Supporting Information (56 pages)

Photochemical conversion of isoxazoles to 5-hydroxyimidazolines

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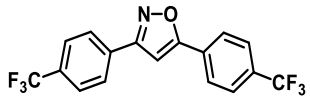
1. General Techniques

NMR spectra were recorded on a Bruker biospin AVANCE Ⅱ (400 MHz for ^{1}H, 100 MHz for ^{13}C) or a Bruker biospin AVANCE Ⅲ (500 MHz for ^{1}H, 125 MHz for ^{13}C) instrument in the indicated solvent. Chemical shifts are reported in units parts per million (ppm) relative to the signal (0.00 ppm) for internal tetramethylsilane for solutions in $CDCl_3$ (7.26 ppm for ^{1}H, 77.0 ppm for ^{13}C) or DMSO-d_6 (2.50 ppm for ^{1}H) or CD_3OD (3.31 ppm for ^{1}H, 49.0 ppm for ^{13}C). Multiplicities are reported using the following abbreviations: s; singlet, d; doublet, dd; doublet of doublets, t; triplet, q; quartet, m; multiplet, br; broad, *J*; coupling constants in Hertz. IR spectra were recorded on a JASCO FT/IR-4200 spectrometer. Only the strongest and/or structurally important peaks are reported as IR data given in $cm^{-1.}$ ESI-TOF Mass spectra were measured using a Bruker micrOTOF II. HRMS (ESI-TOF) was calibrated as Leu-enkephalin or sodium formate. EI Mass spectra were measured using a JMS-700 Mstation. HRMS (EI, 70 eV) was calibrated as perfluorokerosene. All reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) with UV light (254 nm), and were visualized using an aqueous alkaline $KMnO_4$ solution. Gel permeation chromatography (GPC) for purification was performed on Japan Analytical Industry Model LC-9225 NEXT (recycling preparative HPLC) and a Japan Analytical Industry Model UV-600 NEXT ultra violet detector with a polystyrene gel column (JAIGEL-1H, 20 mm × 600 mm), using chloroform as solvent (3.5 mL/min). Column chromatography was performed on Silica Gel 60 N, purchased from Fuji Silysia Chemical Ltd. Preparative thin-layer chromatography (PTLC) was performed using Wakogel B5-F silica coated plates (1.0 mm) prepared in our laboratory. All the photochemical reactions were performed using a 6W UV lamp (wavelength: 254 nm), which was purchased from AS ONE Corporation (model: SLUV-6). A fluorinated ethylene propylene copolymer (FEP) tube was purchased from Flon Industry Co., Ltd (inner diameter: 1.0 mm).

2. Preparation of substrates

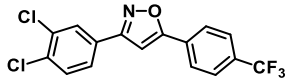
Representative procedure for synthesis of 3,5-bis{4-(trifluoromethyl)phenyl}isoxazole (1f)

To a mixture of *N*-hydroxy-4-(trifluoromethyl)benzimidoyl chloride[1] (894.3 mg, 4.00 mmol, 1.0 equiv.) and 1-ethynyl-4-(trifluoromethyl)benzene (714.5 mg, 4.20 mmol, 1.05 equiv.) in dichloromethane (12.0 mL), triethylamine (1.39 mL, 10.0 mmol, 2.5 equiv.) was added dropwise under an argon atmosphere at room temperature. After being stirred at 40 °C in an oil bath for 30 min, the reaction mixture was passed through a pad of silica gel and concentrated *in vacuo*. The residue was purified by silica gel column chromatography with hexane : ethyl acetate (97 : 3) to afford **1f** (496.0 mg, 1.39 mmol, 35%) as a white solid. Mp 129-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.95 (m, 4 H), 7.78-7.75 (m, 4H), 6.96 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4, 162.0, 132.2 (q, $J_{C\text{-}F}$ = 32.9 Hz), 132.1, 132.1 (q, $J_{C\text{-}F}$ = 32.9 Hz), 130.2, 127.2, 126.1, 126,0, 126.0, 123.8 (q, $J_{C\text{-}F}$ = 272.2 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.2 Hz), 98.9; FT-IR (neat): 1647, 1541, 1456, 1438, 1386, 1329, 1173, 1111, 1016, 951, 846 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{17}H_9F_6NO + Na]^+$ 380.0481: found 380.0475.



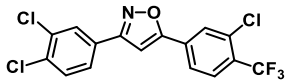
3-(3,4-Dichlorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1a)

Following the representative procedure using 3,4-dichloro-*N*-hydroxybenzimidoyl chloride, purification by PTLC with hexane : ethyl acetate (95 : 5) afforded **1a** (124 mg, 0.345 mmol, 82%) as a white solid. Mp 133-135 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96-7.94 (m, 3H), 7.77 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 8.5 Hz, 1H), 7.57 (d, J = 8.5 Hz, 1H), 6.90 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4, 161.3, 134.5, 133.4, 132.2 (q, J_{C-F} = 32.9 Hz), 131.1, 130.1, 128.7, 128.6, 126,2 (q, J_{C-F} = 5.6 Hz), 125.9, 123.6 (q, J_{C-F} = 272.3 Hz), 98.7; FT-IR (neat): 1646, 1602, 1492, 1444, 1325, 1169, 1068, 1031, 950, 891, 847 cm^{-1}; HRMS (EI, 70 eV): calcd. for $[C_{16}H_8Cl_2F_3NO]^+$, 356.9935: found 356.9934.



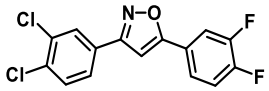
5-{2-Chloro-4-(trifluoromethyl)phenyl}-3-(3,4-dichlorophenyl)isoxazole (1b)

Following the representative procedure using 3,4-dichloro-*N*-hydroxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1b** (217 mg, 0.554 mmol, 69%) as a white solid. Mp 122-124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 2.0 Hz, 1H), 7.80 (s, 1H), 7.73 (dd, J = 8.3, 2.0 Hz, 1H), 7.67 (d, J = 8.3, 1.1 Hz, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.32 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 161.2, 134.6, 133.4, 133.0 (q, J_{C-F} = 33.8 Hz), 132.2, 131.1, 129.8, 129.0, 128.7, 128.6, 128.0 (q, J_{C-F} = 3.9 Hz), 126.0, 124.2 (q, J_{C-F} = 3.5 Hz), 122.8 (q, J_{C-F} = 273.1 Hz), 103.3; FT-IR (neat): 1645, 1427, 1390, 1358, 1322, 1269, 1174, 1128, 1085, 1032, 886 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{16}H_7Cl_3F_3NO + Na]^+$ 413.9438: found 413.9435.



3-(3,4-Dichlorophenyl)-5-(3,4-difluorophenyl)isoxazole (1c)

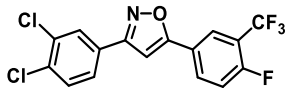
Following the representative procedure using 3,4-dichloro-*N*-hydroxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1c** (56.7 mg, 0.174 mmol, 22%) as a white solid. Mp 144-145 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.70-7.62 (m, 2H), 7.57-7.55 (m, 2H), 7.33-7.26 (m, 1H), 6.76 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 161.2, 151.6 (dd, J_{C-F} = 12.7, 254.1 Hz), 150.7 (dd, J_{C-F} = 13.2, 250.4 Hz), 134.4, 133.4, 131.1, 128.7, 128.6, 125.9, 124,1-124.0 (m), 122.5-122.4 (m), 118.3 (d, J_{C-F} = 18.0 Hz), 115.2 (d, J_{C-F} = 19.4 Hz), 97.8; FT-IR (neat): 1645, 1516, 1497, 1432, 1360, 1273, 1178, 878, 821 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{15}H_7Cl_2F_2NO + Na]^+$ 347.9765: found 347.9768.



3-(3,4-Dichlorophenyl)-5-{4-fluoro-3-(trifluoromethyl)phenyl}isoxazole (1d)

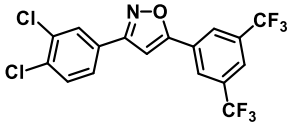
Following the representative procedure using 3,4-dichloro-*N*-hydroxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1d** (106.4 mg, 0.283 mmol, 57%) as a white solid. Mp 100-101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 6.3 Hz, 1H), 8.02-7.99 (m, 1H),

7.93 (d, J = 1.4 Hz, 1H), 7.68 (dd, J = 8.3, 1.5 Hz, 1H), 7.55 (d, J = 8.3 Hz, 1H), 7.35 (dd, J = 9.1, 9.2 Hz, 1H), 6.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 161.3, 160.6 (dq, $J_{C\text{-}F}$ = 1.9, 261.7 Hz), 134.5, 133.4, 131.3 (d, $J_{C\text{-}F}$ = 9.1 Hz), 131.1, 128.6, 128.5, 125.9, 125,0 (dq, $J_{C\text{-}F}$ = 1.7, 4.2 Hz), 123.7 (d, $J_{C\text{-}F}$ = 4.1 Hz), 122.0 (q, $J_{C\text{-}F}$ = 272.5 Hz), 119.5 (dq, $J_{C\text{-}F}$ = 13.4, 33.6 Hz), 118.1 (dq, $J_{C\text{-}F}$ = 17.3, 4.3 Hz), 98.0 (d, J = 3.6 Hz); FT-IR (neat): 1629, 1611, 1510, 1488, 1415, 1332, 1291, 1276, 1217, 1170, 1098, 1032, 968, 836 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{16}H_7Cl_2F_4NO + Na]^+$ 397.9733: found 397.9728.



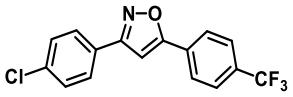
5-{3,5-Bis(trifluoromethyl)phenyl}-3-(3,4-dichlorophenyl)isoxazole (1e)

Following the representative procedure using 3,4-dichloro-*N*-hydroxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1e** (76.2 mg, 0.179 mmol, 26%) as a white solid. Mp 129-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 2 H), 7.97-7.92 (m, 2H), 7.68 (d, J = 7.8 Hz, 1H), 7.56-7.53 (m, 1H), 6.99 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7, 161.5, 134.8, 133.5, 132.9 (q, $J_{C\text{-}F}$ = 33.9 Hz), 131.1, 128.9, 128.7, 128.2, 125.9, 125,8 (q, $J_{C\text{-}F}$ = 3.5 Hz), 123.9-123.7 (m), 122.8 (q, $J_{C\text{-}F}$ = 272.8 Hz), 99.4; FT-IR (neat): 1634, 1557, 1456, 1416, 1371, 1357, 1279, 1188, 1093, 1034, 980, 845 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{17}H_7Cl_2F_6NO + Na]^+$ 447.9701: found 447.9706.



3-(4-Chlorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1g)

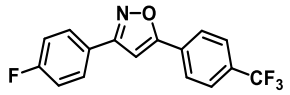
Following the representative procedure using 4-chloro-*N*-hydroxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1g** (141.9 mg, 0.438 mmol, 44%) as a white solid. Mp 129-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.2 Hz, 2H), 7.81-7.79 (m, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.48-7.44 (m, 2H), 6.90 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 162.2, 136.3, 132.0 (q, $J_{C\text{-}F}$ = 32.9 Hz), 130.3, 129.3, 128.1, 127.2, 126.1, 126,1 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.5 Hz), 98.7; FT-IR (neat): 1641, 1603, 1549, 1494, 1468, 1413, 1265, 1175, 1098, 1066, 950, 848 $^{-1}$; HRMS (ESI-TOF): calcd for $[C_{16}H_9ClF_3NO + Na]^+$ 346.0217: found 346.0216.



3-(4-Fluorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1h)

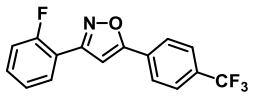
Following the representative procedure using 4-fluoro-*N*-hydroxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1h** (170.3 mg, 0.554 mmol, 69%) as a white solid. Mp 129-132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.2 Hz, 2H), 7.87-7.83 (m, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.18 (dd, J = 8.6, 8.6 Hz, 2H), 6.88 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 163.9 (d,

$J_{C\text{-}F}$ = 250.3 Hz), 162.2, 131.9 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.4, 128.7 (d, $J_{C\text{-}F}$ = 8.5 Hz), 126,1 (q, $J_{C\text{-}F}$ = 3.6 Hz), 126.1, 124.9 (d, $J_{C\text{-}F}$ = 3.3 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.5 Hz), 116.1 (d, $J_{C\text{-}F}$ = 21.9 Hz), 98.7; FT-IR (neat): 1607, 1511, 1435, 1413, 1333, 1173, 1112, 1087, 1070, 951, 845 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{16}H_9F_4NO + Na]^+$ 330.0512: found 330.0507.



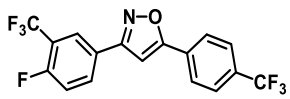
3-(2-Fluorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1i)

Following the representative procedure using 2-fluoro-*N*-hydroxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1i** (118.9 mg, 0.387 mmol, 39%) as a white solid. Mp 129-132 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (t, *J* = 7.3, 7.4 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.48-7.44 (m, 1H), 7.29-7.26 (m, 1H), 7.23-7.19 (m, 1H), 7.08 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 160.3 (d, $J_{C\text{-}F}$ = 251.6 Hz), 131.9 (d, $J_{C\text{-}F}$ = 8.6 Hz), 131.9 (q, $J_{C\text{-}F}$ = 32.7 Hz), 130.5, 129.1 (d, $J_{C\text{-}F}$ = 2.6 Hz), 126.1, 126,1 (q, $J_{C\text{-}F}$ = 3.9 Hz), 124.7 (d, $J_{C\text{-}F}$ = 3.4 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.4 Hz), 116.8 (d, $J_{C\text{-}F}$ = 21.9 Hz), 116.4 (d, $J_{C\text{-}F}$ = 21.9 Hz), 101.5 (d, $J_{C\text{-}F}$ = 9.3 Hz); FT-IR (neat): 1620, 1581, 1502, 1469, 1432, 1327, 1221, 1168, 1112, 1067, 951, 845 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{16}H_9F_4NO + Na]^+$ 330.0512: found 330.0509.



3-{4-Chloro-3-(trifluoromethyl)phenyl}-5-{4-(trifluoromethyl)phenyl}isoxazole (1j)

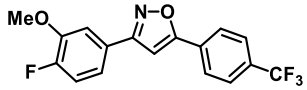
Following the representative procedure using 4-fluoro-*N*-hydroxy-3-(trifluoromethyl)benzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1j** (166.4 mg, 0.443 mmol, 55%) as a white solid. Mp 114-116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11-8.06 (m, 2H), 7.96 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.34 (dd, *J* = 9.2, 9.2 Hz, 1H), 6.93 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 161.2, 160.7 (dq, J = 2.0, 260.8 Hz), 132.3 (q, $J_{C\text{-}F}$ = 32.8 Hz), 132.2 (d, $J_{C\text{-}F}$ = 8.9 Hz), 130.1, 126.2 (q, $J_{C\text{-}F}$ = 3.7 Hz), 126.2, 125.9-125.8 (m), 125.4 (q, $J_{C\text{-}F}$ = 3.8 Hz), 123.6 (q, $J_{C\text{-}F}$ = 272.5 Hz), 122.2 (d, $J_{C\text{-}F}$ =272.7 Hz), 119.5-119.1 (m), 117.9 (d, $J_{C\text{-}F}$ = 21.2 Hz), 98.6; FT-IR (neat): 1627, 1606, 1505, 1415, 1379, 1327, 1242, 1157, 1097, 1057, 1020, 951, 850 cm^{-1}; HRMS (EI, 70 eV): calcd. for $[C_{17}H_8F_7NO]^+$, 375.0494: found 375.0494.



3-(4-Fluoro-3-methoxyphenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1k)

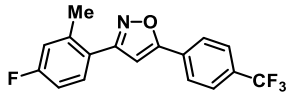
Following the representative procedure using 4-fluoro-*N*-hydroxy-3-methoxybenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1k** (222.5mg,

0.660 mmol, 82%) as a white solid. Mp 121-123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 7.52 (dd, J = 1.6, 8.1 Hz, 1H), 7.31-7.27 (m, 1H), 7.16-7.11 (m, 1H), 6.85 (s, 1H), 3.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 162.3, 153.6 (d, $J_{C\text{-}F}$ = 250.6 Hz), 148.1 (d, $J_{C\text{-}F}$ = 11.1 Hz), 131.9 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.3, 126.0, 125.1 (d, $J_{C\text{-}F}$ = 3.9 Hz), 123.6 (q, $J_{C\text{-}F}$ = 272.2 Hz), 119.7 (d, $J_{C\text{-}F}$ = 7.4 Hz), 116.4 (d, $J_{C\text{-}F}$ = 19.2 Hz), 111.4 (d, $J_{C\text{-}F}$ = 3.0 Hz), 98.7 (d, $J_{C\text{-}F}$ = 3.7 Hz), 56.2; FT-IR (neat): 2979, 1606, 1584, 1574, 1510, 1412, 1370, 1220, 1136, 1035, 1013, 948, 931, 838 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{17}H_{11}F_4NO_2 + Na]^+$ 360.0618: found 360.0614.



3-(4-Fluoro-2-methylphenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1l)

Following the representative procedure using 4-fluoro-*N*-hydroxy-2-methylbenzimidoyl chloride, purification by silica gel column chromatography with hexane: ethyl acetate (97 : 3) afforded **1l** (180.5mg, 0.562 mmol, 70%) as a white solid. Mp 71-72 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.9 Hz, 2H), 7.73 (d, J = 7.9 Hz, 2H), 7.54-7.50 (m, 1H), 7.03-6.96 (m, 2H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 163.3 (d, $J_{C\text{-}F}$ = 249.4 Hz), 162.0, 139.7 (d, $J_{C\text{-}F}$ = 8.2 Hz), 131.9 (q, $J_{C\text{-}F}$ = 32.7 Hz), 131.2 (d, $J_{C\text{-}F}$ = 8.8 Hz), 130.4, 126.0, 126,0 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.5 (d, $J_{C\text{-}F}$ = 2.9 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.3 Hz), 117.8 (d, $J_{C\text{-}F}$ = 21.4 Hz), 113.1 (d, $J_{C\text{-}F}$ = 21.5 Hz), 101.4; FT-IR (neat): 2924, 1613, 1587, 1505, 1446, 1416, 1284, 1234, 1191, 1158, 1011, 967, 874, 845 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{17}H_{11}F_4NO + Na]^+$ 344.0669: found 344.0669.

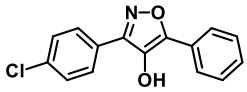


3-(4-Chlorophenyl)-5-phenylisoxazol-4-ol

To a stirred solution of 3-(4-chlorophenyl)-4-iodo-5-phenylisoxazole[2)] (131.3 mg, 0.344 mmol, 1.0 equiv.) in THF (3.44 mL), ^{i}PrMgCl･LiCl in THF (0.82 M, 0.504 mL, 1.2 equiv.) was added dropwise at -78 °C under an argon atmosphere. After being stirred at the same temperature for 30 min, 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborane (84 μL, 0.413 mmol, 1.2 equiv.) was added. After being stirred at 0 °C for 1 h, the reaction mixture was poured into water with ethyl acetate, then acidified with 1 M aq. HCl. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was dissolved in THF (1.1 mL), then H_2O (980 μL), NaOH (41.3 mg, 1.03 mmol, 3.0 equiv.) and 30% H_2O_2 (117 μL, 1.03 mmol, 3.0 equiv.) were added to the solution at 0 °C under an argon atmosphere. After being stirred at 0 °C for 30 min, the reaction mixture was poured into ethyl acetate. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel (hexane : ethyl acetate = 70 : 20) to give 3-(4-chlorophenyl)-5-phenylisoxazol-4-ol (55.9 mg, 0.206 mmol, 60 %) as a white solid.

Mp 147-149 °C. ^{1}H NMR (400 MHz, CD_3OD) δ 8.00-7.96 (m, 4H), 7.54-7.48 (m, 4H), 7.43-7.39 (m, 1H); ^{13}C

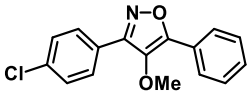
NMR (125 MHz, CD_3OD) δ 157.2, 156.7, 137.4, 134.7, 130.7, 130.6, 130.5, 130.4, 129.6, 129.1, 126.6; FT-IR (neat): 3026, 2925, 1631, 1599, 1444, 1392, 1306, 1270, 1208, 1146, 1049, 945, 919, 838 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{15}H_{10}ClNO_2 - H]^-$ 270.0327: found 270.0332.



3-(4-Chlorophenyl)-4-methoxy-5-phenylisoxazole (1m)

To a stirred solution of 3-(4-chlorophenyl)-5-phenylisoxazol-4-ol (252.0 mg, 0.927 mmol, 1.0 equiv.) in DMF (1.86 mL), Cs_2CO_3 (393.9 mg, 1.21 mmol, 1.3 equiv.) and methyl iodide (115.5 μL, 1.85 mmol, 2.0 equiv.) were added at room temperature. After being stirred at 50 °C in an oil bath for 30 min, the reaction mixture was poured into water. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by PTLC with hexane : ethyl acetate = 90 : 10 to give 3-(4-chlorophenyl)-4-methoxy-5-phenylisoxazole (**1m**) (187.5 mg, 0.656 mmol, 71%).

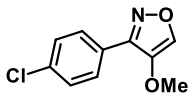
Colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97-7.94 (m, 4H), 7.53-7.44 (m, 5H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 155.9, 137.0, 136.1, 129.8, 129.2, 129.0, 128.4, 127.0, 126.7, 125.4, 61.6; FT-IR (neat): 2935, 1658, 1601, 1549, 1461, 1445, 1423, 1386, 1308, 1215, 1051, 1015, 985, 836 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{16}H_{12}ClNO_2 + Na]^+$ 308.0449: found 308.0443.



3-(4-Chlorophenyl)-4-methoxyisoxazole (1n)

To a stirred solution of 3-(4-chlorophenyl)-isoxazol-4-ol[3)] (101.3 mg, 0.518 mmol, 1.0 equiv.) in DMF (1.0 mL), Cs_2CO_3 (253.1 mg, 0.777 mmol, 1.5 equiv.) and methyl iodide (65 μL, 1.04 mmol, 2.0 equiv.) was added at room temperature. After being stirred at 50 °C in an oil bath for 30 min, the reaction mixture was poured into water. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography on silica gel with hexane : ethyl acetate = 90 : 10 to give 3-(4-chlorophenyl)-4-methoxyisoxazole (**1n**) (78.3 mg, 0.274 mmol, 53%) as a white solid.

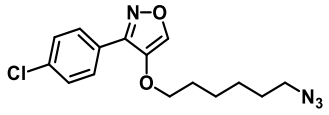
Mp 63-65 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.0, 143.3, 139.6, 135.8, 128.9, 128.5, 126.5, 59.6; FT-IR (neat): 3104, 2834, 1570, 1514, 1466, 1377, 1288, 1258, 1110, 1002, 918, 898, 829 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{10}H_8ClNO_2 + H]^+$ 210.0316: found 210.0309.



4-{(6-Azidohexyl)oxy}-3-(4-chlorophenyl)isoxazole (1o)

To a stirred solution of 3-(4-chlorophenyl) isoxazol-4-ol (20.3 mg, 0.104 mmol, 1.0 equiv.) in DMF (0.600 mL), Cs_2CO_3 (44.0 mg, 0.135 mmol, 1.3 equiv.) and 1-azide-6-bromohexane (27.8 mg, 0.135 mmol, 1.3 equiv.) were added at room temperature. After being stirred at 50 °C in an oil bath for 30 min, the reaction mixture was poured into water. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography on silica gel with hexane : ethyl acetate = 90 : 10 to give 4-{(6-azidohexyl)oxy}-3-(4-chlorophenyl)isoxazole (**1o**) (32.0 mg, 0.0998 mmol, 96%).

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.94 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 3.95 (t, J = 6.4, 2H), 3.28 (t, J = 6.8, 2H), 1.85 (sext, J = 6.8 Hz, 2H), 1.63 (sext, J = 7.0 Hz, 2H), 1.51-1.46 (m, 4H); ^{13}C NMR (125 MHz, CD_3Cl) δ 152.1, 142.1, 140.0, 135.7, 128.9, 128.5, 126.6, 72.6, 51.3, 29.0, 28.7, 26.4, 25.6; FT-IR (neat): 2941, 2863, 2094, 1615, 1514, 1456, 1427, 1255, 1092, 1048, 1015, 921, 895, 836 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{15}H_{17}ClN_4O_2 + Na]^+$ 343.0932: found 343.0926.

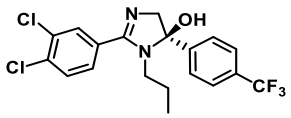


3. Photochemical conversion of isoxazoles 1 to 5-hydroxyimidazolines 2

Representative procedure for the synthesis of 2-(3,4-Dichlorophenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2a).

A solution of 3-(3,4-dichlorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (**1a)** (358.1 mg, 1.00 mmol, 1.0 equiv.) in propylamine (10.0 mL) and H_2O (2.00 mL) was introduced into the tube reactor (FEP tube, inner diameter: 1.0 mm) at room temperature, and the mixture was irradiated with a 6 W UV lamp (Figure S1). After 30 min, the reaction mixture was collected by washing the tube with dichloromethane and methanol, and concentrated in vacuo. The residue was purified by PTLC (dichloromethane: methanol = 77 : 3) to give corresponding imidazoline 2-(3,4-dichlorophenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (**2a**) (274.1 mg, 0.657 mmol, 66% yield). When the reaction was carried out at 0.1 mmol scale (**1a**; 35.8 mg, 0.1 mmol), **2a** was obtained in 73% yield (25.4 mg, 0.0609 mmol) and this result is indicated in Table 1, entry 2. Purification of other compounds **2** was also carried out by PTLC using dichloromethane/methanol (77 : 3) except where indicated.

Decomposition Temperature: 151-153 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.84-7.73 (m, 6H), 7.59 (d, J = 7.9 Hz, 1H), 6.79 (brs, 1H), 3.94 (d, J = 16.4 Hz, 1H), 3.81 (d, J = 16.4 Hz, 1H), 3.13-3.07 (m, 1H), 2.74-2.68 (m, 1H), 1.27-1.17 (m, 1H), 1.00-0.92 (m, 1H), 0.51 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1)) δ 163.1, 146.7, 134.3, 132.9, 131.4, 130.6, 130.1, 129.9, 127.0, 126.6, 125.0 (q, $J_{C\text{-}F}$ = 3.7 Hz), 124.0 (q, $J_{C\text{-}F}$ = 272.0 Hz), 94.4, 69.5, 44.2, 23.9, 11.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -60.8; FT-IR (neat): 3069, 2964, 2932, 1619, 1580, 1455, 1410, 1329, 1295, 1238, 1159, 1125, 1105, 1087, 1067, 1014, 982, 931, 847; HRMS (ESI-TOF): calcd for $[C_{19}H_{17}Cl_2F_3N_2O + H]^+$ 417.0743: found 417.0737.



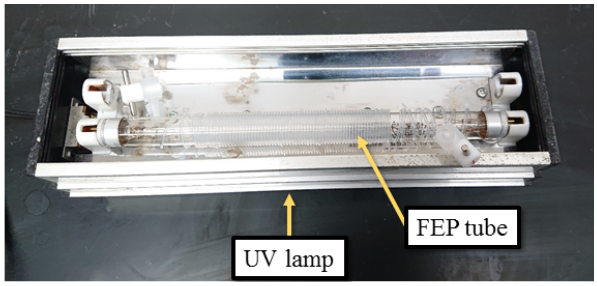
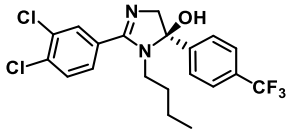


Figure S1. The reactor for photochemical reaction

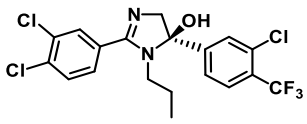
2-(3,4-Dichlorophenyl)-1-butyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2b)

Following the representative procedure, **2b** was obtained (40.6 mg, 0.0941 mmol, 69%) as a white solid from **1a** (48.7 mg, 0.136 mmol). Decomposition Temperature: 168-171 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.84-7.73 (m, 6H), 7.59 (dd, J = 8.3, 1.9 Hz, 1H), 6.78 (brs, 1H), 3.94 (d, J = 16.4 Hz, 1H), 3.82 (d, J = 16.4 Hz, 1H), 3.16-3.10 (m, 1H), 2.78-2.72 (m, 1H), 1.22-1.16 (m, 1H), 0.97-0.89 (m, 3H), 0.54 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1)) δ163.1, 146.7, 134.3, 132.8, 131.4, 130.6, 130.0 (q, $J_{C\text{-}F}$ = 32.7 Hz), 129.8, 127.0, 126.6, 125.0 (q, $J_{C\text{-}F}$ = 3.7 Hz), 123.9 (q, $J_{C\text{-}F}$ = 272.1 Hz), 94.4, 69.6, 42.0, 32.5, 19.8, 13.1; FT-IR (neat): 2957, 2936, 1648, 1558, 1541, 1489, 1457, 1327, 1236, 1067, 1015, 944, 824; HRMS (ESI-TOF): calcd for $[C_{20}H_{19}Cl_2F_3N_2O$ +H]$^+$ 431.0899: found 431.0903.



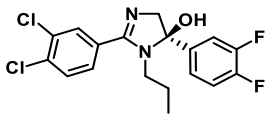
5-{2-Chloro-4-(trifluoromethyl)phenyl}-2-(3,4-dichlorophenyl)-1-propyl-4,5-dihydro-*1H*-imidazol-5-ol (2c)

Following the representative procedure, **2c** was obtained (29.2 mg, 0.0646 mmol, 65%) as a white solid from **1b**. Decomposition temperature: 142-144 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.17 (d, J = 8.3 Hz, 1H), 7.86 (s, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.72 (d, J = 1.4 Hz, 1H), 7.52 (dd, J = 1.4, 8.3, Hz, 1H), 7.02 (brs, 1H), 4.06 (d, J = 16.7 Hz, 1H), 3.86 (d, J = 16.7 Hz, 1H), 3.11-3.05 (m, 1H), 2.68-2.62 (m, 1H), 1.28-1.22 (m, 1H), 1.03-0.92 (m, 1H), 0.51 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ162.5, 143.0, 134.6, 133.2, 133.0, 131.7 (q, $J_{C\text{-}F}$ = 33.1 Hz), 131.1, 130.5, 130.3, 130.2, 128.0 (q, $J_{C\text{-}F}$ = 3.7 Hz), 127.1, 123.4 (q, $J_{C\text{-}F}$ = 3.4 Hz), 123.4 (q, $J_{C\text{-}F}$ = 272.6 Hz), 92.5, 66.4, 44.3, 23.6, 11.3; FT-IR (neat): 3063, 2967, 2932, 1608, 1582, 1484, 1419, 1393, 1326, 1259, 1232, 1172, 1133, 1081, 977, 890, 841; HRMS (ESI-TOF): calcd for $[C_{19}H_{16}C3_2F_3N_2O$ +H]$^+$ 451.0353: found 451.0358.



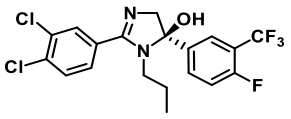
2-(3,4-Dichlorophenyl)-5-(3,4-difluorophenyl)-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2d)

Following the representative procedure, **2d** was obtained (34.4 mg, 0.0893 mmol, 53%) as a white solid from **1c** (55.0 mg, 0.169 mmol). Decomposition temperature: 143-145 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.85 (d, J = 1.7 Hz, 1H), 7.76 (d, J = 8.3 Hz), 7.60-7.53 (m, 2H), 7.45-7.40 (m, 2H), 6.75 (brs, 1H), 3.90 (d, J = 16.3 Hz, 1H), 3.79 (d, J = 16.3 Hz, 1H), 3.11-3.05 (m, 1H), 2.73-2.67 (m, 1H), 1.27-1.20 (m, 1H), 1.00-0.92 (m, 1H), 0.51 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1)) δ 162.8, 149.9 (d, $J_{C\text{-}F}$ = 248.2 Hz), 149.8 (d, $J_{C\text{-}F}$ = 248.2 Hz), 139.9, 134.4, 132.9, 131.5, 130.6, 129.9, 127.0, 122.5, 116.8 (d, $J_{C\text{-}F}$ = 17.3 Hz), 115.7 (d, $J_{C\text{-}F}$ = 18.5 Hz), 93.9, 69.0, 44.2, 23.9, 11.3; FT-IR (neat): 3413, 2967, 2935, 1610, 1583, 1518, 1417, 1376, 1282, 1196, 1110, 1033, 984, 886, 825 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{18}H_{16}Cl_2F_2N_2O$ +H$]^+$ 385.0681: found 385.0678.



2-(3,4-Dichlorophenyl)-5-{4-fluoro-3-(trifluoromethyl)phenyl}-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2e)

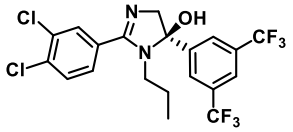
Following the representative procedure, **2e** was obtained (29.1 mg, 0.0669 mmol, 67%) as a white solid from **1d** (37.6 mg, 0.100 mmol). Decomposition temperature: 144-146 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.93-7.84 (m, 3H), 7.78 (d, J = 8.3 Hz, 1H), 7.59 (dd, J = 1.8, 8.2 Hz, 1H), 7.54-7.50 (m, 1H), 6.89 (brs, 1H), 3.93 (d, J = 16.4 Hz, 1H), 3.82 (d, J = 16.4 Hz, 1H), 3.12-3.06 (m, 1H), 2.74-2.68 (m, 1H), 1.24-1.16 (m, 1H), 0.97-0.90 (m, 1H), 0.51 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1)) δ 163.1, 159.3 (d, $J_{C\text{-}F}$ = 257.5 Hz), 139.2, 134.5, 132.9, 132.0 (d, $J_{C\text{-}F}$ = 8.2 Hz), 131.4, 130.6, 129.9, 127.0, 125.3, 122.5 (q, $J_{C\text{-}F}$ = 272.2 Hz), 117.9 (dq, $J_{C\text{-}F}$ = 12.3, 33.4 Hz), 116.6 (d, $J_{C\text{-}F}$ = 20.8 Hz), 94.0, 69.4, 44.1, 23.9, 11.2; FT-IR (neat): 3093, 2968, 1622, 1604, 1583, 1505, 1419, 1323, 1243, 1135, 1082, 1034, 982, 892, 830 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{19}H_{16}Cl_2F_4N_2O$ +H$]^+$ 435.0649: found 435.0646.



5-{3,5-bis(trifluoromethyl)phenyl}-2-(3,4-dichlorophenyl)-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2f)

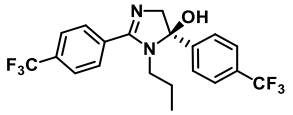
Following the representative procedure, afforded **2f** (20.6 mg, 0.0425 mmol, 54%) as a white solid from **1e** (33.6 mg, 0.0788 mmol). Decomposition temperature: 156-158 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.19 (s, 2H), 8.09 (s, 1H), 7.88 (d, J = 1.7 Hz, 1H), 7.78 (d, J = 8.3 Hz, 1H), 7.63 (dd, J = 1.7, 8.3 Hz, 1H), 7.13 (brs, 1H), 3.97 (d, J = 16.5 Hz, 1H), 3.87 (d, J = 16.5 Hz, 1H), 3.14-3.08 (m, 1H), 2.75-2.69 (m, 1H), 1.19-1.12 (m,

1H), 0.94-0.86 (m, 1H), 0.50 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3/CD_3OD$ (20 : 1)) δ 163.5, 146.0, 134.4, 132.8, 131.4 (q, $J_{C\text{-}F}$ = 33.5 Hz), 131.1, 130.6, 129.8, 127.0, 126.5, 123.1 (q, $J_{C\text{-}F}$ = 272.7 Hz), 121.7, 93.8, 69.2, 43.9, 23.6, 11.0; FT-IR (neat): 3391, 2970, 2939, 1609, 1584, 1551, 1469, 1415, 1372, 1279, 1229, 1180, 1134, 1034, 986, 844, 828 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{20}H_{16}Cl_2F_6N_2O+H]^+$ 485.0617: found 485.0613.



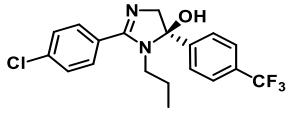
1-Propyl-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2g)

Following the representative procedure, **2g** was obtained (35.5 mg, 0.0853 mmol, 85%) as a white solid from **1f** (35.7 mg, 0.100 mmol). Decomposition temperature: 154-156 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.87 (d, J = 8.2 Hz, 2H), 7.83 (d, J = 8.2 Hz, 2H), 7.78 (d, J = 8.3 Hz, 2H), 7.75 (d, J = 8.3 Hz, 2H), 6.85 (brs, 1H), 3.97 (d, J = 16.3 Hz, 1H), 3.90 (d, J = 16.3 Hz, 1H), 3.13-3.09 (m, 1H), 2.75-2.68 (m, 1H), 1.26-1.17 (m, 1H), 0.97-0.90 (m, 1H), 0.48 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3/CD_3OD$ (25 : 1)) δ164.0, 146.8, 135.1, 132.0 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.1 (q, $J_{C\text{-}F}$ = 33.0 Hz), 128.4, 127.3, 125.5 (q, $J_{C\text{-}F}$ = 3.7 Hz), 125.1 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.0 (q, $J_{C\text{-}F}$ = 272.3 Hz), 123.6 (q, $J_{C\text{-}F}$ = 272.2 Hz), 94.4, 69.5, 44.2, 23.9, 11.2; FT-IR (neat): 3071, 2969, 2928, 1598, 1541, 1457, 1326, 1236, 1167, 1127, 1068, 1018, 965, 846 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{20}H_{18}F_6N_2O+H]^+$ 417.1396: found 417.1398.



2-(4-Chlorophenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2h)

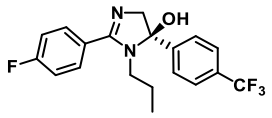
Following the representative procedure, **2h** (22.4 mg, 0.0585 mmol, 59%) as a white solid from **1g** (32.3 mg, 0.100 mmol). Decomposition temperature: 152-154 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.76 (d, J = 8.4 Hz, 2H), 7.74 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.56 (d, J = 8.3 Hz, 2H), 6.80 (brs, 1H), 3.94 (d, J = 16.2 Hz, 1H), 3.80 (d, J = 16.2 Hz, 1H), 3.12-3.06 (m, 1H), 2.74-2.68 (m, 1H), 1.27-1.19 (m, 1H), 0.98-0.91 (m, 1H), 0.48 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3/CD_3OD$ (25 : 1)) δ 164.4, 146.9, 136.1, 130.0 (q, $J_{C\text{-}F}$ = 32.5 Hz), 129.8, 129.2, 128.8, 126.6, 125.0 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.0 (q, $J_{C\text{-}F}$ = 271.7 Hz), 94.4, 69.0, 44.2, 23.8, 11.2; FT-IR (neat): 2967, 2874, 1610, 1588, 1496, 1456, 1379, 1326, 1236, 1163, 1127, 1093, 1014, 968, 833 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{19}H_{18}ClF_3N_2O+H]^+$ 383.1133: found 383.1129.



2-(4-Fluorophenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2i)

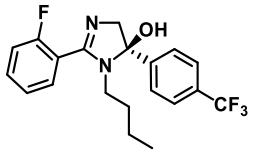
Following the representative procedure, **2i** was obtained (24.0 mg, 0.0655 mmol, 66%) as a white solid from **1h** (30.7 mg, 0.100 mmol). Decomposition temperature: 148-151 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.76 (d,

J = 8.7 Hz, 2H), 7.74 (d, J = 8.7 Hz, 2H), 7.65 (dd, J = 5.7, 8.7 Hz, 2H), 7.33 (dd, J = 8.9, 8.9 Hz, 2H), 6.76 (brs, 1H), 3.93 (d, J = 16.2 Hz, 1H), 3.80 (d, J = 16.2 Hz, 1H), 3.12-3.06 (m, 1H), 2.74-2.68 (m, 1H), 1.26-1.18 (m, 1H), 1.00-0.91 (m, 1H), 0.48 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1)) δ 164.4, 163.6 (d, $J_{C\text{-}F}$ = 250.5 Hz), 146.9, 130.0 (q, $J_{C\text{-}F}$ = 32.1 Hz), 129.9 (d, $J_{C\text{-}F}$ = 8.5 Hz), 127.5 (d, $J_{C\text{-}F}$ = 3.6 Hz), 126.7, 125.0 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.0 (q, $J_{C\text{-}F}$ = 271.9 Hz), 115.7 (d, $J_{C\text{-}F}$ = 21.8 Hz), 94.9, 69.0, 44.3, 23.9, 11.2; FT-IR (neat): 3393, 2968, 2800, 1608, 1573, 1515, 1456, 1402, 1327, 1240, 1159, 1128, 1066, 1011, 975, 923, 837 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{19}H_{18}F_4N_2O$ +H$]^+$ 367.1428: found 367.1423.



1-Butyl-2-(2-fluorophenyl)-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2j)

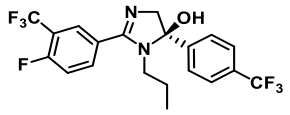
Following the representative procedure, **2j** was obtained (30.5 mg, 0.0802 mmol, 80%) as a white solid from **1i** (30.7 mg, 0.100 mmol). Decomposition temperature: 161-164 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.77 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 8.4 Hz, 2H), 7.58-7.53 (m, 2H), 7.36-7.33 (m, 2H), 6.78 (brs, 1H), 3.98 (d, J = 16.2 Hz, 1H), 3.85 (d, J = 16.2 Hz, 1H), 2.98-2.92 (m, 1H), 2.68-2.62 (m, 1H), 1.14-1.09 (m, 1H), 0.96-0.90 (m, 1H), 0.88-0.82 (m, 2H), 0.46 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1)) δ 160.8, 159.5 (d, $J_{C\text{-}F}$ = 249.0 Hz), 146.9, 131.8 (d, $J_{C\text{-}F}$ = 8.0 Hz), 130.3 (d, $J_{C\text{-}F}$ = 2.7 Hz), 130.0 (q, $J_{C\text{-}F}$ = 33.4 Hz), 126.6, 125.1 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.4 (d, $J_{C\text{-}F}$ = 3.4 Hz), 124.1 (q, $J_{C\text{-}F}$ = 271.7 Hz), 119.7 (d, $J_{C\text{-}F}$ = 15.7 Hz), 115.8 (d, $J_{C\text{-}F}$ = 21.1 Hz), 94.4, 69.6, 42.1, 32.6, 19.8, 13.1; FT-IR (neat): 3420, 2961, 2873, 1628, 1595, 1497, 1458, 1373, 1326, 1298, 1227, 1166, 1068, 1014, 970, 843 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{19}H_{18}F_4N_2O$ +H$]^+$ 367.1428: found 367.1433.



2-{4-fluoro-3-(trifluoromethyl)phenyl}-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2k)

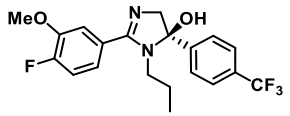
Following the representative procedure, **2k** was obtained (41.3 mg, 0.0951 mmol, 91%) as a white solid from **1j** (39.2 mg, 0.104 mmol). Decomposition temperature: 138-140 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.00-7.96 (m, 2H), 7.81 (d, J = 8.2 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.69-7.65 (m, 1H), 6.80 (brs, 1H), 3.95 (d, J = 16.3 Hz, 1H), 3.83 (d, J = 16.3 Hz, 1H), 3.13-3.06 (m, 1H), 2.74-2.68 (m, 1H), 1.25-1.18 (m, 1H), 0.99-0.91 (m, 1H), 0.50 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1)) δ 162.9, 160.5 (d, $J_{C\text{-}F}$ = 261.1 Hz), 146.5, 133.7 (d, $J_{C\text{-}F}$ = 7.8 Hz), 130.2 (q, $J_{C\text{-}F}$ = 33.2 Hz), 128.0, 127.2 (d, $J_{C\text{-}F}$ = 4.2 Hz), 126.7, 125.1 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.4 (q, $J_{C\text{-}F}$ = 272.2 Hz), 124.2 (q, $J_{C\text{-}F}$ = 272.6 Hz), 118.8 (dq, $J_{C\text{-}F}$ = 12.9, 33.5 Hz), 117.4 (d, $J_{C\text{-}F}$ = 21.1 Hz), 94.5, 69.5, 44.3, 24.0, 11.2; FT-IR (neat): 2973, 2876, 1612, 1582, 1510, 1460, 1326, 1285, 1166, 1128, 1068, 1014, 973, 899, 832 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{20}H_{17}F_7N_2O$ +H$]^+$ 435.1302: found

435.1308.



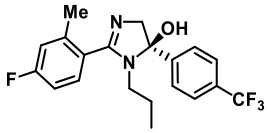
2-(4-fluoro-3-methoxyphenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2l)

Following the representative procedure, **2l** was obtained (22.4 mg, 0.0558 mmol, 56%) as a white solid from **1k** (33.7 mg, 0.100 mol). Decomposition temperature: 166-168 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.79-7.74 (m, 4H), 7.36-7.32 (m, 2H), 7.18 (brs, 1H), 6.78 (brs, 1H), 3.93 (d, J = 16.2 Hz, 1H), 3.89 (s, 3H), 3.81 (d, J = 16.2 Hz, 1H), 3.14-3.08 (m, 1H), 2.77-2.71 (m, 1H), 1.23 (m, 1H), 0.96 (m, 1H), 0.51 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1)) δ 164.5, 153.2 (d, $J_{C\text{-}F}$ = 250.0 Hz), 147.7 (d, $J_{C\text{-}F}$ = 10.9 Hz), 146.8, 130.0 (q, $J_{C\text{-}F}$ = 32.3 Hz), 127.7 (d, $J_{C\text{-}F}$ = 3.6 Hz), 126.6, 125.0 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.0 (q, $J_{C\text{-}F}$ = 271.8 Hz), 120.4 (d, $J_{C\text{-}F}$ = 7.3 Hz), 116.0 (d, $J_{C\text{-}F}$ = 18.9 Hz), 113.4, 94.9, 68.8, 56.2, 44.2, 23.9, 11.2; FT-IR (neat): 3083, 2962, 2932, 1608, 1569, 1519, 1473, 1427, 1325, 1278, 1238, 1181, 1154, 1066, 1013, 980, 849 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{20}H_{20}F_4N_2O_2 + H]^+$ 397.1534: found 397.1528.



2-(4-Fluoro-2-methylphenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1H-imidazol-5-ol (2m)

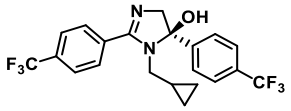
Following the representative procedure, **2m** (22.8 mg, 0.0599 mmol, 60%) as a white solid from **1l** (32.1 mg, 0.100 mmol). Decomposition temperature: 106-109 °C. ^{1}H NMR (500 MHz, DMSO-d_6); δ 7.76 (brs, 4H), 7.41 (dd, J = 6.4, 8.2 Hz, 1H), 7.19-7.17 (m, 1H), 7.15-7.12 (m, 1H), 6.74 (brs, 1H), 3.96 (d, J = 16.0 Hz, 1H), 3.87 (d, J = 16.0 Hz, 1H), 2.83-2.77 (m, 1H), 2.57-2.50 (m, 1H), 2.37 (s, 3H), 1.09-1.01 (m, 1H), 0.95-0.87 (m, 1H), 0.39 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.7, 163.0 (d, $J_{C\text{-}F}$ = 248.9 Hz), 147.5, 139.2 (d, $J_{C\text{-}F}$ = 8.2 Hz), 130.0 (d, $J_{C\text{-}F}$ = 8.5 Hz), 127.3, 126.7, 124.9 (q, $J_{C\text{-}F}$ = 2.3 Hz), 124.1 (q, $J_{C\text{-}F}$ = 272.2 Hz), 123.1, 117.1 (d, $J_{C\text{-}F}$ = 21.4 Hz), 112.6 (d, $J_{C\text{-}F}$ = 21.6 Hz), 93.7, 69.6, 43.9, 23.6, 19.5, 11.3; FT-IR (neat): 2968, 2934, 2873, 1620, 1587, 1455, 1408, 1381, 1327, 1297, 1242, 1165, 1097, 1033, 971, 947, 837 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{20}H_{20}F_4N_2O + H]^+$ 381.1585: found 381.1589.



1-(Cyclopropylmethyl)-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2n)

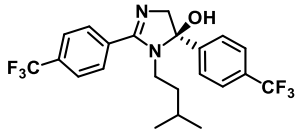
Following the representative procedure, **2n** (31.2 mg, 0.0728 mmol, 73%) as a white solid from **1f** (35.7 mg, 0.100 mmol). Decomposition temperature: : 146-149 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.83 (d, J = 8.3 Hz, 2H), 7.84-7.80 (m, 4H), 7.74 (d, J = 8.3 Hz, 2H), 6.87 (brs, 1H), 4.00 (d, J = 16.3 Hz, 1H), 3.86 (d, J = 16.3 Hz, 1H), 2.84 (d, J = 6.6 Hz, 2H), 0.59-0.51 (m, 1H), 0.10-0.04 (m, 1H), -0.11--0.16 (m, 1H), -0.25--0.29 (m, 1H),

-0.65--0.70 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3/CD_3OD$ (25 : 1)) δ 164.2, 147.2, 135.2, 131.9 (q, $J_{C\text{-}F}$ = 32.7 Hz), 129.8 (q, $J_{C\text{-}F}$ = 32.2 Hz), 128.5. 126.8, 125.4 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.8 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.0 (q, $J_{C\text{-}F}$ = 271.9 Hz), 123.6 (q, $J_{C\text{-}F}$ = 272.4 Hz), 94.0, 69.5, 46.8, 11.4, 5.1, 3.8; FT-IR (neat): 3083, 2933, 2858, 1595, 1520, 1456, 1411, 1325, 1234, 1164, 1126, 1067, 1018, 969, 847 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{21}H_{18}F_6N_2O+H]^+$ 429.1396: found 429.1390.



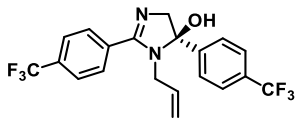
1-Isopentyl-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2o)

Following the representative procedure, **2o** (35.8 mg, 0.0806 mmol, 81%) as a colorless oil from **1f** (35.7 mg, 0.100 mmol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.87 (d, J = 8.2 Hz, 2H), 7.82 (d, J = 8.3 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H), 7.75 (d, J = 8.3 Hz, 2H), 6.83 (brs, 1H), 3.98 (d, J = 16.3 Hz, 1H), 3.87 (d, J = 16.4 Hz, 1H), 3.16-3.10 (m, 1H), 2.80-2.73 (m, 1H), 1.20-1.09 (m, 2H), 0.79-0.73 (m, 1H), 0.47 (d, J = 6.1, 3H), 0.46 (d, J = 6.1, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 147.1, 134.8, 132.1 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.2 (q, $J_{C\text{-}F}$ = 32.2 Hz), 128.6. 126.8, 125.4 (q, $J_{C\text{-}F}$ = 3.5 Hz), 125.1 (q, $J_{C\text{-}F}$ = 3.4 Hz), 124.0 (q, $J_{C\text{-}F}$ = 272.3 Hz), 123.6 (q, $J_{C\text{-}F}$ = 272.2 Hz), 94.3, 69.4, 40.8, 39.5, 25.9, 21.9; FT-IR (neat): 2961, 2932, 2873, 1622, 1600, 1521, 1469, 1412, 1370, 1326, 1235, 1168, 1069, 1018, 966, 847 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{22}H_{22}F_6N_2O+H]^+$ 445.1709: found 445.1706.



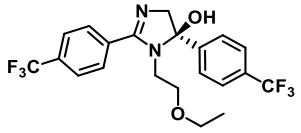
1-Allyl-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2p)

Following the representative procedure, **2p** (27.2 mg, 0.0656 mmol, 66%) as a white solid from **1f** (35.7 mg, 0.100 mmol). Decomposition temperature: 125-127 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.83 (brs, 4H), 7.82 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 8.3 Hz, 2H), 6.89 (brs, 1H), 5.55-5.47 (m, 1H), 4.69 (d, J = 10.3 Hz, 1H), 4.64 (d, J = 17.3 Hz), 4.01 (d, J = 16.4 Hz, 1H), 3.90 (d, J = 16.4 Hz, 1H), 3.78 (dd, J = 6.7, 17.1 Hz, 1H), 3.47 (dd, J = 6.7, 17.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 146.4, 135.3, 134.4, 132.3 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.4 (q, $J_{C\text{-}F}$ = 34.7 Hz), 128.8. 126.9, 125.4 (q, $J_{C\text{-}F}$ = 3.4 Hz), 125.2 (q, $J_{C\text{-}F}$ = 3.1 Hz), 124.0 (q, $J_{C\text{-}F}$ = 272.2 Hz), 123.6 (q, $J_{C\text{-}F}$ = 272.5 Hz), 116.9, 94.7, 69.2, 45.2; FT-IR (neat): 3081, 2939, 2860, 1620, 1560, 1541, 1455, 14121, 1326, 1298, 1235, 1167, 1068, 1018, 969, 846 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{20}H_{16}F_6N_2O+H]^+$ 415.1240: found 415.1237.



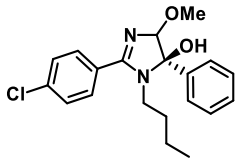
1-(2-Ethoxyethyl)-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2q)

Following the representative procedure, **2q** (37.3 mg, 0.0836 mmol, 84%) as amorphous solid from **1f** (35.7 mg, 0.100 mmol). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.91 (d, J = 8.1 Hz, 2H), 7.86 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H), 7.75 (d, J = 8.3 Hz, 2H), 6.89 (brs, 1H), 4.00 (d, J = 16.4 Hz, 1H), 3.87 (d, J = 16.4 Hz, 1H), 3.33-3.29 (m, 1H), 3.11-3.05 (m, 1H), 3.02-2.94 (m, 4H), 0.91 (t, J = 7.0, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 147.6, 135.1, 132.0 (q, $J_{C\text{-}F}$ = 32.7 Hz), 130.1 (q, $J_{C\text{-}F}$ = 32.0 Hz), 128.8. 126.6, 125.6 (q, $J_{C\text{-}F}$ = 3.8 Hz), 125.3 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.0 (q, $J_{C\text{-}F}$ = 272.0 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.5 Hz), 93.8, 71.1, 69.1, 66.8, 42.4, 14.6; FT-IR (neat): 3066, 2934, 2867, 1620, 1571, 1522, 1411, 1353, 1237, 1163, 1071, 1019, 982, 845 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{21}H_{20}F_6N_2O + H]^+$ 447.1502: found 447.1504.



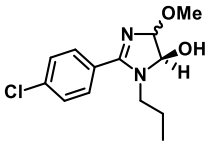
1-Butyl-2-(4-chlorophenyl)-4-methoxy-5-phenyl-4,5-dihydro-1*H*-imidazol-5-ol (2t)

Following the representative procedure, purification by PTLC (hexane : ethyl acetate = 50 : 50) afforded **2t** (13.9 mg, 0.0388 mmol, 39%) as a colorless oil from **1m** (28.6 mg, 0.100 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.8 Hz, 2H), 7.54 (d, J = 7.5 Hz, 2H), 7.44-7.31 (m, 5H), 4.93 (s, 1H), 4.55 (brs, 1H), 3.59 (s, 3H), 3.22-3.14 (m, 1H), 2.97-2.90 (m, 1H), 1.38-1.27 (m, 1H), 1.18-1.08 (m, 1H), 1.00 (sext, J = 7.2 Hz, 2H), 0.64 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 143.3, 136.4, 129.9, 129.5, 128.8, 128.5, 128.1, 125.5, 101.8, 93.0, 57.6, 42.8, 32.4, 20.0, 13.5; HRMS (ESI-TOF): calcd for $[C_{20}H_{23}ClN_2O_2 + H]^+$ 359.1521: found 359.1517.



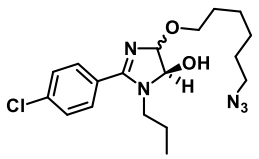
2-(4-Chlorophenyl)-4-methoxy-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2u)

Following the representative procedure, purification by PTLC (hexane : ethyl acetate = 50 : 50) afforded **2u** was obtained (27.4 mg, 0.102 mmol, 52%) as a colorless oil from **1n** (40.9 mg, 0.195 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) For a major isomer: δ 7.50-7.39 (m, 4H), 4.92 (d, J = 1.9 Hz, 1H), 4.77 (d, J = 1.9 Hz, 1H), 3.50 (s, 3H), 3.24-3.20 (m, 1H), 3.11-3.03 (m, 2H), 1.56-1.48 (m, 2H), 0.77 (t, J = 7.4 Hz, 3H); For a minor isomer: δ 7.50-7.39 (m, 4H), 5.19 (d, J = 6.7 Hz, 1H), 5.09 (d, J = 6.7 Hz, 1H), 3.64 (s, 3H), 3.24-3.20 (m, 1H), 3.11-3.03 (m, 2H), 1.58-1.47 (m, 2H), 0.82 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 166.1, 137.1, 136.4, 130.1, 129.6, 129.3, 128.9, 128.8, 128.2, 101.2, 93.8, 90.7, 84.0, 57.3, 55.6, 46.7, 45.7, 22.3, 22.0, 11.2, 11.1; FT-IR (neat): 3265, 2963, 2930, 1647, 1606, 1579, 1557, 1457, 1245, 1092, 1014, 978, 837 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{13}H_{17}ClN_2O_2 + Na]^+$ 291.0871: found 291.0865.



4-{(6-azidohexyl)oxy}-2-(4-chlorophenyl)-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2v)

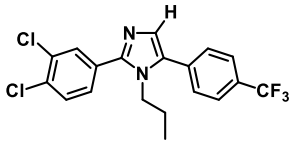
Following the representative procedure, **2v** was obtained (19.6 mg, 0.0516 mmol, 52%) as a colorless oil from **1o** (32.1 mg, 0.100 mmol). ^{1}H NMR (400 MHz, $CDCl_3$) For a major isomer: δ 7.48-7.38 (m, 4H), 4.88 (s, 1H), 4.79 (s, 1H), 3.80 (dt, *J* = 9.0, 6.6 Hz, 1H), 3.52 (dt, *J* = 9.1, 6.6 Hz, 1H), 3.27-3.17 (m, 3H), 3.10-3.01 (m, 1H), 1.68-1.40 (m, 10H), 0.76 (t, *J* = 7.4 Hz, 3H); For a minor isomer: δ 7.48-7.38 (m, 4H), 3.95 (dt, *J* = 9.0, 6.5 Hz, 1H), 3.66 (dt, *J* = 9.0, 6.5 Hz, 1H), 3.27-3.17 (m, 3H), 3.10-3.01 (m, 1H), 1.68-1.40 (m, 10H), 0.80 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 166.0, 136.7, 136.3, 130.1, 129.6, 129.3, 128.8, 128.8, 128.7, 100.7, 92.6, 91.0, 83.9, 69.8, 67.8, 51.4, 51.3, 46.8, 45.7, 29.6, 29.5, 28.8, 28.7, 26.5, 25.7, 25.6, 22.4, 22.0, 11.2, 11.1; FT-IR (neat): 3327, 2934, 2863, 1606, 1582, 1557, 1498, 1457, 1346, 1315, 1243, 1176, 1092, 1015, 957, 836 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{18}H_{26}ClN_5O_2 + H]^+$ 380.1848: found 380.1843.



4. Dehydration of 5-hydroxyimidazolines

2-(3,4-Dichlorophenyl)-1-propyl-5-(4-(trifluoromethyl)phenyl)-1*H*-imidazole (3a)

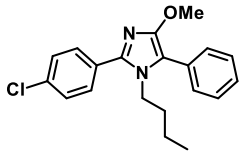
To a stirred solution of 2-(3,4-dichlorophenyl)-1-propyl-5-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1*H*-imidazol-5-ol (**2a**) (20.0 mg, 0.0479 mmol, 1.0 equiv.) in CH_2Cl_2 (0.50 mL), 2.6-lutidine (26.3 μL, 0.240 mmol, 5.0 equiv.) and trifluoroacetic anhydride (10.0 μL, 0.0719 mmol, 1.5 equiv.) were added at 0 °C under an argon atmosphere. After being stirred at the same temperature for 30 min, the reaction mixture was diluted with ethyl acetate and poured into water. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by PTLC (hexane : ethyl acetate = 90 : 10) to give 2-(3,4-dichlorophenyl)-1-propyl-5-(4-(trifluoromethyl)phenyl)-1*H*-imidazole (15.2 mg, 0.0381 mmol, 79%). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 1.8 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.58-7.55 (m, 3H), 7.49 (dd, *J* = 1.8, 8.3 Hz, 1H), 7.21 (s, 1H), 4.07 (t, *J* = 7.4, 2H), 1.35 (sext, *J* = 7.4 Hz, 2H), 0.57 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 134.0, 133.8, 133.3, 133.1, 131.1, 130.8, 130.7, 130.4 (q, $J_{C\text{-}F}$ = 32.5 Hz), 129.4, 128.9, 127.9, 125.9 (q, $J_{C\text{-}F}$ = 3.9 Hz), 124.0 (q, $J_{C\text{-}F}$ = 272.3 Hz), 47.0, 23.8, 10.6; FT-IR (neat): 2939, 1619, 1481, 1423, 1344, 1325, 1167, 1126, 1069, 1015, 943, 890, 849 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{19}H_{15}Cl_2F_3N_2 + H]^+$ 399.0637: found 399.0641.



1-Butyl-2-(4-chlorophenyl)-4-methoxy-5-phenyl-1*H*-imidazole (3b)

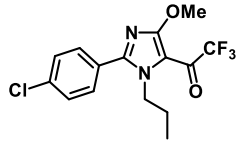
To a stirred solution of 1-butyl-2-(4-chlorophenyl)-4-methoxy-5-phenyl-4,5-dihydro-1*H*-imidazol-5-ol (**2t**) (10.5 mg, 0.0293 mmol, 1.0 equiv.) in CH_2Cl_2 (0.50 mL), 2.6-lutidine (17.0 μL, 0.146 mmol, 5.0 equiv.) and

trifluoroacetic anhydride (8.25 μL, 0.0585 mmol, 2.0 equiv.) were added at 0 °C under an argon atmosphere. After being stirred at the same temperature for 30 min, the reaction mixture was diluted with ethyl acetate and poured into water. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by PTLC (hexane : ethyl acetate = 80 : 20) to give 1-butyl-2-(4-chlorophenyl)-4-methoxy-5-phenyl-1*H*-imidazole (**3b**) (8.4 mg, 0.0246 mmol, 84%). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.3 Hz, 2H), 7.44-7.43 (m, 6H), 7.33-7.29 (m, 1H), 4.03 (t, J = 7.3 Hz, 2H), 3.95 (s, 3H), 1.31-1.24 (m, 2H), 0.93 (sext, J = 7.4, 2H), 0.61 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 141.5, 134.5, 130.3, 129.8, 129.0, 128.9, 128.7, 127.1, 113.1, 56.7, 45.3, 32.2, 19.3, 13.3; FT-IR (neat): 2959, 2930, 1604, 1583, 1519, 1482, 1443, 1329, 1094, 1013, 836 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{20}H_{21}ClN_2O + H]^+$ 341.1415: found 341.1410.



1-{2-(4-Chlorophenyl)-4-methoxy-1-propyl-1*H*-imidazol-5-yl}-2,2,2-trifluoroethan-1-one (3c)

To a stirred solution of 2-(4-chlorophenyl)-4-methoxy-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (**2u**) (32.6 mg, 0.121 mmol, 1.0 equiv.) in CH_2Cl_2 (1.5 mL), 2.6-lutidine (70.6 μL, 0.607 mmol, 5.0 equiv.) and trifluoroacetic anhydride (34.2 μL, 0.243 mmol, 2.0 equiv.) were added at 0 °C under an argon atmosphere. After being stirred at the same temperature for 30 min, the reaction mixture was diluted with ethyl acetate and poured into water. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by PTLC (hexane : ethyl acetate = 80 : 20) to give 1-{2-(4-chlorophenyl)-4-methoxy-1-propyl-1*H*-imidazol-5-yl}-2,2,2-trifluoroethan-1-one (**3c**) (18.6 mg, 0.0536 mmol, 44%). Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J = 8.7 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 4.22-4.19 (m, 2H), 4.09 (s, 3H), 1.70 (sext, J = 7.5 Hz, 2H), 0.82 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, CD_3Cl) δ 168.2 (q, $J_{C\text{-}F}$ = 37.8 Hz), 163.6, 151.1, 136.9, 130.6, 129.3, 127.3, 116.6 (q, $J_{C\text{-}F}$ = 288.4 Hz), 56.7, 49.0, 24.3, 10.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -75.8; FT-IR (neat): 2932, 1658, 1600, 1538, 1484, 1443, 1344, 1235, 1156, 1094, 1015, 982, 946, 838 cm^{-1}; HRMS (ESI-TOF): calcd for $[C_{15}H_{14}ClF_3N_2O_2 + Na]^+$ 369.0588: found 369.0587.



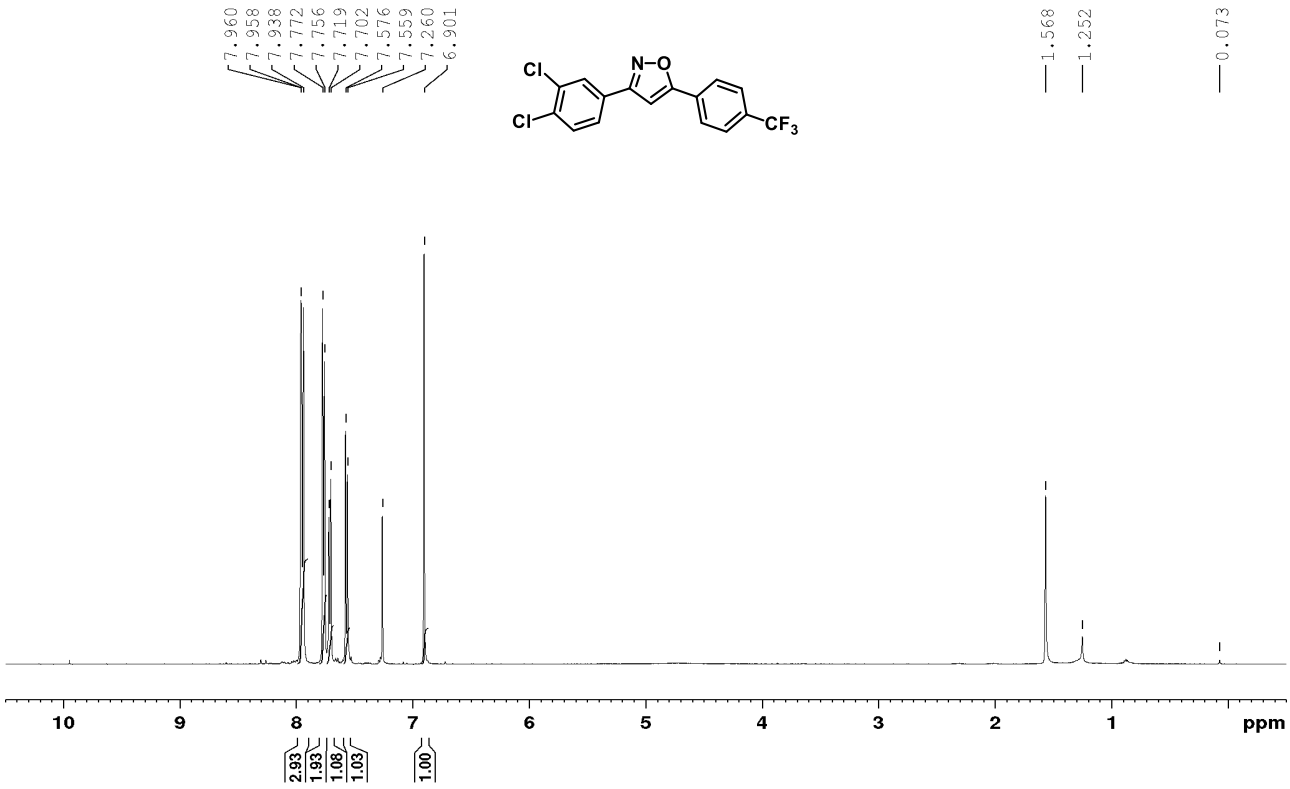
6. References

1. Wang, X. Z.; Jia, J.; Zhang, Y.; Xu, W. R.; Liu, W.; Shi, F. N.; Wang, J. W. *J. Chin. Chem. Soc*. **2007**, *54*, 643-652.
2. Morita, T.; Fuse, S.; Nakamura, H. *Angew. Chem. Int. Ed.* **2016**, *55*, 13580-13584.
3. Morita, T.; Fukuhara, S.; Fuse, S.; Nakamura, H. *Org. Lett.* **2018**, *20*, 433-436.

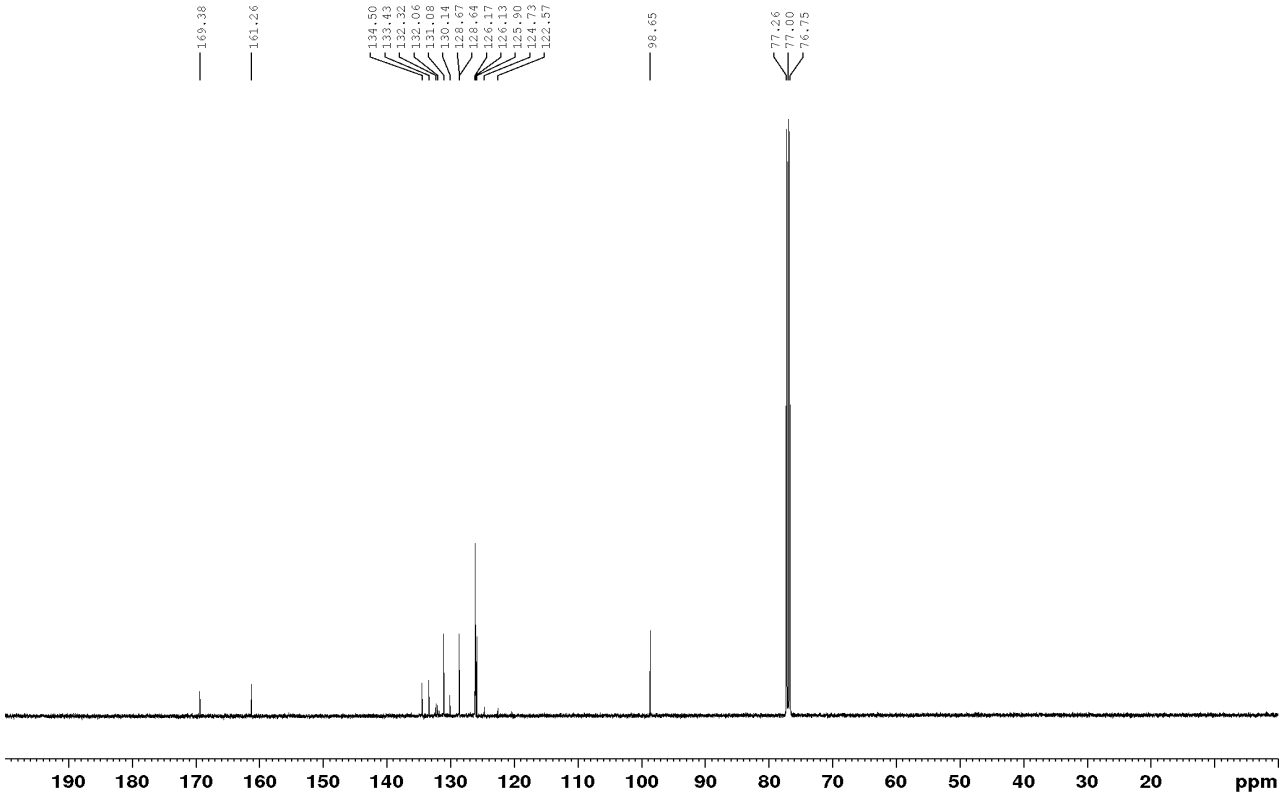
7. NMR Spectra

3-(3,4-Dichlorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1a)

^{1}H NMR (500 MHz, $CDCl_3$)

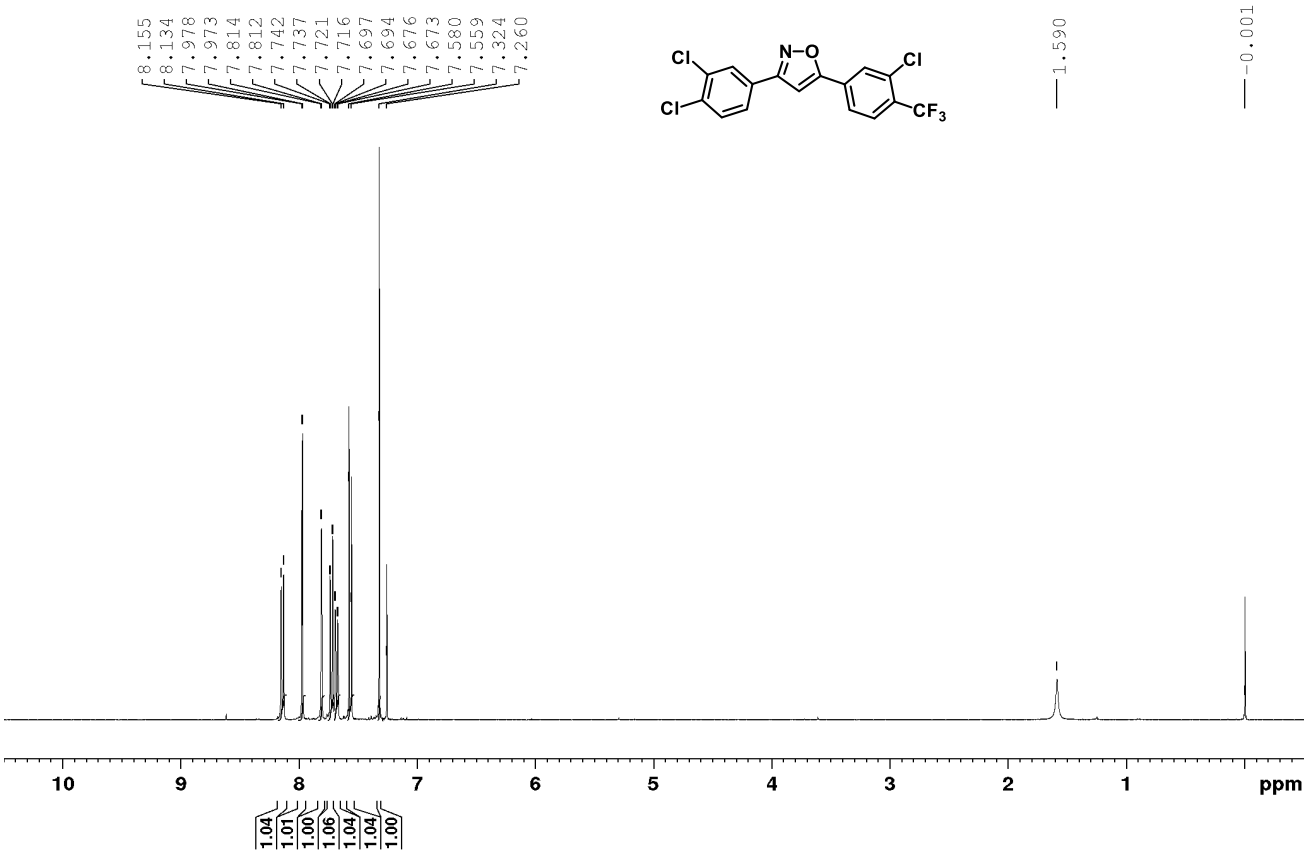


^{13}C NMR (125 MHz, $CDCl_3$)

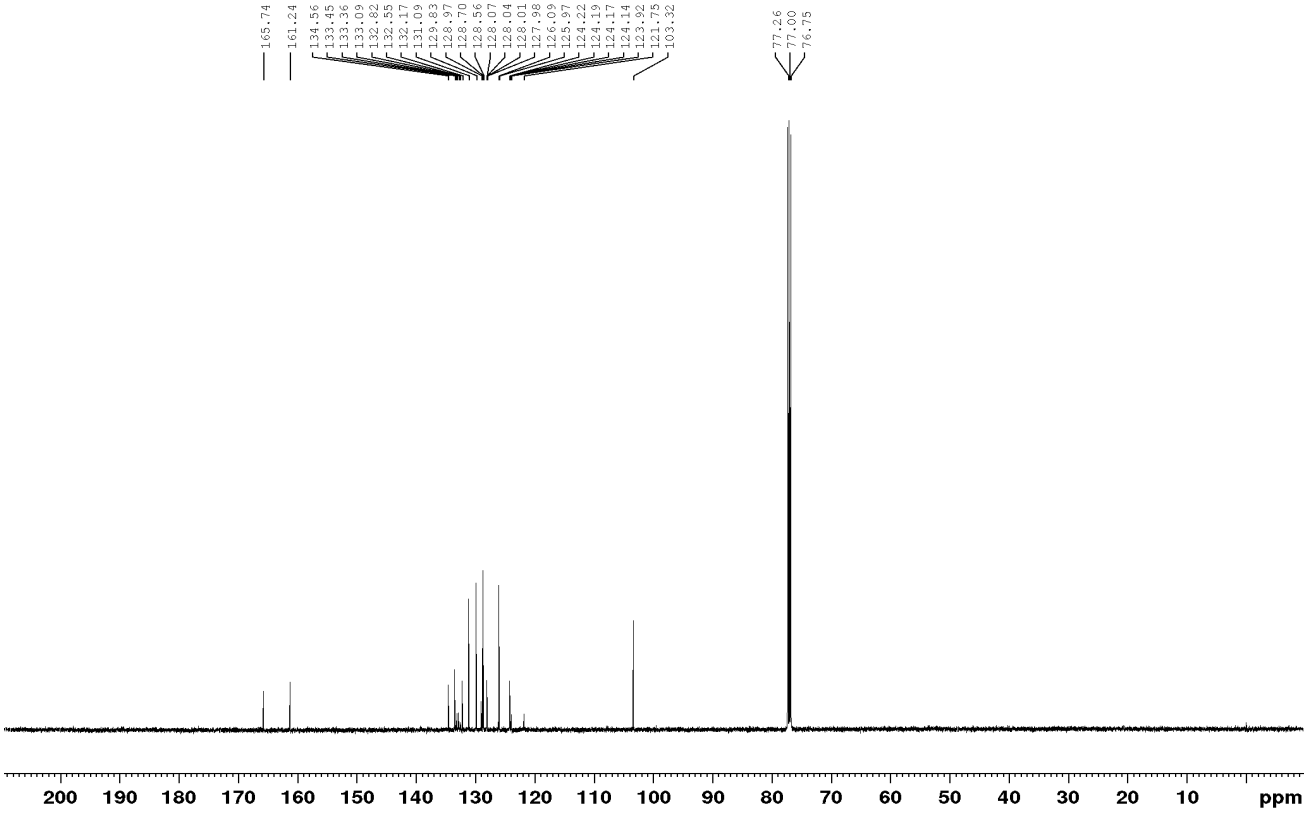


5-{2-Chloro-4-(trifluoromethyl)phenyl}-3-(3,4-dichlorophenyl)isoxazole (1b)

^{1}H NMR (400 MHz, $CDCl_3$)

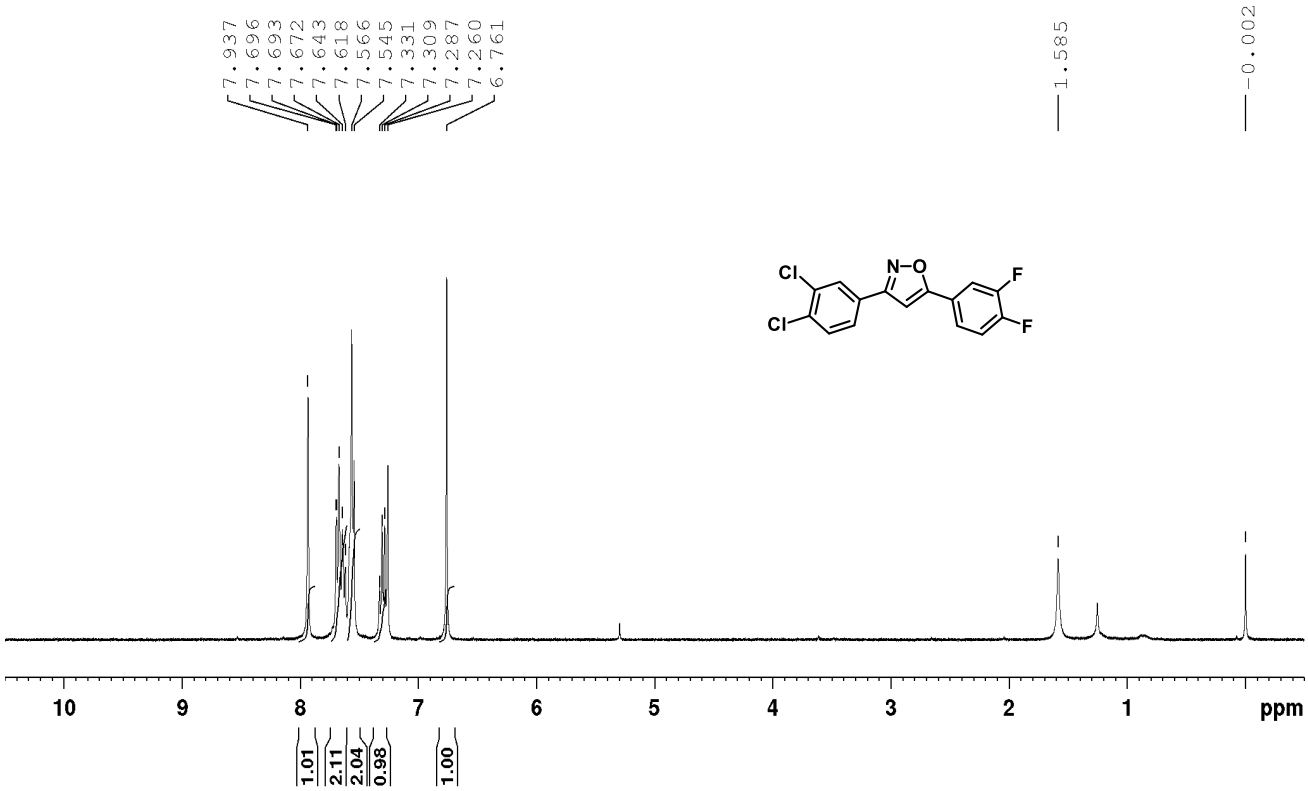


^{13}C NMR (125 MHz, $CDCl_3$)

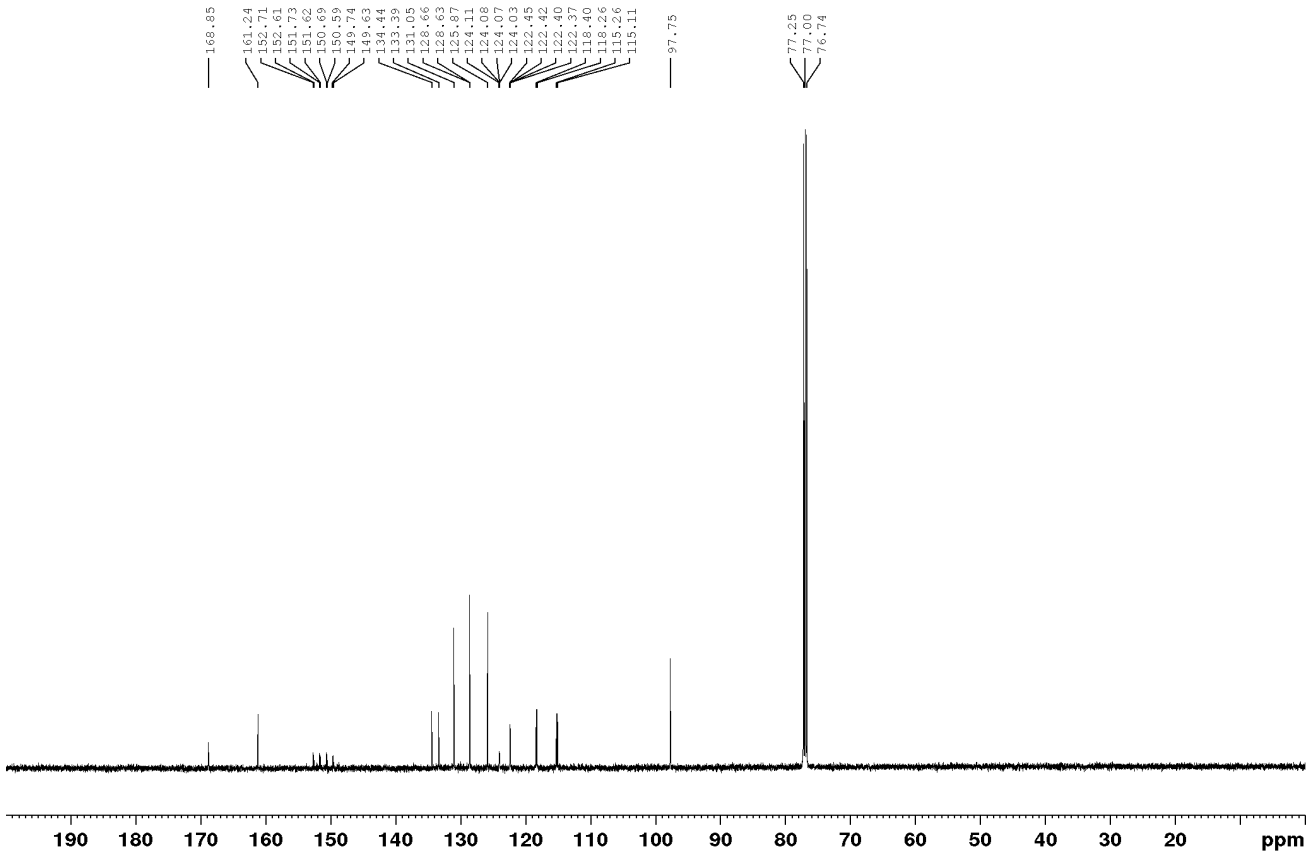


3-(3,4-Dichlorophenyl)-5-(3,4-difluorophenyl)isoxazole (1c)

^{1}H NMR (500 MHz, $CDCl_3$)

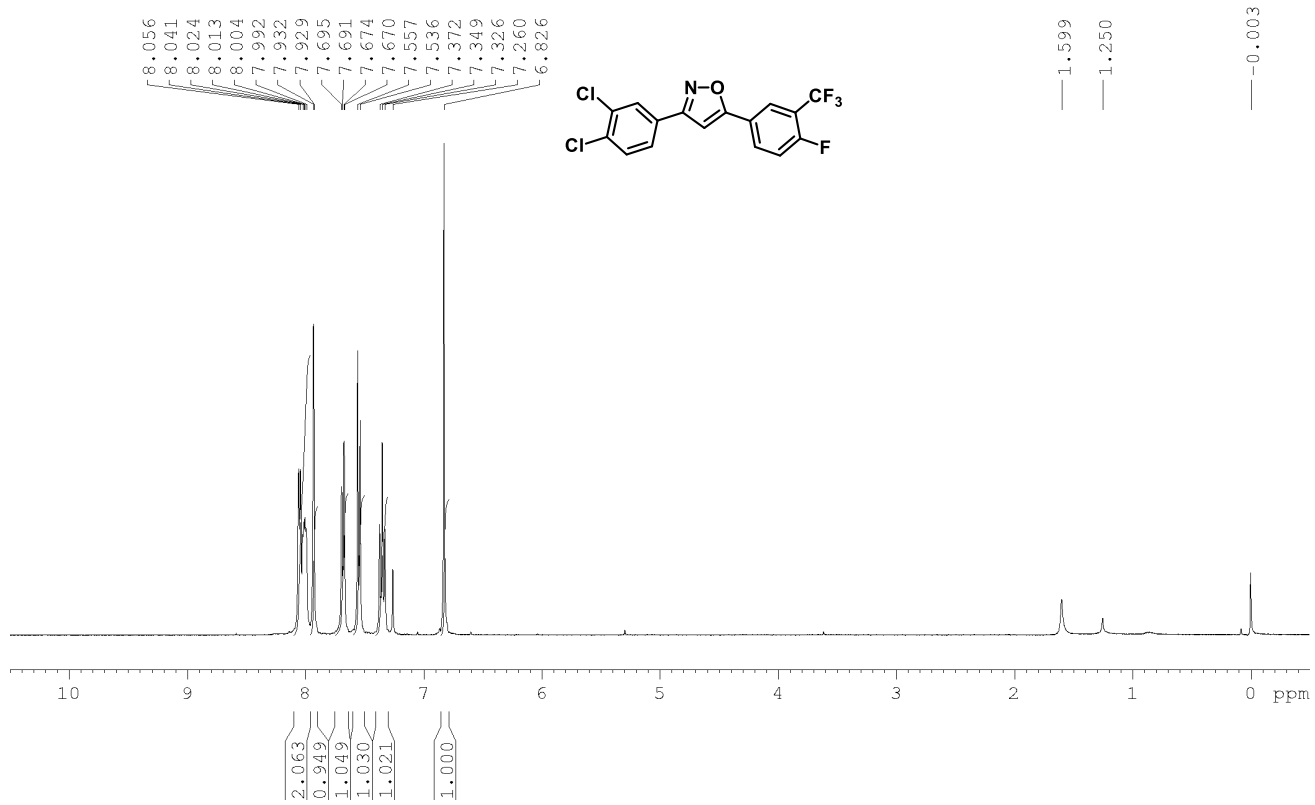


^{13}C NMR (125 MHz, $CDCl_3$)

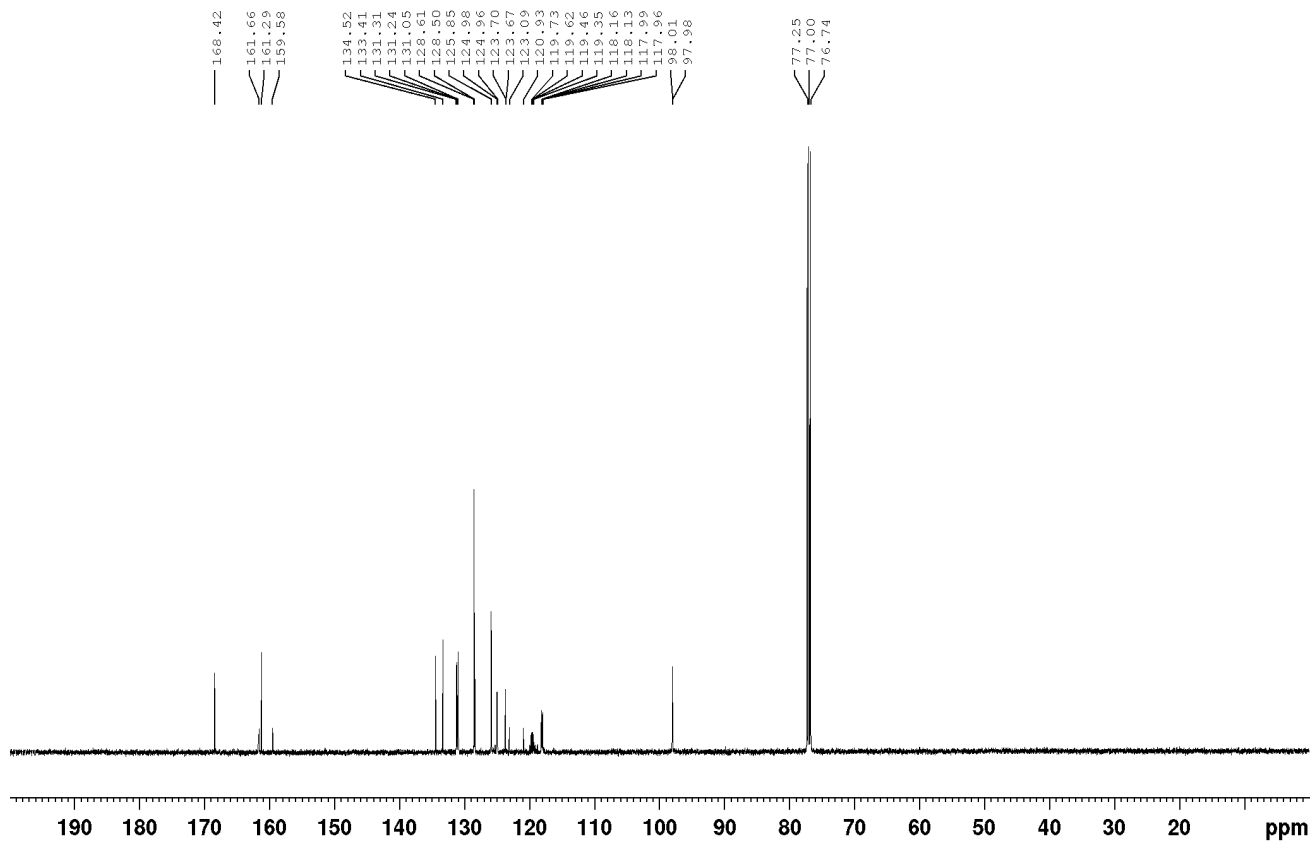


3-(3,4-Dichlorophenyl)-5-{4-fluoro-3-(trifluoromethyl)phenyl}isoxazole (1d)

^{1}H NMR (400 MHz, $CDCl_3$)

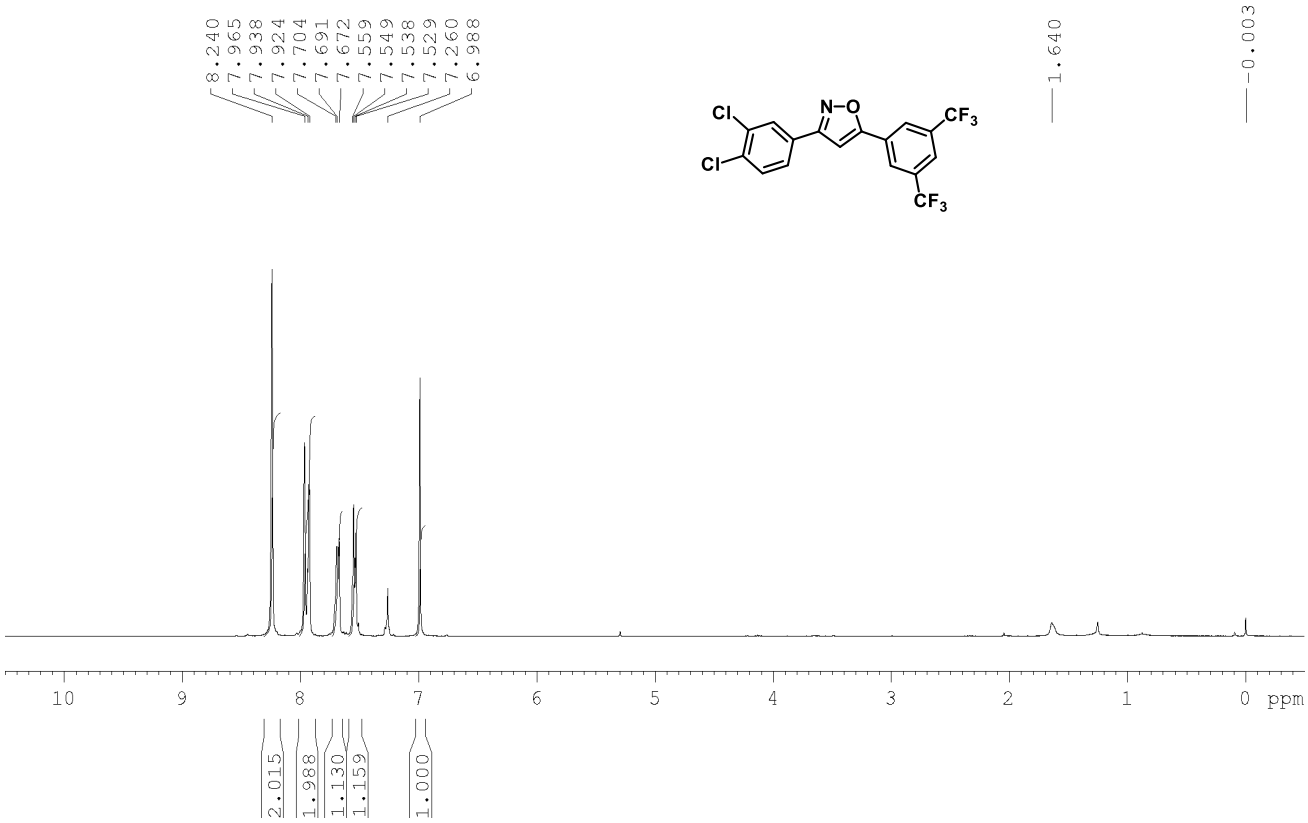


^{13}C NMR (125 MHz, $CDCl_3$)

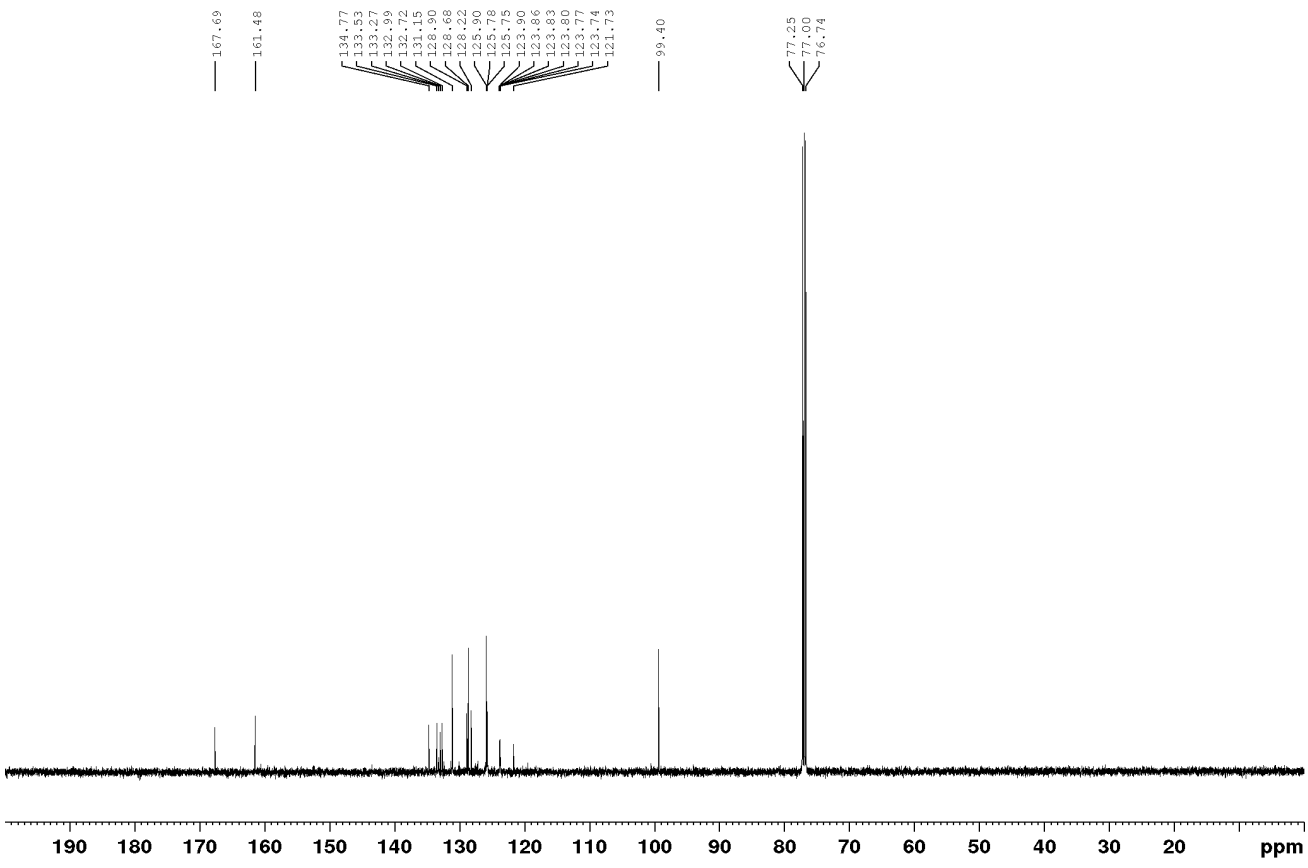


5-{3,5-Bis(trifluoromethyl)phenyl}-3-(3,4-dichlorophenyl)isoxazole (1e)

^{1}H NMR (400 MHz, $CDCl_3$)

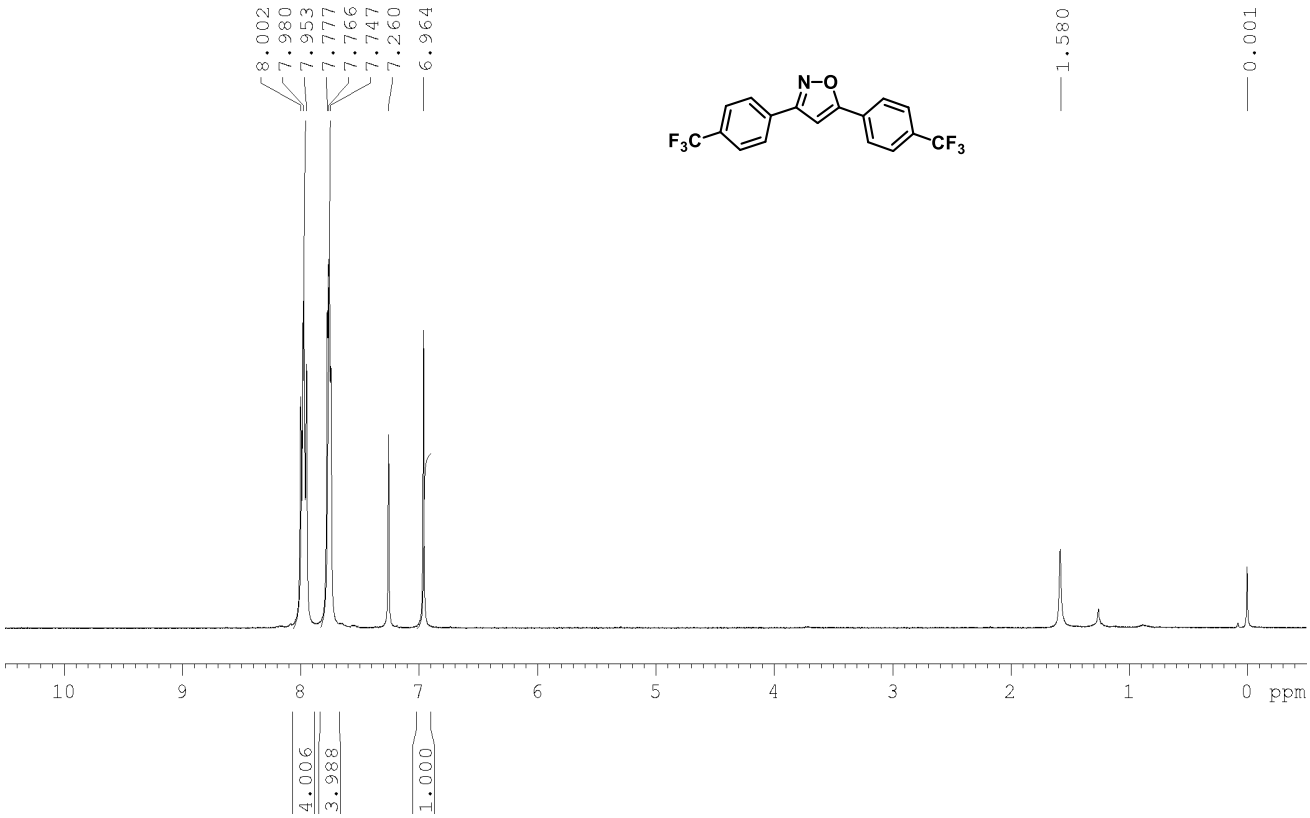


^{13}C NMR (125 MHz, $CDCl_3$)

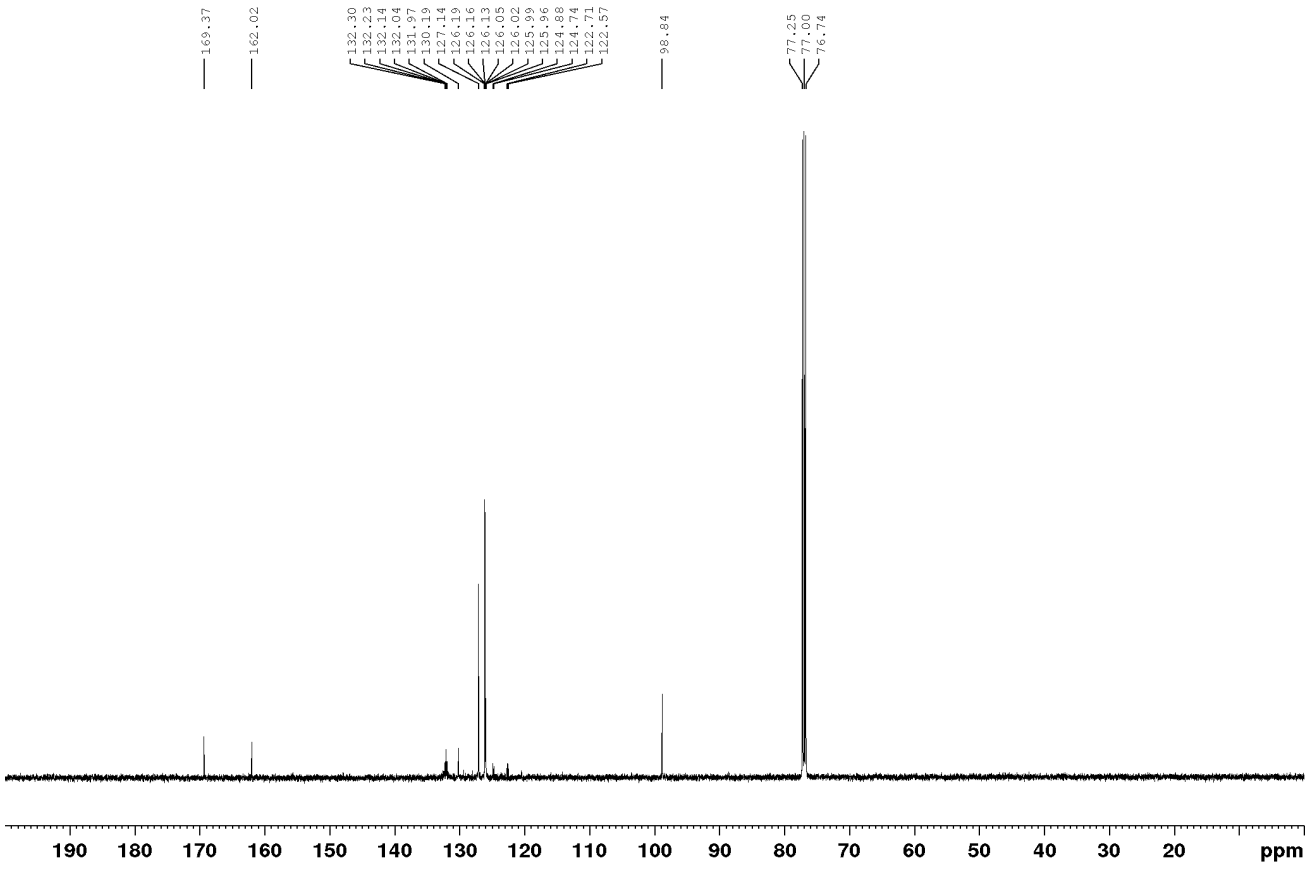


3,5-Bis{4-(trifluoromethyl)phenyl}isoxazole (1f)

^{1}H NMR (400 MHz, $CDCl_3$)

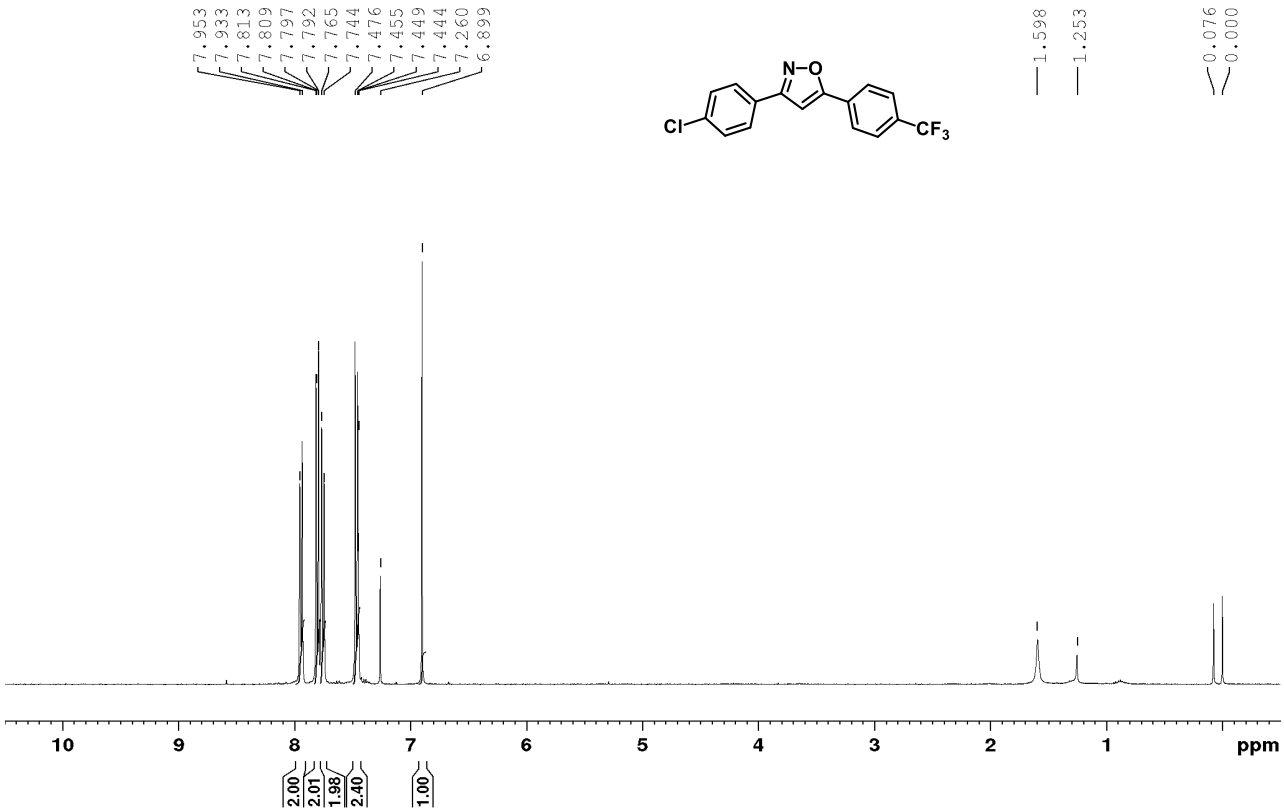


^{13}C NMR (125 MHz, $CDCl_3$)

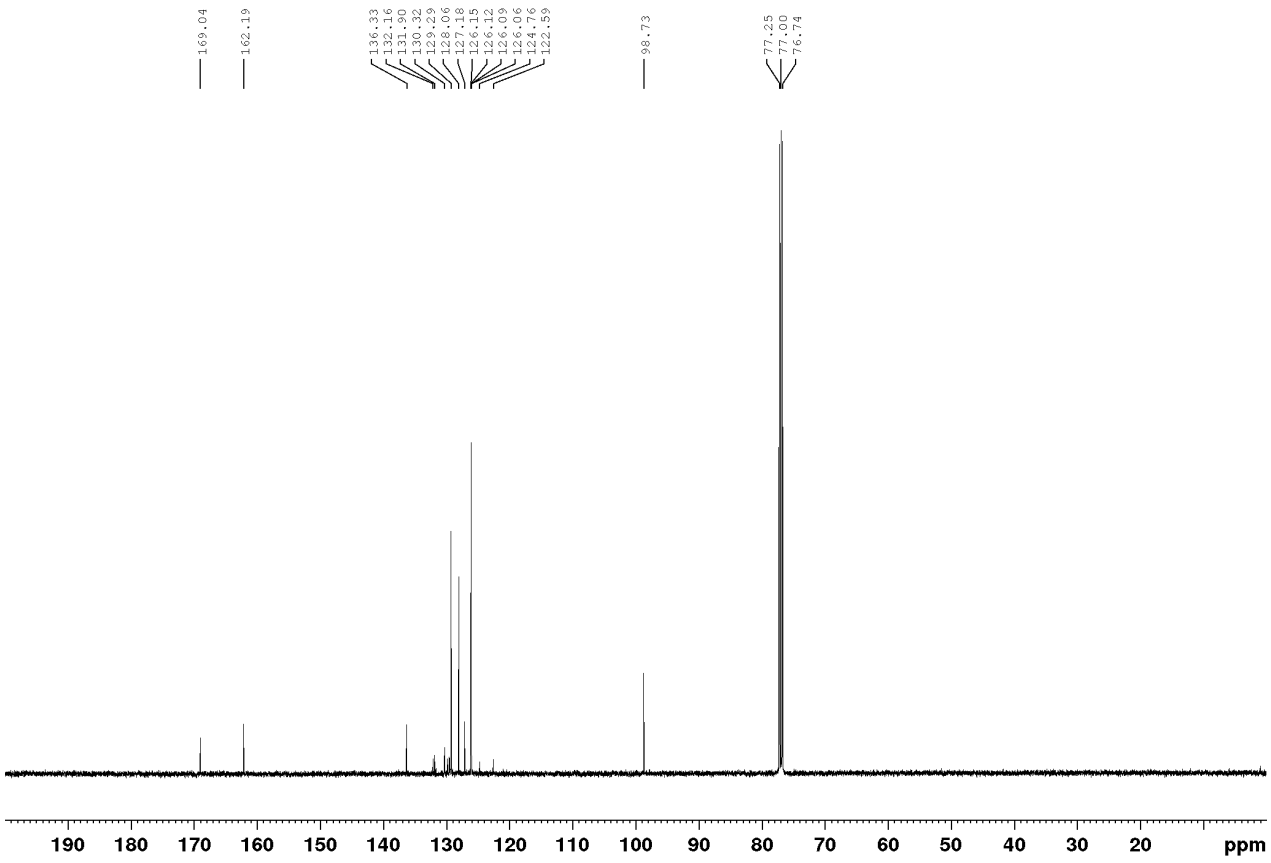


3-(4-Chlorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1g)

^{1}H NMR (400 MHz, $CDCl_3$)

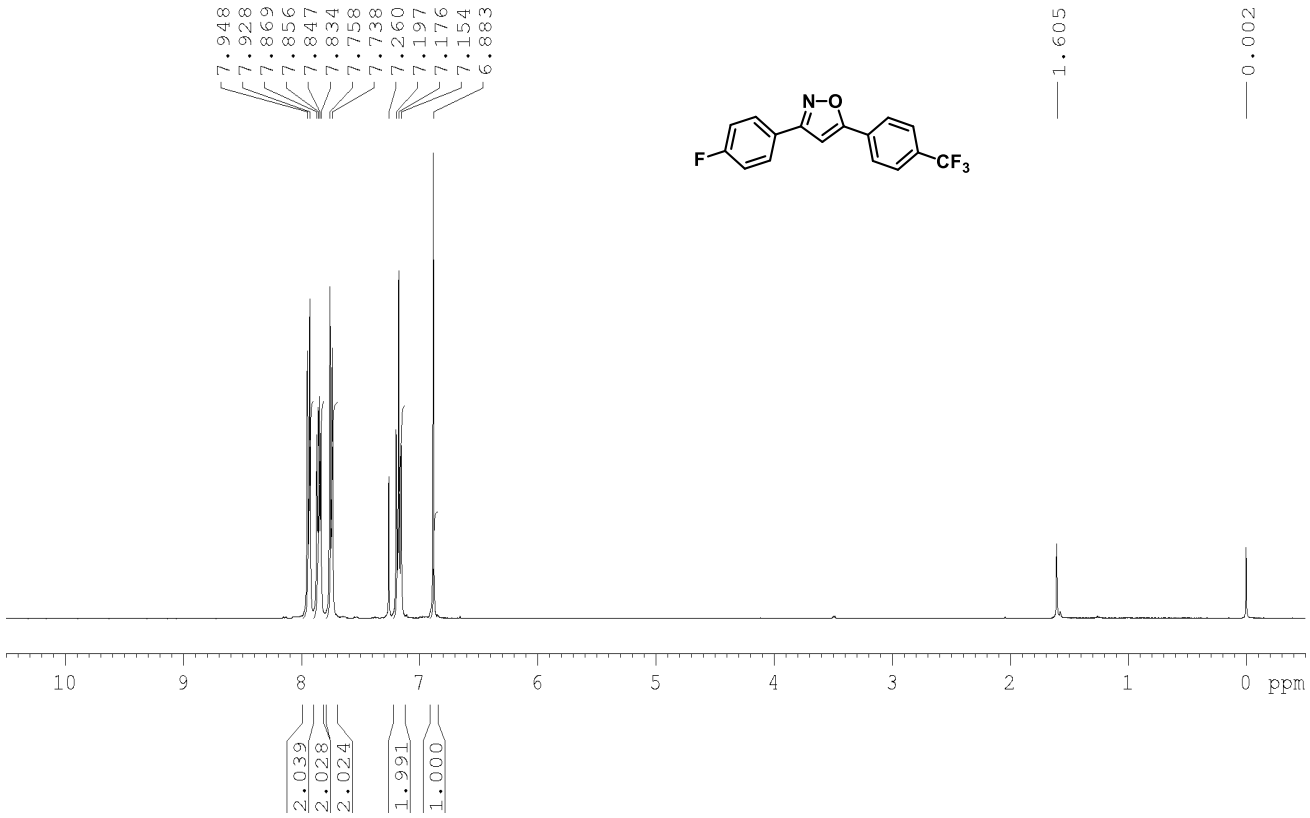


^{13}C NMR (125 MHz, $CDCl_3$)

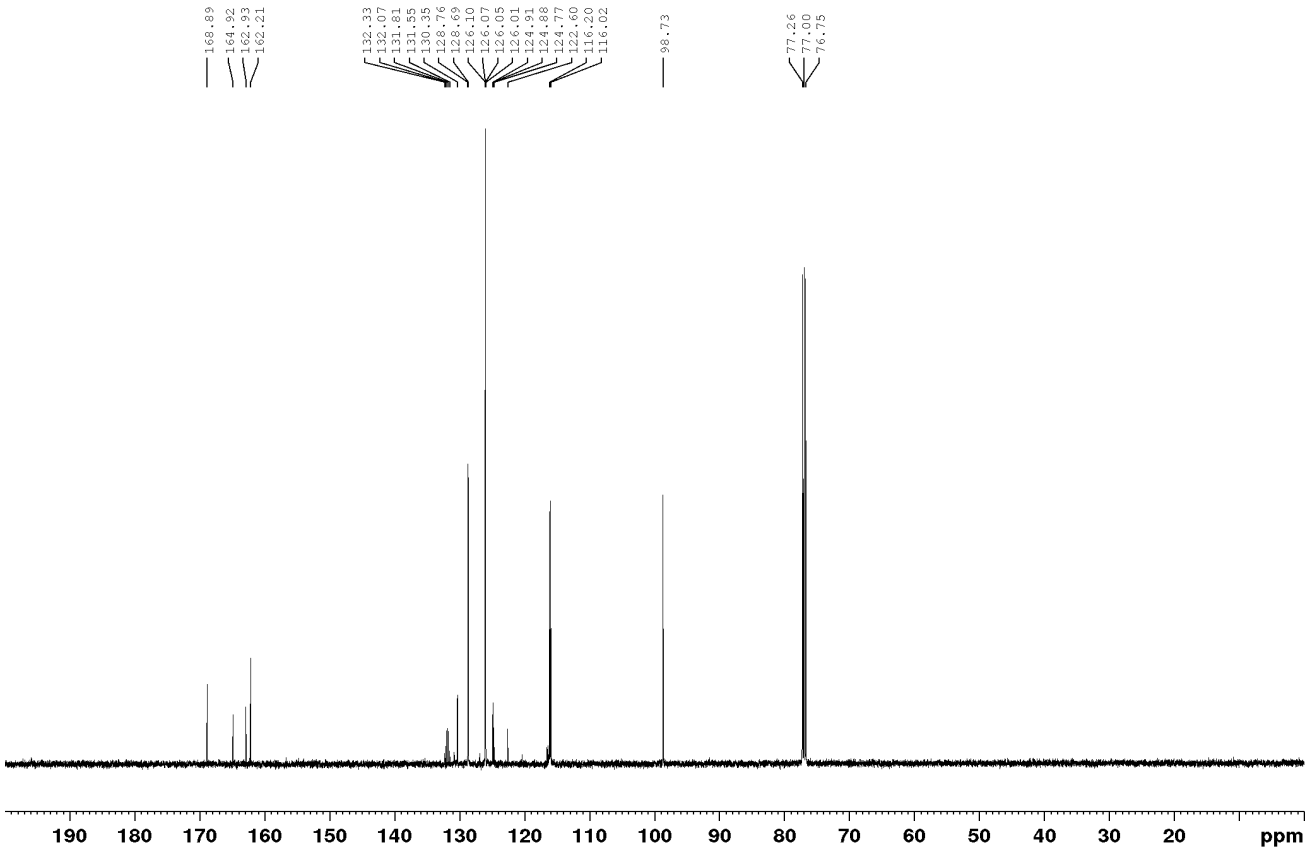


3-(4-Fluorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1h)

^{1}H NMR (400 MHz, $CDCl_3$)

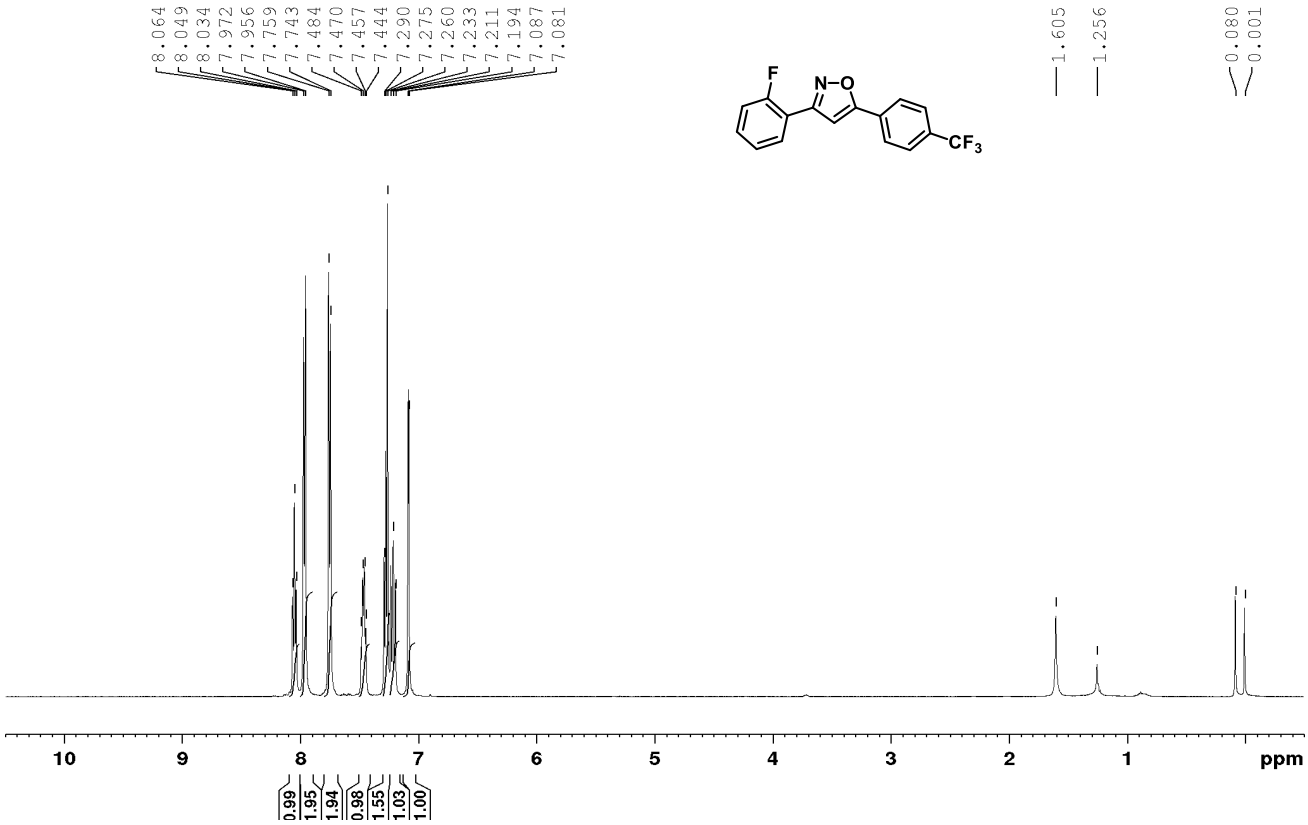


^{13}C NMR (125 MHz, $CDCl_3$)

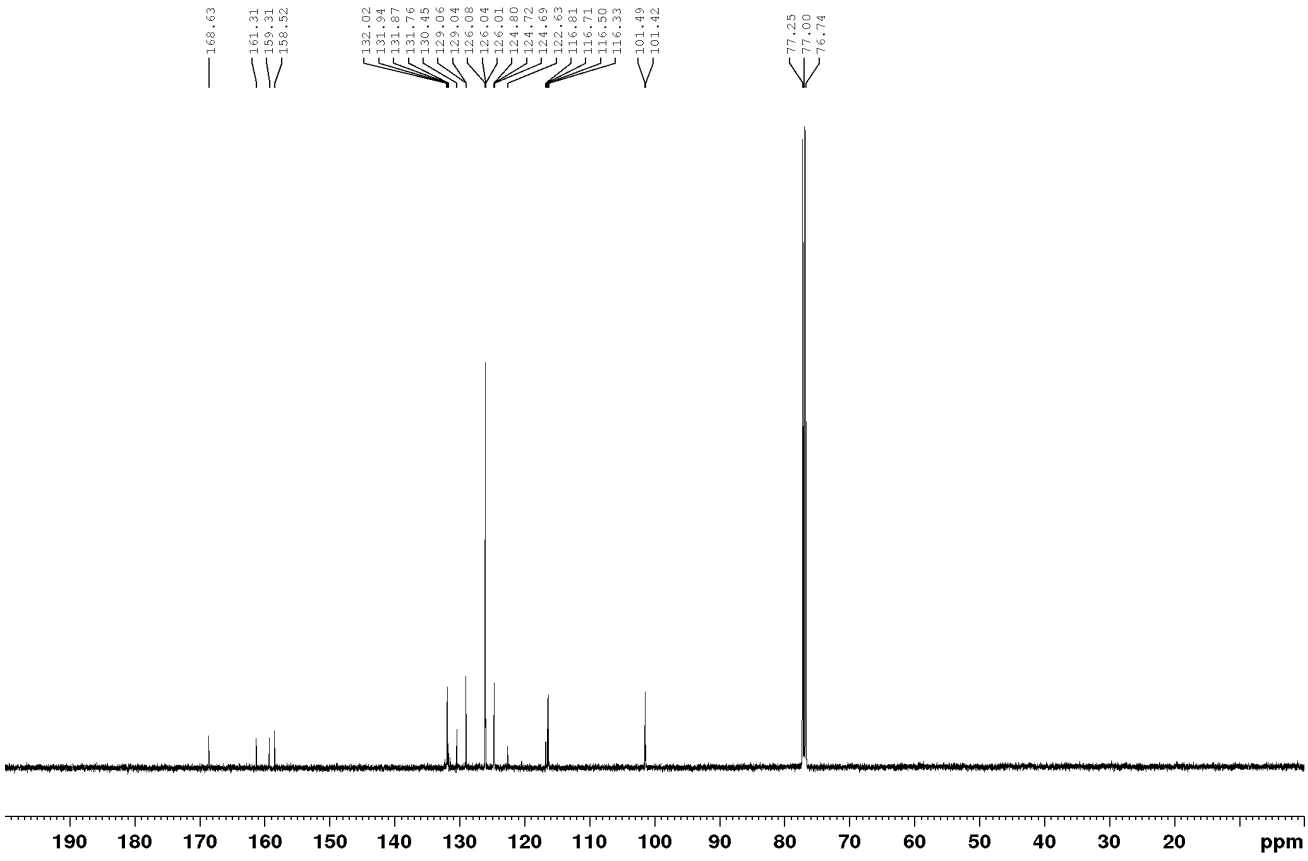


3-(2-Fluorophenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1i)

^{1}H NMR (500 MHz, $CDCl_3$)

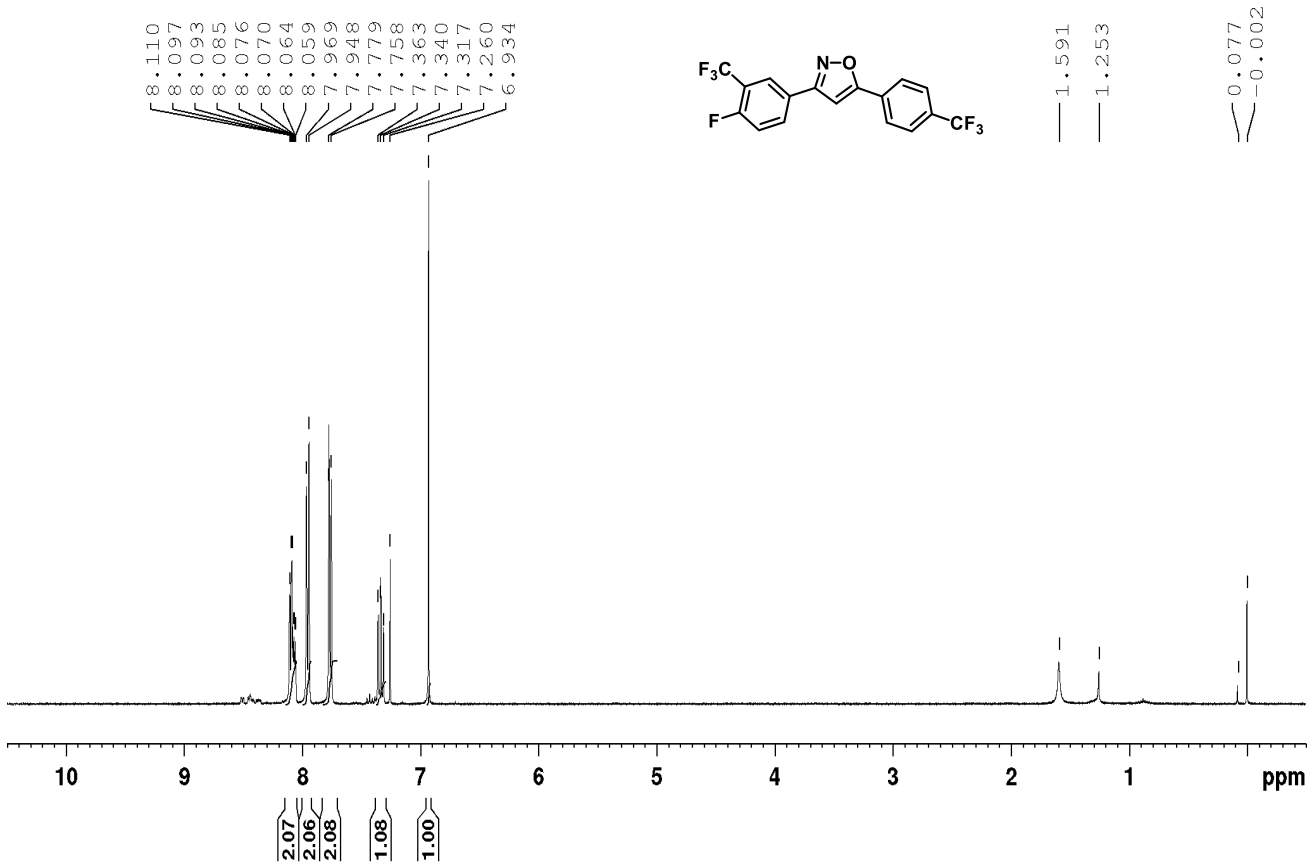


^{13}C NMR (125 MHz, $CDCl_3$)

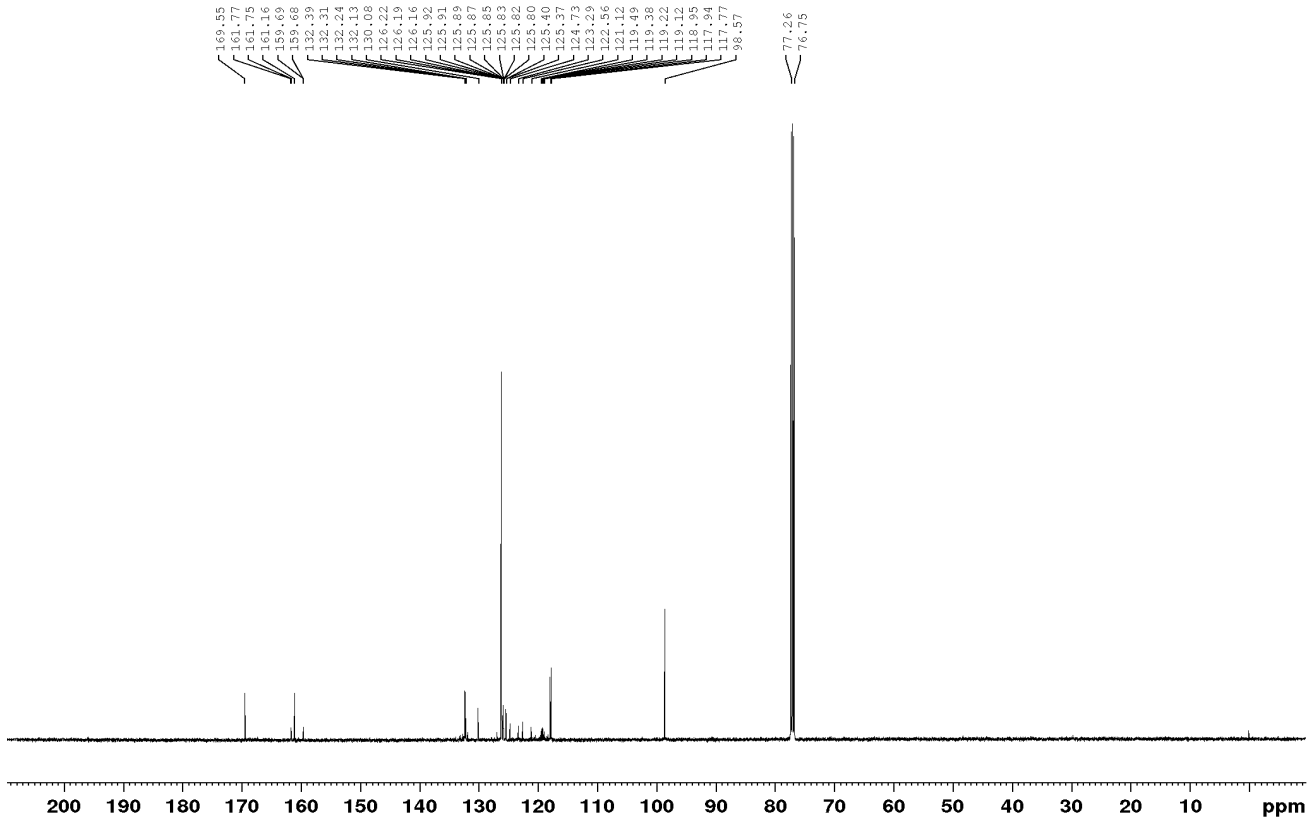


3-{4-Chloro-3-(trifluoromethyl)phenyl}-5-{4-(trifluoromethyl)phenyl}isoxazole (1j)

^{1}H NMR (400 MHz, $CDCl_3$)

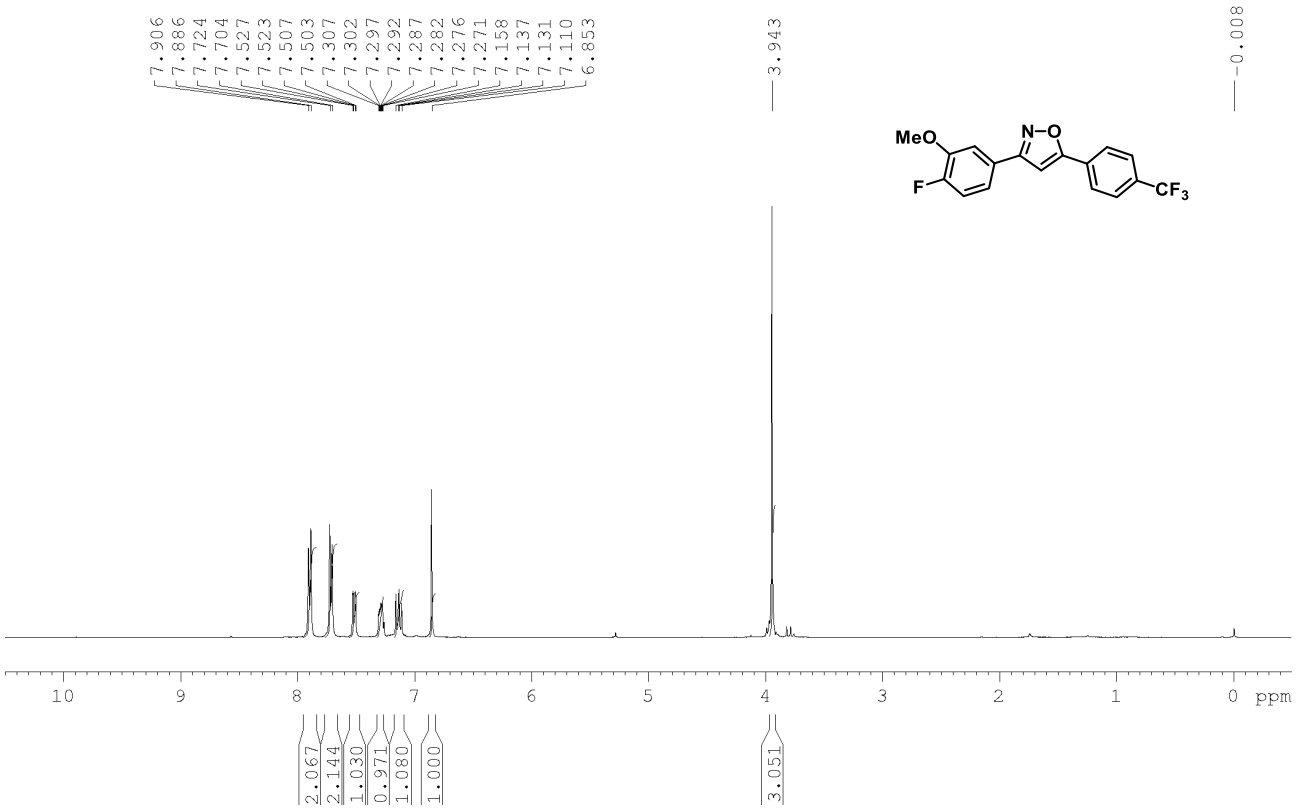


^{13}C NMR (125 MHz, $CDCl_3$)

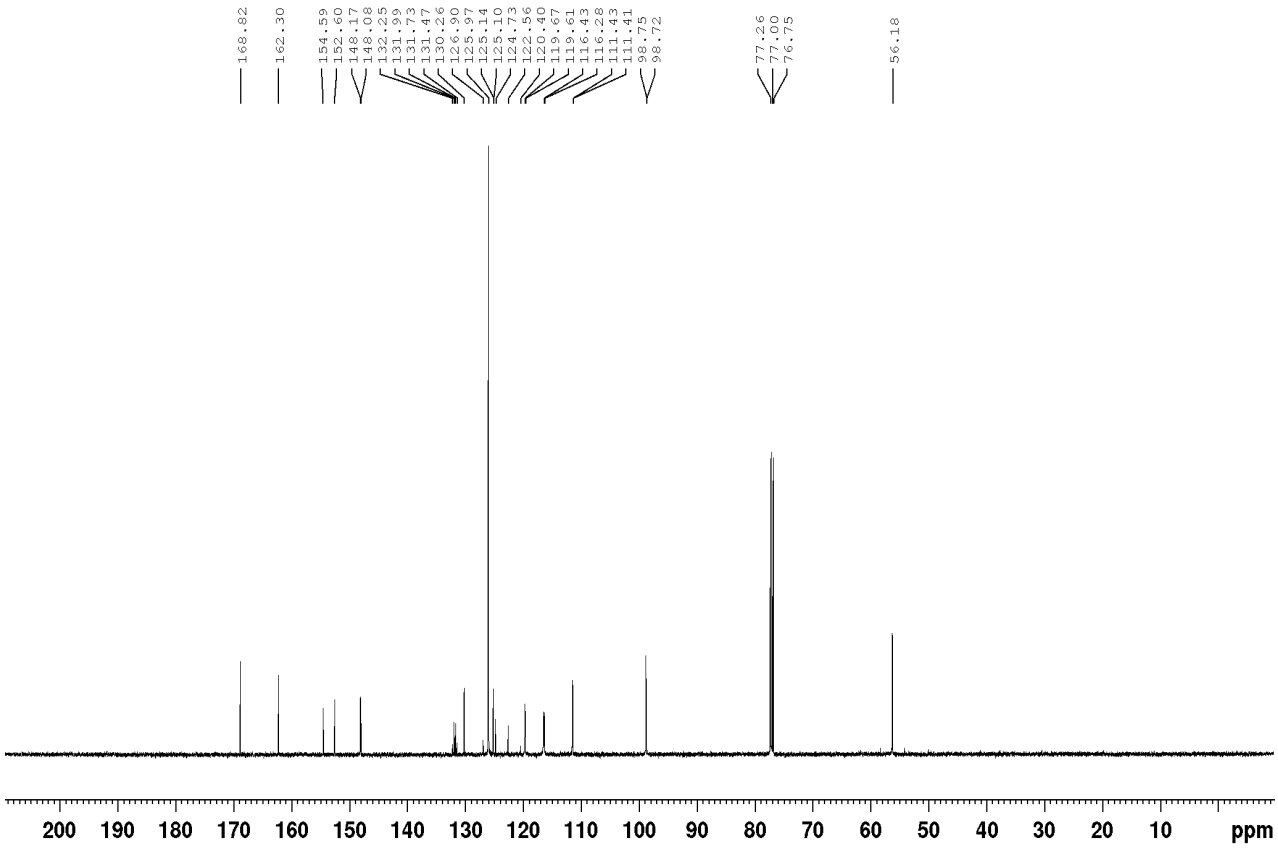


3-(4-Fuoro-3-methoxyphenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1k)

^{1}H NMR (400 MHz, $CDCl_3$)

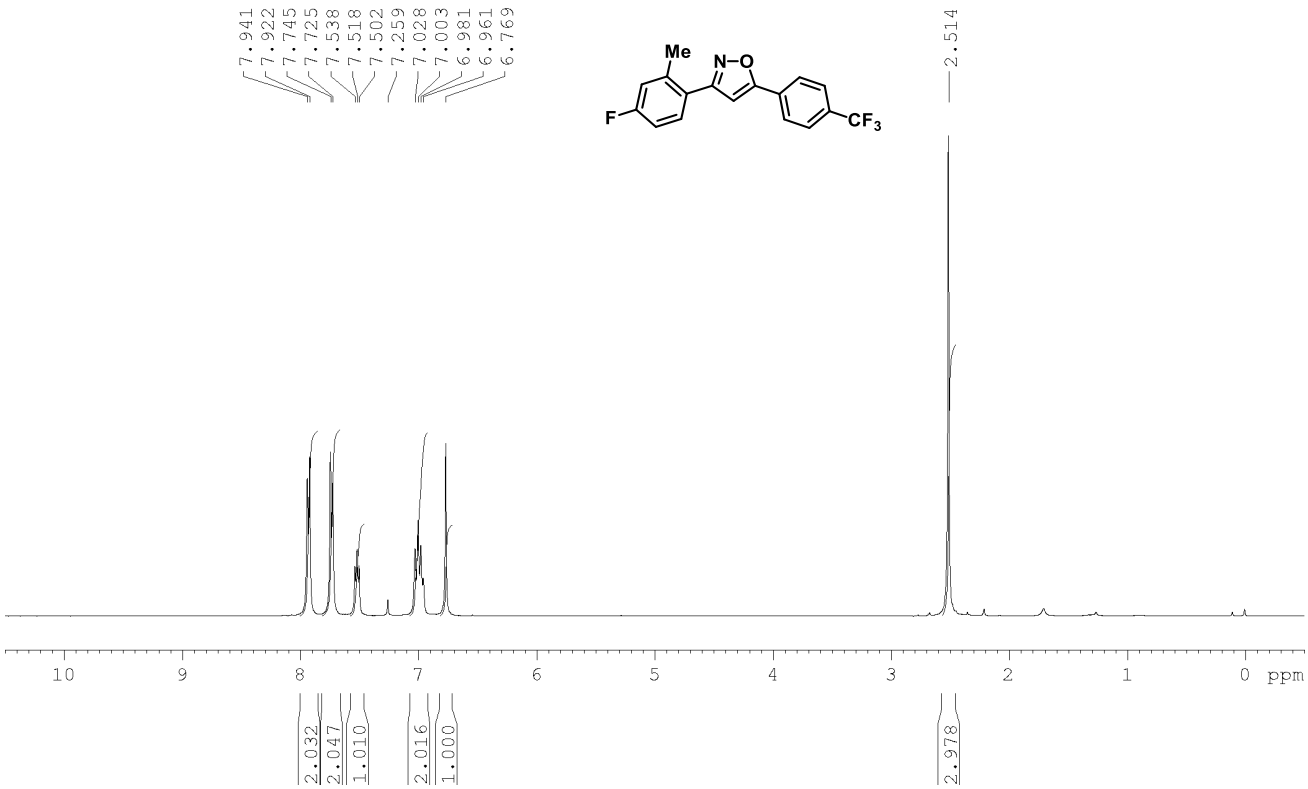


^{13}C NMR (125 MHz, $CDCl_3$)

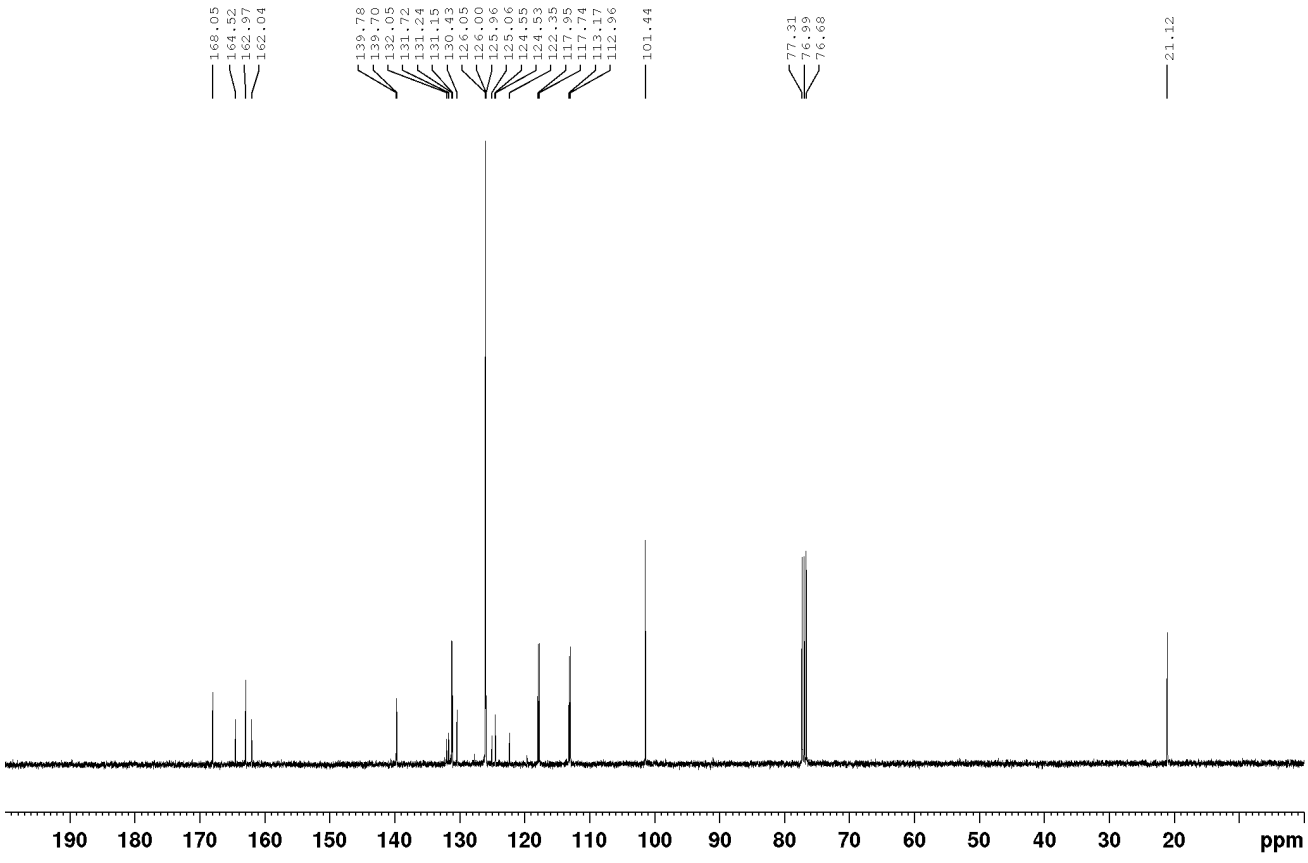


3-(4-Fluoro-2-methylphenyl)-5-{4-(trifluoromethyl)phenyl}isoxazole (1l)

^{1}H NMR (400 MHz, $CDCl_3$)

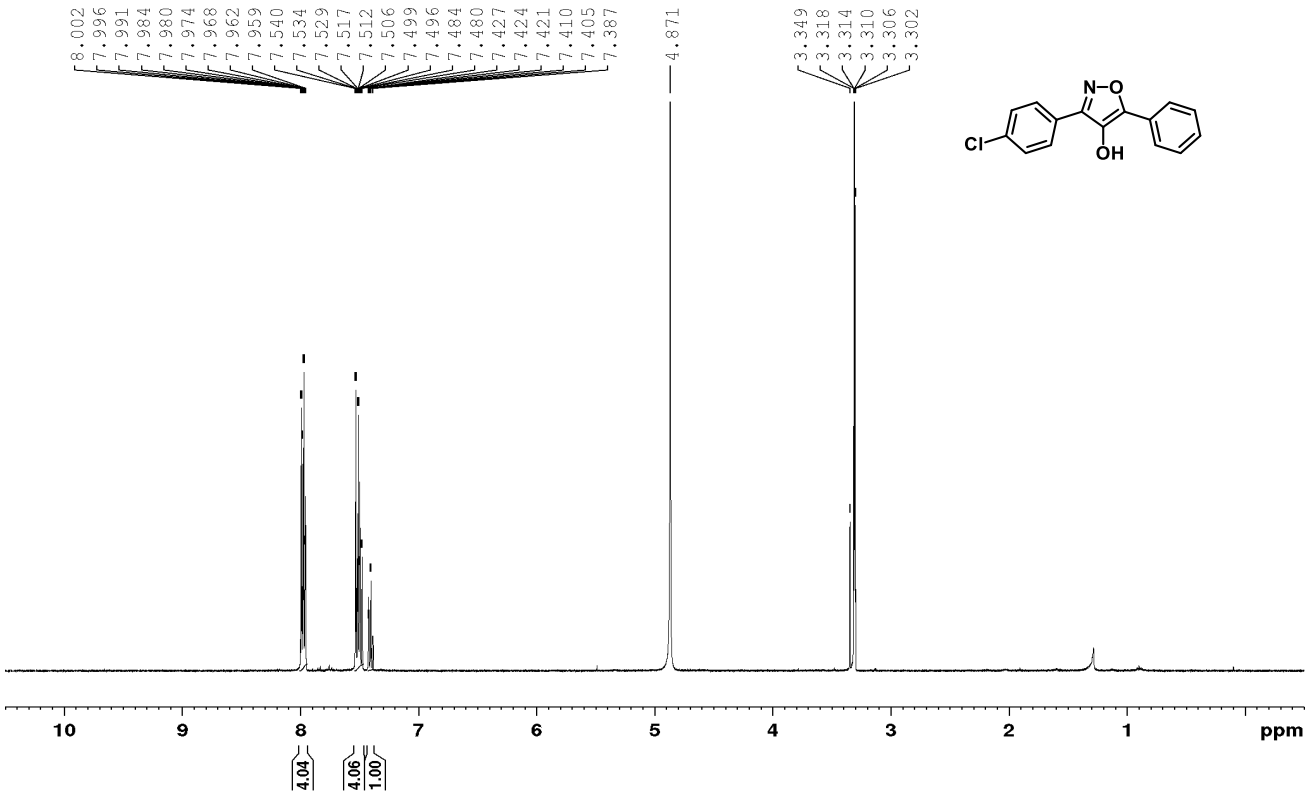


^{13}C NMR (125 MHz, $CDCl_3$)

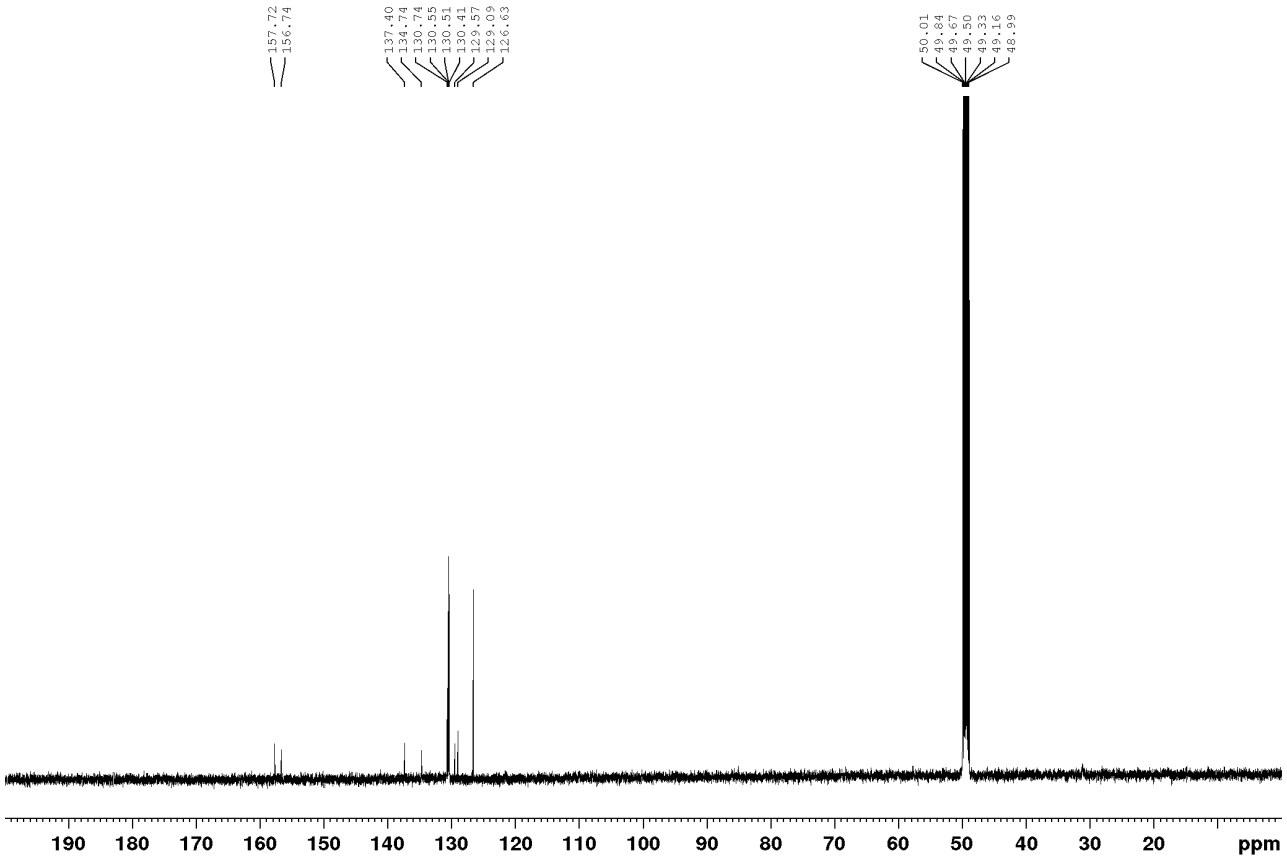


3-(4-Chlorophenyl)-5-phenylisoxazol-4-ol

^{1}H NMR (400 MHz, CD_3OD)

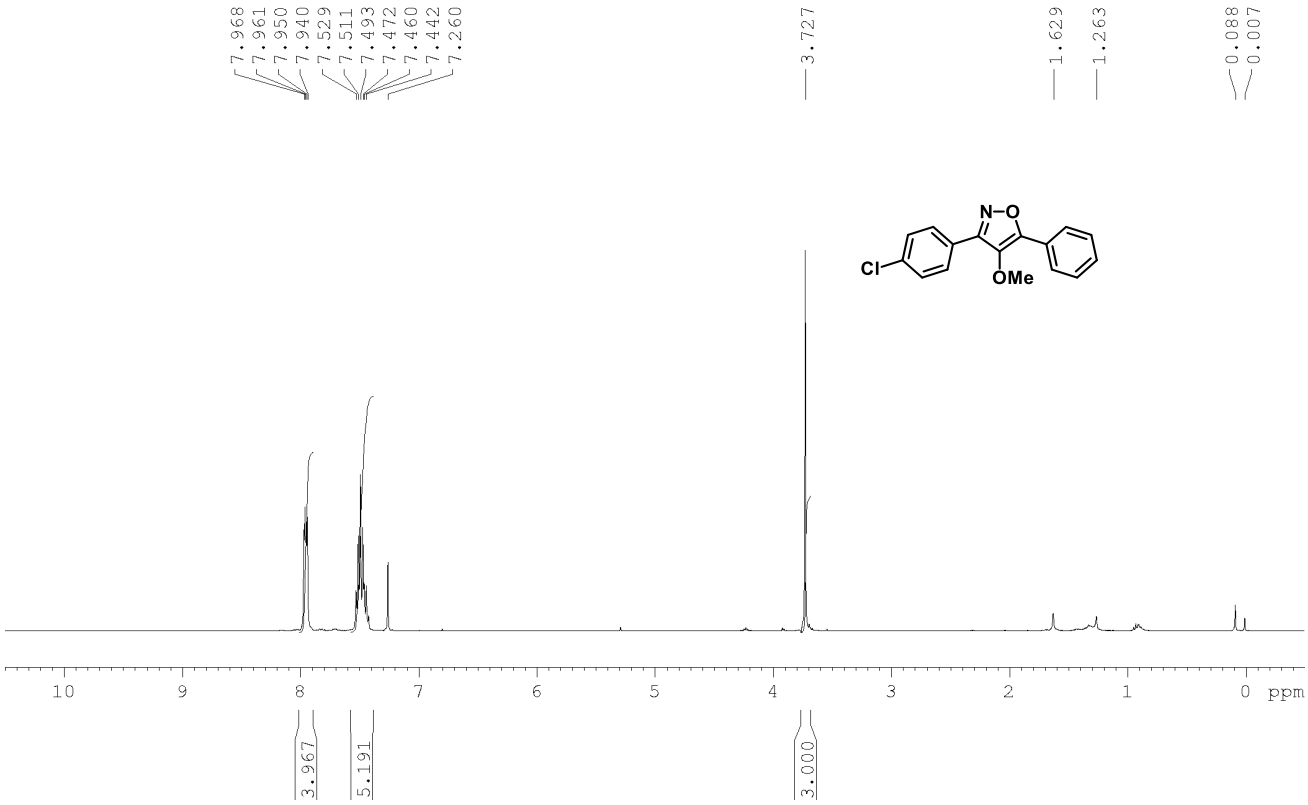


^{13}C NMR (125 MHz, CD_3OD)

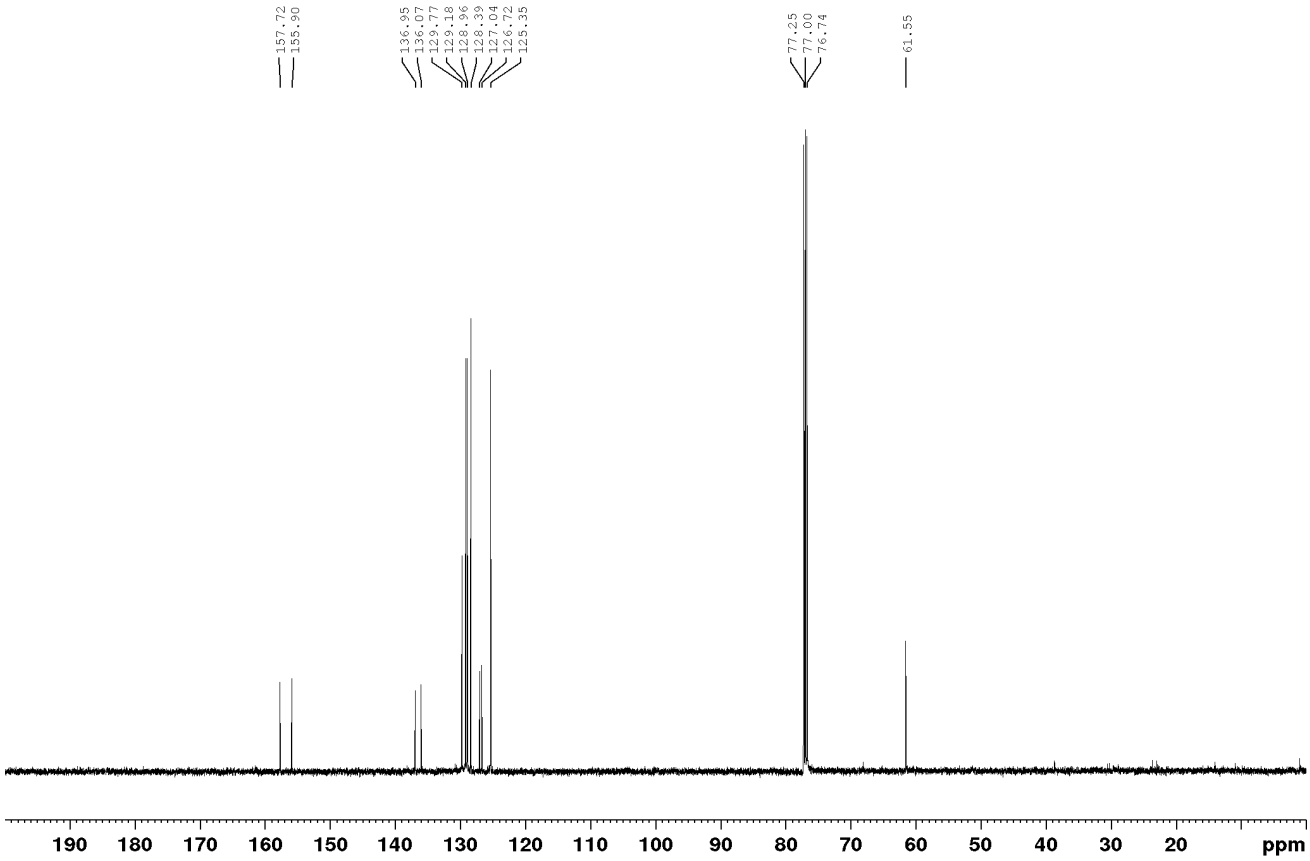


3-(4-Chlorophenyl)-4-methoxy-5-phenylisoxazole (1m)

^{1}H NMR (400 MHz, $CDCl_3$)

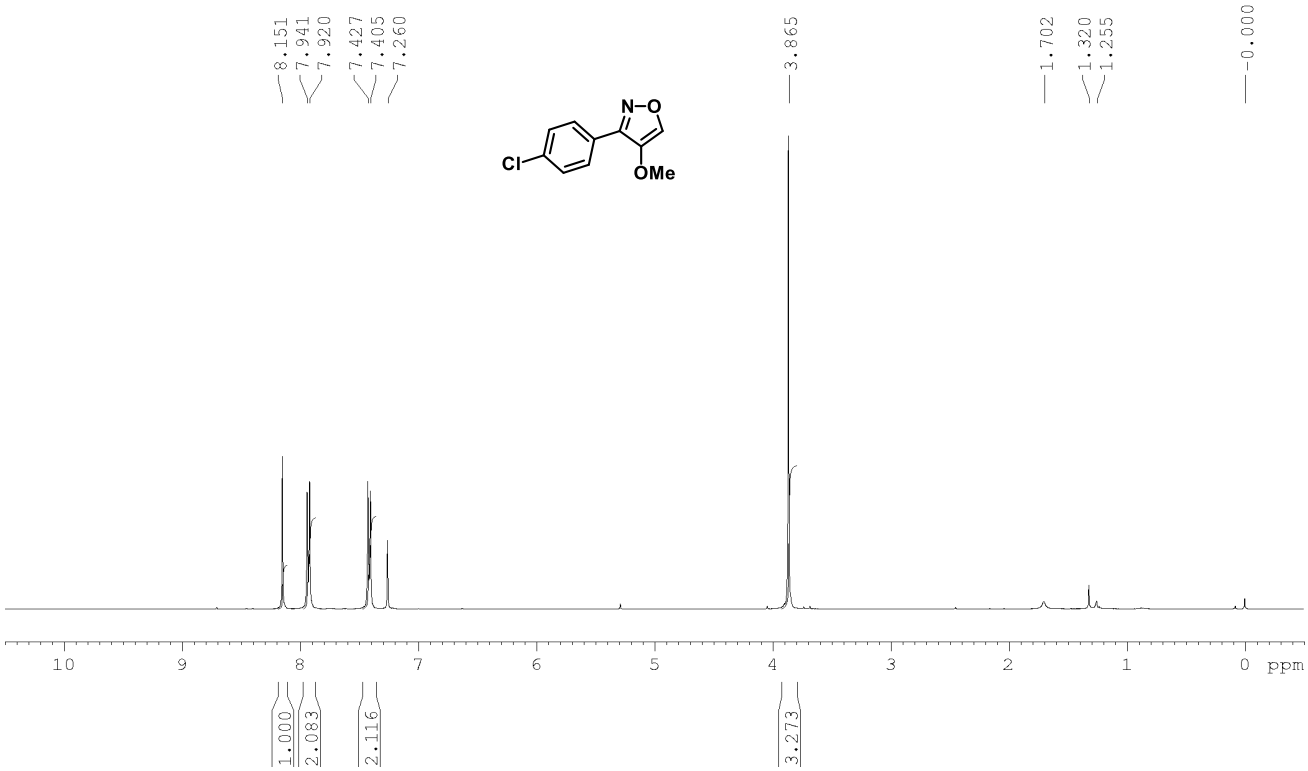


^{13}C NMR (125 MHz, $CDCl_3$)

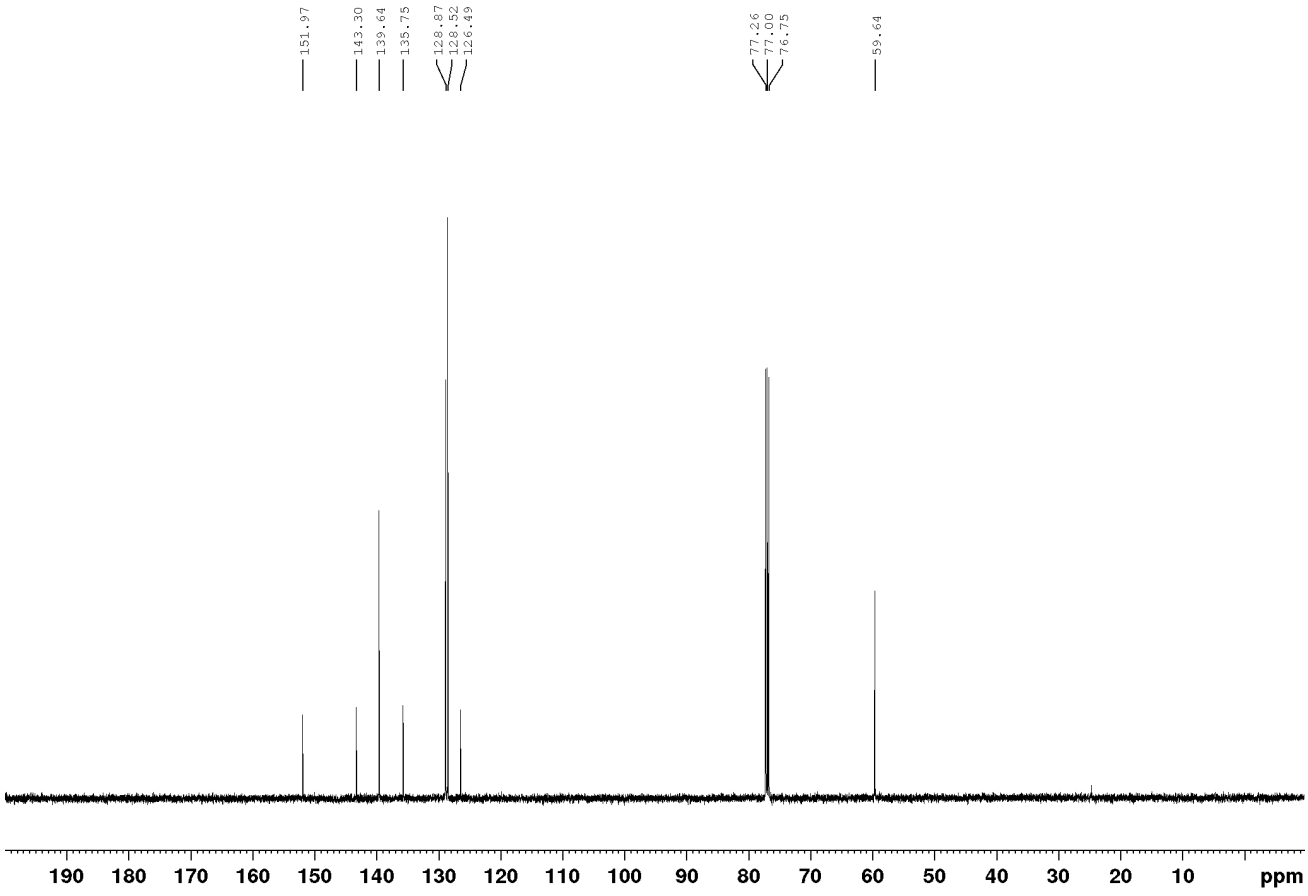


3-(4-Chlorophenyl)-4-methoxyisoxazole (1n)

^{1}H NMR (400 MHz, $CDCl_3$)

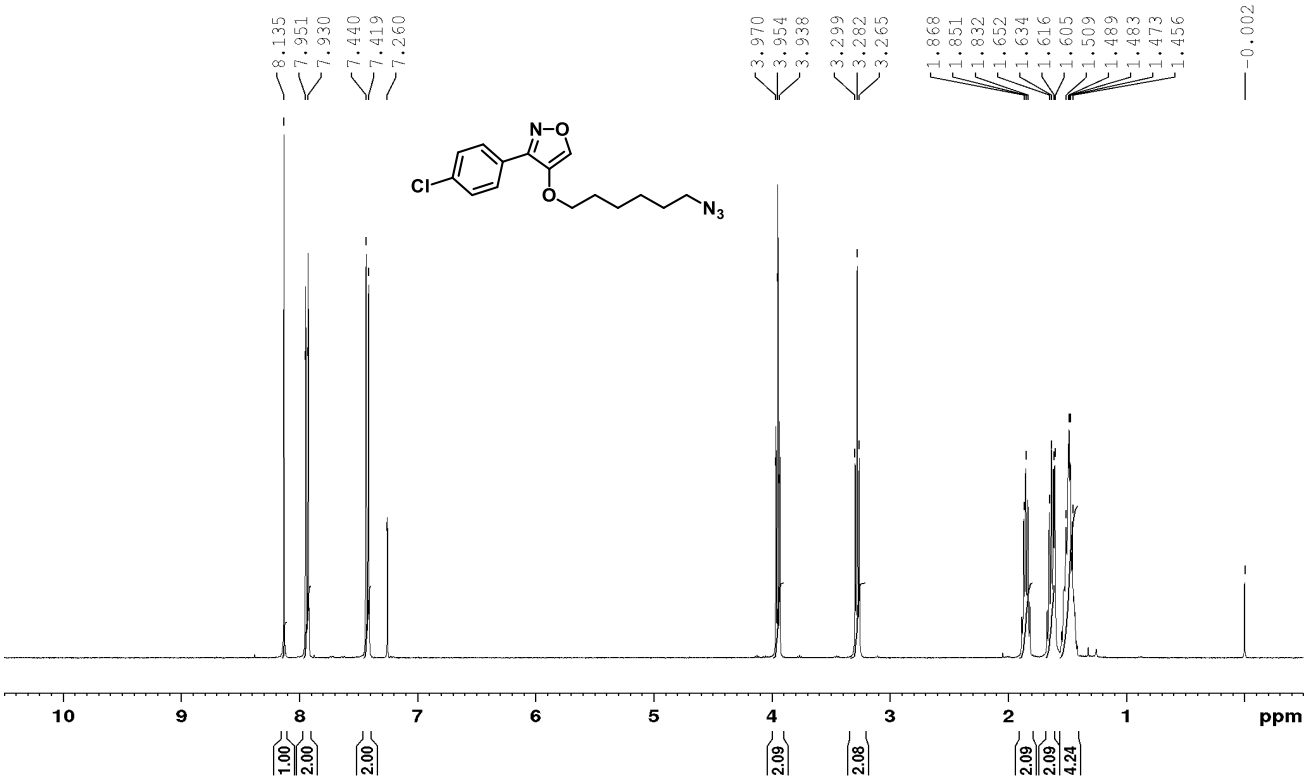


^{13}C NMR (125 MHz, $CDCl_3$)

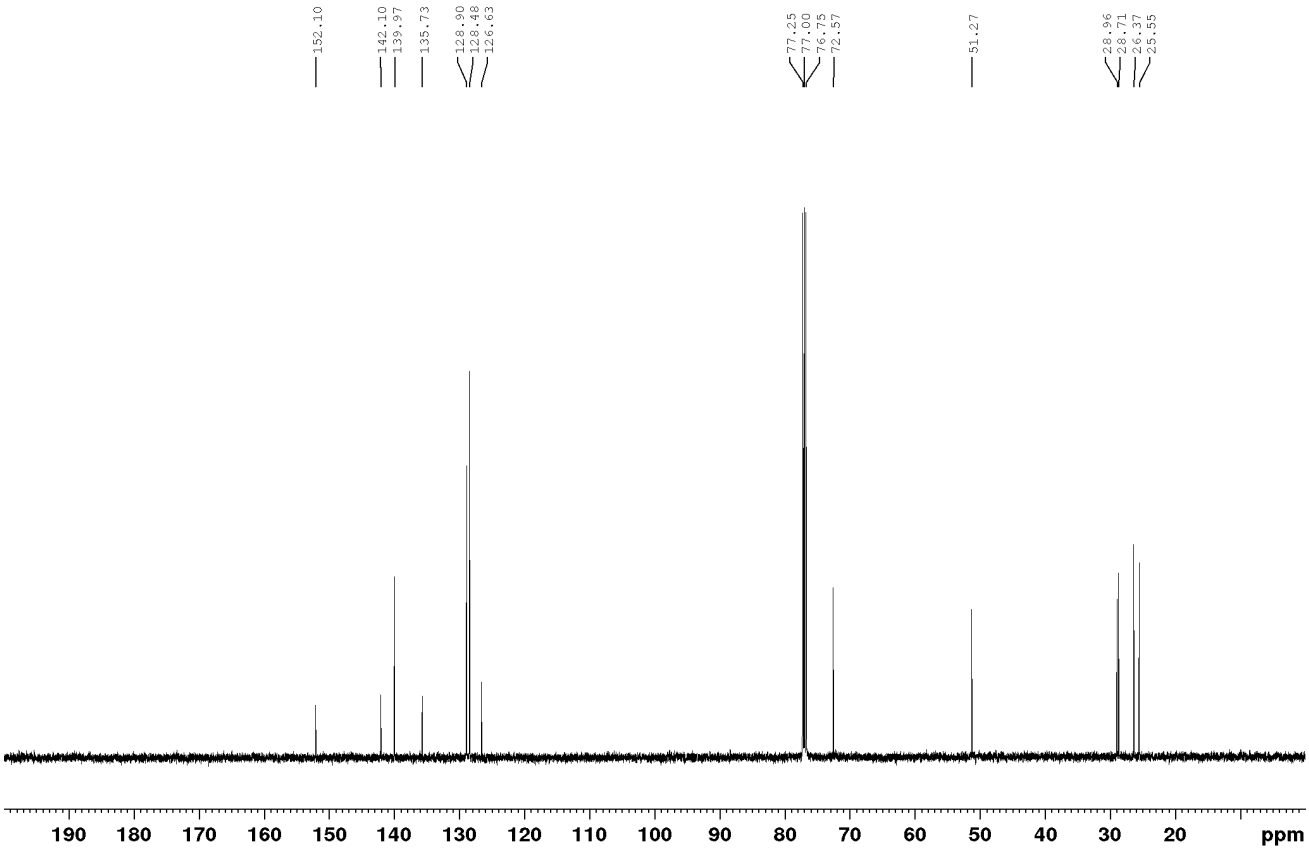


4-{(6-Azidohexyl)oxy}-3-(4-chlorophenyl)isoxazole (1o)

^{1}H NMR (400 MHz, $CDCl_3$)

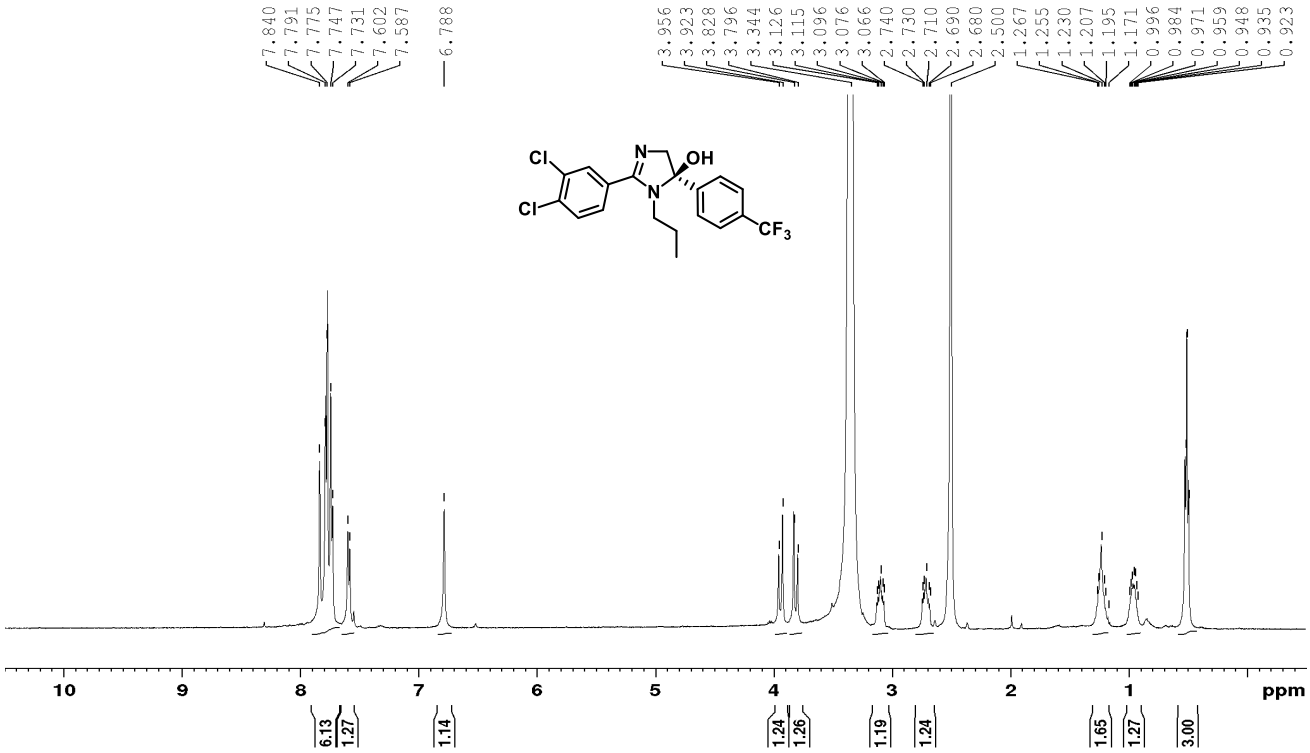


^{13}C NMR (125 MHz, $CDCl_3$)

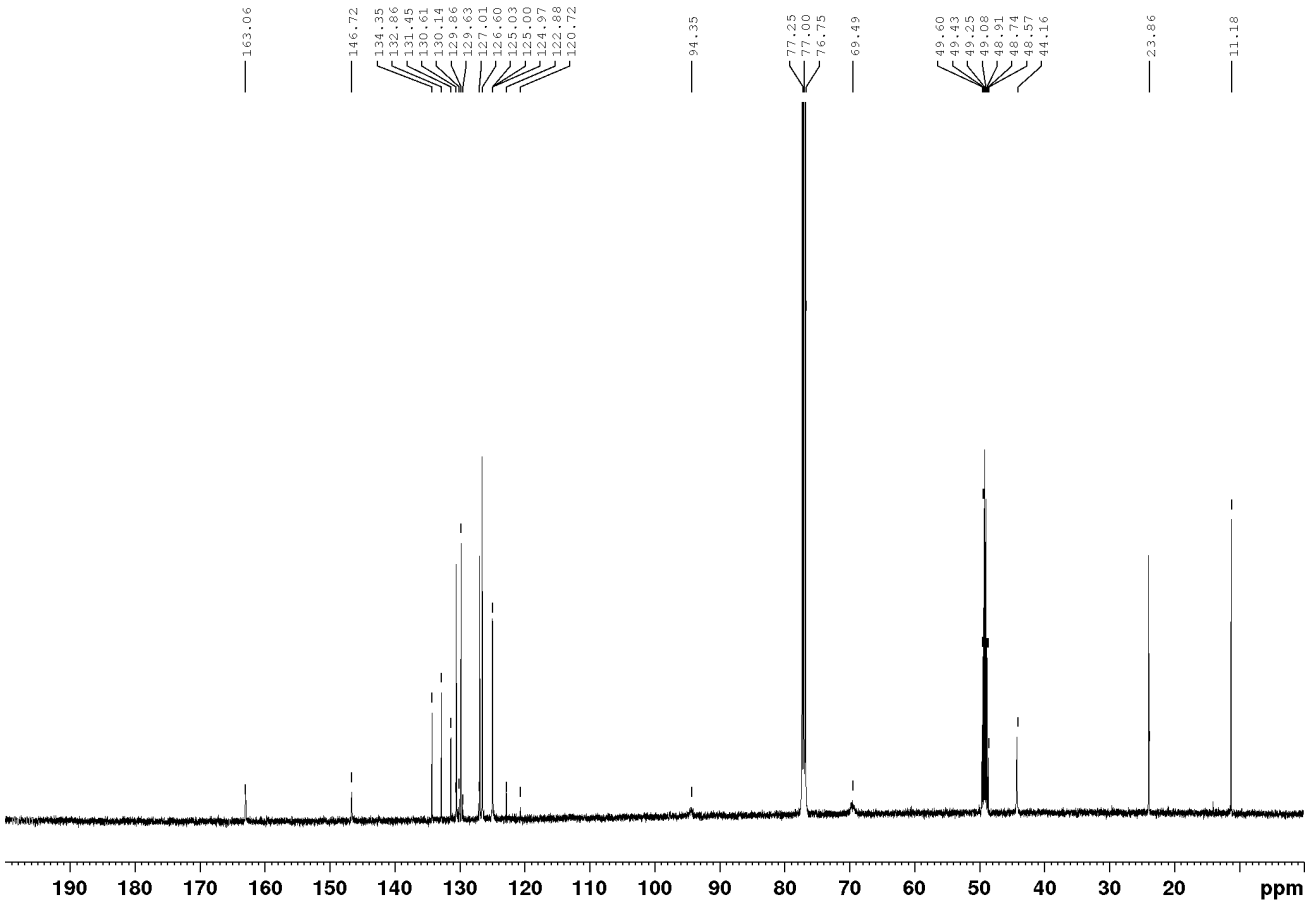


2-(3,4-Dichlorophenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2a)

^{1}H NMR (500 MHz, DMSO-d_6)

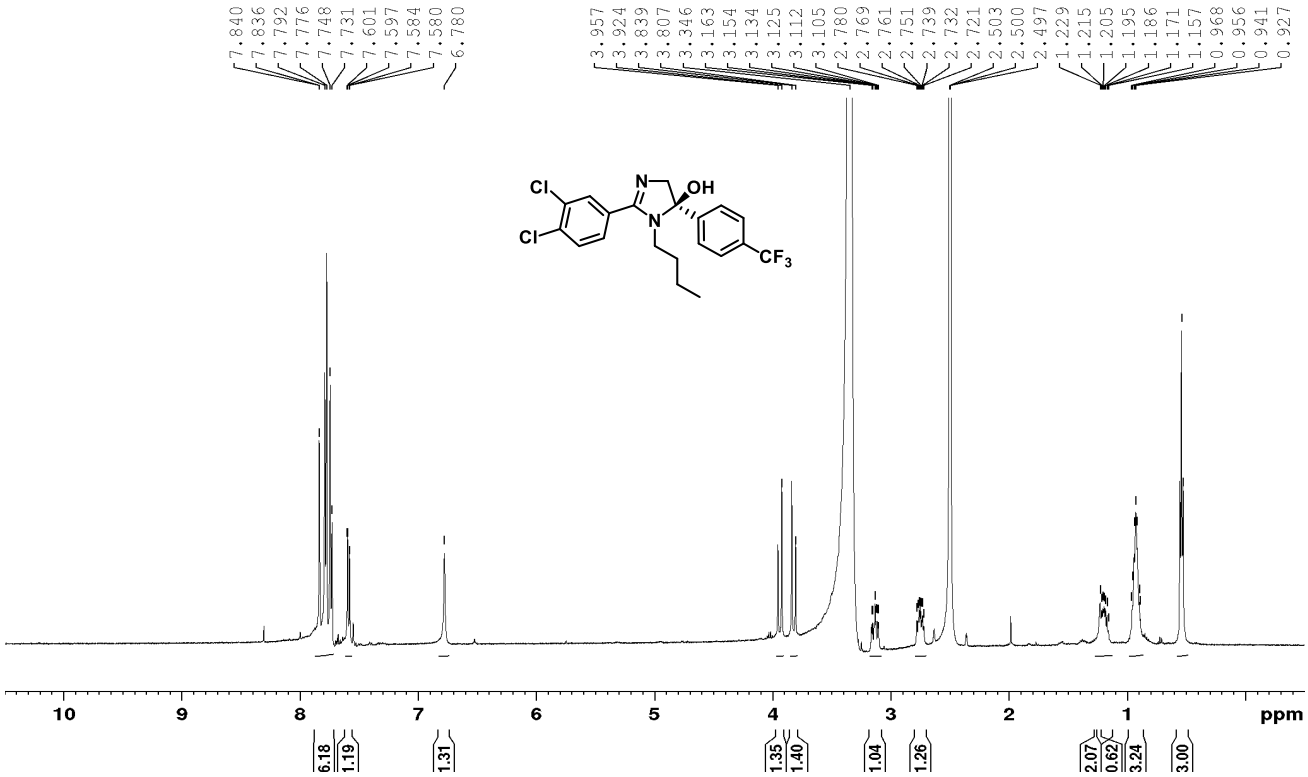


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1))

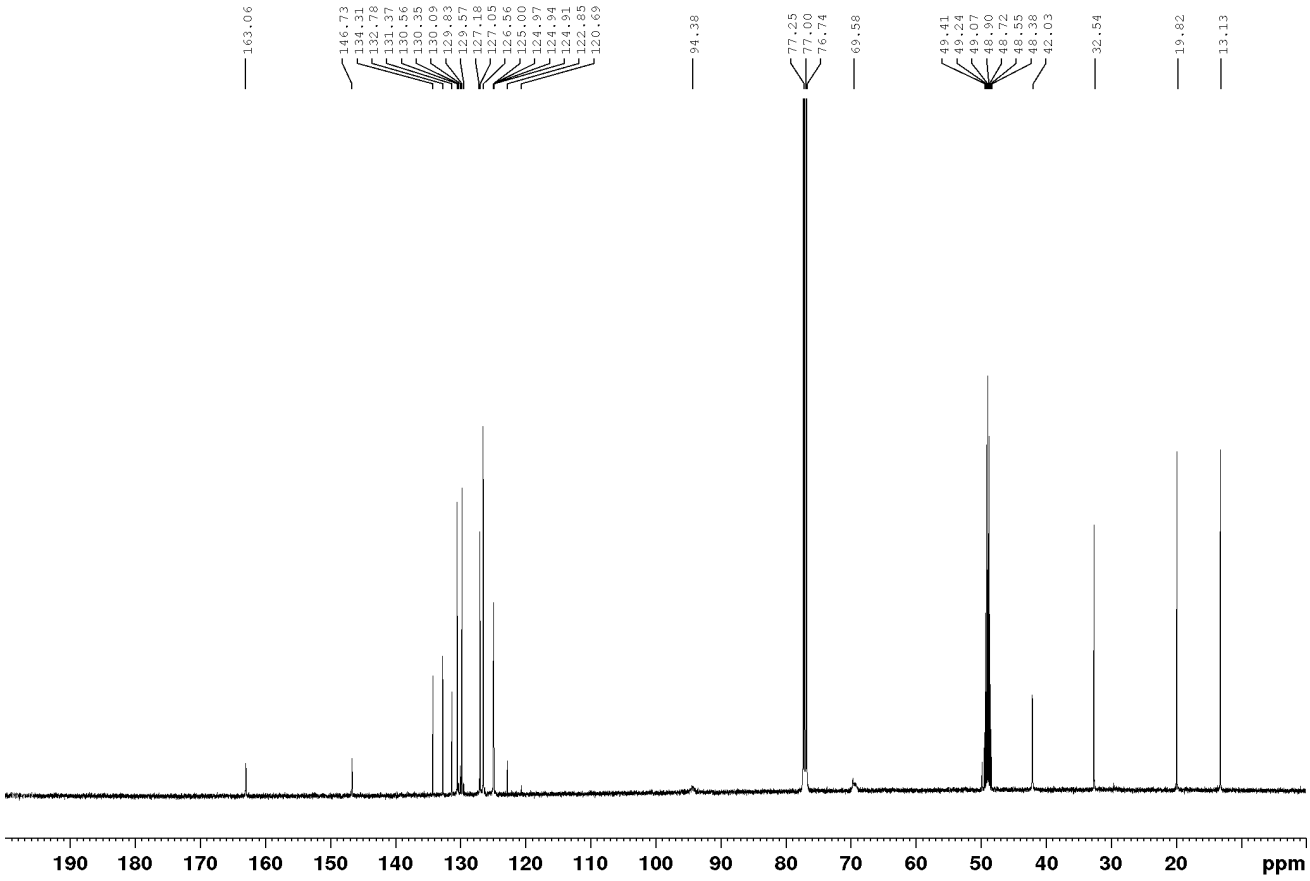


2-(3,4-Dichlorophenyl)-1-butyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2b)

^{1}H NMR (500 MHz, DMSO-d_6)

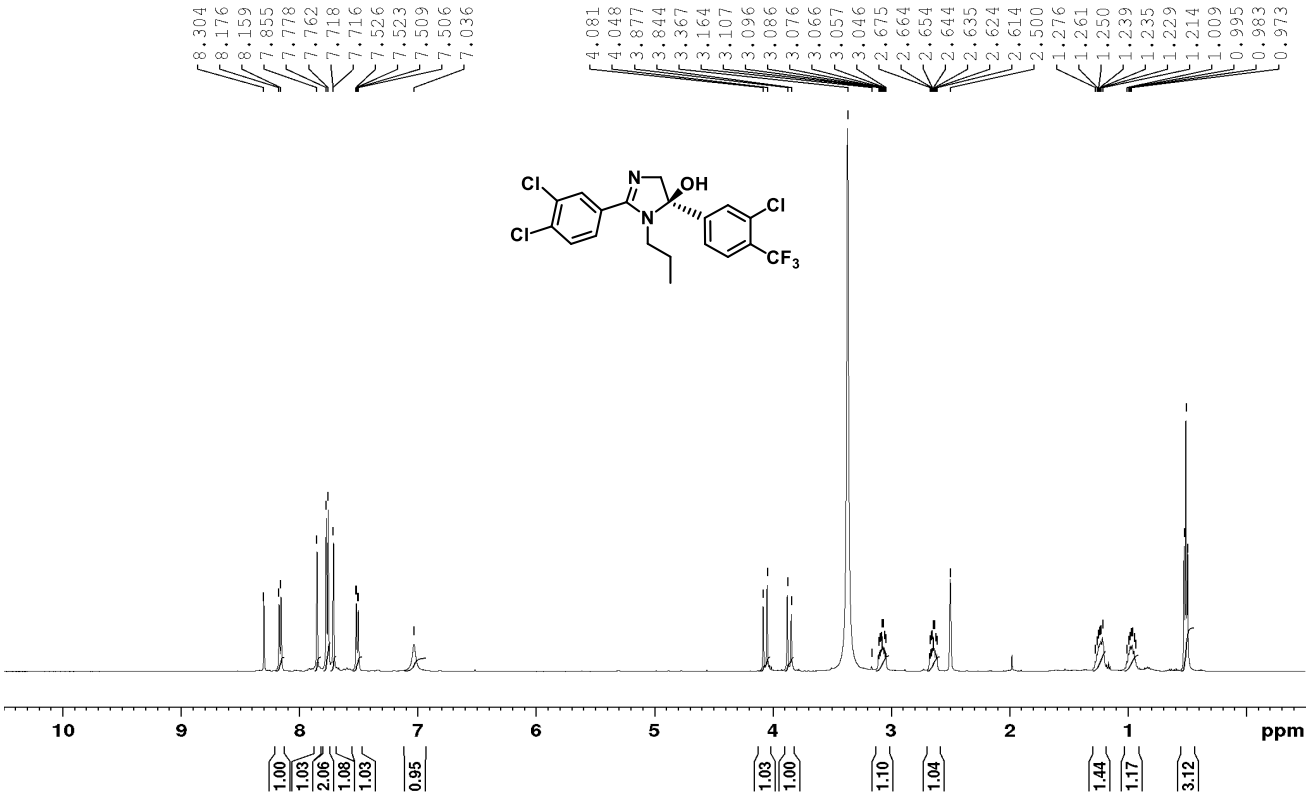


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1))

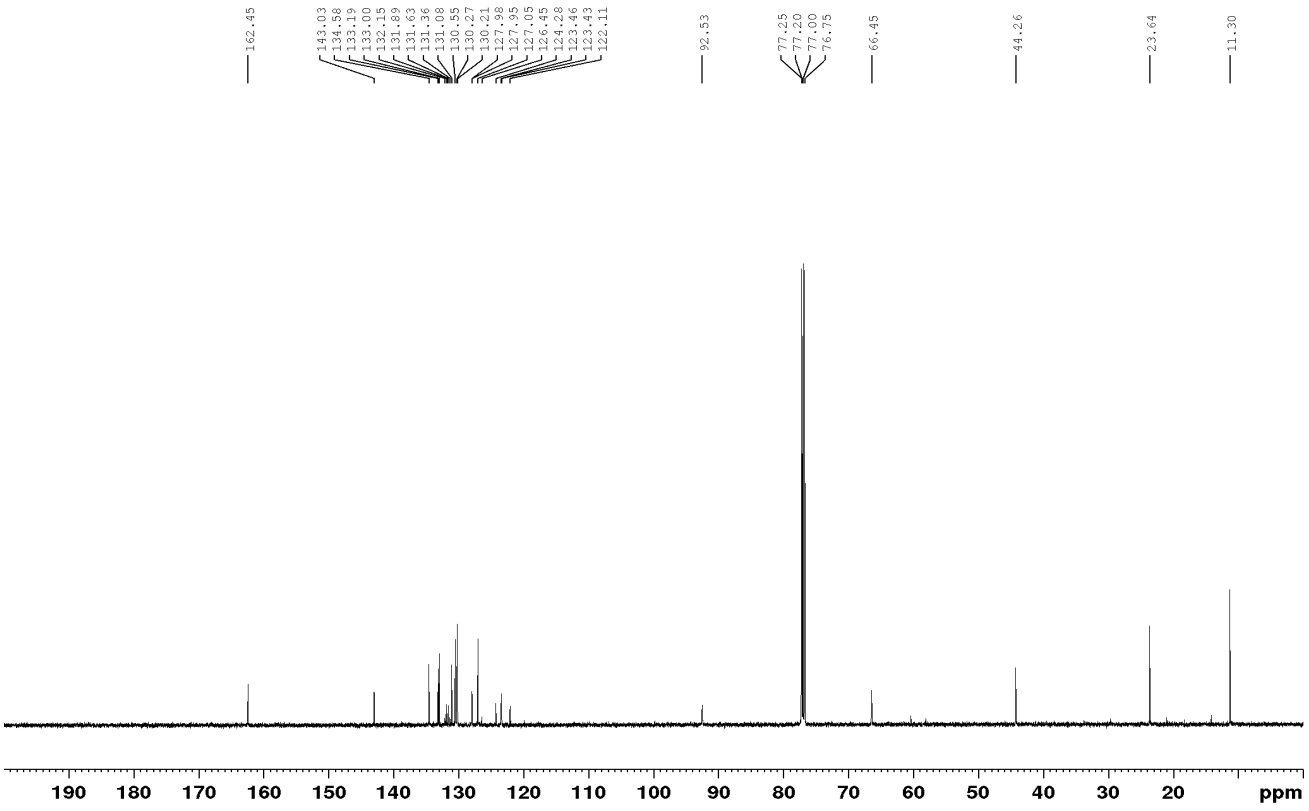


5-{2-Chloro-4-(trifluoromethyl)phenyl}-2-(3,4-dichlorophenyl)-1-propyl-4,5-dihydro-*1H*-imidazol-5-ol (2c)

^{1}H NMR (500 MHz, DMSO-d_6)

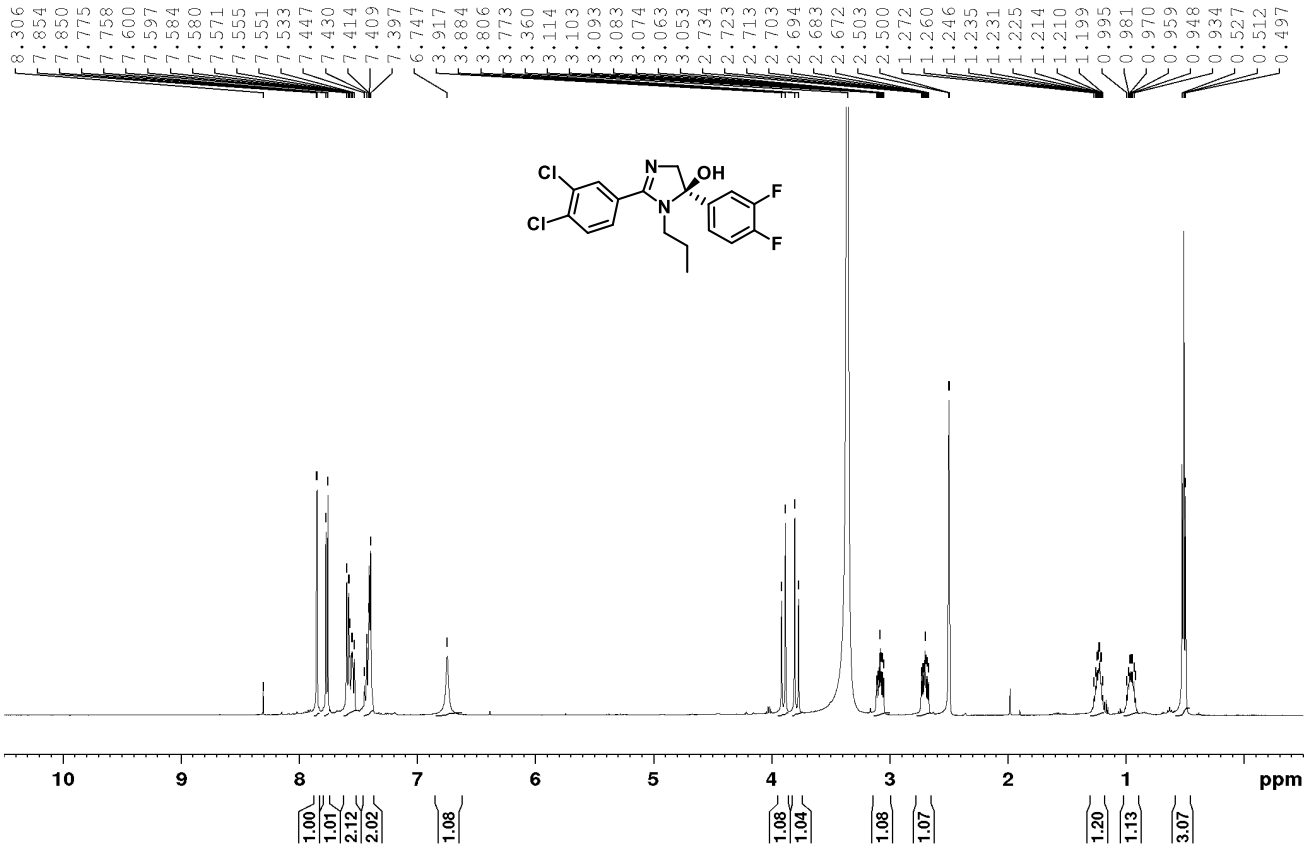


^{13}C NMR (125 MHz, CD_3Cl)

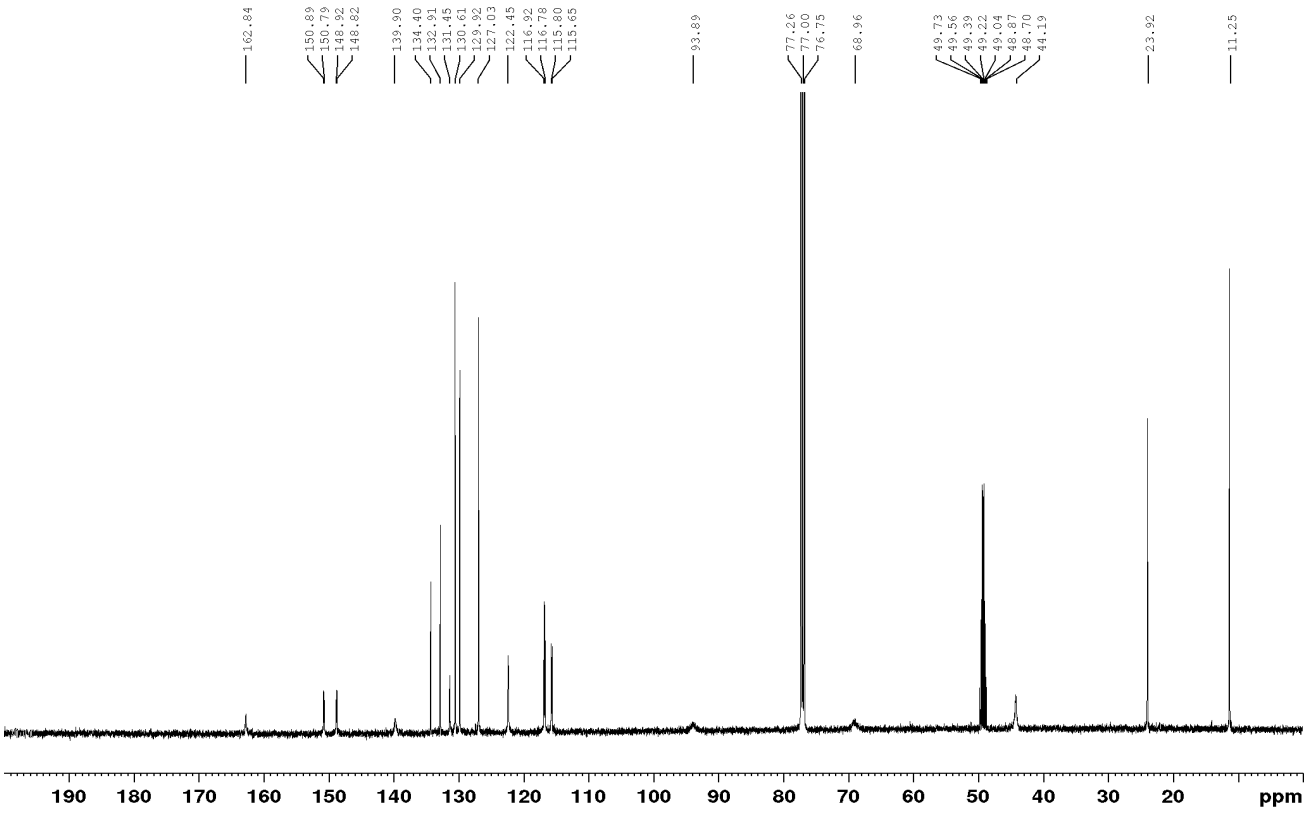


2-(3,4-Dichlorophenyl)-5-(3,4-difluorophenyl)-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2d)

^{1}H NMR (500 MHz, DMSO-d_6)

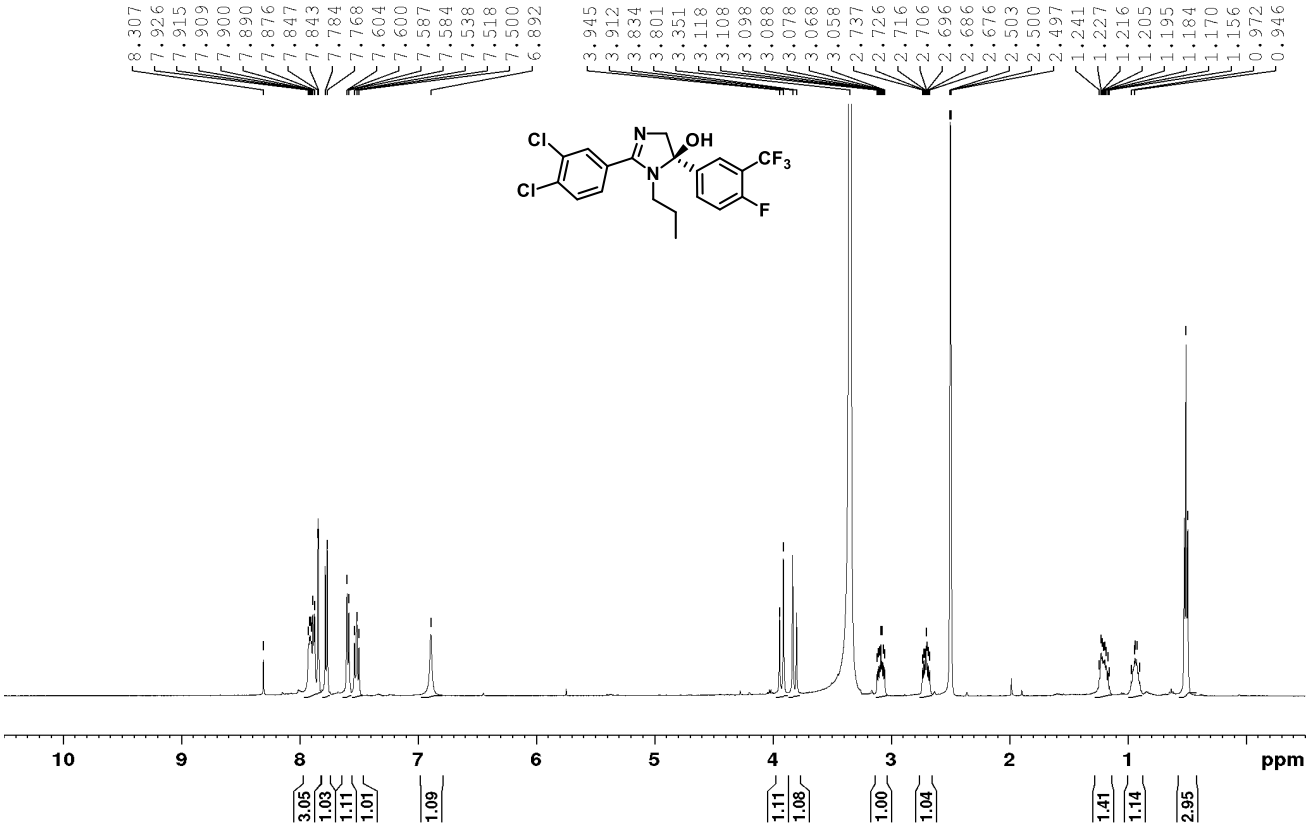


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1))

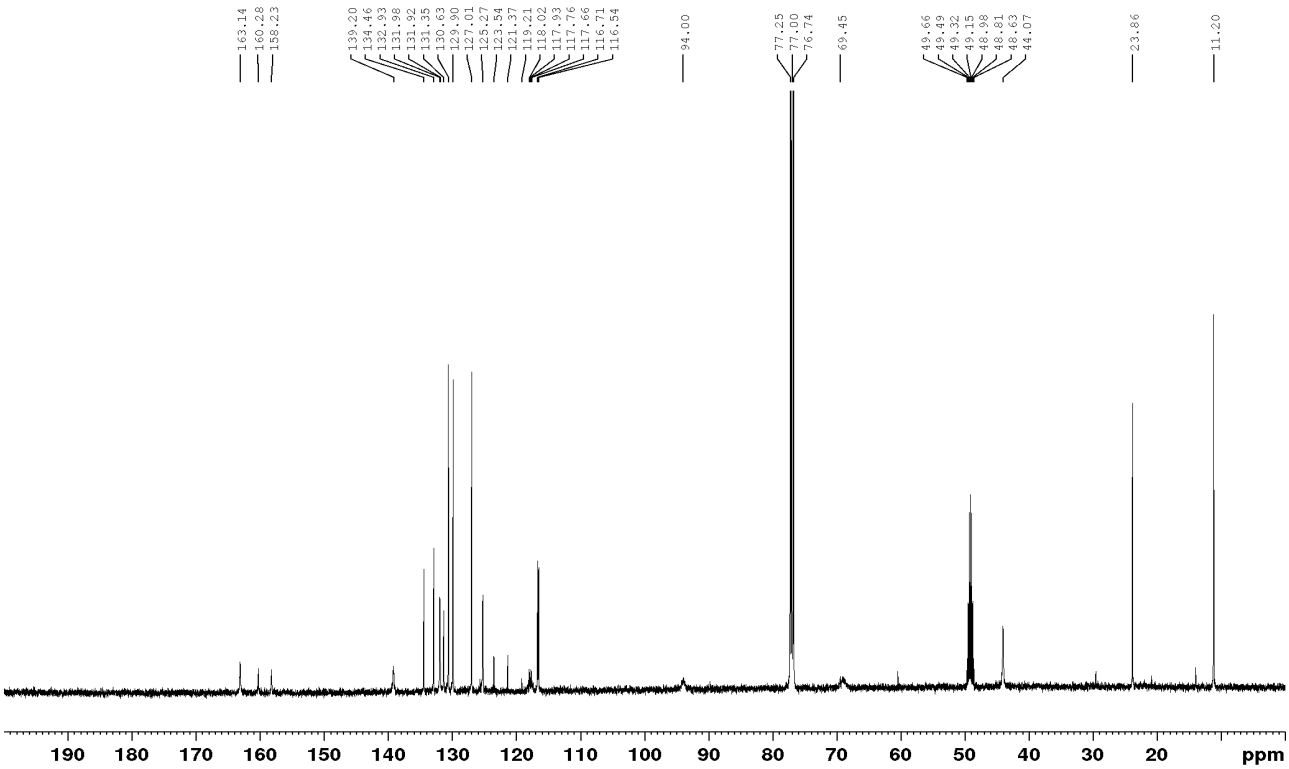


2-(3,4-Dichlorophenyl)-5-{4-fluoro-3-(trifluoromethyl)phenyl}-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2e)

^{1}H NMR (500 MHz, DMSO-d_6)

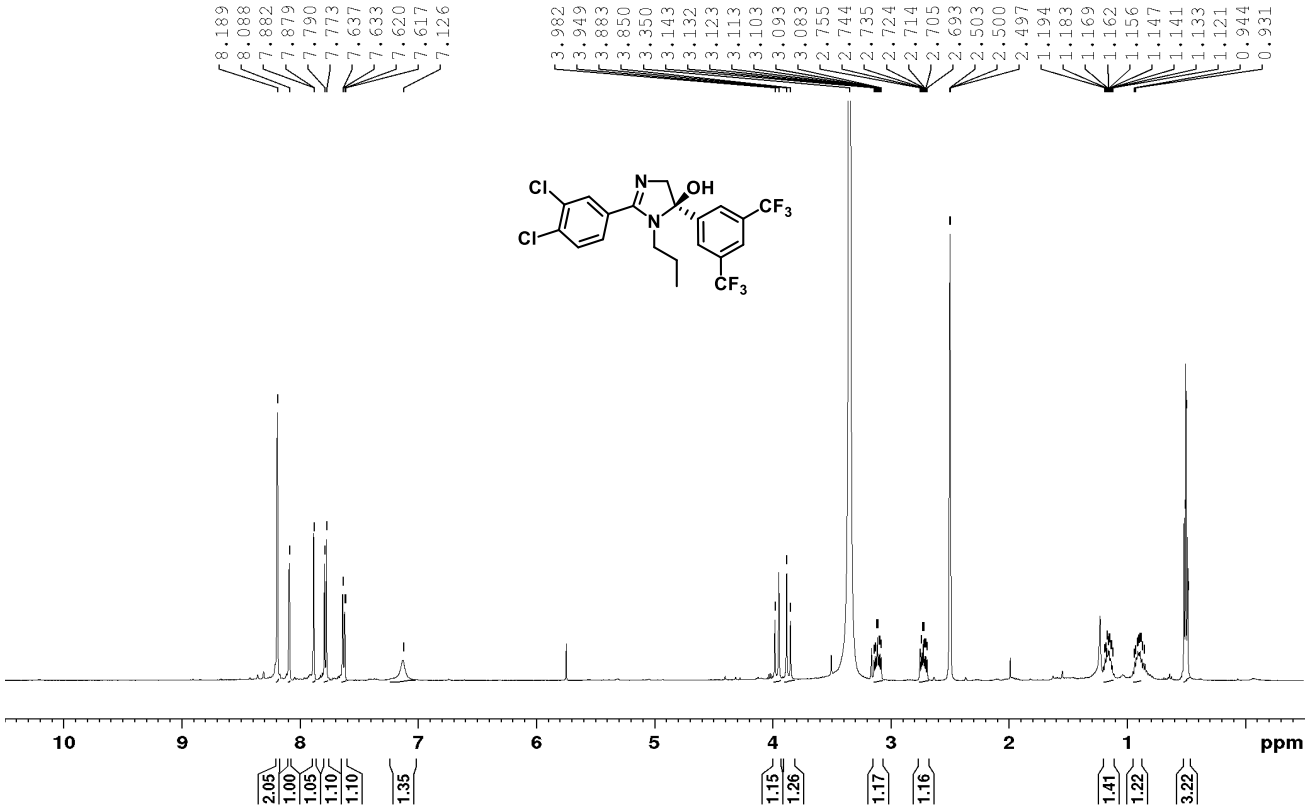


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1))

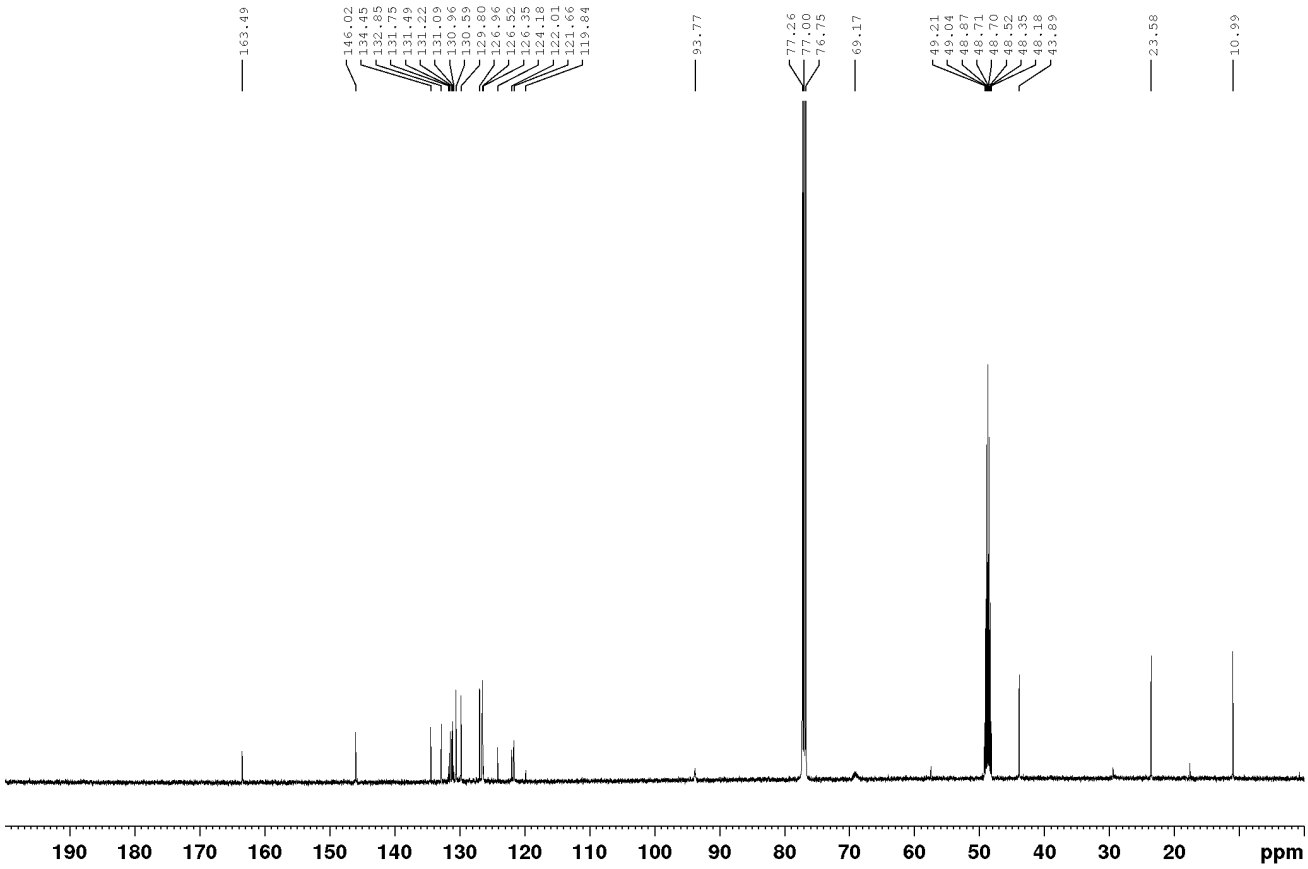


5-{3,5-bis(trifluoromethyl)phenyl}-2-(3,4-dichlorophenyl)-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2f)

^{1}H NMR (500 MHz, DMSO-d_6)

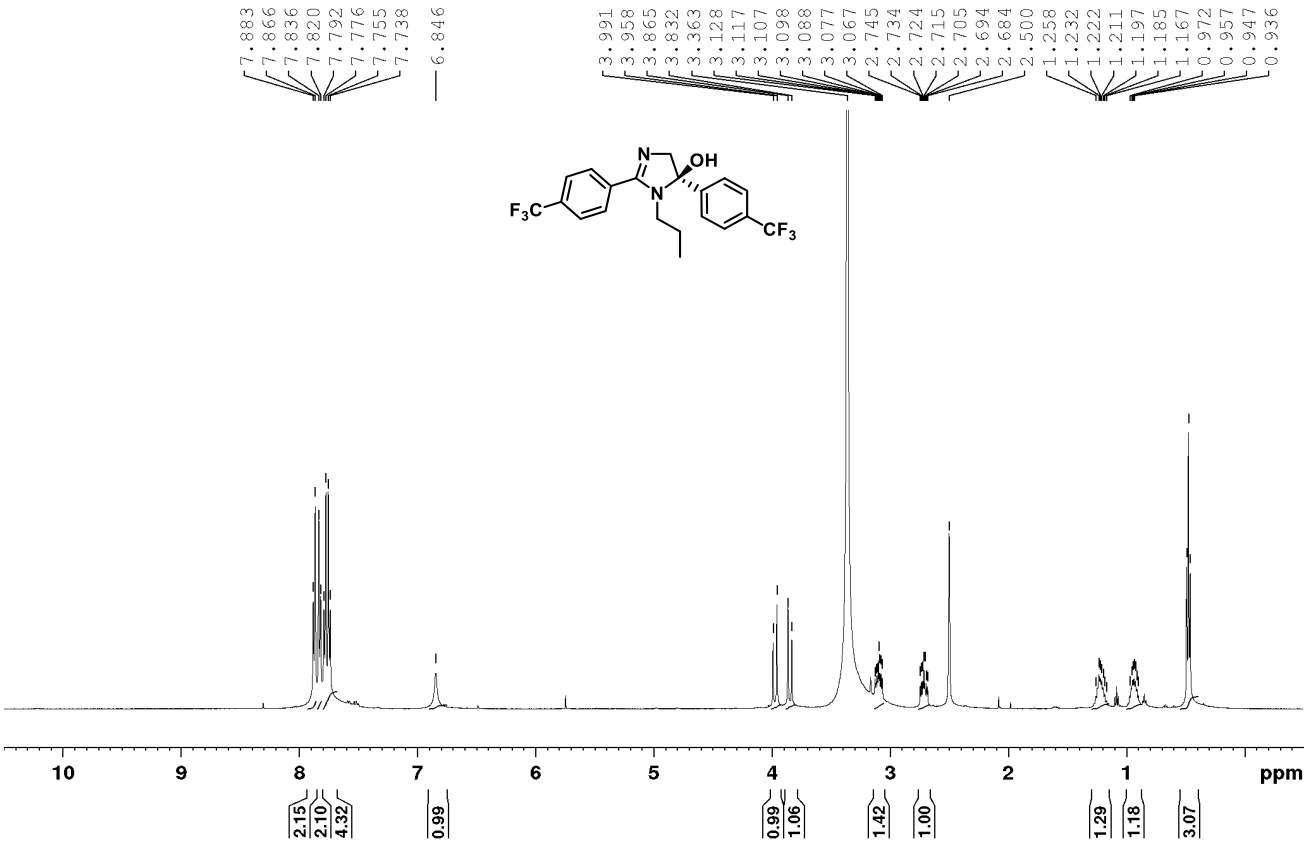


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1))

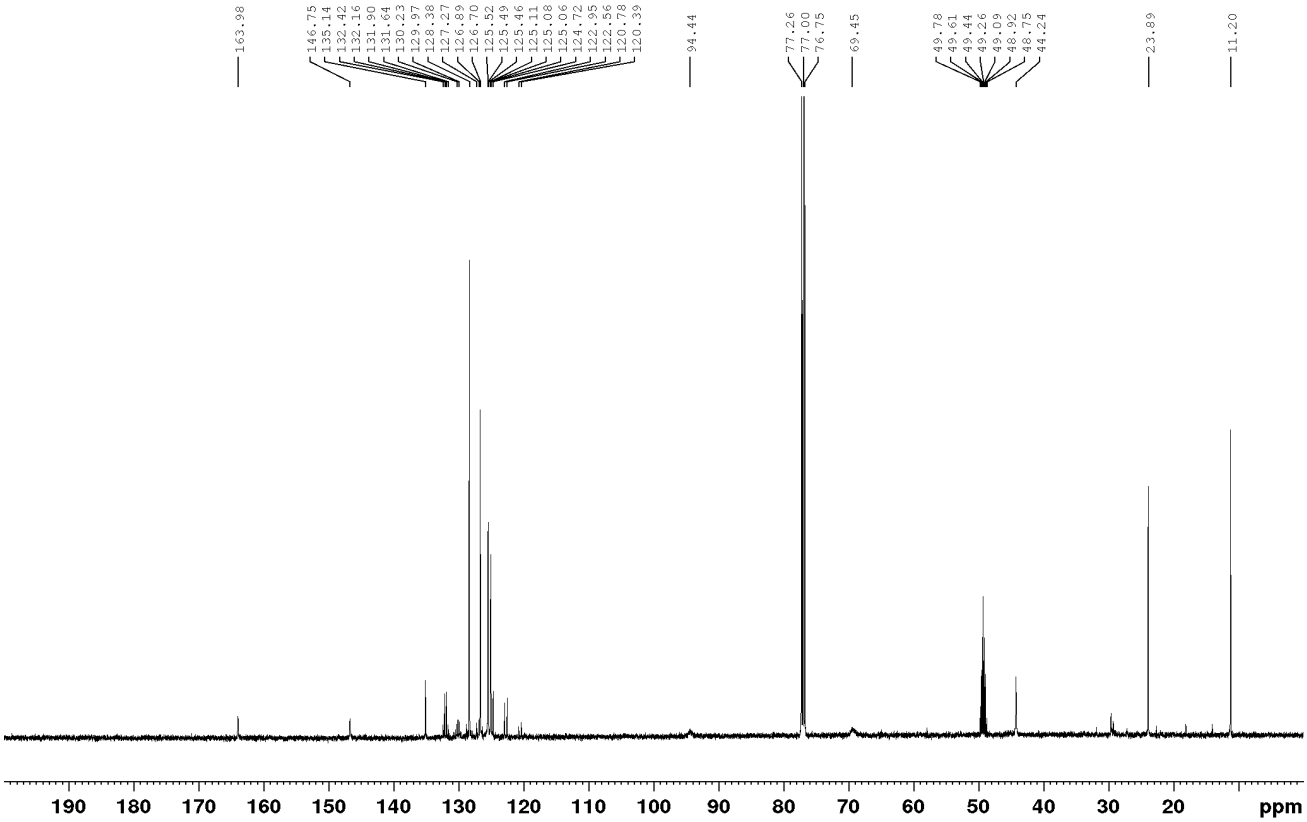


1-Propyl-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2g)

^{1}H NMR (500 MHz, DMSO-d_6)

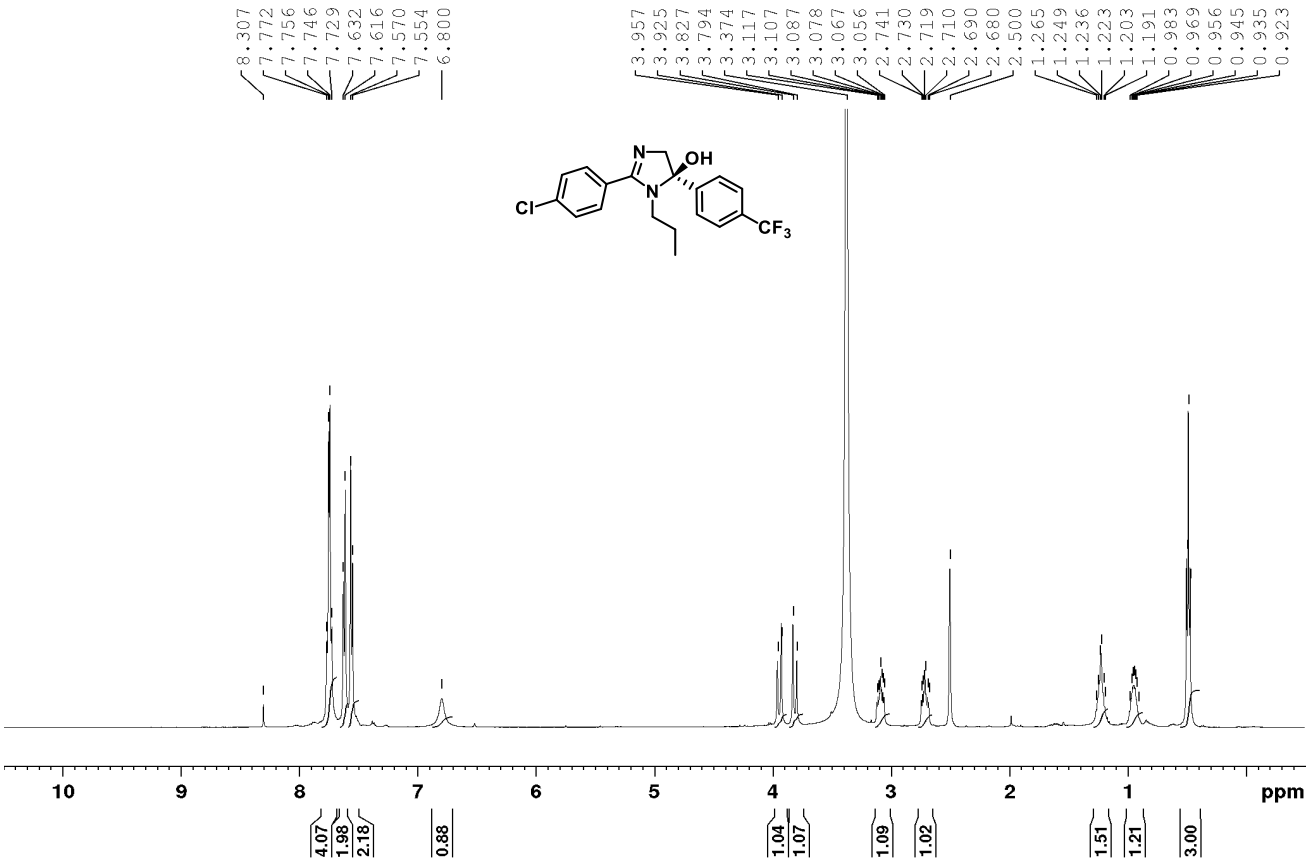


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1))

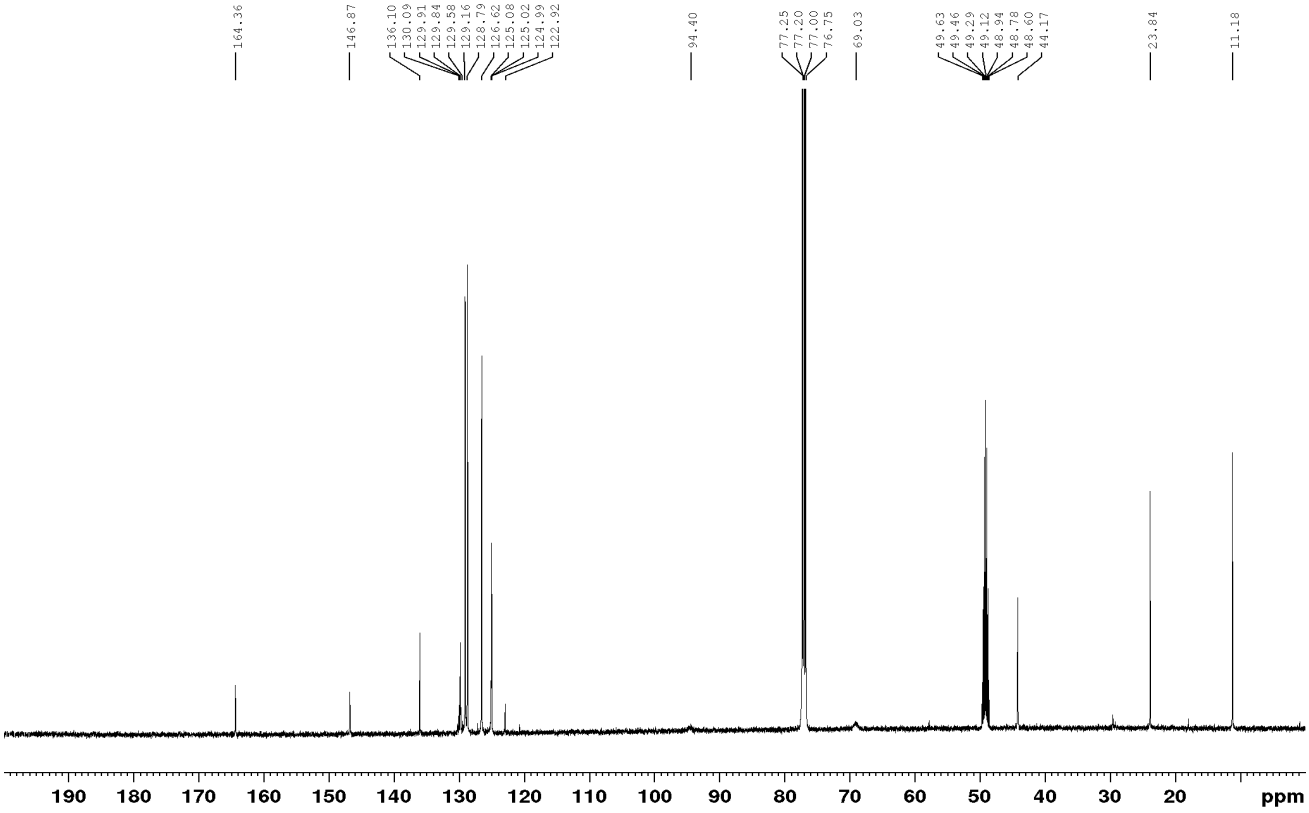


2-(4-Chlorophenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2h)

^{1}H NMR (500 MHz, DMSO-d_6)

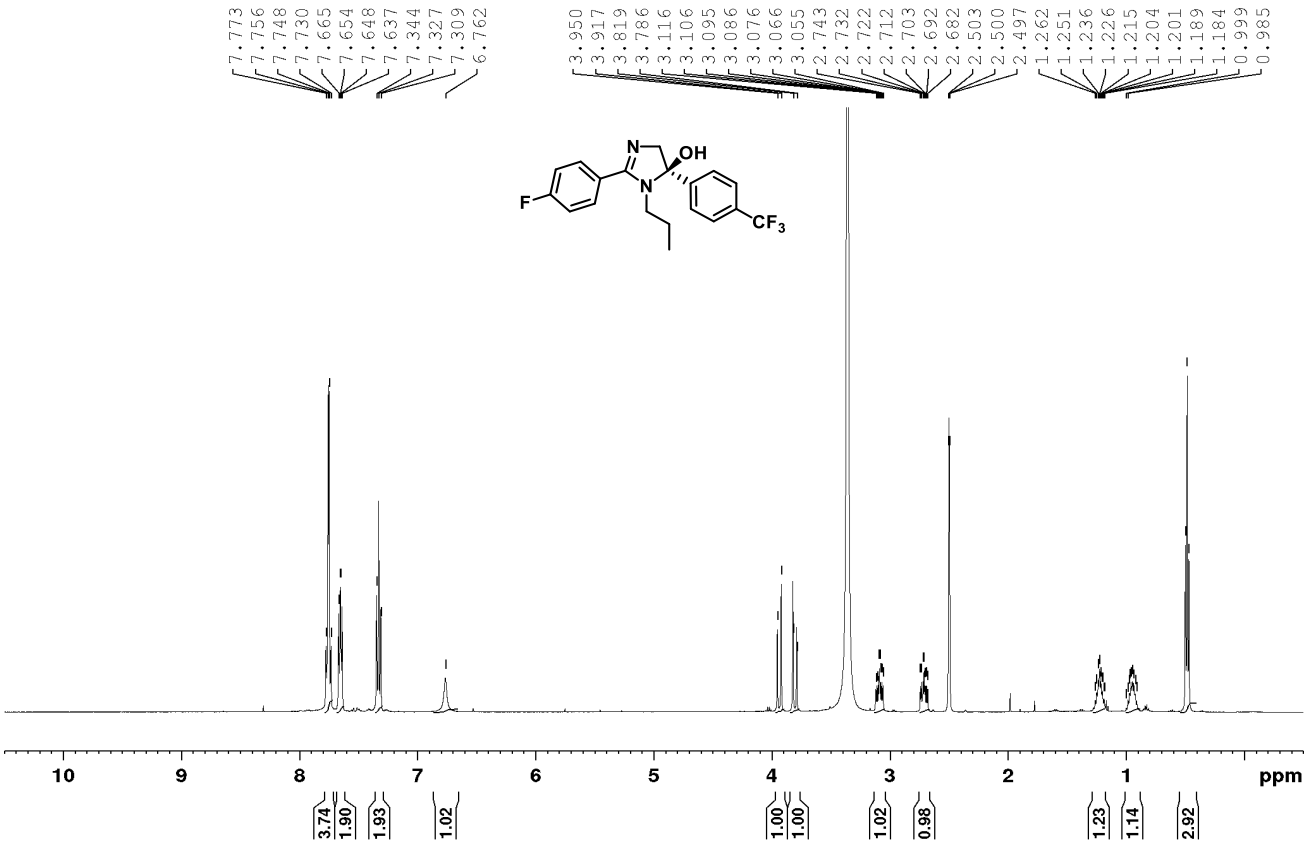


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1))

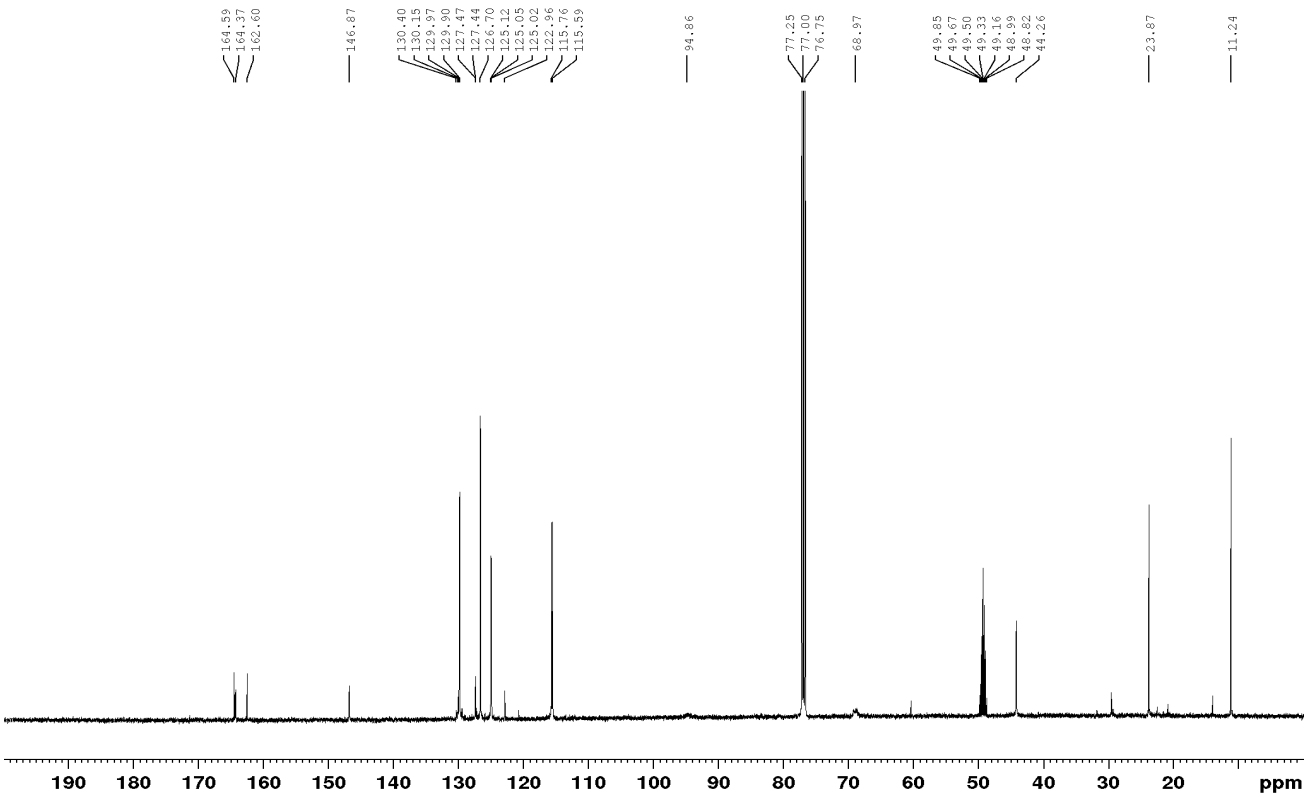


2-(4-Fluorophenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2i)

^{1}H NMR (500 MHz, DMSO-d_6)

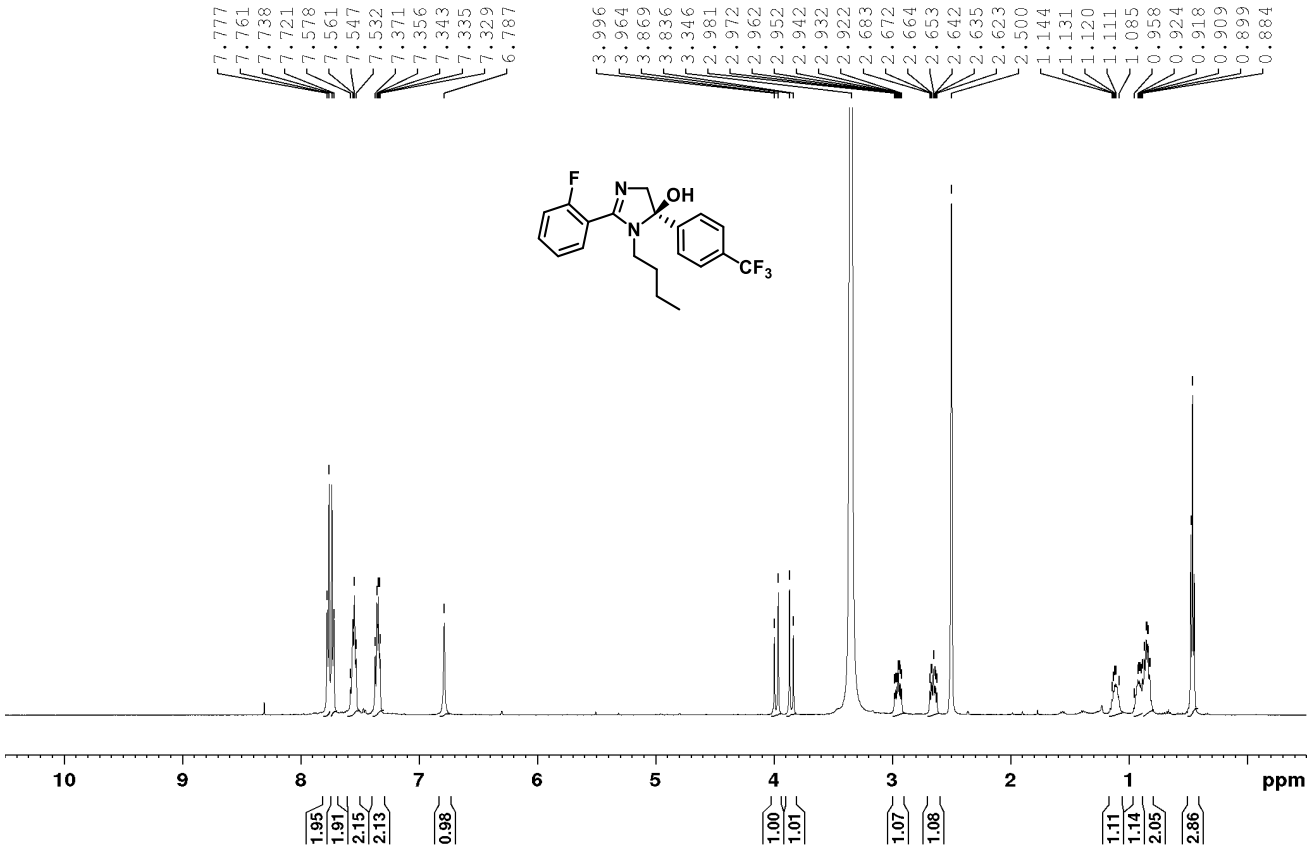


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1))

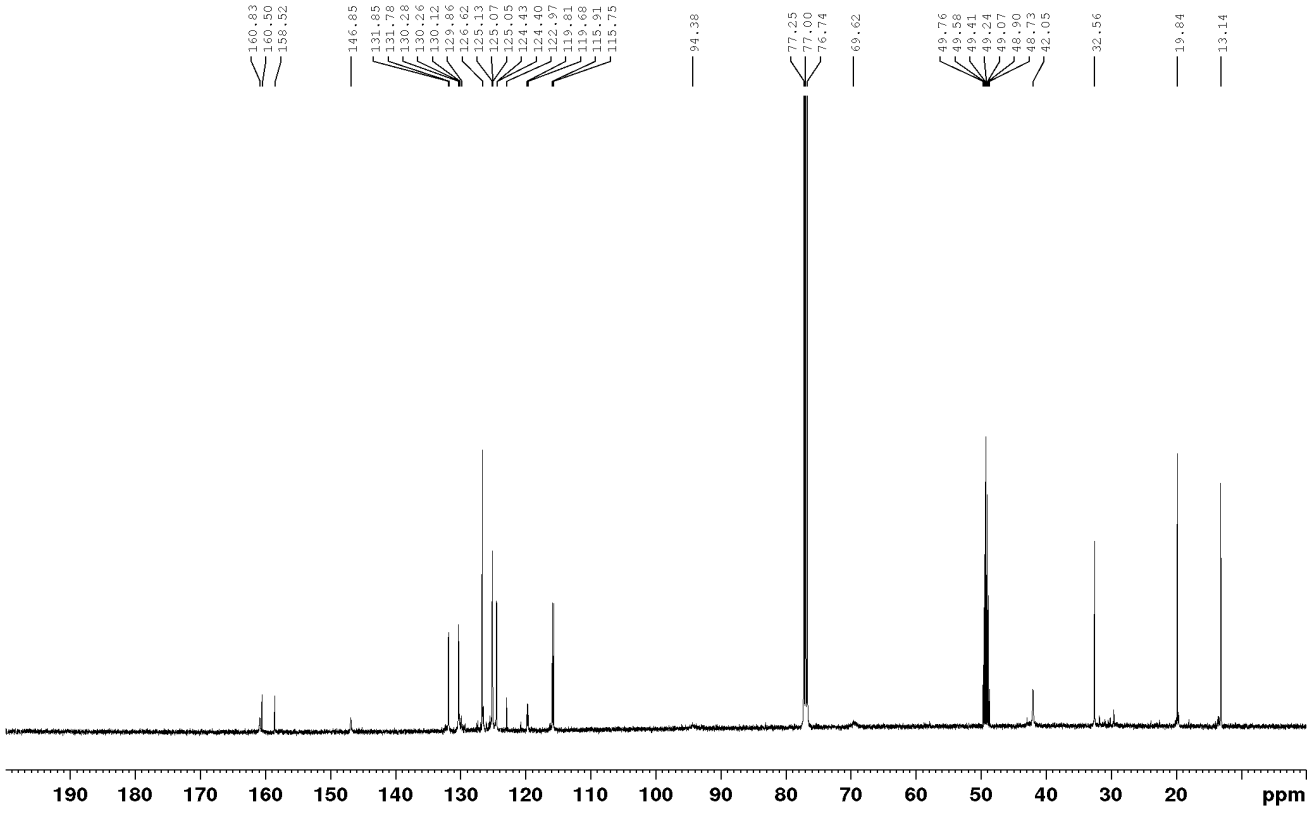


1-Butyl-2-(2-fluorophenyl)-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2j)

^{1}H NMR (500 MHz, DMSO-d_6)

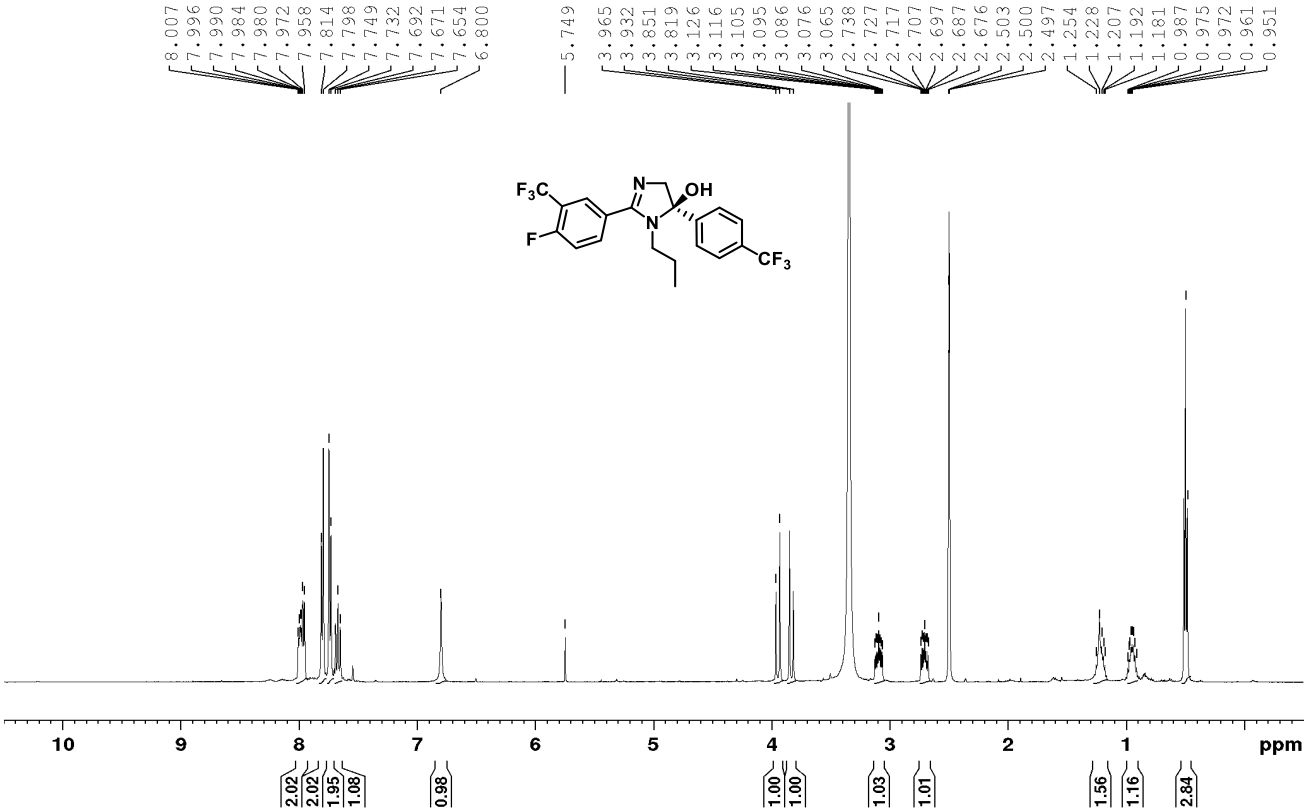


^{13}C NMR (125 MHz, $CDCl_3/CD_3OD$ (20 : 1))

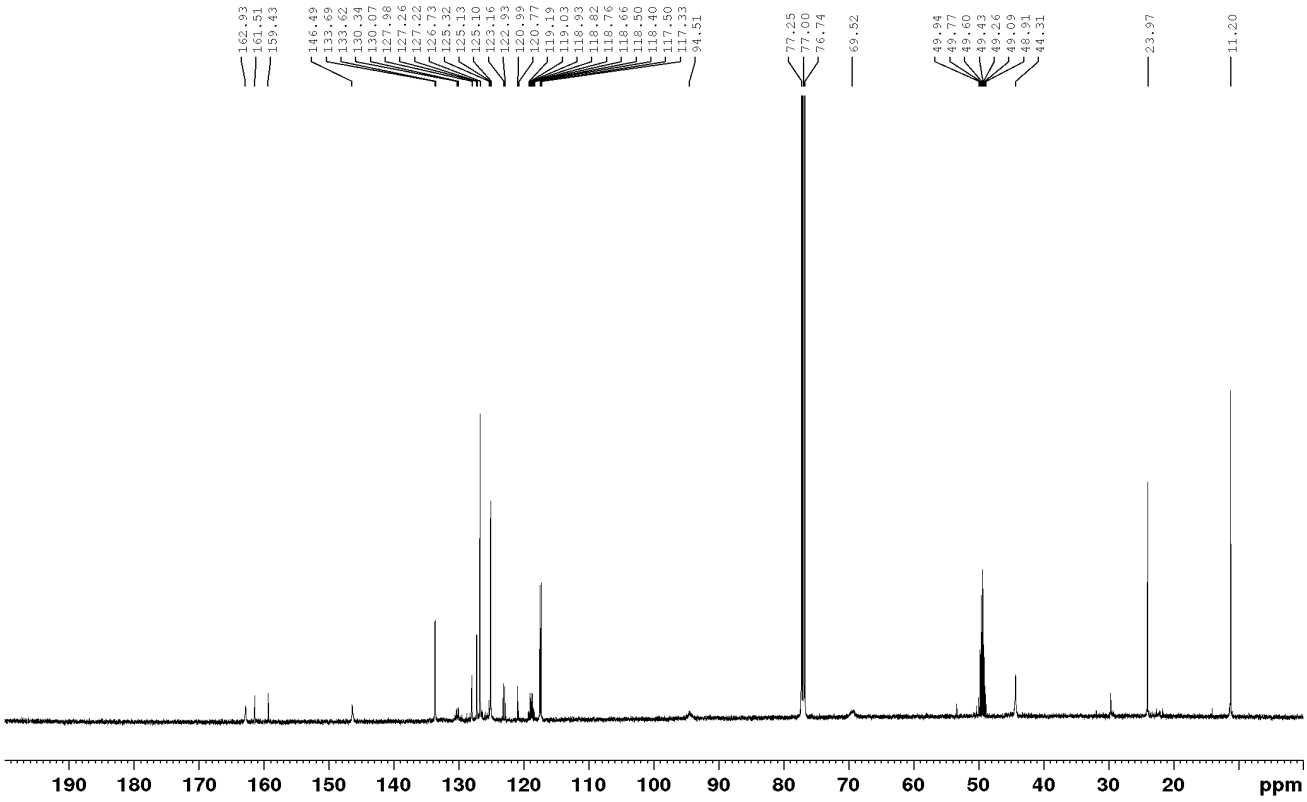


2-{4-fluoro-3-(trifluoromethyl)phenyl}-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2k)

^{1}H NMR (500 MHz, DMSO-d_6)

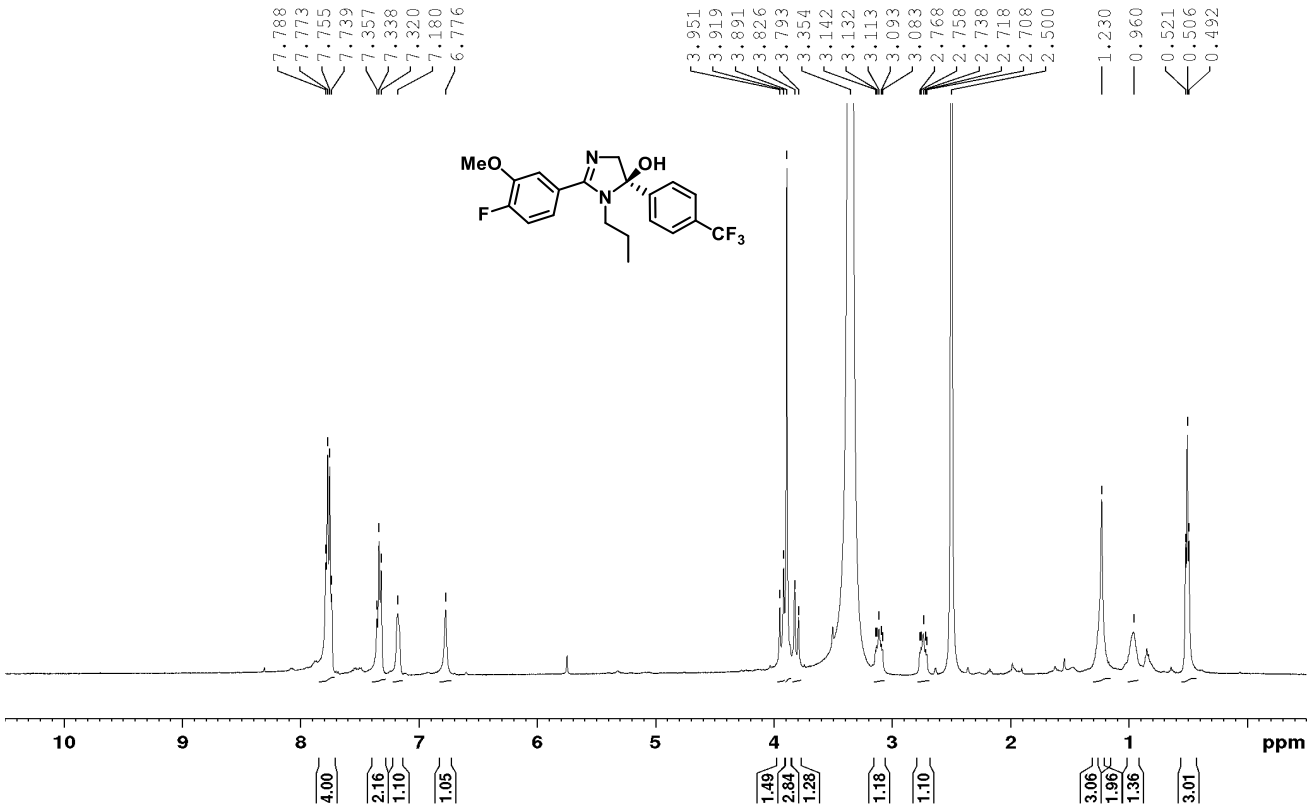


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1))

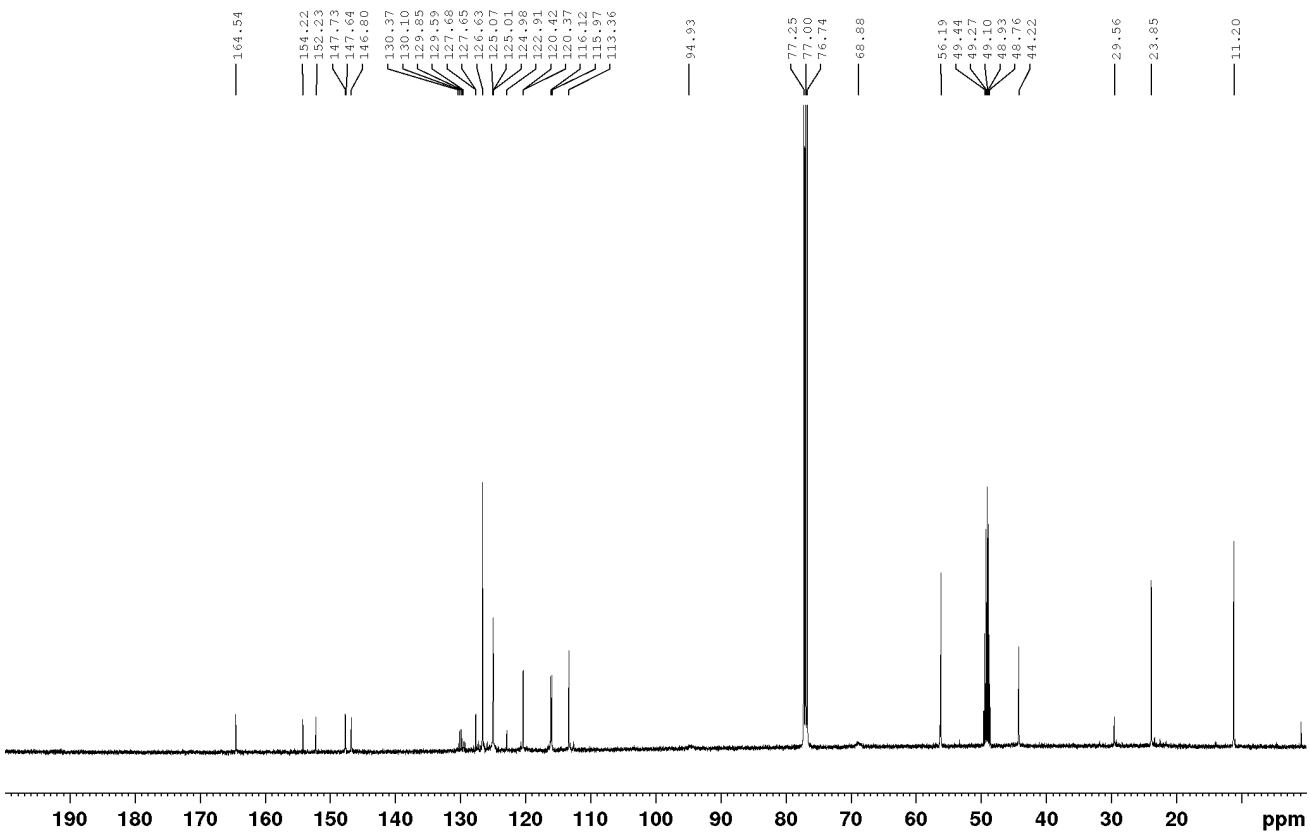


2-(4-fluoro-3-methoxyphenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2l)

^{1}H NMR (500 MHz, DMSO-d_6)

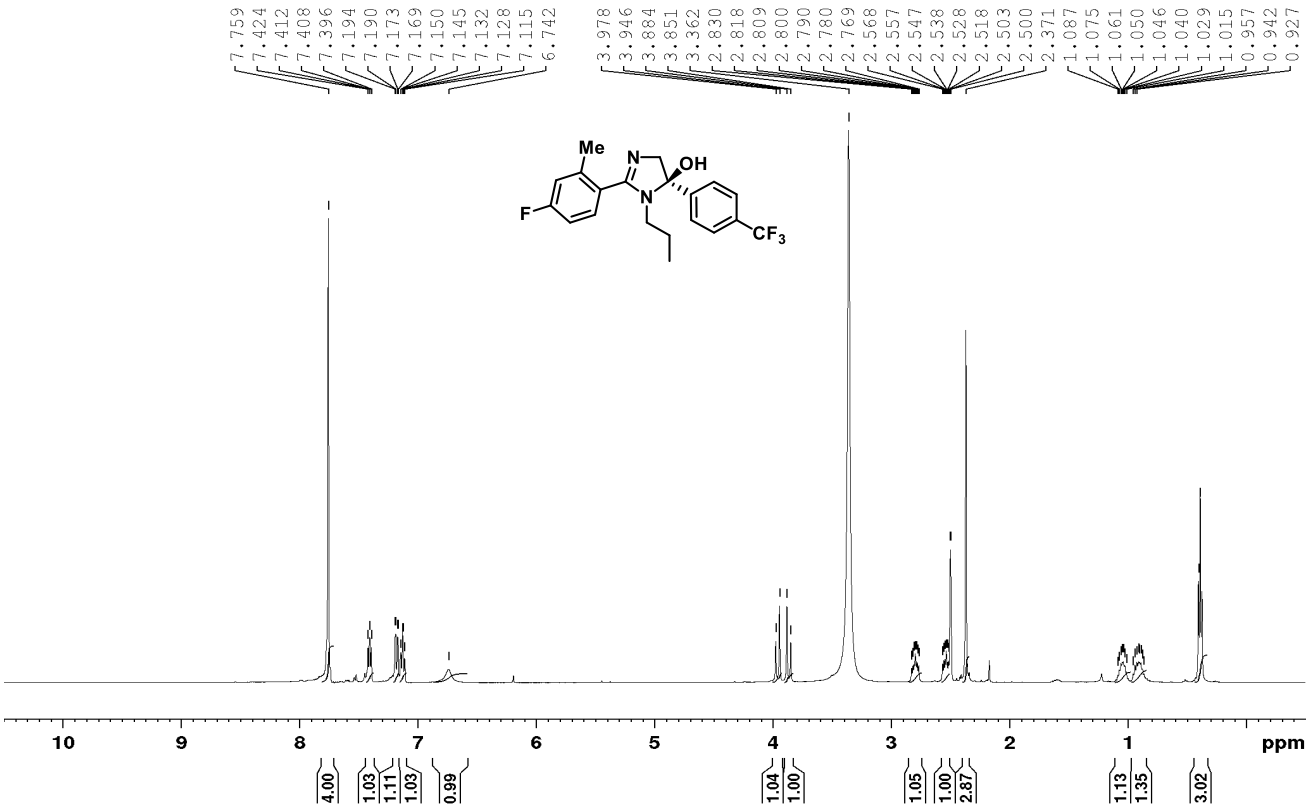


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (20 : 1))

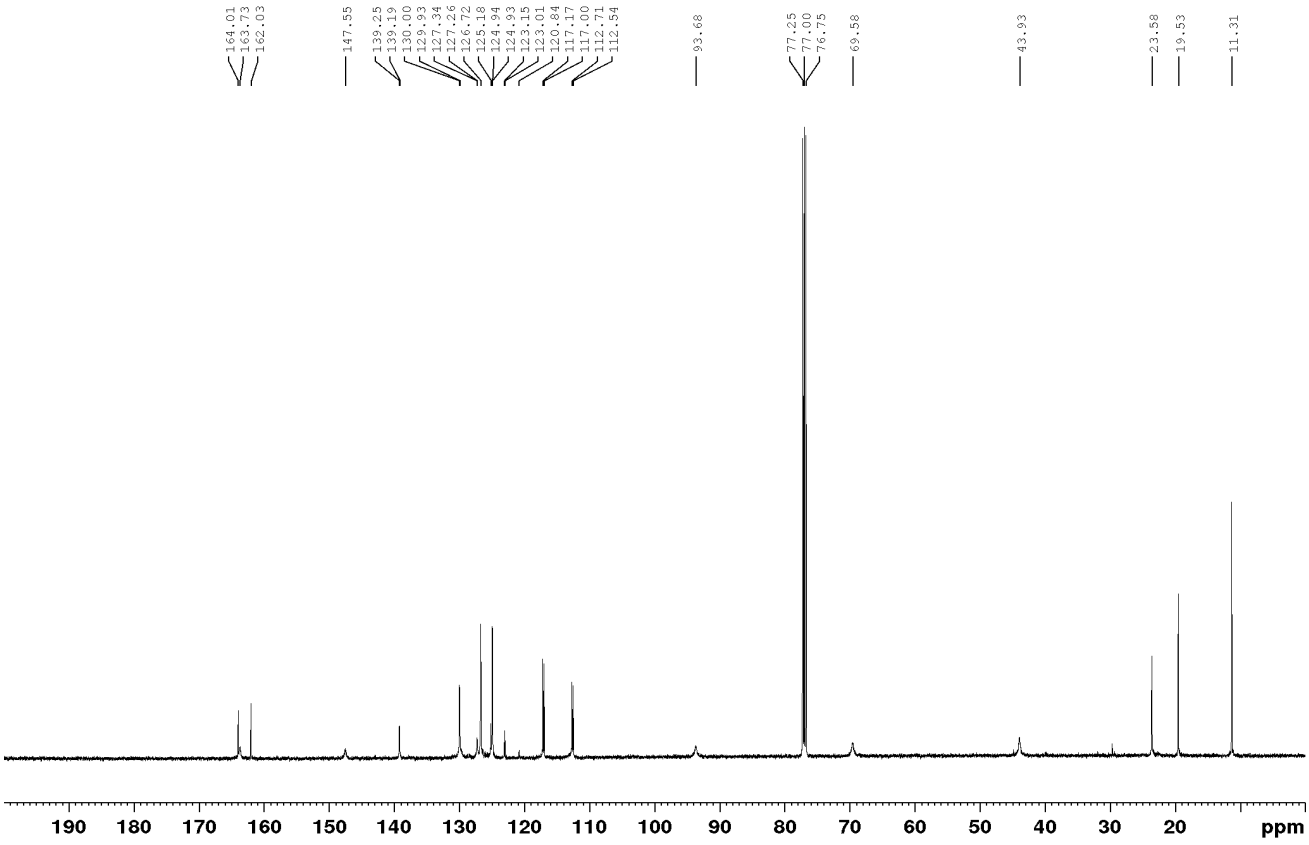


2-(4-Fluoro-2-methylphenyl)-1-propyl-5-{4-(trifluoromethyl)phenyl}-4,5-dihydro-1H-imidazol-5-ol (2m)

^{1}H NMR (500 MHz, DMSO-d_6)

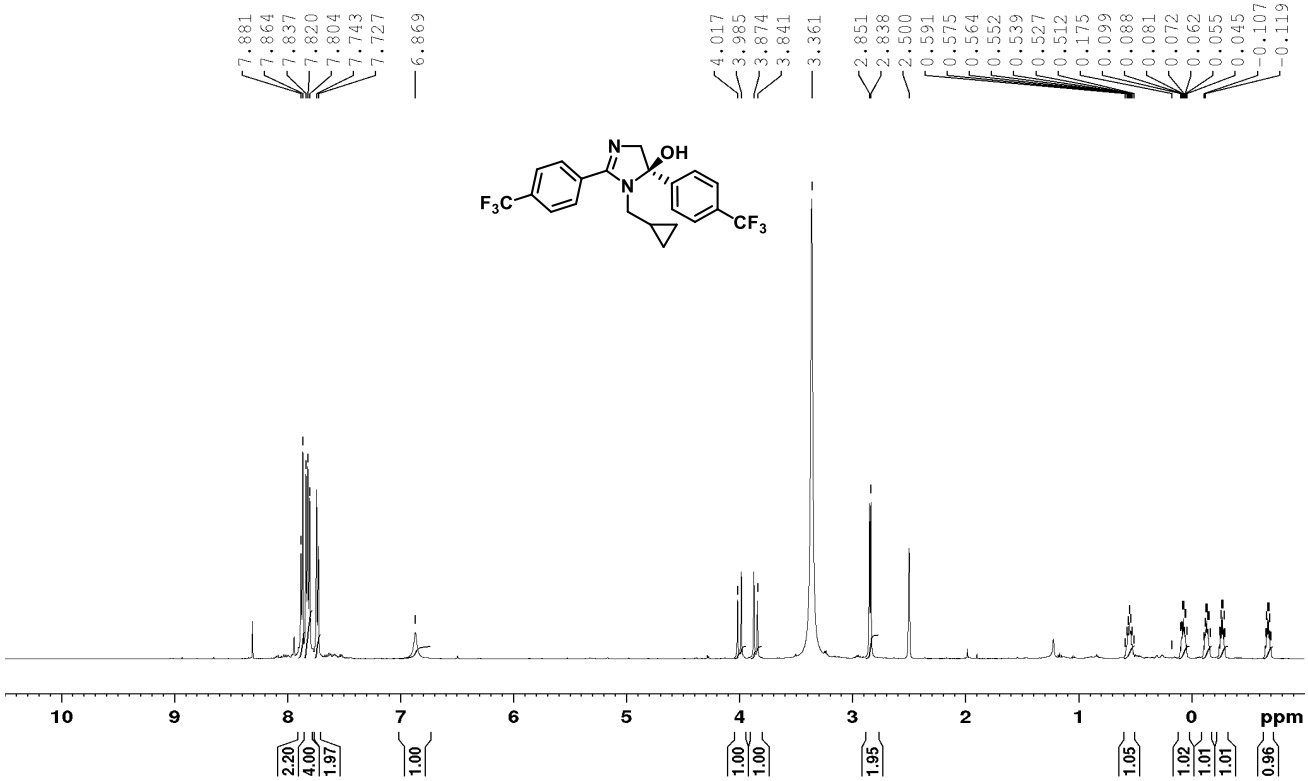


^{13}C NMR (125 MHz, $CDCl_3$)

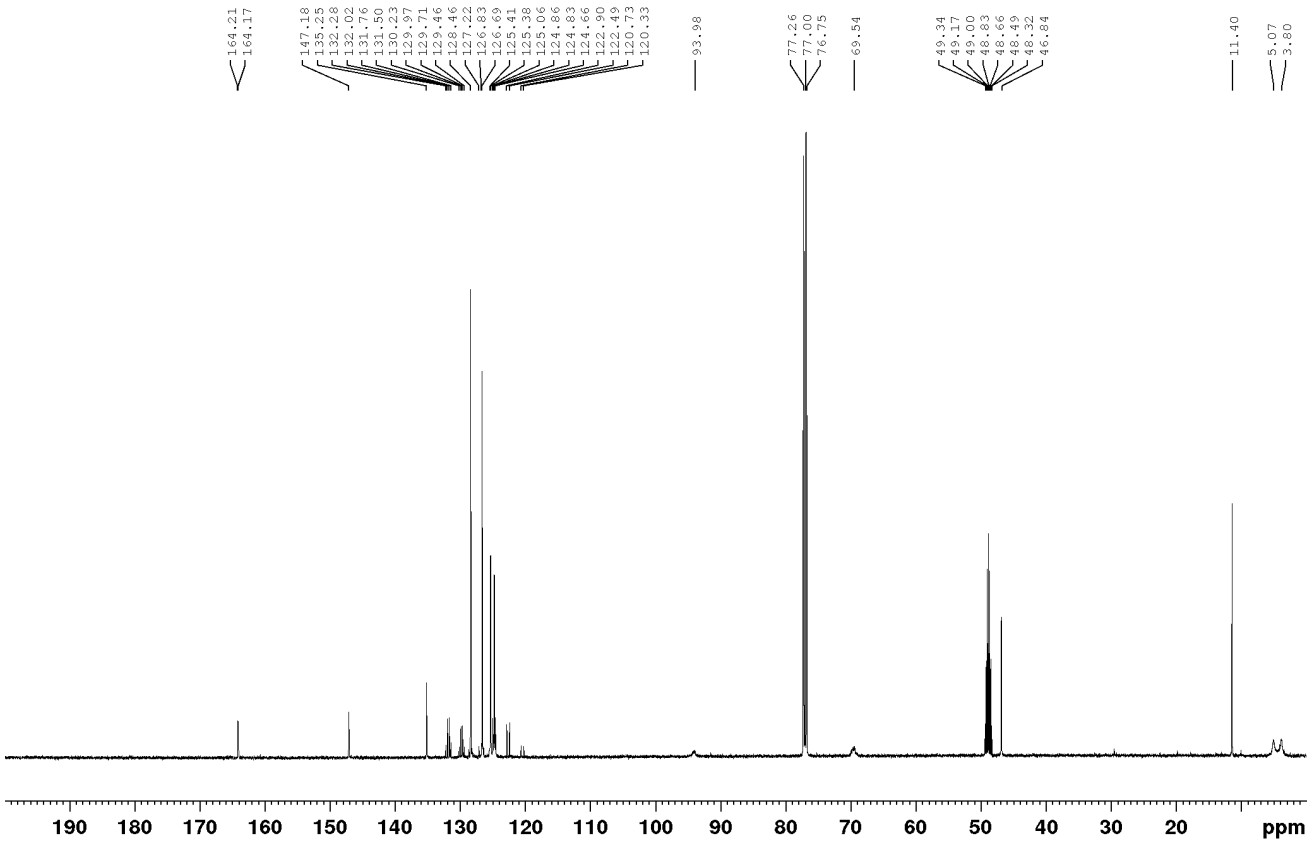


1-(Cyclopropylmethyl)-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2n)

^{1}H NMR (500 MHz, DMSO-d_6)

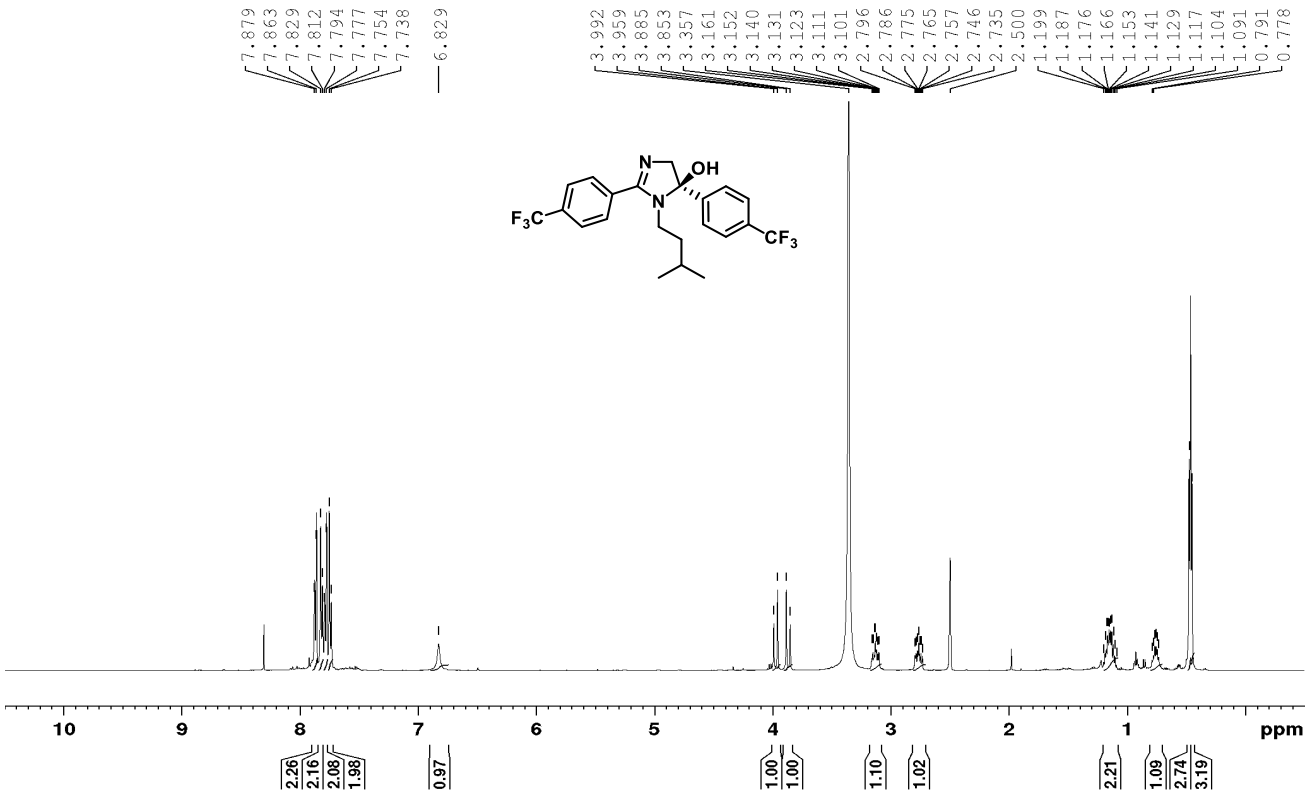


^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD (25 : 1))

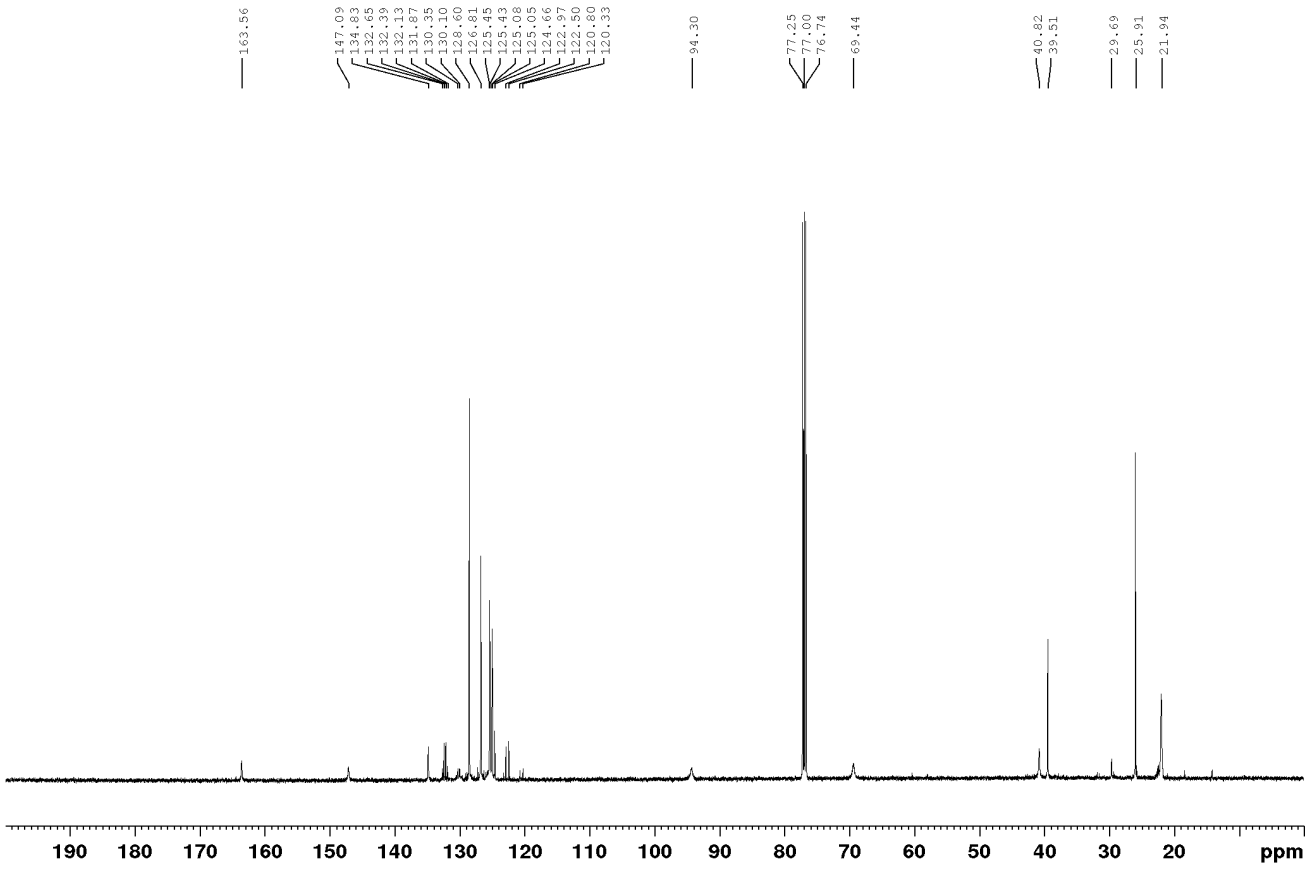


1-Isopentyl-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2o)

^{1}H NMR (500 MHz, DMSO-d_6)

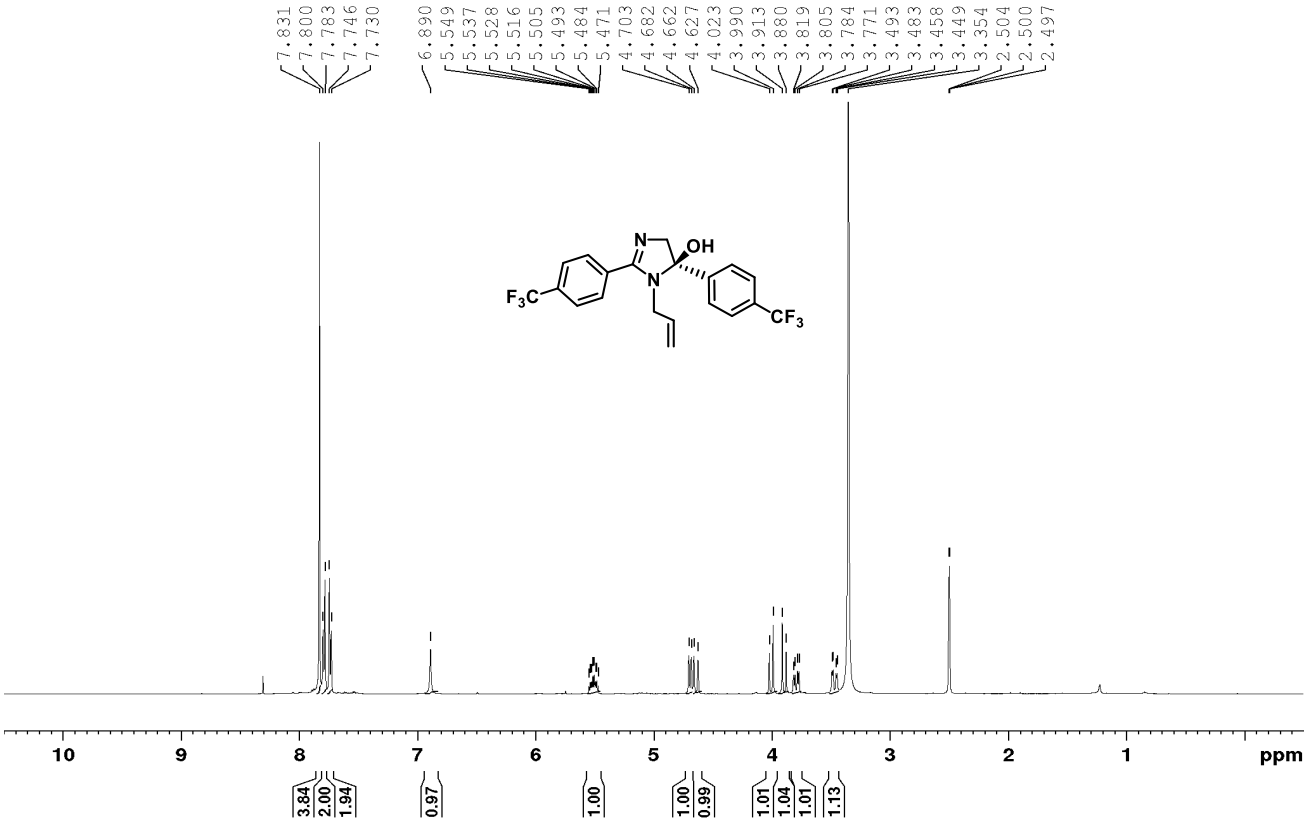


^{13}C NMR (125 MHz, $CDCl_3$)

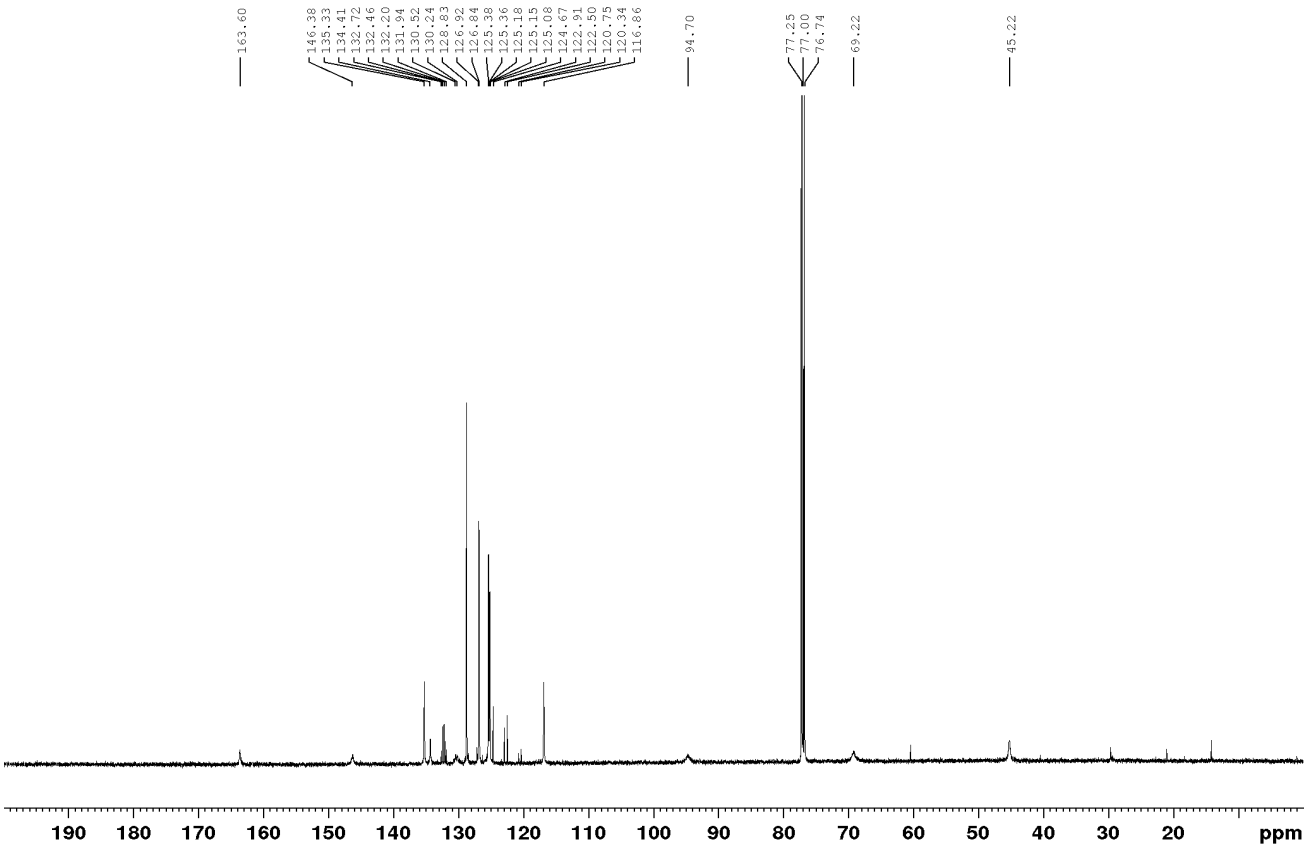


1-Allyl-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2p)

^{1}H NMR (500 MHz, DMSO-d_6)

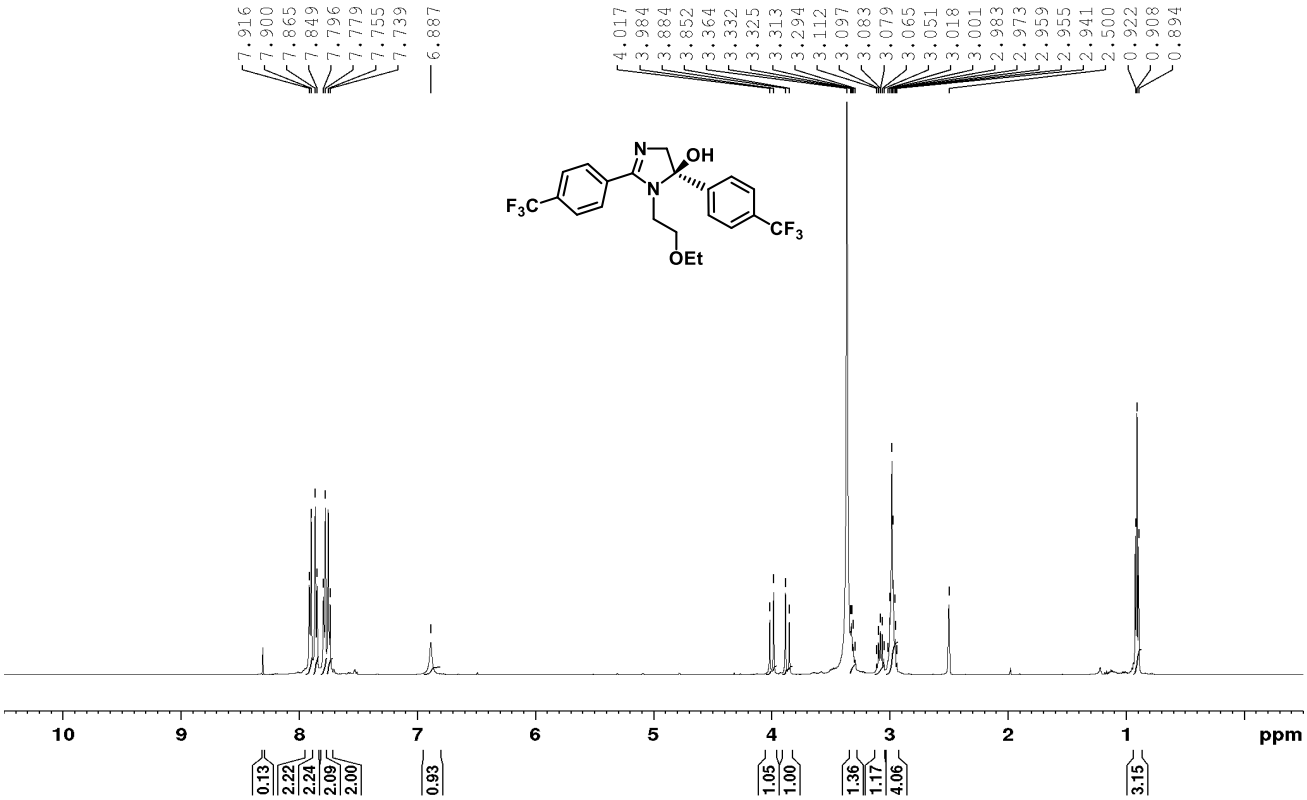


^{13}C NMR (125 MHz, $CDCl_3$)

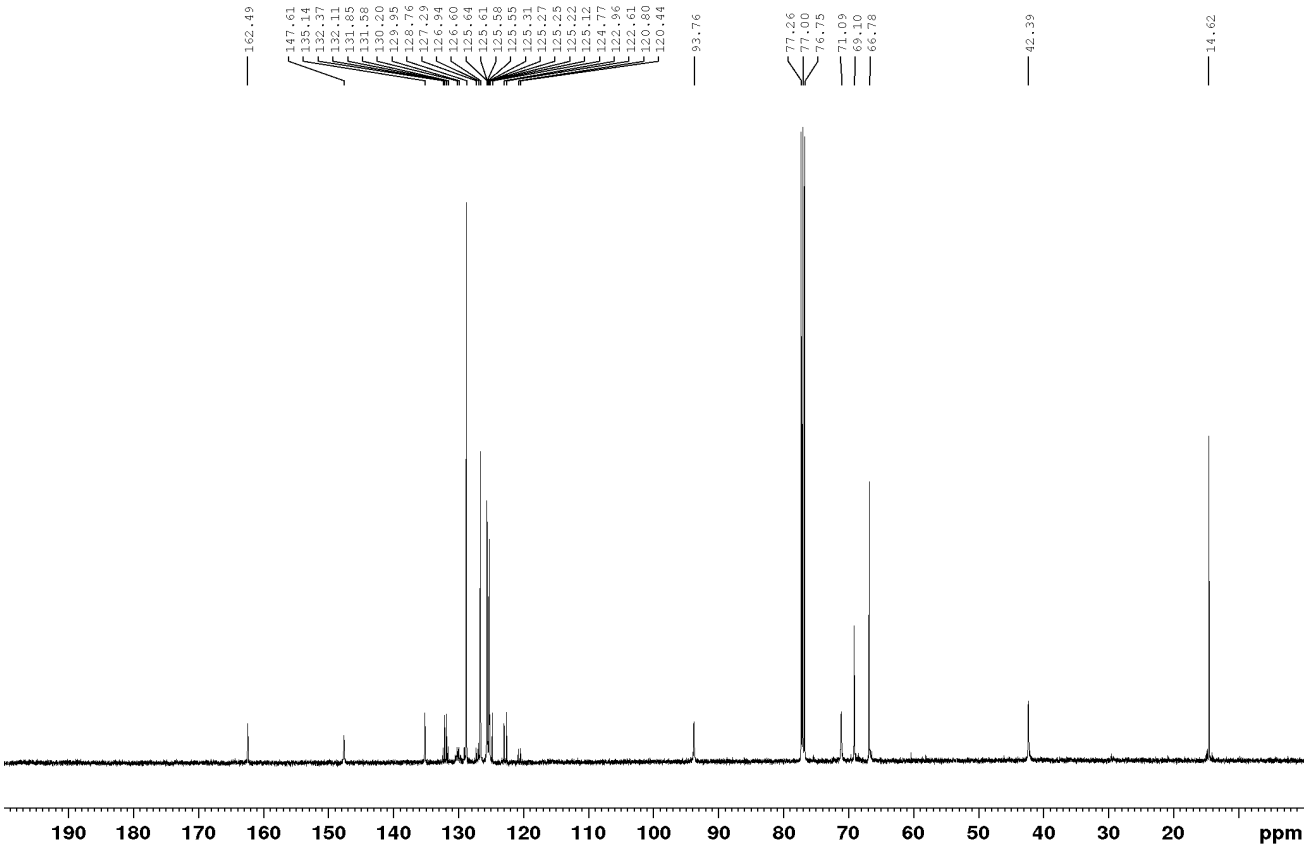


1-(2-Ethoxyethyl)-2,5-bis{4-(trifluoromethyl)phenyl}-4,5-dihydro-1*H*-imidazol-5-ol (2q)

^{1}H NMR (500 MHz, DMSO-d_6)

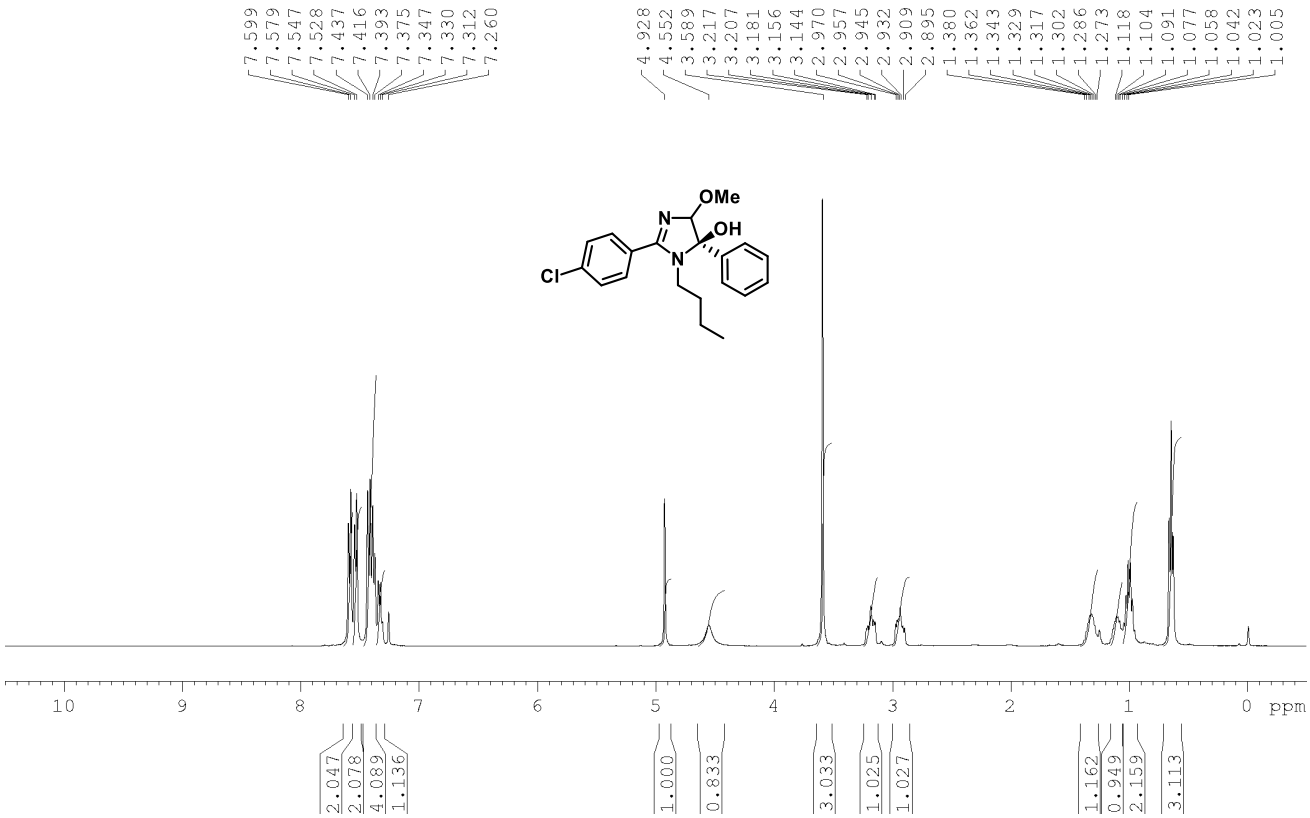


^{13}C NMR (125 MHz, $CDCl_3$)

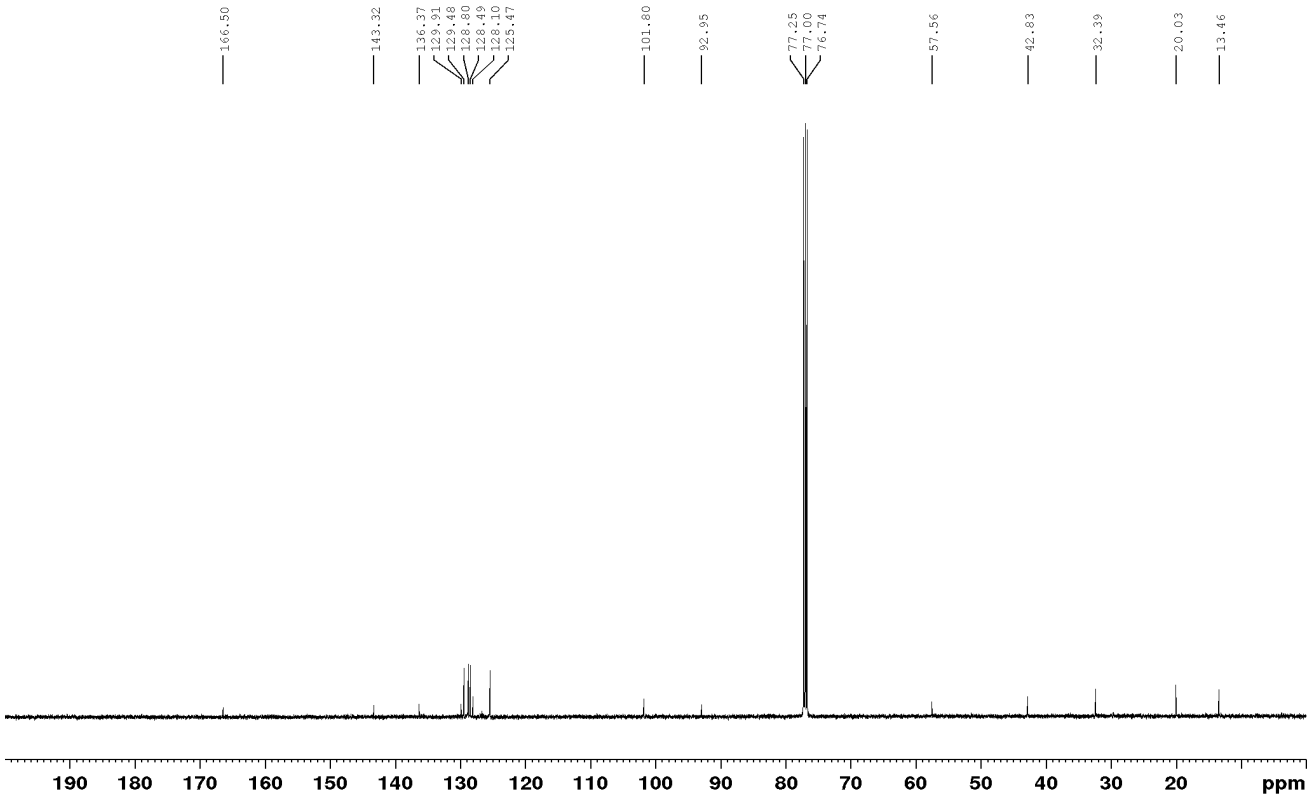


1-Butyl-2-(4-chlorophenyl)-4-methoxy-5-phenyl-4,5-dihydro-1*H*-imidazol-5-ol (2t)

^{1}H NMR (400 MHz, $CDCl_3$)

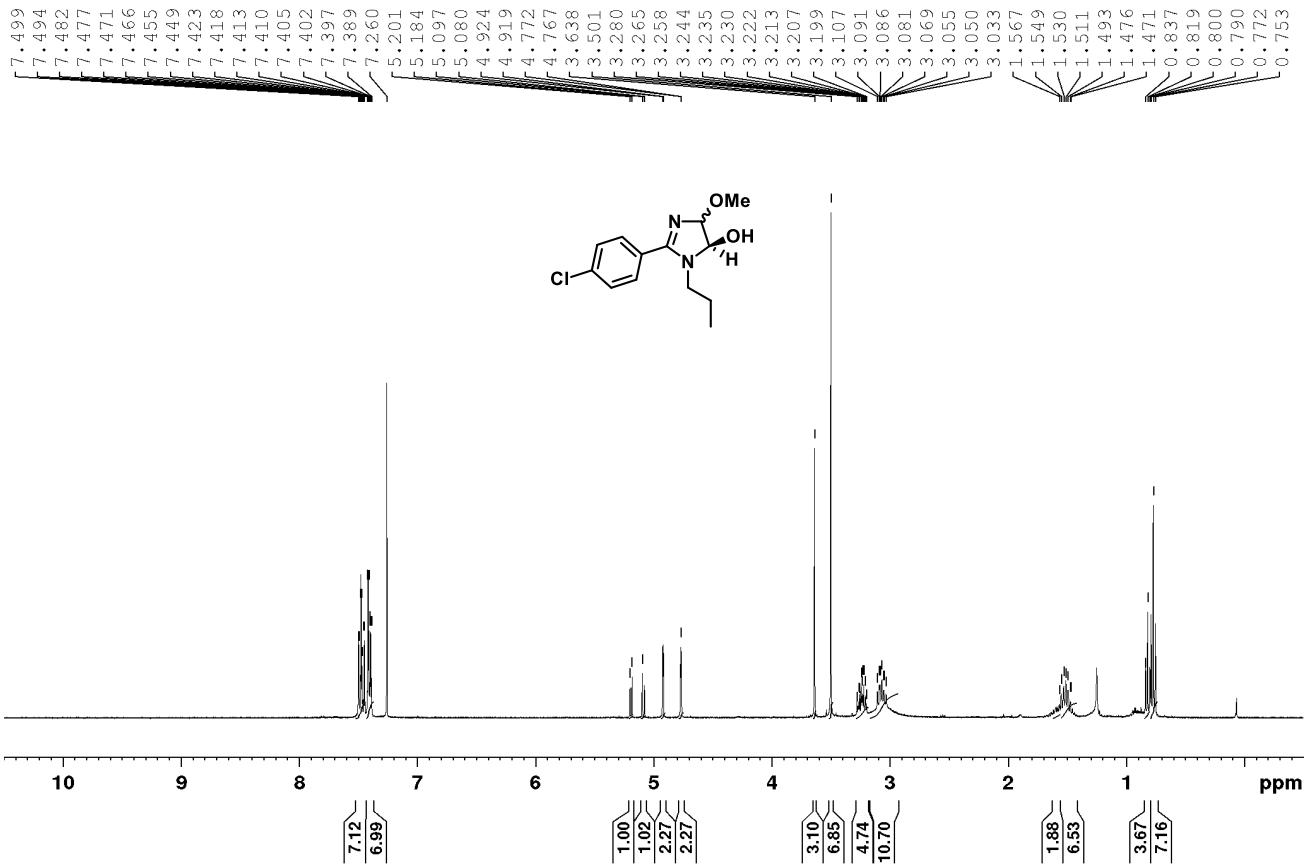


^{13}C NMR (125 MHz, $CDCl_3$)

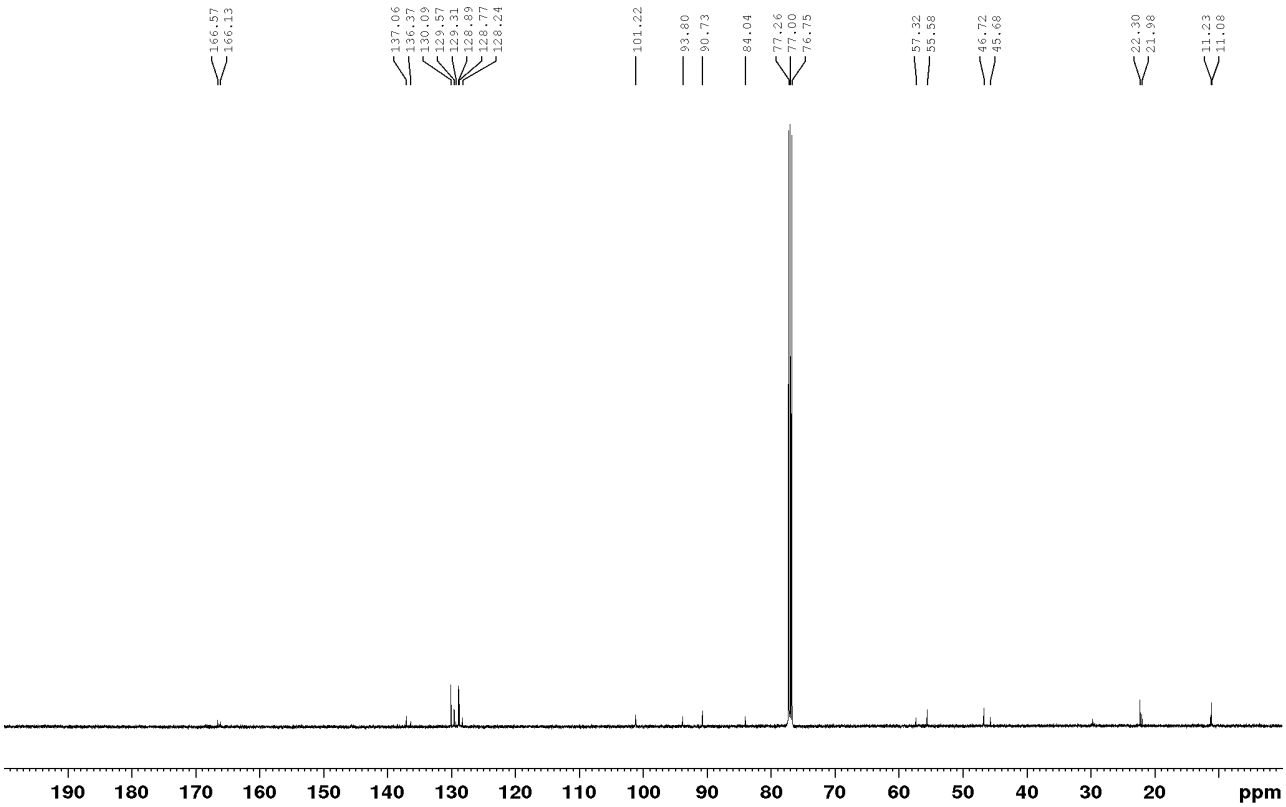


2-(4-Chlorophenyl)-4-methoxy-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2u)

^{1}H NMR (400 MHz, $CDCl_3$)

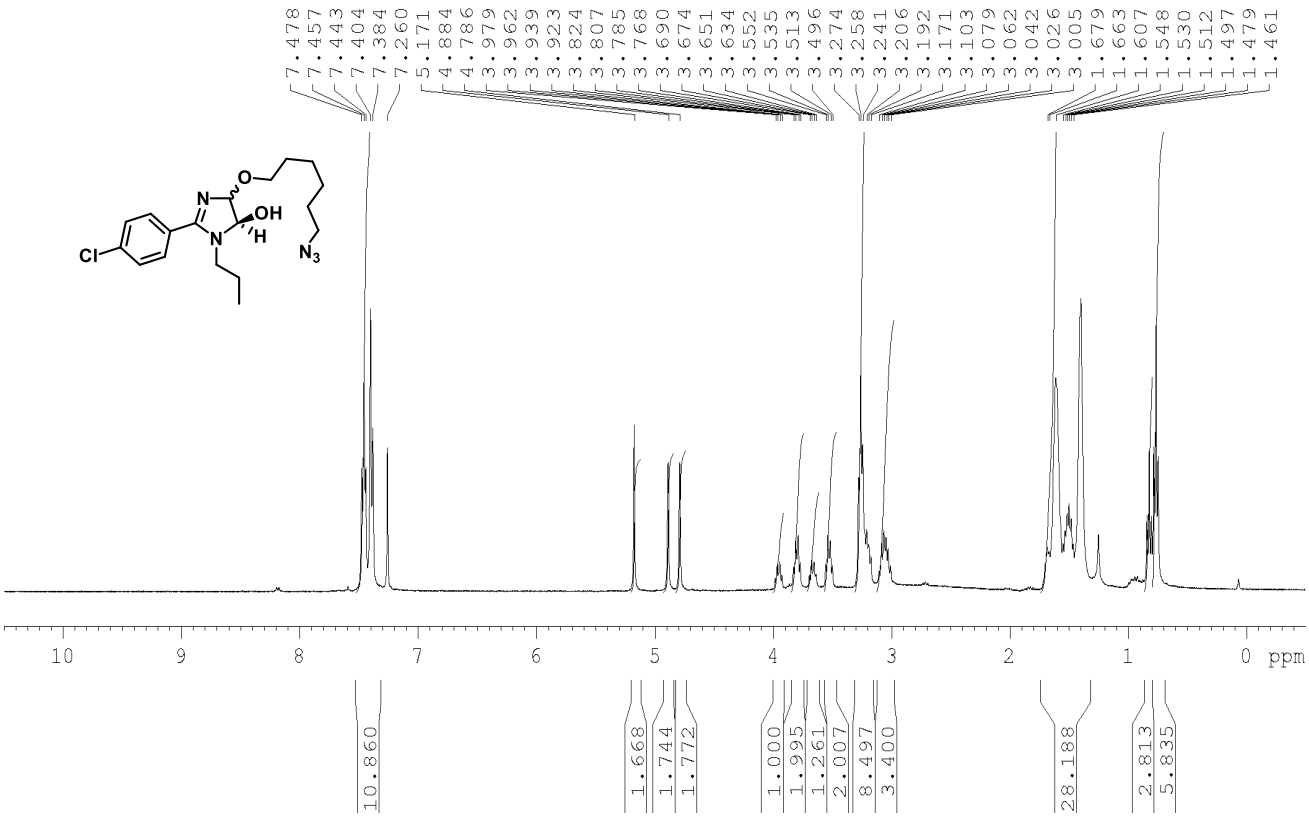


^{13}C NMR (125 MHz, $CDCl_3$)

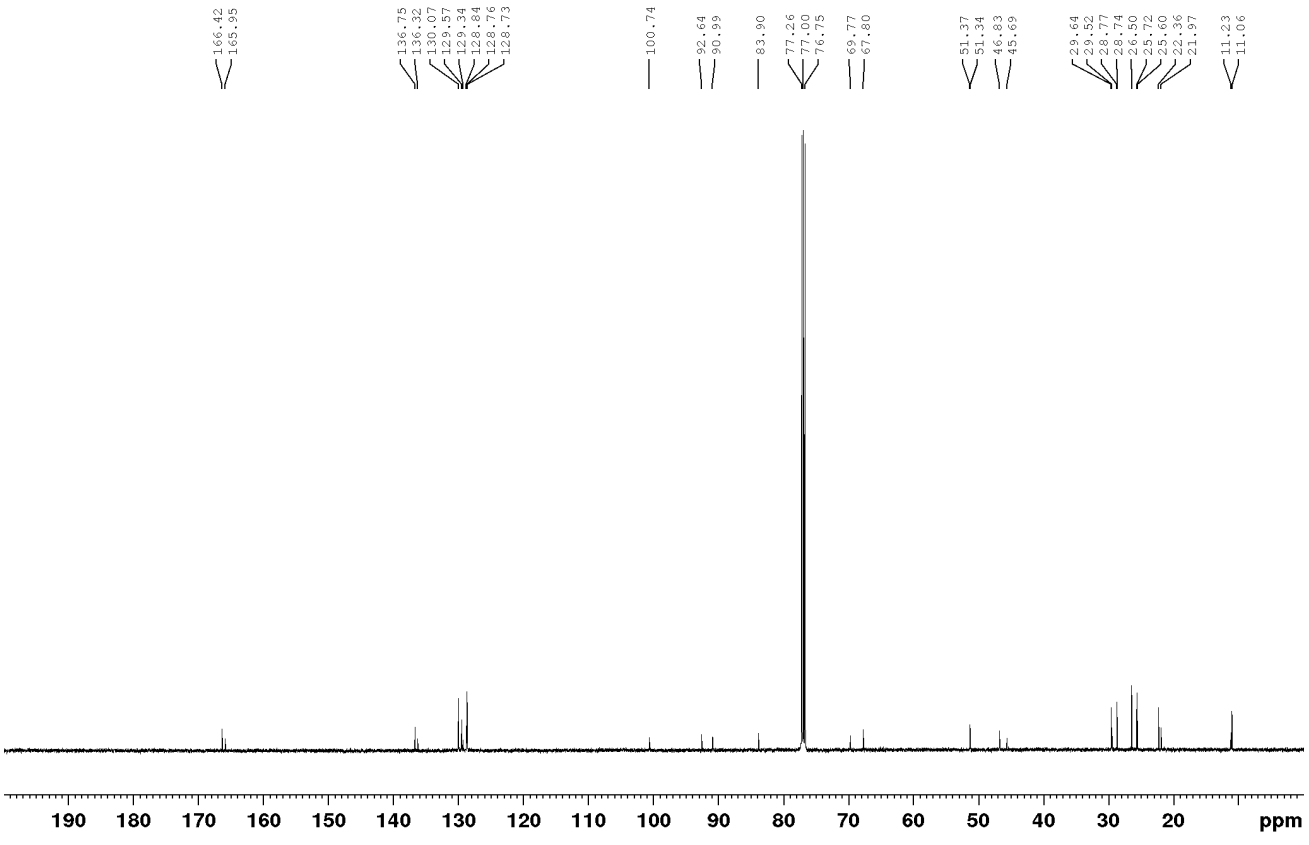


4-{(6-azidohexyl)oxy}-2-(4-chlorophenyl)-1-propyl-4,5-dihydro-1*H*-imidazol-5-ol (2v)

^{1}H NMR (400 MHz, $CDCl_3$)

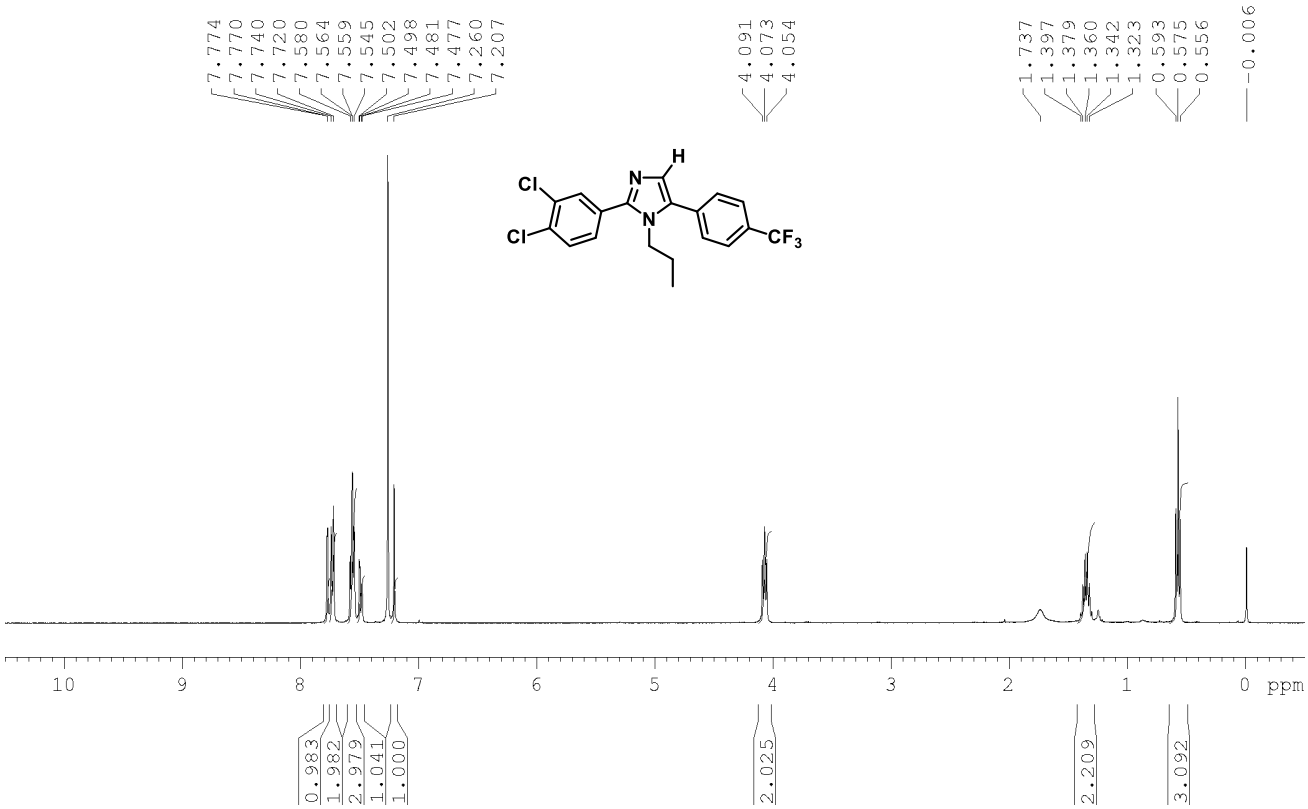


^{13}C NMR (125 MHz, $CDCl_3$)

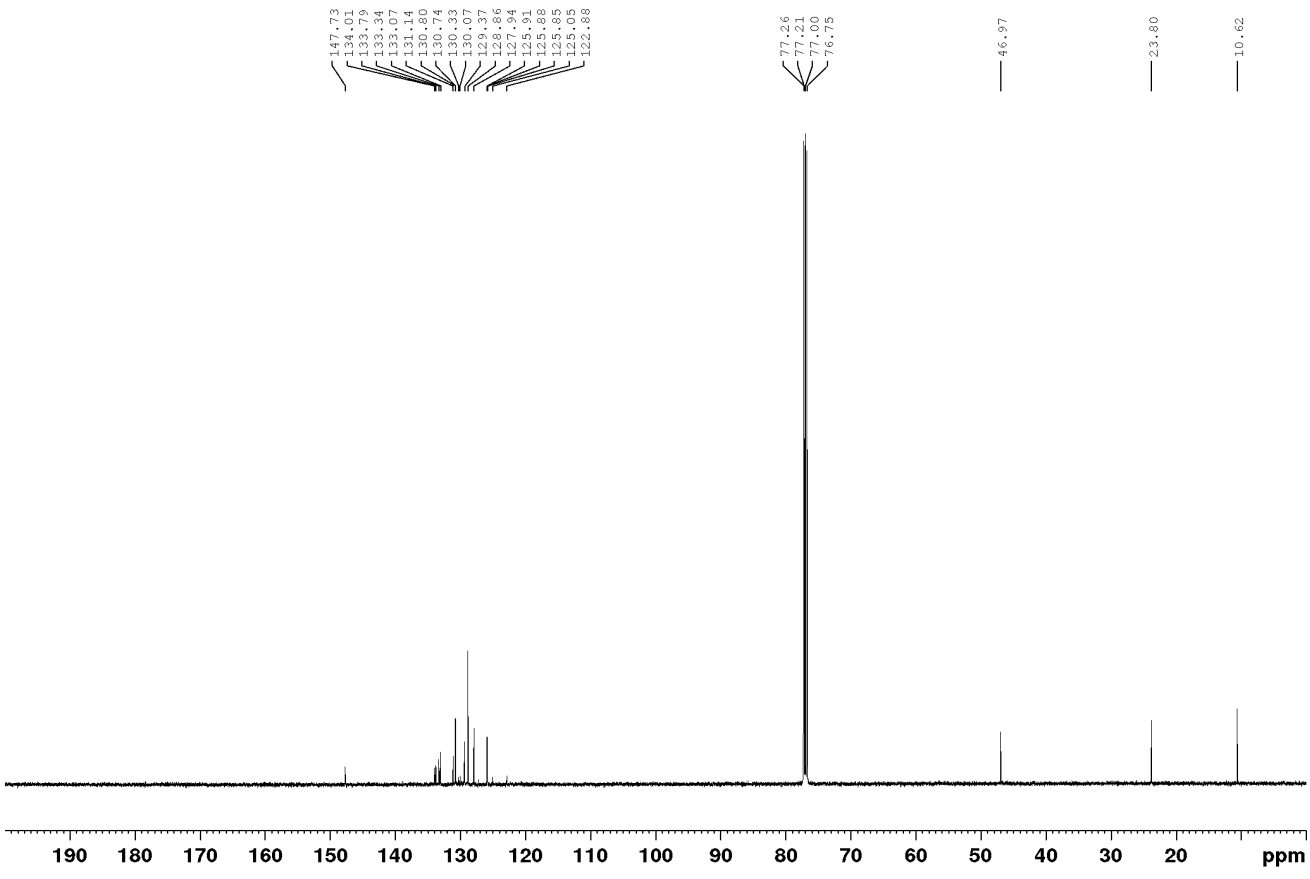


2-(3,4-Dichlorophenyl)-1-propyl-5-(4-(trifluoromethyl)phenyl)-1*H*-imidazole (3a)

^{1}H NMR (400 MHz, $CDCl_3$)

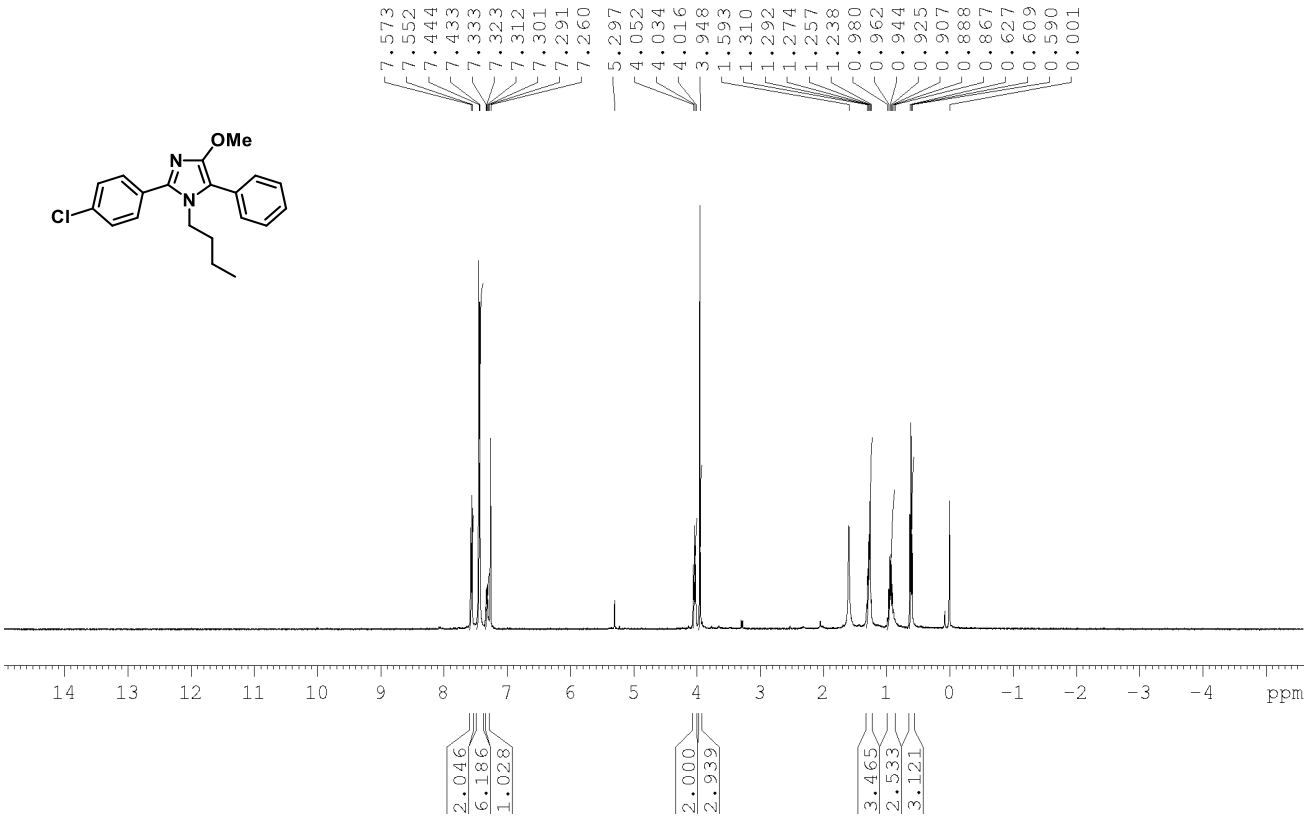


^{13}C NMR (125 MHz, $CDCl_3$)

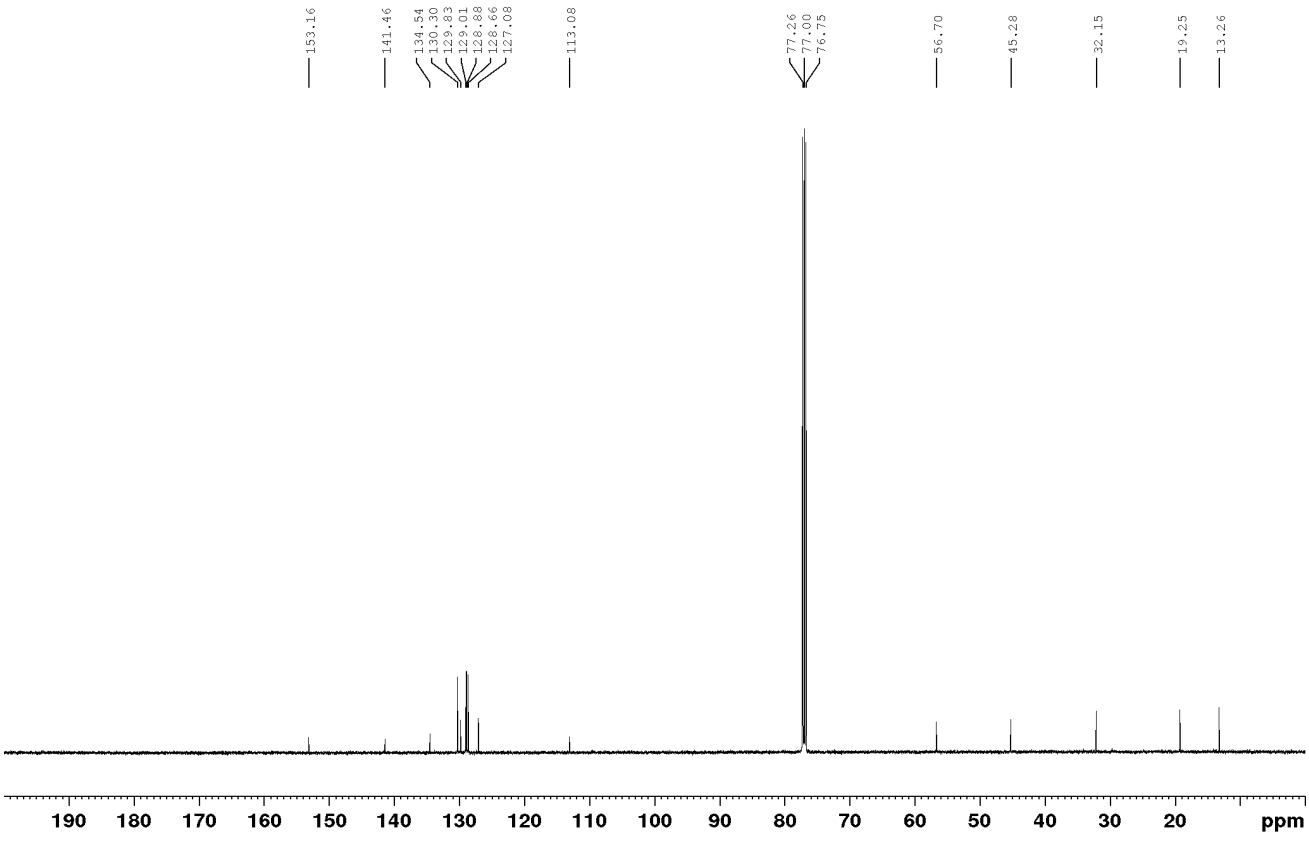


1-Butyl-2-(4-chlorophenyl)-4-methoxy-5-phenyl-1*H*-imidazole (3b)

^{1}H NMR (400 MHz, $CDCl_3$)

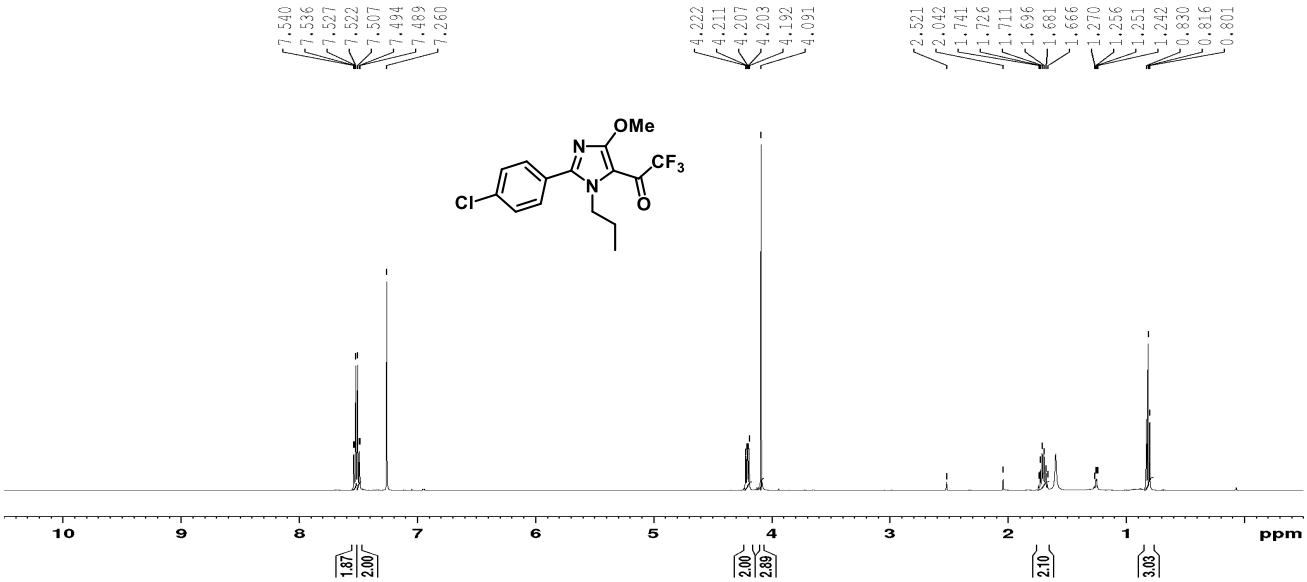


^{13}C NMR (125 MHz, $CDCl_3$)

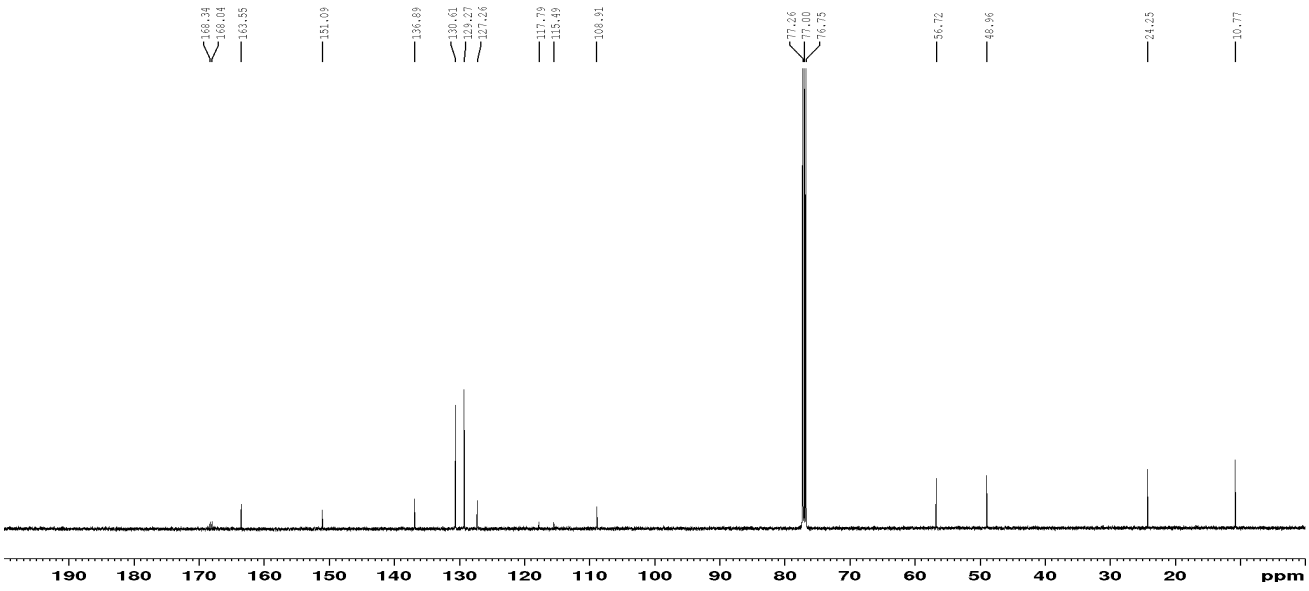


1-{2-(4-Chlorophenyl)-4-methoxy-1-propyl-1*H*-imidazol-5-yl}-2,2,2-trifluoroethan-1-one (3c)

^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (125 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)