Asymmetric Epoxidation of Unfunctionalized Alkenes by Dioxirane Intermediates Generated from Potassium Peroxomonosulphate and Chiral Ketones

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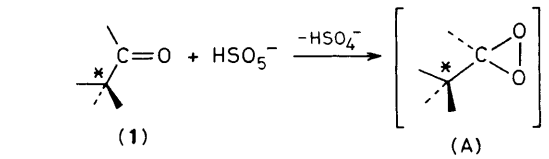
Chiral dioxirane intermediates, which are formed in the reaction of potassium peroxomonosulphate with chiral ketones, allow the epoxidation of simple pro-chiral olefins to the corresponding epoxides to be carried out with enantiomeric excesses in the range 9—12.5%.

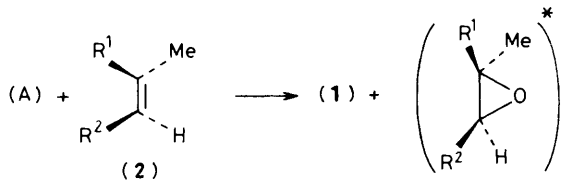
Despite the relevance of chiral epoxides in organic synthesis,[1] methods so far available for the asymmetric epoxidation of unfunctionalized olefins have met with only limited success,[2—9] with the possible exception of microbial oxidations.[10,11] In fact, using chiral organic peroxo-acids or hydroperoxides, the asymmetric bias is rather low [*i.e.* 1—8% enantiomeric excess (e.e.)].[2,8]† Simple olefins have been epoxidized *stoicheiometrically* by the molybdenum(VI) oxide diperoxide complexes $MoO(O_2)_2L^*$ (L^* = chiral bidentate ligand), the reactions showing the highest e.e. (16—35%) for abiotic systems.[4] However, lower (1—7% e.e., in the majority of cases) asymmetric inductions were noted in the *catalytic* epoxidation of unfunctionalized alkenes such as 1-methylcyclohexene with Bu^tOOH in the presence of Mo^{VI} and optically active dialkyl tartrate esters.[5]

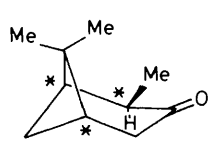
In recent articles we have reported on a new process for olefin epoxidation using potassium peroxomonosulphate (caroate; $KHSO_5$) and ketones, in a CH_2Cl_2–buffered water (pH 7—8) two-phase system in the presence of phase-transfer agents (P.T.A.).[12,13] Kinetic and ^{18}O-labelling experiments suggested that the reactive intermediate responsible for the epoxidation should have a dioxirane-ring structure [*e.g.*, (A)], and that the ketone merely acts to catalyse the process.[12]

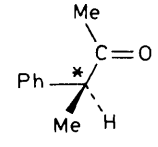
The stereo- and regio-selectivities attainable by using our $KHSO_5$–ketone reagent have been determined.[13] Thus, we decided to explore the enantioselectivities observable in the epoxidation of two representative prochiral, unfunctionalized alkenes, namely 1-methylcyclohexene (**2a**) and (*E*)-β-methylstyrene (**2b**). The chiral ketones chosen as the precursors of chiral dioxirane intermediates were (+)-isopinocamphone (**1a**) and (*S*)-(+)-3-phenylbutan-2-one (**1b**). Both chiral ketones were obtained by literature methods.[14,15]

Ketone-catalysed epoxidations by $KHSO_5$ could readily be carried out at 2—6 °C in a CH_2Cl_2–buffered water two-phase medium, with $Bu_4N^+HSO_4^-$ as P.T.A., according to a pro-









† By contrast, the efficient asymmetric epoxidation of functionalized alkenes, such as allylic alcohols (yielding the corresponding epoxy-alcohols in greater than 90% e.e.), has been described (ref. 9).

Table 1. Chiral-ketone-catalysed asymmetric epoxidation of alkenes by $KHSO_5$ in CH_2Cl_2–water (pH 7—8), with $Bu_4N^+HSO_4^-$ as P.T.A.

Chiral ketone[a]	Alkene	*T*/°C	Alkene to ketone ratio[b]	Epoxide (3)		
				% Yield[c]	Configuration[d]	% E.e.[e]
(+)-(**1a**)	(**2a**)	25	1:1	87	(+)-(1*S*,2*R*)	6
,,	,,	5	1:1	90	,,	10.4
,,	,,	,,	5:1	85	,,	10.2
,,	,,	,,	3:10	80[f]	,,	9.5
(+)-(**1b**)	,,	,,	2:1	92	,,	12
(+)-Monoperoxycamphoric[g] acid	,,	,,	—	85	(−)-(1*R*,2*S*)	5 (8)[h]
(+)-(**1a**)	(**2b**)	5	1:1	60[f]	(+)-(1*R*,2*R*)	12.5
,,	,,	,,	1:2	60[f]	,,	11
,,	,,	,,	5:1	68	,,	11.2
(+)-(**1b**)	,,	,,	1:1	85	,,	9.5
(+)-Monoperoxycamphoric[g] acid	,,	,,	—	88	(−)-(1*S*,2*S*)	4.2 (5.2)[i]

[a] Chiral ketone precursor of chiral dioxirane intermediate as epoxidation agent, unless noted otherwise; the chiral materials were all >95% optically pure. [b] Relatively low ratios were used in order to obtain appropriate reaction times (8—24 h), as the rate is proportional to catalyst concentration (ref. 15). [c] G.l.c. yields, based on the substrate reacted, unless noted otherwise. [d] The configuration of the predominant enantiomer is given (ref. 6). [e] Optical yields determined by ^1H n.m.r.–polarimetry (error limit ±1%), unless noted otherwise. [f] Isolated yields. [g] Not a chiral ketone; reactions using this traditional stoicheiometric epoxidation agent were run in order to compare the enantioselectivities. [h] Based on the value $[\alpha]_D^{20}$ +1.37° (neat) determined after conversion of the enantiomeric epoxides into *cis*-2-methylcyclohexanol using $NaBH_4$–B_2H_6 (ref. 5); the value adopted for enantiomerically pure (+)-(1*S*,2*R*)-*cis*-2-methylcyclohexanol was $[\alpha]_D^{20}$ +17.2° (neat) (ref. 17); the estimated optical yield rises to *ca.* 10% if the value of $[\alpha]_D^{20}$ +13.6° (neat) is adopted (ref. 5) as the maximum rotation for the pure enantiomer. [i] Based on the value $[\alpha]_D^{20}$ −3.8° (*c* 4, EtOH) found for the mixture of enantiomeric epoxides; the maximum recorded rotation of (+)-(1*R*, 2*R*)-1-phenyl-1,2-epoxypropane is $[\alpha]_D^{20}$ +70.8° (*c* 4.4, EtOH) (ref. 18).

cedure already described in detail.[12,13] The epoxides produced could be isolated by column (silica gel) chromatography or reverse-phase semipreparative h.p.l.c.; the same procedure allowed us to recover the optically active ketone catalyst unaltered. The epoxides[5,6,16—18] gave satisfactory physical data and spectra (i.r., n.m.r.); enantiomeric excesses were determined by the ^1H n.m.r. chiral shift method using $Eu(tfc)_3$.[19] The areas of the methyl proton resonances led to the e.e. values summarized in Table 1.

The results demonstrate that, at 5 °C, optical yields ranging from 9 to 12.5% e.e. can be obtained by the $KHSO_5$–chiral ketone epoxidation method. Although no systematic efforts have been made yet to optimize the yields, the enantioselectivities observed are already nearly double those attainable using 'classical' chiral epoxidation reagents such as (+)-monoperoxycamphoric acid. The asymmetric induction observed in the epoxidation of unfunctionalized olefins by our method appears to be surpassed, so far, only by epoxidations using $MoO(O_2)_2L^*$ (see above)[4] or chiral 2-sulphonyloxaziridines.[6] Both these methods, however, are stoicheiometric rather than catalytic.

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