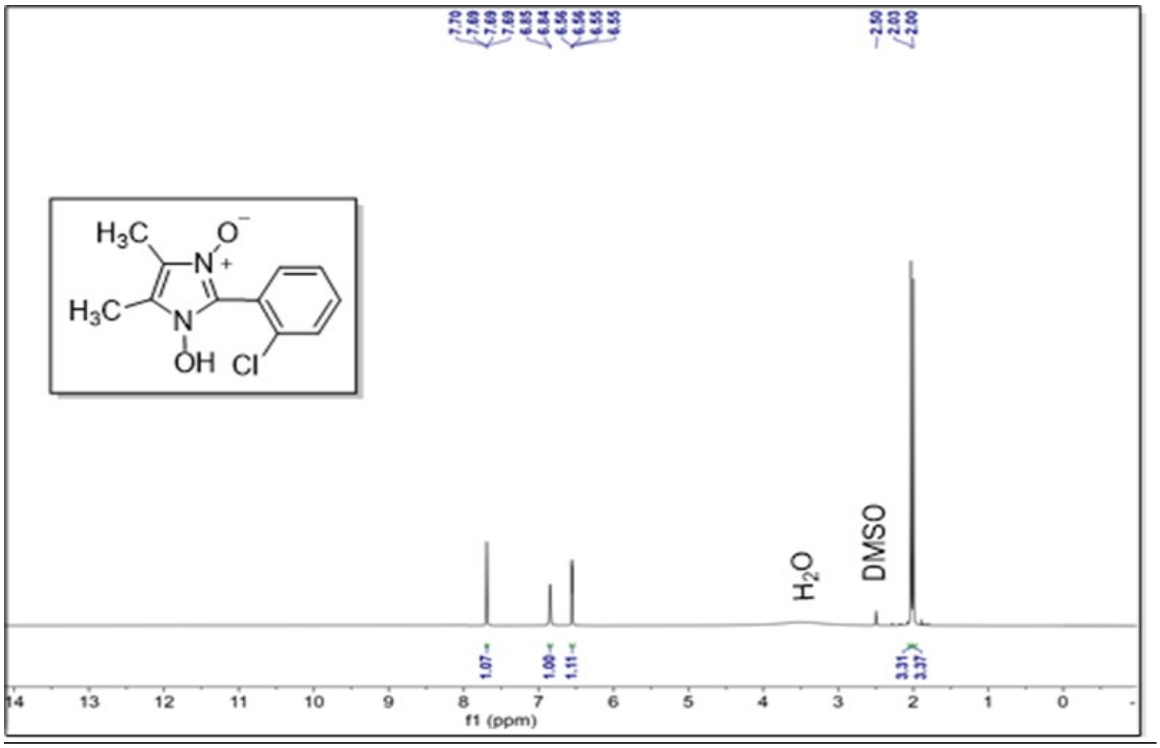
[13]CNMR - 2-(2-chlorophenyl)-1-hydroxy-4,5-dimethyl-1H-imidazole 3-oxide (4au)



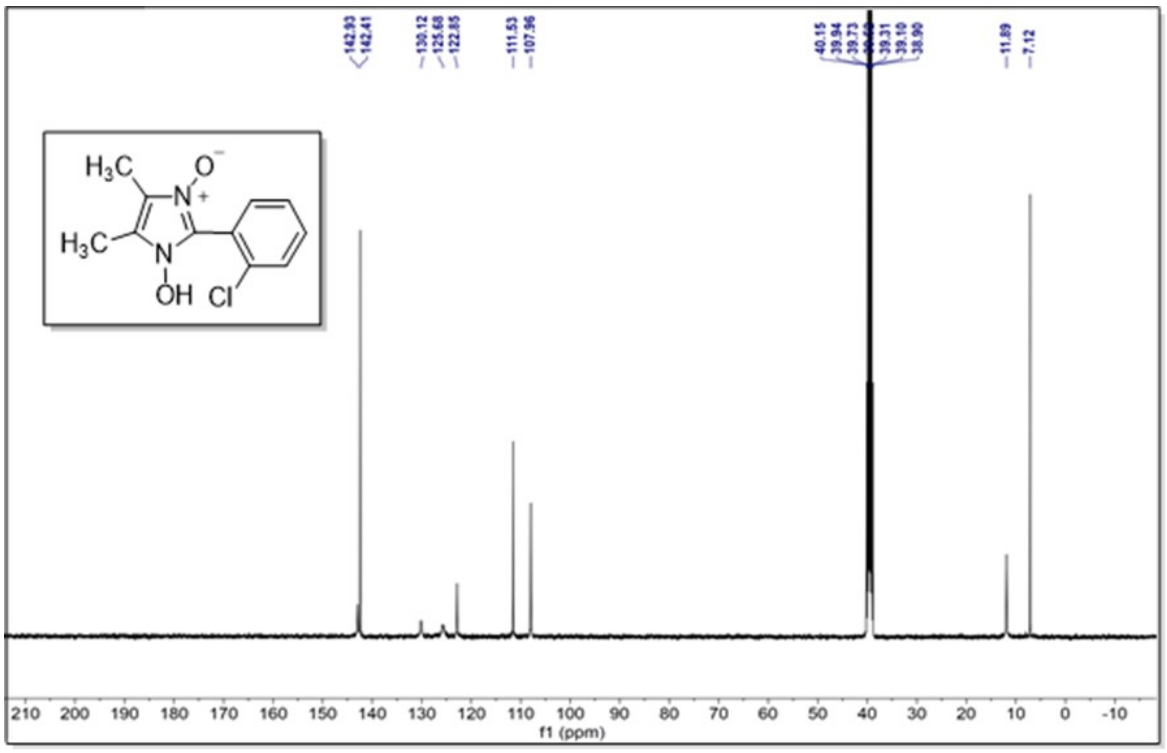
HRMS - 2-(2-chlorophenyl)-1-hydroxy-4,5-dimethyl-1H-imidazole 3-oxide (4au)



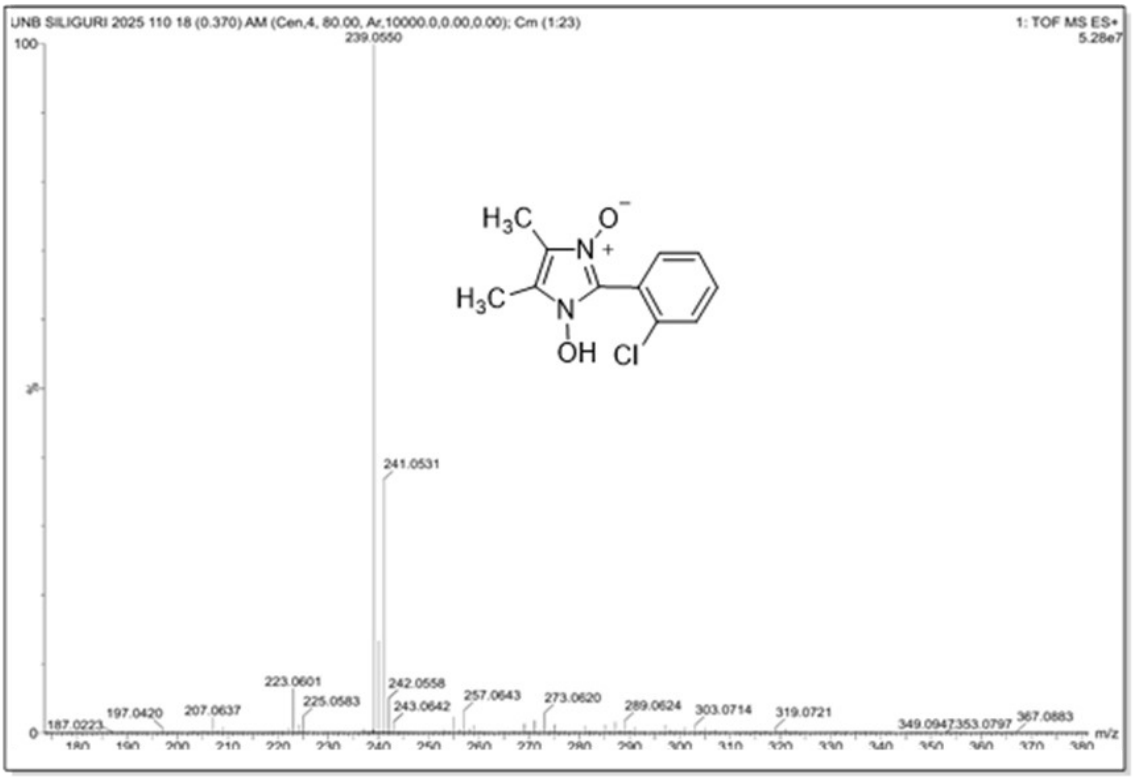
[1]HNMR - 2-(2-chlorophenyl)-1-hydroxy-4,5-dimethyl-1H-imidazole 3-oxide (4av)



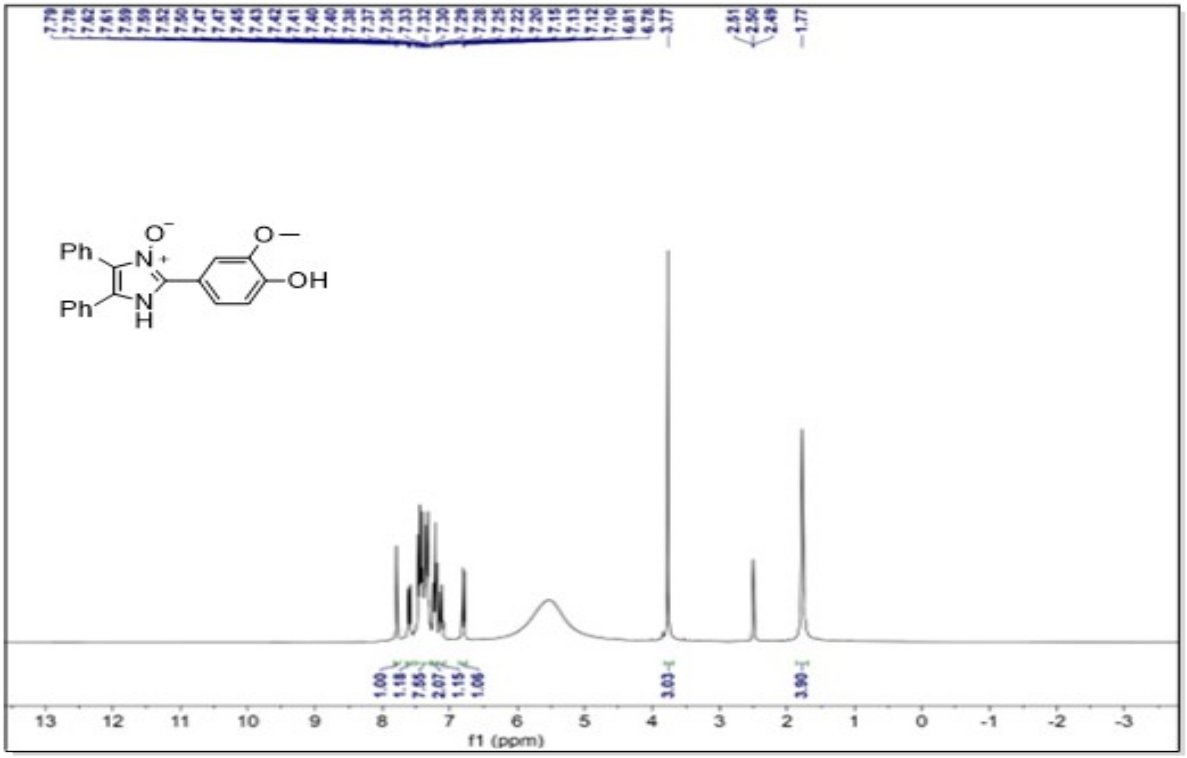
[13]CNMR - 2-(2-chlorophenyl)-1-hydroxy-4,5-dimethyl-1H-imidazole 3-oxide (4av)



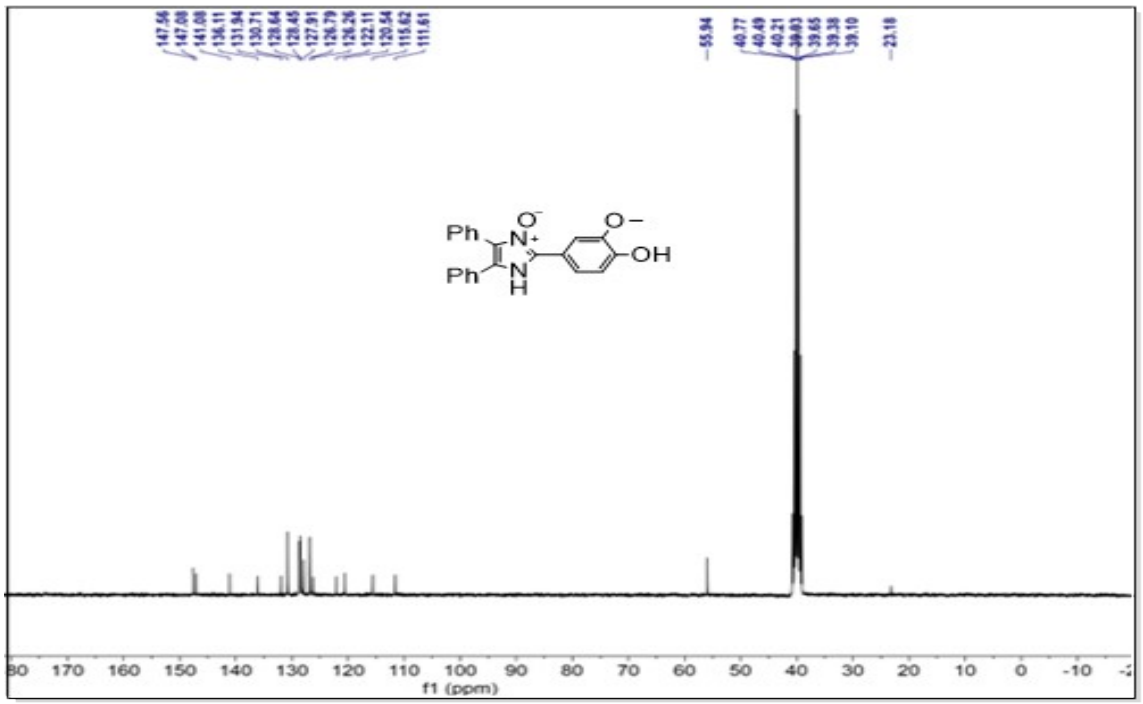
HRMS - 2-(2-chlorophenyl)-1-hydroxy-4,5-dimethyl-1H-imidazole 3-oxide (4av)



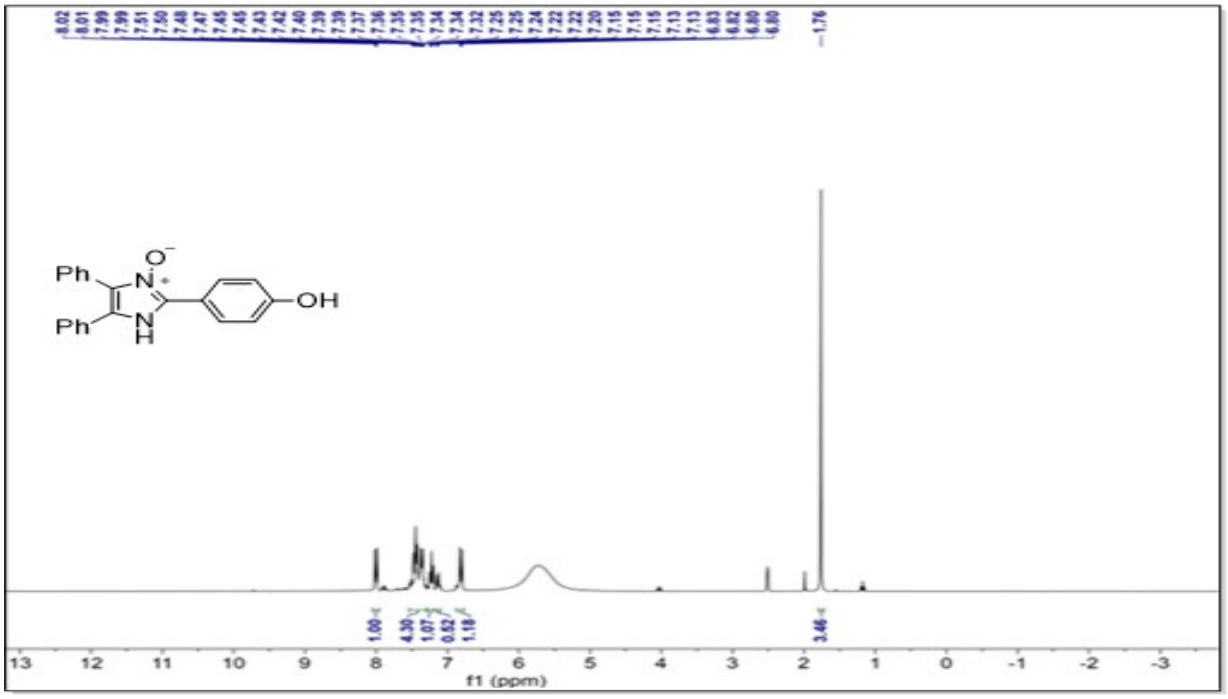
[1]HNMR - 2-(4-Hydroxy-3-methoxyphenyl)-4,5-diphenyl Imidazole 3-oxide (4ba)



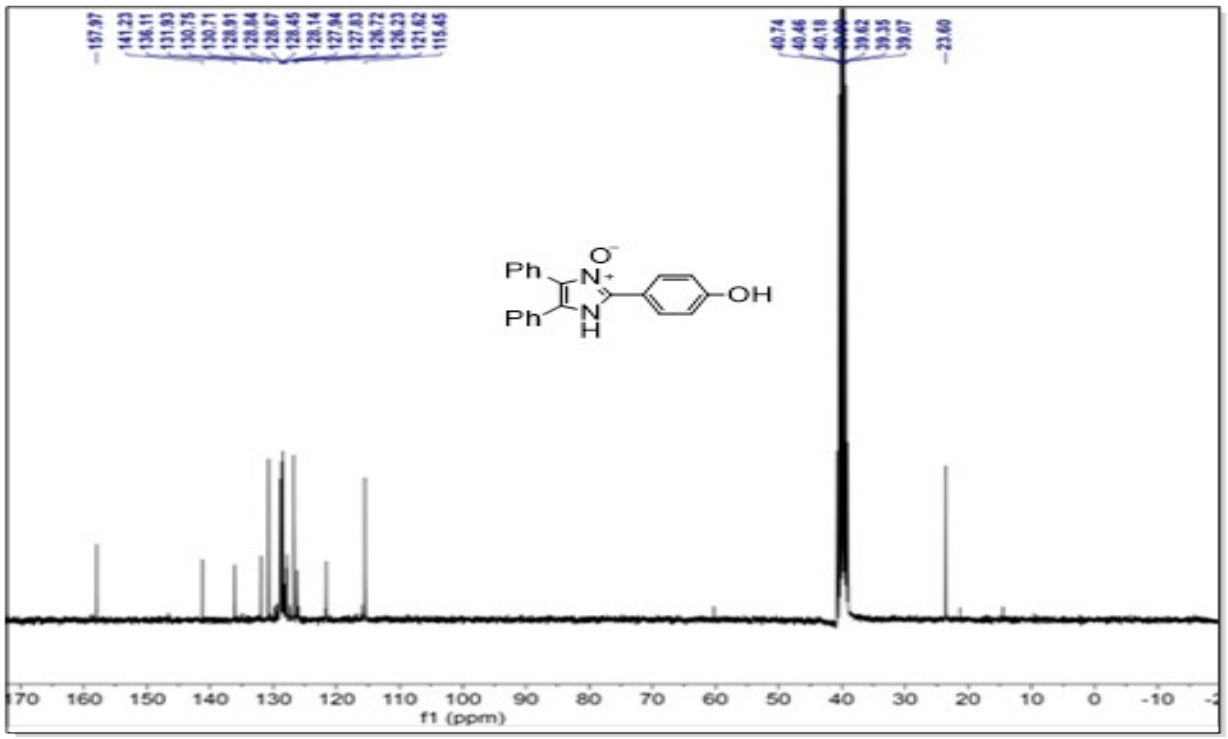
[13]CNMR - 2-(4-Hydroxy-3-methoxyphenyl)-4,5-diphenyl Imidazole 3-oxide (4ba)



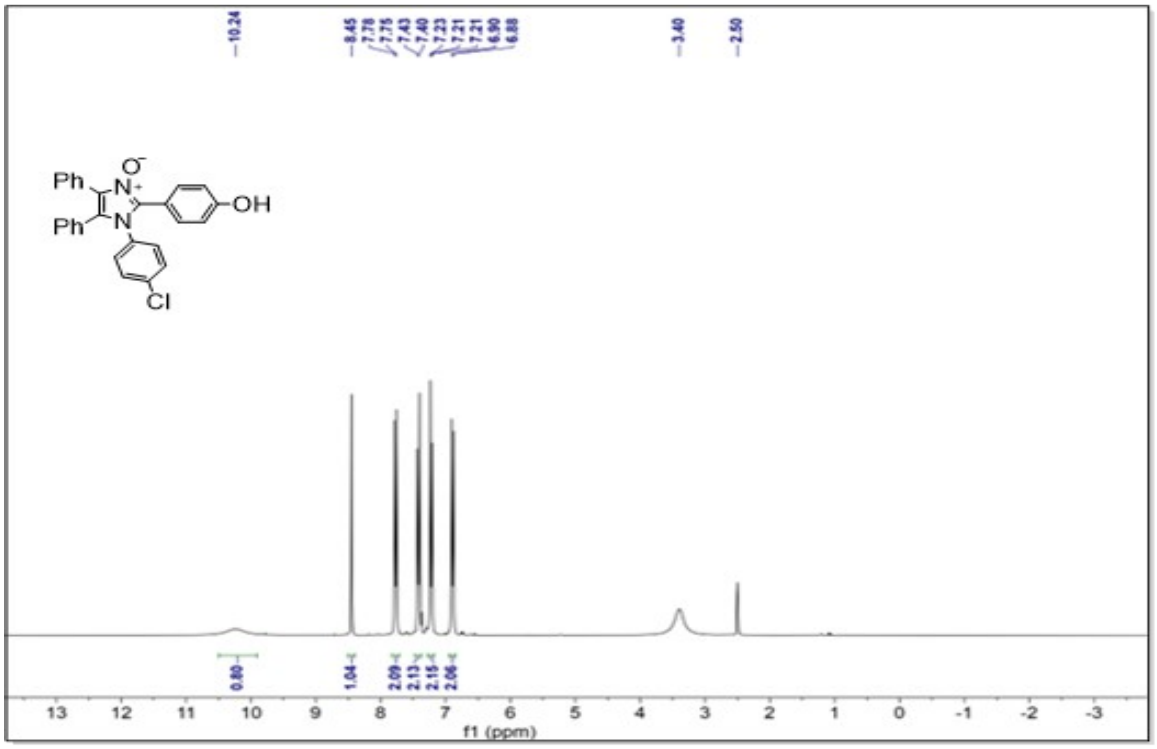
[1]HNMR - 2-(4-Hydroxyphenyl)-4, 5-diphenyl Imidazole 3-oxide (4bc)



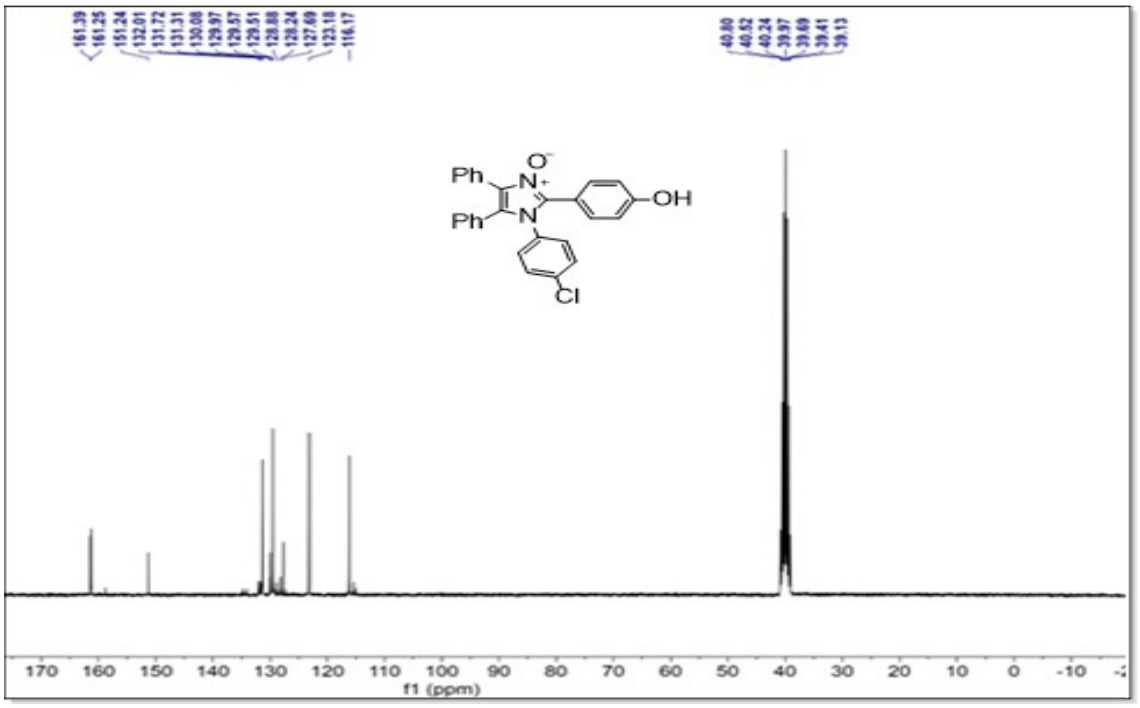
[13]CNMR - 2-(4-Hydroxyphenyl)-4, 5-diphenyl Imidazole 3-oxide (4bc)



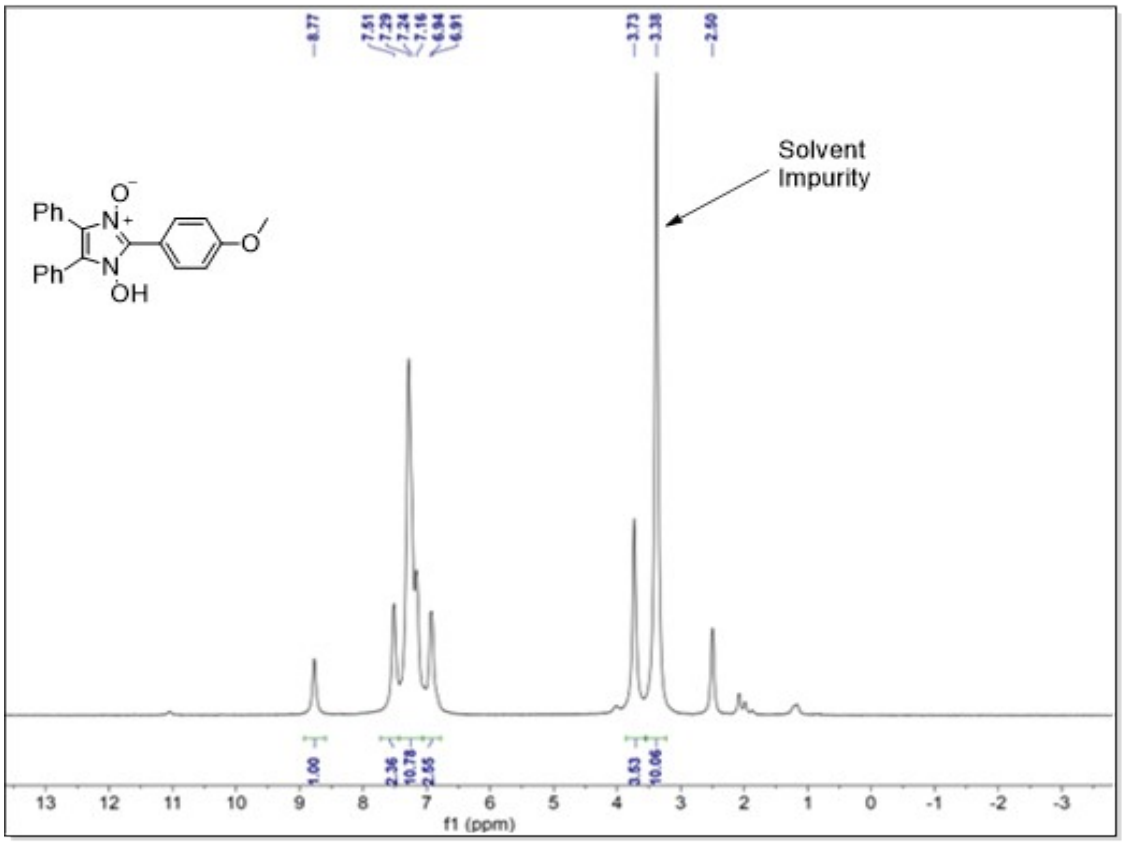
[1]HNMR - 1-(4-Chlorophenyl)-2-(4-hydroxyphenyl)-4,5-diphenyl Imidazole 3-oxide (4bd)



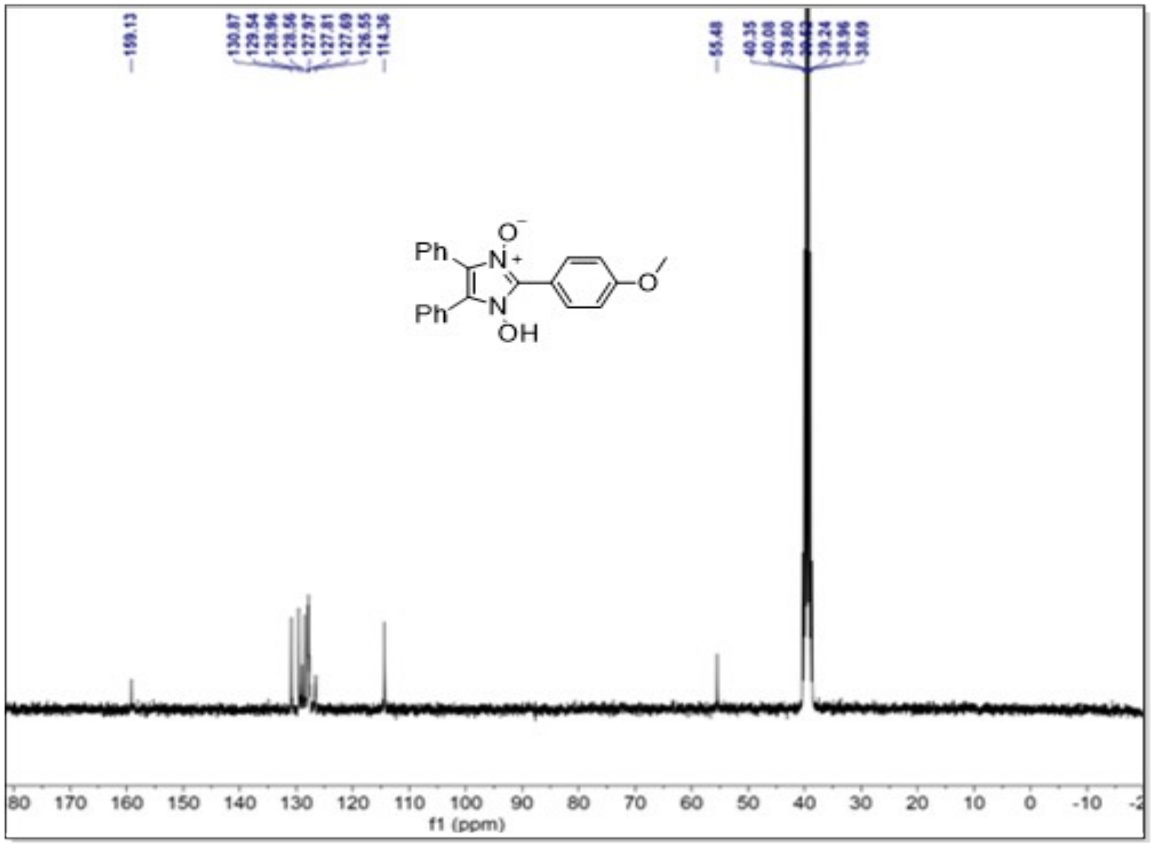
[13]CNMR - 1-(4-Chlorophenyl)-2-(4-hydroxyphenyl)-4,5-diphenyl Imidazole 3-oxide (4bd)



[1]HNMR - 1-Hydroxy-2-(4-methoxyphenyl)-4,5-diphenyl Imidazole 3-oxide (4be)



[13]CNMR - 1-Hydroxy-2-(4-methoxyphenyl)-4,5-diphenyl Imidazole 3-oxide (4be)



Green Chemistry Parameters Calculations

The following formulae were used to calculate the green chemistry parameters: Effective Mass Yield (EMY), Atom Economy (AE), Atom Efficiency (AEf), Carbon Efficiency (CE), Reaction Mass Efficiency (RME), Optimum Efficiency (OE), Process Mass Intensity (PMI), Mass Intensity (MI), Mass Productivity (MP), E-factor, and Solvent and Water Intensity (SI and WI)[3–16]. The calculated data for compounds **4aa—4be** are presented in Table S1, S2, and S3.

$$\text{EMY (\%)} = \frac{Mass\ of\ product}{Mass\ of\ non-benign\ reagents} \times 100$$

$$\text{AE (\%)} = \frac{Molecular\ weight\ of\ product}{Total\ molecular\ weight\ of\ reactants} \times 100$$

$$\text{Aef (\%)} = \text{AE} \times \text{Yield \%}$$

$$\text{CE (\%)} = \frac{Amount\ of\ carbon\ in\ the\ product}{Total\ carbon\ present\ in\ the\ reactants} \times 100$$

$$\text{RME (\%)} = \frac{Mass\ of\ isolated\ product}{Total\ mass\ of\ reactants} \times 100$$

$$\text{OE (\%)} = \frac{RME}{AE} \times 100$$

$$\text{PMI} = \frac{Total\ mass\ of\ input\ material\ in\ the\ whole\ process\ (including\ solvent(s)\ used\ during\ work-up)}{Mass\ of\ product}$$

$$\text{MI} = \frac{Total\ mass\ of\ input\ material\ in\ the\ whole\ process\ (excluding\ solvent(s))}{Mass\ of\ product}$$

$$\text{MP (\%)} = \frac{1}{MI} \times 100$$

$$\text{E-factor} = \frac{Total\ mass\ of\ wastes}{Mass\ of\ product} = \frac{Mass\ of\ raw\ materials\ -\ Mass\ of\ product}{Mass\ of\ product}$$

$$\text{SI} = \frac{Total\ mass\ of\ solvents\ excluding\ water\ in\ the\ whole\ process}{Mass\ of\ product}$$

$$\text{WI} = \frac{Total\ mass\ of\ water\ used\ in\ the\ whole\ process}{Mass\ of\ product}$$

Respective amounts

Reagents: 2,3-Butanedione monoxime: 0.101 g (MW: 101.1050 g); α-Benzil monoxime: 0.225 g (MW: 225.2470); Ammonium acetate: 0.077 g (MW: 77.0830); Hydroxylamine hydrochloride: 0.069 g (MW: 69.4880); 3-Nitrobenzaldehyde: 0.151 g (MW: 151.1210); 2-

Nitrobenzaldehyde: 0.151 g (MW: 151.1210); 4-Methoxybenzaldehyde: 0.136 g (MW: 136.1500); 3-Methoxybenzaldehyde: 0.136 g (MW: 136.1500); 4-(Dimethylamino)benzaldehyde: 0.149 g (MW: 149.1930); 4-Hydroxybenzaldehyde: 0.122 g (MW: 122.1230); 2-Hydroxybenzaldehyde: 0.122 g (MW: 122.1230); 4-Hydroxy-3-methoxybenzaldehyde or Vanillin: 0.152 g (MW: 152.1490); Furan-2-carbaldehyde: 0.096 g (MW: 96.0850); Butan-1-amine: 0.073 g (MW: 73.1390); Naphthalen-1-amine: 0.143 g (MW: 143.1890); 2-Nitroaniline: 0.138 g (MW: 138.126); 4-Aminobenzoic acid: 0.137 g (MW: 137.1380); 4-Methoxyaniline: 0.123 g (MW: 123.1550); 2-Pyridinecarboxaldehyde or Picolinaldehyde: 0.107 g (MW: 107.1120); 4-Chlorobenzaldehyde: 0.140 g (MW: 140.5660); 2-Chlorobenzaldehyde: 0.140 g (MW: 140.5660); 4-Chloroaniline: 0.127 g (MW:127.5710).

Solvents:

Mass of water used as solvents: 2 mL * 0.997 = 1.994 g

Mass of ethanol used as solvents: 3 mL * 0.789 = 2.367 g

Washing solvent EtOAc used: 1 mL * 0.902 = 0.902 g

Table S1. Related information for the calculations of the Green Metrics of the compounds **4aa-4be**.

Compounds	Molecular Weight (MW) of product	Yield (%)	Mass of Product (g)	Total Molecular Weight (MW) of Reactants	Total Mass of Reactants (g)
4aa	233.2270	98	0.229	329.3090	0.329
4ab	233.2270	95	0.222	329.3090	0.329
4ac	218.2560	80	0.175	314.3380	0.314
4ad	218.2560	82	0.18	314.3380	0.314
4ae	231.2990	83	0.193	327.3810	0.327
4af	204.2290	82	0.168	300.3110	0.300
4ag	204.2290	86	0.176	300.3110	0.300
4ah	234.2550	84	0.198	330.3370	0.330
4ai	178.1910	88	0.157	274.2730	0.274
4aj	260.3370	85	0.222	296.3670	0.296
4ak	330.3870	87	0.289	366.4170	0.366
4al	325.3240	80	0.261	361.3540	0.361
4am	324.3360	78	0.254	360.3660	0.360
4an	310.3530	91	0.283	346.3830	0.346
4ao	220.2280	84	0.186	292.7160	0.292
4ap	234.2550	86	0.202	306.7430	0.306
4aq	249.2260	97	0.242	321.7140	0.321
4ar	250.2540	86	0.216	322.7420	0.322
4as	205.2170	88	0.181	277.7050	0.277
4at	222.6720	96	0.214	318.7540	0.318
4au	222.6720	93	0.208	318.7540	0.318
4av	238.6710	97	0.231	311.1590	0.310
4ba	358.3970	82	0.295	454.4790	0.454
4bb	342.3980	77	0.265	438.4800	0.438
4bc	328.3710	80	0.264	424.4530	0.424
4bd	438.9110	81	0.357	474.9410	0.474
4be	358.3970	81	0.292	430.8850	0.430

Representative calculations of green metrics for 2-(3-Nitrophenyl)-4,5-dimethyl Imidazole 3-oxide [4aa]:

$$\text{EMY (\%)} = \frac{Mass\ of\ product}{Mass\ of\ non-benign\ reagents} \times 100 = \frac{0.229\ g}{(0.101\ g + 0.077\ g + 0.151\ g)} \times 100 = \frac{0.229\ g}{0.329\ g} \times 100 = 69.60$$

$$\text{AE (\%)} = \frac{Molecular\ weight\ of\ product}{Total\ molecular\ weight\ of\ reactants} \times 100 = \frac{233.227}{329.309} \times 100 = 70.82$$

$$\text{Aef (\%)} = \text{AE} \times \text{Yield (\%)} = 70.82 \times 98\ (\%) = 69.40$$

$$\text{CE (\%)} = \frac{Amount\ of\ carbon\ in\ the\ product}{Total\ carbon\ present\ in\ the\ reactants} \times 100 = \frac{\left(\frac{0.229}{233.227}\right) \times 11}{(0.001 \times 4 + 0.001 \times 2 + 0.001 \times 7)} \times 100 = 83.08$$

$$\text{RME (\%)} = \frac{Mass\ of\ isolated\ product}{Total\ mass\ of\ reactants} \times 100 = \frac{0.229\ g}{(0.101\ g + 0.077\ g + 0.151\ g)} \times 100 = 69.60$$

$$\text{OE (\%)} = \frac{RME}{AE} \times 100 = \frac{69.40}{70.82} \times 100 = 98.28$$

$$\text{PMI} = \frac{Total\ mass\ of\ input\ material\ in\ the\ whole\ process\ (including\ solvent(s)\ used\ during\ work-up)}{Mass\ of\ product} = \frac{0.101\ g + 0.077\ g + 0.151\ g + 0.05\ g\ (catalyst) + 1.99\ g\ (water) + 2.36\ g\ (ethanol)}{0.229\ g} = 24.58\ (\text{g/g})$$

$$\text{MI} = \frac{Total\ mass\ of\ input\ material\ in\ the\ whole\ process\ (excluding\ solvent(s))}{Mass\ of\ product} = \frac{(0.101\ g + 0.077\ g + 0.151\ g + 0.05\ g\ (catalyst))}{0.229\ g} = 1.66\ (\text{g/g})$$

$$\text{MP (\%)} = \frac{1}{MI} \times 100 = \frac{1}{1.66} \times 100 = 60.42$$

$$\text{E-factor} = \frac{Total\ mass\ of\ wastes}{Mass\ of\ product} = \frac{Mass\ of\ raw\ materials - Mass\ of\ product}{Mass\ of\ product} = \frac{0.101\ g + 0.077\ g + 0.151\ g - 0.229\ g}{0.229\ g} = 0.44$$

$$\text{SI} = \frac{Total\ mass\ of\ solvents\ excluding\ water\ in\ the\ whole\ process}{Mass\ of\ product} = \frac{2.36\ g + 0.9\ g}{0.229\ g} = 14.24\ (\text{g/g})$$

$$\text{WI} = \frac{Total\ mass\ of\ water\ used\ in\ the\ whole\ process}{Mass\ of\ product} = \frac{1.99\ g}{0.229\ g} = 8.69\ (\text{g/g})$$

Table S2. Green Chemistry Parameters (EMY, AE, AEf, CE, RME, OE and MP) for the compounds **4aa-4be**.

Compound	MW	Yield (%)	Mass of Product	EMY (%)	AE (%)	AEf (%)	CE (%)	RME (%)	OE (%)	MP (%)
4aa	233.2270	98%	229	69.60	70.82	69.40	83.08	69.60	98.28	60.42
4ab	233.2270	95	222	67.48	70.82	67.28	80.54	67.48	95.28	58.58
4ac	218.2560	80	175	55.73	69.43	55.54	68.72	55.73	80.27	48.08
4ad	218.2560	82	180	57.32	69.43	56.93	70.69	57.32	82.56	49.45
4ae	231.2990	83	193	59.02	70.56	58.56	72.32	59.02	83.65	51.19
4af	204.2290	82	168	56.00	68.01	55.77	69.61	56.00	82.34	48.00
4ag	204.2290	86	176	58.67	68.01	58.49	72.92	58.67	86.26	50.29
4ah	234.2550	84	198	60.00	70.91	59.56	72.45	60.00	84.61	52.11
4ai	178.1910	88	157	57.30	64.97	57.17	72.09	57.30	88.19	48.46
4aj	260.3370	85	222	75.00	87.84	74.66	85.27	75.00	85.38	64.16
4ak	330.3870	87	289	78.96	90.17	78.45	87.50	78.96	87.57	69.47
4al	325.3240	80	261	72.30	90.03	72.02	80.23	72.30	80.31	63.50
4am	324.3360	78	254	70.56	90.00	70.20	78.31	70.56	78.40	61.95
4an	310.3530	91	283	81.79	89.60	81.54	91.19	81.79	91.29	71.46
4ao	220.2280	84	186	63.70	75.24	63.20	84.46	63.70	84.66	54.39
4ap	234.2550	86	202	66.01	76.37	65.68	86.23	66.01	86.44	56.74
4aq	249.2260	97	242	75.39	77.47	75.15	97.10	75.39	97.31	65.23
4ar	250.2540	86	216	67.08	77.53	66.68	86.31	67.08	86.52	58.06
4as	205.2170	88	181	65.34	73.90	65.03	88.20	65.34	88.42	55.35
4at	222.6720	96	214	67.30	69.86	67.07	81.32	67.30	96.33	58.15
4au	222.6720	93	208	65.41	69.86	64.97	79.04	65.41	93.63	56.52
4av	238.6710	97	231	74.52	76.70	74.40	96.79	74.52	97.15	64.17
4ba	358.3970	82	295	64.98	78.86	64.67	74.83	64.98	82.40	58.53
4bb	342.3980	77	265	60.50	78.09	60.13	70.36	60.50	77.48	54.30
4bc	328.3710	80	264	62.26	77.37	61.90	72.74	62.26	80.48	55.70
4bd	438.9110	81	357	75.32	92.41	74.85	81.34	75.32	81.50	68.13
4be	358.3970	81	292	67.91	83.18	67.38	81.47	67.91	81.64	60.83

Higher is the value, greener is the process.

Table S3. Green Chemistry Parameters (PMI, MI, E-factor, SI and WI) for the compounds **4aa-4be**.

Product	PMI (g/g)	MI (g/g)	E-Factor (g/g)	SI (g/g)	WI (g/g)
4aa	24.58	1.66	0.44	14.24	8.69
4ab	25.36	1.71	0.48	14.68	8.96
4ac	32.08	2.08	0.79	18.63	11.37
4ad	31.19	2.02	0.74	18.11	11.06
4ae	29.16	1.95	0.69	16.89	10.31
4af	33.33	2.08	0.79	19.40	11.85
4ag	31.82	1.99	0.70	18.52	11.31
4ah	28.43	1.92	0.67	16.46	10.05
4ai	35.50	2.06	0.75	20.76	12.68
4aj	25.21	1.56	0.33	14.68	8.96
4ak	19.61	1.44	0.27	11.28	6.89
4al	21.69	1.57	0.38	12.49	7.62
4am	22.28	1.61	0.42	12.83	7.83
4an	19.95	1.40	0.22	11.52	7.03
4ao	30.06	1.84	0.57	17.53	10.70
4ap	27.75	1.76	0.51	16.14	9.85
4aq	23.23	1.53	0.33	13.47	8.22
4ar	26.03	1.72	0.49	15.09	9.21
4as	30.81	1.81	0.53	18.01	10.99
4at	26.25	1.72	0.49	15.23	9.30
4au	27.01	1.77	0.53	15.67	9.57
4av	24.29	1.56	0.34	14.11	8.61
4ba	19.51	1.71	0.54	11.05	6.75
4bb	21.65	1.84	0.65	12.30	7.51
4bc	21.68	1.80	0.61	12.35	7.54
4bd	16.17	1.47	0.33	9.13	5.57
4be	19.62	1.64	0.47	11.16	6.82

Lower is the value, better is the process.

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