A Facile Deprotection of Secondary Acetamides

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General All reagents were obtained from commercial suppliers and used without further purification. Only anhydrous solvents were used for the reactions and these were equally purchased from commercial suppliers. All reactions were performed under nitrogen atmosphere. ^{1}H and ^{13}C NMR were recorded on a Varian Mercury 400 spectrometer in deuterio-solvents with TMS as an internal standard at room temperature. Chemical shifts are reported in ppm on the δ scale along with multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constants, if applicable. HPLC area % values (not adjusted to weight %) in the manuscript Tables 1 and 2 are derived from LC / MS diode array conditions: Solvent A: 0.01 M NH_4Ac in 95% H_2O, 5% MeOH, pH 6.0, Solvent B: 0.01 M NH_4Ac in 100% MeOH on a Phenomenex Luna C18(2), 100A, 2.0 x 30 mm column; Waters 996 PDA, Wavelength (nm): 210 – 400; Resolution (nm): 1.2; Sampling Rate (spectra/s): 1.000. A Waters 2690 HPLC system equipped with 2487 UV detector was used for chiral assays as indicated. High resolution mass spectra were acquired externally by M-Scan Inc.

NOTE: As mentioned in the manuscript, use of this methodology warrants caution due to the rapid gas evolution. The exothermic reaction is readily handled with appropriate precautions. Evolution of CO is accompanied by an equivalent of CO_2, diluting the gaseous by-product stream. To prevent reversion to starting material, the imidoyl chloride intermediate should be handled under anhydrous conditions.

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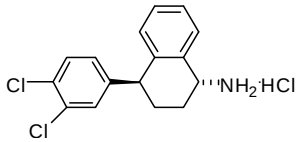
Experimentals

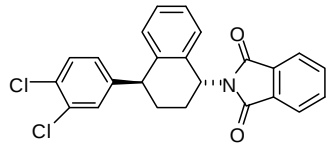
(1*R*,4*S*)-4-(3,4-Dichlorophenyl)-1,2,3,4-tetrahydronaphthalen-1-amine hydrochloride – Compound 1, Scheme 1 / Table 3, entry 1A:



A solution of acetamide (30.0 g, 89.8 mmol) in dry THF (239.3 mL) was treated with pyridine (8.9 mL, 110.0 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (8.9 mL, 101.6 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a yellow slurry. After stirring at 0 °C for 15 min., dry propylene glycol (13.0 mL, 176.0 mmol) was added to maintain an internal temperature below 10 °C and the reaction warmed to 25 °C. During this warming phase, the yellow slurry converted into a lighter yellow slurry. After 10 min., the slurry was treated with 1-propanol (120.5 mL) followed by 6 N HCl (120.0 mL). The reaction was heated to 55 °C and filtered to remove particulates and further heated to distill off THF. Upon concentration, the batch was cooled gradually to 0 °C to facilitate crystallization. A lightly colored solid was filtered off, followed by washing of the filter cake with cold 1-propanol / DI water (75 mL) and M*t*BE (75 mL). The wet cake was dried under vacuum and yielded a white solid (24.8 g, 84.1%): decomp. > 290 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.71 (s, 3H), 7.71 (d, 1H, *J* = 7.7 Hz), 7.53 (d, 1H, *J* = 8.1 Hz), 7.34 (s, 1H), 7.29 (m, 1H), 7.22 (m, 1H), 7.01 (d, 1H, *J* = 8.1 Hz), 6.81 (d, 1H, *J* = 7.7 Hz), 4.56 (s, 1H), 4.26 (s, 1H), 2.26 (m, 1H), 2.15 (m, 1H), 1.83 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.3, 138.8, 133.5, 130.9, 130.5, 130.4, 130.0, 128.9, 128.8, 128.3, 128.1, 126.7, 47.8, 43.0, 27.7, 25.1. Substance data agrees with previously reported information.[1]

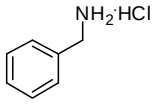
2-((1*R*,4*S*)-4-(3,4-Dichlorophenyl)-1,2,3,4-tetrahydronaphthalen-1-yl)isoindoline-1,3-dione – Table 3, entry 1B:

[1] Han, Z.; Koenig, S.G.; Zhao, H.; Su, X.; Singh, S.P.; Bakale, R.P. *Org. Proc. Res. Dev.* **2007**, *11*, 726.



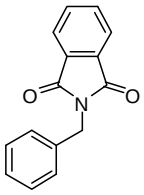
A solution of acetamide (1.67 g, 5.00 mmol) in dry THF (12.5 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a yellow slurry. After stirring at 0 °C for 30 min., dry propylene glycol (0.73 mL, 10.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the yellow slurry converted into a solution before again forming a light yellow slurry. After 1 h, the slurry was treated with phthalic anhydride (1.56 g, 10.0 mmol) and diluted with toluene (12.5 mL). Pyridine (1.21 mL, 15.0 mmol) was added and the mixture heated to reflux, causing the yellow slurry to become orange and then slowly convert to a solution. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (12.5 mL). Refluxing the mixture enabled azeotropic removal of water with toluene. After 12 h, the reaction was cooled and diluted with EtOAc (25 mL). The organic layer was washed successively with 1 N HCl (15 mL), saturated $NaHCO_3$ (15 mL), and brine (15 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded an orange residue. Crude NMR indicated good conversion to phthalimide. The desired product was crystallized from this residue by dissolving in hot EtOH, followed by cooling. Filtration of the solids, washing with EtOH and EtOH/H_2O, and drying gave a yellow, granular solid (1.77 g, 84% yield, single diastereomer): mp 202-203 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (m, 2H), 7.75 (m, 2H), 7.40 (m, 1H), 7.29 (m, 1H), 7.09 (m, 2H), 7.01 (m, 2H), 6.78 (m, 1H), 5.69 (m, 1H), 4.26 (m, 1H), 2.58 (m, 1H), 2.33 (m, 1H), 2.17 (m, 1H), 1.95 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 146.7, 139.4, 135.1, 134.1, 132.0, 130.7. 130.5, 130.4, 129.7, 128.2, 127.2, 126.9, 125.6, 123.4, 49.2, 45.5, 32.7, 27.4. HRMS (*m/z*) [M+H$^+$] calcd for $C_{24}H_{17}Cl_2NO_2$ 422.0715; found, 422.0711. Optical rotation: $[\alpha]^{25}_D$ +196.0 (c = 0.35, $CHCl_3$). New compound.

Phenylmethanamine hydrochloride – Table 3, entry 2A:



A solution of acetamide (0.75 g, 5.00 mmol) in dry THF (12.5 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a light yellow slurry. After stirring at 0 °C for 30 min., dry propylene glycol (0.40 mL, 5.50 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the yellow slurry converted into a solution before again forming a light yellow slurry. The mixture was heated to 60 °C and treated with 3.0 mL MeOH to form an orange solution. Upon cooling to 50 °C, M*t*BE was added slowly before cooling to room temperature. The resulting slurries were filtered off and washed with M*t*BE. After drying, the desired compound was recovered as a light yellow solid (0.35 g, 49% yield): mp 264-265 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (br s, 3H), 7.51 (m, 2H), 7.35 (m, 3H), 3.97 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 134.1, 128.9, 128.4, 128.3, 42.0. Substance data agrees with previously reported information.[2]

2-Benzylisoindoline-1,3-dione – Table 3, entry 2B:

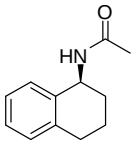


A solution of acetamide (0.75 g, 5.00 mmol) in dry THF (12.5 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a creamy slurry. After stirring at 0 °C for 30 min., dry propylene glycol (0.73 mL, 10.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the yellow slurry converted into a solution before again forming a light yellow slurry. After 1 h, the slurry was

[2] Verkade, J.M.M.; van Hemert, L.J.C.; Quaedflieg, P.J.L.M.; Alsters, P.L.; van Delft, F.L.; Rutjes, F.P.J.T. *Tetrahedron Lett.* **2006**, *47*, 8109.

treated with phthalic anhydride (1.56 g, 10.0 mmol) and diluted with toluene (12.5 mL). Pyridine (1.21 mL, 15.0 mmol) was added and the mixture heated to reflux, causing the yellow slurry to become orange and then slowly convert to a solution. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (12.5 mL). Refluxing the mixture enabled azeotropic removal of water with toluene. After 12 h, the reaction was cooled and diluted with EtOAc (50 mL). The organic layer was washed successively with 1 N HCl (15 mL), saturated $NaHCO_3$ (15 mL), and brine (15 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded a yellow-orange solid. Crude NMR indicated good conversion to phthalimide. The desired product was isolated by column chromatography (SiO_2, gradient 99.9% Hex / 0.1% NEt_3 to 30% EtOAc) to yield an off-white solid (1.00 g, 84% yield): mp 114-116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.70 (m, 2H), 7.43 (m, 2H), 7.29 (m, 3H), 4.85 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 136.3, 134.0, 132.1, 128.7, 128.6, 127.8, 123.3, 41.6. Substance data agrees with previously reported information.[3]

(*S*)-*N*-(1,2,3,4-Tetrahydronaphthalen-1-yl)acetamide – Table 3, entry 3:

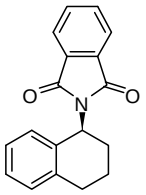


(*S*)-1,2,3,4-tetrahydronaphthalen-1-amine (5.00 mL, 35.6 mmol) was dissolved in dry CH_2Cl_2 (100 mL) and treated with NEt_3 (5.95 mL, 42.7 mmol). The solution was cooled to 0 ºC and treated with acetyl chloride (2.78 mL, 39.2 mmol) to yield a yellow solution which eventually converts into a slurry. The reaction was warmed to room temperature over 16 h prior to quenching with 1 N HCl (25 mL). After separation of the phases, the organic layer was washed with saturated $NaHCO_3$ solution (25 mL) and brine (25 mL), dried over Na_2SO_4, filtered, and concentrated to a yellow solid. The crude solid was recrystallized from 2-PrOH / H_2O and dried to give 4.54 g (67 %) white solid: mp 153-154 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (m, 4H), 5.80 (br, 1H), 5.17 (m, 1H), 2.77 (m, 2H), 2.02 (m, 1H), 2.00 (s, 3H), 1.82 (m, 1H + 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 137.5, 136.6, 129.1, 128.7, 127.2, 126.2, 47.4, 30.1, 29.2, 23.5, 19.9. This

[3] Hsieh, J.-C.; Cheng, C.-H. *Chem. Commun. (Cambridge, U.K.)* **2005**, 4554.

material was used without further purification for the next reaction to produce compound Table 3, entry 3B. Our data for the (*S*)-isomer agrees well with previously reported information for the (*R*)-isomer.[4]

(*S*)-2-(1,2,3,4-Tetrahydronaphthalen-1-yl)isoindoline-1,3-dione – Table 3, entry 3B:

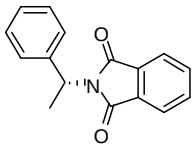


A solution of acetamide (1.90 g, 10.0 mmol) in dry THF (25.0 mL) was treated with pyridine (0.970 mL, 12.0 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.960 mL, 11.0 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a bright yellow slurry. After stirring at 0 °C for 30 min., dry propylene glycol (1.46 mL, 20.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the yellow slurry almost completely dissolved before again forming a yellow slurry. After 90 min., the slurry was treated with phthalic anhydride (3.12 g, 20.0 mmol) and diluted with toluene (25.0 mL). Pyridine (2.41 mL, 29.8 mmol) was added and the mixture heated to reflux, causing the yellow slurry to change in appearance. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (25.0 mL). Refluxing the mixture enabled azeotropic removal of water with toluene. After 16 h, the reaction was cooled and diluted with $CHCl_3$ (80 mL). The organic layer was washed successively with 1 N HCl (30 mL), saturated $NaHCO_3$ (30 mL), and brine (30 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded a crude brown oil. The desired product was purified by column chromatography (SiO_2, gradient 100% Hex to 30% EtOAc) to yield a light yellow solid (2.40 g, 86% yield of a single enantiomer): mp 124-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.72 (m, 2H), 7.15 (s, 1H), 7.14 (s, 1H), 7.06 (m, 1H), 6.94 (m, 1H), 5.55 (m, 1H), 3.03 (m, 1H), 2.83 (m, 1H), 2.43 (m, 1H), 2.11 (m, 2H), 1.85 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 137.8, 134.6, 133.9, 132.0, 129.2, 126.9, 126.0, 125.8, 123.2, 49.3, 29.4, 28.0, 22.4. HRMS (m/z) [M+H$^+$]

[4] Kim, M.-J.; Kim, W.-H.; Han, K.; Choi, Y.K.; Park, J. *Org. Lett.* **2007**, *9*, 1157.

calcd for $C_{18}H_{15}NO_2$ 278.1181; found, 278.1176. The enantiomeric purity (>99.5%) was determined by HPLC conditions: Chiralcel OD, *n*-heptane/2-propanol = 99.0/1.0, flow rate = 1.0 mL/min., UV 215 nm (*S*)-isomer = 6.83 min., (*R*)-isomer = 7.93 min. Optical rotation: $[\alpha]^{25}_{D}$ -125.0 (c = 0.54, MeOH) – our data for the single enantiomer agrees well with that reported for the previous racemic compound.[5]

(*R*)-2-(1-Phenylethyl)isoindoline-1,3-dione – Table 3, entry 4B:

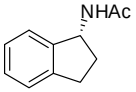


A solution of acetamide (1.63 g, 10.0 mmol) in dry THF (25.0 mL) was treated with pyridine (0.970 mL, 12.0 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.960 mL, 11.0 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a white slurry which became yellow-orange. After stirring at 0 °C for 30 min., dry propylene glycol (1.46 mL, 20.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the yellow slurry almost completely dissolved before again forming a yellow slurry with a separate lower phase. After 90 min., the slurry was treated with phthalic anhydride (3.12 g, 20.0 mmol) and diluted with toluene (25.0 mL). Pyridine (2.41 mL, 29.8 mmol) was added and the mixture heated to reflux, causing the yellow slurry to change in appearance. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (25.0 mL). Refluxing the mixture enabled azeotropic removal of water with toluene. After 16 h, the reaction was cooled and diluted with EtOAc (50 mL). The organic layer was washed successively with 1 N HCl (30 mL), saturated $NaHCO_3$ (30 mL), and brine (30 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded an orange residue. Crude NMR indicated good conversion to phthalimide. The desired product was isolated by column chromatography (SiO_2, gradient 100% Hex to 30% EtOAc) to yield a yellow oil (2.21 g, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$,) δ 7.81 (m, 2H), 7.68 (m, 2H), 7.50 (m, 2H), 7.33 (m, 2H), 7.26 (m, 1H), 5.57 (q, 1H, *J* = 7.3 Hz), 1.92 (d, 1H, *J* = 7.3 Hz). ^{13}C NMR (100 MHz,

[5] Capitosti, S.M.; Hansen, T.P.; Brown, M.L. *Bioorg.Med. Chem.* **2004**, *12*, 327.

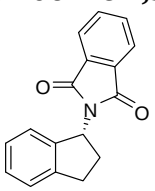
$CDCl_3$) δ 168.1, 140.3, 133.9, 132.0, 128.5, 127.7, 127.4, 123.2, 49.6, 17.5. The enantiomeric purity (>99.5%) was determined by HPLC conditions: Chiralpak AD, hexanes/EtOH/$EtSO_3H$ = 99.0/1.0/0.05, flow rate = 0.75 mL/min., UV 230 nm (*R*)-isomer = 22.0 min., (*S*)-isomer = 24.0 min. Optical rotation: $[\alpha]^{25}_D$ +86.3 (c = 0.31, $CHCl_3$). Substance data agrees with previously reported information, including $[\alpha]^{rt}_D$ +52.2 (c = 0.63, $CHCl_3$).[6]

(*R*)-*N*-(2,3-Dihydro-1*H*-inden-1-yl)acetamide - Table 3, entry 5:



Acetic anhydride (50 mL) was added dropwise to a solution of (*R*)-(-)-1-aminoindane in $CHCl_3$ (50 mL), at 0 °C. The solution was allowed to slowly warm to room temperature and stirred overnight. The reaction mixture was concentrated *in vacuo*. To the residue was added water (50 mL) and extracted twice with $CHCl_3$ (100 mL, 50 mL). The two organic layers were combined and washed with 1 N HCl (50 mL), 5% $NaHCO_3$ (50 mL), dried over Na_2SO_4, filtered and concentrated. The solids were triturated at room temperature with MtBE (30 mL) to afford 11.1 g (84%) of product as a white solid: mp 155-157°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (d, 1H, *J* = 8.00 Hz), 7.23 – 7.14 (m, 4H), 5.25 (q, 1H, *J* = 7.60 Hz), 2.94 – 2.87 (m, 1H), 2.81 – 2.73 (m, 1H), 2.39 – 2.31 (m, 1H), 1.86 (s, 3H), 1.78 – 1.69 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 144.2, 142.9, 127.3, 126.3, 124.5, 123.9. 53.5, 33.1, 29.7, 22.7. The enantiomeric purity (>99.5%) was determined by HPLC conditions: Chiralcel OD, *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min., UV 217 nm (*S*)-isomer = 7.14 min., (*R*)-isomer = 9.57 min. Substance data agrees with previously reported information.[4]

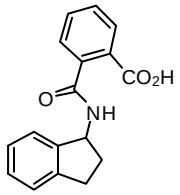
(*R*)-2-(2,3-Dihydro-1*H*-inden-1-yl)isoindoline-1,3-dione – Table 3, entry 5B:



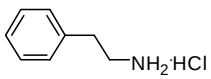
A solution of (*R*)-*N*-(2,3-dihydro-1*H*-inden-1-yl)acetamide (2.0 g, 11.4 mmol) in dry THF (29 mL) was treated with pyridine (1.1 mL, 13.7 mmol) and cooled to 0 °C.

[6] Yang, Q.; Gao, W.; Deng, J.; Zhang, X. *Tetrahedron Lett.* **2006**, *47*, 821.

Dropwise addition of oxalyl chloride (1.1 mL, 12.6 mmol) was accompanied by vigorous bubbling and resulted in a yellow slurry. After stirring at 0 °C for 30 min., dry propylene glycol (1.68 mL, 22.9 mmol) was added in one portion and the reaction warmed to room temperature. After 1 h, the slurry was treated with phthalic anhydride (3.4 g, 23.0 mmol) and diluted with toluene (29 mL). Pyridine (3.0 mL, 37.1 mmol) was added and the mixture was heated to reflux. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (30 mL). The mixture was refluxed overnight. After 19 h, the reaction was cooled and diluted with $CHCl_3$ (100 mL). The organic layer was washed successively with 1 N HCl (43 mL), saturated $NaHCO_3$ (43 mL), and brine (43 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded an oil. The desired product was purified by column chromatography (silica, 9:1 Hex/EtOAc; $R_f = 0.19$), yielding a white solid (2.1 g, 70%): mp 77-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.77 (m, 2H), 7.69 – 7.65 (m, 2H), 7.29 – 7.08 (m, 4H), 5.87 (dd, 1H), 3.40 – 3.33 (m, 1H), 3.03 – 2.95 (m, 1H), 2.58 – 2.43 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 144.0, 140.6, 134.0, 132.1, 128.1, 126.6. 125.0, 123.5, 123.3, 54.8, 31.3, 29.8. HRMS (*m/z*) [M+H$^+$] calcd for $C_{17}H_{13}NO_2$ 264.1025; found, 264.1028. The enantiomeric purity was determined by HPLC conditions: Chiralcel OD, *n*-hexane/2-propanol = 85/15, flow rate = 1.0 mL/min., UV 217 nm (*S*)-isomer = 5.82 min., (*R*)-isomer = 7.31 min. Optical rotation: $[\alpha]^{25}_D$ +194.8 (c = 0.52, $CHCl_3$) – our other data for the (*R*)-isomer agrees well with the previously reported information for the racemic compound.[5] However, that report claimed a "hydrate," with HRMS (*m/z*) [M+H_2O]. We believe that the actual compound reported previously was actually the uncyclized material. This may explain the discrepancy with the reported NMR data as well as mp (173-176 °C).



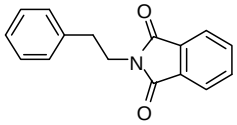
2-Phenylethanamine hydrochloride – Table 4, entry 1A:



A solution of acetamide (0.75 g, 5.00 mmol) in dry THF (12.5 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a bright yellow slurry. After stirring at 0 °C for 30 min.,

dry propylene glycol (0.40 mL, 5.50 mmol) was added in one portion and the reaction warmed to room temperature. Upon warming, the yellow slurry converted into a solution before again forming a light yellow slurry. The mixture was heated to 60 °C and treated with 1.1 mL MeOH to form an orange solution. Upon cooling to 50 °C, M*t*BE was added slowly before cooling to room temperature. The resulting slurries were filtered off and washed with M*t*BE. After drying, the desired compound was recovered as a light yellow solid (0.35 g, 49% yield): mp 220-221 °C. ^{1}H NMR (400 MHz, DMSO) δ 8.25 (br s, 3H), 7.30 (m, 2H), 7.21 (m, 3H), 2.96 (m, 2H), 2.88 (m, 2H). ^{13}C NMR (100 MHz, DMSO) δ 137.4, 128.55, 128.52, 126.6, 39.8, 32.8. Substance data agrees with previously reported information.[7]

2-Phenethylisoindoline-1,3-dione – Table 4, entry 1B:



A solution of acetamide (0.82 g, 5.00 mmol) in dry THF (12.5 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a light yellow slurry. After stirring at 0 °C for 30 min., dry propylene glycol (0.73 mL, 10.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the slurry converted into a solution. After 1 h, the reaction was treated with phthalic anhydride (1.56 g, 10.0 mmol) and diluted with toluene (12.5 mL). Pyridine (1.21 mL, 15.0 mmol) was added and the mixture heated to reflux, causing the yellow slurry to become orange and then slowly convert to a solution. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (12.5 mL). Refluxing the mixture enabled azeotropic removal of water with toluene. After 12 h, the reaction was cooled and diluted with EtOAc (50 mL). The organic layer was washed successively with 1 N HCl (15 mL), saturated $NaHCO_3$ (15 mL), and brine (15 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded a yellow-orange solid (2.3 g crude). Crude NMR indicated good conversion to phthalimide. The desired product was isolated by column

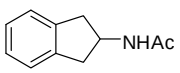
[7] Kitamura, M.; Suga, T.; Chiba, S.; Narasaka, K. *Org. Lett.* **2004**, *6*, 4619.

chromatography (SiO_2, gradient 100% Hex to 30% EtOAc) to yield off-white pearl-like plates (1.07 g, 85% yield): mp 129-131 °C. ^{1}H NMR (400 MHz, $CDCl_3$,) δ 7.83 (m, 2H), 7.71 (m, 2H), 7.25 (m, 5H), 3.92 (t, 2H, *J* = 7.7 Hz), 2.99 (t, 2H, *J* = 7.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 138.0, 133.9, 132.0, 128.8, 128.5, 126.6, 123.2, 39.3, 34.6. Substance data agrees with previously reported information.[8]

Tricyclo[3.3.1.13,7]decan-1-amine hydrochloride – Table 4, entry 2A:

A solution of acetamide (0.97 g, 5.0 mmol) in dry THF (15 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a bright yellow and then turbid orange solution. After stirring at 0 °C for 30 min., dry propylene glycol (0.73 mL, 10.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the solution changed, first turning orange brown before lightening to yellow. The reaction was diluted with ethanol before being concentrated to an orange brown oil. The oil was partitioned between 1 N HCl (10 mL) and M*t*BE (10 mL) and the organic layer washed with 1 N HCl (2 x 5 mL). The combined aqueous layers were basified with 4 N NaOH to pH 11, extracted with EtOAc (3 x 40 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The oily residue was suspended in Et_2O (8 mL) and treated with 1 M HCl in Et_2O (8 mL). This addition formed a lightly colored slurry which was filtered and washed with Et_2O. After drying under vacuum at 50^{o}C for 16 h, 0.66 g of an off-white solid was recovered: decomp. >330 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06 (br s, 3 H), 2.06 (br s, 3H), 1.77 (m, 6H), 1.59 (m, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 50.8, 40.1, 35.1, 28.2. Substance data agrees with previously reported information.[8]

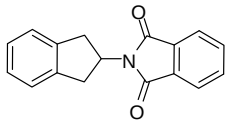
***N*-(2,3-Dihydro-1*H*-inden-2-yl)acetamide – Table 4, entry 3:**



[8] Tang, H.; Wang, X.-D.; Wei, Y.-B.; Huang, S.-L.; Huang, Z.-S.; Tan, J.-H.; An, L.-K.; Wu, J.-Y.; Sun-Chi Chan, A.; Gu, L.-Q. *Eur. J. Med. Chem.* **2008**, *43*, 973.

A mixture consisting of 2-aminoindane hydrochloride (25.0 g, 147.4 mmol), sodium acetate (12.0 g, 146.3 mmol) and acetic anhydride (50 mL) was stirred at room temperature overnight. The reaction mixture was concentrated *in vacuo*. To the residue was added water (150 mL) and extracted twice with $CHCl_3$ (150 mL, 100 mL). The two organic layers were combined and washed with 1 N HCl (100 mL), 5% $NaHCO_3$ (100 mL), dried over $MgSO_4$, filtered and concentrated to afford a tan solid. The solids were triturated at room temperature with MtBE (70 mL) to afford 22.9 g (89%) of product as a beige solid: mp 127-128°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, 1H, J = 6.4 Hz), 7.20 – 7.11 (m, 4H), 4.45 – 4.37 (m, 1H), 3.12 (dd, 2H, J = 16.0, 7.2 Hz), 2.72 (dd, 2H, J = 16.0, 6.0 Hz), 1.78 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.6, 141.9, 127.0, 125.1, 50.6, 23.3. Substance data agrees with previously reported information.[9]

2-(2,3-Dihydro-1*H*-inden-2-yl)isoindoline-1,3-dione – Table 4, entry 3B:

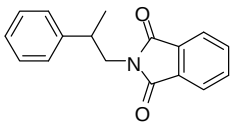


A solution of *N*-(2,3-dihydro-1*H*-inden-2-yl)acetamide (2.0 g, 11.4 mmol) in dry THF (29 mL) was treated with pyridine (1.1 mL, 13.7 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (1.1 mL, 12.6 mmol) was accompanied by vigorous bubbling and resulted in a pale orange slurry. After stirring at 0 °C for 30 min., dry propylene glycol (1.68 mL, 22.9 mmol) was added in one portion and the reaction warmed to room temperature. After 1 h, the slurry was treated with phthalic anhydride (3.4 g, 23.0 mmol) and diluted with toluene (29 mL). Pyridine (3.0 mL, 37.1 mmol) was added and the mixture was heated to reflux. THF (36 mL) was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (36 mL). The mixture was refluxed overnight. The reaction mixture was distilled to dryness. The resulting solids were dissolved in $CHCl_3$ (100 mL). The organic layer was washed successively with 1 N HCl (43 mL), saturated $NaHCO_3$ (43 mL), and brine (43 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded a tan solid. The crude product was triturated by refluxing in EtOH (50 mL) to yield a tan solid (2.6 g, 86%): mp 197-198°C. ^{1}H NMR

[9] Chazalette, C.; Masereel, B.; Rolin, S.; Thiry, A.; Scozzafava, A.; Innocenti, A.; Supuran, C.T. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5781.

(400 MHz, $CDCl_3$) δ 7.86 – 7.82 (m, 2H), 7.73 – 7.66 (m, 2H), 7.25 – 7.17 (m, 4H), 5.20 – 5.11 (m, 1H), 3.63 (dd, 2H, *J* = 15.2, 9.6 Hz), 3.18 (dd, 2H, J = 14.8, 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 141.1, 134.1, 132.2, 126.9, 124.6, 123.4. 50.2, 36.2. Substance data agrees with previously reported information.[10]

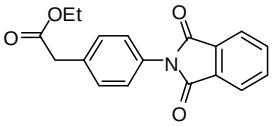
2-(2-Phenylpropyl)isoindoline-1,3-dione – Table 4, entry 4B:



A solution of *N*-(2-phenylpropyl)acetamide (1.77 g, 10.0 mmol) and pyridine (0.97 mL, 12.0 mmol) in dry THF (25.0 mL) was cooled to 0 °C. Oxalyl chloride (0.96 mL, 11.0 mmol) was charged dropwise. After stirring at 0 °C for 30 min., dry propylene glycol (1.46 mL, 20.0 mmol) was added and the reaction warmed to room temperature. After 1 h at room temperature, the slurry was treated with phthalic anhydride (3.12 g, 20.0 mmol), pyridine (2.42 mL, 31.8 mmol) and diluted with toluene (25.0 mL). The reaction mixture was heated to reflux. THF was removed by distillation. Additional toluene (25.0 mL) was added into the reaction mixture and distilled to remove water. The reaction mixture was refluxed with a Dean-Stark apparatus to enable azeotropic removal of water with toluene. After 16 h, the reaction was cooled to room temperature and diluted with EtOAc (70 mL). The organic layer was washed with 1 N HCl (30 mL), saturated $NaHCO_3$ (30 mL), and brine (30 mL), dried over Na_2SO_4, filtered, and concentrated to give an orange crude oil (2.8 g). The crude oil was purified with flash chromatography (SiO_2 gradient 100% Hex to 30% EtOAc) to produce a yellow oil (2.0 g, 75% yield). The product solidified after standing several hours at rt: mp 56-57 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (m, 2H), 7.67 (m, 2H), 7.27 (m, 4H), 7.19 (m, 1H), 3.83 (m, 2H), 3.35 (m, 1H), 1.31 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 143.2, 133.8, 131.8, 128.4, 127.2, 126.7, 123.1, 44.8, 38.4, 18.9. Substance data agrees with previously reported information.[11]

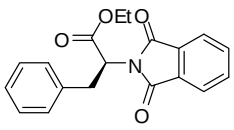
[10] Paleo, M.R.; Dominguez, D.; Castedo, L. *Tetrahedron* **1994**, *50*, 3627.
[11] Suau, R.; Garcia-Segura, R.; Sanchez-Sanchez, C.; Perez-Inestrosa, E.; Pedraza, A.M. *Tetrahedron* **2003**, *59*, 2913.

Ethyl 2-(4-(1,3-dioxoisoindolin-2-yl)phenyl)acetate – Table 4, entry 5B:



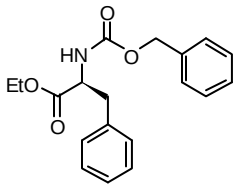
A solution of acetamide (1.11 g, 5.00 mmol) in dry THF (12.5 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a light yellow slurry. After stirring at 0 °C for 30 min., dry propylene glycol (0.73 mL, 10.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the slurry dissipated. After 1 h, the reaction was treated with phthalic anhydride (1.56 g, 10.0 mmol) and diluted with toluene (12.5 mL). Pyridine (1.21 mL, 15.0 mmol) was added and the mixture heated to reflux, causing the orange slurry to become a blood-orange solution. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (12.5 mL). Refluxing the mixture enabled azeotropic removal of water with toluene. After 12 h, the reaction was cooled and diluted with EtOAc (30 mL). The organic layer was washed successively with 1 N HCl (15 mL), saturated $NaHCO_3$ (15 mL), and brine (15 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded a lightly colored solid. The desired product was recrystallized from EtOH to yield an off-white solid (0.85 g). Further solids were isolated from the mother liquors (0.12 g, total yield 63%): mp 147-148 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (m, 2H), 7.80 (m, 2H), 7.42 (m, 4H), 4.16 (q, 2H, J = 7.3 Hz), 3.66 (s, 2H), 1.27 (t, 3H, J = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 167.2, 134.4, 131.7, 130.6, 130.1, 130.0, 126.6, 123.7, 61.0, 41.1, 14.2. HRMS (*m/z*) [M+H$^+$] calcd for $C_{18}H_{15}NO_4$ 310.1079; found, 310.1083. New compound.

(*S*)-Ethyl 2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate –
Table 4, entry 6B:



A solution of acetamide (1.18 g, 5.00 mmol) in dry THF (12.5 mL) was treated with pyridine (0.485 mL, 6.00 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.480 mL, 5.50 mmol) was accompanied by vigorous bubbling and conversion of the clear, colorless solution to a light yellow slurry. After stirring at 0 °C for 30 min., dry propylene glycol (0.73 mL, 10.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the yellow slurry dissolved before again thickening to a slurry. After 3 h, the slurry was treated with phthalic anhydride (1.56 g, 10.0 mmol) and diluted with toluene (12.5 mL). Pyridine (1.21 mL, 15.0 mmol) was added and the mixture heated to reflux, causing the yellow slurry to become orange and then slowly convert to a biphasic solution. THF was removed with a Dean-Stark apparatus before heating the mixture further with additional toluene (12.5 mL). Refluxing the mixture enabled azeotropic removal of water with toluene. After 16 h, the reaction was cooled and the solids dissolved with EtOAc (30 mL). The organic layer was washed successively with 1 N HCl (15 mL), saturated $NaHCO_3$ (15 mL), and brine (15 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded a yellow-orange solid. Crude NMR indicated good conversion to phthalimide. The desired product was isolated by a silica plug to yield a lightly colored oil (1.00 g, 62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (m, 2H), 7.69 (m, 2H), 7.17 (m, 5H), 5.14 (m, 1H), 4.24 (m, 2H), 3.56 (m, 2H), 1.26 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 167.5, 136.8, 134.0, 131.6, 128.8, 128.5, 126.8, 123.4, 62.0, 53.4, 34.6, 14.1. Substance data agrees with previously reported information.[12]

(*S*)-Ethyl 2-(benzyloxycarbonylamino)-3-phenylpropanoate – Table 4, entry 6C:

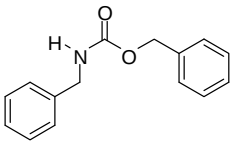


A solution of acetamide (2.35 g, 10.0 mmol) in dry THF (25 mL) was treated with pyridine (0.97 mL, 12.0 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.96 mL, 11.0 mmol) was accompanied by bubbling and conversion to a light yellow

[12] Huang, T.-S.; Li, C.-J. *Org. Lett.* **2001**, *3*, 2037.

slurry. After stirring at 0 °C for 30 min., dry propylene glycol (1.46 mL, 20.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the slurry changed in appearance only slightly. The reaction was diluted with ethanol to form an orange solution. Concentration *in vacuo* yielded a red-orange oil that was taken up in ethyl acetate (25 mL) and water (25 mL). After cooling to 0 ^{o}C, $KHCO_3$ (4.0 g, 40.0 mmol) was added in portions, resulting in vigorous bubbling. Cbz-Cl (5.71 mL, 40.0 mmol) was added slowly, with light bubbling and a transient slurry. After warming to room temperature over 16 h, the layers were separated. The light yellow organic layer was washed with 1 N HCl (15 mL), saturated $NaHCO_3$ (15 mL), and brine (15 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded an orange oil (7.5 g crude). The desired product was isolated by column chromatography (SiO_2, gradient 100% Hex to 30% EtOAc) to yield a colorless oil (1.87 g, 57% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.12 (m, 10H), 5.35 (m, 1H), 5.12 (s, 2H), 4.66 (m, 1H), 4.17 (q, 2H, J = 7.1 Hz), 3.12 (m, 2H), 1.24 (t, 3H, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 155.6, 135.7, 129.6, 129.3, 128.5, 128.2, 128.13, 128.07, 127.07, 66.9, 61.5, 54.8, 38.3, 14.1. The enantiomeric purity (>99.5%) was determined by HPLC conditions: Chiralcel OD, *n*-heptane/2-propanol = 99.0/1.0, flow rate = 1.0 mL/min., UV 215 nm (*S*)-isomer = 12.10 min., (*R*)-isomer = 14.27 min. Optical rotation: $[\alpha]^{25}_{D}$ -14.1 (c = 0.51, MeOH) {lit.: oil; $[\alpha]^{20}_{D}$ -12.7 (c = 1, MeOH)}. Substance data agrees with previously reported information.[13]

Benzyl benzylcarbamate (5) from Scheme 2:



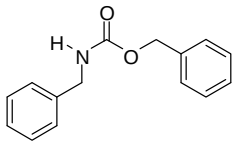
A solution of *N*-benzylacetamide (**3**, 0.75 g, 5.00 mmol) and *N*-benzylbenzamide (**4**, 1.06 g, 5.00 mmol) in dry THF (25 mL) was treated with pyridine (0.97 mL, 12.0 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.96 mL, 11.0 mmol) was accompanied by bubbling and conversion to a yellow slurry. After stirring at 0 °C for 60 min., dry propylene glycol (1.46 mL, 20.0 mmol) was added in one portion and the

[13] Moriniere, J.L.; Danree, B.; Lemoine, J.; Guy, A. *Synth. Commun.* **1988**, *18*, 441.

reaction warmed to room temperature. During this warming phase, the slurry became much thinner. After 2 h, the reaction was diluted with ethanol to form an orange solution. Concentration *in vacuo* yielded a cloudy yellow oil that was partitioned between 1:1 M*t*BE/EtOAc (20 mL) and 0.1 N HCl (20 mL). The separated organic layer – containing unreacted *N*-benzylbenzamide – was extracted with 0.1 N HCl (5 mL) and the combined aq layers extracted with EtOAc (2 x 10 mL). The *N*-benzylbenzamide (**4**) starting material was recovered as a white solid (0.82 g, 78% yield) from the organic layers by concentration and purification by column chromatography (SiO_2, gradient 100% Hex to 50% EtOAc).

The aq phases were carried forward into the subsequent reaction. Basification with 1 N NaOH (16 mL) yielded an orange solution that was extracted with EtOAc (3 x 10 mL). The combined organic layers were diluted with water (50 mL) and cooled to 0 ^{o}C. $KHCO_3$ (2.0 g, 20.0 mmol) was added in portions, resulting in vigorous bubbling. Cbz-Cl (2.85 mL, 20.0 mmol) was added slowly, with light bubbling and the formation of a white slurry. After warming to room temperature over 16 h, the layers were separated. The organic layer was washed with 1 N HCl (20 mL), water (20 mL), and brine (20 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded an orange oil. Benzyl benzylcarbamate (**5**) was isolated by column chromatography (SiO_2, gradient 100% Hex to 33% EtOAc) to yield a colorless solid (0.85 g, 70% yield): mp 59-60 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.26 (m, 10H), 5.28 (br s, 1H), 5.14 (s, 2H), 4.38 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 138.4, 136.5, 128.6, 128.5, 128.1, 127.5, 66.8, 45.1. Substance data agrees with previously reported information.[14]

Benzyl benzylcarbamate (5) from Scheme 3:

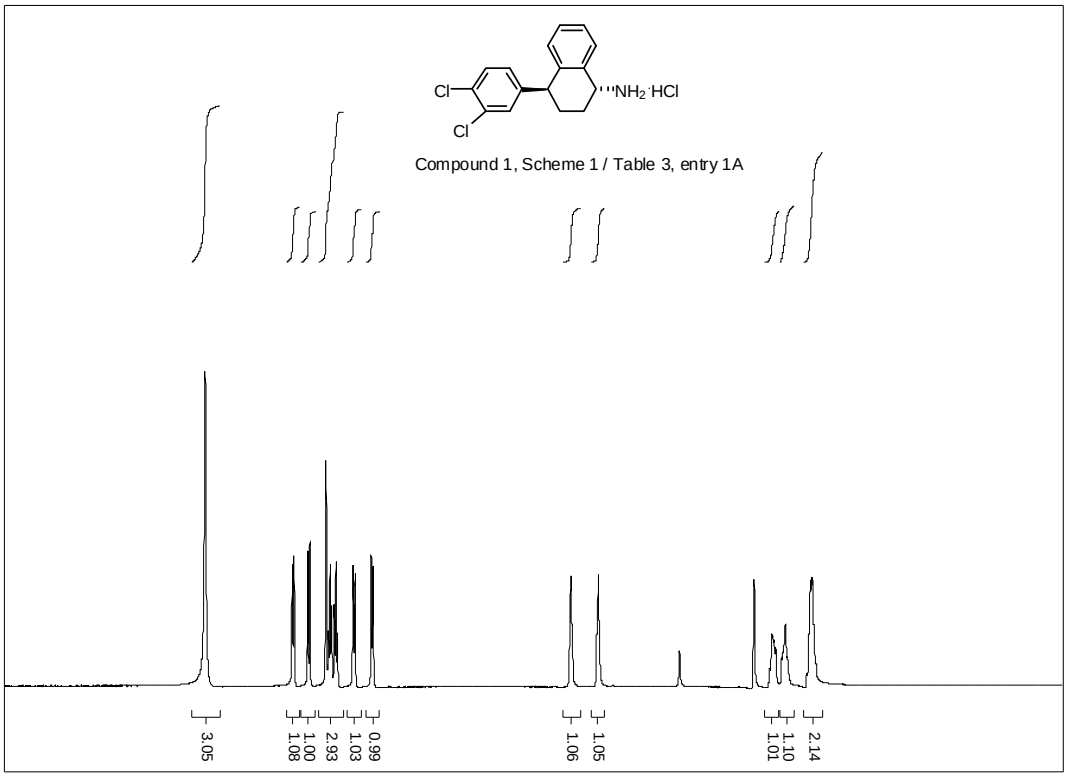


A solution of *N*-benzylacetamide (**3**, 0.37 g, 2.5 mmol) and *N*,*N*-dibenzylacetamide (**6**, 0.60 g, 2.5 mmol) in dry THF (12.5 mL) was treated with pyridine (0.49 mL, 6.0 mmol) and cooled to 0 °C. Dropwise addition of oxalyl chloride (0.48 mL, 5.5 mmol) was

[14] Yang, B.-L.; Tian, S.-K.. *Eur. J. Org. Chem.* **2007**, 4646.

accompanied by bubbling and conversion to a yellow slurry. After stirring at 0 °C for 60 min., dry propylene glycol (0.73 mL, 10.0 mmol) was added in one portion and the reaction warmed to room temperature. During this warming phase, the slurry changed in appearance. After 2 h, the reaction was diluted with ethanol and the solution concentrated *in vacuo* to yield a cloudy yellow oil that was partitioned between EtOAc (10 mL) and 0.1 N HCl (20 mL). The organic layer – containing unreacted *N,N*-dibenzylacetamide – was extracted with 0.1 N HCl (5 mL) and the combined aq layers extracted with EtOAc (2 x 10 mL). The *N,N*-dibenzylacetamide (**6**) starting material was recovered as an orange oil (0.54 g, 90% yield) from the organic layers by concentration and purification by column chromatography (SiO_2, gradient 100% Hex to 33% EtOAc).
The aq phases were carried forward into a subsequent reaction. Basification with 1 N NaOH (20 mL) yielded an orange solution that was extracted with EtOAc (3 x 10 mL). The combined organic layers were diluted with water (25 mL) and cooled to 0 ^{o}C. $KHCO_3$ (1.0 g, 10.0 mmol) was added in portions, resulting in vigorous bubbling. Cbz-Cl (1.43 mL, 10.0 mmol) was added slowly, with light bubbling and the formation of a white slurry. After warming to room temperature over 16 h, the layers were separated. The organic layer was washed with 1 N HCl (20 mL), water (20 mL), and brine (20 mL). Drying over Na_2SO_4, filtration, and concentration *in vacuo* yielded a yellow oil. Benzyl benzylcarbamate (**5**) was isolated by column chromatography (SiO_2, gradient 100% Hex to 33% EtOAc) to yield the same colorless solid (0.47 g, 78% yield).[14]

NMR Spectra


Cl
Cl
NH2·HCl
Compound 1, Scheme 1 / Table 3, entry 1A
3.05
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1.00
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1.03
0.99
1.06
1.05
1.01
1.10
2.14
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6.0
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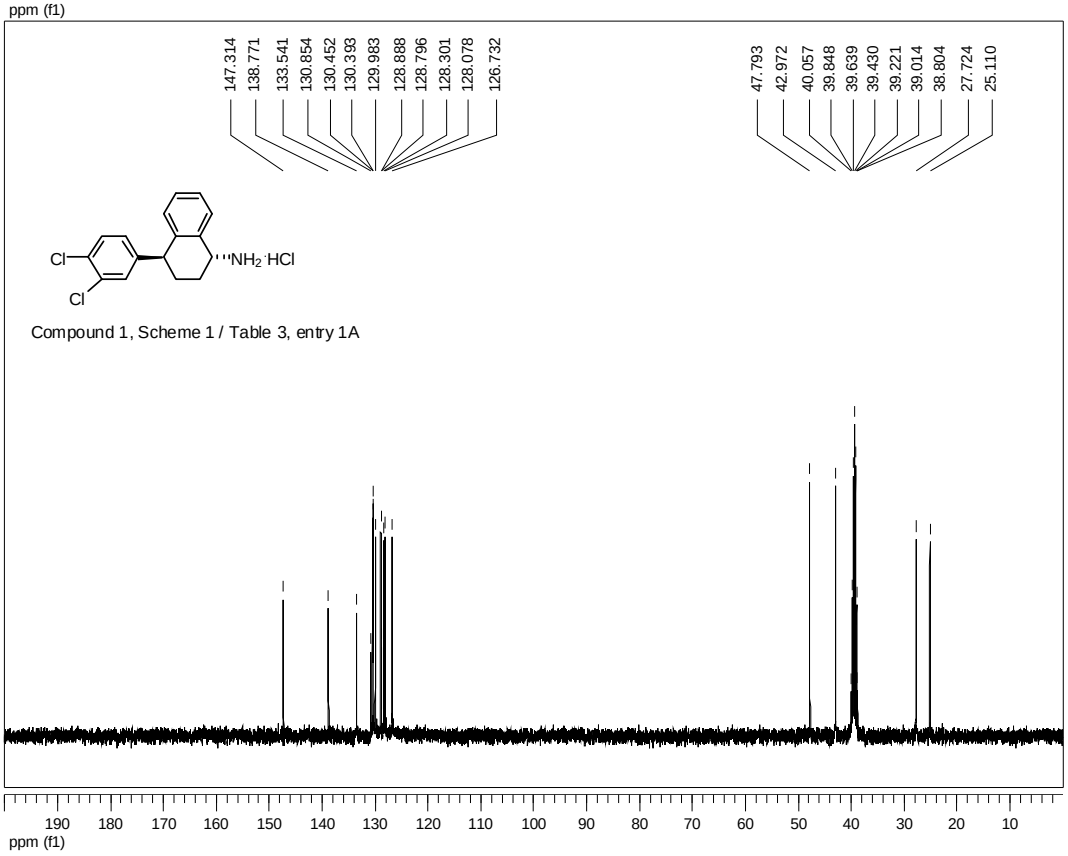
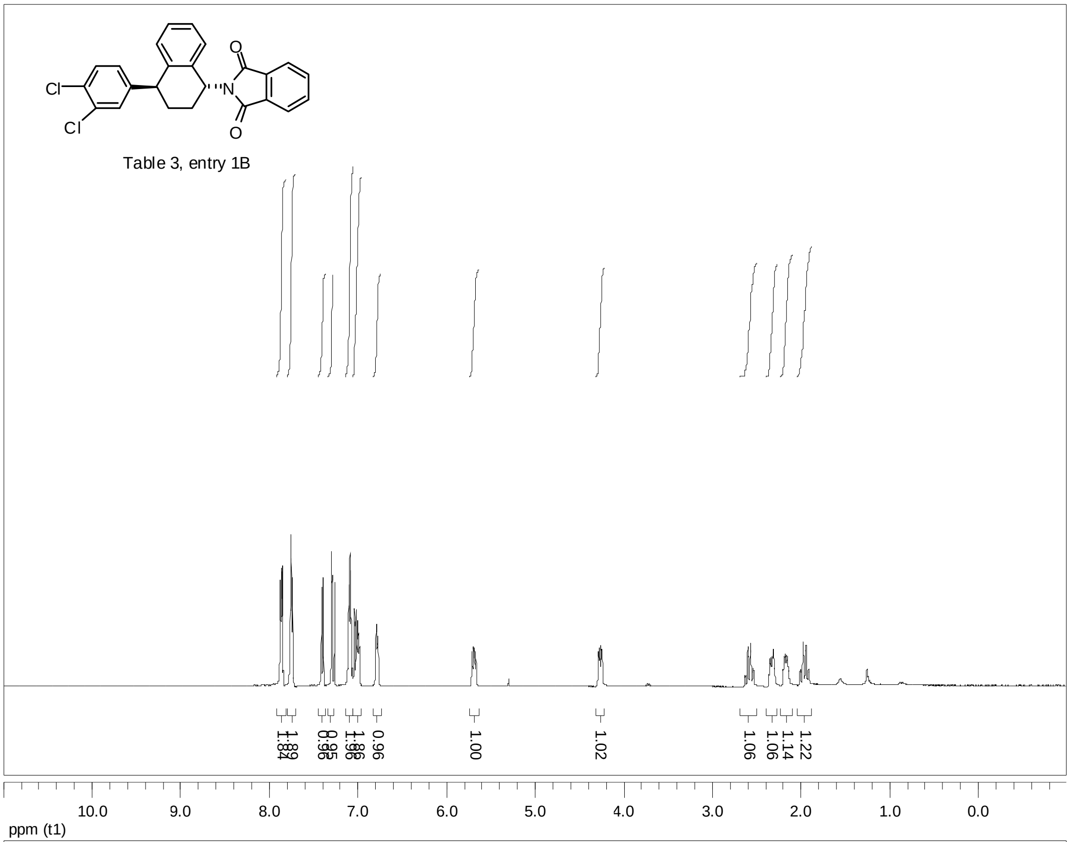
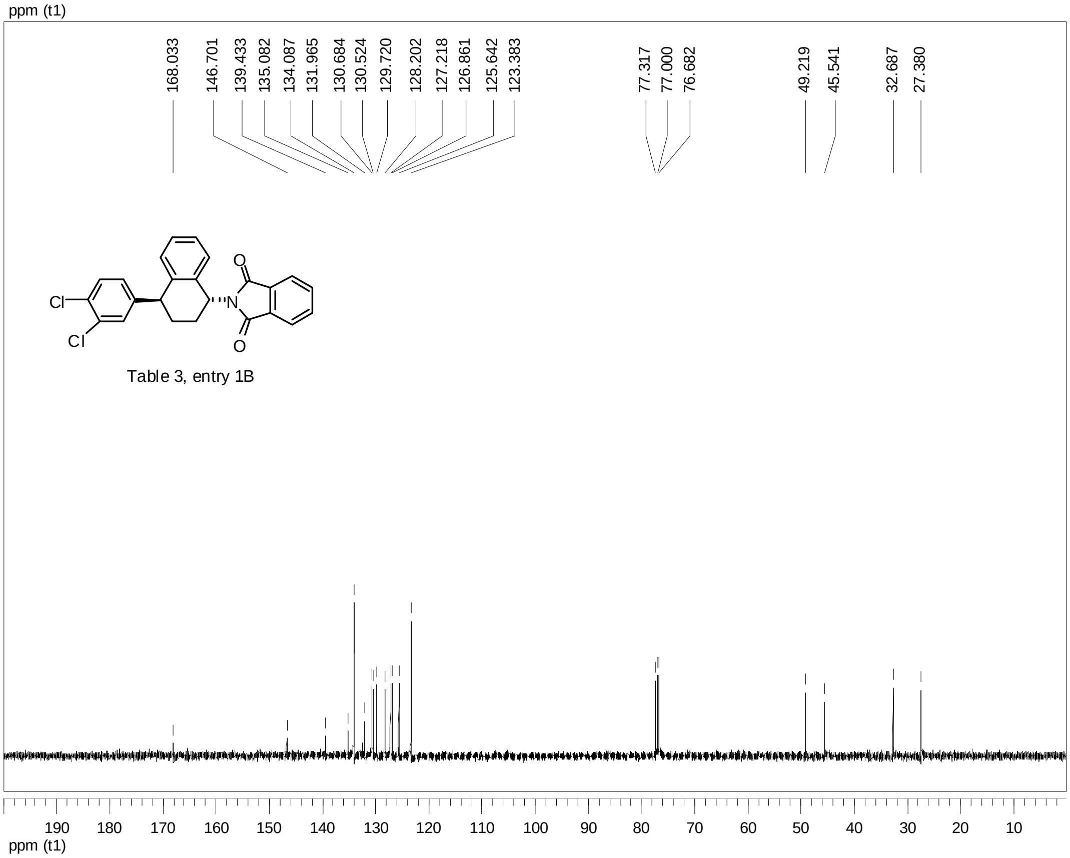
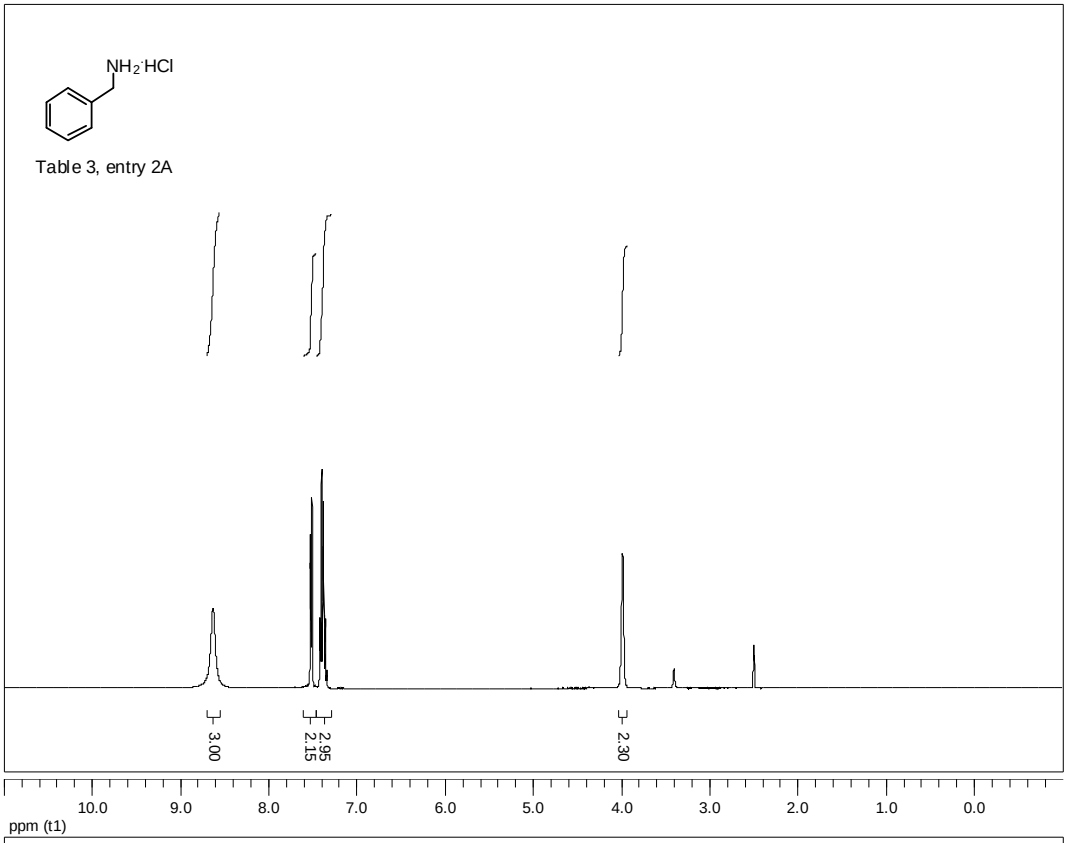
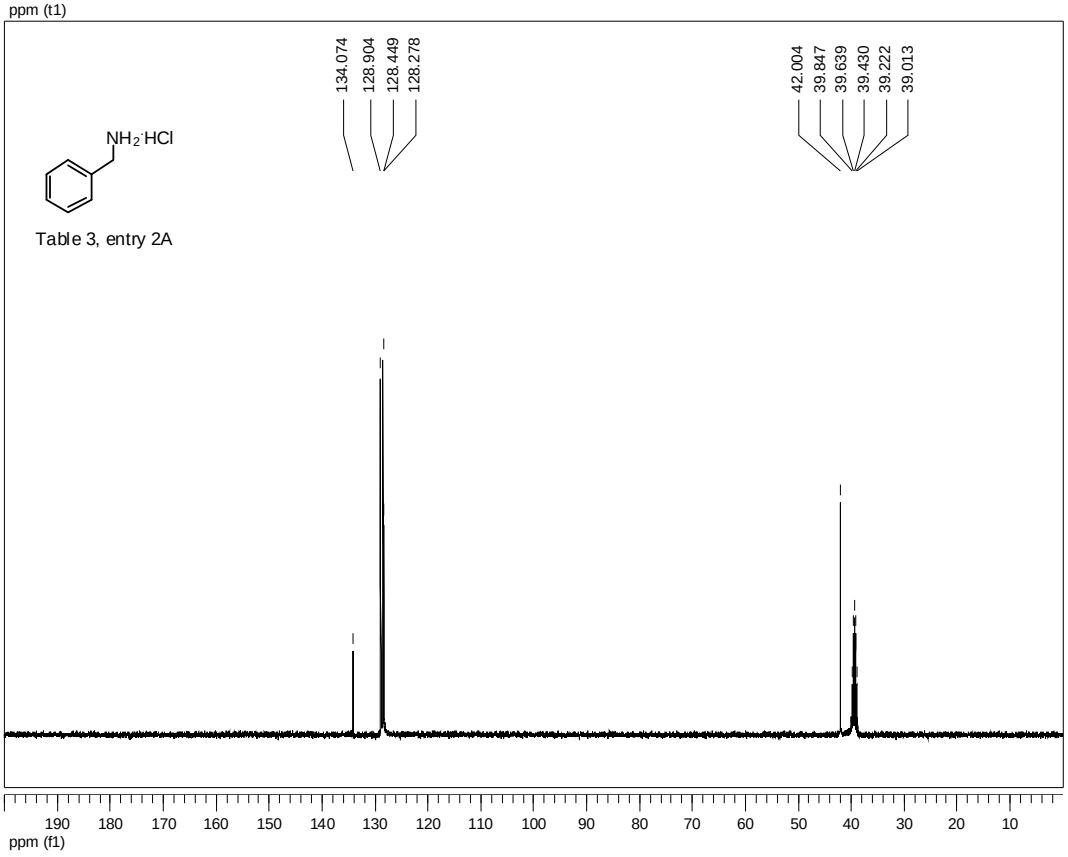
ppm (f1)


147.314
138.771
133.541
130.854
130.452
130.393
129.983
128.888
128.796
128.301
128.078
126.732
47.793
42.972
40.057
39.848
39.639
39.430
39.221
39.014
38.804
27.724
25.110
Cl
Cl
NH2·HCl
Compound 1, Scheme 1 / Table 3, entry 1A
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)


Cl
Cl
N
O
O
Table 3, entry 1B
1.84
1.89
0.95
0.95
1.96
1.96
0.96
1.00
1.02
1.06
1.06
1.14
1.22
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


168.033
146.701
139.433
135.082
134.087
131.965
130.684
130.524
129.720
128.202
127.218
126.861
125.642
123.383
77.317
77.000
76.682
49.219
45.541
32.687
27.380
Cl
Cl
N
O
O
Table 3, entry 1B
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)


NH2·HCl
Table 3, entry 2A
3.00
2.15
2.95
2.30
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


134.074
128.904
128.449
128.278
42.004
39.847
39.639
39.430
39.222
39.013
NH2·HCl
Table 3, entry 2A
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)

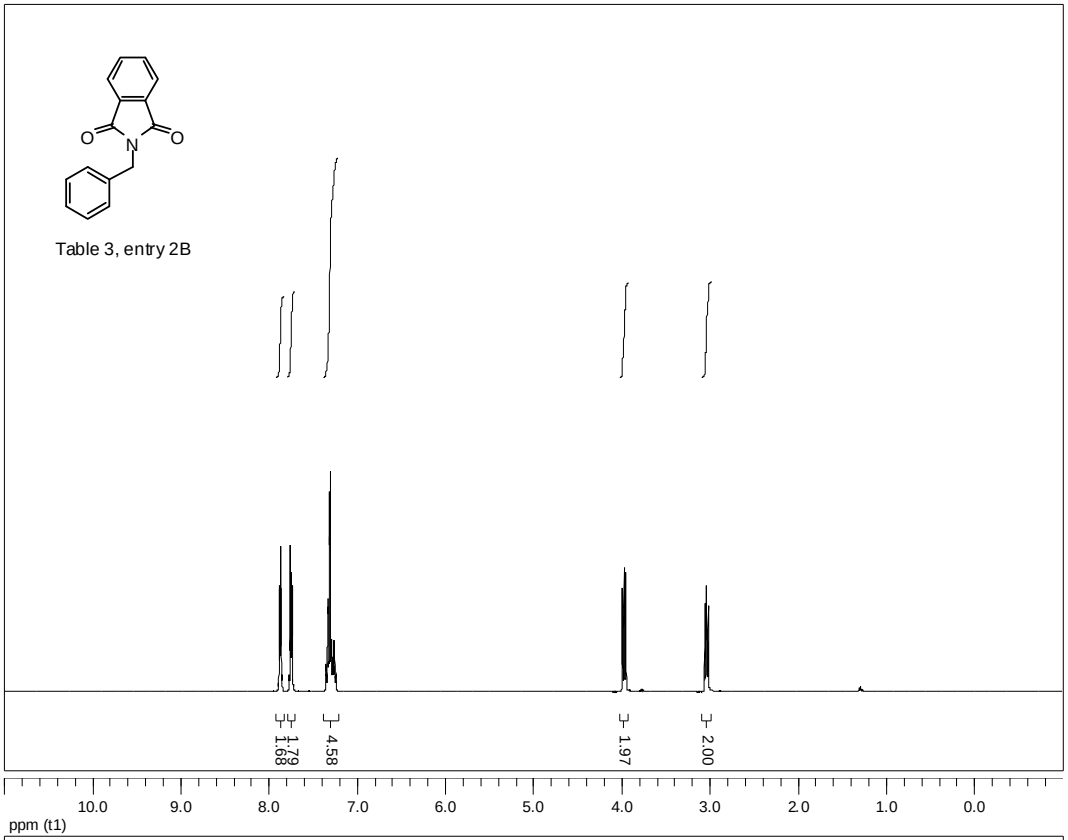
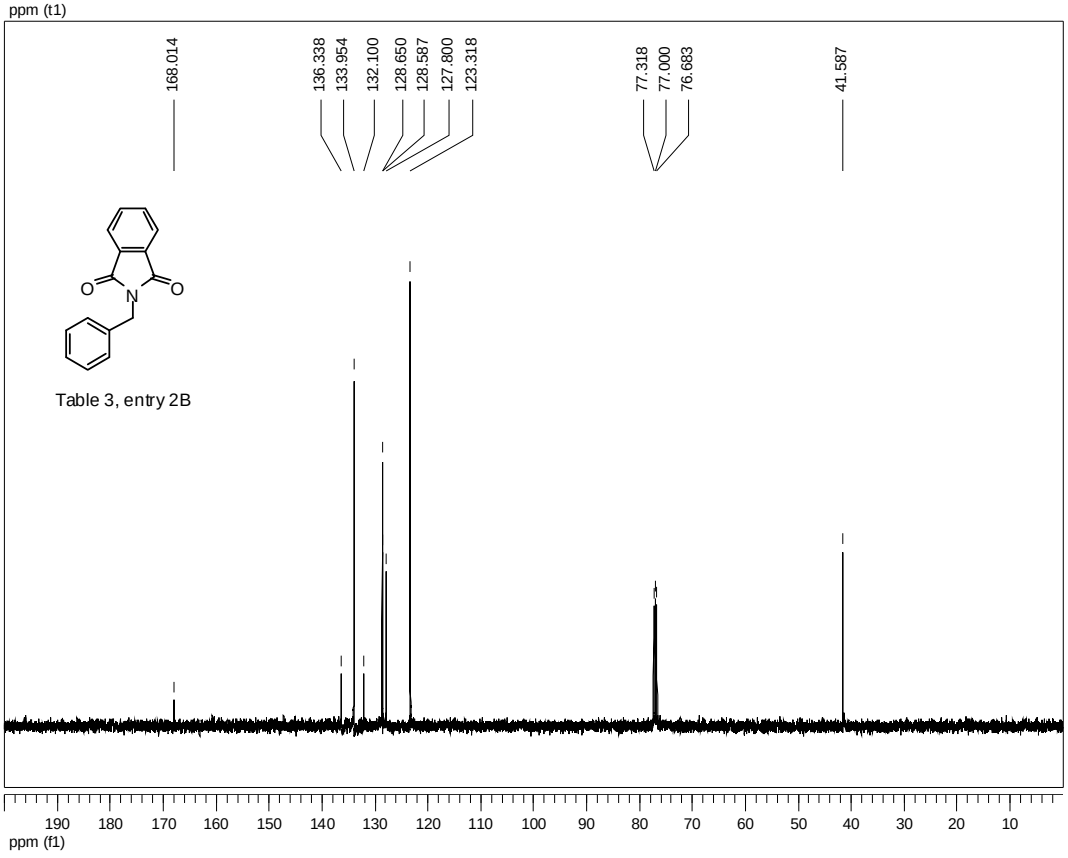
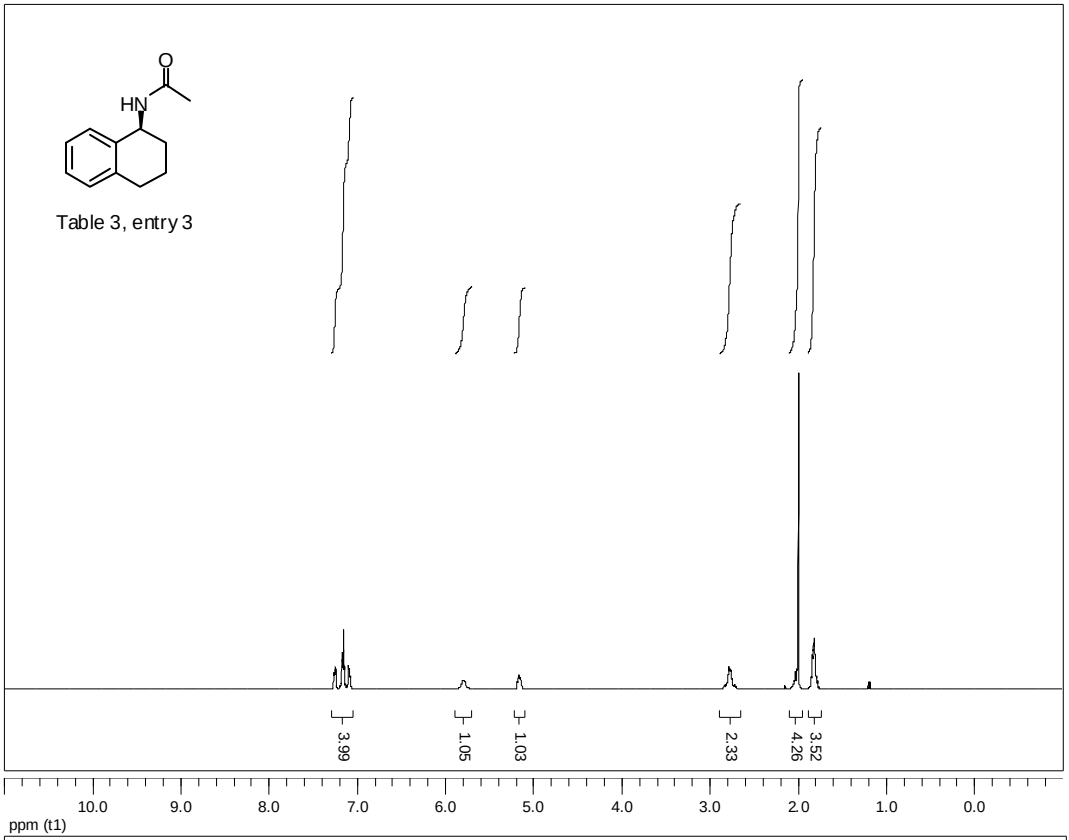
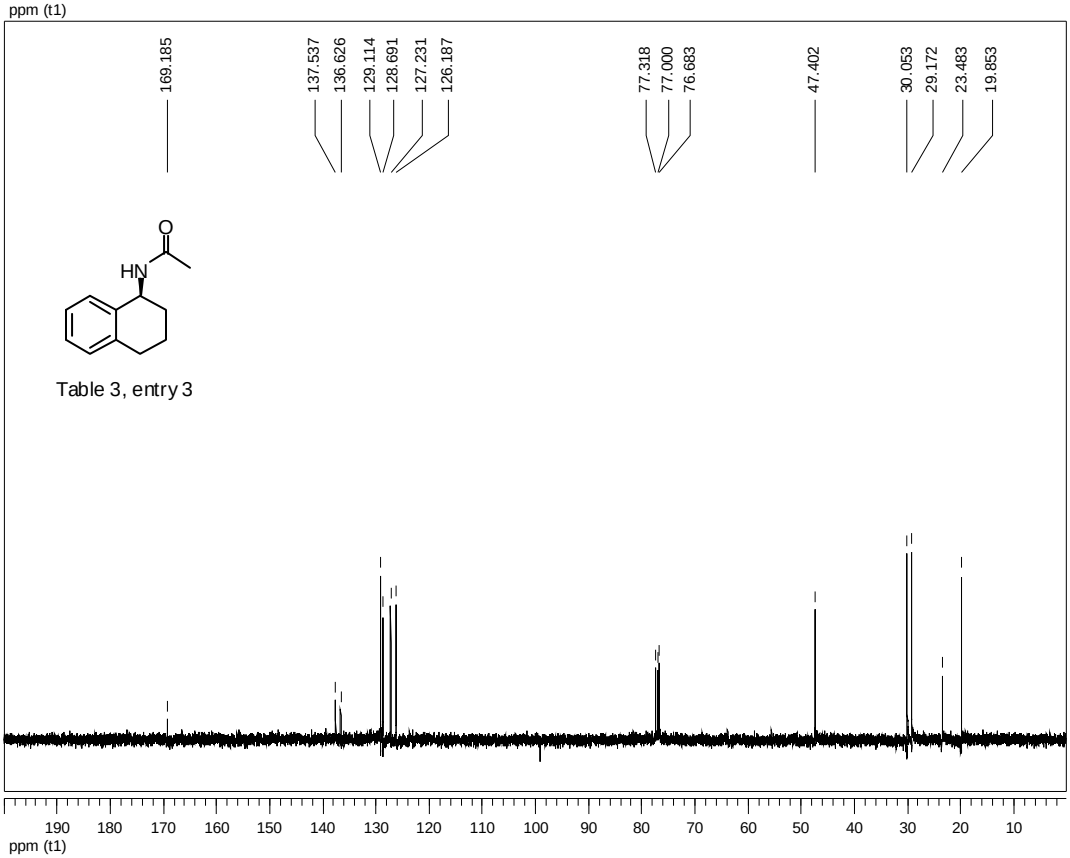


Table 3, entry 2B
1.98
1.79
4.58
1.97
2.00
ppm (t1)


168.014
136.338
133.954
132.100
128.650
128.587
127.800
123.318
77.318
77.000
76.683
41.587
Table 3, entry 2B
ppm (f1)


HN
O
Table 3, entry 3
3.99
1.05
1.03
2.33
4.26
3.52
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


169.185
137.537
136.626
129.114
128.691
127.231
126.187
77.318
77.000
76.683
47.402
30.053
29.172
23.483
19.853
HN
O
Table 3, entry 3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

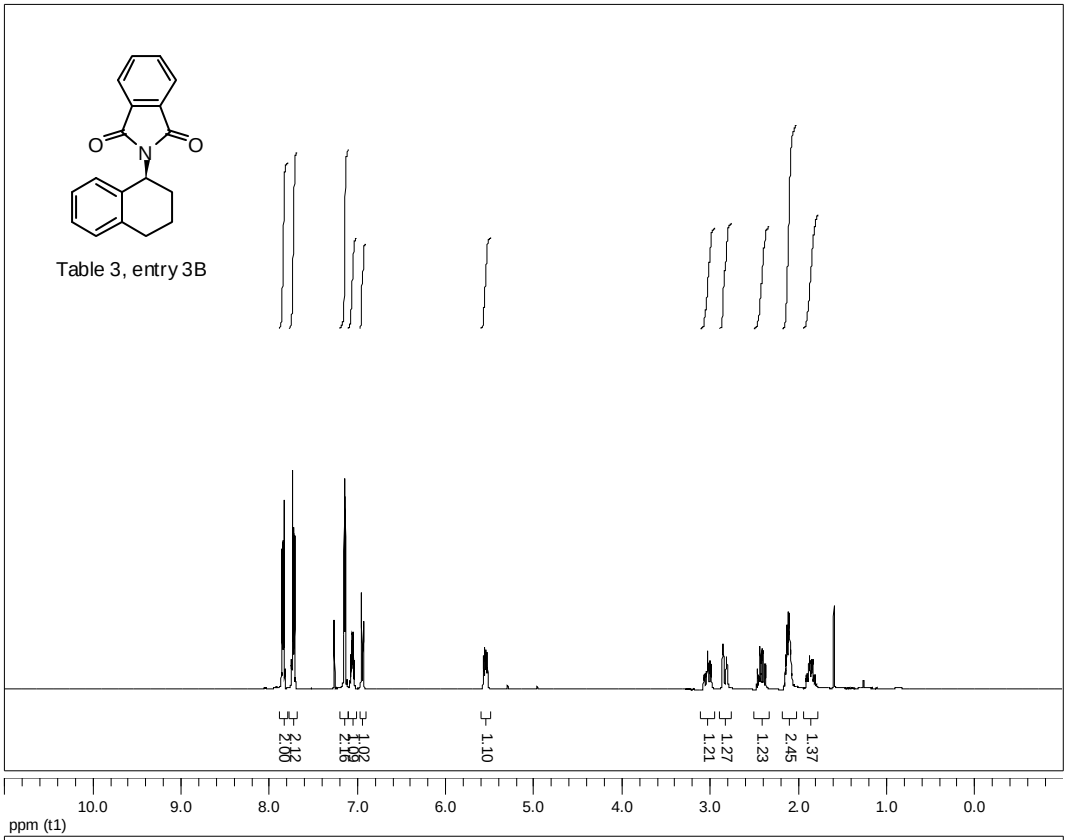
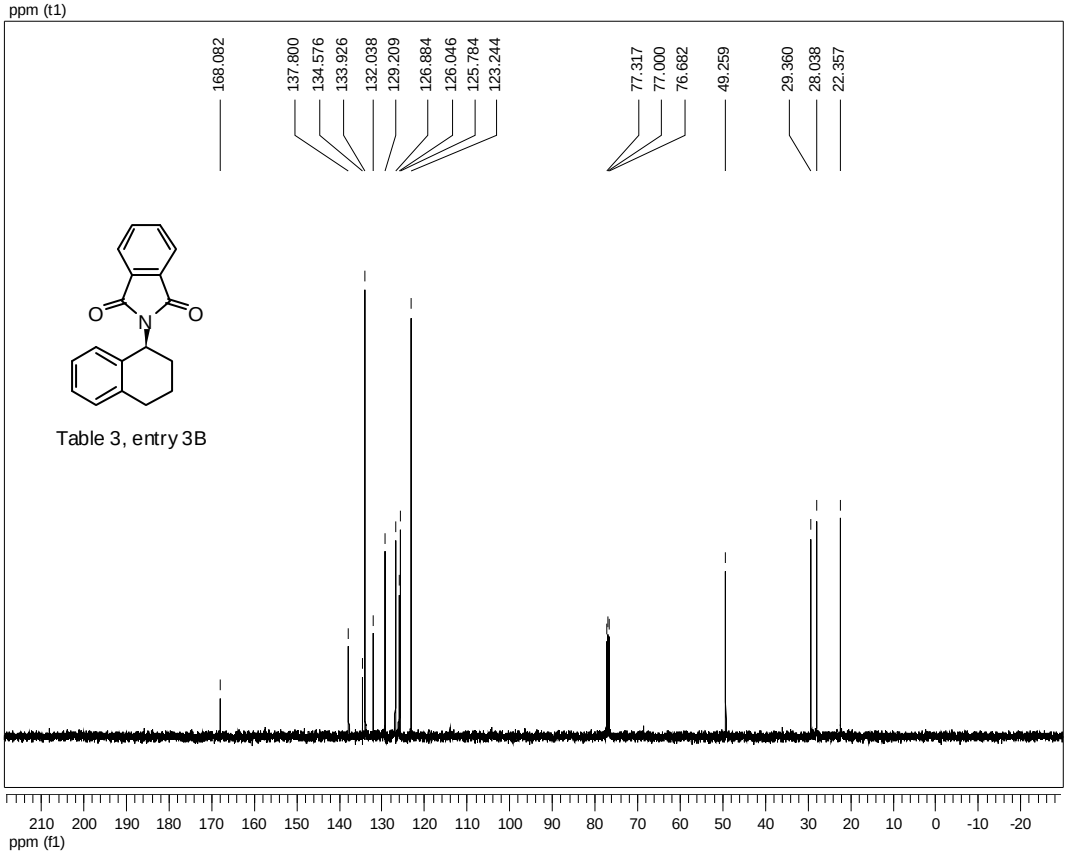


Table 3, entry 3B
2.12
2.06
1.02
2.16
1.10
1.21
1.27
1.23
2.45
1.37
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


168.082
137.800
134.576
133.926
132.038
129.209
126.884
126.046
125.784
123.244
77.317
77.000
76.682
49.259
29.360
28.038
22.357
Table 3, entry 3B
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
ppm (f1)

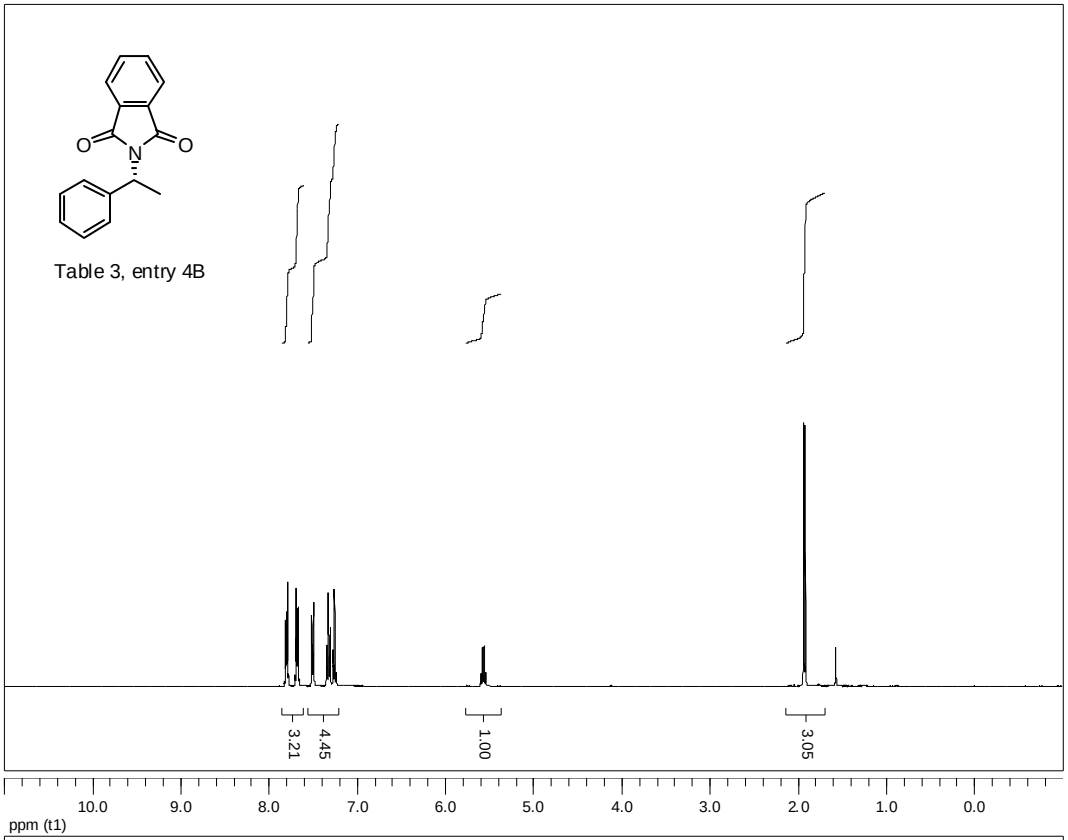
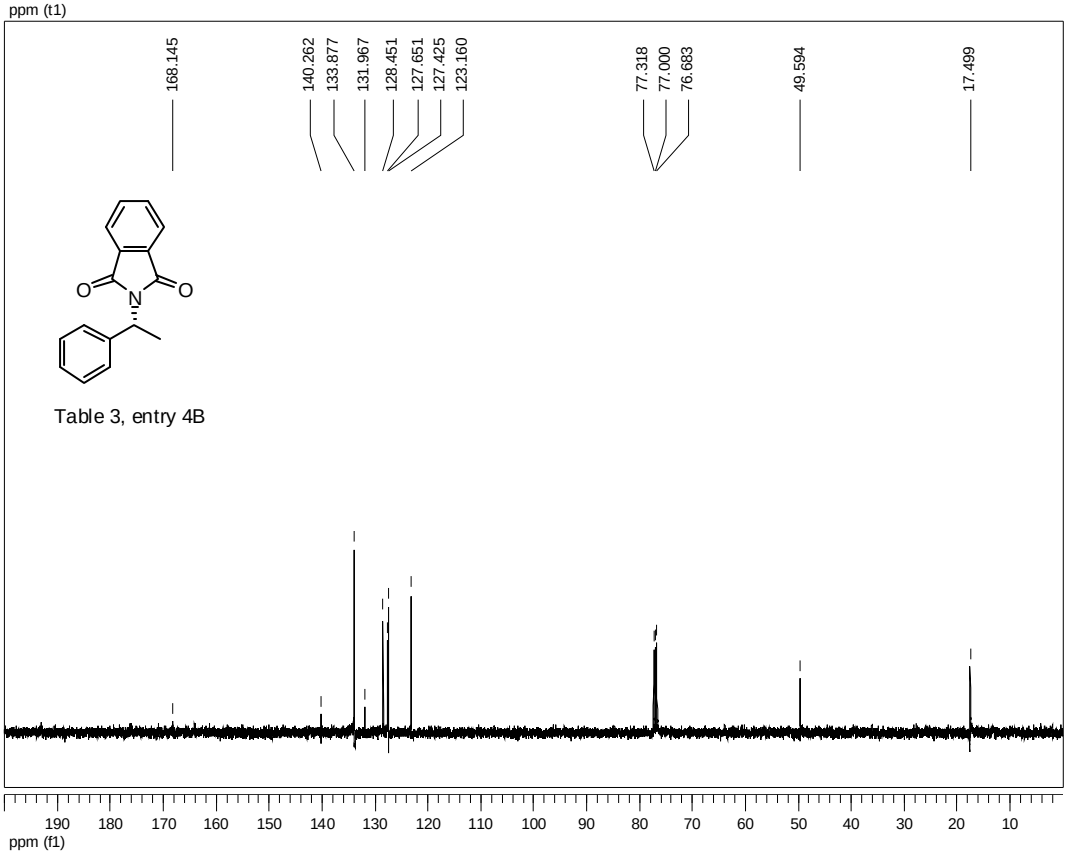
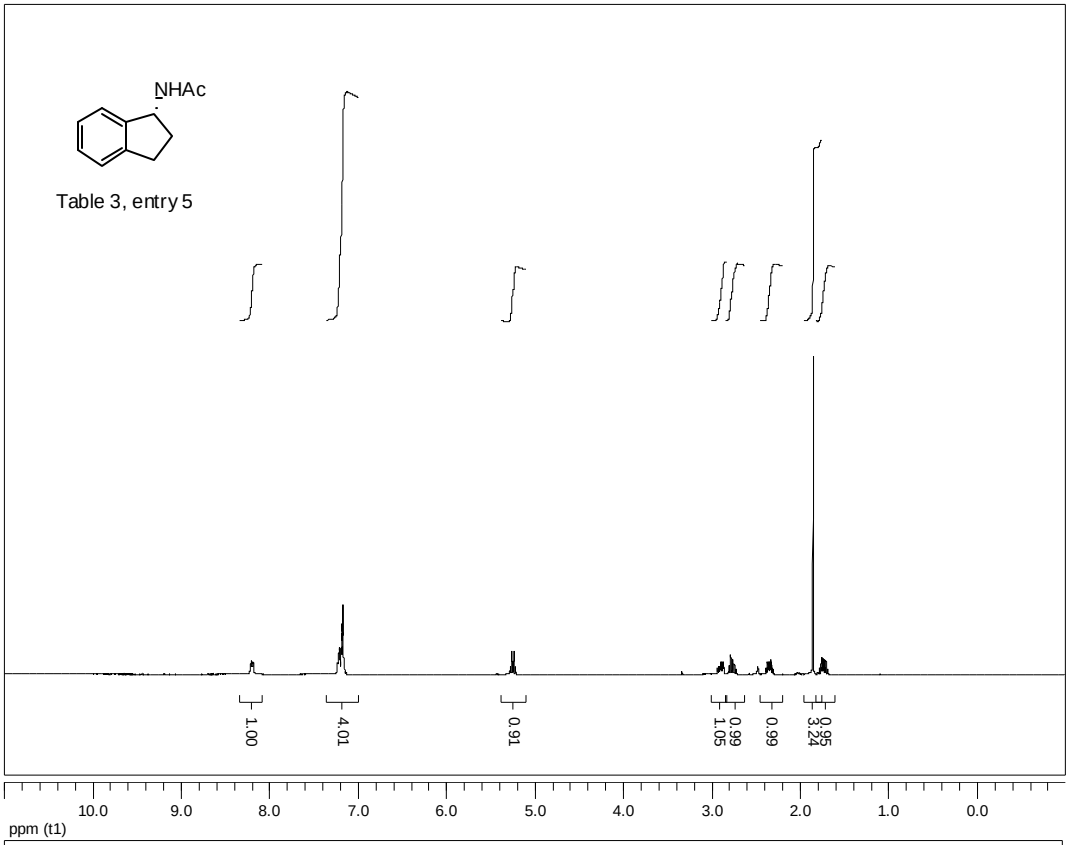
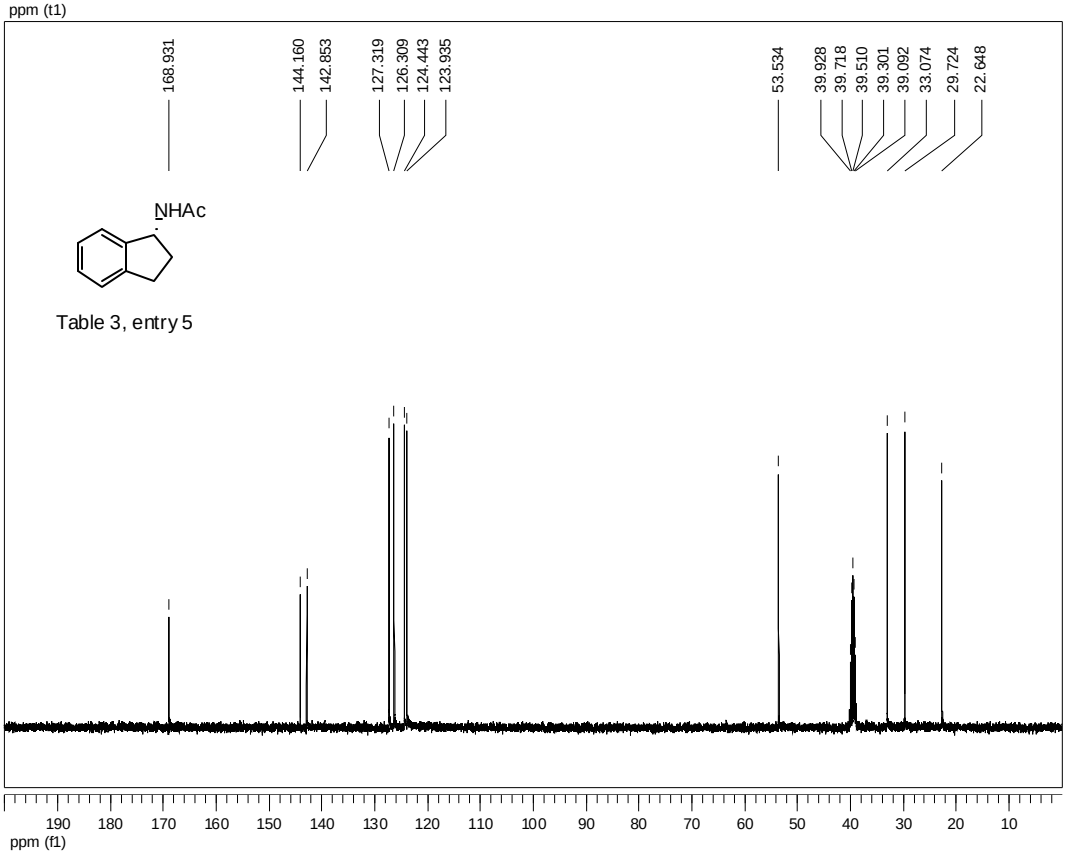


Table 3, entry 4B
3.21
4.45
1.00
3.05
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


168.145
140.262
133.877
131.967
128.451
127.651
127.425
123.160
77.318
77.000
76.683
49.594
17.499
Table 3, entry 4B
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)


NHAc
Table 3, entry 5
1.00
4.01
0.91
1.05
0.99
0.99
3.24
0.95
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


168.931
144.160
142.853
127.319
126.309
124.443
123.935
53.534
39.928
39.718
39.510
39.301
39.092
33.074
29.724
22.648
NHAc
Table 3, entry 5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)

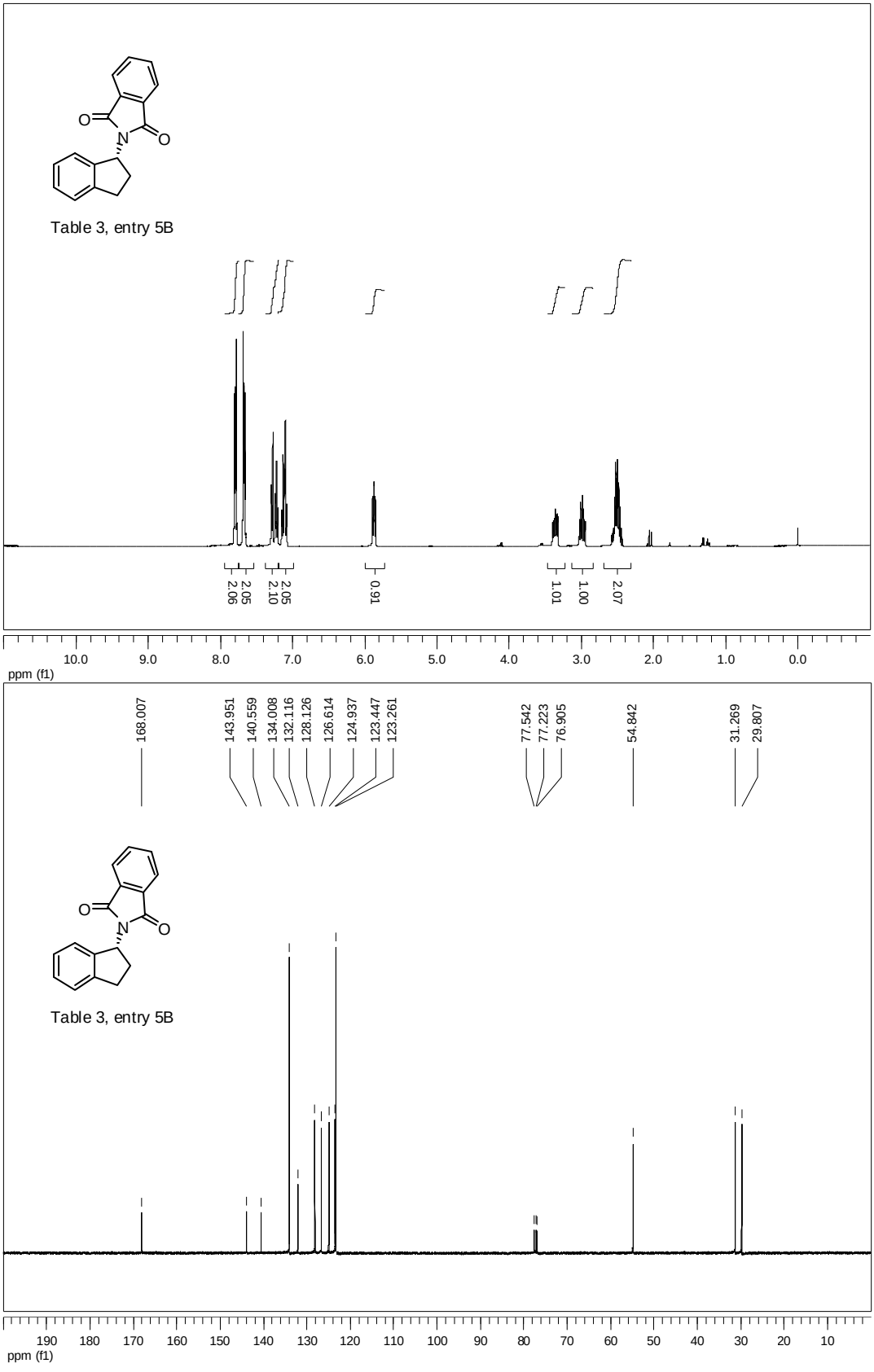
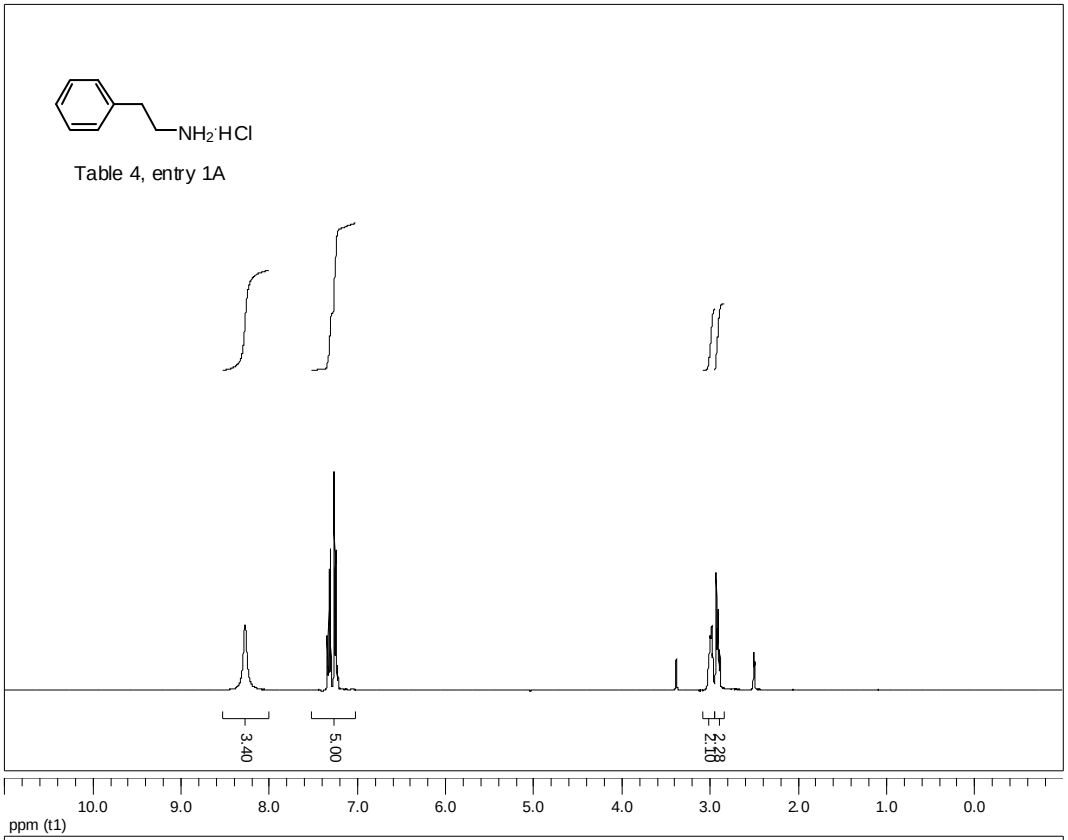
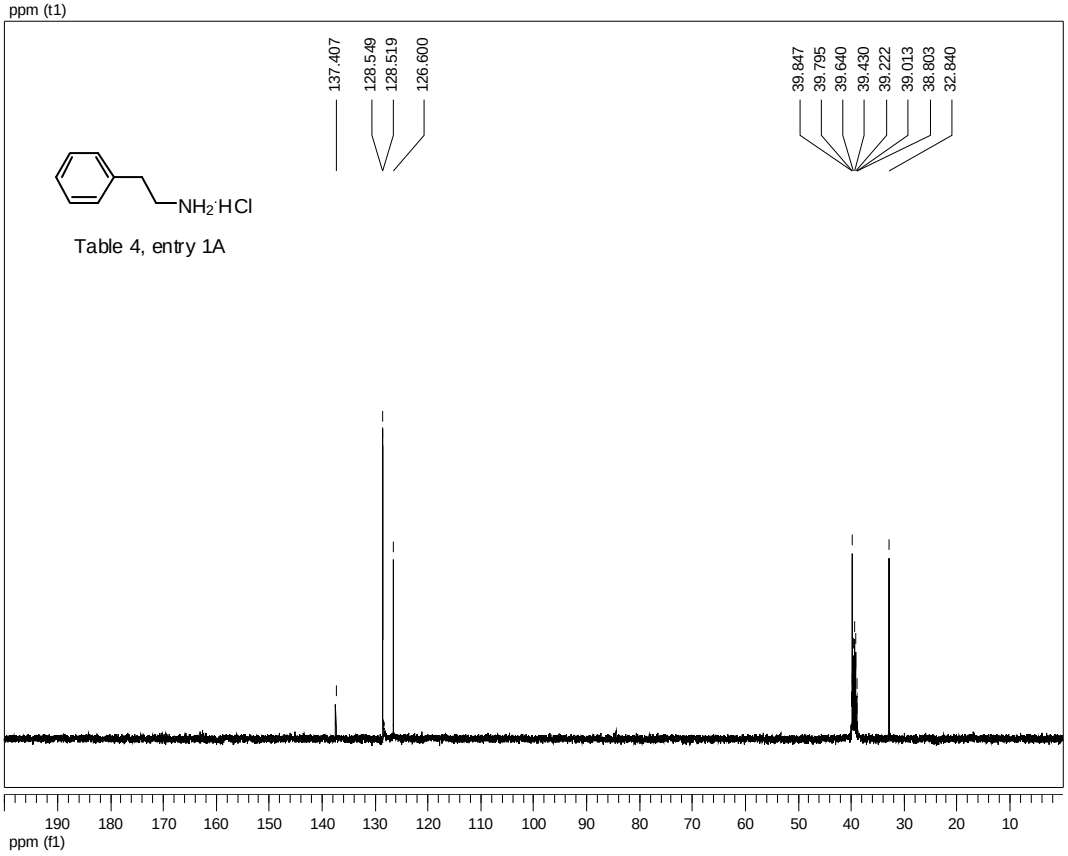


Table 3, entry 5B
2.06
2.05
2.10
2.05
0.91
1.01
1.00
2.07
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
168.007
143.951
140.559
134.008
132.116
128.126
126.614
124.937
123.447
123.261
77.542
77.223
76.905
54.842
31.269
29.807
Table 3, entry 5B
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)


NH2·HCl
Table 4, entry 1A
3.40
5.00
2.10
2.28
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


137.407
128.549
128.519
126.600
39.847
39.795
39.640
39.430
39.222
39.013
38.803
32.840
NH2·HCl
Table 4, entry 1A
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)

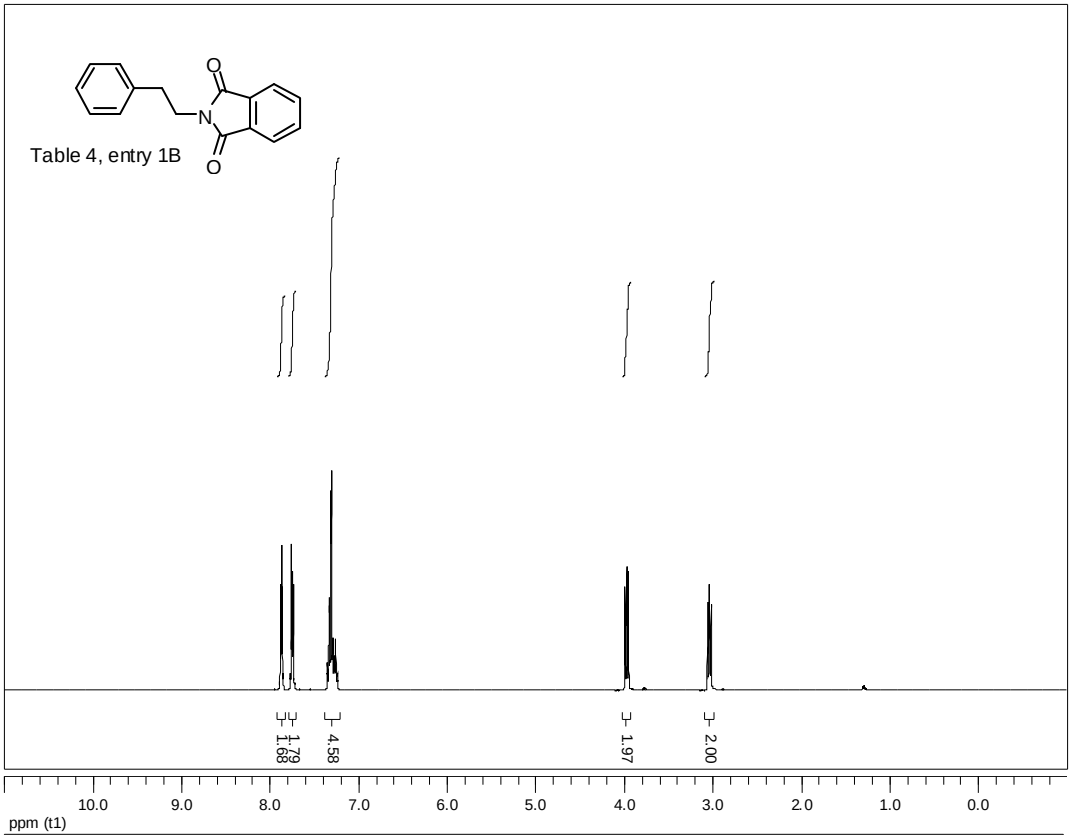
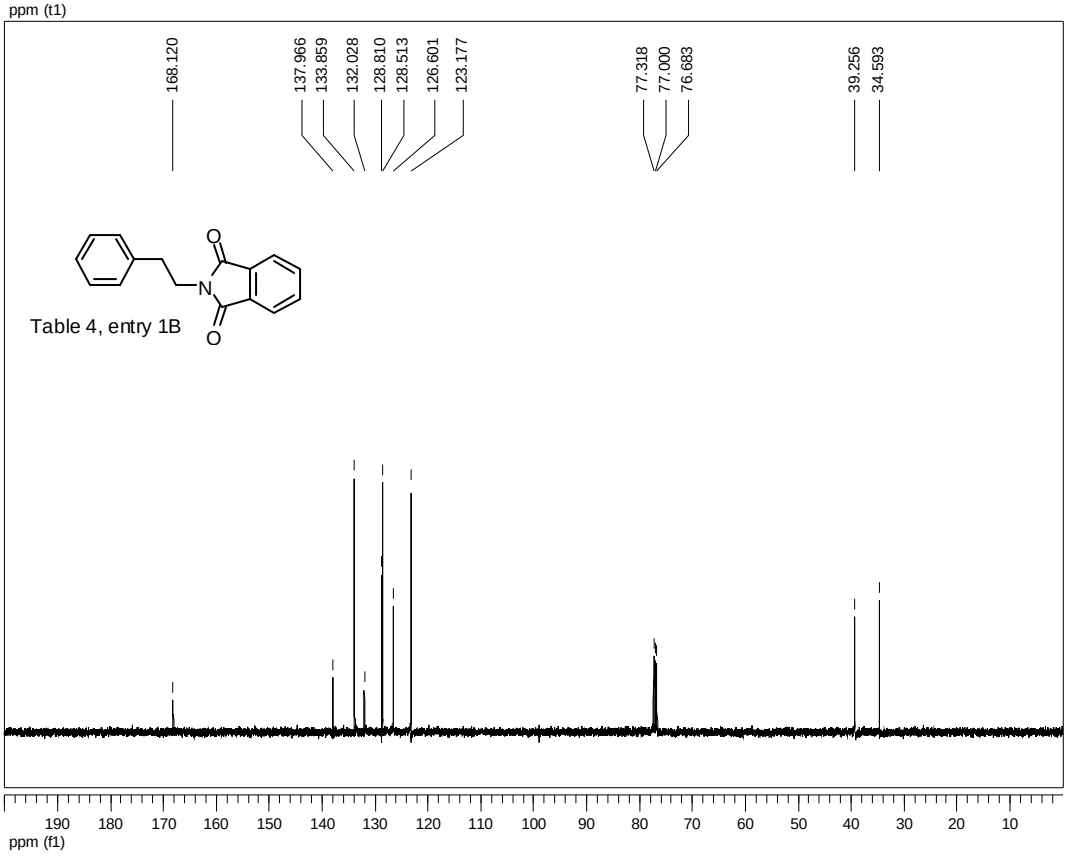
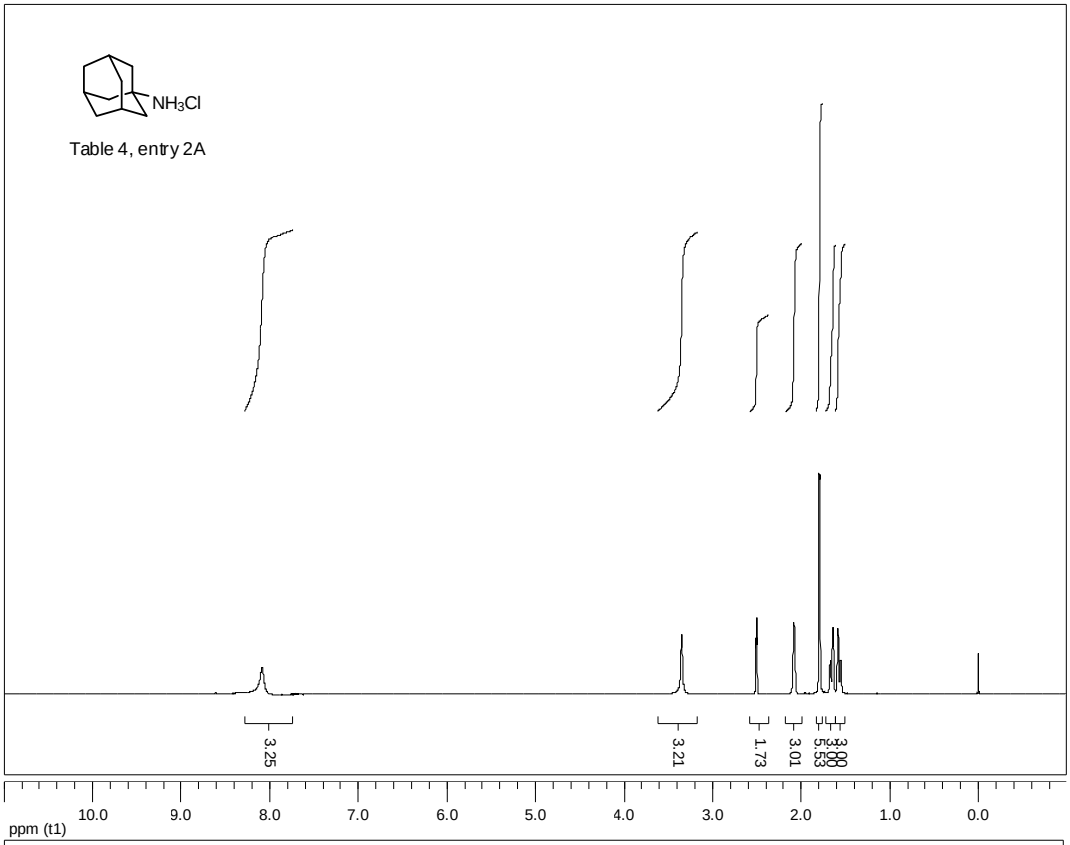
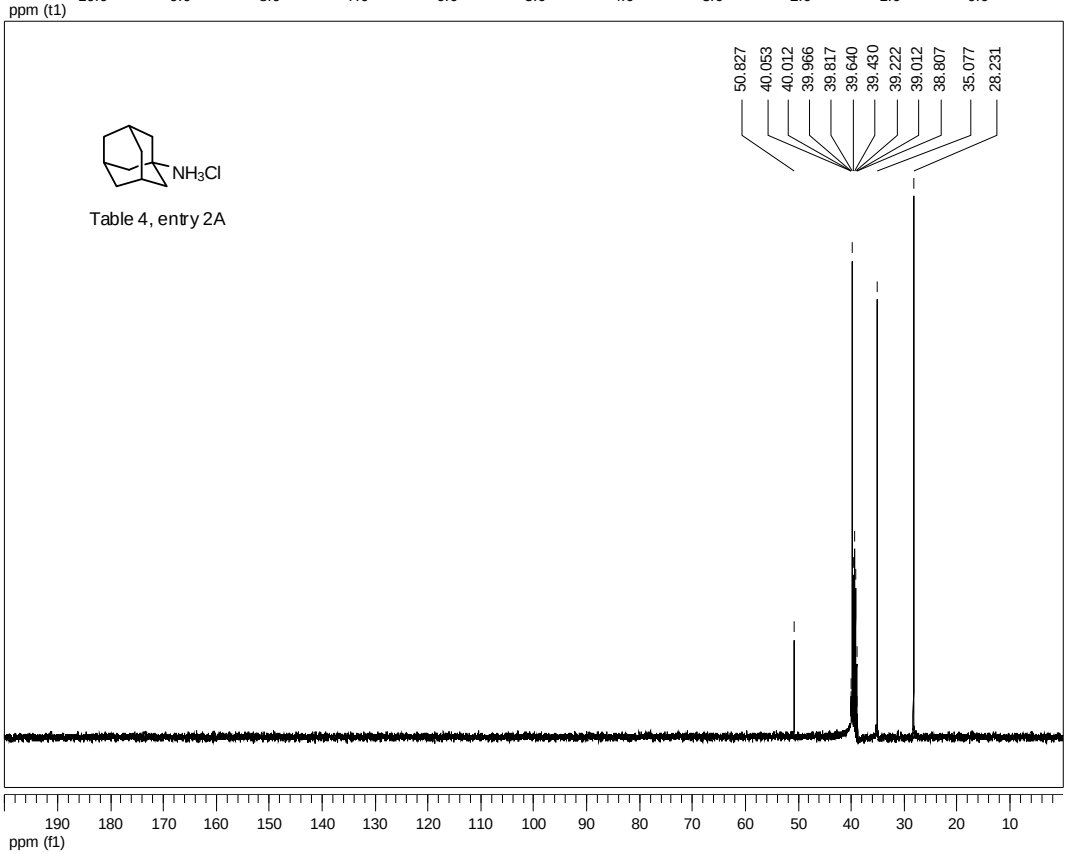
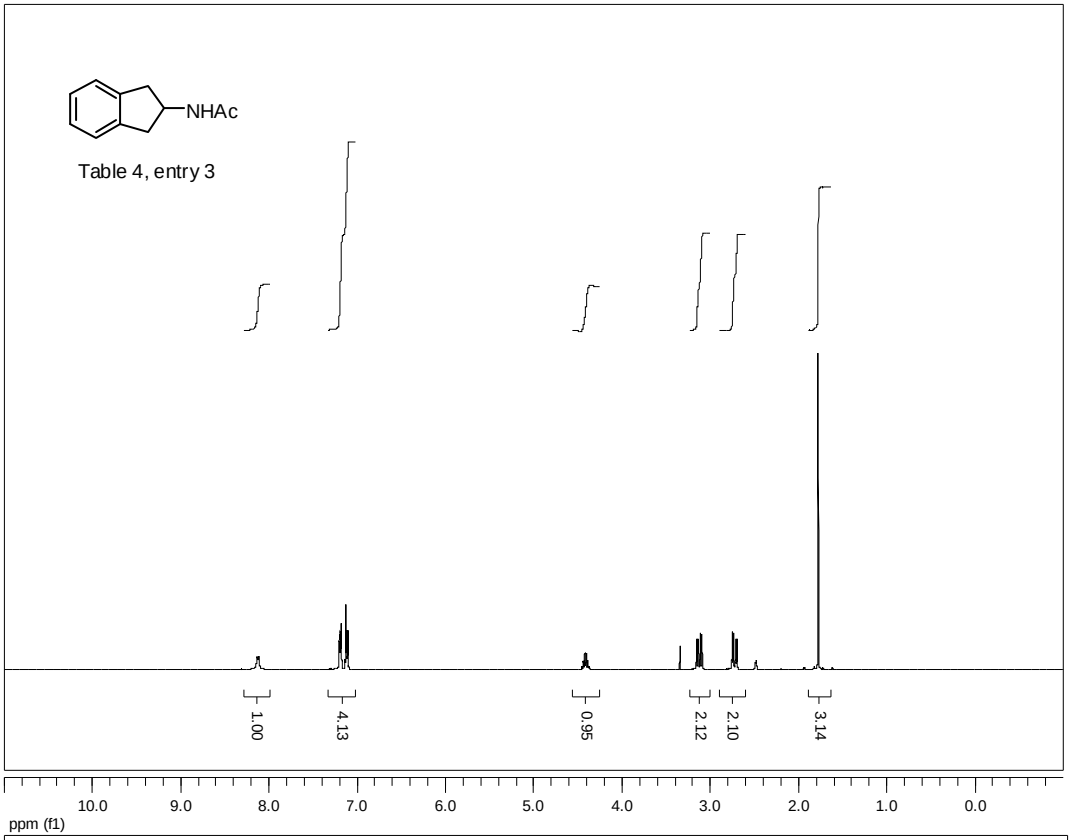


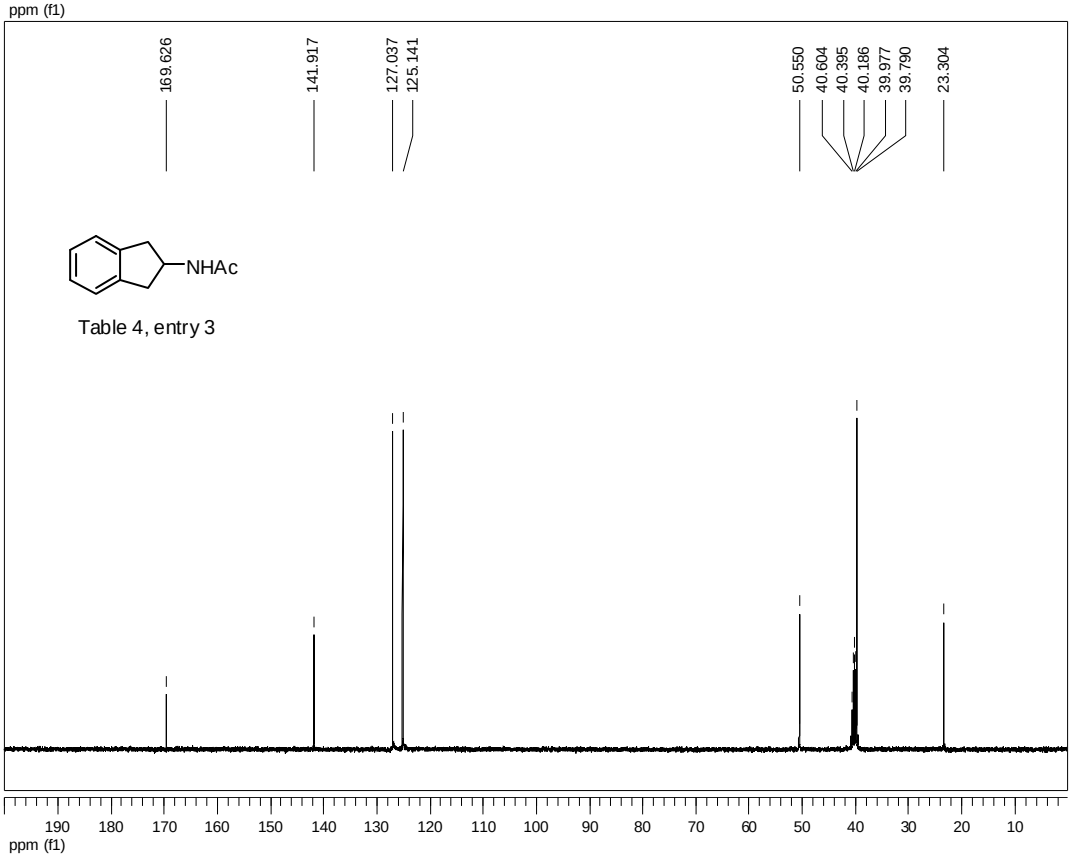
Table 4, entry 1B
1.68
1.79
4.58
1.97
2.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


168.120
137.966
133.859
132.028
128.810
128.513
126.601
123.177
77.318
77.000
76.683
39.256
34.593
Table 4, entry 1B
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)


NH3Cl
Table 4, entry 2A
3.25
3.21
1.73
3.01
5.53
3.00
ppm (t1)


50.827
40.053
40.012
39.966
39.817
39.640
39.430
39.222
39.012
38.807
35.077
28.231
NH3Cl
Table 4, entry 2A
ppm (f1)


NHAc
Table 4, entry 3
1.00
4.13
0.95
2.12
2.10
3.14
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


169.626
141.917
127.037
125.141
50.550
40.604
40.395
40.186
39.977
39.790
23.304
NHAc
Table 4, entry 3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)

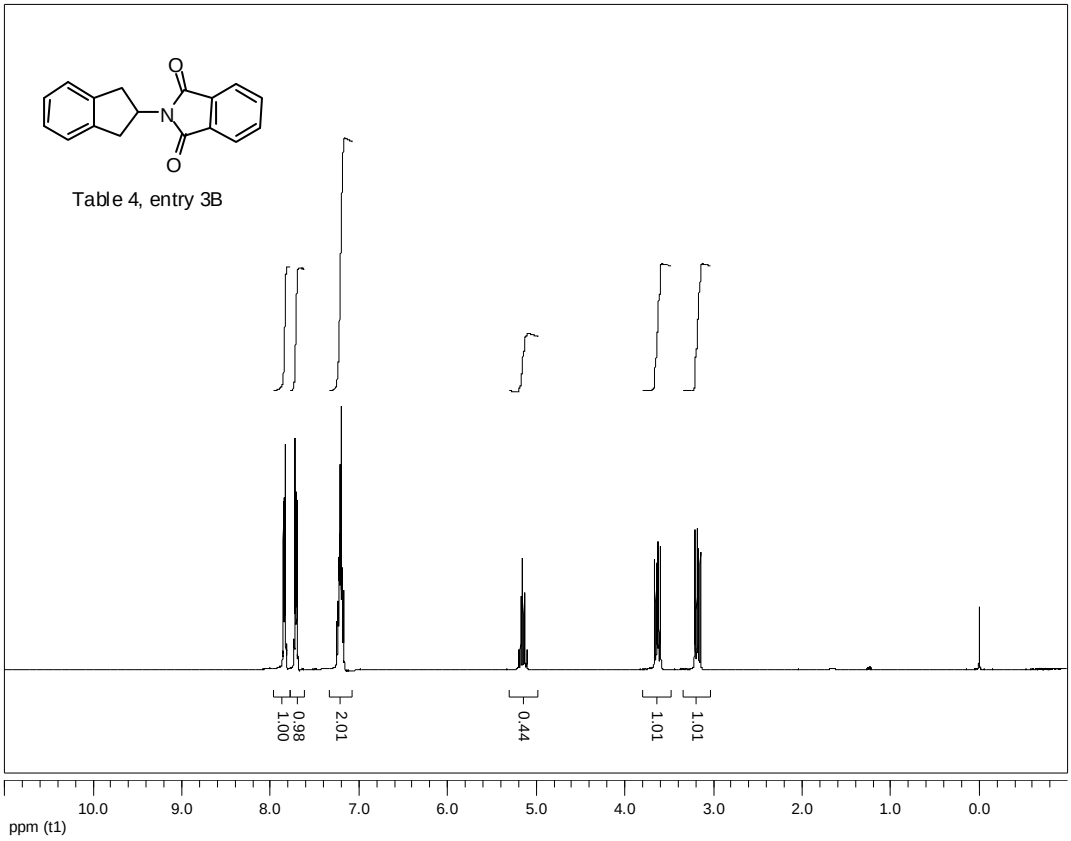
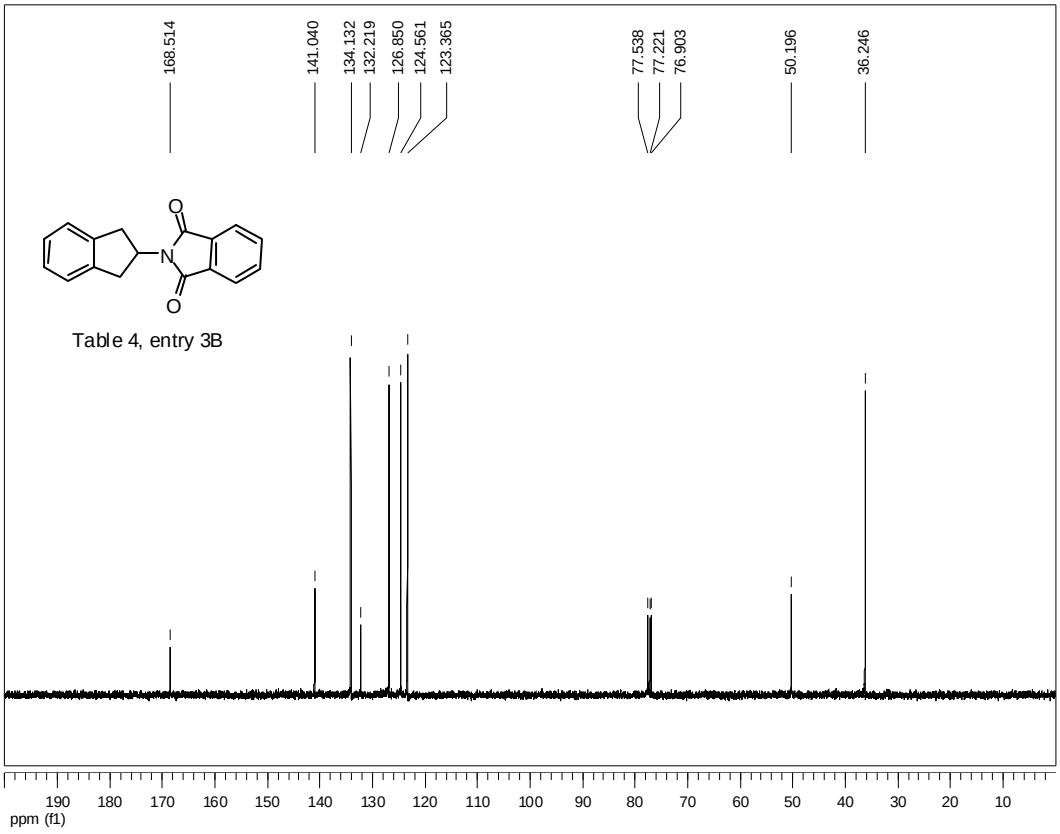


Table 4, entry 3B
1.00
0.98
2.01
0.44
1.01
1.01
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


168.514
141.040
134.132
132.219
126.850
124.561
123.365
77.538
77.221
76.903
50.196
36.246
Table 4, entry 3B
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)

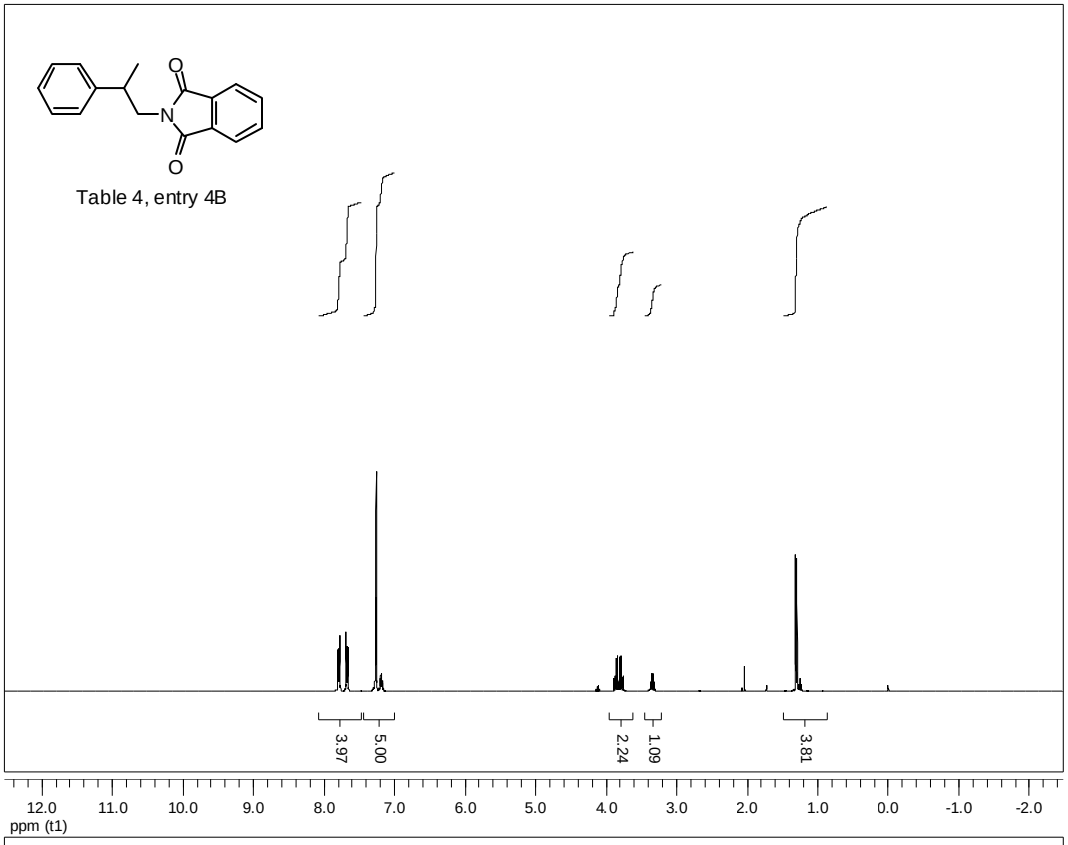
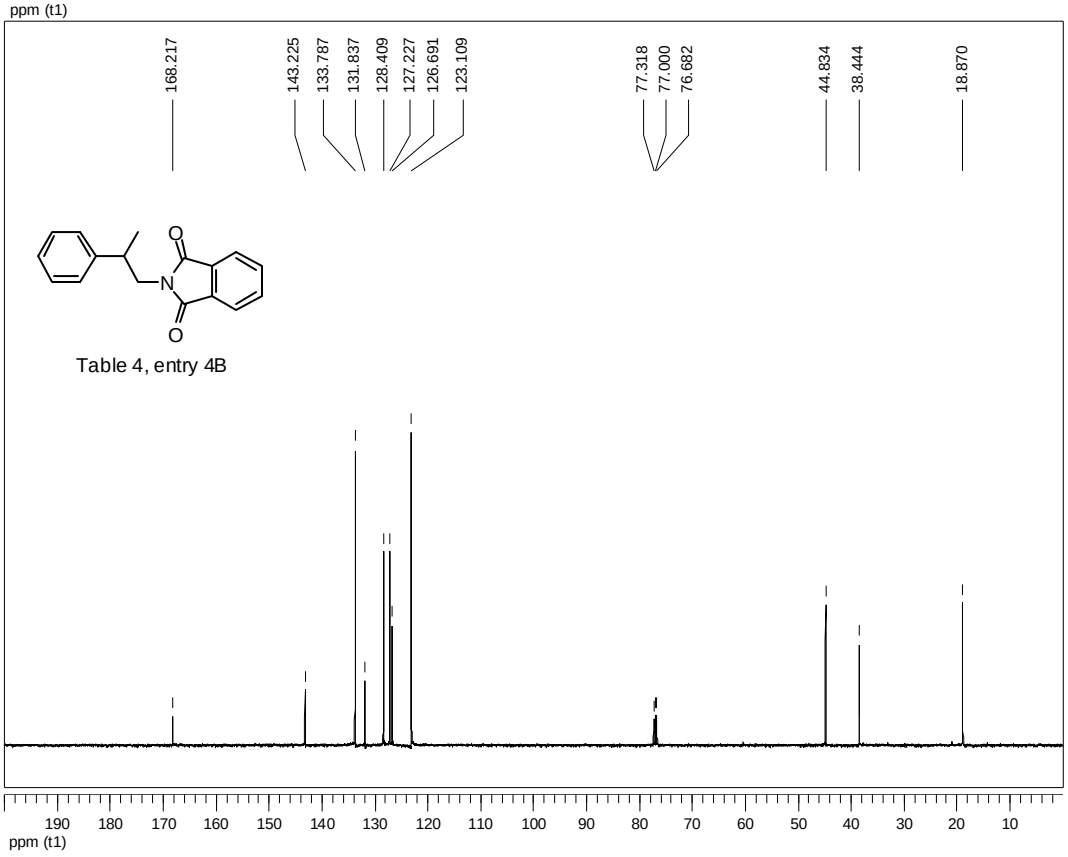
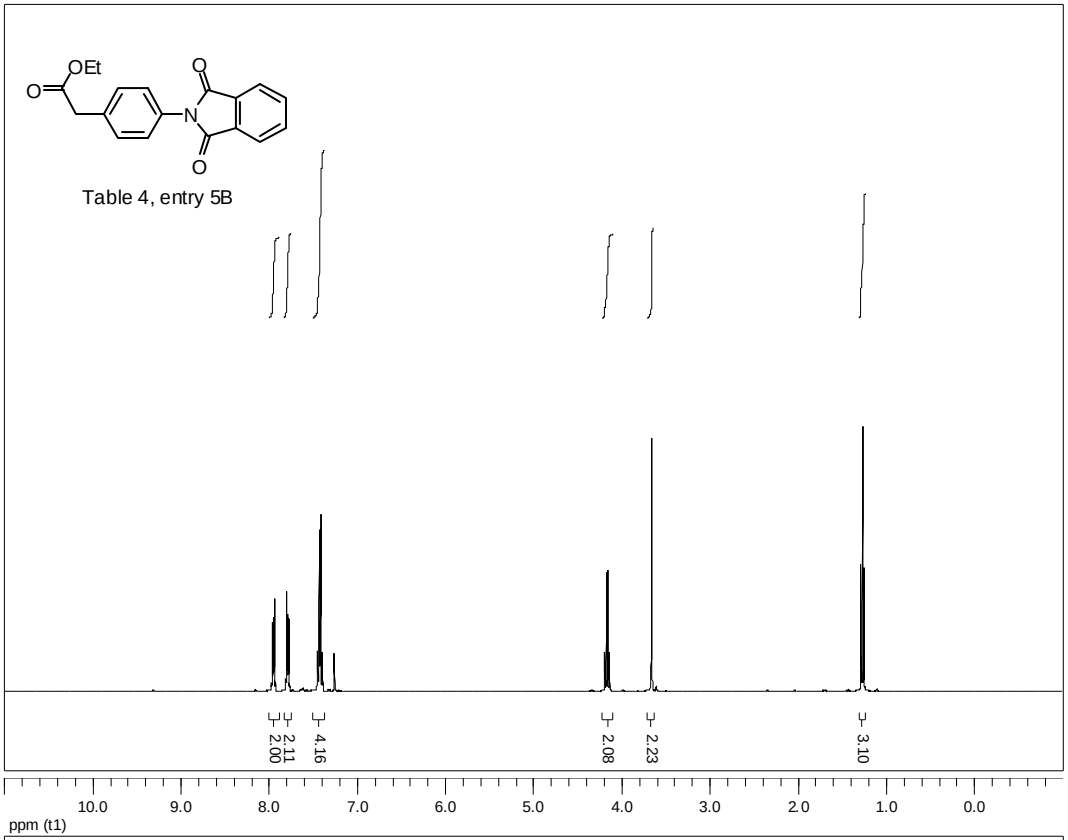
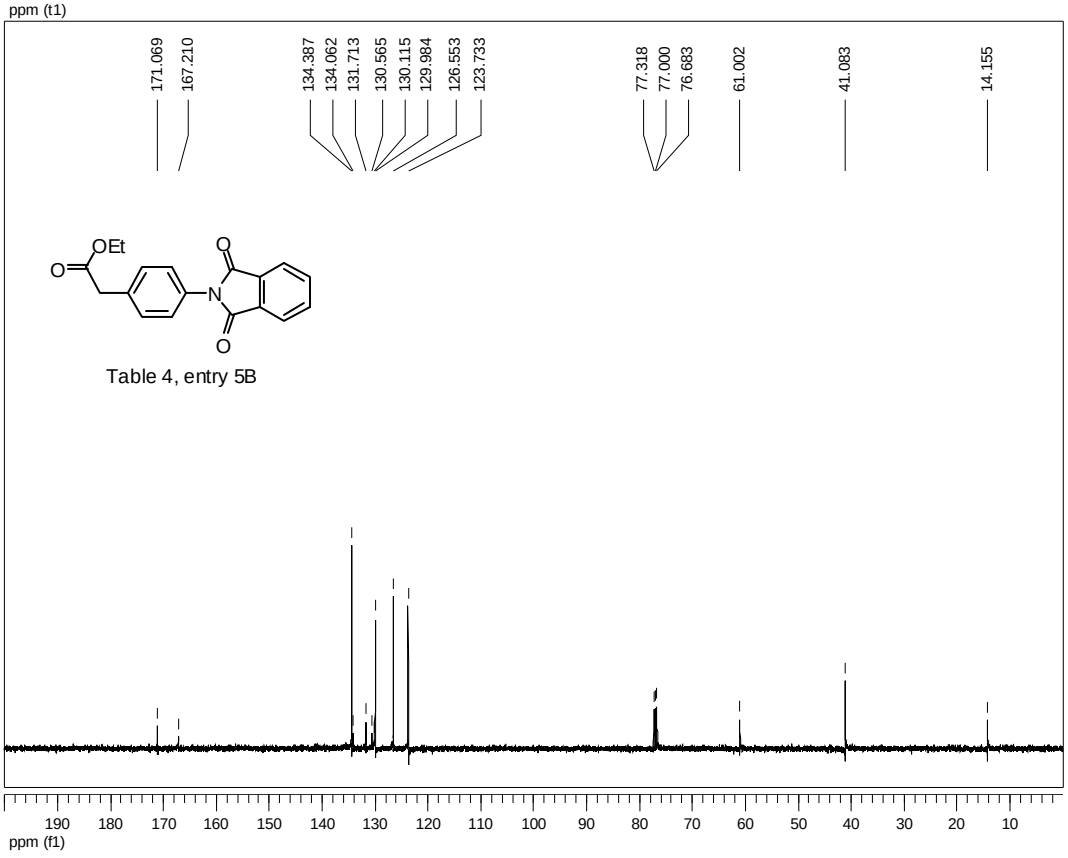
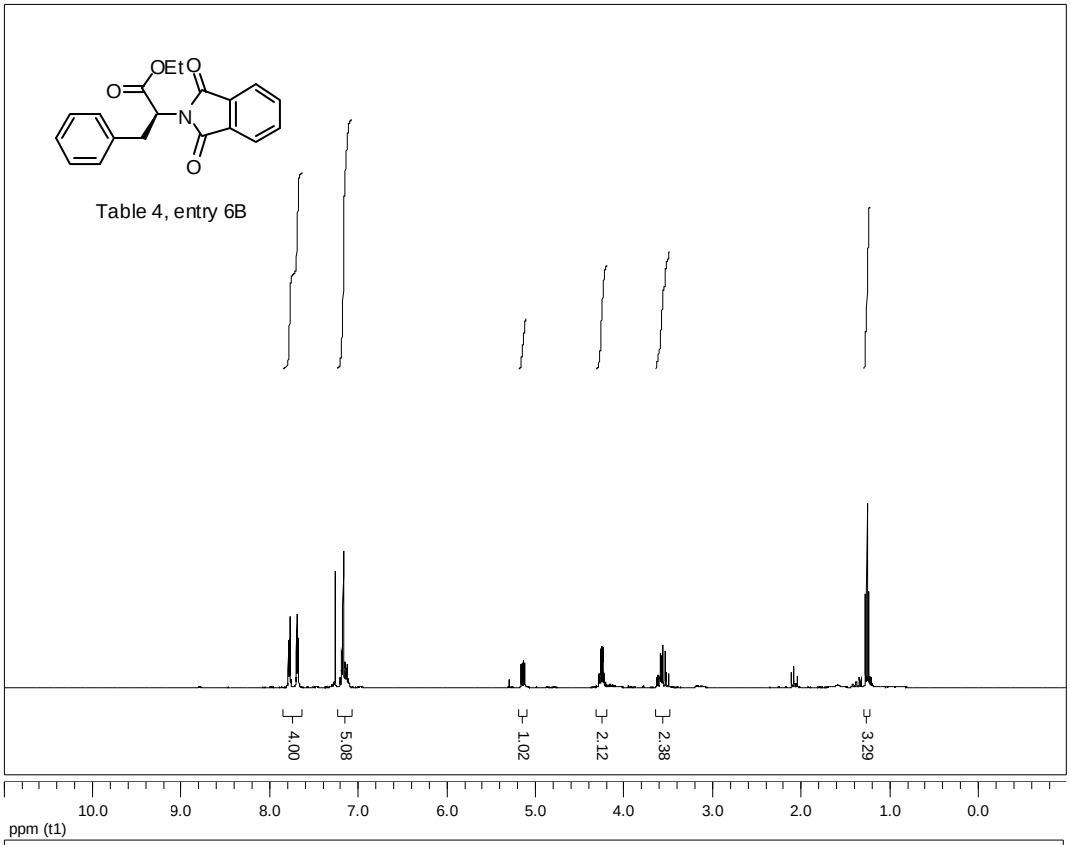


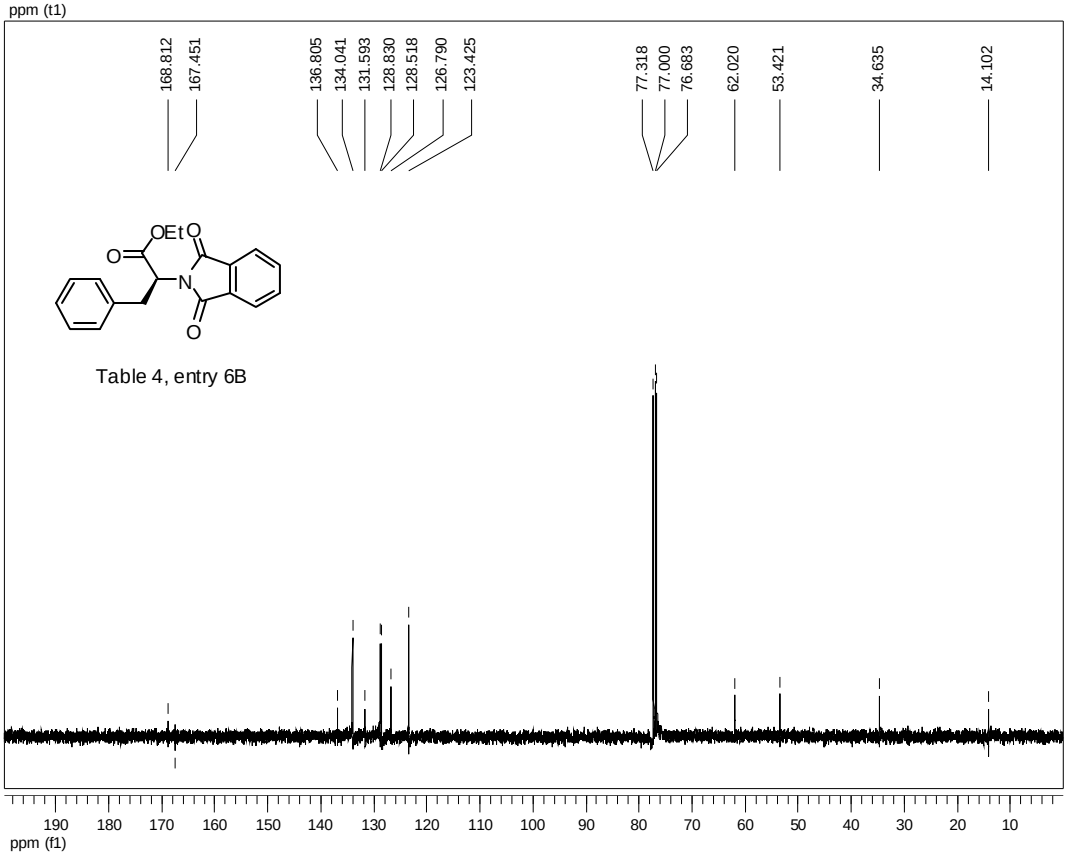
Table 4, entry 4B
3.97
5.00
2.24
1.09
3.81
12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0 -1.0 -2.0
ppm (t1)


168.217
143.225
133.787
131.837
128.409
127.227
126.691
123.109
77.318
77.000
76.682
44.834
38.444
18.870
Table 4, entry 4B
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm (t1)


OEt
O
O
N
O
Table 4, entry 5B
2.00
2.11
4.16
2.08
2.23
3.10
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


171.069
167.210
134.387
134.062
131.713
130.565
130.115
129.984
126.553
123.733
77.318
77.000
76.683
61.002
41.083
14.155
OEt
O
O
N
O
Table 4, entry 5B
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)


OEt
O
O
N
O
Table 4, entry 6B
4.00
5.08
1.02
2.12
2.38
3.29
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


168.812
167.451
136.805
134.041
131.593
128.830
128.518
126.790
123.425
77.318
77.000
76.683
62.020
53.421
34.635
14.102
OEt
O
O
N
O
Table 4, entry 6B
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)

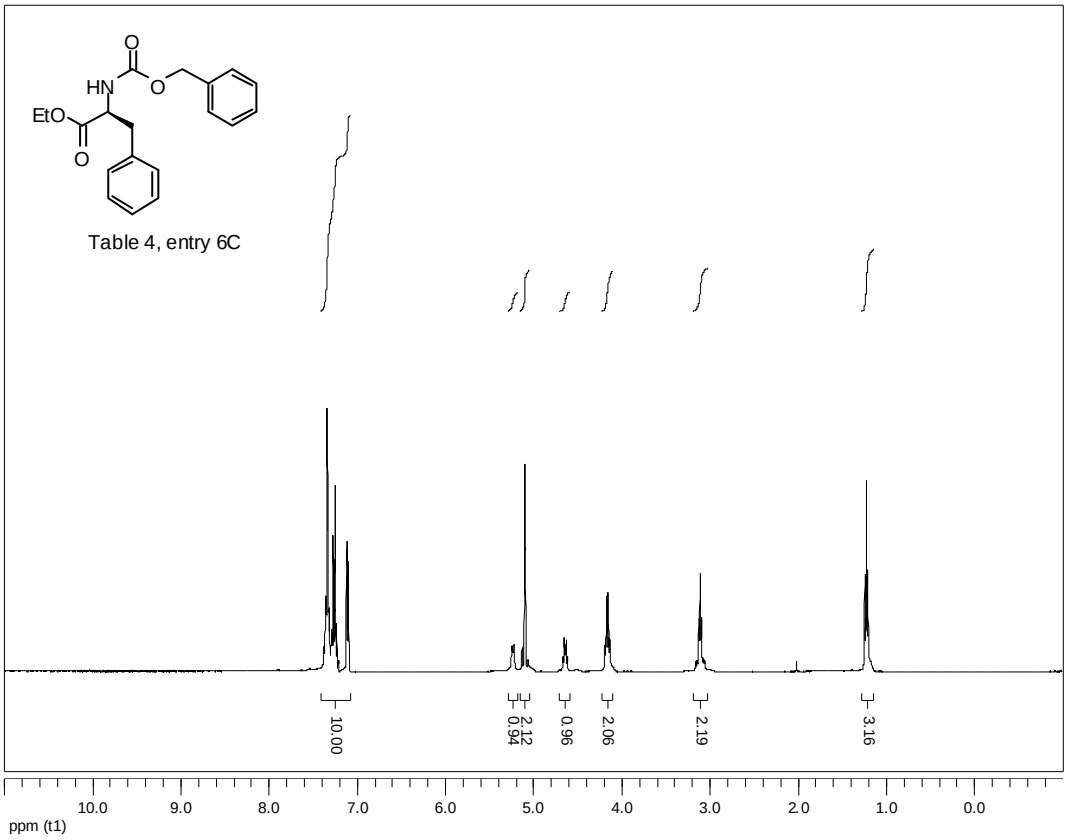
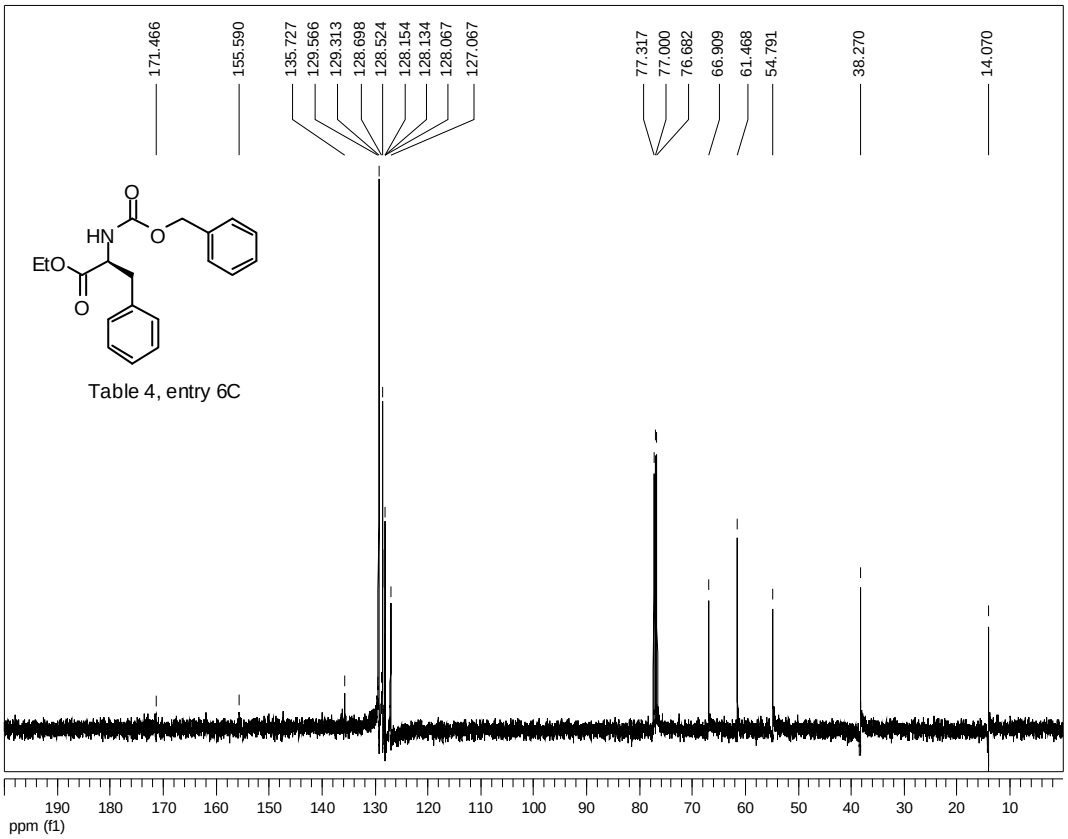
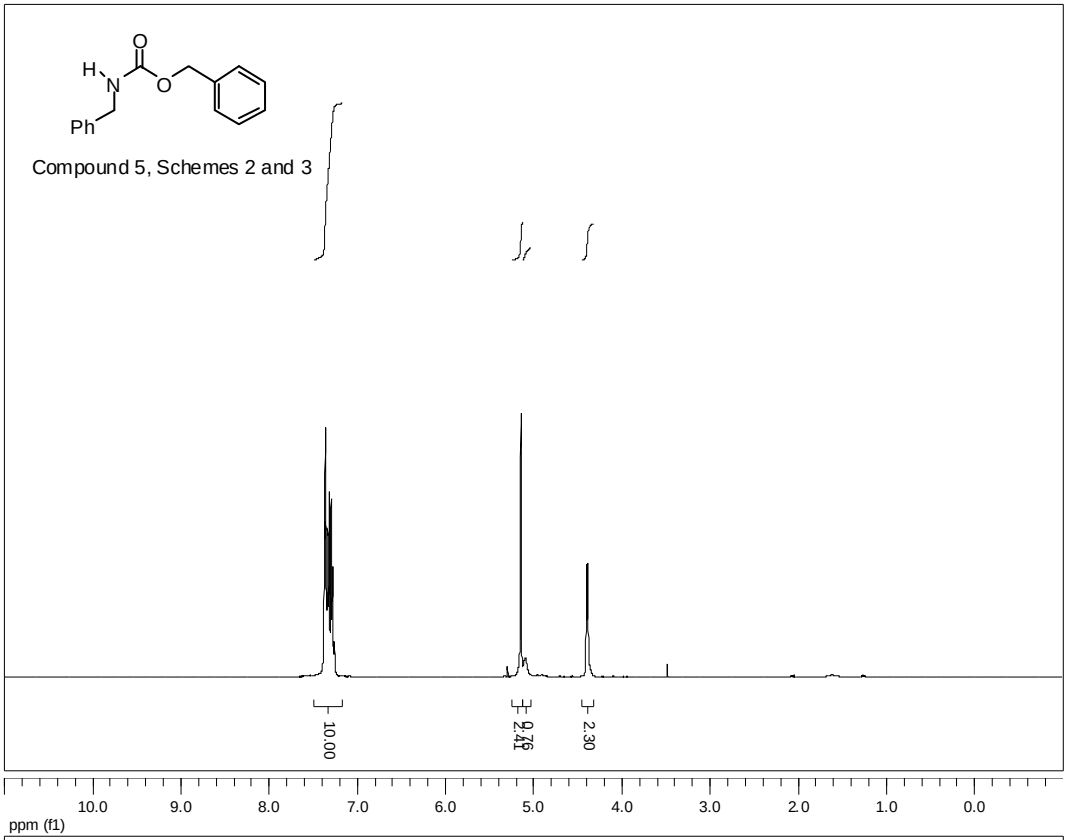
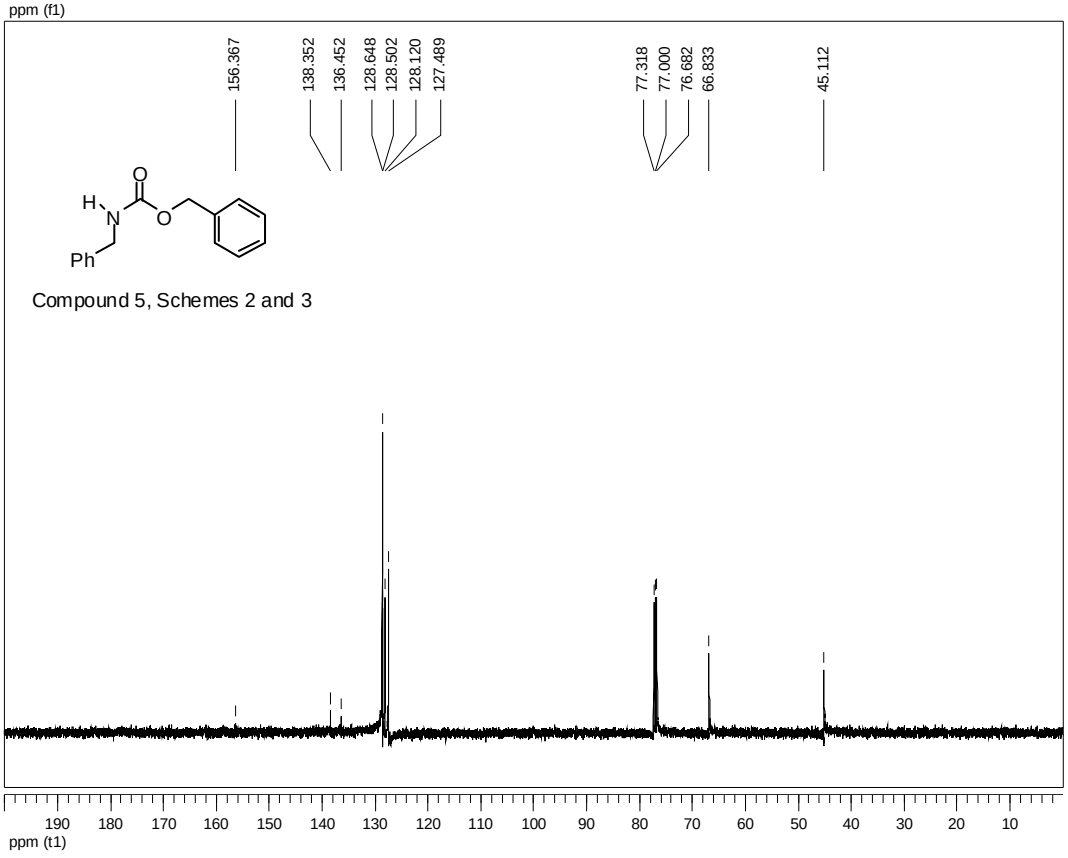


Table 4, entry 6C
10.00
2.12
0.94
0.96
2.06
2.19
3.16
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


171.466
155.590
135.727
129.566
129.313
128.698
128.524
128.154
128.134
128.067
127.067
77.317
77.000
76.682
66.909
61.468
54.791
38.270
14.070
Table 4, entry 6C
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (f1)


Compound 5, Schemes 2 and 3
10.00
2.47
0.76
2.30
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


156.367
138.352
136.452
128.648
128.502
128.120
127.489
77.318
77.000
76.682
66.833
45.112
Compound 5, Schemes 2 and 3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)