

719. Acylation. Part XIII.* Kinetics and Mechanism of the Reaction of Phenols with Acyl Bromides in Acetonitrile.

By J. M. BRIODY and D. P. N. SATCHELL.

The kinetic form of the reaction between acetyl bromide and 2-naphthol in acetonitrile has been determined, both in the presence and the absence of added saline bromide. Other similar reactants have also been studied. The results are considered to provide evidence for acylation by free and ion-paired acylium ions; undissociated acyl bromide may not contribute. The mechanism involves formal catalysis by hydrogen bromide and is one of the first acid-catalysed schemes to implicate the HBr_2^- ion. The literature value for the formation constant of this ion is questioned.

IN Part IX we provided evidence that, in nitromethane, acetyl chloride acylates phenols by a mechanism which involves both the un-ionised and the dissociated acyl halide.¹ Preliminary studies indicated that acetyl bromide behaves similarly. We now report a full study of the acetyl bromide reaction. Since the addition of acyl bromides to nitromethane had been found to lead to the slow formation of (unidentified) precipitates, especially in the presence of added saline bromides, we have used instead acetonitrile, which has a similar dielectric constant.

General Kinetic Form.—To simplify this the phenol (2-naphthol or *p*-methoxyphenol) was kept in at least a ten-fold deficit compared with the acyl bromide. The observed rate of disappearance of phenol (k_{obs}) was then always an accurately first-order process.

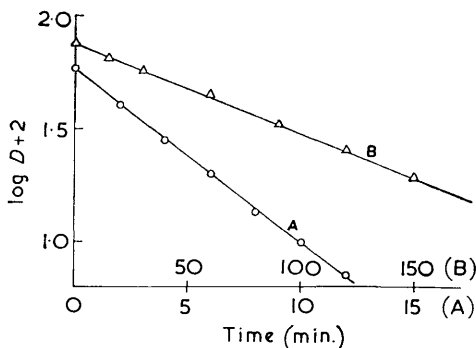


FIG. 1. First-order loss of phenol.

A. 0.540M-Acetyl bromide with 2-naphthol.
B. 0.700M-Isobutyryl bromide plus 0.11 M-saline bromide with 2-naphthol.

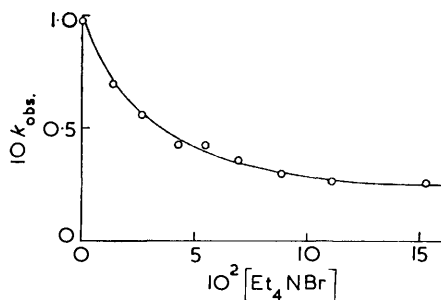


FIG. 2. Effect of added saline bromide. $[\text{AcBr}] = 0.270\text{M}$.

Fig. 1 contains typical plots. The first-order dependence on acyl bromide is illustrated in Table 1. These two results follow the pattern shown by acetyl chloride in nitromethane.¹

TABLE 1.

Acylation of 2-naphthol by acetyl bromide in acetonitrile at 25°; order in acetyl bromide.

k_{obs} = observed first-order rate constant (min.^{-1}) in all Tables; * $[\text{2-naphthol}]_{\text{initial}} \approx 10^{-2}\text{M}$.							
[AcBr]	$10k_{\text{obs}}$	[AcBr]	$10k_{\text{obs}}$	[AcBr]	$10k_{\text{obs}}$	[AcBr]	$10k_{\text{obs}}$
(i) Unrepressed reaction.				(ii) Repressed reaction ($[\text{Et}_4\text{NBr}] = 0.14\text{M}$).			
0.135	0.49	0.338	1.16	0.202	0.18	0.405	0.37
0.203	0.73	0.405	1.42	0.270	0.26	0.540	0.52
0.270	0.98	0.540	1.84				

* Values of k_{obs} were reproducible within $\pm 3\%$.

* Part XII, *J.*, 1963, 3002.

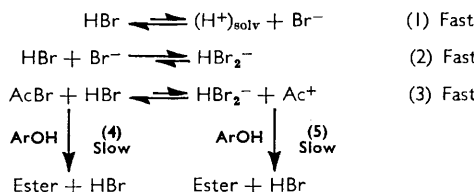
¹ Part IX, *J.*, 1953, 558.

The addition of saline bromide reduces the observed rate (Table 2) and the addition of enough reduces it to an approximately constant value (the "repressed rate"). This effect is shown in Fig. 2. The repressed rate also shows first-order dependence on acetyl bromide concentrations (Table 1).

TABLE 2.
Effect of added tetraethylammonium bromide at 25°.
[2-Naphthol]_{initial} ≈ 10⁻²M.

(i) Acetyl bromide ([AcBr] = 0.270M)				(ii) Isobutyryl bromide ([Bu ^t Br] = 0.700M)	
10 ² [Et ₄ NBr]	10k _{obs}	10 ² [Et ₄ NBr]	10k _{obs}	10 ² [Et ₄ NBr]	10k _{obs}
0	0.98	5.49	0.43	0	0.33
1.34	0.70	6.95	0.36	11.1	0.081
2.68	0.56	8.90	0.30	15.3	0.081
4.32	0.43	11.1	0.27		
		15.3	0.26		

Outline Mechanism.—To explain similar data for the reaction of acetyl chloride in nitromethane we suggested¹ the following mechanism (here expressed in terms of Br rather than Cl).

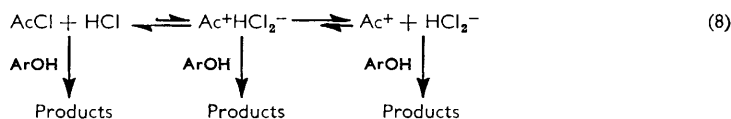


In this scheme ArOH represents the phenol. The existence of the species HBr₂⁻ is well established.² Indeed, values for the equilibrium constants for steps (1) and (2) have been proposed for acetonitrile solution.³ The present Paper is, however, one of the first to cast HBr₂⁻ in a catalytic framework. The mechanism leads to the following rate equation:

$$\begin{aligned}
 -d[\text{ArOH}]/dt &= \{k_4[\text{AcBr}] + k_5[\text{Ac}^+]\}[\text{AcOH}] \\
 &= \{k_4 + k_5K_3(K_1K_2)^{-1}\}[\text{AcBr}][\text{ArOH}] \quad (7)
 \end{aligned}$$

When sufficient saline bromide is added, effectively all the free hydrogen bromide is removed (as HBr₂⁻) and so step (5) is removed. Step (4) then provides a constant contribution at constant acyl bromide concentration, as found. This repressed rate would be expected [from (7)] to be of first order in acyl halide, again as found.

For the chloride system in nitromethane this basic scheme was tentatively elaborated to include the ion-pair Ac⁺HCl₂⁻, the concentration of which increases with the hydrogen halide concentration, and which contributes slightly to the reaction:



This provided an explanation of the additional catalysis [over and above that involved¹ in eqn. (8) with the ion-pair omitted] by hydrogen chloride in nitromethane. We return to the question of ion-pair participation below, but note here that for the present systems we have been unable to study catalysis by added hydrogen bromide because it (as does hydrogen chloride) produces colourless, crystalline precipitates when present in acetonitrile in appreciable quantities. (Mineral acids are unstable in acetonitrile.)³ Presumably the

² Kaufer and Kunz, *Ber.*, 1909, **42**, 385; Tuck and Woodhouse, *Proc. Chem. Soc.*, 1963, 53.

³ Kolthoff, Bruckenstein, and Chantooni, *J. Amer. Chem. Soc.*, 1961, **83**, 3927.

hydrogen bromide formed during the acylation also reacts with the medium, but apparently not sufficiently to disturb the requirements of the mechanism.¹

While the suggested mechanism provides a qualitative explanation of the effects produced by added saline bromide, the exact effects must depend on the values of K_1 and K_2 . The published values³ for K_1 and K_2 imply (for the possible concentration ranges for $[\text{HBr}]_{\text{stoich}}$ in the reaction mixtures, *i.e.*, *ca.* 10^{-4} to *ca.* 10^{-2}M) a very rapid reduction in the $[\text{HBr}]/[\text{HBr}_2^-]$ ratio as bromide is added, even when the incomplete dissociation of the salt³ is taken into account. Consequently a very sudden drop in the rate to the repressed value would be expected [see eqn. (3)]. Our previous results in nitromethane were compatible with such a picture.¹ The fuller results now obtained in acetonitrile are not. There seem two possible explanations: (i) the proposed mechanism needs modification, and (ii) the reported values for K_1 and K_2 are in error. We believe both explanations may be relevant. We deal with (ii) first.

Kolthoff, Bruckenstein, and Chantoonis's equations³ show that it is possible to calculate values of K_2 (called K_{AHA^-} in their Paper) without recourse to either the graphical method they employ or to the limiting condition that $1 \ll [\text{HBr}]K_2$ which this method requires. By using their eqn. (7) and sets of data from their Table II in pairs, values of K_2 can be computed. However, sensible answers are not obtained from the data they quote for hydrogen bromide (K_2 usually appears negative). Furthermore, the condition $1 \ll [\text{HBr}]K_2$ is actually violated in their plot (see their Fig. 2) if the value for K_2 they quote is correct! We conclude that their value for K_2 (and consequently for K_1 also) cannot be relied on. Nevertheless it is a condition of our analysis that the stationary¹ bromide ion concentration is very small in the absence of added salt. The addition of a rather small amount of salt would therefore be expected materially to affect this concentration, and hence the ratio $[\text{HBr}]/[\text{HBr}_2^-]$. We attribute the absence of the implied sudden effect on the rate to the intervention of equilibria like (9), wherein M^+ represents Et_4N^+ , which produce some acylium ions. These equilibria will be most important at low salt concentrations.



As the stoichiometric salt concentration rises the ratio $[\text{M}^+\text{Cl}^-]/[\text{M}^+]$ will rise also (because of incomplete dissociation) and the contribution from this effect could thus become negligible compared with that from route (4), leaving the constant value for k_{obs} found at high salt concentrations.

Structural Changes in the Reactants.—(i) If the mechanism is correct, a reduction in rate on moving from acetyl to isobutyryl bromide would be expected on both polar and steric grounds. [Reaction (4) will be impeded by sufficient chain branching and by electron donation to the carbonyl carbon atom; and route (5) will certainly involve a less reactive acylium ion for the butyryl case, with steric effects possibly also intruding even here.] That isobutyryl bromide acylates 2-naphthol about eight times more slowly than does acetyl bromide, both in the repressed and the unrepressed regions, is therefore a result in the right direction (Tables 1 and 2). However, if the mechanism is correct, the fact that the magnitudes of the rate repressions for the two bromides are very similar implies a nice balance between the change in the extent of ionisation on the one hand and that in the relative reactivities of the reactive entities on the other.

(ii) A change from 2-naphthol to *p*-methoxyphenol produces an increase in rate (Table 3). And the rate repression by salt is changed from a factor of *ca.* 3.4 to one of *ca.* 2.4. The suggested mechanism being assumed these data imply (a) that *p*-methoxyphenol is the more nucleophilic species, and (b) that the change in structure is more effective in increasing the rate when reaction with free Ac^+ ions is not involved. Since both these implications are sensible, the results support the mechanism.

Activation Energies.—The data in Table 3 are limited in extent but two semi-quantitative results emerge: (a) the activation energy is not very dependent on the phenol used, and (b) it is surprisingly similar (for both phenols) for both the repressed and the unrepressed

TABLE 3.

Effect of temperature on the rate of acylation.

2-Naphthol reaction.

[2-Naphthol]_{initial} $\approx 10^{-2}$ M; [AcBr] = 0.270M.

(i) Unrepressed rates.

T (°C)	10 ^k _{obs}
0.0	0.12
25.1	0.98
34.5	1.57

$E = 12.5$ kcal.*

(ii) Repressed rates ([Et₄NBr] = 0.153M).

T (°C)	10 ^k _{obs}
0.0	0.036
25.1	0.26
34.5	0.47

$E = 12.8$ kcal.*

p-Methoxyphenol reaction.[*p*-MeO·C₆H₄·OH]_{initial} $\approx 10^{-2}$ M; [AcBr] = 0.270M.

(i) Unrepressed rates.

T (°C)	10 ^k _{obs}
0.0	0.43
25.1	2.61

$E = 12.0$ kcal.

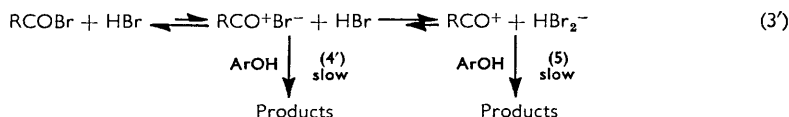
(ii) Repressed rates ([Et₄NBr] = 0.153M).

T (°C)	10 ^k _{obs}
0.0	0.17
25.1	1.13

$E = 12.5$ kcal.

* The activation energy E was calculated from the slope of the best straight line through the points in an Arrhenius plot. The value of E is, in fact, probably somewhat temperature-dependent. However, the essential independence of temperature of the rate repression is to be noted.

reactions. Result (a) is compatible with our mechanism. In fact, *p*-methoxyphenol does provide somewhat smaller activation energies, in accord with its expected greater nucleophilicity and its slightly faster rate of reaction. Result (b), however, is less compatible with the mechanism suggested, for it calls for a fortuitous and rather exact numerical balance between on the one hand the activation energy for step (4) and on the other the activation energy for step (5) [expected to be *appreciably* lower than for (4)] coupled with the heat of reaction for equilibrium (3). As noted above, the virtual identity of the rate repressions for the acetyl and butyryl compounds also calls for a similar fortuitous balance. These implied balances are difficult to accept. Although they are the only results which cast doubt on the mechanism as outlined so far, we nevertheless consider that all the facts are better explained by the following slightly modified scheme:



[The species $\text{RCO}^+\text{HBr}_2^-$ may also be involved at high hydrogen halide concentrations (see p. 3725).] In this scheme acylation by un-ionised acyl halide is unimportant, and predominant attack on the phenol is by the ion-pair and the free ions. If the assumption is made that the positions of the various equilibria (3') are little dependent on temperature (and this is quite possible since the values of ΔH for ionisation of weak electrolytes can be close to zero^{4*}) then the fact that the observed activation energies for the repressed (4') and unrepressed [mainly (5)] routes are so similar is perfectly understandable: the active species changes but little.

The similarities noted between the behaviour of acetyl and butyryl bromides can be explained along the same lines.

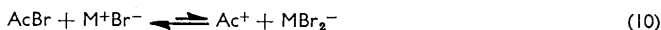
Two Final Matters.—(i) The absence of detectable positive catalysis by added salt at

* Conductivity data⁵ also show that the dissociation constants of salt-like substances in acetonitrile vary little over the temperature ranges here considered.

⁴ Harned and Owen, "The Physical Chemistry of Electrolyte Solutions," Reinhold Publishing Co., New York, 1958.

⁵ Walden and Birr, *Z. physik. Chem.*, 1929, **144**, 269.

the highest salt concentrations suggests that the formation of ionic multiplets, which could promote acylium ion formation *via* processes like (10), is of little consequence in acetonitrile at the concentrations studied.



(ii) Concerning predictions of the effect of addition of saline chloride (rather than bromide), our mechanism implies the possibility of rapid halogen exchange. Provided that equilibrium (11) is favourable to at least some acyl chloride formation, then since acyl



chlorides react less rapidly than the corresponding bromides, and because free saline bromide will also be formed with the acyl chloride, a reduction in rate is to be expected on

TABLE 4.

Effect of saline chloride on the reaction of acetyl bromide at 25°.

	[2-Naphthol] _{initial} ≈ 10 ⁻² M; [AcBr] = 0.270M.		
[Et ₄ NCl]	0	0.095	0.142
10 <i>k</i> _{obs}	0.98	0.23	0.14
(For 0.27M-acetyl chloride alone 10 <i>k</i> _{obs} ≈ 0.01 at 25°.)			

at least two counts. Data in Table 4 illustrate this effect, and provide further circumstantial support for the scheme outlined.

EXPERIMENTAL

Materials and Reaction Stoichiometry.—Acetonitrile was shaken with aqueous potassium hydroxide, dried, and fractionally distilled from either phosphoric oxide or calcium hydride. A cut of b. p. 81.5—81.6° was taken, and stored in a dry atmosphere. Different batches gave essentially identical kinetic data. Acetyl bromide, distilled from isoquinoline, had b. p. 81°. Isobutyryl bromide, fractionally distilled under nitrogen, had b. p. 116.5—117.5°. Tetraethylammonium bromide was recrystallised from ether–alcohol and dried (*in vacuo*) to constant weight; halide analysis indicated a purity of 99.8%. The corresponding chloride, recrystallised from ether–alcohol–chloroform and treated similarly, was 99.5% pure. 2-Naphthol was recrystallised, m. p. 123°. *p*-Methoxyphenol, prepared by the action of dimethyl sulphate in hydroquinone, distilled at 243° and, after recrystallisation from water, had m. p. 54°. 2-Naphthyl acetate and isobutyrate and *p*-methoxyphenyl acetate were prepared under conditions which simulated those obtaining in the kinetic experiments. They were obtained in good yield (>85%) and after recrystallisation had m. p.s 71, 43, and 31°, respectively.

Kinetic Arrangements.—Reaction mixtures were made up from solvent, acyl bromide, and salt (where appropriate) in 10 ml. volumetric flasks and the flasks and contents brought to the required temperature in a thermostat bath. After a further period (usually *ca.* 30 mins.) the reaction was started by addition of the solid phenol (*ca.* 10⁻²M) and sampling begun. With acyl bromide always in a ten-fold excess over phenol, the loss of phenol proved accurately of first order over at least three half-lives (Fig. 1). The object of leaving the acyl bromide in contact with the solvent before the initiation of the main reaction was to ensure the acylation of the majority of any residual water present in the solvent. The water content was not known accurately, but was probably appreciably less than 10⁻²M. Its effect on the stoichiometric acyl halide concentration was thus negligible. The existence of some (any quantity) of free hydrogen bromide in the system is an important prerequisite of the proposed mechanism (see p. 3725).

The sampling process consisted of running aliquot portions into sufficient glacial acetic acid effectively to quench the reaction and to provide solutions with suitable optical densities (*D*). Loss of naphthol was followed by noting the fall in absorption at 3300 Å. With *p*-methoxyphenol measurements were made at 2910 Å. The ester products absorb only slightly at these wavelengths, but when necessary allowance was made. The spectra always eventually (after 10 half-lives) assumed forms close to those expected on the basis of synthetic product mixtures. This is further evidence that the reactions proceed cleanly and in high yield.