5954 *J. Org. Chem.* **1995**, *60*, 5954−5957

Metal Ion Catalysis in Nucleophilic Substitution Reactions Promoted by Complexes of Polyether Ligands with Alkali Metal Salts

Alessandro Gobbi,[†] Dario Landini,[†] Angelamaria Maia,*[,†] and Daniela Secci[‡]

Centro CNR and Dipartimento di Chimica Organica e Industriale dell'Università, Via Golgi 19, I-20133 Milano, Italy, and Dipartimento Farmaco Chimico Tecnologico dell'Università, Via Ospedale 72, I-09124 Cagliari, Italy

Received March 3, 1995[®]

Metal ion effects have been revealed on nucleophilic substitution reactions of *n*-octyl sulfonates **1−3** promoted by complexes of polyether ligands (PEGs, crown ethers, cryptands) with alkali metal salts MY (M = Li, Na, K; Y = I, Br) in low polarity solvents (chlorobenzene, *o*-dichlorobenzene, toluene) at 60 °C. Rate constants increase, in the order $\mathrm{K}^+ < \mathrm{Na}^+ < \mathrm{Li}^+$, with the complexes of crown ethers **5** and **6** and PEG **4**, whereas they are independent of the cation in the case of cryptates of **7**. In the series of sulfonic esters **1−3** these effects progressively diminish with increasing nucleofugality of the leaving group. These results are interpreted on the basis of a transition state where the complexed cation $(\mathrm{Lig}\supset\mathrm{M}^+)$ assists the departure of the leaving group ("electrophilic catalysis").

The anionic reactivity of $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Y}^-$ complexes of alkali and alkaline-earth metal salts with lipophilic polyether ligands (crown ethers, cryptands, podands) is particularly high in weakly polar solvents.[1−3] In fact, in these media, the anion Y^- is considerably activated due to the low interaction with the bulky complexed cation $(\mathrm{Lig}\supset\mathrm{M}^+)$ and weak stabilization by the solvent. The reactivity of these complexes is mainly determined by the charge separation induced by the ligand, increasing in the order open-chain ≤ cyclic < bicyclic polyether. The highest values are obtained with lipophilic cryptates that, due to their particular topology, give rise to very reactive "solvent-separated" ion pairs.[1−3] In such systems little importance is, in general, attributed to a possible involvement of the metal ion in the activation process. By contrast, the fundamental role played by metal ions in biological processes is widely demonstrated, especially in the case of divalent cations (Ca^{2+}, Mg^{2+}, Ba^{2+}).[4−6]

Buncel *et al.* revealed and quantitatively evaluated alkali metal ion catalysis in reactions of alkali metal ethoxides[7] and phenoxides[8] with carbon-, phosphorus-, and sulfur-based esters in ethanol. Recently, cation effects were also recognized in the demethylation of alkyl phosphinates[9] and in Diels−Alder[10] reactions in acetone.

Here, we report a striking example of metal ion catalysis in nucleophilic substitution reactions on alkylsulfonic esters **1−3** promoted by complexes of lipophilic polyethers with alkali metal salts in low polarity media. Cation participation has been studied by systematically changing the inorganic salt, leaving group, complexing agent, and solvent.

Results

Kinetic measurements were carried out by reacting comparable amounts of substrate **1−3** (0.005−0.02 M) and preformed $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Y}^-$ complex (0.004−0.02 M) in chlorobenzene, toluene, or *o*-dichlorobenzene at 60 °C (eq 1).

$$\underset{\mathbf{1-3}}{n\text{-}\mathrm{C_8H_{17}OSO_2R}} + (\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Y}^- \rightarrow n\text{-}\mathrm{C_8H_{17}Y} + (\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{RSO_3}^- \quad (1)$$

R = Me (**1**), 4-$\mathrm{MeC_6H_4}$ (**2**), 4-$\mathrm{NO_2C_6H_4}$ (**3**)
$\mathrm{M}^+ = \mathrm{Li}^+, \mathrm{Na}^+, \mathrm{K}^+$; $\mathrm{Y}^- = \mathrm{I}^-, \mathrm{Br}^-$
Lig = PEG400$\mathrm{Me_2}$ (**4**), PHDB18crown6 (**5**), PHB15crown5 (**6**), [2.2.2, $\mathrm{C_{10}}$] (**7**)

Rates have been measured by potentiometric titration of the nucleophile. Under these conditions reactions follow a regular second-order kinetic equation (2) up to at least 3 half-life times (Figure 1). Results are reported in Tables 1−3.

$$\text{rate} = k[\text{substrate}][(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Y}^-] \qquad (2)$$

In the case of *n*-octyl *p*-nitrobenzenesulfonate (**3**) the reactions are generally very fast and were carried out using the "quenching" technique (see Experimental Section).

[†] Centro CNR and Dipartimento di Chimica Organica e Industriale dell'Università.

[‡] Dipartimento Farmaco Chimico Tecnologico dell'Università.

[®] Abstract published in *Advance ACS Abstracts,* July 15, 1995.

(1) (a) Landini, D.; Maia, A.; Montanari, F.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 2526. (b) Landini, D.; Maia, A.; Montanari, F.; Pirisi, F. M. *J. Chem. Soc., Perkin Trans. 2* **1980**, 46. (c) Landini, D.; Maia, A.; Montanari, F. *J. Am. Chem. Soc.* **1984**, *106*, 2917. (d) Landini, D.; Maia, A.; Podda, G.; Secci, D.; Yan, Y. M. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1721. (e) Maia, A. *Pure Appl.Chem.* **1995**, *67*, 697.

(2) Lehn, J. M. *Pure Appl. Chem.* **1980**, *52*, 2303 and references therein.

(3) Landini, D.; Maia, A. *Gazz. Chim. Ital.* **1993**, *123*, 19.

(4) Suelter, C. H. In *Metal Ions in Biological Systems*; Sigel, H., Ed.; Marcel Dekker: New York, 1976; Vol. 3.

(5) Herschlag, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1990**, 112, 1942 and references therein.

(6) Ito, D. I.; Izumi, S.; Hirata, T.; Suga, T. *J. Chem. Soc., Perkin Trans. 1* **1992**, 37.

(7) (a) Dunn, E. J.; Buncel, E. *Can. J. Chem.* **1989**, *67*, 1440. (b) Pregel, M. J.; Buncel, E. *J. Org. Chem.* **1991**, *56*, 5583 and references therein.

(8) Dunn, E. J.; Moir, R. Y.; Buncel, E.; Purdon, J. G.; Bannard, R. A. B. *Can. J. Chem.* **1990**, *68*, 1837.

(9) Modro, A. M.; Modro, T. A. *Can. J. Chem.* **1993**, *71*, 469.

(10) Casaschi, A.; Desimoni, G.; Faita, G.; Gamba Invernizzi, A.; Lanati, S.; Righetti, P. P. *J. Am. Chem. Soc.* **1993**, *115*, 8002.

0022-3263/95/1960-5954$09.00/0

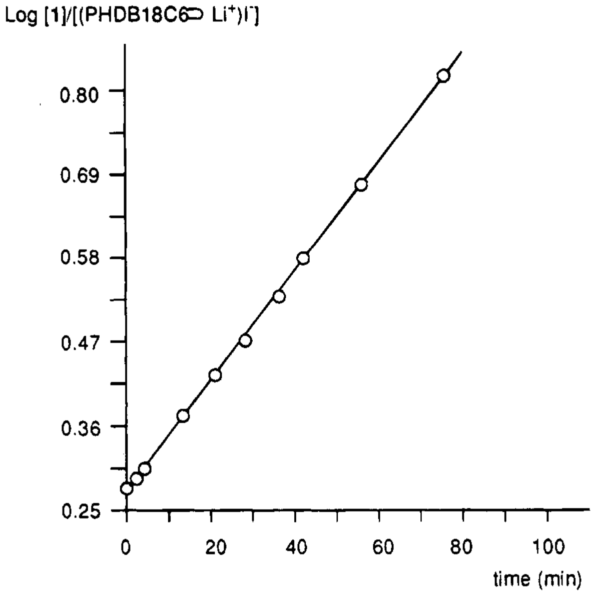


Figure 1. Second-order plot for the reaction of *n*-octyl methanesulfonate (**1**) (0.0186 M) with $(\mathrm{PHDB18C6}\supset\mathrm{Li}^+)\mathrm{I}^-$ (0.0097 M) in chlorobenzene, at 60 °C.

Table 1. Second-Order Rate Constants for the Nucleophilic Substitution of Methanesulfonate in *n*-Octyl Methanesulfonate (1) by Complexes $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Y}^-$ in Chlorobenzene at 60 °C[a]

	10^3k[b] (M^{-1} s^{-1})				
MY	PEG400Me$_2$ (**4**)	PHDB18C6 (**5**)	PHB15C5 (**6**)	[2.2.2,C$_{10}$] (**7**)	
LiI	60.0	26.3	126.0	15.3	
NaI	21.0	19.0	21.5	14.6	
KI	15.5	10.2	17.8	14.5	
QI[c]					6.8
LiBr		12.8	25.0 (26.0)[d]	43.0	
NaBr		13.2	8.0 (8.0)[d]	70.0[e]	
KBr		13.0		44.0	
QBr[c]					20.0

[a] A chlorobenzene solution (30 mL) of substrate (0.005−0.02 M) and $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Y}^-$ complex (0.004−0.02 M). [b] Average of at least two determinations. The error in these values is estimated to be 5%. [c] $Q = (n\text{-}C_8H_{17})_4N^+$. [d] In the case of *n*-octyl tosylate (**2**). [e] See ref 18.

Kinetics with alkali bromides MBr were only possible with good complexing agents like cyclic polyethers **5**−**7** (Table 1).

In DMF and DMSO, where alkali metal iodides MI are largely soluble as such, measurements were performed in the absence of ligand (Table 3). Moreover, it was found that in these solvents reaction 1 goes to the equilibrium; therefore, in this case kinetics were carried out under pseudo-first-order conditions, with a substrate/inorganic salt ratio of 15:1 in order to largely convert the anionic nucleophile I^- to the corresponding $n\text{-}C_8H_{17}I$.

Table 2. Effect of the Leaving Group (OSO_2R) on the Second-Order Rate Constant of Reaction 1 with Complexes $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{I}^-$ in Chlorobenzene at 60 °C[a]

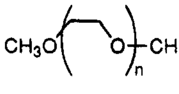
		10^3k[b] (M^{-1} s^{-1})		
R	M	PEG400Me$_2$ (**4**)	PHDB18C6 (**5**)	[2.2.2,C$_{10}$] (**7**)
Me	Li	60.0	26.3	15.3
	Na	21.0	19.0	14.6
	K	15.5	10.2	14.5
4-MeC$_6$H$_4$	Li	40.0	26.6	19.2
	Na	18.0	22.4	22.0
	K	15.0	14.0	19.3
4-NO$_2$C$_6$H$_4$	Li	540	584	1120
	Na	428	540	1200
	K	648	402	1180

[a] A chlorobenzene solution (4−30 mL) of substrate (0.0025−0.02 M) and $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{I}^-$ complex (0.002−0.02 M). [b] Average of at least two determinations. The error in these values is estimated to be 5−10%.

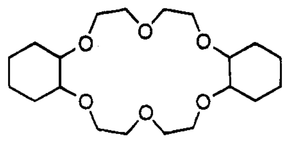
Table 3. Effect of the Solvent Polarity on the Second-Order Rate Constant of the Reaction of *n*-Octyl Methanesulfonate (1) with $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{I}^-$ Complexes at 60 °C

	10^3k[a] (M^{-1} s^{-1})						
	PHDB18C6			PHB15C5			
solvent	Li	Na	K	Li	Na	K	
toluene[b]	77.0	36.0	33.0	230	59.0		
chlorobenzene[b]	26.3	19.0	10.2	126	21.5	17.8	
o-dichlorobenzene[b]	15.3	15.0	9.4	115	19.2	11.7	
DMF[c]							1.85[d,e]
DMSO[c]							0.99[d,e]

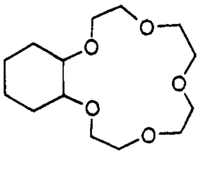
[a] Average of at least two determinations. The error in these values is estimated to be 5%. [b] A solution (30 mL) of substrate (0.005−0.02 M) and $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{I}^-$ complex (0.004−0.02 M). [c] A solution (30 mL) of substrate (0.15−0.25 M) and MI (0.01−0.017 M). [d] In this case the rate constant value was found to be independent of the metal cation. [e] Value obtained by dividing the pseudo-first-order constant by the substrate concentration (see Experimental Section).



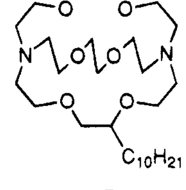
4



5



6



7

Discussion

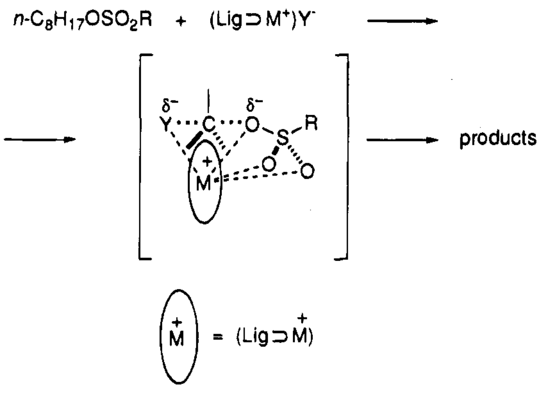
Kinetic data reveal a metal ion participation in the nucleophilic displacement reaction (1) promoted by complexes of polyethers **4**−**7** with alkali metal salts. Catalysis is strictly related to the nature of both the anionic nucleophile Y^- and the leaving group $^-OSO_2R$, but the topology of the ligand is also found to play a major role in determining the entity of such an effect. The results can be explained on the basis of a transition state where the complexed metal cation $(\mathrm{Lig}\supset\mathrm{M}^+)$ interacts with both the anion Y^-, within the ion pair, and the leaving group $^-OSO_2R$ (Scheme 1).

In the activation process the ion pair $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Y}^-$ reacts *via* a concerted "push−pull" mechanism[11] in which the metal cation stabilizes the developing negative charge on the sulfonyl oxygens while the nucleophile Y^- simultaneously attacks the carbon. The higher the

---

[11] A similar mechanism was proposed by Buncel in reactions of alkali metal ethoxides with sulfonate or phosphinate esters.[7b]

Scheme 1



$(\mathrm{Lig}\supset\mathrm{M}^+)\cdots{}^-\mathrm{OSO_2R}$ interaction, the higher the nucleophilic reactivity is expected to be and hence the higher the corresponding rate constants. With the methanesulfonic derivative **1** and the complexes of the alkali iodides MI ($\mathrm{M}^+ = \mathrm{Li}^+, \mathrm{Na}^+, \mathrm{K}^+$) with ligands **4–6**, the sequence found ($k_{\mathrm{KI}} < k_{\mathrm{NaI}} < k_{\mathrm{LiI}}$) reflects the increasing interaction of the leaving group (${}^-\mathrm{OSO_2CH_3}$) with increasing the Lewis acid character of the cation ($\mathrm{K}^+ < \mathrm{Na}^+ < \mathrm{Li}^+$).[12]

As reported in Table 1, on changing from potassium to the corresponding lithium iodide, the rate constants increase from 3-fold up to more than 7-fold. Enhancements obtained with these complexed cations ($\mathrm{Lig}\supset\mathrm{M}^+$) in low polarity media are of the same order of magnitude as those previously reported by other authors with alkali metal ions M^+ in ethanol[8] or acetone.[9]

In contrast, rate constants are lower and independent of the metal ion with the complexes of bicyclic ligand [2.2.2, $\mathrm{C_{10}}$] (**7**) (Table 1). Since cryptands are well known to be powerful cation complexing agents, and hence excellent anion activators,[1–3] the lower reactivity found is clear proof of cation electrophilic assistance to reaction 1.

Similar effects have also been reported by other authors and interpreted in the same sense. For example, the rate of the metal ion assisted reduction of the carbonyl and other functional groups by $\mathrm{LiAlH_4}$ and $\mathrm{NaBH_4}$ noticeably diminishes or is even inhibited when Li^+ and Na^+ are "sequestered" by the cryptand ([2.1.1] and [2.2.1], respectively).[2,13,14]

The proposed mechanism also explains the different cation participation observed in the series of sulfonic esters (Table 2). When tosylate **2** is used instead of the corresponding methanesulfonate **1**, the reactivity sequence is the same ($k_{\mathrm{KI}} < k_{\mathrm{NaI}} < k_{\mathrm{LiI}}$) but flattened into a narrower range. The rate constants are practically independent of the cation ($k_{\mathrm{KI}} \sim k_{\mathrm{NaI}} \sim k_{\mathrm{LiI}}$) in the case of the nosylate **3**, whatever the ligand (Table 2). The results are in line with a decreasing electrophilic assistance demand by increasing the leaving ability of ${}^-\mathrm{OSO_2R}$ on going from **1** to **3**.[15] Contrary to the sulfonic esters **1** and **2** the nucleofugality of *p*-nitrobenzenesulfonate **3** is, in fact, not affected by the metal cation and the sequence of reactivity obtained ($k_{\mathrm{PEG400Me_2}} < k_{\mathrm{PHDB18C6}} < k_{[2.2.2,\mathrm{C_{10}}]}$) is mainly determined by the ability of the polyether to activate the anion in the ion pair.

Cation assistance is also observed with the complexes of alkali bromides, $(\mathrm{Lig}\supset\mathrm{M}^+)\mathrm{Br}^-$ (Table 1). However, catalysis is less pronounced than with the corresponding iodides, probably because in this case the metal ion participation is partially contrasted by a stronger interaction with the harder Br^-, resulting in anion deactivation. As shown in Table 1, the effect is found with both methanesulfonate **1** and tosylate **2**, but only with the PHB15C5 (**6**). The different behavior of this crown ether, in comparison with the larger PHDB18C6, could be attributed to the less efficient shielding of the metal ion charge by **6**, due to the lower number of ether oxygens.[16]

The variation of reactivity with the solvent reveals no substantial difference in the transition state with polarity. The trend found, $k_{\mathrm{Li}^-} > k_{\mathrm{Na}^-} > k_{\mathrm{K}^-}$, is unchanged in the three solvents with both crown ethers **5** and **6** (Table 3). The cation being the same, the obtained sequence $k_{o\text{-dichlorobenzene}} < k_{\text{chlorobenzene}} < k_{\text{toluene}}$ parallels the increasing reactivity of the anion by diminishing the solvating power of the medium. On the other hand, in DMF or DMSO, solvents where alkali metal salts are largely dissociated and the cation much more solvated than the anion,[17] electrophilic catalysis of the former can be reasonably excluded, as confirmed by experimental results (Table 3).

It is worth noting the much higher reactivity of the complexes of crown ethers with alkali metal salts in low polarity media compared with that of the corresponding uncomplexed salts in dipolar aprotic solvents. As Table 3 shows, the $(\mathrm{PHB15C5}\supset\mathrm{Li}^+)\mathrm{I}^-$ ion pair in toluene is about 125 and 233 times more reactive than free I^- solvated by DMF and DMSO, respectively.

These ion pairs, where the cation can give electrophilic assistance to the departure of the leaving group and the anion is highly activated, exhibit a reactivity higher (up to about 20 times) than that of ion pairs where metal ion participation is not expected, like $(n\text{-}\mathrm{C_8H_{17}})_4\mathrm{N}^+\mathrm{I}^-$, or is inhibited by the ligand as for cryptates $(2.2.2,\mathrm{C_{10}}\supset\mathrm{M}^+)\mathrm{I}^-$ (Table 1).

Conclusions

The results reported here underline the different behavior of polyethers **4–7**, depending on the ligand topology. Whereas the cryptand [2.2.2,$\mathrm{C_{10}}$] (**7**), which effectively shields the cations, inhibits metal ion participation,[18] less efficient complexing agents such as crown ethers **5** and **6** or the open-chain $\mathrm{PEG400Me_2}$ (**4**)[1–3] result in catalysis. In the latter case the lower anion activation induced by polyethers **4–6** is largely overcome by the increased cation participation in the transition state.

Metal ion catalysis can therefore be changed by the appropriate choice of the complexing agent. This should not only allow the rate to be increased but should also modify, even markedly, the regio- and stereochemistry of the reaction.

Experimental Section

General Methods. Potentiometric titrations were performed by following a previously described method.[1d] Karl Fischer analyses were carried out with a Metrohm 684 KF

---

[12] Pearson, R. G. *Coord. Chem. Rev.* **1990**, *100*, 403.

[13] Pierre, J. L.; Handel, H. *Tetrahedron Lett.* **1974**, 2317.

[14] Loupy, A.; Seyden-Penne, J. *Tetrahedron* **1980**, *36*, 1937.

[15] March, J. *Advanced Organic Chemistry*; John Wiley and Sons, Inc.: New York, 1992; Chapter 10.

[16] Dhillon, R.; Lincoln, S. F. *Austr. J. Chem.* **1994**, *47*, 123.

[17] Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; Verlag-Chemie: New York, 1988.

[18] The higher rate constant value found for the complex of [2.2.2, $\mathrm{C_{10}}$] with NaBr is probably due to a better Na^+-ligand fitting that produces higher anion reactivity.

coulometer. ^1H NMR spectra were recorded on a Bruker AC 300 spectrometer by using tetramethylsilane as internal standard.

Materials and Solvents. Inorganic salts were Analar grade commercial products, used as such after dehydration of the ground salt in an oven at 110–120 °C for several hours. In all cases the water content is $\leq$0.05 mol of H_2O per mol of salt. *n*-Octyl methanesulfonate (**1**), bp 112–114 °C (2 mm), n^{20}_D 1.4398, was prepared according to the literature [lit.[19] bp 110–114 °C (2 mm), n^{20}_D 1.4392]. *n*-Octyl *p*-toluensulfonate (**2**), bp 198–200 °C (2 mm), n^{20}_D 1.4957, was prepared as previously described [lit.[20] bp 164–166 °C (0.01 mm), n^{20}_D 1.4933]. *n*-Octyl *p*-nitrobenzensulfonate (**3**) was obtained according to an already reported procedure, mp 69–70 °C [lit.[21] mp 70.5–71.9 °C].

Ligands PEG400Me$_2$ (**4**), PHDB18C6 (**5**), and [2.2.2, C$_{10}$] (**7**) are commercially available products, used without further purification.

Perhydrobenzo-15-crown-5 (**6**) was prepared by catalytic hydrogenation of the commercially available benzo-15-crown-5 (**8**) following a known procedure.[22] Crown ether **8** (5.7g, 20 mmol) in ethanol (40 mL) was hydrogenated on 5% Rh/Al_2O_3 (O.5g) in a stainless steel autoclave at 100 atm and 100 °C for 5 h. The catalyst was filtered off over Celite, and the solvent was evaporated under reduced pressure. The residue was stripped under high vacuum by heating at 60–70 °C to afford 5.2 g of **6** as a pale yellow oil (95%), which was used without further purification: n^{23}_D 1.4872; ^1H NMR ($CDCl_3$) δ 1.10–1.95 (m, 8 aliphatic H), 3.50–3.80 (m, 18 ethereal H) [lit.[23] bp 110 °C (0.001 mm)].

Toluene, chlorobenzene, and *o*-dichlorobenzene were Analar grade commercial products, carefully dried before use by standard methods,[24] and stored over molecular sieves under nitrogen. In all cases Karl Fischer titrations showed a water content $\leq$30 ppm. Anhydrous DMSO and DMF were Analar grade commercial solvents used as purchased and stored over molecular sieves under nitrogen. Karl Fischer analysis showed a water content $\leq$50 ppm.

Kinetic Measurements. In a typical procedure a standardized solution (15 mL) of substrate **1** or **2** (0.01–0.04 M) was added to a standardized solution (15 mL) of complexed MY (0.008–0.04 M) in a 50 mL flask thermostated at 60 ± 0.1 °C. Samples (2–5 mL), withdrawn periodically, were quenched in ice-cold MeOH (50 mL), and the unreacted nucleophile Y^- was potentiometrically titrated with 0.01 N $AgNO_3$. The second-order rate constants were evaluated using a least-squares computer program from the equation $1/([B]_o - [A]_o) \ln ([B][A]_o/[A][B]_o) = kt$, where A = substrate and B = complexed MY or *vice versa*. All rates involved at least eight samplings and gave correlation coefficients of 0.997 or better.

The solutions of preformed complexes of **4–7** were prepared by magnetically stirring a standardized solution (30 mL) of ligand in the organic solvent (chlorobenzene, *o*-dichlorobenzene, or toluene) (0.008–0.04 M) with the appropriate quantity of salt MY (0.5–10 mol per mol of ligand) as a solid phase in a flask thermostated at 60 ± 0.1 °C. The system was stirred for 1–2 h and then kept without stirring for an additional 10 min to allow good separation of the two phases. Aliquots (5–8 mL) of the organic phase were centrifuged, and samples (2–5 mL) were withdrawn and titrated with 0.01 N $AgNO_3$. Potentiometric determinations of cryptates $(2.2.2,C_{10}\supset M^+)Y^-$ were performed in acid medium (HNO_3) in order to avoid the simultaneous titration of the free ligand.[1a]

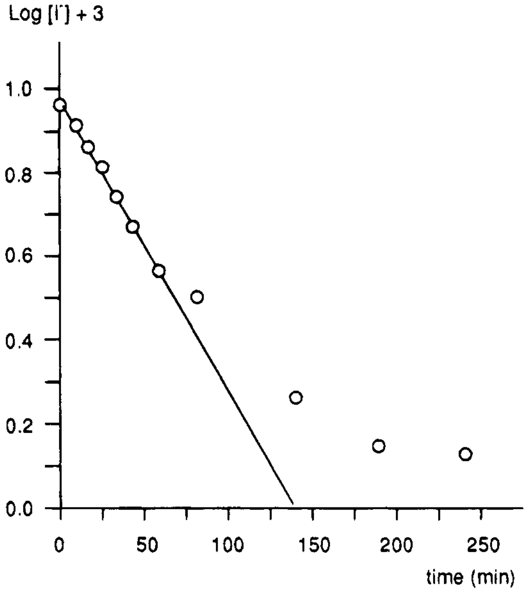


Figure 2. Pseudo-first-order plot for the reaction of *n*-octyl methanesulfonate (**1**) (0.1504 M) with LiI (0.0092 M) in DMF, at 60 °C.

Kinetic determinations with *p*-nitrobenzenesulfonate **3** were carried out by using the "quenching" technique. In a typical procedure standardized solutions (2–3 mL) of substrate **3** (0.005–0.02 M) were added to equal volumes of standardized solutions of complexed MI (0.004–0.015 M) in a series (7–10) of 10 mL flasks thermostated at 60 ● 0.1 °C. At different times the reactions were quenched in ice-cold MeOH (50 mL) and the unreacted nucleophile I^- potentiometrically titrated with 0.01 N $AgNO_3$.

Kinetics in DMF and DMSO were performed under pseudo-first-order conditions by reacting a standardized solution (15 mL) of *n*-octyl methanesulfonate (**1**) (0.15–0.45 M) with a standardized solution (15 mL) of MI (0.01–0.03 M) in a 50 mL flask thermostated at 60 ± 0.1 °C. Samples (2–3 mL), withdrawn at different times, were quenched in ice-cold MeOH (50 mL), and the unreacted I^- was potentiometrically titrated with 0.01 N $AgNO_3$. The pseudo-first-order rate constants, k_{obsd}, were obtained by plotting log [MI] *vs* time. This plot showed an upward curvature due to the existence of an equilibrium for reaction (1) (see Figure 2). The pseudo-first-order rate constants, k_{obsd}, were graphically calculated in the range of conversion 0–40%. The second-order rate constants, k, were calculated by dividing k_{obsd} by the substrate concentration.

Acknowledgment. This work was supported in part by Ministero dell'Università e della Ricerca Scientifica e Tecnologica.

JO9504272

---

[19] William, H. R.; Mosher, H. S. *J. Am. Chem. Soc.* **1954**, *76*, 2984.

[20] Hoffmann, H. M. R. *J. Chem. Soc.* **1965**, 6753.

[21] Snyder, C. H.; Soto, A. R. *J. Org. Chem.* **1964**, *29*, 742.

[22] Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017.

[23] Ikeda, I.; Yamamura, S.; Nakatsuji, Y.; Okahara, M. *J. Org. Chem.* **1980**, *45*, 5355.

[24] Riddick, A.; Bunger, W. B. *Organic Solvents*, 3rd ed.; A. Weissberger: New York, 1970, Vol 2.