SUPPORTING INFORMATION

Lipase-Catalyzed Asymmetric Synthesis of Oxathiazinanones through Dynamic Covalent Kinetic Resolution

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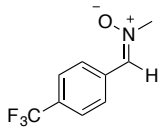
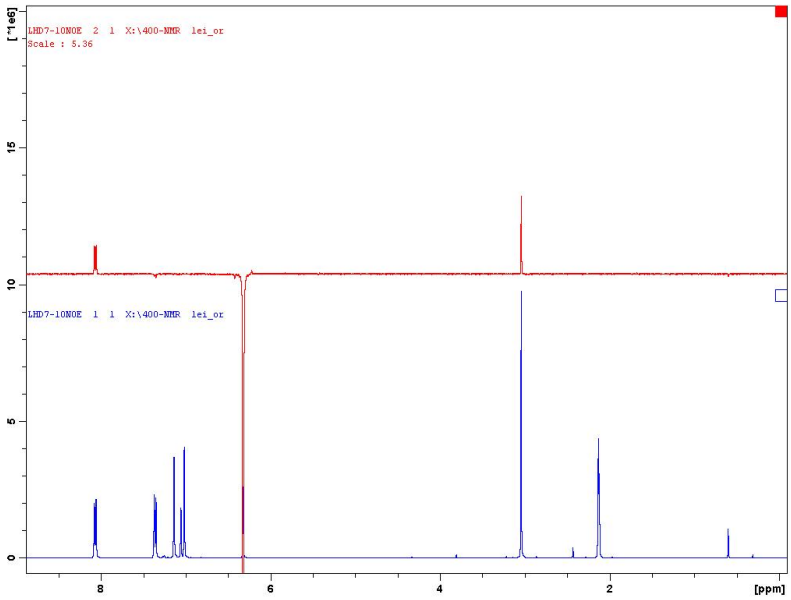
General Methods

Reagents were purchased from Sigma-Aldrich, Lancaster and Apollo and used as received. ^{1}H NMR and ^{13}C NMR data were recorded on a Bruker Avance DMX 500 at 125 MHz. Chemical shifts are reported as δ values (ppm) with $CDCl_3$ (^{1}H NMR δ 7.26, ^{13}C NMR δ 77.16) as internal standard. *J* values are given in Hertz (Hz). Thin layer chromatography (TLC) was performed on precoated Polygram® SIL G/UV silica plates (0.20 mm, Macherey-Nagel), visualized with UV-detection. Flash column chromatography was performed on silica gel 60, 0.040-0.063 mm (SDS). High-resolution mass spectra were analyzed by National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand and School of Medicinal Chemistry, Jinan University, China. Analytical high performance liquid chromatography (HPLC) with chiral stationary phases was performed on HP-Agilent 1110 series controller, using Daicel chiralpak OJ (4.6x250 mm, μm) column. Solvents for HPLC use were of spectrometric grade.

Determination of the nitrone configurations

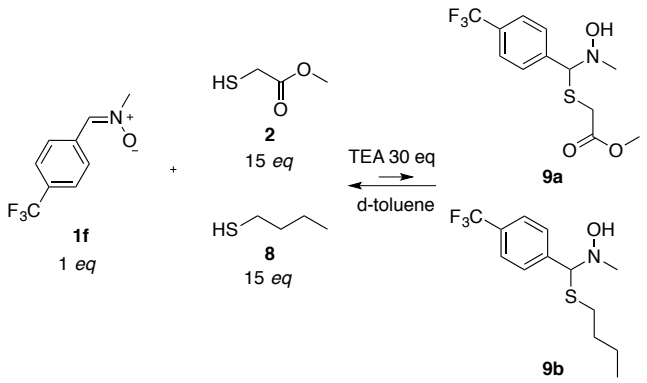
The nitrone configurations were determined by NOE experiments. All nitrones thus displayed *Z*-configuration as shown for nitrone **1f** below.

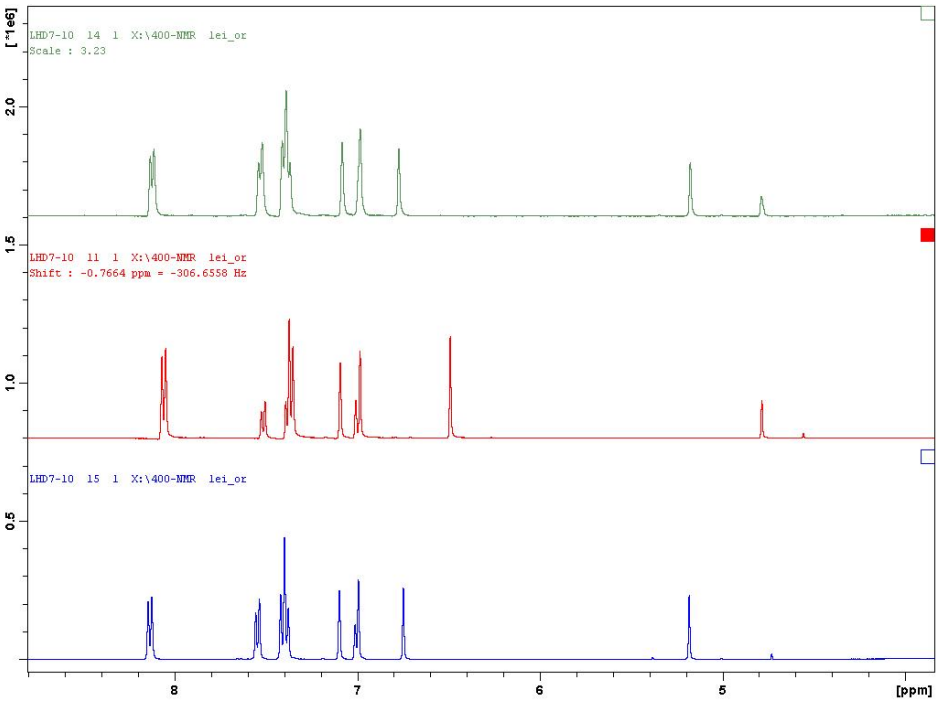




Evaluation of reversibility

The reversibility of the nucleophilic addition was evaluated using ^{1}H NMR spectroscopy with nitrone **1f** and methyl 2-sulfanylacetate **2** in the presence of TEA in *d*-toluene. The equilibrium was attained instantly, forming intermediate **9a** (44%; lower spectrum). Following addition of 1 equivalent of 1-butanethiol **8**, intermediate **9b** (*cf.* middle spectrum) was formed, resulting in the decrease of intermediate **9a** (36%; upper spectrum).





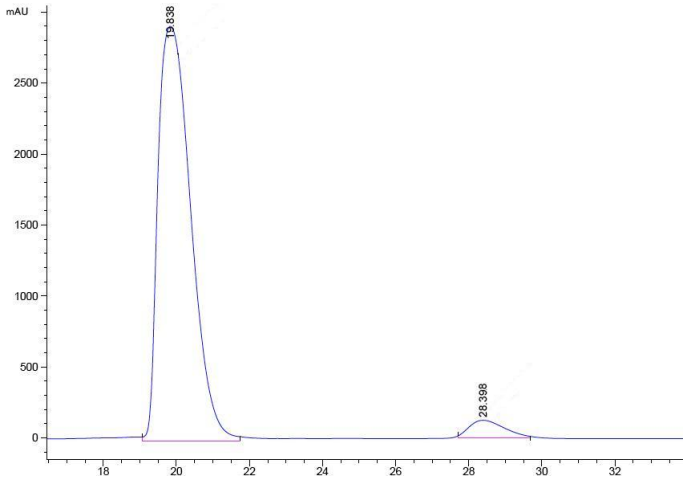
General Procedure for Dynamic Kinetic Resolution

In a typical experiment, a reaction mixture of **1a** (11 μL, 0.1 mmol), methyl 2-sulfanylacetate (**2**) (27.6 μL, 0.3 mmol), triethylamine (14 μL, 0.1 mmol), and isopropenyl acetate (40 μL, 0.36 mmol) in dry toluene (0.5 mL) were added to a sealed-cap vial (1.75 mL) containing *Candida antarctica* lipase B (CALB, Sigma-Aldrich, L4777, 30 mg) together with 200 mg $CaCl_2$. The reaction mixture was heated to 40 °C. After 19 hours, the mixture was cooled to room temperature, filtered and washed with saturated NH_4Cl and brine. The solvent was dried over $MgSO_4$ and removed under vacuum and the crude product was purified by column chromatography: hexane : EtOAc = 15 : 1, affording **3a** (16 mg) as a colorless oil; yield: 85%; *ee*: 90%.

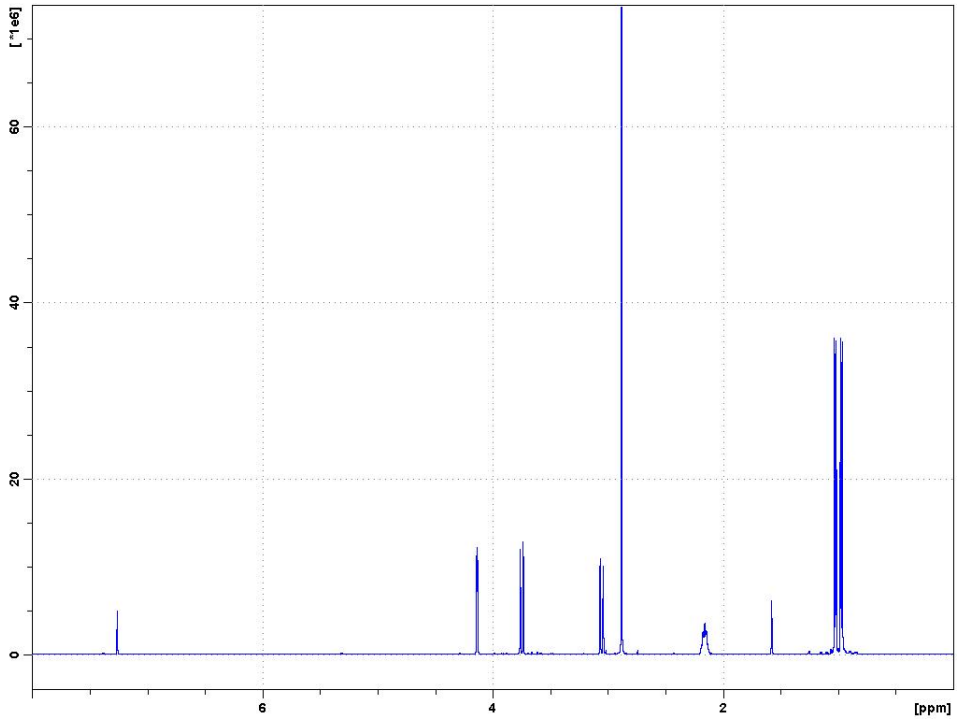
3-isopropyl-2-methyl-1,4,2-oxathiazinan-6-one (3a). The general procedure was followed. Yield: 85%; Enantiomeric excess: 90%, determined by HPLC analysis: Chiral OJ Hex : ^{i}PrOH = 99 : 1, 0.5 mL/min, detection 210 nm, t_R: 19.8 min, 28.3 min; Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 0.99 (6H, dd, *J* = 6.8, 26.9 Hz), 2.11-2.21 (1H, m), 2.88 (3H, s), 3.05 (1H, d, *J* = 12.9 Hz), 3.75 (1H, d, *J* = 12.9 Hz), 4.13 (1H, d, *J* = 2.7 Hz); ^{13}C NMR ($CDCl_3$) δ = 13.8, 20.1, 26.4, 30.21, 42.9, 75.6, 171.7; HRMS (ESI-TOF): 176.0740 ($[M+H]^+$, $C_7H_{14}NO_2S$; calc. 176.0701).

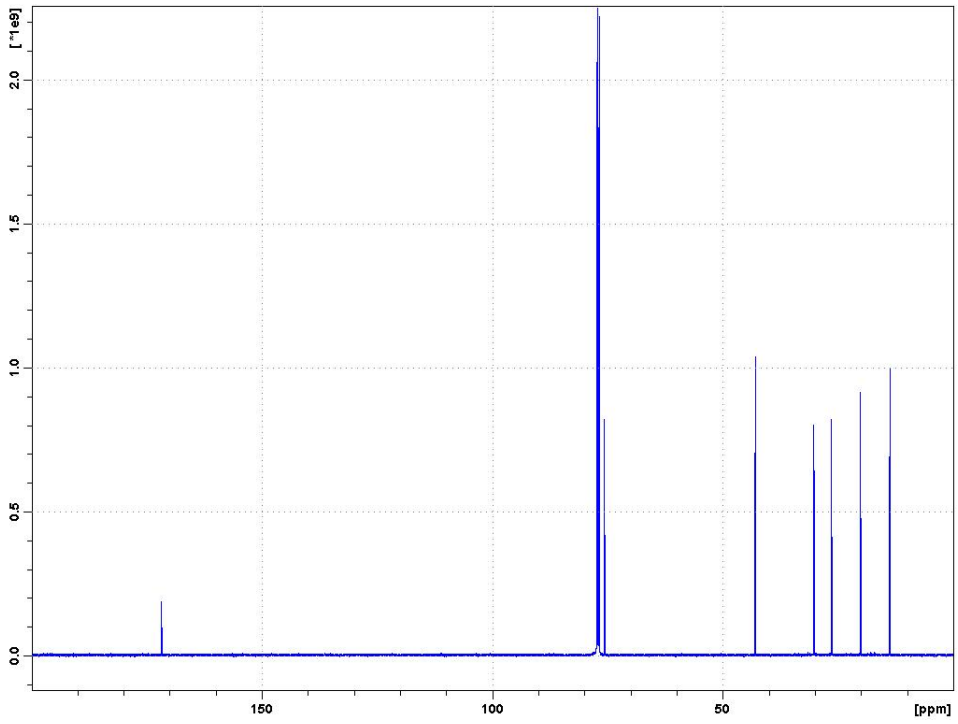
Chiral HPLC of 3a

Peak	Processed Channel	Retention Time (min)	Area	% Area	Height
1	@210 nm	19.838	181858	95.005	2914
2	@210 nm	28.398	8474	4.995	136

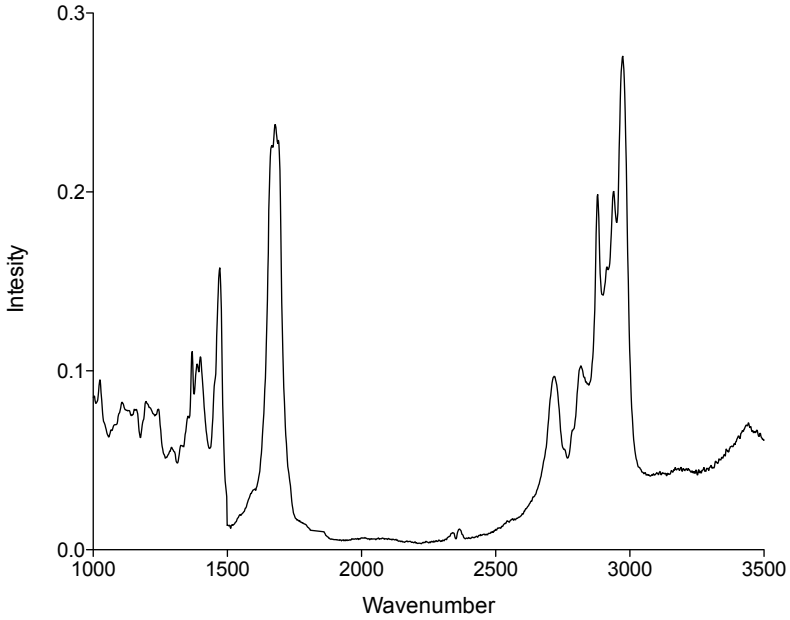


^{1}H NMR and ^{13}C-NMR of 3a





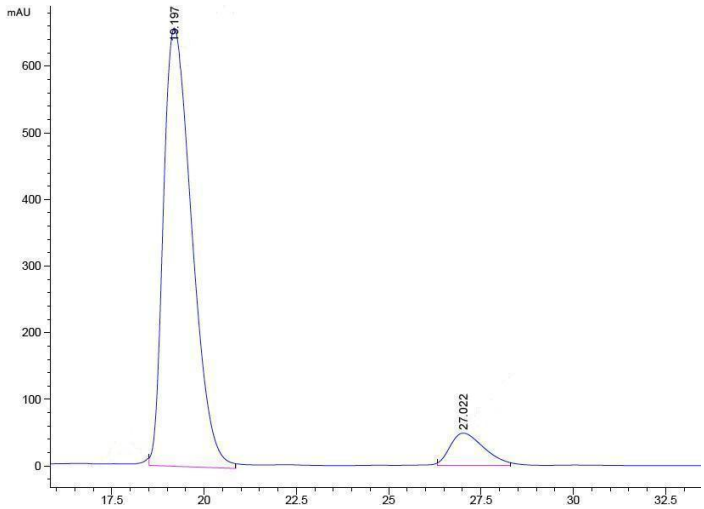
FTIR of 3a



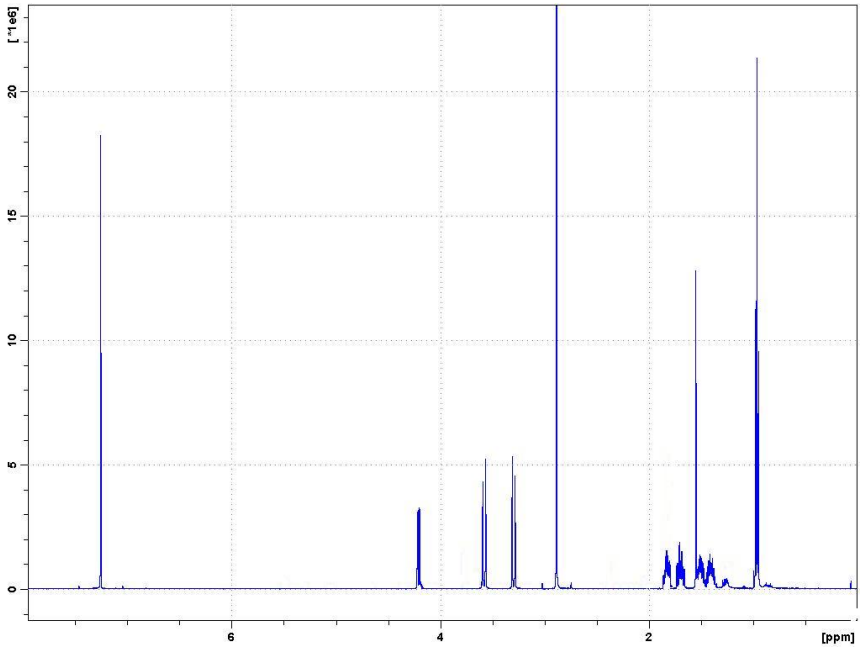
2-methyl-3-propyl-1,4,2-oxathiazinan-6-one (3b). The general procedure was followed. Yield: 87%; Enantiomeric excess: 83%, determined by HPLC analysis: Chiral OJ 99 : 1 = Hex : ^{i}PrOH, 0.5 ml/min, detection 210 nm, t_R: 19.1 min, 27.0 min; Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 0.97 (3H, t, J = 7.27 Hz), 1.36-1.45 (1H, m), 1.46-1.55 (1H, m), 1.65-1.74 (1H, m), 1.78-1.88 (1H, m), 3.30 (1H, d, J = 13.3Hz), 3.58 (1H, d, J = 13.3Hz), 4.21 (1H, dd, J = 3.3, 9.9 Hz); ^{13}C NMR ($CDCl_3$) δ = 13.9, 18.4, 26.5, 34.0, 42.9, 69.3, 171.5; HRMS (ESI-TOF): 176.0697 ($[M+H]^+$, $C_7H_{14}NO_2S$; calc. 176.0701).

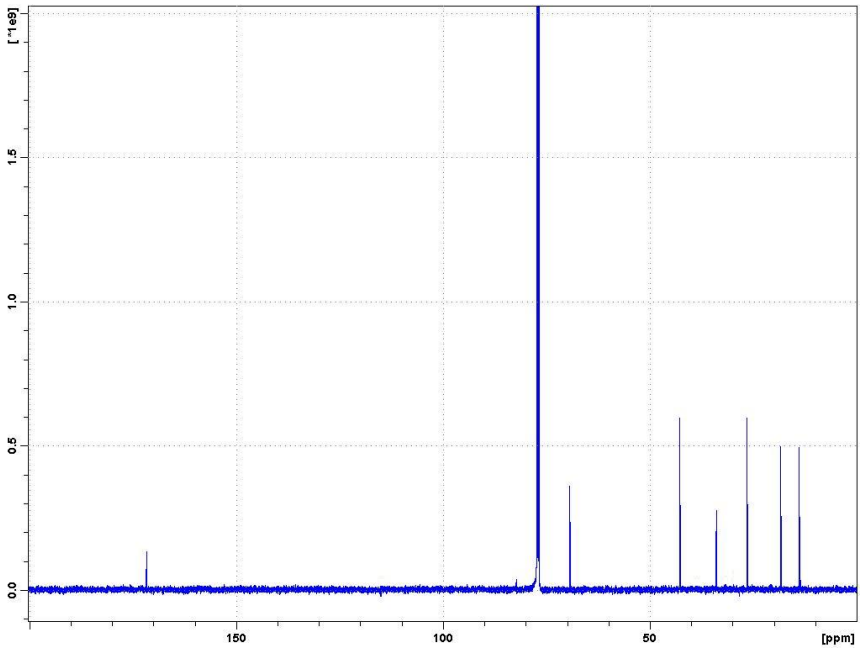
Chiral HPLC of 3b

Peak	Processed Channel	Retention Time (min)	Area	% Area	Height
1	@210 nm	19.197	35199	91.700	650
2	@210 nm	27.022	3068	8.300	42

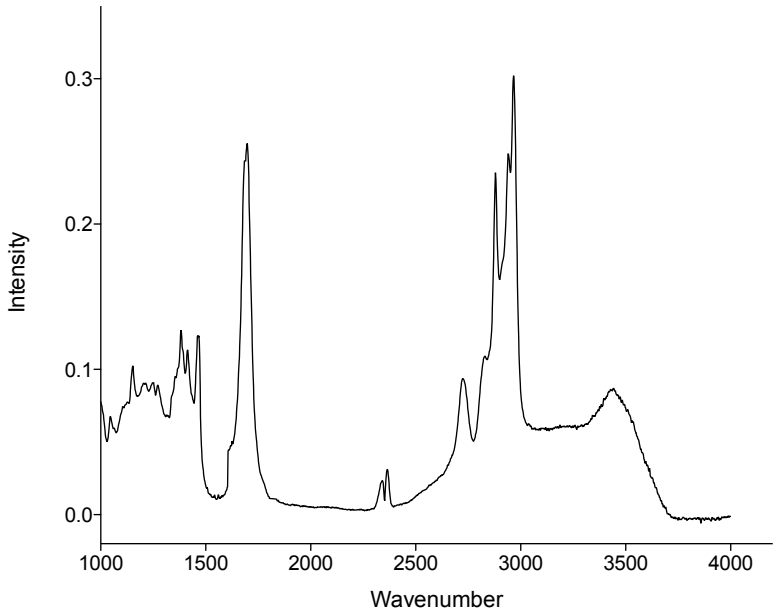


^{1}H NMR and ^{13}C-NMR of 3b





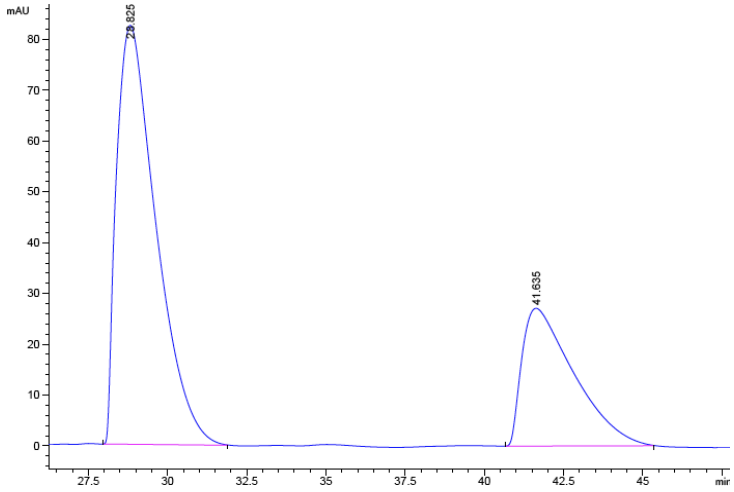
FTIR of 3b



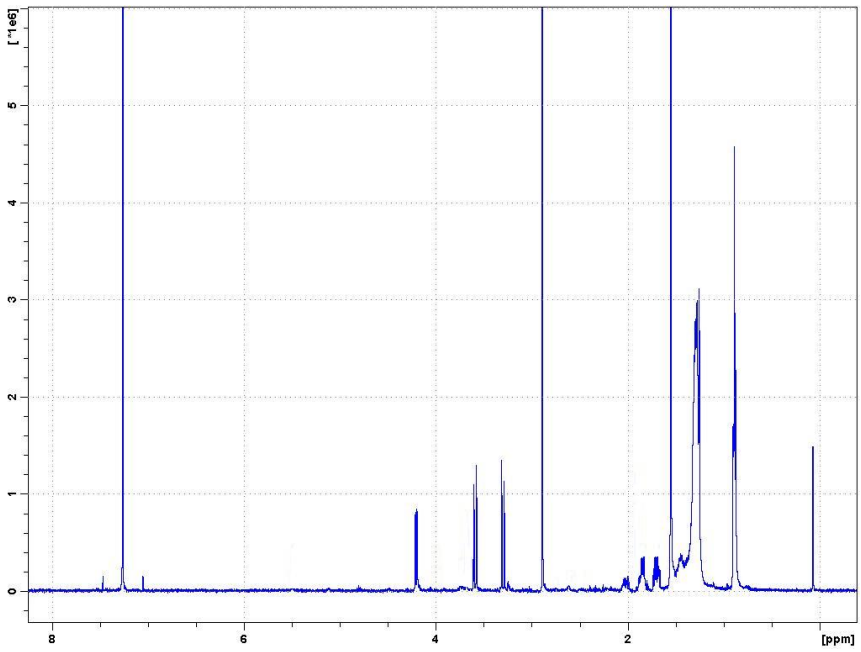
3-heptyl-2-methyl-1,4,2-oxathiazinan-6-one (3c). The general procedure was followed. Yield: 80%; Enantiomeric excess: 31%, determined by HPLC analysis: Chiral OJ 99 : 1 = Hex : ^{i}PrOH, 0.5 ml/min, detection 210 nm, t_R: 28.8 min, 41.6 min; Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 0.89 (3H, t, *J* = *7.4* Hz), 1.17-1.50 (10H, m), 1.65-1.75 (1H, m), 1.78-1.90 (1H, m), 2.89 (3H, s), 3.30 (1H, d, *J* = 13.2 Hz), 3.59 (1H, d, *J* = 13.2 Hz), 4.20 (1H, dd, *J* = 3.3, 9.9 Hz); ^{13}C NMR ($CDCl_3$) δ = 12.6, 21.1, 23.5, 25.0, 27.6, 28.0, 30.3, 30.4, 41.4, 68.1, 170.3; HRMS (ESI-TOF): 232.1320 ($[M+H]^+$, $C_{11}H_{22}NO_2S$; calc. 232.1327).

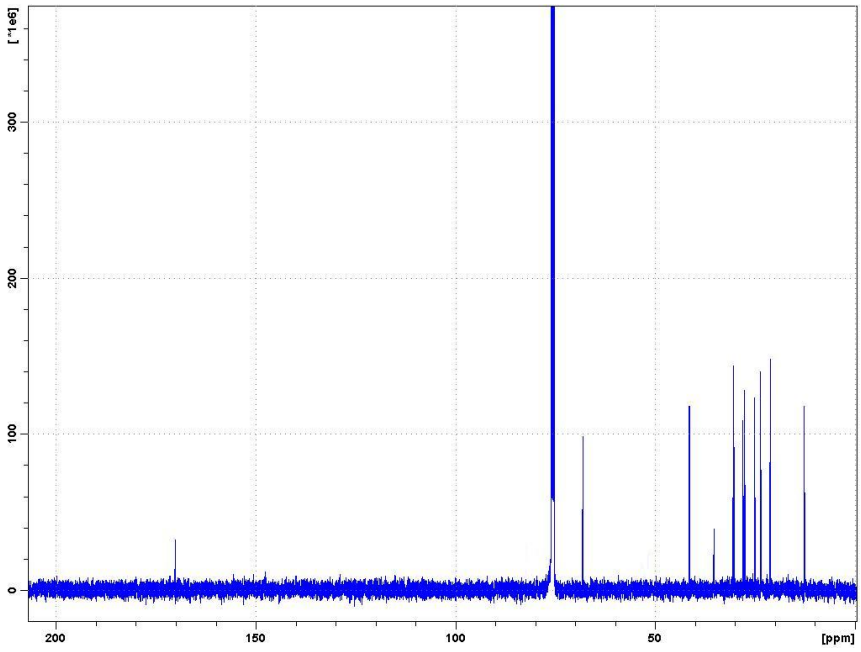
Chiral HPLC of 3c

Peak	Processed Channel	Retention Time (min)	Area	% Area	Height
1	@210 nm	27.791	14302	65.722	152
2	@210 nm	39.243	7459	34.278	54

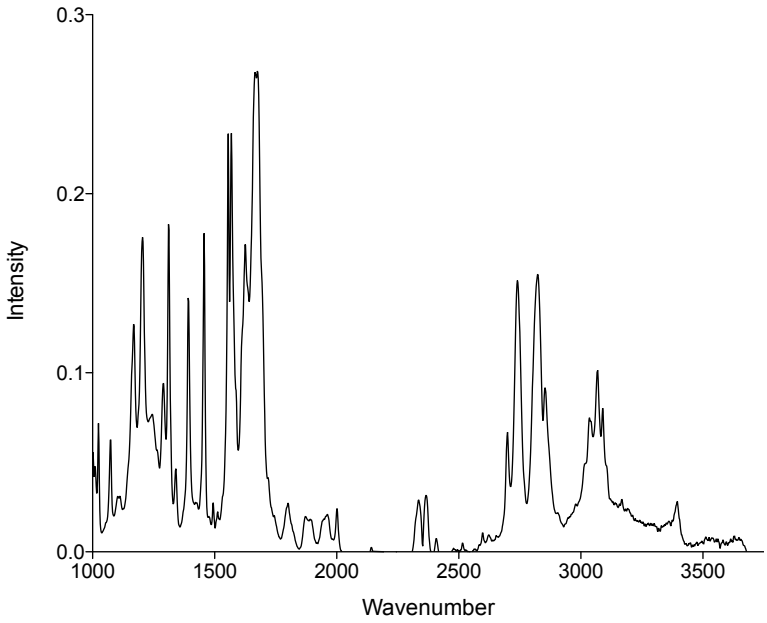


^{1}H NMR and ^{13}C-NMR of 3c





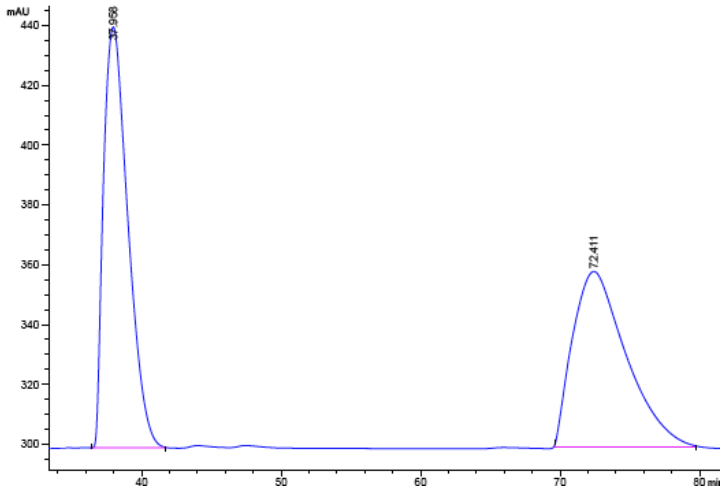
FTIR of 3c



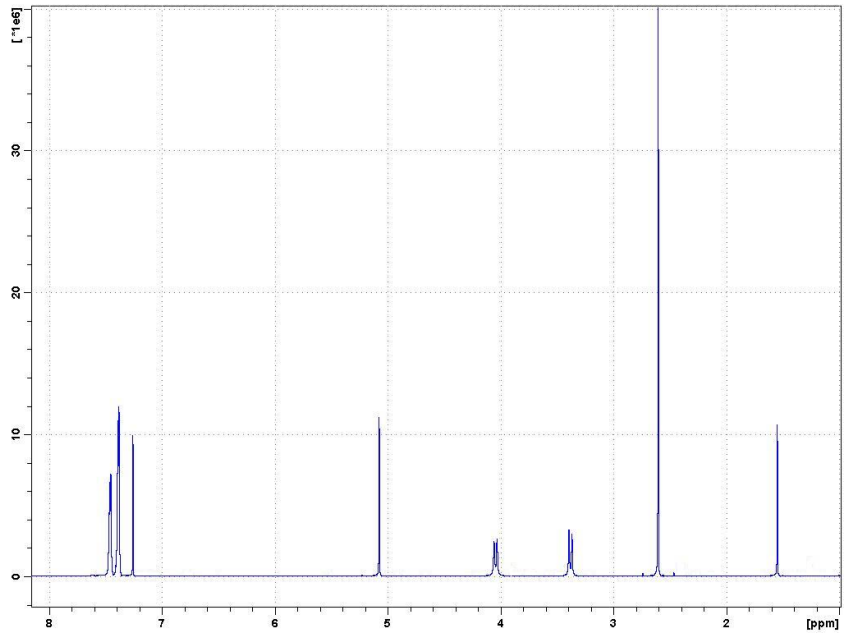
2-methyl-3-phenyl-1,4,2-oxathiazinan-6-one (3d). The general procedure was followed. Yield: 25%; Enantiomeric excess: 3%, determined by HPLC analysis: Hex : ^{i}PrOH = 99 : 1, 0.5 ml/min, detection 210 nm, t_R: 37.9 min, 72.4 min; Colorless oil; ^{1}H NMR ($CDCl_3$) δ = 2.61 (3H, s), 3.39 (1H, d, J = 12.9 Hz), 4.05 (1H, d, J = 12.9 Hz), 5.08 (1H, s), 7.37-7.01 (3H, m), 7.44-7.49 (2H, m); ^{13}C NMR ($CDCl_3$) δ = 27.7, 43.5, 72.1, 128.8, 129.0, 130.0, 136.9, 171.28; HRMS (ESI-TOF): 210.0583 ($[M+H]^+$, $C_{10}H_{12}NO_2S$; calc. 210.0544).

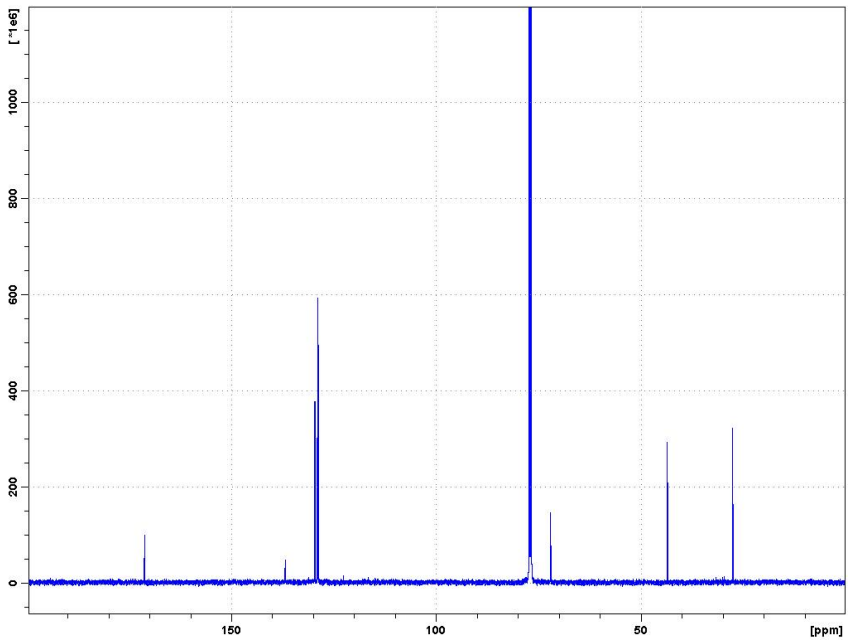
Chiral HPLC of 3d

Peak	Processed Channel	Retention Time (min)	Area	% Area	Height
1	@210 nm	37.958	17127	51.745	140
2	@210 nm	72.411	16011	48.246	59



^{1}H NMR and ^{13}C-NMR of 3d





FTIR of 3d