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Published in:
Organic Letters

DOI:
10.1021/ol800698t

Formation of enantiopure 5-substituted oxazolidinones through enzyme-catalysed kinetic resolution of epoxides

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Contents

General methods

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 300 (^{1}H 300 MHz and ^{13}C 75.5 MHz) spectrometer in $CDCl_3$. Chemical shifts (δ) are given in ppm downfield from TMS as the internal standard. Coupling constants are given in Hz. Mass spectra were recorded on Micromass Quattromicro. Capillary voltage 3.5 kV, cone voltage 40eV. Infrared spectra were recorded on a Bruker-Vector 22 spectrometer. Melting points were determined on Electrothermal 9100 apparatus and are uncorrected. Enzymatic reactions were monitored by GC using a chiral column (Chiraldex G-TA, 30 m x 0.25 mm x 0.25 μm, Astec). GC analysis was performed on a Varian 3350 gas chromatograph equipped with FID detector (set at 250 ^{o}C) and a split injector (set at 250 ^{o}C), using N_2 as a carrier gas, set at a column head pressure of 13 psi. HPLC analysis was performed on a Hewlet-Packard instrument Series 1050 with UV detector at 210 nm using a chiral column (Chirallica PST 1, 250 mm x 4.6 mm x 5 μm, Chirallica d.o.o.). Optical rotations were measured on an Optical Activity LTD automatic polarimeter AA-10. Column chromatography was done using silica gel (Merck type 9385, 230-400 mesh). TLC was performed on 0.25 mm silica gel 60-F plates (Merck). Spots

were visualised after dipping the TLC plate in a mixture of phosphomolybdic acid (25 g): cerium(II)sulfate (7.5 g): sulfuric acid (25 mL): water (495 mL) and subsequent heating.

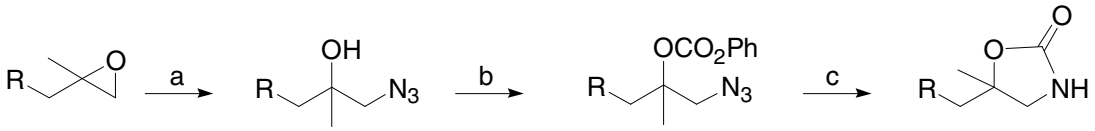
Materials

Wild-type halohydrin dehalogenase from *Agrobacterium radiobacter* (HheC) was produced and purified from recombinant *E. coli* cells as described before.[1] Commercial grade reagents and solvents were used without further purification. The commercially available substrates 1,2-epoxybutane (**1a**), epichlorohydrin (**1e**), glycidol (**1g**), 2,3-epoxypropyl-benzene (**1h**) and enantiomerically pure (*R*)-**1a**, (*R*)-**1e** and (*S*)-**1e**, were supplied by Aldrich, as well as 5-chloromethyl-oxazolidin-2-one (**2e**). 1,2-Epoxy-2-methylbutane (**1b**) and 2-(chloromethyl)-2-methyloxirane (**1c**) were purchased from Acros Organics. 3,3-Dimethyl-1,2-epoxybutane (**1j**) and 1,2-epoxy-3-methylbutane (**1k**) were purchased from Lancaster, and 2-vinyloxyrane (**1l**) from Fluka. 2-Cyclohexyl-oxirane (**1i**) was prepared from corresponding aldehyde as previously described.[2] Other racemic epoxides (**1d** and **1f**) were prepared by *m*-CPBA oxidation of the corresponding alkenes. (*R*)-**1d** (80% ee) was prepared by HheC catalysed kinetic resolution of *rac*-**1d**.

Preparation of racemic oxazolidinones

Racemic 5-ethyl-oxazolidin-2-one (**2a**) was prepared according to a modified literature procedure.[3] A mixture of 1-amino-2-butanol (1.5 g, 16.8 mmol), anhydrous K_2CO_3 (225 mg, 1.6 mmol) and diethyl carbonate (3 mL) was stirred under reflux. Over a period of 1 h the ethanol was distilled from the reaction mixture. The resulting mixture was cooled to room temperature, diluted with CH_2Cl_2 and washed with water. Purification of the residue by column chromatography (SiO_2, EtOAc: hexane =2:8) gave product as a white solid (1.1 g, 57% yield).

Racemic **2b**, **2c** and **2d** were prepared in a three-step procedure starting from *rac* epoxides **1b-1d**.



1b-d

R = CH_3, Cl, Br

(a) NaN_3, H_2O pH 4.2, 30 °C, 5 h; (b) PhOCOCl, Pyridine, CH_2Cl_2, rt; (c) H_2, Pd/C, MeOH, rt, 18 h.

Representative procedure.[4,5] To a soluton of epoxide **1c** (270 mg, 2.5 mmol) in water (4 mL), NaN_3 was added (840 mg, 13.0 mmol) followed by acetic acid (2.3 mL). The reaction mixture was stirred at 30 °C for 5 h. The mixture was extracted with CH_2Cl_2 (2 x 5 mL), saturated with NaCl and extracted again with CH_2Cl_2 (2 x 5 mL). The organic extracts were washed with 10% NaOH and dried over Na_2SO_4. The residue

[1] Tang, L.; van Merode, A. E.; Lutje Spelberg, J. H.; Fraaije, M. W.; Janssen, D. B. *Biochemistry* **2003**, *42*, 14057-14065.
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[3] Gage, J. R.; Evans, D. A. *Organic Synthesis*, Wiley: New York, **1993**, *Coll. Vol. 8, p 528.*
[4] Fringuelli, F.; Piermatti, O.; Piazzo, F.; Vaccaro, L. *J. Org. Chem.* **1999**, *64*, 6094-6096.
[5] Hameršak, Z.; Šepac, D.; Žiher, D.; Šunjić, V. *Synthesis* **2003**, 375-382.

was purified by chromatography (SiO_2, EtOAc: hexane =3:7) providing the pure 1-azido-3-chloro-2-methyl-2-propanol as colorless oil (281 mg, 75% yield). ^{1}H NMR ($CDCl_3$) δ 1.33 (3H, s), 2.34 (1H, s), 3.40 (1H, d, *J*= 12.4 Hz), 3.45 (1H, d, *J*= 12.4 Hz), 3.54 (1H, d, *J*= 11.2 Hz), 3.58 (1H, d, *J*= 11.2 Hz). ^{13}C NMR ($CDCl_3$) δ 22.9, 50.6, 57.5, 72.4

The resulting azidoalcohol (150 mg, 1.0 mmol) was dissolved in 8 mL of CH_2Cl_2, followed by addition of pyridine (200 μL, 4.0 mmol) and phenylchloroformate (400 μL, 2.8 mmol). After stirring overnight at room temperature, the reaction mixture was poured on H_2O (30 mL) and extracted with EtOAc (3 x 40 mL). The extracts were washed with H_2O, aqueous bicarbonate solution, dried with Na_2SO_4, and the solvent was evaporated. The crude product was purified by chromatography (SiO_2, CH_2Cl_2: hexane =2:8) providing the pure 2-azido-1-(chloromethyl)-1-methylethyl phenyl carbonate (247 mg, 91% yield). ^{1}H NMR ($CDCl_3$) δ 1.68 (3H, s), 3.74 (1H, d, *J*= 12.9 Hz), 3.81 (1H, d, *J*= 12.9 Hz), 3.85 (1H, d, *J*= 11.7 Hz), 4.04 (1H, d, *J*= 11.7 Hz), 7.18-7.4 (5H, m). ^{13}C NMR ($CDCl_3$) δ 19.8, 45.9, 54.4, 83.6, 120.9, 121.0, 126.2, 126.3, 129.5, 129.6, 150.7.

The obtained carbonate (242 mg, 0.90 mmol) was dissolved in MeOH (2 mL) and 10% Pd/C (50 mg) was added. Hydrogenation was performed in a closed system at room temperature and at atmospheric pressure of H_2, and the mixture was stirred overnight. The crude product was obtained by filtration of the reaction mixture and purified by chromatography (SiO_2, EtOAc: CH_2Cl_2 =1:1). Pure *rac*-**2c** was obtained in 78% yield (105 mg). The NMR data were identical with biocatalytically prepared (*S*)-**2c**.

Preparation of 3-benzoyl-5-chloromethyl-oxazolidin-2-one (3e)

To a solution of racemic oxazolidinone **2e** (135 mg, 1.0 mmol) in dry THF (4 mL), NaH (1.1 mmol) was added under the inert atmosphere, followed by the addition of benzoyl chloride (300 μL, 2.6 mmol) at 0°C. The reaction mixture was stirred at room temperature for 2.5 h, quenched with an aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4. The residue was purified by chromatography (SiO_2, EtOAc: hexane =1:9 to EtOAc gradient elution) providing the pure *N*-benzoyl oxazolidinone (**3e**) as a white solid (173 mg, 72% yield). ^{1}H NMR ($CDCl_3$) δ 3.76 (1H, dd, J_1= 12.0 Hz, J_2= 3.8 Hz), 3.83 (1H, dd, J_1= 12.0 Hz, J_2= 5.0 Hz), 4.08 (1H, dd, J_1= 11.3 Hz, J_2= 5.6 Hz), 4.29 (1H, dd, J_1= 11.3 Hz, J_2= 8.5 Hz), 4.87-4.95 (1H, m), 7.42-7.69 (5H, m). ^{13}C NMR ($CDCl_3$) δ 44.7, 46.3, 71.7, 127.9, 128.5, 129.0, 132.5, 152.2, 169.4.

Following the same procedure *N*-benzoyl derivative of enantioenriched (*S*)-**2e** was prepared. The NMR data were identical to *rac*-**3e**.

Enzymatic preparation of chiral 5-substituted oxazolidinones

Racemic substrate (0.50 g, 100-250 mM) was dissolved in Tris-SO_4 buffer (0.5 M, pH 7.5) followed by addition of NaOCN and purified halohydrin dehalogenase (HheC). The mixture was stirred at room temperature and stopped at conversion <50%. The mixture was saturated with NaCl and extracted with ethylacetate. The organic phase was dried over Na_2SO_4.

(*R*)-5-ethyl-oxazolidin-2-one (2a). The reaction was carried out for 5 h in 27.5 mL buffer, following the general procedure, and using 0.50 g (6.9 mmol, 250 mM) of racemic **1a**, 230 mg (3.5 mmol) of NaOCN and 10 mg of HheC. After extraction, the solvent was evaporated together with unreacted epoxide. Without further purification **2a** was obtained in 47% yield (374 mg) as a white solid (chemically pure according to NMR); mp 57-58 °C. The product was determined to be in 80% ee by GC analysis. $[\alpha]^{24}_{D}$ +24.0 (c 1.04 $CHCl_3$). MS $(ES^+)[MH]^+$ m/z 116.0. Anal.: Calcd for $C_5H_9NO_2$: C, 52.16; H, 7.88; N, 12.17; Found; C, 52.07; H, 7.95; N, 12.14. ^{1}H NMR ($CDCl_3$) δ 1.01 (3H, t, *J*= 7.5 Hz), 1.66-1.87 (2H, m), 3.25 (1H, dd, J_1= 8.0 Hz, J_2= 8.0 Hz), 3.67 (1H, dd, J_1= 8.5 Hz, J_2= 8.5 Hz), 4.54-4.63 (1H, m), 6.06 (1H, bs). ^{13}C NMR ($CDCl_3$) δ 8.3, 27.4, 45.1, 77.7, 159.9. IR (KBr) 3283, 2968, 2921, 1732, 1244, 1085 cm^{-1}.

(*R*)-5-ethyl-5-methyloxazolidin-2-one (2b). The reaction was carried out for 2.5 h in 23 mL buffer, according the general procedure, and using 0.50 g (5.8 mmol, 250 mM) of racemic **1b**, 190 mg (2.9 mmol) of NaOCN and 10 mg of HheC. After extraction, the solvent was evaporated together with unreacted epoxide. Without further purification **2b** was obtained in 44% yield (330 mg) as a white solid and 97% ee as determined by GC analysis; mp 67-69 °C. $[\alpha]^{20}_{D}$ +10.9 (c 1.33 $CHCl_3$). MS $(ES^+)[MH]^+$ m/z 130.0. Anal.: Calcd for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84; Found; C, 55.74; H, 8.64; N, 10.82. ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, t, *J*= 7.5 Hz), 1.31 (3H, s), 1.61 (2H, q, *J*= 7.5 Hz), 3.16 (1H, d, *J*= 8.5 Hz) 3.28 (1H, d, *J*= 8.5 Hz), 6.58 (1H,bs). ^{13}C NMR ($CDCl_3$) δ 7.1, 24.5, 32.4, 50.2, 82.9, 159.5. IR (KBr) 3275, 2977, 1737, 1263, 1095, 980 cm^{-1}.

(*S*)-5-chloromethyl-5-methyloxazolidin-2-one (2c). The reaction was carried out for 60 min in 23.5 mL buffer, following the general procedure, using 0.50 g (4.7 mmol, 200 mM) of racemic **1c**, 305 mg (4.7 mmol) of NaOCN and 10 mg of HheC. After extraction and purification by chromatography (SiO_2, CH_2Cl_2: EtOAc =1:1), pure (*S*)-**2c** was obtained in 46% yield (325 mg, 93% ee) as a white solid; mp 124 °C. $[\alpha]^{20}_{D}$ – 15.1 (c 0.99 $CHCl_3$). MS $(ES^+)[MH]^+$ m/z 150.0, 151.9, Anal.: Calcd for $C_5H_8ClNO_2$: C, 40.15; H, 5.39; N, 9.36; Found; C, 40.19; H, 5.41; N, 9.33. ^{1}H NMR ($CDCl_3$) δ 1.56 (3H, s), 3.34 (1H, d, *J*= 9.0 Hz), 3.55 (1H, d, *J*= 11.5 Hz), 3.66 (1H, d, *J*= 11.5 Hz). 3.67 (1H, d, *J*= 9.0 Hz), 6.63 (1H, bs). ^{13}C NMR ($CDCl_3$) δ 23.9, 49.0, 63.0, 81.4, 159.0. IR (KBr) 3259, 2953, 1738, 1312, 1095, 988, 760 cm^{-1}.

(*S*)-5-bromomethyl-5-methyloxazolidin-2-one (2d). The reaction was carried out for 60 min in 33 mL Tris-SO_4 buffer, following the general procedure, and using 0.50 g (3.3 mmol, 100 mM) of racemic **1d**, 215 mg (3.3 mmol) of NaOCN and 10 mg of HheC. After extraction and purification by chromatography (SiO_2, CH_2Cl_2: EtOAc =1:1), (*S*)-**2d** (304 mg, 47%, 98% ee) was isolated as a white solid; mp 120 °C. $[\alpha]^{20}_{D}$ –22.8 (c 1.05 $CHCl_3$). MS $(ES^+)[MH]^+$ m/z 193.9, 195.9. Anal.: Calcd for $C_5H_8BrNO_2$: C, 30.95; H, 4.16; N, 7.22; Found; C, 30.99; H, 4.14; N, 7.25. ^{1}H NMR ($CDCl_3$) δ 1.62 (3H, s), 3.36 (1H, d, *J*= 9.0 Hz), 3.45 (1H, d, *J*= 10.5 Hz), 3.56 (1H, d, *J*= 10.5 Hz), 3.68 (1H, d, *J*= 9.0 Hz), 6.55 (1H, bs). ^{13}C NMR ($CDCl_3$) δ 24.5, 37.3, 49.9, 81.0, 158.9. IR (KBr) 3256, 2950, 1737, 1308, 1096, 986, 714 cm^{-1}.

(*S*)-5-chloromethyl-oxazolidin-2-one (2e). Racemic epichlorohydrin (**1e**) (250 mg, 2.7 mmol) was dissolved in Tris-SO_4 buffer (13 mL, 0.5 M, pH 7.5) followed by addition of NaOCN (265 mg, 4.0 mmol) and purified HheC (12.4 mg). The mixture was stirred at room temperature for 3 h (stopped when conversion

reached 100%). The mixture was lyophilized and the solid residue was dissolved in ethylacetate. Solids were removed by filtration and the filtrate was purified by chromatography (SiO_2, EtOAc). (*S*)-**2e** (199 mg, 54% yield) was isolated as a white solid; $[\alpha]^{25}_D$ – 6.7 (c 0.89 $CHCl_3$) and $[\alpha]^{25}_D$ + 12.5 (c 2 CH_2Cl_2). The ee (69%) was determined by HPLC analysis of the corresponding *N*-benzoyl derivative (*S*)-**3e**, prepared as described previously. MS (ES^+)$[MH]^+$ m/z 136.0, 138.0. Anal.: Calcd for $C_4H_6ClNO_2$: C, 35.44; H, 4.46; N, 10.33; Found; C, 35.59; H, 4.44; N, 10.25. ^{1}H NMR ($CDCl_3$) δ 3.56 (1H, ddd, J_1= 9.0 Hz, J_2= 5.8 Hz, J_3= 0.9 Hz), 3.70 (1H, dd, J_1= 11.5 Hz, J_2=6.3 Hz), 3.73 (1H, dd, J_1= 11.5 Hz, J_2=4.6 Hz), 3.78 (1H, dd, J_1= 8.9 Hz, J_2=8.8 Hz), 4.82-4.91 (1H, m), 5.75 (1H, bs). ^{13}C NMR ($CDCl_3$) δ 43.6, 44.4, 74.7, 159.3. IR (KBr) 3363, 3327, 2965, 2908 1748, 1240, 1077, 959, 769 cm^{-1}.

(*S*)-5-chloromethyl-oxazolidin-2-one (2e). (*S*)-epichlorohydrin ((*S*)-**1e**) (100 mg, 1.0 mmol, 97% ee) was dissolved in Tris-SO_4 buffer (10.5 mL, 0.5 M, pH 7.5) followed by addition of NaOCN (249 mg, 3.8 mmol) and purified HheC (3.0 mg). The mixture was stirred at room temperature for 1.5 h (stopped when conversion reached 100 %). The mixture was lyophilized and the solid residue was dissolved in ethylacetate. Solids were removed by filtration and the filtrate was purified by chromatography (SiO_2, EtOAc). (*S*)-**2e** (113 mg, 77% yield, 96% ee) was isolated as a white solid, mp 73-74 °C, $[\alpha]^{24}_D$ – 9.0 (c 1.06 $CHCl_3$), and used to prepare a crystal for X-ray analysis.

Racemisation of (*R*)-1e and (*R*)-1d

To 2.5 mL of Tris-SO_4 buffer (0.5 M, pH 7.5) containing optically pure epoxide (100 mM of (*R*)-**1e** or 50 mM of (*R*)-**1d**) purified HheC was added (0.75 mg). Samples of 100 μL were taken with regular time intervals, extracted with diethyl ether (1 mL), dried over anhydrous Na_2SO_4 and analysed by GC using a chiral column. The racemisation of (*R*)-**1e** was repeated in the presence of NaCl (25 mM). The racemisation of (*R*)-**1d** was repeated (a) in the presence of NaOCN (150 mM) and (b) in the presence of NaOCN (150 mM) and KBr (100 mM).

Determination of absolute configurations

Absolute configurations of epoxides were assigned by chiral GC analysis using reference compounds. The enantiomerically enriched epoxides (*R*)-**1b**,[2] (*S*)-**1c** (77% ee) and (*S*)-**1d** (90% ee) were prepared by (*R,R*)-(salen)CrN_3 catalysed ring opening with $TMSN_3$ according to Label and Jacobsen.[6]

The measured optical rotation of oxazolidinones **2a** and **2e** was compared with the literature values ((*R*)-**2a** 80% ee, $[\alpha]^{24}_D$ + 24.0 (c 1.04 $CHCl_3$), Lit.[7] (*S*)-**2a** 99.9% ee, $[\alpha]^{rt}_D$ – 14.7 (c 1.0 $CHCl_3$); (*S*)-**2e** 69% ee, $[\alpha]^{25}_D$ + 12.5 (c 2 CH_2Cl_2), Lit.[8] (*S*)-**2e** 100% ee, $[\alpha]^{20}_D$ + 18 (c 2 CH_2Cl_2). On the basis of crystal structure determination the absolute configuration of **2e** was confirmed. All other absolute configurations were assigned by analogy.

[6] Label, H.; Jacobsen, E. N. *Tetrahedron Lett*. **1999**, *40*, 7303-7306.
[7] Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Melchiorre, P.; Sambri, L. *Org. Lett*. **2005**, *7*, 1983-1985.
[8] Schierle-Arndt, K.; Kolter, D.; Danilemeier, K.; Steckhan, E. *Eur. J. Org. Chem*. **2001**, 2425-2433.

Crystalographic data

Suitable platelet-shaped crystals were obtained by recrystallisation from dichloromethane/hexane. $C_4H_6ClNO_2$, M_r = 135.55, monoclinic, $P2_1$, a = 9.1140(13), b = 5.6900(8), c = 10.7825(16) Å, β = 90.5123(18)°, V = 559.14(14) Å^3, Z = 4, D_x = 1.610 gcm^{-3}, $F(000)$ = 280, μ = 5.81 cm^{-1}, λ(MoK$\overline{\alpha}$) = 0.71073 Å, T = 100(1) K, 5015 reflections measured, *GooF* = 1.046, $wR(F^2)$ = 0.1321 for 2623 unique reflections and 193 parameters, 1 restraints and $R(F)$ = 0.0509 for 2535 reflections obeying the $F_o \geq 4.0\ \sigma(F_o)$ criterion of observability. The asymmetric unit consisted of two molecules of the title compound, which were linked by N-H…O hydrogen bonds into an infinite two-dimensional network. The adopted labelling scheme and the molecular geometry of the asymmetric unit are illustrated in the *PLUTO*[9] drawings of Fig. 1. The arrangement of molecules in the unit cell is shown in Fig. 2. Each asymmetric unit contains two formula units (= molecule). The monoclinic unit cell contains four moieties of the title compound. The chiral centers of C12 and C22 both showed the *S*-configuration.[10,11]

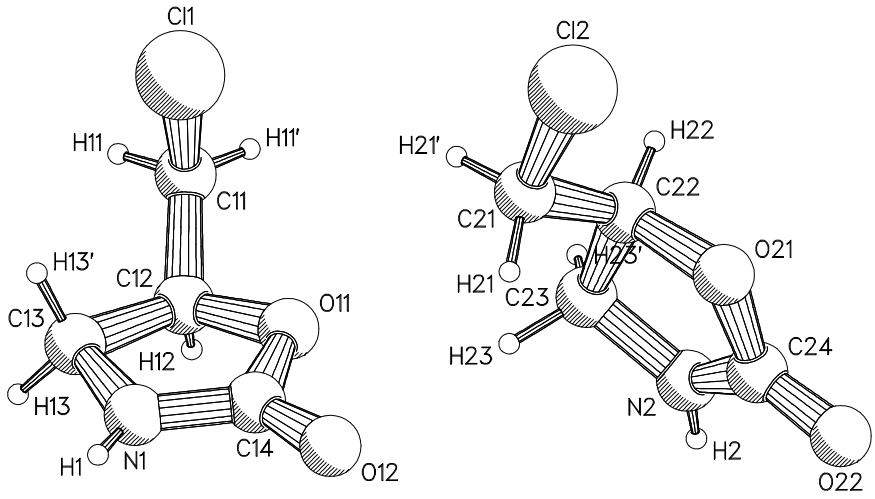


Fig. 1. Perspective *PLUTO*[9] drawings showing the configuration of molecule **1** and molecule **2** of the asymmetric unit with the adopted labelling scheme.

[9] Meetsma, A. (2007). *PLUTO. Molecular Graphics Program*. Version of Dec. 2007. University of Groningen, The Netherlands.
[10] Spek, A.L. (2007). *PLATON. Program for the Automated Analysis of Molecular Geometry* (*A Multipurpose Crystallographic Tool*). Version of Oct. 2007. University of Utrecht, The Netherlands. Spek, A.L. (2003). *J. Appl. Cryst.* **36**, 7-13.
[11] CCDC reference number 680924.

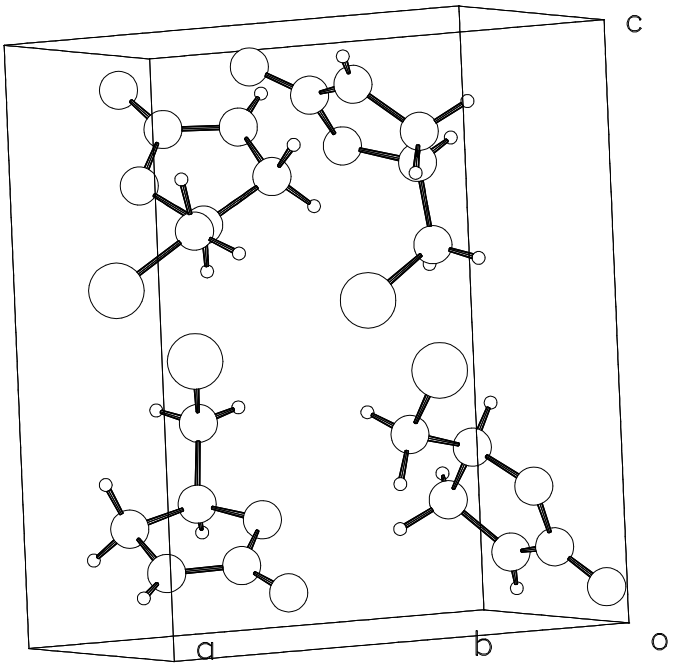


Fig. 2. View of a unit cell with minimal overlap.

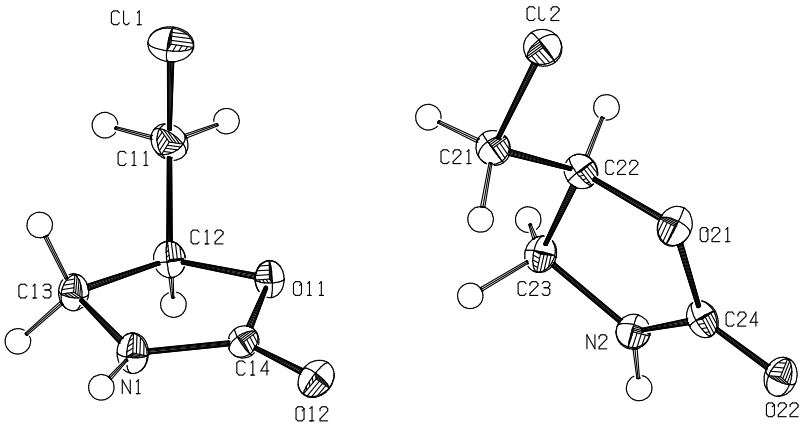


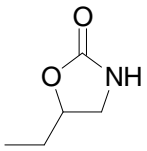
Fig. 3. Perspective *ORTEP*[0] drawing of the two crystallographic independent molecules **1** and molecule **2** of the title compound with the atom-labelling scheme of the non-hydrogen atoms. All atoms are represented by their displacement ellipsoids drawn at the 50% probability level. The hydrogen atoms are drawn with an arbitrary radius.

Determination of enantiomeric purity

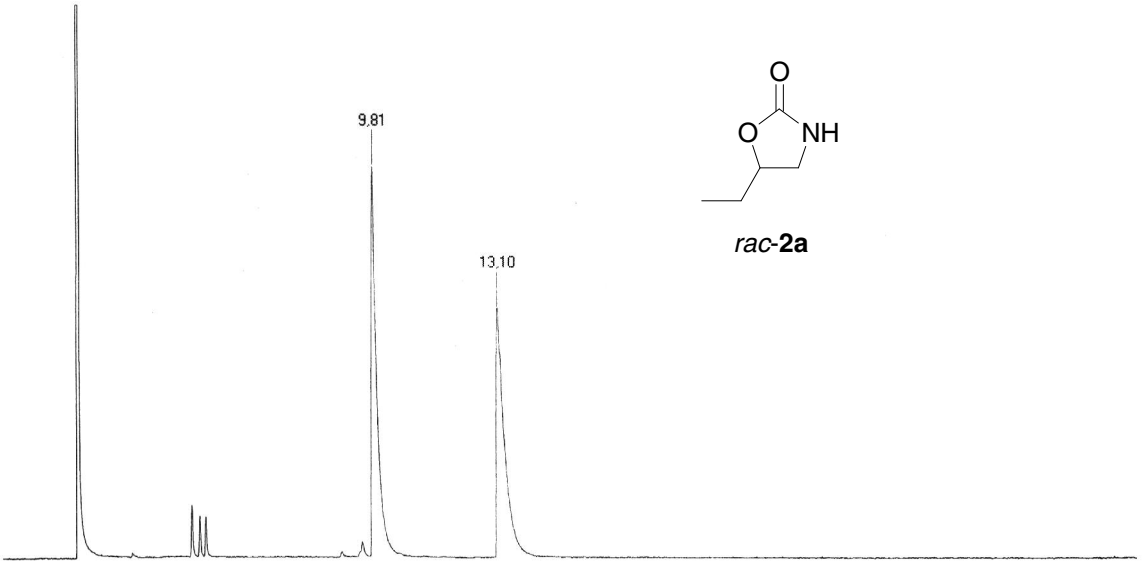
Enantiomeric excesses (ee's) of epoxides and oxazolidinones were determined by chiral GC analysis on a Chiraldex G-TA column (Col I) (30 m x 0.25 mm x 0.25 μm, Astec), or HPLC analysis on a Chirallica PST 1 column (Col II) (250 mm x 4.6 mm x 5 μm, Chirallica d.o.o.) of the corresponding *N*-benzoyl derivative (**3e**).

Table 1. Chiral GC and HPLC analysis.

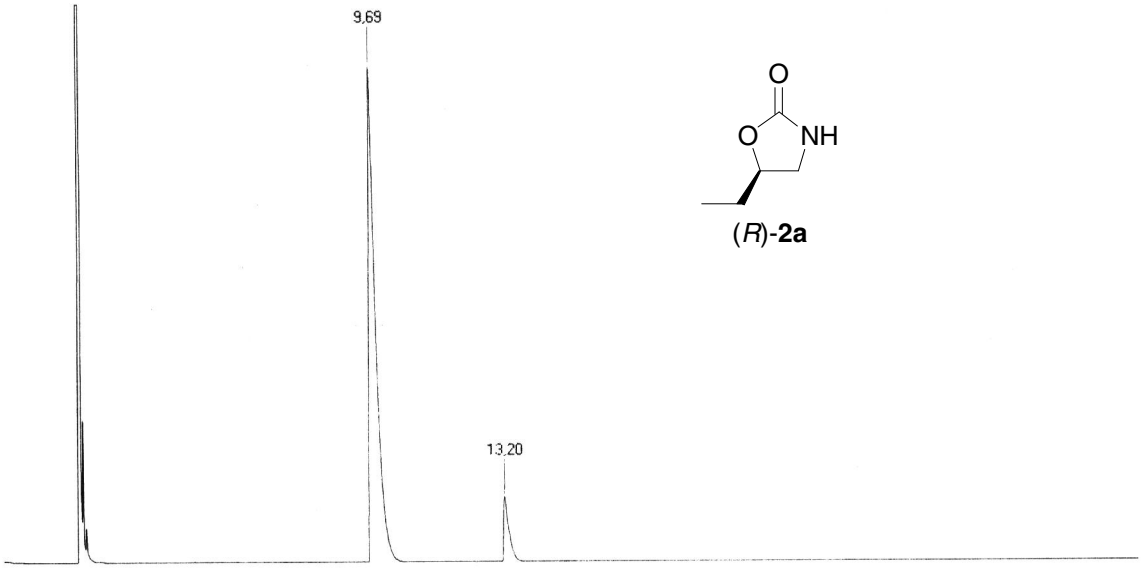
Compound	Col.	Conditions	Retention time (min)
1a	I	40 ºC, isothermal	3.2 (*R*) / 3.5 (*S*)
1b	I	40 ºC, isothermal	4.8 (*R*) / 5.3 (*S*)
1c	I	60 ºC, isothermal	10.2 (*R*) / 10.5 (*S*)
1d	I	70 ºC, isothermal	11.3 (*R*) / 12.1 (*S*)
1e	I	70 ºC, isothermal	6.0 (*S*) / 6.8 (*R*)
2a	I	180 ºC, isothermal	9.7 (*R*) / 13.2 (*S*)
2b	I	180 ºC, isothermal	9.3 (*R*) / 10.2 (*S*)
2c	I	180 ºC, isothermal	16.3 (*R*) / 21.3 (*S*)
2d	I	180 ºC, isothermal	23.3 (*R*) / 29.2 (*S*)
3e	II	EtOH/Hexane (25:75), 1 mL/min	13.1 (*S*) / 14.9 (*R*)



GC conditions: Chiraldex G-TA, 180 ºC, isothermal

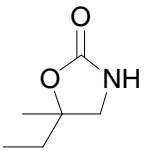


rac-**2a**

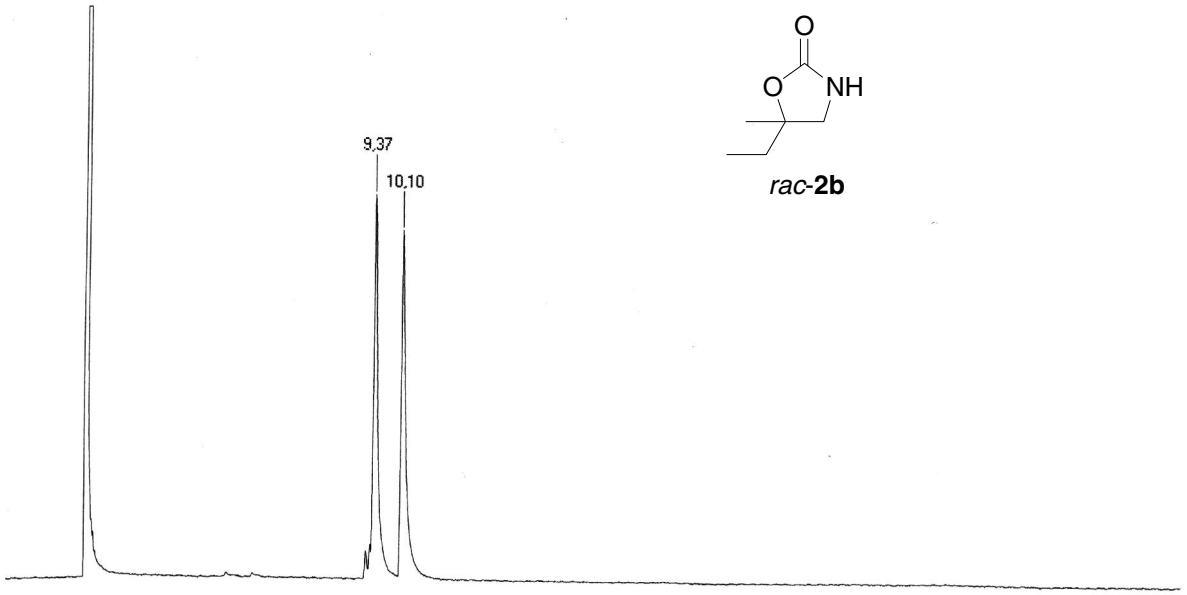


(*R*)-**2a**

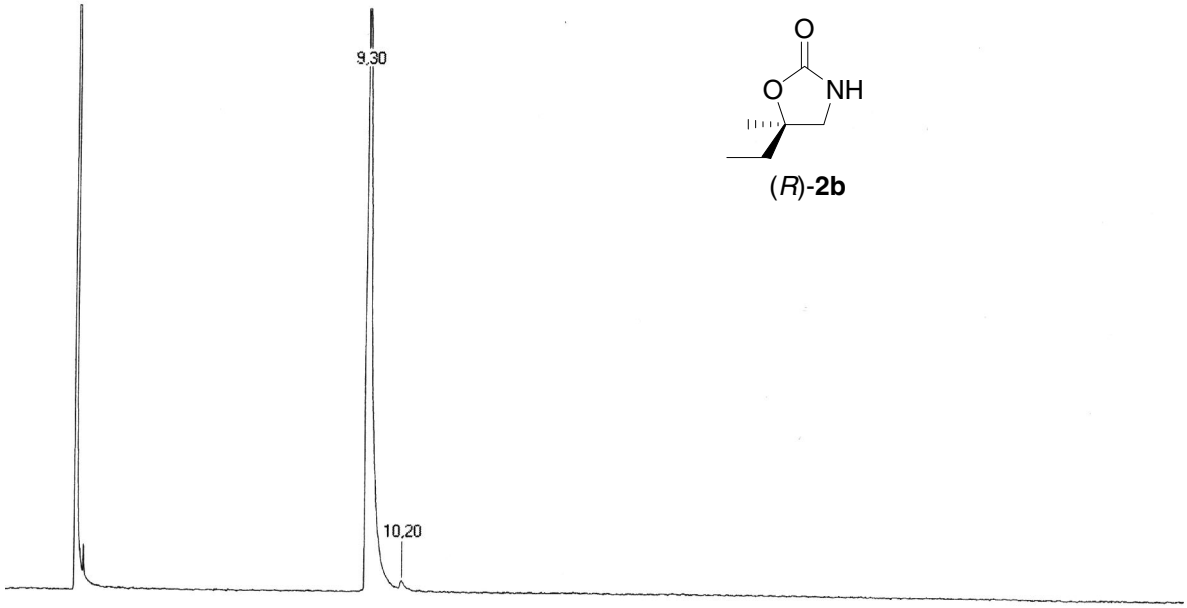
Retention Time	Area	Area %
9.69	133078.0	90.2100
13.2	14442.2	9.7899



GC conditions: Chiraldex G-TA, 180 °C, isothermal

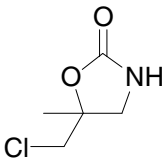


rac-**2b**

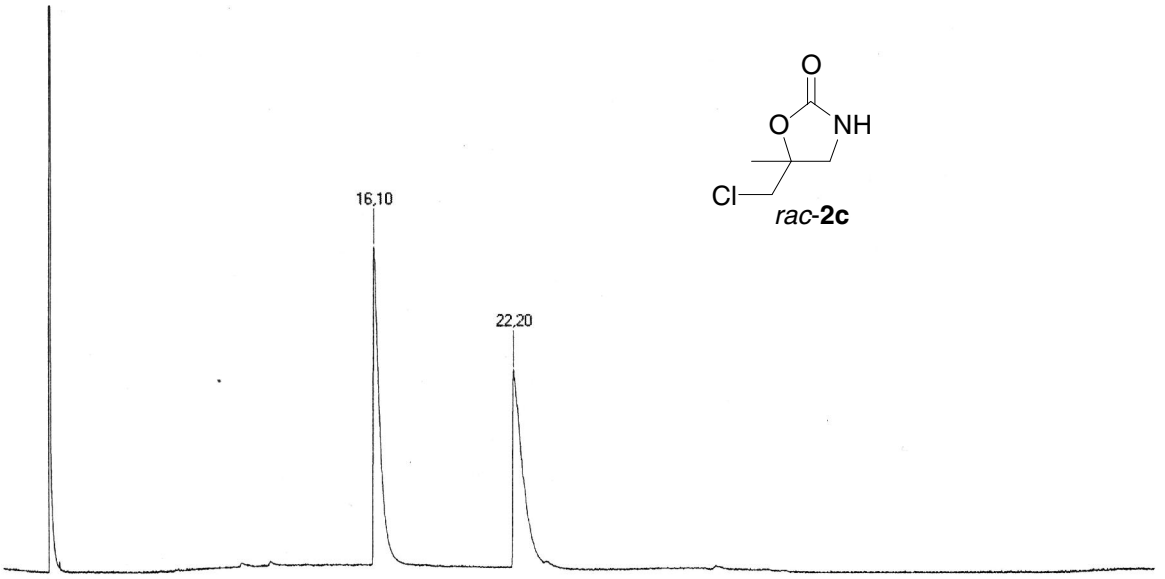


(*R*)-**2b**

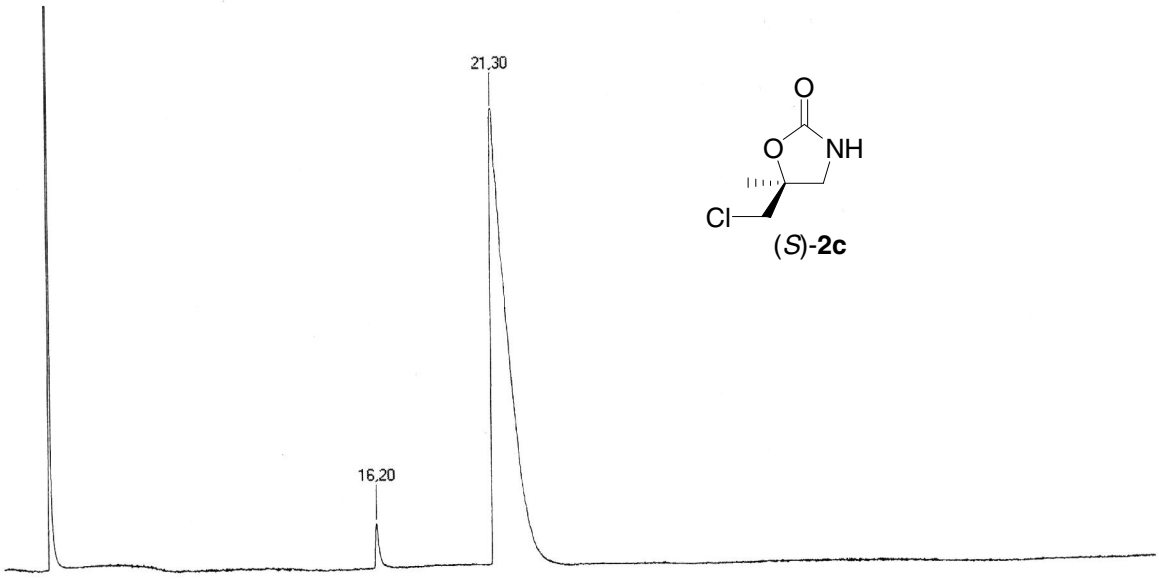
Retention Time	Area	Area %
9.3	136213.7	98.8099
10.2	1640.5	1.1900



GC conditions: Chiraldex G-TA, 180 °C, isothermal

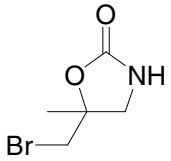


rac-**2c**

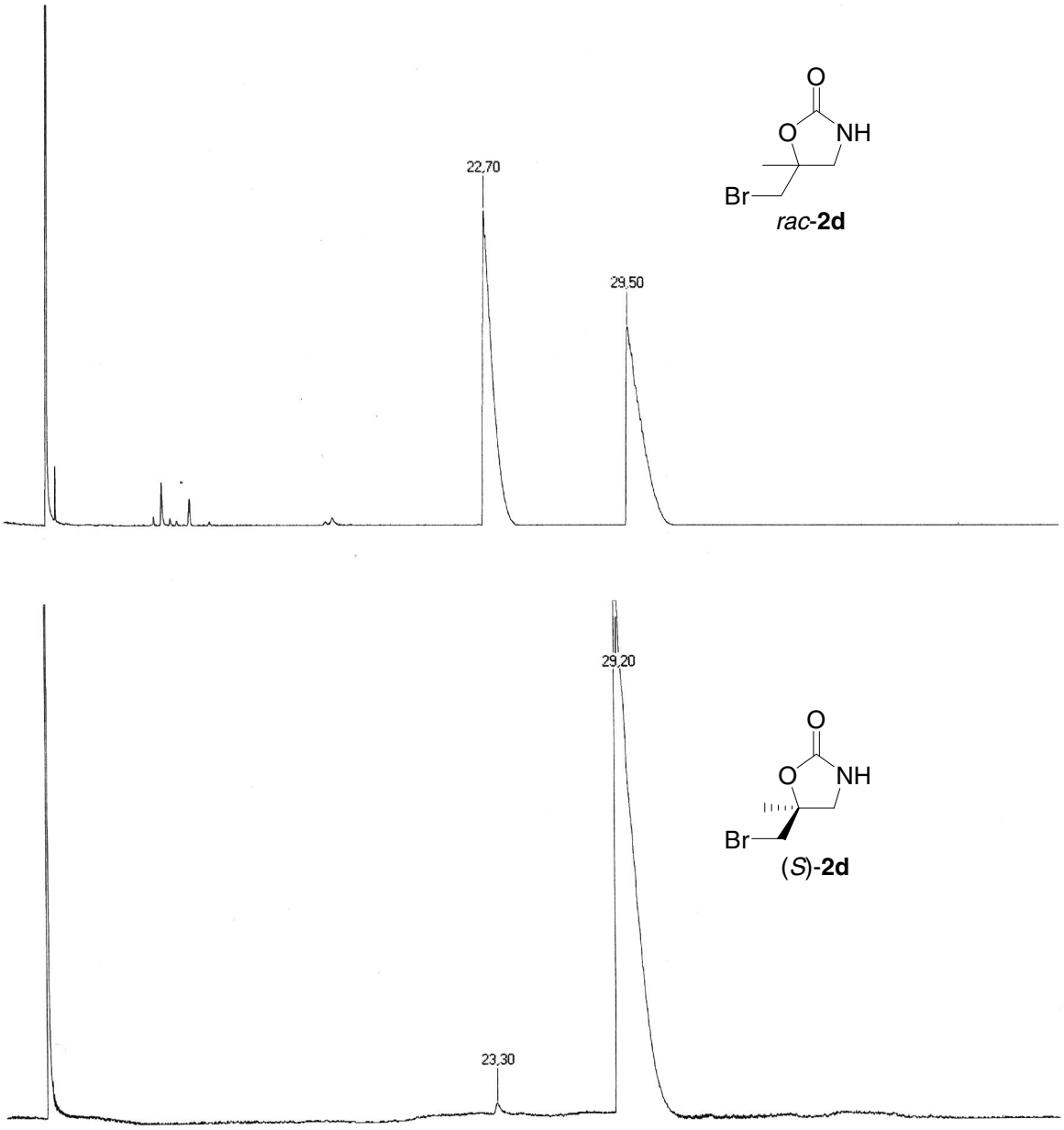


(*S*)-**2c**

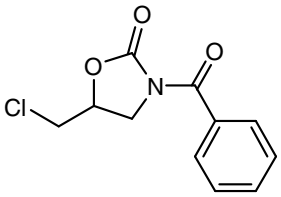
Retention Time	Area	Area %
16.2	6052.7	3.5279
21.3	165509.1	96.4720



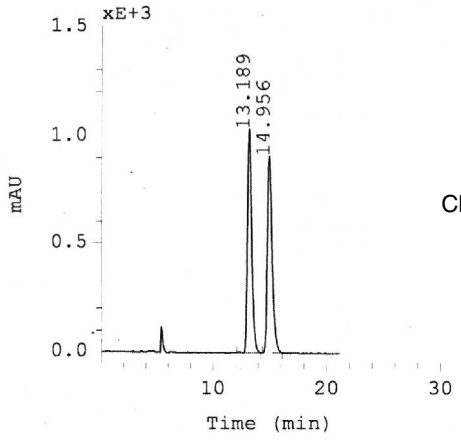
GC conditions: Chiraldex G-TA, 180 ºC, isothermal

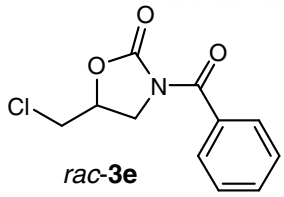


Retention Time	Area	Area %
23.3	1828.0	0.9850
29.2	183755.7	99.0150

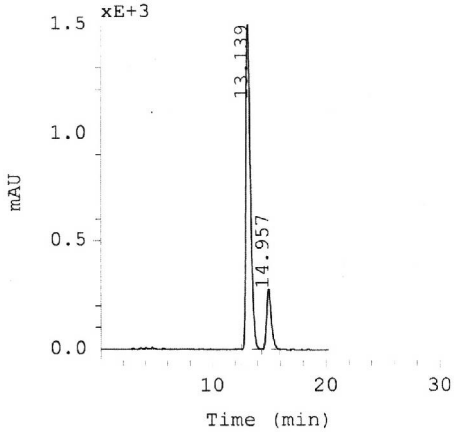


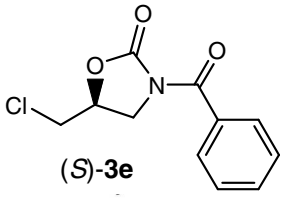
HPLC conditions: Chirallica PST 1, EtOH/Hexane (25:75), 1 mL/min





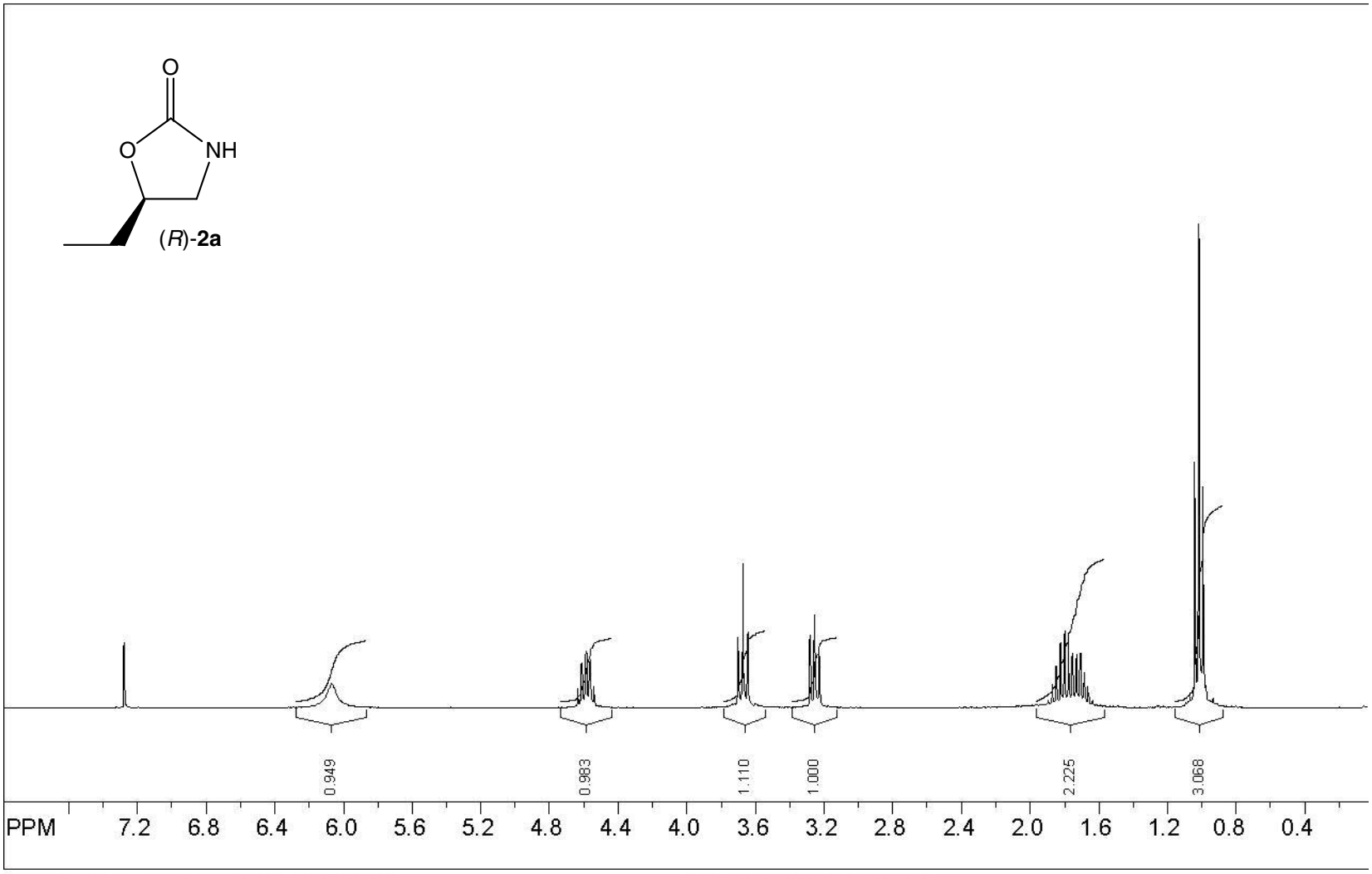
rac-**3e**





(*S*)-**3e**

	Ret.time [min]	Start [min]	End [min]	Height [mAU]	Area [mAU*min]	% Area	Width [min]
1	13.139	12.56	14.35	1501.38	703.164	84.5726	0.426
2	14.957	14.49	15.89	277.576	128.268	15.4274	0.414



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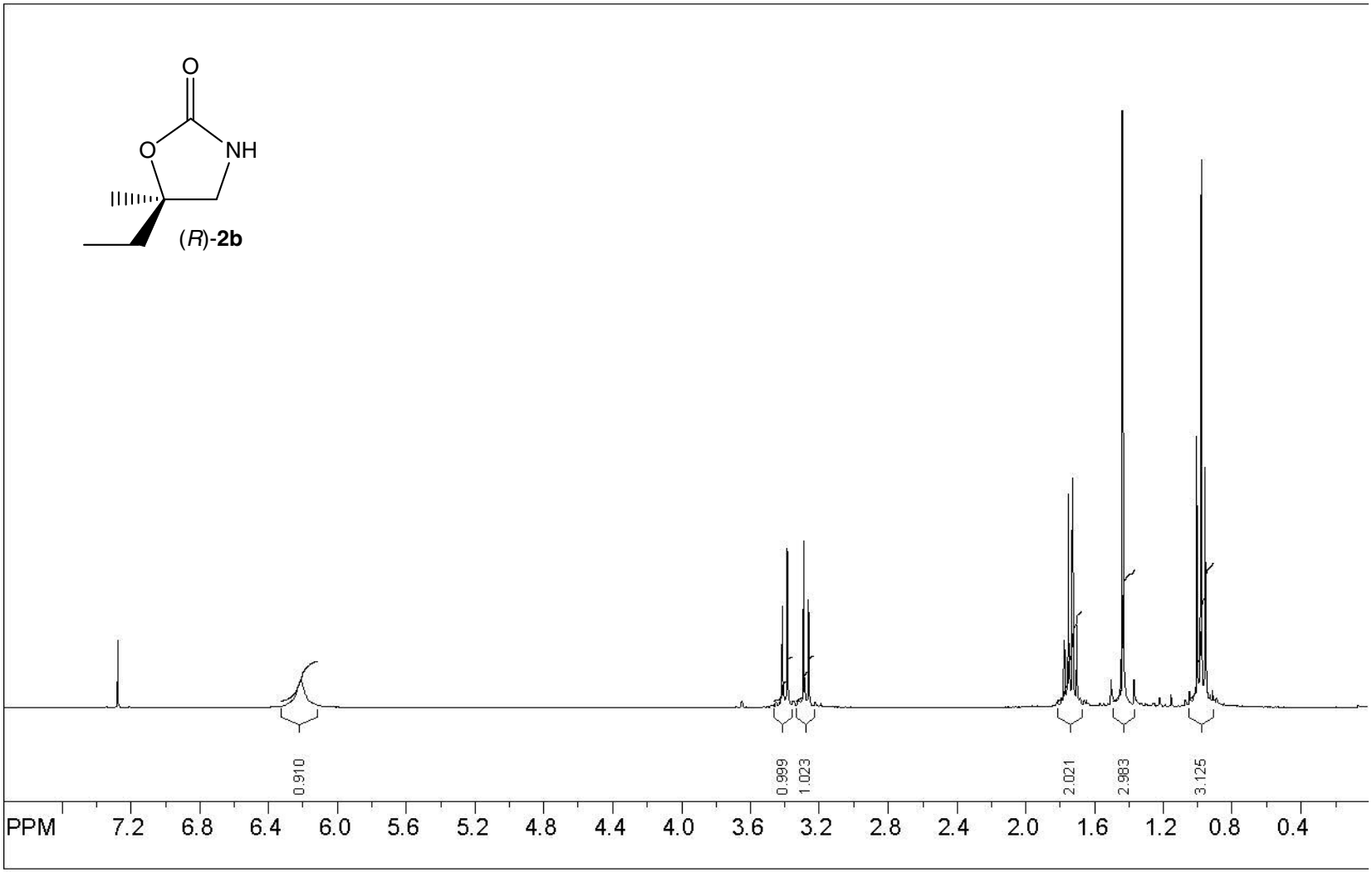
time domain size: 32768 points
width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
number of scans: 8

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000



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number of scans: 32

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
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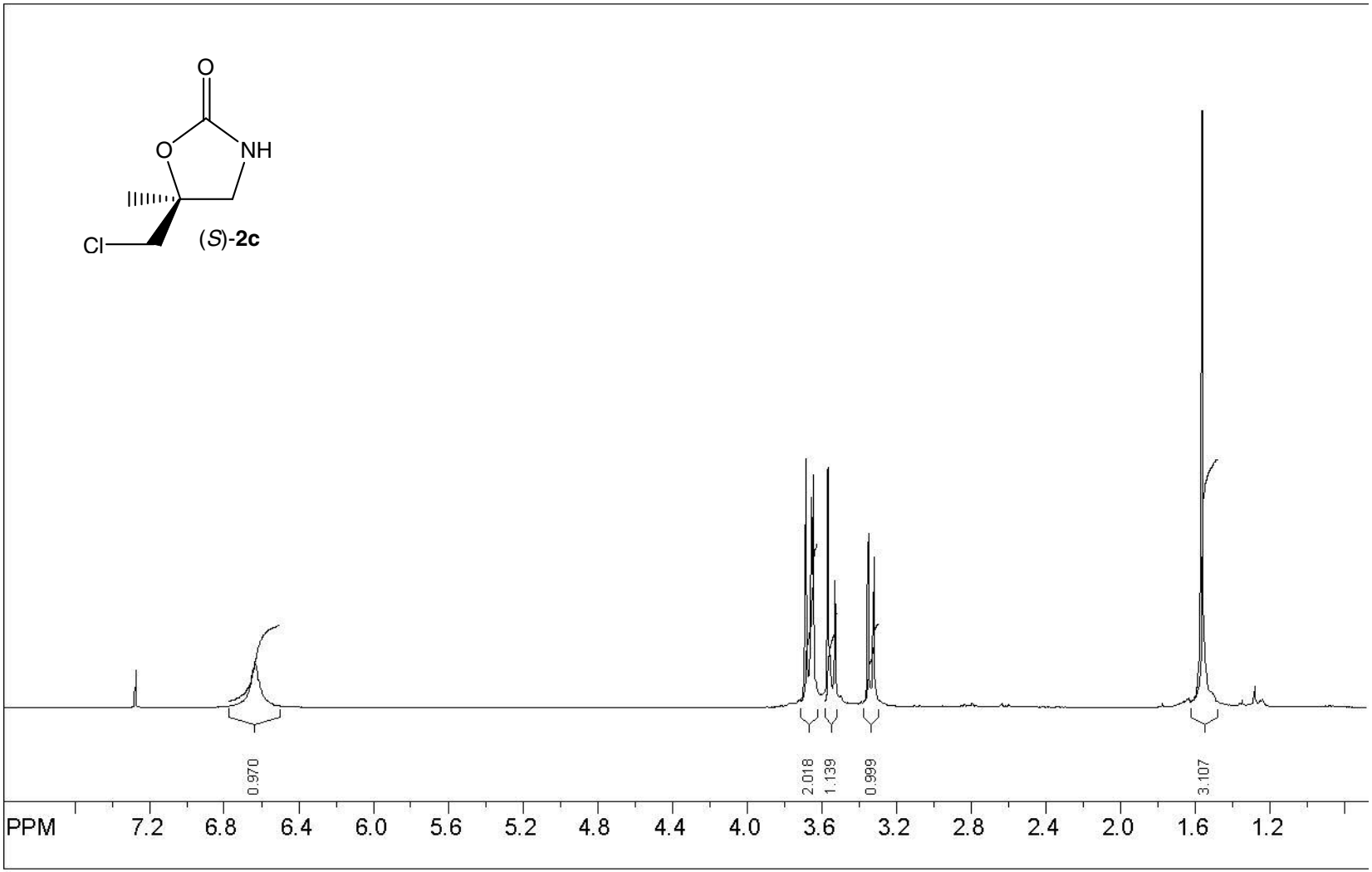

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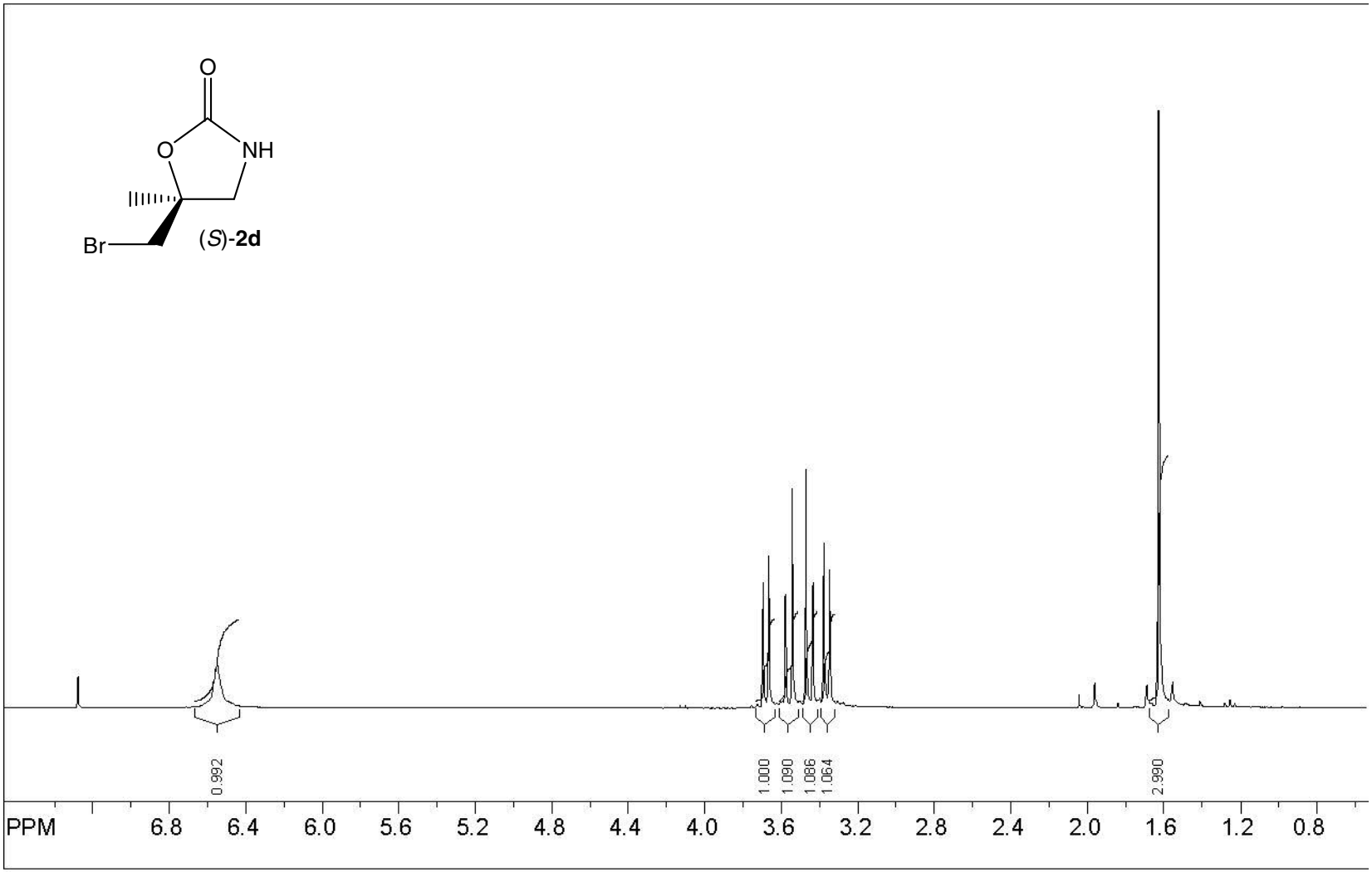

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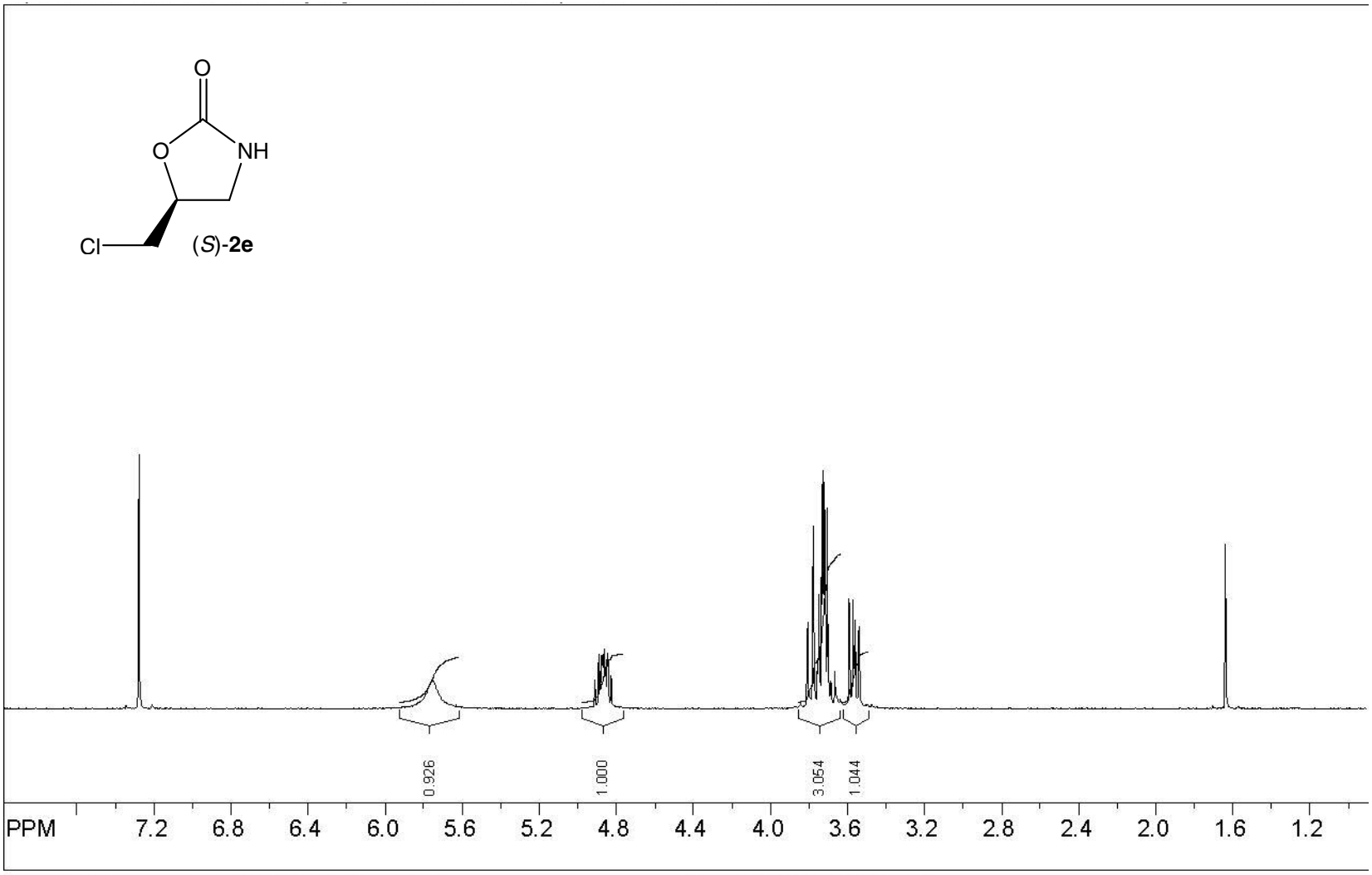
width: 6172.84 Hz = 20.567092 ppm = 0.188380 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000



file: D:\DOKUMENTMaja\NMR\H(70-10)\fid expt: <zg30>
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number of scans: 32

freq. of 0 ppm: 300.130000 MHz
processed size: 32768 complex points
LB: 0.000 GB: 0.0000