Dioxirane Chemistry. Part 25.[1] The Effect of Solvent on the Dimethyldioxirane Carbon–Hydrogen Bond Insertion Reaction

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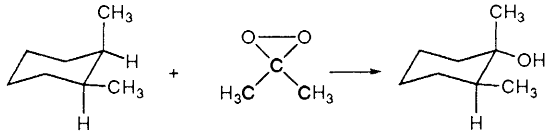
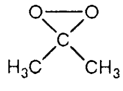
Second order rate coefficients for the insertion reaction of dimethyldioxirane with *cis*-1,2-dimethylcyclohexane have been measured in several binary solvents. The reaction proceeds stereospecifically with retention to give a single alcohol product as reported earlier. The data were treated with the Kamlet–Taft α parameter taken from the multi-parameter solvent effect equation devised by these authors. The α parameter measures the hydrogen bond donor capacity of the solvent. An excellent correlation was observed between the rate coefficients and the α values indicating that the insertion reaction is facilitated by solvents with hydrogen bond donor properties. A spiro type transition state is proposed for the insertion reaction.

Since it was first reported[2] in 1976 the remarkable carbon–hydrogen bond insertion reaction of dimethyldioxirane, **1**, has received an increasing amount of attention. This reaction has permitted the synthesis of previously inaccessible structures.[3] The reaction has also provided simpler access to some functionalities,[2,4–6] and has found an important use in some natural product chemistry.[7–12] The reaction proceeds in a stereospecific fashion thus adding to its utility. The carbon–hydrogen insertion reaction has also been observed[4,8,11–13] for methyltrifluoromethyldioxirane, **2** and cyclohexanespirodioxirane, **3**.[14] We have recently reported[15] that the rate of the dimethyldioxirane epoxidation reaction is dependent on the nature of the second solvent when binary solvents containing 50% acetone are used for the reaction. Treatment of the rate data with a multi-parameter empirical solvent effect equation revealed that the rate is enhanced by hydrogen bond donor solvents and is inhibited by hydrogen bond acceptor solvents. While there are instances in the literature in which a dioxirane is used in a mixed solvent for the carbon–hydrogen insertion reaction, there has been no systematic study of the effect of solvent on this process. Perhaps the most dramatic instance of the effect of solvent change on the insertion reaction is that described[16] by Adam, Curci *et al.* In that work it was shown that oxyfunctionalization of an optically active hydrocarbon by **2** proceeded with complete retention of configuration. Furthermore the reaction was found to have a lower activation energy in methylene chloride than in trifluoroacetone solvent. In the current work we describe the results of a comprehensive study of the effect of solvent on the kinetics of the carbon–hydrogen insertion reaction of **1**. The kinetic data have been correlated with an empirical parameter measuring solvent hydrogen bond donor capacity.



4 **1** **5**

Scheme 1



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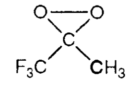

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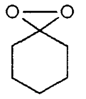

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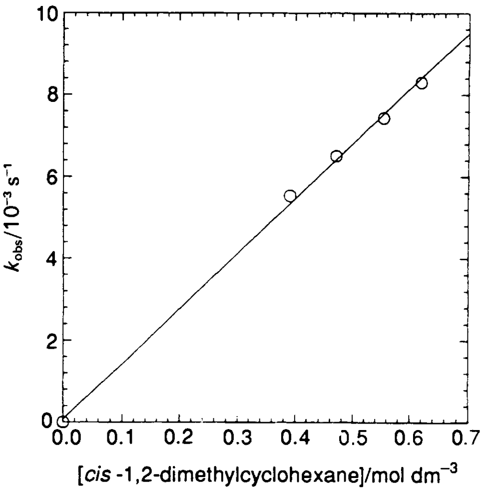


Fig. 1 Plot of k_{obs} *versus* *cis*-1,2-dimethylcyclohexane concentration for the dimethyldioxirane insertion reaction in acetone at 25 °C

Results and Discussion

The general procedure used[15] in the study of the effect of solvent on the epoxidation reaction of **1** was followed in the current work. The rate data were obtained in binary solvents containing 1:1 acetone:solvent X. The substrate chosen for study was *cis*-1,2-dimethylcyclohexane, **4**. Previous work has shown that **4** reacts with **1**[2] or **2**[13] in a stereospecific manner to give alcohol **5** as the sole product (Scheme 1). The kinetic data were obtained at 25 °C under pseudo-first-order conditions with **4** in excess (10–20 fold). As before, the kinetics were followed by observing the decay in the absorption of **1** at 335 nm. Plots of ln $(A_t - A_\infty)$ *versus* time gave straight lines with excellent correlation coefficients (R = 0.998–0.999). The k_{obs} values were obtained from the slopes of these lines. Plots of the k_{obs} values *versus* concentration of **4** gave straight lines ($R > 0.99$) with slopes = k_2. These reactions follow second order kinetics, first order each in **1** and **4**. Fig. 1 shows an example of these plots. A summary of the solvents used, and the kinetic data obtained is given in Table 1. As in the earlier work on the epoxidation reaction only solvents in which it could be shown that there are no competing first or second order processes were used in this study.

In order better to understand the variation in rates observed in the study of the effect of solvent on the epoxidation reaction of **1**, we treated the data with the Kamlet–Taft[17] multi-

Table 1 Second order rate coefficients for the insertion reaction of dimethyldioxirane with *cis*-1,2-dimethylcyclohexane

Solvent[a]	$k_2/10^{-3}$ dm^3 mol^{-1} s^{-1} [b]	Relative reactivity
Acetone	1.37 + 0.03	1.00
Methyl ethyl ketone	1.29 + 0.01	0.94
Ethyl acetate	1.02 + 0.02	0.74
CH_2Cl_2	3.08 + 0.06	2.25
$CHCl_3$	4.44 + 0.13	3.24
$CDCl_3$	4.05 + 0.04	2.96

[a] The second solvent is present in a 1 : 1 volume ratio with acetone. [b] T = 25 °C.

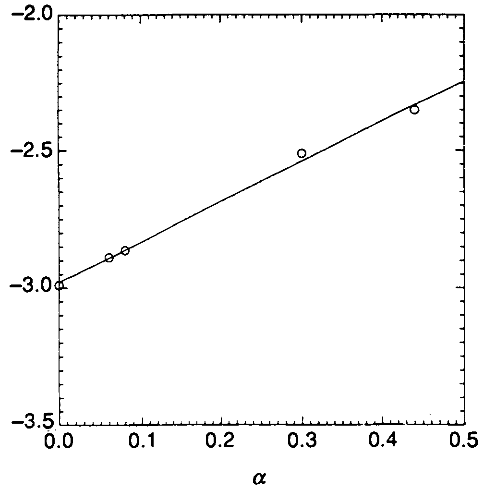


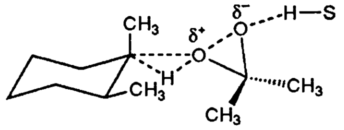
Fig. 2 Plot of log k_2 *versus* the solvent hydrogen bond donor parameter (α) for the dimethyldioxirane insertion reaction of *cis*-1,2-dimethylcyclohexane in several solvents

parameter solvent effect eqn. (1). The equation contains parameters associated with various solvent properties. In the

$$\log k_2 = \log k_0 + s(\pi^* + d\theta) + a\alpha + b\beta + h\delta \quad (1)$$

case of the epoxidation reaction this approach clearly indicated that the parameter α, which is a measure of the solvent hydrogen bond donor (HBD) capacity, was the controlling factor. Solvents with a greater HBD capacity increased the rate of the epoxidation. Based on this experience we decided not to use the full Kamlet–Taft equation to treat the kinetic data on the C–H insertion reaction, but rather went straight to use of the α parameter. Plotting the log k_2 values *versus* α gives an excellent straight line correlation with R = 0.996 (Fig. 2).

These results suggest a transition state for the insertion reaction which has much in common with that suggested[14,18] for the epoxidation reaction. In that case an electrophilic spiro type attack of **1** on the double bond was suggested as leading to partial charge creation at the oxygen atoms of the reacting **1**. A number of suggestions have been made for the transition state for the C–H insertion reaction. In their earlier work on C–H insertions by **2** Curci *et al.*[13] likened the process to that occurring in oxygenations involving ozone. An activated complex involving several resonance contributors, including those involving charged and radical species, was invoked. In subsequent work Curci *et al.*[8] suggested a spiro transition state for a C–H insertion reaction in a steroid substrate. A similar suggestion had been made earlier by Marples.[10] An ordered transition state was proposed[16] for the remarkable insertion reaction in which high configurational retention was observed in the dioxirane oxidation of a chiral hydrocarbon to the derived alcohol. We believe that the spiro type transition state, **6** (S–H is solvent), is most consistent with the results reported here. This structure would permit stabilization by HBD solvents in the same manner as in the epoxidation reaction. The solvent effect data support this kind of weakly polar transition state rather than one which is free radical in character. The solvent effect on rate seen in the current study is less pronounced than that observed for the epoxidation of cyclohexene,[15] for example. This may be attributed to the difference in polarizability of the reacting bonds, that is, a π bond in the epoxidation reaction *versus* an sp^3 σ bond in the insertion reaction. Using a frontier molecular orbital model and water oxide as a model for the dioxirane, Bach *et al.*[19] have described a theoretical model for the electrophilic insertion reaction. This model accounts for the stereospecificity of the reaction as well as the relative reactivity of various C–H bonds. Finally a solvent isotope effect for the insertion reaction was determined for the $CHCl_3/CDCl_3$ pair (= 1.10 at 25 °C). As before, we suggest that the lower rate in the deuteriated solvent is due to the decreased polarizability of the C–D bond.



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Summary.—Treatment of the second order rate coefficients, measured for the dimethyldioxirane C–H insertion reaction in **4**, with the solvent HBD parameter α, derived from the Kamlet–Taft equation, indicates that this reaction is favoured by solvents with greater HBD capacity. The effect is less pronounced than that previously described for the epoxidation reaction of **1**. These results suggest that groups which provide stabilization by intramolecular hydrogen bond donation could be used to provide reaction site selectivity in the insertion reaction.

Experimental

Instrumentation.—UV–VIS spectra were obtained on either: (*a*) a UV–VIS spectrophotometer equipped with a temperature control system (0–80 °C), a kinetic calculation program, a kinetic storage program, and a multi-scan program; (*b*) a UV–VIS spectrophotometer equipped with a UV–VIS six-cell positioner and temperature control at 25, 30 and 37 °C; or (*c*) a UV–VIS spectrophotometer equipped with a constant temperature circulator. Temperature control was from 10–80 °C. Gas chromatography was performed on a capillary GC interfaced with a chromatopic or other integrator. NMR spectra were recorded using a 300 MHz spectrometer.

Materials.—Solvents. All solvents were refluxed 12–48 h with a drying agent followed by distillation. Solvent grades, names of suppliers, and drying agents used are given in Table 2.

Reagents. Oxone, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Dupont), was obtained from Aldrich Chem. Co. and used as such. *cis*-1,2-Dimethylcyclohexane (Wiley Organics Co.) was passed through a neutral alumina column and the purity (> 99%) was verified by GLC. Thioanisole (99% purity) was obtained from Aldrich Chem. Co. and used as such.

Determination of the Kinetics of the C–H *Insertion Reaction of* **1** *into* **4** *in* 1 : 1 *Binary Solvent Systems and Acetone at* 25 °C.—A

Table 2

Solvent	Grade	Supplier	Drying agent/ comments
Acetone	bulk		K_2CO_3
CH_2Cl_2	HPLC	Fisher Scientific	P_2O_5
$CHCl_3$	HPLC	Fisher Scientific	P_2O_5
Butan-2-one	Certified	Eastman Kodak	P_2O_5
Ethyl acetate	Certified	Fisher Scientific	4 Å mol. sieve

freshly prepared solution of **1** was dried (Na_2SO_4 and 4 Å molecular sieves). The concentration of **1** was determined by UV absorption and a previously constructed working curve correlating UV absorption with chemically determined concentrations. The suitable equivalents of *cis*-1,2-dimethylcyclohexane, **4**, were weighed into a 1 cm^3 UV cell. The second solvent (1.0 cm^3) was transferred to the cell using a 1 cm^3 volumetric pipette. The concentrations of **1** and **4** were corrected for the volume of *cis*-dimethylcyclohexane ($d = 0.796$ at 25 °C). UV cells containing the solutions of **1** and **4** were kept in the cell compartment of the UV spectrophotometer in order to permit temperature equilibration. A 1 cm^3 aliquot of the solution of **1** was transferred to the cell containing the solution of **4** using a 1 cm^3 volumetric pipette. The combined solution was shaken vigorously by hand and kinetic data recording begun immediately. The absorption of the solution at 335 nm was monitored *versus* time for 5 min. The reaction solution was kept at room temperature for one or two days in order to record the final absorption (A_∞). This procedure was repeated at several concentrations of **4**. Plots of $-\ln(A_t - A_\infty)$ *versus* time gave straight lines with slopes $= k_{obs}$. Plots of k_{obs} *versus* concentration of **4** gave straight lines with slope $= k_2$. Table 1 summarizes the results of these experiments.

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