JOC Article

Quantitative Evaluation of the Chloride Template Effect in the Formation of Dicationic [1$_4$]Imidazoliophanes

Susana Ramos,[‡] Ermitas Alcalde,[‡] Giancarlo Doddi,*[,†] Paolo Mencarelli,*[,†] and Lluïsa Pérez-García[‡]

Dipartimento di Chimica e CNR-ICCOM-Sezione di Roma, Università di Roma "La Sapienza", P.le Aldo Moro, 2, 00185 Roma, Italy, and Laboratori de Química Orgànica, Facultat de Farmàcia, Universitat de Barcelona, Avda. Joan XXIII s/n, 08028-Barcelona, Spain

paolo.mencarelli@uniroma1.it

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The formation of macrocycles containing two imidazolium rings such as **1**·2X and **2**·2X is anion-directed through hydrogen bonding. The template effect exerted by the chloride anion in the ring-closure reaction of the monocationic model intermediate $\mathbf{9}^+$ to yield the [1$_4$]imidazoliophane $\mathbf{2}^{2+}$ has been evaluated. This effect was quantified following the kinetics of the macrocyclization by using a UV−vis technique. The rate of the ring closure of monocation $\mathbf{9}^+$ is increased up to 10 times, in the presence of Bu_4NCl 0.04 M. This finding confirms that the template effect is operative in the macrocyclization leading to dicationic [1$_4$]imidazoliophanes.

Introduction

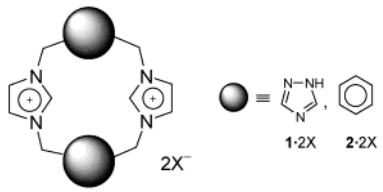
In recent years, the use of template-directed synthesis[1] has enormously benefited the obtention of macrocycles. Countless examples of metal cations and organic neutral molecules as templates have been reported in the preparation of macrocycles. However, despite the increasing use of templates that can be found in the literature, anions have been employed in only a few cases.[2]

It should be noted that generally the evidence of the template effect is based on yield increases,[3] and only a few examples of the evaluation of the operating effect through kinetic studies have been reported.[4]

Part of our research has been focused on the preparation of novel macrocyclic systems built up from heterocyclic betaine subunits, and an ensemble of [1$_n$]heterophanes has been reported.[5] The "3 + 1" convergent stepwise synthesis of several examples of dicationic [1$_4$]heterophanes,[6] frameworks containing two imidazolium rings, such as **1**·2X, is template-controlled in the presence of anions.[7] Moreover, the molecular recognition motifs for anion templating involve the interaction of a multicentered chloride ion with the heteroaromatic and aromatic rings. In fact, there is structural evidence for the existence of hydrogen bonds between chloride ions and the C(2)−H of the imidazolium ring components of the dicationic [1$_4$]heterophanes **1**·2X, as shown by X-ray crystallography;[6] chloride anions selectively increased the yield in comparison with other anions.[7]

The significant increase of the yield in the preparation of dicationic [1$_4$]imidazoliophanes using the chloride

CHART 1



1·2X, **2**·2X

† Università di Roma "La Sapienza".

‡ Universitat de Barcelona.

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(2) For some examples of anion templates in the synthesis of organic molecules and supramolecules see: (a) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486-516. (b) Aoyagi, M.; Biradha, K.; Fujita, M. *J. Am. Chem. Soc.* **1999**, *121*, 7457−7458. (c) Hübner, M.; Gläser, J.; Seel, C.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 383−386. (d) Reuter, C.; Wienand, W.; Hübner, G. M.; Seel, C.; Vögtle, F. *Chem. Eur. J.* **1999**, *5*, 2692−2697. (e) Fyfe, M. C. T.; Glink, P. T.; Menzer, S.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2068−2070. (f) Li, F.; Yang, K.; Tyhonas, J. S.; MacCrum, K. A.; Lindsey, J. S. *Tetrahedron* **1997**, *53*, 12239−12360.

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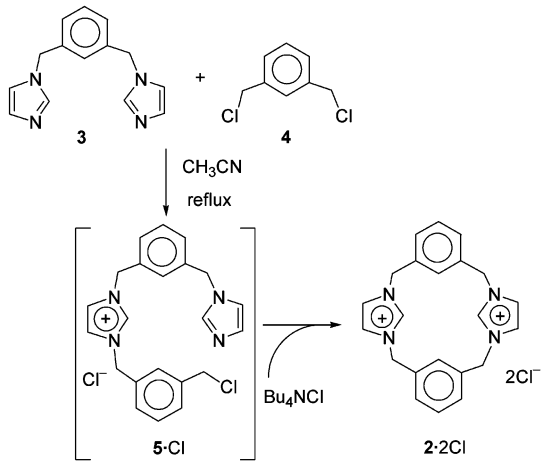
SCHEME 1. "3 + 1" Convergent Synthesis of Dicationic [1$_4$]Heterophane 2·2Cl



anion as template[7] prompted us to carry out a kinetic study of the reaction to quantitatively evaluate the template effect. Here we report the quantitative results obtained for the template-controlled macrocyclization reaction in the presence of chloride anions, leading to the dicationic [1$_4$]imidazoliophane **2**$^{2+}$.

Results and Discussion

The "3 + 1" convergent synthesis leading to the imidazoliophane **2**·2Cl is based on the coupling of protophane **3**[6] with the bis-chloromethyl derivative **4** in acetonitrile under reflux. The reaction occurs in two steps, as shown in Scheme 1, and only the second one, i.e., the ring closure reaction of the intermediate **5**·Cl, should benefit from the template ability of the guest. However compound **5**·Cl has never been isolated.

To evaluate the template effect of the chloride anion in the formation of the cyclophane **2**·2Cl, the preparation of the acyclic intermediate **5**·Cl, the immediate precursor of macrocycle **2**·2Cl along the reaction path, is required.

The preparation of **5**·Cl was attempted according to the route illustrated in Scheme 2. Equimolecular amounts of compounds **3** and **6** were allowed to react in acetonitrile at room temperature for 24 h, affording, after column chromatography, the monocationic ester salt **7**·Br in 20% yield. The ester **7**·Br was converted to the hydrochloride **5H**·2Cl by treatment with 37% HCl, at 95 °C for 24 h and was isolated as **5H**·2PF$_6$, after anion exchange with silver hexafluorophosphate (Scheme 2).

Pure compounds **5H**·2X were isolated and fully characterized both as the chloride and hexafluorophosphate salts **5H**·2Cl and **5H**·2PF$_6$, and their neutralization to **5**·X was attempted. Different experimental conditions were tried in order to carry out the neutralization,[8] but compound **5**·X was never isolated pure: its formation was always accompanied—more or less—by the formation of the macrocyclic compound **2**·2X. The rate of formation of **2**·2X was variable, and it depended on the experimental conditions used (base, solvent, and temperature), and interestingly, it was also counterion dependent: the formation of **2**·2X was always more favored for chloride **5H**·2Cl than for hexafluorophosphate **5H**·2PF$_6$. These facts were in good agreement with the previous results obtained in the formation of dicationic macrocycles such as **2**·2X.[7]

Due to the difficult isolation of compound **5**·X, its protonated form **5H**·2X was selected in order to carry out the deprotonation in situ during the kinetic study, using an organic base, for instance, triethylamine. Initially, the kinetics of cyclization of the more soluble hexafluorophosphate **5H**·2PF$_6$ was examined by ^{1}H NMR in CD_3CN. Unfortunately, fast cyclization of **5H**·2PF$_6$ did not permit us to record sufficient experimental data to calculate meaningful kinetic constants. Furthermore, to avoid the formation of the chloride anions, which could act as templates during the cyclization, the preparation of an alternative intermediate, **9H**·2Pic,[9,10] was taken into consideration. In this case, the use of picrate as leaving group could permit us to follow the kinetics of the reaction by a UV—vis technique.

The preparation of **9H**·2Pic was performed as shown in Scheme 3. The ester **7**·Br, previously synthesized, was converted to the hydrobromide **8H**·2Br by treatment with 48% HBr, at 95 °C for 24 h. The reaction of **8H**·2Br with silver picrate[11a,b] at 60 °C afforded the compound **9H**·2Pic in 98% yield.

Spectroscopic Methods. The structures of new compounds **5/6**—**9H**·2Pic were determined by ^{1}H and ^{13}C NMR spectroscopy. Assignment of the most characteristic signals was made by using NMR experiments (HMBC and HMQC), and the data are shown in Table 1 for compounds **5H,7**—**9H**·2Pic.

Electrospray Ionization Mass Spectrometry. ESI-MS was used to examine charged compounds in the gas phase. ESI-MS was measured as described elsewhere,[12] samples being dissolved in H_2O/CH_3CN (1:1), while the cone voltage was kept at 60 V (Table 2). Compounds **5H**·2PF$_6$, **5H**·2Cl, **8H**·2Br, and **9H**·2Pic (M·2X), containing two aromatic rings and two imidazolium units, show two common characteristic peaks: the ion [M]$^{2+}$ corresponding to the loss of both counterions, and the ion [M—H]$^+$ also corresponding to the loss of both counterions and deprotonation. For compounds **5H**·2Cl and **8H**·2Br, the base peak corresponds to the singly charged fragment ion [**3H**]$^+$ at *m*/*z* 239, due to the protonated trinuclear 1,3-bis(1-imidazolylmethyl)benzene, thus

(8) Neutralization was attempted by adding different aqueous solutions such as NH_4OH, $NaHCO_3$, and Na_2CO_3 to a solution of compound **5H**·2X in H_2O or CH_3NO_2, and fitting the pH to 7—8. Et_3N was also added to a solution of compound **5H**·2X in CH_3CN.

(9) Previously, compound **10H**·2OTs (see Experimental Section) was also considered, which contained in its structure two tosylate counterions and a tosyl as leaving group. The cyclization of compound **10H**·2OTs was followed by ^{1}H NMR in CD_3CN. Similarly to compound **5H**·2PF$_6$, the cyclization reaction was too fast to record enough experimental data to obtain significant kinetic constants.

(10) The reactivity of picrate as leaving group was tested, by reacting 2,4,6-trinitrophenylbenzyl ether **11** (see Experimental Section) and 1-methylimidazole. The quaternization reaction was monitored by UV—vis in CH_3CN at 65 °C. The quaternization was complete after 2 days.

(11) (a) Silver picrate was prepared from 2,4,6-trinitrophenol by treatment with sodium hydroxide and silver nitrate, and after crystallization in water. (b) Kolthoff, I. M.; Lingane, J. J.; Larson, W. D. *J. Am. Chem. Soc.* **1938**, *60*, 2512—2515.

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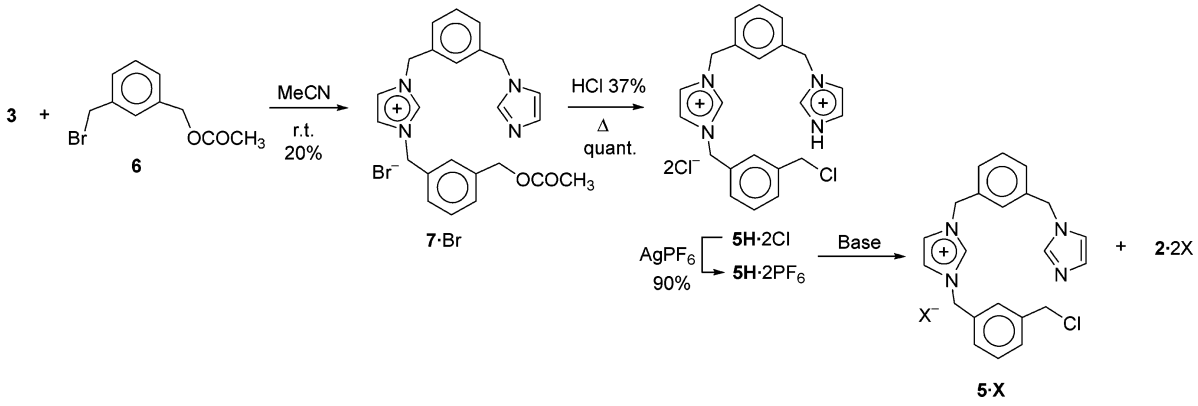
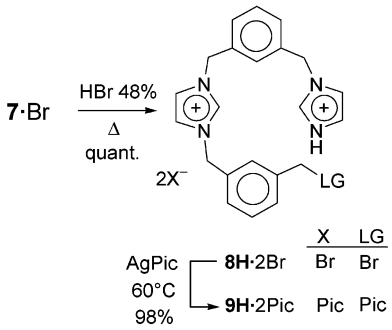
SCHEME 2. Preparation of Precursor 5·X



SCHEME 3. Preparation of the Precursor 9H·2Pic



indicating that fragmentation occurs even under these soft experimental conditions.

Compound **7**·Br (M·X), which has one imidazolium ring in its structure, showed the formation of the ion $[M]^+$, which corresponds to the loss of one counterion, and of the fragment ion $[\mathbf{3H}]^+$ produced with a relative abundance of 91% (V_c = 60 V).

Kinetic Study. The following kinetic scheme (Scheme 4) can be envisaged for the reaction of the monocation $\mathbf{9}^+$ in the presence of chloride anions.

The kinetics of cyclization has been studied by UV−vis spectroscopy in acetonitrile at 25 °C, following the absorbance variation, at λ 370 nm, which is the λ_{max} of the picrate anion. To avoid polymerization reactions, the concentration of the substrate **9**·Pic was kept as low as possible (ca. 7×10^{-4} M).

The first-order rate constant k_0 is the rate constant for the cyclization reaction of the monocation $\mathbf{9}^+$, in the absence of chloride anions, to yield the macrocycle $\mathbf{2}^{2+}$ (Scheme 4). However, since by adding variable amounts of Bu_4NCl the ionic strength of the solution is changed, for each kinetic measurement at a given concentration of Bu_4NCl the k_0 value was evaluated at the same ionic strength, utilizing $Et_4NCF_3CO_2$ as a buffering salt (see Experimental Section for details).

First-order rate constants (k_{obs}) have been obtained in the presence of variable excess amounts of the chloride anion as Bu_4NCl (see Experimental Section), up to its solubility limit. The ratios k_{obs}/k_0, plotted in Figure 1 against the concentration of Bu_4NCl, provide a measure of the rate enhancement produced by the presence of the template. The data show that the ring closure of the monocation $\mathbf{9}^+$·Pic is accelerated by the presence of chloride anions, up to 10 times at $[Bu_4NCl]$ ca. 4×10^{-2} M.

Such rate enhancements can be related to the template concentration by eq 1,

$$\frac{k_{obs}}{k_0} = \frac{1 + (k_1/k_0)K_{sub}[Cl^-]}{1 + K_{sub}[Cl^-]} \qquad (1)$$

which can be obtained from the kinetic Scheme 4 by assuming that the association equilibrium between $\mathbf{9}^+$ and the chloride ion is fast with respect to the ring closure reaction. Equation 1 can be transformed into eq 2

$$\frac{k_{obs}}{k_0} = \frac{1 + K_{T\#}[Cl^-]}{K_{sub}[Cl^-]} \qquad (2)$$

by considering the distribution Scheme 5, which takes into account the association of the template with the open chain precursor $\mathbf{9}^+$ and with the cyclic transition state.[4a,b]

In eq 2 $K_{T\#}$ ($=k_1K_{sub}/k_0$) and K_{sub} have the meaning as the association constant of the template with the cyclic transition state and with the open chain precursor $\mathbf{9}^+$, respectively (Scheme 5).[4c,d]

The ring closure reaction of the monocation $\mathbf{9}^+$, benefits from the template ability of the chloride anion when it binds the transition state more strongly than the reactant.[13] This is mainly due to the preorganization of the cyclic transition state and, secondarily, to the development of a further positive charge on the initially neutral nitrogen atom (Scheme 5).

Nonlinear least-squares fit[14] to eq 1 of the k_{obs}/k_0 ratios provided the following values for the association constants: $K_{T\#} = 941 \pm 78$ M^{-1} and $K_{sub} = 72 \pm 9$ M^{-1}.

The saturation value, which is given by the $K_{T\#}/K_{sub}$ ratio, is the maximum theoretical rate enhancement that would be attained when the substrate is completely bound to the template.[4c,d] This value indicates that the complexed form of $\mathbf{9}^+$ with the chloride ion, is ca. 13 times more reactive than the free one.

In conclusion, the chloride anion serves as a template for the synthesis, leading to the dicationic [1₄]imidazoliophane $\mathbf{2}^{2+}$. The rate enhancement observed, up to 10

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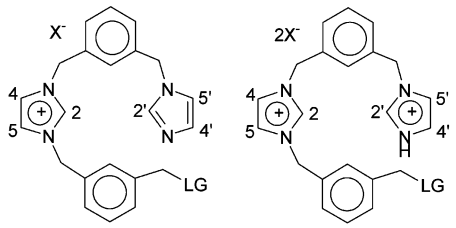
(14) The nonlinear least-squares fitting program used was SigmaPlot Program, SPSS Inc., 233 S. Wacker Drive, 11th floor, Chicago, IL 60606.

TABLE 1. Selected ^{1}H NMR[a] Data for Compounds 7·Br, 5H·2Cl, 5H·2PF$_6$, 8H·2Br, and 9H·2Pic



7·Br X = Br; LG = $OCOCH_3$

	X	LG
5H·2Cl	Cl	Cl
5H·2PF$_6$	PF_6	Cl
8H·2Br	Br	Br
9H·2Pic	Pic	Pic

compd	H-2	H-4	H-5	H-2′	H-4′	H-5′	CH_2-LG	LG
7·Br[b]	9.37	7.83	7.80	7.72	6.89	7.14	5.07	2.05 (CH_3)
5H·2Cl[b]	9.45	7.84	7.80	9.30	7.70	7.76	4.76	
5H·2PF6[b]	9.40	7.84	7.80	8.90	7.54/7.61[c]		4.76	
5H·2PF6[c]	8.60	7.38/7.44[b]		8.60	7.38/7.44		4.69	
8H·2Br[b]	9.51	7.85/7.86[c]		9.37	7.81	7.73	4.69	
9H·2Pic[c]	8.75	7.37/7.46[b]		8.64	7.37/7.46[b]		5.26	8.91 (Pic-LG[d]) 8.72 (Pic-anion)

[a] Previous related compounds have been useful for the assignment of the signals. [b] DMSO-d_6 (500 MHz). [c] CD_3CN (200 MHz). [d] LG means picrate as leaving group.

TABLE 2. Summary of Data Obtained from Positive Ion ESI-MS[a] of 7·Br, 5H·2Cl, 5H·2PF$_6$, 8H·2Br, and 9H·2Pic

	ions, *m*/*z* ratio relative abundance (%)			
compd (M_w)	$[M]^{2+}$	$[M - H]^+$	$[M + X]^+$	**[3H]**$^{+\,b}$
5H·2Cl (449.8)	189.8 23	377.8 68	c	239.7 100
5H·2PF$_6$ (668.8)	189.3 100	377.5 44	523.5 35	239.4 61
8H·2Br (582.1)	211.2 39	421.1 68	c	239.3 100
9H·2Pic (1027.7)	285.8 48	570.0 100	c	c
7·Br (481.4)	400.6[d] 100			239.4 91

[a] V_c = 60 V. [b] Protophane (**3**, M_w 238.3). [c] No signal observed. [d] $[M]^+$.

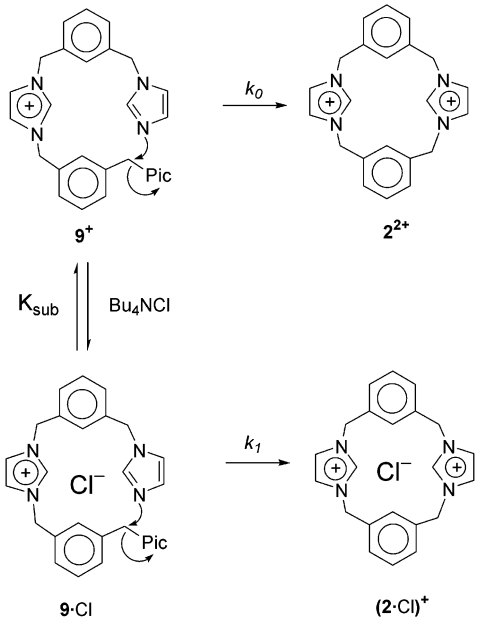
times in the presence of 0.04 M Bu_4NCl, indicates that the ring closure reaction is accelerated in the presence of the template. Thus, the chloride anion stabilizes the transition state, favoring the macrocyclization through hydrogen bonding, as appears to be also suggested by the X-ray structure of the imidazoliophane product **2**·2Cl.[6] The quantitative evaluation of the template effect caused by the chloride anions allows us to justify the improvement of the yields observed for dicationic [1$_4$]imidazoliophanes, and it will be useful to understand and take advantage of the anionic template effect in the preparation of related compounds.

Experimental Section

General and Instrumentation. Thin-layer chromatography (TLC) were carried out on precoated 60 F254 silica gel and precoated 60−200 UV254 aluminum gel plates. Column chromatography was performed on silica gel 60 70−200 mesh (SDS) and aluminum oxide 90 standardized. ^{1}H NMR spectra were recorded at 200, 300, and 500 MHz. ^{13}C NMR spectra were recorded at 50.3 MHz.

Materials. Silver hexafluorophosphate, tetraethylammonium trifluoroacetate (98%), tetrabutylammonium chloride (≥99%), and trifluoroacetic acid (99%) were used without further purification.Triethylamine was distilled from Na, and

SCHEME 4. Kinetic Scheme



HPLC-grade acetonitrile was used in the kinetic experiments without further purification.

3-(Bromomethyl)benzyl Acetate (6). A suspension of 1,3-bis(bromomethyl)benzene (5.3 g, 20.0 mmol) and potassium acetate (1.96 g, 20.0 mmol) was allowed to react in DMF (50 mL) at 80 °C for 24 h. The solvent was removed in vacuo and the solid extracted with ethyl ether (4 × 25 mL). The organic fractions were combined and dried (Na_2SO_4) and the solvent was removed in vacuo. Column chromatography (silica gel, toluene) afforded **7** as a colorless oil (1.5 g, 32%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.12 (s, 3H), 4.49 (s, 2H), 5.10 (s, 2H), 7.26−7.35 (m, 3H), 7.37 (s, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 21.0, 51.8, 65.7, 127.9−128.8, 136.5, 138.1, 170.8; IR (film) 1740, 1223 cm^{-1}; MS (EI) *m*/*z* (%) 163 (100) $[M - Br]^+$, 242 (6) $[M - 1]^+$. Anal. Calcd for $C_{10}H_{11}BrO_2$: C 49.0, H 4.6. Found C 49.1, H 4.6.

1-(3-Acetoxymethyl)benzyl-3-[3-(1-imidazolilmethyl)-benzyl]imidazolium Bromide (7·Br). A solution containing **6** (0.5 mg, 2.05 mmol) in acetonitrile (10 mL) was added dropwise (ca. 5h) to a solution of protophane **3** (0.49 g, 2.05

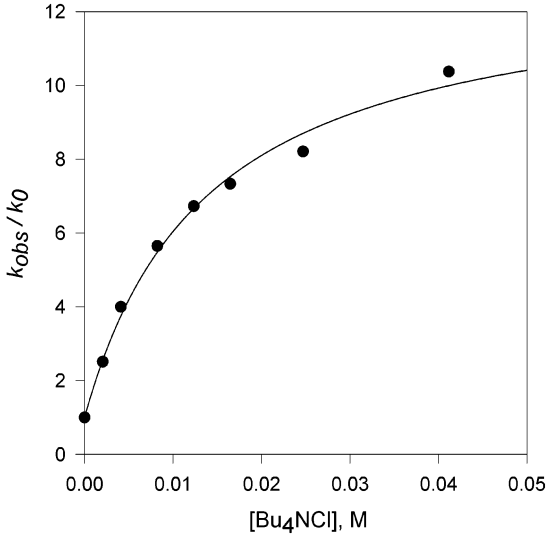
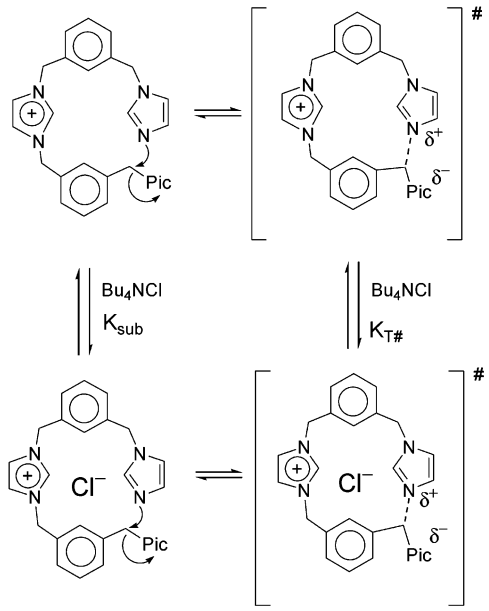


FIGURE 1. Rate enhancement produced by the chloride ion on the ring closure reaction of the monocation **9**$^+$. The points are experimental and the curve is calculated from eq 2.

SCHEME 5. Distribution Scheme



mmol) in acetonitrile (16 mL). The solution was kept at room temperature for 24 h. The solvent was removed in vacuo and the residue was purified by column chromatography (standardized alumina, $CHCl_3/CH_3OH$ increased polarity until 3%). The fractions containing **7**·Br were combined, and the solvent was removed in vacuo, affording **7**·Br as a colorless oil (0.19 g, 20%): ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 21.0, 49.4, 52.1, 65.3, 119.8, 123.2, 127.0, 127.6, 127.8, 128.0, 128.2, 128.6, 128.9, 129.0, 129.5, 129.7, 135.3, 135.5, 136.6, 138.5, 138.9, 170.5; IR (film) 1732, 1230 cm^{-1}.

3-(3-Chloromethyl)benzyl-1-[3*H*-3-(1-imidazoliomethyl)benzyl]imidazolium Dichloride (5*H*·2Cl). The salt **7**·Br (0.25 g, 0.5 mmol) in 37% HCl (7 mL) was heated at 95 °C for 24 h. After cooling, the suspension obtained was filtered and the solvent was evaporated in vacuo, affording **5H**·2Cl as a colorless oil (0.22 g, quant): ^{13}C NMR (50.3 MHz, DMSO-d_6) δ 45.9, 51.5, 51.9, 120.5, 122.3, 123.1, 128.5, 128.7, 128.8, 128.85, 129.0, 129.5, 129.6, 129.9, 135.5, 135.7, 136.1, 136.7, 138.7. Anal. Calcd for $C_{22}H_{23}N_4Cl_3$: C 58.7, H 5.1, N 12.5. Found: C 58.3, H 5.2, N 12.8.

3-(3-Chloromethyl)benzyl-1-[3*H*-3-(1-imidazoliomethyl)benzyl]imidazolium Bishexafluorophosphate (5*H*·2PF$_6$). Silver hexafluorophosphate (0.29 g, 1.14 mmol) was added to an absolute methanol solution (6 mL) of **5H**·2Cl (0.255 g, 0.57 mmol). The gray precipitate formed was filtered and the solvent was removed in vacuo at 25 °C, affording **5H**·$2PF_6$ as a colorless oil (0.34 g, 90%): ^{13}C NMR (50.3 MHz, DMSO-d_6) δ 45.8, 51.4, 51.9, 120.7, 122.4, 123.1, 128.0, 128.1, 128.2, 128.3, 128.4, 129.0, 129.2, 129.5, 130.5, 135.3, 135.5, 135.7, 136.0, 136.6, 138.6. Anal. Calcd for $C_{22}H_{23}N_4ClF_{12}P_2$: C 39.5, H 3.5, N 8.4. Found: C 39.9, H 4.0, N 8.5.

3-(3-Chloromethyl)benzyl-1-[3*H*-3-(1-imidazoliomethyl)benzyl]imidazolium Dibromide (8*H*·2Br). The salt **7**·Br (0.17 g, 0.35 mmol) in 48% HBr (9 mL) was heated at 95 °C for 24 h. After cooling, the suspension obtained was filtered and the solvent was evaporated in vacuo, affording **8H**·2Br as a colorless oil (0.20 g, quant): ^{13}C NMR (50.3 MHz, DMSO-d_6) δ 51.4, 51.8, 52.3, 62.6, 120.4, 122.2, 123.0, 126.4, 126.8, 128.5, 128.7, 128.9, 129.8, 134.7, 135.7, 136.0, 136.5, 143.6.

3-[3-(2,4,6-Trinitrophenoxy)methyl]benzyl-1-[3*H*-3-(1-imidazoliomethyl)benzyl]imidazolium Bis(2,4,6-trinitrophenolate) (9H·2Pic). 8H·2Br (0.1 g, 0.17 mmol) was added to an acetonitrile solution (6 mL) of silver picrate (0.19 g, 0.58 mmol). The solution was kept at 65 °C for 1.5 h. The suspension obtained was filtered and the solvent was removed in vacuo at 25 °C, affording **9H**·2Pic as a colorless oil (0.17 g, 98%). ^{13}C NMR (50.3 MHz, DMSO-d_6) δ 51.6, 52.0, 52.2, 71.5, 120.6, 122.2, 123.1, 124.4, 127.6, 128.0, 128.3, 128.6, 129.2, 129.9, 134.9, 135.6, 135.7, 135.9, 136.6, 139.2, 141.9, 160.9. Anal. Calcd for $C_{40}H_{29}N_{13}O_{21}\cdot 2H_2O$: C 45.1, H 3.1, N 17.1. Found: C 44.9, H 2.7, N 17.2.

Preparation of Compound 10H·2OTs and ^{1}H NMR Study of the Cyclization Reaction. Compound **10H**·2OTs was prepared from the hydrochloride precursor **5H**·2Cl by treatment with silver tosylate as follows.

Silver tosylate (0.19 g, 0.69 mmol) was added to an acetonitrile suspension of **5H**·2Cl (0.1 g, 0.22 mmol) (5 mL). The suspension was kept at 50 °C for 6 h. After this time, the suspension was filtered and the solvent was removed in vacuo at 25 °C, affording **10H**·2OTs as a hygroscopic solid (0.08 g, 42%): ^{1}H NMR (300 MHz, CD_3CN) δ 2.29 (s, 6H), 2.39 (s, 3H), 5.00 (s, 2H), 5.27/5.30/5.33 (3xs, 6H), 7.1−7.8 (m, 24H), 8.91 and 9.27 (s, 2H); ESI-MS (60V) *m*/*z* (%) 513.8 (2) [M − H]$^+$, 239.4 (100) [**3** + H]$^+$.

^{1}H NMR Study. The cyclization reaction was started by adding 1 equiv of triethylamine to a solution of compound **10H**·2OTs in CD_3CN. The reaction progress was monitored by following the disappearance of the CH_2OTs signal and the appearance of a new signal at δ 9.6 ppm (H_2–Im$^+$ of the macrocycle formed). A clean cyclization reaction was observed, but it was too fast to allow us to obtain a sufficient number of experimental data to calculate meaningful kinetic constants.

Preparation of 2,4,6-Trinitrophenylbenzyl Ether (11). Benzyl chloride (43 μL, 0.37 mmol) was added to an acetonitrile solution of silver picrate (0.13 g, 0.47 mmol) (2 mL). The solution was kept at 60 °C for 6 h. After this time, the suspension obtained was filtered and the solvent was removed in vacuo. The residue was partitioned between CH_2Cl_2 (15 mL) and an aqueous saturated solution of K_2CO_3 (10 mL). The aqueous phase was washed again with an aqueous K_2CO_3 solution (2 × 10 mL), and then the organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The yellow solid obtained was crystallized from toluene/hexane, affording **11** (35 mg, 30%). ^{1}H NMR (300 MHz, CD_3CN) δ 5.27 (s, 2H), 7.43 (m, 5H), 8.91 (s, 2H).

Kinetic Measurements. Kinetic measurements were carried out at 25 °C in acetonitrile, in a 3 mL cuvette (optical path 1 cm) kept in the thermostated cell compartment of the spectrophotometer.

TABLE 3. Rate Constants in CH_3CN at 25 °C

$[Bu_4NCl]$ (M)	k_{obs} (s^{-1})	$[Et_4NCF_3CO_2]$ (M)	k_0 (s^{-1})	k_{obs}/k_0
0	9.63×10^{-4}	0	9.63×10^{-4}	1
2.06×10^{-3}	2.49×10^{-3}	2.06×10^{-3}	9.91×10^{-4}	2.51
4.12×10^{-3}	4.18×10^{-3}	4.12×10^{-3}	1.05×10^{-3}	4.00
8.23×10^{-3}	6.00×10^{-3}	8.23×10^{-3}	1.06×10^{-3}	5.65
1.23×10^{-2}	7.41×10^{-3}	1.23×10^{-2}	1.10×10^{-3}	6.73
1.65×10^{-2}	8.43×10^{-3}	1.65×10^{-2}	1.15×10^{-3}	7.33
2.47×10^{-2}	1.01×10^{-2}	2.47×10^{-2}	1.23×10^{-3}	8.21
4.12×10^{-2}	1.39×10^{-2}	4.12×10^{-2}	1.34×10^{-3}	10.37

A stock solution (0.0073 M) of picrate **9H**·2Pic was prepared by dissolving 0.075 g of **9H**·2Pic in 10 mL of acetonitrile containing trifluoroacetic acid 0.2 M. The trifluoroacetic acid was necessary to prevent the dissociation of the protonated imidazole ring of **9H**·2Pic by the picrate ions which are present as counterions [pK_a picric acid = 11 (CH_3CN);[15] pK_a *N*-methylimidazole = 7.4 (CH_3CN);[16] pK_a trifluoroacetic acid = 7.4 (CH_3CN)[17]].

In a typical run, 5 μL of a 0.0073 M solution of **9H**·2Pic was added to 3 mL of acetonitrile solution containg tetrabutylammonium chloride or tetraethylammonium trifluoroacetate at the appropriate concentration (see below). The reaction was started by adding 2 μL of triethylamine [pK_a triethylamine = 18.5 (CH_3CN)[18]] to the cuvette. The progress of reaction was followed at λ 370 nm, which is the λ_{max} of the picrate anion. In all of the cases a first-order behavior was observed.

The concentration of the tetrabutylammonium chloride was varied from 0 to 4.12×10^{-2} M and a total of eight kinetic measurements were carried out. To take into account the effect of the ionic strength which increases on increasing the salt concentration, for each kinetic experiment carried out at a given concentration of tetrabutylammonium chloride (k_{obs}), an independent kinetic was carried out at the same ionic strength by using tetraethylammonium trifluoroacetate at the same concentration (k_0 value). All the kinetic constants obtained are reported in Table 3 together with the k_{obs}/k_0 ratios.

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Supporting Information Available: ^1H spectra for all new compounds and intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

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