Catalytic Asymmetric Epoxidation of α-Branched Enals

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Supporting Information

General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All solvents used in the reactions were distilled from appropriate drying agents prior to use. Reactions were monitored by thin layer chromatography on silica gel pre-coated plastic sheets (0.2 mm, Machery-Nagel). Visualization was accomplished by irradiation with UV light at 254 nm and/or *p*-anisaldehyde stain (0.7 mL p-anisaldehyde, 250 mL EtOH, 9.5 mL conc. H_2SO_4, 2.7 mL glacial AcOH) or potassium permanganate stain (1.5 g $KMnO_4$, 10 g K_2CO_3, 1.25 mL 10% NaOH, 200 mL H_2O). Column chromatography was performed on Merck silica gel (60, particle size 0.040-0.063 mm). Proton and carbon NMR spectra were recorded on Bruker AV-500, Bruker AV-400 or Bruker AV-300 spectrometer in deuterated solvent. Proton chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ δ 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet, br = broad), coupling constants (Hz) and integration. ^{13}C chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, δ 77.0). High resolution mass spectra were determined on a Bruker APEX III FTMS (7 T magnet). Infrared spectra were taken on a Perkin Elmer Spectrum 100 FTIR and are reported in reciprocal centimeters (cm^{-1}). Optical rotations were determined with Autopol IV polarimeter (Rudolph Research Analytical) at 589 nm and 25 °C. Data are reported as follows: $[\alpha]_\lambda^{temp}$, concentration (c in g/100 mL), and solvent. The enantiomeric excesses were determined by GC or HPLC analysis employing a chiral stationary phase column specified in the individual experiment, by comparing the samples with the appropriate racemic mixtures. Diastereomeric ratios were determined by GC or ^1H NMR analysis of the crude reaction mixture.

Chiral GC and HPLC columns

Hydrodex-β TBDAc (25 m x 0.25 mm): heptakis-(2,3-di-*O*-acetyl-6-*O*-*t*-butyldimethyl-sylil)-β-cyclodextrin

BGB-176SE/ SE-52 (30 m x 0.25 mm): 2,3-dimethyl-6-*tert*-butyldimethylsilyl-β-cyclodextrin

Lipodex G (25 m x 0.25 mm): octakis-(2,3-di-O-pentyl-6-O-methyl)-γ-cyclodextrin

BGB-177/BGB-15 (30 m x 0.25 mm): 2,6-dimethyl-3-pentyl-β-cyclodextrin

BGB-174/BGB-1701 (25 m x 0.25 mm): 2,3-dimethyl-6-tert-butyldimethylsilyl-β-cyclodextrin

BGB-178/BGB-15 (30 m x 0.25 mm): 2,3-diethyl-6-tert-butdyldimethylsilyl- β-cyclodextrin

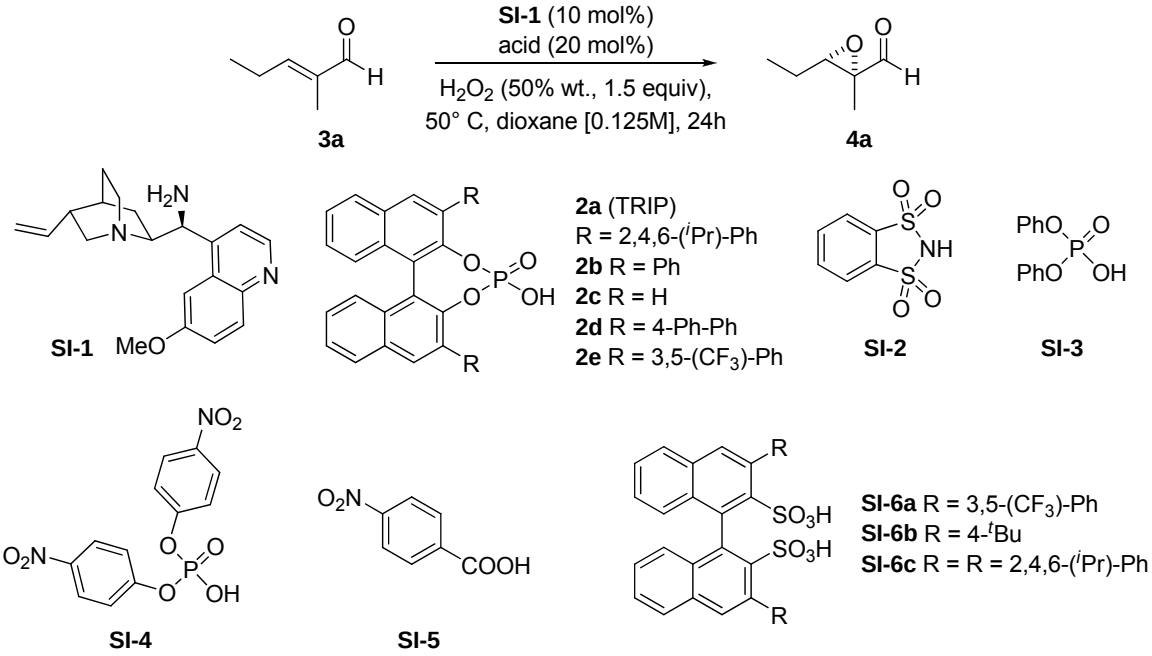
(chiraldex)-G-BP (30 m x 0.25 mm): butyryl- γ-cyclodextrin

Chiralpak AS-RH (150 mm x 4.6 mm): Amylose tris[(S)-a-methylbenzylcarbamate] coated on 5 m silica-gel

Kromasil 3-AmyCoat (150 mm x 4.6 mm): Amylose tris(3,5-dimethylphenylcarbamat) coated on 3 m silica-gel

Optimization data (selected examples)

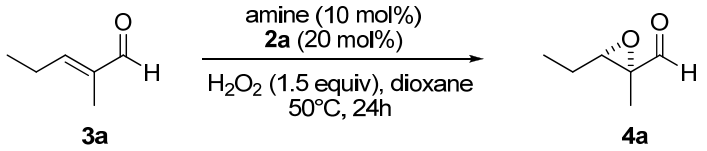
Table 1. Acid co-catalyst screen

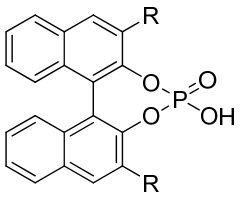


entry	acid	conv, %	dr	er	entry	acid	conv, %	dr	er
1	TFA[a]	37	83:17	93:7	13	(*R*)-**SI-6a**	14	53:47	83:17
2	TCA[b]	32	81:19	92:8	14	(*R*)-**SI-6b**[d]	21	91:9	97.5:2.5
3	(*S*)-**2a**	35	74:26	36:64	15	(*R*)-**SI-6b**	23	31:69	87:13
4	(*R*)-**2a**	50	94:6	99.5:0.5	16	(S)-**SI-6c**[d]	30	89:11	96.5:3.5
5	**SI-2**	25	67:33	74:26	17	(*S*)-**SI-6c**	30	56:44	95:5
6	**SI-3**	58	87:13	95:5	18	(*R*)-**2b**	84	96:4	99.5:0.5
7	pTSA·H_2O	54	86:14	93:7	19	(*S*)-**2b**	84	87:13	81:19
8	**SI-4**	8	77:23	83:17	20	(*R*)-**2c**	78	85:15	95:5
9	H_3PO_4	77	80:20	93:7	21	(*S*)-**2c**	64	80:20	93.5:6.5
10	H_3PO_4[c]	7	80:20	90:10	22	(*R*)-**2d**	71	80:20	85:15
11	**SI-5**	6	54:46	85:15	23	(*S*)-**2e**	72	96:4	99:1
12	(*R*)-**SI-6a**[d]	14	94:6	98.5:1.5					

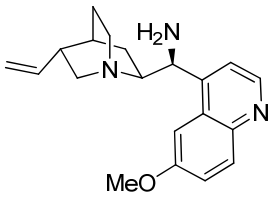
[a] TFA = trifluoroacetic acid; [b] TCA = trichloroacetic acid; [c] 7 mol% were used; [d] 10 mol% were used

Table 2. Amine co-catalyst screen

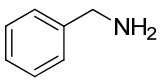




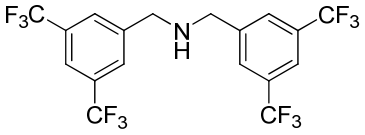
2a R = 2,4,6-(^{i}Pr)-Ph



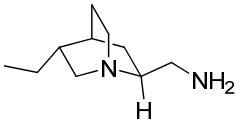
SI-1



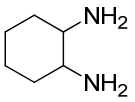
SI-7



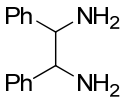
SI-8



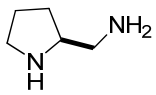
SI-9



SI-10 (meso)
SI-11 (*R*,*R*)



SI-12 (meso)
SI-13 (*R*,*R*)



SI-14

entry	amine	config. of **2a**	conv, %	dr	er
1	**SI-1**	(*R*)	50	94:6	99.5:0.5
2	**SI-1**[a]	(*R*)	43	88:12	99.5:0.5
3	none	(*R*)	<1	-	-
4	**SI-7** [b]	(*R*)	6	69:31	69:31
5	**SI-7**	(*R*)	13	59:41	68:32
6	**SI-8** [b]	(*R*)	2	-	-
7	**SI-9**	(*R*)	48	84:16	95:5
8	**SI-9**	(*S*)	35	67:33	45:54
9	**SI-10**	(*R*)	19	71:29	66:34
10	**SI-11**	(*R*)	28	72:28	58:42
11	**SI-12**	(*R*)	46	58:42	69:31
12	**SI-13**	(*R*)	25	75:25	14:86
13	**SI-13**	(S)	32	81:19	6.5:93.5
14	**SI-14**	(*R*)	18	83:17	88:12

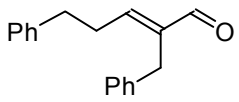
[a] 10 mol% were used; [b]10 mol% of **2a** were used

Synthetic Procedures and Spectral Data

Substrates

Compounds **3a**, **3b** and **3d** were obtained from commercial sources (Sigma-Aldrich, TCI Europe) and used without purification if freshly purchased or distilled prior to use. Chiral binaphthol derived phosphoric acids where prepared according to, or in analogy with the reported procedures.[1] 9-Amino-9-deoxyepiquinine was prepared according to the procedure of Soós et al.[2]

(*E*)-2-benzyl-5-phenylpent-2-enal (3c)



To a solution of 3-phenylpropanal (1g, 7.45 mmol, 1 equiv) in dichloromethane (7.45 mL) was added morpholinium trifluoroacetate[3] (300 mg, 1.49 mmol, 0.2 equiv) and the mixture was stirred at reflux for 19 h. Removal of the solvent under reduced pressure and flash chromatography (10% Et_2O in pentane) afforded **3c** as a colourless oil (800 mg, 3.2 mmol, 86%, E/Z = 97:3). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.43 (s, 1H), 7.30-7.27 (m, 2H), 7.24-7.20 (m, 3H), 7.17-7.09 (m, 5H), 6.61 (apparent t, ^3J = 6.9 Hz), 3.57 (s, 2H), 2.77-2.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.6, 154.8, 142.8, 140.5, 139.1, 128.6, 128.5, 128.4, 128.3, 126.4, 126.1, 34.5, 31.1, 29.7; FTIR (thin film) 3085, 3062, 3027, 2924, 2821, 2716, 1680, 1639, 1601, 1495, 1453, 1137, 1076,

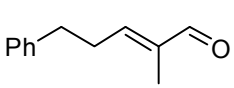
[1] (a) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566. (b) Akiyama, T.; Morita, H.; Itoh, J.; Fuchibe, K. *Org. Lett.* **2005**, *7*, 2583; also see: (c) T. Akiyama, PCT Int. Appl. WO 200409675, 2004. (d) Akiyama, T.; Saitoh, Y.; Morita, H.; Fuchibe, K. *Adv. Synth. Catal.* **2005**, *347*, 1523. (e) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356. (f) Uraguchi, D.; Sorimachi, K.; Terada, M. *J. Am.Chem. Soc.* **2004**, *126*, 11804. (g) Uraguchi, D.; Sorimachi, K.; Terada, M. *J. Am. Chem. Soc.* **2005**, *127*, 9360; also see: (h) Terada, M.; Uraguchi, D.; Sorimachi, K.; Shimizu, H. PCT Int. Appl. WO 2005070875, 2005.

[2] Vakulya, B.;Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005**, *7*, 1967.

[3] Zumbansen, K.; Döring, A.; List, B. *Adv. Synth. Catal.* **2010**, *352*, 1135.

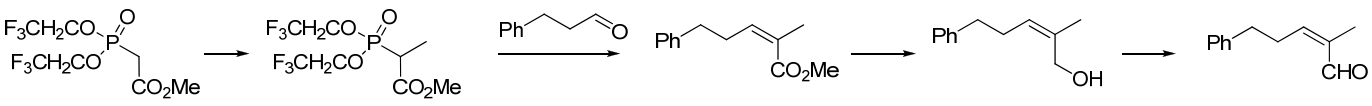
1030, 1002, 883, 733, 697 cm^{-1}; HRMS (*m/z*) calcd for $C_{18}H_{18}O$ $[M]^+$: 250.1358, found: 250.1357. The spectroscopic data are identical in all respects to those previously reported.[4]

(*E*)-2-methyl-5-phenylpent-2-enal (3e)



Prepared by Grubbs metathesis from 4-phenyl-1-butene and methacrylaldehyde according to the reported procedure.[5] Purification by flash chromatography (4% Et_2O in pentane) afforded **3e** as a yellow oil (226 mg, 1.3 mmol, 65%, E/Z > 20:1). ^1H NMR (500 MHz, $CDCl_3$) δ 9.38 (s, 1H), 7.33-7.19 (m, 5H), 6.50 (tq, ^3J = 7.3 Hz, ^4J = 1.3 Hz, 1H), 2.82 (apparent t, ^3J = 7.5 Hz, 2H), 2.68 (apparent q, ^3J = 7.5 Hz, 2H), 1.69 (br. s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.3, 153.3, 140.6, 139.9, 128.6, 128.4, 126.3, 34.4, 30.7, 9.2; FTIR (thin film) 3062, 3028, 2926, 2821, 2713, 1684, 1644, 1454, 1360, 1240, 1015, 700 cm^{-1}; HRMS (*m/z*) calcd for $C_{12}H_{14}O$ $[M]^+$: 174.1045, found: 174.1046. The physical data are identical in all respects to those previously reported.[6]

(*Z*)-2-methyl-5-phenylpent-2-enal ((*Z*)-3e)



SI-16: To a solution of t-BuOK (1.27g, 11.3 mmol, 1.2 equiv) in THF (13 mL) was slowly added methyl bis(2,2,2-trifluoroethyl)phosphonoacetate **SI-15** (2 mL, 9.46 mmol, 1 equiv) at 0 °C under argon. The mixture was stirred at 0 °C for 30 min under argon, and methyl iodide (2.96 mL, 47.3

[4] Erkkilä, A.; Pihko P. M. *Eur. J. Org. Chem.* **2007**, 4205.
[5] Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P, Grubbs, R. H. *J. Am. Chem. Soc*. **2003**, *125*, 11360.

mmol, 5 equiv) was slowly added at 0 °C. The solution was warmed up to room temperature, stirred for 23 h and treated with an saturated aqueous solution of NH_4Cl. The reaction mixture was extracted with EtOAc three times, dried over Na_2SO_4, filtered and concentrated. Flash column chromatography eluting with 30% EtOAc in hexanes afforded **SI-16**[7] as a colourless oil (2.30 g, 6.93 mmol, 73%). ^{1}HNMR (500 MHz, $CDCl_3$) δ: 4.49-4.38 (m, 4H), 3.78 (s, 3H), 3.20 (dq, $^2J_{H,P}$ = 22.8 Hz, ^3J = 7.4 Hz, 1H), 1.52 (dd, $^4J_{H,P}$ = 19.3 Hz, ^3J = 7.4 Hz, 3H).

SI-17[8]: A solution of **SI-16** (332 mg, 1 mmol, 1 equiv) and 18-crown-6 (1.32 g, 5 mmol, 5 equiv) in THF (20 mL) was cooled to -78 °C under argon and treated with KHMDS (199.5 mg, 1 mmol, 1 equiv). 3-Phenylpropanal (133 μL, 1 mmol, 1 equiv) was added and the resulting mixture was stirred at – 78 °C for 1h. Saturated aqueous solution of NH_4Cl was added and the product was extracted with diethyl ether three times, dried over Na_2SO_4, filtered and concentrated. The unsaturated ester **SI-17** (Z/E > 20:1 by ^{1}HNMR) was used without purification. ^{1}HNMR (500 MHz, $CDCl_3$) δ: 7.30-7.17 (m, 5H), 5.98 (td, ^3J = 6.9 Hz, ^4J = 1.2 Hz, 1H), 3.72 (s, 3H), 2.81-2.70 (m, 4H), 1.89 (d, ^4J = 1.2 Hz, 3H).

SI-18[15]: Crude **SI-17** (1 mmol) was dissolved in dichloromethane (3 mL) under argon and cooled to -78 °C. DIBAL (4.8 mL, 1M in hexanes, 4.8 mmol, 4.8 equiv) was added dropwise and the solution was stirred for 1 h at – 78 °C. The reaction was quenched with aqueous Rochelle's salt and stirred vigorously for 2 h. The crude reaction mixture was extracted with dichloromethane three times, dried over Na_2SO_4, filtered and concentrated. Flash column chromatography eluting with 15% diethyl ether in pentane afforded **SI-18** as a colourless oil (93.2 mg, 0.53 mmol, 53% over two steps). ^{1}HNMR (500 MHz, $CDCl_3$) δ: 7.30-7.16 (m, 5H), 5.33 (t, ^3J = 7.6 Hz, 1H), 3.92 (s, 2H), 2.66 (apparent t, ^3J = 7.2 Hz, 2H), 2.37 (centered m, 2H), 1.76 (d, ^4J = 1.1 Hz, 3H).

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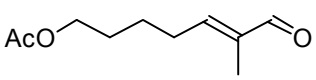
[6] Browder, C. C.; Marmsäter, F. P.; West, F. G. *Can. J. Chem.* **2004**, *82*, 375.
[7] Sano, S.; Takehisa, T.; Ogawa, S.; Yokoyama, K.; Nagao, Y. *Chem. Pharm. Bull.* **2002**, *50*, 1300.
[8] Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.

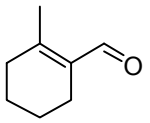
(*Z*)-3e: Oxalyl chloride (50.3 μL, 0.59 mmol, 2 equiv) was dissolved in dichloromethane (9 mL) and the solution was cooled to – 78 °C. DMSO (83.2 μL, 1.17 mmol, 4 equiv) was added dropwise at – 78 °C and the solution was stirred for 30 min. A solution of **SI-18** in dichloromethane (2 mL) was added dropwise and the reaction was stirred for 30 min. Et_3N (244 μL, 1.76 mmol 6 equiv) was added dropwise and the solution was stirred for 1 h at – 78 °C. The reaction was warmed up to room temperature, treated with a saturated aqueous solution of NH_4Cl and extracted with dichloromethane three times, dried over Na_2SO_4, filtered and concentrated. ^{1}H NMR analysis of the crude reaction mixture indicated Z/E ratio of 97:3. Flash column chromatography eluting with 15% diethyl ether in pentane afforded **(*Z*)-3e** as a colourless oil (38.2 mg, 0.22 mmol, 75%, Z:E = 95:5). ^{1}HNMR (500 MHz, $CDCl_3$) δ: 10.0 (s, 1H), 9.38 (s, 0.05 H, *E*-isomer), 7.31-7.17 (m, 5H), 6.53 (td, ^3J = 8.0 Hz, 1H), 2.91-2.78 (m, 4H), 1.76 (d, ^4J = 1.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.0, 147.9, 140.3, 136.6, 128.6, 128.5, 126.4, 35.7, 28.5, 16.4; FTIR (thin film) 3063, 3028, 2925, 2859, 1678, 1645, 1496, 1355, 1242, 1016, 907, 730, 700 cm^{-1}.

(*E*)-6-methyl-7-oxohept-5-en-1-yl acetate (3f)



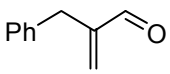
Prepared by Grubbs metathesis from hex-5-en-1-yl acetate and methacrylaldehyde according to the reported procedure.[5] ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.41 (s, 1H), 6.47 (tq, ^3J = 7.3 Hz, ^4J = 1.3 Hz, 1H), 4.10 (t, ^3J = 6.4 Hz, 2H), 2.40 (q, ^3J = 7.5 Hz, 2H), 2.06 (s, 3H), 1.76-1.56 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): 195.2, 171.1, 153.7, 139.8, 64.0, 28.5, 28.3, 24.9, 21.0, 9.3 δ; FTIR (thin film) 2949, 2867, 2715, 2256, 1736, 1684, 1645, 1457, 1388, 1366, 1236, 1047, 908, 729 cm^{-1}; HRMS (*m/z*) calcd for $C_{10}H_{16}O_3$ $[M]^+$: 184.1099, found: 184.1099. The physical data are identical in all respects to those previously reported.[5]

2-methylcyclohex-1-enecarbaldehyde (3g)



To a solution of 1-methylcyclohept-1-ene (200 mg, 1.81 mmol, 1 equiv) in MeCN (9 mL), CCl_4 (9 mL) and water (13 mL) was added $NaIO_4$ (1.6 g, 7.60 mmol, 4.2 equiv) followed by $RuO_2 \bullet xH_2O$ (4.8 mg, 0.036 mmol, 0.02 equiv), and the mixture was stirred vigorously for 1h at room temperature.[9] The mixture was diluted with water and extracted with CH_2Cl_2 three times. The combined organic layers were washed with brine, dried over Na_2SO_4 and the solvent was carefully evaporated. The crude reaction mixture was diluted with CH_2Cl_2 (18 mL) and L-proline (20.7 mg, 0.18 mmol, 0.1 equiv) was added. After 14h, AcOH (104 uL, 1.81 mmol, 1 equiv) was added, and the reaction mixture was stirred at room temperature for 34h after which all of the starting material was consumed. The crude reaction mixture was diluted with ether, washed with sat. aq. $NaHCO_3$ and extracted with ether three times. The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure. Flash chromatography (30% Et_2O in pentane) afforded **3g** as a colourless oil (76.3 mg, 0.61 mmol, 34%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.15 (s, 1H), 2.23-2-16 (m, 4H), 2.14 (br s, 3H), 1.66-1.57 (m, 4H). The spectroscopic data are identical in all respects to those previously reported.[10]

2-benzylacrylaldehyde (5a)

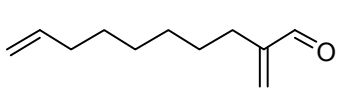


Prepared from 3-phenylpropanal and formaldehyde according to the reported procedure.[4] ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (s, 1H), 7.31-7.17 (m, 5H), 6.10 (s, 1H), 6.07 (s, 1H), 3.57 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.0, 149.8, 138.1, 135.3, 129.2, 128.6, 126.5, 34.2; FTIR (thin film) 3087, 3063, 3029, 2919, 2824, 2701, 1686, 1602, 1496, 1453,

[9] Piers, E.; Skupinska, K. A.; Wallace, D. J. *Synlett* **1999**, 1867.
[10] Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.,***1986**, *108,* 452.

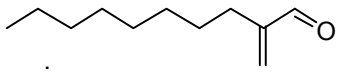
1434, 1245, 1075, 950, 737, 699 cm^{-1}; HRMS (*m/z*) calcd for $C_{10}H_{10}O$ $[M]^+$: 146.0732, found: 146.0733. The physical data are identical in all respects to those previously reported.[4]

2-methylenedec-9-enal (5b)



Prepared from dec-9-enal and formaldehyde according to the reported procedure.[4] ^1H NMR (500 MHz, $CDCl_3$) δ 9.54 (s, 1H), 6.24 (centered m, 1H), 5.98 (br d, ^3J = 0.7 Hz, 1H), 5.80 (ddt, ^3J = 17.1 Hz, ^3J = 10.1 Hz, ^3J = 6.7 Hz), 5.02-4.91 (m, 2H), 2.23 (t, ^3J = 7.5 Hz, 2H), 2.06-2.00 (m, 2H), 1.49-1.29 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.8, 150.5, 139.1, 133.9, 114.2, 33.7, 29.1, 28.9, 28.8, 27.8, 27.7; FTIR (thin film) 3078, 2978, 2928, 2857, 1695, 1641, 1464, 1440, 1329, 995, 942, 910, 850 cm^{-1}; HRMS (*m/z*) calcd for $C_{11}H_{18}O$ $[M]^+$: 166.1358, found: 166.1359. The physical data are identical in all respects to those previously reported.[11]

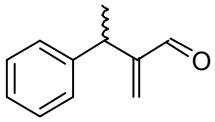
2-methylenedecanal (5c)



Prepared from decanal and formaldehyde according to the reported procedure.[4] ^1H NMR (500 MHz, $CDCl_3$) δ 9.71 (s, 1H), 6.25 (br s, 1H), 5.99 (br s, 1H), 2.23 (t, ^3J = 7.6 Hz, 2H), 1.44 (centered m, 2H), 1.33-1.23 (m, 10H), 0.88 (t, ^3J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.9, 150.5, 134.0, 31.9, 29.4, 29.3, 29.2, 27.77, 27.75, 22.7, 14.1; FTIR (thin film) 2926, 2856, 2256, 1694, 1628, 1466, 1330, 1106, 942, 907, 729 cm^{-1}; HRMS (*m/z*) calcd for $C_{11}H_{20}O$ $[M]^+$: 168.1514, found: 168.1514.

[11] Basu, K.; Richards, J.; Paquette, L. A. *Synthesis* **2004**, 2841.

2-methylene-3-phenylbutanal (rac-5d)

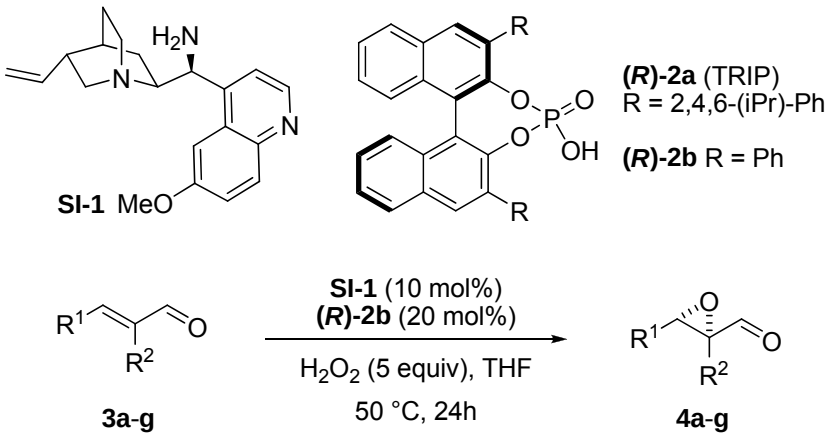


Prepared from 3-phenylbutanal and formaldehyde according to the reported procedure.[4] ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.54 (s, 1H), 7.30-7.18 (m, 5H), 6.24 (br d, ^{3}J = 1.1 Hz, 1H), 6.08 (br s, 1H), 4.03 (q, ^{3}J = 7.2 Hz, 1H), 1.43 (d, 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.9, 154.3, 143.6, 133.7, 128.4, 127.5, 126.4, 37.2, 20.0; FTIR (thin film) 3062, 3029, 2972, 2937, 2878, 2817, 2670, 2256, 1693, 1493, 1453, 1245, 948, 907, 730, 699 cm^{-1}; HRMS (*m/z*) calcd for $C_{11}H_{12}O$ $[M]^{+}$: 160.0888, found: 160.0886. The spectroscopic data are identical in all respects to those previously reported.[4]

Products

General procedure for the enantioselective epoxidation

Procedure A: epoxidation of trisubstituted enals 3a-g

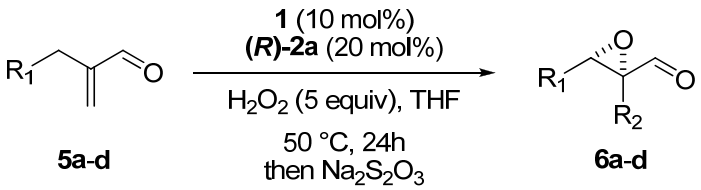


Phosphoric acid **(*R*)-2b** (25.0 mg, 0.05 mmol, 0.2 equiv) and amine **SI-1** (8.08 mg, 0.025 mmol, 0.1 equiv) were dissolved in dry THF (2 mL, 0.125 M) and stirred for 5 min under ambient atmosphere at room temperature. The α-branched enal **3** (0.25 mmol, 1 equiv) was added and the mixture was stirred for an additional 5 min at room temperature. Aqueous hydrogen peroxide (77 μL, 50% w/w, 1.25 mmol, 5 equiv) was added, the reaction vessel was sealed and the reaction mixture was stirred for 24 h at 50 °C under an atmosphere of air. The reaction can be monitored by the disappearance of the starting material; the formed product is masked as a very polar species that appears as a poorly stainable spot on the TLC ($R_f \sim 0.1$) and is presumably a hydroperoxide adduct of the aldehyde **4**. The product **4** is liberated as the free aldehyde when the excess peroxide is quenched. This was performed by stirring the crude reaction mixture with 10% aqueous $Na_2S_2O_3$ (1 mL) for 10 min. The mixture was then diluted with water (5 mL) and diethyl ether (5 mL) and partitioned. The aqueous layer was washed

with diethyl ether (5 mL x 3), and the combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent and flash column chromatography with the specified solvent system afforded the desired product.

Procedure A1: In cases when the epoxyaldehyde products were very volatile or unstable for GC/HPLC analysis, a modified workup procedure was used and the product was reduced to the corresponding alcohol. The crude reaction mixture was quenched by adding solid $Na_2S_2O_3$ (250 mg) and the suspension was stirred for 1 h. It was then filtered through a pad of Celite, washing with 2-5 mL diethyl ether and 2 mL EtOH. To this filtrate was added solid $NaBH_4$ (14.1 mg, 0.375 mmol, 1.5 equiv) and the reaction mixture was stirred for 10 min. Saturated aqueous Na,K-tartrate (Rochelle's salt) was added and the reaction mixture was stirred for 1 h. The resulting biphasic solution was diluted with diethyl ether (5 mL) and water (10 mL) and partitioned. The aqueous layer was washed extracted with EtOAc (5 mL x 2), and the combined organic layers were washed with brine and dried over Na_2SO_4. Evaporation of the solvent and flash column chromatography with the specified solvent system afforded the desired product.

Procedure B: epoxidation of disubstituted enals 5a-3d



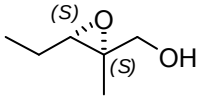
Epoxidation of disubstituted enals **5a-d** was performed exactly as in **Procedure A** for non-volatile products and **Procedure A1** for volatile products, except that phosphoric acid **(*R*)-2a** ((*R*)-TRIP) was used (37.6 mg, 0.05 mmol, 0.2 equiv) instead of **(*R*)-2b**.

Racemates

All racemates of the aldehyde and the corresponding alcohol products were prepared according to the procedure described by Pihko *et al*.[12]

Enantioenriched products 7a-7g and 4a-4g

((2*S*,3*S*)-3-ethyl-2-methyloxiran-2-yl)methanol (7a)



Prepared according to the general procedure **A1** using commercial (*E*)-2-methylpent-2-enal (E/Z >20:1, 0.4 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (50% Et_2O in pentane) afforded **7a** as a colourless oil (19.9 mg, 0.17 mmol, 43%, 92:8 dr, 98.5:1.5 er); $[\alpha]_D^{25}$ – 14.1 (*c* 0.170, $CHCl_3$); Lit[13]: $[\alpha]_D^{22}$ = – 13.5 (c = 0.84, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (dd, ^3J = 4.3 Hz, ^2J = 12.2 Hz, 1H), 3.58 (dd, ^3J = 8.2 Hz, ^2J = 12.2 Hz, 1H), 3.00 (t, ^3J = 6.4 Hz, 1H), 2.82 (minor diastereomer, t, ^3J = 6.4 Hz, 1H), 1.72 (br dd, 1H, exchanges with D_2O), 1.68-1.50 (m, 2H), 1.29 (s, 3H), 1.04 (t, ^3J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) only major diastereomer peaks detected: δ 65.4, 61.3, 60.9, 21.5, 14.1, 10.5; FTIR (thin film) 3427, 2972, 2937, 2878, 1460, 1348, 1040, 909, 732 cm^{-1}; HRMS (*m/z*) calcd for $C_6H_{13}O_2$ $[M+H]^+$: 117.0916, found 117.0915; Chiral GC (Hydrodex-β TBDAc, 20 min at 100 °C, 8 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_2) t_r 9.1 min (major enantiomer, major diastereomer), t_r 11.0 min (major enantiomer, minor diastereomer), t_r 12.0 min (minor enantiomer, major diastereomer), t_r 13.2 min (minor enantiomer, minor diastereomer). The physical data are identical in all respects to those previously reported.[13]

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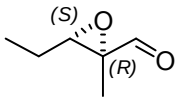
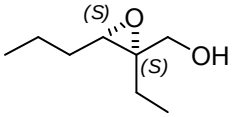
[12] Erkkilä, A., Pihko, P.M., Clarke, M.-R. *Adv. Synth. Catal.* **2007**, *349*, 802.
[13] Colvin, E. W.; Robertson, A. D.; Wakharkar, S. *J. Chem. Soc. Chem. Comm.* **1983**, 312.

(2*R*,3*S*)-3-ethyl-2-methyloxirane-2-carbaldehyde (4a)

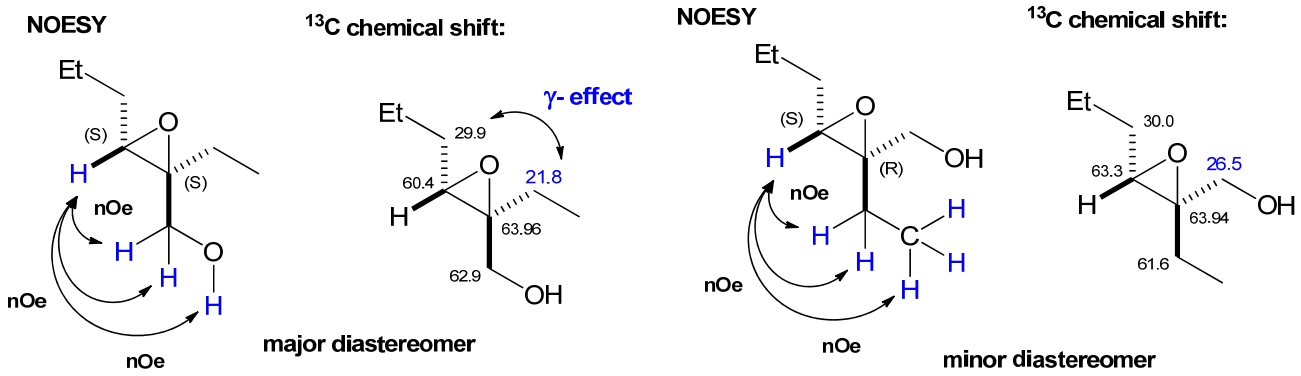


Chiral GC (BGB-176SE/ SE-52, 45 min at 40 °C, 8 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_2) t_r 29.9 min (minor enantiomer, minor diastereomer), t_r 32.2 min (major enantiomer, minor diastereomer), t_r 35.6 min (minor enantiomer, major diastereomer), t_r 35.9 min (major enantiomer, major diastereomer).

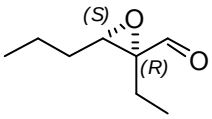
((2*S*,3*S*)-2-ethyl-3-propyloxiran-2-yl)methanol (7b)



Prepared according to the general procedure **A1** using commercial (*E*)-2-ethylhex-2-enal (E/Z = 94:6, 0.36 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (50% Et_2O in pentane) afforded **7b** as a colourless oil (33.1 mg, 0.23 mmol, 64%, 83:17 dr, 99:1 er). $[\alpha]_D^{25}$: – 39.4 (*c* 0.508, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (dd, ^3J = 4.5 Hz, ^2J = 12.1 Hz, 1H), 3.61 (dd, ^3J = 8.2 Hz, ^2J = 12.1 Hz, 1H), 3.67 (minor diastereomer, dd, ^3J = 5.2 Hz, ^2J = 11.8 Hz, 1H), 3.05 (apparent t, ^3J = 5.6 Hz, 1H), 2.87 (minor diastereomer, dd, ^3J = 5.7 Hz, ^2J = 6.6 Hz, 1H), 1.81-1.71 (minor diastereomer, m, 2H), 1.62-1.44 (m, 2H), 1.02-0.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) major diastereomer: δ 63.96, 62.9, 60.4, 29.9, 21.8, 20.1 14.0, 9.3; minor diastereomer: δ 63.94, 63.3, 61.6, 30.0, 26.5, 20.0, 13.9, 8.9; FTIR (thin film) 3431, 2963, 2937, 2876, 1465, 1381, 1048, 908, 733 cm^{-1}; HRMS (*m/z*) calcd for $C_8H_{17}O_2$ $[M+H]^+$: 145.1229. Found 145.1227; Chiral GC (Lipodex G, 70 °C isocratic, 0.5 bar H_2) t_r 29.3 min (minor enantiomer, major diastereomer), t_r 32.0 min (major enantiomer, major diastereomer), t_r 36.1 min (major enantiomer, minor diastereomer), t_r 37.4 min (minor enantiomer, minor diastereomer). The absolute stereochemistry was assigned by analogy with **7a** and **7d**, and the relative stereochemistry was confirmed by NOESY and ^{13}C NMR experiments.

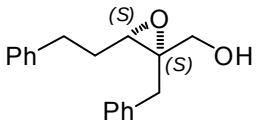


(2*R*,3*S*)-2-ethyl-3-propyloxirane-2-carbaldehyde (4b)



Chiral GC (BGB-177/BGB-15, 35 min at 70 °C, 8 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar H_2) t_r 19.6 min (minor enantiomer, minor diastereomer), t_r 21.4 min (major enantiomer, minor diastereomer), t_r 22.6 min (major enantiomer, major diastereomer), t_r 25.1 min (minor enantiomer, major diastereomer).

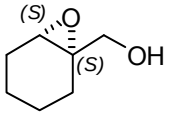
((2*S*,3*S*)-2-benzyl-3-phenethyloxiran-2-yl)methanol (7c)



Prepared according to the general procedure **A1** using (*E*)-2-benzyl-5-phenylpent-2-enal (E/Z >20:1, 0.25 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (20% Et_2O in pentane) afforded **7c** as a colourless oil (51.6 mg, 0.19 mmol, 77%, 90:10 dr, 99:1 er); $[\alpha]_D^{25}$: – 38.0 (*c* 0.548, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.15 (m, 10H), 3.59 (dd, ^3J = 4.2 Hz, ^2J = 12.3 Hz, 1H), 3.48 (dd, ^3J = 8.5 Hz, ^2J = 12.3 Hz, 1H), 3.19 (dd, ^3J = 5.2 Hz, ^3J = 7.5 Hz, 1H), 3.05 (minor diastereomer, d, ^2J = 14.1 Hz, 1H), 2.98 (d, ^2J = 14.8 Hz, 1H), 2.96-2.89 (m, 1H), 2.86-2.77 (m, 1H), 2.70 (d, ^2J = 14.8 Hz, 1H), 2.68-2.64 (minor diastereomer, m, 1H), 2.13-1.99 (m, 2H), 1.92-1.80 (minor diastereomer, m, 1H), 1.52 (dd,

^{3}J = 8.5 Hz, ^{3}J = 4.2 Hz, 1H, -O*H*); ^{13}C NMR (125 MHz, $CDCl_3$) major diastereomer: δ 141.1, 136.5, 129.3, 128.6, 128.54, 128.48, 126.7, 126.2, 63.7, 63.1, 60.0, 35.0, 33.0; minor diastereomer (not all peaks detected): 136.3, 129.8, 128.44, 128.41, 126.3, 62.5, 61.6, 34.9, 32.7, 29.9; FTIR (thin film) 3437, 3063, 3028, 2928, 1603, 1496, 1454, 1068, 1031, 908, 732, 700 cm^{-1}; HRMS (*m/z*) calcd for $C_{18}H_{20}O_2Na$ $[M+Na]^+$: 291.1356. Found 291.1353; Chiral HPLC: *Diastereomer separation:* Zorbax XDB/C18, methanol/water = 70:30, flow rate 1.0 mL/min, 29.2 MPa, 210 nm. *Upon separation, the major diastereomer was switched to a chiral column at 3.32 min till 3.42 min*: Kromasil - AmyCoat, methanol/water = 98:2, flow rate 1.0 mL/min, 12.6 MPa, 220 nm). Major diastereomer: t_r 6.8 min (major enantiomer), t_r 8.4 min (minor enantiomer). The absolute configuration was assigned by analogy with **7a** and **7d**.

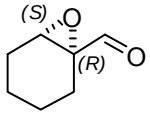
(1*S*,6*S*)-7-oxabicyclo[4.1.0]heptan-1-ylmethanol (7d).



Prepared according to the general procedure **A1** using commercial cyclohex-1-enecarbaldehyde (0.36 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (50% Et_2O in pentane) afforded **7d** as a colourless oil (32.2 mg, 0.25 mmol, 70%, 98.5:1.5 er); $[\alpha]_D^{25}$: – 22.6 (*c* 0.504, $CHCl_3$); Lit[14]: $[\alpha]_D^{25}$: – 22.8 (*c* 2.6, $CHCl_3$, 93% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (dd, ^{3}J = 3.0 Hz, ^{2}J = 12.2 Hz, 1H), 3.59 (dd, ^{3}J = 8.4 Hz, ^{2}J = 12.1 Hz, 1H), 3.26 (d, ^{3}J = 3.4 Hz, 1H), 2.01-1.95 (m, 1H), 1.90-1.64 (m, 4H), 1.54-1.41 (m, 2H), 1.34-1.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 64.5, 60.1, 55.8, 25.3, 24.4, 19.9 19.7; FTIR (thin film) 3417, 2938, 2872, 1435, 1032, 916, 731 cm^{-1}; HRMS (*m/z*) calcd for $C_7H_{13}O_2$ $[M+H]^+$: 129.0916. Found 129.0916. Chiral GC (BGB-177/BGB-15, 90 °C isocratic, 0.6 bar H_2) t_r 32.2 min (minor enantiomer), t_r 32.6 min (major enantiomer). The physical data are identical in all respects to those previously reported.[14]

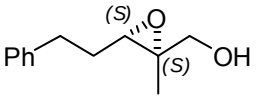
[14] Gao, Y.; Hanson, R. M.; Kluder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(1*R*,6*S*)-7-oxabicyclo[4.1.0]heptane-1-carbaldehyde (4d)



Chiral GC (BGB-177/BGB-15, 65 °C isocratic, 0.7 bar H_2) t_r 31.7 min (minor enantiomer), t_r 34.2 min (major enantiomer).

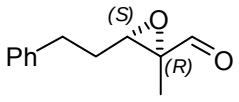
((2*S*,3*S*)-2-methyl-3-phenethyloxiran-2-yl)methanol (7e)



Prepared according to the general procedure **A1** using (*E*)-2-methyl-5-phenylpent-2-enal **3e** (E/Z = 20:1, 0.25 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (50% Et_2O in pentane) afforded **7e** as a colourless oil (36.2 mg, 0.19 mmol, 75%, 95:5 dr, 98.5:1.5 er). $[\alpha]_D^{25}$: – 27.6 (*c* 0.521, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.28 (m, 2H), 7.22-7.19 (m, 3H), 3.63 (dd, ^3J = 3.9 Hz, ^2J = 12.3 Hz, 1H), 3.52 (dd, ^3J = 8.8 Hz, ^2J = 12.3 Hz, 1H), 3.48 (minor diastereomer, dd, ^3J = 5.8 Hz, ^2J = 11.7 Hz, 1H), 3.38 (minor diastereomer, dd, ^3J = 6.2 Hz, ^2J = 11.7 Hz, 1H), 3.09 (t, ^3J = 6.2 Hz, 1H), 2.89-2.83 (m, 1H), 2.76-2.70 (m, 1H), 2.06-1.94 (m, 1H), 1.88-1.81 (m, 1H), 1.65 (br s, 1H), 1.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) major diastereomer: δ 141.2, 128.49, 128.47, 126.2, 65.3, 61.2, 59.6, 32.7, 30.1, 14.1; minor diastereomer (not all signals detected): 142.4, 128.75, 128.6, 126.3, 64.3, 63.7, 20.1; FTIR (thin film) 3427, 3027, 2928, 2861, 1604, 1496, 1454, 1073, 1039, 908, 861, 749, 700 cm^{-1}; HRMS (*m/z*) calcd for $C_{12}H_{16}O_2$ $[M]^+$: 192.1150. Found 192.1151; Chiral HPLC: *Diastereomer separation:* Zorbax XDB/C18, acetonitrile/water = 25:75, flow rate 1.0 mL/min, 22.2 MPa, 210 nm. *Upon separation, each diastereomer was switched to a chiral column at 5.57 min till 5.62 min for the minor diastereomer and 6.06 min till 6.11 min for the major diastereomer:* Chiralpak AS-RH, acetonitrile/water = 30:70, flow rate 1.0 mL/min, 10.1 MPa, 210 nm). Minor diastereomer (**7e**): t_r 10.9 min (major enantiomer), t_r 11.6 min (minor enantiomer). Major diastereomer (**7e'**): t_r 11.5 min (minor enantiomer), t_r 12.21 min (major

enantiomer). The absolute stereochemistry was assigned by analogy with **7a** and **7d**. The minor (2*S*, 3*R*) diastereomer **7e'** has been described.[15]

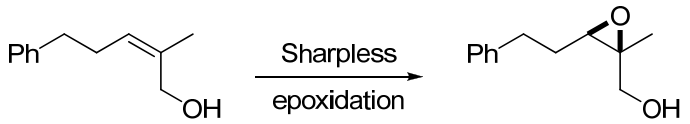
(2*R*,3*S*)-2-methyl-3-phenethyloxirane-2-carbaldehyde (4e)



Chiral GC (BGB-177/BGB-15, 60 min at 120 °C, 10 °C/min until 230 °C, 5 min at 230 °C, 0.7 bar H_2) t_r 40.0 min (major enantiomer, minor diastereomer), t_r 40.6 min (minor enantiomer, minor diastereomer), t_r 45.1 min (major enantiomer, major diastereomer), t_r 45.6 min (minor enantiomer, major diastereomer).

Preparation of an authentic sample for the determination of the absolute stereochemistry of 7e':

((2*S*,3*R*)-2-methyl-3-phenethyloxiran-2-yl)methanol (7e')[15]



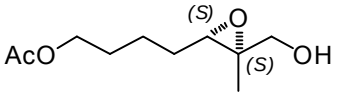
SI-18 **7e'**

A solution of (+)-diisopropyl tartrate (13.2 µL, 0.0625 mmol, 0.22 equiv) in dichloromethane (1 mL) with 4Å molecular sieves (16 mg) was cooled to -20 °C. $Ti(O^iPr)_4$ (4.6 µL, 0.0129 mmol, 0.16 equiv) was added, followed by tert-butylhydroperoxide (77.5 µL, 5.5 M in decanes, 0.426 mmol, 1.5 equiv). A solution of **SI-18** (50 mg, 0.28 mmol, 1 equiv) in dichloromethane (0.2 mL) was added. The reaction mixture was stirred at – 20 °C for 16 h, warmed up to room temperature at treated with H_2O (0.3 mL) and 30% NaOH (0.1 mL). After stirring the biphasic solution for 1h at room temperature, the mixture was extracted with dichloromethane three times, dried over Na_2SO_4, filtered and concentrated. Flash

[15] Prévost, M.; Woerpel, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 14182.

column chromatography elutiong with 35% diethyl ether in pentane afforded **7e'** as a colourless oil (43.6 mg, 0.23 mmol, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.28 (m, 2H), 7.23-7.19 (m, 3H), 3.47 (d, ^2J = 12.0 Hz, 1H), 3.38 (d, ^2J = 12.0 Hz, 1H), 2.89-2.84 (m, 2H), 2.75-2.67 (m, 1H), 2.05-1.98 (m, 1H), 1.87-1.81 (m, 1H), 1.60 (br s, 1H), 1.32 (s, 3H). Chiral HPLC: Chiralpak AS-RH, acetonitrile/water = 30:70, flow rate 1.0 mL/min, 10.1 MPa, 210 nm). t_r 5.55 min (major enantiomer), t_r 6.26 min (minor enantiomer). *Since no diastereomer separation was required in this case, the sample was not pre-eluted on an achiral HPLC column.*

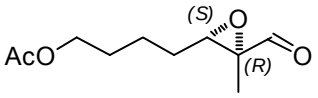
4-((2*S*,3*S*)-3-(hydroxymethyl)-3-methyloxiran-2-yl)butyl acetate (7f)



Prepared according to the general procedure **A1** using (*E*)-6-methyl-7-oxohept-5-enyl acetate **3f** (E/Z >20:1, 0.25 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (50% Et_2O in pentane) afforded **7f** as a colourless oil (33.5 mg, 0.160 mmol, 66%, 97:3 er); $[\alpha]_D^{25}$: – 17.7 (*c* 0.362, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.09 (apparent t, ^3J = 6.6 Hz, 2H), 3.68 (apparent d, ^2J = 11.9 Hz, 1H), 3.58 (dd, ^3J = 6.9 Hz, ^2J = 12.1 Hz, 1H), 3.04 (apparent t, ^3J = 5.6 Hz, 1H), 2.85 (minor diastereomer, apparent t, ^3J = 6.1 Hz, 1H), 2.06 (s, 3H), 2.01 (br s, 1H), 1.74-1.48 (m, 6H), 1.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) major diastereomer: δ 171.3, 65.3, 64.2, 60.9, 59.9, 28.4, 27.8, 23.0, 21.0, 14.2; minor diastereomer (not all peaks detected): 64.6, 64.2, 63.9, 27.7, 23.2, 20.2; FTIR (thin film) 3447, 2955, 2868, 2250, 17365, 1458, 1433, 1387, 1367, 1240, 1035, 911, 868, 729 cm^{-1}; HRMS (*m/z*) calcd for $C_{10}H_{18}O_4Na$ $[M+Na]^+$: 225.1097. Found 225.1099; Chiral GC (Lipodex G, 60 min at 120 °C, 15 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_2): t_r 37.9 min (minor enantiomer, major diastereomer), t_r 39.1 min (major enantiomer, major diastereomer), t_r 41.0 min (major enantiomer, minor diastereomer), t_r 42.2 min (minor

enantiomer, minor diastereomer). The absolute configuration was assigned by analogy with **7a** and **7d**.

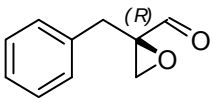
4-((2*S*,3*R*)-3-formyl-3-methyloxiran-2-yl)butyl acetate (4f)



Chiral GC (BGB-174/BGB-1701, 40 min at 155 °C, 10 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_2): t_r 22.1 min (major enantiomer, minor diastereomer), t_r 23.8 min (minor enantiomer, minor diastereomer), t_r 31.6 min (minor enantiomer, major diastereomer), t_r 32.5 min (major enantiomer, major diastereomer).

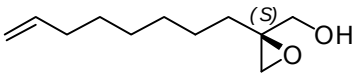
Enantioenriched products 8a-8d and 6a-6d

(*R*)-2-benzyloxirane-2-carbaldehyde (6a)



Prepared according to the general procedure **B** using 2-benzylacrylaldehyde **5a** (0.25 mmol). Purification by flash chromatography (20% Et_2O in pentane) afforded **6a** as a colourless oil (31.7 mg, 0.195 mmol, 78%, 99:1 er); $[\alpha]_D^{25}$: + 47.0 (*c* 0.502, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 7.31-7.20 (m, 5H), 3.21 (d, ^3J = 1.4 Hz, 2H), 3.00 (d, ^3J = 4.6 Hz, 1H), 2.85 (d, ^3J = 4.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.6, 134.8, 129.9, 128.4, 127.0, 61.4, 48.9, 33.1; FTIR (thin film) 3064, 3032, 2826, 1726, 1497, 1454, 1077, 1010, 907, 730 cm^{-1}; HRMS (*m/z*) calcd for $C_{10}H_{10}O_2$ $[M]^+$: 162.0681. Found 162.0682; Chiral GC (BGB-178/BGB-15, 35 min at 115 °C, 8 °C/min until 220 °C, 0.6 bar H_2) t_r 26.0 min (major enantiomer), t_r 27.0 min (minor enantiomer). The physical data are identical in all respects to those previously reported.[12] The absolute stereochemistry was assigned by analogy with **8c**.

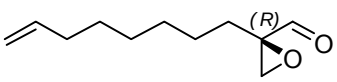
(*S*)-(2-(oct-7-enyl)oxiran-2-yl)methanol (8b)



Prepared according to the general procedure **B** using 2-methylenedec-9-enal **5b** (0.25 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (30% Et_2O in pentane) afforded **8b** as a colourless oil (33.9 mg, 0.184 mmol, 74%, 98.5:1.5 er); $[\alpha]_D^{25}$: – 10.8 (*c* 0.574, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.80 (ddt, ^3J = 17.4 Hz, ^3J = 10.2 Hz, ^3J = 6.7 Hz), 5.03-4.99 (m, 2H), 3.77 (dd, ^3J = 4.2 Hz, ^2J = 12.2, 1H), 3.64 (dd, ^3J = 8.6 Hz, ^2J = 12.2 Hz, 1H), 2.88 (d, ^3J = 4.7 Hz, 1H), 2.66 (d, ^3J = 4.7 Hz, 1H), 2.07-2.00 (m, 2H), 1.82-1.26 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.0, 114.3, 62.8, 59.7, 49.8, 33.7, 32.0, 29.6, 28.9,

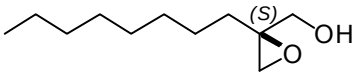
28.8, 24.6; FTIR (thin film) 3429, 3077, 2928, 2857, 2249, 1641, 1464, 1415, 1046, 908, 730 cm^{-1}; HRMS (*m/z*) calcd for $C_{11}H_{21}O_2$ $[M+H]^+$: 185.1542. Found 185.1540; Chiral GC (Hydrodex-β TBDAc, 25 min at 150 °C, 10 °C/min until 220 °C, 0.5 bar H_2) t_r 14.5 min (major enantiomer), t_r 15.4 min (minor enantiomer). The absolute stereochemistry was assigned by analogy with **8c**.

(*R*)-2-(oct-7-enyl)oxirane-2-carbaldehyde (6b)



Chiral GC (BGB-174/BGB-1701, 130 °C isocratic, then baked out at 8 °C/min until 220 °C, 5 min at 220 °C, 0.5 bar H_2): t_r 27.8 min (major enantiomer), t_r 29.3 min (minor enantiomer).

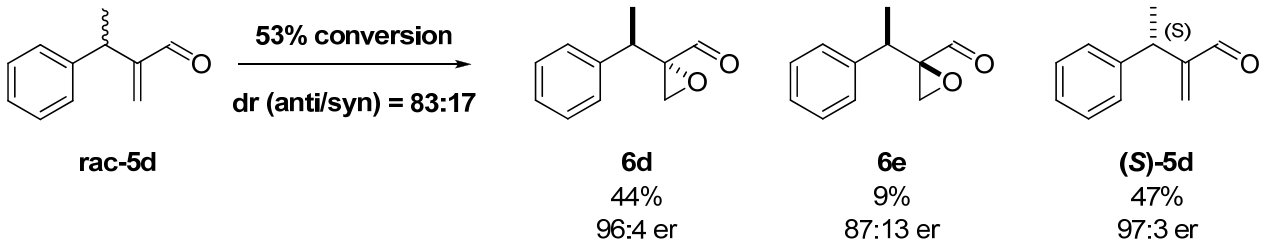
(*S*)-(2-octyloxiran-2-yl)methanol (8c)



Prepared according to the general procedure **B** using 2-methylenedecanal **5c** (0.25 mmol) followed by reduction with $NaBH_4$. Purification by flash chromatography (50% Et_2O in pentane) afforded **8c** as a colourless oil (36.4 mg, 0.196 mmol, 78%, 99:1 er); $[\alpha]_D^{25}$: – 14.8 (*c* 0.595, $CHCl_3$); Lit[16]: $[\alpha]_D^{20}$: – 11.7 (*c* 1.0, $CHCl_3$, 72% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (dd, ^3J = 3.8 Hz, ^2J = 12.1, 1H), 3.64 (dd, ^3J = 8.4 Hz, ^2J = 12.1 Hz, 1H), 2.89 (d, ^3J = 4.7 Hz, 1H), 2.67 (d, ^3J = 4.7 Hz, 1H), 1.80-1.75 (m, 1H), 1.68 (br s, 1H), 1.53-1.47 (m, 1H), 1.39-1.23 (m, 12H), 0.88 (t, ^3J = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 62.7, 59.8, 49.8, 32.0, 31.8, 29.7, 29.2, 24.6, 22.6, 14.1; FTIR (thin film) 3421, 2927, 2857, 2251, 1466, 1364, 1197, 1053, 908, 808, 731 cm^{-1}; HRMS (*m/z*) calcd for $C_{11}H_{23}O_2$ $[M+H]^+$: 187.1698. Found 187.1699; Chiral GC (BGB-177/BGB-15, 140 °C isocratic, then baked out at 220 °C, 0.6 bar

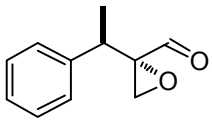
[16] Li, X.; Borhan, B.*J. Am. Chem. Soc.* **2008**, *130*, 16126.

H_2) t_r 19.75 min (major enantiomer), t_r 20.8 min (minor enantiomer). The physical data are identical in all respects to those previously reported.[16]



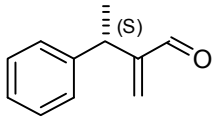
rac-5d | **6d** 44% 96:4 er | **6e** 9% 87:13 er | **(*S*)-5d** 47% 97:3 er

(*S*)-2-((*R*)-1-phenylethyl)oxirane-2-carbaldehyde (6d)



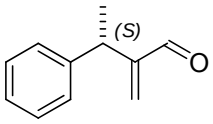
Prepared according to the general procedure **B** using racemic 2-methylene-3-phenylbutanal **rac-5d** (0.25 mmol). Analysis of the crude reaction mixture after 24 h showed 53% conversion of the starting material and two diastereomers **6d** and **6e** with dr = 83:17. Purification by flash chromatography (5% EtOAc in pentane) afforded **6d** as a colourless oil (13.0 mg, 0.074 mmol, 30%, lowered yield due to incomplete separation from (*S*)-**5d,** 96:4 er). $[\alpha]_D^{25}$: + 41.5 (*c* 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (s, 1H), 7.31-7.28 (m, 2H), 7.26-7.21 (m, 3H), 3.68 (q, ^3J = 7.2 Hz, 1H), 2.87 (d, ^3J = 4.6 Hz, 1H), 2.58 (d, ^3J = 4.6 Hz, 1H), 1.38 (d, ^3J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.0, 140.4, 128.5, 128.2, 127.1, 64.6, 48.9, 35.8, 16.2; FTIR (thin film) 30314, 2979, 2940, 2821, 2255, 1733, 1496, 1454, 907, 865, 729 cm^{-1}; HRMS (*m/z*) calcd for $C_{11}H_{12}O_2$ $[M]^+$: 176.0837. Found 176.0839; Chiral GC (G-BP, 40 min at 110 °C, 14 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar H_2): t_r 25.3 min (minor enantiomer, major diastereomer **6d**), t_r 27.0 min (major enantiomer, major diastereomer **6d**), t_r 34.0 min (minor enantiomer, minor diastereomer **6e**), t_r 36.3 min (major enantiomer, minor diastereomer **6e**). The physical data are identical in all respects to those previously reported.[12]

(*S*)-2-methylene-3-phenylbutanal (*S*)-5d



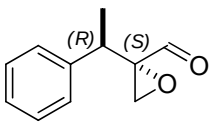
The physical data of this compound are identical in all respects to **rac-5d**. This compound was isolated by flash chromatography (5% EtOAc in pentane) as a colourless oil (8.79 mg, 0.055 mmol, 22%, lowered yield due to incomplete separation from **6d**, 97:3 er); $[\alpha]_D^{25}$: + 48.6 (*c* 0.44, $CHCl_3$), Lit (*R* enantiomer)[17]: $[\alpha]_D^{25}$: – 38.7 (*c* 1.01, $CHCl_3$); Chiral GC (G-BP, 40 min at 110 °C, 14 °C/min until 220 °C, 5 min at 220 °C, 0.6 bar H_2) t_r 13.9 min (major enantiomer), t_r 14.4 min (minor enantiomer).

Assignment of the absolute configuration:



(*S*)-5d

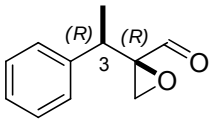
(S)-5d: The absolute configuration was established by comparison of the optical rotation with the literature value.[17]



6d

6d: The relative *anti*-configuration was assigned by comparison of the chemical shifts in ^1H and ^{13}C NMR spectra with the literature values.[12] The absolute configuration was assigned based on the configuration of the recovered enantioenriched starting material (*S*)-**5d**.

[17] Yoo, K. S.; Park, C. P.; Yoon, C. H.; Sakaguchi, S.; O'Neill, J.; Jung, K. W. *Org. Lett.*, **2007**, 9, 3933.



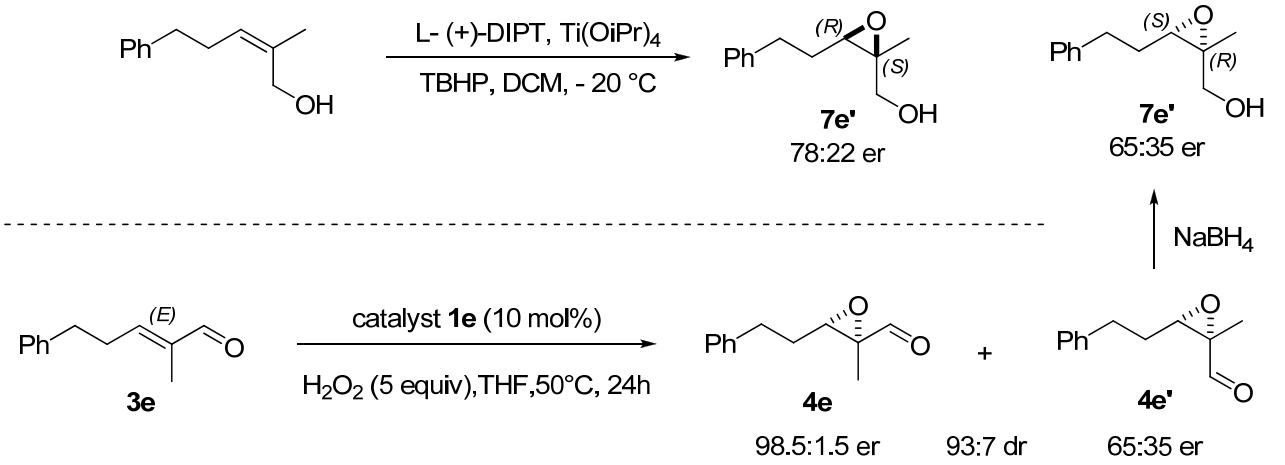
6e

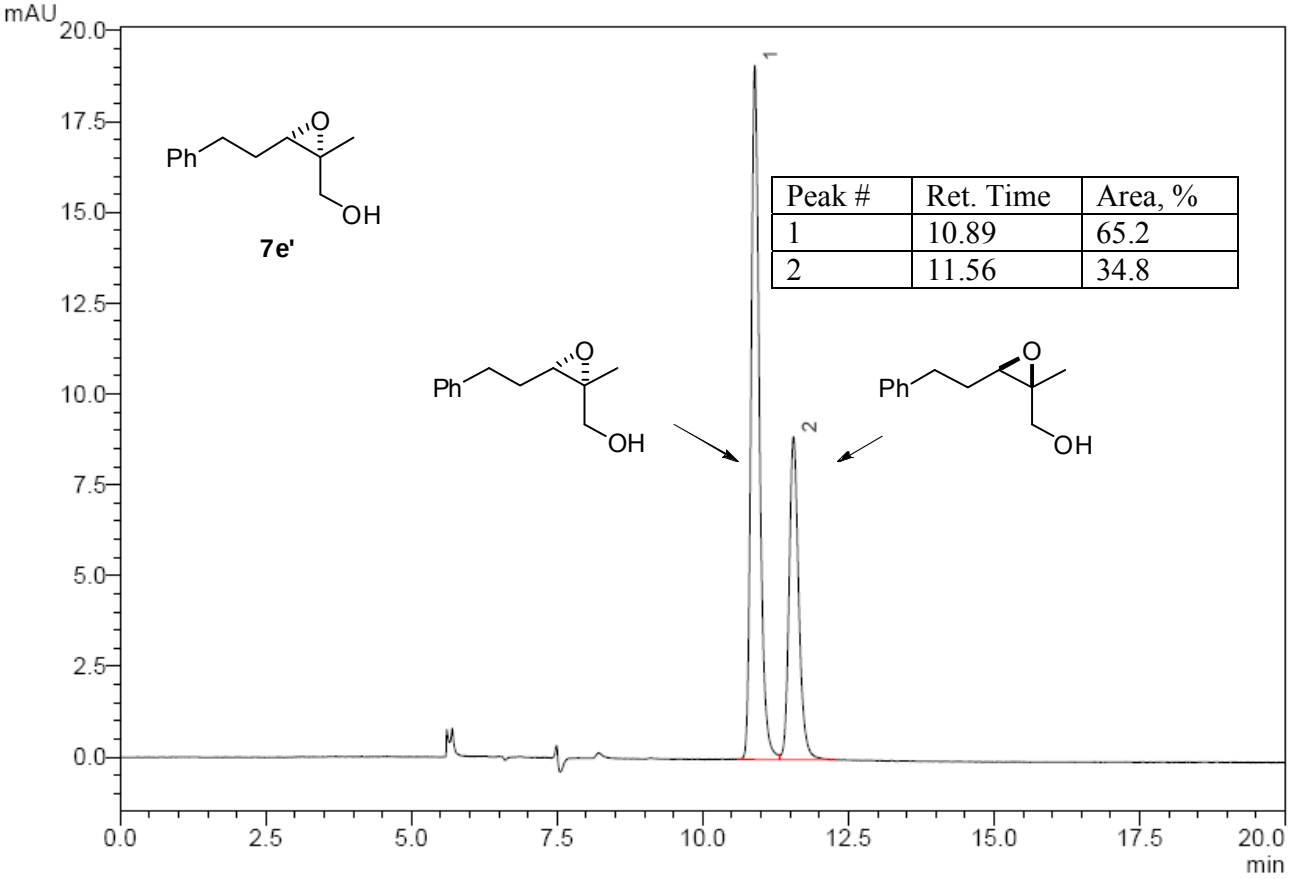
6e: The relative *syn*-configuration was assigned by comparison of the chemical shifts in ^{1}H and ^{13}C NMR spectra with the literature values.[12] The absolute configuration was *tentatively* assigned based on the observed dr and er values of all components of the reaction, such that the stoichiometry of the (*R*) and (*S*) enantiomers at C-3 is balanced. GC and NMR analyses of the crude reaction mixture indicated that (*S*)-**5d**, **6d** and **6e** were the only components of the reaction.

Mechanistic studies

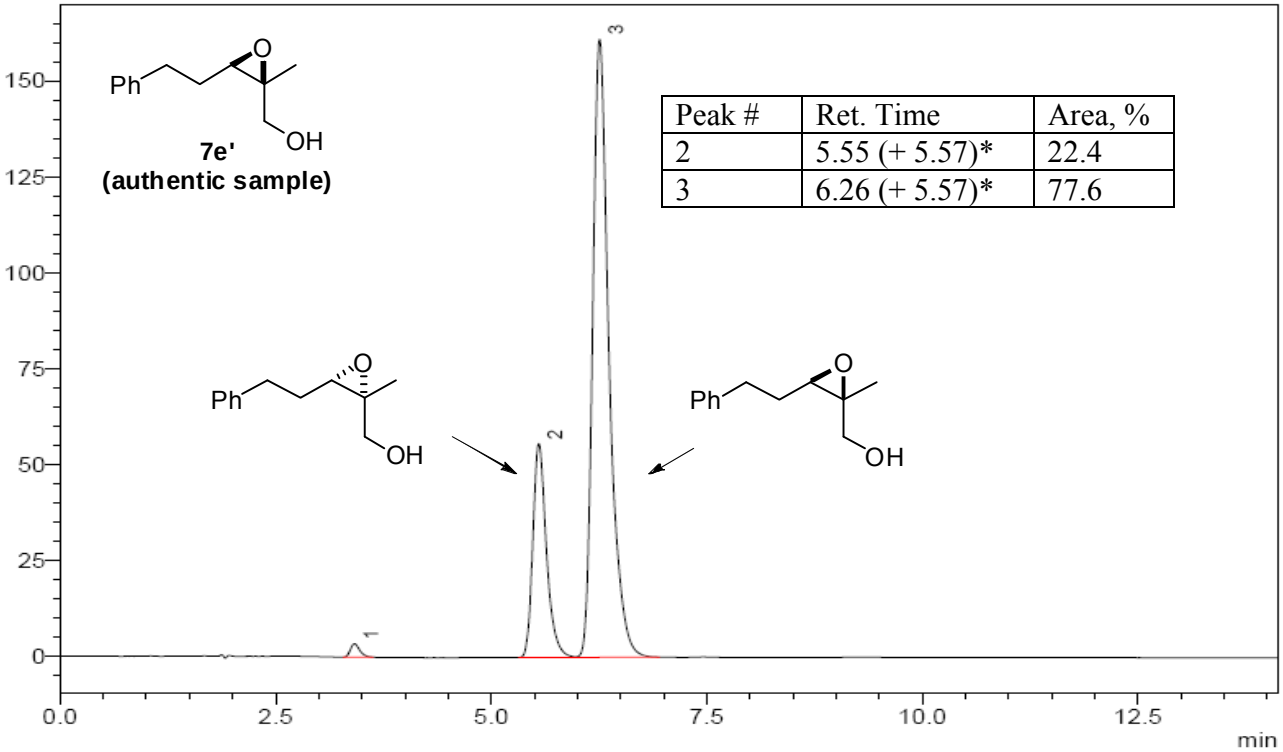
1. Absolute configuration of the minor diastereomer

To determine the absolute configuration of the minor diastereomer, we prepared an authentic sample of the (2S, 3R) epoxide **7e'** using Sharpless epoxidation, and compared its chiral GC trace to the minor diastereomer formed in the reaction of enal **3e** after reduction.





Peak #	Ret. Time	Area, %
1	10.89	65.2
2	11.56	34.8



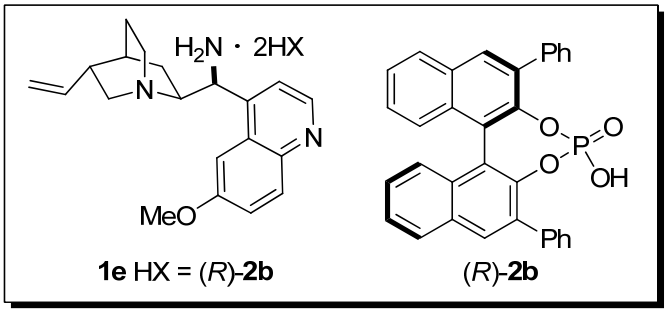
Peak #	Ret. Time	Area, %
2	5.55 (+ 5.57)*	22.4
3	6.26 (+ 5.57)*	77.6

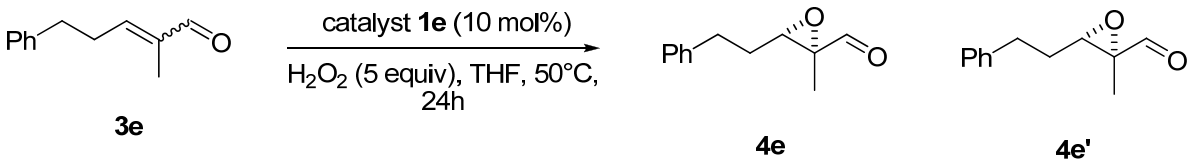
* The minor diastereomer **7e'** was pre-eluted on an achiral column for 5.57 min to separate diastereomers before the switch to the chiral column, while the authentic sample **7e'** was injected directly on the chiral column. Hence the retention times differ by approximately 5.57 min. Column type, solvent system and all other parameters were otherwise identical (see S-18).

2. Epoxidation of the (*Z*)-enal

Submitting the enal (*Z*)-**3e** to the reaction conditions, we found that the epoxidation of (*Z*)-**3e** proceeds with a slightly lower rate than that of (*E*)-**3e** (Table 3, entries 2 and 3), and that the starting material is partially isomerized under the reaction conditions (entry 3). It appears that Z→E isomerization is in direct competition with epoxidation, resulting in parallel reactions of both E and Z isomers. As a result, the overall reaction rate and selectivity is slightly reduced, though some degree of diastereoconvergence is observed.

Table 3. Comparison of E and Z enals in the enantioselective epoxidation



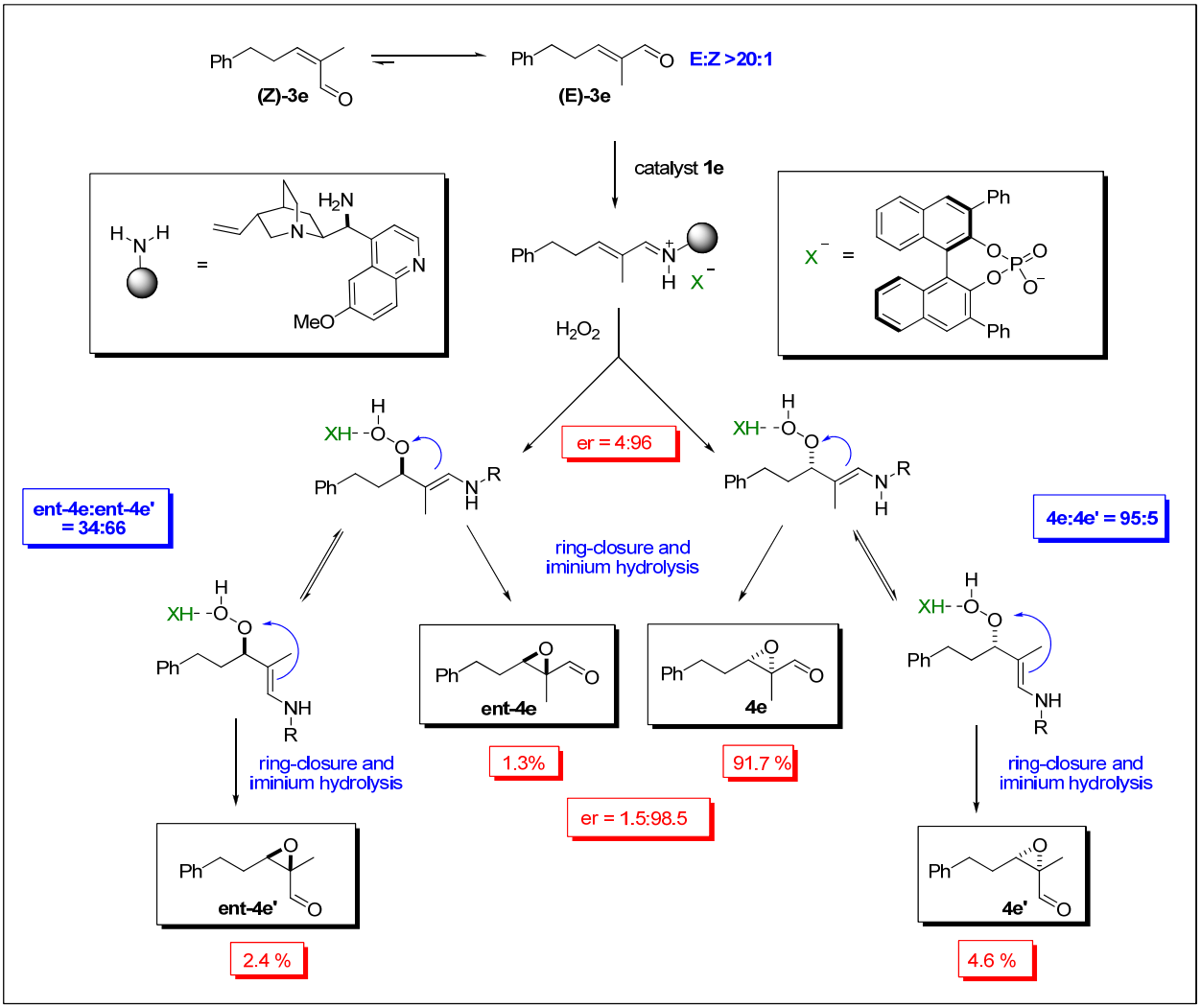


entry	E:Z of **3e**	H_2O_2	conversion	dr	er (**4e**)	er (**4e'**)	E:Z of remaining **3e**
1	>95:5	none	0%	-	-	-	>95:5
2	>95:5	5 equiv	93.5%	95:5	98.5:1.5	65:35	>95:5
3	<5:>95	none	0%	-	-	-	>95:5
4	5:95	5 equiv	85%	76:24	85:15	14:86	76:24

3. Proposed mechanism

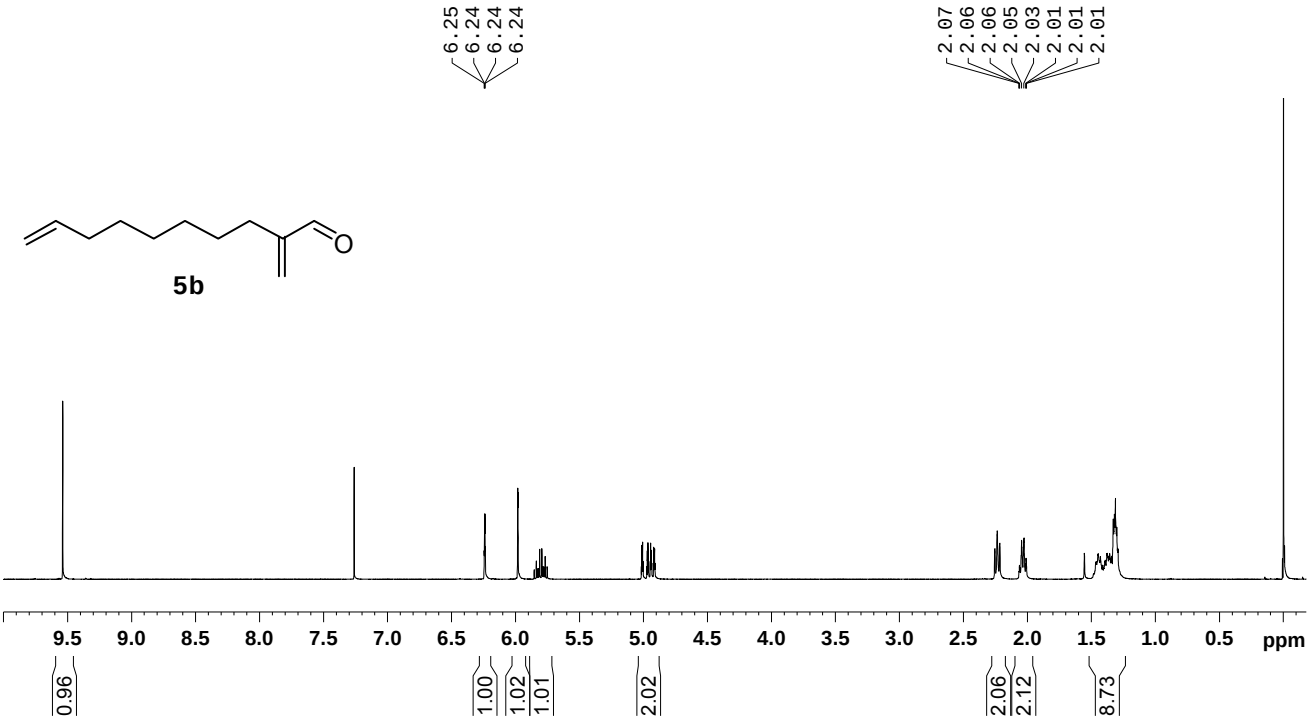
We monitored the epoxidation of (*E*)-**3e** by ^{1}H NMR and observed no traces of E→Z isomerisation under the reaction conditions with or without the peroxide reagent (Table 3, entries 1-2), suggesting that

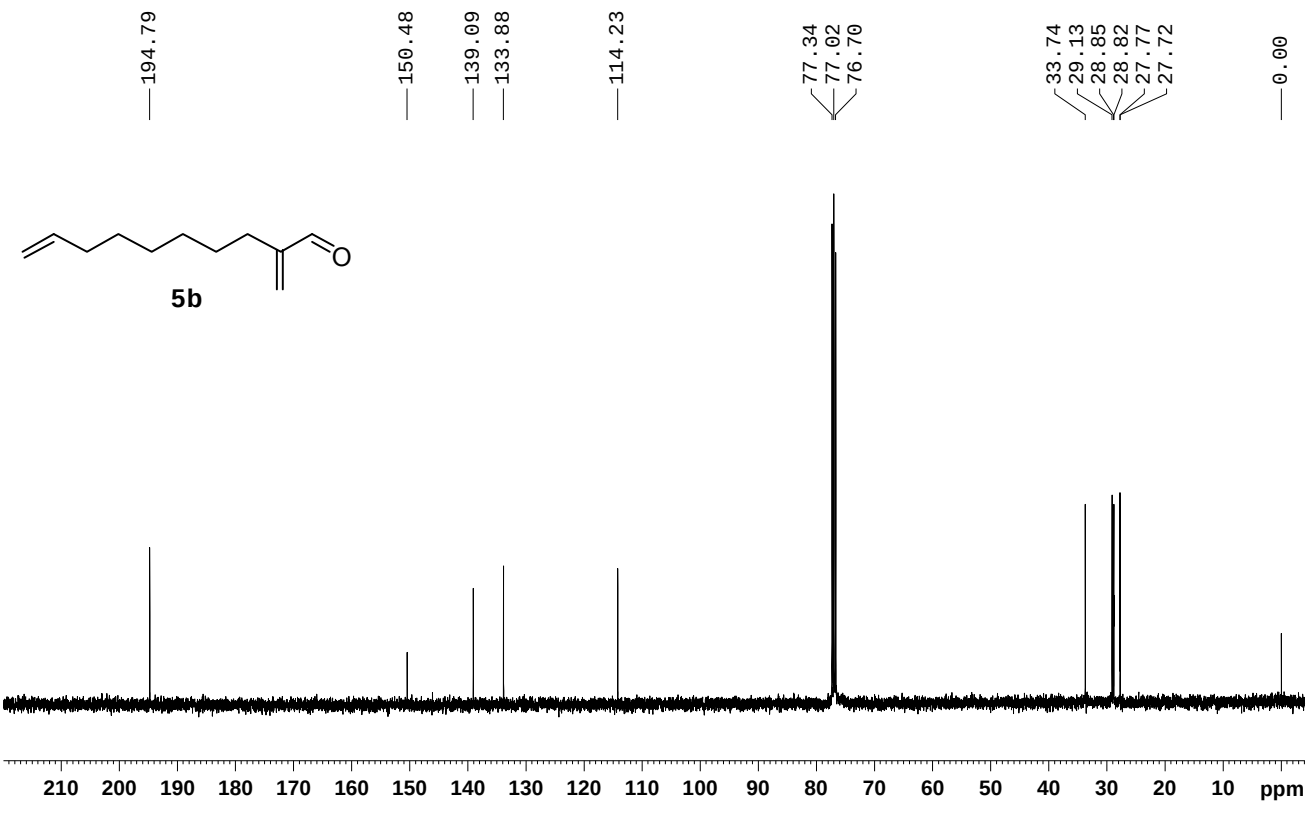
the origin of cis/trans epoxide formation (products **4e** and **4e'**) lies in the rotation of the hydroperoxide adduct (Wright, P.; Abbot, J. *Int. J. Chem. Kinetics* **1993**, *25*, 901.) Based on these results, we propose a mechanistic scheme outlined below. Chiral GC analysis of the crude reaction mixture provided the distribution of the four epoxide isomers formed in the reaction, and suggests a 96:4 er of the initial hydroperoxidation. Rotation of the two initial hydroperoxide adducts results in four different diastereomers which presumably undergo ring-closure at different rates, resulting in an overall enantiomeric enrichment of the major diastereomer **4e** to 98.5:1.5 er.

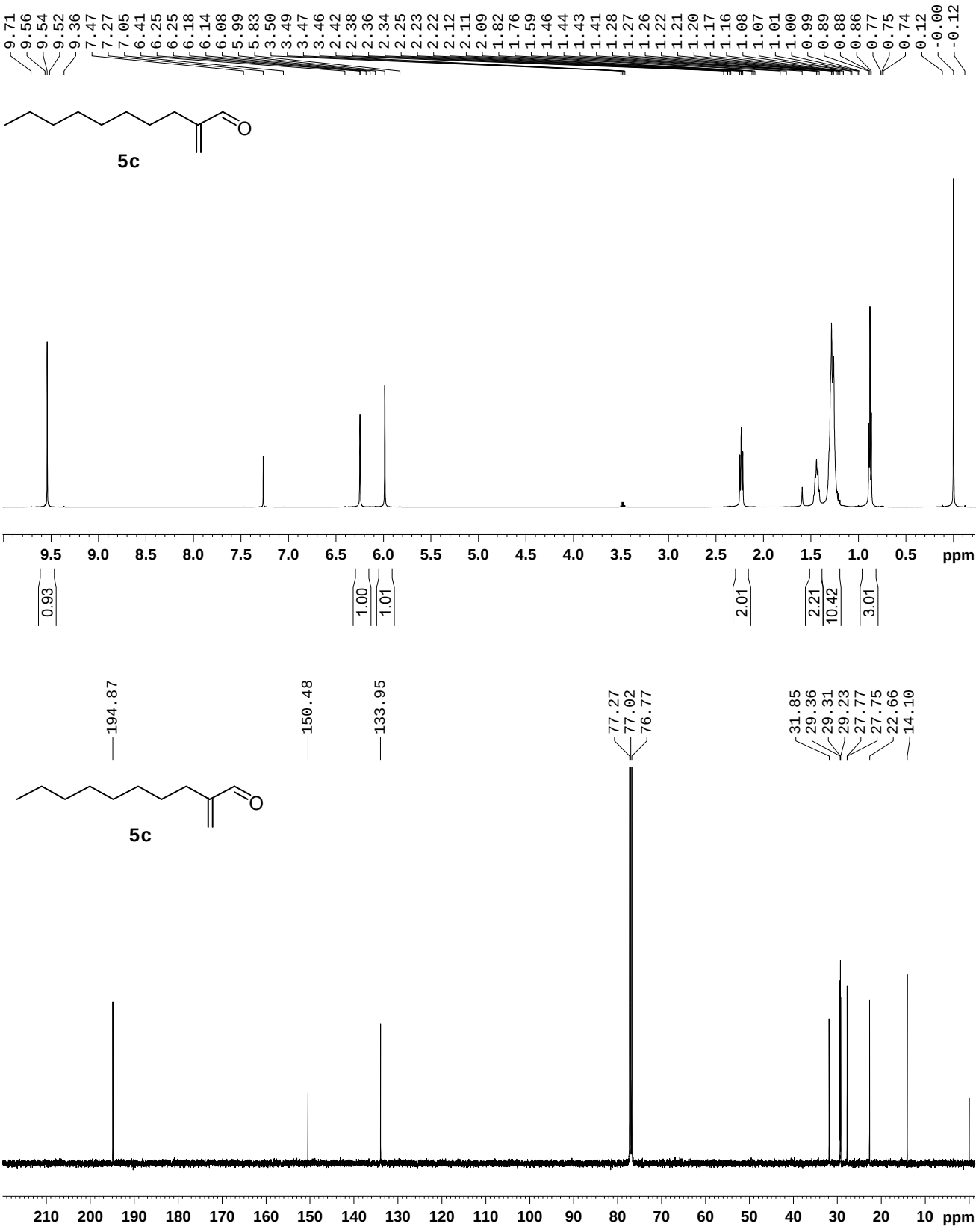


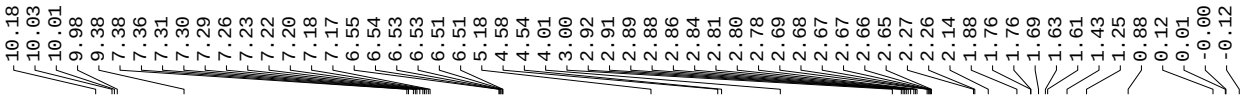
Epoxidation of (*Z*)-enals appears to follow a more complicated pathway which involves Z→E isomerisation of the starting material and the concurrent epoxidation of both E and Z isomers.

Copies of NMR Spectra






9.71 9.56 9.54 9.52 9.36 7.47 7.27 7.05 6.41 6.25 6.18 6.14 6.08 5.99 5.83 3.50 3.49 3.47 3.46 2.42 2.38 2.36 2.34 2.25 2.23 2.22 2.12 2.11 2.09 1.82 1.76 1.59 1.46 1.44 1.43 1.41 1.28 1.27 1.26 1.22 1.21 1.20 1.17 1.16 1.08 1.07 1.01 1.00 0.99 0.89 0.88 0.86 0.77 0.75 0.74 0.12 -0.00 -0.12
O
5c
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.93 1.00 1.01 2.01 2.21 10.42 3.01
194.87 150.48 133.95 77.27 77.02 76.77 31.85 29.36 29.31 29.23 27.77 27.75 22.66 14.10
O
5c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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10.01
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7.38
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7.31
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7.29
7.26
7.23
7.22
7.20
7.18
7.17
6.55
6.54
6.53
6.53
6.51
6.51
5.18
4.58
4.54
4.01
3.00
2.92
2.91
2.89
2.88
2.86
2.84
2.81
2.80
2.78
2.69
2.68
2.67
2.67
2.66
2.65
2.27
2.26
2.14
1.88
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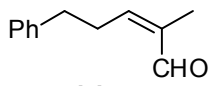
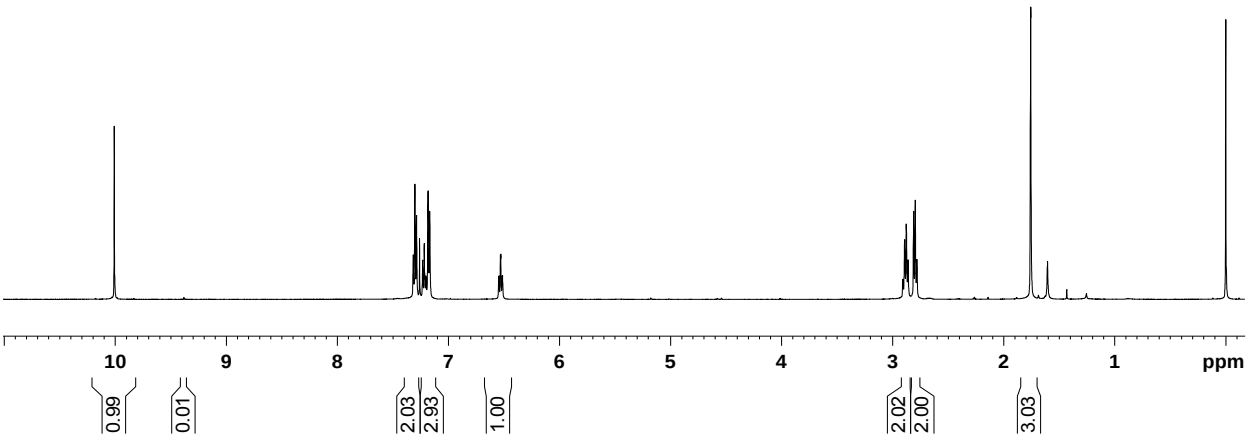
1.63
1.61
1.43
1.25
0.88
0.12
0.01
-0.00
-0.12


Ph
CHO

(Z)-3e


10
9
8
7
6
5
4
3
2
1
ppm
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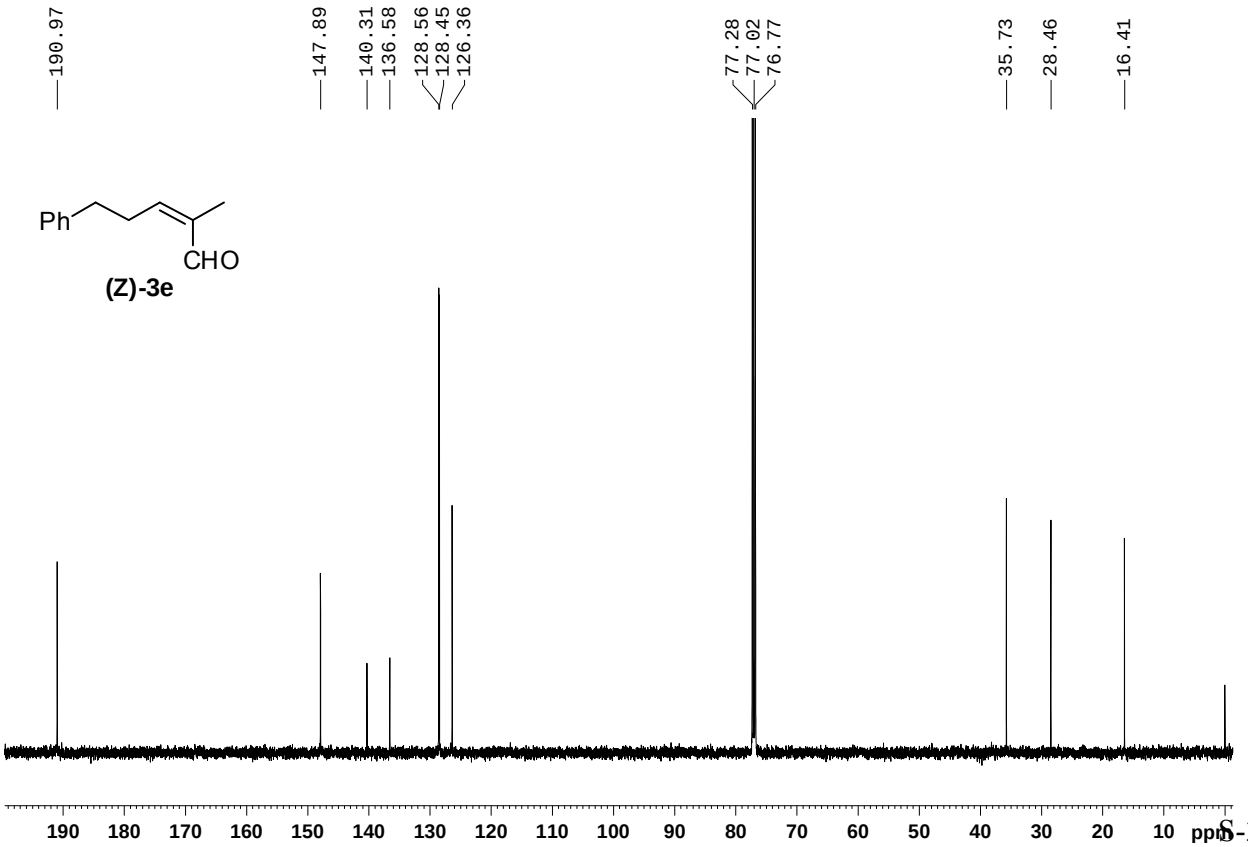
0.01
2.03
2.93
1.00
2.02
2.00
3.03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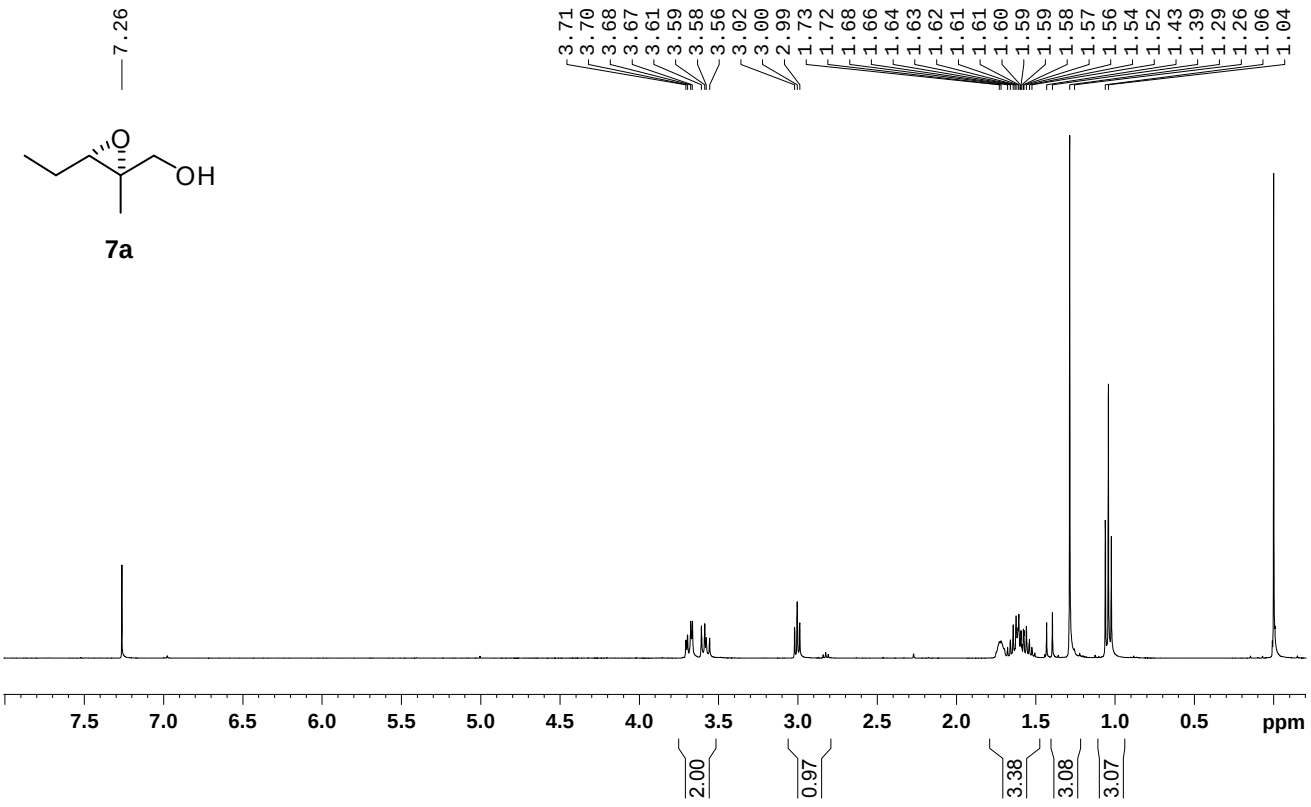
147.89
140.31
136.58
128.56
128.45
126.36
77.28
77.02
76.77
35.73
28.46
16.41
Ph
CHO
(Z)-3e
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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3.68
3.67
3.61
3.59
3.58
3.56
3.02
3.00
2.99
1.73
1.72
1.68
1.66
1.64
1.63
1.62
1.61
1.61
1.60
1.59
1.59
1.58
1.57
1.56
1.54
1.52
1.43
1.39
1.29
1.26
1.06
1.04
O
OH
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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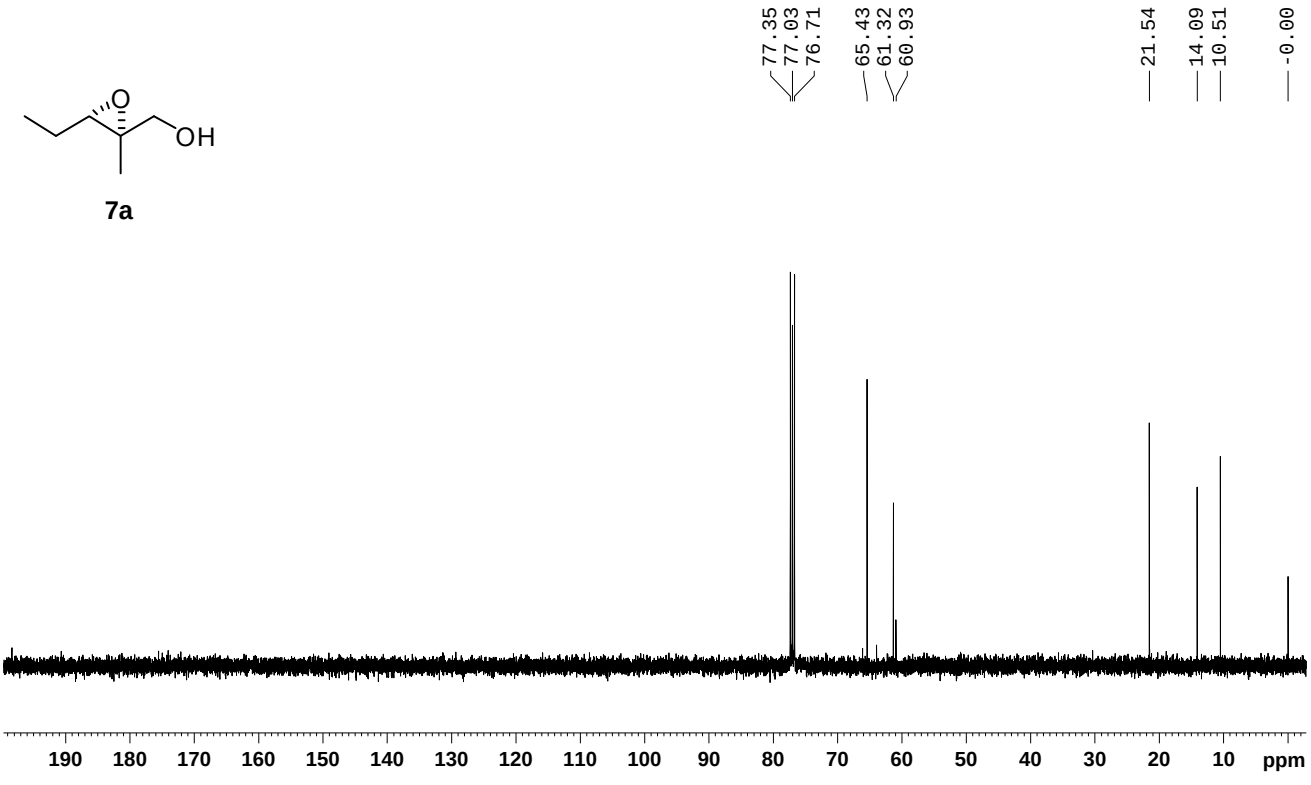
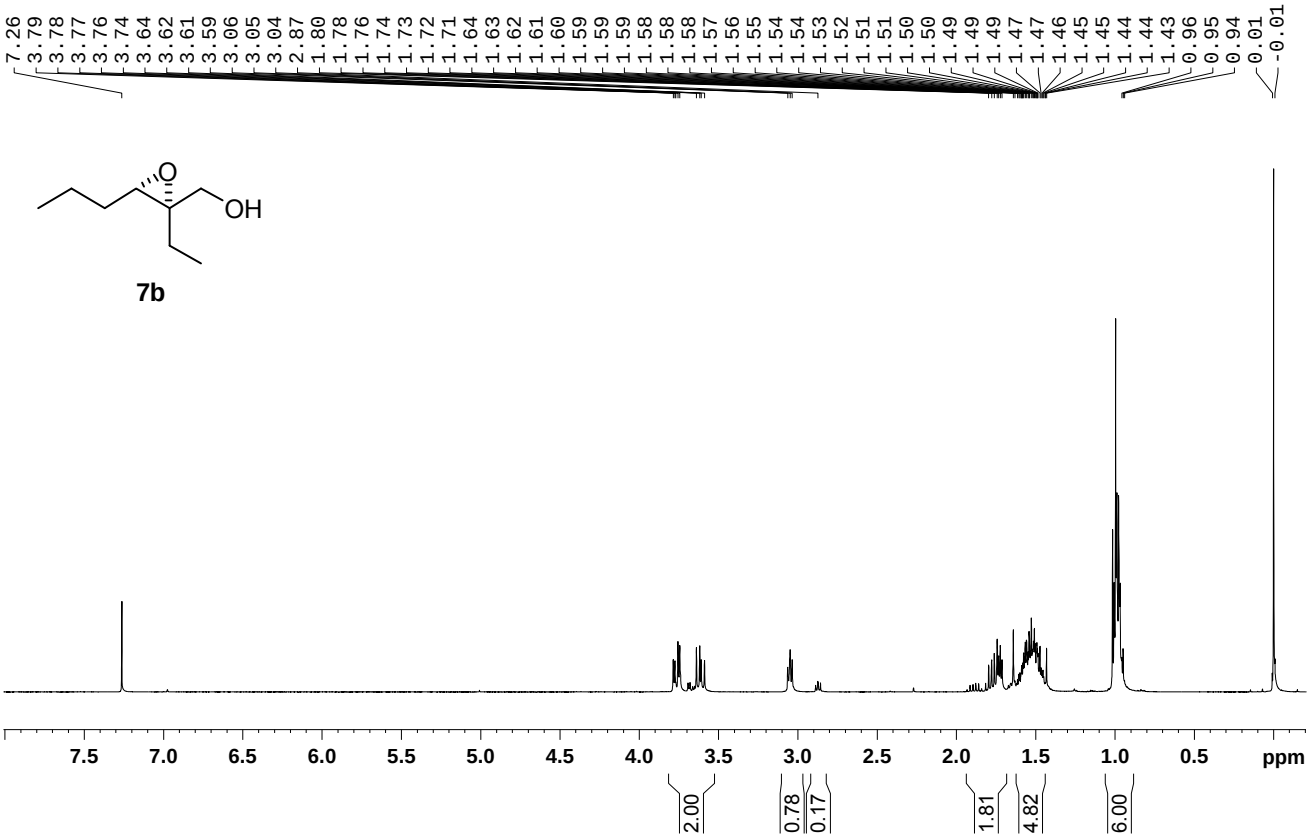
1.5
1.0
0.5
ppm
2.00
0.97
3.38
3.08
3.07

7a


77.35
77.03
76.71
65.43
61.32
60.93
21.54
14.09
10.51
-0.00
O
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

7a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3.74
3.64
3.62
3.61
3.59
3.06
3.05
3.04
2.87
1.80
1.78
1.76
1.74
1.73
1.72
1.71
1.64
1.63
1.62
1.61
1.60
1.59
1.59
1.59
1.58
1.58
1.58
1.57
1.56
1.55
1.54
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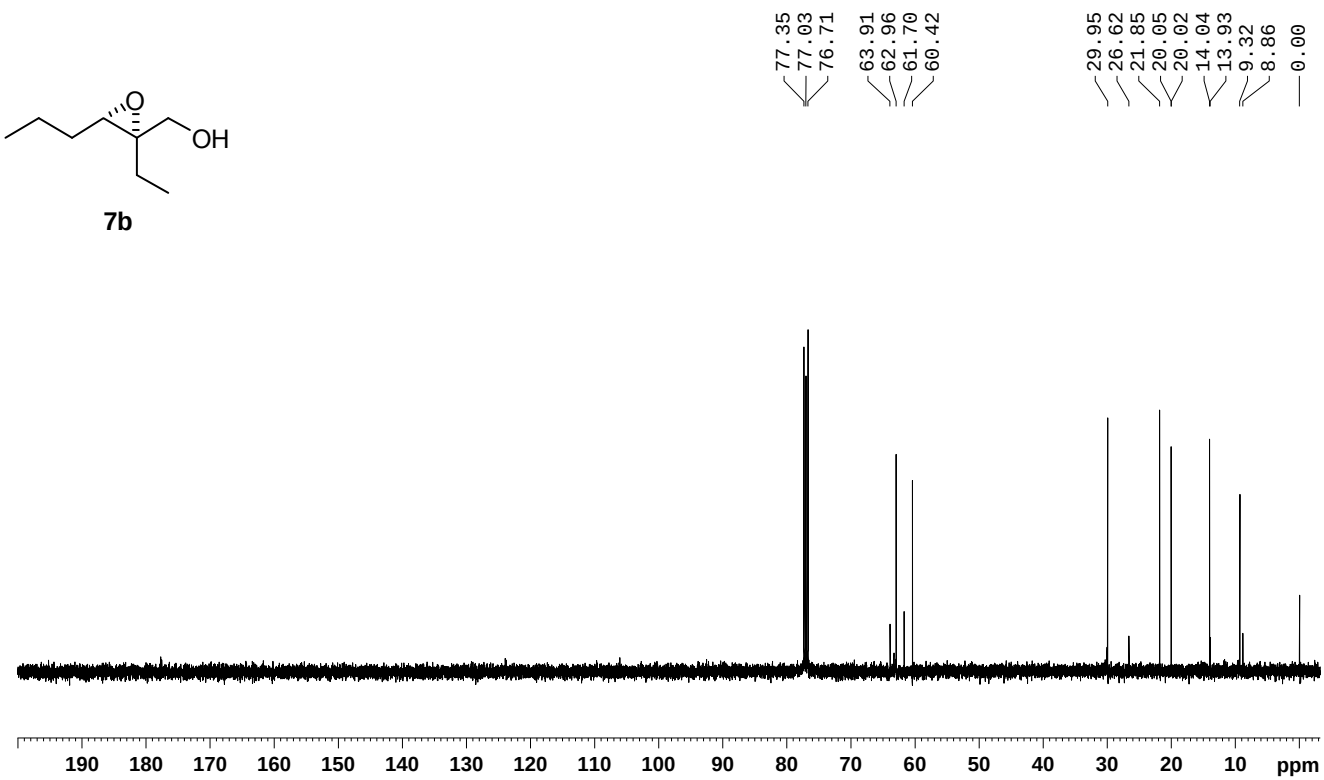
1.51
1.50
1.50
1.49
1.49
1.49
1.47
1.47
1.46
1.45
1.45
1.44
1.44
1.43
0.96
0.95
0.94
0.01
-0.01
O
OH
7b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
0.78
0.17
1.81
4.82
6.00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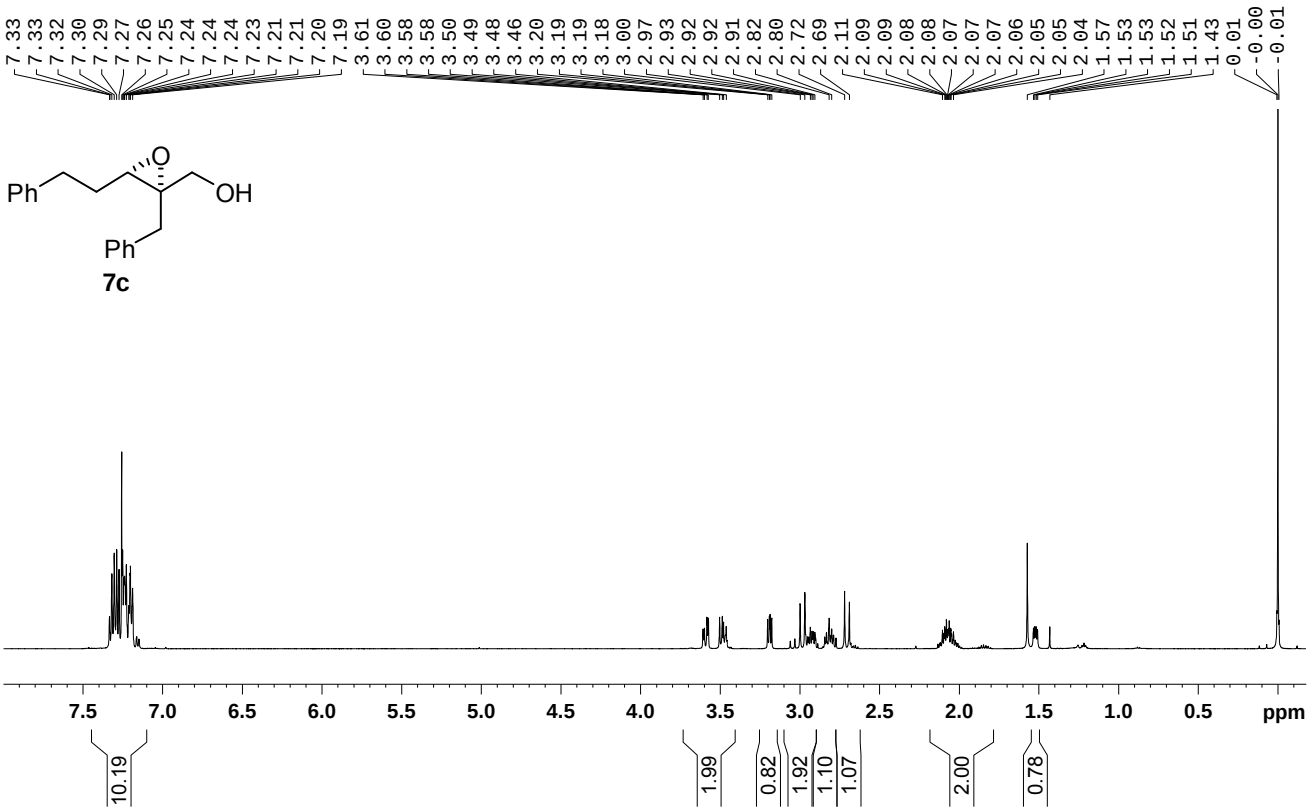
77.03
76.71
63.91
62.96
61.70
60.42
29.95
26.62
21.85
20.05
20.02
14.04
13.93
9.32
8.86
0.00
O
OH
7b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.32
7.30
7.29
7.27
7.26
7.25
7.24
7.24
7.24
7.23
7.21
7.21
7.20
7.19
3.61
3.60
3.58
3.58
3.50
3.49
3.48
3.46
3.20
3.19
3.19
3.18
3.00
2.97
2.93
2.92
2.92
2.91
2.82
2.80
2.72
2.69
2.11
2.09
2.09
2.08
2.08
2.07
2.07
2.07
2.06
2.05
2.05
2.04
1.57
1.53
1.53
1.52
1.51
1.43
0.01
-0.00
-0.01
Ph
O
OH
Ph
7c
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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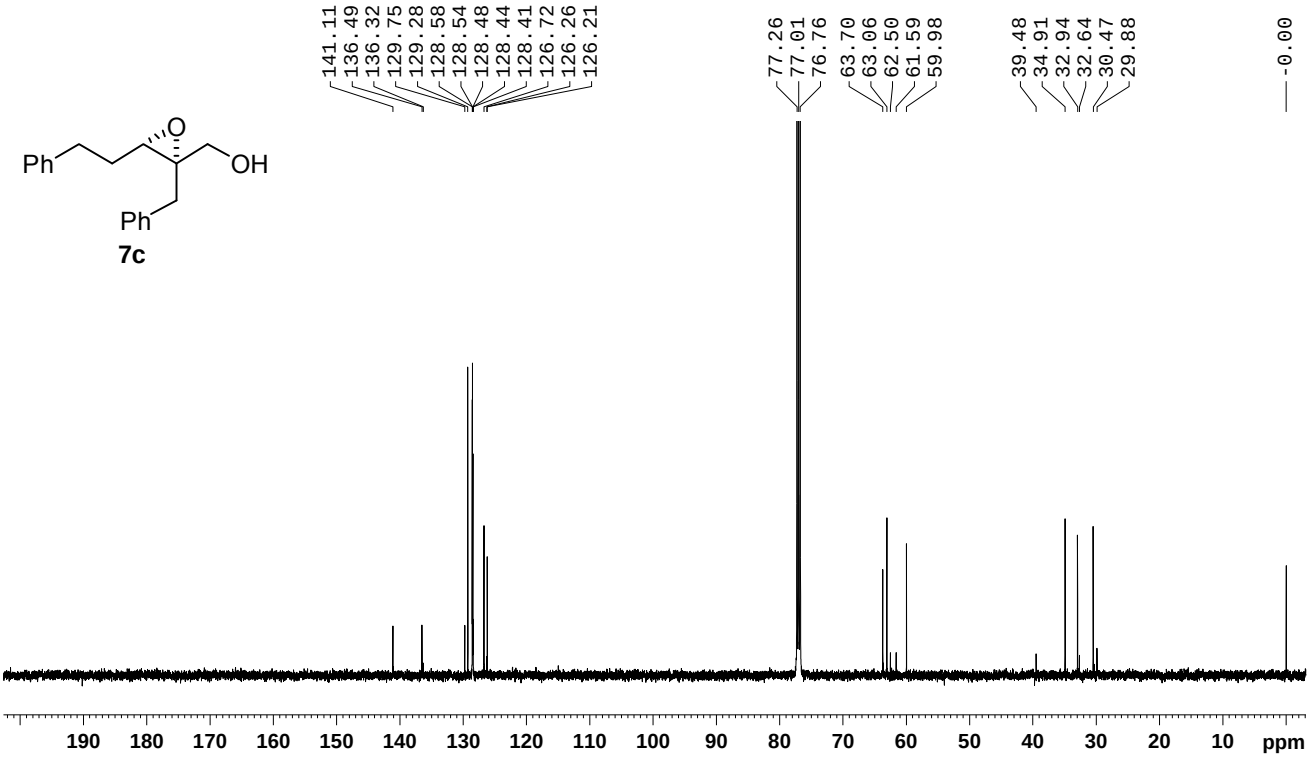
1.99
0.82
1.92
1.10
1.07
2.00
0.78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136.32
129.75
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128.58
128.54
128.48
128.44
128.41
126.72
126.26
126.21
77.26
77.01
76.76
63.70
63.06
62.50
61.59
59.98
39.48
34.91
32.94
32.64
30.47
29.88
-0.00
Ph
O
OH
Ph
7c
190
180
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160
150
140
130
120
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100
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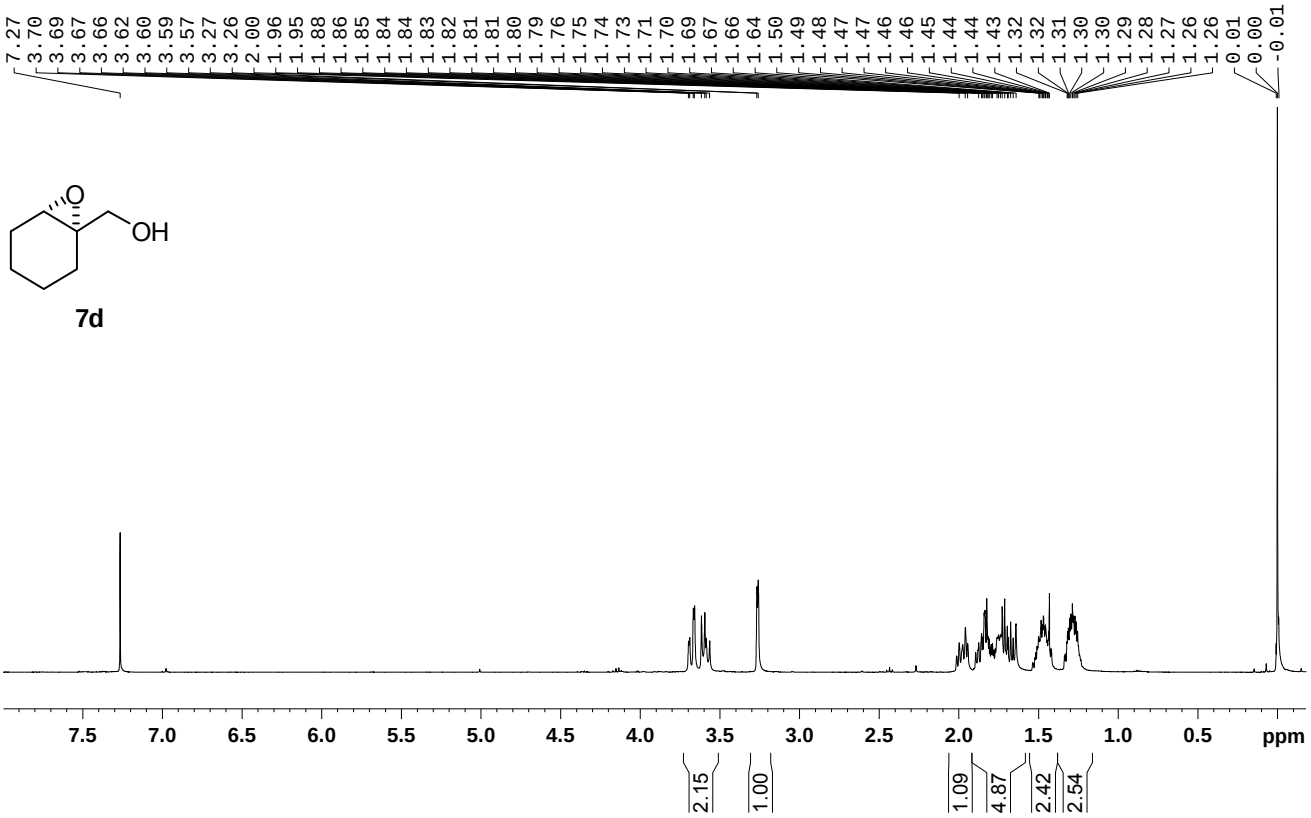
80
70
60
50
40
30
20
10
ppm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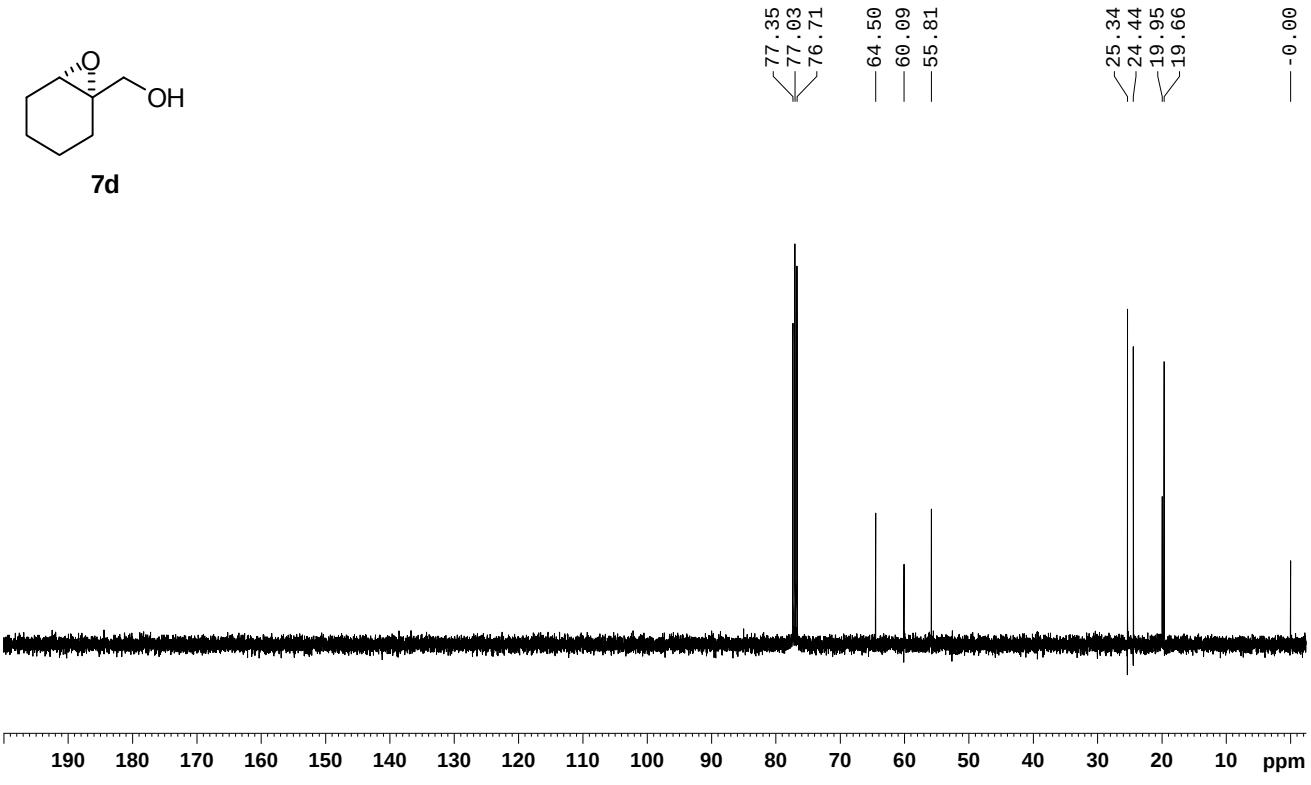
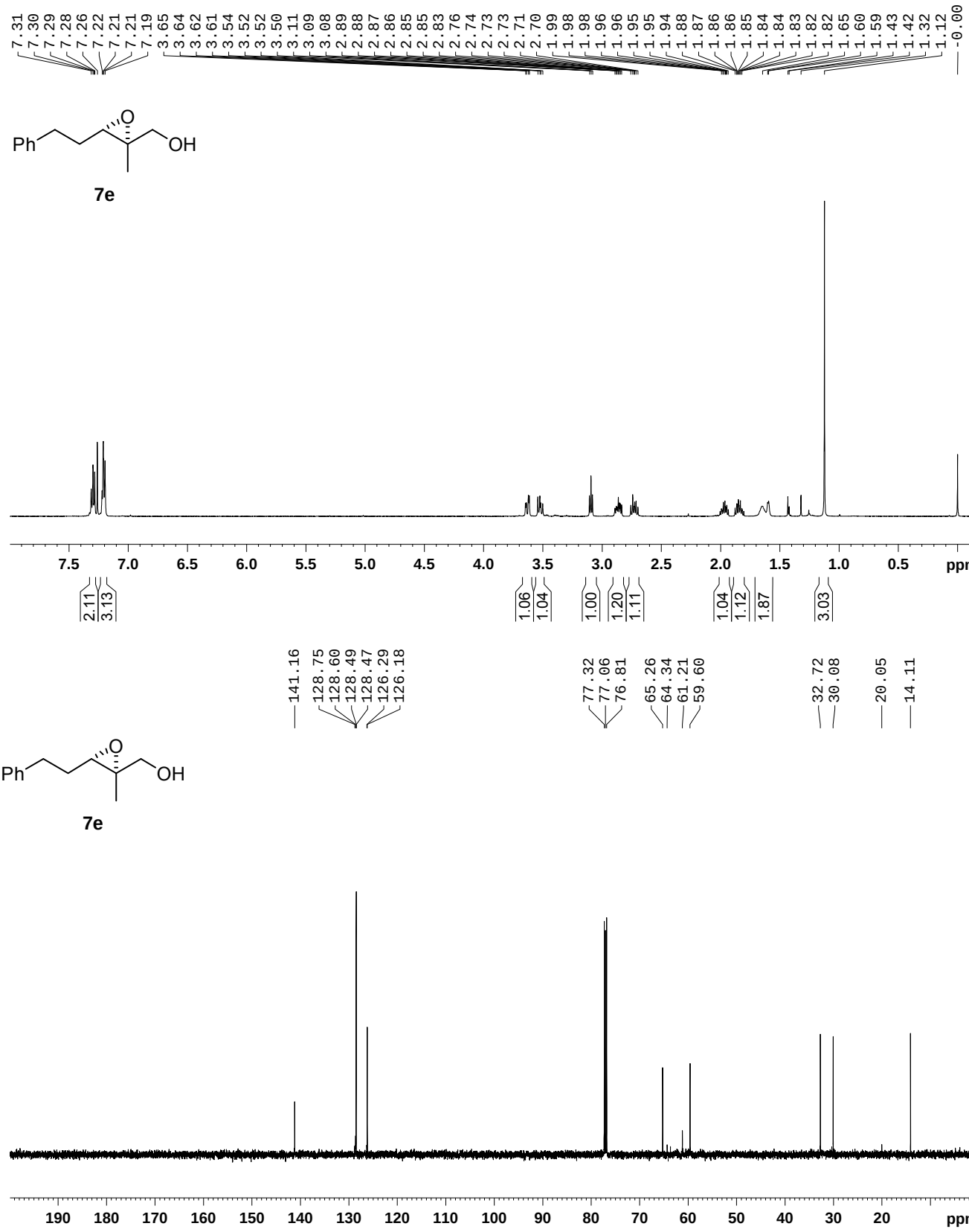
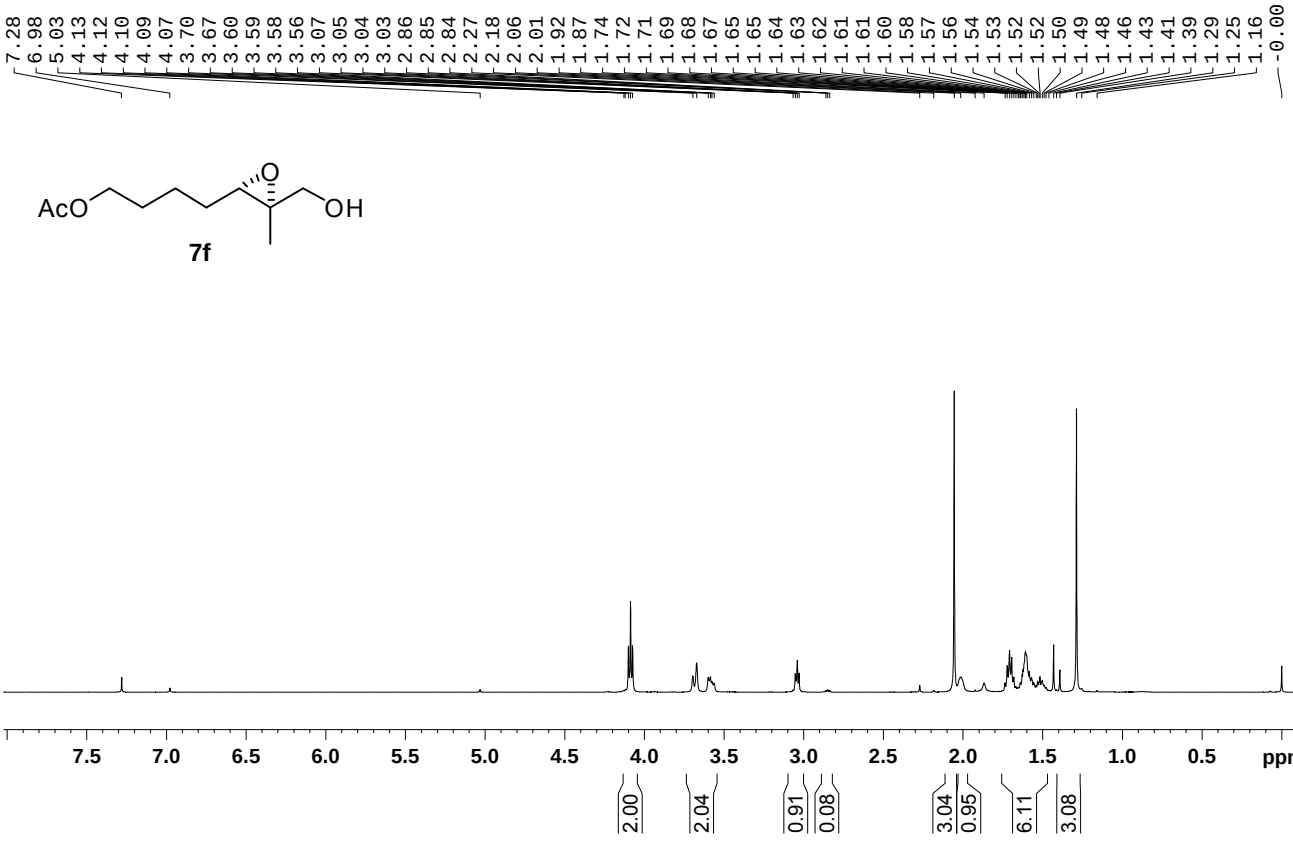
3.62
3.60
3.59
3.57
3.27
3.26
2.00
1.96
1.95
1.88
1.86
1.85
1.84
1.84
1.83
1.82
1.81
1.81
1.80
1.79
1.76
1.75
1.74
1.73
1.71
1.70
1.69
1.67
1.66
1.64
1.50
1.49
1.48
1.47
1.47
1.46
1.46
1.45
1.44
1.44
1.43
1.32
1.31
1.30
1.30
1.29
1.28
1.27
1.26
0.01
0.00
-0.01
O
OH
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.15
1.00
1.09
4.87
2.42
2.54

7d


77.35
77.03
76.71
64.50
60.09
55.81
25.34
24.44
19.95
19.66
-0.00
O
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

7d


7.31 7.30 7.29 7.28 7.26 7.22 7.21 7.21 7.19 3.65 3.64 3.62 3.61 3.54 3.52 3.50 3.11 3.09 3.08 2.89 2.88 2.87 2.86 2.85 2.85 2.83 2.76 2.74 2.73 2.73 2.71 2.70 1.99 1.98 1.98 1.96 1.95 1.95 1.94 1.88 1.87 1.86 1.86 1.85 1.84 1.84 1.83 1.82 1.82 1.65 1.60 1.59 1.43 1.42 1.32 1.12 -0.00
Ph
O
OH
7e
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.11 3.13 1.06 1.04 1.00 1.20 1.11 1.04 1.12 1.87 3.03
141.16 128.75 128.60 128.49 128.47 126.29 126.18 77.32 77.06 76.81 65.26 64.34 61.21 59.60 32.72 30.08 20.05 14.11
Ph
O
OH
7e
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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4.13
4.12
4.10
4.09
4.07
3.70
3.67
3.60
3.59
3.58
3.56
3.07
3.05
3.04
3.03
2.86
2.85
2.84
2.27
2.18
2.06
2.01
1.92
1.87
1.74
1.72
1.71
1.69
1.68
1.67
1.65
1.65
1.64
1.63
1.62
1.61
1.61
1.60
1.58
1.57
1.56
1.54
1.53
1.52
1.52
1.50
1.49
1.48
1.46
1.43
1.41
1.39
1.29
1.25
1.16
-0.00
AcO
OH
7f
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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0.5
ppm
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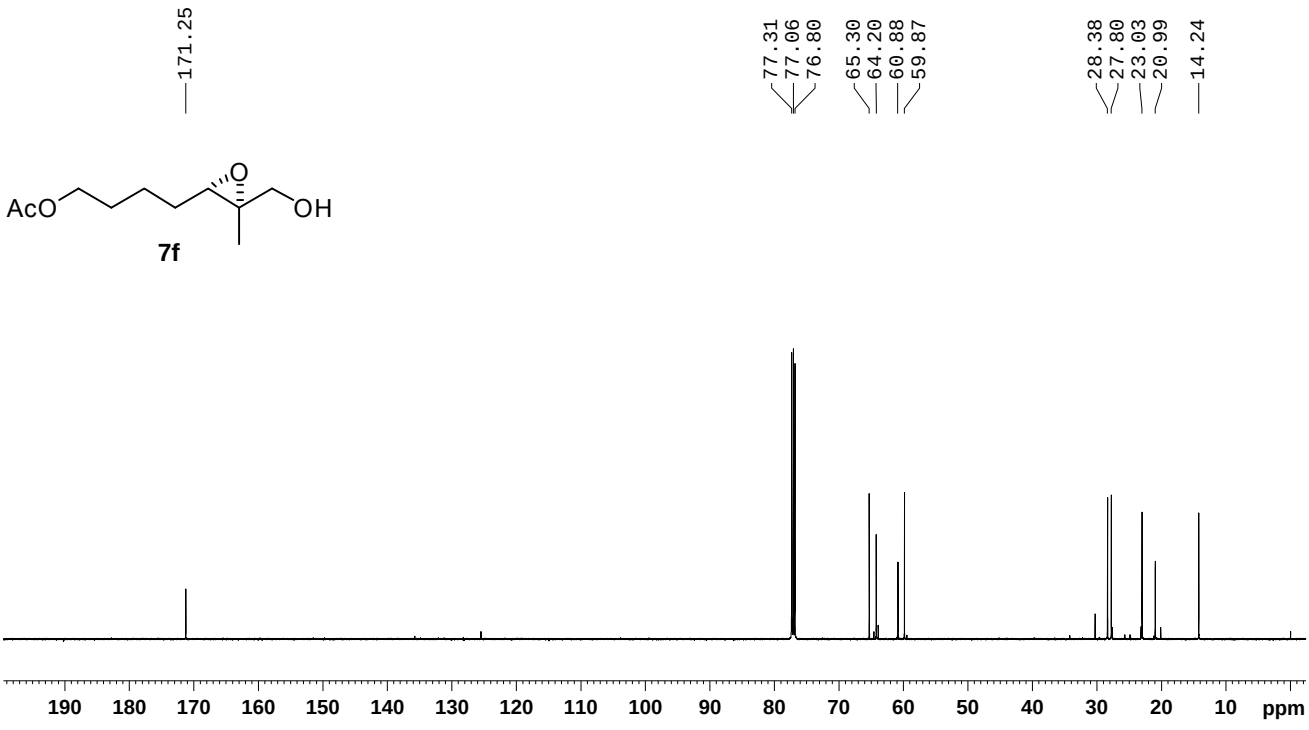
2.04
0.91
0.08
3.04
0.95
6.11
3.08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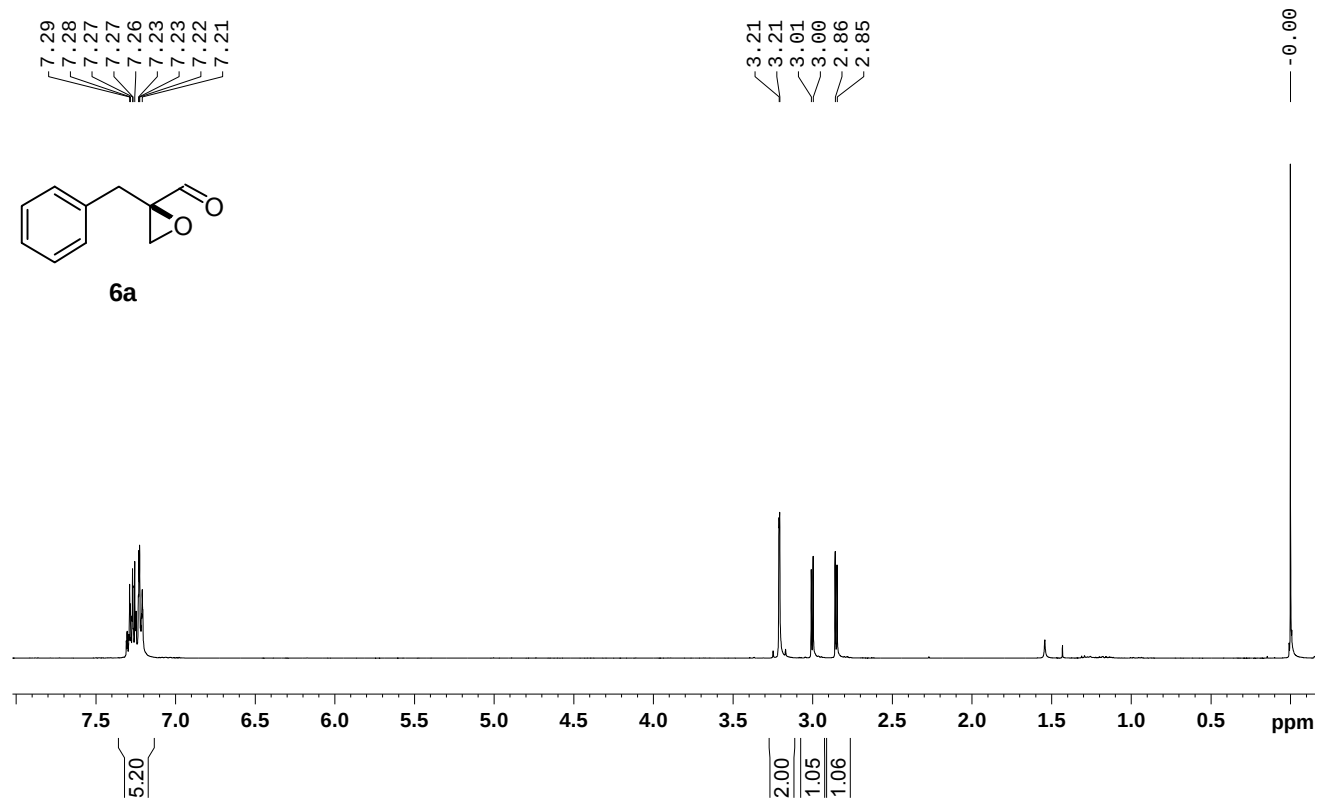
76.80
65.30
64.20
60.88
59.87
28.38
27.80
23.03
20.99
14.24
AcO
OH
7f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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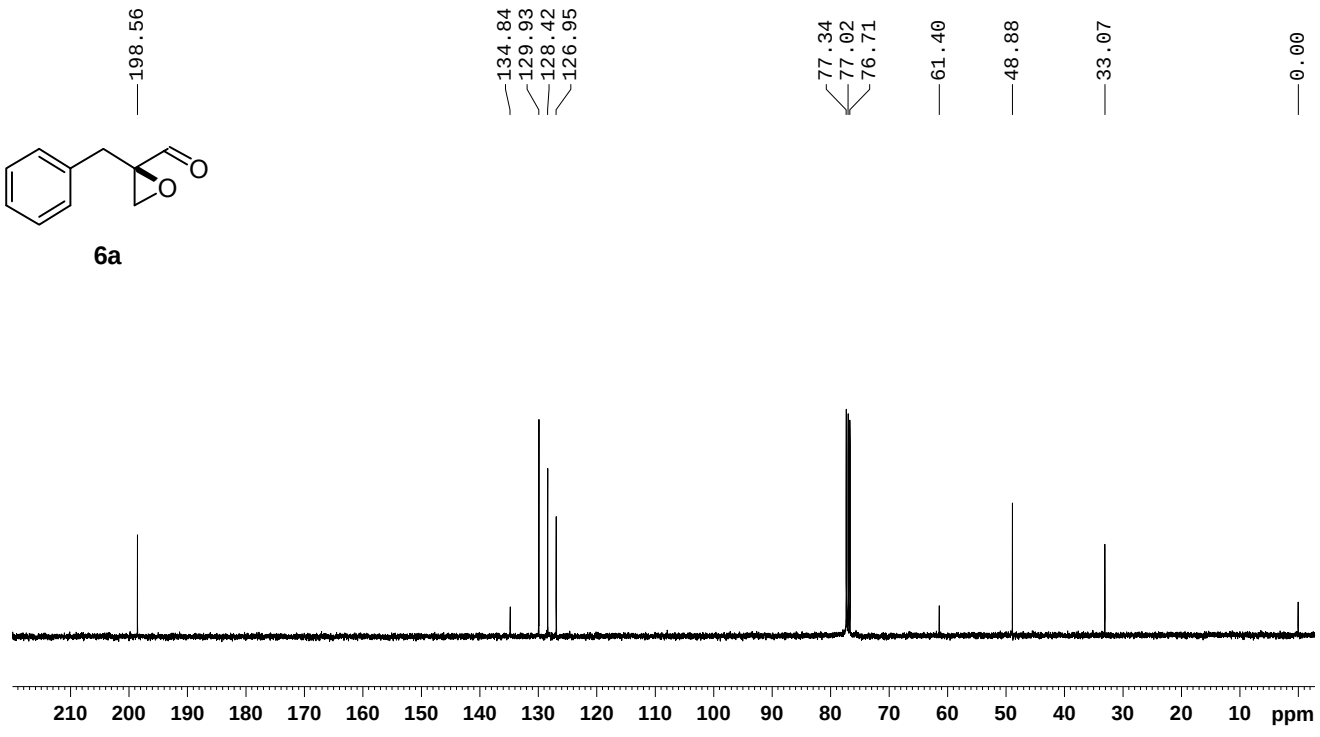
7.27
7.27
7.26
7.23
7.23
7.22
7.21
3.21
3.21
3.01
3.00
2.86
2.85
-0.00
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.20
2.00
1.05
1.06

6a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128.42
126.95
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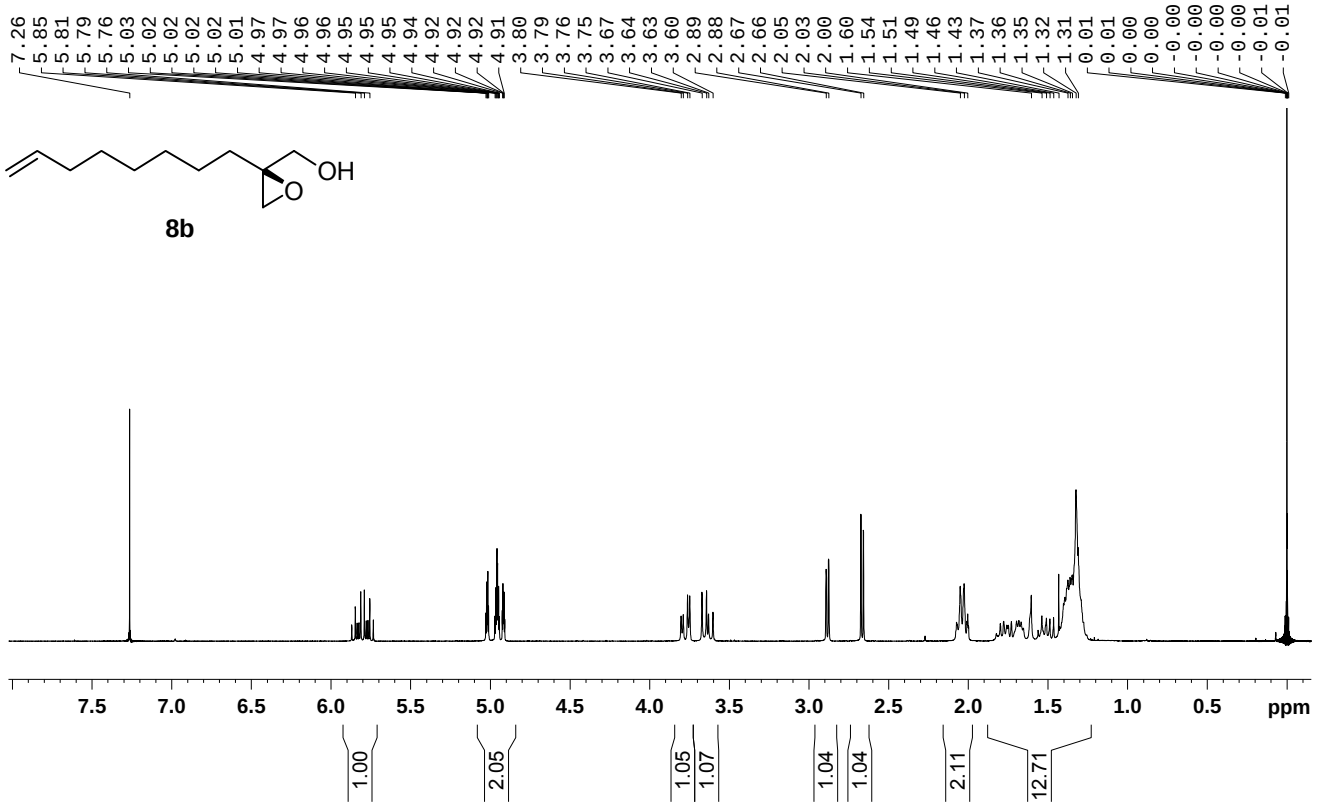
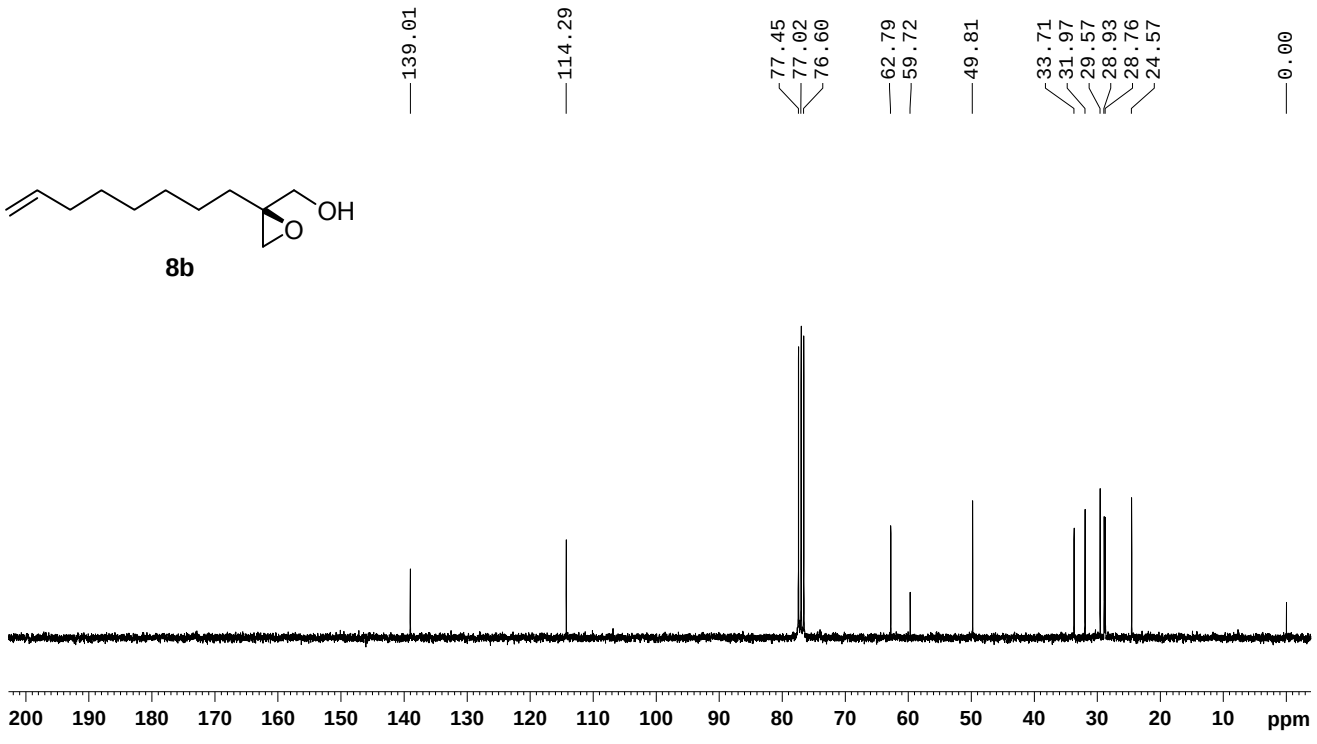
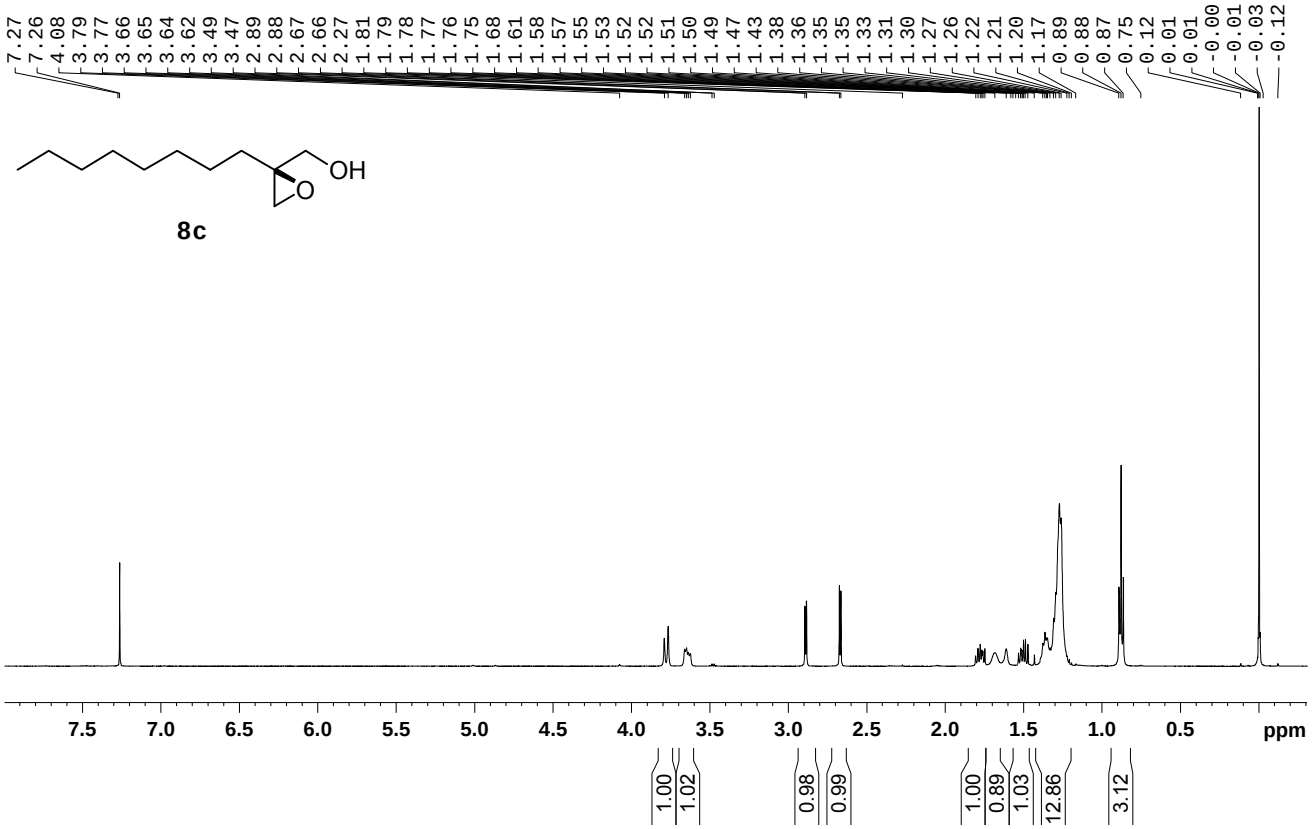
77.02
76.71
61.40
48.88
33.07
0.00
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

6a


7.26 5.85 5.81 5.79 5.76 5.03 5.02 5.02 5.02 5.01 4.97 4.97 4.96 4.96 4.95 4.95 4.95 4.94 4.92 4.92 4.92 4.91 3.80 3.79 3.76 3.75 3.67 3.64 3.63 3.60 2.89 2.88 2.67 2.66 2.05 2.03 2.00 1.60 1.54 1.51 1.49 1.46 1.43 1.37 1.36 1.35 1.32 1.31 0.01 0.01 0.00 0.00 -0.00 -0.00 -0.00 -0.00 -0.01 -0.01
OH
O
8b
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00 2.05 1.05 1.07 1.04 1.04 2.11 12.71


139.01 114.29 77.45 77.02 76.60 62.79 59.72 49.81 33.71 31.97 29.57 28.93 28.76 24.57 0.00
OH
O
8b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.26
4.08
3.79
3.77
3.66
3.65
3.64
3.62
3.49
3.47
2.89
2.88
2.67
2.66
2.27
1.81
1.79
1.78
1.77
1.76
1.75
1.68
1.61
1.58
1.57
1.55
1.53
1.52
1.52
1.51
1.50
1.49
1.47
1.43
1.38
1.36
1.35
1.35
1.33
1.31
1.30
1.27
1.26
1.22
1.21
1.20
1.17
0.89
0.88
0.87
0.75
0.12
0.01
0.01
-0.00
-0.01
-0.03
-0.12
OH
O
8c
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
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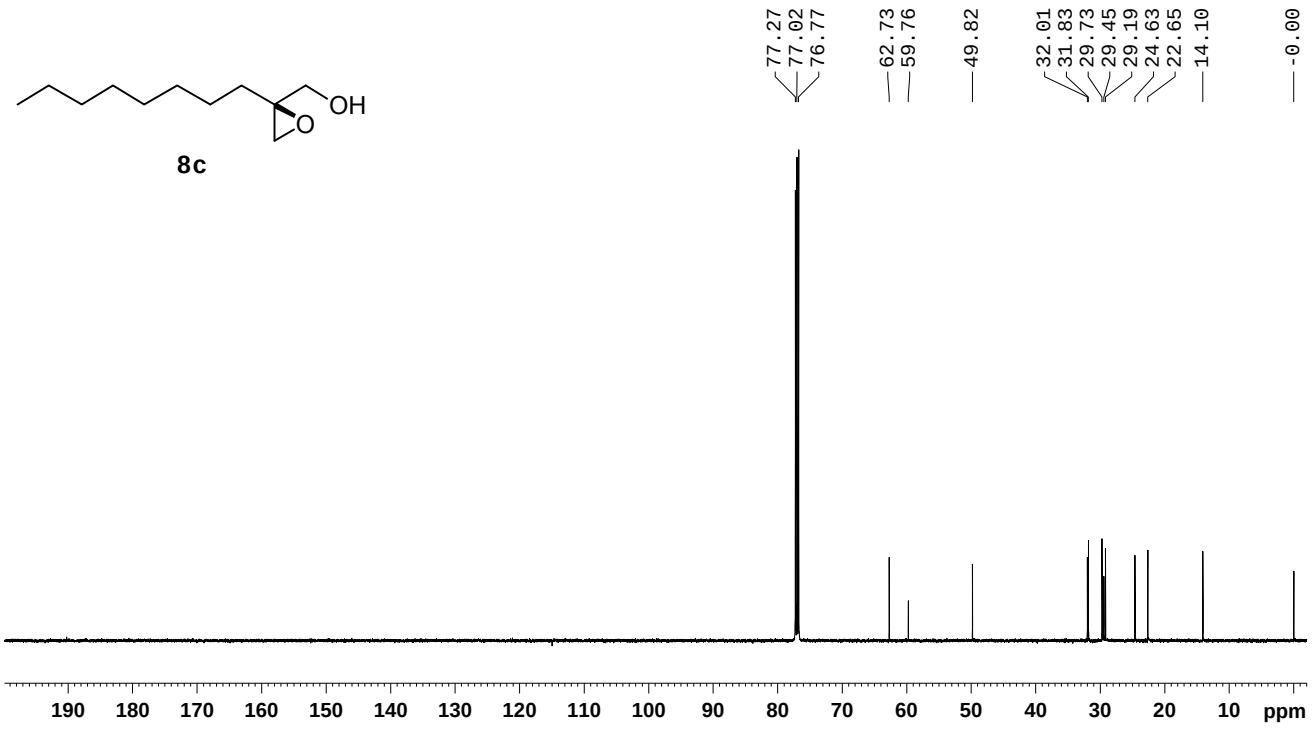
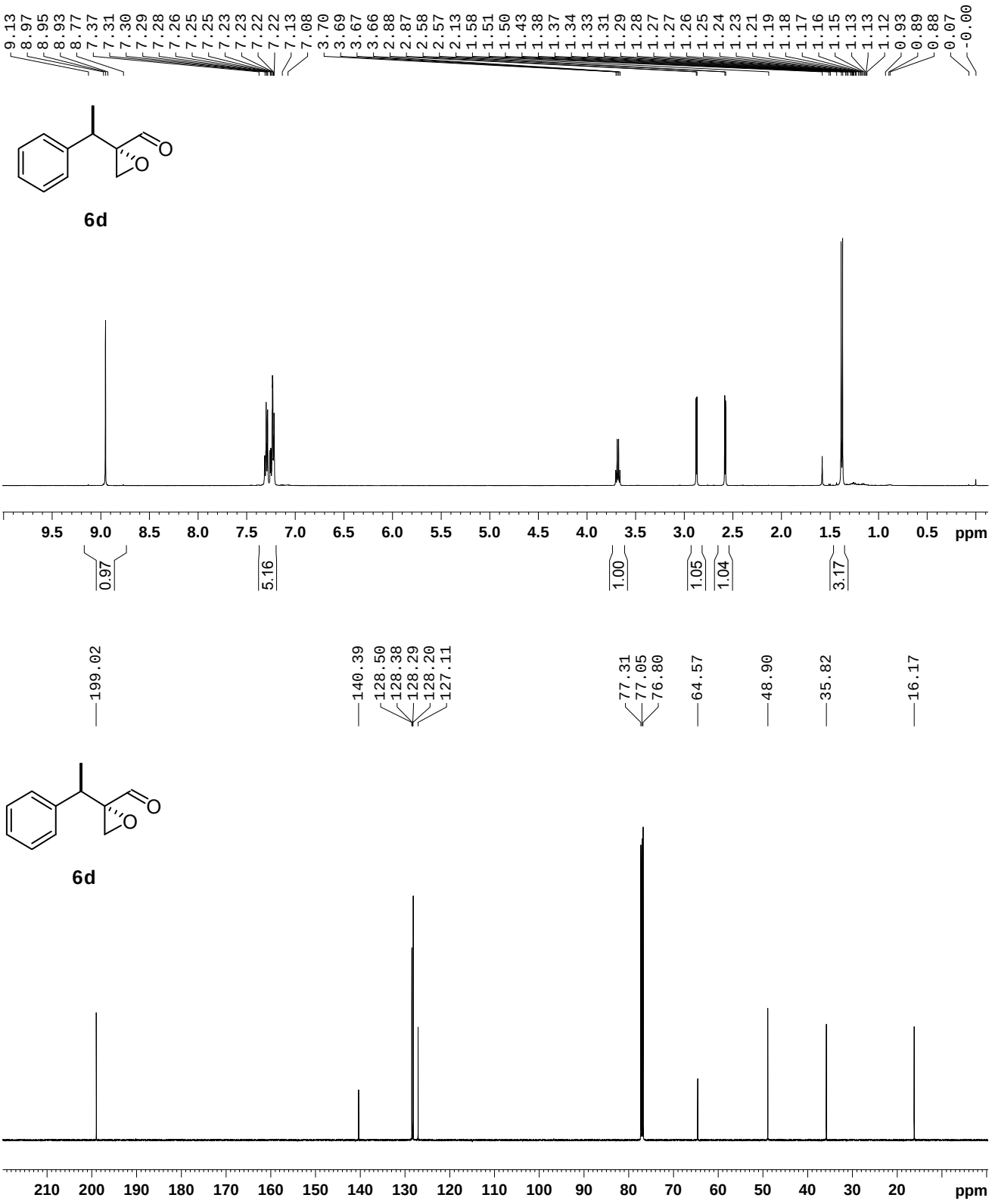
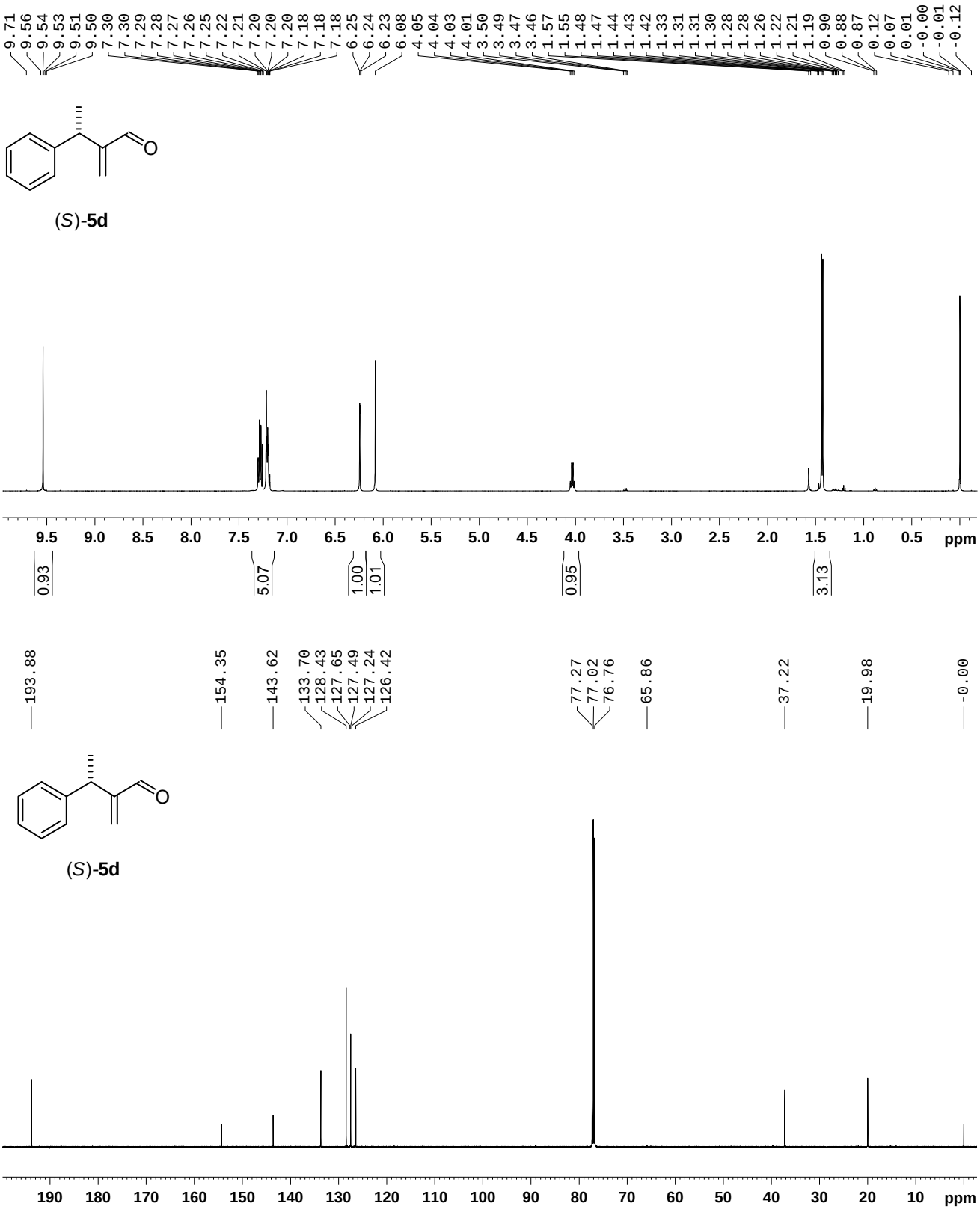
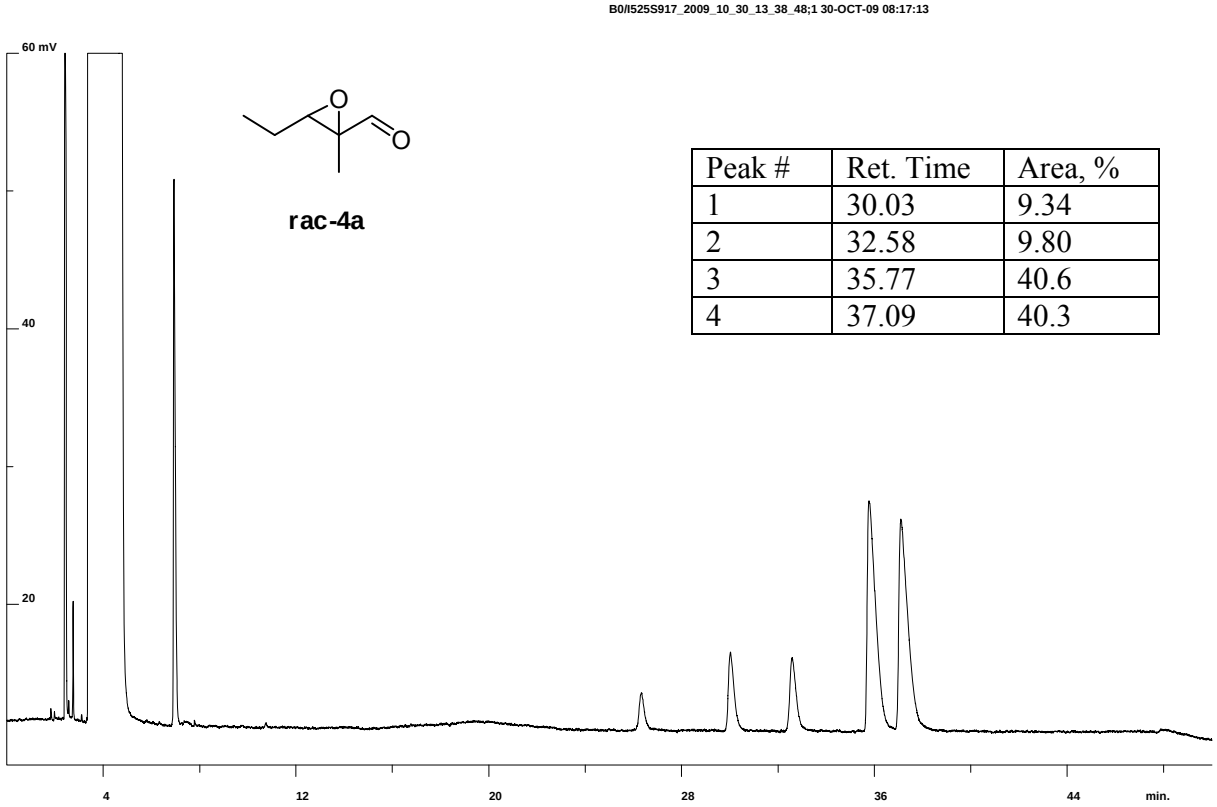
0.98
0.99
1.00
0.89
1.03
12.86
3.12


77.27
77.02
76.77
62.73
59.76
49.82
32.01
31.83
29.73
29.45
29.19
24.63
22.65
14.10
-0.00
OH
O
8c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


9.13
8.97
8.95
8.93
8.77
7.37
7.31
7.30
7.29
7.28
7.26
7.25
7.25
7.23
7.23
7.22
7.22
7.13
7.08
3.70
3.69
3.67
3.66
2.88
2.87
2.58
2.57
2.13
1.58
1.51
1.50
1.43
1.38
1.37
1.34
1.33
1.31
1.29
1.28
1.27
1.27
1.26
1.25
1.24
1.23
1.21
1.19
1.18
1.17
1.16
1.15
1.13
1.13
1.12
0.93
0.89
0.88
0.07
-0.00
O
O
6d
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.97
5.16
1.00
1.05
1.04
3.17
199.02
140.39
128.50
128.38
128.29
128.20
127.11
77.31
77.05
76.80
64.57
48.90
35.82
16.17
O
O
6d
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

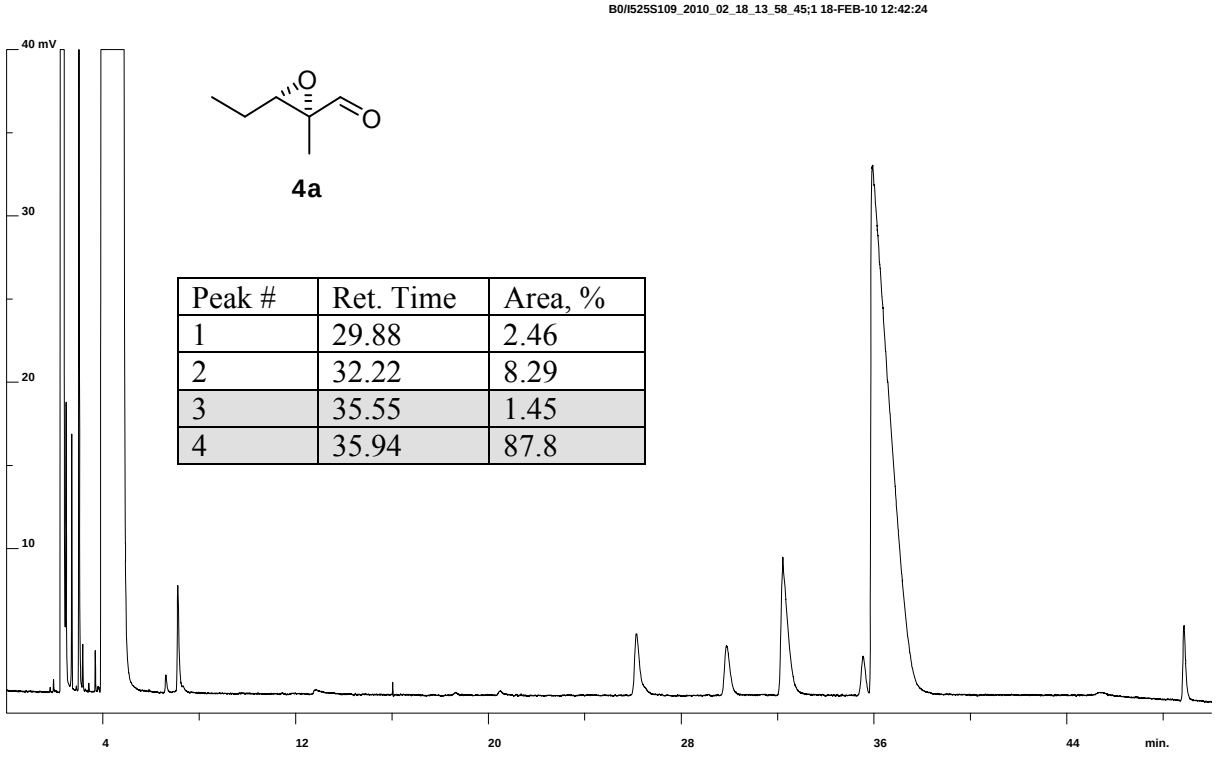

9.71 9.56 9.54 9.53 9.51 9.50 7.30 7.30 7.29 7.28 7.27 7.26 7.25 7.22 7.21 7.20 7.20 7.20 7.18 7.18 6.25 6.24 6.23 6.08 4.05 4.04 4.03 4.01 3.50 3.49 3.47 3.46 1.57 1.55 1.48 1.47 1.44 1.43 1.42 1.33 1.31 1.31 1.30 1.28 1.28 1.26 1.22 1.21 1.19 0.90 0.88 0.87 0.12 0.07 0.01 -0.00 -0.01 -0.12
O
(S)-5d
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.93 5.07 1.00 1.01 0.95 3.13
193.88 154.35 143.62 133.70 128.43 127.65 127.49 127.24 126.42 77.27 77.02 76.76 65.86 37.22 19.98 -0.00
O
(S)-5d
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

GC and HPLC traces



rac-4a

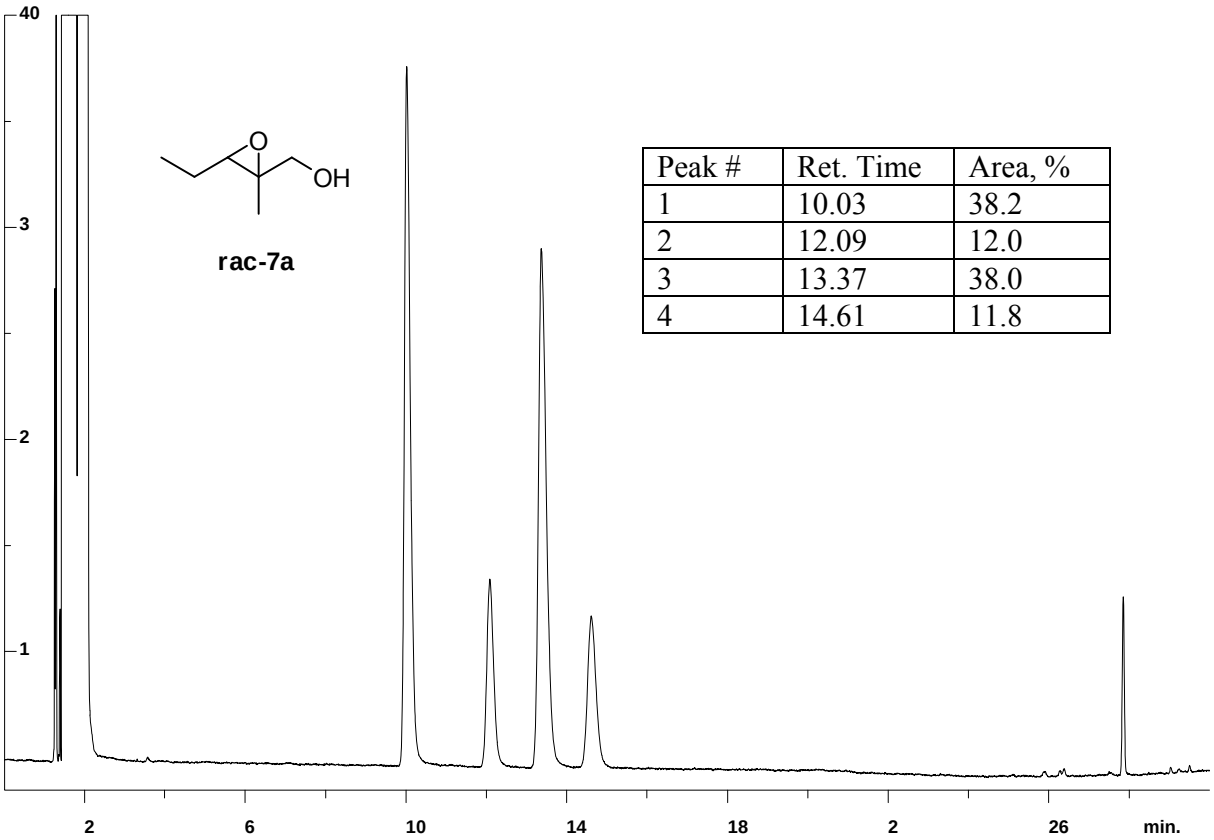
Peak #	Ret. Time	Area, %
1	30.03	9.34
2	32.58	9.80
3	35.77	40.6
4	37.09	40.3



4a

Peak #	Ret. Time	Area, %
1	29.88	2.46
2	32.22	8.29
3	35.55	1.45
4	35.94	87.8

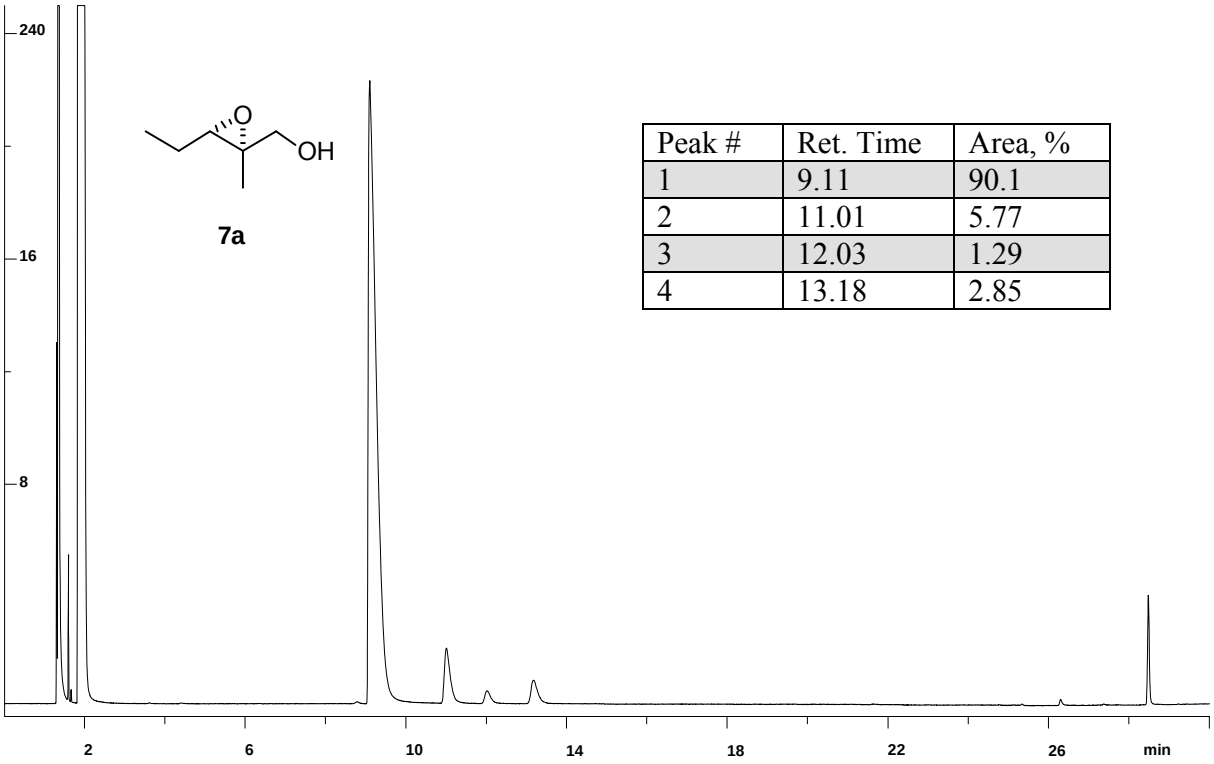
B0/I525S041_2010_01_15_08_34_10;1 14-JAN-10



rac-7a

Peak #	Ret. Time	Area, %
1	10.03	38.2
2	12.09	12.0
3	13.37	38.0
4	14.61	11.8

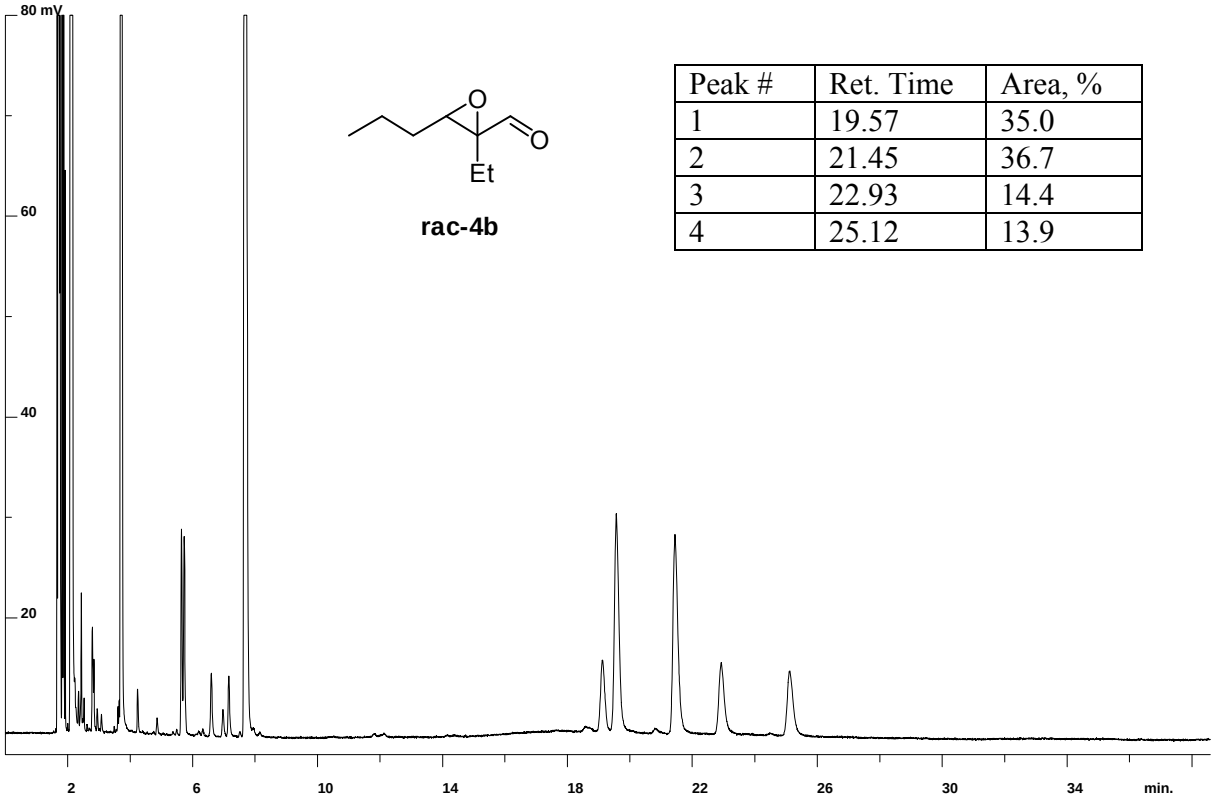
B0/I528S665_2010_02_19_11_58_13;1 19-FEB-10



7a

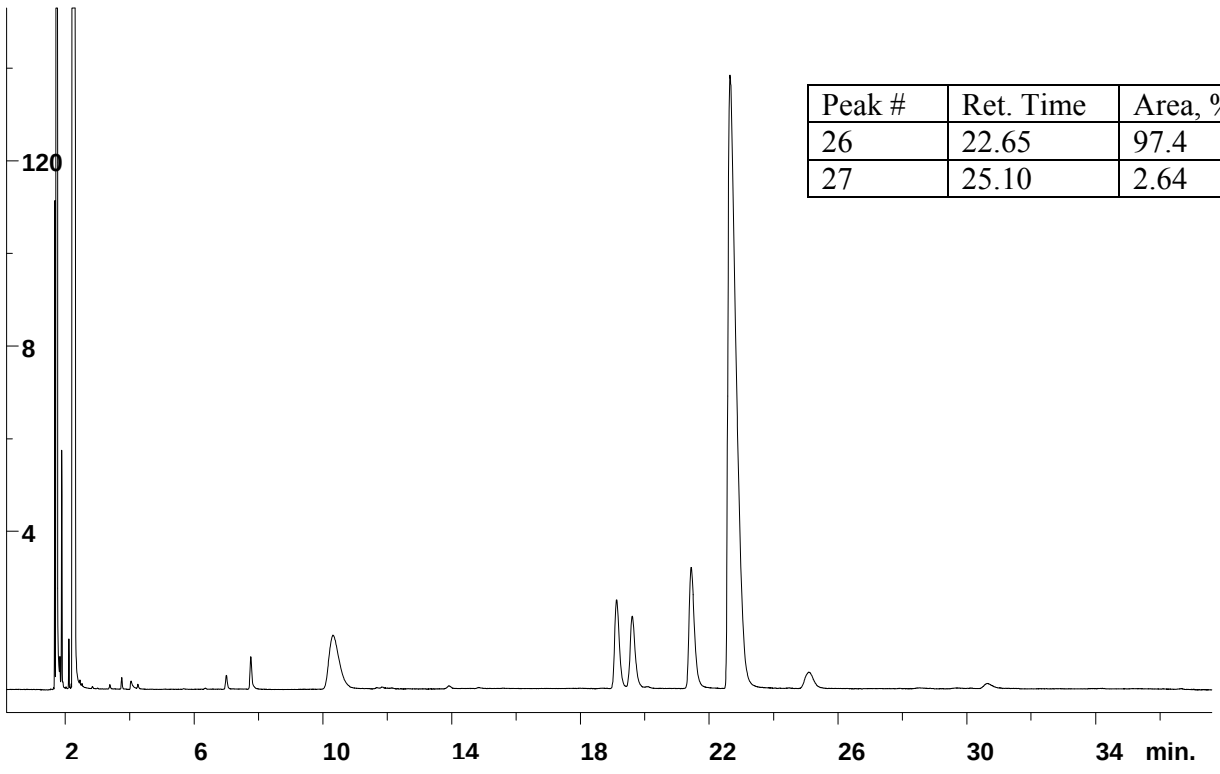
Peak #	Ret. Time	Area, %
1	9.11	90.1
2	11.01	5.77
3	12.03	1.29
4	13.18	2.85

B0/I528S609_2010_01_05_15_54_35;1 5-JAN-10 14:42:11



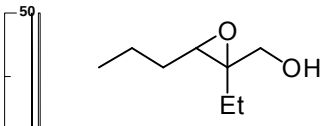
rac-4b

Peak #	Ret. Time	Area, %
1	19.57	35.0
2	21.45	36.7
3	22.93	14.4
4	25.12	13.9



Peak #	Ret. Time	Area, %
26	22.65	97.4
27	25.10	2.64

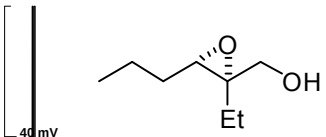
B0/I513S902_2010_02_22_15_12_46;1 22-FEB-10



rac-7b

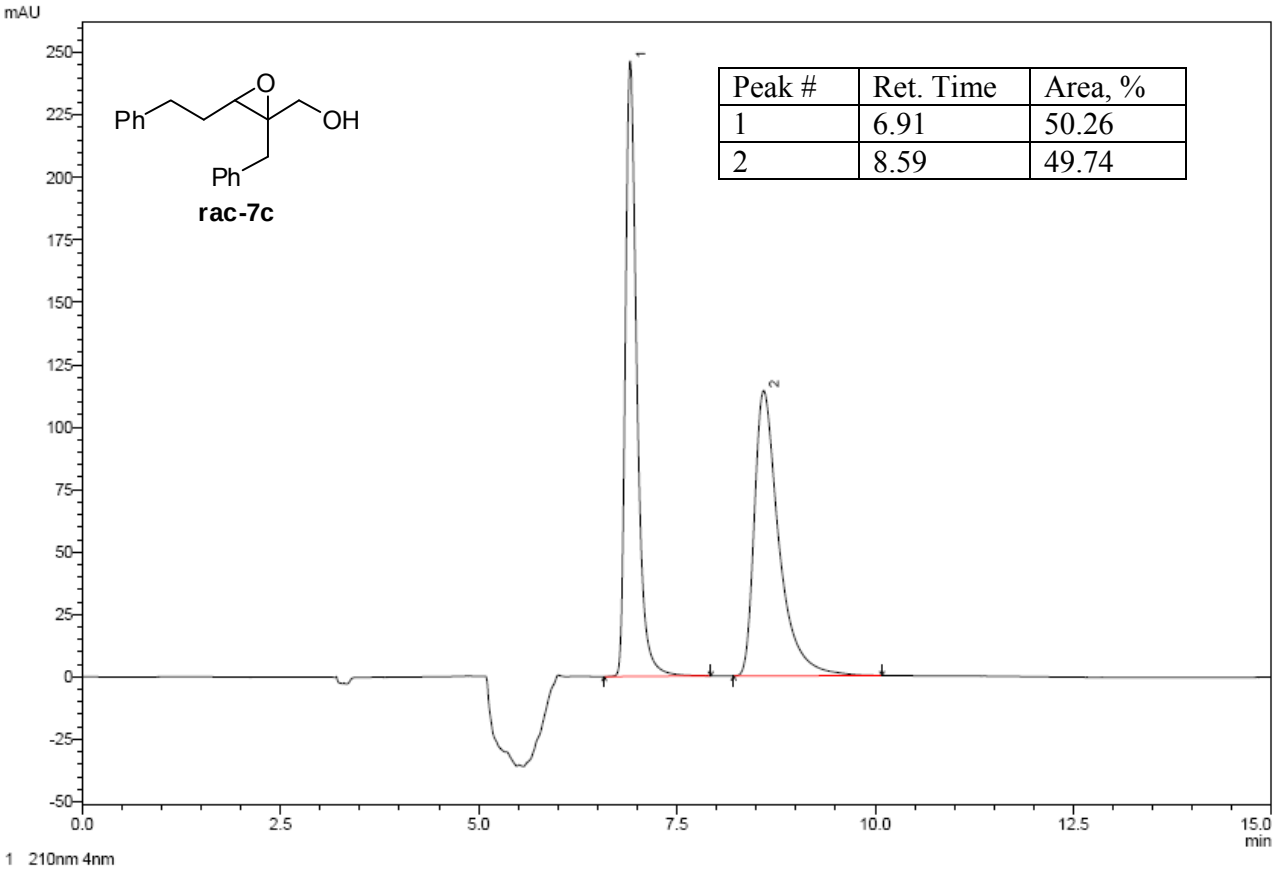
Peak #	Ret. Time	Area, %
1	29.24	17.3
2	32.81	17.5
3	35.89	32.5
4	37.16	32.7

B0/I513S905_2010_02_24_12_05_26;1 23-FEB-10 15:23:59

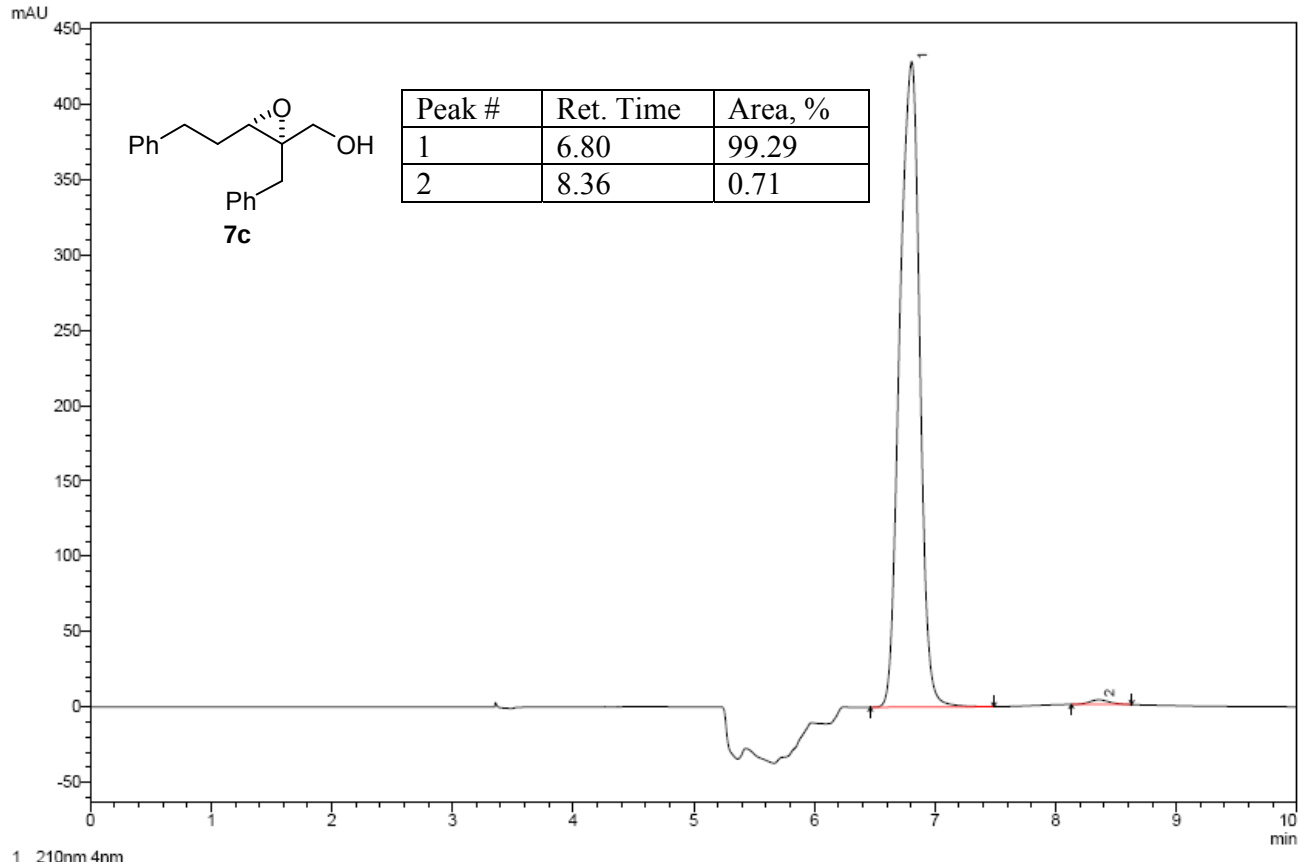


7b

Peak #	Ret. Time	Area, %
1	29.31	1.06
2	32.07	82.2
3	36.06	11.0
4	37.40	5.74

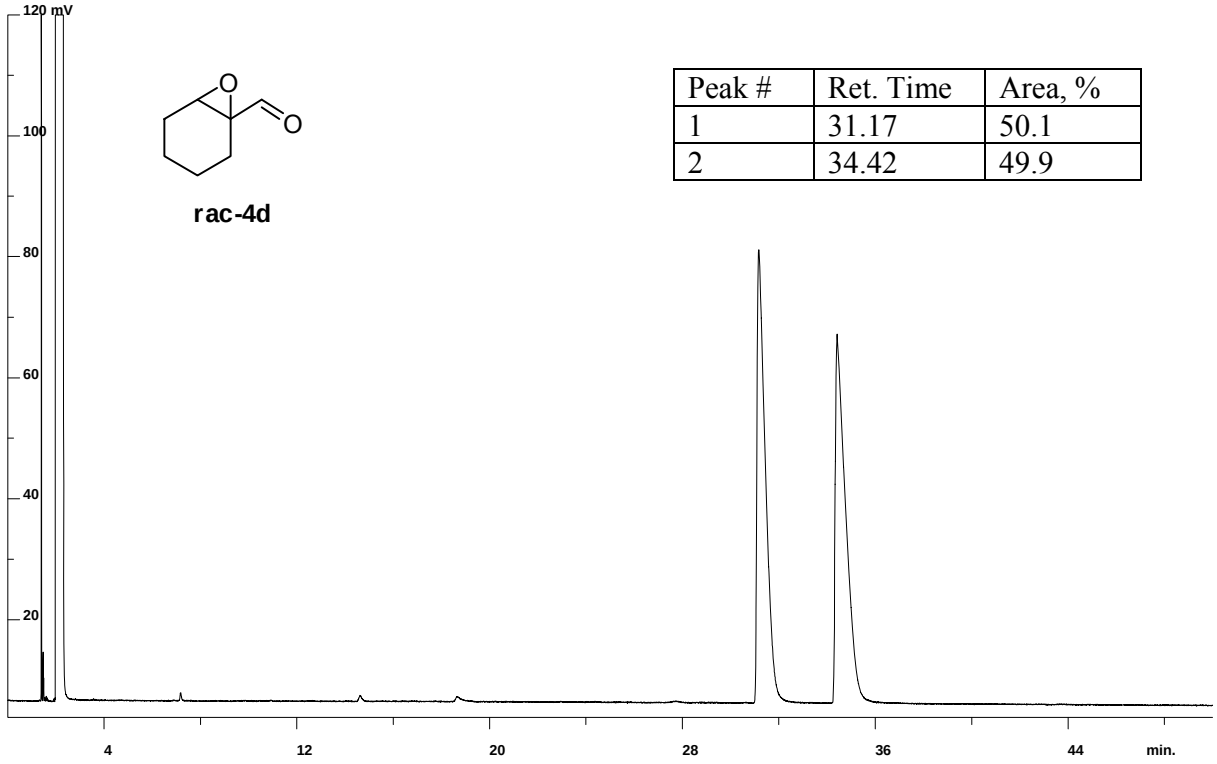


Peak #	Ret. Time	Area, %
1	6.91	50.26
2	8.59	49.74



Peak #	Ret. Time	Area, %
1	6.80	99.29
2	8.36	0.71

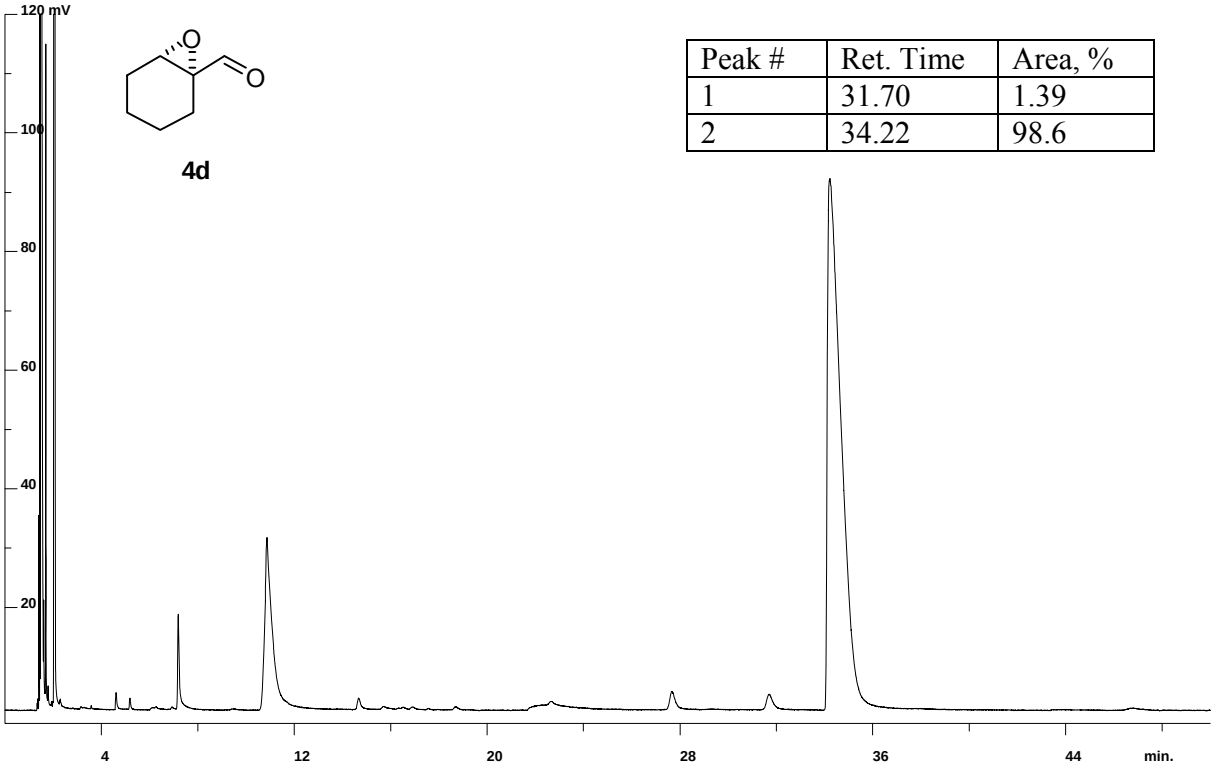
B0/I528S599_2009_12_21_13_32_23;1 21-DEC-09 12:30:06



rac-4d

Peak #	Ret. Time	Area, %
1	31.17	50.1
2	34.42	49.9

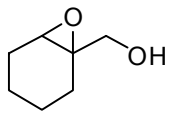
B0/I512S392_2010_01_21_16_18_17;1 21-JAN-10 12:22:13



4d

Peak #	Ret. Time	Area, %
1	31.70	1.39
2	34.22	98.6

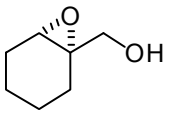
B0/I512S452_2010_02_22_15_56_39;1 22-FEB-10



rac-7d

Peak #	Ret. Time	Area, %
1	31.51	49.9
2	32.73	50.1

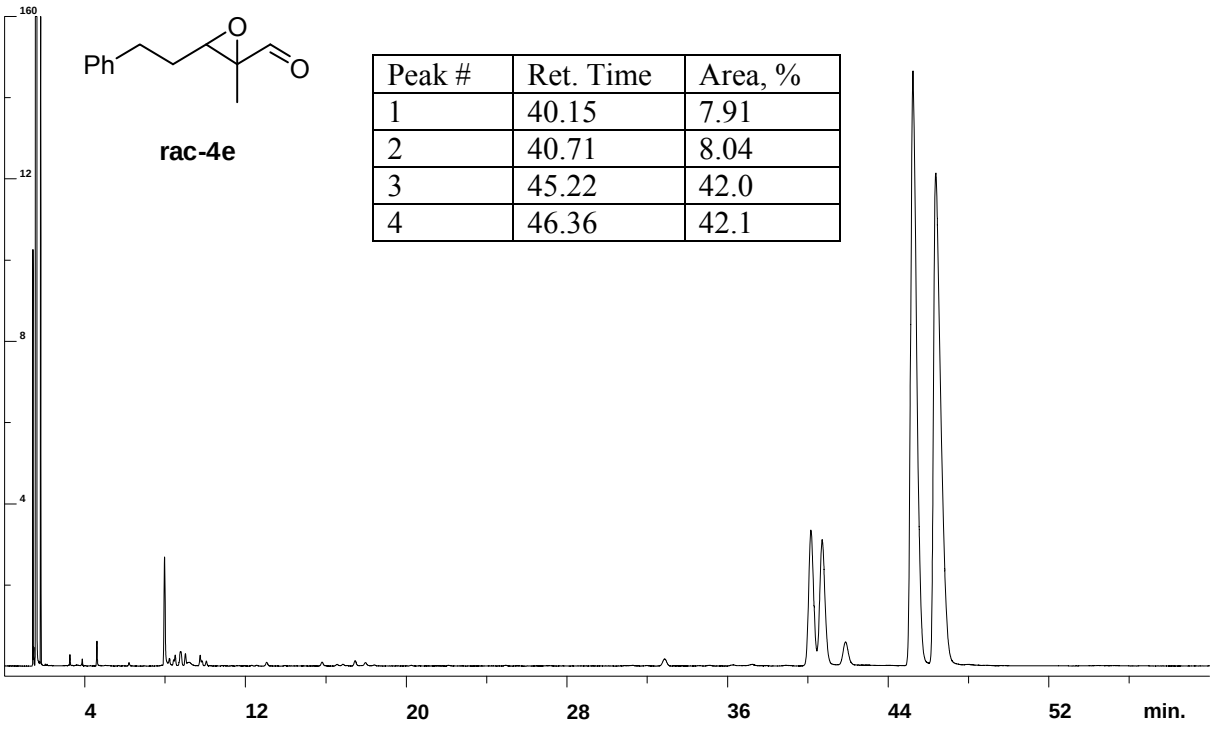
B0/I512S453_2010_02_23_09_06_12;1 23-FEB-10 08:15:37



7d

Peak #	Ret. Time	Area, %
1	32.17	1.58
2	32.60	98.4

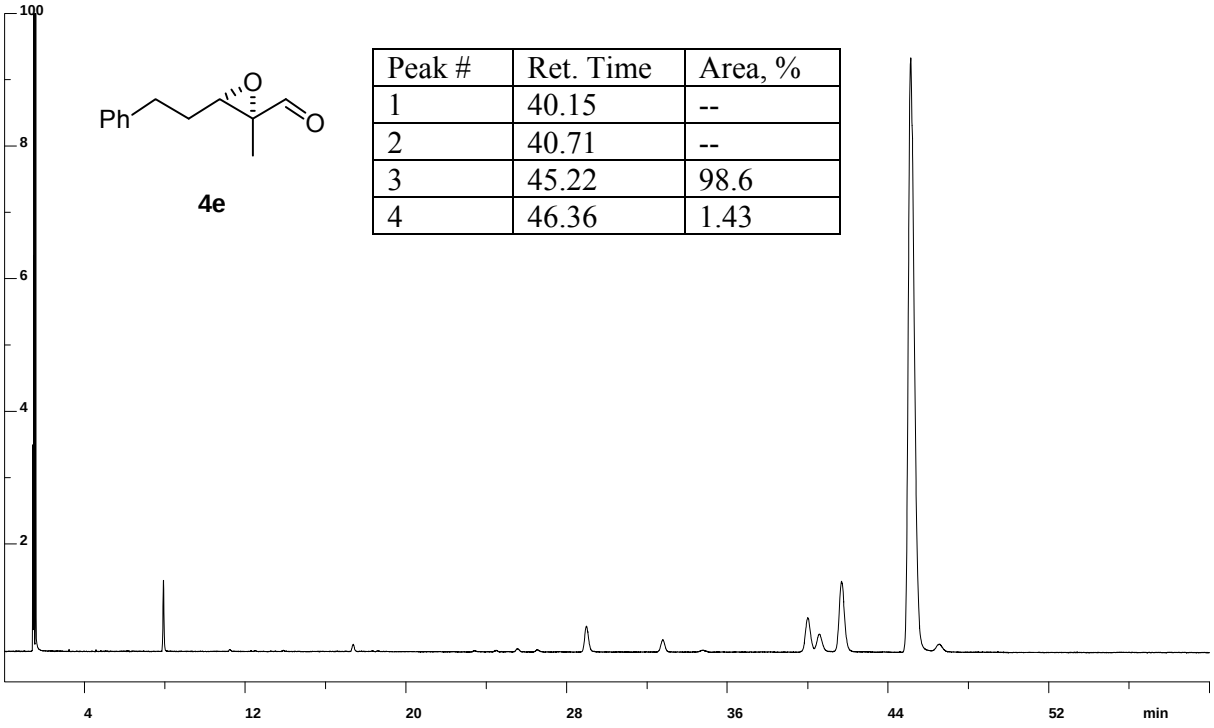
B0/I510S664_2009_12_11_11_35_06;1 11-DEC-09



rac-4e

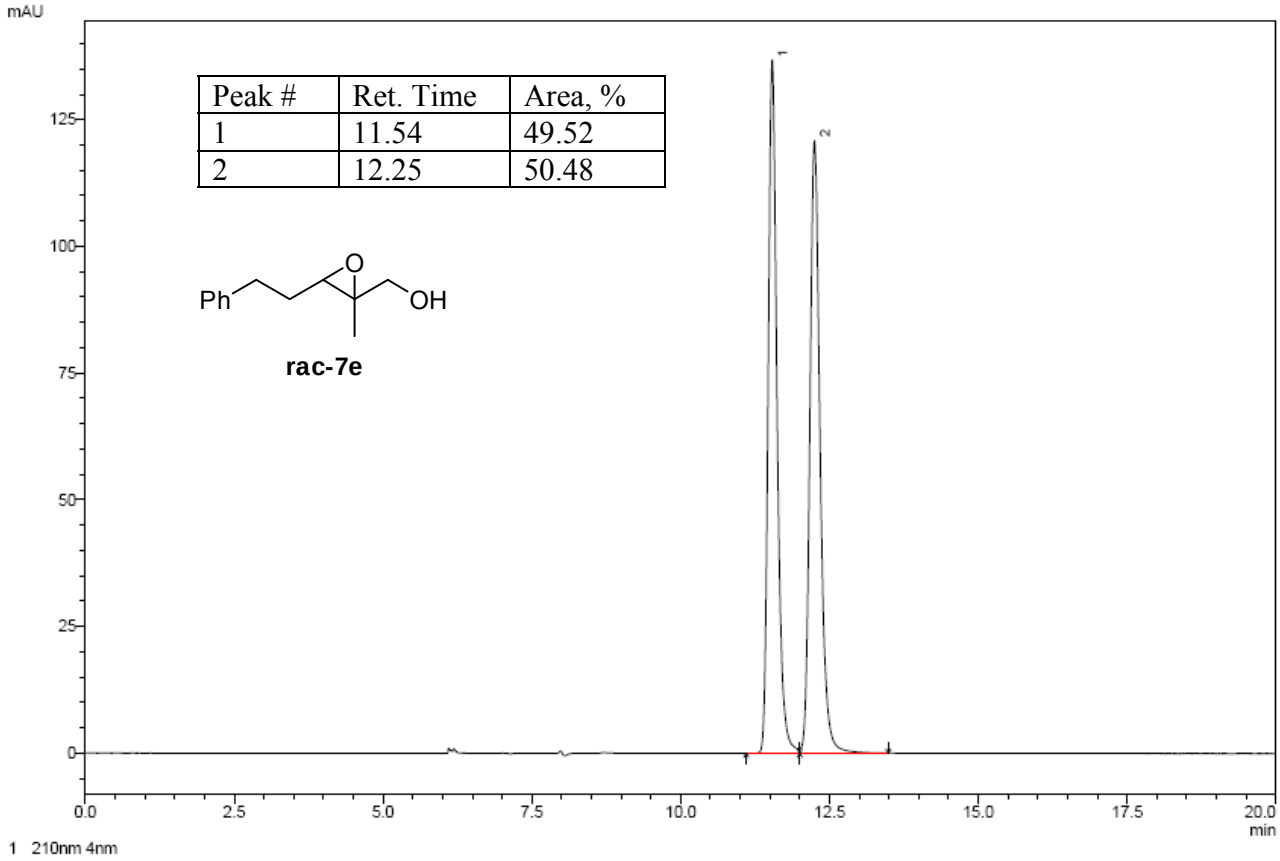
Peak #	Ret. Time	Area, %
1	40.15	7.91
2	40.71	8.04
3	45.22	42.0
4	46.36	42.1

B0/I513S876_2010_01_28_15_58_22;1 28-JAN-10



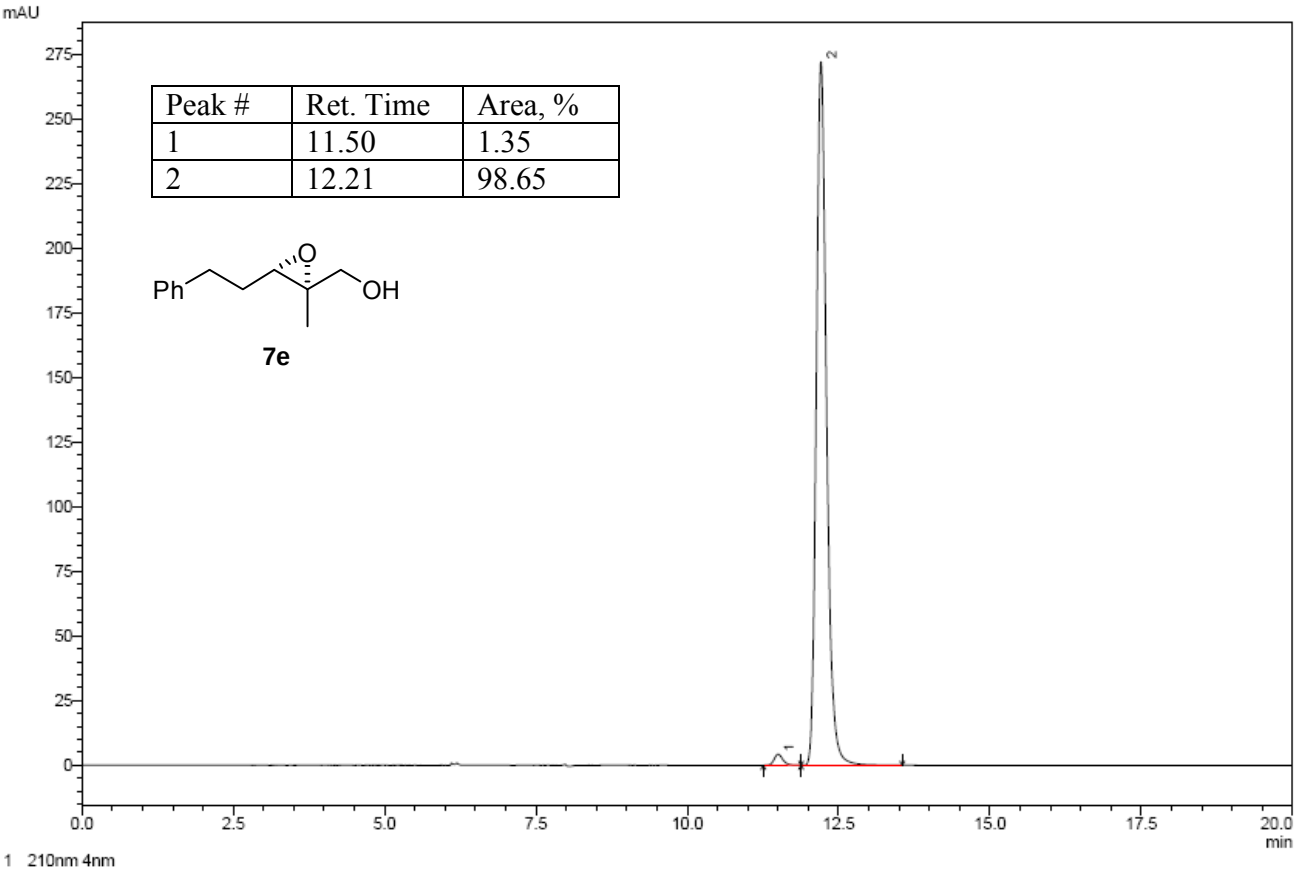
4e

Peak #	Ret. Time	Area, %
1	40.15	--
2	40.71	--
3	45.22	98.6
4	46.36	1.43



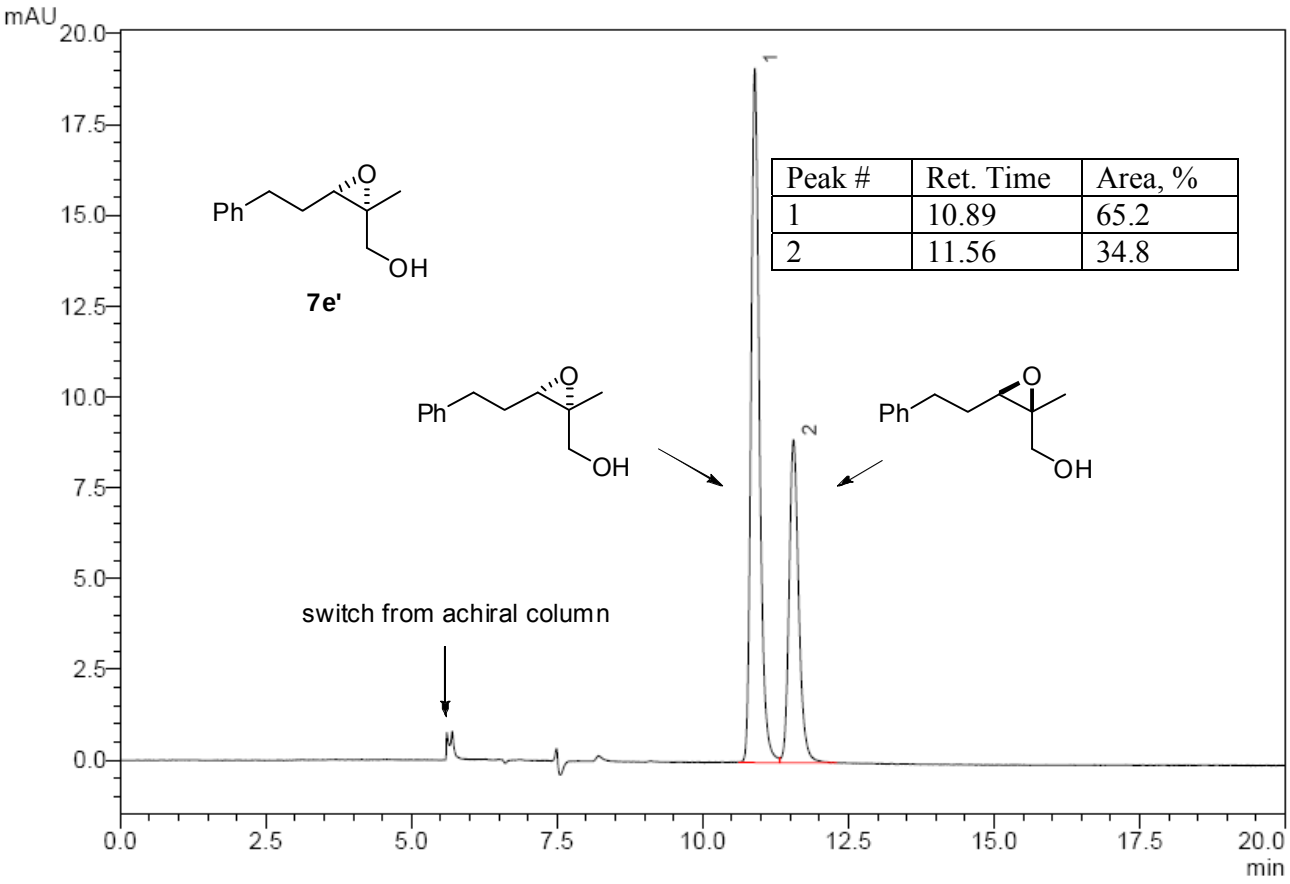
Peak #	Ret. Time	Area, %
1	11.54	49.52
2	12.25	50.48

rac-7e

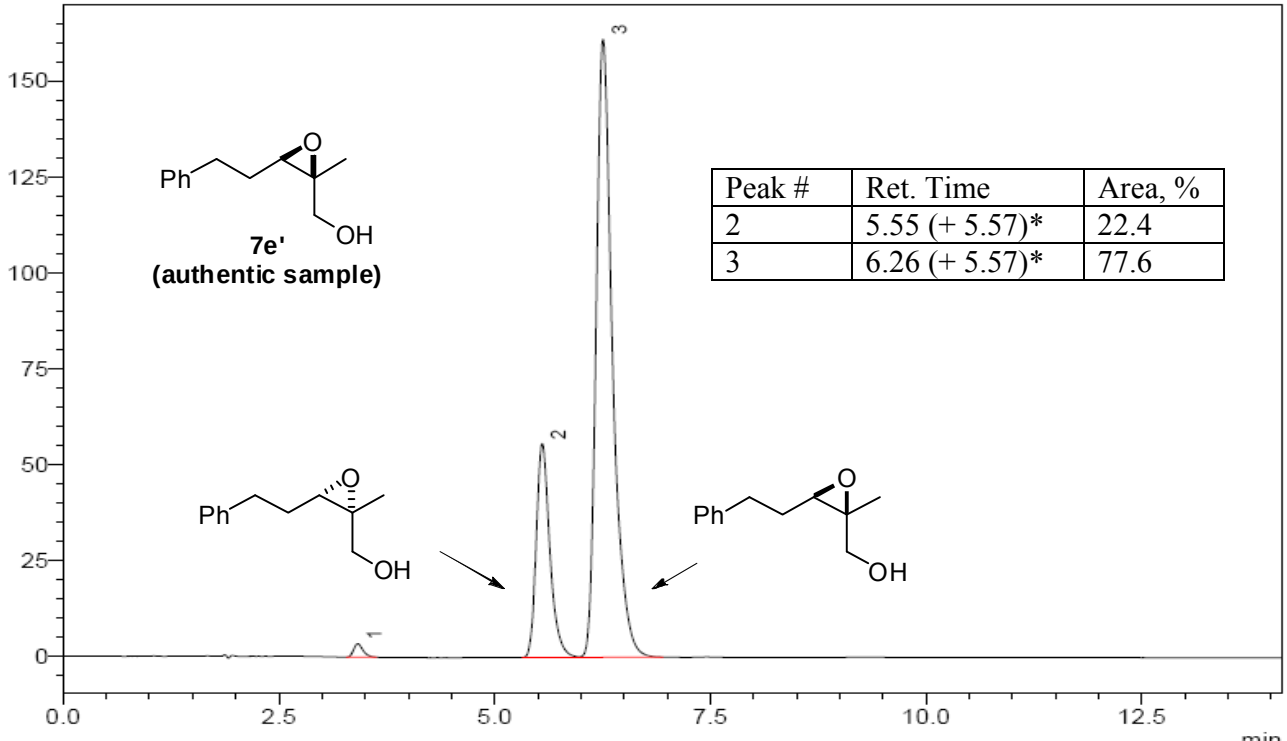


Peak #	Ret. Time	Area, %
1	11.50	1.35
2	12.21	98.65

7e

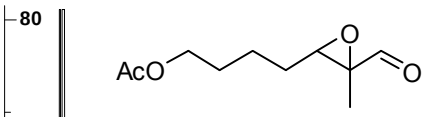


Peak #	Ret. Time	Area, %
1	10.89	65.2
2	11.56	34.8



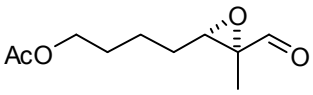
Peak #	Ret. Time	Area, %
2	5.55 (+ 5.57)*	22.4
3	6.26 (+ 5.57)*	77.6

* The minor diastereomer **7e'** was pre-eluted on an achiral column for 5.57 min to separate diastereomers before the switch to the chiral column, while the authentic sample **7e'** was injected directly on the chiral column. Hence the retention times differ by approximately 5.57 min. Column type, solvent system and all other parameters were otherwise identical (see S-18).



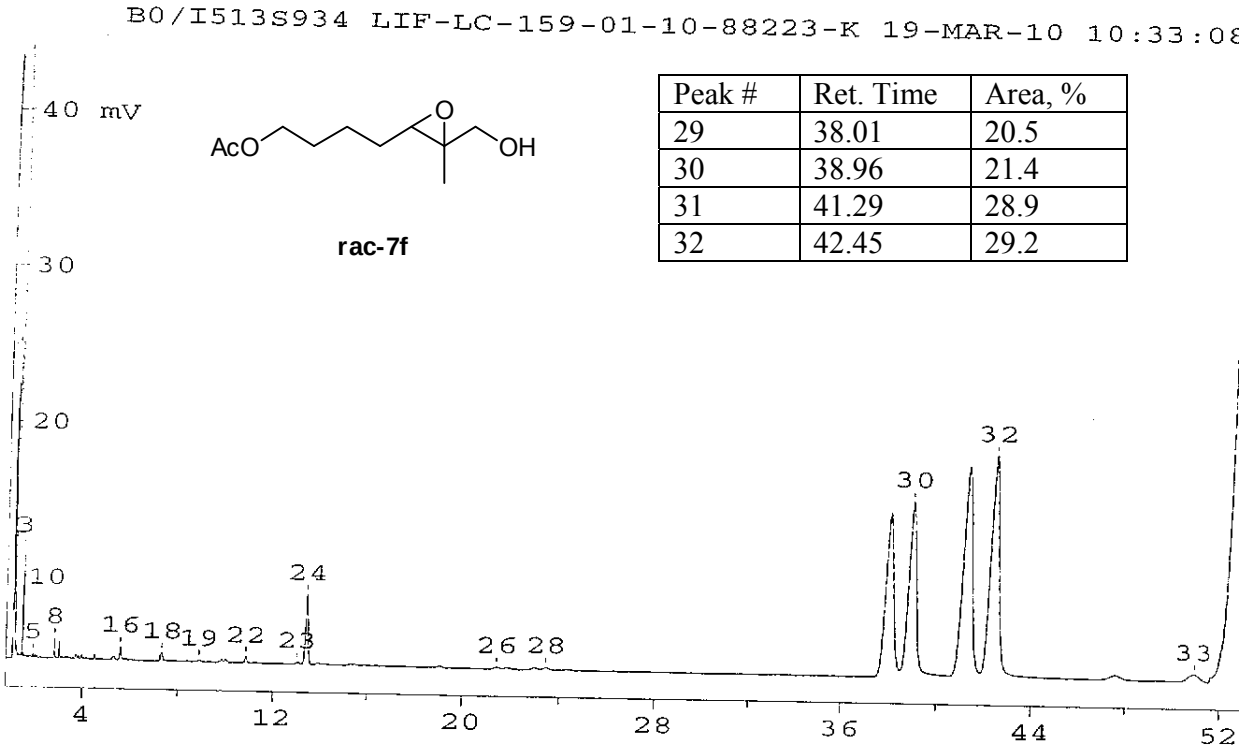
rac-4f

Peak #	Ret. Time	Area, %
1	22.24	25.9
2	23.96	26.3
3	31.82	23.7
4	33.12	24.1

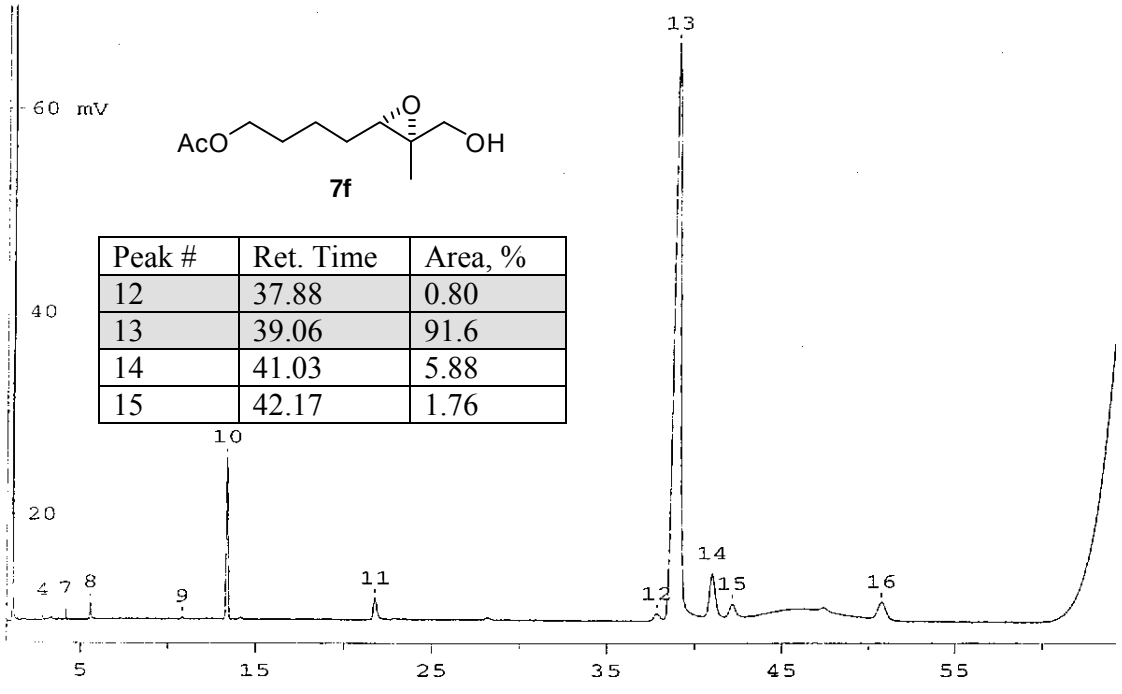


4f

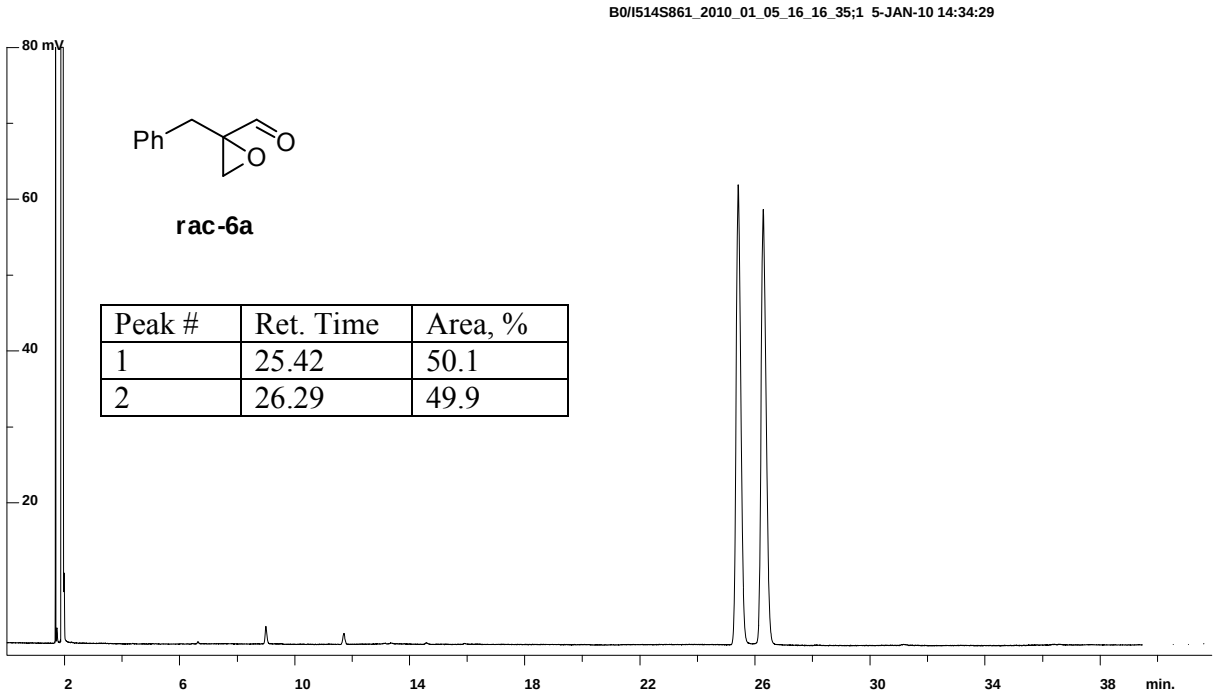
Peak #	Ret. Time	Area, %
1	22.08	5.47
2	23.75	4.21
3	31.57	1.17
4	33.49	89.2



Peak #	Ret. Time	Area, %
29	38.01	20.5
30	38.96	21.4
31	41.29	28.9
32	42.45	29.2

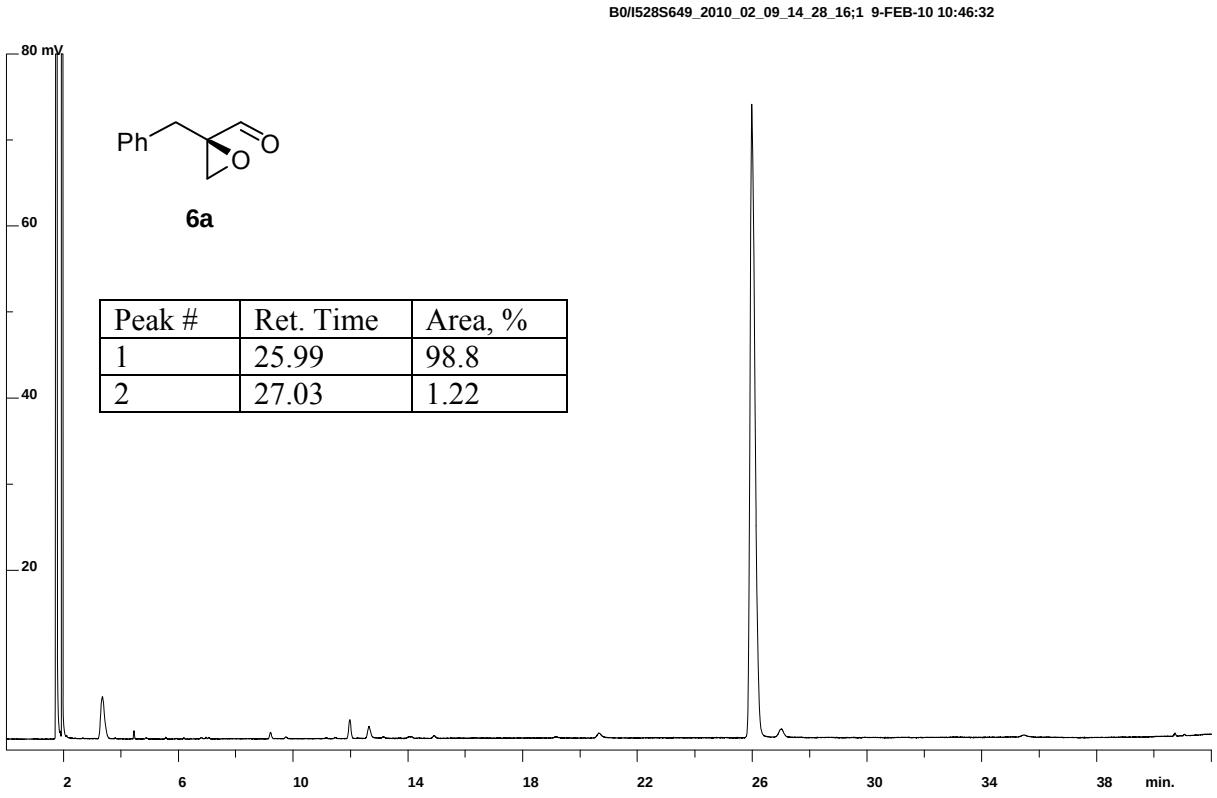


Peak #	Ret. Time	Area, %
12	37.88	0.80
13	39.06	91.6
14	41.03	5.88
15	42.17	1.76



rac-6a

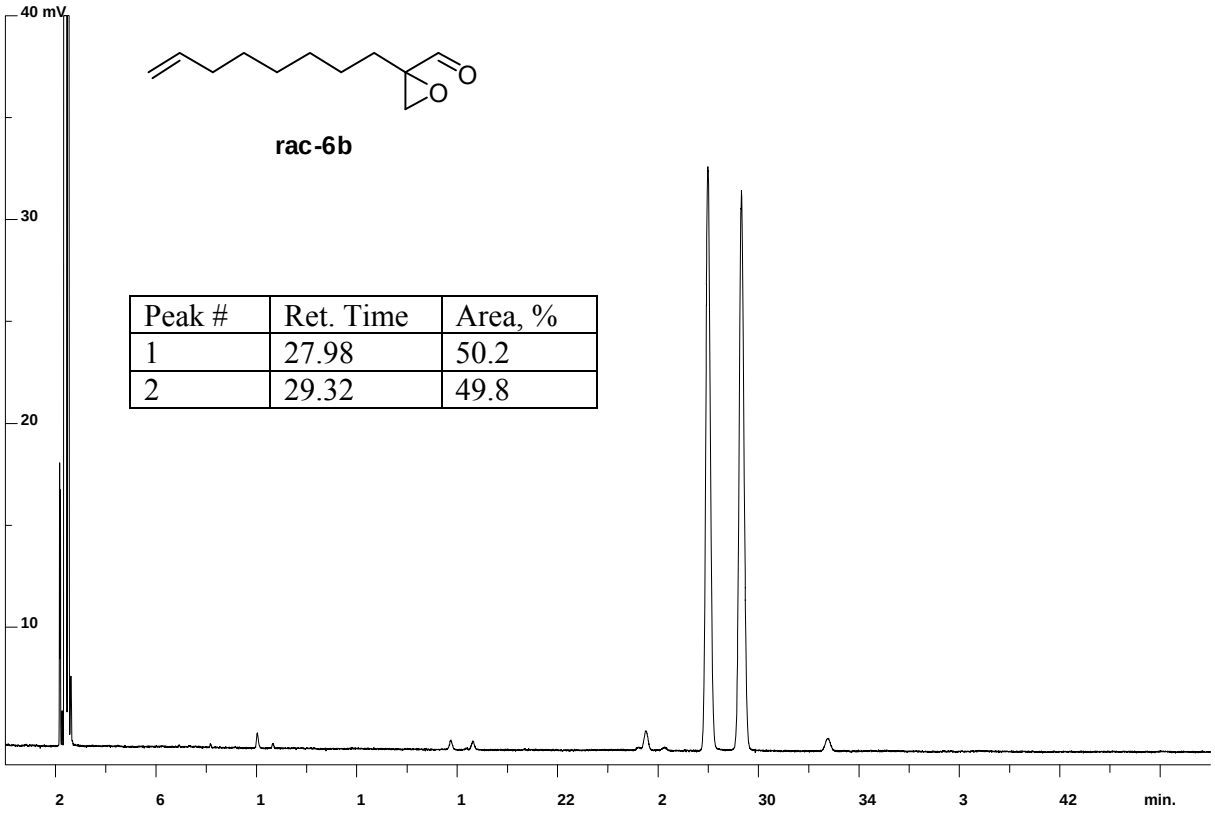
Peak #	Ret. Time	Area, %
1	25.42	50.1
2	26.29	49.9



6a

Peak #	Ret. Time	Area, %
1	25.99	98.8
2	27.03	1.22

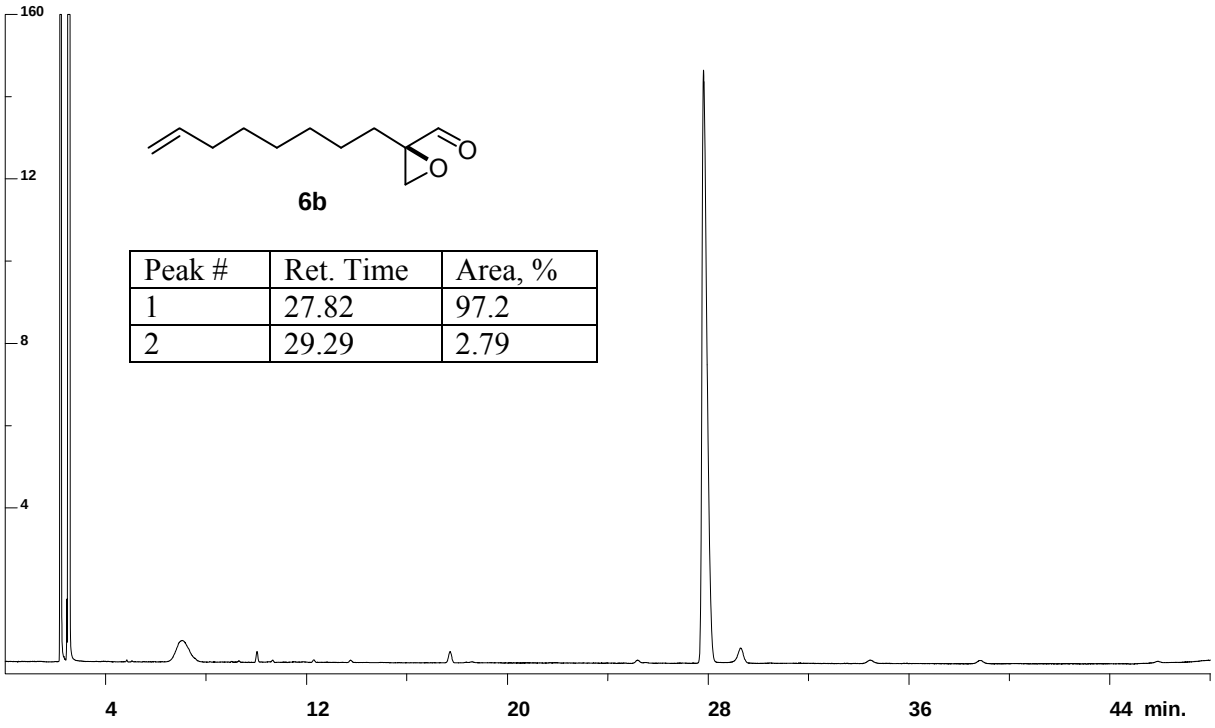
B0/I514S924_2010_02_18_10_04_49;1 18-FEB-10



rac-6b

Peak #	Ret. Time	Area, %
1	27.98	50.2
2	29.32	49.8

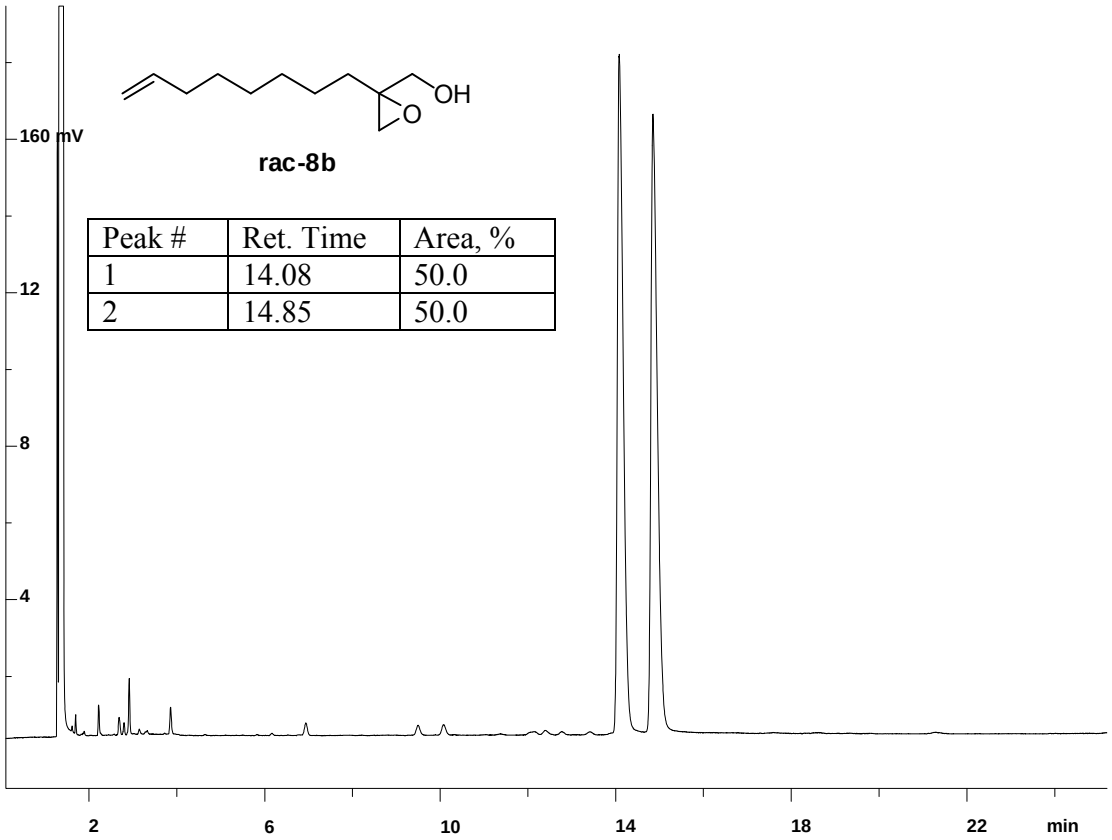
B0/I514S934_2010_02_23_11_26_10;1 23-FEB-10



6b

Peak #	Ret. Time	Area, %
1	27.82	97.2
2	29.29	2.79

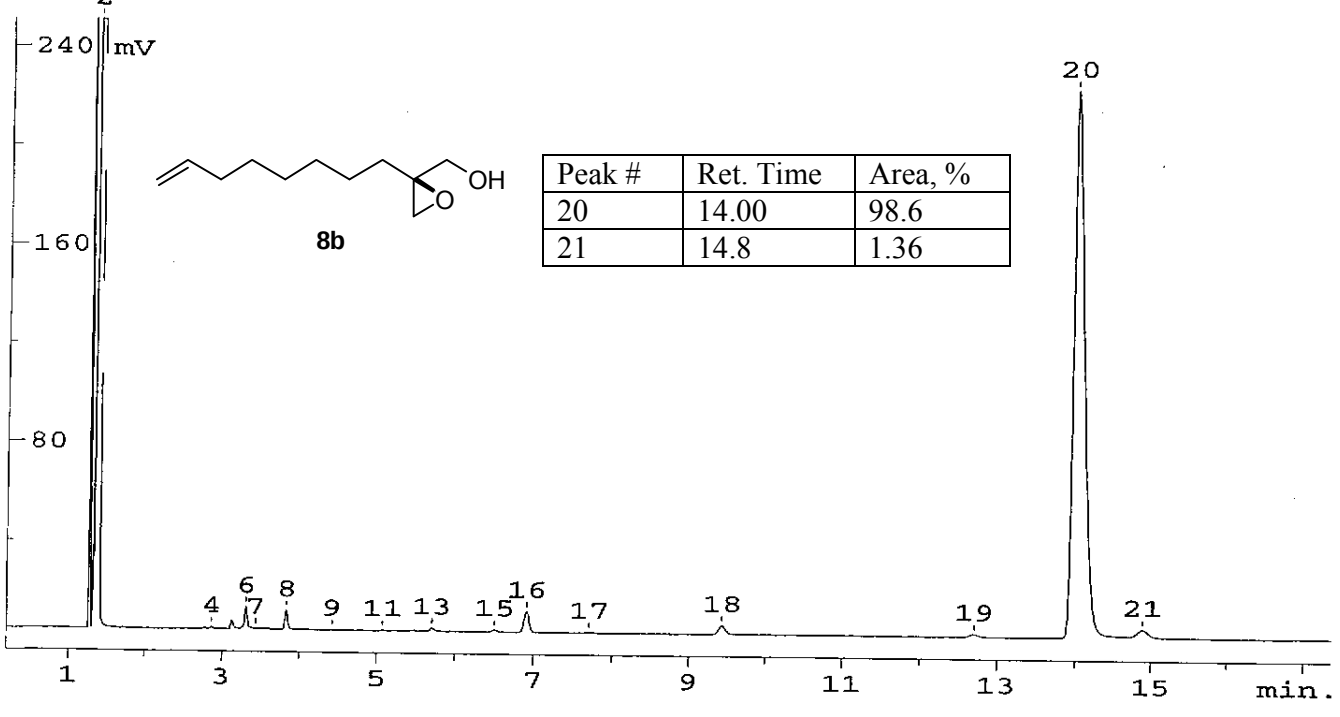
B0/I510S789_2010_02_23_14_06_22;1 23-FEB-10



rac-8b

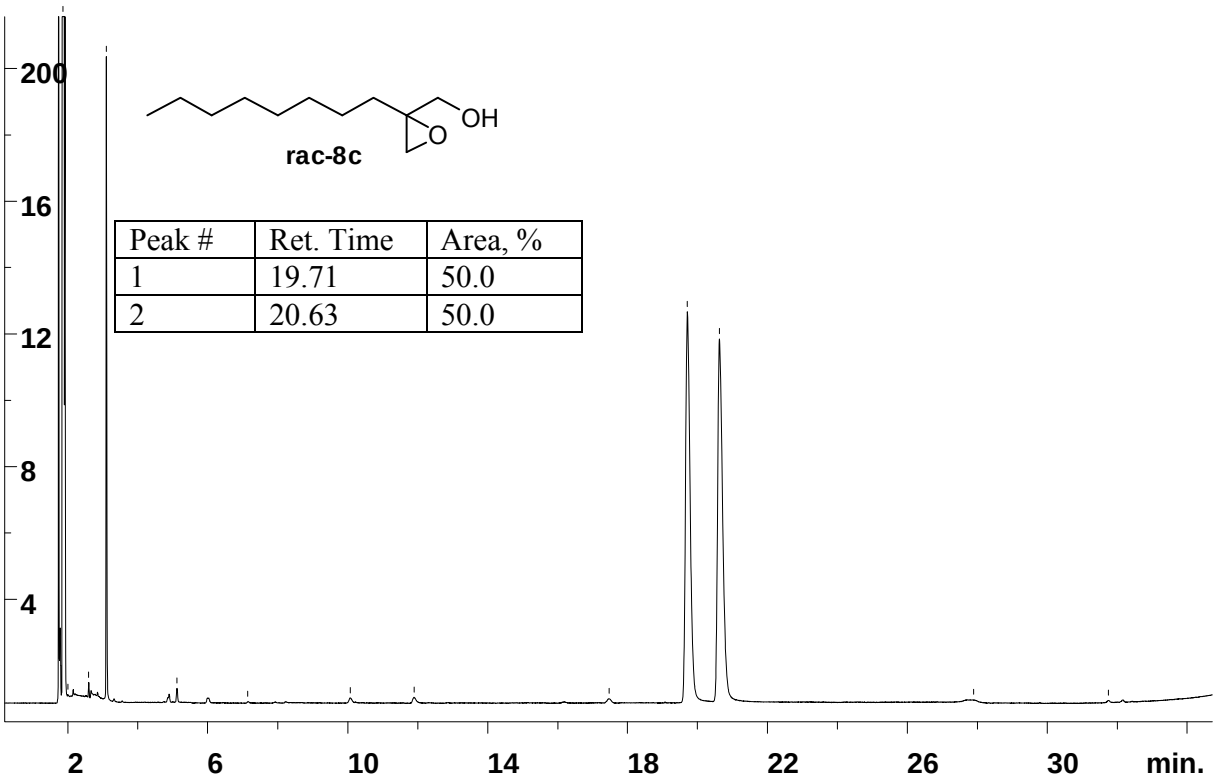
Peak #	Ret. Time	Area, %
1	14.08	50.0
2	14.85	50.0

B0/I513S970 10/88304 LIF-LC-197-01 in CDCl3 22-APR-10 12:31:03



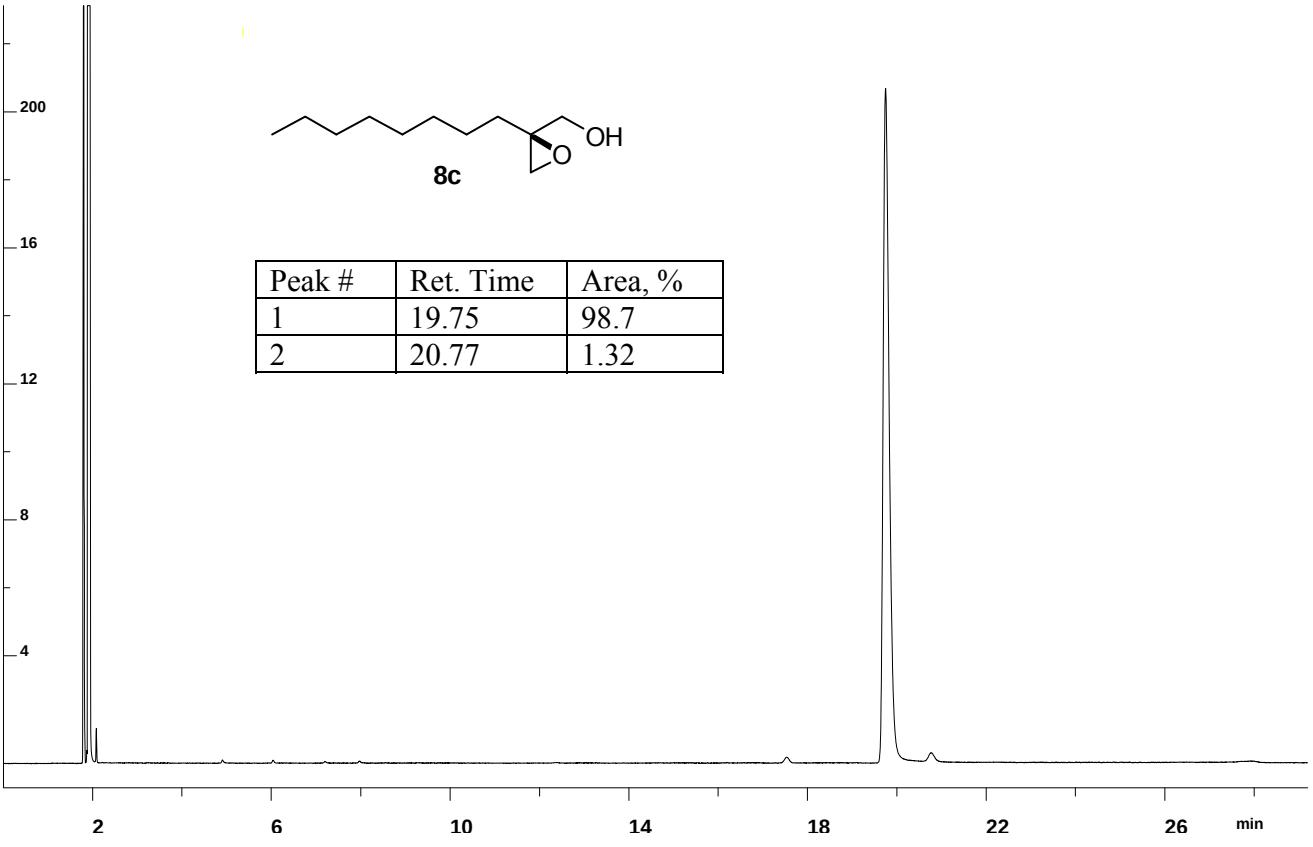
8b

Peak #	Ret. Time	Area, %
20	14.00	98.6
21	14.8	1.36



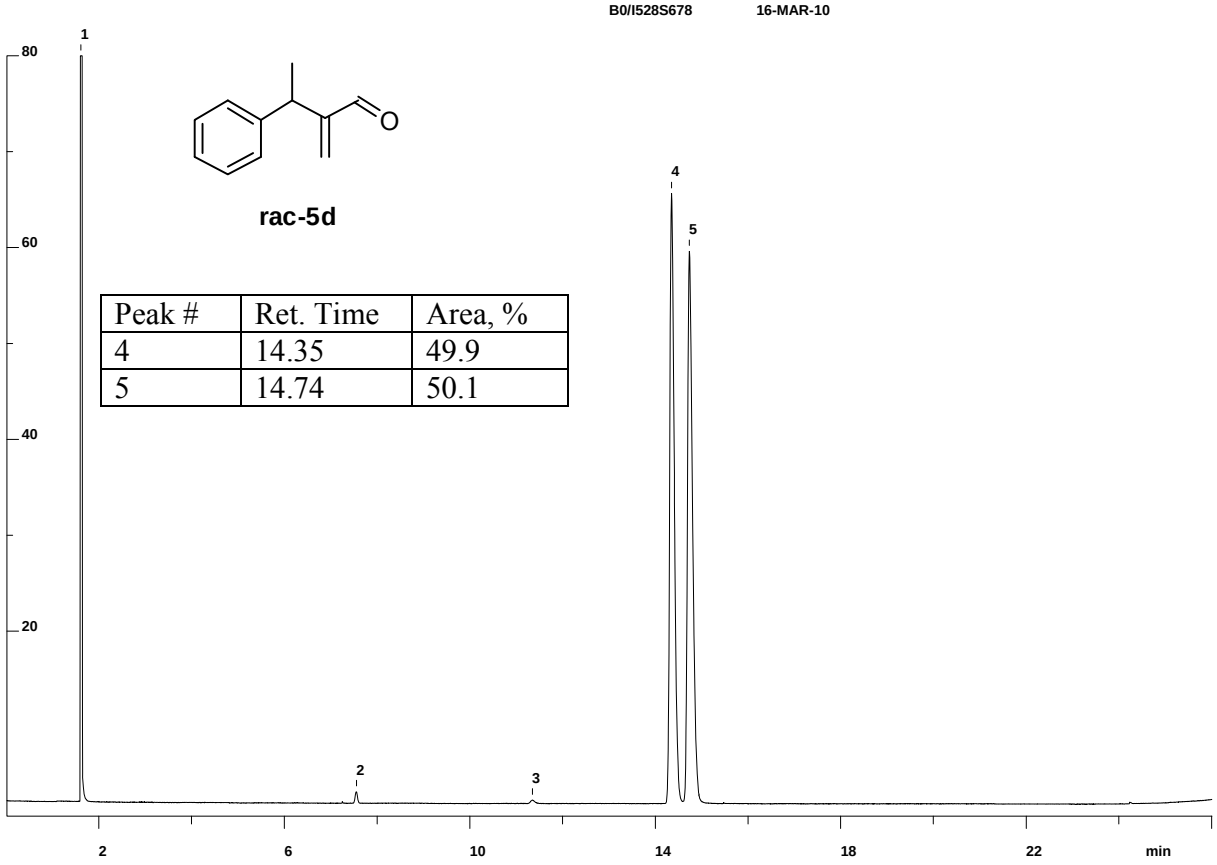
rac-8c

Peak #	Ret. Time	Area, %
1	19.71	50.0
2	20.63	50.0

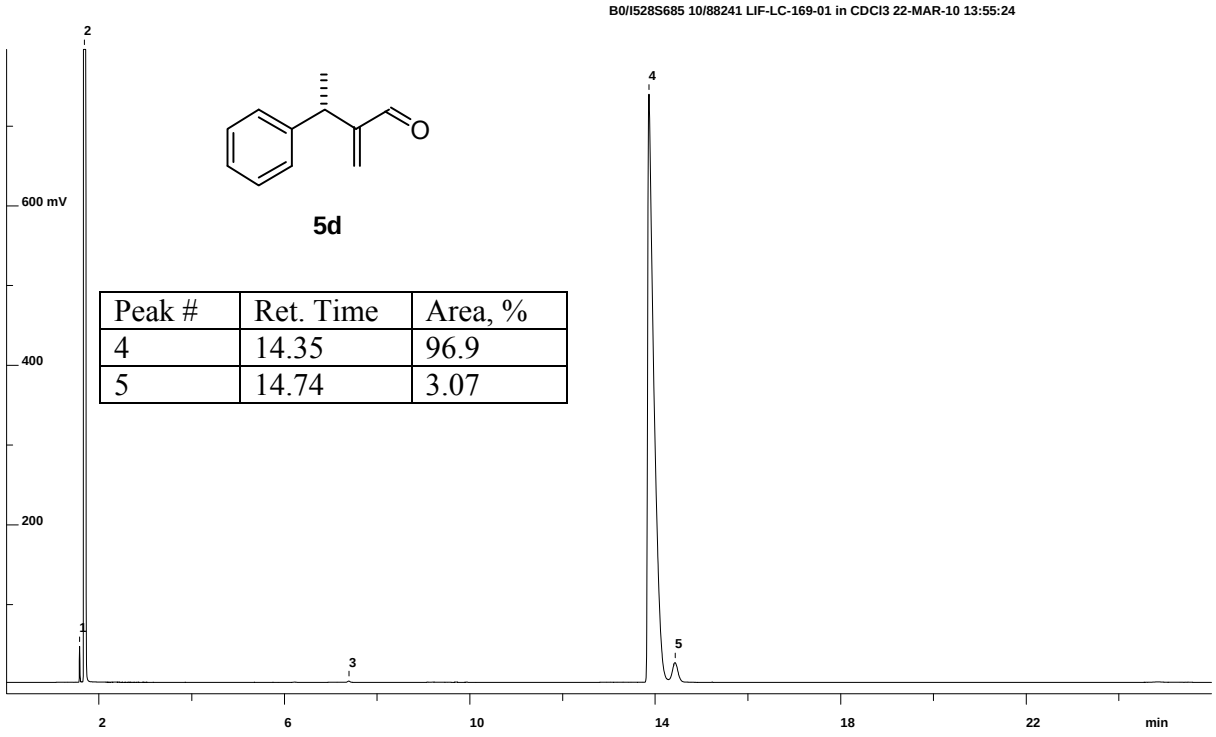


8c

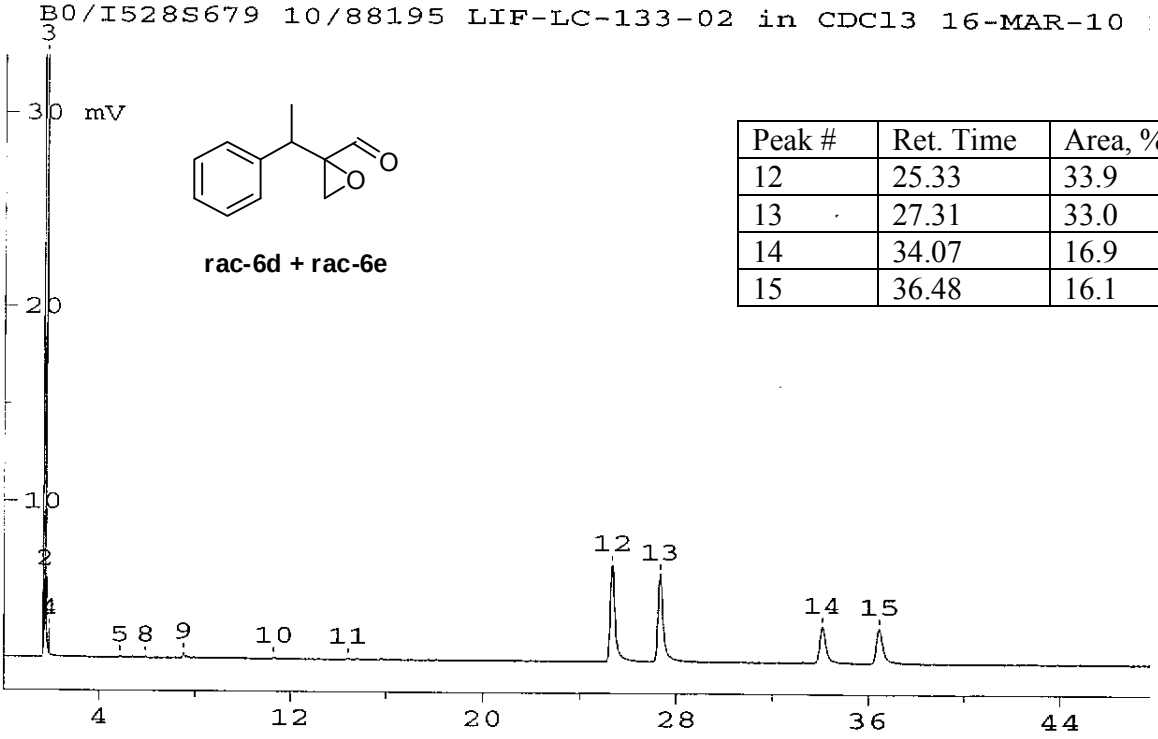
Peak #	Ret. Time	Area, %
1	19.75	98.7
2	20.77	1.32



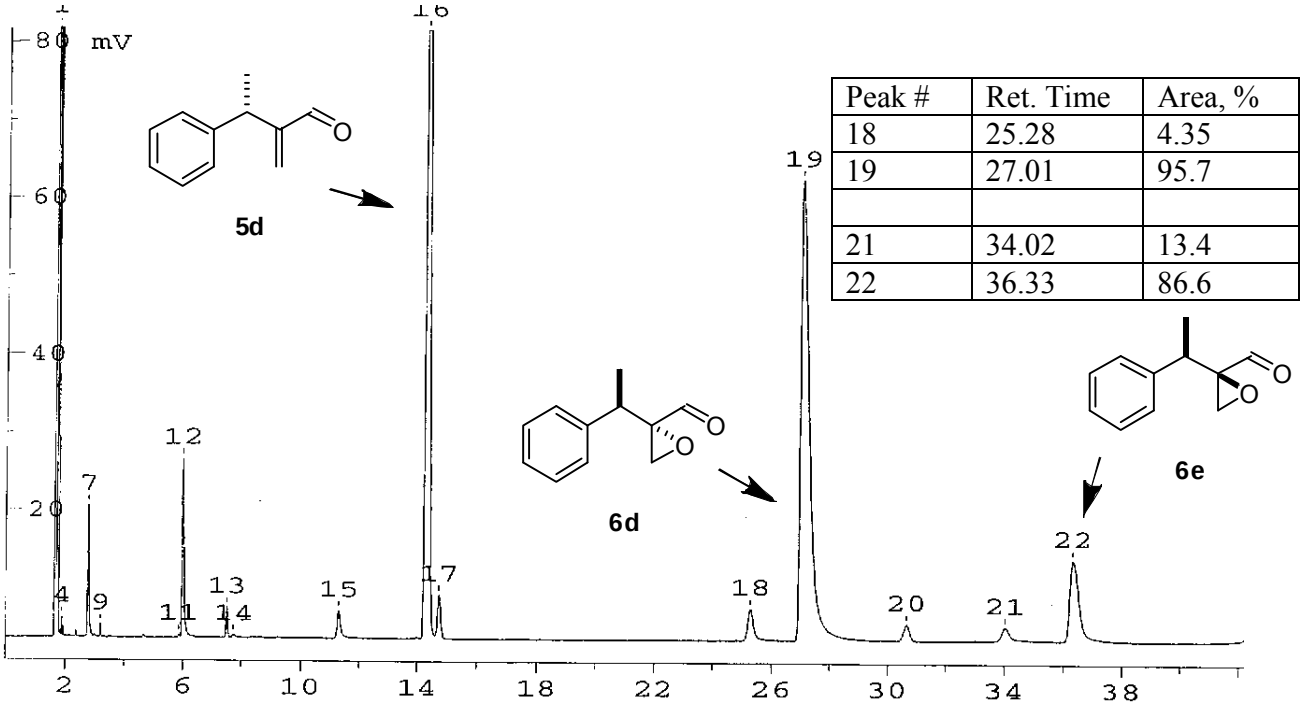
Peak #	Ret. Time	Area, %
4	14.35	49.9
5	14.74	50.1



Peak #	Ret. Time	Area, %
4	14.35	96.9
5	14.74	3.07



Peak #	Ret. Time	Area, %
12	25.33	33.9
13	27.31	33.0
14	34.07	16.9
15	36.48	16.1



Peak #	Ret. Time	Area, %
18	25.28	4.35
19	27.01	95.7
21	34.02	13.4
22	36.33	86.6