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Unsymmetrical chiral salen Schiff base ligands Synthesis and use in metal-based asymmetric epoxidation reactions

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Abstract

Six novel unsymmetrically substituted chiral non-racemic salen ligands were prepared from resolved *trans*-1,2-diaminocyclohexane and two different salicylaldehydes. These were then used to construct cationic chromium(III) and manganese(III) complexes that were employed in studies relevant to catalytic asymmetric epoxidation of alkenes. In the case of the chromium complexes, the yields and enantioselectivities obtained were compared to those obtained with the analogous symmetrically substituted counterparts. In individual cases improved enantioselection and a very strong beneficial effect of phosphine oxide additive was found, but in general the selectivity varied in an unpredictable manner. The results are rationalised through the formation of a mixture of diastereomeric active oxidants. In the case of the manganese complexes, where one of the salicylaldehydes is the 3,5-di-*tert*-butyl case, the standard preparative method leads to substantial scrambling of the ligand and the isolation of mainly Jacobsen's catalyst. One of the preparative methods investigated for the ligand synthesis worked for racemic ligand but failed for the non-racemic version.

Keywords: Chromium; Manganese; Unsymmetrical salen; Epoxidation; Asymmetric; Catalytic

1. Introduction

Complexes of the salen ligand and its derivatives [1] have been known since 1869 [2,3] and were first studied systematically in the 1930s by Pfeiffer and co-workers [4] including the first chiral non-racemic cases [5]. Those specifically derived from non-racemic *trans*-1,2-diaminocyclohexane were first studied in the 1960s [6,7] and, over the subsequent decades, they have been studied widely especially in regard to their use in catalytic asymmetric synthesis [7–9]. Especially notable has been their use in catalytic asymmetric epoxidation of non-functionalised olefins [10–12], exemplified by the very successful manganese(III) complexes derived from *trans*-1,2-diaminocyclohexane developed by the groups of Jacobsen and co-workers [13] and Katsuki and co-workers [14]. The best known and most useful of these is Jacobsen's catalyst **1** [15], whereas the most selective are those developed by Katsuki and co-workers such as **2** [16]. We have reported extensively on the related chromium(III) and (V) complexes [17–27] which are interesting because they have a strikingly different selectivity profile [17,24] from their manganese analogues and also because they allow the study of the stoichiometric variant of the catalytic reaction. The latter is made possible due to the possibility of isolating the chromium(V) complex [28], which is the active oxidant in the catalytic cycle. This in turn, allowed independent study of the stereoselection and the catalysis and led to our best catalyst **3** [20]. In both the manganese and chromium systems, electronic and structural features of the salen ligand have been predominantly tuned at the aryl moieties and can significantly affect the catalytic properties of the resulting complexes

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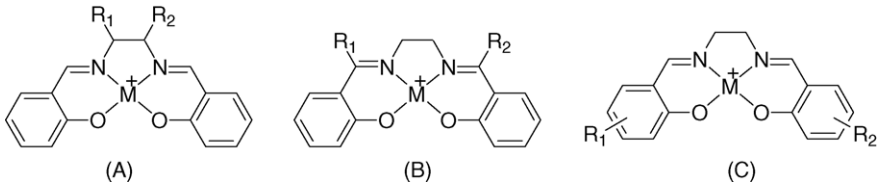
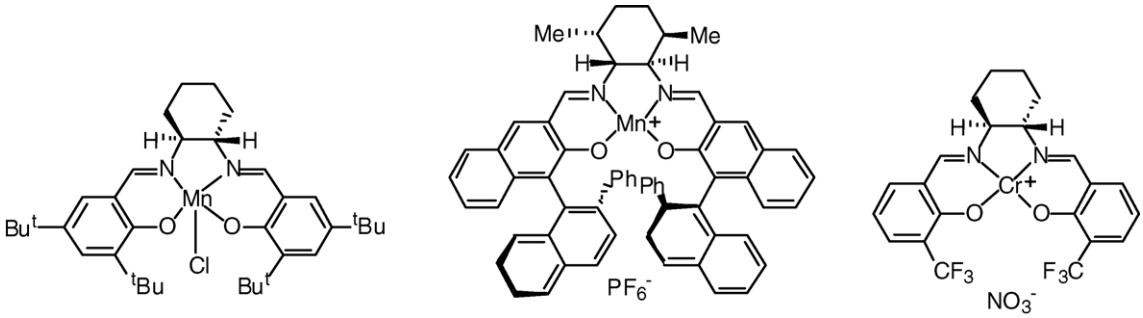


Fig. 1. Types of backbones of non-C_2-symmetric metal salen complexes, $R_1 \neq R_2$.

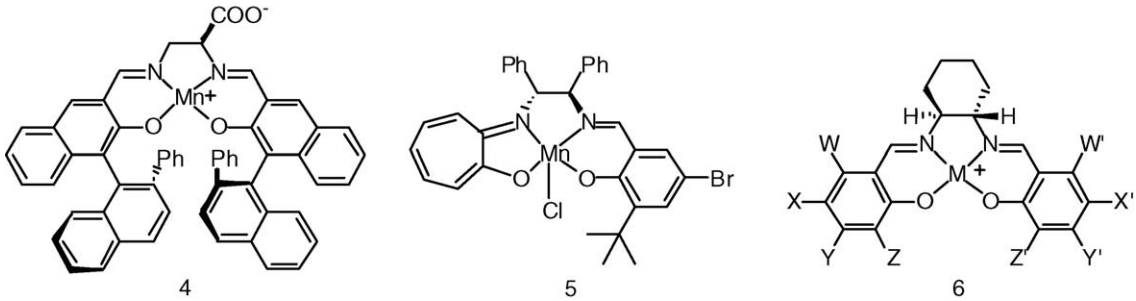
[10,11,21,26,27]. A particular feature of the chromium system is the significant influence exerted by other added ligands for chromium especially phosphine oxides [22].



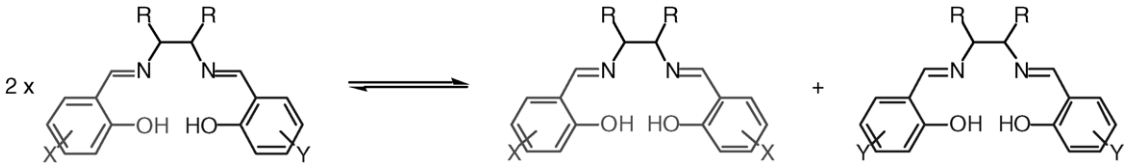
A notable feature of complexes **1**–**3** is that they are C_2-symmetric. This is an important feature because it means that the M(V)=O bond can be formed on either side of the salen plane without generating two different oxidising species. However, a number of years ago, we identified circumstances in which the formation of non-C_2-symmetric chromium salen complexes might offer a possibility for better selectivity in the epoxidation reactions [18,29]. More generally, the construction of such complexes would make available a much greater diversity of metal-salen species and thereby, the possibility of a finer tuning of their electronic and steric parameters.

Conceptually, there are three ways to break C_2-symmetry in metal salen complexes, Fig. 1. Thus the salen ligand could be derived from a non-symmetric diamine (type A); from two different aromatic carbonyls at least one of which is not an aldehyde (type B) or from two different salicylaldehydes (type C).

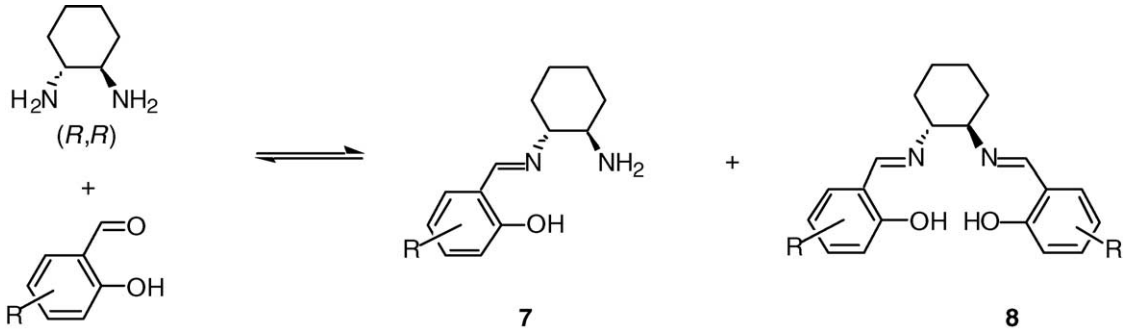
Complexes of types A and B are well known. Those of type A are relatively easy to construct, appear early in the literature and are quite common [5,7]. One that showed promise in catalytic epoxidation was complex **4**, reported by Ito and Katsuki [30]. With care, complexes of type B can also be synthesised, so long as care is taken to ensure that any salicylaldimine segment is constructed last. They are not as common as type A but there are a substantial number in the literature, many of which have been used in catalysis. A noteworthy example used in catalytic epoxidation is complex **5** reported by Jacobsen and co-workers [10]. However, we felt that these types of ligands were not satisfactory for our purposes. First, we had found that chromium complexes derived from biscarbaldimine ligands did not form Cr(V)=O species and so could not be used for catalysis [31]. More seriously, type A and B structures diverge more from the privileged symmetrical bis-salen ligands, such as Jacobsen's catalyst, than do the type C ligands. Thus opportunities for careful fine-tuning of properties are more restricted because they have a more grossly different structure.



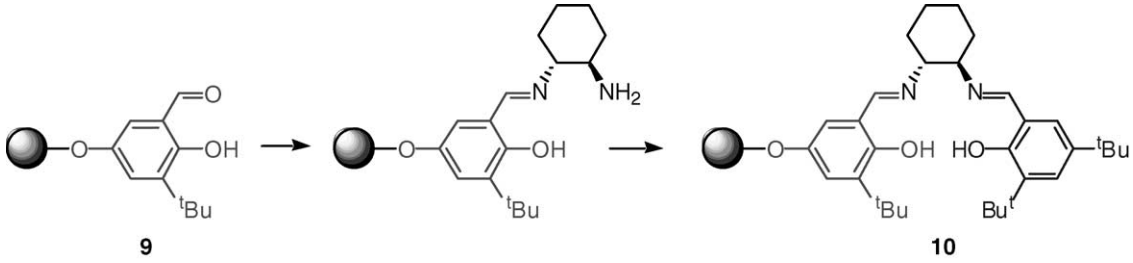
We therefore, sought complexes of the type C and we envisioned that these would have the general structure **6**, which would enable careful fine-tuning of their properties. However, in contrast to types A and B, this type of salen complex is much less common in the literature. This may be ascribed to two factors. First is that symmetrical complexes are straightforward to prepare from the diamine with two equivalents of the relevant aldehyde in a one-pot reaction. However, much



Scheme 1.



Scheme 2.



Scheme 3.

more significant is the ready acid-promoted establishment of an equilibrium between the unsymmetrical salen ligand and the related C_2-symmetric ligands, Scheme 1, resulting in contamination of any resultant complexes. In addition there is a related equilibrium (Scheme 2 below) that makes their synthesis even more difficult.

We now report full details [32,33] of our synthesis of six ligands, which were then used to construct chromium(III) complexes of the type **6**. The latter were subsequently used in stoichiometric asymmetric epoxidation of (*E*)-and (*Z*)-β-methylstyrene and the enantioselectivity results were compared to those obtained using the corresponding C_2-symmetric complexes. We also attempted to construct manganese(III) complexes of the type **6**, and our results have implications for previous reports in this area.

2. Results and discussion

2.1. Preparation of unsymmetrical salen ligands

The fundamental problem that has to be solved (or circumvented) in the synthesis of chiral non-racemic unsymmetrical salens is the nature of the equilibrium shown in Scheme 2, which is related to that in Scheme 1. Thus reaction of, for example, (*R*,*R*)-1,2-diaminocyclohexane with *one* equivalent of a salicylaldehyde results in a mixture of the diamine, monoimine **7** and di-imine **8**. Due to the labile nature of the imine bond towards hydrolysis, an unassisted, step-wise condensation of two different salicylaldehydes with the diamine therefore, affords a mixture of the unsymmetrical and the two C_2-symmetric salen ligands. Catalysed by the phenolic hydrogens, product formation is often completely under thermodynamic control.

For this reason, in all of the 130-year history of work on many thousands of salen ligands and complexes [7,34], including their use as catalysts, probably less than 50 are derived from two dissimilar salicylaldydes [35]. Most of this work is quite recent and a number of strategies have been reported to overcome the problems caused by the equilibria in Schemes 1 and 2. These have included chromatographic separation [36–38], the use of polymeric reagents [38–40] and trapping of species **7** [41] among other methods [42].

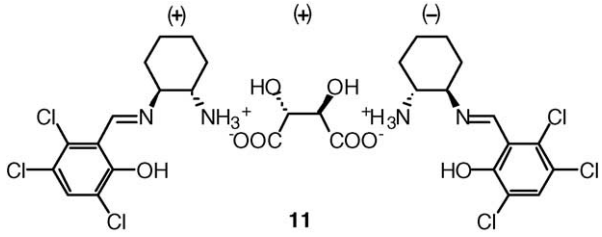
We first examined the usefulness of chromatographic separation for our target ligands for complexes **6** but we found that the position of the equilibrium in Scheme 1 sometimes favoured the symmetrical compounds over the unsymmetri-

cal [43]. This exacerbates an already difficult chromatography and was especially noticeable with combinations of electron withdrawing groups on one side of the salen and electron donating on the other side, a substitution pattern of particular interest to us. Therefore, we did not pursue this route.

We also investigated one of the routes based on polymeric reagents [39], Scheme 3. In these, a salicylaldehyde is first attached to a polymer **9** and the resulting polymer reacted with, in turn, a diamine, a different salicylaldehyde to give the bound ligand **10**. Subsequent treatment with metal generates the bound complex. Although this methodology can be effective for obtaining small samples of non C_2-symmetric complexes, it can be wasteful of both aldehyde and diamine (although both could be recycled). In addition cleavage of the ligand from the support will be problematic because of its propensity to scramble, so that complexes are best made and tested in situ. In principle, the method will be effective if the appropriate loading of metal can be achieved and some characterisation of the bound complexes can be made. However, in our attempts to apply this methodology to the formation of bound chromium complexes, we found [44] that the chromium loading was no more than 30% and we had no way to characterise the bound complexes, so that the four synthetic steps had to be performed more or less "blind". Therefore, we also abandoned this method.

A more attractive strategy would be to find some method to trap mono-Schiff base **7**, which would allow the equilibrium in Scheme 2 to be driven in the desired direction. We expended very substantial efforts trying to find suitable ways to trap species of the type **7**, with little success. These included various partial crystallisations, the use of many different types of acids in attempts to precipitate ammonium salts [43] and the use of many different types of protecting groups for both the free amine and the phenols [45]. Partial success was achieved in some cases but was commonly bedevilled by a too easy reversion to the thermodynamic mixture once the other salicylaldehyde was introduced.

Of all these efforts, only one is worthy of further discussion. Among the acids tried [43] was (+)-tartaric acid and initially this seemed very promising. When used in conjunction with *racemic* 1,2-diaminocyclohexane and trichlorosalicylaldehyde, this gave a near quantitative precipitation of the salt **11**, which yielded a substantial quantity of unsymmetrical salen on treatment with a second salicylaldehyde. However when the same procedure was repeated using *non-racemic* (−)-diamine, only the salt **12** was isolated. It appeared that perhaps the steric requirements of the system were such that they did not allow the formation of a salt such as **11** containing two "half-units" of the same enantiomer.



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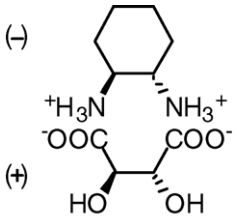

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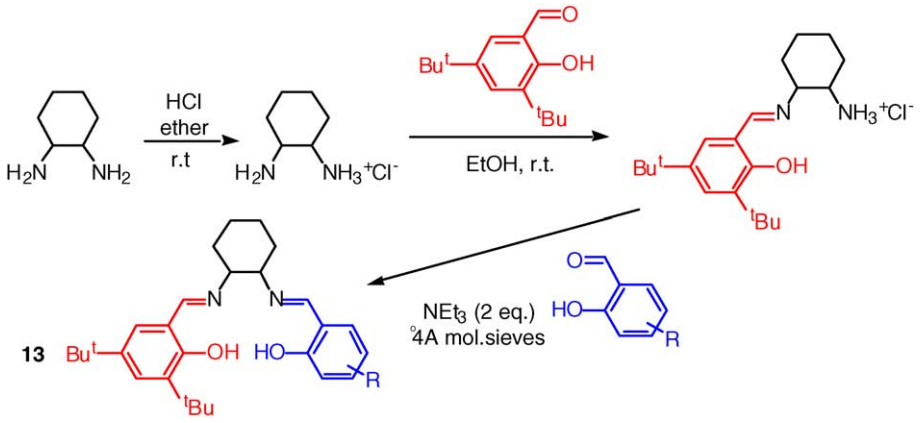
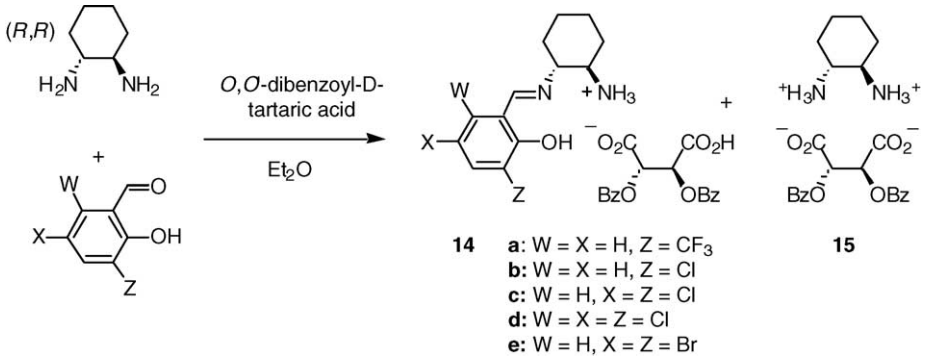
The observations above are relevant to the work of Campbell and Nguyen [41] on the novel, and potentially very effective, synthesis of ligands **13**, outlined in Scheme 4. Anhydrous hydrochloric acid was used to selectively protect one amino group of the vicinal diamine backbone. The resulting ammonium salt was added to a substituted salicylaldehyde providing access to a mono-imine product. This compound was condensed with an equivalent of a different salicylaldehyde in the presence of triethylamine to afford the unsymmetrical salen ligand in good yield. Of the six reported ligands, however, all are racemic. Based on our findings regarding the differing behaviour of racemic and non-racemic mixtures of mono- and bis-condensation products in reaction with a salicylaldehyde, we believe that there may be an issue



Scheme 4.



Scheme 5.

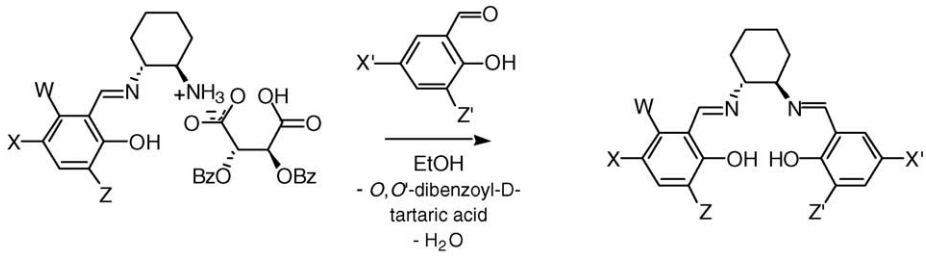
concerning the racemic nature of the ligands reported by Campbell and Nguyen. When the procedure is applied to the synthesis of chiral ligands, the outcome may not be the same.

In the end we decided to persevere with chromatographic separation. We were influenced to do this because our target complexes contained electron-withdrawing groups on one of the salen rings. These are required for reasonable rates in the epoxidation reaction [17,19,21]. We had also previously shown [33,43] that electron-withdrawing substituents on the salicylaldehyde bias the equilibrium in Scheme 2 towards the mono-imine **7**. Thus, for example, an equilibrium mixture formed in $CDCl_3$ from equimolar amounts of 1,2-diaminocyclohexane and 3-chlorosalicylaldehyde contains the mono-imine and bis-imine in a ratio of 3:1. For the di- and tri-chlorosalicylaldehydes this rises to 6:1 and 10:1 respectively. Unfortunately, reaction of these mixtures with a second different salicylaldehyde did not afford a product enriched in unsymmetrical double Schiff base but only traces (<5%) in a mixture of C_2-symmetrical salen ligands, again presumably for thermodynamic reasons. However we were able to trap mono-condensation product **7** with various acids: the most effective being *O*,*O*′-dibenzoyl-D-tartaric acid. This, when added to a mixture of the relevant salicylaldehyde and (−)-*trans*-cyclohexane-1,2-diamine (1:1) in diethyl ether, leads to immediate precipitation of the yellow, mono Schiff base ammonium salts **14a**–**e**, in yields of 75–87%, Scheme 5.

In a number of cases, especially with 3-chlorosalicyclaldehyde, the amino-tartrate salt **15** accounted for 10% of the product, as estimated by ^{1}H-NMR, which also confirmed the presence of an imine signal with the correct integration. Elemental analysis in most cases showed the carbon content to be lower than the theoretical value, to an extent consistent with the observation that the product contains approximately 10% of **15**. The best case was the dibromo case **14e** for which correct analysis was obtained. ^{1}H NMR analysis of the salts was difficult both due to their low solubility and an equilibration that occurs. On addition of acetone-d^6 the salts dissolved fully, but minutes later, precipitation of insoluble dibenzoyl-D-tartaric acid occurred along with production of the symmetrical salen ligand. Recrystallisation of salts **14** was also unsuccessful for the same reason leading only to increased amounts of **15** along with a mixture of the mono- and bis-salen ligands. The salts were therefore, used without purification for the synthesis of unsymmetrical salen ligands. It should be noted that electron withdrawing substitution at the aromatic ring of the salicylaldehyde is vital in order to obtain high yields of the desired half unit, otherwise the product formation gets significantly shifted towards double Schiff base and diamine tartrate salt **15**. We also noted that attempted synthesis of the salt of 5-chlorosalicylaldehyde, the only example not containing a Z-substituent, was unsuccessful, the product consisting mostly of the 5,5′-diCl salen ligand. Again we were content with this restriction since we knew that the presence of Z-substituents was essential in the epoxidation reactions [17,19,21].

With the half units **14a**–**e** at hand, we were able to react them with another salicylaldehyde with electron donating substituents (3,5-di-*t*-butyl and 3-*t*-butyl in one case) to afford the unsymmetrically substituted salen ligands **16a**–**e** and **17** (Scheme 6). In all instances NMR indicated, by examination of the imine signals, a mixture of products with the unsymmetrical ligand being formed in ca. 50%, the remainder consisting of the two corresponding symmetrical ligands and small amounts of either or both salicylaldehyde. Extensive studies on the presence of various bases and/or drying agent in the reactions to give ligands **16c** and **17** showed that these were not helpful in reducing the amounts of the other products [46]. The unsymmetrical ligands were isolated in unavoidably poor yield (average 23%) by column chromatography on silica with dichloromethane as eluting solvent. Several solvent systems were investigated, but dichloromethane consistently showed the best separation. Addition of triethylamine to the eluting solvent (99:1 CH_2Cl_2:Et_3N) was helpful in some cases, notably ligand **16d**.

Several other combinations with different substituted salicylaldehydes were attempted without success. We found it essential to have as great a difference as possible, sterically and electronically, between the two sides of the ligand; electron-withdrawing groups in various positions but including the Z-position on one side, in combination with bulky electron-donating groups on the other side again including the Z-position. This requirement was simply to facilitate separation of the unsymmetrical ligand from the corresponding symmetrical ligands. Smaller steric or electronic differences



	W	X	Z
14a	H	H	CF_3
14b	H	H	Cl
14c	H	Cl	Cl
14d	Cl	Cl	Cl
14e	H	Br	Br

	W	X	Z	X'	Z'
16a	H	H	CF_3	^{t}Bu	^{t}Bu
16b	H	H	Cl	^{t}Bu	^{t}Bu
16c	H	Cl	Cl	^{t}Bu	^{t}Bu
16d	Cl	Cl	Cl	^{t}Bu	^{t}Bu
16e	H	Br	Br	^{t}Bu	^{t}Bu
17	H	Cl	Cl	H	^{t}Bu

Scheme 6.

between the sides did not allow easy separation of the components.

Particular care has to be taken in the characterisation of these types of unsymmetrical ligands and complexes and in assessing their purity. For example, analyses such as optical rotation, IR spectroscopy, even elemental analyses are inconclusive, because it can be argued that the supposed unsymmetrical ligand is simply a mixture with the two corresponding symmetrical ligands. As we shall see, these considerations also apply to unsymmetrical complexes derived from *bona-fide* unsymmetrical ligands. We were therefore, very conscious of the need for definite proof of the proposed unsymmetrically substituted structures, **16a**–**e** and **17**. We drew on evidence from TLC (one spot), melting point (complete melt, narrow range), NMR spectroscopy and mass spectroscopy. Table 1 shows the relevant TLC data. In all cases the symmetrical salen ligand with *tert*-butyl groups was the first fraction isolated by column chromatography at about R_f 0.8. The unsymmetrical ligands ranged in R_f distances from 0.43 to 0.60, the presence of the electron-withdrawing groups thus having a sizeable effect. The corresponding electron-withdrawing symmetrical ligands showed R_f values of 0.20 to 0.44.

The ^{1}H and ^{13}C NMR spectra, obtained before and after chromatography, were particularly significant. As shown in Table 2, the unsymmetrical ligands show clearly different imine hydrogen chemical shifts to the corresponding symmetrical ligands and there is similar difference in signals due to the two different bridgehead protons.

In all cases EI mass spectra showed the expected molecular ion peaks and, gratifyingly, no molecular ion peaks corresponding to the potential symmetrical ligand contaminants. Additional verification is provided by the electrospray mass spectra of the corresponding (salen)chromium(III) complexes, which will be discussed in the next section.

2.2. Preparation of unsymmetrical chromium complexes and their use in asymmetric epoxidation

With the novel ligands in hand, we prepared their corresponding chromium(III) complexes, following both our own previously published syntheses [20,26] and that of Jacobsen and co-workers [47] Scheme 7. The metal was inserted by reaction with chromium(II) chloride and subsequent air oxidation formed the chromium(III) salen chloride complexes **18** and **19**. Yields were only moderate ranging from 42 to 67%. Counter ion exchange with $AgNO_3$ gave the Cr(III)

Table 1
R_f values for unsymmetrical ligands **16a**–**e** and **17** with comparison to their symmetrical counterparts[a]

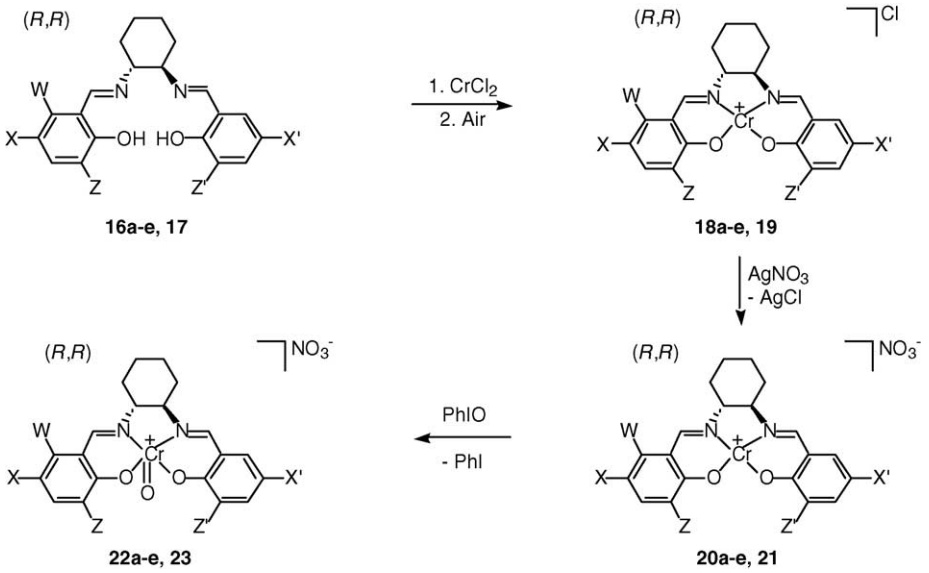
Unsymmetrical ligand	*W*	*X*	*Z*	*X′*	*Z′*	R_f		
						A[b]	B[c]	C[d]
16a	H	H	CF_3	^{t}Bu	^{t}Bu	0.41	0.59	0.78
16b	H	H	Cl	^{t}Bu	^{t}Bu	0.20	0.44	0.82
16c	H	Cl	Cl	^{t}Bu	^{t}Bu	0.42	0.60	0.81
16d	Cl	Cl	Cl	^{t}Bu	^{t}Bu	0.25	0.43	0.82
16e	H	Br	Br	^{t}Bu	^{t}Bu	0.35	0.53	0.84
17	H	Cl	Cl	H	^{t}Bu	0.44	0.56	0.84

[a] On silica with CH_2Cl_2.
[b] A refers to the symmetrical ligand containing electron-withdrawing substituents.
[c] B refers to the unsymmetrical ligand.
[d] C refers to the symmetrical salen ligand containing electron-donating substituents.

Table 2
^{1}H NMR data for ligands **16a**–**e** and **17** and comparison with their symmetrical counterparts[a]

Ligand	*W*	*X*	*Z*	*X′*	*Z′*	Imine chemical shift (δ)		
						A	B	C
16a	H	H	CF_3	^{t}Bu	^{t}Bu	8.33	8.29/8.28	8.29
16b	H	H	Cl	^{t}Bu	^{t}Bu	8.24	8.25/8.26	8.29
16c	H	Cl	Cl	^{t}Bu	^{t}Bu	8.18	8.17/8.24	8.29
16d	Cl	Cl	Cl	^{t}Bu	^{t}Bu	8.69	8.65/8.26	8.29
16e	H	Br	Br	^{t}Bu	^{t}Bu	8.14	8.13/8.23	8.29
17	H	Cl	Cl	H	^{t}Bu	8.18	8.19/8.24	8.26

[a] At 300 MHz, in $CDCl_3$.



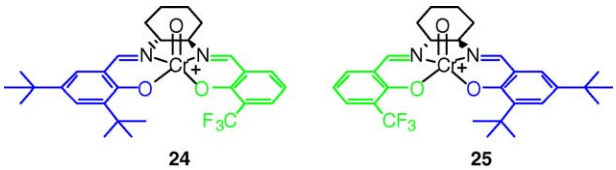
Scheme 7.

nitrate complexes **20** and **21**. All of the complexes showed IR absorptions in the region 1633–1618, characteristic of the imine bond as well as broad OH bands at ca. 3000 cm^{-1}, due to coordinated solvent (H_2O and/or MeOH). Complexes with nitrate counterion showed peaks at ca. 1380 cm^{-1} (symmetrical stretching of the NO_2 group), 862–835 cm^{-1} (stretching of N–O bonds) and 756–720 cm^{-1} (NO_2 bending). A perennial problem with chromium(III) salen complexes, found by ourselves and all other workers, is that they rarely give satisfactory microanalysis data [28,48]. This is caused by the presence of an impurity arising from the $CrCl_2$ insertion process [49], which we have previously shown [19,43,45] is inactive in the oxidation process. The unsymmetrical complexes were no exception and we had to rely on electrospray mass spectrometry for their characterisation. The presence in each case of a peak at *m/z* cationic (salen)Cr(III) complex (M–A) provided verification of structure, and, again gratifyingly, in no case was a signal attributable to the corresponding symmetrical complexes observed.

The nitrate complexes **20** and **21** were then oxidised with iodosylbenzene to the oxo-Cr(V) species **22** and **23**, Scheme 7, which were then used in situ [50,51] as epoxidising agents for our standard substrate (*E*)-β-methylstyrene in stoichiometric reaction at 0 °C in acetonitrile. We conducted two series of experiments, one with no additive and one with equimolar amounts of triphenylphosphine oxide, which we had found to be the best additive [19,22,23]. The reactions were slow, taking days to discharge the green colour of the Cr(V)=O species. We have previously shown [20] that 50% is the maximum yield that can be obtained in the stoichiometric reaction because the Cr(III) species produced reacts with the Cr(V)=O to form an inactive dimer. Even with this restriction, the yields obtained with **22** and **23** were relatively poor (1–11%) with substantial amounts (25–50%) of unreacted alkene recovered. We attribute this to the slower rate of epoxidation caused by the presence of the electron-donating *tert*-butyl groups, which allows other routes to catalyst deactivation. The only by-products observed are benzaldehyde and phenylacetone, both in low yields. The enantioselectivity results are shown in Table 3, along with previously reported results and comparison to the results from the corresponding symmetrical complexes.

The results in Table 3 show no uniform trend. There is indeed one complex (**22e**, entries 11/12) that shows a consistent improvement over its corresponding symmetrical analogues. On the other hand there are complexes that substantially poorer (**22b** and **23**) and others that give results which are an average of the symmetrical cases (**22a** and **22c**). One complex (**22d**) performs better than the symmetrical with Ph_3PO additive present (entry 10) but worse in its absence (entry 9). Mostly the effect of additive is beneficial and in one case (complex **23**, entries 13/14) it is very substantial giving an ee increase of 46%, the largest we have observed to date [19,22,23].

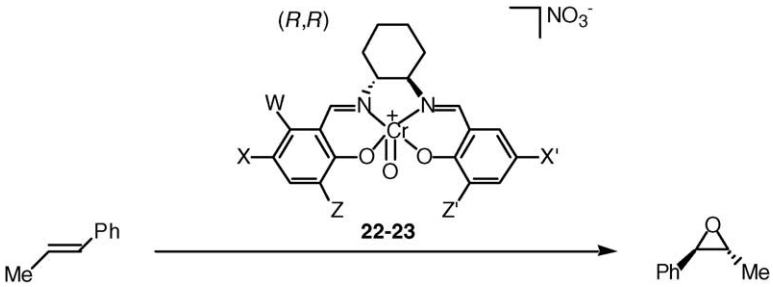
The simplest explanation for the variability of the results in Table 3 is that the loss of C_2-symmetry in the Cr(III) complexes leads, on oxidation, to two diastereomeric Cr(V)=O species, such as **24** and **25** from **20a**. If the alkene interacts differently with the two active oxygen transfer species, there will be two routes to epoxide, and one may be more enantioselective. The observed ee then results from two competing processes.



24 **25**

The existence of two diastereomeric oxochromium species and two competing routes to epoxide implies that

Table 3
Enantioselectivity results from the stoichiometric epoxidation of *E*-β-methylstyrene by complexes **22** and **23** with comparison to their symmetrical counterparts



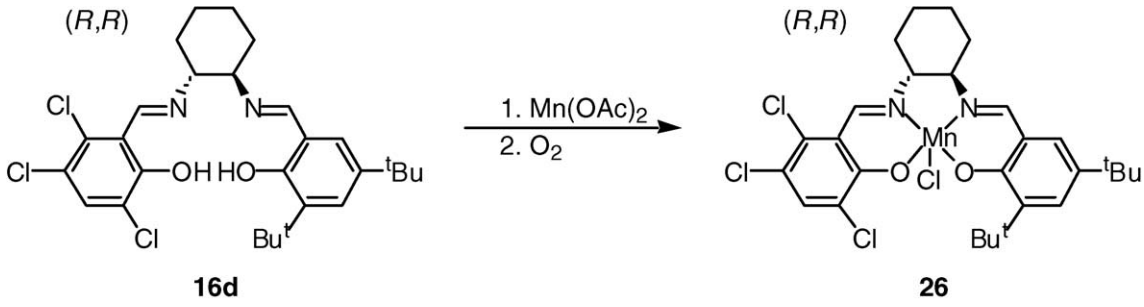
Entry	Complex[a]	*W*	*X*	*Z*	*X′*	*Z′*	Additive	ee A (%)[b,c]	ee B (%)[d]	ee C (%)[c,e,f]
1	**22a**	H	H	CF_3	^{t}Bu	^{t}Bu	None	90	79	65
2	**22a**	H	H	CF_3	^{t}Bu	^{t}Bu	Ph_3PO	92	84	69
3	**22b**	H	H	Cl	^{t}Bu	^{t}Bu	None	81	59	65
4	**22b**	H	H	Cl	^{t}Bu	^{t}Bu	Ph_3PO	88	55	69
5	**22b**[f]	H	H	Cl	^{t}Bu	^{t}Bu	None	80	41[g]	65
6	**22b**[f]	H	H	Cl	^{t}Bu	^{t}Bu	Ph_3PO	86	68[g]	69
7	**22c**	H	Cl	Cl	^{t}Bu	^{t}Bu	None	70[f]	66	65
8	**22c**	H	Cl	Cl	^{t}Bu	^{t}Bu	Ph_3PO	83[f]	79	69
9	**22d**	Cl	Cl	Cl	^{t}Bu	^{t}Bu	None	68[f]	60	65
10	**22d**	Cl	Cl	Cl	^{t}Bu	^{t}Bu	Ph_3PO	72[f]	80	69
11	**22e**	H	Br	Br	^{t}Bu	^{t}Bu	None	63	71	65
12	**22e**	H	Br	Br	^{t}Bu	^{t}Bu	Ph_3PO	77	80	69
13	**23**	H	Cl	Cl	H	^{t}Bu	None	70[f]	25[g]	84
14	**23**	H	Cl	Cl	H	^{t}Bu	Ph_3PO	83[f]	71[g]	78

[a] Nitrate counter ion unless otherwise stated.
[b] A refers to the symmetrical complex containing electron-withdrawing substituents
[c] Results previously reported by us, [17,19–21].
[d] B refers to the unsymmetrical complex
[e] C refers to the symmetrical complex containing electron-donating substituents
[f] With PF_6 counter ion.
[g] Previously incorrectly reported in Ref. [33].

the rational design of highly enantioselective unsymmetrical complexes will not be achievable unless a way can be found to consistently favour one of the diastereomeric oxidants.

2.3. Attempted preparation of unsymmetrical manganese complexes and use in asymmetric epoxidation

The synthesis of complex **26** (Scheme 8) was attempted according to the procedure of Jacobsen and co-workers [15], with slight modification. The reaction was monitored by TLC for complete disappearance of ligand. The product was obtained as a dark brown solid in 34% yield (assuming 100% **26**). The electrospray mass spectrum of the solid did show the expected signal for **26** ($M-Cl$ at m/z 589.1) but this was in only 16% intensity relative to a base peak at m/z 599.3. The latter would be the signal expected for Jacobsen's tetra-*tert*-butyl catalyst ($M-Cl$). Hence we believe that, during the preparation, the unsymmetrical ligand dissociated, forming an equilibrium mixture with both symmetrical ligands, from which the isolation procedure yielded mainly Jacobsen's catalyst. Of course the true proportion of **26** may be higher than the 16 relative% indicated by mass spectrometric analysis. And, indeed, the chlorine content does not equate with the product being mostly tetra-*tert*-butyl complex



Scheme 8.

Table 4
Asymmetric epoxidation of *E*- and *Z*-β-methylstyrene catalysed by **26** and by Jacobsen's Catalyst **1**

Alkene	Product configuration		*trans*-Epoxide		*cis*-Epoxide		Unreacted alkene (%)
	trans	*cis*	ee (%)	Yield (%)	ee (%)	Yield (%)	
E with **26**[a]	(*R*,*R*)		23	51	–	–	10
E with **1**[b]	(*R*,*R*)		22	24	–	–	
Z with **26**[a]	(*S*,*S*)	(2*R*,3*S*)	27	6	91	44	30
Z with **1**	(*S*,*S*)	(2*R*,3*S*)	22[c]	8[c]	92[d]	84[d]	

[a] In the presence of Ph_3PO, this work.
[b] From Ref. [25].
[c] From Ref. [46].
[d] From Ref. [15].

(elemental analysis, theoretical (if 100% **26**): 22.6%; found: 17.8%).

Table 4 shows the results of epoxidations of *E*- and *Z*-β-methylstyrene catalysed with **26** (4 mol%) with comparison to results obtained with authentic Jacobsen's catalyst. Comparison of the results shows that they are very similar.

Thus it appears that using the standard preparative method for Jacobsen's catalyst, the unsymmetrical ligand dissociated to a large extent during the attempted synthesis of **26**, and that the components recombined to leading to isolation of Jacobsen's catalyst. That being the case, manganese complexes of unsymmetrical ligands may never be exclusively formed by the standard preparative method [15]. This has implications for all previous attempts to make unsymmetrical manganese catalysts and the epoxidation reactions reported using them, in that those reports that do not include unambiguous characterisation data should be treated with caution.

3. Conclusions

We have examined a number of possible ways to construct unsymmetrical chiral non-racemic bis-salicylaldimine (salen) complexes of the type **6**. Using chromatographic separation of a biased mixture of symmetrical and unsymmetrical salen ligands, we have constructed a series of novel unsymmetrical bis-salicylaldimine chrmomium(III) complexes (**18**–**21**). These are based on *trans*-1,2-cyclohexanediamine and contain electron deficient aryl rings on one side and electron donating substitution on the other. The derived oxochromium(V) salen complexes **22** and **23** were used in the asymmetric epoxidation of *E*-β-methylstyrene. The obtained yields of epoxide are generally low compared to experiments with the C_2-symmetrically substituted counterparts and the enantioselectivities show no consistent pattern. We explain the results by invoking two diastereomeric oxidising species in the reaction.

Finally in attempts to construct the analogous manganese(III) complexes, only the symmetrical complex was isolated. The latter result should lead to caution in the interpretation of previously reported results in this difficult area.

4. Experimental

4.1. General experimental

Melting points were determined either on a Gallenkamp melting point block or a Reichert Thermovar and are uncorrected. Elemental analyses were carried out by the Microanalytical Laboratory, University College Dublin. Infrared spectra were obtained as potassium bromide discs on a Mattson Instruments Galaxy Series FTIR 3000 spectrometer. Mass spectra at 70 eV were carried out by the Mass Spectrometry Service, University College Dublin. Electrospray mass spectra were run at 200 °C with Source Induced Collision Dissociation turned off and with acetonitrile as solvent unless otherwise stated. Optical rotation values were obtained using a Perkin-Elmer 241 polarimeter. ^{1}H NMR spectra were recorded at 270 MHz on a Joel JNM-GX270 FT spectrometer and at 300 MHz on a Varian Inova 300 spectrometer. ^{13}C NMR spectra were recorded at 75 MHz (Varian). Chemical shifts are reported as *d*-values in ppm relative to internal standard tetramethylsilane (TMS) for ^{1}H and ^{13}C. Chiral stationary phase gas-liquid chromatography (CSP GC) was performed on a Shimadzu GC-8A gas chromatograph coupled to a Shimadzu C-R3A integrator. Detail on chiral columns is described in the relevant sections.

All commercially available solvents were used as supplied, unless otherwise stated. Solvents were dried according to standard procedures [52]. Oxygen-free nitrogen was obtained from BOC gases and was used without further drying. Thin layer chromatography (TLC) was performed on Merck pre-coated Kieselgel $60F_{254}$ and alumina (neutral, type E) plates and realisation was by UV irradiation unless otherwise stated. Flash column chromatography was performed on Merck silica 9385, particle size 0.04–0.063 mm and aluminium oxide 90, standardised (activity II–III), particle size 0.063–0.200 mm (70–230 mesh ASTM). Preparative thin layer chromatography was performed on 0.25 mm × 20 cm silica gel plates (Merck 7748/water, 170 g/390 mL). All chemicals other than those listed below, were from the Aldrich Chemical Company and used as received. 2-(Trifluoromethyl)phenol was obtained from Fluorochem Ltd. *Z*-β-methylstyrene was obtained from Chemsampco Inc.

4.2. Mono-imine salts of racemic and non-racemic trans-cyclohexane-1,2-diamine

4.2.1. Reaction of (+)-tartaric acid and racemic mono-imine

A solution of crude (±)-1-*N*′-(3,5,6-trichlorosaliylidene)cyclohexyl-2-amine (1:10 mixture with bis-imine) was prepared from (±)-*trans*-1,2-cyclohexanediamine (0.25 g, 2.0 mmol) and 3,5,6-trichlorosalicylaldehyde (0.5 g, 2.0 mmol) in ethanol (60 mL). At reflux, solid (+)-tartaric acid (0.12 g, 0.79 mmol) was added. This resulted in a colour change from straw yellow to full intense yellow as a precipitate began to form. The reaction was refluxed for 2 h and the solid formed was filtered hot and washed with hot ethanol (2 × 10 mL) yielding an orange solid (0.36 g, 44%, mp >200 °C), which was insoluble in water. The filtrate was concentrated in vacuo yielding a second solid, the symmetrical Schiff base. The salt obtained (**11**) was used without analysis.

4.2.2. Addition of 3,5-dichlorosalicyaldehyde to racemic tartrate salt ***11***

The salt (0.2 g) was mixed intimately with 3,5-dichlorosalicylaldehyde (0.081 g, 0.42 mmol) with a mortar and pestle. The mixture was added to ethanol (40 mL) and refluxed for 2 h and filtered hot to remove any unreacted salt. The filtrate was concentrated in vacuo whereby a yellow precipitate formed. This was collected by filtration and was washed with cold ethanol (0.096 g (46%). mp 192–194 °C; δH($CDCl_3$) 8.69 (s, 1H, imine), 8.68 (s, 1H, imine), 8.20 (s, 1H, imine), 8.18, (s, 1H, imine), 7.48-7.48 (d, 1H, J = 3.9 Hz, Ar), 7.38–7.38 (d, 1H, J = 2.3 Hz, Ar), 7.08 (d, 1H, J = 2.3 Hz, Ar), 3.49–3.35 (m, 2H, C–H), 2.06–1.30 (m, 8H, cyclohex). Anal. Calcd. for $C_{20}H_{17}N_2O_2Cl_5$: C, 48.56; H, 3.46; N, 5.66; Cl, 35.83. Found: C, 48.58; H, 3.31; N, 5.60; Cl, 35.53. Mass spectroscopic analysis revealed that the compound was a mixture of three Schiff base ligands; the unsymmetrical ligand, the tetrachloro ligand, and the hexachloro ligand; *m*/*z* (rel. intensity) 529 (M^+), 528 (M^{-1}), 496 (M^{+2}, 7), 495 (M^+, 3), 494 (M^+, 11), 462 (M^{+2}, 4), 460 (M^+, 8), 303 (41), 269 (95), 224 (51), 190 (100), 8181).

4.2.3. (+)-Tartaric acid and chiral mono-imine

The procedure in Section 4.2.1 was employed with the same quantities except that (−)-*trans*-1,2-cyclohexanediamine was used instead of racemic. Again, the solid obtained was filtered hot and washed with hot ethanol yielding a white solid (0.21 g, 91%, mp >200 °C. In this case, the salt formed was water-soluble and the filtrate contained exclusively the symmetrical Schiff base. The ^{1}H NMR of the salt was consistent with the tartrate salt of (−)-*trans*-1,2-cyclohexanediamine (**12**): δH(D_2O) 4.29 (s, 2H, CH), 3.34–3.30 (m, 2H, CH), 2.13–2.08 (m, 2H, CH_2), 1.79–1.75 (m, 2H, CH_2), 1.46–1.26 (m, 4H, CH_2).

4.3. Dibenzoyl-D-tartrate salts of mono-salicylaldimines of (R,R)-cyclohexane-1,2-diamine

General procedure. The relevant 2-hydroxybenzaldehyde was added to a solution of (*R*,*R*)-(−)-*trans*-cyclohexane-1,2-diamine (1 equiv.) in diethyl ether (200 mL). The resulting yellow solution was stirred for 10 min then *O*,*O*′-dibenzoyl-D-tartaric acid (1 equiv.) added. Precipitation of the tartrate salt occurred immediately. The mixture was stirred for a further 30 min then filtered, washed with diethyl ether to remove any unreacted salicylaldehyde and water to remove unreacted diamine and dried, usually yielding a yellow solid.

(*R*,*R*)-(−)-*N*-(3-trifluoromethylsalicylidene)-*N*′-(*O*,*O*′-dibenzoyl-D-tartrate)-*trans*-cyclohexane-1,2-diamine (**14a**) was prepared from 2-hydroxy-3-trifluoromethyl benzaldehyde [20] (1.30 g, 6.84 mmol) yielding 3.78 g (86%) of a yellow solid: mp 130–132 °C; IR (KBr, cm^{-1}) 3434, 2943, 2871, 1712, 1631, 1452, 1385, 1333, 1267, 1119, 1027, 717; ^{1}H NMR (300 MHz, acetone-d^6): δ 8.59 (s, 0.2H, N=CH), 8.56 (s, 0.8H, N=CH), 8.12–8.08 (m, 4H, ArH), 7.66–7.48 (m, 8H, ArH), 6.96–6.91 (m, 1H, ArH), 5.93 (s, 2H, BzO–CH), 4.12–4.04 (m, 1H, $CH_2CHN^+H_3$), 3.71–3.62 (m, 1H, CH_2CHN=C), 1.87–1.00 (m, 8H, cyclohexyl-H); Anal. Calcd for $C_{32}H_{31}F_3N_2O_9$: C, 59.63; H, 4.85; F, 8.84; N, 4.35. Found: C, 58.45; H, 5.06; F, 7.68; N, 4.89.

(*R*,*R*)-(−)-*N*-(3-chlorosalicylidene)-*N*′-(*O*,*O*′-dibenzoyl-D-tartrate)-*trans*-cyclohexane-1,2-diamine (**14b**) was prepared from 3-chlorosalicylaldehyde [53] (1.30 g, 8.30 mmol) yielding 3.78 g (75%) of a yellow solid: mp 131–133 °C; IR (KBr, cm^{-1}) 3422, 2938, 2868, 1717, 1630, 1451, 1381, 1268, 1116, 1071, 1027, 717; ^{1}H NMR (300 MHz, acetone-d^6): δ8.54 (s, 0.3H, N=CH), 8.45 (s, 0.7H, N=CH), 8.11–8.08 (m, 4H, ArH), 7.66–7.28 (m, 8H, ArH), 6.86–6.83 (m, 1H, ArH), 5.95 (s, 2H, BzO–CH), 3.90–3.80 (m, 1H, $CH_2CHN^+H_3$), 3.60–3.49 (m, 1H, CH_2CHN=C), 1.85–1.05 (m, 8H, cyclohexyl-H); Anal. Calcd for $C_{31}H_{31}ClN_2O_9$: C, 60.93; H, 5.11; Cl, 5.80; N, 4.58. Found: C, 58.28; H, 5.46; Cl, 6.07; N, 5.54.

(*R*,*R*)-(−)-*N*-(3,5-dichlorosalicylidene)-*N*′-(*O*,*O*′-dibenzoyl-D-tartrate)-*trans*-cyclohexane-1,2-diamine (**14c**) was prepared from commercially available 3,5-dichlorosalicylaldehyde (5.00 g, 26.2 mmol) yielding 13.4 g (79%) of a yellow solid: mp 137–139 °C; IR (KBr, cm^{-1}) 3448, 3058, 2939, 2865, 1715, 1630, 1451, 1382, 1262, 1114, 1070, 1027, 711; ^{1}H NMR (300 MHz, acetone-d^6) δ 8.55 (s, 1H, N=CH), 8.13–8.10 (m, 4H, ArH), 7.68–7.33 (m, 8H, ArH), 6.00 (s, 2H, BzO–CH), 3.83–3.75 (m, 1H, $CH_2CHN^+H_3$), 3.66–3.63 (m, 1H, CH_2CHN=C), 1.92–1.29 (m, 8H, cyclohexyl-H); Anal. Calcd for $C_{31}H_{30}Cl_2N_2O_9$: C, 57.68; H, 4.68; Cl, 10.98; N, 4.34. Found: C, 55.19; H, 4.82; Cl, 10.76; N, 4.75.

(*R*,*R*)-(−)-*N*-(3,5,6-trichlorosalicylidene)-*N*′-(*O*,*O*′-dibenzoyl-D-tartrate)-*trans*-cyclohexane-1,2-diamine (**14d**) was prepared from 3,5,6-trichlorosalicylaldehyde [54] (3.00 g, 13.3 mmol) yielding 7.11 g (79%) of a yellow solid: mp 170–173 °C; IR (KBr, cm^{-1}) 3422, 2939, 2867, 1723, 1626,

1501, 1451, 1382, 1317, 1261, 1177, 1116, 1070, 1027, 769, 717, 625; ^{1}H NMR (300 MHz, acetone-d^6) δ 8.91 (s, 0.4H, N=CH), 8.89 (s, 0.6H, N=CH), 8.12–8.08 (m, 4H, ArH), 7.69–7.50 (m, 7H, ArH), 6.00 (s, 2H, BzO–CH), 4.00–3.92 (m, 1H, $CH_2CHN^+H_3$), 3.88–3.80 (m, 1H, CH_2CHN=C), 1.85–1.10 (m, 8H, cyclohexyl-H); Anal. Calcd for $C_{31}H_{29}Cl_3N_2O_9$: C, 54.76; H, 4.30; Cl, 15.64; N, 4.12. Found: C, 53.91; H, 4.47; Cl, 14.66; N, 4.12.

(*R*,*R*)-(−)-*N*-(3,5-dibromosalicylidene)-*N*′-(*O*,*O*′-dibenzoyl-D-tartrate)-*trans*-cyclohexane-1,2-diamine (**14e**) was prepared from commercially available 3,5-dibromosalicylaldehyde (3.0 g, 10.7 mmol) yielding 6.83 g (87%) of a yellow solid: mp 144–146 °C; IR (KBr, cm^{-1}) 3416, 3059, 2939, 2863, 1717, 1631, 1493, 1451, 1378, 1267, 1176, 1114, 1027, 716; ^{1}H NMR (300 MHz, acetone-d^6) δ 8.53 (s, 0.55H, N=CH), 8.50 (s, 0.45H, N=CH), 8.13–8.10 (m, 4H, ArH), 7.73–7.50 (m, 8H, ArH), 5.99 (s, 2H, BzO–CH), 4.23–4.16 (m, 1H, $CH_2CHN^+H_3$), 3.85–3.75 (m, 1H, CH_2CHN=C), 1.88–1.00 (m, 8H, cyclohexyl-H); Anal. Calcd. for $C_{31}H_{30}Br_2N_2O_9$: C, 50.70; H, 4.12; N, 3.81. Found: C, 50.75; H, 4.36; N, 3.77.

4.4. Unsymmetrical bis-salicylaldimine ligands of (R,R)-cyclohexane-1,2-diamine

General Procedure. To a solution of the appropriate mono *O*,*O*′-dibenzoyl-D-tartrate salt (1 equiv.) in ethanol (50 mL/20 mmol salt) was added the relevant salicylaldehyde (1 equiv.). The resulting yellow/orange solution was refluxed for 1.5 h. After cooling to room temperature the solution was concentrated in vacuo to yield a yellow solid. In all cases analysis by ^{1}H NMR showed that the product contained a mixture of the desired unsymmetrical salen ligand, the two corresponding symmetrical salen ligands and a small amount of one or both salicylaldehydes. The percentage of unsymmetrical Schiff base varied from reaction to reaction. Isolation of the desired ligand was attempted by column chromatography (silica, CH_2Cl_2), however it was difficult to obtain a pure sample of the unsymmetrical ligand due to its decomposition on the silica into the component salicylaldehydes. Yields as expected were very low but it was possible to recover both symmetrical ligands in reasonable yield.

(*R*,*R*)-(−)-*N*-(3-Trifluoromethylsalicylidene)- *N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine (**16a**) was prepared from 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (1.27 g, 5.42 mmol) and **14a** (3.50 g, 5.43 mmol) yielding 0.63 g (23%) of a yellow solid after column chromatography: $[\alpha]_D^{20} = -308^\circ$ (c 1.2, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 14.70 (br s, 1H, OH), 13.57 (br s, 1H, OH), 8.29 (s, 1H, CH=N), 8.28 (s, 1H, CH=N), 7.52 (d, J = 7.0 Hz, 1H, ArH), 7.35–7.28 (m, 2H, ArH), 6.98 (d, J = 2.1 Hz, 1H, ArH), 6.78 (m, 1H, ArH), 3.42–3.32 (m, 1H, C=NCH), 3.32–3.25 (m, 1H, C=NCH), 1.99–1.84 (m, 4H, cyclohexyl-H), 1.81–1.62 (m, 2H, cyclohexyl-H), 1.50–1.27 (m, 2H, cyclohexyl-H), 1.41 (s, 9H, $C(CH_3)_3$), 1.23 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 164.6, 158.1, 161.2, 140.5, 136.6, 135.4, 130.0, 127.3, 126.4, 124.2 (q, $^1J_{C-F}$ = 273 Hz), 119.3, 118.4, 117.9, 117.3, 72.4, 35.2, 34.3, 33.5, 33.1, 31.6, 29.7, 24.4. HRMS Calcd. for $C_{29}H_{37}F_3N_2O_2$: 502.2807. Found: 502.2748.

(*R*,*R*)-(−)-*N*-(3-chlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine (**16b**) was prepared from 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (0.38 g, 1.6 mmol) and **14b** (1.00 g, 1.64 mmol) yielding 0.18 g (24%) of a yellow solid after column chromatography: mp 152–154 °C; $[\alpha]_D^{20} = -471^\circ$ (c 0.4, CH_2Cl_2); IR (KBr, cm^{-1}) 2946, 2860, 1630 (C=N), 1447, 1361, 1272, 1184, 1136, 1098, 829, 772, 740; ^{1}H NMR (300 MHz, $CDCl_3$) δ 14.52 br s, 1H, OH), 13.55 (br s, 1H, OH), 8.26 (s, 1H, CH=N), 8.25 (s, 1H, CH=N), 7.35–7.31 (m, 2H, ArH), 7.04 (d, J = 7.6 Hz, 1H, ArH), 6.98 (d, J = 2.3 Hz, 1H, ArH), 6.69 (apparent t, J = 7.8 Hz, 1H, ArH), 3.43–3.22 (m, 2H, C=NCH), 1.96–1.83 (m, 4H, cyclohexyl-H), 1.74–1.62 (m, 2H, cyclohexyl-H), 1.50–1.27 (m, 2H, cyclohexyl-H), 1.40 (s, 9H, $C(CH_3)_3$), 1.24 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 164.5, 158.5, 158.1, 140.4, 136.6, 132.7, 130.2, 127.3, 126.4, 122.0, 119.4, 118.5, 117.9, 72.7, 72.2, 35.2, 34.3, 33.5, 33.1, 31.7, 29.7, 24.4; HRMS Calcd. for $C_{28}H_{37}ClN_2O_2$: 468.2543. Found: 468.2545. MS (EI) *m*/*z* (relative intensity) 470 (M^{+2}, 6), 468 (M^+, 19), 235 (22), 234 (38), 233 (16), 219 (15), 218 (17), 156 (35), 141 (16), 81 (26), 57 (56), 41 (40), 32 (29), 28 (100); Anal. Calcd. for $C_{28}H_{37}ClN_2O_2$: C, 71.70; H, 7.95; N, 5.97. Found: C, 71.07; H, 7.87; N, 5.69.

(*R*,*R*)-(−)-*N*-(3,5-dichlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine (**16c**) was prepared from 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (1.45 g, 6.19 mmol) and compound **14c** (4.0 g, 6.2 mmol) yielding 0.53 g (17%) of a yellow solid after column chromatography: mp 55–57 °C; $[\alpha]_D^{23} = -369.4^\circ$ (c 1.06, $CHCl_3$); IR (KBr, cm^{-1}) 2960, 2864, 1631 (C=N), 1452, 1362, 1275, 1180, 1101, 867, 743; ^{1}H NMR (300 MHz, $CDCl_3$) δ 14.50 (br s, 1H, OH), 13.50 (br s, 1H, OH), 8.24 (s, 1H, CH=N), 8.17 (s, 1H, CH=N), 7.34 (d, J = 2.3 Hz, 1H, ArH), 7.31 (d, J = 2.6 Hz, 1H, ArH), 7.00 (d, J = 2.3 Hz, 1H, ArH), 6.98 (d, J = 2.6 Hz, 1H, ArH), 3.41 (m, 1H, C=NCH), 3.24 (m, 1H, C=NCH), 2.01–1.82 (m, 4H, cyclohexyl-H), 1.80–1.63 (m, 2H, cyclohexyl-H), 1.53–1.43 (m, 2H, cyclohexyl-H), 1.42 (s, 9H, $C(CH_3)_3$), 1.25 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 163.6, 158.1, 157.6, 140.5, 136.7, 132.4, 129.4, 127.4, 126.4, 123.1, 122.5, 119.4, 117.9, 72.5, 72.2, 35.2, 34.3, 33.4, 32.9, 31.7, 29.7, 24.4 (24.40), 24.4 (24.38); HRMS Calcd. for $C_{28}H_{36}Cl_2N_2O_2$: 502.2153. Found: 502.2164. MS (EI) *m*/*z* (relative intensity) 506 (M^{+4}, 1), 504 (M^{+2}, 7), 502 (M^+, 11), 234 (31), 190 (16), 81 (17), 57 (39), 41 (23), 32 (34), 28 (100); Anal. Calcd for $C_{28}H_{36}Cl_2N_2O_2$: C, 66.79; H, 7.21; N, 5.56; Cl, 14.08. Found: C, 65.78; H, 6.97; N, 5.16; Cl, 14.70.

(*R*,*R*)-(−)-*N*-(3,5,6-trichlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine (**16d**) was prepared from 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde

(0.69 g, 2.9 mmol) and compound **14d** (2.00 g, 2.94 mmol) yielding 2.70 g of a yellow solid. The unsymmetrical salen ligand was isolated in 0.53 g (34%) yield by column chromatography (CH_2Cl_2:Et_3N, 99:1): mp 188–190 °C; $[\alpha]_D^{22} = -593.2$ (c 1, $CHCl_3$); IR (KBr, cm^{-1}) 3060, 2949, 2863, 2357, 1622 (C=N), 1439, 1363, 1273, 1195, 1089, 772; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (s, 1H, CH=N), 8.25 (s, 1H, CH=N), 7.43 (s, 1H, ArH), 7.35 (d, J = 2.6 Hz, 1H, ArH), 6.97 (d, J = 2.6 Hz, 1H, ArH), 3.57 (m, 1H, C=NCH), 3.15 (m, 1H, C=NCH), 2.07–1.78 (m, 4H, cyclohexyl-H), 1.75–1.58 (m, 2H, cyclohexyl-H), 1.42–1.24 (m, 2H, cyclohexyl-H), 1.41 (s, 9H, $C(CH_3)_3$), 1.25 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 164.1, 162.7, 158.1, 140.5, 136.8, 134.0, 131.9, 127.6, 126.4, 124.0, 119.3, 117.6, 114.7, 72.5, 69.8, 35.1, 34.2, 33.5, 32.3, 31.6, 29.6, 24.3, 24.2; HRMS Calcd. for $C_{28}H_{35}Cl_3N_2O_2$: 536.1763. Found: 536.1406. MS (EI) *m*/*z* (relative intensity) 540 (M^{+4}, 8), 538 (M^{+2}, 24), 536 (M^+, 25), 313 (54), 234 (100), 218 (43), 81 (32), 57 (79), 41 (50), 28 (51). Anal. Calcd. for $C_{28}H_{35}Cl_3N_2O_2$: C, 62.52; H, 6.56; N, 5.21; Cl, 19.77. Found: C, 62.34; H, 6.41; N, 4.95; Cl, 20.16.

(*R*,*R*)-(−)-*N*-(3,5-dibromosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine (**16e**) was prepared from 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (0.64 g, 2.7 mmol) and **14e** (2.00 g, 2.72 mmol) yielding 0.37 g (23%) of a yellow solid: IR (KBr, cm^{-1}) 2953, 2860, 1628 (C=N), 1443, 1362, 1274, 1170, 1099, 867, 686; ^{1}H NMR (300 MHz, $CDCl_3$) δ 14.60 (br s, 1H, OH), 13.42 (br s, 1H, OH), 8.23 (s, 1H, CH=N), 8.13 (s, 1H, CH=N), 7.60 (d, J = 2.3 Hz, 1H, ArH), 7.34 (d, J = 2.6 Hz, 1H, ArH), 7.16 (d, J = 2.3 Hz, 1H, ArH), 6.97 (d, J = 2.6 Hz, 1H,), 3.42 (m, 1H, C=NCH), 3.22 (m, 1H, C=NCH), 2.05–1.23 (m, 8H, cyclohexyl-H), 1.42 (s, 9H, $C(CH_3)_3$), 1.25 (s, 9H, $C(CH_3)_3$); C NMR (75 MHz, $CDCl_3$) δ 166.6, 163.5, 159.1, 158.0, 140.6, 138.0, 137.9, 133.1, 127.5, 126.4, 126.2, 119.7, 117.9, 112.6, 109.2, 72.5, 72.1, 35.2, 33.4, 32.8, 31.7, 29.7, 24.4 (24.41), 24.4 (24.39); HRMS Calcd. for $C_{28}H_{36}Br_2N_2O_2$: 592.1126. Found: 591.9851. MS (EI) *m*/*z* (relative intensity) 594 (M^{+4}, 3), 592 (M^{+2}, 4), 590 (M^+, 2), 234 (25), 81 (18), 57 (47), 41 (27), 32 (34), 28 (100); Anal. Calcd. for $C_{28}H_{36}Br_2N_2O_2$: C, 56.77; H, 6.13; N, 4.73; Br, 26.98. Found: C, 53.31; H, 5.72; N, 3.93; Br, 24.53.

(*R*,*R*)-(−)-*N*-(3,5-dichlorosalicylidene)-*N*′-(3′-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine (**17**) was prepared from 3-*tert*-butyl-2-hydroxybenzaldehyde [55] (0.25 g, 1.42 mmol and **14c** (1.0 g, 1.55 mmol) yielding 65 mg of a yellow solid after column chromatography (10%); ^{1}H NMR (270 MHz, $CDCl_3$) δ 14.45 (br s, 1H, OH), 13.60 (br s, 1H, OH), 8.24 (s, 1H, CH=N), 8.19 (s, 1H, CH=N), 7.61 (d, J = 2.5 Hz, 1H, ArH), 7.32 (d, J = 2.5 Hz, 1H, ArH), 7.01 (m, 1H, ArH) 6.95 (t, J = 7.6 Hz, 1H, ArH), 6.75 (t, J = 7.6 Hz, 1H, ArH), 3.42 (m, 1H, C=NCH), 3.25 (m, 1H, C=NCH), 1.98–1.25 (m, 8H, cyclohexyl-H), 1.41 (s, 9H, $C(CH_3)_3$).

4.5. Synthesis of unsymmetrical salenCr(III)Cl complexes

General Procedure: A 100 mL, three-necked round bottom flask with a nitrogen inlet and outlet was charged with a solution of the appropriate Schiff base ligand in dry, degassed THF (20 mL per 2.0 mmol of Schiff base). To the yellow/orange solution, anhydrous chromium(II) chloride (1 equiv. or slight excess) was added. The resulting brown solution was stirred under nitrogen for 3 h and then exposed to air overnight. The reaction was worked up as follows: the brown solution was diluted with methyl *tert*-butyl ether (60 mL), washed with brine (3 × 20 mL) and saturated ammonium chloride (3 × 40 mL) and the organic phase dried over sodium sulfate. The solvent was concentrated to 5 mL when a brown precipitate **a** was collected by filtration, washed with water and dried in an oven at 100 °C. The filtrate was concentrated in vacuo yielding a second product **b**. In the case of complex 3,5-dichloro, 3′,5′-di-*tert*-butyl complex **18c**, three precipitates were obtained. Where no precipitate was observed after concentration of the solution to 5 mL, the Cr(III) salen complex was isolated by concentration to dryness.

[(*R*,*R*)-(−)-*N*-(3-trifluoromethylsalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium (III)] chloride (**18a**) was prepared from **16a** (239 mg, 0.476 mmol) and chromium(II) chloride (60 mg, 0.49 mmol, 1 equiv.) yielding a brown solid (167 mg, 60%). This material was used without further characterisation to form **20a**.

[(*R*,*R*)-(−)-*N*-(3-chlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] chloride (**18b**) was prepared from **16b** (170 mg, 0.362 mmol) and chromium(II) chloride (45 mg, 0.37 mmol, 1 equiv.) yielding an initial precipitate (**18b**(**a**)) (25 mg, 12%). Concentration of the filtrate yielded a second precipitate (**18b**(**b**)) (80 mg, 40%). IR (KBr, cm^{-1}) 2954, 2866, 1621 (C=N), 1592, 1533, 1436, 1393, 1319, 1256, 1170, 1140, 745, 553; MS (Electrospray) *m*/*z* (relative intensity) 600.2 (82), 586.2 (59), 576.2 (26), 518.4 ($M-Cl$, 100). Anal. Calcd. for $C_{28}H_{35}Cl_2CrN_2O_2$: C, 60.65; H, 6.36; Cl, 12.79; Cr, 9.38; N, 5.05. Found: C, 53.89; H, 6.51; Cl, 13.83; Cr, 7.10; N, 5.31.

[(*R*,*R*)-(−)-*N*-(3,5-dichlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] chloride (**18c**) was prepared from **16c** (0.36 g, 0.71 mmol) and chromium(II) chloride (100 mg, 0.81 mmol, 1.1 equiv.) yielding an initial precipitate **18c**(**a**) (25 mg, 6%): MS (Electrospray) *m*/*z* (relative intensity) 634.3 (18), 620.2 (74), 610.2 (42), 592.6 (39), 552.3 ($M-Cl$, 100), 435.4 (15). Anal. Calcd for $C_{28}H_{34}CrCl_3N_2O_2$: C, 57.10; H, 5.82; Cr, 8.83; Cl, 18.06; N, 4.76. Found: C, 48.30; H, 6.47; Cr, 6.04; Cl, 19.91; N, 6.02. Concentration of the filtrate to 5 mL yielded a second precipitate **18c**(**b**) which was filtered and dried (38 mg, 9%): mp >230 °C; IR (KBr, cm^{-1}) 2952, 2864, 1621 (C=N), 1532, 1449, 1389, 1317, 1255, 1171, 864, 766, 552; MS (Electrospray) *m*/*z* (relative intensity) 634.2 (100), 610.1 (46), 592.6 (34), 552.3 ($M-Cl$, 93),

484.5 (16). Anal. Calcd. for $C_{28}H_{34}CrCl_3N_2O_2$: C, 57.10; H, 5.82; Cr, 8.83; N, 4.76. Found: C, 54.42; H, 6.01; Cr, 7.35; N, 4.34. Concentration of the second filtrate to dryness yielded a third product **18c**(**c**) (114 mg, 27%): IR (KBr, cm^{-1}) 2954, 2865, 1619 (C=N), 1533, 1460, 1318, 1256, 1171, 766, 622; MS (Electrospray) *m*/*z* (relative intensity) 812.4 (31), 768.2 (90), 725.3 (35), 636.2 (45), 620.2 (100), 592.5 (17), 552.3 ($M-$Cl, 45), 507.3 (25). Anal. Calcd for $C_{28}H_{34}CrCl_3N_2O_2$: C, 57.10; H, 5.82; Cr, 8.83; N, 4.76. Found: C, 51.99; H, 6.06; Cr, 5.86; N, 3.65.

[(*R*,*R*)-(−)-*N*-(3,5,6-trichlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium (III)] chloride (**18d**) was prepared from **16d** (300 mg, 0.558 mmol) and chromium(II) chloride (75 mg, 0.61 mmol, 1.1 equiv.) yielding a brown solid (245 mg, 70%): mp >230 °C; IR (KBr, cm^{-1}) 2956, 1784, 1622 (C=N), 1533, 1435, 1404, 1173, 772.

[(*R*,*R*)-(−)-*N*-(3,5-dibromosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] chloride (**18e**) was prepared from **16e** (320 mg, 0.540 mmol) and chromium(II) chloride (66 mg, 0.54 mmol, 1 equiv.) yielding 230 mg of a brown solid (63%): mp >230 °C; IR (KBr, cm^{-1}) 2952, 2866, 1619 (C=N), 1444, 1318, 1255, 1156, 717, 653; MS (Electrospray) *m*/*z* (relative intensity) 946.0 (33), 865.1 (20), 724.1 (57), 710.1 (100), 642.2 ($M-$Cl, 40).

[(*R*,*R*)-(−)-*N*-(3,5-dichlorosalicylidene)-*N*′-(3′-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] chloride (**19**) was prepared from **17** (136 mg, 0.304 mmol) yielding a brown solid (108 mg, 57%): mp >230 °C; IR (KBr, cm^{-1}) 2954, 2866, 1619 (C=N), 1534, 1440, 1317, 1267, 1171, 762, 553.

4.6. Synthesis of unsymmetrical chromium salen nitrate complexes

General Procedure: To a solution of the appropriate chromium salen chloride complex in methanol (110 mL per 2 mmol) an excess solution of silver nitrate in water (11 mL per 3 mmol) was added drop-wise. The mixture was stirred for 1 h at room temperature. The resulting white precipitate of silver chloride was gravity filtered and the brown filtrate was concentrated in vacuo to 10 mL. The product was collected by filtration and dried in an oven at 100 °C.

[(*R*,*R*)-(−)-*N*-(3-trifluoromethylsalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium (III)] nitrate (**20a**) was prepared from crude **18a** (140 mg, 0.238 mmol) and silver nitrate (52 mg, 0.306 mmol) yielding a brown solid (74 mg, 47%): mp >230 °C; IR (KBr, cm^{-1}): 2954, 1623 (C=N), 1560, 1448, 1384, 1324, 1123, 1078, 754; MS (Electrospray) *m*/*z* (relative intensity): 651.6 ($M^+ + 1$, 12), 583.6 (15), 552.3 ($M^+ - NO_3$, 100). Anal. Calcd for $C_{29}H_{35}CrF_3N_3O_5.H_2O.MeOH$: C, 54.21; H, 6.22; N, 6.32; Found: C, 54.01; H, 5.74; N, 5.26.

[(*R*,*R*)-(−)-*N*-(3-chlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] nitrate (**20b**) was prepared from **18b** (80 mg, 0.14 mmol) and silver nitrate (27 mg, 0.16 mmol, 1.1 equiv.) yielding a brown solid (75 mg, 89%): mp >230 °C; IR (KBr, cm^{-1}) 2958, 2866, 1724, 1622 (C=N), 1592, 1437, 1384, 1320, 1181, 1139, 744, 555; MS (Electrospray) *m*/*z* (relative intensity) 741.3 (100), 558.6 (16), 518.4 ($M-NO_3$, 41). Anal. Calcd for $C_{28}H_{35}ClCrN_3O_5$: C, 57.88; H, 6.07; Cr, 8.95; N, 7.23; Found: C, 49.08; H, 5.46; Cr, 4.50; N, 5.82.

[(*R*,*R*)-(−)-*N*-(3-chloro)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] hexafluorophosphate was prepared from **18b** (140 mg, 240 mmol) dissolved in the minimum amount of MeOH (150 mL) to which a solution of potassium hexafluorophosphate (52 mg, 290 mmol) in water (5 mL) was added. The resulting solution was stirred overnight at room temperature and concentrated to yield a brown precipitate (128 mg, 76%): mp >230 °C; IR (KBr, cm^{-1}) 2952, 2862, 1623 (C=N), 1534, 1437, 1318, 1254, 1170, 1140; MS (Electrospray) *m*/*z* (relative intensity) 518.4 ($M-PF_6$, 100). Anal. Calcd for $C_{28}H_{35}ClCrF_6N_2O_2P.H_2O.MeOH$: C, 48.78; H, 5.79; N, 3.92. Found: C, 43.69; H, 5.08; N, 3.27.

[(*R*,*R*)-(−)-*N*-(3,5-dichlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] nitrate (**20c**) was prepared from **18c**(**c**) (94 mg, 0.16 mmol) and silver nitrate (30 mg, 0.18 mmol, 1.1 equiv.) yielding a brown solid (80 mg, 81%): mp >230 °C; IR (KBr, cm^{-1}) 2956, 2868, 2361, 1618 (C=N), 1450, 1384, 1314, 1171, 770, 728, 552; MS (Electrospray) *m*/*z* (relative intensity) 642.3 (10), 599.6 (13), 552.4 ($M-NO_3$, 100), 537.4 (11).

[(*R*,*R*)-(−)-*N*-(3,5,6-trichlorosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium (III)] nitrate (**20d**) was prepared from **18d** (237 mg, 0.380 mmol) and silver nitrate (71 mg, 0.42 mmol, 1.1 equiv.) yielding a brown solid (180 mg, 73%): mp >230 °C; IR (KBr, cm^{-1}) 2983, 2866, 1619 (C=N), 1435, 1384, 1321, 1173, 1023, 777, 555; MS (Electrospray) *m*/*z* (relative intensity) 1797.0 (8), 1527.9 (13), 1231.3 (47), 1191.1 (73), 626.6 (22), 588.3 ($M-NO_3$, 100), 571.3 (42). Anal. Calcd for $C_{28}H_{33}Cl_3CrN_3O_5$: C, 51.74; H, 5.12; Cl, 16.36; N, 6.47. Found: C, 43.59; H, 4.43; Cl, 13.36; N, 4.43.

[(*R*,*R*)-(−)-*N*-(3,5-dibromosalicylidene)-*N*′-(3′,5′-di-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] nitrate (**20e**) was prepared from **18e** (218 mg, 0.322 mmol) and silver nitrate (60 mg, 0.35 mmol, 1.1 equiv.) yielding 163 mg of a brown solid (72%): mp >230 °C; IR (KBr, cm^{-1}) 2955, 2867, 1619 (C=N), 1534, 1501, 1444, 1385, 1316, 1255, 1159, 841, 720, 556; MS (Electrospray, CH_3CN) *m*/*z* (relative intensity) 723.4 (7), 682.6 (30), 642.3 ($M-NO_3$, 100), 599.6 (38). MS (Electrospray, CH_3OH) *m*/*z* (relative intensity) 676.3 (21), 642.3 ($M-NO_3$, 100), 627.3 (16). Anal. Calcd. for $C_{28}H_{34}Br_2CrN_3O_5$: C, 47.74; H, 4.86; Br, 22.69; Cr, 7.38; N, 5.97. Found: C, 43.96; H, 4.65; Br, 23.60; Cr, 5.08; N, 4.14.

[(*R*,*R*)-(−)-*N*-(3,5-dichlorosalicylidene)-*N*′-(3′-*tert*-butylsalicylidene)-cyclohexane-1,2-diamine chromium(III)] nitrate (**21**) was prepared from **19** (100 mg, 0.161 mmol) and

silver nitrate (32 mg, 0.19 mmol, 1.2 equiv.) yielding 62 mg (59%) of a brown solid: mp >230 °C; IR (KBr, cm^{-1}) 2958, 2868, 1619 (C=N), 1445, 1383, 1316, 1170, 768, 553.

4.7. Attempted synthesis of [(R,R)-(−)-N-(3,5,6-trichlorosalicylidene)-N′-(3′,5′-di-tert-butylsalicylidene)-cyclohexane-1,2-diamine manganese(III)] chloride (26)

The procedure described by Jacobsen et al. was followed [15]. A 25 mL 2-necked round bottom flask equipped with reflux condenser and addition funnel was charged with manganese(II) acetate tetrahydrate (324 mg, 1.32 mmol) in ethanol (3.5 mL). The stirred solution was heated to reflux and a solution of **16d** (300 mg, 0.558 mmol) in toluene (2.5 mL) was added drop-wise over 30 min. The addition funnel was rinsed with toluene (1 mL) and the mixture refluxed for 2 h. The addition funnel was replaced with a Pasteur pipette connected to a fish-pump and air was bubbled through the reaction mixture, with continued heating for 4 h. The reaction was monitored by TLC (ethyl acetate/hexane 1:4, R_f of ligand = 0.14, R_f of Mn-complex = baseline) until complete ligand disappearance was observed. A saturated solution of sodium chloride (2.5 mL) was added and the mixture cooled to room temperature overnight. The mixture was transferred to a separatory funnel, rinsing the reaction flask with toluene (10 mL). The organic phase was separated, washed with water (2 × 20 mL), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo to yield a brown solid. This was dissolved in dichloromethane (5 mL) and *n*-heptane (5 mL) added. The volume was reduced to ca. 5 mL and the resulting mixture cooled on ice for 1 h and then filtered yielding a brown solid (126 mg, 36%): mp >230 °C; IR (KBr, cm^{-1}) 2953, 2865, 1611 (C=N), 1535, 1431, 1393, 1338, 1312, 1272, 1253, 1177, 842, 779, 569, 548; MS (EI) *m*/*z* relative intensity 599.3 (100[tetra-*t*-Bu $M^+ - Cl$ cation]), 546.4 (29), 313.2 (70), 218.1 (19), 57.1 (71), 41.0 (96). MS (Electrospray) *m*/*z* (relative intensity) 599.6 (100[tetra-*t*-Bu $M^+ - Cl$ cation]), 589.3 (16[unsymm $M - Cl$]). Anal. Calcd. for $C_{28}H_{33}Cl_4MnN_2O_2$: C, 53.69; H, 5.31; Cl, 22.64; Mn, 8.77; N, 4.47. Found: C, 57.20; H, 6.01; Cl, 17.82; Mn, 7.76; N, 4.14.

4.8. Epoxidation reactions

4.8.1. Preparation of oxo-chromium species in situ

Caution, there is evidence [51] that chromium(V)oxo complexes are genotoxic and carcinogenic and thus due care should be taken to avoid inhalation and contact with skin. In a sample bottle, the chromium complexes **20** and **21** (usually 30 mg) were dissolved in acetonitrile (4 mL per 0.08 mmol). To these orange solutions, iodosylbenzene (1.2 equiv.) was added and the resulting black solutions of oxidants **22** and **23** were stirred for 20 min. The excess iodosylbenzene was removed by filtration or decanting and was washed with the same solvent (2 mL).

4.8.2. Stoichiometric epoxidation

The black solution was placed in iced water and the additive added (if required) resulting in a slight colour change from black to black/green. After 10 min equilibration, the substrate alkene (1.2 equiv.) was added via syringe. The resulting solution was stirred until an orange colour persisted, which usually required several days. The solvent was removed in vacuo and diethyl ether (10 mL) was added to the residue. The insoluble complex was washed with diethyl ether (4 × 10 mL) and the combined washings were passed down a short pad of alumina taking care to ensure full elution of organic material. At this stage the chromium complex can be collected for recycling. The eluant was concentrated in vacuo to approximately 1 mL for GC analysis. Decane (1 μL) was added as internal standard to the mixture and 1 μL of this solution injected onto the GC column. The ee of *trans*-β-methylstyrene oxide, its yield and that of starting alkene, phenylacetone and benzaldehyde was determined using a Supelco α-cyclodextrin 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.

4.8.3. Catalytic epoxidations using 26

A solution of commercial household bleach (calculated to be 1.475 M in NaOCl) was diluted to approximately 0.55 M in NaOCl with 0.05 M Na_2HPO_4. **26** (3.86 mg, 6.17×10^{-6} mol, 0.04 equiv.) was added to the relevant

Complex	*W*	*X*	*Z*	*X′*	*Z′*	Additive	ee (%)	Yield (%)	Unreacted alkene (%)
22a	H	H	CF_3	^{t}Bu	^{t}Bu	Ph_3PO	84	2	9
22a	H	H	CF_3	^{t}Bu	^{t}Bu	None	79	2	6
22b	H	H	Cl	^{t}Bu	^{t}Bu	Ph_3PO	55	9	24
22b	H	H	Cl	^{t}Bu	^{t}Bu	None	59	3	40
22c	H	Cl	Cl	^{t}Bu	^{t}Bu	Ph_3PO	79	4	29
22c	H	Cl	Cl	^{t}Bu	^{t}Bu	None	66	3	38
22d	Cl	Cl	Cl	^{t}Bu	^{t}Bu	Ph_3PO	80	11	29
22d	Cl	Cl	Cl	^{t}Bu	^{t}Bu	None	60	6	27
22e	H	Br	Br	^{t}Bu	^{t}Bu	Ph_3PO	80	10	25
22e	H	Br	Br	^{t}Bu	^{t}Bu	None	71	2	51
23	H	Cl	Cl	H	^{t}Bu	Ph_3PO	71	5	nd[a]
23	H	Cl	Cl	H	^{t}Bu	None	25	1	nd[a]

alkene (20 mL, 0.15 mmol, 1 equiv.) and additive (if any) in chloroform (1 mL). Bleach (1.12 mL of 0.55 M, 0.62 mmol, 4 equiv.) was added and the brown solution stirred at 0 °C for 6 h, then warmed to room temperature overnight. Dichloromethane (5 mL) was added, the phases separated and the organic phase washed with water (2 × 5 mL) and brine (5 mL). The solution was dried over sodium sulfate and concentrated in vacuo to yield a brown residue which was purified by flash chromatography (silica, CH_2Cl_2). The solution was concentrated to ca. 1 mL, 1 μL *n*-decane added and *trans*-β-methylstyrene oxide analysed by GC on a Supelco α-cyclodextrin column as before. *cis*-β-Methylstyrene oxide was analysed on a Supelco β-cyclodextrin capillary column, operated at an injection temperature of 250 °C and a gradient column temperature of 77–177 °C over 17 min, with a column pressure of 10 psi. The absolute configuration of *trans*-β-methylstyrene oxide was assigned by comparison of a sample with the data of Witkop and Foltz [56] and of Shi and co-workers [57]. 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 [15].

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