Model System for the Template Effect of Alkali and Alkaline-Earth Metal Ions on the Formation of Benzo-18-crown-6 in MeOH Solution[1]

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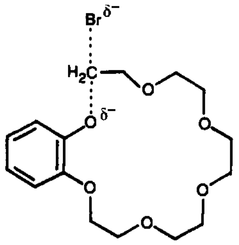
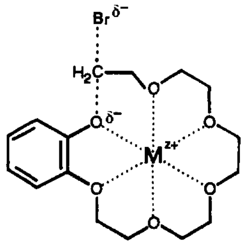
Abstract: Alkali and alkaline-earth metal ions exert a remarkable catalytic effect (template effect) on the cyclization of *o*-hydroxyphenyl 3,6,9,12-tetraoxa-14-bromotetradecyl ether (ArOH) to benzo-18-crown-6 (B18C6) in MeOH solution. This phenomenon is interpreted as resulting from two opposing factors, a rate-enhancing factor due to an increased proximity of chain ends in the cation-associated precursor ArO^- and a rate-retarding factor due to interaction of the nucleophilic end of ArO^- with the metal ion. Combination of previous equilibrium data with kinetic measurements from the present work provides a complete set of equilibrium constants for association of the seven cations Na^+, K^+, Rb^+, and Cs^+ and Ca^{2+}, Sr^{2+}, and Ba^{2+} with the four ligands ArOH, ArO^-, B18C6, and $T^{\ddagger}$, the latter being the transition state for cyclization. Following our earlier suggestion, according to which the proximity effect is viewed as a sort of macrocyclic effect, i.e., the one in which the cyclic ligand is $T^{\ddagger}$ and the acylic ligand is ArO^-, we now present an extrathermodynamic treatment indicating that the magnitude of the above macrocyclic effect is well represented by the K_{B18C6}/K_{ArOH} ratio. This ratio provides an estimate for the upper limit of the template effect. The actually observed values are lower by a factor of ca. 4 because of reduction of nucleophilicity due to cation association.

The base-promoted cyclization of *o*-hydroxyphenyl 3,6,9,12-tetraoxa-14-bromotetradecyl ether (ArOH) to benzo-18-crown-6 (B18C6) in MeOH solution is strongly accelerated by alkali (Na, K, Rb, and Cs) and alkaline earth (Ca, Sr, and Ba) metal ions[2] (template effect). The observed effects could be accounted for in terms of a 1:1 association between ArO^- and M^{z+} (Scheme I)

Beside the uncatalyzed reaction path proceeding through the transition state schematically depicted as $T^{\ddagger}$, an additional reaction path is available in the presence of the metal ions, the one passing through a transition state having the same composition as ArO^-M^{2+}. Arguments have been presented[3] in favor of a fully coordinated structure such as that given by $T^{\ddagger}M^{z+}$ for the transition state that contains M^{z+}. In all cases the reactivity of the ion-paired phenoxide ArO^-M^{z+} (k_{ip}) exceeds that of the unassociated phenoxide ArO^- (k_i), i.e., $k_{ip}/k_i > 1$.



$T^{\neq}$



$T^{\neq}M^{z+}$

In a qualitative description of the phenomenon, we suggested[2] to consider the operation of two opposing factors, (i) a rate-enhancing factor due to an increased *proximity* of chain ends in the cation-associated reactant ArO^-M^{z+} and (ii) a rate-retarding factor due to the expected reduction of the *inherent nucleophilicity* of the nucleophilic end of ArO^- because of cation pairing.

In order to obtain a separation of the two factors, an estimate of at least one of the two is needed. In a recent work on the template effect of alkali metal ions on the formation of B18C6 in 99% Me_2SO solution,[3] the nucleophilicity decrease of ArO^- upon cation pairing was estimated from model reactions. Although possible in principle, this does not seem a viable route in MeOH solution. Alternatively, an independent way to separate the two factors was suggested. It is based on an assessment of the proximity effect by means of comparison of rate data with equilibrium data for association of the metal ions with model ligands. These are ArOH and B18C6, which are taken as neutral models for the initial state, ArO^-, and the transition state, $T^{\ddagger}$, respectively. Thus, cation interaction with the transition state $T^{\ddagger}$ relative to that with the initial state ArO^- is assumed to be mimicked by cation interaction with the cyclic ligand B18C6 relative to that with the acyclic counterpart ArOH, i.e., by the ratio K_{B18C6}/K_{ArOH}, which is usually referred to as the macrocyclic effect.[4,5] However, the goodness of the model could not be properly tested, because of the unavailability of the K_{ArOH} values in Me_2SO solution. As equilibrium data are now available in MeOH solution[6] for associations involving the ligand *o*-$HOC_6H_4(OCH_2CH_2)_4OCH_3$ and its conjugate base, which can safely be assumed[7] to have ligation properties very close to those

Table I. Rate Constants at 25.0 °C and Activation Parameters for the Cyclization of ArO^-M^{z+} to B18C6 in MeOH Solution

metal ion	k, s^{-1} [a]	k_{ip}/k_i [b]	$\Delta H^{\ddagger}$, kcal/mol[c]	$\Delta S^{\ddagger}$, eu[c]
none	$(3.41 \pm 0.05) \times 10^{-7}$		24.3	−6.5
Na^+	$(2.07 \pm 0.01) \times 10^{-5}$	60.7	21.8	−7.0
K^+	$(6.79 \pm 0.09) \times 10^{-5}$	199	20.7	−8.3
Rb^+	$(1.66 \pm 0.01) \times 10^{-5}$	48.7	22.3	−5.8
Cs^+	$(5.84 \pm 0.07) \times 10^{-5}$	17.1	22.3	−7.6
Ca^{2+}	$(1.76 \pm 0.03) \times 10^{-5}$	51.6	20.9	−10.0
Sr^{2+}	$(4.05 \pm 0.01) \times 10^{-4}$	1190	18.3	−12.7
Ba^{2+}	$(1.14 \pm 0.00) \times 10^{-4}$	334	19.4	−11.6

[a] Runs in duplicate. The k value for the free-ion reaction is extrapolated from data at higher temperatures. These are $k = (1.45 \pm 0.01) \times 10^{-4}$ s^{-1} at 75.0 °C (this work), and the k value at 50.0 °C given in ref 2. [b] Specific rate of the metal ion catalyzed reaction relative to that of the uncatalyzed reaction. [c] Calculated from the present kinetic data and from those given in ref 2.

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(1) Part 5 in the series Template Effects. Part 4 in ref 3. A preliminary account of this work was presented at the Sixth IUPAC Symposium on Physical Organic Chemistry, Louvain-la-Neuve, Belgium, July 11-16, 1982.

(2) Ercolani, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1981**, *103*, 2780.

(3) Illuminati, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1983**, *105*, 555.

(4) Poonia, N. S.; Bajaj, A. V. *Chem. Rev.* **1979**, *79*, 389.

(5) Lamb, J. D.; Izatt, R. M.; Christensen, J. J.; Eatough, D. J. In "Coordination Chemistry of Macrocyclic Compounds"; Melson, G. A., Ed.; Plenum Press: New York, 1979.

(6) Ercolani, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1981**, *103*, 7484.

(7) The validity of this assumption is substantiated by available data in Me_2SO solution.[3]

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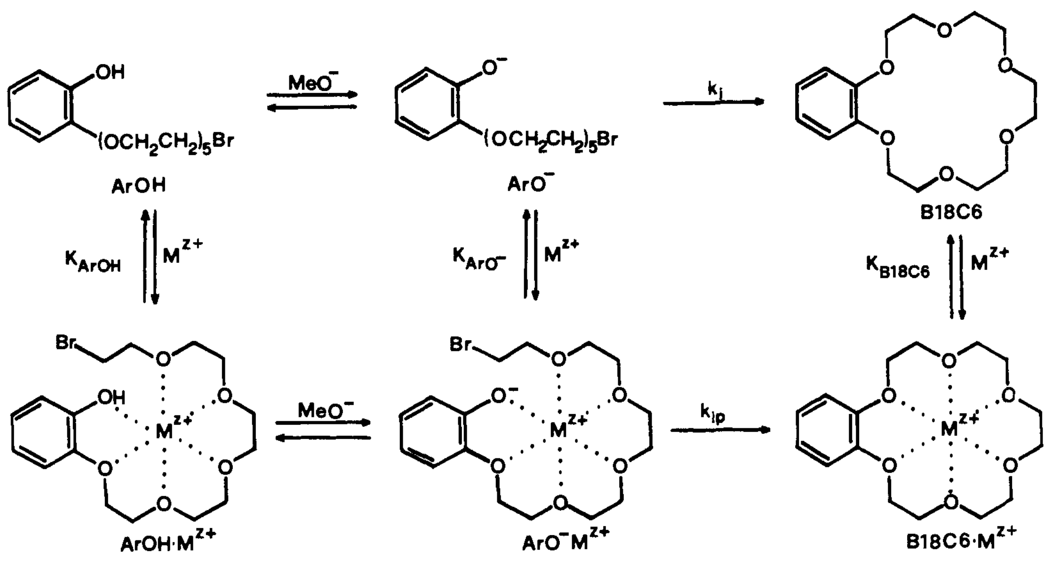
Scheme I



of ArOH and ArO$^-$, respectively, we can show how the macrocyclic effect formulation leads to a reliable assessment of the contribution of the two above-mentioned opposing factors.

Experimental Section

Rate measurements and product analyses in the kinetic runs were carried out as previously reported.[2]

The kinetics of the uncatalyzed reaction was carried out by a sealed-ampule technique.

Results and Discussion

Since our previous kinetic measurements[2] were carried out at 50.0 °C, whereas the equilibrium measurements were carried out at 25.0 °C,[6] rate constants at 25.0 °C have now been obtained (Table I). These were directly measured at 25.0 °C for the metal ion catalyzed reactions and extrapolated from data at higher temperatures for the uncatalyzed reaction. A complete chemical potential diagram can now be drawn for any of the metal-ion-catalyzed reactions. One example is shown in Figure 1.

Let $\Delta\mu_i^{\ddagger}$ and $\Delta\mu_{ip}^{\ddagger}$ be the standard potential of activation for the uncatalyzed and metal ion catalyzed reactions, respectively, and $\Delta\mu^\circ_{ArO^-}$ the standard potential change for association of M^{z+} to ArO$^-$. The standard potential change $\Delta\mu^\circ_{T^{\ddagger}}$ for association of M^{z+} to $T^{\ddagger}$ is given by

$$\Delta\mu^\circ_{T^{\ddagger}} = \Delta\mu_{ip}^{\ddagger} - \Delta\mu_i^{\ddagger} + \Delta\mu^\circ_{ArO^-} \quad (1)$$

which is easily demonstrated by inspection of Figure 1. The transition states $T^{\ddagger}$ and $T^{\ddagger}M^{z+}$ are in equilibrium in the sense that they appear simultaneously and in proportion corresponding to the equilibrium constant $K_{T^{\ddagger}}$[8,9]

$$K_{T^{\ddagger}} = \exp(-\Delta\mu^\circ_{T^{\ddagger}}/RT) \quad (2)$$

which may reasonably be called the ion pairing constant of $T^{\ddagger}$. Equation 1 can be written in the form

$$K_{T^{\ddagger}} = (k_{ip}/k_i)K_{ArO^-} \quad (3)$$

which provides a convenient operational definition of $K_{T^{\ddagger}}$. Thus, combining the present kinetic data with previous equilibrium data, a complete set of 28 equilibrium constants for associations of the seven cations Na$^+$, K$^+$, Rb$^+$, Cs$^+$, Ca^{2+}, Sr^{2+}, and Ba^{2+}, with the four ligands ArOH, ArO$^-$, $T^{\ddagger}$, and B18C6 is now available (Table II).

Owing to eq 3 the problem of the influence of the metal ion on reactivity resolves itself into questions of the response to the

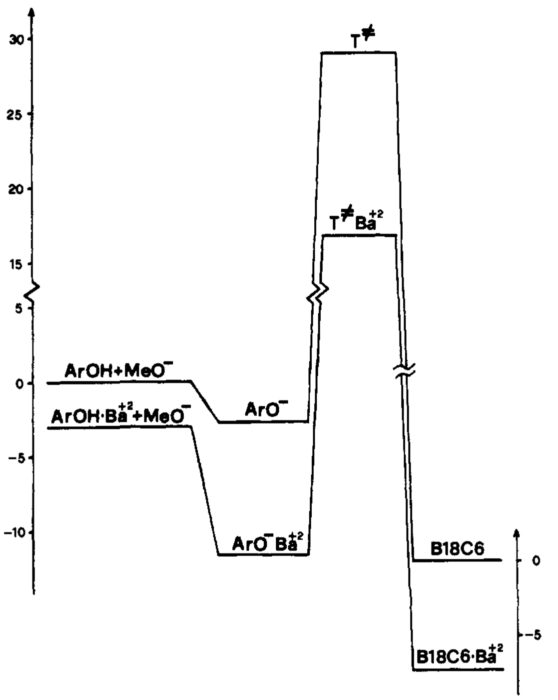


Figure 1. Standard potential diagram for uncatalyzed and Ba^{2+}-catalyzed formation of B18C6 in MeOH at 25.0 °C. Units in kilocalories per mole. Since the standard potential changes for cyclization are unknown, the two ordinates are independent from each other.

Table II. log K Values for Association of ArOH, ArO$^-$, $T^{\ddagger}$, and B18C6 with Alkali and Alkaline-Earth Metal Ions in MeOH at 25.0 °C

	log K_{ArOH}[a]	log K_{ArO^-}[a]	log $K_{T^{\ddagger}}$[b]	log K_{B18C6}[c]
Na$^+$	2.00	2.99	4.77	4.03
K$^+$	2.34	3.40	5.70	5.27
Rb$^+$	2.19	3.34	5.03	4.62
Cs$^+$	1.93	3.15	4.38	3.66
Ca^{2+}	1.20	6.20	7.91	3.50
Sr^{2+}	1.86	6.26	9.34	4.92
Ba^{2+}	2.18	6.43	8.95	5.35

[a] As based on the assumption that the ligation abilities of ArOH and ArO$^-$ are equal to those of o-$HOC_6H_4(OCH_2CH_2)_4OCH_3$ and its conjugate base, respectively. Data from ref 6. [b] Calculated according to eq 3. The k_{ip}/k_i values are given in Table I. [c] Data from ref 6.

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(8) Hammett, L. P. "Physical Organic Chemistry"; McGraw-Hill: New York, 1970; p 138.

(9) Rudakov, E. S.; Kozhevnikov, I. V.; Zamashichikov, V. V. *Russ. Chem. Rev. (Engl. Transl.)* **1974**, *43*, 305.

Table III. Negative Charge Effect and Macrocyclic Effect for Association of Alkali and Alkaline-Earth Metal Ions with a Series of Polyether Ligands

	negative charge effect		macrocyclic effect	
	$\log \frac{K_{ArO^-}}{K_{ArOH}}$	$\log \frac{K_{T^{\ddagger}}}{K_{B18C6}}$	$\log \frac{K_{B18C6}}{K_{ArOH}}$	$\log \frac{K_{T^{\ddagger}}}{K_{ArO^-}}$ [a]
Na^+	0.99	0.74	2.03	1.78
K^+	1.06	0.43	2.93	2.30
Rb^+	1.15	0.41	2.43	1.69
Cs^+	1.22	0.72	1.73	1.23
Ca^{2+}	5.00	4.41	2.30	1.71
Sr^{2+}	4.40	4.42	3.06	3.08
Ba^{2+}	4.25	3.60	3.17	2.52

[a] According to eq 3 the ratio $K_{T^{\ddagger}}/K_{ArO^-}$ is equal to k_{ip}/k_i.

metal ion of the relative ligation abilities of the ligands $T^{\ddagger}$ and ArO^-. It is clear from the data that interaction of the metal ions with the transition state is the strongest, i.e., $T^{\ddagger}$ is the best ligand out of the four species ArOH, ArO^-, $T^{\ddagger}$, and B18C6. These are all sexadentate oxygen ligands, but belong to different structural types. Both ArOH and ArO^- are open chained, but the former is neutral and the latter is a singly charged anion. Similarly, the cyclic ligands $T^{\ddagger}$ and B18C6 differ for the presence of a negative charge on the former. ArOH can be viewed as the acyclic counterpart of B18C6, so can ArO^- with respect to $T^{\ddagger}$, with the significant difference that the negative charge on $T^{\ddagger}$ is presumably more spread than that on ArO^-. That $T^{\ddagger}$ binds all the given cations more strongly than the other ligands is understandable, since $T^{\ddagger}$ is both cyclic and negatively charged. Cyclic multidentate ligands with certain ring sizes are well-known to bind cations more strongly than their cyclic counterparts (macrocyclic effect),[4,5] and the effect of a negative charge, though somewhat spread, should provide an additional driving force for association. These effects are easily analyzed when the data from Table II are put in the form shown in Table III.

As pointed out previously,[6] the effect of the negative charge on the K_{ArO^-}/K_{ArOH} ratio is largely dependent upon cation charge. It is relatively small—1 order of magnitude—for the monovalent cations, but increases to 4–5 powers of ten with the divalent cations. Much the same situation is found with the $K_{T^{\ddagger}}/K_{B18C6}$ ratios. Thus the increased stability of the $T^{\ddagger}M^{z+}$ pairs with respect to the $B18C6{\cdot}M^{z+}$ pairs primarily depends on those factors that make ArO^- a better ligand than ArOH. The $\log (K_{T^{\ddagger}}/K_{B18C6})$ values show the tendency to be lower than the $\log (K_{ArO^-}/K_{ArOH})$ values in a regular way, but some scatter is present. The quantity P, defined as

$$P = \log (K_{ArO^-}/K_{ArOH}) - \log (K_{T^{\ddagger}}/K_{B18C6}) \qquad (4)$$

is 0.62 ± 0.06 for the five cations K^+, Rb^+, Cs^+, Ca^{2+}, and Ba^{2+}. It is 0.25 for Na^+ and vanishingly small for Sr^{2+}. In spite of the fact that the uncertainities in the individual log K values may combine in an unfavorable way, the scatter for Sr^{2+} seems to be real, but the situation for Na^+ is uncertain. In any event, it seems very remarkable, but somewhat surprising (vide infra), that a single type of behavior is observed, irrespective of the monovalent or divalent nature of the metal ions.

As long as B18C6 and ArOH are good models for the ligation abilities of hypothetical neutral ligands having exactly the same structure and geometry of $T^{\ddagger}$ and ArO^-, respectively, the quantity P is easily interpreted as the loss of Coulombic stabilization on going from initial to transition state because of dispersal of the negative charge of ArO^- on a three-atom system in the reaction zone of the S_N2-type transition state. Combining eq 3 with eq 4, one obtains

$$\log (k_{ip}/k_i) = \log (K_{B18C6}/K_{ArOH}) - P \qquad (5)$$

Equation 5 relates the extent of catalysis by metal ions to available equilibrium data for metal ion associations in model systems. Also, it provides a pictorial interpretation of the template effect. Catalysis by metal ions on the formation of the crown ether is viewed as a manifestation of the macrocyclic effect due to the fact that $T^{\ddagger}$ is a cyclic ligand whereas ArO^- is acyclic. To a reasonable approximation the magnitude of this macrocyclic effect is given by (K_{B18C6}/K_{ArOH}). Apart from some deviant values, observed rate enhancements are lower than the K_{B18C6}/K_{ArOH} ratios by a factor of ca. 4 because of reduction of cation–anion interactions on going from initial to transition state. Thus, the K_{B18C6}/K_{ArOH} ratios set an upper limit to the extent of catalysis. This is well illustrated by a plot of $\log (k_{ip}/k_i)$ vs. $\log (K_{B18C6}/K_{ArOH})$ (Figure 2).[10]

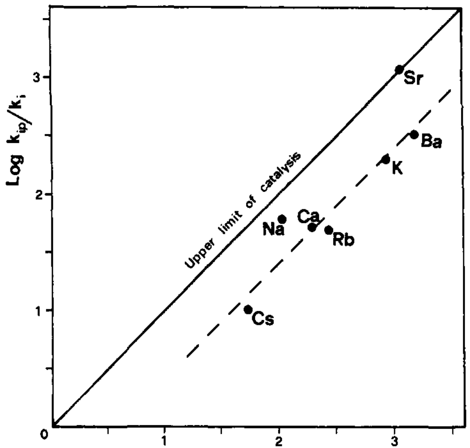

Figure 2. Catalysis by alkali and alkaline-earth metal ions in the formation of B18C6. Catalytic effect vs. macrocyclic effect in the model system B18C6/ArOH. The full line has zero intercept and unit slope. The broken parallel line is displaced downward by 0.6 log unit.

We also note that eq 5, describing the extent of catalysis as the algebraic sum of two independent quantities, puts into quantitative form our previous suggestion[2] that the template effect results from the superposition of a proximity effect and a chemical effect arising from cation pairing of the nucleophilic end of the reactant. The extrathermodynamic analysis on the basis of eq 4 is essentially equivalent to the assumption that the quantities $\log (K_{B18C6}/K_{ArOH})$ and P represent the effect of interaction of the metal ion outside and inside the reaction zone,[12] respectively. It seems therefore natural to take the former as a measure of the proximity effect, and the latter as a measure of the nucleophilicity decrease of the phenoxide upon ion pairing.

It might seem odd that the nucleophilicity decrease is the same irrespective of the charge of the metal ion. In fact, at first we expected a greater nucleophilicity decrease upon association with the alkaline-earth metal ions, because of the larger Coulombic stabilization of ArO^- upon association with a doubly charged cation than with a singly charged one. Evidence has been obtained[6] that the ArO^-M^{z+} pairs are solvent separated, possibly by one solvent molecule, as shown below. The bridging solvent molecule(s) weakens the interaction between the opposite charges. Were the ArO^-M^{z+} pairs contact pairs, their stability would be expected to exhibit a greater sensitivity to cation charge than that actually observed. But in the cavity of the transition state that contains M^{z+} there is no room for any solvent molecule, which renders it plausible to believe that the nucleophilic oxygen and the metal ion are in contact in $T^{\ddagger}M^{z+}$. Thus, as a tentative

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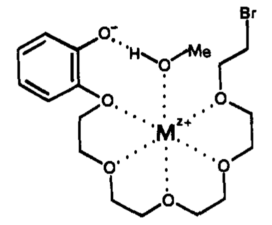
[10] Treating the previously published data[11] on the catalytic effects of Ba^{2+} and Sr^{2+} on the formation of B18C6 in water at 50 °C by means of eq 7 in ref 3, we calculate: $(k_{ip}/k_i) = 97$ and $K_{ArO^-} = 38$ M for Ba^{2+}; $(k_{ip}/k_i) = 80$ and $K_{ArO^-} = 28$ M for Sr^{2+}. Thus, in water solution the catalytic effectiveness of Sr^{2+} is slightly lower than that of Ba^{2+}, which is exactly what one could find in methanol if the Sr^{2+}-catalyzed reaction fitted to the linear correlation given by the dashed line of Figure 2. It appears therefore that the anomalous behavior of Sr^{2+} in methanol might well be due to solvation effects. But how and why solvation should act in the observed way is hard to understand.

[11] Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* 1977, *99*, 7709.

[12] For a definition of "reaction zone" see: Leffler, J. E.; Grunwald, E. "Rates and Equilibria of Organic Reactions"; Wiley: New York, 1963; p 140.

J. Am. Chem. Soc. 1983, 105, 6149-6151



explanation for the observed insensitiveness of the *P* values to cation charge, we postulate a situation in which the greater loss of Coulombic energy suffered during the activation process by the ArO^-M^{2+} pairs upon dispersion of the negative charge is exactly compensated by the greater gain of Coulombic energy due to contact pairing resulting from solvent extrusion.

By a similar reasoning one would predict a substantially larger decrease of the nucleophilicity of ArO^- upon contact pairing with M^{z+} than upon solvent-separated pairing. To this end it is interesting to compare the results from the present work with those obtained in connection with a study of the template effect of alkali metal ions on the formation of B18C6 in 99% aqueous Me_2SO.[3] In the essentially aprotic 99% Me_2SO, in which contact pairing occurs in the ArO^-M^+ pairs, the nucleophilicity decrease upon cation pairing could be measured on the basis of a proper model reaction. The reactivity of the ion pair was found to be ca. $^{1}/_{30}$ as large as that of the free ion in the case of sodium and ca. $^{1}/_{15}$ in the case of the heavier metal ions. When compared with the estimated fourfold drop of nucleophilicity of ArO^- upon cation pairing with the alkali-metal ions in MeOH solution, these data strongly argue in favor of the conclusion that loss of Coulombic energy on going from initial to transition state should be larger in the case of contact pairing in the initial state than in the case of solvent-separated pairing.

Proximity Effect. An Entropy Phenomenon?

On the basis of the simple consideration that a major contribution to the standard entropy of chain molecules arises from internal rotations around single bonds and that a significant fraction of this conformational entropy is presumably lost when the chain is wrapped around a metal template, one reaches the conclusion that the metal ion associated reactant should reach the transition state with a lesser entropic penalty than the unassociated reactant. However, as it often happens with polar reactions as carried out in polar solvents, a significant contribution to the observed thermodynamic quantities is made by solvation effects,[13] which can obscure the internal thermodynamic quantities of the reaction. This is also the case with the present reaction. Although the activation parameters (Table I) are but moderately accurate since they were obtained from two temperatures only, there seems to be no doubt that the expected entropic advantage of the metal ion catalyzed cyclizations over the uncatalyzed one does not show up in the measured $\Delta S^{\ddagger}$ values. This is not really surprising, as a significant desolvation of the phenoxide end during the activation process is likely to produce a positive $\Delta S^{\ddagger}_{\mathrm{solv}}$ term.[14] It seems also reasonable to postulate that the $\Delta S^{\ddagger}_{\mathrm{solv}}$ term is more positive for the uncatalyzed reaction than for the catalyzed ones, since the free phenoxide should be more heavily solvated than the ion-paired phenoxide. If this hypothesis is correct, one must conclude that for the alkali metal ion catalyzed cyclizations the $\Delta\Delta S^{\ddagger}_{\mathrm{solv}}$ and $\Delta\Delta S^{\ddagger}_{\mathrm{int}}$ contributions are opposite in sign and of comparable magnitude, with the net result that the $\Delta S^{\ddagger}$ values are similar to that of the uncatalyzed reaction. With the alkaline-earth metal ions the $\Delta\Delta S^{\ddagger}_{\mathrm{solv}}$ term predominates, thus yielding $\Delta S^{\ddagger}$ values appreciably more negative than the $\Delta S^{\ddagger}$ value for the uncatalyzed reaction. As a matter of fact, in both series the template effect turns out to be enthalpic in origin.

We may further note that also the thermodynamic macrocyclic effect related to polyether neutral ligands, which has served as a model for the template effect, might be expected to be entropic in origin as a result of the presumably smaller conformational entropy of the macrocycle as compared to the acyclic ligand. But experimental evidences not always fulfill this expectation and solvation contributions can be held responsible, at least in part, for the enthalpic origin of the effect as observed in many instances.[5]

Registry No. ArOH, 77963-49-6; B18C6, 14098-24-9; Na^+, 17341-25-2; K^+, 24203-36-9; Rb^+, 22537-38-8; Cs^+, 18459-37-5; Ca^{2+}, 14127-61-8; Sr^{2+}, 22537-39-9; Ba^{2+}, 22541-12-4.

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(13) Jencks, W. P. "Catalysis in Chemistry and Enzymology"; McGraw-Hill: New York, 1969; p 313.

(14) For an estimate of this contribution in 75% ethanol see: Illuminati, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1975**, *97*, 4960.

Communications to the Editor

Polyvalent Porphyrins. Properties of Tetrakis(3,5-di-*tert*-butyl-4-hydroxyphenyl)porphyrin (1-P) and Its Fe^{III} and Zn^{II} Derivatives

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The peroxidases react with hydrogen peroxide to cleave the O–O bond and produce a protohemin derivative that is $2e^-$ equiv more oxidized than the resting Fe(III) porphyrin.[2,3] Recent evidence suggests that at least one of the electrons is removed from the porphyrin π system to give a cation radical that is responsible for much of the electron transfer involved in substrate oxidations.[4,5] The radical nature of the intermediates has prompted us to investigate complexes of the porphyrin 1-P[6] in which advantage is taken of the steric protection afforded by the *tert*-butyl groups, which so effectively stabilizes species such as the tri-*tert*-butylphenoxyl radical.[7] 1-P was synthesized by the Rothemund procedure[8,9] and purified[10] by chromatography on silica with 1:1

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(1) On leave from the Department of Chemistry, University of Surrey, Guildford, Surrey GU2 5XH, U.K.

(2) George, P. *J. Biol. Chem.* **1953**, *201*, 413-426.

(3) Newson, W. D.; Hager, L. P. In "The Porphyrins"; Dolphin, D., Ed.; Academic Press: New York, 1979; Vol. 7, pp 295-332.

(4) Roberts, J. E.; Hoffman, B. M.; Rutter, R.; Hager, L. P. *J. Biol. Chem.* **1981**, *256*, 2118-2121.

(5) Schonbaum, G. R.; Lo, S. *J. Biol. Chem.* **1972**, *247*, 3353-3360.

(6) While this work was in progress the preparation of 1-P and its oxidation with ferricyanide were reported by Melezhik, A. V.; Pokhodenko, V. D. *Zh. Org. Khim.* **1982**, *18*, 1054-1056. However, the oxidized forms were not purified nor characterized and some of the proposed structures (e.g., that for 2-Zn) do not agree with our assignment.

(7) Ingold, K. U. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 1, pp 37-112.

(8) Badger, G. M.; Jones, R. A.; Lawlett, R. L. *Aust. J. Chem.* **1964**, *17*, 1028-1035.

(9) Kim, J. B.; Adler, A. D.; Longo, F. R. in "The Porphyrins"; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. 1, Part A, pp 85-100.

(10) The parent compounds 1-P, 1-Zn, and $1\text{-}Fe^{III}Cl$ were characterized by elemental analysis and mass, electronic, IR, and in the first two cases NMR spectroscopies. See also: Shroyer, A. L. W.; Lorberau, C.; Eaton, S. S.; Eaton, G. R. *J. Org. Chem.* **1980**, *45*, 4296-4302.

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