temperature, the solvent was removed, and the product was partitioned between CH_2Cl_2 and an aqueous solution of saturated $NaHCO_3$. The layers were separated, and the aqueous layer was washed with CH_2Cl_2 (5 mL). All organic layers were washed with brine and dried through Na_2SO_4. The product was placed on a Florisil column (2 × 10 cm) and eluted with 30% Et_2O/PE: 0–50 mL, nil; 50–250 mL, 395 mg (49% yield based on benzocyclobutenone) of **27** as a white solid, which was recrystallized from PE, mp 83.5–84.5 °C [IR (KBr) 2950 (m), 1680 (s), 1250 (s), 1235 (m) 1155 (m), 1128 (s), 1080 (s), 1049 (m), 985 (m), 917 (m), 750 (m); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.54 (str d, J = 7 H, 1 H), 7.37–7.16 (m, 3 H), 6.04 (d, J = 1.5 Hz, 1 H), 5.08 (d, J = 6.1 Hz, 1 H), 3.96 (d of d, J = 1.6, 6.1 Hz, 1 H), 3.49 (s, 3 H), 3.38 (s, 3 H), 3.37 (s, 3 H), 3.30 (s, 3 H), 2.50 (s, 3 H); exact mass calcd for $C_{18}H_{22}O_5$ m/e 318.1461, obsd 318.1504]. Anal. Calcd for $C_{18}H_{22}O_5$ C, 67.91; H, 6.97. Found: C, 67.51; H, 7.00.

Elution was continued as follows: 250–750 mL, 218 mg (27% yield based on benzocyclobutenone) of **26** as a yellow solid, which was recrystallized from Et_2O/PE, mp 110–112.5 °C [IR (KBr) 3450 (s, br), 2940 (m), 1610 (m), 1560 (s), 1420 (m), 1296 (m), 1275 (m), 1243 (s), 1140 (s), 1095 (s), 915 (m), 748 (m); ^1H NMR (C_6D_6, 200 MHz) 7.49–7.45 (m, 1 H), 7.04–7.00 (m, 3 H), 6.07 (d of d, J = 10.3, 1.8 Hz, 1 H), 5.63 (d, J = 10.3 Hz, 1 H), 4.94 (d, J = 1.8 Hz, 1 H), 3.50 (s, 3 H), 3.28 (s, 3 H), 3.06 (s, 3 H). 2.71 (s, 3 H), 2.46 (s, 2 H); exact mass calcd for $C_{18}H_{22}O_5$, m/e 318.1461, obsd 318.1483].

1,4-Dimethoxyspiro[anthracene-9(10*H*),2′-[1,3]dithiolan]-10-one (29). A solution of 3,3,6,6-tetramethoxy-1-bromo-1,4-cyclohexadiene (279 mg, 1.0 mmol) in dry THF (6 mL), maintained under argon atmosphere, was treated with a 1.54 M solution (0.65 mL, 1.0 mmol) of *n*-BuLi in hexane at −65 °C. After 4 min, this mixture was treated with a solution of **28** (229 mg, 1.1 mmol) in dry THF (1.0 mL) at a rate to maintain the reaction temperature below −60 °C. After being stirred for 30 min at −65 °C, the red reaction mixture was warmed to room temperature and heated to reflux for 3 h. The cooled reaction mixture was quenched with CH_3OH (2 mL) and concentrated in vacuo. The residue was partitioned between water (10 mL) and CH_2Cl_2 (4 × 10 mL). The combined organic layers were dried through anhydrous $CaSO_4$ and concentrated in vacuo to yield 409 mg of a light orange foam as a mixture of **29** and 1,4-dimethoxy-9,10-anthraquinone. Pure **29** was obtained via preparative TLC with Et_2O as eluant, followed by recrystallization from Et_2O/PE to yield light orange crystals: mp 144–146 °C: IR (KBr) 3020 (m), 1670 (s), 1590 (m), 1495 (m), 1330 (m), 1260 (s), 1060 (m), 970 (m), 735 (m); ^1H NMR ($CDCl_3$, 60 MHz) δ 8.20–7.95 (m, 2 H), 7.70–7.20 (m, 2 H), 7.0 (center of AB, $\Delta\nu$ = 15.6 Hz, J = 10 Hz, 2 H), 3.94 and 3.90 (overlapping s, 10 H); exact mass calcd for $C_{18}H_{16}O_3S_2$, m/e 344.0541, obsd 344.0549.

The yield of the annelation process was determined by hydrolysis of **29** to the 1,4-dimethoxy-9,10-anthraquinone. The remainder of the crude orange foam and the pure **29** was dissolved in acetone/water (25 mL:5 mL) and treated with 543 mg of mercuric chloride. After being refluxed for 3 h, the mixture was cooled and filtered. The filtrate was concentrated in vacuo, and the residue was partitioned between water (10 mL) and CH_2Cl_2 (4 × 5 mL). The combined organic layers were washed with 1 M potassium iodide (2 × 50 mL) and dried through anhydrous $CaSO_4$. Concentration in vacuo yielded an orange oil, which was chromatographed on a preparative TLC plate with Et_2O as the eluant. The products from this and the previous plate were combined and crystallized to yield 122 mg (46%) of pure 1,4-dimethoxy-9,10-anthraquinone which was identical with a known sample.[3a]

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Registry No. **1**, 60316-53-2; **2**, 6383-64-8; **3**, 71192-84-2; **8**, 89278-93-3; **9**, 89278-94-4; **10**, 78752-32-6; **11**, 89278-97-7; **12**, 89278-98-8; **13a**, 89278-96-6; **13b**, 89278-95-5; **14a**, 89278-99-9; **14b**, 89279-00-5; **15**, 89279-02-7; **16**, 89302-31-8; **17**, 89279-01-6; **18a**, 89279-03-8; **18c**, 89279-04-9; **19a**, 89302-32-9; **19c**, 89302-34-1; **20a**, 89279-05-0; **20c**, 89279-06-1; **21a** (isomer 1), 89361-39-7; **21a** (isomer 2), 89361-40-0; **21b** (isomer 1), 89362-80-1; **21b** (isomer 2), 89361-41-1; **21c**, 89279-09-4; **22a**, 89279-07-2; **22c**, 89279-08-3; **23**, 89279-10-7; **24**, 89279-11-8; **25**, 3469-06-5; **26**, 89279-13-0; **27**, 89279-14-1; **28**, 79190-97-9; **29**, 89279-12-9; $CH_2(OH)CH(CH_3)OH$, 57-55-6; 3,3,6,6-tetramethoxy-1-bromocyclohexa-1,4-diene, 60316-51-0; 3-bromocyclohex-2-en-1-one 1,2-ethanediyl dithioketal, 81770-76-5; 2-bromocyclohex-2-en-1-one ethylene glycol ketal, 70156-98-8; 1,4-dimethoxy-9,10-anthraquinone, 6119-74-0.

Supplementary Material Available: ^1H NMR data for **13a**, **13b**, **14a**, and **14b**; lanthanide shift studies for **13a**; graphs of chemical shifts vs. concentration of lanthanide shift reagents; and a discussion of lanthanide shift studies (11 pages). Ordering information is given on any current masthead page.

Kinetic and Thermodynamic Study of the Reaction of 2,4,6-Triphenylthiopyrylium Ion with Butylamine and Cyclohexylamine in Dimethyl Sulfoxide

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A kinetic and thermodynamic study of the reaction of the 2,4,6-triphenylthiopyrylium ion (1) with butylamine and cyclohexylamine has been performed in Me_2SO at 25 °C. The reaction involves the initial formation of both the corresponding 2*H*- and 4*H*-thiopyrans, which equilibrate to form only the more stable 2*H* adduct. The kinetic data are consistent with a two-step process wherein the formation of the protonated 2*H*- and 4*H*-thiopyran intermediates is the rate-controlling step. A comparison with the addition reaction of 1 with CH_3O^- shows that the relative stabilities of the 2*H* and 4*H* isomers are strongly affected by the charge of the thiopyran derivative. Equilibrium data indicate that the acidity of the ammonium ion is strongly enhanced by the presence of the thiopyranyl moiety.

In recent years the heteroaromatic pyrylium and thiopyrylium cations have found valuable biological, industrial, and synthetic applications.[1] These ions are also of interest because, in contrast to benzenoid systems, they are in-

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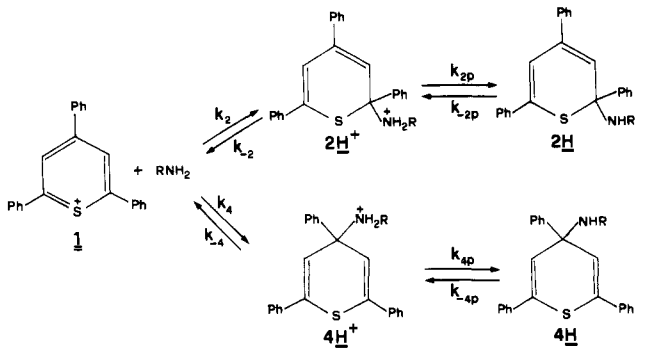
Scheme I



trinsically reactive toward nucleophilic reagents. Quantum mechanical calculations show that the strongly electronegative oxygen atom in pyrylium ion promotes a higher positive charge density on the α position than on the γ position.[2] In thiopyrylium ion the charge distribution seems to be similar on both the α and γ positions.[2] Thus the positional selectivity toward nucleophilic attack on the two cations should be different.[3] There are only limited data for a quantitative assessment of the reactivity of these cations with nucleophiles.[1,3-6]

We wish to report on a detailed kinetic study of the reaction of 2,4,6-triphenylthiopyrylium perchlorate (1) with the neutral nucleophiles butylamine and cyclohexylamine, which have different steric requirements, in Me_2SO at 25 °C.

Results

Study of the reaction of 1 with butylamine and cyclohexylamine in Me_2SO by ^{13}C and ^1H NMR showed the complete conversion of 1 into the corresponding 2*H*-thiopyran adducts.[7] Transient signals indicating formation of the 4*H* isomer were detected by ^1H NMR. A kinetic study carried out in a stopped-flow spectrophotometer by mixing 1 with a large excess of amine/ammonium buffers showed two processes. At 350 nm, where both 1 and the 2*H* adduct absorb, we noted an initial decrease in absorbance followed by a slower increase up to a constant value, indicating complete formation of the 2*H* adduct. The separation between the two processes increased on increasing the amine/ammonium ratio. When the two processes were well separated, 1, whose change was monitored at 410 nm, disappeared completely when the first process was over.

This pattern can be interpreted by Scheme I, in which the fast process is the formation of both the 4*H* and 2*H* adducts, and the slower one is equilibration of the system to the more stable 2*H*-thiopyran.

The k_p and k_{-p} terms refer to proton transfer and are defined as

$$k_p = k_p^{s} + k_p^{am}[am]$$

$$k_{-p} = k_{-p}^{sH}[sH] + k_{-p}^{amH}[amH]$$

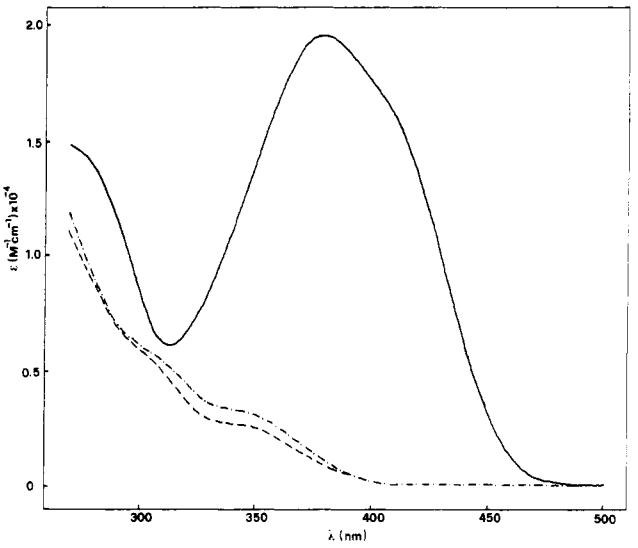


Figure 1. UV-vis spectra of 1 and the corresponding 2*H* adducts with butylamine (– –) and cyclohexylamine (·–·) in Me_2SO.

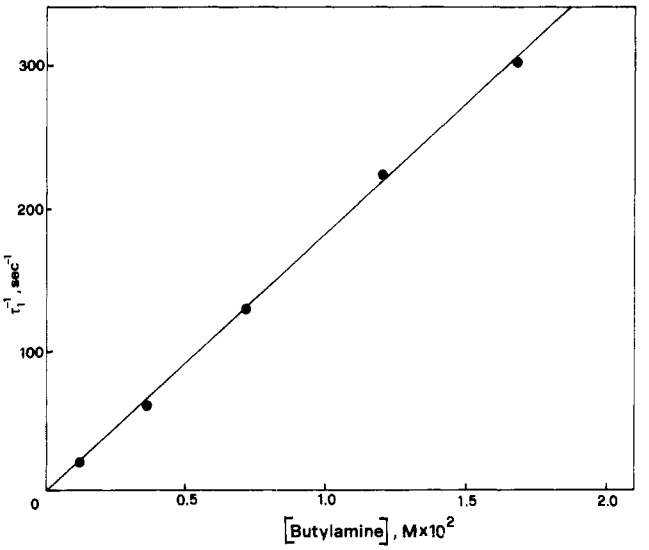


Figure 2. Plot of τ_1^{-1} vs. [butylamine] at [butylammonium] = 0.1 M.

k_p^{s}, k_p^{am} are the rate constants for the deprotonation of the charged adducts by the solvent and amine, respectively, and k_{-p}^{sH}, k_{-p}^{amH} are rate constants for the protonation of neutral adducts by the solvated proton and the conjugate acid of the amine, respectively.

According to this scheme, considering that the equilibrium is completely shifted toward the 2*H* adduct and using the steady-state approximation with respect to $4H^+$ and $2H^+$,[8] the following relationships can be written:[9]

$$1/\tau_1 + 1/\tau_2 = \frac{k_2[am]k_{2p}}{k_{-2} + k_{2p}} + \frac{k_4[am]k_{4p}}{k_{-4} + k_{4p}} + \frac{k_{-4}k_{-4p}}{k_{-4} + k_{4p}} \quad (1)$$

$$1/\tau_1 \times 1/\tau_2 = \frac{k_2[am]k_{2p}}{k_{-2} + k_{2p}} \times \frac{k_{-4}k_{-4p}}{k_{-4} + k_{4p}} \quad (2)$$

τ_1 and τ_2 are the relaxation times of the two processes.

(1) Balaban, A. T.; Dinculescu, A.; Dorofeenko, G. N.; Fischer, G. W.; Koblik, A. V.; Mezheritskii, V. V.; Schorth, W. "Pyrylium Salts"; Academic Press: New York, 1982.
(2) Palmer, M. H.; Findlay, R. H.; Moyes, W.; Gaskell, A. J. *J. Chem. Soc., Perkin Trans. 2* **1975**, 841.
(3) Doddi, G.; Illuminati, G.; Insam, N.; Stegel, F. *J. Org. Chem.* **1982**, *47*, 960.
(4) Brouillard, R.; El Hage Chahine, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 5375.
(5) McClelland, R. A.; Gedge, S. *J. Am. Chem. Soc.* **1980**, *102*, 5838.
(6) Ritchie, C. D.; Kubisty, C.; Ting, G. Y. *J. Am. Chem. Soc.* **1983**, *105*, 279.
(7) Cordischi, V. C.; Doddi, G.; Stegel, F. *J. Org. Chem.* **1982**, *47*, 3496.

(8) The steady-state approximation can be applied if the following relationships hold: $k_4[am] + k_{-4p} << k_{-4} + k_{4p}$ and $k_2[am] + k_{-2p} << k_{-2} + k_{2p}$. The data reported in Table III show that $K_2[am]$ and $K_4[am]$ are $<<1$ (i.e., $k_{-2} >> k_2[am]$ and $k_{-4} >> k_4[am]$) moreover $K_2^{am}[am]/[amH]$ and $K_4^{am}[am]/[amH]$ are $>>1$ (i.e., $k_{2p} >> k_{-2p}$ and $k_{4p} >> k_{-4p}$), under all experimental conditions.
(9) For an exhaustive treatment of the relaxation processes see Bernasconi, C. F. "Relaxation Kinetics"; Academic Press: New York, 1976.

Table I. Kinetic Data of the Reaction of 1 with Butylamine/Butylammonium Buffers in Me_2SO at 25 °C

A. [butylammonium] = 0.1 M; [butylamine], M	$1/\tau_1$, s^{-1}	$1/\tau_2$, s^{-1}	$1/\tau_1 \times 1/\tau_2$, s^{-2}
1.20×10^{-3}	20.7	4.07×10^{-1}	8.42
3.61×10^{-3}	61.5	1.34×10^{-1}	8.24
7.20×10^{-3}	129	6.56×10^{-2}	8.46
1.20×10^{-2}	224	4.05×10^{-2}	9.07
1.68×10^{-2}	300	2.84×10^{-2}	8.52
B. [butylamine] = 3.53×10^{-4} M;[a] [butylammonium], M	**$1/\tau_1$, s^{-1}**	**$1/\tau_2$, s^{-1}**	**$1/\tau_1 + 1/\tau_2$, s^{-1}**
0	6.06	$<<1/\tau_1$	6.06
2.50×10^{-2}	7.81	0.316	8.13
5.00×10^{-2}	8.60	0.517	9.12
7.50×10^{-2}	9.99	0.636	10.63
1.00×10^{-1}	11.67	0.737	12.41
C. [butylamine] = 2.15×10^{-4} M;[a] [butylammonium], M	**$1/\tau_1$, s^{-1}**	**$1/\tau_2$, s^{-1}**	**$1/\tau_1 + 1/\tau_2$, s^{-1}**
0	3.58	$<<1/\tau_1$	3.58
2.50×10^{-2}	6.61	0.365	6.97
5.00×10^{-2}	8.06	0.518	8.58
7.50×10^{-2}	12.28	0.588	12.87
1.00×10^{-1}	14.63	0.627	15.26

[a] μ = 0.1 M, with $KClO_4$ as the compensating electrolyte.

Butylamine A. Study of the Two Relaxation Processes. As already mentioned, when the reaction is carried out with amine/ammonium buffers, with [amine] $\sim 10^{-3}$ to 10^{-2} M and [ammonium] = 0.1 M, the complete fast disappearance of 1 is observed and the condition $1/\tau_1 >> 1/\tau_2$ is fulfilled (see Table IA). Under this condition the following approximate expression of $1/\tau_1$ holds:

$$1/\tau_1 = \frac{k_2[\mathrm{am}]k_{2p}}{k_{-2} + k_{2p}} + \frac{k_4[\mathrm{am}]k_{4p}}{k_{-4} + k_{4p}} \qquad (3)$$

A plot of $1/\tau_1$ vs. [amine] is linear with intercept 0 (Figure 2). This result indicates that $k_{2p} >> k_{-2}$ and $k_{4p} >> k_{-4}$, and eq 3 reduces to $1/\tau_1 = (k_2 + k_4)[\mathrm{am}]$, from which $(k_2 + k_4)$ is the slope of Figure 2. Therefore the rate-controlling step for the butylamine reaction is nucleophilic attack of the amine to yield the charged thiopyrans.

The product $(1/\tau_1) \times (1/\tau_2)$ does not change with the amine concentration within experimental error (Table IA). This result indicates that for this reaction

$$k_{4p}^{am}[\mathrm{am}] >> k_{4p}^{s}, k_{-4p}^{amH}[\mathrm{amH}] >> k_{-4p}^{sH}[\mathrm{sH}]$$

and eq 2 reduces to:

$$1/\tau_1 \times 1/\tau_2 = k_2 \frac{k_{-4}k_{-4p}^{amH}[\mathrm{amH}]}{k_{4p}^{am}} \qquad (4)$$

When the reaction is carried out with buffers having a lower [amine]/[ammonium] ratio (Table IB, IC), the more general eq 1 must be considered. However, since $k_{2p} >> k_{-2}$, $k_{4p} >> k_{-4}$, $k_{4p}^{am}[\mathrm{am}] >> k_{4p}^{s}$, and $k_{-4p}^{amH}[\mathrm{amH}] >> k_{-4p}^{sH}[\mathrm{sH}]$, the following simplified equation holds:

$$1/\tau_1 + 1/\tau_2 = (k_2 + k_4)[\mathrm{am}] + \frac{k_{-4}k_{-4p}^{amH}[\mathrm{amH}]}{k_{4p}^{am}[\mathrm{am}]} \qquad (5)$$

Actually a plot of $(1/\tau_1 + 1/\tau_2)$ vs. [butylammonium], with [butylamine] constant, is linear with a slope that decreases if the experiment is performed at slightly higher amine concentration (Figure 3). The values of the products of the slope by the corresponding amine concentrations

$$\frac{k_{-4}k_{-4p}^{amH}}{k_{4p}^{am}}$$

are coincident within experimental error, while the ratios between the intercepts and the corresponding amine concentrations coincide with the $(k_2 + k_4)$ term previously obtained. The

$$\frac{k_{-4}k_{-4p}^{amH}}{k_{4p}^{am}}$$

term so obtained can be used to evaluate k_2 by eq 4, and consequently also the value of k_4. The product

$$k_4 \frac{k_{4p}^{am}}{k_{-4}k_{-4p}^{amH}}$$

gives the equilibrium constant (K_{4T}) for the following reaction:

$$1 + 2\ \mathrm{amine} \overset{K_{4T}}{\rightleftharpoons} 4H + \mathrm{ammonium}$$

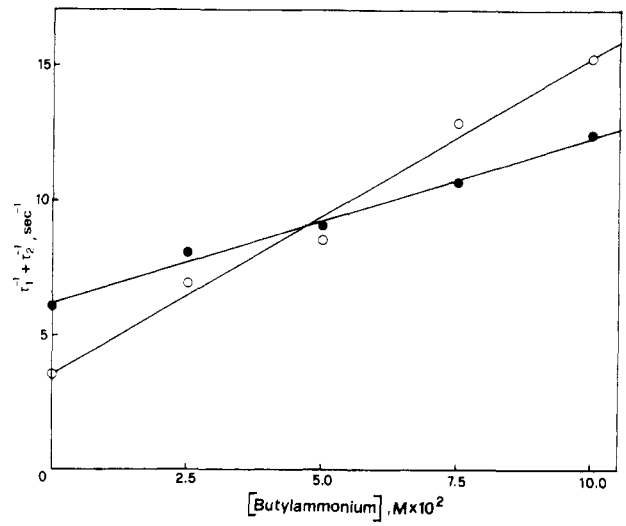


Figure 3. Plot of $\tau_1^{-1} + \tau_2^{-1}$ vs. [butylammonium] at [butylamine] = 2.15×10^{-4} M (○) and [butylamine] = 3.53×10^{-4} M (●).

Table II. pH Jump Experiments with the (Butylamino)thiopyran Adducts and *p*-Toluenesulfonic Acid[a]

2*H* adduct		4*H* adduct	
[TsOH], M	k_{obsd2}, s^{-1}	[TsOH], M	k_{obsd4}, s^{-1}
1.75×10^{-3}	539	1.75×10^{-3}	629
3.73×10^{-3}	544	3.73×10^{-3}	677
9.67×10^{-3}	550	5.72×10^{-3}	682

[a] μ = 0.1 M, with $KClO_4$ as the compensating electrolyte.

B. pH Jump Experiments. These experiments were performed to evaluate k_{-2} and k_{-4} (Table II) by study of the decomposition of the adducts into the reactants in acidic media.

Butylamine and 1 were premixed to assure complete formation of the 2*H* adduct. This solution was subjected to a pH jump by mixing it with a Me_2SO solution of *p*-toluenesulfonic acid. The reaction was studied in the stopped-flow spectrophotometer by monitoring the ap-

Table III. Kinetic and Thermodynamic Constants for the Reaction of 1 with Butylamine and Cyclohexylamine in Me_2SO at 25 °C[a]

	butylamine (K_a = 1.3 × 10^{-11} M)	cyclohexylamine (K_a = 1.3 × 10^{-11} M)
k_2, M^{-1} s^{-1} [b]	3.7 × 10^3	7.0 × 10^2
k_{-2}, s^{-1}	5.4 × 10^2	>7 × 10^2 [c]
K_2, M^{-1}	7	
K_{2T}, M^{-1}	1.6 × 10^7	4.8 × 10^6
K_2^{am}	2.3 × 10^6	
K_{2a}, M	3 × 10^{-5}	
k_4, M^{-1} s^{-1}	1.4 × 10^4	2.7 × 10^3
k_{-4}, s^{-1}	6.5 × 10^2	>7 × 10^2 [c]
K_4, M^{-1}	22	
K_{4T}, M^{-1}	6 × 10^5	2.5 × 10^4
K_4^{am}	2.9 × 10^4	
K_{4a}, M	4 × 10^{-7}	

[a] μ = 0.1 M. [b] Uncorrected for the statistical factor. [c] Upper limit by the stopped-flow method.

pearance of 1 at 410 nm. As shown in Table II the reaction rate is independent of the concentration of the strong acid within experimental error. This result indicates that under this condition all the 2*H*-thiopyran is rapidly and completely converted into the $2H^+$ adduct, and that the rate-controlling step is detachment of the butylamino group from this compound to yield 1. Therefore k_{obsd2} coincides with k_{-2}.

We have evaluated k_{-4} by performing the pH jump immediately after the solution of 1 and amine was prepared, before any significant equilibration between the two adducts had occurred. Monitoring the reaction at 410 nm revealed only one relaxation process, indicating that the decompositions of the two neutral thiopyrans to yield 1 occur at similar rates. The observed relaxation curve is given by the summation of the two exponential functions related to the decomposition process of each adduct:[10]

$$\Delta OD = \Delta OD_2^\circ \exp(-k_{obsd2}t) + \Delta OD_4^\circ \exp(-k_{obsd4}t) \quad (6)$$

ΔOD_2° and ΔOD_4° are the amplitudes related to the decomposition of the 2*H* and 4*H* adducts. These terms are given by the following expressions:

$$\Delta OD_2^\circ = \Delta OD^\circ k_2/(k_2 + k_4)$$

$$\Delta OD_4^\circ = \Delta OD^\circ k_4/(k_2 + k_4)$$

ΔOD° is the amplitude of the entire process. Rearranging eq 6 affords:

$$\exp(-k_{obsd4}t) = \frac{\Delta OD - \Delta OD_2^\circ \exp(-k_{obsd2}t)}{\Delta OD_4^\circ} \quad (7)$$

Since $k_{obsd2} = k_{-2}$, the k_{obsd4} term can be obtained. As shown in Table II, k_{obsd4} is also independent of the concentration of the acid within experimental error, hence $k_{obsd4} = k_{-4}$. The kinetic and thermodynamic parameters for the butylamine reaction are given in Table III.

Although K_{2T} was measured directly, the values of the reported equilibrium constants were obtained from either kinetic data or a combination of kinetic and thermodynamic data. These parameters are defined as follows: $K_2 = k_2/k_{-2}$, $K_4 = k_4/k_{-4}$ (equilibrium constants for the formation of $2H^+$ and $4H^+$ adducts, respectively); K_{2T} (equilibrium constant for the reaction 1 + 2 amine $\rightleftharpoons$ 2*H* + ammonium); K_{4T} is defined similarly (see text for its determination); $K_2^{am} = K_{2T}/K_2$ (equilibrium constant for the reaction $2H^+$ + amine $\rightleftharpoons$ 2*H* + ammonium); and $K_4^{am} = K_{4T}/K_4$, $K_{2a} = K_2^{am}K_a$, $K_{4a} = K_4^{am}K_a$ (acid dissociation constants of $2H^+$ and $4H^+$ adducts, respectively).

Cyclohexylamine. The kinetic and thermodynamic parameters for the cyclohexylamine reaction were determined in the same way as those for the butylamine reaction (Table III).

At variance with what was observed for the sterically less hindered butylamine, the detachment of the cyclohexylamino group was too fast to be determined by the stopped-flow technique. An estimate of k_{-2} and k_{-4} can be made on the assumption that the effect of the thiopyranyl group on the acidity of the ammonium ion, as indicated by K_2^{am} and K_4^{am}, is the same for both amines. From the relationships $k_{-2} = k_2K_2^{am}/K_{2T}$ and $k_{-4} = k_4K_4^{am}/K_{4T}$ we estimate that k_{-2} and k_{-4} for this reaction should not exceed the corresponding constants for the butylamine reaction by more than one order of magnitude.

Discussion

As shown in Table III butylamine has a higher rate of reaction with 1 than cyclohexylamine (k_2, k_4) in spite of their identical basicity. The same behavior has been observed in the reaction of 2,4,6-triphenylpyrylium ion with amines in methanol[10] and can be ascribed to some steric interaction with the phenyl group bound to the reaction center. The decrease in reactivity for the cyclohexylamine reaction is similar at the C-2 and C-4 positions in agreement with the similar steric environment at these sites.

The rate constants for expulsion of cyclohexylamine (k_{-2}, k_{-4}) are greater than those for butylamine, presumably a consequence of steric strain in the charged adducts that is relieved by the departure of the amine. The contribution of steric factors to the amino group detachment step has been established in addition reactions of amines.[11]

With butylamine (and probably also with cyclohexylamine) the $4H^+$ adduct is both the kinetically and thermodynamically favored product with respect to the $2H^+$ isomer. This behavior differs from that observed for the reaction of 1 with CH_3O^- in methanol, in which the 4*H*-thiopyran is the kinetically controlled product, whereas the 2*H* isomer is the thermodynamically favored one.[3] Although the absolute values of kinetic and equilibrium constants are greatly affected by the change in solvent, we expect that the relative reactivities of the α and γ positions with a nucleophile should not be strongly solvent dependent,[12] and a comparison between the two reactions should be meaningful.

The presence of a more delocalized π system can account for the higher stability of 2-methoxy-2*H*-thiopyran compared with the 4*H* isomer. On the other hand, for the amine reaction, the location of a positively charged atom near the electron-withdrawing sulfur atom overwhelms this stabilizing effect, and the $4H^+$ adduct is more stable than the $2H^+$. The ratios k_{-4}/k_{-2} for the methoxide reaction (estimated >14) and the amine reaction (~1) reflect the difference between the two reactions.

Although the rate of the methoxide reaction is ~100× that of the amine reaction,[13] the selectivities of the two are

(10) Doddi, G.; Illuminati, G.; Mecozzi, M.; Nunziante, P. *J. Org. Chem.* **1983**, *48*, 5268.

(11) (a) Bernasconi, C. F.; Muller, M. C.; Schmid, P. *J. Org. Chem.* **1979**, *44*, 3189. (b) Bernasconi, C. F.; Carrè, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 2698.

(12) Ritchie has recently shown that the relative reactivity of different organic cations toward nucleophiles is not affected by changing the solvent from water to Me_2SO: Ritchie, C. D.; Van Verth, J. E.; Virtanen, P. O. I. *J. Am. Chem. Soc.* **1982**, *104*, 3491.

(13) The reactivity of the methoxide ion should be greatly enhanced if the reaction is performed in Me_2SO.[12] The relative reactivity of methoxide ion and butylamine toward 1 can be roughly estimated by the reaction of the 2,4,6-triphenylpyrylium ion in methanol.[3,10] A value ~10^3 is calculated for the $k_{MeO}/k_{butylamine}$ ratio.

comparable (k_4/k_2 = 1.4 and 3.8, respectively). This feature, which is observed for many reactions of organic cations with nucleophiles,[14] does not necessarily imply a similar location of the transition state along the reaction coordinate. Thus, in the highly exothermic methoxide ion reaction the k_4/k_2 ratio should reflect long-range interactions between nucleophile and substrate.[3] In contrast, in the amine reaction the relative reactivities of the 2 and 4 positions should be more affected by the stabilities of the reaction products.

If the stability of the neutral amino adducts with respect to the substrate is considered (K_{2T} and K_{4T}), the 2*H* adduct should be the favored product. This feature is also observed for the neutral methoxide adducts, but the cause for this behavior is to be found in the higher acidity of $2H^+$ with respect to $4H^+$. Clearly this feature is related to the proximity of the electron-withdrawing sulfur atom.[15]

Noteworthy is the dramatic difference in acidity between the charged adducts and the parent amine as measured by K_2^{am} and K_4^{am}. This difference indicates that the thiopyran moiety is a strong electron-withdrawing group because changing the amino group from primary (reagent) to secondary (product) can account only for 1 pK_a unit.[16]

As mentioned above, in the reaction of butylamine the rate-determining step is the nucleophilic attack of the amine:

$$k_{-2} < k_{2p}^{am}[am] + k_{2p}^{s} \text{ and } k_{-4} < k_{4p}^{am}[am] + k_{-4p}^{s}$$

An increase in steric hindrance of the amine should increase the k_{-4} and k_{-2} terms[11] and decrease the k_{4p} and k_{2p} constants.[11b,c,17] With cyclohexylamine an increase in k_{-4} and k_{-2} is observed, but the hypothetical reduction of parameters k_{4p} and k_{2p} does not allow the relationships $k_{-4} > k_{4p}^{am}[am] + k_{4p}^{s}$ and $k_{-2} > k_{2p}^{am}[am] + k_{2p}^{s}$ to be verified. This behavior differs from that observed for the trinitrobenzene reaction in Me_2SO, wherein the deprotonation of ammonium ion adduct is the slow process with both secondary amines and the less hindered primary one.[17]

A behavior similar to the reaction of 1 has been recently observed for the reaction of 2,4,6-triphenylpyrylium ion with amines in methanol.[10] Also for this process the rate-determining step is nucleophilic attack by both butylamine and cyclohexylamine, whereas with cyclic secondary amines, such as piperidine, pyrrolidine, and morpholine, proton transfer seems to be the rate-controlling step.

It will be interesting to extend this study to the sterically more hindered secondary amines in order to determine whether the increase of steric crowding about the nitrogen atom in the adduct can reduce the rate of such a thermodynamically favored proton-transfer process, so that it may become the rate-controlling step of the reaction.

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

(15) The pK_a values of aliphatic amines having a β sulfur atom are 2 pK_a units lower than the unsubstituted ones: Gonick, E.; Fernelius, W. C.; Douglas, B. E. *J. Am. Chem. Soc.* **1954**, *76*, 4671. Hall, Jr., H. K. *Ibid.* **1956**, *78*, 2570.

(16) Kolthoff, I. M.; Chantooni, Jr., M. K.; Bhowmik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23.

(17) Crampton, M. R.; Gibson, B. *J. Chem. Soc., Perkin Trans. 2* **1981**, 533.

Experimental Section

Materials. 2,4,6-Triphenylthiopyrylium perchlorate was available from our previous work.[3]

Me_2SO (Carlo Erba R.P.E.) was dried over sodium hydride, fractionally distilled under reduced pressure, keeping the temperature of the pot at 40 °C, and stored under argon. The amines were refluxed over sodium for 2 h and distilled under argon.

Butylammonium and cyclohexylammonium perchlorates were prepared from the respective amines and aqueous 70% perchloric acid. After removal of the water, the salts were purified by solution in dioxane and reprecipitation with dry ether. Piperidino and pyrrolidino perchlorates were prepared in the same way and recrystallized twice from benzene–acetone (3:1) and (4:1), respectively. Tetraethylammonium perchlorate was prepared by neutralization of an aqueous solution of tetraethylammonium hydroxide with aqueous perchloric acid and recrystallized from water or acetone. All the salts were dried by warming at 80 °C in vacuum. Caution must be used in the handling of these potential explosive salts.

Spectra. The UV–vis spectra of the substrate and the corresponding 2*H* adducts with butylamine and cyclohexylamine (Figure 1) were recorded on a Cary 219 spectrophotometer. The spectrum of a solution of 1 recorded after one day did not show appreciable changes.

Rate Measurements. The kinetics were carried out on a Durrum 110 stopped-flow spectrophotometer at 25 °C under pseudo-first-order conditions, [1] $\sim 10^{-5}$ M. Ionic strength was kept at 0.1 M by addition of appropriate amounts of $KClO_4$. The reaction solutions were freshly prepared and handled under argon.

Equilibrium Measurements. All the determinations were carried out at 25 °C on a Cary 219 spectrophotometer. The pK_a values of butylamine (10.9) and cyclohexylamine (10.9) in Me_2SO at ionic strength 0.1 M were determined on a set of amine/ammonium buffers by measuring the absorbance of the blue form of bromthymol blue at 633 nm. The pK_a of the indicator (10.5) was determined using the pK_a values at μ = 0.1 M of piperidine (10.6)[18] and pyrrolidine (10.8).[18] The ionic strength was maintained at 0.1 M with tetraethylammonium perchlorate.

The equilibrium constant K_{2T} of the equilibrium 1 + 2 amine $\rightleftharpoons$ 2*H* + ammonium (Scheme I) was obtained by measuring the residual absorbance of 1 at 410 nm, where only it absorbs, after equilibration of a mixture of 1 ($\sim 10^{-4}$ M), amine ($\sim 10^{-3}$ M), and ammonium perchlorate (0.1 M) in a Teflon-stoppered 10-cm quartz cell. The values of K_{2T} were calculated according to the following equation:

$$K_{2T} = \frac{([1]_0 - [1]_{eq})\,[amH]}{[1]_{eq}\,[am]_{eq}^2}$$

where

$$[am]_{eq} = [am]_0 - 2([1]_0 - [1]_{eq})$$

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Registry No. 1, 18342-83-1; 1 (perchlorate), 2930-37-2; **2*H*** (R = Bu), 82338-23-6; **2*H*** (R = cyclohexyl), 89232-72-4; **2*H*$^+$** (R = Bu), 89255-67-4; **2*H*$^+$** (R = cyclohexyl), 89232-73-5; **4*H*** (R = Bu), 89232-70-2; **4*H*** (R = cyclohexyl), 89232-74-6; **4*H*$^+$** (R = Bu), 89232-71-3; **4*H*$^+$** (R = cyclohexyl), 89232-75-7; cyclohexylamine, 108-91-8; butylamine, 109-73-9.

(18) Courtot-Coupez, J.; Le Demezet, M. *Bull. Soc. Chim. Fr.* **1969**, 1033.