Definition of the Predominant Tautomeric Form of 3-Methyl-1-phenylpyrazoline-5-thione in Solution by ^{1}H and ^{13}C NMR Spectroscopy

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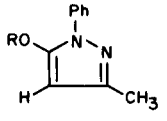
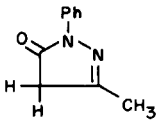
Conjoint use of pmr allylic coupling constants and of ^{13}C nmr chemical shift patterns defines the predominant tautomeric form of 3-methyl-1-phenylpyrazoline-5-thione in solution in aprotic dipolar and in non-polar solvents as the thiol species, 3-methyl-1-phenylpyrazole-5-thiol. The tautomeric preference thus differs from that of the oxygen analog, and is opposite to that noted for thiol-thione tautomerism in six-membered heteroaromatic species.

Introduction.

Feeney, Newman, and Pauwels (1) have examined the ^{13}C nmr spectrum of 3-methyl-1-phenylpyrazolin-5-one dissolved in dimethyl sulfoxide, and conclude that it exists in the OH form **1** (5-hydroxy-3-methyl-1-phenylpyrazole) in the aprotic dipolar solvent. However, pmr spectra of this compound in deuteriochloroform (2) indicate very strongly that it exists predominantly as the CH form **2** in this solvent. Quantum-chemical calculations of the relative energies of the OH form **1**, the CH form **2**, and the NH form **3** suggest (3) that species **2** is the most stable as an isolated (unsolvated) molecule, yet the actual energy differences are small enough to allow solvent influences to determine the favored tautomeric form. The influence of dimethyl sulfoxide is surely to stabilize the OH form through its hydrogen-bond acceptor character (4), and on this basis, stabilization by this type of hydrogen bonding should be much less effective with the thio-analog (3-methyl-1-phenylpyrazoline-5-thione), so that solvent influences on the favored forms



1 R = H
7 R = CH_3



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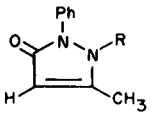
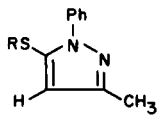
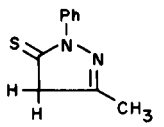


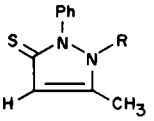
3 R = H
8 R = CH_3



4 R = H
9 R = CH_3



5



6 R = H
10 R = CH_3

among the SH (**4**), CH (**5**), and NH (**6**) species should be less significant. Further, Albert and Barlin (5) have shown that the "mercapto" derivatives of six-membered ring azaheteroaromatic species favor the thioamide (-NH-C(:S)-) form over the thiol (-N:C(-SH)-) to a much greater extent than the "hydroxy" derivatives favor the non-enolic forms, and extrapolation of this tendency to the five-membered ring species would suggest that forms **5** and **6** would be favored over **4**.

From a study of the ionization, uv, ir, and pmr chemical shift properties of 3-methyl-1-phenylpyrazoline-5-thione and related compounds, Tanaka (6) proposes that the NH form **6** is favored in aqueous solution, while the SH form **4** predominates in chloroform. However, the pmr spectra cited for the fixed species **9** and **10** are closely similar to that of the parent compound and thus fail to distinguish clearly between the SH and NH forms (we noted that for 3-methyl-1-phenylpyrazolin-5-one, Feeney and co-workers point out that pmr chemical shifts do not distinguish clearly between the OH and NH forms, and ir and uv evidence is similarly equivocal [*cf.* various citations in reference (2)]. Consequently, in this paper we have examined (i) the coupling constant patterns in the pmr spectra of 3-methyl-1-phenylpyrazolin-5-one, 3-methyl-1-phenylpyrazoline-5-thione and the fixed derivatives **7**, **8**, **9**, and **10**, and (ii) the ^{13}C nmr spectra of 3-methyl-1-phenylpyrazoline-5-thione, in attempts to decide unequivocally between the species **1** and **3**, and **4** and **6**.

Results and Discussion.

Our pmr data are summarized in Table I: the positions of the signals are in close agreement with those reported by Tanaka (6). Comparisons for 3-methyl-1-phenyl-

TABLE I

Proton Magnetic Resonance Spectra of
3-Methyl-1-phenylpyrazolin-5-one, -5-thione, Derivatives

Compound	Solvent	Signals (intensity, multiplicity (with J), assignment)
3-Methyl-1-phenyl pyrazolin-5-one	$CDCl_3$	2.11 (3, s, 3-methyl), 3.33 (2, s, 4-CH_2), 7.23-7.90 (5, m, phenyl)
	DMSO-d_6	2.13 (3, d (0.4), 3-Me), 5.40 (1, q (0.4), 4-CH), 7.25-7.83 (5, m, phenyl)
	HMPA (a)	5.32 (1, s, 4-CH), 7.25-8.00 (5, m, phenyl), 12.50 (1, s, 5-OH)
5-Methoxy-3-methyl-1-phenyl-pyrazole	DMSO-d_6	2.17 (3, d (0.4), 3-Me), 3.90 (3, s, 5-OCH_3), 5.70 (1, q (0.4), 4-CH), 7.25-7.80 (5, m, phenyl)
2,3-Dimethyl-1-phenyl-pyrazolin-5-one	$CDCl_3$	2.23 (3, d (0.8), 3-Me), 3.06 (3, s, 2-Me), 5.38 (1, q (0.8), 4-CH), 7.30-7.50 (5, m, phenyl)
	DMSO-d_6	2.23 (3, d (0.8), 3-Me), 3.03 (3, s, 2-Me), 5.27 (1, q (0.8), 4-CH), 7.30-7.50 (5, m, phenyl)
3-Methyl-1-phenyl-pyrazoline-5-thione	$CDCl_3$	2.28 (3, d (0.4), 3-Me), 3.43 (1, br s, 5-SH), 6.24 (1, q (0.4), 4-CH), 7.47 (5, m, phenyl)
	DMSO-d_6	2.29 (3, d (0.4), 3-Me), 4.00 (1, br s, 5-SH), 6.23 (1, q (0.4), 4-CH), 7.55 (5, m, phenyl)
	C_6D_6	2.18 (3, d (0.4), 3-Me), 2.82 (1, s, 5-SH), 6.00 (1, q (0.4), 4-CH), 7.17 (5, m, phenyl)
5-Methylthio-3-methyl-1-phenylpyrazole	$CDCl_3$	2.27 (6, br s, 3-Me & 5-SMe), 6.12 (1, q (0.4), 4-CH), 7.25-7.51 (5, m, phenyl)
	DMSO-d_6	2.23 (3, d (0.4), 3-Me), 2.62 (3, s, 5-SMe), 6.33 (1, q, (0.4), 4-CH), 7.52 (5, m, phenyl)
2,3-Dimethyl-1-phenyl-	$CDCl_3$	2.30 (3, d (0.8), 3-Me, 3.30 (3, s, 2-Me), 6.15 (1, q (0.8), 4-CH), 7.50 (5, m, phenyl)
	DMSO-d_6	2.28 (3, d (0.8), 3-Me), 3.30 (3, s, 2-Me), 6.02 (1, q (0.8), 4-CH), 7.52 (5, m, phenyl)

(a) Hexamethylphosphoramide: 3-Methyl signal is obscured in this solvent.

TABLE II

Carbon-13 Magnetic Resonance Spectra of 1-Phenylpyrazole Species

Substituents in 1-Phenylpyrazole moiety:	Chemical Shifts, ppm from Tetramethylsilane				
	5-Hydroxy, 3-methyl (1)	5-Hydroxy	3-Methyl, 5-thiol (4)	3-Methyl, 5-methylthio (9)	2,3-Dimethyl 5-thione (10)
Solvent	DMSO	DMSO	$CDCl_3$	$CDCl_3$	$CDCl_3$
Carbon Assignment					
3-Pyrazole	150.8 (a)	141.8 (a)	143.2	143.8	146.5
4-Pyrazole	90.8	90.8	115.7	112.1	111.8
5-Pyrazole	157.8	155.3	153.5	153.6	170.5
1'-Phenyl	140.8	140.8	140.0	141.8	134.6
2'-Phenyl	130.8	130.8	133.0	132.8	129.0
3'-Phenyl	122.8	127.8	129.5	128.4	129.6
4'-Phenyl	126.8	127.8	132.0	131.3	130.0
3-Methyl	14.8		17.5	17.6	11.9
2-Methyl					34.6
S-Methyl				21.7	

(a) Chemical shifts converted from the data of Feeney and co-workers (1).

pyrazolin-5-one and 3-methyl-1-phenylpyrazoline-5-thione in deuteriochloroform and in perdeuterated dimethyl sulfoxide show that these compounds do not have parallel tautomer preferences: the relative signal intensities for the thio-analog in both solvents (and also in perdeuterated benzene) show that the CH species **5** is not a major

constituent. One-proton signals at δ 3.43 (in deuteriochloroform), 4.00 (DMSO-d_6) and 2.82 (perdeuteriobenzene) all exchange rapidly with added deuterium oxide indicating attachment to electronegative atoms, but these signals fall in regions characteristic both of -NH- and of -SH proton signals in these solvents (7,8, and unpublished results). Further, the 4-CH proton signals of the fixed models **9** (3-methyl-5-methylthio-1-phenylpyrazole) and **10** (2,3-dimethyl-1-phenylpyrazoline-5-thione) each fall in a similar region to the parent (the same pattern is evident for the 4-CH shifts for the fixed species **7** and **8**).

With the exception of the spectra of 3-methyl-1-phenylpyrazolin-5-one in hexamethylphosphoramide, where the very low field one-proton signal at δ 12.50 is characteristic of an enolic proton, permitting assignment to form **1**, the chemical shift data provide no conclusive information about tautomer preferences. The coupling constant patterns are more informative, since corresponding species will have closely similar magnitudes for the allylic couplings between the protons of the 3-methyl group and the 4-proton. Thus, the bond order of the 3-4 bond in species **1** is certainly less than for **3**, and for species **4** less than for species **6**; the fixed model compounds **7** and **8**, and **9** and **10**, provide satisfactory models for **1** and **3**, and for **4** and **6**. From Table I it is evident that two characteristic values of the allylic couplings are present: the larger (0.8 Hz) found for compounds **8** and **10**, (typical of values in other five-membered ring species with localized double bonds in the allylic moiety (9,10)), and the smaller (0.4 Hz) found for 3-methyl-1-phenylpyrazolin-5-one in DMSO-d_6, for 3-methyl-1-phenylpyrazoline-5-thione in deuteriochloroform, DMSO-d_6, and perdeuteriobenzene and for compounds **7** and **9** (reflecting the delocalization of the electrons of the 3-4 bond through the pyrazole ring [*cf.* Rottendorf and Sternhell (11)]). These results identify the predominant tautomeric form of the thio-compound as the SH species **4** (3-methyl-1-phenylpyrazole-5-thiol), excluding **6**, and are consistent with Feeney and coworkers finding that the OH form 1 predominates in aprotic dipolar media.

The ^{13}C nmr spectral data of Table II confirm the identification of **4** (3-methyl-1-phenylpyrazole-5-thiol) as the predominant tautomeric form: the chemical shift patterns for 3-methyl-5-methylthio-1-phenylpyrazole (**9**) and the putative **4** are closely similar to one another. The 5-carbon shifts are virtually identical (153.5 ppm for **4**, 153.6 ppm for **9**) and differ markedly from that for the model compound for the NH form (*i.e.* **10**, 2,3-dimethyl-1-phenylpyrazoline-5-thione), which is at 170.5 ppm. We conclude that predictions of tautomeric preferences in the hydroxypyrazole-pyrazolethiol series using the analogies outlined in the Introduction are risky exercises; it would be of obvious interest to see if quantum-chemical calculations of the relative energies of species **4**, **5**, and **6** successfully reproduce the observed preponderance of **4**.

EXPERIMENTAL

Sources of Materials.

The pyrazolin-5-one and pyrazoline-5-thione derivatives were prepared by routes reported in a standard monograph (12), starting from the commercially available 3-methyl-1-phenylpyrazolin-5-one. The melting points of these products (Fisher-Johns apparatus) were concordant with those reported previously, and the pmr spectra were consistent with the gross structural features. For the tautomerically fixed model compounds, the pmr spectra demonstrated that these consisted of over 97% of the postulated species. Solvents for the nuclear magnetic resonance spectra were supplied by Merck Sharp and Dohme, Montreal.

Spectra.

The pmr spectra were obtained using a Varian A-60D spectrometer. Chemical shifts refer to dilute solutions (< 2% w/v) and are expressed in the ppm scale, downfield from internal tetramethylsilane. Coupling constants were measured using the 50 Hz sweep width setting, calibrated using a Hewlett-Packard 5332B counter. Measurements were reproducible to 0.02 Hz. The ^{13}C nmr spectra were obtained for deuteriochloroform solutions using Varian CFT-20 or XL-100 spectrometers (Fourier transform mode) with full proton decoupling.

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