

Organocatalytic asymmetric biomimetic transamination of aromatic ketone to optically active amine

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Supporting Information

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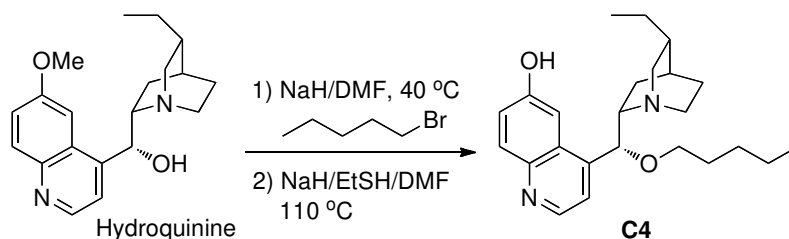
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General Methods. All commercially available reagents were used without further purification. Toluene was distilled from sodium-benzophenone. Dichloromethane was distilled from CaH₂. *N,N*-Dimethylformamide was dried over 4 Å molecular sieves (activated at 180 °C in vacuo 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 and ¹³C NMR spectra were recorded on a 100 MHz NMR spectrometer. IR spectra were recorded on a FT-IR spectrometer. Melting points were uncorrected. *o*-HOPhCH₂NH₂ was prepared from 2-methoxybenzylamine through demethylation using BBr₃,¹ and hydroquinine was prepared according to the reported procedure.²

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

(2) C. Palacio and S. J. Connon, *Org. Lett.*, 2011, **13**, 1298.

Preparation of Catalyst C4



To a solution of hydroquinine (2.0 g, 6.1 mmol) in DMF (20 mL) was added NaH (70% suspension in mineral oil) (0.627 g, 18.3 mmol). After the reaction mixture was stirred at rt for 1 h, 1-bromopentane (1.84 g, 12.2 mmol) was added in one portion. Upon stirring at 40 °C overnight, the reaction mixture was quenched with H₂O (20 mL), extracted with EtOAc (40 mL x 3), washed with brine (20 mL x 3), dried over MgSO₄, filtered, and concentrated to give a yellow oil, which was used directly for the next step.

To a suspension of NaH (70% suspension in mineral oil) (2.1 g, 61.3 mmol) (washed with *n*-hexane, dried in vacuo) in DMF (20 mL) was added EtSH (7.58 g, 122.0 mmol) dropwise at 0 °C under N₂ over 10 min. After the reaction mixture was

stirred at rt for 20 min, a solution of the crude product from the previous step in DMF (10 mL) was added in one portion. Upon stirring at 110 °C overnight, the reaction mixture was cooled to rt, acidified with concentrated HCl, washed with *n*-hexane (40 mL x 3), brought to pH = 10 with NH₄OH, extracted with EtOAc (60 mL x 3), washed with H₂O and brine, dried over MgSO₄, filtered, concentrated, and purified by flash column chromatography (silica gel, packed with EtOAc containing 1% Et₃N) (eluent: EtOAc/MeOH = 40/1 to 10/1) to give compound **C4** as a yellow solid (1.26 g, 54% overall). mp. 82-85 °C; $[\alpha]_D^{20} = -66.8$ (*c* 0.99, CHCl₃); IR (film) 3072, 1618, 1464, 1241, 1118 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 11.38 (br s, 1H), 8.67 (d, *J* = 4.4 Hz, 1H), 8.23 (s, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.38 (d, *J* = 4.4 Hz, 1H), 7.30 (dd, *J* = 9.2, 1.6 Hz, 1H), 5.34 (s, 1H), 3.71-3.56 (m, 1H), 3.30-3.16 (m, 3H), 3.05-2.80 (m, 2H), 2.42-2.26 (m, 1H), 2.12-1.98 (m, 1H), 1.98-1.86 (m, 1H), 1.86-1.78 (m, 1H), 1.66-1.48 (m, 4H), 1.45-1.22 (m, 5H), 1.22-1.08 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.75 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.7, 146.4, 144.0, 143.5, 131.4, 128.0, 123.6, 117.8, 106.1, 78.7, 69.4, 59.3, 58.0, 43.5, 37.0, 29.8, 28.5, 27.5, 27.3, 25.4, 22.5, 19.7, 14.1, 11.9; HRMS Calcd for C₂₄H₃₅N₂O₂ (M+H): 383.2693; Found: 383.2686.

X. Xiao, Y. Xie, C. Su, M. Liu and Y. Shi, *J. Am. Chem. Soc.*, 2011, **133**, 12914.

Representative procedure for transamination of ketones (Table 2, entry 1).

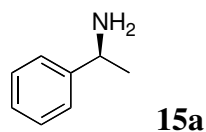
To a Schlenk tube was added ketone **14a** (0.120 g, 1.00 mmol), *o*-HOPhCH₂NH₂ (0.185 g, 1.50 mmol), catalyst **C4** (0.077 g, 0.20 mmol), and toluene (5 mL). After stirring at 110 °C for 72 h, the reaction mixture was concentrated and subjected to flash column chromatography (silica gel, eluent: PE/EtOAc = 30/1) to remove *o*-HOPhCH₂NH₂, catalyst, and other byproducts. The resulting aldimine along with small amounts of ketone **14a** was dissolved in THF (1 mL) and 1N HCl (4 mL). Upon stirring at 20 °C for 24 h, the reaction mixture was washed with *n*-hexane (15 mL x 3), brought to pH > 7 with solid K₂CO₃, extracted with CH₂Cl₂ (30 mL x 3),

dried over MgSO₄, filtered, and concentrated to give amine **15a** as a yellow oil (0.080 g, 66%).

Preparation of *N*-benzoyl derivative of amine for the determination of the enantiomeric excess.

To a solution of amine **15a** (0.012 g, 0.10 mmol) in CH₂Cl₂ (1 mL) were added Et₃N (0.018 g, 0.18 mmol) and PhCOCl (0.018 g, 0.15 mmol). Upon stirring at rt for 30 min, the reaction mixture was purified by flash column chromatography (silica gel, eluent: PE/EtOAc = 8/1) to give *N*-benzoyl amine **16a** as a white solid (0.019 g, 82%). The sample was subjected to chiral HPLC (Chiralpak AD-H column) to determine the enantiomeric excess.

Table 2, entry 1

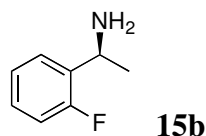


Yellow oil; $[\alpha]_D^{20} = -26.5$ (*c* 0.33, CHCl₃) (80% ee); IR (film) 3442, 1629, 1453 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.28 (m, 4H), 7.26-7.19 (m, 1H), 4.10 (q, *J* = 6.8 Hz, 1H), 1.47 (br s, 2H), 1.38 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 148.0, 128.6, 126.9, 125.8, 51.5, 25.9.

(1) Y. Chu, Z. Shan, D. Liu and N. Sun, *J. Org. Chem.*, 2006, **71**, 3998.

(2) D. Guijarro, Ó. Pablo and M. Yus, *J. Org. Chem.*, 2010, **75**, 5265.

Table 2, entry 2

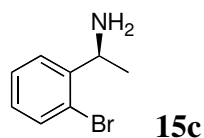


Light yellow oil; $[\alpha]_D^{20} = -23.1$ (*c* 1.08, CHCl₃) (84% ee); IR (film) 3360, 1584, 1489 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.38 (m, 1H), 7.23-7.16 (m, 1H),

7.15-7.08 (m, 1H), 7.04-6.97 (m, 1H), 4.38 (q, $J = 6.4$ Hz, 1H), 1.59 (br s, 2H), 1.42 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 161.8, 159.3, 134.7, 134.5, 128.3, 128.2, 126.89, 126.85, 124.40, 124.37, 115.7, 115.5, 45.59, 45.56, 24.2; HRMS Calcd for $\text{C}_8\text{H}_{11}\text{FN}$ (M+H): 140.0870; Found: 140.0868.

L. M. Klingensmith, K. A. Nadeau and G. A. Moniz, *Tetrahedron Lett.*, 2007, **48**, 4589.

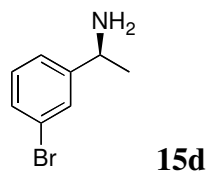
Table 2, entry 3



Yellow oil; $[\alpha]_{\text{D}}^{20} = -21.1$ (c 1.19, CHCl_3) (71% ee); IR (film) 3441, 1631, 1468 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.54-7.47 (m, 2H), 7.35-7.27 (m, 1H), 7.12-7.04 (m, 1H), 4.49 (q, $J = 6.4$ Hz, 1H), 1.76 (br s, 2H), 1.38 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 146.3, 133.1, 128.4, 128.0, 126.7, 123.3, 50.2, 23.9; HRMS Calcd for $\text{C}_8\text{H}_{11}\text{BrN}$ (M+H): 200.0069; Found: 200.0069.

L. M. Klingensmith, K. A. Nadeau and G. A. Moniz, *Tetrahedron Lett.*, 2007, **48**, 4589.

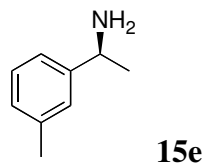
Table 2, entry 4



Yellow oil; $[\alpha]_{\text{D}}^{20} = -19.7$ (c 0.95, CHCl_3) (78% ee); IR (film) 3374, 1594, 1567, 1474 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.50 (s, 1H), 7.35 (d, $J = 7.6$ Hz, 1H), 7.26 (d, $J = 8.0$ Hz, 1H), 7.21-7.14 (m, 1H), 4.12-4.03 (m, 1H), 1.66 (br s, 2H), 1.36 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.2, 130.2, 130.0, 129.1, 124.6, 122.7, 51.1, 25.8; HRMS Calcd for $\text{C}_8\text{H}_{11}\text{BrN}$ (M+H): 200.0069; Found:

200.0065.

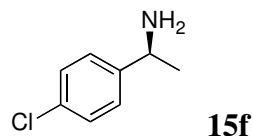
Table 2, entry 5



Yellow oil; $[\alpha]_D^{20} = -29.2$ (*c* 1.15, CHCl_3) (82% ee); IR (film) 3441, 1608, 1450 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.17 (m, 1H), 7.17-7.09 (m, 2H), 7.07-7.01 (m, 1H), 4.06 (q, *J* = 6.8 Hz, 1H), 2.34 (s, 3H), 1.75 (br s, 2H), 1.37 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 147.8, 138.2, 128.5, 127.7, 126.6, 122.9, 51.4, 25.7, 21.6; HRMS Calcd for $\text{C}_9\text{H}_{13}\text{NNa}$ (*M*+*Na*): 158.0940; Found: 158.0937.

M. Pallavicini, E. Valoti, L. Villa and O. Piccolo, *Tetrahedron: Asymmetry*, 2001, **12**, 1071.

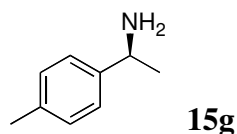
Table 2, entry 6



Yellow oil; $[\alpha]_D^{20} = -26.2$ (*c* 0.99, CHCl_3) (79% ee); IR (film) 3361, 1592, 1492 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.26 (m, 4H), 4.10 (q, *J* = 6.4 Hz, 1H), 1.88 (br s, 2H), 1.36 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 146.0, 132.6, 128.8, 127.4, 50.9, 25.7; HRMS Calcd for $\text{C}_8\text{H}_{11}\text{ClN}$ (*M*+*H*): 156.0575; Found: 156.0571.

D. Guijarro, Ó. Pablo and M. Yus, *J. Org. Chem.*, 2010, **75**, 5265.

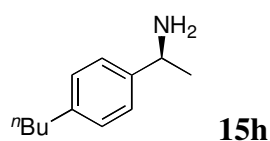
Table 2, entry 7



Yellow oil; $[\alpha]_D^{20} = -36.3$ (*c* 1.02, CHCl_3) (83% ee); IR (film) 3286, 1514, 1455 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.27-7.20 (m, 2H), 7.17-7.11 (m, 2H), 4.13-4.03 (m, 1H), 2.33 (s, 3H), 1.78 (br s, 2H), 1.37 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.0, 136.5, 129.3, 125.8, 51.2, 25.8, 21.2; HRMS Calcd for $\text{C}_9\text{H}_{13}\text{NNa}$ ($\text{M}+\text{Na}$): 158.0940; Found: 158.0936.

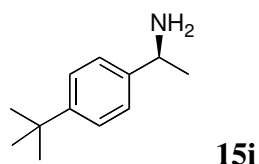
D. R. J. Hose, M. F. Mahon, K. C. Molloy, T. Raynham and M. Wills, *J. Chem. Soc., Perkin Trans. 1*, 1996, 691.

Table 2, entry 8



Yellow oil; $[\alpha]_D^{20} = -23.2$ (*c* 1.12, CHCl_3) (78% ee); IR (film) 3290, 1512, 1456 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.24 (d, $J = 8.0$ Hz, 2H), 7.13 (d, $J = 8.0$ Hz, 2H), 4.07 (q, $J = 6.4$ Hz, 1H), 2.59 (t, $J = 7.6$ Hz, 2H), 1.72 (br s, 2H), 1.64-1.53 (m, 2H), 1.41-1.29 (m, 5H), 0.92 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 145.1, 141.6, 128.6, 125.7, 51.2, 35.4, 33.8, 25.7, 22.5, 14.1; HRMS Calcd for $\text{C}_{12}\text{H}_{20}\text{N}$ ($\text{M}+\text{H}$): 178.1590; Found: 178.1590.

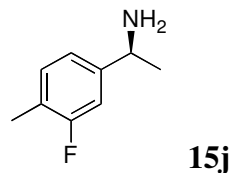
Table 2, entry 9



Yellow oil; $[\alpha]_D^{20} = -20.0$ (*c* 1.28, CHCl_3) (76% ee); IR (film) 3291, 1509, 1461 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.37-7.33 (m, 2H), 7.29-7.23 (m, 2H), 4.08 (q, $J = 6.4$ Hz, 1H), 1.73 (br s, 2H), 1.38 (d, $J = 6.4$ Hz, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 149.8, 144.9, 125.50, 125.49, 51.1, 34.6, 31.5, 25.7; HRMS

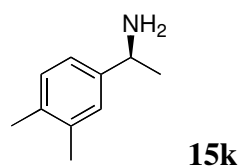
Calcd for C₁₂H₂₀N (M+H): 178.1590; Found: 178.1586.

Table 2, entry 10



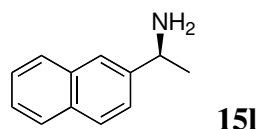
Yellow oil; $[\alpha]_D^{20} = -25.5$ (*c* 1.17, CHCl₃) (85% ee); IR (film) 3291, 1580, 1505 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.15-7.08 (m, 1H), 7.04-6.97 (m, 2H), 4.08 (q, *J* = 6.4 Hz, 1H), 2.24 (d, *J* = 1.2 Hz, 3H), 1.83 (br s, 2H), 1.36 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 160.4, 147.9, 131.6, 131.5, 123.3, 123.1, 121.20, 121.17, 112.5, 112.3, 50.9, 25.8, 14.39, 14.35; HRMS Calcd for C₉H₁₃FN (M+H): 154.1027; Found: 154.1023.

Table 2, entry 11



Yellow oil; $[\alpha]_D^{20} = -27.0$ (*c* 1.21, CHCl₃) (83% ee); IR (film) 3291, 1504, 1451 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.15-7.04 (m, 3H), 4.12-4.00 (m, 1H), 2.27 (s, 3H), 2.25 (s, 3H), 1.67 (br s, 2H), 1.38 (d, *J* = 6.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 145.4, 136.8, 135.2, 129.9, 127.2, 123.2, 51.2, 25.8, 20.0, 19.5; HRMS Calcd for C₁₀H₁₅NNa (M+Na): 172.1097; Found: 172.1093.

Table 2, entry 12

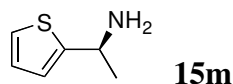


Light red oil; $[\alpha]_D^{20} = -21.0$ (*c* 0.98, CHCl₃) (81% ee); IR (film) 3364, 3287, 1601, 1507, 1451 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.86-7.76 (m, 4H), 7.52-7.41 (m, 3H), 4.29 (q, *J* = 6.4 Hz, 1H), 1.74 (br s, 2H), 1.48 (d, *J* = 6.4 Hz, 3H); ¹³C NMR

(100 MHz, CDCl₃) δ 145.2, 133.7, 132.8, 128.4, 127.9, 127.8, 126.2, 125.7, 124.7, 123.9, 51.6, 25.7; HRMS Calcd for C₁₂H₁₃NNa (M+Na): 194.0940; Found: 194.0938.

D. Guijarro, Ó. Pablo and M. Yus, *J. Org. Chem.*, 2010, **75**, 5265.

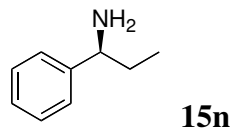
Table 2, entry 13



Yellow oil; $[\alpha]_D^{20} = -8.6$ (*c* 0.79, CHCl₃) (70% ee); IR (film) 3441, 1630, 1450, 1372, 1309 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.18-7.14 (m, 1H), 6.95-6.88 (m, 2H), 4.36 (q, *J* = 6.8 Hz, 1H), 1.73 (br s, 2H), 1.48 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 153.0, 126.7, 123.5, 122.2, 47.5, 26.5.

D. Guijarro, Ó. Pablo and M. Yus, *J. Org. Chem.*, 2010, **75**, 5265.

Table 2, entry 14



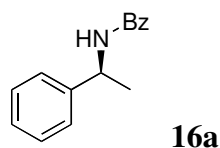
Yellow oil; $[\alpha]_D^{20} = -14.5$ (*c* 0.60, CHCl₃) (77% ee); IR (film) 3418, 1628, 1454 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.28 (m, 4H), 7.26-7.20 (m, 1H), 3.80 (t, *J* = 6.4 Hz, 1H), 1.80-1.60 (m, 4H), 0.87 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 146.6, 128.6, 127.1, 126.6, 58.0, 32.6, 11.1; HRMS Calcd for C₉H₁₃NNa (M+Na): 158.0940; Found: 158.0937.

(1) Y. Chu, Z. Shan, D. Liu and N. Sun, *J. Org. Chem.*, 2006, **71**, 3998.

(2) D. Guijarro, Ó. Pablo and M. Yus, *J. Org. Chem.*, 2010, **75**, 5265.

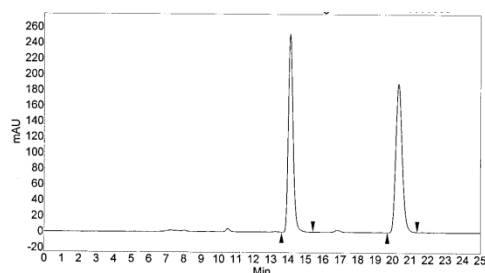
The chromatograms for determination of enantioselectivity

Table 2, entry 1



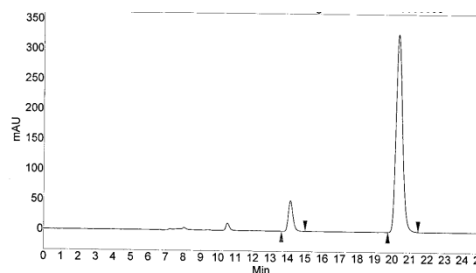
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



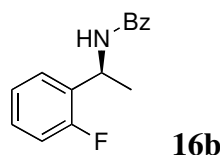
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.12	49.875	13.62	15.43
2	20.32	50.125	19.69	21.39
Total		100.000		

Enantio-enriched product



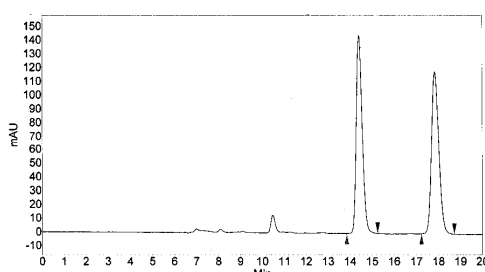
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.16	10.049	13.65	15.02
2	20.35	89.951	19.74	21.47
Total		100.000		

Table 2, entry 2



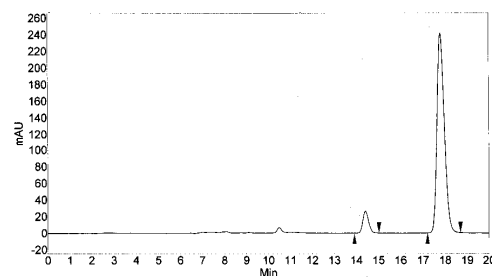
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



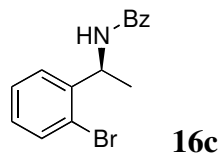
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.43	49.961	13.85	15.25
2	17.85	50.039	17.23	18.72
Total		100.000		

Enantio-enriched product



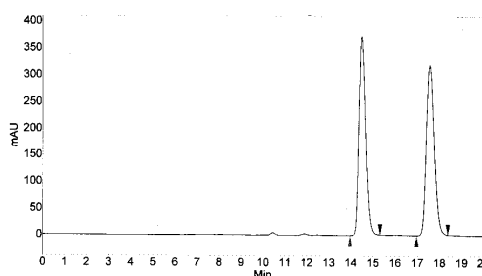
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.41	7.927	13.91	15.03
2	17.81	92.073	17.21	18.70
Total		100.000		

Table 2, entry 3



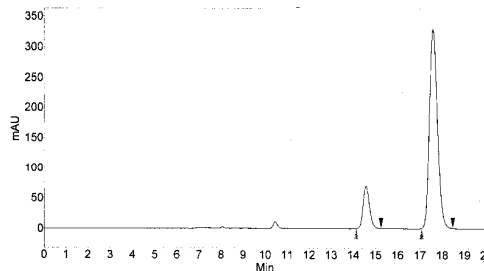
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



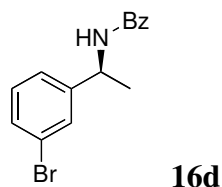
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.49	49.729	13.97	15.32
2	17.57	50.271	16.96	18.38
Total		100.000		

Enantio-enriched product



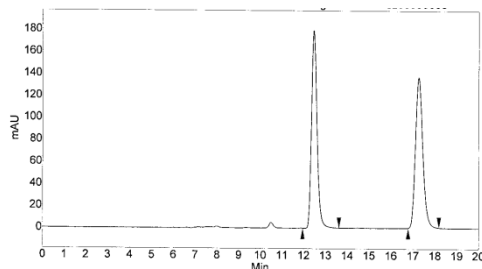
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.57	14.435	14.13	15.25
2	17.60	85.565	17.08	18.48
Total		100.000		

Table 2, entry 4



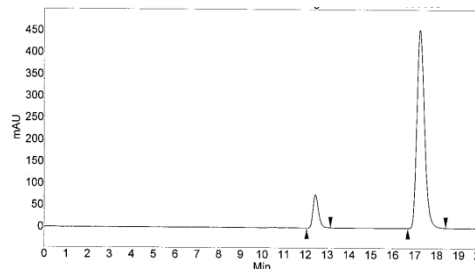
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



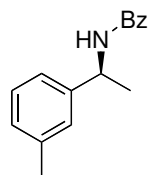
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	12.45	49.950	11.95	13.62
2	17.25	50.050	16.78	18.18
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	12.45	10.760	12.05	13.15
2	17.24	89.240	16.68	18.41
Total		100.000		

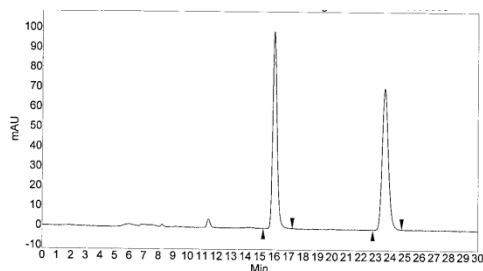
Table 2, entry 5



16e

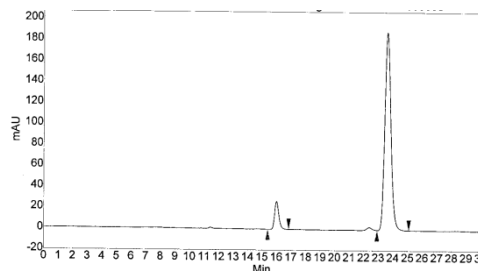
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (90/10); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



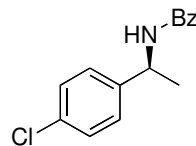
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	16.00	49.868	15.23	17.24
2	23.61	50.132	22.79	24.77
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	16.00	8.949	15.39	16.84
2	23.60	91.051	22.91	25.08
Total		100.000		

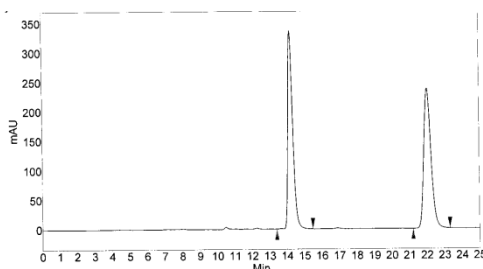
Table 2, entry 6



16f

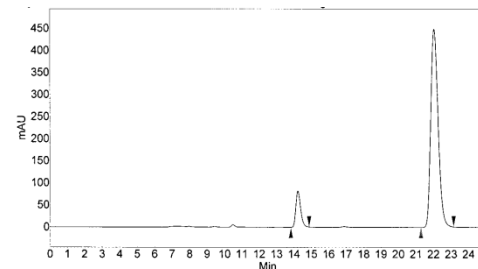
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



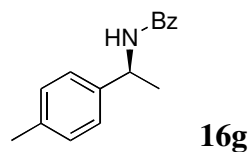
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	14.21	49.607	13.42	15.48
2	22.03	50.393	21.21	23.30
Total		100.000		

Enantio-enriched product



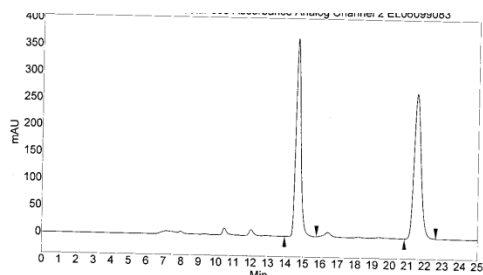
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	14.24	10.646	13.83	14.89
2	22.04	89.354	21.29	23.14
Total		100.000		

Table 2, entry 7



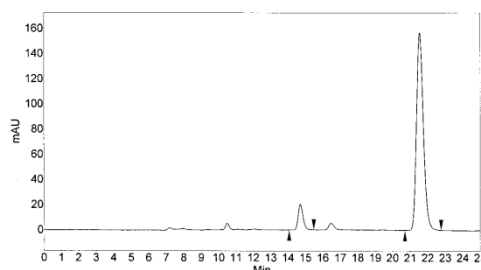
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



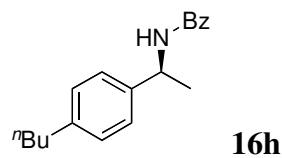
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.67	49.738	13.96	15.79
2	21.51	50.262	20.82	22.60
Total		100.000		

Enantio-enriched product



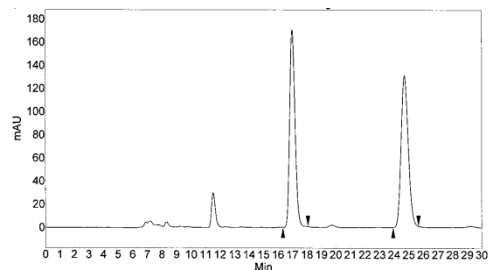
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	14.71	8.490	14.06	15.48
2	21.55	91.510	20.69	22.76
Total		100.000		

Table 2, entry 8



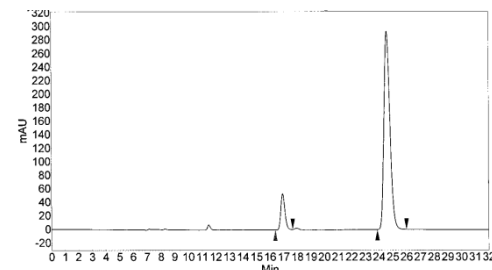
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (90/10); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



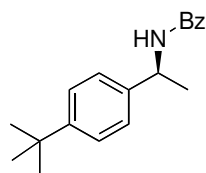
Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	16.99	49.676	16.35	18.08
2	24.71	50.324	23.93	25.67
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area % [%]	Start [Min]	End [Min]
1	16.93	11.024	16.38	17.67
2	24.59	88.976	23.88	25.99
Total		100.000		

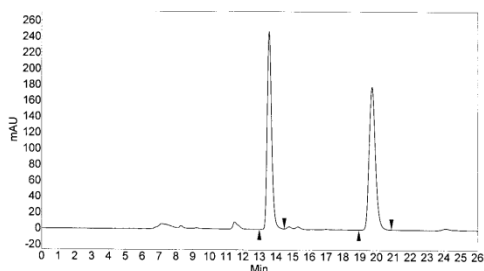
Table 2, entry 9



16i

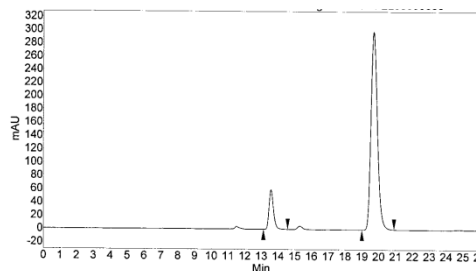
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (90/10); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



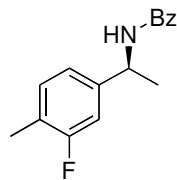
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	13.57	49.689	12.99	14.49
2	19.72	50.311	18.94	20.88
Total		100.000		

Enantio-enriched product



Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	13.57	12.177	13.12	14.57
2	19.69	87.823	19.00	20.90
Total		100.000		

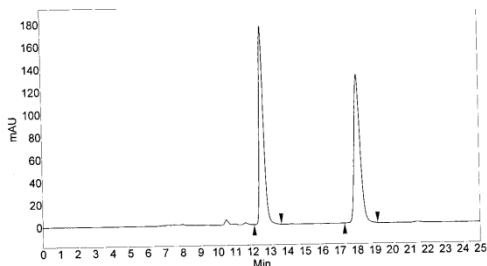
Table 2, entry 10



16j

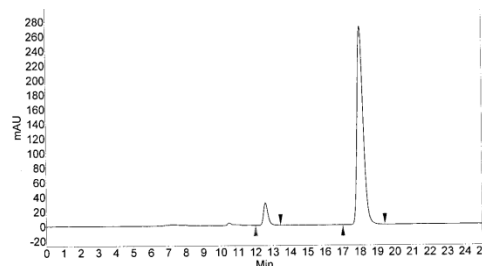
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



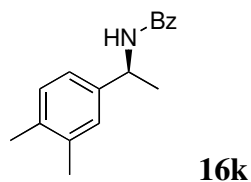
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	12.57	49.648	12.10	13.65
2	18.05	50.352	17.29	19.17
Total		100.000		

Enantio-enriched product



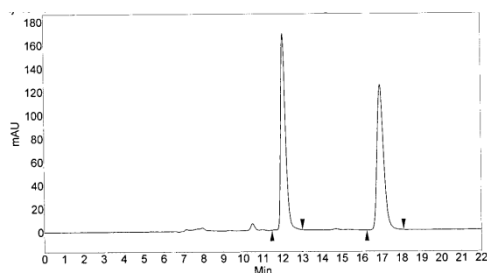
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	12.57	7.565	12.00	13.44
2	18.05	92.435	17.03	19.43
Total		100.000		

Table 2, entry 11



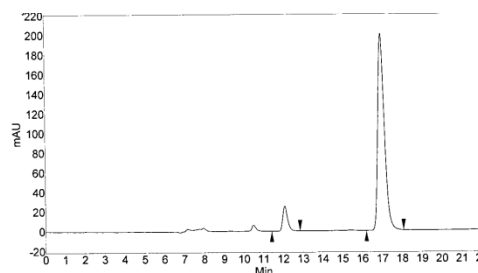
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



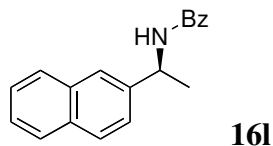
Index	Time [Min]	Area %	Start [Min]	End [Min]
1	12.05	49.980	11.47	13.01
2	16.95	50.020	16.26	18.10
Total		100.000		

Enantio-enriched product



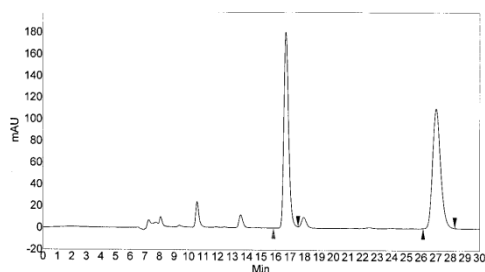
Index	Time [Min]	Area %	Start [Min]	End [Min]
1	12.08	8.323	11.42	12.85
2	16.97	91.677	16.21	18.07
Total		100.000		

Table 2, entry 12



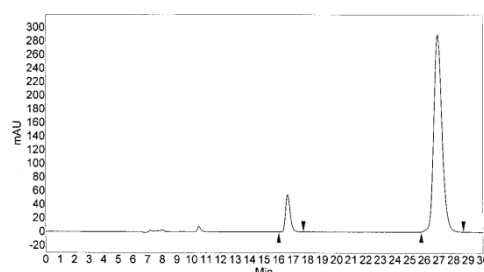
HPLC Condition: Column: Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



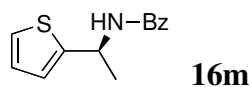
Index	Time [Min]	Area %	Start [Min]	End [Min]
1	16.71	49.641	15.85	17.55
2	27.01	50.359	26.13	28.30
Total		100.000		

Enantio-enriched product



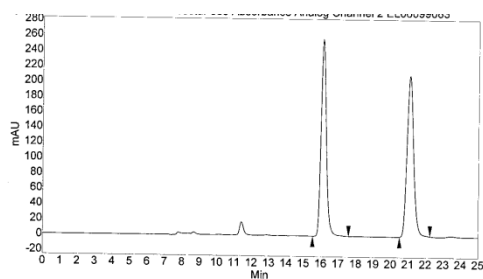
Index	Time [Min]	Area %	Start [Min]	End [Min]
1	16.63	9.666	16.01	17.71
2	26.91	90.334	25.79	28.67
Total		100.000		

Table 2, entry 13



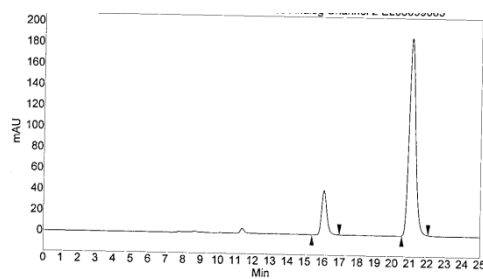
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard



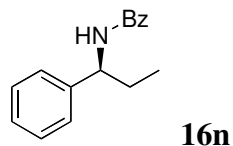
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	16.11	49.662	15.53	17.60
2	21.07	50.338	20.51	22.24
Total		100.000		

Enantio-enriched product



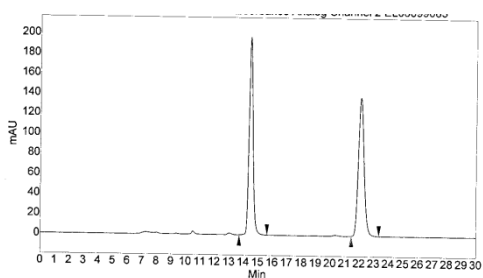
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	16.09	15.188	15.40	16.98
2	21.07	84.814	20.54	22.03
Total		100.000		

Table 2, entry 14



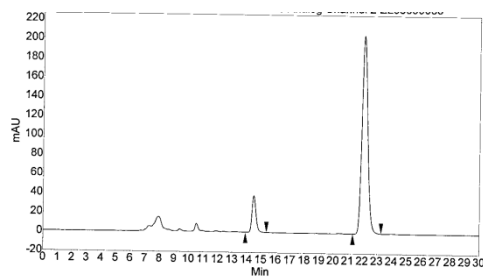
HPLC Condition: **Column:** Chiralpak AD-H, Daicel Chemical Industries, Ltd.;
Eluent: Hexanes/IPA (85/15); **Flow rate:** 0.5 mL/min; **Detection:** UV230 nm.

Racemic standard

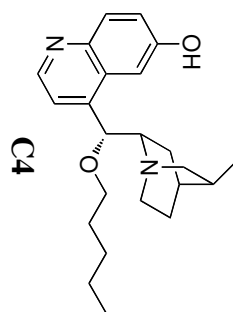
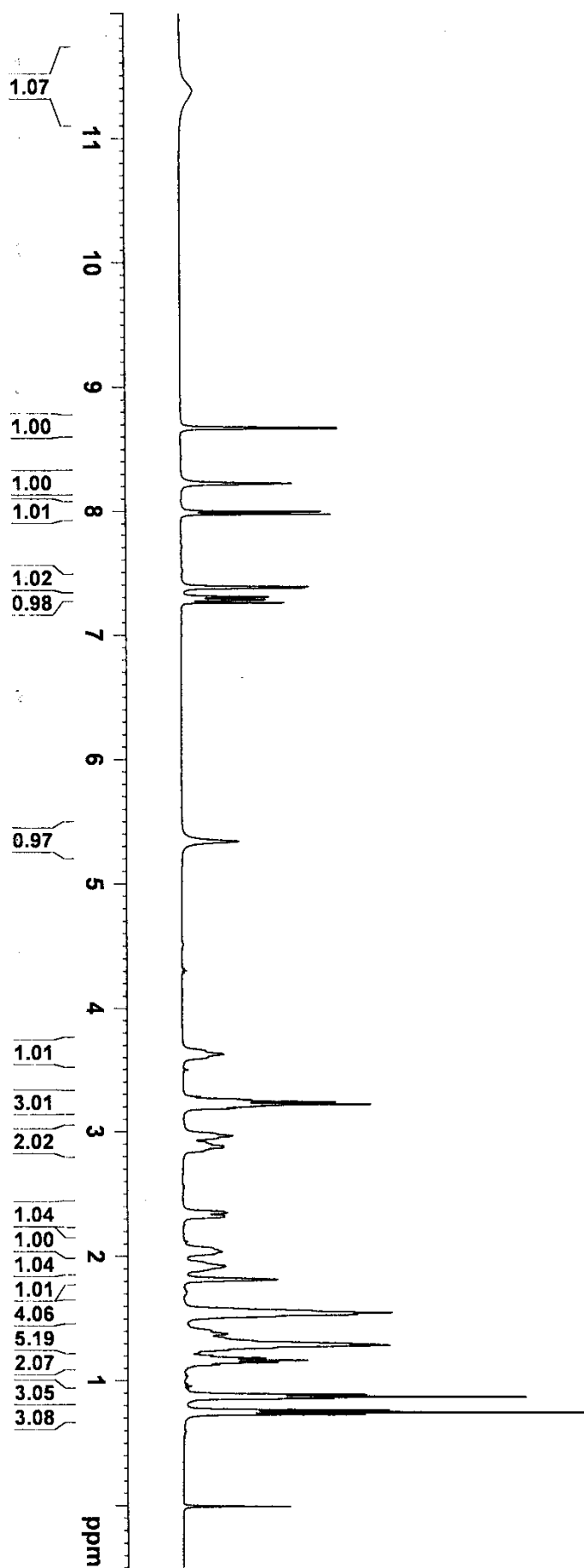


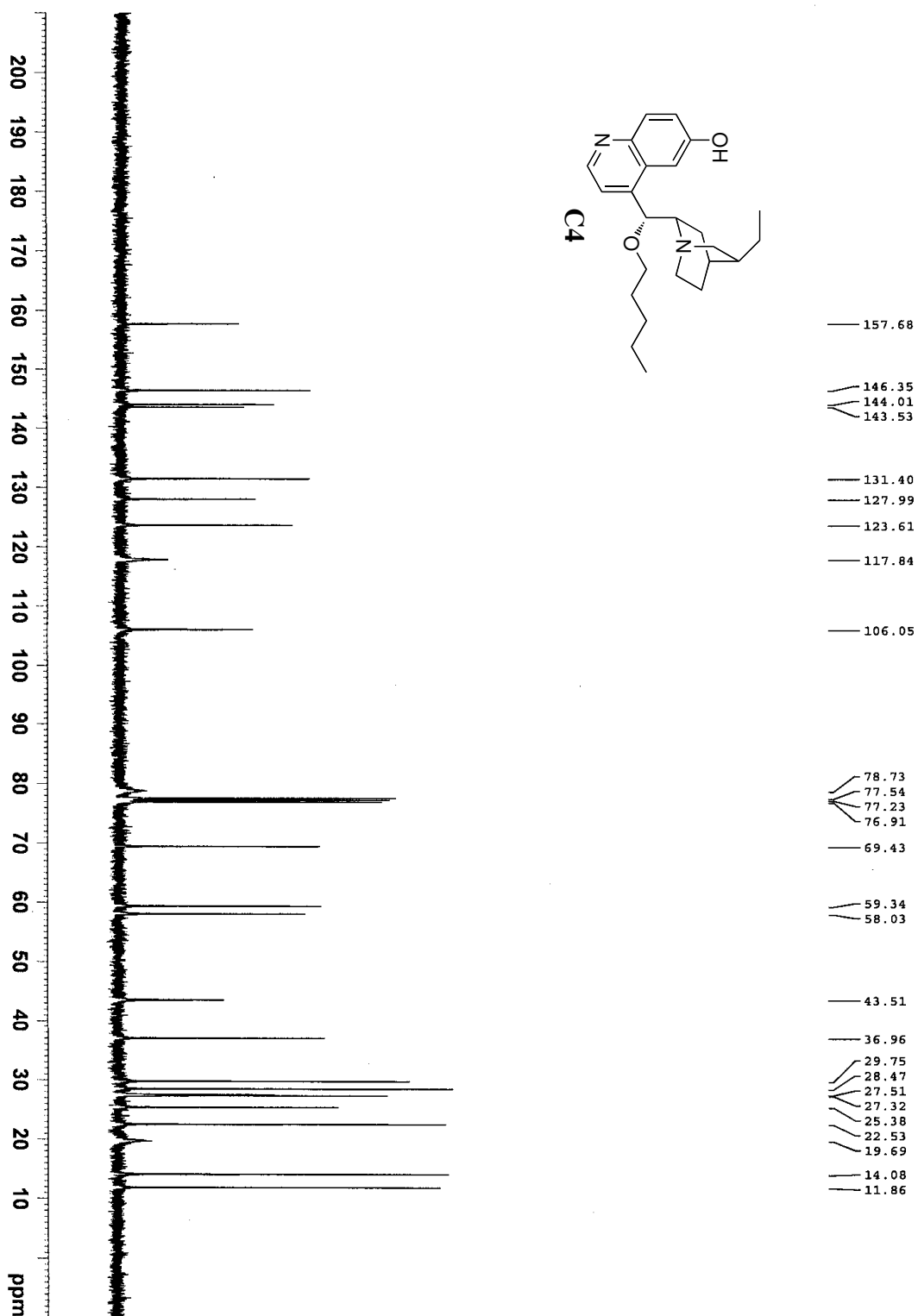
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	14.47	49.954	13.72	15.63
2	22.08	50.046	21.46	23.34
Total		100.000		

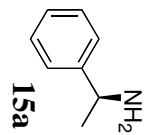
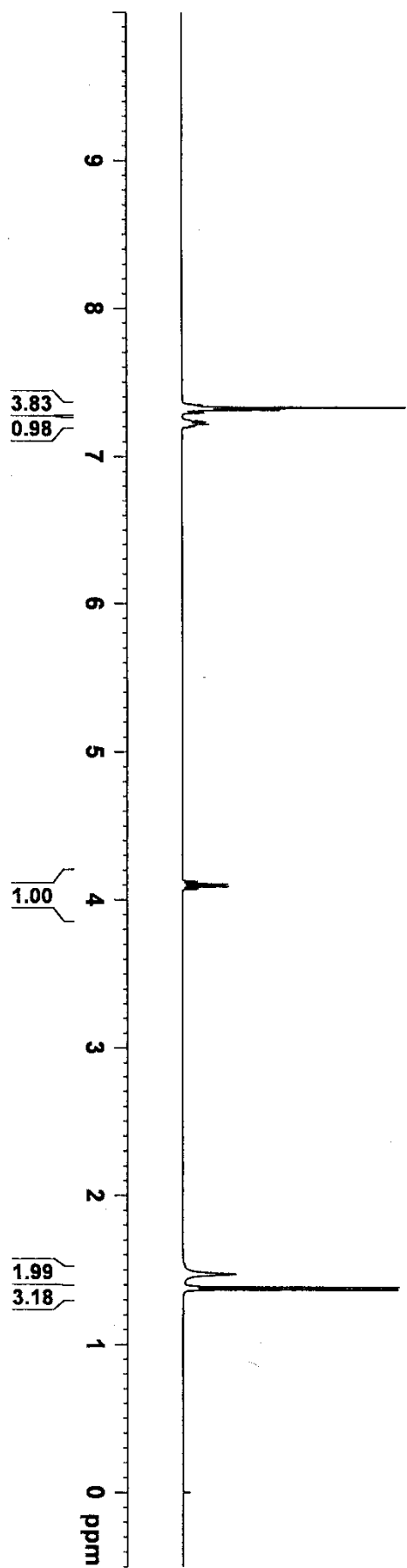
Enantio-enriched product

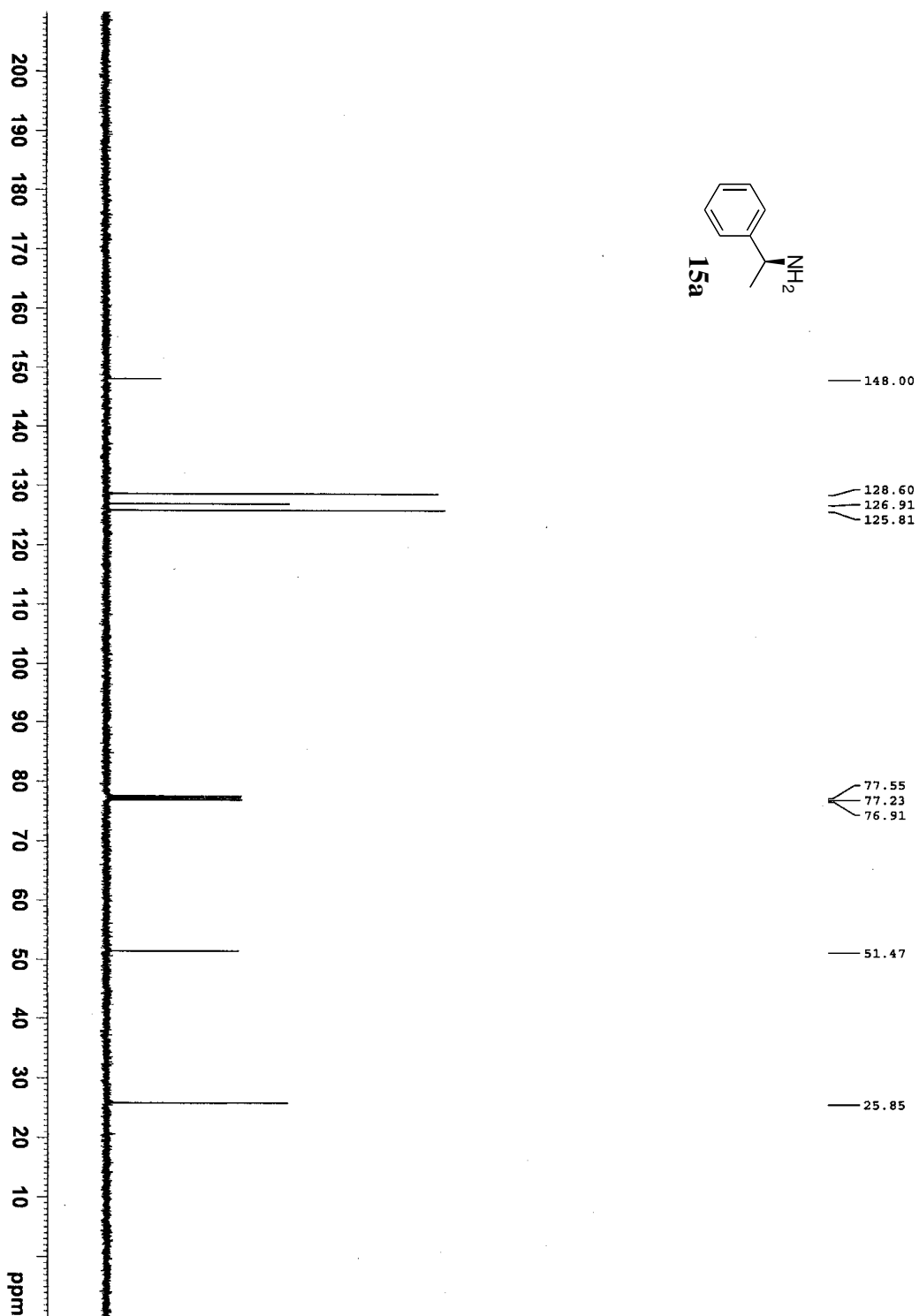


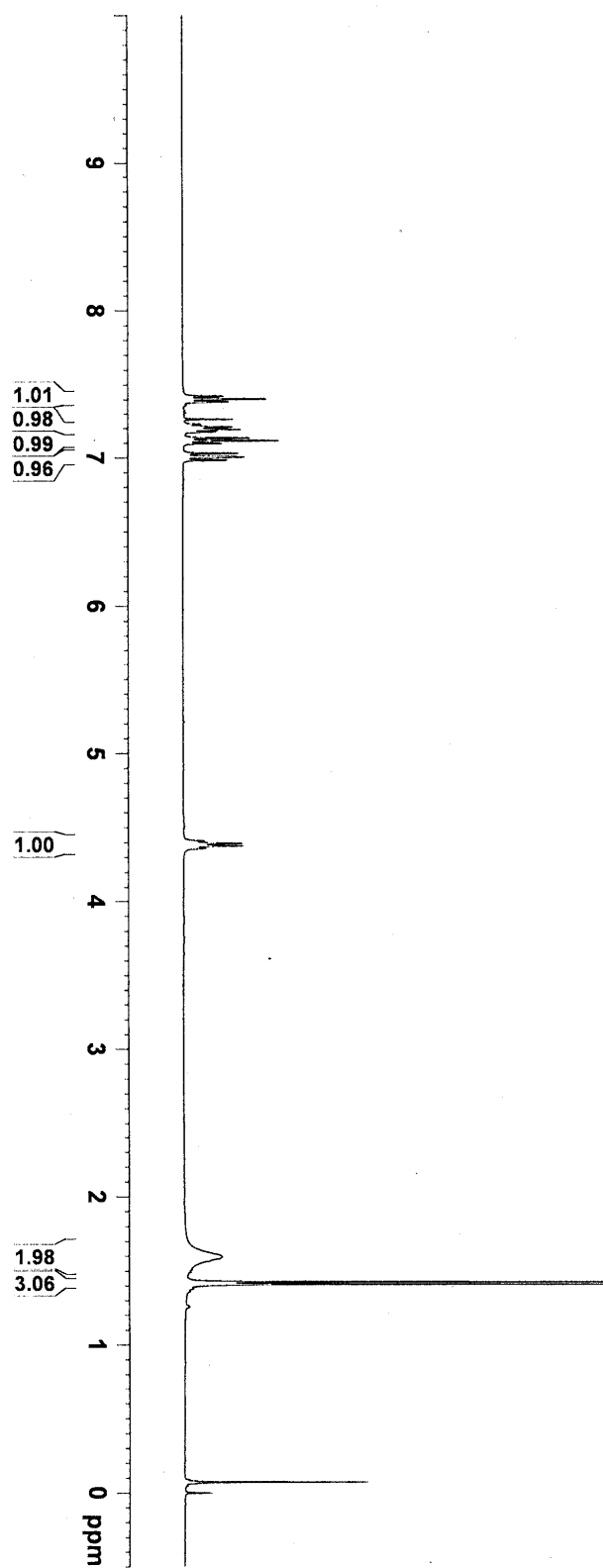
Index	Time [Min]	Area [%]	Start [Min]	End [Min]
1	14.51	11.348	13.93	15.39
2	22.09	88.652	21.33	23.28
Total		100.000		



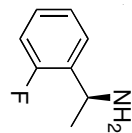


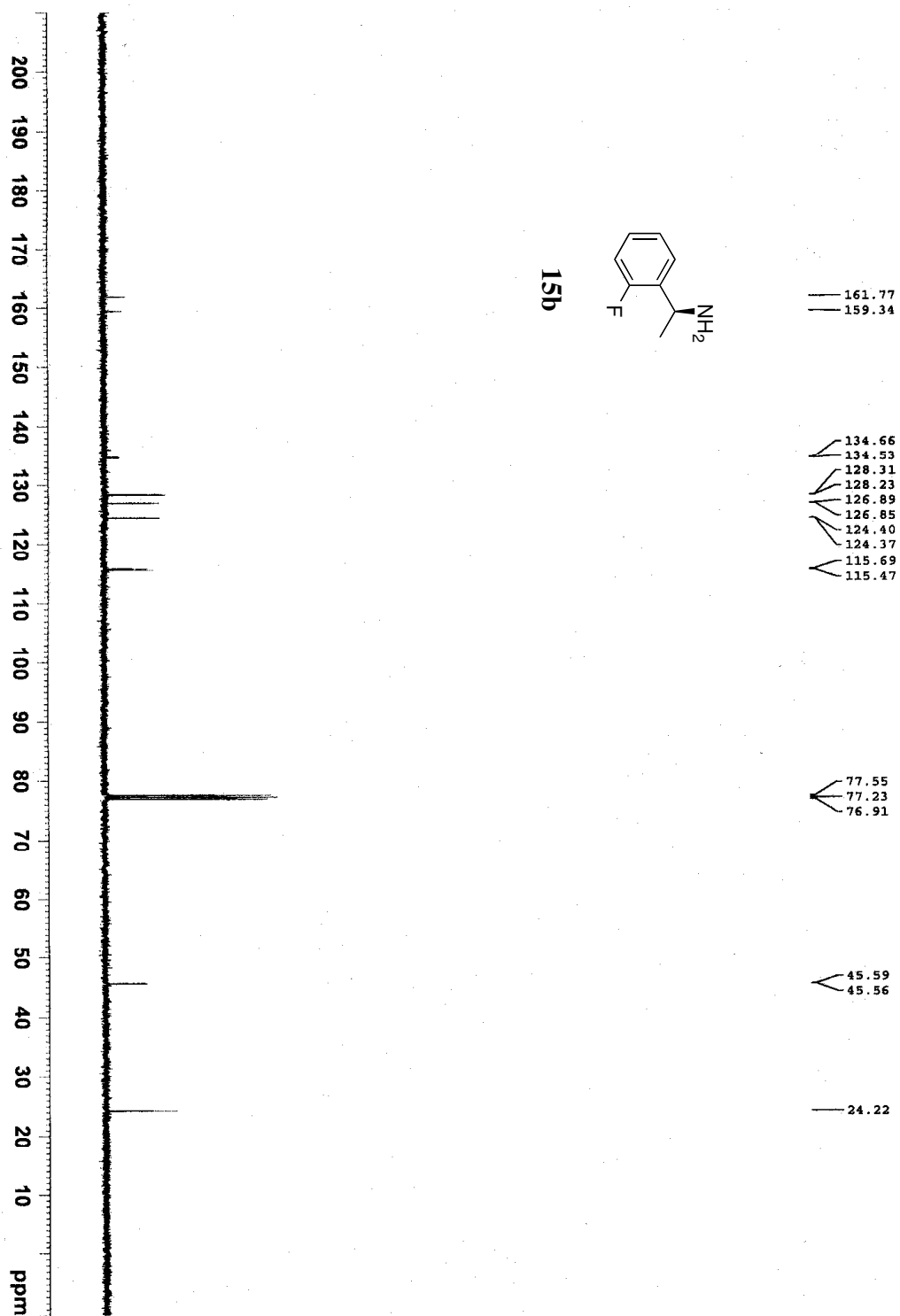


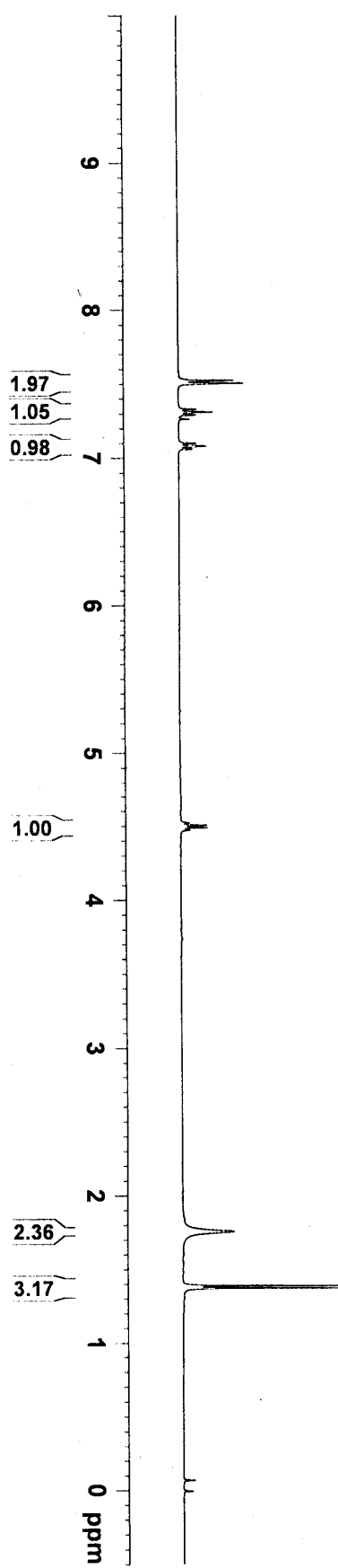




15b







15c

