Alkali-metal Ion Catalysis and Inhibition of Acetyl Transfer from *p*-Nitroaryl Acetates to Hexanoate Ion

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Deacetylation of 2-acetoxy-5-nitro-1,3-xylylene-18-crown-5 (21-acetoxy-18-nitro-2,5,8,11,14-pentaoxa[18]metacyclophane) by hexanoate ion in DMF is strongly inhibited by Li^+ ion, slightly retarded by Na^+ ion, and significantly promoted by the larger alkali-metal ions. In contrast, the analogous reaction of the simple model *p*-nitrophenyl acetate is inhibited by all of the alkali-metal ions. These effects are discussed in terms of differential binding of metal ions to reactants and transition states. In line with conclusions from previous works, it is confirmed that coordinative binding of metal ions with the oxygen donors of the polyether bridge of the crown-ether substrate is an effective force for catalysis.

Coordinative interactions with hard donor atoms, such as the ether oxygens of crown ethers, and electrostatic interactions with negatively charged groups provide two basic modes for binding hard metal ions. Clearly, enhanced stability of metal complexes is found with multidentate ligands bearing a negatively charged group, in which the two modes act synergically.

These concepts have focused our interest on reacting systems, such as 2-X-substituted 1,3-xylylene-crown ethers, where the neutral electrophilic group X undergoes attack by a negatively charged nucleophile Y^- [eqn. (1)]. The transition state TS can be viewed as a negatively charged macrocyclic ligand which can bind ions more strongly than do the reactants. Our previous works in this field[1-6] have shown that alkali- and alkaline-earth-metal ions can act as efficient catalysts of methyl and acetyl transfer reactions (X = OMe and OAc, respectively). It was concluded that coordinative binding of metal ions to the crown ether bridges is an effective force for catalysis.

In the present work we assess the ability of added alkali-metal salts to act as catalysts or inhibitors for the acetyl transfer reaction from 2-AcO-5-NO_2-18C5 to tetramethylammonium hexanoate in dimethylformamide (DMF) at 25 °C [eqn. (2)].

The corresponding reaction of the simple model compound *p*-nitrophenyl acetate (*p*NPOAc) was also investigated for comparison purposes [eqn. (3)]. The results are discussed in terms of differential binding of metal ions to transition states and reactants.

Results

Deacylation of the *p*-nitroarylacetates was carried out by treating very dilute substrate solutions (*ca.* 0.01 mmol dm^{-3}) with an excess of tetramethylammonium hexanoate (*ca.* 1 mmol dm^{-3}), either in the absence or presence of alkali-metal ions. The nucleophile was generated *in situ* by partial neutralisation of hexanoic acid with a calculated amount of a freshly prepared stock solution of tetramethylammonium hydroxide in DMF.

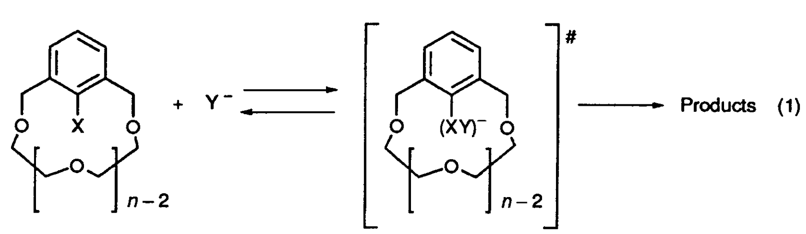
Table 1 Influence of alkali-metal salts on the rate of acetyl transfer from *p*-NPOAc to hexanoate ion in DMF at 25.0 °C[a]

Salt	c_{salt}/mol dm^{-3}	k_{obs}/dm^3 mol^{-1} s^{-1} [b]
$LiClO_4$	1.00×10^{-3}	0.456
$NaClO_4$	1.01×10^{-3}	0.565
	3.18×10^{-3}	0.255
	1.00×10^{-2}	0.109
$KClO_4$	1.01×10^{-3}	0.893
	3.16×10^{-3}	0.657
	1.01×10^{-2}	0.477
RbBr	9.84×10^{-4}	0.936
	3.15×10^{-3}	0.797
	9.40×10^{-3}	0.583
$CsClO_4$	2.48×10^{-3}	0.796
	1.00×10^{-2}	0.540

[a] k_0 = 1.06 dm^3 mol^{-1} s^{-1}. [b] Mean errors of the order of ± 4%.

Tetramethylammonium was chosen as the reference counterion since tetraalkylammonium ions do not associate to an appreciable extent with alkanoates in DMF.[7] Sources of alkali-metal ions were the perchlorate salts, with the sole exception of Rb^+ which was added as the bromide. The influence of added alkali-metal salts was investigated over a wide concentration range, whose upper limit in the case of K^+ and Rb^+ ions was imposed by the limited solubility of their salts. Hexanoate ion was the reactant of choice instead of the simpler acetate ion, in order to avoid any possible complication arising from the low solubility of alkali-metal acetates, notably CH_3CO_2K, in DMF solution.

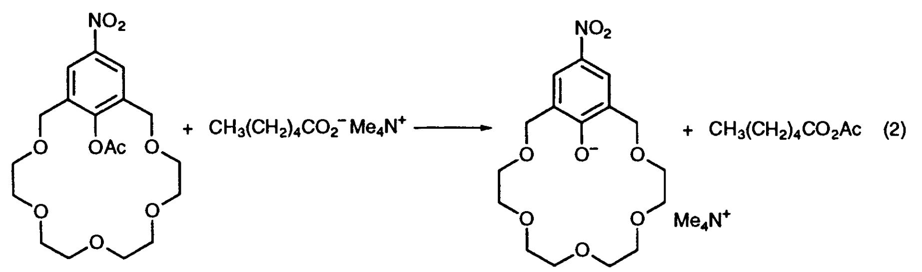
The kinetics were followed spectrophotometrically by monitoring the liberation of the *p*-nitroaryloxide ions in the



(1)

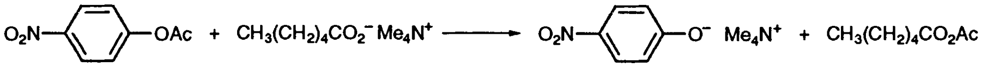
2-X-3(*n*+1)C*n*

TS



(2)

2-AcO-5-NO$_2$-18C5



(3)

*p*NPOAc

Table 2 Influence of alkali-metal salts on the rate of acetyl transfer from 2-AcO-5-NO$_2$-18C5 to hexanoate ion in DMF at 25.0 °C[a]

Salt	c_{salt}/mol dm^{-3}	k_{obs}/dm^3 mol^{-1} s^{-1} [b]
LiClO$_4$	2.02×10^{-4}	7.53×10^{-2}
	3.94×10^{-4}	6.55×10^{-2}
	7.95×10^{-4}	4.70×10^{-2}
NaClO$_4$	2.03×10^{-4}	8.98×10^{-2}
	6.31×10^{-4}	7.71×10^{-2}
	1.02×10^{-3}	7.14×10^{-2}
	2.50×10^{-3}	7.30×10^{-2}
	6.31×10^{-3}	7.13×10^{-2}
	1.59×10^{-2}	6.10×10^{-2}
	3.96×10^{-2}	5.61×10^{-2}
	0.100	5.45×10^{-2}
KClO$_4$	2.02×10^{-4}	0.141
	1.01×10^{-3}	0.284
	1.78×10^{-3}	0.390
	3.16×10^{-3}	0.553
	5.62×10^{-3}	0.755
	1.00×10^{-2}	0.968
RbBr	9.96×10^{-4}	0.209
	1.99×10^{-3}	0.289
	4.23×10^{-3}	0.423
	9.40×10^{-3}	0.575
CsClO$_4$	1.00×10^{-3}	0.144
	2.51×10^{-3}	0.200
	6.31×10^{-3}	0.257
	1.58×10^{-2}	0.273
	3.98×10^{-2}	0.233
	0.100	0.158

[a] $k_o = 8.60 \times 10^{-2}$ dm^3 mol^{-1} s^{-1}. [b] Mean errors of the order of ± 4%.

415–440 nm interval. Clean first-order behaviour was observed in all cases, with stable and reproducible infinity readings strictly corresponding to virtually complete reaction. Thus, deacylation of the *p*-nitroaryl acetates occurred smoothly and quantitatively under the conditions of our kinetic measurements, showing the insignificance of reacylation of the liberated *p*-nitroaryloxides by the mixed anhydride.

Pseudo-first-order rate constants measured in the presence of added salts were translated into second-order rate constants k_{obs}. The corresponding quantities k_o measured in the absence of added salts, *i.e.*, when Me_4N^+ is the sole counterion present, provide good reference values for a quantitative measure of metal-ion effects on rates. The variation of k_{obs} with the concentration of alkali-metal salts is shown in Tables 1 and 2. log plots of k_{obs}/k_o *vs.* concentration of added salt are given in Figs. 1 and 2, respectively.

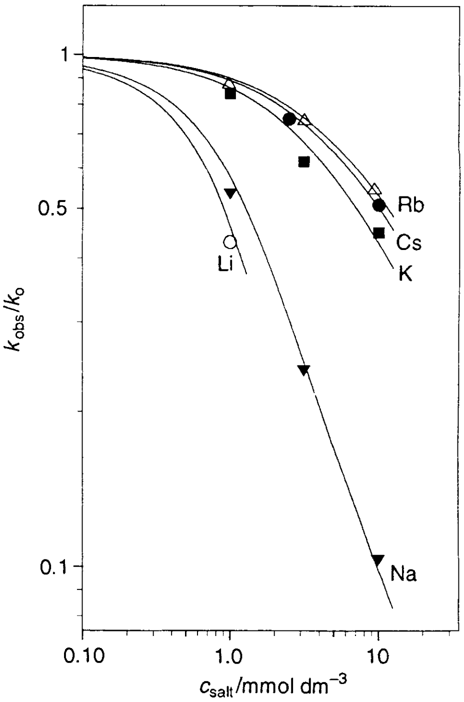


Fig. 1 Influence of alkali-metal salts on the rate of acetyl transfer from *p*-NPOAc to hexanoate ion in DMF at 25 °C [the curve for Li$^+$ is calculated according to eqn. (8) with the K_{ip} value obtained from analysis of rate data of 2-AcO-5-NO$_2$-18C5; the point is experimental]

The magnitude of metal-ion effects on deacylation rates is not only a marked function of cation concentration and nature, but also of substrate identity. With the model compound *p*NPOAc, all of the metal ions are rate depressing to extents increasing on increasing salt concentration, and decreasing on increasing cation size (Fig. 1). Since extensive ion pairing is known[7] to take place between alkali-metal ions and alkanoates in DMF in the order Li$^+$ > Na$^+$ > K$^+$ > Cs$^+$,* it seems logical to ascribe the rate depressing effects observed in the deacylation of *p*NPOAc to the formation of cation–alkanoate pairs which are less reactive than free alkanoate.

In contrast with the monotonic rate depressing effects of all

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* A reversal in the Li$^+$/Na$^+$ order, namely Na$^+$ > Li$^+$, occurs with less basic carboxylates, such as 3-bromopropanoate and benzoate (see refs. 7 and 8, respectively).

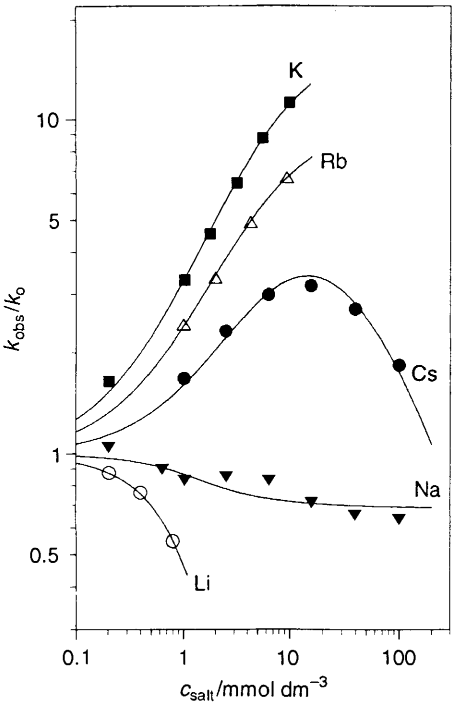

Fig. 2 Influence of alkali-metal salts on the rate of acetyl transfer from 2-AcO-5-NO$_2$-18C5 to hexanoate ion in DMF at 25 °C

of the alkali-metal ions in the reaction of *p*NPOAc, a highly structured reactivity picture is seen in the reactions of the crown-ether substrate 2-AcO-5-NO$_2$-18C5 (Fig. 2). The magnitude of the rate-retarding effect of Li$^+$ ion is the same as that observed in the corresponding reaction of *p*NPOAc. With Na$^+$ ion a slight rate retardation is found, that amounts to a reactivity decrease of about $\frac{1}{3}$ upon variation of the metal-ion concentration of nearly three orders of magnitude. Significant rate enhancements are observed with the larger metal ions. A monotonic reactivity increase with increasing metal ion concentration is seen in the K$^+$ and Rb$^+$ reactions, with a definite tendency to saturation, that is even more evident in plots of k_{obs}/k_o *vs.* c_{salt} (not shown here). A rate maximum is present in the concentration–rate profile of the Cs$^+$ reaction. This behaviour, which is well precedented in deacylations of 2-acetoxy-1,3-xylylene crown ethers,[1,2] can be taken with confidence as indicative of significant associations of the metal ion with both reactants.

Treatment of Rate Data.—The variation of rate constants with added salt concentration was treated according to the standard binding isotherm,[9] eqn. (4), that is derived from transition-state theory and expresses catalysis or inhibition by

$$k_{obs}/k_o = \frac{1 + K_{T^\#}\gamma^2[M^+]}{(1 + K_S[M^+])(1 + K_{ip}\gamma^2[M^+])} \qquad (4)$$

metal ions in terms of associations of 1:1 stoichiometry with reactants * and transition state.[1,2] Since the salts used as sources of alkali-metal ions behave as strong electrolytes in DMF solution,[10] the quantity [M$^+$] appearing in eqn. (4) was taken as the analytical concentration of added salt c_{salt}, corrected for the amount of metal ion sequestered by the hexanoate ion (see the Experimental section). Thus eqn. (4) relates the observable quantities k_{obs}/k_o to the total concentration of added salt by means of a relation that contains three unknown quantities. The equilibrium constants K_S and K_{ip} for association of metal ions with the ester substrate and with hexanoate, defined in eqns. (5) and (6), respectively, can either be obtained from independent measurements or treated as adjustable parameters in a standard curve-fitting procedure. On the other hand, the third quantity $K_{T\#}$, which has the meaning of the formal conversion of the transition state T$^\#$ which does not contain M$^+$ into one which does contain M$^+$ [eqn. (7)], can be obviously obtained

$$\mathrm{ArOAc} + \mathrm{M}^+ \overset{K_S}{\rightleftharpoons} \mathrm{ArOAc{\cdot}M}^+ \qquad (5)$$

$$\mathrm{CH_3(CH_2)_4CO_2^-} + \mathrm{M}^+ \overset{K_{ip}}{\rightleftharpoons} \mathrm{CH_3(CH_2)_4CO_2^-{\cdot}M^+} \qquad (6)$$

$$\mathrm{T}^\# + \mathrm{M}^+ \overset{K_T\#}{\rightleftharpoons} \mathrm{T^\#{\cdot}M^+} \qquad (7)$$

from the kinetics only. The mean activity coefficient γ can be calculated as before[7] according to the extended Debye–Hückel equation $\log \gamma = -1.59\,\mu^{\frac{1}{2}}/(1 + 2.88\mu^{\frac{1}{2}})$, which corresponds to a value of 36.71 for the relative permittivity of DMF and of 6 Å for the Bjerrum distance.

Treatment of rate data related to the model compound *p*NPOAc required the use of a simplified form of eqn. (4) since any association of *p*NPOAc with alkali-metal ions is unlikely. We found that the simple eqn. (8) with the best-fit equilibrium

$$k_{obs}/k_o = \frac{1}{1 + K_{ip}\gamma^2[M^+]} \qquad (8)$$

parameters K_{ip} listed in Table 3 adequately describes the variation of k_{obs} with metal-ion concentration, which means that the contribution to the overall rate of the metal-ion assisted path is negligibly small, *i.e.*, $K_{T\#}\gamma^2[M^+] \ll 1$ for all the metal ions in the investigated concentration ranges. This is tantamount to saying that the rate depression on addition of alkali-metal salts reflects, within the precision of the data, the decrease in free hexanoate concentration caused by the mass-law effect exerted by increasing amounts of metal ions in solution, the cation–alkanoate pairs being in all cases totally unreactive.

Application of the general eqn. (4) to the reactions of 2-AcO-5-NO$_2$-18C5 is less straightforward, in view of the well known adaptability of equations containing many adjustable parameters. Therefore, independent evidence for association of alkali-metal ions with the crown-ether substrate was sought. In MeOH solution[2] K_S (dm^3 mol^{-1}) for binding of metal ions to 2-AcO-18C5 is negligibly small for Li$^+$, but is 51 for Na$^+$, 1,800 for K$^+$, 2,200 for Rb$^+$ and 1,700 for Cs$^+$. However, equilibrium constants for complexation of alkali-metal ions by crown-ether hosts are one to two orders of magnitude smaller in DMF than in MeOH.[11] Thus, the existence of substrate–cation complexes of definite stability can be ruled out for Li$^+$, is unlikely for Na$^+$, but is still conceivable for the larger metal ions. Clear-cut evidence for association with Cs$^+$ was obtained by means of UV spectroscopy. Addition of increasing amounts of CsClO$_4$ to a solution of 2-AcO-5-NO$_2$-18C5 caused small, but reproducible absorbance changes (Fig. 3) that were consistent with the formation of a 1:1 complex with a K_S value of 50 dm^3 mol^{-1}. No spectral changes were observed upon addition of KClO$_4$ or RbBr, but it should be considered that the limited solubility of these salts prevented investigation of the concentration range above 0.01 mol dm^{-3}, where spectral changes in the Cs$^+$ case became significant. As expected, no

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* The formation of triple ions of the type + − + between Li$^+$ and alkanoate becomes significant at Li$^+$ concentrations much larger than those used in the present work (see ref. 7).

Table 3 Binding of alkali-metal ions to reactants and transition states[a]

Metal ion	log K_{ip}[b]	log $K_{T\#}$
*p*NPOAc		
Li^+	3.5[c]	—
Na^+	3.2	—
K^+	2.4	—
Rb^+	2.2	—
Cs^+	2.3	—
2-AcO-5-NO_2-18C5		
Li^+	3.5	—
Na^+	3.2[d]	3.1
K^+	2.3	3.6
Rb^+	2.4	3.4_5
Cs^+[e]	1.9	3.0

[a] Estimated accuracy in log K is ± 0.1–0.2. [b] log K_{ip} values previously determined (ref. 7) for association with 15-bromopentadecanoate in DMF at 45 °C are as follows: 3.24 (Li^+), 2.98 (Na^+), 1.85 (Cs^+). [c] From analysis of rate data obtained in the reaction of 2-AcO-5-NO_2-18C5. [d] From analysis of rate data obtained in the reaction of *p*NPOAc. [e] log K_S = 1.7 from spectrophotometric measurements.

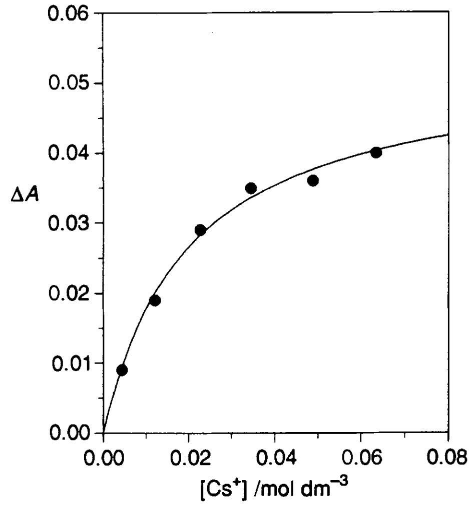


Fig. 3 Spectrophotometric determination of K_S for binding of Cs^+ to 2-AcO-5-NO_2-18C5 in DMF at 25 °C. The curve is calculated by means of eqn. (10), with K_S = 50 dm^3 mol^{-1}.

spectral changes were observed upon addition of $NaClO_4$ up to concentrations in the order of 0.1 mol dm^{-3}.

Treatment of rate data as obtained in the presence of $CsClO_4$ was carried out by means of eqn. (4), which on introduction of the known K_S value of 50 dm^3 mol^{-1} reduces to an equation containing two adjustable parameters only. Consistent with the lack of evidence of significant association of 2-AcO-5-NO_2-18C5 with K^+ and Rb^+ ions, the pertinent rate data were analysed by means of eqn. (9), the form to which eqn. (4) reduces

$$k_{obs}/k_o = \frac{1 + K_{T\#}\gamma^2[M^+]}{1 + K_{ip}\gamma^2[M^+]} \qquad (9)$$

whenever $K_S[M^+]$ is negligible with respect to 1. The same equation was used in the analysis of the data of the Na^+ reaction. A word of caution is appropriate here, as the variation of k_{obs} values is very small. Consequently, there is such a wide range of pairs of values of the parameters showing nearly equal goodness of fit to the data, that the standard curve-fitting procedure where the two unknowns are treated as adjustable parameters is practically meaningless. For this reason, the K_{ip} value determined from the corresponding reaction of *p*NPOAc was introduced into eqn. (9), which is thus reduced to an equation containing $K_{T\#}$ as the sole adjustable parameter. Finally, rate data of the Li^+ reaction could be fit to a good precision to the simple eqn. (8), which clearly indicates that the only productive pathway in this case is that involving unassociated reactants.

The equilibrium constants obtained from analysis of rate data are summarised in Table 3. The overall good quality of the fits shown in Figs. 1 and 2 supports the general validity of our analysis. This is further confirmed by the fact that the two sets of K_{ip} values, whenever independently determined, are not only in fair agreement with each other, but compare well with the K_{ip} values previously determined for binding alkali-metal ions to a long-chain alkanoate ion under closely similar conditions (see footnote *b* to Table 3).

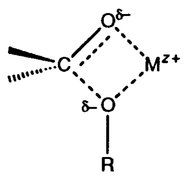
Discussion

Before discussing the influence of the metal ions on the cleavage of the crown ether aryl acetate, we first consider the model reactions of alkali-metal hexanoates with *p*NPOAc, for which contributions from the ion-pair pathway were found to be insignificant in all cases. This finding is seemingly in keeping with the well-known concept that ion pairs are less reactive than free ions,[12] but it should be borne in mind that this rule applies strictly to nucleophilic reactions of S_N2-type only. Less known, yet well documented, is the fact that ion pairs exhibit enhanced reactivity relative to free ions in nucleophilic addition to carbonyl carbon. Thus, alkali- and alkaline-earth-metal alkoxides in solutions of their parent alcohols have been reported to be more reactive than free alkoxides in reactions with aryl acetates.[1–3,13,14] There is also good evidence that Na^+-paired *m*-methoxyphenolate ion is more reactive than free *m*-methoxyphenolate towards *p*NPOAc in CH_3CN solution.[15] It seems likely that metal ions bind more strongly to transition states ($T^{\#}$) than to RO^- because of the occurrence of chelate structures in the ($T^{\#}\cdot M^{z+}$) complexes. The latter presumably have the form of the four-membered contact ion pair **I**, but in protic solvents the six-membered solvent-shared structures **II** and **III** may play a role. Chelate structures of varying nature and geometry have been suggested for the metal-ion-assisted nucleophilic attack of oxygen nucleophiles at sulfonyl[16] and phosphoryl[17] groups.

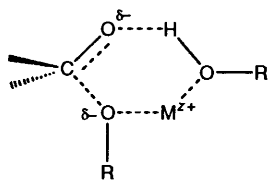
The negligible reactivity of the hexanoate–cation pairs towards *p*NPOAc would thus indicate that stabilization of the transition state by chelation of the metal ions is lacking, in marked contrast with the behaviour of alkoxide- and aryloxide-cation pairs in analogous reactions. It has been suggested that the oxygen–oxygen distance in alkanoate ions is such as to permit a certain degree of chelation with alkali-metal ions,[8] as shown in **IV**, with the possible exception of Li^+ ion, which is too small to interact with both oxygens.[18] On the other hand, in either of the two chelate structures **V** and **VI**, which can be envisaged for the ($T^{\#}\cdot M^+$) complexes, contact between M^+ and the fractional negative charge localized on one of the two carboxylate oxygens is perforce lost. We suggest that the resulting loss of electrostatic interaction is responsible for the lack of stabilization of the transition state by metal ions, and, therefore, for the negligible reactivity of the hexanoate–cation pairs.

Comparison of the rate profiles plotted in Fig. 2 with those in Fig. 1 shows that the polyether bridge of 2-AcO-5-NO_2-18C5 is clearly responsible for a dramatic alteration of the reactivity pattern. The data provide a clear-cut confirmation of the proposal that interaction of metal ions with a polyether bridge proximal to the reaction zone is an effective force for catalysis.

The only metal ion for which such an effect is lacking is Li^+. It seems likely that its largest solvation energy[19] and smallest



I



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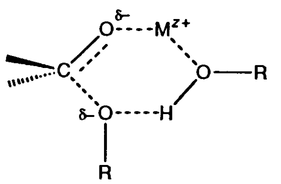
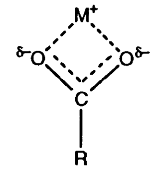
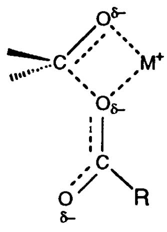


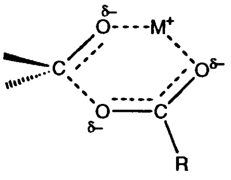
III



IV



V



VI

size are responsible for a negligible affinity with the transition state. On the other hand, the larger metal ions exhibit a significant affinity with the transition state, as quantitatively measured by the log $K_{T\#}$ values listed in Table 3. The data peak at K^+ ion, but selectivity among cations is not very high, probably on account of the high adaptability of the cavity delimited by the functional group undergoing nucleophilic attack and the flexible polyether bridge. It is worth noting that Na^+ is as effective as Cs^+ in binding to the transition state, and not much less effective than K^+ and Rb^+. Yet K^+, Rb^+ and Cs^+ catalyse the reaction, whereas Na^+ acts as a weak inhibitor. This can be ascribed entirely to the stronger binding of the latter to the alkanoate reactant. It appears therefore that selectivity among cations in the metal-ion assisted acetyl transfer from 2-AcO-5-NO_2-18C5 to hexanoate reflects their relative binding ability to hexanoate more than to the transition state.

A final comment is devoted to the question of the microscopic or detailed mechanism of the metal-ion-assisted acetyl transfer reaction. A dualism exists between the ion-pair mechanism, in which a cation paired nucleophile adds to the carbonyl group of a free substrate molecule, and a pre-association mechanism in which a free nucleophile anion reacts with a cation–substrate complex. Discussions aimed at distinguishing between these two possibilities can be found in the recent literature.[16a] Application of the standard methods of classical kinetics to the two mechanisms leads to kinetic equations[14] which are not only operationally indistinguishable from each other, but also from eqn. (4), which is derived from transition state theory and bears no relation to the microscopic mechanism. Our view on this question has been discussed at length in previous papers.[1,2,14] Briefly, we stress again, in line with Hammett's arguments,[20] that, when the reagents are in mobile equilibrium, the question of the microscopic mechanism is irrelevant to any presently observable phenomena. It is clear that for quantitative discussion it suffices to refer to the influence of metal ions on the standard potential of reactants and transition states, *i.e.*, to the quantities listed in Table 3. None of these quantities depends on the detailed mechanism by which the transition state is attained.

Experimental

NMR spectra were recorded in $CDCl_3$ on a Bruker WP-80 spectrometer (*J* values in Hz). UV–VIS measurements were carried out on a Cary 219 spectrophotometer with a thermostatted cell compartment.

Materials.—*N*,*N*-Dimethylformamide (Carlo Erba) was stirred for 24 h over anhydrous copper(II) sulfate, filtered, distilled from fresh anhydrous copper(II) sulfate at reduced pressure (b.p. 60–62 °C at 40 mmHg), thoroughly purged with argon and stored in an automatic burette under argon. The alkali-metal perchlorates and RbBr were of analytical reagent grade and were kept under vacuum. Hexanoic acid (Aldrich) and *p*-nitrophenyl acetate (Fluka) were used without further purification. 2-AcO-5-NO_2-18C5 was prepared by acetylation of the parent phenol[21] (m.p. 89.5–91.0 °C, lit.,[21] 91.0–91.5 °C) with EtOTl–AcCl.[2] Purification was carried out by flash chromatography on acid-washed silica gel (230–400 mesh) using petroleum ether (b.p. 40–70 °C)–chloroform (1:1 v/v) as the eluent; δ_H 8.25 (2 H, s, ArH), 4.26–4.90 (4 H, AB system, *J* 12, $ArCH_2$), 3.36–3.84 (16 H, m, OCH_2CH_2O), 2.43 (3 H, s, $COCH_3$) (Found: C, 54.7; H, 6.5; N, 3.2. $C_{18}H_{25}NO_9$ requires C, 54.1; H, 6.3; N, 3.5). Stock solutions of the base (0.05 mol dm^{-3}) were freshly prepared by dilution with DMF of commercial tetramethylammonium hydroxide (25% methanol solution, Janssen). The assumption is made that the extremely low methanol content (0.05%) of the solutions used in the kinetic runs does not appreciably alter the properties of pure DMF.

Rate Measurements.—Solutions were freshly prepared and handled under argon to prevent contamination by atmospheric carbon dioxide.

In the quantitative analysis of rate data, when association of the metal ion with the anionic nucleophile is taken into account, the concentration of free metal ion is given by the following equation:[14]

$$[M^+] = \{-J + [(J^2 + 4K_{ip}c_{salt})]^{\frac{1}{2}}\}/2K_{ip}$$

In this equation $J = 1 + K_{ip}\ (c_{Nu} - c_{salt})$, where c_{Nu} is the analytical concentration of the hexanoate nucleophile. Association of the metal ion with the anionic reactant was analogously taken into account when the ionic strength μ was calculated. Full expressions of $[M^+]$ and γ were introduced into the equations used for fitting of rate data.

Equilibrium Measurements.—Spectrophotometric determination of K_S for binding of Cs^+ ion to 2-AcO-5-NO_2-18C5 was carried out as previously described.[22] The data were fitted by means of a non-linear least-squares procedure to eqn. (10),

$$\Delta A = \frac{(\Delta A)_\infty K_S [M^+]}{1 + K_S [M^+]} \qquad (10)$$

where ΔA is the absorbance change measured at $\lambda = 300$ nm at a given metal ion concentration, and the subscript ∞ refers to substrate fully complexed by M^+. The quantities $(\Delta A)_\infty$ and K_S were treated as adjustable parameters.

Computational Details.—Non-linear least-squares calculations were carried out by means of the program SIGMA PLOT 2.0 (Jandel Scientific).

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