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Crystal and Molecular Structures of Pyrazol-3-one Derivatives. I. 1,2-Dihydro-5-methyl-2-phenyl-4-(9*H*-thioxanthen-9-yl)-3*H*-pyrazol-3-one

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The crystal and molecular structure of 1,2-dihydro-5-methyl-2-phenyl-4-(9*H*-thioxanthen-9-yl)-3*H*-pyrazol-3-one was examined by the X-ray diffraction method to establish the predominant tautomeric form (**3b**) due to the pyrazol-3-one ring in the solid state. The title compound, $C_{23}H_{18}N_2OS$, crystallizes in space group Cc with lattice parameters $a = 17.675$ (8), $b = 12.421$ (3), $c = 11.374$ (7) Å, $\beta = 132.57$ (3)°, and $Z = 4$. In crystals, molecules of **3b** are linked by an intermolecular hydrogen bond between the NH and C=O groups.

Keywords——X-ray analysis; crystal structure; pyrazol-3-one; 2,4-dihydro-5-methyl-2-phenyl-3*H*-pyrazol-3-one; 1,2-dihydro-5-methyl-2-phenyl-4-(9*H*-thioxanthen-9-yl)-3*H*-pyrazol-3-one

Some of the pyrazol-3-ones have the important use in medicine as analgesics and antipyretics, and in color photography as magenta dye formers.[1] The relative abundance of the various tautomeric forms[2-5] of 2,5-disubstituted pyrazol-3-ones has been the subject of much work since Konn's synthesis[6] of the first example of this class. During our studies on the reactivity of 5-amino- and 5-methyl-2,4-dihydro-2-phenyl-3*H*-pyrazol-3-one with the various possible tautomeric forms (CH-, NH-, and OH-forms in Chart 1), we found that these pyrazol-3-ones underwent dehydration at the 4-position active methylene of the pyrazol-3-one ring with the OH group of xanthen-9-ol or thioxanthen-9-ol to give **3a**-type condensed products.[7]

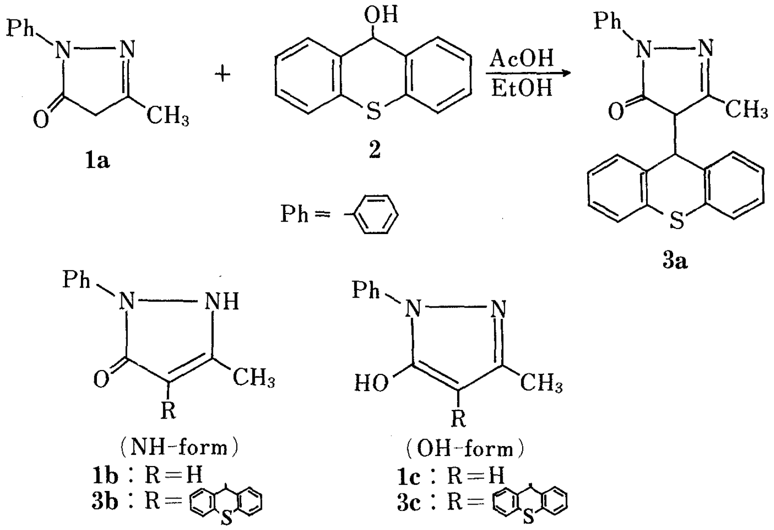


Chart 1

The purpose of the present work was to determine the preferred tautomeric form of **3a** in the solid state by the X-ray diffraction method and to compare the result with the structures of **1b** and **1c**[8] that exist as two crystallographically independent molecules in the unit cell corresponding to the different tautomeric forms (the NH-form (**1b**) and OH-form (**1c**)).

TABLE I. Positional and Thermal Parameters of Compound **3b**

Atom	X	Y	Z	B_{eq}
N1	0.7974 (6)	0.4809 (4)	0.8702 (5)	2.2
N2	0.8455 (6)	0.5128 (4)	1.0259 (5)	2.4
C3	0.8458 (5)	0.4282 (5)	1.1031 (5)	2.2
O4	0.8713 (5)	0.4345 (4)	1.2360 (4)	1.4
C5	0.8091 (6)	0.3353 (5)	0.9998 (6)	1.9
C6	0.7793 (6)	0.3733 (5)	0.8593 (6)	1.9
C7	0.7342 (7)	0.3209 (5)	0.7038 (6)	3.1
C8	0.7962 (7)	0.2251 (5)	1.0461 (7)	1.9
C9	0.7415 (5)	0.1454 (4)	0.9073 (5)	3.3
C10	0.6359 (7)	0.1329 (5)	0.8649 (7)	4.0
C11	0.5829 (7)	0.0685 (7)	0.6679 (7)	6.0
C12	0.6359 (7)	0.0161 (6)	0.6370 (7)	5.7
C13	0.7406 (7)	0.0241 (5)	0.7377 (6)	3.0
C14	0.7938 (6)	0.0892 (5)	0.8738 (6)	3.4
S15	0.9285 (5)	0.1033 (3)	0.9999 (5)	3.1
C16	0.9632 (6)	0.1258 (5)	1.1848 (6)	2.5
C17	1.0618 (7)	0.0878 (6)	1.3249 (7)	5.1
C18	1.0916 (7)	0.1073 (6)	1.4687 (7)	8.6
C19	1.0283 (6)	0.1621 (5)	1.4832 (7)	6.1
C20	0.9339 (7)	0.1975 (6)	1.3462 (7)	3.4
C21	0.9010 (6)	0.1820 (5)	1.1954 (6)	1.5
C22	0.8607 (6)	0.6249 (5)	1.0659 (6)	1.7
C23	0.9503 (7)	0.6573 (6)	1.2127 (7)	4.1
C24	0.9633 (7)	0.7659 (6)	1.2489 (7)	4.3
C25	0.8914 (7)	0.8362 (6)	1.1427 (7)	1.4
C26	0.7989 (7)	0.8064 (6)	0.9957 (7)	1.9
C27	0.7838 (7)	0.6976 (6)	0.9537 (7)	2.4
Atom	X	Y	Z	B_{iso}
HC71	0.780 (6)	0.280 (6)	0.720 (6)	5.4
HC72	0.715 (6)	0.372 (5)	0.613 (6)	6.4
HC73	0.671 (6)	0.278 (5)	0.644 (6)	4.5
HC8	0.753 (6)	0.225 (5)	1.087 (4)	1.3
HC10	0.590 (6)	0.156 (4)	0.834 (6)	3.0
HC11	0.516 (6)	0.042 (5)	0.598 (6)	4.4
HC12	0.600 (4)	−0.022 (4)	0.532 (4)	2.0
HC13	0.784 (5)	−0.016 (5)	0.721 (5)	2.5
HC17	1.099 (5)	0.039 (4)	1.306 (5)	2.3
HC18	1.146 (6)	0.077 (5)	1.552 (6)	5.4
HC19	1.058 (6)	0.178 (5)	1.610 (6)	4.3
HC20	0.881 (5)	0.235 (5)	1.363 (5)	3.1
HC23	1.014 (6)	0.612 (5)	1.281 (6)	4.5
HC24	1.037 (6)	0.784 (4)	1.354 (6)	5.6
HC25	0.901 (6)	0.897 (4)	1.168 (6)	3.2
HC26	0.735 (6)	0.849 (5)	0.908 (6)	5.0
HC27	0.709 (6)	0.674 (5)	0.838 (6)	4.4

For non-hydrogen atoms $B_{eq}=\frac{8}{3}\Sigma_i\Sigma_jB_{ij}a_ia_j$.

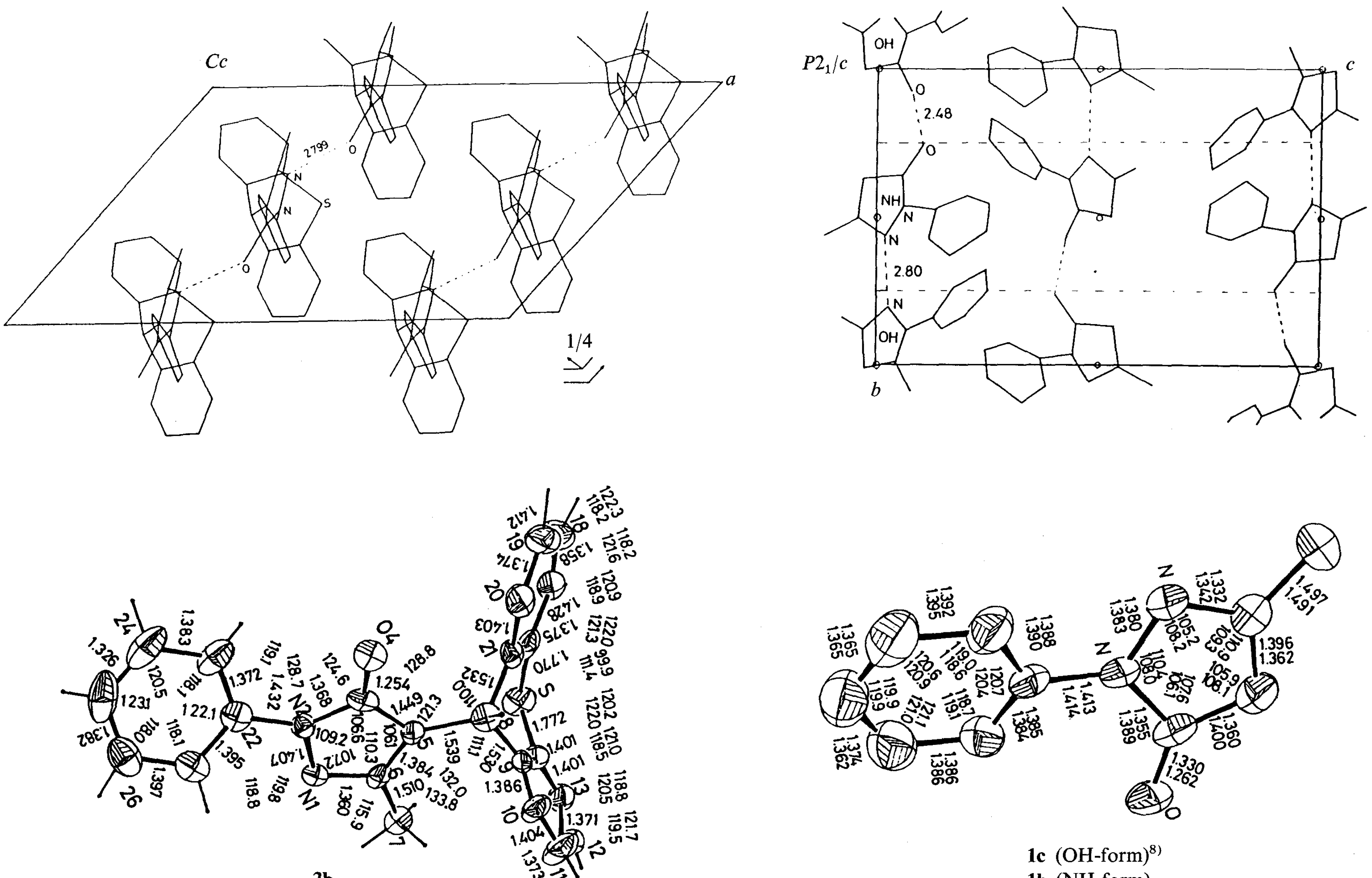
Structure Determination of 3b

A crystal of **3b**, $C_{23}H_{18}N_2OS$,[7] having dimensions 0.20 × 0.25 × 0.30 mm was selected for investigation. Systematic absences were unique for the monoclinic space group *Cc*, and the unit cell dimensions, obtained by least-squares refinement using Bragg angles (Mo $K\alpha$, $\lambda=0.791069$ Å) of 30 reflections ($25° < 2\theta < 30°$) are: $a=17.675$ (8), $b=12.421$ (3), $c=11.374$ (7) Å, $\beta=132.57$ (3)°, $Z=4$, volume $=1839.2$ Å^3, $D_c=1.30\,\mathrm{g\,cm^{-3}}$, $\mu=2.02\,\mathrm{cm^{-1}}$. Intensity data were collected at room temperature on a Rigaku four-circle diffractometer using Zr-filtered Mo $K\alpha$ radiation by the ω-2θ scan mode. Scans of $1°\,\mathrm{min^{-1}}$ were used with a scan range in 2θ which varied from 0 to $8.0°\,\mathrm{min^{-1}}$ depending directly upon the number of counts obtained in a short preliminary count of the peak. Background counts were taken at both ends of the scan with ω displaced $\pm 3.0°$ from the $K\alpha$ peak. A total of 2924 unique reflections were measured in the range $2\theta < 60°$; 2350 reflections had intensities greater than $3\sigma(I)$. The intensities of 3 standard reflections measured after every 60 reflections, showed no significant variation during data collection. Lorentz and polarization corrections were applied, but no absorption corrections were made. Standard deviations in the intensities, $\sigma(I)$, and in the structure amplitudes, $\sigma(F)$, were derived directly from counting statistics. The structure was solved by direct methods using MULTAN[9] to calculate phases for the $300|E|$ values greater than 1.30. The *E*-map obtained from the phase set with the largest combined figure of merit (2.82) revealed all the non-hydrogen atoms. The 2350 reflections were used for the block-diagonal least-squares refinement of the structure, in which the function minimized was $\sum w(|F_o|-|F_c|)^2$ where $w=1/\sigma^2(F_o)$. Refinement[10] of non-hydrogen atoms with anisotropic temperature factors and hydrogen atoms with isotropic temperature factors was terminated at a conventional *R* of 0.059 and a weighted $R_w=0.072$ ($R_w=(\sum w(|F_o|-|F_c|)^2/\sum w|F_o|^2)^{1/2}$). The atomic scattering factors for S, O, N and C were those of Cromer and Waber;[11] for H, the scattering factors of Stewart, Davidson, and Simpson[12] were used. The final positional and thermal parameters are given in Table I. The hydrogen atom of the NH group in the pyrazol-3-one ring could not be found on the difference Fourier maps calculated from the structure factors of the last cycle refinement.

Discussion

The method nuclear magnetic resonance (NMR) spectroscopy of **3a** in dimethyl sulfoxide (DMSO) solution showed one singlet proton at δ 4.98 due to the thioxanthenyl 9-H, and there was no evidence of a resonance with the proton of the 4-position in the pyrazol-3-one ring, so we concluded that the NH-form (**3b**) or the OH-form (**3c**) is predominant in the solution. In the solid state, additional factors affecting the tautomeric forms are likely, owing to the possibility of strong hydrogen bonding. The infrared (IR) spectra[3,7] of **1a** and **3a** are remarkably simple in the 1500—1600 cm^{-1} region, comprising two phenyl ring vibrations. Compound **3a** is expected to favor either the NH- (**3b**) or OH-form (**3c**) in the solid state as well as in solutions, because no C=O band is present around 1680 cm^{-1} in the IR spectrum.[7]

From the present X-ray work, the predominant tautomeric form of **3a** in the solid state is now well established, and it has become clear that **3a** exists in the NH-form (**3b**). Figure 1 compares some significant bond distances, angles and molecular packing schemes connected by the hydrogen bond of **3b** with those of **1a**.[8] In the case of **1a**,[8] it has been reported that there are two crystallographically independent molecules (the NH-form (**1b**) and OH-form (**1c**)) in the unit cell, and hydrogen bonds characterized by the O–H···O (2.48 Å) and N–H···N (2.80 Å) lengths. On the other hand, the molecules of **3b** are packed with a hydrogen bond between the NH and CO groups (2.799 Å) to form endless chains along the *c*-axis as shown in Fig. 1. With regard to the bond lengths of the two compounds (**3b** and **1b**), the C–C or C–N bonds of the pyrazol-3-one ring reflect their tautomeric forms and are slightly



3b

1c (OH-form)[8]
1b (NH-form)

Fig. 1. Thermal Ellipsoids are Drawn at the 50% Probability Level

The e.s.d.'s of bond lengths and angles are 0.006—0.009 Å and 0.4—0.7° for **2b**.

TABLE II. Least-Squares Planes and Deviations of Atoms from the Planes

Plane 1: a plane defined by the atoms C16–C21.
$-0.4952X-0.8657Y-0.0739Z+6.0105=0$
C16 0.009; C17 0.002; C18 −0.010
C19 0.001; C20 0.010; C21 −0.017

Plane 2: a plane defined by the atoms C9–C14.
$0.3251X+0.7860Y-0.5259Z+0.5966=0$
C9 0.011; C10 −0.011; C11 0.001
C12 0.009; C13 −0.007; C14 −0.006

Plane 3: a plane defined by the atoms N1, N2, C3, C5 and C6.
$-0.9090X+0.2069Y-0.3619Z+8.1439=0$
C1 0.022; C2 −0.051; C3 0.033
C5 −0.027; C6 −0.007

Plane 4: a plane defined by the atoms C22–C27.
$-0.9176X-0.1173Y+0.3798Z+3.9331=0$
C22 −0.020; C23 −0.017; C24 −0.014
C25 −0.039; C26 0.000; C27 −0.027

The dihedral angles between planes are as follows:
Between planes 1 and 2: 143.37°
Between planes 1 and 3: 72.68
Between planes 1 and 4: 58.14
Between planes 2 and 3: 86.71
Between planes 2 and 4: 126.17
Between planes 3 and 4: 47.75

shortened or elongated from the normal values. But they show the intermediate bond lengths resulted from some electron delocalization; the distances of C5–C6 and N1–C6 of **3b** (1.384 and 1.360 Å respectively) are compared with the corresponding ones in the NH-form (**1b**) (1.362 and 1.342 Å, respectively). The bond distances of the carbonyl groups are 1.254 and 1.262 Å for **3b** and the NH-form (**1b**) of **1a**, respectively, and are in good agreement within the experimental errors. It is well known that the dihedral angle of the related thioxanthene nucleus is quite sensitive to alterations in the electronic nature of its substituents,$^{13)}$ as seen in the change of the dihedral angle in going from phenothiazine (158.5 °) to thioxanthen-9-ol (132.4°).$^{13-16)}$ Table II gives the best least-squares planes together with the displacement of atoms from the best planes. A final point of particular interest was the dihedral angles between the planes of the pyrazol-3-one and phenyl rings; 47.8° for **3b** compared with 23° and 38° for **1b** and **1c**, respectively.$^{8)}$

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