Asymmetric Catalytic Synthesis of Enantiopure *N*-Protected 1,2-Amino Alcohols

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General Methods. The ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts (δ) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvents ($CHCl_3$). Coupling constants are given in Hz. Carbon types were determined from DEPT ^{13}C NMR experiments. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal. Purification of reaction products was carried out by flash chromatography (FC) on silica gel (230-400 mesh). Melting points are uncorrected. Optical rotations are reported as follows: $[\alpha]^{rt}_{D}$ (*c* in g per 100 mL, solvent).

Materials. Commercial grade reagents and solvents were used without further purification; otherwise, where necessary, they were purified as recommended.[1]
Racemic epoxides: propylene oxide, 1,2-epoxy hexane, 1,2-epoxy-7-octene, phenyl glycidyl ether, epichlorohydrin and styrene oxide were purchased from Aldrich and used as received. Other racemic epoxides were prepared by *m*-CPBA oxidation of the corresponding alkenes.[2]
Carbamates **3a-c** were purchased from Aldrich and used as received.
Carbamate **3d** was purchased from Fluka and used as received.
Both (R,R) and (S,S)-(salen)-Co(II) complexes **2** (Aldrich) are commercially available.

Determination of Enantiomeric Purity. The enantiomeric excess (ee) of the products was determined by HPLC analysis on the *N*-protected 1,2-amino alcohols for aminols **5a-d** and **7e-i** and on the corresponding *O*-benzyl derivatives for aminols **7a-d**. Daicel Chiralpak AD-H or AS-H columns with i-PrOH/hexane as the eluent were used. HPLC traces were compared to racemic samples prepared with racemic (salen)-Co^{III} complexes as the catalyst.

[1] Armarengo, W. L. F.; Perrin, D. D.; In *Purification of Laboratory Chemicals*, 4th ed.; Butterworth Heinemann: Oxford, 1996.
[2] Moyna, G.; Williams, H. J.; Scott, A. L. *Synth. Commun.* **1996**, *26*, 2235.

Determination of Regiochemistry. The regiochemistry of the ring opening reactions was determined by careful GC and NMR analysis of the crude reaction mixtures and by comparison with literature data.

Determination of Absolute Configuration. The measured optical rotation of *N*-Boc protected 1-amino-2-ols **7a**,[3] **7d**,[4] and **7g**[5] and of *N*-Cbz protected 1-amino-2-ol **7gb**[6] were compared with the literature value. The optical rotation of (S)-propanolol **8**[3] and (S)-propanolol hydrochloride **8**·**HCl**[7] were also compared to the literature values. All other absolute configurations were assigned by analogy.

Calculation of conversion (*c*) and determination of selectivity factor *s*.[8] Calculation of selectivity factor *s* was accomplished by using the equation: $s = k_{rel} = \ln[1 - c(1+ee)]/\ln[1 - c(1-ee)]$, where ee is the enantiomeric excess of the amino alcohol product and *c* is the conversion. The conversion was set to equal the isolated yield of the amino alcohol product, so calculated values for *c* actually represent lower limits: the value for *c* was calculated by multiplying the isolated yield times 0.454 (Table S1).

Table S1. *s* values for the AKR of Terminal Epoxides with Carbamates

Table 1 entry	Table 2 entry	product	yield	*c*	ee	*s*
8		**5a**	0.99	0.45	98.9	454
9		**5b**	0.93	0.42	99.5	865
10		**5c**	0.97	0.44	99.0	473
11		**5d**	0.67	0.304	99.5	610
	1	**7a**	0.99	0.45	99.3	725
	2	**7b**	0.99	0.45	99.2	630
	3	**7c**	0.99	0.45	99.7	1695
	4	**7d**	0.84	0.38	99.9	3750
	5	**7e**	0.95	0.43	99.5	900
	6	**7f**	0.87	0.395	99.9	3950
	7	**7g**	0.90	0.41	99.9	4160
	8	**7gb**	0.52	0.236	99.5	540
	9	**7h**	0.76	0.345	99.8	1690
	10	**7i**	0.62	0.28	99.8	1460

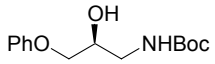
[3] Kawamoto, A. M.; Martin, M. *J.Chem.Soc.Perkin Trans.1* **2001**,*16*; 1916.
[4] Enders, D.; Haertwig, A.; Raabe, G.; Runsink, J. *Eur. J. Org. Chem.* **1998**, 1771.
[5] Adderley, N. J.; Buchanan, D. J.; Dixon, D. J.; Lainé D. I. *Angew. Chem. Int. Ed.* **2003**, *42*, 4241.
[6] Nesterenko, V.; Byers, J. T.; Hergenrother, P. J. *Org. Lett.* **2003**, *5*, 281.
[7] Klunder J. M.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710.
[8] Kagan, H. B.; Fiaud, J. C. In *Topics in Stereochemistry*; Allinger, N. L.; Eliel, E. L. Eds.; Interscience: New York, 1987; Vol. 14, p 249.

The determination of accurate *s* values is dependent of accurate measurement of both ee and conversion, and for highly selective processes ($s > 50$) even small errors in these measurements can originate large errors in the calculation of the selectivity factor.[9]
The accuracy of ee's values were evaluated by carrying out each AKR reactions almost three times: it was found that the ee varied by ±0.1 %.
Lowest sensitivity to errors in the measurement of conversion is attained with evaluation at low conversion. We therefore run the AKR reactions using 0.2 equiv of carbamates **3** relative to racemic epoxides, but under these conditions the amino alcohol products were always recovered in enantiomerically pure form (ee = 99.9). For this reason the *s* values were calculated considering the data obtained in reactions carried out using 0.454 equiv of carbamates **3** relative to racemic epoxides. Under these conditions, in some cases, the optical purity of the products is slightly affected by concentration effects.[10]
Considering the extraordinarily levels of selectivities ($s > 400$) observed in the AKR reactions, the relative magnitude of *s* factors can provide useful guidelines of evaluation of AKR strategy, but the absolute values for the best substrates (*s* exceeding 3000) are certainly lacking precision.

General Procedure for the *O*-Benzylation of *N*-Boc protected amino alcohols. Under an inert atmosphere, pure *N*-Boc protected amino alcohols **7a-d** were dissolved in THF followed by the addition of NaH (1.1 equiv) at 0°C. After addition of benzyl bromide (1.2 equiv) and $(Bu)_4NI$ (0.2 equiv), the reaction mixture was allowed to rise to room temperature. After being stirred for 3 hours, the reaction was quenched with $NaHCO_3$, extracted with Et_2O and dried over anhydrous $MgSO_4$. Purification by flash chromatography (hexane/AcOEt 9/1) afforded pure *O*-benzyl *N*-protected amino alcohols.

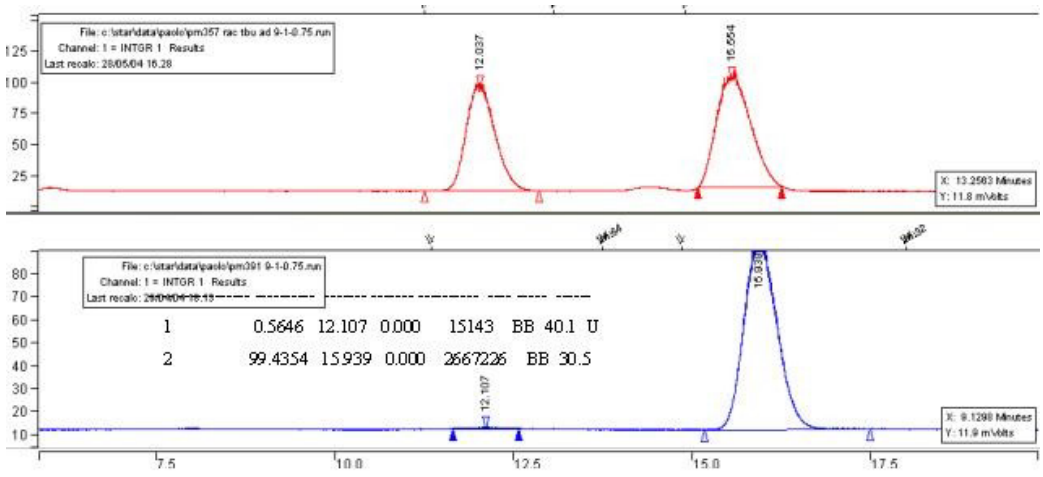
General Procedure for the AKR of Racemic Terminal Epoxides. All the reactions were carried out in undistilled solvent without any precautions to exclude water. In an ordinary test tube equipped with a magnetic stirring bar, the (salen)-Co^{II} complex **2** (0.022 mmol) was dissolved in 0.15 mL of TBME. After addition of the oxidizing agent (*p*-nitro benzoic acid, 0.044 mmol), the tube was closed with a rubber stopper and the mixture was stirred at room temperature till the red colour turned to dark brown. Then the carbamate **3** (0.5 mmol) and TBME (0.05 mL) were added. After 5 minutes stirring, the epoxide (1.1 mmol) was added and stirring was continued at room temperature until GC analysis showed disappearance of the carbamate. Then the crude reaction mixture was flushed through a plug of silica. Solvent was removed in vacuo, and the residue was purified by flash chromatography to give the *N*-protected 1,2-amino alcohol in enantiomerically pure form.

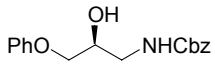
[9] Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307.
[10] As the resolution approaches completion, the concentration of the less reactive enantiomer is much greater than that of the more reactive one, and so the two enantiomers react equally, owing to the balance between the intrinsic rate and the available concentration. See: Eames, J. *Angew. Chem. Int. Ed.* **2000**, *39*, 885.



((S)-2-Hydroxy-3-phenoxy-propyl)-carbamic acid *tert*-butyl ester (5a)[3] – The reaction was carried out at room temperature for 24 h using 2 mol% of (*S,S*)-(salen)Co^{II} **2** and 4 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (DCM/AcOEt 9/1) as a white solid; melting point: 82-85 C°. The ee was determined by HPLC analysis using a Chiralpak AD-H column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 12.1 min; τ_S = 15.9 min). $[\alpha]^{rt}_D$= -10.4° (*c* = 2, $CHCl_3$, 98.9% ee). ESI-MS *m/z* 266 $[M-H]^-$, 290 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 1.46 (s, 9H), 3.20 (bs, 1H, OH), 3.25-3.35 (m, 1H), 3.43-3.53 (m, 1H), 3.90-4.02 (m, 2H), 4.05-4.15 (m, 1H), 4.99 (bs, 1 H, NH), 6.90-7.00 (m, 3H), 7.27-7.32 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (CH_3, 3C), 43.5 (CH_2), 69.3 (CH_2), 69.9 (CH), 79.9 (C), 114.5 (CH, 2C), 121.2 (CH), 129.5 (CH, 2C), 157.1 (C), 158.4 (C).

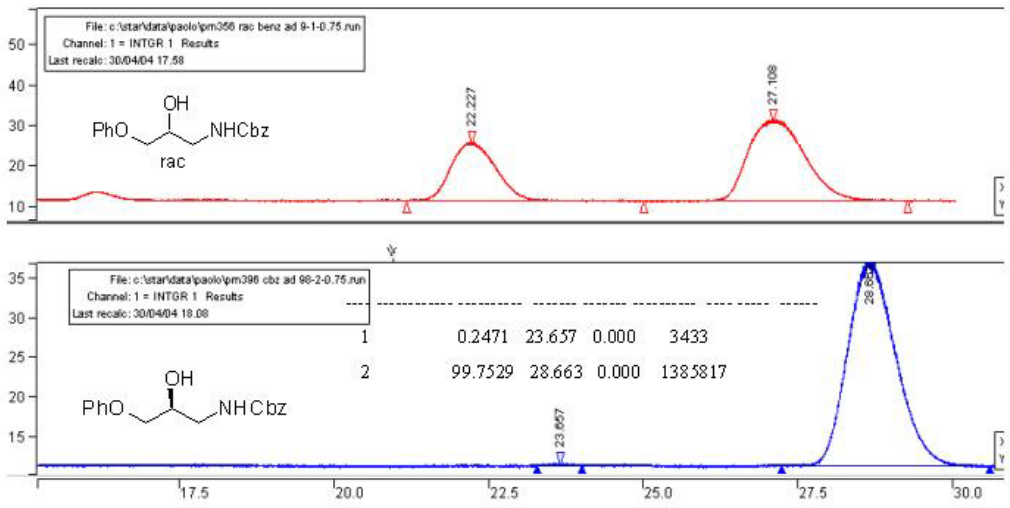
HPLC conditions: AD-H, hexane / *i*-PrOH 9/1 flux: 0.75 mL/min

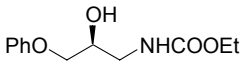




((S)-2-Hydroxy-3-phenoxy-propyl)-carbamic acid benzyl ester (5b) – The reaction was carried out at room temperature for 24 h using 4 mol% of (*S,S*)-(salen)Co^{II} **2** and 8 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 75/25) as a white solid; melting point: 79-82 C°. The ee was determined by HPLC analysis using a Chiralpak AD-H column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 23.6 min; τ_S = 28.6 min). $[\alpha]^{rt}_D$= -6.8° (*c* = 1.04, $CHCl_3$, 99.5% ee). ESI-MS *m/z* 300 $[M-H]^-$, 324 $[M+Na]^+$. ^{1}H NMR ($CDCl_3$): δ = 2.92 (d, *J* = 4.0, 1H, OH), 3.35-3.43 (m, 1H), 3.50-3.60 (m, 1H), 3.90-4.02 (m, 2H), 4.08-4.18 (m, 1H), 5.13 (s, 2 H), 5.20 (bs, 1 H, NH), 6.85-7.00 (m, 3H), 7.27-7.40 (m, 7H); ^{13}C NMR ($CDCl_3$): δ = 43.7 (CH_2), 66.9 (CH_2), 69.3 (CH_2), 69.5 (CH), 114.5 (CH, 2C), 121.2 (CH), 128.0 (CH), 128.1 (CH), 128.5 (CH, 2C), 129.5 (CH, 2C), 136.2 (C), 157.2 (C), 158.2 (C).

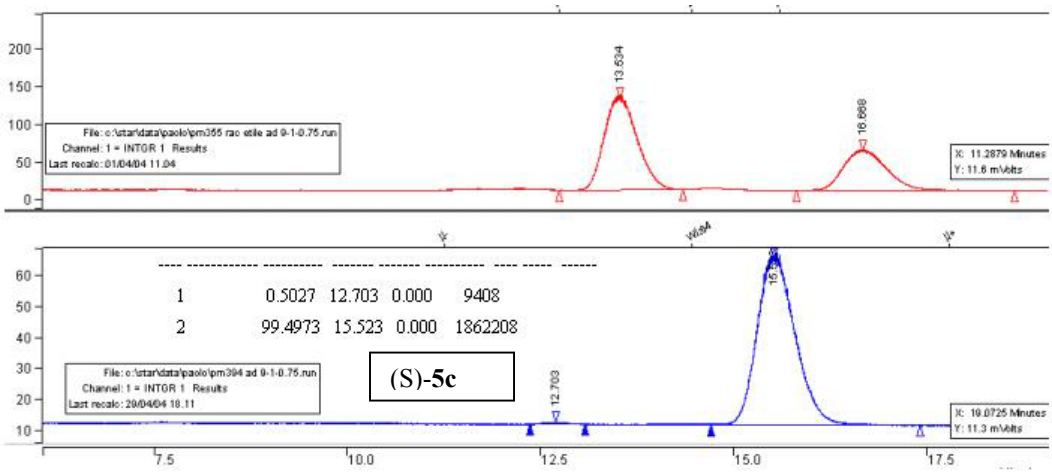
HPLC conditions: AD-H, hexane / *i*-PrOH 9/1 flux: 0.75 mL/min

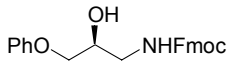




((S)-2-Hydroxy-3-phenoxy-propyl)-carbamic acid ethyl ester (5c) – The reaction was carried out at room temperature for 24 h using 2 mol% of (*S,S*)-(salen)Co^{II} **2** and 4 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 7/3) as a colourless oil. The ee was determined by HPLC analysis using a Chiralpak AD-H column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 12.7 min; τ_S = 15.5 min). $[\alpha]^{rt}_D$= -8.6° (*c* = 1.04, $CHCl_3$, 99.0% ee). ESI-MS *m/z* 238 $[M-H]^-$, 262 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 1.25 (t, *J* = 7.2, 3H), 3.12 (bs, 1H, OH), 3.30-3.40 (m, 1H), 3.48-3.58 (m, 1H), 3.95 (dd, *J* = 6.4, 9.6, 1H), 3.99 (dd, *J* = 4.8, 9.6, 1H), 4.07-4.15 (m, 1H), 4.13 (q, *J* = 7.2, 2H), 5.14 (bs, 1H, NH), 6.88-7.00 (m, 3H), 7.27-7.32 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.5 (CH_3), 43.7 (CH_2), 61.1 (CH_2), 69.3 (CH_2), 69.5 (CH), 114.4 (CH, 2C), 121.2 (CH), 129.4 (CH, 2C), 157.6 (C), 158.3 (C).

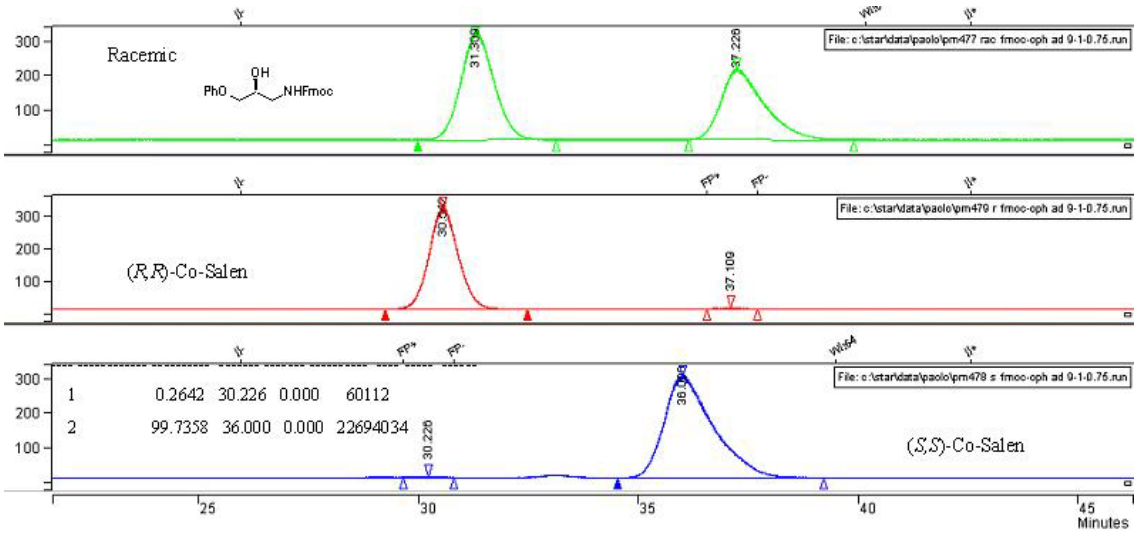
HPLC conditions: AD-H, hexane / *i*-PrOH 9/1 flux: 0.75 mL/min

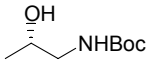




((S)-2-Hydroxy-3-phenoxy-propyl)-carbamic acid 9*H*-fluoren-9-ylmethyl ester (5d) – The reaction was carried out at room temperature for 50 h using 4 mol% of (*S,S*)-(salen)Co^{II} **2** and 8 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (DCM/AcOEt 92/8) as a white solid; melting point: 108-110 C°. The ee was determined by HPLC analysis using a Chiralpak AD-H column (90/10 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 30.2 min; τ_S = 36.0 min). $[\alpha]^{rt}_D$= -3.6° (*c* = 2.1, $CHCl_3$, 99.5% ee). ESI-MS *m/z* 388 $[M-H]^-$, 412 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 2.98 (bs, 1H, OH), 3.31-3.41 (m, 1H), 3.50-3.60 (m, 1H), 3.90-4.00 (m, 2H), 4.08-4.16 (m, 1H), 4.22 (t, *J* = 6.8, 1H), 4.44 (d, *J* = 6.8, 2H), 5.23 (bs, 1H, NH), 6.90 (d, *J* = 8.0, 2H), 6.98 (t, *J* = 7.2, 1H), 7.28-7.34 (m, 4H), 7.40 (t, *J* = 7.2, 2H), 7.59 (d, *J* = 7.6, 2H), 7.76 (d, *J* = 7.6, 2H),; ^{13}C NMR ($CDCl_3$): δ = 43.8 (CH_2), 47.2 (CH), 66.9 (CH_2), 69.3 (CH_2), 69.6 (CH), 114.5 (CH, 2C), 119.9 (CH, 2C), 121.3 (CH), 124.9 (CH, 2C), 127.1 (CH, 2C), 127.7 (CH, 2C), 129.6 (CH, 2C), 141.3 (C, 2C), 143.8 (C, 2C), 157.3 (C), 158.3 (C).

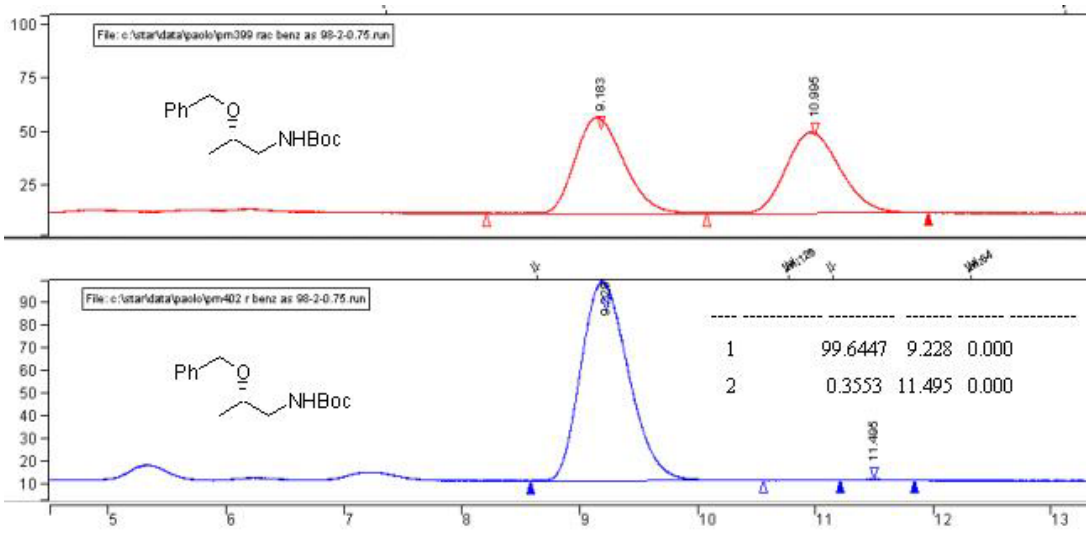
HPLC conditions: AD-H, hexane / *i*-PrOH 9/1 flux: 0.75 mL/min

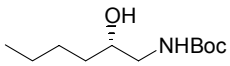




((S)-2-Hydroxy-propyl)-carbamic acid *tert*-butyl ester (7a)[3,4] – The reaction was carried out at room temperature for 24 h using 2 mol% of (*R,R*)-(salen)Co^{II} **2** and 4 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 65/35) as a colourless oil. The ee was determined by HPLC analysis on the corresponding *O*-benzyl derivative, prepared following the described general procedure, using a Chiralpak AS-H column (98/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S = 9.2 min; τ_R = 11.5 min). $[\alpha]^{rt}_D$= +22.3° (*c* = 1.0, $CHCl_3$, 99.3% ee), lit.[4] $[\alpha]^{rt}_D$= -23.2°, (R)-**7a** (*c* = 0.65, $CHCl_3$, >96% ee). ESI-MS *m/z* 174 $[M-H]^-$, 198 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 1.17 (d, *J* = 6.4, 3H), 1.44 (s, 9H), 2.44 (bs, 1H, OH), 2.95-3.05 (m, 1H), 3.20-3.30 (m, 1H), 3.86-3.96 (m, 1H), 4.95 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 20.6 (CH_3), 28.3 (CH_3, 3C), 47.9 (CH_2), 67.6 (CH), 79.6 (C), 156.9 (C).

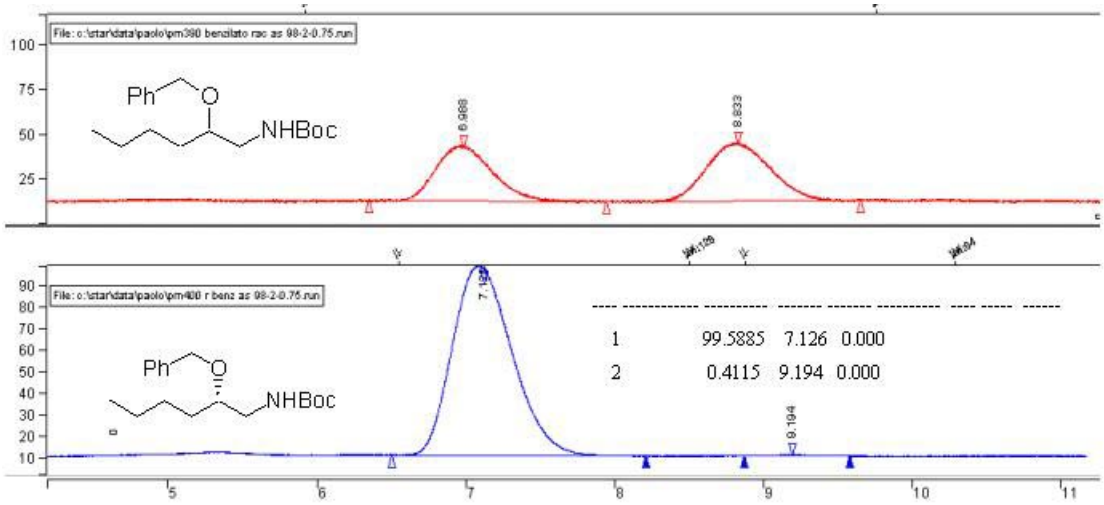
HPLC conditions: AS-H, hexane / *i*-PrOH 98/2 flux: 0.75 mL/min

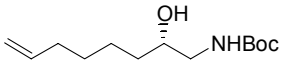




((S)-2-Hydroxy-hexyl)-carbamic acid *tert*-butyl ester (7b) – The reaction was carried out at room temperature for 24 h using 2 mol% of (*R,R*)-(salen)Co^{II} **2** and 4 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 75/25) as a colourless oil. The ee was determined by HPLC analysis on the corresponding *O*-benzyl derivative, prepared following the described general procedure, using a Chiralpak AS-H column (98/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S = 7.1min; τ_R = 9.2 min). $[\alpha]^{rt}_D$= +14.2° (*c* = 0.9, $CHCl_3$, 99.2% ee). ESI-MS *m/z* 216 $[M-H]^-$, 240 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 0.88 (t, *J* = 7.2, 3H), 1.25-1.40 (m, 4H), 1.40-1.50 (m, 2H), 1.43 (s, 9H), 2.62 (bs, 1H, OH), 2.94-3.02 (m, 1H), 3.24-3.34 (m, 1H), 3.61-3.71 (m, 1H), 5.02 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 13.9 (CH_3), 22.6 (CH_2), 27.6 (CH_2), 28.3 (CH_3, 3C), 34.4 (CH_2), 46.6 (CH_2), 71.5 (CH), 79.5 (C), 156.8 (C).

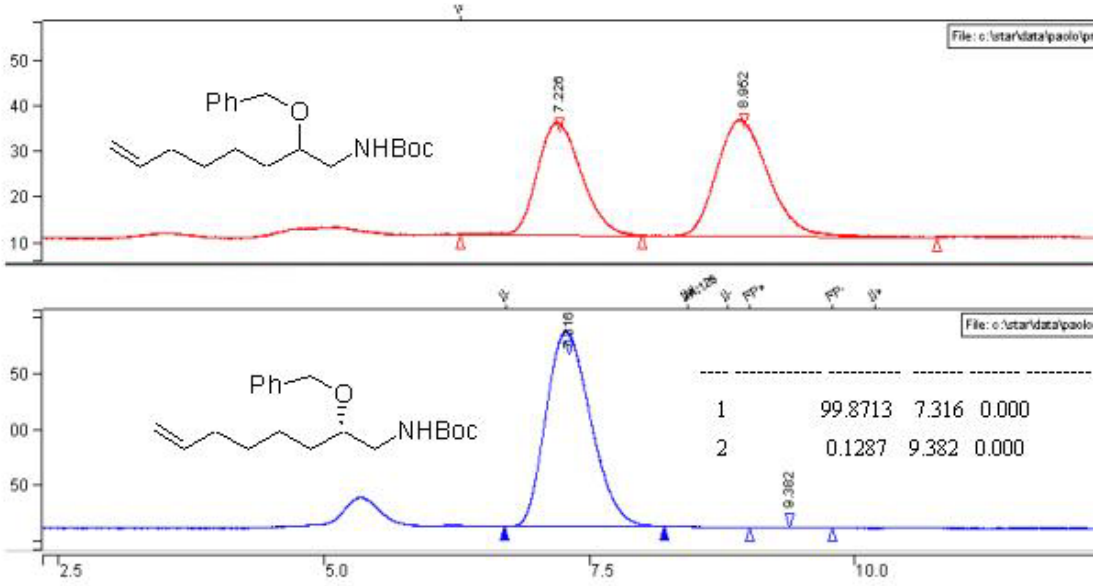
HPLC conditions: AS-H, hexane / *i*-PrOH 98/2 flux: 0.75 mL/min

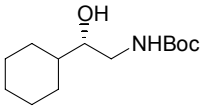




((S)-2-Hydroxy-oct-7-enyl)-carbamic acid *tert*-butyl ester (7c) – The reaction was carried out at room temperature for 24 h using 2 mol% of (*R,R*)-(salen)Co^{II} **2** and 4 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 75/25) as a colourless oil. The ee was determined by HPLC analysis on the corresponding *O*-benzyl derivative, prepared following the described general procedure, using a Chiralpak AS-H column (98/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S = 7.3 min; τ_R = 9.4 min). $[\alpha]^{rt}_D$= +10.6° (*c* = 0.9, $CHCl_3$, 99.7% ee). ESI-MS *m/z* 242 $[M-H]^-$, 266 $[M+Na]^+$. ^{1}H NMR ($CDCl_3$): δ = 1.25-1.50 (m, 6H), 1.44 (s, 9H), 2.00-2.10 (m, 2H), 2.33 (bs, 1H, OH), 2.95-3.05 (m, 1H), 3.25-3.35 (m, 1H), 3.62-3.72 (m, 1H), 4.85-5.00 (m, 3H, CH_2=, NH), 5.75-5.85 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 24.9 (CH_2), 28.3 (CH_3, 3C), 28.8 (CH_2), 33.6 (CH_2), 34.6 (CH_2), 46.6 (CH_2), 71.5 (CH), 79.6 (C), 114.4 (CH), 138.7 (CH_2), 156.8 (C).

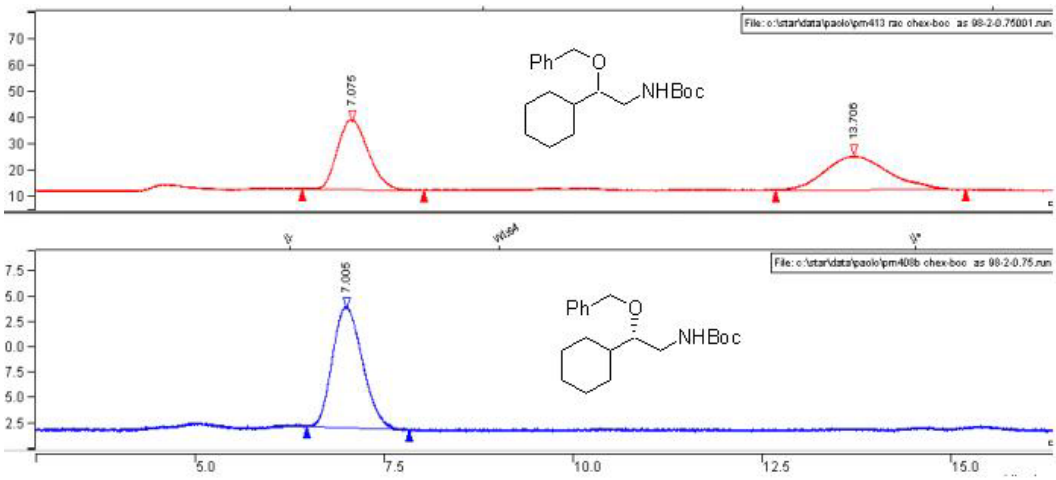
HPLC conditions: AS-H, hexane / *i*-PrOH 98/2 flux: 0.75 mL/min

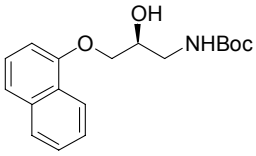




((S)-2-Cyclohexyl-2-hydroxy-ethyl)-carbamic acid *tert*-butyl ester (7d)[4] – The reaction was carried out at room temperature for 24 h using 4 mol% of (*R,R*)-(salen)Co^{II} **2** and 8 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 8/2) as a white solid; melting point: 82-83 C°. The ee was determined by HPLC analysis on the corresponding *O*-benzyl derivative, prepared following the described general procedure, using a Chiralpak AS-H column (98/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S = 7.0 min; τ_R = 13.7 min). $[\alpha]^{rt}_D$= +16.7° (*c* = 1.1, $CHCl_3$, 99.9% ee); lit.[4] $[\alpha]^{rt}_D$= -19.4°, (R)-**7d** (*c* = 1.25, CH_2Cl_2, 94% ee). ESI-MS *m/z* 244 $[M+H]^+$, 266 $[M+Na]^+$. ^{1}H NMR ($CDCl_3$): δ = 1.00-1.10 (m, 2H), 1.10-1.30 (m, 3H), 1.30-1.40 (m, 1H), 1.44 (s, 9H), 1.62-1.70 (m, 2H), 1.70-1.80 (m, 2H), 1.80-1.89 (m, 1H), 2.25 (bs, 1H, OH), 3.01-3.09 (m, 1H), 3.29-3.39 (m, 1H), 3.39-3.45 (m, 1H), 4.90 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): δ = 25.9 (CH_2), 26.0 (CH_2), 26.3 (CH_2), 28.2 (CH_2), 28.3 (CH_3, 3C), 28.8 (CH_2), 41.7 (CH), 44.4 (CH_2), 75.7 (CH), 79.4 (C), 156.8 (C).

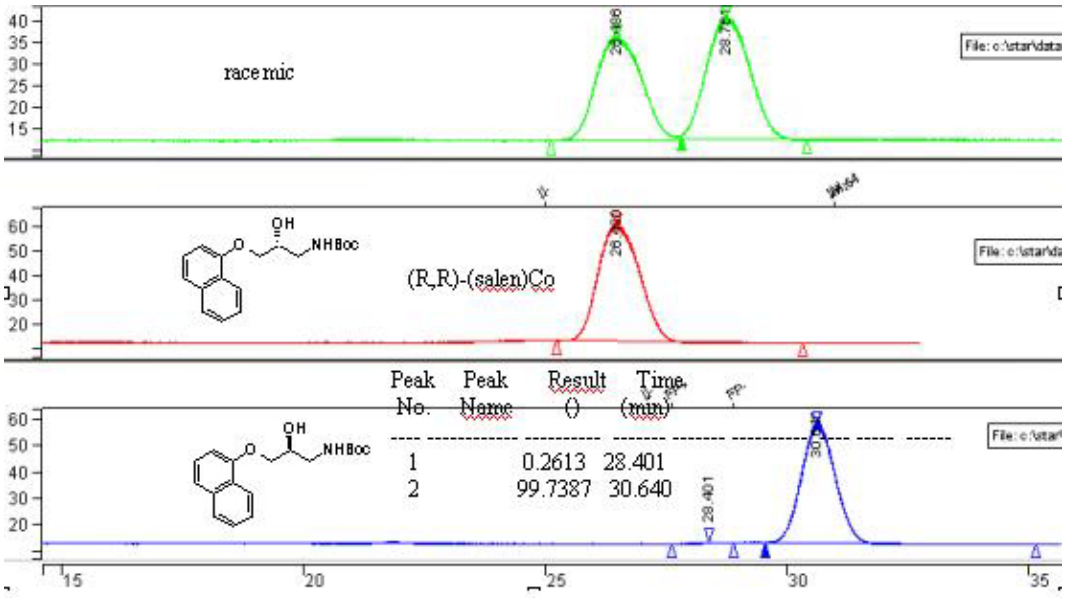
HPLC conditions: AS-H, hexane / *i*-PrOH 98/2 flux: 0.75 mL/min

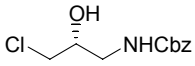




[(S)-2-Hydroxy-3-(naphthalen-1-yloxy)-propyl]-carbamic acid *tert*-butyl ester (7e) – The reaction was carried out at room temperature for 24 h using 4 mol% of (*S,S*)-(salen)Co^{II} **2** and 8 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 75/25) as a white solid; melting point: 102-105 C°. The ee was determined by HPLC analysis using a Chiralpak AD-H column (95/5 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 28.4 min; τ_S = 30.6 min). $[\alpha]^{rt}_D$= -16.3° (*c* = 0.85, $CHCl_3$, 99.5% ee). ESI-MS *m/z* 318 $[M+H]^+$, 340 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 1.47 (s, 9H), 3.36 (bs, 1H, OH), 3.38-3.48 (m, 1H), 3.54-3.64 (m, 1H), 4.16 (d, *J* = 5.6, 2H), 4.23-4.30 (m, 1H), 5.03 (bs, 1 H, NH), 6.80-6.85 (m, 1H), 7.35-7.40 (m, 1H), 7.44-7.54 (m, 3H), 7.79-7.84 (m, 1H), 8.18-8.23 (m, 1H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (CH_3, 3C), 43.8 (CH_2), 69.6 (CH_2), 70.1 (CH), 80.0 (C), 104.9 (CH), 120.8 (CH), 121.6 (CH), 125.3 (CH), 125.4 (C), 125.8 (CH), 126.5 (CH), 127.6 (CH), 134.5 (C), 154.0 (C), 157.3 (C).

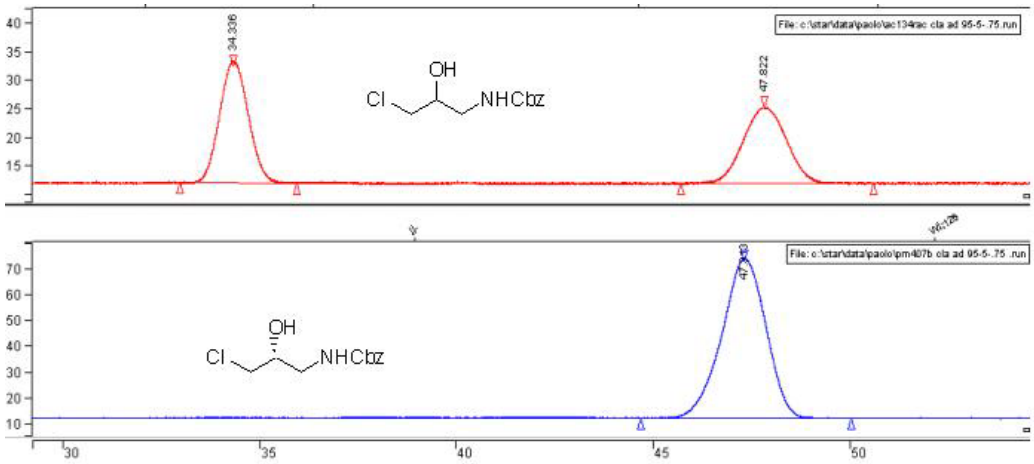
HPLC conditions: AD-H, hexane / *i*-PrOH 95/5 flux: 0.75 mL/min

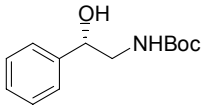




((R)-3-Chloro-2-hydroxy-propyl)-carbamic acid benzyl ester (7f) – The reaction was carried out 0 °C for 24 h using 4 mol% of (*R,R*)-(salen)Co^{II} **2**, 8 mol% of *p*-nitro benzoic acid as the additive and benzyl carbamate **3b** as the nucleophile. The title compound was isolated by column chromatography (DCM/AcOEt 85/15) as a colourless oil. The ee was determined by HPLC analysis using a Chiralpak AD-H column (95/5 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_S = 34.3 min; τ_R = 47.4 min). $[\alpha]^{rt}_D$= +10.3° (*c* = 0.92, $CHCl_3$, 99.9% ee). ESI-MS *m/z* 244 $[M+H]^+$, 266 $[M+Na]^+$. ^{1}H NMR ($CDCl_3$): δ = 3.15 (bs, 1H, OH), 3.25-3.35 (m, 1H), 3.44-3.52 (m, 1H), 3.52-3.62 (m, 2H), 3.90-4.00 (m, 1H), 5.11 (s, 2H), 5.22 (bs, 1H, NH), 7.29-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 44.1 (CH_2), 46.6 (CH_2), 67.1 (CH_2), 70.9 (CH), 128.1 (CH), 128.2 (CH), 128.5 (CH), 136.1 (C), 157.4 (C).

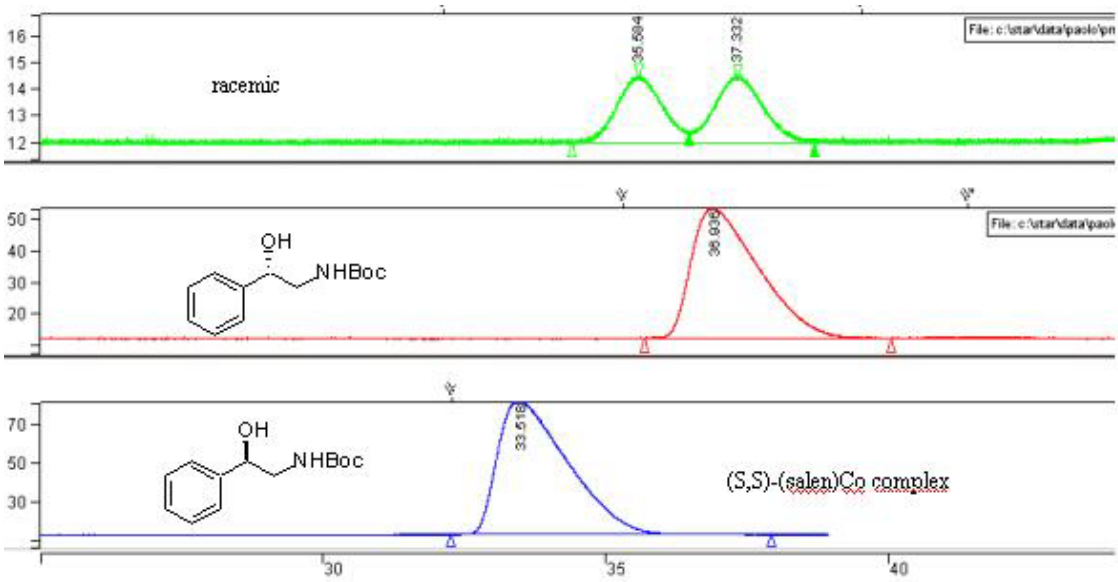
HPLC conditions: AD-H, hexane / *i*-PrOH 95/5 flux: 0.75 mL/min

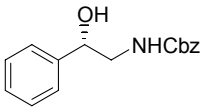




((S)-2-Hydroxy-2-phenyl-ethyl)-carbamic acid *tert*-butyl ester (7g)[5] – The reaction was carried out at room temperature for 36 h using 4 mol% of (*R,R*)-(salen)Co^{II} **2** and 8 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (hexane/AcOEt 8/2) as a white solid; melting point: 122-125 C°. The ee was determined by HPLC analysis using a Chiralpak AS-H column (98/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 35.5 min; τ_S = 37.3 min). $[\alpha]^{rt}_D$= +52.4° (*c* = 1.5, $CHCl_3$, 99.9% ee); lit.[5] $[\alpha]^{rt}_D$= -57.5°, (R)-**7g** (*c* = 1.01, CH_2Cl_2, >98% ee). ESI-MS *m/z* 238 $[M+H]^+$, 260 $[M+Na]^+$. ^{1}H NMR ($CDCl_3$): δ = 1.45 (s, 9H), 2.99 (bs, 1H, OH), 3.22-3.32 (m, 1H), 3.44-3.54 (m, 1H), 4.78-4.86 (m, 1H), 4.92 (bs, 1H, NH), 7.27-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (CH_3, 3C), 48.3 (CH_2), 73.9 (CH), 79.8 (C), 125.8 (CH, 2C), 127.7 (CH), 128.4 (CH, 2C), 141.8 (C), 156.9 (C).

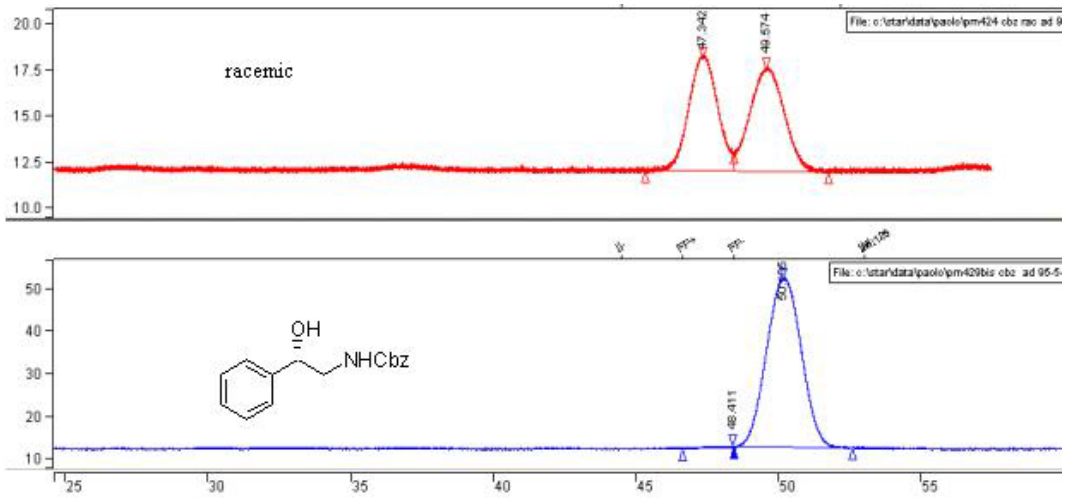
HPLC conditions: AS-H, hexane / *i*-PrOH 98/2 flux: 0.75 mL/min





((S)-2-Hydroxy-2-phenyl-ethyl)-carbamic acid benzyl ester (7gb)[6] – The reaction was carried out at room temperature for 48 h using 5 mol% of (*R,R*)-(salen)Co^{II} **2**, 8 mol% of *p*-nitro benzoic acid as the additive and benzyl carbamate **3b** as the nucleophile. The title compound was isolated by column chromatography (DCM/AcOEt 85/15) as a white solid; melting point: 92-94 C°. The ee was determined by HPLC analysis using a Chiralpak AD-H column (95/5 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 48.4 min; τ_S = 50.1 min). $[\alpha]^{rt}_D$= +25.2° (*c* = 1.03, $CHCl_3$, 99.5% ee), lit.[6] $[\alpha]^{rt}_D$= +27.1°, (S)-**7gb** (*c* = 0.93, CH_2Cl_2, 99% ee). ESI-MS *m/z* 272 $[M+H]^+$, 294 $[M+Na]^+$. ^{1}H NMR ($CDCl_3$): δ = 2.73 (bs, 1H, OH), 3.33 (ddd, *J* = 5.2, 8.0, 14.2 Hz, 1H), 3.53-3.63 (m, 1H), 4.80-4.88 (m, 1H), 5.10 (s, 2H), 5.17 (bs, 1H, NH), 7.29-7.40 (m, 10H); ^{13}C NMR ($CDCl_3$): δ = 48.5 (CH_2), 66.9 (CH_2), 73.5 (CH), 125.8 (CH, 2C), 127.9 (CH), 128.1 (CH, 2C), 128.2 (CH), 128.49 (CH), 128.52 (CH, 2C), 136.3 (C), 141.5 (C), 157.1 (C).

HPLC conditions: AD-H, hexane / *i*-PrOH 95/5 flux: 0.75 mL/min



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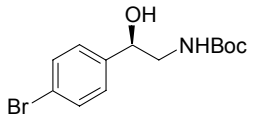
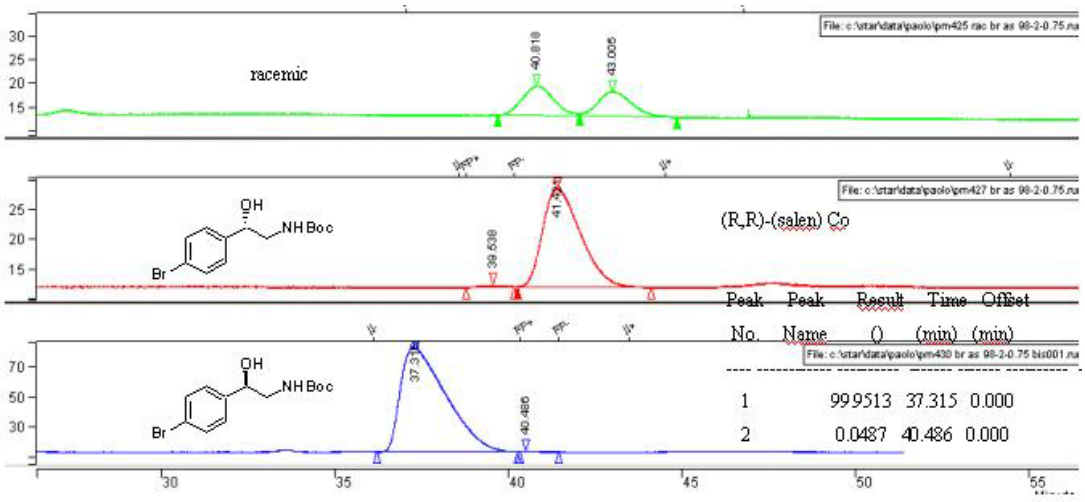
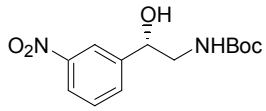
Totals:		100.0000		0.000	3394222			



[(R)-2-(4-Bromo-phenyl)-2-hydroxy-ethyl]-carbamic acid *tert*-butyl ester (7h) – The reaction was carried out at room temperature for 48 h using 5 mol% of (*S,S*)-(salen)Co^{II} **2** and 8 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (DCM/AcOEt 9/1) as a white solid; melting point: 91-96 C°. The ee was determined by HPLC analysis using a Chiralpak AS-H column (98/2 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 37.3 min; τ_S = 40.5 min). $[\alpha]^{rt}_D$= -31.5° (*c* = 2.08, $CHCl_3$, 99.8% ee). ESI-MS *m/z* 316 $[M+H]^+$, 338 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 1.44 (s, 9H), 3.16-3.26 (m, 1H), 3.28 (bs, 1H, OH), 3.40-3.50 (m, 1H), 4.76-4.84 (m, 1H), 4.90 (bs, 1H, NH), 7.23-7.27 (m, 2H), 7.45-7.50 (m, 2H); ^{13}C NMR (CDCl3): δ = 28.3 (CH_3, 3C), 48.2 (CH_2), 73.2 (CH), 80.0 (C), 121.5 (C), 127.6 (CH, 2C), 131.5 (CH, 2C), 140.8 (C), 157.0 (C).

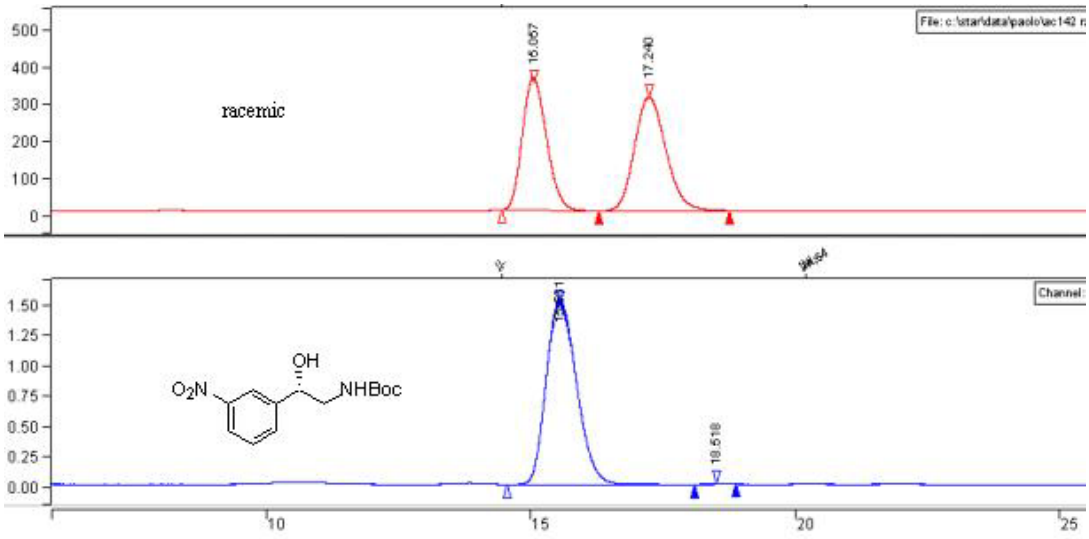
HPLC conditions: AS-H, hexane / *i*-PrOH 98/2 flux: 0.75 mL/min





[(R)-2-Hydroxy-2-(3-nitro-phenyl)-ethyl]-carbamic acid *tert*-butyl ester (7i) – The reaction was carried out at room temperature for 48 h using 5 mol% of (*R,R*)-(salen)Co^{II} **2** and 8 mol% of *p*-nitro benzoic acid as the additive. The title compound was isolated by column chromatography (DCM/AcOEt 9/1) as a white foam. The ee was determined by HPLC analysis using a Chiralpak AS-H column (9/1 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 15.5 min; τ_S = 18.5 min). $[\alpha]^{rt}_D$= +35.9° (*c* = 2.3, $CHCl_3$, 99.8% ee). ESI-MS *m/z* 283 $[M+H]^+$, 305 $[M+Na]^+$. ^1H NMR ($CDCl_3$): δ = 1.44 (s, 9H), 3.23-3.33 (m, 1H), 3.48-3.56 (m, 1H), 3.94 (bs, 1H, OH), 4.91-5.01 (m, 2H, 1 NH), 7.50-7.54 (m, 1H), 7.69-7.73 (m, 1H), 8.12-8.16 (m, 1H), 8.24-8.26 (m, 1H); ^{13}C NMR (CDCl3): δ = 28.2 (CH_3, 3C), 48.3 (CH_2), 73.1 (CH), 80.4 (C), 121.5 (CH), 122.6 (CH), 129.3 (CH), 132.0 (CH), 144.3 (C), 148.3 (C), 157.4 (C).

HPLC conditions: AS-H, hexane / *i*-PrOH 9/1 flux: 0.75 mL/min



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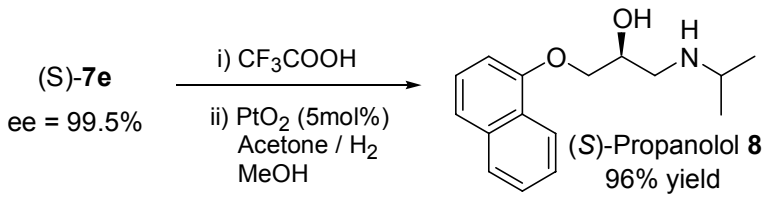
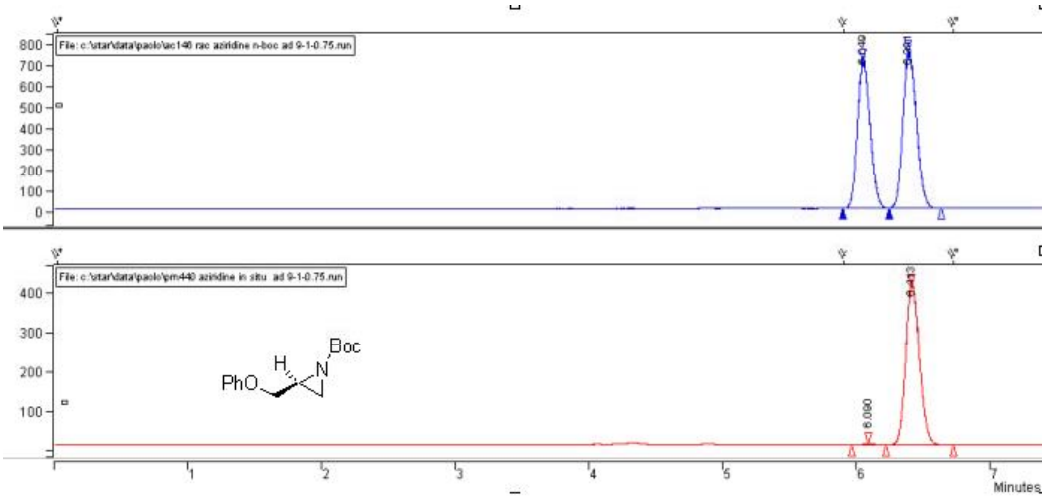
2		0.1027	18.518	0.000	62211	PB	25.9	U
Totals:		100.0000		0.000	60591095			

Synthesis of (*S*)-Propanol (8). Trifluoroacetic acid (2 mL) was added dropwise to a stirred solution of the *N*-Boc protected amino alcohol **(S)-7e** (1 mmol, 99.5% ee, prepared by AKR of **6e** with *tert*-Butyl carbamate using (*S,S*)-(salen)-Co^{III} complex) in CH_2Cl_2 (3 mL) at room temperature. After 1 h stirring, the mixture was evaporated under reduced pressure. Then the residue was dissolved in 20% aqueous NaOH, extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The material was dissolved in 5 mL MeOH and PtO_2 (12 mg, 0.05 mmol), 4 Å molecular sieves (400 mg) and acetone (110 μL, 1.1 mmol) were added. The flask was then flushed with hydrogen (1 atm) and the reaction was allowed to stir for 4 h at room temperature. The mixture was filtered through Celite and the filtrate was concentrated by rotary evaporation. The resulting opaque white solid was recrystalized from cyclohexane to yield (*S*)-(-)-Propanolol **8** (249 mg, 96% yield): $[\alpha]^{rt}_D$= -11.6° (*c* = 1.3, $CHCl_3$), lit.[3] $[\alpha]^{rt}_D$= +5.1°, (R)-**8** (*c* = 1.6, EtOH, 84% ee). ^{1}H NMR ($CDCl_3$): δ = 1.11 (d, *J* = 6.0 Hz, 6H), 2.82-2.90 (m, 2H), 3.00 (dd, *J* = 2.7, 12.0 Hz, 1H), 4.12-4.24 (m, 3H), 6.83 (d, *J* = 5.7, 1H), 7.37 (t, *J* = 7.6, 1H), 7.43-7.52 (m, 3H), 7.78-7.83 (m, 1H), 8.23-8.27 (m, 1H); ^{13}C NMR (CDCl3): δ = 22.91 (CH_3), 22.96 (CH_3), 48.8 (CH), 49.6 (CH_2), 68.4 (CH), 70.8 (CH_2), 104.8 (CH), 120.5 (CH), 121.8 (CH), 125.1 (CH), 125.5 (C), 125.8 (CH), 126.3 (CH), 127.4 (CH), 134.4 (C), 154.3 (C).

The hydrochloride salt **8**·**HCl** was formed as a white solid by precipitation from ether using gaseous hydrochloride acid: $[\alpha]^{rt}_D$= -24.8° (*c* = 0.85, EtOH), lit.[7] $[\alpha]^{rt}_D$= -25.5°, (S)- **8**·**HCl** (*c* = 1.18, EtOH).



One-pot Synthesis of (*S*)-2-Phenoxymethyl-aziridine-1-carboxylic acid *tert*-butyl ester (9). In an ordinary test tube equipped with a magnetic stirring bar, the (*R,R*)-(salen)-Co^{II} complex **2** (13.2 mg, 0.022 mmol) was dissolved in 0.15 mL of TBME. After addition of the oxidizing agent (*p*-nitro benzoic acid, 7.3 mg, 0.044 mmol), the tube was closed with a rubber stopper and the mixture was stirred at room temperature till the red colour turned to dark brown. Then the tert-butyl carbamate **3a** (58.6 mg, 0.5 mmol) and TBME (0.05 mL) were added. After 5 minutes stirring, the (±)-glycidyl phenyl ether **4** (150 µL, 1.1 mmol) was added and stirring was continued at room temperature for 24 h. After the addition of 3 mL of THF, tosyl chloride (TsCl, 0.8 mmol) and NaH (19.2 mg, 0.8 mmol) were added at 0 °C, the reaction mixture was allowed to rise to room temperature. After being stirred for 2 hours, 2 mL of THF and 2 mmol of NaH (48 mg) were added. After 3 hours stirring at room temperature, the mixture was diluted with Et_2O and the reaction was quenched with some drops of methanol. The mixture was washed with $NaHCO_3$, extracted with Et_2O and dried over anhydrous $MgSO_4$. Purification by flash chromatography (hexane/AcOEt 98/2) afforded pure (*S*)-2-Phenoxymethyl-aziridine-1-carboxylic acid *tert*-butyl ester **(9)** as a colourless oil (97 mg, 78% yield).[3] The ee was determined by HPLC analysis using a Chiralpak AD-H column (9/1 hexane/*i*-PrOH; flow rate 0.75 mL/min; τ_R = 6.1 min; τ_S = 6.4 min). $[\alpha]^{rt}_D$= -59.8° (*c* = 1.7, $CHCl_3$, 98.9% ee). ^{1}H NMR ($CDCl_3$): δ = 1.44 (s, 9H), 2.25 (d, *J* = 3.6 Hz, 1H), 2.38 (d, *J* = 6.0 Hz, 1H), 2.80-2.86 (m, 1H), 4.00 (dd, *J* = 4.8, 10.4 Hz, 1H), 4.17 (dd, *J* = 4.8, 10.4 Hz, 1H), 6.89-6.98 (m, 3H), 7.27-7.31 (m, 2H); ^{13}C NMR (CDCl3): δ = 27.8 (CH_3, 3C), 29.5 (CH_2), 35.8 (CH), 67.5 (CH_2), 81.4 (C), 114.6 (CH, 2C), 121.1 (CH), 129.4 (CH, 2C), 158.3 (C), 161.7 (C).



Peak	Peak	Result	Time	Offset	Area	Sep.	1/2
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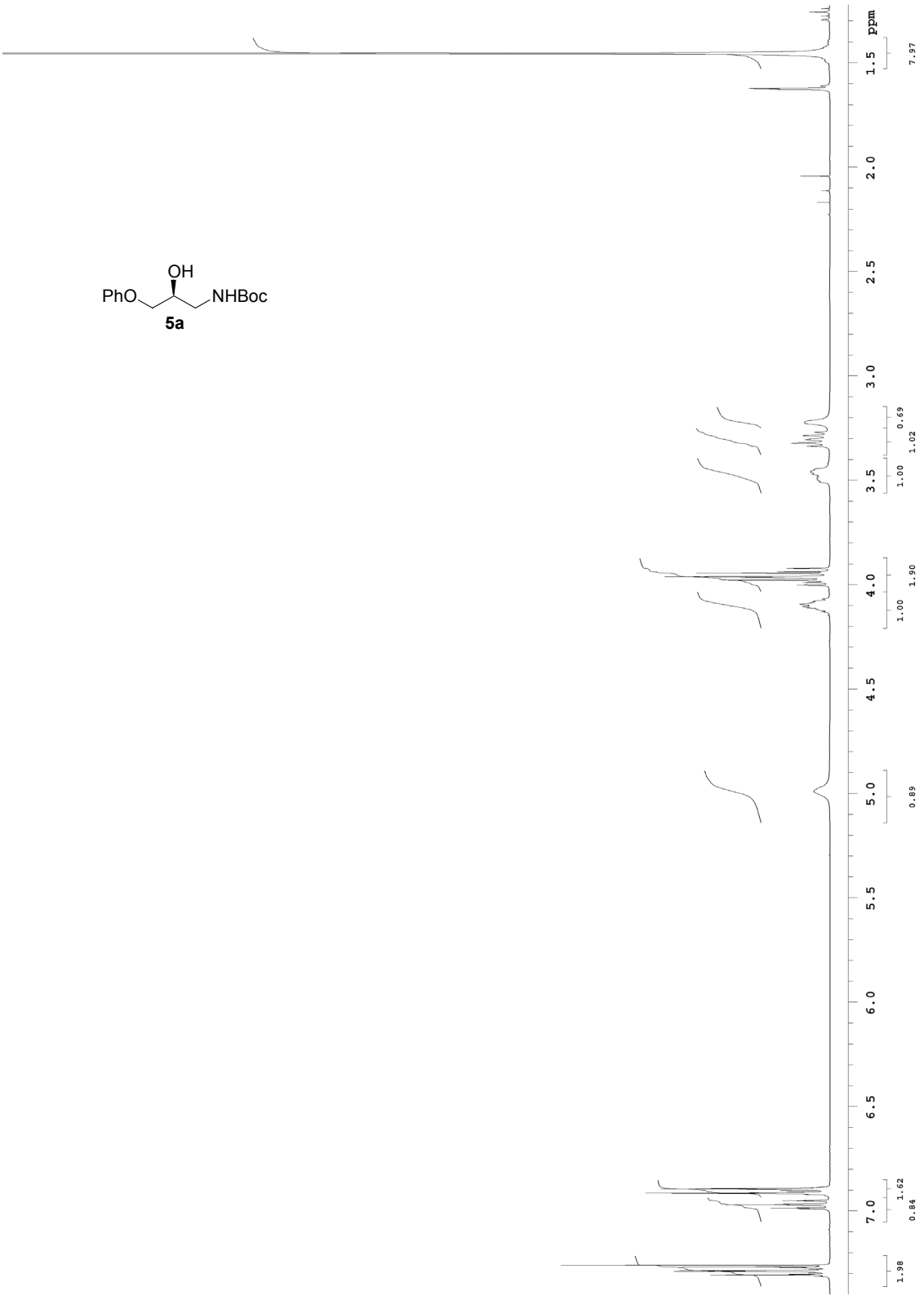
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5.5
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1.00
1.90
1.00
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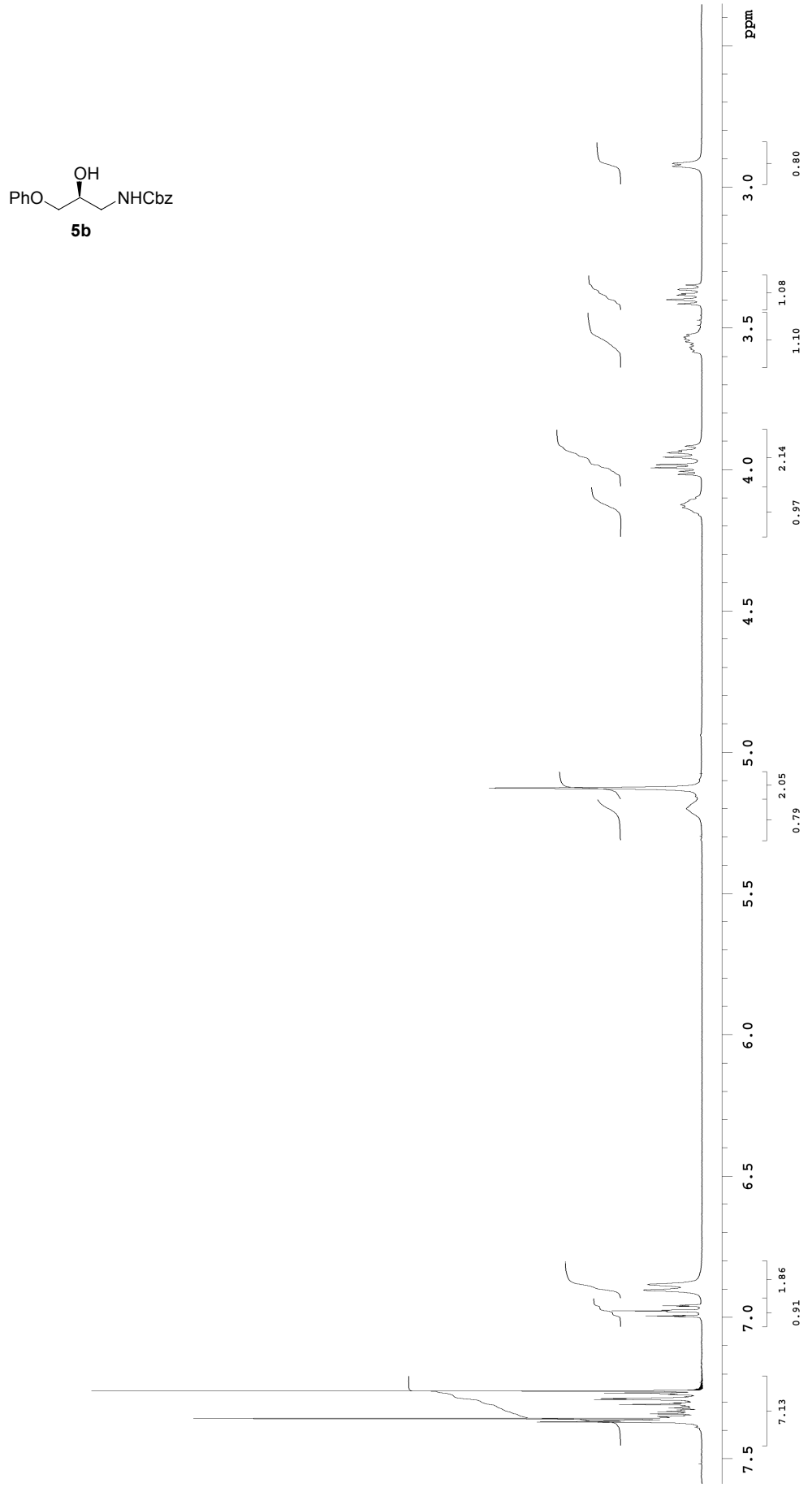
1.62
0.84
1.98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2.14
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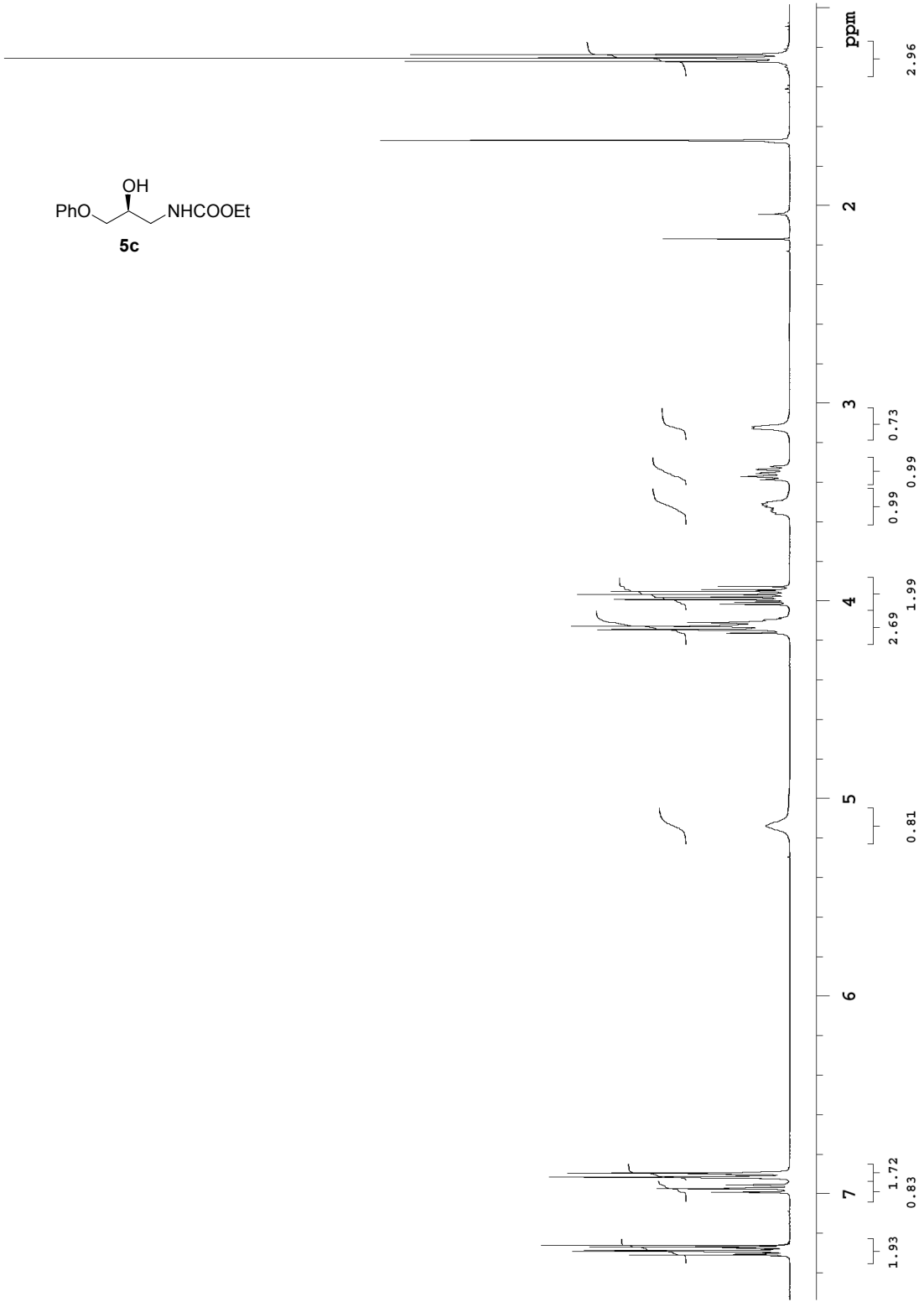
1.08
1.10
0.80


OH
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ppm
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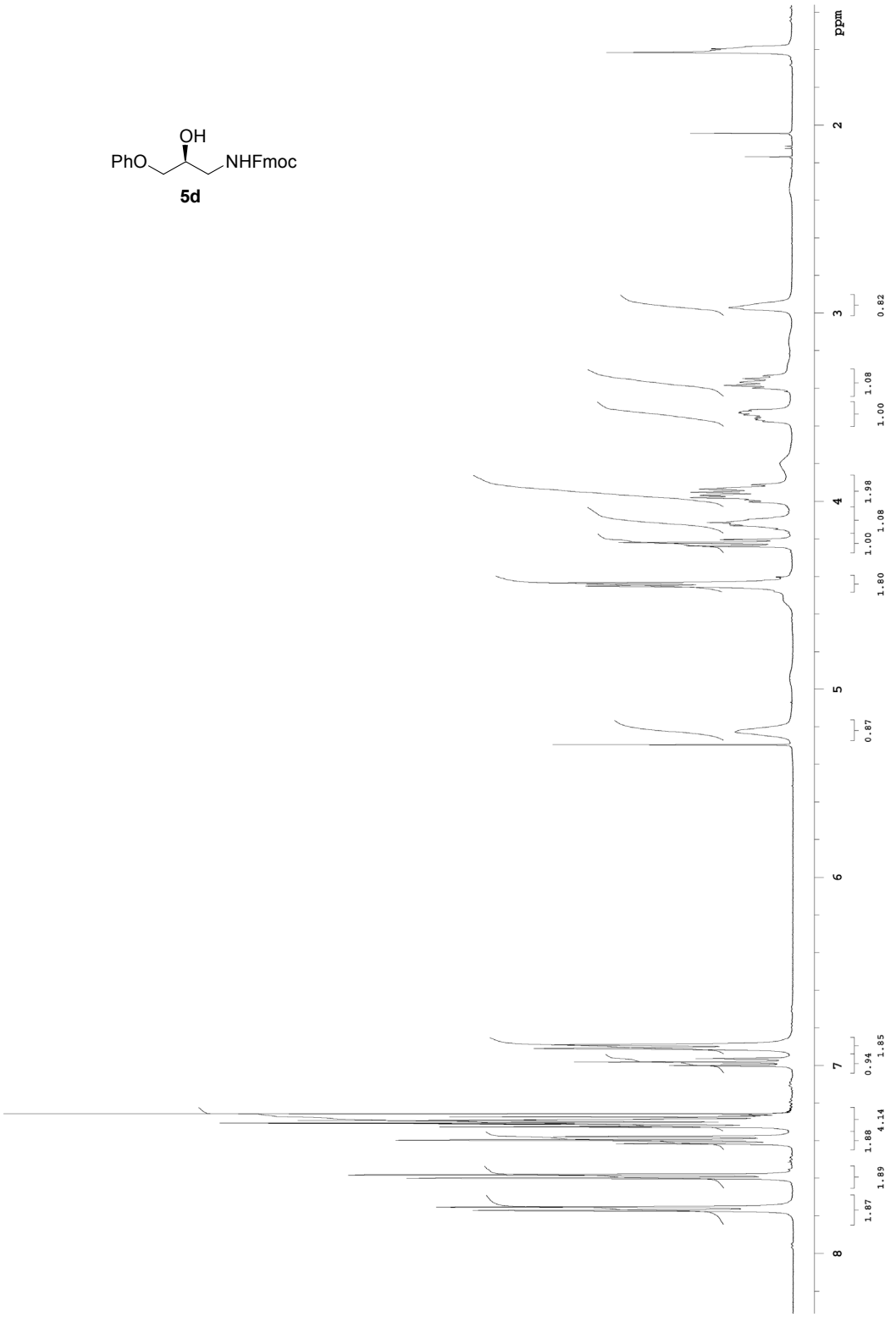
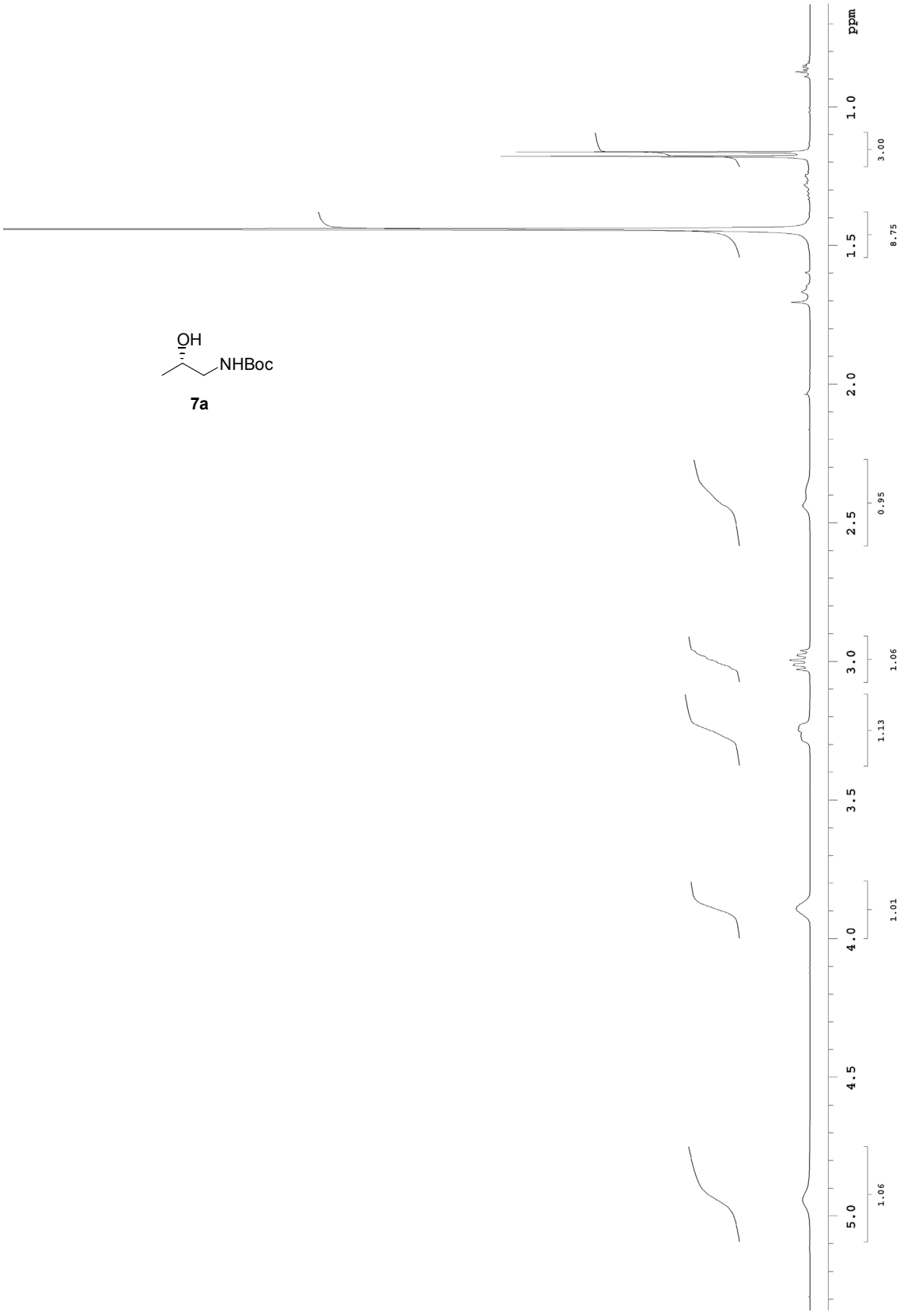
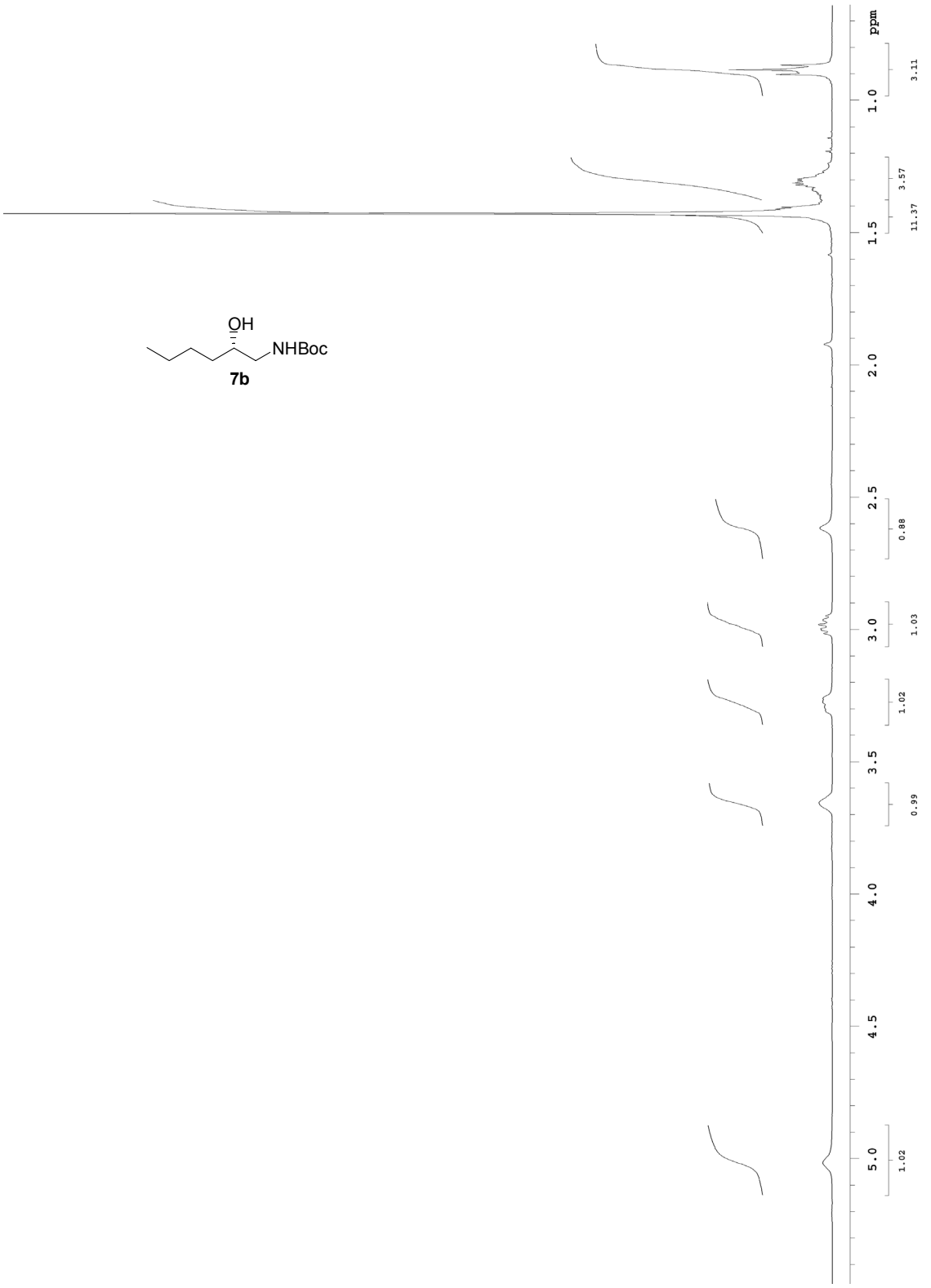
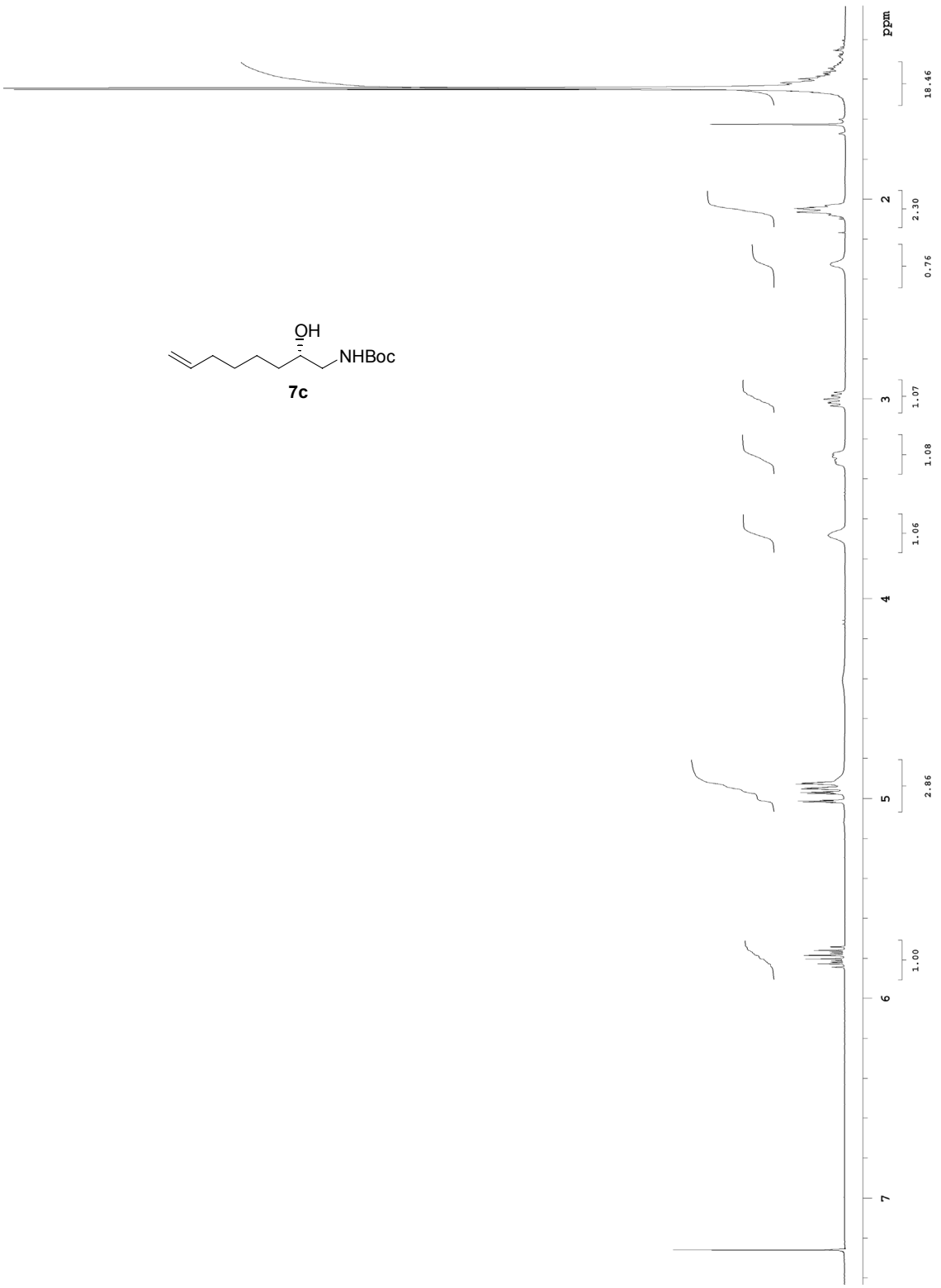
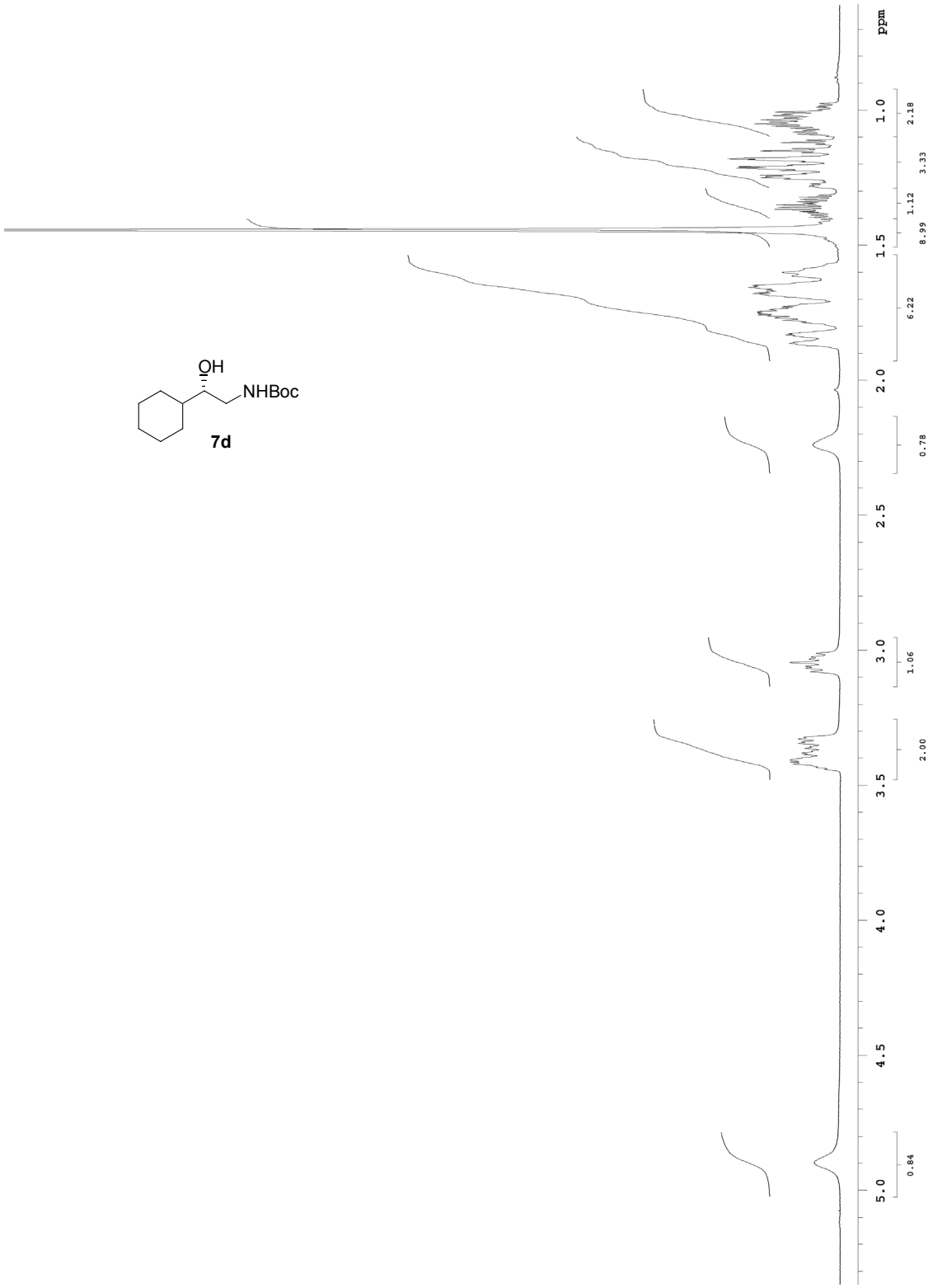
4
5
6
7
2.96
0.73
0.99
0.99
2.69
1.99
0.81
1.72
0.83
1.93

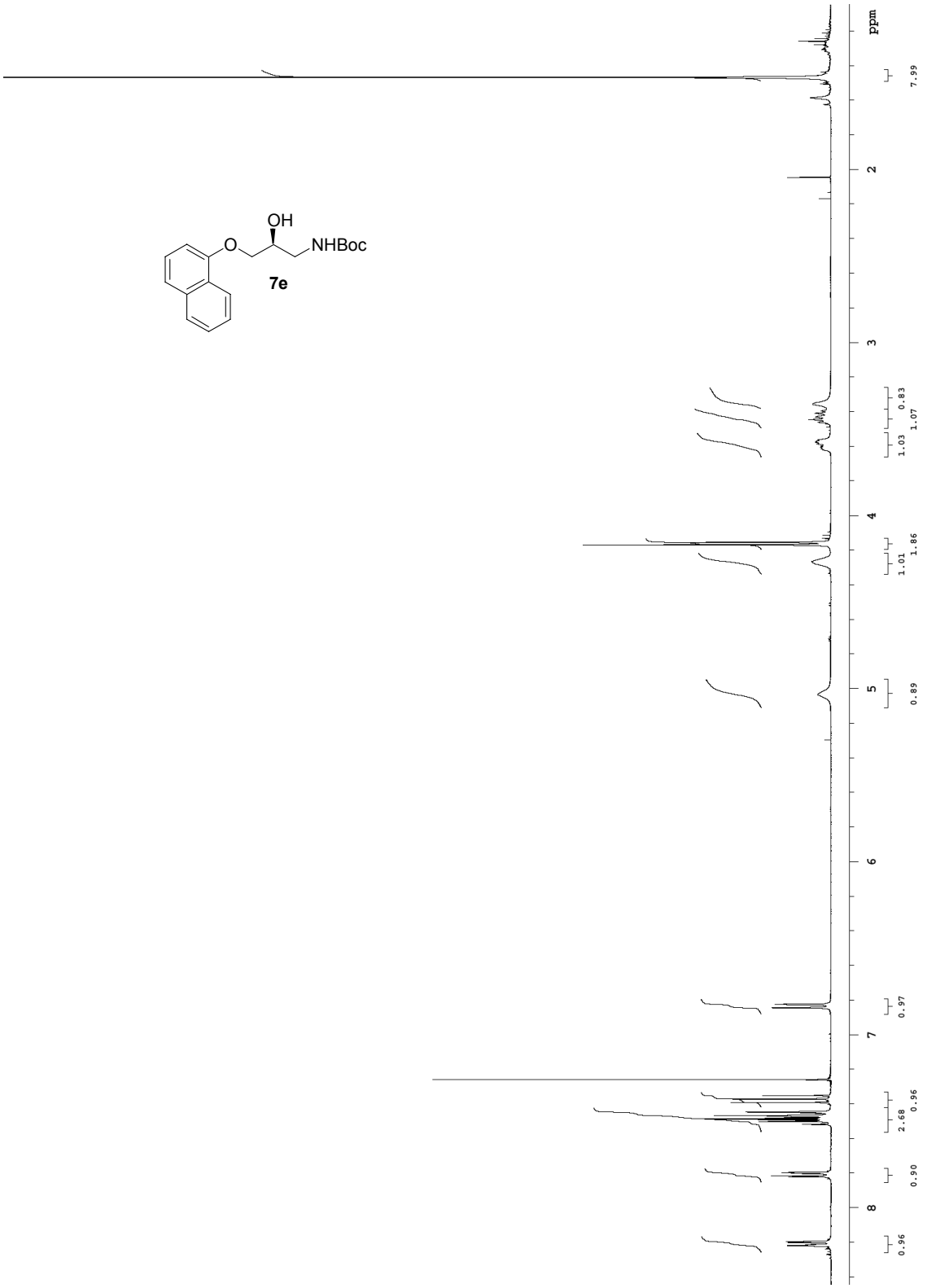

OH
PhO
NHFmoc
5d
ppm
2
3
4
5
6
7
8
0.82
1.08
1.00
1.98
1.08
1.00
1.80
0.87
0.94
1.85
1.88
4.14
1.89
1.87

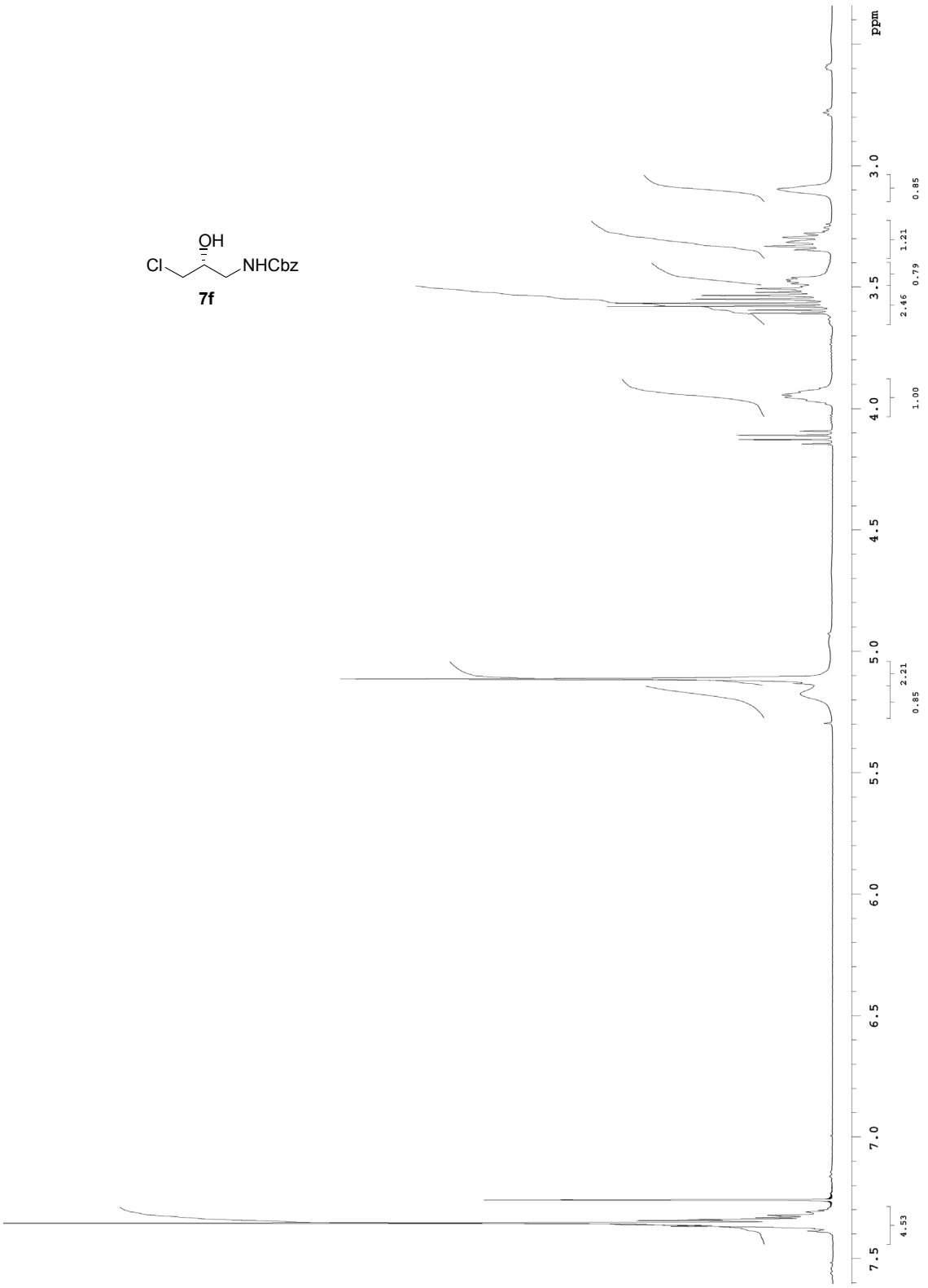

OH
NHBoc
7a
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
3.00
8.75
0.95
1.06
1.13
1.01
1.06

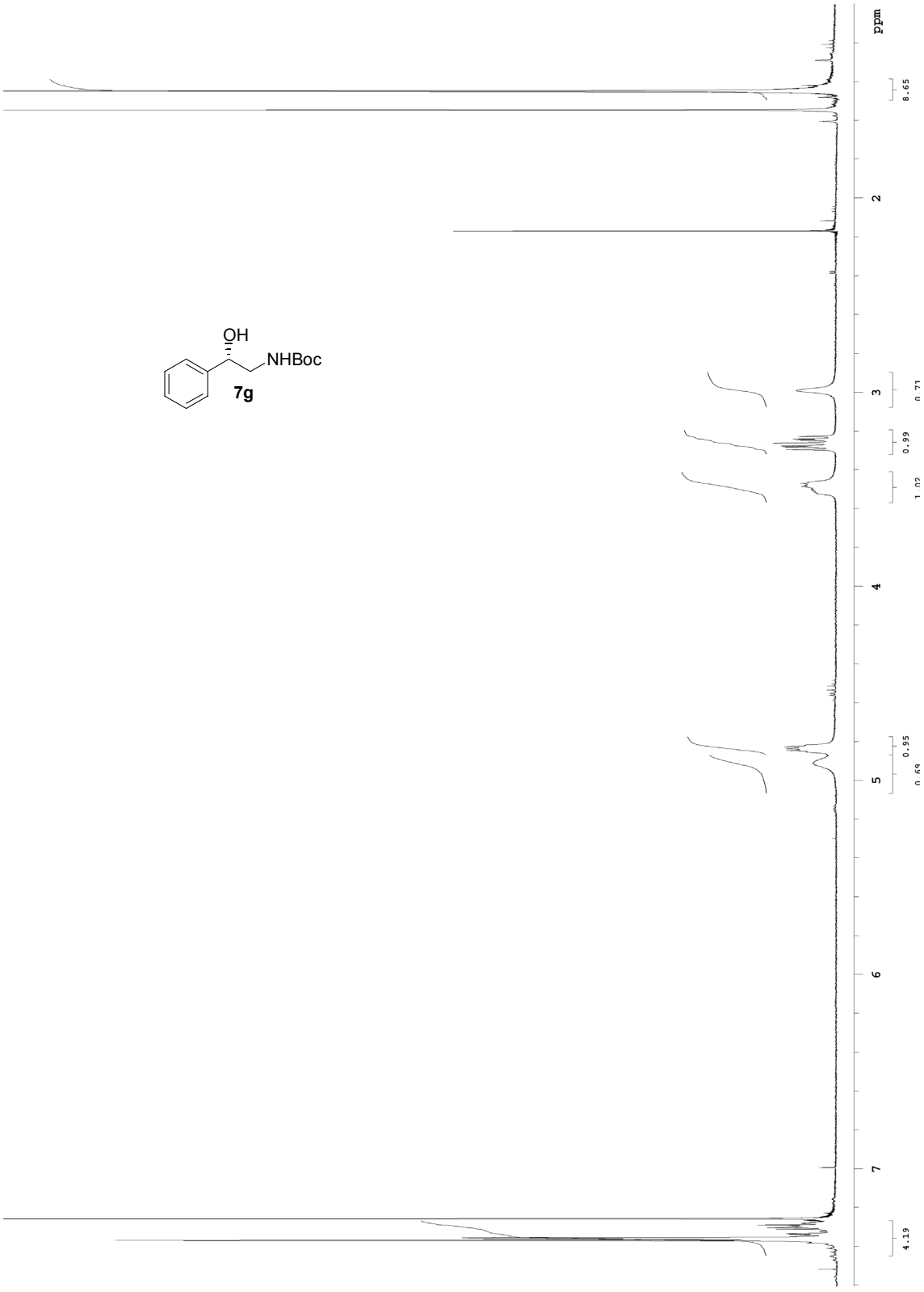

OH
NHBoc
7b
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
3.11
3.57
11.37
0.88
1.03
1.02
0.99
1.02

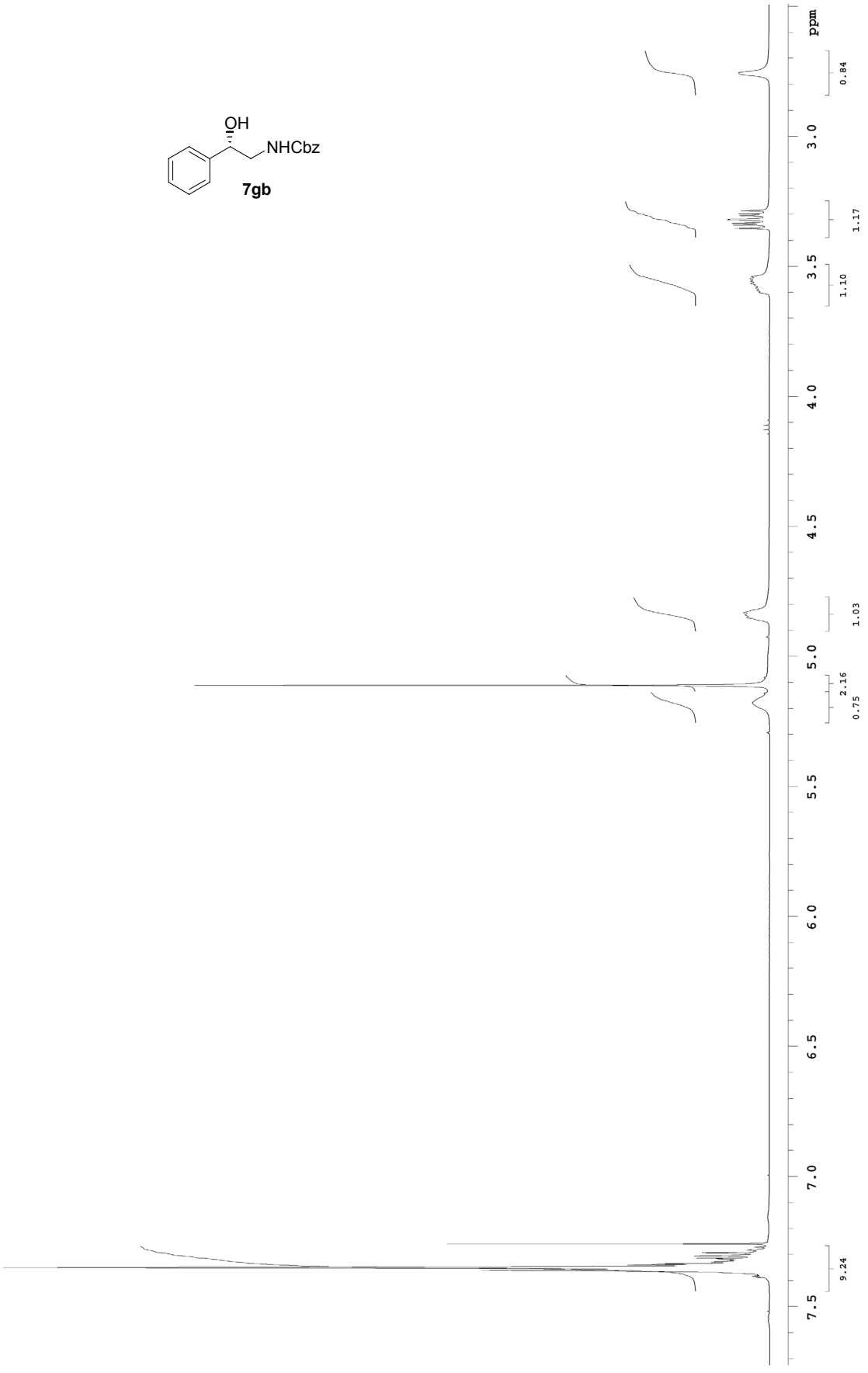

OH
NHBoc
7c
ppm
1
2
3
4
5
6
7
18.46
2.30
0.76
1.07
1.08
1.06
2.86
1.00

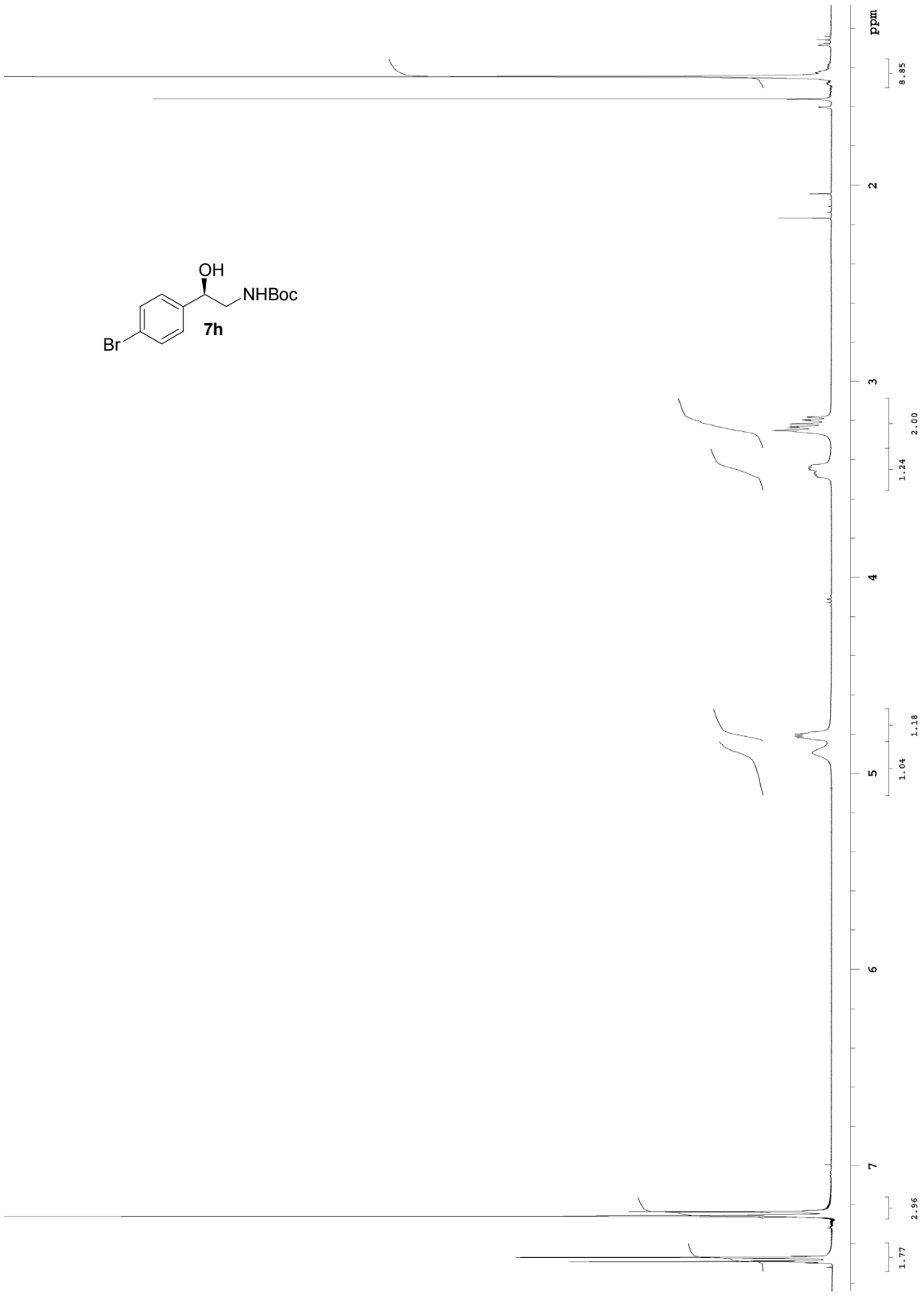

OH
NHBoc
7d
ppm
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.84
2.00
1.06
0.78
6.22
8.99
1.12
3.33
2.18


OH
O
NHBoc
7e
ppm
7.99
0.83
1.07
1.03
1.86
1.01
0.89
0.97
0.96
2.68
0.90
0.96

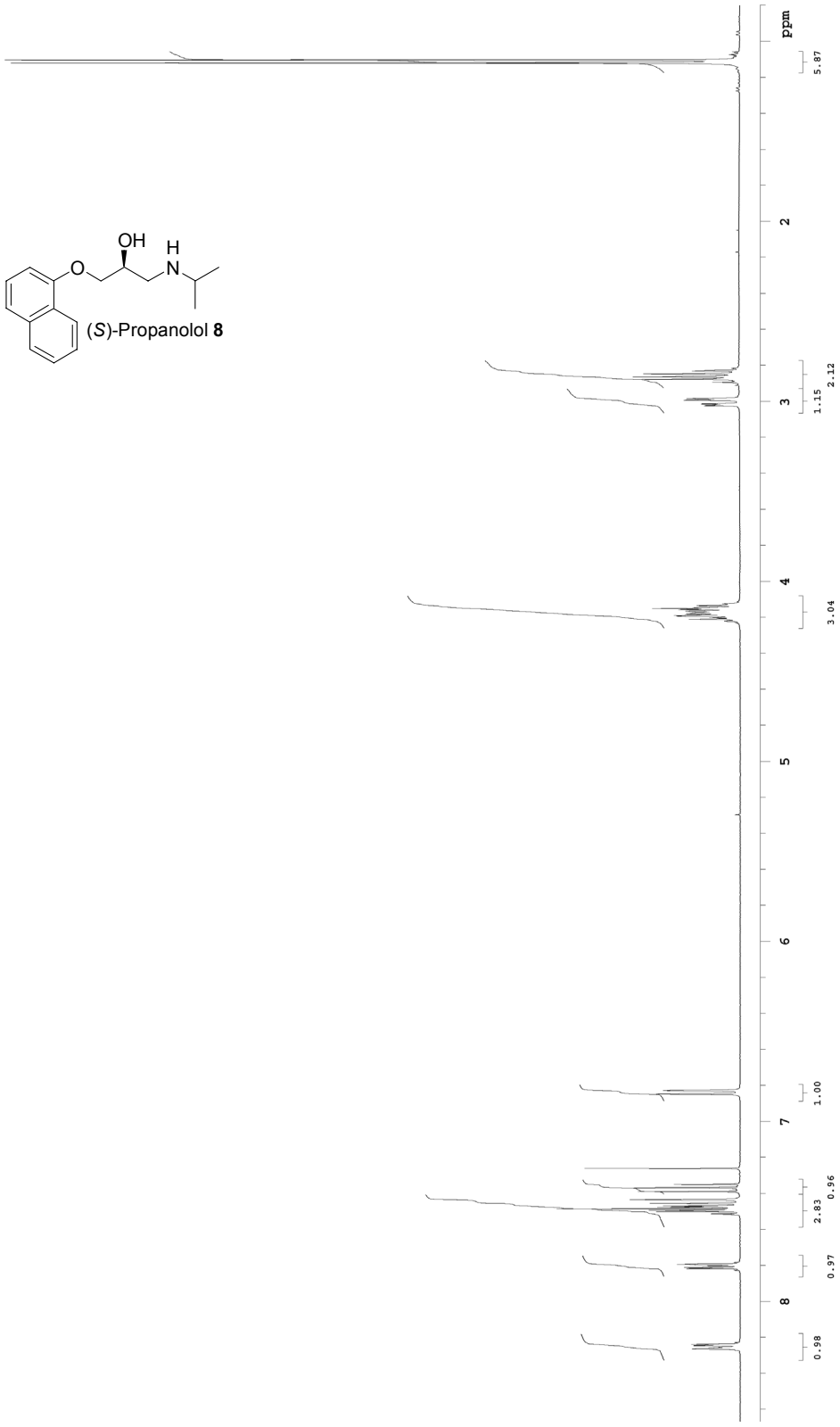

OH
Cl
NHCbz
7f
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
4.53
2.21
0.85
1.00
2.46
0.79
1.21
0.85

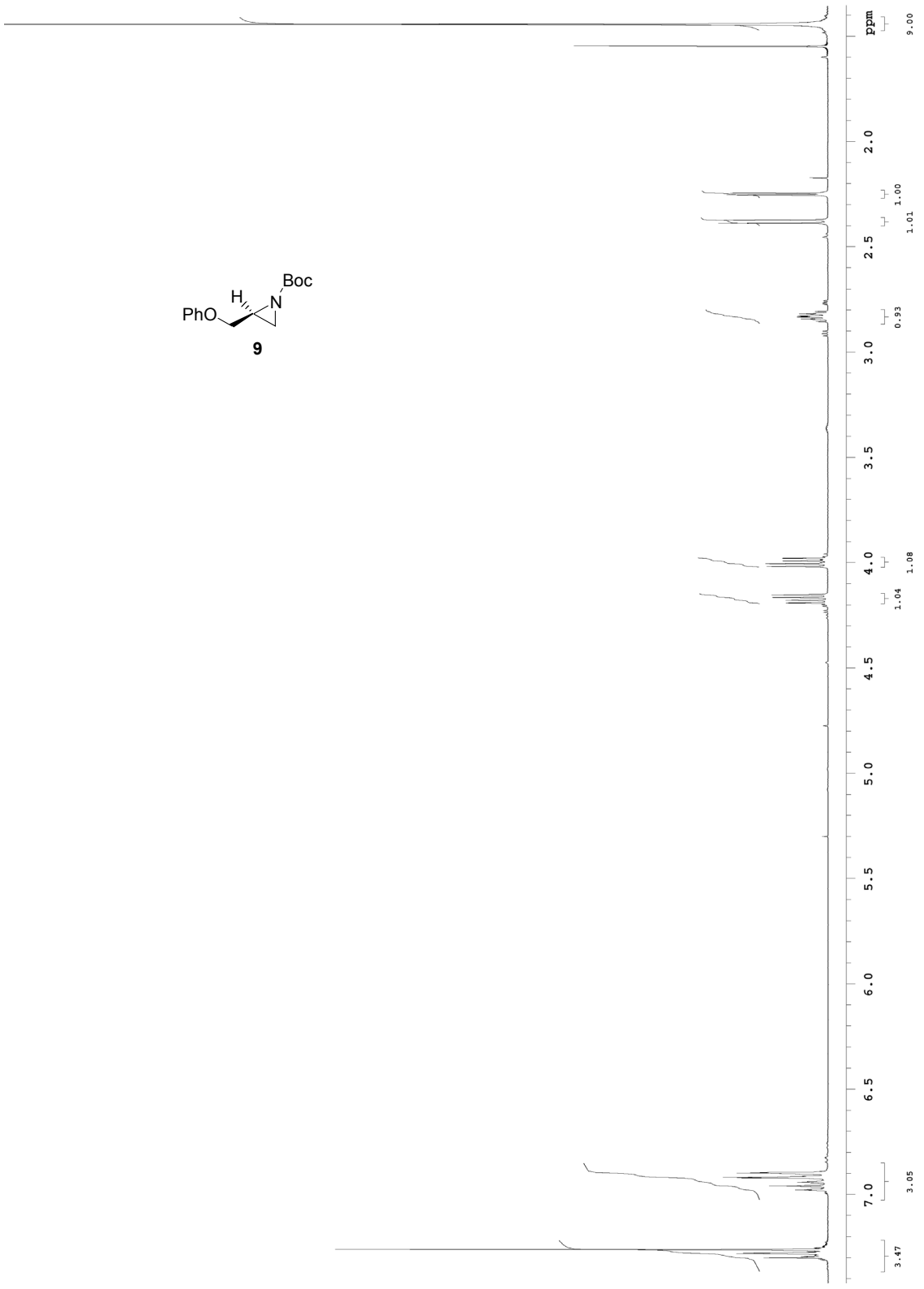

OH
NHBoc
7g
ppm
8.65
0.71
0.99
1.02
0.95
0.69
4.19


OH
NHCbz
7gb
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
9.24
0.75
2.16
1.03
1.10
1.17
0.84


OH
NHBoc
Br
7h
ppm
8.85
2.00
1.24
1.18
1.04
2.96
1.77


OH
O2N
NHBoc
7i
ppm
9.70
1.14
1.14
0.84
1.04
1.06
1.00
1.02
0.96
0.90


OH
H
N
O
(S)-Propanolol 8
ppm
1
2
3
4
5
6
7
8
5.87
1.15
2.12
3.04
1.00
2.83
0.96
0.97
0.98


Boc
H
N
PhO
9
ppm
9.00
2.0
1.00
1.01
2.5
0.93
3.0
3.5
4.0
1.04
1.08
4.5
5.0
5.5
6.0
6.5
7.0
3.05
3.47