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CHEMO-ENZYMATIC SYNTHESIS OF 1,2- AND 1,3- AMINO-ALCOHOLS AND THEIR USE IN THE ENANTIOSELECTIVE REDUCTION OF ACETOPHENONE AND ANTI-ACETOPHENONE OXIME METHYL ETHER WITH BORANE.

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Abstract: New chiral amino-alcohols were enantioselectively synthesized using bio-transformations as the key steps. They were used as ligand in the enantioselective borane reduction of acetophenone and of the corresponding *anti* oxime methyl ether.

1) Introduction.

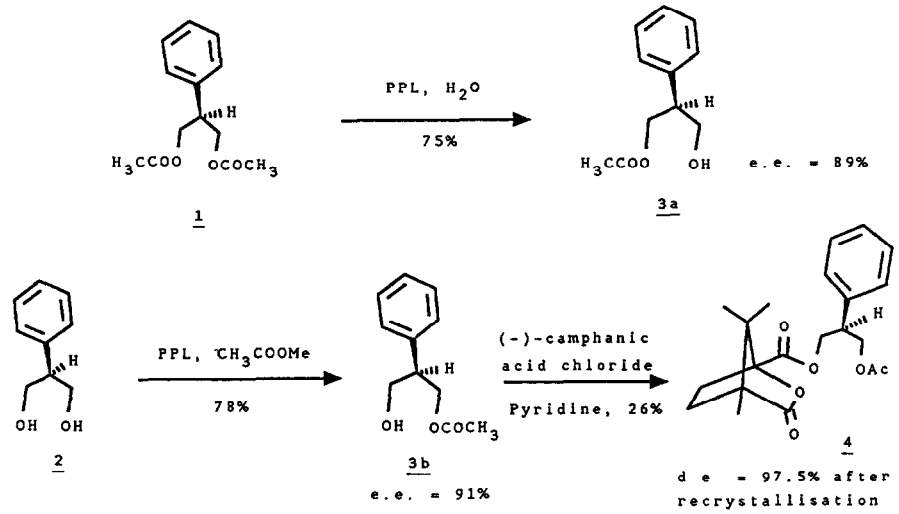
The use of chiral amino-alcohols derived from amino acids as ligands in the enantioselective borane reduction of carbonyl compounds and in some cases of their corresponding oxime ethers has already been described [1]. In this communication we wish to report the synthesis of (S)-3-amino-2-phenylpropan-1-ol 7a ,(1S,2R)-2--amino-cyclopentan-1-ol 14a ,(1S,2R)- and (1R,2S)-1-amino-indan-2-ol 23 and 24 and some of their N-monoalkylated derivatives as well as their use in the reactions cited above.

2) EPC-synthesis of 1,2- and 1,3-amino-alcohols.

The enantioselective key steps in the synthesis of the amino alcohols were bio-transformations . In the case of the propanolamine series 7a-c , we used the lipase from porcine pancreas (PPL) which was shown to catalyze hydrolysis of *meso*-diacetylated diols and acylation of meso-diols with high enantiotopic group differentiation[2].

The hydrolysis of the *meso*-diacetate 1 in aqueous media gave the (S)-(-)-monoacetate 3a in 75 % yield with 89 % e.e.. Acylation of the diol 2 in organic media gave the (R)-(+)-monoacetate 3b in 78 % yield with 91 % e.e..

The absolute configuration in this series was determined by X-ray analysis of the diastereomerically pure ester 4 prepared from (-)-camphanic acid chlorid and 3b *(Scheme 1, figure 1).*



Scheme 1

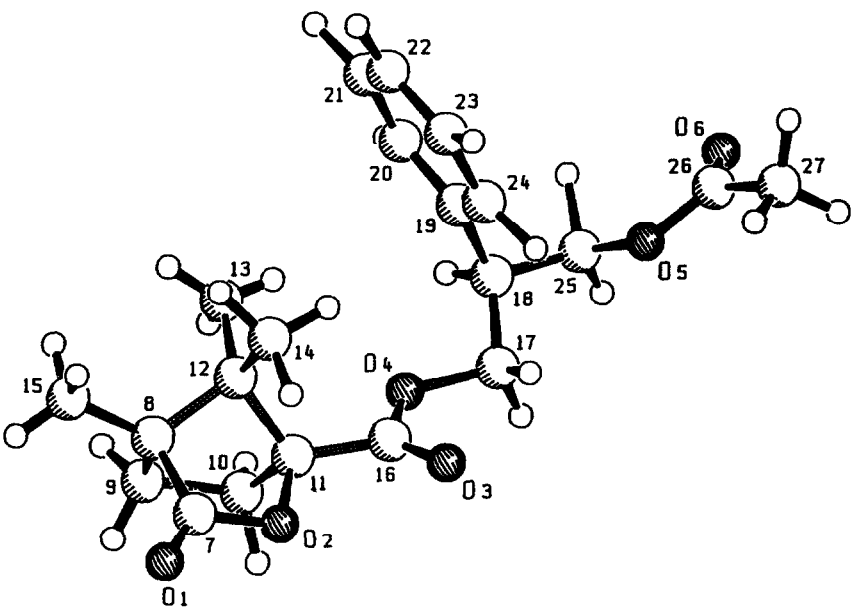
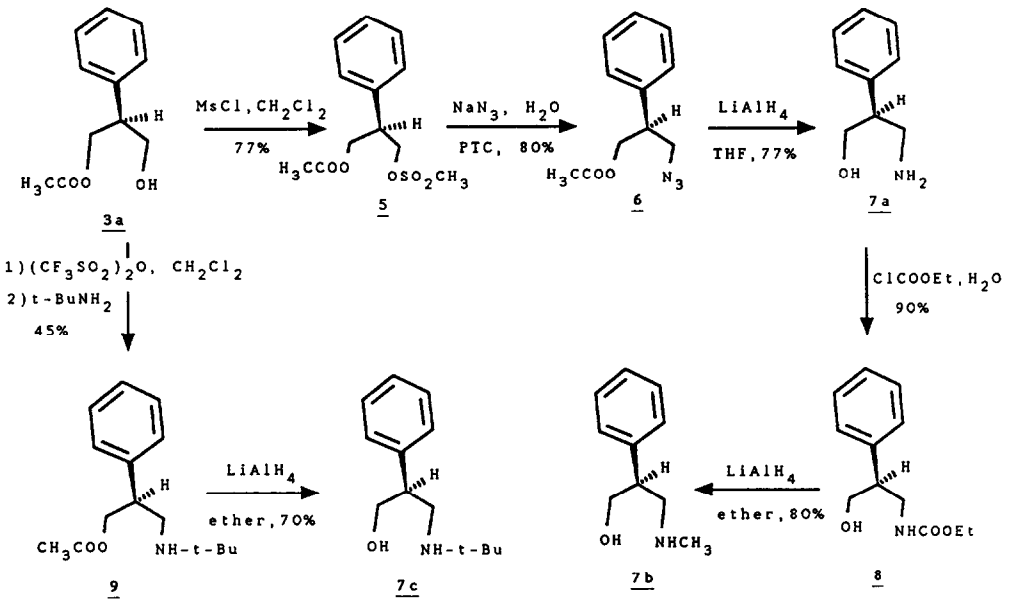


Figure 1: Molecular structure and atomic numbering scheme of 4 (Schakal)[13].

The monoacetate 3a (e.e.= 89%) was subsequently transformed to the desired compounds 5-9 by means of standard chemical transformations *(Scheme 2)*.



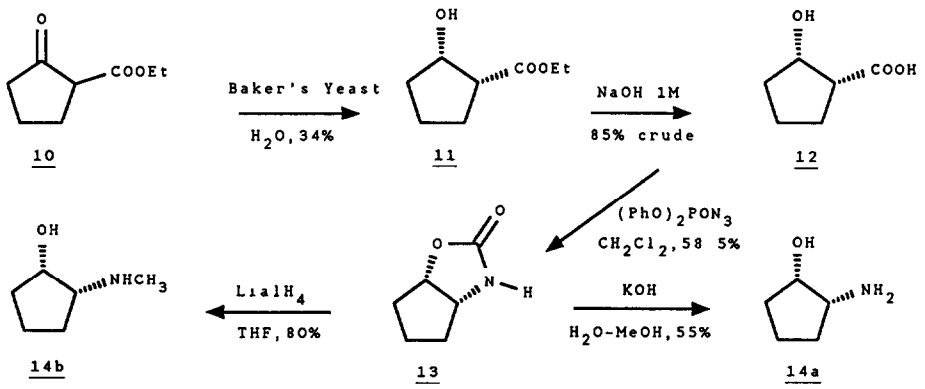
Scheme 2

The (S)-(-)-3-amino-2-phenylpropan-1-ol 7a was prepared via the mesylated compound 5 and the azido compound 6 without detectable racemisation (e.e.= 92%). The optical purity of 7a was brought up to more than 95% via the recrystallization of the corresponding HCl-salt. The N-methylated derivative 7b was prepared using a classical method of monomethylation[3].

As the mesylated derivative 5 was found to react sluggish with tert. butylamine, the more reactive triflate was prepared . The reaction with tert. butylamine gave the compound 9 with 59% ee due to partial racemisation. The reduction of 9 afforded the compound 7c (e.e.= 55%) which was obtained in optical pure form via recrystallization of the HCl-salt.

The 2-amino-cyclopentan-1-ol 14a-b series were prepared starting from the enantiomerically pure hydroxy-ester 11 which on his side was obtained by Baker's Yeast reduction[4] of the corresponding β-ketoester 10, in 34 % yield with high enantio- and diastereoselectivity (e.e.> 97%, d.e. > 99%). The corresponding hydroxy acid 12 was

converted into the oxazolidin-2-one 13 by means of a modified Curtius reaction using diphenylphosphorazide (DPPA)[5] in methylene chloride *(Scheme 3)*.

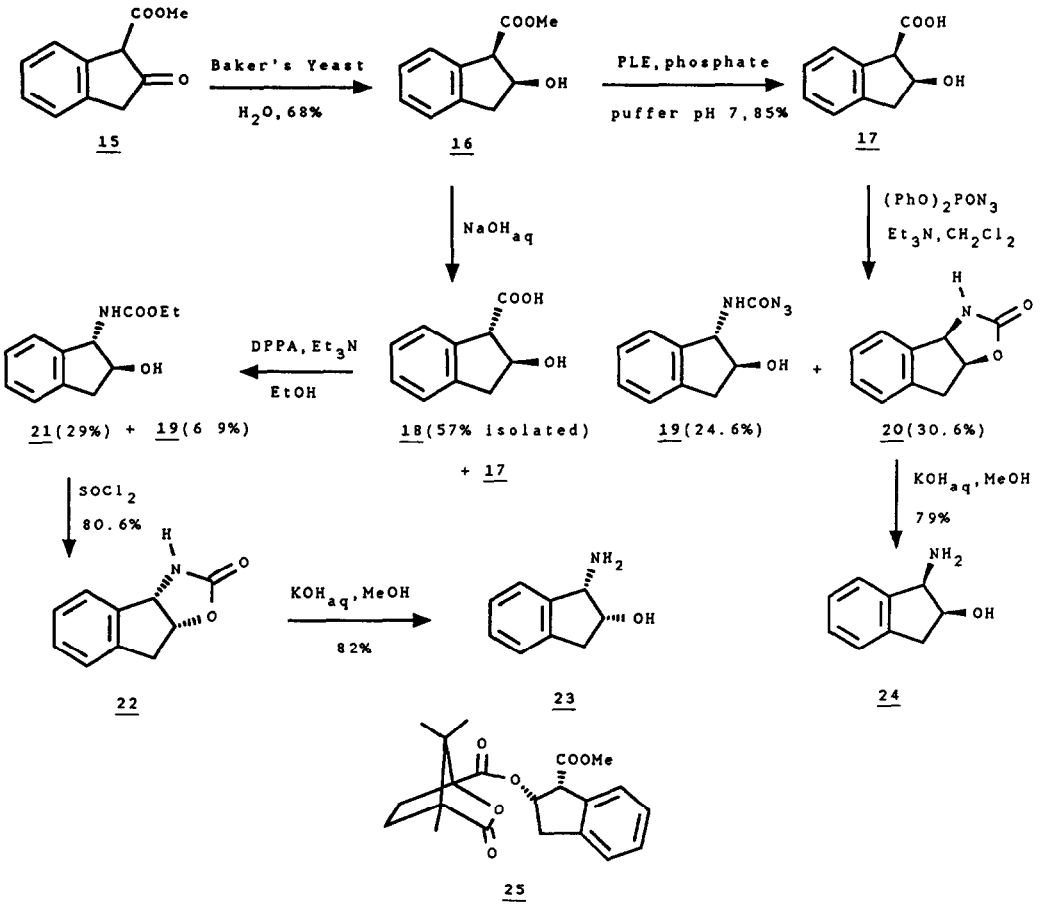


Scheme 3

The same approach was used to prepare both enantiomeric forms 23 and 24 of the 1-amino-indan-2-ol. We started from the optical pure hydroxy ester 16 obtained by Baker's Yeast reduction of the β-ketoester 15 (e.e.=99.5%, d.e.>99%). The absolute configuration of 16 was determined by X-ray analysis of the corresponding camphanic ester 25 *(Scheme 4,figure 2)*.

The hydrolysis of the methyl ester 16 with aqueous sodium hydroxyde at RT gave a mixture of *cis*- and *trans*-hydroxy acid (17/18:66/34). Only the *trans*-isomer 18 could be isolated in pure form by crystallization of the mixture (57%). The *cis*-isomer was then prepared by enzymatic hydrolysis of the ester with Pig Liver Esterase (PLE)[6] in neutral medium (85%).

The $COOH \rightarrow NH_2$ interconversions were performed as described above by reaction with DPPA. The reaction of *cis*-hydroxy-acid 17 with DPPA at RT in methylene chloride gave the oxazolidin-2-one 20 and as major by-product, the N-acyl azide 19[7]. The *trans*-hydroxy-acid 18 was first transformed into the ethylcarbamate 21 with DPPA by refluxing in ethanol (19 was obtained as major by-product) and the further reaction with thionyl chloride[8] gave the oxazolidin-2-one 22 . Hydrolysis of the oxazolidin-2-ones gave the corresponding 1-amino-indan-2-ols 23 and 24 *(Scheme 4)*.



Scheme 4

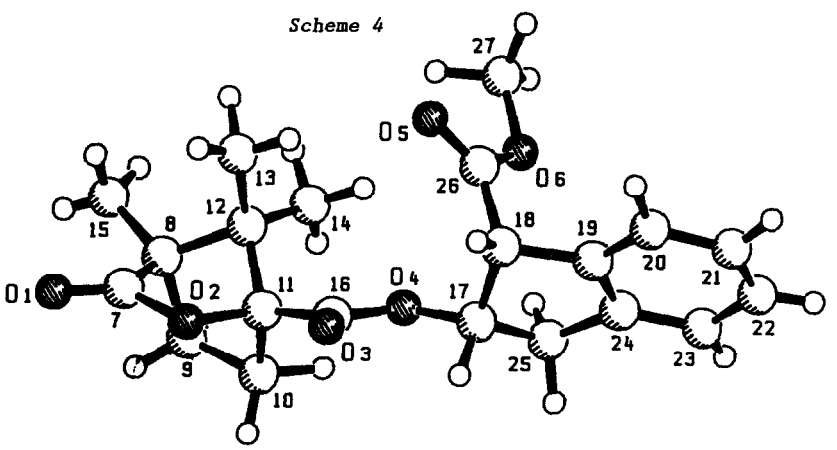
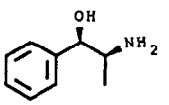


Figure 2: Molecular structure and atomic numbering scheme of 25 (Schakal)[13].

3) Enantioselective reductions.

1,3,2-oxazaborolidines, prepared by reaction of chiral 1,2-amino-alcohols with borane catalyze borane-reduction of ketones and oximes ethers with in some cases very good enantioselectivities[1]. We investigated reductions with 1,3,2-oxazaborolidines and tetrahydro-1,3,2-oxazaborines as catalyst which were prepared *in situ* by reaction of borane-THF 1M with the previously synthetised 1,2- and 1,3-amino-alcohols. (-)-Norephedrine 26, (-)-Ephedrine 27, (+)-trityl-Norephedrine 28 [9] were also investigated as ligands for comparison purposes *(Scheme 5)*.



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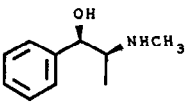

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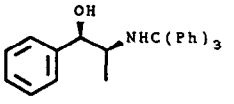

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Scheme 5

In some cases, the reductions were carried out with different stoichiometries in order to evaluate the catalytic behaviour of the ligands. The results are summarized in *tables 1* and *2*.

In both reactions types, the best enantioselectivities were obtained with 1,2-amino alcohols *(table 1, entries 4,7,8,9; table 2, entries 3,6,8,10)* Introduction of a bulky substituent on nitrogen caused a pronounced decrease in the ee values *(table 1, entries 3,12; table 2, entry 11)*. A methyl substituent on nitrogen showed a variable effect on the ee values depending on the ligand *(table 1, entries 1,2; 4,5 and 8,9 ; table 2, entries 3,5 and 8,9)*.

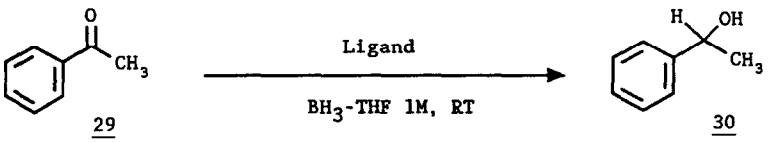
With stoichiometric amounts of the ligand, all the reductions of acetophenone required more time than the reduction with borane alone (15 minutes with one mol equivalent of BH_3 in THF at 25°C). Consequently no system was found to be efficient with catalytic amounts of ligand *(table 1, entries 6,10,11)*.

In the case of the anti oxime methyl ether 31[10], we obtained the amine 33 as well as the hydroxylamine methyl ether 32. The ratio 32/33 depends on the amount of borane used and on the nature of the ligand too the N-alkylated ligands affording more amine and less 32 than the not alkylated *(table 2, entries 2,5,11)*. Very high enantioselectivities were obtained only with stoichiometric amounts of not alkylated 1,2-amino-alcohols *(table 2, entries 3,6 and 8)*.

Finally, the cyclic structures of the amino-cyclopentanol 14a and amino-indanol 23 were found to be as good as aliphatic structures of Norephedrine-type and its seems , as shown in previous works[1], that disubstitution in α-position of the hydroxyl group was necessary to attain high selectivities as well as good catalytic effects

TABLE 1

REDUCTION OF ACETOPHENONE[a)]



29 30

Entry	Ligand	Equiv. ligand : Borane : 29	% conversion[b)] (time in h.)	Configuration of 30 (% ee)[c)]
1	*(S)-3-amino-2-phenyl propan-1-ol* 7a	1 : 2.3 : 0.8	> 95% (2)	R (17.0%)
2	*(S)-3-methylamino-2-phenylpropan-1-ol* 7b	1 : 2.3 : 0.8	> 95% (2)	R (29.5%)
3	*(S)-3-t-butylamino-2-phenylpropan-1-ol* 7c	1 : 2.1 : 0.8	> 95% (2)	R (5.5%)
4	*(1S,2R)-2-amino cyclopentan-1-ol* 14a	1 : 2.3 : 0.8	> 95% (3)	S (76.7%)
5	*(1S,2R)-2-methylamino cyclopentan-1-ol* 14b	1 : 2.16 : 0.8	> 95% (2)	S (50.8%)
6		1 : 12.5 : 10	> 95% (2)	S (23.2%)
7	*(1S,2R)-1-amino indan-2-ol* 23	1 : 2.3 : 0.8	> 95% (1)	R (86.9%)
8	*(1R,2S)-Norephedrine* 26	1 : 2 : 0.8	> 95% (2)	R (74.5%)
9	*(1R,2S)-Ephedrine* 27	1 : 2 : 0.8	> 95% (2)	R (78 7%)
10		1 : 5 : 3.5	> 95% (2)	R (61.4%)
11		1 : 12.5 : 10	> 95% (2)	R (34.0%)
12	*(1R,2S)-N-trityl norephedrine* 28	1 : 2.1 : 0.8	> 95% (2)	R (4.4%)

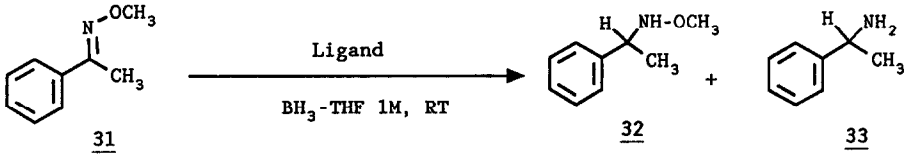
a) for the procedure, see experimental

b) Determined by GC: Carbowax 20M, 10%, 2m., 200°C

c) Determined by HPLC. Chiralcel OB (Daicel), hexane/isopropanol 90/10 1ml/min., UV 215 nm

TABLE 2

REDUCTION OF ANTI-ACETOPHENONE OXIME METHYL ETHER[a)]



31 32 33

Entry	Ligand	Equiv. ligand : Borane : 31	Composition[b)] 31/32/33(%)(h.)	Configuration 33 (% ee)[c)]
1	*(S)-3-amino-2-phenyl propan-1-ol* 7a	1 : 2.3 : 0.8	5.1/88.6/4.8 (24)	R (42.9%)
2	*(S)-3-methylamino-2-phenylpropan-1-ol* 7b	1 : 2.3 : 0.8	14.0/46.2/39.8 (24)	R (49.0%)
3	*(1S,2R)-2-amino cyclopentan-1-ol* 14a	1 : 2.3 : 0.8	0.0/72.0/24.8 (40)[d)]	R (95.0%)
4		1 : 5 : 3.5	31.1/22.3/46.5 (40)	R (70.6%)
5	*(1S,2R)-2-methylamino cyclopentan-1-ol* 14b	1 : 2.1 : 0.8	21.9/29.9/47.9 (24)	R (6.4%)
6	*(1S,2R)-1-amino indan-2-ol* 23	1 : 2.3 : 0.8	0.0/93.2/6.8 (30)[d)]	S (94.5%)
7		1 : 23 : 8	0.0/16.2/83.8 (30)[d)]	S (45.9%)
8	*(1R,2S)-Norephedrine* 26	1 : 2.1 : 0.8	0.0/77.9/22.0 (24)[d)]	S (93.2%)
9		1 : 5 : 3.5	19.3/27.9/52.5 (24)	S (87.0%)
10	*(1R,2S)-Ephedrine* 27	1 : 2.1 : 0.8	6.7/68.7/24.5 (24)	S (71.0%)
11	*(1R,2S)-N-trityl norephedrine* 28	1 : 2.1 : 0.8	0.6/2.4/97.0 (24)	- (0.0%)

a) for the procedure: see experimental.

b) Determined by GC OV 101, 3%, 4m, 130°C

c) Determined by HPLC of the 3,5-dinitrobenzamides· Pirkle covalent D-Naphtylalanine, hexane/isopropanol 80/20, 1ml/min., UV 240 nm

d) After complete elimination of oxime ether 31, an excess of 1M-BH_3-THF was added and the mixture was heated at 70°C up to completion of the reduction (33> 95% by GC). We observed no loss of optical purity.

Experimental section.

General:

Melting points and boiling points are uncorrected. Melting points were determined with a Büchi 535 apparatus. Bulb-to-bulb distillations were performed with a Büchi GKR-50 apparatus. Optical rotations were measured on a Perkin-Elmer Model 241 polarimeter at 23±2°C.

Flash chromatographies were performed on Silica Gel 60 (Merck, 230-400 mesh), analytical TLC on Silica Gel 60 F_{254}(Merck).

Capillary GC and GC with packed columns were performed respectively with Carlo Erba HRGC 5160 Mega series and Carlo Erba GC 6000 Vega series apparatus, HPLC on a Waters 840 system.

IR spectra were recorded on a Perkin Elmer 1420 spectrophotometer, ^{1}H NMR spectra on Varian EM 360L (60MHz), Brücker AC-F250 (250Mhz), and Brücker AM 300 (300Mhz) spectrometers and mass spectra on a Finigan MAT 212 spectrometer(IE, 70 eV).

Starting materials, reagents and solvents:

Diol 2 was prepared by LAH-reduction of the commercially available 2-phenyl-diethylmalonate[10]. Diacetate 1 was obtained by reaction in ether of diol 2 with 2.5 mol.eq.of acetylchloride and 2.5 mol.eq. of triethylamine at 0°C (80 %). β-keto ester 10 was commercially available and β-keto ester 15 was prepared by the procedure of Schroth[11].

The crude lipase from porcine pancreas (PPL) and esterase from pig liver were available by Sigma (Nr.L 3126, E 3128) and Baker's Yeast by Klipfel AG (Rheinfelden, Switzerland).

Anhydrous ether and THF were obtained by distillation over sodium. Hexanes naming corresponds to the isomers mixture.

Experimental procedures and characterisation of products:

Hydrolysis of the 1,3-diacetoxy-2-phenyl propane 1 to the (S)-(-)-1-acetoxy-2-phenyl propan-3-ol 3a.

Typical procedure: 2g of crude Lipase were suspended in 25 ml phosphate buffer (pH 7) and centrifugated 30 min. at 2500 trs/min. The surnagent was decanted and diacetate 1 (0.5g, 2.11 mmol) was added. The mixture was stirred at RT and the pH was kept constant during the hydrolysis by continous addition of 1N-NaOH solution from an autoburette. After addition of one equivalent of base, the reaction was stopped, the solution extracted with ether, the organic layer dried over $MgSO_4$ and the solvent evaporated *in vacuo*. The crude product was flash chromatographied in ether/hexanes : 2/1 and bulb-to-bulb distilled (135°C, 5.10^{-3}mbar) to give an colorless oil (0.31g,75%).

3a: $C_{11}H_{14}O_3$ (194.23); $[\alpha]_D$= -58.8° (c=0.66,$CHCl_3$); IR (CH_2Cl_2): 3600, 3490, 1735; ^{1}HNMR (60MHz,$CDCl_3$): δ 7.32 (s,5H, Ar-H); 4.40 (d,J=7Hz, 2H,CH_2OAc); 3.86 (d,J=7Hz, 2H,CH_2OH); 3.14 (qi,J=7Hz, 1H,CH); 2.32 (s,1H,OH); 2.05 (s,3H,CH_3); Anal. found: C,67.1; H,7.3; O,24.7 Calc.: C,68.0; H,7.3; O,24.7.

The e.e. (89.3%) was determined by HPLC: Chiracel OB (Daicel), Hex/i-PrOH: 90/10, 1ml/min., UV 215 nm.

Acetylation of the 2-phenylpropane-1,3-diol to the (R)-(+)-3b.

Typical procedure: a solution of diol 2 (0,34g,2.23mmol) in 34ml of methylacetate (previously dried on 4 Angströms molecular sieves) was mixed with 1.7g of crude PPL and stirred at RT for 5 hours. After filtration and evaporation of the solvent, the crude product was purified and analysed as described before to yield 0.34g (78%) of compound 3b: e.e.= 90.7% by HPLC.

Preparation of (R)-1-acetoxy-2-phenyl-3-mesyloxy propan 5:

To a solution of 3a (4.9g, 25.2 mmol) and Et_3N (9.8ml,70mmol) in 60 ml CH_2Cl_2 mesylchloride was added dropwise at -10°C (3.9 ml, 50mmol) . Then the solution was stirred for 2 hours at 0°C, washed successively with ice-water, 1N-HCl, saturated bicarbonate solution and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was flash chromatographied in ether to give a colorless oil (19.5 mmol ,77%) which is to use rapidly in the next step.

5: $C_{12}H_{16}O_5S$ (272.32); IR (CCl_4): 1750, 1370, 1230, 1180; ^1H NMR (60MHz,$CDCl_3$): δ 7.31 (s,5H,Ar-H); 4.50 (d,J=6Hz, CH_2-OSO_2); 4.40 (d,J=6HZ, 2H,CH_2OAC); 3.38 (qi,J=6HZ, 1H,CH); 2.83 (s,3H,CH_3-SO_2); 2.03 (s,3H,CH_3CO); MS M/z; 212(28), 177(2), 176 (4), 134(17), 133(51), 105(24), 104(91), 91(10), 77(8),43(100).

Preparation of (S)-(-)-1-acetoxy-3-azido-2-phenyl propane 6:

The mesylated compound 5 (5.3g,19.5 mmol) was added to a stirred solution of sodium azide (2.53g,3.9mmol) and tri-n-octylmethylammonium chloride (400mg,0.97mmol) in 15 ml water. The mixture was vigourously stirred and heated at 80°C for 6 hours. The solution was extracted with CH_2Cl_2, dried and concentrated *in vacuo*. The crude product was flash chromatographied in ether/hexanes:2/5 to give a colorless oil (3.45g,15 7mmol,80%).

6: $C_{11}H_{13}N_3O_2$ (219.25); $[\alpha]_D$= -20.13° (c=1.0,$CHCl_3$); IR (CCl_4): 2100, 1750, ^1H NMR (250Mhz, $CDCl_3$): δ 7.40-7.20 (m,5H,Ar-H); 4.32 (d,J=6.5Hz, 2H,CH_2OAc); 3 63 (d,J=6.5Hz, 2H,CH_2N_3); 3.20 (qi,J=6.5Hz, 1H,CH); 2.05 (s,3H,CH_3); MS: m/z, 193(0.1)(M+.), 177(0.1), 176(0.7), 163(4), 159(5), 131(3), 130(14), 104(32) , 103(12), 91(8), 77(7), 43(100).

Preparation of (S)-(-)-3-amino-2-phenyl propan-1-ol 7a:

To a suspension of $LiAlH_4$ (13g, 342 mmol) in 800 ml anhydrous THF was added dropwise a solution of 6 (38g,173mmol) in 200 ml anhydrous THF. The mixture was then refluxed for 3 hours. After hydrolysis with 100 ml of freshly prepared saturated aqueous ammonium sulfate, the insoluble salts were filtered and washed thoroughly with ether. The combined filtrates were concentrated *in vacuo* to give 37g of crude product.

An aliquot was transformed into N,O-bis-PFP derivatives and injected in GC (Chirasil-L-Val, Chrompack, 25m x 0.25 mm, 105°C (35min.), 10°C/min.,110°C, e.e = 92%).

The crude product was dissolved in ether and HCl-gas was bubbled to precipitate 25g (133 mmol,77%) of the corresponding HCl-salt (m.p.: 172-173°C).

Recrystallization in 175 ml CH_3COOEt and 215 ml MeOH gave a first batch B1 (11.2g, m.p.:189-190°C) and after addition of CH_3COOEt to the mother solution, two other batches B2 (0.9g, m.p.: 189-190°C) and B3 (6.57g,m.p.:188-189°C) were obtained. Batch B3 was again recrystallized (45 ml CH_3COOEt, 56 ml MeOH) to give B4 (3.48g,m.p.:189-190°C), B5 (1.28g,m.p.: 189-190°C) and B6 (m.p.< 188°C).

Batches B1,B2,B4 and B5 were combined (16.86g, 52%).

7a(HCl): $C_9H_{14}NOCl$ (187 67); $[\alpha]_D$= -23.74° (c=0.914, HCl 1N); Anal. found C,57.6, H,7.4; N,7.5, O,8.4; Cl,18.9 calc.: C,57.6; H,7.52, N,7.46; O,8 52, Cl,18.89.

15g (80 mmol) of the salt were dissolved in 80 ml 2M-NaOH and stirred vigourously for an hour. The mixture was extracted 3 times with CH_2Cl_2, the solution dried over $MgSO_4$ and concentrated in vacuo to give 12.2g of product which was bulb-to-bulb distilled (180°C/ 10^{-1} mbar) to give 10.7g of 7a as colorless oil (71 mmol, 88%).

As previously, e.e. (> 95%) was determined by GC.

7a: $C_9H_{13}NO$ (151.21); $[\alpha]_D$= -32.25° (c= 1.47, MeOH); IR(CH_2Cl_2): 3660, 3600, 3400, 3320, 1060; ^1H NMR (300 MHz,$CDCl_3$): δ 7.38-7.15 (m,5H,Ar-H); 3 91 (m,2H,CH_2-O); 3.13 (m,2H,CH_2-N); 2.95 (m,1H,CH); 2.35 (s,3H,OH,NH_2).

Preparation of (S)-(+)-3-carbetoxyamino-2-phenyl propan-1-ol 8:

To a stirred solution of enantiomerically pure 7a (5.7g, 37.7mmol) in 200 ml water, were dropped at 0°C first 1.9ml (20.4 mmol) ethylchloroacetate and then simultanously 19 ml 2M-NaOH and another 1.9 ml chloroester. The mixture was stirred at 0°C for. 2 hours and 1 for hour at RT. The solution was acidified (1N-HCl), extracted with ether, the organic layer washed with water, dried over $MgSO_4$ and concentrated *in vacuo*. Bulb-to-bulb distillation (220°C/ 6 10^{-3} mbar) gave 8 as a colorless oil (7.56g, 90%).

8: $C_{12}H_{17}NO_3$ (223.27); $[\alpha]_D$= +20.96° (c=0.93, $CHCl_3$); IR(CH_2Cl_2): 3620, 3460, 1720 ; ^1H NMR(60MHz,$CDCl_3$): δ 7.25 (s,5H,Ar-H); 4.97 (s,1H,NH); 4.09 (qa,J=7Hz, 2H,CH_2-CH_3); 3.68-3.34 (m,2H,CH_2-O); 3.79 (d,J=6Hz, 2H,CH_2-N); 3.22-2 67 (m,2H,CH+OH); 1.23(t,J=7Hz,3H,CH_3). Anal. found. C,64.1; H,7.8; N,6.3; O,21.7, calc.: C,64.56; H,7.68; N,6.28; O,21.50.

Preparation of (S)-(-)-3-N-methylamino-2-phenyl propan-1-ol 7b :

To a suspension of $LiAlH_4$ (5.14g,135mmol) in 100ml anhydrous ether were added dropwise 7.5g (33mmol) of 8 in 50 ml anhydrous ether. The mixture was refluxed for 10 hours and then hydrolysed with 30%-NaOH and water to precipitate aluminium hydroxydes. After filtration, washing with ether and concentration *in vacuo*, the crude product (4.9g) was purified by bulb-to-bulb distillation (160°/8 10^{-3} mbar) to give a colorless oil (4.6g,80%).

7b: $C_{10}H_{15}NO$ (165.24); $[\alpha]_D$= -23.17° (c=1.079,MeOH); IR (CH_2Cl_2): 3660, 3600, 3310, 3230, 1035; ^1H NMR (300MHz,DMSO d_6): 7.20-7.15 (m,5H,Ar-H); 3.60 (m,2H, CH_2-O); 3.33 (s,2H, OH,NH); 2.65 (m,2H, CH_2-N); 2.50 (m,1H,CH); 2.24 (s,3H,CH_3), MS; m/z: 165(0.5)(M+.), 147(15), 104(8), 44(100).

Preparation of (S)-(-)-1-acetoxy-3-(N-tertbutylamino)-2-phenyl propan 9:

To a stirred solution of monoacetate 3b (20g, 103 mmol) and Et_3N (9.4ml, 130ml) in 400 ml of methylene chloride, was dropped at -10°C a solution of trifluoromethane sulfonic acid anhydride (21ml, 130mmol) in 20 ml CH_2Cl_2. The solution was stirred at 0°C for 5 hours and rapidly washed successively with cold 1N-HCl,ice-water dried over $MgSO_4$ and filtered. To this solution was added dropwise at RT tertbutylamine (32ml, 300mmol) and the mixture stirred overnight. The organic layer was extracted twice with 1N-HCl, the aqueous layer basified with 1N-NaOH and extracted twice with ether. After drying and concentration of the solution, the crude product (22.8g) was flash chromatographied in ethyl acetate and bulb-to-bulb distilled (210°C/ 10^{-1}mbar) to afford a colorless oil (11,5g, 45%).

9: $C_{15}H_{23}NO_2$ (249.36); $[\alpha]_D$= -7.88°(c=1.066,$CHCl_3$); IR ($CHCl_3$): 1733; ^1H NMR ($CDCl_3$,250MHz): δ 7.38-7.18 (m,5H,Ar-H); 4.28 (m,2H,CH_2-O); 3.08 (m,1H,CH); 2.88 (m,2H,CH_2-N); 2.02 (s,3H,CH_3CO); 1.04 (s,9H,CH_3); 0.84 (s,1H,NH); MS; m/z 249(1)(M+.), 234(4), 117(12), 104(15), 91(12), 86(100), 57(23), 43(28).

The e.e.(59%) was determined by ^1H NMR ($CDCl_3$,300MHz) in the presence of (S)-(+)-TAE.

Preparation of (S)-(-)-3-(N-tertbutylamino)-2-phenyl propan-1-ol 7c:

To a suspension of $LiAlH_4$ (3.4g, 88mmol) in 200ml anhydrous ether was dropped a solution of 9 (11g, 44mmol) in 100ml anhydrous ether. The mixture was refluxed for 2 hours and hydrolysed with 2N-NaOH. The salts were filtered, washed thouroughly with ether and the organic phase dried and concentrated *in vacuo* The residue (8.5g) was dissolved in ether and HCl-gas was bubbled through the solution to precipitate 7.54g (70%) of the corresponding hydrochloride salt.

An e.e. of 55% was determined from crude product in the same manner as for 9

Recrystallization of the salt in ethyl acetate/methanol:10/1 afforded three successive batches of crystals:

B1 3.00g m.p.: 142.7-145.6°C
B2 1.65g m.p.: 137.6-138.9°C
B3 1.75g m.p.: 129.8-132.2°C
Batch B2 was again recrystallized to give:
B4 1.12g m.p.: 143.8-145°C
Batches B1 and B4 were combined (4.12g, 51.5%).

7c(HCl): $C_{13}H_{22}NOCl$ (243.78); $[\alpha]_D$= -38.7° (c=0.76,HCl-0.1N); Anal. found. C,64.0; H,9.1; N,5.7; =,6.5; Cl,14.6 calc.: C,64.05; H,9.10; N,5.75; O,6.56, Cl,14.54.

The salt (4g, 16.4 mmol) was dissolved in 15 ml 2M-NaOH and stirred for an 1 hour. The mixture was saturated with NaCl and extracted twice with ether. After drying and evaporation of the solvent *in vacuo*, the crude product was bulb-to-bulb distilled (180°C/ 7 10^{-3} mbar) to give an oil which crystallized at RT (2.85g, 84%)(e.e.>95%).

7c: $C_{13}H_{21}NO$ (207.32); colorless cristals, m.p.: 49.5-50.5°C (ether / pentane: 5/30); $[\alpha]_D$=-28.15°C (c=1.05,MeOH); IR (CH_2Cl_2): 3220, 2980, 1040; ^1H NMR (300MHz, DMSO d_6): 7.33-7.13 (m,5H,Ar-H); 5.17 (s,1H,OH); 3.65 (m,1H,CH_2-O); 3 53 (m,1H,CH_2-O); 2.87 (m,1H.CH); 2.75 (m,2H,CH_2-N); 1.25 (s,1H,NH); 0.98 (s,9H,CH_3); Anal. found: C,75.5; H,10.2, N,6.9; O,7.8; calc.: C,75.32; H,10.21; N,6.76; O,7.72.

Preparation of ethyl (1R,2S)-2-hydroxycyclopentane carboxylate 11:

In a 6 *l.* flask equiped with a mechanic stirrer, 2.4 *l.*tap water, 450g saccharose and 300g Baker's Yeast were introduced. The mixture was stirred at RT for an hour and keto-ester 10 (20g,17.5 ml,128mmol) was introduced. After 24 hours of stirring, a solution of saccharose (300g in 1 l. tap water) was again added and an hour later 30g,(26ml,192mmol) of 10. The mixture was stirred for 48 hours and after addition of Celite (120g), filtered The aqueous solution was extracted three times with ether (1.5*l.*), the organic phase dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography in ethylacetate/hexanes to give 11 as a colorless oil (17.21g, 109mmol,34%).

11: $C_8H_{14}O_3$ (158.2): $[\alpha]_D$= +14.24°(c=1.96,$CHCl_3$); Bulb-to-bulb distillation 56°C/10^{-1}mbar; All spectral data were identical to those given in the literature.

The d.s. (>99%) was determined by GC with a 10% Carbowax 20M phase on 80/100 chromosorb W AW (Supelco)(packed column 2m.,200°C), the e.e. (98.5%) by GC of the isopropylurethane derivative on a Chirasil-L-Val (Chrompack) 25m x 0.25mm (145°C)

Preparation of (4R,5S)-cyclopentano[d]oxazolidin-2-one 13:

600 ml 1M-NaOH were added to the hydroxyester 11 (59g,373mmol) and the mixture was stirred vigourously for an hour. After neutralization with 1M-HCl,the solution was extracted 4 times with ether, the combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The crude product 12 (41.4g, 318mmol) was dissolved in 2.5 l CH_2Cl_2 and 33 ml (456mmol) Et_3N, 81 ml (456mmol) diphenylphosphorylazide (DPPA) were added. The mixture was stirred at RT for 24 hours. After evaporation of the solvent *in vacuo*, the crude product was flash chromatographied in ethyl acetate to give 23.69g (50% from hydroxyester) of 13.

13: $C_6H_9NO_2$ (127.14); colorless crystals (CH_2Cl_2/hexanes); m.p.:132.5°C, $[\alpha]_D$=-42.4° (c=0.98,$CHCl_3$), IR (CH_2Cl_2). 3460,3260,1748; ^1H NMR ($CDCl_3$,250 MHz) δ 5.98 (s,1H,NH); 5.06(m,1H,CH-O); 4.28(m,1H,CH-N); 2.18-2.04 (m,1H,CH_2); 1.94-1 05 (m,5H,CH_2); Anal. found: C,56.7; H,7.3; N,11.10; O,25.25; Calc.: C,56.69; H, 7.14, N,11.02; O,25.17.

The e e. (>98%) was determined by GC of 13 on a Chirasil-L-Val (Chrompack) 25m x 0.25mm (145°C,5min; 10°C/min; 190°C).

Preparation of (1S,2R)-2-amino cyclopentan-1-ol 14a:

To compound 13 (4.5g,35.4mmol) was added a solution of KOH (8g,142mmol) in 90 ml MeOH/H_2O:1/1. The mixture was refluxed for 30 hours, saturated with NaCl and extracted 4 times with ether to give 1.9g of crude product (53%) which cristallyzed in ether/hexanes at -18°C to give hygroscopic colorless crystals of 14a. The product was also characterised by the HCl-salt.

14a(HCl): $C_5H_{12}NOCl$ (137.61); m.p.: 228-229°C (decomp.); Anal. found: C,43.7; H,8.9; N,10.2; O,11.5; Cl,25.6; Calc.: C,43.64; H,8.79; N,10.18; O,11.63; Cl,25.76.

14a: $C_5H_{11}NO$ (101.15); $[\alpha]_D$= + 17.8°(c= 1.264, MeOH); IR (CH_2Cl_2): 3400, 2970, 2920, 2890; ^1H NMR($CDCl_3$,300Mhz): δ 3.87 (m,1H,CH-O); 3.21 (m,1H, CH-N); 2.85-1.32 (m+s,9H,CH_2,OH,NH_2).

Preparation of (1S,2R)-2-N-methylamino cyclopentan-1-ol 14b:

To a suspension of $LiAlH_4$ (10g,260mmol) in 300 ml anhydrous THF, was dropped at 10°C a solution of 13 (8g,63mmol) in 180 ml THF. The mixture was refluxed for 4 hours and hydrolysed with freshly prepared saturated aqueous Na_2SO_4 solution. The salts were filtered, washed with ether, the combined solutions were dried and concentrated *in vacuo*. The crude product (9.88g) was bulb-to-bulb distilled (65°C/4 10^{-2}mbar) to give 14b as a colorless oil.

14b: $C_6H_{13}NO$ (115.18): $[\alpha]_D$ = -17.0° (c=0.96,$CHCl_3$); IR (CH_2Cl_2): 3370, 2970, 2910, 1020, ^1H RMN (300MHz,$CDCl_3$): δ 4.00 (m,1H,CH-O); 2.81 (m,1H,CH-N); 2.43 (s,3H,CH_3); 2.23 (s,2H,OH+NH); 1.90-1.31 (m,6H,CH_2); MS: m/z 115(12)(M+.), 86(19),71(25),70(100),58(13),57(26), 56(37), 55(21), 44(68), 43(28), 42(81), 41(31), 40(20), 39(23).

Preparation (1R,2S)-2-hydroxy indan-1- carboxylic acid ethyl ester 16:

Typical procedure: A 40 *l.* reactor was charged with 20 *l.* tap water and 6 kg Baker's Yeast which were added with stirring. The mixture was stirred for an half hour at about 35°C and β-keto ester 15 (31.5g,165mmol) was added. The fermenting suspension was then stirred for 48 hours at 30-35°C (TLC control). The suspension was filtered over Celite, the clarified aqueous solutions were extracted three times with 5 *l.* ethyl acetate and after usual work-ups, the crude product was purified by flash chromatography in ethyl acetate and by recrystallization in ether/hexanes to give 16 as colorless crystals (21.7g,113mmol,68%)

16: $C_{11}H_{12}O_3$ (192.22): m.p.:73.2°C; $[\alpha]_D$= +48.3° (c=1.0,$CHCl_3$); IR (CH_2Cl_2): 3600, 3650, 1745, 1725; ^1H NMR ($CDCl_3$,300MHz): δ 7.40 (m,1H,Ar-H); 7.23 (m,3H,Ar-H); 4.84 (m,1H,CH-OH); 4.12 (d,J=5Hz, 1H,CH-COOMe); 3.80 (s,3H,CH_3); 3.23 (d,J=7.5Hz, 1H,OH); 3.13 (m,2H,CH_2); Anal. found: C,68.82; H,6.39; O,25.03; calc.: C,68.73; H,6.29; O,24.97.

E.e. (99.5%) and d.s. (>99%) were determined by HPLC on Chiracel OB (Daicel): Hexane/i-PrOH: 95/5, 1ml/min., UV 210nm.

Preparation of (1R,2S)-2-hydroxy indan-1-carboxylic acid 17:

The hydroxy ester 16 (2.12g,11mmol) was suspended in 70 ml phosphate puffer (pH=7) and 2 ml of the suspended PLE (22mg, 5060 U) were added . Then the mixture was stirred at RT for 5 hours, the pH was readjusted to 7 with 1M-NaOH and stirred overnight. 0.5 ml of the suspended enzyme was again added and the pH was readjusted. The mixture was stirred for 60 hours and the solution was acidified with 1N-HCl and extracted four times with ether. After drying and evaporation of the solvent *in vacuo*, the crude product was recrystallized in ethyl acetate/n-hexane to give 17 as colorless crystals (1.67g,85%).

17: $C_{10}H_{10}O_3$ (178.19); m.p.: 121.5-122.5°C; $[\alpha]_D$ = +29.3° (c=1.02,EtOH); IR (KBr): 3330, 2970, 2710, 2600, 1705; ^1H NMR (DMSO d_6, 250 MHz): δ 7.35-7.07 (m,4H,Ar-H); 4.70 (m,1H,CH-O); 3.97 (d, J=5Hz, 1H,CH-CO); 3.33 (s,1H,OH); 3.08-2.82 (m,2H,CH_2); Anal. found: C,67.70; H,5.70; O,26.80; Calc.: C,67.41; H,5.66; O,26.94.

Preparation of (1S,2S)-2-hydroxy indan-1-carboxylic acid 18:

To the hydroxy ester 16 (22.3g,116mmol) were added 200ml 1M-NaOH and the mixture was stirred at RT for an hour. After acidification with 1M-HCl, the solution was extracted three times with ether, the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was then recrystallized in ethyl acetate/ pentane to give a first batch of crystals (11.8g,66mmol,57%) which were identified as the pure trans hydroxy acid 18, the second batch (4.38g, 24.6mmol,21.1%) was found to contain a mixture of cis and trans isomers.

18: $C_{10}H_{10}O_3$ (178.19); m.p.: 151.5-152°C; $[\alpha]_D$ = + 61.21° (c=0.89, EtOH); IR (KBr): 3320,2960, 1705; ^1H NMR (DMSO d_6,250 MHz): δ 7.29-7.08 (m,4H,Ar-H); 5.30 (s,1H,OH); 4.65 (m,1H,CH-O); 3.75 (d,J=5Hz,1H,CH-CO); 3.28-2.67 (m,2H,CH_2); Anal. found: C,67.50; H,5.77; Calc.: C,67.41; H,5.66.

Preparation of (4R,5S)-indano[1,2-d]oxazolidin-2-one 20 and (1S,2S)-N-(-2-hydroxy-1-indan)acylazide 19:

To a solution of the cis hydroxy acid 17(0.3g,68mmol) in 15 ml CH_2Cl_2 were added DPPA (0.37ml,1.72mmol) and Et_3N (0.24ml,1.72mmol) and the mixture was stirred for 24 hours at RT. The solution was successively washed with 1N-HCl, saturated $NaHCO_3$ solution and water, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product (0.64g) was purified by flash chromatography in ethyl acetate/hexanes : 1/1 to give first 19 (90mg,24.5%) and 20 (90mg,30.6%).

19: $C_{10}H_{10}N_4O_2$ (218.21); colorless crystals, m.p.: 163-164°C (ethyl acetate/hexanes); $[\alpha]_D$ = + 227° (c=1.44, EtOH); IR (THF): 3410, 3259, 2140, 1715; ^1H NMR (DMSO d_6, 250 MHz): δ 8.43 (d,J=8.5Hz, 1H,NH); 7.28-7.08 (m,4H,Ar-H); 5.40 (d,J=5Hz,1H,OH); 4.85 (m,1H,CH-N); 4.20 (m,1H,CH-O); 3.29-2.60 (m,2H,CH_2); Anal. found: C,55.19; H,4.70; N,25.26; Calc.: C,55.04; H,4.62; N,25.68.

20: $C_{10}H_9NO_2$ (175.19): colorless crystals, m.p.: 204.5-205.5°C (ethyl acetate/hexanes); $[\alpha]_D$= + 76.6° (C=0.65,CH_3COOEt); IR (CH_2Cl_2): 3450, 3250, 1755; ^1H NMR (DMSO d_6, 250 MHz): δ 8.24 (s,1H,NH); 7.20 (s,4H,Ar-H); 5.23 (m,1H,CH-N); 5.05 (d,J=7.5Hz,1H,CH-O); 3.48-2.97 (m,2H,CH_2); Anal. found: C,68.26; H,5.27; N,8.55; O,18.20; Calc.: C,68.56; H,5.18; N,8.00; O,18.27.

Preparation of (1S,2S)-ethyl-N-(-2-hydroxy-1-indan) carbamate 21:

To a solution of the trans hydroxy acid 18 (9.5g, 53.3mmol) in 150 ml ethylalcohol were added DPPA (64mmol, 11.2ml) and Et_3N (64mmol, 4.6ml) and the mixture was refluxed overnight. After work-up and purification as for the previous procedure, compound 19 (0.78g, 3.66mmol,6.7%) and 21 (3.42g, 15.4 mmol, 29%) were obtained.

21. $C_{12}H_{15}NO_3$ (221.16), colorless crystals, m.p : 121-122°C (ethyl acetate/hexanes); $[\alpha]_D$= + 121.3° (c= 0.48,EtOH); IR (CH_2Cl_2). 3590, 3440, 1705; ^1H NMR ($CDCl_3$, 250 MHz)· δ 7.33-7.12 (m,4H,Ar-H); 5.18 (s,1H,NH); 4.9 (t,J=6.5Hz,1H,CH-N); 4.42 (m,1H,CH-O); 4.18 (qa,J=7.5Hz,2H,CH_2); 4.12 (s,1H,OH); 3.39-2.82 (m,2H,CH_2); 1.30 (t,J=6.5Hz,3H,CH_3); Anal. found: C,65.12; H,6.82; N,6.49; O,21.79; Calc.: C,65.14, H,6 83; N,6.33; O,21.69.

Preparation of (4S,5R)-indano[1,2.d]oxazolidin-2-one 22:

Ethylcarbamate 21 (1.21g, 5.46 mmol) was dissolved in 10 ml $SOCl_2$ and the solution was stirred overnight at RT. The excess of thionyl chloride was evaporated *in vacuo* and the crude product was recrystallized in ethyl acetate to give 0.77g (4.4mmol,80.6%) of colorless crytals.

22: $C_{10}H_9NO_2$ (175.19); m.p.: 206-207°C; $[\alpha]_D$= -78.7°C (c=0.56, CH_3COOEt); IR and ^1H NMR spectra were identical to those of compound 20; Anal. found: C,67.92; H,5.31; N,7.97; O,18.58; Calc.: C,68.56; H,5.18; N,8.00; 18.27.

Preparation of (1S,2R) and (1R,2S)-1-amino indan-2-ols 23 and 24:

To a solution of 22 (0.85g,4.85mmol) in 20 ml EtOH was added a solution of 1.09g KOH (4 eq.) in 20 ml H_2O. The mixture was refluxed for 24 hours. Ethanol was evaporated *in vacuo* and the aqueous phase was three times extracted with ether an after usually work-ups, the crude product was recrystallyzed in CH_2Cl_2/n-hexane to give 23 (0.6g, 4mmol,82.5%) as colorless crystals. The same procedure was used for 20 (160mg, 0.91mmol in 5 ml EtOH, 0.2g KOH in 5 ml H_2O) to afford 24 (108mg, 79%).

23: $C_9H_{11}NO$ (149.19); m.p. 116-117°C; $[\alpha]_D$= - 61.5° (c= 0.478,$CHCl_3$), IR (CH_2Cl_2): 3600, 3410, 3340; ^1H NMR ($CDCl_3$,250MHz): δ 7.42-7.13 (m,4H,Ar-H); 4.38 (s,2H,CH); 3.20-2.86 (m,2H,CH_2); 2.20(s,3H,OH,NH_2); Anal. found: C,71.82; H,7.54; N,9.38; O,10.92; Calc.: C,72.46; H,7.43; N,9.39; O,10.72.

24: m.p.: 115-116°; $[\alpha]_D$= + 65.12°C (c= 0.238, $CHCl_3$); Anal. found: C,72.06, H,7.47; N,9.45; O,10.92; Calc.: C,72.46; H,7.43; N,9.39; O,10.72.

Reduction of acetophenone:

Typical procedure: 2.5mmol of ligand were dissolved under argon in THF (2.5ml, freshly distilled a over sodium). Then the desired quantity of 1M-borane solution in THF was added dropwise at 0-5°C and the mixture was stirred overnight at the same temperature under light overpressure of argon. Freshly distilled acetophenon a (2mmol, 0.23 ml) was added dropwise to the solution at 0-5°C and the mixture was then stirred at room temperature for two hours. After hydrolysis with 2M-HCl and evaporation of THF *in vacuo* , the aqueous layer was extracted twive with ether, the organic layer dried over $MgSO_4$ and evaporated *in vacuo* to give an oil which was analysed in GC (Carbowax, 20M, 10%, 2m., 200°C) and in HPLC (Chiralcel OB (Daicel), hexane/isopropanol: 90/10, 1ml/min., UV 215 nm).

Reduction of anti-acetophenone oxime methyl ether:

Typical procedure: 2.5 mmol of the ligand were dissolved under argon in THF (2.5ml,freshly distilled over sodium). Then the desired quantity of 1M-borane solution in THF was added dropwise at 0-5°C and the mixture was stirred for 6-7 hours at the same temperature under light overpressure of argon. A solution of oxime ether (2mmol, 0.3g) in 1.5 ml abs. THF was added dropwise at 0-5°C and the mixture was stirred at RT. After hydrolysis (2M-HCl) and evaporation of THF, the aqueous solution was extracted with ether, basified with ammonium hydroxyde and extracted twice with ether. The organic layer was dried and concentrated *in vacuo*. The 3,5-dinitrobenzamide was prepared from this crude product for HPLC analysis (Pirkle covalent D-Naphtylalanine (Regis), hexane/isopropanol: 80/20, 1ml/min., UV 240 nm). For GC analysis (OV 101, 3%, 4m.,130°C), an aliquot of the reaction mixture was hydrolysed with 2M-HCl, basified with NH_4OH, extracted with ether and injected.

X-Ray structure of the derivatives 4 and 25.

Preparation of (1S,4R)-camphanic acid-[(R)-(+)-3-acetoxy-2- phenyl propan-1 -ol] ester 4:

A solution of monoacetate 3b (174mg, 0.9mmol) and (-)-camphanic acid chloride (0.28g, 1.3mmol) in 5 ml pyridine was stirred at RT overnight. 16 ml of CCl_4 were added to the mixture and the solution was filtered and evaporated *in vacuo*. The product was dissolved in 50 ml ether, the solution successively washed with 1N-HCl, water and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was recrystallized from ether/n-hexane to give a first batch of colorless crystals (90mg,26%).

4: $C_{21}H_{26}O_6$ (374.43); m.p.: 66.6-67°C; $[\alpha]_{365}$= -10.33° (c=0.96,$CHCl_3$); IR (CH_2CL_2): 1787, 1740; ^1H NMR (250MHz,$CDCl_3$): δ 7.49-7.20 (m,5H, Ar-H); 4.51 (m,2H, CH_2-O); 4.32 (m,2H,CH_2-O); 3.41 (qi,J=6Hz, 1H,CH); 2.38 (m,1H,CH_2); 2.05 (s,3H,$COCH_3$); 1.90 (m,2H,CH_2); 1.65 (m,1H,CH_2); 1.08 (s,3H,CH_3); 0.86 (s,3H,CH_3); 0.78 (s,3H,CH_3). Anal. found: C,67.0; H,6.93 Calc.: C,67.36; H,7.0.; HPLC: Spherisorb Si 80,10μ, Hex/i-PrOH:95/5, 1ml/min., UV 210 nm, d.e. = 97.5%.

Preparation of (1S,4R)-camphanic acid-[(1R,2S)-2-hydroxy indan-1-carboxylic acid ethyl ester] ester 25:

To a solution of hydroxy ester 16 (384mg,2mmol) and (-)-camphanic acid chloride (433mg,2mmol) in 40 ml methylene chloride was dropped a solution of 4-dimethylaminopyridine (245mg,2mmol) in 8 ml CH_2Cl_2. The mixture was refluxed for 3 hours and the organic layer was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography in ether/hexanes: 1/1 to afford 280mg (37%) of 25. Colorless crystals were obtained by recrystallization in ethyl acetate/ n-hexane.

25: $C_{21}H_{24}O_6$ (372.42); m.p.: 105.5°C; $[\alpha]_D$ = + 13.57° (c = 1.08, $CHCl_3$); IR (CH_2Cl_2): 1790, 1745; ^1H NMR ($CDCl_3$,250 MHz): δ 7.39 (m,1H,Ar-H); 7.25 (m,3H,Ar-H); 5.85 (m,1H,CH-O); 4.36 (d,J=7Hz,1H,CH-CO); 3.75 (s,3H,CH_3CO); 3.29 (m,2H,CH_2); 2.32 (m,1H,CH_2); 2.08-1.79 (m,2H,CH_2); 1.65 (m,1H,CH_2); 1.10 (s,3H,CH_3); 1.00 (s,3H,CH_3); 0.93 (s,3H,CH_3); Anal. found: C,67.83; H,6.61; Calc.: C,67.73; H,6.50.

Table 3: Crystal Data of the structure 4 and 25[a].

Compound	4	25
Formula	$C_{21}H_{26}O_6$	$C_{21}H_{24}O_6$
Crystal system	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$
a, A°	6.615(1)	6.338(1)
b, A°	10.016(1)	10.383(1)
c, A°	30.127(2)	29.115(2)
V, $A^{\circ 3}$	1996	1916
Z	4	4
Calc. density g cm^{-3}	1.246	1.291
No. of reflections	2415	3269
No. of nonzero reflections	2252	2058
No. of parameters	348	340
Final R factor	0.058	0.051

a) The structure were solved with direct methods (SDP Multan 82)[14,15] *and refined by full-matrix least-squares techniques*[16].

b) Nonius CAD4 diffractometer was used (Cu K_α 1.54178 A°).

c) Philips PW 1100 diffractometer was used (Mo K_α 0.70926 A°).

Table 4: Bond distances (A°) in 4 with esd's in parentheses.

O1	C7	1.203(6)	C11	C12	1.547(6)
O2	C7	1.365(6)	C11	C16	1.485(6)
O2	C11	1.468(5)	C12	C13	1.546(6)
O3	C16	1.194(6)	C12	C14	1.541(6)
O4	C16	1.345(5)	C17	C18	1.520(7)
O4	C17	1.459(5)	C18	C19	1.528(7)
O5	C25	1.439(7)	C18	C25	1.529(7)
O5	C26	1.349(7)	C19	C20	1.378(8)
O6	C26	1.21(1)	C19	C24	1.409(8)
C7	C8	1.520(7)	C20	C21	1.403(9)
C8	C9	1.582(6)	C21	C22	1.39(1)
C8	C12	1.555(6)	C22	C23	1.37(1)
C8	C15	1.511(7)	C23	C24	1.420(8)
C9	C10	1.580(7)	C26	C27	1.54(1)
C10	C11	1.555(6)			

Table 5: Bond distances (A°) in 25 with esd's in parentheses.

O1	C7	1.192(9)	C11	C12	1.560(9)
O2	C7	1.386(9)	C11	C16	1.501(9)
O2	C11	1.464(8)	C12	C13	1.55(1)
O3	C16	1.188(9)	C12	C14	1.53(1)
O4	C16	1.340(9)	C17	C18	1.562(9)
O4	C17	1.455(8)	C17	C25	1.55(1)
O5	C26	1.197(9)	C18	C19	1.525(9)
O6	C26	1.334(9)	C18	C26	1.508(9)
O6	C27	1.46(1)	C19	C20	1.407(9)
C7	C8	1.496(9)	C19	C24	1.41(1)
C8	C9	1.568(9)	C20	C21	1.40(1)
C8	C12	1.565(9)	C21	C22	1.39(1)
C8	C15	1.52(1)	C22	C23	1.41(1)
C9	C10	1.57(1)	C23	C24	1.39(1)
C10	C11	1.550(9)	C24	C25	1.52(1)

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16) The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.