A Novel Counterion Effect on the Diastereoselectivity in the Mn^{III}(salen)-Catalyzed Epoxidation of Phenyl-Substituted *cis*-Alkenes

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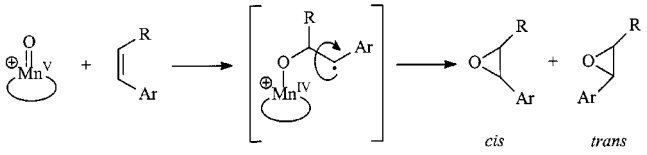
The catalytic oxidation of the phenyl-substituted *cis* alkenes **1a,b** by the Mn^{III}(salen)X complexes **3a–f** with iodosyl benzene (PhIO) as oxygen source affords the corresponding epoxides **2a,b** in *cis*/*trans* ratios of 79:21 to 26:74. The diastereoselectivity (*cis*/*trans* ratio) depends on the counterion of the Mn^{III}(salen)X complexes **3a–f**. Thus, for the complexes **3a–c** (Cl^-, Br^- and AcO^- as ligating counterions) extensive isomerization (*cis*/*trans* ratio ca. 30:70) takes place, while for the complexes **3d–f** (BF_4^-, PF_6^- and SbF_6^- as nonligating counterions) only moderate isomerization (*cis*/*trans* ratio ca. 75:25) is observed. This counterion effect may be rationalized in terms of the two-state reactivity paradigm; specifically, the axial ligand in the radical intermediate alters the triplet-quintet energy gap.

Introduction

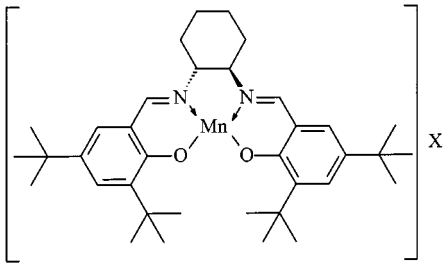
Direct oxygen transfer to olefins is a well-established and popular route to prepare epoxides, which are valuable building blocks in synthetic organic chemistry.[1] In recent years, there has been much effort to conduct this transformation selectively under catalytic conditions.[2] To date, the best known method to epoxidize unfunctionalized olefins enantioselectively is the Jacobsen-Katsuki epoxidation in which optically active Mn^{III}(salen) complexes are employed as catalysts and PhIO or NaOCl as oxygen source, with the Mn^{V}-oxo species as the active oxidant.[2,3] Although the synthetic value of this reaction is undisputed, its mechanism is currently under intensive debate.[3] Of considerable concern has been isomerisation, i.e., by starting from *cis* olefins, a mixture of *cis* and *trans* epoxides is formed (Scheme 1), a process which is particularly serious for phenyl-substituted olefins.[2,3] To account for this loss of stereoselectivity, a radical intermediate has been proposed, which leads to *cis*/*trans* epoxides through isomerisation by simple bond rotation.[3] Several experimental parameters such as solvent effects and salen and substrate structure have been shown to influence the *cis*/*trans* ratio; however, the behaviour of the counterion appears not to have been examined. In this preliminary report we wish to call attention to the fact that the ligation propensity of the counterion in the Mn(salen)X complex **3** influences profoundly the diastereoselectivity in the epoxidation of *cis* olefins. Thus, for the phenyl-substituted olefins **1a,b**, the *cis*/*trans*-epoxide ratio **2a,b** is ca. 30:70 (extensive isomerization) when the complexes **3a–c** with the ligating counterions Cl^-, Br^- and AcO^- are employed, while the *cis*/*trans* ratio is ca. 75:25 (moderate isomerization) for the complexes **3d–f** with the nonligating counterions BF_4^-, PF_6^- and SbF_6^-.



Scheme 1. Mechanism for the isomerization in the Jacobsen-Katsuki epoxidation of phenyl-substituted *cis* alkenes

Results and Discussion

The manganese catalysts **3b–f** (Figure 1) were synthesized as stated in the Supporting Information. Authentic samples of *cis*- and *trans*-epoxides **2a,b** were prepared by DMD epoxidation of the corresponding olefins **1a,b**. The manganese-catalyzed epoxidations of alkenes **1a,b** were carried out with 10 mol-% of catalyst **3** and 1 equiv. of iodosyl benzene (PhIO) as oxygen source. The results are summarized in Table 1.



Mn^{III}(salen)X comlexes **3a-f**
(X = Cl, Br, OAc, BF_4, PF_6, SbF_6)

Figure 1. The Mn^{III}(salen)X complexes **3a-f**

From these data it is obvious that the Mn-complexes **3a–f** fall into two broad classes of catalysts in regard to

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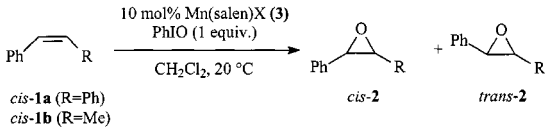
  1434–193X/00/1121–3519 $ 17.50+.50/0

Table 1. Counterion effects on the *cis*/*trans* ratio[a] of epoxides **2** in the Mn-catalyzed epoxidation of cis-substituted alkenes **1**



entry	alkene	catalyst	time	mb [%]	convn. [%]	*cis* : *trans*
1		**3a** (X = Cl)	45 min[b]	92	25	31 : 69
2			16 h	n.d.	43	29 : 71
3		**3b** (X = Br)	14 h	n.d.	40	26 : 74
4		**3c** (X = OAc)	14 h	n.d.	42	29 : 71
5	Ph Ph	**3d** (X = BF_4)	5 min[c]	76	59	76 : 24
6	*cis*-**1a**		5 min[c]	76	64	76 : 24
7[d]		**3e** (X = PF_6)	2 h	86	65	64 : 36
8[e]			15 h	98	29	23 : 77
9		**3f** (X = SbF_6)	5 min[c]	51	55	79 : 21
10	Ph Me	**3a** (X = Cl)	15 h	n.d.	33	35 : 65
11	*cis*-**1b**	**3e** (X = PF_6)	15 h	n.d.	92	78 : 22

[a] The *cis*/*trans* ratios were determined by ^{1}H NMR analysis of the crude product; error ±5 % of the stated values. – [b] Not all PhIO was consumed. – [c] Complete consumption of PhIO. – [d] 5 mol% of TEBA was added. – [e] 11 mol% of TEBA was added.

diastereoselectivity: While for complexes **3a–c** with the ligating counterions Cl^-, Br^- and AcO^- mainly the *trans*-epoxide **2** (*cis*/*trans* ratio ca. 30:70; entries 1–4, 10) is observed, complexes **3d–f**, with the nonligating counterions BF_4^-, PF_6^- and SbF_6^-, respectively, afford mainly the *cis* product (*cis*/*trans* ratio ca. 75:25; entries 5–7, 9, 11). Control experiments showed that the *cis*- and *trans*-epoxides **2** persist under the reaction conditions (see Supporting Information) and, thus, the inversion of the *cis*/*trans* ratio takes place in the oxygen-transfer step.

Diminution of the reaction time to 45 min for catalyst **3a** (Cl^-) revealed that the diasteroselectivity does not depend on the extent of conversion (cf. entries 1, 2). The time required for complete consumption of the PhIO is also influenced by the nature of the counterion. While the epoxidations of the complexes **3d–f** with the nonligating counterions BF_4^-, PF_6^- and SbF_6^- (entries 5, 6, 9) occur within minutes, complex **3a** with Cl^- as ligating anion retards the reaction rate to several hours (entry 2).

The addition of a slight excess of triethylbenzylammonium chloride (TEBA) relative to the Mn catalyst (11 mol-% TEBA versus 10 mol-% Mn catalyst) to the reaction mixture of catalyst **3e** (PF_6^-) gave the same the *cis*/*trans* ratio and rate (entry 8) as when the complex **3a** (Cl^-) is used (entry 2), whereas substoichiometric amounts of TEBA (5 mol-%) had only a small effect (entry 7). Since it has been shown previously that simple quaternary ammonium salts have no significant effect on the diastereoselectivity,[4] the present TEBA results imply irreversible binding of the externally added chloride ion to the "naked" cation **3e** (PF_6^-) to form complex **3a** (Cl^-). In the case of stoichiometric amounts of TEBA (entry 8), all of the complex **3e** (PF_6^-) is converted into **3a** (Cl^-) and the characteristic reactivity (slow rate) and diastereoselectivity (extensive isomerisation) is observed for the latter (compare entries 1, 6 and 8). When a substoichiometric amount is employed, a mixture of complexes **3a** (Cl^-) and **3e** (PF_6^-) is formed, and since **3e** (PF_6^-) reacts much faster than **3a** (Cl^-), a similar diastereoselectivity (little isomerisation) results as without TEBA, i.e., the *cis*/*trans* ratios are 64:36 for substoichiometric amounts of TEBA (entry 7) and 76:24 for none (entry 6).

The above-mentioned difference in reaction rates of the two complexes **3a** (Cl^-) and **3e** (PF_6^-) substantiates that the binding of the external chloride ion to the "naked" cation is irreversible. Were this Cl^- complexation reversible, even a small amount of **3e** (PF_6^-) would react so much faster than **3a** (Cl^-) that a *cis*/*trans* ratio of about 70:30 (entries 6, 7) should have been observed. But the experimental *cis*/*trans* ratio is 23:77 (entry 8) and, thus, this may be reconciled if ligation of the chloride ion is irreversible.

It remains to suggest a mechanistic rationale, why epoxidation by the hexafluorophosphate complex **3e** (nonligating PF_6^- counterion) proceeds mainly with retention of the *cis* configuration (*cis*:*trans* ca. 75:25, entries 6, 11), while for the complex **3a** with the chloride ion as ligating counterion, extensive isomerisation to the thermodynamically preferred *trans*-epoxides **2** (*cis*:*trans* ca. 30:70, entries 1, 2, 10) takes place. This counterion effect may be explained on the basis of the theoretical work by Linde et al.,[5] who in terms of the two-state reactivity paradigm[6] suggested that the point of spin crossover from the triplet (t) to quintet (q) state in the Mn^V-oxo complex is decisive in the control of reactivity and selectivity in high-spin systems. The later spin crossover occurs, the longer is the lifetime of the radical intermediate and the more *trans*-epoxide **2** may form by means of bond rotation. If it is assumed that the t-q gap of the chloride-ligated radical intermediate is larger than for the "naked" one (a model for the complex **3e** with nonligating PF_6^- anion), spin crossover for the complex **3a** (Cl^-) comes later and, therefore, more *trans*-epoxide **2** should be formed than for complex **3e** (PF_6^-). In this context, it should be recalled that the dependence of the diastereoselectivity in the Mn^{III}-catalyzed epoxidation on the electronic nature of the olefin, i.e., it was demonstrated that electron-rich olefins are more diastereoselective (less *cis*/*trans* isomerization) than electron-poor ones,[7] has been accounted for by Linde et al.[5] in terms of such changes in the t-q energy gap. Consequently, we suggest that an axial chloride ligand in the radical intermediate alters the t-q gap compared to the "naked" one due to changes in the electronic properties of the manganese centre. Indeed, recent calculations by the Houk group[8] reveal that the t-q energy gap of the Mn^V-oxo species is strongly affected by the axial ligand; unfortunately, these computations have been carried out only on the Mn^V-oxo species and the Mn^{III} resting state, but would be required for the radical intermediate (Scheme 1) with and without an axial chloride ligand to corroborate our mechanistic speculations.

In conclusion, we have demonstrated that the ligating nature of the counterion, i.e., the ligating Cl^-, Br^- and AcO^- ions in complexes **3a−c** versus the nonligating BF_4^-, PF_6^- and SbF_6^- ions in complexes **3d−f,** has a definitive influence on the diastereoselectivity of the Mn^{III}-catalysed epoxidation of phenyl-substituted *cis* alkenes. This may be caused by ligand-induced changes in the t-q energy gap of the putative radical intermediate, a novel phenomenon that should be worthwhile for further exploration to understand and control selectivities in such metal-catalysed oxidations.

Experimental Section

General Remarks: ^{1}H NMR (200 MHz): Bruker AC 200 ($CHCl_3$, at δ = 7.26 as internal standard). *cis*-Stilbene **(1a)** was purchased from Aldrich. − *cis*-β-methylstyrene **(1b)** was prepared by hydrogenation of 1-phenylpropyne with the Lindlar catalyst.

Manganese-Catalyzed Epoxidation of Alkenes 1a,b: A solution of the particular Mn(salen)X **3** (50.0 μmol, 10 mol-%)in CH_2Cl_2 (5 mL) was stirred for 3 min at room temp. (ca. 20 °C). After addition of the alkene **1** (500 μmol), the mixture was stirred for another 2 min and PhI=O (110 mg, 500 μmol) was added in small portions during 2 min. The resulting suspension was stirred for up to 16 h until a clear, brown solution was obtained. After removal of the solvent (20 °C, 400 mbar), the residue was transferred onto a short column of silica gel (ca. 10 g) and eluted with 200 mL of a PE/Et_2O mixture (1:1). After removal of the solvent (30 °C, 10 mbar), the resulting colourless oil was analysed by ^{1}H NMR spectroscopy (1,1,2,2-tetrachlorethane as internal standard). The results are summarized in Table 1.

Acknowledgments

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