Stereoconvergent Amine-Directed Alkyl–Alkyl Suzuki Reactions of Unactivated Secondary Alkyl Chlorides

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Supporting Information

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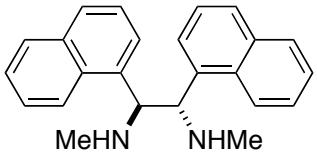
I. General

The following reagents were purchased and used as received: 9-BBN dimer (Aldrich), $NiBr_2$•diglyme (Aldrich; somewhat hygroscopic), KO*t*-Bu (Acros or Strem), *n*-hexanol (Aldrich; anhydrous), and *i*-Pr_2O (Aldrich; anhydrous). Unless otherwise noted, reactions were conducted with stirring in oven-dried glassware under an inert atmosphere.

II. Preparation of Materials



(1*S*,2*S*)-*N*^{1},*N*^{2}-Dimethyl-1,2-di(naphthalen-1-yl)ethane-1,2-diamine (1). The title compound was synthesized from 2,2'-((1*R*,2*R*)-1,2-diaminoethane-1,2-diyl)diphenol and 1-naphthaldehyde according to a procedure by Chin,[1] methylated according to a procedure by Alper,[2] and purified by flash chromatography (2:33:65 NEt_3:EtOAc:hexanes) to provide the desired ligand.

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(1) Kim, H.; Nguyen, Y.; Yen, C. P.-H.; Chagal, L.; Lough, A. J.; Kim, B. M.; Chin, J. *J. Am. Chem. Soc.* **2008**, *130*, 12184–12191.
(2) Kuznetsov, V. F.; Jefferson, G. R.; Yap, G. P. A.; Alper, H. *Organometallics* **2002**, *21*, 4241–4248.

The (*R*,*R*) enantiomer was synthesized by the same method, except starting with 2,2'-((1*S*,2*S*)-1,2-diaminoethane-1,2-diyl)diphenol.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27–8.14 (m, 2H), 7.72–7.54 (m, 6H), 7.41–7.30 (m, 6H), 4.69 (s, 2H), 2.23 (s, 6H), 2.08 (br s, 2H).

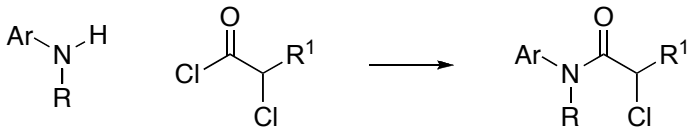
^{13}C NMR (100 MHz, $CDCl_3$) δ 137.3, 133.9, 132.3, 128.8, 127.6, 125.5, 125.3, 125.2, 125.1, 123.3, 35.1.

FT-IR (KBr) 2945, 2790, 1943, 1596, 1507, 1394, 1162, 1136, 1104 cm^{-1}.

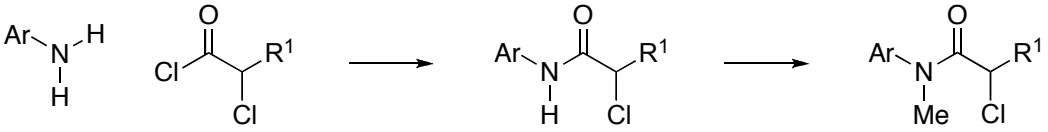
MS (APCI + ESI) *m*/*z* (M^+) calcd for $C_{24}H_{24}N_2$: 340.2, found: 340.1.

$[\alpha]^{23}_D$ = +77° (c = 0.011, $CHCl_3$).

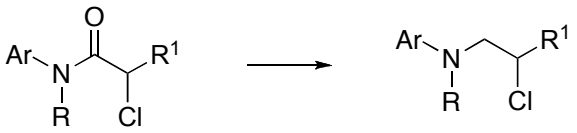
Synthesis of starting materials. These procedures have not been optimized.



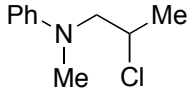
Representative procedure for the synthesis of tertiary amides from secondary amines: Triethylamine (4.2 mL, 30 mmol) and then the α-chloro acyl chloride (20 mmol) were added dropwise to a 0 °C solution of the secondary amine (20 mmol) in CH_2Cl_2 (150 mL) in a 500-mL round-bottom flask. Then, the reaction was allowed to warm to room temperature and stirred for 2 h. Next, an aqueous solution of HCl (1 M; 50 mL) was added. The organic layer was separated, washed with water (50 mL) and brine (50 mL), dried over Na_2SO_4, filtered, and concentrated.



Representative procedure for the synthesis of tertiary amides from primary amines: The secondary amide was synthesized from the primary amine according to the preceding procedure. The unpurified secondary amide (20 mmol) was dissolved in dry THF (100 mL) in a 250-mL round-bottom flask, and the solution was cooled to 0 °C. Sodium hydride (0.48 g, 20 mmol) was added, and the mixture was stirred at 0 °C for 30 min. Next, MeI (1.2 mL, 20 mmol) was added dropwise over 1 min. Then, the reaction mixture was stirred at 0 °C for 2 h, after which the reaction was quenched by the addition of water (20 mL). The solvent was removed by rotary evaporation, and Et_2O (100 mL) and water (100 mL) were added to the residue. The organic layer was separated, washed with water (50 mL) and brine (50 mL), dried over Na_2SO_4, and concentrated.



Representative procedure for the reduction of amides to arylamines: Borane–THF (1.0 M; 1.0 equiv) was added dropwise to a solution of the amide in dry THF (100 mL) in a 3-neck, 300-mL round-bottom flask equipped with a stir bar and a reflux condenser. After the addition was complete, the solution was heated at reflux for 18 h. Next, it was allowed to cool to room temperature, and then the reaction was quenched by the addition of an aqueous solution of NaOH (1 M; 10 mL). The THF was removed by rotary evaporation, and the resulting mixture was diluted with Et_2O (100 mL). The organic layer was separated, washed with water (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered, and concentrated.



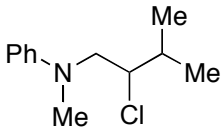
***N*-(2-Chloropropyl)-*N*-methylaniline.** Synthesized from *N*-methylaniline (3.5 mL, 32.3 mmol) and 2-chloropropanoyl chloride (3.1 mL, 31.9 mmol). Purified by chromatography (0%→50% Et_2O/hexanes): 4.66 g (78% over 2 steps). Clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.23 (m, 2H), 6.76–6.67 (m, 3H), 4.28 (sextet, 1H, J = 7.2 Hz), 3.68–3.61 (dd, 1H, J = 6.5, 15.2 Hz), 3.52–3.45 (dd, 1H, J = 7.3, 15.2 Hz), 3.04 (s, 3H), 1.53 (d, 3H, J = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 129.5, 116.9, 112.0, 61.2, 55.3, 40.0, 23.2.

FT-IR (neat) 2976, 1601, 1509, 1353, 748, 692 cm^{-1}.

MS (APCI + ESI) m/z (M^+) calcd for $C_{10}H_{14}ClN$: 183.1, found: 183.1.



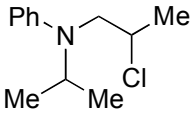
***N*-(2-Chloro-3-methylbutyl)-*N*-methylaniline.** Synthesized from *N*-methylaniline (3.10 g, 20.0 mmol) and 2-chloro-3-methylbutanoyl chloride (2.16 mL, 20.0 mmol). Purified by chromatography (0%→50% Et_2O/hexanes): 1.36 g (32% over 2 steps). Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.21 (m, 2H), 6.75–6.66 (m, 3H), 4.21–4.15 (m, 1H), 3.68 (dd, 1H, J = 6.0, 15.4 Hz), 3.55 (dd, 1H, J = 7.6, 15.4 Hz), 3.03 (s, 3H), 2.09–2.00 (m, 1H), 1.08–1.02 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 129.5, 116.8, 112.1, 67.1, 57.9, 40.1, 31.7, 20.8, 16.4.

FT-IR (neat) 2968, 2914, 1600, 1507, 1362, 1210, 747, 692 cm^{-1}.

MS (APCI + ESI) m/z (M^+) calcd for $C_{12}H_{18}ClN$: 211.1, found: 211.1.



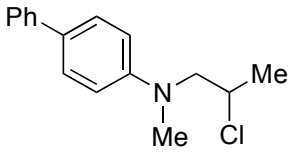
***N*-(2-Chloropropyl)-*N*-isopropylaniline.** Synthesized from *N*-isopropylaniline (4.50 mL, 31.1 mmol) and 2-chloropropionyl chloride (3.10 mL, 31.1 mmol). Purified by chromatography (0%→50% Et_2O/hexanes): 1.74 g (27% over 2 steps). Light-yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.23 (m, 2H), 6.88–6.86 (m, 2H), 6.82–6.78 (m, 1H), 4.17–4.01 (m, 1H), 3.99 (septet, 1H, *J* = 6.7 Hz), 3.50–3.45 (dd, 1H, *J* = 5.2, 14.8 Hz), 3.26–3.20 (dd, 1H, *J* = 8.6, 14.6 Hz), 1.50 (d, 3H, *J* = 6.8 Hz), 1.20 (d, 3H, *J* = 6.8 Hz), 1.13 (d, 3H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 129.4, 118.8, 116.8, 55.2, 52.4, 52.1, 23.2, 20.9, 20.0.

FT-IR (neat) 2974, 1599, 1497, 1378, 1293, 1224, 1185, 1121, 1048, 1013, 910, 752, 696 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{12}H_{18}ClN$: 211, found: 211.



***N*-(2-Chloropropyl)-*N*-methylbiphenyl-4-amine.** Synthesized from 4-biphenylamine (3.38 g, 20.0 mmol) and 2-chloropropanoyl chloride (1.97 mL, 20.0 mmol). Purified by chromatography (5%→100% Et_2O/hexanes): 2.08 g (40% over 3 steps). White solid.

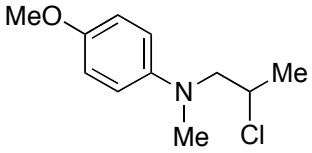
mp 157 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.46 (m, 4H), 7.42–7.35 (m, 2H), 7.29–7.23 (m, 1H), 6.79–6.73 (m, 2H), 4.32 (sextet, 1H, *J* = 6.7 Hz), 3.68 (dd, 1H, *J* = 6.5, 15.2 Hz), 3.54 (dd, 1H, *J* = 7.3, 15.2 Hz), 3.09 (s, 3H), 1.57 (d, 3H, *J* = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 141.7, 129.2, 128.4, 127.8, 126.2, 126.0, 112.1, 60.0, 55.0, 39.8, 23.2.

FT-IR (neat) 2924, 2845, 1612, 1505, 1456, 1201, 816, 761, 697 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{18}ClN$: 259.1, found: 259.1.



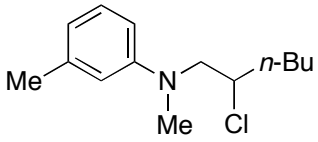
***N*-(2-Chloropropyl)-4-methoxy-*N*-methylaniline.** Synthesized from 4-methoxy-*N*-methylaniline (2.17 g, 15.8 mmol) and 2-chloropropanoyl chloride (1.5 mL, 15.5 mmol). Purified by chromatography (5%→100% Et_2O/hexanes): 2.89 g (86% over 2 steps). Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87–6.82 (m, 2H), 6.71–6.65 (m, 2H), 4.24 (sextet, 1H, *J* = 6.6 Hz), 3.77 (s, 3H), 3.54 (dd, 1H, *J* = 6.4, 15.0 Hz), 3.37 (dd, 1H, *J* = 7.3 Hz, 15.0 Hz), 2.97 (s, 3H), 1.52 (d, 3H, *J* = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 143.7, 115.1, 114.0, 62.3, 56.0, 55.4, 40.3, 23.2.

FT-IR (neat) 2928, 1513, 1246, 1040, 814 cm^{-1}.

MS (APCI + ESI) *m*/*z* (M^+) calcd for $C_{11}H_{16}ClNO$: 213.1, found: 213.1.



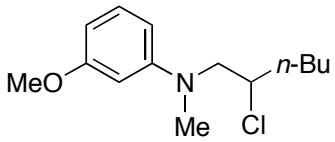
***N*-(2-Chlorohexyl)-*N*,3-dimethylaniline.** Synthesized from *N*-methyl-*m*-toluidine (2.00 g, 16.5 mmol) and 2-chlorohexanoyl chloride (2.47 mL, 16.5 mmol). Purified by chromatography (5%→100% Et_2O/hexanes): 2.31 g (58% over 2 steps). Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16–7.10 (m, 1H), 6.65–6.46 (m, 3H), 4.20–4.11 (m, 1H), 3.63–3.51 (m, 2H), 3.02 (s, 3H), 2.32 (s, 3H), 1.89–1.78 (m, 1H), 1.72–1.55 (m, 2H), 1.47–1.25 (m, 3H), 0.91 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 138.8, 129.1, 112.9, 110.4, 109.4, 59.2, 59.0, 39.7, 36.8, 28.9, 23.5, 22.2, 14.2.

FT-IR (neat) 2929, 2860, 1602, 1499, 1065, 764, 693, 668 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{14}H_{22}ClN$: 239.1, found: 239.1.



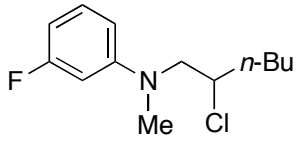
***N*-(2-Chlorohexyl)-3-methoxy-*N*-methylaniline.** Synthesized from 3-methoxyaniline (1.37 g, 10.0 mmol) and 2-chlorohexanoyl chloride (1.69 g, 10.0 mmol). Purified by chromatography (5%→100% Et_2O/hexanes): 1.63 g (62% over 3 steps). Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (t, 1H, *J* = 8.2 Hz), 6.28 (d, 2H, *J* = 8.0 Hz), 6.20 (t, 1H, *J* = 2.2 Hz), 4.17–4.11 (m, 1H), 3.78 (s, 3H), 3.55 (d, 2H, *J* = 6.8 Hz), 3.01 (s, 3H), 1.85–1.76 (m, 1H), 1.66–1.54 (m, 2H), 1.43–1.25 (m, 3H), 0.89 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 150.2, 130.2, 105.2, 101.5, 98.8, 60.9, 60.2, 55.3, 40.2, 35.9, 28.8, 22.5, 14.2.

FT-IR (neat) 2956, 2931, 2872, 1612, 1577, 1500, 1456, 1247, 1169, 1056, 824, 750, 687 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{14}H_{22}ClNO$: 255.1, found: 255.1.



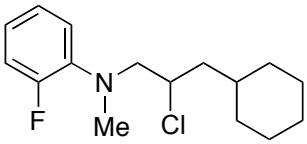
***N*-(2-Chlorohexyl)-3-fluoro-*N*-methylaniline.** Synthesized from 3-fluoro-*N*-methylaniline (1.13 mL, 10.0 mmol) and 2-chlorohexanoyl chloride (1.69 g, 10.0 mmol). Purified by chromatography (5%→50% Et_2O/hexanes): 1.78 g (74% over 2 steps). Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.10 (m, 1H), 6.45–6.38 (m, 2H), 6.38–6.31 (m, 1H), 4.18–4.10 (m, 1H), 3.57 (d, 2H, *J* = 6.8 Hz), 3.03 (s, 3H), 1.85–1.77 (m, 1H), 1.70–1.61 (m, 1H), 1.64–1.21 (m, 4H), 0.91 (t, 3H, *J* = 7.1 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4 (d, *J* = 243 Hz), 150.4, 130.4 (d, *J* = 10 Hz), 107.6 (d, *J* = 22 Hz), 99.1 (d, *J* = 26 Hz), 60.7, 60.0, 40.2, 35.8, 28.7, 22.5, 14.1.

FT-IR (neat) 2988, 2931, 2886, 1621, 1577, 1502, 1362, 1235, 1162, 1009, 822, 754, 682 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{13}H_{19}ClFN$: 243.1, found: 243.1.



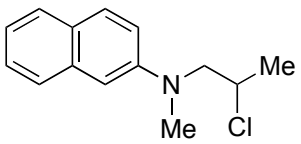
***N*-(2-Chloro-3-cyclohexylpropyl)-2-fluoro-*N*-methylaniline.** Synthesized from 2-fluoroaniline (1.44 mL, 15.0 mmol) and 2-chloro-3-cyclohexylpropionyl chloride (3.14 g, 15.0 mmol). Purified by chromatography (5%→50% Et_2O/hexanes): 1.80 g (42% over 3 steps). Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07–6.80 (m, 4H), 4.26–4.17 (m, 1H), 3.55–3.47 (m, 1H), 3.43–3.35 (m, 1H), 2.96 (s, 3H), 1.79–1.47 (m, 7H), 1.33–1.05 (m, 3H), 1.00–0.73 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8 (d, *J* = 304.8 Hz), 139.2 (d, *J* = 10.3 Hz), 124.6 (d, *J* = 4.2 Hz), 121.0 (d, *J* = 9.8 Hz), 119.2 (d, *J* = 4.5 Hz), 116.5 (d, *J* = 26.5 Hz), 62.4 (d, *J* = 7.3 Hz), 59.2 (d, *J* = 2.3 Hz), 43.8, 41.3, 34.9, 34.2, 32.1, 26.9, 26.5, 26.2.

FT-IR (neat) 2923, 2852, 1614, 1505, 1448, 1230, 746 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{23}ClFN$: 283.2, found: 283.1.



***N*-(2-Chloropropyl)-*N*-methylnaphthalen-2-amine.** Synthesized from 2-naphthylamine (2.00 g, 14.0 mmol) and 2-chloropropionyl chloride (1.38 mL, 14.0 mmol). Purified by chromatography (0%→100% Et_2O/hexanes): 1.82 g (55% over 3 steps). White solid.

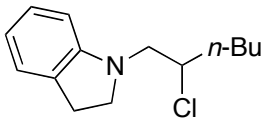
mp 153 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.62 (m, 3H), 7.40–7.34 (m, 1H), 7.25–7.18 (m, 1H), 7.13–7.09 (m, 1H), 6.90–6.87 (m, 1H), 4.33 (sextet, 1H, *J* = 6.8 Hz), 3.76 (dd, 1H, *J* = 6.6, 15.2 Hz), 3.61 (dd, 1H, *J* = 7.3, 15.2 Hz), 3.15 (s, 3H), 1.55 (d, 3H, *J* = 6.6 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 135.4, 128.8, 127.6, 126.5, 126.3, 126.2, 121.8, 116.1, 105.5, 59.9, 55.2, 39.8, 23.8.

FT-IR (neat) 2924, 2855, 1629, 1512, 824, 743 cm^{-1}.

MS (APCI + ESI) *m*/*z* (M^+) calcd for $C_{14}H_{16}ClN$: 233.1, found: 233.1.



1-(2-Chlorohexyl)indoline. Synthesized from indoline (1.12 mL, 10.0 mmol) and 2-chlorohexanoyl chloride (1.69 g, 10.0 mmol). Purified by chromatography (0%→50% Et_2O/hexanes): 1.09 g (46% over 2 steps). Clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11–7.04 (m, 2H), 6.70–6.64 (m, 1H), 6.48–6.44 (m, 1H), 4.13–4.04 (m, 1H), 3.52–3.45 (m, 2H), 3.35 (dd, 1H, *J* = 6.6, 14.3 Hz), 3.29 (dd, 1H, *J* = 6.6, 14.3 Hz), 3.05–3.00 (m, 2H), 1.99–1.88 (m, 1H), 1.77–1.55 (m, 2H), 1.50–1.22 (m, 3H), 0.93 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 129.5, 127.5, 124.7, 117.9, 106.5, 61.6, 57.6, 54.7, 35.9, 28.9, 28.8, 22.5, 14.2.

FT-IR (neat) 2956, 2930, 2859, 1607, 1489, 1267, 743 cm^{-1}.

MS (APCI + ESI) *m*/*z* (M^+) calcd for $C_{14}H_{20}ClN$: 237.1, found: 237.1.

III. Stereoconvergent Suzuki Cross-Coupling Reactions

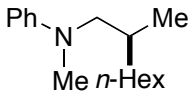
General procedure (conducted in a glovebox; however, see the note below). The trialkylborane was prepared by adding 9-BBN dimer (440 mg, 1.80 mmol), *i*-Pr_2O (1.0 mL), and the alkene (3.60 mmol) in turn to a 4-mL vial. The vial was capped and removed from the glovebox. The reaction mixture was stirred at 60 °C for 1 h, and then it was allowed to cool to r.t. The vial was taken back into the glovebox, and the reaction mixture was diluted with *i*-Pr_2O to furnish a 1.5 M solution. Next, a portion of this solution (0.9 mL, 1.35 mmol) was added to a solution of KO*t*-Bu (101 mg, 0.900 mmol) in *n*-hexanol (188 μL, 1.50 mmol) in a 4-mL vial. The resulting mixture was stirred at r.t. for 30 min.

A solution of $NiBr_2$·diglyme (26.7 mg, 0.075 mmol) and (1*R*,2*R*)-N^1,N^2-dimethyl-1,2-di(naphthalen-1-yl)ethane-1,2-diamine (30.8 mg, 0.090 mmol) in *i*-Pr_2O (5.5 mL) in a 20-mL vial was stirred at r.t. for 30 min. Next, the electrophile (0.75 mmol) was added, along with an *i*-Pr_2O rinsing (0.5 mL), and then the solution of the activated trialkylborane was added dropwise over 2 min. The reaction mixture was stirred at r.t. for 40 h, and then it was filtered through silica gel, eluting with Et_2O (20 mL). The solvent was removed by rotary evaporation, and the

residue was diluted with hexanes (10 mL). The resulting solution was filtered through an acrodisc and then concentrated by rotary evaporation.

A second run was performed with the (1*S*,2*S*) enantiomer of ligand **1**.

Note: For the sake of convenience, the stereoconvergent Suzuki cross-couplings described in Table 1 were conducted in a glovebox. However, this method does *not* require the use of a glovebox. When carried out without a glovebox, the coupling illustrated in entry 1 of Table 1 proceeded in 88% ee and 82% yield.



(*S*)-*N*-Methyl-*N*-(2-methyloctyl)aniline (Table 1, entry 1). *N*-(2-Chloropropyl)-*N*-methylaniline (138 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-hexene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Clear oil. First run: 146 mg (83%, 88% ee). Second run (6 mmol scale): 1.20 g (86%, 88% ee).

The ee was determined by HPLC on an OJ-H column (hexanes, 1.0 mL/min) with t_r = 9.0 min (minor), 9.7 min (major).

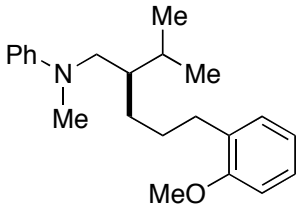
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.19 (m, 2H), 6.70–6.63 (m, 3H), 3.21 (dd, 1H, *J* = 6.6, 14.5 Hz), 3.02 (dd, 1H, *J* = 8.1, 14.5 Hz), 2.95 (s, 3H), 1.98–1.82 (m, 1H), 1.44–1.04 (m, 10H), 0.92–0.83 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 129.3, 115.7, 112.0, 60.1, 39.7, 35.0, 32.5, 32.1, 29.9, 27.3, 22.9, 18.0, 14.3.

FT-IR (neat) 2956, 2926, 2856, 1729, 1600, 1507, 1465, 992, 746, 691 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{16}H_{27}N$: 233.2, found: 233.2.

$[\alpha]^{23}_D$ = +7.3° (c 0.0075, $CHCl_3$).



***N*-(2-Isopropyl-5-(2-methoxyphenyl)pentyl)-*N*-methylaniline (Table 1, entry 2).** *N*-(2-Chloro-3-methylbutyl)-*N*-methylaniline (155 mg, 0.73 mmol) and a solution of the reagent prepared by hydroboration of 2-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.32 mmol) were used with $NiBr_2$·diglyme (51.6 mg, 0.146 mmol) and (1*R*,1*R*)-N^1,N^2-dimethyl-1,2-di(naphthalen-1-yl)ethane-1,2-diamine (59.8 mg, 0.176 mmol). The product was purified by flash chromatography on reverse-phase silica gel (10%

acetonitrile/water→acetonitrile). Yellow oil. First run: 126 mg (53%, 95% ee). Second run: 123 mg (52%, 98% ee).

The ee was determined by SFC on an OJ-H column (5% MeOH/CO_2(*l*), 3.0 mL/min, 100 bar) with t_r = 10.6 min (minor), 12.7 min (major).

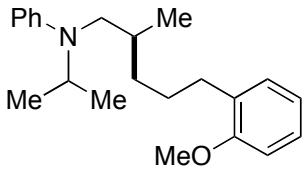
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.12 (m, 4H), 6.92–6.85 (m, 2H), 6.73–6.68 (m, 3H), 3.83 (s, 3H), 3.28 (dd, 1H, *J* = 7.2, 14.8 Hz), 3.20 (dd, 1H, *J* = 7.4, 14.6 Hz), 2.93 (s, 3H), 2.64–2.60 (m, 2H), 1.89–1.76 (m, 2H), 1.70–1.61 (m, 2H), 1.47–1.39 (m, 1H), 1.35–1.25 (m, 1H), 0.95 (d, 3H, *J* = 6.8 Hz), 0.93 (d, 3H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 149.9, 130.1, 129.7, 129.0, 126.8, 120.3, 115.5, 111.9, 110.1, 55.2, 54.5, 41.9, 39.3, 30.7, 28.3, 27.9, 27.6, 19.5, 18.3.

FT-IR (neat) 2955, 2361, 1600, 1507, 1465, 1359, 1242, 1128, 1051, 1033, 992, 929, 858, 749, 692 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{22}H_{31}NO$: 325, found: 325.

$[\alpha]^{24}_D$ = +8.6° (c 0.0095, CH_2Cl_2).



(*S*)-*N*-Isopropyl-N-(5-(2-methoxyphenyl)-2-methylpentyl)aniline (Table 1, entry 3). *N*-(2-Chloropropyl)-*N*-isopropylaniline (158 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 2-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 167 mg (69%, 81% ee). Second run: 182 mg (75%, 82% ee).

The ee was determined by HPLC on an OD-H column (100% hexanes, 1.0 mL/min) with t_r = 20.6 min (major), 23.8 min (minor).

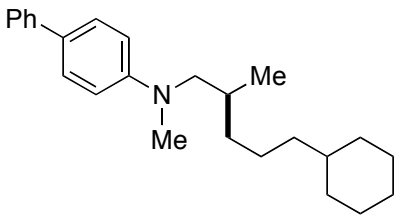
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21–7.08 (m, 4H), 6.88–6.80 (m, 4H), 6.70 (t, 1H, *J* = 7.2 Hz), 3.97 (septet, 1H, *J* = 6.8 Hz), 3.79 (s, 3H), 2.96 (dd, 1H, *J* = 6.2, 14.2 Hz), 2.75 (dd, 1H, *J* = 8.0, 14.4 Hz), 2.65–2.63 (m, 2H), 1.81–1.79 (m, 2H), 1.66–1.51 (m, 2H), 1.21–1.19 (m, 1H), 1.13 (d, 3H, *J* = 6.4 Hz), 1.09 (d, 3H, *J* = 6.8 Hz), 0.85 (d, 3H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 149.8, 131.1, 129.8, 128.7, 126.8, 120.2, 117.1, 116.3, 110.1, 55.1, 51.9, 49.9, 34.9, 30.7, 30.5, 27.3, 20.3, 19.8, 17.9.

FT-IR (neat) 2930, 1599, 1496, 1464, 1362, 1290, 1243, 1195, 1126, 1051, 1032, 752, 696 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{22}H_{31}NO$: 325 found: 325.

$[\alpha]^{24}_D$ = –33° (c 0.011, CH_2Cl_2; from (1*S*,2*S*)-**1**).



(*S*)-*N*-(5-Cyclohexyl-2-methylpentyl)-*N*-methylbiphenyl-4-amine (Table 1, entry 4). *N*-(2-Chloropropyl)-*N*-methylbiphenyl-4-amine (195 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of allylcyclohexane with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 184 mg (70%, 85% ee). Second run: 172 mg (66%, 85% ee).

The ee was determined by HPLC on an OJ-H column (1% isopropanol/hexanes, 1.0 mL/min) with t_r = 19.3 min (minor), 23.8 min (major).

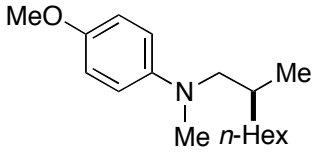
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.54 (m, 2H), 7.52–7.47 (m, 2H), 7.42–7.36 (m, 2H), 7.27–7.22 (m, 1H), 6.77–6.72 (m, 2H), 3.27 (dd, 1H, *J* = 6.6, 14.6 Hz), 3.07 (dd, 1H, *J* = 8.1, 14.6 Hz), 3.01 (s, 3H), 2.00–1.90 (m, 1H), 1.74–1.53 (m, 4H), 1.47–1.06 (m, 10H), 0.92 (d, 3H, *J* = 6.8 Hz), 0.94–0.80 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 141.5, 128.8, 128.4, 127.9, 126.4, 126.0, 112.1, 60.0, 39.8, 38.1, 37.9, 35.2, 33.8, 33.6, 32.5, 31.1, 27.0, 26.7, 24.5, 18.0.

FT-IR (neat) 2922, 2850, 1612, 1525, 1490, 1200, 816, 761, 696 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{25}H_{35}N$: 349.3, found: 349.3.

$[\alpha]^{23}_D$ = +7.6° (c 0.0060, $CHCl_3$).



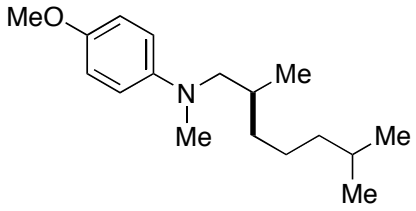
(*S*)-4-Methoxy-*N*-methyl-*N*-(2-methyloctyl)aniline (Table 1, entry 5). *N*-(2-Chloropropyl)-4-methoxy-*N*-methylaniline (160 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-hexene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 152 mg (77%, 88% ee). Second run: 148 mg (75%, 86% ee).

The ee was determined by HPLC on an OJ-H column (1% isopropanol/hexanes, 1.0 mL/min) with t_r = 7.4 min (major), 8.3 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86–6.80 (m, 2H), 6.69–6.62 (m, 2H), 3.76 (s, 3H), 3.11 (dd, 1H, *J* = 6.6, 14.3 Hz), 2.93 (dd, 1H, *J* = 8.1, 14.3 Hz), 2.87 (s, 3H), 1.91–1.78 (m, 1H), 1.44–1.00 (m, 10H), 0.91–0.84 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 145.3, 114.9, 113.9, 61.3, 56.1, 40.1, 35.0, 32.5, 32.1, 29.9, 27.3, 22.9, 18.1, 14.4.

FT-IR (neat) 2955, 2926, 2855, 1513, 1464, 1244, 1181, 1043, 811 cm^{-1}.
MS (EI) *m*/*z* (M^+) calcd for $C_{17}H_{29}NO$: 263.2, found: 263.2.
$[\alpha]^{23}_D$ = +4.4° (c 0.0051, $CHCl_3$).



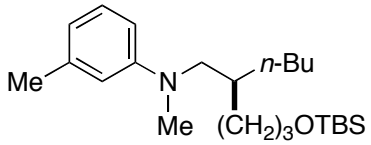
(*S*)-*N*-(2,6-Dimethylheptyl)-4-methoxy-N-methylaniline (Table 1, entry 6). *N*-(2-Chloropropyl)-4-methoxy-*N*-methylaniline (160 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-methylpent-1-ene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 150 mg (76%, 84% ee). Second run: 155 mg (79%, 85% ee).

The ee was determined by SFC on an OD-H column (2.5% MeOH/CO_2(*l*), 3.0 mL/min, 100 bar) with t_r = 5.7 min (minor), 6.0 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86–6.80 (m, 2H), 6.69–6.63 (m, 2H), 3.76 (s, 3H), 3.10 (dd, 1H, *J* = 6.8, 14.4 Hz), 2.93 (dd, 1H, *J* = 8.0, 14.4 Hz), 2.87 (s, 3H), 1.90–1.80 (m, 1H), 1.58–1.46 (m, 1H), 1.42–1.31 (m, 2H), 1.31–1.19 (m, 1H), 1.18–1.01 (m, 3H), 0.91–0.84 (m, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 145.3, 115.0, 113.9, 61.3, 56.1, 40.1, 39.6, 35.2, 32.3, 28.2, 25.0, 23.0, 22.8, 18.1.

FT-IR (neat) 2954, 2928, 2868, 1514, 1244, 1181, 1043, 811, 700 cm^{-1}.
MS (APCI + ESI) *m*/*z* (M^+) calcd for $C_{17}H_{29}NO$: 263.2, found: 263.1.
$[\alpha]^{23}_D$ = +4.3° (c 0.0080, $CHCl_3$).



(*S*)-*N*-(2-(3-(tert-Butyldimethylsilyloxy)propyl)hexyl)-*N*,3-dimethylaniline (Table 1, entry 7). *N*-(2-Chlorohexyl)-*N*,3-dimethylaniline (180 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of allyloxy(*tert*-butyl)dimethylsilane with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 166 mg (59%, 90% ee). Second run: 191 mg (67%, 92% ee).

The ee was determined by HPLC of the corresponding desilylated alcohol[3] on an OJ-H column (1% isopropanol/hexanes, 1.0 mL/min) with t_r = 21.5 min (major), 23.0 min (minor).

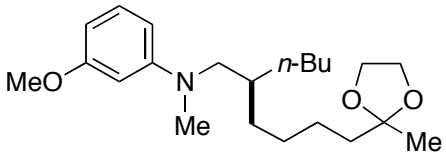
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11–7.07 (m, 1H), 6.48–6.47 (m, 3H), 3.56 (t, 2H, *J* = 6.6 Hz), 3.15–3.12 (m, 2H), 2.90 (s, 3H), 2.29 (s, 3H), 1.80 (br s, 1H), 1.54–1.52 (m, 2H), 1.28–1.27 (m, 8H), 0.87 (s, 12 H), 0.02 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 138.6, 128.9, 116.6, 112.6, 109.2, 63.6, 57.6, 39.5, 36.4, 31.3, 29.8, 28.7, 27.6, 26.0, 23.2, 22.0, 18.3, 14.1, –5.3.

FT-IR (neat) 2928, 1602, 1499, 1255, 1099, 835, 774, 692 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{23}H_{43}NOSi$: 377, found: 377.

$[\alpha]^{24}_D$ = –7.9° (c 0.011, CH_2Cl_2; from (1*S*,2*S*)-**1**).



(*S*)-*N*-(2-Butyl-6-(2-methyl-1,3-dioxolan-2-yl)hexyl)-3-methoxy-*N*-methylaniline (Table 1, entry 8). *N*-(2-Chlorohexyl)-3-methoxy-*N*-methylaniline (180 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 2-(but-3-enyl)-2-methyl-1,3-dioxolane with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 229 mg (85%, 94% ee). Second run: 238 mg (88%, 93% ee).

The ee was determined by SFC on an OD-H column (5% MeOH/CO_2(*l*)→20% MeOH/CO_2(*l*), 3.0 mL/min, 100 bar) with t_r = 7.2 min (minor), 8.8 min (major).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, 1H, *J* = 8.2 Hz), 6.29–6.26 (m, 1H), 6.23–6.18 (m, 2H), 3.91–3.89 (m, 4H), 3.77 (s, 3H), 3.12 (d, 2H, *J* = 7.6 Hz), 2.90 (s, 3H), 1.80 (br s, 1H), 1.62–1.59 (m, 2H), 1.28–1.25 (m, 15H), 0.86 (m, 3H).

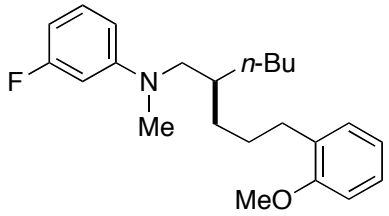
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 151.1, 129.6, 110.1, 105.1, 100.4, 98.3, 64.6, 57.6, 55.0, 39.6, 39.2, 36.6, 31.6, 31.3, 28.7, 26.8, 24.6, 23.7, 23.2, 14.1.

FT-IR (neat) 2930, 1611, 1502, 1378, 1244, 1169, 1057, 948, 828, 750, 688 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{22}H_{37}NO_3$: 363, found: 363.

$[\alpha]^{23}_D$ = –4.6° (c 0.011, CH_2Cl_2; from (1*S*,2*S*)-**1**).

(3) The silyl ether was treated with TBAF in THF (1 M; 5 equiv) and stirred for 2 h at room temperature.



(*S*)-3-Fluoro-*N*-(2-(3-(2-methoxyphenyl)propyl)hexyl)-*N*-methylaniline (Table 1, entry 9). *N*-(2-Chlorohexyl)-3-fluoro-*N*-methylaniline (180 mg, 0.74 mmol) and a solution of the reagent prepared by hydroboration of 2-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 183 mg (69%, 92% ee). Second run: 187 mg (71%, 92% ee).

The ee was determined by SFC on an OJ column (gradient 5%→20% MeOH/CO_2(*l*), 3.0 mL/min, 100 bar) with t_r = 5.9 min (minor), 6.9 min (major).

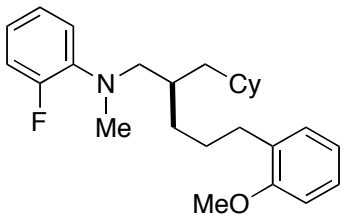
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.14 (m, 3H), 6.93 (t, 1H, *J* = 7.4 Hz), 6.88 (d, 1H, *J* = 8.0 Hz), 6.46–6.37 (m, 3H), 3.84 (s, 3H), 3.20 (d, 2H, *J* = 7.2 Hz), 2.94 (s, 3H), 2.64 (t, 2H, *J* = 7.8 Hz), 1.90 (br s, 1H), 1.72–1.59 (m, 3H), 1.47–1.33 (m, 7H), 0.94 (t, 3H, *J* = 6.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1 (d, *J* = 240 Hz), 157.4, 151.3 (d, *J* = 11 Hz), 130.8, 129.9 (d, *J* = 10 Hz), 129.7 (d, *J* = 11 Hz), 126.9, 120.3, 110.1, 107.3 (d, *J* = 2 Hz), 101.8 (d, *J* = 21 Hz), 98.5 (d, *J* = 25 Hz), 57.3, 55.1 (d, *J* = 4 Hz), 39.4, 36.2, 31.4, 31.2, 30.7, 28.6, 26.6, 23.1, 14.1.

FT-IR (neat) 2929, 1620, 1579, 1504, 1465, 1360, 1290, 1243, 1158, 1128, 1051, 1032, 1010, 910, 821, 752, 683, 649 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{23}H_{32}FNO$: 357, found: 357.

$[\alpha]^{24}_D$ = +6.3° (c 0.010, CH_2Cl_2).



(*R*)-*N*-(2-(Cyclohexylmethyl)-5-(2-methoxyphenyl)pentyl)-2-fluoro-*N*-methylaniline (Table 1, entry 10). *N*-(2-Chloro-3-cyclohexylpropyl)-2-fluoro-*N*-methylaniline (215 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 2-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 242 mg (80%, 72% ee). Second run: 252 mg (84%, 70% ee).

The ee was determined by SFC on an OJ column (gradient 5%→20% MeOH/CO_2(*l*), 3.0 mL/min, 100 bar) with t_r = 6.8 min (minor), 7.4 min (major).

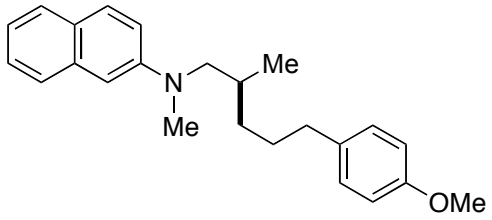
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.13 (m, 2H), 7.05–6.97 (m, 2H), 6.94–6.89 (m, 2H), 6.87–6.80 (m, 2H), 3.82 (s, 3H), 3.05–2.95 (m, 2H), 2.83 (s, 3H), 2.59 (t, 2H, *J* = 7.6 Hz), 1.90–1.84 (m, 1H), 1.69–1.50 (m, 7H), 1.44–1.10 (m, 8H), 0.92–0.77 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 155.2 (d, *J* = 243 Hz), 140.7 (d, *J* = 8 Hz), 131.1, 129.7, 126.8, 124.1 (d, *J* = 3 Hz), 120.4 (d, *J* = 8 Hz), 120.3 (d, *J* = 7 Hz), 119.2 (d, *J* = 4 Hz), 116.1 (d, *J* = 21 Hz), 110.1, 59.6 (d, *J* = 4 Hz), 55.1, 40.4 (d, *J* = 2 Hz), 40.2, 34.9, 34.1, 33.5, 32.7, 32.2, 30.6, 26.7, 26.4.

FT-IR (neat) 2922, 1612, 1503, 1450, 1290, 1242, 1116, 1033, 909, 823, 749, 649 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{26}H_{36}FNO$: 397, found: 397.

$[\alpha]^{24}_D$ = +5.8° (c 0.0115, CH_2Cl_2).



(*S*)-*N*-(5-(4-Methoxyphenyl)-2-methylpentyl)-*N*-methylnaphthalen-2-amine (Table 1, entry 11). *N*-(2-Chloropropyl)-*N*-methylnaphthalen-2-amine (176 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 4-allylanisole with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 180 mg (69%, 83% ee). Second run: 185 mg (71%, 83% ee).

The ee was determined by HPLC on an OD-H column (1% isopropanol/hexanes, 1.0 mL/min) with t_r = 17.1 min (major), 18.6 min (minor).

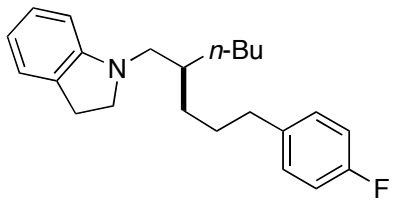
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.58 (m, 3H), 7.36–7.29 (m, 1H), 7.18–7.02 (m, 4H), 6.84–6.76 (m, 3H), 3.76 (s, 3H), 3.29 (dd, 1H, *J* = 6.8, 14.6 Hz), 3.14 (dd, 1H, *J* = 8.0, 14.6 Hz), 3.01 (s, 3H), 2.56–2.46 (m, 2H), 2.03–1.91 (m, 1H), 1.90–1.34 (m, 3H), 1.21–1.10 (m, 1H), 0.90 (d, 3H, *J* = 6.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 147.8, 135.4, 134.8, 129.4, 128.8, 127.6, 126.5, 126.3, 126.2, 121.8, 116.1, 113.9, 113.7, 105.5, 59.9, 55.4, 39.8, 35.4, 34.4, 32.4, 31.1, 29.4, 17.9.

FT-IR (neat) 2929, 2857, 1628, 1600, 1512, 1245, 1177, 1036, 823, 744 cm^{-1}.

MS (EI) *m*/*z* (M^+) calcd for $C_{24}H_{29}NO$: 347.2, found: 347.2.

$[\alpha]^{23}_D$ = +11.9° (c 0.0072, $CHCl_3$).



(*S*)-1-(2-(3-(4-Fluorophenyl)propyl)hexyl)indoline (Table 1, entry 12). 1-(2-Chlorohexyl)indoline (180 mg, 0.75 mmol) and a solution of the reagent prepared by hydroboration of 1-allyl-4-fluorobenzene with 9-BBN dimer (1.5 M solution in *i*-Pr_2O; 0.90 mL, 1.35 mmol) were used. The product was purified by flash chromatography on reverse-phase silica gel (10% acetonitrile/water→acetonitrile). Yellow oil. First run: 154 mg (55%, 90% ee). Second run: 152 mg (59%, 93% ee).

The ee was determined by SFC on an OJ column (gradient 5%→20% MeOH/CO_2(*l*), 3.0 mL/min, 100 bar) with t_r = 7.3 min (major), 7.8 min (minor).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–7.09 (m, 2H), 7.08–7.02 (m, 2H), 6.99–6.92 (m, 2H), 6.62 (t, 1H, *J* = 7.3 Hz), 6.41 (d, 1H, *J* = 7.7 Hz), 3.36–3.25 (m, 2H), 2.95 (t, 2H, *J* = 8.4 Hz), 2.88 (d, 2H, *J* = 7.2 Hz), 2.58 (t, 2H, *J* = 7.7 Hz), 1.76–1.57 (m, 3H), 1.49–1.23 (m, 8H), 0.90 (t, 3H, *J* = 6.8 Hz).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, *J* = 243.0 Hz), 153.6, 138.4 (d, *J* = 3.2 Hz), 129.9 (d, *J* = 7.6 Hz), 129.8, 127.5, 124.5, 117.2, 115.1 (d, *J* = 21.0 Hz), 106.5, 54.7, 54.4, 37.1, 35.7, 31.8, 31.7, 29.1, 28.9, 28.8, 23.4, 14.3.

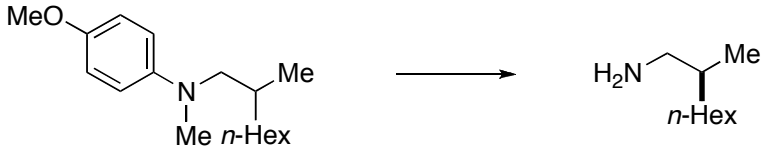
FT-IR (neat) 2928, 2857, 1607, 1510, 1489, 1460, 1221, 1156, 832, 743, 714 cm^{-1}.

MS (APCI + ESI) *m*/*z* (M^+) calcd for $C_{23}H_{30}FN$: 339.2, found: 339.1.

$[\alpha]^{23}_D$ = +0.97° (c 0.0071, $CHCl_3$).

IV. Assignment of Absolute Stereochemistry

These procedures have not been optimized.



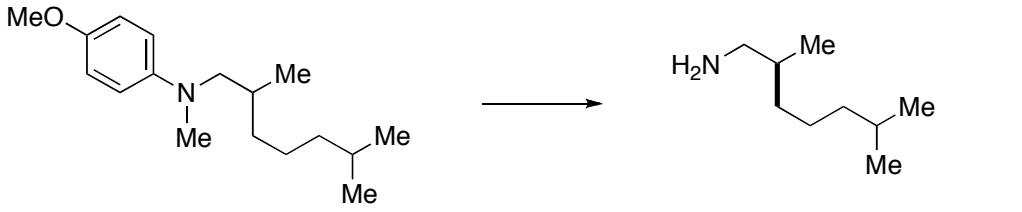
88% ee, from (1*R*,1*R*)-**1**

$[\alpha]^{21}_D$ = –9.0°

$[\alpha]^{21}_D$ = –8.4°; >95% ee (lit.)

(*S*)-2-Methyloctan-1-amine (derived from the product of Table 1, entry 5). Anhydrous calcium oxide (476 mg, 8.5 mmol) was added to a solution of 4-methoxy-*N*-methyl-*N*-(2-methyloctyl)aniline (150 mg, 0.57 mmol) in a mixture of THF (anhydrous; 3.2 mL) and MeOH (anhydrous; 2.4 mL) in a 20-mL vial. The mixture was cooled to 0 °C, and a solution of iodine (635 mg, 2.5 mmol) in THF (1 mL) was added. The reaction mixture was stirred at 0 °C for 3.5 h. Next, it was diluted with CH_2Cl_2 (20 mL), and the reaction was quenched by the addition of aqueous sodium thiosulfate (15%; 50 mL). The organic layer was separated and then washed

with water (20 mL) and brine (10 mL), dried over Na_2SO_4, and concentrated by rotary evaporation to give a dark-brown oil. The oil was dissolved in a mixture of acetonitrile (0.8 mL) and water (0.8 mL), and then trichloroisocyanuric acid (116 mg, 0.50 mmol) was added in a single portion, followed by aqueous HCl (2 M; 1 mL). The reaction mixture was stirred at r.t. for 4 h, and then the acetonitrile was removed by rotary evaporation. The product was extracted into CH_2Cl_2, and the solution was concentrated on a rotary evaporator. The product was purified by Kugelrohr distillation (oven temperature: 90 °C; 9 torr), which provided the product as a colorless oil (34 mg, 42%). The absolute stereochemistry was determined to be (*S*) by comparison with a reported optical rotation.[4]



84% ee, from (1*R*,1*R*)-**1**

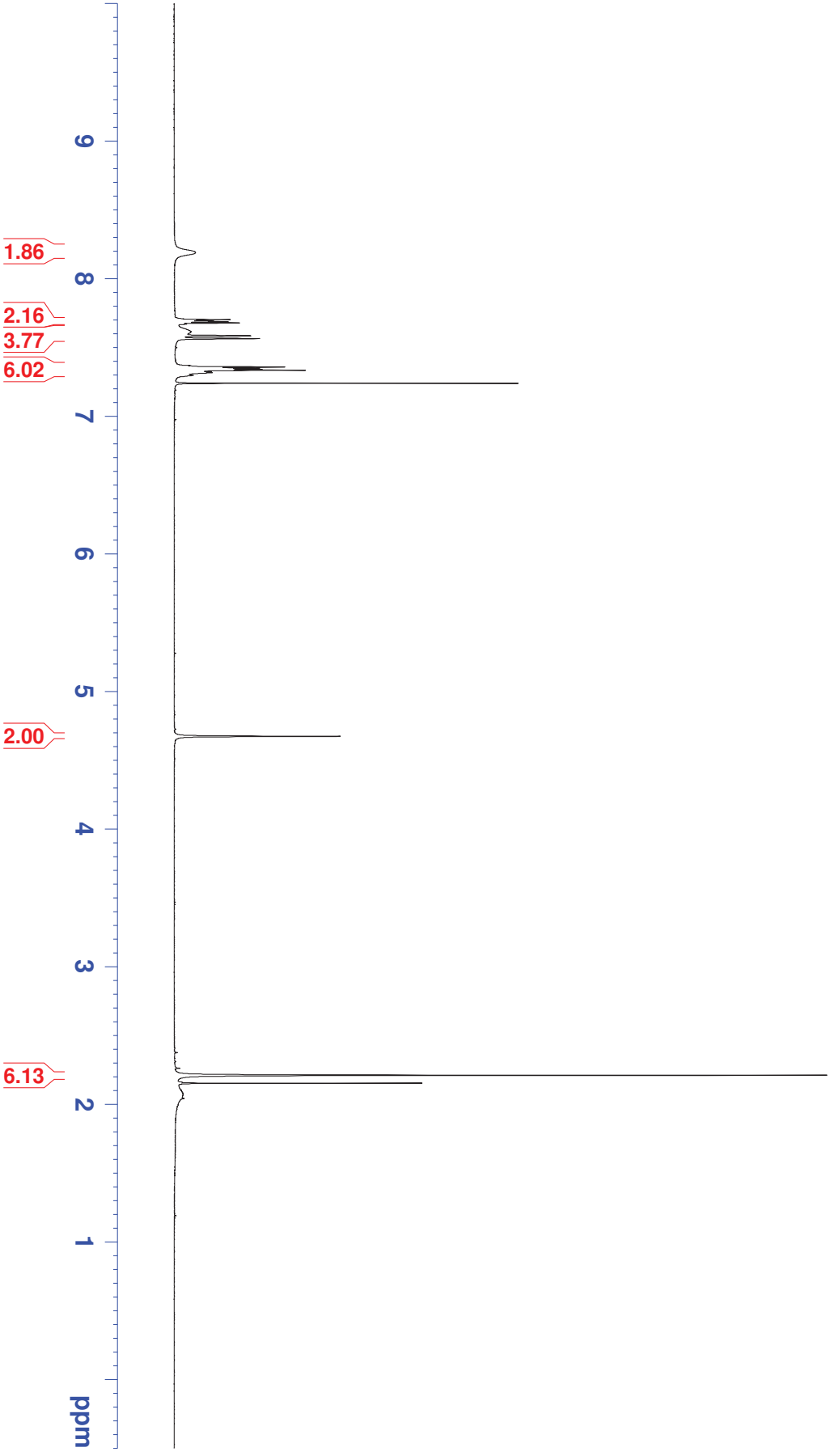
$[\alpha]^{21}_D = -7.4°$

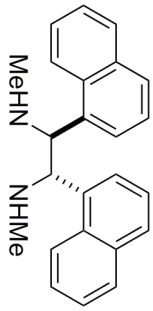
$[\alpha]^{21}_D = -10.6°$; >95% ee (lit.)

(*S*)-2,6-Dimethylheptan-1-amine (derived from the product of Table 1, entry 6). The same conditions employed for the synthesis of (*S*)-2-methyloctan-1-amine were used, except with *N*-(2,6-dimethylheptyl)-4-methoxy-*N*-methylaniline (150 mg, 0.57 mmol) as the starting material. Yield (unoptimized): 31 mg, 38%. The absolute stereochemistry of the cross-coupling product obtained with ligand (1*R*,1*R*)-**1** was determined to be (*S*) by comparison with a reported optical rotation.[4]

(4) Enders, D.; Schubert, H. *Angew. Chem Int. Ed. Engl.* **1984**, *23*, 365–366.

V. ^{1}H NMR Spectra





(S,S)-1

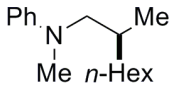
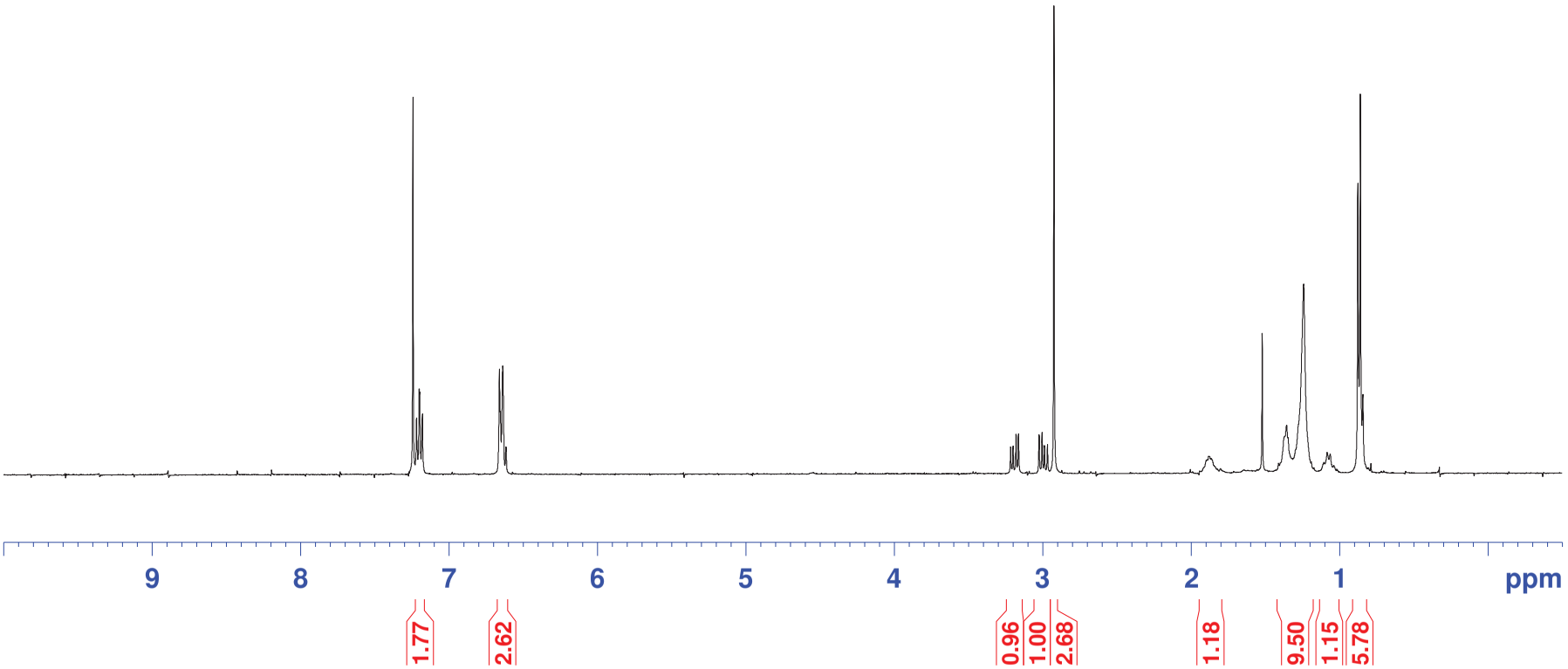


Table 1, entry 1



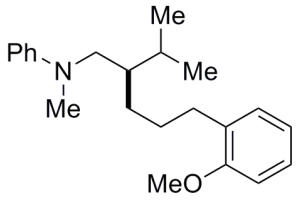
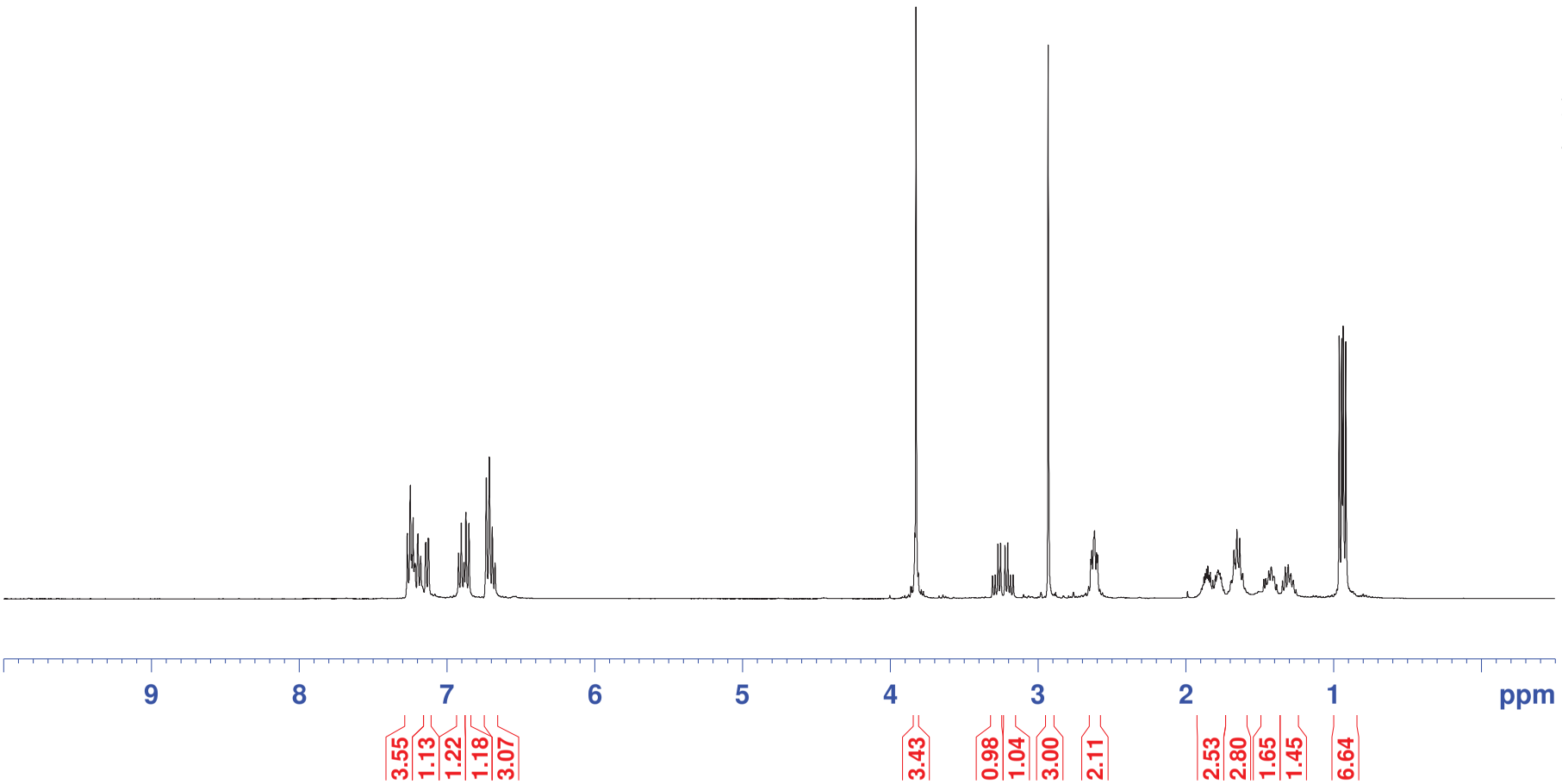


Table 1, entry 2



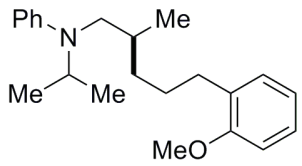
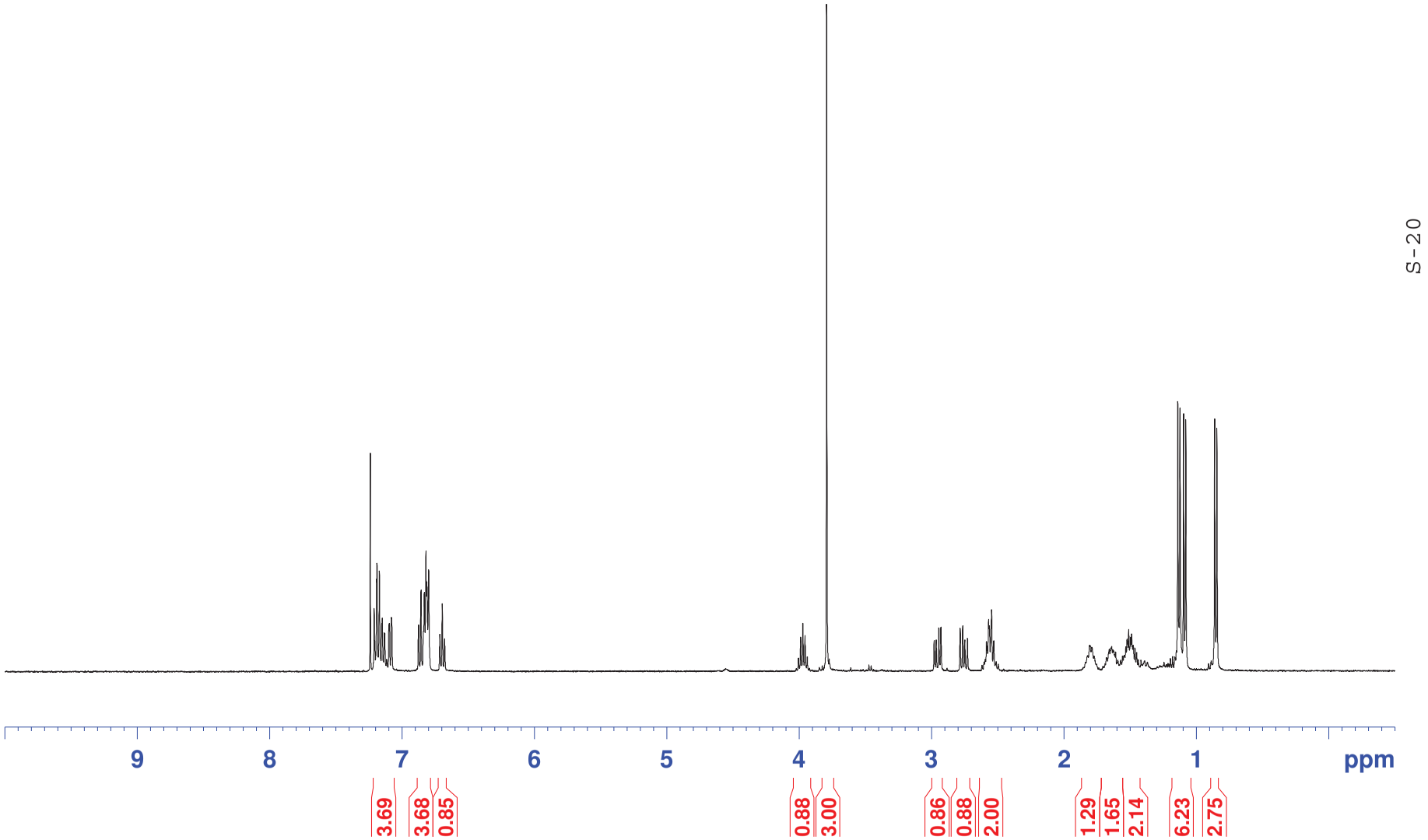


Table 1, entry 3



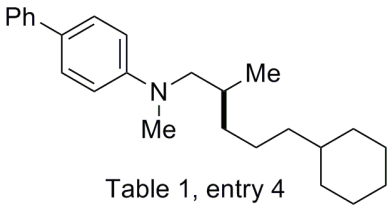
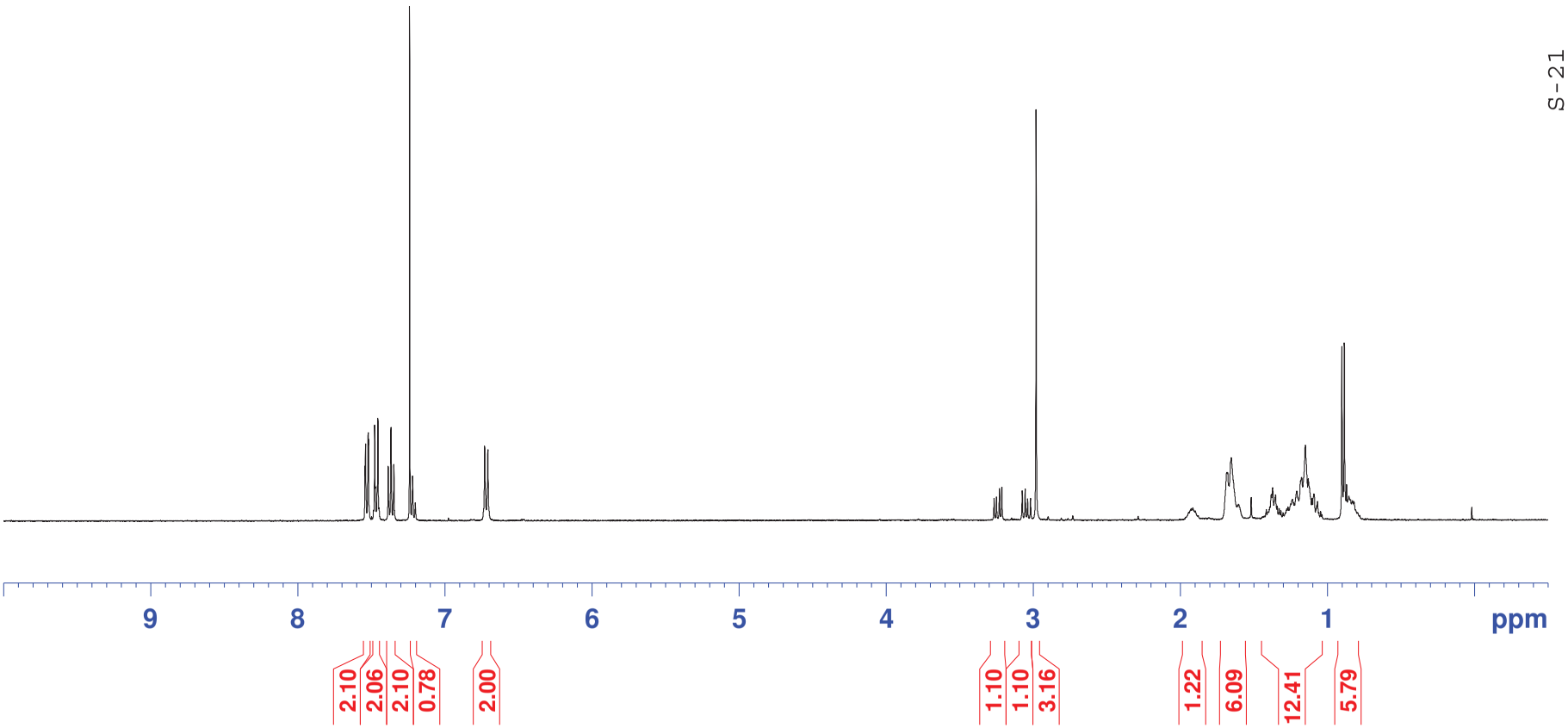


Table 1, entry 4



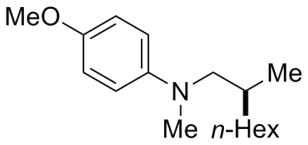
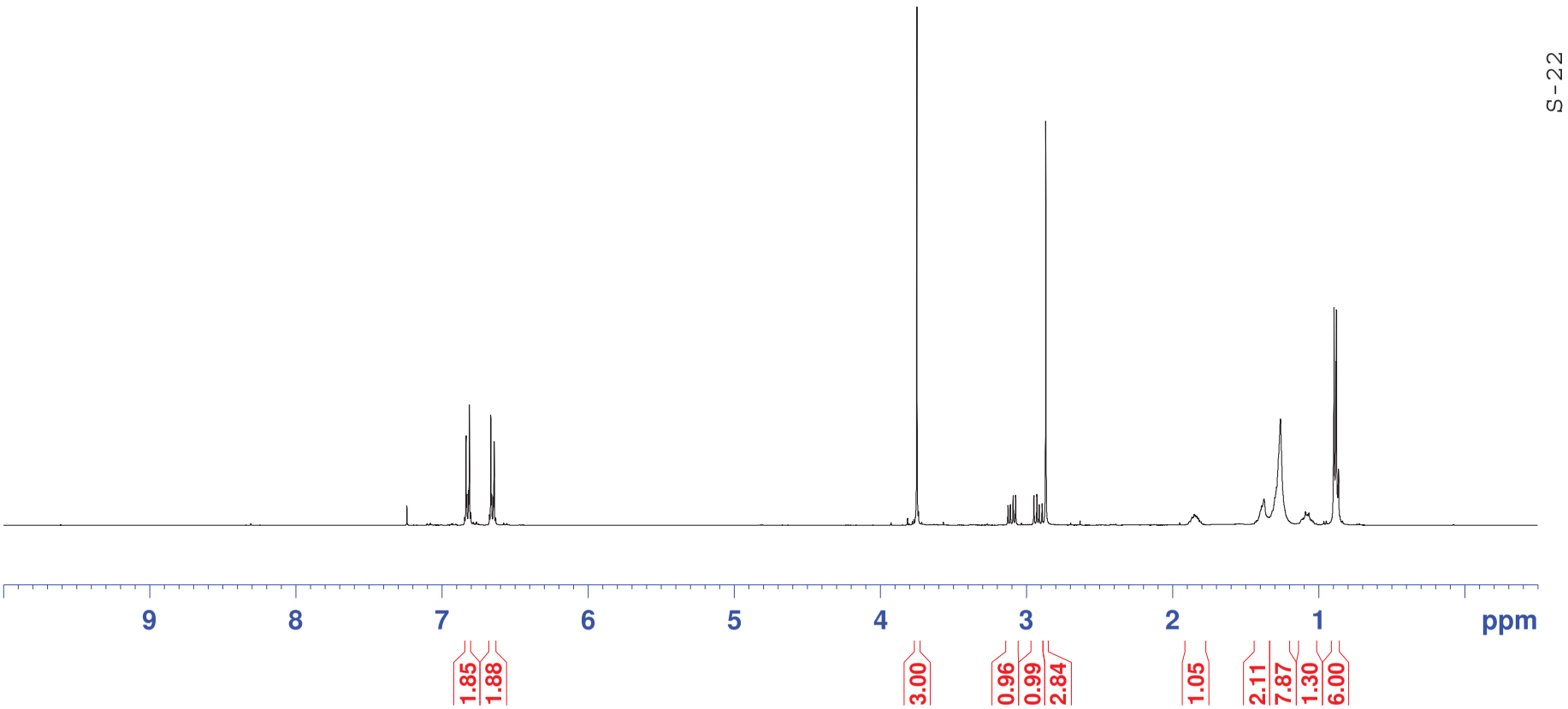


Table 1, entry 5



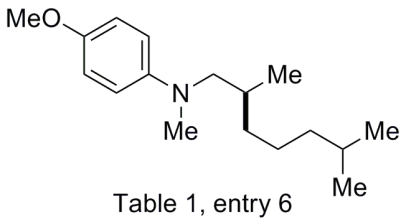
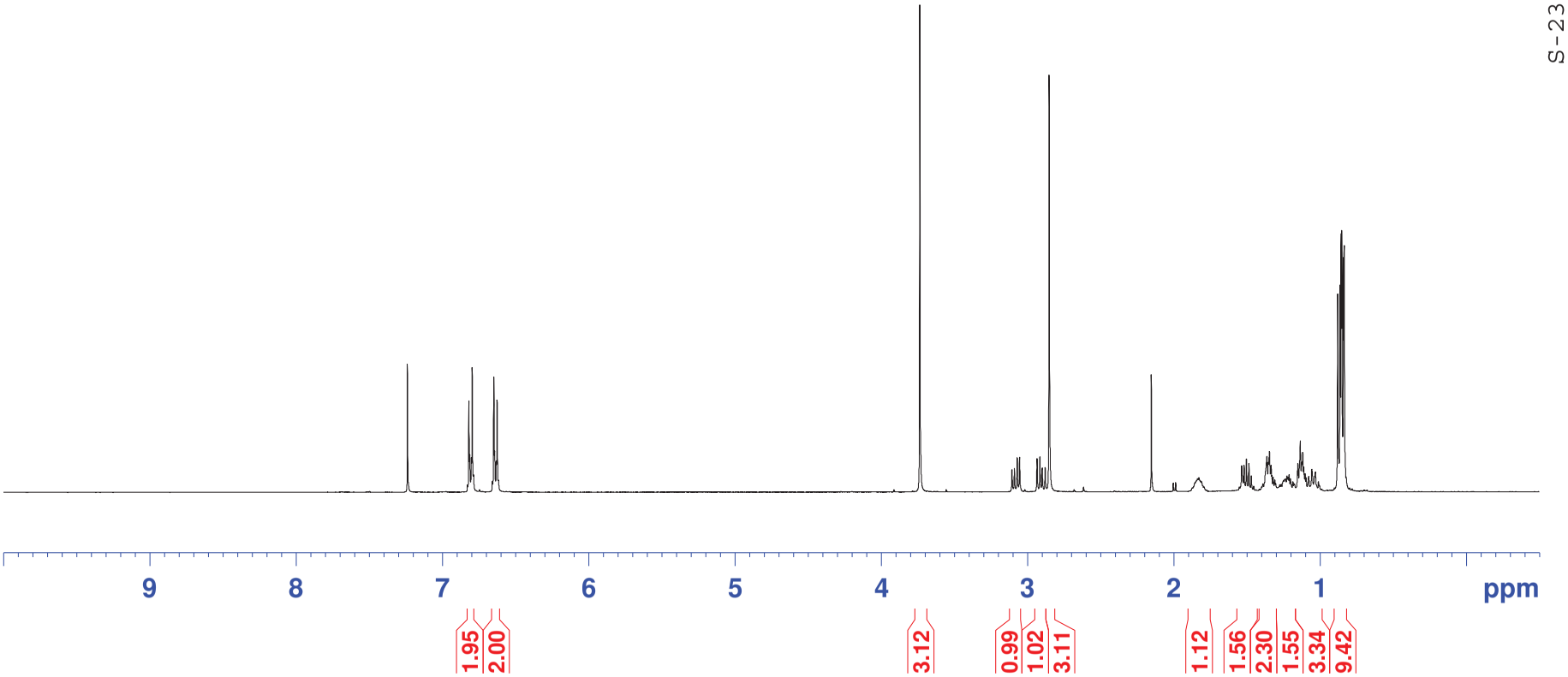


Table 1, entry 6



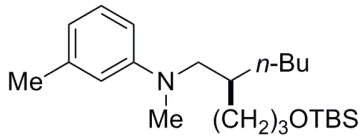
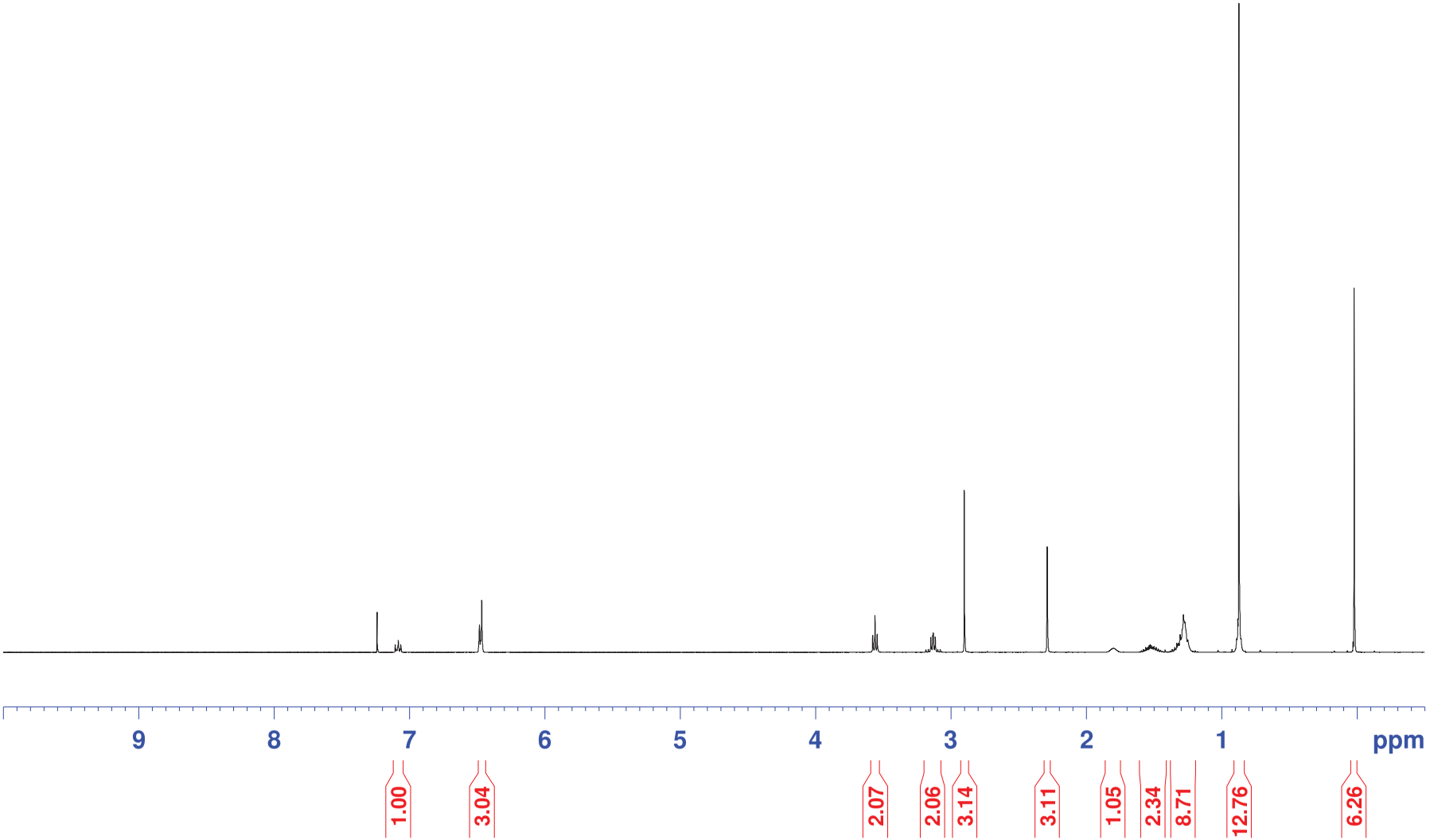


Table 1, entry 7



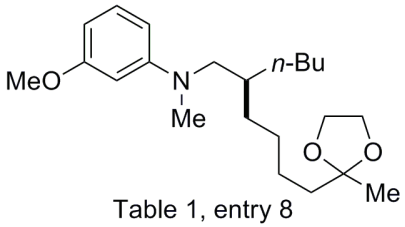
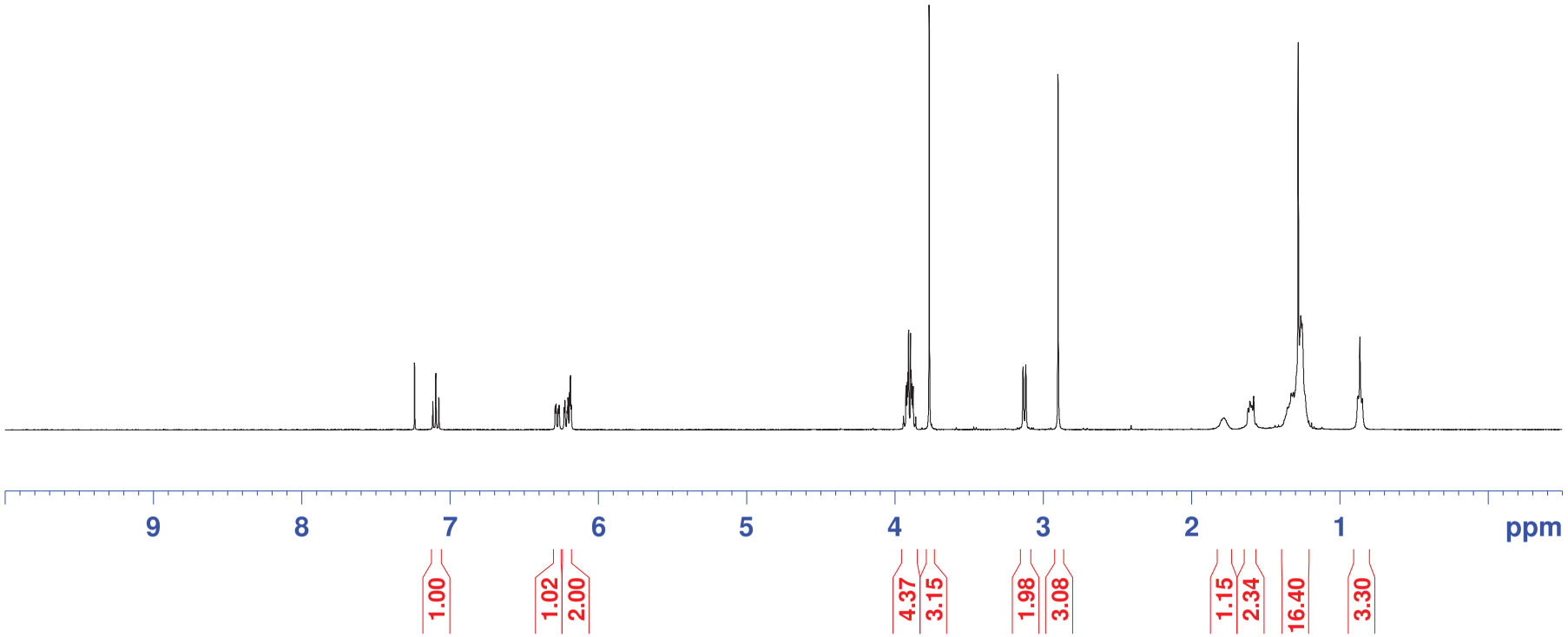


Table 1, entry 8



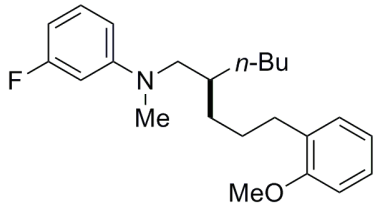
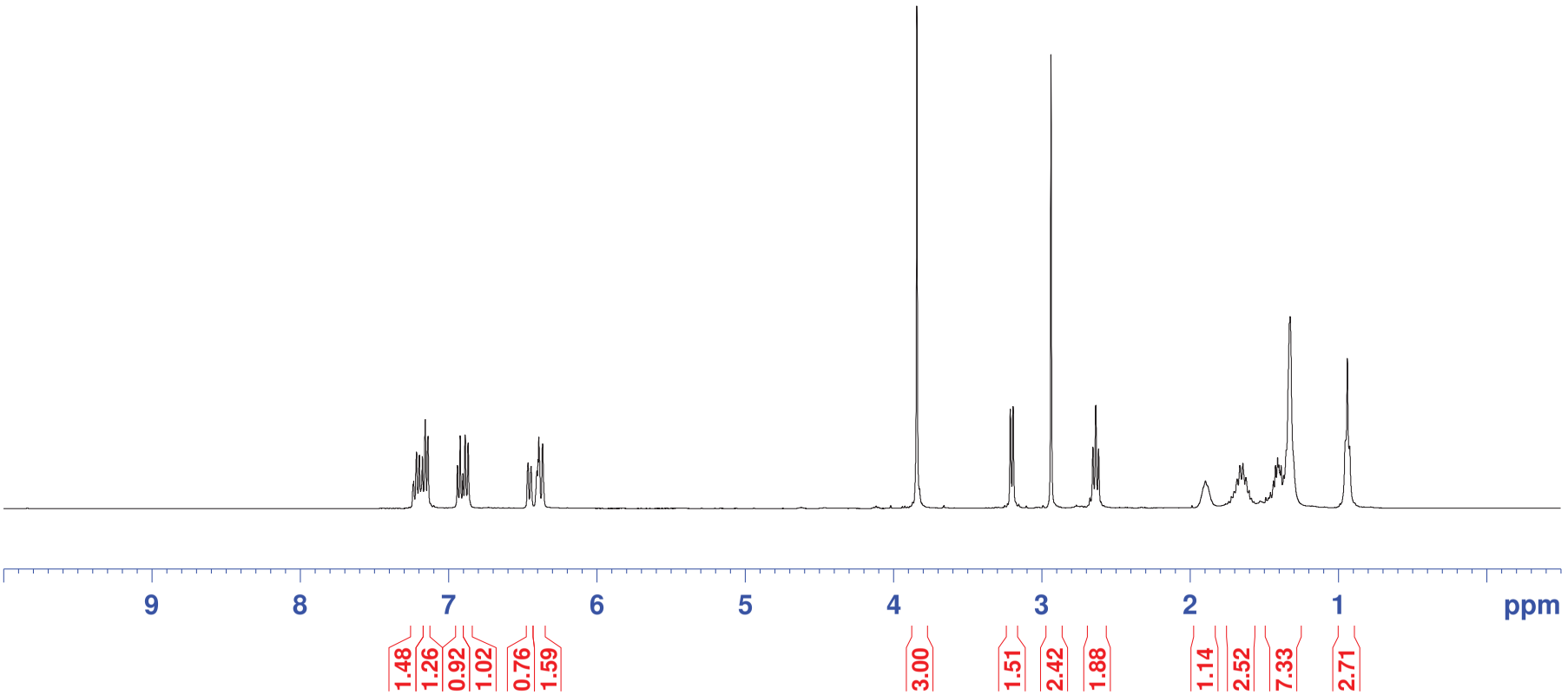


Table 1, entry 9



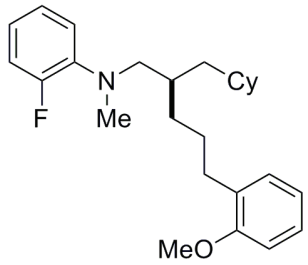
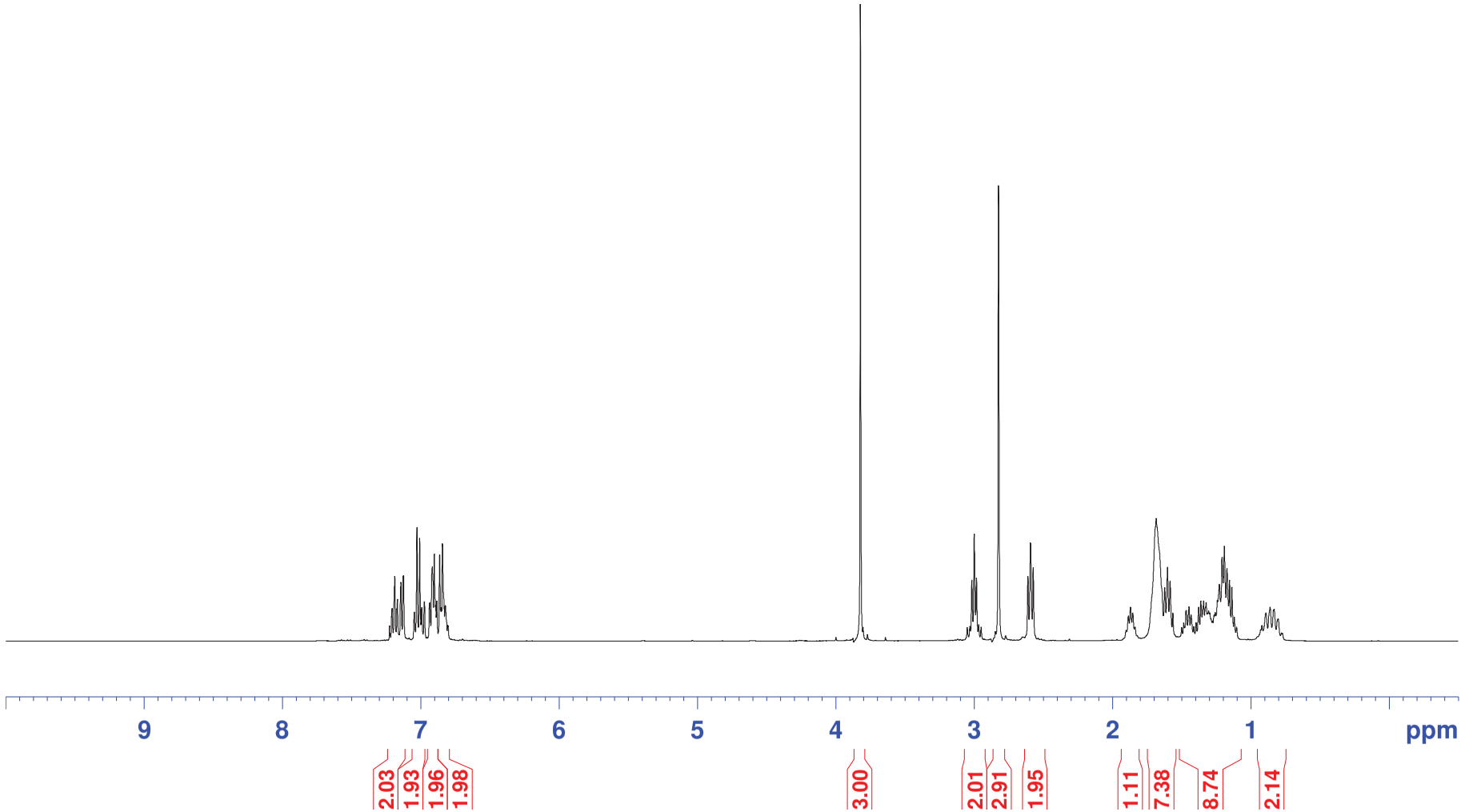


Table 1, entry 10



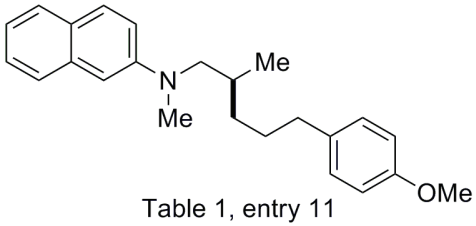
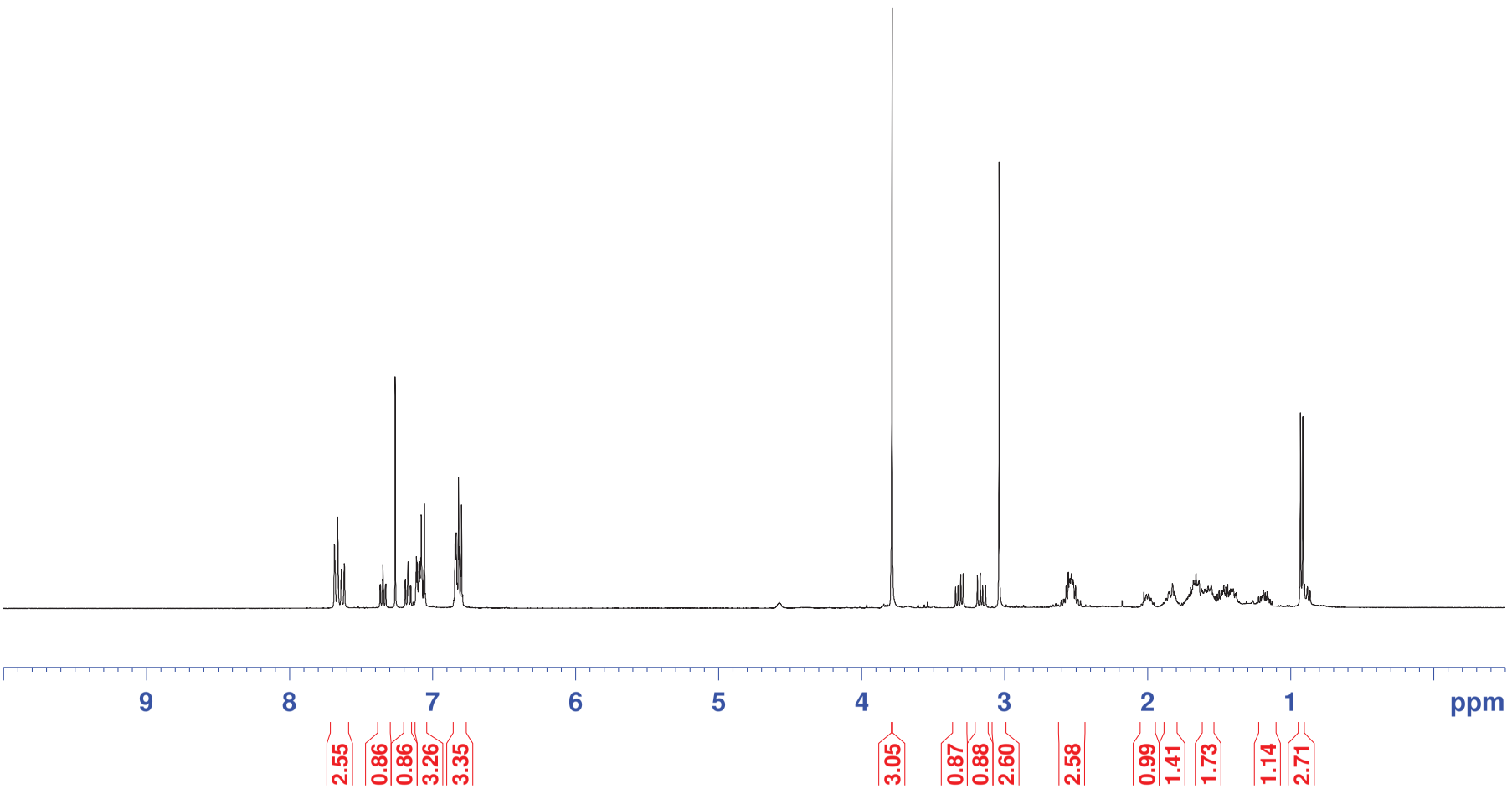


Table 1, entry 11



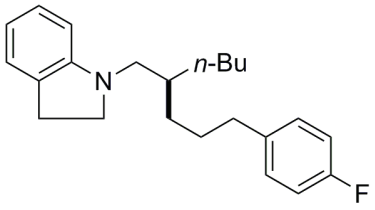


Table 1, entry 12