in CH_3OH (15 mL) a solution of MCPBA (1.0 g, 5 mmol) in methanol was added in 15 min at 22–25 °C. After 1 h at room temperature, the reaction mixture was cooled to 0–10 °C and filtered. The greenish yellow precipitate was washed with cold CH_3OH and dried (0.20 g, 53%); mp 118–120 °C (lit.[18] mp 118.5–119 °C). Anal. Calcd for $C_6H_4N_2O_3$: C, 47.4; H, 2.65; N, 18.4. Found: C, 47.2; H, 2.91; N, 19.2.

Oxidation of *S,S*-Dimethyl-*N*-(*p*-nitrophenyl)sulfilimine (17) to Sulfoximine (21) by Preformed MCPBA Anion. To a stirring solution of MCPBA (1.0 g, 5 mmol) in ethanol (6 mL) at 0 °C a solution of K_2CO_3 (1.8 g, 13 mmol) in water (6 mL) was added. After 20 min at 0 °C, **17** (0.5 g, 2.5 mmol) in ethanol (30 mL) was added in one portion, the cooling bath was then removed, and stirring was continued at room temperature for 1 h. The reaction mixture was concentrated under vacuum (to about 5 mL) and water was added (20 mL) followed by extraction with CH_2Cl_2 (2 × 30 mL). The organic phase was washed successively with concentrated NaCl solution (20 mL), dried over anhydrous $MgSO_4$, and filtered. Evaporation of solvent yielded an orange solid consisting (TLC) largely of sulfoximine (**21**) contaminated with **18** and **19**. Recrystallization from methanol yielded pure **21**; mp 158–160 °C (0.48 g, 90%) (lit.[14] mp 160–162 °C).

Hydrolysis of 17 to 20. A solution of sulfilimine **17** (0.25 g, 1.25 mmol) in 95% C_2H_5OH (10 mL) was stirred with a solution of K_2CO_3 (0.5 g) in water (2 mL) at room temperature for 20 h. The reaction mixture was diluted with H_2O (10 mL), cooled, and filtered. The dried yellow solid (0.13 g, mp 145–147 °C, 75% yield) was identical wiith authentic *p*-nitroaniline (**20**).

MCPBA Oxidation of *p*-Nitroaniline (20). A solution of **20** (1.38 g, 10 mmol) and MCPBA (85%) (2.2 g, 11 mmol) in CH_3OH was stirred at room temperature for 90 min (a yellow precipitate formed after 5 min). The reaction mixture was cooled to ca. 0 °C and filtered. The light brown solid obtained (0.83 g) was mainly **19** with a trace of **20** (TLC). No evidence of **18** was found.

Acknowledgment.[22] This research was supported by Grant CA12227 awarded by the National Cancer Institute, DHEW, Instrument Grant CHE 76-05757 from the National Science Foundation, Grant IN88J from the American Cancer Society, and the Samuel S. Fels Fund.

Registry No. 3, 13150-75-9; **4**, 22236-45-9; **6** ($R^1 = R^2 = CH_3$, R^3 = Cl-*p*-$C_6H_4SO_2$), 61706-01-2; **6** ($R^1 = R^2 = CH_3$, $R^3 = C_6H_5SO_2$), 22236-46-0; **6** ($R^1 = R^2 = CH_3$, $R^3 = O_2N$-*p*-$C_6H_4SO_2$), 61706-02-3; **6** ($R^1 = R^2 = CH_3$, $R^3 = CH_3SO_2$), 70355-69-0; **6** ($R^1 = R^2 = C_6H_5$, R^3 = CH_3-*p*-$C_6H_4SO_2$), 38764-58-8; **6** ($R^1 = R^2 = CH_3$, $R^3 = O_2N$-*p*-$C_6H_4C{=}O$), 3532-29-4; **6** ($R^1 = R^2 = CH_3$, $R^3 = Cl_2CHC{=}O$), 66406-35-7; **6** ($R^1 = R^2 = C_6H_5$, $R^3 = CH_3C{=}O$), 70355-70-3; **6** ($R^1 = R^2 = CH_3$, $R^3 = O_2N$-*p*-C_6H_4), 56158-00-0; **7**, 52259-84-4; **8**, 19871-30-8; **9**, 18922-58-2; **10**, 13553-68-9; **11**, 13150-76-0; **12**, 70355-71-4; **13**, 52259-85-5; **14**, 6026-68-2; **15**, 42397-41-1; **17**, 27691-52-7; **18**, 4485-08-9; **19**, 614-25-5; **20**, 100-01-6.

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Orientation of the Sulfoxide Bond as a Stereochemical Probe. Synthesis and ^1H and ^{13}C NMR of Substituted Thiopyrano[4,3-*c*]pyrazoles

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Received February 9, 1979

The synthesis of the novel substituted thiopyrano[4,3-*c*]pyrazole ring system is reported. Proton (^1H NMR) and carbon-13 (^{13}C NMR) magnetic resonance studies, utilizing shift reagents, were used to make conformational assignments in this bicyclic system, taking advantage of the chemical shift sensitivity to the orientation of the exocyclic sulfur oxygen observed in **8a** and **8b**. Single-crystal X-ray results and NMR evidence are presented to show that the thiopyran ring of **7–9** exists in the chair conformation and that the S→O bond in **8a** is α-axial, while in **8b** the S→O bond is β-equatorial.

From earlier ^1H NMR studies, empirical correlations for the determination of configurations and conformations in cyclic sulfoxides have been proposed; these correlations have been subsequently strengthened by solvent-effect and shift-reagent studies.[2] More recently, the analysis of the ^{13}C NMR data of cyclic sulfides, sulfoxides, and sulfones has provided stronger evidence of axial–equatorial orientation of the S→O bond.[3,4] Most of the reported data pertains to simple four-, five-, or six-membered cyclic compounds. The objective of this study was to utilize the orientation of the S→O bond for conformational assignments in a new bicyclic system (thiopyrano[4,3-*c*]pyrazole), employing ^1H NMR spectrometry, shift reagents, and ^{13}C NMR spectrometry. Few studies are available wherein all three techniques are utilized on the same sulfoxide system.

Chemistry

Tetrahydro-4*H*-thiopyran-4-one (**1**),[5] the 1-oxide **2**,[6] and the 1,1-dioxide **3**[7] were prepared by literature methods. Tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one (**4**) was prepared by the condensation of benzaldehyde and ketone **1** with concentrated hydrochloric acid in ethanol, which in our hands was preferred over the method of Leonard.[8] The bis-aldol sulfoxide **5** could not be obtained

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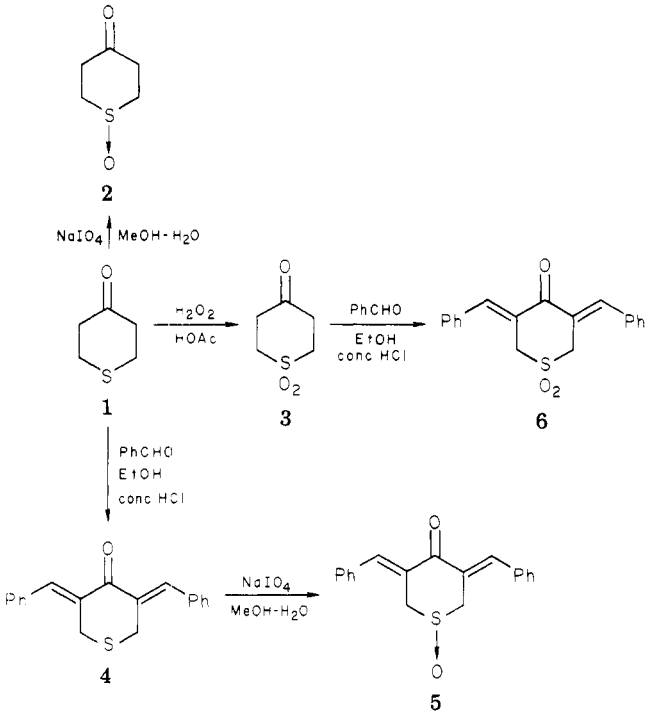
Table I. ^1H and ^{13}C NMR of Compounds 1-6[a]

	1	2	3	4	5	6
carbons						
C(2,6)	29.6	46.8	47.9	29.9	50.3	53.1
C(3,5)	43.6	31.9	37.2	133.5	126.2	126.5
C(4)	207.2	204.4	201.2	188.2	187.3	185.9
=CH				136.3	144.0	144.0
protons						
H(2,6)	2.85 m	3.30 m	3.30 m	2.85 s	4.18 s	4.40 s
H(3,5)	2.72 m	2.75 m	2.90 m			
=CH				7.75 s	8.03 s	8.05 s
C_6H_5				7.35 s	7.42 s	7.45 s

[a] The ^{13}C chemical shifts were calculated from the central peak of the solvent, $CDCl_3$, taken as 76.9 ppm from Me_4Si. The ^1H chemical shifts are relative to Me_4Si and are on the δ scale.

Scheme I



by condensation of benzaldehyde with ketone **2** because of apparent decomposition of ketone **2** under the conditions of the reaction; rather, oxidation of bis-aldol sulfide **4** with sodium metaperiodate in aqueous methanol afforded **5** in 80–89% yield. On the other hand, the sulfone ketone **3** gave the bis-aldol sulfone **6** in good yield when concentrated hydrochloric acid in ethanol was used (Scheme I—preparation of **2**–**6**).

Reaction of ketones **4** and **6** with *n*-propylhydrazine in refluxing methanol gave 2,3,3a,4,6,7-hexahydrothiopyrano[4,3-*c*]pyrazoles **7** and **9**, respectively. The corresponding reaction with bis-aldol sulfoxide ketone **5** gave two isomers, **8a** (major) and **8b** (minor), which could be separated by fractional crystallization. In some cases a dehydro (pyrazole) product could be isolated as a minor component from the reaction mixture[9] (Scheme II—preparation of **7**–**9**).

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(9) The structural relationships between dihydro and dehydro products is discussed in the following paper in this issue.

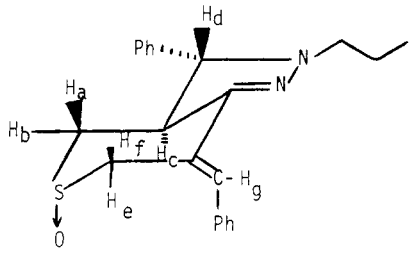


Figure 1. Conformation of **8a**.

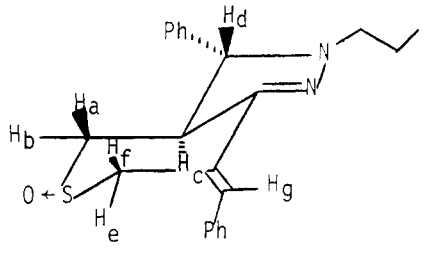


Figure 2. Conformation of **8b**.

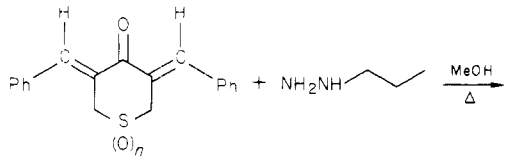
Compounds **7**–**9** were shown to have antiinflammatory activity; the structure–activity relationships of these and related analogues will be reported elsewhere.

Discussion of NMR

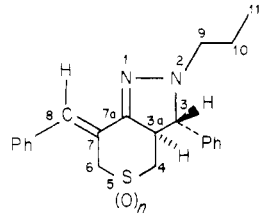
^1H and ^{13}C NMR data of symmetrically substituted thiopyrans **1**–**6**, which were used as precursors for the bicyclic systems, are presented in Table I. The chemical shift assignments of the protons and the carbon atoms of **1**–**6** are straightforward.[3,10a] The $Eu(dpm)_3$ shift reagent studies of **4** indicated that the vinylic protons shifted farther downfield than the other protons. At a concentration of 10 mg each of reagent and substrate in 0.5 mL of $CDCl_3$ the relative order of shifts was =CH (2.7) > CH_2 (1.0) ≫ C_6H_5 (0.1). Since the shift reagent coordinates with the carbonyl function, the downfield effect on the vinylic proton is consistent with the *Z* configuration (=CH protons cis to C=O). Additional ^{13}C experiments indicated that the vinylic carbons (=CH) move farther downfield ($\Delta(\sigma)$ = 2.5 ppm) than the C(3,5) carbons ($\Delta(\delta)$ = 1.5 ppm) upon addition of $Eu(fod)_3$.[11]

(10) M. S. Chauhan and I. W. J. Still, *Can. J. Chem.*, **53**, 2880 (1975); I. W. J. Still, N. Plavac, D. M. McKinnon, and M. S. Chauhan., *ibid.*, **54**, 280 (1976).
(11) As one might expect, the $Eu(fod)_3$ ^{13}C experiment indicates only that the vinylic carbon is closer to the carbonyl than are the C(3,5) and aromatic carbons.

Scheme II



4, $n = 0$
5, $n = 1$
6, $n = 2$



7, $n = 0$
8a, $n = 1$
8b, $n = 1$ sulfoxide isomers
9, $n = 2$

Table II. Dihedral Angles (deg)

angle	crystalline 7	8a
H_d-C(3)-C(3a)-H_c	162	162
H_c-C(3a)-C(4)-H_b	−54	−45
H_c-C(3a)-C(4)-H_a	176	153

The isolation of isomeric sulfoxides **8a** and **8b** from the hydrazine cyclization reaction (Scheme II) prompted us to extend the knowledge gained by us and by others[2,3,4,10] to the assignment of the configuration and conformation of this novel bicyclic system.

A large vicinal proton–proton coupling constant ($J_{H_cH_d}$ = 14 Hz) (proton assignments as in Figure 1) indicated a trans diaxial relationship for these protons for sulfide **7**; H_c and H_d assignments were confirmed by homonuclear proton decoupling. Because of substantial overlap of proton resonances, additional evidence for conformational assignments of **7** could not be obtained. Therefore, the solid-state structure was determined by single-crystal X-ray analysis. The results established the chemical structure and stereochemistry shown for **7**. In crystalline **7** the thiopyran ring exists in a chair conformation with a calculated dihedral angle H_d–C(3)–C(3a)–H_c = 162°, which is in good agreement with the value of 159° calculated from the NMR data. Other dihedral angles in crystalline **7** are compared in Table II with NMR derived values for sulfoxide **8a**.

The proton NMR spectrum of **8a** was assigned by using the LAOCN-3 program as a six-spin system of protons designated as H_a–H_f (see Figure 1 for proton assignments). However, because of the influence of the S→O bond, the greater separation of proton resonances led to a better fit (R (root mean square) = 0.3) between the observed and calculated spectra than was observed for **7**. The values of the chemical shifts and coupling constants obtained from the fit are shown in Table III and are accurate to about ±0.03 ppm. The calculated spectrum established the trans diaxial relationship of H_a–H_c (J = 12.8 Hz) and H_c–H_d (J = 14.4 Hz) protons. Thus, **8a** exists in the chair form as does **7**.

The proton NMR spectrum of **8b** was also assigned by using the LAOCN-3 program (R = 0.3). The values of the chemical shifts and coupling constants obtained from the fit are shown in Table III. The ^{1}H NMR data of sulfone **9** are comparable to those of the sulfoxides (Table III).

To further support the structural assignments of **8a** and **8b**, we studied the compounds in the presence of the shift

Table III. ^{1}H NMR Data for 7-9[a]

	chemical shifts, δ			
	7	8a[b]	8b[b]	9
H_a	2.8	2.66	~2.89	3.3
H_b	3.2	3.25	3.50	3.65
H_c	3.4	4.36	4.45	4.35
H_d	3.7	3.42	3.75	4.0
H_e	3.7	3.79	3,13	3.3
H_f	3.75	3.97	4.02	4.0
H_g	7.2	7.58[c]	7.5	7.4
aryl H	7.3	7.3-7.4	7.35-7.4	7.35-7.4
NCH_2	2.8	2.85[d]	2.88[d]	2.85
		2.89[d]	2.90[d]	
CH_2	1.75	1.75	1.72	1.68
CH_3	0.9[e]	0.88[e]	0.92[e]	0.88[e]
	coupling constants, Hz			
	7	8a	8b	9
$J_{a,b}$	NA	−11.0	−12.0	NA
$J_{a,c}$	NA	12.8	12.1	10-15
$J_{a,e}$	NA	2[f]	2[f]	~1[f]
$J_{b,c}$	NA	5.0	4.9	NA
$J_{b,f}$	NA	2[g]	2.2[g]	NA
$J_{c,d}$	14	14.4	13.9	14
$J_{e,f}$	NA	−15.2	13.2	−13

[a] 100-MHz spectra in $CDCl_3$ containing Me_4Si as internal reference. [b] Protons H_a to H_f assigned by LAOCN-3: **8a**, R = 0.3; **8b**, R = 0.3. Others were assigned by visual inspection. [c] J = 2 Hz; probably long-range coupling to H_f or H_e. [d] Overlapping triplets, J = 7 Hz. [e] Triplet, J = 7 Hz. [f] Possible assignment of coupling; likely coupling to vinyl proton H_g. [g] Possible coupling to vinyl proton H_g. NA = not assigned.

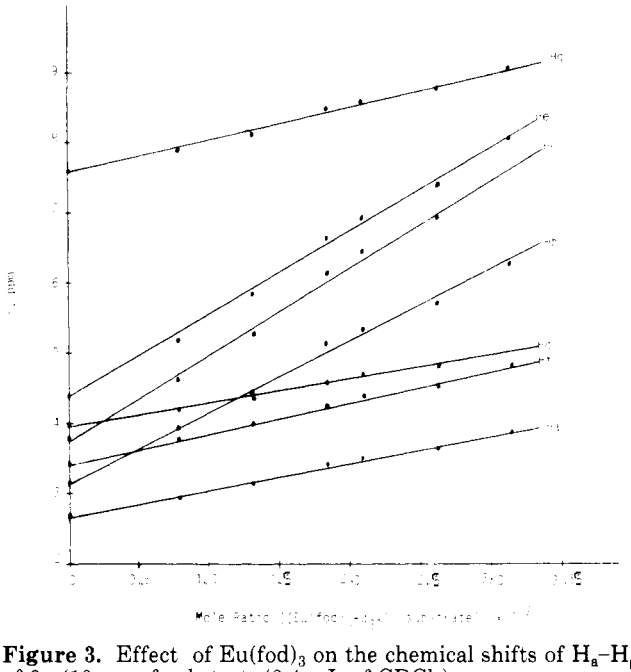


Figure 3. Effect of Eu(fod)$_3$ on the chemical shifts of H_a–H_g of **8a** (10 mg of substrate/0.4 mL of $CDCl_3$).

reagent Eu(fod)$_3$. The relative downfield shifts of protons of **8a** are in the order H_c (3.7) > H_e (3.5) > H_b (3.1) > H_g (1.4) > H_f (1.3) > H_a (1.1) > H_d (1.0) (Figure 3). H_c is α-axial and 1,3-cis to the S→O bond, whereas H_b and H_e are α-1,3-diequatorial to each other and are both cis-1,2 to the S→O bond. Since the shift reagent chelates with the S→O bond, these data are consistent with the S→O bond being α-axial in **8a** (Figure 1).

Similar studies with **8b** gave the following relative downfield shifts: H_f (5.8) > H_a (5.7) > H_e (4.7) > H_b (4.0) > H_c (2.2) > H_g (1.3) > H_d (1.0) (Figure 4). Since co-

Table IV. ^{13}C NMR Data for Compounds 7-9[a]

	7[b]	8a	8b	9
C(2,6)	31.4, 29.6	48.8, 47.7	52.9	53.1, 52.8
C(3)	56.5	45.9	49.8	51.6
C(4)	151.0	148.0	147.6	145.7
C(5)	129.2	120.4	120.8	120.9
C(7)	126.3	133.9	132.2	132.2
C(8)	78.3	79.8	79.7	78.8
C(9)	56.5	56.1	56.1	55.7
C(10)	21.1	21.0	20.9	20.7
C(11)	11.7	11.7	11.5	11.5

[a] XL-100-15 NMR spectrometer operating at 25.2 MHz. The chemical shifts are with reference to $\delta(CDCl_3) = 76.9$. [b] For the purpose of comparing ^{13}C chemical shifts with compounds 1-6 (Table I), carbon atoms of 7-9 have here been assigned as noted for 7 above and should not be confused with proper numbering as noted in Scheme II.

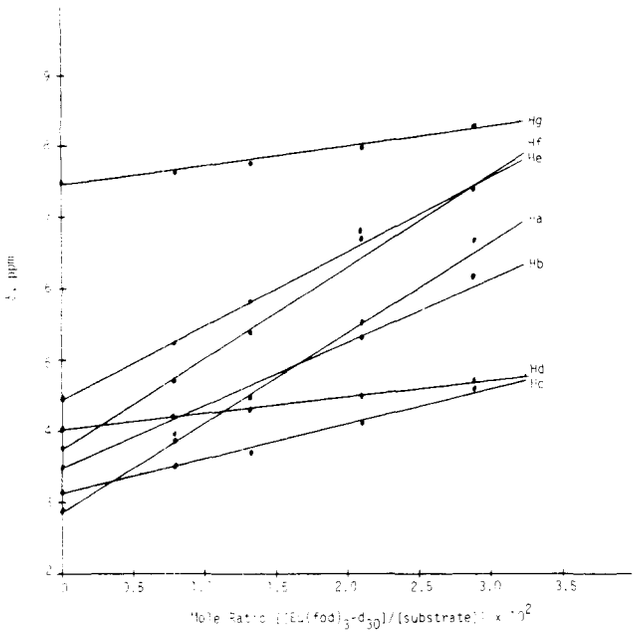


Figure 4. Effect of $Eu(fod)_3$ on the chemical shifts of H_a-H_g of **8b** (10 mg of substrate/0.4 mL of $CDCl_3$).

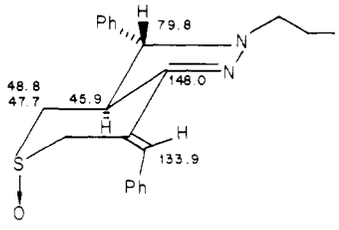
ordination occurs with the S→O bond, assumed β-equatorial in **8b**, protons closest to the S→O bond move substantially downfield; H_f and H_a, both being β-axial and *cis*-1,2 to the S→O bond, undergo the most dramatic shifts. Other protons showing large shifts are H_e and H_b, both being α-equatorial and trans-1,2 to the S→O bond. Although the points on the curve for H_a and H_b deviate somewhat from linearity, the conclusions remain that they suffer considerable downfield shifting upon addition of shift reagent. In contrast to **8a**, H_c in **8b** is not substantially influenced by the shift reagent because shift-reagent coordination occurs on the β face. On the other hand, H_d was affected about the same in both **8a** and **8b**. These data are consistent with structure **8b** (Figure 2).

In order to study the effect of introduction of an S→O bond on the carbon shifts of the methylene carbons α to sulfur, we investigated the ^{13}C NMR of the intermediates **1-6** (Table I) and of the bicyclic products **7-9** (Table IV). Two observations are worthy of comment.

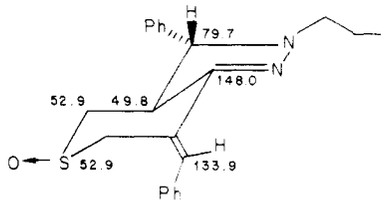
First, the introduction of an oxygen atom on sulfur affects adjacent carbons; for example, the oxygen atom in **8a** has a deshielding effect on the carbon β to oxygen and a shielding effect on carbons γ and δ to oxygen. In **8b** the deshielding effect on the carbon β to oxygen was larger than for that of **8a**. The magnitudes of these effects are comparable to the reported data on monocyclic compounds.[3]

	8a	8b
β effect	+17	+22
γ effect	-10, -9	-6, -8
δ effect	-3	-3

Second, the chemical shifts of the methylene carbons of **7**, **8a**, and **8b** are comparable to the values reported by Buchanan and Durst[4] for 4-*tert*-butylthiopyran and its axial and equatorial sulfoxides. The chemical shifts of sulfone **9** are comparable to those of the sulfoxides **8a** and **8b**; thus, the influence of another oxygen atom is by no means additive.



8a



8b

Experimental Section

Melting points were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected. $Eu(fod)_3$ (europium(III) 6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate) and $Eu(dpm)_3$ (europium(III) 2,2,6,6-tetramethyl-3,5-heptanedionate) were obtained commercially from Thompson-Packard. Proton and ^{13}C NMR studies were carried out on a Varian Associates XL-100-15 NMR spectrometer equipped with Fourier transform accessories from Nicolet Technology Corp. The calculations of the theoretical NMR spectra from chemical shifts and coupling constants were carried out by using the LAOCN-3 program from Nicolet Technology Corp. Root mean square (*R*)

values of 0.3 were obtained for both **8a** and **8b**. The geminal coupling constants were taken as negative and all others are positive. The chemical shifts are relative to Me_4Si (^1H) and $CDCl_3$ (δ = 76.9) (^{13}C). Proton NMR spectra were also obtained on a Perkin-Elmer PE R12B operating at 60 MHz. Fully decoupled, off-resonance, and gated NMR spectra were obtained to differentiate between methyl, methylene, and methine types of carbons. Infrared spectra were obtained on a Perkin-Elmer Model 621 spectrometer. New compounds gave elemental analyses that were within 0.3% of the calculated values.

Preparation of Tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one (4). A solution of ketone 1[4] (11.6 g, 0.1 mol) and benzaldehyde (22.2 g, 0.2 mol) in 60 mL of ethanol containing 6 mL of concentrated HCl was heated on a steam bath for 1 h. After the solution was cooled in an ice bath, the product was collected and washed twice with fresh ethanol and dried in vacuo to give 7.7 g of **4**; mp 150–151.5 °C. The combined mother liquor and washings were concentrated to the original volume, treated with 6 mL of concentrated HCl, and heated on a steam bath for 1 h. After collection of the product (16.6 g, mp 149–150 °C) as above, this procedure was repeated, giving another 3.0 g of **4**, mp 149–151 °C, for a combined yield of 27.3 g (93%); lit. mp 150–151 °C.

Preparation of Tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one 1-Oxide (5). A solution of $NaIO_4$ (10.4 g, 0.048 mol) in 50 mL of H_2O was added to a stirred suspension of sulfide **4** (7.0 g, 0.024 mol) in 300 mL of MeOH maintained at 25 °C by a water bath. After 3 days, solvent was removed in vacuo and the residue was dissolved in $CHCl_3$ and filtered. The filtrate was concentrated in vacuo and the residue was crystallized from 150 mL of MeOH to give 6.9 g (89%) of product: mp 155–160 °C; IR (KBr) 1650 (CO), 1560 and 1590 (PhCH=C), 1040 (S→O) cm^{-1}. Anal. Calcd for $C_{19}H_{16}SO_2$: C, 74.00; H, 5.23; S, 10.40. Found: C, 73.76; H, 5.28; S, 10.39.

Preparation of Tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one 1,1-Dioxide (6). The procedure is analogous to that described for **4**. The yield was 82%; mp 198–200 °C (lit.[7] mp 198–199 °C).

Preparation of 2,3,3a,4,6,7-Hexahydro-3-phenyl-7-(phenylmethylene)-2-propylthiopyrano[4,3-*c*]pyrazole (7). A mixture of sulfide **4** (5.84 g, 0.02 mol) and *n*-propylhydrazine (1.48 g, 0.02 mol) in 100 mL of MeOH was heated at reflux temperature for 3 h. After the mixture had cooled the formed crystals were collected and washed with MeOH. Recrystallization from MeOH and then from CH_3CN (2×) afforded 2.0 g of **7**: mp 119.5–122 °C (28%); IR (KBr) 1540, 1595 (PhC=CC=N) cm^{-1}. Anal. Calcd for $C_{22}H_{24}N_2S$: C, 75.82; H, 6.94; N, 8.04; S, 9.20. Found: C, 76.02; H, 6.99; N, 8.03; S, 9.07.

Preparation of 2,3,3a,4,6,7-Hexahydro-3-phenyl-7-(phenylmethylene)-2-propylthiopyrano[4,3-*c*]pyrazole 5-Oxide (8a and 8b). A mixture of sulfoxide **5** (1.9 g, 6.16 mmol) and *n*-propylhydrazine (570 mg, 7.70 mmol) in 60 mL of MeOH was heated at reflux temperature for 2 h. Solvent was removed in vacuo and the residue was stirred with Et_2O. Filtration afforded 1.2 g of a product mixture (**8a** and **8b**). The filtrate was concentrated in vacuo and the residue was leached with hot hexane. After the solution cooled, another 0.2 g of product mixture was obtained. Recrystallization of the combined product mixture from CH_3CN/H_2O (2×) gave **8a** (31%): mp 176.5–178 °C; IR (KBr) 1570, 1595, 1615 (PhC=CC=N), 1030 (S→O) cm^{-1}. Anal. Calcd for $C_{22}H_{24}N_2OS$: C, 72.49; H, 6.64; N, 7.69; S, 8.80. Found: C, 72.43; H, 6.79; N, 7.69; S, 8.56.

The mother liquors from **8a** were combined and concentrated in vacuo, and the residue was recrystallized from CH_3CN several times to give **8b** (9%): mp 164–166 °C; IR (KBr) 1565, 1580, 1595, 1615 (PhC=CC=N), 1025 (S→O) cm^{-1}. Anal. Calcd for $C_{22}H_{24}N_2OS$: C, 72.49; H, 6.64; N, 7.69; S, 8.80. Found: C, 72.46; H, 6.59; N, 7.81; S, 8.55.

Preparation of 2,3,3a,4,6,7-Hexahydro-3-phenyl-7-(phenylmethylene)-2-propylthiopyrano[4,3-*c*]pyrazole 5,5-Dioxide (9). A mixture of sulfone **6** (3.24 g, 0.01 mol) and *n*-propylhydrazine (0.88 g, 0.012 mol) was combined in 100 mL of MeOH and heated at reflux temperature for 2 h. After the mixture cooled, 3.05 g of crude product was collected and then stirred with 500 mL of CCl_4 overnight. A small amount of solids was removed by filtration and the filtrate was concentrated in vacuo leaving a residue which was twice crystallized from MeOH to give 2.0 g (53%) of product: mp 198–199.5 °C; IR (KBr) 1555, 1595, 1615 (PhC=CC=N), 1115, 1310 (SO_2) cm^{-1}. Anal. Calcd for $C_{22}H_{24}N_2O_2S$: C, 69.44; H, 6.36; N, 7.36; S, 8.43. Found: C, 69.40; H, 6.47; N, 7.33; S, 8.17.

Table V. Fractional Coordinates and Errors in Parentheses

atom[a]	x	y	z
N(1)	0.369 (2)	0.711 (1)	0.807 (1)
N(2)	0.215 (2)	0.669 (1)	0.678 (1)
C(3)	0.075 (3)	0.716 (1)	0.590 (2)
C(3a)	0.263 (3)	0.776 (1)	0.623 (2)
C(4)	0.153 (3)	0.847 (1)	0.620 (2)
S(5)	0.401 (1)	0.912 (0)	0.693 (1)
C(6)	0.503 (3)	0.899 (1)	0.885 (2)
C(7)	0.572 (3)	0.824 (1)	0.885 (2)
C(7a)	0.400 (2)	0.770 (1)	0.778 (2)
C(8)	0.769 (3)	0.805 (1)	0.976 (2)
C(9)	0.051 (3)	0.619 (1)	0.716 (2)
C(10)	0.209 (3)	0.566 (1)	0.792 (2)
C(11)	0.366 (3)	0.524 (1)	0.687 (2)
C(1′)	0.962 (3)	0.847 (1)	1.096 (2)
C(2′)	1.185 (3)	0.815 (1)	1.136 (2)
C(3′)	1.379 (3)	0.851 (1)	1.247 (2)
C(4′)	1.351 (3)	0.920 (1)	1.319 (2)
C(5′)	1.127 (3)	0.952 (1)	1.287 (2)
C(6′)	0.931 (3)	0.916 (1)	1.174 (2)
C(1″)	−0.002 (3)	0.682 (1)	0.423 (1)
C(2″)	−0.229 (3)	0.699 (1)	0.339 (2)
C(3″)	−0.298 (3)	0.670 (1)	0.182 (2)
C(4″)	−0.144 (3)	0.624 (1)	0.110 (2)
C(5″)	0.079 (3)	0.607 (1)	0.194 (2)
C(6″)	0.150 (3)	0.635 (1)	0.350 (2)
H_a	0.06 (2)	0.85 (1)	0.68 (1)
H_b	0.09 (2)	0.85 (1)	0.52 (1)
H_c	0.36 (2)	0.77 (1)	0.57 (1)
H_d	−0.04 (2)	0.73 (1)	0.63 (1)
H_e	0.63 (2)	0.93 (1)	0.92 (1)
H_f	0.39 (2)	0.91 (1)	0.92 (1)
H_g	0.77 (2)	0.76 (1)	0.96 (1)
H(9a)	−0.04 (2)	0.59 (1)	0.62 (1)
H(9b)	−0.02 (2)	0.65 (1)	0.80 (1)
H(10a)	0.10 (2)	0.54 (1)	0.79 (1)
H(10b)	0.31 (2)	0.59 (1)	0.88 (1)
H(2′)	1.20 (2)	0.76 (1)	1.09 (1)
H(3′)	1.49 (2)	0.82 (1)	1.27 (1)
H(4′)	1.46 (2)	0.94 (1)	1.40 (1)
H(5′)	1.11 (2)	0.99 (1)	1.33 (1)
H(2″)	−0.32 (2)	0.73 (1)	0.39 (1)
H(3″)	−0.43 (2)	0.68 (1)	0.13 (1)
H(4″)	−0.19 (2)	0.61 (1)	0.00 (1)
H(5″)	0.15 (2)	0.58 (1)	0.16 (1)
H(6″)	0.27 (2)	0.62 (1)	0.41 (1)
H(6′)	0.75 (2)	0.95 (1)	1.15 (1)

[a] Carbon and proton numbering corresponds to that shown in structure **7** and Figures 1 and 2; benzylidene phenyl atoms are primed and the other phenyl atoms are double primed.

X-ray Structure Analysis of 7. $C_{22}H_{24}N_2S$ had two molecules in a triclinic ($P\bar{1}$) unit cell with a = 5.521 (2) Å, b = 19.833 (7) Å, c = 9.267 (4) Å, α = 103.3 (1)°, β = 101.9 (1)°, γ = 88.9 (1)°, and a measured density of 1.23 g cm^{-3} (calculated density 1.20 g cm^{-3}). Intensities were recorded by using the θ–2θ variable scan rate technique with backgrounds B_1 and B_2 measured for $^1/_{20}$th of the scan time on each side of the reflection. Errors (σ) were assigned according to $\sigma = r[C + 100(B_1 + B_2)]^{1/2}$, where C is the total reflection count and r is the scan rate. Of the 1988 total reflections measured on a Syntex $P2_1$ diffractometer, 1317 were observed with intensity $I > 3\sigma$. The structure was solved by direct methods and refined by full-matrix least-squares analysis in which all coordinates and anisotropic temperature factors were allowed to vary. The refinements minimizing $\sum w(F_o^2 - F_c^2)^2$, where $w = \sigma^{-2}$, converged to $R = \sum||F_o| - |F_c||/\sum|F_o| = 0.11$ for the observed reflections. Only peaks attributable to hydrogen atoms were evident in a difference map at this stage. Inclusion of all hydrogens except those of the methyl group and further refinements (the

coordinates but not the assigned isotropic temperature factor of 4.2 Å^2 for the hydrogens were also refined) converged the final R value to 0.09. The final atomic coordinates are given in Table V.

Acknowledgments. We are indebted to Mr. J. Alicino and Ms. Mary Young for microanalysis and to Ms. Virginia Shu for chemical synthesis.

Registry No. 1, 1072-72-6; 2, 17396-36-0; 3, 17396-35-9; 4, 70332-83-1; 5, 70332-84-2; 6, 70332-85-3; 7, 70355-01-0; 8a, 70355-02-1; 8b, 70355-03-2; 9, 70355-04-3; benzaldehyde, 100-52-7; propylhydrazine, 5039-61-2.

Supplementary Material Available: X-ray data consisting of tables of temperature factors, bond distances, and bond angles (3 pages). Ordering information is given on any current masthead page.

Preparation of Thiopyrano- and Pyrano[4,3-*c*]pyrazoles. Structure Elucidation of Dehydro Coproducts

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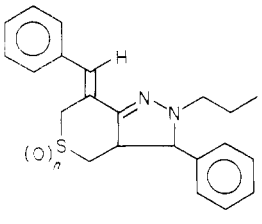
Received February 13, 1979

Reaction of *n*-propylhydrazine with tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one gives 2-propylhexahydrothiopyrano[4,3-*c*]pyrazole (**1**) as the major product. However, this reaction provides a dehydro coproduct whose structure has been shown to be the 1-substituted isomer B rather than the 2-substituted isomer A. Analogous reactions give varying amounts of the 1-substituted dehydro coproducts, the proportion being determined, probably, by both steric and electronic effects. Structure determination of the dehydro coproducts was aided by ^{1}H NMR spectroscopy, by X-ray crystallography of one of the 1-substituted dehydro coproducts (**14**), and by synthesis of the isomeric 2-substituted dehydro product **23** by dehydrogenation of **13**.

In a previous paper[1] we described a method for preparing 2,3,3a,4,6,7-hexahydrothiopyrano[4,3-*c*]pyrazoles (**1–3**) and discussed our studies using ^{1}H NMR and ^{13}C

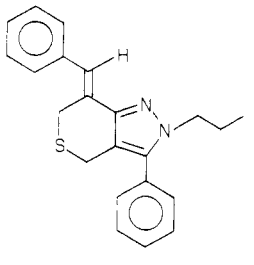


1, n = 0
2, n = 1 (two sulfoxide isomers)
3, n = 2

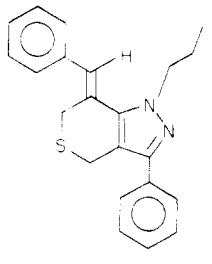
NMR in which shift reagents were utilized in making conformational assignments in this bicyclic system. The utility of the S→O bond in making assignments in a relatively complex rigid system was demonstrated, the conformational assignment being confirmed in one case by X-ray crystallographic data. We mentioned but did not elaborate therein on the finding of dehydro coproducts during the isolation of the major products **1** and **3**. This paper describes our studies on the elucidation of the structure of these pyrazole coproducts.

Chemistry and Discussion

When tetrahydro-3,5-bis(phenylmethylene)-4*H*-thiopyran-4-one[2] is treated with *n*-propylhydrazine in refluxing methanol for 3 h and the mixture cooled, **1** deposits as the major product; several recrystallizations are required to obtain the product pure. The TLC of the mother liquor revealed the presence of a slightly more polar coproduct. Concentration of the mother liquor afforded a low yield of the minor product, which was further purified by several recrystallizations. This product possessed m/e 346 (M^+), indicating a loss of two hydrogens relative to **1**, while the ^{1}H NMR ($CDCl_3$) spectrum showed the presence of an *n*-propyl group at δ = 1.1 (t, J = 7.0 Hz, CH_3), 2.1 (m, CH_2), and 4.35 (t, J = 7.0 Hz, NCH_2); the position of the NCH_2 signal was shifted downfield 1.5 ppm relative to the NCH_2 signal of **1** (δ = 2.8), consistent with attachment of the propyl group to an aromatic pyrazole nitrogen. We were, thus, afforded the option that the dehydro coproduct was one of two possible pyrazole structures (A or B), indistinguishable on the basis of spectral data alone.



A



B

Our initial observations led us to favor structure B; for example, prolonged heating or the addition of excess *n*-propylhydrazine to the reaction mixture failed to increase the amount of pyrazole coproduct formed, making it unlikely that the observed dehydro coproduct was derived by dehydrogenation of **1**. Likewise, compound **1** remained unchanged when heated in methanol in the presence of *n*-propylhydrazine. In fact, we found compound **1** to be quite stable to various dehydrogenating conditions, such as *p*-chloranil in either refluxing *tert*-butyl alcohol or xylene solution, DDQ in refluxing dioxane, or 5% palladium/charcoal or sulfur in refluxing DMF solution. Extended reaction times led in some cases only to

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(2) N. J. Leonard and D. Choudhury, *J. Am. Chem. Soc.*, **79**, 156 (1957).

0022-3263/79/1944-2518$01.00/0