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Supporting Information

Efficient Base Catalyzed Alkylation Reactions with Aziridine Electrophiles

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Contents

Experimental

1) *Solvents and Reagents*

All reagents bought from commercial sources were used as sold. Organic solvents were concentrated under reduced pressure using a Büchi rotary evaporator. Syringes, needles and cannulae were oven dried at 140 ^{o}C. Anhydrous tetrahydrofuran was freshly distilled from sodium-benzophenone under an atmosphere of nitrogen. Anhydrous dichloromethane, toluene and $HN^{i}Pr_2$ were purified by distillation over calcium hydride.

2) *Chromotography*

TLC analyses were performed using Merck aluminium-backed or glass-backed plates pre-coated with silica (0.25 mm, 60 F_{254}) and visualized under UV light (254 nm) and/or by the use of potassium permanganate using the solvent system indicated. Systems using 'petroleum ether' refer to light petroleum 40-60 ^{o}C. Column chromatography was performed on silica (Kieselgel 60 (40-60 µm).

3) *Spectra*

Infrared spectra were recorded on an ATI Matison: Genesis Series FTIR spectrometer from a thin film or with Nujol deposited on a sodium chloride plate, with absorption maxima (v_{max}) recorded in wavenumbers (cm^{-1}), and labelled as broad (br), strong (s), medium (m), or weak (w). Only selected absorptions are recorded. NMR spectra were recorded using a Bruker Avance 500 MHz spectrometer, chemical shifts (δ) are quoted in parts per million referenced to the residual solvent peak (7.26

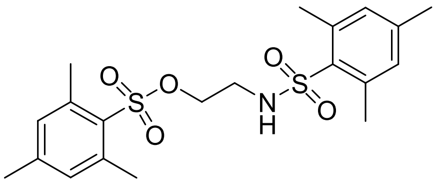
$CDCl_3$ ^1H, 77.1 $CDCl_3$ ^{13}C). The multiplicity of each signal is designated using the following abbreviations; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (*J*) are reported in Hertz (Hz). Low resolution mass spectra were recorded on a Fissions VG Trio 2000 quadrupole mass spectrometer. High resolution mass spectra were recorded on a Thermo Finnigan Mat 95XP mass spectrometer. Melting points were obtained using a Griffin melting point apparatus and remain uncorrected.

4) Starting Materials

N-tosyl (**2a**), N-Nosyl (**2d**), N-Phosphoryl (**2e**) and N-CbZ (**2c)** aziridines were synthesised according to known procedures.[S1-S4] The starting material for **3f** was synthesised by esterification of adipoyl dichloride followed by Dieckmann condensation.[S5] The starting material for **3g** and **3o** was synthesised by treatment of 1-indanone with NaH and dimethylcarbonate.[S6] Starting materials for **3h** was synthesised by a transesterification reaction from the methyl ester.[S7] Starting material for **3k** was obtained from a Thorpe-Ziegler condensation.[S8] Starting material for **3i** was synthesised by treatment of pyrrolidin-2-one with Boc_2O and 10 mol% DMAP at room temperature in CH_2Cl_2 followed by esterification with LiHMDS and dimethylcarbonate at -78 °C. The starting material for **3p** was synthesised *via* an SN_{Ar} reaction of 2-fluoronitrobenzene and dimethyl malonate with NaH, followed by reduction of the aromatic nitro group with H_2 / Pd according to a known procedure.[S9]

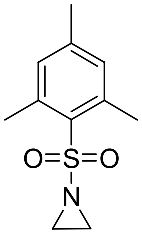
2.2 Reactions and Preparations

2,4-(Dimesitylsulfonyl)ethanolamine



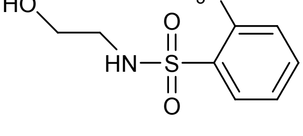
Ethanolamine (1.0 g, 16.4 mmol) in 1.0 mL dry pyridine was added to a stirred solution of 2,4,6-trimethylbenzene sulfonyl chloride (7.52 g, 34.4 mmol) in 5 mL dry pyridine at -10 ^{o}C. Following warming to room temperature, the solution was stirred overnight. Water (5 mL) and CH_2Cl_2 (10 mL) were added, and the two layers were separated. The organic layer was washed with 1 N HCl (2 x 10 mL), and the combined aqueous layers were extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were washed with a saturated copper sulfate solution (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the titled product as a white solid (5.66 g, 81 %); m.p. 82-84 ^{o}C; ν_{max} (nujol)/cm^{-1} 3328 (br, NH), 2852 (s), 1601 (w), 1464 (s), 1455 (s), 1377 (m), 1316 (w, SO_2), 1303 (w, SO_2), (s), 1170 (w, SO_2), 1147 (w, SO_2); δ_H (500MHz, $CDCl_3$) 6.97 (s, 2 H, O-Mes aromatic), 6.94 (s, 2 H, NH-Mes aromatic), 4.95 (t, 1 H, *J* = 6, NH), 3.97 (t, 2 H, *J* = 6, CH_2O), 3.20 (q, 2 H, *J* = 6, $C\mathit{H_2}NH$), 2.59 (s, 6 H, 2 x CH_3, O-Mes), 2.57 (s, 6 H, 2 x CH_3, N-Mes), 2.32 (s, 3 H, CH_3, O-Mes), 2.30 (s, 3 H,-CH_3, N-Mes); δ_C (125MHz, $CDCl_3$) 143.8 (C), 142.5 (C), 139.9 (C), 139.0 (C), 133.3 (C), 132.1 (CH), 131.9 (CH), 130.0 (C), 67.7 (CH_2O), 41.8 (CH_2N), 22.9 (2 x CH_3), 22.6 (2 x CH_3), 21.1 (CH_3), 21.0 (CH_3); *m/z* (CI^+, NH_3) 443 ($[M+NH_4]^+$, 100), 261 (21), 243 (37), 226 (72), 167 (22), 136 (25), 119 (23); HRMS 443.1663 $[M+NH_4]^+$, $C_{20}H_{31}O_5N_2S_2$ requires 443.1669.

N-mesityl sulfonyl aziridine 2b



Potassium hydroxide (3.70 g, 65.9 mmol) in 18 mL water was added in one portion to 2,4-(dimesitylsulfonyl)ethanolamine (5.60 g, 13.2 mmol) in 100 mL benzene, and the biphasic mixture was stirred rapidly at room temperature overnight. The two layers were separated and the benzene layer was washed with water (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure to give an off-white solid. The residue was purified by column chromatography [diethyl ether / petroleum ether] (1:2) to give the titled product as a crystalline white solid (2.81 g, 95 %); m.p 59-62 ^oC; v_{max} (neat)/cm^{-1} 3056 (m), 2986 (m), 2942 (m), 2306 (m), 1751 (m), 1605 (m), 1456 (m), 1442 (m), 1320 (s, SO_2), 1266 (s), 1157 (s, SO_2); δ_H (500MHz, $CDCl_3$) 6.96 (s, 2 H, CH aromatic), 2.68 (s, 6 H, 2 x CH_3), 2.40-2.25 (s, 4 H, 2 x CH_2), 2.29 (s, 3 H, CH_3); δ_C (125MHz, $CDCl_3$) 143.1 (C), 140.2 (2 x C), 132.5 (C), 131.8 (2 x CH), 26.6 (2 x CH_2), 23.0 (2 x CH_3), 21.0 (CH_3); *m/z* (CI^+, NH_3) 226 ($[M+H]^+$, 100%); HRMS ($[M+NH_4]^+$) 243.1168, $C_{11}H_{19}O_2N_2S$ requires 243.1162.

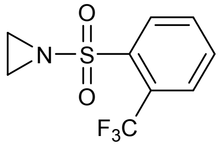
N-(2-(Trifluoromethane)benzenesulfonyl)ethanolamine



Ethanolamine (1.25 g, 20.44 mmol) and triethylamine (2.86 mL, 20.44 mmol) in 10 mL CH_2Cl_2 were added dropwise to a solution of 2-(Trifluoromethyl)benzenesulfonyl chloride (5.0 g, 20.44 mmol) in 15 mL CH_2Cl_2 at 0

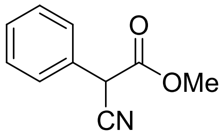
^{o}C. Following warming to room temperature, the solution was stirred overnight. 1 N HCl was added (10 mL), and the two layers were separated. The organic layer was washed with 1 N HCl (2 x 20 mL). The combined aqueous fractions were extracted with CH_2Cl_2 (20 mL). The combined organic fractions were then dried (Na_2SO_4) and concentrated. The residue was filtered through a silica plug (Et_2O) to give the titled product as a white solid (4.90 g, 79 %). ν_{max} (neat)/cm^{-1} 3367 (br, OH, NH), 1310 (s, SO_2), 1166 (s, SO_2); δ_H (500MHz, $CDCl_3$) 8.21 (dd, 1 H, *J* = 6, 8, CH), 7.87 (dd, 1 H, *J* = 6, 8.0, CH), 7.74-7.69 (m, 2 H, 2 x CH), 5.48 (t, 1 H, *J* = 6, NH), 3.70 (t, 2 H, *J* = 6, CH_2), 3.12 (q, 2 H, *J* = 6, 11, CH_2N); δ_C (125MHz, $CDCl_3$) 138.3 (*i*-C), 132.8 (CH), 132.5 (CH), 131.5 (CH), 128.6 (q, *J* = 4, CH), 127.5 (q, *J* = 33, *C*(CF_3)), 122.9 (q, *J* = 274, CF_3), 61.2 (CH_2O), 45.3 (CH_2N); *m/z* (CI^+, NH_3) 287 ($[M+NH_4]^+$, 100%), 270 (12), 62 (10); HRMS (ES, $[M+NH_4]^+$ 287.0669, $C_9H_{14}O_3N_2F_3S$ requires 287.0672.

N-2-(Trifluoromethane)benzenesulfonyl aziridine 2f



Triethylamine (3.81 mL, 27.24 mmol) and mesitylsulfonyl chloride (2.84 g, 12.97 mmol) in 5 mL CH_2Cl_2 were added to a solution of *N*-(2-(Trifluoromethane)benzenesulfonyl)ethanolamine (3.49g, 12.97 mmol) in 10 mL CH_2Cl_2 at -20 ^{o}C over 30 minutes. Following warming to 0 ^{o}C, the solution was stirred for 16 h. 1 N HCl was added (10 mL), and the two layers were separated. The organic layer was washed with 1 N HCl (2 x 15 mL). The combined aqueous fractions were extracted with CH_2Cl_2 (15 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated. The residue was dissolved in benzene (100 mL) and potassium hydroxide (2.83 g, 50.47 mmol) in 14 mL H_2O was added. The biphasic mixture was stirred vigorously for 16 h. Water (25 mL) was added and the two layers were separated. The organic layer was dried (Na_2SO_4) and concentrated to give the titled compound as a white solid (2.44 g, 75 %). m.p. 54-56 ^{o}C; ν_{max} (neat)/cm^{-1} 3020 (m), 1361 (m), 1314 (s, SO_2), 1216 (s), 1162 (s, SO_2);); δ_H (500MHz, $CDCl_3$) 8.80 (dd, 1 H, *J* = 6, 8, CH), 7.85 (dd, 1 H, *J* = 6, 8, CH), 7.75-7.68 (m, 2 H, 2 x CH), 2.40 (s, 4 H, 2 x CH_2); δ_C (125MHz, $CDCl_3$) 137.2 (*i*-C), 133.6 (CH), 132.4 (CH), 131.9 (CH), 128.7 (q, *J* = 34, *C*(CF_3)), 128.4 (q, *J* = 6, CH), 122.4 (q, *J* = 274, CF_3), 28.8 (2 x CH_2); *m/z* (ES) 268 ($[M+NH_4]^+$ 36), 252 (25), 199 (100); HRMS 252.0295 $[M+H]^+$, $C_9H_9O_2N_1F_3S$ requires 252.0301.

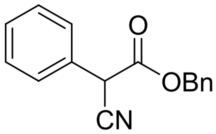
Methyl 2-cyano-2-phenylacetate



Phenylacetonitrile (3.80 mL, 33.0 mmol) followed by dimethyl carbonate (13.9 mL, 264.0 mmol) were added to a suspension of sodium hydride (2.64 g, 66.0 mmol, 60% dispersion in mineral oil) in 80 mL of toluene at room temperature. Following warming to 80 ^{o}C for 30 min, a white and pale yellow cake formed, which was heated at 80 ^{o}C for a further 1 h. 1 N HCl was added until the solid dissolved (~ 60 mL), and the solution was extracted with EtOAc (2 x 40 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated, and the resulting yellow oil was purified by column chromatography [diethyl ether / petroleum ether] (1:3) to give the titled product as a clear oil (5.51 g, 95%); ν_{max} (neat)/cm^{-1} 2957 (m), 2252 (w, CN), 1750 (s, C=O), 1497 (m), 1456 (s), 1436 (s), 1313 (s), 1257 (s), 1236 (s); δ_H (500MHz,

$CDCl_3$) 7.22-7.13 (m, 5 H, 5 x CH), 4.54 (s, 1 H), 3.52 (s, 3 H, OCH_3); δ_C (125MHz, $CDCl_3$) 165.6 (C=O), 130.0 (C), 129.4 (2 x CH), 129.1 (CH), 128.0 (2 x CH), 115.8 (CN), 53.9 (OCH_3), 43.5 (CH); *m/z* (CI^+, NH_3) 193 ($[M+NH_4]^+$, 100%); HRMS 193.0965 $[M+NH_4]^+$, $C_{10}H_{13}O_2N_2$ requires 193.0977.

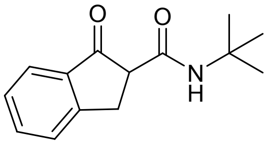
Benzyl 2-cyano-2-phenylacetate



BuLi (1.6M solution in hexanes, 8.1 mL, 13.0 mmol) was added dropwise to a solution of diisopropylamine (1.82 mL, 13.0 mmol) in 40 mL dry THF at -78 °C. Following warming to 0 °C for 20 min, phenylacetonitrile (1.0 mL, 8.7 mmol) was added in 5 mL dry THF dropwise and the solution was stirred for 20 min. Benzyl chloroformate (1.83 mL, 13.0 mmol) was then added in 10 mL dry THF and the solution was stirred at 0 °C for 48 h and then at RT for 16 h. 1 N HCll was added (50 mL), and the solution was extracted with CH_2Cl_2 (2 x 30 mL). The combined organic portions were washed with 1 N HCl (2 x 30 mL), brine (30 mL), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography [diethyl ether / petroleum ether] (1:2) to give the titled product as a white solid (1.72 g, 80 %); m.p. 32-35 °C; v_{max} (neat)/cm^{-1} 2975 (m), 2254 (w, CN), 1748 (s, C=O), 1497 (s), 1456 (s), 1378 (m), 1194 (s); δ_H (500MHz, $CDCl_3$) 7.38-7.17 (m, 10 H, 2 x Phenyl), 5.02 *and* 5.01 (d *and* d, *J* = 12 *and* 12, CH_2OCO), 4.68 (s, 1 H, CHCN); δ_C (125MHz, $CDCl_3$) 164.9 (C=O), 134.4 (C), 129.8 (C, Bn), 129.4 (CH), 129.3 (CH) , 128.8 (CH), 128.7 (CH), 128.2 (CH), 128.0 (CH), 115.5 (CN), 68.7 (CH_2O), 43.8 (*C*HCN); *m/z* (CI^+,

NH_3) 269 ($[M+NH_4]^+$, 100%), 108 (32), 91 (47) HRMS 269.1277 $[M+NH_4]^+$, $C_{16}H_{17}O_2N_2$ requires 269.1280.

1-Oxo-indan-2-carboxylic acid *tert*-butylamide



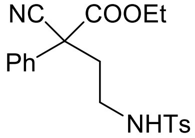
NaH (60% dispersion, 636 mg, 15.9 mmol) was suspended in 10 mL dry THF under nitrogen in an oven dried flask. Following stirring for 10 minutes, the suspension was allowed to settle and the THF was syringed off. The residue was suspended in dry THF (15 mL). Following warming to reflux, *tert*-butyl isocyanate (726 μL, 6.4 mmol) and 1-indanone (750 mg, 6.4 mmol) was added in 2 mL THF over 10 minutes. Following stirring at reflux for 1 h, a white/yellow cake formed which was heated for a further 3 h. After cooling to 0 ^oC, 1 N HCl was added cautiously until the solid had completely dissolved (c.a 20 mL). The solution was extracted with Et_2O (2 x 20 mL) and the organic phase was washed with sat $NaHCO_3$ (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated. The residue was triturated with Et_2O to give the titled compound as a white solid (760 mg, 58 %); m.p. 134-136 ^oC; v_{max} (neat)/cm^{-1} 3561 (br, NH), 3054 (m), 1698 (m, C=O ketone), 1665 (m, C=O amide), 1233 (s); δ_H (500MHz, $CDCl_3$) 7.72 (d, 1 H, *J* = 8, CH), 7.60 (t, 1 H, *J* = 7, CH), 7.49 (d, 1 H, *J* = 8, CH), 7.36 (t, 1 H, *J* = 7, CH), 7.00 (br, NH), 3.75 (dd, 1 H, *J* = 4, 18, C*H*H’), 3.48 (dd, *J* = 4, 8, CH), 3.28 (dd, *J* = 8, 18, CH*H’*), 1.37 (s, 9 H, 3 x CH_3); δ_C (125MHz, $CDCl_3$) 203.8 (C=O ketone), 165.2 (C=O amide), 154.4 (C), 135.7 (CH), 135.4 (C), 127.5 (CH), 126.7 (CH), 124.3 (CH), 53.5 (CH), 51.4 (*C*(CH_3)$_3$), 29.2 (3 x CH_3), 28.5 (CH_2);

m/z (ES) 254 ([M+Na]$^+$ 100%); HRMS 254.1159 [M+Na]$^+$, $C_{14}H_{17}O_2N_1Na$ requires 254.1157.

General procedure for the base catalyzed ring opening of *N*-protected aziridines

BEMP (10.4 µL, 0.036 mmol) was added to a stirred solution of pro-nucleophile (0.72 mmol) in 700 µL THF and the solution was stirred at room temperature for 10 minutes. Aziridine (0.36 mmol) was added and the solution was stirred at room temperature. After completion of the reaction, the solution was concentrated under reduced pressure and the residue was purified by flash column chromatography [diethyl ether / petroleum ether].

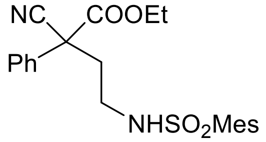
Compound 3a



Following general procedure, the titled product was obtained as a colourless oil (129 mg, 93%) after flash column chromatography [diethyl ether / petroleum ether] (1:1)]; ν_{max} (neat)/cm^{-1} 3283 (br, NH), 2980 (m), 2240 (m, CN), 1743 (s, C=O), 1332 (s, SO_2), 1158 (s, SO_2); δ_H (500MHz, $CDCl_3$) 7.74 (d, 2 H, *J* = 8, 2 x CH), 7.53-7.40 (m, 5 H, Ph), 7.34 (d, 2 H, *J* = 8, 2 x CH), 4.75 (br, 1 H, NH), 4.34-4.18 (m, 2 H, OCH_2), 3.26-3.00 (m, 2 H, CH_2N), 2.68 (ddd, 1 H, *J* = 7, 9, 14, C*H*CH_2N), 2.47 (s, 3 H, CH_3), 2.47-2.37 (m, 1 H, C*H’*CH_2N), 1.27 (t, 3 H, *J* = 7, CH_3); δ_C (125MHz, $CDCl_3$) 167.3 (C=O), 144.0 (C), 136.7, 133.8, 130.1, 129.6, 129.5, 127.4, 126.1, 117.9 (CN), 63.9 (OCH_2), 52.3 (quaternary C), 40.0 (CH_2), 37.9 (CH_2), 21.8 (CH_3), 14.0 (CH_3); *m/z*

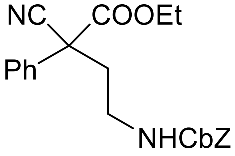
(CI^+, NH_3) 501 ($[M+NH_4]^+$ 40%), 387 (28), 279 (65), 110 (100), 102 (43), 91 (22); HRMS (ES) $[M+H]^+$ 387.1370, $C_{20}H_{23}O_4N_2S$ requires 387.1373.

Compound 3b



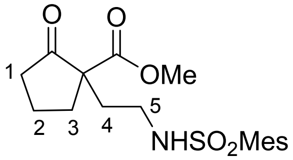
Following general procedure, the titled product was obtained as a colourless oil (150 mg, 99 %) after flash column chromatography [diethyl ether / petroleum ether] (1:1)]; v_{max} (neat)/cm^{-1} 3322 (br, NH), 3059m(w), 2983 (m), 2934 (m), 2245 (w, CN), 1744 (s, C=O), 1604 (m), 1450 (s), 1330 (s, SO_2), 1265 (s), 1229 (s), 1155 (s, SO_2); δ_H (500MHz, $CDCl_3$) 7.45-7.36 (m, 5 H, 5 x CH phenyl), 6.93 (s, 2 H, 2 x CH), 5.03 (t, 1 H, *J* = 6, NH), 4.25-4.14 (m, 2 H, *J* = 7, 11, OCH_2), 3.00 (tdd, 1 H, *J* = 6, 10, 13, CHN), 2.88 (dddd, *J* = 5, 6, 10, 12, 1 H CH'N), 2.61-2.58 (m, 1 H, C*H*CH_2N), 2.57 (s, 6 H, 2 x CH_3), 2.38-2.33 (m, 1 H, C*H'*CH_2N), 2.28 (s, 3 H, CH_3), 1.20 (t, 3 H, *J* = 7, CH_3); δ_C (125MHz, $CDCl_3$) 167.0 (C=O), 142.4 (C), 139.2 (2 x C Mes), 133.5 (C), 133.3 (C phenyl), 132.1 (2 x CH Mes), 129.4 (2 x CH phenyl), 129.2 (2 x CH phenyl), 125.9 (CH phenyl), 117.7 (CN), 63.6 (OCH_2), 52.0 (quaternary C), 39.1 (CH_2N), 37.6 (CH_2), 22.9 (2 x CH_3), 20.9 (CH_3), 13.7 (CH_3 ester); *m/z* (CI^+, NH_3) 432 ($[M+NH_4]^+$ 34), 415 ($[M+H]^+$ 100), 386 (15), 369 (20), 231 (27), 183 (12), 136 (25), 119 (22); HRMS 415.1696 $[M+H]^+$, $C_{22}H_{27}O_4N_2S_1$ requires 415.1686.

Compound 3c



Following general procedure (50mg, 0.28mmol of aziridine was used), the titled product was obtained as a colourless oil (86 mg, 83%), after flash column chromatography [dichloromethane / methanol] (99:1)]; ν_{max} (neat)/cm^{-1} 3350 (br, NH), 2990 (m), 2245 (m, CN), 1740 (s, C=O), 1710 (s, C=O); δ_H (500MHz, $CDCl_3$) 7.55 (d, 2 H, *J* = 7, CH), 7.42-7.31 (m, 8 H, 8 x CH), 5.07 (s, 2 H, CH_2 benzyl), 4.92 (t, 1 H, *J* = 7, NH), 4.25-4.14 (m, 2 H, CH_2O), 3.36 (q, 2 H, *J* = 7, CH_2N), 2.69-2.63 (m, 1 H, C*H*CH_2N), 2.44-2.39 (m, 1 H, C*H'*CH_2N), 1.22 (t, 3 H, *J* = 7, CH_3); δ_C (125MHz, $CDCl_3$) 167.7 (C=O ester), 156.5 (C=O carbamate), 136.8 (C), 134.3 (C), 129.7 (CH), 129.5 (CH), 128.9 (CH), 128.6 (CH), 128.6 (CH), 126.4 (CH), 118.4 (CN), 67.2 (CH_2 benzyl), 63.9 (OCH_2), 53.9 (quaternary C), 38.1 (CH_2N), 37.8 (CH_2), 14.2 (CH_3); *m/z* (CI^+, NH_3) 384 ($[M+NH_4]^+$ 50), 367 (45), 323 (47), 276 (41), 233 (22), 204 (37), 108 (100), 91 (75); HRMS $[M+H]^+$, 367.1657 $C_{20}H_{22}O_4N_2$ requires 367.1658.

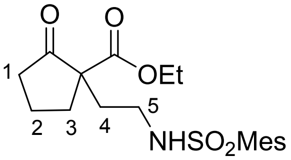
Compound 3d



Following general procedure, the titled product was obtained as a colourless oil (129 mg, 98 %) after flash column chromatography [diethyl ether / petroleum ether] (3:2); ν_{max} (neat)/cm^{-1} 3393(NH), 2979 (w), 2956 (w), 2254 (m), 1748 (m, C=O), 1726 (m, C=O ester), 1329 (m, SO_2), 1157 (s, SO_2); δ_H (500MHz, $CDCl_3$) 6.93

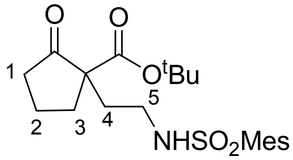
(s, 2 H, CH aromatic), 5.02 (t, 1 H, *J* = 6, NH), 3.64 (s, 3 H, OCH_3), 2.95 (q, 2 H, *J* = 6, CH_2N), 2.60 (s, 6 H, 2 x CH_3), 2.47-2.37 (m, 2 H, $C(1)H_2$), 2.28 (s, 3 H, CH_3), 2.31-2.23 (m, 1 H, C(4)H) 2.06-1.80 (m, 5 H, C(4)H’, $C(2)H_2$, $C(3)H_2$) ; δ_C (125MHz, $CDCl_3$) 215.1 (C=O ester), 171.7 (C=O ketone), 142.1 (C), 139.0 (2 x C), 133.5 (C), 132.0 (2 x CH), 58.9 (quaternary C), 52.8 (OCH_3), 39.9 (CH_2N), 37.7 (CH_2CH_2N), 33.5 ($C(1)H_2$), 33.1 ($C(3)H_2$), 22.9 (2 x CH_3), 20.9 (CH_3), 19.6 ($C(2)H_2$); *m/z* (CI^+, NH_3) 385 ($[M+NH_4]^+$, 70), 368 ($[M+H]^+$, 25), 350 (70), 336 (15), 243 (18), 203 (23), 168 (100), 160 (12); HRMS ($[M+H]^+$) 368.1528 $[M+H]^+$, $C_{18}H_{26}O_5N_1S_1$ requires 368.1526.

Compound 3e



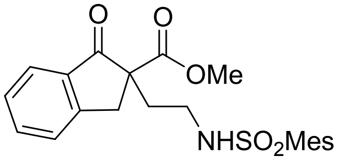
Following general procedure, the titled product was obtained as a colourless oil (134 mg, 99 %) after flash column chromatography [diethyl ether / petroleum ether] (3:2); ν_{max} (neat)/cm^{-1} 3307 (br, NH), 2979 (w), 2256 (w), 1748 (s, C=O), 1722 (s, C=O ester), 1327 (s, SO_2), 1155 (s, SO_2); δ_H (500MHz, $CDCl_3$) 6.93 (s, 2 H, CH aromatic), 5.06 (t, 1 H, *J* = 6, NH), 4.13-4.06 (q, 2 H, *J* = 7, OCH_2), 2.95 (q, 2 H, *J* = 6, CH_2N), 2.60 (s, 6 H, 2 x CH_3), 2.43-2.37 (m, 2 H, $C(1)H_2$), 2.97-2.22 (m, 1 H, C(4)H), 2.27 (s, 3 H, CH_3), 2.05-1.79 (m, 5 H, $C(2)H_2$, C(4)H’, $C(3)H_2$), 1.10 (t, 3 H, *J* = 7, CH_3 ester); δ_C (125MHz, $CDCl_3$) 215.2 (C=O), 171.2 (C=O ester), 142.1 (C), 139.0 (2 x C), 133.5 (C), 131.9 (2 x CH), 61.7 (OCH_2), 58.9 (quaternary C), 38.9 (CH_2N), 37.7 (CH_2CH_2N), 33.6 ($C(1)H_2$), 33.0 ($C(3)H_2$), 22.9 (2 x CH_3), 20.9 (CH_3), 19.6 ($C(2)H_2$), 14.0 (CH_3 ester); *m/z* (CI^+, NH_3) 399 ($[M+NH_4]^+$, 15), 364 (23), 182 (100), 174 (16); HRMS ($[M+NH_4]^+$) 399.1949 $[M+NH_4]^+$, $C_{19}H_{31}O_5N_2S_1$ requires 399.1948.

Compound 3f



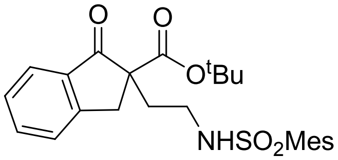
Following general procedure, the titled product was obtained as a colourless oil (116 mg, 78 %) after flash column chromatography [diethyl ether / petroleum ether] (3:2); ν_{max} (neat)/cm^{-1} 3325 (br, NH), 3054 (m), 2983 (m), 2925 (m), 2305 (w), 1745 (s, C=O), 1720 (s, C=O ester), 1604 (w), 1456 (w), 1422 (w), 1369 (w), 1328 (s, SO_2), 1265 (s), 1155 (s, SO_2); δ_H (500MHz, $CDCl_3$) 6.93 (s, 2 H, 2 x CH), 5.17 (t, 1 H, *J* = 6, NH), 2.95 (q, 2 H, *J* = 6, CH_2N), 2.61 (s, 6 H, 2 x CH_3), 2.42-2.33 (m, 2 H, $C(1)H_2$), 2.27 (s, 3 H, CH_3), 2.26-2.18 (m, 1 H, C(4)H), 1.97-1.76 (m, 5 H, C(4)H', $C(2)H_2$, $C(3)H_2$), 1.36 (s, 9 H, 3 x CH_3); δ_C (125MHz, $CDCl_3$) 215.6 (C=O ketone), 170.5 (C=O ester), 142.0 (C), 139.0 (2 x C), 133.5 (C), 131.9 (2 x CH), 82.6 ($OC(CH_3)_3$), 59.8 (quaternary C), 38.9 (CH_2N), 37.6 (CH_2CH_2N) 34.0 ($C(1)H_2$), 32.8 ($C(3)H_2$), 27.7 (3 x CH_3), 22.9 (2 x CH_3), 20.9 (CH_3), 19.6 ($C(2)H_2$); *m/z* (CI^+, NH_3) 427 ($[M+NH_4]^+$ 10), 392 (100), 354 (15), 310 (10), 170 (11), 136 (14), 110 (13); HRMS 427.2255 $[M+NH_4]^+$, $C_{21}H_{35}O_5N_2S_1$ requires 427.2261.

Compound 3g



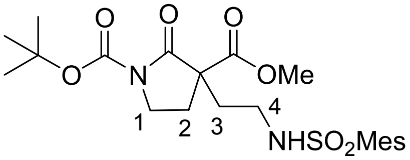
Following general procedure, the titled product was obtained as a colourless oil, which crystallized upon storage (130 mg, 88 %) after flash column chromatography [diethyl ether / petroleum ether] (2:1); m.p. 82-85 °C; ν_{max} (neat)/cm^{-1} 3315 (br, NH), 2979 (m), 2930 (m), 1741 (s, C=O), 1715 (C=O ester), 1601 (s), 1456 (m), 1329 (s, SO_2), 1154 (s, SO_2); δ_H (500MHz, $CDCl_3$) 7.72 (d, 1 H, *J* = 8, CH), 7.62 (t, 1 H, *J* = 8, CH), 7.40 (d, 1 H, *J* = 8, CH), 7.38 (t, 1 H, *J* = 8, CH), 6.91 (s, 2 H, CH aromatic), 5.09 (t, 1 H, *J* = 6, NH), 3.64 (d, 1 H, J = *17*, C*H*H' indanone), 3.62 (s, 3 H, OCH_3), 3.07 (d, 1 H, *J* = 17, CH*H'* indanone), 3.05-3.00 (m, 2 H, CH_2N), 2.58 (s, 6 H, 2 x CH_3), 2.26 (s, 3 H, CH_3), 2.26-2.24 (m 1 H, C*H*CH_2N), 2.04-1.99 (m, 1 H, C*H'*CH_2N); δ_C (125MHz, $CDCl_3$) 201.0 (C=O), 170.3 (C=O ester), 151.7 (C), 141.1 (C), 137.9 (2 x C), 134.7 (C), 133.5 (C), 132.6 (CH), 130.9 (2 x CH), 127.0 (CH), 125.4 (CH), 123.9 (CH), 57.9 (quaternary C), 51.9 (O-CH_3), 38.0 (CH_2N), 36.2 (CH_2CH_2N), 33.4 (C(7)H_2), 21.9 (2 x CH_3), 19.9 (CH_3); *m/z* (CI^+, NH_3) 433 ($[M+NH_4]^+$ 53%), 416 ($[M+H]^+$ 63), 401 (38), 384 (15), 234 (32), 216 (100), 208 (33), 202 (18), 159 (31), 151 (21), 137 (54), 123 (33), 112 (25), 97 (21), 84 (23), 69 (19), 59 (34); HRMS 416.1526 $[M+H]^+$, $C_{22}H_{26}O_5N_1S_1$ requires 416.1526.

Compound 3h



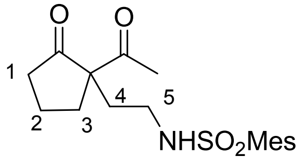
Following general procedure, the titled product was obtained as a white solid (148 mg, 91 %) after flash column chromatography [diethyl ether / petroleum ether] (1:1); m.p 24-26 ^{o}C; v_{max} (neat)/cm^{-1} 3311 (br, NH), 2977 (m), 2932 (m), 1738 (s, C=O), 1716 (C=O ester), 1605 (s), 1455 (m), 1328 (s, SO_2), 1152 (s, SO_2); δ_H (500MHz, $CDCl_3$) 7.70 (d, 1 H, *J* = 8, C(1)H), 7.59 (t, 1 H, *J* = 8, C(3)H), 7.42 (d, 1 H, *J* = 8, C(4)H), 7.36 (t, 1 H, *J* = 8, C(2)H), 6.90 (s, 2 H, CH aromatic), 5.11 (t, 1 H, *J* = 6, NH), 3.56 (d, 1 H, *J* = 17, C(5)H), 3.05-2.97 (m, 3 H, C(5)H’, CH_2N), 2.59 (s, 6 H, 2 x CH_3), 2.25 (s, 3 H, CH_3), 2.22-2.15 (m, 1 H, C*H*CH_2N), 1.97-1.93 (m, 1 H, C*H’*CH_2N), 1.30 (s, 9 H, 3 x CH_3 *tert* butyl); δ_C (125MHz, $CDCl_3$) 202.5 (C=O ketone), 169.9 (C=O ester), 152.7 (C), 142.1 (C), 139.0 (2 x C), 135.5 (C), 134.8 (C), 133.6 (CH), 131.9 (2 x CH), 127.8 (CH), 126.3 (CH), 124.8 (CH), 82.4 (quaternary C ester), 59.9 (quaternary C), 39.1 (CH_2N), 37.4 (CH_2CH_2N), 34.1 (CH_2), 27.7 (3 x CH_3), 22.9 (2 x CH_3), 20.9 (CH_3); *m/z* (CI^+, NH_3) 475 ($[M+NH_4]^+$ 10), 458 (21), 419 (60), 402 (100), 358 (62), 276 (29), 258 (40), 218 (30), 193 (39), 174 (25), 168 (17), 158 (58), 136 (24), 120 (21), 91 (13), 59 (16); HRMS 475.2261 $[M+NH_4]^+$, $C_{25}H_{35}O_5N_2S_1$ requires 475.2261.

Compound 3i



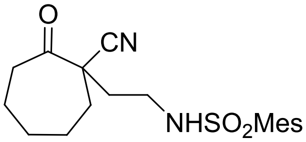
Following general procedure, the titled product was obtained as a colourless oil (121 mg, 73 %) after flash column chromatography [diethyl ether / petroleum ether (1:1) then chloroform / diethyl ether (4:1)]; ν_{max} (neat)/cm^{-1} 3309 (br, NH), 3021 (m), 2980 (m), 2954 (m), 2938 (m), 1782 (s, C=O), 1728 (br, C=O carbamate and C=O amide), 1605 (m), 1456 (m), 1369 (s, SO_2), 1305 (s), 1215 (s), 1154 (s, SO_2); δ_H (500MHz, $CDCl_3$) 6.94 (s, 2 H, 2 x CH), 4.99 (t, 1 H, *J* = 6, NH), 3.73-3.69 (m, 2 H, C(1)H_2), 3.71 (s, 3 H, OCH_3), 3.01 (q, 2H, *J* = 7, C(4)H_2N), 2.60 (s, 6 H, 2 x CH_3), 2.44 (ddd, 1 H, *J* = 4, 7, 13, C(2)H), 2.28 (s, 3 H, CH_3), 2.21 (td, 1 H, *J* = 7, 14, C(3)H), 2.02-1.97 (m, 1H), 1.92 (td, 1 H, *J* = 9, 13), 1.52 (s, 9 H, 3 x CH_3); δ_C (125MHz, $CDCl_3$) 171.2 (C=O), 170.7 (C=O), 149.8 (C=O carbamate), 142.2 (C), 139.0 (2 x C), 133.5 (C), 132.0 (2 x CH), 83.7 (*C*(CH_3)$_3$), 56.1 (OCH_3), 53.2 (quaternary C), 43.9 (C(1)H_2), 38.7 (C(4)H_2), 33.8 (C(3)H_2), 28.0 (3 x CH_3), 27.8 (C(2)H_2), 22.9 (2 x CH_3), 20.9 (CH_3); *m/z* (CI$^+$, NH_3) 486 ([M+NH_4]$^+$ 10), 385 (30), 369 (100), 287 (15), 256 (12), 185 (11), 172 (11); HRMS 486.2274 [M+NH_4]$^+$, $C_{22}H_{36}O_7N_3S_1$ requires 486.2268.

Compound 3j



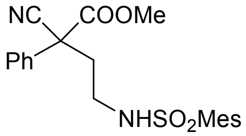
Following general procedure, the titled product was obtained as a colourless oil (91 mg, 73 %) after flash silica chromatography [diethyl ether / petroleum ether] (3:2); ν_{max} (neat)/cm^{-1} 3397 (br, NH), 1738 (m, C=O), 1703 (m, C=O), 1330 (m, SO_2), 1217 (s), 1156 (m, SO_2); δ_H (500MHz, $CDCl_3$) 6.94 (s, 2 H, 2 x CH), 4.78 (t, 1 H, *J* = 6, NH), 2.88-2.75 (m, 2 H, CH_2N), 2.60 (s, 6 H, 2 x CH_3) 2.56-2.49 (m, 1 H, C(1)H), 2.35-2.24 (m, 1 H, C(4)H), 2.29 (s, 3 H, CH_3), 2.16 (s, 3 H, CH_3 acetyl), 2.10-2.06 (m, 1 H, C(1)H'), 1.95-1.69 (m, 5 H, C(2)H_2, C(3)H_2, C(4)H'); δ_C (125MHz, $CDCl_3$) 216.05 (C=O ketone cyclic), 204.4 (C=O ketone), 142.3 (C), 138.9 (2 x C), 133.4 (C), 132.0 (2 x CH), 67.2 (quaternary C), 38.9 (CH_2N), 38.1 (C*H₂*CH₂N), 34.1 (C(1)H_2), 31.1 (C(3)H_2), 26.1 (CH_3 acetyl), 22.9 (2 x CH_3), 20.9 (CH_3), 19.5 (C(2)H_2) ; *m/z* (CI$^+$, NH_3) 369 ([M+NH$_4$]$^+$ 12), 352 (12), 334 (100), 152 (20), 127 (12); HRMS 352.1571 [M+H]$^+$, $C_{18}H_{26}O_4N_1S_1$ requires 352.1577.

Compound 3k



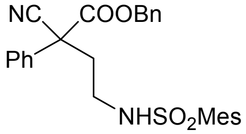
Following general procedure, the reaction was stirred at reflux (65 ^oC). The titled product was obtained as a white solid (55 mg, 43 %) after flash column chromatography [diethyl ether / petroleum ether] (3:1)]; m.p. 90-93 ^oC; ν_{max} (nujol)/cm^{-1} 3290 (br, NH), 2851 (s), 2324 (w, CN), 1457 (m), 1376 (m), 1330 (w, SO_2), 1164 (s, SO_2); δ_H (500MHz, $CDCl_3$) 6.95 (s, 2 H, 2 x CH), 4.88 (t, 1 H, *J* = 6, NH), 3.09-2.94 (m, 2 H, CH_2N), 2.71-2.62 (m, 2 H, CH_2), 2.60 (s, 6 H, 2 x CH_3), 2.29 (s, 3 H, CH_3), 2.26-2.13 (m, 2 H, CH_2), 1.97-1.89 (m, 4 H, 2 x CH_2), 1.71-1.54 (m, 3 H, CH_2, C*H*H'), 1.33-1.24 (m, 1 H, C*H'*H); δ_C (125MHz, $CDCl_3$) 205.8 (C=O), 142.5 (C), 139.0 (2 x C), 133.1 (C), 132.1 (2 x CH), 119.6 (CN), 53.6 (quaternary C), 40.5 (CH_2), 38.9 (CH_2), 37.0 (CH_2), 36.3 (CH_2), 28.7 (CH_2), 25.6 (CH_2), 24.6 (CH_2), 23.0 (2 x CH_3), 21.0 (CH_3); *m/z* (CI^+, NH_3) 380 ($[M+NH_4]^+$, 28), 363 (40), 179 (23), 163 (100), 136 (20); HRMS 363.1737 $[M+H]^+$, $C_{19}H_{27}O_3N_2S_1$ requires 363.1737.

Compound 3l



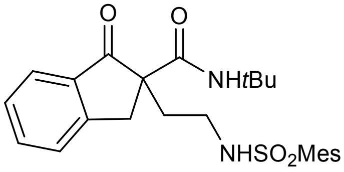
Following general procedure, the titled product was obtained as a colourless oil (141 mg, 99 %) after flash column chromatography [diethyl ether / petroleum ether] (1:1)]; ν_{max} (neat)/cm^{-1} 3325 (br, NH), 2954 (m), 2246 (w, CN), 1746 (s, C=O), 1603 (m), 1450 (s), 1329 (s, SO_2), 1247 (s), 1155 (s, SO_2); δ_H (500MHz, $CDCl_3$) 7.45-7.36 (m, 5 H, 5 x CH phenyl), 6.94 (s, 2 H, CH aromatic), 5.03 (t, 1 H, *J* = 6, NH), 3.75 (s, 3 H, OCH_3), 3.00 (tdd, 1 H, *J* = 6, 10, 13, CHN), 2.99-2.92 (m, 1 H, CH'N), 2.64-2.59 (m, 1 H, C*H*CH_2N), 2.57 (s, 6 H, 2 x CH_3), 2.40-2.34 (m, 1 H, C*H'*CH_2N), 2.29 (s, 3 H, CH_3); δ_C (125MHz, $CDCl_3$) 167.6 (C=O), 142.4 (C), 139.2 (2 x C), 133.3 (C Mes), 133.3 (C phenyl), 132.1 (2 x CH Mes), 129.4 (2 x CH phenyl), 129.3 (2 x CH phenyl), 125.8 (CH), 117.6 (CN), 54.2 (OCH_3), 51.8 (quaternary C), 39.0 (CH_2N), 37.7 (C*H₂*CH_2N), 22.9 (2 x CH_3), 20.9 (CH_3); *m/z* (CI^+, NH_3) 418 ($[M+NH_4]^+$ 100), 401 (56), 219 (10); HRMS 418.1794 $[M+NH_4]^+$, $C_{21}H_{28}O_4N_3S_1$ requires 418.1795.

Compound 3m



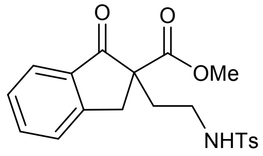
Following general procedure, the titled product was obtained as a colourless oil (166 mg, 98 %) after flash silica chromatography [diethyl ether / petroleum ether] (1:1)]; ν_{max} (neat)/cm^{-1} 3325 (br, NH), 2939 (w), 2246 (w, CN), 1747 (s, C=O), 1450 (m), 1329 (s, SO_2), 1218 (s), 1156 (s, SO_2); δ_H (500MHz, $CDCl_3$) 7.31-7.29 (m, 2 H, 2 x CH), 7.25-7.23 (m, 3 H, 3 x CH), 7.20-7.16 (m, 3 H, 3 x CH), 7.08-7.06 (m, 2 H, 2 x CH), 6.83 (s, 2 H, 2 x CH), 5.07 *and* 5.06 (d *and* d, 1 H *and* 1H, *J* = 14 *and* 14, CH_2O), 4.89 (t, 1 H, *J* = 6, NH), 2.98 (tdd, 1 H, *J* = 6, 10, 13, CHN), 2.86 (dddd, 1 H, *J* = 5, 6, 10, 12, CH'N), 2.54-2.48 (m, 1 H, C*H*CH_2N), 2.47 (s, 6 H, 2 x CH_3), 2.31-2.23 (m, 1 H, C*H'*CH_2N), 2.19 (s, 3 H, CH_3); δ_C (125MHz, $CDCl_3$) 166.8 (C=O), 142.4 (C Mes), 139.2 (2 x C, Mes), 134.3 (C Bn), 133.3 (C Mes), 133.2 (C phenyl), 132.1 (2 x CH Mes), 129.4 (2 x CH phenyl), 129.2 (2 x CH phenyl), 128.6 (2 x CH Bn), 128.6 (2 x CH Bn), 127.8 (CH benzyl), 125.9 (CH phenyl), 117.5 (CN), 68.8 (OCH_2), 52.0 (quaternary C), 39.0 (CH_2N), 37.5 (CH_2), 23.0 (2 x CH_3), 21.0 (CH_3); *m/z* (CI^+, NH_3) 494 ($[M+NH_4]^+$, 24), 477 (13), 386 (11), 360 (44), 295 (43), 269 (17), 217 (16), 204 (59), 161 (100), 136 (27), 120 (18), 106 (22), 91 (17); HRMS 494.2101 $[M+NH_4]^+$, $C_{27}H_{32}O_4N_3S_1$ requires 494.2108.

Compound 3n



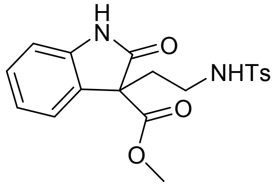
Following general procedure, the titled product was obtained as a white solid (153 mg, 94 %) after flash silica chromatography [diethyl ether / petroleum ether] (1 :1)]; m.p. 38-40 °C; ν_{max} (neat)/cm^{-1} 3349 (br, 2 x NH), 2976 (m), 1700 (C=O ketone), 1658 (C=O amide), 1537 (m), 1465 (m), 1328 (m, SO_2), 1266 (s), 1156 (s, SO_2); δ_H (500MHz, $CDCl_3$) 7.71 (d, 1 H, *J* = 8, CH), 7.63 (dt, 1 H, *J* = 1, 8, CH), 7.45 (d, 1 H, *J* = 8, CH), 7.37 (t, 1 H, *J* = 8, CH), 7.11 (s, 1 H, NH amide), 6.92 (s, 2 H, 2 x CH sulfonamide), 5.22 (t, 1 H, *J* = 7, NH sulfonamide), 3.89 (d, 1 H, *J* = 18, C*H*H'), 3.09 (d, 1 H, *J* = 18, CH*H'*), 3.02 (dtd, 1 H, *J* = 5, 8, 13, C*H*H'N), 2.90 (dd, 1 H, *J* = 6, 12, CH*H'*N), 2.61 (s, 6 H, 2 x CH_3), 2.27 (s, 3 H, CH_3), 2.07 (ddd, 1 H, *J* = 5, 7, 13, C*H*CH_2N), 1.86 (td, 1 H, *J* = 8, 14, C*H'*CH_2N), 1.26 (s, 9 H, 3 x CH_3); δ_C (125MHz, $CDCl_3$) 207.3 (C=O ketone), 168.0 (C=O amide), 153.3 (C), 142.1 (C), 139.0 (C), 136.3 (CH), 134.4 (CH), 133.5 (C), 132.0 (2 x CH), 127.8 (CH), 126.7 (CH), 124.6 (CH), 59.6 (quaternary C), 51.4 (*C*$(CH_3)_3$), 39.6 (CH_2), 39.5 (CH_2), 36.3 (CH_2), 28.5 (3 x CH_3), 22.9 (2 x CH_3), 20.9 (CH_3); *m/z* (ES, NH_3) 479 ($[M+Na]^+$ 45), 457 ($[M+H]^+$, 100); HRMS 457.2154 $[M+H]^+$, $C_{25}H_{33}O_4N_2S$ requires 457.2156.

Compound 3o



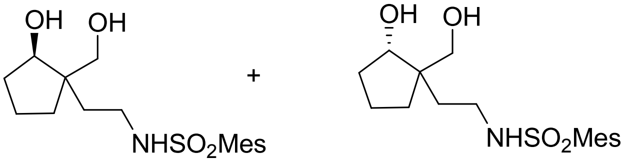
Following general procedure, the titled product was obtained as a white solid (135 mg, 97%), after flash silica chromatography [diethyl ether / petroleum ether] (2 :1)]; v$_{max}$ (neat)/cm^{-1} 3287 (br, NH), 1739 (m, C=O), 1711 (s, C=O ester), 1329 (s, SO_2), 1155 (s, SO_2);); δ$_H$ (500MHz, $CDCl_3$) 7.67 (d, 1 H, *J* = 8, CH), 7.62 (d, 2 H, *J* = 8, 2 x CH tosyl), 7.57 (dt, 1 H, *J* = 1, 8, CH), 7.40 (d, 1 H. *J* = 8, CH), 7.33 (t, 1 H, *J* = 8, CH), 7.20 (d, 2 H, *J* = 8, 2 x CH tosyl), 4.92 (t, 1 H, *J* = 6, NH), 3.60 (d, 1 H, *J* = 17, C*H*H'), 3.57 (s, 3 H, CH_3), 3.04 (d, 1 H, *J* = 17, CH*H'*), 3.08-2.97 (m, 2 H, CH_2N), 2.33 (s, 3 H, CH_3 tosyl), 2.22 (ddd, 1 H, *J* = 6, 8, 14, C*H*CH_2N), 1.96 (ddd, 1 H, *J* = 6, 8, 14, C*H'*CH_2N); δ$_C$ (125MHz, $CDCl_3$) 202.1 (C=O), 171.4 (C=O), 152.3 (C), 143.4 (C), 136.8 (C), 135.7 (CH), 134.6 (C), 129.7 (CH), 128.0 (CH), 127.0 (CH), 126.5 (CH), 125.0 (CH), 59.0 (quaternary C), 53.0 (OCH_3), 39.7 (CH_2), 37.0 (CH_2), 34.4 (CH_2), 21.5 (CH_3); *m/z* (ES, NH_3) 388 ($[M+H]^+$, 100), HRMS $[M+H]^+$, 388.1219 $C_{20}H_{21}O_4N_1S$ requires 388.1219.

Compound 3p



Following general procedure, the titled product was obtained as a white solid (136 mg, 98 %) after flash silica chromatography [chloroform / acetone] (9 :1)]; ν_{max} (neat)/cm^{-1} 3283 (br, NH), 1741 (s, C=O), 1714 (s, C=O), 1329 (s, SO_2), 1158 (s, SO_2), δ_H (500MHz, $CDCl_3$) 9.17 (s, 1 H, NH oxindole), 7.63 (d, 2 H, *J* = 8, 2 x CH tosyl), 7.32 (dt, 1 H, *J* = 1, 8, CH), 7.22 (d, 2 H, *J* = 8, 2 x CH tosyl), 7.18 (d, 1 H, *J* = 7, CH), 7.09 (t, 1 H, *J* = 8, CH), 7.01 (d, 1 H, *J* = 8, CH), 5.83 (dd, 1 H, *J* = 3, 9, NH), 3.67 (s, 3 H, OCH_3), 2.92-2.84 (m, 1 H, CHN), 2.80-2.76 (m, 1 H, CH'N), 2.58 (ddd, 1 H, *J* = 5, 10, 15, C*H*CH_2N), 2.49 (td, 1 H, *J* = 5, 15, C*H'*CH_2N), 2.37 (s, 3 H, CH_3 tosyl); δ_C (125MHz, $CDCl_3$) 177.3 (C=O), 169.7 (C=O), 143.2 (C), 142.0 (C), 136.4 (C), 129.8 (CH), 129.6 (CH), 127.1 (CH), 123.7 (CH), 122.9 (CH), 111.1 (CH), 58.4 (quaternary C), 53.5 (OCH_3), 39.3 (CH_2N), 32.3 (CH_2), 21.5 (CH_3); *m/z* (ES, NH_3) 406 $[M+NH_4]^+$ 100), 389 (50); HRMS $[M+NH_4]^+$ 406.1431, $C_{19}H_{24}O_5N_3S$ requires 406.1431.

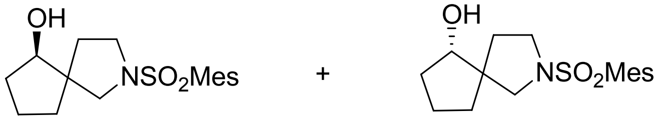
Diol-alcohol **6**



LiAlH$_4$ (2.0 M solution in THF, 0.91 mL) was added dropwise to a solution of **3d** (190 mg, 0.52 mmol) in 4 mL dry Et_2O at 0^{o}C. Following stirring at this temperature for 4 h, the solution was diluted with Et_2O (5 mL), and water (5 mL) was added cautiously whilst maintaining cooling at 0°C. The layers were separated, and the aqueous layer was acidified to pH 2 with 1.0 N HCl. The aqueous portion was then extracted with Et_2O (3 x 10 mL), and the combined organic fractions were dried (Na_2SO_4) and concentrated. The residue was purified by flash column chromatography (Et_2O) to give the titled compound as a clear oil (155 mg, 88%); ν_{max} (neat)/cm^{-1} 3488 (br, OH *and* NH), 3055 (m), 2962 (m), 1734 (w), 1605 (m), 1451 (m), 1422 (m), 1321 (s, SO_2), 1266 (s), 1155 (s, SO_2); δ_H (500MHz, $CDCl_3$) 6.95 (s, 2 H, 2 x CH), 5.62 (t, 1 H, *J* = 6, NH), 3.99 *and* 3.92 (q *and* q, 0.75 H *and* 0.25 H, *J* = 4 *and* 7), 3.45 *and* 3.33 (dd *and* dd, 0.8 H *and* 1.2 H, *J* = 4, 11 *and* 4, 11, C*H₂*OH), 3.00-2.85 (m, 2 H, CH_2N), 2.56 (s, 6 H, 2 x CH_3), 2.50 (t, 1 H, *J* = 4, OH), 2.29 (s, 3 H, CH_3), 2.00-1.84 (m, 2 H), 1.69-1.62 (m, 1 H), 1.58-1.24 (m, 5 H); δ_C (125MHz, $CDCl_3$) 142.1 (C), 139.1 (2 x C), 133.5 (C), 131.9 (2 x CH), 81.0 *and* 78.7 (CHOH), 67.9 *and* 65.3 (CH_2OH), 48.7 *and* 47.5 (quaternary C), 39.1 *and* 39.0 (CH_2N), 33.5 *and* 32.7 (CH_2), 32.8 *and* 31.4 (CH_2), 29.4 (CH_2), 23.0 (2 x CH_3), 20.9 (CH_3), 20.3 *and* 19.8 (CH_2); *m/z* (CI^+, NH_3) 342 ($[M+H]^+$, 81%), 322 (10), 217 (11), 167 (49), 160 (72), 140 (100), 126 (12), 120 (27), 110 (14); HRMS $[M+H]^+$ 342.1734, $C_{17}H_{28}O_4NS$ requires 342.1734

.

Spiro-fused mono-alcohol **7**



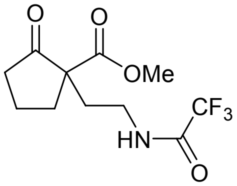
Diol **6** (100mg, 0.29 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise to a solution of Et_3N (189 µL, 1.35 mmol), TsCl (54 mg, 0.29 mmol) and a single crystal of DMAP in CH_2Cl_2 (1 mL) and the solution was stirred at RT for 1 h, before warming to reflux and stirring for a further 48 h. Following cooling to RT, CH_2Cl_2 (3 mL) was added and the solution was washed with 1.0 N HCl (3 x 3 mL) and brine (3 mL). The HCl portions were extracted with CH_2Cl_2 (2 x 5 mL), dried (Na_2SO_4), and concentrated. The residue was purified by flash column chromatography ([diethyl ether / petroleum ether] (1:1 to 100:0) to give the spiro cyclised adduct (67 mg) and 10 mg of the starting diol (78% brsm); ν_{max} (neat)/cm^{-1} 3511 (br, OH *and* NH), 3055 (m), 2986 (m), 1712 (m), 1310 (m, SO_2), 1266 (s), 1153 (m, SO_2); δ_H (500MHz, $CDCl_3$) 6.94 (s, 2 H, 2 x CH), 3.95 (t, 0.35 H, *J* = 4, C*H*OH minor), 3.87-3.86 (m, 0.65 H, C*H*OH major), 3.52 (d, 0.65 H, *J* = 10, C*H*H'N, major), 3.47 (ddd, 0.35 H, *J* = 7, 8, 10, C*H*H'N minor), 3.39-3.30 (m, 1.30 H, CH_2N, major), 3.24 (ddd, 0.35 H, *J* = 6, 8, 9, CH*H'*N, minor), 3.11 (d, 0.35 H, *J* = 10, C*H*H', minor), 3.00 (d, 0.35 H, *J* = 10, CH*H*', minor), 2.92 (d, 0.65 H, *J* = 10, CH*H'*, major), 2.63 (s, 3.9 H, 2 x CH_3, major), 2.62 (s, 2.1 H, 2 x CH_3, minor), 2.30 (s, 3 H, CH_3), 2.04-1.95 (m, 2 H, CH_2), 1.80-1.43 (m, 6 H, 3 x CH_2); δ_C (125MHz, $CDCl_3$) 142.5 (*i*-C), 140.1 (2 x C), 132.8 (*p*-C), 131.9 (2 x CH), 77.6 *and* 77.5 (CHOH), 55.7 *and* 51.3 (CH_2N), 54.4 *and* 53.9 (quaternary C), 46.2 *and* 45.8 (CH_2), 35.8 (CH_2), 33.9 *and* 33.5 (CH_2), 31.2 *and* 29.7 (CH_2), 22.9 *and*

22.8 (2 x CH_3), 21.0 (*p*-CH_3), 21.0 *and* 20.3 (CH_2); *m/z* (CI^+, NH_3) 324 ($[M+H]^+$, 100%), 140 (60); HRMS HRMS $[M+H]^+$ 324.1623, $C_{17}H_{26}O_3NS$ requires 324.1628.

General procedure for one pot trifluoroacetylation / sulfonamide cleavage:

Trifluoroacetic anhydride (197 μL, 1.37 mmol) was added to a stirred solution of sulfonamide (0.68 mmol) and Et_3N (206 μL, 1.37 mmol) in dry CH_2Cl_2 (10 mL) under N_2. Following stirring at RT for 30 mins, the residue was concentrated under reduced pressure, and diluted with dry THF (5 mL). The solution was cooled to -78 ^oC, and SmI_2 (0.1 M in THF) was added dropwise until the blue/green colour persisted for 20 minutes (typically 5 equivs). Following exposure to air until the solution turned yellow, the solution was concentrated, and filtered through a plug of silica (eluent: Et_2O). The filtrate was concentrated, and purified by flash column chromatography.

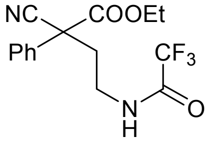
Compound 8a



Following the general procedure, the titled product was obtained as a pale yellow oil (145 mg, 74 %) after flash column chromatography [diethyl ether / petroleum ether] (3 : 2)]; v_{max} (neat)/cm^{-1} 3340 (br, NH), 1730 (m, C=O ketone), 1708 (br, C=O ester, amide), 1556 (m), 1213 (m), 1162 (m); δ_H (500MHz, $CDCl_3$) 7.36 (br, 1 H, NH), 3.72 (s, 3 H, OCH_3), 3.50 (dt, 1 H, *J* = 6, 13, CHN), 3.39 (dt, 1 H, *J* = 6, 13, CH'N), 2.51-2.46 (m, 2 H), 2.35 (m, 1 H), 2.10-1.92 (m, 5 H); δ_C (125MHz,

$CDCl_3$) 215.3 (C=O ketone), 171.9 (C=O ester), 157.2 (q, *J* = 37, C=O amide), 115.8 (q, *J* = 286, CF_3), 59.1 (quaternary C), 52.9 (OCH_3), 37.1 (CH_2N), 36.3 (CH_2), 34.3 (CH_2), 32.0 (CH_2), 19.7 (CH_2); *m/z* (ES) 299 ($[M+NH_4]^+$, 100); HRMS 299.1222 $[M+NH_4]^+$, $C_{11}H_{18}O_4N_2F_3$ requires 299.1219.

Compound 8b



Following the general procedure, the titled product was obtained as a pale yellow oil, (162 mg, 73 %) after flash column chromatography [diethyl ether / petroleum ether] (3 : 2)]; ν_{max} (neat)/cm^{-1} 3335 (br, NH), 2249 (w, CN), 1735 (s, C=O), 1704 (br, C=O ester, amide), 1556 (m), 1451 (m), 1215 (s), 1182 (s); δ_H (500MHz, $CDCl_3$) 7.53-7.52 (m, 2 H, 2 x CH), 7.44-7.38 (m, 3 H, 3 x CH), 6.92 (br, 1 H, NH), 4.23 (dq, 2 H, *J* = 7, 11, OCH_2), 3.57-3.44 (m, 2 H, CH_2N), 2.67 (td, 1 H, *J* = 7, 14, C*H*CH_2N), 2.50 (ddd, 1 H, *J* = 6, 8, 14, C*H'*CH_2N), 1.22 (t, 3 H, *J* = 7, CH_3); δ_C (125MHz, $CDCl_3$) 167.0 (C=O), 157.4 (q, *J* = 37, C=O amide), 133.3 (C), 129.5 (2 x CH), 129.4 (CH), 125.8 (2 x CH), 117.7 (CN), 115.6 (q, *J* = 288, CF_3), 63.6 (OCH_2), 52.2 (quaternary C), 36.7 (CH_2), 36.2 (CH_2), 13.7 (CH_3); *m/z* (ES) 346 ($[M+NH_4]^+$, 100); HRMS 346.1365 $[M+NH_4]^+$, $C_{15}H_{19}O_3N_3F_3$ 346.1373.

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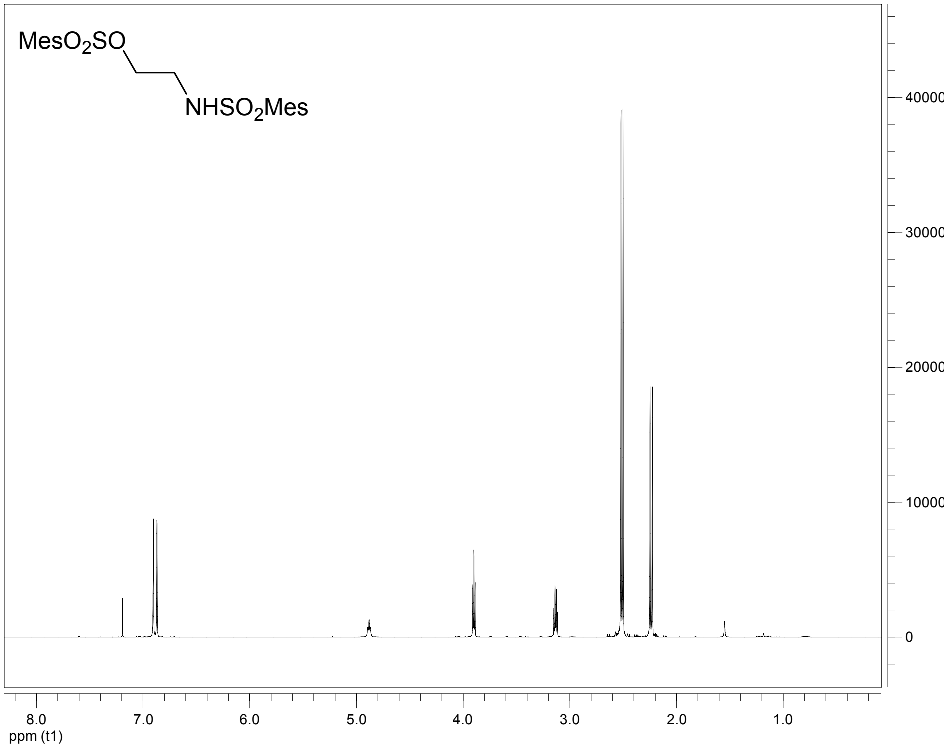
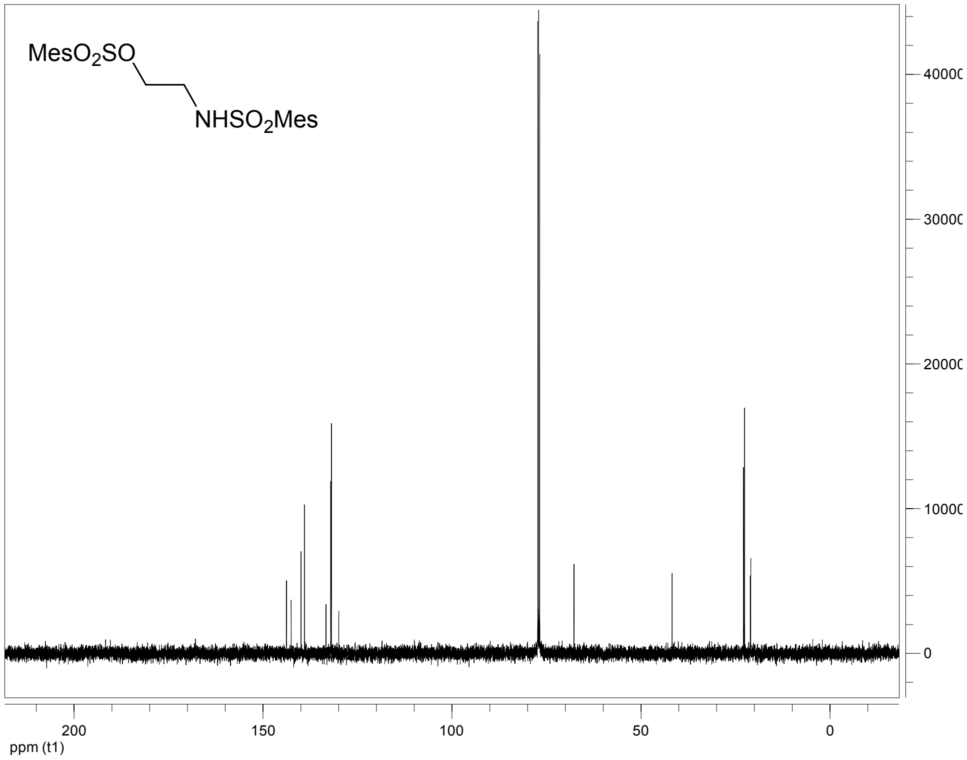
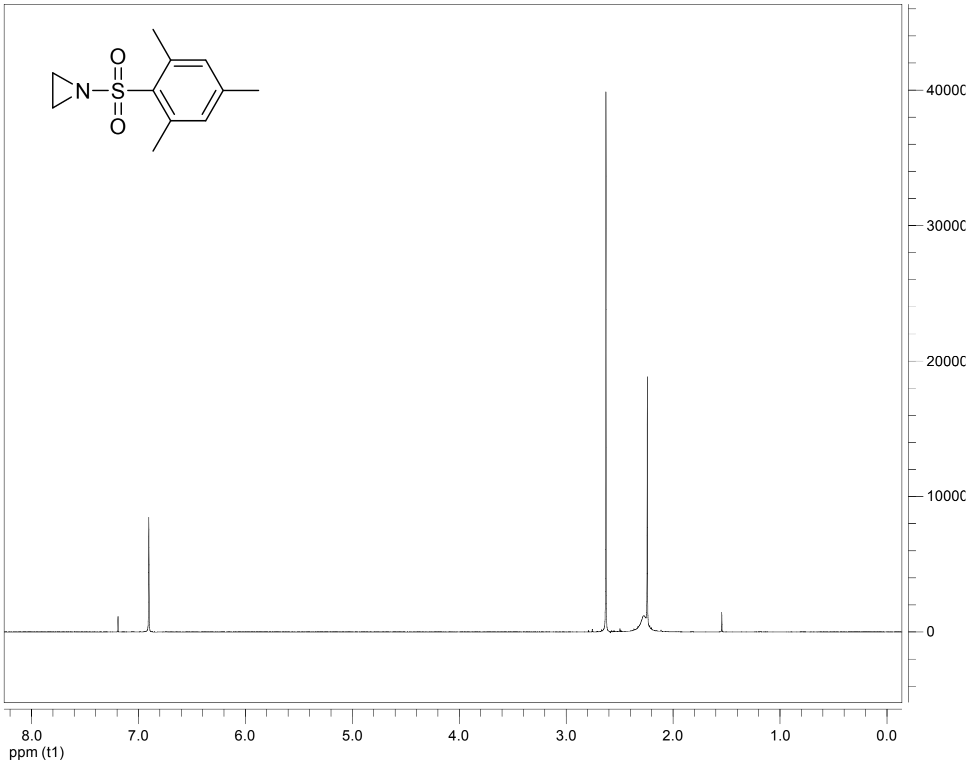
^{1}H NMR of 2,4-(Dimesitylsulfonyl)ethanolamine



^{13}C NMR of 2,4-(Dimesitylsulfonyl)ethanolamine



^{1}H NMR of *N*-mesitylsulfonyl aziridine **2b**



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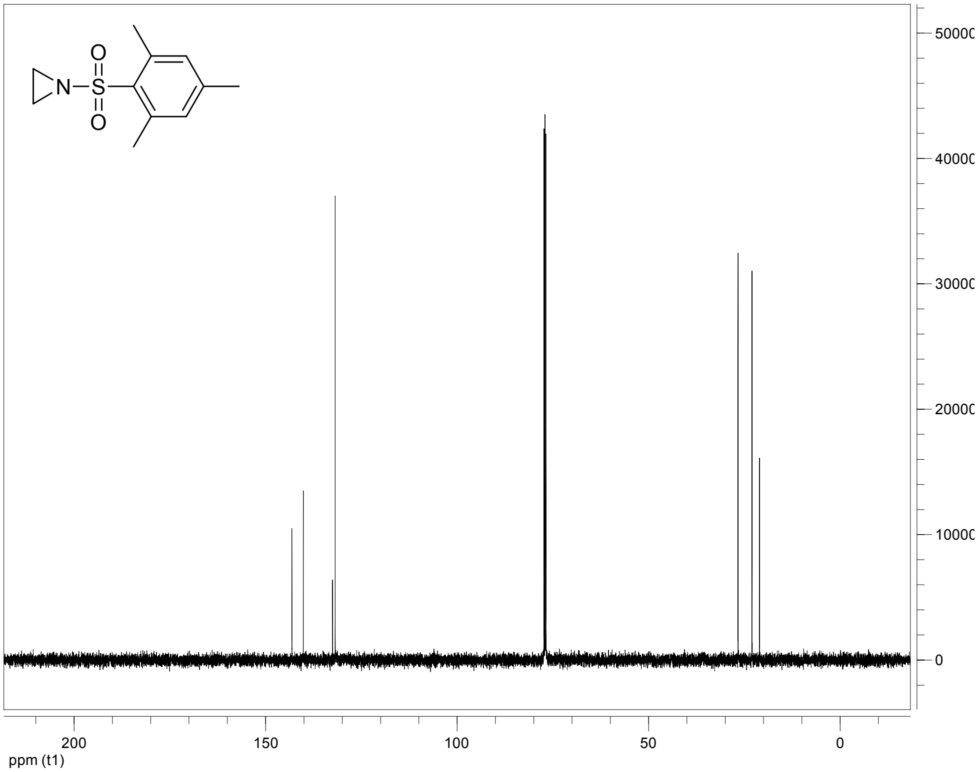
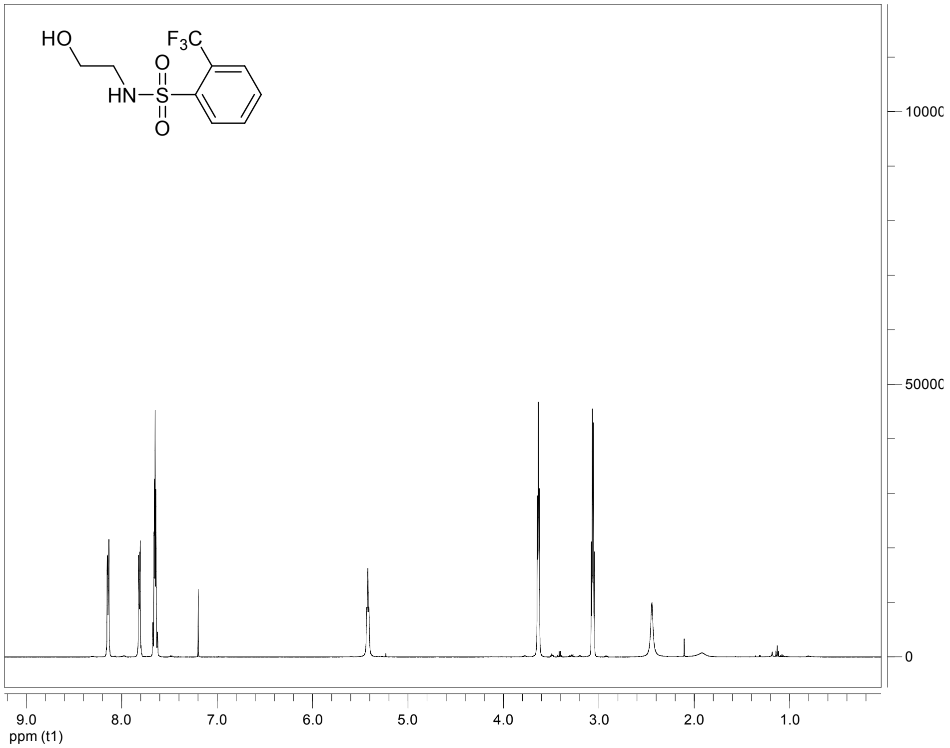


^{1}H NMR of *N*-(2-(Trifluoromethane)benzenesulfonyl)ethanolamine



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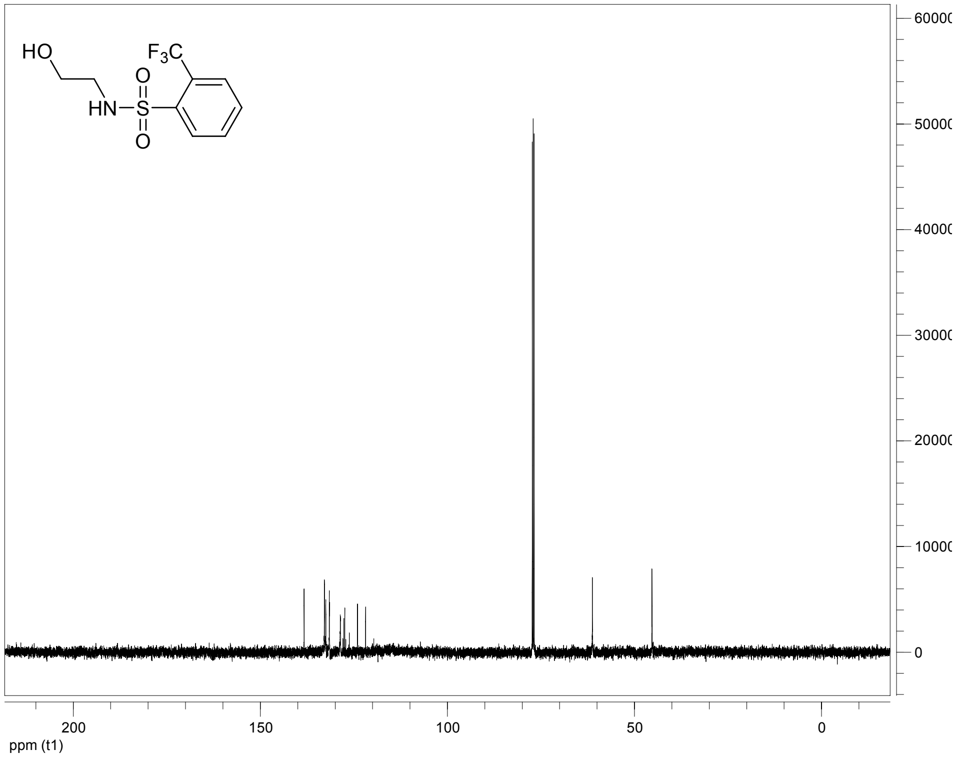
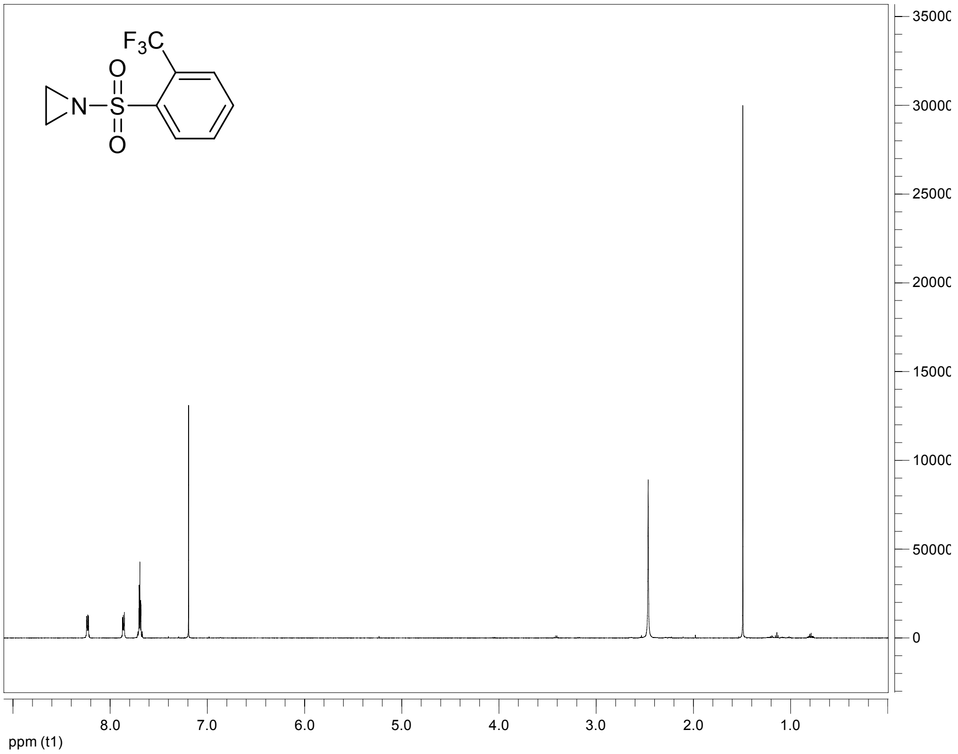
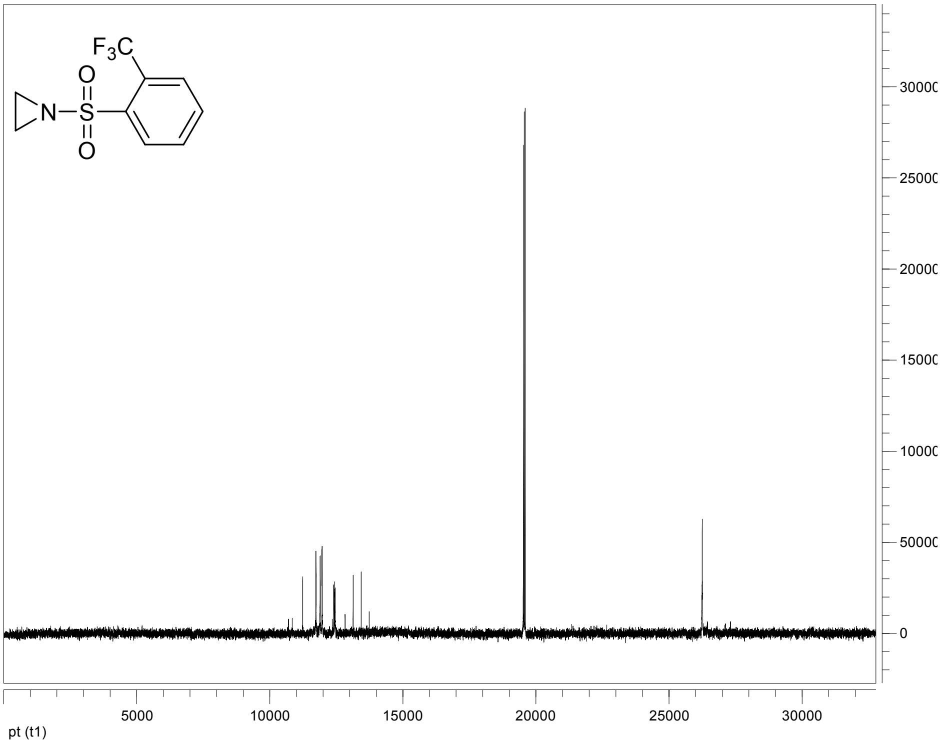


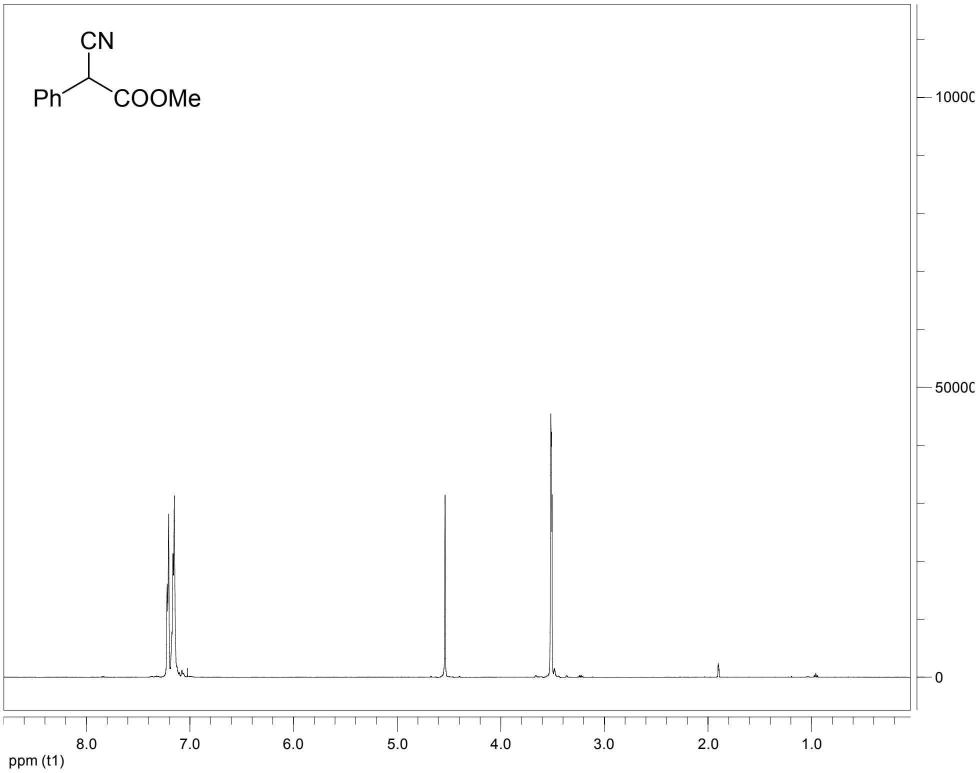
^{1}H NMR of *N*-(2-(Trifluoromethane)benzenesulfonyl aziridine **2f**



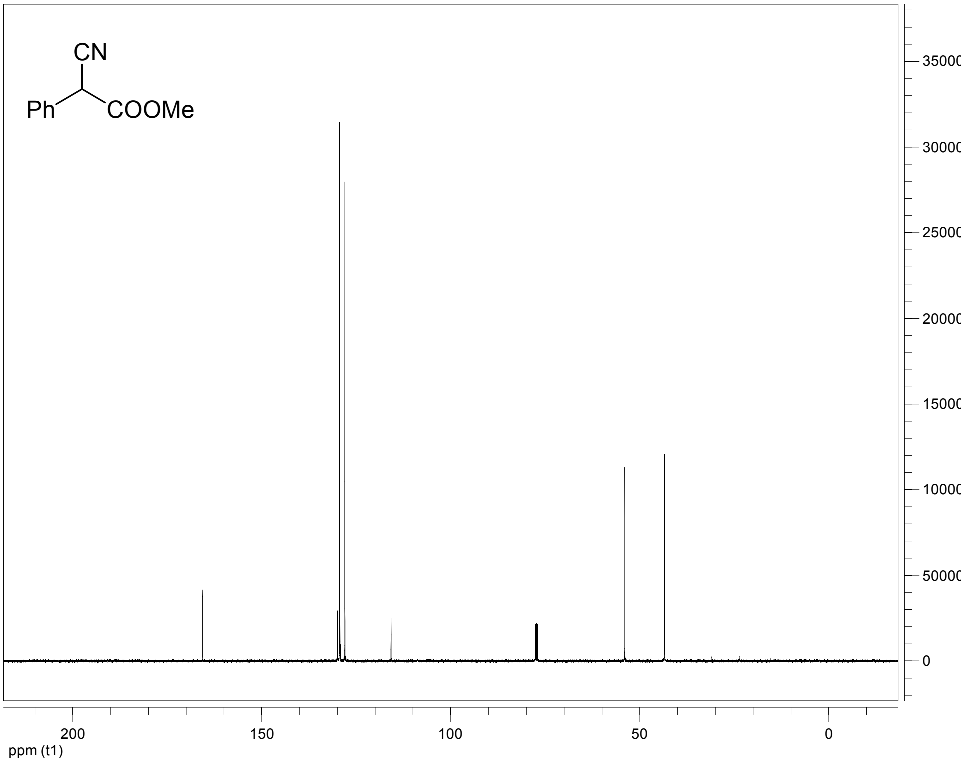
^{13}C NMR of *N*-(2-(Trifluoromethane)benzenesulfonyl aziridine **2f**



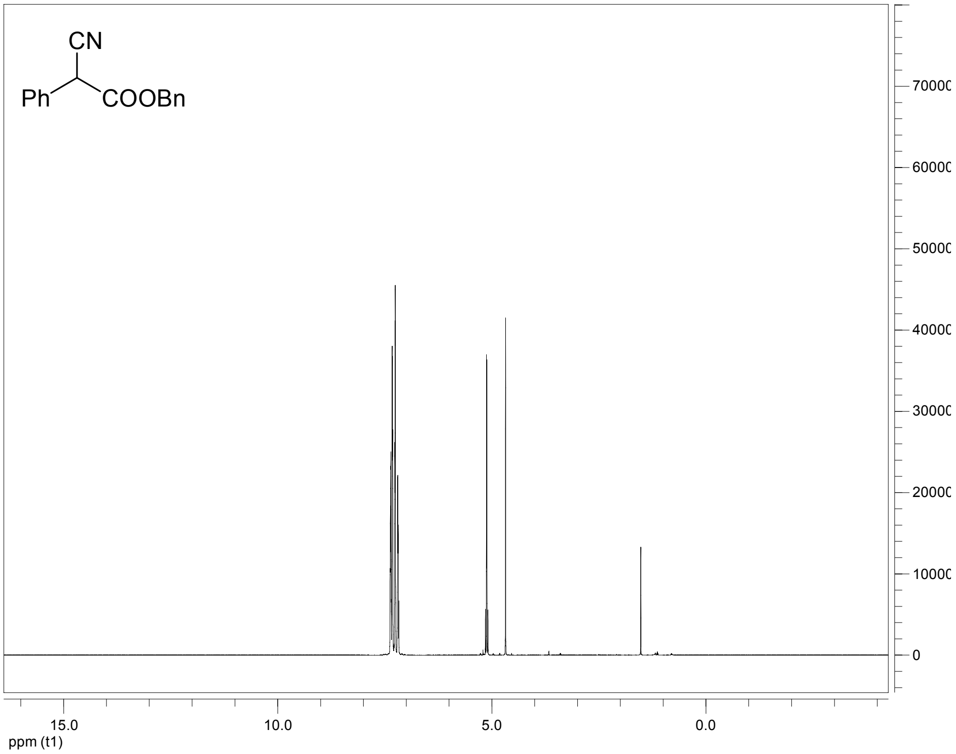
^{1}H NMR for Methyl 2-cyano-2-phenylacetate



^{13}C NMR of Methyl 2-cyano-2-phenylacetate



^{1}H NMR of Benzyl 2-cyano-2-phenylacetate



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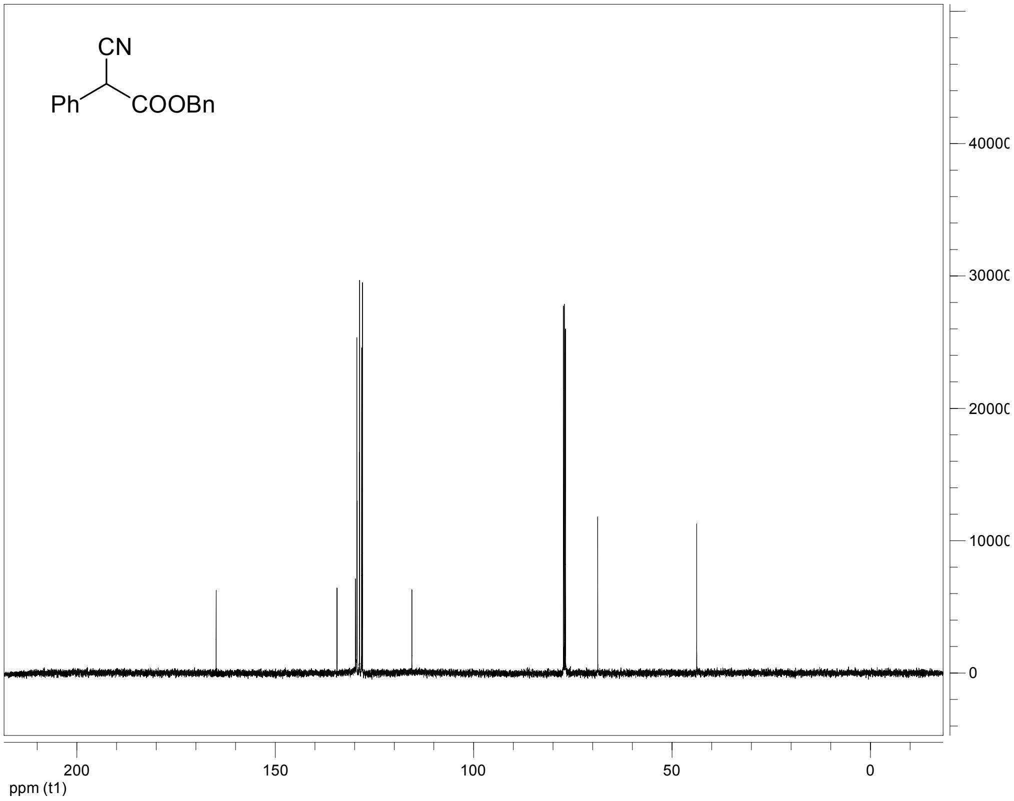
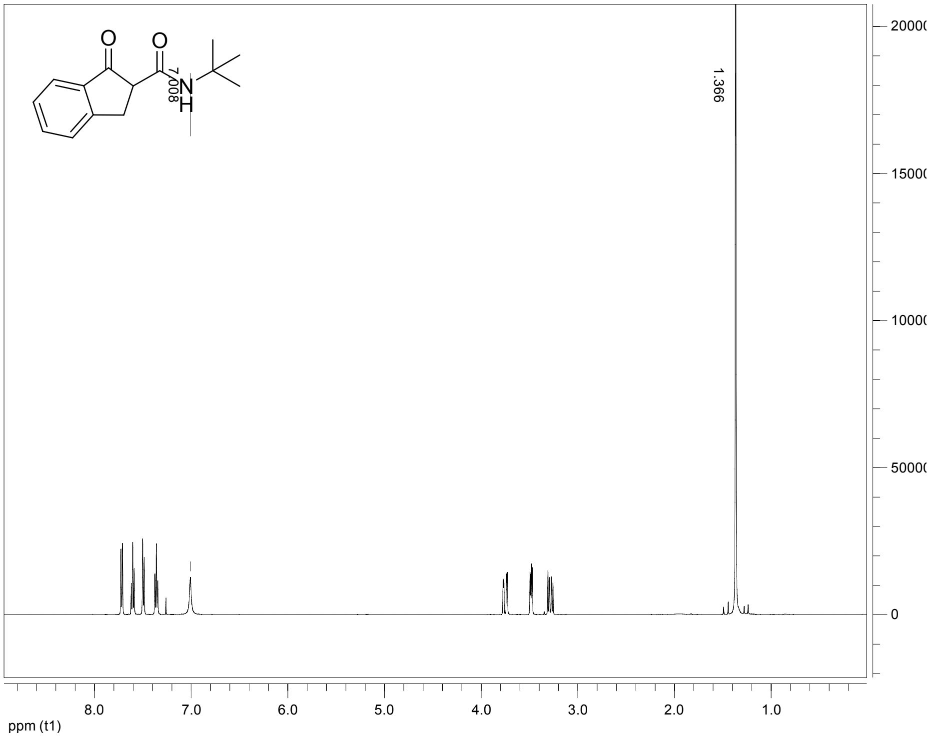


^{1}H NMR of 1-Oxo-indan-2-carboxylic acid tert-butylamide



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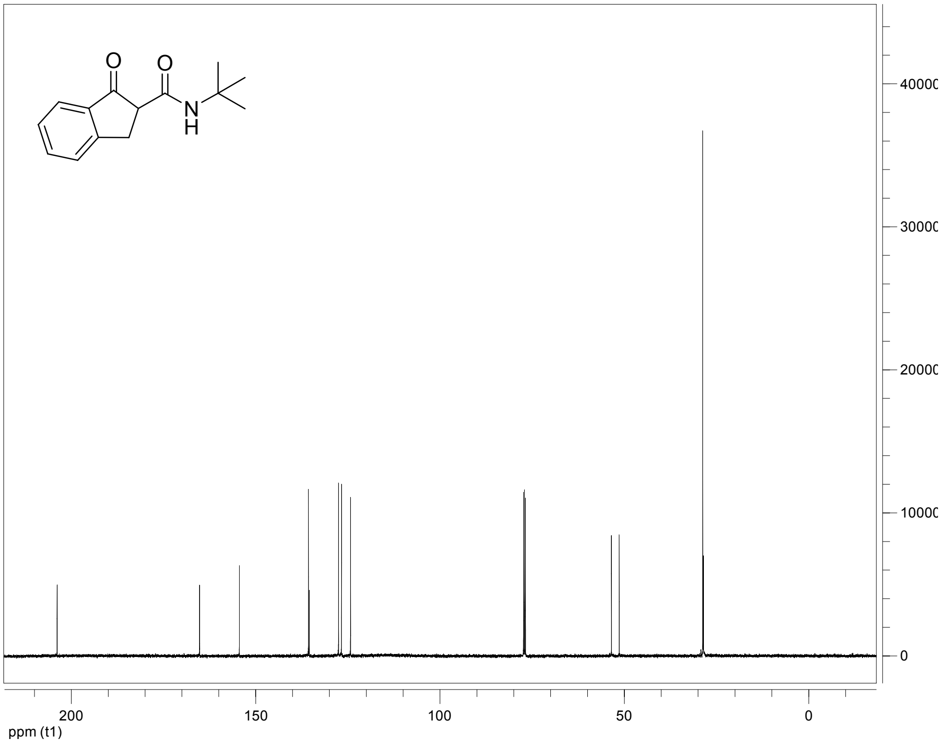
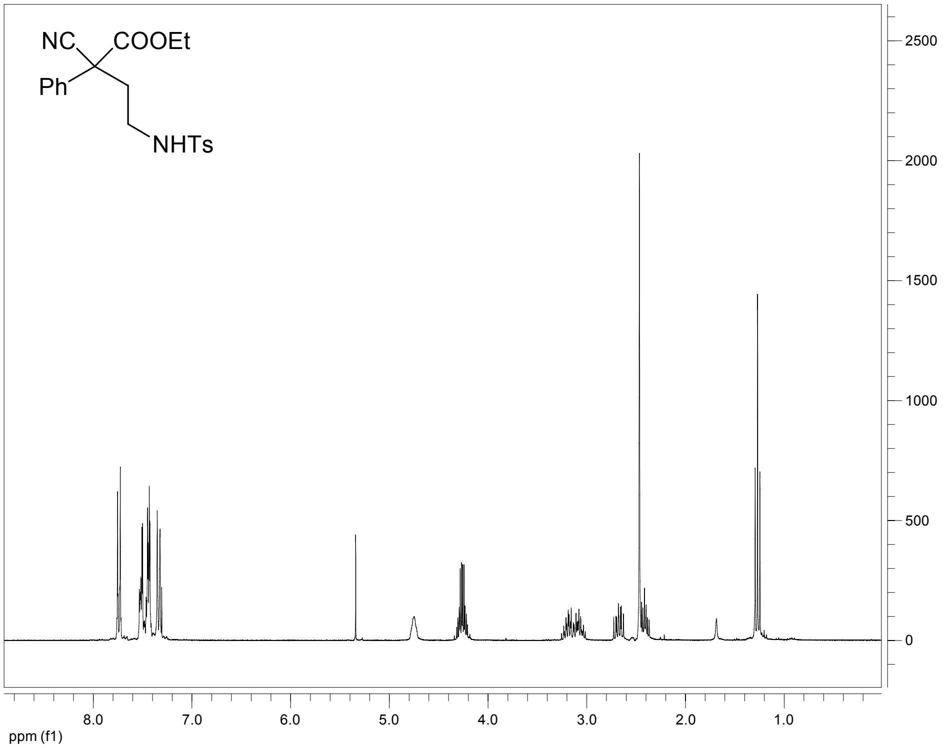
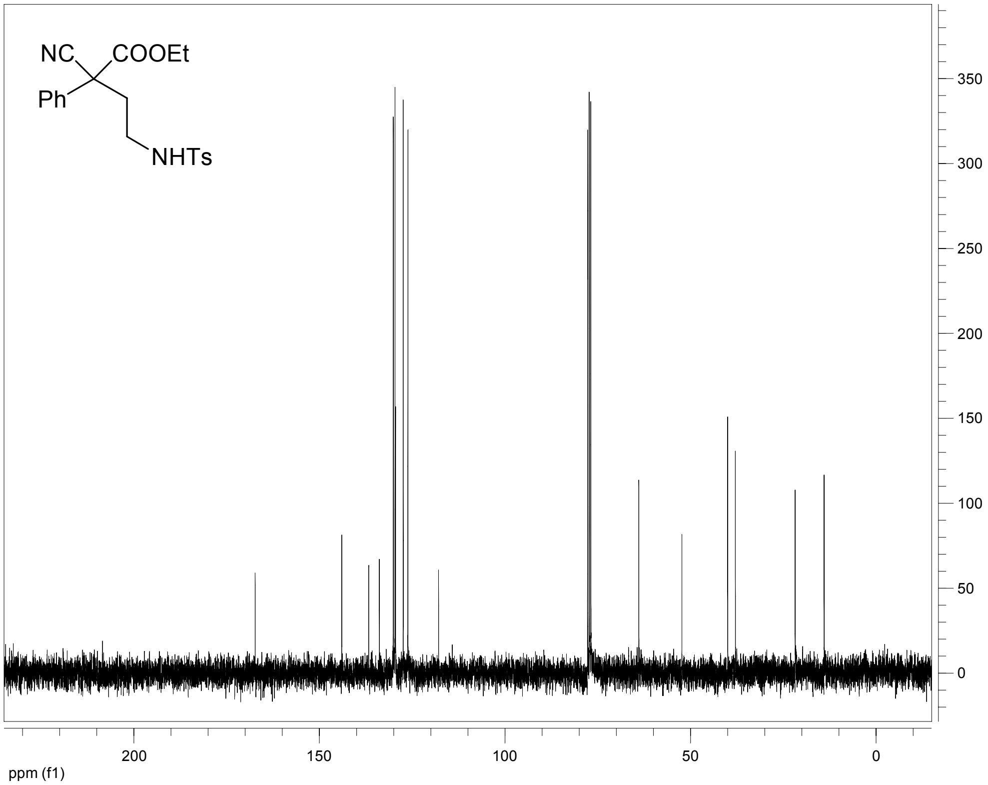


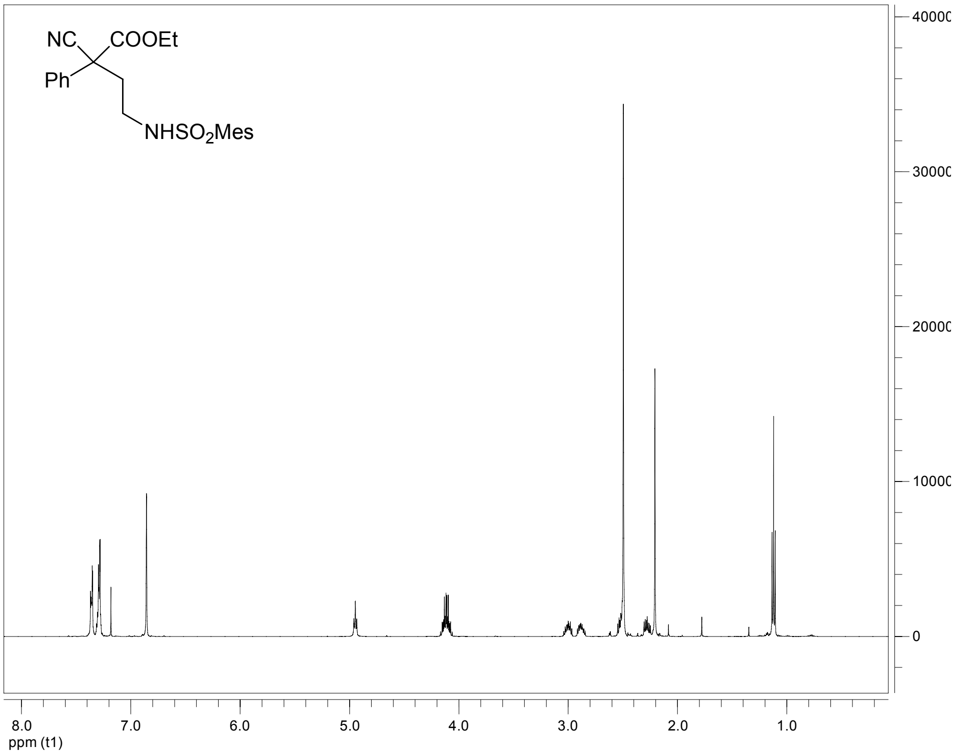
^{1}H NMR of compound **3a**



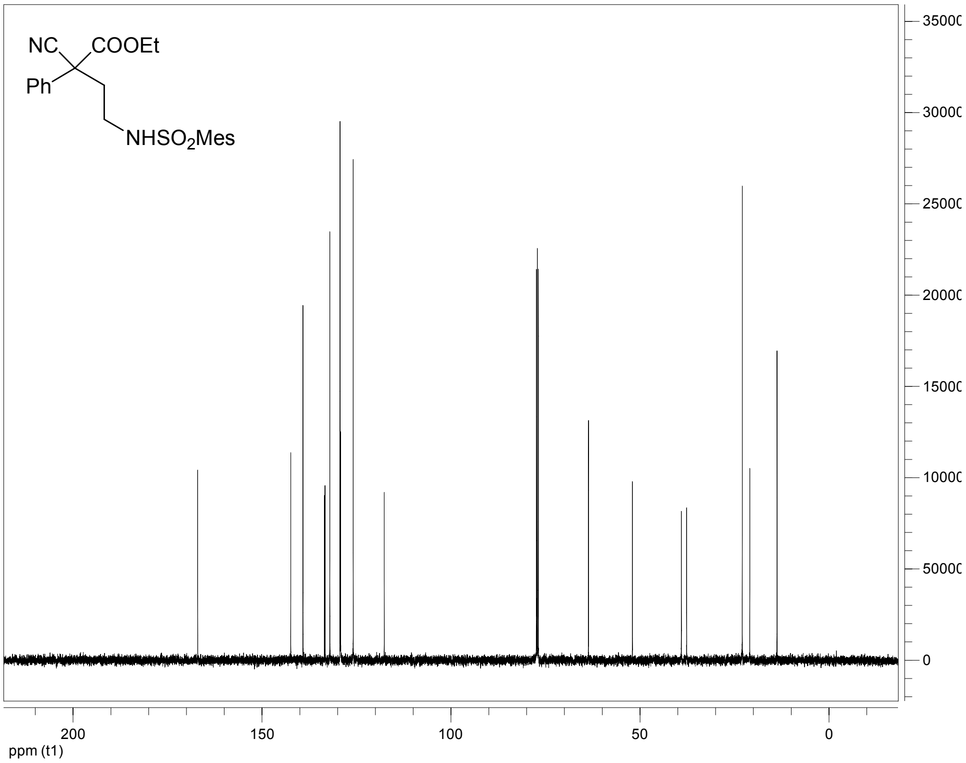
^{13}C NMR of compound **3a**



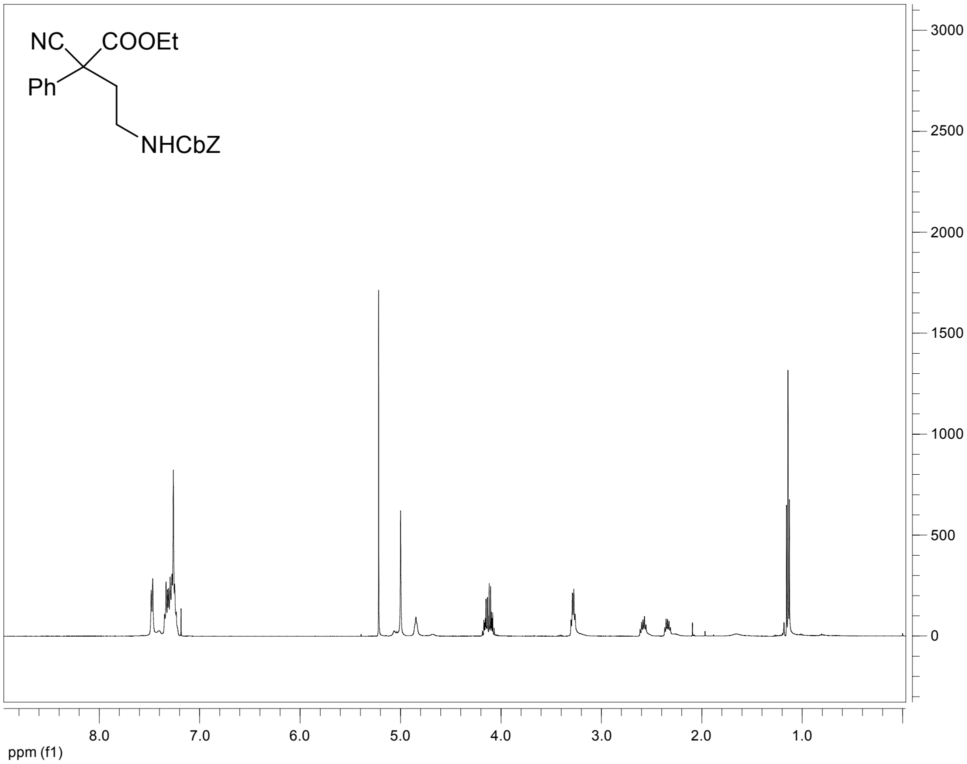
^{1}H NMR of compound **3b**



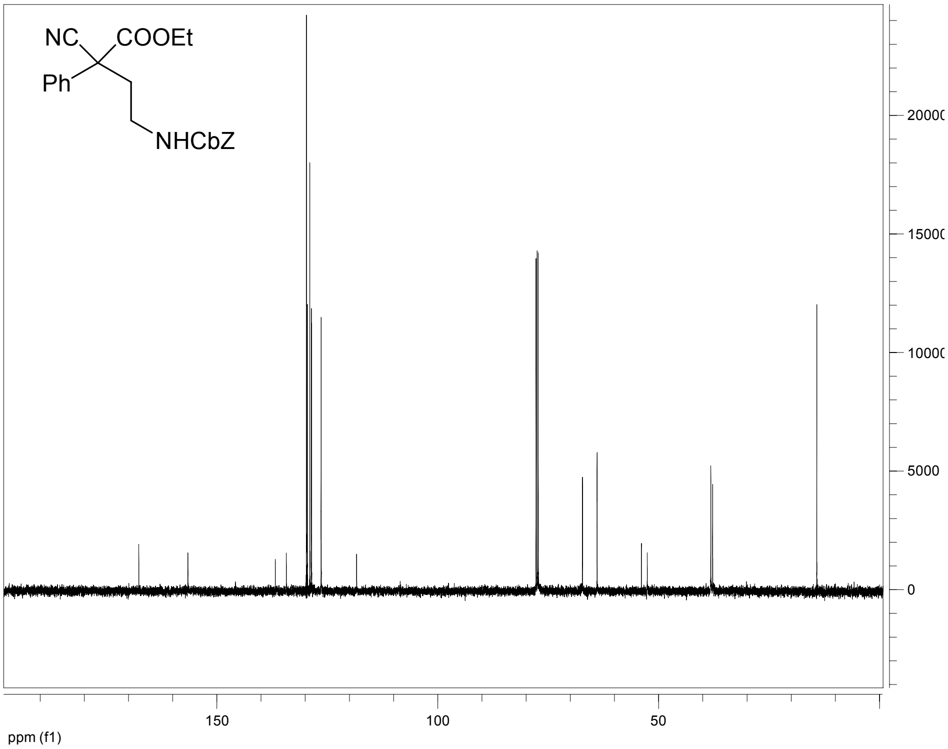
^{13}C NMR of compound **3b**



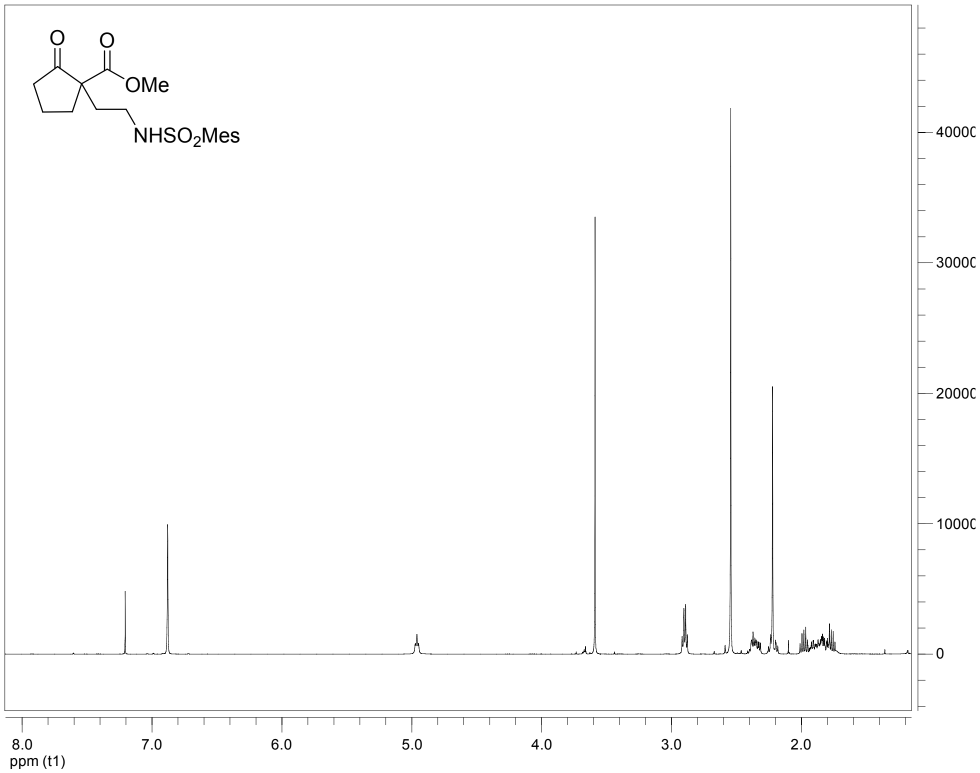
^{1}H NMR of compound **3c**



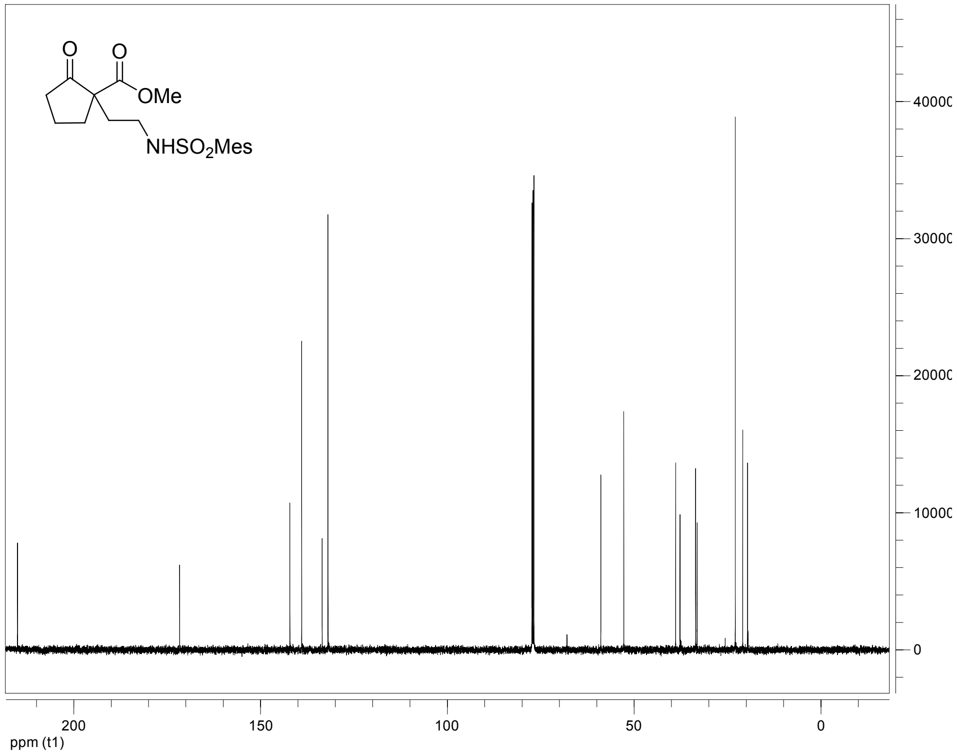
^{13}C NMR of compound **3c**



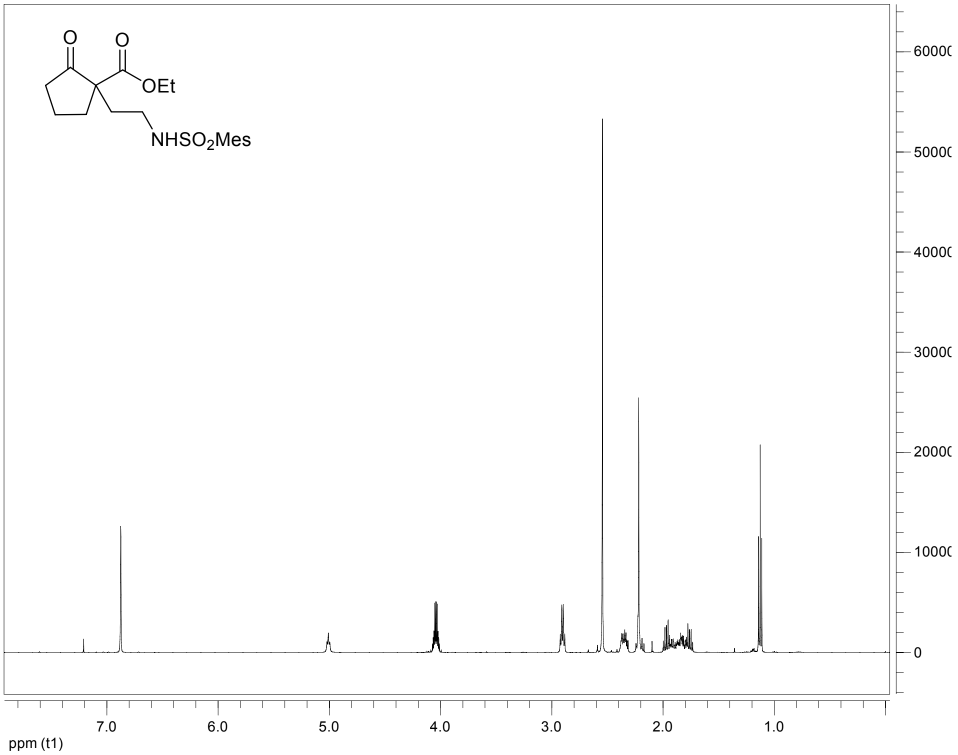
^{1}H NMR of compound **3d**



^{13}C NMR of compound **3d**



^{1}H NMR of compound **3e**



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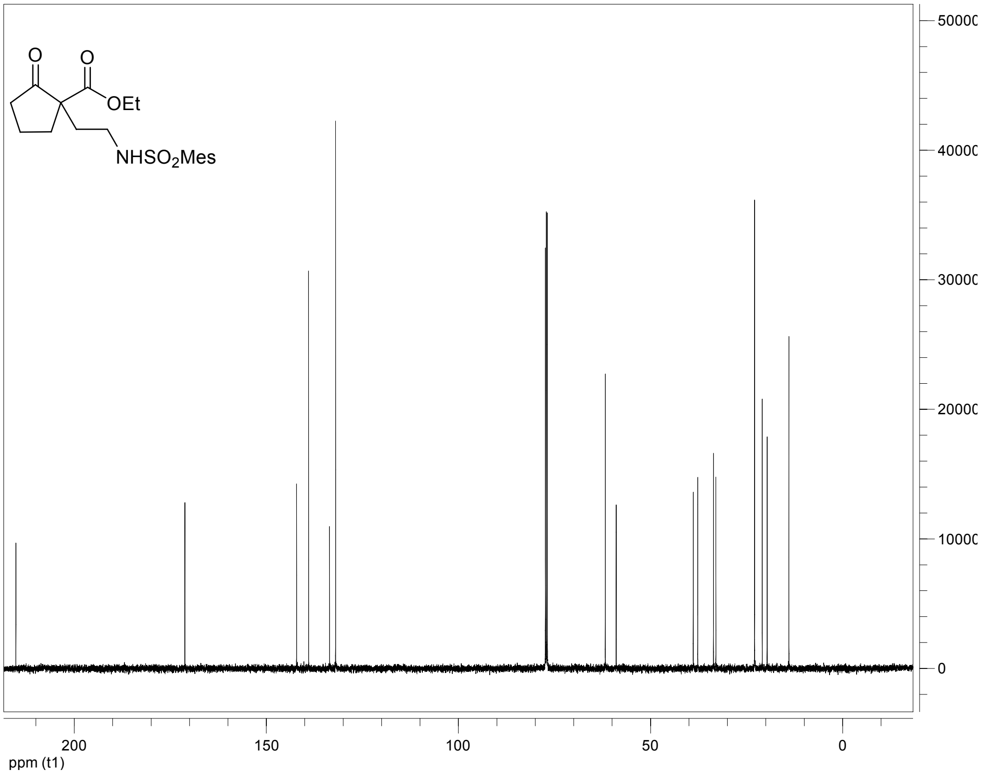
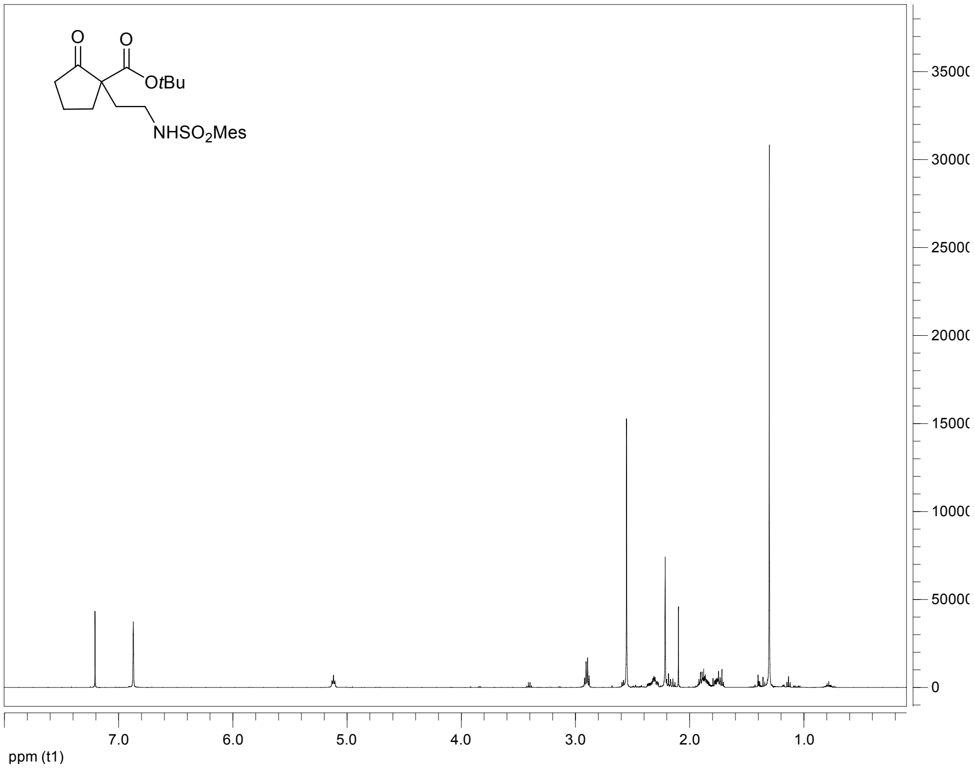
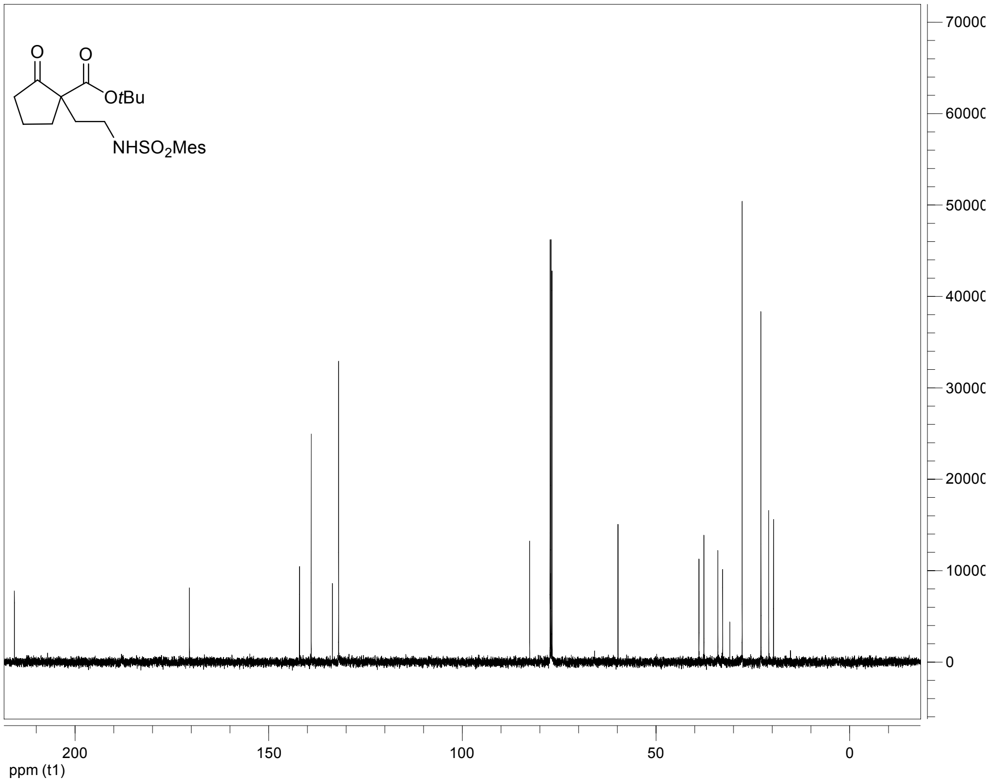


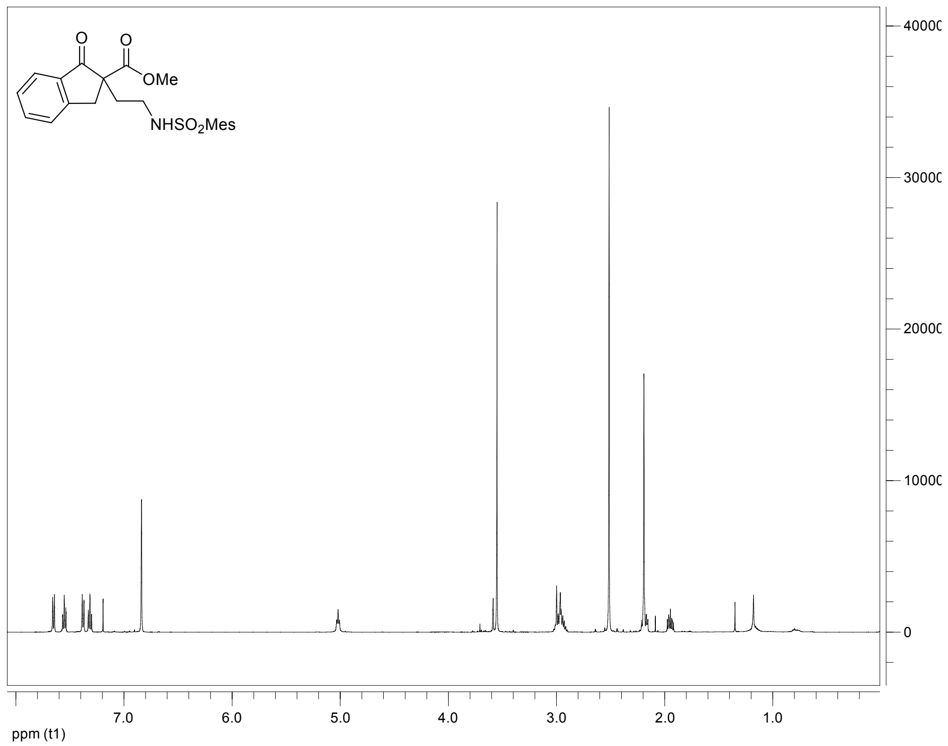
^{1}H NMR of compound **3f**



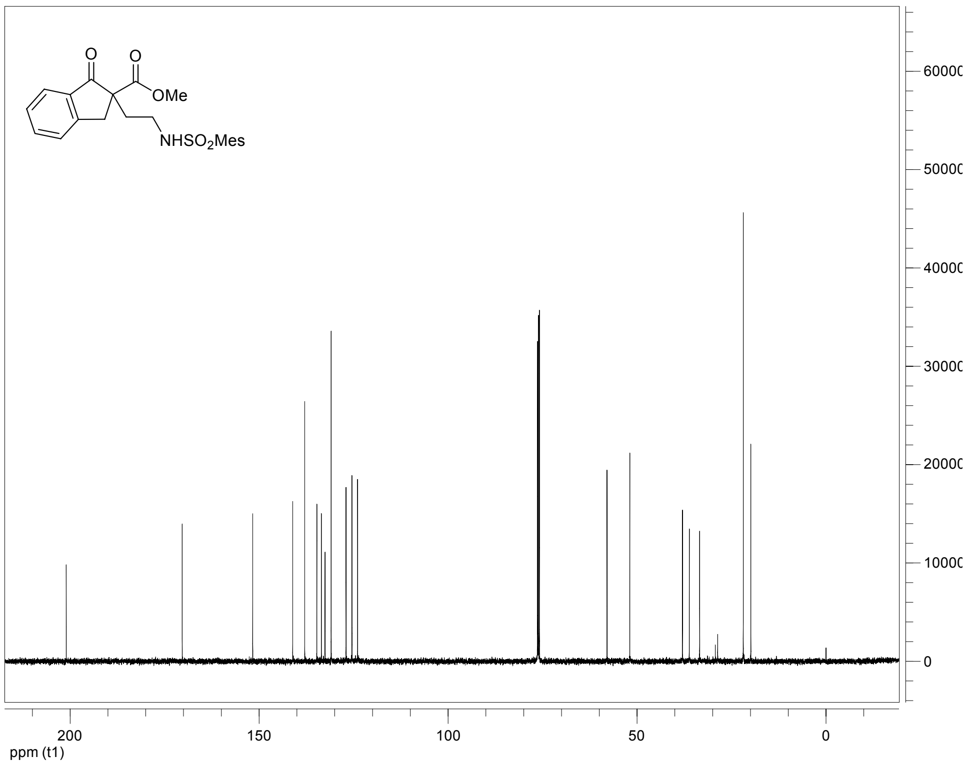
^{13}C NMR of compound **3f**



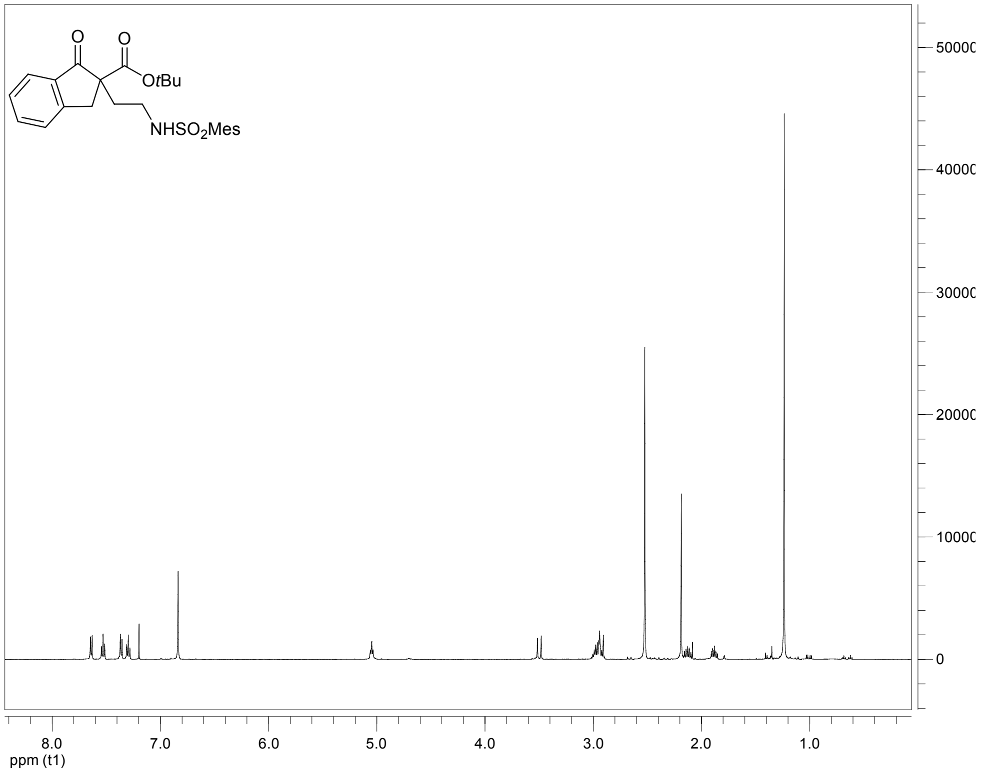
^{1}H NMR of compound **3g**



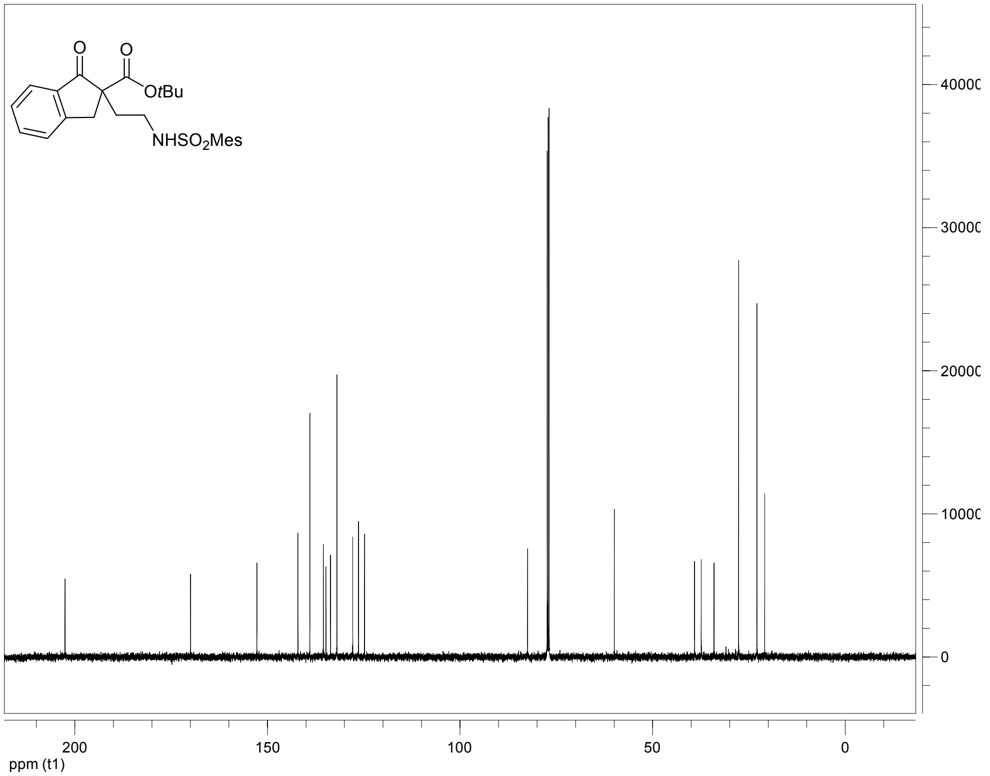
^{13}C NMR of compound **3g**



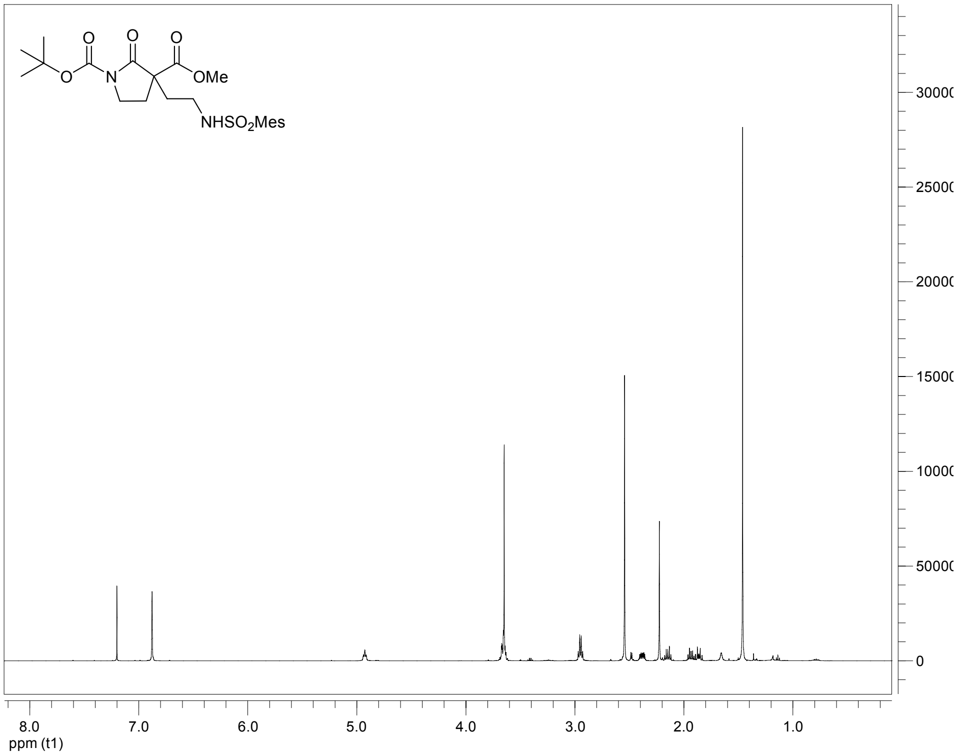
^{1}H NMR of compound **3h**



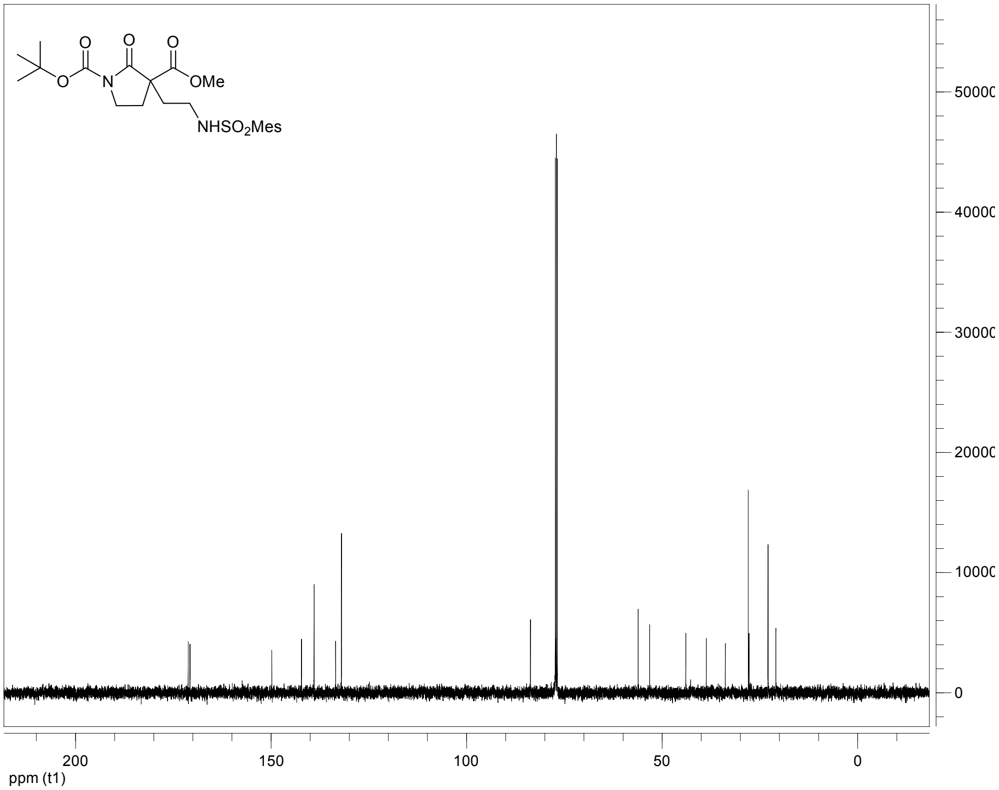
^{13}C NMR of compound **3h**



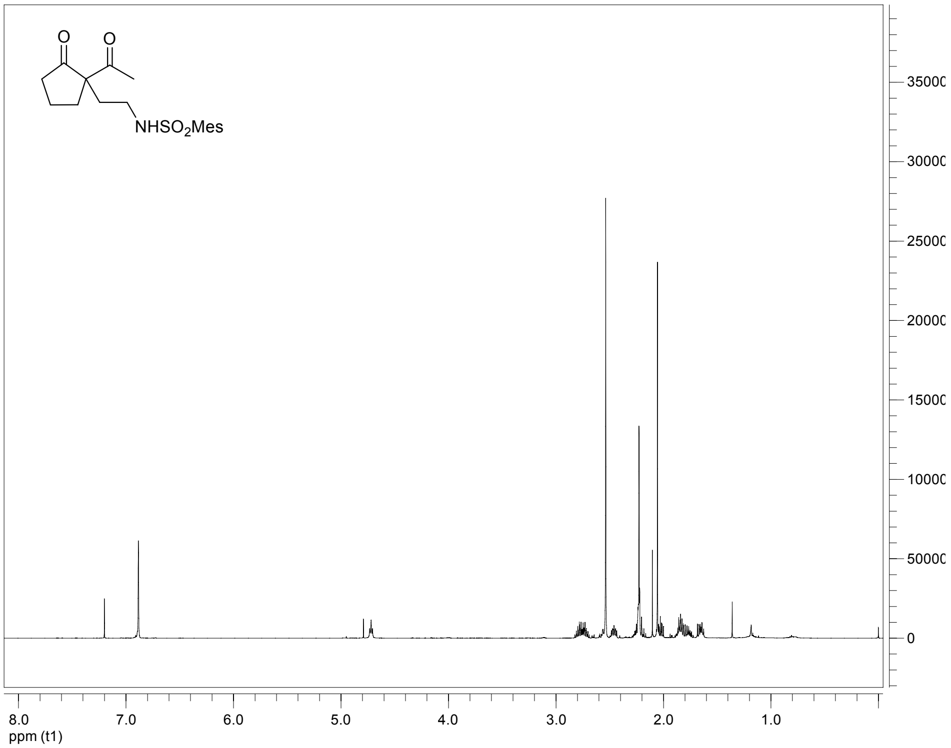
^{1}H NMR of compound **3i**



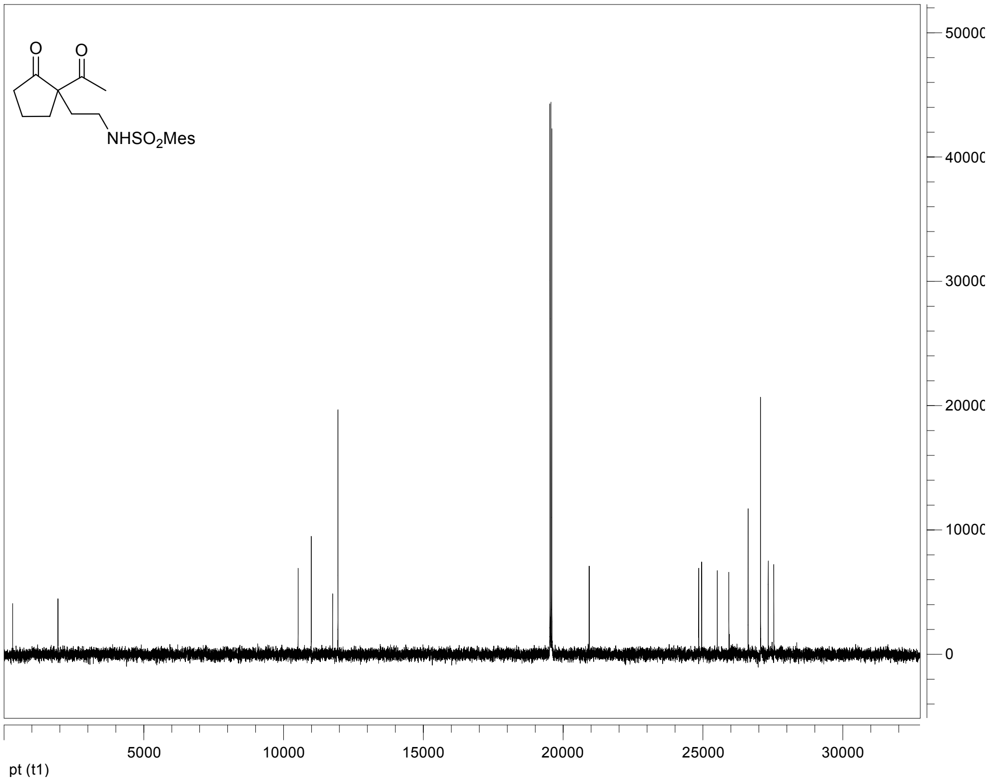
^{13}C NMR of compound **3i**



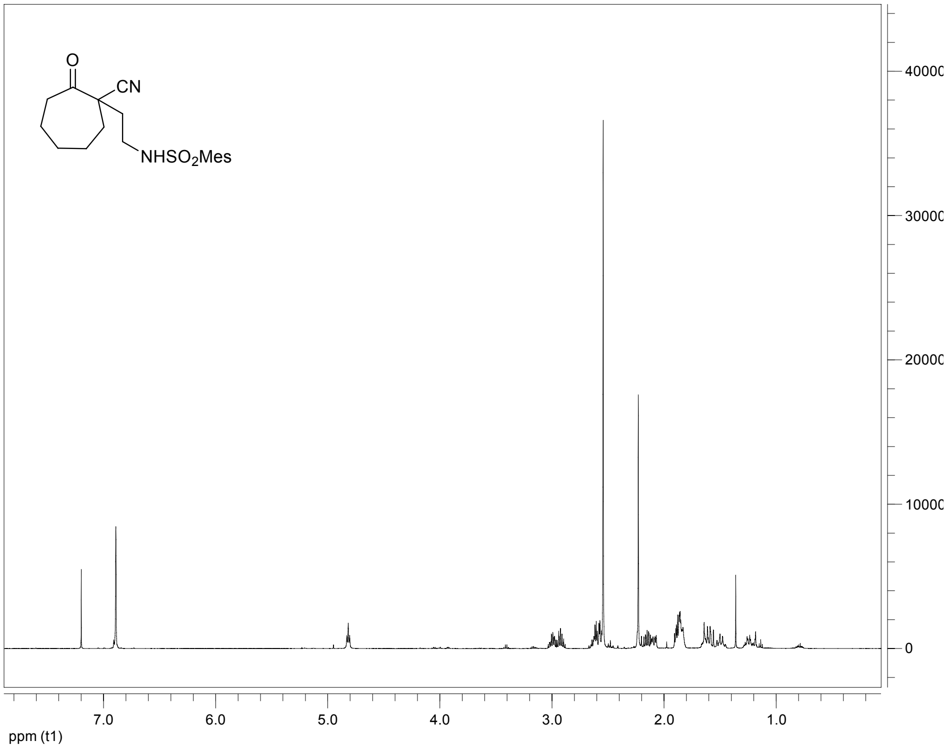
^{1}H NMR of compound **3j**



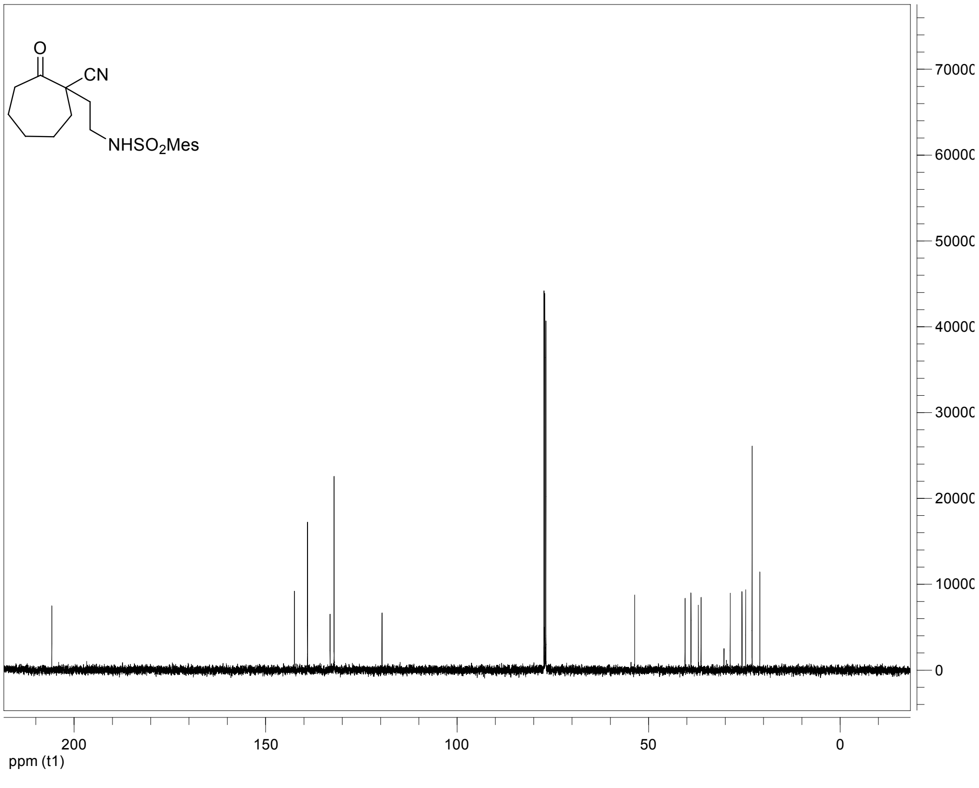
^{13}C NMR of compound **3j**



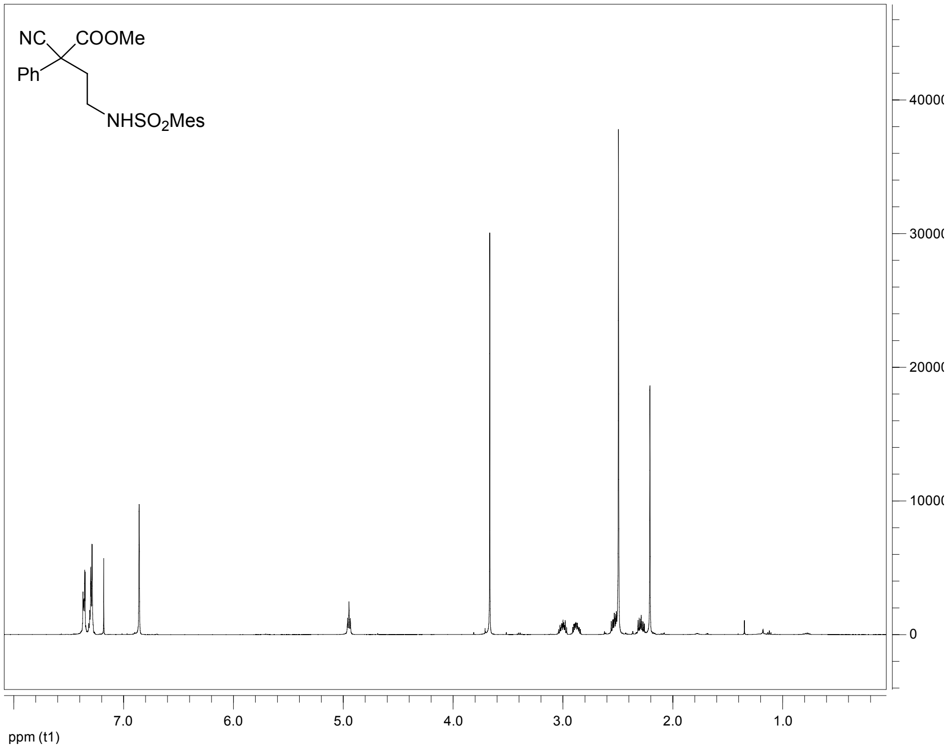
^{1}H NMR of compound **3k**



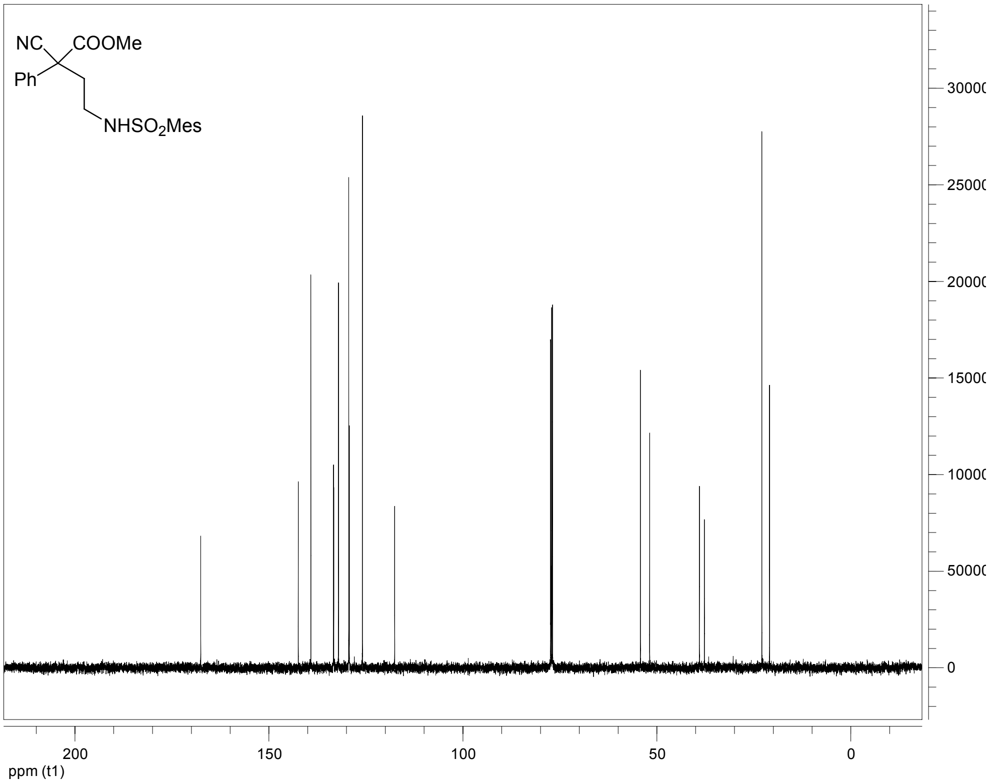
^{13}C NMR of compound **3k**



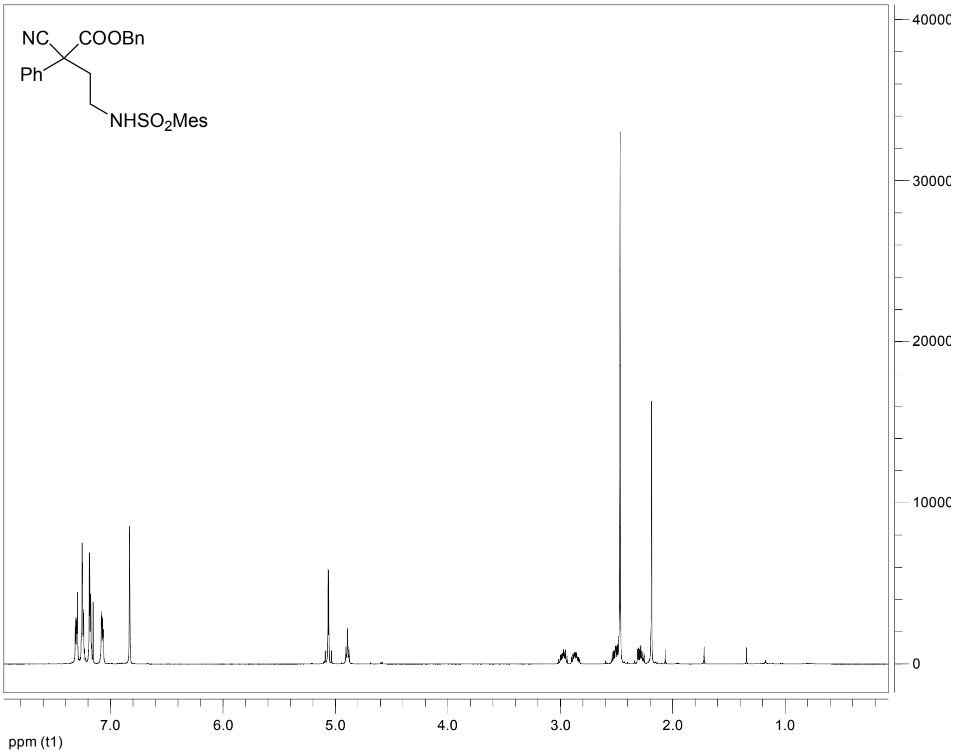
^{1}H NMR of compound **3l**



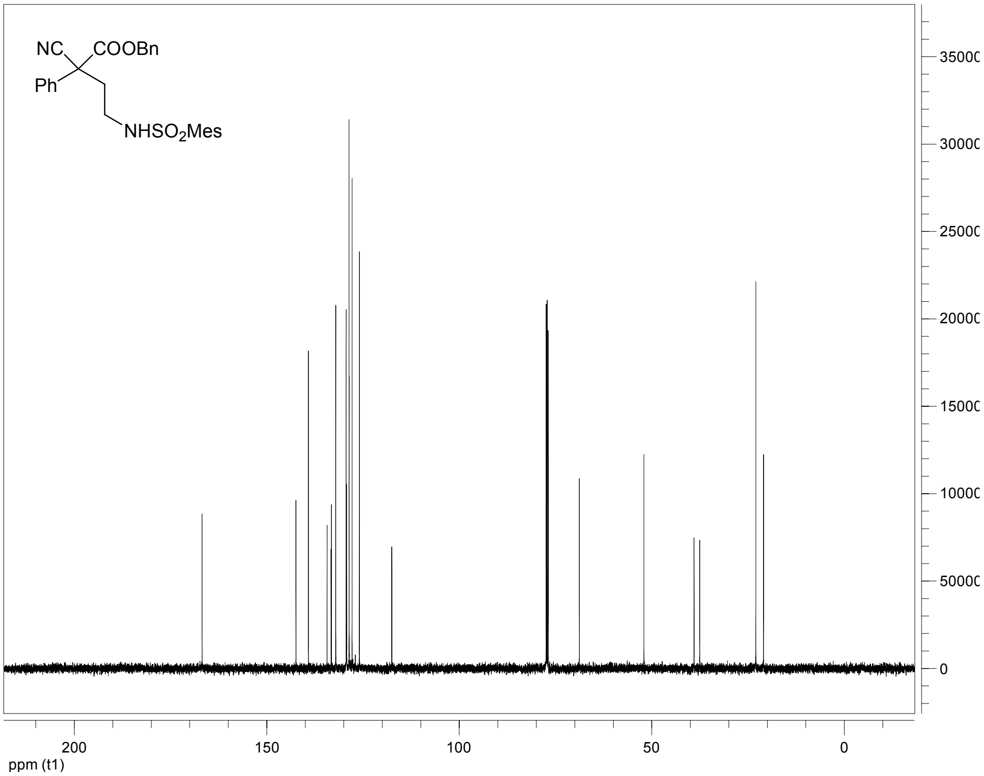
^{13}C NMR of compound **3l**



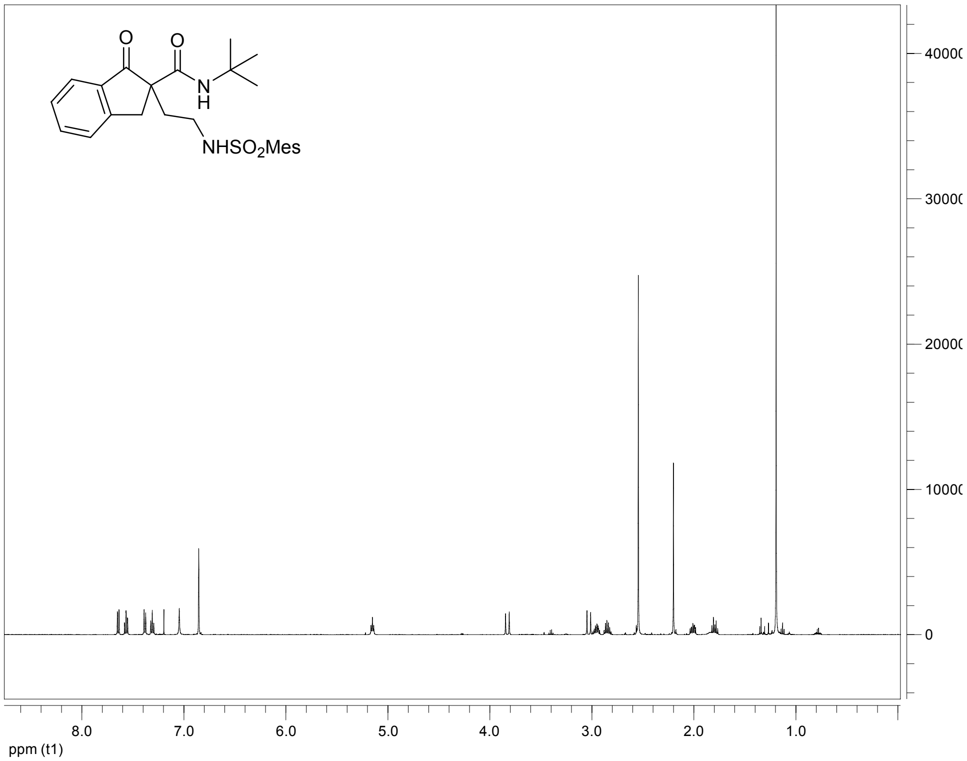
^{1}H NMR of compound **3m**



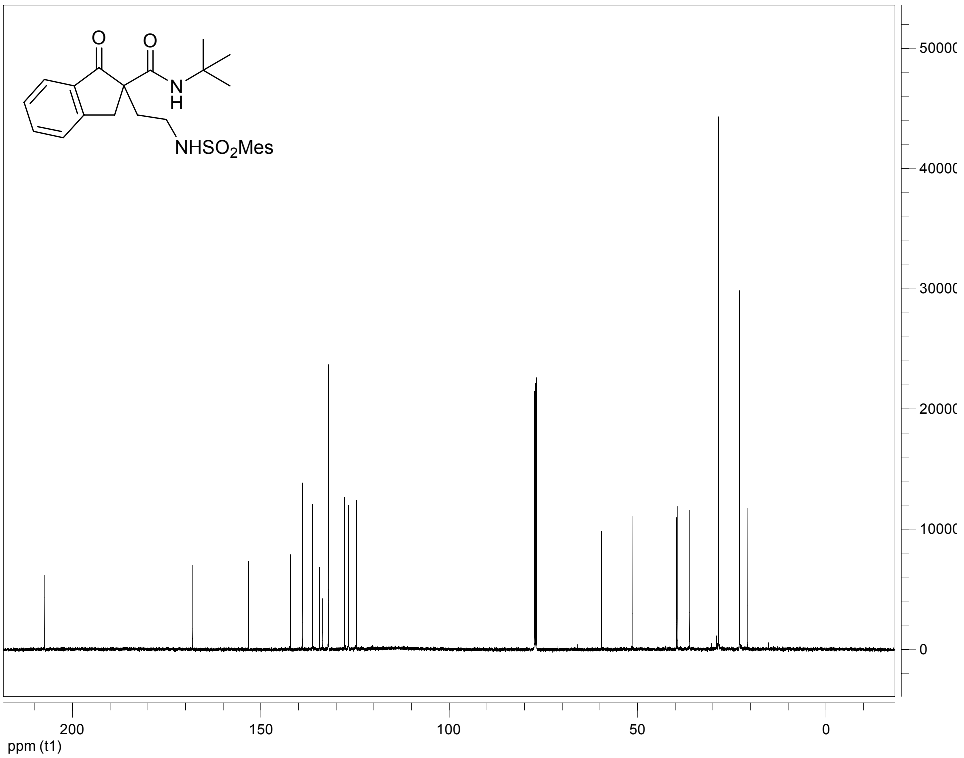
^{13}C NMR of compound **3m**



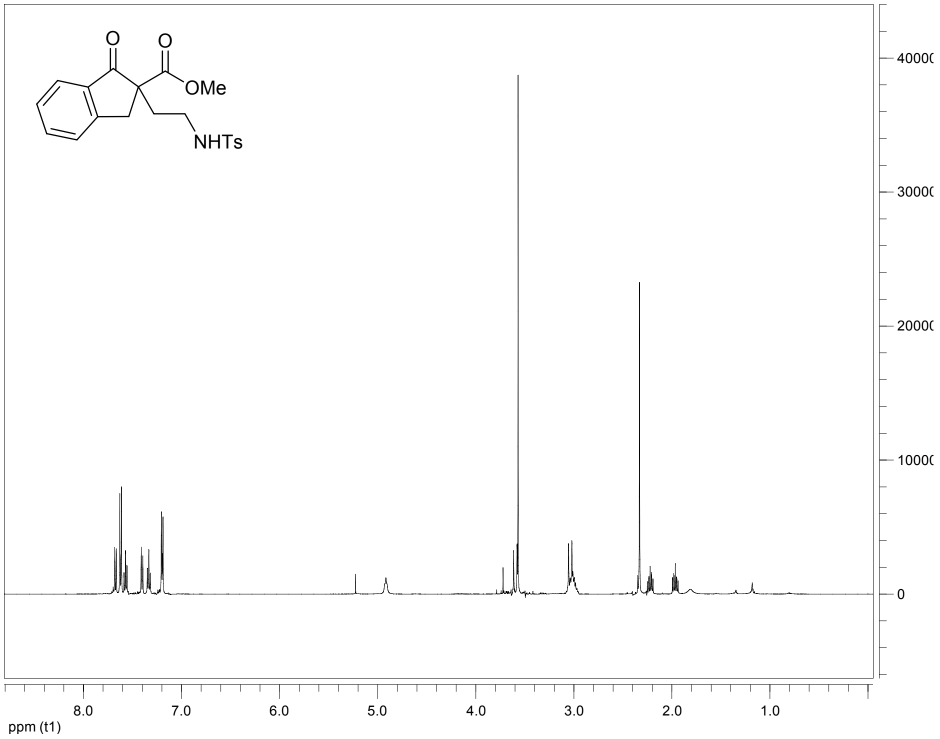
^{1}H NMR of compound **3n**



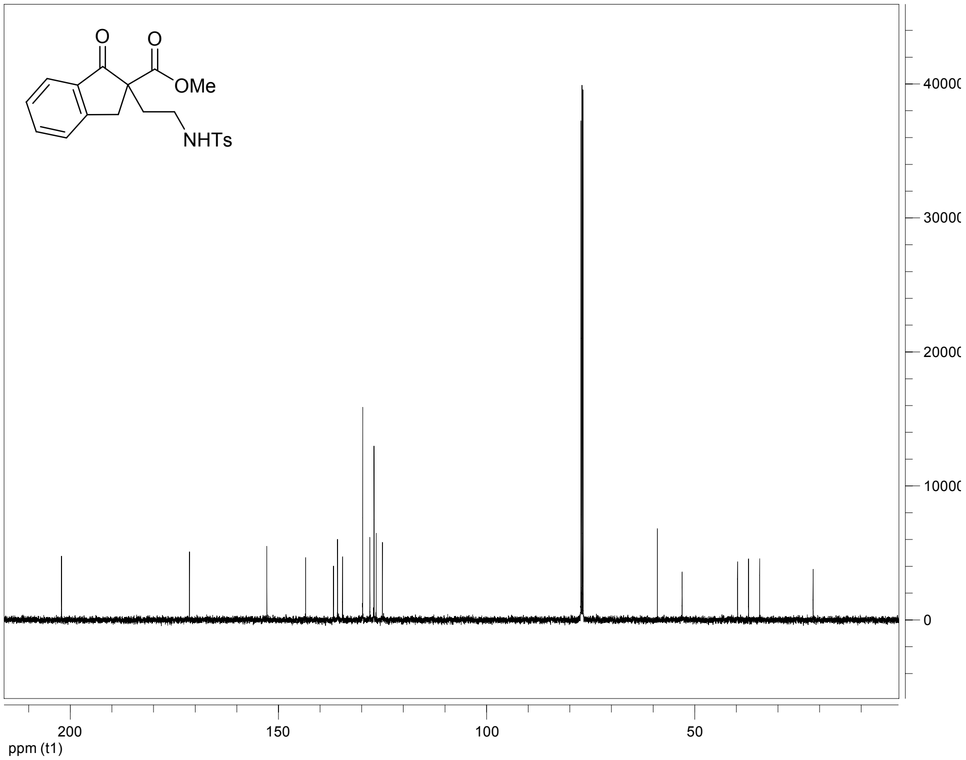
^{13}C NMR of compound **3n**



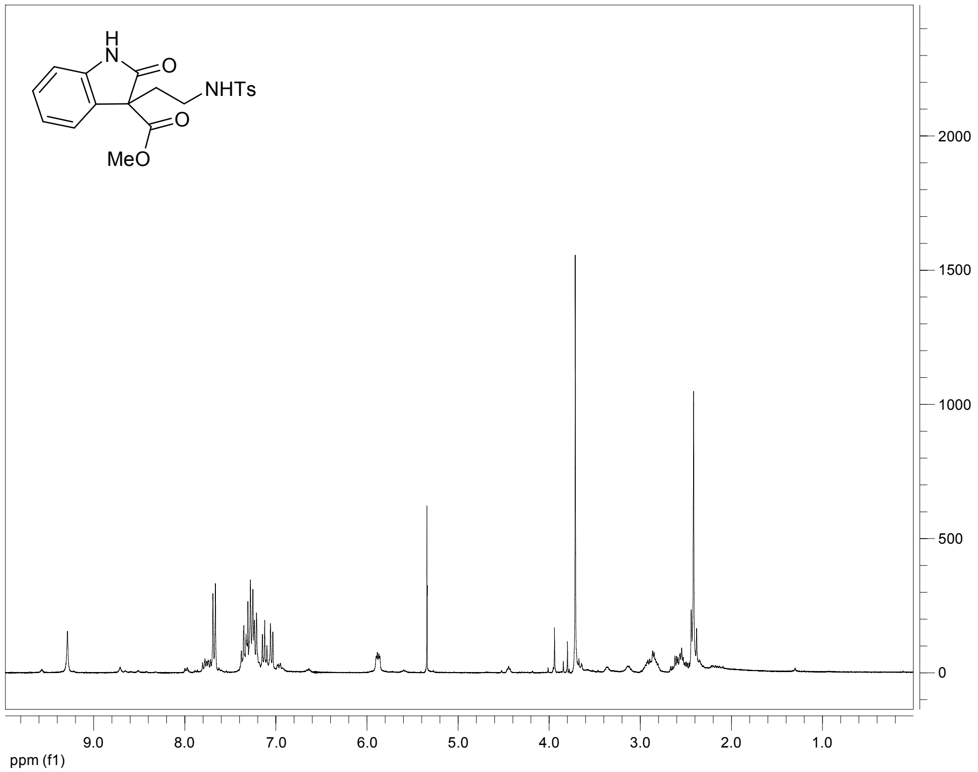
^{1}H NMR of compound **3o**



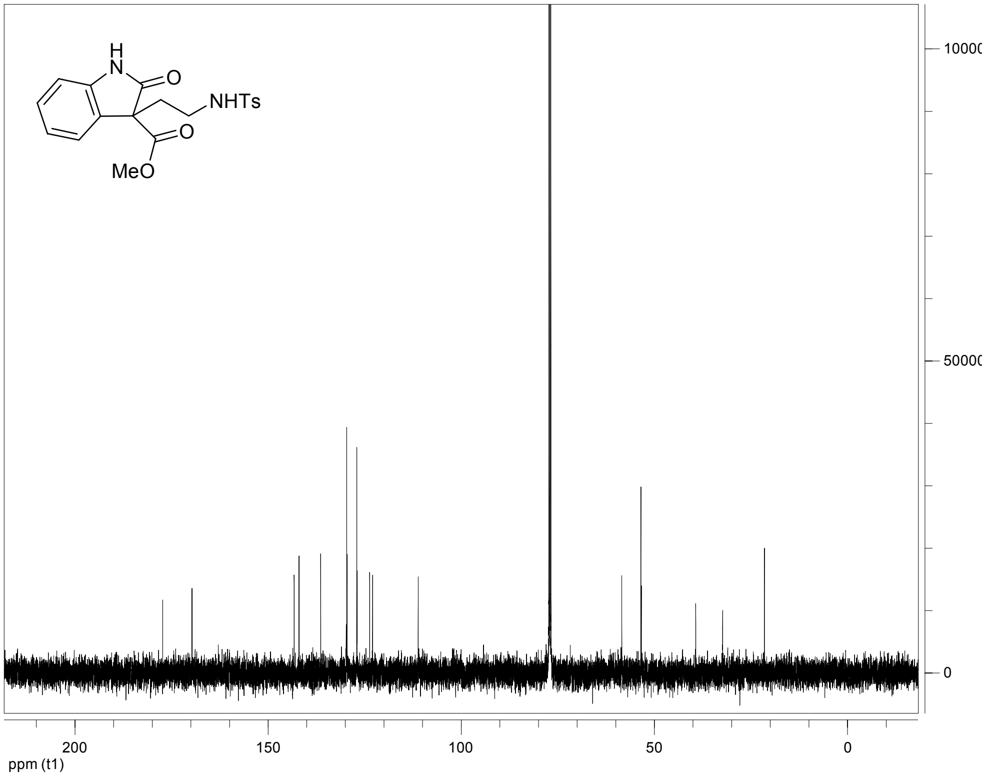
^{13}C NMR of compound **3o**



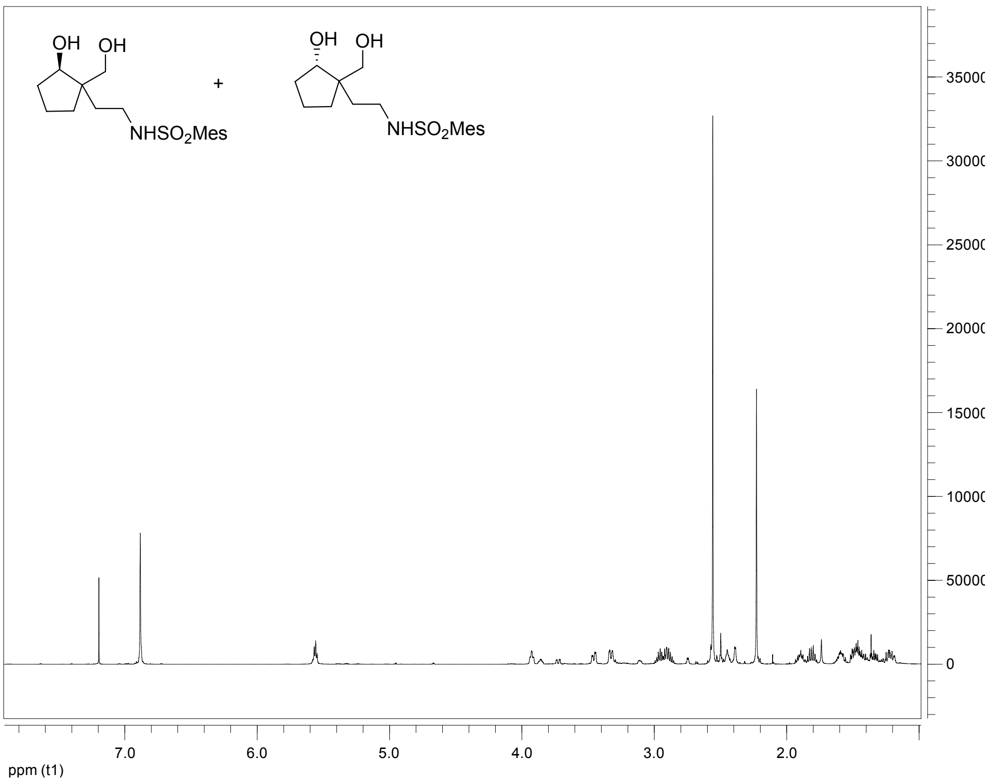
^{1}H NMR of compound **3p**



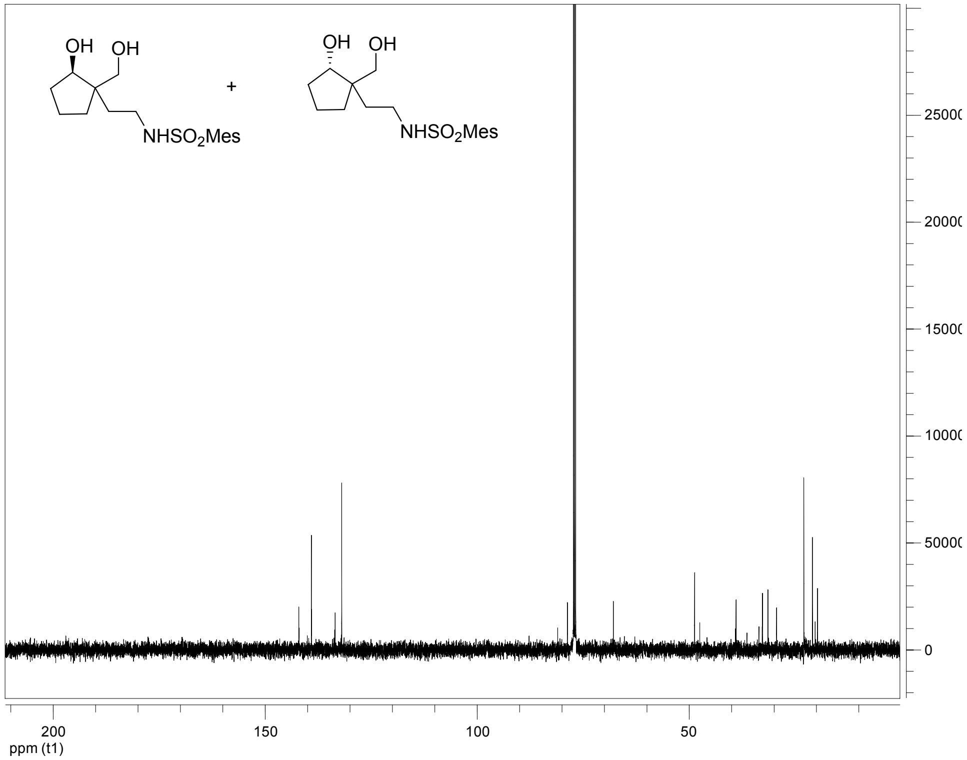
^{13}C NMR of compound **3p**



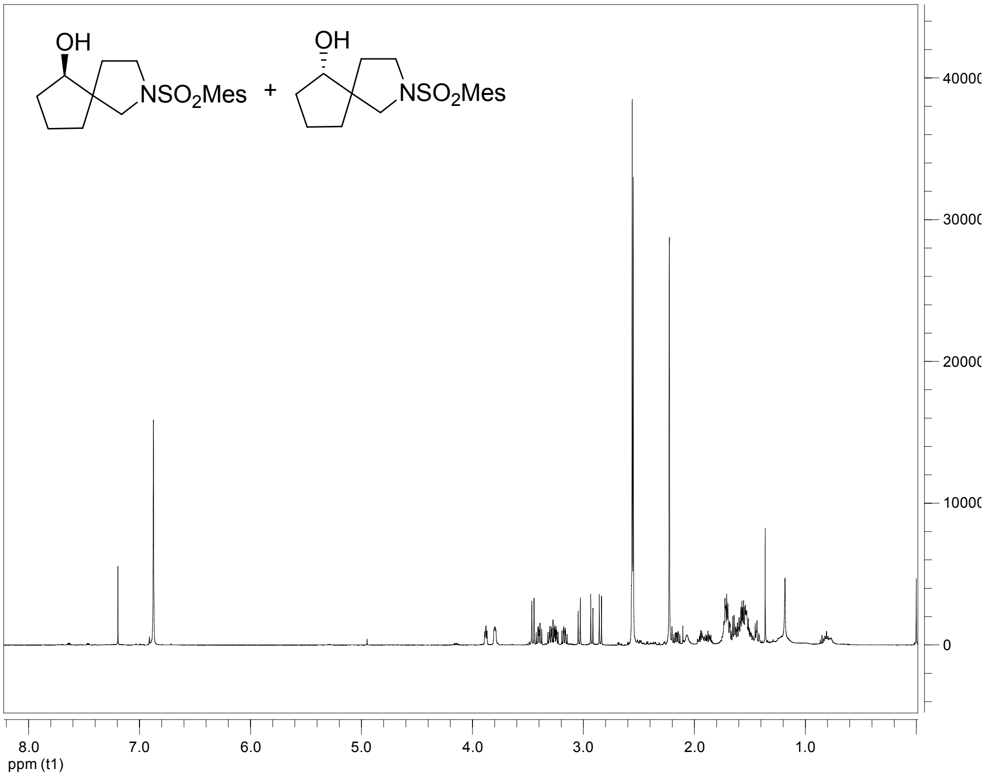
^{1}H NMR of Di-alcohol **6**



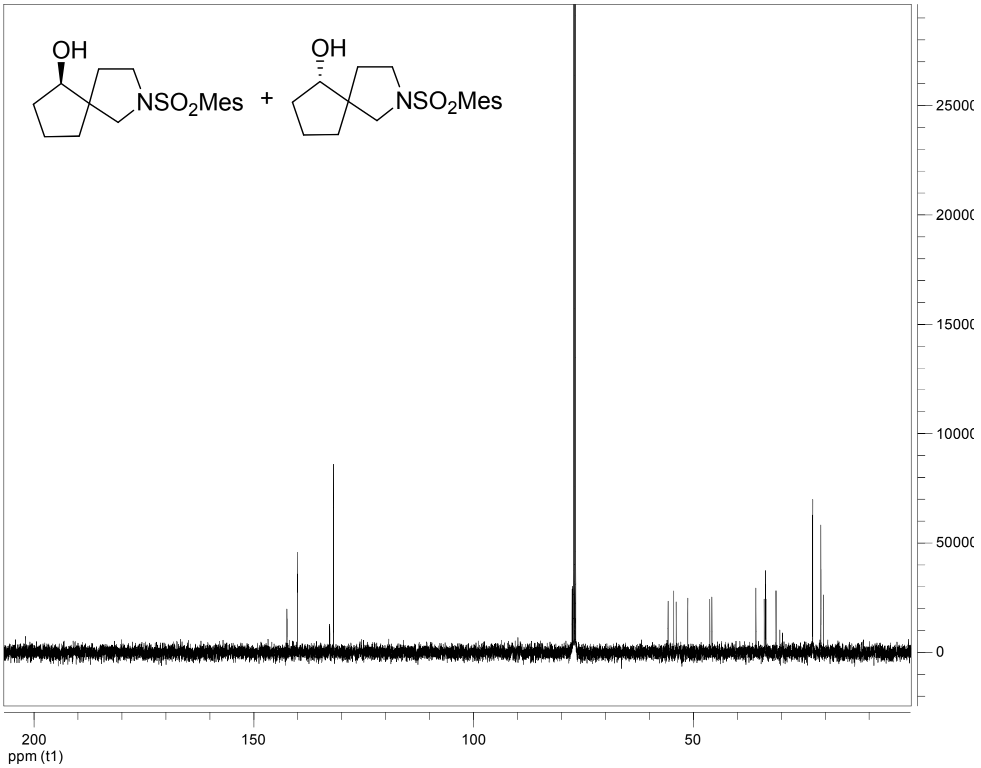
^{13}C NMR of Di-alcohol **6**



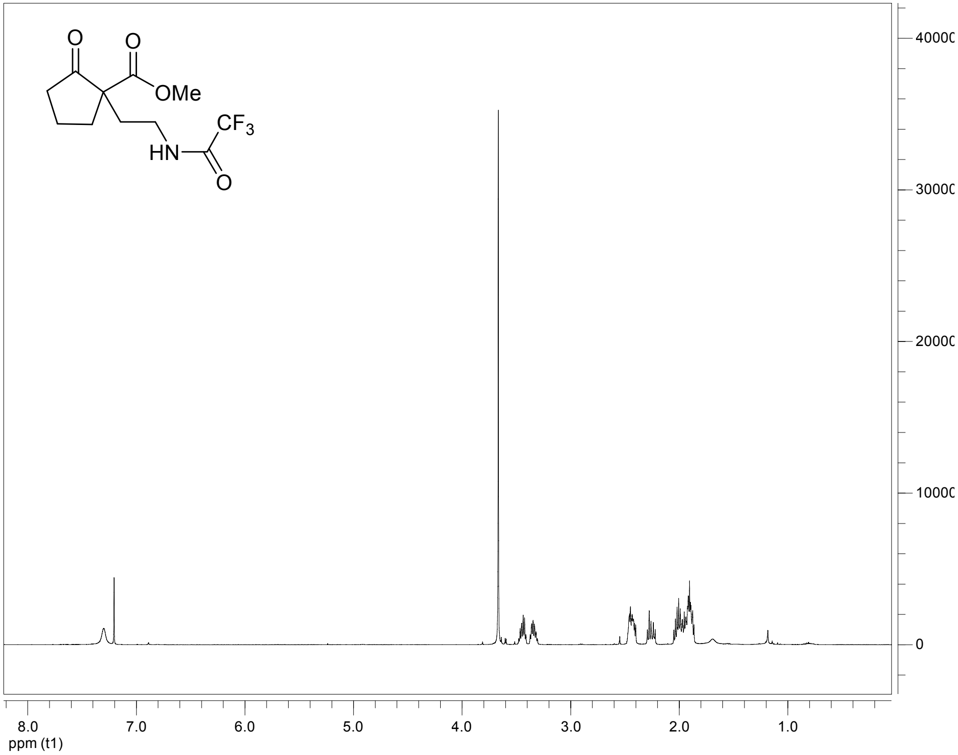
^{1}H NMR of spiro-fused mono alcohol **7**



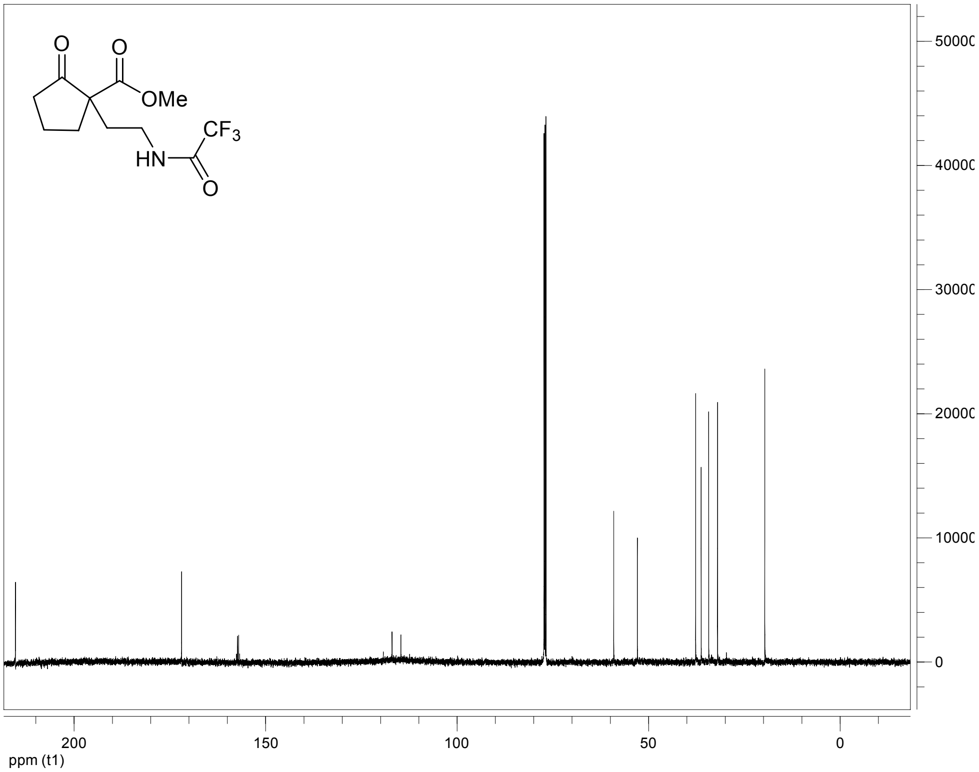
^{13}C NMR of spiro-fused mono alcohol **7**



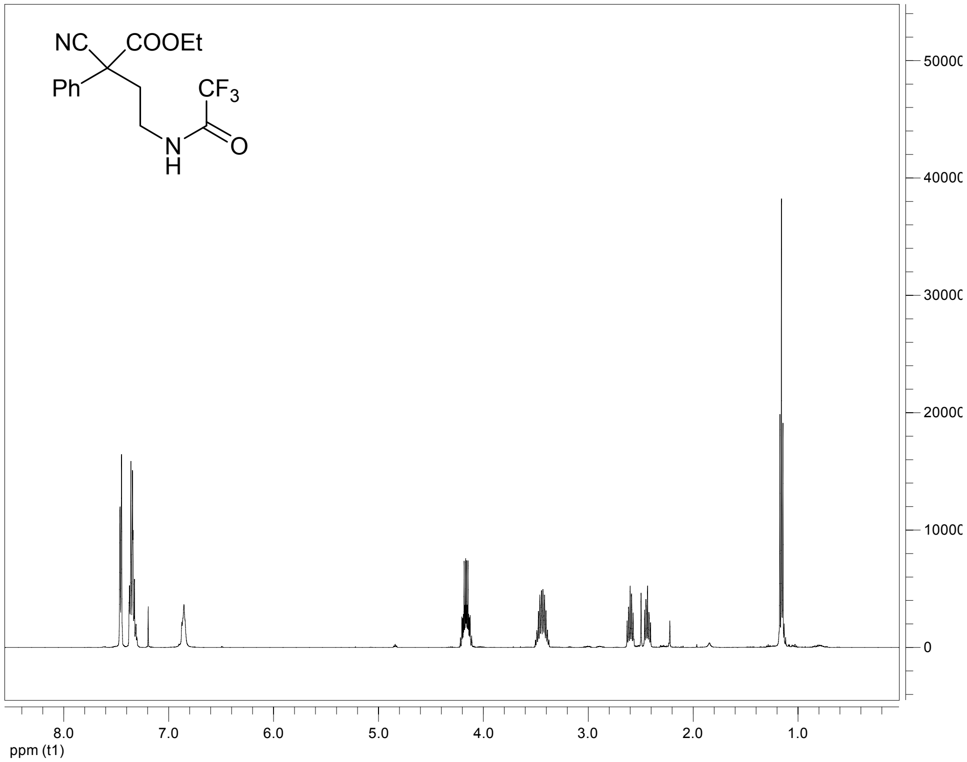
^{1}H NMR compound **8a**



^{13}C NMR of compound **8a**



^{1}H NMR of compound **8b**



^{13}C NMR of compound **8b**