Enantioselective oxidation using transition metal catalysts

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Chapter 5

Catalytic α-Hydroxylation Using Manganese(III) Complexes

5.1 Introduction

α-Hydroxy ketones play an important role in synthetic organic chemistry. Achiral α-hydroxy ketones can be produced in a number of ways, i.e. ring closure of dialdehydes under the influence of thiazolium salts and triethylamine generates cyclic hydroxy ketones,[1] whereas acid catalyzed ring opening and oxidation of epoxides using DMSO as oxidant has been performed, providing, for instance, 2-hydroxy-1-phenylethanone starting from styrene oxide with yields up to 71 %.[2]

Ketones have been converted to the corresponding α-hydroxy ketones using bis(trifluoroacetoxy)iodobenzene with yields up to 94 % for cyclohexanone.[3] The synthesis of α-hydroxy ketones starting from a halide, an isocyanide and a carbonyl compound under the influence of samarium(II) iodide with yields up to 91 % is described by Ito and co-workers.[4]

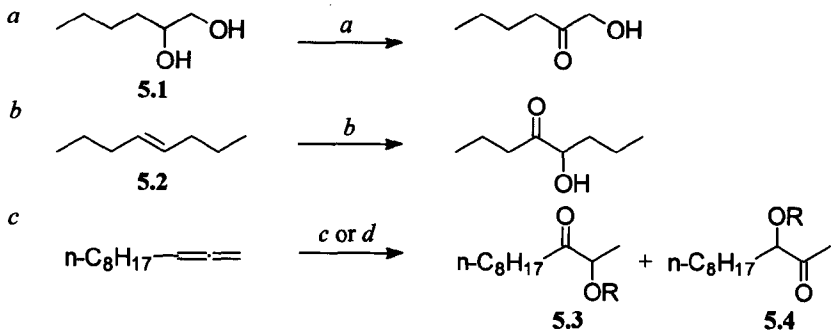
A transition metal catalyst employed in the oxidation of 1,2-diols to α-hydroxy ketones is peroxotungstophosphate, used in combination with acidic hydrogen peroxide in a two phase system (aqueous hydrogen peroxide/chloroform).[5] Regioselective oxidation takes place with a maximum yield of 93 % in case of 1,2-hexanediol (**5.1**, scheme 5.1a).

Olefins have been used as starting materials, that are converted to the corresponding epoxide with subsequent acid mediated ring opening,[6] followed by oxidation to the hydroxy ketone with a maximum yield of 63 % for 4-octene (**5.2**, scheme 5.1b). Unsymmetrical olefins yield a mixture of regioisomers. Hydrogen peroxide oxidation of allenes such as 1,2-undecadiene, in an acetic acid/chloroform system, gives 50 % of the corresponding α-keto acetate **5.3** regioselectively, whereas the reaction performed in *tert*-BuOH gave an approximately 1 : 1 mixture of both regioisomers **5.3** and **5.4** (scheme 5.1c).[7]

Ishii and co-workers use zirconium in the synthesis of α-hydroxy carbonyl compounds starting from 1,2-diols, generating α-hydroxy aldehydes in the case of acyclic diols (1,2-butanediol) and an α-hydroxy ketone for 1,2-cyclohexanediol.[8] A reduction method using hafnocene dihydride and α-diketones gave the corresponding hydroxy ketones with a regioselectivity up to 98 % in case of 2,3-dioxobutane.[9]

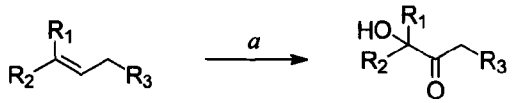
Simple ruthenium salts give rise to α-hydroxy ketones starting from olefins as described in a patent by Takasago.[10] The best result for unsubstituted alkenes is obtained using ruthenium(III) chloride for the oxidation of cyclohexene (74 %).

Mukaiyama and co-workers[11] used osmium tetroxide in combination with a nickel(II) catalyst in the oxidation of olefins (scheme 5.2). Isobutyraldehyde is used as terminal oxidant



Scheme 5.1 *Synthesis of α-hydroxy ketones using peroxotungstophosphate (PCWP). a. PCWP, hydrogen peroxide, chloroform, r.t. 93 %; b. see a. but with addition of sulphuric acid, reflux, 63 %; c. see b, but with addition of acetic acid. 5.4: R = Ac: 50 %; d. see b. but with tert-butanol as solvent, 5.3 and 5.4: 56 %, ratio 5.3 : 5.4 = 1 : 1.1.*

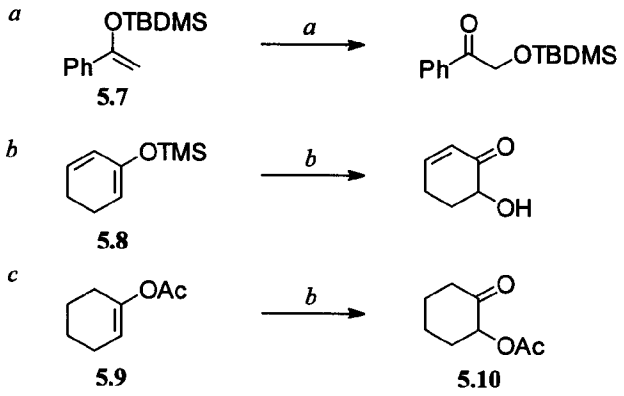
and molecular oxygen plays an important role, since reaction under an argon atmosphere did not give any oxygenation products. The highest yield is obtained for prenyl benzoate (**5.5**: 82 %). The less activated olefin 1-undecene (**5.6**) gave the corresponding α-hydroxy ketone in 67 % yield.



5.5: $R_1 = R_2 = Me$, $R_3 = OBz$
5.6: $R_1 = R_2 = H$, $R_3 = n\text{-}C_8H_{17}$

Scheme 5.2 *Synthesis of α-hydroxy ketones. a. bis(3-methyl-2,4-pentanedionato) nickel(II) (Ni(mac)$_2$), osmium tetroxide, O_2, 2,6-lutidine, isopropylaldehyde, THF, r.t.*

With silyl enol ethers as starting materials, Mukaiyama and co-workers use a nickel(II) catalyst in combination with an aldehyde and molecular oxygen (scheme 5.3a). Excellent yields were obtained for the *tert*-butyldimethylsilyl enol ether of acetophenone (**5.7**, 93 %).[12] Cobalt(II) mediated catalysis can be performed, with the highest yield in the oxidation of 2-trimethylsilyloxy cyclohexadi-1,3-ene (**5.8**, 87 %, scheme 5.3b).[13] Furthermore, enol acetates like cyclohex-1-enyl acetate (**5.9**) can be oxidized yielding 2-keto-cyclohexylacetate (**5.10**, scheme 5.3c, 89 %). Also, MCPBA is used as oxidant in this reaction, with yields up to 77 %.[14]

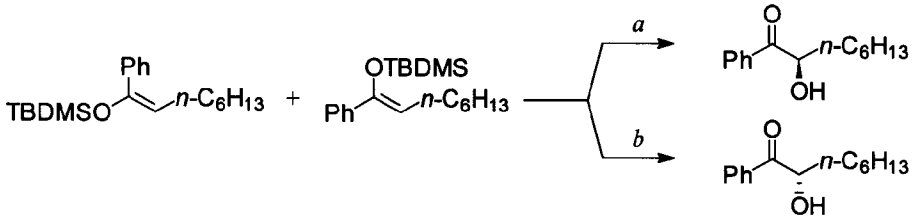


Scheme 5.3 *Oxidation of protected enols to (protected) α-hydroxy ketones. a. $Ni(mac)_2$, O_2, isobutyraldehyde, r.t., 93 %; b. $Co(mac)_2$, propionaldehyde diethylacetal, 4Å MS, 45 °C.*

Chandrasekaran and co-workers[15] reported a heterogeneous permanganate base catalyst. A finely ground mixture of potassium permanganate, copper(II) sulphate pentahydrate, with *tert*-butanol and a trace of water in dichloromethane gave α-hydroxy ketones in up to 59 % yield (cycloheptene).

Only a very limited number of enantioselective syntheses of α-hydroxy ketones have been reported, for instance, oxidation of 1,2-diols using alcohol dehydrogenase yielded α-hydroxy aldehydes with enantioselectivities exceeding 97 %.[16]

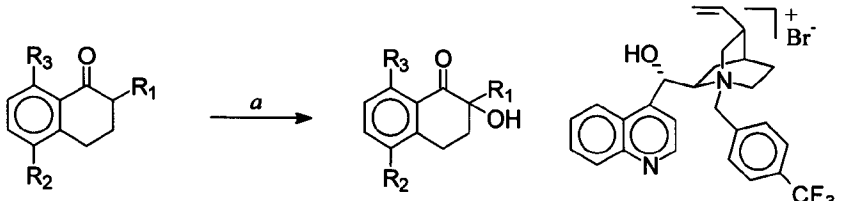
Sharpless and co-workers[17] reported the osmium catalyzed enantioselective oxidation of enol ethers (methyl or *tert*-butyldimethylsilyl derivatives) using AD-mix-α or AD-mix-β,[18] with enantioselectivities up to 99 % (scheme 5.4).



Scheme 5.4 *Enantioselective oxidation of enol ethers. a. AD-mix-β, b. AD-mix-α.*

A method based on the use of chiral phase transfer catalysts is reported by Shiori and co-workers,[19] employing quaternary ammonium salts of chinchona alkaloids with α-alkylated

ketones as substrates. The best results were obtained with *para*-trifluoromethylbenzyl cinchonium bromide (**5.11**, scheme 5.5) in the oxidation of 8-chloro-3,4-dihydro-5-methoxy-2-methyl-1-naphthalenone (**5.12**, e.e. 79 %). With non-functionalized ketones the highest enantioselectivity, 77 %, is reached for 3.4-dihydro-2-(1-methylethyl)-naphthalenone (**5.13**).

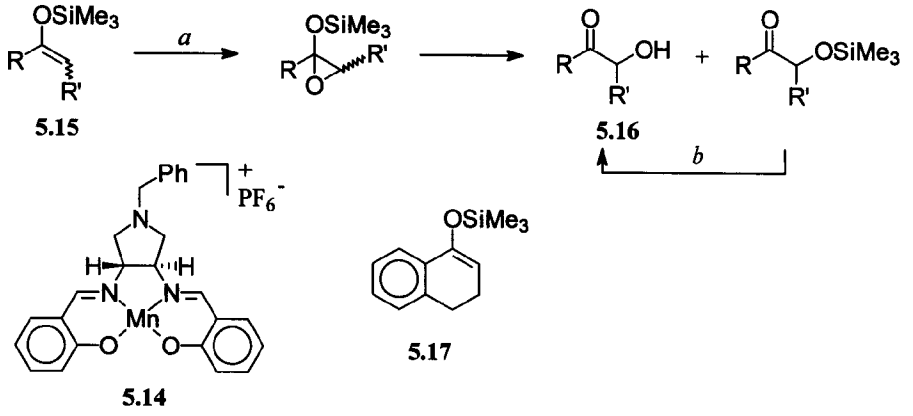


5.12: R_1 = Me, R_2 = OMe, R_3 = Cl
5.13: R_1 = *iso*-Pr, R_2 = R_3 = H

5.11

Scheme 5.5 *Enantioselective oxidation of ketones to α-hydroxy ketones. a. **5.11**, O_2, 50 % aqueous NaOH, toluene, triethylphosphite, r.t.*

Reddy and Thornton published a synthesis of hydroxy ketones starting from silyl enol ethers using a chiral pyrrolidine derived salen complex (**5.14**, scheme 5.6).[20] The procedure involves epoxidation of the enol double bond in **5.15** using catalyst **5.14** and iodosylbenzene, followed by desilylation with potassium fluoride, resulting in the formation of the α-hydroxy ketone **5.16**. An enantioselectivity of 61 % was found for the silyl enol ether derived from α-tetralone (**5.17**, scheme 5.6).



5.15

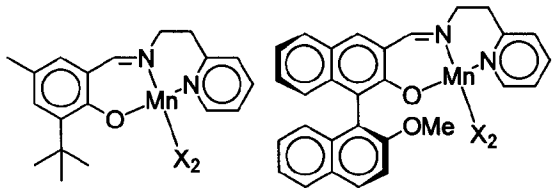
5.16

5.17

5.14

Scheme 5.6 *α-Oxidation of the silyl enol ethers **5.15** using mononuclear manganese salen complex **5.14**. a. **5.14**, PhIO, acetonitrile, r.t.; b. KF, methanol.*

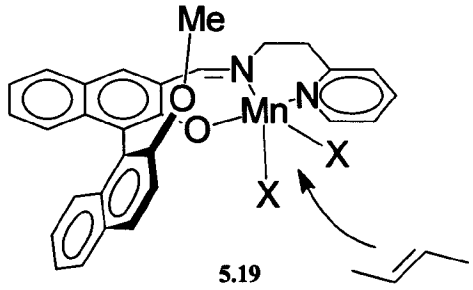
Since diaminocyclohexane-based catalysts are not suitable for the oxidation of *trans*-olefins (or trisubstituted olefins) because steric interactions are too severe, we decided to synthesize the "half-salen" manganese complexes **5.18** and **5.19**, as depicted in figure 5.1, and examine these complexes in the α-hydroxylation and epoxidation of *trans*-alkenes.



5.18 **5.19**

Figure 5.1 *"Half-salen" complexes **5.18** and **5.19**.*

As is shown in figure 5.2, the "front side" of the half-salen complexes is less sterically encumbered, and a phenolic unit of the salen ligand is replaced by a monodentate ligand (X), generally more prone to dissociation. Attack of the olefin to the proposed manganese oxo species might be possible from this direction, making the approach for in particular a *trans*-olefin feasible. The "half-salen" manganese catalysts **5.18** and **5.19** seem excellently suited to investigate oxidation of *trans*-olefins and trisubstituted olefins.



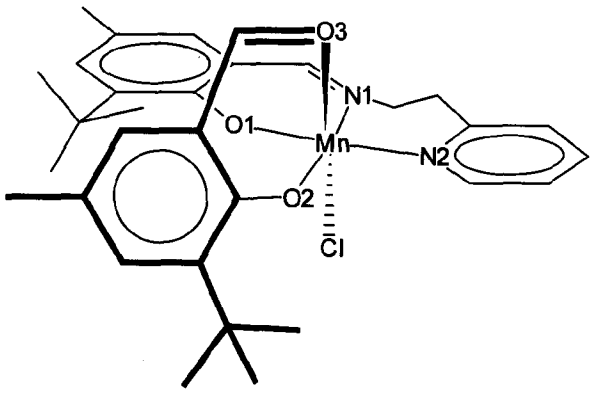
5.19

Figure 5.2 *Possible attack of the olefin to the manganese catalyst **5.19**.*

5.2 Synthesis of (2-*tert*-Butyl-4-methyl-6-(2-pyridin-2-yl-ethylimino-methyl)-phenolato) (2-*tert*-butyl-4-methyl-6-formyl)-phenolato)manganese(III) chloride (5.20)

We tried to synthesize complex **5.18** by complexation of $Mn(OAc)_2 \cdot 4H_2O$ with 2-*tert*-butyl-4-methyl-6-(2-pyridin-2-yl-ethylimino-methyl)-phenol (**5.21**, synthesized as described in chapter 4), followed by air oxidation to the manganese(III) complex and subsequent anion

exchange (LiCl), analogously to the literature procedure for the Jacobsen catalyst (described in chapter 3).[21] Recrystallization of the dark-brown product from acetonitrile afforded black crystals. Unexpectedly, the elemental analysis indicated a composition of $C_{31}H_{38}N_2O_3MnCl$ instead of $C_{19}H_{23}N_2OMnCl$. In order to establish unequivocally the structure of complex **5.20**, a molecular structure determination was performed. Surprisingly, complex **5.18** was not formed, but instead one equivalent of imine was hydrolysed to afford the starting aldehyde, that is bonded to manganese. The molecular structure of complex **5.20** is given in figure 5.3.



5.20

Figure 5.3

The *ORTEP*-picture (figure 5.4) clearly shows a distorted octahedral geometry around manganese(III). The half-salen ligand binds in an equatorial fashion with O1, O2, and N1 of the ligand coordinated to the manganese(III) atom. A salicylaldehyde moiety binds with the phenoxo oxygen (1.914(5) Å) at the remaining equatorial position, with the O-coordinated aldehyde (2.270(5) Å) at an apical position. The chloride (2.456(2) Å) occupies the remaining apical coordination site (figure 5.4). The bond angle Cl1-Mn1-O3, (O3 of the coordinating aldehyde) shows significant bending (172.5(2)°) from the expected 180°. This could signify strain in the molecule due to the steric interaction between the two *tert*-butyl groups. Comparison of the bond lengths and angles with values found in the literature can not be made, since to our knowledge this is the first example of a half-salen salicylaldehyde complex. A $(salicylaldehyde)_3Mn$ complex is known.[22] However, only UV-VIS and IR-spectra and no crystallographic data are given.

Further experiments did not result in a successful synthesis of complex **5.18**.

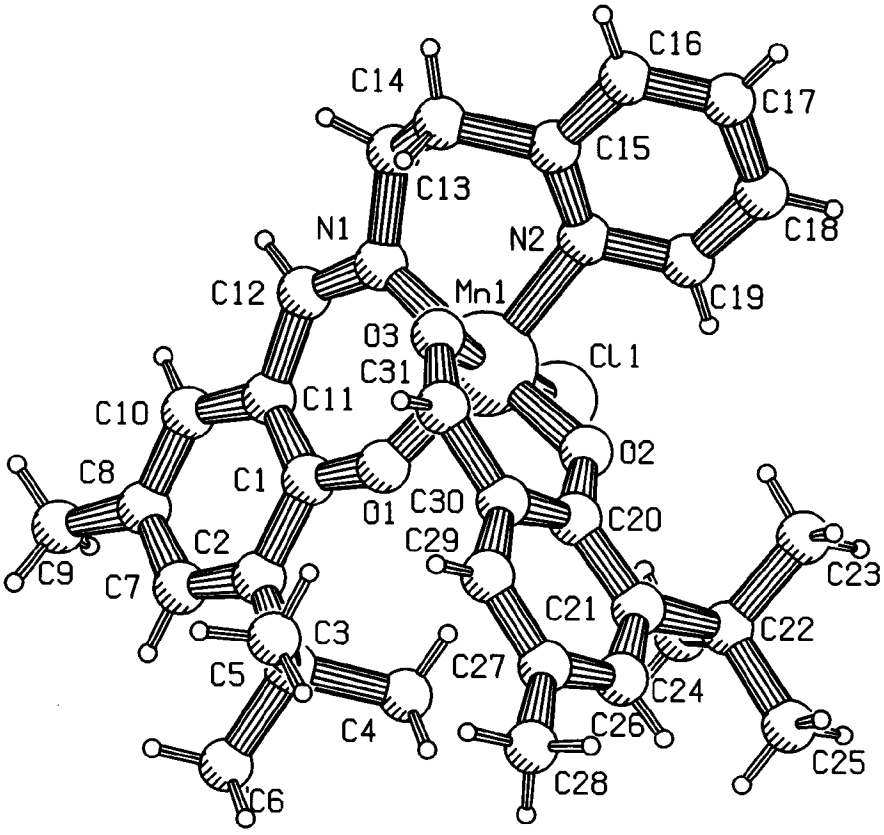


Figure 5.4 *Molecular structure of (2-tert-Butyl-4-methyl-6-(2-pyridin-2-yl-ethylimino-methyl)-phenolato)-(2-tert-Butyl-4-methyl-phenolato)manganese(III) chloride (**5.20**) (PLUTO) with adopted numbering scheme. Selected bond distances (Å) and angles (deg) (standard deviations in parentheses): Mn1-Cl1: 2.456(2); Mn1-O1: 1.874(5); Mn1-O2: 1.914(5); Mn1-O3: 2.270(5); Mn1-N1: 2.000(7); Mn1-N2: 2.094(7); Cl1-Mn1-O1: 97.77(16); Cl1-Mn1-O2: 91.05(16); Cl1-Mn1-O3: 172.48(15); Cl1-Mn1-N1: 92.40(19); Cl1-Mn1-N2: 92.76(18); O1-Mn1-O2: 93.1(2); O1-Mn1-O3: 85.8(2); O1-Mn1-N1: 89.3(2); O1-Mn1-N2: 169.3(2); O2-Mn1-O3: 82.1(2); O2-Mn1-N1: 175.5(3); O2-Mn1-N2: 88.7(2); O3-Mn1-N1: 94.3(2); O3-Mn1-N2: 83.9(2); N1-Mn1-N2: 88.4(3).*

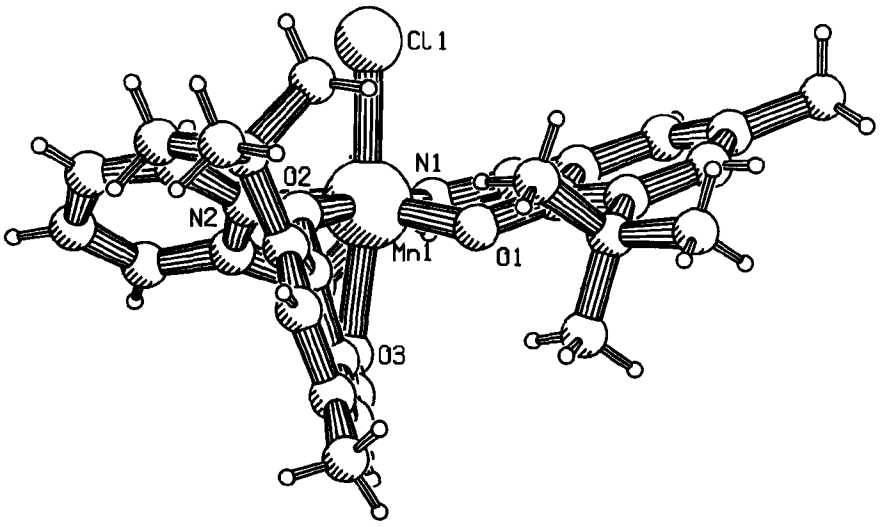
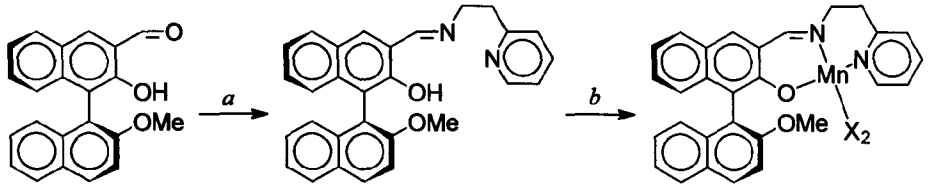


Figure 5.5 *Side view from the aldehyde towards the N1 along the manganese nitrogen bond of 5.20 (PLUTO).*

5.3 Synthesis of 3-(2-Pyridin-2-yl-ethylimino-methyl)-[2'-methoxy[(*S*)-1,1'-bi-naphthalen]-2-olato]-manganese(III) chloride (5.19)

Retrosynthetic analysis of complex **5.19** offers imine **5.22** and ultimately aldehyde **5.23** as precursors for **5.19**.

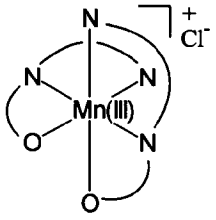
Aldehyde **5.23** was prepared from bis-β-naphthol as described in chapter 3. Imine formation was carried out by reaction of **5.23** with 2-pyridylethylamine in ethanol heated under reflux. Subsequently, complexation with manganese(II) acetate in ethanol, using the procedure published by Jacobsen,[21] was performed (scheme 5.7).



5.23 **5.22** **5.19**

Scheme 5.7 *Synthesis of catalyst 5.19. a. 2-pyridylethylamine, ethanol, Δ, 100 %; b. manganese(II) acetate tetrahydrate, O_2, LiCl, MeOH, Δ, 47 %.*

Elemental analysis of complex **5.19** was not satisfactory. However, it is known that these type of complexes are extremely difficult to characterize by elemental analysis. Ion spray mass spectroscopy gave a parent ion at m/e 917, corresponding to a structure of two ligands binding to the manganese ion as in **5.24** (figure 5.6), with loss of a chloride anion. This is consistent with the observed behaviour of these type of complexes, the ion spray mass spectroscopy of the di(*tert*-butyl) Jacobsen catalyst **5.25** (figure 5.6) showed a parent peak at m/e 599, corresponding to the catalyst with loss of the chloride anion.[23]



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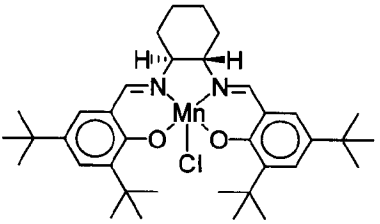


5.25

Figure 5.5

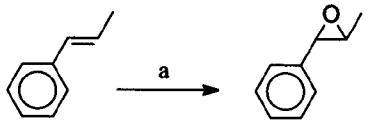
5.4 Oxidation Study

5.4.1 Oxidation of *trans*-β-Methylstyrene and 3,4-Dihydro-1-trimethylsilyloxy naphthalene by Complex 5.20

Evaluation of complex **5.20** suggested that it may still be a suitable catalyst for oxidation reactions. The coordinating aldehyde could be displaced by an oxidant, or could aid the displacement of the chloride anion for the oxidant. In the latter situation, it could be imagined that the activity of the ensuing oxygenated complex would be enhanced by electron donation of the aldehyde to the metallo-complex as has been demonstrated in porphyrin and salen complexes (see chapter 1).

As a model compound for the epoxidation of *trans*-olefins *trans*-β-methylstyrene (**5.26**) was chosen. Epoxidation of this olefin under phase transfer conditions with bleach (scheme 5.8) yielded less than 5 % epoxide after 16 h, demonstrating that **5.20** is not a suitable catalyst in the epoxidation of *trans*-β-methylstyrene.

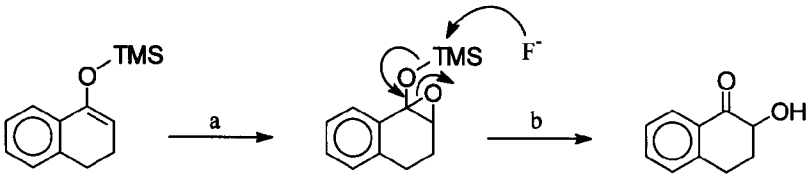
As model compound for the α-hydroxylation of silyl enol ethers and for the epoxidation of trisubstituted olefins, the silyl enol ether of α-tetralone was chosen (scheme 5.9). The α-hydroxylation of the substrate is performed by epoxidation of the enol double bond, yielding the trimethylsilyl epoxide **5.27**. Subsequently, ring opening of the epoxide takes place,



5.26

Scheme 5.8 *Attempted oxidation of trans-β-methylstyrene (5.26) using 5.20 as catalyst. a. 5.20 (1.5 mol%), NaOCl, CH_2Cl_2, H_2O (pH = 9.0), 16 h., r.t.*

generating α-hydroxy ketone **5.28** and the trimethylsilyloxy-analogue of **5.28** (see also scheme 5.6). The remaining protected hydroxy compound is deprotected using KF in methanol.



5.17 5.27 5.28

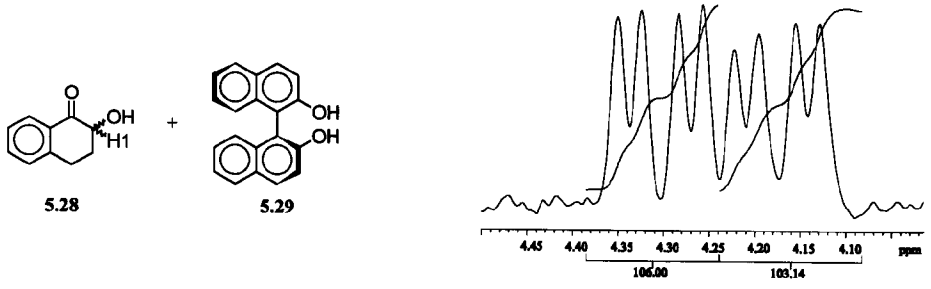
Scheme 5.9 *Attempted oxidation of 5.17 using 5.20 as catalyst. a. 5.20, PhIO, acetonitrile, r.t.; b. KF, MeOH, r.t.*

Epoxidation of the silyl enol ether of α-tetralone, (2.0 mol% of **5.20** followed by desilylation using KF in methanol) yielded less than 5 % of the α-hydroxy tetralone **5.28**. The main product of the reaction was α-tetralone, which is simply the product of desilylation of the starting material. This shows that **5.20** does not catalyze the epoxidation of this substrate either.

5.4.2 Oxidation of 3,4-Dihydro-1-trimethylsilyloxy-naphthalene by Complex 5.19

The use of complex **5.19** (2.0 mol%) to catalyze the α-hydroxylation of α-silyl enol ether **5.17** (scheme 5.9) resulted in a very fast reaction. Epoxidation was observed to be complete within 20 minutes. The reaction mixture, containing both α-hydroxy and α-silyloxy ketone (^{1}H NMR), was quenched with a solution of KF in methanol, to provide 80 % of the α-hydroxy ketone **5.28**. The catalyst gives a slightly better yield in the same time-scale compared to that reported by Reddy and Thornton[20] (80 % *versus* 72 %). The enantiomeric excess of hydroxy ketone **5.28** was examined by ^{1}H NMR using a chiral organic shift reagent (figure 5.7). Hydroxy ketone **5.28** and a 10-fold excess of (*S*)-bis-β-naphthol (**5.29**) were dissolved in chloroform-*d3*. The H1-proton (see figure 5.7) could be used for the

determination of the enantiomeric excess of racemic **5.28**; a double doublet was obtained for each of the enantiomers. When the product of the epoxidation (scheme 5.9) was examined a double doublet with equal intensity was obtained and it was evident that racemic hydroxy ketone was formed in the reaction.



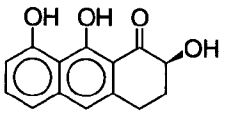
5.28 **5.29**

Figure 5.7 *E.e.-determination of α-hydroxy tetralone **5.28** using (S)-bis-β-naphthol (**5.29**) as organic shift reagent; ^1H NMR absorptions of H1.*

To ascertain that the formation of racemic **5.28** was due to the reaction conditions, catalyst **5.30** was synthesized according to a literature procedure (scheme 5.10).[20,21]

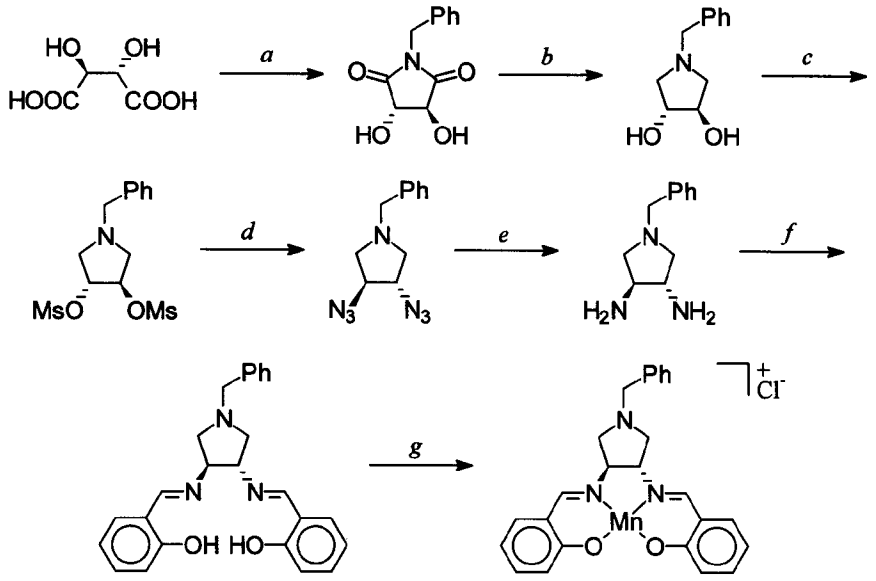
In this catalyst, the stereogenic centres are sited on the top side of the molecule in contrast to the dissymmetric biaryl unit present in the "lower" part of **5.19**.

When this catalyst was used in the α-hydroxylation of **5.17**, racemic hydroxy ketone **5.28** was again obtained, as shown by our ^1H NMR analysis, contrary to the selectivity reported in the literature (detection by HPLC).[20] Possible reasons include racemization under our reaction conditions, although they are very similar to those reported.[20] Although enantiomerically stable α-hydroxy ketones have been synthesized, α-hydroxy ketone **5.32** is known to racemize rapidly under basic conditions (figure 5.8).[24]



5.32

Figure 5.8



5.31 5.30

Scheme 5.10 *a. benzylamine, para-xylene, Dean Stark, 85 %; b. LAH, THF, r.t., 64 %; c. MsCl, Et_3N, THF, r.t., 36 %; d. NaN_3, DMF, r.t., 37 %; e. LAH, THF, r.t., 56 %; f. salicylaldehyde, methanol, r.t., 64 %; g. manganese(II) acetate tetrahydrate, O_2, methanol, LiCl, r.t., 40%.*

It could be imagined that acidic conditions, e.g. present during chromatography on a silica gel column, also could induce racemization at the α-carbon atom of the substrate. Another possibility would be that the reaction is not catalyzed by the half-salen manganese(III) catalyst, but proceeds in an achiral fashion. Reactions that might shed light on this puzzling result include the blank reaction, reaction with simple manganese(III) salts as catalysts, performing the reaction at a lower temperature suppressing the non catalyzed reaction and conducting the reaction with different, less activated, oxidants such as sodium hypochlorite, hydrogen peroxide or alkyl hydrogen peroxide. These conditions are under current investigation.

When a model of complex **5.28** is build, it can be seen that the steric bulk, if present, and the stereogenic centres in catalyst **5.28** are situated at the top side of the catalyst. Therefore, the approach of the silyl enol ether towards the proposed manganese oxo species is probably from the bottom side of the catalyst. It is reasonable to assume that the differences in interaction between the two π-faces of the silyl enol ether and the catalyst are small.

Therefore, is not clear where the enantioselectivity reported in the literature for the α-hydroxylation of **5.17** using chiral manganese catalyst **5.30** in the asymmetric oxygenation stems from.

Another possibility is that the enantiomeric excess determination gives incorrect data, since this method has not be applied to enantiomerically enriched α-hydroxy tetralone yet.

5.5 Conclusions

We have synthesized two new manganese(III) complexes, **5.19** and **5.20**, the latter showing a salenaldehyde bidentate coordination to the manganese centre. Complex **5.20** shows, as far as we know, unprecedented coordination behaviour, since the salicylaldehyde is coordinating with an equatorial phenoxy moiety and an axial aldehyde oxygen. Catalyst **5.19** is not a suitable epoxidation catalyst for *trans*-olefins since only 5 % epoxide was observed in the case of *trans*-β-methyl styrene. Catalyst **5.20** is not suited for epoxidation of *trans*-olefins or α-hydroxylation of silyl enol ethers. In both cases < 5 % product was obtained. However, complex **5.19** is very active in the α-hydroxylation of silyl enol ethers. In 20 minutes 80 % of the α-hydroxy ketone (or the α-trimethylsilyloxy ketone) was obtained. The use of (*S*)-bis-β-naphthol as chiral shift reagent for ^{1}H NMR showed the α-hydroxyketone to be racemic. Control experiments with catalyst **5.30** did not give rise to an enantioselective oxidation, contrary to the results described in the literature.

5.6 Experimental Section

5.6.1 General Remarks

For general remarks concerning materials and instrumentation, see § 2.7. *trans*-β-Methylstyrene was obtained from Aldrich. *trans*-β-Methylstyrene oxide and 3,4-Dihydro-1-trimethylsilyloxy-naphthalene were synthesized following to a literature procedure.[25,26] Iodosyl benzene was synthesized from iodobenzene diacetate (Acros) following literature procedures.[27]

5.6.2 Molecular Structure Determination

Molecular Structure Determination of (2-tert-Butyl-4-methyl-6-(2-pyridin-2-yl-ethyl imino-methyl)-phenolato)-(2-tert-Butyl-4-methyl-phenolato)manganese(III) chloride (5.20). Crystals suitable for X-ray determination were grown from acetonitrile. Crystal data for **5.20**: $C_{31}H_{38}N_2O_3MnCl$, M = 577.04, crystal size = 0.25 x 0.15 x 0.08 mm, triclinic,

spacegroup *P*-1, a = 9.1397(9), b = 9.5529(9), c = 17.470(3) Å, α = 100.029(9)°, β = 103.039(10)°, γ = 101.853(8)°, V = 1414.9(3) Å^3, Z = 2, D_x = 1.355 g cm^{-3}, λ(Mo $K\bar{\alpha}$) = 0.71073 Å, μ(Mo $K\bar{\alpha}$) = 6.0 cm^{-1}, F(000) = 608, T = 150 K, ω scan, $\Delta\omega$ = 1.03 + 0.35 tg θ, 1.2 < θ < 25.0, total unique data 4983 (R_{int} = 0.1191), No. of observations [$I \geq 2.0\ \sigma(I)$] 2176, R = 0.084, R_w = 0.1525, maximum peak in final Fourier difference synthesis 0.53 e/Å^3.

5.6.3 Reactions

2'-Methoxy-3-(2-pyridin-2-yl-ethyl-imino-methyl)-[1,1']binaphthalenyl-2-ol 5.22. Aldehyde **5.23** (656 mg, 2.0 mmol) and pyridylethylamine (244 mg, 2.0 mmol) were dissolved in EtOH (100 mL), and subsequently heated under reflux for 30 min. After cooling the mixture to room temperature the solvent was removed *in vacuo*, yielding pure **5.22** (863 mg, 100 %); m.p. 191.0-191.6 °C; ^{1}H NMR: δ 13.11 (br s, 1H), 8.60-8.52 (m, 2H), 8.07-7.79 (m, 4H), 7.59-7.47 (m, 2H), 7.39-7.09 (m, 8H), 4.08 (t, J = 7.2, 2H), 3.81 (s, 3H), 3.17 (t, J = 7.2, 2H); ^{13}C NMR: 165.56, 158.98, 155.11, 154.53, 149.41, 136.42, 135.34, 133.80, 132.99, 129.64, 129.37, 128.67, 128.04 (2 x), 127.31, 126.42, 125.12, 124.83, 123.71, 123.55, 123.15, 121.50, 120.80, 118.92, 117.17, 114.27, 59.40, 56.99, 32.24. HRMS calcd for $C_{29}H_{24}N_2O_2$ 432.184, found 432.184. Anal. Calcd for $C_{29}H_{24}N_2O_2$: C, 80.53; H, 5.59; N, 6.48. Found: C, 80.30; H, 5.64; N, 6.39.

Bis-(3-(2-pyridin-2-yl-ethylimino-methyl)-[2'-methoxy[(*S*)-1,1'-binaphthalen]-2-olato])-manganese(III) chloride (5.19). Imine **5.22** (432 mg, 1.0 mmol) and manganese(II) acetate tetrahydrate (490 mg, 2.0 mmol) were dissolved in EtOH (50 mL), and the solution was heated under reflux for 30 min in air. LiCl (255 mg, 6.0 mmol) was added and the solution was heated under reflux for a further 30 min. Subsequently, the mixture was cooled to room temperature, and the solvent removed *in vacuo*. The residue was dissolved in CH_2Cl_2 and filtered to remove the inorganic salts. After evaporation of the solvent *in vacuo*, **5.22** (261 mg, 47 %) was obtained as a brown powder. A sample for analysis was obtained by precipitation from acetonitrile. Anal. Calcd for $C_{56}H_{46}N_4O_4MnCl$: C, 72.37; H, 4.99; N, 6.03; Mn, 5.91; Cl, 3.81. Found: C, 63.31; H, 4.76; N, 5.32; Mn, 6.35; Cl, 8.81.

(2-tert-Butyl-4-methyl-6-(2-pyridin-2-yl-ethylimino-methyl)-phenolato)-(2-tert-Butyl-4-methyl-6-formyl-phenolato)manganese(III) chloride (5.20). Imine **5.22** (888 mg, 3.0 mmol) and manganese(II) acetate tetrahydrate (1.47 g, 6.0 mmol) were dissolved in EtOH (50 mL), and the solution was heated under reflux for 30 min. LiCl (765 mg, 18.0 mmol) was added and the solution was heated under reflux for another 30 min. Subsequently, the mixture was cooled to room temperature, and the solvent was removed *in vacuo*. The residue was dissolved

in CH_2Cl_2 and filtered to remove the inorganic salts. After evaporation of the solvent *in vacuo*, **5.20** (479 mg, 55 %) was obtained as a brown powder. An analytical sample was obtained by crystallization from acetonitrile. Anal. Calcd for $C_{31}H_{38}N_2O_3 \cdot H_2O$: C, 62.57; H, 6.78; N, 4.71; Mn: 9.23; Cl, 5.96. Found: C, 62.17; H, 6.36; N, 4.71; Mn, 9.66; Cl, 6.23.

***N,N'*-Di(salicydene)-3,4-diamino-1-benzyl-pyrrolidine-manganese(III) chloride (5.28).** Complex **5.30** was synthesized according to a literature procedure.[20] Spectral properties were in accordance with the literature. Data for *N,N'*-di(salicydene)-3,4-diamino-1-benzyl-pyrrolidine (**5.31**); m.p. 106.3-108.1 °C; $[\alpha]_D^{21.5}$ = -424.1° (c 1.38, $CHCl_3$); ^{1}H NMR: δ 8.27 (s, 2H), 7.41-6.83 (m, 13H), 4.02-3.98 (m, 2H), 3.81-3.68 (m, 2H), 3.19-3.14 (m, 2H), 2.97-2.91 (m, 2H); ^{13}C NMR: 165.42, 160.90, 138.31, 132.59, 131.61, 128.74, 128.40, 127.22, 118.82, 118.48, 116.96, 75.26, 60.27, 60.00. HRMS calcd for $C_{25}H_{25}N_3O_2$ 399.195, found 399.195.

Epoxidation Reactions. General Remarks. Domestic bleach was used for the preparation of the NaOCl solutions (commercial bleach (Piek, 25 mL, about 0.4 M) was added to 0.05 M Na_2HPO_4 (10 mL) and the resulting solution was adjusted to pH = 11.3 ± 0.1 with 1 M aqueous NaOH). The turnover was determined by GC (HP-1 (Crosslinked Methyl Silicone Gum)) using an internal standard method (n-hexadecane). The enantioselectivity of the epoxidation was determined by chiral GC analysis (CP-cyclodextrin-β-2,3,6 M-19 (df = 0.25 μm) column).

Epoxidation Reactions. *trans*-β-Methylstyrene (**5.26**, 118 mg, 1.0 mmol) and catalyst (*S*)-**5.19** (10.0 mg, 1.0 mol%) or **5.20** (1.0 mol%) were dissolved in CH_2Cl_2 (1.0 mL) and the sodium hypochlorite solution (see general remarks, *vide supra*, 4 mL) was added. The reaction was performed under vigorous stirring for 16 h. The mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and analyzed by GC.

α-Hydroxylation of 3,4-Dihydro-1-trimethylsilyloxy-naphthalene (5.17). Silyl enol ether **5.17** (218 mg, 1.0 mmol), iodosyl benzene (330 mg, 1.5 mmol) and catalyst **5.19** (15.5 mg, 2.0 mol%) were stirred in MeCN (3.5 mL) for 20 min. KF (50 mg) in MeOH (20 mL) was added, and the resulting mixture was stirred for a further 20 min. The mixture was extracted with ether (3 x 25 mL), the combined ether layers were dried over Na_2SO_4, filtered, and the solvent was removed *in vacuo*. The α-hydroxy ketone **5.28** was purified using column chromatography (silica gel, ether : hexane = 1 : 1, detection *via* charrying with a vanillin spray[28] (vanillin (1.0 g) and sulphuric acid (1.0 mL) were dissolved in EtOH (100 mL), R_f = 0.2) yielding pure **5.28** (129 mg, 80 %). ^{1}H NMR δ 8.08-8.04 (m, 1H), 7.58-7.50

(m, 1H), 7.40-7.27 (m, 2H), 4.40 (m, 1H), 3.93 (br s, 1H), 3.27-2.98 (m, 2H), 2.61-2.49 (m, 1H), 2.16-1.95 (m, 1H);[29] ^{13}C NMR: δ 199.58, 144.28, 134.11, 130.43, 128.88, 127.50, 126.83, 73.84, 31.84, 27.72.

Determination of Enantiomeric Excess of α-Hydroxy-α-tetralone (5.26). Racemic **5.28** (1.0 mg, 3.1 x 10^{-2} mmol) and (*S*)-bis-β-naphthol (**5.29**, 8.8 mg, 3.1 x 10^{-2}, 1.0 equiv.) were dissolved in $CDCl_3$ (1.0 mL). The ^1H NMR spectrum showed 2 double doublets at δ = 4.30 and 4.17 ppm (J = 5.3, J = 2.2) in a ratio of 1 : 1.

5.7 References and Notes

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