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The synthesis and use in asymmetric epoxidation of metal salen complexes derived from enantiopure *trans*-cyclopentane- and cyclobutane-1,2-diamine

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Abstract—A complete synthesis of enantiopure *trans*-cyclopentane-1,2-diamine and *trans*-cyclobutane-1,2-diamine is described. These diamines have been used as components of novel chiral salen ligands whose chromium and manganese complexes were then evaluated as oxygen transfer agents in the asymmetric epoxidation of alkenes.

1. Introduction

There continues to be great interest in the development of general reagents for catalytic asymmetric alkene epoxidation,[1–3] the most notable successes being the systems of Sharpless and Jacobsen/Katsuki[1,3,4] The chiral manganese salen complex **1** developed by Jacobsen and co-workers was the first catalyst to enable the asymmetric epoxidation of unfunctionalised alkenes in high ee. This and other similar manganese complexes catalyse the epoxidation of *Z*- and tri-substituted alkenes, often with excellent selectivity (e.g. 92% ee in the epoxidation of (*Z*)-β-methylstyrene). However, the major limitation of **1** is the low selectivity displayed in the epoxidation of *E*-1,2-disubstituted alkenes (e.g. 22% ee in the epoxidation of (*E*)-β-methylstyrene).

For some time we have been working on the development of epoxidation catalysts based on a chromium salen template (**2**,**3**, Table 1).[5–12] The stability of the oxochromium(V) species[13] **3** allows the reaction to be run in both stoichiometric and catalytic mode. The most notable aspect of our system is that *E*-alkenes give much better selectivity than *Z* isomers. This is in contrast to the manganese salen based system and indeed nearly all other metal oxo based oxidants.[14,15] Very recently we have improved the ee in our standard test reaction, the epoxidation of (*E*)-β-methylstyrene, to 92% using complex **3** (L = triphenylphosphine oxide (Ph_3PO)) in stoichiometric mode.[9]

We[2,6,7,12] and others[16–19] have suggested that the stereoselection obtained using manganese and chromium salen complexes is due to a non-planar complex. This non-planarity can be observed in a number of X-ray crystal structures[16] and arises as a result of the sp^3 centres on the diimine bridge of the ligand. Thus, the N–C–C–N dihedral angle (Fig. 1) between the two nitrogen atoms of the ligand is a measure of the resultant twist or step in the complex. For complexes derived from *trans*-cyclohexane-1,2-diamine the rigid nature of the cyclohexane ring, with a set N–C–C–N dihedral angle, is a major influence on the complex conformation. Since our group has previously suggested that chromium salen complexes facilitate selective epoxidation of *E*-alkenes by their stepped nature[6] we felt that investigation of smaller ring diamines might lead to more enantioselective epoxidation catalysts by increasing the N–C–C–N dihedral angle and thus altering the ligand conformation in a favourable manner.

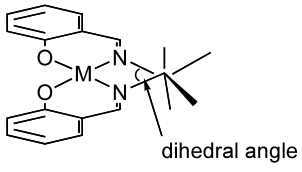

Figure 1. Illustration of the N–C–C–N dihedral angle in metal salen complexes.

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Despite the widespread use of metal salen complexes in asymmetric catalysis there has been no previous report of ligands containing such diamines (Scheme 1).

2. Results and discussion

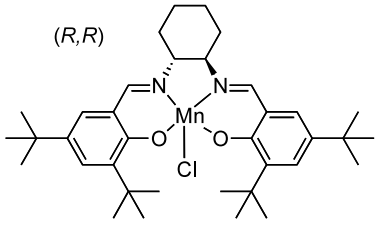
We initially investigated synthetic routes to the chiral diamines *trans*-cyclopentane-1,2-diamine **4** and *trans*-cyclobutane-1,2-diamine **5**. The easier to make appeared to be the cyclopentyl species **4**, although it is not as conformationally rigid as the cyclobutyl species **5**. Although we were particularly interested in the use of these diamines as components of chiral salen complexes they also have numerous other potential applications in asymmetric synthesis.[20,21]

2.1. Synthesis of (*R*,*R*)-*trans*-cyclopentane-1,2-diamine, 4

Two syntheses of *trans*-cyclopentane-1,2-diamine **4** had previously been reported. The route of Jaeger and Blumendal involved the reduction of cyclopentane-1,2-dione dioxime using sodium.[22] Attempts to repeat this procedure were unsuccessful and the yields obtained were considerably lower than those reported in the literature.

An alternative route reported by Potter et al.[23] involved the hydrogenation of diazide **6** over PtO_2 to yield the diamine **4**. Our initial attempts to synthesise **6** were from cyclopentene via the analogous dibromide. However, despite evaluating a variety of reaction conditions to convert the dibromide to diazide **6** we found that competing elimination led to a mixture of two products. Therefore, the procedure of Minisci and co-workers for the synthesis of 1,2-diazidocyclohexane **6**, directly from cyclopentene was followed.[24] This produced a 15:1 mixture of the *trans*- and *cis*-isomers of **6** in poor yield (13%). Separation of the small amount of *cis* isomer was possible by column chromatography; however, this was not carried out in most runs of the experiment since separation of the isomers was possible in the later resolution step.

Reduction of the diazide by hydrogenation over PtO_2 proved unsuccessful, contrary to the report of Potter et al.[23] Instead we found that Pd/C was effective and using hydrogen at 3 atm pressure gave *trans*-cyclopentane-1,2-diamine **4** in 73% yield (Scheme 2). This racemic material was resolved using tartaric acid according to the method of Toftlund and Pedersen.[25] The assignment of an (*R*,*R*) configuration to the resolved diamine is on the basis of a crystal structure of the tartrate salt obtained by Toftlund and Pedersen.[25] A procedure from the same authors was used to release the enantiopure diamine,[25] which, due to its air sensitivity, was used immediately for the generation of salen ligands. While this work was in progress an alternative method for the preparation of **4** was reported; however, this starts from the expensive *trans*-cyclopentane-1,2-dicarboxylic acid.[26]



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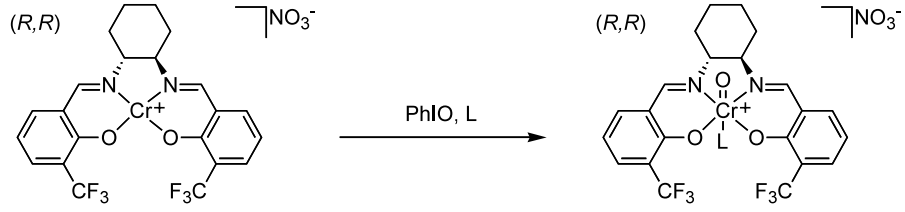
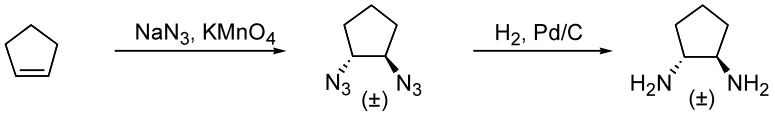


2 **3**

Scheme 1.



6 **4**

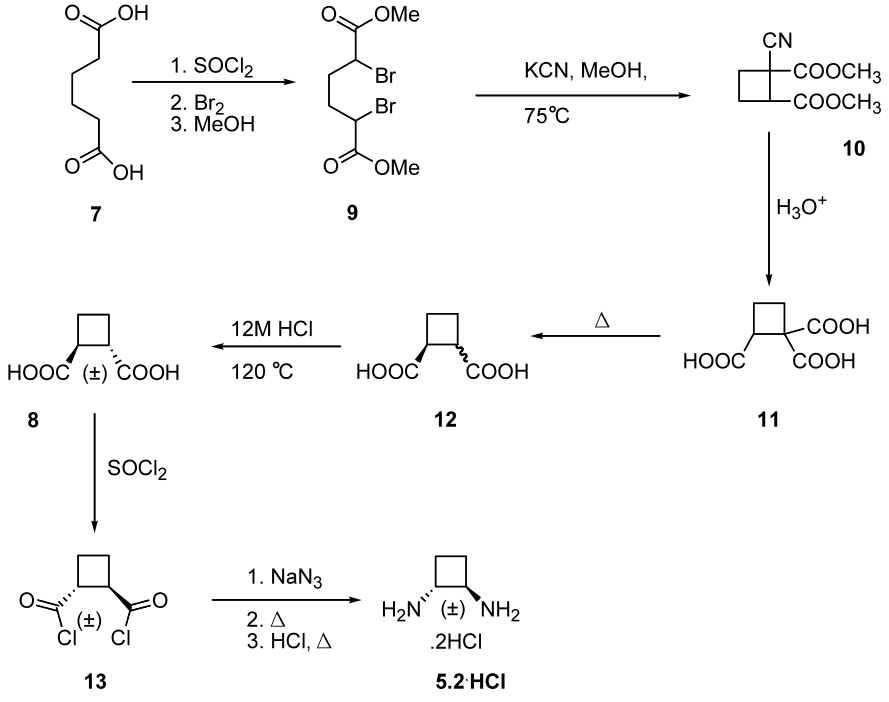
Scheme 2.

2.2. Synthesis of (+)-*trans*-cyclobutane-1,2-diamine, 5

Again, only two routes to *trans*-cyclobutane-1,2-diamine **5** have been published. The most recent of these was developed from a by-product of a different reaction, which was being investigated by the same workers.[27] The starting iminonitrile species requires a three step synthesis in its own right[28] so this route was not examined further.

Instead the synthesis carried out by Buchman et al. was used as a starting point.[29] The general scheme of this synthesis involves the conversion of adipic acid **7** into *trans*-cyclobutane-1,2-dicarboxylic acid **8**. A Schmidt rearrangement, using hydrazoic acid, is then used to convert this to the analogous diamine **5**. At approximately the same time, a similar synthesis was reported by Shuikina, which involved a Hoffman rearrangement for the conversion of the diacid to the diamine.[30] Since the publication of these works a small number of reports have been made of their use, either as a whole, or in part.[31–33] Watson and O'Neill reported improved yields for the initial step[34] and Cory and co-workers found that the Schmidt rearrangement was unsuccessful and used the Curtius rearrangement instead.[31] However, none of these authors described their synthesis in detail, and we therefore feel it is appropriate to describe the route we followed. This is shown in Scheme 3 and was developed on the basis of all the work mentioned above. The formation of the dibromo-dimethyl ester of adipic acid **9** was carried out as a one pot procedure giving 57% yield.[34] The ring-closure step to yield **10** was carried out using potassium cyanide with suitable precautions to ensure a basic environment. Buchman's procedure[29] for this step calls for distillation of the reaction mixture to obtain the product; however, we found it more satisfactory to remove the excess methanol by distillation at atmospheric pressure and then flush the residue through a pad of silica gel using CH_2Cl_2. In this manner a mixture of the two isomers of nitrile diester **10** was obtained in 71% yield. It was possible to separate these products since one crystallises from the mother liquor, leaving the other behind as a liquid. This separation was carried out initially; however, it only leads to loss of material and is unnecessary since the distinction between isomers is immediately lost in the subsequent hydrolysis to triacid **11**, heating of which (180°C at 20 mmHg) yields cyclobutane-1,2-diacid as a 70:30 mixture of *trans*- and *cis*-isomers **12**. The combined hydrolysis and decarboxylation were carried out in 65% yield.

This mixture of isomers of **12** was equilibrated by heating in 12 M HCl at 120°C for 6 days.[35] Subsequent cooling led to crystallisation of pure *trans*-isomer **8** in 54% yield. After further heating of the mother liquor under similar conditions, a further sample of **8** was isolated. As mentioned above, Buchman and co-workers converted this diacid **8** to the diamine **5** by the Schmidt rearrangement in 55% yield.[29] However, given the difficulties in handling hydrazoic acid and the reported failure of this method[31] we instead used a Curtius rearrangement. This necessitated initial formation of the foul smelling diacid chloride **13**. Using thionyl chloride this was accomplished in 96% yield. Initially we attempted to isolate the diacyl azide derivative of **13** prior to the Curtius rearrangement, as previously reported for the cyclopropyl analogue,[36] however a small sample of the diazide exploded violently very shortly after being removed from the rotary evaporator, fortunately leading to no serious injuries. We therefore abandoned this procedure and instead used a one-pot



Scheme 3.

procedure[37] in which neither the diacylazide nor its diisocyanate rearrangement product were isolated. The diamine dihydrochloride **5·2HCl** was isolated in 46% yield, in agreement with the previous report for the cyclopropyl analogue by Sturm et al.[31]

A resolution of *trans*-cyclobutane-1,2-diamine has never previously been reported. However, diacid **8** has been resolved in reasonable yield using cinchonidine.[35] The recent development of the 'Dutch resolution' technique,[38] based on the use of mixtures of three resolving agents, had given us confidence when originally embarking on this synthesis, that resolution of the diamine would not prove problematic. The authors reported that addition of a suitable mixture or 'family' of resolving agents to a racemic substrate in the appropriate solvent led to the almost immediate formation of a salt. This salt is composed of a mixture of the substrate and each of the three resolving agents. In many cases[38] the salt contains just one substrate enantiomer in 30–50% yield after one recrystallisation. Given that tartaric acid has proved useful for resolving both the cyclohexyl and cyclopentyl analogues of **5** we chose the family of tartaric acid derivatives 'T-mix' for our initial attempts.

We did observe the formation of a salt, but to our disappointment and surprise, liberation of diamine **5** from this salt yielded only racemic material. This failure of the 'Dutch resolution' method is notable. It may be that we would have been successful using other 'families'; however, these are not readily available. On the other hand very few difunctionalised species and no diamines were reported among the many successfully resolved substrates in the original communication of Vries et al.[38]

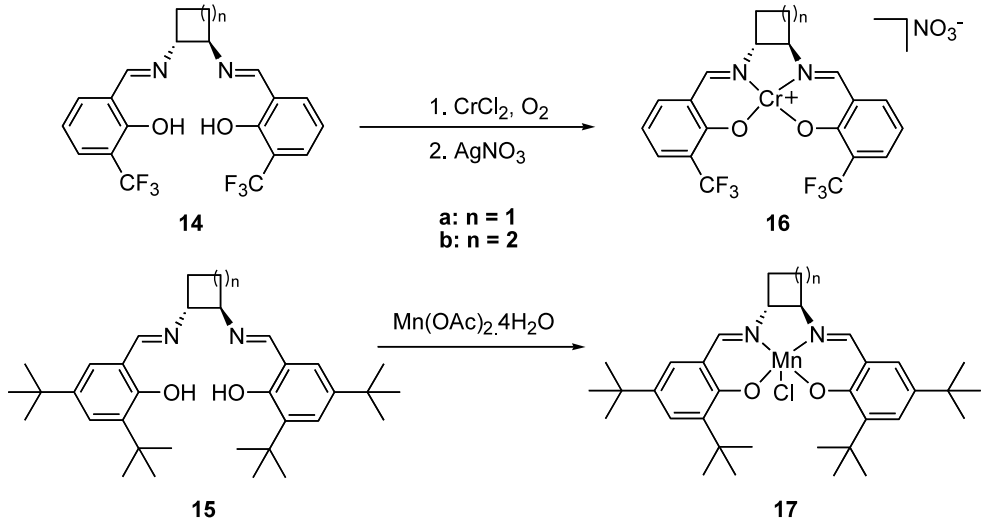
We thus resorted to tartaric acid as a resolving agent and we followed Toftlund and Pedersen's procedure for *trans*-cyclopentane-1,2-diamine **4** to give enantiopure (+)-*trans*-cyclobutane-1,2-diamine in 10% yield.[25] The enantiopurity of the resolved diamine was confirmed by chiral HPLC analysis of the derived salen ligand **14a**.

The mother liquor from the initial resolution step was reacted to regenerate the remaining diamine, and this was then reacted with unnatural (−)-tartaric acid. The salt obtained from this procedure contained, after one recrystallisation, the (−)-diamine in enantiopure form.

2.3. Synthesis of chromium and manganese salen complexes

The four salen ligands **14a**,**b** and **15a**,**b** were synthesised by simple condensation of the relevant diamine and salicylaldehyde. Formation of the (salen)Cr(III) and (salen)Mn(III) complexes of these ligands was then attempted by reaction of the appropriate salen ligand with anhydrous chromium(II) chloride[39] and manganese(II) acetate respectively (Scheme 4).[40] Using the cyclopentyl ligands **14b**, **15b** both these reactions proceeded without difficulty yielding the desired complexes **16b**, **17b**, which were characterised by electrospray mass spectroscopy and IR spectroscopy.

We then attempted to synthesise the cyclobutane-containing (salen)Cr(III) complex **16a** using chromium(II) chloride (Scheme 4). For all the (salen)Cr(III) complexes which have previously been synthesised by us, addition of chromium(II) chloride to a solution of the yellow solution of the ligand in THF leads to an immediate colour change to dark brown. Unusually we observed a green coloured solution instead. Nevertheless, the reaction was continued as before and a green solid was isolated. This was reacted with silver nitrate yielding a precipitate of silver chloride and leading to the isolation of a further green solid. The IR spectrum of this solid contained the characteristic imine stretch at 1624 cm^{-1}. However, the electrospray mass spectrum indicated that only a small proportion of the substance had the correct m/z value of 480 for **16a**. The other components of the mixture are not readily identifiable from their mass spectrum or IR spectrum.



Scheme 4.

In order to further investigate the synthetic possibilities of *trans*-cyclobutane-1,2-diamine the tetra *tert*-butyl substituted salen **15a** was also prepared. This was then reacted with manganese(II) acetate tetrahydrate in an attempt to synthesise **17a**. A brown powder was obtained as product of the reaction; however, the electrospray mass spectrum of this material showed no trace of a signal at the correct m/z of 571, instead a number of other peaks were present, with the base peak at m/z 631. We would suggest that in both the attempted insertions described above the product consisted of polymeric material. It is likely that in the cyclobutyl case the N–C–C–N angle has become too large and the ligand is no longer able to bind the metal effectively.

2.4. Asymmetric epoxidation mediated by complexes 16 and 17

We evaluated the epoxidation of (*E*)- and (*Z*)-β-methylstyrene using the four complexes **16** and **17** described above. For the chromium complexes, Ph_3PO was used as a donor ligand additive and reactions were carried out in stoichiometric mode using iodosylbenzene as terminal oxidant. The manganese salen complexes were used at a catalyst loading of 2.5 mol% with bleach as terminal oxidant.[41]

Unfortunately, but not entirely unexpectedly, epoxidation of (*E*)-β-methylstyrene using the Cr(V)=O derivative of cyclopentane diamine derived **16b** in stoichiometric mode led to a slightly reduced ee (87%) compared to the cyclohexyl case **3** (92%). We suggest that the conformational flexibility of the cyclopentane ring, which can exist in either the half-chair or envelope conformations (Fig. 2), is not favourable for achieving high ee.

The results obtained using the manganese complex **17b** are presented in Table 1 and they are compared to the results obtained with the cyclohexyl analogue **1**. Interestingly, there is a slight improvement in the selectivity and yield with respect to Jacobsen's catalyst **1** for *E*-alkenes, but a deterioration for the *Z* isomers.

Despite the apparent failure to synthesise the complexes **16a** and **17a**, the products of the attempted complexation reactions were evaluated as epoxidation catalysts. In the case of the chromium species the characteristic black colour of the derived (salen)Cr(V)=O species was not generated and the reaction product showed only a 0.2% yield of *trans*-β-methylstyrene oxide. Similarly, the product of the manganese insertion reaction gave an insignificant yield of epoxide.

3. Conclusion

1,2-Diamines have been used extensively as the source of chiral information in asymmetric synthesis[20,21] and we have drawn together here a complete synthesis of two such diamines. From these, four new chiral ligands have been synthesised with the possibility existing of numerous other derivatives. Chromium and manganese complexes of the salen ligands derived from *trans*-cyclopentane-1,2-diamine were synthesised. The chromium complex **16b** epoxidises an *E*-alkene in high ee, whereas the manganese complex **17b** shows excellent selectivity for a *Z*-alkene. Neither chromium nor manganese were suitable metals for complexing to the salen ligands derived from *trans*-cyclobutane-1,2-diamine. This indicates that these ligands are most likely highly non-planar, however perhaps other metals would be suitable for complexation.

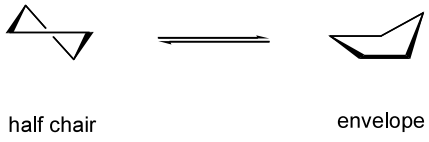
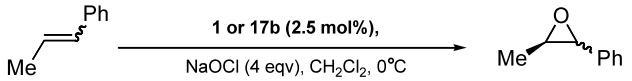


Figure 2. Conformations of cyclopentane.

Table 1. Comparison of manganese salen catalysts **1** and **17b** for epoxidation of *E*- and *Z*-β-methylstyrenes



Substrate	Catalyst	ee (%)	Yield (%)	Product configuration
E-β-Methylstyrene	**17b**	28	67	(2*R*,3*R*)
E-β-Methylstyrene	**1**	22	24	(2*R*,3*R*)
Z-β-Methylstyrene	**17b**	84	25	(2*R*,3*S*)[a]
Z-β-Methylstyrene	**1**	90	55	(2*R*,3*S*)[a]

[a] (2*R*,3*S*) refers to 2-methyl-3-phenyloxirane (β-methylstyrene oxide).

4. Experimental

4.1. General experimental

Melting points were determined either on a Gallenkamp melting point block or a Reichert Thermovar and are uncorrected. Optical rotation values were obtained using a Perkin–Elmer 241 polarimeter. ^{1}H NMR spectra were recorded at 270 MHz on a Jeol JNM-GX270 FT spectrometer and at 300 MHz on a Varian INOVA 300 spectrometer. ^{13}C NMR spectra were recorded at 67 MHz (Jeol) or 75 MHz (Varian). Chemical shifts are reported as δ values in ppm relative to internal standard tetramethylsilane (TMS) for ^{1}H spectra. Chiral gas–liquid chromatography (GC) was performed on a Shimadzu GC-8A gas chromatograph coupled to a Shimadzu C-R3A integrator. High-performance liquid chromatography was performed using a Waters 501 HPLC pump with a Waters 486 Tunable Absorbance detector coupled to a Shimadzu C-R5A integrator. All commercially available solvents were

used as supplied, unless otherwise stated. Solvents were dried according to standard procedures.[42] Flash column chromatography was performed on Merck silica 9385, particle size 0.04–0.063 mm. Iodosylbenzene was prepared according to a standard procedure.[43] 2-(Trifluoromethyl)phenol was obtained from Fluorochem Ltd. *Z*-β-Methylstyrene was obtained from Chemsampco Inc., 40 Enterprise Avenue, Trenton, NJ 08638, USA, tel.: +1-609-656-2440. All other chemicals were obtained from the Aldrich Chemical Company and used as received.

4.2. (±)-*trans*-1,2-Diazido-cyclopentane, 6

Potassium permanganate (23.2 g, 0.147 mol) was added portionwise over 4 h to a mixture of sodium azide (38.2 g, 0.587 mol) and cyclopentene (20.0 g, 0.294 mol) in MeOH (150 mL). The reaction was stirred for a further 4 h and water (100 mL) was added. The reaction was carefully acidified using conc. H_2SO_4 (20 mL was required, caution, very exothermic). The resulting brown suspension was extracted with Et_2O (3×100 mL) and the extracts were washed with saturated Na_2HCO_3 (100 mL), dried over Na_2SO_4 and the solvent was removed in vacuo to yield an orange liquid (13.0 g, 29%). This was purified by flash chromatography to yield a sample of *trans*-1,2-diazidocyclopentane (3.77 g, 8%) and a sample of a 9:1 mixture of the *trans* and *cis*-1,2-diazidocyclopentane (2.04 g, 5%) In subsequent repeats of this experiment the small amount of *cis* isomer produced was not removed and the mixture was used in the next reaction: IR (neat, cm^{-1}) 2958, 2100 (N_3), 1268; ^1H NMR (300 MHz, $CDCl_3$) δ (*trans* isomer) 3.78–3.52 (m, 2H, CHN_3), 2.10–2.00 (m, 2H, cyclopentyl-H), 1.84–1.66 (m, 4H, cyclopentyl-H); ^{13}C NMR (67 MHz, $CDCl_3$) δ (*trans* isomer) 67.0, 29.3, 20.9. Anal. calcd for $C_5H_8N_6$: C, 39.47; H, 5.30; N, 55.23. Found C, 39.04; H, 5.18; N. 56.08%.

4.3. (±)-*trans*-Cyclopentane-1,2-diamine, 4

(±)-*trans*-1,2-Diazido-cyclopentane **6** (6.0 g, 39 mmol) was hydrogenated at 45 psi for 24 h over Pd/C (400 mg of 10% w/w, 0.38 mmol). The suspension was then filtered and the filtrate was evaporated in vacuo to give a yellow liquid (2.88 g, 73%). This was not purified further but instead was resolved immediately: IR (neat, cm^{-1}) 2955, 2361, 1600; ^1H NMR (270 MHz, $CDCl_3$) δ 2.77–2.70 (m, 2H, CHN), 2.05–1.93 (m, 2H, cyclopentyl-H), 1.72–1.58 (m, 2H, cyclopentyl-H), 1.60 (br s, 4H, NH_2), 1.39–1.28 (m, 2H, cyclopentyl-H).

4.4. (*R*,*R*)-(−)-*trans*-Cyclopentane-1,2-diamine di-(+)-tartrate

(±)-*trans*-Cyclopentane-1,2-diamine **4** (2.88 g, 28.8 mmol) and (+)-tartaric acid (10.1 g, 67.3 mmol) were reacted according to the procedure of Toftlund and Pedersen[25] to give an off-white precipitate which was filtered and dried (5.21 g, 90% based on one enantiomer). This solid was recrystallised 3 times from water/MeOH to give white crystals (1.23 g, 22% based on one enantiomer): mp 126–127°C (lit.[25] 128–130°C); $[\alpha]_D^{20} = +10.0$ (*c* 2, H_2O, lit.[25] +10.1°); ^1H NMR (270 MHz, D_2O) δ 4.31 (s, 4H, C*H*OH), 3.60–3.56 (m, 2H, CHN), 2.12–2.05 (m, 2H, cyclopentyl-H), 1.69–1.58 (m, 4H, cyclopentyl-H); ^{13}C NMR (67 MHz, D_2O) δ 179.2, 75.6, 57.7, 32.3, 24.3.

4.5. (*R*,*R*)-(−)-*trans*-Cyclopentane-1,2-diamine, (*R*,*R*)-4

Following the procedure of Toftlund and Pedersen the product of Section 4.4 was reacted to give a pale yellow liquid (194 mg, 70%). Due to the known air sensitivity of 1,2 diamines this was used immediately (see Sections 4.9 and 4.10): ^1H NMR (270 MHz, $CDCl_3$) δ 2.77–2.70 (m, 2H, CHN), 2.05–1.93 (m, 2H, cyclopentyl-H), 1.72–1.58 (m, 2H, cyclopentyl-H), 1.60 (br s, 4H, NH_2), 1.39–1.28 (m, 2H, cyclopentyl-H).

4.6. 2-(Methoxymethoxy)-1-(trifluoromethyl)benzene

Sodium hydride (6.40 g of a 60% dispersion in mineral oil, 160 mmol) was washed with hexane and transferred to a two-neck 250 mL round bottom flask under an atmosphere of N_2. After addition of anhydrous DMF (50 mL) the slurry was cooled with stirring to 0°C. To the resulting grey suspension was added dropwise a solution of 2-(trifluoromethyl)phenol (24.00 g, 150 mmol) in anhydrous DMF (25 mL) at such a rate that the evolution of hydrogen did not become too vigorous. After complete addition the ice bath was removed and the brown reaction mixture stirred for 1 h. Chloromethylmethyl ether (12.4 mL, 160 mmol) was added dropwise and the resulting white suspension stirred overnight. Ice/water (100 mL) was added cautiously and the mixture extracted with Et_2O (3×100 mL). The combined Et_2O extracts were washed with NaOH (2 M, 100 mL), HCl (2 M, 100 mL), and brine (100 mL). The solution was dried over $MgSO_4$ and the solvent was removed in vacuo to yield a colourless liquid (28.2 g, 92%): IR (neat, cm^{-1}) 2961, 2919, 2849, 1609, 1496, 1463, 1323, 1244, 1116, 1056, 989, 758, 648; ^1H NMR (270 MHz, $CDCl_3$) δ 7.58 (d, $J=7.6$ Hz, 1H, ArH), 7.50–7.44 (m, 1H, ArH), 7.26–7.21 (m, 1H, ArH), 7.04 (d, $J=7.9$ Hz, 1H, ArH), 5.26 (s, 2H, OCH_2O), 3.49 (s, 3H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0, 133.2, 127.1, 123.7 (q, $J_{C-F}=273$ Hz), 121.1, 119.5 (q, $J_{C-F}=31$ Hz), 115.2, 94.2, 56.3; MS (EI) *m*/*z* (relative intensity) 206 (M^+, 2), 145 (M–OCH_2CH_3, 3), 127 (2), 95 (2), 63 (3), 45 (100). Anal. calcd for $C_9H_9F_3O_2$: C, 52.43; H, 4.40; F, 27.65. Found: C, 53.05; H, 4.62; F, 27.20%.

4.7. 2-(Methoxymethoxy)-3-(trifluoromethyl)benzaldehyde

To a solution of 2-(methoxymethoxy)-1-(trifluoromethyl)benzene (31.9 g, 155 mmol) in anhydrous THF (200 mL) at −78°C (acetone/dry ice) under an atmosphere of N_2 was added *n*-butyllithium (68.0 mL of a 2.5 M solution, 170 mmol) dropwise with stirring. After an additional hour stirring at this temperature, a mixture of anhydrous DMF (13.2 mL, 170 mmol) and anhydrous THF (10 mL) was added to the green mixture and the resulting solution was allowed to warm to

rt and stirred overnight. The yellow solution was hydrolysed by the addition of water (150 mL) and the mixture extracted with Et_2O (3×150 mL). The combined Et_2O extracts were then washed with 2 M HCl (100 mL) and brine (100 mL), dried over $MgSO_4$ and the solvent was removed in vacuo to yield a viscous yellow liquid. This was distilled in vacuo to yield a pale yellow liquid (29.3 g, 81%): bp 153°C (0.5 mmHg); IR (neat, cm^{-1}) 2956, 2923, 2866, 2360, 1672 (C=O), 1623, 1454, 1335, 1117, 1075, 985, 923, 757; ^1H NMR (270 MHz, $CDCl_3$) δ 10.31 (s, 1H, CHO), 8.07 (dd, $J=1.7$ Hz, 7.9 Hz, 1H, ArH), 7.90–7.87 (m, 1H, ArH), 7.38 (apparent t, $J=7.9$ Hz, 1H, ArH), 5.13 (s, 2H, OCH_2O), 3.63 (s, 1H, OCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.6, 158.6, 132.7, 132.5, 131.5, 124.8, 123.0 (q, $J_{C-F}=273$ Hz), 118.4, 102.5, 58.1; MS (EI) m/z (relative intensity) 234 (M^+, 9), 203 (M–OCH_3, 4), 188 (3), 132 (2), 113 (3), 69 (6), 63 (5), 45 (100), 29 (47). Anal. calcd for $C_{10}H_9F_3O_3$: C, 51.29; H, 3.87; F, 24.34. Found: C, 51.13; H, 4.03; F, 24.14%.

4.8. 2-Hydroxy-3-(trifluoromethyl)benzaldehyde

2-(Methoxymethoxy)-3-(trifluoromethyl)benzaldehyde (15.0 g, 64.0 mmol) was dissolved in MeOH (300 mL) and AcOH (0.2 M, 200 mL). The mixture was heated under reflux for 8 h, at which stage TLC analysis (silica, CH_2Cl_2) indicated the complete disappearance of starting material. After cooling overnight white needle like crystals formed in the reaction. These were filtered off, and dried in a dessicator until of constant weight (5.44 g, 45%). Drying under vacuum had to be avoided as it led to loss of material by sublimation. The filtrate was concentrated to a yield a further crop which were dried similarly (3.27 g, 27%): mp 58–59°C; IR (KBr, cm^{-1}) 3103, 2867, 1680 (C=O), 1622, 1487, 1451, 1337, 1190, 1118, 747, 671, 486; ^1H NMR (270 MHz, $CDCl_3$) δ 11.73 (s, 1H, OH), 9.96 (s, 1H, CHO), 7.85–7.76 (m, 2H, ArH), 7.15–7.09 (m, 1H, ArH); ^{13}C NMR (67 MHz, $CDCl_3$) δ 196.3, 159.7, 137.4, 134.2, 122.9 (q, $J_{C-F}=273$ Hz), 121.2, 119.2, 118.9 (q, $J_{C-F}=32$ Hz); MS (EI) m/z (relative intensity) 191 (M+1, 18), 190 (M+, 100), 189 (M−1, 33), 172 (29), 171 (19), 170 (4), 169 (66), 144 (23), 143 (7), 142 (65), 141 (47), 114 (42), 63 (37), 29 (39). Anal. calcd for $C_8H_5F_3O_2$: C, 50.54; H, 2.65; F, 29.98. Found: C, 50.21; H, 2.67; F, 30.04%.

4.9. 4.8(*R*,*R*)-(−)-*N*,*N*′-Bis(3-trifluoromethylsalicylidene)-*trans*-cyclopentane-1,2-diamine, 14b

(*R*,*R*)-(−)-*trans*-Cyclopentane-1,2-diamine (*R*,*R*)-**4** (194 mg, 1.94 mmol) was dissolved in EtOH (70 mL) and 2-hydroxy-3-trifluoromethylbenzaldehyde (737 mg, 3.87 mmol) added to the solution. The resulting bright yellow mixture was refluxed for 2 h, cooled and the solvent was removed in vacuo to yield a solid which was recrystallised from hexane to give bright yellow needles (765 mg, 89%): mp 138°C; $[\alpha]_D^{20}=-437$; IR (KBr, cm^{-1}) 2969, 2882, 1633, 1497, 1457, 1333, 1190, 1160, 1077, 842, 752, 685, 609; ^1H NMR (270 MHz, $CDCl_3$) δ 14.48 (s, 2H, OH), 8.34 (s, 2H, HC=N), 7.59 (dd, $J=7.9$ Hz and 1.1 Hz, 2H, ArH), 7.38 (dd, $J=7.8$ Hz and 1.1 Hz, 2H, ArH), 6.90 (apparent t, $J=7.8$ Hz, 2H, ArH), 3.82–3.75 (m, 2H, N-CH), 2.28–2.15 (m, 2H, cyclopentyl H), 2.05–1.91 (m, 4H, cyclopentyl-H); ^{13}C NMR (67 MHz, $CDCl_3$) δ 164.5, 160.2, 135.1, 129.9, 123.6 (q, $J_{C-F}=283$ Hz), 119.1, 118.4, 117.7, 76.0, 33.0, 21.9; MS (EI) m/z (relative intensity) 444 (M^+, 5), 255 (100), 190 (20), 170 (28), 155 (20), 127 (25), 67 (30), 41 (29). Anal. calcd for $C_{21}H_{18}F_6N_2O_2$: C, 56.76; H, 4.08; N, 6.30. Found: C, 56.57; H, 4.05; N, 6.15%.

4.10. (*R*,*R*)-(−)-*N*,*N*′-Bis(3,5-di-*tert*-butylsalicylidene)-*trans*-cyclopentane-1,2-diamine, 15b

(*R*,*R*)-(−)-*trans*-Cyclopentane-1,2-diamine (***R***,***R***)-**4** (188 mg, 1.88 mmol) and 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (880 mg, 3.75 mmol) were refluxed in EtOH (10 mL) for 2 h. On cooling to rt crystals formed which were filtered and dried (741 mg, 74%): mp 166–168°C; $[\alpha]_D^{20}=-365$ (*c* 1, CH_2Cl_2); ^1H NMR (270 MHz, $CDCl_3$) δ 13.67 (s, 2H, OH), 8.31 (s, 2H, N=CH), 7.34 (d, $J=2.5$ Hz, 2H, ArH), 7.02 (d, $J=2.5$ Hz, 2H, ArH), 3.76–3.72 (m, 2H, C=N-CH), 2.27–2.13 (m, 2H, cyclopentyl-H), 2.05–1.91 (m, 4H, cyclopentyl-H), 1.44 (s, 9H, $C(CH_3)$), 1.26 (s, 9H, $C(CH_3)$); ^{13}C NMR (67 MHz, $CDCl_3$) δ 165.7, 158.0, 140.1, 136.5, 126.9, 126.2, 117.8, 76.5, 35.1, 34.2, 33.3, 31.5, 29.5, 22.2; MS (EI) m/z (relative intensity) 533 (M+1, 9) 532 (M^+, 27), 299 (100), 251 (25), 234 (13), 218 (10), 57 (26). Anal. calcd for $C_{35}H_{52}N_2O_2$: C, 78.90; H, 9.84; N, 5.26. Found: C, 78.54; H, 9.47; N, 5.40%.

4.11. *meso*-Dimethyl 2,5-dibromohexane-1,6-dioate, 9

A combination of the procedures of Buchman et al.[29] and Watson and O'Neill[34] were used. Thionyl chloride (323 g, 2.71 mol) was added in 70 mL portions over 2 h to adipic acid **7** (197 g, 1.35 mol) heated at 80°C in a two-neck 1 L round bottom flask equipped with a reflux condenser and a pressure equalised dropping funnel. After heating until gas evolution ceased some solid (adipic acid) still remained in the reaction. Therefore, a further 100 mL of thionyl chloride was added and heating continued until gas evolution ceased. The addition took 7 h in total. Following this bromine (473 g, 2.96 mol) was added dropwise to the pale yellow hot reaction mixture over 12 h and heating was then continued for a further 3 h. After cooling to rt, N_2 was passed through the reaction to remove excess bromine. The resulting brown reaction mixture was added dropwise to MeOH (275 mL) in a 1 L round bottom flask cooled in an ice bath. A white precipitate formed during the addition and this was filtered as soon as addition was complete and recrystallised from MeOH (201 g, 45%). On standing further precipitate formed in the mother liquor which was also recrystallised from MeOH (52 g, 12%). The two crops were identical: mp 76–77°C (lit.[34] 75–76°C); ^1H NMR (270 MHz, $CDCl_3$) δ 4.30–4.23 (m, 2H, CHBr), 3.80 (s, 6H, OCH_3), 2.36–2.35 (m, 2H, CH-CBr), 2.10–2.02 (m, 2H, CH-CBr); ^{13}C NMR (67 MHz, $CDCl_3$) δ 170.2, 53.7, 44.8, 33.0.

4.12. 1-Cyano-cyclobutane-1,2-dicarboxylic acid dimethyl ester, 10

Using a modification of the procedure of Buchman et al.,[29] *meso*-dimethyl 2,5-dibromohexane-1,6-dioate **9** (200 g, 0.602 mol) and potassium cyanide (88.3 g, 1.36 mol) were added to a 1 L round bottom flask containing MeOH (400 mL). The reaction mixture was heated at 75°C for 56 h. After cooling to rt the MeOH was distilled at atmospheric pressure and the residue was flushed through a pad of silica with CH_2Cl_2. The solvent was removed in vacuo to yield a yellow liquid (84.1 g, 71%). ^{1}H NMR indicated this to be a 43:57 mixture of the two isomers of product. On standing crystals formed in the liquid and these were filtered and dried (21.4 g, 18%). Distillation of the mother liquor yielded a colourless liquid (bp 94°C at 0.2 mmHg (lit.[29] 119–120°C at 2 mmHg), 30.9 g, 26%): Crystalline isomer: mp 92–93°C (lit.[29] 89.5–90°C) from MeOH; ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.85 (s, 3H, OCH_3), 3.79–3.72 (m, 1H, cyclobutyl-H), 3.72 (s, 3H, OCH_3), 2.75–2.53 (m, 3H, cyclobutyl-H), 2.42–2.26 (m, 1H, cyclobutyl-H); ^{13}C NMR (67 MHz, $CDCl_3$) δ 170.2, 167.8, 118.7, 53.7, 52.4, 45.3, 42.2, 28.4, 21.4; liquid isomer: bp 94°C at 0.2 mmHg (lit.[29] 119–120°C at 2 mmHg); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.88 (s, 3H, OCH_3), 3.83–3.76 (m, 1H, cyclobutyl-H), 3.80 (s, 3H, OCH_3), 2.69–2.53 (m, 3H, cyclobutyl-H), 2.35–2.27 (m, 1H, cyclobutyl-H); ^{13}C NMR (67 MHz, $CDCl_3$) δ 169.9, 167.8, 117.5, 54.1, 52.6, 43.9, 43.6, 29.0, 20.2.

4.13. Cyclobutane-1,2-dicarboxylic acid, 12

Using a modification of the procedure of Buchman et al.[29] a mixture of the two isomers of 1-cyano-cyclobutane-1,2-dicarboxylic acid dimethyl ester **10** (46.3 g, 0.234 mol) and 6 M HCl (117 mL) were refluxed for 12 h. The mixture was concentrated in vacuo until a white solid precipitated. Et_2O (200 mL) was added to the residue and the mixture filtered. The filtrate was washed with water (50 mL), dried over Na_2SO_4 and the solvent was removed in vacuo to yield a pale yellow liquid (33.4 g). This liquid was heated at 180°C under vacuum (water pump) until gas evolution ceased ($\sim$2.5 h). On cooling a brown solid was formed (21.0 g, 62%). ^{1}H NMR indicated this to be a 70:30 mixture (**12**) of the trans and *cis* diacids: ^{1}H NMR (270 MHz, D_2O) δ (*trans* isomer) 3.09–3.02 (m, 2H, CHC=O), 1.79–1.76 (m, 4H, cyclobutyl-H); ^{1}H NMR (270 MHz, D_2O) δ (*cis* isomer) 3.17–3.11 (m, 2H, CHC=O), 1.87–1.84 (m, 4H, cyclobutyl-H).

4.14. *trans*-Cyclobutane-1,2-dicarboxylic acid, 8

The mixture of *cis*- and *trans*-cyclobutane-1,2-dicarboxylic acid **12** (18.9 g, 0.131 mol) from the previous reaction was subjected to the equilibration procedure of Neibecker and co-workers[35] to give grey crystals (10.3 g, 54%). ^{1}H and ^{13}C NMR indicated these to be the pure *trans*-isomer: mp 133–135°C (lit.[29] 130–131°C); ^{1}H NMR (270 MHz, D_2O) δ 3.09–3.02 (m, 2H, CHC=O), 1.79–1.76 (m, 4H, cyclobutyl-H); ^{13}C NMR (67 MHz, D_2O) δ 178.0, 40.2, 21.4.

4.15. *trans*-Cyclobutane-1,2-dicarbonyl dichloride, 13

trans-Cyclobutane-1,2-dicarboxylic acid **8** (7.99 g, 55.4 mmol) and thionyl chloride (15 mL, 206 mmol) were heated at 70°C in benzene (35 mL) for 24 h. Benzene and excess thionyl chloride were distilled off and the brown residue dried under water pressure and purified by Kugelrohr distillation to yield a colourless liquid (9.62 g, 96%): bp $\sim$65°C at 0.1 mmHg, (lit.[44] 51°C at 0.2 mmHg); ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.96–3.86 (m, 2H, CHC=O), 2.47–2.27 (m, 4H, cyclobutyl-H); ^{13}C NMR (67 MHz, $CDCl_3$) δ 173.2, 50.4, 22.1.

4.16. *trans*-Cyclobutane-1,2-diamine dihydrochloride, 5·2HCl

A solution of *trans*-cyclobutane-1,2-dicarbonyl dichloride (**13**) (9.50 g, 52.5 mmol) in benzene (60 mL) was added dropwise over 5 min to a solution of sodium azide (11.9 g, 184 mmol) in water (60 mL) cooled to 0°C. The resulting two phase mixture was stirred vigorously for 2 h after which time the phases were separated and the organic phase was washed with 5% Na_2HCO_3 (20 mL), water (20 mL) and dried over $CaCl_2$. This benzene solution of diacyl azide (**CAUTION**: explosion risk) was decanted into a fresh flask equipped with a reflux condenser and oil bubbler and heated slowly to 50°C. Initial slow evolution of gas became vigorous at $\sim$40°C so heat was removed for a period. After gas evolution had ceased heat was reapplied at 50°C for a further hour. After cooling to rt 20% HCl (20 mL) was added and the reaction heated to 90°C for 4 h, then allowed to cool to rt overnight. The benzene layer was separated and washed with water (50 mL). The aqueous layers were combined, washed with benzene (100 mL) and the water removed in vacuo to yield a brown solid which was recrystallised from MeOH/Et_2O to give a white solid (6.29g, 46%): mp 256–257°C (lit.[27] 248–251°C); ^{1}H NMR (270 MHz, D_2O) δ 3.82–3.74 (m, 2H, CHN), 2.20–2.09 (m, 2H, cyclobutyl-H), 1.87–1.72 (m, 2H, cyclobutyl-H); ^{13}C NMR (75 MHz, D_2O) δ 48.6, 20.7.

4.17. (±)-*trans*-Cyclobutane-1,2-diamine, 5

trans-Cyclobutane-1,2-diamine dihydrochloride, **5.2·HCl** (1.22 g, 7.67 mmol) was dissolved in water (3 mL) and added to a separatory funnel containing freshly ground KOH (1.72 g, 30.7 mmol). The mixture was shaken vigorously and then extracted with $CHCl_3$ (4×10 mL). The $CHCl_3$ extracts were dried over Na_2SO_4 and the solvent was removed in vacuo to a pale yellow liquid (612 mg, 93%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.90–2.79 (m, 2H, CHN), 2.09–1.96 (m, 2H, cyclobutyl-H), 1.66 (br s, 4H, NH_2), 1.39–1.16 (m, 2H, cyclobutyl-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.8, 26.1.

4.18. Resolution of *trans*-cyclobutane-1,2-diamine using tartaric acid

(±)-*trans*-Cyclobutane-1,2-diamine (**5**) (2.11 g, 24.5 mmol) was reacted with (+)-tartaric (8.64 g, 57.6 mmol)

acid according to the procedure of Toftlund and Pederson,[25] to give a white precipitate (1.95 g, 20%) with $[\alpha]_D^{20}=+23.0$ (*c* 1, H_2O). ^1H NMR analysis suggested that this substance is a salt containing a 2:1 ratio of (+)-tartaric acid and *trans*-cyclobutane-1,2-diamine: ^1H NMR (300 MHz, D_2O) δ 4.46 (s, 4H), 4.0–3.9 (m, 2H), 2.38–2.26 (m, 2H), 2.02–1.88 (m, 2H); ^{13}C NMR (67 MHz, D_2O) δ 179.2, 75.6, 50.9, 23.3. Three recrystallisations of this material from MeOH/H_2O (1:1) gave white crystals (961 mg, 10%); $[\alpha]_D^{20}=+28.0$ (*c* 1, H_2O) mp 124–126°C; IR (KBr, cm^{-1}) 3318, 3269, 2975, 1565, 1474, 1408, 1304, 1263, 1214, 1135, 1066, 677, 483; ^1H NMR (300 MHz, D_2O) δ 4.46 (s, 4H), 4.0–3.9 (m, 2H), 2.38–2.26 (m, 2H), 2.02–1.88 (m, 2H); ^{13}C NMR (67 MHz, D_2O) δ 179.2, 75.6, 50.9, 23.3. Further recrystallisation failed to change the specific rotation value any further. The enantiomeric excess of the diamine component of the salt was determined using a modification of the method of Jacobsen and co-workers:[40] a small sample of the salt (25 mg) was suspended in CH_2Cl_2 (2 mL) in a test tube and a NaOH solution (4 M, 0.5 mL) was added. This mixture was mixed vigorously using a 'whirlimixer'. 2-Hydroxy-3-(trifluoromethyl)benzaldehyde (10 mg) was added and after further vigorous mixing a 250 μL aliquot was removed, diluted to 5 mL with hexane and analysed by chiral HPLC (Chiralcel AD column, hexane/*i*PrOH 99:1, 0.6 mL/min). This indicated the presence of only one enantiomer of the diamine derivative **14a**.

Further precipitate subsequently appeared in the mother liquor of the initial reaction. This was recrystallised twice from MeOH/H_2O (1:1) to give white crystals (304 mg, 3%) with $[\alpha]_D^{20}=+12.2$ (*c* 1, H_2O). Application of the procedure for determination of ee of the diamine indicated that this salt contained the opposite enantiomer to the initial precipitate, in enantiopure form.

The remaining mother liquors from the reaction were combined and treated with KOH to regenerate **5** (220 mg, 2.55 mmol). This was reacted, in the same manner as before, but with (−)-tartaric acid, to give a white solid (300 mg, 30%). ^1H NMR indicated this to be bis-salt. One recrystallisation of this material from MeOH/H_2O (1:1) gave white crystals (115 mg, 12%) with $[\alpha]_D^{20}=-27.9$ (*c* 1, H_2O). Given that this shows opposite specific rotation to the initial salt above it is a confirmation of the success of the resolution. HPLC analysis by the method above confirmed the presence of enantiopure (−) diamine.

4.19. (+)-*N*,*N*′-Bis(3-trifluoromethylsalicylidene)-*trans*-cyclobutane-1,2-diamine (14a)

(+)-*trans*-cyclobutane-1,2-diamine, (+)-**5** (53 mg, 613 μmol), obtained from its bis-tartrate salt using the procedure in Section 4.5, was reacted with 2-hydroxy-3-(trifluoromethyl)benzaldehyde (233 mg, 1.23 mmol) according to the method in Section 4.9 to give a yellow oil. Recrystallisation from hexane gave a yellow solid (198 mg, 75%): $[\alpha]_D^{20}=+485$ (*c* 1, CH_2Cl_2); mp 115°C; IR (KBr, cm^{-1}) 2995, 2957, 2895, 1629, 1452, 1331, 1185, 1147, 1114, 1060, 842, 754, 618; ^1H NMR (300 MHz, $CDCl_3$) δ 14.48 (s, 2H, OH), 8.34 (s, 2H, HC=N), 7.62 (dd, $J=7.6$ Hz and 0.9 Hz, 2H, ArH), 7.43 (dd, $J=7.6$ Hz and 1.5 Hz, 2H, ArH), 6.90 (dd, $J=7.6$ Hz and 7.6 Hz, 2H, ArH), 4.19–4.14 (m, 2H, N-CH), 2.40–2.35 (m, 2H, cyclobutyl H), 2.14–2.11 (m, 2H, cyclobutyl-H); ^{13}C NMR (67 MHz, $CDCl_3$) δ 163.9, 160.4, 135.6, 130.3 (q, $J_{C-F}=5$ Hz), 123.9 (q, $J_{C-F}=273$ Hz), 119.3, 118.5, 117.9, 68.7, 33.0, 24.2. Anal. calcd for $C_{20}H_{16}F_6N_2O_2$ C, 55.82; H, 3.75; N, 6.51. Found: C, 55.54; H, 3.69; N, 6.39. MS (EI) *m*/*z* (relative intensity) 430 (M^+, 1), 411 (3), 241 (100), 200 (28), 186 (43), 168 (26), 80 (24), 67 (23).

4.20. (+)-*N*,*N*′-Bis(3,5-di-*tert*-butylsalicylidene)-*trans*-cyclobutane-1,2-diamine, 15a

(+)-*trans*-Cyclobutane-1,2-diamine, **5** (32 mg, 376 μmol) and 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (176 mg, 752 μmol) were refluxed in EtOH (10 mL) for 2 h. On cooling to rt crystals formed which were filtered and dried (160 mg, 82%): mp 165–166°C; $[\alpha]_D^{20}=+400$ (*c* 1, CH_2Cl_2); IR (KBr, cm^{-1}) 2955, 2900, 1627 (C=N), 1464, 1436, 1360, 1272, 1250, 1171, 802, 763; ^1H NMR (300 MHz, $CDCl_3$) δ 13.65 (s, 2H, OH), 8.32 (s, 2H, N=CH), 7.37 (d, $J=2.3$ Hz, 2H, ArH), 7.07 (d, $J=2.3$ Hz, 2H, ArH), 4.16–4.08 (m, 2H, C=N-CH), 2.37–2.27 (m, 2H, cyclopentyl-H), 2.19–2.03 (m, 2H, cyclopentyl-H), 1.45 (s, 9H, $C(CH_3)$), 1.29 (s, 9H, $C(CH_3)$); ^{13}C NMR (67 MHz, $CDCl_3$) δ 164.8, 158.0, 140.2, 136.6, 127.1, 126.2, 117.6, 69.0, 35.0, 34.1, 31.5, 29.7, 24.1; MS (EI) *m*/*z* (relative intensity) 518 (M^+, 1), 285 (69), 244 (23), 234 (20), 57 (100). Anal. calcd for $C_{34}H_{50}N_2O_2$: C, 78.72; H, 9.71; N, 5.40. Found: C, 78.63; H, 9.76; N, 5.44%.

4.21. [(*R*,*R*)-(−)-*N*,*N*′-Bis(3-trifluoromethylsalicylidene)-*trans*-cyclopentane-1,2-diamine chromium(III)] nitrate, 16b

(*R*,*R*)-(−)-*N*,*N*′-Bis(3-trifluoromethylsalicylidene)-*trans*-cyclopentane-1,2-diamine (350 mg, 787 μmol) and chromium(II) chloride (97 mg, 787 μmol) were reacted according to the procedure of Jacobsen and co-workers [39] to give a brown solid (250 mg, 60%). This was redissolved in methanol (25 mL) and a solution of silver nitrate (88 mg, 1.1 equiv.) in water (2 mL) was added. The resulting precipitate of silver chloride was filtered and the filtrate concentrated to yield a brown solid (126 mg, 46%): mp >230°C; IR (KBr, cm^{-1}) 2948, 2749, 1643, 1561, 1439, 1384, 1301, 1180, 1120, 1077, 860, 762, 647. Anal. calcd for $C_{21}H_{16}CrF_6N_3O_5.H_2O.MeOH$: C, 43.57; H, 3.66; N, 6.93. Found: C, 43.15; H, 3.70; N, 6.32%. MS (Electrospray) *m*/*z* (relative intensity) 557.6 (M^++1, 10), 525.6 (32), 511.5 (65), 494.3 (M−NO_3, 100).

4.22. [(*R*,*R*)-(−)-*N*,*N*′-Bis(3,5-di-*tert*-butylsalicylidene)-*trans*-cyclopentane-1,2-diamine manganese(III)] chloride, 17b

Following the method of Jacobsen[45] manganese(II) acetate tetrahydrate (897 mg, 3.66 mmol) and (*R*,*R*)-(−)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-*trans*-cyclopentane-

1,2-diamine (650 mg, 1.22 mmol) were reacted to yield a brown oil. This was purified by flash chromatography (silica, CH_2Cl_2 then EtOH) to yield unreacted ligand (189 mg, 29%) and the desired complex as a brown solid (37 mg, 8%): mp>300°C; IR (KBr, cm^{-1}) 2958, 1620, 1534, 1432, 1358, 1344, 1305, 1271, 1250, 1174, 839, 749, 542; MS (Electrospray) m/z 585 (M−Cl, 100). Anal. calcd for $C_{35}H_{50}ClMnN_2O_2 \cdot 1/2H_2O$: C, 66.71; H, 8.16; Cl, 5.63; N, 4.45. Found: C, 66.70; H, 8.01; Cl, 5.81; N, 4.32%.

4.23. Procedures for analysis of epoxidation reaction product mixtures

Typically the worked up reaction mixture (see below) was dissolved in ~1 mL of Et_2O and 1 μL of *n*-decane was added as an internal standard. 1 μL of this solution was injected onto a GC column. The ee of *trans*-β-methylstyrene oxide was determined with a Supelco cyclodextrin-α capillary column (alphadex 120), 30 m× 0.25 mm i.d., 0.25 μm film operated at an injection temperature of 230°C and a column temperature of 93°C, with a column pressure of 18 psi. The ee of *cis*-β-methylstyrene oxide was determined with a Supelco cyclodextrin-β capillary column (betadex 120), 30 m×0.25 mm i.d., 0.25 μm film. This was operated at an injection temperature of 230°C and a column temperature of 77°C with a column pressure of 20 psi. The absolute configuration of *trans*-β-methylstyrene oxide was assigned by comparison of a sample with the data of Witkop and Foltz[46] and of Shi and co-workers.[47] The absolute configuration of *cis*-β-methylstyrene oxide was assigned by comparison of the GC retention times to those of a sample made according to the Jacobsen method.[41]

4.24. Epoxidation of (*E*)-β-methylstyrene by the Cr(V)=O derivative of 16b

Iodosylbenzene (1.2 equiv.) was added to a stirred solution of **16b** (30 mg, 1 equiv.) in CH_3CN (5 mL). A deep blue/black colour appeared almost immediately. After stirring for 30 min this solution was filtered and the filtrate cooled to 0°C using an ice/water bath. Ph_3PO (1 equiv.) was added, followed 5 min later by (*E*)-β-methylstyrene (1 equiv.). The reaction mixture was stirred at 0°C until the brown colour of the **16b** complex returned completely (~1.5 h). The solvent was removed in vacuo and the residue treated with Et_2O. The Et_2O washings were flushed through a short alumina column using Et_2O as eluant. The eluant was concentrated in vacuo to a small volume (~1 mL) and this sample was analysed by GC as described above.

4.25. Epoxidation of alkenes catalysed by manganese complex 17b

Epoxidation of both (*E*)-β-methylstyrene and (*Z*)-β-methylstyrene was carried out according to the procedure of Jacobsen and co-workers.[41] The worked up reaction mixture was analysed by GC as described above.

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