Electronic Supplementary Material (ESI) for Chemical Communications

An efficient synthesis of optically active trifluoromethyl aldimines via asymmetric biomimetic transamination

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Supporting Information

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General Methods. All commercially available reagents were used without further purification. All dry solvents were freshly distilled under nitrogen from appropriate drying agents before use. Benzene, tetrahydrofuran, and ethyl ether were distilled from sodium-benzophenone. Dichloromethane was distilled from CaH_2. Chloroform was distilled from P_2O_5. *N*,*N*-Dimethylformamide was dried over 4 Å molecular sieves (activated at 180 ^oC over 8 h in vacuum). Column chromatography was performed on silica gel (200-300 mesh). ^1H NMR spectra were recorded on a 400 MHz NMR spectrometer, ^{19}F NMR spectra were recorded on a 376 MHz NMR spectrometer, and ^{13}C NMR spectra were recorded on a 100 MHz NMR spectrometer. IR spectra were recorded on a FT-IR spectrometer. Melting points were uncorrected. α-Trifluoromethyl ketones were prepared according to the reported procedures.[1-4] (2-Chloro-4-cyano)benzylamine was prepared from 3-chloro-4-methylbenzonitrile by benzylic bromination with NBS[5] and subsequent amination with hexamethylenetetramine.[6] α-Trifluoromethyl imines were prepared according to the reported procedure with slight modification[7] and purified by flash chromatography or recrystallization.

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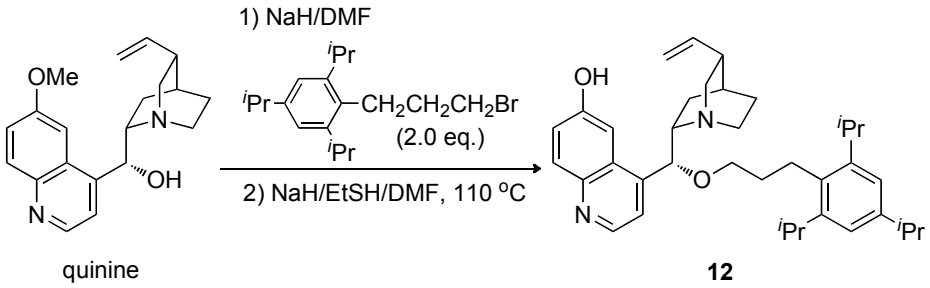
Preparation of catalyst C10



quinine **12**

To a solution of quinine (10.18 g, 31.4 mmol) in dry DMF (80 mL) was added NaH (70% suspension in mineral oil) (3.23 g, 94.2 mmol) portionwise at rt under N_2.[1,2] After the reaction mixture was stirred at rt for 1 h, a solution of 2-(3-bromopropyl)-1,3,5-triisopropylbenzene[3] (19.90 g, 61.3 mmol) in DMF (20 mL) was added. Upon stirring at 40 °C overnight, the reaction mixture was quenched with brine (100 mL), extracted with EtOAc (3 x 200 mL), washed with brine (5 x 100 mL), dried over $MgSO_4$, filtered, and concentrated. The resulting crude product was subjected to the next step without further purification.

To a suspension of NaH (70% in mineral oil) (5.38 g, 157.0 mmol) (washed with hexane, dried under vacuum) in dry DMF (122 mL) was added EtSH (19.82 g, 314.0 mmol) dropwise at 0 °C under N_2 over 20 min. After the reaction mixture was stirred at rt for 20 min, a solution of the above crude product in dry DMF (60 mL) was added dropwise at rt over 10 min. Upon stirring at 110 ºC overnight, the reaction mixture was acidified with 4N HCl to pH 3, diluted with brine (100 mL), and extracted with EtOAc (3 x 200 mL). The organic phase was brought to pH 10 with NH_4OH, washed with brine (3 x 100 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, EtOAc/MeOH = 20/1-5/1) to give compound **12** as a light yellow solid (14.97 g, 86% overall yield). mp. 95-97 °C; $[\alpha]^{20}_D$ = -27.4 (*c* 1.02, $CHCl_3$); IR (film) 3414, 1618, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.25 (br s, 1H), 8.74 (d, *J* = 4.4 Hz, 1H), 8.18 (s, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 7.50 (d, *J* = 4.0 Hz, 1H), 7.36 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.02 (s, 2H), 5.75-5.59 (m, 1H), 5.50 (s, 1H), 4.94 (d, *J* = 17.2 Hz, 1H), 4.89 (d, *J* = 10.4 Hz, 1H), 3.86-3.65 (m, 1H), 3.61-3.45 (m, 2H), 3.36-3.18 (m, 3H), 3.14-3.00 (m, 1H), 3.00-2.74 (m, 4H), 2.73-2.60 (m, 1H), 2.48-2.34 (m, 1H), 2.25-2.10 (m, 1H), 2.08-1.75 (m, 4H), 1.75-1.61

(m, 1H), 1.60-1.45 (m, 1H), 1.42-1.18 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 146.8, 146.59, 146.55, 144.7, 143.9, 141.0, 133.1, 131.4, 128.3, 123.4, 121.2, 118.0, 115.2, 107.4, 79.0, 69.7, 59.8, 56.6, 43.5, 39.7, 34.3, 32.7, 29.4, 28.1, 27.2, 25.1, 24.8, 24.7, 24.3, 20.1; HRMS Calcd for $C_{37}H_{51}N_2O_2$ (M+H): 555.3945; Found: 555.3943.

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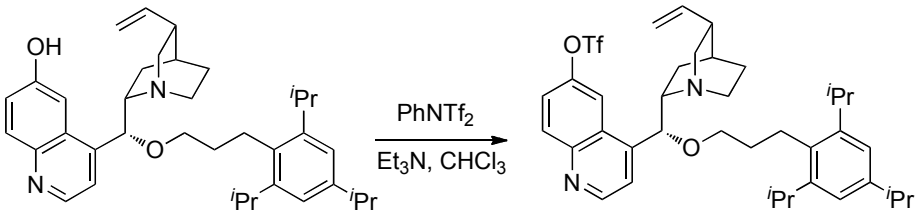

12 **13**

To a solution of compound **12** (14.97 g, 27.0 mmol) and $PhNTf_2$ (11.56 g, 32.4 mmol) in $CHCl_3$ (200 mL) was added Et_3N (6.28 g, 62.1 mmol) at rt.[1] Upon stirring at rt overnight, the reaction mixture was washed with 2N HCl (2 x 40 mL), saturated Na_2CO_3 aqueous (2 x 40 mL), dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, packed with EtOAc containing 2% Et_3N) (eluted with EtOAc/MeOH/Et_3N = 200/5/2) to give compound **13** as an orange oil (18.19 g, 98% yield). $[\alpha]^{20}_D$ = -14.1 (*c* 1.29, $CHCl_3$); IR (film) 1508, 1425, 1142 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, *J* = 4.4 Hz, 1H), 8.35-8.20 (m, 2H), 7.66-7.52 (m, 2H), 7.01 (s, 2H), 5.87-5.74 (m, 1H), 5.10-4.91 (m, 3H), 3.55-3.45 (m, 2H), 3.44-3.28 (m, 1H), 3.28-3.12 (m, 3H), 3.09-2.98 (m, 1H), 2.93-2.56 (m, 5H), 2.33-2.23 (m, 1H), 1.92-1.70 (m, 6H), 1.63-1.50 (m, 1H), 1.37-1.13 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 147.82, 147.75, 147.3, 146.61, 146.57, 142.1, 133.4, 133.1, 126.9, 123.9, 122.9, 121.2, 120.8, 120.7, 117.5, 116.3, 114.5, 114,3, 83.0, 70.3, 61.2, 57.0, 43.0, 40.1, 34.3, 32.5, 29.4, 28.2, 28.1, 24.9, 24.7, 24.3, 24.0; HRMS Calcd for $C_{38}H_{50}F_3N_2O_4S$(M+H): 687.3438; Found: 687.3439.

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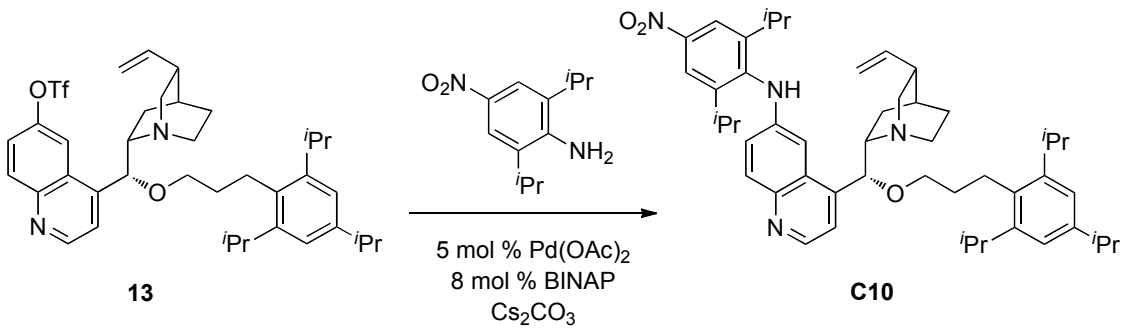

To a flask charged with 2,6-diisopropyl-4-nitroaniline[1] (5.728 g, 25.77 mmol), $Pd(OAc)_2$ (0.241 g, 1.07 mmol), BINAP (1.070 g, 1.72 mmol), and Cs_2CO_3 (9.798 g, 30.07 mmol) was added a solution of compound **13** (14.755 g, 21.48 mmol) in toluene (210 mL) under N_2.[2] Upon stirring at reflux for 15 h, the reaction mixture was filtered through a Celite pad, washed with EtOAc, concentrated, and purified by flash chromatography (silica gel, CH_2Cl_2/MeOH = 55/1) to give a residue, which was purified again by flash chromatography (silica gel, packed with CH_2Cl_2 containing 2% Et_3N) (eluted with CH_2Cl_2/MeOH = 80/1) to give compound **C10** as a yellow solid (11.724 g, 72% yield). mp. 154-156 °C; $[\alpha]^{20}_D$ = -44.5 (*c* 1.04, $CHCl_3$); IR (film) 3387, 1624, 1328 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.8 Hz, 1H), 8.14 (s, 2H), 7.98 (d, *J* = 9.2 Hz, 1H), 7.43 (d, *J* = 2.8 Hz, 1H), 7.06-6.96 (m, 4H), 5.77-5.65 (m, 2H), 5.06-4.87 (m, 3H), 3.51-3.12 (m, 7H), 3.08-2.70 (m, 5H), 2.70-2.57 (m, 1H), 2.57-2.46 (m, 1H), 2.30-2.20 (m, 1H), 1.92-1.68 (m, 5H), 1.58-1.44 (m, 2H), 1.30-1.15 (m, 30H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 147.1, 147.0, 146.5, 146.4, 145.1 144.7, 144.0, 142.0, 141.6, 133.1, 132.0, 128.1, 121.1, 119.9, 119.4, 118.6, 114.3, 102.8, 80.9, 69.7, 60.3, 57.2, 43.3, 40.2, 34.2, 32.6, 29.3, 29.0, 28.1, 27.9, 24.9, 24.7, 24.6, 24.2, 23.8, 23.4, 21.7; HRMS Calcd for $C_{49}H_{67}N_4O_3$ (M+H): 759.5208; Found: 759.5190.

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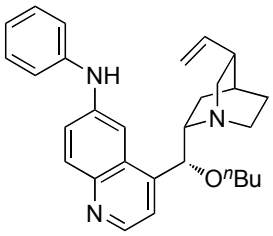
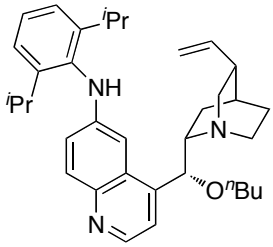


C7

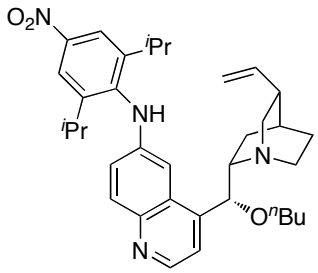
Prepared in a manner similar to **C10**. Brown solid (67% yield from the corresponding triflate); mp. 65-67 °C; $[\alpha]^{20}_D$ = -136.9 (*c* 1.02, $CHCl_3$); IR (film) 3282, 1597, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 3.6 Hz, 1H), 8.00 (d, *J* = 8.8 Hz, 1H), 7.65 (s, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.42-7.23 (m, 3H), 7.18 (d, *J* = 7.6 Hz, 2H), 6.99 (t, *J* = 6.8 Hz, 1H), 6.51 (s, 1H), 5.80-5.67 (m, 1H), 5.10 (br s, 1H), 5.02-4.88 (m, 2H), 3.55-3.41 (m, 1H), 3.41-3.27 (m, 2H), 3.23-3.05 (m, 2H), 2.82-2.66 (m, 2H), 2.38-2.26 (m, 1H), 1.92-1.75 (m, 3H), 1.67-1.47 (m, 4H), 1.46-1.34 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 144.7, 144.6, 142.5, 142.0, 141.8, 131.6, 129.7, 127.9, 122.2, 122.1, 118.8, 118.5, 114.7, 106.8, 80.9, 69.5, 60.5, 57.2, 43.4, 40.1, 32.3, 28.1, 27.7, 21.8, 19.7, 14.1; HRMS Calcd for $C_{29}H_{36}N_3O$ (M+H): 442.2853; Found: 442.2855.



C8

Prepared in a manner similar to **C10**. Yellow solid (48% yield from the corresponding triflate); mp. 204-206 °C; $[\alpha]^{20}_D$ = -130.7 (*c* 1.14, $CHCl_3$); IR (film) 3333, 1621, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.0 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.38-7.20 (m, 5H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.20 (br s, 1H), 5.76-5.63 (m, 1H), 5.32 (br s, 1H), 5.10-4.97 (m, 2H), 3.78-3.58 (m, 1H), 3.50-3.38 (m, 2H), 3.37-3.18 (m, 4H), 3.03-2.85 (m, 2H), 2.56-2.45 (m, 1H), 2.10-1.89 (m, 3H), 1.79-1.67 (m, 1H), 1.67-1.51 (m, 3H), 1.49-1.36 (m, 2H), 1.51 (t, *J* = 8.0 Hz, 12H), 0.94 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 147.2, 145.9, 143.4, 142.9, 140.9, 134.9, 131.6, 128.2, 128.0, 124.2, 118.9, 118.4, 115.2, 101.4, 79.6, 69.5, 60.1, 56.6, 43.4, 39.5, 32.3, 28.6, 28.0, 27.0, 24.2, 24.0, 21.2,

19.7, 14.1; HRMS Calcd for $C_{35}H_{48}N_3O$ (M+H): 526.3792; Found: 526.3788.



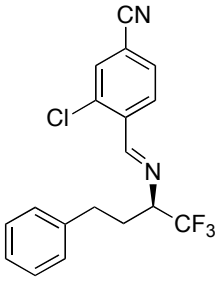
C9

Prepared in a manner similar to **C10**. Yellow solid (70% yield from the corresponding triflate); mp. 234-235 °C; $[\alpha]^{20}_D$ = -89.9 (*c* 0.95, $CHCl_3$) ; IR (film) 3383, 1623, 1328 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 4.4 Hz, 1H), 8.12 (s, 2H), 7.95 (d, *J* = 9.2 Hz, 1H), 7.36 (d, *J* = 4.4 Hz, 1H), 7.08-6.97 (m, 2H), 5.77 (s, 1H), 5.74-5.63 (m, 1H), 4.98-4.78 (m, 3H), 3.35-3.17 (m, 5H), 3.04-2.95 (m, 1H), 2.95-2.86 (m, 1H), 2.63-2.51 (m, 1H), 2.51-2.34 (m, 1H), 2.27-2.17 (m, 1H), 1.78-1.61 (m, 3H), 1.60-1.32 (m, 6H), 1.21 (d, *J* = 6.8 Hz, 6H), 1.18 (d, *J* = 6.8 Hz, 6H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 147.2, 147.1, 144.89, 144.86, 144.2, 142.2, 141.7, 132.0, 128.2, 119.9, 119.3, 119.1, 114.3, 103.3, 81.5, 69.5, 60.4, 57.3, 43.2, 40.3, 32.3, 29.0, 28.1, 27.9, 23.8, 23.5, 22.3, 19.7, 14.1; HRMS Calcd for $C_{35}H_{47}N_4O_3$ (M+H): 571.3643; Found: 571.3640.

Representative procedure for asymmetric [1,3]-proton shift of trifluoromethyl ketimine (Table 2, entry 1)

To a tube charged with imine **7a** (0.175 g, 0.50 mmol) and catalyst **C10** (0.038 g, 0.050 mmol) was added dry benzene (0.5 mL). Upon stirring at 20 °C for 72 h, the reaction mixture was purified by flash chromatography (silica gel, hexane/Et_2O = 15/1) to give product **8a** as a colorless oil (0.174 g, 99% yield). The sample was subjected to chiral HPLC (chiralpak AD-H column) to determine the enantiomeric excess.

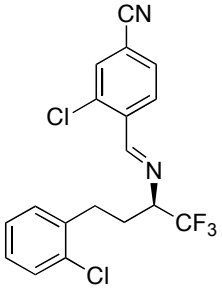
Table 2, entry 1



8a

Colorless oil; $[\alpha]^{20}_{D}$ = +160.5 (*c* 1.10, $CHCl_3$) (94% ee); IR (film) 3028, 2233, 1641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 1.2 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.34-7.27 (m, 2H), 7.25-7.18 (m, 1H), 7.18-7.13 (m, 2H), 3.81-3.70 (m, 1H), 2.78-2.68 (m, 1H), 2.57-2.47 (m, 1H), 2.36-2.19 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 139.8, 136.1, 135.9, 133.2, 130.4, 129.4, 128.7, 128.4, 126.4, 125.1 (q, $J_{C\text{-}F}$ = 279.0 Hz), 116.9, 115.9, 70.8 (q, $J_{C\text{-}F}$ = 28.0 Hz), 31.1, 29.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{18}H_{15}ClF_3N_2$ (M+H): 351.0870; Found: 351.0872.

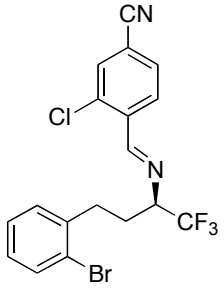
Table 2, entry 2



8b

Yellow oil; $[\alpha]^{20}_{D}$ = +119.7 (*c* 1.26, $CHCl_3$) (94% ee); IR (film) 2233, 1642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 1.2 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 7.6 Hz 1H), 7.22-7.12 (m, 3H), 3.85-3.75 (m, 1H), 2.80-2.66 (m, 2H), 2.37-2.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 137.9, 136.4, 136.3, 134.2, 133.6, 130.7, 130.5, 130.0, 129.8, 128.2, 127.2, 125.1 (q, $J_{C\text{-}F}$ = 279.0 Hz), 117.2, 116.2, 71.5, (q, $J_{C\text{-}F}$ = 28.0 Hz), 29.4, 28.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{18}H_{14}Cl_2F_3N_2$ (M+H): 385.0481; Found: 385.0482.

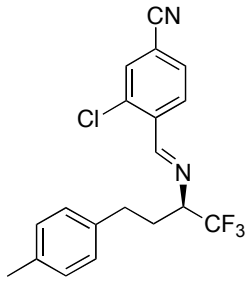
Table 2, entry 3



8c

Colorless oil; $[\alpha]^{20}_{D}$ = +108.5 (*c* 1.11, $CHCl_3$) (94% ee); IR (film) 2233, 1642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 1H), 7.60 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.2Hz, 1H), 7.27-7.17 (m, 2H), 7.10-7.03 (m, 1H), 3.88-3.77 (m, 1H), 2.80-2.67 (m, 2H), 2.36-2.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 139.6, 136.4, 136.2, 133.4, 133.2, 130.6, 130.4, 129.7, 128.3, 127.8, 125.1 (q, $J_{C\text{-}F}$ = 279.0 Hz), 124.5, 117.1, 116.1, 71.4 (q, $J_{C\text{-}F}$ = 28.0 Hz), 31.9, 29.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.3 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{18}H_{14}BrClF_3N_2$ (M+H): 428.9976; Found: 428.9980.

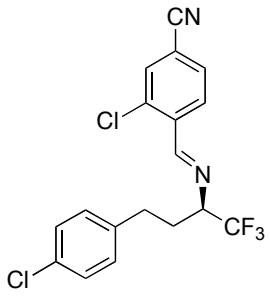
Table 2, entry 4



8d

Colorless oil; $[\alpha]^{20}_{D}$ = +154.2 (*c* 1.05, $CHCl_3$) (94% ee); IR (film) 2233, 1641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 1.2 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 3.79-3.69 (m, 1H), 2.74-2.64 (m, 1H), 2.53-2.42 (m, 1H), 2.32 (s, 3H), 2.30-2.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 136.7, 136.3, 136.09, 136.07, 133.4, 130.6, 129.6, 129.5, 128.4, 125.2 (q, $J_{C\text{-}F}$ = 279.0 Hz), 117.1, 116.0, 71.0 (q, $J_{C\text{-}F}$ = 28.0 Hz), 30.8, 29.9, 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{19}H_{17}ClF_3N_2$ (M+H): 365.1027; Found: 365.1027.

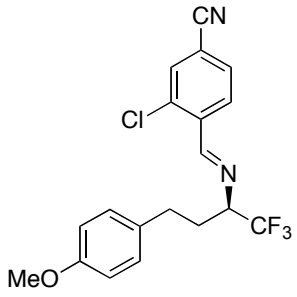
Table 2, entry 5



8e

Colorless oil; $[\alpha]^{20}_{D}$ = +150.2 (*c* 1.07, $CHCl_3$) (93% ee); IR (film) 2233, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 1.2 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 3.79-3.68 (m, 1H), 2.72-2.62 (m, 1H), 2.56-2.45 (m, 1H), 2.31-2.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 138.5, 136.24, 136.18, 133.5, 132.4, 130.6, 129.9, 129.7, 129.0, 125.1 (q, J_{C-F} = 279.0 Hz), 117.1, 116.2, 71.1 (q, J_{C-F} = 28.0 Hz), 30.8, 29.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 3.8 Hz); HRMS Calcd for $C_{18}H_{14}Cl_2F_3N_2$ (M+H): 385.0481; Found: 385.0483.

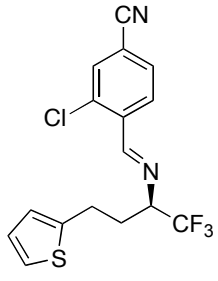
Table 2, entry 6



8f

Colorless oil; $[\alpha]^{20}_{D}$ = +178.8 (*c* 1.13, $CHCl_3$) (94% ee); IR (film) 2232, 1638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.22 (d, *J* = 8.4 Hz, 1H), 7.72 (s, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 3.82-3.68 (m, 4H), 2.72-2.61 (m, 1H), 2.51-2.40 (m, 1H), 2.31-2.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 158.4, 136.4, 136.2, 133.5, 131.8, 130.6, 129.7, 129.5, 125.2 (q, J_{C-F} = 279.0 Hz), 117.2, 116.1, 114.3, 71.1 (q, J_{C-F} = 28.0 Hz), 55.4, 30.4, 30.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{19}H_{17}ClF_3N_2O$ (M+H): 381.0976; Found: 381.0978.

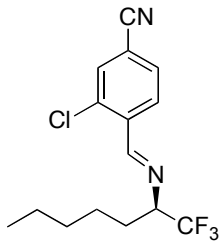
Table 2, entry 7



8g

Yellow oil; $[\alpha]^{20}_{D}$ = +155.5 (*c* 1.04, $CHCl_3$) (91% ee); IR (film); 2233, 1640 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 1.2 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.18-7.13 (m, 1H), 6.97-6.91 (m, 1H), 6.80 (d, *J* = 3.2 Hz, 1H), 3.87-3.75 (m, 1H), 2.98-2.88 (m, 1H), 2.81-2.70 (m, 1H), 2.38-2.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 142.5, 136.3, 136.2, 133.5, 130.6, 129.7, 127.2, 125.14 (q, $J_{C\text{-}F}$ = 279.0 Hz), 125.08, 124.0, 117.1, 116.2, 70.6 (q, $J_{C\text{-}F}$ = 28.0 Hz), 30.3, 25.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{16}H_{13}ClF_3N_2S$ (M+H): 357.0435; Found: 357.0438.

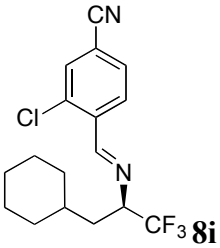
Table 2, entry 8



8h

Colorless oil; $[\alpha]^{20}_{D}$ = +118.4 (*c* 0.99, $CHCl_3$) (94% ee); IR (film) 2234, 1643 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.69 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 3.79-3.67 (m, 1H), 1.96-1.79 (m, 2H), 1.37-1.15 (m, 6H), 0.86 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 136.5, 136.1, 133.4, 130.6, 129.7, 125.3 (q, $J_{C\text{-}F}$ = 279.0 Hz), 117.1, 116.0, 72.1 (q, $J_{C\text{-}F}$ = 28.0 Hz), 31.3, 28.8, 25.0, 22.5, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.6 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{15}H_{17}ClF_3N_2$ (M+H): 317.1027; Found: 317.1027.

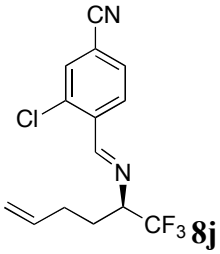
Table 2, entry 9



8i

White solid; mp. 71-72 °C; $[\alpha]^{20}_{D}$ = +135.7 (*c* 1.12, $CHCl_3$) (94% ee); IR (film) 2234, 1643 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.72 (s, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 3.94-3.83 (m, 1H), 1.88-1.60 (m, 7H), 1.24-1.10 (m, 4H), 1.08-0.96 (m, 1H), 0.96-0.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 136.6, 136.1, 133.5, 130.7, 129.7, 125.4 (q, J_{C-F} = 279.0 Hz), 117.2, 116.0, 69.4 (q, J_{C-F} = 28.0 Hz), 36.0, 34.2, 33.1, 31.9, 26.5, 26.2, 26.0**;** ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.6 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{17}H_{19}ClF_3N_2$ (M+H): 343.1183; Found: 343.1183.

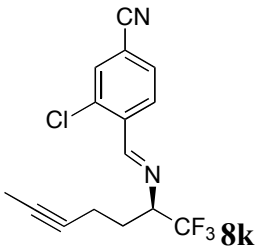
Table 2, entry 10



8j

Colorless oil; $[\alpha]^{20}_{D}$ = +133.6 (*c* 1.25, $CHCl_3$) (91% ee); IR (film) 2234, 1642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 1.2 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 5.81-5.69 (m, 1H), 5.10-5.01 (m, 2H), 3.86-3.75 (m, 1H), 2.19-2.09 (m, 1H), 2.05-1.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 136.6, 136.4, 136.2, 133.5, 130.7, 129.8, 125.3 (q, J_{C-F} = 281.0 Hz), 117.2, 116.6, 116.1, 71.1 (q, J_{C-F} = 28.0 Hz), 29.2, 27.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.5 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{14}H_{13}ClF_3N_2$ (M+H): 301.0714; Found: 301.0712.

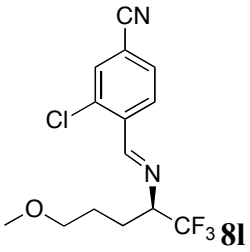
Table 2, entry 11



8k

Colorless oil; $[\alpha]^{20}_{D}$ = +275.1 (*c* 1.01, $CHCl_3$) (90% ee); IR (film) 2234, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 1.2 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 4.09-3.98 (m, 1H), 2.32-2.22 (m, 1H), 2.11-1.90 (m, 3H), 1.80-1.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5, 136.5, 136.3, 133.5, 130.6, 129.7, 125.3 (q, $J_{C\text{-}F}$ = 279.0 Hz), 117.1, 116.1, 78.1, 76.3, 70.2 (q, $J_{C\text{-}F}$ = 28.0 Hz), 27.5, 14.7, 3.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 3.8 Hz); HRMS Calcd for $C_{15}H_{13}ClF_3N_2$ (M+H): 313.0714; Found: 313.0713.

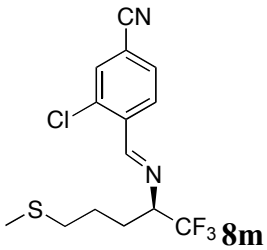
Table 2, entry 12



8l

Colorless oil; $[\alpha]^{20}_{D}$ = +94.1 (*c* 1.00, $CHCl_3$) (86% ee); IR (film) 2234, 1641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 1.2 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 3.87-3.76 (m, 1H), 3.46-3.36 (m, 2H), 3.32 (s, 3H), 2.09-1.88 (m, 2H), 1.58-1.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 136.5, 136.2, 133.5, 130.6, 129.7, 125.2 (q, $J_{C\text{-}F}$ = 279.0 Hz), 117.2, 116.1, 72.20, 71.9 (q, $J_{C\text{-}F}$ = 28.0 Hz), 58.8, 26.2, 25.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.6 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{14}H_{15}ClF_3N_2O$ (M+H): 319.0820; Found: 319.0819.

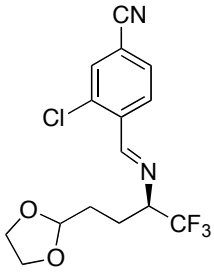
Table 2, entry 13



8m

Yellow oil; $[\alpha]^{20}_{D}$ = +116.7 (*c* 1.03, $CHCl_3$) (90% ee); IR (film) 2233, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.71 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 3.82-3.72 (m, 1H), 2.52 (t, *J* = 7.2 Hz, 2H), 2.11-1.92 (m, 5H), 1.65-1.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 136.3, 136.1, 133.4, 130.6, 129.6, 125.0 (q, J_{C-F}= 279.0 Hz), 117.0, 116.0, 71.7 (q, J_{C-F} = 28.0 Hz), 33.7, 28.1, 24.9, 15.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.4 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{14}H_{15}ClF_3N_2S$ (M+H): 335.0591; Found: 335.0591.

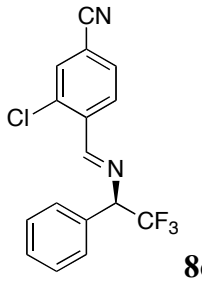
Table 2, entry 14



8n

Yellow oil; $[\alpha]^{20}_{D}$ = +95.1 (*c* 0.99, $CHCl_3$) (86% ee); IR (film) 2234, 1640, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 1.6 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 4.89 (t, *J* = 4.4 Hz, 1H), 4.00-3.92 (m, 2H), 3.92-3.81 (m, 3H), 2.16-2.06 (m, 1H), 2.06-1.94 (m, 1H), 1.75-1.65 (m, 1H), 1.63-1.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 136.5, 136.2, 133.5, 130.6, 129.8, 125.2 (q, J_{C-F} = 280.0 Hz), 117.2, 116.1, 103.9, 71.4 (q, J_{C-F} = 30.0 Hz), 65.3, 65.1, 29.3, 23.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -74.7 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{15}H_{15}ClF_3N_2O_2$ (M+H): 347.0769; Found: 347.0770.

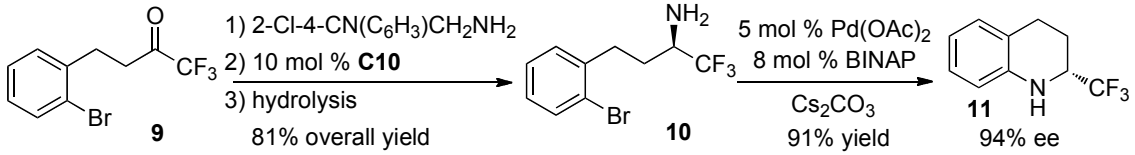
Table 2, entry 15



8o

White solid; mp. 80-81 °C; $[\alpha]^{20}_{D}$ = +93.5 (*c* 0.98, $CHCl_3$) (67% ee); IR (film) 1638, 706 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 1.2 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.57-7.50 (m, 2H), 7.46-7.37 (m, 3H), 4.92 (q, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 136.5, 136.4, 134.3, 133.5, 130.6, 129.8, 129.5, 129.0, 128.9, 124.5 (q, J_{C-F} = 280.0 Hz), 117.2, 116.2, 75.4 (q, J_{C-F} = 29.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.7 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{16}H_{11}ClF_3N_2$ (M+H): 323.0557; Found: 323.0556.

Preparation of 2-trifluoromethyltetrahydroquinoline (11) (Scheme 2)



To a flask charged with 2-Cl-4-CN-benzylamine (0.625 g, 3.75 mmol) and 4 Å molecular sieves (1.20 g) were added $CHCl_3$ (7.0 mL) and acetic acid (0.338 g, 5.63 mmol) under N_2. After the mixture was stirred at rt for 20 min, trifluoromethyl ketone **9** (0.703 g, 2.5 mmol) was added. The reaction mixture was refluxed for 5 h, cooled to rt, diluted with Et_2O (20 mL), filtered through a layer of silica gel (3 cm height) by suction, and washed with Et_2O (60 mL). The filtrate was concentrated, diluted with hexane/Et_2O = 7:1 (30 mL), filtered through a layer of silica gel (3 cm height) by suction again, washed with hexane/Et_2O = 7:1 (50 mL), and concentrated to give the corresponding ketimine as a white solid.

A mixture of the above ketimine and **C10** (0.190 g, 0.25 mmol) in benzene (2.5 mL) was stirred at 20 °C for 72 h, diluted with hexane/Et_2O = 7:1 (10 mL), filtered through a layer of silica gel (3 cm height) by suction, washed with hexane/Et_2O = 7:1 (60 mL), and concentrated to a residue, which was dissolved in Et_2O (12.5 mL), followed by the addition of ethylene glycol (25.0 mL) and 6N HCl (25.0 mL). The reaction mixture was stirred at rt

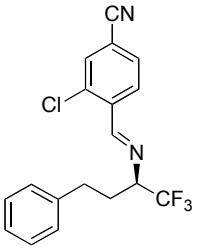
for 4 h and washed with Et_2O (2 x 10 mL). The organic phase was extracted with 2N HCl (10 mL). The combined aqueous phase was diluted with water (100 mL) and washed with Et_2O (4 x 30 mL). The organic phase was extracted with 2N HCl (30 mL), and the aqueous phase was washed with Et_2O (2 x 20 mL). The above aqueous phases were combined, and CH_2Cl_2 (20 mL) was added. The mixture was brought to pH 10 with solid Na_2CO_3, extracted with CH_2Cl_2 (5 x 40 mL), dried over Na_2SO_4, filtered, concentrated, and purified by flash chromatography (silica gel, hexane/Et_2O = 5/1) to give amine **10** as a colorless oil (0.566 g, 81% overall yield). $[\alpha]^{20}_D$ = +29.2 (*c* 1.14, $CHCl_3$); IR (film) 3407, 1623 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.27-7.21 (m, 2H), 7.11-7.04 (m, 1H), 3.20-3.01 (m, 2H), 2.88-2.78 (m, 1H), 2.11-2.00 (m, 1H), 1.72-1.61 (m, 1H), 1.39 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 133.2, 130.6, 128.2, 127.8, 126.9 (q, J_{C-F} = 280.0 Hz), 124.6, 53.6 (q, J_{C-F} = 29.0 Hz), 32.4, 30.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -78.9 (d, *J* = 7.9 Hz); HRMS Calcd for $C_{10}H_{12}BrF_3N$ (M+H): 282.0100; Found: 282.0098.

To a flask charged with $Pd(OAc)_2$ (0.006 g, 0.025 mmol), BINAP (0.025 g, 0.04 mmol) and Cs_2CO_3 (0.228 g, 0.7 mmol) was added a solution of amine **10** (0.141 g, 0.5 mmol) in toluene (5 mL) under N_2.[1] Upon stirring at reflux until the reaction was completed as judged by TLC (around 4 h), the reaction mixture was filtered through Celite, concentrated, and purified by flash chromatography (silica gel, hexane/Et_2O = 20/1) to give compound **11** as a white solid (0.092 g, 91% yield). mp. 54-55 °C; $[\alpha]^{20}_D$ = -24.4 (*c* 1.05, $CHCl_3$) (94% ee); IR (film) 3415, 1611 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.07-6.97 (m, 2H), 6.74-6.68 (m, 1H), 6.59 (d, *J* = 8.0 Hz, 1H), 4.08 (br s, 1H), 3.92-3.81 (m, 1H), 2.82 (t, *J* = 6.8 Hz, 2H), 2.17-2.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 129.2, 127.4, 126.0 (q, J_{C-F} = 279.0 Hz), 120.9, 118.6, 114.8, 53.0 (q, J_{C-F} = 30.0 Hz), 24.5, 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.6 (d, *J* = 7.5 Hz); HRMS Calcd for $C_{10}H_{11}F_3N$ (M+H): 202.0838; Found: 202.0835.

1) A. S. Guram and S. L. Buckwald, *J. Am. Chem. Soc.,* 1994, **116**, 7901.

The chromatograms for determination of enantioselectivity

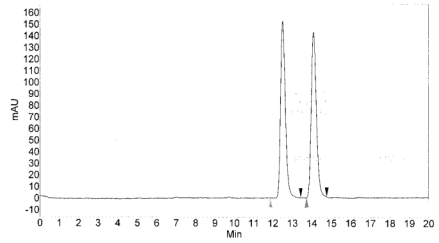
Table 2, entry 1



8a

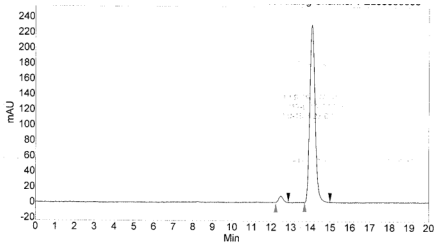
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



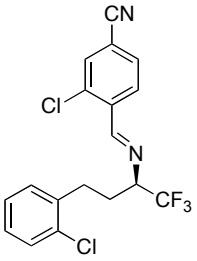
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	12.52	49.866	11.87	13.43
2	14.11	50.134	13.73	14.77
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	12.49	2.890	12.24	12.88
2	14.08	97.110	13.71	15.00
Total		100.000		

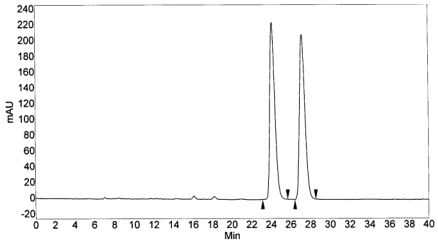
Table 2, entry 2



8b

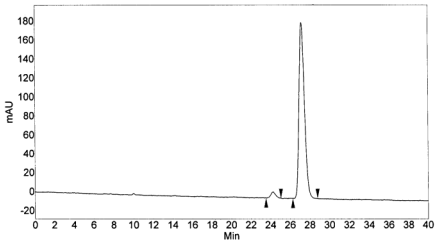
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



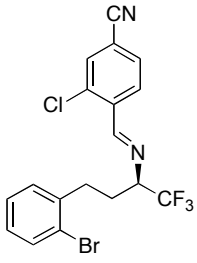
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	24.15	49.761	23.13	25.69
2	27.20	50.239	26.42	28.54
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	24.25	3.004	23.53	25.04
2	27.19	96.996	26.27	28.78
Total		100.000		

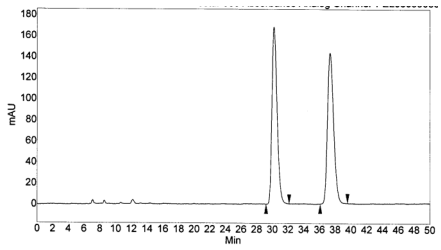
Table 2, entry 3



8c

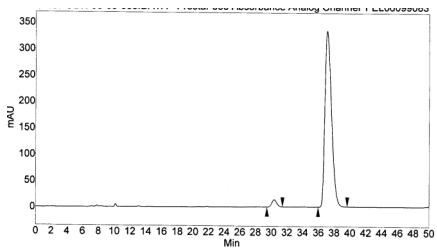
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



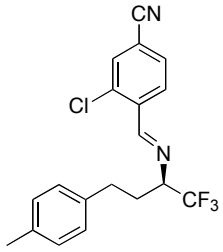
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	30.21	49.917	29.20	32.15
2	37.33	50.083	36.08	39.55
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	30.39	2.941	29.44	31.43
2	37.09	97.059	35.96	39.63
Total		100.000		

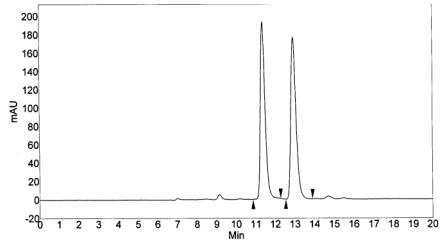
Table 2, entry 4



8d

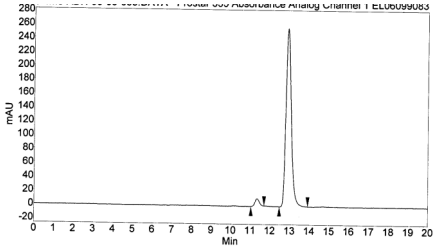
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



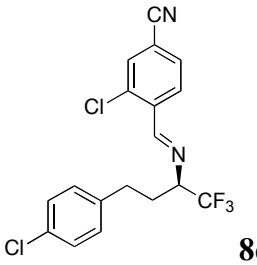
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	11.37	49.717	10.87	12.28
2	12.93	50.283	12.54	13.91
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	11.35	3.235	11.04	11.71
2	12.91	96.765	12.48	13.93
Total		100.000		

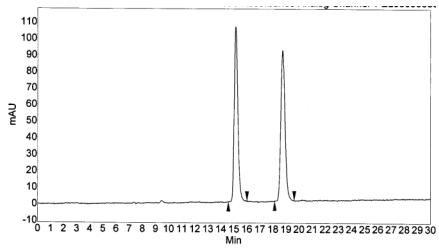
Table 2, entry 5



8e

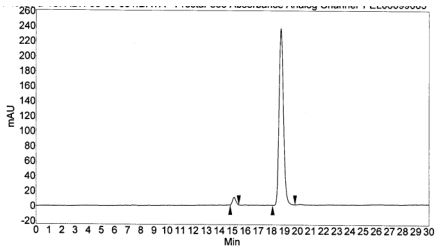
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



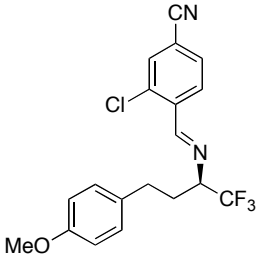
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	15.15	49.886	14.57	16.01
2	18.75	50.114	18.13	19.64
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	15.13	3.265	14.83	15.50
1	18.73	96.735	18.10	19.81
Total		100.000		

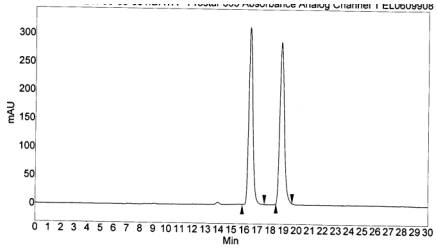
Table 2, entry 6



8f

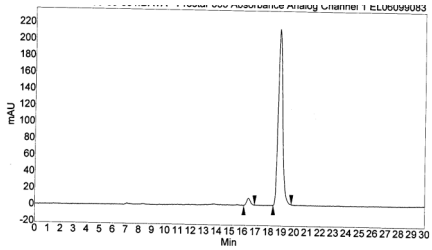
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



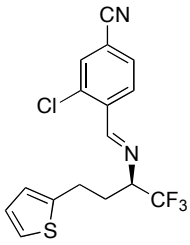
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	16.43	49.803	15.83	17.53
2	18.83	50.197	18.42	19.64
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	16.47	3.184	16.10	16.94
1	18.85	96.816	18.37	19.77
Total		100.000		

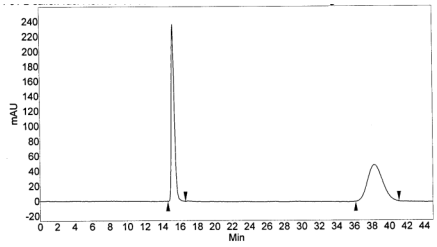
Table 2, entry 7



8g

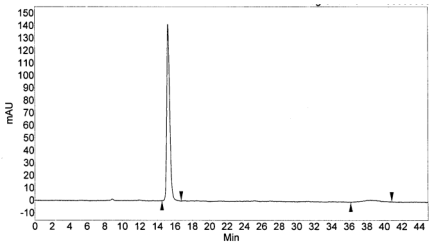
HPLC Condition: **Column:** Chiralpak AS-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



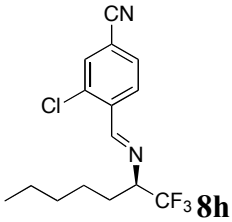
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	15.24	50.018	14.62	16.62
2	38.37	49.982	36.18	41.10
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	15.25	95.306	14.52	16.73
1	38.47	4.694	36.18	40.84
Total		100.000		

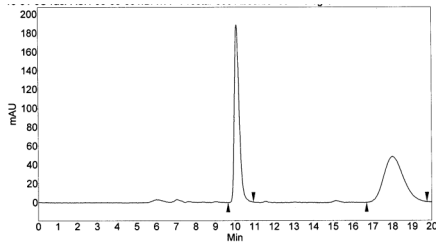
Table 2, entry 8



8h

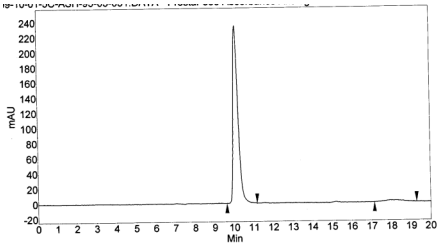
HPLC Condition: **Column:** Chiralpak AS-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



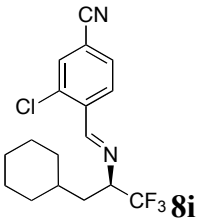
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	10.11	49.753	9.65	10.95
2	18.01	50.247	16.69	19.75
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	10.11	96.878	9.63	11.17
2	18.01	3.122	17.14	19.28
Total		100.000		

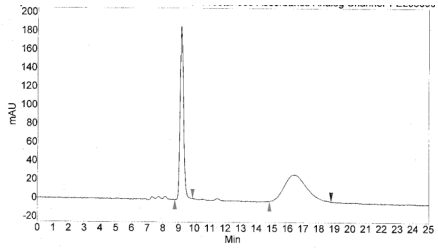
Table 2, entry 9



8i

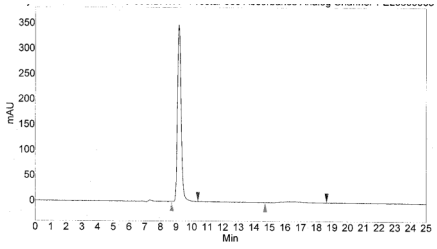
HPLC Condition: **Column:** Chiralpak AS-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



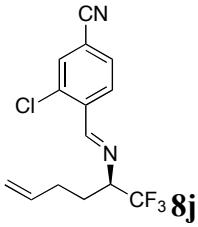
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	9.17	49.935	8.75	9.88
2	16.44	50.065	14.84	18.78
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	9.17	96.998	8.72	10.40
2	16.28	3.002	14.72	18.65
Total		100.000		

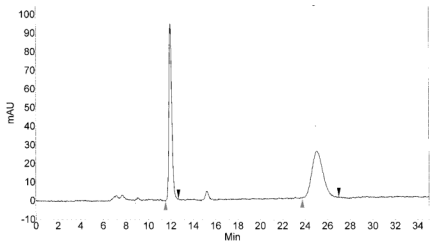
Table 2, entry 10



8j

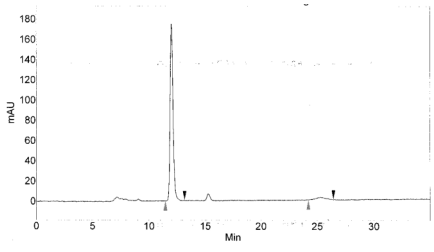
HPLC Condition: **Column:** Chiralpak AS-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



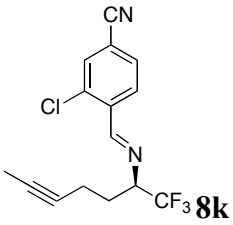
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	11.96	49.819	11.52	12.68
2	25.03	50.181	23.75	27.00
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	12.00	95.472	11.45	13.15
2	25.45	4.528	24.21	26.43
Total		100.000		

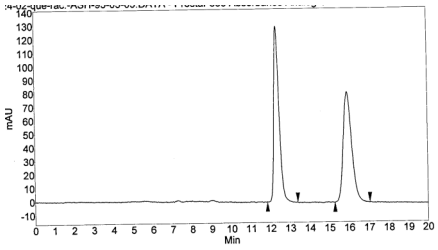
Table 2, entry 11



8k

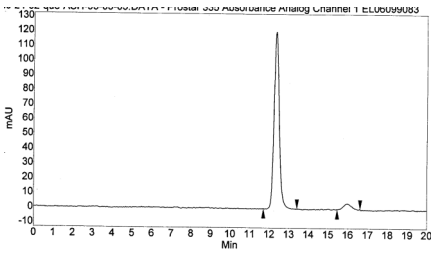
HPLC Condition: **Column:** Chiralpak AS-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



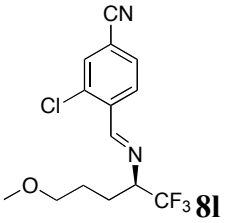
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	12.35	49.819	11.84	13.38
2	15.92	50.181	15.28	17.04
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	12.33	95.236	11.70	13.42
2	15.99	4.764	15.46	16.62
Total		100.000		

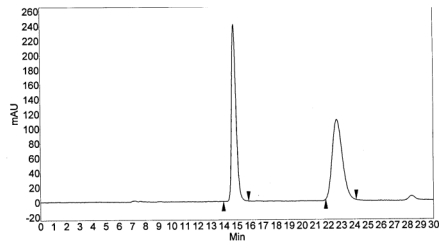
Table 2, entry 12



8l

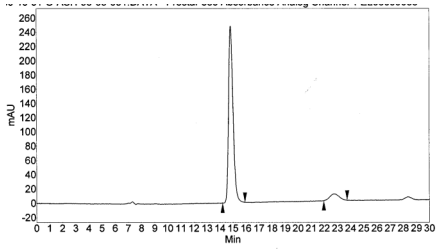
HPLC Condition: **Column:** Chiralpak AS-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



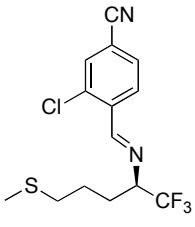
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.80	49.845	13.97	15.90
2	22.68	50.155	21.81	24.12
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.84	92.909	14.20	15.93
2	22.76	7.091	21.97	23.73
Total		100.000		

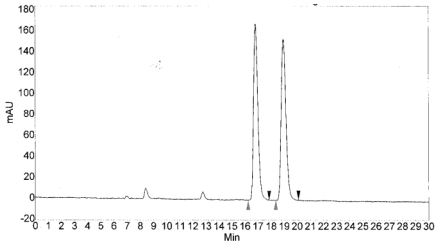
Table 2, entry 13



8m

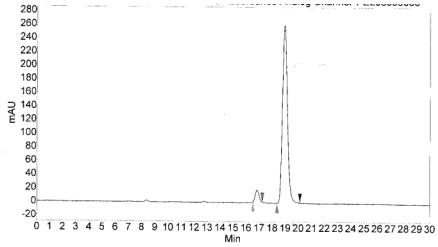
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/05); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



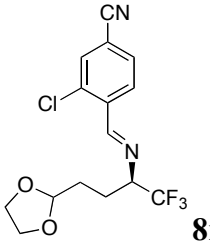
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	16.83	49.868	16.25	17.85
2	18.96	50.132	18.37	20.10
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	16.84	4.998	16.52	17.25
2	18.93	95.002	18.38	20.12
Total		100.000		

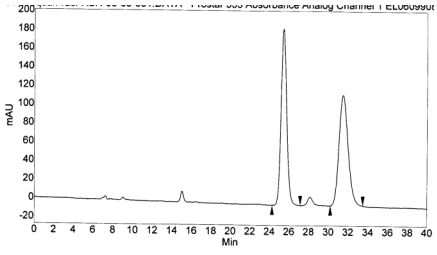
Table 2, entry 14



8n

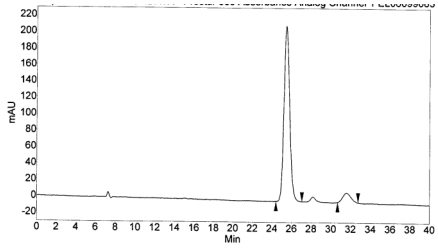
HPLC Condition: Column: Chiralpak AS-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



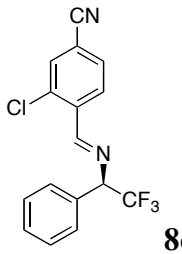
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	25.41	49.969	24.26	27.14
2	31.47	50.031	30.19	33.48
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	25.45	93.013	24.40	27.06
2	31.57	6.987	30.69	32.75
Total		100.000		

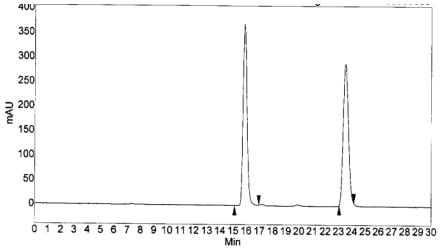
Table 2, entry 15



8o

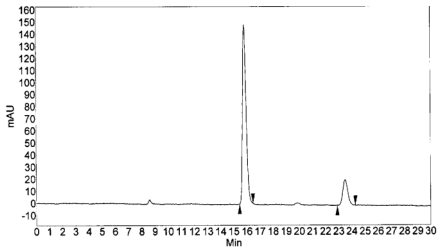
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV215 nm; 25°C.

Racemic standard



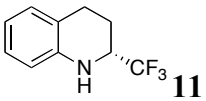
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
2	15.87	49.952	15.11	16.95
1	23.51	50.048	23.04	24.15
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	15.84	83.509	15.45	16.47
2	23.48	16.491	22.89	24.25
Total		100.000		

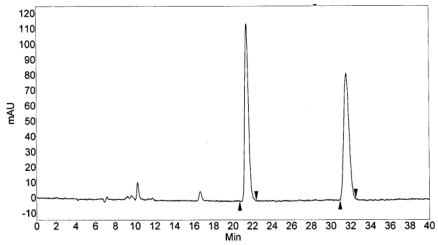
Scheme 2



11

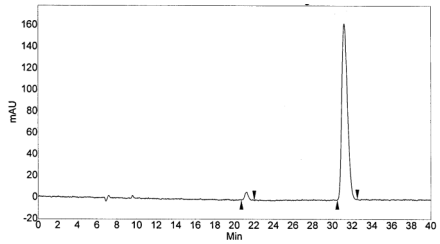
HPLC Condition: Column: Chiralcel OD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (90/10); **Flow rate:** 0.5 mL/min; **Detection:** UV209 nm; 25°C.

Racemic standard



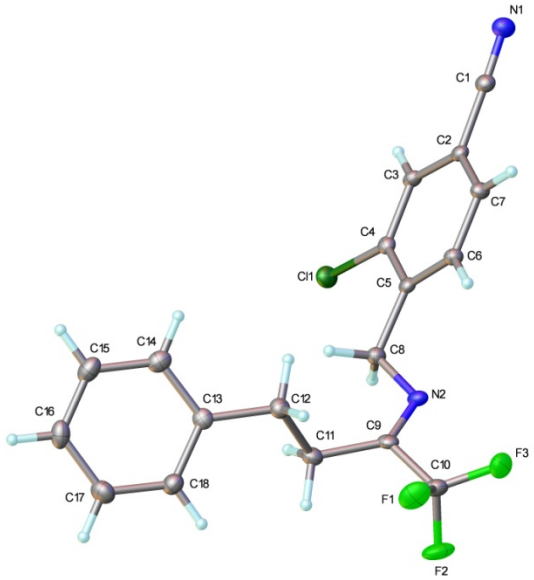
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	21.44	49.767	20.71	22.39
2	31.59	50.233	30.92	32.52
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	21.24	2.880	20.72	22.04
2	31.21	97.120	30.51	32.53
Total		100.000		

The X-ray structure of compound **7a**



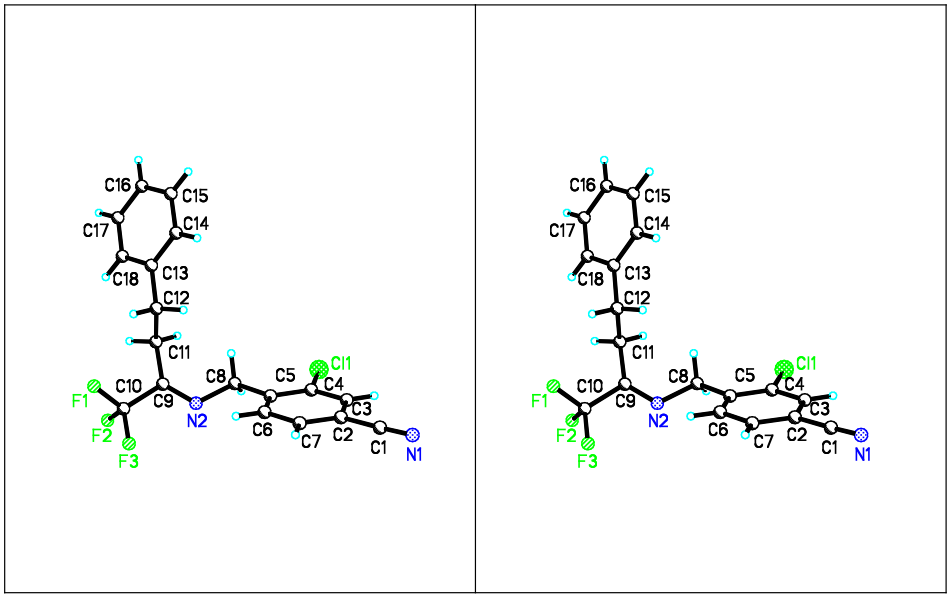


Table 1. Crystal data and structure refinement for a.

Identification code	a
Empirical formula	C18 H14 Cl F3 N2
Formula weight	350.76
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 14.103(3) A alpha = 90 deg.
	b = 7.6310(15) A beta = 114.36(3) deg.
	c = 16.683(3) A gamma = 90 deg.
Volume	1635.6(6) A^3
Z, Calculated density	4, 1.424 Mg/m^3
Absorption coefficient	0.266 mm^-1
F(000)	720
Crystal size	0.42 x 0.41 x 0.09 mm
Theta range for data collection	1.59 to 25.00 deg.
Limiting indices	-16<=h<=16, -9<=k<=9, -19<=l<=19
Reflections collected / unique	9557 / 2842 [R(int) = 0.0570]
Completeness to theta = 25.00	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.5608
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2842 / 0 / 217
Goodness-of-fit on F^2	1.219
Final R indices [I>2sigma(I)]	R1 = 0.0654, wR2 = 0.2023
R indices (all data)	R1 = 0.0938, wR2 = 0.2744
Largest diff. peak and hole	1.172 and -1.162 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for a.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Cl(1)	-1169(1)	8013(1)	1115(1)	31(1)
F(1)	4466(2)	7388(4)	4568(2)	52(1)
F(2)	3419(2)	7800(4)	5196(1)	54(1)
F(3)	3447(2)	5328(3)	4602(1)	49(1)
N(1)	-1256(2)	978(4)	-655(2)	35(1)
N(2)	1914(2)	6730(4)	3258(2)	25(1)
C(1)	-860(3)	1983(4)	-104(2)	27(1)
C(2)	-378(2)	3302(4)	571(2)	22(1)
C(3)	-942(2)	4819(4)	534(2)	23(1)
C(4)	-470(2)	6104(4)	1165(2)	22(1)
C(5)	541(2)	5897(4)	1824(2)	21(1)
C(6)	1079(2)	4378(4)	1821(2)	23(1)
C(7)	633(3)	3069(4)	1196(2)	24(1)
C(8)	1032(3)	7349(5)	2478(2)	26(1)
C(9)	2668(3)	7751(5)	3648(2)	25(1)
C(10)	3503(3)	7043(5)	4500(2)	32(1)
C(11)	2853(3)	9590(5)	3417(2)	28(1)
C(12)	3386(3)	9596(5)	2774(2)	29(1)
C(13)	3553(2)	11414(5)	2490(2)	26(1)
C(14)	3348(3)	11729(5)	1608(2)	32(1)
C(15)	3529(3)	13366(6)	1338(2)	37(1)
C(16)	3922(3)	14716(5)	1929(2)	37(1)
C(17)	4128(3)	14425(5)	2807(3)	38(1)
C(18)	3950(3)	12796(5)	3083(2)	31(1)

Table 3. Bond lengths [A] and angles [deg] for a.

Cl(1)-C(4)	1.740(3)
F(1)-C(10)	1.341(4)
F(2)-C(10)	1.346(4)
F(3)-C(10)	1.326(4)
N(1)-C(1)	1.150(5)
N(2)-C(9)	1.261(4)
N(2)-C(8)	1.459(4)
C(1)-C(2)	1.453(5)
C(2)-C(7)	1.388(5)
C(2)-C(3)	1.392(5)
C(3)-C(4)	1.391(4)
C(3)-H(3)	0.9500
C(4)-C(5)	1.405(5)
C(5)-C(6)	1.387(5)
C(5)-C(8)	1.509(4)
C(6)-C(7)	1.392(4)
C(6)-H(6)	0.9500
C(7)-H(7)	0.9500
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(11)	1.506(5)
C(9)-C(10)	1.522(5)
C(11)-C(12)	1.543(4)
C(11)-H(11B)	0.9900
C(11)-H(11A)	0.9900
C(12)-C(13)	1.516(5)
C(12)-H(12B)	0.9900
C(12)-H(12A)	0.9900
C(13)-C(18)	1.395(5)
C(13)-C(14)	1.397(5)
C(14)-C(15)	1.387(6)
C(14)-H(14)	0.9500
C(15)-C(16)	1.375(6)
C(15)-H(15)	0.9500
C(16)-C(17)	1.389(5)
C(16)-H(16)	0.9500
C(17)-C(18)	1.384(6)
C(17)-H(17)	0.9500
C(18)-H(18)	0.9500

C(9)-N(2)-C(8)	119.2(3)
N(1)-C(1)-C(2)	178.0(4)
C(7)-C(2)-C(3)	122.1(3)
C(7)-C(2)-C(1)	120.1(3)
C(3)-C(2)-C(1)	117.8(3)
C(2)-C(3)-C(4)	117.8(3)
C(2)-C(3)-H(3)	121.1
C(4)-C(3)-H(3)	121.1
C(3)-C(4)-C(5)	121.8(3)
C(3)-C(4)-Cl(1)	117.9(3)
C(5)-C(4)-Cl(1)	120.3(2)
C(6)-C(5)-C(4)	118.2(3)
C(6)-C(5)-C(8)	121.9(3)
C(4)-C(5)-C(8)	119.9(3)
C(5)-C(6)-C(7)	121.5(3)
C(5)-C(6)-H(6)	119.2
C(7)-C(6)-H(6)	119.2
C(2)-C(7)-C(6)	118.6(3)
C(2)-C(7)-H(7)	120.7
C(6)-C(7)-H(7)	120.7
N(2)-C(8)-C(5)	112.0(3)
N(2)-C(8)-H(8A)	109.2
C(5)-C(8)-H(8A)	109.2
N(2)-C(8)-H(8B)	109.2
C(5)-C(8)-H(8B)	109.2
H(8A)-C(8)-H(8B)	107.9
N(2)-C(9)-C(11)	129.9(3)
N(2)-C(9)-C(10)	115.2(3)
C(11)-C(9)-C(10)	114.9(3)
F(3)-C(10)-F(1)	107.2(3)
F(3)-C(10)-F(2)	106.3(3)
F(1)-C(10)-F(2)	106.8(3)
F(3)-C(10)-C(9)	114.0(3)
F(1)-C(10)-C(9)	112.1(3)
F(2)-C(10)-C(9)	110.1(3)
C(9)-C(11)-C(12)	111.5(3)
C(9)-C(11)-H(11B)	109.3
C(12)-C(11)-H(11B)	109.3
C(9)-C(11)-H(11A)	109.3
C(12)-C(11)-H(11A)	109.3
H(11B)-C(11)-H(11A)	108.0
C(13)-C(12)-C(11)	113.8(3)
C(13)-C(12)-H(12B)	108.8
C(11)-C(12)-H(12B)	108.8

C(13)-C(12)-H(12A)	108.8
C(11)-C(12)-H(12A)	108.8
H(12B)-C(12)-H(12A)	107.7
C(18)-C(13)-C(14)	117.7(3)
C(18)-C(13)-C(12)	122.6(3)
C(14)-C(13)-C(12)	119.7(3)
C(15)-C(14)-C(13)	120.7(4)
C(15)-C(14)-H(14)	119.6
C(13)-C(14)-H(14)	119.6
C(16)-C(15)-C(14)	121.0(3)
C(16)-C(15)-H(15)	119.5
C(14)-C(15)-H(15)	119.5
C(15)-C(16)-C(17)	119.0(4)
C(15)-C(16)-H(16)	120.5
C(17)-C(16)-H(16)	120.5
C(18)-C(17)-C(16)	120.4(4)
C(18)-C(17)-H(17)	119.8
C(16)-C(17)-H(17)	119.8
C(17)-C(18)-C(13)	121.2(3)
C(17)-C(18)-H(18)	119.4
C(13)-C(18)-H(18)	119.4

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for a.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Cl(1)	31(1)	28(1)	33(1)	1(1)	11(1)	7(1)
F(1)	28(1)	79(2)	40(1)	4(1)	5(1)	-4(1)
F(2)	66(2)	69(2)	21(1)	-12(1)	12(1)	8(1)
F(3)	58(2)	39(2)	36(1)	9(1)	6(1)	5(1)
N(1)	38(2)	35(2)	30(2)	-4(1)	10(1)	-3(2)
N(2)	28(2)	30(2)	18(1)	-4(1)	10(1)	-5(1)
C(1)	31(2)	29(2)	23(2)	-1(1)	13(2)	-2(2)
C(2)	24(2)	25(2)	16(1)	0(1)	9(1)	-3(1)
C(3)	21(2)	29(2)	17(1)	0(1)	6(1)	-4(1)
C(4)	25(2)	24(2)	22(2)	1(1)	14(1)	0(1)
C(5)	24(2)	23(2)	17(1)	1(1)	11(1)	-2(1)
C(6)	22(2)	26(2)	20(1)	-2(1)	7(1)	-2(1)
C(7)	26(2)	24(2)	22(2)	-3(1)	10(1)	1(1)
C(8)	28(2)	24(2)	23(2)	-1(1)	9(1)	0(2)
C(9)	29(2)	29(2)	20(2)	-9(1)	13(1)	-4(2)
C(10)	33(2)	39(2)	23(2)	-6(1)	9(2)	-4(2)
C(11)	29(2)	27(2)	28(2)	-6(1)	13(1)	-2(2)
C(12)	30(2)	27(2)	31(2)	-1(1)	15(2)	1(2)
C(13)	19(2)	30(2)	32(2)	0(1)	15(1)	-1(1)
C(14)	25(2)	42(2)	30(2)	1(2)	11(2)	1(2)
C(15)	30(2)	50(2)	32(2)	11(2)	12(2)	0(2)
C(16)	30(2)	33(2)	48(2)	13(2)	17(2)	2(2)
C(17)	36(2)	35(2)	43(2)	-7(2)	16(2)	-9(2)
C(18)	32(2)	35(2)	27(2)	2(1)	12(2)	-2(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for a.

	x	y	z	U(eq)
H(3)	-1627	4972	93	28
H(6)	1769	4227	2255	28
H(7)	1012	2039	1198	29
H(8A)	1269	8286	2194	31
H(8B)	503	7858	2658	31
H(11B)	3296	10224	3961	34
H(11A)	2179	10214	3145	34
H(12B)	4069	9003	3058	35
H(12A)	2955	8910	2245	35
H(14)	3081	10812	1190	39
H(15)	3379	13557	735	45
H(16)	4051	15830	1740	44
H(17)	4393	15351	3221	46
H(18)	4101	12614	3687	38

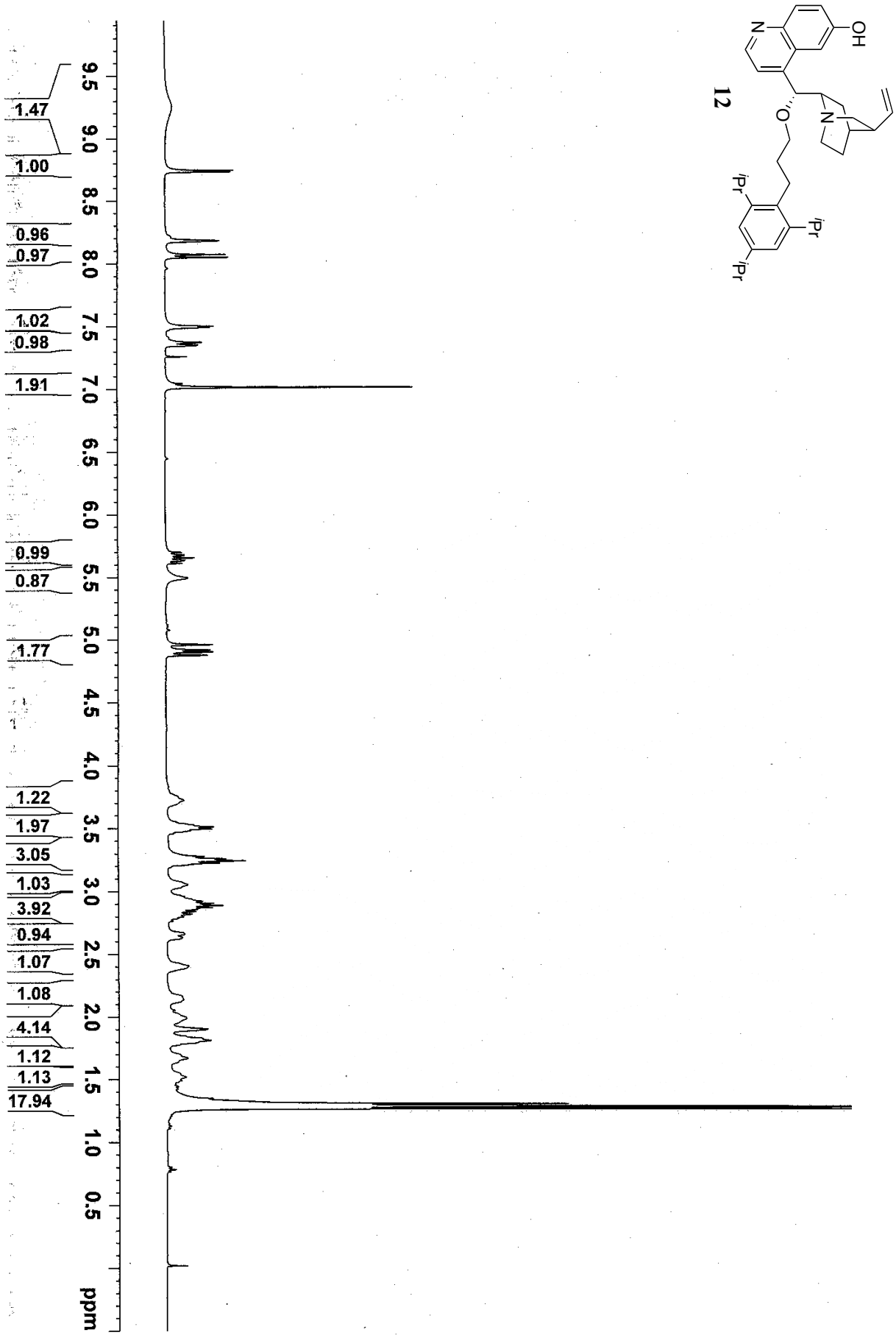
Table 6. Torsion angles [deg] for a.

N(1)-C(1)-C(2)-C(7)	-144(11)
N(1)-C(1)-C(2)-C(3)	33(11)
C(7)-C(2)-C(3)-C(4)	-1.7(4)
C(1)-C(2)-C(3)-C(4)	-178.2(3)
C(2)-C(3)-C(4)-C(5)	-0.2(4)
C(2)-C(3)-C(4)-Cl(1)	179.4(2)
C(3)-C(4)-C(5)-C(6)	1.6(4)
Cl(1)-C(4)-C(5)-C(6)	-178.0(2)
C(3)-C(4)-C(5)-C(8)	178.2(3)
Cl(1)-C(4)-C(5)-C(8)	-1.3(4)
C(4)-C(5)-C(6)-C(7)	-1.2(4)
C(8)-C(5)-C(6)-C(7)	-177.8(3)
C(3)-C(2)-C(7)-C(6)	2.0(5)
C(1)-C(2)-C(7)-C(6)	178.5(3)
C(5)-C(6)-C(7)-C(2)	-0.5(5)
C(9)-N(2)-C(8)-C(5)	147.4(3)
C(6)-C(5)-C(8)-N(2)	-21.5(4)
C(4)-C(5)-C(8)-N(2)	162.0(3)
C(8)-N(2)-C(9)-C(11)	-3.0(5)
C(8)-N(2)-C(9)-C(10)	174.7(3)
N(2)-C(9)-C(10)-F(3)	15.1(4)
C(11)-C(9)-C(10)-F(3)	-166.8(3)
N(2)-C(9)-C(10)-F(1)	137.1(3)
C(11)-C(9)-C(10)-F(1)	-44.9(4)
N(2)-C(9)-C(10)-F(2)	-104.2(4)
C(11)-C(9)-C(10)-F(2)	73.8(4)
N(2)-C(9)-C(11)-C(12)	-86.6(4)
C(10)-C(9)-C(11)-C(12)	95.7(3)
C(9)-C(11)-C(12)-C(13)	177.7(3)
C(11)-C(12)-C(13)-C(18)	45.6(4)
C(11)-C(12)-C(13)-C(14)	-137.2(3)
C(18)-C(13)-C(14)-C(15)	-0.4(5)
C(12)-C(13)-C(14)-C(15)	-177.7(3)
C(13)-C(14)-C(15)-C(16)	0.5(5)
C(14)-C(15)-C(16)-C(17)	-0.7(6)
C(15)-C(16)-C(17)-C(18)	0.7(6)
C(16)-C(17)-C(18)-C(13)	-0.6(6)
C(14)-C(13)-C(18)-C(17)	0.4(5)
C(12)-C(13)-C(18)-C(17)	177.7(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for a [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)


12
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N
O
N
iPr
iPr
iPr
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1.00
0.96
0.97
1.02
0.98
1.91
0.99
0.87
1.77
1.22
1.97
3.05
1.03
3.92
0.94
1.07
1.08
4.14
1.12
1.13
17.94
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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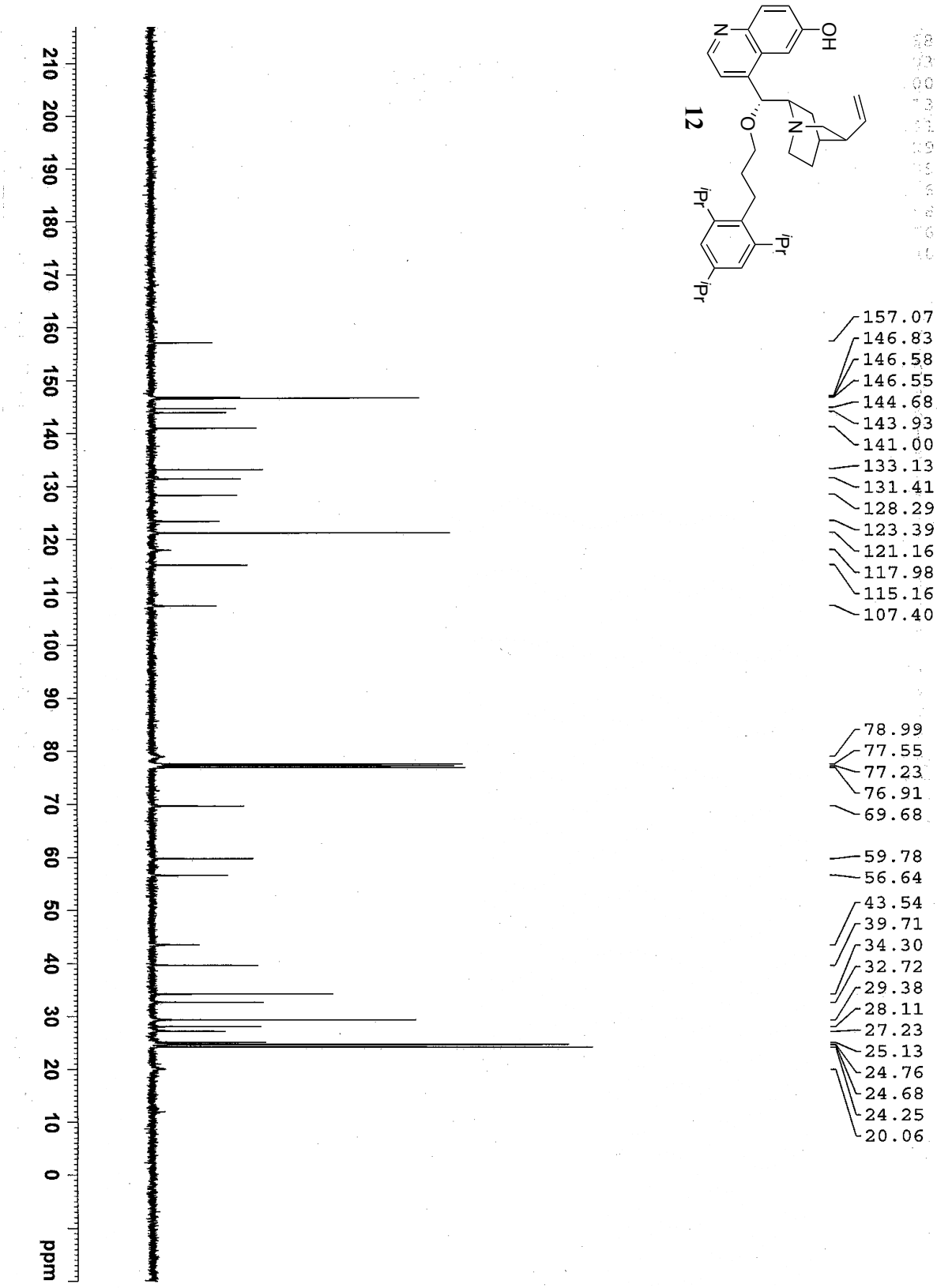
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


12
OH
N
O
N
iPr
iPr
iPr
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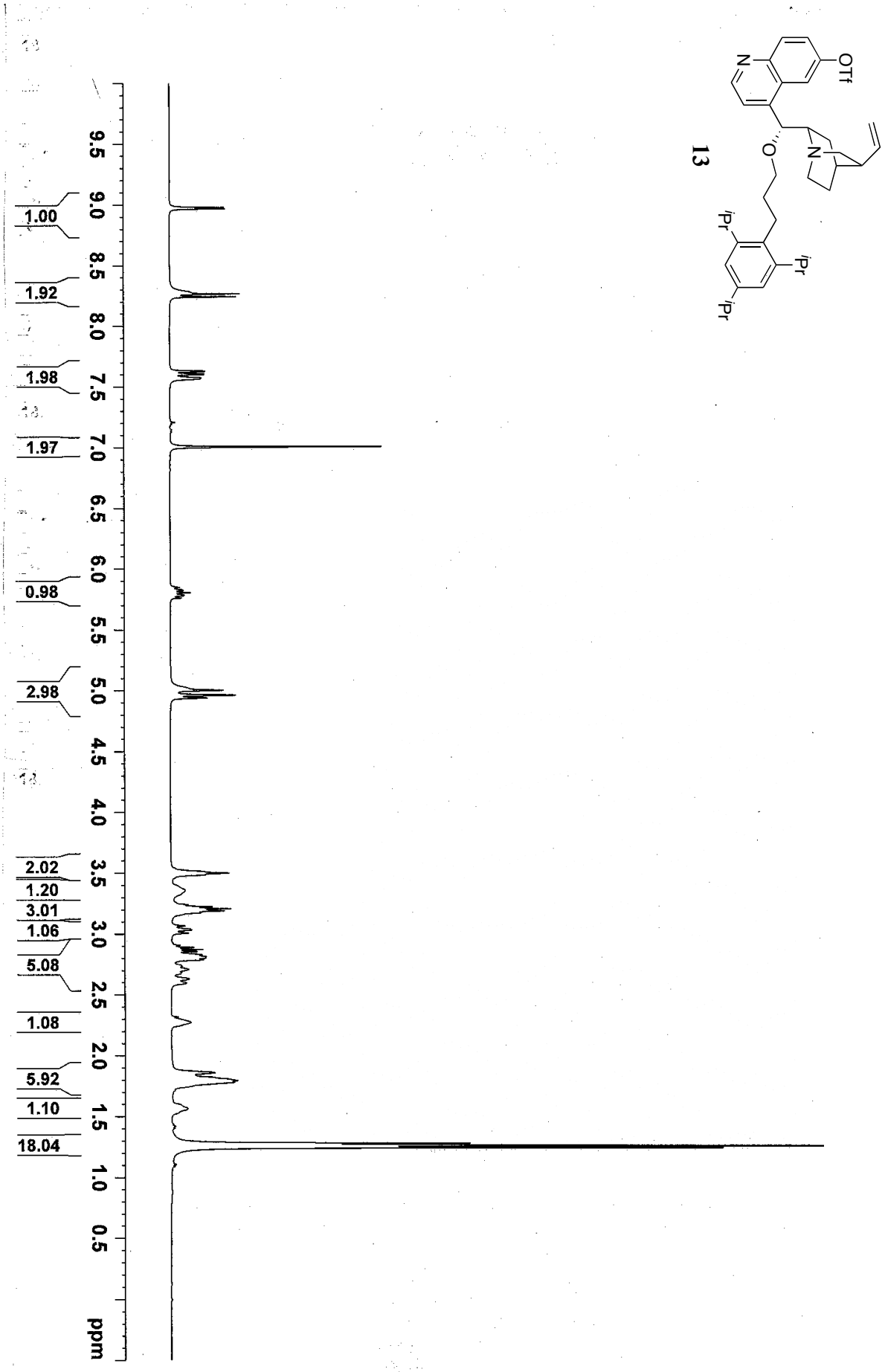
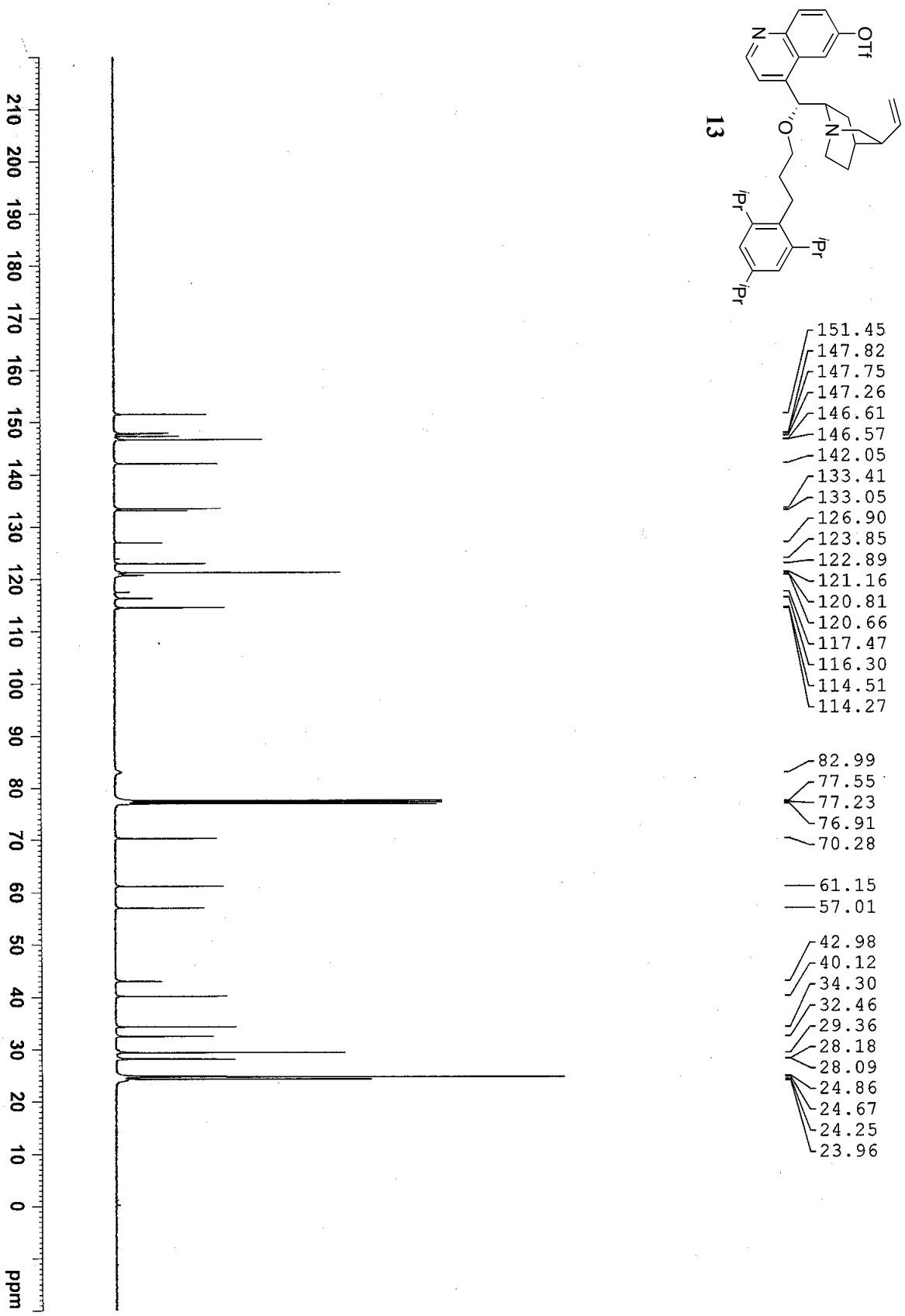
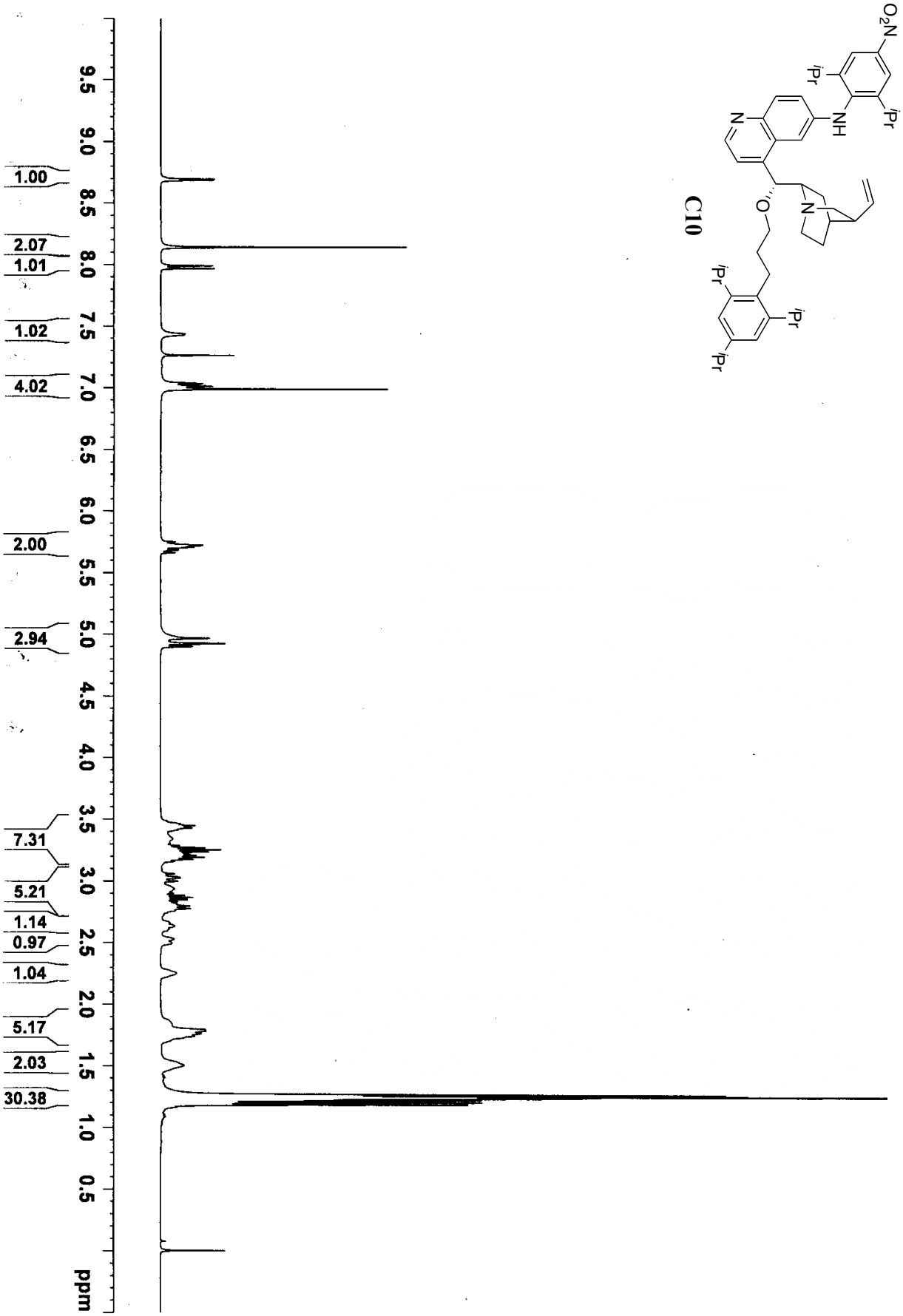
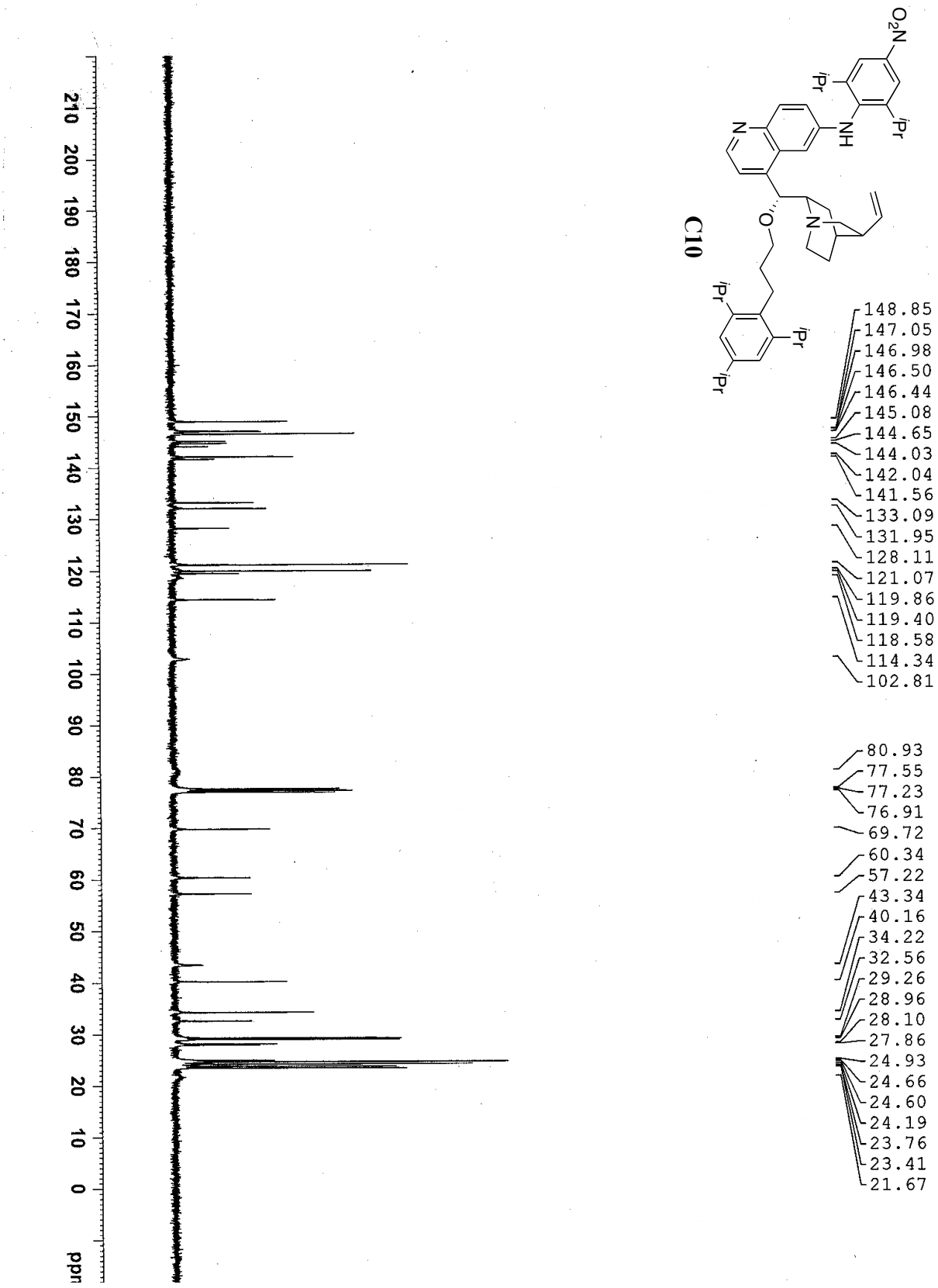
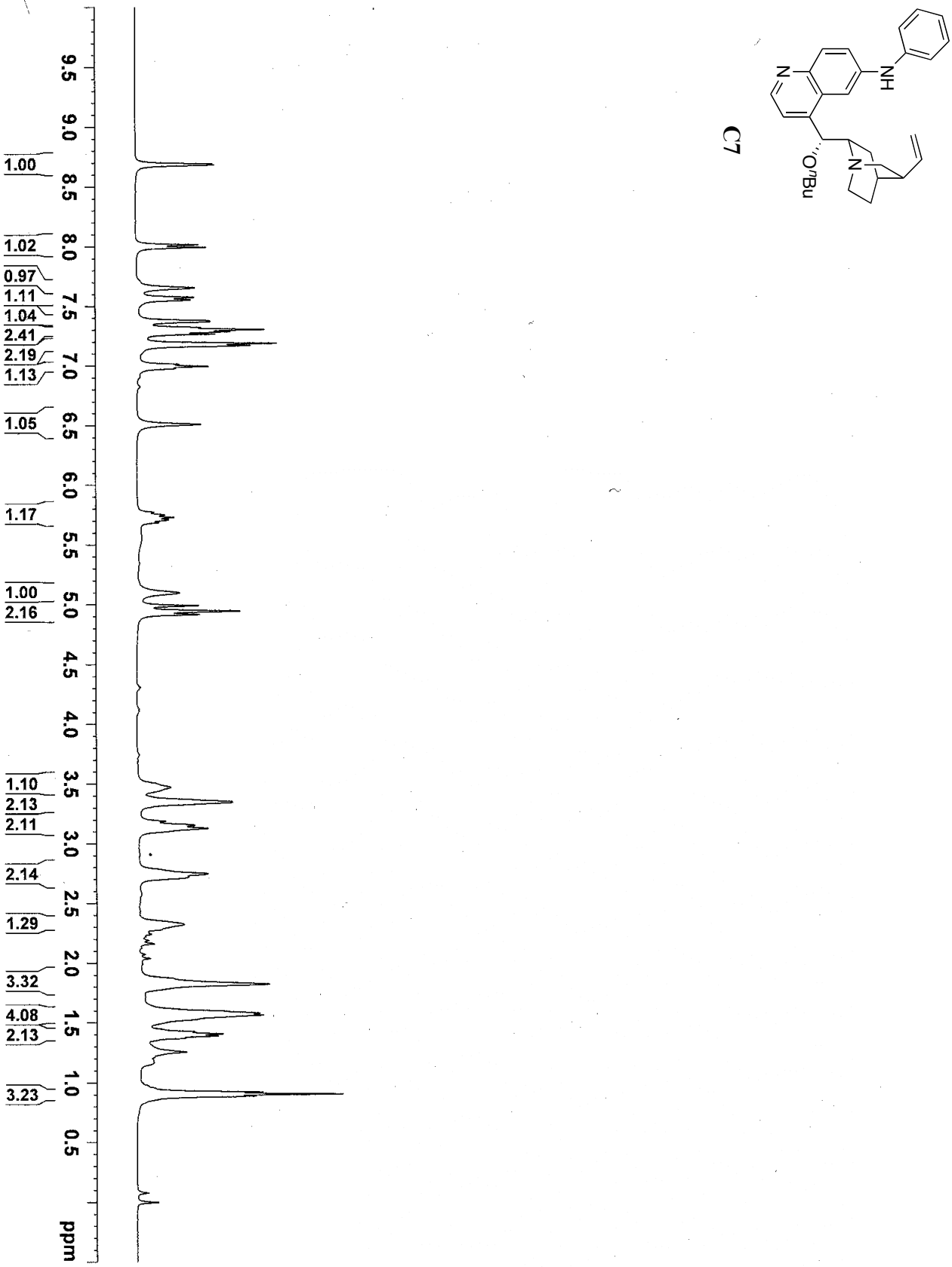
146.58
146.55
144.68
143.93
141.00
133.13
131.41
128.29
123.39
121.16
117.98
115.16
107.40
78.99
77.55
77.23
76.91
69.68
59.78
56.64
43.54
39.71
34.30
32.72
29.38
28.11
27.23
25.13
24.76
24.68
24.25
20.06
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

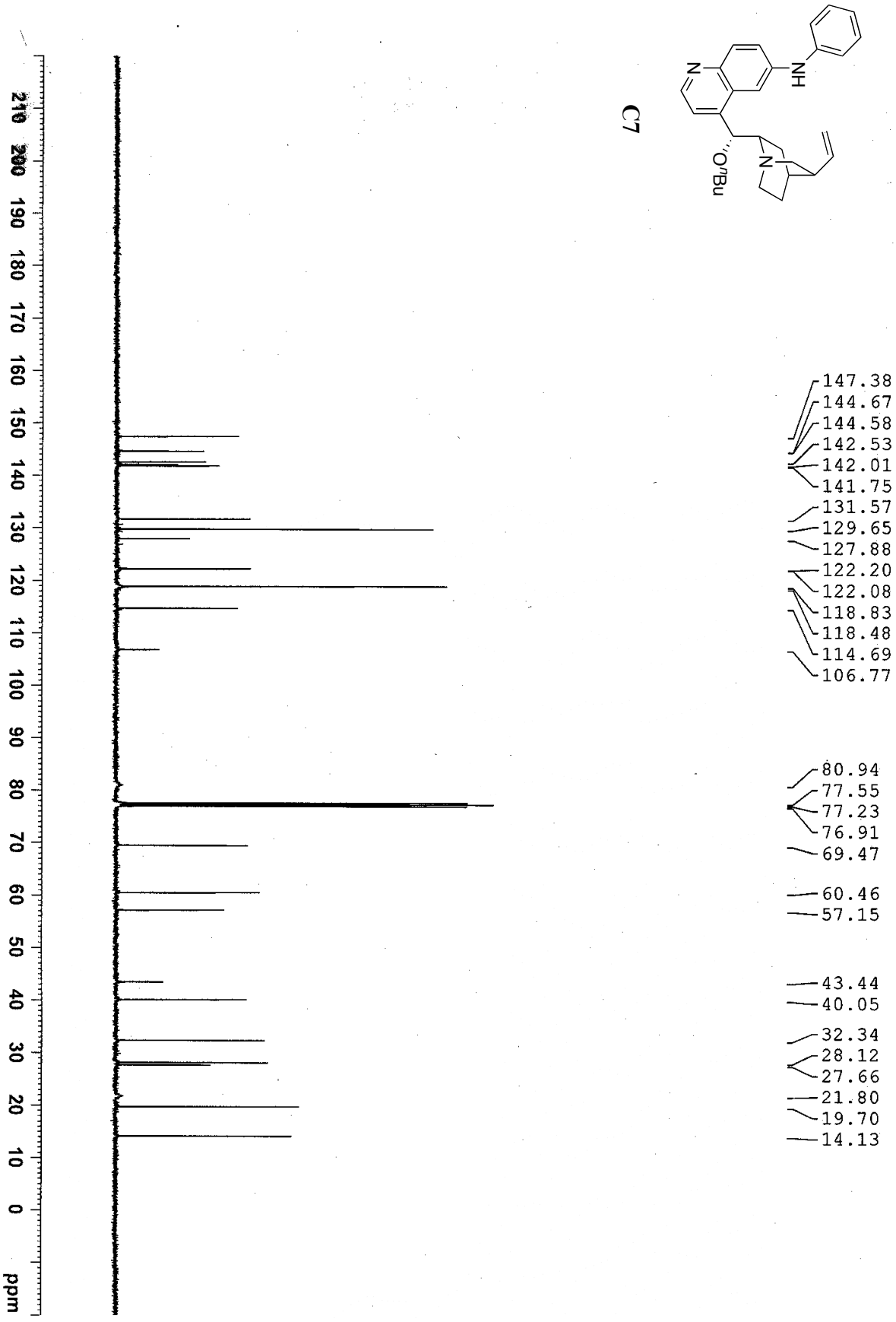


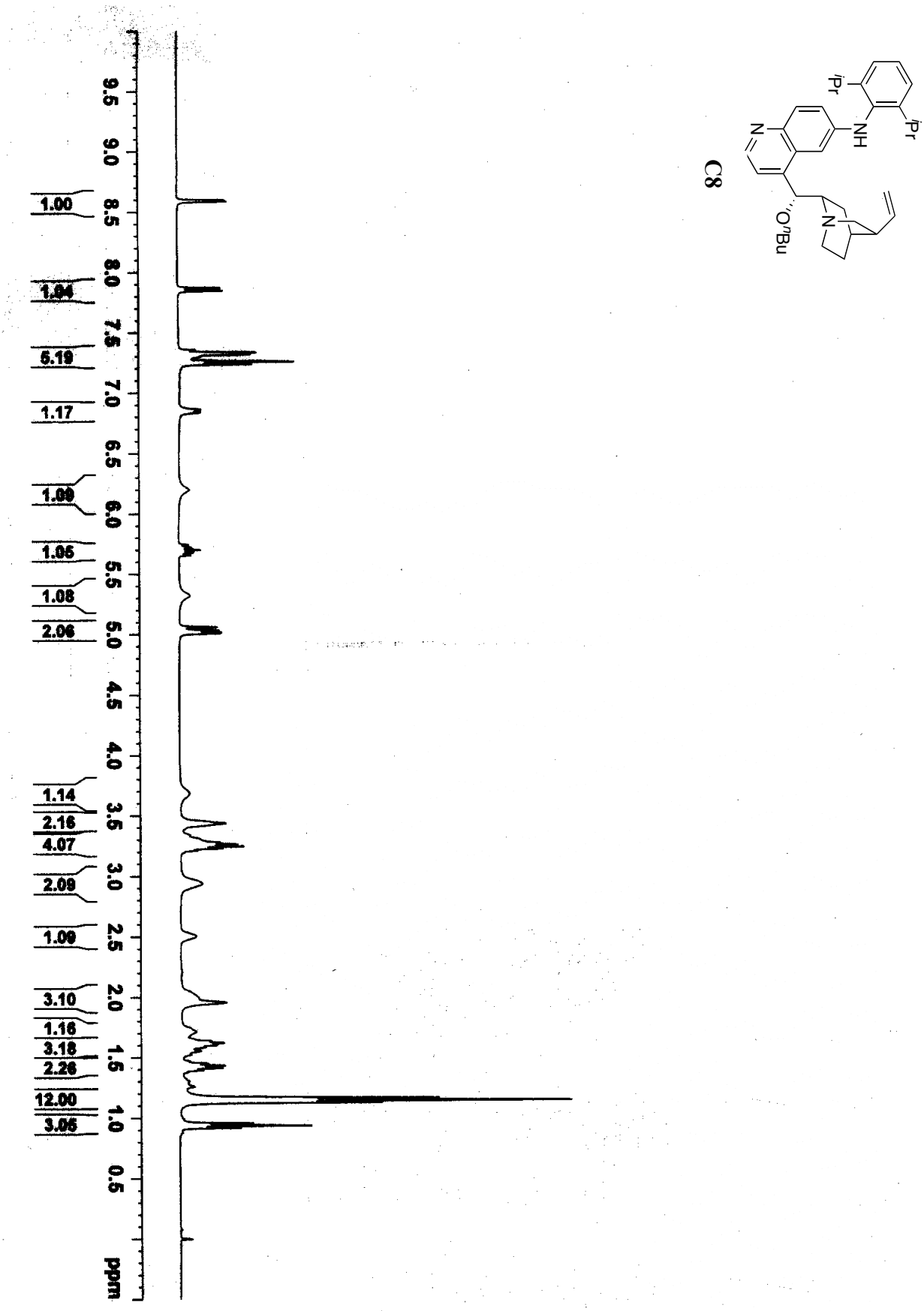

13
OTf
N
O
N
iPr
iPr
iPr
151.45
147.82
147.75
147.26
146.61
146.57
142.05
133.41
133.05
126.90
123.85
122.89
121.16
120.81
120.66
117.47
116.30
114.51
114.27
82.99
77.55
77.23
76.91
70.28
61.15
57.01
42.98
40.12
34.30
32.46
29.36
28.18
28.09
24.86
24.67
24.25
23.96
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm




C10
148.85
147.05
146.98
146.50
146.44
145.08
144.65
144.03
142.04
141.56
133.09
131.95
128.11
121.07
119.86
119.40
118.58
114.34
102.81
80.93
77.55
77.23
76.91
69.72
60.34
57.22
43.34
40.16
34.22
32.56
29.26
28.96
28.10
27.86
24.93
24.66
24.60
24.19
23.76
23.41
21.67
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

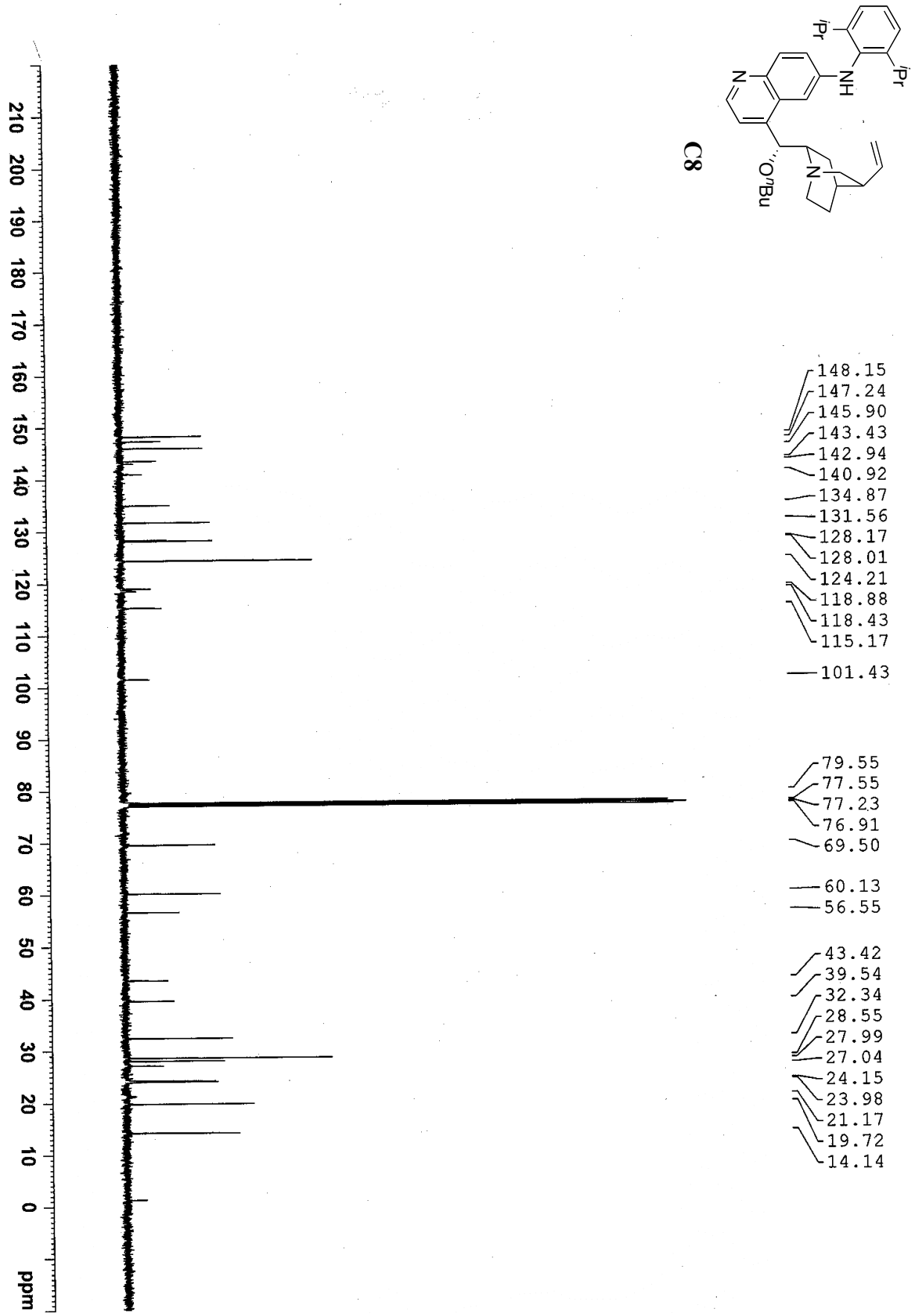

1.00
1.02
0.97
1.11
1.04
2.41
2.19
1.13
1.05
1.17
1.00
2.16
1.10
2.13
2.11
2.14
1.29
3.32
4.08
2.13
3.23
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
C7
N
NH
N
O^{n}Bu


C7
147.38
144.67
144.58
142.53
142.01
141.75
131.57
129.65
127.88
122.20
122.08
118.83
118.48
114.69
106.77
80.94
77.55
77.23
76.91
69.47
60.46
57.15
43.44
40.05
32.34
28.12
27.66
21.80
19.70
14.13
ppm


1.00
1.04
5.19
1.17
1.09
1.05
1.08
2.06
1.14
2.16
4.07
2.09
1.09
3.10
1.16
3.18
2.26
12.00
3.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

iPr
NH
iPr
N
O"Bu
N

C8


C8
148.15
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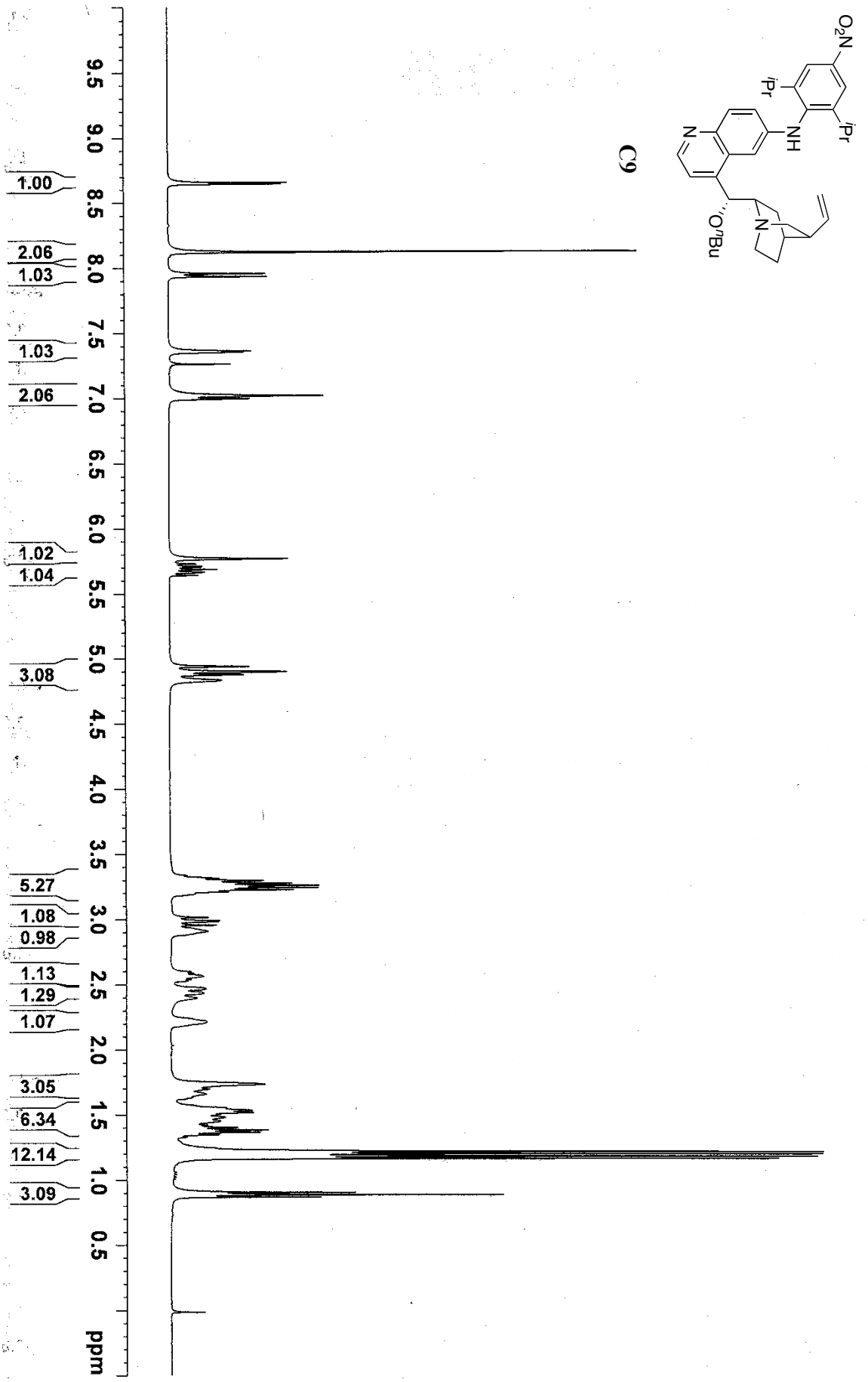
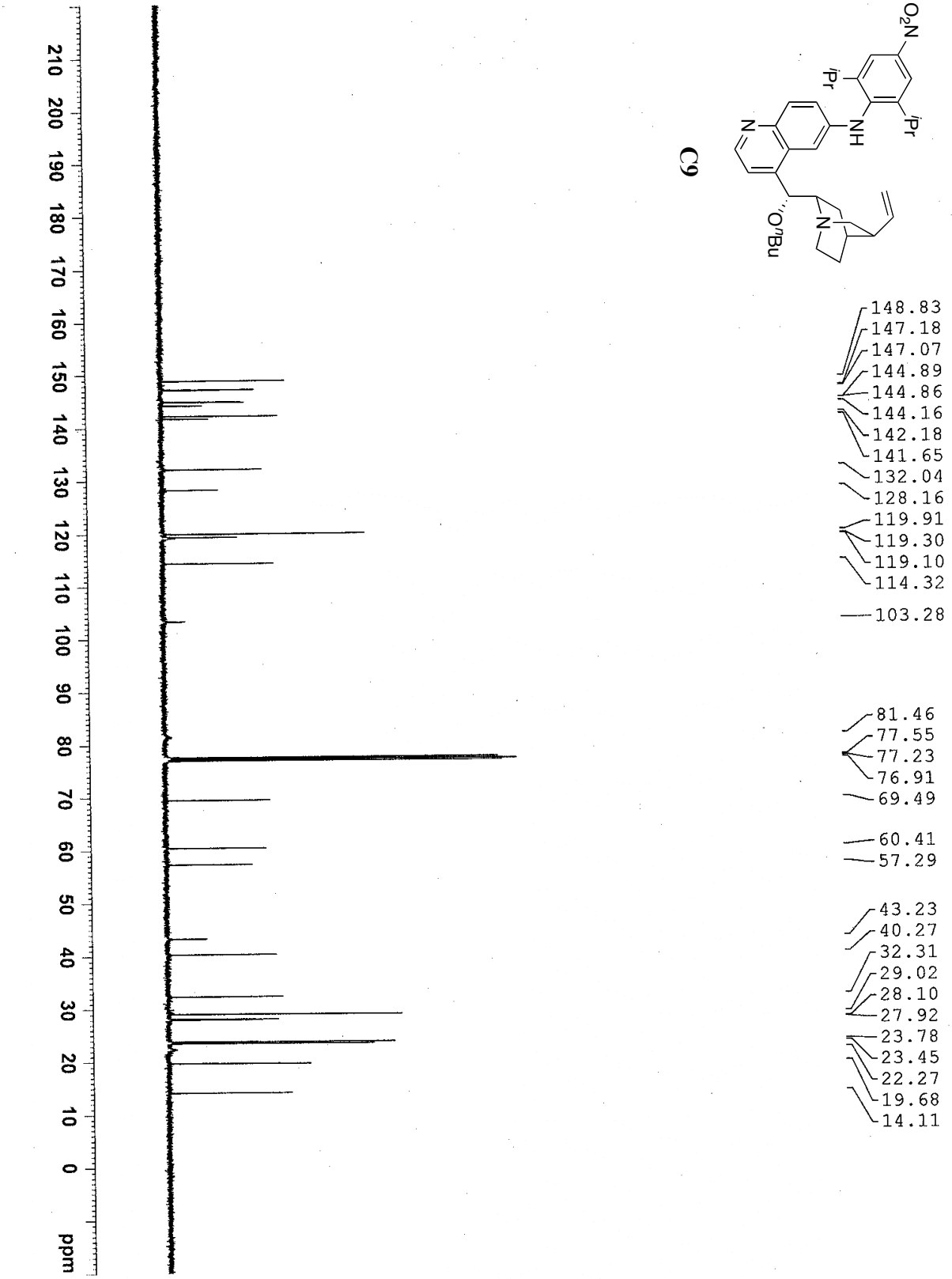
145.90
143.43
142.94
140.92
134.87
131.56
128.17
128.01
124.21
118.88
118.43
115.17
101.43
79.55
77.55
77.23
76.91
69.50
60.13
56.55
43.42
39.54
32.34
28.55
27.99
27.04
24.15
23.98
21.17
19.72
14.14
ppm


C9
O2N
iPr
iPr
NH
N
N
OnBu
1.00
2.06
1.03
1.03
2.06
1.02
1.04
3.08
5.27
1.08
0.98
1.13
1.29
1.07
3.05
6.34
12.14
3.09
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


C9
148.83
147.18
147.07
144.89
144.86
144.16
142.18
141.65
132.04
128.16
119.91
119.30
119.10
114.32
103.28
81.46
77.55
77.23
76.91
69.49
60.41
57.29
43.23
40.27
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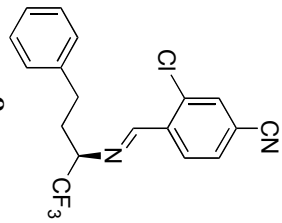
28.10
27.92
23.78
23.45
22.27
19.68
14.11
ppm

Table 2, entry 1

8a



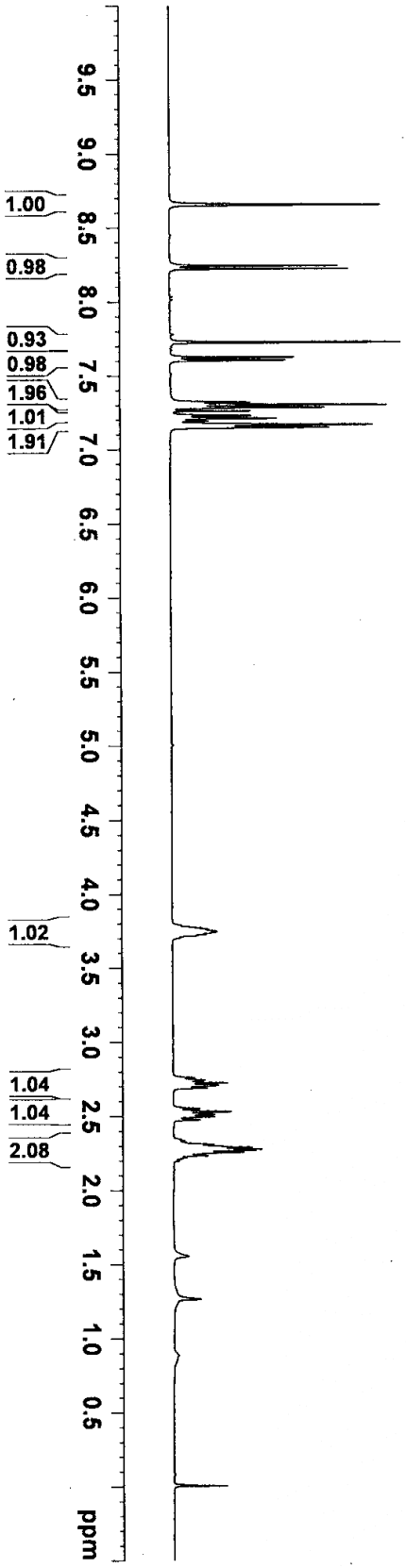


Table 2, entry 1

8a

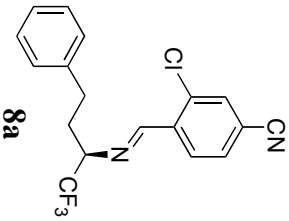


Table 2, entry 1

8a

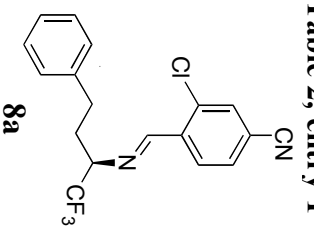
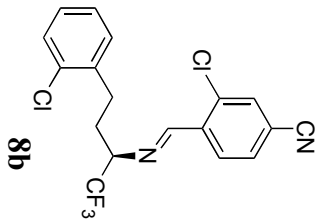


Table 2, entry 2



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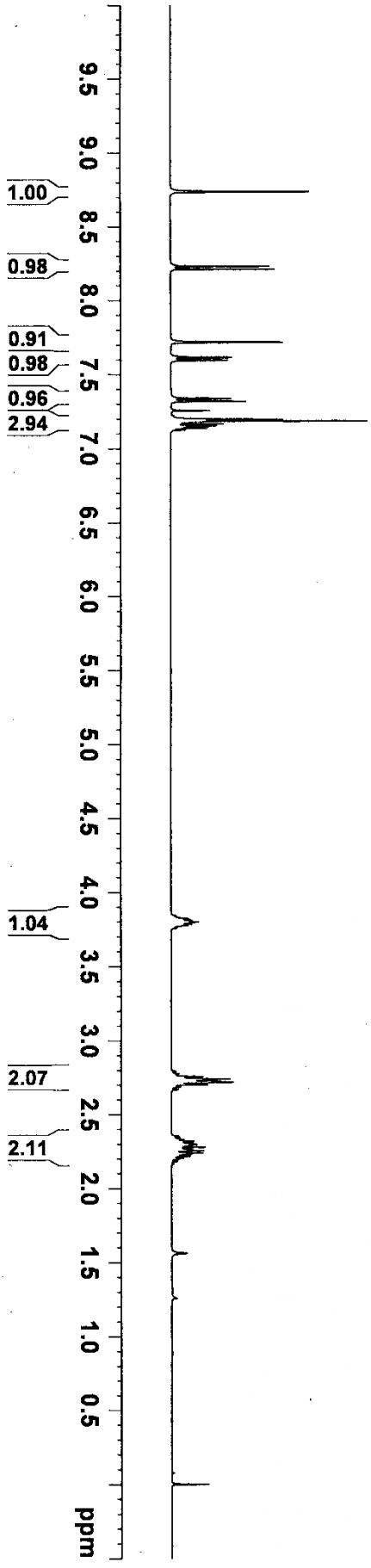
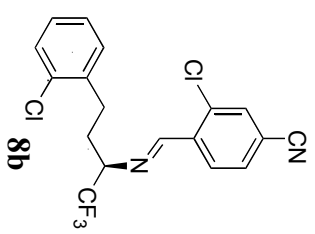
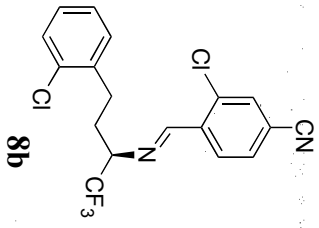


Table 2, entry 2



8b

Table 2, entry 2



8b

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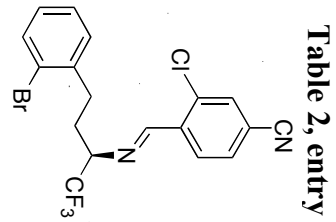

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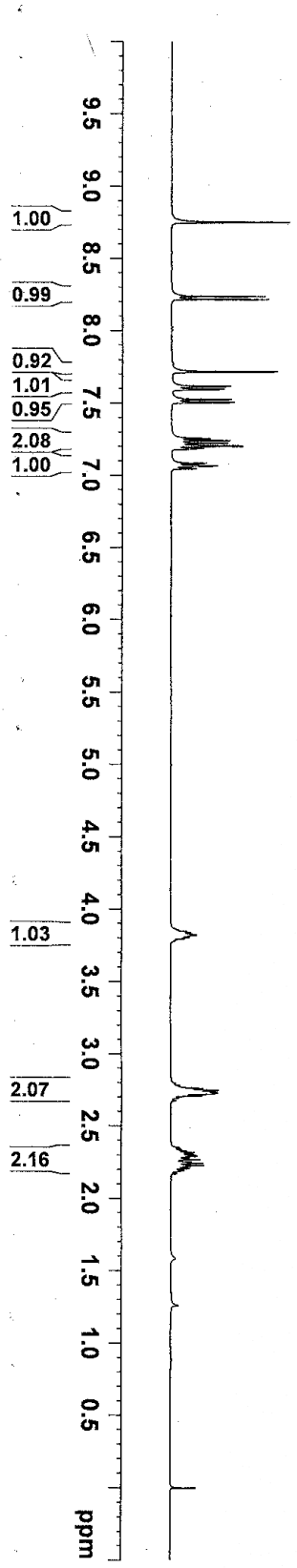

Table 2, entry 3

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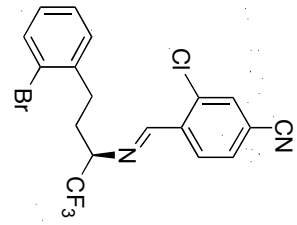

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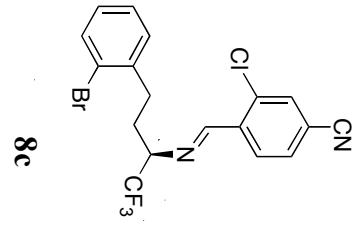

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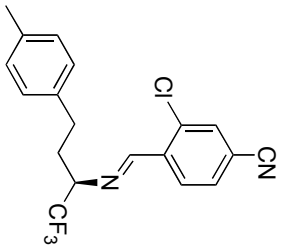
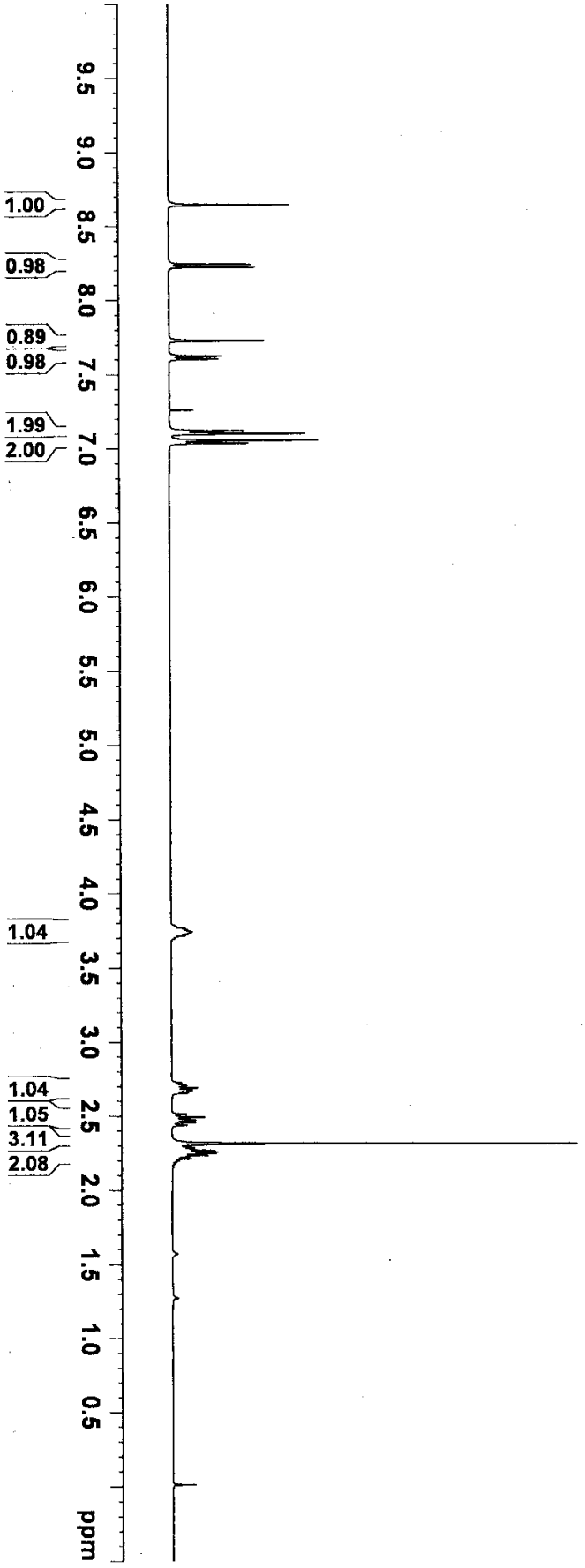
Table 2, entry 4

8d





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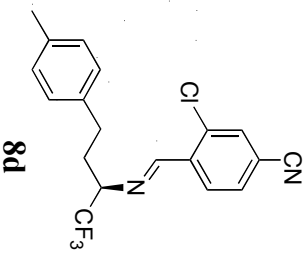

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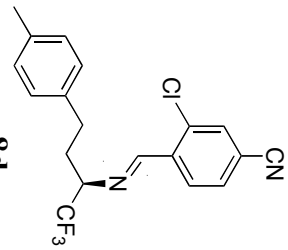

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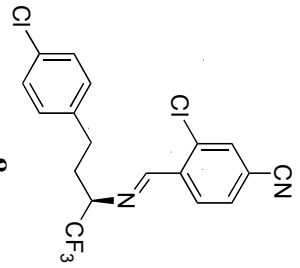

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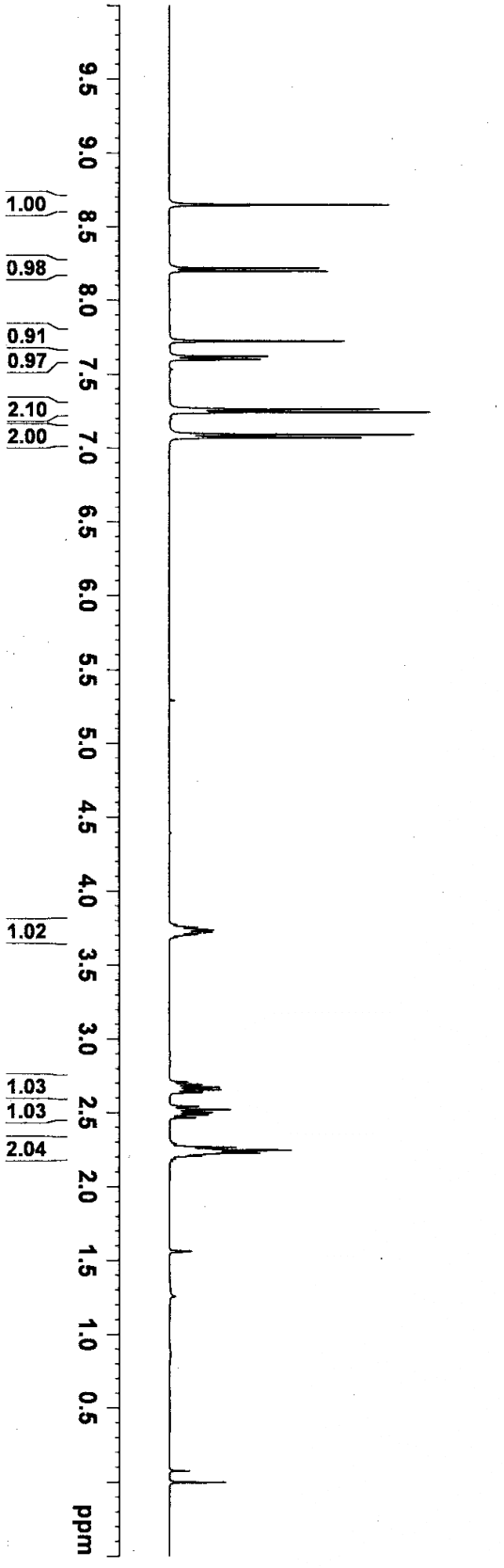

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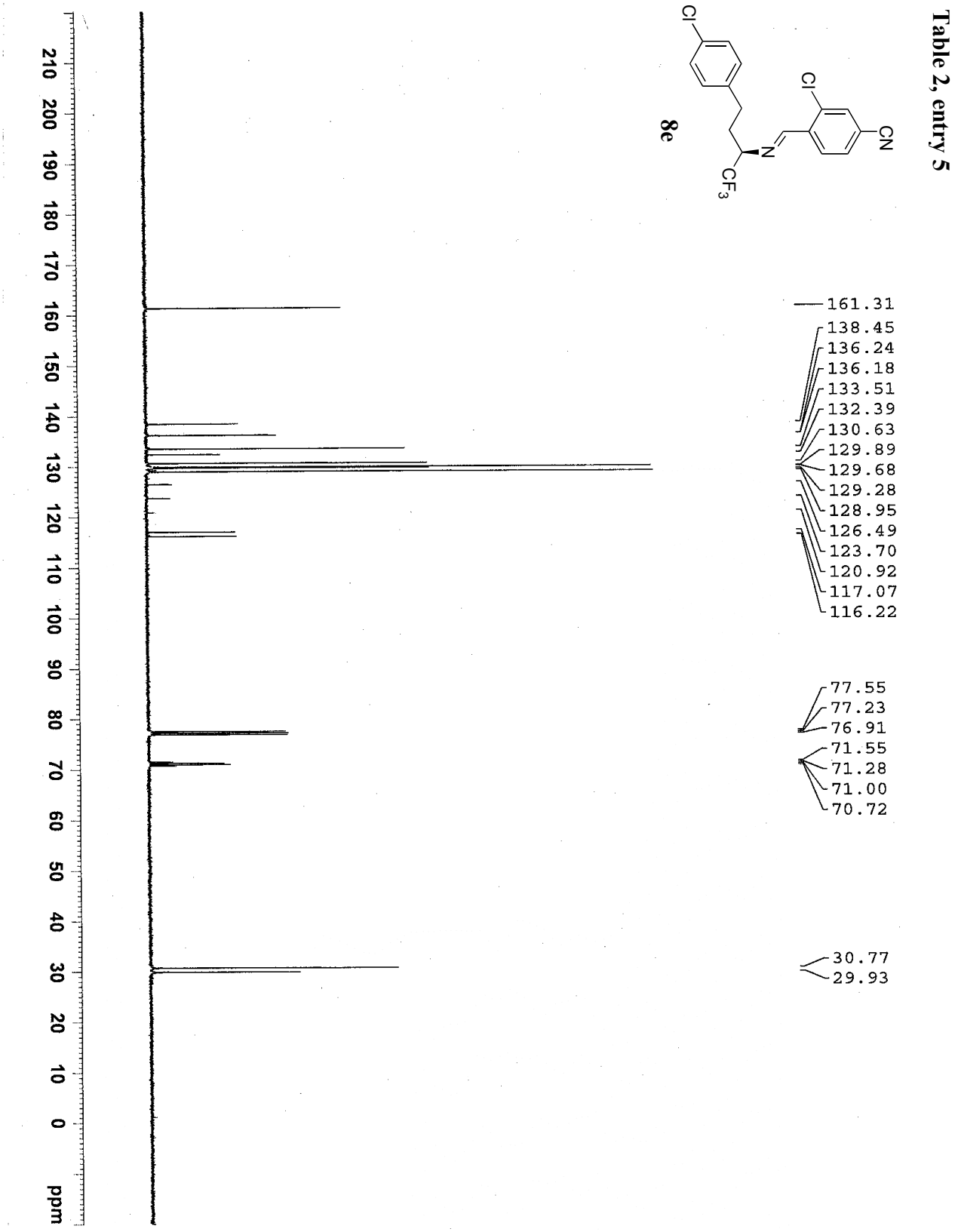

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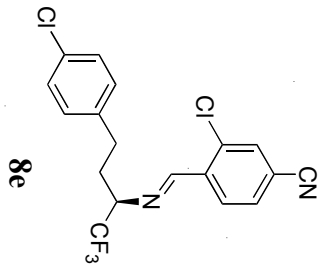

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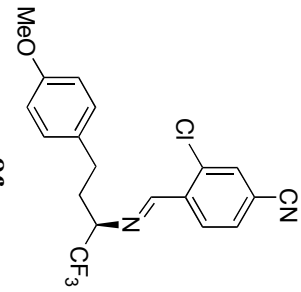

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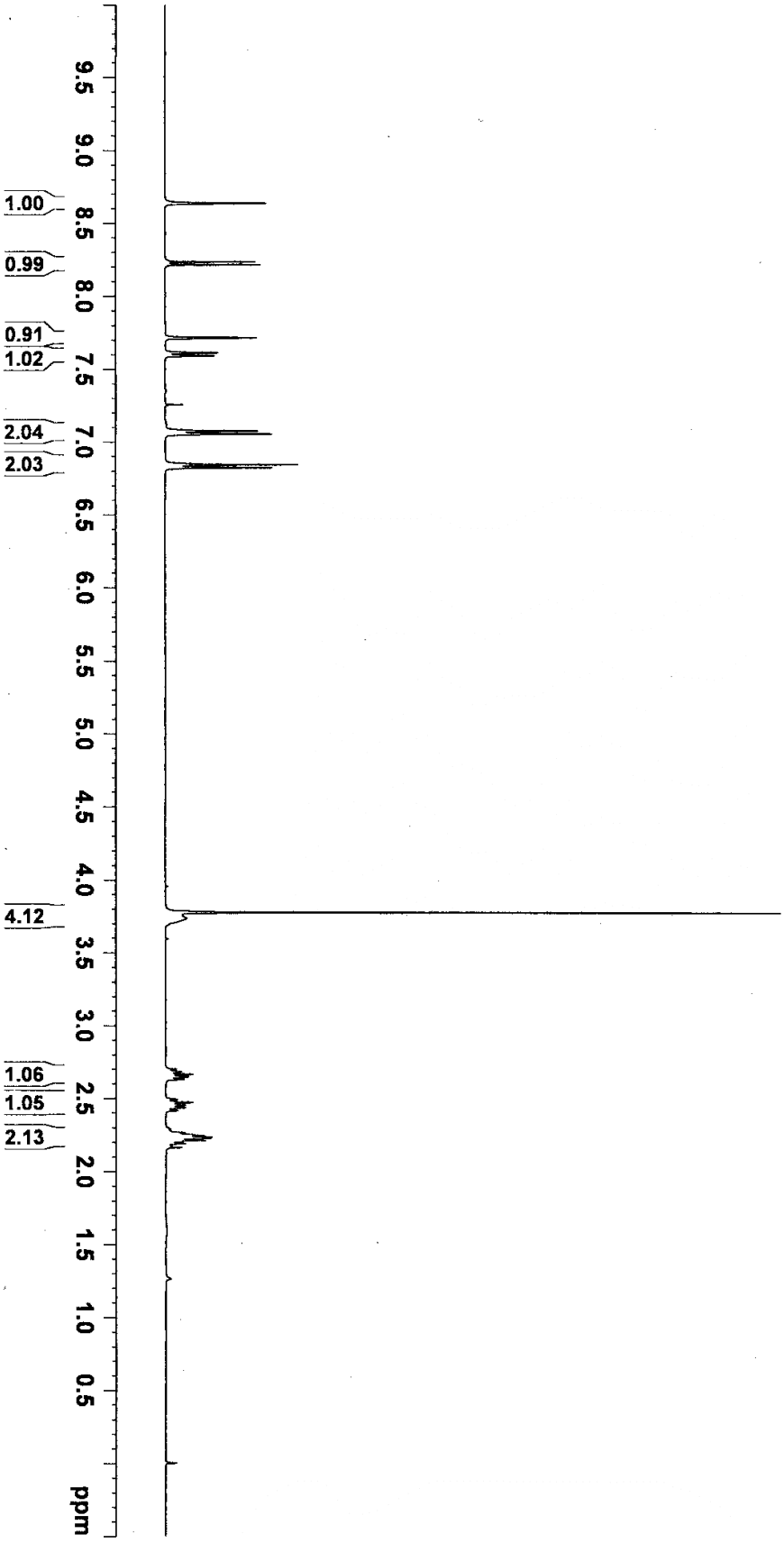

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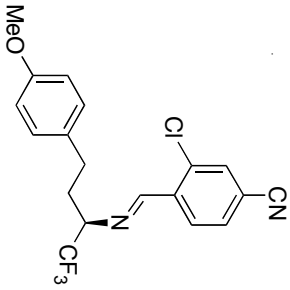

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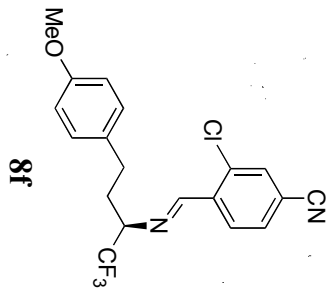

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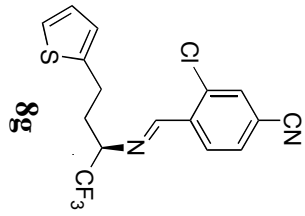
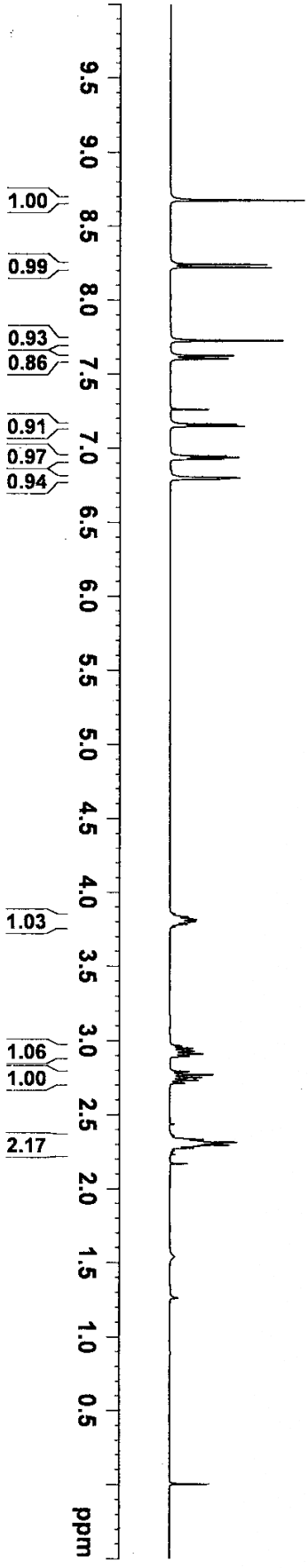


8g



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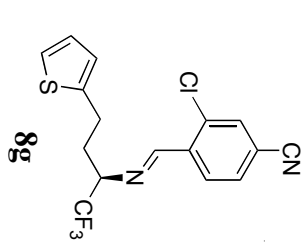

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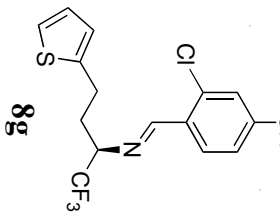

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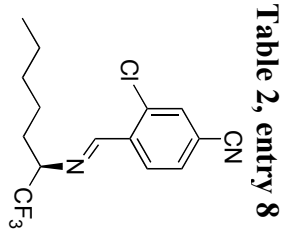
Table 2, entry 8

8h



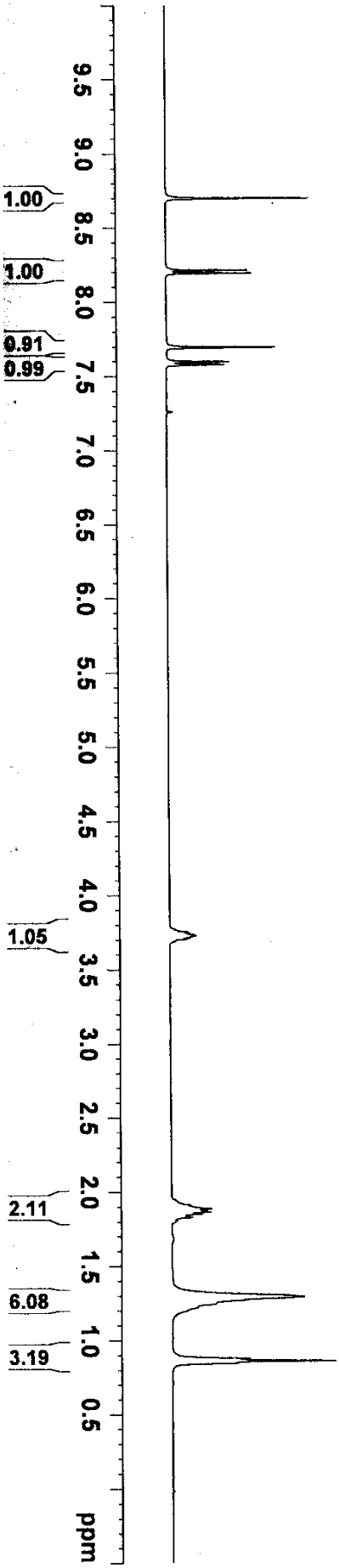


Table 2, entry 8

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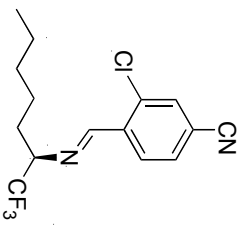

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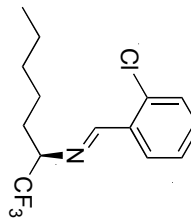

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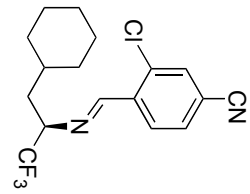

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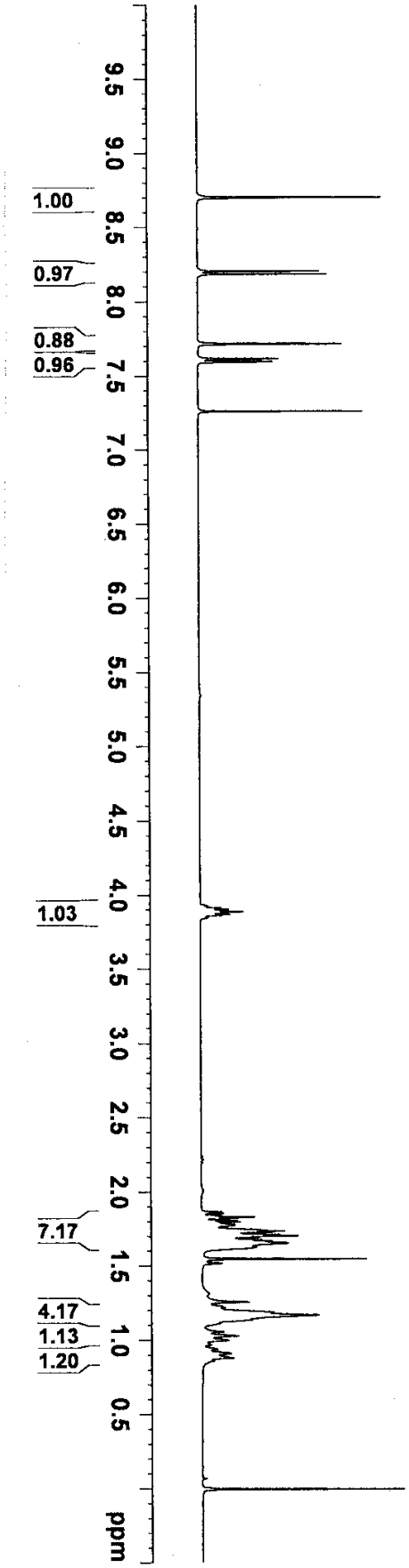

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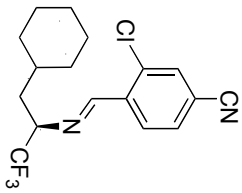

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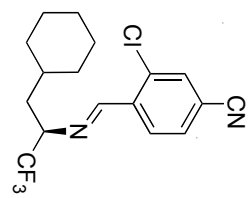

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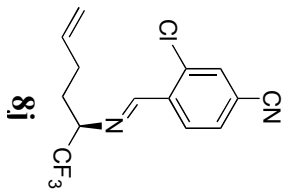

8j

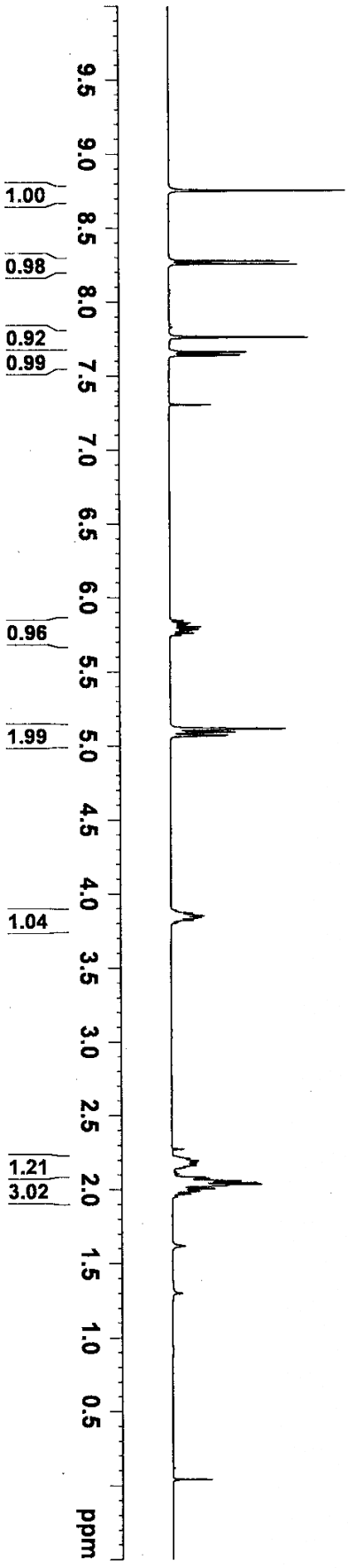

Table 2, entry 10

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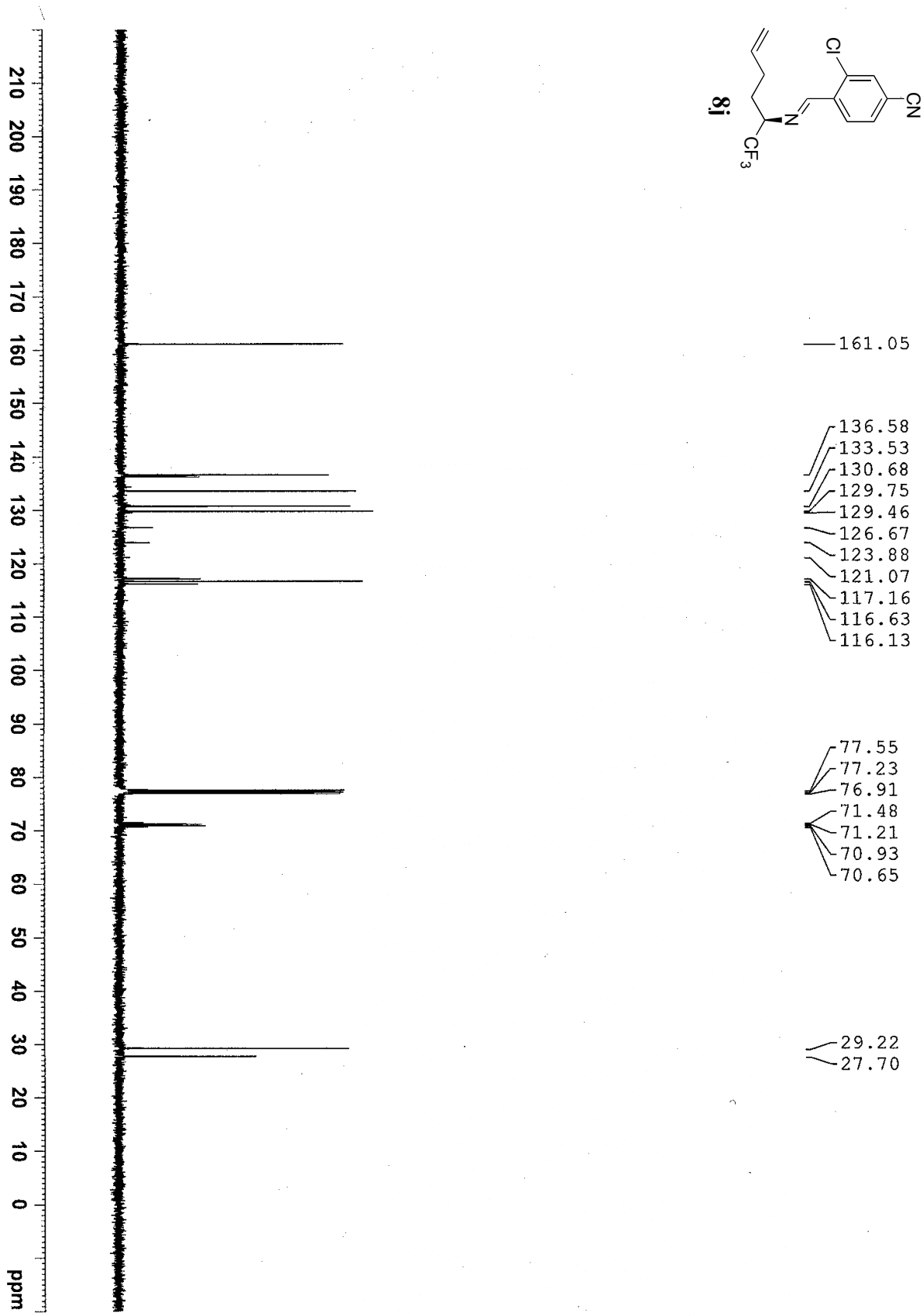

Table 2, entry 10

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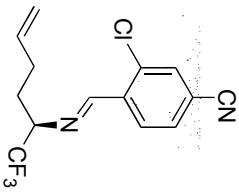

Table 2, entry 11

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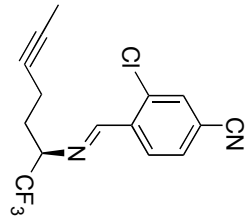

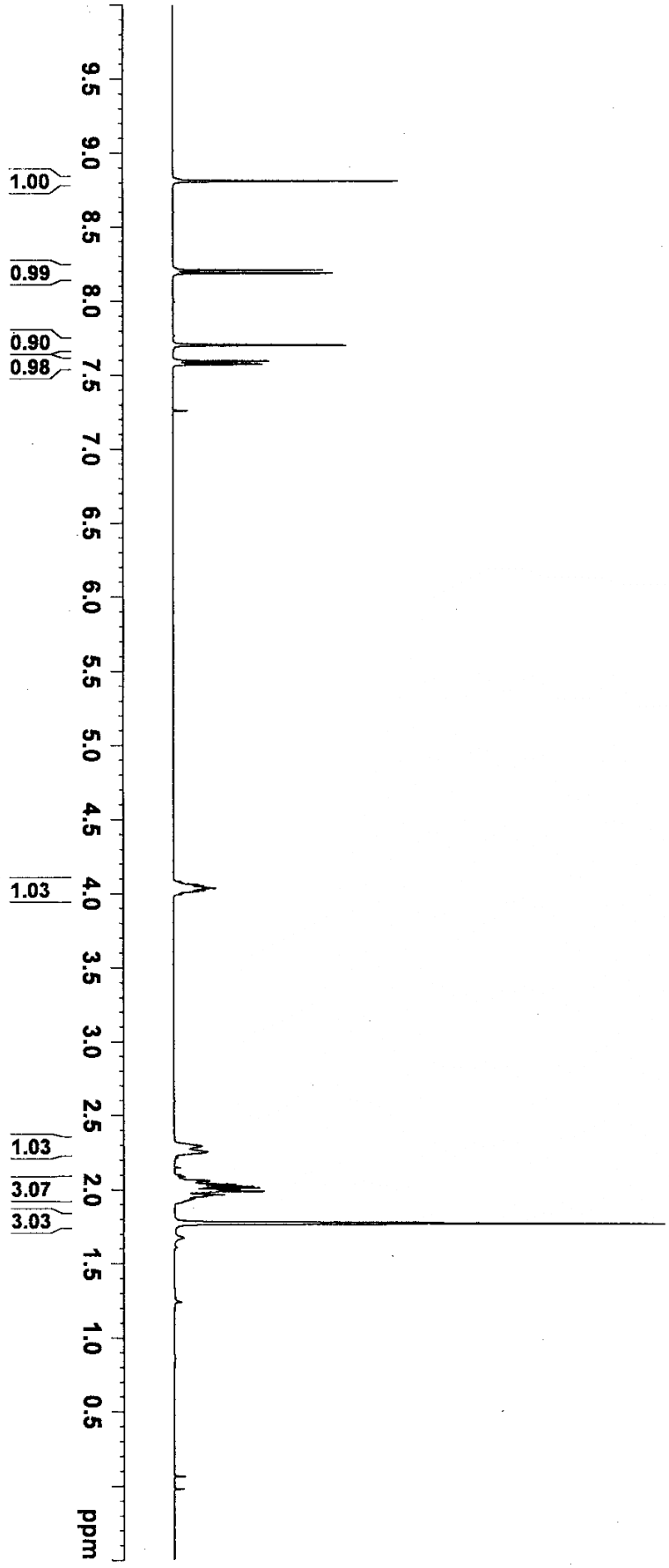

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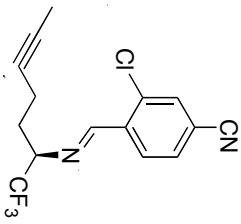

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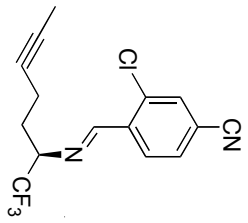
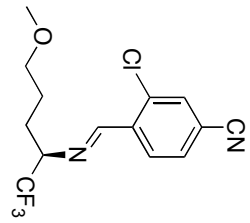
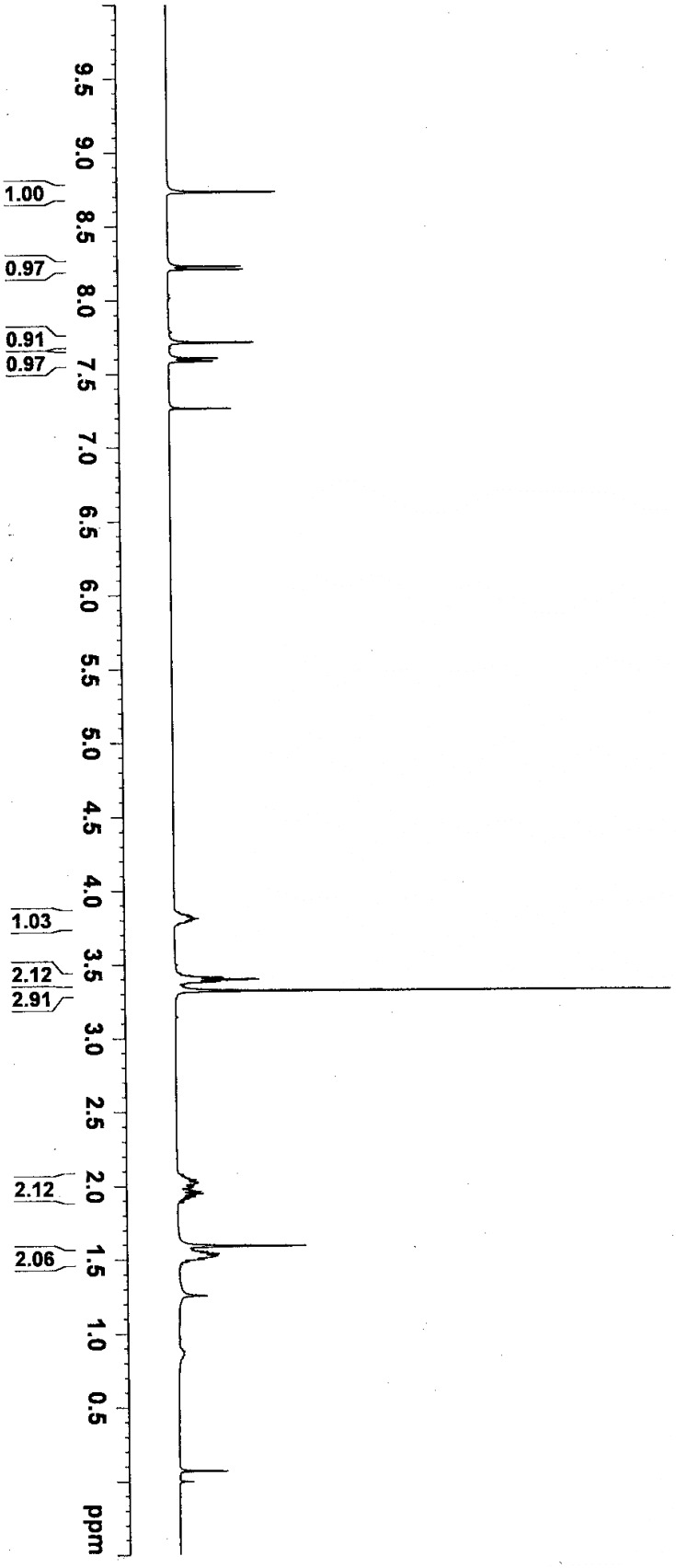


Table 2, entry 12



8l



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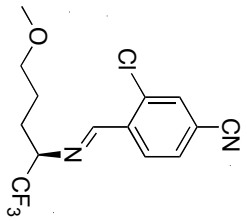
8l



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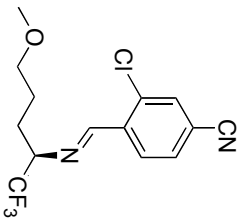

8l

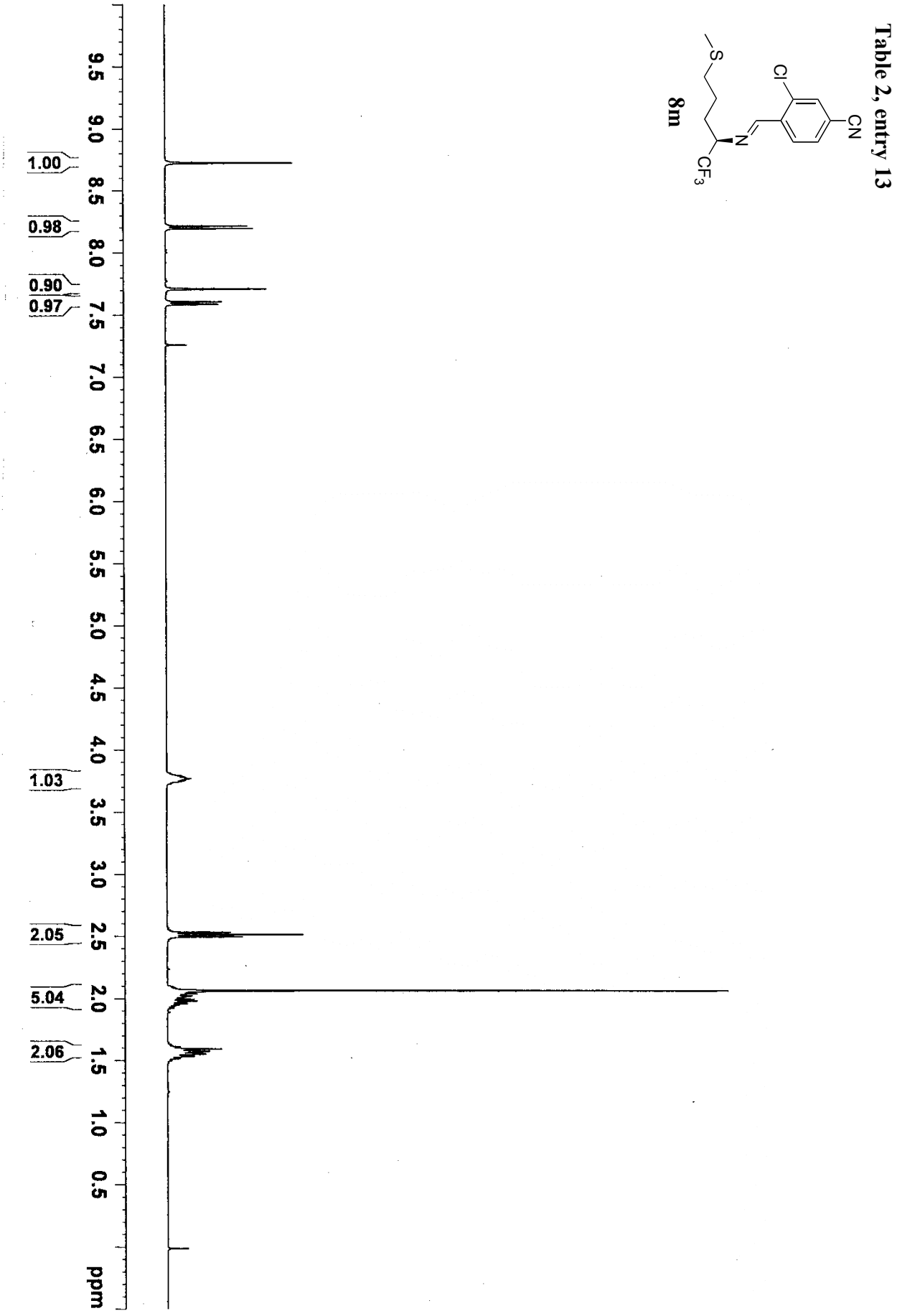
Table 2, entry 13
8m
S
Cl
CN
N
CF3
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.98
0.90
0.97
1.03
2.05
5.04
2.06

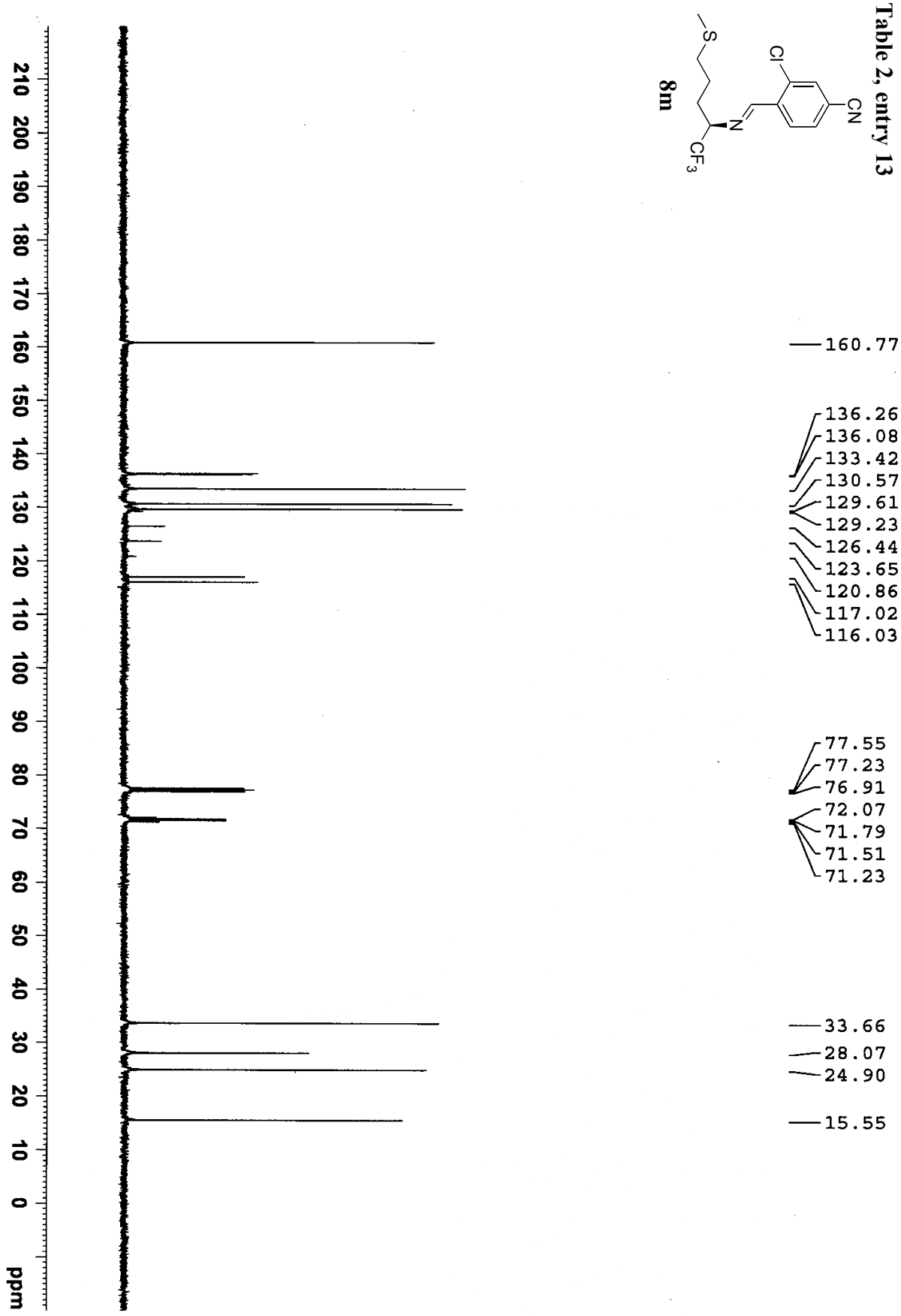
Table 2, entry 13
8m
S
Cl
CN
N
CF3
160.77
136.26
136.08
133.42
130.57
129.61
129.23
126.44
123.65
120.86
117.02
116.03
77.55
77.23
76.91
72.07
71.79
71.51
71.23
33.66
28.07
24.90
15.55
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

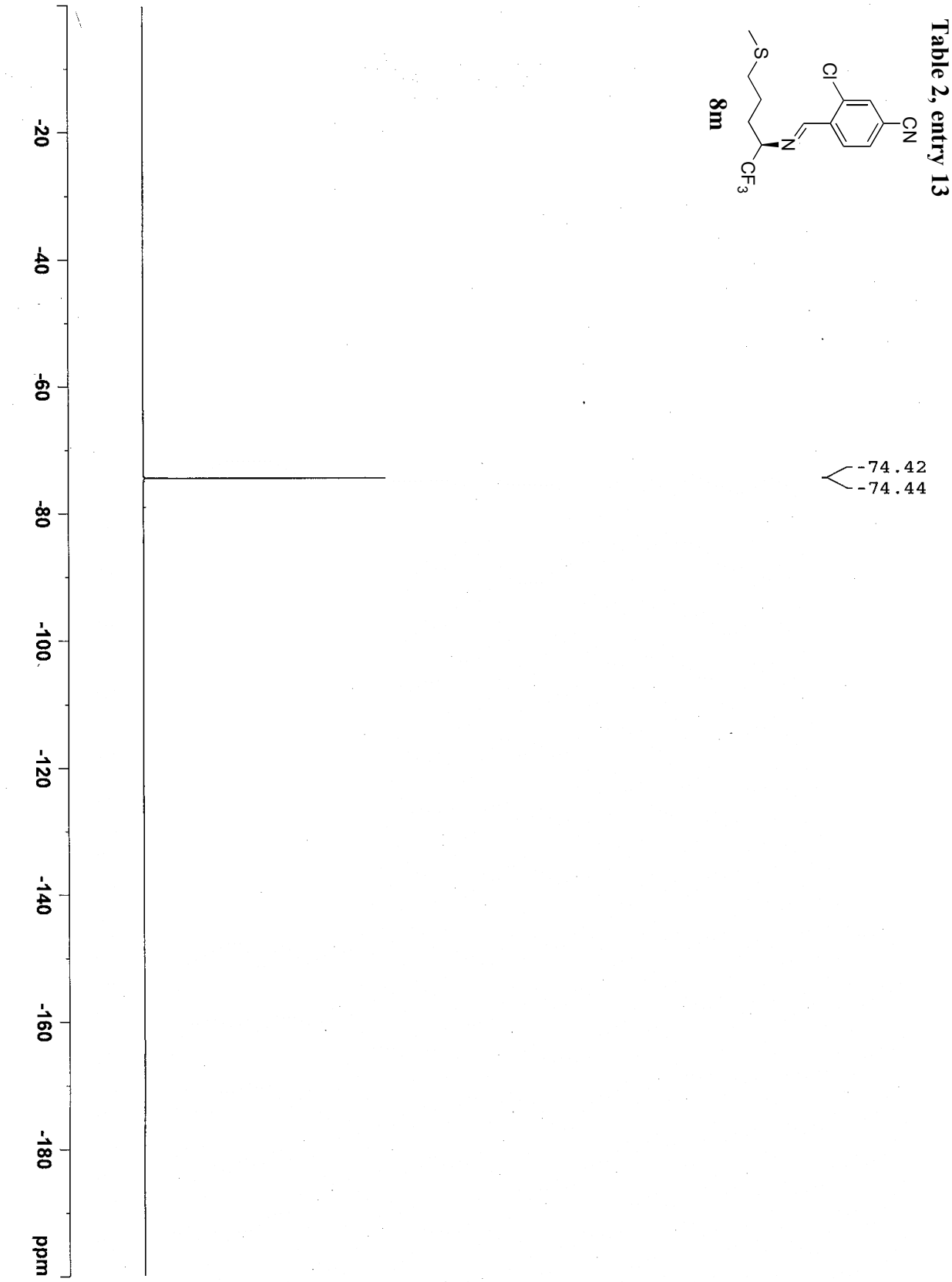
Table 2, entry 13
8m
S
Cl
CN
N
CF3
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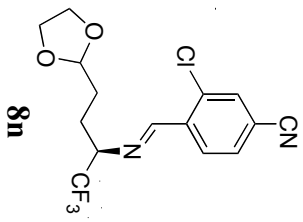
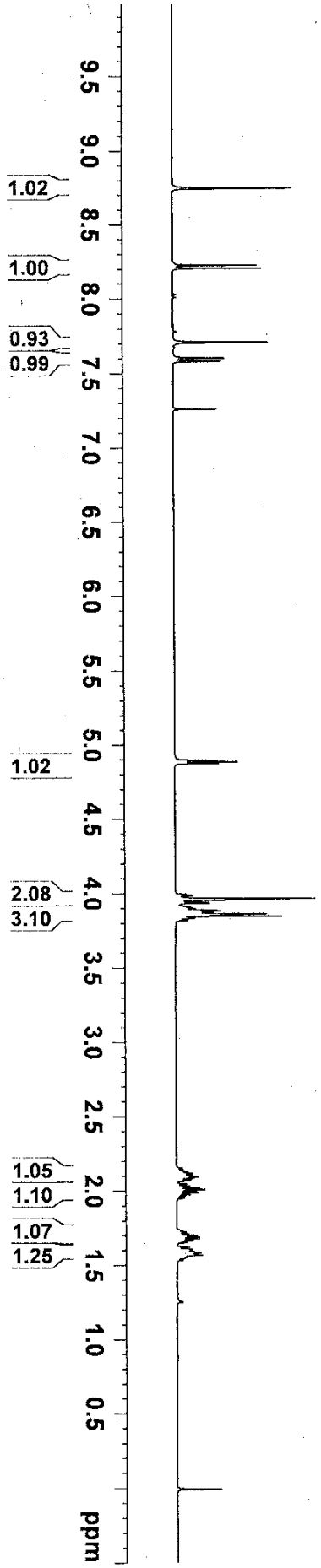
-74.44
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

Table 2, entry 14



8n



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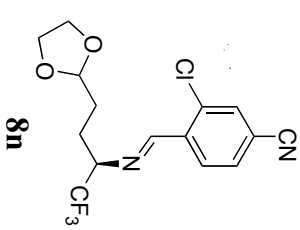
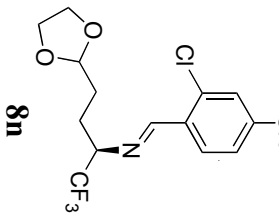


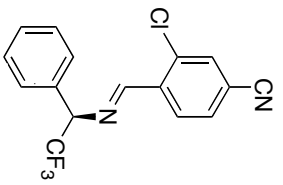
8n

Table 2, entry 14



8n

Table 2, entry 15



8o

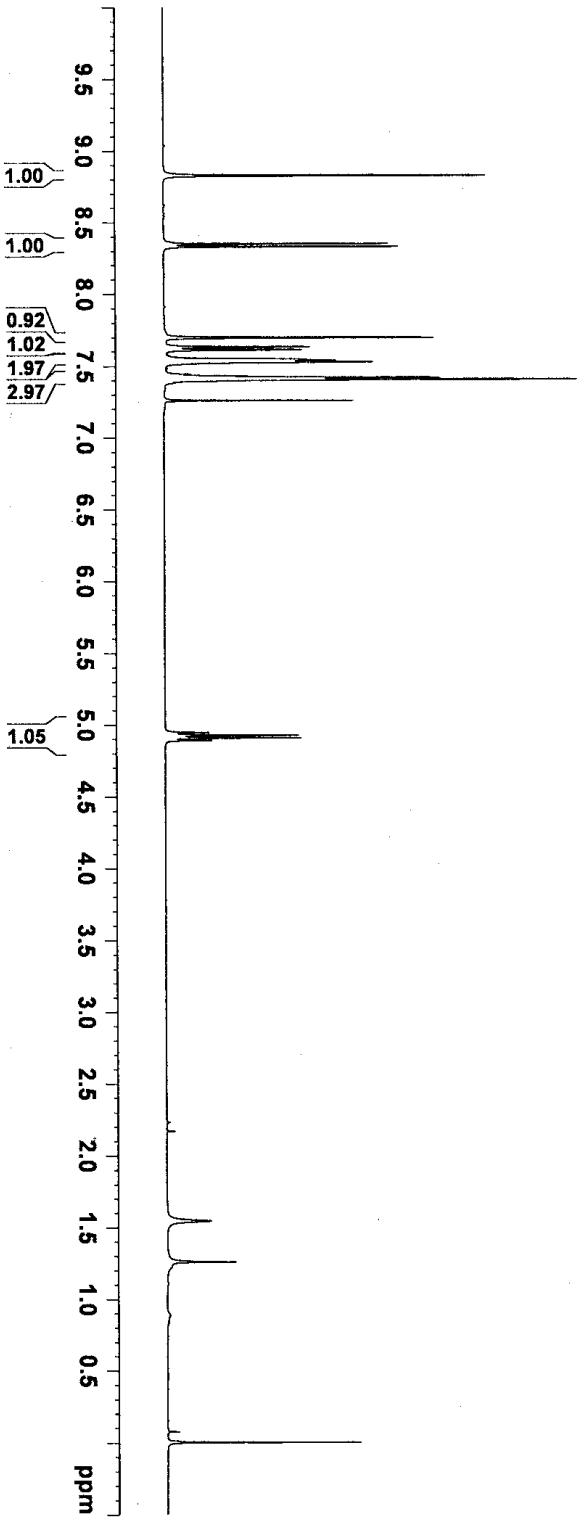
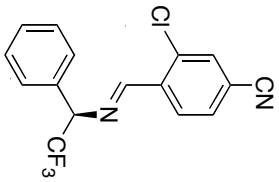
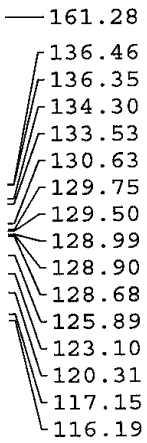
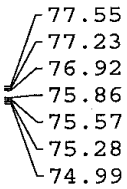


Table 2, entry 15

8o







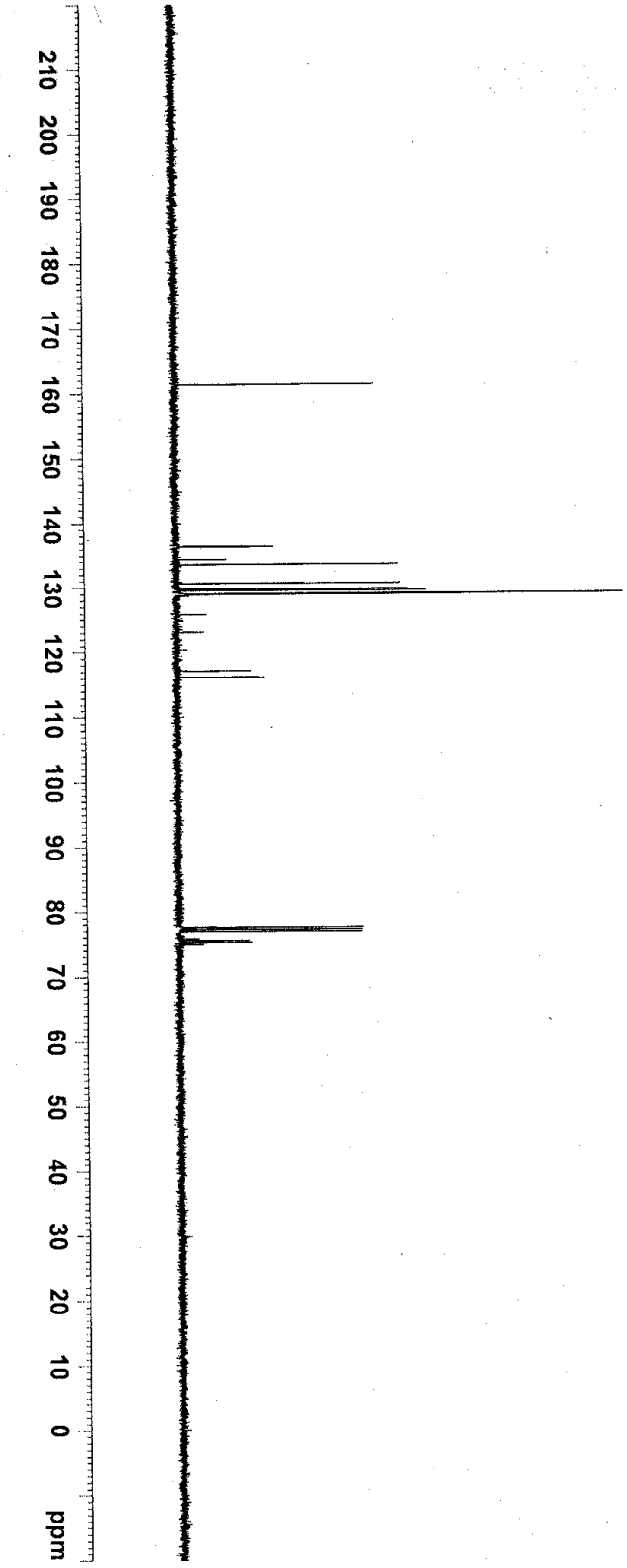
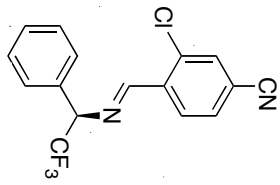
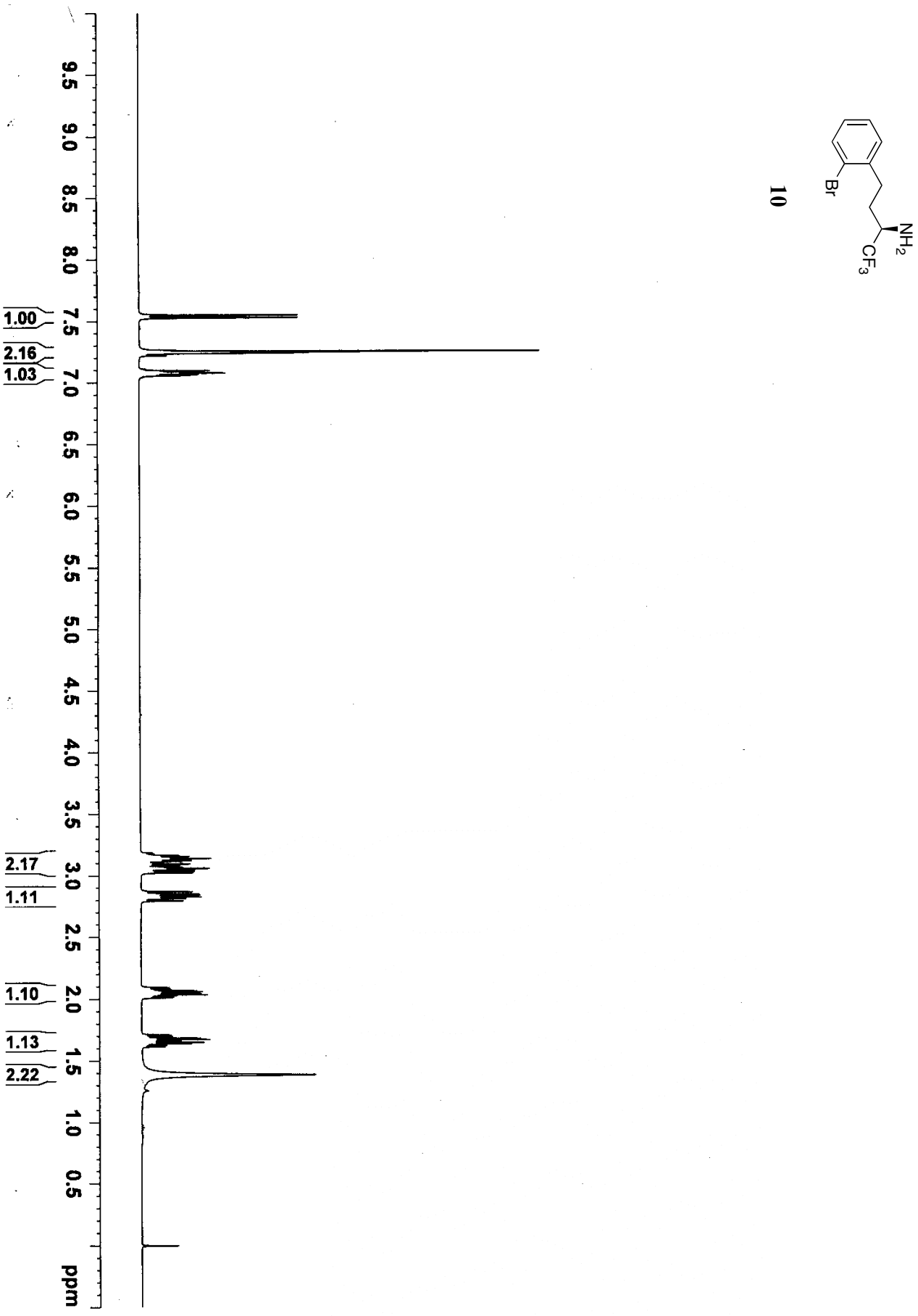
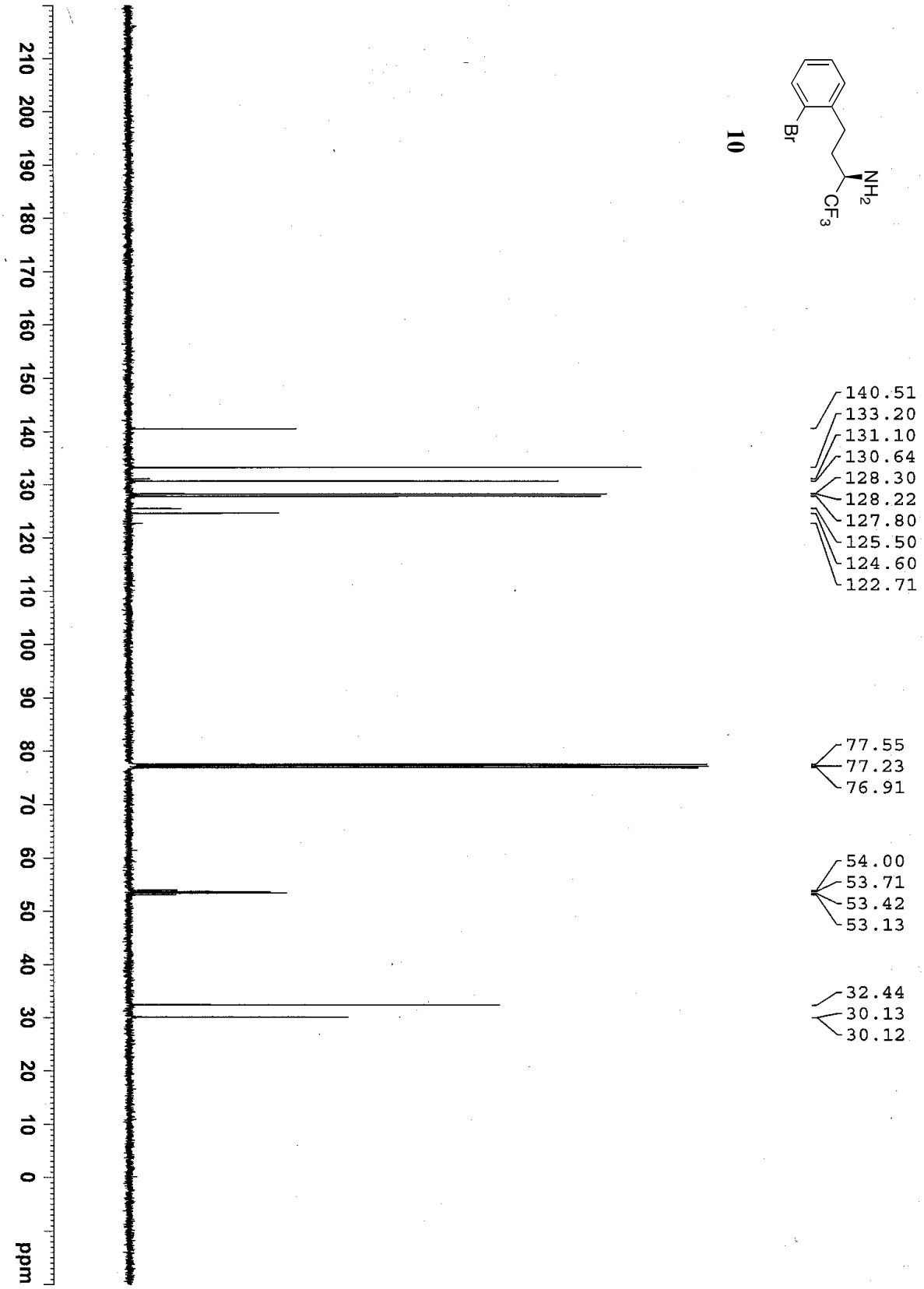


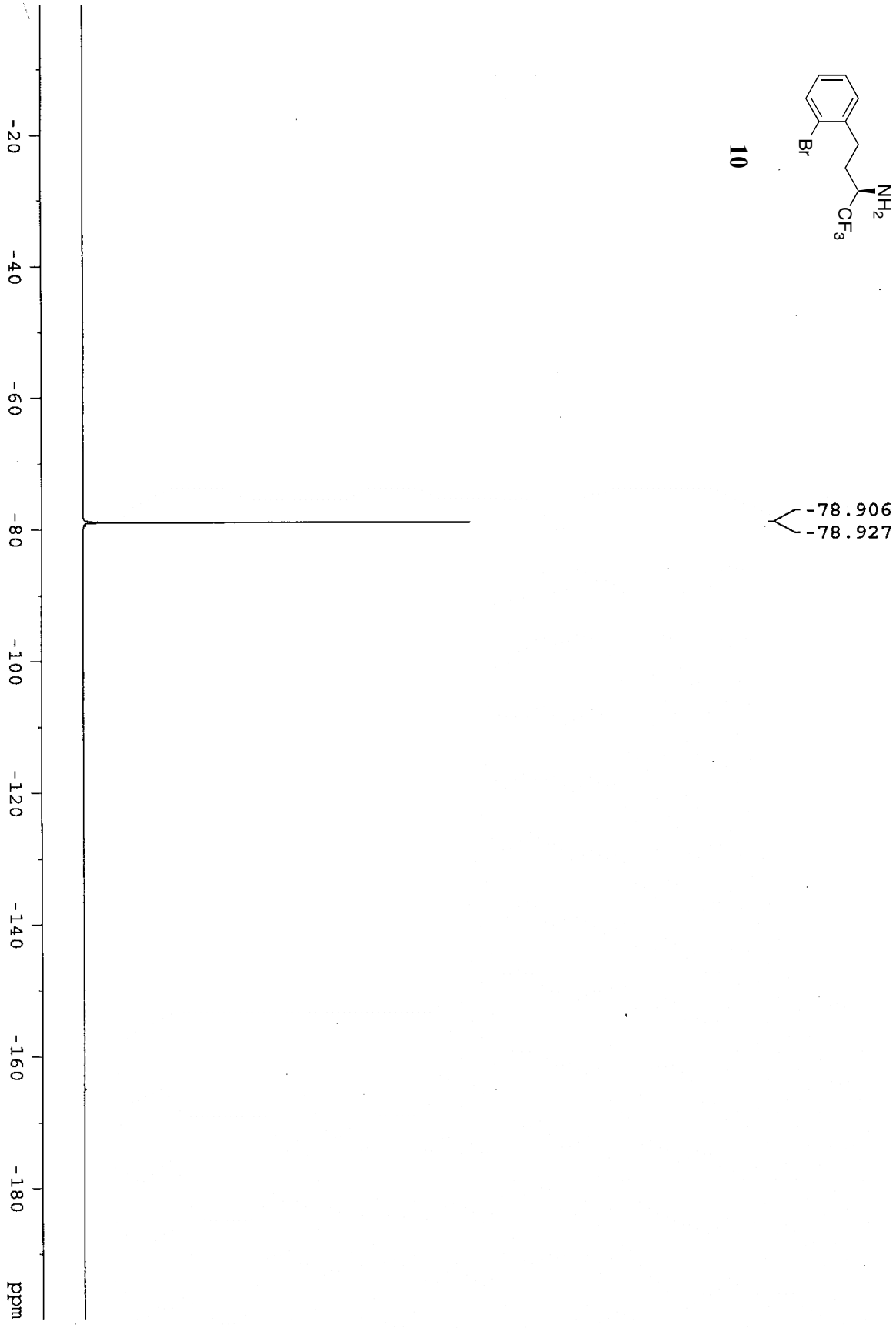
Table 2, entry 15

8o

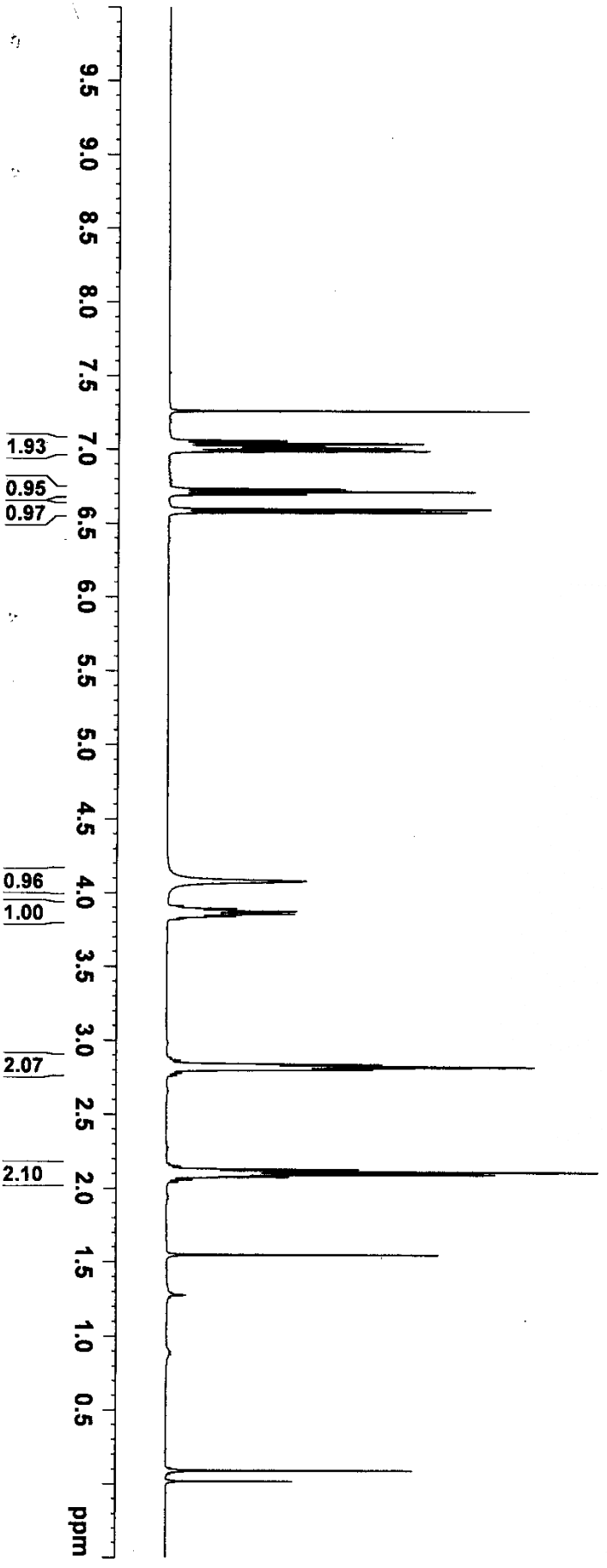




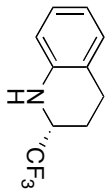

10
Br
NH2
CF3
140.51
133.20
131.10
130.64
128.30
128.22
127.80
125.50
124.60
122.71
77.55
77.23
76.91
54.00
53.71
53.42
53.13
32.44
30.13
30.12
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

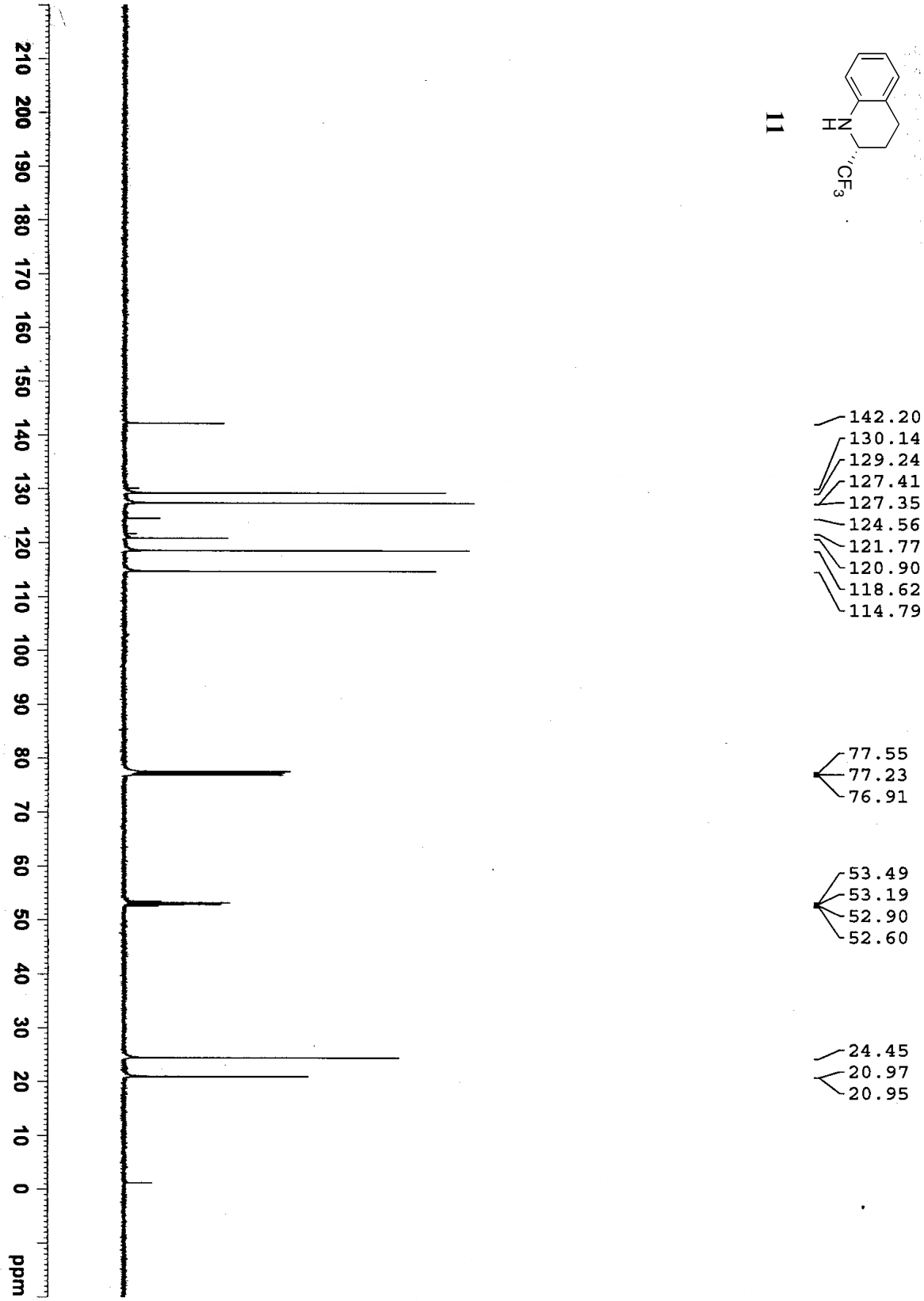


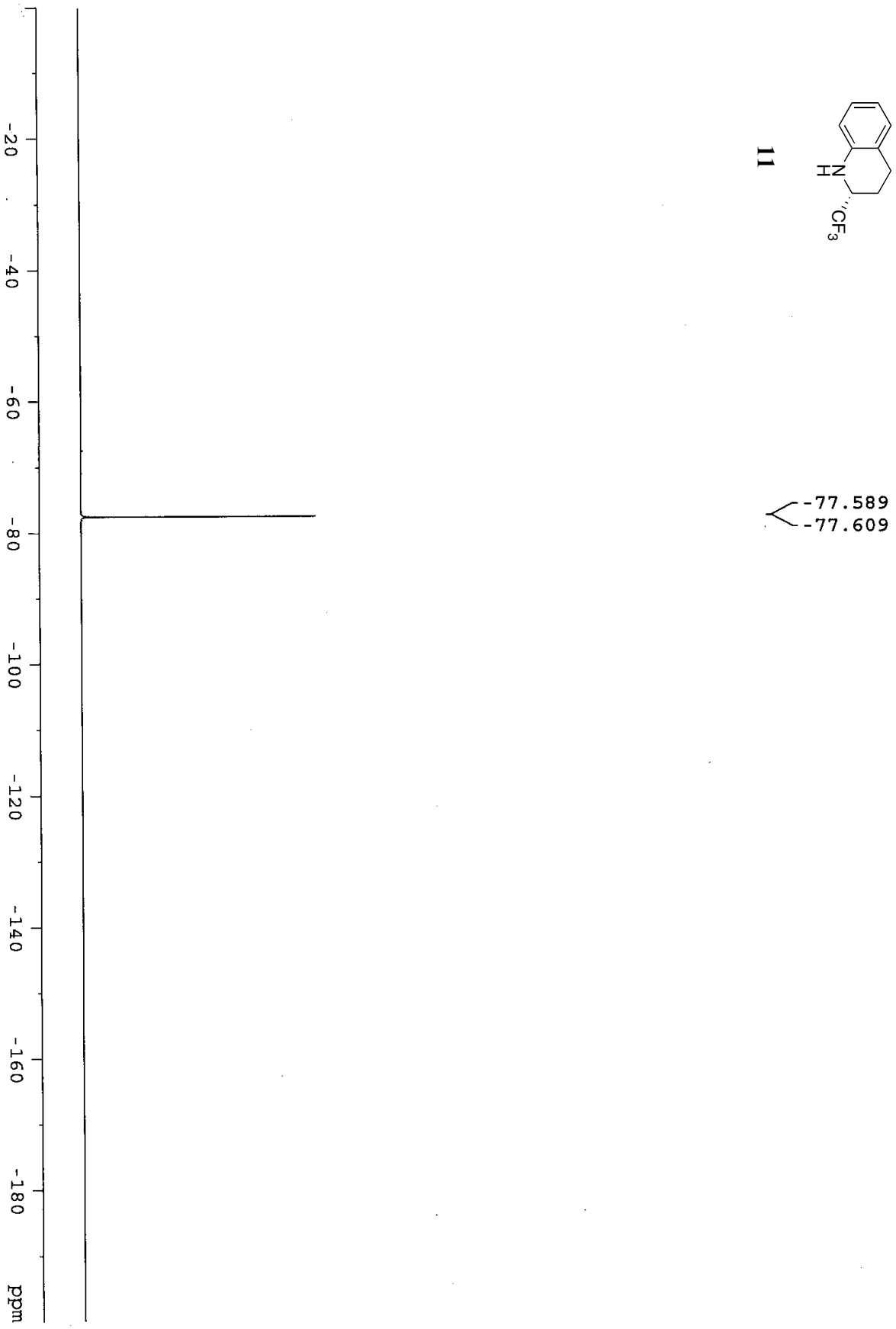
10


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.93
0.95
0.97
0.96
1.00
2.07
2.10

11


N
H
CF3


11
142.20
130.14
129.24
127.41
127.35
124.56
121.77
120.90
118.62
114.79
77.55
77.23
76.91
53.49
53.19
52.90
52.60
24.45
20.97
20.95
ppm


11
-77.589
-77.609
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm