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A comparative study of the asymmetric epoxidation of aromatic olefins using the first generation manganese salen epoxidation catalysts and their light fluorous variants: an interesting discovery on the use of benzotrifluoride as a cosolvent

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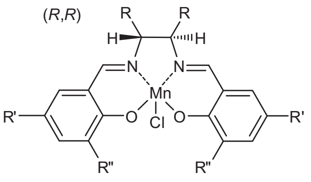
We dedicate this paper to Prof. Yasuyuki Kita on the occasion of his 70th birthday

ABSTRACT

The asymmetric epoxidation of aromatic olefins using optically active first generation manganese salen catalysts and light fluorous variants was examined. Although a slight decrease in the enantioselectivity of the product was observed when light fluorous catalysts were employed, the activities of these catalysts were higher than those of the non-fluorous catalysts. Additionally the influence on enantioselectivity of the oxidation was examined when fluorous cosolvents were used. The enantioselectivity of the oxidation increased with the addition of benzotrifluoride (BTF) regardless of whether a fluorous or non-fluorous salen catalyst was used.

1. Introduction

Optically active manganese(III) (salen) complexes[1] are known to be useful chiral catalysts in the asymmetric epoxidation of unfunctionalized olefins.[2] By using these same catalysts, the asymmetric oxidation of benzylic and allylic C—H bonds, and oxidative kinetic resolutions can be achieved.[3] Since the initial report of these salen catalysts, the structure has continued to be modified[4] and these variants have been used in several key reactions for the introduction of asymmetry in the synthetic sequence of various optically active compounds.[5] The salen complexes **1a** and **1b** in Figure 1 represent the (*R*,*R*)-first generation-type salen catalysts, which were reported by Jacobsen et al.[6] and Katsuki et al.[2b] at about the same time. In 1998, the heavy fluorous variants of salen catalysts **1a** and **1b** were reported by Pozzi et al. (Fig. 1c and d).[7] Since these heavy fluorous catalysts were selectively soluble in perfluorocarbons, an efficient epoxidation of olefins under fluorous biphasic conditions was successfully achieved.[8] Herein we report an asymmetric oxidation of triphenylethylene using light-fluorous versions of the first generation salen catalysts **1a** and **1b**, that is, catalysts **1e** and **1f** (Fig. 1). The light-fluorous catalysts, unlike the heavy fluorous variants, are soluble in general organic solvents, and we could expect to influence the stereoselectivity of the oxidation reactions by the addition of flourous co-solvents.[9]



1a : R = Ph, R' = ^{t}Bu, R'' = ^{t}Bu
1b : (R-R) = $(CH_2)_4$, R' = ^{t}Bu, R'' = ^{t}Bu
1c : R = Ph, R' = C_8F_{17}, R'' = C_8F_{17}
1d : (R-R) = $(CH_2)_4$, R' = C_8F_{17}, R'' = C_8F_{17}
1e : R = Ph, R' = C_4F_9, R'' = ^{t}Bu
1f : (R-R) = $(CH_2)_4$, R' = C_4F_9, R'' = ^{t}Bu

Figure 1. Non-fluorous **1a**, **1b**, heavy **1c**, **1d**, and light-fluorous **1e**, **1f** first generation salen complexes.

2. Results and discussion

The light-fluorous manganese salen complexes **1e** and **1f** were synthesized according to previously reported procedures.[2] For the key reaction to introduce the perfluorobutyl group into the chiral ligand structure, we utilized an effective perfluoroalkylation

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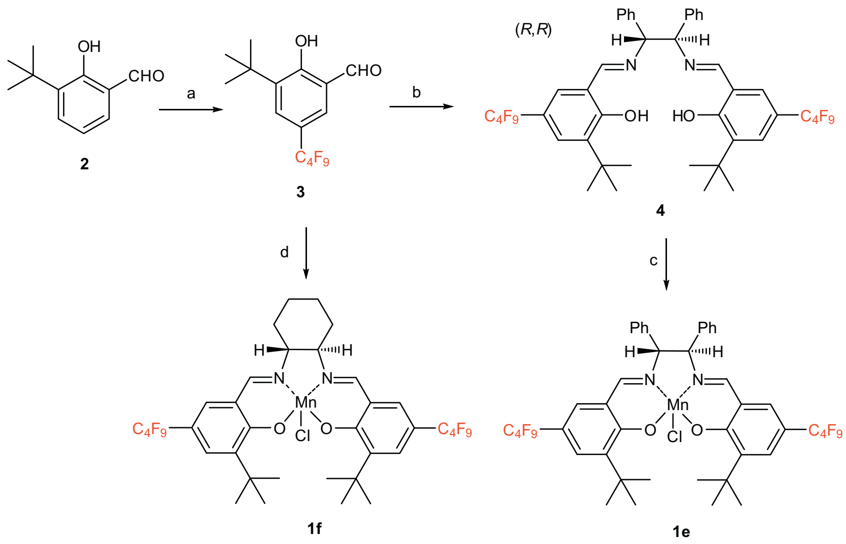


Scheme 1. Synthesis of light-fluorous salen complexes **1e** and **1f**. Reagents and conditions: (a) 1.5 equiv C_4F_9I, 1.0 equiv V-70L, 8.0 equiv Cs_2CO_3, DMF, rt, 20 h, 71%; (b) 0.6 equiv (1*R*,2*R*)-1,2-diphenylethane-1,2-diamine, 3 Å MS, EtOH, reflux, 1 h, 89%; (c) 2.0 equiv $Mn(OAc)_2·4H_2O$, 3.0 equiv LiCl, 3 Å MS, EtOH, reflux, 4 h, 91%; (d) 0.6 equiv (1*R*,2*R*)-cyclohexane-1,2-diamine, 3 Å MS, EtOH, reflux, 1 h, then 2.0 equiv $Mn(OAc)_2·4H_2O$, 3.0 equiv LiCl, 3 Å MS, EtOH, reflux, 4 h, 54%.

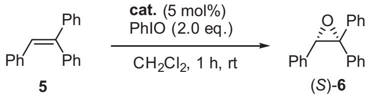
reaction of free-phenol derivatives.[10] The synthesis started by treating 3-(*tert*-butyl)-2-hydroxybenzaldehyde **2** with C_4F_9I in the presence of a radical initiator V-70L to give perfluorobutylated compound **3** with perfect regioselectivity in 71% yield. The condensation reaction of **3** with (1*R*,2*R*)-1,2-diphenylethane-1,2-diamine was conducted in the presence of 3 Å molecular sieves to obtain chiral ligand **4** in 89% yield. Subsequent ligation of ligand **4** with $Mn(OAc)_2$ in the presence of LiCl gave the target salen complex **1e** in 91% yield. The light fluorous cyclohexyl based catalyst **1f** was also prepared in 54 % yield from **3** via a one-pot reaction using (1*R*,2*R*)-cyclohexane-1,2-diamine in refluxing EtOH as shown in Scheme 1.

First, we examined the catalytic activity of the light-fluorous salen complexes **1e** and **1f** in the epoxidation of triphenylethylene **5** in dichloromethane as shown in Table 1. Iodosobenzene (PhIO, 2.0 equiv) was used as the oxidizing agent[2a] and we stopped the reaction after exactly one hour to allow for direct comparison of the activity of the different catalysts. As shown in Table 1, we found that the enantioselectivity of the epoxidation using the light-fluorous salen complexes was 32% and 31% ee (entries 1 and 2) which was lower than the corresponding original salen complexes which gave enantioselectivities of 59% and 39% (entries 3 and 4).[11] This observed phenomenon was the same as for the heavy fluorous versions of the catalysts carried out under fluorous biphasic conditions and previously reported by Pozzi et al.[7] However, the catalytic activity for the oxidation using this light-fluorous catalysts was higher than for the original complexes. There was a noteworthy difference in the oxidative activity between the light-fluorous **1f** and the original salen catalyst **1b** under the same conditions in dichloromethane (Table 1, entries 2 and 4) where 78% and 15% conversion were obtained respectively.

The asymmetric epoxidation of **5** using light-fluorous and non-fluorous catalysts was examined using acetonitrile as the solvent,[12] and the results are shown in Table 2. We found that the reaction rate was higher in acetonitrile than in dichloromethane with complete conversion being achieved in almost all cases in as little as 20 min. While acetonitrile showed less pronounced differences in terms of catalytic activity across the four catalysts, it did improve the enantioselectivities for the epoxide products of all four catalysts when compared to the results obtained in dichloromethane. Again, as was the case with dichloromethane, the fluorous catalysts systematically gave lower enantioselectivities for the epoxidation than the non-fluorous variants (Table 2, entries 1–2 vs 3–4). Unfortunately, these examples clearly show that the introduction of light-fluorous tags onto the salen complex tends to reduce the stereoselectivity of the epoxide product.

We next turned our attention to exploring the use of fluorous cosolvents in the oxidation of the triphenylethylene with a family of salen catalysts and our results are summarized in Table 3. We found that there was a definite impact on the enantioselectivity

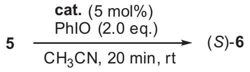
Table 1
Asymmetric oxidation of triphenylethylene **5** to epoxide (*S*)-**6** in CH_2Cl_2



entry	cat.	conv. (%) [a]	ee (%) [b]
1	**1e**	89	32
2	**1f**	78	31
3	**1a**	85	59
4	**1b**	15	39

[a] Determined by ^{1}H NMR.
[b] Determined by HPLC (DAICEL CHIRALCEL OD-3, hexane/^{i}PrOH = 9/1, flow rate 0.4 mL min^{-1}).

Table 2
Asymmetric oxidation of triphenylethylene **5** to epoxide (*S*)-**6** in CH_3CN



entry	cat.	conv. (%) [a]	ee (%) [b]
1	**1e**	100	49
2	**1f**	95	57
3	**1a**	100	73
4	**1b**	77	47

[a] Determined by ^{1}H NMR.
[b] Determined by HPLC (DAICEL CHIRALCEL OD-3, hexane/^{i}PrOH = 9/1, flow rate 0.4 mL min^{-1}).