Supporting Information

Polymer supported *Cinchona*-based bifunctional sulfonamide catalyst: A highly enantioselective, recyclable heterogeneous organocatalyst

Sung Hun Youk, Sang Ho Oh, Ho Sik Ro, Je Eun Lee, Ji Woong Lee and Choong Eui Song*

Department of Chemistry, Institute of Basic Science, Sungkyunkwan University, Suwon 440-746, Korea; E-mail : s1673@skku.edu

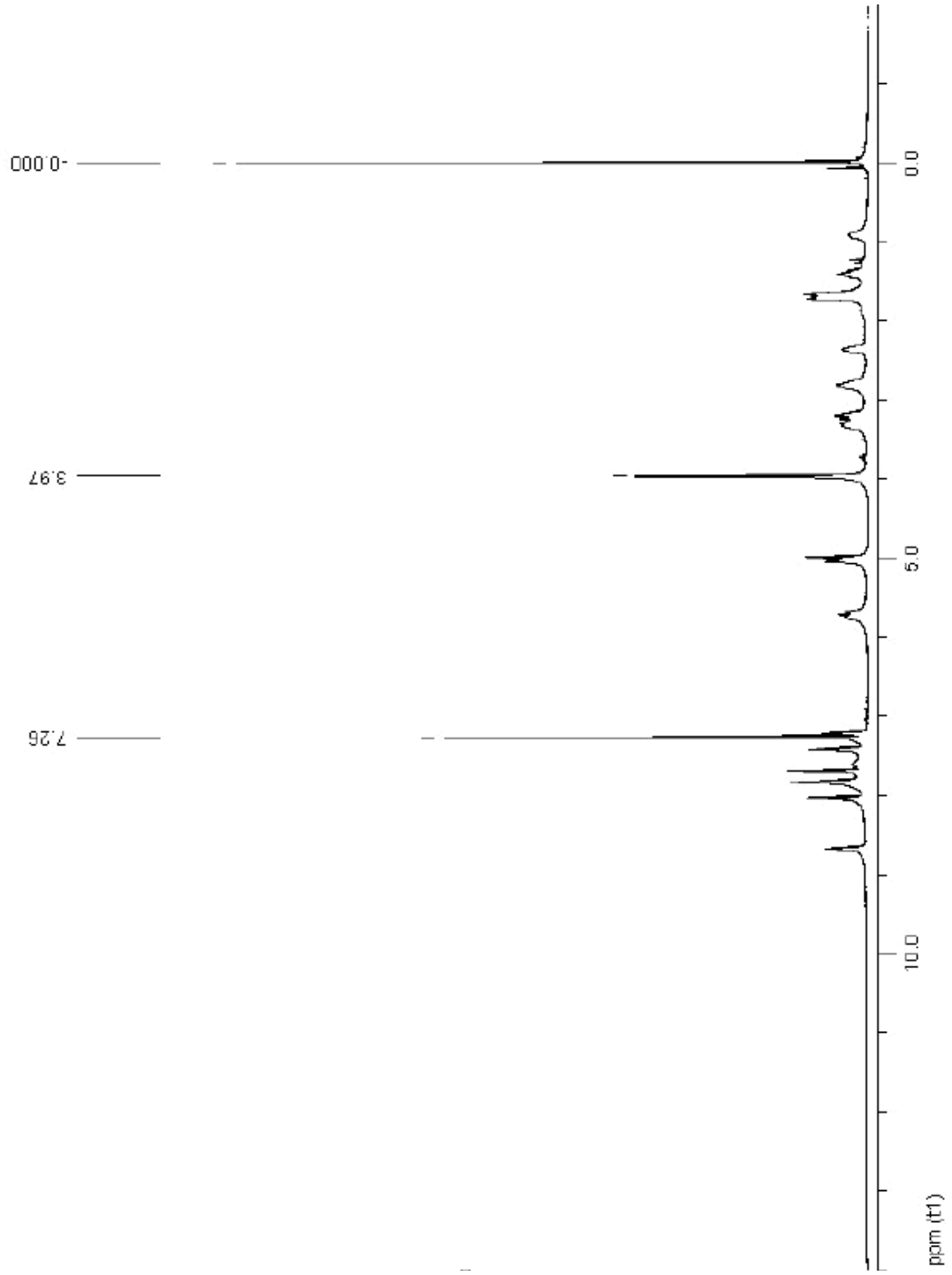
Contents

1. General

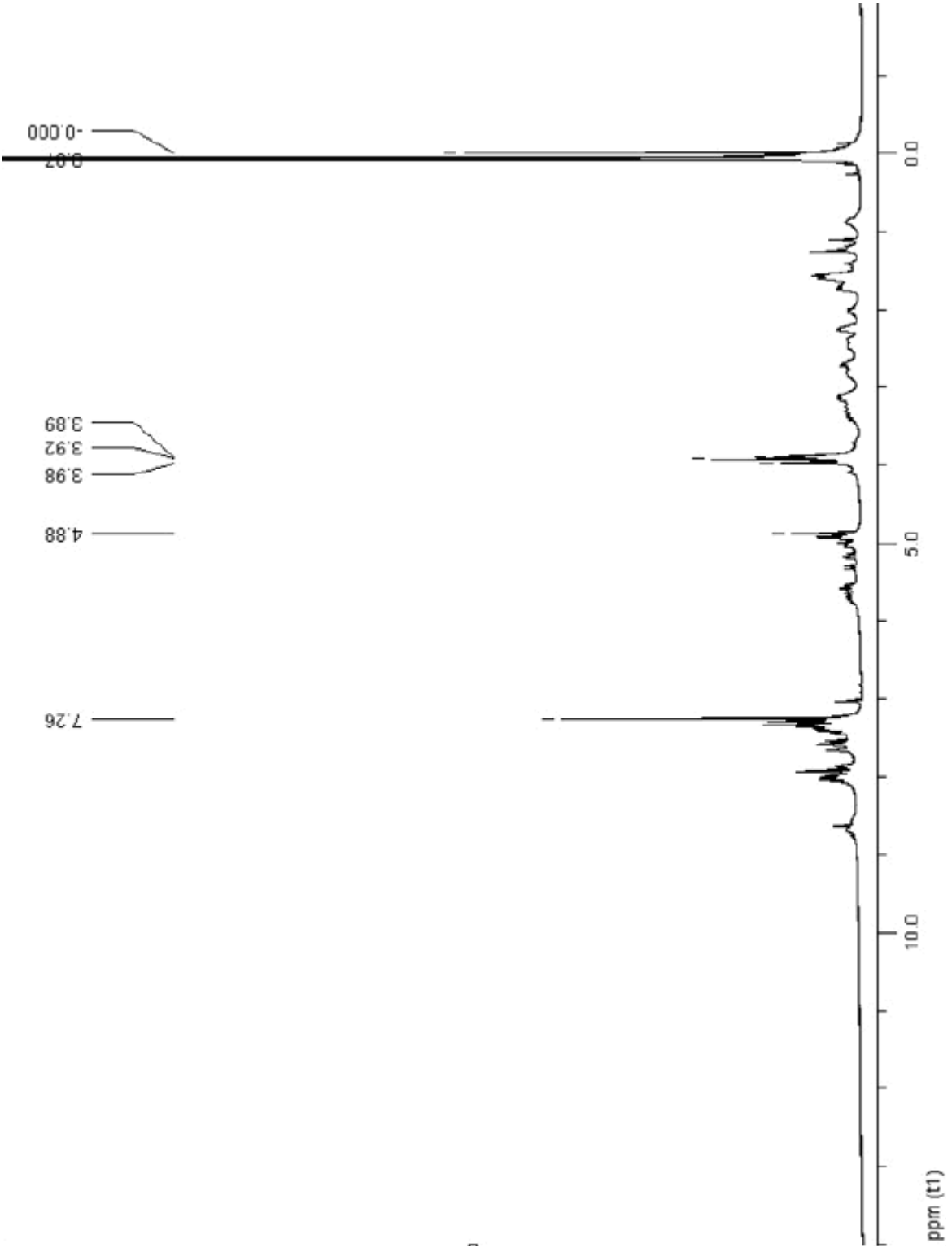
Anhydrides (**1a**, **1b**, **1c**, **1e**) were purchased from Aldrich and used without further purification. Anhydride **1d** was obtained by the hydrogenation of **1a**. Anhydrides **1f** and **1g** were obtained from the corresponding diacids which are commercially available. Quinine was purchased from Aldrich and used without further purification. Thin-layer chromatography was carried out on Merck silica gel 60F plates. HPLC analyses were performed on a Varian star series and a Jasco 1100 series instrument equipped with an isostatic pump using a Hypersil Column (250 × 4.6 mm) or a Kromasil column (250 × 4.6 mm). The ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 300 or Brucker 400 spectrometers and the ^{13}C CP/MAS solid-state NMR spectra were recorded on a Brucker DSX 400 spectrometer at KBSI in Taegu (Korea). The IR spectra were obtained using a Brucker vertex 70 spectrometer. The HRMS spectra were recorded on a Jeol JMS-700 Mstation. Elemental analysis was performed with a Fisons EA 1108 CHNS-O. The melting points were determined on a Buchi melting point B-540 apparatus and were uncorrected. The optical rotation was measured on a Perkin Elmer 343 plus polarimeter.

2. ^{1}H NMR spectra of catalyst I (before heating and after heating)

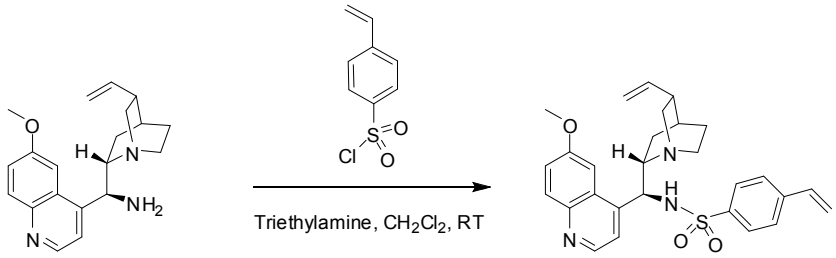
Before heating



After heating (110^{o}C in chlorobenzene for 12h)



3. Preparation and characterization of III

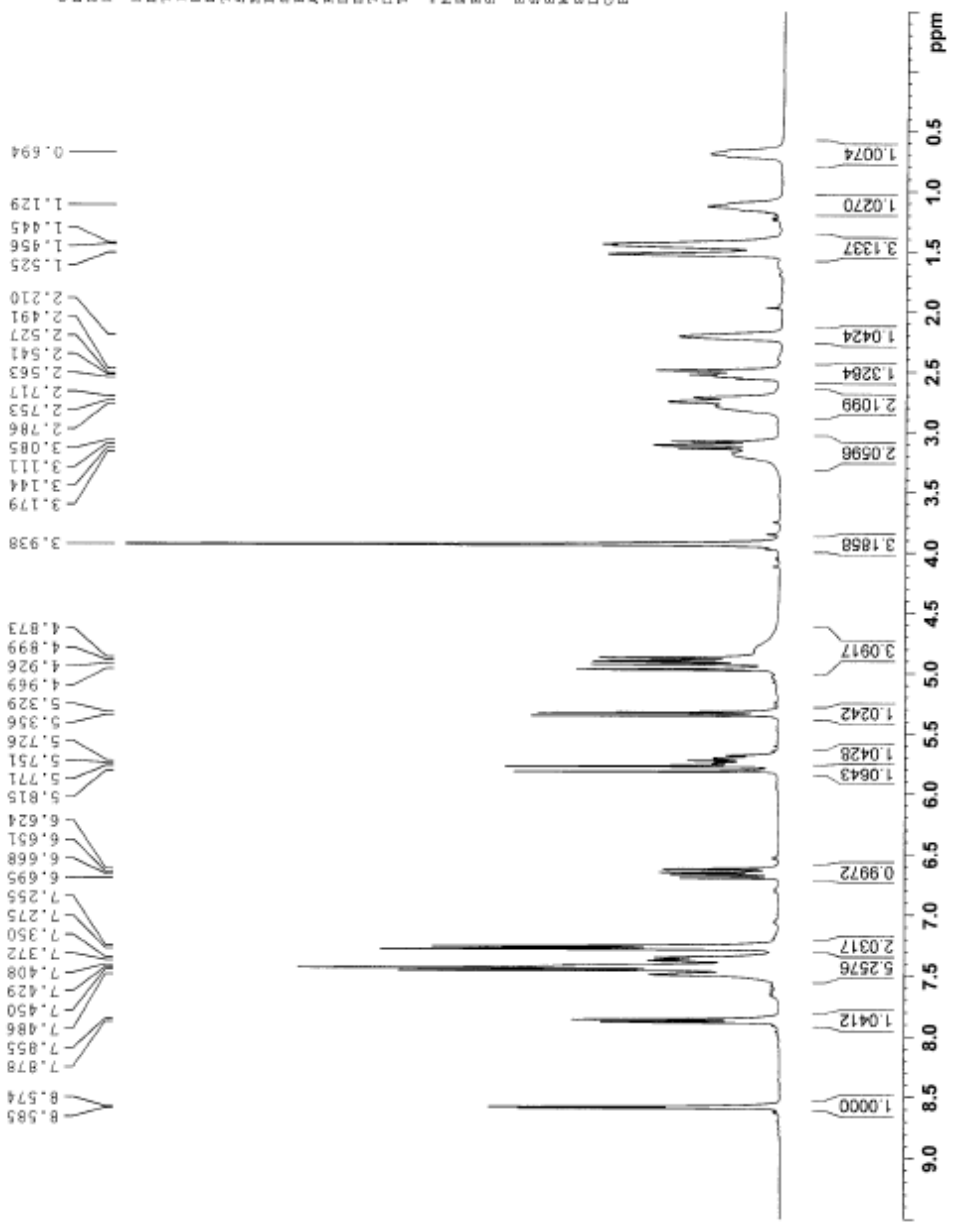


III

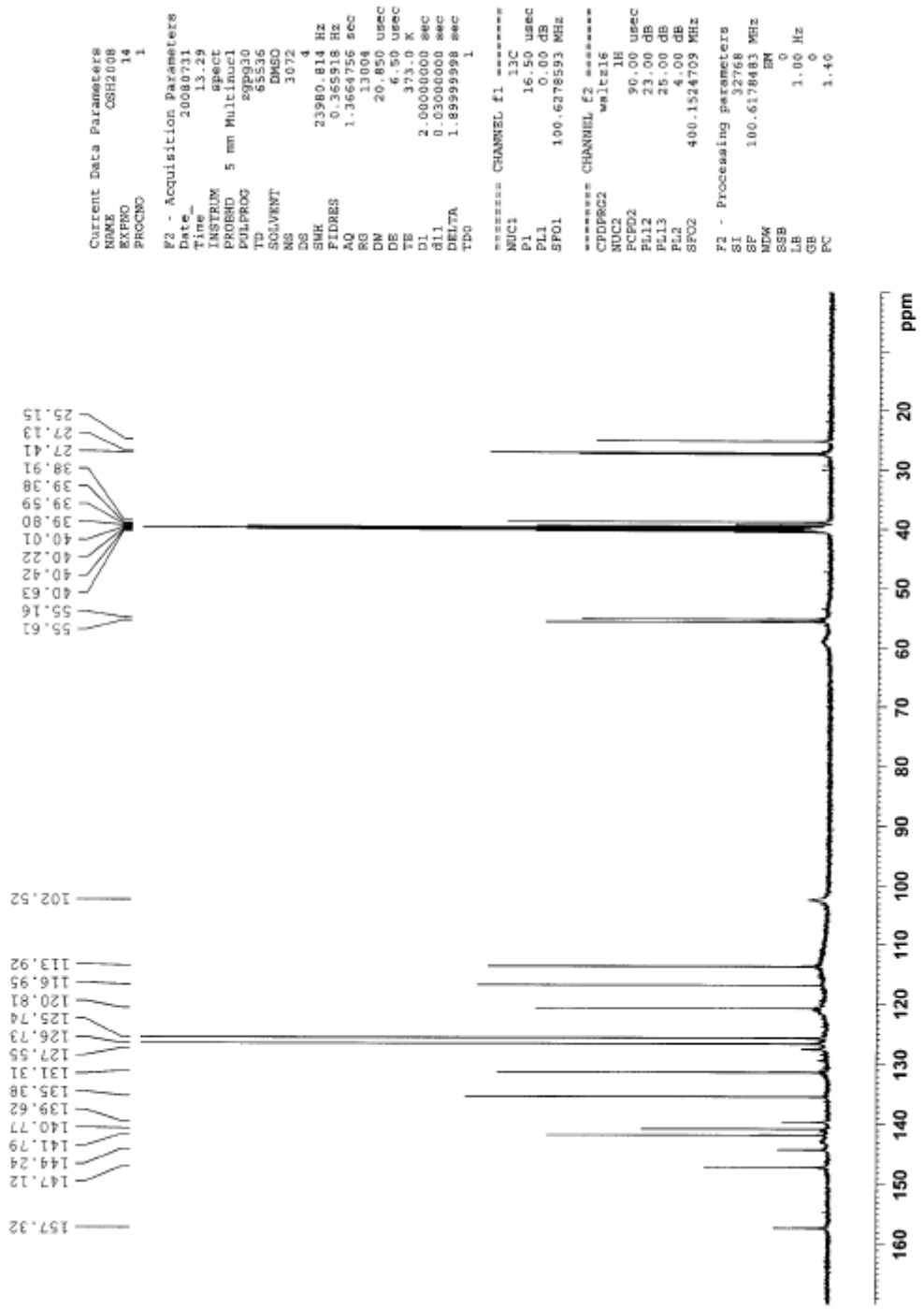
To a solution of 9-amino(9-deoxy)epiquinine[1] (9.0 g, 27.8 mmol) and 4-vinylbenzenesulfonyl chloride[2] (4.45 g, 21.9 mmol) in CH_2Cl_2 (200 mL) was added NEt_3 (3.4 mL, 24.4 mmol) at room temperature. The mixture was stirred at room temperature under an Ar atmosphere for 2h. After the addition of 120 mL of water, the mixture was extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4, filtered and then the filtrate was evaporated *in vacuo*. The residue was purified by column chromatography on a silica gel with EtOAc-MeOH (20 : 1) to afford compound **III** (8.5 g, 79.1% yield) as a white solid. Mp 79.9 ^{o}C; $[\alpha]_D^{20}$ = +32.19 (*c* = 1 in $CHCl_3$); ^{1}H NMR (400 MHz, d_6-DMSO, 110 ^{o}C) δ 0.65 – 0.75 (m, 1H), 1.05 – 1.20 (m, 1H), 1.35 – 1.55 (m, 3H), 2.47 – 2.60 (m, 1H, overlapped with DMSO), 2.67 – 2.90 (m, 2H), 3.05 – 3.30 (m, 1H), 3.93 (s, 3H), 4.60 – 5.00 (m, 3H), 5.34 (d, *J* = 10.8 Hz, 1H), 5.30 – 5.81 (m, 2H), 6.66 (dd, *J* = 17.8, *J* = 10.8 Hz, 1H), 7.26 (d, *J* = 8 Hz, 2H), 7.35 – 7.48 (m, 5H), 7.86 (d, *J* = 9.2 Hz, 1H), 8.58 (d, *J* = 4.4 Hz, 1H) ppm; ^{13}C NMR (400 MHz, d_6-DMSO, 110 ^{o}C) δ 25.15, 27.13, 27.41, 55.16, 55.61, 102.52, 113.92, 116.95, 120.81, 125.74, 126.73, 127.55, 131.31, 135.38, 139.62, 140.77, 141.79, 144.24, 147.12, 157.32 ppm; IR(KBr) ν 3584, 3202, 3074, 2940, 1919, 1620, 1396, 1323, 1228, 1155,

1029 cm^{-1}; HRMS (FAB) Calcd for $[C_{28}H_{31}N_3O_3S+H]^+$: 490.2164; found: 490.2166; Anal. Calcd for $C_{28}H_{31}N_3O_3S$: C, 68.68; H, 6.38; N, 8.58; S, 6.55. Found: C, 68.60; H, 6.38; N, 8.39; S, 6.56.

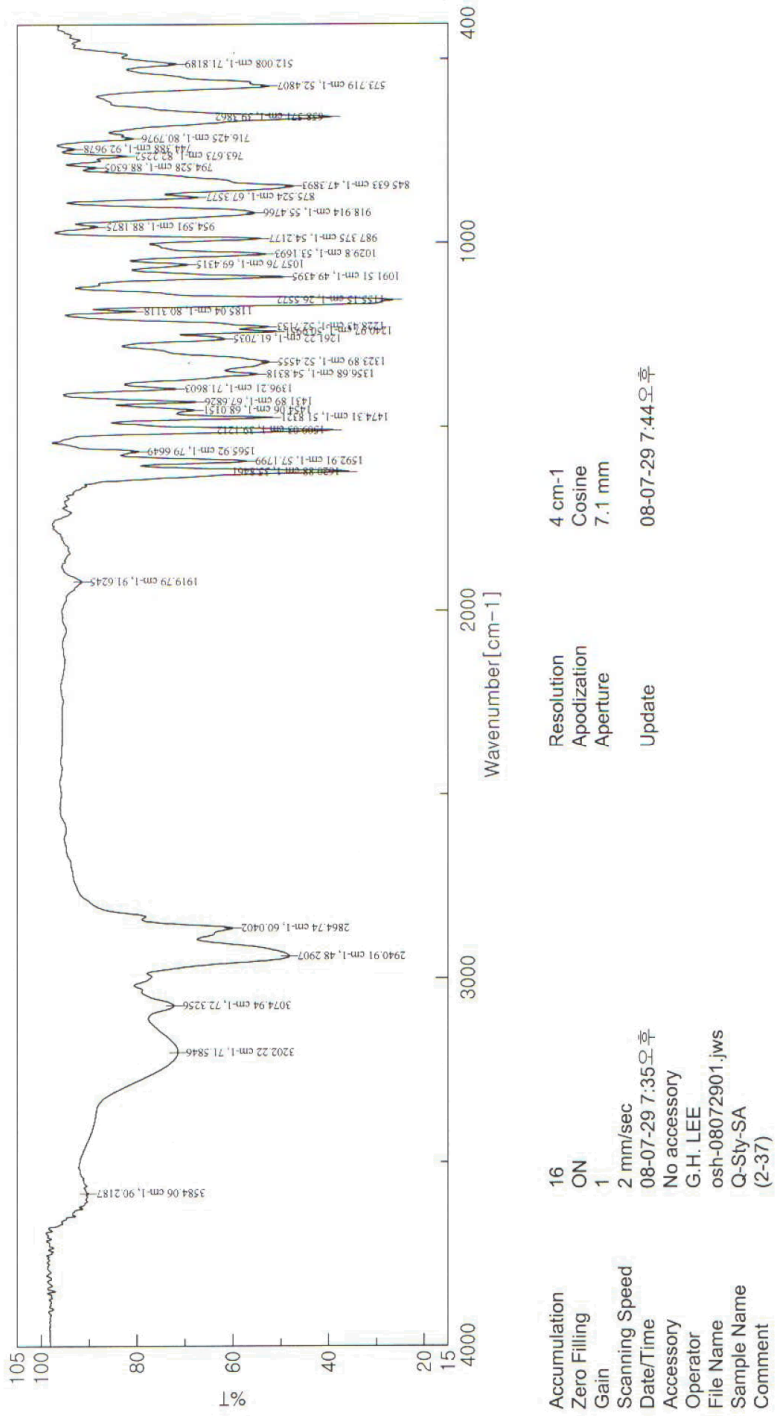
^{1}H-NMR spectrum of catalyst III (d_6-DMSO, 110 ^{o}C)



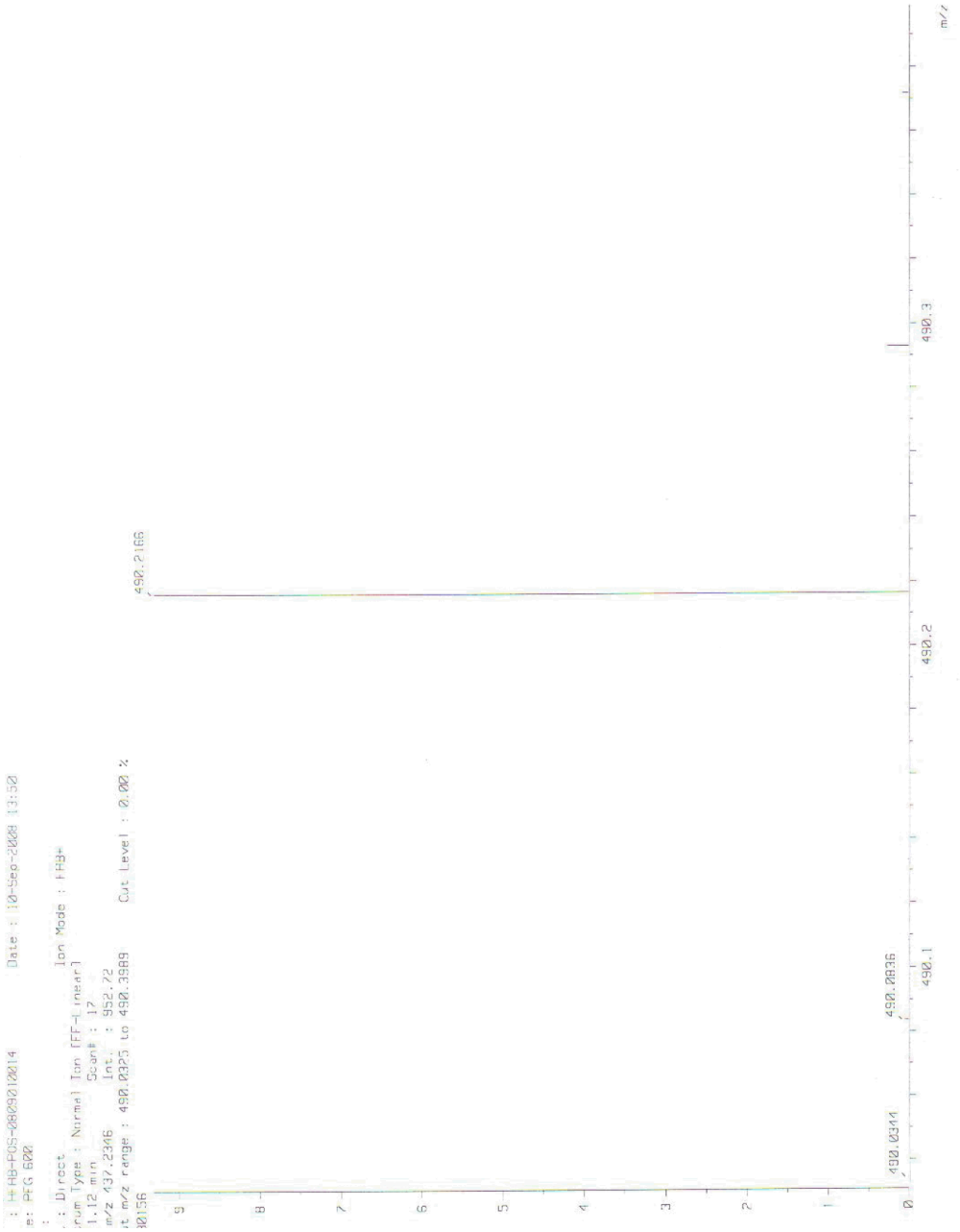
^{13}C-NMR spectrum of catalyst III (d_6-DMSO, 110 ^{o}C)



IR spectrum of catalyst III (KBr)



HRMS spectrum of catalyst III

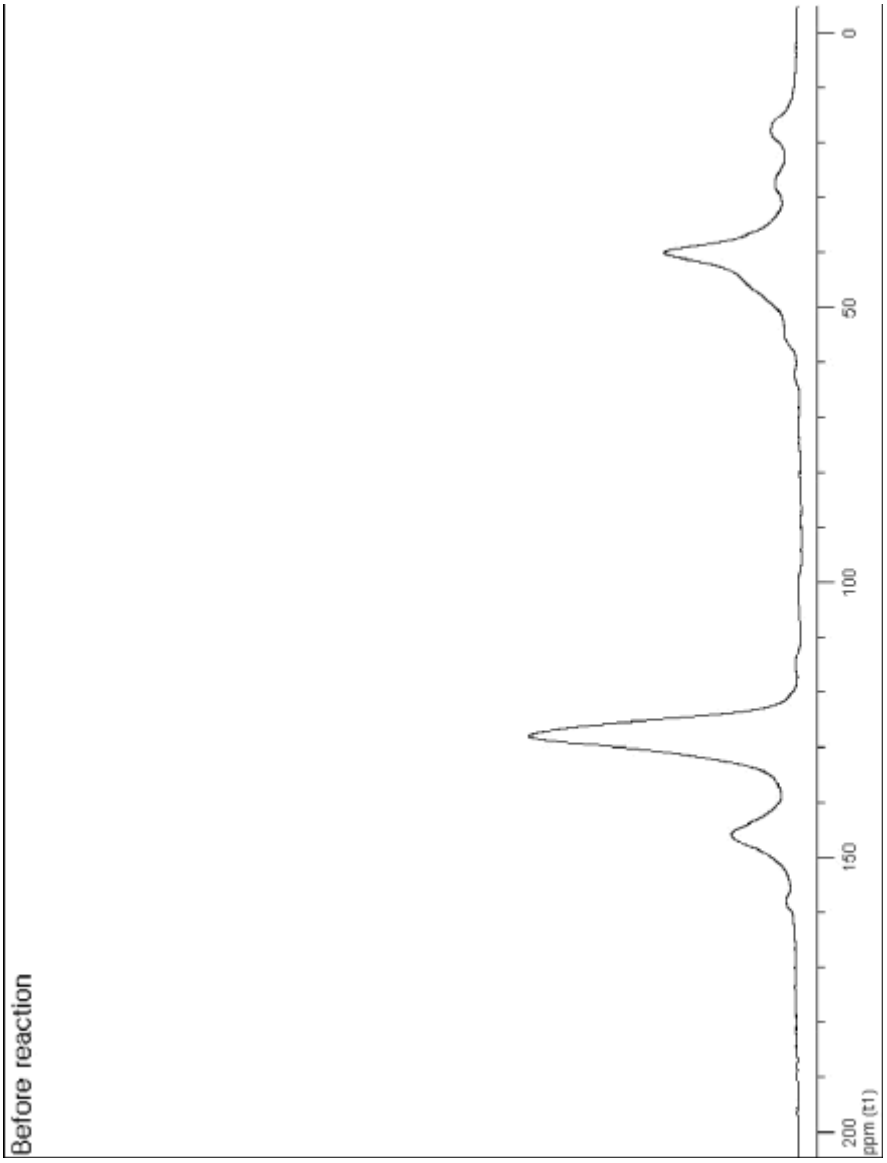


4. Preparation and characterization of catalyst IV

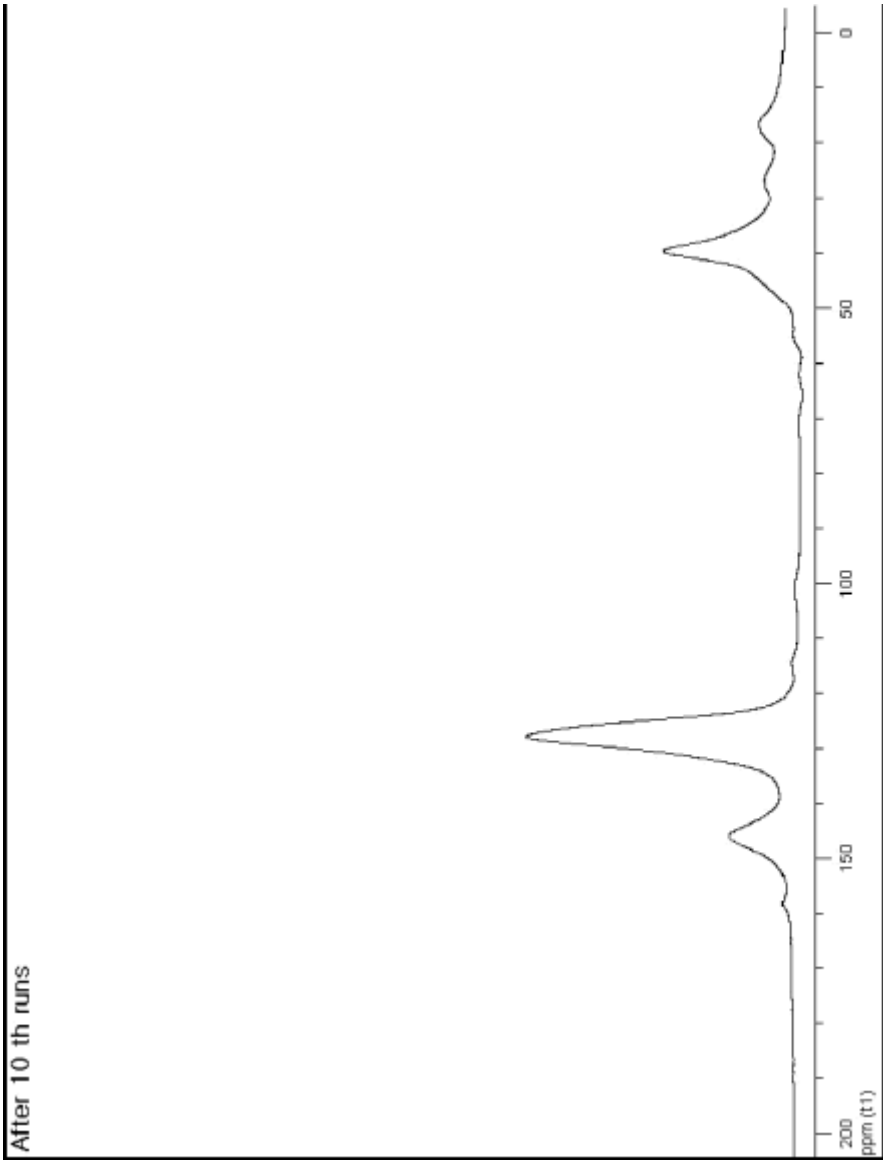
The stabiliser (t-butyl catechol) was first removed from styrene and commercial 1,4-divinylbenzene by washing samples with an excess of 1 per cent aqueous sodium hydroxide and twice with water. To a solution of water (112 mL), acacia gum (5.7 g) and sodium chloride (3.6 g), was added a styrene (67.8 mmol, 7.8 mL), 1,4-divinyl benzene (1.3 mmol, 195 μL), azobisisobutyronitrile (1.3 mmol, 213 mg), catalyst **III** (3.4 mmol, 1.66 g) and chlorobenzene (12.6 mL). The reaction mixture was deoxygenated by pursing with argon atmosphere for at least 30 min at room temperature. Then, the reaction vessel was heated to 110 □ and stirred for 12 hours under Ar atmosphere. After cooling to room temperature, the reaction mixture was filtered and washed with water. The polymeric residue was suspended in 300 mL of water and stirred for at least 1 hour and then filtered. The filtered residue was suspended in 400 mL of methanol and stirred for at least 1 hour and then filtered. After washing successively with methanol, dichloromethane and diethyl ether, the polymer was dried overnight in *vacuo* to afford 6 g of catalyst **IV** as a white solid. IR (KBr) ν 3399, 3081, 3001, 2920, 1621, 1600, 1356, 1240, 1154, 1028 cm^{-1}; Anal. Calcd for : N, 2.16; S, 1.66. Found: N, 2.01; S, 1.31.

^{13}C CP/MAS solid-state NMR (400 MHz) spectrum of catalyst IV

Before reaction

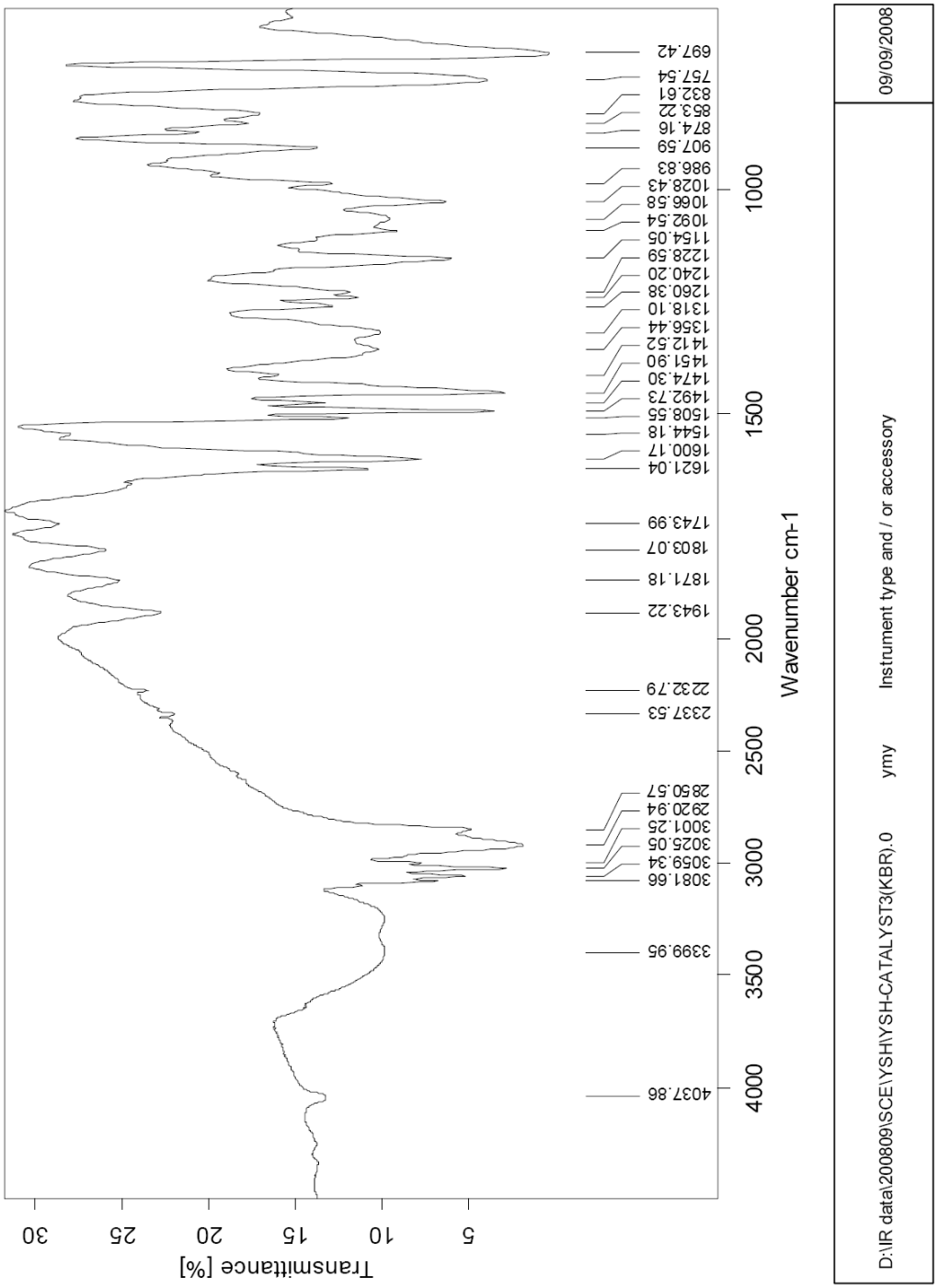


After 10 runs

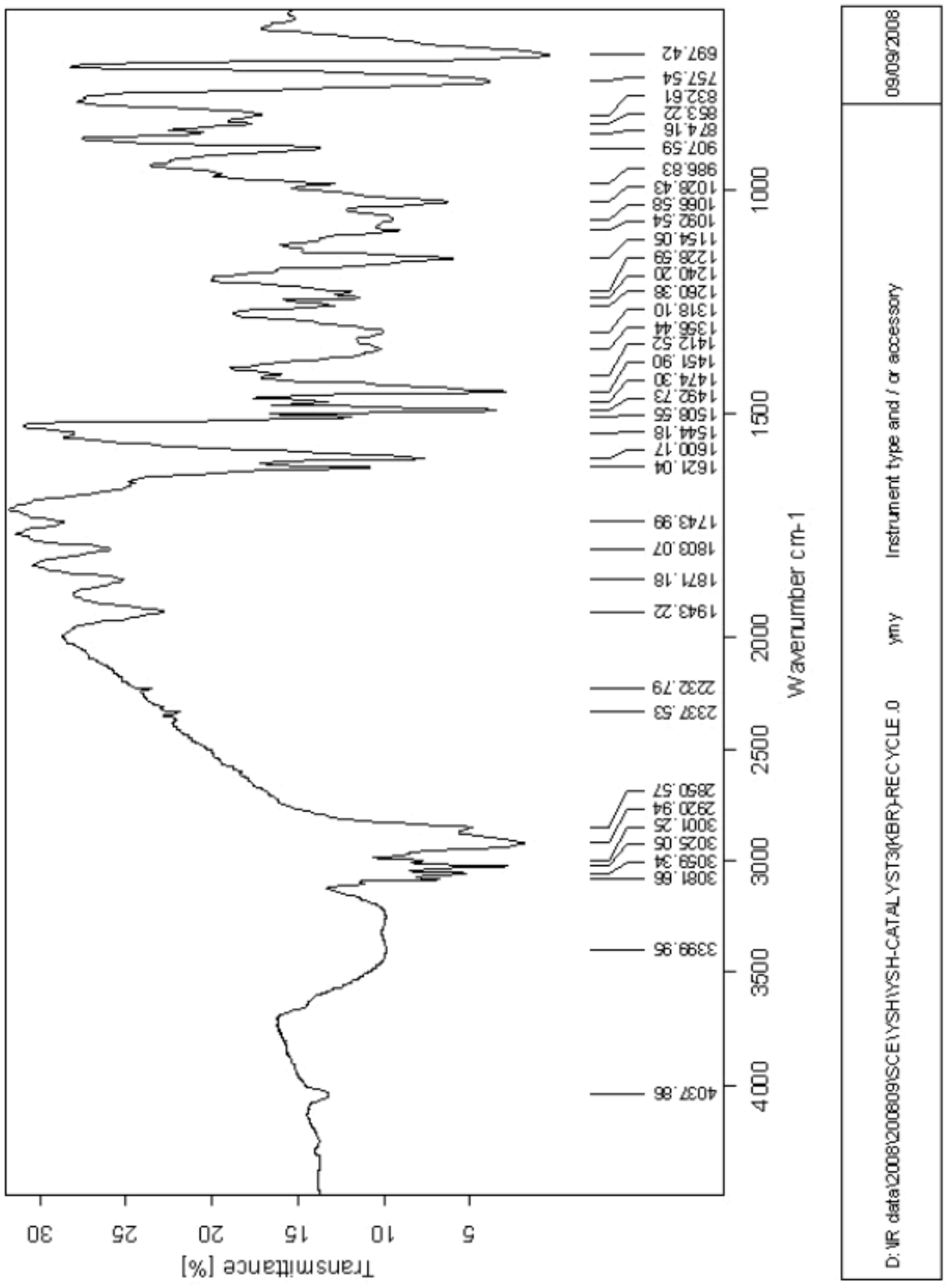


IR spectrum of catalyst IV (KBr)

Before reaction



After 10 runs

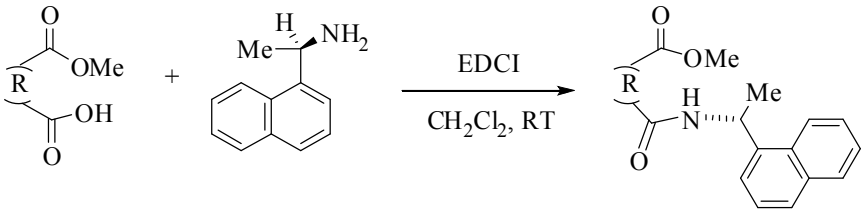


5. General procedure for methanolysis of prochiral cyclic anhydrides

Methanol (202 μL, 5 mmol) was added dropwise to a stirred solution of anhydrides (0.5 mmol) and catalysts (10 mol %) in appropriate solvents (10 mL) at the temperature indicated in Scheme 2, Table 1. The reaction mixture was stirred at that temperature until the starting material was consumed, as indicated by TLC analysis. After filtration of resin, the filtrate was concentrated *in vacuo* to yield the pure hemiester products (**2a**–**2g**) in nearly quantitative yields.

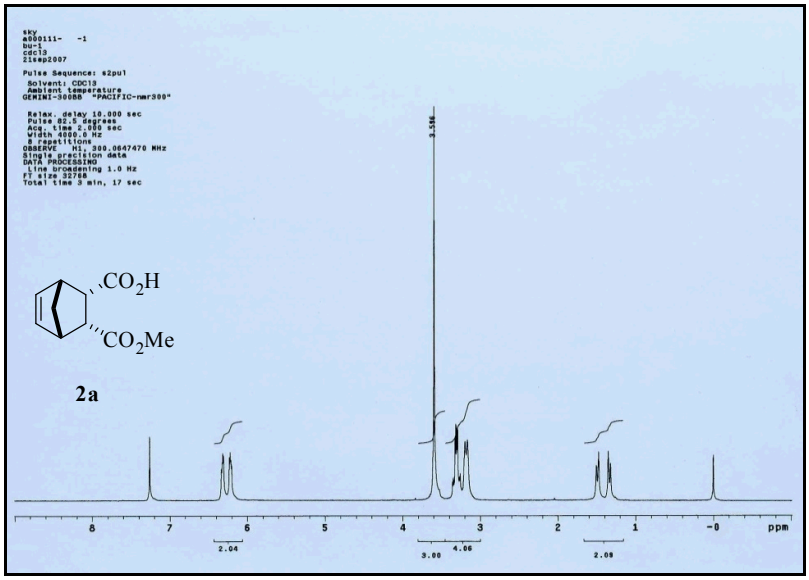
The enantiomeric excess (*ee*) of each product was determined by HPLC analysis of a diastereomeric mixture of the corresponding amide-ester prepared from the hemiester according to the literature procedure[3] (Scheme 1).

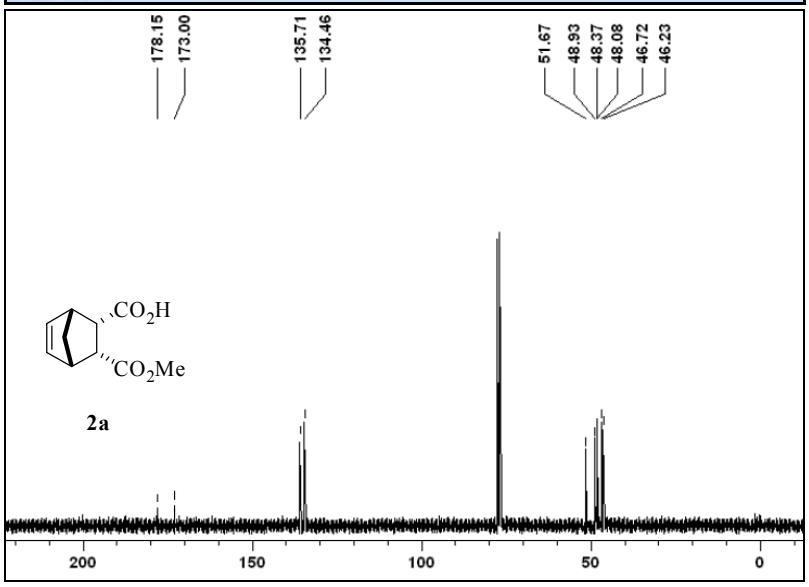
Scheme 1



6. ^{1}H and ^{13}C NMR spectra of 2a-2g

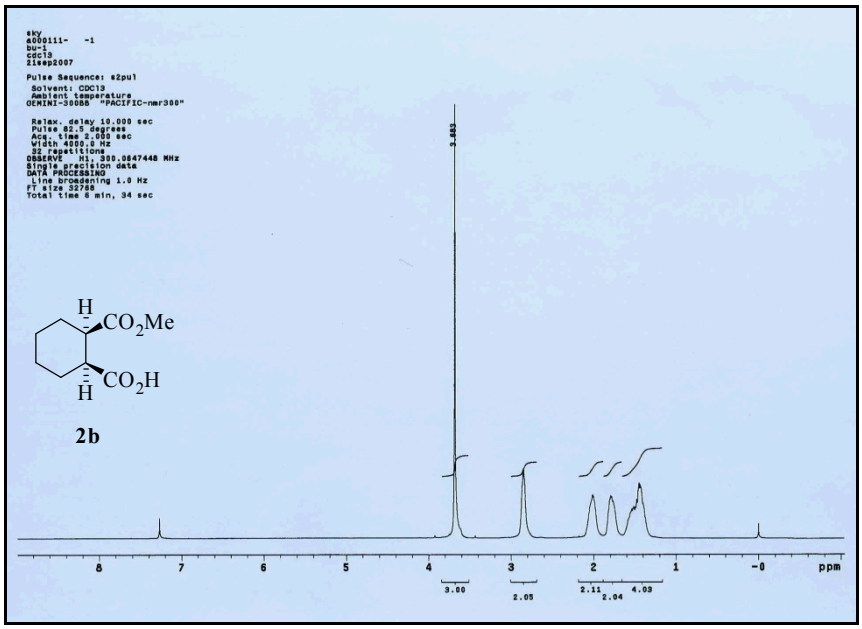
NMR Spectra of 2a

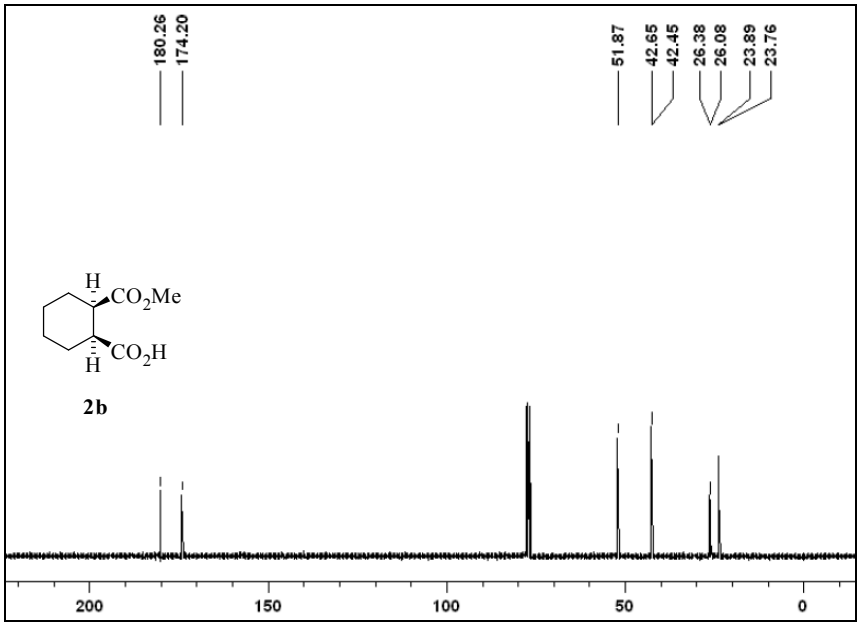




^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (bd, J = 9.0 Hz, 1H), 1.50 (dt, J = 9.0 Hz and 1.8 Hz, 1H), 3.01-3.41 (m, 4H), 3.59 (s, 3H), 6.21 (dd, J = 5.0 and 3.0 Hz, 1H), 6.33 (dd, J = 5.0 and 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.23, 46.72, 48.08, 48.37, 48.93, 51.67, 134.46, 135.71, 173.00, 178.15.

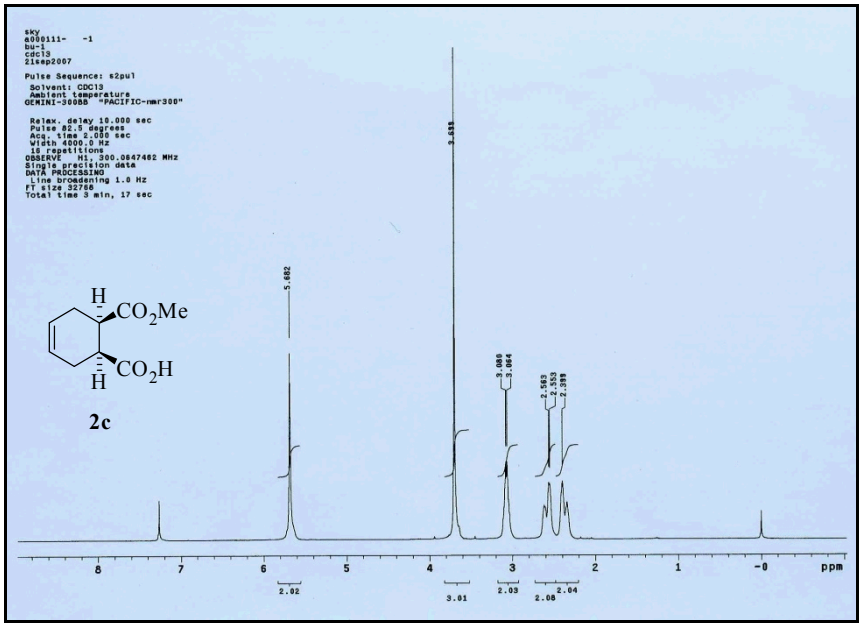
NMR spectra of 2b

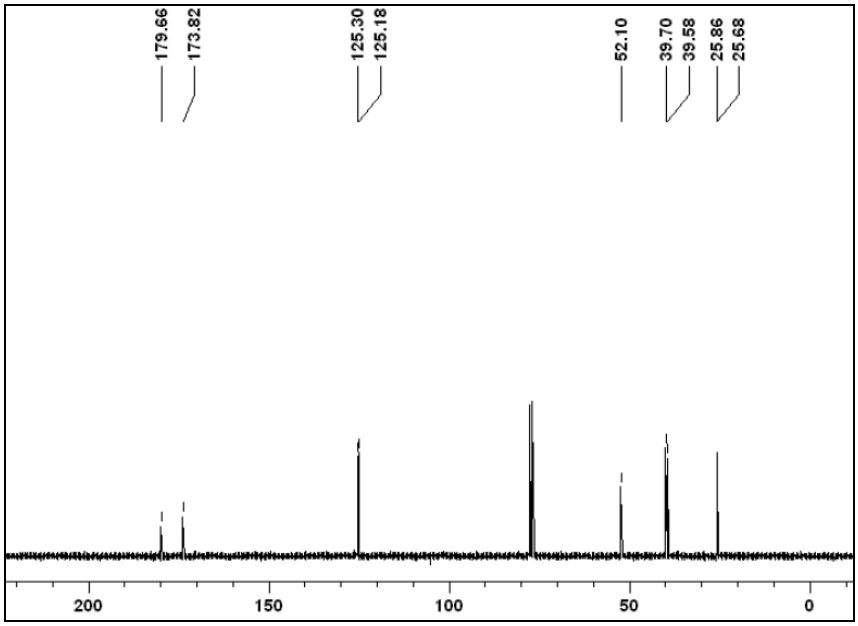




^{1}H NMR (300 MHz, $CDCl_3$): δ 1.36-1.62 (m, 4H), 1.72-1.84 (m, 2H), 1.96-2.10 (m, 2H), 2.80-2.92 (m, 2H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.76, 23.89, 26.08, 26.38, 42.45, 42.65, 51.87, 174.20, 180.26.

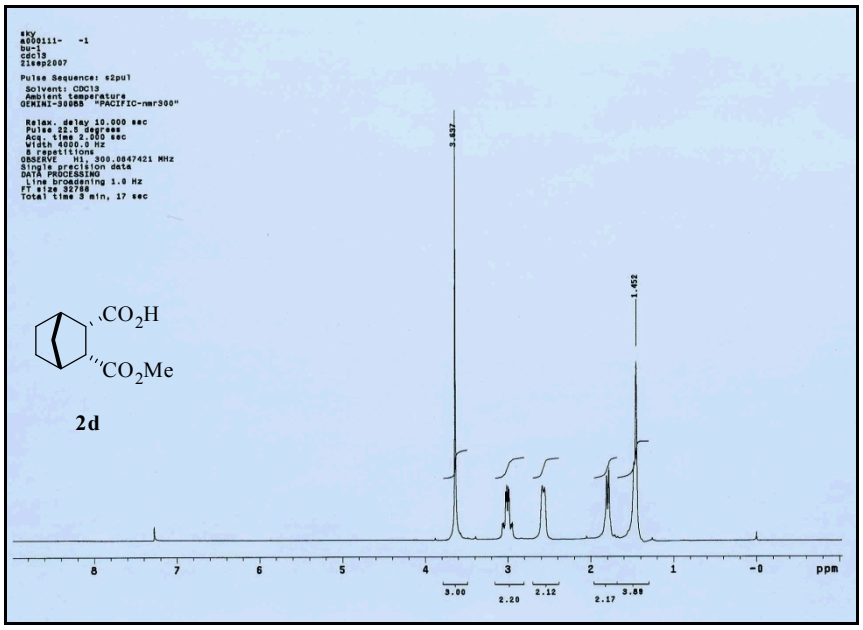
NMR Spectra of 2c

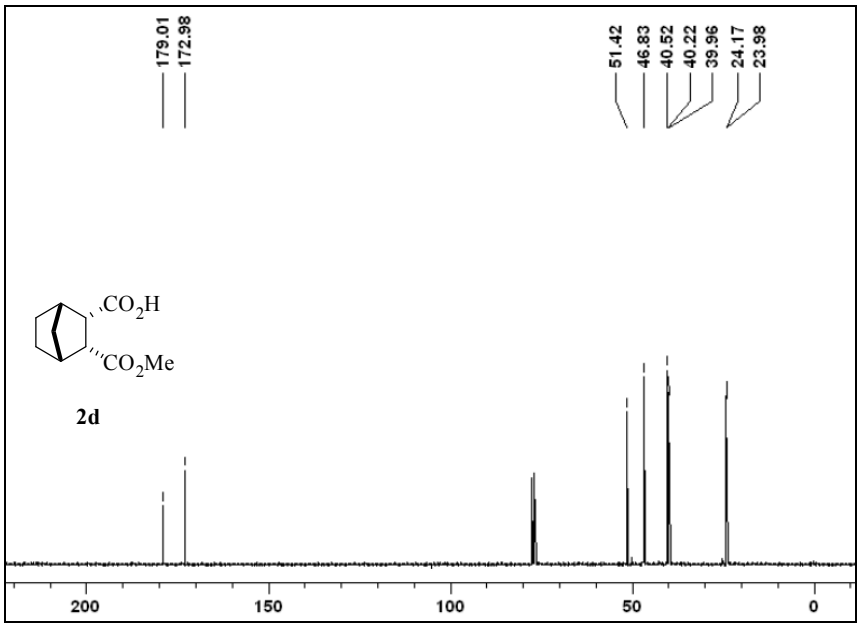




^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32-2.65 (m, 4H), 3.02-3.12 (m, 2H), 3.69 (s, 3H), 5.68 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.68, 25.86, 39.58, 39.70, 52.10, 125.18, 125.30, 173.82, 179.66.

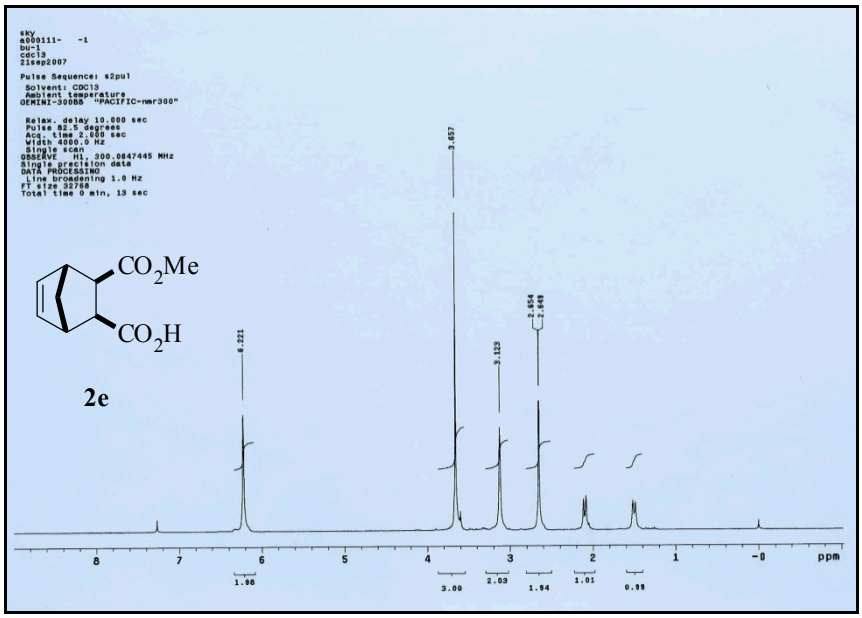
NMR spectra of 2d

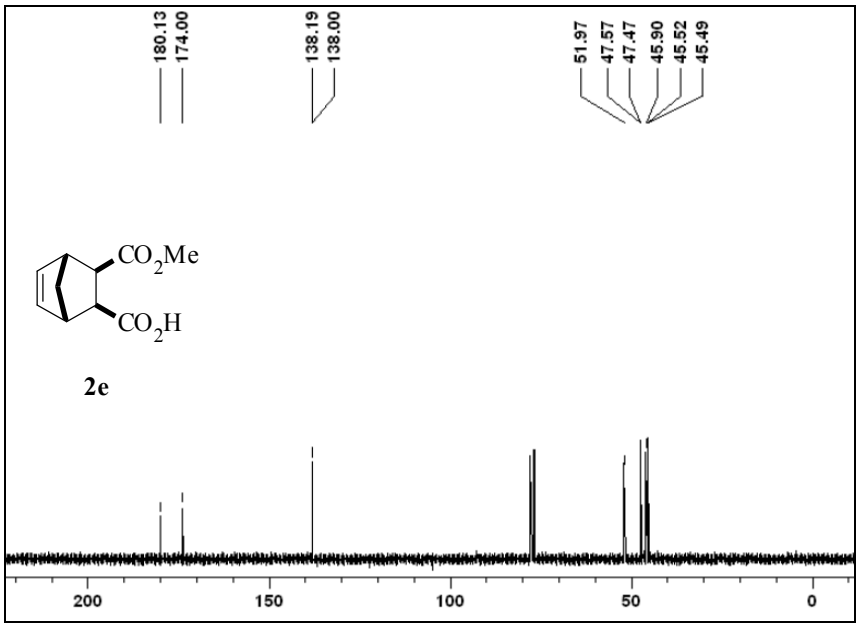




^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35-1.58 (m, 4H), 1.75-1.83 (m, 2H), 2.57-2.62 (m, 2H), 2.82-3.04 (m, 2H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.98, 24.17, 39.96, 40.22, 40.52, 46.83, 51.42, 172.98, 179.01.

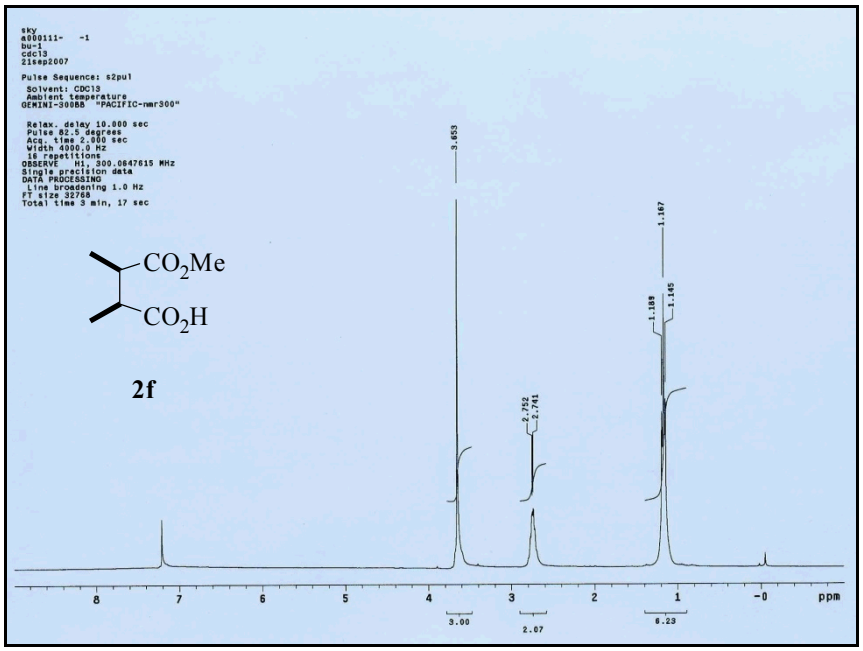
NMR Spectra of 2e

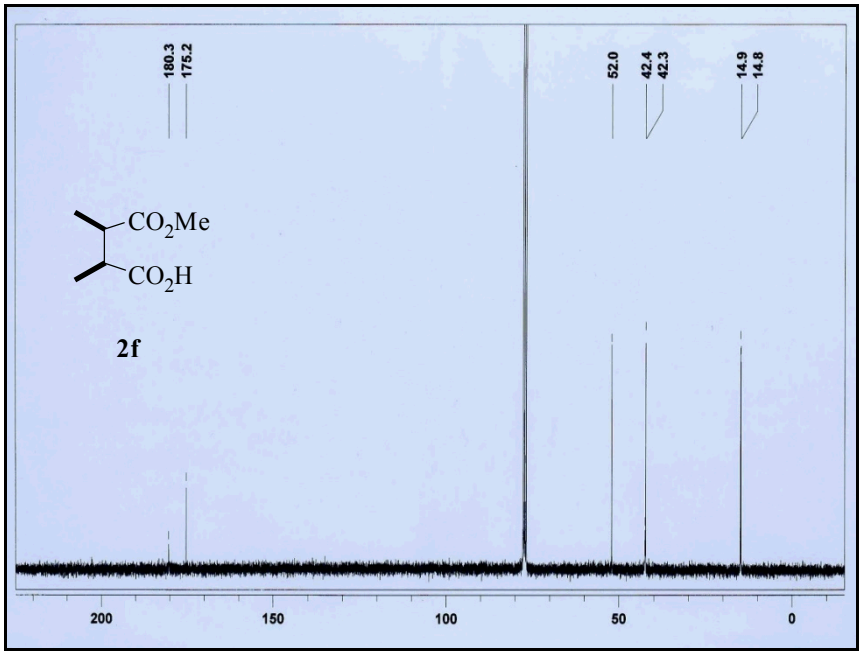




^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42 (bd, J = 9.0 Hz, 1H), 2.13 (bd, J = 9.0 Hz, 1H), 2.62 (m, 2H), 3.09 (m, 2H), 3.65 (s, 3H), 6.22 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.49, 45.52, 45.90, 47.47, 47.57, 51.97, 138.00, 138.19, 174.00, 180.13

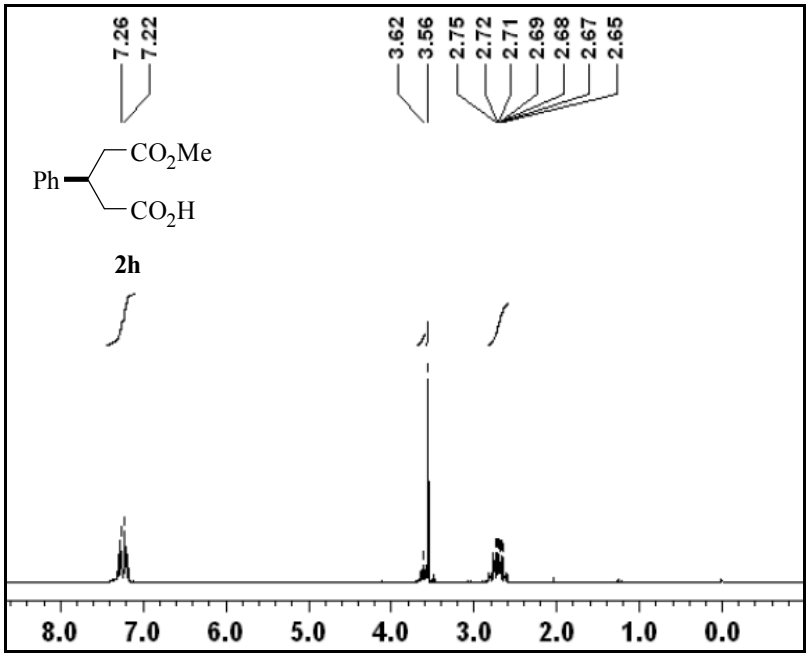
NMR Spectra of 2f

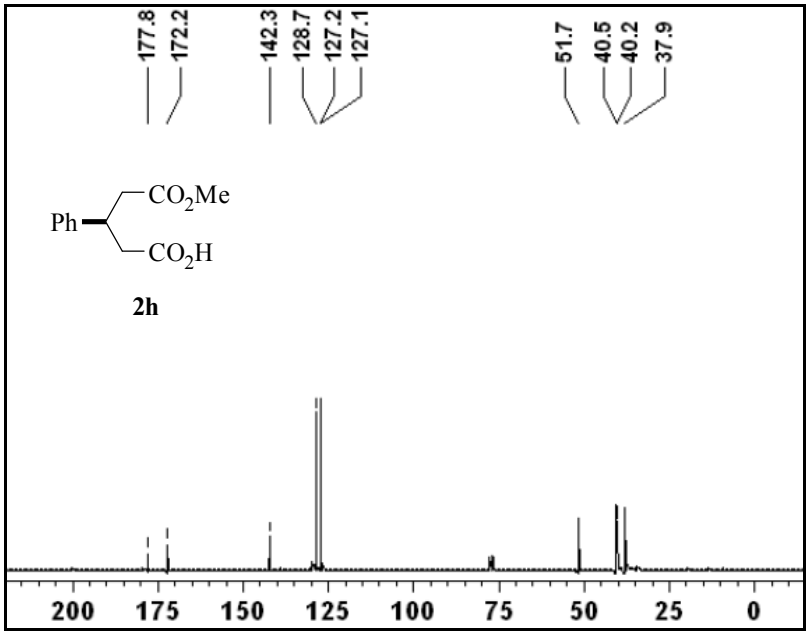




^{1}H NMR (300MHz, $CDCl_3$): δ 1.02 – 1.21 (m, 6H), 2.71 – 2.79 (m, 2H), 3.66(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.8, 14.9, 42.3, 42.4, 52.0, 175.2, 180.3̃

NMR Spectra of 2g

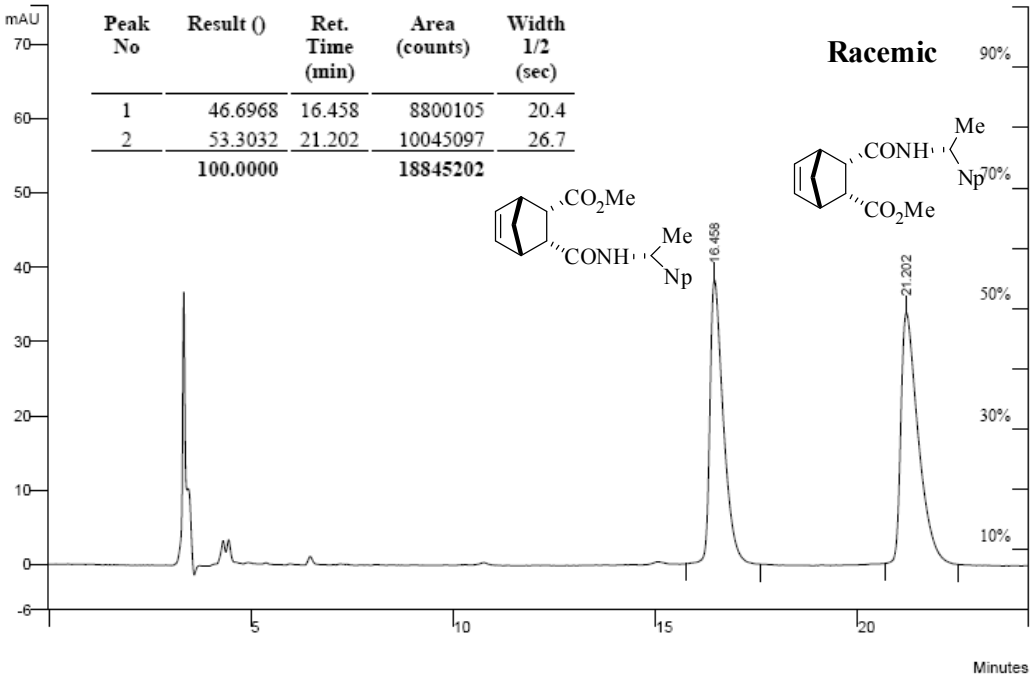




^{1}H NMR (300MHz, $CDCl_3$): δ 2.6 – 2.8 (m, 4H), 3.56 (s, 3H), 3.58 – 3.67 (m, 1H), 7.10–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 37.9, 40.2, 40.5, 51.7, 127.1, 127.2, 128.7, 142.3, 172.2, 177.8.

7. HPLC spectra for Scheme 2.

The ee value was determined by the HPLC analysis (Hypersil, 40 : 1, Hexanes : IPA, 1 mL/min, t(minor) = 16.74 min, t(major) = 21.05 min) of the diastereomeric mixture of the corresponding amide-ester, which was prepared as described previously.



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
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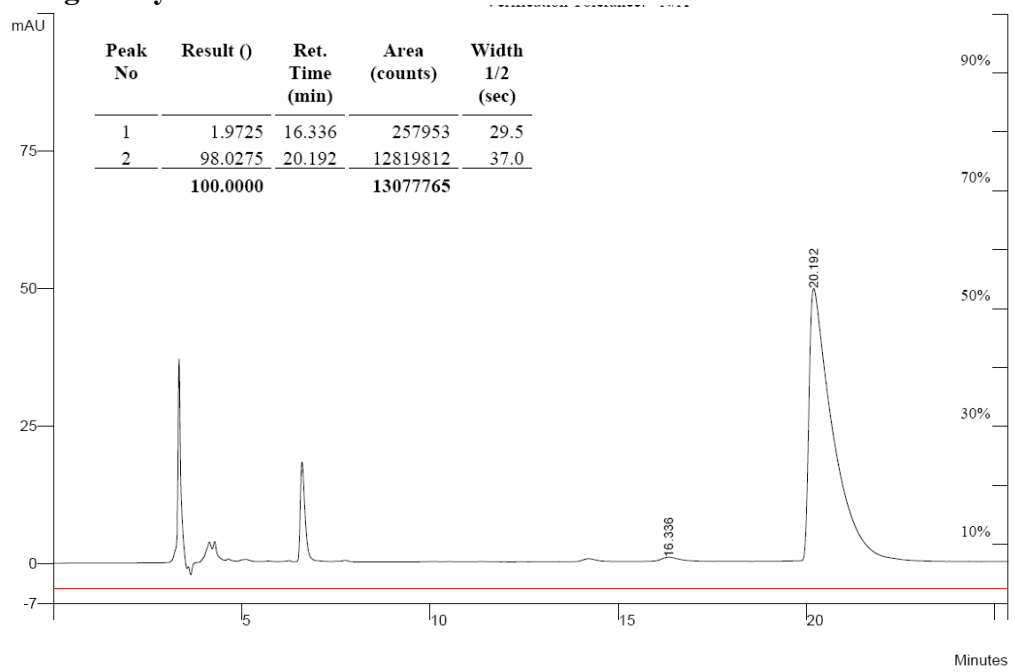
Using catalyst III



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
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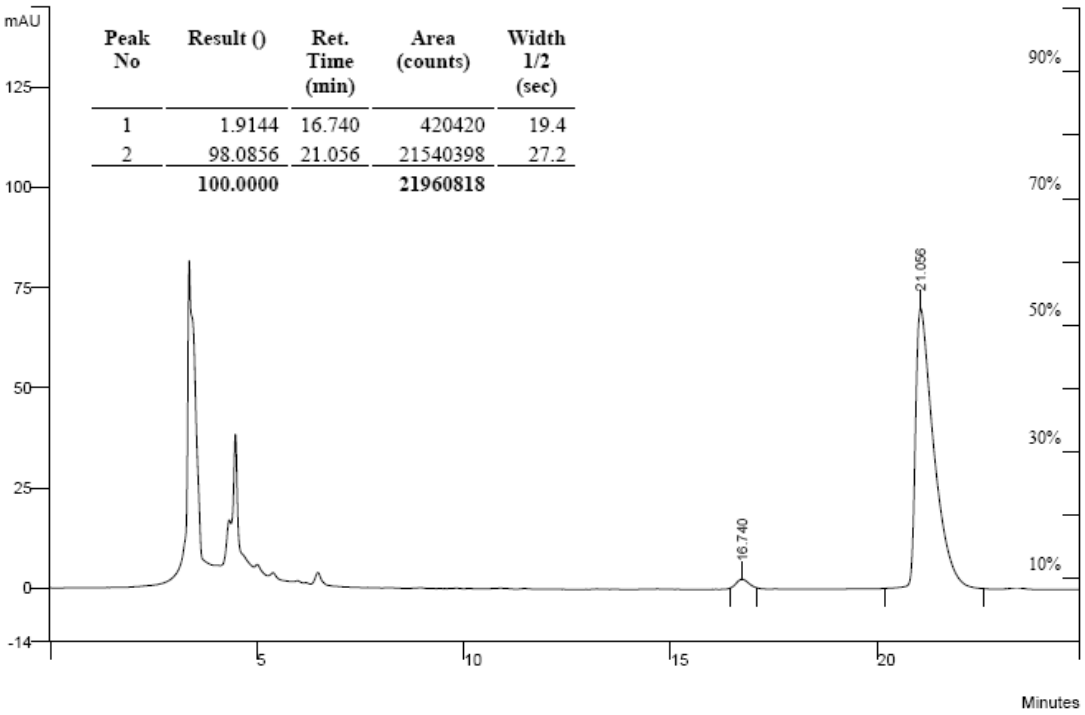
Using catalyst IV



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
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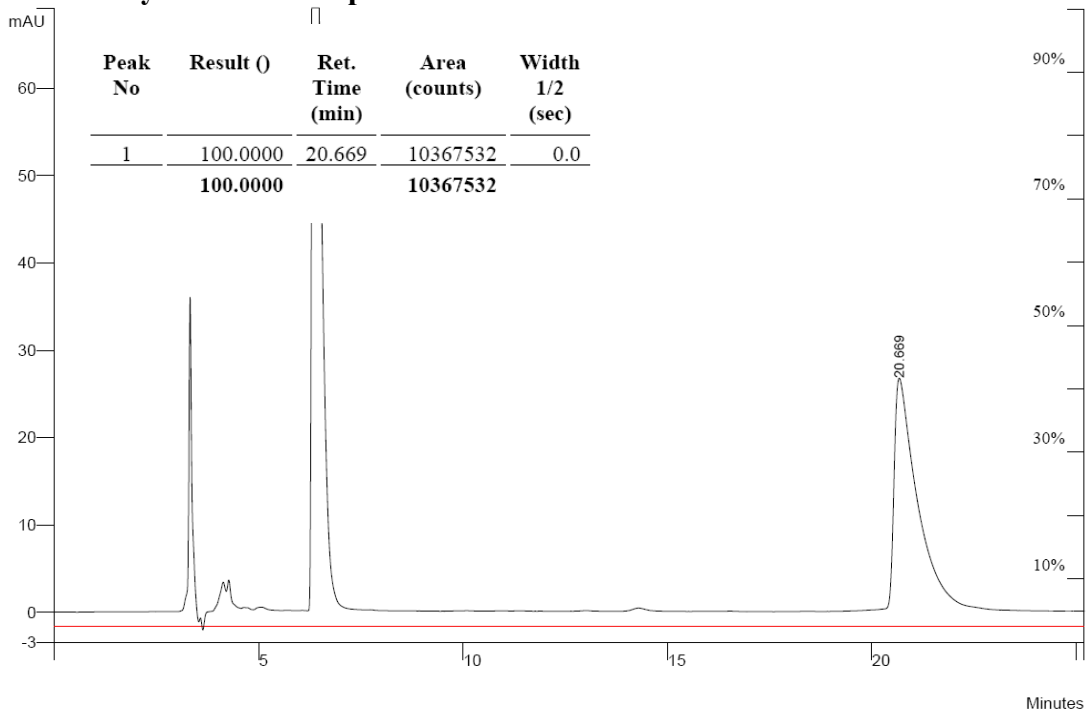
	100.0000		**21960818**	

After recrystallization of product

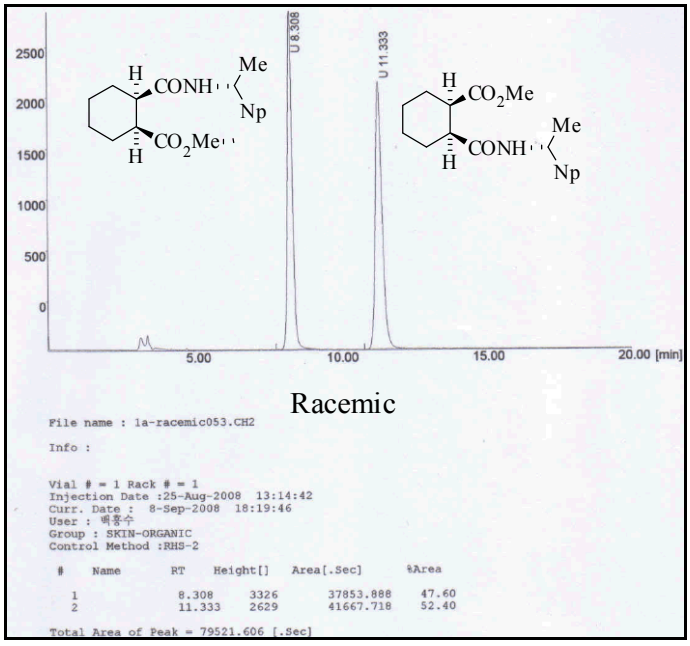


Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	100.0000	20.669	10367532	0.0
	100.0000		**10367532**	

8. HPLC spectra for Table 1.

Table 1 - Entry 1.

The ee value was determined by the HPLC analysis (Hypersil, 40 : 1, Hexanes : IPA, 1 mL/min, t(minor) = 8.30 min, t(major) = 11.33 min) of the diastereomeric mixture of the corresponding amide-ester, which was prepared as described previously.



Racemic

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Group : SKIN-ORGANIC
Control Method :RHS-2

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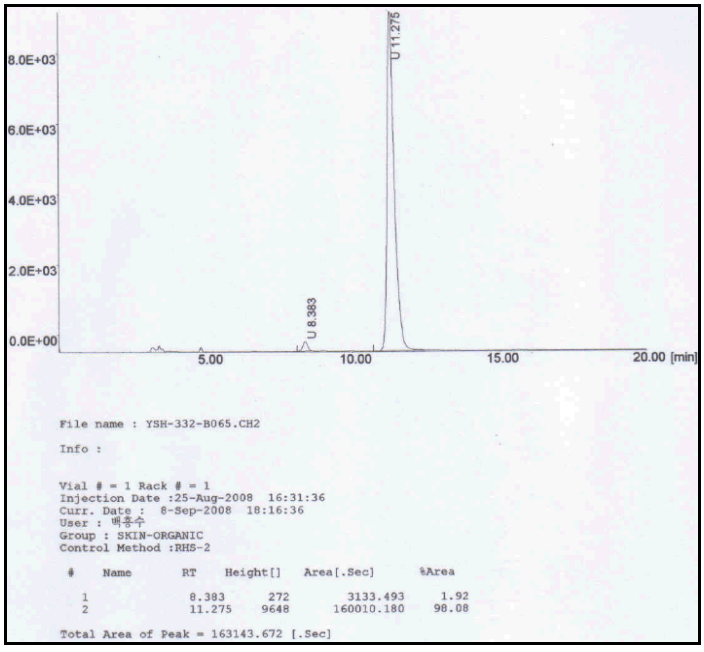


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Control Method :RHS-2

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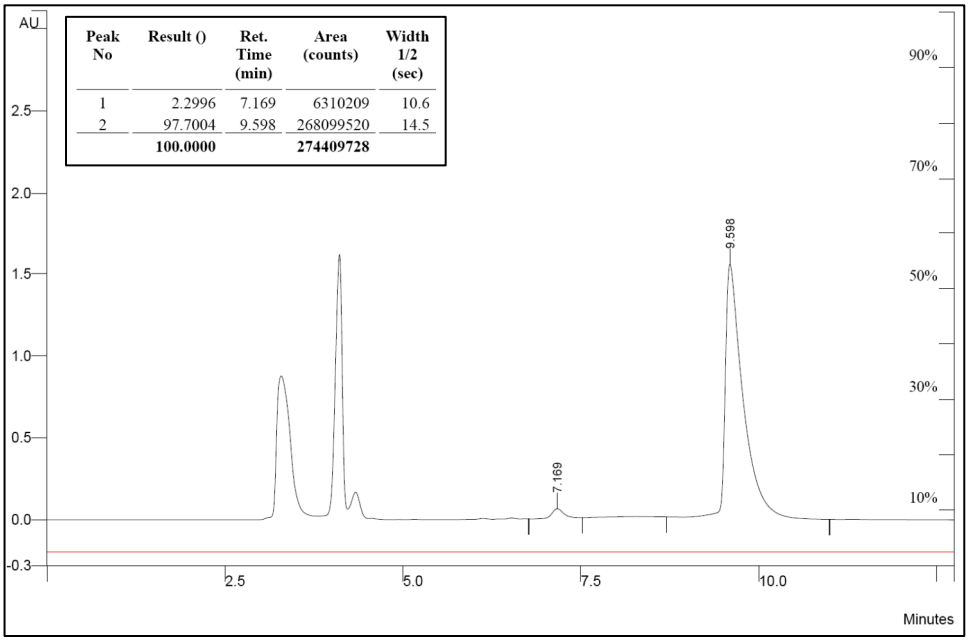
Table 1 - Entry 2.



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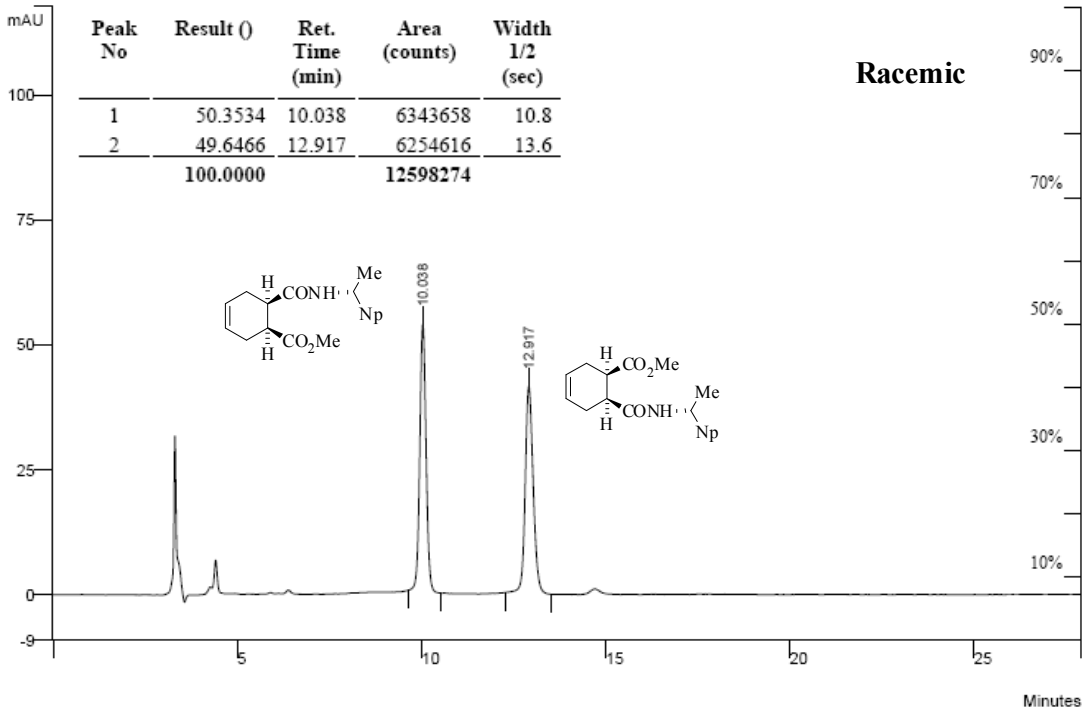
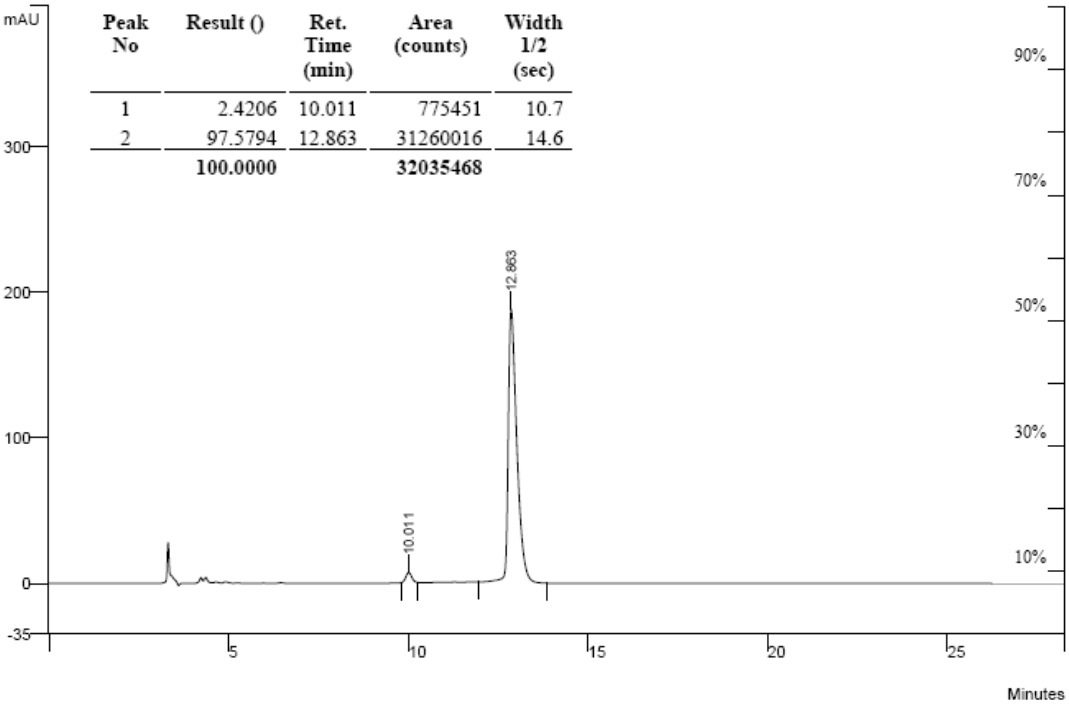
	100.0000		**274409728**	

Table 1 - Entry 3.

The ee value was determined by the HPLC analysis (Hypersil, 40 : 1, Hexanes : IPA, 1 mL/min, t(minor) = 10.01 min, t(major) = 12.86 min) of the diastereomeric mixture of the corresponding amide-ester, which was prepared as described previously.



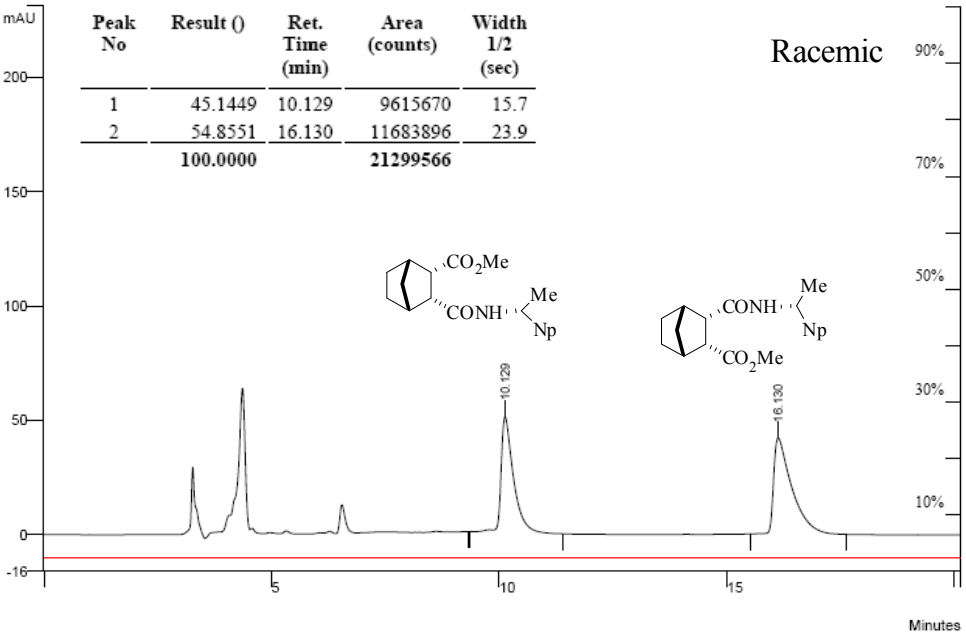
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.3534	10.038	6343658	10.8
2	49.6466	12.917	6254616	13.6
	100.0000		**12598274**	



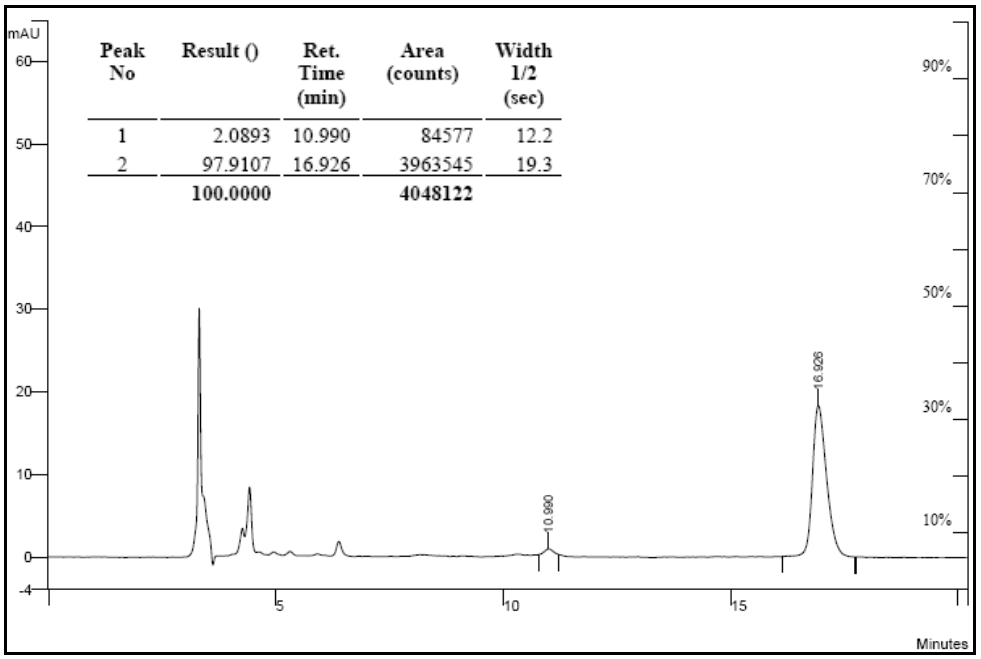
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	2.4206	10.011	775451	10.7
2	97.5794	12.863	31260016	14.6
	100.0000		**32035468**	

Table 1 - Entry 4.

The ee value was determined by the HPLC analysis (Hypersil, 40 : 1, Hexanes : IPA, 1 mL/min, t(minor) = 10.99 min, t(major) = 16.92 min) of the diastereomeric mixture of the corresponding amide-ester, which was prepared as described previously.



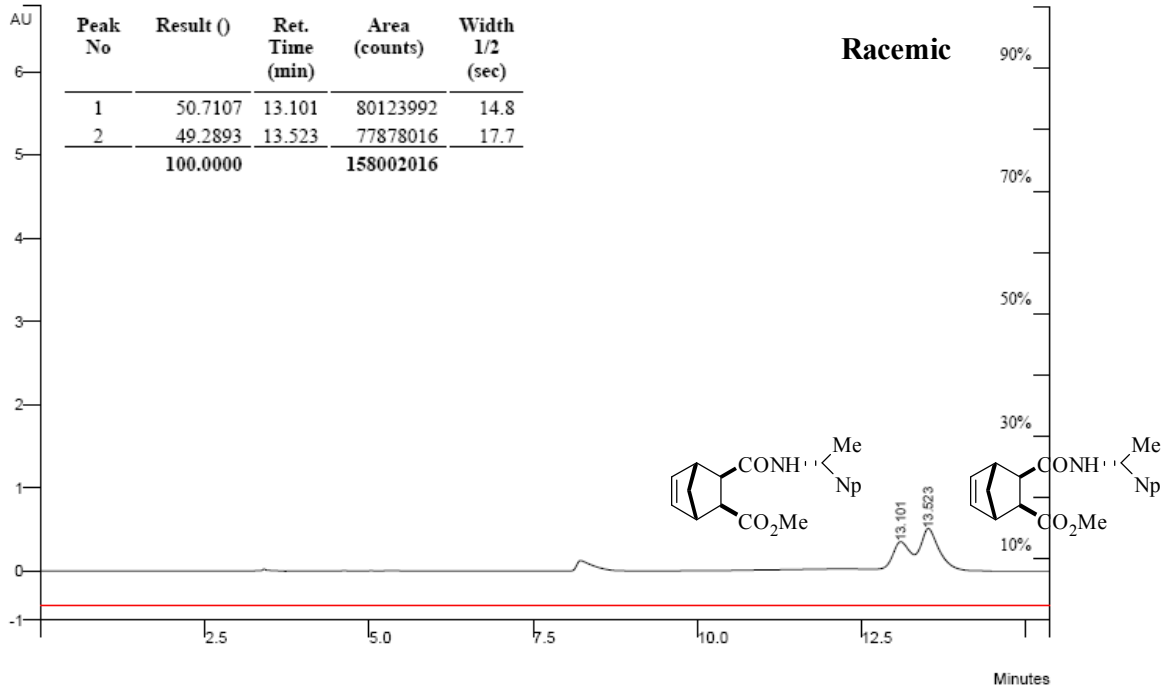
Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	45.1449	10.129	9615670	15.7
2	54.8551	16.130	11683896	23.9
	100.0000		**21299566**	



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	2.0893	10.990	84577	12.2
2	97.9107	16.926	3963545	19.3
	100.0000		**4048122**	

Table 1 - Entry 5.

The ee value was determined by the HPLC analysis (Kromasil, 40 : 1, Hexanes : IPA, 1 mL/min, t(minor) = 13.73 min, t(major) = 15.17 min) of the diastereomeric mixture of the corresponding amide-ester, which was prepared as described previously.



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	50.7107	13.101	80123992	14.8
2	49.2893	13.523	77878016	17.7
	100.0000		**158002016**	

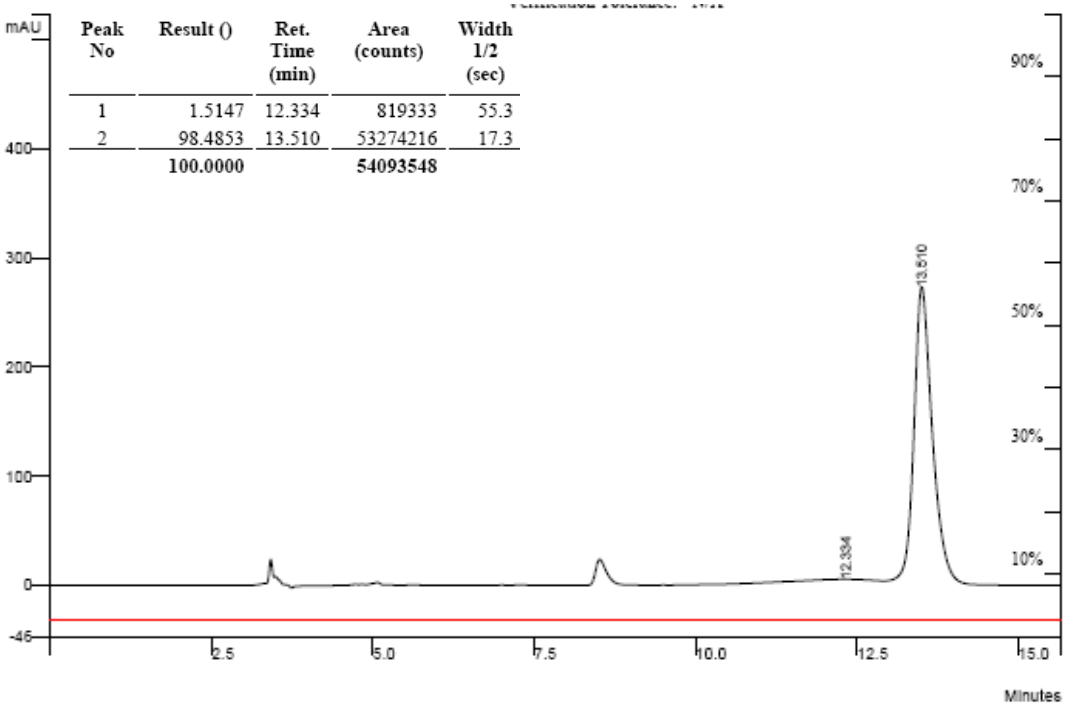
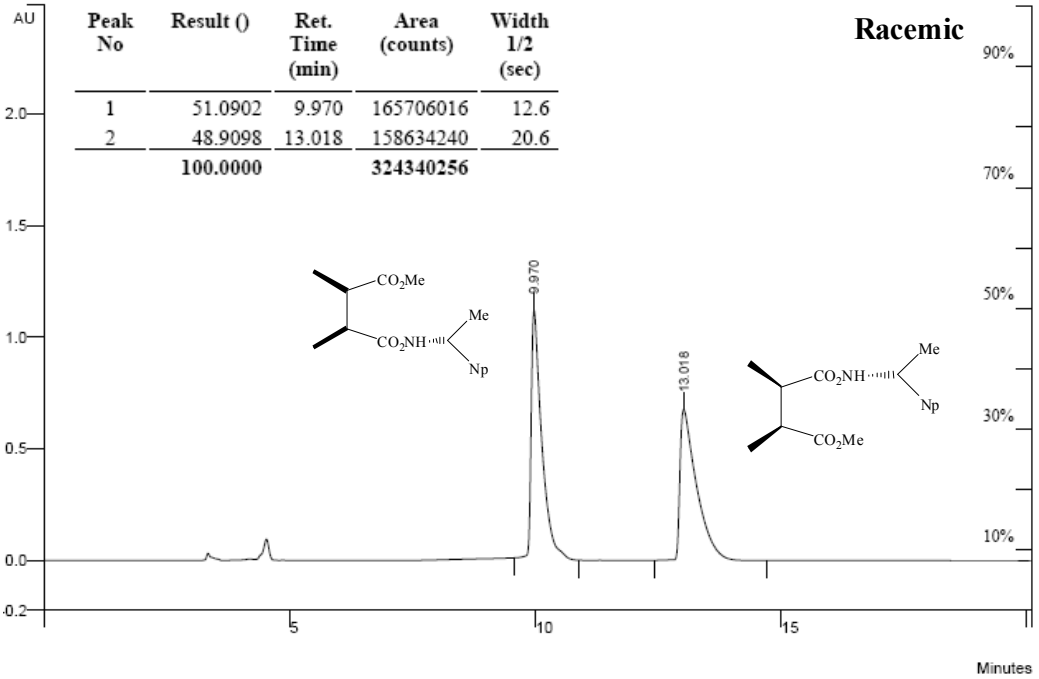
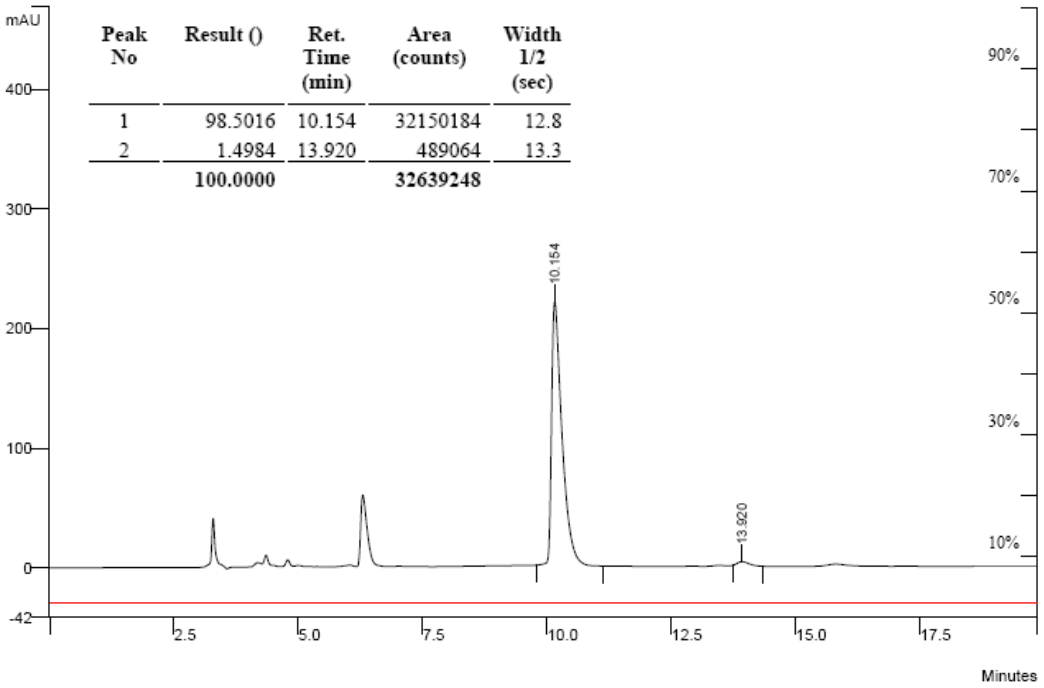


Table 1 - Entry 6.

The ee value was determined by the HPLC analysis (Hypersil, 40 : 1, Hexanes : IPA, 1 mL/min, t(major) = 10.15 min, t(minor) = 13.92 min) of the diastereomeric mixture of the corresponding amide-ester, which was prepared as described previously.

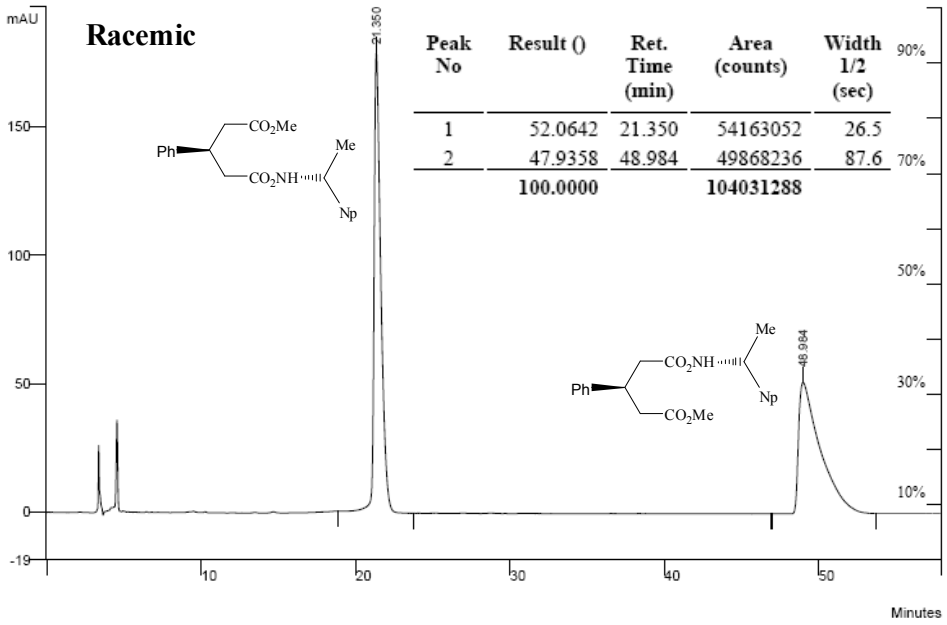




Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	98.5016	10.154	32150184	12.8
2	1.4984	13.920	489064	13.3
	100.0000		**32639248**	

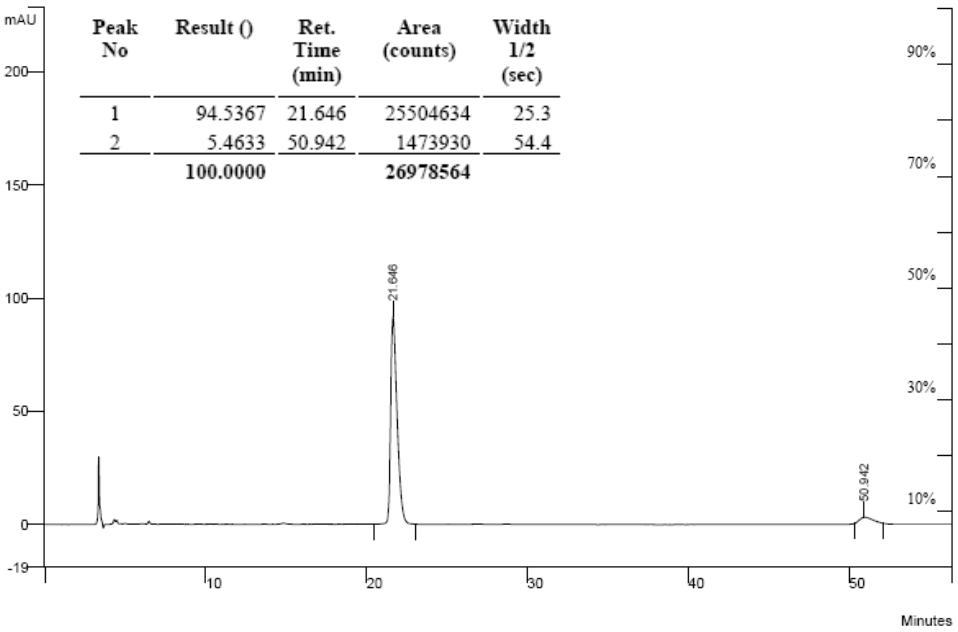
Table 1 - Entry 7.

The ee value was determined by the HPLC analysis (Hypersil, 20 : 1, Hexanes : IPA, 1 mL/min, t(major) = 21.64 min, t(minor) = 50.94 min) of the diastereomeric mixture of the corresponding amide-ester, which was prepared as described previously.



Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	52.0642	21.350	54163052	26.5
2	47.9358	48.984	49868236	87.6
	100.0000		**104031288**	

Peak No	Result ()	Ret. Time (min)	Area (counts)	Width 1/2 (sec)
1	94.5367	21.646	25504634	25.3
2	5.4633	50.942	1473930	54.4
	100.0000		**26978564**	



9. References.

1. B. Vakulya, S. Varga, A. Csampai and T. Soos, *Org. Lett*., 2005, **7**, 1967.

2. D. J. Berrisford, P. A. Lovell, N. R. Suliman and A. Whiting, *Chem. Commun*., 2005, 5904.

3. Y. M. Song, J. S. Choi, J. W. Yang and H. Han, *Tetrahedron Lett*., 2004, **45**, 3301.