

Supporting Information

A One-Pot Preparation of 1,3-Disubstituted Azetidines.

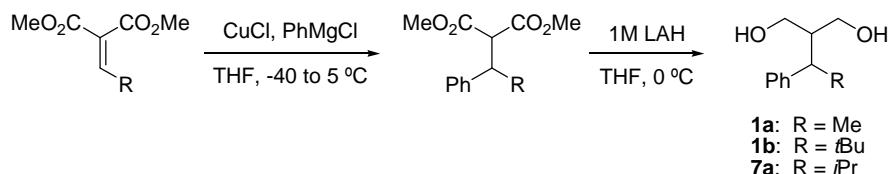
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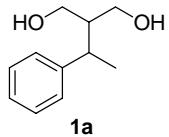
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General Methods. Unless otherwise stated, solvents and reagents were reagent grade and used without further purification. Melting points ranges were determined on a Büchi B-545 melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded using PTFE or NaCl plate IR cards and evaporating from the solvent indicated, and are reported in wavenumbers (cm⁻¹). ¹H (400 MHz or 500 MHz) and ¹³C (100 MHz or 126 MHz) NMR spectra were obtained using a 400 MHz or 500 MHz instrument as indicated, and chemical shifts are reported in parts per million (ppm). Coupling constants are reported in hertz (Hz). Spectral splitting patterns are designated as: ap, apparent; s, singlet; br, broad; d, doublet; t, triplet; q, quartet; m, multiplet; and comp, complex multiplet. Hi-resolution mass spectra was obtained using a time of flight (TOF) mass spectrometer. Determination of enantiomeric ratios for chiral products was carried out using a supercritical fluid chromatography (SFC) apparatus under the conditions and using the columns indicated.

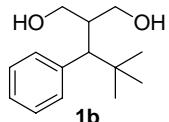


General Racemic Diol Formation Procedure. To a cooled solution of alkylidene malonate in dry THF (100 mL) at -40 °C was added catalytic CuCl (3 mmol) followed by a solution of phenyl magnesium chloride in THF (25 wt%, 78 mmol) over 10 min. The reaction was warmed to 5 °C over 15-30 min., quenched with sat. NH₄Cl (40 mL), diluted with MTBE (300 mL), and treated with 0.5 N HCl (40 mL). The biphasic mixture was separated, the organics were dried (MgSO₄), filtered and concentrated to give the crude malonate adduct. This material was dissolved in THF (120 mL), cooled to 0 °C under N₂, slowly treated with 1.0 M LAH in THF (120 mL, 120 mmol) over 30 min., and then stirred overnight to rt. The resulting solution was cooled to 0 °C and slowly treated with water (4.6 mL, **CAUTION: EXOTHERMIC**), 15% NaOH (4.6 mL), and water (13.7 mL) and the resulting slurry was stirred for 1 hr then filtered. The filtrate was concentrated in vacuo, and the

crude oil purified via column chromatography eluting with EtOAc/hexanes and the product was recrystallized as indicated.

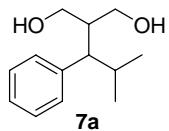


2-(1-phenylethyl)propane-1,3-diol (1a) was prepared in 70 % overall yield from dimethyl ethylidene malonate according to the general racemic diol formation procedure as an oil; ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.18 (comp, 5 H), 3.98 (dd, *J* = 3.3, 10.8 Hz, 1 H), 3.85 (dd, *J* = 6.8, 10.8 Hz, 1 H), 3.64 (dd, *J* = 3.3, 10.7 Hz, 1 H), 3.48 (dd, *J* = 6.8, 10.7 Hz, 1 H), 2.90-2.83 (m, 1 H), 2.76 (s, 2 H), 1.91-1.83 (m, 1 H), 1.30 (d, *J* = 7.1 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 145.7, 128.6, 127.4, 126.4, 65.0, 64.3, 47.8, 37.7, 19.7; IR ν 3336, 2964, 2931, 1891, 1653, 1054, 1022, 701 cm⁻¹; mass spectrum (TOF) calcd. for C₁₁H₁₆O₂+H: M+H (theory), 181.12231; M+H (found), 181.12316.

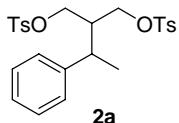


2-(2,2-dimethyl-1-phenylpropyl)propane-1,3-diol (1b) was prepared from dimethyl (2,2-dimethylpropylidene)malonate¹ according to the general racemic diol formation procedure. The product was recrystallized from hexanes to give **1b** in 59% overall yield as a solid: mp 103-105 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.17 (comp, 5 H), 3.96 (dd, *J* = 2.8, 10.9 Hz, 1 H), 3.83 (dd, *J* = 4.6, 10.6 Hz, 1 H), 3.75 (dd, *J* = 8.0, 10.6 Hz, 1 H), 3.43 (dd, *J* = 8.0, 10.9 Hz, 1 H), 3.10 (brs, 1 H), 2.75 (brs, 1 H), 2.47 (d, *J* = 10.6 Hz, 1 H), 2.33-2.28 (m, 1 H), 1.00 (s, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ 141.6, 130.0, 128.0, 126.4, 67.4, 65.6, 55.3, 42.8, 34.5, 29.6; IR ν 3245, 2949, 1652, 1456, 1034, 702 cm⁻¹; mass spectrum (TOF) calcd. for C₁₄H₂₂O₂+H: M+H (theory), 223.16926; M+H (found), 223.17011.

¹ Provencher, L.; Wynn, H.; Jones, J. B.; Krawczyk, A. R. *Tetrahedron: Asymm.* **1993**, *4*, 2025-2040.



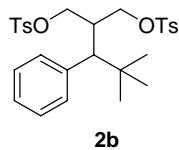
2-(2-methyl-1-phenylpropyl)propane-1,3-diol (7a) was prepared from dimethyl (2-methylpropylidene)malonate² according to the general racemic diol formation procedure. The product was recrystallized from hexanes to give **7a** in 55% overall yield as a solid: mp 85-87 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.28-7.18 (comp, 3 H), 7.08-7.06 (comp, 2 H), 3.87 (dd, *J* = 3.4, 10.7 Hz, 1 H), 3.71 (dd, *J* = 3.4, 10.7 Hz, 1 H), 3.67 (dd, *J* = 7.3, 10.7 Hz, 1 H), 3.45 (dd, *J* = 7.7, 10.7 Hz, 1 H), 3.31 (brs, 1 H), 3.14 (brs, 1 H), 2.52 (dd, *J* = 6.8, 8.5 Hz, 1 H), 2.27-2.19 (m, 1 H), 2.17-2.07 (m, 1 H), 0.87 (d, *J* = 6.7 Hz, 3 H), 0.78 (d, *J* = 6.7 H, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 140.5, 129.5, 128.0, 126.4, 65.3, 64.4, 50.5, 42.8, 28.3, 21.8, 18.6; IR ν 3336, 1959, 1456, 1027, 104 cm⁻¹; CHN calcd. for C₁₃H₂₀O [208.30]: C, 74.96; H, 9.68. Found: C, 74.67; H, 9.52.



2-{[(p-toluenesulfonyl)oxy]methyl}-3-phenylbutyl p-toluenesulfonate (2a). A solution of the diol **1a** (290 mg, 1.6 mmol) in dry CH₂Cl₂ (3 mL) at 0 °C was treated with Et₃N (0.86 mL, 6.2 mmol), *p*-toluenesulfonic anhydride (Ts₂O, 1.85 g, 5.7 mmol), and catalytic dimethylaminopyridine (DMAP, 20 mg, 0.2 mmol) and the reaction was warmed to rt and stirred overnight at rt. Solvent was concentrated in vacuo and the crude product was purified by flash chromatography eluting with EtOAc/Hexanes (1:1) to give 0.66 g (85 %) of the bis-tosylate **2a** as an oil; ¹H NMR (500 MHz, CDCl₃) δ 7.81 (apt, *J* = 2.0 Hz, 1 H), 7.79 (apt, *J* = 1.8 Hz, 1 H), 7.62 (apt, *J* = 2.0 Hz, 1 H), 7.60 (apt, *J* = 1.8 Hz, 1 H), 7.40-7.38 (comp, 2 H), 7.30-7.28 (comp, 2 H), 7.24-7.19 (comp, 3 h), 7.01-6.99

² Cardillo, C.; Fabbroni, S.; Gentilucci, L.; Gianotti, M.; Tolomelli, A. *Synth. Commun.* **2003**, 33, 1587-1594.

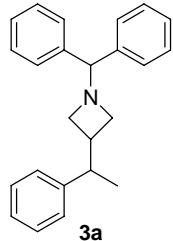
(comp, 2 H), 4.20 (dd, J = 3.8, 10.0 Hz, 1 H), 4.13 (dd, J = 5.5, 10.0 Hz, 1 H), 3.83 (dd, J = 4.0, 10.0 Hz, 1 H), 3.68 (dd, J = 7.3, 10.0 Hz, 1 H), 2.79-2.73 (m, 1 H), 2.49 (s, 3 H), 2.46 (s, 3 H), 2.17-2.12 (m, 1 H), 1.19 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (126 MHz, CDCl_3) δ 145.1, 144.9, 143.3, 132.5, 132.4, 130.0, 129.9, 128.8, 128.0, 127.9, 127.1, 126.8, 67.7, 67.0, 44.1, 37.2, 21.7, 21.6, 19.1; IR ν 2969, 1598, 1361, 1177, 980, 814, 667 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{25}\text{H}_{28}\text{O}_6\text{S}_2+\text{H}$: M+H (theory), 511.12195; M+H (found), 511.12356.



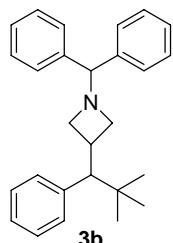
4,4-Dimethyl-2-[(*p*-toluenesulfonyl)oxy]methyl-3-phenylpentyl *p*-toluenesulfonate (2b) was prepared from **1b** according to the same procedure as for **2a** except that the reaction was heated to reflux in CH_2Cl_2 to give **2b** in 70% yield after purification by silica gel chromatography and recrystallization of the resulting solid from EtOAc/Hexanes: mp 88-90 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.79-7.76 (comp, 2 H), 7.65-7.62 (comp, 2 H), 7.36 (d, J = 8.0 Hz, 2 H), 7.29 (d, J = 8.0 Hz, 2 H), 7.17-7.13 (comp, 3 H), 6.93 (brs, 2 H), 4.21 (dd, J = 3.4, 10.2 Hz, 1 H), 4.06 (dd, J = 5.0, 9.8 Hz, 1 H), 3.98 (dd, J = 7.0, 9.8 Hz, 1 H), 3.38 (dd, J = 8.7, 10.2 Hz, 1 H), 2.58 (d, J = 6.3 Hz, 1 H), 2.56-2.49 (m, 1 H), 2.47 (s, 3 H), 2.45 (s, 3 H), 0.87 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.1, 145.0, 139.3, 132.8, 132.6, 103.0, 132.6, 130.0, 129.9, 128.2, 128.1, 127.9, 126.8, 69.1, 68.7, 53.9, 39.2, 34.2, 29.5, 21.7, 21.6; IR ν 2962, 1363, 1153, 1176, 948, 666 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{28}\text{H}_{34}\text{O}_6\text{S}_2+\text{H}$: M+H (theory), 553.16890; M+H (found), 553.17066.

General Azetidine Formation Procedure: To a solution of the diol (5 mmol) in dry ACN (10 mL) at -20 $^{\circ}\text{C}$ was slowly added trifluoromethanesulfonic anhydride (10.5 mmol) over 10-20 min. followed by diisopropylethyl amine (DIEA, 12.5 mmol) over 10-20 min. Both reagents were added at such a rate as to maintain the internal reaction temperature below -10 $^{\circ}\text{C}$, and the resulting reaction mixture was aged for 10 min. at -20 to -10 $^{\circ}\text{C}$. Additional DIEA (12.5 mmol) was then added over 5

min. followed by the amine (4.75 mmol) over 5 min., the reaction was heated to 70 °C for 1-2 hrs and then cooled to rt. Solvent was removed in vacuo, and the resulting crude solid was purified via silica gel chromatography eluting with EtOAc/hexanes to give the azetidine products in the yields indicated below.

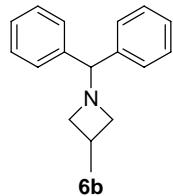


1-(diphenylmethyl)-3-(1-phenylethyl)azetidine (3) was prepared from 2-(1-phenylethyl)propane-1,3-diol (**1a**) and aminodiphenylmethane according to the general azetidine formation procedure in 85% yield as an oil; ¹H NMR (500 MHz, CDCl₃) δ 7.49-7.44 (comp, 4 H), 7.38-7.28 (comp, 6 H), 7.27-7.19 (comp, 5 H), 4.37 (s, 1 H), 3.55 (dt, *J* = 1.7, 6.7 Hz, 1 H), 3.24-3.20 (m, 1 H), 2.92-2.86 (m, 2 H), 2.78-2.70 (m, 2 H), 1.22 (d, *J* = 6.9 Hz, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 145.3, 142.5, 142.4, 128.5, 128.4, 128.3, 127.6, 127.5, 127.2, 127.1, 127.0, 126.0, 78.6, 59.1, 45.0, 36.9, 19.7; IR ν 3061, 3025, 2956, 2817, 1491, 1451, 1028, 743, 700 cm⁻¹; mass spectrum (TOF) calcd. for C₂₄H₂₅N+H: M+H (theory), 328.20598; M+H (found), 328.20720.

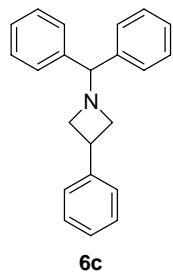


1-(diphenylmethyl)-3-(2,2-dimethyl-1-phenylpropyl)azetidine (3b) was prepared from 2-(2,2-dimethyl-1-phenylpropyl)propane-1,3-diol (**1b**) according to the general azetidine formation procedure in 95% yield as a solid: mp 107-109 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.54-7.45 (comp, 2 H), 7.41-7.37 (comp, 2 H), 7.34-7.31 (comp, 2 H) 7.25-7.22 (comp, 5 H), 7.19-7.13 (comp, 2H), 7.10 (brs, 1 H), 7.09 (brs, 1 H), 4.27 (s, 1 H), 3.68 (dt, *J* = 2.9 7.0 Hz, 1 H), 3.26-3.19 (m, 1 H), 3.15 (dt, *J*

= 2.9, 7.2 Hz, 1 H), 2.85 (t, J = 7.6 Hz, 1 H), 2.56 (d, J = 10.9 Hz, 1 H), 2.28 (t, J = 7.4 Hz, 1 H), 0.86 (s, 9 H); ^{13}C NMR (126 MHz, CDCl_3) δ 142.5, 142.2, 141.3, 128.5, 128.4, 127.5, 127.4, 127.1, 127.0, 126.0, 78.1, 63.1, 61.6, 59.9, 34.5, 31.8, 28.2; IR ν 2952, 2813, 1490, 1451, 1069, 909, 733, 703 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{27}\text{H}_{31}\text{N}+\text{H}$: M+H (theory), 370.25293; M+H (found), 370.25397.

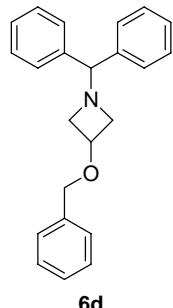


1-(diphenylmethyl)-3-methylazetidine (6b) was prepared from 2-methyl-1,3-propanediol and aminodiphenylmethane according to the general azetidine formation procedure in 64% yield as a solid: mp 46-48 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.44-7.41 (comp, 4 H), 7.31-7.26 (comp, 4 H), 7.23-7.17 (comp, 2 H), 4.33 (s, 1 H), 3.40 (dd, J = 6.0, 7.5 Hz, 1 H), 3.39 (dd, J = 6.5, 7.5 Hz, 1 H), 2.69 (dd, J = 7.1, 8.0 Hz, 1 H), 2.69 (dd, J = 6.8, 7.0 Hz, 1 H), 2.63-2.51 (m, 1 H), 1.16 (d, J = 6.9 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 142.4, 128.3, 127.5, 126.8, 78.5, 61.3, 25.0, 19.4; IR ν 3060, 2953, 2813, 1450, 1206, 1151, 743, 702 cm^{-1} ; CHN calcd. for $\text{C}_{17}\text{H}_{19}\text{N}$ [237.34]: C, 86.03; H, 8.07; N, 5.90. Found: C, 85.76; H, 8.06; N, 5.81.

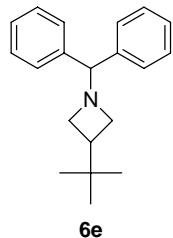


1-(diphenylmethyl)-3-phenylazetidine (6c) was prepared from 2-phenyl-1,3-propanediol and aminodiphenylmethane according to the general azetidine formation procedure in 92% yield as a solid: mp 73-74 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.55-7.54 (comp, 4 H), 7.42-7.34 (comp, 8 H), 7.31-7.25 (comp, 3 H), 4.50 (s, 1 H), 3.80-3.72 (comp, 2 H), 3.25 (t, J = 6.5 Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 143.2, 142.3, 128.6, 128.5, 127.6, 127.2, 127.0, 126.4, 78.3, 60.7, 34.9; IR ν 3082,

3059, 2948, 2826, 1491, 1451, 1208, 1151, 751, 698 cm^{-1} ; CHN calcd. for $\text{C}_{22}\text{H}_{21}\text{N}$ [299.41]: C, 88.25; H, 7.07; N, 4.68. Found: C, 88.08; H, 7.10; N, 4.58.

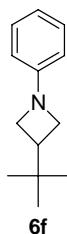


3-(benzyloxy)-1-(diphenylmethyl)azetidine (6d) was prepared from 2-benzyloxy-1,3-propanediol and aminodiphenylmethane according to the general azetidine formation procedure in 92% yield as an oil; ^1H NMR (400 MHz, CDCl_3) δ 7.48-7.45 (comp, 4 H), 7.39-7.30 (comp, 9 H), 7.27-7.17 (comp, 2 H), 4.46 (s, 2 H), 4.43 (s, 1 H), 4.32-4.27 (m, 1 H), 3.57 (dd, J = 6.1, 8.7 Hz, 1 H), 3.57 (dd, J = 4.1, 6.7 Hz, 1 H), 3.02 (dd, J = 6.1, 8.7 Hz, 1 H), 3.02 (dd, J = 4.1, 6.7 Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 142.3, 137.9, 128.5, 128.0, 127.9, 127.6, 127.2, 78.6, 71.1, 67.8, 61.0; IR ν 3059, 3025, 2939, 2830, 1490, 1452, 1352, 1207, 1152 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}+\text{H}$: M+H (theory), 330.18524; M+H (found), 330.18562.

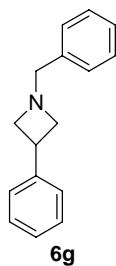


3-tert-butyl-1-(diphenylmethyl)azetidine (6e) was prepared from 2-tert-butyl-1,3-propanediol and aminodiphenylmethane according to the general azetidine formation procedure in 86% yield as a solid: mp 74-75 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.47-45 (comp, 4 H), 7.32-7.28 (comp, 4 H), 7.23-7.19 (comp, 2 H), 4.34 (s, 1 H), 3.23 (t, J = 7.9 Hz, 2 H), 2.88 (t, J = 8.0 Hz, 2 H), 2.43-2.36 (m, 1 H), 0.90 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 142.6, 128.3, 127.5, 126.9, 77.8, 54.8, 40.8, 30.3,

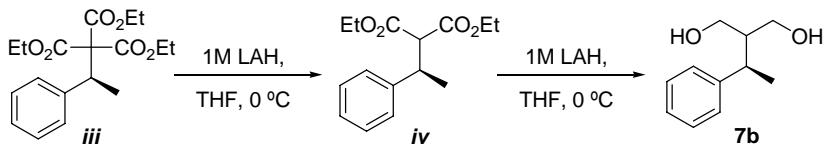
26.8; IR ν 2946, 2831, 1203, 1150 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{20}\text{H}_{25}\text{N}+\text{H}$: M+H (theory), 280.20598; M+H (found), 280.20738.



3-tert-butyl-1-phenylazetidine (6f) was prepared from 2-*t*butyl-1,3-propanediol and aniline according to the general azetidine formation procedure in 32% yield as a low melting solid; ^1H NMR (400 MHz, CDCl_3) δ 7.31-7.27 (comp, 2 H), 6.80-6.78 (m, 1 H), 6.53 (d, J = 8.2 Hz, 2 H), 3.90 (apt, J = 7.7 Hz, 2 H), 3.69 (apt, J = 6.6 Hz, 2 H), 2.70-2.64 (m, 1 H), 0.99 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 151.7, 128.9, 117.0, 113.3, 53.0, 40.9, 30.7, 26.3; IR ν 2961, 2900, 2842, 1602, 1506, 1475, 1363, 1127, 748, 691 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{13}\text{H}_{19}\text{N}+\text{H}$: M+H (theory), 190.15903; M+H (found), 190.15898.



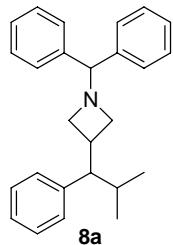
1-benzyl-3-phenylazetidine (6g) was prepared from 2-phenyl-1,3-propanediol and aniline according to the general azetidine formation procedure in 58% yield as an oil; ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.23 (comp, 10 H), 3.81-3.73 (comp, 3 H), 3.69 (s, 2 H), 3.30-3.19 (comp, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 142.5, 138.1, 128.4, 128.3, 128.2, 126.9, 126.9, 126.3, 63.7, 61.4, 35.7; IR ν 3061, 2947, 2821, 1652, 1496, 1028, 697 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{16}\text{H}_{17}\text{N}+\text{H}$: M+H (theory), 224.14338, M+H (found), 224.14429.



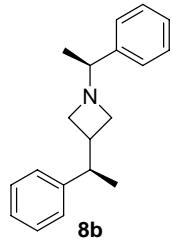
2-[(1*R*)-1-phenylethyl]propane-1,3-diol (7b).³ To a solution of triethyl (2*S*)-2-phenylpropane-1,1,1-tricarboxylate⁴ **iii** (3.9 g, 11.5 mmol) in THF (55 mL) was slowly added 1M LAH in THF (23 mL, 23 mmol) and the reaction was warmed to rt over 2 h. The reaction mixture was recooled to 0 °C, slowly quenched with water (0.9 mL), 15% NaOH (0.9 mL), and water (2.7 mL) and the resulting slurry was filtered. The collected precipitate was washed with MTBE (2 x 50 mL) and the collected filtrate was dried (MgSO_4), filtered, and concentrated to give the crude malonate adduct **iv**. This material was redissolved in THF (40 mL), cooled to 0 °C, treated with 1M LAH in THF (20 mL, 20 mmol), and warmed to rt over 2 h. The reaction mixture was recooled to 0 °C, slowly quenched with water (0.9 mL), 15% NaOH (0.9 mL), and water (2.7 mL) and the resulting slurry was filtered. The collected precipitate was washed with MTBE (2 x 50 mL) and the collected filtrate was dried (MgSO_4), filtered, and concentrated. This crude product was purified by silica gel chromatography eluting with 100% EtOAc to give 0.8g (40%) of **7b** as a solid: 69-71 °C; $[\alpha]^{23}_D$ -106.9 (*c* 0.38, CH_2Cl_2); 94% ee; chiral SFC: Chirapak AD column, 4% EtOH in CO_2 for 4 min. then ramp to 40% EtOH @ 2% per min, t_R = 12.8 min. (*S*), 14.2 min. (*R*). The spectral data for the chiral diol **7b** matched that found for the racemic derivative **1a**.

³ Reduction of the tris-ester **iii** provided only the malonate adduct **iv**, thus a two-step protocol for the synthesis of the diol **7b** was utilized.

⁴ Hillier, M. C.; Desrosiers, J-N.; Marcoux, J-F; Grabowski, E. J. *J. Org. Lett.* **2004**, 6, 573-576.

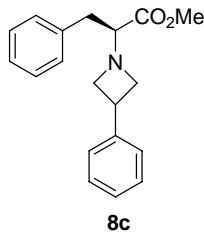


1-(diphenylmethyl)-3-(2-methyl-1-phenylpropyl)azetidine (8a) was prepared from 2-(2-methyl-1-phenylpropyl)propane-1,3-diol (**7a**) and aminodiphenylmethane according to the general azetidine formation procedure in 92% yield as a solid: mp 138-140 °C; ¹H NMR (500 MHz, CDCl₃) δ 7.46-7.44 (comp, 2 H), 7.39, 7.38 (comp, 2 H), 7.33-7.09 (comp, 11 H), 4.29 (s, 1 H), 3.63 (dt, *J* = 2.4, 7.1 Hz, 1 H), 3.11 (dt, *J* = 2.4, 7.3 Hz, 1 H), 3.03-2.98 (m, 1 H), 2.84 (t, *J* = 7.6 Hz, 1 H), 2.46 (dd, *J* = 7.2, 10.9 Hz, 1 H), 2.43 (t, *J* = 7.9 Hz), 1.84-1.78 (m, 1 H), 0.89 (d, *J* = 6.8 Hz, 3 H), 0.72 (d, *J* = 6.8 Hz, 3 H); ¹³C NMR (126 MHz, CDCl₃) 142.4, 142.3, 142.2, 128.6, 128.5, 128.4, 128.0, 127.5, 127.4, 127.1, 127.0, 126.1, 78.7, 61.5, 59.3, 58.2, 34.0, 33.1, 21.0, 20.3; IR ν 3060, 2954, 2871, 2914, 1491, 1451, 1074, 909, 701 cm⁻¹; mass spectrum (TOF) calcd. for C₂₆H₂₉N+H: M+H (theory), 356.23728; M+H (found), 356.23832.

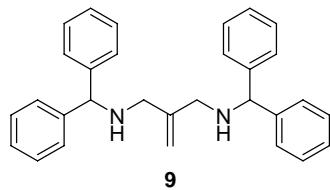


3-[(1R)-1-phenylethyl]-1-[(1S)-1-phenylethyl]azetidine (8b) was prepared from 2-[(1R)-1-phenylethyl]propane-1,3-diol (**7b**, 94 % ee) and (*S*)-α-methylbenzyl amine (98% ee) according to the general azetidine formation procedure in 95% yield as a solid: mp 66-67 °C; [α]²³_D -20.2 (c 2.40, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.37-7.16 (comp, 10 H), 3.42-3.31 (comp, 2 H), 3.28 (q, *J* = 6.5 Hz, 1 H), 2.89-2.76 (comp, 2 H), 2.73-2.67 (comp, 2 H), 1.22 (d, *J* = 6.5 Hz, 3 H), 1.16 (d, *J* = 6.9 Hz, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 145.3, 143.7, 128.4, 128.2, 127.2, 127.1, 127.0, 126.2, 69.0,

58.7, 58.6, 45.0, 36.4, 21.1, 19.7; IR ν 3026, 2960, 2808, 1652, 1208, 1152, 760, 699 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{19}\text{H}_{23}\text{N}+\text{H}$: $\text{M}+\text{H}$ (theory), 266.19033 $\text{M}+\text{H}$ (found), 266.19064.

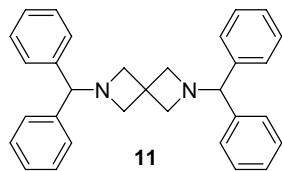


Methyl (2S)-3-phenyl-2-(3-phenylazetidin-1-yl)propanoate (8c) was prepared from 2-phenyl-1,3-propanediol **7c** and (S)-phenylalanine methyl ester according to the general azetidine formation procedure in 73% yield as an oil; $[\alpha]^{23}_{\text{D}} -5.0$ (c 3.90, CH_2Cl_2); 99% ee; chiral SFC: Chiralcel OJ-H column, 4% EtOH in CO_2 for 4 min. then ramp to 40% EtOH @ 2% per min, $t_{\text{R}} = 8.1$ min. (*S*), 8.8 min. (*R*). ^1H NMR (400 MHz, CDCl_3) δ 7.34-7.20 (comp, 10 H), 3.87-3.74 (comp, 3 H), 3.65 (s, 3 H), 3.40 (dd, $J = 6.2, 7.7$ Hz, 1 H), 3.37 (t, $J = 6.7$ Hz, 1 H), 2.96 (dd, $J = 7.8, 13.6$ Hz, 1 H), 2.91 (dd, $J = 6.2, 13.6$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.0, 141.9, 137.2, 129.0, 128.3, 127.0, 126.9, 126.6, 126.4, 71.1, 60.0, 59.6, 51.5, 36.7, 35.6; IR δ 3028, 2950, 2835, 1733, 1167, 756, 689, 667 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{19}\text{H}_{21}\text{NO}_2+\text{H}$: $\text{M}+\text{H}$ (theory), 296.16451; $\text{M}+\text{H}$ (found), 296.16410.

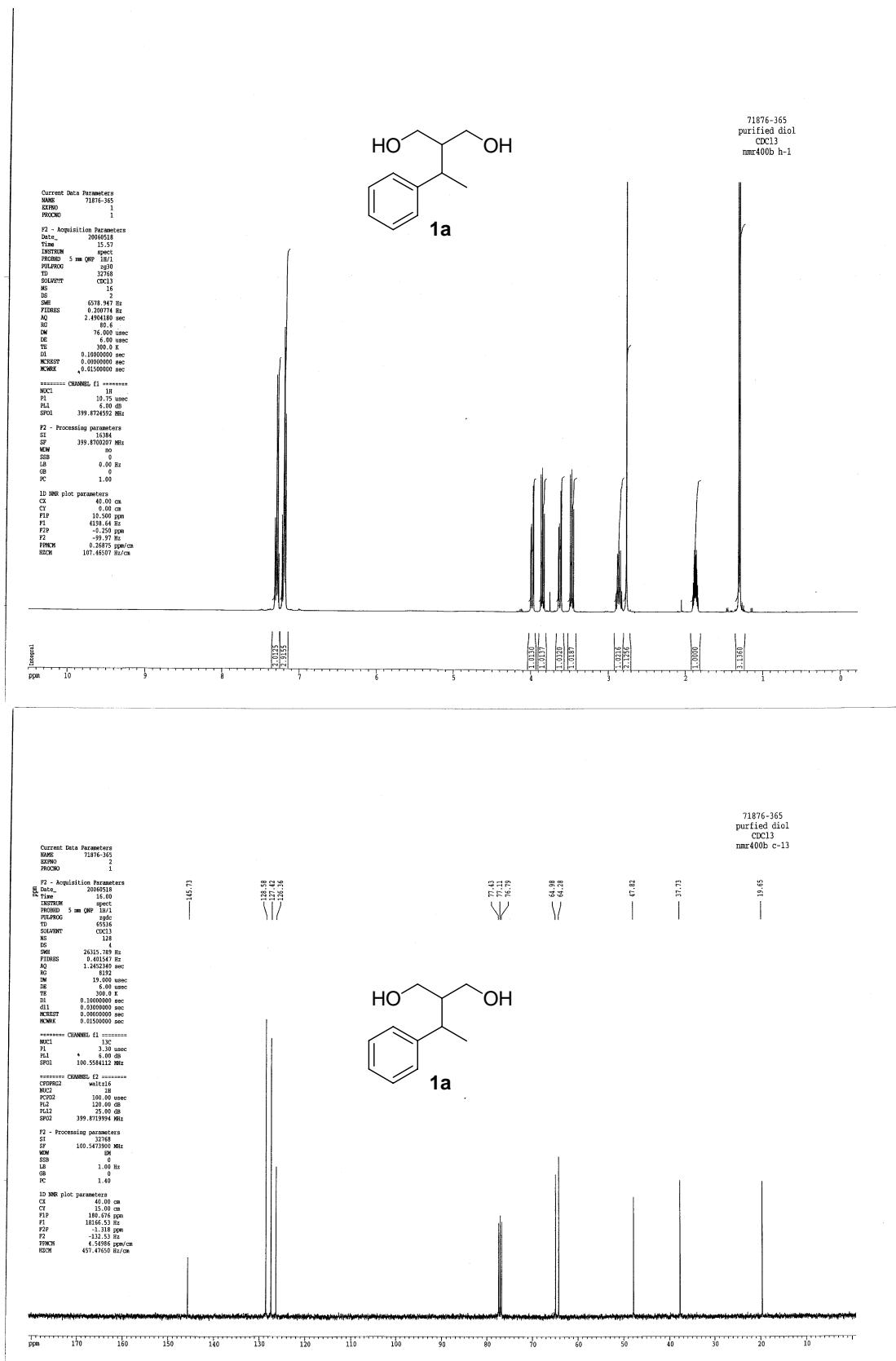


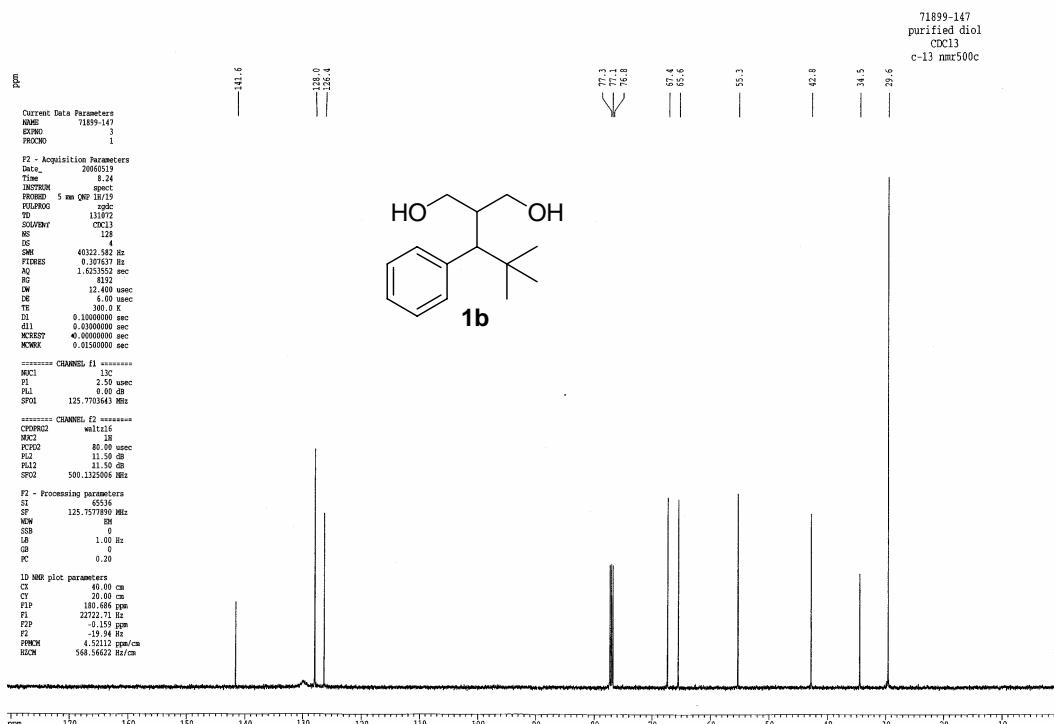
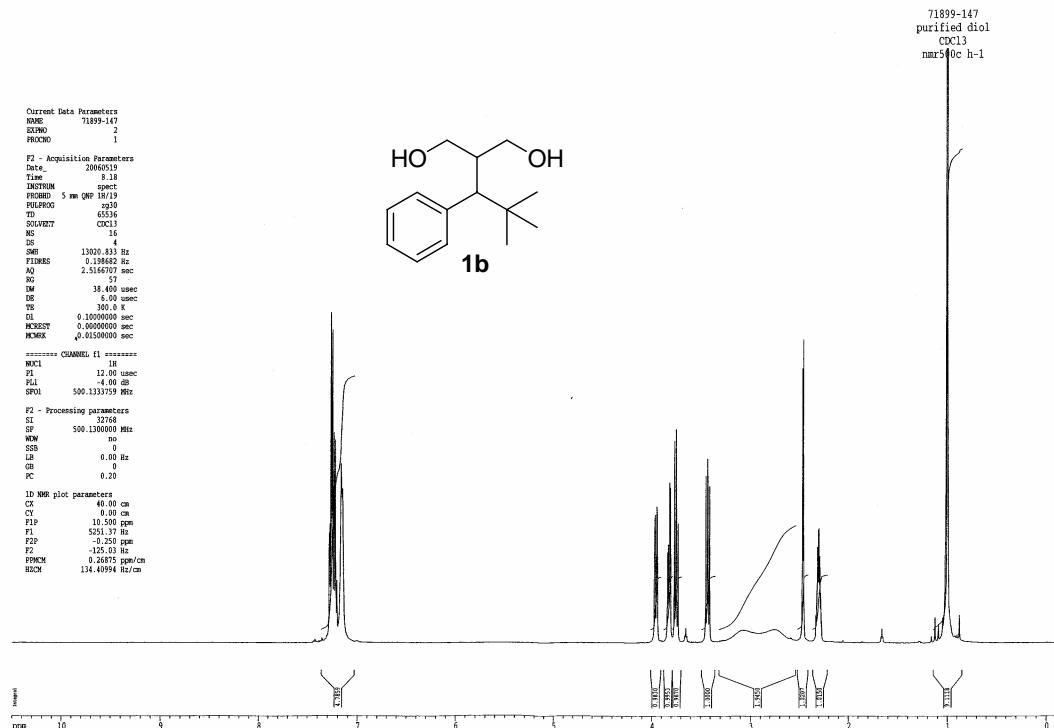
N,N'-diphenylmethyl-2-methylenepropane-1,3-diamine (9) was prepared from 2-(hydroxymethyl)-1,3-propanediol and aminodiphenylmethane according to the general azetidine formation procedure in 32% yield as an oil; ^1H NMR (500 MHz, CDCl_3) δ 7.50-7.26 (comp, 20 H), 5.18 (s, 2 H), 4.90 (s, 2 H), 3.34 (s, 4 H), 2.35 (brs, 2 H); ^{13}C NMR (126 MHz, CDCl_3) δ 143.8, 128.6, 128.5, 127.5, 127.4, 127, 113, 66.6, 51.9; IR ν 3312, 3061, 3025, 2825, 1491, 1425, 1028, 909, 744,

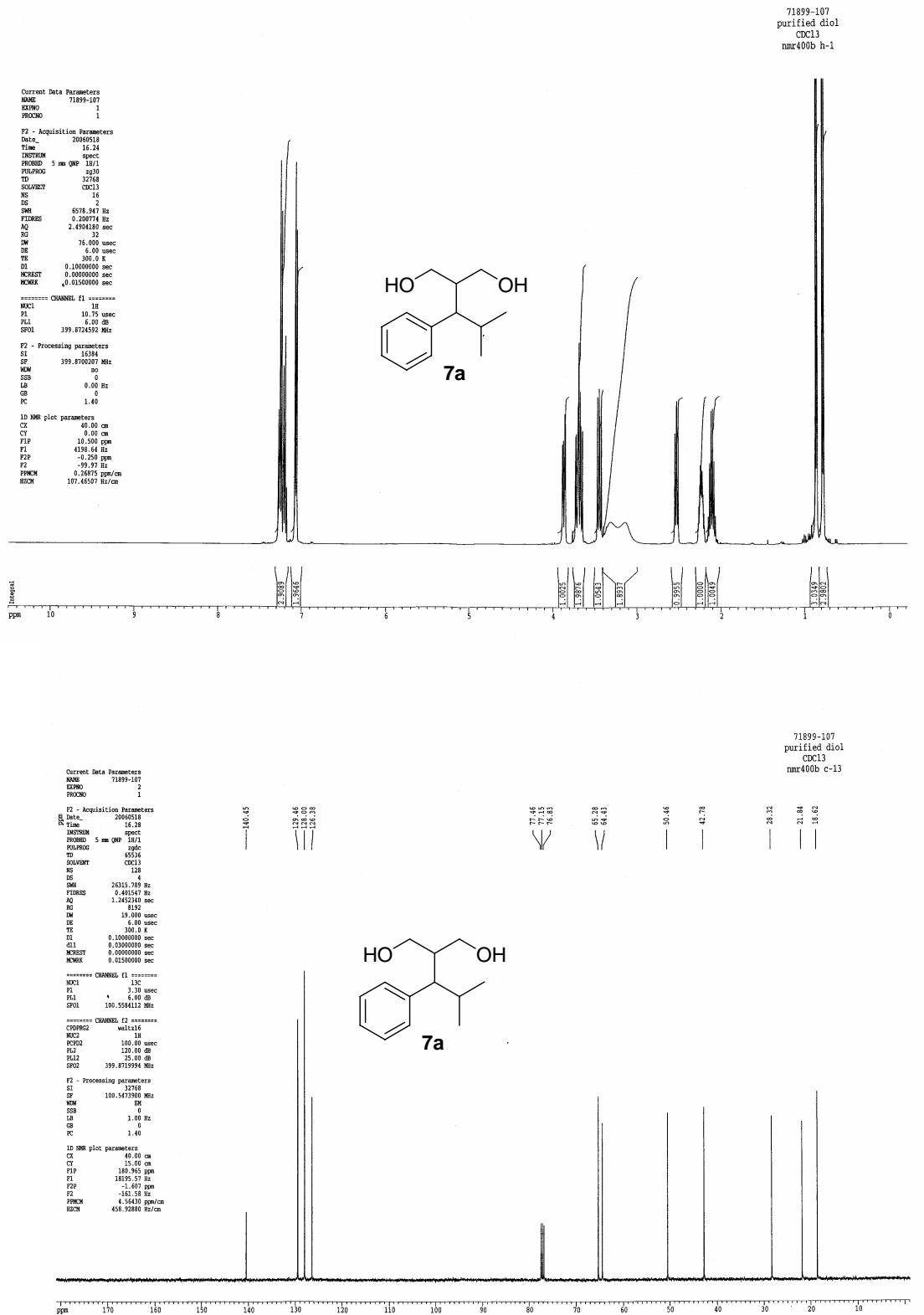
701 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{30}\text{H}_{30}\text{N}_2+\text{H}$: $\text{M}+\text{H}$ (theory), 419.24818; $\text{M}+\text{H}$ (found), 419.25058.

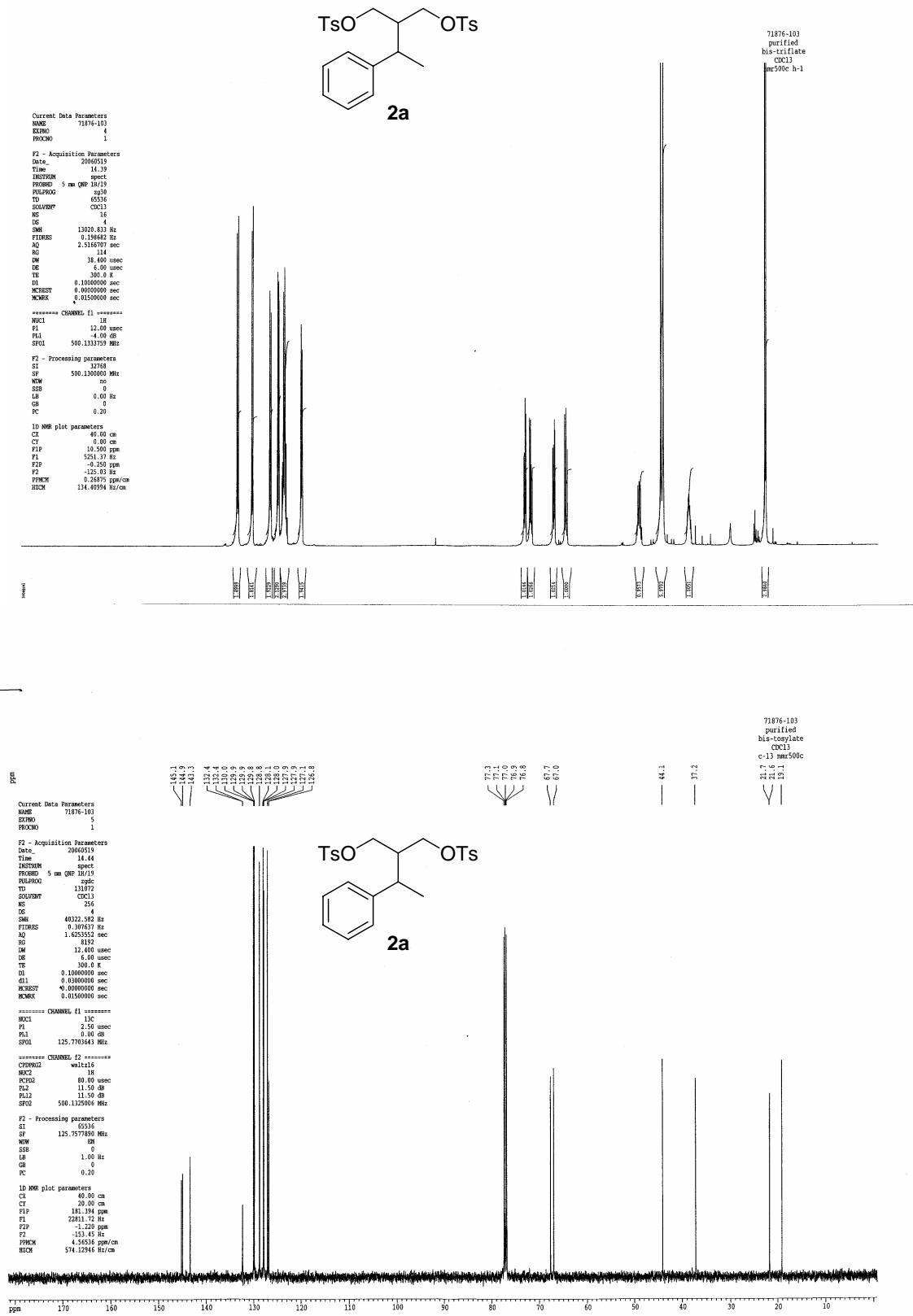


2,6-diphenylmethane-2,6-diazaspiro[3.3]heptane (11) was prepared from pentaerythritol **10** and aminodiphenylmethane according to the general azetidine formation procedure in 35% yield as a solid: mp 88-90 $^{\circ}\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.43-7.41 (comp, 8 H), 7.32-7.29 (comp, 8 H), 7.24-7.20 (comp, 4 H), 4.31 (s, 2 H), 3.27 (s, 8 H); ^{13}C NMR (126 MHz, CDCl_3) δ 142.4, 128.4, 127.5, 127.0, 78.0, 63.9, 33.0; IR ν 3083, 3060, 3025, 2937, 2814, 1490, 1451, 1244, 909, 736, 703 cm^{-1} ; mass spectrum (TOF) calcd. for $\text{C}_{13}\text{H}_{30}\text{N}_2+\text{H}$: $\text{M}+\text{H}$ (theory), 431.24818, $\text{M}+\text{H}$ (found), 431.25028.









71899-211
purified.
tosylate
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nmr400b h-1

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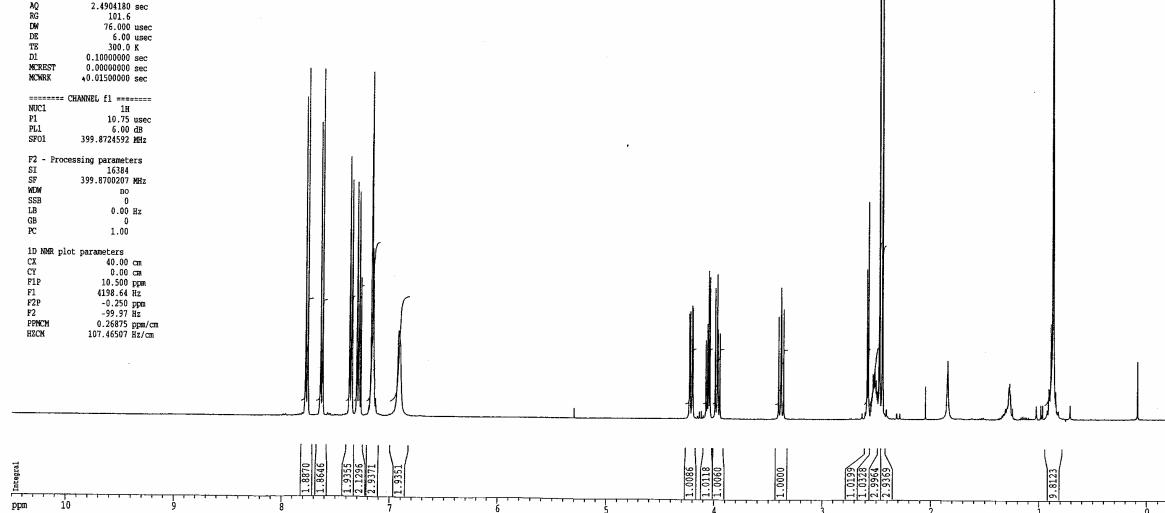
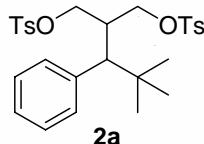
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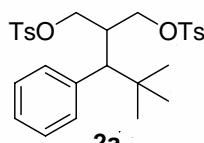


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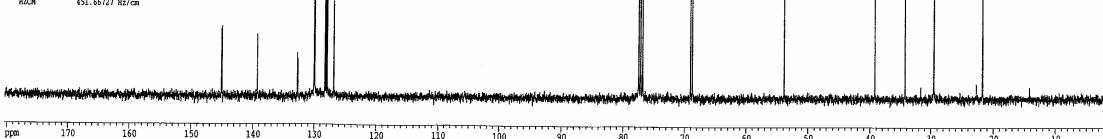
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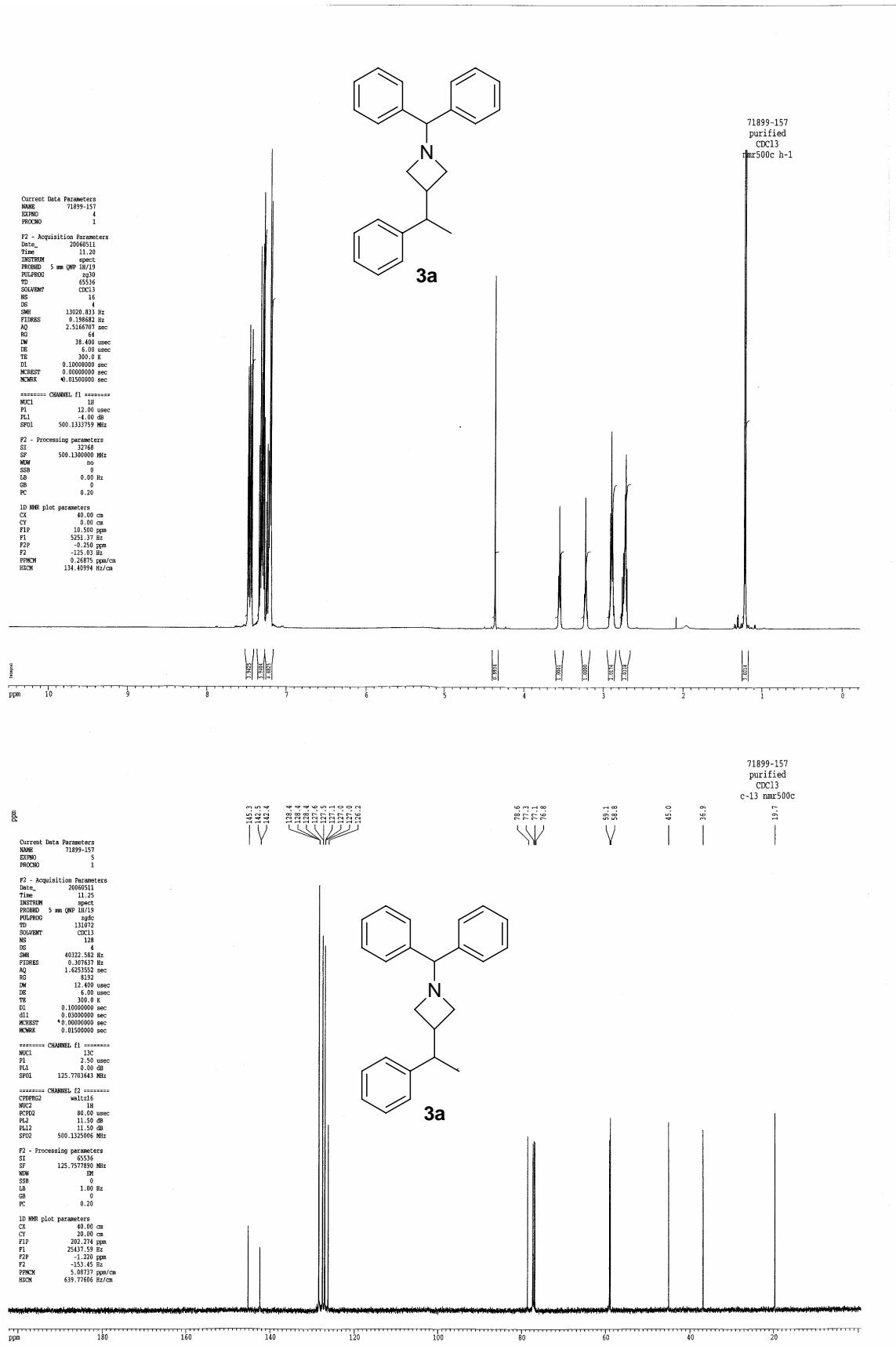
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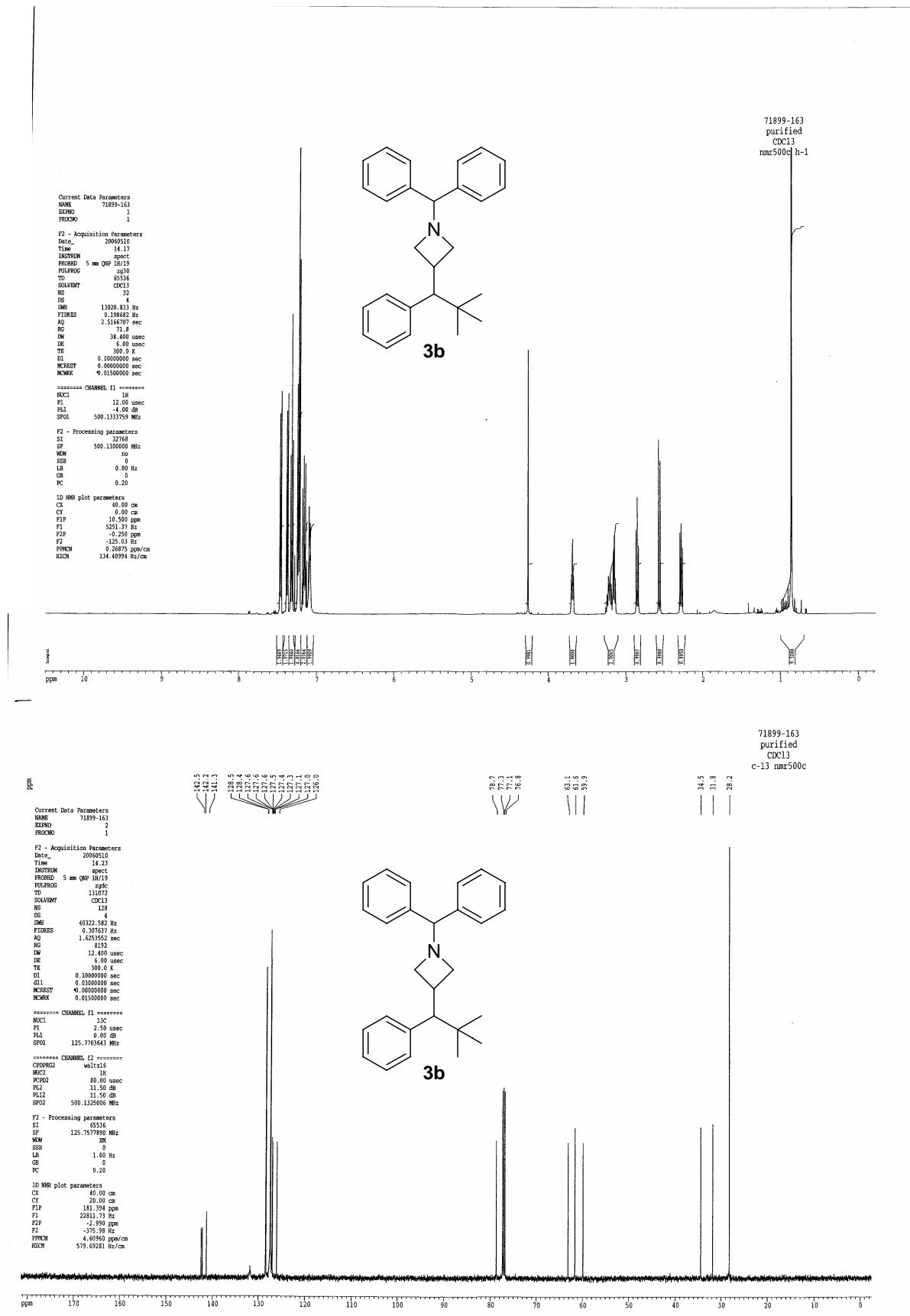
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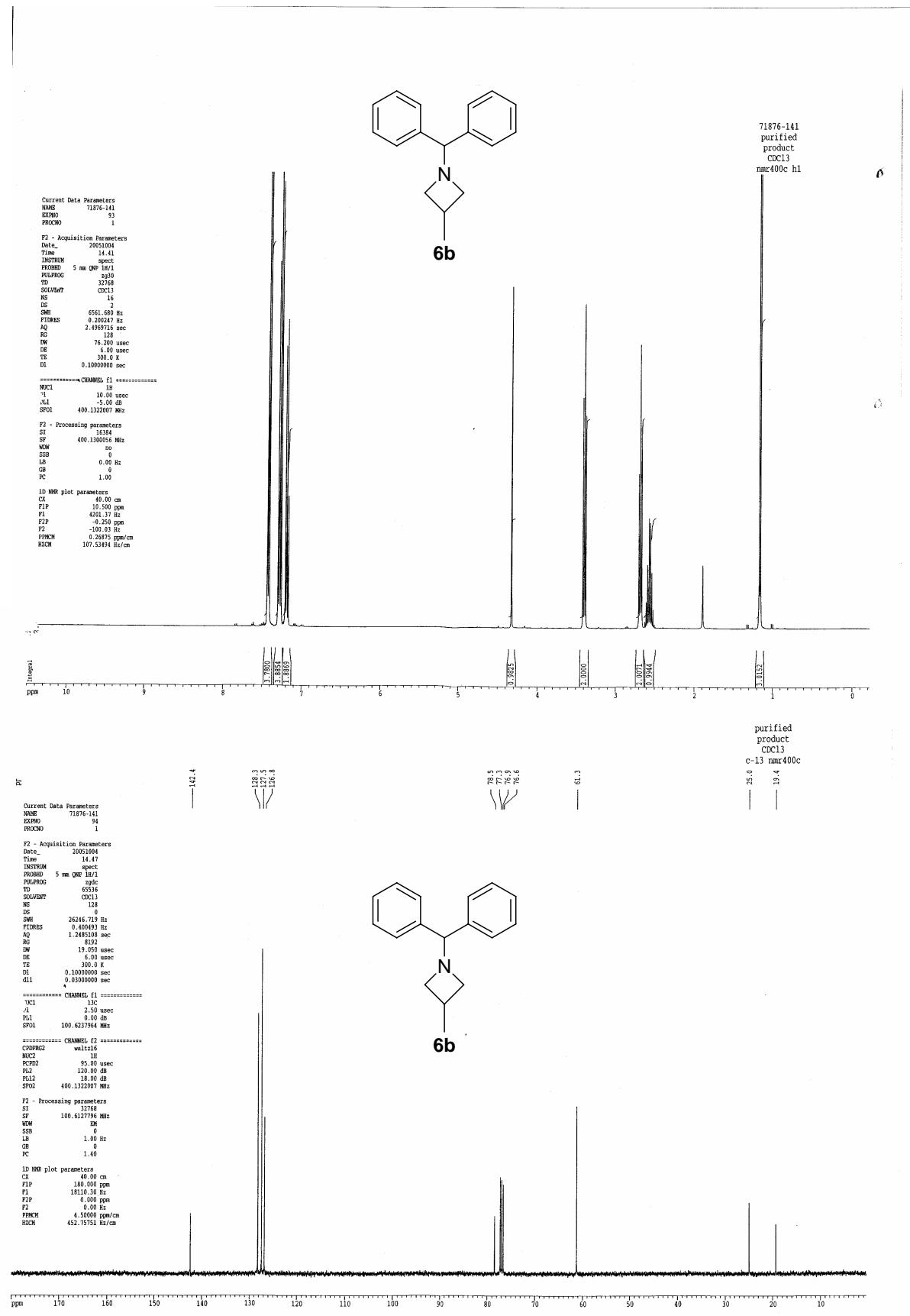
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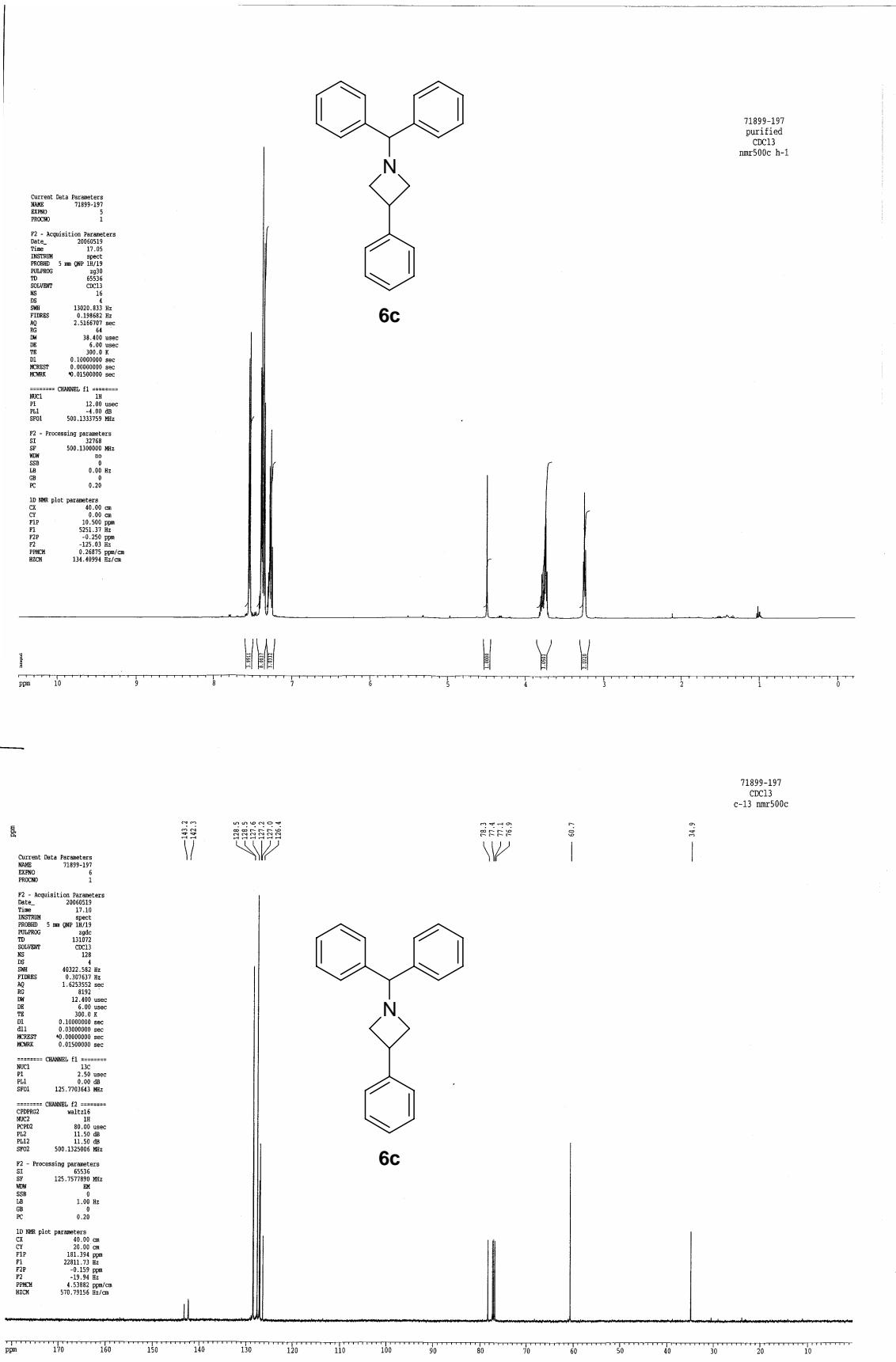
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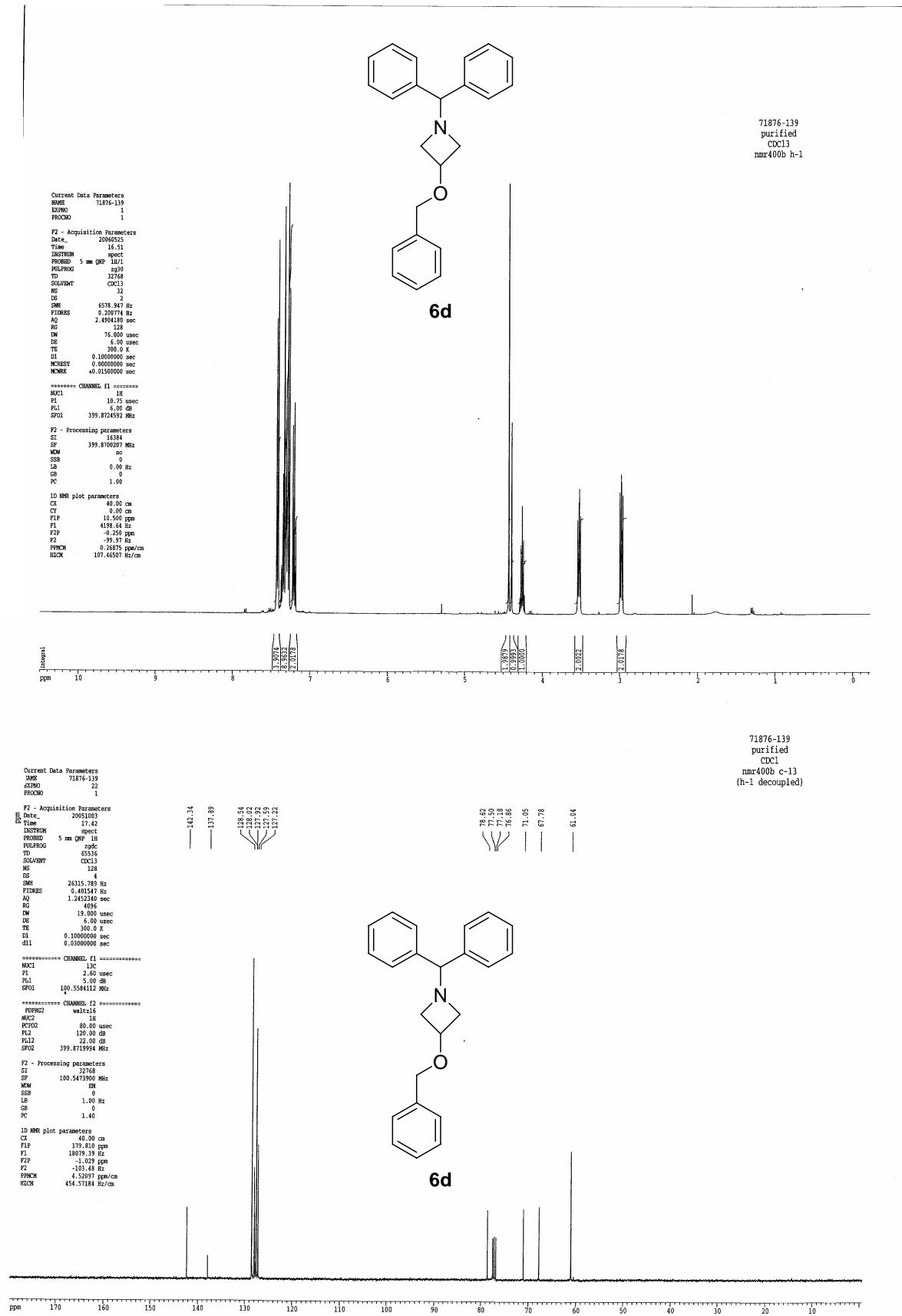


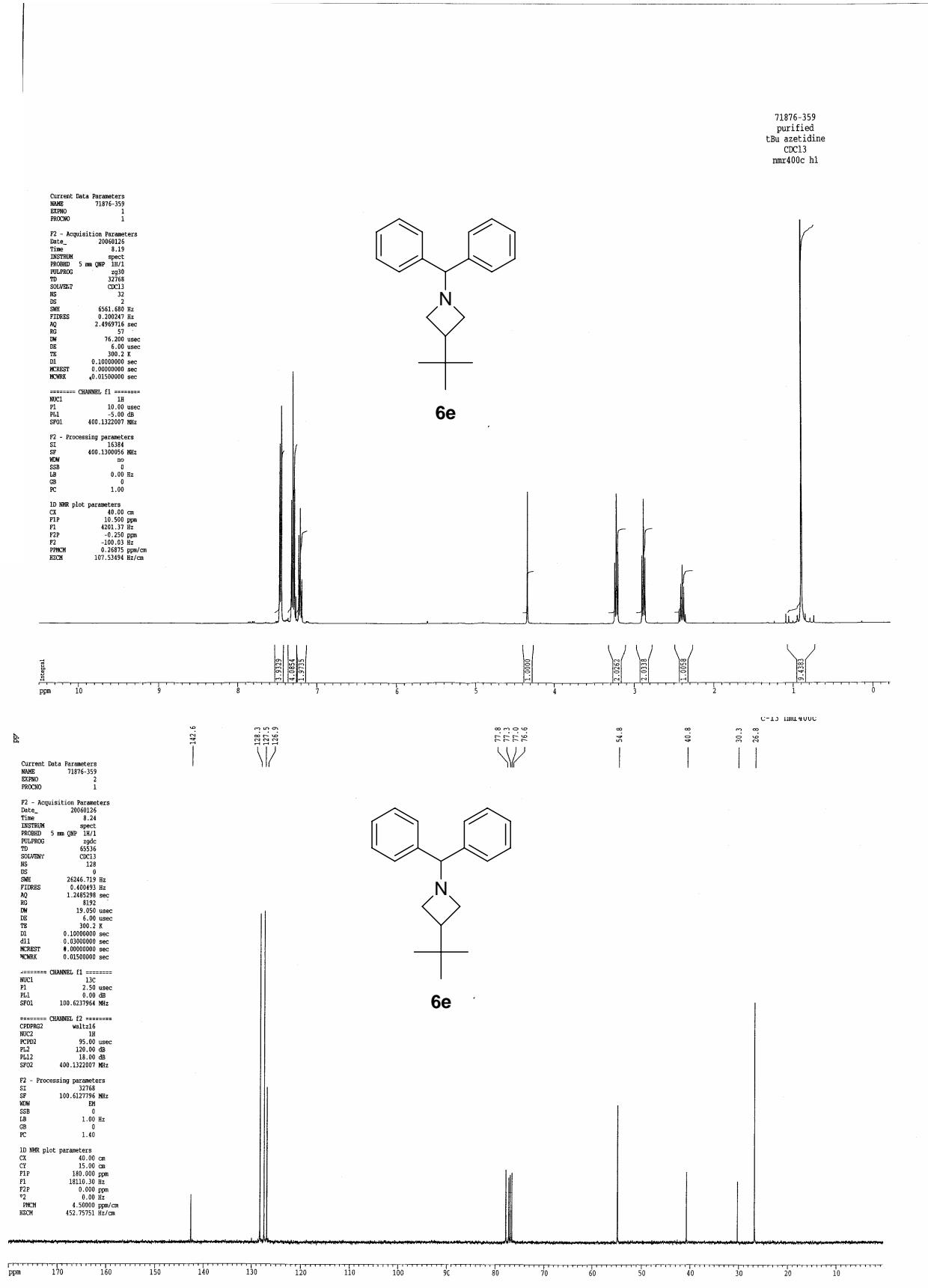


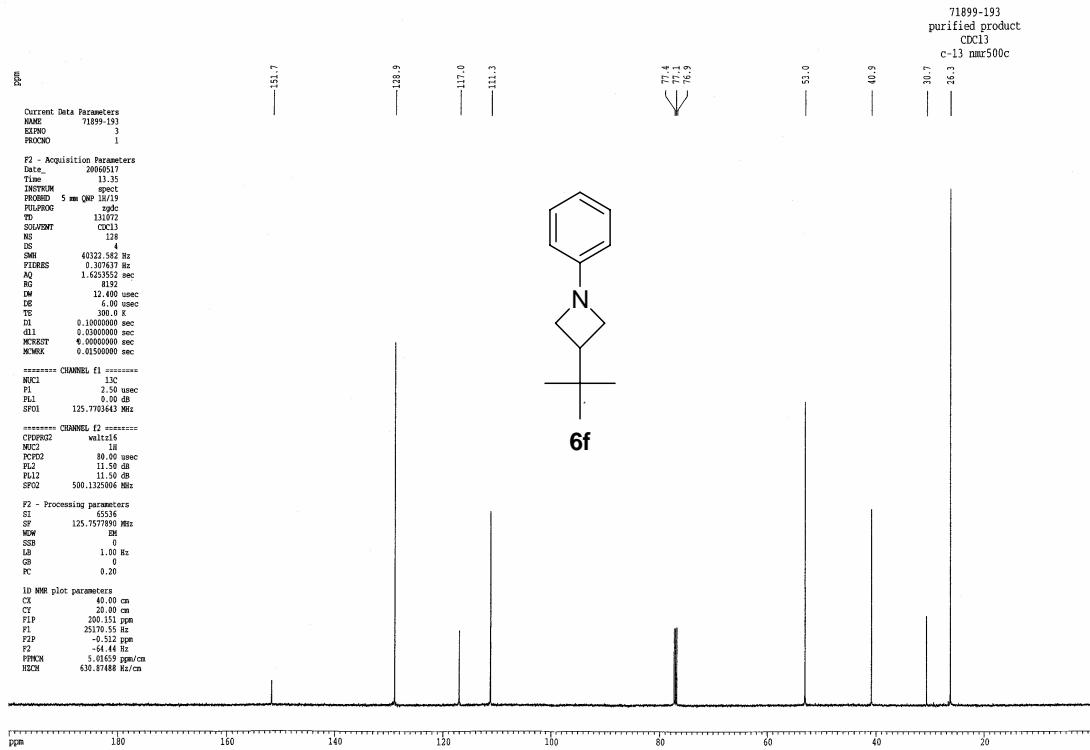
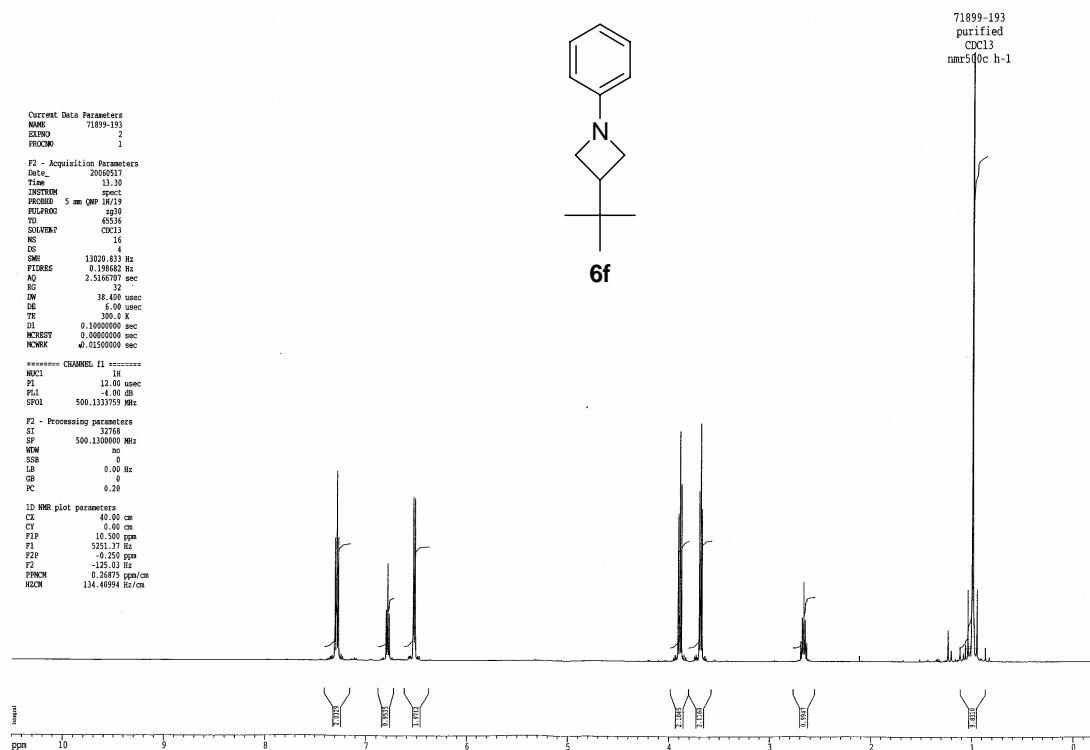


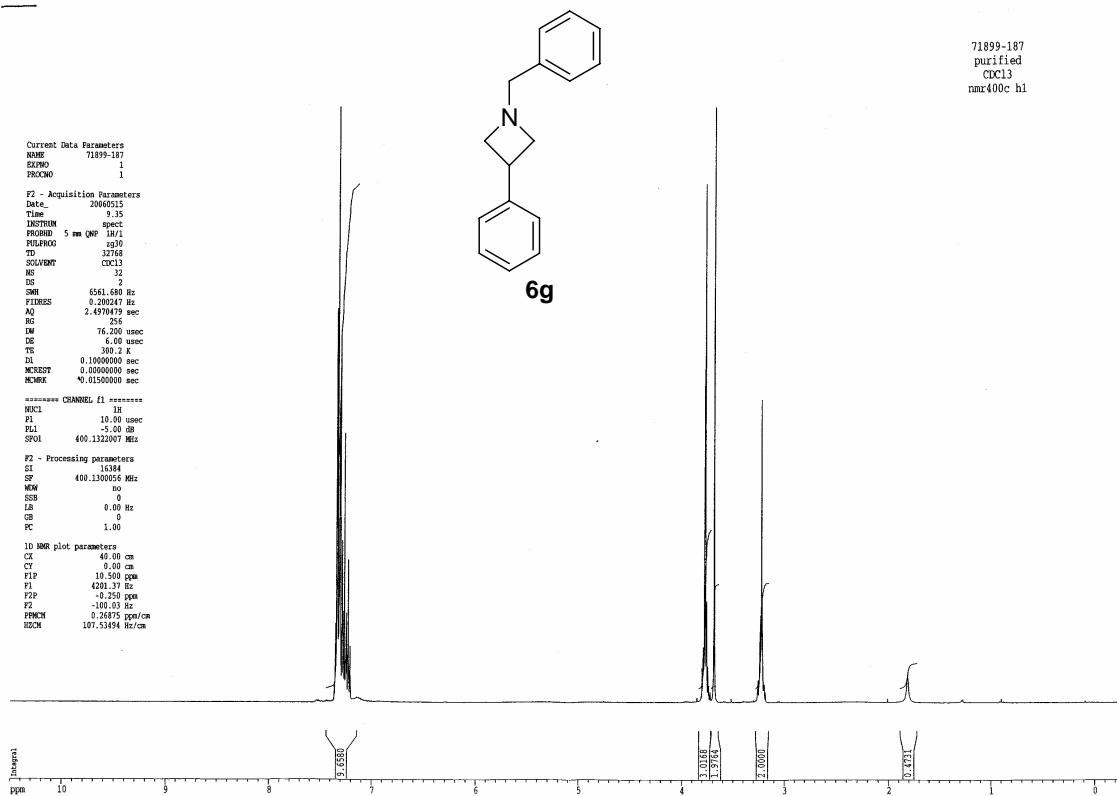












c-13 nmr400c

