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Effect of Alkali Cations on the Methoxide Ion Addition to Corands Incorporating a Thiopyrylium Subunit

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Abstract: The incorporation of a thiopyrylium ring in a corand structure forms a system with a weak binding ability in methanol towards the alkali cations K^+, Rb^+ and Cs^+. The binding substantially increases in basic solution because of the reversible addition of methoxide ion to the heteroaromatic ring to form a neutral 4*H* adduct. The effect of the length of the polyoxyethylene chain and of the presence of a bulky group (*tert*-butyl) in the γ position of the heteroaromatic ring has been quantitatively investigated. Results obtained from molecular mechanics calculations were used to rationalise the depressing effect of the γ *tert*-butyl group on the ligand ability of thiopyrans.

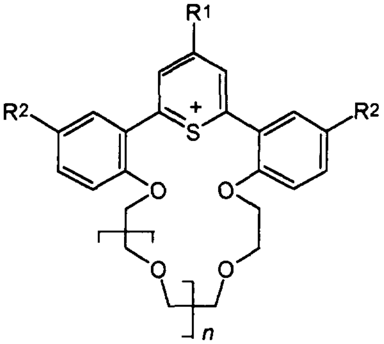
Introduction

Much interest is currently devoted to responsive macrocyclic receptor molecules whose binding strength and/or selectivity towards guest species can be reversibly influenced by physical and chemical means.[1] An important class of such receptors is constituted by pH-responsive crown ethers which change their cation binding ability in response to the pH of their environment. Usually they contain one or more proton-ionizable functional groups attached to the periphery or incorporated into the backbone of the macrocyclic structure.[1,2] However pH-responsive receptors can be also obtained by incorporating in the crown ether ring an electrophilic group capable of reversibly adding the conjugate base of the solvent. An example of this approach regarding the addition of methoxide ion to an aldehydic group attached to a podand structure has been recently investigated by us.[3]

In search of additional electrophilic groups to be incorporated in a polyether structure we focused our attention on the thiopyrylium ring, since it can undergo the reversible addition of anionic nucleophiles to yield neutral adducts.[4] Accordingly we wish to report the results of an investigation regarding the effects of the alkali cations Na^+, K^+, Rb^+ and Cs^+ on the reversible addition of methoxide ion in methanol to the corands **1a**-**3a**.

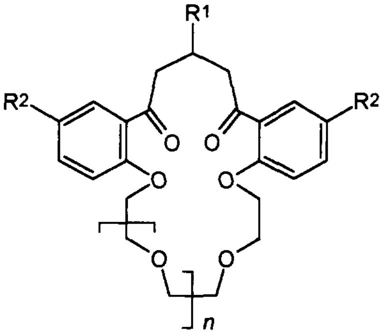
Results and Discussion

In order to assess the behaviour of thiopyrylium corands we considered the compounds **1a**-**3a**. These were chosen in order to evaluate the effect of the crown ether size (**1a** *vs.* **2a**) and of the presence of a bulky group in the γ position of the heteroaromatic ring (**2a** *vs.* **3a**).



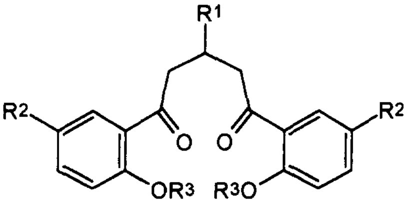
1a-3a

1a R1 = H, R2 = Me, *n* = 2
2a R1 = H, R2 = Me, *n* = 3
3a R1 = *t*-Bu, R2 = H, *n* = 3



4, 5

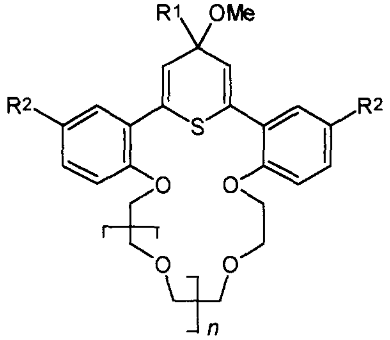
4 R1 = H, R2 = Me, *n* = 3
5 R1 = *t*-Bu, R2 = H, *n* = 3



6 R1 = H, R2 = Me, R3 = H
7 R1 = *t*-Bu, R2 = H, R3 = H
8 R1 = *t*-Bu, R2 = H, R3 = Me

Syntheses. The preparation of the compound **1a** had been previously reported.[5] The compounds **2a** and **3a** were prepared by heterocyclization of the corresponding macrocyclic 1,5-pentanediones **4** and **5** with P_4S_{10}. These in turn were prepared by two-component cyclization of the appropriate bis-phenol, **6** or **7**, with pentaethylene glycol ditosylate. The compound **6** was prepared in one step by reaction of *p*-methylanisole with glutaryl dichloride and $AlCl_3$ in CH_2Cl_2 [5] (the presence of the *para* methyl group makes the reaction regiospecific addressing the acylation in the *ortho* position only), whereas the compound **7** was prepared in three steps: *i*) condensation of *o*-methoxyacetophenone with trimethylacetaldehyde; *ii*) Michael addition of *o*-methoxyacetophenone to the resulting enone to yield **8**; *iii*) demethylation of **8** with trimethylsilyl iodide generated *in situ*.

^{1}H NMR Study. ^{1}H NMR spectra of CD_3OD solutions of cations **1a-3a**, recorded at 25 °C after the addition of an equivalent of CD_3ONMe_4 in CD_3OD showed the fast and complete conversion of the substrates into the corresponding 4*H* adducts **1b-3b** (^{1}H NMR data are reported in the Experimental). The assignment of the chemical structures was based on the multiplicity of the signals and on the comparison with data reported for related reactions.[6,7] The behaviour of the cation **3a** was unexpected, because it is in contrast with that of 2,6-diphenyl-4-*tert*-butylthiopyrylium ion which is known to react with methoxide ion to yield both the 4*H* and 2*H* adducts.[7] The different behaviour is due to the presence of the polyoxyethylene chain that evidently decreases the stability of the 2*H* adduct.



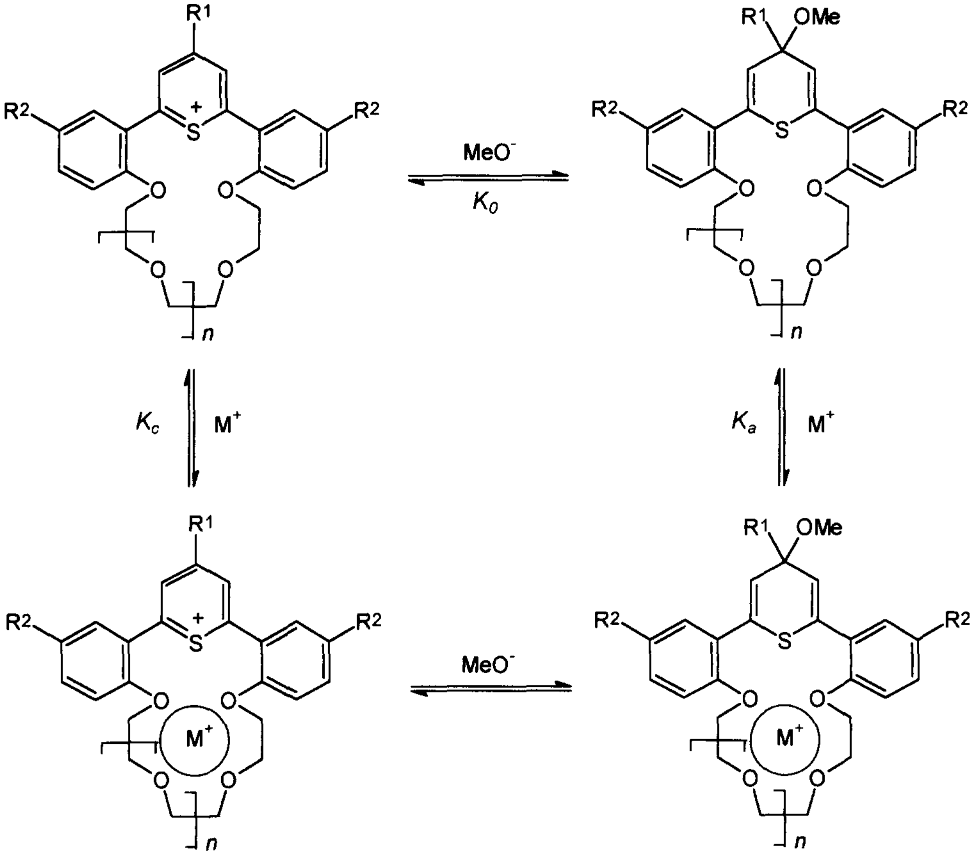
1b-3b

1b R1 = H, R2 = Me, *n* = 2
2b R1 = H, R2 = Me, *n* = 3
3b R1 = *t*-Bu, R2 = H, *n* = 3

Any association between the adducts **1b-3b** and tetramethylammonium ion was ruled out because of the large ionic radius of the latter with respect to the cavity size of the corands. To check the possibility of complexation of the alkali cations Na^+, K^+, Rb^+ and Cs^+ by the adducts **1b-3b**, an NMR investigation was carried out in the presence of the corresponding alkali bromides. In fact chemical shift variations of the signals of the adducts after the addition of the alkali cations K^+, Rb^+, and Cs^+, were observed. In contrast the presence of NaBr did not cause any appreciable variation in the ^{1}H NMR spectrum of the adducts.

The ^{1}H NMR spectra of the cations **1a-3a** were unaffected by the presence of the alkali cations Na^+, K^+, $Rb^+$and Cs^+.

Equilibrium Measurements. Equilibrium measurements were carried out spectrophotometrically at 25.0 °C and at constant ionic strength (0.15 M) by measuring the absorbance of a buffered solution of the given thiopyrylium corand after the addition of increasing amounts of an alkali cation solution. The buffer (Et_3N / Et_3NH^+) was chosen in order to have initially almost equal concentrations of thiopyrylium ion and 4*H* adduct in equilibrium. Absorbance measurements were carried out at a wavelength where only the thiopyrylium corand absorbs. Since the 4*H* adduct is expected to be a better ligand than the thiopyrylium cation, addition of an alkali cation is expected to shift the equilibrium toward the 4*H* adduct thus causing a decrease of the absorbance. Indeed the experimental results confirmed our expectaction, and the observed decrease of absorbance was accounted for by Scheme 1.



Scheme 1

Even though there were no NMR evidences for the association of thiopyrylium corands with Na^+, K^+, Rb^+ and Cs^+, there was the necessity to consider this equilibrium in order to accomodate the spectrophotometric results.

The possibility that alkali bromides could affect the basicity of the buffer was ruled out in that no absorbance variations were observed when a thiopyrylium salt lacking the polyoxyethylene chain, i.e. 2,6-di-*tert*-butyl-4-phenylthiopyrylium, was treated under the same conditions.

The absorbance mesurements allowed the evaluation of the ratio R of the concentration of $4H$ adduct to that of thiopyrylium corand. The equilibrium constant for the addition of methoxide ion to thiopyrylium corand is given by the ratio R / $[MeO^-]$. In the absence of added alkali cations, this ratio coincides with the equilibrium constant K_0 , whereas in the presence of alkali cations, coincides with the apparent equilibrium constant K_{app} defined as shown in Eq. 1, where A and $A{\cdot}M^+$ stand for the free and metal ion associated $4H$ adduct, C and $C{\cdot}M^+$ stand for the free and metal ion associated thiopyrylium corand.

$$K_{app} = \frac{([A]+[A\cdot M^+])}{([C]+[C\cdot M^+])[MeO^-]} \tag{1}$$

The ratio K_{app}/K_0 (= K_{rel}) provides a measure of the effect of the metal ion on the ease of formation of the 4*H* adduct. In fact K_{rel} values were calculated as the ratio of the quantity *R* measured in the presence of added salt over that measured in its absence. The value of K_{rel} is related to the metal ion concentration by Eq. 2, where K_a and K_c are the association contants of 4*H* adduct and thiopyrylium corand, respectively, with metal ions.

$$K_{rel} = \frac{1+K_a[M^+]}{1+K_c[M^+]} \tag{2}$$

Apart from the case of sodium ion which proved to be ineffective with all of the substrates, all the reactions showed an increase of K_{rel} on increasing $[M^+]$. The dependence of K_{rel} on metal ion concentration is practically linear if $K_c \times [M^+]$ is lower than 0.1, otherwise a significant downward curvature is observed. Two typical profiles are reported in Fig. 1 and 2.

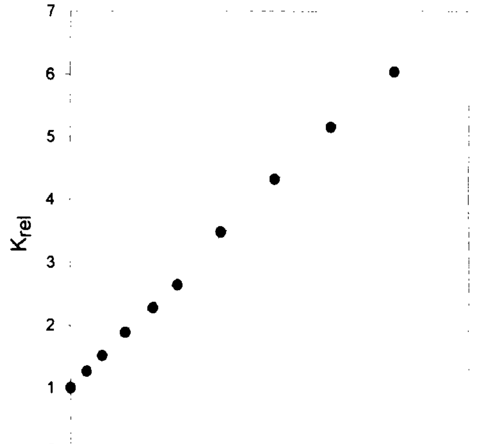


Figure 1 Variations of K_{rel} with the analytical concentration of Cs^+ for the substrate **1a** in MeOH at 25 °C and ionic strength = 0.15 mol L^{-1}.

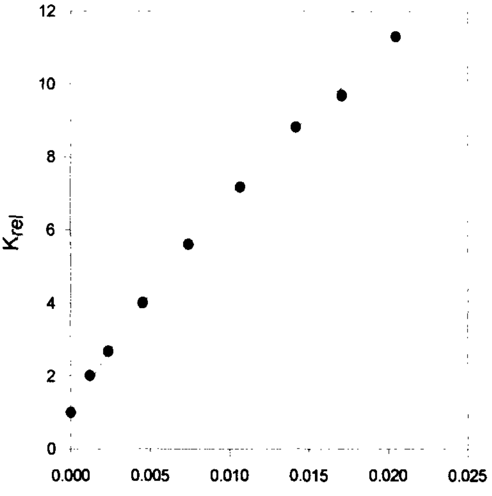


Figure 2 Variations of K_{rel} with the analytical concentration of Cs^+ for the substrate **2a** in MeOH at 25 °C and ionic strength = 0.15 mol L^{-1}. The curve is calculated by Eq. 2.

In Table 1 are reported the association constants obtained by non-linear least square curve fitting of the experimental data according to Eq. 2. As expected the neutral ligands are more effective than the positively charged ones, however it is noteworthy that the thiopyrylium corands, in spite of the positive charge, show a non-negligible ligand ability. This is greater for the corands **2a** and **3a** which have a longer polyoxyethylene chain thus suggesting that an increase of the number of binding sites can compensate for the unfavourable coulombic interactions between the metal ion and the charged heteroaromatic ring. However the association constants K_c are rather low and this would explain why interaction of the thiopyrylium corands with the metal ions Na^+, K^+, Rb^+ and Cs^+ did not produce appreciable NMR variations.

Table 1 Association constants (mol^{-1} L) of the heteroaromatic cations **1a-3a** and the corresponding adducts **1b-3b**, with the alkali cations K^+, Rb^+ and Cs^+ in MeOH at 25 °C.[a,b]

		K^+	Rb^+	Cs^+
K_c	**1a**	-	2.4 (0.7)	2 (1)
	2a	19 (1)	15 (1)	22 (2)
	3a	17 (2)	22 (2)	13 (2)
K_a	**1b**	104 (6)	244 (4)	220 (6)
	2b	82 (5)	339 (6)	744 (24)
	3b	26 (2)	55 (3)	75 (3)

[a] Standard deviations in parenthesis. [b] Association constants lower than 1 are not reported.

The neutral adducts, besides being better ligands, show some selectivity. This is illustrated in Fig. 3 where the constants K_a are reported against the ionic radius of K^+, Rb^+, and Cs^+. It appears that **2b** which has a polyoxyethylene chain longer than **1b** and lacks the *tert*-butyl group in the position 4 of the thiopyran ring, is not only the best ligand but also the most selective.

It is interesting to note that the presence of the bulky *tert*-butyl group has a relevant depressing effect on the ligand ability of thiopyrans, whereas it is ineffective on the binding strength of the corresponding thiopyrylium cations. The reduced coordination properties of **3b** with respect to **2b** cannot be ascribed to the absence on the aromatic rings of the electron releasing methyl groups because the ligand properties of a number of aryl substituted crown ethers, *e.g.*, dibenzo-18-crown-6 derivatives, are practically insensitive to this kind of substitution.[8] In order to understand the effect of the γ *tert*-butyl group on the ligand ability of 4*H*-thiopyrans we decided to carry out molecular mechanics calculations on the thiopyrans **2b** and **3b** and on their K^+, Rb^+ and Cs^+ complexes.

Molecular Mechanics Calculations. A thorough exploration of the conformational space of each compound was carried out by the Monte Carlo method in order to find the lowest energy conformation (global minimum).

Two features emerged from the results. The first one is that the free thiopyrans and their alkali cation complexes exhibit a U shaped conformation in which the cavity formed by the polyoxyethylene chain is bent over the thiopyran ring, not far from the γ methoxy group. This evidence suggests that the oxygen atom of the methoxy group may have a role in the complexation of the metal cation.

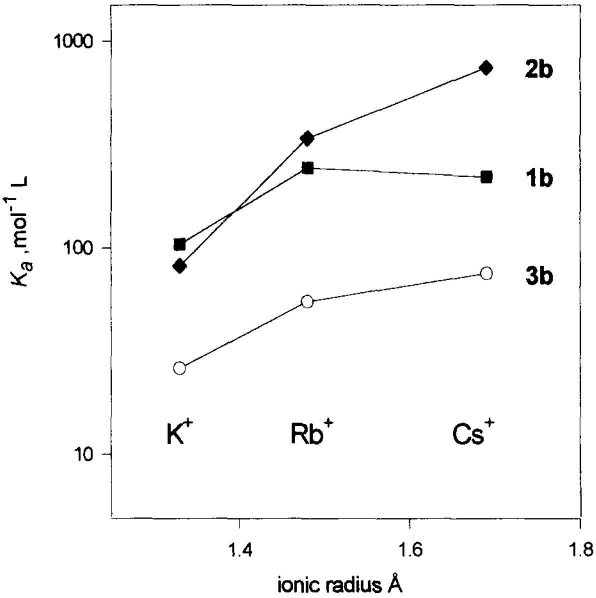


Figure 3 Plot of associations constants K_a vs. the ionic radius

The second point is that in the metal ion associated thiopyran **2b**, independently of the type of alkali metal ion, the methoxy group orients itself with the oxygen atom pointing toward the cation in the cavity, whereas in the case of **3b** the methoxy group, in order to avoid the unfavourable steric interaction between the methyl and the geminal bulky *tert*-butyl group, has rotated thus pointing the oxygen atom away from the cavity. This behaviour is clearly evident in Fig. 4 and 5 in which, as an exemplification, the global minimum structures of the complexes of **2b** and **3b** with the rubidium cation are shown. In Table 2 are reported all the metal cation–oxygen atoms distances measured in the global minima found for the complexes of thiopyrans **2b** and **3b** with K^+, Rb^+ and Cs^+. It is evident from the table that, for all the cations, the two different orientations of the methoxy group have a relevant effect on the $CH_3O - M^+$ distance.

In conclusion the molecular mechanics calculations suggests an active participation in the metal ion complexation of the methoxy group in the case of the thiopyran **2b**, whereas in the case of **3b** this participation is precluded by an unfavourable orientation of the methoxy group forced by steric interactions with the *tert*-butyl group.

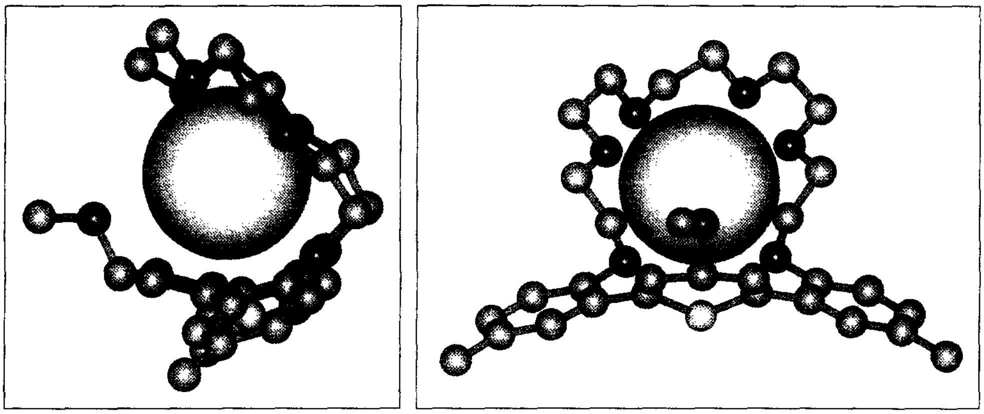


Figure 4 Two orthogonal views of the global minimum structure found for the complex of **2b** with the Rb^+ ion (hydrogen atoms omitted).

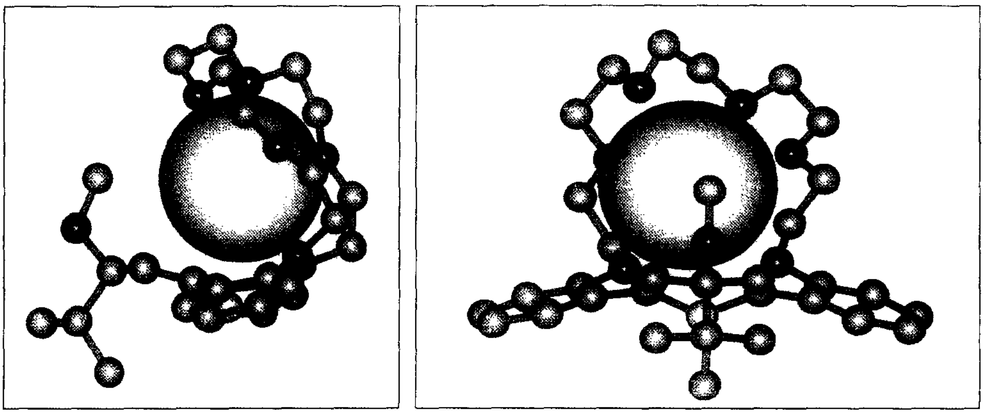


Figure 5 Two orthogonal views of the global minimum structure found for the complex of **3b** with the Rb^+ ion (hydrogen atoms omitted).

Table 2 Metal cation-oxygen atoms distances (Å) in the global minimum structures of adducts **2b** and **3b**

Adduct	Cation	$-CH_3\mathbf{O}$	$Ar\mathbf{O}-$	$-CH_2CH_2\mathbf{O}-$
	K^+	2.96	3.48 ; 3.51	2.78 ; 2.51 ; 2.44 ; 2.75
2b	Rb^+	3.24	3.58 ; 3.37	2.82 ; 2.69 ; 2.64 ; 2.83
	Cs^+	3.18	4.19 ; 3.41	3.15 ; 3.03 ; 2.84 ; 3.42
	K^+	4.41	2.94 ; 3.33	2.68 ; 2.54 ; 2.56 ; 2.66
3b	Rb^+	4.50	3.06 ; 3.34	2.35 ; 2.75 ; 2.69 ; 2.79
	Cs^+	4.62	3.14 ; 3.56	3.09 ; 2.86 ; 2.97 ; 3.08

Experimental

Melting points are uncorrected. ^{1}H NMR spectra were recorded with a Bruker WP-80 SY and a Bruker AC 300 P. All the prepared compounds gave clean ^{1}H NMR spectra. MS-EI and MS-FAB spectra were obtained with a VG 4. Spectrophotometric measurements were carried out at 25.0 °C in 10 mm quartz cuvettes with a Varian Cary 219. The purity of the thiopyrylium corands (> 98 %) was checked by spectrophotometric titration in MeOH with a methanolic solution of NaOMe of known concentration.

Materials. Acetone-d_6, acetonitrile-d_3, chloroform-d and methanol-d_4 for NMR spectroscopy were from Carlo Erba. Purification of triethylamine and drying of methanol were carried out as previously reported.[9] AR-grade Et_4NBr, and Et_3NHBr[10] were dried in vacuum at 110 °C. Pentaethylene glycol ditosylate was from Aldrich. Tetramethylammonium hydroxide (25 wt % in methanol) was from Janssen. Diketone **6**, and perchlorate of **1a** were available from our previous work.[5,11] CD_3OD solution of CD_3ONMe_4 was obtained by repeated evaporation, under vacuum, and dissolution in this solvent of a known quantity of the methanolic Me_4NOH solution.

5',4"-Dimethyl-4,7,10,13,16,19-hexaoxa-26-thionia-2,3;20,21-dibenzobicyclo[20,3,1]hexacosa-1(26), 2,20,22,24-pentaene perchlorate[11] (**2a**) was obtained in 50 % yield, from diketone **4** following the published method for the synthesis of **1a**.[5] This salt decomposes by air exposure, therefore it was kept and handled under argon. M$^+$ calcd 511.21, found 511.2. For ^{1}H NMR and UV-vis data *vide infra.*

24-*Tert*-butyl-4,7,10,13,16,19-hexaoxa-26-thionia-2,3;20,21-dibenzobicyclo[20,3,1]hexacosa-1(26),2,20,22,24-pentaene perchlorate[11] (**3a**). The synthesis of this salt from diketone **5** was carried out according to the published method for the synthesis of **1a**.[5] The purification procedure was modified with respect to that reported because the crude product consisted in a mixture of the expected thiopyrylium salt and of the corresponding pyrylium salt (the molar ratio thiopyrylium:pyrylium evaluated by ^{1}H NMR was 1.3:1). The thiopyrylium content was raised by dissolving the crude product in acetone (1 g in 40 mL) and adding a solution of 0.41 g of $Na_2S{\cdot}9H_2O$ in 10 mL of water. The resulting solution was warmed at 40 °C for 30 m, then, after cooling at room temperature, it was added to a solution of 0.5 mL of $HClO_4$ in 250 mL of water and extracted with CH_2Cl_2. The organic extracts were dried and, after having reduced the volume to 10 mL, ethyl ether was added until complete precipitation of a solid that the ^{1}H NMR analysis revealed to be thiopyrylium: pyrylium mixture 4:1. This procedure was repeated a second time raising the thiopyrylium content to 8.6:1. The final purification of **3a** was accomplished according to a previously described procedure[12] that relied on the selective attachment of methoxide ion to the pyrylium ring to yield the neutral 2*H*-pyran which can be easily removed. Overall yield 19 %; mp 58-59 °C (dec.). M$^+$ calcd 539.25, found 538.9. For ^{1}H NMR and UV-vis data *vide infra.*

5',4"-Dimethyl-8,11,14,17,20,23-hexaoxa-6,7;24,25-dibenzocyclopentacosa-6,24-diene-1,5-dione (**4**) was prepared by reaction of **6** with pentaethylene glycol ditosylate according to a cognate synthesis.[5] The crude product was purified by flash chromatography (ethyl acetate): yield 20 %; mp 68-69 °C; ^{1}H NMR ($CDCl_3$) 2.02 (p, 2H, J 7.3 Hz, $CH_2CH_2CH_2$), 2.26 (s, 6H, CH_3), 3.12 (t, 4H, J 7.3 Hz, $CH_2CH_2CH_2$), 3.60 (s, 4H), 3.64 (s, 8H), 3.75-3.95 (m, 4H, $ArOCH_2CH_2$), 4.05-4.25 (m, 4H, $ArOCH_2CH_2$), 6.7-7.5 (m, 6H, Ar*H*).

3-*Tert*-butyl-8,11,14,17,20,23-hexaoxa-6,7;24,25-dibenzocyclopentacosa-6,24-diene-1,5-dione (**5**). A 100 mL solution of **7** (1.0 g, 2.94 mmol) and pentaethylene glycol ditosylate (1.61 g, 2.94 mmol) in dry DMF was added over a 5 h period to a stirred suspension of 1.3 g (9.4 mmol) of anhydrous K_2CO_3 in 200 mL of dry DMF, maintained at 70 °C. After the addition was completed the reaction mixture was kept at this temperature for 5 h. By removal of the solvent under reduced pressure an oil was obtained that was poured into water and extracted with ethyl ether. The extracts were dried ($CaCl_2$), the solvent removed and the residue purified by column chromatography (silica gel, benzene/ethyl acetate 1:1) to give a solid product : yield 45 %; mp 88.5-89.5 °C; ^{1}H NMR ($CDCl_3$) 0.92 (s, 9H, CH_3), 2.6-3.3 (m, 5H,), 3.64 (s, 12H), 3.7_5-3.9 (m. 4H, $ArOCH_2CH_2$), 4.0-4.2 (m, 4H, $ArOCH_2CH_2$), 6.8-7.7 (m, 8H, Ar*H*).

1,5-Bis(2-hydroxyphenyl)-3-*tert*-butylpentane-1,5-dione (**7**) was obtained by demethylation of **8** with an excess of trimethylsilyl iodide (8:1), according to a published procedure.[13] The reaction was carried out at 85 °C for 7 h. The crude product was purified by flash chromatography (CH_2Cl_2) to give a solid compound: yield 80%; mp 88-89 °C; ^{1}H NMR ($CDCl_3$) 1.00 (s, 9H, CH_3), 2.6-3.3_5 (m, 5H), 6.8-7.8 (m, 8H, Ar*H*), 12.08 (s, 9H, O*H*).

1,5-Bis(2-methoxyphenyl)-3-*tert*-butylpentane-1,5-dione (**8**) was prepared by refluxing for 18 h 7 g of trimethylacetaldehyde (0.08 mol) with 12 g of 2-methoxyacetophenone (0.08 mol) in 70 mL of methanolic sodium methoxide (1.25 M). The residue obtained by solvent removal was poured in water and extracted with ethyl ether. The extracts were dried and the solvent evaporated to give an oil that was added together with 13.6 g of 2-methoxyacetophenone (0.091 mol) to a 90 mL benzene suspension of 5 g of sodium amide (0.128 mol). The reaction mixture was refluxed for 20 h under argon, then poured into water and extracted with ethyl ether. The extracts were washed with water and dried (Na_2SO_4). After removal of the solvent the residue was recrystallized from a 1:1 *n*-hexane/methanol mixture: yield 38 %; mp 82-83 °C; ^{1}H NMR ($CDCl_3$) 0.89 (s, 9H, CH_3), 2.6-3.3_5 (m, 5H) 3.85 (s, 6H, OCH_3), 6.8_5-7.6 (m, 8H, Ar*H*).

^{1}H NMR Study. The spectra of **1a-3a** recorded in CD_3OD (ca. 5×10^{-3} mol L^{-1}) were the following:

1a: δ 2.44 (s, 6H, CH_3); 3.3-3.5 (m, OCH_2CH_2O); 3.7-3.8 (m, 4H, $ArOCH_2CH_2O$); 4.3-4.4 (m, 4H, $ArOCH_2CH_2O$); 7.2_5-7.6_8 (m, 6H, ArH); 8.87 (A_2B-system, J 9 Hz, 1H, H-21); 9.92 (A_2B-system, J 9 Hz, 2H, H-20 and H-22).

2a: δ 2.43 (s, 6H, CH_3), 3.6-3.7 (m, 12H, OCH_2CH_2O), 3.7_5-3.8_5 (m, 4H, $ArOCH_2CH_2O$), 4.2-4.4 (m, 4H, $ArOCH_2CH_2O$), 7.2-7.7_5 (m, 6H, ArH), 9.17 (A_2B- system, J 6.7 Hz, 1H, H-24), 9.27 (A_2B-system, J 6.7 Hz, 2H, H-23 and H-25).

3a: δ 1.61 (s, 9H, CH_3), 3.4-3.5 (m, 12H), 3.8_5-3.9_5 (m, 4H, $ArOCH_2CH_2$), 4.3_5-4.4_5 (m, 4H, $ArOCH_2CH_2$), 7.3-7.8 (m, 8H, ArH), 8.98 (s, 2H, H-23 and H-25).

The spectra of adducts **1b-3b** were recorded after the addition of 6 µl of a CD_3OD solution of CD_3ONMe_4 (ca. 0.5 M) to 500 µl of a CD_3OD solution of the corresponding cations **1a-3a** (ca. 5×10^{-3} mol L^{-1}). The signals of the adducts remained unchanged after ten hours.

1b: δ 2.28 (6H, s, CH_3); 3.6-3.9 (12H, m); 4.0-4.2_5 (4H, m, $ArOCH_2$); 5.16 (1H, t, J 5.0 Hz, *H*γ); 5.92 (2H, d, J 5.0 Hz, *H*β); 6.8_6-7.2 (6H, m, *Ar*).

2b: δ 2.28 (6H, s, CH_3); 3.6-3.9 (16H, m); 4.0-4.2_5 (4H, m, $ArOCH_2$); 5.16 (1H, t, J 5.3 Hz, *H*γ); 6.03 (2H,d, J 5.3 Hz, *H*β); 6.8_6-7.2 (6H, m, *Ar*).

3b: δ 1.03 (9H, s, CH_3); 3.5_4-3.6 (12H, m); 3.8_3-3.9 (4H, m, $ArOCH_2CH_2$); 4.1-4.2 (4H, m, $ArOCH_2CH_2$); 5.75 (2H, s, *H*β); 6.9-7.4 (8H, m, *Ar*).

Equilibrium Measurements. UV-vis spectra of the thiopyrylium corands **1a-3a** and of the 4*H* adducts **1b-3b** recorded in methanol were the following:

1a: λ_{max}, nm (ε) 454 (11500), 358 (6500), 310 (7000), 245 (20500).

2a: λ_{max}, nm (ε) 460 (12200), 358 (5000), 307 (6900), 244 (21000).

3a: λ_{max}, nm (ε) 431 (11900), 346 (4600), 280 sh, 263 (15000), 241 (18300).

1b: λ_{max}, nm (ε) 287 (8200), 240 sh.

2b: λ_{max}, nm (ε) 289 (8700), 240 sh.

3b: λ_{max}, nm (ε) 287 (8600), 240 sh.

Absorbance measurements were carried out at 25.0 °C in 10 mm quartz cuvettes at a wavelength where only the thiopyrylium corand absorbs (**1a**: 454 nm; **2a**: 460 nm; **3a**: 431 nm). It was verified that the presence of the alkali cations Na^+, K^+, Rb^+ and Cs^+ does not significantly affect the spectra of the thiopyrylium corands.

In a typical run 2 mL of a buffered solution (Et_3N *ca.* 10^{-3}-10^{-2} mol L^{-1} / Et_3NHBr *ca.* 10^{-2} mol L^{-1}) of the corand (*ca.* 2-3x10^{-5} mol L^{-1}) whose ionic strength is adjusted to 0.15 mol L^{-1} with Et_4NBr, are placed in a cuvette and the absorbance measured. The ratio R is evaluated as $(A_0 - A) / A$, where A_0 is the absorbance of the substrate solution under acid conditions (*vide infra*), and A the measured absorbance. Increasing amounts of a 0.15 mol L^{-1} NaBr, or 0.1 mol L^{-1} KBr, or 0.057 mol L^{-1} RbBr, or 0.055 mol L^{-1} CsBr solution (whose ionic strength is adjusted to 0.15 mol L^{-1} with Et_4NBr if necessary) are added with a Hamilton microsyringe to the sample cuvette. After each addition the absorbance value is recorded with allowance being made for thermal equilibration. After correction for dilution, the absorbance value is used to calculate the new R value, this was then translated into the value of the constant K_{rel}. In Fig. 6 is reported the plot of the absorbance, corrected for dilution, as a function of the metal ion concentration in a typical run. The value of A_0 is evaluated as follows: to 2 ml of the initial solution placed in a cuvette is added an axcess of methanolic $HClO_4$ thus completely shifting the equilibrium toward the thiopyrylium substrate; the measured absorbance is then corrected for dilution affording the value of A_0

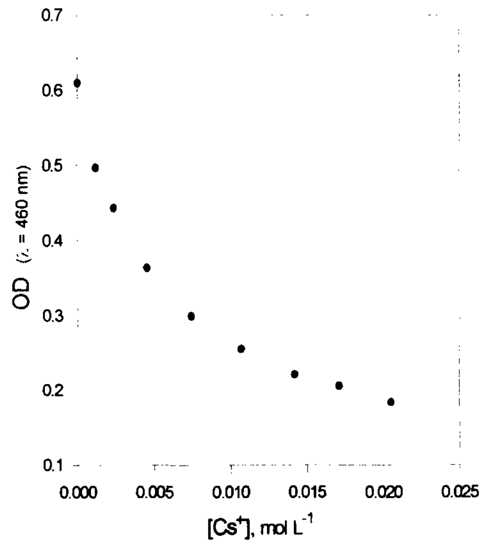


Figure 6 Plot of absorbance *vs* Cs+ concentration. [**2a**]= 6.50×10^{-5} mol L^{-1}; [Et_3N]= 4.00×10^{-3} mol L^{-1} ; [Et_3NH^+]= 4.00×10^{-2} mol L^{-1} ; [Et_4N^+]= 1.10×10^{-1} mol L^{-1} .

Metal ion concentrations were considered coincident with the corresponding analytical concentration in that alkali metal salts generally behave as strong electrolytes in methanol.[14]

Non-linear least-squares curve fitting of the experimental data was carried out by the SIGMA PLOT program.[15]

Computational Procedure. All the calculations were carried out utilizing the Force Field MM+, an extension of the MM2 Force Field[16] as implemented in the HyperChem, Release 4 for Windows, Molecular Modeling System.[17]

Some Force Field parameters, relative to some structural features of the thiopyran subunit, that were inappropriate or missing, were added by us to the MM+ Force Field. The choice of the parameters (force constants, standard bond lengths, and standard bond angles) was based on x-ray data of a thiopyran derivative[18] and on structural data obtained by semiempirical (PM3) MO calculations on 2,6-diphenyl-4*H*-thiopyran. The appropriate parameters for the van der Waals interactions of the alkali cations, that were missing in the original MM+ Force Field, were added to the Force Field as described elsewhere.[19] Each calculation was carried out *in vacuo* ($\varepsilon = 1.5$). The non-bonded electrostatic interactions were calculated by using the partial atomic charges obtained by a semiempirical (PM3) MO calculation. The exploration of the conformational space of thiopyrans **2b** and **3b** and of their alkali cation complexes was carried out by the Monte Carlo approach[20] as implemented in the Conformational Search module of the ChemPlus extensions for HyperChem.

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