Copper-Mediated Amidation of Heterocyclic and Aromatic C-H Bonds

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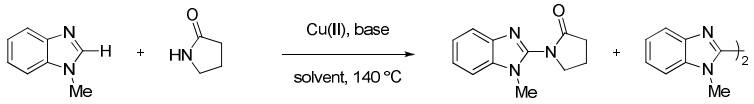
Material and Method.

Except as otherwise noted, commercial reagents and solvents were used as received without further purification. Proton nuclear magnetic resonance (1H NMR) spectra and carbon nuclear magnetic resonance (13C NMR) spectra were recorded with Varian Unity/Inova 500 (500 MHz/125 MHz) or Bruker Biospin 300 (300 MHz/75 MHz) spectrometer. Fluoride nuclear magnetic resonance (19F NMR) spectra were recorded with Bruker Biospin 300 (282 MHz). Chemical shifts for protons are reported in parts per million (δ scale) and are referenced to residual protium in the NMR solvents ($CHCl_3$: δ 7.27, D_2HCOD: δ 3.31). Chemical shifts for carbon are reported in parts per million (δ scale) and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0, CD_3OD: δ 49.1, $(CD_3)_2SO$: δ 40.5). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant in Hz, and integration. Infrared spectra were recorded using a Perkin-Elmer FT-IR spectrometer (thin film or neat, as indicated). High-resolution mass spectra were obtained through the Harvard University mass spectrometry facilities. Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Flash chromatography was performed on a CombiFlash companion system (Teledyne ISCO, Inc.) with pre-packed FLASH silica gel columns (Biotage, Inc.).

Supplementary tables.

Table S1. Selected screening results for coupling reaction of **1** with amide nucleophile **2a**.



1 **2a** **3a** **4**

Entry	Reaction condition (equiv of the reagents)	Solvent	Time	Yield[b] of **3a/4/1** (%)
1	**1** (1.0), **2a** (2.0), $Cu(OAc)_2$ (0.2), Na_2CO_3(2.0)	Toluene	24 h	10/-/81
2	**1** (1.0), **2a** (2.0), $Cu(OAc)_2$ (0.2), Na_2CO_3(2.0), Pyr. (5.0)	Toluene	24 h	58/30/-
3	**1** (1.0), **2a** (5.0), $Cu(OAc)_2$ (0.2), Na_2CO_3(2.0), Pyr. (5.0)	Toluene	24 h	16/-/79
4	**1** (1.0), **2a** (5.0), $Cu(OAc)_2$ (0.2), Na_2CO_3(2.0), pyr. (10.0)	Toluene	36 h[c]	88[d]/6/-
5	**1 (1.0), 2a (5.0), $Cu(OAc)_2$ (0.2), Na_2CO_3(2.0), pyr. (20.0)**	**Toluene**	**12 h**[c]	**82[d]/10/-**
6	1 (1.0), 2a (5.0), $Cu(OAc)_2$ (1.0), Na_2CO_3(2.0), pyr. (20.0)	Toluene	4 h[c]	65[d]/23/-
7	**1** (1.0), **2a** (5.0), $CuCl_2$ (0.2), Na_2CO_3(2.0), pyr. (20.0)	Toluene	16 h	74/-/12
8	**1** (1.0), **2a** (5.0), $CuBr_2$ (0.2), Na_2CO_3(2.0), pyr. (20.0)	Toluene	16 h	9/-/56
9	**1** (1.0), **2a** (5.0), $Cu(OTf)_2$ (0.2), Na_2CO_3(2.0), pyr. (20.0)	Toluene	16 h	28/-/52
10	**1** (1.0), **2a** (5.0), $Cu(OCOCF_3)_2$ (0.2), Na_2CO_3(2.0), pyr. (20.0)	Toluene	16 h	13/-/81
11	**1** (1.0), **2a** (5.0), $Cu(OAc)_2$ (0.2), Na_2CO_3(2.0), lutidine (20.0)	Toluene	16 h	14/-/81
12	**1** (1.0), **2a** (5.0), $Cu(OAc)_2$ (0.2), Na_2CO_3(2.0), TMEDA (20.0)	Toluene	16 h	14/-/77

[a]Standard condition: **1** (0.3 mmol), toluene (10 mL), O_2 (balloon), 140 °C. [b]Yields of **3a**, **4** and **1** determined by ^{1}H-NMR. [c]Required reaction time for completely consuming **1**. [d]Isolated yield of **3a**. [e]Abbreviations: pyr. = pyridine, TMEDA = *N,N'*-tetramethylethylenediamine.

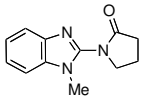
General procedure for the copper-mediated amidation reaction.

To a dry flask, were added the heterocycle, the amide nucleophile, the base and $Cu(OAc)_2$ respectively. An atmosphere of oxygen was introduced by briefly evacuating the flask, then flushing with pure oxygen (1 atm). Toluene and pyridine were added to the flask. The resulting green mixture was allowed to stir at room temperature for 30 mins and then heat at 120-140 ºC for 12-30 h. After the limiting starting material was completely consumed, the reaction mixture was cooled down to room temperature and diluted with EtOAc. The mixture was washed with aqueous ammonium, brine, and dried over Na_2SO_4. The dried solution was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was further purified by silica gel chromatography.

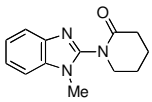
Procedure for the preparation of bezimidazole precursors 9 and 10.

To the colorless solution of Tosyl-Cl (106 mg, 0.56 mmol) in CH_2Cl_2 (5 ml), was added 2-(1H-benzo[*d*]imidazol-1-yl)ethanamine hydrochloride or 3-(1H-benzo[*d*]imidazol-1-yl)propan-1-amine hydrochloride (0.51 mmol) slowly at room temperature. The solution was stirred for 2 h and then diluted with water. The aqueous layer was separated and extracted with EtOAc. The combined organic layers were washed with brine and dried over Na_2SO_4. The dried solution was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was further purified by silica gel chromatography.

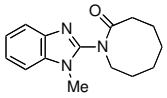
Characterizations of new compounds.



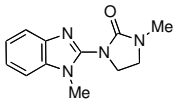
1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)pyrrolidin-2-one (3a). Yield: 82%. R_f = 0.25 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.64 (m, 1H), 7.35-7.30 (m, 1H), 7.30-7.21 (m, 2H), 4.08 (t, *J* = 7.0 Hz, 2H), 3.69 (s, 3H), 2.61 (t, *J* = 8.0 Hz, 2H), 2.27 (tt, *J* = 8.0, 7.0 Hz, 2H); ^{13}C NMR (126 MHz, CDCl3) δ 175.1, 146.2, 140.7, 134.9, 122.4, 122.2, 118.9, 109.3, 49.2, 31.3, 31.2, 19.1; IR (neat): 2984, 294, 1735, 1516, 1373, 1235, 1043 cm^{-1}. HRMS–ESI (*m/z*)-ESI *m/z* calcd. for $C_{12}H_{13}N_3ONa$ [M+Na] 238.0951; Found: 238.0948.



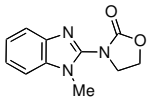
1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)piperidin-2-one (3b). Yield: 55%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, CDCl3) δ 7.72 (d, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 7.3 Hz, 1H), 7.33-7.25 (m, 2H), 3.92 (t, *J* = 5.5 Hz, 2H), 3.62 (s, 3H), 2.64 (t, *J* = 6.3 Hz, 2H), 2.14-1.94 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 149.3, 140.9, 134.7, 122.7, 122.2, 119.5, 109.5, 50.7, 32.9, 30.3, 23.2, 21.2; IR (neat): 3056, 2948, 1668, 1509, 1480, 1442, 1396, 1329, 1285, 1160, 908, 740 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{13}H_{15}N_3ONa$ [M+Na] 252.1107; Found: 252.1112.



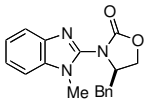
1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)azocan-2-one (3c). Yield: 55%. R_f = 0.30 (100% ethyl acetate); ^{1}H NMR (500 MHz, CDCl3) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.37 – 7.25 (m, 3H), 4.01 (t, *J* = 6.0 Hz, 2H), 3.64 (s, 3H), 2.76 (t, *J* = 5.0 Hz, 2H), 2.06-1.89 (m, 4H), 1.85–1.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.9, 149.1, 140.8, 134.7, 122.6, 122.0, 119.6, 109.4, 50.2, 34.1, 30.5, 30.3, 28.5, 26.1, 24.7; IR (neat): 2926, 1664, 1508, 1475, 1439, 1392, 1329, 12383, 1129, 912, 727, 561 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{15}H_{20}N_3O$ [M+1]: 258.1601; Found: 258.1604.



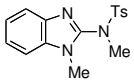
1-methyl-3-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)imidazolidin-2-one (3d). Yield: 45%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.0 Hz, 1H), 7.35 (d, *J* = 7.0 Hz, 1H), 7.32-7.27 (m, 2H), 4.16 (t, *J* = 7.6 Hz, 2H), 3.81 (s, 3H), 3.63 (t, *J* = 7. 6 Hz, 2H), 2.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 148.0, 140.8, 135.4, 122.0, 121.9, 118.5, 109.2, 44.9, 43.5, 31.5, 31.1; IR (neat): 3051, 1717, 1523, 1482, 1429, 1398, 1278, 1264, 1230, 726 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{12}H_{14}N_4ONa$ [M+Na]: 253.1060, Found: 253.1066.



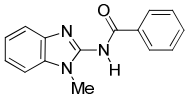
3-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)oxazolidin-2-one (3e). Yield: 72%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, CDCl3) δ 7.69 (d, *J* = 7.0 Hz, 1H), 7.36-7.27 (m, 3H), 4.61 (t, *J* = 7.5 Hz, 2H), 4.34 (t, *J* = 7.5 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 145.2, 140.4, 135.1, 122.7, 122.5, 118.9, 109.4, 63.4, 46.3, 31.2; IR (neat): 2911, 1763, 1524, 1483, 1449, 1401, 1228, 1209, 1133, 1037, 746 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{11}H_{12}N_3O_2$ [M+1]: 218.0924; Found: 218.0926.



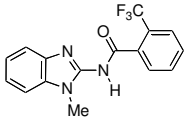
4-benzyl-3-(1-methyl-1*H*-benzimidazol-2-yl)-1,3-oxazolidin-2-one (3f). Yield: 64%. R_f = 0.30 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90-7.62 (m, 1H), 7.41-7.22 (m, 6H), 7.08 (d, *J* = 7.2 Hz, 2H), 5.18 (qd, *J* = 8.5, 4.0 Hz, 1H), 4.55 (t, *J* = 8.5 Hz, 1H), 4.34 (t, J = 8.5 Hz, 1H), 3.73 (s, 3H), 3.23 (dd, *J* = 13.8, 4.0 Hz, 1H), 2.95 (dd, *J* = 13.8, 8.5 Hz,1H,); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.4, 144.4, 140.9, 135.0, 134.5, 129.2, 128.8, 127.3, 122.8, 122.5, 119.3, 109.5, 68.1, 58.0, 37.8, 30.8; IR (neat): 1762, 1709, 1399, 1360, 1220, 729, 702 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{18}H_{17}N_3O_2Na$ [M+Na]: 330.1213, Found: 330.1209.



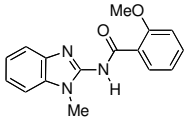
***N*,4-dimethyl-*N*-(1-methyl-1*H*-benzimidazol-2-yl)benzenesulfonamide (3g).** Yield: 50%. R_f = 0.30 (30% ethyl acetate-hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.43 – 7.38 (m, 1H), 7.36 (dd, *J* = 6.9, 1.2 Hz, 1H), 7.34 – 7.25 (m, 3H), 3.91 (s, 3H), 3.20 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.7, 144.8, 140.3, 134.7, 132.1, 129.7, 128.8, 123.4, 122.6, 119.6, 110.0, 38.1, 30.8, 21.6; IR (neat): 3055, 1394, 1352, 1160, 779, 700 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{16}H_{17}N_3O_2SNa$ [M+Na]: 338.0934, Found: 338.0928.



***N*-(1-methyl-1*H*-benzimidazol-2-yl)benzamide (3h).** Yield: 85%. R_f = 0.30 (30% ethyl acetate-hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 6.9 Hz, 2H), 7.60 – 7.41 (m, 3H), 7.40 – 7.21 (m, 4H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 153.9, 137.9, 131.2, 130.2, 129.2, 128.3, 127.9, 123.0 (2), 111.2, 108.9, 28.2. HRMS cald for $C_{15}H_{14}N_3O$ [M+H]: 252.1131, Found: 252.1136.

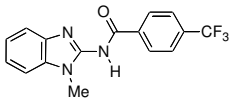


***N*-(1-methyl-1*H*-benzo[d]imidazol-2-yl)-2-(trifluoromethyl)benzamide (3i).** Yield: 91%. R_f = 0.30 (20% ethyl acetate-hexanes); ^{1}H NMR (500 MHz, D_2O) δ 12.27 (brs, 1H), 7.93 (d, , *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.32-7.22 (m, 4H), 3.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.9, 153.5, 139.8, 131.4, 130.0, 129.9, 129.0, 128.0, 127.8 (q, *J* = 31.5 Hz), 126.4 (q, *J* = 5.5 Hz), 124.2 (q, *J* = 274.5 Hz), 123.4, 123.3, 111.3, 109.2, 28.3; IR (neat): 3274,1736, 1571, 1484, 1383, 1365, 1315, 1135 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{16}H_{12}F_3N_3ONa$ [M+Na]: 342.0825; Found: 342.0825.

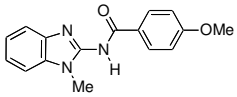


2-methoxy-*N*-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)benzamide (3j). Yield: 72%. R_f = 0.30 (20% ethyl acetate-hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.45 (brs, 0.5H), 10.15 (brs, 0.5H), 8.18 (d, , *J* = 6.6 Hz, 1H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.36-7.18 (m, 3H), 7.17-6.86 (m, 2H), 4.02 (s, 3H), 3.75 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ

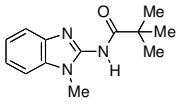
1169.4, 159.5, 147.4, 136.8, 135.3, 134.2, 132.6, 124.8, 124.6, 123.4, 122.2, 117.2, 113.3, 111.3, 56.9, 30.4; IR (neat): 3298, 1602, 1571, 1483, 1375, 1244, 747 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{16}H_{15}N_3O_2Na$ [M+Na]: 304.1057; Found: 304.1054.



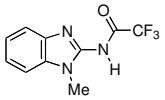
***N*-(1-methyl-1*H*-benzo[d]imidazol-2-yl)-4-(trifluoromethyl)benzamide (3k).** Yield: 70%. R_f = 0.30 (20% ethyl acetate-hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 12.28 (s, 1H), 8.46 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.41 – 7.22 (m, 4H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, DMSO) δ 171.8, 152.3, 141.8, 130.6 (q, *J* = 32.0 Hz), 129.8, 129.1, 128.5, 124.6 (q, *J* = 3.0 Hz), 124.0 (q, *J* = 272.5 Hz), 122.5 (2C), 111.8, 109.3, 28.1; IR (neat): 3278, 1578, 1560, 1321, 1104, 1064, 746 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{16}H_{13}F_3N_3O$ [M+1] 320.1005; Found: 320.1045.



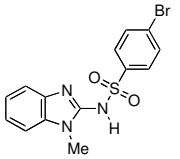
4-methoxy-*N*-(1-methyl-1*H*-benzimidazol-2-yl)benzamide (3l). Yield: 67%. R_f = 0.30 (20% ethyl acetate-hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.6 Hz, 2H), 7.44 – 7.15 (m, 4H), 6.96 (d, *J* = 8.6 Hz, 2H), 3.89 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 162.3, 154.2, 131.1, 130.8, 130.3, 128.3, 123.0, 114.1, 113.2, 111.0, 108.9, 55.3, 28.2; IR (neat): 1572, 1321, 1251, 689, 668 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{16}H_{15}N_3O_2Na$ [M+Na]: 304.1057; Found: 304.1054.



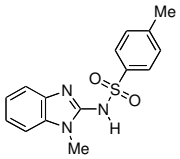
***N*-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)pivalamide (3m).** Yield: 58%. R_f = 0.30 (20% ethyl acetate-hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 12.16 (brs, 1H), 7.25-7.17 (m, 4H), 3.63 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 154.0, 130.7, 129.1, 122.8, 122.6, 111.2, 108.8, 41.1, 28.2, 28.1; IR (neat): 3253, 2952, 1593, 1548, 1477, 1391, 739 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{13}H_{18}N_3O$ [M+H]:232.1444; Found: 232.1455.



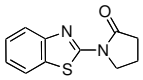
2,2,2-trifluoro-N-(1-methyl-1H-benzo[d]imidazol-2-yl)acetamide (3n). Yield: 68%. R_f = 0.30 (20% ethyl acetate-hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 11.97 (brs, 1H), 7.48 (d, *J* = 6.6 Hz, 2H), 7.41-7.32 (m, 3H), 3.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8 – 165.8 (m), 153.1, 129.8, 127.8, 124.3, 124.2, 117.2 (q, *J* = 286.0 Hz), 112.1, 109.8, 28.7; IR (neat): 3230,2922, 1549, 1481, 1124, 741 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{10}H_9F_3N_3O$ [M+1]: 244.0692; Found: 244.0696.



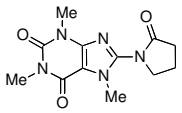
4-bromo-*N*-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)benzenesulfonamide (3o). Yield: 97%. R_f = 0.30 (20% ethyl acetate-hexanes); ^1H NMR (500 MHz, $CDCl_3$) δ 10.62 (brs, 1H), 7.87 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 7.35-7.31 (m, 1H), 7.24-7.18 (m, 2H), 7.13 (d, *J* = 7.0 Hz, 1H), 3.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 142.7, 131.9, 130.3, 128.2, 127.6, 126.4, 123.5, 123.2, 111.1, 108.9, 28.4; IR (neat): 3357, 3091, 1578, 1483, 1271, 1129, 1084, 1001, 821, 735, 637 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{14}H_{13}BrN_3O_2S$ [M+1]: 365.9906; Found: 365.9915.



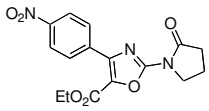
4-methyl-*N*-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)benzenesulfonamide (3p). Yield: 86%. R_f = 0.30 (20% ethyl acetate-hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.69 (brs, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.36-7.29 (m, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.21-7.15 (m, 2H), 7.13-7.07 (m, 1H), 3.50 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.8, 142.2, 140.8, 130.3, 129.3, 128.3, 126.0, 123.2, 122.9, 111.1, 108.7, 28.3, 21.4; IR (neat): 3312, 2925, 1711, 1585, 1275, 1132, 1084, 829, 746, 673, 533 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{15}H_{16}N_3O_2S$ [M+1]: 302.0956; Found: 302.0964.



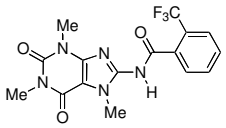
1-(benzo[*d*]thiazol-2-yl)pyrrolidin-2-one (5a). Yield: 45%. R_f = 0.50 (50% ethyl acetate-hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79-7.86 (t, *J* = 7.7 Hz, 2H), 7.43 (td, *J* = 7.7, 1.3 Hz, 1H), 7.31 (td, *J* = 7.7, 1.3 Hz, 1H), 4.27 (t, *J* = 7.2 Hz, 2H), 2.74 (t, *J* = 8.0 Hz, 2H), 2.29 (tt, *J* = 8.0, 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 157.1, 148.7, 132.4, 126.0, 123.9, 121.3 (2C), 48.2, 31.9, 18.1; IR (neat): 3034, 1709, 1510, 1360, 1221, 917, 730, 529 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{11}H_{10}N_2OSNa$ [M+Na]: 241.0406; Found: 241.0398.



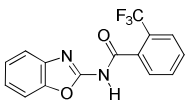
1,3,7-trimethyl-8-(2-oxopyrrolidin-1-yl)-1*H*-purine-2,6(3*H*,7*H*)-dione (6a). Yield: 42%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.97 (t, *J* = 7.0 Hz, 2H,), 3.86 (s, 3H), 3.52 (s, 3H), 3.40 (s, 3H), 2.61 (t, *J* = 8.1 Hz, 2H), 2.29 (tt, *J* = 8.1, 7.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 155.1, 151.6, 146.7, 144.3, 106.5, 49.0, 33.2, 31.0, 29.7, 27.9, 19.1; IR (neat): 1701, 1661, 1512, 1452, 1216 cm^{-1}. HRMS–ESI (*m/z*) calcd. for $C_{12}H_{16}N_5O_3$ [M+1]: 278.1248. Found: 278.1253.



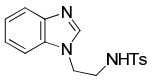
Ethyl 4-(4-nitrophenyl)-2-(2-oxopyrrolidin-1-yl)-1,3-oxazole-5-carboxylate (7a). Yield: 84%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 9.0 Hz, 2H), 8.26 (d, *J* = 9.0 Hz, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 4.10 (t, *J* = 7.2 Hz, 2H), 2.65 (t, *J* = 8.1 Hz, 2H), 2.25 (tt, *J* = 8.1, 7.2 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl3) δ 172.7, 161.6, 152.5, 149.0, 147.8, 132.4, 128.7, 128.5, 123.6, 61.9, 47.5, 31.9, 18.3, 14.2; IR (neat): 2984, 1737, 1585, 1344, 1188, 1082, 856, 728 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{16}H_{15}N_3O_6Na$ [M+Na]: 268.0853; Found: 368.0858.



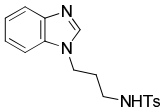
2-(trifluoromethyl)-*N*-(1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-yl)benzamide (6i). Yield: 63%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, CDCl3) δ 8.43 (brs, 1H), 7.85-7.80 (m, 1H), 7.77-7.65 (m, 3H), 3.97 (s, 3H), 3.43 (s, 3H), 3.40 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d6) δ 167.5, 155.1, 151.7, 147.0, 144.1, 135.0, 133.2, 131.4, 129.5, 127.2 (q, *J* = 4.5 Hz), 126.9 (q, *J* = 31.0 Hz), 124.4 (q, *J* = 273.5 Hz), 106.3, 32.5, 30.1, 28.2; IR (neat): 3196, 2925, 1709, 1651, 1505, 1315, 1172, 1131 1036, 736 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{16}H_{14}F_3N_5O_3Na$ [M+Na]: 404.0941; Found: 404.0947.



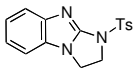
***N*-(1,3-benzoxazol-2-yl)-2-(trifluoromethyl)benzamide (8i).** Yield: 76%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.81 (brs, 1H), 7.91 – 7.69 (m, 2H), 7.67 – 7.53 (m, 2H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.26 (td, *J* = 7.6, 1.2 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.75 (brs, 1H). ^{13}C NMR (125 MHz, DMSO) δ 166.4, 155.9, 148.4, 140.9, 135.6, 133.6, 131.8, 129.7, 127.5(q, *J* = 5.0 Hz), 127.0 (q, *J* = 31.5 Hz), 125.8, 125.0, 124.7(q, *J* =271.5 Hz), 119.2, 111.2; IR (neat): 2927, 1628, 1578, 1552, 1314, 1132, 1109, 743 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{15}H_9F_3N_2O_2Na$ [M+Na]:329.0508; Found: 329.0527.



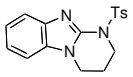
***N*-[2-(1*H*-benzimidazol-1-yl)ethyl]-4-methylbenzenesulfonamide (9).** Yield: 59%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.76 (s, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 4.30 (t, *J* = 4.9 Hz, 2H), 3.39 (t, *J* = 4.9 Hz, 2H), 2.39 (s, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 143.2, 142.5, 137.3, 132.8, 129.7, 126.8, 123.0, 122.3, 119.3, 109.3, 45.7, 42.1, 21.5. IR (neat): 3093, 1498, 1327, 1157, 1093, 744 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{16}H_{17}N_3O_2SNa$ [M+Na]: 338.0934; Found: 338.0930.



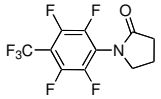
***N*-[3-(1*H*-benzimidazol-1-yl)propyl]-4-methylbenzenesulfonamide (10).** Yield: 59%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.84 – 7.73 (m, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.32 (m, 1H), 7.30 – 7.17 (m, 4H), 6.84 (t, *J* = 5.9 Hz, 1H), 4.31 (t, *J* = 6.6 Hz, 2H), 2.88 (q, *J* = 5.9 Hz, 2H), 2.38 (s, 3H), 2.10 – 2.04 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 143.4, 136.5, 133.3, 129.7, 126.9, 123.0, 122.3, 120.1, 109.7, 41.7, 39.6, 29.2, 21.4. IR (neat): 3056, 1501, 1318, 1153, 748, 551cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{17}H_{19}N_3O_2SNa$ [M+Na]: 352.1090; Found: 352.1097.



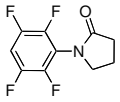
1-[(4-methylphenyl)sulfonyl]-2,3-dihydro-1*H*-imidazo[1,2-*a*]benzimidazole (11). Yield: 86%. R_f = 0.50 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.14 – 7.06 (m, 2H), 4.36 (t, *J* = 7.6 Hz, 2H), 4.10 (t, *J* = 7.6 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 147.5, 145.2, 133.2, 131.4, 129.9, 128.0, 122.1, 121.7, 119.6, 108.4, 51.6, 39.8, 21.6. IR (neat): 1544, 1434, 1277, 1170, 1089, 572 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{16}H_{15}N_3O_2SNa$ [M+Na]: 336.0777; Found: 336.0775.



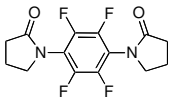
1-[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydropyrimido[1,2-*a*]benzimidazole (12). Yield: 90%. R_f = 0.50 (100% ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.3 Hz, 2H), 7.22 – 7.05 (m, 3H), 4.04 (t, *J* = 5.5 Hz, 2H), 3.98 (t, *J* = 6.2 Hz, 2H), 2.37 (s, 3H), 2.30 (tt, *J* = 6.2, 5.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 144.5, 141.1, 135.3, 133.1, 129.4, 128.5, 122.2, 121.1, 118.9, 107.8, 44.7, 40.7, 21.9, 21.6. IR (neat): 1525, 1436, 1286, 1150, 671 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{17}H_{18}N_3O_2S$ [M+1]: 328.1114; Found: 328.1120.



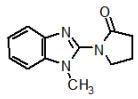
1-[2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl]pyrrolidin-2-one (13a). Yield: 22%. R_f = 0.40 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (t, *J* = 7.0 Hz, 2H), 2.62 (t, *J* = 8.0 Hz, 2H), 2.35 (tt, *J* = 8.0, 7.0 Hz, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -56.24 (t, *J* = 21.8 Hz, 3F), -139.62 – -140.63 (m, 2F), -141.26 – -142.13 (m, 2F). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 146.6, 145.7 – 144.4 (m), 143.6 – 142.4, 121.8, 94.7, 48.9 (t, *J* = 2.1 Hz), 30.0, 19.6. IR (neat): 1728, 1503, 1346, 1272, 1145, 987, 715 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{11}H_7NF_7NO$ [M+1]: 302.0410; Found: 302.0423.



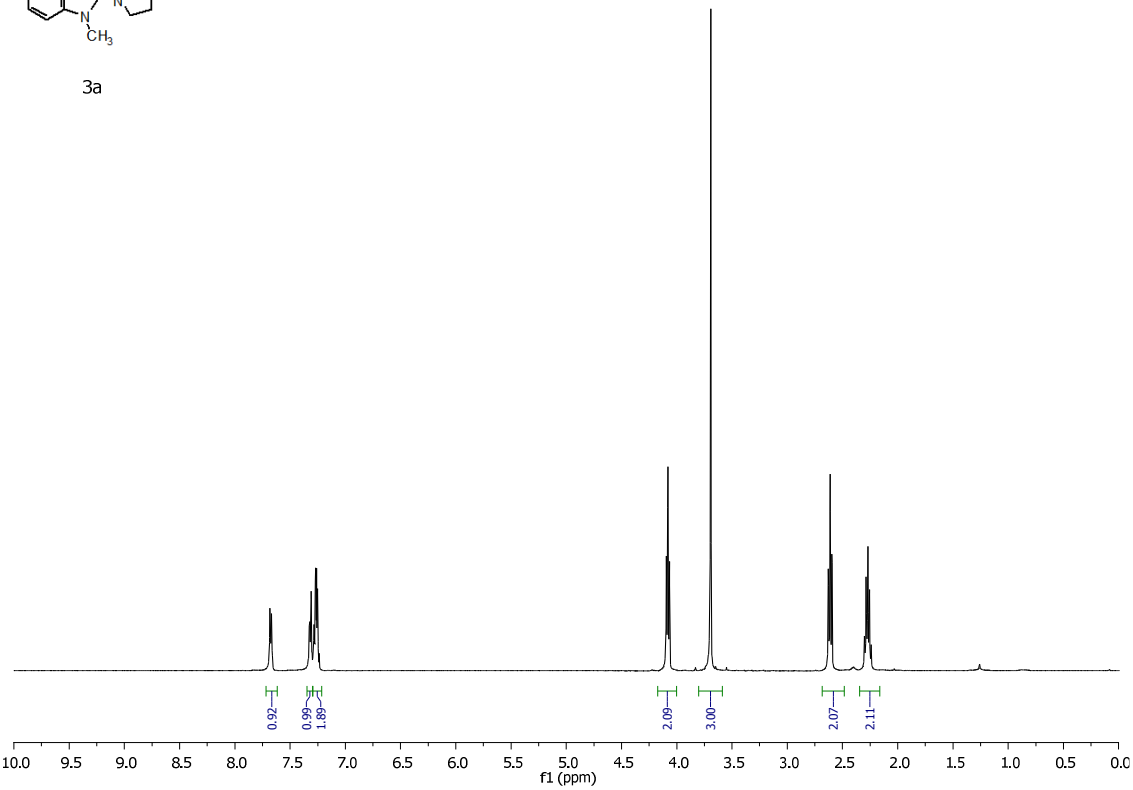
1-(2,3,5,6-tetrafluorophenyl)pyrrolidin-2-one (14a). Yield: 33%. R_f = 0.50 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (tt, *J* = 9.7, 7.2 Hz, 1H), 3.80 (t, *J* = 7.0 Hz, 2H), 2.59 (t, *J* = 8.1 Hz, 2H), 2.31 (tt, *J* = 8.1, 7.0 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ -138.42 – -138.67 (m, 2F), -144.14 – -144.85 (m, 2F). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5, 146.07 (dddd, *J* = 248.7, 13.0, 11.5, 4.1 Hz), 144.54 – 141.90 (ddt, *J* = 248.7, 14.4, 3.6 Hz), 118.45 (tt, *J* = 14.4, 2.7 Hz), 105.03 (t, *J* = 22.8 Hz), 49.08 (t, *J* = 1.8 Hz), 30.1, 19.4. IR (neat): 3046, 1698, 1514, 1495, 1251, 945 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{11}H_7NF_7NO$ [M+1]: 302.0410; Found: 302.0423.

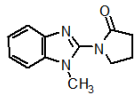


1,1'-(2,3,5,6-tetrafluorobenzene-1,4-diyl)dipyrrolidin-2-one (14aa). Yield: 71%. R_f = 0.20 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (t, *J* = 7.0 Hz, 4H), 2.59 (t, *J* = 8.1 Hz, 4H), 2.31 (tt, *J* = 8.1, 7.0 Hz, 4H); ^{19}F NMR (282 MHz, $CDCl_3$) δ -144.42 (s, 4F); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 145.6 – 141.9 (m), 117.4 – 117.0 (m), 49.1, 30.0, 19.4. IR (neat): 1705, 1502, 1395, 1251, 977 cm^{-1}, HRMS–ESI (*m/z*) calcd. for $C_{14}H_{12}F_4N_2O_2Na$ [M+Na]: 339.0727; Found: 39.0734.



3a


0.92
0.99
1.89
2.09
3.00
2.07
2.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



3a

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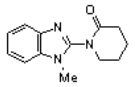
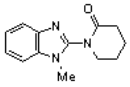
f1 (ppm)



3b

0.93
3.16
2.09
3.00
2.09
4.21
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



3b

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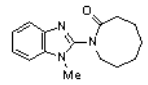
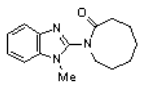
f1 (ppm)

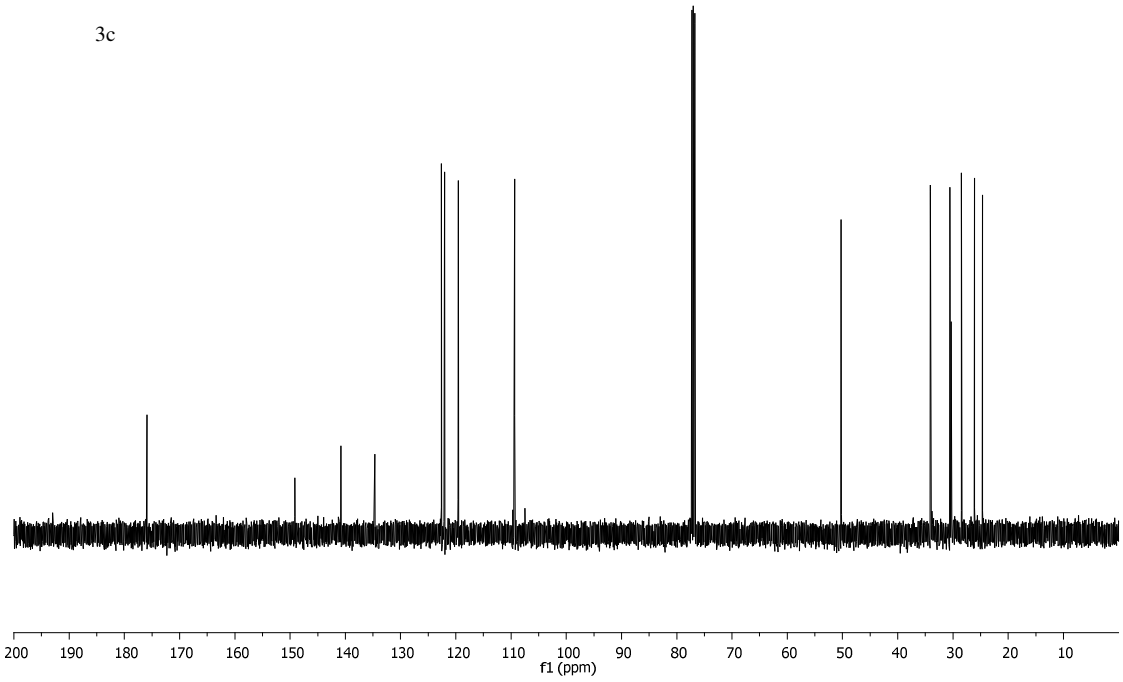

O
N
N
Me

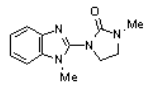
3c

0.93
3.02
2.10
3.00
2.10
4.62
4.29
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

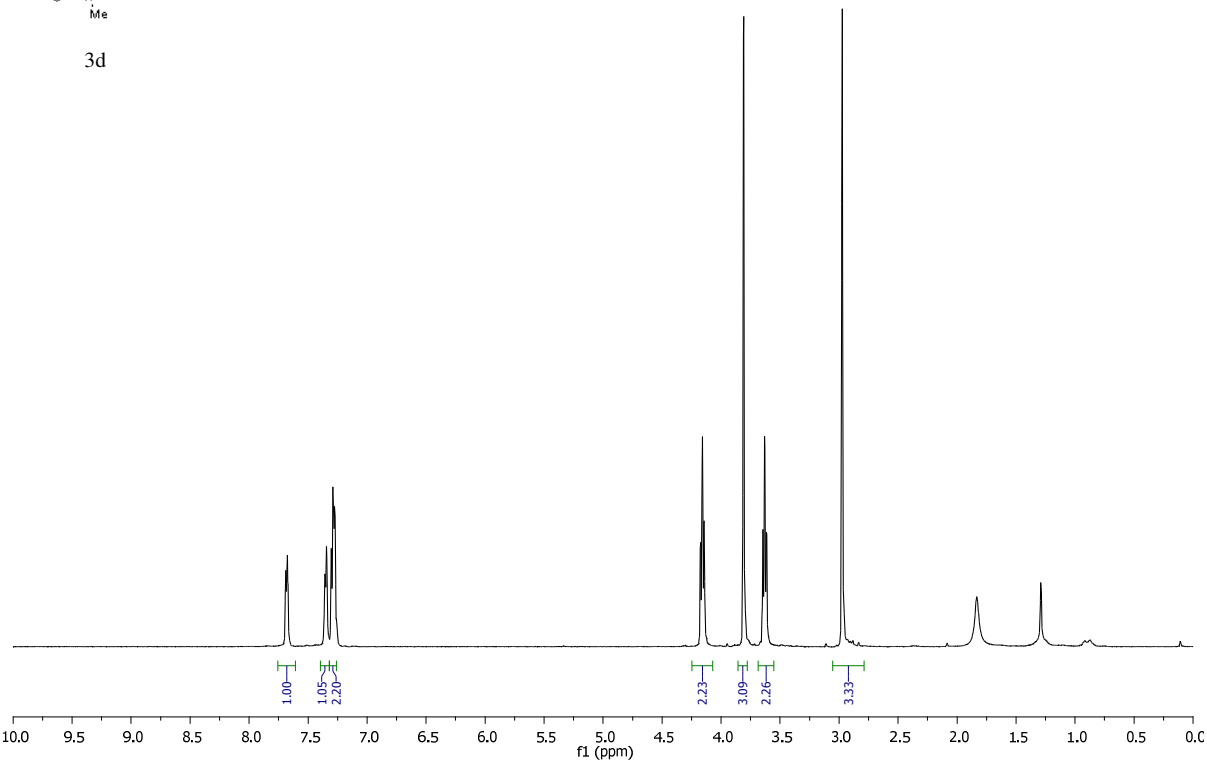

O
N
N
Me

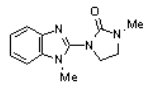
3c


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

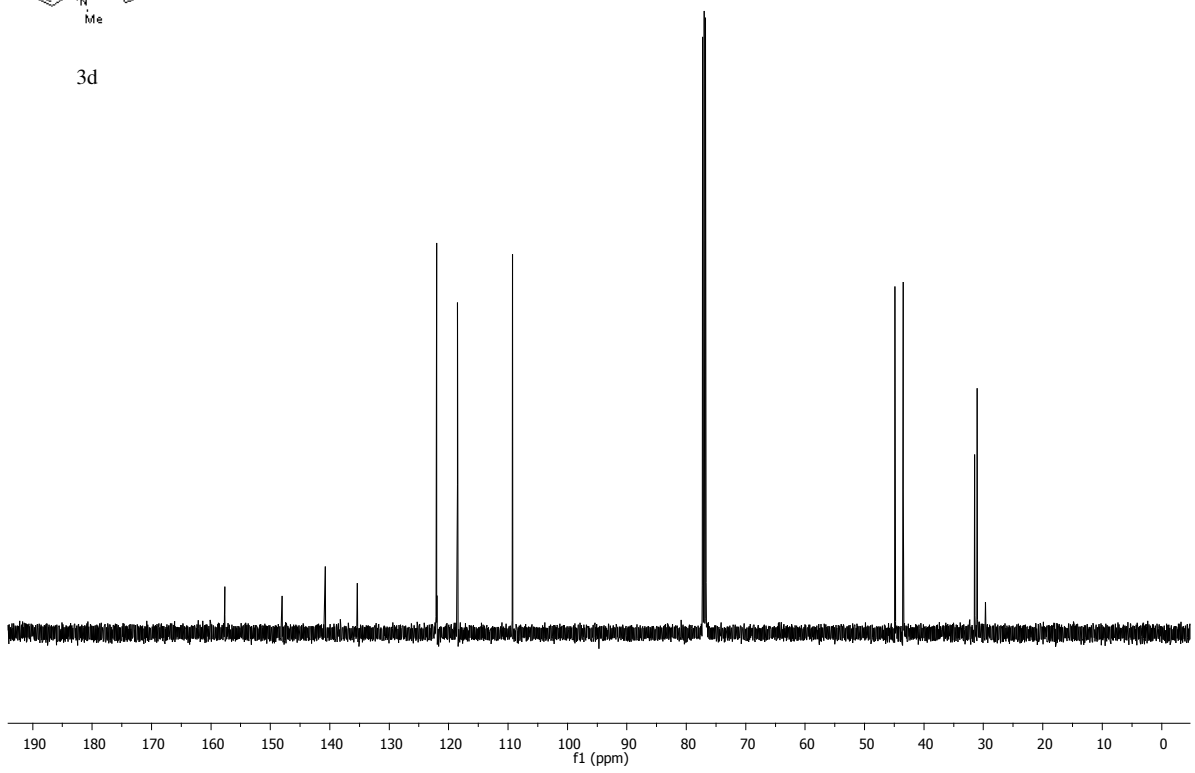


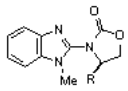
3d


1.00
1.05
2.20
2.23
3.09
2.26
3.33
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

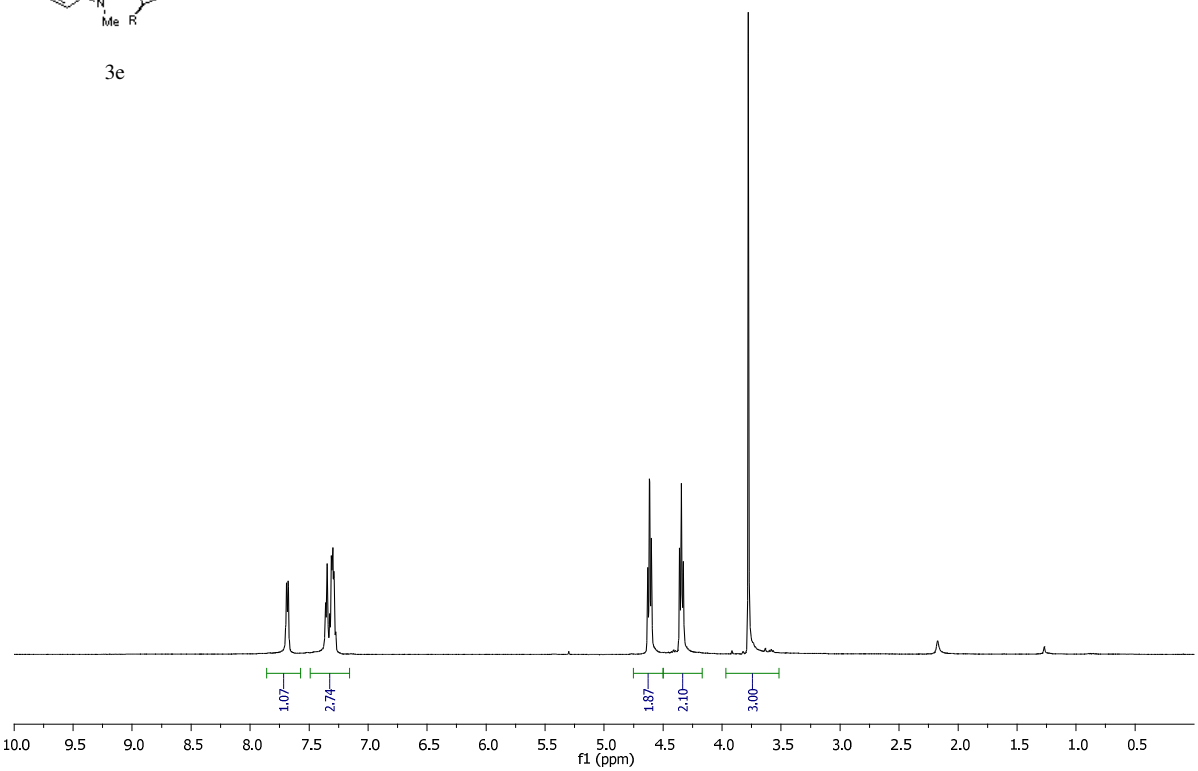


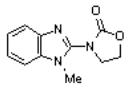
3d


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

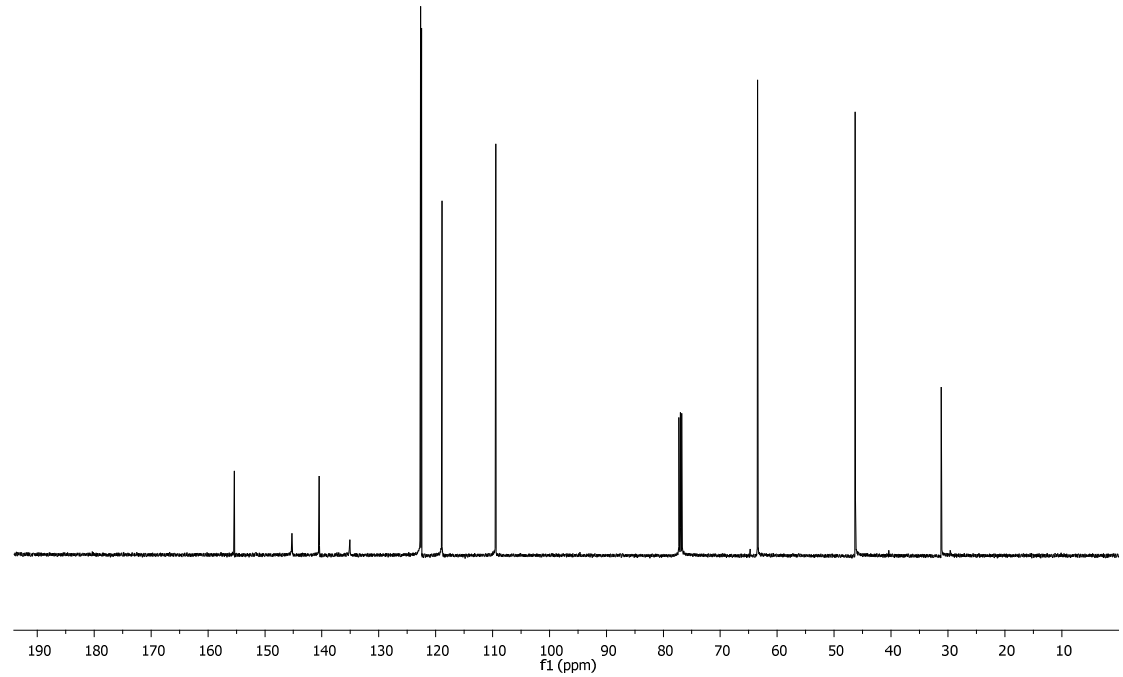

O
N
O
N
Me
R

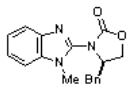
3e


1.07
2.74
1.87
2.10
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


O
N
O
N
Me

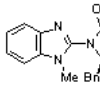
3e


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


Me Bn

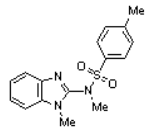
3f

1.03
6.48
1.93
1.01
1.11
1.12
3.00
1.09
1.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

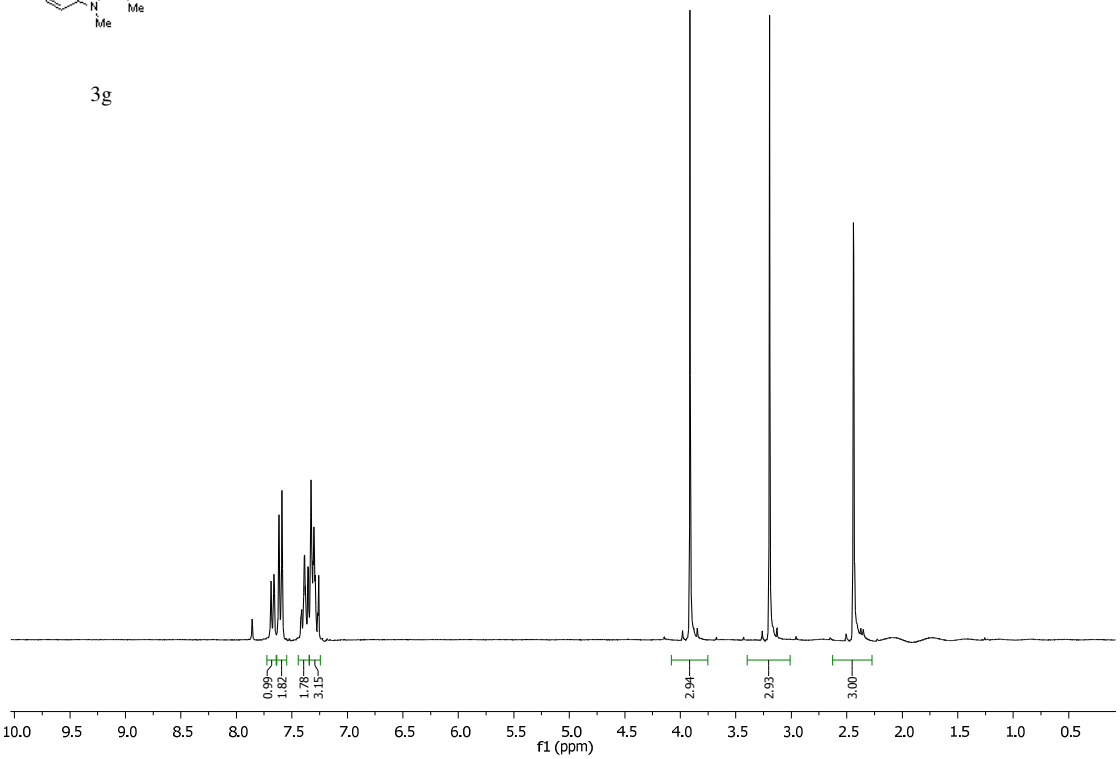

Me Bn

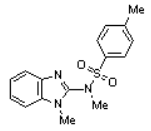
3f

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

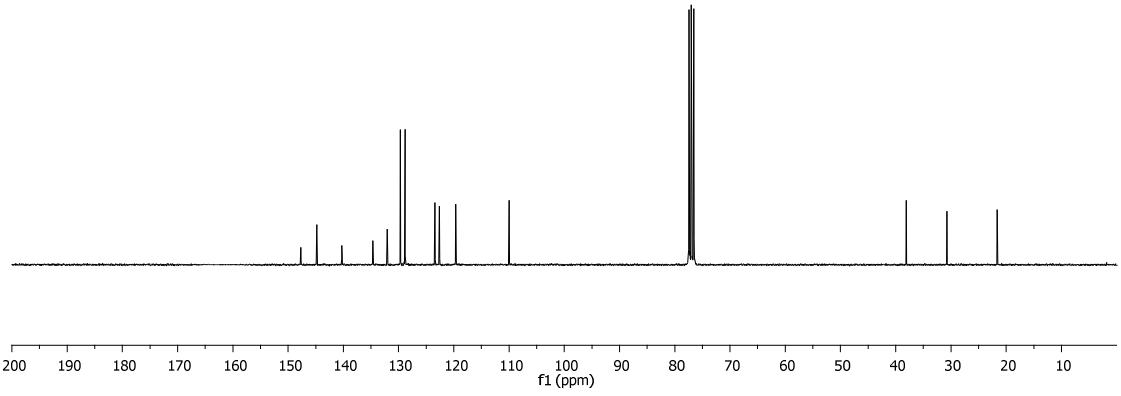


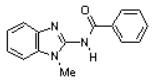
3g


0.99
1.82
1.78
3.15
2.94
2.93
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

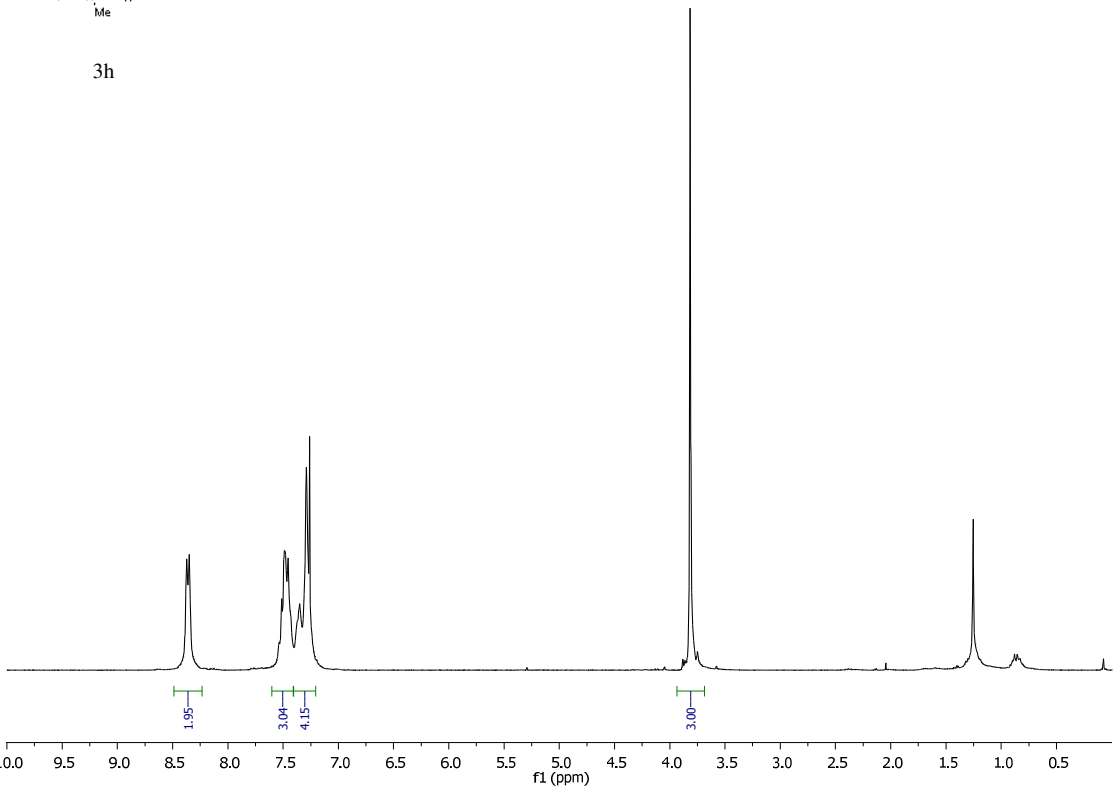


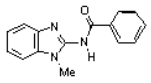
3g


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

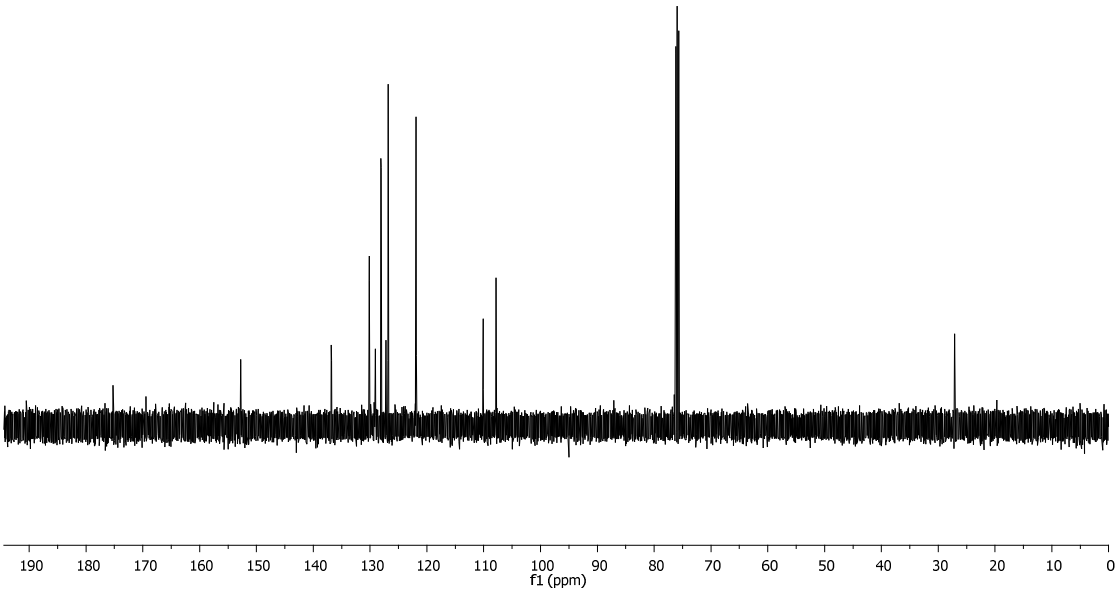


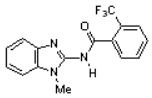
3h


1.95
3.04
4.15
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

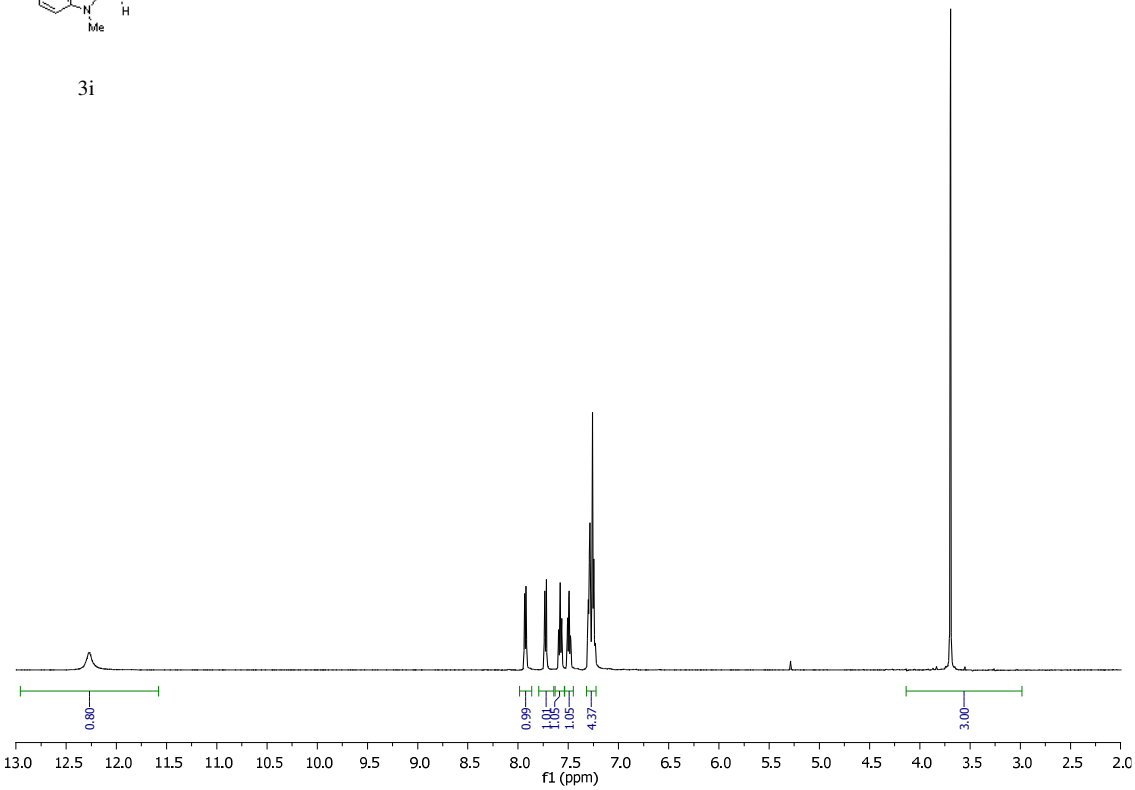


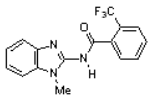
3h


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



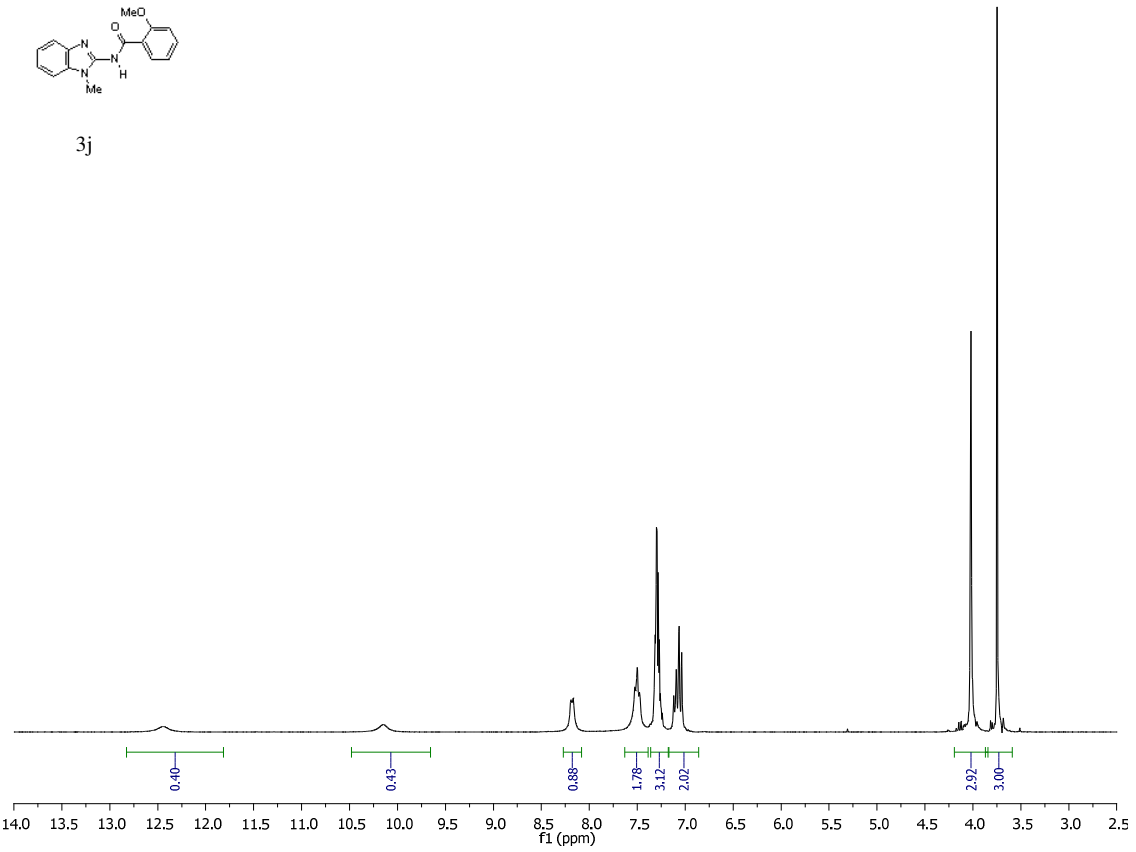
3i

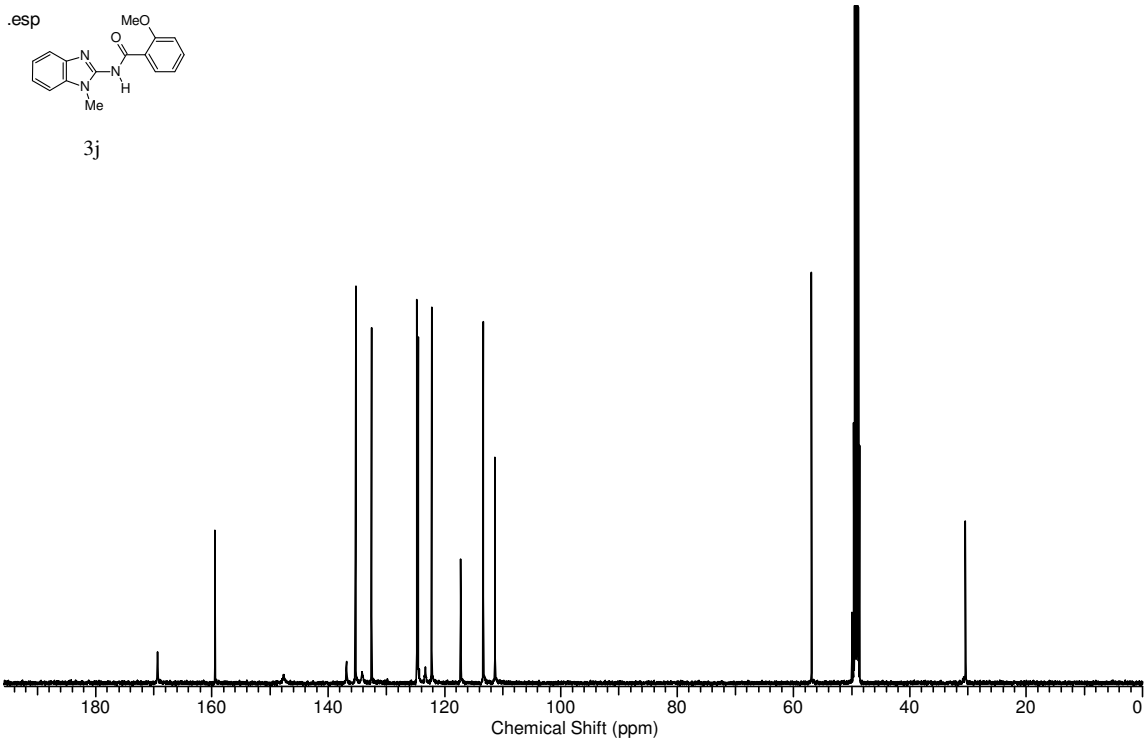

0.80
0.99
1.01
1.05
1.05
4.37
3.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0
f1 (ppm)

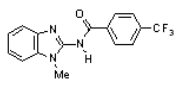


3i

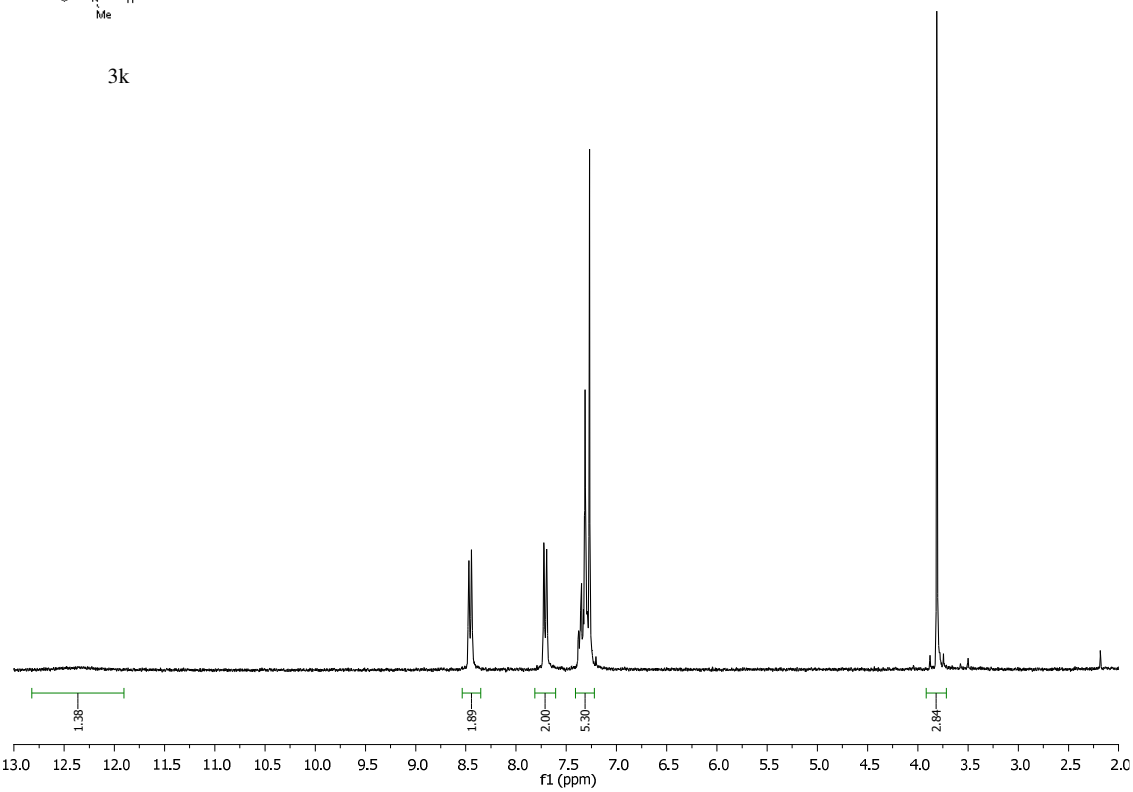
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


MeO
O
N
N
H
Me
3j
0.40
0.43
0.88
1.78
3.12
2.02
2.92
3.00
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5
f1 (ppm)

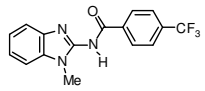

.esp
MeO
O
N
N
H
Me
3j
180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)



3k

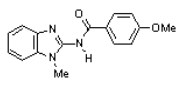

1.38
1.89
2.00
5.30
2.84
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0
f1 (ppm)

.esp



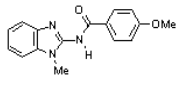
3k

129.09
124.60
122.53
122.49
109.32
111.81
28.06
171.78
152.27
141.84
130.71
130.45
129.76
128.54
121.65
180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)



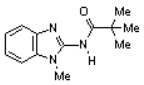
3l

2.10
7.71
2.26
3.07
3.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5
f1 (ppm)



3l

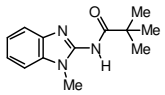
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



3m

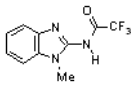
0.64
4.26
3.00
9.45
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

.esp

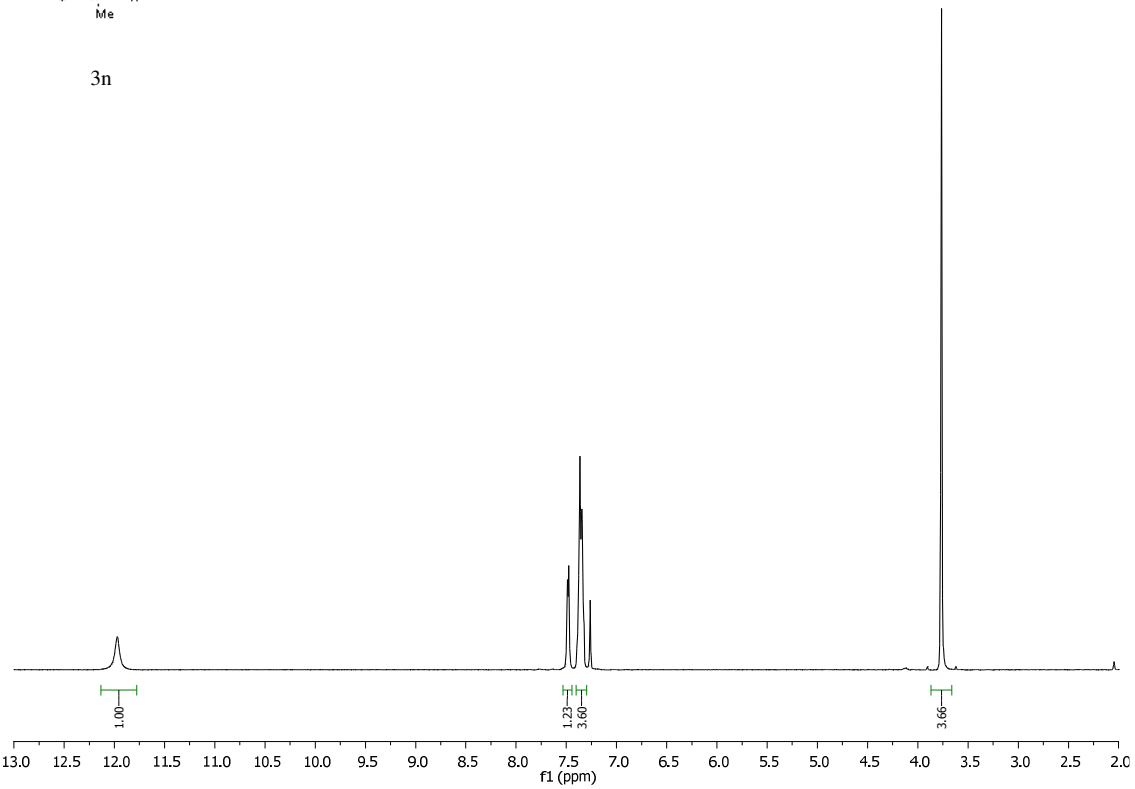


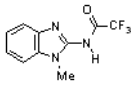
3m

173.64
154.04
130.65
128.99
122.76
122.68
111.21
108.76
41.14
28.20
28.09
180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)



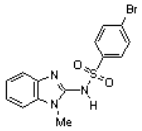
3n


1.00
1.23
3.60
3.66
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0
f1 (ppm)

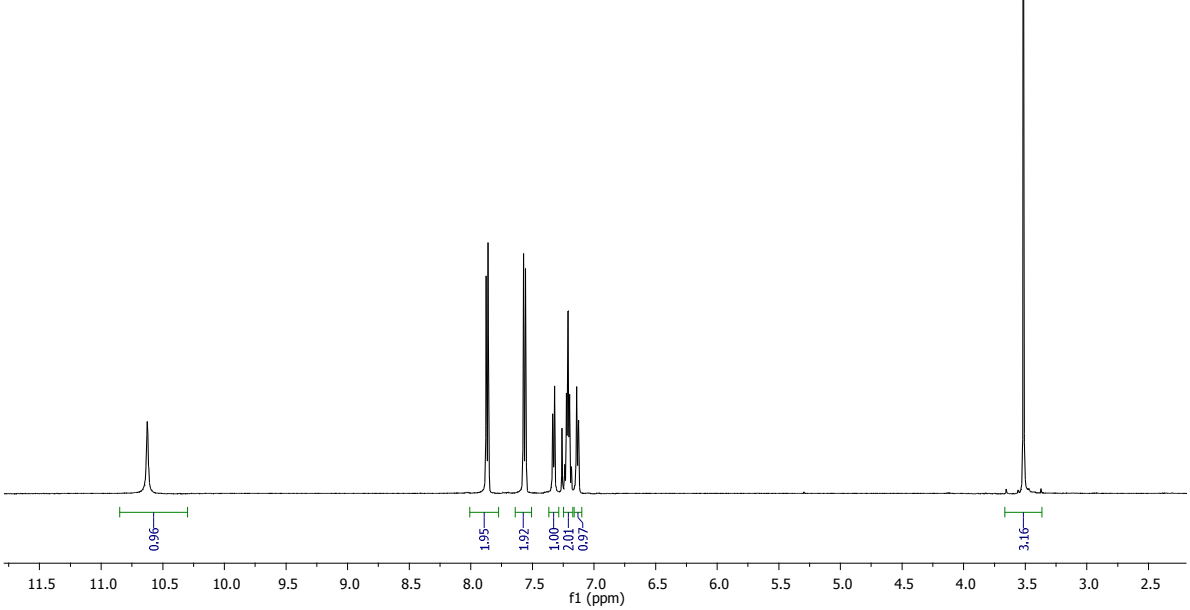


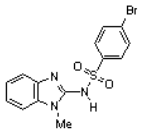
3n

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Br
O
S
O
N
H
N
N
Me

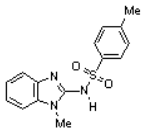
3o


0.96
1.95
1.92
1.00
2.01
0.97
3.16
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f1 (ppm)

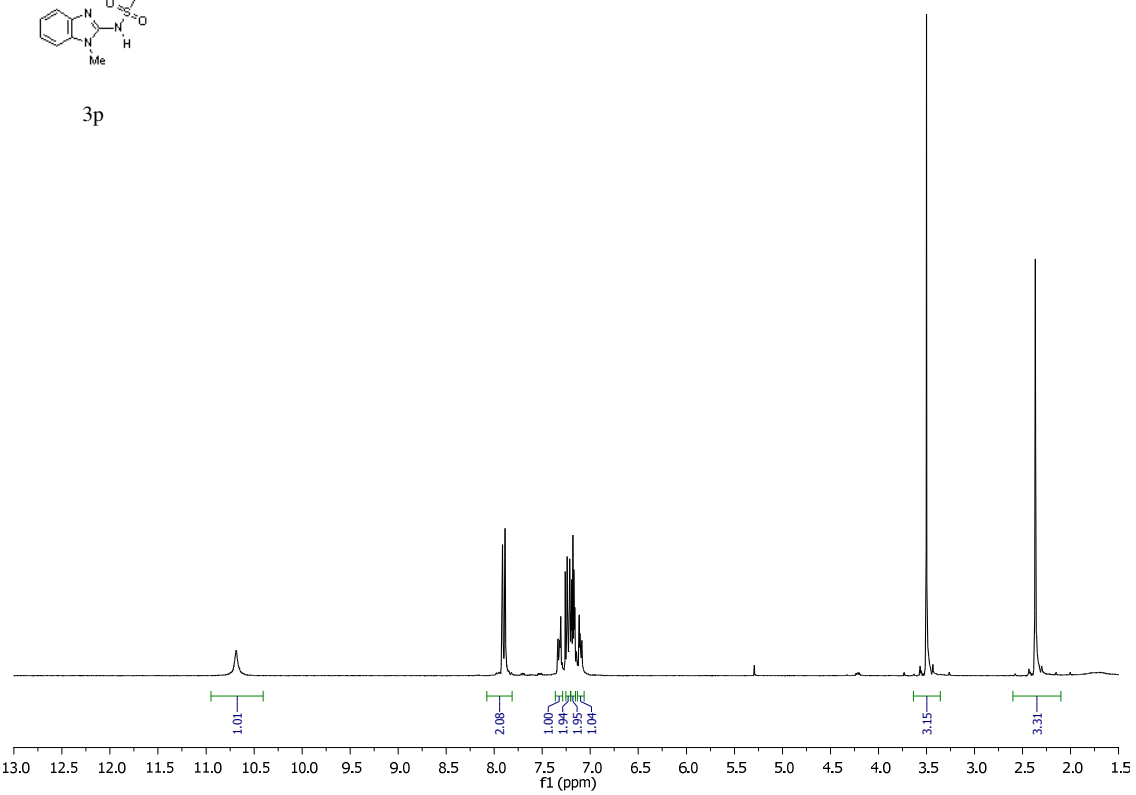

Br
O
S
O
N
H
N
N
Me

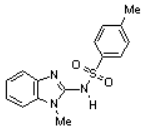
3o

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



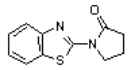
3p


1.01
2.08
1.00
1.94
1.95
1.04
3.15
3.31
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
f1 (ppm)

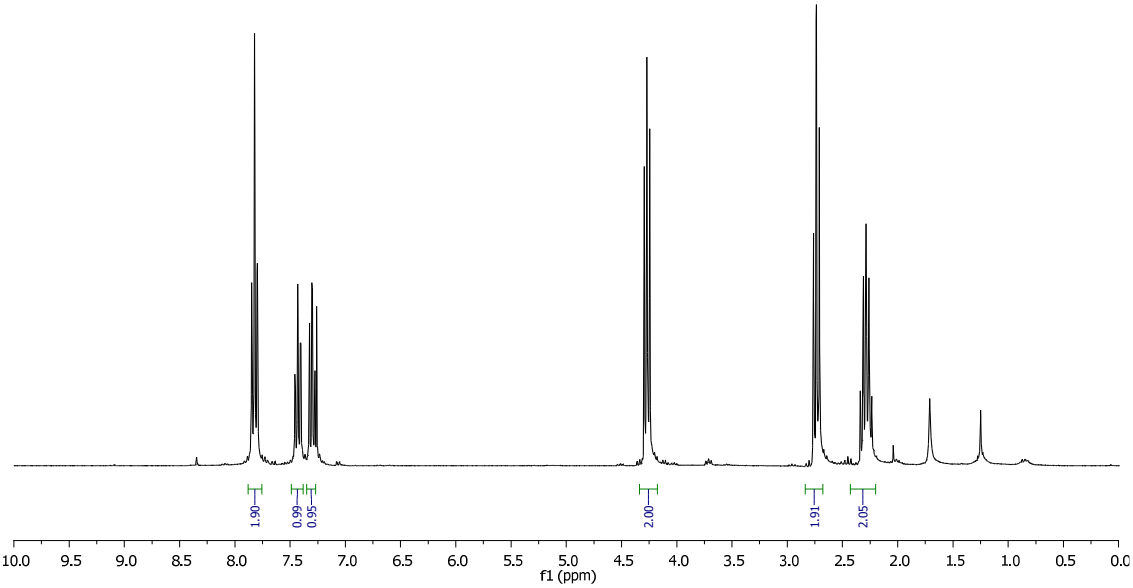


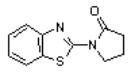
3p

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



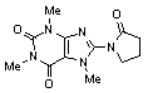
5a


1.90
0.99
0.95
2.00
1.91
2.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

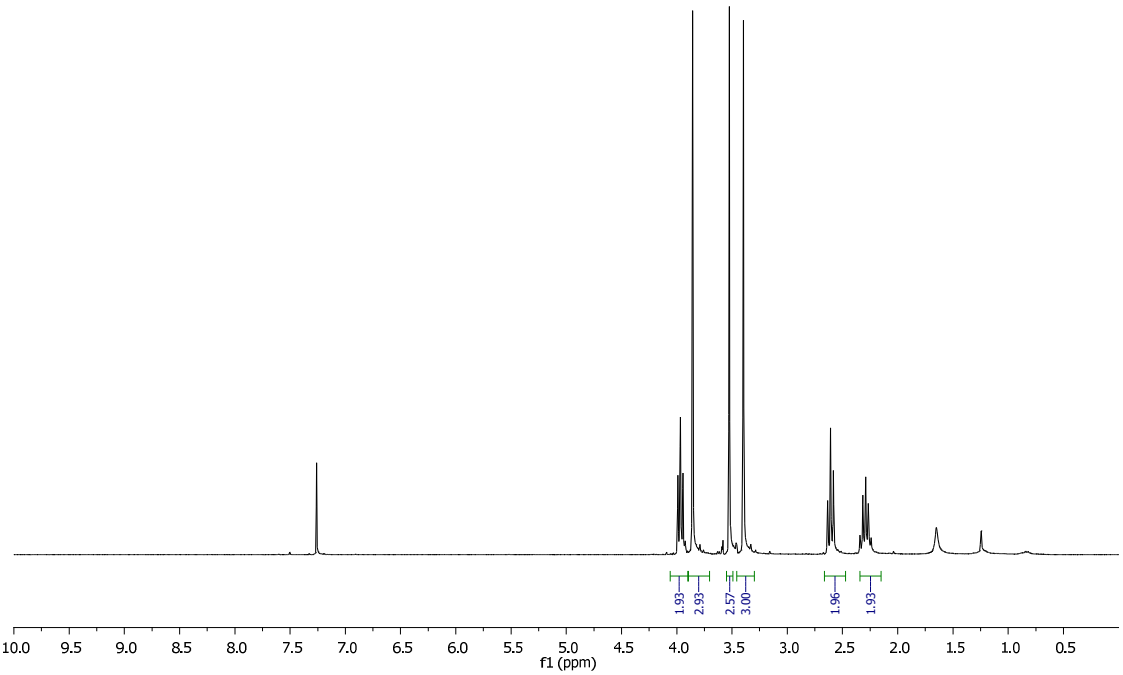


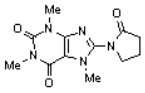
5a

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



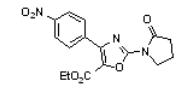
6a


1.93
2.93
2.57
3.00
1.96
1.93
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

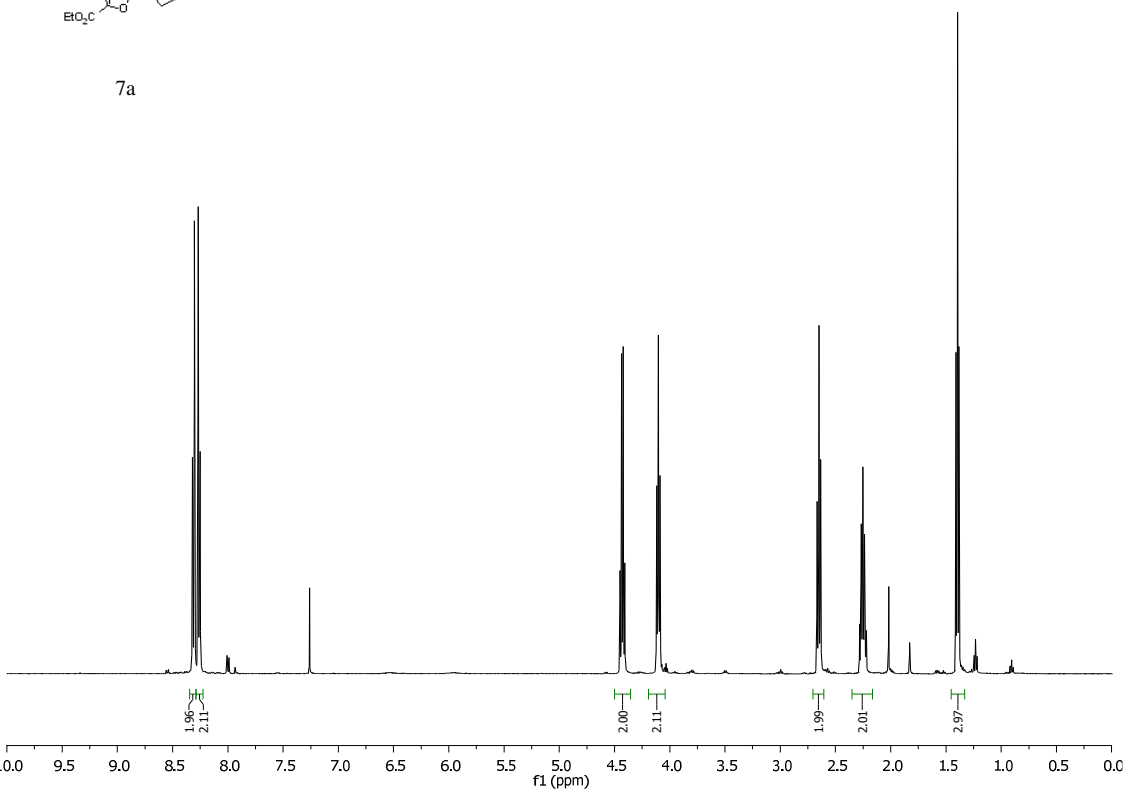


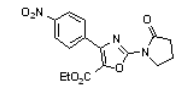
6a

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

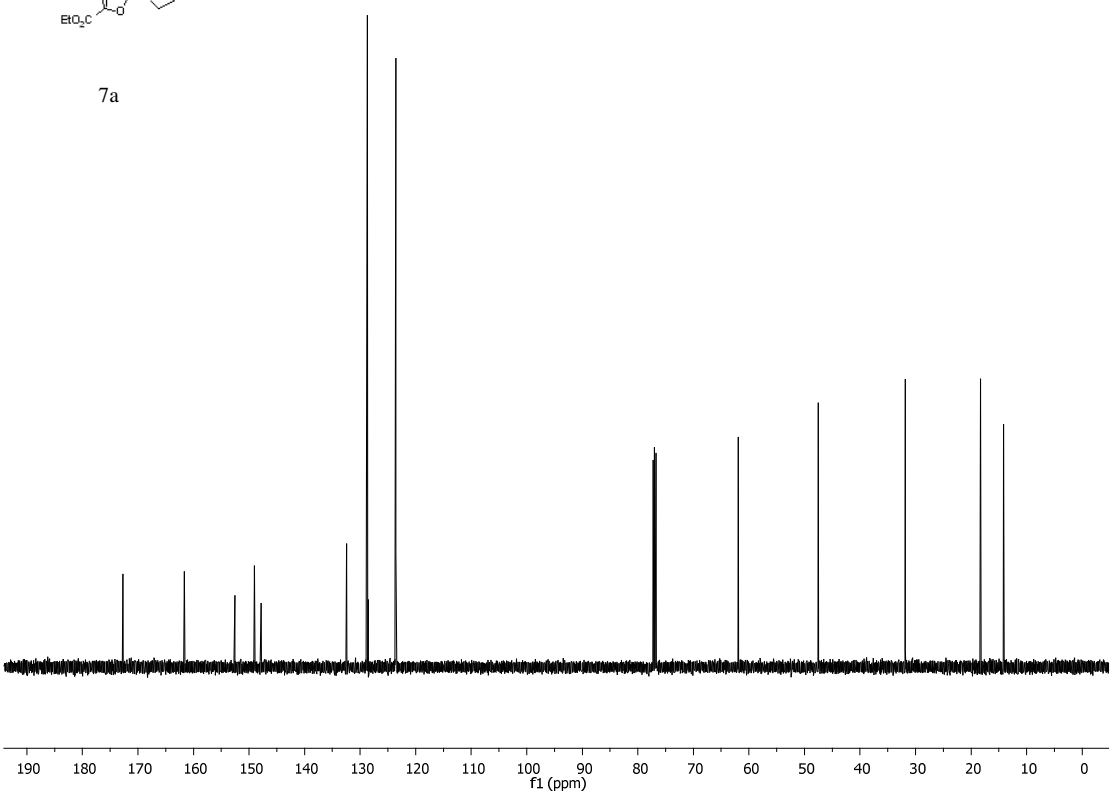


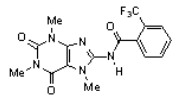
7a


1.96
2.11
2.00
2.11
1.99
2.01
2.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

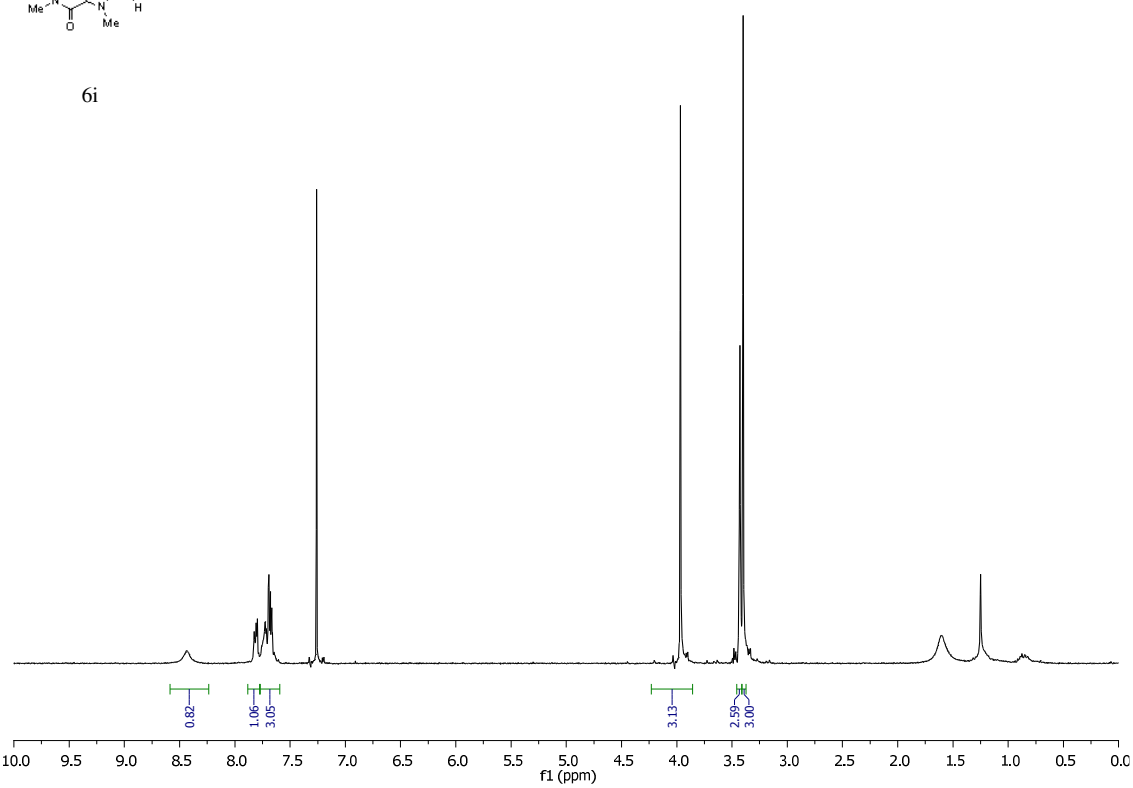


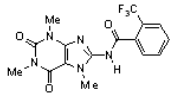
7a


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



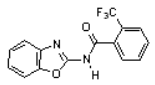
6i


0.82
1.06
3.05
3.13
2.59
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

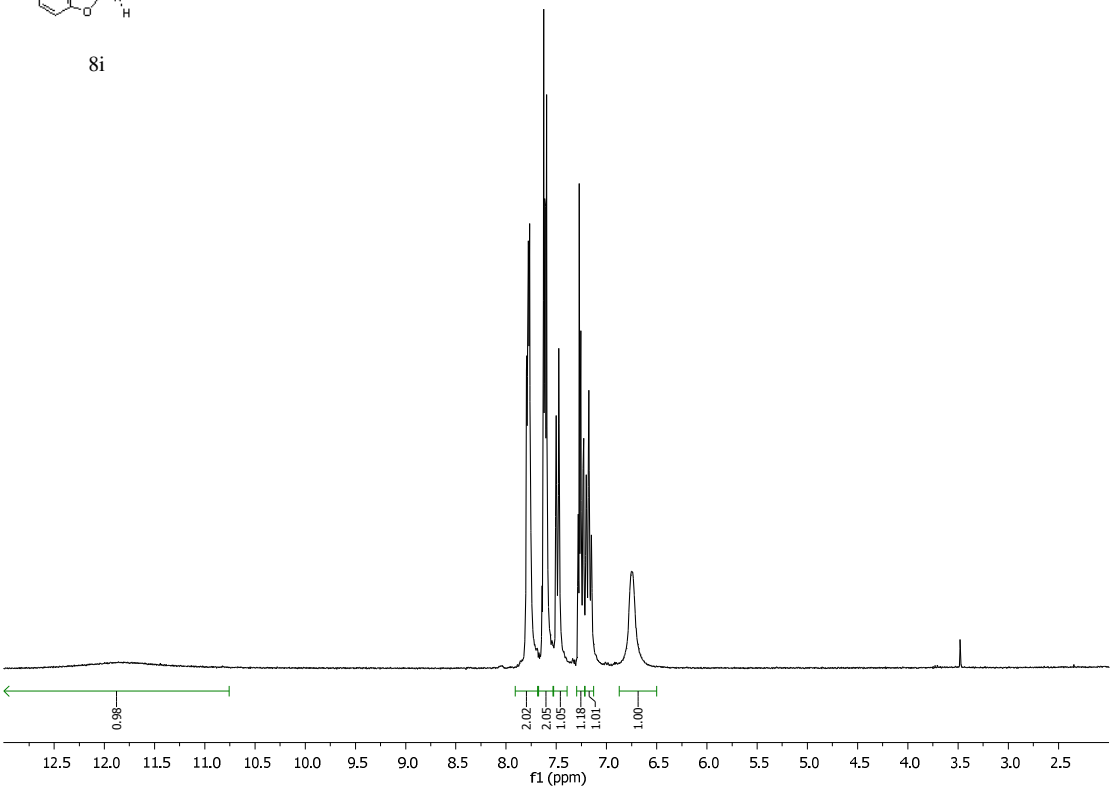


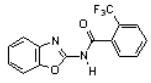
6i

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



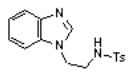
8i


0.98
2.02
2.05
1.05
1.18
1.01
1.00
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5
f1 (ppm)

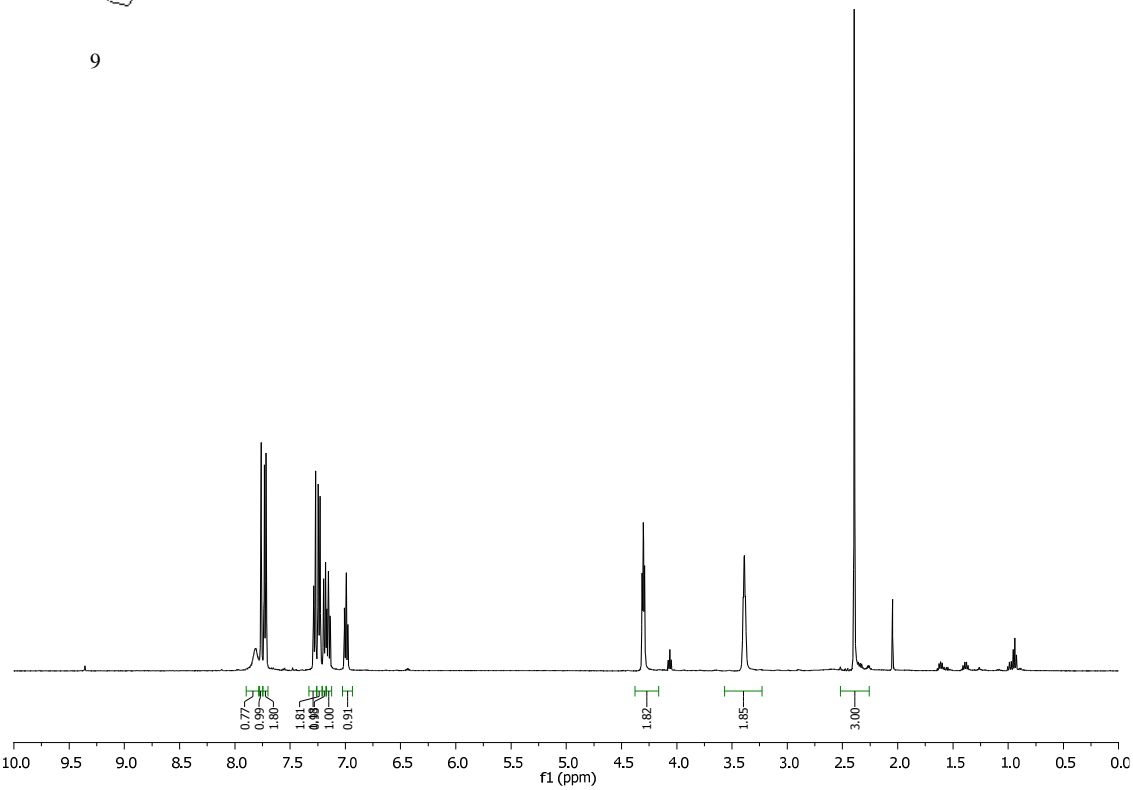


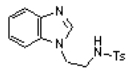
8i

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

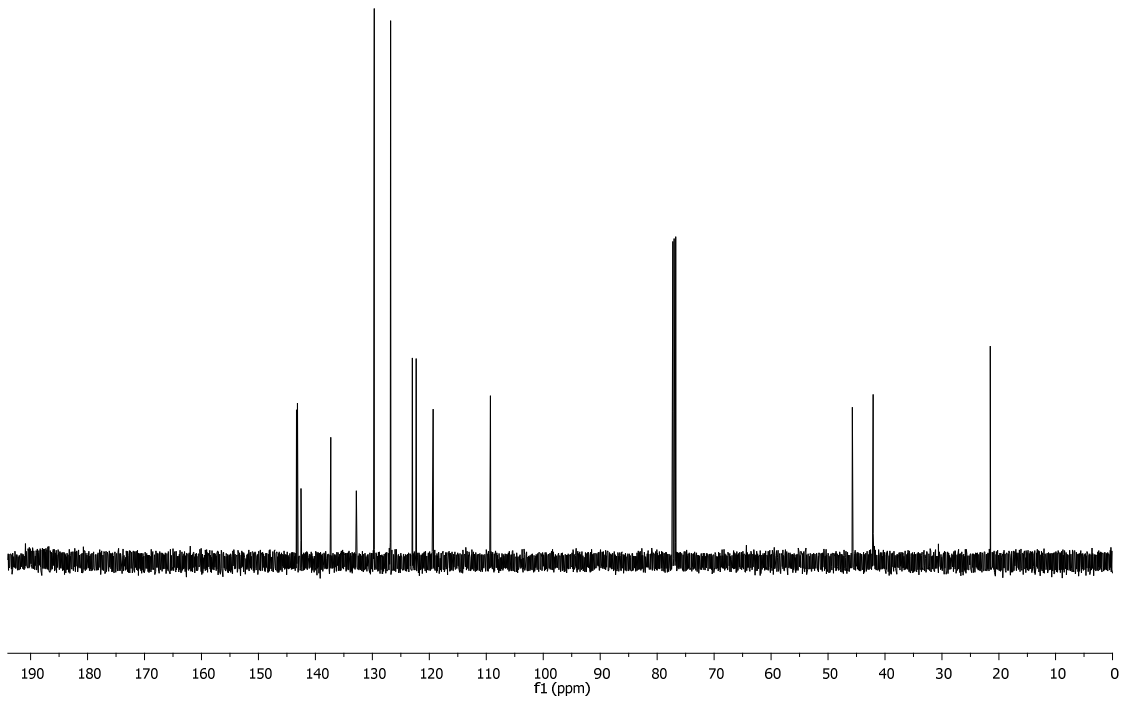


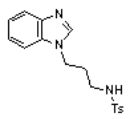
9


0.77
0.99
1.80
1.81
1.00
0.91
1.82
1.85
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

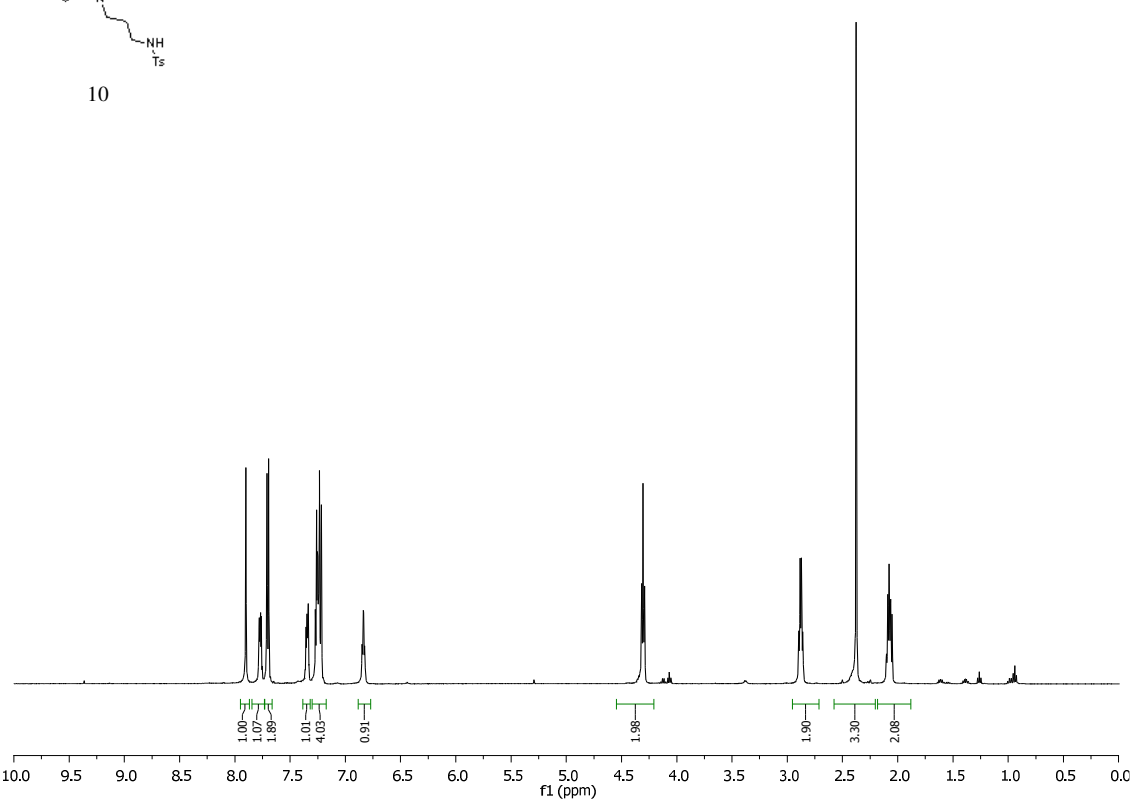


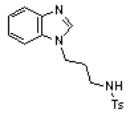
9


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



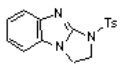
10


1.00
1.07
1.89
1.01
4.03
0.91
1.98
1.90
3.30
2.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

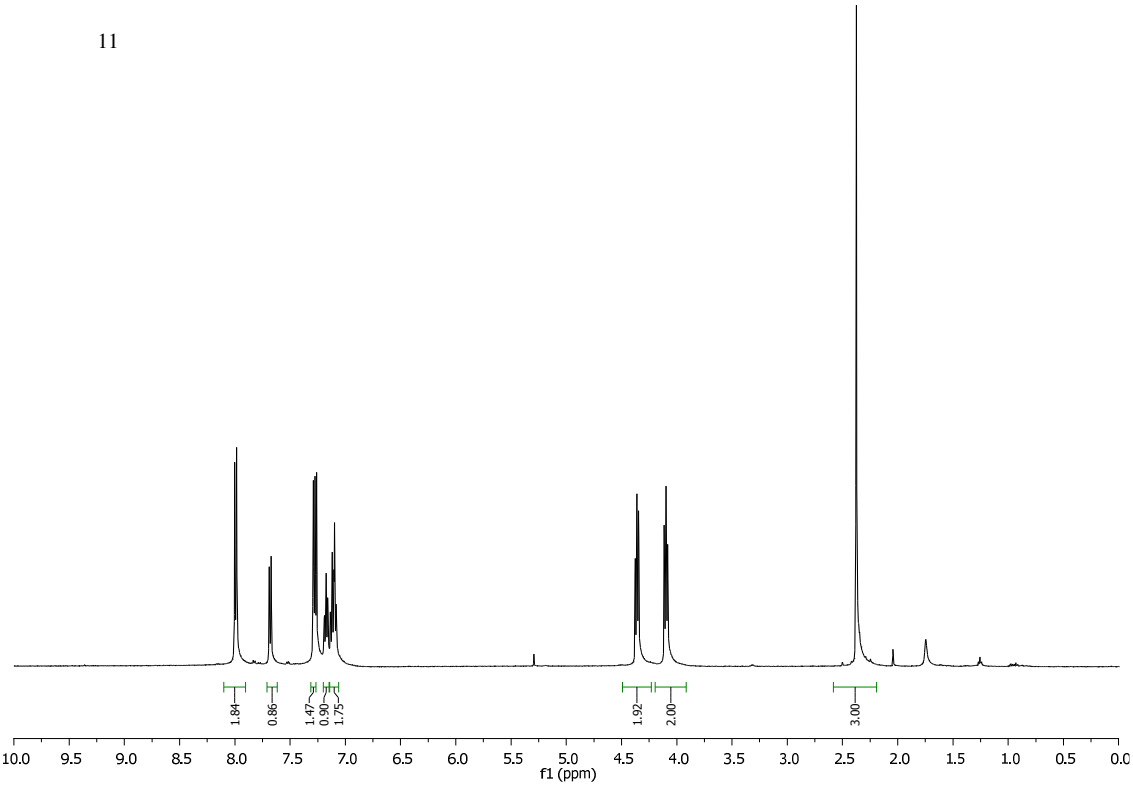


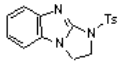
10

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

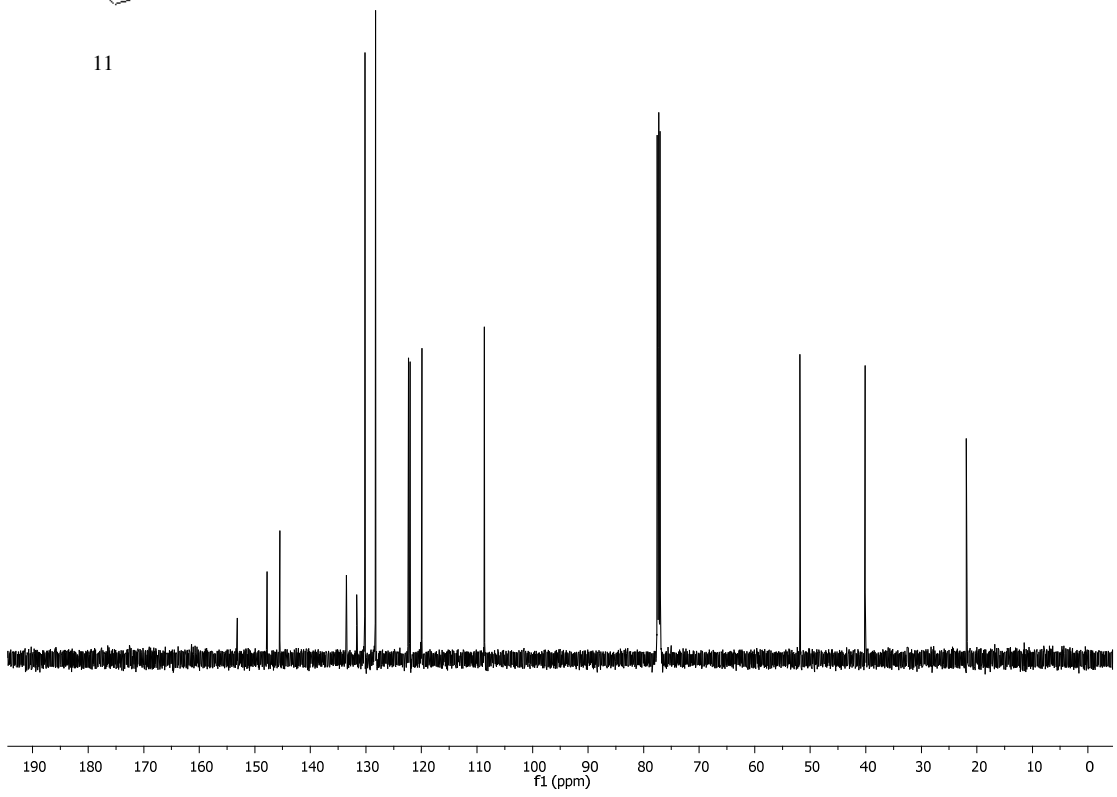


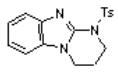
11


1.84
0.86
1.47
0.90
1.75
1.92
2.00
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

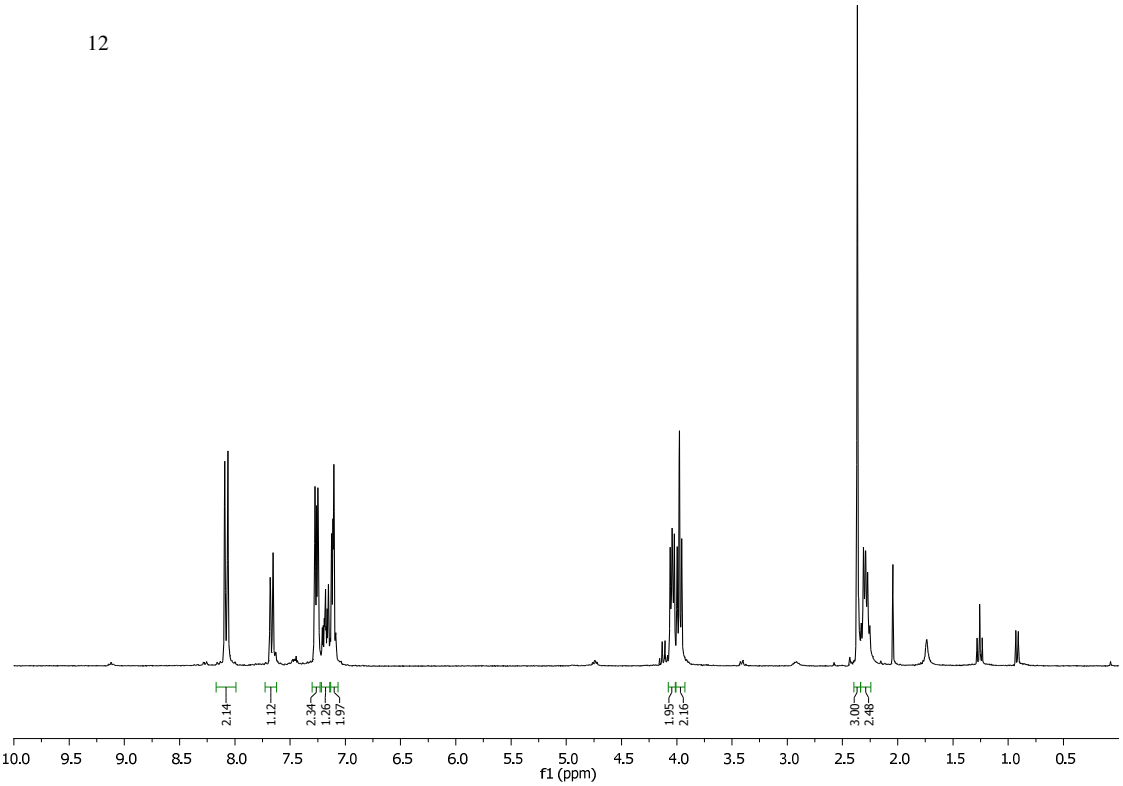


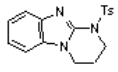
11


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

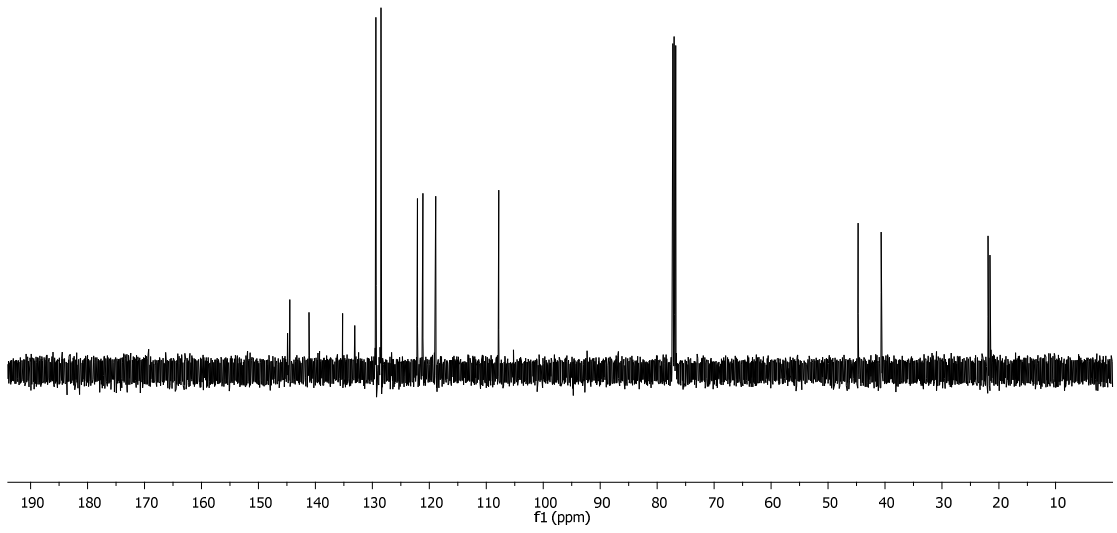

Ts
N
N
N

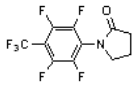
12


2.14
1.12
2.34
1.26
1.97
1.95
2.16
3.00
2.48
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

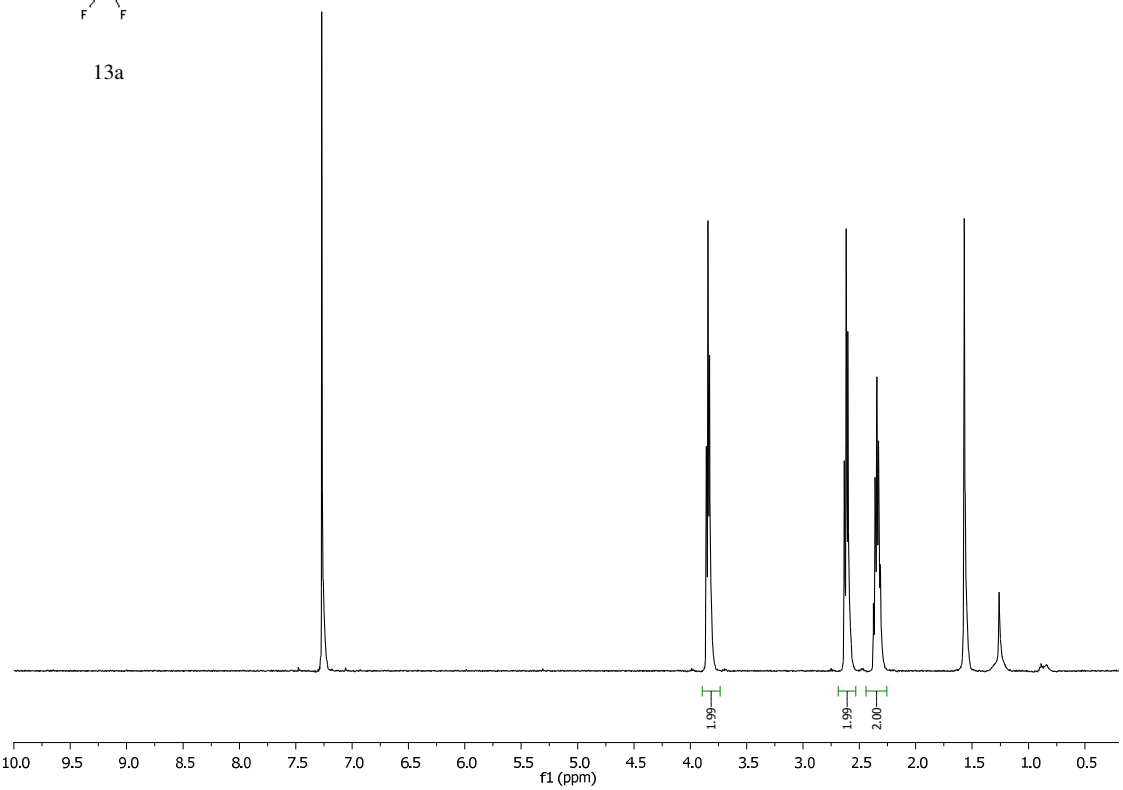

Ts
N
N
N

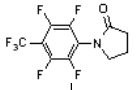
12


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

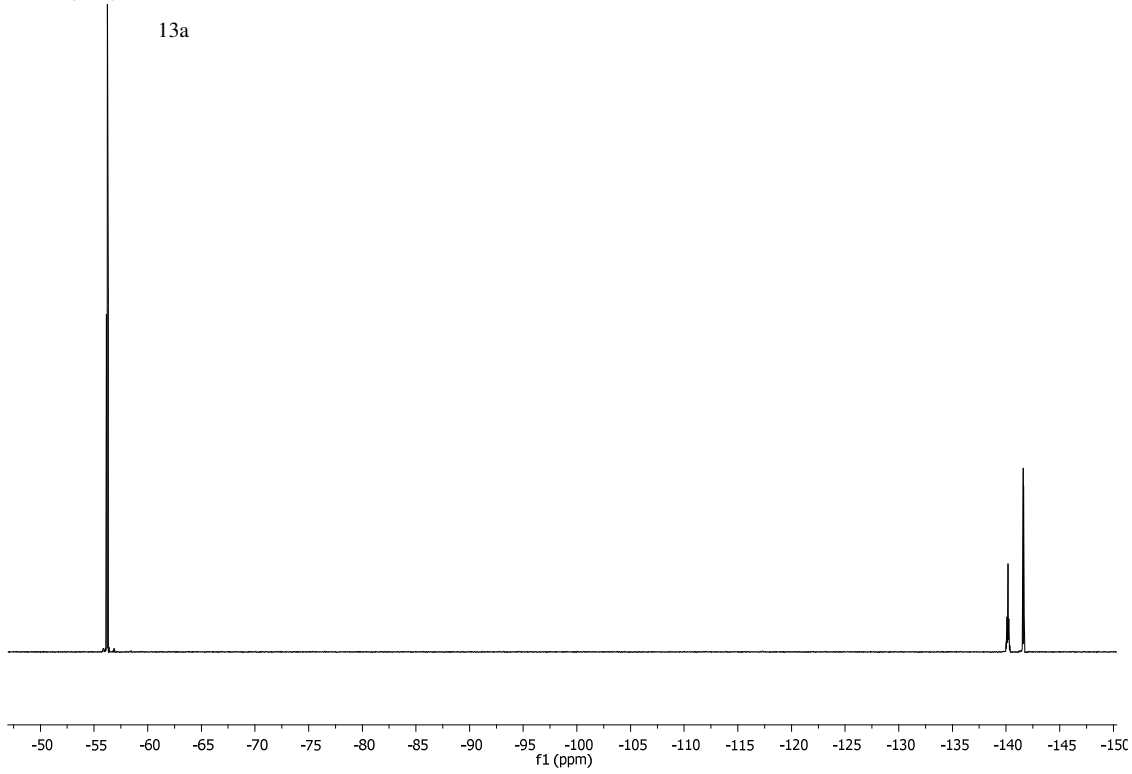


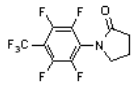
13a


1.99
1.99
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



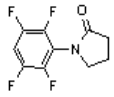
13a


-50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150
f1 (ppm)

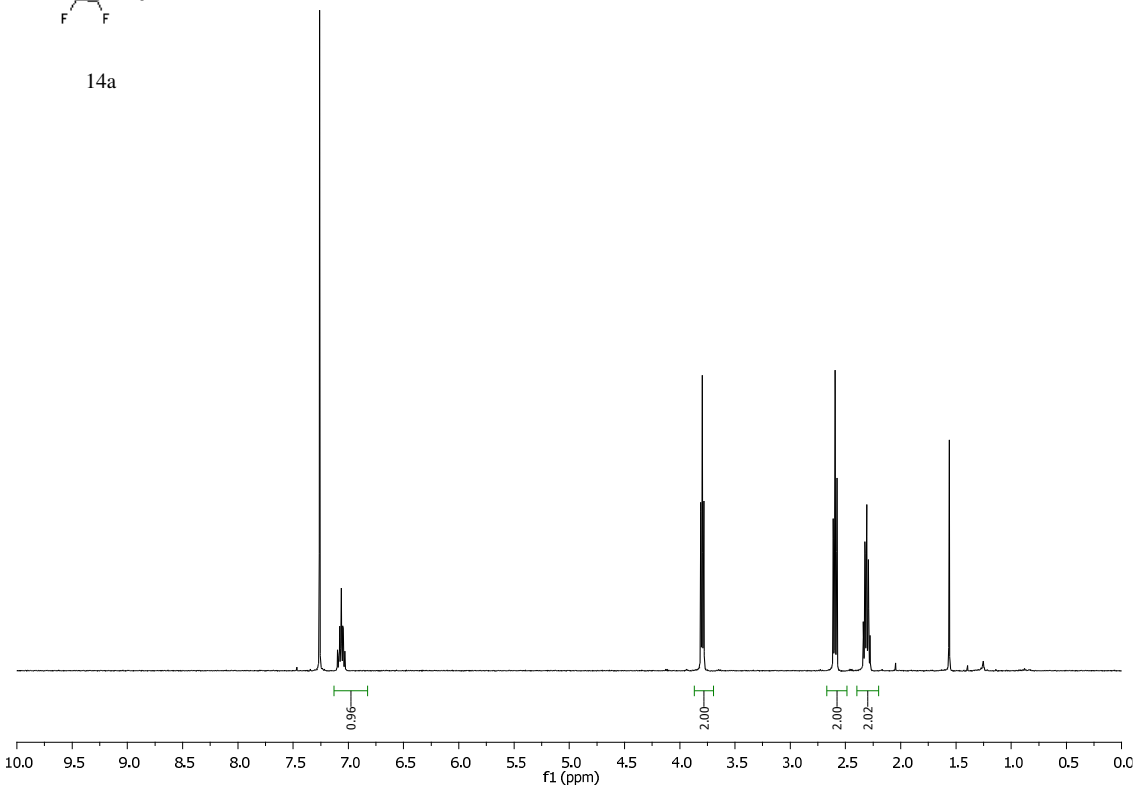


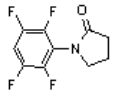
13a

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

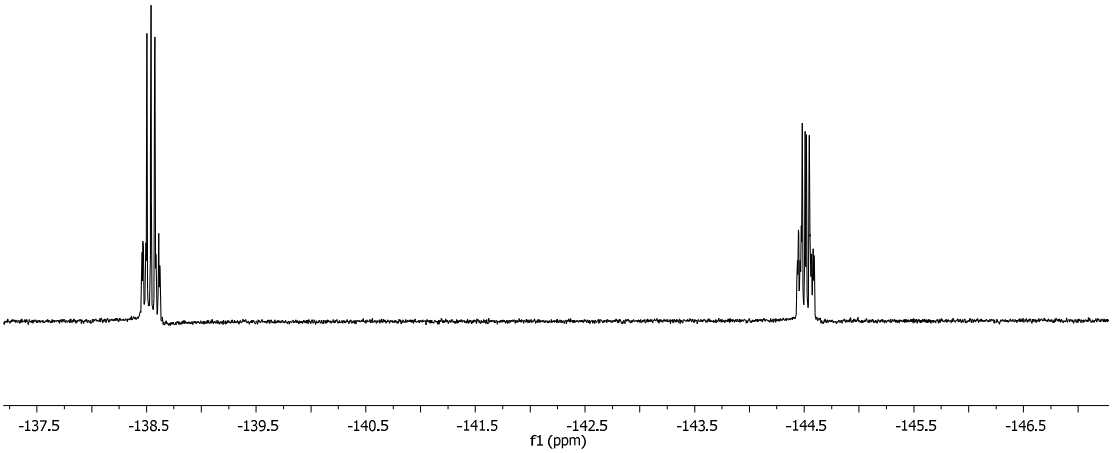


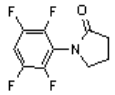
14a


0.96
2.00
2.00
2.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

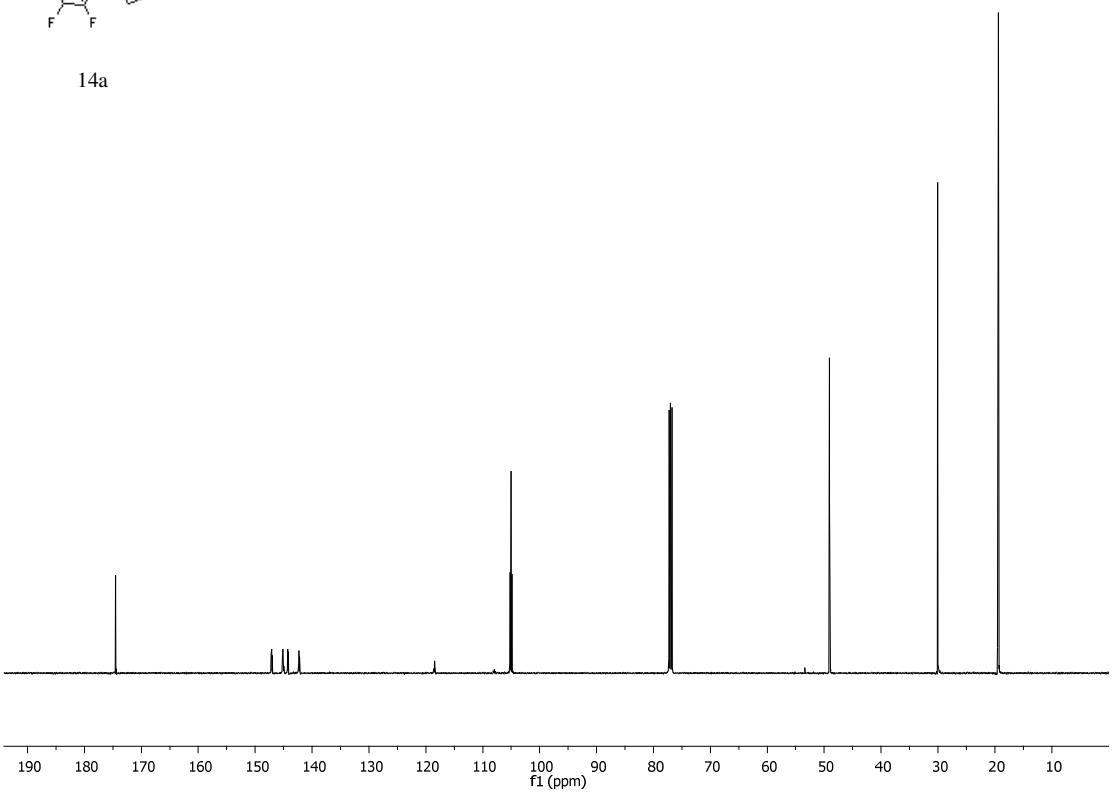


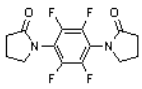
14a


-137.5
-138.5
-139.5
-140.5
-141.5
-142.5
-143.5
-144.5
-145.5
-146.5
f1 (ppm)

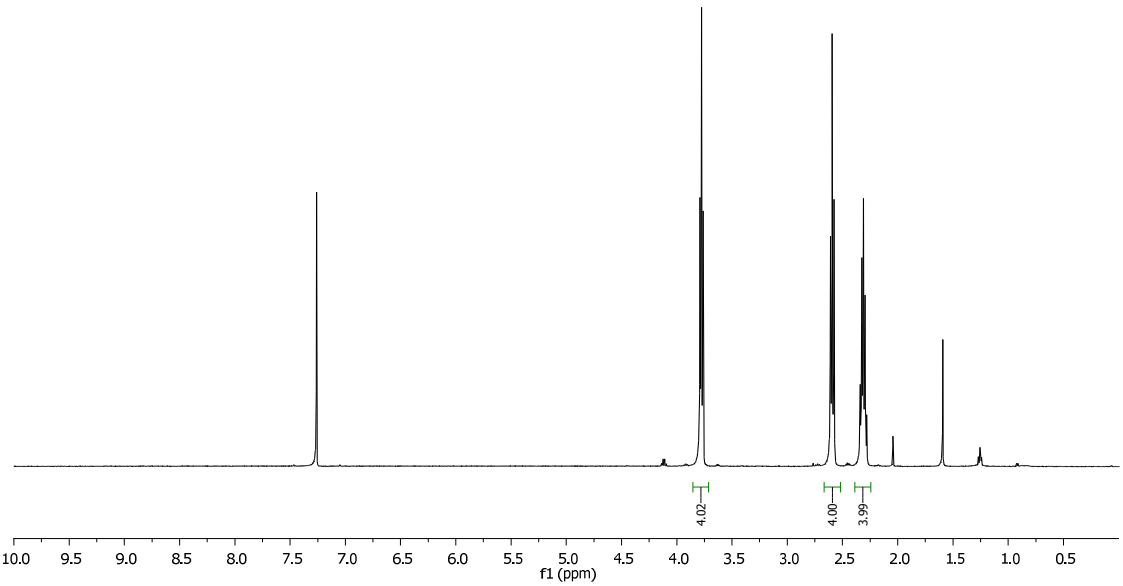


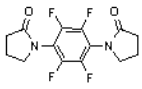
14a


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

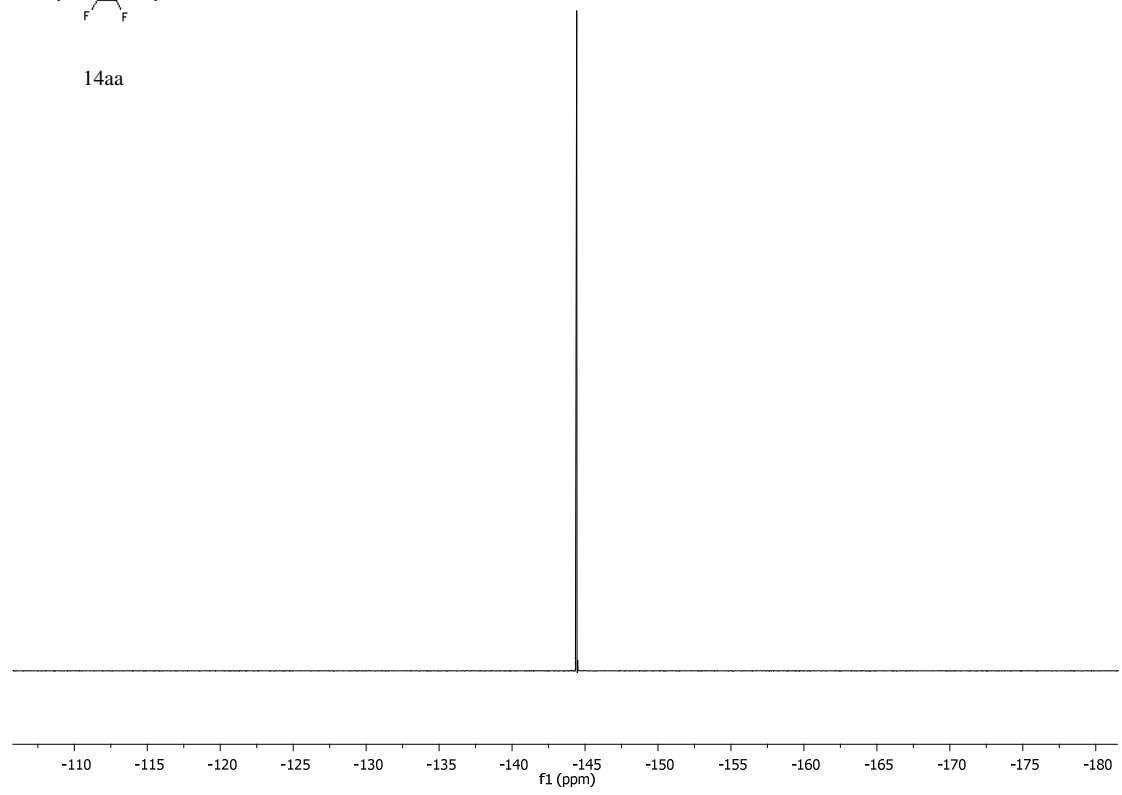


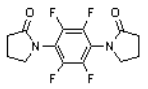
14aa


4.02
4.00
3.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)



14aa


-110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180
f1 (ppm)



14aa

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)