

**Modification of chiral dimethyl tartrate through transesterification:  
Immobilisation on POSS and enantioselectivity reversion in Sharpless  
asymmetric epoxidation**

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## **Abstract**

Modification of dimethyl tartrate has been investigated through transesterification with aminoalcohols to provide reactive functionalities for the covalent bonding of chiral tartrate to polyhedral oligomeric silsesquioxanes. The transesterification of dimethyl tartrate has been widely studied by means of using different catalytic systems and reaction conditions. Through the proper selection of both, the catalytic system and the reaction conditions, it is possible to achieve the mono- or the bis-substituted tartrate derivative as sole products. All the intermediate chiral tartrate-derived ligands were successfully used in the homogeneous enantioselective epoxidation of allylic alcohols providing moderate enantiomeric excess over the products. Attached amine groups have been used to support the modified tartrate ligands onto a haloaryl-functionalized silsesquioxane moiety. This final chiral tartrate ligand displays enantioselectivity reversion in the asymmetric epoxidation of allylic alcohols with regards to the starting dimethyl tartrate ligand, having both molecules them the same chiral sign. However, the POSS-containing ligand can be easily recovered in almost quantitative yield and reused in asymmetric epoxidation reactions. In addition, recovered silsesquioxane-pendant ligand, though displaying decreasing catalytic activity in recycling epoxidation tests, showed very stable enantioselective behavior.

**Keywords:** Tartrate ligands; Transesterification; Asymmetric epoxidation; Enantioselectivity reversal; POSS;

## Introduction

The development of the titanium-tartrate system as a chiral catalyst for the asymmetric epoxidation of allylic alcohols (Sharpless asymmetric epoxidation) has been one of the major breakthroughs in enantioselective synthesis [1]-[3], as revealed by the large number of publications related to this topic [4]. Thus, the asymmetric epoxidation of allylic alcohols has become a valuable tool for the synthesis of enantiopure epoxy-alcohols, which are versatile chiral building blocks [5]-[6]. However, one of the main drawbacks of this process is the complexity of the work-up procedure for carrying out the oxidation and quenching the reaction. In this sense not only large amounts of solvents are necessary to purify the products, but also the reuse or recovery of the catalyst becomes impossible. Different attempts, more or less successful, have been carried out in order to overcome these inconveniences. Some of them deal with the possibility of supporting the chiral ligands on different solids, both organic or inorganic, to obtain heterogeneous analogues to the Sharpless homogeneous catalyst [7]-[10]. In this way the quenching of the reaction is largely simplified, since the filtration of the catalysts is enough to stop the reaction and also the catalyst is reusable. However, the immobilization of the catalytic species leads, in most of the cases, to a great decrease of the catalytic activity because of mass transfer becomes a limiting stage of the reaction process. An interesting way to prepare reusable catalysts without introducing mass transfer restrictions consists of using a carrier for the catalytic active species which helps the recovering of the catalytic complex. One of the possibilities deals with the handling of polyhedral oligomeric silsesquioxanes – POSS – which easily dissolve or precipitate depending on the organic solvent, allowing their recovering. Silsesquioxanes are organosilicon compounds usually employed as models for the study of the behaviour of certain species immobilized onto the surface of silica-based supports.

Those compounds have been applied to the immobilization of both, either metal species [11]-[13] or organic compounds [14],[15], giving an approximate idea of the catalytic behaviour of the grafted species onto the surface of solid supports. However, operating with these species simplifies the working procedures since, through the proper choice of the solvent, silsesquioxane can dissolve to form homogeneous catalytic systems but they are easily recovered by selective precipitation in other solvents – usually THF –.

The work herein described presents the modification of chiral tartrate molecules, starting from dimethyl L-(+)-tartrate **1**, suitable for covalent bonding to properly functionalized silsesquioxanes. This approach is based on the modification of the ester groups which minimizes the structural change with respect to catalyst enantioselectivity (Scheme 1). The enantiopure tartrate derived ligands were used, together with titanium isopropoxide, in the asymmetric epoxidation of various allylic alcohols, using tert-butyl hydroperoxide (TBHP) as oxidant agent, providing good asymmetric induction. Silsesquioxane-pendant tartrate ligand showed reversal enantioselective with regards non-modified tartrate in the epoxidation of cinnamyl alcohol, being this result attributed to the bulky size of the silicon substituent. Recycling test with POSS-functionalized tartrate ligands provided constant enantioselectivity though the activity decreases for reutilization runs.

## **Results and Discussion**

### **Design and synthesis of mono (3) and di-amino (4) ester.**

#### *Synthesis optimization*

For anchoring purposes on an appropriately functionalized silsesquioxane, *N*-methylethanolamine **2**, was chosen as the amine functionality for carrying out a

transesterification reaction. To avoid undesired reactions the hydroxylamine **2** was BOC protected to afford the carbamate **5** as colourless oil in 95 % yield.

The starting material dimethyl L-tartrate **1**, was first protected as the bisacetal by using 2,3-butanedione, accordingly to the methodology developed by Dixon et al. [16], yielding a white solid of (2,3,5,6)-dimethoxy-5,6-dimethyl-[1,4]-dioxane-dimethyl tartrate **6** in 90-95 % yield after purification by recrystallization, or by using dimethyl-benzyl acetal, following the Seebach procedure [17], yielding a white solid of 2,3-O-benzyliden-dimethyl tartrate **7**, in 90-95% yield after recrystallization (Scheme 2). In both cases, the chirality of the starting tartrate was maintained. The use of different protecting group strategies was justified because of the different de-protection procedures to be employed. Thus, while the dimethoxy-[1,4]-dioxane protecting group in **6** may be removed by acid hydrolysis with trifluoroacetic acid (TFA), the benzylidene acetal in **7** may be removed by hydrogenolysis.

The next step in the tartrate modification protocol consisted of the transesterification of the protected starting materials **6** and **7**. In this step both the mono **9** and **11** and disubstituted compounds **10** and **12** can be obtained (Scheme 3). For the synthesis of monosubstituted compounds **9** and **11**, the acetals **6** and **7** were reacted with BOC ethanolamine **5** using a titanium alkoxide, following a similar procedure to that described by Dixon et al. [18]. *N*-methyl-*tert*-butoxycarbonylethanolamine **5**, was treated with titanium tetrachloride in the presence of triethylamine as catalyst to give the corresponding titanium alkoxide, **8**, (Scheme 4) to be used as a transesterification catalyst. The synthesis of **8** was targetted bearing in mind that transesterification reactions catalysed by titanium alkoxides take place by the alkoxide binding to the metallic center with transfer to the ester group [19] (Scheme 4).

Table 1 summarizes the results obtained for the transesterification of **6** and **7** with **5** using **8** as catalyst. The investigated titanium alkoxide to tartrate ratios seem to confirm the high catalytic activity of the titanium alkoxide **8**, since better yields for the transesterification products are obtained as the titanium content increases (Table 1, entries 1-4). At this point it is noteworthy that the monosubstituted compound **9** is produced as the unique product with Ti/tartrate ratios of 0.05-0.15 (Table 1, entries 1-3). The influence of the solvent polarity on the product distribution has also been investigated (Table 1, entries 5 and 6). Thus, similar results were found when THF or chloroform were used, while the use of a non-polar solvent such as benzene led to a remarkable increase in the yield of the monoester **9**, without detecting any presence of diester **10** (Table 1, entry 6). These results suggest a strong influence of the polarity of the solvent on the reaction outcome, since less polar solvents provide higher yields of transesterified product **9**.

Comparison between the two differently protected starting tartrates revealed that **7** was more reactive than **6** as evidenced from the shorter transesterification reaction times to achieve similar yields of **9** and **11** + **12**, respectively (Table 1, entries 6-7). The monitorization of the reaction media during the transesterification reactions, did not reveal the presence of diester **10** when using **6** as starting material, unlike protected dimethyl tartrate **7**, which led to diester **12** after few hours. This difference in behaviour could be probably explained by the smaller number of coordinating OR groups in **7**, making the alkoxide more available.

Since the above described methodology is clearly effective in achieving selective monosubstitution, an alternative procedure was employed to synthesize the disubstituted products **10** and **12**. A strongly acidic catalyst, n-butyl-stannonic acid, has been described as an effective catalyst for the transesterification reaction of diesters [20].

Bearing in mind the effect of the solvent in the monosubstitution transesterifications, benzene was used as the reaction solvent. These results are detailed in Table 2.

Increasing the molar ratio of **5**:**7** led to higher yields of **12** as the main product (Table 2, entries 1, 2 and 3). Additionally, further improvements in the yield of diesters **10** and **12** were obtained by varying the catalyst amount. The effect of this parameter was more pronounced than altering the amine/DMT molar ratio. Here, the bis-substituted product **10** or **12** was the sole product when the Ti:substrate ratio is raised to 0.5:1 (Table, 2, entries 5 and 6).

The next step in the procedure was the removal of the protecting groups in **9-12**, for which two different approaches were used (Scheme 5). In the first route each group was removed separately. Thus, the benzylidene acetal protecting group in modified tartrates **11** and **12** was firstly removed by hydrogenation, using the method described by Kocienski [21]. This procedure gave the corresponding diols **13** and **14** in 95% yield after purification by preparative HPLC. Subsequent cleavage of the BOC protecting group was then carried out by acid hydrolysis with CF<sub>3</sub>COOH. This gave the deprotected amine modified tartrates **3** and **4** in 70-85% yield after crystallization. Alternatively, a method similar to that developed by Dixon et al. [18] was used to remove the protecting groups from tartrates **9** and **10**. Thus, attempted BOC and dimethoxy acetal deprotection was investigated using CF<sub>3</sub>COOH at r.t. However, using this procedure only the BOC protecting group was removed. It was found that a second treatment increasing the temperature and reaction time up to 24 h yielded the unprotected tartrate **3** and **4**.

#### *Synthesis of silsesquioxane-pendant tartrate ligands*

In order to evaluate the behaviour of the tartrate derived compounds as chiral ligands, a step forward in terms of the synthesis of silsesquioxane immobilized ligands (Scheme

6) has been carried out. Initially the haloaryl functionalized silsesquioxane was reacted with **2** to give product **15**. The resultant product **15** displays, as did the protected compound **5**, the ability to react only with the protected tartrate through the hydroxyl group. Thus, **15** was reacted with the benzilidene acetal protected dimethyl tartrate **7** to give the transester **16**. Protected dimethyltartrate **7** was chosen as the starting material for this study because unlike the butanedione derivative **6**, which requires strong acid treatment for its cleavage, the benzilidene acetal protecting group can be easily removed using mild hydrogenation conditions. In this way, the integrity of the rest of the molecule was ensured by the cleavage of **16** with Pd/C to give **17**. All the steps of this sequence have led to similar results to that achieved for the analogue product **11**, although butyl stannonic acid was used as catalyst for the transesterification reaction because of its readily availability and its capability to mainly produce symmetric bis-substituted tartrates through transesterification. The crude reaction was then submitted to hydrogenation in presence of Pd/C as catalyst for the cleavage of the benzylidene acetal, giving product **17** as a white solid.

### Catalytic tests

The enantioselective epoxidation of different allylic alcohols with *tert*-butyl hydroperoxide (TBHP) were performed at -20°C in presence of either **3**, **4**, **13**, **14** or **17** as chiral ligands and using Ti(O-*i*Pr)<sub>4</sub> as titanium source. Ligands **13** and **14**, containing the BOC protecting groups, were studied for comparison purposes, to contrast the enantio- and catalytic activity in ligands **3** and **4**, showing free amino functionalities. These tests also allowed checking the different modifications carried out during consecutive protection, transesterification and deprotection reactions did not caused ligand razemization. The results have been summarized in table 3.

The best activity and enantioselectivity were found for the BOC protected ligands **13** and **14** (Table 3, entries 3 and 4). Using ligand **14** as the chiral catalyst with titanium tetraisopropoxide gave the epoxy alcohol in up to 70% ee. In contrast, using tartrates with free amino group i.e. **3** and **4** (entries 1 and 2) led to the generation of lower epoxide yields and enantioselectivities, which could be caused by the formation of different titanium-tartrate derivative complexes when amino groups, free from protective group, are present within the chiral ligand. In general, these results are repeated for the different tested substrates, independently of the structure of the oxidized allylic alcohol. These results suggest only moderate efficiency in the formation of the tartrate–titanium complex, the essential active catalytic species for the Sharpless epoxidation catalyst.

On the other hand, it is particularly noteworthy that the tartrate-derived chiral ligand supported on silsesquioxane **17** shows a similar activity to that of the Boc-protected tartrate analogue, although the most interesting result for this reaction lies in the reversed enantioselectivity showed by this ligand. The measured enantiomeric excess is in the same range than using ligand **13**, but the achieved chiral induction is completely reversed, yielding an excess of the opposite enantiomer to the major one achieved with the rest of the L-(+)-dimethyl tartrate derivatives. Enantioreversion has been previously observed in several ligands because of different reasons [22]-[28]. For instance, the molar ratio between components [22] or just the reaction solvent [25] causes the reversal on the enantioselectivity of a certain catalyst. Immobilising on polymer supports has also been described to produce reversal enantioselectivity [26],[27]. Actually, Janda et al. [27] found enantioreversal induction in the epoxidation of 2-hexen-1-ol when using poly(ethylene glycol) transesterified chiral tartrates. These authors have shown that the Sharpless' catalyst enantioselection can be reversed

depending on the size of the ester substituents at the tartrate ligands, so that if the size of the substituent is higher than 750 a.m.u. the sign of the optical rotation of the product is reversed. Bearing in mind the silsesquioxane fragment attached to the tartrate ligand is larger than 1,100 a.m.u., a similar enantioversional behaviour could arise with this ligand as well. With regards to the reusability of the silsesquioxane-pendant tartrate chiral ligand, the same was recovered from the reaction media, after epoxidation of cinnamyl alcohol, by means of precipitation with THF, washed with dichloromethane and dried before being used in a second assay (Table 3, entry 6). Results indicate the enantioselectivity of the complex is well preserved during the recycling test, leading to the same enantiomeric excess on the final glycidol product. On the other hand, the catalytic activity is largely decreased for the reutilization test, since less than a half of the initial epoxide yield is achieved. This loss of catalytic activity could be related to the inactivation of some fraction of the chiral complex during the recycling test. Preliminary results on the epoxidation of different allylic alcohols indicate a similar behaviour for other substrates, finding the same enantioselective reversion observed for cinnamyl alcohol

Finally, in order to determine whether this is the cause of enantioversion or just the presence of the benzyl group in the aminoalcohol used for transesterifying the chiral tartrate ligand, a new compound was prepared. In this case, N-benzyl N-methyl amino ethanol was used for the transesterification of dimethyl tartrate starting from **7** and carrying out the transesterification reaction in presence of butylstannonic acid (Scheme 7). The resultant product, obtained after acetal cleavage, **18** was used as chiral ligand in the asymmetric epoxidation of cinnamyl alcohol inducing the usual chiral configuration onto the resultant phenyl glycidol (Table 3, entry 7). In this way, the enantioselectivity

reversal observed for the POSS-functionalized material should be ascribed to the size of the silsesquioxane fragment more than to the presence of the aromatic ring.

## Conclusions

A straightforward strategy for modifying tartrates has been developed in order to attach the resultant chiral ligands onto properly-functionalized polyhedral oligomeric silsesquioxanes. The reaction conditions for transesterification were optimized to achieve either the mono- or bis-substituted tartrate derivative as the sole product. The chiral tartrate-derived ligands so-obtained were used in the asymmetric epoxidation of cinnamyl alcohol achieving up to 70% ee in the resulting epoxy-alcohol. C2-symmetrical diesters **4** and **14** gave higher enantiomeric excess than the asymmetric monosubstituted tartrate derivatives **3** and **13**. Finally, the amino-groups allowed anchoring the tartrate derived ligands to a silsesquioxane fragment resulting in an enantioselectivity reversal of the chiral ligand. Further studies on the application of this heterogeneization strategy to the anchoring of tartrate derived ligands onto the surface of silica supports are being developed.

## Experimental

Materials and general procedures.

Dimethyl-L-tartrate (DMT, Acros, +99%) and N-methyl ethanolamine (NMEA, Aldrich, 99%) were distilled under inert atmosphere before being used. N-butyl tin hydroxide oxide (Aldrich, 97%) was used as received. Titanium chloride was used and stored in dry box. *Tert*-butyl hydroperoxide anhydrous solution in dichloromethane was prepared from aqueous solution (TBHP, Aldrich, 70%) by extraction with

dichloromethane followed by azeotropic distillation in a dean-stark for solvents heavier than water. The obtained solution was characterized by iodometric titration and stored at low temperature (+4°C) in presence of activated 3Å molecular sieves.

All non-aqueous reactions were carried out under inert atmosphere (usually nitrogen or argon) using standard Schlenk techniques, avoiding all times the presence of traces of water in the starting materials. Solvents were distilled prior their use as follows: CHCl<sub>3</sub> from P<sub>2</sub>O<sub>5</sub>; THF from Na/benzophenone; benzene and toluene from Na. Melting points were determined using a *Mettler Toledo DSC822e*. NMR spectra were recorded on a *Varian Mercury 400 MHz* spectrometer. Chemical shifts are reported in parts per million (ppm), in reference to the residual proton signals from the deuterated solvents. FTIR analysis were acquired on a *Mattson Infinity series FT-IR* spectrometer using the KBr buffer technique. Elemental analyses were performed on a *Elementar Vario EL III*. TLC was carried out using precoated sheets (Aldrich silica gel) and visualizing the products by developing with phosphomolybdic acid/ethanol or ammonium molybdate and ceric sulphate in H<sub>2</sub>SO<sub>4</sub>/H<sub>2</sub>O [28]. Product purification was carried out, unless otherwise stated, on a semi-preparative scale *HPLC Varian Prepstar* fitted with a normal phase *Dynamax Microsorb 100-8 Si* column (250 mm length, 41.4 mm I.D.) using n-hexane:i-propanol mixtures as solvent.

#### Protection of starting materials

*tert-Butyl 2-hydroxyethyl(methyl)carbamate (5)*. To a solution of **2** (10 g, 0.133 mol) in THF (50 ml) at 0°C, was added a solution of di-*tert*-butyl dicarbonate (32 g, 0.146 mol) in THF (10 ml) dropwise. The reaction mixture was stirred overnight at room temperature and then concentrated in *vacuo*. The residue was purified by semi-preparative HPLC to give the title compound (21.5 g, 0.123 mol, 92 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.36 (s, 9H; -C(CH<sub>3</sub>)<sub>3</sub>), 2.82 (s, 3H; -N-CH<sub>3</sub>), 3.25 (m, 2H; -N-CH<sub>2</sub>-);

3.61 ppm (m, 2H;  $-CH_2-OH$ ).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 28.2 ( $-C(CH_3)_3$ ), 34.9 ( $-N-CH_3$ ), 51.3 ( $-CH_2-OH$ ), 60.8 ( $-N-CH_2-$ ), 79.5 ( $-C(CH_3)_3$ ), 156.7 ppm ( $-N-CO_2-tBu$ ). IR  $\nu_{max}$  (neat): 1682 (C=O), 2975 (C-H), 3435  $cm^{-1}$  (O-H). Elemental analysis calcd (%) for  $C_8H_{17}NO_3$ : C 54.84, H 9.78, N, 7.99; found: C 54.81, H 9.77, N 8.03.

*Dimethyl (2R,3R,5R',6R') 5,6-dimethoxy-5,6-dimethyl-1,4-dioxane-2,3-dicarboxylate (6)*. To a solution of **1** (10.0 g, 55.6 mmol), trimethylorthoformate (TMOF, 17.8 g, 166.9 mmol) and 2,3-butanodione (6.0 g, 67.6 mmol) in methanol, was added camphorsulfonic acid (CSA, 1.3 g, 54.8 mmol). The mixture was then heated under reflux and stirring was continued overnight. The reaction was quenched by slow addition of  $NaHCO_3$  (10 g, 119 mmol) and reflux was maintained for two more hours. The resultant suspension was filtered and concentrated to dryness, giving a brown solid. The residue was then purified by recrystallization from n-hexane/ethyl acetate to give the desired product as a white solid (14.3 g, 49.0 mmol, 88.1%). m.p. 105.2°C.  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 1.34 (s, 6H;  $-C-CH_3$ ), 3.30 (m, 6H;  $-O-CH_3$ ), 3.75 (s, 6H;  $-CO_2CH_3$ ), 4.51 ppm (m, 2H;  $-O-CH-$ ).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 17.4 ( $-C-CH_3$ ), 48.5 ( $-O-CH_3$ ), 52.5 ( $-CO_2CH_3$ ), 68.7 ( $-O-CH-$ ), 99.0 ( $C-CH_3$ ), 168.1 ppm ( $-CO_2CH_3$ ). IR  $\nu_{max}$  (KBr): 1030, 1141, 1204, 1756 (C=O), 2956 (C-H)  $cm^{-1}$ . Elemental analysis calcd (%) for  $C_{12}H_{20}O_8$ : C 49.31, H 6.90; found: C 49.47, H 6.94.

*Dimethyl (4R,5R) 2-phenyl-1,3-dioxolane-4,5-dicarboxylate (7)*. A solution of **1** (10.0 g, 55.6 mmol) was mixed with benzaldehyde dimethyl acetal (9.4 g, 61.1 mmol) in benzene (50 ml). To this mixture was added p-toluenesulfonic acid (0.05 g, 0.3 mmol) in a 100 ml round bottom flask connected to Dean-Stark apparatus for solvents lighter than water. The mixture was heated under reflux for 12 hours during which time the solvent was withdrawn from the Dean-Stark trap in order to displace the equilibrium. The reaction was allowed to cool and then quenched with  $K_2CO_3$  (4.2 g, 30.0 mmol).

The resultant suspension was filtered and concentrated in vacuo to give a yellowish solid. The residue was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>/n-hexane to give compound **7** (13.1 g, 49 mmol, 89%). m.p. 73.2°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 3.84 (s, 3H; -CO<sub>2</sub>CH<sub>3</sub>), 3.89 (s, 3H; -CO<sub>2</sub>CH<sub>3</sub>), 4.92 (d, 2H, *J*=4.0Hz; -O-CH-), 6.15 (s, 1H; -CH-Ph); 7.47 ppm (5H; HAr). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 52.9 (-CO<sub>2</sub>CH<sub>3</sub>), 76.7 (-O-CH-), 106.6 (CH-Ph), 127.0, 128.2 and 129.9 (HC<sup>Ar</sup>), 135.0 (C<sup>Ar</sup>), 169.8 (-CO<sub>2</sub>CH<sub>3</sub>). IR ν<sub>max</sub> (KBr): 1108, 1244, 1435, 1754 (C=O), 2958 (C-H) cm<sup>-1</sup>. Elemental analysis calcd (%) for C<sub>13</sub>H<sub>14</sub>O<sub>6</sub>: C 58.65, H 5.30; found: C 58.40, H 5.37.

Preparation of transesterification catalyst: (*2-Methyl-boc-amino*)ethyl orthotitanate (**8**). To a solution of TiCl<sub>4</sub> (0.10 g, 0.53 mmol) in CHCl<sub>3</sub> (10 ml), was added **5** (0.37 g, 2.1 mmol) dropwise to give a yellowish solution. The resultant mixture was then stirred for 30 min and then triethylamine (0.21 g, 2.1 mmol) was added via syringe, giving a colourless suspension. The reaction was then stirred for an additional hour before being used as catalyst for transesterification reactions without further purification.

#### Transesterification Products

Transesterification reactions were carried out by mixing acetal protected DMT, **6** or **7** (3.5 mmol scale), and compound **5** (3.5 mmol for monosubstitution reactions, 7.7 mmol for disubstitution reactions) in dry solvents (200 ml), typically benzene. To the resultant mixtures were added the transesterification catalysts: compound **8** (0.53 mmol) and butylstannonic acid (1.7 mmol) for the mono- and disubstitution reactions respectively. The so-prepared suspensions were then heated at reflux for 1 to 3 days, then filtered off through a column of florisil to remove the organometallic species and concentrated *in vacuo*. The residues were purified by semi-preparative scale HPLC and the fractions were collected for the main products. In each case the resultant fractions were concentrated *in vacuo* to give the following products:

2{2-[(*tert*-butoxycarbonyl)(methyl)amino]ethyl}-3-methyl (2*R*,3*R*) 5,6-dimethoxy 5,6-dimethyl-1,4-dioxane-2,3-dicarboxylate (**9**). Compound obtained as a colourless oil (1.43 g, 3.2 mmol, 93%) starting from **6**. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (s, 6H; -C-CH<sub>3</sub>), 1.44 (s, 9H; -C(CH<sub>3</sub>)<sub>3</sub>), 2.90 (s, 3H; CH<sub>3</sub>-N-), 3.30 (s, 6H; -O-CH<sub>3</sub>), 3.45 (m, 2H; -N-CH<sub>2</sub>-), 3.74 (s, 3H; -CO<sub>2</sub>CH<sub>3</sub>), 4.24 (m, 2H; -CH<sub>2</sub>-O-), 4.50 ppm (m, 2H; -CH-O-). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 17.5 (-C-CH<sub>3</sub>), 28.7 (-C(CH<sub>3</sub>)<sub>3</sub>), 35.5 (-N-CH<sub>3</sub>), 47.3 (-N-CH<sub>2</sub>-), 48.4 (-O-CH<sub>3</sub>), 52.4 (-CO<sub>2</sub>CH<sub>3</sub>), 64.2 (-CH<sub>2</sub>-O-), 68.7 (-CH-O-), 80.0 (-C(CH<sub>3</sub>)<sub>3</sub>), 99.2 (-C-CH<sub>3</sub>), 154.9 (-N-CO<sub>2</sub>tBu), 167.9 ppm (-CO<sub>2</sub>-R). IR ν<sub>max</sub> (neat): 1043, 1153, 1394, 1459, 1700, 1749, 2959 cm<sup>-1</sup>. Elemental analysis calcd (%) for C<sub>19</sub>H<sub>33</sub>NO<sub>10</sub>: C 52.40, H 7.64, N 3.22; found: C 51.96, H 7.52, N 3.35.

Bis{2-[(*tert*-butoxycarbonyl)(methyl)amino]ethyl} (2*R*,3*R*)-5,6-dimethoxy-5,6-dimethyl-1,4-dioxane-2,3-dicarboxylate (**10**). This compound was obtained as a colourless oil (2.00 g, 3.47 mmol, 99%) starting from **6**. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.30 (m, 6H; -C-CH<sub>3</sub>), 1.42 (s, 18H; -C(CH<sub>3</sub>)<sub>3</sub>), 2.91 (s, 6H; CH<sub>3</sub>-N-), 3.43 (m, 4H; -N-CH<sub>2</sub>-), 4.22 (m, 4H; -CH<sub>2</sub>-O-), 4.47 ppm (2H; -CH-O-). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 17.7 (-C-CH<sub>3</sub>), 28.6 (-C(CH<sub>3</sub>)<sub>3</sub>), 35.8 (-N-CH<sub>3</sub>), 48.6 (-N-CH<sub>2</sub>-), 52.8 (-O-CH<sub>3</sub>), 64.4 (-CH<sub>2</sub>-O-), 68.6 (-CH-O-), 80.1 (-C(CH<sub>3</sub>)<sub>3</sub>), 99.4 (-C-CH<sub>3</sub>), 155.8 (-N-CO<sub>2</sub>tBu), 167.9 ppm (-CO<sub>2</sub>-CH<sub>2</sub>-). Elemental analysis calcd (%) for C<sub>26</sub>H<sub>46</sub>N<sub>2</sub>O<sub>12</sub>: C 53.97, H 8.01, N 4.84; found: C 54.12, H 7.88, N 4.65.

4-{2-[(*tert*-butoxycarbonyl)(methyl)amino]ethyl}-5-methyl (4*R*,5*R*)-2-phenyl-1,3-dioxolane-4,5-dicarboxylate (**11**). This compound was obtained as a colourless oil (0.72 g, 1.76 mmol, 46.8%) starting from **7**. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.41 (m, 9H; -C(CH<sub>3</sub>)<sub>3</sub>), 2.86 (s, 3H; CH<sub>3</sub>-N-), 3.28 (s, 2H; -N-CH<sub>2</sub>-), 3.88 (m, 3H; -CO<sub>2</sub>CH<sub>3</sub>), 4.24 (m, 2H; -CH<sub>2</sub>-O-), 4.86 (m, 2H; -CH-O-), 6.07 (s, 1H; -CH-Ph), 7.42 ppm (m, 5H; HAr). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 28.6 (-C(CH<sub>3</sub>)<sub>3</sub>), 35.3 (-N-CH<sub>3</sub>), 47.4 (-N-CH<sub>2</sub>-

), 52.8 (-CO<sub>2</sub>CH<sub>3</sub>), 63.7 (-CH<sub>2</sub>-O-), 77.7 (-CH-O-), 80.1 (-C(CH<sub>3</sub>)<sub>3</sub>), 98.9 (-CH-Ph), 126.7, 127.6 and 129.2 (HC<sup>Ar</sup>), 135.2 (C<sup>Ar</sup>), 155.2 (-N-CO<sub>2</sub>tBu), 167.9 ppm (-CO<sub>2</sub>R). Elemental analysis calcd (%) for C<sub>20</sub>H<sub>27</sub>NO<sub>8</sub>: C 58.67, H 6.65, N 3.42; found: C 58.55, H 6.63, N 3.57.

*Bis*{2-[(*tert*-butoxycarbonyl)(methyl)amino]ethyl} (4*R*,5*R*)-2-phenyl-1,3-dioxolane-4,5-dicarboxylate (**12**). This compound was obtained as a colourless oil (1.91 g, 3.46 mmol, 92%) starting from **7**. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.43 (s, 18H; -C(CH<sub>3</sub>)<sub>3</sub>), 2.91 (s, 6H; CH<sub>3</sub>-N-), 3.46 (m, 4H; -N-CH<sub>2</sub>-), 4.30 (m, 4H; -CH<sub>2</sub>-O-), 4.92 (d, 2H; *J*=17.9Hz, -CH-O-), 6.09 (s, 1H; -CH-Ph), 7.44 ppm (m, 5H; H<sub>Ar</sub>). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 28.7 (-C(CH<sub>3</sub>)<sub>3</sub>), 35.8 (-N-CH<sub>3</sub>), 47.8 (-N-CH<sub>2</sub>-), 64.4 (-CH<sub>2</sub>-O-), 77.7 (-CH-O-), 80.3 (-C(CH<sub>3</sub>)<sub>3</sub>), 107.0 (-CH-Ph), 127.4, 128.5 and 130.1 (HC<sup>Ar</sup>), 135.6 (C<sup>Ar</sup>), 155.3 (-N-CO<sub>2</sub>tBu), 169.3 ppm (-CO<sub>2</sub>CH<sub>3</sub>). Elemental analysis calcd (%) for C<sub>27</sub>H<sub>40</sub>N<sub>2</sub>O<sub>10</sub>: C 58.68, H 7.30, N 5.07; found: C 58.32, H 7.78, N 4.98.

*Bis*{2-[(benzyl)(methyl)amino]ethyl} (2*R*,3*R*)-2,3-dihydroxybutanedioate (**18**). This compound was obtained as a yellowish oil (2.06 g, 3.46 mmol, 92%) starting from **7** and subsequent deprotection with Pd/C in ethanol. The product was purified by flash chromatography on silica with hexane:diethyl ether 50:50 vol. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 39.5 (-N-CH<sub>3</sub>), 54.8 (-N-CH<sub>2</sub>-), 60.5 (-N-CH<sub>2</sub>-Ph), 62.1 (-CH<sub>2</sub>-O-), 74.1 (-CH-O-), 126.7, 128.1 and 128.6 (HC<sup>Ar</sup>), 135.6 (C<sup>Ar</sup>), 137.7 (-C<sup>Ar</sup>), 169.0 ppm (-CO<sub>2</sub>CH<sub>2</sub>-). Elemental analysis calcd (%) for C<sub>24</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>: C 64.85, H 7.26, N 6.30; found: C 64.98, H 7.27, N 6.32.

Cleavage of transesterification products

After transesterification reactions and with the purpose of using modified tartrates as chiral ligands in the asymmetric epoxidation of cinnamyl alcohol, the protecting groups were removed as follows:

i) Benzyl acetal protected transesters were treated with catalytic amounts Pd/C (10%) in methanol under H<sub>2</sub> atmosphere for at least 24 h. The reactions were carried out until no substrate was detected by TLC and then filtered and concentrated *in vacuo*.

ii) The 2,3-butanedione and BOC protecting groups were removed by acid treatment with TFA in CH<sub>2</sub>Cl<sub>2</sub>. The reactions were carried out in ultrasonic bath until completion and then concentrated in vacuo. The resultant products were purified by crystallization from MeOH/CH<sub>2</sub>Cl<sub>2</sub> at -30°C.

*1*-{2-[(*tert*-butyloxycarbonyl)(methyl)amino]ethyl} 4-methyl (2*R*,3*R*)-2,3-dihydroxybutanedioate (**13**). Starting from **11** (1.0g, 2.44 mmol) and using deprotection procedure i), the title product was obtained as a light yellow oil (0.78 g, 2.43 mmol, 99%). <sup>1</sup>H NMR (400 MHz, DMSO-D<sub>3</sub>): δ = 1.38 (s, 9H; -C(CH<sub>3</sub>)<sub>3</sub>), 2.80 (s, 3H; CH<sub>3</sub>-N-), 3.41 (m, 2H; -N-CH<sub>2</sub>-), 3.64 (s, 3H; -CO<sub>2</sub>CH<sub>3</sub>), 4.15 (2xt, 2H; *J*=4.8Hz, *J*=11.8Hz, *J*=17.4Hz, -CH<sub>2</sub>-O-), 4.39 ppm (m, 2H; -CH-OH). <sup>13</sup>C NMR (100 MHz, DMSO-D<sub>3</sub>): δ = 27.6 (-C(CH<sub>3</sub>)<sub>3</sub>); 33.8 (-N-CH<sub>3</sub>); 46.7 (-N-CH<sub>2</sub>-); 51.2 (-CO<sub>2</sub>CH<sub>3</sub>); 62.0 (-CH<sub>2</sub>-O-); 72.1 (-CH-OH); 78.3 (-C(CH<sub>3</sub>)<sub>3</sub>); 153.8 (-N-CO<sub>2</sub>tBu); 170.7 ppm (-CO<sub>2</sub>R). Elemental analysis calcd (%) for C<sub>13</sub>H<sub>23</sub>NO<sub>8</sub>: C 48.59, H 7.21, N 4.36; found: C 48.77, H 7.23, N 4.42.

*Bis*{2[(*tert*-butyloxycarbonyl)(methyl)amino]ethyl} (2*R*,3*R*)-2,3-dihydroxybutanedioate (**14**). Starting from **12** (1.0 g, 1.80 mmol) and the title compound was obtained using deprotection method i) (0.82 g, 1.76 mmol, 97.5%). <sup>1</sup>H NMR (400 MHz, DMSO-D<sub>3</sub>): δ = 1.39 (s, 18H; -C(CH<sub>3</sub>)<sub>3</sub>), 2.84 (s, 6H; CH<sub>3</sub>-N-), 3.47 (m, 4H; -N-CH<sub>2</sub>-), 4.25 (s, 4H; -

$CH_2-O-$ ), 4.50 ppm (s, 2H;  $-CH-OH$ ).  $^{13}C$  NMR (100 MHz, DMSO- $D_3$ ):  $\delta$  = 28.2 ( $-C(CH_3)_3$ ), 35.1 ( $-N-CH_3$ ), 47.4 ( $-N-CH_2-$ ), 62.9 ( $-CH_2-O-$ ), 72.0 ( $-CH-OH$ ), 79.5 ( $-C(CH_3)_3$ ), 155.5 ( $-N-CO_2tBu$ ), 170.4 ppm ( $-CO_2CH_3$ ). IR  $\nu_{max}$  (neat): 1203, 1433, 1463, 1679, 1759, 3030, 3345  $cm^{-1}$ . Elemental analysis calcd (%) for  $C_{20}H_{36}N_2O_{10}$ : C 51.71, H 7.81, N 6.03; found: C 51.85, H 7.74, N 5.97.

*1-Methyl 4-[2-(methylamino)ethyl] (2R,3R)-2,3-dihydroxybutanedioate (3)*. Starting from **13** (0.583 g; 1.81 mmol), using deprotection method ii) gave compound **3** (0.280g, 1.27 mmol, 70%) is achieved as needle-shaped crystals after crystallization from  $CH_2Cl_2/EtOH$ . The same compound was produced starting from **9** using procedure iii). m.p. = 123,32°C.  $^1H$  NMR (400 MHz, DMSO- $D_3$ ):  $\delta$  = 2.60 (s, 3H;  $CH_3-N-$ ), 3.22 (s, 2H;  $-N-CH_2-$ ), 3.66 (s, 3H;  $-CO_2CH_3$ ), 4.28 (m, 2H;  $-CH_2-O-$ ), 4.53 ppm (m, 2H;  $-CH-OH$ ).  $^{13}C$  NMR (100 MHz, DMSO- $D_3$ ):  $\delta$  = 32.1 ( $-N-CH_3$ ), 46.2 ( $-N-CH_2-$ ), 51.2 ( $-CO_2CH_3$ ), 59.1 ( $-CH_2-O-$ ), 71.5 ( $-CH-OH$ ), 170.7 ppm ( $-CO_2R$ ). IR  $\nu_{max}$  (KBr): 1158, 1253, 1399, 1459, 1694, 1754, 2975, 3470  $cm^{-1}$ . Elemental analysis calcd (%) for  $C_8H_{15}NO_6$ : C 43.44, H 6.83, N 6.33; found: C 43.67, H 6.92, N 6.52.

*(R,R) bis[2-(methylamino)ethyl] tartrate (4)*. Starting from **14** (0.634 g; 1.36 mmol) using deprotection method ii) gave compound **4** (0.312, 1.18 mmol, 87%) as a solid from  $CH_2Cl_2/EtOH$ . The same compound was produced starting from **10** using procedure iii). m.p.= 133.73°C.  $^1H$  NMR (400 MHz, DMSO- $D_3$ ):  $\delta$  = 2.61 (s, 6H;  $CH_3-N-$ ), 3.22 (m, 4H;  $-N-CH_2-$ ), 4.31 (m, 4H;  $-CH_2-O-$ ), 4.63 ppm (d, 2H;  $J=0.8Hz$ ,  $-CH-OH$ ).  $\delta_C$  ppm (DMSO- $D_6$ , 100 MHz): 32.4 ( $-N-CH_3$ ), 46.3 ( $-N-CH_2-$ ), 59.7 ( $-CH_2-O-$ ), 72.0 ( $-CH-OH$ ), 170.4 ppm ( $-CO_2CH_3-$ ). Elemental analysis calcd (%) for  $C_{10}H_{20}N_2O_6$ : C 45.45, H 7.63, N 10.60; found: C 45.31, H 7.70, N 10.67.

Silsesquioxane derived molecules

(*N*-methyl, methylphenylethyl-POSS)-aminoethanol, **15**. A solution of chloromethyl)phenylethyl-POSS (1-[2-[(Chloromethyl)phenyl]ethyl]-3,5,7,9,11,13,15-heptacyclopentylpentacyclo[9.5.1.1<sup>3,9</sup>.1<sup>5,15</sup>.1<sup>7,13</sup>]octasiloxane) (1 g, 1 mmol) in dichloromethane was treated with **2** (1,5 eq) and pyridine (0,2 eq). The resultant solutions was heated to reflux and stirred for 24 hours. After reaction completion the solvent was removed under reduced pressure and the crude reaction was suspended in a small quantity of dichloromethane. The product was then recovered by precipitation in acetonitrile in nearly quantitative yield. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.93 (m, 2H; -Si-CH<sub>2</sub>-), 0.96 (m, 7H; -Si-CH), 1.47, 1.57 and 1.73 (m, 56H; -(CH<sub>2</sub>)-), 2.33 (s, 3H; CH<sub>3</sub>-N-), 2.65 (m; 2H; -N-CH<sub>2</sub>-), 2.71 (m; 2H; -CH<sub>2</sub>-Ph-), 3.80 (s, 3H; -O-CH<sub>3</sub>), 3.83 (m, 2H; -CH<sub>2</sub>-OH), 3.87 (m, 2H; Ar-CH<sub>2</sub>-N-), 7.24 and 7.75 ppm (m, 8H; -CH<sup>Ar</sup>-). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 22.4, 27.2 (C<sup>Cp</sup>), 41.1 (CH<sub>3</sub>-N-), 49.9 (Si-CH-), 51.5 (-O-CH<sub>3</sub>), 57.1 (-CH<sub>2</sub>-OH), 57.8 (-Ph-CH<sub>2</sub>-N), 61.4 (-N-CH<sub>2</sub>-), 126.2, 129.1, 130.2 and 140.4 ppm (-C<sup>Ar</sup>). IR ν<sub>max</sub> (neat): 504, 1115, 1450, 2860, 2950, 3431 cm<sup>-1</sup>. Elemental analysis calcd (%) for C<sub>47</sub>H<sub>81</sub>NO<sub>13</sub>Si<sub>8</sub>: C 51.66, H 7.47, N 1.28; found: C 51.51, H 7.52, N 1.25.

**16**. A solution of **15** (0.750 g, in benzene was treated with **7** (1.0 eq) in presence of butylstannonic acid (0,05 eq). The resultant suspension was then refluxed for 3 days, using a dean-stark apparatus to displace the equilibrium, filtered off through a column of florisil and the clean solution concentrated in vacuo to give a yellow solid. The crude product was suspended in 5 mL of dichloromethane and 50 mL of acetonitrile were added to precipitate the silsesquioxane products. The title compound was then purified to give a white product by flash chromatography on silica using n-hexane:diethyl ether (0,725 g, 0,53 mmol, 76%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.91 (m, 2H; -Si-CH<sub>2</sub>-), 1.00 (m, 7H; -Si-CH), 1.42, 1.50 and 1.72 (m, 56H; -(CH<sub>2</sub>)-), 2.41 (s, 3H; CH<sub>3</sub>-N-),

2.65 (m; 2H; -N-CH<sub>2</sub>-), 2.68 (m; 2H; -CH<sub>2</sub>-Ph-), 3.68 (m, 2H; -CH<sub>2</sub>-O-), 3.76 (s, 3H; -O-CH<sub>3</sub>), 3.85 (m, 2H; Ar-CH<sub>2</sub>-N-), 5.01 (m, 2H; -CH-O-), 6.17 (s, 1H; -CH-Ph), 7.24, 7.43, 7.75 ppm (m, 18H; *H*-Ar). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 22.4 and 27.2 (C<sup>Cp</sup>), 40.9 (CH<sub>3</sub>-N-), 49.9 (Si-CH-), 51.2 (-O-CH<sub>3</sub>), 58.4 (-Ph-CH<sub>2</sub>-N), 61.9 (-CH<sub>2</sub>-O-), 62.6 (-N-CH<sub>2</sub>-), 80.1 (-CH-O-), 127.4, 128.5, 130.2, 135.5 and 142.1 (-C<sup>Ar</sup>), 169.5 ppm (-CO<sub>2</sub>-). IR ν<sub>max</sub> (neat): 501, 1112, 1450, 1746, 2868, 2950 cm<sup>-1</sup>. Elemental analysis calcd (%) for C<sub>59</sub>H<sub>91</sub>NO<sub>18</sub>Si<sub>8</sub>: C 53.40, H 6.91, N 1.06; found: C 53.47, H 6.74, N 0.98.

**17.** The cleavage of the benzilidene acetal group in **16** (0.4 g, 0.36 mmol) was carried out using the same abovementioned deprotection method i) giving **17** as a white solid after washing with acetonitrile (0.417 g, 0.32 mmol, 89%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 0.93 (m, 2H; -Si-CH<sub>2</sub>-), 0.97 (m, 7H; -Si-CH), 1.45, 1.51 and 1.73 (m, 56H; -(CH<sub>2</sub>-), 2.39 (s, 3H; CH<sub>3</sub>-N-), 2.67 (m; 2H; -N-CH<sub>2</sub>-), 2.71 (m; 2H; -CH<sub>2</sub>-Ph-), 3.74 (m, 2H; -CH<sub>2</sub>-O-), 3.79 (s, 3H; -O-CH<sub>3</sub>), 3.83 (m, 2H; Ar-CH<sub>2</sub>-N-), 4.58 (m, 2H; -CH-OH), 7.21 and 7.43 ppm (m, 8H; *H*-Ar). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 22.5 and 27.2 (C<sup>Cp</sup>), 41.2 (CH<sub>3</sub>-N-), 50.0 (Si-CH-), 51.4 (-O-CH<sub>3</sub>), 58.0 (-Ph-CH<sub>2</sub>-N), 62.3 (-CH<sub>2</sub>-O-), 62.5 (-N-CH<sub>2</sub>-), 73.0 (-CH-OH), 127.4, 128.5, 130.5 and 141.9 (-C<sup>Ar</sup>), 170.9 ppm (-CO<sub>2</sub>-). IR ν<sub>max</sub> (neat): 501, 1112, 1746, 2868, 2950, 3411 cm<sup>-1</sup>. Elemental analysis calcd (%) for C<sub>52</sub>H<sub>87</sub>NO<sub>18</sub>Si<sub>8</sub>: C 50.41, H 7.08, N 1.13; found: C 50.29, H 7.04, N 1.19.

General procedure for the asymmetric epoxidation of allylic alcohols

For comparison purposes the chiral ligands prepared accordingly to the above mentioned procedures have been used in the asymmetric epoxidation of several allylic alcohols in presence of titanium isopropoxide as the metallic source and tert-butyl hydroperoxide as the oxidant. In a typical assay 1.0 g of 4A molecular sieves were suspended, under inert atmosphere, in 50 ml of dry CH<sub>2</sub>Cl<sub>2</sub> before cooling the resultant

suspension down to  $-20^{\circ}\text{C}$ . The next step consisted of the addition of 42 mg of freshly distilled  $\text{Ti}(\text{OiPr})_4$  (0.15 mmol), an equimolar amount of the chiral ligand (0.15 mmol) and 2.15 mL of an anhydrous solution of TBHP in dry  $\text{CH}_2\text{Cl}_2$  (120 mmol). The resultant suspension was then stirred for 1 hour before adding the substrate (30 mmol) by dropping during 1 hour using a syringe pump. The reaction was then stirred for another additional hour. The resultant epoxides were then recovered and purified by semi-preparative HPLC. The isolated products were analyzed either by using a GC, fitted with a chiral capillary column (Chiraldex G-TA; 40m x 0.25mm) and a FID detector, or by HPLC using n-Heptane:Isopropanol in a chiral column ((S,S)-Whelk-01; 25cm x 2.5mm) fitted with a UV diode-array detector.

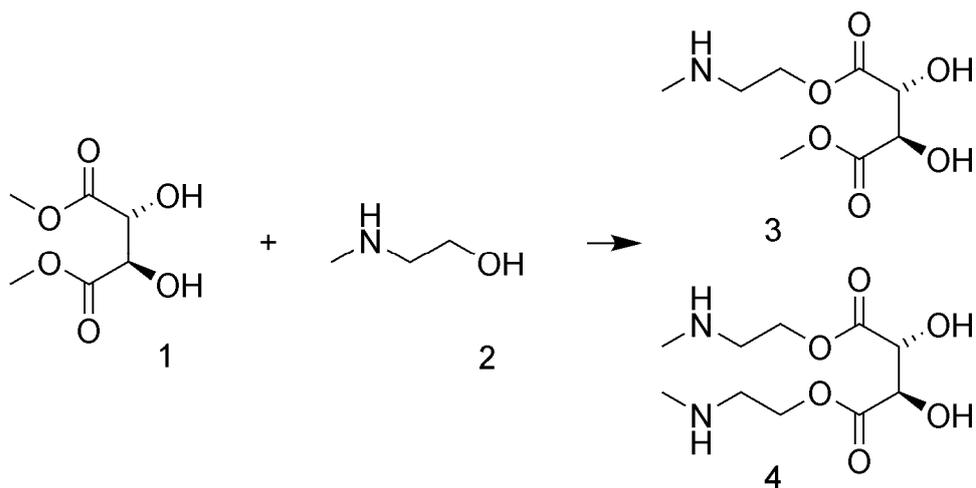
## References

- [1] Katsuki T, Sharpless KB. The first practical method for asymmetric epoxidation. *J Am Chem Soc* 1980;102:5974-5976.
- [2] Martin VS, Woodard SS, Katsuki T, Yamada Y, Ikeda M, Sharpless KB. Kinetic resolution of racemic allylic alcohols by enantioselective epoxidation. A route to substances of absolute enantiomeric purity?. *J Am Chem Soc* 1981;103:6237-6240.
- [3] Hanson RM, Sharpless KB. Procedure for the catalytic asymmetric epoxidation of allylic alcohols in the presence of molecular sieves. *J Org Chem* 1986;51:1922-1925.
- [4] The topic 'Sharpless asymmetric epoxidation' gives 581 entries in a search performed on SciFinder Scholar.

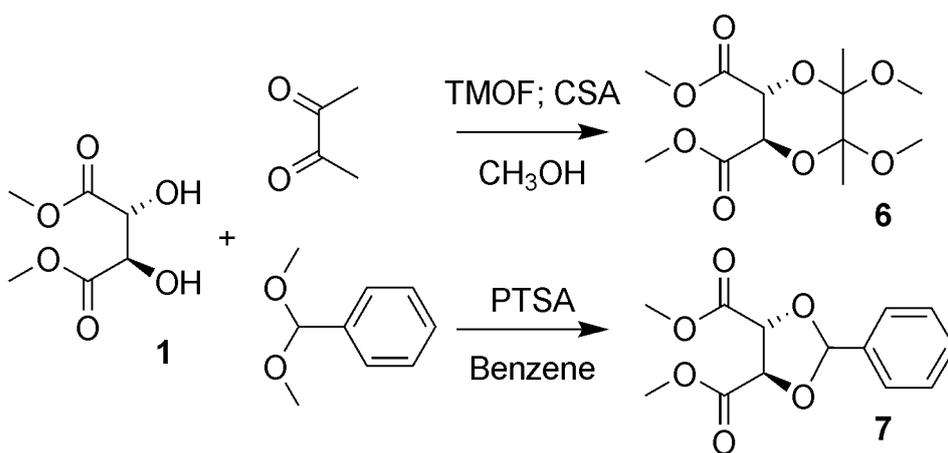
- [5] Gao Y, Sharpless KB. Asymmetric synthesis of both enantiomers of Tomoxetine and Fluoxetine. Selective reduction of 2,3-Epoxypropenyl alcohol with Red-Al. *J Org Chem* 1988;53:4081-4084.
- [6] Katsuki T, Martin VS. *Organic Reactions*. New York: Wiley; 1996. 1-299 p.
- [7] Canali L, Karjalainen JK, Sherrington DC, Hormi O. Efficient polymer-supported sharpless alkene epoxidation catalyst. *Chem Commun* 1997:123-124.
- [8] Meunier D, Piechaczyk A, de Mallmann A, Basset JM. Silica supported tantalum catalysts for asymmetric epoxidations of allylic alcohols. *Angew Chem Int Ed* 1999;38:3540-3542.
- [9] Xiang S, Zhang Y, Xin Q, Li C. Asymmetric epoxidation of allylic alcohol on organic-inorganic hybrid chiral catalysts grafted onto the surface of silica and in the mesopores of MCM-41. *Angew Chem Int Ed Engl* 2002;41:821-824.
- [10] Zhao W, Hao ZP, Hu C, Li J, Xu X. The epoxidation of allylic alcohol on Ti-complex/MCM-48 catalysts. *Microporous Mesoporous Mater* 2008;112:133-137.
- [11] Riollet V, Quadrelli EA, Copéret C, Basset JM, Andersen RA, Köhler K, Böttcher RM, Herdtweck E. Grafting of  $[Mn(CH_2tBu)_2(tmeda)]$  on silica and comparison with its reaction with a silsesquioxane. *Chem Eur J* 2005;11:7358-7365.
- [12] Mintcheva N, Tanabe M, Osakada K. Preparation and structure of new phenylplatinum complexes containing silsesquioxane as a monodentate or bidentate ligand. *Organometallics* 2006;25:3776-3783.
- [13] Pérez Y, Pérez Quintanilla D, Fajardo M, Sierra I, del Hierro I. Immobilization of titanium chiral alkoxides on SBA-15 and modelling the active sites of heterogeneous catalyst using titanium silsesquioxane complexes. *J Mol Catal A* 2007;271:227-237.

- [14] Kawasaki T, Ishikawa K, Sekibata H, Sato I, Soai K. Enantioselective synthesis induced by chiral organic-inorganic hybrid silsesquioxane in conjunction with asymmetric autocatalysis. *Tetrahedron Lett* 2004;45:7939-7941.
- [15] Ionescu G, van der Vlugt JI, Abbenhuis HCL, Vogt D. Synthesis and applications of chiral phosphite ligands derived from incompletely condensed silsesquioxane backbones. *Tetrahedron Asymmetry* 2005;16:3970-3975.
- [16] Barlow JS, Dixon DJ, Foster AC, Ley SV, Reynolds DJ. New building blocks for efficient and highly diastereoselective polyol production – synthesis and utility of (*R',R',S,S*) and (*S',S',R,R*)-2,3-butane diacetal protected butane tetrol derivatives. *J Chem Soc Perkin Trans 1* 1999;12:1627-1630.
- [17] Seebach D. *Modern Synthetic Methods*. Frankfurt/Main: Wiley. 1980. 113-171 p.
- [18] Dixon DJ, Foster AC, Ley SV, Reynolds DJ. Preparation of desymmetrised meso-tartrate derivatives – synthesis and utility of (*R',R',S,R*)-2,3-butane diacetal protected butane tetrol. *J Chem Soc Perkin Trans 1* 1999;12:1631-1633.
- [19] Uri A, Tuulmets A, Palm V. Transesterification of esters of carboxylic acids by titanium-alcoholates 2. Transesterification of esters of aromatic acids. *Organic Reactivity (Tartu)* 1983;20:122-131.
- [20] Furlán RLE, Mata EG, Mascaretti OA. Butylstannonic acid catalyzed transesterification of carboxylic esters. *Tetrahedron Lett* 1998;39:2257-2260.
- [21] Kociensky PJ. *Protecting groups*. Stuttgart: Thieme. 1994. 96-102 p.
- [22] Shimizu I, Matsumoto Y, Shoji K, Ono T, Satake A, Yamamoto A. Enantioselective elimination reaction of a 6,6-Membered Bicyclic Allylic Carbonate. Importance of chirality reversal depending on the palladium-chiral phosphine ratio. *Tetrahedron Lett* 1996;37:7115-7118.

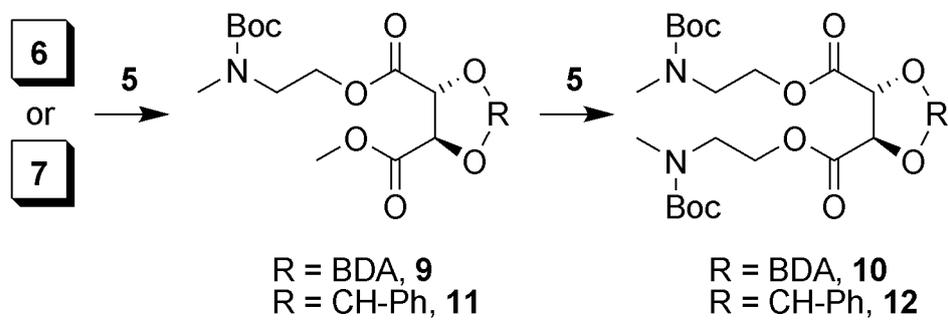
- [23] Altava B, Berruguete MI, Fraile JM, Garcia JI, Luis SV, Mayoral JA, Vicent MJ. How important is the inner matrix of supported enantiomeric catalysts? Reversal of topicity with two polystyrene backbones. *Angew Chem Int Ed* 2000;39:1503-1506.
- [24] Trost BM, Fettes A, Shireman BT. Direct catalytic asymmetric aldol additions of methyl ynones. Spontaneous reversal in the sense of enantioinduction. *J Am Chem Soc* 2004;126:2660-2661.
- [25] Arseniyadis S, Valleix A, Wagner A, Miokowski C. Kinetic resolution of amines: a highly enantioselective and chemoselective acetylating agent with a unique solvent-induced reversal of stereoselectivity. *Angew Chem Int Ed* 2004;43:3314-3317.
- [26] Altava B, Berruguete MI, Garcia-Verdugo E, Luis SV, Vicent MJ. Functional monolytic resins for the development of enantioselective versatile catalytic minireactors with long-term stability: TADDOL supported systems. *Green Chem* 2006;8:717-726.
- [27] Reed NN, Dickerson TJ, Boldt GE, Janda KD. Enantio-reversal in the Sharpless asymmetric epoxidation reaction controlled by the molecular weight of a covalently appended achiral polymer. *J Org Chem* 2005;70:1728-1731.
- [28] Lutz F, Igarashi T, Kawasaki T, Soai K. Small amounts of chiral  $\beta$ -amino alcohols reverse the enantioselectivity of chiral catalysts in cooperative asymmetric autocatalysis. *J Am Chem Soc* 2005; 127:12206-12207.
- [29] Gao Y, Hanson RM, Klunder JM, Ko Soo Y, Masamune H, Sharpless KB. Catalytic asymmetric epoxidation and kinetic resolution: modified procedures including in situ derivatization. *J Am Chem Soc* 1987;109:5765-5780.



Scheme 1



Scheme 2



Scheme3

