The Crystal and Molecular Structure of 3-Methyl-3-pyrazolin-5-one

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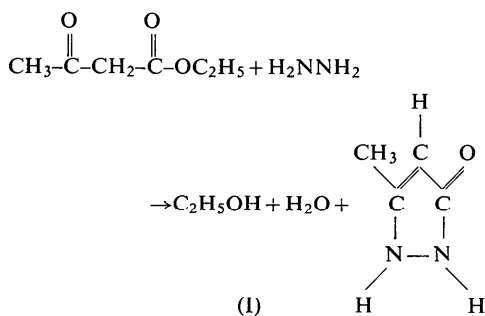*Chemistry Department, University of Maryland, College Park, Maryland* 20742, *U.S.A.*

The crystal structure of 3-methyl-3-pyrazolin-5-one ($C_4H_6N_2O$) has been determined by X-ray diffraction as a model for the pyrazolin-5-one compounds. The space group is $P2_1/a$. Cell dimensions are $a = 10.520$ (3), $b = 6.499$ (2), $c = 8.052$ (1) Å, $\beta = 114.45$ (1)°, $Z = 4$, $D_x = 1.299$ (1) g.cm^{-3}. Three-dimensional X-ray data were collected using Mo $K\alpha$ radiation. The structure was solved using statistical methods of phase determination, and refined by the full-matrix least-squares method to $R = 0.071$ (unit weights). Hydrogen-bonded layers are found parallel to the ab plane. The predominant tautomer is established as 3-methyl-3-pyrazolin-5-one. A comparison of structures based on data gathered by moving-crystal moving-counter and stationary-crystal stationary-counter methods shows no significant differences in bond lengths and angles calculated from atomic parameters refined on either set of data.

Introduction

In the process of a literature search for bond lengths, it became clear that few crystallographic structure determinations have been reported for oxo derivatives of the pyrazole system. Structural data may be found for derivatives of antipyrine, both the *p*-bromo derivative (Romain, 1958) and also several metal complexes (Vijayan & Viswamitra, 1966, 1967, 1968). Recently, bond lengths and angles were determined for 1,1-dimethyl-3-phenylpyrazolium 5-oxide (De Camp & Stewart, 1970) which suggested unusual bonding in the heterocyclic ring. The lack of appropriate data for comparison prompted us to prepare and determine the structure of a simple pyrazolin-5-one compound. Synthetic considerations made 3-methyl-3-pyrazolin-5-one the logical choice.

The technique of Knorr (1883) [reaction (I)] was used

$$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OC_2H_5 + H_2NNH_2$$

$$\rightarrow C_2H_5OH + H_2O + \quad \begin{array}{c} H \\ | \\ CH_3 \; C \; O \\ \diagdown / \diagdown / \\ C \quad C \\ | \quad | \\ N — N \\ / \quad \diagdown \\ H \quad\quad H \end{array}$$

(I)

for the preparation of 3-methyl-3-pyrazolin-5-one, referred to hereafter as MPYRAZ. The melting point [experimental 215°, literature value 215° (Wiley & Wiley, 1964)], elemental analysis [calculated for $C_4H_6N_2O$: C, 49.98; H, 6.12; N, 28.57; O, 16.33%; found: C, 49.20; H, 6.17; N, 28.50; O (by difference), 16.13%] and infrared spectrum (Refn, 1961) all confirmed the chemical structure of the product.

Experimental

Crystals of MPYRAZ were grown from dimethylformamide solution, after attempts with other solvents had produced microcrystalline masses. Monoclinic plates were formed which cleaved readily normal to the short axis. X-ray examination of these crystals showed repeatedly that they were not single, but consisted of several individuals stacked in approximately the same orientation. In the usual case, the various parts of the crystal differed by a rotation of a few degrees around the short axis of the plate. Since this axis was parallel to the direction of the polarized light under the microscope, detection of the multiple nature of the crystals was difficult unless the plate was viewed edge-on.

All crystals examined in this manner showed varying degrees of mis-stacking. One individual was finally found that appeared to be single both when examined by polarized light and from inspection of X-ray photographs, and it was selected for intensity measurements on the diffractometer. It should be noted that even this crystal was eventually shown to be composed of two individuals that were mis-stacked by approximately 0.5°. The assignment of unit-cell axes was such that the

Table 1. *Crystal data*

3-Methyl-3-pyrazolin-5-one, $C_4H_6N_2O$; F.W. 98.11;
  m.p. 215°C
Monoclinic, $a = 10.520 \pm 0.003$, $b = 6.499 \pm 0.002$,
  $c = 8.052 \pm 0.001$ Å, $\beta = 114.45 \pm 0.01°$, at 21 °C
Volume of unit cell = 501.5 ± 0.4 Å^3
Calculated density = 1.299 ± 0.001 g.cm^{-3} ($Z = 4$)
Mo $K\alpha$ radiation ($\lambda = 0.71069$ Å), Nb filter
Crystal size $0.3 \times 0.2 \times 0.2$ mm
μ(Mo $K\alpha$) = 1.04 cm^{-1}
1393 reflections measured (934 observed) to 60° 2θ
Systematically absent reflections: $h0l$ for $h = 2n + 1$; $0k0$ for
  $k = 2n + 1$
Space group $P2_1/a$ (C^5_{2h})

cleavage faces were (001). Unit-cell dimensions were determined by least-squares refinement based on accurate measurements of nineteen 2θ values. The crystal data for MPYRAZ are summarized in Table 1.

The crystal was mounted for study on the diffractometer in such a manner that the c axis of the unit cell was collinear with the φ axis of the quarter-circle Eulerian cradle. Several intense reflections at various settings of χ and φ were carefully scanned to detect any anisotropy of the peak-profile characteristics. At this point, it became clear that the supposedly single crystal was actually two individuals differing in orientation by approximately 0·5° in φ at $\chi=0°$. Because this appeared to be the best crystal which could be obtained, we proceeded with data collection. However, the split nature of the crystal meant that both crystals could not be brought into the diffracting condition simultaneously at low settings of χ. Consequently, the scanning range was increased from its recommended value (Alexander & Smith, 1962) to 2·3 + tan θ degrees, so that the integrated intensity of both crystals would be measured. However, this implied that each crystal would necessarily be slightly mis-set in φ by an amount that would be greatest for the $hk0$ reflections, and progressively less for reflections with higher values of l (and consequently higher settings of χ). At the chosen φ settings, the integrated intensity of a strong $hk0$ reflection was found to be unaffected by changes of about 0·2° on φ. This demonstrated that the approximation of choosing an intermediate value of φ appeared to be an appropriate compromise with reality.

Measurements of reflection intensities were made by both the moving-crystal moving-counter (2θ scan) and stationary-crystal stationary-counter (peak height) methods. Peak-height measurements were converted to integrated intensities by the use of

$$I_s = I_p \times (0\cdot8349 + 1\cdot6945t + 8\cdot8191t^2 - 8\cdot4871t^3), \quad (1)$$

where I_s is the calculated integrated intensity, I_p is the measured peak-height intensity and t is tan θ. The equation was developed by a linear least-squares procedure from 272 comparisons of peak height and scan measurements of the same reflection. Based on a comparison of the measured and calculated values of the integrated intensity for these 272 reflections, the conversion process had an average error of 22%. This high value appears to be due to errors in the peak-height measurements, which are more sensitive to small errors in the angular settings of the diffractometer, and which are more seriously affected by the splitting of the crystal.

A total of 4625 individual measurements of 1393 independent reflections were made, of which 1935 were peak height and 2690 were scan measurements. Measurements were made by both methods in order to investigate the effect of peak-height measurements on the final structure. Reflections in the hkl and $\bar{h}kl$ octants of reciprocal space were measured. In addition,

Table 2. *Atomic positional and thermal parameters for 3-methyl-3-pyrazolin-5-one*

All values are multiplied by 10^4; the anisotropic temperature factor is given by
$$\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)];$$
an asterisk (*) indicates parameters on which refinements were not made; U(isotropic) is defined as $(U_{11}U_{22}U_{33})^{1/3}$

	X/a	Y/b	Z/c	U_{11}	U_{22}	U_{33}	$2U_{12}$	$2U_{13}$	$2U_{23}$	U(isotropic)
O	3823 (2)	4298 (3)	6098 (3)	0483 (14)	0554 (13)	0692 (16)	0139 (9)	0381 (11)	0217 (10)	0570
N(1)	5846 (2)	2890 (4)	6179 (3)	0386 (14)	0409 (13)	0409 (14)	0025 (13)	0221 (11)	0053 (12)	0401
N(2)	6617 (2)	1144 (3)	6812 (3)	0344 (14)	0449 (13)	0327 (11)	0060 (13)	0153 (11)	0005 (10)	0370
C(3)	6011 (3)	0025 (4)	7667 (3)	0390 (14)	0404 (15)	0240 (11)	−0041 (13)	0093 (11)	−0039 (12)	0336
C(4)	4854 (3)	1027 (4)	7587 (4)	0414 (19)	0496 (17)	0341 (14)	−0038 (13)	0196 (14)	0051 (12)	0412
C(5)	4739 (3)	2855 (4)	6592 (4)	0344 (14)	0437 (15)	0376 (14)	0000 (13)	0174 (11)	0002 (12)	0384
C(6)	6647 (4)	−1967 (5)	8534 (5)	0692 (28)	0533 (21)	0488 (19)	0117 (19)	0174 (18)	0121 (17)	0565
H(1)	6118 (33)	3869 (41)	5532 (42)							0646 (101)
H(2)	7431 (32)	0950 (39)	6557 (39)							0583 (88)
H(4)	4244 (27)	0629 (35)	8064 (37)							0405 (76)
H(61)	5823 (45)	−2811 (58)	8374 (51)							1013*
H(62)	7292 (42)	−1589 (59)	9613 (59)							1013*
H(63)	7080 (39)	−2666 (53)	7776 (54)							1013*

for reflections below 2θ of 30°, reflections in the symmetrically equivalent octants hkl and $\bar{h}kl$ were also measured. Multiple measurements of equivalent reflections were averaged, with a general agreement of 15%. Structure-factor amplitudes were calculated, 934 being observed at the 3σ level of significance. Lorentz and polarization corrections were applied, but no absorption correction was applied.

Structure solution and refinement

Quasi-normalized structure-factor amplitudes (ε's) were calculated (Dickinson, Stewart & Holden, 1966). Phases were determined statistically for 140 reflections with high ε values following the modified symbolic addition procedure used in $XRAY67$ (Stewart, 1970). An E map constructed with these phases revealed seven peaks

forming a chemically reasonable molecule of the anticipated geometry. The two nitrogen atoms were identified from the bonding geometry of the ring. The oxygen atom could not be distinguished with certainty, so all other atoms were tentatively identified as carbon. After two cycles of full-matrix least-squares refinement, bond lengths clearly differentiated between exocyclic bonds, and the oxygen atom could be determined. Several additional refinement cycles, varying positional and anisotropic thermal parameters, reduced the unweighted R index to 10%. The quantity minimized was $\Sigma w||F_o| - |F_c||$, where w is the weight defined as

$$w = \frac{0.1}{\text{maximum } (\sigma F_{\text{rel}}, \, 0.005 \, F_{\text{rel}})}. \tag{2}$$

Hydrogen atoms were located from a difference map

Table 3. *Comparison of observed and calculated structure factors*

Values of F_o and F_c are multiplied by 10. Unobserved reflections are indicated with an asterisk.

at this point, and the refinement continued, varying positional parameters for all atoms, isotropic thermal parameters for hydrogen, and anisotropic thermal parameters for all other atoms. The temperature factors for the methyl hydrogen atoms became unreasonably high, and were removed from the refinement, assigning them a constant value of 8·0 Å . Similar failure of methyl hydrogen atoms to refine has been observed for methyl groups with high thermal motion (Stout, Stout & Welsh, 1963).

The final R indexes were 0·071 (unit weights) and 0·069 (weighted) including all reflections observed at the 3σ level. This large value of R is probably due to the difficulty with the splitting described above. In the last cycle, no parameter was shifted by more than 0·51 of its estimated standard deviation. Only 35 of the 459 reflections coded as unobserved had F_c greater than the threshold value of F_o based on the 3σ criterion. A difference map constructed from the final set of positional and thermal parameters was essentially featureless, showing no differences between the observed and calculated electron density greater than 0·3 Å^{-3}. The final atomic positional and thermal parameters are shown in Table 2. A comparison of the observed and calculated structure factors is found in Table 3. The atomic scattering factor calculations were taken from *International Tables for X-ray Crystallography* (1968) for C, N, and O. The values for hydrogen were taken from Stewart, Davidson & Simpson (1965).

To demonstrate that the conversion of peak-height measurements to integrated intensities by use of equation (1) did not introduce any significant systematic error, full-matrix least-squares refinements were carried out on data sets consisting of (a) only measurements made by the 2θ-scan method, (b) all peak-height measurements, plus the 272 peak-to-scan comparisons, with equation (1) applied to the peak-height measurements, and (c) the combination of sets (a) and (b). Two cycles of refinement gave R indexes of 0·060 for set (a) and 0·095 for set (b), in comparison with 0·071 for the merged set (c). When compared to the scan-data set (a), 34% of the final parameters from set (b) and 12% of the final parameters based on set (c) were different at a 3σ level of significance. Almost without exception, the affected parameters were temperature factors (principally U_{13} and U_{33}) and hydrogen positional parameters. Significant differences were also found for the F_c scale factor in both sets (b) and (c). Bond lengths and angles, however, were found to be substantially identical, except for a few angles involving hydrogen atoms. None of the observed differences would have caused any alteration in our interpretation of the structure. Similar results have been reported by Palenik (1970).

Discussion of the structure

The final structure, including bond lengths and angles, is shown in Fig. 1. The packing of the molecules into the unit cell is illustrated in Fig. 2.

The molecule of MPYRAZ is essentially planar, with all cyclic atoms showing trigonal bonding, corresponding to Fig. 3(e). A least-squares plane was calculated based on seven atoms (Schomaker, Waser, Marsh & Bergman, 1959). The results are shown in Table 4, including the distance of all other atoms from the plane. The standard deviation of the distances of the defining atoms from the plane is 0·009 Å.

Table 4. *Least-squares plane for*
3-*methyl*-3-*pyrazolin*-5-*one*

Equation of plane: $2 \cdot 105x + 3 \cdot 115y + 5 \cdot 601z = 5 \cdot 575$, where x, y, and z are the fractional unit-cell coordinates of points lying on the plane.

	Distance from plane (Å)
*O	−0·016
*N(1)	0·017
H(1)	0·012
*N(2)	−0·010
H(2)	−0·030
*C(3)	−0·007
*C(4)	0·016
H(4)	0·027
*C(5)	0·005
*C(6)	−0·003
H(61)	−0·523
H(62)	0·881
H(63)	0·557

* Indicates an atom defining the plane.

The trigonal hybridization of C(4) was an unexpected finding. Based on the structure of the molecules involved in reaction (1) as well as on the evidence revealing that C(4) shows reactivity typical of an active methylene group, MPYRAZ has been considered to have structure 3(a), which is a 2-pyrazolin-5-one (Wiley & Wiley, 1964) structure. This requires that C(4) be tetrahedral, that N(2) have no hydrogen atom bonded to it, and that the N(2)–C(3) bond be a double bond. This
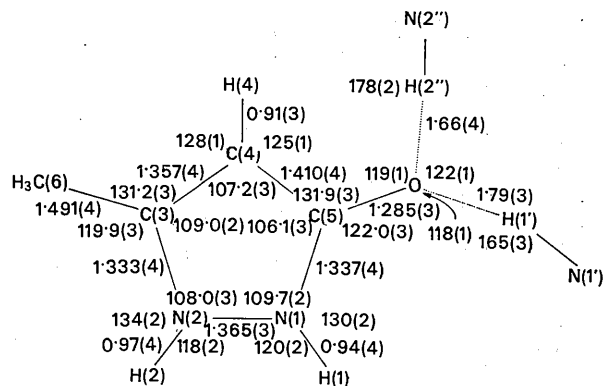

Fig. 1. Bond lengths (in Å) and angles (in degrees) for 3-methyl-3-pyrazolin-5-one. The estimated standard deviation in the last digit is given in parentheses. Symmetry operations to produce hydrogen-bonded atoms are: prime $' = 1 - x, 1 - y, 1 - z$; double prime $'' = -\frac{1}{2} + x, \frac{1}{2} - y, z$.
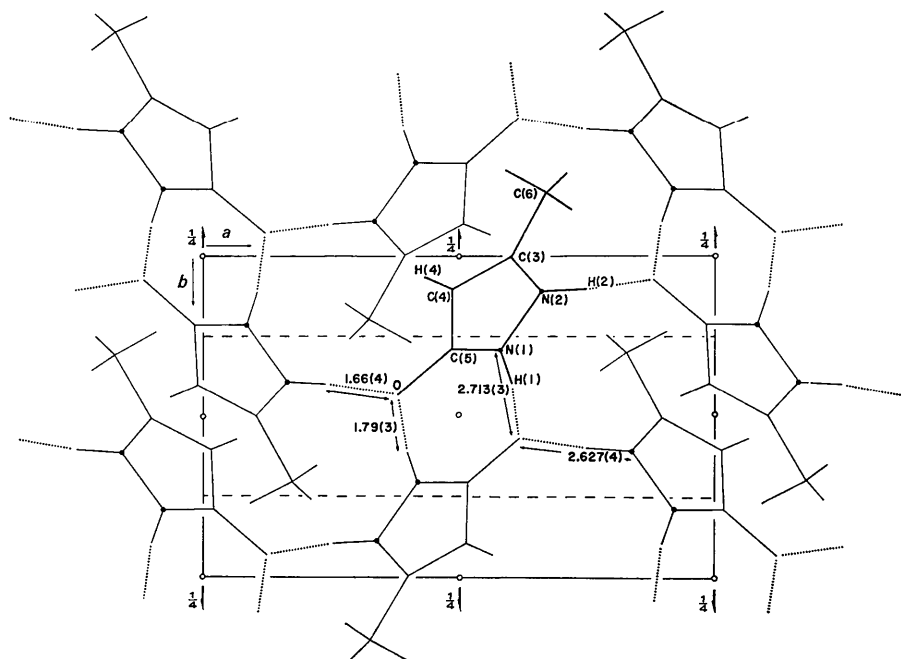
Fig. 2. Hydrogen-bonding network in 3-methyl-3-pyrazolin-5-one viewed along c^*. Nitrogen atoms are indicated by filled circles and hydrogen bonds by dotted lines. The labelled molecule corresponds to the parameters given in Table 2. Hydrogen-bonding distances are given in Å.

postulated structure clearly does not conform to our observed structure. N(2)–C(3) is intermediate in length between the C–N bond lengths found in melamine (Hughes, 1941) and sym-triazine (Coppens, 1967). Bond characters are fixed by symmetry in these cases at $1\frac{1}{3}$ and $1\frac{1}{2}$, respectively, and the bond lengths are correspondingly reported to be 1·346 and 1·313 Å. The length found for C(3)–C(4) is several e.s.d.'s longer than the normal C–C double bond of 1·335 (5) Å (Sutton, 1965), but substantial double-bond character is clearly present. Our structural evidence, as a result, clearly shows that MPYRAZ must be regarded chemically as 3-methyl-3-pyrazolin-5-one.

Each molecule of MPYRAZ forms N–H···O hydrogen bonds with two other molecules, as shown in Fig. 2. The carbonyl oxygen acts as an acceptor of hy-

drogen bonds from N(1) of the molecule related by a center of symmetry at $\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$, and from N(2) of the molecule related by the a glide plane at $y=\frac{1}{4}$. The O···H(2″)–N(2″) bond has a shorter-than-average length, suggesting that it is unusually strong. The tendency of hydrogen bonds to be linear (Donohue, 1968) and for the hydrogen atoms involved in the bonds to be close to the plane of the molecule (Donohue, 1969) has been noted. Our results support his observations, since the stronger bond is not only linear within experimental error, but is also closer to the plane defined by O, N(1′), and N(2″). H(1′) lies 0·09 Å from this plane, while H(2″) is only 0·02 Å distant.

The length of the C(5)–O bond was found to be 1·285 (5) Å. This is clearly longer than the generally accepted value of 1·215 (5) Å for aldehyde and ketone carbonyls (Sutton, 1965). Mackay & Mathieson (1969) have reported a lengthening of approximately 0·07 Å in a lactam carbonyl, strongly hydrogen-bonded to a water molecule. Such inductive effects may also account for the abnormally long C–O bond in MPYRAZ.

The tautomerism of the pyrazolin-5-one class has been extensively studied by spectroscopic methods. De Stevens, Halamandaris, Wenk & Dorfman (1959) reported strong absorption in the infrared spectrum of MPYRAZ in the region from 2700 to 2400 cm⁻¹, and concluded that the predominant structure was the zwitterionic form 3(b). Refn (1961) noted the absence of carbonyl absorption in the solid state infrared spectra of several pyrazolin-5-one compounds. In each case, an aromatic structure was not excluded by sub-
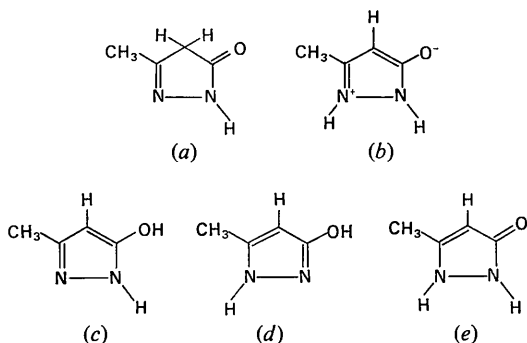

Fig. 3. Proposed structures for 3-methyl-3-pyrazolin-5-one.

stitution. Carbonyl absorption was observed, however, in cases where substitution required the system to be nonaromatic, e.g., disubstitution at C(4). The conclusion was drawn that, for compounds similar to MPYRAZ, a tautomeric equilibrium between the aromatic hydroxypyrazole structures 3(c) and 3(d) was preferred. Vinokurov, Troitskaya, Grandberg & Pentin (1963) have also found spectroscopic evidence supporting the existence of the hydroxypyrazole forms in the crystalline state.

In contrast, Jones, Ryan, Sternhell & Wright (1963) made infrared and n.m.r. studies which suggested the absence of any tautomeric equilibrium. In the case of MPYRAZ, a keto structure 3(e) was found to be favored in $CHCl_3$, D_2O, or pyridine solution. UV studies (Katritzky, Maine & Golding, 1965) suggest a shift of the tautomeric equilibrium with solvents of different polarity. Aqueous solutions of MPYRAZ were found to favor forms such as 3(e) while the predominant structure in cyclohexane solution was 3(d). Evans, Whelan & Johns (1965) concluded that 3(c) is the most representative structure for MPYRAZ based on solid-state infrared spectra. N.m.r. data supported structure 3(e) in pyridine solution, and also suggested that H(4) is readily exchanged by recrystallization from D_2O. Elguero, Jacquier & Tarrago (1967) pointed out that the findings reported in the literature clearly indicate the predominance of solvent effects in determining the nature of the tautomeric equilibrium.

An attempt was made to resolve the above situation with respect to the most stable tautomer of MPYRAZ in the solid state. The coordinates of H(1) were changed to the position that H(1) would occupy if it were part of a hydroxyl group which was hydrogen-bonded to N(1). Two cycles of full-matrix least-squares refinement including all parameters (except the methyl-hydrogen temperature factors) shifted the H atom back almost to its original position. Similar treatment of H(2) produced similar results. While this cannot exclude minor contributions from structures such as 3(c) or 3(d), it appears that our data favor the predominance of the keto tautomer 3(e) in the crystalline state.

Crystallographic computations were carried out using *X-RAY 67* (Stewart, 1967) on a Univac 1108 computer. Computer time was provided by the Computer Science Center, University of Maryland, under grant Nsg 398 from the National Aeronautics and Space Administration. Use of the diffractometer was provided through the courtesy of the Biochemistry Division, Walter Reed Army Institute of Research. The authors would like to acknowledge the assistance of Mr Jerald J. Zeger who performed the synthetic work, and Dr Franz Kasler who performed the organic microanalyses.

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