Ozonolysis of 9 in Trifluoroethanol/Methylene Chloride. A 1:1 trifluoroethanol/methylene chloride solution (20 mL) of 9 (200 mg) was treated with 2 equiv of ozone at 0 °C. After workup, the products were separated by column chromatography on silica gel. Elution with benzene gave trifluoroethyl benzoate (13): oil; IR 1740, 1295, 1255, 1165, 705 cm^{-1}; ^{1}H NMR (CCl_4) δ 4.67 (q, J = 8 Hz, 2 H), 7.3–7.7 (m, 3 H), 8.0–8.1 (m, 2 H). Elution with 1:50 ether/benzene gave 1-phenyl-2-acetoxyacenaphthylene ozonide (11, 116 mg, 51%): mp 137–138 °C (methanol, 50 °C); ^{1}H NMR ($CDCl_3$) δ 6.99 (d, J = 6 Hz, 1 H), 7.2–8.1 (m, 14 H), 8.19 (d, J = 6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 112.09 (1 C), 119.43 (1 C), 119.54 (1 C), 125.00–134.21 (21 C), 161.74 (1 C); IR 1760 cm^{-1}. Anal. Calcd for $C_{25}H_{16}O_5$: C, 75.75; H, 4.07. Found: C, 75.74; H, 3.89. Elution with ether gave 3-phenyl-3-hydroperoxynaphtho[1,8-*cd*]pyran-1(3*H*)-one (12) (71 mg, 42%): mp 183–185 °C (ethyl acetate/hexane); IR 3270, 1690, 1300 cm^{-1}; CIMS (isobutane) *m*/*e* 293 ($M^+ + 1$); ^{1}H NMR (CD_3COCD_3) δ 7.4–8.5 (m, 11 H), 11.72 (s, 1 H); ^{13}C NMR (CD_3COCD_3) δ 110.15 (1 C), 121.08 (1 C), 127.27–130.39 (12 C), 132.83 (1 C), 134.88 (1 C), 140.45 (1 C), 163.33 (1 C). Anal. Calcd for $C_{18}H_{12}O_4$; C, 73.97; H, 4.14. Found: C, 73.90; H, 3.96.

Ozonolysis of 9 in Methanol/Methylene Chloride. A 1:1 methanol/methylene chloride solution (20 mL) of 9 (300 mg) was treated with 2 equiv of ozone at −70 °C. After workup, the products were separated by column chromatography on silica gel. Elution with benzene initially gave 15 mg (5%) of 9. Continued elution gave the ozonide 11 (240 mg, 70%). Elution with 1:50 ether/benzene gave 3-phenyl-3-methoxynaphtho[1,8-*cd*]pyran-1(3*H*)-one (14) (19 mg, 8%): oil; IR 1710, 1275, 705 cm^{-1}; ^{1}H NMR (CCl_4) δ 3.91 (s, 3 H), 7.2–8.1 (m, 11 H). Anal. Calcd for $C_{19}H_{14}O_3$: C, 83.21; H, 5.11. Found: C, 83.50; H, 5.08. Elution with 1:5 ether/benzene gave 12 (22 mg, 9%).

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Registry No. 1a, 131080-08-5; 1b, 131080-09-6; 4, 2881-31-4; 5a, 131080-11-0; 5b, 131080-13-2; 6a, 131080-12-1; 6b, 131080-14-3; 7, 131080-15-4; 8a, 65-85-0; 9, 131080-10-9; 11, 131080-16-5; 12, 131080-17-6; 13, 1579-72-2; 14, 22422-09-9; 2-phenyl-1-indanone, 16619-12-8.

Isomerization Equilibria of 2*H*- and 4*H*-Thiopyrans

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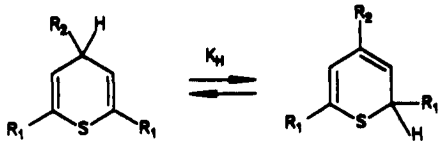
2*H*- and 4*H*-thiopyrans have been the subject of numerous studies;[1] nevertheless, little is known about their relative thermodynamic stability, especially from a quantitative standpoint.[2-4]

Recently we provided the first quantitative data on the reversible isomerization of a number of 4-methoxy-4*H*-thiopyrans into the corresponding 2-methoxy-2*H* isomers.[5-7] However these data, owing to possible geminal interactions between the methoxy group and the ring sulfur atom, might depend only to a limited extent on the intrinsic stability of the heterocyclic systems. This prompted us to investigate a number of isomerization equilibria, shown in Scheme I, in which the migration of hydrogen, instead of the methoxy group, is involved. The results of such an investigation are reported herein.

Scheme I



1a – 6a

1b – 6b

1 R₁=Ph, R₂=H
2 R₁=Ph, R₂=Ph
3 R₁=Ph, R₂=Bu^t
4 R₁=Bu^t, R₂=H
5 R₁=Bu^t, R₂=Ph
6 R₁=Bu^t, R₂=Bu^t

Table I. Equilibrium Constants[a] for the Isomerization of 4*H*-Thiopyrans into 2*H*-Thiopyrans

thiopyran	K_H[b]	K_{OMe}[c]
1	0.16[d]	0.52[e]
2	7.1[d]	33[e]
3	0.24[d]	0.80[e]
4	1.8[f]	3.2[g]
5	36[f]	94[h]
6	4.2[f]	4.2[g]

[a] Corrected for statistical factors. [b] In CD_3CN. [c] At 25 °C in MeOH. K_{OMe} values have been calculated from equilibrium data referring to the attachment of MeO^- to the corresponding thiopyrylium cations. [d] At 25 °C. [e] Reference 6. [f] At 100 °C. [g] Reference 7. [h] Reference 5.

Results and Discussion

Isomerization of the thiopyran mixtures (for their preparation and composition, see the Experimental Section) was carried out in CD_3CN in the presence of the corresponding thiopyrylium cation. This catalyzes the isomerization by a hydride transfer mechanism,[4] as shown in Scheme II. However, despite the catalyst, the equilibration processes were very slow. The 2,6-diphenyl-substituted thiopyrans 1–3 required from ca. 5 to 15 days to equilibrate at 25 °C, whereas the 2,6-di-*tert*-butyl-substituted thiopyrans 4–6 could be equilibrated, in a reasonable elapse of time (up to ca. 10 days), only at 100 °C. In each of the two series the order of the rate of equilibration as a function of the substituent R^2 was H > Ph > *t*-Bu. This pattern, which suggests the operation of steric effects, can be easily explained by the mechanism depicted in Scheme II. Indeed in order for the hydride transfer to occur the thiopyran and the thiopyrylium ion must closely approach each other, the approach becoming more difficult as the steric hindrance of the substituents increases.

In Table I are reported the statistically corrected equilibrium constants for the isomerization process K_H. These were evaluated dividing the final ratios of the isomers [2*H*]/[4*H*] by the factor 4 in the case of the thiopyrans 1 and 4, and by the factor 2 in all the other cases. Indeed one has to consider that the 4*H*-thiopyrans 1a and 4a have a 2-fold axis of symmetry passing through the

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(1) Kuthan, J. *Adv. Heterocycl. Chem.* **1983**, *34*, 145.

(2) It has been reported that 3,5-dimethyl-2,6-diphenyl-4*H*-thiopyran[3] and 2,4,6-triphenyl-4*H*-thiopyran[4] isomerize to the corresponding 2*H*-thiopyran.

(3) Kharchenko, V. G.; Kleimenova, V. I.; Yakoreva, A. R. *Khim. Geterotsikl. Soedin.* **1970**, 900.

(4) Øestensen, E. T.; Abdallah, A. A.; Skaare, S. H.; Mishrikey, M. M. *Acta Chem. Scand.* **1977**, *B31*, 496.

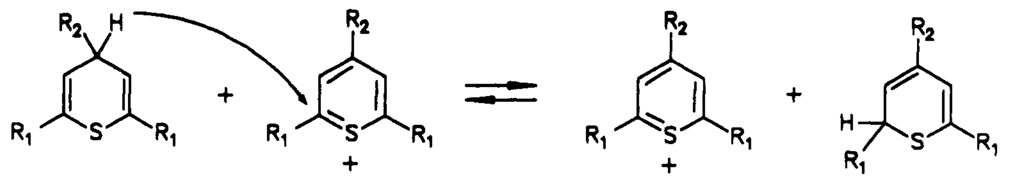
(5) Di Vona, M. L.; Doddi, G.; Ercolani, G.; Illuminati, G. *J. Am. Chem. Soc.* **1986**, *108*, 3409.

(6) Doddi, G.; Ercolani, G.; Nunziante, P. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1427.

(7) Doddi, G.; Ercolani, G. *J. Chem. Soc., Perkin Trans. 2* **1989**, 1393.

0022-3263/91/1956-1674$02.50/0

Scheme II



atoms S and C-4, and that all of the 2*H*-thiopyrans are formed as racemic modifications.[8] For comparative purposes the corrected equilibrium constants K_{OMe} referring to the isomerization of 2,6-R^1-4-R^2-4-methoxy-4*H*-thiopyrans into the corresponding 2-methoxy-2*H*-thiopyrans, are also reported.

Let us evaluate the effect of the substituents Ph and *t*-Bu on the stability of the thiopyrans. If one makes the reasonable assumption that the π energy of the 4*H*-thiopyrans is not affected by the nature of R^2, then the effect of R^2 on the stability of the 2*H*-thiopyrans can be evaluated. In fact if the π energy of **1a** is assumed to coincide with that of **2a**, then the $\Delta\Delta G°$ at 25 °C for the substitution of H with Ph in the 4-position of the 2*H*-thiopyran amounts to −2.2 kcal/mol. This value is obtained by eq 1, where $K_H{}^H$ and $K_H{}^{Ph}$ stand for the K_H values relative to 1 and 2, respectively.

$$\Delta\Delta G° = -RT \ln \frac{K_H{}^{Ph}}{K_H{}^{H}} \qquad (1)$$

From the K_H values for the thiopyrans 4 and 5, the $\Delta\Delta G°$ calculated at 100 °C by eq 1 amounts to −2.2 kcal/mol. The two values, which, considering the different temperature, are very similar, provide a measure of the resonance stabilization of the 2*H*-thiopyran brought about by the 4-phenyl group. Analogous calculations on the methoxy-substituted thiopyrans had been made in a previous work, yielding a $\Delta\Delta G°$ value of ca. −2.4 kcal/mol. However, the effect had been misinterpreted in that it had been erroneously attributed to a destabilizing geminal interaction of the groups OMe and Ph.[6]

When analogous calculations are made for the substitution of H with *t*-Bu, $\Delta\Delta G°$ values of −0.2 kcal/mol at 25 °C and −0.6 kcal/mol at 100 °C are obtained which indicate a small interaction, if any, of the 4-*tert*-butyl group with the π system of the 2*H*-thiopyran. Owing to the smallness of this interaction, one can assume that the effect of the *tert*-butyl groups on the energy of **6a** and **6b** is comparable, therefore the K_H constant for the thiopyans 6 should reflect the intrinsic stabilities of the 2*H*- and 4*H*-thiopyrans. The conclusion is that the two heterocyclic systems have very similar stabilities, the free energy difference being less than 1 kcal/mol.

Before comparing the K_H with the corresponding K_{OMe} constants, it should be noted that in the 2-methoxy-2*H*-thiopyrans there is the possibility of a stabilizing geminal O, S interaction. The magnitude of this effect, known either as generalized anomeric effect or negative hyperconjugation, is not however firmly established in the case of second-row substituents.[9,10] Although by inspection of Table I it appears that the K_{OMe} constants are generally higher than the corresponding K_H constants, the difference is remarkably small being in all of the cases less than a factor 5. Admittedly the comparison is not homogeneous because of the different solvent, and, in the case of the thiopyrans 4–6, also the different temperature of reaction. However, the present results seem to exclude a significant stereoelectronic stabilization.

Experimental Section

^1H NMR measurements were carried out in CD_3CN solution on a Bruker WP 80 SY spectrometer. CD_3CN for NMR spectroscopy was from Erba.

The following thiopyrylium perchlorates were prepared according to literature procedures: 2,6-diphenylthiopyrylium,[11] 2,4,6-triphenylthiopyrylium,[12] 2,6-diphenyl-4-*tert*-butylthiopyrylium,[13] 2,6-di-*tert*-butylthiopyrylium,[11] 4-phenyl-2,6-di-*tert*-butylthiopyrylium,[14] 2,4,6-tri-*tert*-butylthiopyrylium.[14]

Preparation of the Mixtures of Thiopyrans. $NaBH_4$ (0.076 g, 2 mmol) was gradually added to a well-stirred solution (or suspension) of the appropriate thiopyrylium perchlorate (2.5 mmol) in methanol (20 mL), maintained at −15 °C. After hydrogen evolution, the solution was evaporated under vacuum and the residue was extracted with *n*-hexane (3 × 10 mL). The extracts were collected, washed with water, dried over anhydrous Na_2SO_4, and evaporated under vacuum. The residue, dissolved in CD_3CN and analyzed by ^1H NMR, was constituted by a mixture of 2*H*- and 4*H*-thiopyrans. The isomer ratios [2*H*]:[4*H*] were as follows: 1 0:100; **2**, 31:69; **3**, 4:96; **4**, 9:91; **5**, 91:9; **6**, 31:69.

When the procedure was repeated with a different $NaBH_4$ specimen, slightly different isomer ratios were obtained.

Isomerization of 2*H*- and 4*H*-Thiopyrans. To the mixture of the thiopyrans dissolved in CD_3CN was added a comparable amount of the parent thiopyrylium salt. The resulting solution was transferred in a NMR tube which was sealed and thermostated at the proper temperature (25 or 100 °C). ^1H NMR measurements were carried out at regular time intervals until constant ratios of the two isomers were attained.

Supplementary Material Available: ^1H NMR data for the thiopyrylium salts and the thiopyrans and ^1H NMR spectra of the mixtures of thiopyrans as obtained from the reduction of the corresponding thiopyrylium salts (8 pages). Ordering information is given on any current masthead page.

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