Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 18 (2007) 1926–1933

Synthesis of new calix[4]arene based chiral ligands bearing β-amino alcohol groups and their application in asymmetric transfer hydrogenation

Adrien Quintard, Ulrich Darbost, Francis Vocanson,* Stéphane Pellet-Rostaing* and Marc Lemaire

ICBMS, Institut de Chimie et Biochimie Moléculaire et Supramoléculaire, UMR-CNRS 5246, Université de Lyon, Université Claude Bernard Lyon 1, CPE Lyon, 43 Bd du 11 Novembre 1918, 69622 Villeurbanne Cedex, France

Received 6 July 2007; accepted 20 July 2007
Available online 4 September 2007

Abstract—A new series of chiral calix[4]arenes bearing β-amino alcohol groups have been synthesised. The crucial steps consist of the binding of glycidyl groups on the lower rim of the calix[4]arenas, followed by their regioselective opening with amines. These ligands were successfully tested in an asymmetric transfer hydrogenation. The best results (conversion max = 97% and ee max = 87%) were obtained using calix[4]arene mono-functionalised ligands. These results are the best ones obtained using calixarene based ligands in asymmetric catalysis.

1. Introduction

Obtaining enantiomerically pure species is one of the greatest challenges in fine and medicinal chemistry. In this respect, enantioselective catalysis, a method of choice often used in the industry, fulfils this purpose.

Among the numerous asymmetric reactions developed by chemists, the asymmetric transfer hydrogenation of prochiral ketones has received a lot of interest over the last decade since it occurs under mild and environmentally friendly conditions, essential in modern synthesis.[1] Research efforts over the last decade have led to the discovery of several efficient systems in terms of either activity or selectivity. Among the Ir, Rh or Ru complexes, the latter are the most common ones. The best results are obtained when Ru(II) is associated with monotosylated diamines[2] or β-amino alcohol ligands.[3] Noyori showed that the amino alcohols cause a significant acceleration effect on the reduction.[4] Among these amino alcohols, our group has described the use of amino alcohol trityl-ether ligands, which gave good results in terms of enantioselectivities (ee = 88%) and conversions (97%) on the reduction of acetophenone,[5] and better than the Pericas et al. ether amino alcohol type ligand.[6]

Calixarenes are pre-organised molecules useful in ion and metal complexation because of their orientation power depending on their conformation and their relatively easy functionalisation.[7] These metal complexation and orientation properties have been translated to metal-catalysis by many groups, in particular Matt et al. with surprisingly good results in hydroformylation[8] and C–C bond forming reactions.[9]

Although these are good results, the use of calix[4]arenes as a platform for chiral ligands in asymmetric catalysis has been less studied and only a few applications have been described without giving significant results. In the first, Matt made use of chiral diphosphine calix[4]arenes in allylic alkylation with 67% ee and hydrogenation with 48% ee. Despite these poor transfers of chirality, he obtained excellent results in terms of conversion (100%).[10] More recently, Neri reported the synthesis of amino-acid calix[4]arene-like ligands applied to an aldol reaction with limited enantioselectivities (ee max = 28%),[11] while Tomaselli et al. used a salen calixarene ligand in an asymmetric epoxidation obtaining up to 72% ee.[12]

* Corresponding authors. Tel.: +33 04 72 43 14 07; fax: +33 04 72 43 14 08; e-mail: pellet@univ-lyon1.fr

0957-4166/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2007.07.018

Herein, we report the synthesis of new chiral calix[4]arene ligands bearing β-amino alcohol groups and their use in the metal-catalyzed transfer hydrogenation of ketones, which was compared to the reference β-amino alcohol ligand **7** already published by our group.[5] The role of a number of amino-alcohols and the symmetry of the ligand have been well established.

2. Results and discussion

2.1. Ligands synthesis

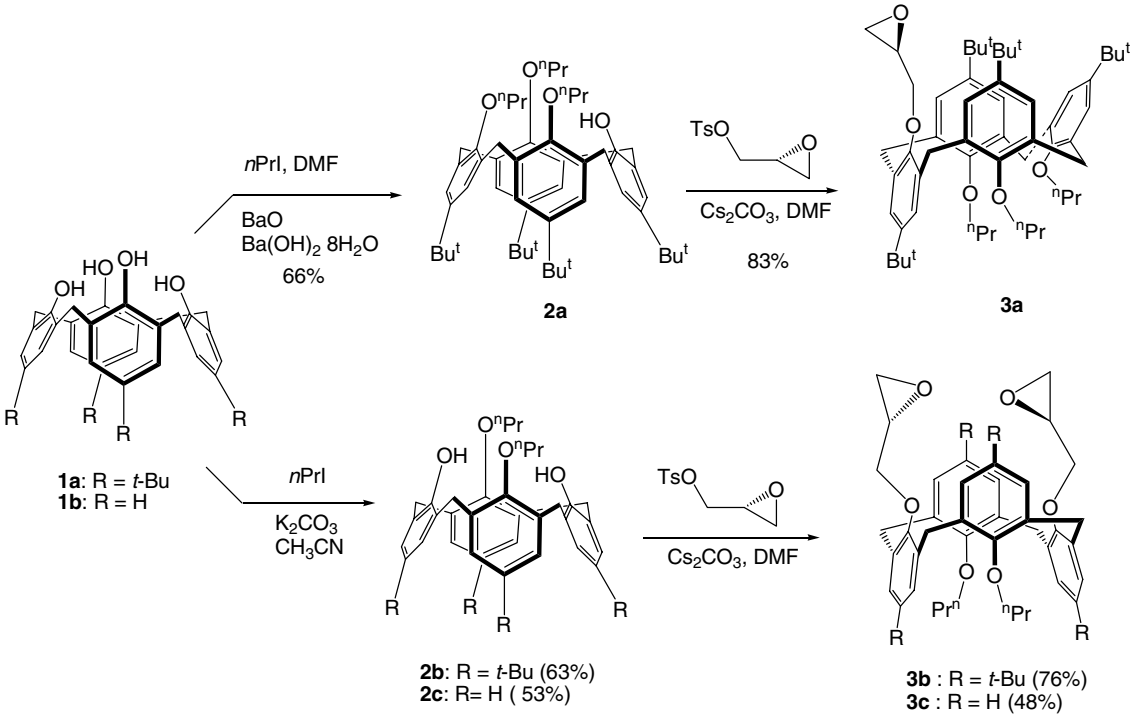
As the starting point of our work, we decided to protect a determined number of phenolic groups, in order to not let them disturb the metal coordination during the catalysis. When using an *n*-propyl as the protecting group with a *tert*-butyl group at the upper rim, the system was seen to rigidify. However with H at the upper rim, it was seen to induce flexibility. The di-functionalisation of the lower rim was supposed to give C_2 symmetric ligands, which are famous for their strong activity in catalysis.

The methodology used for the second step was previously described by Neri and Takata during the tetra-functionalisation of calix[4]arenes with glycidyl groups.[13] Reactions of (*R*)-glycidyl tosylate in the presence of Cs_2CO_3 in DMF easily gave the products **3a**–**c** in good yields (48–83%) (Scheme 1). Attempts to add glycidyl groups in the presence of K_2CO_3 or NaH with the use of (*R*)-epichlorhydrin or (*R*)-glycidyl tosylate failed. As previously described,[13] the regioselective attack on the tosylate-bearing carbon was confirmed by the absence of diastereoisomeric peaks in ^{1}H NMR for the compounds bearing two glycidyl groups. This indicated that the stereochemistry of the starting material was recovered in the calix[4]arenes. The same result was postulated on the calix[4]arene bearing only one glycidyl function.

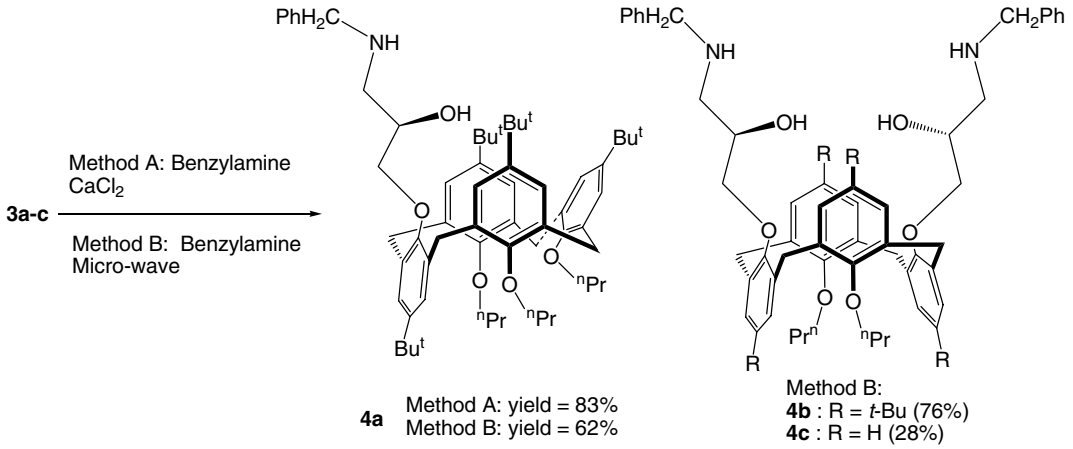
The conformations of all compounds were established by ^{1}H and ^{13}C NMR spectra and compared to the literature.[14] In the ^{1}H NMR spectrum of **3a** the presence of two doublets (3.03 and 4.08 ppm, $J = 12$ Hz) and a singlet around 3.5 ppm for $ArCH_2Ar$ groups indicated a partial cone conformation. Furthermore, the three $ArCH_2Ar$ signals observed at 30.9, 37.6 and 37.9 ppm in the ^{13}C NMR spectrum confirmed this assignment. The partial cone conformation of **3a** with the glycidyl group was firmly established by NOESY experiment.

In the ^{13}C NMR spectrum of compounds **3b** and **3c** the presence of two $ArCH_2Ar$ signals around 38 ppm indicates an 1,3 alternate structure. Corroborating these observations, the ^{1}H NMR spectrum displayed a singlet for two $ArCH_2Ar$ and an AB system for the two others. The simplified NMR spectrum of those two compounds agrees with a C_2 symmetrical structure.

The regioselective opening of glycidyl by amines has already been described in the literature using numerous methodologies.[15] Surprisingly, the reactivity of the compounds was weak and the opening by benzylamine failed, using classical methods such as reaction in DMF or $CHCl_3$ in the presence of $CaCl_2$ as Lewis acid. These results prompted us to realise the reaction using pure benzylamine as solvent in the presence of $CaCl_2$. This methodology gave compound **4a** after 11 h; this compound was easily purified by simple precipitation in MeOH in 81% yield.



Scheme 1.



Scheme 2.

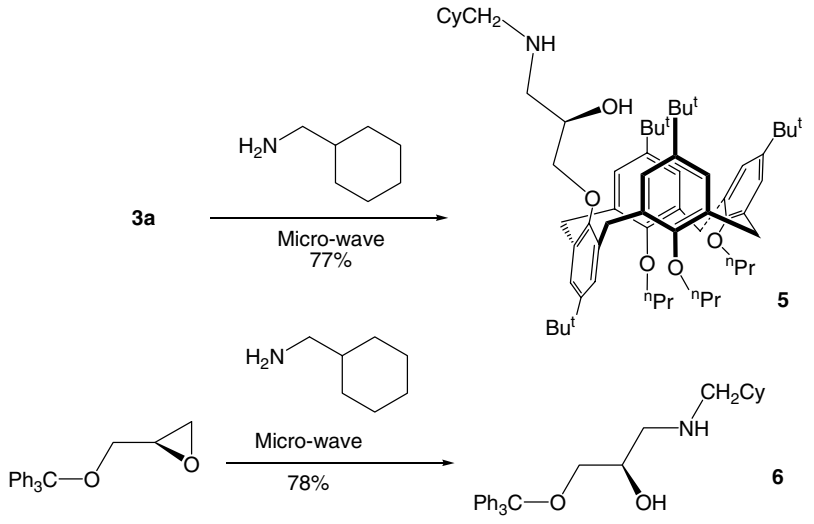
Attempts to apply this methodology to the synthesis of compounds **4b** and **4c** failed since the reaction gave a mixture of inseparable products. Fortunately, the use of an alternative microwave procedure on those compounds gave a notable acceleration of the reaction without a Lewis acid as previously described by Zhao.[16] Moreover, the number of side products was diminished which allowed an easy purification by simple precipitation or recrystallisation. Compounds **4a**–**c** were obtained using this method in 28–76% yield in 1.5 h at 200 W and 150 °C (Scheme 2). The specific opening at the least hindered position of the epoxide was firmly proven by the presence in all the ^{13}C spectra of the CH(OH) signal around 67 ppm and the two CH_2NH_2 signals around 54 and 51 ppm. The ^{1}H and ^{13}C NMR indicated that the conformation of the final compounds was unchanged. Indeed, the $ArCH_2Ar$ signals retained the same characteristics after the reaction.

In order to study the influence of the amino group on the catalysis, compounds **5** and **6** were synthesised using the same microwave methodology (Scheme 3). Good yields (77% and 78%) were obtained after 1 h of reaction and simple purification by recrystalisation or precipitation. As with compound **4a**, compound **5** was in a partial cone conformation.

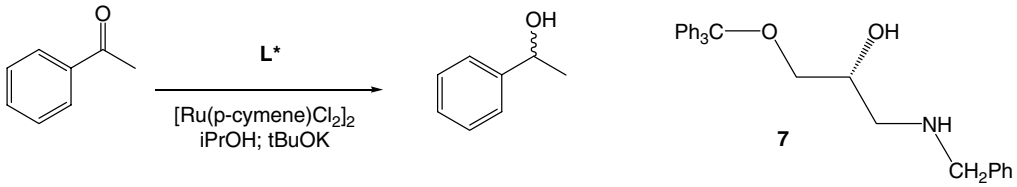
2.2. Application of ligands to asymmetric transfer hydrogenation

The catalytic activity of the new ligands was studied under standard conditions on the transfer hydrogenation of acetophenone (Scheme 4). A ruthenium(II) complex was prepared in situ by heating the $[Ru(p\text{-cymene})Cl_2]_2$ precursor at 80 °C with the ligand in 2-propanol for 30 min. Initial studies were performed using an S/C = 100 ratio at room temperature. The results are summarised in Table 1.

The reduction of acetophenone is not quantitative using the different ligands. The loss of enantiomeric excess after prolonged reaction times is due to the formation of the thermodynamic products. The best results in terms of conversion (97%) were obtained using ligand **4a**. The good conversion (97%) and enantioselectivity (87%) (entry 1) can be compared to those obtained using reference ligand



Scheme 3.



Scheme 4.

Table 1. Asymmetric transfer hydrogenation of acetophenone

Entry[a]	Ligand	L*/Ru	S/C	Time (h)	Conversion[b] (%)	ee (%) enantiomer (*S*)[b]
1	**4a**	2	100	1(3)	75(97)	87(86)
2	**4a**	1	100	1(3)	47(67)	87(87)
3	**4b**	1	100	1(3)	12(18)	84(83)
4	**4c**	1	100	1(3)	14(16)	87(78)
5	**4c**	1	100	22(6 days)	55(71)	74(69)
6	**5**	2	100	1(24)	39(60)	90(88)
7	**5**	2	100	48	71	88
8	**6**	2	100	1(24)	42(47)	89(87)
9	**7**[5]	2	100	1(15)	71(95)	88(87)

[a] Reaction conditions: acetophenone (0.5 mmol); [Ru(*p*-cymene)Cl_2]$_2$ (0.005 mmol); and *t*-BuOK (0.6 mmol) in 6 ml 2-propanol at room temperature.
[b] Conversion and ee were determined by chiral GC analysis.

7 (entry 9). Using an L*/Ru ratio of 1 (entry 2) caused a small decrease in conversion. This was surprising since the [Ru(*p*-cymene)Cl_2]$_2$ is known to bind to two amino-alcohols. A hypothesis to explain this result can be that the active species is an RuL_2^* complex while the remaining Ru is deactivated by another species such as the excess base.

The disappointing low conversions (18%) while keeping good ee values (around 85%) obtained using C_2 symmetry ligands **4b** and **4c** (entries 3 and 4) might be due to a strong steric hindrance of the complex. This results in a difficulty of the acetophenone to gain access to the metal. The better conversion obtained after prolonged reaction time with ligand **4c** (entry 5) corroborates this hypothesis since the absence of *tert*-butyl group in this ligand results in a decrease of the steric hindrance.

As expected, ligands **5** and **6** (entries 6 and 8) caused a small increase in the enantiomeric excess (ee max = 90%). Unfortunately, this gain in enantiomeric excess goes with a loss in terms of conversion. The activity after a prolonged reaction time of the calixarene ligand **5** (entry 7) versus trityl ether ligand **6** can be due the better resistance of the associated Ru–**5** complex to deactivation.

3. Conclusion

To conclude, we have developed an efficient and easy synthesis of new calix[4]arene β-amino alcohol ligands. This synthesis was conducted through the binding of glycidyl groups followed by the regioselective opening by two different amines. The yields obtained were acceptable to good, depending on the type of the calix[4]arenes.

These ligands were studied on the asymmetric transfer hydrogenation of acetophenone to give good enantioselectivities (ee max = 90%) and very good conversions (conversion max = 97%) using mono-branched ligands **4a** and **5**. Results were rather disappointing with ligands **4b** and **4c** containing C_2 symmetry.

The results obtained are actually the best obtained by using calixarene based ligands in asymmetric catalysis. This shows that those supramolecules can be efficiently used in asymmetric synthesis. To increase the activity of our ligands, works are currently under study in our laboratory by diversifying the amine at the last step and modifying the alkyl groups on the calixarenes.

4. Experimental

All the organic and organometallic reagents used were pure commercial products. Acetonitrile was distilled over CaH_2 under nitrogen. ^1H and ^{13}C NMR spectra were recorded with a Bruker-ALS-300 (300 MHz for ^1H and 75 MHz for ^{13}C) in $CDCl_3$ or DMSO as solvent. The following symbols are used to describe the spectrums: s: singlet, d: doublet, t: triplet, q: quadruplet, m: multiplet, *J*: coupling constant in hertz. Trimethylsilane was used as the internal standard in $CDCl_3$: 7.26 ppm in ^1H NMR, 77.0 ppm in ^{13}C NMR. DMSO: 2.50 ppm in ^1H NMR. Mass spectra were recorded in electrospray mode on a thermo LCQ avantage at the centre commun de spéctrométrie de masse (University Claude Bernard Lyon1). Polarimetric measurements were performed on a Perkin–Elmer 241 apparatus at ambient temperature. Melting points were performed on electrothermal 9100 apparatus. IR spectra were performed on a Perkin–Elmer spectrum-one FT-IR spectrometer.

4.1. Compound 2a

p-tert-Butyl-calix[4]arene (1.0 g, 1.5 mmol), 1.6 g (10.5 mmol) of BaO and 1.7 g (5.39 mmol) of $Ba(OH)_2$·

8H_2O were dissolved under nitrogen in 20 ml of DMF for 30 min. Then 4.5 ml (46 mmol) of *n*-PrI was added and the mixture was stirred under nitrogen for 1 h. Then 60 ml of H_2O was added and the mixture was stirred for ten more minutes. The aqueous layer was extracted by 3×30 ml CH_2Cl_2. The organic layer was then washed by 30 ml of brine and by 2×20 ml H_2O (pH 9), dried over Na_2SO_4, filtrated and evaporated. The obtained solid was dissolved in 20 ml of ethyl acetate and filtrated. The filtrate was evaporated to give crude product that was purified by re-crystallisation in CH_2Cl_2/MeOH to give 0.76 g (0.98 mmol) of **2a**[14b] as white crystals. Yield = 66%. TLC: eluant: CH_2Cl_2/*n*-heptane: 1/1. Visualisation: UV + iodine. $R_f = 0.65$. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.13 (s, 2H, *H*–Ar); 7.04 (s, 2H, *H*–Ar); 6.51 (s, 4H, *H*–Ar); 5.58 (s, 1H, O*H*); 4.35 (t, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar); 3.84 (t, 2H, $J = 8.4$ Hz, O–CH_2–CH_2–CH_3); 3.75 (t, 4H, $J = 6.7$ Hz, 2O–CH_2–CH_2–CH_3); 3.21 (d, 2H, $J = 13.1$ Hz, Ar–CH_2–Ar); 3.15 (d, 2H, $J = 12.6$ Hz, Ar–CH_2–Ar); 2.30–2.38 (m, 2H, O–CH_2–CH_2–CH_3); 1.84–2.02 (m, 4H, 2O–CH_2–CH_2–CH_3); 1.10 (t, 6H, $J = 7.3$ Hz, 2O–CH_2–CH_2–CH_3); 1.33 (s, 18H, *t*-Bu); 0.95 (t, 3H, $J = 7.5$ Hz, O–CH_2–CH_2–CH_3); 0.82 (s, 18H, *t*-Bu).

4.2. Compound 2b

p-tert-Butyl-calix[4]arene (1.0 g, 1.5 mmol) and 1.3 g (9.4 mmol) of K_2CO_3 were stirred under nitrogen in 50 ml of anhydrous CH_3CN for 30 min. 1-Iodopropan (0.6 ml, 6.1 mmol) was added to the obtained suspension. The mixture was then refluxed under nitrogen for 24 h and then stopped. The solvent was evaporated, and the residue dissolved in 60 ml of CH_2Cl_2 and 40 ml of H_2O. After separation, the organic layer was washed by a 20 ml solution of HCl (1 M), then by 3×30 ml H_2O. The organic layer was then dried over Na_2SO_4, filtrated and evaporated. The crude product was purified by re-crystallisation (CH_2Cl_2/MeOH) to give 0.69 g (0.95 mmol) of **2b**[14b] as white crystals. Yield = 63%. TLC: eluant: CH_2Cl_2/*n*-heptane: 1/1. Visualisation: UV + iodine. $R_f = 0.52$. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.89 (s, 2H, O*H*); 7.03 (s, 4H, *H*–Ar); 6.85 (s, 4H, *H*–Ar); 4.30 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar); 3.94 (t, 4H, $J = 6.4$ Hz, 2O–CH_2–CH_2–CH_3); 3.30 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar); 2.00–2.06 (m, 4H, 2O–CH_2–CH_2–CH_3); 1.28 (s + t, 24H, 2O–CH_2–CH_2–CH_3 + *t*-Bu); 1.01 (s, 18H, *t*-Bu).

4.3. Compound 2c

Calix[4]arene (1 g, 2.3 mmol) and 1.3 g (9.4 mmol) of K_2CO_3 were stirred under nitrogen in 50 ml of anhydrous CH_3CN for 30 min. 1-Iodopropane (0.9 ml, 9.4 mmol) was added to the obtained suspension. The mixture was then refluxed under nitrogen for 18 h and then stopped. The solvent was evaporated, and the residue dissolved in 45 ml of CH_2Cl_2. The aqueous layer was then extracted by 2×40 ml CH_2Cl_2. The resulting organic extract was washed by 2×45 ml H_2O, dried over Na_2SO_4, filtrated and then evaporated. The crude product was purified by re-crystallisation (CH_2Cl_2/MeOH) to give 0.620 g (1.2 mmol) of **2c**[17] as white crystals. Yield = 52%. TLC: eluant: CH_2Cl_2/*n*-heptane: 1/1. Visualisation: UV + iodine. $R_f = 0.48$. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 8.32 (s, 2H, O*H*); 7.05 (d, 4H, $J = 7.5$ Hz, *H*–Ar); 6.,92 (d, 4H, $J = 7.7$ Hz, *H*–Ar); 6.75 (t, 2H, $J = 7.5$ Hz, *H*–Ar); 6.64 (t, 2H, $J = 7.5$ Hz, *H*–Ar); 4.32 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar); 3.98 (t, 4H, $J = 6.2$ Hz, 2O–CH_2–CH_2–CH_3); 3.38 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar); 2.04–2.11 (m, 4H, 2O–CH_2–CH_2–CH_3); 1.32 (t, 6H, $J = 7.3$ Hz, 2O–CH_2–CH_2–CH_3).

4.4. Compound (*R*)-3a

Compound **2a** (0.40 g, 0.5 mmol) and 0.843 g (2.60 mmol) of Cs_2CO_3 were dissolved under nitrogen in 7 ml of DMF for 30 min. Then 0.18 g (0.77 mmol) of (*R*)-glycidyl-tosylate was added and the mixture stirred at 80 °C under nitrogen for 8 h and then stopped. Twenty millilitres of H_2O was added and the aqueous layer extracted by 3×20 ml CH_2Cl_2. The resulting organic layer was then washed by 4×30 ml of H_2O, dried over Na_2SO_4, filtrated and evaporated. The pure product **3a** (0.353 g, 0.425 mmol) was obtained as a white powder by re-crystallisation (CH_2Cl_2/MeOH). Yield = 83%. TLC: eluant: CH_2Cl_2/*n*-heptane: 1/1. Visualisation: UV. $R_f = 0.72$. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.20 (d, 2H, $J = 6$ Hz, *H*–Ar); 7.09 (s, 2H, *H*–Ar); 7.01 (d, 1H, $J = 2.4$ Hz, *H*–Ar); 6.90 (d, 1H, $J = 2.7$ Hz, *H*–Ar); 6.58 (s, 2H, *H*–Ar); 4.08 (d, 2H, $J = 12.0$ Hz, Ar–CH_2–Ar); 3.99 (dd, 1H, $J = 11.5$, 3.0 Hz, O–CH_2–CHO); 3.37–3.78 (m, 11H, 3O–CH_2–CH_2–CH_3; 1O–CH_2–CHO and 2Ar–CH_2–Ar); 3.20 (m, 1H, O–CH_2–C*H*O–CH_2); 3.03 (d, 2H, $J = 12.6$ Hz, Ar–CH_2–Ar); 2.85 (t, 1H, $J = 4.8$ Hz, CH_2–CHO–CH_2–O); 2.52 (dd, 1H, $J = 5.1$, 2.7 Hz, CH_2–CHO–CH_2–O); 1.88–1.80 (m, 4H, 2O–CH_2–CH_2–CH_3); 1.48–1.56 (m, 2H, O–CH_2–CH_2–CH_3); 1.39 (s, 9H, *t*-Bu); 1.34 (s, 9H, *t*-Bu); 1.04 (s, 18H, *t*-Bu); 1.00 (t, 6H, $J = 7.5$ Hz, 2O–CH_2–CH_2–CH_3); 0.70 (t, 3H, $J = 7.3$ Hz, O–CH_2–CH_2–CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): 153.8 (Ar*C*–O–CH_2); 153.6 (Ar*C*–O–CH_2); 144.9 (Ar*C*–*t*-Bu); 143.5 (Ar*C*–*t*-Bu); 135.9 (Ar*C*–CH_2); 133.2 (Ar*C*–CH_2); 132.4 (Ar*C*–CH_2); 131.8 (Ar*C*–CH_2); 127.8 (Ar*C*H); 125.6 (Ar*C*H); 125.3 (Ar*C*H); 76.2 (ArO*C*H$_2$–CH_2); 75.4 (Ar-O*C*H$_2$–CH_2); 73.6 (O–*C*H_2–CHO); 50.77 (O–CH_2–*C*HO–CH_2); 45.1 (*C*H_2–CHO–CH_2–O); 37.9 (Ar–*C*H_2–Ar); 37.6 (Ar–*C*H_2–Ar); 34.1 (Ar–*C*$(CH_3)_3$); 33.68 (Ar–*C*$(CH_3)_3$); 31.7 (*C*H_3); 30.9 (Ar–*C*H_2–Ar); 23.7 (O–CH_2–*C*H_2–CH_3); 21.6 (O–CH_2–*C*H_2–CH_3); 10.7 (O–CH_2–CH_2–*C*H_3); 9.4 (O–CH_2–CH_2–*C*H_3). ES-MS $m/z = 831.3$ $[M+H]^+$. IR (solid): $\nu = 2958$, 2873, 1474, 1196, 1120, 1044, 1012, 869. $[\alpha]_D^{20} = -2.2$ (*c* 1.135, $CHCl_3$), mp = 279–283 °C.

4.5. Compound (*R*,*R*)-3b

Compound **2b** (0.497 g, 0.68 mmol) and 1.78 g (5.43 mmol) of Cs_2CO_3 were dissolved under nitrogen in 8 ml of DMF for 30 min. Then 0.464 g (2.04 mmol) of (*R*)-glycidyl-tosylate was added and the mixture stirred at 80 °C under nitrogen for 13.5 h and then stopped. Then 20 ml of H_2O was added and the aqueous layer extracted by 3×25 ml CH_2Cl_2. The resulting organic layer was then washed by 2×30 ml of H_2O, dried over Na_2SO_4, filtrated and evaporated. The pure product **3b** (0.436 g, 0.515 mmol) was obtained as a white powder by re-crystallisation (CH_2Cl_2/

MeOH). Yield = 76%. TLC: eluant: CH_2Cl_2/*n*-heptane: 8/2. Visualisation: UV, $R_f = 0.54$, ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.11 (d, 2H, $J = 2.4$ Hz, *H*–Ar); 7.01 (d, 2H, $J = 2.7$ Hz, *H*–Ar); 6.98 (s, 4H, *H*–Ar); 3.87–3.71 (s + AB, 8H, 4Ar–C*H*$_2$–Ar); 3.54 (dd, 2H, $J = 11.2$, 3.3 Hz, O–C*H*$_2$–CHO); 3.38 (t, 4H, $J = 7.5$ Hz, 2O–C*H*$_2$–CH$_2$–CH$_3$); 3.23 (dd, 2H, $J = 11.3$, 5.2 Hz, O–C*H*$_2$–CHO); 2.79 (m, 2H, 2O–CH$_2$–C*H*O–CH$_2$); 2.57 (t, 2H, $J = 5.1$ Hz, C*H*$_2$–CHO–CH$_2$–O); 2.30 (dd, 2H, $J = 5.4$, 2.7 Hz, C*H*$_2$–CHO–CH$_2$–O); 1.38–1.15 (m, 43H, 2O–CH$_2$–C*H*$_2$–CH$_3$, 4*t*-Bu and 1O–CH$_2$–CH$_2$–C*H*$_3$); 0.73 (t, 3H, $J = 7.8$ Hz, O–CH$_2$–CH$_2$–C*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): 154.7 (Ar*C*–O–CH$_2$); 154.0 (Ar*C*–O–CH$_2$); 143.9 (Ar*C*–*t*-Bu); 143.8 (Ar*C*–*t*-Bu); 133.3 (Ar*C*–CH$_2$); 133.0 (Ar*C*–CH$_2$); 126.4 (Ar*C*H); 72.3 (O–*C*H$_2$–CH$_2$–CH$_3$); 71.4 (O–*C*H$_2$–CHO); 50.7 (O–CH$_2$–*C*HO–CH$_2$); 44.6 (*C*H$_2$–CHO–CH$_2$); 38.8 (Ar–*C*H$_2$–Ar); 38.6 (Ar–*C*H$_2$–Ar); 33.9 (Ar–*C*(CH$_3$)$_3$); 31.4 (*C*H$_3$); 22.4 (O–CH$_2$–*C*H$_2$–CH$_3$); 10.0 (O–CH$_2$–CH$_2$–*C*H$_3$). ES-MS $m/z = 845.3$ $[M+H]^+$, IR (solid): $\nu = 2961$, 2870, 1473, 1454, 1361, 1197, 1117, 1029, 1012, 909, 869. $[\alpha]_D^{20} = -6.2$ (*c* 0.975, $CHCl_3$), decomposition if $T > 305$ °C.

4.6. Compound (*R*,*R*)-3c

Compound **2c** (0.40 g, 0.80 mmol) and 2.10 g (6.4 mmol) of Cs_2CO_3 were dissolved under nitrogen in 8 ml of DMF for 30 min. (*R*)-Glycidyl-tosylate (0.500 g, 2.18 mmol) was then added and the mixture stirred at 80 °C under nitrogen for 11 h and then stopped. Twenty milliliters of H_2O were added and the aqueous layer extracted by 3×20 ml CH_2Cl_2. The resulting organic layer was then washed by 3×30 ml of H_2O (pH 6), dried over Na_2SO_4, filtrated and evaporated. The pure product **3c** (0.238 g, 0.383 mmol) was obtained as a yellowish-white powder by re-crystallisation (CH_2Cl_2/MeOH). Yield = 48%. TLC: eluant: CH_2Cl_2/*n*-heptane: 8/2. Visualisation: UV, $R_f = 0.12$, ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.10 (t, 4H, $J = 5.6$ Hz, *H*–Ar); 7.02 (d, 4H, $J = 7.3$ Hz, *H*–Ar); 6.73 (t, 4H, $J = 5.6$ Hz, *H*–Ar); 3.82 (dd, 2H, $J = 6.7$, 2.4 Hz, O–C*H*$_2$–CHO); 3.46–3.65 (m, 14H, 3O–C*H*$_2$ and 4Ar–C*H*$_2$–Ar); 3.12 (m, 2H, O–CH$_2$–C*H*O–CH$_2$); 2.79 (t, 2H, $J = 4.1$ Hz, C*H*$_2$–CHO–CH$_2$–O); 2.55 (dd, 2H, $J = 2.8$, 2.6 Hz, C*H*$_2$–CHO–CH$_2$–O); 1.68–1.56 (m, 4H, O–CH$_2$–C*H*$_2$–CH$_3$); 0.90 (t, 6H, $J = 7.4$ Hz, O–CH$_2$–CH$_2$–C*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): 156.7 (Ar*C*–O–CH$_2$); 156.6 (Ar*C*–O–CH$_2$); 133.9 (Ar*C*–CH$_2$); 130.1 (Ar*C*H); 121.8 (Ar*C*H); 121.7 (Ar*C*H); 73.4 (O–*C*H$_2$–CH$_2$–CH$_3$); 71.7 (O–*C*H$_2$–CHO); 50.9 (O–CH$_2$–CHO–CH$_2$); 44.7 (CH$_2$–CHO–CH$_3$); 38.7 (Ar–CH$_2$–Ar); 38.5 (Ar–CH$_2$–Ar); 22.5 (O–CH$_2$–CH$_2$–CH$_3$); 10.1 (O–CH$_2$–CH$_2$–CH$_3$). ES-MS $m/z = 621.2$ $[M+H]^+$, IR (solid): $\nu = 2933$, 1449, 1245, 1188, 1008, 759. $[\alpha]_D^{20} = -8.5$ (*c* 1.015, $CHCl_3$), mp = 217–221 °C.

4.7. Compound (*R*)-4a

Compound **3a** (0.196 g, 0.267 mmol) and 0.123 g (1.06 mmol) of $CaCl_2$ were stirred at 80 °C in 2 ml (18.4 mmol) of benzylamine. The reaction was stopped after 11 h by adding 10 ml of a solution of aqueous NH_4Cl, followed by extraction by 3×20 ml of CH_2Cl_2, The resulting organic mixture was then washed twice with 10 ml H_2O, dried over Na_2SO_4, filtrated and evaporated. The pure product **4a** (0.204 g, 0.217 mmol) was obtained as a white powder by precipitation in the residual benzylamine. Yield = 81%. TLC: eluant: *n*-heptane/ethyl acetate: 8/2. Visualisation: UV, $R_f = 0.3$, ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.30–7.35 (m, 5H, *H*–Ar); 7.21 (s, 2H, *H*–Ar); 7.08 (s, 2H, *H*–Ar); 6.92 (d, 1H, $J = 3.0$ Hz, *H*–Ar); 6.87 (d, 1H, $J = 3.0$ Hz, *H*–Ar); 6.63 (dd, 2H, $J = 6.7$, 1.0 Hz, *H*–Ar); 4.14–4.21 (m, 1H, O–CH$_2$–C*H*(OH)–CH$_2$); 4.10 (d, 2H, $J = 12.3$ Hz, Ar–C*H*$_2$–Ar); 3.84–3.91 (AB, 2H, $J = 13.2$ Hz, O–C*H*$_2$–CH(OH)); 3.43–3.76 (m, 12H, 3O–C*H*$_2$–CH$_2$–CH$_3$, 2Ar–C*H*$_2$–Ar and NH–C*H*$_2$–Ar); 3.04 (d, 2H, $J = 12.6$ Hz, Ar–C*H*$_2$–Ar); 2.75 (dd, 1H, $J = 8.2$, 3.9 Hz C*H*$_2$NHCH$_2$Ar); 2.66 (dd, 1H, $J = 9.6$, 6.9 Hz C*H*$_2$NHCH$_2$Ar); 1.81–1.85 (m, 4H, 2O–CH$_2$–C*H*$_2$–CH$_3$); 1.51–1.59 (m, 2H, O–CH$_2$–C*H*$_2$–CH$_3$); 1.39 (s, 9H, *t*-Bu); 1.33 (s, 9H, *t*-Bu); 0.95–1.08 (m, 24H, 2*t*-Bu and 2O–CH$_2$–CH$_2$–C*H*$_3$); 0.71 (t, 3H, $J = 7.5$ Hz, O–CH$_2$–CH$_2$–C*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): 154.7 (Ar*C*–O–CH$_2$); 153.8 (Ar*C*–O–CH$_2$); 145.0 (Ar*C*–*t*-Bu); 143.8 (Ar*C*–*t*-Bu); 135.7 (Ar*C*–CH$_2$); 132.6 (Ar*C*–CH$_2$); 132.4 (Ar*C*–CH$_2$); 128.5 (Ar*C*H); 127.2 (Ar*C*H); 76.2 (ArO*C*H$_2$–CH$_2$); 75.4 (ArO*C*H$_2$–CH$_2$); 74.7 (O–*C*H$_2$–CH(OH)); 69.1 (O–CH$_2$–*C*H(OH)–CH$_2$); 53.5 (NH–*C*H$_2$–Ar); 50.9 (*C*H$_2$–CH(OH)–CH$_2$–O); 37.8 (Ar–*C*H$_2$–Ar); 37.6 (Ar–*C*H$_2$–Ar); 34.0 (Ar–*C*(CH$_3$)$_3$); 31.4 (*C*H$_3$); 30.8 (Ar–*C*H$_2$–Ar); 23.6 (O–CH$_2$–*C*H$_2$–CH$_3$); 21.7 (O–CH$_2$–*C*H$_2$–CH$_3$); 10.6 (O–CH$_2$–CH$_2$–*C*H$_3$); 9.4 (O–CH$_2$–CH$_2$–*C*H$_3$). ES-MS $m/z = 938.7$ $[M+H]^+$, IR (solid) $\nu = 2958$, 2873, 1474, 1197, 1119, 1045, 1011, 868, 733, 697. $[\alpha]_D^{20} = -2.5$ (c 0.91, $CHCl_3$), mp = 238–239 °C.

4.8. Compound (*R*,*R*)-4b

Compound **3b** (0.102 g, 0.120 mmol) was dissolved in 1 ml (9.2 mmol) of benzylamine in a micro-wave vial. The mixture was heated in the microwave for 1.5 h at 150 °C; 200 W. Benzylamine was then reduced to third and the pure product **4b** (0.036 g, 0.033 mmol) was obtained as white crystals through crystallisation by adding MeOH. Yield = 28%. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.21–7.30 (m, 10H, *H*–Ar); 7.03 (d, 2H, $J = 2.1$ Hz, *H*–Ar); 6.97 (m, 6H, *H*–Ar); 3.78–3.92 (m, 8H, 4Ar–C*H*$_2$–Ar); 3.70 (s, 4H, 2NH–C*H*$_2$–Ar); 3.57 (t, 2H, $J = 8.7$ Hz, 1O–C*H*$_2$–CH(OH)); 3.44 (m, 2H, 2O–CH$_2$–C*H*(OH)–CH$_2$); 3.37 (dd, 2H, $J = 5.4$, 2.4 Hz, O–C*H*$_2$–CH(OH)); 3.25 (t, 4H, $J = 7.8$ Hz, 2O–C*H*$_2$–CH$_2$–CH$_3$); 2.42 (AB, 4H, $J = 3.9$ Hz, 2C*H*$_2$NHCH$_2$Ar); 1.37 (s, 2H, *t*-Bu); 1.26–1.27 (2s, 34H, *t*-Bu); 0.83 (m, 4H, 2O–CH$_2$–C*H*$_2$–CH$_3$); 0.58 (t, 6H, $J = 7.8$ Hz, 2O–CH$_2$–CH$_2$–C*H*$_3$), ^{13}C NMR (300 MHz, $CDCl_3$, 298 K): 154.7 (Ar*C*–O–CH$_2$); 154.4 (Ar*C*–O–CH$_2$); 149.8 (Ar*C*–*t*-Bu); 132.7 (Ar*C*–CH$_2$); 132.2 (Ar*C*–CH$_2$); 128.8 (Ar*C*H); 12.9 (Ar*C*H); 125.87 (Ar*C*H); 73.4 (O–*C*H$_2$–CH$_2$–CH$_3$); 71.9 (O–*C*H$_2$–CH(OH)); 68.2 (O–CH$_2$–*C*H(OH)–CH$_2$); 53.3 (NH–*C*H$_2$–Ar); 51.0 (CH(OH)–*C*H$_2$–NH); 39.2 (Ar–*C*H$_2$–Ar); 39.0 (Ar–*C*H$_2$–Ar); 33.9 (Ar–*C*(CH$_3$)$_3$); 31.5 (*C*H$_3$); 21.9 (O–CH$_2$–*C*H$_2$–CH$_3$); 9.8 (O–CH$_2$–CH$_2$–*C*H$_3$), ES-MS $m/z =$ 1059.6 $[M+H]^+$, IR solid $\nu = 3513$, 2959, 2901, 2870, 1760, 1481, 1361, 1208, 1122, 1015, 867, 744, 697.

$[\alpha]_D^{20} = +3.4$ (c 0.75, $CHCl_3$), mp decomposition if $T > 224$ °C.

4.9. Compound (*R*,*R*)-4c

Compound **3c** (0.105 g, 0.169 mmol) was dissolved in 1 ml (9.2 mmol) of benzylamine in a micro-wave vial. The mixture was heated in the microwave for 2 h at 150 °C; 200 W. Benzylamine was then reduced to third, 40 ml of CH_2Cl_2 added and the organic layer was washed by a 30 ml solution of HCl (1 M), then by 40 ml of H_2O, dried over Na_2SO_4, filtrated and evaporated. The product **4c** (0.103 g, 0.123 mmol) was precipitated from the obtained oil by adding ether to give a yellow powder. Yield = 73%. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.54–7.66 (m, 5H, *H*–Ar); 7.37–7.41 (m, 5H, *H*–Ar); 6.78–7.03 (m, 12H, *H*–Ar); 4.27 (s, 4H, 2Ar–C*H*$_2$–Ar); 3.67–3.93 (m, 10H, 2O–CH$_2$–C*H*(OH)–CH$_2$; 2Ar–C*H*$_2$–Ar and 2NH–C*H*$_2$–Ar); 3.28 (t, 4H, $J = 8.1$ Hz, O–C*H*$_2$–CH$_2$–CH$_3$); 3.19 (t, 4H, $J = 7.5$ Hz, O–C*H*$_2$–CH(OH)); 2.42 (m, 4H, C*H*$_2$NHCH$_2$Ar); 0.94 (m, 4H, O–CH$_2$–C*H*$_2$–CH$_3$); 0.60 (t, 6H, $J = 7.2$ Hz, 2O–CH$_2$–CH$_2$–C*H*$_3$), ^{13}C NMR (300 MHz, $CDCl_3$, 298 K): 157.2 (Ar*C*–O–CH$_2$); 155.7 (Ar*C*–O–CH$_2$); 134.2 (Ar*C*–CH$_2$); 133.9 (Ar*C*–CH$_2$); 130.8 (Ar*C*H); 130.2 (Ar*C*H); 129.6 (Ar*C*H); 128.6 (Ar*C*H); 124.0 (Ar*C*H); 123.4 (Ar*C*H); 72.4 (O–*C*H$_2$–CH$_2$–CH$_3$); 71.5 (O–*C*H$_2$–CH(OH)); 65.8 (O–CH$_2$–*C*H(OH)–CH$_2$); 51.4 (NH–*C*H$_2$–Ar); 48.3 (CH(OH)–*C*H$_2$–NH); 38.5 (Ar–*C*H$_2$–Ar); 38.3 (Ar–*C*H$_2$–Ar); 22.4 (O–CH$_2$–*C*H$_2$–CH$_3$); 10.2 (O–CH$_2$–CH$_2$–*C*H$_3$), ES-MS $m/z = 835.3$ $[M+H]^+$, IR (solid) $\nu = 3291$, 3022, 2956, 2926, 2873, 1455, 1205, 1092, 1012, 751, 697. $[\alpha]_D^{20} = -36.3$ (c 0.885, $CHCl_3$), mp decomposition if $T > 217$ °C.

4.10. Compound (*R*)-5

Compound **3a** (0.122 g, 0.146 mmol) was dissolved in 1 ml (7.7 mmol) of cyclohexanemethylamine in a micro-wave vial. The mixture was heated in the microwave for 1 h at 150 °C; 200 W. The pure product **5** (0.108 g, 0.114 mmol) was obtained as white crystals through precipitation by adding MeOH. Yield = 78%. TLC: eluant: *n*-heptane/ethyl acetate: 8/2. Visualisation: UV, $R_f = 0.16$, ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ 7.21 (s, 2H, *H*–Ar); 7.09 (s, 2H, *H*–Ar); 6.96 (s, 1H, *H*–Ar); 6.86 (s, 1H, *H*–Ar); 6.62 (d, 2H, $J = 5.8$, 2.1 Hz, *H*–Ar); 4.10 (d, 2H, $J = 12.1$ Hz, Ar–C*H*$_2$–Ar + covered O–CH$_2$–C*H*(OH)–CH$_2$); 3.43–3.74 (m, 12H, O–C*H*$_2$–CH(OH), 3O–C*H*$_2$–CH$_2$–CH$_3$ and 2Ar–C*H*$_2$–Ar); 3.04 (d, 2H, $J = 12.3$ Hz, Ar–C*H*$_2$–Ar); 2.45–2.68 (m, 4H, C*H*$_2$NHCH$_2$Ar and NH–C*H*$_2$–Ar); 1.20–1.86 (m, 35H, 3O–CH$_2$–C*H*$_2$–CH$_3$, 2*t*-Bu and cyclohexane protons); 1.04 (s, 18H, 2*t*-Bu); 1.00 (t, 6H, $J = 6$ Hz, 2O–CH$_2$–CH$_2$–C*H*$_3$); 0.71 (t, 3H, $J = 7.2$ Hz, O–CH$_2$–CH$_2$–C*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): 154.7 (Ar*C*–O–CH$_2$); 153.8 (Ar*C*–O–CH$_2$); 145.0 (Ar*C*–*t*-Bu); 143.8 (Ar*C*–*t*-Bu); 135.7 (Ar*C*–CH$_2$); 132.6 (Ar*C*–CH$_2$); 132.1 (Ar*C*–CH$_2$); 128.0 (Ar*C*H); 125.9 (Ar*C*H); 125.7 (Ar*C*H); 125.3 (Ar*C*H); 76.2 (ArO*C*H$_2$–CH$_2$); 75.4 (ArO*C*H$_2$–CH$_2$); 74.9 (O–*C*H$_2$–CH(OH)); 68.8 (O–CH$_2$–*C*H(OH)–CH$_2$); 56.3 (NH–*C*H$_2$–Ar); 51.7 (*C*H$_2$–CH(OH)–CH$_2$–O); 37.8 (CH$_2$–*C*H–2(CH$_2$)); 37.7 (Ar–*C*H$_2$–Ar); 37.6 (Ar–*C*H$_2$–Ar); 34.0 (Ar–*C*(CH$_3$)$_3$); 33.7 (Ar–*C*(CH$_3$)$_3$); 31.5 (*C*H$_3$); 31.3 (Ar–*C*H$_2$–Ar); 31.2 (CH–2(*C*H$_2$)); 26.6 (*C*H–2(CH$_2$)) 25.9 (*C*H$_2$–2(CH$_2$)); 23.6 (O–CH$_2$–*C*H$_2$–CH$_3$); 21.7 (O–CH$_2$–*C*H$_2$–CH$_3$); 10.7 (O–CH$_2$–CH$_2$–*C*H$_3$); 9.4 (O–CH$_2$–CH$_2$–*C*H$_3$). ES-MS $m/z = 944.8$ $[M+H]^+$, IR (solid) $\nu = 3548$, 2952, 2926, 2864, 1474, 1197, 1120, 1044, 1011, 871. $[\alpha]_D^{20} = +1.4$ (c 0.93, $CHCl_3$), mp = 226–227 °C.

4.11. Compound (*R*)-6

(*R*)-Glycidyl tritylether (0.198 g, 0.62 mmol) was dissolved in 1 ml (7.7 mmol) of cyclohexanemethylamine in a micro-wave vial. The mixture was heated in the microwave for 1 h at 150 °C; 200 W. 40 ml of CH_2Cl_2 was added and the organic layer washed by a 20 ml solution of HCl 1 N, then by 2 × 20 ml H_2O, dried over Na_2SO_4, filtrated and evaporated. The pure product **6** (0.205 g, 0.477 mmol) was obtained as a white powder by recrystallisation (CH_2Cl_2/ethyl acetate). Yield = 77%. ^{1}H NMR (300 MHz, DMSO, 298 K): δ 8.66 (s, 1H, N*H*); 7.54–7.66 (m, 5H, *H*–Ar); 7.27–7.41 (m, 15H, *H*–Ar); 5.70 (s, 1H, –O*H*); 4.10 (m, 1H, O–CH$_2$–C*H*(OH)–CH$_2$); 3.02–3.11 (m, 2H, O–C*H*$_2$–CH(OH)); 3.78–2.89 (m, 4H, 2NH–C*H*$_2$); 1.61–1.81 (m, 6H, C*H*$_2$ of cyclohexane); 1.10–1.27 (m, 3H, C*H*$_2$ and C*H* of cyclohexane); 0.87–0.98 (m, 2H, C*H*$_2$ of cyclohexane). ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): 146.8 (Ar*C*); 129.6 (Ar*C*H); 128.6 (Ar*C*H); 127.9 (Ar*C*H); 127.2 (Ar*C*H); 82.0 (Ph$_3$–*C*–O); 67.4 (O–CH$_2$–*C*H(OH)–CH$_2$); 64.1 (O–*C*H$_2$–CH(OH)); 54.6 (NH–*C*H$_2$–Ar); 51.3 (*C*H$_2$–CH(OH)–CH$_2$–O); 34.4 (CH$_2$–*C*H–2(CH$_2$)); 30.6 (CH–2(*C*H$_2$)); 25.8 (*C*H–2(CH$_2$)); 25.3 (*C*H$_2$–2(CH$_2$)). ES-MS $m/z = 430.0$ $[M+H]^+$, IR (solid) $\nu = 3301$, 2919, 2847, 2760, 1492, 1445, 1096, 1072, 754, 699. $[\alpha]_D^{20} = +10.6$ (c 1, $CHCl_3$), mp = 196–197 °C.

4.12. General procedure for reduction of acetophenone

[Ru(*p*-cymène)Cl$_2$]$_2$ (3.1 mg, 0.005 mmol) and an appropriate amount of chiral ligand were dissolved in 2 ml of 2-propanol and stirred at 80 °C under argon for 30 min. The solution turned to red. The mixture is cooled down to room temperature and *t*-BuOK (0.60 mg, 0.600 mmol) in 3 ml of 2-propanol added followed by acetophenone (60 mg, 0.500 mmol) in 1 ml of 2-propanol. The solution was stirred under argon for the time indicated. The reaction is monitored by chiral GC.

GC: Shimadzu GC-14A. Column: J&W Scientific Inc, Clycodex B, Integrator: Shimadzu C-R6A Chromatopac, Program: initial temperature: 50 °C, initial time: 5 min, program rate: 1 °C/min, final temperature: 200 °C, final time: 1 min, retention time: 21.9 min for acetophenone, 30.0 min for (*R*)-phenylethanol and 31.0 min for (*S*)-phenylethanol.

References

1. For recent reviews on asymmetric hydrogenation see: (a) Noyori, R.; Yamakawa, M.; Hashiguchi, S. *J. Org. Chem.* **2001**, *66*, 7931–7944; (b) Blaser, H. U.; Malan, C.; Pugin, B.; Spindler, F.; Steinder, H.; Studer, M. *Adv. Synth. Catal.* **2003**,

345, 103–151; (c) Evareare, K.; Mortreux, A.; Carpentier, J.-F. *Adv. Synth. Catal.* **2003**, *345*, 67–77; (d) Clapham, S. E.; Hadzovic, A.; Morris, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2201–2237; (e) Gladiali, S.; Alberico, E. *Chem. Soc. Rev.* **2006**, *35*, 226–236; (f) Wu, X.; Xiao, J. *Chem. Commun.* **2007**, 2449–2466.

2. (a) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562–7563; (b) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97–102; (c) Schwink, L.; Ireland, T.; Püntener, K.; Knochel, P. *Tetrahedron: Asymmetry* **1998**, *9*, 1143–1163; (d) Ohkuma, T.; Utsumi, N.; Tsutsmi, K.; Murata, K.; Snadoval, C.; Noyori, R. *J. Am. Chem. Soc.* **2006**, *128*, 8724–8725.
3. (a) Palmer, M.; Walsgrove, T.; Wills, M. *J. Org. Chem.* **1997**, *62*, 5226–5228; (b) Alonso, D. A.; Guijarro, D.; Pinho, P.; Temme, O.; Andersson, P. G. *J. Org. Chem.* **1998**, *63*, 2749–2751; (c) Nordin, S. J. M.; Roth, P.; Tarnai, T.; Alonso, D. A.; Brandt, P.; Andersson, P. G. *Chem. Eur. J.* **2001**, *7*, 1431–1436; (d) Hayes, A.; Clarkson, G.; Wills, M. *Tetrahedron: Asymmetry* **2004**, *15*, 2079–2084.
4. Takehara, J.; Hashigushi, S.; Fujii, A.; Inoue, S.-I.; Ikariya, T.; Noyori, R. *Chem. Commun.* **1996**, 233–234.
5. Harfouche, J.; Hérault, D.; Tommasino, M. L.; Pellet-Rostaing, S.; Lemaire, M. *Tetrahedron: Asymmetry* **2004**, *15*, 3413–3418.
6. Pasto, M.; Riera, A.; Pericas, M.-A. *Eur. J. Org. Chem.* **2002**, *14*, 2337–2341.
7. (a) Wieser, C.; Dieleman, C. B.; Matt, D. *Coord. Chem. Rev.* **1997**, *165*, 93–161; (b) Karakhanov, E. E.; Maskimov, A. L.; Runova, E. A.; Kardasheva, Y. S.; Terenina, M. V.; Buchneva, T. S.; Guchkova, A. Y. *Macromol. Symp.* **2003**, *204*, 159–173; (c) Petrella, A. J.; Raston, C. L. *J. Organomet. Chem.* **2004**, *689*, 4125–4136.
8. (a) Steyer, S.; Jeunesse, C.; Harrowfield, J.; Matt, D. *J. Chem. Soc., Dalton Trans.* **2005**, *24*, 1301–1309; (b) Plourde, F.; Gilbert, K.; Gagnon, J.; Harvey, P. D. *Organometallics* **2003**, *22*, 2862; (c) Steyer, S.; Jeunesse, C.; Matt, D.; Welter, R.; Wesolek, M. *J. Chem Soc., Dalton Trans.* **2002**, *22*, 4264–4275; (d) Parlevliet, F. J.; Kiener, C.; Fraanje, J.; Goubitz, K.; Lutz, M.; Spek, A. L.; Kamer, P. C. J. *J. Chem. Soc., Dalton Trans.* **2000**, *7*, 1113–1122; (e) Paciello, R.; Siggel, L.; Ropper, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 1920–1923; (f) Csók, Z.; Szalontai, G.; Czira, G.; Kollár, L. *J. Organomet. Chem.* **1998**, *570*, 23.
9. (a) Semeril, D.; Lejeune, M.; Jeunesse, C.; Matt, D. *J. Mol. Catal. A* **2004**, *217*, 59; (b) Frank, M.; Maas, G.; Schatz, J. *Eur. J. Org. Chem.* **2004**, *3*, 607–613.
10. Dieleman, C.; Steyer, S.; Jeunesse, C.; Matt, D. *J. Chem. Soc., Dalton Trans.* **2001**, *17*, 2508–2517.
11. Gaeta, C.; De Rosa, M.; Fruilo, M.; Soriente, A.; Neri, P. *Tetrahedron: Asymmetry* **2005**, *16*, 2333–2340.
12. Amato, M. E.; Ballistreri, F. P.; Pappalardo, A.; Tomaselli, G. A.; Toscano, R. M.; Williams, D. J. *Eur. J. Org. Chem.* **2005**, *16*, 3562–3570.
13. (a) Neri, P.; Bottino, A.; Geraci, C.; Piattelli, M. *Tetrahedron: Asymmetry* **1996**, *7*, 17–20; (b) Takata, T.; Takagi, H.; Furusho, Y. *Enantiomer* **2002**, *7*, 129–132.
14. (a) Jaime, C.; De Mendoza, J.; Prados, P.; Nieto, P. M.; Sanchez, C. *J. Org. Chem.* **1991**, *56*, 3372–3376; (b) Iwamoto, K.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1991**, *56*, 4955–4962.
15. Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561–2576.
16. Tan, W.; Zhao, B.-X.; Sha, L.; Jiao, P.-F.; Wan, M.-S. *Synth. Commun.* **2006**, *36*, 1353–1359.
17. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M.-J.; Egberink, R.; De Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767–2777.