The Effects of Ion-pairing on the Rates of Fragmentation of Alkali-metal Salts of Tertiary Alcohols

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The lithium, sodium, and potassium salts of 1,2,3-triphenylpropan-2-ol (**1**) decompose in DMSO solution at convenient rates yielding deoxybenzoin and toluene. Under conditions of excess of base, deoxybenzoin is rapidly converted into its enolate, whose u.v. absorption permits spectroscopic rate determinations. Following expectations from earlier work, rates for (**1**) are in the order 1:122:1 330 for the lithium, sodium, and potassium salts. The effects of added cryptands and common ion metal iodide have been studied and are shown to be consistent with an earlier proposed reaction scheme involving differential reactivity of associated and 'free' alkoxide anions. Use of cryptands has allowed estimate of the rate of decomposition of the unassociated alkoxide of (**1**), $8.5 \times 10^3\ s^{-1}$ at 18.6°, and this is at least 100-fold faster than its ion-pair with potassium. Reactions are strongly inhibited by added iodides and again, this is shown to be consistent with the reaction scheme. The salts of 3-methyl-1,2,3-triphenylbutan-2-ol (**2**) have also been studied. Under similar conditions these are 10^3 times more reactive than those of (**1**), fragmenting to deoxybenzoin and cumene. Steric inhibition of ion-pairing and steric enhancement of reactivity of the free alkoxide both contribute to the observed reactivity. Steric effects alone appear to be responsible for the regioselectivity of its fragmentation.

Alkoxide solution reactions almost always also show dependence on the nature of the inevitable countercation.[1] These effects have been noted in intermolecular reactions with alkoxides exhibiting both nucleophilic[2] and basic[3] behaviour patterns, but are most dramatically displayed in the intramolecular processes exemplified in Figure 1.

Alkali-metal salts of tertiary alcohols may fragment yielding ketone and hydrocarbon, a reaction course rationalised as collapse of the alkoxide to ketone, with expulsion of a carbanion, commonly benzylic, which is subsequently protonated.[4] Both steric course, and facility of this anionic cleavage, depend strongly on solvent and metallic counterion, with rates of cleavage increasing by 3—4 orders of magnitude on changing from Li^+ to K^+. Similar dependence has also been found in alkoxide rearrangements, including anionically accelerated pericyclic processes exemplified by the anionic oxy-Cope reaction,[5] and in hydride shifts from alkoxide methine to carbonyl carbon.[6,7] In all examples, formal collapse of the alkoxide anion to carbonyl yields a strongly basic leaving group, to be trapped either intermolecularly by solvent, or intramolecularly, probably with bond formation and cleavage being concerted.

The cation dependences, Cram suggested,[4] could be formally treated in terms of differential reactivity of alkoxide ions in their 'free' and various associated forms. In organic solvents, the alkoxides would exist largely as unreactive ion-pairs, in equilibrium with more reactive dissociated anions. The stereochemical course of alkoxide fragmentations demanded recognition of both intimate and solvent-separated ion-pairs, but a simplified scheme, basically that of Acree,[8] accomodates the kinetic behaviour, at least qualitatively.

$$RO^- + M^+ \overset{K_{ip}}{\rightleftharpoons} ROM \qquad (1)$$

$$RO^- \xrightarrow{k_i} P \qquad (2)$$

$$ROM \xrightarrow{k_p} P \qquad (3)$$

Scheme 1.

Scheme 1 leads to relationship (4) for reaction velocity in terms of reactivity of free ion (k_i), the ion-pair (k_p) and the ion-pairing constant (K_{ip}). In a given solvent, the ion-pairing

$$v = \{(k_i + k_pK_{ip}[M^+])/(1 + K_{ip}[M^+])\}[ROH_{tot}] \qquad (4)$$
$$\text{where } [ROH_{tot}] = [RO^-] + [ROH]$$

constant will depend on the cation, as will the reactivity of the ion-pairs. The reactivity of free ions, should be cation-independent, and larger than that of associated species. At one extreme, with K_{ip} very large and $k_i \gg k_p$ the relationship simplifies to (5), so that observed reactivity ratios simply reflect differences

$$\begin{aligned} v &= \{k_1/(1 + K_{ip}[M^+])\}[ROH_{tot}] \\ &\sim \{k_1/(K_{ip}[M^+])\}[ROH_{tot}] \end{aligned} \qquad (5)$$

in ion-pairing constants. Conductivity measurements on t-butoxide solutions[9] have shown that even in 'good' aprotic dipolar organic solvents such as DMSO, ion-pairing constants are large enough (see Table 1) and vary with cation in the fashion required to account for the behaviour. Higher alkoxide aggregates may also form; cryoscopic measurements on these solutions show that at between 0.85 and 0.5M, even potassium t-butoxide in DMSO is dimeric or trimeric, and lithium t-butoxide is tetrameric even in very dilute solutions.[10] These aggregates are not well characterised, but their structures may well resemble those found in crystal structures of t-butoxides, which have been determined for potassium, rubidium, and caesium salts.[11]

At the other extreme, when ion-pairing is reduced, possibly by change of solvent, or by addition of metal-ion-selective complexing agents, observed rates should tend to k_i. Crowns and cryptands have been used in efforts to obtain rates characteristic of organic anions rather than their associated forms.[7,12] Measurements have not yet been undertaken on the alkoxide fragmentations, where reaction is completed by

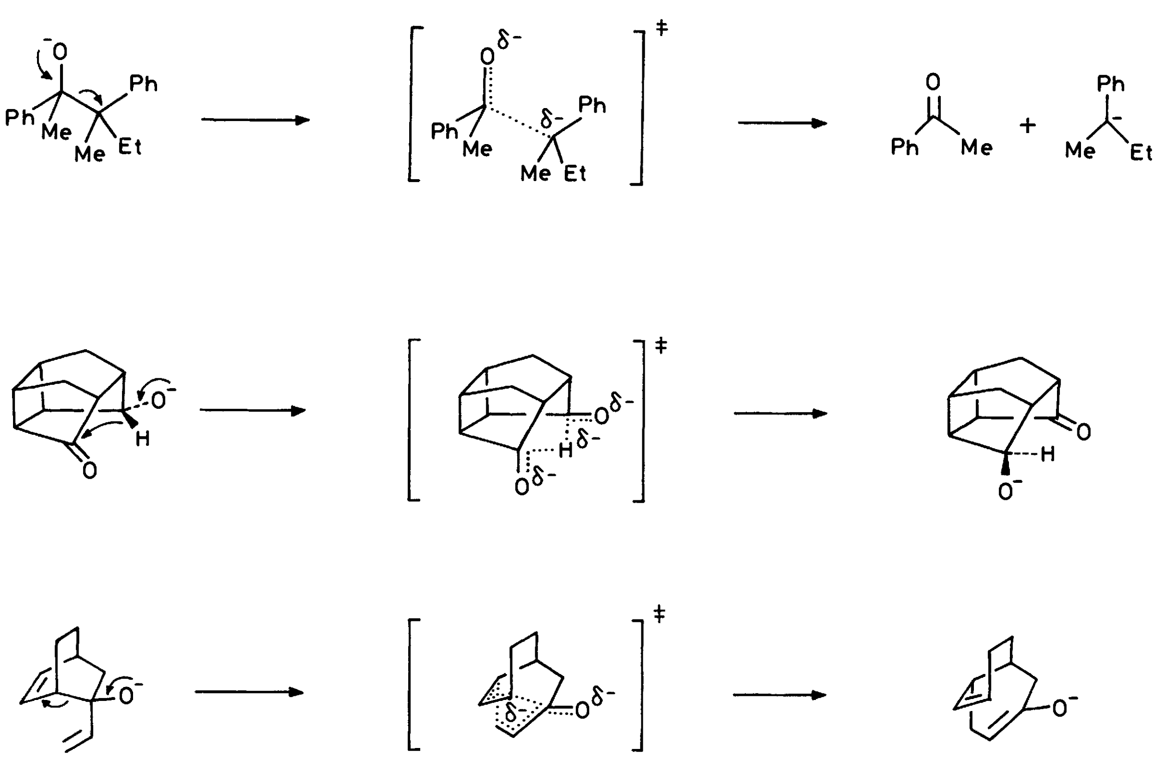


Figure 1. Cleavages and rearrangements of alkoxides showing strong cation and solvent dependence

Table 1. Literature values of equilibrium constants of relevant alkali-metal ion-pairing (K_{dim}, K_{ip}, or K_x) and cryptand formation (K_{crp}) in DMSO (25 °C)

	$CH_3SOCH_2^-$	Bu^tO^-	I^-	[2.2.2]	[2.1.1]
Li	370	$\sim 10^8$		<10	6.3×10^5
Na	127	$\sim 10^6$	0.0	2.0×10^5	4.0×10^4
K	15	270	0.08	6.3×10^6	<100
Cs	5	200	1.32	25	

Data taken from refs. 9, 26, and 28.

solvent protonation of the leaving group, and we describe here attempts to quantify the effects of ion-pairing in these reactions.

Results

We have prepared tertiary alcohols (1), (2), and (5), structurally similar to those used by Cram, and examined their reactions with strong base. We have searched particularly for alcohols whose behaviour would allow reaction monitoring by conventional u.v. spectroscopic methods, and whose reactions proceeded at comfortable rates in DMSO solution at room temperature. Two compounds, 1,2,3-triphenylpropan-2-ol (1) and 3-methyl-1,2,3-triphenylbutan-2-ol (2), readily available by addition of phenyl-lithium or benzylmagnesium bromide to the appropriate ketone (Scheme 2) have satisfied these requirements rather well.

Tertiary alcohols are converted quantitatively into their salts by treatment with excess of lithium-, sodium-, or potassium-dimsyl in DMSO.[13,14] These salts of (1) and (2) are not stable in DMSO solution, reacting to yield, as sole products after quenching by aqueous acid and extraction, deoxybenzoin (3) and either toluene or cumene. The salts of 1,2-diphenyl-3-methylbutan-2-ol (5) similarly yield cumene and acetophenone. When [$^2H_6$]DMSO was used as solvent, the recovered cumene was $>94\%$ monodeuteriated.

These alcohols themselves show no significant u.v. absorption above 270 nm, but the basic DMSO solutions of (1) and (2) develop a new absorption at $\lambda_{max.}$ 395 (± 2) nm with small variations depending on the cation. The same u.v. spectra could be obtained by treating DMSO solutions of deoxybenzoin with excess of lithium-, sodium-, or potassium-dimsyl, and we associate the developing absorption with formation of deoxybenzoin enolate (6), $\lambda_{max.}$ 395 nm (log ε 4.8), presumably its *trans*-isomer. Under conditions of excess of base (typically alcohol concentration *ca.* 10^{-5}M, and dimsyl $>10^{-2}$M) the enolate growth curve showed accurate first-order behaviour, with half-lives ranging from <1 s to over 48 h at room temperature, depending on the exact conditions.

The solutions of (5) similarly developed a new absorption at 328 nm (log ε 3.11), occurring as a shoulder on the absorption from dimsyl anion. This was shown to arise from acetophenone enolate, in principle, affording a spectroscopic handle on this reaction also. In practice, the changes in absorbance at this wavelength were difficult to measure accurately because of the high background absorbance at the relatively high dimsyl concentrations used.

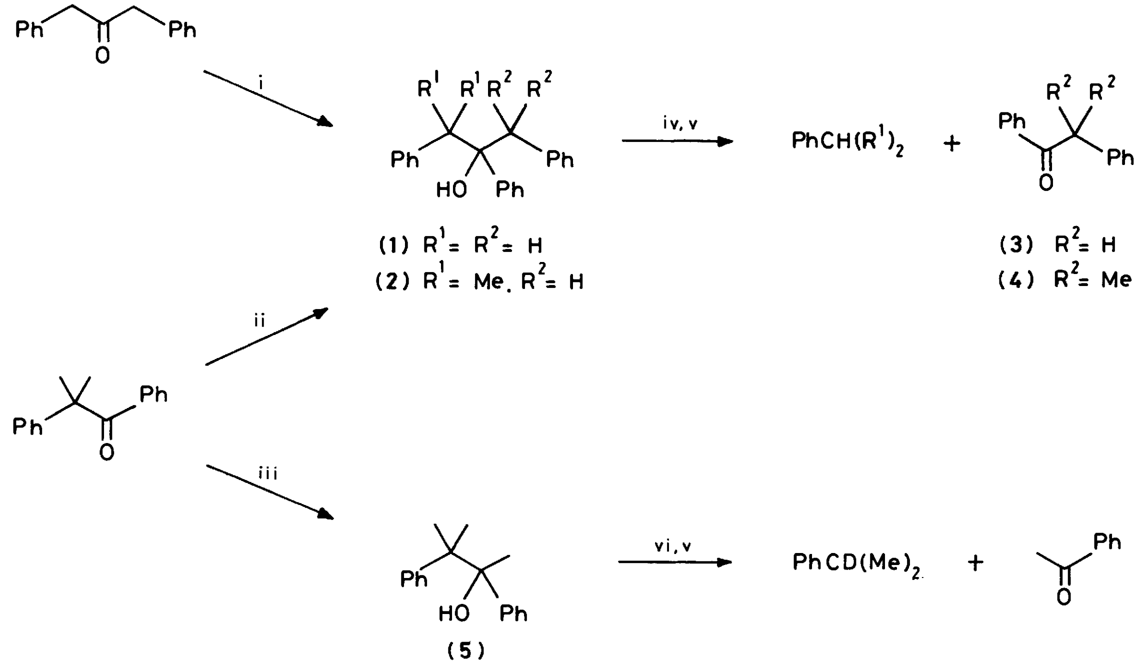
Most experiments have been carried out on 1,2,3-triphenylpropan-2-ol (1), monitoring changes at the deoxybenzoin enolate absorption. The resulting pseudo-first-order rate constants obtained showing the effects of variation of metal ion,

Table 2. Rate data for fragmentation of lithium, sodium, and potassium salts of 1,2,3-triphenylpropan-2-ol in DMSO with added [2.2.2] or [2.1.1] cryptands

Alkoxide and cryptand	T/°C	[Dimsyl]/M	[ROH]/M	[Cryp$_{tot}$]/M	$k_{obs.}$/s^{-1}
Lithium salt–added [2.1.1]cryptand	18.6	0.015	6.5×10^{-5}	0	3.02×10^{-6}
				7.08×10^{-3}	1.97×10^{-5}
				9.55×10^{-3}	7.82×10^{-5}
				1.17×10^{-2}	1.08×10^{-3}
				1.54×10^{-2}	4.89×10^{-3}
				1.93×10^{-2}	5.57×10^{-3}
				2.37×10^{-2}	7.42×10^{-3}
				3.08×10^{-2}	8.16×10^{-3}
Sodium salt–added [2.2.2]cryptand	18.6	0.015	6.5×10^{-5}	0	3.70×10^{-4}
				5.85×10^{-3}	8.90×10^{-4}
				9.75×10^{-3}	2.30×10^{-3}
				1.17×10^{-2}	7.60×10^{-2}
				1.50×10^{-2}	9.89×10^{-2}
				1.75×10^{-2}	9.93×10^{-2}
				1.95×10^{-2}	1.00×10^{-2}
Potassium salt–added [2.2.2]cryptand	18.6	0.015	6.5×10^{-5}	0	3.88×10^{-3}
				3.97×10^{-3}	4.89×10^{-3}
				7.94×10^{-3}	6.70×10^{-3}
				1.00×10^{-2}	8.19×10^{-3}
				1.19×10^{-2}	8.57×10^{-3}
				1.47×10^{-2}	8.61×10^{-3}
				1.71×10^{-2}	8.39×10^{-3}
				1.99×10^{-2}	8.66×10^{-3}

Table 3. Values of parameters used in calculation rates of fragmentation of salts of 1,2,3-triphenylpropan-2-ol (**1**) and of 3-methyl-1,2,3-triphenylbutan-2-ol (**2**) in DMSO. Calculated lines are displayed in Figures 2—4

Salt	T/°C	Addend	K_{ip}	K_{dim}	K_{crp} or K_x	k_i	k_p	[Base]/M
(**1**)-K	18.6	[2.2.2]Cr.	1.2×10^{1}	10	8.0×10^{6}	8.5×10^{-3}	8.5×10^{-5}	0.012
(**1**)-Na	18.6	[2.2.2]Cr.	3.4×10^{3}	130	5.0×10^{5}	8.5×10^{-3}	8.5×10^{-6}	0.012
(**1**)-Li	18.6	[2.1.1]Cr.	2.0×10^{5}	300	9.0×10^{5}	8.5×10^{-3}	8.5×10^{-8}	0.012
(**1**)-K	26.0	KI	8.5×10^{1}	15	8.0×10^{-2}	2.0×10^{-2}	2.0×10^{-5}	0.027
(**1**)-Na	30.8	NaI	2.5×10^{3}	130	1.0×10^{-2}	4.0×10^{-2}	4.0×10^{-7}	0.019
(**2**)-Na	18.6	NaI	1.0×10^{3}	130	1.0×10^{-2}	8.0	8.0×10^{-3}	0.025
(**2**)-Li	18.6	LiI	3.5×10^{4}	300	1.0×10^{-2}	8.0	8.0×10^{-3}	0.020



Scheme 2. *Reagents:* i, PhLi–Et_2O; ii, PhMgBr–Et_2O; iii, MeLi–Et_2O; iv, $CH_3SOCH_2^-$–DMSO; v, H^+–H_2O; vi, $CD_3SOCD_2^-$–[$^2H_6$]DMSO

Table 4. Rate data for fragmentation of sodium and potassium salts of 1,2,3-triphenylpropan-2-ol in DMSO with added potassium or sodium iodide

Alkoxide and salt	T/°C	[Dimsyl]/M	[ROH]/M	$[M_{tot}]$/M	$k_{obs.}$/s^{-1}
Sodium salt–added sodium iodide Data set 1	30.8	0.019	7.1×10^{-5}	1.91×10^{-2}	1.73×10^{-3}
				2.48×10^{-2}	1.25×10^{-3}
				3.43×10^{-2}	8.51×10^{-4}
				3.49×10^{-2}	7.61×10^{-4}
				5.00×10^{-2}	5.24×10^{-4}
				6.53×10^{-2}	3.80×10^{-4}
				2.12×10^{-1}	7.80×10^{-5}
Sodium salt–added sodium iodide Data set 2	30.8	0.019	7.1×10^{-5}	1.91×10^{-2}	1.67×10^{-3}
				2.51×10^{-2}	1.23×10^{-3}
				2.93×10^{-2}	8.66×10^{-4}
				4.22×10^{-2}	6.75×10^{-4}
				4.71×10^{-2}	5.12×10^{-4}
				9.66×10^{-2}	1.87×10^{-4}
				2.05×10^{-1}	6.71×10^{-5}
				2.32×10^{-1}	6.11×10^{-5}
Potassium salt–added potassium iodide Data set 1	26.0	0.026	7.1×10^{-5}	2.61×10^{-2}	8.33×10^{-3}
				3.09×10^{-2}	6.82×10^{-3}
				3.19×10^{-2}	6.62×10^{-3}
				3.75×10^{-2}	6.03×10^{-3}
				5.65×10^{-2}	4.35×10^{-3}
				7.11×10^{-2}	3.60×10^{-3}
				9.87×10^{-2}	2.56×10^{-3}
				1.21×10^{-1}	2.06×10^{-3}
				2.16×10^{-1}	1.31×10^{-3}
				2.33×10^{-1}	1.06×10^{-3}
Potassium salt–added potassium iodide Data set 2	26.0	0.028	7.1×10^{-5}	2.81×10^{-2}	8.12×10^{-3}
				3.47×10^{-2}	6.84×10^{-3}
				4.70×10^{-2}	5.30×10^{-3}
				5.72×10^{-2}	4.39×10^{-3}
				8.64×10^{-2}	3.26×10^{-3}
				1.08×10^{-1}	2.58×10^{-3}
				1.50×10^{-1}	1.90×10^{-3}
				1.99×10^{-1}	1.30×10^{-3}
				3.26×10^{-1}	8.00×10^{-4}
				4.42×10^{-1}	5.50×10^{-4}

Data sets represent rates determined in different batches of DMSO.

of its concentration, and of added complexing agent on the rates of fragmentation of its alkoxide are presented in Tables 2 and 4. Similar measurements showing the effect of metal ion on the rates of fragmentation of salts of (**5**) are contained in Table 5. Before discussing our rate data, however, a comment on their reproducibility is in order. These reactions were conducted in as nearly anhydrous DMSO as was possible. Typically, Karl Fischer titration gave water contents <25 p.p.m. in the batches of solvent used. Rates determined using DMSO from the same batch of solvent and dimsyl preparation were reproducible routinely to within ±5%. However, in common with other workers,[15] we experienced difficulties in obtaining reproducible rate data with different batches of DMSO and dimsyl. Rates could vary by up to 20% and we believe this is caused by small, varying amounts of adventitious water. In a sense, the experiments are 'ill conditioned' in their sensitivity to trace moisture, and indeed, many workers[16] sensibly avoid the problem by using DMSO with a measured 1—0.5% of added water. These alcohols do not fragment at measurable rates in these aqueous DMSO mixtures, presumably because hydroxide in 99% or 99.5% DMSO does not generate any appreciable amount of alkoxide anion.[17] In our hands also, solutions of dimsyl in DMSO decayed[18] sufficiently fast at $T > 30$ °C to complicate measurements on slow runs at that temperature.

Discussion

The observations are most economically rationalised by the outline Scheme 3, involving the anticipated fragmentation of the alkoxide salts by expulsion of either benzyl or cumyl anion (An^-). Ketone (**3**) is then deprotonated by dimsyl, and benzylic anion protonated by DMSO, *i.e.*, $k_4[An^-] \ll k_2[CH_3SOCH_2^-]$. In the case of alcohol (**2**), an alternative fragmentation yielding the non-enolisable ketone (**4**) is not observed, and we return to this aspect of its reaction later.

Scheme 3 leads to relationships between a pseudo-first-order rate constant for formation of the enolate and the phenomenological constants. The individual constants in the ratio

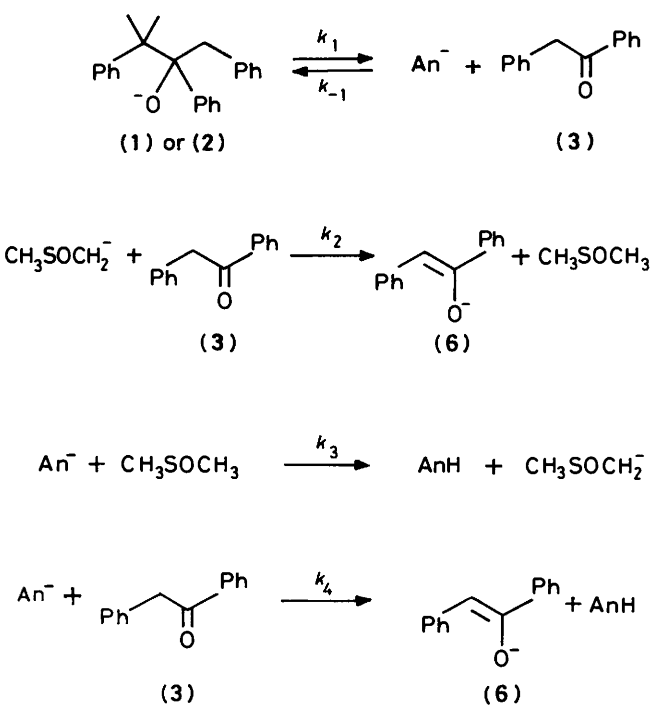
$$k_{obs} = k_1\{(k_{-1}/k_2)([An^-]/[CH_3SOCH_2] + 1\} \qquad (6)$$

k_{-1}/k_2 are not known, but both should be large and may well approach diffusion-control limits.[19] A Brønsted relationship for deprotonations of carbon acids by dimsyl anion is not available, but the second-order rate constant for deprotonation of triphenylmethane by dimsyl anion[20] is 8×10^3 l mol^{-1} s^{-1} (25 °C), and with deoxybenzoin being 13 pK_a units more acidic[21] than triphenylmethane, even a low Brønsted coefficient (β *ca.* 0.52) would give k_2 *ca.* 10^{10} l mol^{-1} s^{-1}. Neither are there rates available for addition of carbanions to ketonic carbonyl.

Table 5. Rate data for fragmentation of lithium and sodium salts of 3-methyl-1,2,3-triphenylpropan-2-ol in DMSO with added lithium or sodium iodide

Alkoxide and salt	T/°C	[Dimsyl]/M	[ROH]/M	$[M_{tot}]$/M	$k_{obs.}/s^{-1}$
Lithium alkoxide–added lithium iodide Data set 1	18.6	0.012	1.1×10^{-2}	1.21×10^{-2}	6.50×10^{-2}
				1.48×10^{-2}	5.76×10^{-2}
				1.89×10^{-2}	4.10×10^{-2}
				1.97×10^{-2}	3.26×10^{-2}
				2.54×10^{-2}	2.41×10^{-2}
				2.70×10^{-2}	2.16×10^{-2}
				4.53×10^{-2}	1.08×10^{-2}
Lithium alkoxide–added lithium iodide Data set 2	18.6	0.025	1.1×10^{-4}	2.50×10^{-2}	4.02×10^{-2}
				2.64×10^{-2}	2.84×10^{-2}
				3.05×10^{-2}	2.62×10^{-2}
				3.17×10^{-2}	2.44×10^{-2}
				3.34×10^{-2}	1.68×10^{-2}
				4.61×10^{-2}	1.06×10^{-2}
				4.75×10^{-2}	9.90×10^{-3}
				7.00×10^{-2}	5.90×10^{-3}
				9.21×10^{-2}	4.01×10^{-3}
Sodium alkoxide–added sodium iodide Data set 1	18.6	0.019	1.1×10^{-4}	1.86×10^{-2}	9.10×10^{-1}
				2.11×10^{-2}	6.64×10^{-1}
				2.78×10^{-2}	6.26×10^{-1}
				3.12×10^{-2}	4.26×10^{-1}
				4.74×10^{-2}	3.39×10^{-1}
				5.18×10^{-2}	2.43×10^{-1}
				6.04×10^{-2}	1.89×10^{-1}
				1.05×10^{-1}	1.12×10^{-1}
				1.32×10^{-1}	9.60×10^{-2}
Sodium alkoxide–added sodium iodide Data set 2	18.6	0.027	1.1×10^{-4}	2.65×10^{-2}	7.97×10^{-1}
				2.81×10^{-2}	6.84×10^{-1}
				3.22×10^{-2}	5.65×10^{-1}
				3.71×10^{-2}	4.27×10^{-1}
				5.44×10^{-2}	3.12×10^{-1}
				6.09×10^{-2}	2.58×10^{-1}
				6.87×10^{-2}	2.09×10^{-1}
				1.31×10^{-2}	1.14×10^{-1}

The different sets represent runs using different batches of DMSO.



Scheme 3.

However, nucleophilic aromatic substitutions by fluorenide anions in DMSO have been studied.[22] Depending on the aromatic, these show $0.71 < \beta_{nuc} < 47$. A second-order rate constant of *ca.* 10^8 l mol^{-1} s^{-1} can be extrapolated for hypothetical reaction of benzyl anion with *p*-cyanofluorobenzene. The extension to a carbonyl addition is not entirely satisfactory, but the data at least indicate the possibility of diffusion-limited addition of the benzyl anion to deoxybenzoin.

The form of relationship (6) thus depends on the value of the ratio $[An^-]/[CH_3SOCH_2^-]$. As noted above, the reactions are carried out in *ca.* 10^3 molar excess of dimsyl, so that it must be $< 10^{-3}$. Benzyl anion is also being consumed by protonation by DMSO, a process for which rates are again unavailable.[23] The expression then simplifies such that the observed pseudo-first-order rate constants can be identified with k_1, governing the rate of production of deoxybenzoin in a form which can be intercepted to yield its enolate.

The rates of fragmentation of the lithium, sodium, and potassium alkoxides of (**1**) in presence of 0.015M-metal dimsyl (Table 2) are in the ratio 1:122:1330, a span of 10^3 across the series. With excess of base, the basic ion-pairing Scheme 1 must be expanded to include of ion-pairing of the metal dimsyl, *i.e.*, equation (7). With the dimsyl in large excess, the 'free' metal ion

$$\text{Dimsyl}^- + M^+ \overset{K_{dim}}{\rightleftharpoons} \text{Dimsyl M} \qquad (7)$$

concentration is governed largely by this equilibrium. This being the case, the ratio of observed rates can be shown to

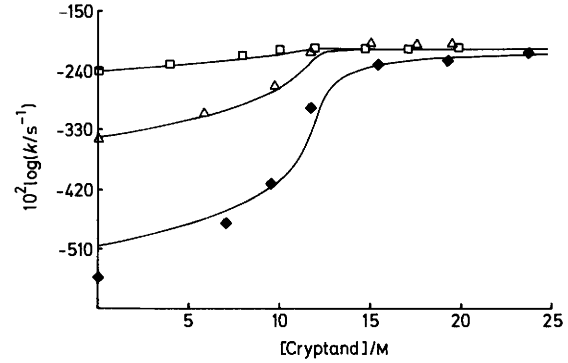


Figure 2. Effect of added [2.2.2] cryptand on rates of fragmentation in DMSO solution at 18.6 °C of potassium (□) and sodium (△) salts of 1,2,3-triphenylpropan-2-ol, and of [2.1.1] cryptand on the lithium salt (◆)

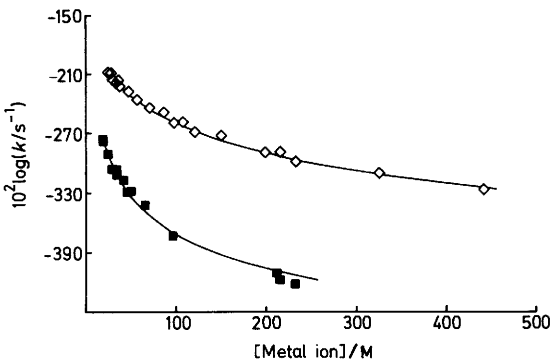


Figure 3. The effect of added common metal ion iodides on rates of fragmentation of the sodium (■) and potassium (◇) salts of 1,2,3-triphenylpropan-2-ol in DMSO solution, at 30.80 and 26.0 °C, respectively

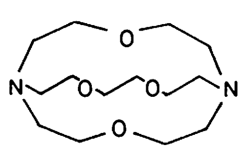
correspond approximately to the ratio $(K_{dim}/K_{ip})_{Li}:(K_{dim}/K_{ip})_{Na}:(K_{dim}/K_{ip})_{K}$.

With the available measurements of ion-pairing constants for the alkali-metal dimsyls (included in Table 1) it becomes possible to extract an approximate ratio of ion-pairing constants, $3.3 \times 10^4:9.2 \times 10^2:1$ for the lithium, sodium, and potassium alkoxides of 1,2,3-triphenylpropan-2-ol. Although the cation dependence is substantial, it is less than that reported for t-butoxides where the corresponding ratio is *ca.* $3.7 \times 10^5:3.7 \times 10^3:1$. Presumably the difference lies in the bulk of the groups attached to the tertiary centre, and it is also likely that the absolute values of the ion-pairing constants are lower in the larger alcohol. Arnett has already suggested that steric inhibition of ion-pairing is responsible at least partially for the high reactivity of tri-t-butylcarbinol salts in DMSO.[24]

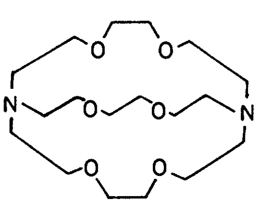
Table 2 also contains rate data for fragmentation of these alkoxides in presence of added cryptands. These associate rapidly[25] and strongly[26] with alkali-metal cations in DMSO [equation (8)]. With the sodium and potassium alkoxides,

$$M^+ + \text{Crypt} \overset{K_{crp}}{\rightleftharpoons} \text{M.Crypt}^+ \qquad (8)$$

[2.2.2]cryptand was used since its association constants with these cations are $>10^5$ (Table 1) so that the cryptand should compete efficiently with alkoxide for the alkali-metal cation. The graph of log rate against concentration of added cryptand (Figure 2) shows that is indeed the case. With potassium alkoxide, a relatively small enhancement is observed, but after addition of cryptand equivalent to the total metal present, the rate effectively becomes constant. For sodium alkoxide, the enhancement is more pronounced, but the same limiting value of the rate is reached near stoicheiometric equivalence between metal and cryptand. The association constant of [2.2.2]cryptand and lithium cation in DMSO is only *ca.* 10 and the effect of this cryptand on the rates of the lithium alkoxide was not studied. However, the [2.1.1]cryptand forms a stable cryptate with lithium, and the effect of its addition was examined. The rate enhancements are the largest found, but as shown graphically, the rates only approach asymptotically the limiting value achieved by sodium and potassium alkoxides.



[2.1.1] cryptand



[2.2.2] cryptand

The equilibria in equations (1), (7), and (8) yield a cubic relating $[M^+]$ to the measurable quantities of total metal ion concentrations $[M_{tot}]$ and cryptand $[\text{Cryp}_{tot}]$,[27] equation (9)

$$[M^+]^3 + P[M^+]^2 + Q[M^+] + R = 0 \qquad (9)$$

with relationships (10)—(12).

$$P = (K_{crp} + K_{dim} + K_{crp}K_{dim}[\text{Crp}_{tot}])/K_{crp}K_{dim} \qquad (10)$$

$$Q = (1 + K_{crp}[\text{Crp}_{tot}] - K_{crp}[M_{tot}])/K_{crp}K_{dim} \qquad (11)$$

$$R = -[M_{tot}]/K_{crp}K_{dim} \qquad (12)$$

The solid lines in Figure 2 represent calculated dependence of rates on the concentrations of the added cryptands, using these relationships. If the values of k_i in Scheme 1 is taken as the limiting rate approached by all the alkoxides with excess of cryptand, k_p and K_{ip} for each salt can be treated as adjustable parameters in a fit of the lines to the data. The lines shown are 'eyeball fits' to the data and the values of the parameters used in generating the lines are given in Table 3.

In view of the difficulties of obtaining fully reproducible rate data the values quoted for the parameters should be treated only as good order of magnitude estimates. However, two points of interest emerge. First, the values of K_{ip} required to produce reasonable fits are entirely reasonable when compared with Exner's experimental values for t-butoxide, given the larger organic anion here. Secondly, the ratio k_i/k_p, governing the relative reactivity of dissociated and associated alkoxides, is cation-dependent in the anticipated fashion, and is large. Provided the ratio is >100, the fits are not strongly sensitive to this ratio, but even for the potassium salt, where stabilisation of negative charge in the oxyanion by association with cation is least, the ratio is *ca.* 100.

Data showing the effects of added common ion sodium and potassium iodides on rates of fragmentation of (**1**) are presented in Table 4 and graphically in Figure 3. These iodides are only weakly associated in DMSO.[28] Values for ion-pairing constants for equation (13) are presented in Table 1. Observed rates

$$M^+ + X^- \overset{K_x}{\rightleftharpoons} MX \qquad (13)$$

should therefore be depressed by the raising of $[M^+]$, in the expression for $k_{obs.}$ and qualitatively the effect is observed, and was sufficient to force use of higher temperatures to obtain

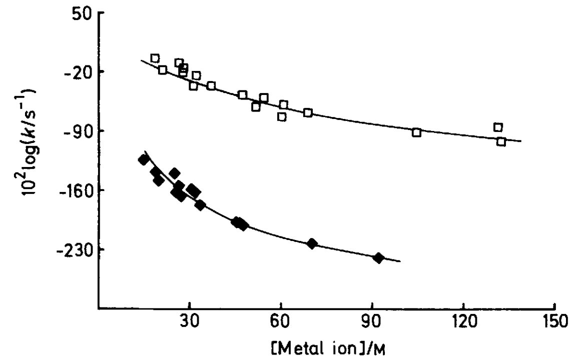


Figure 4. The effect of added common metal ion iodides on the rates of fragmentation of the lithium (◆) and sodium (□) salts of 3-methyl-1,2,3-triphenylbutan-2-ol in DMSO solution at 18.6 °C

reasonable rates. This effect should be superimposed on a normal Brønsted ionic strength effect, which we can only assume is relatively small. The solid lines in Figure 3 represent behaviour calculated using the known ion-pairing constants in equilibria (1), (7), and (13) to calculate $[M^+]$ in terms of the measurable quantities, $[M_{tot}]$ and total iodide $[X_{tot}]$. Again the relationship is the cubic,[27] with the constants now given by equations (14)—(16). The lines are 'eyeball fits' obtained by

$$P = (K_x + K_{dim})/K_{dim}K_{crp} \quad (14)$$

$$Q = (1 - K_x[M_{tot}] - K_{dim}[X_{tot}])/K_{dim}K_x \quad (15)$$

$$R = (K_x[_{tot}] - [M_{tot}])/K_{dim}K_x \quad (16)$$

adjusting K_{ip} and k_i. The values of the parameters used are given in Table 3, and it is satisfying that this and the added cryptand experiments yield similar values for the sodium and potassium alkoxide ion-pairing constants. The values of k_i used also represent a conventional temperature dependence of k_i.

With added lithium iodide, the fragmentations of (1) became too slow for collection of reliable rate data. The alkoxides of (2), however, turned out to be *ca.* 5 × 10^3 more reactive, fragmenting to yield the same enolate, now by expulsion of the cumyl anion from the alkoxide. The reactivity was too high for rate measurements on the potassium salts, or on solutions with added cryptands with our available equipment, but the effects of added lithium and sodium iodide on observed rates of fragmentation are presented in Table 5 and Figure 4. The data here is considerably more scattered than our measurements on (1), and reflect the difficulties in stop-flow measurements on these air- and moisture-sensitive solutions. As before, the solid lines were generated by adjusting K_{ip}, k_i, and k_p. As is clear from the form of the relationship between $k_{obs.}$ and these constants, K_{ip} and k_i, are strongly covariant, and reasonable fits to data could be obtained with a range of K_{ip}–k_i combinations. Values of K_{ip} between 10 and 10^2 smaller than those for (1) were necessary, presumably reflecting the effect of greater steric crowding at the co-ordination site. It was also necessary to set the reactivity of free alkoxide, k_i for (2), to between 141 and 940 times larger than for (1). The unfortunate absence of a limiting-rate measurement does not allow selection of a particular value k_i. The best-fit values are incorporated in Table 3, but the widespread possible individual values must be recognised.

The enhanced observed reactivity of (2) over (1) thus reflects the combined effect of structural change on ion-pairing equilibria, and a direct effect on reactivity of the alkoxide anions. As noted earlier, the fragmentation of (2) proceeds by expulsion of a cumyl rather than benzyl anion. This

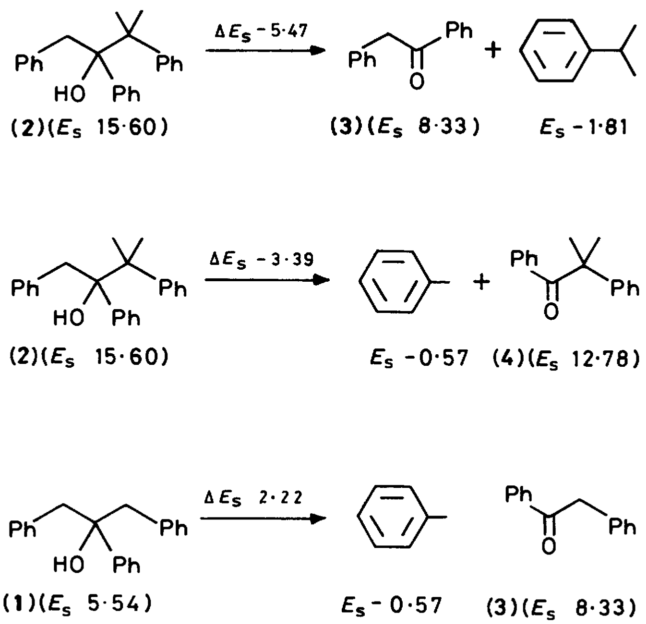


Figure 5. Steric energy changes in cleavages of alcohols (1) and (2). All E_s in kcal mol^{-1}

regioselectivity, and > 140-fold reactivity of the anion of (2) over (1), should reflect relative stabilities of the carbanions, and differential relief of ground-state strain in the fragmentation processes. The relative importance of these factors is not clear, but with strained alkoxides, either where all substituents at the carbinol are bulky,[24,29,30] or where reaction would involve cleavage of a small ring,[31] fragmentations involving expulsion of unstabilised alkyl carbanions occur. Lomas[30] has attempted to quantify the steric effects by calculating the difference in strain between saturated alcohols of the type $R^1R^2R^3COH$, and the possible ketonic and hydrocarbon products using a standard empirical force method.[32] Cumene is reckoned to be 0.5 pK_a units more acidic than toluene,[33] so that cumyl anion may be marginally the better of the two leaving groups in our reactions. Following Lomas, we have calculated the change in steric energy in the net conversion of alcohols (1) and (2) into their possible fragmentation products (see Figure 5), and clearly any effect from carbanion stabilities operate in sympathy with strain relief. For (2), formation of deoxybenzoin (3) and cumene is favoured, by 2.08 kcal mol^{-1} over its alternative unobserved fragmentation to (4) and toluene, and by 7.64 kcal mol^{-1} over the fragmentation of (1). The difference in reactivity between the 'free alkoxides of (1) and (2) would require expression of < 50% of this $\Delta\Delta E_s$, suggesting an early transition state.

Conclusions.—In this work, we have revisited the experiments of Cram and his collaborators on fragmentation of t-alkoxides, focusing on the cation dependence of reactivity. Rates of fragmentation of the salts of 1,2,3-triphenylpropan-2-ol have been determined in DMSO in the presence of added salts or cryptands. Within the limits of accuracy, Cram's original reaction scheme involving differential reactivity of paired and free alkoxide anions qualitatively and quantitatively accounts for the rate data. Similar conclusions follow from the behaviour of 3-methyl-1,2,3-triphenylbutan-2-ol. Rate enhancement in its fragmentation is the combined result inhibition of ion-pairing and an intrinsically more reactive anion. Steric effects are clearly important in determining the direction of fragmentation of unsymmetrical alkoxides.

Experimental

^1H N.m.r. spectra were recorded on either a Perkin-Elmer 90 MHz R32 or Varian SC 300 MHz spectrometer. Unless otherwise stated, the solvent was deuteriochloroform, with tetramethylsilane internal standard. I.r. spectra were determined on a Pye–Unicam SP3-200 spectrophotometer, using 0.1 mm solution cells with carbon tetrachloride as solvent. Mass spectra were recorded on a Kratos MS 25 machine operating at 70 eV for electron impact ionisation. G.l.c.–m.s. spectra were run on a Perkin-Elmer Sigma 3 g.l.c. machine in conjuncton with the Kratos MS 25 instrument. For all chemical ionisation spectra, ammonia was the chemical ionisation reagent used. U.v. spectra were carried out on a Pye–Unicam SP8-300 u.v.–visible spectrophotometer, with the cell block kept at constant temperature by a Haake E3 thermostat bath. For g.l.c., a Carlo Erba Strumentazione machine with a 20 m OV-1 glass capillary column using hydrogen carrier gas and a flame ionisation detector was used in all cases. Merck G alumina was used for alumina columns, Merck Kieselgel 60 H silica for silica columns, and Merck Kieselgel 60 PF254 silica for preparative t.l.c. For t.l.c., Merck pre-coated silica-backed plates with a 0.2 mm layer of Kieselgel 60 F254 were used. All microanalyses were carried out by the University of Manchester Microanalysis Laboratory under the direction of Mr. M. Hart. For atomic absorption spectroscopy, a Perkin-Elmer 603 spectrophotometer was used in all cases. Water contents were measured by coulometric Karl Fischer titration on a Metrohm 652KF coulometer. Empirical force field calculations were carried out using the MM2 program mounted on the CDC7600 at UMRCC.

1,2,3-*Triphenylpropan*-2-*ol* (**1**).—A three-necked flask (100 ml), fitted with a reflux condenser and two septum caps, was flame dried and allowed to cool under a flow of nitrogen. To this was added magnesium (0.24 g) and dry ether (10 ml), and the mixture was stirred magnetically. A solution of bromobenzene (1.53 g) in dry ether (15 ml) was then added slowly, and the mixture stirred until all magnesium had dissolved. To this was added a solution of 1,3-diphenylpropan-2-one (2.0 g) in dry ether (20 ml), and the mixture was then refluxed for 1 h. After cooling to room temperature, ice (5 g) was added, followed by a saturated aqueous solution of EDTA (50 ml). The organic layer was separated, the aqueous layer washed with ether (3 × 15 ml), the organic layers combined, and dried (Na_2SO_4). The organic layer was then filtered, and the ether removed under reduced pressure to give the product as a solid (1.62 g, 60%). The product was purified by silica column chromatography using a pentane–ether gradient, and then was recrystallised to give the *pure alcohol*, m.p. 85—86 °C (Found: C, 87.4; H, 7.0. $C_{21}H_{20}O$ requires C, 87.5; H, 6.9%); $\nu_{max.}$(CCl_4) 3 560 (m), 3 100—3 020 (m), 2 960 (s), 2 930 (s), 1 600 (w), 1 495 (m), 1 450 (m), and 1 100 (m) cm^{-1}; δ_H($CDCl_3$) 7.4–6.9 (15 H, m), 3.25 (2 H, d, *J* 13 Hz), 3.02 (2 H, d, *J* 13 Hz), and 1.68 (1 H, s, removed by D_2O); *m*/*z* (E.I.) 270 (5%), 198 (44), 197 (100), 105 (92), 91 (86), and 77 (80); (C.I.) 306 (6), 289 (2), 288 (12), 271 (53), 197 (75), 105 (100), and 91 (92).

3-*Methyl*-1,2,3-*triphenylbutan*-2-*ol* (**2**).—A solution of benzylmagnesium chloride in ether was prepared as described by Prout *et al.*[34] from magnesium turnings (0.135 g, 5.6×10^{-3} mol) and distilled benzyl chloride (0.6 ml, 5.2×10^{-3} mol). A solution of 1,2-diphenyl-2-methylpropan-1-one[35] (0.8 g, 3.6×10^{-3} mol) in distilled toluene (6 ml) was then added and the mixture refluxed for 1 h, before pouring onto crushed ice (10 g). An ammoniacal solution of EDTA (20 ml of a saturated solution), was then added and the layers separated. The aqueous layer was extracted twice with ether (10 ml), the organic layers combined, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. This gave a viscous yellow liquid (0.91 g) which contained the product as the major component of a mixture (*ca.* 55% of the mixture, a yield of 44%). The product was purified by silica column chromatography, eluting with a hexane–ether gradient, and by crystallisation from petroleum (b.p. 100—120 °C) to give a *crystalline solid*, m.p. 86—87 °C (Found: C, 87.7; H, 7.8. $C_{23}H_{24}O$ requires C, 87.4; H, 7.8%); $\nu_{max.}$(CCl_4) 3 560 (m), 3 040 (m), 2 960 (s), 1 600 (w), 1 440 (s), 1 375 (m), 1 355 (w), and 1 102 (m) cm^{-1}; δ_H($CDCl_3$) 6.9—7.65 (15 H, m), 3.44 (1 H, d, *J* 14 Hz), 3.05 (1 H, d, *J* 14 Hz), 1.55 (1 H, s), 1.48 (3 H, s), and 1.43 (3 H, s); *m*/*z* (E.I.) No M^+, 298 (1%), 197 (100), 147 (30), 119 (71), 105 (99), 91 (83), and 77 (76); (C.I.) 334 (M + 18, 15), 315 (M + 1, 2), 197 (57), 167 (22), 119 (100), 105 (61), and 91 (22).

2,3-*Diphenyl*-3-*methylbutan*-2-*ol* (**5**).—This was synthesised using the method of Shilton.[36] A solution of 1,2-diphenyl-2-methylpropan-1-one (3.4 g, 1.52×10^{-2} mol) in dry diethyl ether (10 ml) was stirred under a flow of nitrogen for 15 min. To this solution was added methyl-lithium solution (14 ml of a 1.2M solution in ether, 1.6×10^{-2} mol) dropwise by syringe, whilst keeping the solution under a flow of nitrogen. After addition was complete, the solution was refluxed for 5 min, then propan-2-ol (10 ml) was added with stirring, followed by water (25 ml). The organic layer was separated and the aqueous layer washed with ether. The combined organic layers were then dried (Na_2SO_4), filtered, and evaporated under reduced pressure to yield a pale viscous yellow liquid (3.0 g) which was purified by bulb-to-bulb distillation under reduced pressure (150 °C and 0.15 mmHg), silica column chromatography (eluting with a hexane–ether gradient), and preparative t.l.c. This gave a crystalline solid, m.p. 68—69.5 °C (lit.,[36] 70 °C) which on recrystallisation from aqueous ethanol gave crystals, m.p. 69—70 °C (Found: C, 84.6; H, 8.5. Calc. for $C_{16}H_{16}O$: C, 85.0; H, 8.4%); $\nu_{max.}$(CCl_4) 3 600 (m), 3 060 (w), 2 990 (s), 1 600 (w), 1 385 (m), 1 070 (m), and 1 035 (m) cm^{-1}; δ_H($CDCl_3$) 7.2—7.42 (10 H, m), 1.73 (1 H, s), 1.48 (3 H, s), 1.36 (3 H, s), and 1.14 (3 H, s); *m*/*z* (E.I.) 222 (M − water, 16%), 121 (100), 105 (73), 91 (44), 77 (42), and 43 (64); C.I. 240 (M^+, 7), 223 (100), 121 (43), 119 (40), 105 (52), and 91 (28).

Purification of DMSO.—The purification procedure used was as described by Bordwell,[13] by distillation from sodium amide at 0.1 mmHg, keeping the pot temperature below 60 °C, directly into storage flasks fitted with a Rotaflow stopcock that was then kept closed after distillation. The vacuum was released with argon and the DMSO was stored under argon.

Metal-dimsyl Solutions.—(i) *Dimsyl-lithium*. Freshly distilled DMSO (13 ml) was added to a flask (25 ml) on an argon line and was fitted with a magnetic stirrer. To this was added n-butyl-lithium (3 ml of a 1.6M solution in hexane) using a gas-tight syringe. A solid appeared in the hexane layer, which dissolved in DMSO on stirring. After 5 min no more gas was evolved, and the hexane was removed by oil-pump vacuum, the vacuum being released with argon. This gave a clear solution of dimsyl-lithium, best results being obtained with a butyl-lithium solution that had been prepared in these laboratories[37] and stored on the argon line. Commercially available n-butyl-lithium solution invariably yielded yellow dimsyl solutions.

(ii) *Dimsylsodium and Dimsylpotassium*. A gas-line flask (50 ml) was fitted with a magnetic stirrer and flushed with argon. To this was added a suspension of the metal amide in toluene. Sodium amide was from Fluka; potassium amide was prepared by the method of Hauser and Dunnavant.[38] The flask was rapidly replaced on the argon line, evacuated, and the vacuum then released with argon. The amide was then washed four times with petroleum (b.p. 40—60 °C) (5 ml). In the case of potassium, it was especially necessary to prevent contact with oxygen at any stage, since this resulted in the amide turning yellow which in turn gave yellow dimsylpotassium. The flask was then evacuated with stirring to give the amide as a fine powder. The flask was cooled in water, and DMSO (25 ml) was added to the stirred mixture. Reaction was complete in *ca.* 5 min and the solution was then evacuated to remove ammonia formed, and when no further gas was evolved the vacuum was released with argon, to give a clear solution of the appropriate metal-dimsyl solution.

Base concentrations were then determined as previously described.[39] Generally, quantities of amide or butyl-lithium were used giving dimsyl concentrations <0.1M. Solutions more concentrated than this did not store well, even when kept at low temperature under argon.

Rate Measurements.—For slower runs (*i.e.*, $t_{\frac{1}{2}} > 1$ min) reactions were carried out in modified Thunberg cuvettes.[40] These were evacuated (0.5 mmHg), the vacuum then being released with argon to put the whole apparatus under argon. Using a gas-tight syringe, dimsyl solution (2.4 ml) was added through a septum cap into the larger of the two 'arms', and alcohol solution (0.4 ml, 2.5×10^{-3}M in DMSO) was added to the smaller. The apparatus was then clamped with the two arms and the u.v. cell below the water level of the bath which thermostatted the cell block of the u.v. spectrometer. After 15 min, it was removed, swiftly dried with a tissue, and the reactants mixed by repeated pouring from one arm to the other. The mixed solution was then poured into the u.v. cell itself and the apparatus placed in the cell block of the spectrometer to monitor absorbance changes at the indicated wavelength.

For the runs with 'added solutions' (metal halides or cryptands in DMSO), the dimsyl arm of the apparatus had dimsyl solution (2.0 ml) injected into it, and 0.5 ml of a mixture of DMSO and the added solution. The composition of the mixture varied from no added solution (*i.e.*, 0.5 ml DMSO) to being all added solution.

For faster runs, (with $t_{\frac{1}{2}} < 1$ min), a Hi-Tech SFA-11 stopped-flow apparatus was used in conjunction with the same spectrophotometer. Before use, the apparatus was stored in a vacuum oven at 40 °C and 0.1 mmHg overnight, set up while still warm, and flushed with argon for 30 min. The plastic solution reservoir syringes supplied with the apparatus were replaced by Weber 10 ml glass syringe barrels, fitted with rubber septum caps. At all times, the apparatus and contents of the reservoir syringes were kept under positive argon pressure. To one of the syringes was added dimsyl solution (10 ml), and to the other reservoir syringe was added alcohol solution in DMSO (10 ml). For runs with added solutions (metal halides, cryptands), the added solution was mixed with the dimsyl solution using a 5 ml gas-tight syringe, in the reservoir syringe. For new concentrations, the reservoir syringe was replaced with a clean, dry reservoir syringe (flushed with argon) for each new concentration.

With both fast and slow reactions, the output of the spectrometer was led to a 12-bit A/D converter and logged automatically on a BBC/B microcomputer. At least 40 points over three half-lives were recorded and rates obtained by non-linear least-squares fit of the first-order decay to the data.[41] Runs in which calculated and experimental infinity values did not agree within experimental error were rejected. In cases when drift of infinity value occurred, it was found to be associated with failure of seals allowing diffusion of atmospheric oxygen into the apparatus.

After completion of reactions, cell contents were collected and 1.0 ml thereof diluted with a known volume of distilled water for determination of cation concentration by atomic emission spectroscopy.

Added Halide Solutions.—The alkali-metal halide (*ca.* 2 g), was placed in a flask (25 ml) on an argon line. The flask was then evacuated, and the contents of the flask heated strongly (500 °C) for 5—10 min to remove any water present. The flask and its contents were then allowed to cool under vacuum to room temperature, before release of the vacuum by argon. A septum cap was attached to the stopcock attachment of the flask and DMSO (15 ml) added. A sonic bath was then placed so that the flask was immersed in the water of the bath, and the sonic bath was then switched on for 1 h. The solutions obtained in this way always contained undissolved halide, and for the kinetics, the halide solution was removed by syringe from above the undissolved material.

Added Cryptand Solutions.—The cryptands [2.1.1] and [2.2.2] were obtained from Merck, and were purified by bulb-to-bulb distillation under reduced pressure at 200 °C and 0.3 mmHg, and 170 °C at 0.3 mmHg, respectively, immediately before making up the solutions in DMSO. An appropriate amount of cryptand (*ca.* 100 mg) was quickly weighed into a gas-line flask, attached to the gas line, and the flask evacuated (0.5 mmHg). The vacuum was then released with argon, and DMSO (2 ml) added. The mixture was then stirred until all the cryptand dissolved, after which the solution was used as an 'added solution', as described above.

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