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Study of the Reaction of Bis- and Tris-pyrylium and -thiopyrylium Cations with Methoxide Ion. Electronic Effects of the Heterocyclic Rings as Substituents

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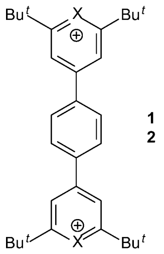
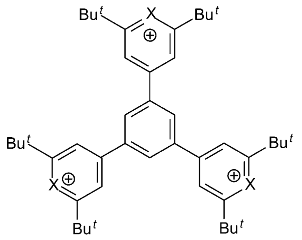


1 X = O
2 X = S



3 X = O
4 X = S

The bis- and tris-pyrylium and thiopyrylium cations **1**−**4** were prepared in gram scale by heterocyclization of the corresponding bis- and tris-1,5-pentanediones **6** and **8**. Their reaction with CD_3ONa in CD_3OD was studied by ^1H NMR at −40 °C and at +25 °C. At low temperature, kinetically controlled mixtures of 2*H* and/or 4*H* adducts were detected, whereas at room temperature the mixtures equilibrated to yield, in all of the cases, the more stable 2*H* adducts exclusively. A spectrophotometric study of the reactions with sodium methoxide in methanol was carried out at 25.0 °C with the aim of determining the stepwise equilibrium constants for the addition of MeO^- at the α position of the heteroaromatic rings. The obtained equilibrium constants allowed the evaluation of the electronic effects of chalcogenopyrylium and 2*H*-chalcogenopyran subunits as substituents. Despite the different sensitivity to electronic effects, pyrylium and thiopyrylium rings have a similar electron-withdrawing effect with a $\sigma^+_p \sim 0.8$ and a $\sigma^+_m \sim 0.5$. Apart from the expected importance of the inductive effect due to the positive charge, the difference between these two values remarks the importance of the resonance contribution. In contrast both the neutral 2*H*-pyranyl and thiopyranyl rings have a negligible effect as substituents, independently of the position, para or meta, they occupy.

Introduction

Dynamic covalent chemistry[1] requires reversible reactions to selectively build template-driven assemblies under thermodynamic control. In the course of our ongoing research on the physical basis of template effects and self-assembly,[2] we planned to investigate the behavior of covalent dynamical systems based on pyrylium[3] and thiopyrylium[4] cations, as these heteroaromatic units are known to undergo reversible addition by a number of nucleophiles to yield neutral adducts.

As a preliminary study, we report here the preparation of the bis- and tris-pyrylium and thiopyrylium cations **1**−**4** (see the Abstract graphic) and a quantitative study of their reaction with methoxide ion in methanol, aimed at elucidating the electronic effects of chalcogenopyrylium and chalcogenopyran subunits on addition equilibria.

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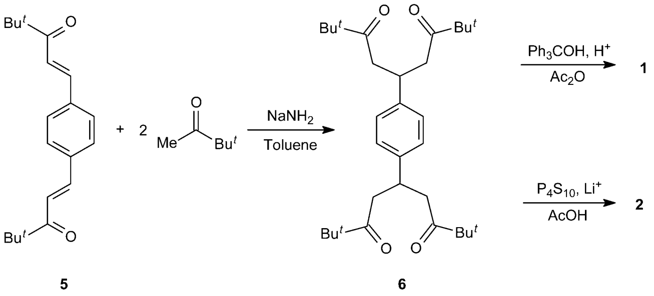
10.1021/jo050884a CCC: $30.25

SCHEME 1



Results

Synthesis of 1−4. The bispyrylium **1** was prepared by an improved procedure that proved to be simpler and slightly more efficient than that reported in the literature (72% vs 61% total yield):[5] Michael addition of 2 equiv of pinacolone to the bisenone **5**, promoted by heterogeneous sodium amide in toluene, yielded the bispentanedione **6** in 80% yield; this was converted into the bispyrylium cation **1** in high yield (91%) by oxidation in acetic anhydride with triphenylcarbenium tetrafluoroborate generated in situ (Scheme 1).

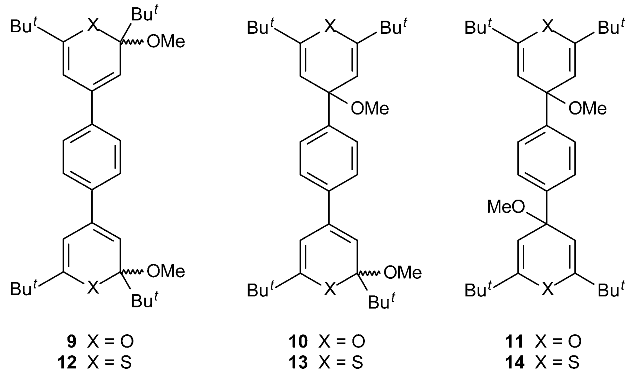
Since the 1,5-pentanedione substructure may be regarded as a synthetic precursor of the thiopyrylium ring as well, the bispentanedione **6** was also converted into the bisthiopyrylium cation **2** (yield 42%) by the method of Strzelecka and Gionis,[6] i.e., by reaction in acetic acid with P_4S_{10} in the presence of lithium perchlorate (Scheme 1).

Analogous procedures were used for the preparation of the triscations **3** and **4**, as illustrated in Scheme 2.

The tris-enone **7** was prepared in 63% yield by NaOH-catalyzed condensation in aqueous ethanol of benzene-1,3,5-tricarbaldehyde with 3 equiv of pinacolone. Michael addition of 3 equiv of pinacolone to the tris-enone **7**, promoted by heterogeneous sodium amide in toluene, yielded the tris-pentanedione **8** in 77% yield. This was converted into both the tris-pyrylium cation **3** (yield 90%) and the tris-thiopyrylium cation **4** (yield 21%) by the same methods followed for the syntheses of **1** and **2**. It should be noted that the low yield of the thiopyrylium salts **2** and **4** is mainly due to the purification procedure that required repeated recrystallizations in order to remove mixed pyrylium−thiopyrylium byproducts.

^{1}H NMR Study of the Reactions of 1−4 with Methoxide Ion. We had previously studied the reaction of a number of simple pyrylium and thiopyrylium cations, symmetrically substituted in the 2,6-positions, with methoxide ion in methanol by ^{1}H NMR.[7] Besides providing quantitative data about the effects of the ring-heteroatom and of substituents in pyrylium and thiopyrylium ions, these studies were aimed at gaining a deeper understanding of cation−anion combination reactions. The reactions of the bis- and tris-cations **1**−**4** were studied by the same approach, i.e., by recording ^{1}H NMR spectra at low temperature (≈ −40 °C) immediately after the mixing of the reactants, and at room temperature (≈ 25 °C). At low temperature, the reaction is under kinetic control, and thus, the observed composition of the mixture of the adducts reflects the relative magnitude of the kinetic constants for the nucleophilic attack. In contrast, at room temperature, the mixture rapidly attains equilibration, and thus, its composition reflects the relative stabilities of the adducts. In all cases, the addition of the solid substrate to an excess CD_3ONa solution in CD_3OD thermostated at −40 °C within the NMR probe led to the immediate disappearance of the signals of the substrates and the appearance at higher fields, owing to the neutralization of the positive charges, of the signals of the corresponding adducts. The reaction of cations **1** and **2** with excess methoxide ion can give in principle the bis-pyrans **9**−**11** and bis-thiopyrans **12**−**14**, respectively (Chart 1). The ^{1}H NMR technique proved to be unsuccessful in discriminating between the diastereomers represented by the general structures **9** and **12**, probably because the stereogenic centers that are formed upon addition of methoxide ion to the α positions of the various heteroaromatic nuclei, are remote from each other. In contrast constitutional isomers, due to the attack of either α or γ position, could be easily distinguished.

CHART 1



SCHEME 2

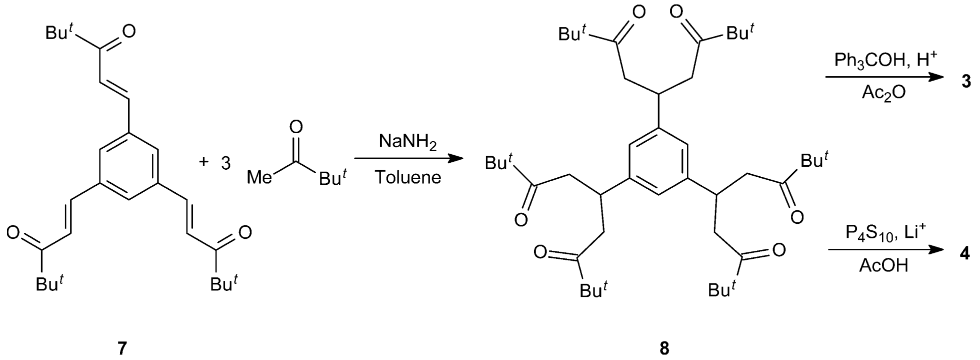
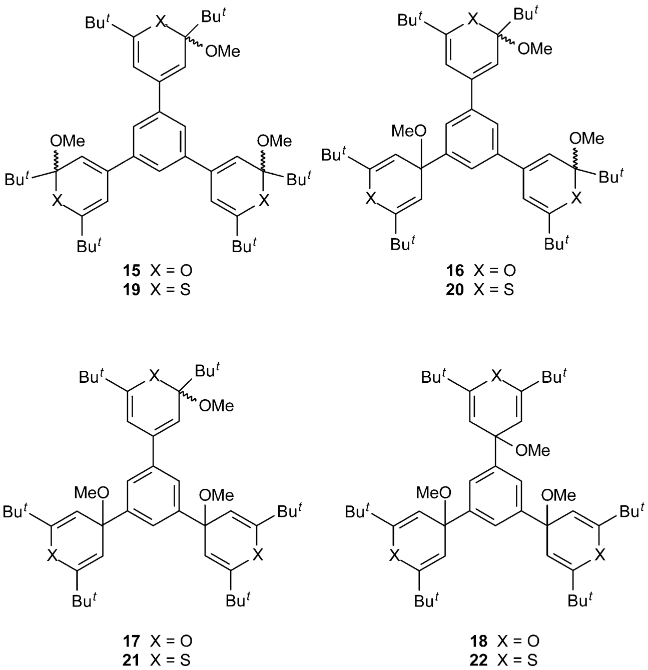


CHART 2



15 X = O
19 X = S
16 X = O
20 X = S
17 X = O
21 X = S
18 X = O
22 X = S

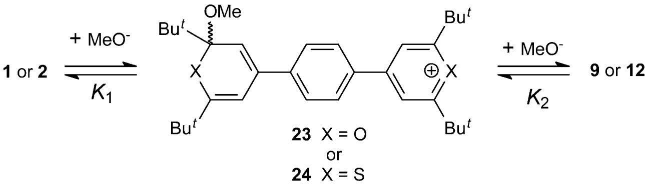
In the case of the bis-pyrylium **1**, only the bis-adducts **9** and **10** in a ratio 4:1 were observed at −40 °C. By raising the temperature at 25 °C, the bis-adduct **10** completely converted into the bis-adduct **9**. In contrast, the addition of the bis-thiopyrylium cation **2** to the CD_3ONa/CD_3OD solution at −40 °C led to the immediate precipitation of a white solid. The precipitate was dissolved in $CDCl_3$ at room temperature and then subjected to ^{1}H NMR analysis. In $CDCl_3$, the equilibration among the adducts is slow even at room temperature, so the composition of the isomeric mixture has still not reached equilibrium. The mixture was constituted by the adducts **12** and **13** in a ratio 10:1 with trace amounts of the adduct **14**. To attain equilibration, it was necessary to add a small percent of CD_3OD and raise the temperature at about 45 °C. After equilibration, only one product was observed, namely the bis-adduct **12**.

The reaction of the tris-cations **3** and **4** is in principle more complicated because four constitutional isomers can form, namely the tris-pyrans **15**−**18** and the tris-thiopyrans **19**−**22** (Chart 2).

Indeed, at low temperature, the ^{1}H NMR spectrum of the tris-pyrylium **3** in CD_3ONa/CD_3OD solution showed an indiscernible mixture of isomers. It was only possible to evaluate the global ratio between 2*H*- and 4*H*-pyranyl rings, equal to 1:5. Upon raising the temperature at 25 °C, the mixture completely converted into a unique product, namely the tris-pyran **15**. In contrast, the reaction of the tris-thiopyrylium **4** appeared much simpler to decipher: at low temperature the ^{1}H NMR revealed only the presence of the tris-4*H* adduct **22**, whereas at 25 °C only the thermodynamically more stable tris-2*H* adduct **19** was detected.

In conclusion all the examined cations react with CD_3ONa/CD_3OD at −40 °C to yield a kinetically controlled mixture of 2*H*- and/or 4*H*-adducts that equilibrates at 25 °C to yield, in all of the cases, the more stable 2*H* adducts exclusively.

SCHEME 3



Spectrophotometric Study of the Equilibria of 1−4 with Methoxide Ion. The ^{1}H NMR study showed that at 25 °C the addition of methoxide ion to the cations **1**−**4** is thermodynamically controlled and occurs exclusively at the α positions. We carried out a spectrophotometric study of the reactions in methanol at 25 °C to evaluate the corresponding stepwise equilibrium constants. The reactions were monitored by following the absorbance of the pyrylium or thiopyrylium nucleus, at a wavelength where it is the only chromophore absorbing, as a function of the methoxide ion concentration. Since the required concentrations of methoxide ion to follow the reactions were very low, suitable buffers or a strong acid ($HClO_4$) were necessary to modify the pH of the solutions.

In the case of the divalent cations **1** and **2**, a two-step process can be envisaged as shown in Scheme 3.

The absorbance as a function of the methoxide ion concentration is given by eq 1

$$A = \frac{c_{\mathrm{sub}}(\epsilon_{\mathrm{sub}} + \epsilon_{2H}K_1[\mathrm{MeO}^-])}{1 + K_1[\mathrm{MeO}^-] + K_1K_2[\mathrm{MeO}^-]^2} \qquad (1)$$

where c_{sub} is the analytical concentration of the substrate (**1** or **2**) and ϵ_{sub} and ϵ_{2H} are the molar extinction coefficients of the substrate and of the monoadduct (**23** or **24**), respectively. It should be noted that since the absorption at the chosen wavelength is only due to the

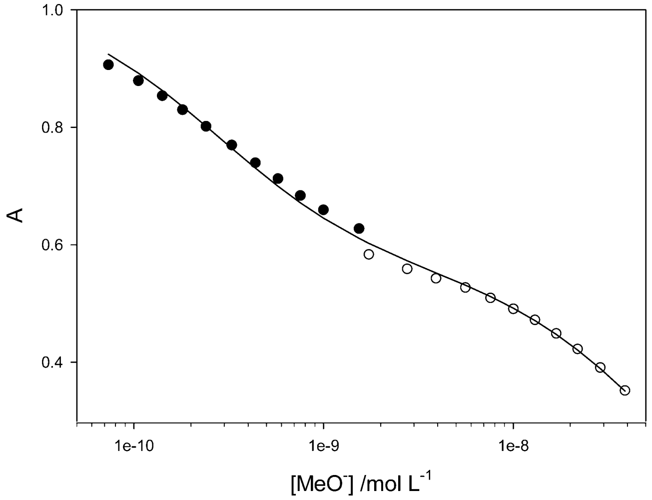


FIGURE 1. Absorbance at λ = 370 nm of a 2.2 × 10^{-5} M solution of **2** as a function of methoxide ion concentration. Filled and empty circles refer to experiments carried out in the presence of $ClCH_2CO_2H/ClCH_2CO_2^-$ and $PhCO_2H/PhCO_2^-$ buffers, respectively; the best fit curve is calculated by eq 1.

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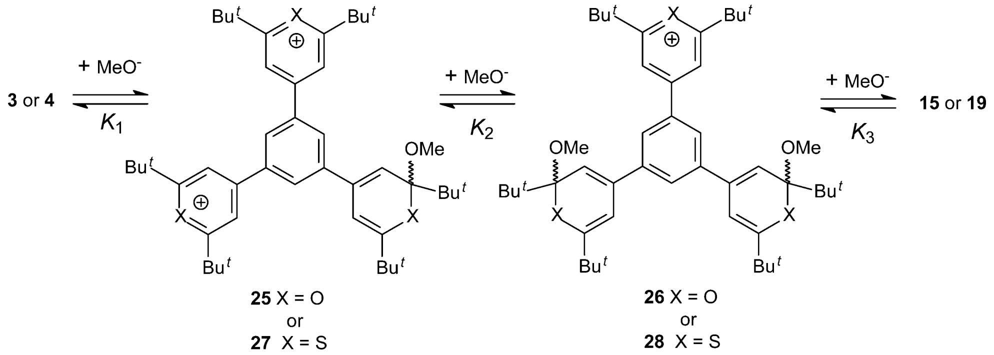
(5) Boldt, P.; Bruhnke, D.; Gerson, F.; Scholz, M.; Jones, P. G.; Bär, F. *Helv. Chim. Acta* **1993**, *76*, 1739.

(6) Gionis, V.; Strzelecka, H. *Synth. Commun.* **1984**, *14*, 775.

(7) Doddi, G.; Ercolani, G. *J. Chem. Soc., Perkin Trans. 2* **1986**, 271.

SCHEME 4



pyrylium or thiopyrylium cromophore, the molar extinction coefficients ϵ_{sub} and ϵ_{2H} were expected to be approximately in a 2:1 ratio; this was successively verified experimentally. In the case of the bis-pyrylium cation **1**, the methoxide ion concentration in solution was modulated by $Cl_3CCO_2H/Cl_3CCO_2^-$ and by $ClCH_2CO_2H/ClCH_2CO_2^-$ buffers, while in the case of the bis-thiopyrylium cation **2**, $ClCH_2CO_2H/ClCH_2CO_2^-$ and $PhCO_2H/PhCO_2^-$ buffers were used (see the Experimental Section). The experimental absorbance as a function of methoxide ion concentration was fitted by nonlinear least-squares to eq 1 by considering c_{sub} and ϵ_{sub} as known parameters and ϵ_{2H}, K_1, and K_2 as adjustable parameters. For the sake of illustration, the experimental points and the calculated curve in the case of the bis-thiopyrylium cation **2** are reported in Figure 1.

In the case of the trivalent cations **3** and **4**, the addition of methoxide ion occurs in three steps as shown in Scheme 4.

Accordingly, the equation yielding the absorbance as a function of the methoxide ion concentration is as follows

$$A = \frac{c_{\mathrm{sub}}(\epsilon_{\mathrm{sub}} + \epsilon_{2H}K_1[\mathrm{MeO}^-] + \epsilon_{2H,2H}K_1K_2[\mathrm{MeO}^-]^2)}{1 + K_1[\mathrm{MeO}^-] + K_1K_2[\mathrm{MeO}^-]^2 + K_1K_2K_3[\mathrm{MeO}^-]^3} \tag{2}$$

where c_{sub} is the analytical concentration of the substrate (**3** or **4**) and ϵ_{sub}, ϵ_{2H}, and $\epsilon_{2H,2H}$ are the molar extinction coefficients of the substrate, of the mono-adduct (**25** or **27**), and of the bis-adduct (**26** or **28**), respectively. In this case, the molar extinction coefficients ϵ_{sub}, ϵ_{2H}, and $\epsilon_{2H,2H}$ were expected to be approximately in a 3:2:1 ratio; this was successively verified experimentally. In the case of the tris-pyrylium cation **3**, the methoxide ion concentration in solution was modulated by $HClO_4$ and by $Cl_3CCO_2H/Cl_3CCO_2^-$ and $ClCH_2CO_2H/ClCH_2CO_2^-$ buffers, while in the case of the tris-thiopyrylium cation **4**, $Cl_2CHCO_2H/Cl_2CHCO_2^-$, $ClCH_2CO_2H/ClCH_2CO_2^-$, and $PhCO_2H/PhCO_2^-$ buffers were used (see the Experimental Section). The experimental absorbance as a function of methoxide ion concentration was fitted by nonlinear least-squares to eq 2 by considering c_{sub} and ϵ_{sub} as known parameters and ϵ_{2H}, $\epsilon_{2H,2H}$ K_1, K_2, and K_3 as adjustable parameters. The obtained equilibrium constants for the reaction of cations **1**−**4** are reported in Table 1.

TABLE 1. Equilibrium Constants for the Reaction of Cations 1−4 with MeO⁻ in MeOH at 25.0 °C[a]

cations	log K_1	log K_2	log K_3
1	12.6	10.1	
2	9.4	7.2	
3	13.1	11.3	9.7
4	10.0	8.4	6.6

[a] Estimated error is ± 0.2 log units.

Discussion

Cations **1**−**4** react with CD_3ONa/CD_3OD at −40 °C to yield a kinetically controlled mixture of 2*H*- and/or 4*H*-adducts that equilibrates at 25 °C to yield, in all of the cases, the more stable 2*H*-adducts exclusively. This pattern of reactivity had been previously observed in simple pyrylium and thiopyrylium cations.[7−11] Indeed, previous studies of the reaction of pyrylium and thiopyrylium cations with methoxide ion in methanol showed that (i) pyrylium ions are more reactive than the corresponding thiopyrylium ions from both a kinetic and a thermodynamic point of view and (ii) the kinetically favored product is not always that thermodynamically more stable. The first observation finds justification in the higher carbocationic character of the pyrylium ring, which in turn is due to the higher electronegativity of oxygen. The second observation indicates that the transition states are significantly different from the final products. Indeed, there are evidences suggesting that the rates of nucleophilic attack are dominated by coulombic interactions,[12] whereas the thermodynamic regioselectivity is dominated by the greater stability of the 2*H*-adducts. Indeed, MNDO and AM1 calculations showed that 2-methoxy-2*H*-pyrans are much more stable than the corresponding 4*H*-isomers because of negative hyperconjugative effects between the geminal oxygen atoms.[13] This effect is less important in 2-methoxy-2*H*-thiopyrans as shown by the lower equilibrium constants for their formation.[8−11]

The equilibrium constants reported in Table 1 provide the first quantitative data about the thermodynamic reactivity of polyvalent pyrylium and thiopyrylium cations and merit to be discussed in some detail. The sequential addition of methoxide ion to the α positions

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[8] Doddi, G.; Ercolani, G. *J. Org. Chem.* **1986**, *51*, 4385.

[9] Di Vona, M. L.; Doddi, G.; Ercolani, G.; Illuminati, G. *J. Am. Chem. Soc.* **1986**, *108*, 3409.

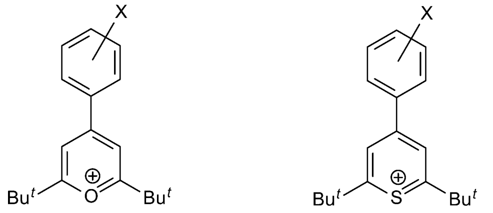
[10] Doddi, G.; Ercolani, G. *J. Org. Chem.* **1988**, *53*, 1729.

[11] Doddi, G.; Ercolani, G. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1393.

[12] Cerichelli, G.; Doddi, G.; Ercolani, G. *Gazz. Chim. Ital.* **1988**, *118*, 291.

[13] Doddi, G.; Ercolani, G.; Mencarelli, P. *J. Org. Chem.* **1992**, *57*, 4431.

CHART 3



	X		X
29	p-NO$_2$	**36**	p-NO$_2$
30	m-Cl	**37**	m-Cl
31	p-Cl	**38**	p-Cl
32	H	**39**	H
33	p-Me	**40**	p-Me
34	p-OMe	**41**	p-OMe
35	p-NMe$_2$	**42**	p-NMe$_2$

of chalcogenopyrylium rings is well differentiated in free energy terms; i.e., the first addition is significantly more favored than the second one, and in the case of the tris-cations **3** and **4**, the second addition is also significantly more favored than the third one. This is principally due to the fact that the chalcogenopyrylium ring, because of its positive charge, behaves as an electron-withdrawing substituent, whereas the neutral 2*H*-chalcogenopyranyl ring is expected to be less effective. Thus, in the case of bis-chalcogenopyrylium ions, for example, the addition of the first methoxide ion is favored by the electron-withdrawing effect of the other chalcogenopyrylium ring not undergoing nucleophilic attack, whereas the addition of the second methoxide ion is only slightly affected by the electronic behavior of the 2*H*-chalcogenopyranyl ring formed in the previous step. Another effect, although of secondary importance, favoring the first attack over the second one, and, in the case of the tris-cations, also the second attack over the third one, is the statistical factor. Indeed, considering the bis-chalcogenopyrylium ions, the first equilibrium is favored by a factor 2 because there are two equivalent rings that can undergo the attack, whereas the second equilibrium is disfavored by a factor 2 (or favored by a factor 1/2), because in the reverse reaction, both the 2*H*-chalcogenopyranyl rings can release methoxide ion. In the case of the tris-chalcogenopyrylium ions, for the same reasons, the first equilibrium is favored by a factor 3, the second equilibrium by a factor 1, and the third equilibrium by a factor 1/3.

Comparing the equilibrium constants of the bis-pyrylium cation **1** with those of the bis-thiopyrylium cation **2**, as well as those of the tris-pyrylium cation **3** with those of the tris-thiopyrylium cation **4**, it is evident, as expected, the higher reactivity of pyrylium with respect to thiopyrylium. However it is useful to go deep in the analysis of the electronic effects by comparing the obtained results with those previously obtained for the series of 2,6-di-*tert*-butyl-4-arylpyrylium, **29**−**35**,[8] and thiopyrylium **36**−**42** (Chart 3).[9]

As shown in Figure 2, the equilibrium constants for the addition of methoxide ion to the α position of cations **29**−**42** are linearly correlated to the Brown σ^+ values,[14] with the following parameters: pyrylium series, slope (ρ) = 2.55, intercept ($\log K_0$) = 10.2, corr coeff. (r^2) = 0.987;[8] thiopyrylium series, slope (ρ) = 1.99, intercept ($\log K_0$) = 7.4, corr coeff (r^2) = 0.985.[9]

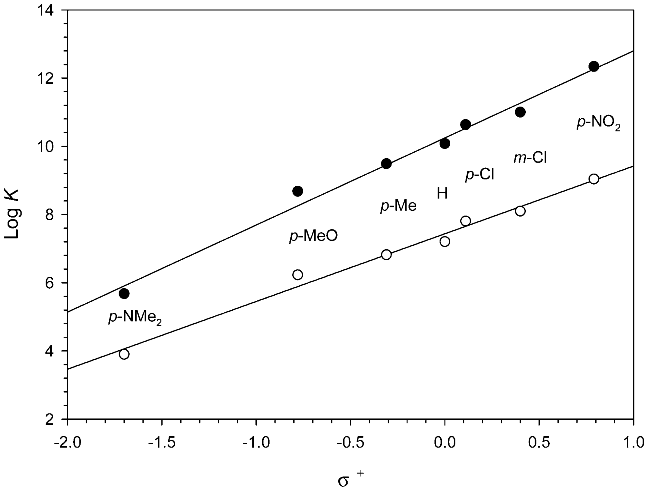


FIGURE 2. Plots of log K for the addition of MeO$^-$ to the α position of pyrylium ions **29**−**35** (filled circles) and thiopyrylium ions **36**−**42** (empty circles).

By correcting the equilibrium constants K_1 of the bis-cations in Table 1, for the statistical factor 2, and interpolating from the corresponding σ^+ correlation, one obtains the value of $\sigma^+_p = 0.81$ for the 2,6-di-*tert*-butylpyrylium ring and of $\sigma^+_p = 0.84$ for the 2,6-di-*tert*-butylthiopyrylium ring. The data reveal that both pyrylium and thiopyrylium moieties behave as good electron-withdrawing substituents, whose effect is comparable to that of the nitro group ($\sigma^+_p = 0.79$).[14] The effect is mainly due to the positive charge on the two heteroaromatic rings, with a negligible effect of the nature of the ring heteroatom.

Analogously, by correcting the equilibrium constants K_2 of the bis-cations in Table 1, for the statistical factor 1/2, and interpolating from the corresponding σ^+ correlation, one obtains the value of $\sigma^+_{\rm p} = 0.06$ for the 2,6-di-*tert*-butyl-2-methoxy-2*H*-pyranyl and $\sigma^+_{\rm p} = 0.03$ for the 2,6-di-*tert*-butyl-2-methoxy-2*H*-thiopyranyl, showing that both rings are substantially electron-neutral.

A similar approach can be applied to the tris-cations by correcting the equilibrium constant K_1 for the statistical factor 3 and considering the effect of the two chalcogenopyrylium rings in the meta position as additive. In this case, one obtains upon interpolation the value of $\sigma^+_{\rm m} = 0.47$ for the 2,6-di-*tert*-butylpyrylium and $\sigma^+_{\rm m} = 0.53$ for 2,6-di-*tert*-butylthiopyrylium. Also in this case the effect of the two rings is the same within the experimental errors. It is noteworthy, however, that $\sigma^+_{\rm p}$ is significantly higher than $\sigma^+_{\rm m}$ (about 0.3 units), indicating that a significant component of the electron-withdrawing effect exerted in the para position by the chalcogenopyrylium ring is due to resonance. This behavior is quite unusual for electron-withdrawing substituents as generally the difference $\sigma^+_{\rm p} - \sigma^+_{\rm m}$ does not exceed 0.1 unit.[14]

By correcting the equilibrium constant K_3 of the tris-cations for the statistical factor 1/3, and by considering the effect of the two 2*H*-chalcogenopyrans rings in the meta position as additive, one obtains upon interpolation the value of $\sigma^+_{\rm m} = -0.01$ for the 2,6-di-*tert*-butyl-2-methoxy-2*H*-pyranyl and $\sigma^+_{\rm m} = -0.09$ for the 2,6-di-*tert*-

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(14) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 5th ed.; Wiley: New York, 2001; p 370.

butyl-2-methoxy-2*H*-thiopyranyl, showing, also in this case, that both of the rings are substantially electron-neutral.

It is interesting to note that the constants K_2 of the tris-cations provide a useful test for the assumption of additivity of the electronic effects of the groups in the meta position. Indeed, by this assumption, the equilibrium constant K_2 can be calculated from the σ^+_m of the cationic 2,6-di-*tert*-butylchalcogenopyrylium ring [$(\sigma^+_m)_{cat}$] and the σ^+_m of the 2,6-di-*tert*-butyl-2-methoxy-2*H*-chalcogenopyranyl ring [$(\sigma^+_m)_{2H}$], as shown in eq 3.

$$\log K_2 = \rho[(\sigma_m{}^+)_{cat} + (\sigma_m{}^+)_{2H}] + \log K_0 \qquad (3)$$

The calculated values of log K_2 for the tris-pyrylium **3** (= 11.4) and the tris-thiopyrylium **4** (= 8.3) cations are in excellent agreement with the corresponding experimental values reported in Table 1, thus supporting the assumption of additivity of electronic effects.

Conclusions

The reaction of bis- and tris-pyrylium and thiopyrylium cations with methoxide ion in methanol is a useful reaction to probe the effect of the two chalcogenopyrylium rings as substituents in the para and meta position, respectively. Despite the different sensitivity to electronic effects of pyrylium and thiopyrylium rings, as measured by the different ρ values (see Figure 2), the two rings have a similar electron-withdrawing effect with a $\sigma^+_p \sim 0.8$ and a $\sigma^+_m \sim 0.5$. Apart from the expected importance of the inductive effect due to the positive charge, the difference between these two values remarks the importance of the resonance contribution. In contrast, both the neutral 2*H*-pyranyl and thiopyranyl rings have a negligible effect as substituents, independent of the position, para or meta, they occupy.

Experimental Section

Materials and Instrumentation. Solvents (A.R. grade) were distilled before use. Deuterated solvents for NMR spectroscopy and other chemicals (A.R. grade) were used as received. Stock solutions of sodium methoxide were prepared by dissolving the appropriate amount of clean sodium in either methanol or methanol-d_4 under an argon atmosphere. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts are given in ppm from TMS as internal standard. Melting points are uncorrected. 1,1′-(1,4-Phenylene)bis(4,4-dimethylpent-1-en-3-one)[5] (**5**) and benzene-1,3,5-tricarbaldehyde[15] were prepared by literature procedures.

5,5′-(1,4-Phenylene)bis(2,2,8,8-tetramethylnonane-3,7-dione) (6). A solution of **5** (3.3 g, 11 mmol) in 25 mL of toluene was added to a stirred suspension of sodium amide (2.15 g, 55 mmol) and pinacolone (4.4 g, 44 mmol) in 40 mL of toluene, under a dry nitrogen atmosphere, at room temperature. After 2 h, water (40 mL) was added and the resulting mixture extracted with CHCl$_3$. The organic extracts were dried over CaCl$_2$ and evaporated to dryness to yield a crude solid. Recrystallization from EtOH gave 4.40 g of pure **6** as white crystals (yield 80%). Mp: 204−206 °C (lit.[5] mp 210 °C). ^{1}H NMR (CDCl$_3$): δ 0.99 (s, 36 H), 2.75 (m, 8H), 3.70 (m, 2H), 7.09 (s, 4H). Anal. Calcd for $C_{32}H_{50}O_4$ (498.75): C, 77.06; H, 10.10. Found: C, 76.92; H, 10.06.

4,4′-(1,4-Phenylene)bis(2,6-di-*tert*-butylpyrylium) Bistetrafluoroborate (1). The bis-pentanedione **6** (2.5 g, 5 mmol) and triphenylmethanol (2,86 g, 11 mmol) were dissolved in 73 mL of acetic anhydride by gently warming. To this mixture was added dropwise under stirring a solution of 50% HBF$_4$ (4.04 g, 23 mmol) in 48 mL of acetic anhydride, prepared by adding the HBF$_4$ in drops to the ice cooled acetic anhydride. The reaction mixture was then kept at 50 °C for 30 m. After the mixture was cooled to room temperature, diethyl ether was added until complete precipitation of **1**, which was filtered, washed with diethyl ether, and purified by dissolution in the least amount of dichloromethane followed by reprecipitation with diethyl ether: 2.8 g of white crystals were obtained (yield 91%). Mp: 280−282 °C dec (lit.[5] mp 270−272 °C dec). ^{1}H NMR (CD$_3$CN): δ 1.60 (s, 36 H), 8.26 (s, 4H), 8.39 (s, 4H). ^{13}C NMR (CD$_3$CN): δ 28.5, 40.3, 118.0, 131.8, 139.0, 167.0, 188.6. UV−vis (CH$_3$CN): log ϵ (λ_{max} = 350 nm) = 4.62. Anal. Calcd for $C_{32}H_{44}O_2B_2F_8$ (634.31): C, 60.59; H, 6.99. Found: C, 60.33; H, 6.82.

4,4′-(1,4-Phenylene)bis(2,6-di-*tert*-butylthiopyrylium) bisperchlorate (2). (**CAUTION**: organic perchlorates are potentially explosive and must be handled with all necessary precautions.) A mixture of the bis-pentanedione **6** (1.8 g, 3.6 mmol), phosphorus pentasulfide (4.80 g, 10.8 mmol), and lithium perchlorate (4.60 g, 43.2 mmol) in 35 mL of acetic acid was refluxed for 3 h under stirring. The resulting mixture was filtered, and the solid residue, after being washed with hot acetic acid, was eliminated. The cooled filtrate was then added with diethyl ether until complete precipitation of a solid that was redissolved in the least amount of CH$_3$CN and reprecipitated with diethyl ether to yield 1.77 g of a gray solid. The ^{1}H NMR spectrum of this material was consistent with the expected bis-thiopyrylium cation and the corresponding pyrylium−thiopyrylium cation in a 10:1 molar ratio. Double recrystallization of the crude solid from CH$_2$Cl$_2$ provided 1.05 g of **2** as yellow crystals. Mp: 280−282 °C dec. ^{1}H NMR (CD$_3$CN): δ 1.70 (s, 36H), 8.29 (s, 4H), 8.81 (s, 4H). ^{13}C NMR (CD$_3$CN): δ 31.3, 43.3, 131.8, 131.9, 141.5, 160.8, 186.7. UV−vis (CH$_3$CN): log ϵ (λ_{max} = 368 nm) = 4.65. HRMS: m/z = 246.1438 (M)$^{2+}$. Anal. Calcd for $C_{32}H_{44}O_8S_2Cl_2$ (691.72): C, 55.56; H, 6.41; S, 9.27. Found: C, 55.61; H, 6.54; S, 9.10.

1,1′,1″-Benzene-1,3,5-triyltris(4,4-dimethylpent-1-en-3-one) (7). Benzene-1,3,5-tricarbaldehyde (0.50 g, 3.1 mmol) was added to a stirred mixture of pinacolone (1.85 g, 18.5 mmol), EtOH (3.8 mL), and H$_2$O (0.8 mL). After heating to 40 °C, a solution of NaOH (0.037 g, 93 mmol) in H$_2$O (2 mL) was added dropwise. After 3 h, the precipitate was filtered, washed with H$_2$O and EtOH, and recrystallized from EtOH to yield 0.79 g of **7** as white crystals (yield 63%). Mp: 172−174 °C. ^{1}H NMR (CDCl$_3$): δ 1.24 (s, 27 H), 7.15 (d, J = 15.5 Hz, 3H), 7.71 (d, J = 15.5 Hz, 3H), 7.71 (s, 3H). ^{13}C NMR (CDCl$_3$): δ 26.2, 43.3, 122.3, 128.9, 141.3, 136.3, 203.8. IR (CHCl$_3$): $\nu_{max(C=O)}$ 1683 cm^{-1}, $\nu_{max(C=C)}$ 1609 cm^{-1}. Anal. Calcd for $C_{27}H_{36}O_3$ (408.58): C, 79.37; H, 8.88. Found: C, 79.29; H, 9.00.

5,5′,5″-Benzene-1,3,5-triyltris(2,2,8,8-tetramethylnonane-3,7-dione) (8). A solution of **7** (0.57 g, 1.4 mmol) in 4 mL of toluene was added to a stirred suspension of sodium amide (0.41 g, 10 mmol) and pinacolone (0.84 g, 8.4 mmol) in 4 mL of toluene, under a dry nitrogen atmosphere, at room temperature. After 48 h, 8 mL of water was added and the resulting mixture extracted with CHCl$_3$. The organic extracts were dried over CaCl$_2$ and evaporated to dryness to yield a crude solid. Recrystallization from EtOH gave 0.76 g of pure **8** as white crystals (yield 77%). Mp: 154−156 °C. ^{1}H NMR (CDCl$_3$): δ 0.96 (s, 54 H), 2.71 (m, 12H), 3.65 (m, 3H), 6.83 (s, 3H). ^{13}C NMR (CDCl$_3$): δ 26.1, 35.7, 42.5, 43.9, 125.1, 144.3, 213.6. IR (CHCl$_3$): $\nu_{max(C=O)}$ 1704 cm^{-1}. Anal. Calcd for $C_{45}H_{72}O_6$ (709.06): C, 76.23; H, 10.23. Found: C, 76.19; H, 10.42.

4,4′,4″-Benzene-1,3,5-triyltris(2,6-di-*tert*-butylpyrylium) Trisperchlorate (3). (**CAUTION**: Organic perchlorates are potentially explosive and must be handled with all

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[15] Fourmigué, M.; Joahnssen, I.; Boubekeur, K.; Nelson, C.; Batali, P. *J. Am. Chem. Soc.* **1993**, *115*, 3752.

the necessary precautions). The tris-pentanedione **8** (0.17 g, 0.24 mmol) and triphenylmethanol (0.206 g, 0.79 mmol) were dissolved in 5.3 mL of acetic anhydride by gently warming. To this mixture was added dropwise under stirred a solution of 60% $HClO_4$ (0.278 g, 1.66 mmol) in 3.5 mL of acetic anhydride, prepared by adding the $HClO_4$ in drops to the ice-cooled acetic anhydride. The reaction mixture was kept at 50 °C for 30 min. After the mixture was cooled to room temperature, diethyl ether was added until complete precipitation of **3**, which was filtered, washed with Et_2O, and purified by dissolution in the least amount of dichloromethane followed by reprecipitation with diethyl ether: 0.215 g of white needles were obtained. Mp: 290−292 °C dec. ^{1}H NMR (CD_3CN): δ 1.64 (s, 54 H), 8.49 (s, 6H), 8.92 (s, 3H). ^{13}C NMR (CD_3CN): δ 28.5, 40.5, 118.8, 135.9, 137.3, 166.4, 189.0. UV−vis (CH_3CN): log ϵ (λ_{max}= 306 nm) = 4.95. HRMS: m/z = 375.2116 $(M + ClO_4)^{2+}$. Anal. Calcd for $C_{45}H_{63}O_{15}Cl_3$ (950.35): C, 56.87; H, 6.68. Found: C, 56.50; H, 7.03.

4,4′,4′′-Benzene-1,3,5-triyltris(2,6-di-*tert*-butylthiopyrylium) Trisperchlorate (4). (**CAUTION**: Organic perchlorates are potentially explosive and must be handled with all necessary precautions). A mixture of the tris-pentanedione **8** (0.5 g, 0.7 mmol), phosphorus pentasulfide (1.41 g, 3.18 mmol), and lithium perchlorate (1.35 g, 12.7 mmol) in 11 mL of acetic acid was refluxed for 3 h under stirring. The resulting mixture was filtered, and the solid residue, after washing with hot acetic acid, was eliminated. The cooled filtrate was added with diethyl ether until complete precipitation of a solid that was redissolved in the least amount of CH_3CN and reprecipitated with diethyl ether to yield 0.53 g of gray solid. The ^{1}H NMR spectrum of this material was consistent with the expected tris-thiopyrylium cation and the corresponding bis-thiopyrylium−pyrylium cation in a 6:1 molar ratio. Triple recrystallization of the crude solid from ethyl alcohol provided 0.147 g of pure **4** as yellow crystals. Mp: 286−288 °C dec. ^{1}H NMR (CD_3CN): δ 1.72 (s, 54H), 8.70 (s, 3H), 8.99 (s, 6H). ^{13}C NMR (CD_3CN): δ 31.2, 43.4, 132.6, 134.8, 140.4, 160.0, 186.9. UV−vis (CH_3CN): log ϵ (λ_{max}= 322 nm) = 4.88. HRMS: m/z = 399.1804 $(M + ClO_4)^{2+}$. Anal. Calcd for $C_{45}H_{63}O_{12}S_3Cl_3$ (998.53): C, 54.13, H, 6.36; S, 9.63. Found: C, 53.95; H, 6.43; S, 9.53.

^{1}H NMR Measurements. Low-temperature spectra were recorded just after the addition of the substrate (ca. 0.02 mmol of solid sample) to a ca. 0.5 mL of a 0.5 M solution of CD_3ONa in CD_3OD, thermostated at ∼−40 °C in the NMR probe. Apart from the case of the substrate **2** that showed the precipitation of a white solid upon addition to the CD_3ONa/CD_3OD solution, the ^{1}H NMR spectra were also recorded at ∼25 °C after equilibration of the reaction mixtures was attained.

In the case of the substrate **2**, the precipitate was separated by filtration, washed with CD_3OD, dissolved in 0.5 mL of $CDCl_3$ at room temperature, and subjected to ^{1}H NMR analysis. The pattern of the signals was attributed to the kinetically controlled formation of the adducts. After equilibration of the mixture, attained by adding 0.01 mL of CD_3OD and warming the solution up to 45 °C, a second ^{1}H NMR spectrum was recorded.

Details on the composition of the reaction mixtures under both kinetic and thermodynamic control are reported in the Results.

^{1}H NMR spectral data of the detected species are as follows:

9: δ 1.01 (s, 18H), 1.24 (s, 18H), 5.44 (s, 2H), 5.46 (s, 2H), 7.54 (s, 4H).

10: *2H*-pyran moiety, δ 1.01 (s, 9H), 1.24 (s, 9H), 5.39 (s, 1H), 5.44 (s, 1H); 4*H*-pyran moiety, δ 1.22 (s, 18H), 4.65 (s, 2H), 7.37−7.49 (m, 4H).

12: δ 1.09 (s, 18H), 1.30 (s, 18H), 5.52 (s, 2H), 6.32 (s, 2H), 7.44 (s, 4H).

13: 2*H*-thiopyran moiety, δ 1.10 (s, 9H), 1.31 (s, 9H), 5.50 (s, 1H), 6.30 (s, 1H); 4*H*-thiopyran moiety, δ 1.27 (s, 18H), 5.46 (s, 2H), 7.35−7.43 (m, 4H).

14: δ 1.25 (s, 36H), 7.31 (s, 4H); note that H-3 and H-5 signals are hidden.

15: δ 1.03 (s, 27H), 1.25 (s, 27H), 5.43 (d, J = 1.4 Hz, 3H), 5.44 (d, J = 1.4 Hz, 3H), 7.46 (s, 3H).

18: δ 1.20 (s, 54H), 4.59 (s, 6H), 7.39 (s, 3H).

19: δ 1.10 (s, 27H), 1.32 (s, 27H), 5.55 (s, 3H), 6.34 (s, 3H), 7.40 (s, 3H).

22: δ 1.24 (s, 54H), 5.34 (s, 6H), 7.15 (s, 3H).

UV−vis Spectrophotometric Determination of the Equilibrium Constants. Determination of the equilibrium constants was carried out by spectrophotometric titrations of the given substrate at 25.0 °C in 10-mm quartz cuvettes. Typically, 2 mL of a methanol solution of the chalcogenopyrylium ion in the range $(1-3) \times 10^{-5}$ M and containing the acid component of the given buffer in excess (from 1×10^{-3} to 2×10^{-2} M) was added with successive aliquots of a 0.1−0.4 M methanol solution of sodium methoxide by microliter syringes. After each addition, allowance was made for thermal equilibration, and then the absorbance value was recorded and corrected for dilution. The actual methoxide ion concentration after each addition was calculated by the composition of the buffer, the known pK_a of the buffer acid, and the methanol autoprotolysis constant ($pK_{MeOH} = 16.92$ at 25 °C).[16] The acids used as buffers and their pK_a in methanol are the following: trichloroacetic acid (4.98);[17] dichloroacetic acid (6.41);[17] chloroacetic acid (7.7);[18] benzoic acid (9.1).[18] Only in one case, namely substrate **3** at the lower pH values, were the required methoxide ion concentrations in the cuvette attained by direct addition of aliquots of a methanol solution of the strong acid $HClO_4$. The absorbance measurements were carried out at a fixed wavelength, λ, where either the pyrylium or thiopyrylium nucleus is the only chromophore absorbing. The value of the molar extinction coefficients of the substrates, ϵ_{sub}, at this wavelength was previously determined by UV−vis spectra carried out in the presence of 0.05 M HBF_4. The values of λ in nm and log ϵ_{sub} for the substrates **1**−**4** are the following: **1**, 354 (4.61); **2**, 370 (4.66); **3**, 320 (5.79); **4**, 340 (6.75). The values of the absorbances vs the corresponding methoxide ion concentrations were fitted by either eq 1 or 2 as further detailed in the Results.

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