

SUPPORTING INFORMATION

The smallest organocatalyst in highly enantioselective direct aldol reaction in wet solvent-free conditions

Sudipto Bhowmick[†], Sunita S. Kunte[#] and Kartick C. Bhowmick^{†,*}

[†] Division of Organic Synthesis, Department of Chemistry, Visva-Bharati University; Bolpur, West Bengal-731 235, India

[#] Division of Organic Chemistry, Analytical Section, National Chemical Laboratory, Pune-411 008, India

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Experimental Section

General Methods. Routine monitoring of reaction was performed by TLC, using pre-coated silica gel TLC plates obtained by E-Merck. All the column chromatographic separations were done by using silica gel (60-120 mesh). Petroleum ether used was of boiling range 60-80 °C. Proton nuclear magnetic resonance (¹H NMR) spectra were recorded on BRUKER-400 MHz spectrometer. Chemical shifts are expressed in ppm downfield from TMS as internal standard. Infrared (IR) spectra were recorded on a FT-IR spectrometer (Shimadzu). Melting points were measured on a digital melting point apparatus. Analytical high performance liquid chromatography (HPLC) was carried out on (Shimadzu CLASS-VP V6.12 SP5) instrument using Chiralpak AD-H (4.6mm×250mm), Chiralpak Kromasil 5-AmyCoat (4.6 mm×250mm), and Chiralcel OD-H (4.6 mm×250 mm) columns. Optical rotations were measured on a Bellingham+Stanley ADP410 Polarimeter at $\lambda=589$ nm.

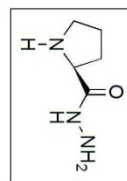
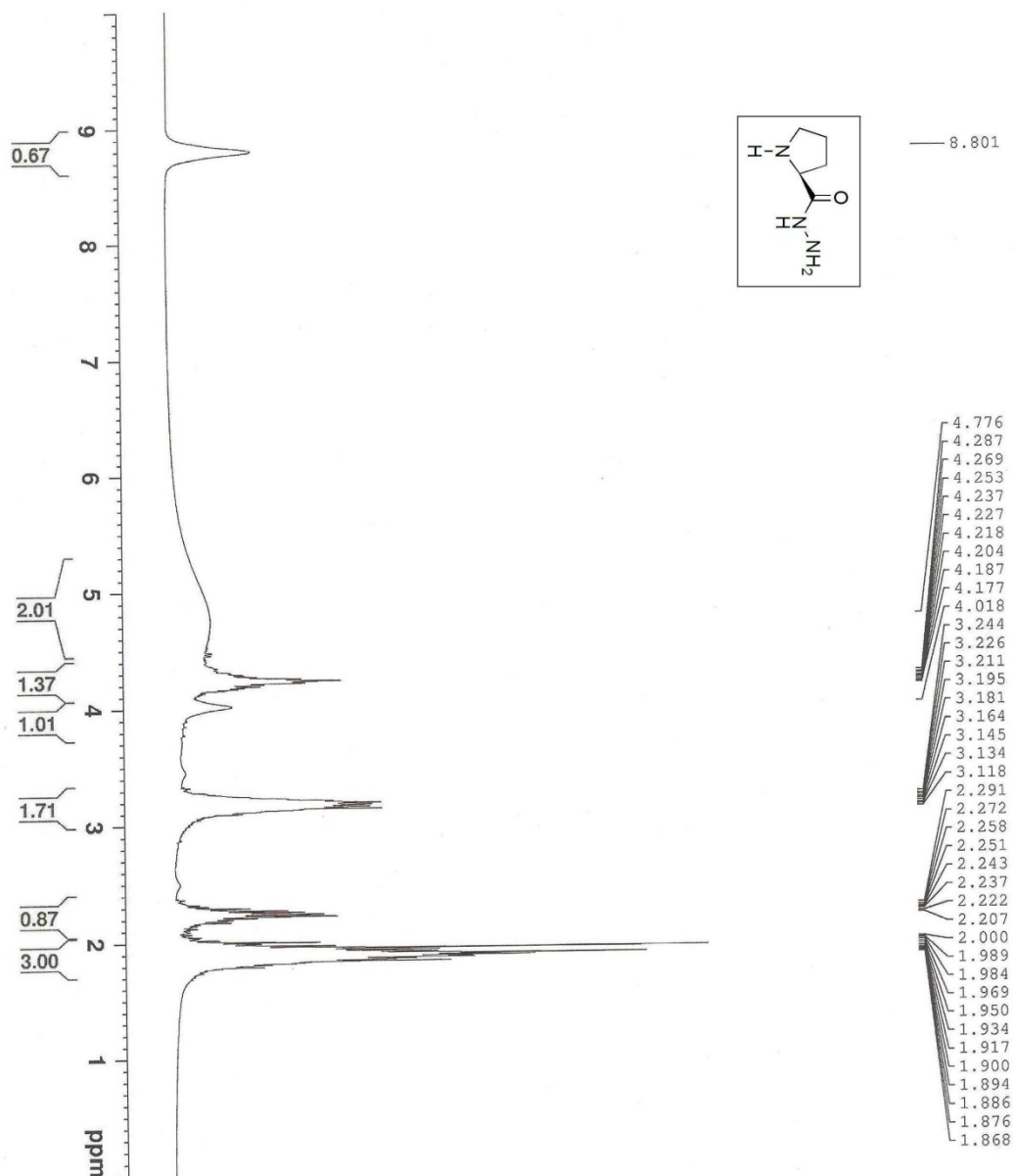
Synthesis of L-proline hydrazide, 1

The following procedure is a partially modified one from the reported procedure in literature.^{1,2}

A solution of L-proline (10 mmol, 1.15g) was dissolved in 5 ml of MeOH and was cooled to 0 °C followed by slow addition of 1 mL of acetyl chloride. The mixture was stirred at refluxed for 12 h and then allowed to attain room temperature. The solution was concentrated under reduced pressure. The methyl ester hydrochloride of L-proline so obtained was washed with Et₂O (2×25 mL), dried over Na₂SO₄ and concentrated under reduced pressure to give a crude brownish liquid product (1.57 g, 95%). Then to the crude product in MeOH (9 mL), 98% hydrazine hydrate (8.1 mL) was added drop wise and the mixture was stirred for 24 h. A white precipitate generated was removed by filtration and the filtrate was concentrated under reduced pressure. The yellow oily residue was washed with MeOH (2 x 20 mL) followed by drying under vacuum to give the pure product as a colourless oil (0.99 g, 81%). The ¹H NMR, ¹³C NMR and IR is consistent with the literature reports.²

¹H NMR (CDCl₃, 400 MHz) δ 1.87 (3H, m), 2.22 (1H, m), 3.13 (2H, m), 4.01 (1H, br, s), 4.22 (1H, m), 4.77 (2H, br, s), 8.80 (1H, br, s); ¹³C NMR (CDCl₃, 101 MHz) δ 25.3, 30.8, 45.8, 59.5, 173.1; IR (film, cm⁻¹): 3328 (NH), 3311, 3251, 3153, 3031, 2869, 1741, 1616, 1595, 1446, 1240, 1178, 1087, 894. ESI-MS (m/z): calcd for C₅H₁₁N₃O [M +H]⁺: 130.0982; found: 130.0858.

¹H NMR Spectrum of L-Proline hydrazide, 1



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 EXPNO 58
 PROCNO 1

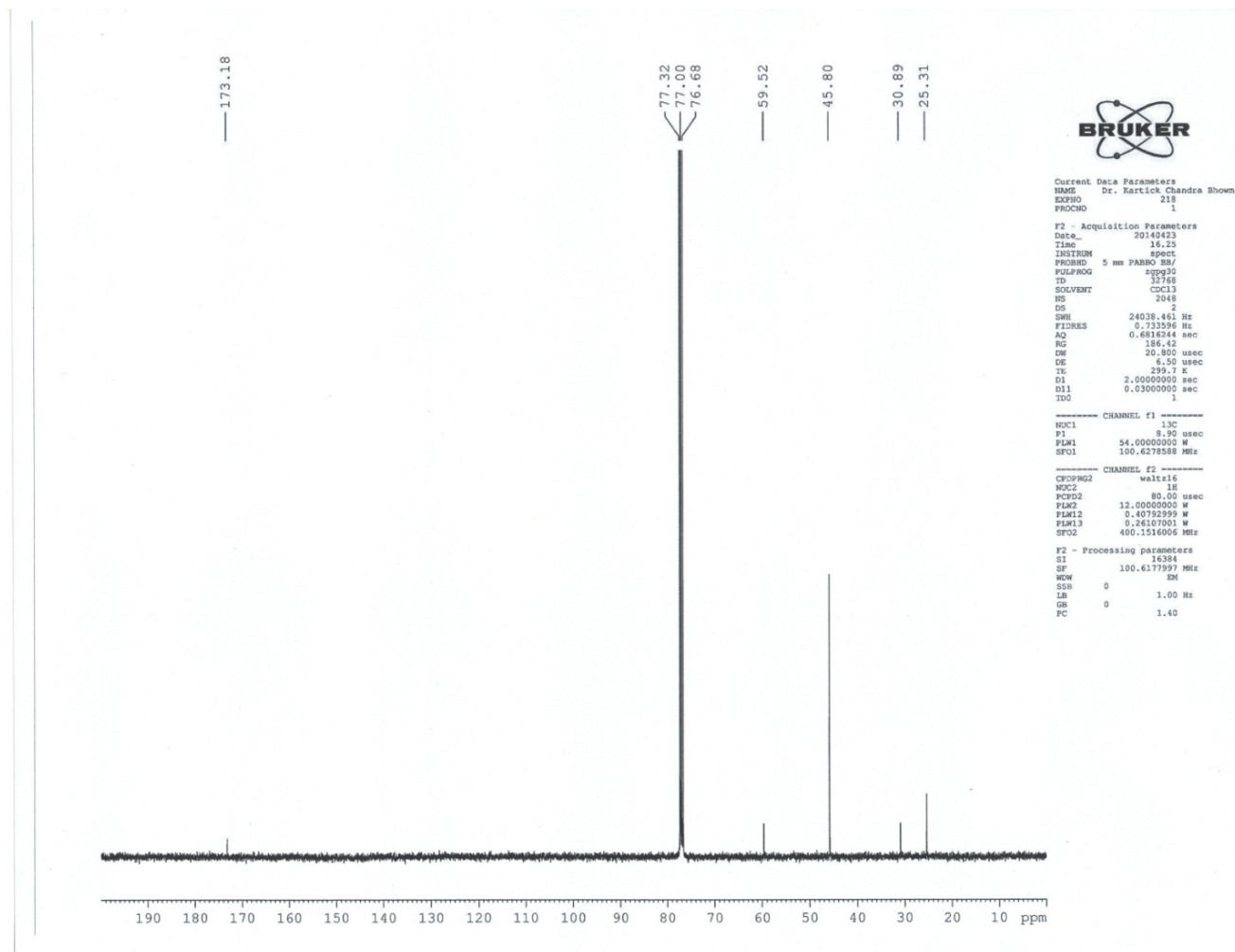
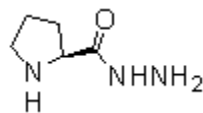
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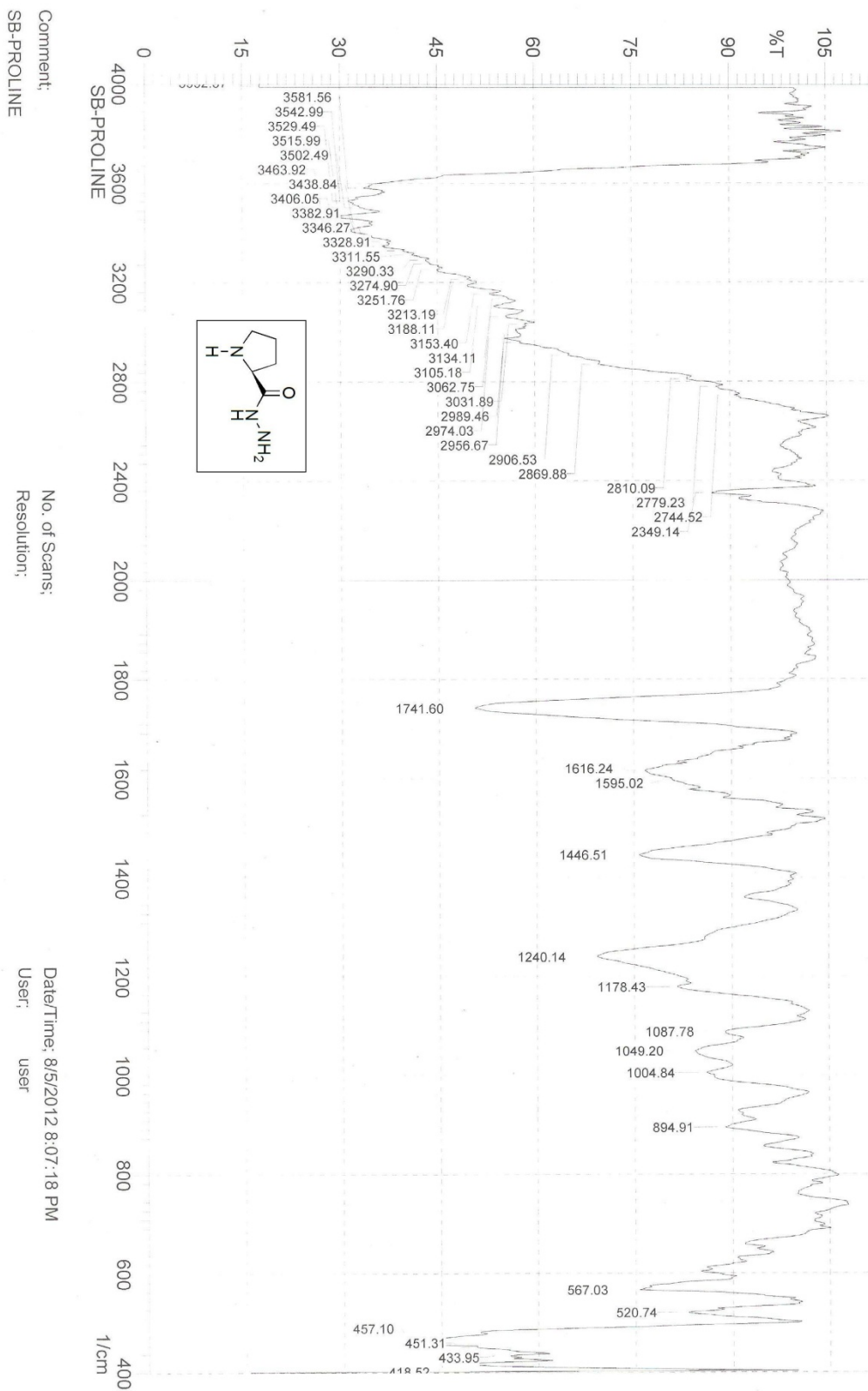
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¹³C NMR Spectrum of L-Proline hydrazide, 1



FT-IR Spectrum of L-Proline hydrazide, 1

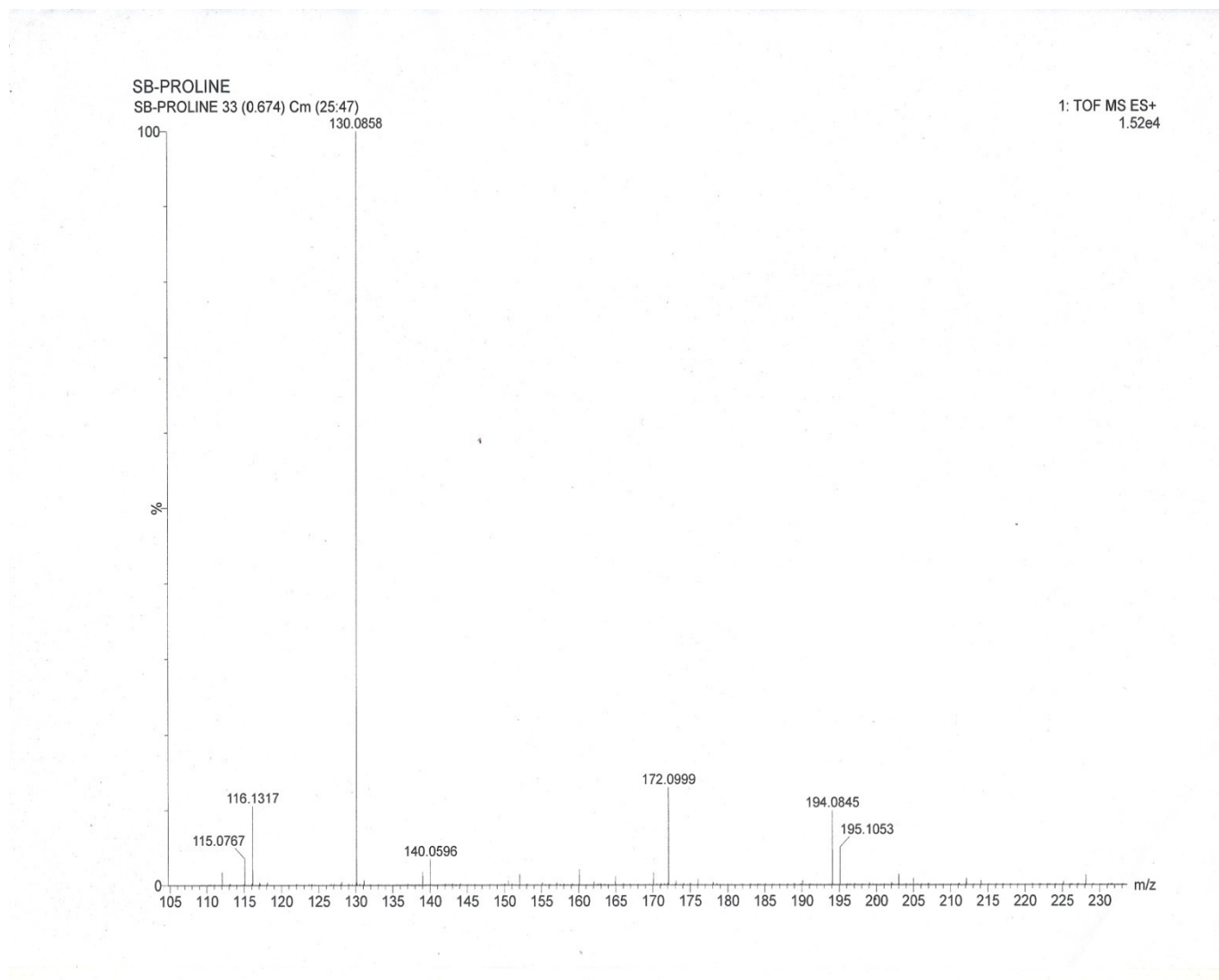
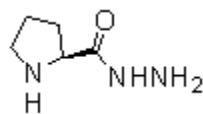


SR-262



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ESI-MS Spectrum of L-Proline hydrazide, 1

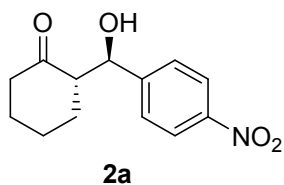


General procedure for the enantioselective direct aldol reaction.

To a mixture of catalyst **1** (0.1 mmol) and acid additive (0.05 mmol) in water (0.01 mL), ketone (4.0 mmol) was added followed by aromatic aldehyde (1.0 mmol). The resulting mixture was stirred at room temperature, an emulsion was formed. The reaction was monitored by TLC. It was then quenched with 10 mL of saturated NaHCO₃ solution, extracted with EtOAc (3×10 mL), and brine (15 mL), dried over Na₂SO₄. Purification by column chromatography afforded the corresponding pure products as a mixture of *syn* and *anti* isomers. The ee of the *anti* isomers were determined by chiral HPLC analysis.

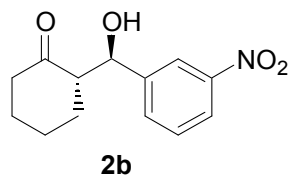
HPLC data for chiral aldol products

(2*S*,1'*R*)-2-[Hydroxy(4-nitrophenyl)methyl]cyclohexan-1-one (**2a**).³



The spectroscopic NMR data are in agreement with the previously reported ones.³ The enantiomeric excess of this sample was determined to be 97% by chiral HPLC analysis (Chiralpak Kromasil 5-CelluCoat, hexanes/*i*PrOH 95/5), flow rate = 1.0 mL/min; λ = 254 nm; t_R (major)=24.5 min, t_R (minor)=34.9 min.

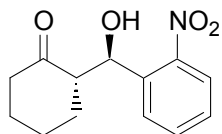
(2*S*,1'*R*)-2-[Hydroxy(3-nitrophenyl)methyl]cyclohexan-1-one (**2b**).⁴



The spectroscopic NMR data are in agreement with the previously reported ones.⁴ The enantiomeric excess of this sample was determined to be 98% by chiral HPLC analysis

Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (15:85), flow rate = 0.5 mL/min;
 $\lambda = 254 \text{ nm}$; t_R (major) = 20.7 min, t_R (minor) = 27.9 min.

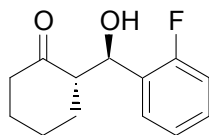
(2*S*,1'*R*)-2-[Hydroxy(2-nitrophenyl)methyl]cyclohexan-1-one (2c).³



2c

The spectroscopic NMR data are in agreement with the previously reported ones.³ The enantiomeric excess of this sample was determined to be 88% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (15:85), flow rate = 0.5 mL/min; $\lambda = 254 \text{ nm}$; t_R (major) = 17.5 min, t_R (minor) = 20.0 min.

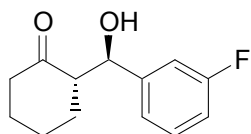
(2*S*,1'*R*)-2-[Hydroxy(2-fluorophenyl)methyl]cyclohexan-1-one (2d).⁵



2d

The spectroscopic NMR data are in agreement with the previously reported ones.⁵ The enantiomeric excess of this sample was determined to be 68% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (05:95), Flow rate: 0.5 mL/min; $\lambda = 254 \text{ nm}$; t_R (major) = 16.2 min, t_R (minor) = 20.7 min.

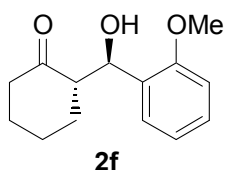
(2*S*,1'*R*)-2-[Hydroxy(3-fluorophenyl)methyl]cyclohexan-1-one (2e).



2e

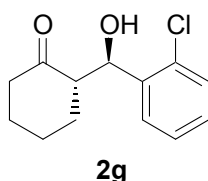
The spectroscopic NMR data are in agreement with the previously reported ones. The enantiomeric excess of this sample was determined to be 32% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (05:95), Flow rate: 0.5 mL/min; $\lambda = 254$ nm; t_R (minor) = 16.5 min, t_R (major) = 18.5 min.

(2*S*,1'*R*)-2-[Hydroxy(2-methoxyphenyl)methyl]cyclohexan-1-one (2f).⁶



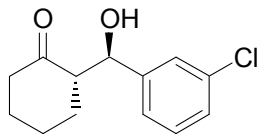
The spectroscopic NMR data are in agreement with the previously reported ones.⁶ The enantiomeric excess of this sample was determined to be 89% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (05:95), Flow rate: 0.5 mL/min; $\lambda = 254$ nm; t_R (major) = 24.8 min, t_R (minor) = 28.8 min.

(2*S*,1'*R*)-2-[Hydroxy(2-chlorophenyl)methyl]cyclohexan-1-one (2g).³



The spectroscopic NMR data are in agreement with the previously reported ones.³ The enantiomeric excess of this sample was determined to be 64% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (05:95), Flow rate: 0.5 mL/min; $\lambda = 254$ nm; t_R (major) = 12.1 min, t_R (minor) = 17.0 min.

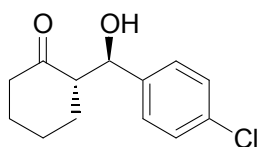
(2*S*,1'*R*)-2-[Hydroxy(3-chlorophenyl)methyl]cyclohexan-1-one (2h).³



2h

The spectroscopic NMR data are in agreement with the previously reported ones.³ The enantiomeric excess of this sample was determined to be 46% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (05:95), Flow rate: 0.5 mL/min; $\lambda = 254$ nm; t_R (major) = 19.2 min, t_R (minor) = 21.0 min.

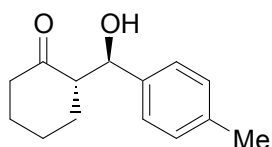
(2*S*,1'*R*)-2-[Hydroxy(4-chlorophenyl)methyl]cyclohexan-1-one (2i).³



2i

The spectroscopic NMR data are in agreement with the previously reported ones.³ The enantiomeric excess of this sample was determined to be 91% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (10:90), Flow rate: 0.5 mL/min; $\lambda = 254$ nm; t_R (major) = 16.5 min, t_R (minor) = 18.8 min.

(2*S*,1'*R*)-2-[Hydroxy(4-methylphenyl)methyl]cyclohexan-1-one (2j).⁴

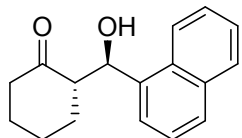


2j

The spectroscopic NMR data are in agreement with the previously reported ones.⁴ The enantiomeric excess of this sample was determined to be 49% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (3:97), Flow rate: 0.5 mL/min;

$\lambda = 254 \text{ nm}$; t_R (major) = 14.2 min, t_R (minor) = 18.6 min.

(2*S*, 1'*R*)-2-[Hydroxy(naphthalen-1-yl)methyl]cyclohexan-1-one (2k).⁴

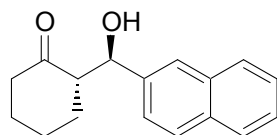


2k

The spectroscopic NMR data are in agreement with the previously reported ones.⁴ The enantiomeric excess of this sample was determined to be 44% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (3:97), Flow rate: 0.5 mL/min;

$\lambda = 254 \text{ nm}$; t_R (major) = 16.2 min, t_R (minor) = 23.5 min.

(2*S*, 1'*R*)-2-[Hydroxy(naphthalen-2-yl)methyl]cyclohexan-1-one (2l).⁴

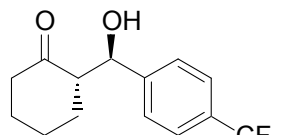


2l

The spectroscopic NMR data are in agreement with the previously reported ones.⁴ The enantiomeric excess of this sample was determined to be 61% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (10:90), Flow rate: 0.5 mL/min;

$\lambda = 254 \text{ nm}$; t_R (major) = 26.4 min, t_R (minor) = 33.4 min.

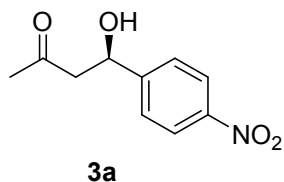
(2*S*, 1'*R*)-2-[Hydroxy(4-trifluoromethylphenyl)methyl]cyclohexan-1-one (2m).⁴



2m

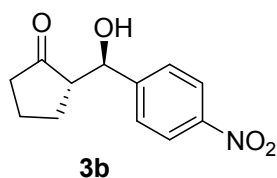
The spectroscopic NMR data are in agreement with the previously reported ones.⁴ The enantiomeric excess of this sample was determined to be 80% by chiral HPLC analysis Chiralcel OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (20:80), Flow rate: 0.5 mL/min; $\lambda = 254$ nm; t_R (major) = 19.3 min, t_R (minor) = 21.4 min.

(4*R*)-4-Hydroxy-p-nitrophenylbutan-2-one (3a).⁷



The spectroscopic NMR data are in agreement with the previously reported ones.⁷ The enantiomeric excess of this sample was determined to be 98% by chiral HPLC analysis Chiralcel-OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (8.5:91.5), Flow rate: 0.7 mL/min; $\lambda = 254$ nm; t_R (major) = 38.2 min, t_R (minor) = 45.0 min.

(2*S*,1'*R*)-2-[Hydroxy(4-nitrophenyl)methyl]cyclopentan-1-one (3b).⁷

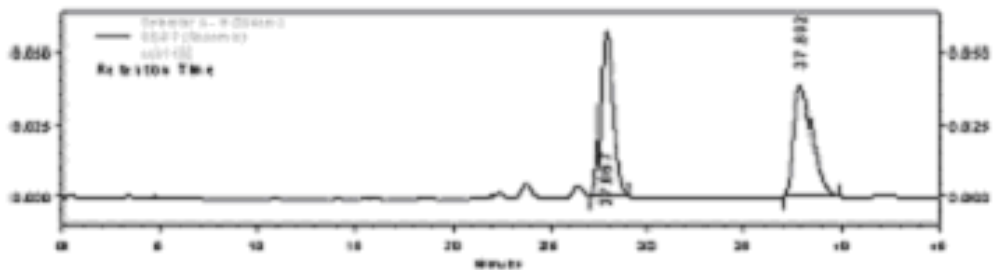


The spectroscopic NMR data are in agreement with the previously reported ones. The enantiomeric excess of this sample was determined to be >99.9% by chiral HPLC analysis Chiralpak Kromasil-5AmyCoat (254 x 4.6), Mobile phase: IPA:Pet Ether (10:90), Flow rate : 1 mL/min; $\lambda = 265$ nm; t_R (minor) = 20.0 min, t_R (major) = 21.5 min.

References:

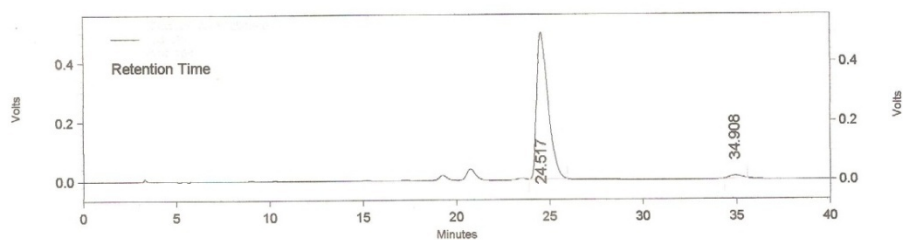
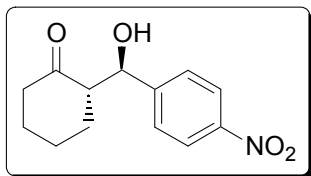
1. V. Gauchot and A. R. Schmitzer, *J. Org. Chem.*, 2012, **77**, 4917-4923.
2. A. Kudelko, W. Zielinski and K. Ejsmont, *Tetrahedron*, 2011, **67**, 7838-7845.
3. M. Gruttadauria, F. Giacalone, A. M. Marculescu, P. Lo Meo, S. Riela and R. Noto, *Eur. J. Org. Chem.*, 2007, 4688-4698.
4. C. Wu, X. Fu, X. Ma and S. Li, *Tetrahedron: Asymmetry*, 2010, **21**, 2465-2470.
5. F. Giacalone, M. Gruttadauria, P. Lo Meo, S. Riela and R. Noto, *Adv. Synth. Catal.*, 2008, **350**, 2747-2760.
6. Y. -J. An, Y. -X. Zhang, Y. Wu, Z. -M. Liu, C. Pi and J. -C. Tao, *Tetrahedron: Asymmetry*, 2010, **21**, 688-694.
7. N. Mase, Y. Nakai, N. Ohara, H. Yoda, K. Takabe, F. Tanaka and C. F. Barbas III, *J. Am. Chem. Soc.* 2006, **128**, 734-735.

2a (Racemic) (HPLC Conditions: Chiralpak Kromasil 5-CelluCoat, hexanes/iPrOH 95/5), flow rate = 0.7 mL/min; λ = 254 nm)



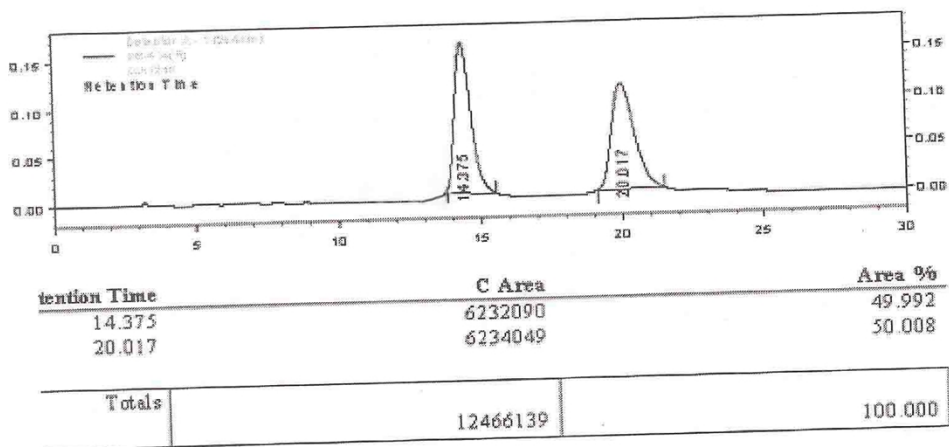
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2a (Chiral HPLC done under conditions mentioned in the above experimental section)

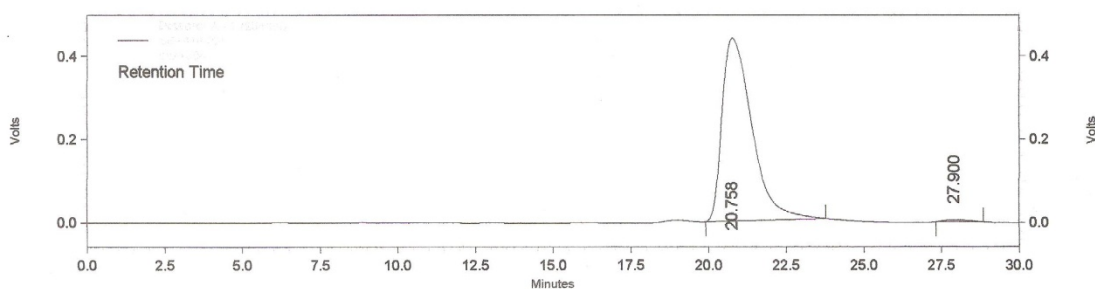
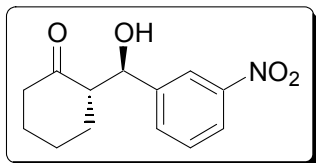


Detector A - 1 (254nm)			
Retention Time	C Area	Area %	
24.517	20943388	98.181	
34.908	387911	1.819	
Totals	21331299	100.000	

2b (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (15:85), flow rate = 0.7 mL/min; λ = 254 nm)

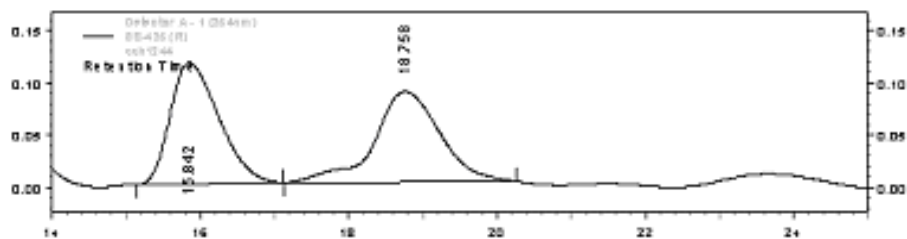


2b (Chiral HPLC done under conditions mentioned in the above experimental section)



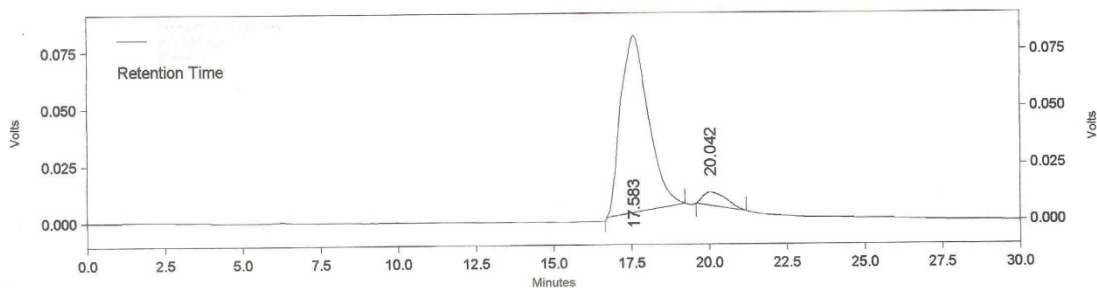
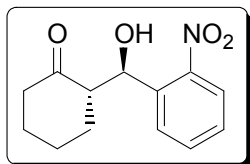
Detector A - 1 (254nm)			
Pk #	Retention Time	Area	Area %
1	20.758	29329234	99.160
2	27.900	248385	0.840
Totals		29577619	100.000

2c (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (10:90), flow rate = 0.7 mL/min; λ = 254 nm)



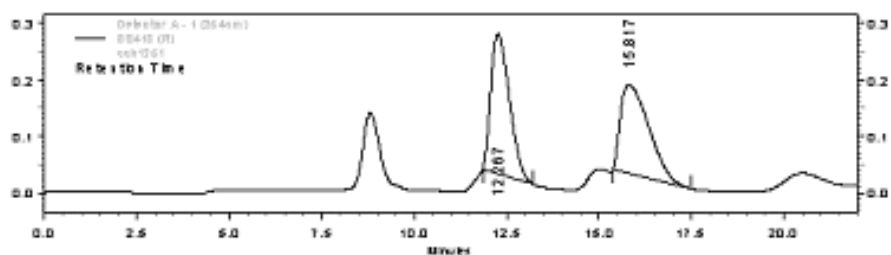
Retention Time	C Area	Area %
15.842	5292208	49.828
18.758	5328658	50.172
Totals	10620866	100.000

2c (Chiral HPLC done under conditions mentioned in the above experimental section)



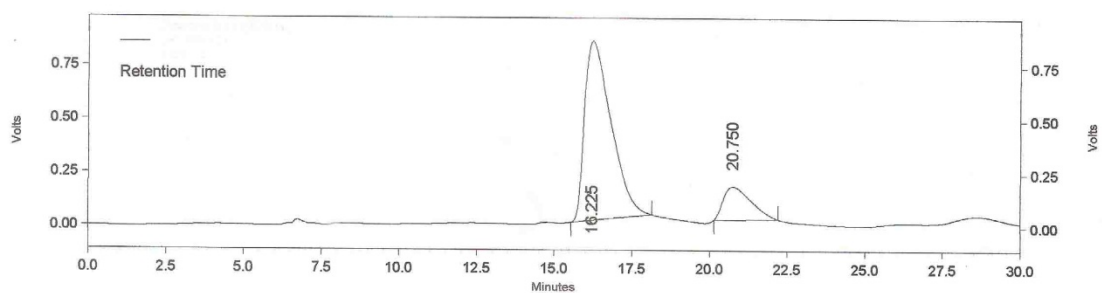
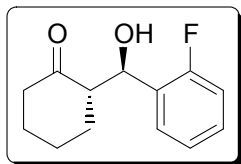
Detector A - 1 (254nm)			
Pk #	Retention Time	Area	Area %
1	17.583	4820161	94.009
2	20.042	307167	5.991
Totals		5127328	100.000

2d (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (05:95),
Flow rate: 0.7 ml/min; $\lambda = 254$ nm; t_R (major) = 12.2 min, t_R (minor) = 16.3 min.)



Retention Time	C Area	Area %
12.267	8714354	50.730
15.817	8463523	49.270
Totals	17177877	100.000

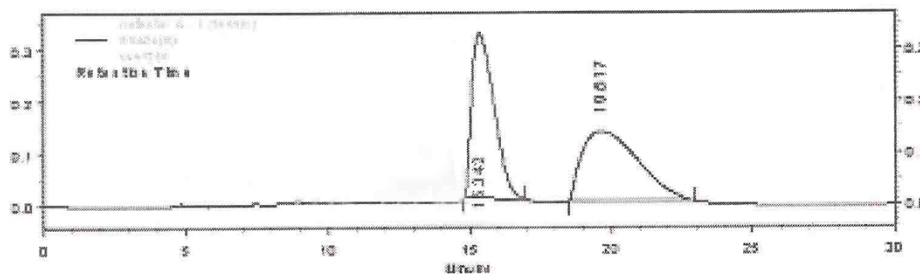
2d (Chiral HPLC done under conditions mentioned in the above experimental section)



Detector A - 1 (254nm)

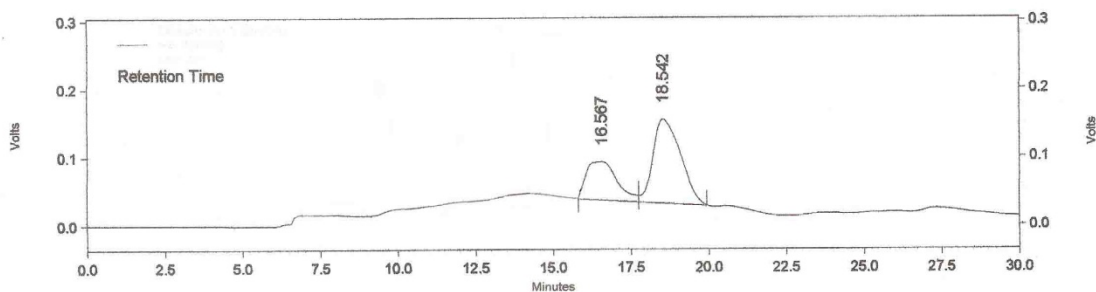
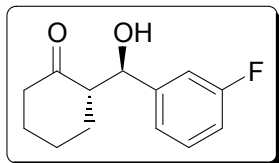
Pk #	Retention Time	Area	Area %
1	16.225	49988442	83.764
2	20.750	9689486	16.236
Totals		59677928	100.000

2e (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (05:95), Flow rate: 0.7 ml/min; $\lambda = 254$ nm)



Retention Time	C Area	Area %
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19.617	18682253	51.527
Totals	36257071	100.000

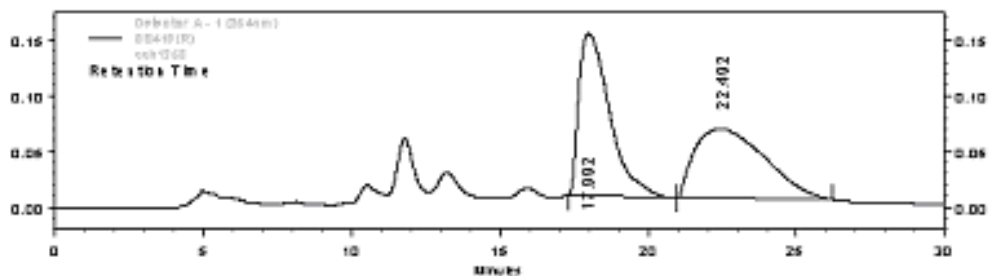
2e (Chiral HPLC done under conditions mentioned in the above experimental section)



Detector A - 1 (254nm)

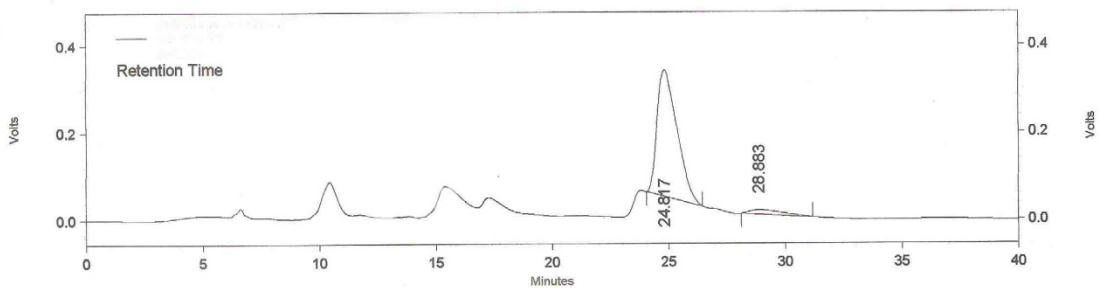
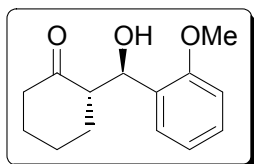
Pk #	Retention Time	Area	Area %
1	16.567	3890271	33.801
2	18.542	7619096	66.199
Totals		11509367	100.000

2f (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (05:95), Flow rate: 0.7 ml/min; λ = 254 nm)



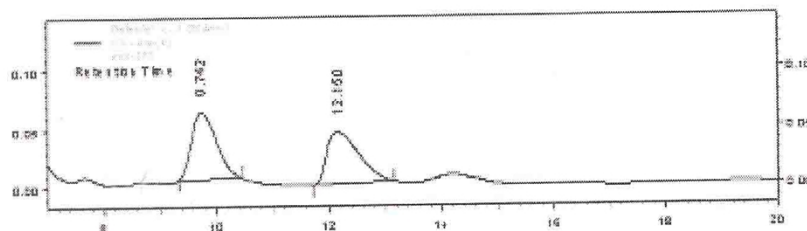
Retention Time	C Area	Area %
17.992	10643567	50.766
22.492	10322192	49.234
Totals		100.000

2f (Chiral HPLC done under conditions mentioned in the above experimental section)



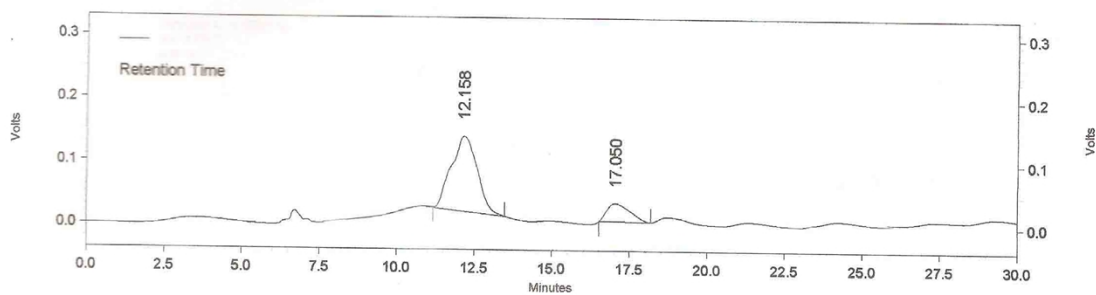
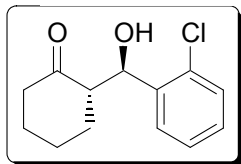
Detector A - 1 (254nm)			
PK #	Retention Time	Area	Area %
1	24.817	17408725	94.432
2	28.883	1026463	5.568
Totals		18435188	100.000

2g (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (05:95), Flow rate: 0.7 ml/min; $\lambda = 254$ nm)



Retention Time	C Area	Area %
9.742	1741746	50.307
12.150	1720479	49.693
Totals	3462225	100.000

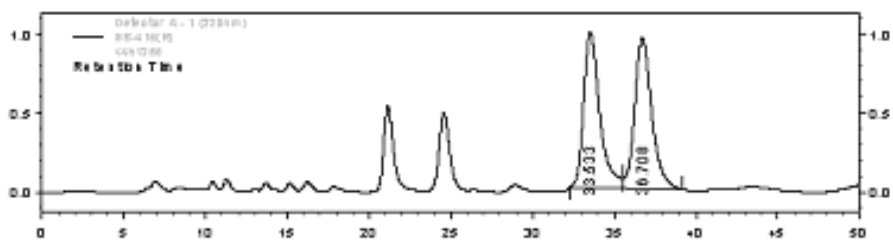
2g (Chiral HPLC done under conditions mentioned in the above experimental section)



Detector A - 1 (254nm)

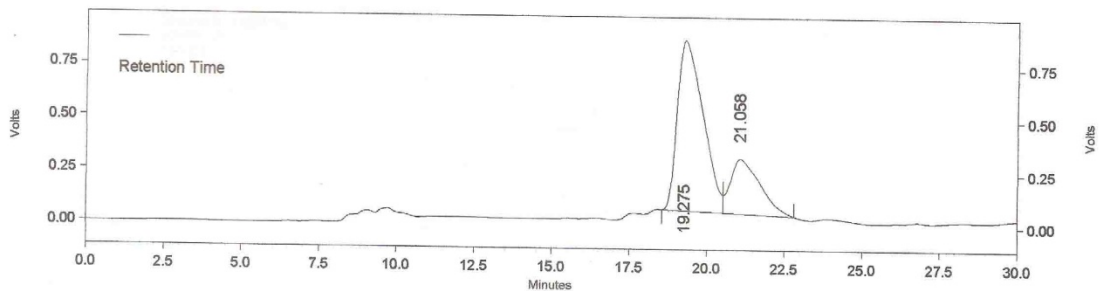
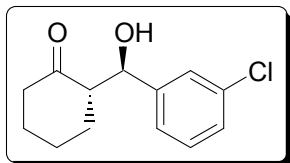
Pk #	Retention Time	Area	Area %
1	12.158	6932352	82.173
2	17.050	1503941	17.827
Totals		8436293	100.000

2h (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (05:95), Flow rate: 0.7 ml/min; $\lambda = 254$ nm)



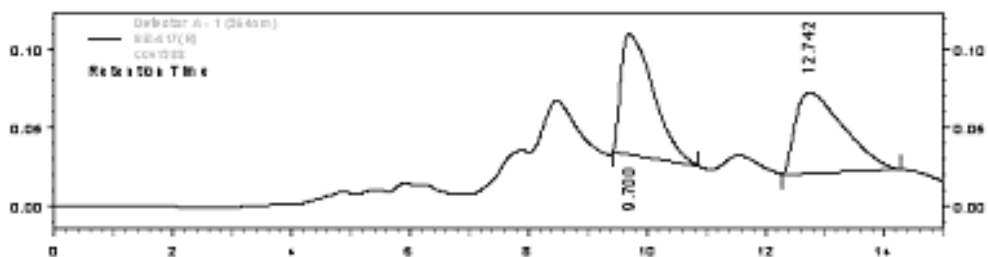
Retention Time	C Area	Area %
33.533	67083106	49.133
36.708	69449347	50.867
Totals	136532453	100.000

2h (Chiral HPLC done under conditions mentioned in the above experimental section)



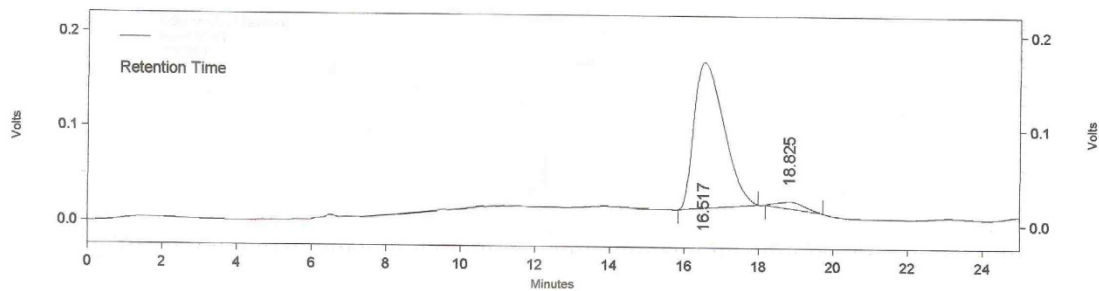
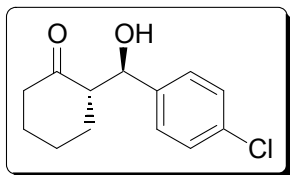
Detector A - 1 (254nm)	Pk #	Retention Time	Area	Area %
	1	19.275	46804610	72.919
	2	21.058	17382431	27.081
Totals			64187041	100.000

2i (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (15:85), Flow rate: 0.7 ml/min; $\lambda = 254$ nm)



Retention Time	C Area	Area %
9.700	2938444	50.546
12.742	2874979	49.454
Totals	5813423	100.000

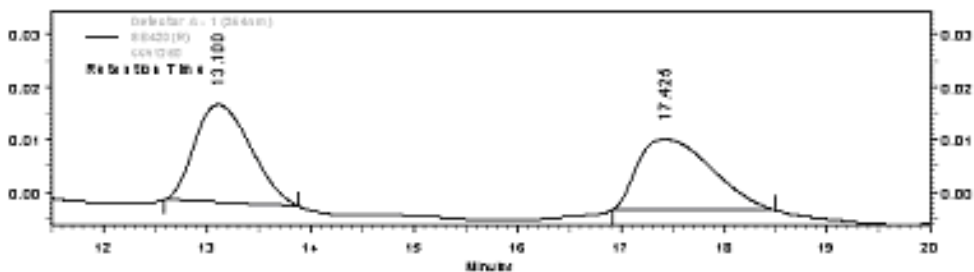
2i (Chiral HPLC done under conditions mentioned in the above experimental section)



Detector A - 1 (254nm)

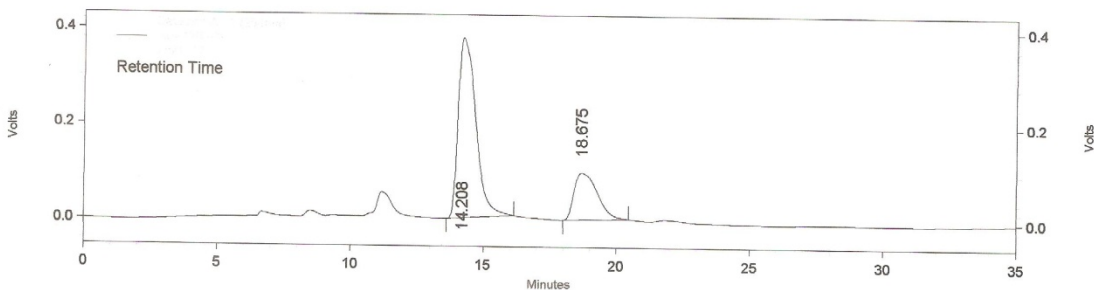
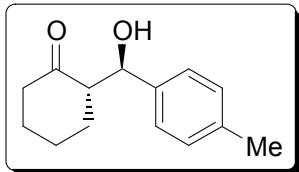
Pk #	Retention Time	Area	Area %
1	16.517	8518553	95.738
2	18.825	379267	4.262
Totals		8897820	100.000

2j (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (3:97), Flow rate: 1 ml/min; λ = 254 nm)



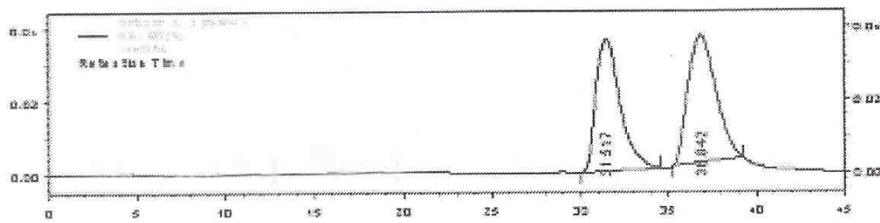
Retention Time	C Area	Area %
13.100	233973	51.176
17.425	223220	48.824
Totals	457193	100.000

2j (Chiral HPLC done under conditions mentioned in the above experimental section)



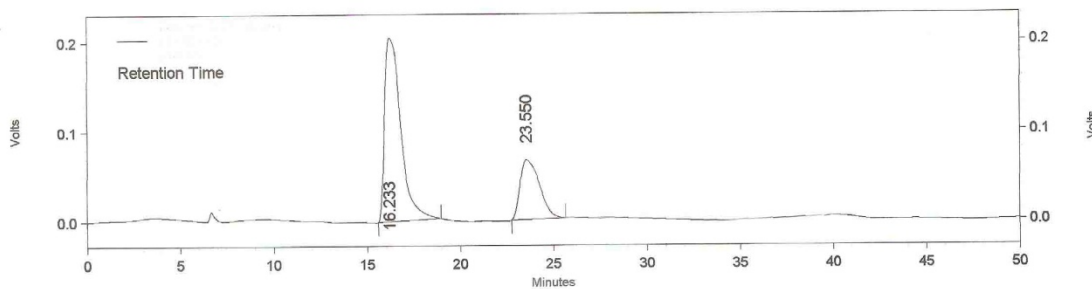
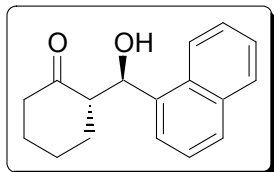
Detector A - 1 (254nm)			
Pk #	Retention Time	Area	Area %
1	14.208	17287453	74.368
2	18.675	5958510	25.632
Totals		23245963	100.000

2k (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (3:97), Flow rate: 1 ml/min; $\lambda = 254$ nm)



Retention Time	C Area	Area %
31.517	3431581	47.140
36.842	3847940	52.860
Totals	7279521	100.000

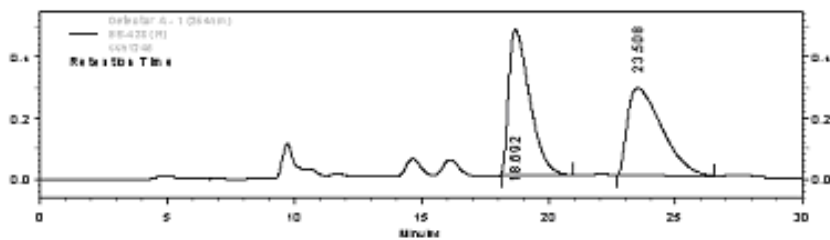
2k (Chiral HPLC done under conditions mentioned in the above experimental section)



Detector A - 1 (254nm)

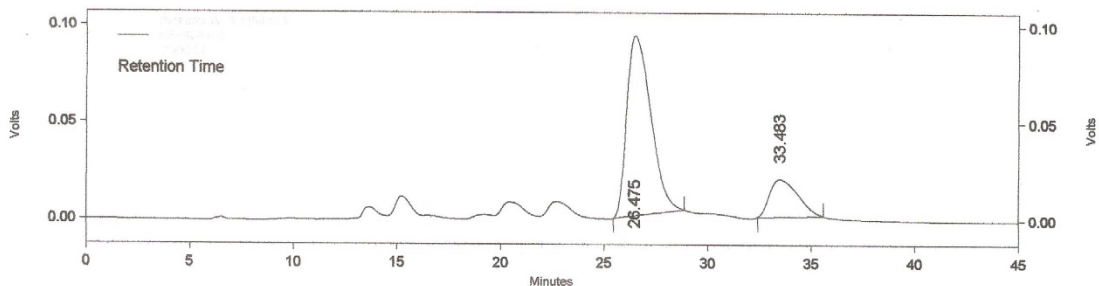
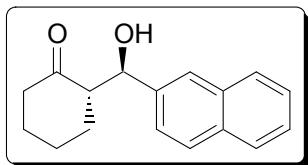
Pk #	Retention Time	Area	Area %
1	16.233	12406598	72.112
2	23.550	4798023	27.888
Totals		17204621	100.000

2l (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), IPA:n-Hexane (10:90), Flow rate: 0.7 ml/min; $\lambda = 254$ nm)



Retention Time	C Area	Area %
18.692	27382960	50.208
23.508	27155710	49.792
Totals	54538670	100.000

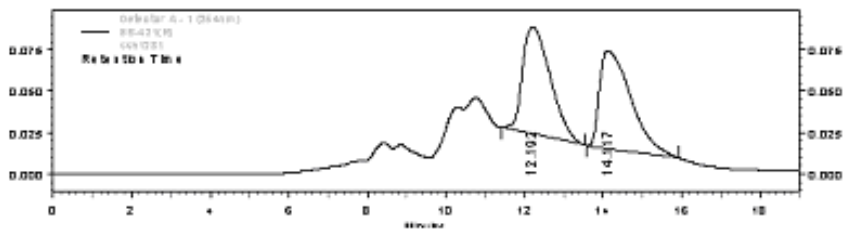
2l (Chiral HPLC done under conditions mentioned in the above experimental section)



Detector A - 1 (254nm)

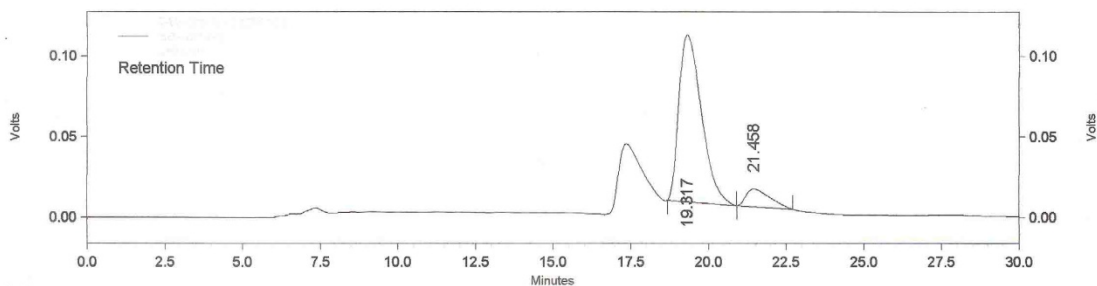
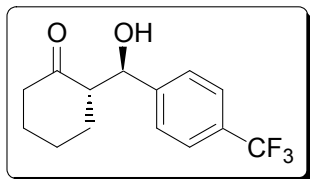
Pk #	Retention Time	Area	Area %
1	26.475	7503953	80.344
2	33.483	1835873	19.656
Totals		9339826	100.000

2m (Racemic) (HPLC conditions: Chiralcel OD-H (250 x 4.6 mm), Mobile phase: IPA:n-Hexane (20:80), Flow rate: 0.5 ml/min; $\lambda = 254$ nm)



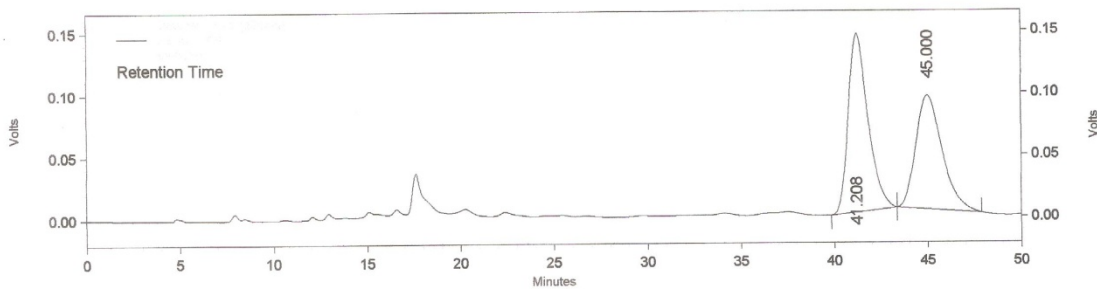
Retention Time	C Area	Area %
12.192	3203444	49.349
14.117	3288005	50.651
Totals	6491449	100.000

2m (Chiral HPLC done under conditions mentioned in the above experimental section)



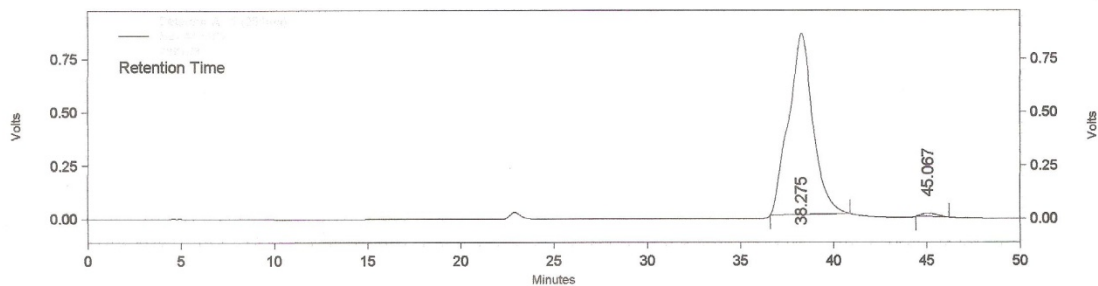
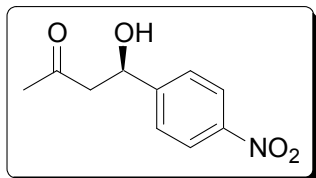
Detector A - 1 (254nm)			
Pk #	Retention Time	Area	Area %
1	19.317	5264546	89.893
2	21.458	591932	10.107
Totals		5856478	100.000

3a (Racemic) (HPLC conditions mentioned above)



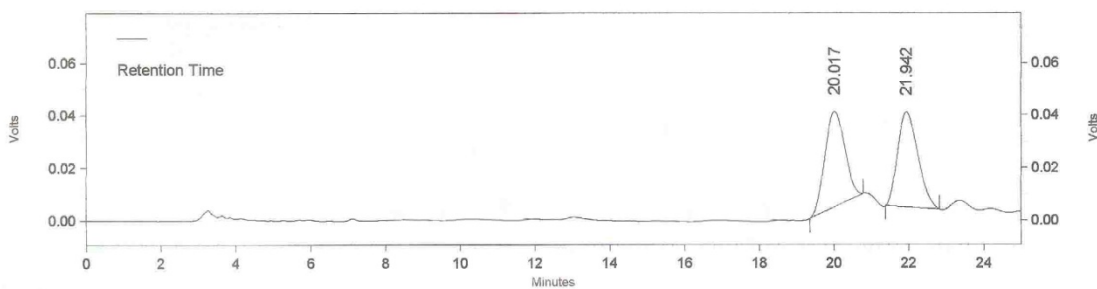
Detector A - 1 (254nm)			
Pk #	Retention Time	Area	Area %
1	41.208	10492794	53.982
2	45.000	8944643	46.018
Totals		19437437	100.000

3a (Chiral) (Same HPLC conditions like racemic mentioned above)



Detector A - 1 (254nm)			
Pk #	Retention Time	Area	Area %
1	38.275	77098041	98.832
2	45.067	911231	1.168
Totals		78009272	100.000

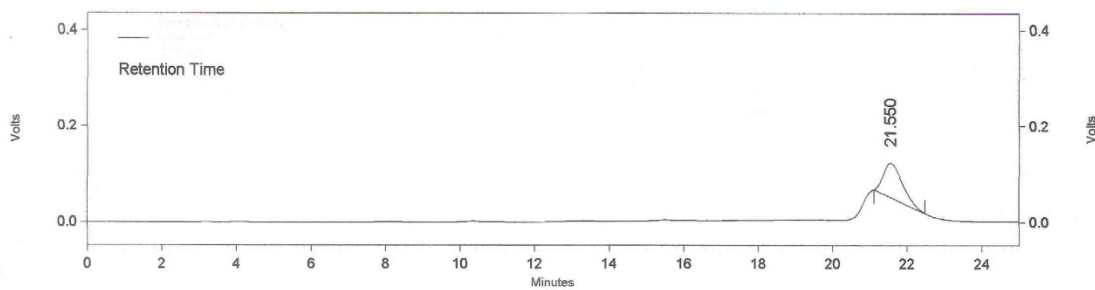
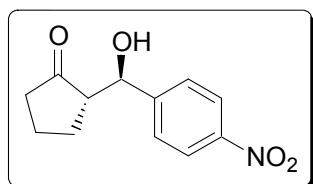
3b (Racemic) (HPLC conditions mentioned above)



Detector A - 1 (265nm)

Pk #	Retention Time	Area	Area %
1	20.017	672927	49.626
2	21.942	683071	50.374
Totals		1355998	100.000

3b (Chiral) (Same HPLC conditions like racemic mentioned above)



Detector A - 1 (265nm)

Pk #	Retention Time	Area	Area %
1	21.550	1273155	100.000
Totals		1273155	100.000

Table 2

Effect of the acid additives in the aldol reaction between 4-nitrobenzaldehyde and cyclohexanone catalyzed by **1**

Cyclohexanone (4 mmol) + 4-nitrobenzaldehyde (1 mmol) $\xrightarrow[\text{Additive (5 mol\%), H}_2\text{O (0.01 ml), rt}]{\text{Catalyst 1 (10 mol\%)}}$ Product **2a**

Entry	Additive (pK _a)	Time (h)	Yield ^a (%)	<i>anti/syn</i> ^b (%)	ee ^c (%)
1	PTSA (-2.8)	72	99	93/7	97
2	Methane sulfonic acid (-1.9)	24	85	81/19	60
3	TFA (0.23)	32	91	84/16	88
4	Picric acid (0.38)	84	97	84/16	97
5	L-Tartaric acid (2.89)	36	93	80/20	87
6	Citric acid (3.14)	24	87	89/11	73
7	4-Nitrobenzoic acid (3.41)	24	95	86/14	93
8	2,4-dinitrophenol (4.11)	17	96	84/16	93
9	Benzoic acid (4.2)	36	91	82/18	86
10	Adipic acid (4.43)	48	88	82/18	66
11	Oleic acid (9.85)	22	97	80/20	76
12	Stearic acid (10.15)	18	87	78/22	76

^a Isolated yield after purification by column chromatography. ^b Diastereomer ratios (*anti/syn*) were determined by ¹H NMR spectrum of the crude product mixture. ^c Determined by chiral HPLC analysis.