Supporting Information

Enantio-differentiation of *O*-Heterocycles Using a Binol-derived Disulfonimide as Chiral Solvating Agent

Aline Couffin, O. Thillaye du Boullay, Marc Vedrenne, Christophe Navarro, Blanca Martin-Vaca*

and Didier Bourissou*

Contents:

General conditions.

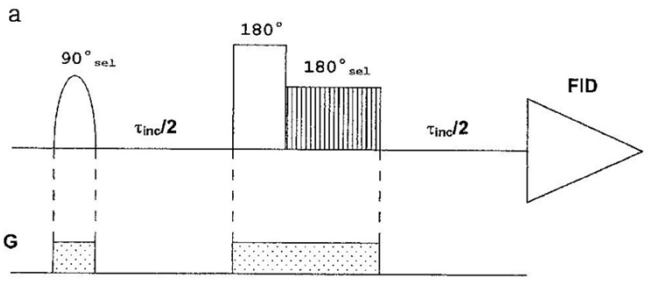
Solvent, toluene (>99.9%) was dried prior to use with a Braun solvent-pacificator system, chloroform and benzene deuterated was dried under molecular sieves and degazed before used.

(*R*)-1,1'-binaphthyl-2,2'-bis(sulfuryl)imide was prepared according to literature procedures.[1] *Meso*-lactide was obtained from ThyssenKrupp Uhde GmbH as a mixture with *D,L*-lactide (40% *meso*-lactide and 60% *D,L*-lactide) and purified according to literature procedure.[2]

All spectra were recorded on a Bruker Avance 500, 400 and 300 spectrometers equipped with a 5 mm triple resonance inverse Z-gradient probe (TBI ^{1}H). All chemical shifts for ^{1}H were relative to TMS using ^{1}H (residual) chemical shifts of the solvent as a secondary standard.

2D ROESY experiments. Spectra were acquired at 183K using a mixing time of 300 ms, 8 averages for each *t*1 value after 8 dummy scans, a datum set of 2048 time domain data point in the t2 dimension with 256 *t*1 increments, and the States-TPPI method for quadrature detection in the *t*1 dimension.

Instant ZS-decoupling experiments. Experiments were acquired on a Bruker AVANCE I 500 MHz spectrometer equipped either with a 5 mm TBI 1H {BB,^{13}C} probehead or a 5mm TCI 1H {13C,31P} cryoprobe. NMR spectra were recorded in $CDCl_3$ at 298K. The pulse program used to obtain one dimensional proton decoupled proton spectra is described below.[3]



This pulse program produces a pseudo 2D experiment where the delay (tau_c = 8 ms) between excitation and detection is incremented stepwise. Gaussian selective excitations were used for excitation and inversion. A program to extract the first data points of each series of FIDs from the pseudo 2D experiment has been developed. These points are then arranged to form a new FID that can be processed by using a classic Fourier transformed. Total acquisition times were approximately 1 day with a sample of 60 mM with the 5 mm TBI 1H {BB,^{13}C} probehead. When the same experiment is done in the same conditions but with a 5mm TCI 1H {^{13}C,^{31}P} cryoprobe, the one dimensional proton decoupled proton spectra is recorded in only 30 minutes.

---

[1] A. Berkessel, P. Christ, N. Leconte, J. -M. Neudörfl and M. Schäfer, *Eur. J. Org. Chem.* **2010**, 5165.
[2] M. Muller, J. Hess, W.-G. Schenell, D. Bendix, G. Entenmann, US patent 5214159, May 24, **1993**.
[3] K. Zangger, H. Sterk, *J. Magn. Reson*. **1997**, *124*, 486.

Analytical procedure for the determination of the ee of lactide:

Mixtures with different ratios of *D*- and *L*-lactide were dissolved in $CDCl_3$. One equivalent of (*R*)-**1** was added. Experiment was acquired on a Bruker Avance 400 MHz spectrometer at 298 K. Specific pulse program: zghd and irradiation at 1.6 ppm (irradiation power: 45 dB).

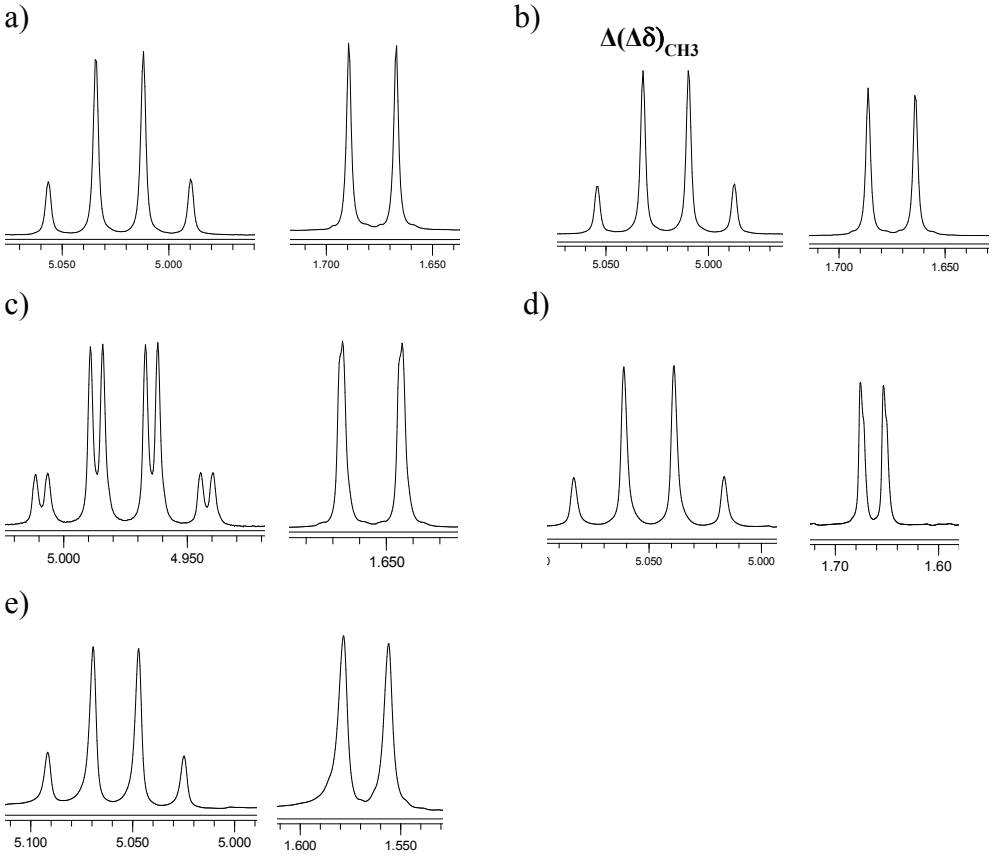


Figure S1: Overlaid ^{1}H NMR (300 MHz) spectrum of a 60 mM solution of a 1:1 mixture of (*D,L*)-Lactide in $CDCl_3$ and a) (*R,R*)-(+)-Hydrobenzoin **A**, b) (4*S*,5*S*)-4,5-Bis(diphenylhydroxymethyl)-2,2-dimethyldioxolane **B**, c) (*R*)-(+)-Binol **C**, d) Disulfonamide **D**, d) Disulfonamide **E**

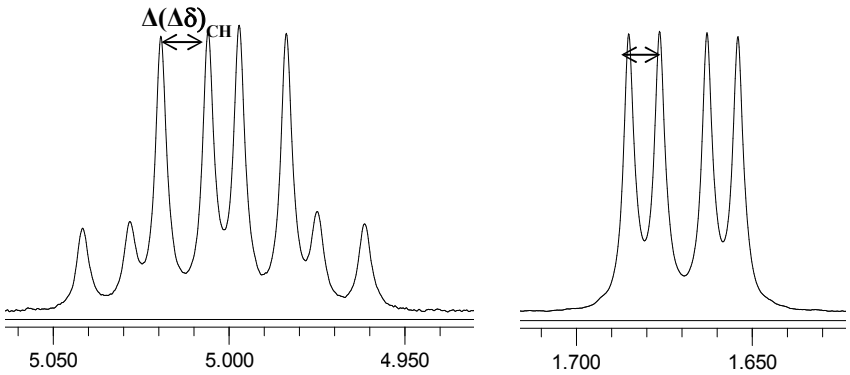


Figure S2: Overlaid ^{1}H NMR (300 MHz) spectrum of a 10 mM solution of a 1:1 mixture of (*R*)-**2** with (*D,L*)-Lactide in $CDCl_3$. $\Delta(\Delta\delta)_{CH} = 0.018$ ppm, $\Delta(\Delta\delta)_{CH3} = 0.009$ ppm

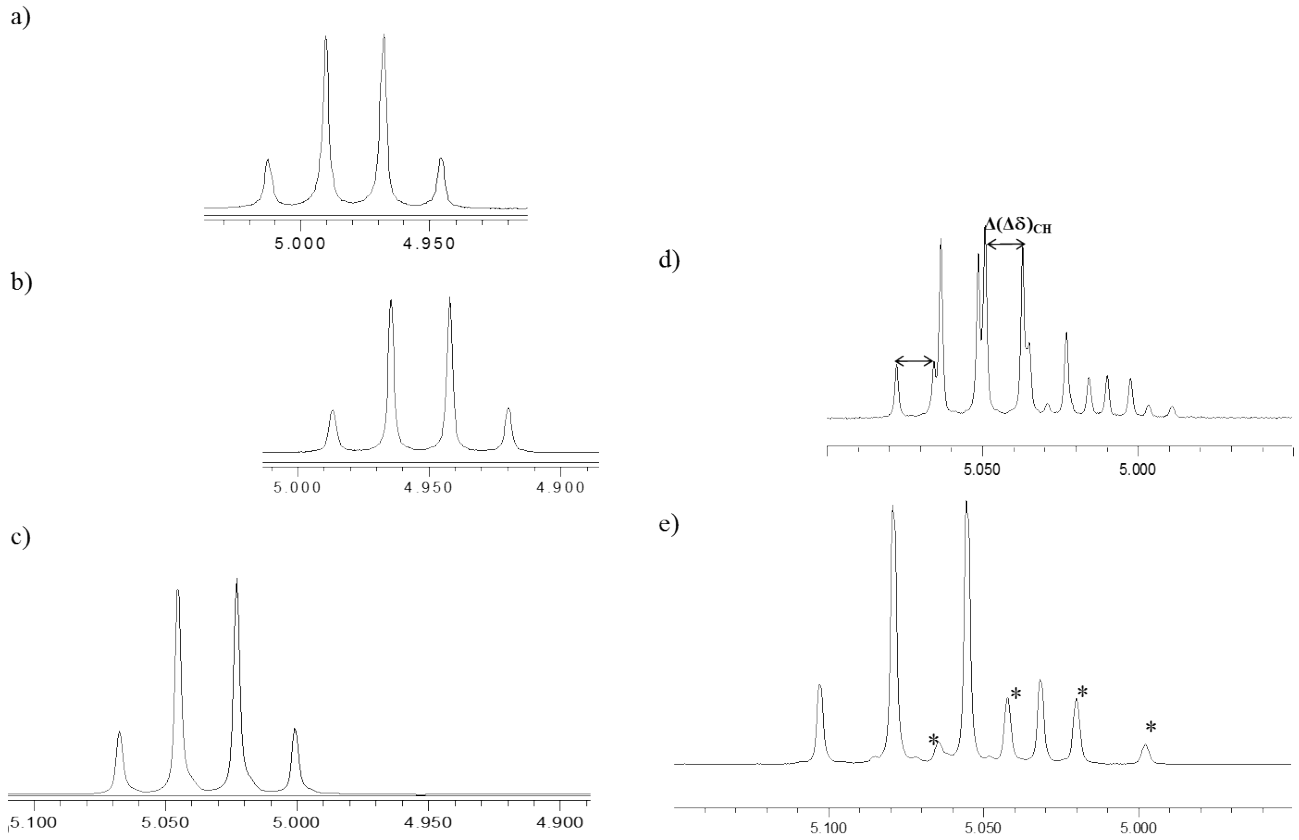


Figure S3: Overlaid ^{1}H NMR (300 MHz) spectra of 10 mM solutions of a 1:1 mixture of (*R*)-**1** with a) *L*-lactide ($(\Delta\delta)_{CH}$ = 0,055 ppm), b) *D*-lactide ($(\Delta\delta)_{CH}$ = 0,081 ppm), c) free *D,L*-lactide;.d) *meso*-lactide ($(\Delta\delta)_{CH}$ = 0,025 and 0.038ppm) and e) free *meso* –lactide; * = 20% of *D,L* lactide present in *meso*-lactide.

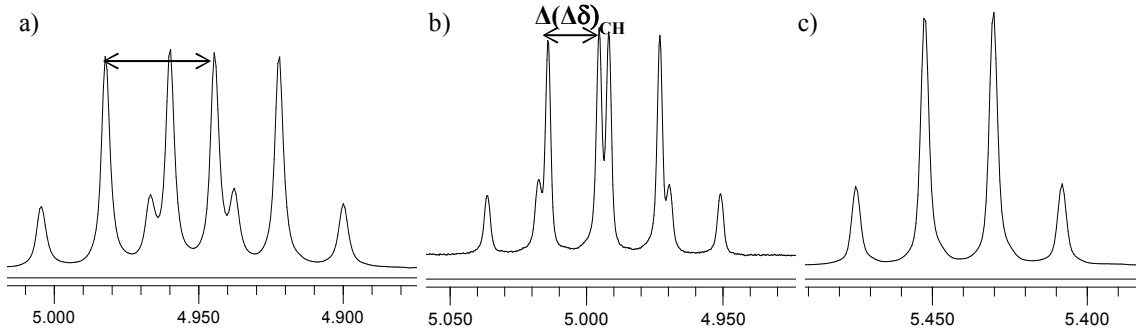


Figure S4: Overlaid ^{1}H NMR (300 MHz) spectra of a 1:1 mixture of (*R*)-**1** with (*D,L*)-Lactide in a) $CDCl_3$, b) CD_3CN and c) $(CD_3)_2CO$.

Job Plots.

Equimolar amounts of (*R*)-**1** (Host) and *D*- and *L*- Lactide (Guest) were dissolved separetively in $CDCl_3$. These solutions were distributed among nine NMR tubes, with the molar fractions of host and guest in the resulting solutions increasing from 0.1 to 0.9 (resp. decreasing from 0.9 to 0.1).

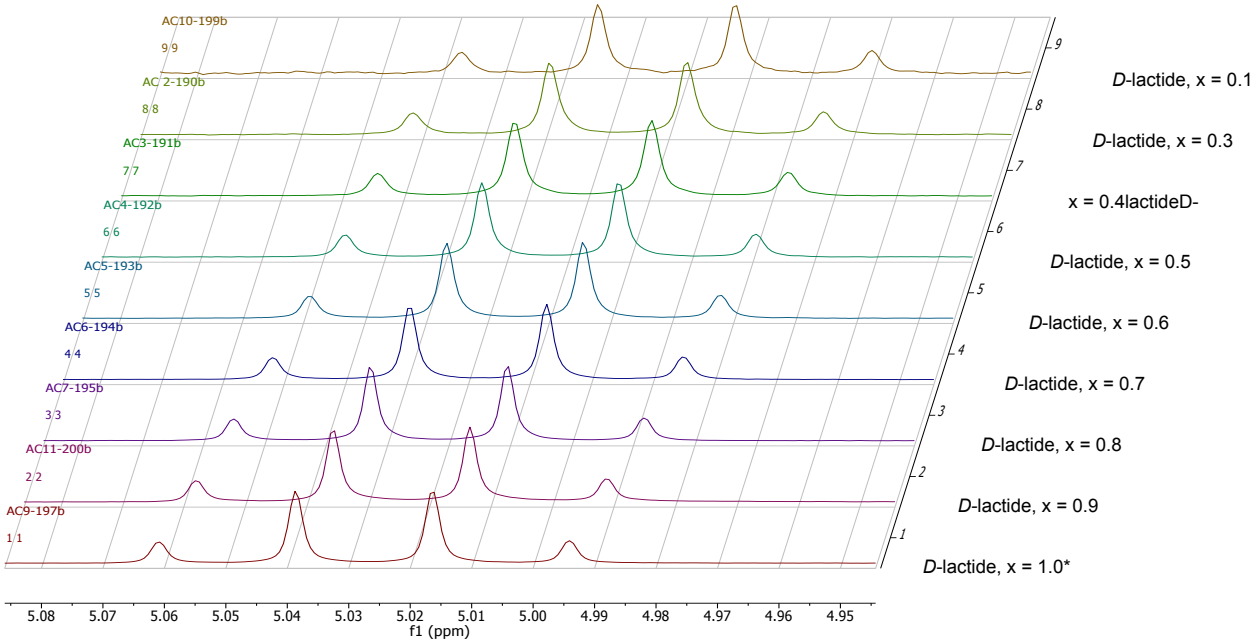


Figure S5: Overlaid of a selected region (δ from 4.95 to 5. 08 ppm) of ^{1}H NMR (300 MHz) spectra of 10 mM solution of a mixture of (*R*)-**1** and *D*-lactide with variable molar fractions (molar fraction of *D*-lactide x from 0.1 to 1).

The displacement of the methyl chemical shift $(\Delta\delta)_{CH}$ or $(\Delta\delta)_{CH3}$ induced by association was plotted against the molar fractions of the guest, lactide, [G]/([G]+[H]). For each enantiomer, the nine samples of enantiopure lactide (Guest) and (*R*)-**1** (Host) were analyzed in $CDCl_3$ at 298 K.

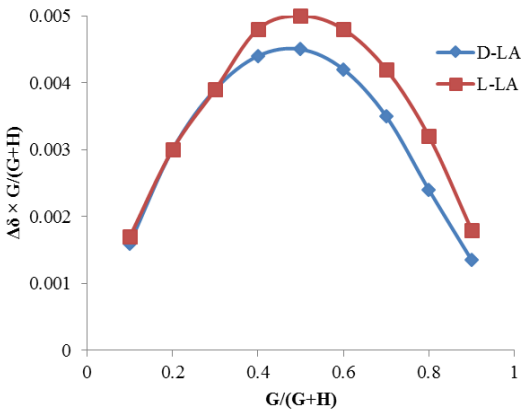


Figure S6: Job's plots for the association of (*R*)-**1** (Host) with (*D*)- and (*L*)-lactide (Guest) [G/(G+H) = molar fraction of lactide, Δδ = chemical shift variation of the CH_3 signal of (*D*)- and (*L*)-lactide]. Maxima at 0.5 molar fraction indicates a 1:1 stoichiomety.

Determination of the association constants by ^{1}H NMR titrations.

^{1}H NMR titration was achieved at 25°C on a series of samples in which the concentration of lactide was kept constant (typically, 10mM in dry $CDCl_3$) while that of (*R*)-**1** was gradually increased. The corresponding binding constant K_{ass} values were estimated from the variation of the chemical shift of the methine and methyl signals taking into account the 1:1 stoechiometry of the (*R*)-**1** / lactide adducts K_{ass} values were determined by means of the nonlinear least-square method applied to the CH and CH_3 signals downfield shifted upon association.

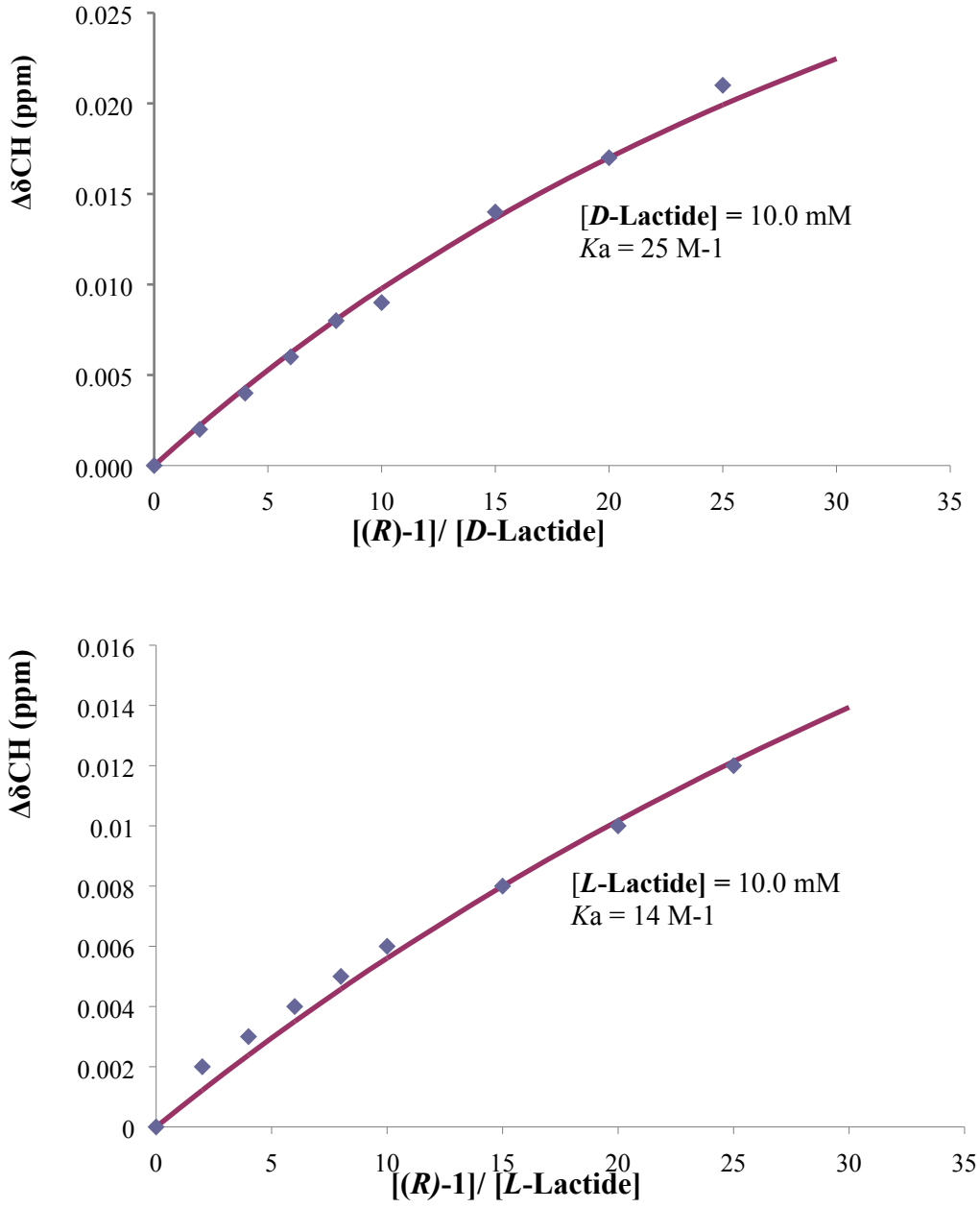


Figure S7: ^{1}H NMR (500 MHz, $CDCl_3$) titration data obtained for the association of (*R*)-**1** and *D*- or *L*-lactide. Estimated error ±15%.

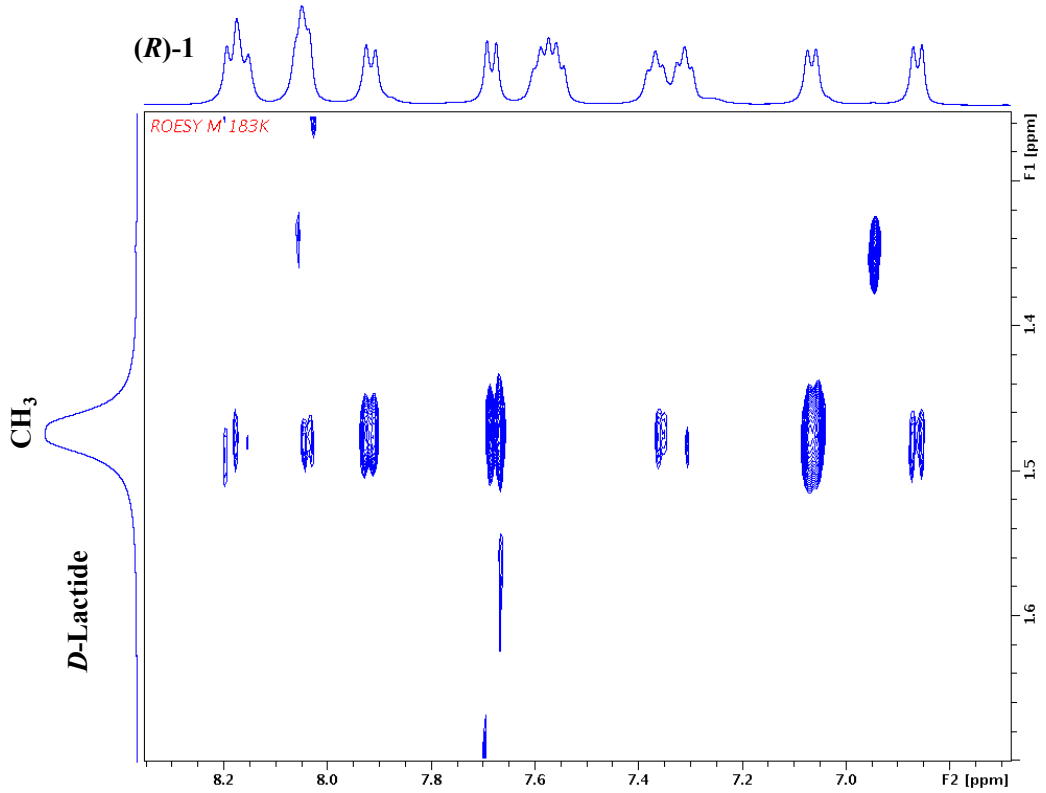


Figure S8: Portion of the 2D ROESY spectra (500 MHz, 183 K, 10mM in CD_2Cl_2) of a 1:1 mixture of (*R*)-**1** and *D*-LA: cross correlation peaks between H binaphtyls of (*R*)-**1** with the methyl protons of *D*-LA.

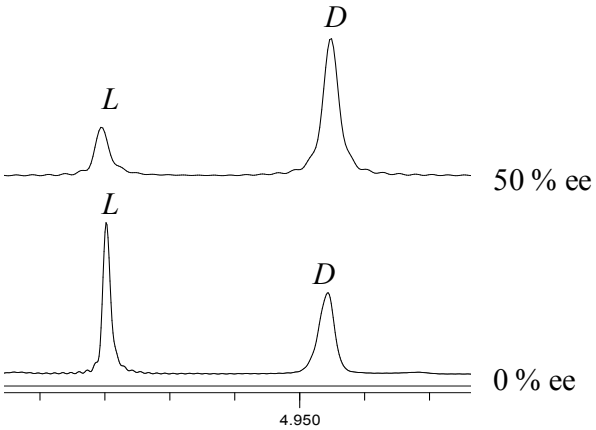
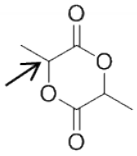
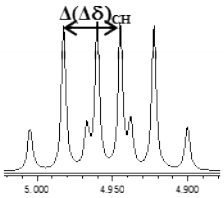
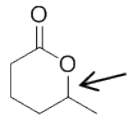
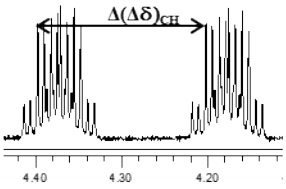
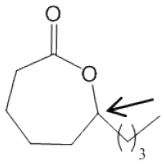
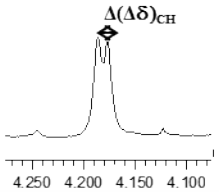
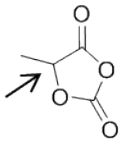
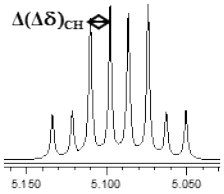
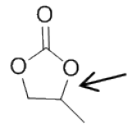
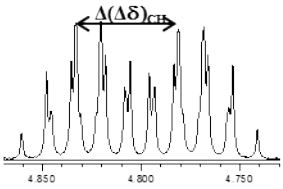
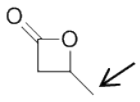
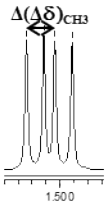
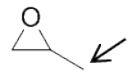
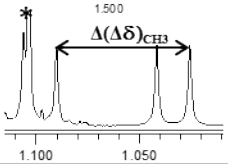


Figure S9. CH spectral region of the homo-decoupled ^{1}H NMR spectra of solutions of (*R*)-**1** and two different D/L lactide mixtures.

Table S1. Enantio-differentiation of various chiral ROP monomers with (*R*)-**1**.[a]

entry	racemic monomer	Δ(Δδ) (ppm)	relevant part of the ^{1}H NMR spectrum
1		0.038	
2		0.195	
3		0.008[b]	
4		0.013	
5		0.052	
6		0.013	
7		0.065	

[a] The ^{1}H NMR spectra were recorded in the presence of (*R*)-**1** (60 mM, 1 equiv.) in $CDCl_3$ at 25°C: 500 MHz for entry 4; 400 MHz for entries 2 and 6; 300 MHz for entries 1, 3 and 5. *Residual Et_2O from (*R*)-**1**. [b] Homonuclear broadband decoupled spectrum.

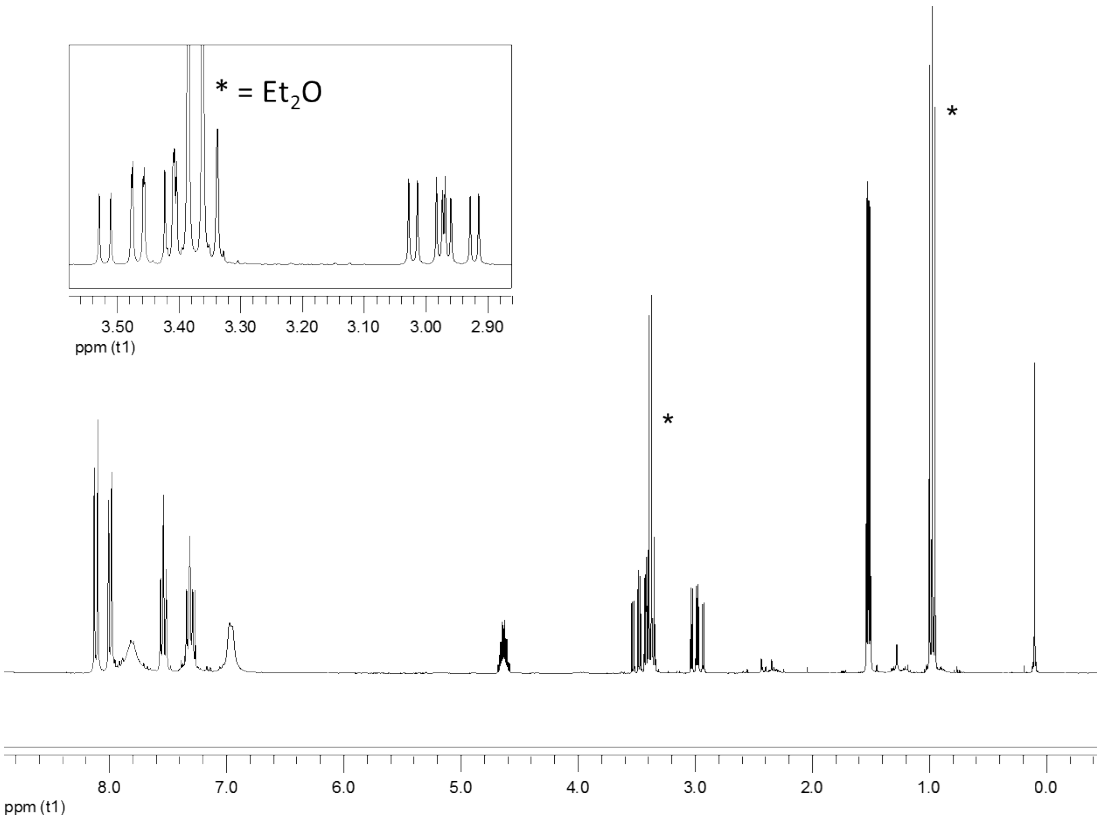


Figure S10. Standard ^{1}H NMR spectrum of a solution of (*R*)-**1** and β-butyrolactone (60 mM, 1 equiv.).

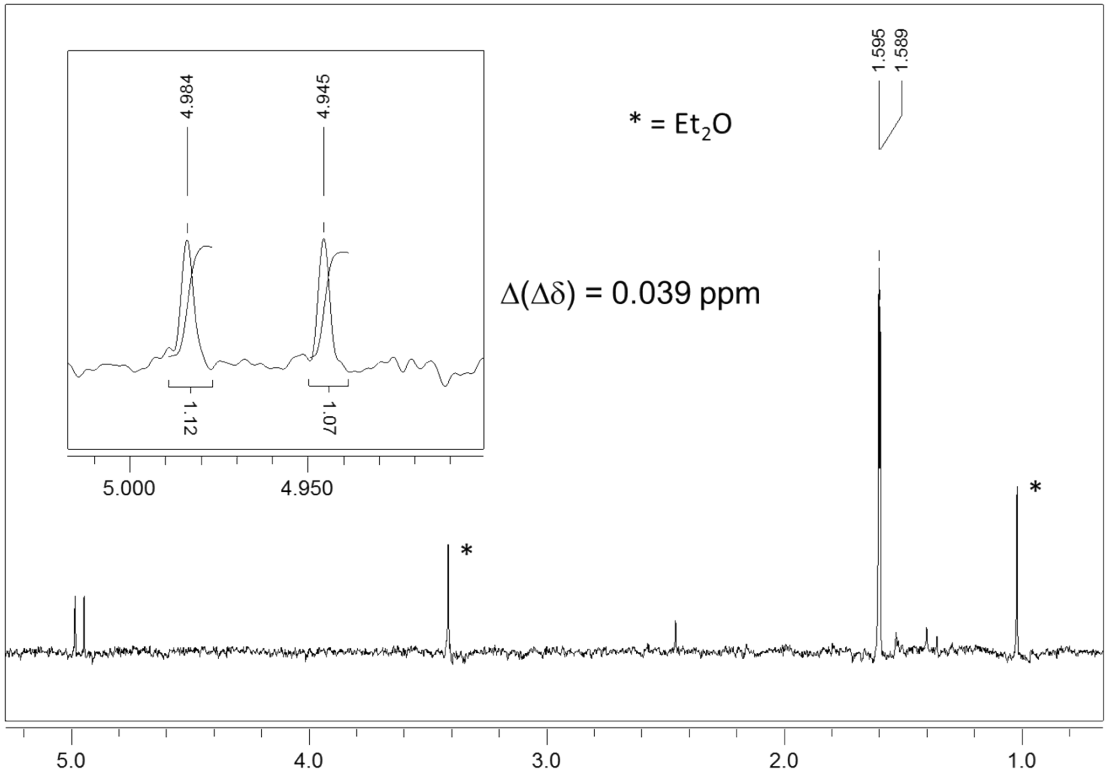


Figure S11. Instant homo-decoupled ^{1}H NMR spectrum of a solution of (*R*)-**1** and *D,L*-lactide (60 mM, 1 equiv.). Δ(Δδ) = 0.039 ppm