J. Am. Chem. Soc. **1984**, *106*, 861-869

Reaction Mechanism and Factors Influencing Phase-Transfer Catalytic Activity of Crown Ethers Bonded to a Polystyrene Matrix

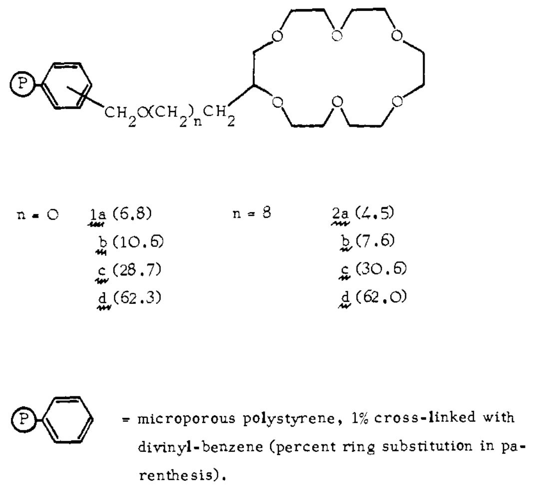
Pier Lucio Anelli, Bronislaw Czech, Fernando Montanari,* and Silvio Quici*

Contribution from the Centro CNR and Istituto di Chimica Industriale dell'Universita', Via Golgi 19, 20133 Milano, Italy. *Received June 27, 1983*

Abstract: Polymer-supported crown ethers **1** and **2** were prepared by reaction of 1% cross-linked chloromethylated polystyrene, with (hydroxymethyl)- and (ω-hydroxynonyl)-18-crown-6, respectively. Their phase-transfer catalytic activity was tested in anion-promoted nucleophilic aliphatic substitutions and compared with that of structurally similar soluble crown ethers and of polymer-supported and soluble phosphonium salts. Catalytic efficiency of crown ethers **1** and **2** depends on a combination of three parameters: the nature of the nucleophile, the percent ring substitution, and the presence of a spacer chain. Complexation of potassium salts largely depends on the anion, with a high degree for soft nucleophiles like I^- and SCN^- and a lower degree for smaller and less polarizable nucleophiles like Br^- and CN^-. This corresponds to high and low catalytic efficiency, respectively. Spaced catalysts **2** are on the average 2–4 times more reactive than directly bonded catalysts **1**. The extent of ring substitution noticeably influences catalytic activity, the variation depending on the nature of the nucleophile. With soft nucleophiles the observed rates progressively diminish as loading increases, following a linear correlation on a semilogarithmic scale, whereas with harder nucleophiles the observed rates reach a maximum at 30% ring substitution. All reactions follow a pseudo-first-order kinetics, and rates are linearly dependent on molar equivalents of polymer-supported crown ethers. Hydrophilicity of catalysts and the extent of complexation increase with the extent of loading. Phenol is exclusively O-alkylated, even in the presence of the most hydrophilic catalysts. The data, as a whole, lead to the conclusion that the reactions occur in the organic shell surrounding a complexed crown ether, following a mechanism analogous to that demonstrated for immobilized quaternary salts.

The use of polymer-supported macrocyclic and macrobicyclic polyethers as phase-transfer catalysts was first described by us a few years ago[1] and further developed more recently.[2] Compared with onium quaternary salts, which are by far the most studied polymer-supported phase-transfer catalysts, macrocyclic and macrobicyclic polyethers feature the great advantage of much greater chemical stability.[2c] Indeed, quaternary salts may easily undergo Hofmann elimination and retro-Menshutkin reactions, thus limiting the possibility of catalyst recycling and therefore not fulfilling the main objective for catalyst immobilization on the polymer.

Chart I



On the other hand, crown ethers and especially cryptates are much more difficult to prepare than quaternary salts. These drawbacks are eliminated if virtually unlimited recycling is possible. Many authors have described the immobilization of crown ethers on a polymer matrix,[3,4] usually polystyrene. Crown ethers also have been inserted into the polymer backbone,[3f,g,5] or bonded to polymers other than polystyrene,[6] or even to inorganic supports.[7] Generally polymeric crown ethers have been used for complexation and selective transport of cations.[3a–h,5c] Some papers concerned the use of these systems as phase-transfer catalysts.[1,2,4] Synthetic approaches, as well as a few parameters ruling catalytic activity, have been examined, such as the following: the molar crown ether/substrate ratio,[2b,8] the presence of spacer chains,[1b,9]

---

(1) (a) Cinquini, M.; Colonna, S.; Molinari, H.; Montanari, F.; Tundo, P. *J. Chem. Soc., Chem. Commun.* **1976**, 394–396. (b) Molinari, H.; Montanari, F.; Tundo, P. *Ibid.* **1977**, 639–641.

(2) (a) Montanari, F.; Tundo, P. *Tetrahedron Lett.* **1979**, 5055–5058. (b) Montanari, F.; Tundo, P. *J. Org. Chem.* **1981**, *46*, 2125–2130. (c) Montanari, F.; Tundo, P. *Ibid.* **1982**, *47*, 1298–1302.

(3) (a) Bradshaw, J. S.; Stott, P. E. *Tetrahedron* **1980**, 461–510. (b) Kahovec, J.; Svec, F. *Chem. Listy* **1981**, *75*, 33–65. (c) Akelah, A.; Sherrington, D. C. *Chem. Rev.* **1981**, *81*, 557–587. (d) Smid, J. "Progress in Macrocyclic Chemistry"; Izatt, R. M., Christensen, J. J., Eds.; Wiley-Interscience: New York, 1981; Vol. II, Chapter 3. (e) Smid, J. *Pure Appl. Chem.* **1982**, *54*, 2129–2140. (f) Blasius, E.; Janzen, K. P. In "Host–Guest Complex Chemistry"; Vögtle, F., Ed.; Springer-Verlag: West Berlin, 1981; Vol. I; *Top. Curr. Chem.* **1981**, *98*, 163–189. (g) Blasius, E.; Janzen, K. P. *Pure Appl. Chem.* **1982**, *54*, 2115–2128. (h) Warshawsky, A. *Angew. Makrom. Chem.* **1982**, *109/110*, 171–196. (i) Dotsevi, G.; Sogah, Y.; Cram, D. J. *J. Am. Chem. Soc.* **1976**, *98*, 3038–3041.

(4) (a) Regen, S. L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 421–429. (b) Manecke, G.; Krämer, A.; Winter, H.-J.; Reuter, P. *Nouv. J. Chim.* **1982**, *6*, 623–628. (c) Montanari, F.; Landini, D.; Rolla, F. In "Host–Guest Complex Chemistry"; Vögtle, F., Ed.; Springer-Verlag: West Berlin, 1982; Vol. II; *Top. Curr. Chem.* **1982**, *101*, 147–200 and references therein.

(5) (a) Bormann, S.; Brossas, J.; Franta, E.; Gramain, P.; Kirch, M.; Lehn, J.-M. *Tetrahedron* **1975**, *31*, 2791–2793. (b) Mathias, L. J.; Al-Jumah, K. *J. Polym. Sci.* **1980**, *18*, 2911–2919. (c) Gramain, P.; Frère, Y. *Ind. Eng. Chem. Prod. Res. Dev.* **1981**, *20*, 524–530. (d) Cho, I.; Chang, S.-K. *Makromol. Chem., Rapid Commun.* **1981**, *2*, 155–160. (e) Mathias, L. J.; Canterberry, J. B. *Polym. Prepr., Am. Chem. Soc.* **1982**, *23*, 171–173. (f) Takekoshi, T.; Webb, J. L. U.S. Patent 3824215, 1974; *Chem. Abstr.* **1975**, *82*; 17465-w.

(6) (a) Shchori, E.; Jagur-Grodzinski, J. *J. Appl. Polym. Sci.* **1976**, *20*, 773–788. (b) van Beijnen, A. J. M.; Nolta, R. J. M.; Zwikker, J. W.; Drenth, W. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 409–410. (c) Anzai, J.; Ueno, A.; Suzuki, Y.; Osa, T. *Makromol. Chem., Rapid Commun.* **1982**, *3*, 55–58. (d) Anzai, J.; Sakata, Y.; Ueno, A.; Osa, T. *Ibid.* **1982**, *3*, 399–403. (e) Fyles, T. M.; McGavin, C. A.; Thompson, D. E. *J. Chem. Soc., Chem. Commun.* **1982**, 924–925. (f) Yagi, K.; Ruiz, J. A.; Sanchez, M. C.; Guerrero, C. *Polym. Prepr., Am. Chem. Soc.* **1982**, *23*, 169–170. (g) Krespan, C. G. U.S. Patent 3952015, 1976; *Chem. Abstr.* **1976**, *85*, 4678-p. (h) Frost, L. W. U.S. Patent 3956136, 1976; *Chem. Abstr.* **1976**, *85*, 161153-x.

(7) (a) Dotsevi, G.; Sogah, Y.; Cram, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 1259–1261. (b) Yagi, K.; Sanchez, M. C. *Makromol. Chem., Rapid Commun.* **1981**, *2*, 311–315. (c) Waddel, T. G.; Leyden, D. E. *J. Org. Chem.* **1981**, *46*, 2406–2407.

(8) van Zon, A.; de Jong, F.; Onwezen, Y. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 429–432.

0002-7863/84/1506-0861$01.50/0

Table I. Analytical Data of Polymer-Supported Crown Ethers

	titer (mequiv of 18-crown-6/g)			
catalyst	by wt increase	by elemental anal (% O in parentheses)	% ring substitution[a]	% yield of binding
1a[b,c]	0.42	0.54 (6.07)	6.8	94.7
1b[b,d]	0.72	0.76 (8.54)	10.6	92.7
1c[b,e]	1.33	1.44 (16.15)	28.7	91.7
1d[b,f]	1.83	2.00 (22.40)	62.3	91.3
2a[b,c]	g	0.34 (3.86)	4.5	63.0[h]
2b[b,d]	g	0.50 (5.56)	7.6	66.7[h]
2c[b,e]	1.17	1.30 (14.58)	30.6	97.7
2d[b,f]	1.52	1.60 (17.96)	62.0	90.9

[a] Calculated on the elemental analysis. [b] From (chloromethyl)-polystyrene 1% cross-linked with divinylbenzene. [c] 0.67 mequiv of Cl/g; 7.2% ring substitution. [d] 1.04 mequiv of Cl/g; 11.4% ring substitution. [e] 2.63 mequiv of Cl/g; 31.3% ring substitution. [f] 5.0 mequiv of Cl/g; 68.2% ring substitution. [g] Not valuable. [h] Conditions were not optimized.

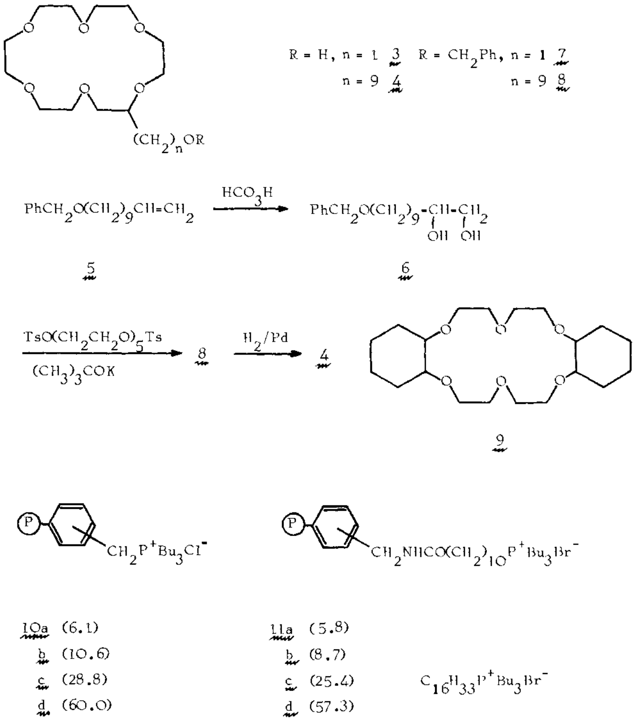
the amount of cross-linking in the polymer support,[10] and the stirring speed.[8] In some instances the catalytic activity of crown ethers has been compared with that of other phase-transfer catalysts bonded to a polymer matrix, such as quaternary salts, cryptands, and polyglymes.[1,2,8,9,11] However, the analyses are mostly qualitative, and conclusions are not complete and sometimes contradictory.[1,2,8,9]

Our study of this problem was based on the same heuristic principle previously followed for quaternary salts,[12] i.e., polymer-supported crown ethers should behave, to a great extent, like soluble crown ethers of similar structure. Since structural factors governing the activity of soluble crown ethers in classical phase-transfer catalysis are well-known,[13,14] it was important to know how the same factors work when crown ethers are immobilized on a polymer: in particular, the specific solvation of the crown ether moiety and the extent of complexation. Therefore a comparison was required, under the same experimental conditions, of soluble and polymer-supported quaternary salts, for which the role of various parameters was already known. The aim was to study the nature of the reaction microenvironment and, eventually, the mechanism of phase-transfer reactions catalyzed by crown ethers immobilized on a polymer matrix.

Results

The polymeric catalysts studied have structures **1** and **2**. Catalysts **1a–d** were obtained by condensation of (hydroxymethyl)-18-crown-6 (**3**)[2a,c] with commercial chloromethylated polystyrene, 1% cross-linked with divinylbenzene, with 0.67, 1.04, 2.63, and 5.0 mequiv of Cl/g, respectively. Reactions were carried out in the presence of NaH for 4 days in boiling THF and gave 95, 93, 92, 91% yield, respectively. Yields were evaluated, with good precision, through the weight increase of the polymer and were more accurately defined on the basis of oxygen elemental analysis (Table I).[15] Catalysts **2a–d** were similarly obtained by condensation of (ω-hydroxynonyl)-18-crown-6 (**4**) with the same chloromethylated polystyrenes with 0.67 to 5.0 mequiv of Cl/g. Yields were 63, 67, 98, and 91% for catalysts **2a**, **2b**, **2c**, and **2d**, respectively, as indicated by oxygen elemental analysis. For the synthesis of crown ether **4**, 11-(benzyloxy)-1-undecene (**5**) was oxidized to diol **6**. Condensation with pentaethyleneglycol ditosylate in THF in the presence of potassium *tert*-butoxide gave (ω-benzyloxynonyl)-18-crown-6 (**8**), which was finally converted to **4** by hydrogenolysis (Scheme I).

Scheme I



The catalytic activity of polymer-supported crown ethers **1** and **2** was evaluated in nucleophilic substitutions by I^-, Br^-, CN, and SCN^- on *n*-octyl methanesulfonate (reactions 1–4) and, in part, in the Br-I exchange reaction in *n*-octyl bromide (reaction 5). The

$$n\text{-}C_8H_{17}OMes + Y^- \rightarrow n\text{-}C_8H_{17}Y + MesO^- \qquad (1\text{-}4)$$

$$Y = I \text{ (eq 1)}; \; Y = Br \text{ (eq 2)};$$

$$Y = CN \text{ (eq 3)}; \; Y = SCN \text{ (eq 4)}$$

$$n\text{-}C_8H_{17}Br + I^- \rightarrow n\text{-}C_8H_{17}I + Br^- \qquad (5)$$

$$\text{rate} = k_{\text{obsd}}[\text{substrate}] \qquad (6)$$

reactions were carried out in toluene–H_2O and/or chlorobenzene–H_2O at 60 °C in the presence of 0.05 molar equiv of catalyst. Catalysts were first conditioned by stirring the reaction mixture for 12 h at 200 rpm and at 60 °C in the absence of the substrate, which was added at zero time. For reactions with CN^-, in order to limit hydrolysis of the latter to formate, conditioning was made in the presence of water and the organic solvent only.

Rates were measured by GLC analysis, and the stirring speed was maintained at 1300 rpm in order to minimize the influence of diffusion.[12] Under these conditions, the reactions followed the pseudo-first-order eq 6 up to a conversion of at least 80%, and the observed rate-constants (k_{obsd}, s^{-1}) were linearly related to the molar equivalents of the polymer-bound crown ethers (Figure 1).

---

(9) Fukunishi, K.; Czech, B.; Regen, S. L. *J. Org. Chem.* **1981**, *46*, 1219–1221.

(10) Manecke, G.; Krämer, A. *Makromol. Chem.* **1981**, *182*, 3017–3030.

(11) Blasius, E.; Janzen, K.-P.; Klotz, H.; Toussaint, A. *Makromol. Chem.* **1982**, *183*, 1401–1411.

(12) Molinari, H.; Montanari, F.; Quici, S.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 3920–3927.

(13) Landini, D.; Maia, A.; Montanari, F. *J. Chem. Soc., Perkin Trans. 2* **1980**, 46–51.

(14) Stott, P. E.; Bradshaw, J. S.; Parish, W. W. *J. Am. Chem. Soc.* **1980**, *102*, 4810–4815.

(15) The synthesis of (hydroxymethyl)-18-crown-6 (**3**) has been previously described by us[2a,c] and, independently, by Manecke[10,16] and subsequently modified.[9,17] Other hydroxymethyl or aminomethyl crown ethers have been described.[18]

(16) Hiratani, K.; Reuter, P.; Manecke, G. *J. Mol. Catal.* **1979**, *58*, 241–245.

(17) (a) Woo, E. P. U.S. Patent 4256859 (1979); *Chem. Abstr.* **1981**, *95*, 81039f. (b) Czech, B. *Tetrahedron Lett.* **1980**, 4197–4198. (c) Ikeda, I.; Yamamura, S.; Nakatsuji, Y.; Okahara, M. *J. Org. Chem.* **1980**, *45*, 5355–5358.

(18) (a) Tomoi, M.; Abe, O.; Ikeda, M.; Kihara, K.; Kakiuchi, H. *Tetrahedron Lett.* **1978**, 3031–3034. (b) Hsu, Y.-Y.; Chin, H.-L.; Huang, K.-H.; War, C.-C.; Huang, Y.-C. *K'o Hsueh Tung Pao* **1981**, *26*, 408–410; *Chem. Abstr.* **1981**, *95*, 43735x. (c) Maeda, H.; Kikui, T.; Nakatsuji, Y.; Okahara, M. *J. Org. Chem.* **1982**, *47*, 5167–5171 and references therein. (d) Czech, B.; Kang, S. I.; Bartsch, R. A. *Tetrahedron Lett.* **1983**, 457–460. (e) Dishong, D. M.; Diamond, C. J.; Cinoman, M. I.; Gokel, G. W. *J. Am. Chem. Soc.* **1983**, *105*, 586–593 and references therein.

Table II. Comparison of Catalytic Activities of Soluble and Polymer-Supported Crown Ethers[a]

catalyst	solvent	$k_{obsd} \times 10^6$, s^{-1} [b,c] Y = I	Y = SCN	Y = Br	Y = CN
7	PhCl-H_2O	146.0	21.9	12.4	22.7
1a		30.0 (0.20)	4.9 (0.22)		
1c				2.9 (0.23)	5.9 (0.26)
8		90.0	17.0	8.3	14.9
2a		31.0 (0.34)	6.2 (0.36)		
2c				4.7 (0.57)	8.3 (0.56)
7	PhMe-H_2O	93.0	27.8	2.6	6.1
1a		47.8 (0.51)	10.0 (0.36)		
1c				2.8 (1.08)	6.5 (1.06)
8		194.0	30.9	4.4	6.7
2a		91.9 (0.47)	10.1 (0.32)		
2c				8.0 (1.82)	10.4 (1.55)

[a] For reactions 1-4 at 60 °C. [b] The ratios k^1/k^7 or k^2/k^8 are in parentheses. [c] For polymer-supported catalysts only the data for the best catalysts are reported: 1a, 2a for Y = I, SCN; 1c, 2c for Y = Br, CN.

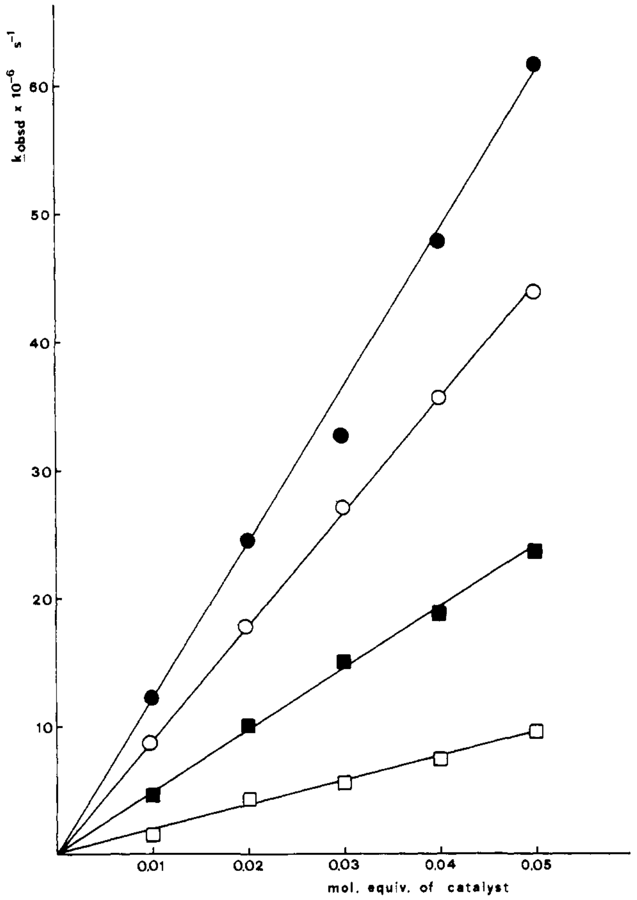


Figure 1. Dependence of the observed pseudo-first-order rate constants (k_{obsd}) on molar equivalents of polymer-supported crown ether units for the OMes-I exchange reaction of *n*-octyl methanesulfonate in toluene–water at 60 °C: catalyst **1a** (●), **1b** (○), **1c** (■), and **1d** (□).

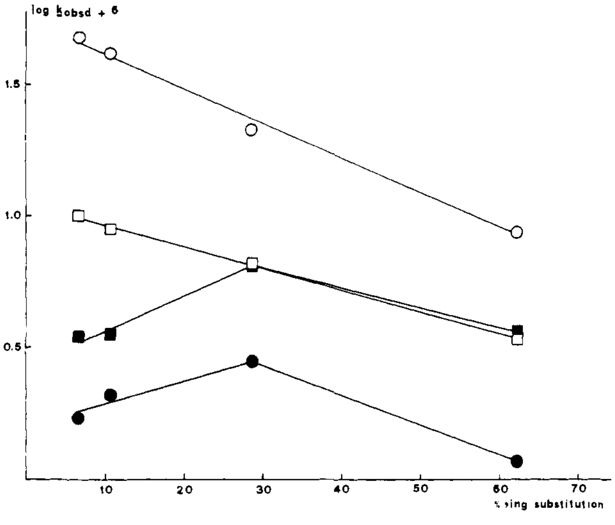


Figure 2. Dependence of the observed pseudo-first-order rate constants (k_{obsd}) on percent ring substitution for OMes-X exchange reactions of *n*-octyl methanesulfonate in toluene–water at 60 °C, catalysts **1a–d**: X = I (○), SCN (□), Br (●), and CN (■).

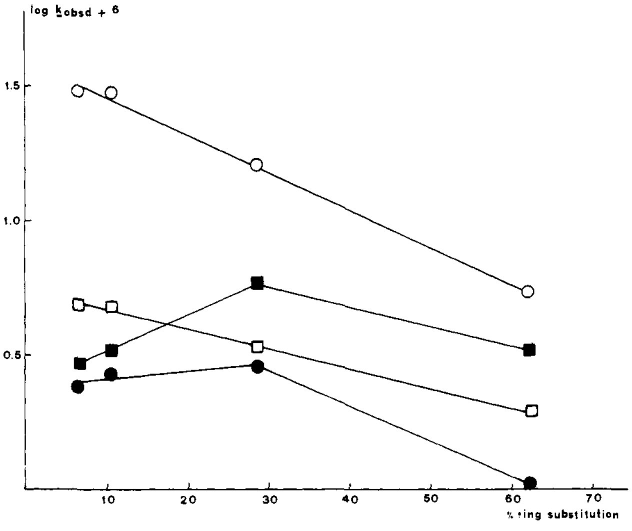


Figure 3. Dependence of the observed pseudo-first-order rate constants (k_{obsd}) oh percent ring substitution for OMes-X exchange reactions of *n*-octyl methanesulfonate in chlorobenzene–water at 60 °C, catalysts **1a–d**: X = I (○), SCN (□), Br (●), and CN (■).

The catalytic activity of polymeric crown ethers was compared with that of soluble crown ethers **7** and **8**, structurally related to **1** and **2**, respectively, and with that of polymer bound **10** and **11** or soluble **12** quaternary phosphonium salts (Tables II–IV and Figures 2–5).

The extent of complexation of soluble crown ethers **7** and **8** in the organic phase was measured under the reaction conditions in toluene–H_2O and chlorobenzene–H_2O at 60 °C. The values are reported in Table V.

None of the commonly used methods[19] could be used to measure the percent of complexation of polymer-supported crown ethers (see Discussion), nor was it possible to work under conditions equal to those of the kinetic measurements, due to the enormous excess of salts. Therefore, we chose conditions which could at least give information on the variations of the stability of complexes on

---

(19) (a) Pedersen, C. J.; Frensdorff, H. K. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 16–25. (b) de Jong, F.; Reinhoudt, D. N. *Adv. Phys. Org. Chem.* **1980**, *17*, 279–433.

Table III. Catalytic Efficiency, $E_{pol}^{CE/QX}$, of Polymer-Supported Crown Ethers. Comparison with Polymer-Supported Phosphonium Salts[a, b]

		X = Br; Y = I		X = OMes; Y = I		X = OMes; Y = Br	
catalyst	% ring substitution	$k_{obsd} \times 10^6$, s^{-1}	$E_{pol}^{CE/QX}$	$k_{obsd} \times 10^6$, s^{-1}	$E_{pol}^{CE/QX}$	$k_{obsd} \times 10^6$, s^{-1}	$E_{pol}^{CE/QX}$
1a	6.8			47.8	2.1	1.6	0.07
10a	6.1			22.7		23.9	
1b	10.6	29.4	0.88	41.4	2.1	2.1	0.10
10b	10.6	33.3		19.6		21.7	
1c	28.7	13.1	0.88	21.3	2.3	2.8	0.22
10c	28.8	14.8		9.1		12.7	
1d	62.3	3.5	0.92	8.8	3.3	1.2	0.36
10d	60.0	3.8		2.7		3.3	
2b	7.6			85.5	2.5	3.5	0.15
11b	8.7			33.8		22.8	
2c	30.6			49.9	3.1	8.0	0.74
11c	25.4			16.1		10.8	
2d	62.0			28.3	2.5	4.7	0.72
11d	57.3			11.2		6.5	

[a] In toluene-H_2O, at 60 °C, for reactions $C_8H_{17}X + Y^- \rightarrow C_8H_{17}Y + X^-$ (eq 1, 2, and 5). [b] For catalysts 10b-d and 11b-d, values taken from ref 26.

Table IV. Catalytic Efficiency, $E_{sol}^{CE/QX}$, of Soluble Crown Ethers. Comparison with Hexadecyltributylphosphonium Salts[a]

		Y = I		Y = SCN		Y = Br		Y = CN	
catalyst	solvent	$k_{obsd} \times 10^6$, s^{-1}	$E_{sol}^{CE/QX}$	$k_{obsd} \times 10^6$, s^{-1}	$E_{sol}^{CE/QX}$	$k_{obsd} \times 10^6$, s^{-1}	$E_{sol}^{CE/QX}$	$k_{obsd} \times 10^6$, s^{-1}	$E_{sol}^{CE/QX}$
12	PhMe-H_2O	110.2		23.6		106.6		410.0	
7		93.0	0.8	27.8	1.3	2.6	0.02	6.1	0.015
8		194.4	1.8	30.9	0.8	4.4	0.04	6.7	0.02
12	PhCl-H_2O	47.6		18.0		61.2		320.6	
7		145.8	3.1	21.9	1.2	12.4	0.2	22.7	0.07
8		90.0	1.9	17.0	0.9	8.3	0.1	14.9	0.05

[a] For reaction $C_8H_{17}OMes + Y^- \rightarrow C_8H_{17}Y + MesO^-$, at 60 °C (eq 1-4). [b] Values for $E_{sol}^{CE/QX}$ (CE = 9; QX = 12) in chlorobenzene-H_2O at 70 °C (from ref 13): I, 2.4; SCN, 1.3; Br, 0.4; CN, 0.03.

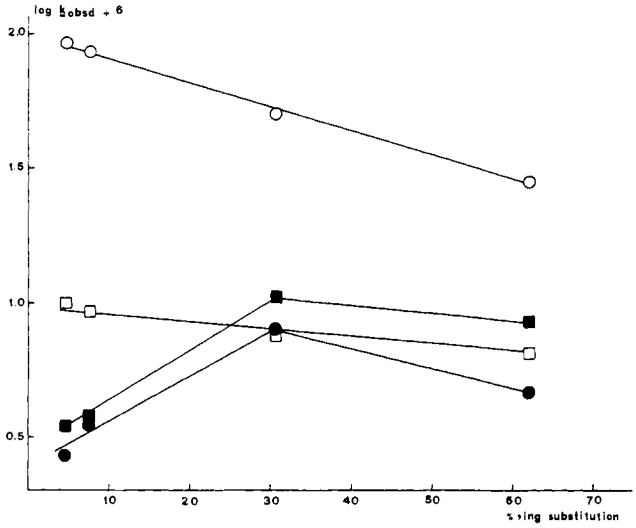


Figure 4. Dependence of the observed pseudo-first-order rate constants (k_{obsd}) on percent ring substitution for OMes-X exchange reactions of *n*-octyl methanesulfonate in toluene-water at 60 °C, catalysts **2a-d**: X = I (○), SCN (□), Br (●), and CN (■).

changing the percent ring substitution. In practice, we equilibrated polymeric crown ethers swelled in toluene with a small excess (4 molar equiv for crown ether unit) of a 0.3 M aqueous solution of KI or KBr and then titrated the uncomplexed salt. The values are reported in Table VI. They indicate a higher extent of complexation of KI compared to KBr. For both salts complexation increases as loading increases.

A new methodology for evaluating the hydrophilicity of polymeric crown ethers and the amounts of organic solvents and water adsorbed by these catalysts under the reaction conditions was needed. Indeed, the methods described up to now[12,20] are based on the amount of solvent that remains imbibed in the polymer after equilibration and subsequent filtration under standard

Table V. Percent Complexation of Soluble Crown Ethers under Phase-Transfer Conditions[a]

		% complexation	
crown ethers	salt	toluene-H_2O	chlorobenzene-H_2O[b]
7	KI	29[c]	82
	KSCN	66[c]	90
	KBr	2.6	12
	KCN	4.4	12
8	KI	72	89
	KSCN	92	93
	KBr	2.4	10.2
	KCN	5.6	11.9

[a] In the organic phase, after 3 h of stirring at 60 °C of a 0.025 M solution of 7 or 8 in toluene or chlorobenzene with a 4 M aqueous solution of potassium salt (see Experimental Section). [b] Percent complexation of perhydrodibenzo-18-crown-6 in PhCl-H_2O at 70 °C: KI (92.8), KSCN (83.0), KBr (16.8), KCN (12.2), from ref 13. [c] A third oily phase (essentially complexed crown 7) is separated at the interface (see Experimental Section).

Table VI. Percent Complexation of Polymer-Supported Crown Ethers 1[a]

catalyst	KI	KBr[b]
1a	13.7	*c*
1b	29.0	*c*
1c	58.2	18.0 (28.0)
1d	64.0	29.0 (42.0)

[a] 0.3 mequiv of catalyst in 4.0 mL of toluene equilibrated with 4.0 mL of a 0.3 M aqueous solution of KI or KBr for 3 h at 20 °C. [b] In parentheses: percent complexation under the same conditions, but in the absence of toluene. [c] Not valuable.

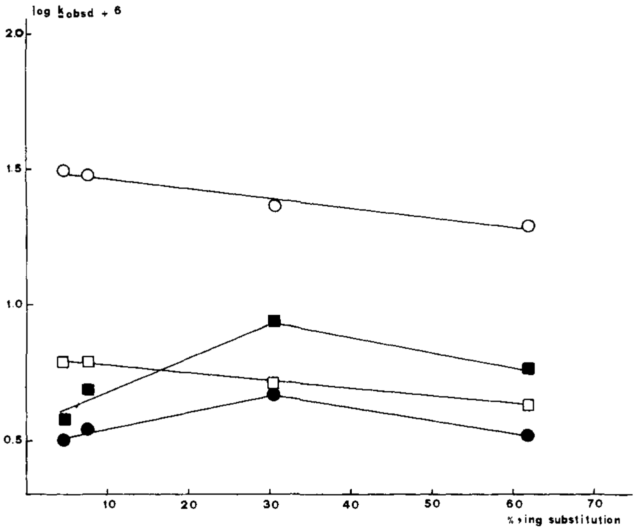


Figure 5. Dependence of the observed pseudo-first-order rate constants (k_{obsd}) on percent ring substitution for OMes-X exchange reactions of *n*-octyl methanesulfonate in chlorobenzene–water at 60 °C, catalysts **2a–d**: X = I (○), SCN (□), Br (●), and CN (■).

Table VII. Swelling and Hydration of Polymer-Supported Catalysts[a]

	swelling, mL/g			% H_2O in the imbibed solvent	
catalyst	H_2O[b]	toluene	H_2O/toluene[b,c]	toluene/aqueous KI[b,c]	toluene/aqueous KBr[b,c]
1a	1.2	7.0	4.3	9.8	11.5
1b	2.4	6.0	4.0	18.9	28.0
1c	2.6	4.2	2.6	53.1	38.0
1d	3.4	4.0	3.4	80.5	75.6
2b				10.9	11.6
2c				19.6	30.8

[a] At 20 °C. [b] 4 M aqueous solution of Kl (or KBr). [c] 1:1 v/v.

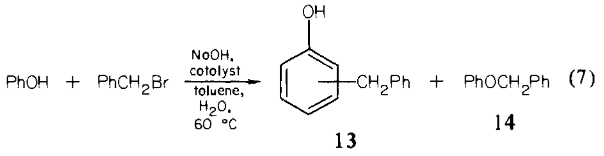
conditions. All these methods are largely imprecise, and their results are difficult to reproduce. Therefore we tried to develop a new technique to afford more reliable results, better reflecting the specific solvation of polymeric catalysts under phase-transfer conditions. A given weight of catalyst was put in a graduated test tube and equilibrated by shaking at room temperature[21] with a measured amount of (i) a 4 M aqueous solution of the appropriate salt, (ii) the organic solvent, or (iii) both the aqueous solution and the organic solvent. The test tube was then centrifuged, and in this way the catalyst was stratified in a compact layer above, below, and at the interface in cases i, ii, and iii, respectively. We assume the volume taken up by the centrifuged polymeric phase is proportional to the liquid adsorbed under swelling conditions. The values reported in Table VII indicate that the amount of adsorbed aqueous solution increases almost 3 times passing from **1a** to **1d**, whereas an opposite trend is observed for the adsorbed toluene. Under phase-transfer conditions, both solvents are adsorbed, and the water/toluene ratio increases as the loading increases. Ratios were measured by drawing samples of the centrifuged polymers, mixing them with excess Me_2SO-d_6, and analyzing the filtered solution by NMR.

For the study of the distribution of the aqueous and the organic phase inside the polymer, i.e., on the solvation shell of the catalytic site, C/O-alkylation of phenol was performed in the presence of catalytic amounts of polymeric crown ethers, under previously described conditions (eq 7).[12,22] The fact that exclusive O-alkylation was found, even with the most hydrophilic catalysts, indicates that reactions occur in an organic solvation shell surrounding the catalytic site, a behavior identical with that already observed for polymer-supported quaternary salts.[12,22,23]

Table VIII. Reactions in the Absence of Stirring[a]

	% conversion[c]	
catalyst[b]	Y = I	Y = Br
1a	3.5	
1b	3.8	
1c	4.8	0.7
1d	16.6	1.7

[a] $C_8H_{17}OMes + Y^- \rightarrow C_8H_{17}Y + OMes^-$ in toluene–H_2O at 60 °C (eq 1 and 2). [b] 0.05 molar equiv. [c] After 24 h.



13

14

Finally, some reactions were repeated in the absence of stirring. The observed rates (Table VIII) were in any case extremely low, compared to those found under standard conditions. As expected, they were relatively faster with highly loaded and more hydrophilic catalysts: 16 and 1.7% conversion with I^- and Br^- as nucleophiles in reactions 1 and 2, after 24 h at 60 °C, respectively.

Discussion

Accessibility and Analysis of Polymer-Bonded Crown Ethers. Crown ether moieties can be introduced on to a cross-linked polystyrene matrix in two ways: (i) copolymerization of styrene and cross-linker with a styrene unit containing the crown ether; and (ii) attack of the crown ether on a reactive functional group previously introduced on to the polystyrene matrix.[25] Both approaches have been used by different authors.[1-5] Copolymerization has the advantage of giving a polymer generally well defined in structure, as well as the number and distribution of functional groups. However, some of the groups introduced in this way may be relatively inaccessible for any subsequent chemical reaction.[25] Introduction of a functional group by chemical modification of cross-linked polystyrene gives rise to a polymer whose features are much more difficult to define, but all the groups thus introduced are generally accessible for further exploitation.[25]

In this paper, as in our previous papers,[1,2,12,26] we have functionalized beads of commercial chloromethylated polystyrene, with different percent ring substitution. Therefore, this synthesis method ensures that all crown ethers introduced into the polymers should be accessible to reagents.

In a preceding paper[2b] we assayed three possible ways for titrating polymer-bonded crown ethers. Among these, addition of a molar excess of potassium picrate to a methylene chloride–water suspension of the resin, followed by spectrophotometric analysis of noncomplexed picrate in the aqueous phase, had given

---

(20) (a) Gregor, H. P.; Hoechschele, G. K.; Potenza, J.; Tsuk, A. G.; Feinland, R.; Shida, M.; Teyssié, P. *J. Am. Chem. Soc.* **1965**, *87*, 5525–5534. (b) Ohtani, N.; Wilkie, C. A.; Nigam, A.; Regen, S. L. *Macromolecules* **1981**, *14*, 516–520. (c) Tomoi, M.; Ford, W. T. *J. Am. Chem. Soc.* **1981**, *103*, 3821–3828.

(21) A more correct, but experimentally more difficult, procedure would be the equilibration and centrifugation at 60 °C, i.e., at the same temperature of kinetic measurements. We believe that the observed trend of swelling of the catalysts should be very similar at 20 and 60 °C.

(22) Montanari, F.; Quici, S.; Tundo, P. *J. Org. Chem.* **1983**, *48*, 199–202.

(23) The use of β-naphthol instead of phenol did not afford reliable results because of the competitive uncatalyzed alkylation, as observed for polymer-supported quaternary salts.[22] O-Alkylation only was obtained[24] in the reaction of sodium phenoxide with allyl chloride in benzene, in the presence of poly(vinylmonobenzo-18-crown-6).

(24) Akabori, S.; Miyamoto, S.; Tanabe, H. *J. Polym. Sci., Polym. Lett. Ed.* **1978**, *16*, 533–537.

(25) (a) Sherrington, D. C. In "Polymer-supported Reactions in Organic Synthesis"; Hodge, P., Sherrington, D. C., Eds.; Wiley: Chichester, 1981; Chapter 1. (b) Sherrington, D. C. *Nouv. J. Chim.* **1982**, *6*, 661–668.

(26) Anelli, P. L.; Montanari, F.; Quici, S. *J. Chem. Soc., Perkin Trans. 2*, in press.

the best results. However, when this method was applied to the analysis of polymeric catalysts **1** and **2** described in the present paper, in some cases complexation of crown ether with potassium picrate could not be carried to completion even with a tenfold excess of the latter. Thus the experimental error was unacceptably high.

However, oxygen elemental analysis gave much more reliable results on the functionalization degree of polymeric catalysts (seven oxygen atoms introduced into the polymer for each crown ether unit), consistent in all cases with the weight increase of chloromethylated polystyrene (Table I).

Catalytic Efficiency of Polymer-Bonded Crown Ethers. As shown in Figures 2–5, catalytic activity of polymer-supported crown ethers **1** and **2** depends on the complex interplay of several factors. In evaluating these factors, a first comparison can be made between the reactivity of soluble catalysts **7** and **8** and the most reactive polymeric catalysts within the series **1a–d** and **2a–d**.

As shown in Table II, the reactivity of the best polymer-supported crown ethers (**1a** and **2a** for reactions with I^- and SCN^-; **1c** and **2c** for reactions with Br^- and CN^-) was on the average 2–5 times lower than that of the corresponding soluble catalysts **7** and **8**—a behavior similar to that observed[12] for the polymer-supported quaternary salts. In some cases the reactivity ratios were even reversed, and the rates with polymeric crown ethers were slightly higher than those observed with **7** or **8**. This means that more favorable complexation effects (see below) may prevail over adverse diffusional and polar factors.

For a more significant evaluation of catalytic activity, both polymer-supported and soluble crown ethers were compared with the corresponding phosphonium quaternary salts. Efficiency coefficients, $E_{\text{pol}}{}^{\text{CE/QX}}$ and $E_{\text{sol}}{}^{\text{CE/QX}}$ defined by eq 8 and 9, are reported in Tables III and IV.

$$E_{\text{pol}}{}^{\text{CE/QX}} = k_{\text{obsd}}{}^{1}/k_{\text{obsd}}{}^{10} \text{ or } k_{\text{obsd}}{}^{2}/k_{\text{obsd}}{}^{11} \tag{8}$$

$$E_{\text{sol}}{}^{\text{CE/QX}} = k_{\text{obsd}}{}^{7}/k_{\text{obsd}}{}^{12} \text{ or } k_{\text{obsd}}{}^{8}/k_{\text{obsd}}{}^{12} \tag{9}$$

We previously demonstrated[13] that in the presence of catalytic amounts of lipophilic crown ethers, such as perhydrodibenzo-18-crown-6 (**9**), nucleophilic substitutions carried out under aqueous–organic two-phase conditions follow the classic mechanism of phase-transfer catalysis: the observed pseudo-first-order rate constants are linearly related to the amount of complexed crown ether in the organic phase; moreover they are independent of the stirring rate above 400 rpm, which excludes the possibility that reactions occur at the interface. However, the catalytic efficiency of crown ethers dramatically depends not only on cation but also on the nature of the anion, both responsible for the stability of the complex in the organic phase. For example, catalytic efficiency of **9**, $E_{\text{sol}}{}^{\text{CE/QX}}$ (CE = **9**, QX = **12**), in chlorobenzene–water at 70 °C goes from 2.4 and 1.3 for I^- and SCN^-, respectively, to 0.4 and 0.03 for Br^- and CN^-, respectively.[13] Very similar values were found for crown ethers **7** and **8** in the same solvent at 60 °C (Table IV). The catalytic efficiency of **7** and **8** is noticeably lower in toluene–water, because of the lower degree of complexation of all the salts in toluene compared to the complexation in the more polar chlorobenzene (Table V). In any case, the dramatic difference among the values of $E_{\text{sol}}{}^{\text{CE/QX}}$ depending on the soft or hard character of the anion is maintained.

Catalytic efficiencies of polymer-bonded crown ethers **1** and **2**, expressed in this case by $E_{\text{pol}}{}^{\text{CE/QX}}$, largely reflect those of soluble crown ethers. As shown in Table III, in the OMes-I exchange reactions 1 in toluene–water at 60 °C, percent ring substitution being constant, crown ethers **1a–d** and **2b–d** are 2.1–3.3 times more reactive than the corresponding tributylphosphonium salts **10a–d** and **11b–d**, respectively. This factor is independent of loading and of the presence of a spacer chain. Catalytic efficiency decreases to about 0.9 in the Br-I exchange reaction 5, but it becomes very much lower in the presence of poorly polarizable nucleophiles, as exemplified by OMes-Br exchange reaction 2. As a consequence, the observed rate constants decrease up to 40 times passing, for example, from reaction 1 to reaction 2, i.e. from I^- to Br^- as nucleophile.

In the two series of catalysts **1a–d** and **2b–d** coefficients $E_{\text{pol}}{}^{\text{CE/QX}}$ gradually shift from 0.07 to 0.4 and from 0.15 to 0.70, respectively, by increasing loading. Therefore, values obtained with I^-, and the highest of those obtained with Br^-, compare well with values found for soluble crown ethers. They show, in other words, that under optimum conditions, crown ethers and quaternary salts, free or bonded to a polymer matrix, behave in a similar manner: with soft anions, crown ethers are on the average more efficient than quaternary salts, but the situation is completely reversed on passing to hard anions, in agreement with different extents of complexation (see below). Polymer-supported crown ethers are sometimes slightly more reactive than the corresponding soluble catalysts.

Complexation of Polymer-Bonded Crown Ethers. In the presence of a small excess of potassium halide, the percent of complexation of polymer-bonded crown ethers is always higher for soft anions than for less polarizable anions (Table VI). This trend is identical with that observed in soluble crown ethers **7** and **8** (Table V) and confirms Pedersen's[19a] and our[13] results for other soluble crown ethers.[27]

As shown in Table VII, hydrophilicity of catalysts **1** and **2** increases as loading increases. For example, in toluene–water under the reaction conditions, the ratio of the two solvents adsorbed by catalysts **1a–d** is 90:10 and 20:80 at 7% and 60% ring substitution, respectively. The values reported in Table VI indicate that percents of complexation increase in the same way, with greater increases for Br^- than for I^-. Although these values have been measured in the presence of a relatively small excess of salt, the same trend is expected to occur under the reaction conditions.

The increase of salt binding ability with loading increase requires some further comments. The vast majority of complexation constants of soluble crown ethers have been determined in the presence of picrate or other similar organic anions, all highly lipophilic and easily analyzable by spectroscopic techniques.[19] The main object of these studies was to understand relationships between the macrocycle structure and the nature of the cation, whereas very little is known on the influence of anions, especially those with high charge density and low polarizability. It has been reported by Pedersen and Frensdorff[19a] that the amount of potassium halide dissolved in benzene by perhydrodibenzo-18-crown-6 (**9**) increases in the order KCl < KBr < KI. Addition to benzene of quite small quantities of methanol largely increases the amount of salt dissolved by **9**, with greater increases for the more electronegative anions: 290-, 13-, and 5-fold for Cl^-, Br^-, and I^-, respectively. Accordingly, we found that the presence of a few molecules of water which selectively accompany the anion in the organic solvent under phase-transfer conditions, in the case of small and less polarizable anions, appreciably increases the stability of the complexes of crown ether **9** with respect to the anhydrous organic solution.[13]

In conclusion, it seems very likely that, under these reaction conditions, a progressive increase of water adsorbed by polymeric catalysts **1** and **2** is related to a progressive increase of complexing capability by pendant crown ethers, the more relevant the harder the anion.[28]

---

[27] Blasius[3f,8] prepared several polymers with crown ethers and cryptands included in the backbone, or attached as pendant groups, and used them as the stationary phase in elution chromatography. In agreement with our results, elution with water of a homogeneous series of sodium halides separated the salts in the order of increasing polarizability of anions.

[28] A complexation increase with loading increase could also be attributed to intervention of a "sandwich effect". This kind of cooperative effect has been observed in the case of bis-crown ethers linked by an alkyl chain: it depends on the distance between the two ligands and is usually observed when the cation diameter exceeds that of the crown ether cavity.[29] A similar effect has been observed in polymers.[30] Since in our case potassium cation perfectly adapts to the cavity of 18-crown-6, the occurrence of a sandwich effect seems to be improbable even at high loadings. A study of the role played by the cation in these systems is in progress.

[29] (a) Bourgoin, M.; Wong, K. H.; Hui, J. Y.; Smid, J. *J. Am. Chem. Soc.* **1975**, *97*, 3462–3467. (b) Wong, K. H.; Ng, H. L. *J. Coord. Chem.* **1981**, *11*, 49–55. (c) Maeda, T.; Ouchi, M.; Kimura, K.; Shono, T. *Chem. Lett.* **1981**, 1573–1574. (d) Shono, T.; Okahara, M.; Ikeda, I.; Kimura, K.; Tamura, H. *J. Electroanal. Chem.* **1982**, *132*, 99–105.

Percent Ring Substitution and Spacer Chains. The influence of percent ring substitution and of the insertion of a spacer chain on the catalytic activity of polymeric crown ethers **1** and **2** is in some aspects similar to but in others quite different from that found[26] in tributyl phosphonium salts **10** and **11**.

In the case of quaternary salts **10** directly bonded to the polymer matrix, used as catalysts in nucleophilic substitutions 1 and 2, reaction rates decreased about one order of magnitude on passing from 10% to 60% ring substitution; the log's of k_{obsd} were linearly related to the loading of catalytic sites. Insertion of a linear spacer chain (catalysts **11**) resulted in a k_{obsd} increase (1.7–3.1-fold) with respect to directly bonded catalysts **10**, an increase which was noticeably higher (up to 10-fold) at 60% ring substitution. The different behavior of catalysts **10** and **11** was explained by the combination of two opposite effects: (i) a polarity increase at the catalytic site with an increase in percent ring substitution; and (ii) a polarity decrease with insertion of a spacer chain, due to the intrinsic lipophilicity of the alkyl chains, as well as the more even distribution of catalytic sites within the polymer matrix. Behavior of catalysts **10** and **11** was independent of reaction temperature and charge density and/or polarizability of nucleophiles.[26]

In highly loaded polymer-supported crown ethers k_{obsd} increases on the average 2–4-fold on going from directly bonded catalysts **1** to spaced catalysts **2** (Figures 2–5), whereas the maximum increase is 2-fold in less loaded catalysts. These ratios are practically the same as those found for polymer-supported quaternary salts.[1,12,26,31] However, unlike catalysts **10** and **11**, in crown ethers **1** and **2** the nature of the nucleophile influences the relationship between the observed rate constants and percent ring substitution more than the introduction of a spacer chain: with polarizable anions (I^-, SCN^-) k_{obsd} progressively diminish as loading increases in both series of polymeric crowns **1a–d** and **2a–d**, following a linear relationship on a semilogarithmic scale. The decrease is larger for catalysts **1** than for more spaced catalysts **2** (up to 5.4 and 3.2 times, going from **1a** to **1d** and from **2a** to **2d**, respectively). This behavior is observed in both toluene–water and chlorobenzene–water. With less polarizable anions (Br^-, CN^-), k_{obsd} increase up to 3 times by increasing loading up to 30% ring substitution (catalysts **1c** and **2c**) and subsequently decrease on going to 62% ring substitution (catalysts **1d** and **2d**).

In the case of soft anions results indicate that one factor (or several cooperating factors) limits reaction rates. In the case of harder anions, clearly two or more factors operate in an opposite manner.

As noted above, complexation of polymer-supported crown ethers is directly related to the amount of water within the catalyst. More water also leads to higher diffusion rates of salts through the polymer matrix.[32] Both factors lead to an increase of reaction rates. Higher percent ring substitution and the resulting higher hydrophilicity result in increased polarity within the polymer, and therefore a lower anion reactivity. The sum of these opposite factors should be responsible for the observed behavior of catalysts **1** and **2** as a function of loading, spacer chain, and the nature of the anion.

Microenvironment of Reaction. Formation of O-alkylation product **14** only in the reaction of phenol with benzyl bromide in the presence of catalysts **1a–d** strongly supports the hypothesis that reactions occur within an organic solvation shell surrounding the catalytic site. The same mechanism should apply to the most hydrophilic and polar catalysts, like **1d**. As in the case of soluble crown ethers, anions should exchange at the water–organic solvent interface, without requiring a concomitant transfer of the cationic counterparts.[13] Complexed crown ether moieties possibly surrounded by the aqueous phase should be catalytically inefficient.

Other Factors Influencing Catalytic Activity: Catalyst Particle Size, Percent of Cross-Linking, Absence of Stirring. Tomoi and Ford have demonstrated[20c] that, in the case of polymer-bonded quaternary salts, eventual diffusion controls lead to an inverse rate dependence on particle size. It was not possible to include a systematic analysis in this sense here since the catalysts were not available in sufficient amounts to allow sieving in different mesh ranges. However, in agreement with our observations[26] in the synthesis of phosphonium salts **10** and **11**, chemical modification of a chloromethylated polystyrene, previously sieved within a narrow mesh range, cannot significantly change the average particle size. Any low-mesh fractions obtained by sieving catalyst beads after the introduction of crown ether moieties derive from a weak aggregation of particles, as found for catalysts **10** and **11**. This aggregation rapidly disappears during catalyst conditioning, as observed by microscopic inspection of suspensions of catalysts **1** and **2** in the organic solvent.

All polymeric catalysts used in this work are 1% cross-linked with divinylbenzene. A cross-linking increase gives rise to reduced swelling properties and therefore, in the case of diffusion control, to a lowering of reaction rates.[25] This same behavior has been observed by Manecke[4b,10] in polymeric crown ethers, obtained by copolimerization of styrenes already containing crown ether functionalities with varying amounts of cross-linkers.

It was recently reported by van Zon[8] that catalytic activity of polystyrene-supported crown ethers structurally similar to catalysts **1** (50% ring substitution with benzo-18-crown-6 moieties) increased by a factor of about 7 on going from a magnetic stirring speed of 100 rpm to nonstirring conditions. In contrast with these results we find a dramatic decrease of k_{obsd} passing from the standard 1300-rpm stirring speed to a nonstirred system (Table VIII). It was demonstrated by us[12] and by others[20c] that, for polymer-supported quaternary salts, a 400–800-rpm stirring speed is necessary to reach a plateau of reactivity. On the other hand, it has been observed by Regen that when a polymer-supported phase-transfer catalyst can settle itself on a large surface of separation between the two liquid phases, the reaction substantially proceeds at the same rate with or without stirring. According to the model proposed by Regen,[4a] inside the polymeric catalyst there are microscopic aqueous and organic pools, the composition of which is similar to the external bulk phases. In other words, extensive pool–pool phase boundaries are generated inside the polymer, thereby increasing the rate of diffusion between the two liquid phases, as the polymer serves like a "pseudo-high-speed stirrer". When a larger amount of catalyst is used and/or the surface of the liquid interface becomes smaller, stirring becomes necessary in order to secure the continuous contact of liquid phases with the polymeric catalyst. Since van Zon claims that a possible physical removal of the catalyst from the liquid/liquid interface by adhesion to the inside walls of the reaction vessel has been avoided,[8] his results remain unexplained.

Conclusion

The results obtained in the present work may be summarized as follows. (i) In anion-promoted nucleophilic aliphatic substitutions carried out under phase-transfer conditions, catalytic efficiency of polystyrene-supported crown ethers essentially depends on three parameters: nature of the nucleophile, percent ring substitution, and presence of a spacer chain. These parameters govern various factors which directly influence reaction rates, i.e.,

---

(30) (a) Kopolow, S.; Hogen Esch, T. E.; Smid, J. *Macromolecules* **1973**, *6*, 133–142. (b) Gramain, P.; Frère, Y. *Polymer* **1980**, *21*, 921–924. (c) Smid, J. *Makromol. Chem. Suppl.* **1981**, *5*, 203–215. (d) Kimura, K.; Maeda, T.; Shono, T. *Makromol. Chem.* **1981**, *182*, 1579–1586.

(31) (a) Brown, J. M.; Jenkins, J. A. *J. Chem. Soc., Chem. Commun.* **1976**, 458–459. (b) Chiles, M. S.; Reeves, P. C. *Tetrahedron Lett.* **1979**, 3367–3370. (c) Chiles, M. S.; Jackson, D. D.; Reeves, P. C. *J. Org. Chem.* **1980**, *45*, 2915–2918. (d) Tomoi, M.; Ogawa, E.; Kakiuchi, N. "Resumês des Communications", Colloque International sur les Reactifs Supportês en Chimie Organique, Lyon, 1982; p 130.

(32) It has been suggested[33] that in the attachment of amino acids to chloromethylated polystyrene these highly polar molecules find difficulty in penetrating the hydrophilic polystyrene matrix, but when the latter is made significantly more polar by substitution of chlorine atoms for dimethylsulfonium groups, amino acids diffuse much more easily through the polymers.

(33) Petit, M. A.; Jozefonvicz, J. *J. Appl. Polym. Sci.* **1977**, *21*, 2589–2596.

(34) Regen, S. L.; Besse, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 4059–4063.

(35) Williams, M. R. Mosher, H. S. *J. Am. Chem. Soc.* **1954**, *76*, 2984–2987.

(36) Fenton, D. E.; Parkin, D.; Newton, R. F. *J. Chem. Soc., Perkin Trans. 1* **1981**, 449–454.

percent complexation and selective solvation by the organic phase of complexed crown ether, polarity of the reaction microenvironment, hydrophilicity of the catalyst, and diffusion of reagents within the polymer matrix. (ii) Potassium salts of soft nucleophiles, like I^- and SCN^-, are highly complexed; this corresponds to a polymeric catalyst efficiency 2–3-fold higher than that of structurally related tributyl alkyl phosphonium salts. (iii) With smaller and less polarizable anions, like Br^- and CN^-, complexation is much lower, and thus catalytic efficiency becomes noticeably lower. (iv) Insertion of a ten-atom linear spacer chain leads on the average to a 2–4-fold rate increase, depending on the loading. (v) As in polymer-supported quaternary salts, a loading variation noticeably influences catalytic activity, but in this case the observed variation depends on the nature of the nucleophile. With soft nucleophiles k_{obsd} progressively diminish (up to 5-fold) as loading increases, whereas with hard nucleophiles k_{obsd} reach a maximum at 30% ring substitution. (vi) Loading increase is accompanied by a progressive increase of hydrophilicity of polymeric catalysts, the main consequence being a concomitant increase both in complexation and in local polarity. (vii) Reaction of phenol with benzyl bromide leads exclusively to the O-alkylation product. (viii) Reactions follow a pseudo-first-order kinetics, and k_{obsd} are linearly related to the molar equivalents of crown ethers bonded to the resin.

The observed data, as a whole, indicate that, as for the related quaternary salts, phase-transfer reactions promoted by polymer-supported crown ethers follow a mechanism identical with that observed for soluble catalysts. As described in eq 10, the

$$\begin{array}{ccccccl} \textcircled{P}\text{—CE}\bullet\text{MY} & + & \text{RX} & \longrightarrow & \textcircled{P}\text{—CE}\bullet\text{MX} & + \ \text{RY} & \text{organic phase} \\ \upharpoonleft\downharpoonright & & & & \upharpoonleft\downharpoonright & & \qquad (10) \\ \text{Y}^- & + & \text{M}^+ & + & \text{X}^- & & \text{aqueous phase} \end{array}$$

reactions occur in the organic shell surrounding a complexed crown ether. Anions are exchanged at the water–organic solvent interface, the exchange not requiring the concomitant transfer of cationic counterparts.

Experimental Section

Chlorobenzene and toluene used for kinetics were Analar grade chemical solvents; organic and inorganic reagents, ACS grade, were used without further purification. Chloromethylated polystyrene, 200–400 mesh, cross-linked with 1% divinylbenzene with 0.67, 1.04, 2.63, and 5.0 mequiv of Cl/g were purchased from Fluka AG. GLC analyses were performed on a Hewlett-Packard Model 5840 flame ionization instrument (2 ft × 0.125 in UCW 982–10% on Chromosorb W column). NMR spectra were recorded with a Varian EM-390 90-MHz NMR spectrometer. Potentiometric titrations were performed with a Metrohm Titroprocessor E636 and Metrohm Dosimat E635. *n*-Octyl methanesulfonate,[35] pentaethyleneglycol ditosylate,[36] and hydroxymethyl-18-crown-6[2a,c] were prepared following standard procedures.

11-(Benzyloxy)-1-undecene (5). A solution of 68.4 g (0.40 mol) of benzyl bromide in 100 mL of anhydrous THF was added dropwise to a vigorously stirred suspension of 51.6 g (0.46 mol) of t-BuO$^-$K$^+$ and 68.1 g (0.40 mol) of 10-undecen-1-ol in 300 mL of anhydrous THF at reflux temperature. Reflux and stirring were maintained for 15 h. After being cooled at room temperature the reaction mixture was filtered and the solid precipitate was washed with 100 mL of methylene chloride. The combined filtrate and washing were evaporated in vacuo. The residue was dissolved in 200 mL of ethyl ether, washed with brine (3 × 80 mL), and dried over $MgSO_4$. Evaporation of the solvent gave 95.0 g of a crude oily product which was distilled under vacuum to afford 68.5 g (66%) of **5**: bp 153–155 °C (1 torr); n^{20}_D 1.4918; ^{1}H NMR ($CDCl_3$) δ 1.10–1.85 (m, 16 H), 1.85–2.22 (m, 2 H), 3.45 (t, 2 H), 4.50 (s, 2 H), 4.8–5.1 (m, 2 H), 5.45–6.0 (m, 1 H), 7.30 (m, 5 H). Anal. Calcd for $C_{18}H_{28}O$: C, 83.00; H, 10.86. Found: C, 82.87; H, 10.62.

11-(Benzyloxy)-1,2-undecanediol (6). A solution of 31.24 g (0.120 mol) of **5** in 40 mL of 99% formic acid was added dropwise at room temperature to a stirred solution of 10.9 mL (0.126 mol) of 35% hydrogen peroxide in 100 mL of 99% formic acid. The reaction mixture was stirred for 24 h at room temperature. The excess of acid was evaporated under vacuum, and the product was directly saponified with 100 mL of 3 N KOH in EtOH (1 h, reflux).

The solvent was evaporated and the residue was acidified with 100 mL of 3 N HCl and extracted with ethyl ether (3 × 100 mL). The organic phase was washed with 100 mL of H_2O and dried over $MgSO_4$. Evaporation of the solvent afforded 32.8 g (93%) of a white solid: mp 43–45 °C (*n*-hexane); ^{1}H NMR ($CDCl_3$) δ 1.10–1.90 (m, 16 H), 2.45 (br s, 2 H) 3.30–3.92 (m, 5 H), 4.50 (s, 2 H), 7.30 (m, 5 H). Anal. Calcd for $C_{18}H_{29}O_3$: C, 73.66; H, 9.98. Found: C, 73.43; H, 9.90.

2-(9-(Benzyloxy)nonyl)-18-crown-6 (8). A solution of 25.2 g (0.046 mol) of pentaethyleneglycol ditosylate in 200 mL of anhydrous THF was added dropwise to a vigorously stirred suspension of 11.4 g (0.102 mol) of t-BuO$^-$K$^+$ and 13.6 g (0.046 mol) of **6** in 300 mL of THF at reflux temperature. Reflux and stirring were maintained for 40 h. After being cooled at room temperature the reaction mixture was filtered and the solid precipitate was washed with 100 mL of CH_2Cl_2. The combined filtrate and washing were evaporated in vacuo; the residue dissolved in 200 mL of CH_2Cl_2 was washed with 100 mL of 3 N HCl and then water (2 × 50 mL). The organic phase was dried over $MgSO_4$ and evaporated to give 21 g of reddish viscous oil. Column chromatography (neutral alumina, EtOAc) gave 6.86 g (30%) of **8** as a thick colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.2–1.7 (m, 16 H), 3.43 (t, 2 H), 3.65 (br s, 23 H), 4.47 (s, 2 H), 7.30 (m, 5 H); mass spectrum, *m/e* 496 (M^+). Anal. Calcd for $C_{28}H_{48}O_7$: C, 67.69; H, 9.76. Found: C, 67.49; H, 9.88.

2-(9-Hydroxynonyl)-18-crown-6 (4). A sample of 2.1 g (4.2 mmol) of **8** dissolved in 80 mL of 95% ethanol was hydrogenated for 3 h at room temperature in the presence of 10% Pd/C (250 mg). Filtration of the catalyst and evaporation of the solvent in vacuo afforded 1.71 g (quantitative yield) of **4** as a colorless thick oil: ^{1}H NMR ($CDCl_3$) δ 1.2–1.8 (m, 16 H), 2.15 (br s, 1 H), 3.4–3.85 (m, 25 H). Anal. Calcd for $C_{21}H_{42}O_7$: C, 62.02; H, 16.82. Found: C, 61.90; H, 16.66.

Polymer-Supported Crown Ethers 1a–d and 2a–d. Functionalized crown ethers **3** and **4** were linked to commercially available 1% cross-linked chloromethylated polystyrenes by refluxing the amount of polymer corresponding to 1 mmol of chlorine with 1.2 mmol of **3** or **4** in THF (50 mL for 1 g of polymer) and 2 mmol of 80% NaH in mineral oil for 4 days. At the end of reaction the polymer was washed with water, methanol, ethyl ether, methylene chloride, ethyl ether, methanol, methylene chloride, and ethyl ether and then dried for 3 h (65 °C, 2 torr). The amount of crown ether bonded to the polymer was estimated by weight increase and elemental analysis of oxygen (Table I).

Kinetic Measurements. Kinetics were run in a 50-mL flask, equipped with a Teflon-lined screw cap, thermostated at 60 °C with circulating butyl phthalate and magnetic stirrer. The temperature was controlled to within ±0.01 °C by a Exacal 200 Bath Circulator. Stirring speed (1300 ± 50 rpm) was controlled by using a strobe light. The flask was charged with 12.5 mL of a 4 M aqueous solution of potassium salt (KX, X = I, Br, CN, SCN), 3 mL of toluene or chlorobenzene, tetradecane as internal standard (2 mL of a 0.1 M solution in toluene or chlorobenzene), and 0.25 mequiv of catalyst. The mixture was left at 60 °C for 12 h at 200-rpm stirring speed in order to condition the catalyst. *n*-Octyl methanesulfonate or *n*-octyl bromide (5 mL of a 1 M solution in toluene or chlorobenzene) was added at zero time and the mixture stirred at 1300 rpm. The reactions were followed by GLC analysis. The pseudo-first-order rate constants (k_{obsd}) were obtained by plotting ln [substrate] vs. time and determining the slope of the straight lines.

Reactions of Potassium Phenoxide with Benzyl Bromide. The flask used for the kinetic measurements thermostated at 60 °C was charged with 5 mL of a 0.2 M solution of phenol in 0.3 M aqueous KOH, 0.2 mequiv of catalyst **1**, 3 mL of toluene, and tetradecane as internal standard (1 mL of a 0.1 M solution in toluene). The mixture was left at 60 °C for 5 h at 200-rpm stirring speed in order to condition the catalyst. Benzyl bromide (2.5 mL of a 0.5 M solution in toluene) was added, and the reaction mixture was stirred at 1300 rpm at 60 °C for 18 h. After being cooled at room temperature the mixture was acidified with 5 mL of 3 N HCl and the organic phase was analyzed by GLC (6 ft × 0.125 in. SE-30–10% on Chromosorb W 80–100 mesh, in a program temperature from 140 to 180 °C). Benzyl phenyl ether was the only product observed: yields were 78, 82, 87, and 96% for catalysts **1a**, **1b**, **1c**, and **1d**, respectively.

Extent of Complexation of Crown Ethers 7 and 8. A 2.5×10^{-2} M chlorobenzene or toluene solution (12 mL) of **7** or **8** and a 4 M aqueous solution (10 mL) of potassium salt (KX, X = I, Br, CN, SCN) was stirred for 2 h in a flask thermostated at 60 °C. Solutions were left without stirring for an additional 2 h to allow good separation of the two phases. A 4-mL sample of the organic phase was titrated with 0.01 N silver nitrate (potentiometric titration). Results are reported in Table V. Experimental error was within ±5% of the obtained values. In the complexation of catalyst **7** with KI and KSCN in toluene–water a third oily layer was formed at the interface. ^{1}H NMR spectra and titration of weighted samples indicated that this layer was essentially the complexed crown ether.

Extent of Complexation of Polymer-Supported Crown Ethers 1a–d. A weighted amount of catalyst, corresponding to 0.3 mequiv of crown ether

J. Am. Chem. Soc. 1984, 106, 869-879

units, was stirred with a 0.3 M aqueous solution (4 mL) of KI or KBr and toluene (4 mL) in a 20-mL centrifuge test tube for 3 h at room temperature. The tube was centrifuged at 3000 rpm for 20 min. Aliquots of the aqueous phase were potentiometrically titrated with 0.01 N silver nitrate. Results are reported in Table VI. Values are the average of at least two measurements. The experimental error was within ±5% of the obtained values.

Swelling and Hydration of Catalysts 1a–d. A 0.5-g sample of catalyst was shaken for 3 h at room temperature in a 10-mL graduated centrifuge test tube with 8 mL of toluene, or 8 mL of a 4 M aqueous solution of KI (or KBr), or 4 mL of toluene and 4 mL of a 4 M aqueous solution of potassium salt and then centrifuged for 20 min at 3000 rpm; the catalyst stratified in a compact layer above, below, and at the interface, respectively. The observed swelling volumes of polymers are reported in Table VII. Measurements were reproducible within ±0.1 mL. Samples of centrifuged catalyst were carefully withdrawn, shaken by hand with 1 mL of anhydrous Me_2SO-d_6, filtered, and analyzed by ^1H NMR. The percent of water in the mixture of solvents adsorbed by the catalyst is reported in Table VII. Values are the average of at least two measurements. The experimental error was within ±5%.

Acknowledgment. This paper was supported by a grant from the Progetto Finalizzato di chimica fine e secondaria of Consiglio Nazionale delle Ricerche (CNR), Roma.

Registry No. 4, 88106-63-2; **5**, 81518-75-4; **6**, 88106-65-4; **7**, 76377-04-3; **8**, 88106-64-3; **9**, 16069-36-6; **12**, 14937-45-2; octyl methanesulfonate, 16156-52-8; octyl bromide, 111-83-1.

Kinetic Isotope Effects and Tunneling in Cyclic Double and Triple Proton Transfer between Acetic Acid and Methanol in Tetrahydrofuran Studied by Dynamic ^1H and ^2H NMR Spectroscopy

Detlef Gerritzen and Hans-Heinrich Limbach*

Contribution from the Institut für Physikalische Chemie der Universität Freiburg i.Br., D-7800 Freiburg, West Germany. *Received December 28, 1982*

Abstract: We have extended our previous studies of proton exchange and hydrogen bonding between acetic acid (A) and methanol (B) in tetrahydrofuran-d_8 to the study of the primary kinetic H/D isotope effects of the exchange. For this purpose a new combination of dynamic ^1H and ^2H NMR spectroscopy has been used to perform an "NMR proton inventory". The following rate law was obtained at deuterium fractions $D = 0$ and $D = 1$ of the exchangeable protonic sites: $v = k^{LL}C_AC_B + k^{LLL}C_A{}^2C_B$ (L = H, D). This was attributed to a superposition of cyclic double and triple proton exchange involving one and two molecules of acetic acid and one molecule of methanol. Additional experiments were carried out at intermediate deuterium fractions. Thus, we have succeeded in measuring the kinetic HH/HD/DD and HHH/HHD/DDD isotope effects of the exchange as a function of the temperature. This has been achieved for the first time for well-defined intermolecular multiple-proton-transfer reactions. We discuss the possibility of determining the number of protons transferred in a chemical reaction by performing an NMR proton inventory. The rule of the geometric mean (RGM) is fulfilled for the kinetic isotope effects of the LLL process, which are almost independent of temperature within the margin of error. By contrast, the RGM is not fulfilled for the LL process, and the kinetic isotope effects depend strongly on the temperature. The energies of activation and frequency factors fit Bell's criteria of tunneling. Our kinetic results are not in good agreement with predictions of transition-state theory but can be explained by an intermolecular tunneling model. The results are proof that acetic acid and methanol form cyclic hydrogen-bonded 1:1 and 2:1 complexes which have a very low concentration in tetrahydrofuran.

Noncatalyzed proton-transfer reactions (HH reactions) of the type

$$AH + XH^* = BH^* + XH \tag{1}$$

can take place between a variety of molecules in protic and aprotic[1-20] media and in the gaseous and the solid[21-24] state. In organic and biochemical systems they are related to bifunctional catalysis[25-33] and biological activity.[34-36] On the other hand, these

---

(1) Bell, R. P. "The Tunnel Effect in Chemistry"; Chapman and Hall: London, 1980.

(2) Grunwald, E. In "Proton Transfer"; Caldin, E., Gold, V., Eds.; Chapman and Hall: London, 1975; p 103.

(3) Denisov, G. S.; Bureiko, S. F.; Golubev, N. S.; Tokhadze, K. G. In "Molecular Interactions"; Ratajczak, H., Orville-Thomas, W. J., Eds.; Wiley: Chichester, 1980; Vol. 2, p 107.

(4) Limbach, H. H. In "Aggregation Processes in Solution"; Gormally, J., Wyn Jones, E., Eds.; Elsevier: Amsterdam, 1983; Studies in Physical and Theoretical Chemistry, Vol. 26, Chapter 16, p 411.

(5) Limbach, H. H.; Seiffert, W. *Ber. Bunsenges. Phys. Chem.* **1974**, *78*, 641.

(6) Limbach, H. H. *Ber. Bunsenges. Phys. Chem.* **1977**, *81*, 1112.

(7) Limbach, H. H. *J. Magn. Reson.* **1979**, *36*, 287.

(8) Hennig, J.; Limbach, H. H. *J. Chem. Soc., Faraday Trans. 2* 1979, 75, 752.

(9) Limbach, H. H.; Hennig, J. *J. Chem. Phys.* **1979**, *71*, 3120.

(10) Limbach, H. H.; Seiffert, W. *J. Am. Chem. Soc.* **1980**, *102*, 538.

(11) Gerritzen, D.; Limbach, H. H. *J. Phys. Chem.* **1980**, *84*, 799.

(12) Limbach, H. H.; Gerritzen, D.; Seiffert, W. *Bull. Magn. Reson.* **1980**, *2*, 315.

(13) Gerritzen, D.; Limbach, H. H. *Ber. Bunsenges. Phys. Chem.* **1981**, *85*, 527.

(14) Limbach, H. H.; Hennig, J.; Gerritzen, D.; Rumpel, H. *Faraday Discuss. Chem. Soc.* **1982**, *74*, 229.

(15) Hennig, J.; Limbach, H. H. *J. Magn. Reson.* **1982**, *49*, 322.

(16) Limbach, H. H.; Hennig, J.; Stulz, J. *J. Chem. Phys.* **1983**, *78*, 5432.

(17) Bureiko, S. F.; Denisov, G. S.; Golubev, N. S.; Lange, I. Y. *React. Kinet. Catal. Lett.* **1979**, *11*, 35.

(18) Bren, V. A., Chernoivanov, V. A.; Konstantinovskii, L. E.; Nivorozhkin, L. E.; Zhdanov, Y. A.; Minkin, V. I. *Dokl. Akad. Nauk SSSR* **1980**, *251*, 1129.

(19) Nesmeyanov, A. N.; Babin, V. N.; Zavelovitch, E. B.; Kochetkova, N. S. *Chem. Phys. Lett.* **1976**, *37*, 184.

(20) Graf, F. *Chem. Phys. Lett.* **1979**, *62*, 291.

(21) Schuster, P., Zundel, G., Sandorfy, C., Eds.; "The Hydrogen Bond"; North-Holland Publishing Co.: Amsterdam, 1976.

(22) Nagoka, S.; Terao, T.; Imashiro, F.; Saika, A.; Hirota, N.; Hayashi, S. *Chem. Phys. Lett.* **1981**, *80*, 580.

(23) Meier, B. H.; Graf, F.; Ernst, R. R. *J. Chem. Phys.* **1982**, *76*, 767.

(24) Baugham, S. L.; Duerst, R. W.; Rowe, W. F.; Smith, Z.; Wilson, E. B. *J. Am. Chem. Soc.* **1981**, *103*, 6286.

(25) Swain, C. G.; Brown, J. F. *J. Am. Chem. Soc.* **1952**, *74*, 2534, 2538.

0002-7863/84/1506-0869$01.50/0