J. Am. Chem. Soc. **1986**, *108*, 3409–3415

Rates and Equilibria of the Methoxide Attachment to 2,6-Di-*tert*-butyl-4-arylthiopyrylium Cations. Can Ion Pair Formation Be Rate Determining in Anion–Cation Combination Reactions?

M. L. Di Vona, G. Doddi,* G. Ercolani,* and G. Illuminati[†]

Contribution from the Centro C. N. R. di Studio sui Meccanismi di Reazione, Dipartimento di Chimica, Università di Roma "La Sapienza", I-00185 Roma, Italy. *Received August 19, 1985*

Abstract: The complete set of kinetic and equilibrium constants for the methoxide attachment to a series of 2,6-di-*tert*-butyl-4-arylthiopyrylium cations (aryl = X–C_6H_4 with X = *p*-NO_2, *m*-Cl, *p*-Cl, H, *p*-Me, *p*-OMe, *p*-NMe_2) has been obtained in MeOH at 25 °C. The reaction involves the kinetically controlled formation of both the corresponding 2*H*- and 4*H*-thiopyrans which equilibrate to form only the thermodynamically more stable 2*H* adduct. The observed kinetic patterns show that the rate-determining step is the combination of the nucleophile with the cations to give the adducts, thus disproving the views indicating the ion pair formation as the rate-determining step in anion–cation combination reactions. Moreover the experimental data clearly indicate that the Leffler–Hammond postulate cannot be held valid for this class of reactions. The different selectivity observed for the methoxide attachment to the α and γ positions is explained on the basis of the different transmission efficiency of the electronic substituent effects.

Interactions between nucleophiles and stable organic cations, owing to their fundamental role in organic chemistry, have been the object of numerous experimental studies.[1] Nevertheless the comprehension of these processes is not satisfactory, with special regard to the nature of the transition state and the factors that affect its energy.[1a]

The study of positional selectivity is in general one of the fundamentals in the understanding of chemical reactivity; nevertheless investigations on regioselectivity in nucleophile–cation combination reactions have never been considered. The heteroaromatic thiopyrylium cations are well suited to perform such studies because they can be attacked by nucleophiles on the two reactive α and γ positions.[2]

In the present paper we report the results of the reactions between 2,6-di-*tert*-butyl-4-arylthiopyrylium **1a–7a** and methoxide ions, in methanol, at 25.0 °C, to give the corresponding adducts, namely, 4*H*- (**1b–7b**) and 2*H*-thiopyrans (**1c–7c**).

We will show how the electronic effects influence the regioselectivity and, more significantly, how the observed kinetic patterns give valuable insights on the nature of the transition state.

Results

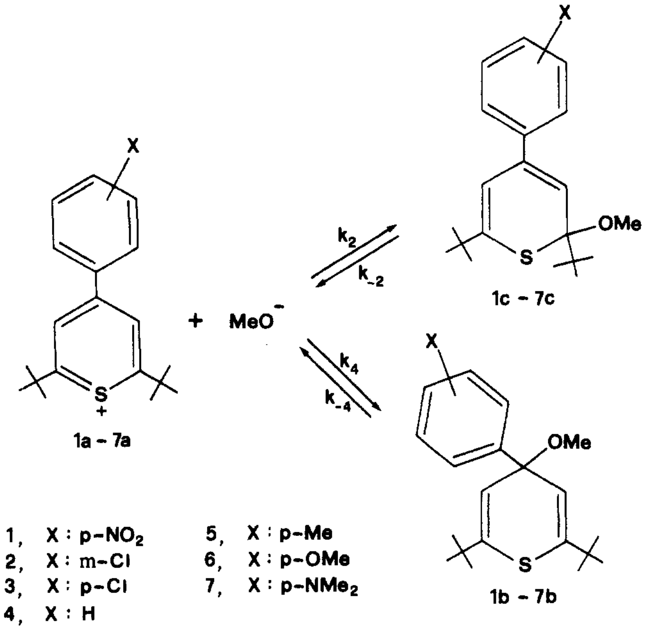
^{1}H NMR Study. The ^{1}H NMR study of the reaction was performed at −40 and 30 °C, respectively.

The experiments carried out at low temperature, with an excess of CD_3O^-, lead to the immediate disappearance of the signals of the substrates and the appearance at higher fields, owing to the neutralization of the positive charge, of the signals of the corresponding 2*H* and 4*H* adducts (Scheme I). At variance with the other cations, compound **7a** shows the formation of only the 2*H* adduct **7c**.

When the temperature is raised to 30 °C, the complete conversion of the 4*H* adducts **1b–6b** to the 2*H* isomers **1c–6c** is observed. The ^{1}H NMR data are reported in the Experimental Section.

Kinetic Study. The kinetic experiments were carried out under pseudo-first-order conditions in a stopped-flow spectrophotometer by mixing the substrates **1a–7a** ($\sim 1 \times 10^{-5}$ M after the mixing) with an excess of sodium methoxide (2×10^{-4} to 2×10^{-3} M after the mixing), in methanol, at 25.0 °C. The reaction was monitored at two wavelengths: wavelength *A*, where only the substrate absorbs, and wavelength *B*, where both the substrate and the corresponding 2*H* adduct absorb (see Experimental Section for λ_A and λ_B values). The only exception was cation **1a**, whose kinetics were followed at only one wavelength because it absorbs in the same region as the corresponding 2*H* and 4*H* adducts.

Scheme I



Three different kinetic patterns were observed, as follows: (i) The reaction of cations **2a–4a**, when monitored at wavelength *A*, show one process, linearly dependent on [MeO$^-$], that leads to the complete disappearance of the substrate. Following the reaction at wavelength *B*, two widely separated processes are observed. The first one coincides with that observed at wavelength *A* and shows a decrease of absorbance up to a constant value (at this wavelength the substrate absorbs more than the 2*H* adduct). The second one, which involves an increase of absorbance, does not depend on [MeO$^-$] and is referred to the complete conversion of the 4*H* adduct to the 2*H* isomer. The reaction of **1a**, monitored at λ = 330 nm, shows a pattern analogous with that observed for

---

[†] Deceased in Rome, January 22nd, 1986.

(1) (a) Ritchie, C. D. *J. Am. Chem. Soc.* **1983**, *105*, 7313 and references therein. (b) Bunton, C. A.; Davoudzadeh, F.; Jagdale, M. J. *J. Chem. Soc., Perkin Trans. 2* **1984**, 395 and references therein.

(2) (a) Doddi, G.; Illuminati, G.; Insam, N.; Stegel, F. *J. Org. Chem.* **1982**, *47*, 960. (b) Doddi, G.; Ercolani, G. *Ibid.* **1984**, *49*, 1806. (c) Doddi, G.; Ercolani, G. *J. Am. Chem. Soc.* **1984**, *106*, 7082.

(3) For an exhaustive treatment of the relaxation processes, see: Bernasconi, C. F. *Relaxation Kinetics*; Academic: New York, 1976.

0002-7863/86/1508-3409$01.50/0

the cations **2a**–**4a** at wavelength *B* and is referred to the same processes (at $\lambda = 330$ nm the molar absorbance decreases in the order **1a** > **1c** > **1b**).

(ii) The reaction of cations **5a** and **6a**, monitored at wavelength *A*, shows two not well separated processes, whose separation increases on increasing [MeO$^-$], that lead to the complete disappearance of the substrate. The same processes are observed at wavelength *B*, yielding the 2*H* adduct as the final product.

(iii) At both wavelengths *A* and *B*, cation **7a** shows only one process, linearly dependent on [MeO$^-$], leading to the equilibrium mixture of the substrate and the 2*H* adduct only.

It must be emphasized that the observation of a certain kinetic pattern (i–iii) depends, for a given cation, only on the methoxide ion concentration. In fact the reaction of cations **1a**–**4a** at methoxide concentrations as low as 10^{-7} to 10^{-5} M (from Et_3N/Et_3NH^+ buffers) shows the occurrence of pattern ii, at [MeO$^-$] > 5×10^{-3} M cations **5a** and **6a** show pattern i, and in the range [MeO$^-$] ~ 10^{-2} to 10^{-1} M cation **7a** shows pattern ii, thus indicating the formation of the 4*H* adduct **7b** that escaped NMR detection, probably because of too rapid equilibration of the system. These observations indicate that on increasing [MeO$^-$] the observed kinetic pattern changes in the following order: iii → ii → i.

All the kinetic patterns can be rationalized by Scheme I. In the Discussion section we will show that this kinetic scheme is the only one that can account for all the observed kinetic patterns. For Scheme I the following equations can be written:

$$\tau_1^{-1} + \tau_2^{-1} = (k_2 + k_4)[\mathrm{MeO^-}] + k_{-2} + k_{-4} \qquad (1)$$

$$\tau_1^{-1}\tau_2^{-1} = (k_2k_{-4} + k_4k_{-2})[\mathrm{MeO^-}] + k_{-2}k_{-4} \qquad (2)$$

τ_1 and τ_2 are the relaxation times of the two processes. In case i, the two processes being widely separated and the equilibrium completely shifted toward the 2*H* adduct, the above equations reduce to

$$\tau_1^{-1} = (k_2 + k_4)[\mathrm{MeO^-}] \qquad (3)$$

$$\tau_2^{-1} = \frac{k_2k_{-4}}{k_2 + k_4} \qquad (4)$$

In case ii, with the two processes not well separated and with the 2*H* adduct the only final product, eq 1 and 2 simplify to

$$\tau_1^{-1} + \tau_2^{-1} = (k_2 + k_4)[\mathrm{MeO^-}] + k_{-4} \qquad (5)$$

$$\tau_1^{-1}\tau_2^{-1} = k_2[\mathrm{MeO^-}]k_{-4} \qquad (6)$$

In case iii the relationship

$$k_{-4} \gg k_4[\mathrm{MeO^-}] \qquad (7)$$

holds, and only the reversible formation of the 2*H* adduct is observed, i.e.

$$\tau^{-1} = k_2[\mathrm{MeO^-}] + k_{-2} \qquad (8)$$

The kinetic constants have been evaluated as follows: In case i relative to the cations **1a**–**4a**, plots of τ_1^{-1} vs. [MeO$^-$] are linear with slopes equal to $(k_2 + k_4)$ according to eq 3 (Tables S1–S4). As indicated in eq 4, τ_2^{-1} is independent of [MeO$^-$] (Tables S1–S4), and the product $\tau_2^{-1}(k_2 + k_4)$ affords k_2k_{-4}. Since at the end of the first process the substrate is completely converted into the 4*H* and 2*H* adducts, the ratio of their concentrations ($[2H]_1/[4H]_1$) coincides with the k_2/k_4 term. Considering that at the end of the reaction the concentration of 2*H* adduct ($[2H]_2$) coincides with $[2H]_1 + [4H]_1$, the following relationship is obtained:

$$\frac{k_2}{k_4} = \frac{[2H]_1}{[2H]_2 - [2H]_1} \qquad (9)$$

In the case of cations **2a**–**4a**, absorbance measurements carried out at wavelength *B*, at the end of the first and the second process, respectively, afford k_2/k_4 by eq 9. The k_2/k_4 ratio for cation **1a** cannot be obtained with the above procedure because the 4*H* adduct **1b** absorbs in the same region as the 2*H* isomer **1c**. The estimation of this ratio will be described below.

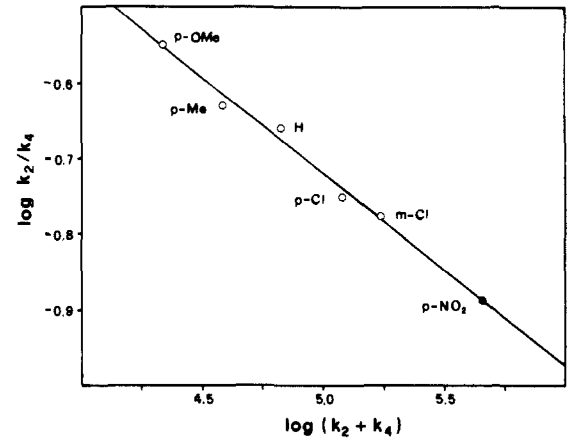


Figure 1. Dependence of log (k_2/k_4) on log $(k_2 + k_4)$. The solid circle is extrapolated log (k_2/k_4) for cation **1a**.

For cations **5a** and **6a** (case ii), plots of $(\tau_1^{-1} + \tau_2^{-1})$ vs. [MeO$^-$] (Tables S5 and S6) give straight lines, with slopes equal to $(k_2 + k_4)$ (eq 5). Actually, the intercept of this plot should give the k_{-4} constant; however, since this term in our experimental conditions is small, its determination is affected by a large error, and therefore the value of the intercept was not taken into account for the determination of k_{-4}. According to eq 6, plots of $(\tau_1^{-1}\tau_2^{-1})$ vs. [MeO$^-$] (Tables S5 and S6) are linear with slopes equal to k_2k_{-4}. Experiments performed at [MeO$^-$] $\simeq 5 \times 10^{-3}$ to 10^{-2} M, showing the kinetic pattern i, permit the evaluation of the k_2/k_4 ratio by eq 9, as described above (we assume that this ratio is not affected by the higher ionic strength).

We observed an empirical linear correlation between log (k_2/k_4) and log $(k_2 + k_4)$ for the cations **2a**–**6a** (Figure 1). This correlation was used to estimate the k_2/k_4 value for the cation **1a**.

From the values of $(k_2 + k_4)$, k_2k_{-4}, and k_2/k_4 the kinetic constants k_2, k_4, and k_{-4} and the equilibrium constant K_4 ($=k_4/k_{-4}$) are determined.

In the case of cation **7a**, the experiments carried out at [MeO$^-$] $\simeq 2 \times 10^{-4}$ to 2×10^{-3} M (Table S7) yield the constant k_2 (eq 8). Also in this case the intercept was not taken into account for the k_{-2} determination. The kinetic experiments performed at [MeO$^-$] $\simeq 10^{-2}$ to 10^{-1} M (Table S8), which indicate also the formation of the 4*H* adduct (eq 5 and 6), were used only to obtain an estimate of the kinetic constants k_4 and k_{-4}, owing to the large effects of ionic strength and methoxide ion association. The analytical methoxide ion concentration was corrected for the sodium methoxide association.[4] A plot of $(\tau_1^{-1} + \tau_2^{-1})$ vs. the free methoxide ion concentration is linear with slope equal to $(k_2 + k_4)$ and intercept equal to k_{-4} (eq 5). Plotting $(\tau_1^{-1}\tau_2^{-1})$ vs $[\mathrm{MeO^-}]_{\mathrm{free}}$ affords k_2k_{-4} as the slope (eq 6). Strictly speaking, these empirical "constants" depend on the ionic strength, which was not kept constant; therefore the parameters obtained are apparent kinetic constants averaged by the least-squares treatment over the range of ionic strength. We indicate these constants as k_2^* ($=47$ M^{-1} s^{-1}), k_4^* ($=590$ M^{-1} s^{-1}), and k_{-4}^* ($=41$ s^{-1}), to distinguish them from the constants obtained in dilute solutions. We point out that the value of k_2^*, being lower than k_2 ($=75$ M^{-1} s^{-1}), is consistent with the retarding salt effect expected for an anion–cation combination reaction.[5] Our estimate of k_4 is based on the assumption that the two constants k_2 and k_4 are similarly affected by the medium effects, i.e., $k_2^*/k_4^* = k_2/k_4$, thus affording $k_4 \simeq 900$ M^{-1} s^{-1}. The apparent kinetic constant k_{-4}^* should be an upper limit for k_{-4} (i.e., $k_{-4} < 41$ s^{-1}) since the

---

(4) The precise value of the ion association constant of sodium methoxide is not known, but a value close to 10 M^{-1} seems reasonable: (a) Terrier, F. *Ann. Chim. (Paris)* **1969**, *4*, 153. (b) Barthel, J.; Justice, J.-C.; Wachter, R. *Z. Phys. Chem. (Munich)* **1973**, *84*, 100.

(5) (a) Bunton, C. A.; Huang, S. K. *J. Am. Chem. Soc.* **1972**, *94*, 3536. (b) Fox, B. M.; Hepworth, J. D.; Mason, D.; Hallas, G. *J. Chem. Soc., Perkin Trans. 2* **1982**, 987.

Table I. Rates and Equilibrium Constants for the Reaction of Cations **1a–7a** with MeO⁻, in Methanol at 25.0 °C

cation	k_4, s^{-1} M^{-1}	k_{-4}, s^{-1}	K_4, M^{-1}	k_2, s^{-1} M^{-1}	k_{-2}, s^{-1}	K_2, M^{-1}
1a	4.0×10^{5a}	6.3×10^{-2a}	6.4×10^{6a}	5.2×10^{4a}	4.7×10^{-5a}	1.1×10^{9b}
2a	1.5×10^{5}	1.6×10^{-1}	9.2×10^{5}	2.5×10^{4}	2.0×10^{-4}	1.2×10^{8c}
						1.3×10^{8b}
3a	1.0×10^{5}	3.0×10^{-1}	3.3×10^{5}	1.8×10^{4}	2.8×10^{-4}	6.4×10^{7c}
4a	5.4×10^{4}	6.4×10^{-1}	8.5×10^{4}	1.2×10^{4}	7.7×10^{-4}	1.6×10^{7c}
5a	3.1×10^{4}	1.3	2.4×10^{4}	7.4×10^{3}	1.1×10^{-3}	6.6×10^{6c}
6a	1.7×10^{4}	1.7	9.9×10^{3}	4.8×10^{3}	2.7×10^{-3}	1.7×10^{6c}
7a	9×10^{2a}	3×10^{a}	3×10^{a}	7.5×10	9.5×10^{-3}	7.8×10^{3d}
						8.0×10^{3c}

[a] Estimated value; see text. [b] Obtained in the presence of chloroacetic acid/chloroacetate buffers. [c] Obtained in the presence of triethylammonium buffers. [d] Obtained with MeONa.

transition state is more polar than the neutral 4*H* adduct.[6] From the relationship 7, which holds in the range [MeO⁻] $\simeq 2 \times 10^{-4}$ to 2×10^{-3} M, k_{-4} must be at least 10-fold greater than k_4[MeO⁻], also at the higher methoxide ion concentration (2×10^{-3} M), i.e., $k_{-4} > 18$ s^{-1}. Therefore an average value for $k_{-4} \simeq 30$ s^{-1} seems appropriate. An approximate value for $K_4 \simeq 30$ M^{-1} can now be estimated.

Equilibrium Measurements. The equilibrium constants k_2 were obtained spectrophotometrically at very low methoxide ion concentrations, with buffer solutions. The K_2 value for the cation **7a** was obtained also with diluted solutions of sodium methoxide ([MeO⁻] ~ 10^{-4} to 10^{-3} M). Further details are reported in the Experimental Section. From the values of K_2 and k_2, the kinetic constants k_{-2} ($=k_2/K_2$) can be calculated.

The kinetic and equilibrium constants for the reaction of cations **1a–7a** are reported in Table I. These constants are estimated to be accurate to within ±10% on the basis of some independent duplication of the measurements, unless indicated as estimated values in the table. The constants k_2 and K_2 were not corrected for the statistical factor.

Discussion

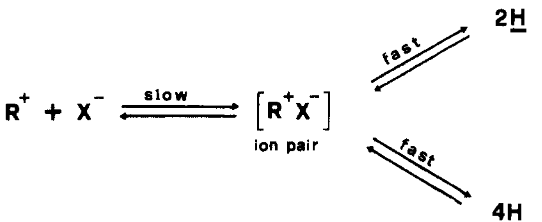
The Nature of the Transition State. The kinetic patterns observed in the reaction of cations **1a–7a** with MeO⁻ give useful insights on the nature of the transition state of anion–cation combinations. However, before discussing our data it is appropriate to consider the principal results known for such reactions. Ritchie showed that these reactions are reasonably well correlated by the simple "constant selectivity" N_+ relationship[7] (eq 10), in

$$\log \frac{k}{k_0} = N_+ \qquad (10)$$

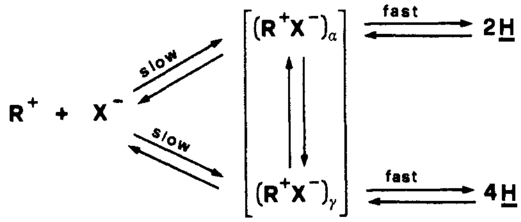
which k is the rate constant for the reaction of a preformed cation with a given nucleophilic system (i.e., a given nucleophile in a given solvent), k_0 is the rate constant for a reference nucleophile, and is dependent only on the identity of the cation,[8] and N_+ is a parameter dependent only on the nucleophilic system.

In spite of frequent inexplicable deviations,[1a,9] there is a large body of data that follows eq 10. At variance with rate data, there was no corresponding rate–equilibrium or equilibrium–equilibrium correlation.[7] These features lead Ritchie to the conclusion that the nucleophile and electrophile are completely separated in the transition state, with electrophile solvation little perturbed. Hence, quoting Ritchie,[7] "the transition state for the rate-determining step is either between the intimate and solvent-separated ion pair, or, with the modification of the mechanism suggested by Atkinson,[10] between the two-solvent-separated and one-solvent-separated ion pairs". In both cases the transition state should be very close in structure to the one-solvent-separated ion pair.[7] An alternative explanation consistent with the reactivity–selectivity principle, and involving a balanced partial desolvation of the cation at the transition state, was offered by Pross.[11] The common features of these explanations are that the activation barrier is only due to desolvation factors and that, apart from the different degree of desolvation of the transition state, the formation of an ion pair intermediate is the rate-determining step.

Scheme II



Scheme III



Successively, the application of the N_+ scale to reactions of nucleophilic reagents with acyl compounds forced Ritchie to retract any kind of detailed description of the nature of the transition state.[12,13]

It is evident that the experimental data produced to date do no allow a firm assessment of the mechanism of these reactions.

As indicated above, our experimental results provide useful insight about this matter.

In the Results section we have rationalized the observed kinetic patterns according to Scheme I. Now we will show that alternative kinetic schemes that involve the rate-determining formation of ion pairs as intermediates are not consistent with observed kinetic pattern ii. Let us consider Scheme II, which refers to the rate-determining formation of an ion pair that successively yields the two adducts in a fast process. In this case, since the rate law is not affected by all the steps beyond the rate-limiting one, the substrate R⁺, in the presence of a large excess of the nucleophile, must always disappear following a simple first-order process. The conversion of the 4*H* adduct into the 2*H* one must occur through the intermediacy of the ion pair that is present in steady-state concentration. This process does not affect the decay of the substrate.

Actually, the observation of pattern ii, which involves the disappearance of the substrate R⁺ through two processes, indicates that R⁺ participates in the conversion of the 4*H* adduct into the 2*H* one, thus ruling out Scheme II.

---

(6) Bunnett, J. F. In *Investigation of Rates and Mechanisms of Reactions*; Friess, S. L., Lewis, E. S., Weissberger, A., Eds.; Interscience: New York, 1974; pp 372–373.

(7) Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348.

(8) Successively, Ritchie showed that log k_0 is also solvent dependent.[9]

(9) Ritchie, C. D. *Pure Appl. Chem.* **1978**, *50*, 1281.

(10) Atkinson, G.; Kor, S. K. *J. Phys. Chem.* **1967**, *71*, 673.

(11) Pross, A. *J. Am. Chem. Soc.* **1976**, *98*, 776.

(12) Ritchie, C. D. *J. Am. Chem. Soc.* **1975**, *97*, 1170.

(13) However the application of the N_+ scale to nucleophilic reactions of acyl compounds has been recently criticized: Palling, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 4869.

Alternatively, the rate-determining formation of two oriented ion pairs[14] that yield the 2*H* and 4*H* adducts, respectively, could be formulated as a hypothetical kinetic scheme (Scheme III). The equilibration of the two oriented ion pairs reported in the square brackets refers to the process that occurs within the solvent cage. This process is expected to be faster than the equilibration of the two oriented ion pairs through the reactants, because it should involve a lesser degree of solvent reorganization. On the basis of this reasonable condition the conversion of the 4*H* adduct into the 2*H* one occurs through the equilibration of the two oriented ion pairs within the solvent cage and does not involve the substrate R^+. Once again R^+, in the presence of a large excess of the nucleophile, must disappear following a simple first-order process, which is in contrast with the experimental observation of pattern ii. Therefore, Scheme III must be rejected also.

It can be argued that a reaction, such as the methoxide attachment carried out in methanol, is a particular case of an anion–cation combination reaction, since, in principle, the methoxide ion could act as a general base by activating attachment of a methanol molecule. However, for an analogous nucleophilic system (OH^-/H_2O), Bunton et al. pointed out that there is no reason to believe that this mechanism operates, thus suggesting a normal behavior for OH^-.[15] Moreover, since we also reported the observation of pattern ii in the reaction of 2,4,6-triphenylthiopyrylium ion with amines in Me_2SO,[2b,c] the results here reported should be general for nucleophile–cation combination reactions.

It should be pointed out that, since Scheme I holds, we do not have any evidence for the intermediacy of ion pairs; however, if they exist as intermediates along the reaction path, their formation cannot be rate-determining, in contrast with the earlier proposals of Ritchie and with the model of Pross.

Our results show, more generally, that the possible formation of any common species that precedes the 2*H* and 4*H* adducts such as an ion pair or a donor–acceptor complex[16] cannot be rate-determining and indicate that there are two rate-determining transition states in which the nucleophile and each electrophilic center specifically interact. An important consequence of these findings is that each electrophilic site, behaving like an independent electrophile, should follow independently the Ritchie equation.

More recently Ritchie suggested that a partial electron transfer between nucleophile and electrophile can occur at the transition state.[1a] However, since we observe two distinct rate-determining transition states for the formation of the 2*H* and 4*H* adducts, respectively, if such partial electron transfer occurs, it must involve a specific interaction between the nucleophile and the electrophilic site.

Bunton reported that there is no change in orbital rehybridization from sp^2 at the reaction center of diferrocenylmethyl cation, on going to the transition state for the attachment of anionic nucleophilies.[15] Since, in addition, our results indicate a specific interaction between the nucleophile and the electrophilic site, the transition state for anion–cation combination reaction seems to look like an intimate ion pair, with little, if any, bond formation.

Substituent Effects on Equilibria. We found a remarkably good linear correlation of gradient 1.04 between log K_4 and log K_2 (r = 0.999), spanning 5 powers of 10 (Figure 2). This feature indicates that the relative thermodynamic stability of 2*H* and 4*H* adducts ($K_2/K_4 \sim 200$) is negligibly affected by the substitution on the phenyl ring. Considering that the mode of transmission of the substituent effects in the two adducts should be different, since the aryl group could in principle interact with the π system of the 2*H* adduct, the above observation forces the conclusion that the substituents poorly affect the stability of the two adducts. This feature seems to indicate that the aryl groups are scarcely conjugated with the 2*H* adduct π system. Therefore the influence of the substituents on the equilibrium constants should essentially reflect variations in the cations' thermodynamic stability.

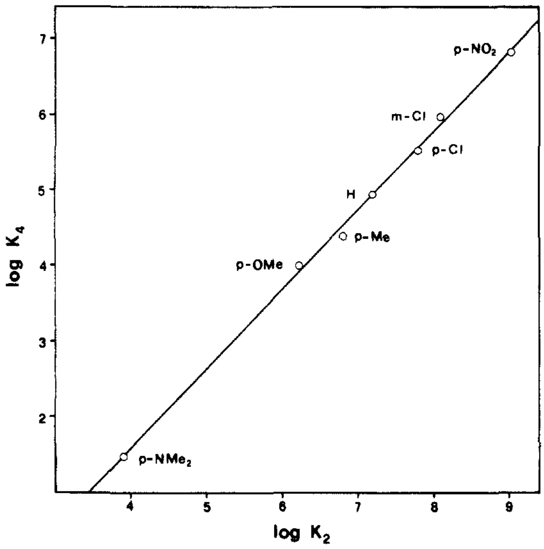


Figure 2. Correlation between the equilibrium constants for the formation of 4*H*-thiopyrans and the equilibrium constants for the corresponding 2*H* isomers.

The higher thermodynamic stability of 2*H* with respect to the 4*H* isomers is a general feature, observed in reversible nucleophile attachment to pyrylium and thiopyrylium cations, and can be ascribed to the different π system of the two adducts.[17]

The equilibrium constants K_2 and K_4 are well correlated by the σ^+ constants of the substituents ($\rho_2^{eq} = 2.0$, $r = 0.993$; $\rho_4^{eq} = 2.1$, $r = 0.991$). Structural X-ray investigations performed on such related systems as 2,4,6-triphenylthiopyrylium[18] and 2,6-diphenyl-4-(*p*-(dimethylamino)phenyl)thiopyrylium[19] show that the γ-aryl groups are twisted with respect to the mean plane of the thiopyrylium ring (15.8° and 12.4°, respectively). The good correlations of the equilibrium constants against σ^+ indicate that the observed degree of noncoplanarity of the rings does not affect the transmission of resonance substituent effects. Eaborn et al. reached similar conclusions by studying the transmission of substituent effects in biphenyl systems.[20]

Substituent Effects on Rates. It is commonly accepted that the structural changes connecting reactants and products are at some intermediate stage of completion at the transition state. This idea is the basis of the so-called Leffler–Hammon postulate[21] that can be expressed quantitatively by the rate–equilibrium relationship

$$\delta\Delta G^{\ddagger} = \alpha\delta\Delta G^{\circ} \qquad (11)$$

where α is a factor, limited to values between 0 and 1, which specifies the contribution of reactant and product free energy differences to that of the transition state. A value of α close to 0 indicates a reactantlike transition state, whereas α close to 1 indicates a productlike transition state. Even though eq 11 tends to focus attention on the thermodynamic component of the activation barrier, it is recognized that in some cases other factors must be taken into account.[21d] Typical situations, as the reaction here reported, are those in which the thermodynamically less stable product is formed faster than the more stable one. Hence, in these cases, there must be additional factors which are present in the transition state, but absent in the reactants and products. These

---

[14] For a case in which oriented ion pairs were detected, see: Oakes, J.; Symons, M. C. R. *Trans. Faraday Soc.* **1970**, *66*, 10.

[15] Bunton, C. A.; Carrasco, N., Davoudzadeh, F.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1520.

[16] It was suggested that donor-acceptor complexes could be transient intermediates in the reaction of pyrylium cations with nucleophiles: Fărcasiu, M.; Fărcasiu, D. *Tetrahedron Lett.* **1967**, 4833.

[17] Doddi, G.; Ercolani, G. *J. Chem. Soc., Perkin Trans. 2* **1986**, 271.

[18] Batsanov, A. S.; Struchkov, Yu. T.; Ukkin, L. Yu.; Dolgopolova, N. A. *Inorg. Chem. Acta* **1982**, *63*, 17.

[19] Dulmage, W. J.; Ligth, W. A.; Marino, S. J.; Salzberg, C. D.; Smith, D. L.; Staudenmayer, W. J. *J. Appl. Phys.* **1978**, *49*, 5543.

[20] Baker, R.; Bott, R. W.; Eaborn, C.; Greasley, P. M. *J. Chem. Soc.* **1964**, 627.

[21] (a) Pross, A. *Adv. Phys. Org. Chem.* **1977**, *14*, 69. (b) Leffler, J. E. *Science* **1953**, *117*, 340. (c) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963. (d) Murdoch, J. R.; Magnoli, D. E. *J. Am. Chem. Soc.* **1982**, *104*, 3792.

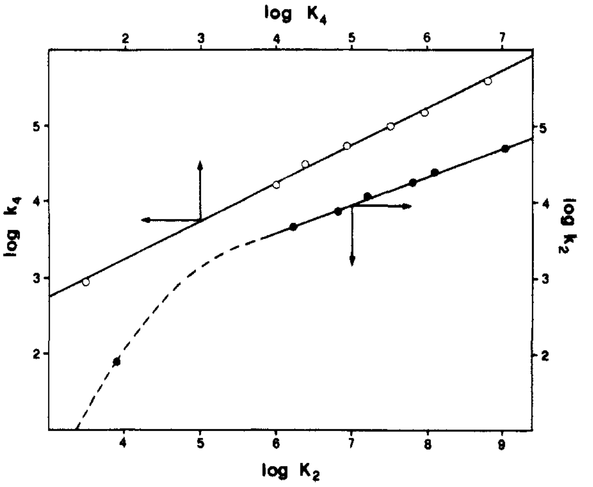


Figure 3. Rate–equilibrium relationships for the formation of 2*H*- (●) and 4*H*- (○) thiopyrans.

additional factors could be regarded as kinetic factors since they do not affect the $\Delta G°$ for the reaction. It should be pointed out that in the reaction reported here these kinetic factors cannot be ascribed to steric effects, because the steric interactions in the transition states should be intermediate between reactants and products.[22] Assuming that thiopyrylium cations are well-behaved with respect to the Ritchie equation, the comprehension of the nature of these kinetic factors is strictly connected with the understanding of the factors that make the Ritchie relationship (eq 10) work. Although this goal is far from being reached, these kinetic components probably originate from electrostatic factors due to electrophile–nucleophile interactions and solvent reorganization. It follows that electronic substituent effects do influence these kinetic components.

In Figure 3 are reported the plots of log k_4 vs. log K_4 and log k_2 vs. log K_2. All the points of the first plot are well interpolated by a straight line of gradient 0.50 ($r = 0.999$). Also, the points on the log k_2–log K_2 plot, with the exception of the dimethylamino group, are well interpolated by a straight line of slope 0.37 ($r = 0.998$).[23] However, since (from the above considerations) the substituents affect the kinetic factors of the activation barrier, the application of eq 11 is improper and the α values (slopes of Figure 3 plots) are no longer meaningful. This conclusion should be general for anion–cation combination reactions.

The kinetic constants k_2 (with an exception for **7a**) and k_4 are well correlated by the σ^+ constants, as shown in Figure 4 ($\rho_2^{\text{kin}} = 0.67$, $r = 0.990$; $\rho_4^{\text{kin}} = 1.0$, $r = 0.991$). The order $\rho_4^{\text{kin}} > \rho_2^{\text{kin}}$ cannot be ascribed to the different steric hindrance to solvation of the two reactive centers, because a higher sensitivity to the electronic effects would be expected for the more hindered α center. This conclusion stems from the comparison of ρ values for the dissociation constants of 2,6-di-*tert*-butyl-4-X-phenols with respect to the 2,6-unsubstituted ones.[24] We believe that the different ρ values reflect the different transmission efficiencies of electronic effects between the substituent and the two reactive centers.[25] In fact the substituent effects are directly transmitted to the γ position as in the Brown–Okamoto reference reaction,[21c] whereas they are transmitted to the α position by the heteroaromatic ring. The large deviation observed in the log k_2–σ^+ plot (Figure 4) for the dimethylamino group (1 order of magnitude lower than the value predicted by the corresponding regression line) is also observed in nucleophilic attachment on para-substituted phenyltropylium ions. In fact, there are good linear correlations when the methoxide attachment to the α position is reported against the methoxide (in methanol) or hydroxide (in water) attachment to para-substituted phenyltropylium ions. The former correlation involving the *p*-Cl, H, *p*-OMe, and *p*-NMe$_2$ groups[26] has a slope of 1.2 and a correlation coefficient of 0.998; the latter, involving the *p*-Cl, H, *p*-Me, *p*-OMe, and *p*-NMe$_2$ groups,[27] has a slope of 1.3 and the same correlation coefficient. Since these additions do not occur on the phenyl-substituted position of the tropylium ring,[28] the above correlations indicate that the deviation of the *p*-dimethylamino group, with respect to σ^+, is observed whenever the electronic substituent effect is transmitted by the positively charged aromatic system.

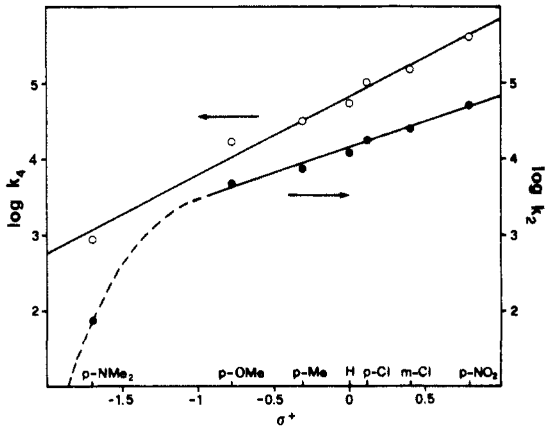


Figure 4. Rate–σ^+ relationships for the formation of 2*H*- (●) and 4*H*- (○) thiopyrans.

We think that the dimethylamino group introduces a too large perturbation in charged aromatic systems, as evidenced by the large contribution of quinoid-type structure in this class of compounds.[19,29] With reference to the reaction here reported, this feature would affect only the nucleophilic attachment to the α position, being the γ one connected with the substituent as in the Brown–Okamoto reference reaction.

Conclusions

The results obtained in this investigation indicate that in anion–cation combination reactions there are no rate-determining steps preceding the formation of the adducts and show that each electrophilic site of an ambident cation behaves like an independent electrophile. Moreover, our results clearly indicate that the Leffler–Hammond postulate does not apply to this class of reactions.

Experimental Section

Materials. Methanol-d_4 for NMR spectroscopy was from Merck. Dry methanol was obtained as previously reported.[30] Stock solutions of sodium methoxide were prepared by dissolving the appropriate amount of clean sodium in methanol (or methanol-d_4) under an argon atmosphere. Methanolic $HClO_4$ was prepared by a published procedure.[31] Purification of triethylamine and preparation of triethylamine/triethylammonium buffers were carried out as previously indicated.[30] Chloroacetic acid (Aldrich Gold Label) was used without further purification. Chloroacetic acid/chloroacetate buffers were prepared by partial neutralization of the acid with sodium methoxide solutions.

---

(22) The sterics effects are due (i) in the reactants, to the interaction of α and λ bulky substitutents with the flanking ring hydrogen atoms and (ii) in the product, to the increased crowding of the reaction center with respect to the starting cation.

(23) One of the referees pointed out that the α_2 value calculated by the ratio $\rho_2^{\text{kin}}/\rho_2^{\text{eq}}$ (0.335) does not agree with the reported value (0.37). The different α_2 value obtained by $\rho_2^{\text{kin}}/\rho_2^{\text{eq}}$ is due to the fact that in the evaluation of ρ_2^{eq} was included also the K_2 constant for the NMe$_2$ group, whereas this value was not considered in the log k_2 vs. log K_2 plot. At variance the slightly different α_4 value obtained by the ratio $\rho_4^{\text{kin}}/\rho_4^{\text{eq}}$ (0.48) is only due to round-off errors in ρ_4^{kin} and ρ_4^{eq}.

(24) Cohen, L. A.; Jones, W. M. *J. Am. Chem. Soc.* **1963**, *85*, 3397.

(25) Mc Lennan, D. J. *Tetrahedron* **1978**, *34*, 2331 and references therein.

(26) Ritchie, C. D.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1972**, *94*, 4963.

(27) (a) Ritchie, C. D.; Fleischhauer, H. *J. Am. Chem. Soc.* **1972**, *94*, 3481. (b) Virtanen, P. O. I.; Vaskuri, J.; Väisänen, S. *Finn. Chem. Lett.* **1975**, 159.

(28) Jutz, C.; Voithenleitner, F. *Chem. Ber.* **1964**, *97*, 29.

(29) Bigelow, R. W. *J. Chem. Phys.* **1980**, *73*, 3864.

(30) Doddi, G.; Fornarini, S.; Illuminati, G.; Stegel, F. *J. Org. Chem.* **1979**, *44*, 4496.

(31) Ritchie, C. D.; Skinner, G. A.; Badding, V. G. *J. Am. Chem. Soc.* **1972**, *94*, 4963.

2,6-Di-*tert*-butyl-4-(*p*-chlorophenyl)thiopyrylium (**3a**), 2,6-di-*tert*-butyl-4-phenylthiopyrylium (**4a**), 2,6-di-*tert*-butyl-4-(*p*-methylphenyl)thiopyrylium (**5a**), and 2,6-di-*tert*-butyl-4-(*p*-methoxyphenyl)thiopyrylium (**6a**) perchlorates were available from our previous work.[32]

Syntheses. 2,6-Di-*tert*-butyl-4-(*p*-nitrophenyl)thiopyrylium perchlorate (**1a**) was prepared by a slight modification of the method reported by Le Fèvre and Le Fèvre[33] relative to the nitration of 2,4,6-triphenylpyrylium perchlorate.

2,6-Di-*tert*-butyl-4-phenylthiopyrylium perchlorate (**4a**) (1.92 g) was dissolved in 100% HNO_3 (40 mL) at 0 °C and left for 30 min. Dilution was performed, at 0 °C, by stirring in successively AcOH (40 mL) and 30% $HClO_4$ (80 mL). The resulting solution was poured into ice–water (500 mL). After 1 h the solid was collected by filtration and air-dried. The salt was purified by dissolution in the least amount of CH_2Cl_2 followed by precipitation with dry ether: yield 1.05 g (49%); mp 194–195 °C. Anal. Calcd for $C_{19}H_{24}ClNO_6S$: C, 53.08; H, 5.63; N, 3.26. Found: C, 53.17; H, 5.80; N, 3.38.

2,6-Di-*tert*-butyl-4-(*m*-chlorophenyl)thiopyrylium perchlorate (**2a**) was prepared according to the following synthetic sequence: 2,2,8,8-tetramethyl-5-(*m*-chlorophenyl)nonane-3,7-dione (**8**) → 2,6-di-*tert*-butyl-4-(*m*-chlorophenyl)pyrylium perchlorate (**9**) → **2a**.

Compound **8** was prepared according to the general procedure previously described for analogous compounds[32] and was recrystallized from *n*-hexane at −20 °C: yield 79%; mp 82–83 °C. Anal. Calcd for $C_{19}H_{27}ClO_2$: C, 70.68; H, 8.43. Found: C, 70.62; H, 8.40.

Conversion of **8** to **9** was accomplished as follows: Compound **8** (3.2 g) and triphenylmethanol (2.6 g) were dissolved in Ac_2O (50 mL) by gently warming the solution. To the well-stirred solution was added over 30 min 70% $HClO_4$ (3 g) in Ac_2O (40 mL) (this solution must be prepared by adding the $HClO_4$ in drops to the ice-cooled and well-stirred Ac_2O). Ether was added to the reaction mixture until complete precipitation of the product **9**, which was collected and washed with ether. The crude solid was purified by dissolution in the least amount of CH_2Cl_2 followed by precipitation with dry ether: yield 3.6 g (86%); mp 219–221 °C. Anal. Calcd for $C_{19}H_{24}Cl_2O_5$: C, 56.59; H, 6.00. Found: C, 56.45; H, 5.88. The reaction of **9** with sodium sulfide in aqueous acetone, carried out as described for the preparation of 2,4,6-triphenylthiopyrylium perchlorate,[34] afforded a 2:1 mixture of **2a** and **9**, respectively. The thiopyrylium content was raised to 9:1 by treating the product mixture with sodium sulfide in aqueous acetone for a second time. The final purification of the thiopyrylium salt **2a** was accomplished according to a previously described procedure[32] that relied on the selective attachment of methoxide ion to the pyrylium ring to yield the neutral 2*H*-pyran which can then be easily removed; overall yield 22%; mp 182–183 °C. Anal. Calcd for $C_{19}H_{24}Cl_2O_4S$: C, 54.42; H, 5.77. Found: C, 54.62; H, 5.81.

2,6-Di-*tert*-butyl-4-(*p*-(dimethylamino)phenyl)thiopyrylium perchlorate (**7a**) was prepared by a modification of the method reported by Wizinger and Angliker[35] for the preparation of 2,6-diphenyl-4(*p*-(dimethylamino)phenyl)thiopyrylium perchlorate.

2,6-Di-*tert*-butylthiopyrylium perchlorate[36] (**10**) (1.54 g), *N*,*N*-dimethylaniline (0.65 g), anhydrous sodium acetate (0.43 g), and AcOH (50 mL) were refluxed for 4 days. The volume was reduced to about 10 mL by partial distillation of the solvent, CCl_4 (200 mL) was then added, and the solution was left at 0 °C for 1 h. The precipitate was collected by filtration and dissolved in the least amount of CH_2Cl_2. The residue (sodium salts) was removed by filtration, and ethyl ether/petroleum ether 40–70 °C (1:1 v/v) was added to the solution until complete precipitation of the product **7a**:[37] yield 0.85 g (40%); mp 241–243 °C. Anal. Calcd for $C_{21}H_{30}ClNO_4S$: C, 58.93; H, 7.07; N, 3.27. Found: C, 58.90; H, 7.03; N, 3.31.

^{1}H NMR Measurements. All spectra were recorded on a Bruker WP 80 SY spectrometer. Chemical shifts were quoted in ppm relative to Me_4Si. Low-temperature NMR spectra were recorded just after the addition of the substrate (ca. 0.05 mmol of solid sample) to ca. 0.5 mL of a solution of CD_3ONa 0.5 M in CD_3OD, thermostated at −40 °C inside the NMR probe. Room temperature (~30 °C) NMR measurements were carried out after equilibrium of the reaction mixtures was attained. ^{1}H NMR data for cations **1a**–**7a**, 4*H*-thiopyrans **1b**–**6b**, and 2*H*-thiopyrans **1c**–**7c** are the following:[38]

1a: δ 1.73 (s, 18 H, *t*-Bu), 8.27 (A_2B_2 system, 2 H, *J* = 8.8 Hz, H-3′), 8.50 (A_2B_2 system, 2 H, *J* = 8.8 Hz, H-2′), 8.95 (s, 2 H, H-3). **2a**: δ 1.71 (s, 18 H, *t*-Bu), 7.7–8.2 (m, 4 H, aryl), 8.89 (s, 2 H, H-3). **3a**: δ 1.71 (s, 18 H, *t*-Bu), 7.70 (A_2B_2 system, 2 H, *J* = 8.8 Hz, H-3′), 8.08 (A_2B_2 system, 2 H, *J* = 8.8 Hz, H-2′), 8.86 (s, 2 H, H-3). **4a**:[17] δ 1.70 (s, 18 H, *t*-Bu), 7.7–8.2 (m, 5 H, phenyl), 8.82 (s, 2 H, H-3). **5a**: δ 1.70 (s, 18 H, *t*-Bu), 2.50 (s, 3 H, Me), 7.52 (A_2B_2 system, 2 H, *J* = 8.5 Hz, H-3′), 8.01 (A_2B_2 system, 2 H, *J* = 8.5 Hz, H-2′), 8.84 (s, 2 H, H-3). **6a**: δ 1.69 (s, 18 H, *t*-Bu), 3.96 (s, 3 H, OMe), 7.23 (A_2B_2 system, 2 H, *J* = 9.1 Hz, H-3′), 8.15 (A_2B_2 system, 2 H, *J* = 9.1 Hz, H-2′), 8.79 (s, 2 H, H-3). **7a**: δ 1.62 (s, 18 H, *t*-Bu), 3.23 (s, 6 H, NMe_2), 7.00 (A_2B_2 system, 2 H, *J* = 9.4 Hz, H-3′), 8.18 (A_2B_2 system, 2 H, *J* = 9.4 Hz, H-2′), 8.57 (s, 2 H, H-3).

1b: δ 1.25 (s, 18 H, *t*-Bu), 5.34 (s, 2 H, H-3), 7.57 (A_2B_2 system, 2 H, *J* = 8.0 Hz, H-2′), 8.24 (A_2B_2 system, 2 H, *J* = 8.0 Hz, H-3′). **2b**: δ 1.24 (s, 18 H, *t*-Bu), 5.30 (s, 2 H, H-3), 7.0–7.7 (m, 4 H, aryl). **3b**: δ 1.25 (s, 18 H, *t*-Bu), 5.36 (s, 2 H, H-3), 7.30 (psuedo-s, 4 H, aryl). **4b**[17] δ 1.26 (s, 18 H, *t*-Bu), 5.39 (s, 2 H, H-3), 7.32 (pseudo-s, 5 H, phenyl). **5b**: δ 1.26 (s, 18 H, *t*-Bu), 2.31 (s, 3 H, Me), 5.38 (s, 2 H, H-3), 7.14 (pseudo-s, 4 H, aryl). **6b**: δ 1.26 (s, 18 H, *t*-Bu), 3.77 (s, 3 H, OMe), 5.39 (s, 2 H, H-3), 6.85 (A_2B_2 system, 2 H, *J* = 8.9 Hz, H-3′), 7.20 (A_2B_2 system, 2 H, *J* = 8.9 Hz, H-2′). **7b**: Not observed.

1c: δ 1.09 (s, 9 H, *t*-Bu-2), 1.32 (s, 9 H, *t*-Bu-6), 5.59 (s, 1 H, H-3), 6.32 (s, 1 H, H-5), 7.66 (A_2B_2 system, 2 H, *J* = 8.9 Hz, H-2′), 8.27 (A_2B_2 system, 2 H, *J* = 8.9 Hz, H-3′). **2c**: δ 1.08 (s, 9 H, *t*-Bu-2), 1.31 (s, 9 H, *t*-Bu-6), 5.46 (s, 1 H, H-3), 6.25 (s, 1 H, H-5), 7.3–7.4 (m, 4 H, aryl). **3c**: δ 1.08 (s, 9 H, *t*-Bu-2), 1.31 (s, 9 H, *t*-Bu-6), 5.47 (s, 1 H, H-3), 6.28 (s, 1 H, H-5), 7.39 (pseudo-s, 4 H, aryl). **4c**:[17] δ 1.10 (s, 9 H, *t*-Bu-2), 1.33 (s, 9 H, *t*-Bu-6), 5.48 (s, 1 H, H-3), 6.33 (s, 1 H, H-5), 7.40 (pseudo-s, 5 H, phenyl). **5c**: δ 1.08 (s, 9 H, *t*-Bu-2), 1.31 (s, 9 H, *t*-Bu-6), 2.34 (s, 3 H, Me), 5.43 (s, 1 H, H-3), 6.31 (s, 1 H, H-5), 7.19 (A_2B_2 system, 2 H, *J* = 8.1 Hz, H-3′), 7.27 (A_2B_2 system, 2 H, *J* = 8.1 Hz, H-2′). **6c**: δ 1.08 (s, 9 H, *t*-Bu-2), 1.31 (s, 9 H, *t*-Bu-6), 3.81 (s, 3 H, OMe), 5.41 (s, 1 H, H-3), 6.30 (s, 1 H, H-5), 6.93 (A_2B_2 system, 2 H, *J* = 9.0 Hz, H-3′), 7.34 (A_2B_2 system, 2 H, *J* = 9.0 Hz, H-2′). **7c**: δ 1.07 (s, 9 H, *t*-Bu-2), 1.30 (s, 9 H, *t*-Bu-6), 2.93 (s, 6 H, NMe_2), 4.83 (s, 1 H, H-3), 6.32 (s, 1 H, H-5), 6.77 (A_2B_2 system, 2 H, *J* = 9.0 Hz, H-3′), 7.23 (A_2B_2 system, 2 H, *J* = 9.0 Hz, H-2′).

UV-Vis Spectra. The UV-vis spectra of the substrates and the corresponding 2*H* adducts in methanol were recorded on a Cary 219 spectrophotometer. The values of λ_{max} (log ε) are the following:

1a, 322 nm (4.44); **2a**, 321 nm (4.31); **3a**, 355 nm (4.34); **4a**, 348 nm (4.22); **5a**, 368 (4.40), 314 nm (4.02); **6a**, 408 (4.48), 312 (3.84), 254 nm (3.80); **7a**, 533 (4.73), 293 (4.02), 260 nm (3.96).

1c, 300 nm (4.22); **2c**, 312 (3.53), 250 nm (4.18); **3c**, 310 (3.56), 253 nm (4.31); **4c**, 308 (3.41), 246 nm (4.04); **5c**, 307 (3.51), 248 nm (4.17); **6c**, 271 (4.06), 247 nm (4.12); **7c**, 304 (4.25), 256 nm (4.15).

Rate Measurements. Kinetic experiments were carried out on a Durrum 110 stopped-flow spectrophotometer at 25.0 °C under pseudo-first-order conditions. Typical errors in rate measurements are ±4%. The ionic strength was not kept constant. The reaction solutions were freshly prepared and handled under argon. The reaction kinetics of cations **2a**–**7a** were followed at wavelengths *A* and *B* (see Results). The values of λ_A and λ_B (nm), in order, are the following: **2a**, 355, 320; **3a**, 355, 320; **4a**, 360, 320; **5a**, 370, 320; **6a**, 410, 320; and **7a**, 530, 320. The reaction of cation **1a** was monitored only at λ = 330 nm. The k_2/k_4 ratio for cations **2a**–**6a** was determined from absorbance measurements at wavelength *B* (see Results). The same values of k_2/k_4 were obtained by performing the measurements at wavelengths *B* ±10 nm, thus indicating a negligible contribution of the 4*H* adducts to the absorbance in this region, as previously indicated for cognate compounds.[39] At variance, the 4*H* adduct **1b** shows an appreciable absorbance in the same region where the 2*H* isomer **1c** absorbs.

Equilibrium Measurements. The determination of K_2 values was carried out at 25.0 °C on a Cary 219 spectrophotometer by measuring the residual absorbance of the substrate (OD_∞) after equlibration with buffer solutions, at λ_A for the cations **2a**–**7a** and at λ = 330 nm for the cation **1a**. The addition of an excess of methanolic $HClO_4$ to these mixtures shifts the equilibrium completely toward the substrate, thus permitting the measurement of OD_0 after correction of the observed OD value for dilution.

The K_2 values were obtained by the equation

---

[32] Cordischi, V. C.; Doddi, G.; Ercolani, G. *J. Chem. Res., Synop.* **1985**, 62.

[33] LeFèvre, C. G.; Le Fèvre, R. J. W. *J. Chem. Soc.* **1932**, 2894.

[34] Maryanoff, B. E.; Stackhouse, J.; Senkler, G. H., Jr.; Mislow, K. *J. Am. Chem. Soc.* **1975**, *97*, 2718.

[35] Wizinger, R.; Angliker, H. J. *Helv. Chim. Acta* **1966**, *49*, 2046.

[36] Doddi, G.; Ercolani, G. *Synthesis* **1985**, 789.

[37] In some runs small amounts of **10** (<5%) were recovered together with the final product **7a**. In these cases the purification procedure of **7a** relied on the higher tendency of **10** to yield with methoxide ion easily removable neutral adducts and was accomplished as previously reported in analogous cases.[32]

[38] In view of the use of deuterated methanol, the chemical shift values of the 2- and 4-methoxy groups in the 2*H* and 4*H* adducts, respectively, are not quoted.

[39] Dimroth, K.; Wolfe, K.; Kroke, H. *Liebigs Ann. Chem.* **1964**, *678*, 183.

J. Am. Chem. Soc. **1986**, *108*, 3415–3422

$$K_2 = \frac{(\mathrm{OD}_0 - \mathrm{OD}_\infty)}{\mathrm{OD}_\infty[\mathrm{MeO}^-]}$$

In the case of the cation **1a**, owing to the absorbance contribution of the 2*H* adduct **1c**. the observed OD_∞ value ($\mathrm{OD}_\infty{}^{\mathrm{obs}}$) must be corrected by the equation

$$\mathrm{OD}_\infty = \frac{\mathrm{OD}_\infty{}^{\mathrm{obsd}}\epsilon_{1a} - \mathrm{OD}_0\epsilon_{1c}}{\epsilon_{1a} - \epsilon_{1c}}$$

where ϵ_{1a} and ϵ_{1c} are the molar absorbances for **1a** and **1c** at $\lambda = 330$ nm, respectively. The buffers used were triethylamine/triethylammonium ($\mathrm{p}K_a = 10.88$)[31] for cations **2a**–**7a** and chloroacetic acid/chloroacetate ($\mathrm{p}K_a = 7.7$)[40] for cations **1a** and **2a**. The methoxide ion concentration of each buffer was calculated from the methanol autoprotolysis constant ($\mathrm{p}K_s = 16.92$ at 25 °C).[41] The K_2 value for the cation **7a** was also obtained with diluted solutions of sodium methoxide ($[\mathrm{MeO}^-] \sim 10^{-4}$ to 10^{-3} M). The ionic strength was always lower than 2×10^{-3} M. The concentration of the substrates was in the range $(1-4) \times 10^{-5}$ M. The absorbance measurements were carried out with Teflon-stoppered 1-cm quartz cells, with the exception of cations **2a** (with triethylamine/triethylammonium buffer) and **3a** for which 10-cm quartz cells were used.

Note Added in Proof. M.L.D.V., G.D., and G.E. remember with great sorrow the sudden decease of their inspiring teacher Prof. Gabriello Illuminati.

Acknowledgment. We wish to thank Prof. C. A. Bunton and Prof. F. Stegel for criticisms and suggestions, G. Frachey for the technical assistance in NMR measurements, and the Servizio di Microanalisi, Area della Ricerca di Roma del C.N.R., for elemental analyses.

Supplementary Material Available: Tables S1–S8 summarizing all the kinetic measurements (4 pages). Ordering information is given on any current masthead page.

---

[40] Clare, B. W.; Cook, D.; Ko, E. C. F.; Mac, Y. C.; Parker, A. J. *J. Am. Chem. Soc.* **1966**, *88*, 1911.

[41] Koskikallio, J. *Suom. Kemistil. B* **1957**, *30*, 111.

Solid-State and Solution Studies of Lithiated 2-Carbomethoxycyclohexanone Dimethylhydrazone and Lithiated Cyclohexanone Phenylimine

Robert A. Wanat, David B. Collum,* Greg Van Duyne, Jon Clardy,* and Randall T. DePue

Contribution from the Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853-1301. *Received August 21, 1985*

Abstract: Treatment of 2-carbomethoxycyclohexanone dimethylhydrazone with lithium diisopropylamide as a hydrocarbon solution afforded the corresponding lithiated hydrazone as a tetrahydrofuran solvate **1**. An X-ray crystallographic structure determination showed **1** to be dimeric in the solid state. Solution molecular weight and spectroscopic studies in aromatic hydrocarbon solvents uncovered a dissociative process involving either monomer–dimer equilibrium or solvent dissociation. Treatment of cyclohexanone phenylimine with lithium diisopropylamide in hydrocarbon solution afforded the corresponding lithiated derivative as the diisopropylamine solvate **2**. An X-ray crystallographic structure determination showed **2** to exist as a dimer with significant disorder in the cyclohexenyl and phenyl moieties. Lithium–carbon contacts of the η^3-azaallyl type were not observed. ^{6}Li and ^{13}C NMR studies showed **2** to exist as a 2:1 mixture of two rapidly equilibrating forms. By titration of the corresponding solvent-free anion ($\mathbf{2}_{\text{solvent-free}}$) with diisopropylamine, the two species were shown to be bis-solvated dimers in close analogy to the solid-state structure. The structures are discussed in light of the stereochemistry of imine alkylation and the syn effect of lithiated imines.

We became interested in the mechanism of the alkylations of metalated Schiff's bases (azaallyllithiums).[1,2] Although on first inspection the C═N—R moiety and C═O ketone carbonyl group appear to be interchangeable, studies by Corey, Enders, Fraser, and others uncovered some notable differences in the alkylation stereoselectivities.[3,4] For example, metalated Schiff's bases derived from conformationally anchored cyclohexanones exhibit axial alkylation selectivities of a significantly greater magnitude than those of the corresponding ketone enolates (eq 1).[5] In the specific case of dimethylhydrazone alkylation, the axial selectivities are sensitive to substituents on the carbanionic carbon. Cyano- and (methylthio)-substituted lithiated hydrazones alkylate with high axial selectivities. However, the corresponding carbomethoxy-substituted derivative exhibits a lower selectivity more characteristic of ketone enolates. Equally intriguing is the propensity of the 3- and 6-substituted lithiated cyclohexanone dimethylhydrazones to alkylate from the *more* hindered face.[1]

---

[1] Collum, D. B.; Kahne, D.; Gut, S. A.; DePue, R. T.; Mohamadi, F.; Wanat, R. A.; Clardy, J.; Van Duyne, G. *J. Am. Chem. Soc.* **1985**, *106*, 4865.

[2] Wanat, R. A.; Collum, D. B. *J. Am. Chem. Soc.* **1985**, *107*, 2078.

[3] Reviews of the chemistry of metalated Schiff's bases: (a) Hickmott, P. W. *Tetrahedron* **1982**, *38*, 1975. (b) Enders, D. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pergamon: New York, 1983. (c) Whitesell, J. K.; Whitesell, M. A. *Synthesis* **1983**, 517. (d) Fraser, R. R. In *Comprehensive Carbanion Chemistry*; Elsevior: New York, 1980.

[4] The nitroso derivatives of 4-*tert*-butylpiperidines exhibit high alkylation stereoselectivities that seem to imply a close mechanistic relationship to lithiated Schiff's base alkylations (cf. ref 3d).

[5] Huff, B. J. L.; Tuller, F. N.; Caine, D. *J. Org. Chem.* **1969**, *34*, 3070. House, H. O.; Umen, M. J. *J. Org. Chem.* **1973**, *38*, 1000. Howe, R.; McQuillin, F. J. *J. Chem. Soc.* **1958**, 1194. Kuwajima, I.; Nakamura, E. *J. Am. Chem. Soc.* **1975**, *97*, 3257. Djerassi, C.; Osiecki, J.; Eisenbraun, E. J. *J. Am. Chem. Soc.* **1961**, *83*, 4433. House, H. O.; Tefertiller, B. A.; Olmstead, H. D. *J. Org. Chem.* **1968**, *33*, 935. Kuehne, M. E. *J. Org. Chem.* **1970**, *35*, 171. Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1982**, *104*, 1025.

0002-7863/86/1508-3415$01.50/0