289 (2), 221 (20), 105 (100); ^{1}H NMR δ 7.5–6.7 (m, 9 H), 4.60 (br s, 1 H), 3.70 (br dd, J = 8, 2.5 Hz, 1 H), 2.50 (m, 1 H), 2.2 (m, 1 H), 1.95 (m, 1 H), 0.86 (m, 1 H), 0.52 (m, 2 H), 0.14 (m, 2 H) ppm.

The last (third) fraction yielded 10 mg of an oil whose GC indicated it to be the major product of the mixture (i.e., that comprising 50% of the adducts). This was identified as **15**: M$^+$ 289.1462, calcd 289.1466; ^{1}H NMR δ 7.5–6.7 (m, 9 H), 5.6 (br, 2 H), 4.88 (br s, 1 H), 3.71 (ddd, J = 4, 8, 11 Hz, 1 H), 2.4 (m, 2 H), 2.3 (m, 2 H), 2.0 (m, 2 H) ppm.

Registry No. 1, 1496-76-0; **11g**, 135733-81-2; **15**, 135733-80-1; **21a**, 135733-79-8; **27**, 135733-78-7; $Me_2C{=}CMe_2$, 563-79-1; $H_2C{=}CH(CH_2)_3CH{=}CH_2$, 3070-53-9; vinylcyclopropane, 693-86-7.

Effects of Metal Ions on the Equilibria of Methanol and Methoxide Ion Addition to Benzaldehydes. Effect of a Poly(oxyethylene) Side Arm

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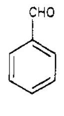
The effect of added alkali (Na, K) and alkaline-earth (Sr, Ba) metal bromides on the equilibria for the addition of methanol and methoxide ion to 2-(1,4,7,10,13-pentaoxatetradecyl)benzaldehyde (2) has been studied in methanol at 25 °C. Whilst alkali cations do not significantly perturb the above equilibria, alkaline-earth metal ions cause a dramatic increase of the equilibrium constant for the addition of methoxide ion (ca. 420 and 150 times in the presence of 0.1 M $SrBr_2$ and $BaBr_2$, respectively). A detailed study of the system afforded equilibrium constants for associations of metal ions with all of the species involved in the process. An analogous set of equilibrium measurements was carried out for comparison purposes with benzaldehyde (1). All of the added salts did not affect both the addition of methanol and methoxide ion to 1, thus indicating that a substantial contribution to the ligand ability of the hemiacetal anion of 2 arises from interaction of metal ions with at least some of the donor sites of the polyether side arm.

A large number of organic reactions are carried out in the presence of either alkali or alkaline-earth metal ions whose effects on reaction rates and equilibria are very often neglected or underestimated at best.[1] The principal obstacle to a detailed analysis of metal ion effects on organic reactions is due to the formation of aggregates of unknown composition and structure, which becomes important in solvents of low dielectric constant. On the other hand, in more polar solvents, associations with metal ions are weaker and not always recognizable. A possible approach to overcome this difficulty is to modify the substrate structure by adding a number of suitable coordinating sites capable of holding the metal ion in close proximity to the reaction center. Hopefully, the information gained about the interaction between metal ion and reaction zone will contribute also to the understanding of some of the many facets of supramolecular reactivity and catalysis.

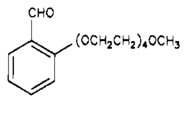
To date, only a limited number of reaction types have been studied in detail by this approach, namely, nucleophilic substitution,[2] base-induced methanolysis of esters,[3] and acid–base equilibria.[4] Here, we report a study of the effects of alkali (Na, K) and alkaline-earth (Sr, Ba) cations on the equilibria for the addition of methanol and methoxide ion to benzaldehyde (1) and to a substituted benzaldehyde bearing in ortho position a polyether chain (2).

Table I. Equilibrium Constants for the Formation of the Hemiacetals (K_{SH}) and Hemiacetal Anions (K_{S^-}) of Benzaldehydes 1 and 2 in MeOH at 25 °C

aldehyde	K_{SH}	K_{S^-}, mol^{-1} L
1	0.055	0.20
2	0.068	0.060



1



2

Results and Discussion

Equilibria in the Absence of Metal Ions. Benzaldehydes (a) in neutral and alkaline methanolic solutions undergo the reversible addition of methanol (eq 1) and methoxide ion (eq 2) to yield the corresponding hemiacetals (h) and hemiacetal anions (ha).[5,6] The formation

$$\underset{a}{ArCHO} \ (+\ MeOH) \xrightleftharpoons{K_{SH}} \underset{h}{ArCH(OMe)OH} \qquad (1)$$

$$\underset{a}{ArCHO} + MeO^- \xrightleftharpoons{K_{S^-}} \underset{ha}{ArCH(OMe)O^-} \qquad (2)$$

of acetals, rather than hemiacetals, is known to occur in

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[1] (a) Gordon, J. E. *The Organic Chemistry of Electrolyte Solutions*; Wiley: New York, 1975. (b) Loupy, A.; Tchoubar, B. *Effects de Sels en Chimie Organique et Organométallique*; Dunod: Paris, 1988.

[2] Illuminati, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1983**, *105*, 555–563.

[3] (a) Ercolani, G.; Mandolini, L. *J. Am. Chem. Soc.* **1990**, *112*, 423–427. (b) Cacciapaglia, R.; Lucente, S.; Mandolini, L.; van Doorn, A. R.; Reinhoudt, D. N.; Verboom, W. *Tetrahedron* **1989**, *45*, 5293–5304.

[4] Ercolani, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1981**, *103*, 7484–7489.

[5] Crampton, M. R. *J. Chem. Soc., Perkin Trans. 2* **1975**, 185–189.

[6] Arora, M.; Cox, B. G.; Sørensen, P. E. *J. Chem. Soc., Perkin Trans. 2* **1979**, 103–107.

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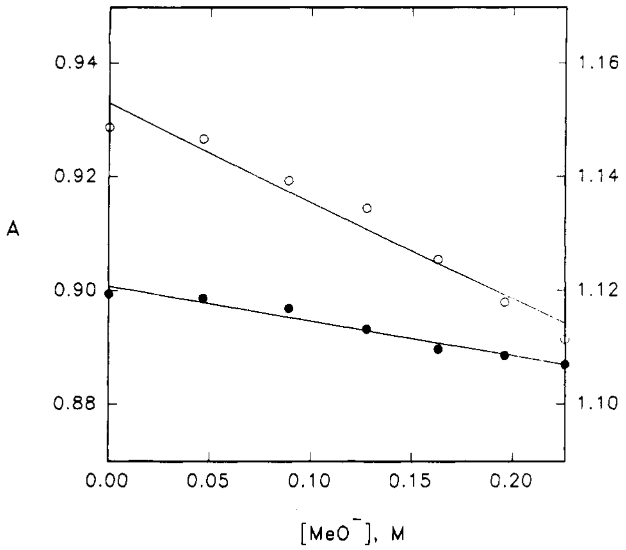


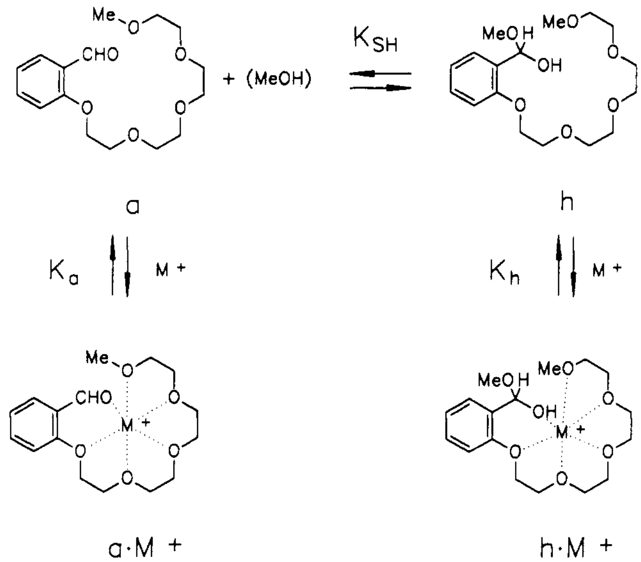
Figure 1. Absorbance of the aldehydes **1** (○, left scale) and **2** (●, right scale) as a function of methoxide ion concentration.

acidic solutions but not in neutral or basic media.[7]

The equilibrium constants K_{SH} (= [h]/[a]) for the aldehydes **1** and **2** were determined in CD_3OD at 25 °C by FT ^1H NMR. Since the equilibrium between h and a is slow on the NMR time scale, the two species give rise to distinct resonance signals. The ratio of the areas under the peaks of the aldehydic and hemiacetalic CH proton gave the K_{SH} values listed in Table I.[8] The data for benzaldehyde compares fairly well with those reported in the literature (0.090;[5] 0.038[9]) that were obtained in CH_3OH by indirect methods.

The equilibrium constants K_{S^-} for the benzaldehydes **1** and **2** were evaluated spectrophotometrically in MeOH at 25 ± 0.1 °C by measuring the absorbance of a solution of the aldehyde at increasingly greater concentrations of Me_4NOMe (up to ca. 0.2 M). Tetramethylammonium was the counterion of choice because any association with the species appearing in eqs 1 and 2 is unlikely. Experiments were completed within 1 h of dissolution of the benzaldehydes. In this time no appreciable decomposition by the Cannizzaro reaction or methoxide reduction occurred.[10] Measurements were carried out in correspondence of the absorption maxima of the aldehydes; at 244 nm for compound **1** and at 318 nm for compound **2**. Because at these wavelengths the corresponding acetals did not show any significant absorbance,[11] it was assumed that also the corresponding hemiacetals and hemiacetal anions do not absorb. It was assumed, moreover, that, up to ca. 0.2 M ionic strength activity coefficients of neutral species are unity whereas activity coefficients of similarly charged ions are equal.[12] Taking into account the above assumptions, the absorbance A of the aldehyde is related to methoxide ion concentration by eq 3, where A_0 is the absorbance of the aldehyde in equilibrium with the hemiacetal, under neutral conditions. The constant K_{S^-} was obtained by a

Scheme I



$$A = \frac{A_0(1 + K_{SH})}{1 + K_{SH} + K_{S^-}[\mathrm{MeO^-}]} \tag{3}$$

nonlinear least-squares treatment of the data according to eq 3, considering A_0 and K_{S^-} as adjustable parameters and K_{SH} as a known term. Typical experimental results for the two aldehydes together with the corresponding calculated curves are reported in Figure 1. Such curves are practically straight lines because of the low conversion of the aldehydes into the corresponding hemiacetal anions, even at the highest concentrations of MeO^-. In fact, a Maclaurin series expansion of eq 3 truncated at the term of first degree (eq 4) fits the experimental points equally well. The obtained values of K_{S^-} are listed in Table I.

$$A = A_0 - \frac{A_0K_{S^-}}{1 + K_{SH}}[\mathrm{MeO^-}] \tag{4}$$

Despite the small absorbance variations, the data were quite reproducible and are believed to be accurate within ±20%. The constant K_{S^-} for the benzaldehyde was previously evaluated by ^1H NMR measurements in more concentrated methoxide ion solutions (up to ca. 3 M).[5] The reported value (0.14 ± 0.01 mol^{-1} L) satisfactorily agrees with that obtained in the present work.

In conclusion, it appears that in the absence of metal cations, the benzaldehydes **1** and **2** show a similar behavior toward the addition of methanol and methoxide ion, as indicated by the K_{SH} values that are practically coincident and by the K_{S^-} values that differ by less than a factor of 4.

Equilibria in the Presence of Metal Ions under Neutral Conditions. Before considering the effects of alkali and alkaline-earth metal ions on the equilibria (1) and (2) a comment about their ion-pairing properties in methanol solution is needed. Whilst alkali metal salts generally behave as strong electrolytes,[13] the picture is more complicated with alkaline-earth metal salts. The difficulty arises from the fact that divalent metal ions are presumably strongly associated in methanol solution, but

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[7] Bell, J. M.; Kubler, D. G.; Sartwell, P.; Zepp, R. G. *J. Org. Chem.* **1965**, *30*, 4284.

[8] It has been reported[5] that only benzaldehydes containing electron-withdrawing groups yield sufficient amounts of hemiacetal to allow accurate determination of K_S by integration of peak areas. However, this statement was referred to measurements carried out with old CW NMR spectrometers.

[9] Fuchs, R.; Young, T. M.; Rodewald, R. F. *Can. J. Chem.* **1973**, *51*, 4122–4124.

[10] Swain, C. G.; Powell, A. L.; Lynch, T. J.; Alpha, S. R.; Dunlap, R. P. *J. Am. Chem. Soc.* **1979**, *101*, 3584–3587.

[11] UV spectra of the acetals were obtained from methanolic solutions of the aldehydes ca. 1 × 10^{-4} M in the presence of HBF_4 ca. 1 × 10^{-3} M.

[12] An example of the validity of this assumption can be found in ref 4.

[13] Notable exceptions are found with counterions such as NO_3^- and ClO_4^- probably due to the existence of chelate interactions: Fernândez-Prini, R. In *Physical Chemistry of Organic Solvent Systems*; Covington, A. K., Dickinson, T., Eds.; Plenum: London, 1973; pp 568–571.

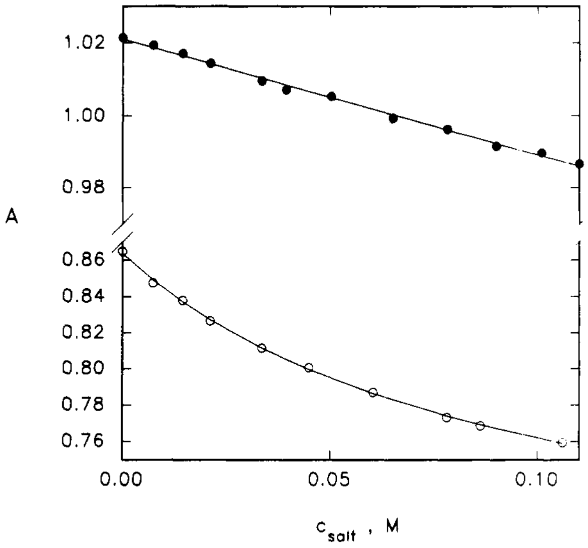

Figure 2. Absorbance of the aldehyde 2 as a function of the concentration of NaBr (●) and of BaBr$_2$ (○).

the pertinent association constants are generally unknown. A plausible simplifying assumption, that proved to be useful in previous work,[3,14] is to consider the alkaline-earth cations present in solution as monoassociated singly charged species of the type (MX)$^+$.

In the absence of added methoxide ion, formation of the hemiacetal anion can be neglected. The relevant equilibria, illustrated in Scheme I for the case of aldehyde 2, involve only 1:1 associations of the species a and h with the metal ions. The symbol M$^+$ in Scheme I stands either for Na$^+$, K$^+$ or for (SrBr)$^+$, (BaBr)$^+$, in that the alkaline-earth cations were added as bromides.

^{1}H NMR spectra of the two aldehydes were recorded in CD$_3$OD in the presence of 0.1 M Me$_4$NBr, NaBr, KBr, SrBr$_2$, or BaBr$_2$. The spectra for benzaldehyde did not show any change with respect to the spectrum recorded in the absence of salts, whereas the spectra for the compound 2, with the exception of that recorded in the presence of Me$_4$NBr, showed some chemical shift variations (see Experimental Section). These variations are seemingly due to fast equilibrium associations, on the NMR time scale, of the species a and h with the metal ions. However, the ratio of the integrated peak areas of hemiacetalic and aldehydic protons was in all of the cases coincident with the K_{SH} value. In order to put this result in the proper perspective, it is useful to make use of the concept of primitive concentration.[15] In the present case this is referred to the total concentration of a species, irrespective of the various forms actually present in solution through the establishment of association equilibria with a metal ion. Therefore, the peak ratio determined in the presence of metal salts is the primitive value of the constant K_{SH} (K_{SH}*), in that it is operationally defined in terms of the primitive concentrations of a and h ($K_{SH}^* = [h^*]/[a^*]$ where $[a^*] = [a] + [aM^+]$, and $[h^*] = [h] + [hM^+]$). The ratio K_{SH}^*/K_{SH}, which provides a measure of the effect of the metal ions on the hemiacetal formation, is related to the metal ion concentration by eq 5. Equation

$$\frac{K_{SH}^*}{K_{SH}} = \frac{1 + K_h[M^+]}{1 + K_a[M^+]} \qquad (5)$$

Table II. Association Constants for the Species Involved in the Addition of MeOH and MeO$^-$ to 2 at 25.0 °C[a,b]

metal ion	log K_a (≈log K_h)	log K_{ha}	log K_{MeO}
Na$^+$			
K$^+$	1.08 ± 0.06	(≈log K_a)	
Sr^{2+}		4.7 ± 0.2[c]	2.0 ± 0.2[c]
Ba^{2+}	1.04 ± 0.04	4.2 ± 0.1[c]	1.6 ± 0.1[c]

[a] The values of the association constants not reported are to be considered significantly lower than 10 mol^{-1} L. [b] Reported errors are standard deviations as obtained from the regression analysis. [c] Conditional constant that holds for solutions having the same ionic composition as that used for the experimental evaluation of the constant (see text).

5 is based on the assumption that activity coefficients of neutral species are unity and that $\gamma_{aM^+} = \gamma_{hM^+} = \gamma_{M^+}$. Because in the present cases $K_{SH}^*/K_{SH} = 1$, the constants K_h and K_a are either very similar or very small. UV spectra of the two aldehydes in 0.1 M solutions of the above salts were fully consistent with the NMR observations. Benzaldehyde did not show any spectral change, whereas the compound 2 showed small, but measurable, spectral changes in the presence of the metal salts. Both NMR and UV evidences led us to the conclusion that, in contrast with the compound 2, benzaldehyde is completely not associated with the metal cations. In order to evaluate the association constants K_a and K_h for the compound 2, we found it more convenient to exploit the UV rather than the NMR changes because of the greater sensitivity of the spectrophotometric technique. Experiments were carried out at 25 ± 0.1 °C by measuring the absorbance at 318 nm of a solution of the aldehyde 2 at increasingly greater concentrations of the given metal bromide (up to ca. 0.1 M). The absorbance is related to the metal ion concentration by eq 6, where A_∞ stands for the limit value to which the ab-

$$A = \frac{A_0 + A_\infty K_a[M^+]}{1 + K_a[M^+]} \qquad (6)$$

sorbance tends when the metal ion concentration tends, in strict mathematical terms, to infinity. A derivation of eq 6 is presented in Appendix 1. Since the fraction of metal ion sequestered by the neutral species a and h is negligibly small, in view of their low concentration, [M$^+$] can be set equal to the analytical concentration of the salt, c_{salt}. A nonlinear least-squares fitting procedure of the experimental data according to eq 6, considering A_0, A_∞, and K_a as adjustable parameters, proved to be effective in the case of potassium and barium, but an unacceptable high degree of correlation between A_∞ and K_a was found in the case of sodium and strontium. Plotting the experimental data one notes that, in contrast with potassium and barium, the data points for strontium and sodium practically lie along straight lines. Sodium and barium curves are shown, for comparison, in Figure 2. The different behavior is due to the fact that in the case of sodium and strontium, the constant K_a is significantly lower than 10 mol^{-1} L.[16] A Maclaurin series expansion of eq 6 truncated at the term of first degree (eq 7) correctly fits the experimental data for sodium and strontium. Of

$$A = A_0 + (A_\infty - A_0)K_a[M^+] \qquad (7)$$

course, while in the case of potassium and barium it was

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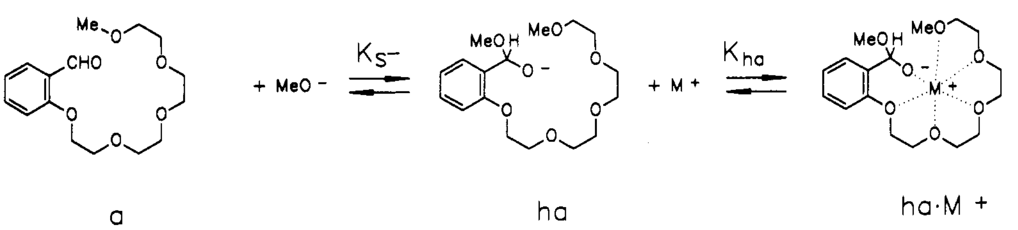
(14) (a) Cacciapaglia, R.; Mandolini, L. *J. Org. Chem.* **1988**, *53*, 2579–2582; (b) *Tetrahedron* **1990**, *46*, 1353–1366.

(15) Hammett, L. P. *Physical Organic Chemistry*; McGraw-Hill: New York, 1970; p 16.

(16) This can be shown considering the Maclaurin series expansion of eq 6 truncated at the term of second degree: $A = A_0 + (A_\infty - A_0)K_a[M^+] - (A_\infty - A_0)K_a^2[M^+]^2$. The absence of deviation from linearity indicates that the second-order term is negligible with respect to the first order one, i.e., $|A_\infty - A_0|K_a[M^+] \gg |A_\infty - A_0|K_a^2[M^+]^2$. Cancelling out and considering that $[M^+] \leq 0.1$ M, it follows that eq 7 holds when $K_a \ll 10$ mol^{-1} L.

Scheme II



possible to evaluate the constant K_a (Table II), in the case of sodium and strontium only the composite term $(A_\infty - A_0)K_a$ was affordable, by linear regression analysis.

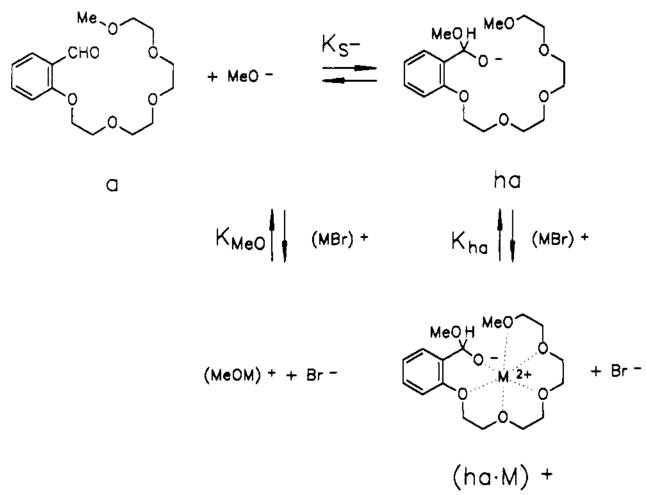
In conclusion, while the simple benzaldehyde and the corresponding hemiacetal did not show any tendency to associate with the metal salts, clear experimental evidences for the association of **2** were gathered for all of the cations, but the relevant association constants turned out to be very small. The constants for potassium and barium were of the order of 10 mol^{-1} L, whereas in the case of sodium and strontium the associations were so low that a significant measurement could not be obtained. The same considerations also hold for the corresponding hemiacetal in that from the NMR measurements $K_h \approx K_a$ for all the examined cations.

Equilibria in the Presence of Metal Ions under Basic Conditions. Now, let us consider the experiments carried out in the presence of a fixed methoxide ion concentration, first taking into account the effects of the alkali metal ions. In the presence of methoxide ion and of an alkali cation, besides the equilibria shown in Scheme I, also the equilibria shown in Scheme II must be considered. Experiments were carried out in MeOH at 25 ± 0.1 °C by measuring the absorbance of a dilute solution of the aldehyde containing Me_4NOMe (4.00×10^{-2} M) and Et_4NBr (0.110 M) after progressive additions of small aliquots of a 0.110 M solution of NaBr (or KBr) containing Me_4NOMe (4.00×10^{-2} M). By this procedure ionic strength was held constant (= 0.15 M) throughout the experiments, thus avoiding complications due to variations of activity coefficients in the expression of K_{ha}. In the case of benzaldehyde the absorbance, corrected for dilution, did not change, thus indicating that the constant K_{ha} for sodium and potassium is negligible. In the case of the aldehyde **2**, the absorbance variations were only due to the formation of the complex aM^+, thus indicating that these cations do not perturb both the addition of methanol (vide supra) and of methoxide ion. This means that in the case of NaBr and KBr, the primitive constant $K_{S^-}{}^*$ is equal to the constant K_{S^-} measured in the absence of metal salts. Since eq 8 holds, the constant K_{ha} is similar to the constant K_a in the case of potassium and very small in the case of sodium.

$$\frac{K_{S^-}{}^*}{K_{S^-}} = \frac{1 + K_{ha}[M^+]}{1 + K_a[M^+]} \tag{8}$$

In the case of the alkaline-earth metal ions, besides the equilibria shown in Scheme I, also the equilibria shown in Scheme III must be considered. Experiments were carried out by measuring the absorbance of a set of solutions containing the aldehyde, Me_4NOMe (4.00×10^{-2} M), variable amounts of $SrBr_2$ (or $BaBr_2$) up to 0.1 M, and variable amounts of Et_4NBr to adjust the total salt concentration to 0.15 M. These conditions were aimed at keep both ionic strength and bromide ion concentration essentially constant. It is useful to introduce the conditional constants $\bar{K}_{ha}$ and $\bar{K}_{MeO}$ coincident with $K_{ha}/[Br^-]$ and $K_{MeO}/[Br^-]$, respectively. Assuming that the constant for

Scheme III



the association of a with $(MOMe)^+$ is equal to the value of K_a obtained with $(MBr)^+$, one can easily obtain eq 9, where c_{salt} (= $[(MBr)^+] + [(MOMe)^+]$) is the analytical concentration of the alkaline-earth cation under investigation. Specifying $[(MBr)^+]$ in eq 9 as a function of c_{salt},

$$\frac{K_{S^-}{}^*}{K_{S^-}} = \frac{1 + \bar{K}_{ha}[(MBr)^+]}{(1 + K_a c_{salt})(1 + \bar{K}_{MeO}[(MBr)^+])} \tag{9}$$

c_{MeO} (= 4.00×10^{-2} M), and $\bar{K}_{MeO}$, one obtains eq 10, where $J = 1 + \bar{K}_{MeO}(c_{MeO} - c_{salt})$. The primitive constant $K_{S^-}{}^*$

$$\frac{K_{S^-}{}^*}{K_{S^-}} = \frac{1 + (\bar{K}_{ha}/2\bar{K}_{MeO})[-J + (J^2 + 4\bar{K}_{MeO}c_{salt})^{1/2}]}{(1 + K_a c_{salt})[1 + [-J + (J^2 + 4\bar{K}_{MeO}c_{salt})^{1/2}]/2]} \tag{10}$$

is obtained from the absorbance readings as described in Appendix 2. Let us consider first the experiments carried out with compound **2**. Nonlinear least-squares curve fitting of the experimental data to eq 10, considering $\bar{K}_{ha}$ and $\bar{K}_{MeO}$ as adjustable parameters, was remarkably good (Figure 3) despite the many, perhaps rough, approximations involved in the treatment. Note that in the case of strontium, the constant K_a appearing in eq 10 is negligible, whereas in the case of barium it is a known term (11 mol^{-1} L). This causes eq 10 to describe qualitatively different profiles for the two cations. Indeed, while on increasing the concentration of $SrBr_2$ the ratio $K_{S^-}{}^*/K_{S^-}$ should tend to a plateau value coincident with $\bar{K}_{ha}/\bar{K}_{MeO}$, on increasing the concentration of $BaBr_2$ the ratio $K_{S^-}{}^*/K_{S^-}$ should reach a maximum and then decrease. As a matter of fact, the experimental points in the case of strontium do not permit to verify this prediction; however, in the case of barium a maximum is clearly discernible (see Figure 3). The effects of strontium and barium salts on the methoxide addition to the aldehydic group is remarkable. Indeed as shown in Figure 3, at the maximum concentrations of $SrBr_2$ and $BaBr_2$ the constant $K_{S^-}{}^*$ is, respectively, ca. 420 and 150 fold greater than K_{S^-}. The values of the constants

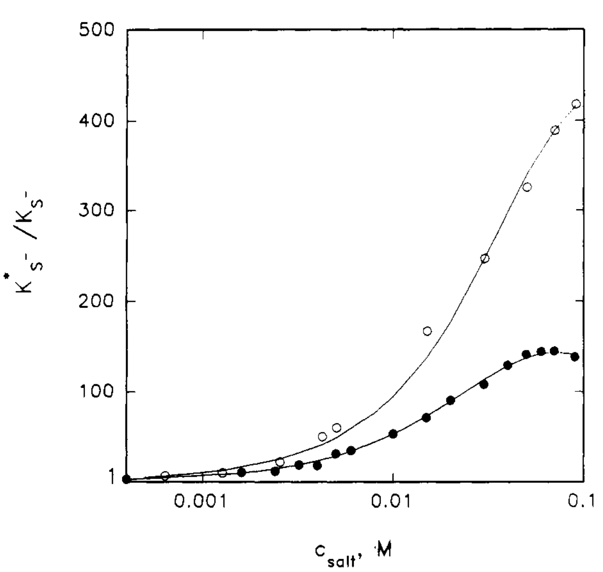


Figure 3. Effect of $SrBr_2$ (○) and $BaBr_2$ (●) on the Equilibrium for the Formation of the Hemiacetal Anion of **2**.

$\bar{K}_{ha}$ and $\bar{K}_{MeO}$ for strontium and barium are listed in Table II. The constants $\bar{K}_{MeO}$ are in good agreement with those obtained by a kinetic study on the base-induced methanolysis of esters in solutions of similar ionic composition.[3b]

In the case of benzaldehyde, the same absorbance was measured irrespective of the concentration of $SrBr_2$ or $BaBr_2$, thus indicating that K_{S^-}* is equal to K_{S^-}. Considering that in the case of benzaldehyde K_a is always negligible, eq 10 indicates that $\bar{K}_{ha}$ is equal to $\bar{K}_{MeO}$ for both strontium and barium.

In order to discuss the observed phenomena, let us consider the simple benzaldehyde **1** as the reference compound for the evaluation of the effect of the polyether side arm present in **2**. As expected, all the species involved in the reaction of benzaldehyde did not show any tendency to associate with the metal salts, the only notable exception being the hemiacetal anion that binds the alkaline-earth cations as strongly as MeO^- (see Table II for $\bar{K}_{MeO}$ constants). Evidently, the driving force for the association is provided in both the anionic species only by the negative charge localized on the oxygen atom, without any participation of the geminal methoxy group in the hemiacetal anion, which in principle could behave as an additional donor site.

Let us now consider the association constants of the species involved in the reaction of the aldehyde **2**. As far as the alkali cations are concerned, the ligand ability of the hemiacetal anion is similar to that of the neutral hemiacetal. This, although might appear as surprising, would indicate that the presence of a negative charge does not bring on a more significant coordination of the alkali cations with respect to the neutral hemiacetal. A previous study[4] on the acid–base equilibria of a phenol having the same polyether chain showed that the corresponding phenoxide ion binds sodium and potassium ions about 10 times better than the neutral phenol. Two advantages of the phenoxide ion over the hemiacetal anion of **2** can be envisaged: one due to the symmetrical placement of the negative oxygen atom in the favorable 1,4 alternation of donor sites[17] and the other due to the reduced conformational freedom of the negative oxygen atom. A possible disadvantage due to the reduced basicity of the phenoxide ion as compared to the hemiacetal anion is probably compensated by a lighter solvation. In light of this comparison the poor ligand ability of the hemiacetal anion toward Na^+ and K^+ seems not to be so strange. By contrast, the hemiacetal anion of **2** behaves as a good ligand for the alkaline-earth cations. This is consistent with expectations because of the greater coulombic interaction between the negative charge of the ligand and the doubly charged cations. However, the effect of strontium and barium salts on the addition of methoxide ion to the aldehydic group depends not only on the association of the hemiacetal anion but also on that of MeO^-, the two associations having opposite effects on the constant K_{S^-}*. In particular, since the former is a better ligand than the latter (see Table II) an increase of the constant K_{S^-}* is observed. There is little doubt that the advantage of the hemiacetal anion over methoxide is due to the additional binding sites for the metal ion provided by at least some of the oxygen donors of the polyether side arm.

Conclusions

In the absence of metal cations, the benzaldehydes **1** and **2** show a similar behavior toward the addition of methanol and methoxide ion. When in the presence of the alkali cations, the two aldehydes still behave similarly ($K_{SH}^* \approx K_{SH}$ and $K_{S^-}^* \approx K_{S^-}$), but a dramatic difference of behavior is observed when the reaction is carried out in the presence of the alkaline-earth cations. The difference does not regard the addition of methanol, but rather that of methoxide ion which is strongly favored in the case of the compound **2** (ca. 420 and 150 times in the presence of 0.1 M $SrBr_2$ and $BaBr_2$, respectively). These results prove that the presence of a suitably placed poly(oxyethylene) chain can enhance the effect of cations on the addition of methoxide ion to the formyl group.

Experimental Section

^1H NMR spectra were recorded with a Bruker WP-80 SY spectrometer. Chemical shifts were quoted in ppm relative to TMS. High-resolution EI mass spectra were obtained with a Kratos MS-80 spectrometer. Spectrophotometric measurements were carried out in the thermostated cell compartments of a Varian Cary 219 instrument; temperature control was within ±0.1 °C.

Materials. AR-grade methanol (water content lower than 0.08%) and AR-grade NaBr, KBr, $SrBr_2{\cdot}H_2O$, and $BaBr_2{\cdot}2H_2O$ were used without further purification. Tetramethylammonium hydroxide (25 wt % solution in methanol) was from Janssen; methanolic stock solutions of the base were titrated with standard acid. AR-grade Me_4NBr and Et_4NBr were dried in vacuo at 110 °C. Benzaldehyde was distilled in vacuo. 3,6,9,12-Tetraoxatridecyl tosylate was prepared by a literature procedure.[18] All of the materials were stored and handled under argon. Solutions were freshly prepared.

2-(1,4,7,10,13-Pentaoxatetradecyl)benzaldehyde (2). To a mixture of salicylaldehyde (1.83 g, 15 mmol), 3,6,9,12-tetraoxatridecyl tosylate (4.71 g, 13 mmol), and 30 mL of distilled THF was added, under stirring, a solution of tetramethylammonium hydroxide (7 mL of the 25 wt % solution in MeOH, 14 mmol) in 8 mL of THF. When the addition was complete, the mixture was refluxed for 2.5 h. After being cooled to room temperature the reaction solution was poured into 200 mL of 10% NaOH aqueous solution and extracted with ethyl ether. The ethereal extracts were washed with water and dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to give a viscous oil that was purified by flash chromatography (silica gel, benzene/ethyl acetate (35:65)): yield 32%; ^1H NMR ($CDCl_3$, 80 MHz) 10.40 (d, J = 0.66 Hz, 1 H, CHO), 7.8–6.9 (m, 4 H, ArH), 4.3–4.1

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[18] Ouchi, M.; Inoue, Y.; Wada, K.; Iketani, S.; Hakushi, T.; Weber, E. *J. Org. Chem.* **1987**, *52*, 2420–2427.

(m, 2 H, ArOC*H*$_2$CH$_2$), 4.0–3.8 (m, 2 H, ArOCH$_2$C*H*$_2$), 3.8–3.4 (m, 12 H, $(OCH_2CH_2)_3O$), 3.34 (s, 3 H, CH$_3$); UV λ_{max} (MeOH) 318 nm; HRMS calcd for $C_{16}H_{24}O_6$ 312.1573, found (*m/z*) 312.1562.

^{1}H NMR Measurements. ^{1}H NMR spectra of the compounds **1** and **2**, concentration 0.04 M, were recorded in CD_3OD at 25 °C. The chemical shifts of the aldehydic and hemiacetalic protons were, respectively, the following: **1**, 10.00 and 5.51 ppm; **2**, 10.46 and 5.82 ppm. ^{1}H NMR spectra of the compounds **1** and **2** were also recorded in the presence of Me_4NBr, NaBr, KBr, $SrBr_2$, $BaBr_2$, concentration 0.1 M. Some chemical shift variations were observed for the compound **2** in the presence of the metal salts, the most significant being that related to the aldehydic proton. The chemical shift of the latter in the presence of the metal salts was the following: NaBr, 10.42 ppm; KBr, 10.34 ppm; $SrBr_2$, 10.39 ppm; $BaBr_2$, 10.31 ppm. Values of K_{SH} and K_{SH}^* were obtained from integrated peak areas of aldehydic and hemiacetalic protons. The equilibrium position was reached within the time necessary to prepare the samples and record the spectra (a few minutes).

Spectrophotometric Measurements. The evaluation of the equilibrium constants K_{S^-} was carried out spectrophotometrically at 25.0 °C in 10-mm quartz cuvettes. The aldehyde concentration in the cuvette was in the order of 7×10^{-5} M for compound **1** and 3×10^{-4} M for compound **2**. Increasing amounts of 1 M Me_4NOMe solution were stepwise dispensed to both the sample and reference cuvettes by means of a mycrosyringe, with care being taken to minimize contamination by atmospheric CO_2. After each addition the absorbance value at 244 nm for compound **1** and at 318 nm for compound **2** was recorded with allowance being made for thermal equilibration. Volume additivity was assumed to calculate the methoxide ion concentration in the cuvette and to correct the observed OD value for dilution.

A strictly analogous experimental procedure was adopted for the experiments carried out in the absence of added methoxide ion, but in the presence of metal salts, the only difference was in the composition of the added solution, which was ca. 0.3 M NaBr, $SrBr_2$, or $BaBr_2$ or 0.1 M KBr. Details of the experiments carried out in the presence of methoxide ion and metal salts are given in the Results.

Appendix 1

A derivation of eq 6 is presented here. At 318 nm the absorbance is due to the independent contributions of the free and associated aldehyde in accordance with eq 11,

$$A = [a](\epsilon_a + \epsilon_{aM}K_a[M^+]) \qquad (11)$$

where ϵ_a and ϵ_{aM} stand for the molar extinction coefficients of a and aM^+, respectively. A useful expression for [a] can be obtained considering that the analytical concentration of the aldehyde c_a (= [a*] + [h*]) can be expressed by eq 12. Considering that, from the NMR experiments, K_{SH}^*

$$c_a = [a^*](1 + K_{SH}^*) \qquad (12)$$

= K_{SH} up to 0.1 M concentration of the metal salts, and taking into account eq 13, eq 12 can be rewritten in the form of eq 14. Substitution of eq 14 into eq 11 yields eq

$$[a^*] = [a](1 + K_a[M^+]) \qquad (13)$$

$$[a] = \frac{c_a}{(1 + K_a[M^+])(1 + K_{SH})} \qquad (14)$$

15. When $[M^+] = 0$, eq 15 becomes $A_0 = c_a\epsilon_a/(1 + K_{SH})$,

$$A = \frac{c_a(\epsilon_a + \epsilon_{aM}K_a[M^+])}{(1 + K_a[M^+])(1 + K_{SH})} \qquad (15)$$

whereas when $[M^+]$ tends to infinity, eq 15 tends to $A_\infty = c_a\epsilon_{aM}/(1 + K_{SH})$. Substitution of the expression for A_0 and A_∞ into eq 15 yields eq 6.

Appendix 2

Here it is illustrated how the primitive constant $K_{S^-}^*$ (= $[ha^*]/[a^*][MeO^{-*}]$) is evaluated from the absorbance readings. Considering eq 11 and eq 13, eq 16 is obtained

$$[a^*] = A\frac{(1 + K_a c_{salt})}{\epsilon_a + \epsilon_{aM}K_a c_{salt}} \qquad (16)$$

in which $[M^+]$ has been substituted with the more appropriate term c_{salt}. In the case of barium, since eq 6 proved to be effective, K_a, ϵ_a, and ϵ_{aM} (the two last obtained by the definition of A_0 and A_∞ given in Appendix 1) are known quantity and [a*] could be immediately evaluated. Since, in the case of strontium, eq 6 reduces to eq 7 and since the term that multiplies *A* in eq 16 is strictly analogous to the inverse of the right hand side of eq 6, eq 16 reduces, in the case of strontium, to eq 17. Because the

$$[a^*] = \frac{A}{\epsilon_a + (\epsilon_{aM} - \epsilon_a)K_a c_{salt}} \qquad (17)$$

composite term $(\epsilon_{aM} - \epsilon_a)K_a$ is a known quantity, also in the case of strontium, [a*] could be evaluated.

From the mass balance of the aldehyde (c_a = [a*] + [h*] + [ha*]), remembering that $[h^*] = K_{SH}^*[a^*] = K_{SH}[a^*]$, eq 18 is easily obtained. Finally, since $[MeO^{-*}] = c_{MeO}$,

$$[ha^*] = c_a - [a^*](1 + K_{SH}) \qquad (18)$$

the constant $K_{S^-}^*$ can be easily evaluated.

Registry No. 1, 100-52-7; 2, 135733-61-8; 2-HOC_6H_4CHO, 90-02-8; $Ts(OCH_2CH_2)_4OMe$, 62921-76-0.