Organocatalytic asymmetric biomimetic transamination of α-keto acetal to chiral α-amino acetal

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Supporting Information

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General Methods. All commercially available reagents were used without further purification. Toluene and benzene were distilled from sodium-benzophenone. Dichloromethane and 1,2-dichloroethane were distilled from CaH_2. Dimethyl sulfoxide was dried over 4 Å molecular sieves (activated at 180 ^oC under vacuum over 8 h). Column chromatography was performed on silica gel (200-300 mesh). ^1H NMR spectra were recorded on a 400 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. *o*-$HOPhCH_2NH_2$ was prepared from 2-methoxybenzylamine through demethylation using BBr_3.[1] Catalysts **C1-C5** were prepared according to the reported procedure.[2] Ketones **4a, 4b,** and **4e-4q** were prepared by addition of the corresponding Grignard reagents to ethyl dimethoxyacetate or ethyl diethoxyacetate.[3] Ketones **4c** and **4d** were prepared from ketone **4a** via acid-catalyzed acetal exchange according to the reported procedure.[4]

(1) A. J. Hallett, G. J. Kwant and J. G. Vries, *Chem.-Eur. J.,* 2009, **15**, 2111.

(2) (*a*) X. Xiao, Y. Xie, C. Su, M. Liu and Y. Shi, *J. Am. Chem. Soc.,* 2011, **133**, 12914; (*b*) Y. Xie, H. Pan, X. Xiao, S. Li and Y. Shi, *Org. Biomol. Chem.,* 2012, **10**, 8960.

(3) M. Adamczyk, D. D. Johnson, P. G. Mattingly, Y. Pan and R. E. Reddy, *Synth. Commun.,* 2002, **32**, 3199.

(4) S.-K. Tian, R. Hong and L. Deng, *J. Am. Chem. Soc.,* 2003, **125**, 9900.

Representative procedure for transamination of α-keto acetals (Table 2, entry 1).

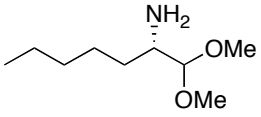
To a Schlenk tube was added α-keto acetal **4a** (0.101 g, 0.50 mmol), *o*-$HOPhCH_2NH_2$ (0.092 g, 0.75 mmol), catalyst **C5** (0.038 g, 0.10 mmol), and toluene (2.5 mL). Upon stirring at 110 ^oC for 72 h, the reaction mixture was cooled to room temperature, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 30/1) to remove *o*-$HOPhCH_2NH_2$, catalyst, and other byproducts. The resulting aldimine was dissolved in THF (1.0 mL) and 1 N HCl (2.0 mL). Upon stirring at 20 ^oC for 24 h, the reaction mixture was diluted with water (20 mL), washed with hexanes (15 mL x 3), concentrated to remove THF, brought to pH > 7 with solid K_2CO_3, extracted with CH_2Cl_2 (30 mL x 3), dried over $MgSO_4$, filtered, and concentrated to give α-amino acetal **6a** as a yellow

oil (0.066 g, 65% yield, 85% ee).

Preparation of *N*-benzoyl derivative of α-amino acetal for the determination of the enantiomeric excess.

To a solution of α-amino acetal **6a** (0.020 g, 0.10 mmol) in CH_2Cl_2 (1.0 mL) was added Et_3N (0.018 g, 0.18 mmol) and PhCOCl (0.018 g, 0.15 mmol). Upon stirring at room temperature for 30 min, the reaction mixture was purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 8/1) to give *N*-benzoyl amine **10a** as a white solid (0.027 g, 88%). The sample was subjected to chiral HPLC (Chiralpak AD-H column) to determine the enantiomeric excess.

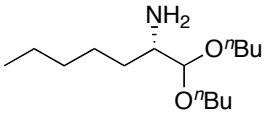
Table 1, entry 10



6b

Yellow oil; $[\alpha]^{20}_D$ = -11.4 (*c* 0.35, $CHCl_3$) (82% ee); IR (film) 3379, 2954, 1116, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.99 (d, *J* = 4.8 Hz, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 2.84-2.74 (m, 1H), 1.58-1.48 (m, 1H), 1.47-1.35 (m, 2H), 1.33-1.16 (m, 7H), 0.85 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 108.5, 55.2, 55.0, 52.8, 32.4, 32.1, 25.9, 22.8, 14.2; HRMS Calcd for $C_9H_{22}NO_2$ (M+H): 176.1645; Found: 176.1642.

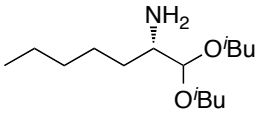
Table 1, entry 11



6c

Yellow oil; $[\alpha]^{20}_D$ = -6.4 (*c* 0.39, $CHCl_3$) (76% ee); IR (film) 3384, 2957, 1115, 1071 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.22-4.06 (m, 1H), 3.72-3.56 (m, 2H), 3.52-3.38 (m, 2H), 2.91-2.72 (m, 1H), 1.61-1.50 (m, 6H), 1.44-1.33 (m, 6H), 1.33-1.20 (m, 6H), 0.95-0.84 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.0, 67.9, 67.6, 53.6, 32.19, 32.17, 32.14, 32.0, 25.9, 22.8, 19.57, 19.56, 14.3, 14.1; HRMS Calcd for $C_{15}H_{34}NO_2$ (M+H): 260.2584; Found: 260.2584.

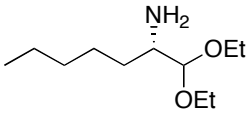
Table 1, entry 12



6d

Yellow oil; $[\alpha]^{20}_D$ = -4.8 (*c* 0.31, $CHCl_3$) (77% ee); IR (film) 3379, 2956, 1469, 1117, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.10 (d, *J* = 5.2 Hz, 1H), 3.43 (dd, *J* = 8.8, 6.4 Hz, 1H), 3.36 (dd, *J* = 8.8, 6.4 Hz, 1H), 3.22-3.13 (m, 2H), 2.83-2.75 (m, 1H), 1.89-1.76 (m, 2H), 1.59-1.49 (m, 1H), 1.49-1.36 (m, 3H), 1.36-1.17 (m, 6H), 0.92-0.83 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.7, 74.6, 74.4, 53.4, 32.4, 32.2, 28.91, 28.89, 26.0, 22.8, 19.64, 19.61, 14.2; HRMS Calcd for $C_{15}H_{33}NNaO_2$ (M+Na): 282.2404; Found: 282.2406.

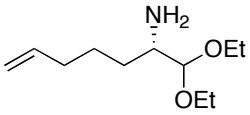
Table 2, entry 1



6a

Yellow oil; $[\alpha]^{20}_D$ = -7.6 (*c* 1.01, $CHCl_3$) (85% ee); IR (film) 3379, 1118, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.15 (d, *J* = 5.6 Hz, 1H), 3.77-3.60 (m, 2H), 3.56-3.46 (m, 2H), 2.81-2.72 (m, 1H), 1.78-1.60 (m, 2H), 1.59-1.49 (m, 1H), 1.49-1.38 (m, 1H), 1.34-1.22 (m, 6H), 1.22-1.15 (m, 6H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.5, 63.5, 63.2, 53.7, 32.4, 32.2, 26.0, 22.8, 15.6, 14.2; HRMS Calcd for $C_{11}H_{25}NNaO_2$ (M+Na): 226.1778; Found: 226.1775.

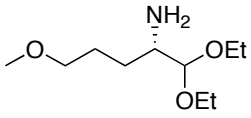
Table 2, entry 2



6e

Yellow oil; $[\alpha]^{20}_D$ = -6.7 (*c* 1.22, $CHCl_3$) (84% ee); IR (film) 3379, 2976, 1594, 1117, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.85-5.72 (m, 1H), 4.98 (d, *J* = 17.2 Hz, 1H), 4.92 (d, *J* = 10.0 Hz, 1H), 4.14 (d, *J* = 4.8 Hz, 1H), 3.77-3.60 (m, 2H), 3.56-3.46 (m, 2H), 2.82-2.73 (m, 1H), 2.13-1.97 (m, 2H), 1.63-1.50 (m, 2H), 1.50-1.32 (m, 3H), 1.31-1.24 (m, 1H), 1.24-1.15 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 114.7, 106.5, 63.5, 63.2, 53.5, 34.0, 32.0, 25.7, 15.6; HRMS Calcd for $C_{11}H_{23}NNaO_2$ (M+Na): 224.1621; Found: 224.1618.

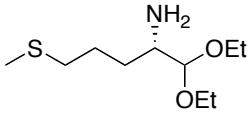
Table 2, entry 3



6f

Yellow oil; $[\alpha]^{20}_D$ = -5.0 (*c* 1.03, $CHCl_3$) (83% ee); IR (film) 3379, 2975, 1118, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.17 (d, *J* = 5.2 Hz, 1H), 3.77-3.63 (m, 2H), 3.57-3.47 (m, 2H), 3.39 (t, *J* = 6.4 Hz, 2H), 3.32 (s, 3H), 2.83-2.75 (m, 1H), 1.82-1.70 (m, 1H), 1.70-1.47 (m, 4H), 1.34-1.24 (m, 1H), 1.24-1.18 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.5, 73.1, 63.6, 63.3, 58.7, 53.6, 29.1, 26.5, 15.6; HRMS Calcd for $C_{10}H_{23}NNaO_3$ (M+Na): 228.1570; Found: 228.1569.

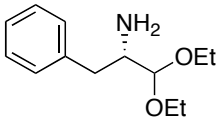
Table 2, entry 4



6g

Yellow oil; $[\alpha]^{20}_D$ = -8.9 (*c* 1.00, $CHCl_3$) (84% ee); IR (film) 3370, 2974, 1118, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.16 (d, *J* = 4.8 Hz, 1H), 3.78-3.64 (m, 2H), 3.57-3.47 (m, 2H), 2.84-2.75 (m, 1H), 2.57-2.43 (m, 2H), 2.09 (s, 3H), 1.86-1.73 (m, 1H), 1.72-1.57 (m, 2H), 1.47-1.28 (m, 3H), 1.25-1.18 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.5, 63.6, 63.4, 53.5, 34.5, 31.7, 26.1, 15.7, 15.6; HRMS Calcd for $C_{10}H_{24}NO_2S$ (M+H): 222.1522; Found: 222.1518.

Table 2, entry 5

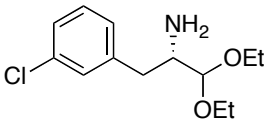


6h

Yellow oil; $[\alpha]^{20}_D$ = -14.7 (*c* 0.98, $CHCl_3$) (83% ee); IR (film) 3376, 2975, 1495, 1454, 1118, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (m, 2H), 7.25-7.18 (m, 3H), 4.25 (d, *J* = 5.2 Hz, 1H), 3.83-3.68 (m, 2H), 3.63-3.51 (m, 2H), 3.17-3.05 (m, 1H), 2.99 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.52 (dd, *J* = 13.2, 9.6 Hz, 1H), 1.69-1.46 (m, 2H), 1.28-1.20 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 129.5, 128.7, 126.5, 105.8, 63.8, 63.5, 55.1, 38.8, 15.6;

HRMS Calcd for $C_{13}H_{22}NO_2$ (M+H): 224.1645; Found: 224.1646.

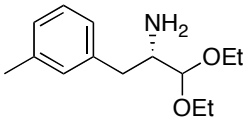
Table 2, entry 6



6i

Yellow oil; $[\alpha]^{20}_D$ = -13.9 (*c* 0.95, $CHCl_3$) (82% ee); IR (film) 3383, 2975, 1597, 1573, 1477, 1118, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.16 (m, 3H), 7.13-7.08 (m, 1H), 4.23 (d, *J* = 4.4 Hz, 1H), 3.81-3.67 (m, 2H), 3.62-3.50 (m, 2H), 3.13-3.04 (m, 1H), 3.00-2.92 (m, 1H), 2.54-2.43 (m, 1H), 1.50-1.30 (m, 2H), 1.28-1.20 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 134.4, 129.9, 129.6, 127.7, 126.6, 105.8, 63.7, 63.5, 54.9, 38.6, 15.6; HRMS Calcd for $C_{13}H_{21}ClNO_2$ (M+H): 258.1255; Found: 258.1257.

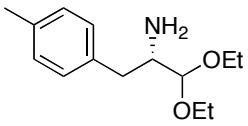
Table 2, entry 7



6j

Yellow oil; $[\alpha]^{20}_D$ = -16.5 (*c* 1.00, $CHCl_3$) (84% ee); IR (film) 3383, 2974, 1608, 1444, 1118, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22-7.15 (m, 1H), 7.08-6.98 (m, 3H), 4.25 (d, *J* = 5.2 Hz, 1H), 3.83-3.68 (m, 2H), 3.63-3.51 (m, 2H), 3.15-3.05 (m, 1H), 3.02-2.90 (m, 1H), 2.46 (dd, *J* = 12.4, 9.6 Hz, 1H), 2.33 (s, 3H), 1.46-1.33 (m, 2H), 1.29-1.20 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 138.2, 130.3, 128.5, 127.2, 126.5, 106.0, 63.7, 63.4, 55.00, 38.8, 21.6, 15.6; HRMS Calcd for $C_{14}H_{24}NO_2$ (M+H): 238.1802; Found: 238.1803.

Table 2, entry 8

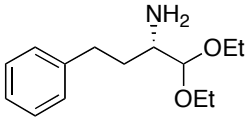


6k

Yellow oil; $[\alpha]^{20}_D$ = -16.0 (*c* 1.02, $CHCl_3$) (86% ee); IR (film) 3379, 2975, 1515, 1444, 1110, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13-7.03 (m, 4H), 4.23 (d, *J* = 5.2 Hz, 1H),

3.82-3.67 (m, 2H), 3.62-3.51 (m, 2H), 3.13-3.03 (m, 1H), 2.99-2.90 (m, 1H), 2.47 (dd, J = 13.2, 9.6 Hz, 1H), 2.31 (s, 3H), 1.43-1.29 (m, 2H), 1.27-1.20 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2, 135.8, 129.3, 106.0, 63.7, 63.3, 55.0, 38.4, 21.2, 15.6; HRMS Calcd for $C_{14}H_{23}NNaO_2$ (M+Na): 260.1621; Found: 260.1618.

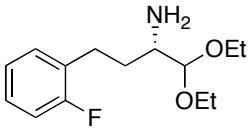
Table 2, entry 9



6l

Yellow oil; $[\alpha]^{20}_D$ = -12.2 (*c* 0.98, $CHCl_3$) (84% ee); IR (film) 3379, 2975, 1496, 1455, 1116, 1062 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.24 (m, 2H), 7.24-7.14 (m, 3H), 4.19 (d, J = 4.4 Hz, 1H), 3.79-3.60 (m, 2H), 3.58-3.45 (m, 2H), 2.90-2.78 (m, 2H), 2.71-2.60 (m, 1H), 1.96-1.85 (m, 1H), 1.66-1.40 (m, 3H), 1.26-1.16 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 128.6, 128.5, 125.9, 106.4, 63.5, 63.2, 53.2, 34.3, 32.7, 15.5; HRMS Calcd for $C_{14}H_{23}NNaO_2$ (M+Na): 260.1621; Found: 260.1619.

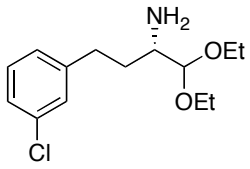
Table 2, entry 10



6m

Yellow oil; $[\alpha]^{20}_D$ = -11.2 (*c* 1.14, $CHCl_3$) (84% ee); IR (film) 3376, 2975, 1492, 1456, 1114, 1061 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.18 (m, 1H), 7.18-7.10 (m, 1H), 7.07-6.94 (m, 2H), 4.19 (d, J = 4.8 Hz, 1H), 3.78-3.59 (m, 2H), 3.56-3.45 (m, 2H), 2.89-2.76 (m, 2H), 2.76-2.64 (m, 1H), 1.94-1.82 (m, 1H), 1.62-1.50 (m, 1H), 1.50-1.37 (m, 2H), 1.23-1.16 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 160.1, 130.83, 130.78, 129.3, 129.1, 127.7, 127.6, 124.13, 124.10, 115.4, 115.2, 106.4, 63.6, 63.2, 53.3, 33.0, 25.9, 25.8, 15.5; HRMS Calcd for $C_{14}H_{23}FNO_2$ (M+H): 256.1707; Found: 256.1708.

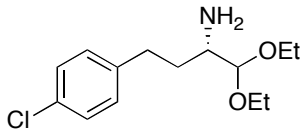
Table 2, entry 11



6n

Yellow oil; $[\alpha]^{20}_{D}$ = -12.5 (*c* 1.14, $CHCl_3$) (83% ee); IR (film) 3376, 2975, 1597, 1573, 1477, 1116, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.13 (m, 3H), 7.12-7.06 (m, 1H), 4.18 (d, *J* = 3.6 Hz, 1H), 3.79-3.61 (m, 2H), 3.58-3.46 (m, 2H), 2.88-2.74 (m, 2H), 2.69-2.58 (m, 1H), 1.94-1.81 (m, 1H), 1.62-1.49 (m, 1H), 1.48-1.30 (m, 2H), 1.26-1.17 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 134.2, 129.7, 128.7, 126.8, 126.1, 106.5, 63.6, 63.4, 53.2, 34.1, 32.4, 15.6; HRMS Calcd for $C_{14}H_{22}ClNNaO_2$ (M+Na): 294.1231; Found: 294.1232.

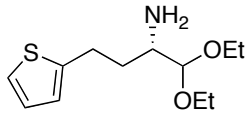
Table 2, entry 12



6o

Yellow oil; $[\alpha]^{20}_{D}$ = -11.7 (*c* 1.01, $CHCl_3$) (85% ee); IR (film) 3376, 2975, 1492, 1115, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.20 (m, 2H), 7.16-7.10 (m, 2H), 4.17 (d, *J* = 5.2 Hz, 1H), 3.78-3.60 (m, 2H), 3.56-3.45 (m, 2H), 2.85-2.74 (m, 2H), 2.67-2.57 (m, 1H), 1.92-1.81 (m, 1H), 1.60-1.47 (m, 1H), 1.44-1.32 (m, 2H), 1.24-1.17 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 131.6, 130.0, 128.6, 106.5, 63.6, 63.4, 53.2, 34.2, 32.0, 15.6; HRMS Calcd for $C_{14}H_{22}ClNNaO_2$ (M+Na): 294.1231; Found: 294.1233.

Table 2, entry 13

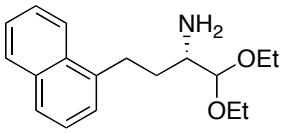


6p

Yellow oil; $[\alpha]^{20}_{D}$ = -15.4 (*c* 1.04, $CHCl_3$) (82% ee); IR (film) 3376, 2974, 1443, 1373, 1116, 1062 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.12-7.07 (m, 1H), 6.93-6.87 (m, 1H), 6.83-6.78 (m, 1H), 4.18 (d, *J* = 4.8 Hz, 1H), 3.78-3.61 (m, 2H), 3.57-3.46 (m, 2H), 3.09-2.99 (m, 1H), 2.96-2.79 (m, 2H), 2.01-1.90 (m, 1H), 1.68-1.56 (m, 1H), 1.46-1.30 (m, 2H), 1.25-1.17 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 126.9, 124.3, 123.1, 106.4, 63.6,

63.3, 53.0, 34.6, 26.8, 15.5; HRMS Calcd for $C_{12}H_{21}NNaO_2S$ (M+Na): 266.1185; Found: 266.1185.

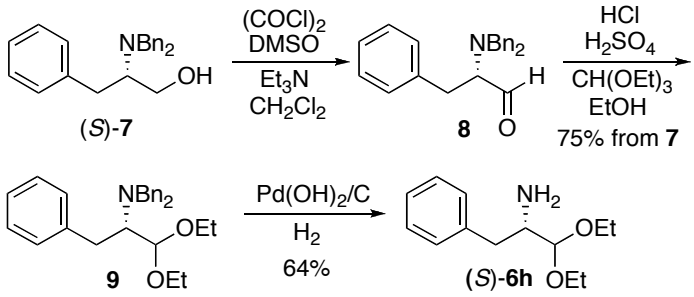
Table 2, entry 14



6q

Yellow oil; $[\alpha]^{20}_D$ = -18.0 (*c* 0.91, $CHCl_3$) (82% ee); IR (film) 3376, 2974, 1596, 1510, 1444, 1116, 1061 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.55-7.44 (m, 2H), 7.43-7.34 (m, 2H), 4.21 (d, *J* = 4.8 Hz, 1H), 3.81-3.70 (m, 1H), 3.69-3.59 (m, 1H), 3.58-3.46 (m, 2H), 3.40-3.28 (m, 1H), 3.18-3.07 (m, 1H), 3.00-2.91 (m, 1H), 2.10-1.98 (m, 1H), 1.80-1.67 (m, 1H), 1.66-1.50 (m, 2H), 1.26-1.16 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 134.0, 132.0, 128.9, 126.7, 126.1, 125.9, 125.7, 125.6, 124.1, 106.4, 63.6, 63.2, 53.7, 33.8, 29.9, 15.54, 15.52; HRMS Calcd for $C_{18}H_{25}NNaO_2$ (M+Na): 310.1778; Found: 310.1775.

The determination of the absolute configuration of α-amino acetal 6h (Scheme 2)



To a solution of oxalyl chloride (1.40 g, 11.0 mmol) in CH_2Cl_2 (25.0 mL) was added a solution of dimethyl sulfoxide (1.72 g, 22.0 mmol) in CH_2Cl_2 (5.0 mL) at -61 ^oC over 3 min under N_2. After the reaction mixture was stirred at -61 ^oC for 5 min, a solution of (*S*)-2-(*N,N*-dibenzylamino)-3-phenyl-1-propanol (**7**) (3.31 g, 10.0 mmol) in CH_2Cl_2 (12.0 mL) was added over 5 min. After stirring at -61 ^oC for another 30 min, triethylamine (5.06 g, 50.0 mmol) was added. Upon stirring at -61 ^oC for 1 h, the reaction mixture was taken out from the cooling bath, stirred for 2 h, quenched with water (60 mL), extracted with CH_2Cl_2 (50 mL x 3), dried over $MgSO_4$, filtered, and concentrated to give crude aldehyde **8** as a yellow oil (3.30 g).

A solution of the above aldehyde in EtOH (10.0 mL) was added to a solution of triethylorthoformate (14.82 g, 100.0 mmol), HCl (33% w/w in EtOH, 10.0 mL), and concentrated sulfuric acid (0.25 mL) in EtOH (50.0 mL) under N_2. Upon stirring at room temperature for 2 days, the reaction mixture was brought to pH > 7 with saturated $NaHCO_3$ aqueous solution, extracted with Et_2O (75 mL x 3), washed with H_2O (30 mL x 3), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 10/1) to give *N,N*-dibenzylamino acetal **9** as a yellow oil (3.02 g, 75% overall yield). $[\alpha]^{20}_D$ = -24.5 (*c* 0.94, $CHCl_3$) [lit.[1] for (*S*)-**9**; $[\alpha]_D$ = -17.8 (*c* 0.9, $CHCl_3$)]; IR (film) 1494, 1453, 1117, 1060 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.07 (m, 15H), 4.58 (d, *J* = 4.4 Hz, 1H), 3.79 (d, *J* = 13.6 Hz, 2H), 3.74 (d, *J* = 13.6 Hz, 2H), 3.71-3.66 (m, 1H), 3.63-3.46 (m, 2H), 3.41-3.32 (m, 1H), 3.13-3.06 (m, 1H), 2.94 (dd, *J* = 14.4, 4.8 Hz, 1H), 2.89 (dd, *J* = 14.4, 9.2 Hz, 1H), 1.20 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$)

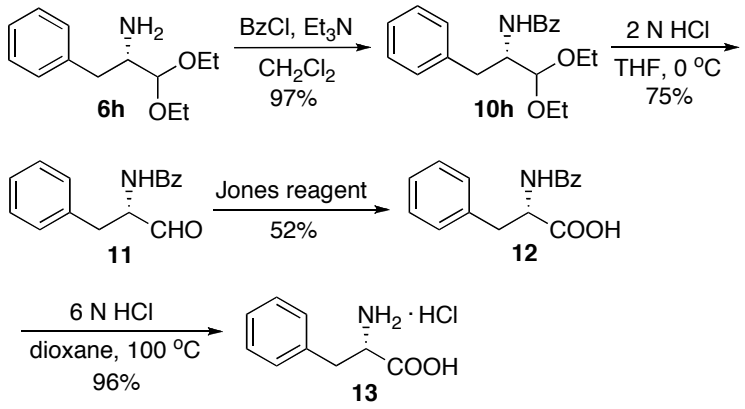
δ 141.3, 140.6, 129.9, 128.9, 128.2, 128.1, 126.7, 125.8, 105.1, 63.31, 63.26, 60.4, 54.6, 32.8, 15.7, 15.6; HRMS Calcd for $C_{27}H_{34}NO_2$ (M+H): 404.2584; Found: 404.2583.

(1) M. A. Graham, A. H. Wadsworth, A. Zahid and C. M. Rayner, *Org. Biomol. Chem.,* 2003, **1**, 834.

To a solution of *N,N*-dibenzylamino acetal **9** (0.404 g, 1.0 mmol) in MeOH (20.0 mL) was added $Pd(OH)_2/C$ (20%, 0.060 g).[1] Upon stirring at room temperature overnight under H_2 (1 atm), the reaction mixture was filtered through a pad of Celite, washed with CH_2Cl_2 (80 mL), concentrated, and purified by flash column chromatography (silica gel, eluent: EtOAc/MeOH = 60/1 to 40/1) to give α-amino acetal **6h** as a yellow oil (0.142 g, 64%). $[\alpha]^{20}_D$ = -19.0 (*c* 1.05, $CHCl_3$) (99.5% ee).

(1) J. Huang, F. Wang, D.-M. Du and J. Xu, *Synthesis,* 2005, 2122.

The transformation of α-amino acetal 6h to corresponding α-amino acid (Scheme 3)



To a solution of α-amino acetal **6h** (0.112 g, 0.50 mmol) in CH_2Cl_2 (5.0 mL) were added Et_3N (0.091 g, 0.90 mmol) and PhCOCl (0.090 g, 0.75 mmol). Upon stirring at room temperature for 30 min, the reaction mixture was purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 8/1) to give *N*-benzoyl amine **10h** as a white solid (0.159 g, 97%). mp. 93-94 °C; $[\alpha]^{20}_D$ = -28.7 (*c* 0.95, $CHCl_3$); IR (film) 3270, 1638, 1541, 1066 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73-7.67 (m, 2H), 7.52-7.45 (m, 1H), 7.44-7.38 (m, 2H), 7.32- 7.25 (m, 4H), 7.24-7.17 (m, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 4.61-4.52 (m, 1H), 4.45 (d, *J* = 2.8 Hz, 1H), 3.85-3.76 (m, 1H), 3.67-3.46 (m, 3H), 3.05 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.97 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 138.3, 134.9, 131.6, 129.5, 128.70, 128.66, 127.1, 126.6, 102.1, 63.9, 63.8, 52.8, 35.9, 15.54, 15.49; HRMS Calcd for $C_{20}H_{25}NNaO_3$ (M+Na): 350.1727; Found: 350.1732.

To a solution of **10h** (0.131 g, 0.40 mmol) in THF (6.5 mL) was added 2 N HCl (26.0 mL). Upon stirring at 0 °C overnight,[1] the reaction mixture was neutralized to pH = 7 by solid $NaHCO_3$, extracted with CH_2Cl_2 (40 mL x 3), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: CH_2Cl_2/MeOH = 50/1) to give *N*-benzoylphenylalaninaldehyde (**11**) as a white solid (0.076 g, 75%). mp. 135-137 °C; $[\alpha]^{20}_D$ = -90.3 (*c* 0.98, EtOH) [lit.[2] for (*S*)-**11**; $[\alpha]_D$ = -109 (*c* 3, EtOH)]; IR (film) 3307, 1636, 1542 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.77-7.68 (m, 2H), 7.56-7.49

(m, 1H), 7.47-7.38 (m, 2H), 7.35- 7.23 (m, 3H), 7.22-7.15 (m, 2H), 6.73 (d, J = 4.4 Hz, 1H), 4.96-4.87 (m, 1H), 3.34 (dd, J = 14.0, 6.0 Hz, 1H), 3.27 (dd, J = 14.0, 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 167.5, 135.7, 133.8, 132.2, 129.6, 129.1, 128.9, 127.5, 127.2, 60.4, 35.4; HRMS Calcd for $C_{16}H_{16}NO_2$ (M+H): 254.1176; Found: 254.1172.

(1) T. Schmidlin and C. Tamm, *Helv. Chim. Acta*, 1980, **63**, 121.

(2) M. S. Silver and J. H. Haskell, *J. Med. Chem.*, 1989, **32**, 1253.

To a solution of **11** (0.071 g, 0.28 mmol) in acetone (2.0 mL) was added Jones reagent (1.0 mL) dropwise at 0 °C over 30 min.[1] After the reaction mixture was stirred at 0 °C for 3 h, a few drops of isopropyl alcohol was added. The reaction mixture was concentrated, dissolved in H_2O (30 mL), extracted with CH_2Cl_2 (30 mL x 3), dried over $MgSO_4$, filtered, concentrated, and purified by flash column chromatography (silica gel, eluent: CH_2Cl_2/MeOH = 50/1) to give *N*-benzoyl-(*S*)-phenylalanine (**12**) as a white solid (0.039 g, 52%). mp. 179-181 °C; $[\alpha]^{20}_D$ = -29.9 (*c* 0.86, MeOH) [lit.[2] for (*S*)-**12**; $[\alpha]_D$ = -41.4 (*c* 1.0, MeOH)]; IR (film) 3427, 3322, 1610, 1537 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.73-7.68 (m, 2H), 7.54-7.48 (m, 1H), 7.45-7.38 (m, 2H), 7.31-7.25 (m, 4H), 7.22-7.16 (m, 1H), 4.87-4.83 (m, 1H), 3.34 (dd, J = 14.0, 9.6 Hz, 1H), 3.12 (dd, J = 14.0, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 174.9, 170.2, 138.7, 135.3, 132.8, 130.2, 129.5, 129.4, 128.3, 127.8, 55.6, 38.2; HRMS Calcd for $C_{16}H_{16}NO_3$ (M+H): 270.1125; Found: 270.1122.

(1) J. Mulzer, A. Angermann, B. Schubert and C. Seilz, *J. Org. Chem.*, 1986, **51**, 5294.

(2) A. Miyashita and H. Takaya, *Tetrahedron*, 1984, **40**, 1245.

A solution of (*S*)-**12** (0.032 g, 0.12 mmol) in 6 N HCl (3.0 mL) and dioxane (0.5 mL) was stirred at 100 °C overnight.[1,2] The reaction mixture was cooled to rt and washed with Et_2O (3.0 mL x 3). The aqueous phase was concentrated to give amino acid hydrochloride **13** as a white solid (0.023 g, 96%). mp. 230-231 °C; $[\alpha]^{20}_D$ = +34.0 (*c* 0.50, 1N HCl) [lit.[3] for (*S*)-**13**; $[\alpha]^{25}_D$ = +43 (*c* 0.5, 1N HCl)]; IR (film) 3417, 2539, 1658, 1631 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.41-7.35 (m, 2H), 7.34-7.28 (m, 3H), 4.29-4.23 (m, 1H),

3.37-3.33 (m, 1H), 3.18 (dd, J = 14.4, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.2, 135.6, 130.5, 130.1, 128.9, 55.1, 37.3; HRMS Calcd for $C_9H_{12}NO_2$ (M-Cl): 166.0863; Found: 166.0864.

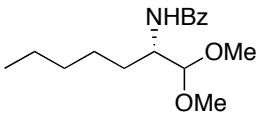
(1) X. Xiao, M. Liu, C. Rong, F. Xue, S. Li, Y. Xie and Y. Shi, *Org. Lett.*, 2012, **14**, 5270.

(2) D. M. Coe, R. Perciaccante and P. A. Procopiou, *Org. Biomol. Chem.*, 2003, **1**, 1106.

(3) H. Josien, A. Martin and G. Chassaing, *Tetrahedron Lett.*, 1991, **32**, 6547.

The chromatograms for the determination of enantioselectivity

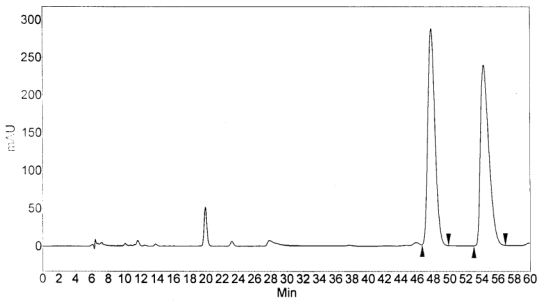
Table 1, entry 10



10b

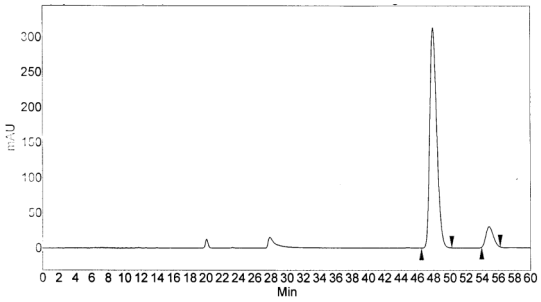
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (98/2); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



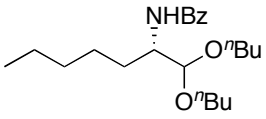
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	47.75	50.049	46.63	49.85
2	54.23	49.951	53.00	56.90
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	47.95	91.026	46.50	50.22
2	54.85	8.974	53.93	56.22
Total		100.000		

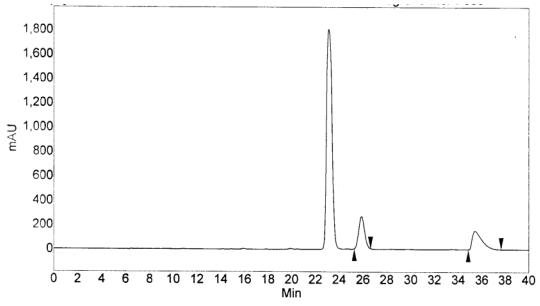
Table 1, entry 11



10c

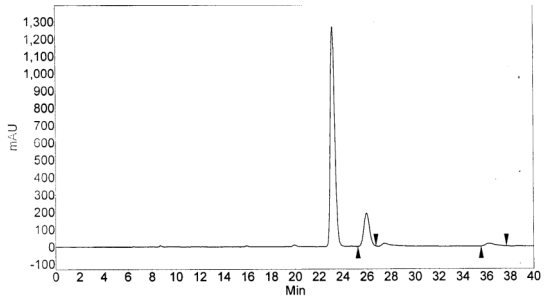
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (98/2); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



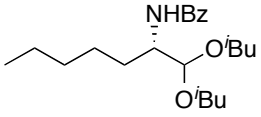
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	25.87	50.174	25.26	26.63
2	35.41	49.826	34.84	37.65
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	25.99	88.184	25.24	26.75
2	36.21	11.816	35.55	37.68
Total		100.000		

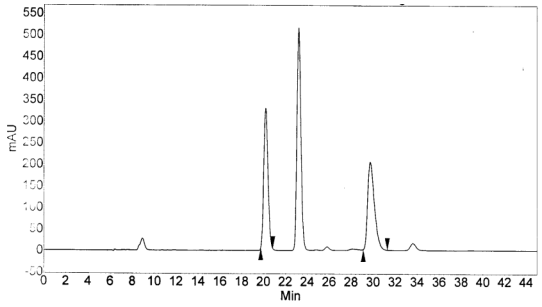
Table 1, entry 12



10d

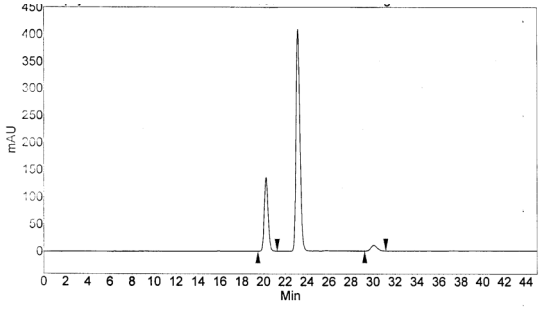
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (98/2); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



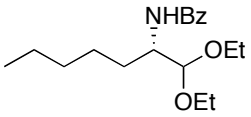
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	20.21	49.978	19.74	20.85
2	29.76	50.022	29.12	31.30
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	20.23	88.696	19.46	21.27
2	30.08	11.304	29.26	31.16
Total		100.000		

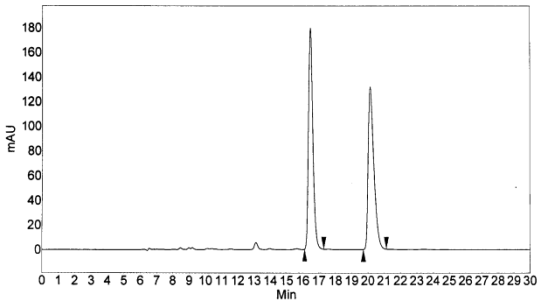
Table 2, entry 1



10a

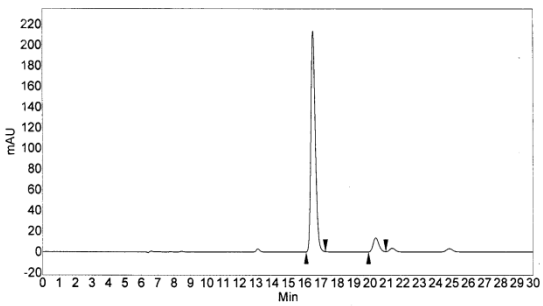
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



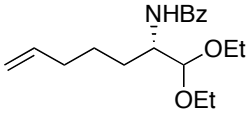
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	16.52	50.068	16.13	17.31
2	20.19	49.932	19.72	21.15
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	16.53	92.588	16.10	17.28
2	20.35	7.412	19.91	20.96
Total		100.000		

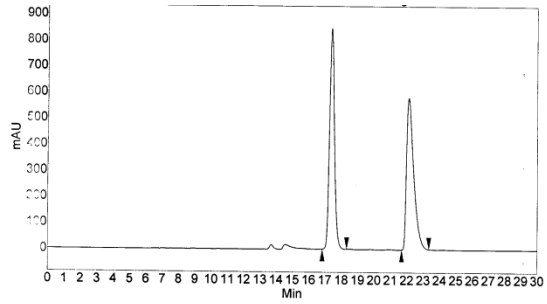
Table 2, entry 2



10e

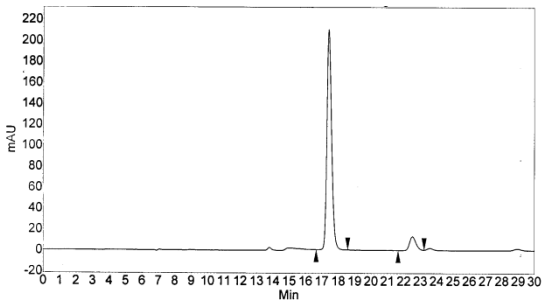
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



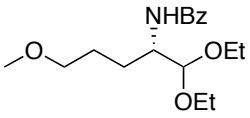
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	17.39	49.817	16.83	18.33
2	22.11	50.183	21.68	23.34
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	17.44	92.156	16.66	18.58
2	22.52	7.844	21.64	23.22
Total		100.000		

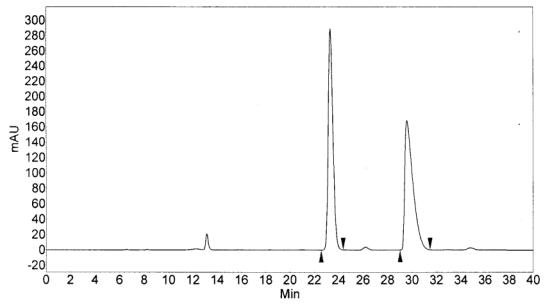
Table 2, entry 3



10f

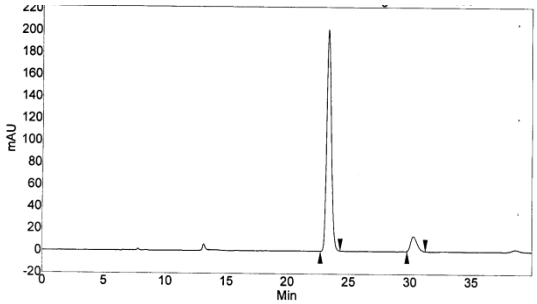
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



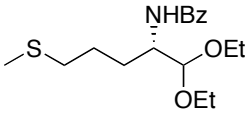
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	23.35	49.991	22.57	24.36
2	29.59	50.009	29.03	31.49
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	23.36	91.581	22.70	24.31
2	30.27	8.419	29.75	31.24
Total		100.000		

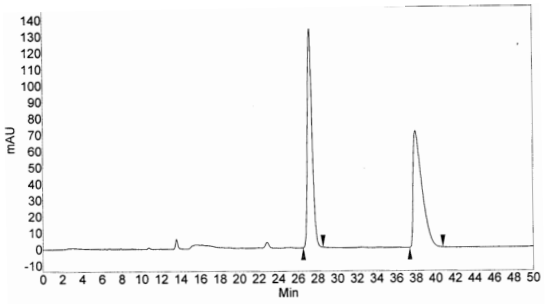
Table 2, entry 4



10g

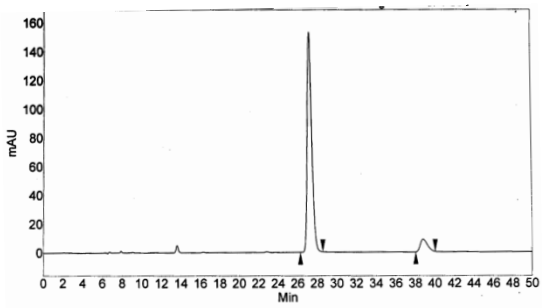
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



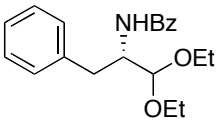
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.25	50.025	26.52	28.53
2	38.00	49.975	37.36	40.71
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.28	92.020	26.28	28.57
2	38.81	7.980	38.06	40.04
Total		100.000		

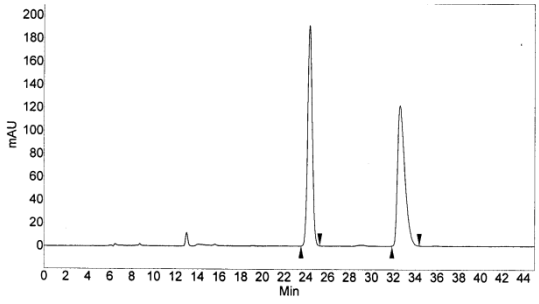
Table 2, entry 5



10h

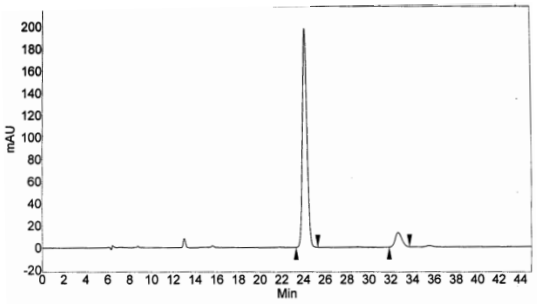
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



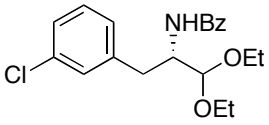
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	24.35	49.996	23.54	25.26
2	32.60	50.004	31.86	34.37
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	24.16	91.456	23.31	25.31
2	32.68	8.544	31.86	33.72
Total		100.000		

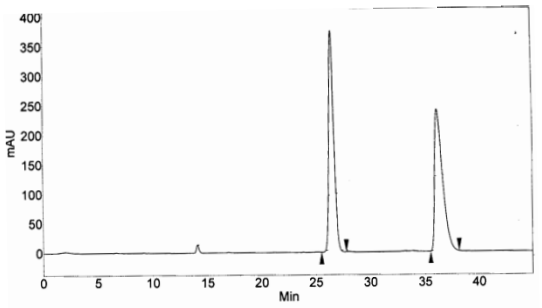
Table 2, entry 6



10i

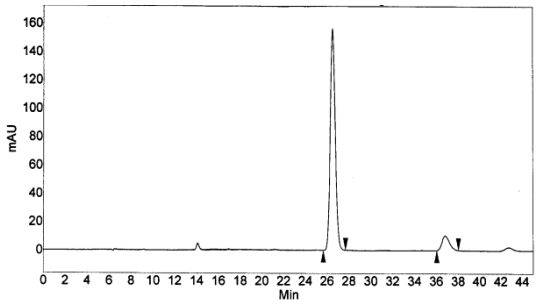
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



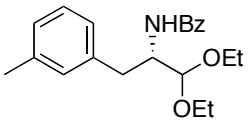
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	26.49	49.919	25.52	27.77
2	36.19	50.081	35.51	38.14
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	26.49	90.959	25.63	27.68
2	36.81	9.041	36.04	38.03
Total		100.000		

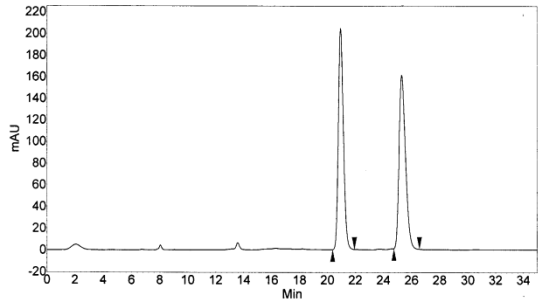
Table 2, entry 7



10j

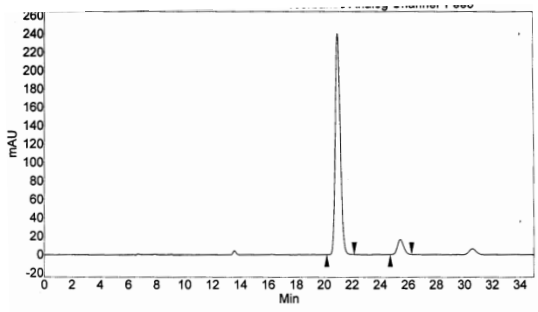
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



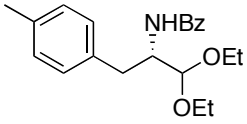
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	20.96	50.105	20.37	21.92
2	25.29	49.895	24.74	26.55
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	20.97	92.274	20.19	22.14
2	25.43	7.726	24.71	26.22
Total		100.000		

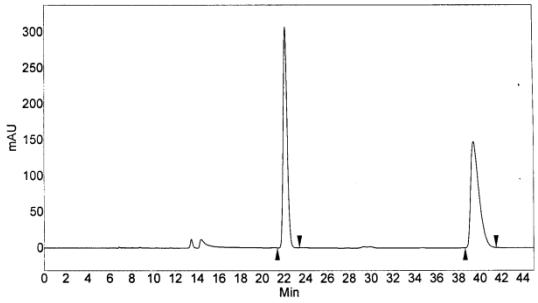
Table 2, entry 8



10k

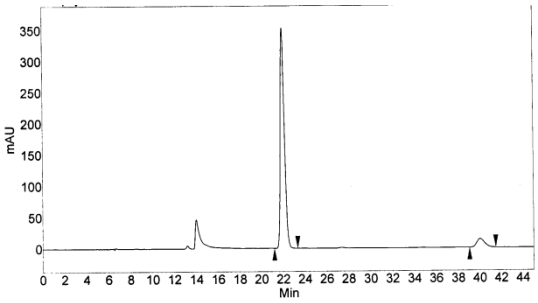
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



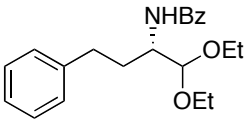
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	22.13	50.128	21.39	23.42
2	39.43	49.872	38.64	41.50
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	21.97	93.068	21.18	23.31
2	40.03	6.932	39.06	41.47
Total		100.000		

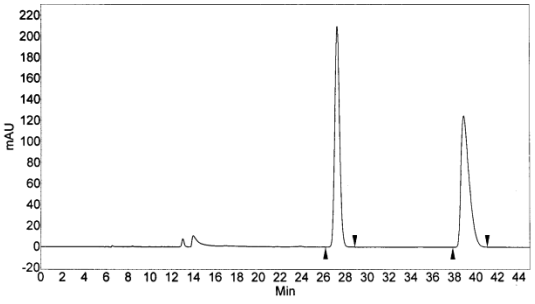
Table 2, entry 9



10l

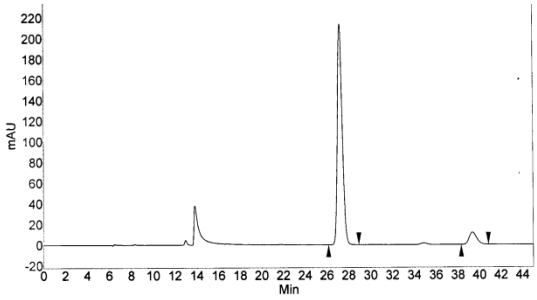
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



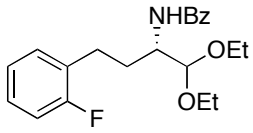
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.29	49.984	26.19	28.89
2	38.89	50.016	37.85	41.05
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.25	92.130	26.15	28.93
2	39.36	7.870	38.31	40.82
Total		100.000		

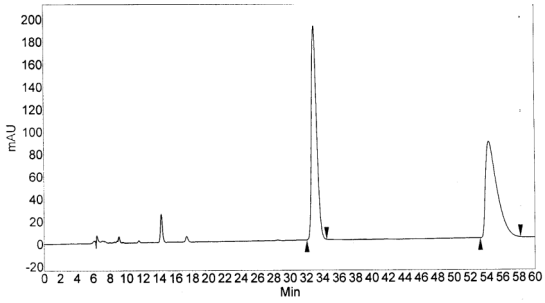
Table 2, entry 10



10m

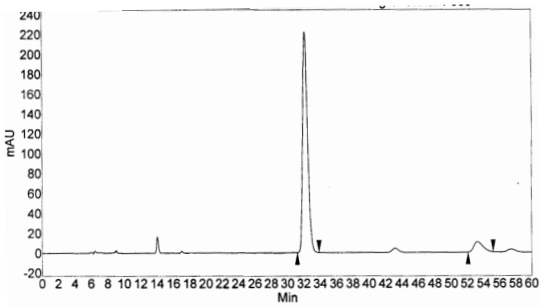
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



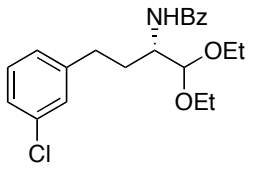
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	33.03	50.082	32.07	34.49
2	54.33	49.918	53.25	58.21
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	32.20	92.188	31.21	33.87
2	53.20	7.812	52.08	55.17
Total		100.000		

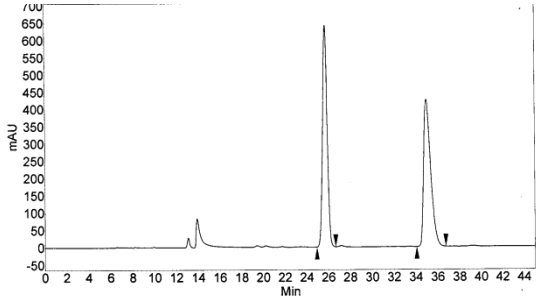
Table 2, entry 11



10n

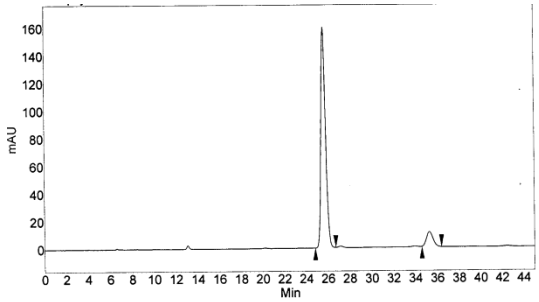
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



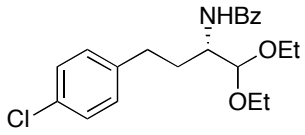
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	25.75	49.826	24.94	26.66
2	35.00	50.174	34.09	36.73
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	25.63	91.480	24.82	26.70
2	35.27	8.520	34.58	36.37
Total		100.000		

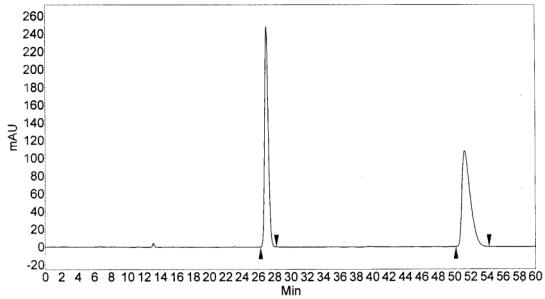
Table 2, entry 12



10o

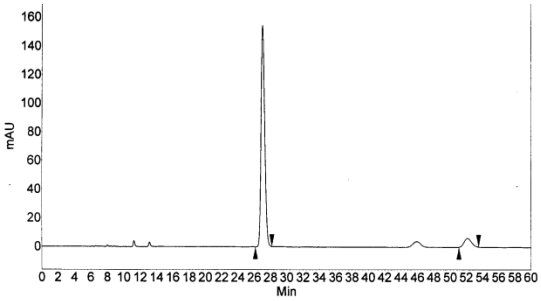
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



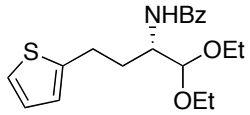
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.07	50.086	26.28	28.22
2	51.29	49.914	50.18	54.24
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.09	92.557	26.13	28.17
2	52.13	7.443	51.08	53.50
Total		100.000		

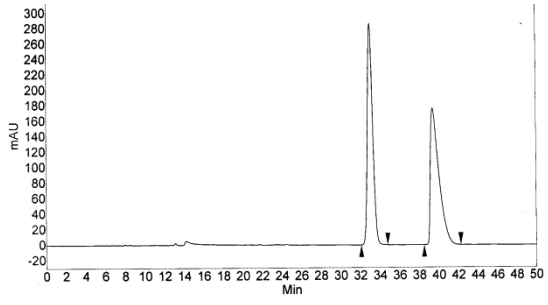
Table 2, entry 13



10p

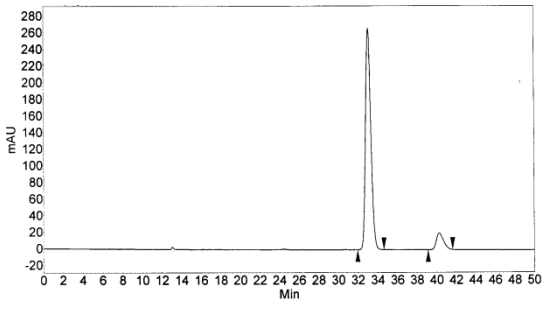
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic



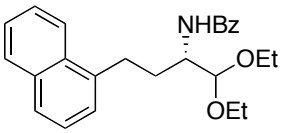
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	33.05	50.047	32.10	34.78
2	39.40	49.953	38.49	42.21
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	33.07	90.968	31.96	34.62
2	40.24	9.032	39.10	41.61
Total		100.000		

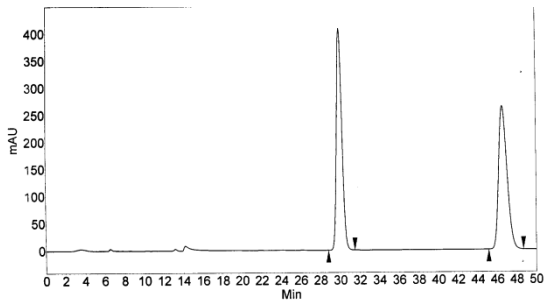
Table 2, entry 14



10q

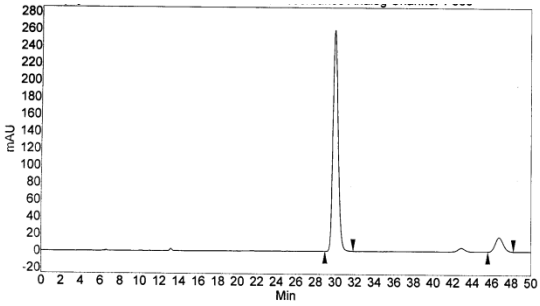
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



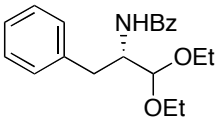
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	29.93	49.905	28.79	31.48
2	46.53	50.095	45.10	48.66
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	30.01	90.839	28.95	31.84
2	46.72	9.161	45.56	48.19
Total		100.000		

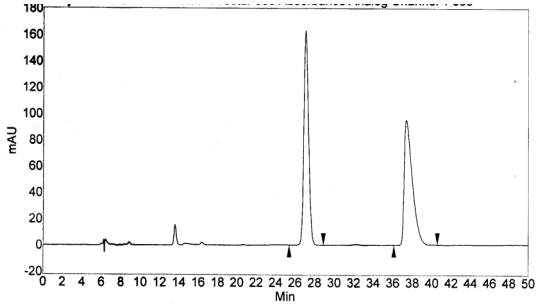
Scheme 2



10h

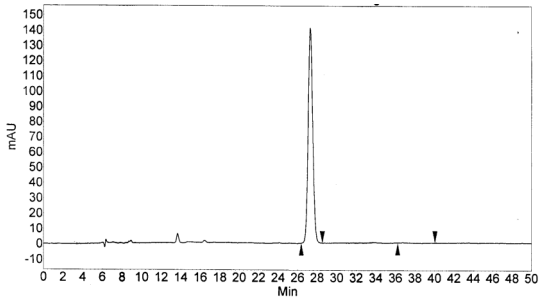
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.; **Eluent:** Hexanes/IPA (95/5); **Flow rate:** 0.5 mL/min; **Detection:** UV220 nm.

Racemic



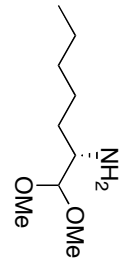
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.16	50.009	25.39	28.90
2	37.43	49.991	36.12	40.56
Total		100.000		

Chiral



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	27.31	99.811	26.37	28.53
2	36.69	0.189	36.22	40.04
Total		100.000		

Table 1, entry 10



6b

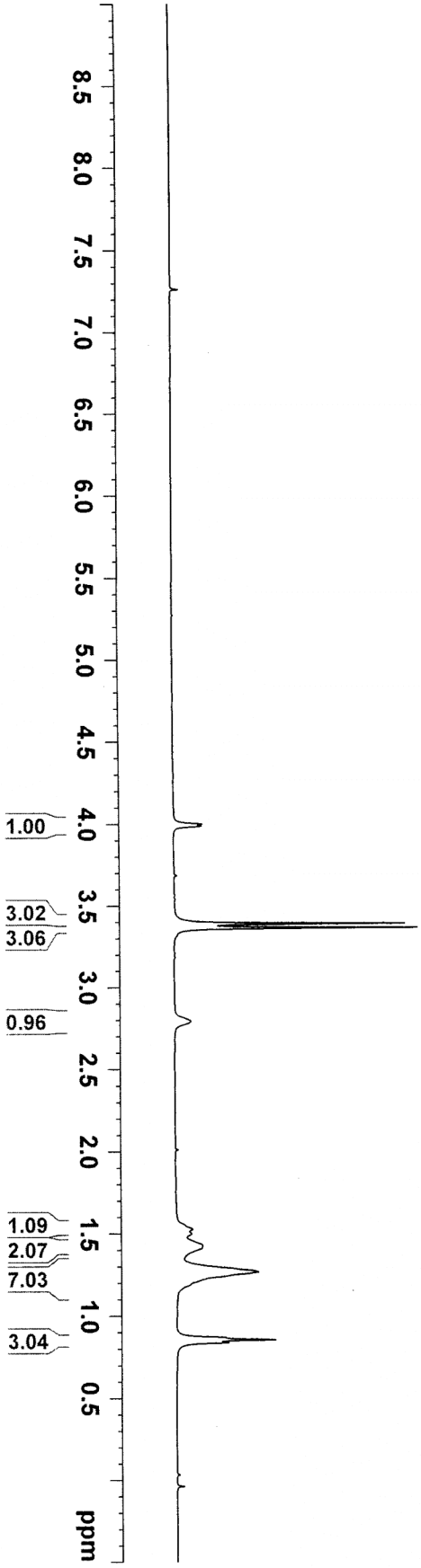


Table 1, entry 10

6b

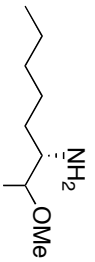
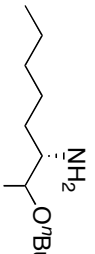
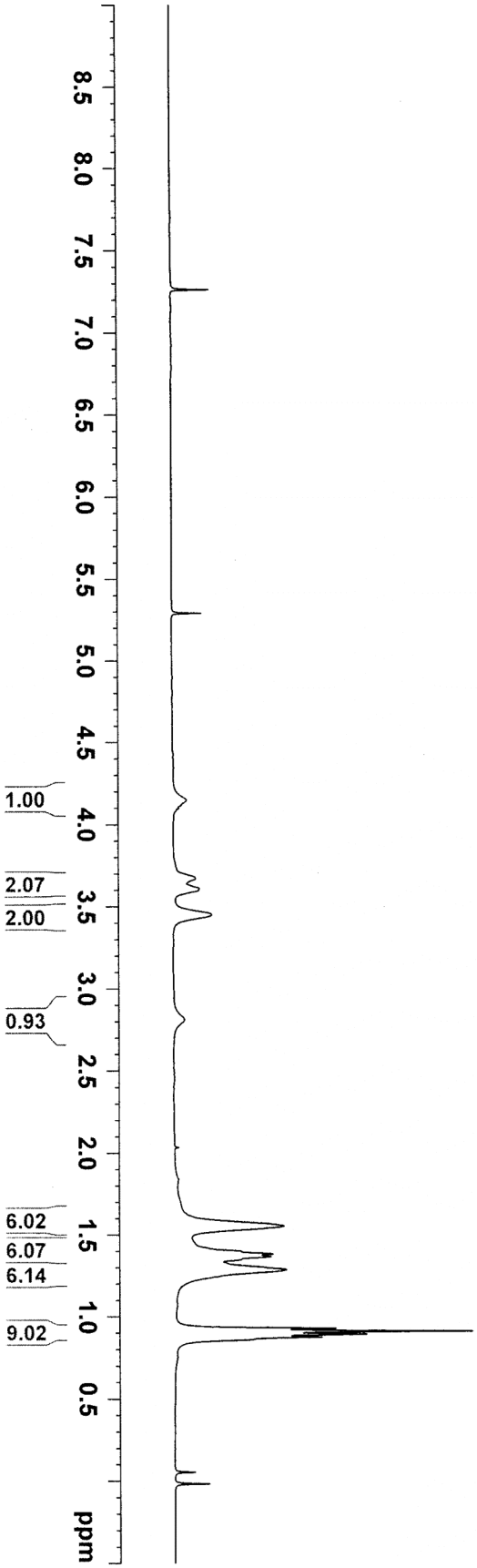


Table 1, entry 11

6c





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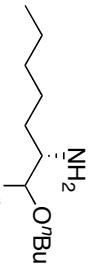

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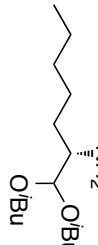

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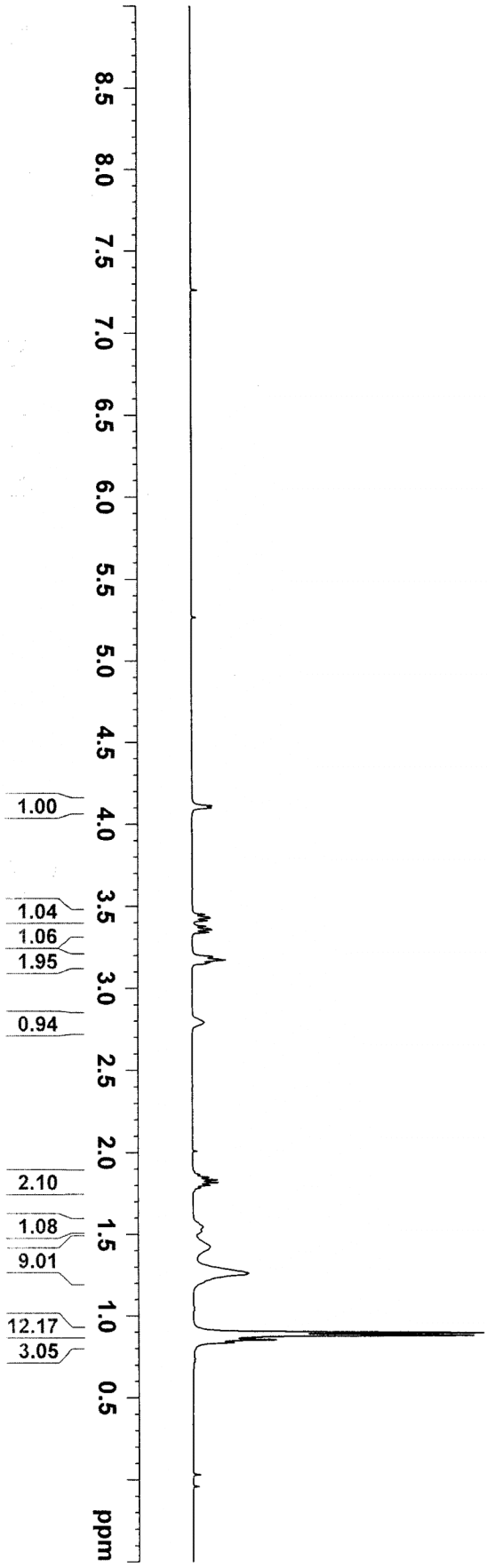

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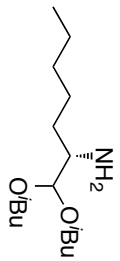

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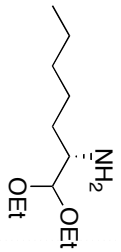

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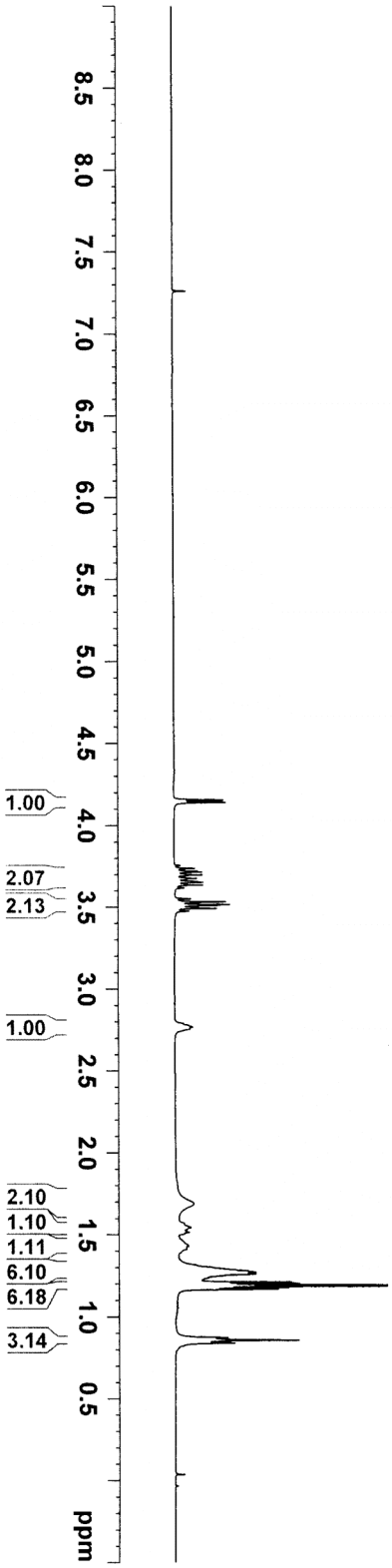

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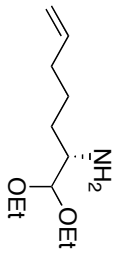
Table 2, entry 2



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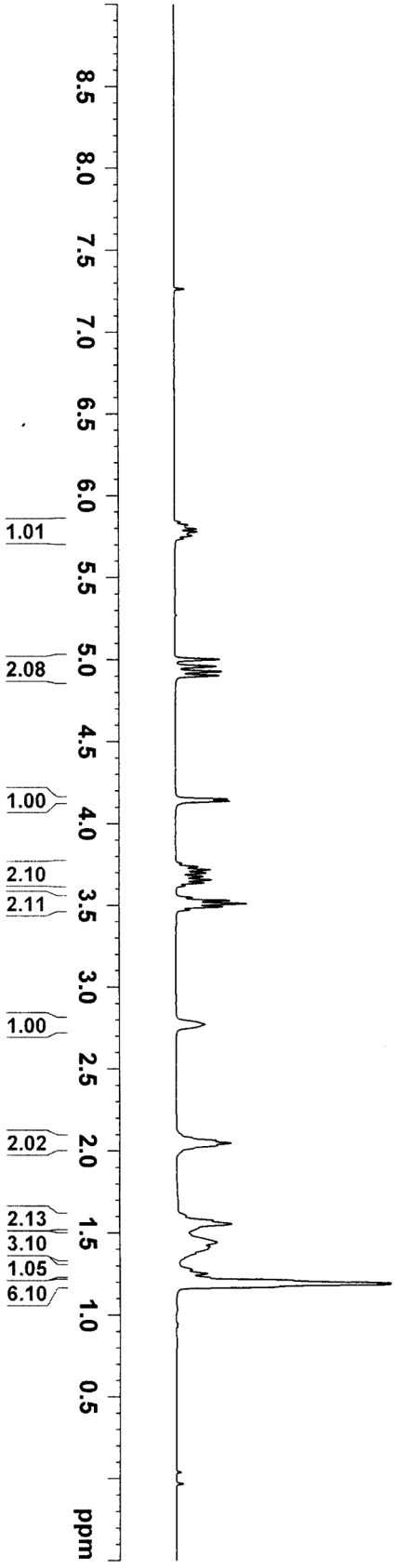

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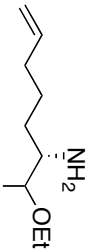

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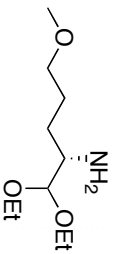

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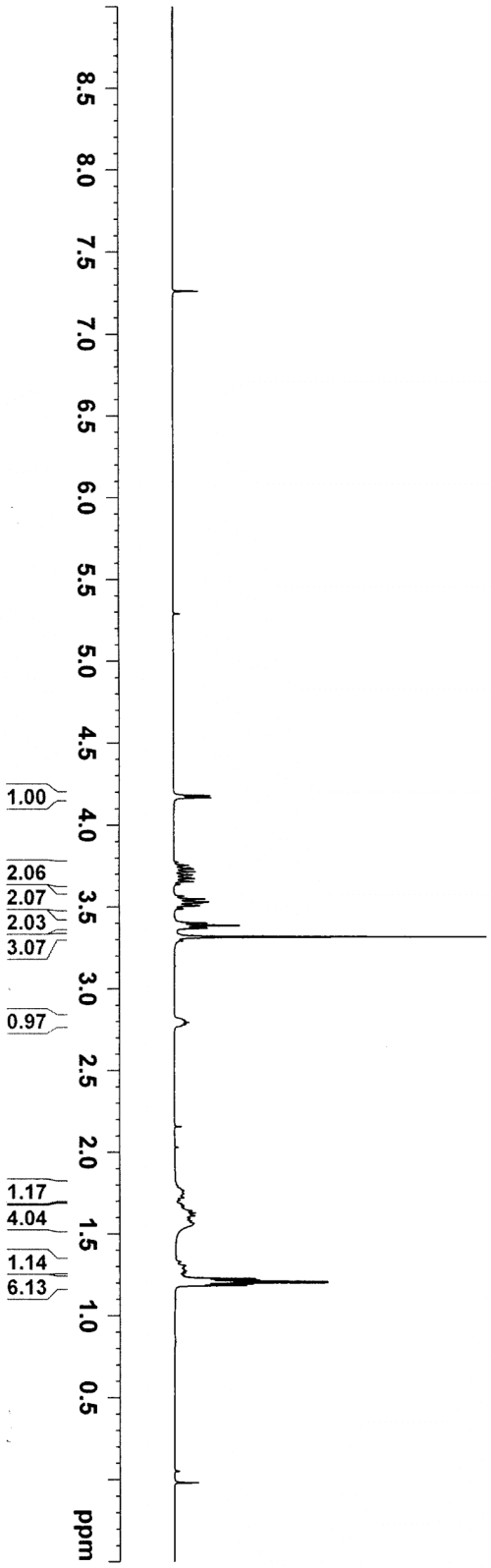

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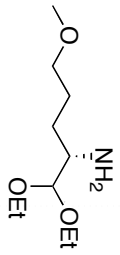

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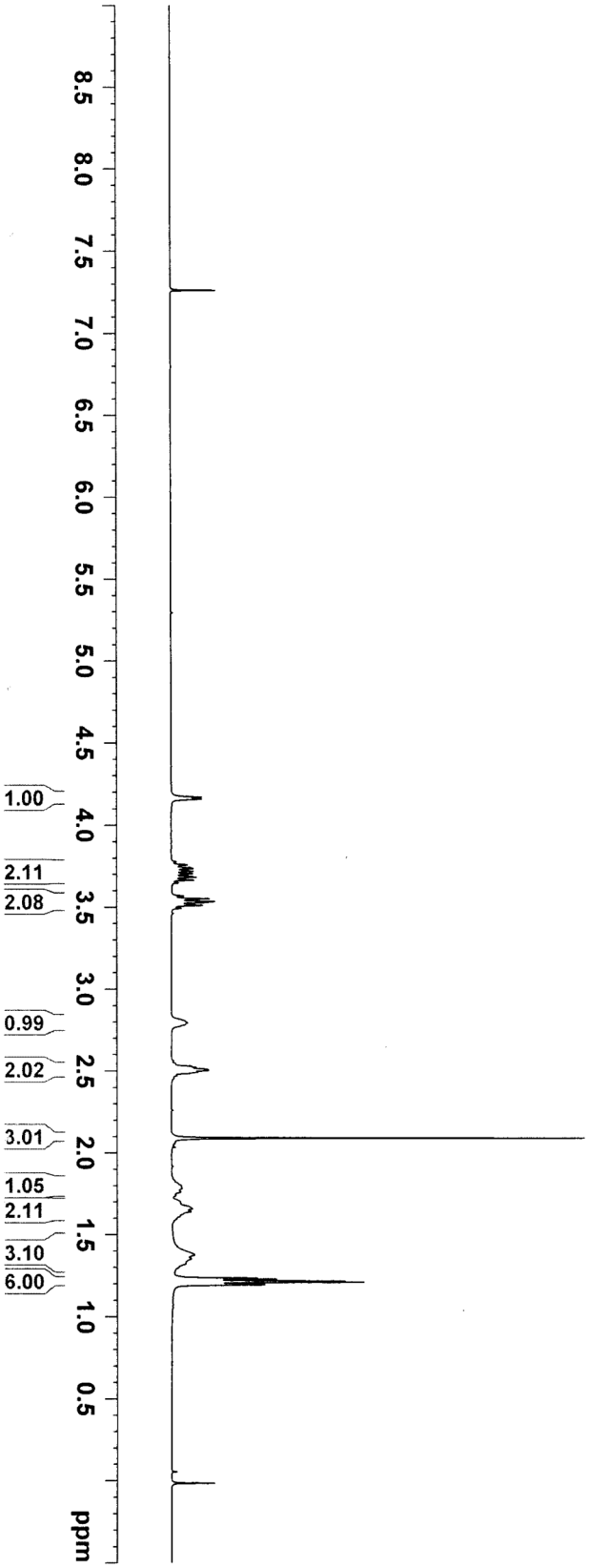

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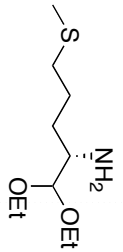

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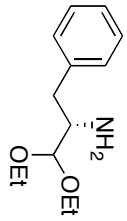

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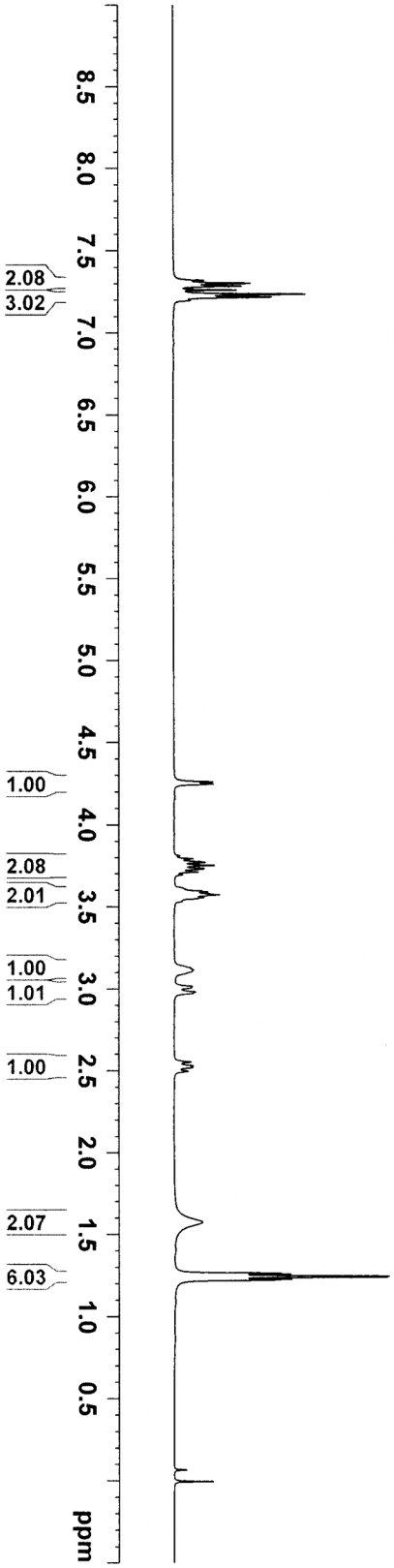

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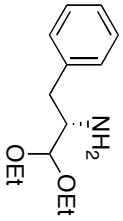

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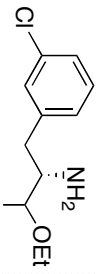

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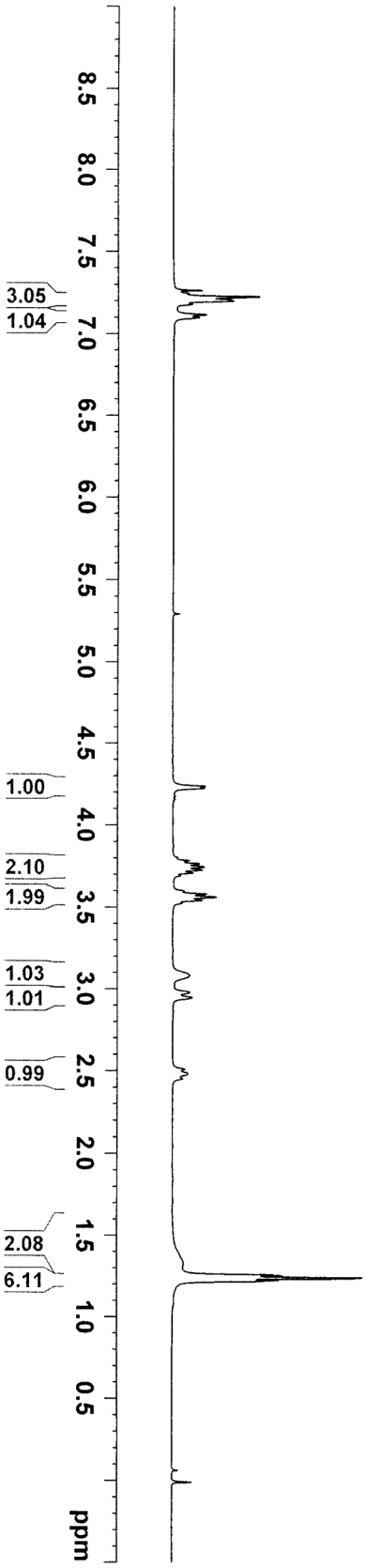

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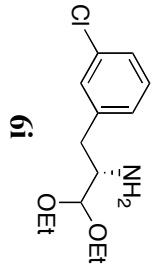

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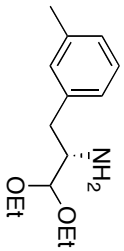

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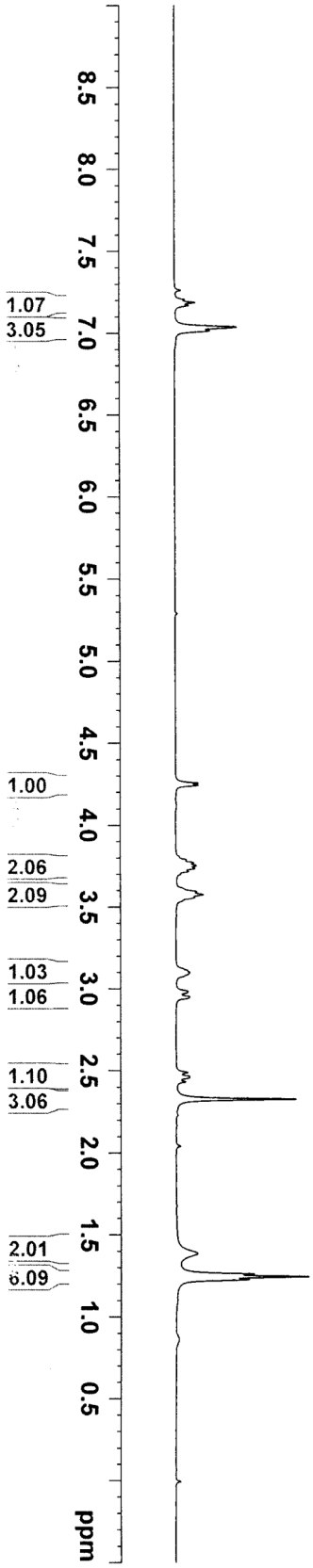

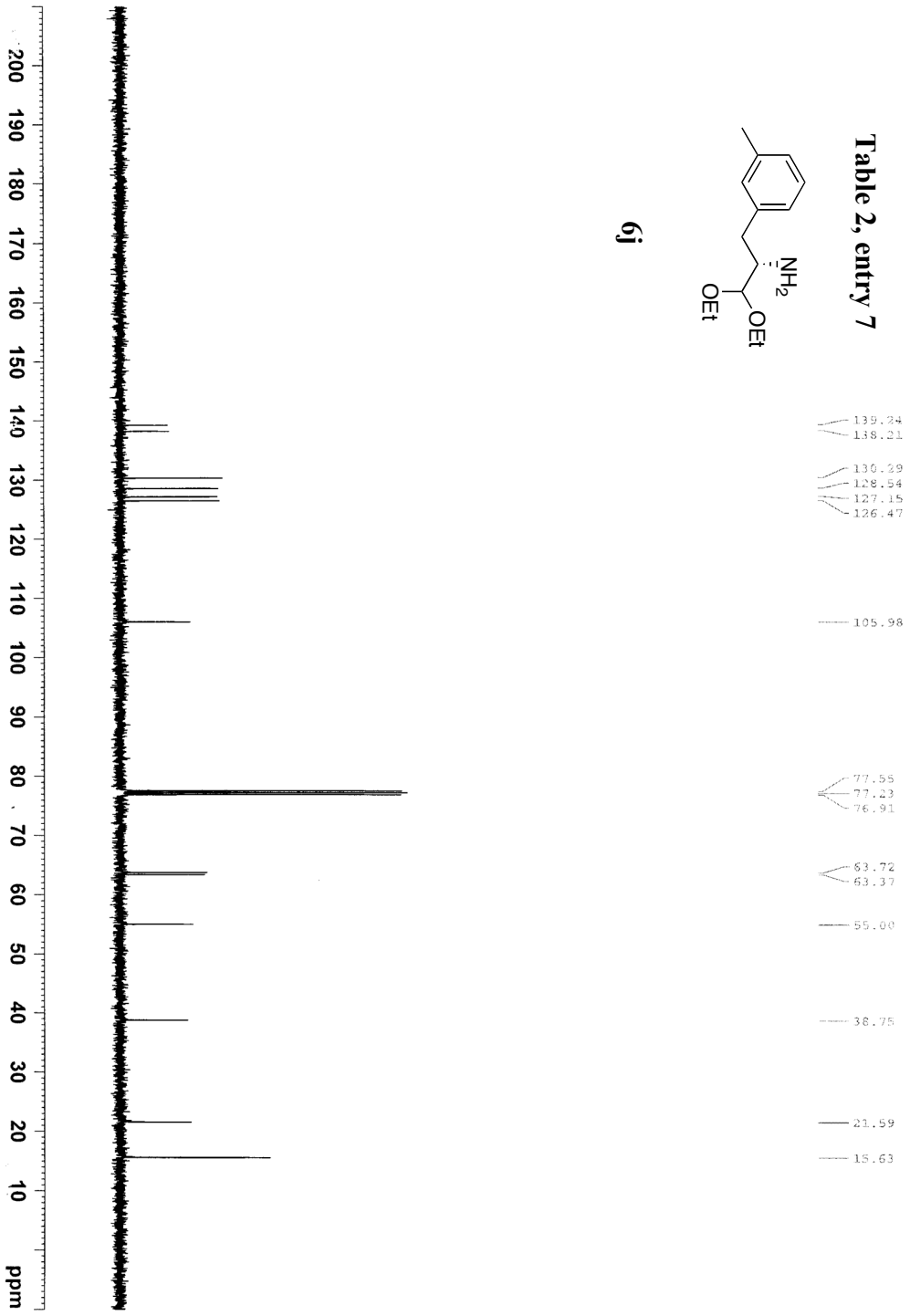

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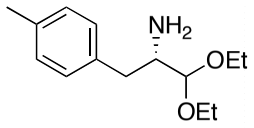

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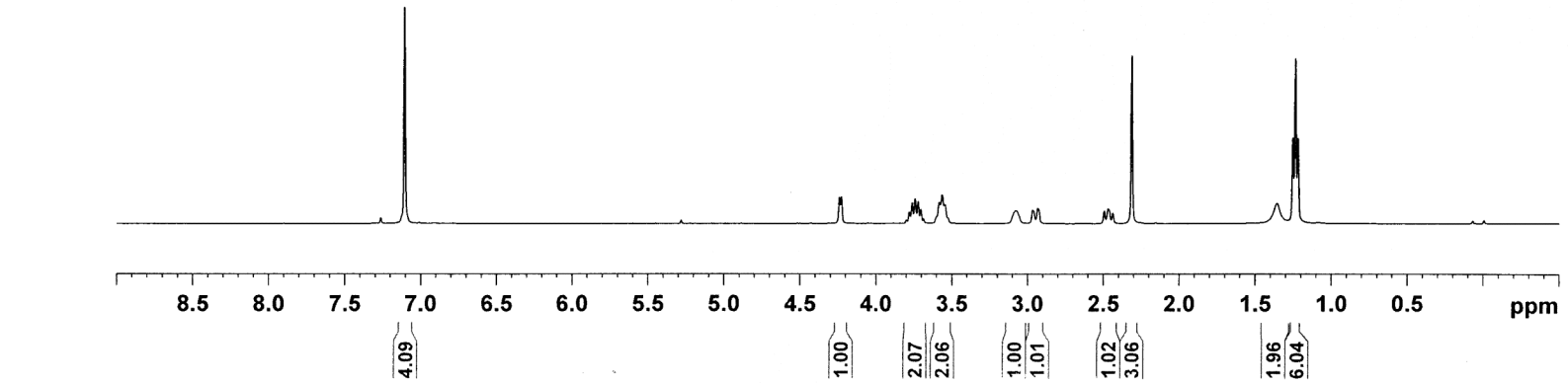

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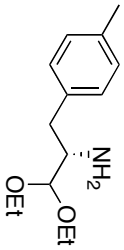

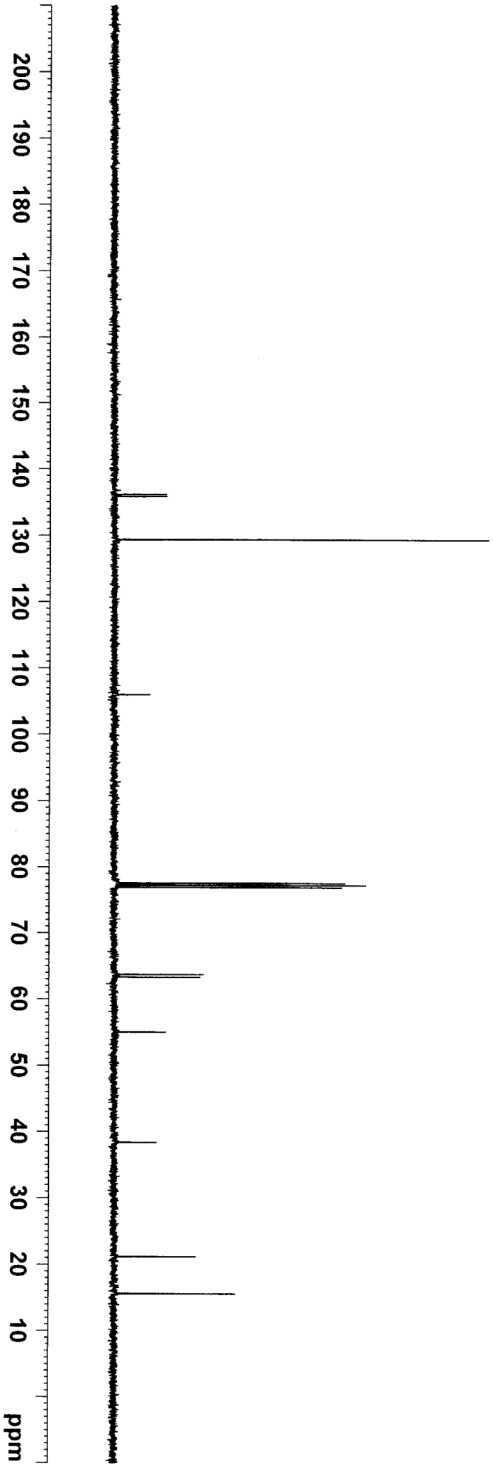

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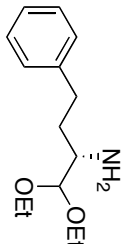
15.61

Table 2, entry 9



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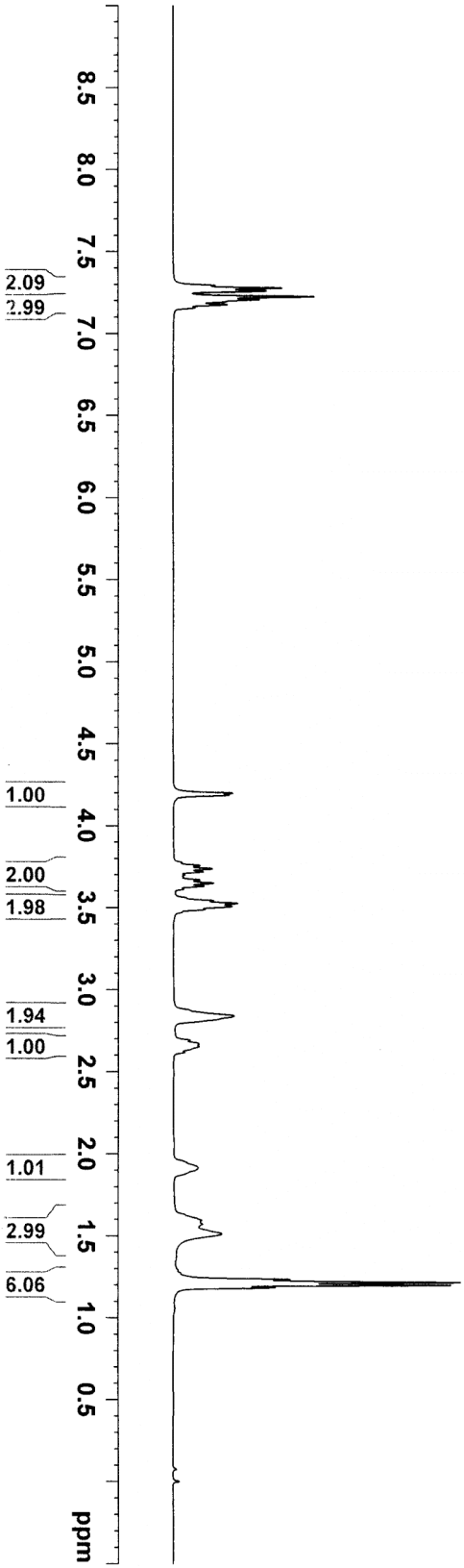

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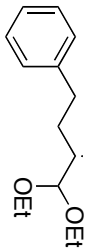

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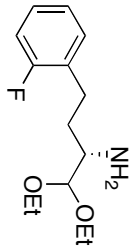

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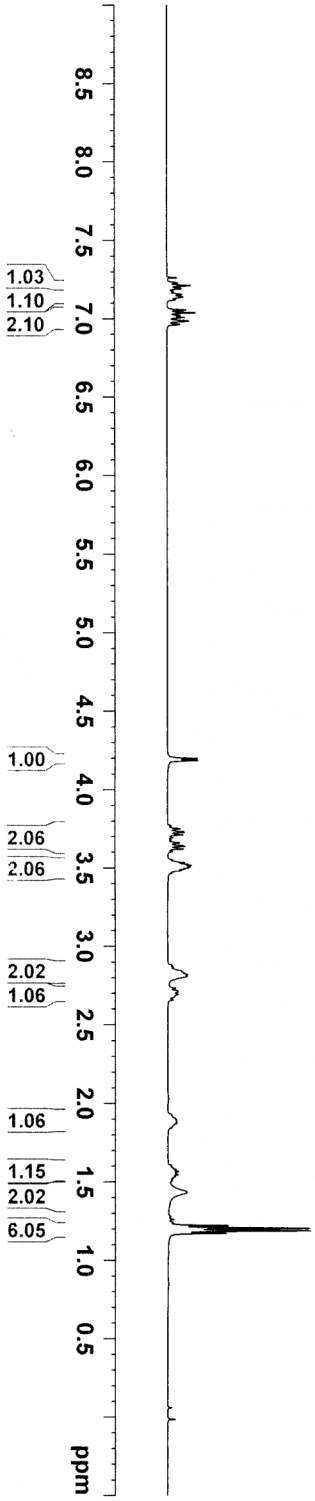

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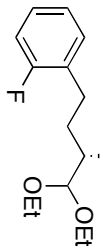

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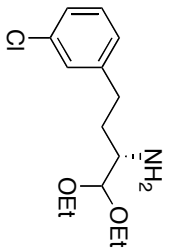

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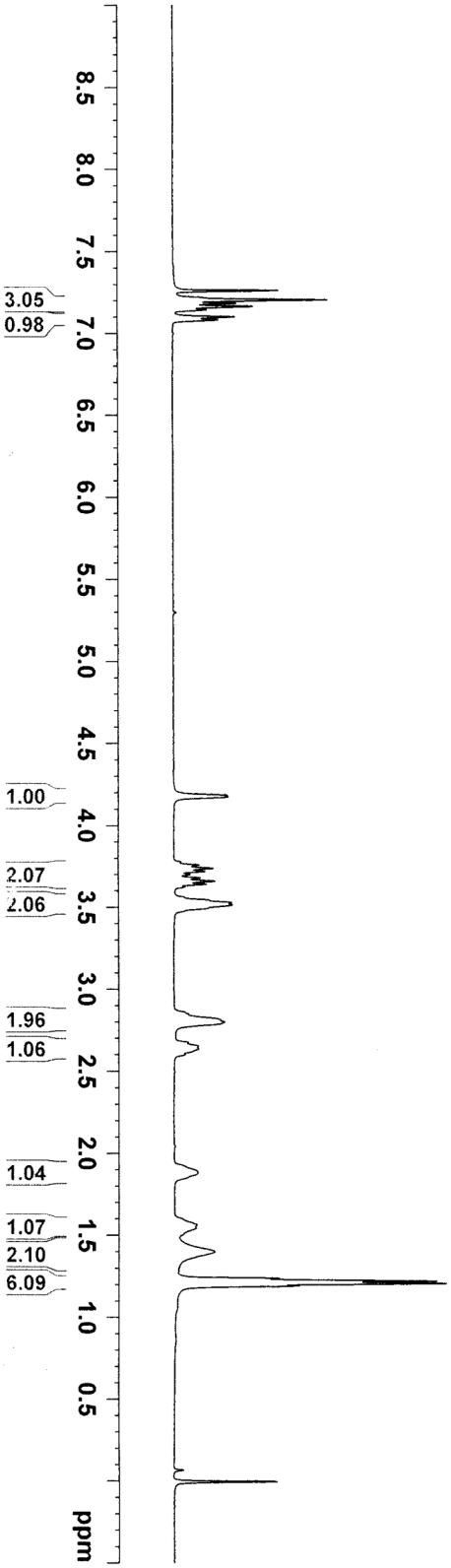

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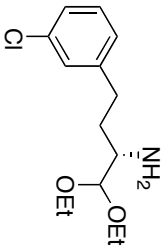

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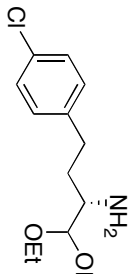

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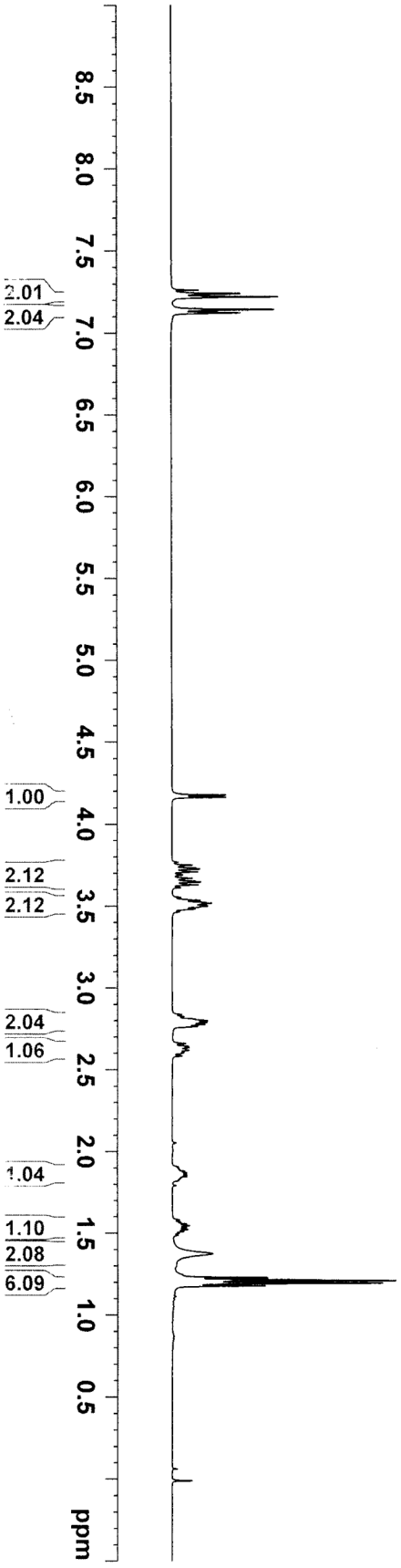

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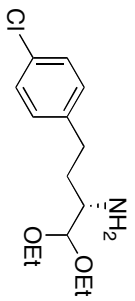

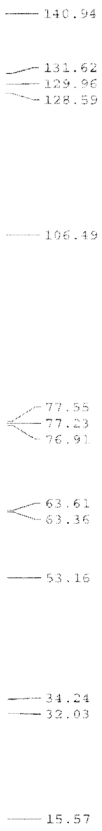

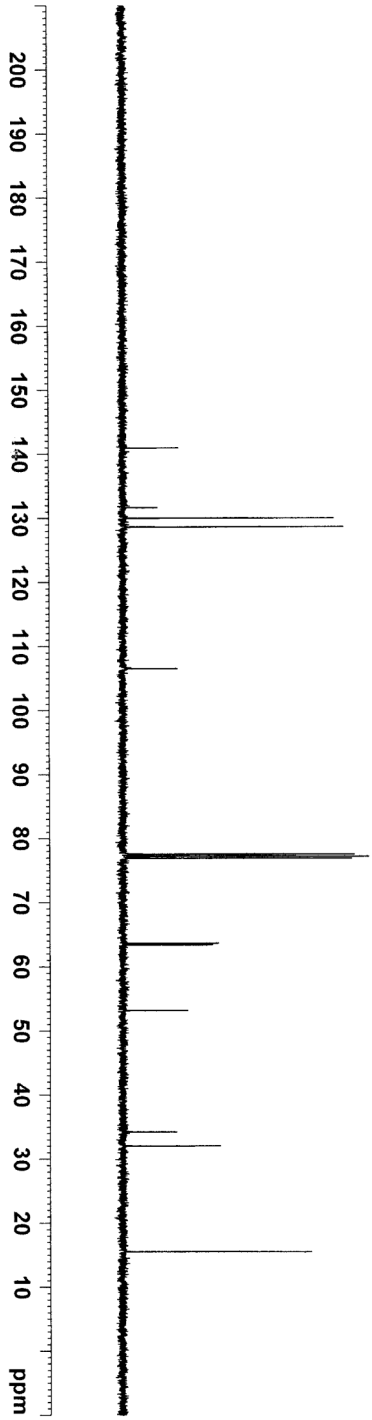

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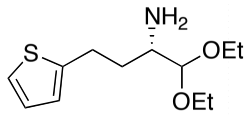

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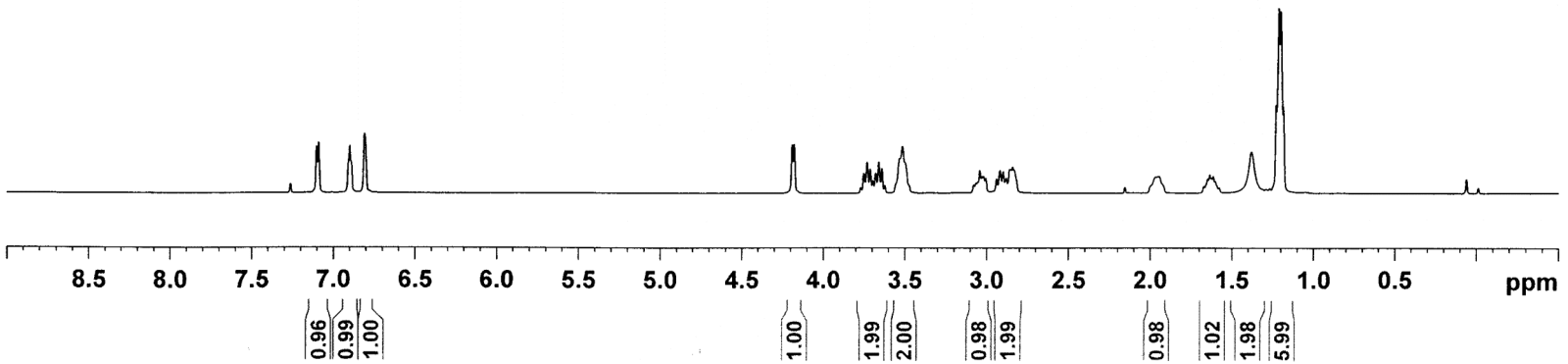

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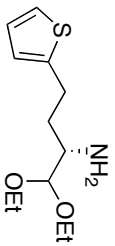

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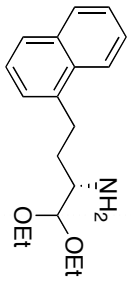

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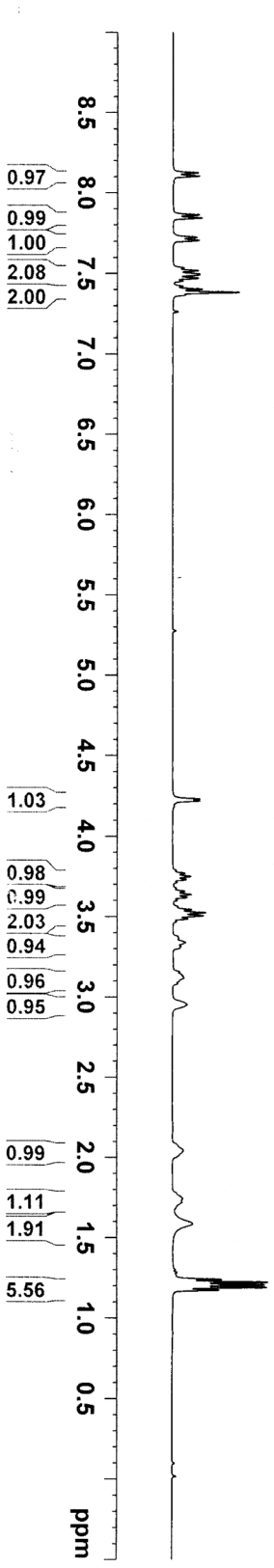

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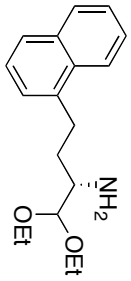
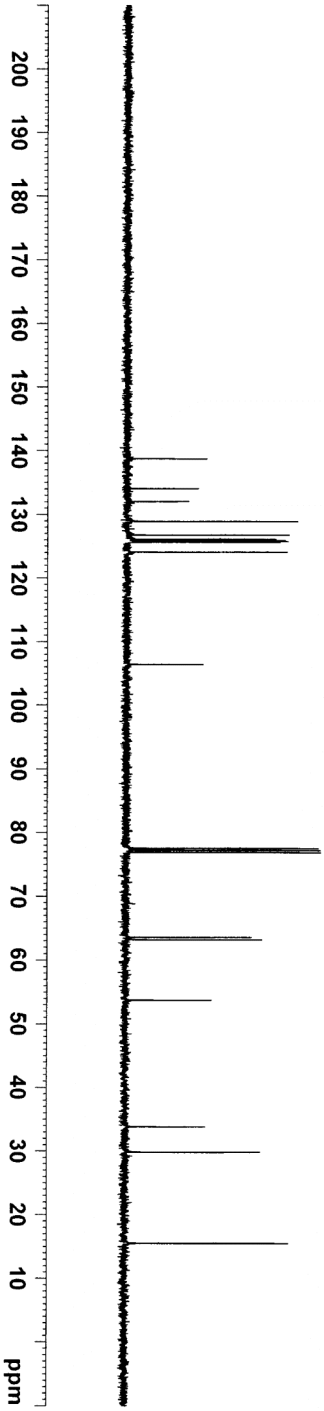
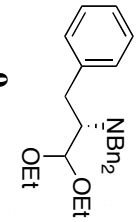




Scheme 2



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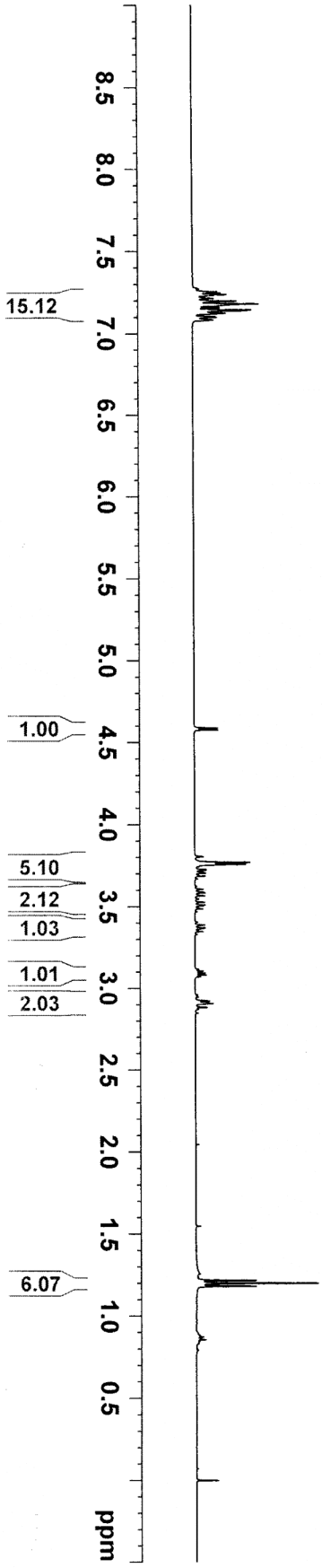
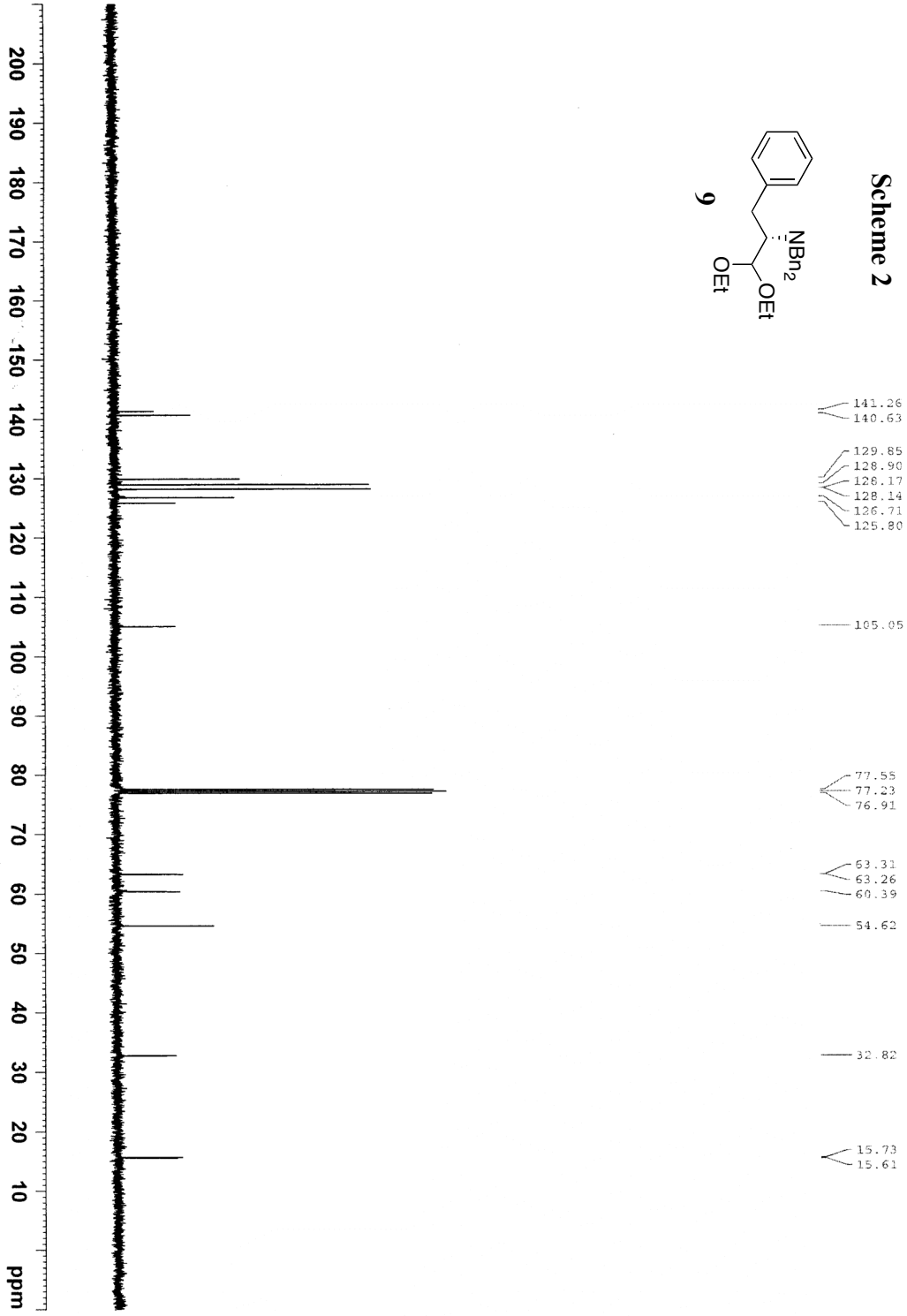
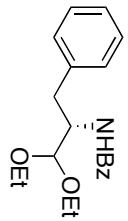




Scheme 3



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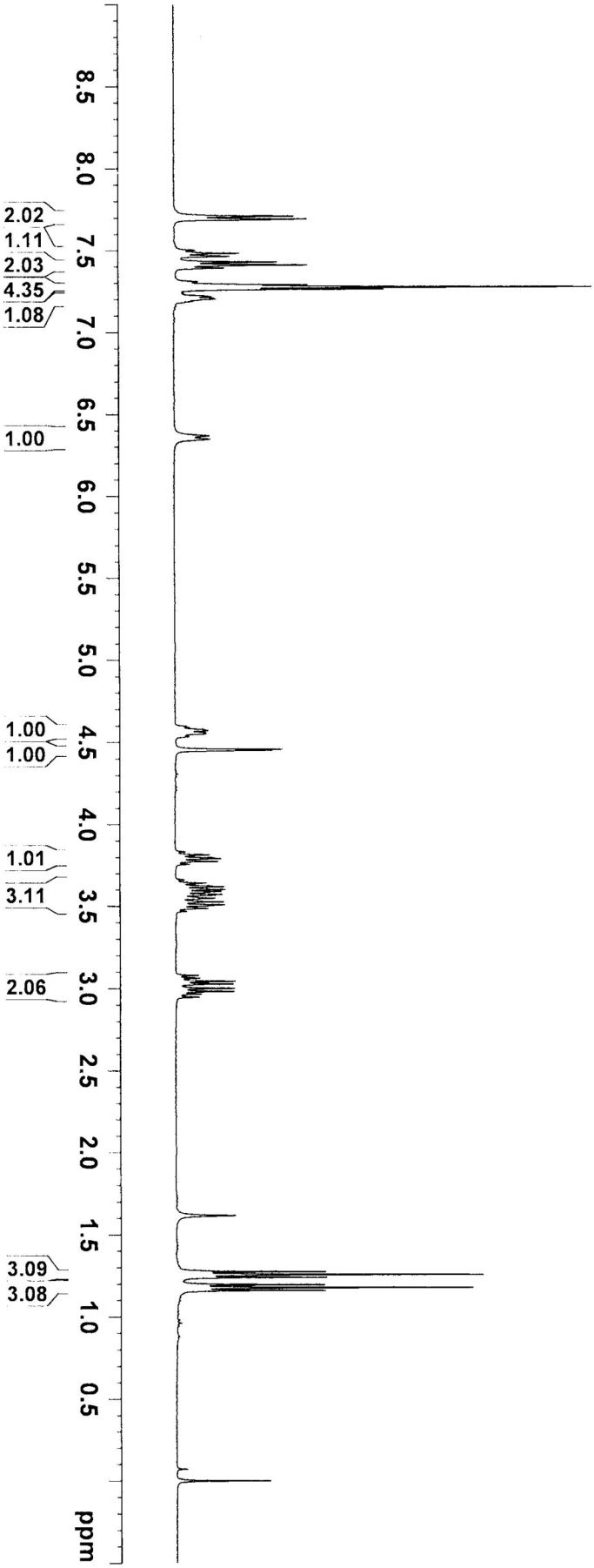
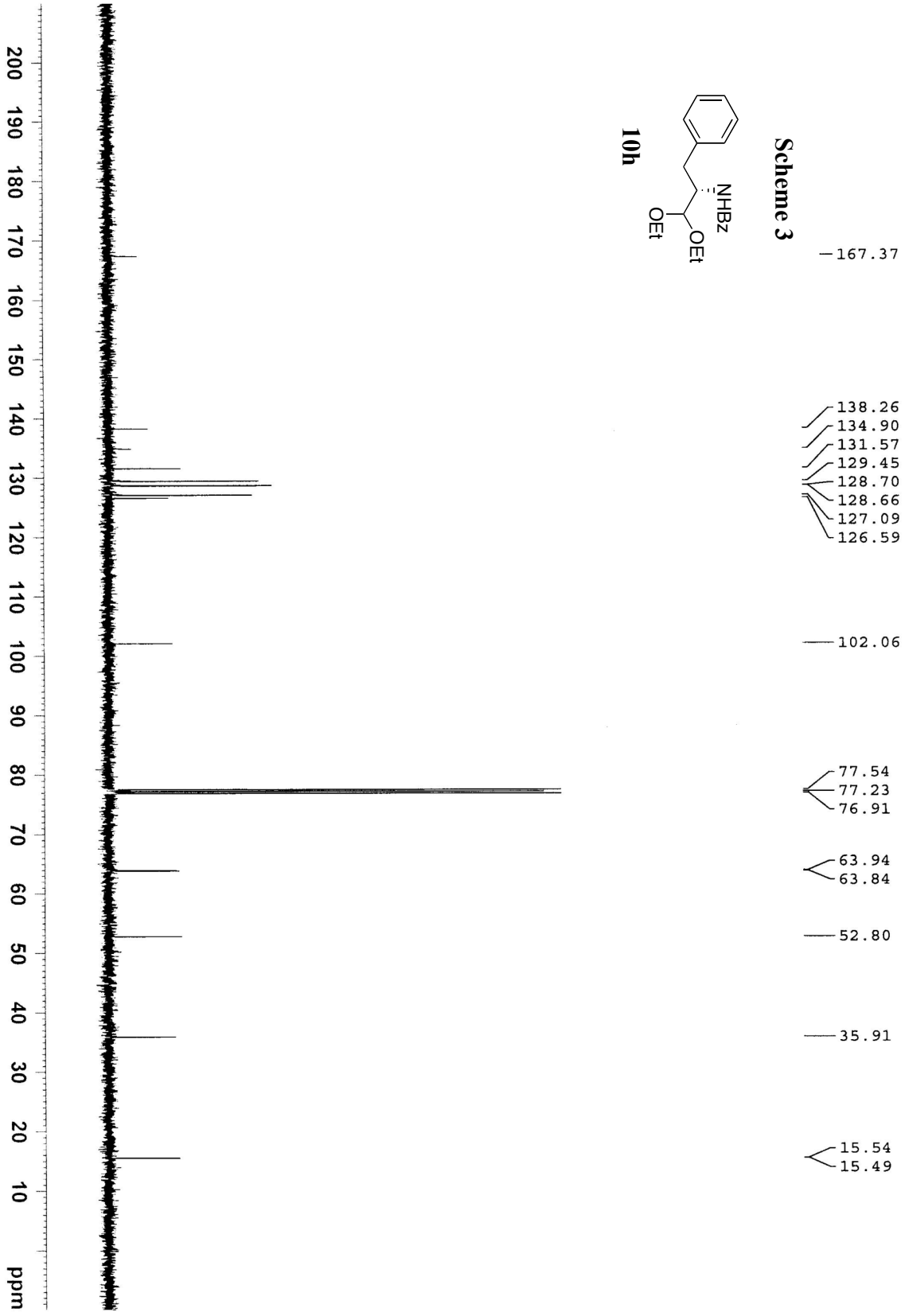
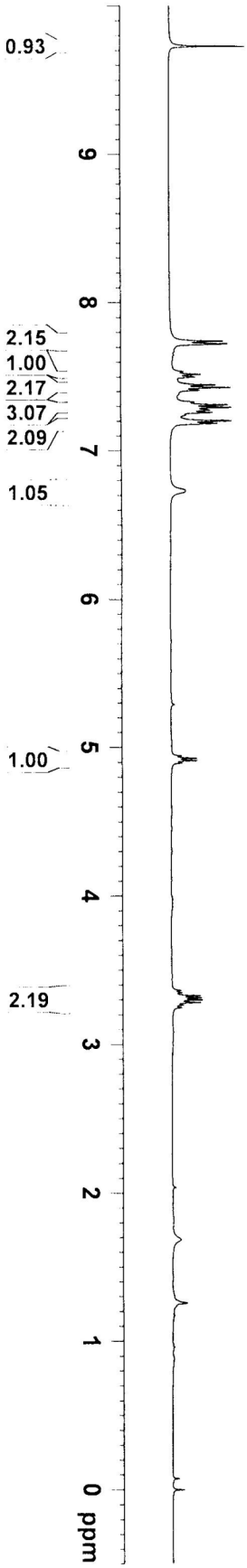
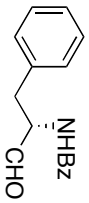






Scheme 3



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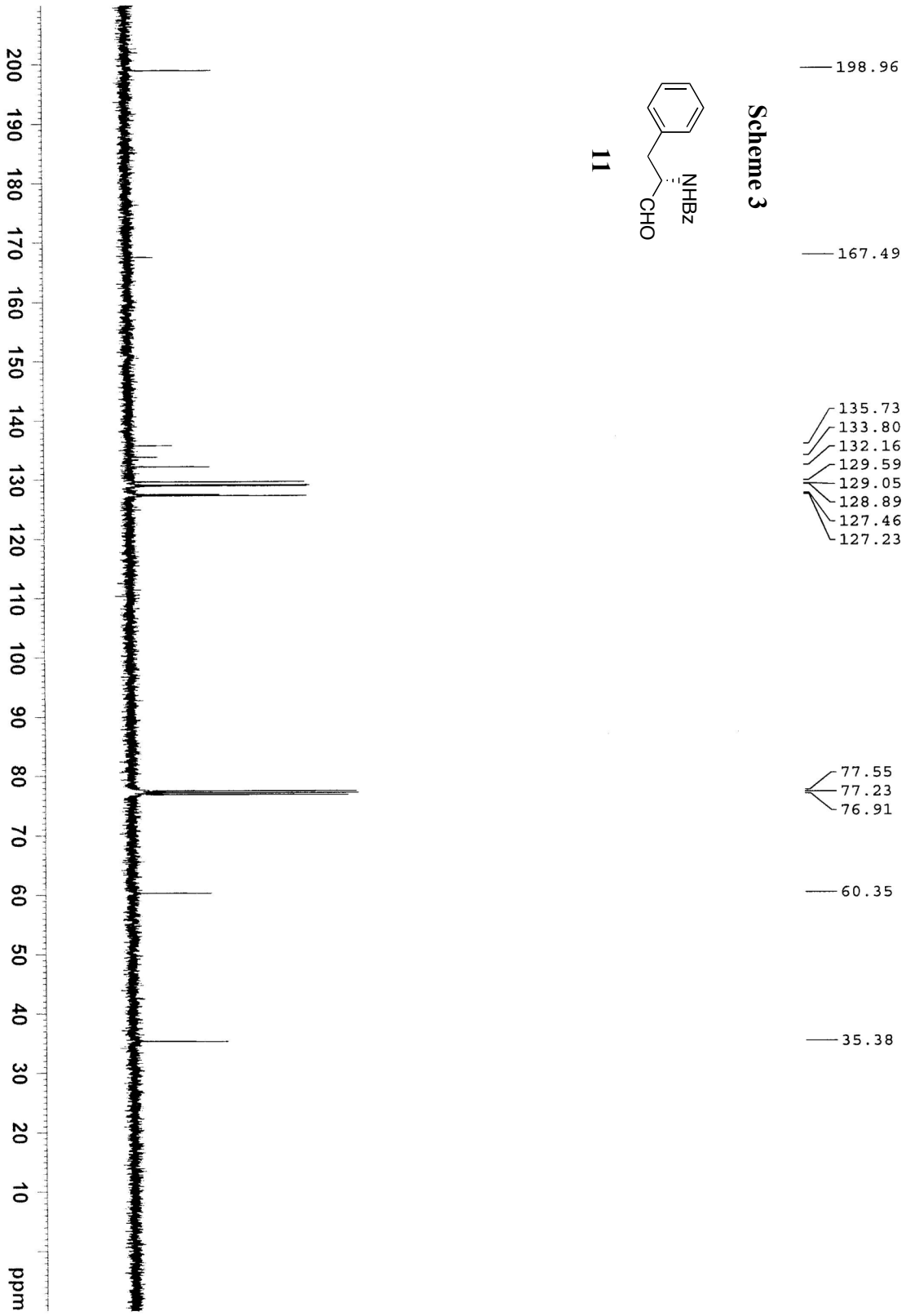
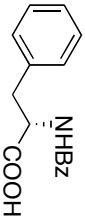


Scheme 3



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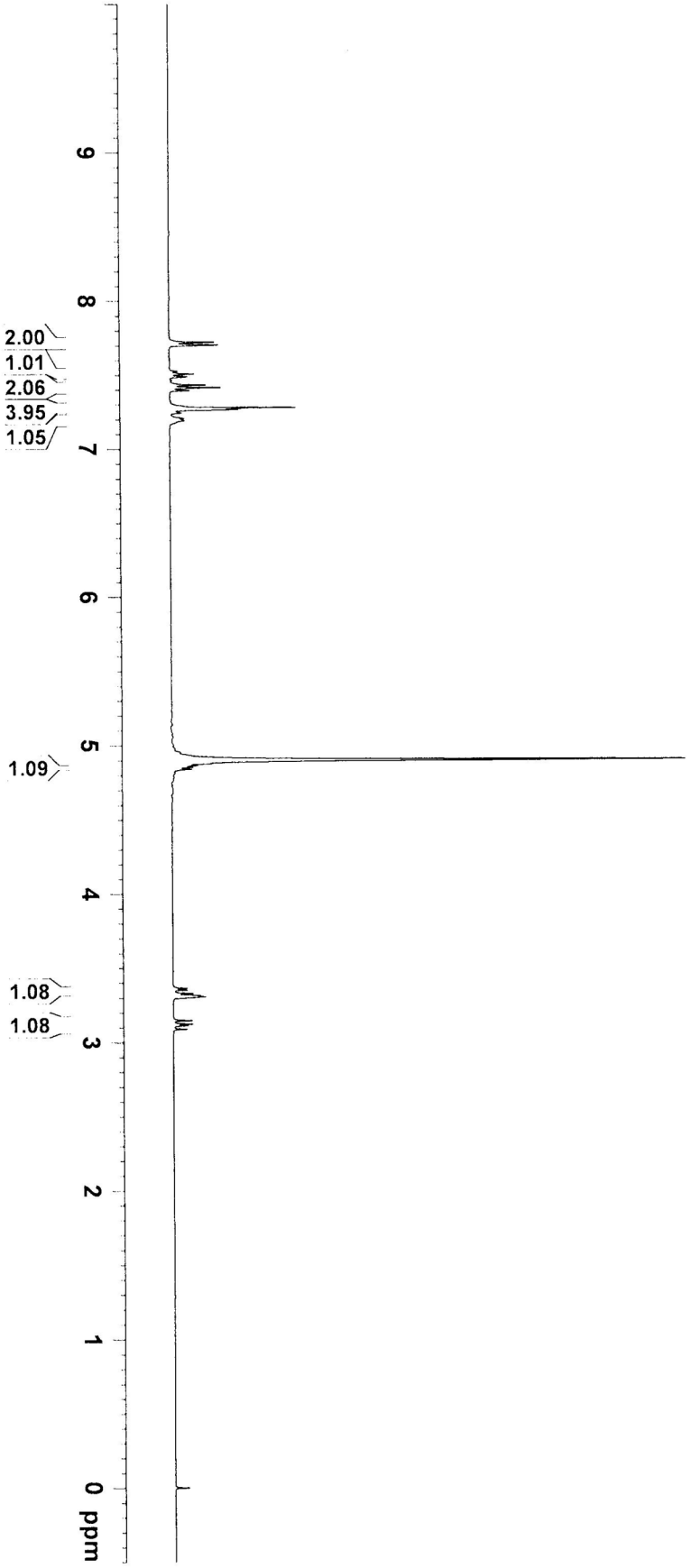
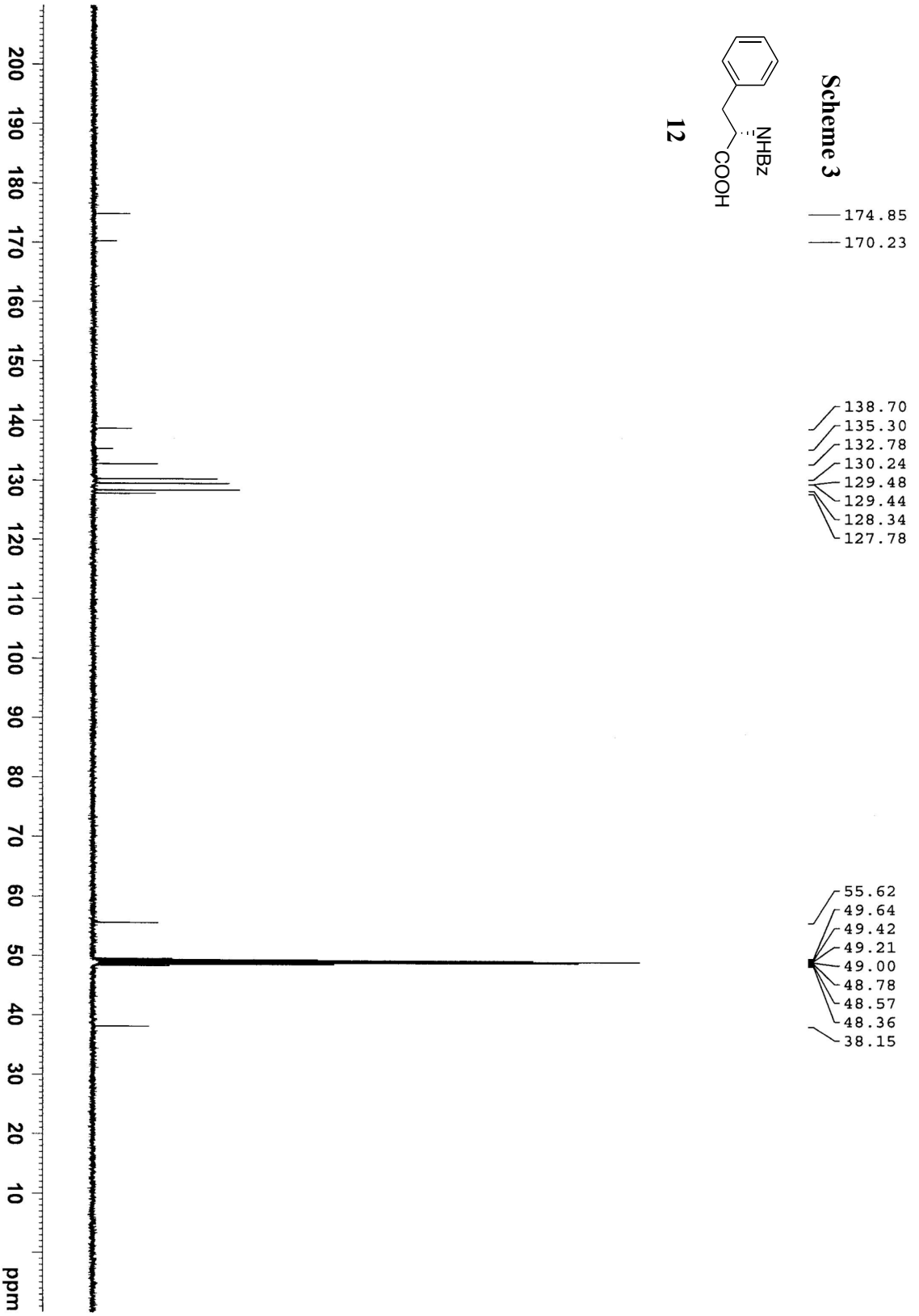
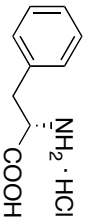




Scheme 3



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