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THE EFFECT OF PRESSURE ON SWERN–MOFFATT OXIDATIONS

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Rates of oxidation of cyclohexanol by dimethyl sulphoxide in conjunction both with acetic anhydride and with dicyclohexylcarbodiimide have been measured with variation of both temperature and pressure. Activation volumes were found to be −25 and −34 cm^3 mol^{-1}, respectively, and the absence of an α–d PKIE was noted. The reaction mechanism is discussed in the context of these values.

INTRODUCTION

The use of dimethyl sulphoxide (DMSO) as an oxidising agent for alcohols has been shown to occur with many minor modifications of the conditions but the basic mechanism is believed to require initial coordination of an electrophile to the sulphoxide oxygen which leads to a dimethylalkoxysulphonium ion (**1**) with nucleofugic oxygen. The oxygen is then displaced by the alcohol which is to be oxidised and the resulting alkoxysulphonium compound (**2**) undergoes a β-elimination with the expulsion of the carbonyl product (Scheme 1).[1]

The Pfitzner–Moffatt method[2] for oxidation of alcohols uses as the activating electrophile, dicyclohexylcarbodiimide (DCC) and a proton source (e.g. pyridinium trifluoroacetate) (Scheme 2). Acetic anhydride (Swern oxidation) may be also used to *O*-acetylate the DMSO[3] and the same intermediate (**2**; E = OAc) may be generated by forming the chloroformate of the alcohol which reacts with DMSO with decarboxylation.[4] The electrophilic species may be a carbocation or diazonium ion derived from a primary amine and nitrous acid which then only needs the final elimination to complete the reaction.[5] Oxidations by these routes are generally mild and can give very high yields of the carbonyl products including aldehydes from primary alcohols. The family of reactions are widely used in synthesis but mechanistic information is by no means complete.

We now report some kinetic studies of two forms of this oxidation with variation both of temperature and pressure to obtain the appropriate activation parameters and find also a lack of a primary kinetic isotope effect to establish the rate-determining step.

EXPERIMENTAL

The oxidation of cyclohexanol by acetic anhydride and DMSO. Solutions of cyclohexanol and acetic anhydride, 0·2 M and 2·0 M, respectively, in DMSO (dried and distilled), were prepared immediately before use. The two solutions were allowed to reach the desired reaction temperature, equal volumes were mixed and the mixture was then placed in a thermostatted spectrophotometer cell and the absorbance at 300 nm monitored. For reactions followed at elevated pressures the same procedure was followed. The spectrophotometer cell was sealed with a silicone rubber cap to allow pressure equalisation and was then placed in the high-pressure optical cell as previously described.[6] The progress of the reaction was monitored as before. Under these conditions the appearance of the carbonyl absorption was observed to follow a first-order rate law to at least 50% reaction. Nonetheless the reaction is a complex multistep process and no significance can be attributed to composite rate constants obtained in this way. The variation of pseudo-first-order rate coefficients does, however, lead to a composite volume of activation. Rates were observed to be sensitive to the

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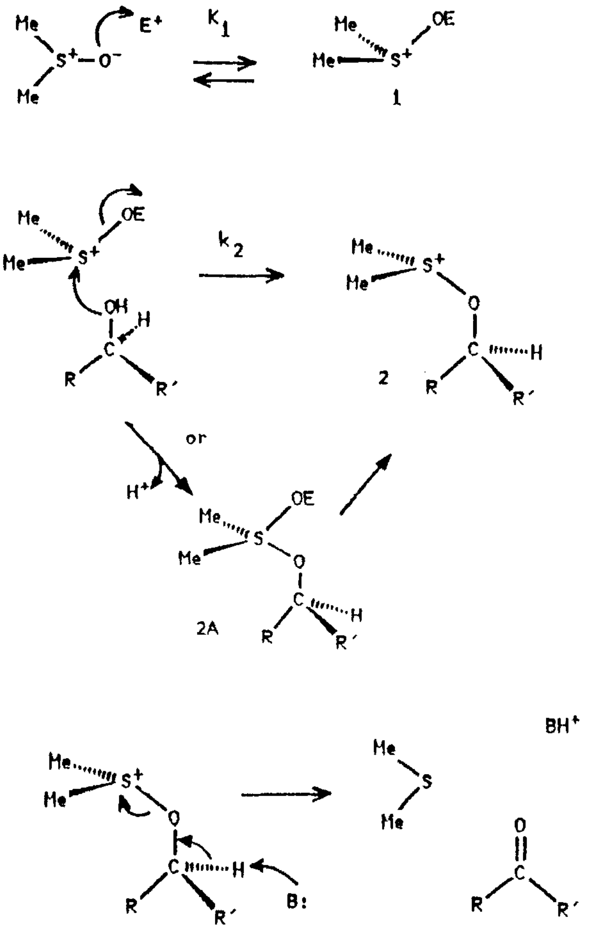
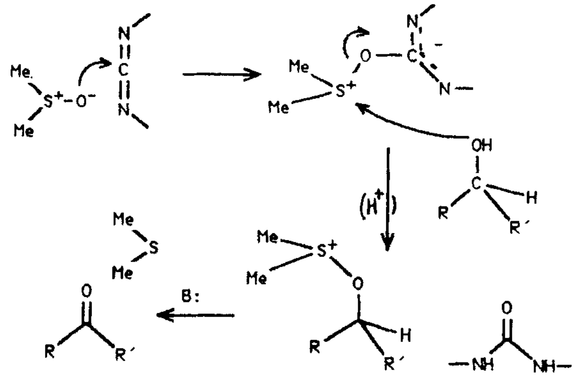
concentration of acetic anhydride although were not affected by small amounts of added acetic acid or triethylamine. However, rate constants of the acetic anhydride reactions were observed to fall off significantly at long reaction times. This is due to the loss of some of the alcohol, which directly reacts with acetic anhydride and is converted to acetate which cannot undergo oxidation. Measured rate constants were obtained by the Guggenheim method[7] and activation volumes were calculated by equation (1) using a least-squares linear fit, and are given in Table 1[8], and Figure 1.

$$_{\mathrm{D}}V^* = -RT\cdot \mathrm{d}p(\ln k) \qquad (1)$$



Scheme 1



Scheme 2

Table 1. Oxidation of cyclohexanol by DMSO–Acetic Anhydride

	T(°C)	$10^4 k$(s^{-1})	SD(%)
	45·0	3·27	1
	50·0	7·10	3
	58·0	13·1	0·5
	60·0	20·1	2
	66·0	28·3	1
	70·0	44·5	1
Apparent Arrhenius activation energy, $E_A = 90\cdot 0 \pm 2$ kJ mol^{-1}			
$T = 58\cdot 0$°C	p(bar)	$10^4 k$(s^{-1})	SD(%)
	1	13·1	4
	500	20·2	4
	750	26·5	3
	850	29·7	4
	1000	34·4	5
Volume of activation, $\Delta V^* = -25\cdot 2$ cm^3 mol^{-1}			

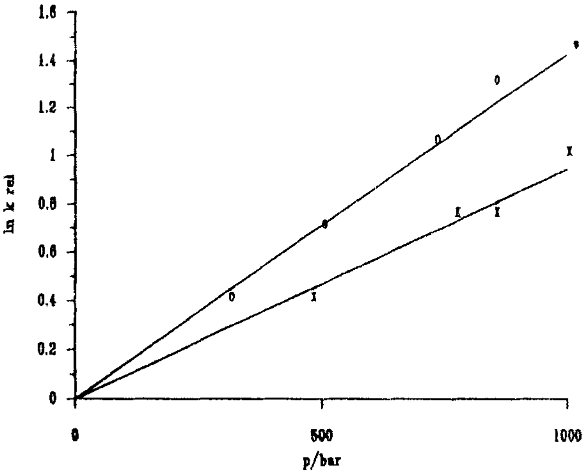


Figure 1. Effect of pressure on rates of oxidation of cyclohexanol by DMSO; X = acetic anhydride method, O = DCC method

Table 2. Oxidation of cyclohexanol by DMSO–DCC

T(°C)	$10^4\,k$(s^{-1})	SD(%)
31·0	2·75	1·8
35·0	3·75	4·5
40·0	8·17	2·0
45·0	11·65	1·3

Apparent Arrhenius activation energy, $E_A = 83$ kJ mol^{-1}

$T = 31$°C	p(bar)	$10^4\,k$(s^{-1})	SD(%)
	1	2·75	1·8
	300	4·25	2
	510	6·55	1
	740	7·77	1
	880	8·30	1
	1020	11·8	2·5

Volume of activation, $\Delta V^* = -34$ cm^3 mol^{-1}

The oxidation of cyclohexanol by DCC in DMSO. Solutions were prepared of, on the one hand, cyclohexanol (0·1 M), trifluoroacetic acid (0·05 M) and pyridine (0·1 M) in a DMSO : chloroform (1 : 3 v/v) mixture and, on the other, DCC (0·5 M) in the same DMSO : chloroform solvent, all materials being the purest available. The chloroform was necessary in order to retain in solution dicyclohexylurea which forms as one product. Equal volumes of the thermally equilibrated solutions were mixed, placed in the spectrophotometer cell as described above and the absorption at 310 nm monitored as a function of time to about 75% completion. Pseudo-first-order rate constants were evaluated by the Guggenheim procedure and the volume of activation according to equation (1) (Table 2, Figure 1).

DISCUSSION

Volumes of activation are strongly negative for both systems and especially so for the oxidation by DCC. The observed values may be accounted for as follows. Each of the two oxidations takes place by a sequence of at least three steps (Schemes 1 (E = OAc) and 2). The slow step we assume to be the second, the displacement by the alcohol of the intermediate alkoxysulphonium ion. The evidence for this is twofold. Firstly, on mixing DMSO with acetic anhydride or with DCC spectroscopic changes are noted immediately though the reaction is far from complete, suggesting that there is a rapid equilibrium between the reagents prior to product formation. Secondly, the oxidation of cyclohexanol-1-*d* occurs at the same rate as the 1-*h* compound and the absence of a kinetic isotope effect confirms the final elimination as being subsequent to the rate-determining step. The volume of activation therefore should be the sum of the volume of reaction for step (1) and the volume of activation for step (2):

$$\Delta V^*_{\text{obs}} = \Delta V_1 + \Delta V_2^* \qquad (2)$$

ΔV_1 should be negative in both cases since the reactions are associative and, in addition, would contain an element of electrostriction due to the formation of the sulphonium ion. However, one would expect a more negative volume change for the reaction between DMSO and DCC than that between DMSO and acetic anhydride if it is assumed that the former reaction is an addition, the two molecules combining to a single product whereas the latter is a concerted displacement at sulphur, acetate being simultaneously released.[9] However there is the possibility that the rate-determining step is also an addition to form the sulphurane **2A** which subsequently and rapidly releases acetate. This sequential displacement would be parallel to that known to occur in the Pummerer reaction[10*] and would be associated with a more negative volume change than would the concerted reaction. There is, in addition, the imponderable effect of solvent change to be taken into account. The electrostrictive volume change, ΔV_e, given by the Drude–Nernst equation:[11]

$$\Delta V_e = Lq^2/2r \cdot \Phi \qquad (3)$$

depends upon the dielectric constant function, Φ, which would be greater for a non-polar solvent such as chloroform than for DMSO. One would expect a rather more negative contribution from electrostriction for the DCC reaction in the mixed solvent than for one in pure DMSO but the difference is hard to estimate. All in all, values of -10 and -20 cm^3 mol^{-1} for the respective values of ΔV_1 would seem reasonable. The second step, the displacement of the oxygen leaving group by alcohol, is again associative and in both cases ΔV^* should be negative and very similar, a figure of around -10 cm^3 mol^{-1}, comparable with many S$_N$2 reactions, being a reasonable estimate.[9] The pressure effects on the rates of these two oxidations therefore seem to be in accordance with the presumed mechanism and lend support to it.

The application of pressure to these reactions could have practical use in promoting difficult oxidations. For example, a mixture of cyclohexanol (10 mmol), acetic anhydride (100 mmol) and DMSO (30 mL) at 25 °C undergoes no detectable reaction over 10 h although oxidation fo cyclohexanone is complete within 4 h at 60 °C. Complete reaction was also achieved at 25 °C within 10 h at 10 kbar pressure. We are examining further the preparative applications of this technique.

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