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Facile oxidative cyclization to access C2-quaternary 2-hydroxy-indolin-3-ones: Synthetic studies towards matemone

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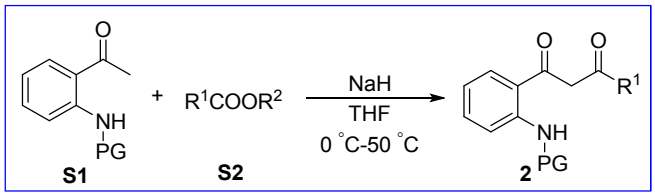
Contents

1. General information

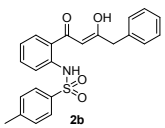
Unless otherwise noted, all the reagents were purchased from commercial suppliers and used without further purification. ^{1}H NMR spectra were recorded at 400 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration. ^{13}C NMR data were collected at 100 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Infrared spectra (IR) were measured by FT-IR apparatus. High resolution mass spectroscopy (HRMS) was recorded on TOF MS ES+ mass spectrometerand acetonitrile and dichloromethane were used to dissolve the sample. Column chromatography was carried out on aluminum oxide (200-300 mesh).

2. Experimental procedures and characterization data

***General Procedure for Synthesis of Diketone* 2b, 2d and 2e**:

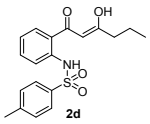


To a solution of 2-amino-acetophenone derivatives (10.0 mmol) in THF (40 mL) was added NaH (1.50 g, 60% dispersion in mineral oil) and the mixture was stirred at r.t. for 10 min. To the mixture was added ester (20.0 mmol) dropwise, and the reaction mixture was heated at 50°C for 4 hours. Then, the mixture was cooled to 0°C, quenched with water, acidified with 3NHCl, and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by silica gel column chromatography (ethyl acetate/petroleum ether = 19:1) to provide the desired diketone **2**.



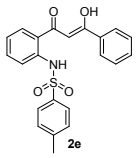
Diketone **2b**: Orange solid (3.39 g, 83% yield); m.p. 144-146°C; IR (KBr) *v* 3063, 1573, 1494, 1163, 921 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, *enolform*) δ (ppm) 15.44 (s, 1H), 10.78 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.64 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.47 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.27-7.42 (m, 6H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.02 (td,

J= 8.0, 0.8 Hz, 1H), 5.90 (s, 1H), 3.64 (s, 2H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 188.2, 181.7, 139.0, 134.6, 131.6, 130.1, 129.2, 124.8, 124.7, 124.5, 124.1, 122.7, 122.5, 118.7, 118.5, 115.9, 92.5, 38.5, 16.8; HR-MS (TOF-ES+) m/z: $[M+H]^+$calcd for $C_{23}H_{22}NO_4S$ 408.1270, found 408.1290.



2d

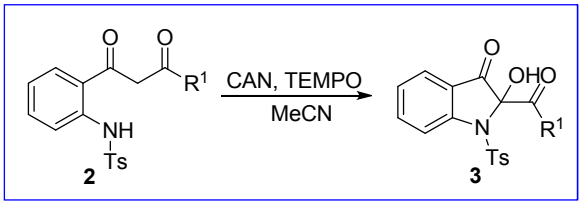
Diketone **2d**: Purple solid (3.48 g, 97% yield); m.p. 70-71^{o}C; IR (KBr) *v* 3063, 2962, 1603, 1576, 1153 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, *enolform*) δ (ppm) 15.46 (s, 1H), 10.75 (s, 1H), 7.65-7.68 (m, 3H), 7.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.42 (td, *J* = 8.4, 1.2 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.06 (td, *J* = 8.0, 1.2 Hz, 1H), 5.92 (s, 1H), 2.28-2.37 (m, 7H), 1.64-1.71 (m, 4H), 0.91-1.01 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 193.2, 188.84, 143.7, 139.2, 136.4, 133.7, 129.6, 129.3, 124.0, 123.4, 121.1, 97.0, 38.7, 21.5, 19.8, 13.7; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{19}H_{21}NO_4SNa$ 382.1089, found 382.1106.



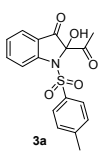
2e

Diketone **2e**: Yellow solid (3.42 g, 87% yield); m.p. 164-165^{o}C; IR (KBr) *v* 3196, 1489, 1158, 909, 763 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz, *enol form*) δ (ppm) 16.00 (s, 1H), 10.44 (s, 1H), 7.89 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.49-7.71 (m, 8H), 7.10-7.16 (m, 3H), 6.46 (s, 1H), 2.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 193.4, 179.8, 143.8, 138.6, 136.0, 133.6, 133.5, 132.8, 129.6, 129.1, 128.9, 127.2, 126.9, 125.7, 124.1, 122.4, 94.6, 21.3; HR-MS (TOF-ES+) m/z: $[M+H]^+$calcd for $C_{22}H_{20}NO_4S$394.1113, found 394.1111.

***General Procedure of Oxidative Cyclization for the synthesis of 3a-3e*:**



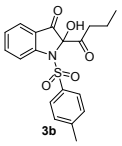
To a solution of 1,3-dicarbonyl substrate (0.5 mmol) in MeCN (5 mL) was added ceric ammonium nitrate (CAN, 548 mg, 1.0 mmol, 2.0 equiv.) and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 94 mg, 0.6 mmol, 1.2 equiv.). And the mixture was stirred at r.t. for the given time. After completion of the reaction monitored by TLC, the mixture was filtered and the filtrate was concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:9-1:5) to provide indolin-3-one **3a-3e**.



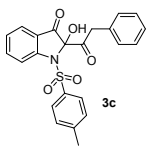
3a

2-Acetyl-2-hydroxy-1-tosylindolin-3-one **3a**: Yellow solid (63% yield); m.p. 89-90^{o}C; IR (KBr) *v* 3587, 3473, 3089, 1748, 1602, 1354, 1153 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500

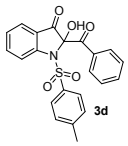
MHz) δ (ppm) 8.00 (d, J = 8.0 Hz, 2H), 7.67-7.76 (m, 3H), 7.33 (d, J = 8.0 Hz, 2H), 7.20-7.23 (m, 1H), 5.78 (s, 1H), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 197.6, 191.6, 152.6, 145.2, 138.6, 135.7, 129.8, 128.1, 125.9, 124.2, 120.8, 114.2, 91.8, 23.2, 21.7; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{17}H_{15}NO_5SNa$ 368.0569, found 368.0567.



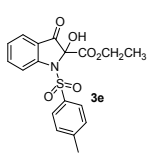
Indolin-3-one **3b**: Amber oil (57% yield); IR (KBr) ν 2967, 1743, 1601, 1359, 1164 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.98 (d, J = 8.4 Hz, 2H), 7.64-7.73 (m, 3H), 7.30 (d, J = 8.4 Hz, 2H), 7.19 (t, J = 7.6 Hz, 1H), 5.86 (s, 1H), 2.90-2.98 (m, 1H), 2.40 (s, 3H), 2.19-2.27 (m, 1H), 1.69-1.76 (m, 2H), 0.91 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 200.2, 191.9, 152.6, 145.2, 138.5, 135.5, 129.8, 128.3, 125.8, 124.1, 120.8, 114.1, 91.6, 37.7, 16.9, 13.4; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{19}H_{19}NO_5SNa$ 396.0882, found 396.0873.



Indolin-3-one**3c**: Yellow solid (67% yield); m.p. 143-145^{o}C; IR (KBr) ν 3390, 1748, 1599, 1464, 1342, 951 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.99 (d, J = 8.4 Hz, 2H), 7.61-7.70 (m, 2H), 7.54 (d, J = 7.6 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 7.11-7.18 (m, 6H), 5.80 (s, 1H), 4.22 (d, J = 16.8 Hz, 1H), 3.87 (d, J = 17.2 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 198.7, 191.0, 152.2, 145.3, 138.2, 135.4, 130.8, 130.5, 129.8, 128.5, 128.2, 127.5, 125.8, 124.0, 120.7, 114.0, 91.6, 43.5, 21.7; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{23}H_{19}NO_5SNa$ 444.0882 , found 444.0883.



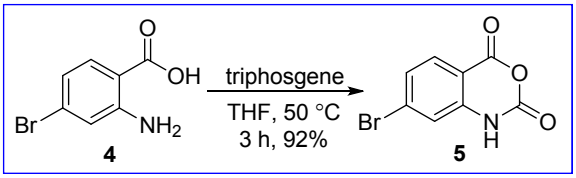
Indolin-3-one **3d**: White solid (70% yield); m.p. 157-159 ^{o}C; IR (KBr) ν 3352, 1735, 1688, 1599, 1493 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.97 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 7.6 Hz, 2H), 7.78 (d, J = 8.0 Hz, 1H), 7.70 (dd, J = 8.0, 1.2 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 7.6 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 7.21-7.26 (m, 1H), 6.47 (s, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 191.6, 190.9, 152.0, 145.2, 138.4, 135.6, 134.6, 131.6, 129.8, 129.1, 129.0, 128.3, 126.2, 124.4, 120.7, 114.5, 90.3, 21.6; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{22}H_{17}NO_5SNa$ 430.0725, found 430.0714.



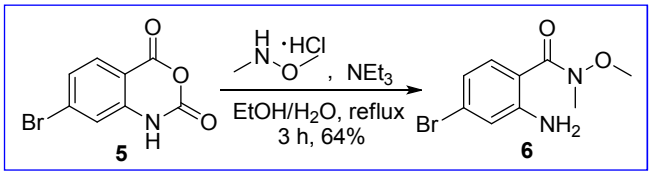
Indolin-3-one **3e**: White solid (99% yield); m.p. 141-142^{o}C; IR (KBr) ν 3402, 1762, 1729, 1599, 1463, 1145 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.01 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 7.6 Hz, 1H), 7.54-7.66 (m, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.17 (td, J = 8.0, 1.2 Hz, 1H), 5.34 (s, 1H), 4.30-4.50 (m, 2H), 2.43 (s, 3H), 1.28-1.36 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 191.2, 167.2, 152.3, 145.1, 138.3, 136.0, 129.9, 128.0,

125.8, 123.8, 120.1, 113.7, 87.2, 64.5, 21.7, 13.9; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{18}H_{17}NO_6SNa$ 398.0674 , found 398.0658.

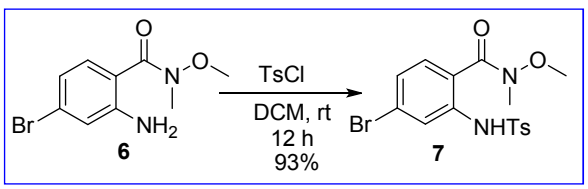
Synthethesis for the Core Structure of Metamone:



4-Bromoisatoic anhydride**5**was prepared as the reported procedure[1]: To a solution of 4-bromoanthranilic acid (**4**, 2.16 g, 10.0 mmol) in 50 mL of THF was added triphosgene (1.00 g, 3.4 mmol). The mixture was heated at 50°C for 3 hours. Then the reaction mixture was allowed to cool to room temperature. The solution was concentrated *in vacuo* and *n*-hexane was added. The precipitate was filtered, washed by *n*-hexane and dried to give the crude product as a tan powder (2.23 g, 92% yield), which was used without further purification.

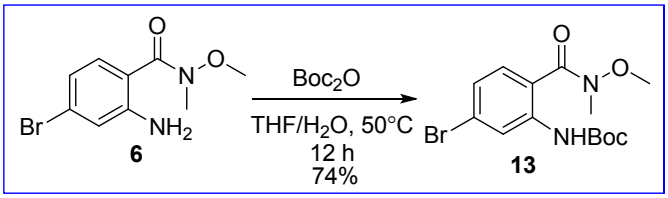


2-Amino-4-bromo-*N*-methoxy-*N*-methylbenzamide**6**was prepared as the reported procedure[2]:To a solution of *N*,*O*-dimethylhydroxylamine hydrochloride (0.91 g, 9.3 mmol) in 12 mL of 90% aqueous ethanol was added triethylamine (0.94 g, 9.3 mmol). After 10 min of stirring at room temperature, isatoic anhydride (1.50 g, 6.2 mmol) was added in portions. Then the mixture was refluxed for 2 hours and poured into 20 mL of mixture of ice and saturated sodium bicarbonate. And ethanol was removed *in vacuo*, and the remains were extracted with ethyl acetate (3 × 20 mL), and the organic layers werecombined, washed with water (20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give crude product as an amber oil (1.03 g, 64% yield). The crude product was also used without further purification.

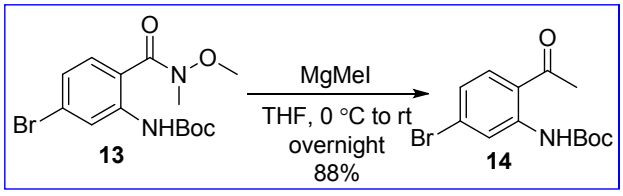


A solution of **6** (0.78g, 3.0 mmol), TsCl (1.72 g, 9.0 mmol, 3.0 equiv.) and pyridine (145 μL,

1.8 mmol, 0.6 equiv.) in DCM (40 mL) was stirred overnight. Then, the mixture was washed with saturated copper sulfate solution (3 × 40 mL), and brine (50 mL). The organic layer was dried over Na_2SO_4, concentrated *in vacuo*, and the residue was purified *via*silica gel column chromatography (ethyl acetate/petroleum ether = 1:19) to provide tosyl-protected product **7**as colorless oil (1.15 g, 93% yield). IR (KBr) *v*3200, 1617, 1584, 1488, 1163, 668 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 9.10 (*br* s, 1H), 7.85 (d, *J* = 1.6 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 10.4 Hz, 2H), 7.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 3.22 (s, 3H), 3.17 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 167.2, 144.0, 138.3, 136.5, 130.5, 129.7, 127.3, 126.7, 125.9, 125.2, 121.2, 61.0, 33.4, 21.5; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{16}H_{17}N_2O_4SBrNa$ 434.9990, found 434.9990.



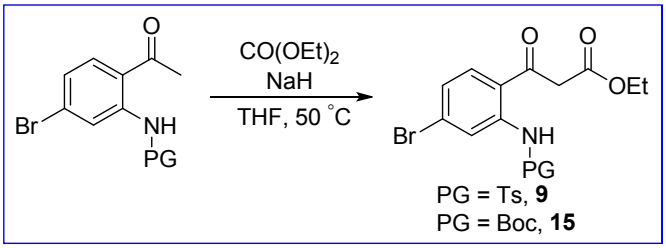
A solution of crude product **6** (0.78g, 3.0 mmol), Boc_2O (1.96 g, 9.0 mmol, 3.0 equiv.) and NaOH (0.24 g, 6.0 mmol, 2.0 equiv.) in THF/H_2O (1:1, 6 mL) was stirred at 60 ^{o}Covernight. After the completion, the mixture was acidified by HCl (3N) andwashed with ethyl acetate (3 × 10 mL). The collected organic layer was washed with brine(10 mL), dried over Na_2SO_4, and concentrated *in vacuo*.The residue was purified *via*silica gel column chromatography (EtOAc/petroleum ether = 1:9) to provide Boc-protected product **13**as yellowish oil (0.80 g, 74% yield). IR (KBr) *v*3354, 1734, 1627, 1585, 1569, 1505, 1152 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm)8.62 (s, 1H), 8.49 (s, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.13 (dd, *J* = 8.4, 2.0 Hz, 1H), 3.55 (s, 3H), 3.37 (s, 3H), 1.51 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 168.2, 152.5, 139.7, 130.1, 126.0, 124.4, 122.8, 118.7, 81.0, 61.5, 34.0, 28.3; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{14}H_{19}N_2O_4BrNa$ 381.0426, found 381.0442.



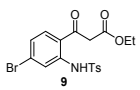
To a solution of **13** (2.4 mmol) in THF (30 mL) was added 2.4 mL of 3M methylmagnesiumiodide (in diethyl ether) by syringe at 0^{o}C. After the addition, the mixture was

allowed to warm to room temperature and be stirred overnight. When the reaction was completed as monitored by TLC, the mixture was quenched with saturated ammonium chloride solution (30 mL), extracted with ethyl acetate (3 × 30 mL), and the organic layers were washed with brine (50 mL), dried over Na_2SO_4, and concentrated *in vacuo*. And the residue was purified by silica gel column chromatography (EtOAc/petroleum ether = 1:9-1:3) to provide 4'-Bromo-2'-(*N*-*tert*-butyloxylcarbonyl-aminoacetophenone(**14**) as colorless oil (0.66 g, 88% yield); IR (KBr) ν 3448, 2981, 1664, 1246, 1158, 743cm-1; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 11.00 (s, 1H), 8.74 (d, J = 2.0 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.15 (dd, J = 8.4, 2.0 Hz, 1H), 2.61 (s, 3H), 1.53 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 201.5, 152.8, 142.8, 132.7, 130.1, 124.1, 122.0, 119.8, 81.0, 28.5, 28.2.

***Experimental Procedure of Acylation*:**



To a solution of protected 2'-amino-4'-bromoacetophenone (2.0mmol) in THF (10 mL) was added NaH (0.40 g, 60% dispersion in mineral oil) and the mixture was stirred at r.t. for 10 min. To the mixture was added diethyl oxalate (4.0 mmol) dropwise, and the reaction mixture was heated at 50^{o}C for 4 hours. After completion, the mixture was cooled to 0^{o}C, quenched with water, acidified with 3NHCl, and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated*in vacuo*, and purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1:19) to provide the desired ketoester.



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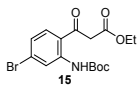
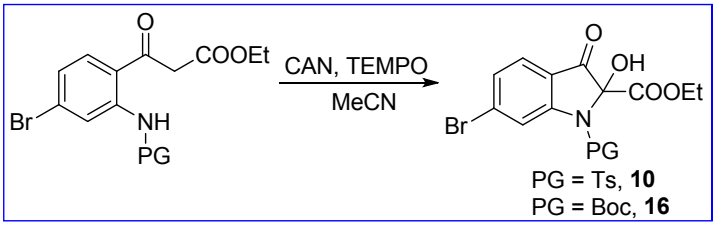
Ketoester **9**:Crimson oil (0.62g, 70% yield);IR (KBr) *v*2982, 1732, 1645, 1595, 1159 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 11.28 (s, 1H), 7.91 (d, J = 1.6 Hz, 1H), 7.78 (d, J = 8.4 Hz, 2H), 7.56 (d, J = 8.8 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 7.18 (dd, J = 8.8, 2.0 Hz, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.90 (s, 2H), 2.39 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 195.8, 166.6, 144.5, 141.7, 136.1, 132.6, 130.8, 129.9, 127.4, 125.7, 121.6, 119.6, 61.9, 47.1, 21.6, 14.0; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{18}H_{18}NO_5SBrNa$ 461.9987, found 462.0009.



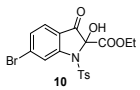
15

Ketoester **15**:White solid(0.54 g, 70% yield);m.p.: 69-70°C;IR (KBr) *v*2984, 1734, 1656, 1571, 1511, 1149 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 10.81 (s, 1H), 8.79 (d, J = 1.6 Hz, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.17 (dd, J = 8.8, 1.6 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.98 (s, 2H), 1.52 (s, 9H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 195.6, 167.1, 152.7, 143.4, 132.3, 131.1, 124.3, 122.2, 118.8, 81.3, 61.8, 47.8, 28.2, 14.1; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{16}H_{20}NO_5BrNa$ 408.0423, found 408.0419.

***Experimental Procedure for Oxidative Cyclization*:**

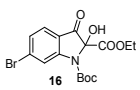


To a solution of ketoester (0.5 mmol) in MeCN (5 mL) was added ceric ammonium nitrate (548 mg, 1.0 mmol) and 2,2,6,6-tetramethylpiperidinooxy (94 mg, 0.6 mmol). The mixture was stirred at r.t. for the given time.Then, the solvent was removed *in vacuo* and the residue was purified *via* silica gel column chromatography (ethyl acetate/petroleum ether =1:19-1:9) to provide the corresponding indolin-3-one.



10

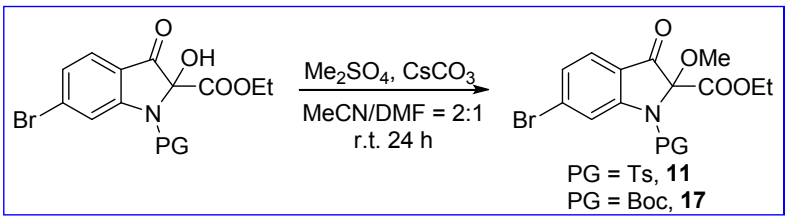
Indolin-3-one**10**:Pink solid (210 mg, 92% yield);m.p.: 140-141°C;IR (KBr) *v*3425, 1757, 1598, 1364, 1162 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.97 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 1.6 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.29 (dd, J = 8.4, 1.6 Hz, 1H), 5.34 (s, 1H), 4.27-4.48 (m, 2H), 2.43 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 190.1, 166.8, 152.7, 145.4, 135.7, 134.0, 130.0, 127.9, 127.5, 126.6, 119.0, 117.2, 87.6, 64.6, 21.7, 13.9; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{18}H_{16}NO_6SBrNa$ 475.9779, found 475.9756.



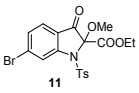
16

Indolin-3-one**16**:Colorless oil (194 mg, 97% yield);IR (KBr) ν 3450, 1726, 1633, 1429, 1263, 570 cm-1; ^1H NMR (DMSO-d_6, 400 MHz) δ (ppm) 8.28 (s, 1H), 7.93 (s, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.48 (dd, J = 8.4, 1.6 Hz, 1H), 4.09-4.24 (m, 2H), 1.49 (s, 9H), 1.13 (t, J = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm) 192.4, 165.7, 149.7, 133.2, 127.5, 126.9, 119.4, 118.9, 87.7, 84.1, 62.6, 28.0, 14.4; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{16}H_{18}NO_6BrNa$ 422.0215, found 422.0255.

***Experimental Procedure of Methylation*[3]:**

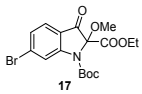


To a solution of protected indolin-3-one(0.5 mmol) in CH_3CN/DMF (2:1, 3.6 mL) was added Cs_2CO_3 (570 mg, 1.75 mmol) and Me_2SO_4 (48 μL, 1.75 mmol). The reaction was stirred at room temperature for 24 hours. After completion, the solvent was removed *in vacuo* and the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = -1:9-1:5) to provide the desired product.



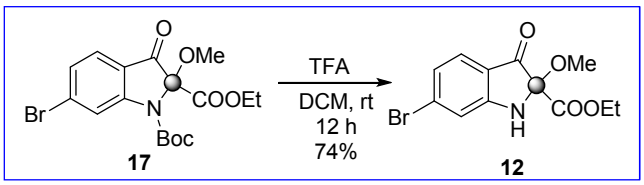
11

Indolin-3-one**11**: White solid (218 mg, 93% yield);m.p.: 161-162^{o}C;IR (KBr) ν2969, 1725, 1596, 1425, 1098, 948 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.06 (d, J = 1.2 Hz, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.32 (dd, J = 8.0, 1.2 Hz, 1H), 4.22-4.38 (m, 2H), 2.90 (s, 3H), 2.45 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 190.0, 163.6, 153.7, 145.5, 136.1, 134.3, 130.0, 127.6, 127.3, 126.1, 119.6, 117.2, 93.3, 63.2, 52.8, 21.7, 13.9; HR-MS (TOF-ES+) m/z: [M+Na]$^+$calcd for $C_{19}H_{18}NO_6SBrNa$ 489.9936, found 489.9921.



17

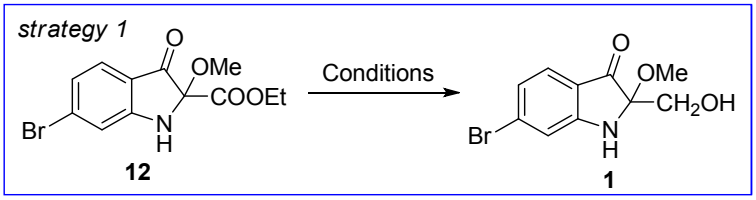
Indolin-3-one**17**: Colorless oil (163 mg, 79% yield);IR (KBr) ν2981, 1777, 1725, 1600, 1428, 1354, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.49 (s, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 4.18-4.30 (m, 2H), 3.30 (s, 3H), 1.55 (s, 9H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 191.3, 163.8, 154.3, 149.8, 134.1, 127.3, 125.4, 119.94, 119.88, 91.4, 84.3, 62.8, 52.2, 28.0, 14.0; HR-MS (TOF-ES+) m/z: [M+Na]$^+$calcd for $C_{17}H_{20}NO_6BrNa$ 436.0372, found 436.0373.



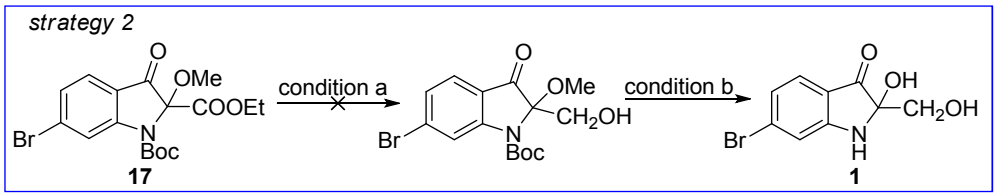
A solution of Boc-protected indolin-3-one**17**(124 mg, 0.3 mmol) in DCM (6 mL) was added trifluoroacetic acid (225 μL, 3.0 mmol). The reaction mixture was stirred at room temperature overnight. After completion, the mixture was allowed to cool to 0^{o}C, acidified by aqueous ammonia, and washed with ethyl acetate(3 × 20 mL). The combined organic layers were washed

with brine (30 mL), dried over anhydrous Na_2SO_4, concentrated*in vacuo*, and purified *via* silica gel column chromatography (ethyl acetate/petroleum ether = 1:9-1:5) to provide deprotectedindolin-3-one**12**as yellow oil (70 mg, 74% yield).IR (KBr) *v*3335, 1751, 1716, 1607, 1451, 914 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.45 (d, J = 8.4 Hz, 1H), 7.18 (s, 1H), 7.07 (dd, J = 8.0, 1.2 Hz, 1H), 5.41 (s, 1H), 4.25-4.35 (m, 2H), 3.35 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 193.0, 166.0, 160.9, 134.0, 126.2, 124.6, 118.4, 116.4, 91.7, 63.4, 52.1, 14.0; HR-MS (TOF-ES+) m/z: $[M+Na]^+$calcd for $C_{12}H_{12}NO_4BrNa$ 335.9847, found 335.9846.

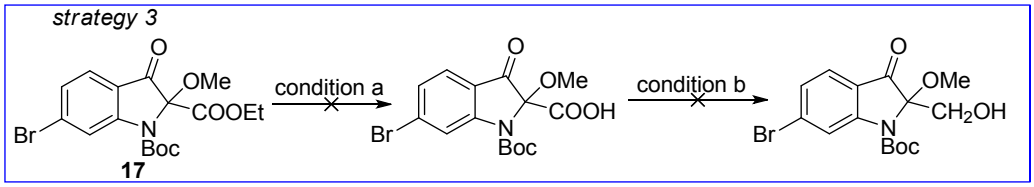
Efforts to the Reduction ofEster to Matemone



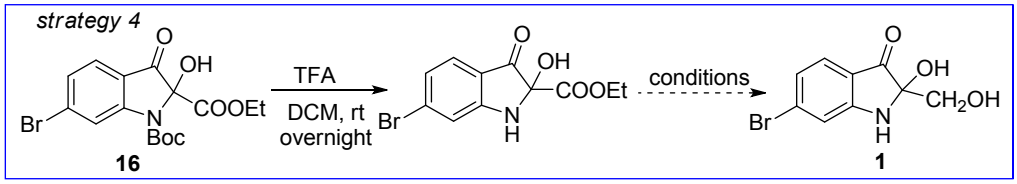
Entry	Conditions	Result
1	1.5 eq. $NaBH_4$	NR
2	1.5 eq. $LiAlH_4$	ND
3	3.0 eq. $LiAlH_4$	ND
4	3.0 eq. $LiAlH_4$ reflux	ND
5	10.0 eq. $LiAlH_4$	Complex
6	8.0 eq. $LiAlH_4$	Complex
7	1.5 eq. $NaBH_4$/ 3.0 eq. $CaCl_2$	Complex
8	1.5 eq. $NaBH_4$/ 3.0 eq. $CaCl_2$, 0 ^0C	ND
9	1.5 eq. BH_3-THF	ND
10	5.0 eq. BH_3-THF	ND



Entry	Condition a	Condition b	result
1	1.5 eq. $NaBH_4$	TFA	ND
2	1.5 eq. $LiAlH_4$	--	Complex
3	1.5 eq. BH_3-THF	--	NR
4	5.0 eq. BH_3-THF	--	trace

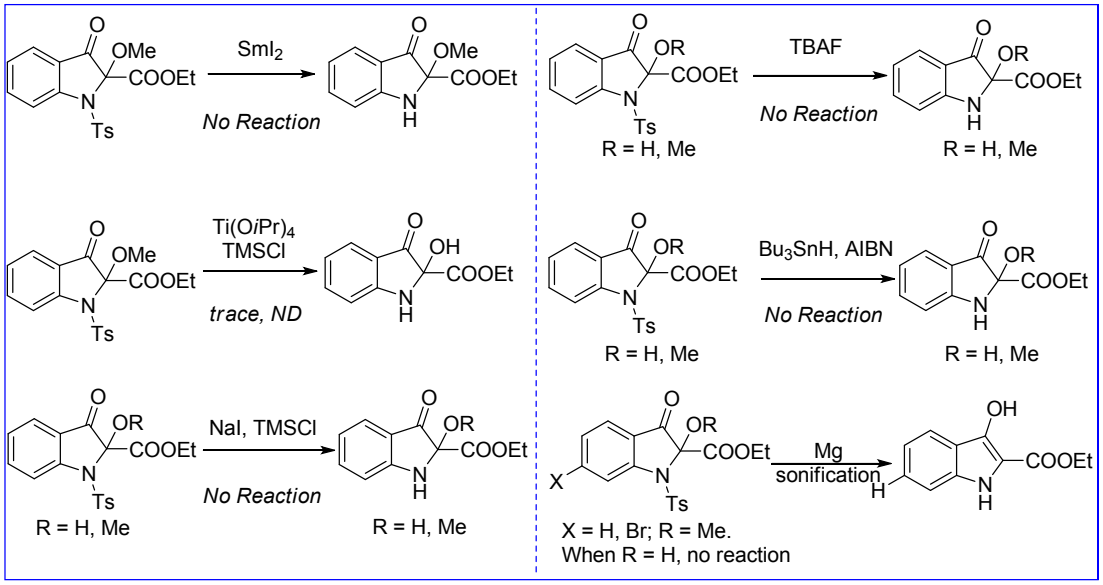


Entry	Condition a	Condition b	result
1	NaOH	1.5 eq. BH_3-THF	NR
2	NaOH	1.5 eq. BH_3-THF reflux	NR
3	NaOH	5.0 eq. BH_3-THF	Trace
4	NaOH	NMM/ IBCF/ $NaBH_4$	complex



Entry	Conditions	Result
1	5.0 eq. $NaBH_4$	Complex
2	5.0 eq. BH_3-THF	Complex
3	12.0 eq. $NaBH_4$, 7.0 eq. $CaCl_2$	Complex
4	6.0 eq. $NaBH_4$, 3.5 eq. $CaCl_2$	Complex
5	10.0eq. $LiAlH_4$	Complex
6	5.0eq. $LiAlH_4$	Complex

Removal of Tosyl Group:

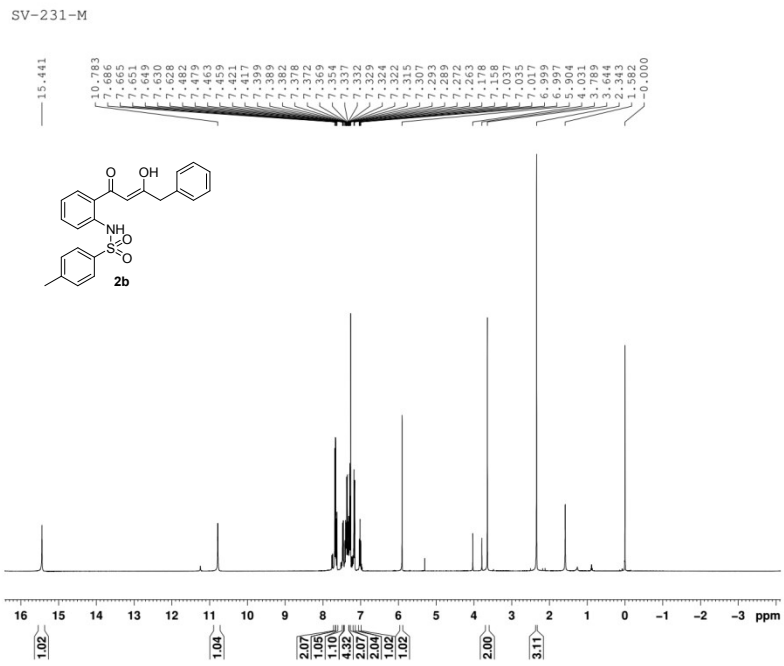


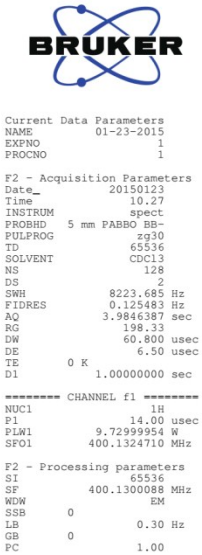
[1] Darras, F. H.; Kling, B.; Heilmann, J.; Decker, M. *ACS Med. Chem. Lett.***2012**, *3*, 914-919.

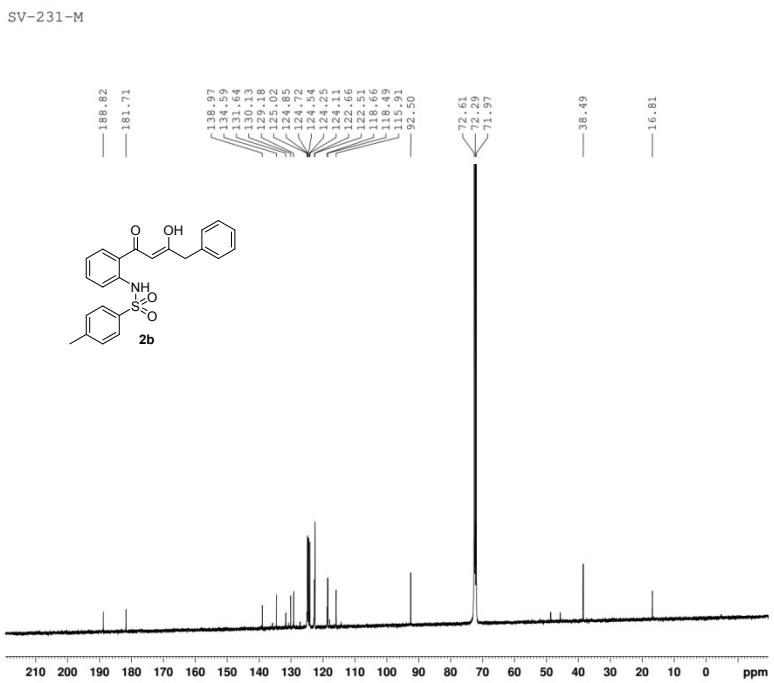
[2] Frye, S. V.; Johnson, M. C.; Valvano, N. L. *J. Org. Chem.***1991**, *56*, 3750-3752.

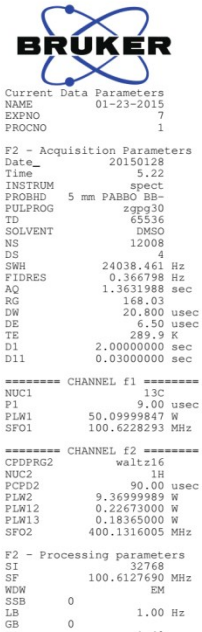
[3] Ren, Q.; Huang, J.; Wang, L.; Li, W.; Liu, H.; Jiang, X.; Wang, J. *ACS Catalysis***2012**, *12*, 2622-2625.

3. NMR Spectra of New Compounds

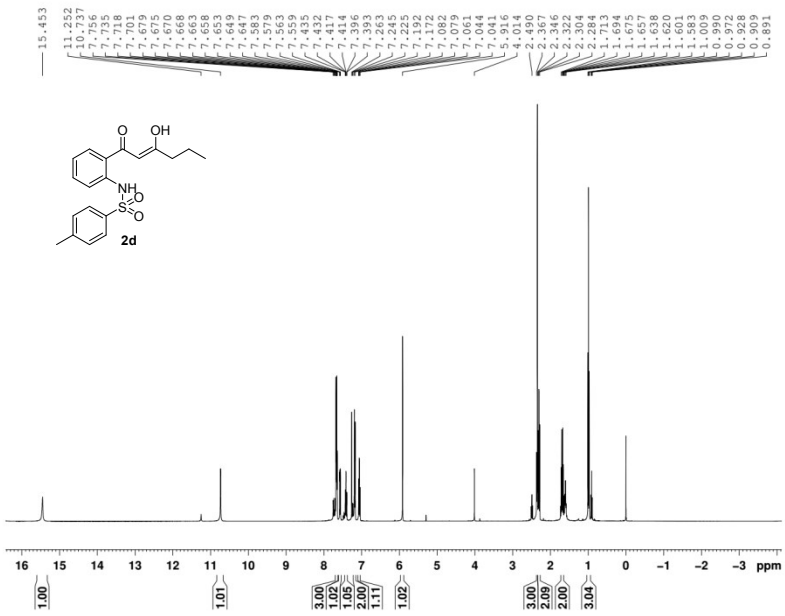








SV-252



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PROCNO 1

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RG 152.51
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DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec

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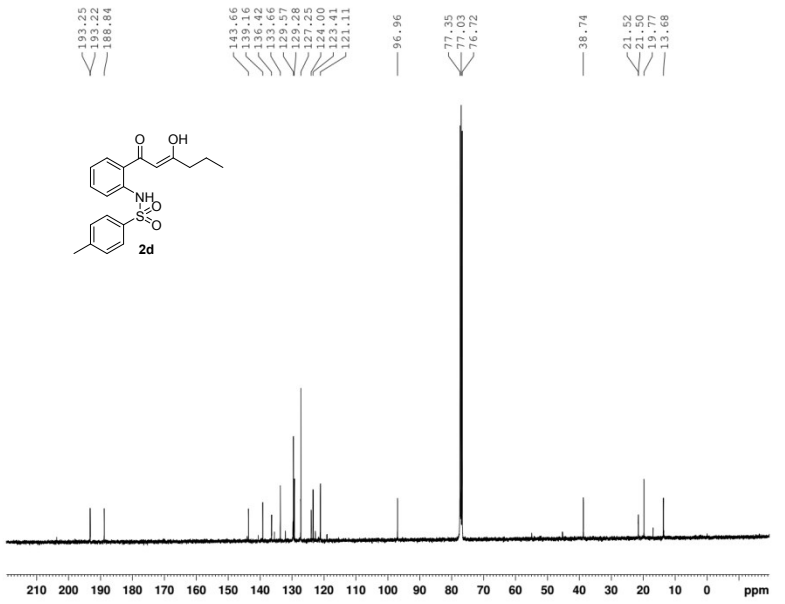
SV-252



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PROCNO 1

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FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 168.03
DW 20.800 usec
DE 6.50 usec
TE 299.9 K
D1 2.00000000 sec
D11 0.03000000 sec

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P1 9.00 usec
PLW1 50.09999847 W
SFO1 100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 9.36999989 W
PLW12 0.22673000 W
PLW13 0.18365000 W
SFO2 400.1316005 MHz

F2 - Processing parameters
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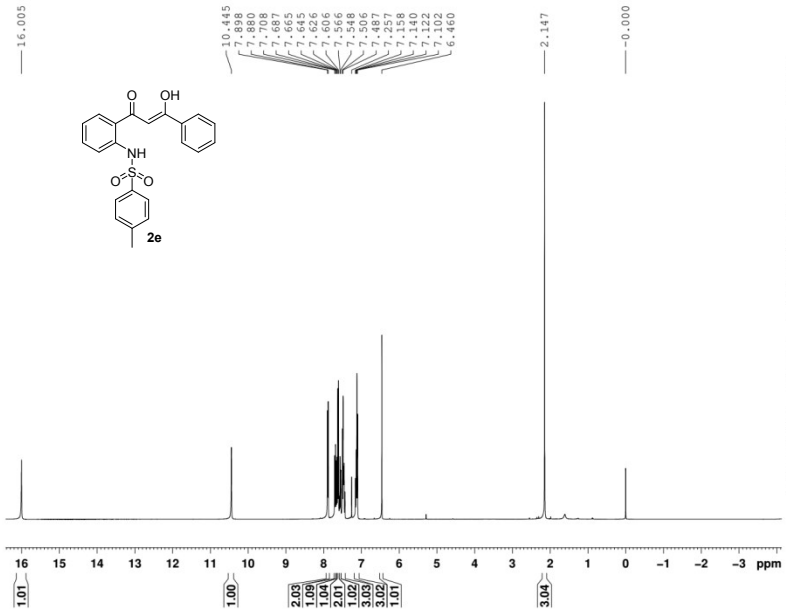
SV-275-M

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PROCNO                         1

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TD                        65536
SOLVENT                   CDCl3
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DS                            2
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AQ                     3.9846387 sec
RG                        106.96
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TE                        518.1 K
D1                    1.00000000 sec

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F2 - Processing parameters
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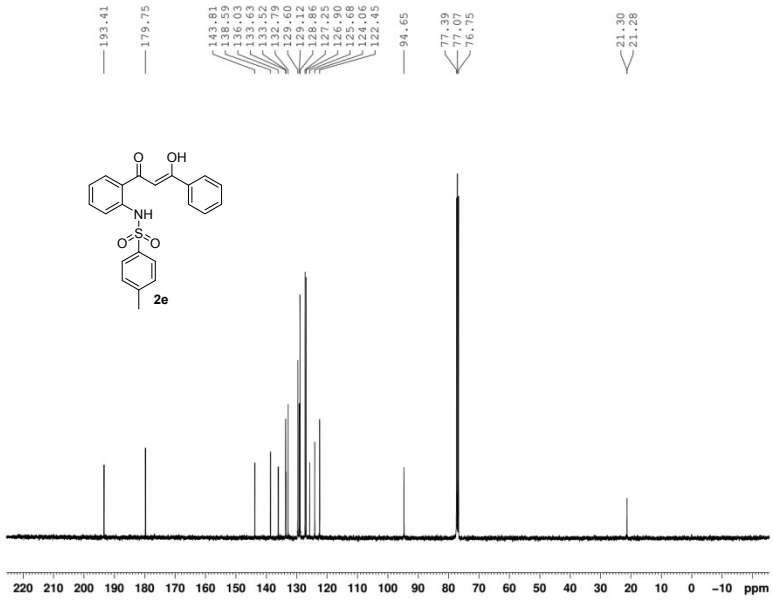
SV-275-M

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P1                         9.00 usec
PLW1                 50.09999847 W
SFO1                100.6228293 MHz

======== CHANNEL f2 ========
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NUC2                         1H
PCPD2                     90.00 usec
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PLW12                 0.22673000 W
PLW13                 0.18365000 W
SFO2                400.1316005 MHz

F2 - Processing parameters
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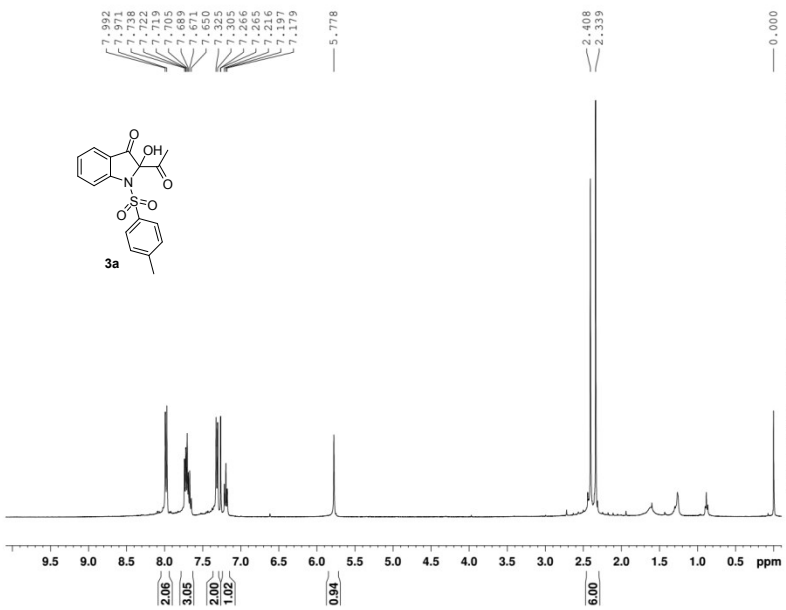
SV-208



BRUKER

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PROCNO                         1

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FIDRES                0.125483 Hz
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RG                       198.33
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TE                       291.7 K
D1                    1.00000000 sec

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PLW1                 9.72999954 W
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F2 - Processing parameters
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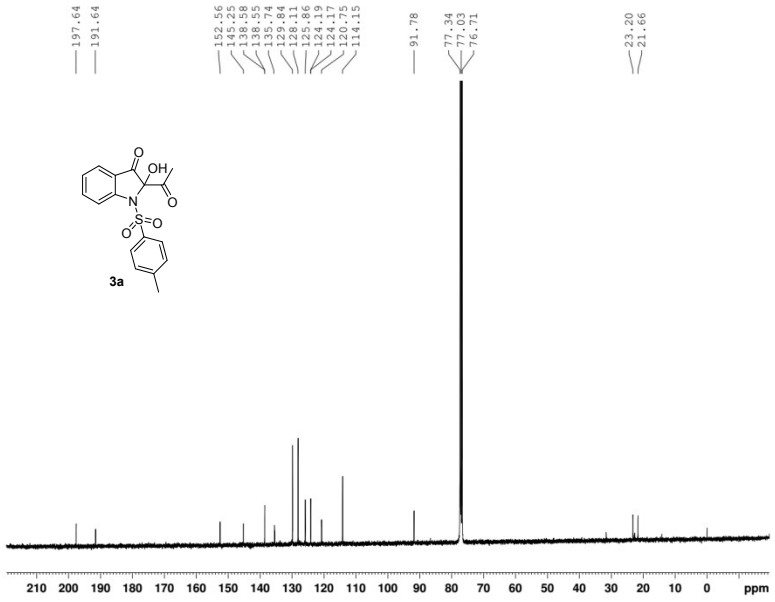
SV-208



BRUKER

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PROCNO                         1

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FIDRES                0.366798 Hz
AQ                    1.3631988 sec
RG                       168.03
DW                       20.800 usec
DE                        6.50 usec
TE                       293.5 K
D1                    2.00000000 sec
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======== CHANNEL f1 ========
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PLW1                50.09999847 W
SFO1               100.6228293 MHz

======== CHANNEL f2 ========
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NUC2                         1H
PCPD2                    90.00 usec
PLW2                 9.36999989 W
PLW12                0.22673000 W
PLW13                0.18365000 W
SFO2               400.1316005 MHz

F2 - Processing parameters
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WDW                             EM
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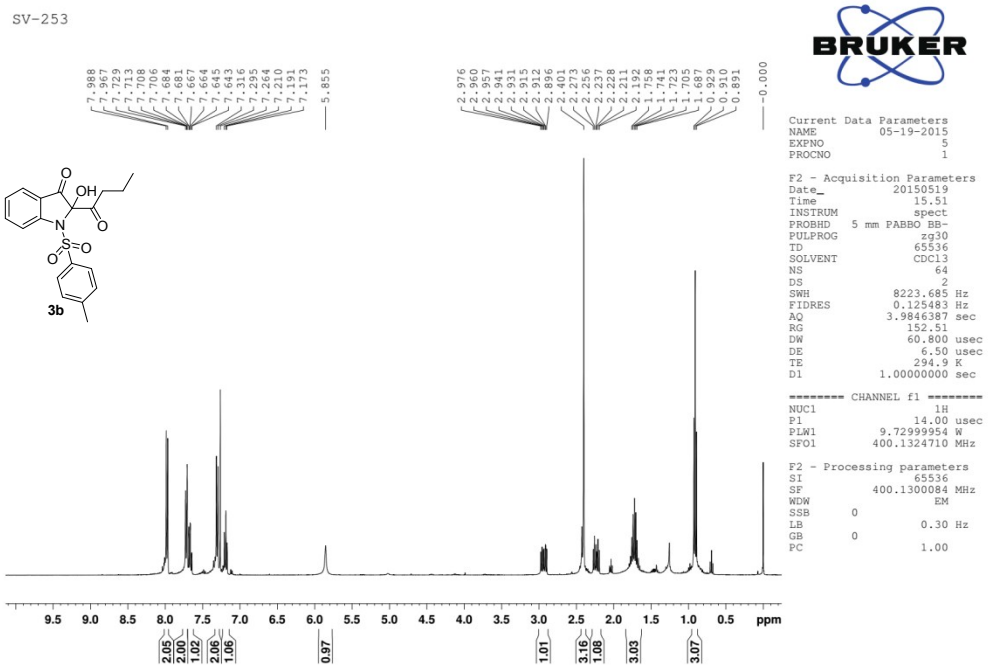
SV-253
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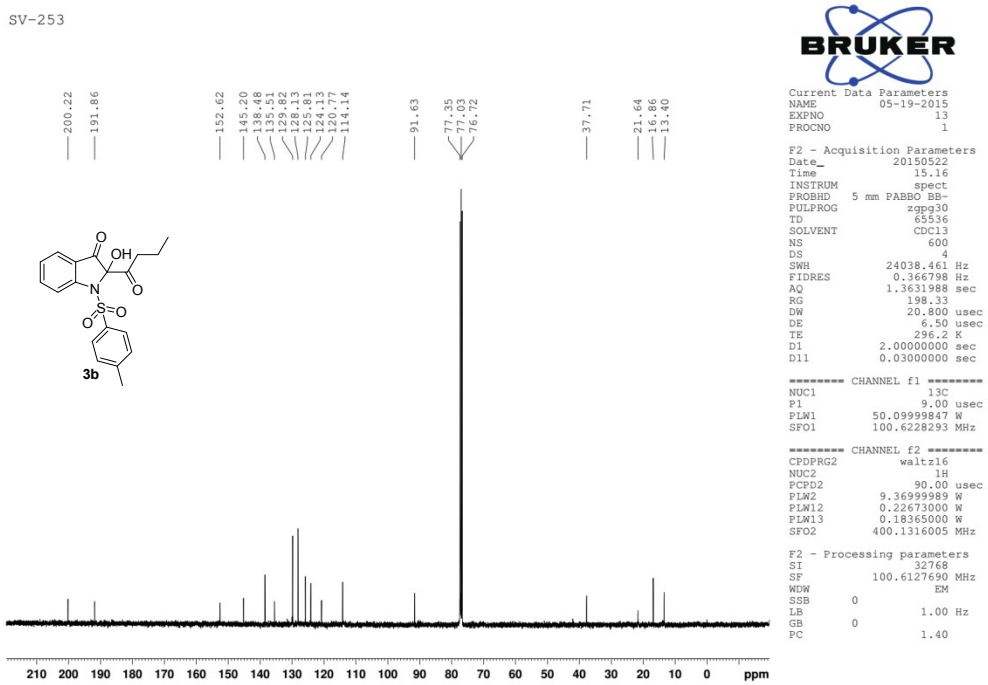
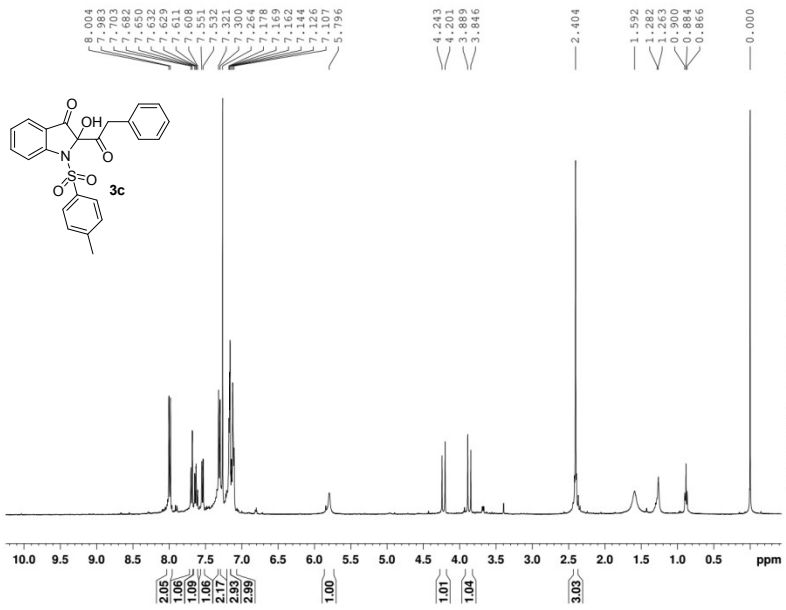
2.915
2.912
2.896
2.401
2.273
2.256
2.237
2.228
2.211
2.192
1.758
1.741
1.723
1.705
1.687
0.929
0.910
0.891
0.000
OH
O
O
N
S
O
O
3b
Current Data Parameters
NAME 05-19-2015
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150519
Time 15.51
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 64
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 152.51
DW 60.800 usec
DE 6.50 usec
TE 294.9 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PLW1 9.72999954 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 65536
SF 400.1300084 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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 ppm
2.05
2.00
1.02
2.06
1.06
0.97
1.01
3.16
1.08
3.03
3.07


SV-253
BRUKER
200.22
191.86
152.62
145.20
138.48
135.51
129.82
128.13
125.81
124.13
120.77
114.14
91.63
77.35
77.03
76.72
37.71
21.64
16.86
13.40
OH
O
O
N
S
O
O
3b
Current Data Parameters
NAME 05-19-2015
EXPNO 13
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150522
Time 15.16
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 600
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 198.33
DW 20.800 usec
DE 6.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PLW1 50.09999847 W
SFO1 100.6228293 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 9.36999989 W
PLW12 0.22673000 W
PLW13 0.18365000 W
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

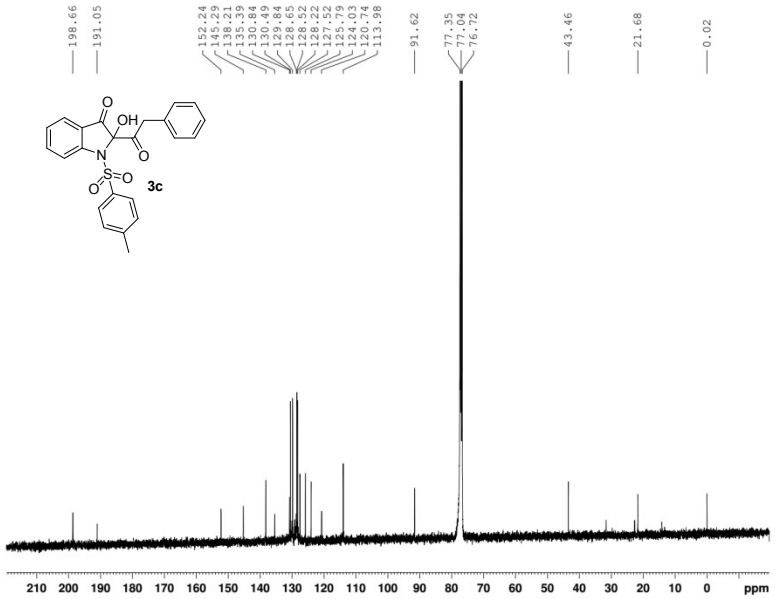
SV-231



BRUKER

```
Current Data Parameters
NAME                  01-16-2015
EXPNO                          5
PROCNO                         1

F2 - Acquisition Parameters
Date_              20150116
Time                   12.31
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       52
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                 3.9846387 sec
RG                     198.33
DW                   60.800 usec
DE                    6.50 usec
TE                    288.3 K
D1                1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                     14.00 usec
PLW1              9.72999954 W
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF               400.1300083 MHz
WDW                        EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

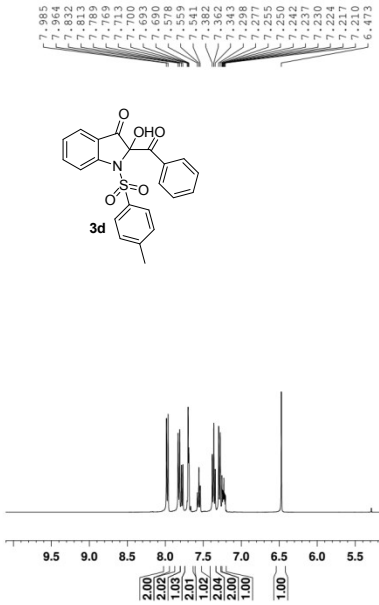
SV-231



BRUKER

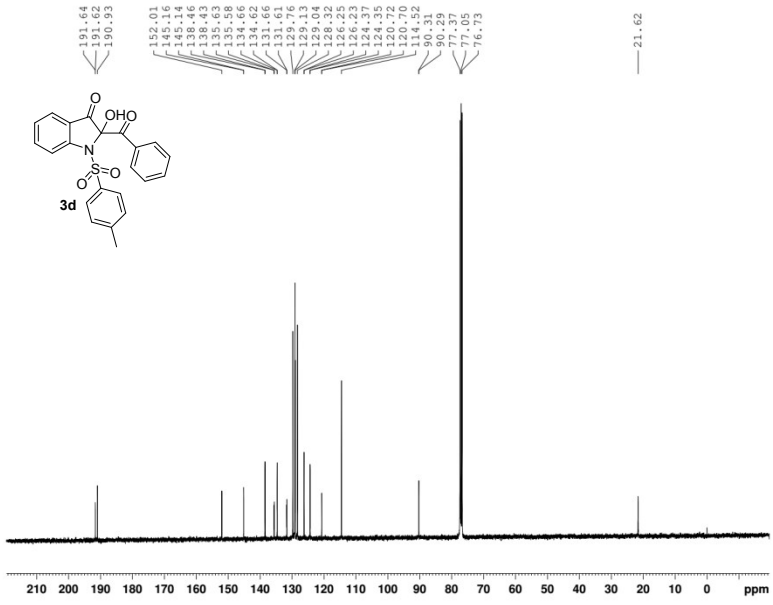
```
Current Data Parameters
NAME                  01-16-2015
EXPNO                         18
PROCNO                         1

F2 - Acquisition Parameters
Date_              20150123
Time                    6.39
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     12004
DS                        4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                 1.3631988 sec
RG                     152.51
DW                   20.800 usec
DE                    6.50 usec
TE                    0 K
D1                 2.00000000 sec
D11                0.03000000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                      9.00 usec
PLW1             50.09999847 W
SFO1            100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                  90.00 usec
PLW2              9.36999989 W
PLW12             0.22673000 W
PLW13             0.18365000 W
SFO2             400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF               100.6127690 MHz
WDW                        EM
SSB          0
LB                     1.00 Hz
GB           0
PC                     1.40
```

SV-275

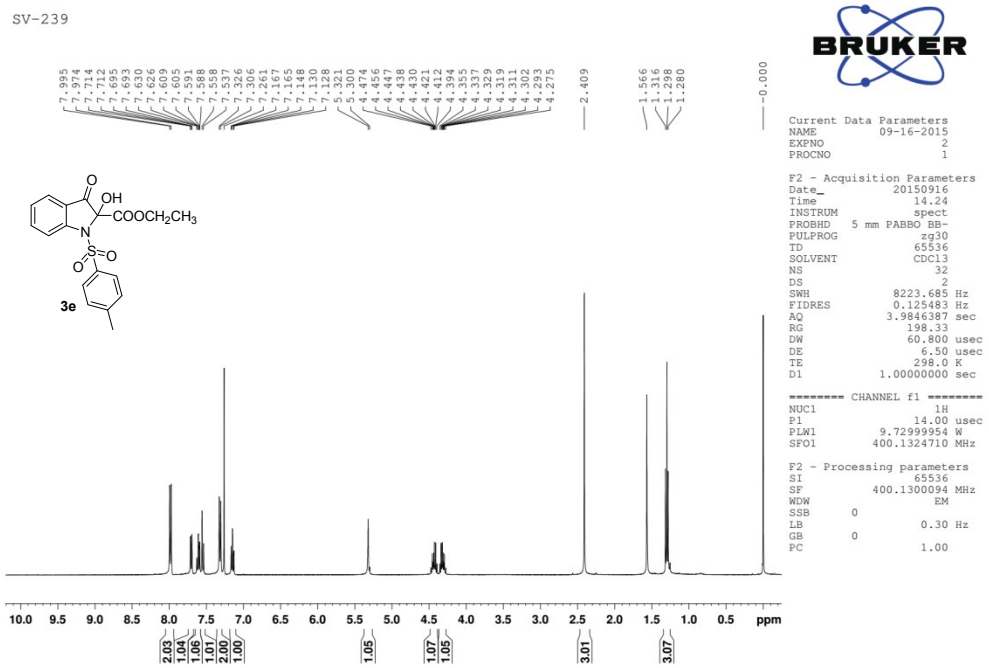


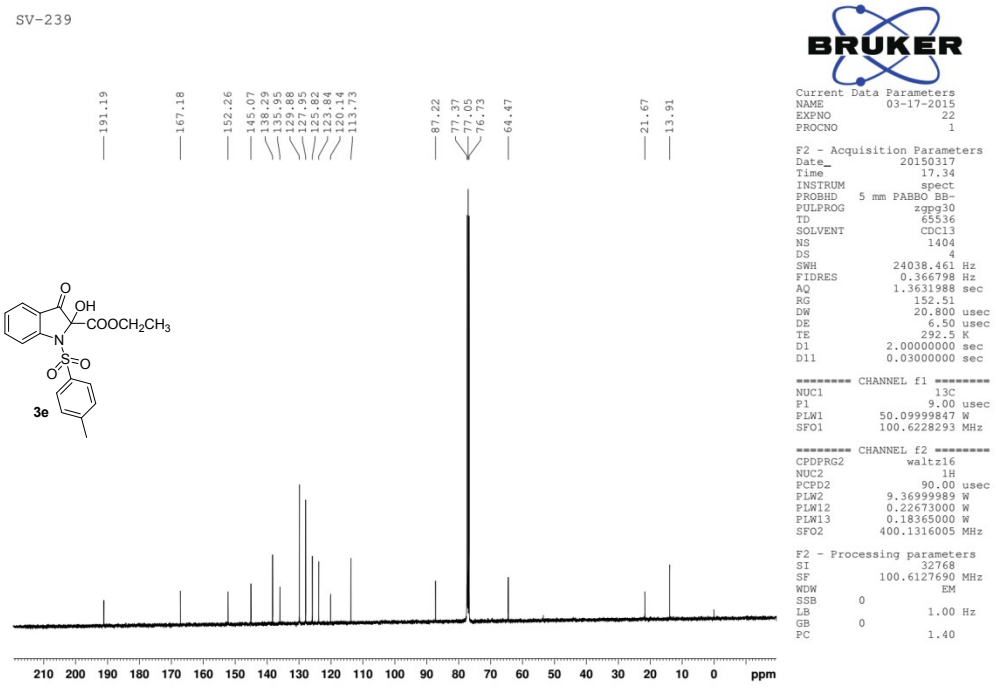

```
Current Data Parameters
NAME                  09-24-2015
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_              20150924
Time                  10.58
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       36
DS                        2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                    138.14
DW                  60.800 usec
DE                   6.50 usec
TE                  0 K
D1                  1.00000000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                    14.00 usec
PLW1             9.72999954 W
SFO1           400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF               400.1300122 MHz
WDW                       EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

SV-275

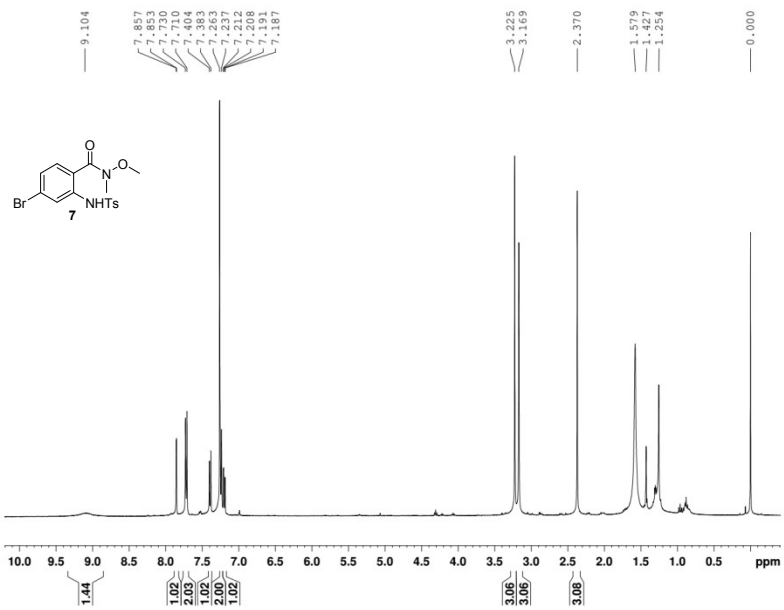



```
Current Data Parameters
NAME                  09-24-2015
EXPNO                         16
PROCNO                         1

F2 - Acquisition Parameters
Date_              20150925
Time                  15.56
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     1360
DS                        4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631988 sec
RG                    198.33
DW                  20.800 usec
DE                   6.50 usec
TE                   518.1 K
D1                 2.00000000 sec
D11                0.03000000 sec

======== CHANNEL f1 ========
NUC1                     13C
P1                     9.00 usec
PLW1            50.09999847 W
SFO1           100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                      1H
PCPD2                 90.00 usec
PLW2             9.36999989 W
PLW12            0.22673000 W
PLW13            0.18365000 W
SFO2           400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF               100.6127690 MHz
WDW                       EM
SSB          0
LB                     1.00 Hz
GB           0
PC                     1.40
```


SV-239
7.995
7.974
7.714
7.712
7.695
7.693
7.630
7.626
7.609
7.605
7.591
7.588
7.558
7.537
7.326
7.306
7.261
7.167
7.165
7.148
7.130
7.128
5.321
5.300
4.474
4.456
4.447
4.438
4.430
4.421
4.412
4.394
4.355
4.337
4.329
4.319
4.311
4.302
4.293
4.275
2.409
1.566
1.316
1.298
1.280
0.000
OH
COOCH2CH3
N
S
O
O
3e
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 ppm
2.03
1.04
1.06
1.01
2.00
1.00
1.05
1.07
1.05
3.01
3.07
BRUKER
Current Data Parameters
NAME 09-16-2015
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150916
Time 14.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 198.33
DW 60.800 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PLW1 9.72999954 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 65536
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

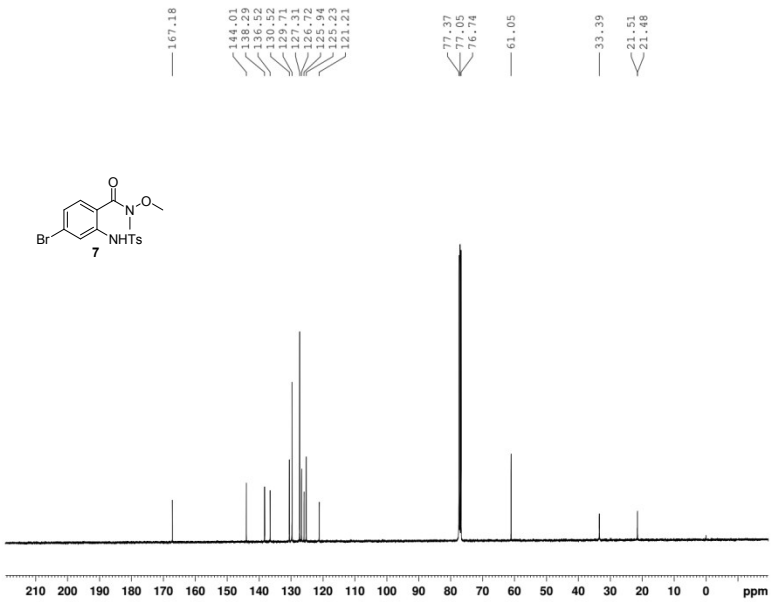

SV-239
191.19
167.18
152.26
145.07
138.29
135.95
129.88
127.95
125.82
123.84
120.14
113.73
87.22
77.37
77.05
76.73
64.47
21.67
13.91
OH
COOCH2CH3
N
S
O
O
3e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
BRUKER
Current Data Parameters
NAME 03-17-2015
EXPNO 22
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150317
Time 17.34
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1404
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 152.51
DW 20.800 usec
DE 6.50 usec
TE 292.5 K
D1 2.00000000 sec
D11 0.03000000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PLW1 50.09999847 W
SFO1 100.6228293 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 9.36999989 W
PLW12 0.22673000 W
PLW13 0.18365000 W
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

SV-260



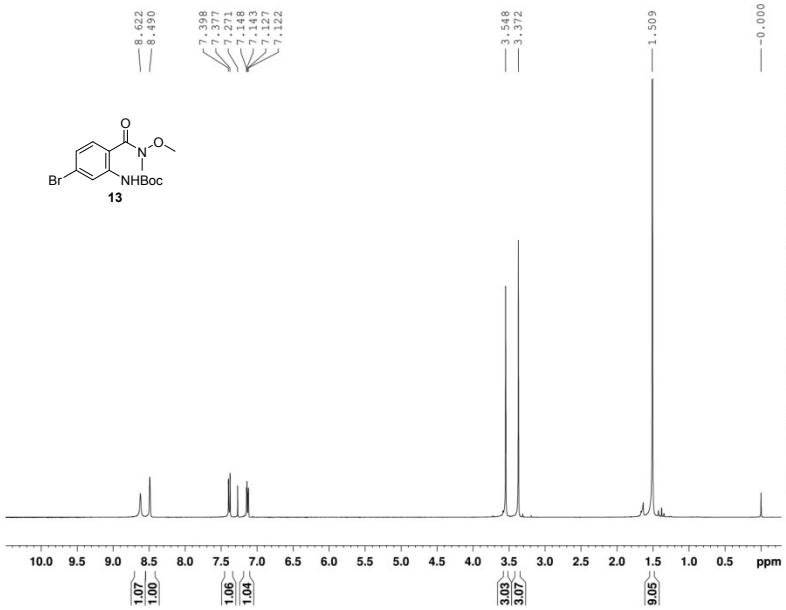

```
Current Data Parameters
NAME                  06-05-2015
EXPNO                          4
PROCNO                         1

F2 - Acquisition Parameters
Date_                  20150605
Time                      14.11
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                   zg30
TD                           65536
SOLVENT                   CDCl3
NS                             128
DS                               2
SWH                   8223.685 Hz
FIDRES                0.125483 Hz
AQ                    3.9846387 sec
RG                          198.33
DW                        60.800 usec
DE                         6.50 usec
TE                         297.0 K
D1                    1.00000000 sec

======== CHANNEL f1 ========
NUC1                          1H
P1                         14.00 usec
PLW1                  9.72999954 W
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                           65536
SF                  400.1300091 MHz
WDW                             EM
SSB                0
LB                         0.30 Hz
GB                 0
PC                         1.00
```

SV-260




```
Current Data Parameters
NAME                  09-24-2015
EXPNO                          5
PROCNO                         1

F2 - Acquisition Parameters
Date_                  20150924
Time                      13.31
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                           65536
SOLVENT                   CDCl3
NS                            1988
DS                               4
SWH                  24038.461 Hz
FIDRES                0.366798 Hz
AQ                    1.3631988 sec
RG                          198.33
DW                        20.800 usec
DE                         6.50 usec
TE                 0 K
D1                    2.00000000 sec
D11                   0.03000000 sec

======== CHANNEL f1 ========
NUC1                         13C
P1                          9.00 usec
PLW1                 50.09999847 W
SFO1                100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2                  waltz16
NUC2                          1H
PCPD2                      90.00 usec
PLW2                  9.36999989 W
PLW12                 0.22673000 W
PLW13                 0.18365000 W
SFO2                400.1316005 MHz

F2 - Processing parameters
SI                           32768
SF                  100.6127690 MHz
WDW                             EM
SSB                0
LB                         1.00 Hz
GB                 0
PC                         1.40
```

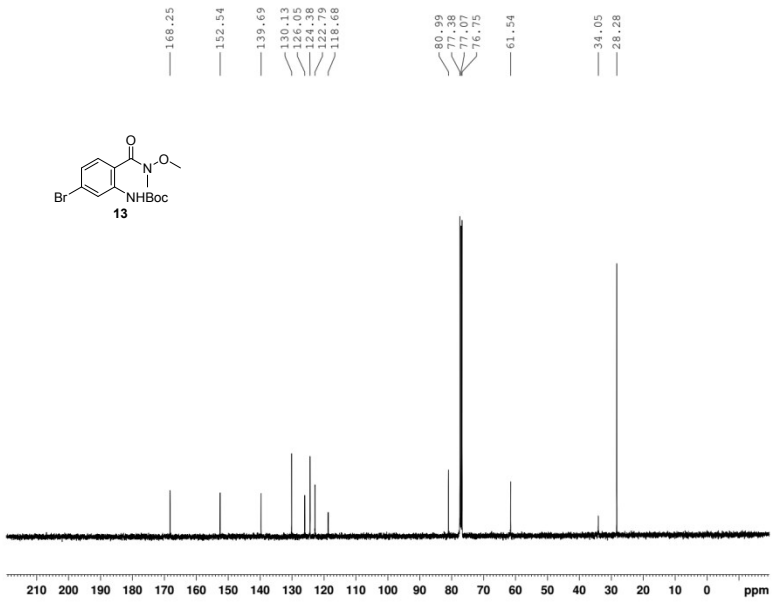
SV-320



BRUKER

```
Current Data Parameters
NAME                  03-24-2016
EXPNO                          3
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160324
Time                   17.18
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8223.685 Hz
FIDRES              0.125483 Hz
AQ                  3.9846387 sec
RG                     124.55
DW                    60.800 usec
DE                     6.50 usec
TE                     291.7 K
D1                 1.00000000 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                     14.00 usec
PLW1               9.72999954 W
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF                 400.1300059 MHz
WDW                          EM
SSB             0
LB                      0.30 Hz
GB              0
PC                        1.00
```

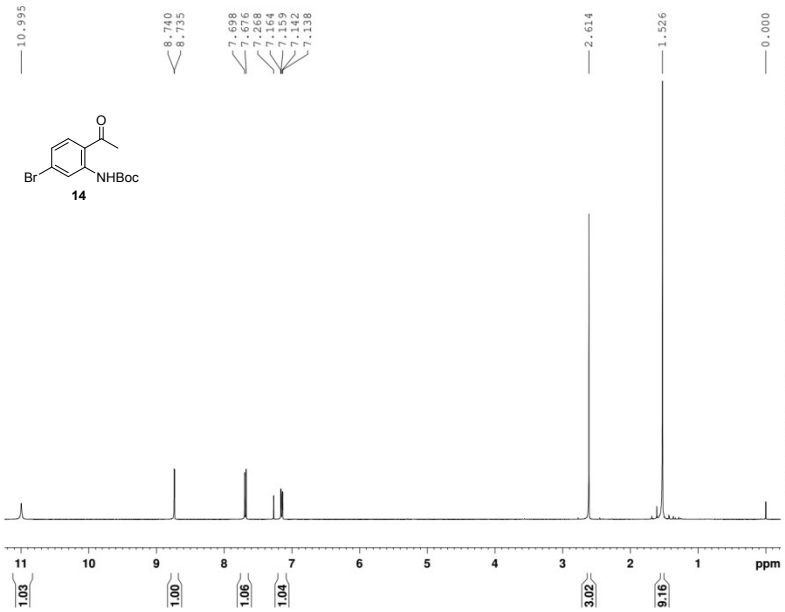
SV-320



BRUKER

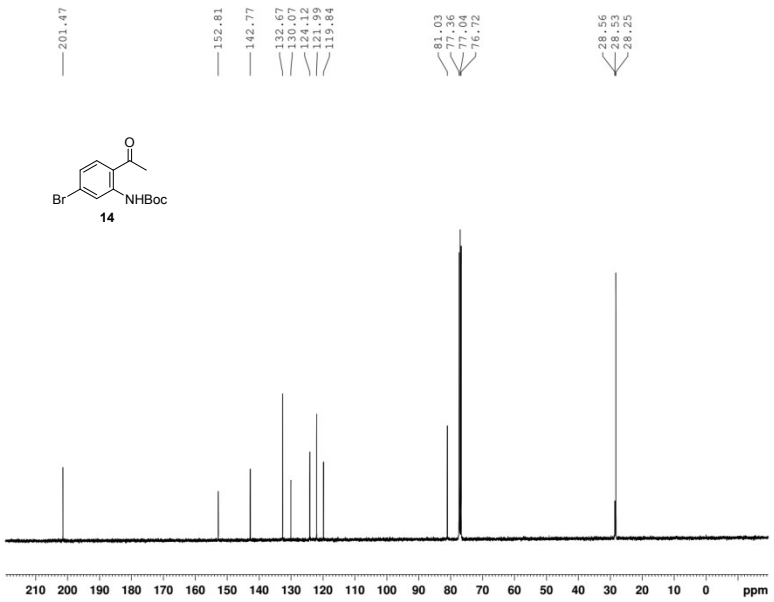
```
Current Data Parameters
NAME                  03-24-2016
EXPNO                         12
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160326
Time                   11.50
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT                CDCl3
NS                       256
DS                         4
SWH                24038.461 Hz
FIDRES              0.366798 Hz
AQ                  1.3631988 sec
RG                     168.03
DW                    20.800 usec
DE                     6.50 usec
TE                     290.9 K
D1                 2.00000000 sec
D11                0.03000000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                      9.00 usec
PLW1              50.09999847 W
SFO1             100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                       1H
PCPD2                  90.00 usec
PLW2               9.36999989 W
PLW12              0.22673000 W
PLW13              0.18365000 W
SFO2             400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF                 100.6127690 MHz
WDW                          EM
SSB             0
LB                      1.00 Hz
GB              0
PC                        1.40
```

SV-328



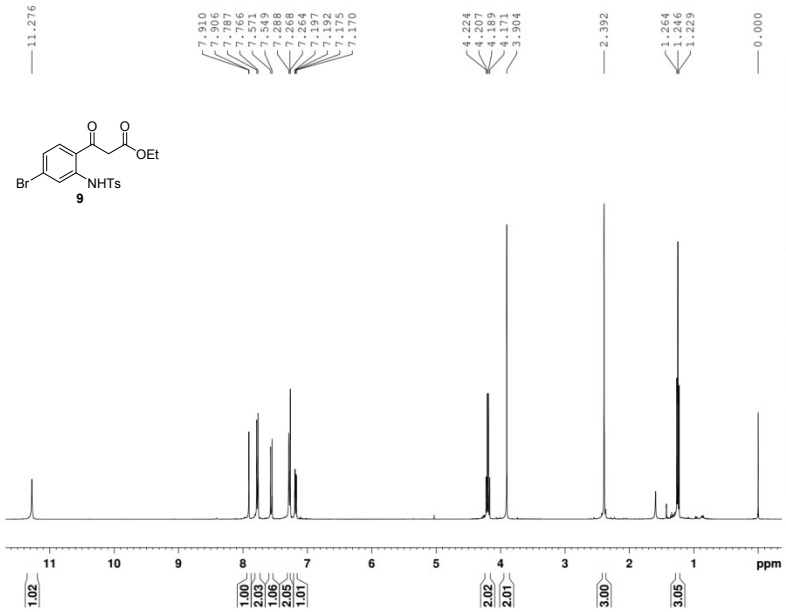

```
Current Data Parameters
NAME                  05-03-2016
EXPNO                          5
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160503
Time                      13.01
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          13
DS                           2
SWH                   8223.685 Hz
FIDRES                0.125483 Hz
AQ                    3.9846387 sec
RG                       124.55
DW                       60.800 usec
DE                        6.50 usec
TE                       297.6 K
D1                    1.00000000 sec

======== CHANNEL f1 ========
NUC1                         1H
P1                       14.00 usec
PLW1                 9.72999954 W
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                           65536
SF                  400.1300069 MHz
WDW                             EM
SSB          0
LB                        0.30 Hz
GB           0
PC                        1.00
```

SV-328



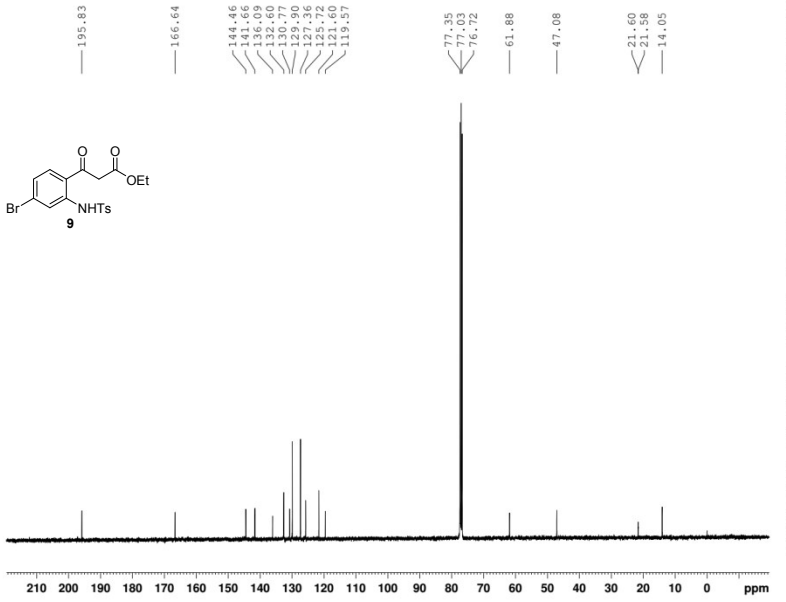

```
Current Data Parameters
NAME                  05-03-2016
EXPNO                         10
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160504
Time                      14.49
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          700
DS                           4
SWH                  24038.461 Hz
FIDRES                0.366798 Hz
AQ                    1.3631988 sec
RG                       198.33
DW                       20.800 usec
DE                        6.50 usec
TE                       297.1 K
D1                    2.00000000 sec
D11                   0.03000000 sec

======== CHANNEL f1 ========
NUC1                        13C
P1                        9.00 usec
PLW1                50.09999847 W
SFO1               100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                    90.00 usec
PLW2                 9.36999989 W
PLW12                0.22673000 W
PLW13                0.18365000 W
SFO2                400.1316005 MHz

F2 - Processing parameters
SI                           32768
SF                  100.6127690 MHz
WDW                             EM
SSB          0
LB                        1.00 Hz
GB           0
PC                        1.40
```

SV-261

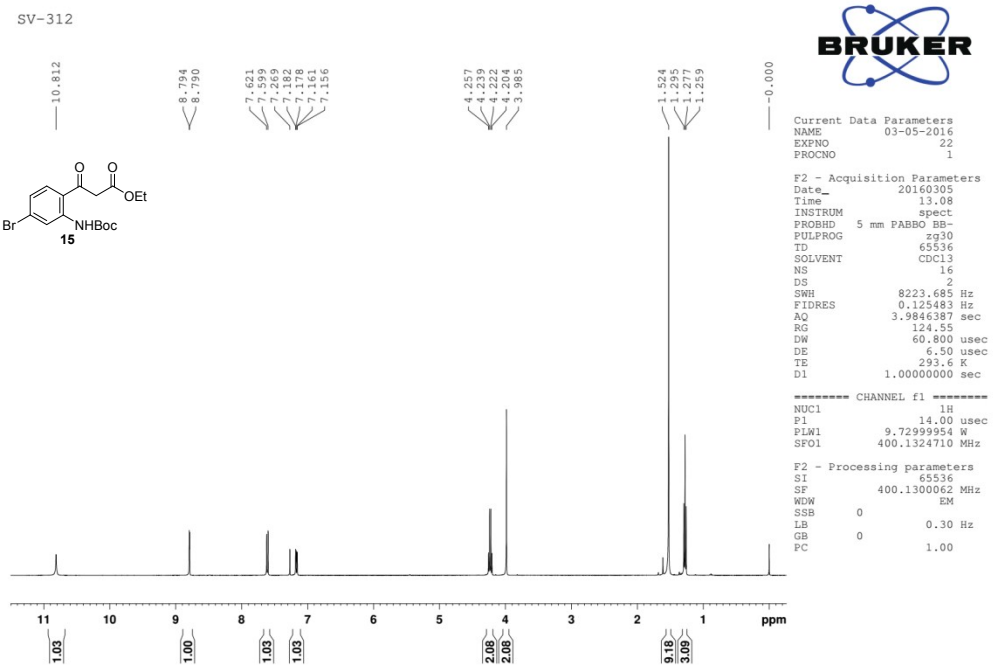


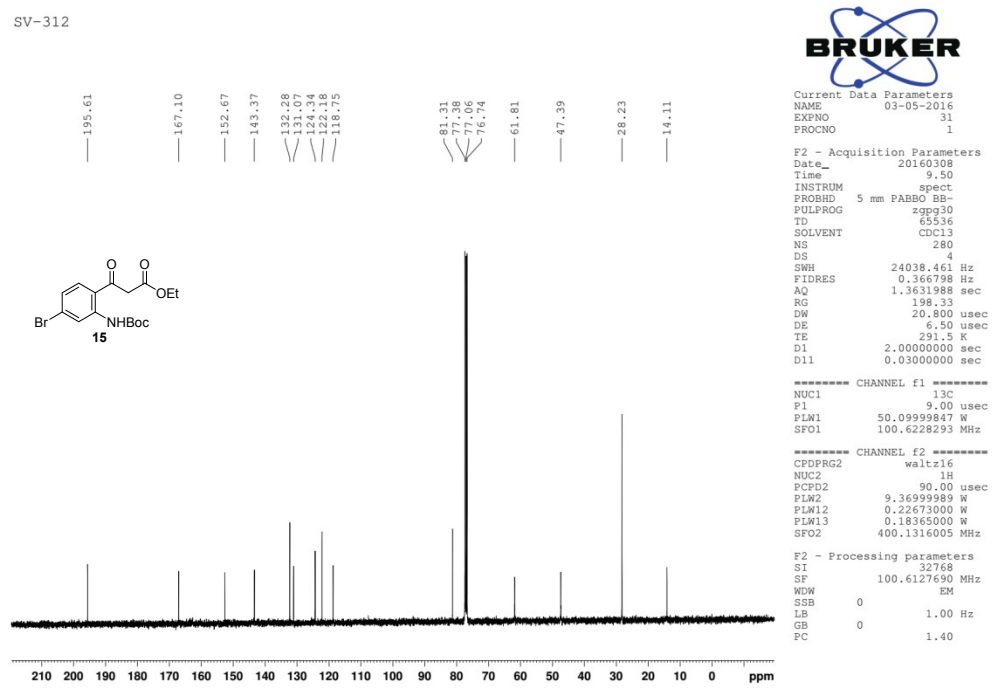

```
Current Data Parameters
NAME                  06-11-2015
EXPNO                          4
PROCNO                         1

F2 - Acquisition Parameters
Date_                  20150611
Time                      11.22
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          58
DS                           2
SWH                   8223.685 Hz
FIDRES                0.125483 Hz
AQ                    3.9846387 sec
RG                       168.03
DW                     60.800 usec
DE                      6.50 usec
TE                      295.9 K
D1                 1.00000000 sec

======== CHANNEL f1 ========
NUC1                        1H
P1                     14.00 usec
PLW1                9.72999954 W
SFO1               400.1324710 MHz

F2 - Processing parameters
SI                       65536
SF                 400.1300085 MHz
WDW                         EM
SSB             0
LB                      0.30 Hz
GB              0
PC                      1.00
```

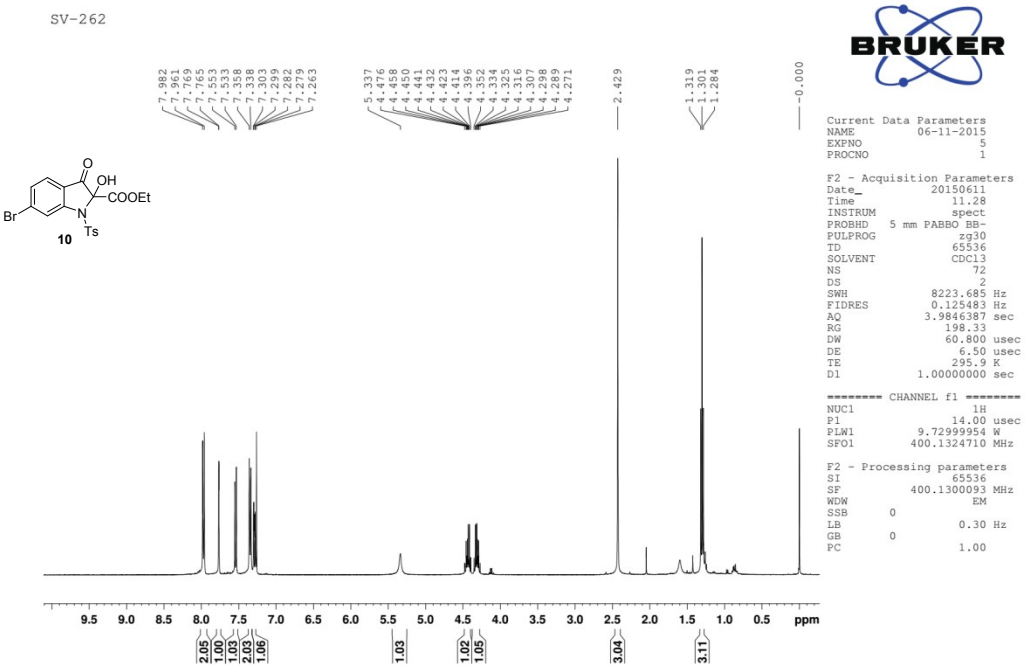
SV-261

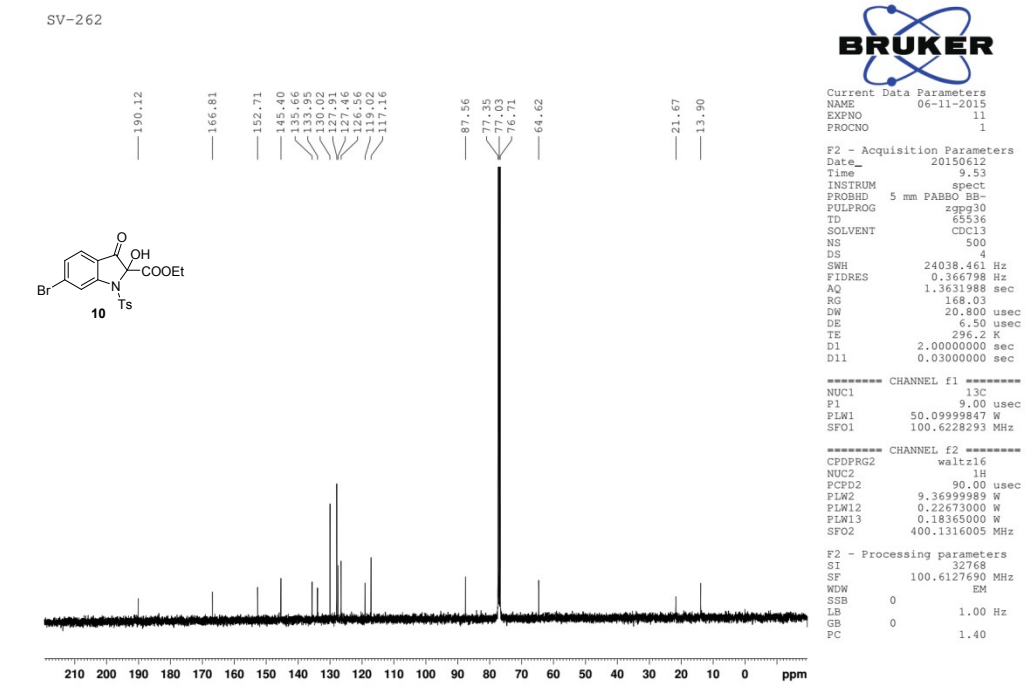



```
Current Data Parameters
NAME                  06-11-2015
EXPNO                         10
PROCNO                         1

F2 - Acquisition Parameters
Date_                  20150611
Time                      16.40
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                        1024
DS                           4
SWH                  24038.461 Hz
FIDRES                0.366798 Hz
AQ                    1.3631988 sec
RG                       198.33
DW                     20.800 usec
DE                      6.50 usec
TE                      296.8 K
D1                 2.00000000 sec
D11                0.03000000 sec

======== CHANNEL f1 ========
NUC1                       13C
P1                      9.00 usec
PLW1               50.09999847 W
SFO1              100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                  90.00 usec
PLW2                9.36999989 W
PLW12               0.22673000 W
PLW13               0.18365000 W
SFO2               400.1316005 MHz

F2 - Processing parameters
SI                       32768
SF                100.6127690 MHz
WDW                         EM
SSB             0
LB                      1.00 Hz
GB              0
PC                      1.40
```

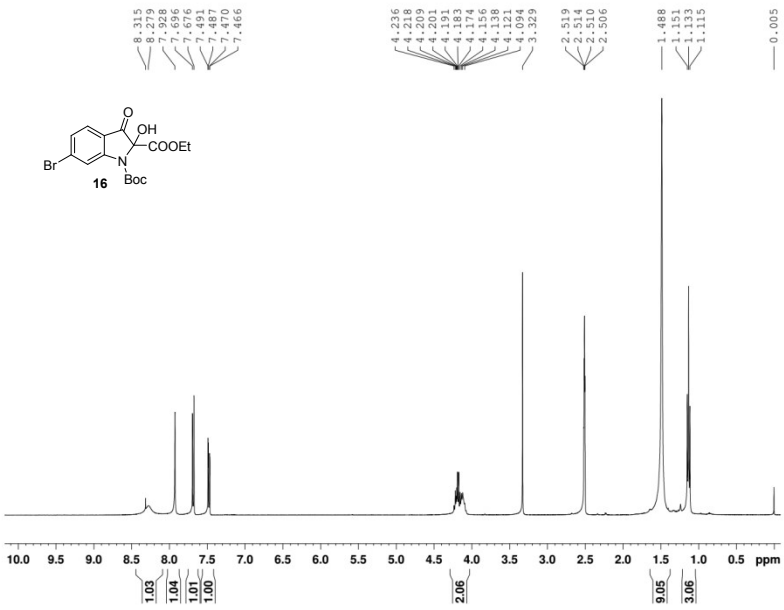

SV-312
10.812
8.794
8.790
7.621
7.599
7.269
7.182
7.178
7.161
7.156
4.257
4.239
4.222
4.204
3.985
1.524
1.295
1.277
1.259
0.000
O
O
OEt
Br
NHBoc
15
Current Data Parameters
NAME 03-05-2016
EXPNO 22
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160305
Time 13.08
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 124.55
DW 60.800 usec
DE 6.50 usec
TE 293.6 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PLW1 9.72999954 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 65536
SF 400.1300062 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 ppm
1.03 1.00 1.03 1.03 2.08 2.08 9.18 3.09


SV-312
195.61
167.10
152.67
143.37
132.28
131.07
124.34
122.18
118.75
81.31
77.38
77.06
76.74
61.81
47.39
28.23
14.11
O
O
OEt
Br
NHBoc
15
Current Data Parameters
NAME 03-05-2016
EXPNO 31
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160308
Time 9.50
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 280
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 198.33
DW 20.800 usec
DE 6.50 usec
TE 291.5 K
D1 2.00000000 sec
D11 0.03000000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PLW1 50.09999847 W
SFO1 100.6228293 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 9.36999989 W
PLW12 0.22673000 W
PLW13 0.18365000 W
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


SV-262
7.982
7.961
7.769
7.765
7.553
7.533
7.358
7.338
7.303
7.299
7.282
7.279
7.263
5.337
4.476
4.458
4.450
4.441
4.432
4.423
4.414
4.396
4.352
4.334
4.325
4.316
4.307
4.298
4.289
4.271
2.429
1.319
1.301
1.284
-0.000
OH
COOEt
Br
N
Ts
10
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 ppm
2.05
1.00
1.03
2.03
1.06
1.03
1.02
1.05
3.04
3.11
BRUKER
Current Data Parameters
NAME 06-11-2015
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150611
Time 11.28
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 72
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 198.33
DW 60.800 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PLW1 9.72999954 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 65536
SF 400.1300093 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


SV-262
190.12
166.81
152.71
145.40
135.66
133.95
130.02
127.91
127.46
126.56
119.02
117.16
87.56
77.35
77.03
76.71
64.62
21.67
13.90
OH
COOEt
Br
N
Ts
10
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
BRUKER
Current Data Parameters
NAME 06-11-2015
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150612
Time 9.53
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 500
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 168.03
DW 20.800 usec
DE 6.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PLW1 50.09999847 W
SFO1 100.6228293 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 9.36999989 W
PLW12 0.22673000 W
PLW13 0.18365000 W
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

SV-327-2



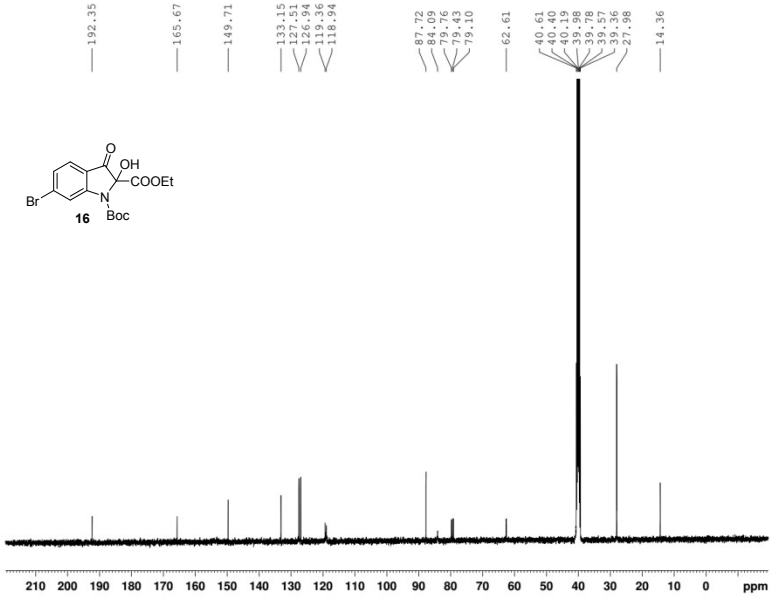
Current Data Parameters
NAME 05-03-2016
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20160503
Time 13.37
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 20
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 168.03
DW 60.800 usec
DE 6.50 usec
TE 297.7 K
D1 1.00000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PLW1 9.72999954 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 65536
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

SV-327-2



Current Data Parameters
NAME 05-03-2016
EXPNO 12
PROCNO 1

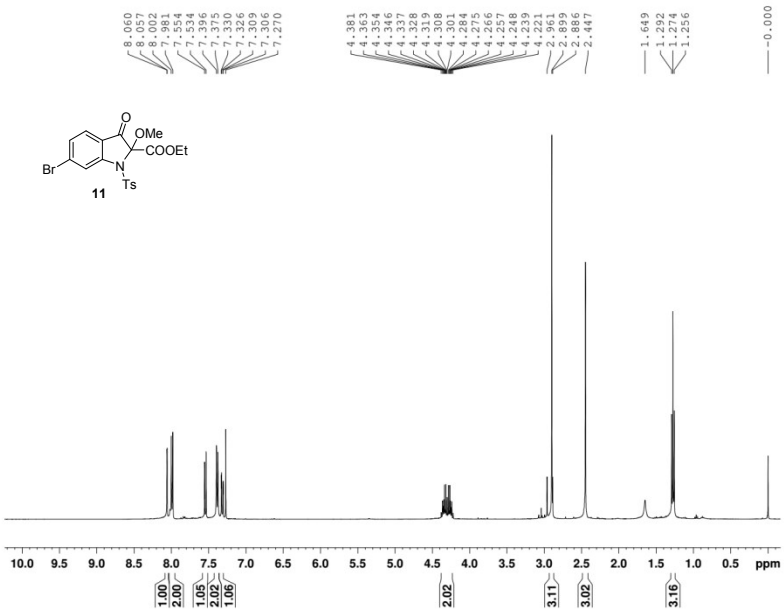
F2 - Acquisition Parameters
Date_ 20160504
Time 16.03
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1184
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 198.33
DW 20.800 usec
DE 6.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PLW1 50.09999847 W
SFO1 100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PLW2 9.36999989 W
PLW12 0.22673000 W
PLW13 0.18365000 W
SFO2 400.1316005 MHz

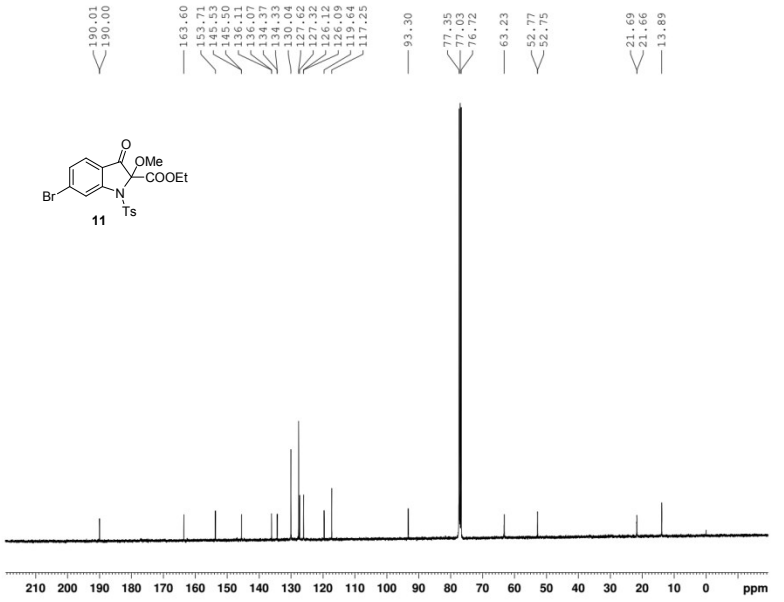
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

SV-281



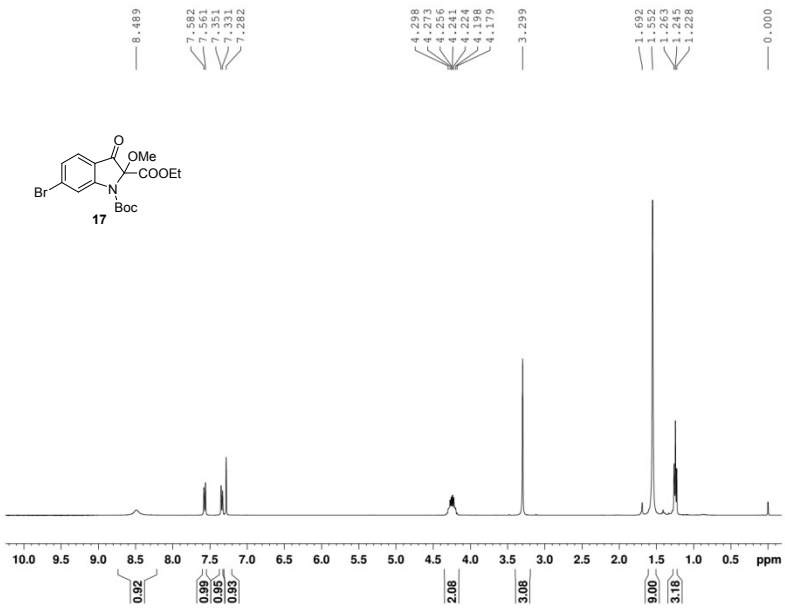

```
Current Data Parameters
NAME                  10-09-2015
EXPNO                          4
PROCNO                         1

F2 - Acquisition Parameters
Date_              20151010
Time                   11.24
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                CDCl3
NS                        68
DS                         2
SWH                 8223.685 Hz
FIDRES              0.125483 Hz
AQ                  3.9846387 sec
RG                     152.51
DW                    60.800 usec
DE                     6.50 usec
TE                     296.6 K
D1                 1.00000000 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                     14.00 usec
PLW1               9.72999954 W
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                        65536
SF                400.1300060 MHz
WDW                          EM
SSB          0
LB                      0.30 Hz
GB           0
PC                        1.00
```

SV-281




```
Current Data Parameters
NAME                  10-09-2015
EXPNO                         15
PROCNO                         1

F2 - Acquisition Parameters
Date_              20151019
Time                   21.18
INSTRUM                spect
PROBHD   5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT                CDCl3
NS                      3600
DS                         4
SWH                24038.461 Hz
FIDRES              0.366798 Hz
AQ                  1.3631988 sec
RG                     198.33
DW                    20.800 usec
DE                     6.50 usec
TE                     297.6 K
D1                 2.00000000 sec
D11                0.03000000 sec

======== CHANNEL f1 ========
NUC1                      13C
P1                      9.00 usec
PLW1              50.09999847 W
SFO1             100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                       1H
PCPD2                  90.00 usec
PLW2               9.36999989 W
PLW12              0.22673000 W
PLW13              0.18365000 W
SFO2             400.1316005 MHz

F2 - Processing parameters
SI                        32768
SF                100.6127690 MHz
WDW                          EM
SSB          0
LB                      1.00 Hz
GB           0
PC                        1.40
```

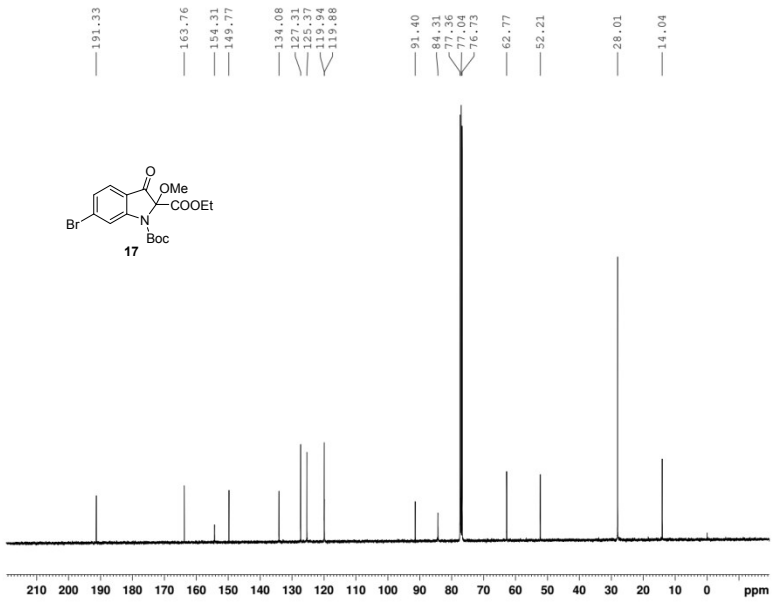
SV-314



17

```
Current Data Parameters
NAME                  03-12-2016
EXPNO                          6
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160312
Time                  13.21
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                    94.96
DW                   60.800 usec
DE                    6.50 usec
TE                   290.3 K
D1               1.00000000 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                   14.00 usec
PLW1            9.72999954 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   65536
SF             400.1300017 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

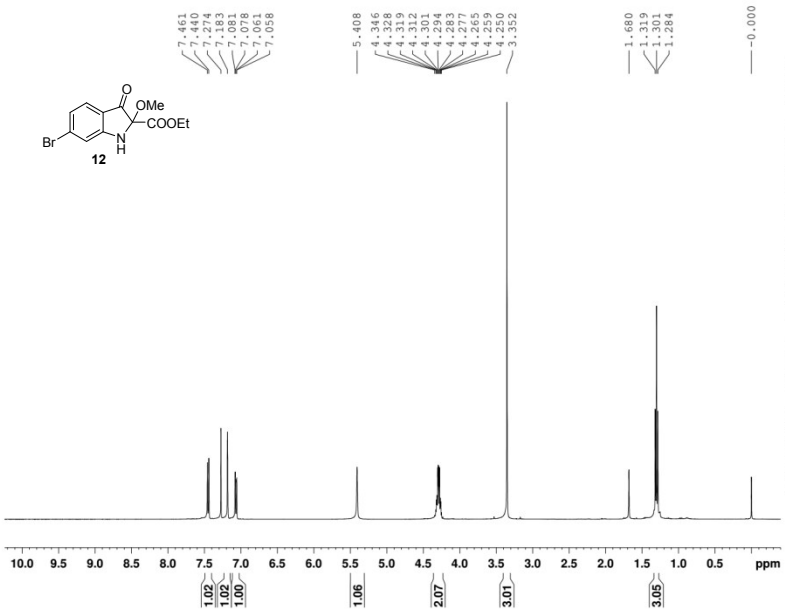
SV-314



17

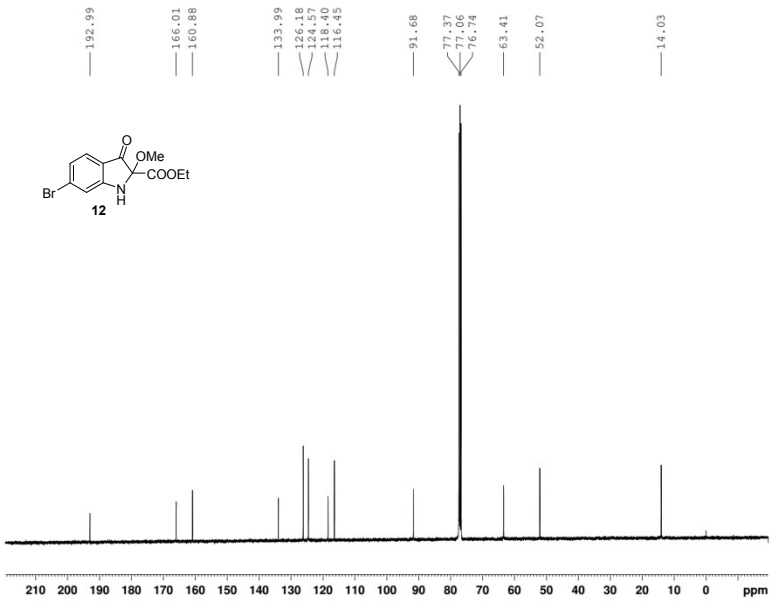
```
Current Data Parameters
NAME                  03-12-2016
EXPNO                         10
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160314
Time                  14.47
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    1296
DS                       4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631988 sec
RG                   198.33
DW                   20.800 usec
DE                    6.50 usec
TE                   297.9 K
D1               2.00000000 sec
D11              0.03000000 sec

======== CHANNEL f1 ========
NUC1                    13C
P1                    9.00 usec
PLW1           50.09999847 W
SFO1          100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                90.00 usec
PLW2            9.36999989 W
PLW12           0.22673000 W
PLW13           0.18365000 W
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF             100.6127690 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

SV-318



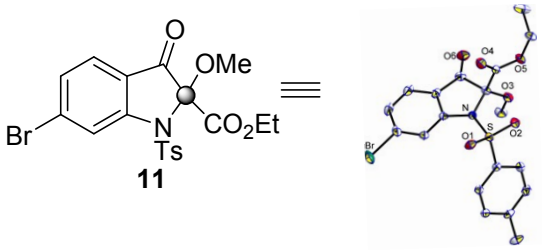

```
Current Data Parameters
NAME                  03-17-2016
EXPNO                          6
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160317
Time                  13.52
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH                8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                    138.14
DW                  60.800 usec
DE                   6.50 usec
TE                   291.1 K
D1                1.00000000 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                    14.00 usec
PLW1            9.72999954 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   65536
SF             400.1300042 MHz
WDW                     EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

SV-318




```
Current Data Parameters
NAME                  03-17-2016
EXPNO                         23
PROCNO                         1

F2 - Acquisition Parameters
Date_              20160321
Time                  12.12
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    1628
DS                       4
SWH               24038.461 Hz
FIDRES            0.366798 Hz
AQ                1.3631988 sec
RG                    198.33
DW                  20.800 usec
DE                   6.50 usec
TE                   293.4 K
D1                2.00000000 sec
D11               0.03000000 sec

======== CHANNEL f1 ========
NUC1                    13C
P1                    9.00 usec
PLW1           50.09999847 W
SFO1          100.6228293 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2                90.00 usec
PLW2            9.36999989 W
PLW12           0.22673000 W
PLW13           0.18365000 W
SFO2          400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF             100.6127690 MHz
WDW                     EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    1.40
```

4. X-ray crystallographic data of compound11



X-ray crystal of **11** (showing the thermal ellipsoids at 20%probability level).

Compound **11**		
Bond precision: C-C = 0.0041 A	Wavelength= 0.71073	
a = 10.6287	b = 12.6972	c = 15.0254
alpha = 90	beta = 96.572	gamma = 90
Cell setting: Monoclinic	Moiety formula: $C_{13}H_{14}SO_3$	
Cell volume= 2014.42	Space group: P21/c	
Data completeness= 0.994	Theta(max)= 25.030	
R(reflections)= 0.0362	WR2(reflections)= 0.1058	
S = 1.052	Radiation type: MoK\a	
Measurement device type: CCD area detector	Measurement method: phi and omega scans	
Structure solution: SHELXS-97	Structure refinement: SHELXL-97	
Solution primary: direct	Solution secondary: difmap	
Solution hydrogens: geom	Hydrogen treatment: mixed	