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Stereoselective Epoxidation of Cyclic Alkenes Using *m*-CPBA and Oxone®/Trifluoroacetone – a Comparison

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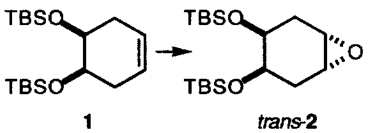
Abstract: A comparison of the observed diastereoselectivity of epoxidation of cyclic alkenes using *m*-CPBA and Oxone®/trifluoroacetone is reported. The results indicate that dioxirane epoxidations are sterically controlled and provide a crude model for determination of whether hydrogen bonding is operating in the *m*-CPBA epoxidations.

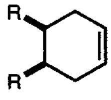
Keywords: epoxidation; diastereoselection; dioxiranes

Diastereoselective epoxidations of cyclic and acyclic alkenes using *m*-CPBA have proved to be useful transformations in organic synthesis.[1] With the advent of dioxiranes (*eg* dimethyldioxirane) as epoxidising reagents,[2] recent attention has focused on assessing the levels of diastereoselectivity exhibited by these reagents. Indeed, Adam *et al.*[3] and Murray *et al.*[4] have shown that, with an appropriate solvent, dioxiranes exhibit *cis*-directed epoxidations which is reminiscent of known[1] results with peracids. There have, however, been few reports directly comparing observed diastereoselectivities in peracid and dioxirane epoxidations.[5] And, no examples of stereoselective epoxidations using *in situ* generated methyl(trifluoromethyl)dioxirane in an acetonitrile-water solvent system[6] have been disclosed.



1 trans-2

Oxone®/ CF_3COCH_3	*m*-CPBA/ CH_2Cl_2
trans : *cis* 98 : 2	*trans* : *cis* 56 : 44



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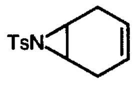

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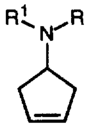

5

During an epoxidation study detailed in the preceding paper,[7] we compared the diastereoselectivity observed in the transformation of alkene **1** into epoxides **2** using *m*-CPBA in CH_2Cl_2 with that obtained using *in situ* generated methyl(trifluoromethyl)dioxirane (Yang's conditions[6]). Under Yang's conditions, complete *trans* selectivity was observed whereas only a 56:44 mixture of *trans*- and *cis*-**2** was obtained using *m*-CPBA. We interpreted these results by suggesting that some degree of *cis*-direction (due to hydrogen bonding) was occurring with *m*-CPBA.[7] This suggested to us that a comparison of the diastereoselectivity observed with the two different reagents could be used as a crude test to determine whether any hydrogen bonding was operating in the *m*-CPBA epoxidations. Herein, we describe the results obtained with a range of alkenes **3**-**5**.

All of the epoxides were prepared in quantitative crude yield from alkenes **3**-**5** using either *m*-CPBA in CH_2Cl_2 or Yang's conditions (Oxone®/trifluoroacetone) and the *trans* : *cis* ratios were determined by ^1H NMR spectroscopy on the crude products (see Table).[8] The stereochemistry of the epoxides was established as follows: (i) entries 1, 2, 3 and 6 have previously been reported;[7] (ii) *trans*-epoxide in entry 4 was independently synthesised;[9] (iii) entries 5 and 10 were assigned by literature precedence;[10] (iv) entry 7 is a

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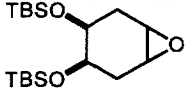
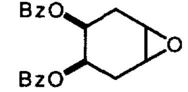
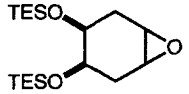
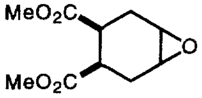
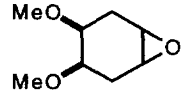
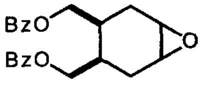
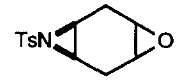
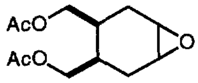
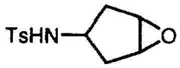
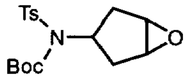
known reaction;[11] and (v) entries 8 and 9 were assigned by literature precedence.[12]

The results fit into two categories. Entries 1-5 show significant differences in stereoselectivity between the two types of epoxidising reagents indicating that with *m*-CPBA, hydrogen bonding is operating. However, entries 6-10 show essentially the same levels of stereocontrol with the two epoxidising systems. In these cases, the substituents do not contain any available lone pairs or protons for hydrogen bonding interactions with *m*-CPBA and steric control (to a similar degree with both reagents) is observed.

Table: *Stereoselective Epoxidations of Alkenes 3-5 Using m-CPBA and Yang's Conditions – a Comparison*

Entry	Epoxide	*m*-CPBA[a] *trans* : *cis*	Oxone®[b] *trans* : *cis*	Entry	Epoxide	*m*-CPBA[a] *trans* : *cis*	Oxone®[b] *trans* : *cis*
1		56 : 44	98 : 2	6		80 : 20	81 : 19
2		39 : 61	98 : 2	7		62 : 38	72 : 28
3		75 : 25	94 : 6	8		78 : 22	81 : 19
4		39 : 61	91 : 9	9		83 : 17	90 : 10
5		16 : 84	60 : 40	10		98 : 2	98 : 2

[a] *m*-CPBA, $NaHCO_3$, CH_2Cl_2, rt, 16-20 h; [b] Oxone®, trifluoroacetone, Na_2•EDTA, MeCN-water, $NaHCO_3$, 0 °C, 2-3 h

In summary, we have described the first comparison of stereoselective epoxidation reactions using Oxone®/trifluoroacetone and *m*-CPBA. These results suggest a useful and potentially general way of establishing whether hydrogen bonding is operating in *m*-CPBA epoxidations and also demonstrate that dioxirane-mediated epoxidations can lead to synthetically useful levels of diastereoselectivity where *m*-CPBA fails (Entries 1-4).

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References and Notes

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