Rapid Communication

Enantioselective epoxidation of 2,2-Dialkyl-2H-chromenes with Oxone^R and Jacobsen's (S,S)-Mn(III)(Ph-salen)Cl complex : Solvent effect[†]

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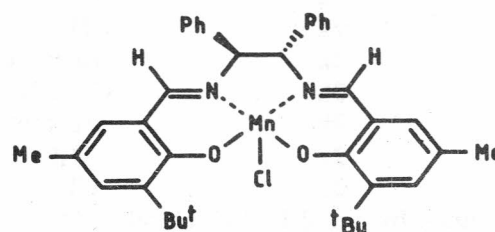Hyderabad 500 007, India
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(S,S) - (Ph - Salen)Cl (1)

a) R^1 = Me , R^2 = CN

b) R^1 = Me , R^2 = H

c) R^1 = -(CH$_2$)$_5$- = R^1 , R^2 = H

Enantioselective epoxidations of 2,2-dialkyl-2H-chromenes 2a-2c to 3a-c with oxone in the presence of (S-S)-Mn(III)(Ph-salen)Cl as a catalyst, in various solvents are described.
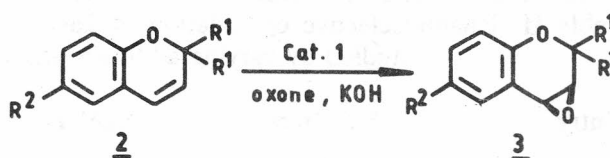
Chiral manganese salen complexes are effective in enantioselective epoxidation of alkenes[1,2]. Recent development in this area includes designing of new ligands[3] and discovering new nucleophilic oxidants. After the pioneering research by Jacobsen with NaOCl[2], several other oxidants such as iodosobenzene[2], molecular oxygen[4], H_2O_2[5], Bu$_4$NIO$_4$[6], dimethyldioxirane[7] and mCPBA[8] were explored. Oxone^R has found a great deal of importance in organic chemistry as a cheap oxidising agent[9]. However, its utility in enantioselective epoxidation has not been fully[8] explored. In this report, we wish to present oxone as a suitable and alternative oxidant in combination with Jacobsen's Mn(III)-salen catalyst 1 for enantioselective epoxidation of 2,2-dialkyl-2H-chromenes 2a-2c. The enantioselectivity markedly depends upon the solvent used and the solvent CH$_3$CN was distinctly superior.

We first studied (cf. Table I) the epoxidation of 2a with 2.5 equiv. of oxone under essentially the similar conditions [0.03 equiv. of (S,S)-1, and 0.3 equiv. of 4-phenylpyridine-N-oxide (4-PPNO)] reported[10] by others using CH$_2$Cl$_2$ as a solvent at 0°C. Although the reaction went to completion in 12 hr, the enantiomeric excess of 19.8% (chiral HPLC), observed for the epoxide 3a, was rather disappointing. We reasoned that the low enantioselectivity was perhaps due to the slow rate of the reaction in CH$_2$Cl$_2$.

The effect of solvents[11] on chiral Mn-salen complex catalysing the enantioselective epoxidation of alkenes has not been fully investigated. We

observed that when compound 2a was treated with oxone (2.5 equiv.), (S,S)-1 and 4-PPNO, but with CH$_3$CN as a solvent, the optical purity of 3a dramatically improved to 85% ee (chiral HPLC) (entry 2). In addition the epoxidation reaction was completed in just 15 minutes. We could not explain the dramatic enhancement in rate of the reaction and the enantioselectivity with CH$_3$CN as a solvent. However, the result was indeed appealing and therefore deserved further investigation. Table I indicates the number of reactions with different solvents carried out with model substrates 2a-2c.

We have also studied (cf. Table II) the effect of additives[12] on the course of the epoxidation keeping CH$_3$CN as a common solvent. Entries 1-4 indicate that there was no dramatic effect on the enantioselectivity of the epoxidation of 2a either by changing the ratio of 4-PPNO or by using other additives. Entry 5, where no additive[13] was added, the enantiomeric excess of 95% was noted for the epoxide 3a (chiral HPLC and optical rotation). Entries 6 and 7 represent reactions carried out without the additive.

In conclusion we have described oxone as a cheap and complimentary nucleophilic oxidant in the enantioselective epoxidation with chiral Mn(III)-salen catalyst. The effect of solvent in the epoxidation was indeed interesting. Further re-

Table I—Enantioselective epoxidation with Oxone (2.5 equiv.), Mn(III)-salen catalyst **1** (10 mol%) and 4-PPNO (0.3 equiv.)

Entry	Substrate	Solvent (Reaction period)	Product	ee(%)[a]	Yield (%)[b]
1	**2a**	CH_2Cl_2 (12 hr)	**3a**	19.8	61
2	**2a**	CH_3CN (15 min.)	**3a**	85.0	67
3	**2a**	Acetone (12 hr)	**3a**	60.8	62
4	**2b**	CH_3CN (15 min.)	**3b**	65.0	79
5	**2b**	Acetone (12 hr)	**3b**	32.9	61
6	**2c**	CH_3CN (15 min.)	**3c**	85.6	81
7	**2c**	CH_2Cl_2 (12 hr)	----------no reaction---------		

[a]ee determined by chiral HPLC (chiralcel OD with isopropanol-hexane as eluents and at 254 nm) and or by optical rotations.
[b]Isolated yields

Table II—Enantioselective epoxidation of **2a-2c** with Oxone (2.5 equiv.) and Mn(III)-salen catalyst **1** studied by varying additives and using CH_3CN as a common solvent

Entry	Substrate	(S,S)-**1**	Additive (equiv.)	ee (%)[a] (hplc)	Yield (%)[b]
1	**2a**	10 (mol%)	4-PPNO (1.2)	86.5	82
2	**2a**	10 (mol%)	NMO (5.0)	87.5	85
3	**2a**	10 (mol%)	Imidazole (1)	83.9	83
4	**2a**	15 mol%)	No additive	95.0	86
5	**2b**	15 (mol%)	No additive	91.0	80
6	**2c**	15 (mol%)	No additive	90.0	75

[a]ee determined by optical rotation and HPLC.
[b]Isolated yield.

search to improve the enantioselectivity with other catalyst in this domain will be forthcoming.

Experimental Section

General procedure for epoxidation of 2,2-dialkylchromene 2a-2c. Oxone (1.35 mmoles) was dissolved in water (3 mL) and then basified to pH 11 by adding 1N KOH solution. This solution was then added to a mixture of olefin (**2a-2c**)[14] (0.54 mmole) and catalyst (15 mol%) in acetonitrile (5 mL) at 0°C. The reaction was monitored by TLC The two layers were separated and the organic layer was dried over Na_2SO_4 and concentrated. The residue was chromatographed over silica gel (60-120·mesh) using 5% ethyl acetate in n-hexane as eluent to give the epoxide (**3a-3c**).
^{1}H NMR ($CDCl_3$, Varian Gemini 200 MHz) of:

3a: δ 1.28, 1.53 (2s, 6H), 3.46 (d, J=4.2 Hz, 1H), 3.86 (d, J=4.2 Hz, 1H), 6.78 (d, J=8.5 Hz, 1H), 7.42 (dd, J=8.5, 1.5 Hz, 1H), 7.57 (d, J=1.5 Hz, 1H).

3b: δ 1.25 (s, 3H), 1.57 (s, 3H), 3.42 (d, J=4.25 Hz, 1H), 3.83 (d, J=4.25 Hz, 1H), 6.7-6.95 (m, 2H), 7.15-7.35 (m, 2H).

3c: δ 1.2-2.2 (m, 10H), 3.42 (d, J=4.25 Hz,

1H), 3.80 (d, J=4.25 Hz, 1H), 6.75-6.95 (m, 2H), 7.15-7.35 (m, 2H).

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