product is a primary ozonide, then it has a remarkable thermal stability. The most stable primary ozonides observed in our earlier studies were those of tetramethylethylene[1] and vinyl chloride,[5] whose decomposition rates became appreciable at about −90 and −70 °C, respectively. Although these temperatures are not very different from the decomposition temperature of −55 °C for our styrene ozonide, neither of the previous primary ozonides survived warming to room temperature. It may be that the weak spectrum we observed in our residual samples at room temperature is due to a secondary ozonide whose intense bands are indistinguishable from those of the primary ozonide, but that does not seem very likely.

If, on the other hand, our ozonide is a styrene secondary ozonide, this assignment raises some experimental difficulties. First, styrene ozonide becomes the only secondary ozonide for which we have failed to detect by low-temperature infrared spectroscopy the associated primary ozonide. Second, C_6H_5CHO should be a precursor to the secondary ozonide, and it should have been readily observed under our experimental conditions. Finally, the thermal stability of our ozonide is very different from that of a styrene secondary ozonide prepared by Criegee and Korber.[11] These authors found their ozonide to be stable up to 50 °C in a neat state or in solutions of benzene, CCl_4, or $CHCl_3$. In several other solvents, their ozonide was unstable and decomposed by a first-order kinetics giving C_6H_5CHO as the exclusive aldehyde. The decomposition half-life was the shortest in CH_3OH solvent, being about 22 min at 50 °C. In isopropyl alcohol the half-life was 113 h at the same temperature. Compared to these results, our ozonide decomposition became appreciable at −100 °C in the presence of CH_3OH and at about −55 °C by itself. On the basis of these data, we prefer to suggest that our ozonide may be a styrene primary ozonide. A tentative assignment of the infrared spectrum, where the oxolane ring modes have been distinguished from those characteristic of the styrene,[12] is presented in Table I.

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Lipophilic [2.2.2] Cryptands as Phase-Transfer Catalysts. Activation and Nucleophilicity of Anions in Aqueous–Organic Two-Phase Systems and in Organic Solvents of Low Polarity

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Abstract: Kinetics of nucleophilic substitutions by a homogeneous series of anions in *n*-octyl methanesulfonate, catalyzed by lipophilic cryptand [2.2.2, C_{14}] **1**, have been measured in a chlorobenzene-water two-phase system. Cryptand **1** behaves as a phase-transfer catalyst, and reactions follow a mechanism identical with that found for quaternary salts Q^+Y^-. The observed pseudo-first-order rate constants are linearly related to the concentration of cryptate $[K^+\subset(2.2.2, C_{14})]Y^-$ in the organic phase. They can be simulated in a homogeneous PhCl solution by adding the amount of water associated with the cryptate and with the substrate in the $PhCl-H_2O$ two-phase system, the reactivity scale being $N_3^- > CN^- > Br^- \sim I^- > Cl^- > SCN^-$. The hydration state of anions in $[K^+\subset(2.2.2, C_{14})]Y^-$ is the same as that found for Q^+Y^-. In anhydrous PhCl reaction rates increase up to 15-fold and the reactivity scale ($CN^- > N_3^- > Cl^- > Br^- > I^- > SCN^-$) becomes identical with the well-known sequence in dipolar aprotic solvents. Lipophilic cryptates exist as monomeric species in low-polarity solvents. In these conditions they probably represent the best approach to a model of solvent-separated ion pair. Owing to the low polar interaction and the absence of association, the reactivity shown by the unsolvated anion is probably the maximum obtainable in solution.

The mechanism of liquid to liquid phase-transfer catalysis (PTC) by lipophilic onium salts is well established.[2-6] In addition to onium salts, several systems capable of forming inclusion complexes with metal cations have been used as phase-transfer catalysts: crown ethers,[7] cryptands,[8] and polypode ligands.[9] Common properties for all these catalysts are a high lipophilic character, which allows transfer of anions from the aqueous phase to organic media of low polarity, and a topology imposing a large separation between the anion and the cationic center;[10] thus the weak solvation and the slight interaction between the opposite ions lead to strong anion activation.

However, these similarities do not mean that the reaction mechanism demonstrated for quaternary salts also applies to all other cases. Other mechanisms cannot a priori be excluded, expecially the possibility that reactions occur at the water-organic solvent interface.

Azamacrobicyclic polyethers (cryptands) are particularly attractive for anion activation, since they form stable cation inclusion complexes (cryptates) in which a spheroidal ligand

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Table I. Second-Order Rate Constants for the Reaction of *n*-Octyl Methanesulfonate with Various Nucleophiles (Y^-)[a] in Chlorobenzene–Water Two-Phase System under Phase-Transfer Conditions, and in Anhydrous and Wet Chlorobenzene, at 60 °C

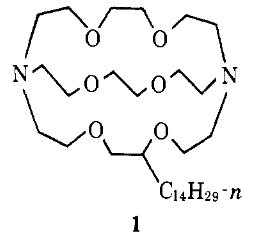
	phase-transfer conditions ($PhCl{-}H_2O$)[b]				homogeneous conditions			
					anhydrous PhCl[c]			wet PhCl[d]
Y^-	$k \times 10^3$, $M^{-1}\,s^{-1}$[e,f]	k_{rel}	hydration state *n* of $[K^+\subset(2.2.2, C_{14})]Y^-\cdot nH_2O$[g]	% complexation	$k \times 10^3$, $M^{-1}\,s^{-1}$[h]	k_{rel}	% complexation	$k \times 10^3$, $M^{-1}\,s^{-1}$[f,i]
N_3^-	28.6	6.1	4.8 ± 0.2	95	150.0	17.3	90	24.5
CN^-	15.5	3.3	7.2 ± 0.3	97	183.3	21.1	45	15.2
Cl^-	3.5	0.7	5.3 ± 0.2	95	50.8	5.8	43	6.5
Br^-	5.6	1.2	4.3 ± 0.2	97	36.6[j]	4.2	97	6.8
I^-	4.7	1.0	3.2 ± 0.1	100	8.7	1.0	100	5.0
SCN^-	1.1	0.23	2.8 ± 0.2	100	1.5	0.17	100	0.95

[a] From $[K^+\subset(2.2.2, C_{14})]Y^-$. [b] 20 mL of a chlorobenzene solution of substrate (6×10^{-1} M) and of $[K^+\subset(2.2.2, C_{14})]Y^-$ ($0.5{-}5 \times 10^{-2}$ M), and 15 mL of an aqueous solution of KY (6.2 M). [c] [Substrate] = $2{-}6 \times 10^{-2}$ M; [cryptate] = $1{-}4 \times 10^{-2}$ M. [d] [Substrate] = 6×10^{-1} M; [cryptate] = $1{-}3 \times 10^{-2}$ M; the extent of complexation is the same as that found in the two-phase system. [e] *k* is defined as $k = k_{obsd}/[\text{cryptate}]$. [f] Average of at least two runs. [g] Average from at least three determinations. [h] The rate constants are computer generated using least-squares analysis and are the average of at least two runs. [i] *k* is defined as $k_{obsd}/[\text{substrate}]$. [j] $k = 54.4 \times 10^{-3}\ M^{-1}\,s^{-1}$ in anhydrous toluene.

of about 10-Å diameter surrounds the cation, replacing its solvation sphere.[15] Therefore in cryptates interaction between the opposite ions is minimized, and they are expected to display a very high anionic reactivity in nonpolar media.[15] While an enormous amount of work has been developed on the stability and the selectivity of cryptation as a function of ligand topology,[15] relatively little is known about anion activation by cryptates,[8,13,14,15b] and practically nothing about kinetic parameters. Likely, this is also due to the low solubility of classical unsubstituted cryptates in nonpolar organic media,[15] so that lipophilic systems must be specially designed for such studies.

The synthesis of lipophilic azamacrobicyclic polyethers related to the [2.2.2] cryptand has been independently described by us[8] and by Lehn and co-workers.[13b] Such compounds, bearing one or two linear alkyl chains of 10–20 carbon atoms, were found to be highly efficient catalysts for several representative reactions under liquid to liquid and solid to liquid PTC conditions.[8,13b]

We report in this paper a study of the reaction mechanism and the nucleophilicity of anions in nucleophilic aliphatic substitutions catalyzed by [2.2.2, C_{14}] cryptand **1** in aqueous–organic two-phase systems. The study has been extended to nucleophilic substitutions by $[K^+\subset(2.2.2, C_{14})]Y^-$ cryptates in organic solvents of low polarity, to evaluate the influence of the specific hydration of cryptate in the organic phase on the reactivity of anions under phase-transfer conditions.



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Results

As for kinetic measurements under phase-transfer conditions in the presence of quaternary salts as catalysts,[5] *n*-octyl methanesulfonate (**2**) was chosen as substrate. Rates of displacement of the methanesulfonic group by a homogeneous series of anionic nucleophiles (Cl^-, Br^-, I^-, SCN^-, N_3^-, CN^-) were measured at 60 °C in a water–chlorobenzene two-phase system in the presence of catalytic amounts of [2.2.2, C_{14}] cryptand **1** (0.008 33–0.0833 mol/mol of substrate) and with a 5:1 molar ratio of inorganic salt/substrate (reaction 1).

$$\underset{\mathbf{2}}{n\text{-}C_8H_{17}OSO_2Me} + KY \xrightarrow[PhCl\text{-}H_2O]{[2.2.2,\ C_{14}]} \underset{\mathbf{3}}{n\text{-}C_8H_{17}Y} + MeSO_3K \qquad (1)$$

$$Y = Cl, Br, I, SCN, N_3, CN$$

The reactions were carried out with stirring at 1000 rpm, to ensure that the reaction rates were independent of the ion diffusion rates at the interface.[5] The rates were measured by following the disappearance of the substrate by ^1H NMR spectroscopy in the presence of benzyl phenyl ether as internal standard. The complexation percents of cryptates were determined by potentiometric titration of the anion in the organic phase. They remained constant during the reaction and were found in the range 95–100% (Table I).

By using liquid membranes with the already described methodology,[4,5] it was established that catalyst **1** is entirely in the organic phase, as a cryptand or cryptate. Moreover, titrimetric measurements indicated that no detectable amount of methanesulfonate ion is in the organic phase under the reaction conditions. This ensures that the methanesulfonate is quantitatively transferred to the aqueous phase, so that equilibrium 2 is fully shifted to the right.

$$([K^+\subset(2.2.2, C_{14})]MeSO_3^-)_{org} + (Y^-)_{aq} \rightleftarrows$$
$$\rightleftarrows ([K^+\subset(2.2.2, C_{14})]Y^-)_{org} + (MeSO_3^-)_{aq} \qquad (2)$$

The reactions follow pseudo-first-order kinetics (eq 3) up to at least 3 half-lives. In the absence of catalyst no appreciable conversion was detected after 20 half-lives with respect to the slowest catalyzed reaction.

$$\text{rate} = k_{obsd}\,[\text{substrate}] \qquad (3)$$

The observed rate constants (k_{obsd}, s^{-1}) are linearly dependent on the cryptate $[K^+\subset(2.2.2, C_{14})]Y^-$ concentration in the range examined ($0.5{-}5 \times 10^{-2}$ M, Figure 1). The second-order rate constants ($k_{obsd}/[\text{cryptate}]$, $M^{-1}\,s^{-1}$) are reported in Table I.

A few molecules of water are associated with the cryptate in the organic phase. In the absence of complexable salts and under the same conditions (temperature and solvent) as the kinetic measurements, cryptand **1** is associated with 2 molar equiv of water (Karl Fischer analysis), whereas an additional amount of water depending on the anion (1–5 molar equiv) is associated with the cryptate (Table I).

Kinetic measurements were extended to homogeneous solutions in anhydrous chlorobenzene and toluene, with comparable concentrations of substrate ($3{-}4 \times 10^{-2}$ M) and cryptate ($0.5{-}3 \times 10^{-2}$ M). Rates were measured by poten-

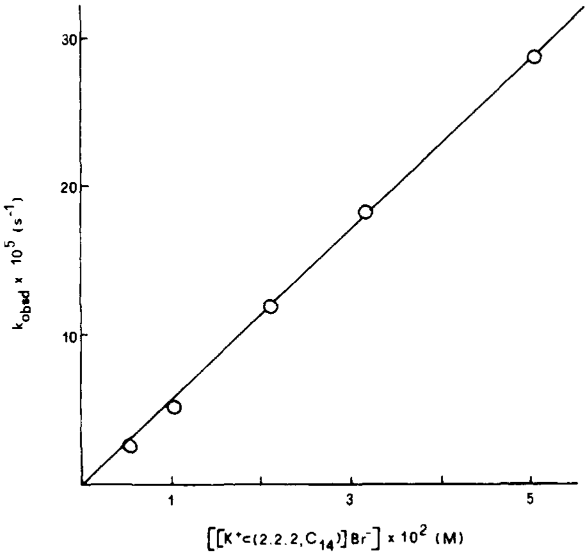

Figure 1. Dependence of the observed rate constants (k_{obsd}) on the catalyst concentration, $[K^+\subset(2.2.2, C_{14})]Br^-$, for the reaction of *n*-octyl methanesulfonate with bromide ion in PhCl-H_2O two-phase system at 60 °C. For the reaction conditions see footnote *b*, Table I.

tiometric titration of the nucleophile, and reactions 4 were found to follow a second-order kinetic equation 5 (Table I).

$$n\text{-}C_8H_{17}OSO_2Me + [K^+\subset(2.2.2, C_{14})]Y^- \rightarrow n\text{-}C_8H_{17}Y + [K^+\subset(2.2.2, C_{14}]MeSO_3^- \quad (4)$$

$$\text{rate} = k[\text{substrate}][\text{cryptate}] \quad (5)$$

Adding to chlorobenzene an amount of water identical with that associated with the substrate[5] and the cryptate under two-phase conditions ($[H_2O] = 0.04–0.31$ M for substrate and cryptate concentrations equal to 0.6 and 0.01–0.03 M, respectively), the reactions followed a pseudo-first-order kinetic equation 6.

$$\text{rate} = k_{obsd}\,[\text{cryptate}] \quad (6)$$

Second-order rate constants ($k_{obsd}/[\text{substrate}]$) are reported in Table I. In all cases they are lower than those measured in the anhydrous solvent, but very similar to those measured under two-phase conditions.

Isopiestic measurements on the homogeneous solution of $[K^+\subset(2.2.2, C_{14})]Br^-$ in anhydrous chlorobenzene did not show any association of cryptate, at least in the range of concentration used in the kinetic runs.

Discussion

Reaction Mechanism. All the typical aspects of reactions carried out under PTC conditions in the presence of quaternary salts[4,5] are shown by reactions performed in chlorobenzene–water two-phase system in the presence of catalytic amounts of the lipophilic cryptand [2.2.2, C_{14}] **1**, i.e., (1) reactions follow regular pseudo-first-order kinetics, and the observed rate constants are linearly related to the effective concentration of the nucleophile associated with cryptate in the organic phase (Figure 1 and Table I); (2) the reaction rates in two-phase conditions can be simulated in homogeneous organic solution by reproducing the hydration of cryptate and substrate (Table I).

Therefore the mechanism demonstrated[2,4,5] for PTC in the presence of quaternary salts applies also to this case: the lipophilic cryptate transfers the anion from the aqueous to the organic phase, where the reaction occurs, and the leaving group moves to the aqueous phase; the rate-determining step of the process is nucleophilic attack on the substrate, with transport through the interface and reestablishment of equilibria as fast steps. This excludes the possibility that the reaction occurs at the interface or in the aqueous phase. Both the cryptate and the free ligand remain entirely in the organic phase, so that exchange of anions at the interface does not require the concomitant transfer of the cationic counterpart. These conclusions are summarized by eq 7, which is similar to that proposed[5] for phase-transfer reactions catalyzed by quaternary salts.

$$\begin{tikzcd}
\begin{matrix}RX\\+\\ {[K^+\subset(2.2.2, C_{14})]Y^-}\end{matrix} \arrow[r] & RY + [K^+\subset(2.2.2, C_{14})]X^- \arrow[d] & \text{(organic phase)} \\
Y^- + K^+ \arrow[u] & + \quad X^- & \text{(aqueous phase)}
\end{tikzcd} \quad (7)$$

Reactivity of Anions. As shown in Table I, the reactivity scale of a homogeneous series of anions under PTC conditions in the two-phase system PhCl-H_2O is $N_3^- > CN^- > Br^- \sim I^- > Cl^- > SCN^-$. This scale is identical with that found[5] in the presence of quaternary salts, although the absolute rates are 1.5–2 times higher. It lies in a narrow range and is anomalous with regard to the well-known reactivity scales, both in protic and dipolar aprotic solvents.

The specific solvation of cryptate and substrate in the organic phase by a limited number of water molecules is the main reason for the reactivity sequence found in the two-phase system, as demonstrated by reproduction of almost identical rate constants[16] in homogeneous solution of wet chlorobenzene. It is important to point out that the number of water molecules associated with the anion in the cryptate is always the same as that found[5] for the corresponding quaternary salts. Changing from PTC conditions to homogeneous solution in anhydrous chlorobenzene, rate increases are always observed. These depend on the nature of the anion, and are the highest for highly electronegative and/or slightly polarizable anions. The reactivity scale becomes $CN^- > N_3^- > Cl^- > Br^- > I^- > SCN^-$, and reflects the well-known sequence of the same anions in dipolar aprotic solvents.[17] The strict parallelism between the behavior of quaternary salts and cryptates in PhCl-H_2O and in anhydrous PhCl is best shown in Figure 2.

Rate increases in going from PTC conditions to homogeneous conditions in anhydrous PhCl are on the average slightly higher than those found[5] for quaternary salts, for example, 14.5 times for Cl^- and 6.5 times for Br^- cryptates, as compared with 11 and 2.5 times[5] for the corresponding quaternary salts, respectively. Unlike the latter, the second-order rate constants of cryptates in anhydrous PhCl remain constant upon variation of the cryptate concentration. It is thus consistent that association measurements indicate that in these conditions cryptates exist as monomeric species, whereas quaternary salts, as previously supposed,[5] show a variable association state (between 1 and 2 in the same concentration range).[18] Therefore the unsolvated anion associated with the cryptate shows maximum reactivity, probably the highest which can actually be obtained in solution.

Reactivities increase upon diminishing the polarity of the solvent. For example, the second-order rate constants in toluene by $[K^+\subset(2.2.2, C_{14})]Br^-$ are 1.4-fold higher than in chlorobenzene, a factor which is comparable with that (1.3) found[5] for $C_{16}H_{33}P^+Bu_3Br^-$ in the same solvents.

It would be interesting to measure reaction rates of anions associated with the cryptate in a solvent of very low polarity and polarizability, such as cyclohexane. Unfortunately, cryptates like $[K^+\subset(2.2.2, C_{14})]Br^-$ are not soluble in this solvent. In order to balance the low cation–anion interaction and lack of aggregation, solubilization of cryptates requires polar or polarizable solvents or specific solvation by a limited number of polar molecules. From this it is derived that the stability constants of $[K^+\subset(2.2.2, C_{14})]Cl^-$ and $[K^+\subset(2.2.2, C_{14})]CN^-$ cryptates are much higher in wet than in anhydrous chlorobenzene (Table I), and that the specific solvation by one molecule of $CHCl_3$ is required to stabilize a solution of $[K^+\subset(2.2.2, C_{10})]F^-$ cryptate in anhydrous benzene.[13b]

A further comment is required regarding the comparison between the nucleophilic reactivity of cryptates and quaternary salts in low-polarity organic solvents.

Cryptates represent what is probably the best actual approach to a model "solvent-separated ion pair". In spite of their partial association, quaternary salts of appropriate topology[5] react on the average only two to five times more slowly than cryptates both in PTC and in homogeneous conditions. This confirms the validity of the choice of quaternary salts as anion activators, since they combine very high reactivity with easy preparation. Forcing the comparison with cryptates, quaternary salts may probably be considered as good models of "loose ion pairs" in low-polarity organic solvents.

Lipophilic quaternary salts and cryptates, in addition to lipophilic complexed crown ethers,[19] constitute a spectrum of salt-like systems which allows comparative study and reliable understanding of the properties of ion pairs. As already pointed out,[13b] owing to their higher ion-pair separation, lipophilic cryptates open a new way for the study, in organic solution, of properties similar to those found in the gas phase.

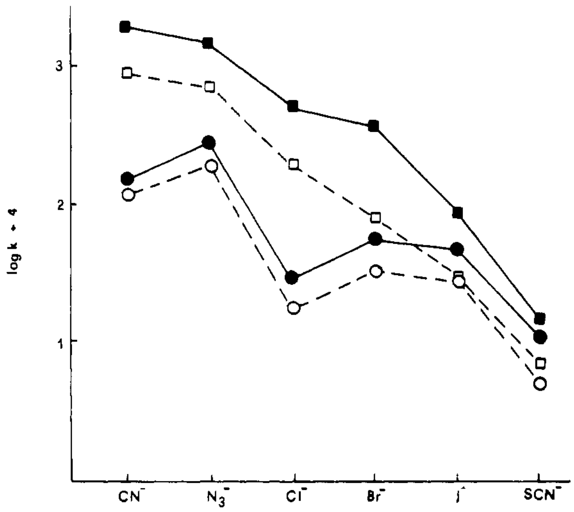

Figure 2. Comparison of the second-order rate constants, k ($M^{-1}\ s^{-1}$), for the reaction of n-octyl methanesulfonate with various nucleophiles Y^- associated with $[K^+\subset(2.2.2, C_{14})]$ and $C_{16}H_{33}P^+Bu_3$ in anhydrous PhCl and in PhCl-H_2O two-phase system at 60 °C: $[K^+\subset(2.2.2, C_{14})]Y^-$ = PhCl (■), PhCl-H_2O (●); $C_{16}H_{33}P^+Bu_3Y^-$ = PhCl (□), PhCl-H_2O (○), data from ref 5.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer using tetramethylsilane as internal standard; potentiometric titrations were performed with a Metrohm Potentiograph type E576 using silver and calomel electrodes, the latter isolated with potassium sulfate bridge; molecular weight measurements were carried out with a Hitachi Perkin-Elmer Model 115 apparatus.

Materials and Solvents. All inorganic salts were Analar grade commercial products; potassium azide was prepared according to the literature.[20] They were used without further purification, except for the experiments carried out in anhydrous conditions in which they were carefully dried and stored in a desiccator.

n-Octyl methanesulfonate (**2**), bp 112–114 °C (2 mm), $n^{20}{}_D$ 1.4398, was prepared according to the literature [lit.[21] bp 110–114 °C (2 mm), $n^{20}{}_D$ 1.4392]. The synthesis of [2.2.2, C_{14}] cryptand **1**, isolated as a complex with $NaBF_4$, mp 91.5–92.5 °C, has been previously reported.[8b] The free ligand was obtained by continuous extraction for several days with n-pentane of a suspension of $[Na^+\subset(2.2.2, C_{14})]BF_4^-$ cryptate (6.82 g, 10 mmol) in 40 mL of 5% aqueous NaOH and 10 mL of methanol. Pentane was evaporated under vacuum, a small amount of pentane was added to the residue, the solution was filtered from a small amount of cryptate, and the solvent was evaporated again to afford cryptand **1**. The product contained some water, which was converted to ice by freezing and then removed by vacuum sublimation (0.5 mmHg). The process was repeated three times to give the pure ligand **1** as a hygroscopic oil, $n^{20}{}_D$ 1.4830 (5.4 g, 94.4% yield). ^1H NMR spectra ($CDCl_3$) showed three sets of signals at δ 0.6–1.5 (29 H, alkyl chain), 2.4–2.9 (12 H, NCH) and 3.2–3.8 (23 H, OCH). Anal. Calcd for $C_{32}H_{64}N_2O_6$: C, 67.10; H, 11.26; N, 4.89. Found: C, 66.93; H, 11.02; N, 5.09.

Chlorobenzene and toluene were Analar grade chemical solvents, used without further purification in the reactions carried on under phase-transfer conditions. For the experiments performed under anhydrous conditions, they were carefully purified and dried as previously reported.[5] Karl Fischer titrations showed water contents ≤50 ppm.

Extent of Complexation and Distribution Coefficients. The extent of complexation of cryptand **1** under phase-transfer conditions was determined by stirring 20 mL of a standardized chlorobenzene solution of **1** ($2\text{-}4 \times 10^{-2}$ M) with 15 mL of an aqueous solution (4.2 M) of potassium salt in a flask thermostated at 60 °C. The system was stirred for 60 min, then kept without stirring for an additional 30–60 min to allow good separation of the two phases. Aliquots of the organic phase were withdrawn and titrated with 0.01 N silver nitrate (potentiometric titration). Ancillary experiments showed that in all cases a stirring time of about 60 min was sufficient to obtain a constant value of complexation.

Equilibrium 2 was studied under the same conditions described above, with the addition to the system of 12 mmol of potassium methanesulfonate corresponding to the amount formed in reaction 1 at 100% conversion.

The extent of complexation in anhydrous conditions was determined by stirring 20 mL of a standardized chlorobenzene solution of cryptand **1** ($2\text{-}4 \times 10^{-2}$ M), thermostated at 60 °C, with 1.2 mmol of anhydrous potassium salt, as solid phase. Samples of the solution were withdrawn at various times by stopping the stirrer for 30–60 min, and titrated potentiometrically with 0.01 N silver nitrate. This procedure was repeated until a constant value was obtained (2–6 h). Potentiometric determinations must be performed in the absence of free ligand **1**, since the latter is also titrated by silver nitrate. Therefore, the measurements were either carried out in acid medium (HNO_3), in which the ligand is protonated, or, in the case of CN^- and N_3^-, in the presence of excess of potassium nitrate, to ensure that all **1** is complexed.

Hydration State of Cryptates. The hydration state of cryptates was determined by stirring for 60 min 20 mL of a standardized organic solution of $[K^+\subset(2.2.2, C_{14})]Y^-$ ($2\text{-}4 \times 10^{-2}$ M) with 15 mL of an aqueous solution (4.2 M) of the corresponding potassium salt in a flask thermostated at 60 °C. Stirring was stopped and aliquots of the organic phase withdrawn at intervals until a constant content of water was measured (Karl Fischer analysis, 2–4 h). Concentration of complexed KY in the organic layer was measured in parallel by potentiometric titration. The hydration state of free ligand **1** was determined as described above, using an aqueous solution of tetramethylammonium chloride instead of potassium salt. Potentiometric titration of the organic layer did not show any detectable amount of Cl^-.

Kinetic Measurements. The apparatus used for kinetic measurements under phase-transfer conditions has been previously described.[5] In a typical procedure, the reaction flask was thermostated at 60 ± 0.1 °C and charged with 15 mL of an aqueous solution of potassium salt (4.2 M) and 20 mL of a standardized chlorobenzene solution of cryptand **1** ($1\text{-}10 \times 10^{-2}$ M). This mixture was stirred for 60 min, then two aliquots (5 mL) of the organic phase were withdrawn, and the percent of complexation was determined by potentiometric titration. A chlorobenzene solution (10 mL) of substrate **2** (1.2 M) and benzyl phenyl ether (0.8 M) as internal standard, already at 60 ± 0.1 °C, was added to the flask, and stirring and timing were started. Aliquots of the organic phase were withdrawn at various times by stopping the stirrer for 40–60 s to allow adequate separation. These were quenched by cooling in an ice bath and analyzed by ^1H NMR. Reaction rates were determined by following the disappearance of the triplet (CH_2OSO_2Me) centered at δ 4.05 and using the singlet at δ

4.80 (OCH_2Ph) as standard. The pseudo-first-order rate constants (k_{obsd}) were obtained by plotting log [substrate] vs. time and determining the slope of the straight lines. The second-order rate constants, k, were evaluated by dividing k_{obsd} by the cryptate concentration.

In the kinetic measurements under anhydrous homogeneous conditions 10 mL of a standardized solution of substrate ($5-20 \times 10^{-2}$ M) were added to 40 mL of a standardized solution of cryptate ($0.6-6 \times 10^{-2}$ M) in a 100-mL flask thermostated at 60 ± 0.1 °C. The solution of the cryptate was prepared as described above. Aliquots of 3-5 mL, withdrawn periodically, were quenched in 50 mL of ice-cold MeOH in the presence of 3 mL of 6 M HNO_3 or, for CN^- and N_3^- ions, of 0.5 g of KNO_3, and unreacted nucleophile was determined using 0.01 N silver nitrate (potentiometric titration).

From eq $1/([B_0] - [A_0]) \ln [BA_0]/[AB_0] = kt$,[5] where [A] = [substrate] and [B] = [cryptate], or vice versa, the second-order rate constants were calculated using a least-squares computer program. All rates involved at least eight samplings and gave correlation coefficients of 0.996 or better.

In the reactions in wet chlorobenzene, 40 mL of a standardized solution (A) of cryptand **1** ($2-6 \times 10^{-2}$ M) and 40 mL of a stock solution (B) of substrate (1.2 M) were separately equilibrated with 30 mL of an aqueous solution (4.2 M) of the corresponding inorganic salt, as described for the determinations of hydration state. At zero time 25 mL of solution B was added to 25 mL of solution A in a 100-mL flask, thermostated at 60 ± 0.1 °C. Aliquots of 3 mL, withdrawn periodically, were quenched with 50 mL of ice-cold MeOH, and unreacted nucleophile was determined as described above. All the runs were carried on with large excess of substrate, and the pseudo-first-order rate constants, k_{obsd}, were obtained by plotting log [cryptate] vs. time and determining the slope of the line. The second-order rate constants, k, were evaluated by dividing k_{obsd} by the substrate concentration.

Aggregation State of Cryptates. The state of aggregation of crypates, $[K^+ \subset (2.2.2, C_{14})]Y^-$, in anhydrous PhCl at 60 °C was performed through vapor pressure (isopiestic) determinations, using a Hitachi Perkin-Elmer apparatus, calibrated with a standard chlorobenzene solution of benzil. The measurements, carried on in the concentration range $0.3-3 \times 10^{-2}$ M, showed that cryptates were present as monomeric species.

Liquid Membranes. In a "U" system, thermostated at 60 °C, 30 mL of a standardized chlorobenzene solution (A) of $[K^+ \subset (2.2.2, C_{14})]Y^-$ (2×10^{-2} M) and 30 mL of chlorobenzene (B) were connected through 90 mL of an aqueous solution of the corresponding KY inorganic salt (4.2 M). The system was stirred and samples of organic phases (A) and (B) were independently withdrawn at various times by stopping the stirrer for 20 min to allow adequate separation, and titrated with 0.01 N silver nitrate (potentiometric titration). These measurements showed that no transfer of $[K^+ \subset (2.2.2, C_{14})]Y^-$ from (A) to (B) could be detected even after several days. The experiments with the free ligand **1** were performed as described above, using an aqueous solution of tetramethylammonium chloride (4.2 M) instead of potassium salts. Also in this case no transfer of **1** from (A) to (B) was detected.

Reaction Products. The products of the reactions between *n*-octyl methanesulfonate (**2**) and various anions under kinetic conditions were isolated with almost quantitative yields. They were chemically homogeneous and were identified by their physical and spectroscopic properties.

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