Tetrahedron Letters,Vol.28,No.29,pp 3311-3314,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

Epoxidation of Alkenes by Dimethyldioxirane: Evidence for a Spiro Transition State

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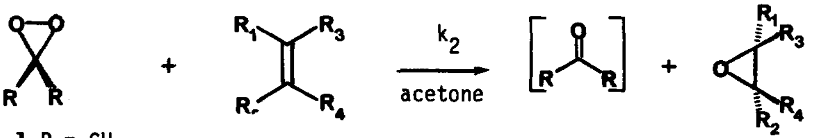
Summary: The relative reactivity series for the epoxidation of alkenes by dimethyldioxirane showed the reaction to be unexpectedly sensitive to steric factors; <u>cis</u> compounds were ~8 times as reactive as the <u>trans</u> isomers.

Dioxiranes, three-membered cyclic peroxides, are of high reactivity in oxygen-atom transfer chemistry.[1] Dioxiranes are also of interest because of their relationship to carbonyl oxides (ozonolysis mechanisms).[2] Edwards and Curci, based on extensive kinetic, stereochemical, and ^{18}O-labeling data, suggested[1a] that dimethyldioxirane was the oxygen-atom transfer reagent in the potassium peroxymonosulfate-acetone system. Recently, Murray has shown[1c] that dialkyldioxiranes may be isolated by low-temperature distillation from the reaction mixture of caroate (oxone) and ketones. The isolated dioxiranes have been characterized[1c,3] by physical and spectral data; dimethyldioxirane can be obtained as <0.1 M solutions. We have recently reported[4a] the electrophilic oxygen-atom transfer chemistry of α-azohydroperoxides. Epoxidation (stereospecific) by α-azohydroperoxides has been shown[4] to be mechanistically similar to that by peracids. It is therefore of interest to compare and contrast the kinetic data for epoxidation of a series of alkenes with dimethyldioxirane with those for α-azohydroperoxides and peracids. We wish to report a kinetics study of the epoxidation of a series of alkenes by dimethyldioxirane (reaction 1), the relative reactivity of which shows unexpected trends in relation to alkene substitution patterns.



(1)

1 R = CH_3

1d R = CD_3

Dimethyldioxirane (**1**) or dimethyldioxirane-d_6 (**1d**) was prepared by the reaction of potassium monoperoxysulfate (oxone) with acetone or acetone-d_6, respectively.[1] Solutions (~0.1 M) of the dioxirane (**1 or 1d**) in acetone or acetone-d_6, respectively, were obtained by the distillation procedure developed by Murray and co-workers.[1c] The concentration of dioxirane was determined by oxidation of excess Ph_3P (subsequent GC analysis) and was in good agreement with that determined by UV methods.[5] Product studies for the epoxidation of a series of alkenes by dimethyldioxirane-d_6 in acetone-d_6 were carried out by ^1H NMR spectroscopy. For all thirteen cases (Table 1), addition of one equivalent of dioxirane **1d** to the alkene resulted in the quantitative formation of the epoxide (reaction 1). As previously reported,[1a-c] the reaction was found to be stereospecific. Epoxidation of *trans*-alkenes yielded only *trans*-epoxides while oxidation of the *cis* compounds produced only the *cis*-epoxides.

The kinetic study of the epoxidation reactions was carried out by UV techniques. The epoxidation reaction was shown to be of the first order in both alkene and peroxide. The loss of dimethyldioxirane was monitored in all cases. Pseudo first order conditions with 1:10 and 10:1 alkene/peroxide ratios gave the same k_2 values within experimental error. Tetrasubstituted alkenes were approx. two orders of magnitude more reactive than monosubstituted or *trans*-dialkyl compounds. *cis*-Dialkyl alkenes were found to be seven to nine fold more reactive than the *trans* compounds. The E/Z trisubstituted isomers were found to be of roughly similar reactivity. 2-Methyl-2-butene was noted to undergo epoxidation faster than 1,2-dimethylcyclohexene while the other trisubstituted compounds were only slightly slower (a factor of 2 or less). The data are summarized in Table 1.

Table 1. Second Order Rate Constants for the Epoxidation of Alkenes by Dimethyldioxirane (**1**) in Acetone at 25°C.

Alkene	$k_2M^{-1}s^{-1}$[a]	Rel. React.	Alkene	$k_2M^{-1}s^{-1}$[a]	Rel. React.
$Me_2C{=}CMe_2$	7.1±0.6	106.	Cyclopentene	0.62±0.01	9.3
1,2-Dimethylcyclohexene	2.0±0.1	30.	*cis*-3-Hexene	0.57±0.02	8.5
			trans-3-Hexene	0.067±0.001	1.0
$Me_2C{=}CHMe$	2.4±0.1	36.	*cis*-2-Hexene	0.61±0.01	9.1
1-Methylcyclohexene	1.59±0.06	23.7	*trans*-2-Hexene	0.084±0.002	1.3
Z-3-Methyl-3-hexene	1.61±0.06	24.0	2-Methyl-1-pentene	0.31±0.01	4.6
E-3-Methyl-3-hexene	1.08±0.04	16.1			
			1-Nonene	0.035±0.005	0.5

a. Determined under pseudo first order conditions with 1:10 and 10:1 alkene to 1 ratios.

The relative reactivity series for epoxidation by dimethyldioxirane is qualitatively similar to that expected for electrophilic oxygen-atom transfer reactions based on results with peracids[6] or α-azohydroperoxides, but shows a number of surprising differences. For epoxidations by peracids and α-azohydroperoxides the relative reactivity series generally observed[4,6,7] is $R_2C{=}CR_2 > R_2C{=}CHR > R_2C{=}CH_2 \cong$ *cis*-RCH=CHR $\cong$ *trans*-RCH=CHR > $RCH{=}CH_2$; each additional substituent increases the reactivity by an order of magnitude. In contrast, epoxidation by dimethyldioxirane is much less sensitive to the number of alkyl substituents. For example, a trisubstituted alkene was found to be of greater reactivity than a tetrasubstituted compound. Several disubstituted *trans* alkenes were only roughly a factor of two more reactive than the monosubstituted example and ~8 fold less reactive than their *cis* isomers. Thus steric interactions are more important here than in peracid epoxidations[6,7] or those by α-azohydroperoxides.[4]

The mechanism[7] of oxygen-atom transfer oxidation of alkenes by peracids that is generally shown is a cyclic planar concerted process ("butterfly" transition state) suggested by Bartlett.[7b] A spiro transition state[7a,8] has also been considered. Sharpless has proposed[9] an intermediate orientation for epoxidation of allylic alcohols. The oxygen-atom transfer reactions of oxaziridines with alkenes have been reported by Davis.[10] Based on a detailed study with chiral oxaziridines, he showed that the experimentally observed epoxide configuration was consistent with a planar ("butterfly"-type) transition state. Molecular orbital (ab initio) calculations by Bach[11] support the planar mechanism of oxygen-atom transfer of oxaziridines. Rebek has synthesized[12a] "selective peracids" which showed different selectivities in epoxidation when compared to simple peracids. These results were interpreted to favor a planar transition state due to steric interactions from the other half of the reagent. Interestingly, many of the unusual selectivity trends observed by Rebek are very similar to those observed with dimethyldioxirane.[12b]

The mechanism of epoxidation by dimethyldioxirane can be viewed in terms of the transition states of the two mechanistic extremes for electrophilic[13] oxygen-atom transfer: planar or spiro (Scheme 1). The observed relative reactivity series seems to strongly favor the spiro transition state. In particular it is easy to rationalize the *cis/trans* selectivity by use of the spiro arrangement since one side of the *cis* alkenes ($R_3{=}R_4{=}H$ above) can be attached preferentially. Similar steric interactions of the *cis* or the *trans* alkene and the

Scheme 1

planar

spiro

methyl group of the dioxirane would be expected in the planar transition state. As seen for oxaziridines,[10] the increased sensitivity to steric factors may be viewed as a consequence of the greater proximity of alkyl groups of the reagent to those of the alkene. Only the datum for the 1,1-disubstituted example in Table 1 does not fit readily the proposed model.[14] The results do not require that all epoxidations by dioxiranes proceed via the spiro transtion state. However, this work suggests that the energy difference between the two extreme transition states is small enough to be readily overcome. The present results clearly show that dioxiranes should be valuable in selective oxidation of disubstituted alkenes. The selectivity could be greatly increased by the use of different dioxiranes with bulky alkyl groups.

Acknowledgment is made to the National Science Foundation (CHE-8506665) for support of this work. ALB was a fellow of the Camille and Henry Dreyfus Foundation, 1981-86.

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    b) Perhaps the addition of H_2O_2 to the acid chloride in the presence of the other carbonyl derivative yields an epoxidizing agent different from that originally thought.
13. A recent Hammett study on the oxidation of sulfides by dimethyldioxirane has concluded that the reaction is electrophilic in character; see Murray, R.W.; Jeyaraman, R.; Pillay, M.K., J. Org. Chem., 52, 746 (1987).
14. This example could be explained by a distortion to an intermediate orientation or that the planar geometry is favored for monosubstituted alkenes.

(Received in USA 7 May 1987)