The Kinetics and Mechanism of Addition of Bulky Alcohols to Dimethyl Ketene and to *p*-Nitrophenyl Isocyanate in Iso-octane and Carbon Tetrachloride Solutions

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We report on the kinetics of addition of pentan-3-ol to *p*-nitrophenyl isocyanate and to dimethyl ketene in iso-octane, of t-butyl alcohol to the isocyanate in iso-octane, and of pentan-3-ol to the isocyanate in carbon tetrachloride. The extent of self-association of the alcohols in iso-octane has also been examined. For all the additions, our results are compatible with a mechanism that involves slow attack by both alcohol monomers and trimers, the latter being the more reactive. Conclusions from previous work with pentan-3-ol are not supported.

There exists much evidence that the alcoholysis of ketenes and isocyanates in non-hydroxylic solvents involve predominantly polymeric (H-bonded) forms of the alcohol.[1–4] The reactivity of monomeric alcohol appears relatively small. The reaction order in stoichiometric alcohol concentration, $[ROH]_S$, that is observed depends upon the reaction conditions:[2] when these favour a predominance of monomer species in solution (*e.g.* at low concentrations or in solvents to which the OH group can H-bond) then orders >1, and often 2–3, are normally found, whereas when polymers predominate (*e.g.* at low temperatures, or at relatively high values of $[ROH]_S$) the reaction order in $[ROH]_S$ can fall to *ca.* 1. Many authors who have studied these reactions using non-hydroxylic solvents accept the involvement of polymers (when these are present in kinetically significant concentrations) but there exists one crucial study of alcoholysis of several ketenes in such solvents by the bulky alcohol pentan-3-ol that has been interpreted in terms of monomer participation only.[5] This study used second-order reaction conditions (approximately equal stoicheiometric concentrations of ketene and alcohol of *ca.* 0.05 mol dm^{-3}). The change in $[ROH]_S$ during the reaction will therefore have been from *ca.* 0.05 to <0.01 mol dm^{-3} over 3 half-lives. This is a concentration region in which the relative amounts of monomer and polymer would be expected[3,6] to change substantially with $[ROH]_S$. The finding of accurate second-order behaviour (*i.e.* first order in $[ROH]_S$) is therefore surprising; it suggests that pentan-3-ol is much less associated than might be expected, and/or that its polymers are relatively unreactive. We have now reinvestigated alcoholysis by pentan-3-ol using both dimethyl ketene and *p*-nitrophenyl isocyanate with iso-octane as the solvent, and have measured the extent of polymerisation of the alcohol in this solvent. We also report results for carbon tetrachloride as the solvent, and have studied another bulky alcohol, t-butyl alcohol.

Experimental

Pentan-3-ol and t-butyl alcohol were the Aldrich products and were used without further purification. The carbon tetrachloride was of AnalaR grade and was stored over molecular sieves. The sources and treatment of the other materials, and the general kinetic procedures, have been described previously for ethanolysis.[2,3] All kinetic runs were conducted under pseudo-first-order conditions (excess of alcohol), and k_{obs}, the observed first-order rate constant for loss of ketene (or isocyanate), was always reproducible to within ±10%. Excellent isosbestic points for the conversion of reactants into products were obtained. Our concentrations and other conditions are given in the Tables and Figures. Preparative-scale reactions showed that the expected products [equations (1) and (2)] are formed

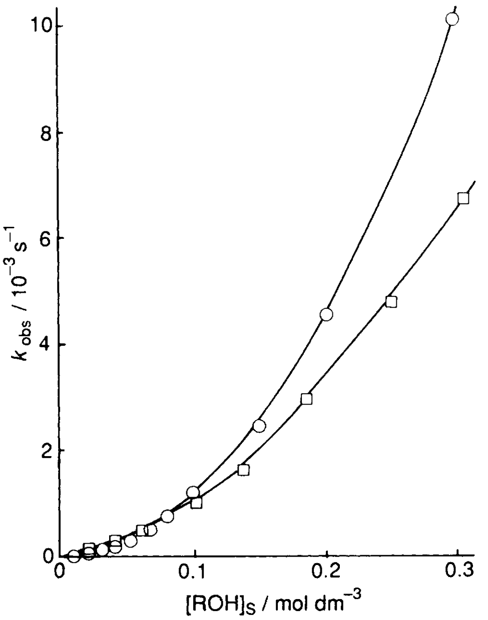


Figure 1. Reaction of pentan-3-ol with dimethyl ketene and *p*-nitrophenyl isocyanate in iso-octane: $[\text{ketene}]_{\text{initial}} \simeq 2 \times 10^{-3}$ mol dm^{-3}; $[\text{isocyanate}]_{\text{initial}} \simeq 7.5 \times 10^{-5}$ mol dm^{-3}; $T_p \simeq 25$ °C (Table 2); for k_{obs} see the text; □, dimethyl ketene; ○, *p*-nitrophenyl isocyanate.

$$Me_2C{=}C{=}O + ROH \longrightarrow Me_2CHCO_2R \qquad (1)$$

$$p\text{-}NO_2C_6H_4N{=}C{=}O + ROH \longrightarrow p\text{-}NO_2C_6H_4NHCO_2R \qquad (2)$$

in very high yields. The self-association of the alcohols in iso-octane was investigated as before[3] by IR spectroscopy at 26 ± 1 °C. The O–H stretching absorption of monomer occurs at 3 620 and at 3 605 cm^{-1} for pentan-3-ol and t-butyl alcohol, respectively.

Results and Discussion

(*a*) Figures 1 and 2 show our k_{obs} values for all the systems studied. In no case does the alcoholysis show a simple first-order

Table 1. Derived rate and equilibrium constants.[a]

			Rate and equilibrium constants in iso-octane				
		Temp./°C	$k_1/10^{-3}$ dm^3 mol^{-1} s^{-1}	k_3K_3/dm^9 mol^{-3} s^{-1}	k_3/dm^3 mol^{-1} s^{-1}	K_3/dm^6 mol^{-2}	k_3/k_1
p-Nitrophenyl isocyanate	Ethanol[3]	24.5	0.50	12.5	0.36	35	720
	t-Butyl alcohol	25.0	0.15	0.32	0.008	40	53
	Pentan-3-ol	25.0	2.7	1.5	0.11	14	41
Dimethyl ketene	Pentan-3-ol	24.7	5.0	0.93	0.066	14	13

[a] For k_{obs}, k_1, k_3, and K_3 see the text.

Table 2. Effects of temperature on alcoholysis by pentan-3-ol.

Compound	Solvent	[ROH]$_S$/mol dm^{-3}	T_p/°C	$k_{obs}/10^{-3}$ s^{-1}	$\Delta H^\ddagger$/kJ mol^{-1}	$\Delta S^\ddagger$/J K^{-1} mol^{-1}
Dimethyl ketene	Iso-octane	0.26	24.7 37.0 44.3	5.20 5.41 5.70	1.0 ± 0.5	−284 ± 25
p-Nitrophenyl isocyanate	Carbon tetrachloride	0.08	18.0 25.0 35.0	0.354 0.298 0.202	−28 ± 5	−386 ± 30

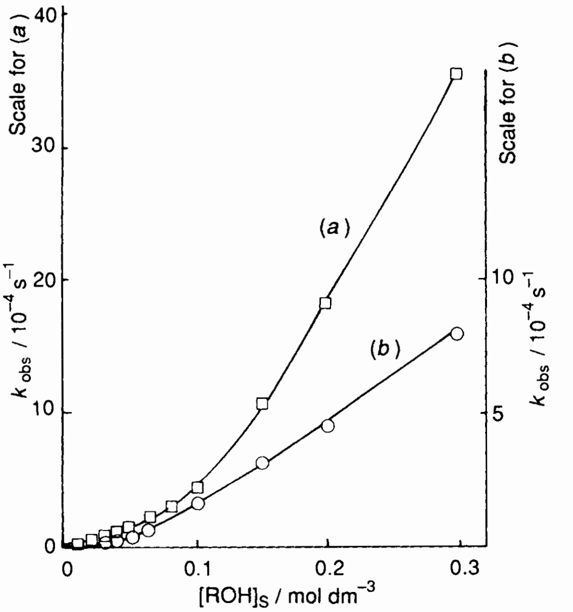


Figure 2. Reaction of *p*-nitrophenyl isocyanate with pentan-3-ol in carbon tetrachloride and t-butyl alcohol in iso-octane. Conditions as for Figure 1: (*a*) pentan-3-ol; (*b*) t-butyl alcohol.

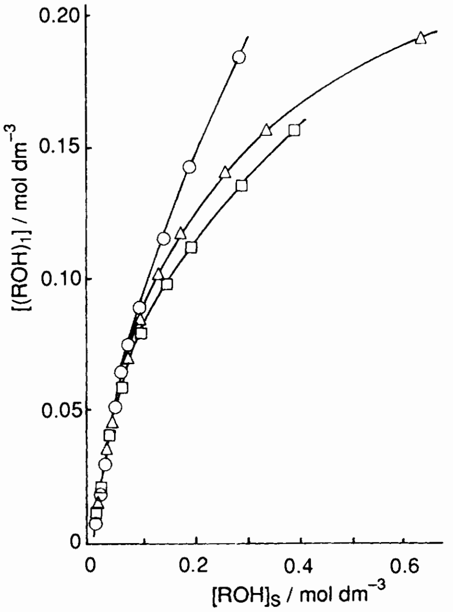


Figure 3. Plots of [(ROH)$_1$] against [ROH]$_S$ at 26 ± 2 °C: ○, pentan-3-ol; □, t-butyl alcohol; △, ethanol.

dependence on [ROH]$_S$. The results for dimethyl ketene cast doubt on the conclusion of Brady *et al.*[5] that the reaction of pentan-3-ol with dimethyl and other ketenes is simple first-order in [ROH]$_S$. Their use of the second-order rate equation is an insensitive test for the order in alcohol; this has been found in other contexts.[1]

(*b*) Figure 3 shows the alcohol monomer concentration, [(ROH)$_1$], as a function of [ROH]$_S$ for pentan-3-ol, t-butyl alcohol, and ethanol[3] in iso-octane solution. The extent of association is in the sequence t-butyl alcohol > ethanol > pentan-3-ol. Our results for t-butyl alcohol are in reasonable agreement with those of Rytting *et al.*,[6] and of Tucker and Becker[7] for this alcohol in hexadecane. The relative extents of self-assocation suggest (tentatively) that chain length may be more important than chain branching in reducing association.[6] It is postulated below that for the present systems the polymeric alcohol is largely the trimer. Tucker and Becker also favour the trimer,[7] Rytting the tetramer.[6]

(*c*) Since there is no doubt that both monomeric and polymeric alcohol species coexist in the reaction mixtures, the possible involvement of both must be considered in the alcoholyses. We do this first. The association equilibrium can be written as equation (3). Previous work with ethanol and the isocyanate shows[3] that k_{obs} has the form of equation (4), and

$$x(\mathrm{ROH})_1 \rightleftharpoons (\mathrm{ROH})_x \quad K_x, \text{ Fast} \qquad (3)$$

suggests that the active form of the polymer is the trimer. As for ethanol, plots of k_{obs}/[(ROH)$_1$] *versus* [(ROH)$_1$]^2 are rectilinear (Figure 4).

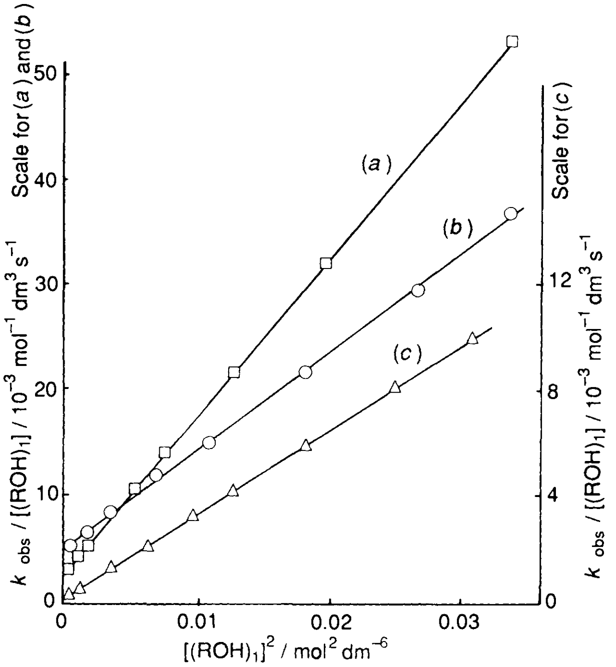


Figure 4. Plots of equation (4). (*a*) *p*-nitrophenyl isocyanate and pentan-3-ol (25 °C); (*b*) dimethyl ketene and pentan-3-ol (24.7 °C); (*c*) *p*-nitrophenyl isocyanate and t-butyl alcohol (25.0 °C).

$$\begin{aligned} k_{obs} &= k_1[(ROH)_1] + k_3[(ROH)_3] \\ &= k_1[(ROH)_1] + k_3K_3[(ROH)_1]^3 \qquad (4) \end{aligned}$$

Analogous plots that test for the additional involvement of two or four molecules of alcohol in the transition state suggest that the dimer and tetramer contribute relatively little or nothing to the alcoholyses. Equation (4) corresponds to the mechanism of equations (5)–(7) (in which $Me_2C{=}C{=}O$ can

$$3(ROH)_1 \rightleftharpoons (ROH)_3 \quad K_3, \text{Fast} \qquad (5)$$

$$(ROH)_1 + ArNCO \longrightarrow ArNHCO_2R \quad k_1, \text{slow} \qquad (6)$$

$$(ROH)_3 + ArNCO \longrightarrow ArNHCO_2R + 2(ROH)_1 \quad k_3, \text{slow} \qquad (7)$$

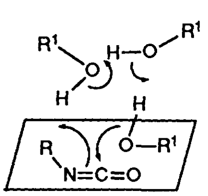
replace ArNCO). Values of k_1 and k_3K_3 can be calculated from plots such as those in Figure 4, and are given in Table 1. Assuming, as an approximation, that the associated alcohol is largely trimer, estimates of K_3 and k_3 can be obtained for iso-octane (Table 1). The results in Table 1 show that the reactivity of pentan-3-ol towards dimethyl ketene and *p*-nitrophenyl isocyanate is rather similar. The values of k_1 and k_3 for the three alcohols suggest that both electron release and steric bulk are important in determining nucleophilicity. The ratio k_3/k_1 varies widely, but the efficacy of the trimer as reactant is apparent everywhere.

An interpretation of the greater-than-first-order dependence of k_{obs} on $[ROH]_S$ entirely in terms of polymer involvement ignores any effect of increase in $[ROH]_S$ on the bulk polarity of the solvent. This appears justified at the alcohol concentrations involved.[10] However, it also ignores any independent specific solvation of the ketene (or isocyanate) and transition state by alcohol molecules. It is reasonable to think that the more alcohol molecules there are in the transition state the better will it be stabilised. The third-order term in $[(ROH)_1]$ could be explained as arising from a fast pre-equilibrium solvation of the ketene (or isocyanate) by two monomers followed by a slow nucleophilic attack by another monomer. Yet if such an explanation was valid it is difficult to understand why second-order terms are absent, and it is reasonably certain that polymers do react, since k_{obs} does not fall at alcohol concentrations where polymers predominate. Therefore it seems to us simplest (even if over-simple) to express the mechanism in terms of polymer involvement. It should be noted that Baker-type mechanisms, in which an alcohol-substrate intermediate can undergo a partially rate-determining, alcohol-catalysed, prototropic rearrangement to product, are incompatible with the kinetic form observed.[1,8,9]

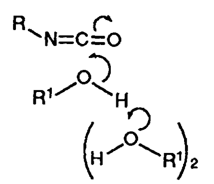
At 25 °C values for k_{obs} for reaction of pentan-3-ol with the isocyanate in carbon tetrachloride are *ca.* 2.7 times smaller than in iso-octane at the same value of $[ROH]_s$ (Figure 2). These solvents have similar relative permittivity.* A possible reason for the smaller k_{obs} values is that there may be less alcohol association in carbon tetrachloride (owing to competing H-bond interactions with the solvent, $ROH \cdots ClCCl_3$). At very low alcohol concentrations results of Moodie and Sansom[11] suggest that kinetically insignificant amounts of polymers exist in this solvent. It has been claimed[12] that photo-acceleration of alcoholyses of isocyanates can occur in halogenated solvents, but we found our rate constants were unaffected by the amount of light (at 306 nm) to which reaction mixtures were exposed.

The effects of temperature on the alcoholysis of the isocyanate in carbon tetrachloride, and on that of dimethyl ketene by pentan-3-ol in iso-octane, are given in Table 2. The activation parameters are consistent with those found previously for similar reactions,[1–3] and are compatible with the mechanism of equations (5)–(7) since the small positive or negative values of $\Delta H^\ddagger$ can arise from the opposing effects of temperature on the fast and slow steps, and the large negative values of $\Delta S^\ddagger$ from the substantial loss of freedom involved in reaching the transition state.

(*d*) If we accept the mechanism of equations (5)–(7) for the present solvents (and note that in largely aqueous media the hydration of ketenes is thought to involve at least two molecules of water[13]) there still remain questions of detail. One point still debated[2,13,14] is whether the transition states are cyclic and involve addition of the C=C (or N=C) double bond perpendicular to the molecular plane [*e.g.* (I)], or involve in-plane attack at the carbonyl carbon atoms with any additional molecules of alcohol (or water) possibly acting as general-base catalysts [*e.g.* (II)]. Calculations suggest[15,16] that the latter is favoured for polar solvents, and the former for non-polar. Contrary to Tidwell's views,[13,14] the fact that polar substituents have a (moderate) effect on the rates of addition to ketenes and isocyanates in both high and low relative permittivity solvents does not mean that the polarity of the transition state will not be minimised as far as possible in non-polar media.



(I)



(II)

Steric effects are clearly important in the additions. In-plane attack will be more subject to these effects but they will not be absent for bulky nucleophiles in perpendicular attack. Polymeric alcohols will make stringent steric demands. Our relative k_1 and k_3 values are not easy to interpret and we doubt that steric effects will permit an unambiguous distinction

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* This quantity was formerly called dielectric constant.

between cyclic and non-cyclic transition states. Other evidence leads us to favour the former.[1,2]

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