X-ray Structure Analysis Online

Cocrystallization of Two Tautomers: 1-Phenyl-3-(propan-2-yl)-1,2-dihydro-pyrazol-5-one and 1-Phenyl-3-(propan-2-yl)-1*H*-pyrazol-5-ol

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Two different tautomeric forms, namely the *keto* [1-phenyl-3-(propan-2-yl)-1,2-dihydro-pyrazol-5-one] and the *enol* form, [1-phenyl-3-(propan-2-yl)-1*H*-pyrazol-5-ol], $C_{12}H_{14}N_2O{\cdot}2C_{12}H_{14}N_2O$, are present in the crystal in a 1:2 ratio. During crystallization, 1-phenyl-3-(propan-2-yl)-1,2-dihydro-pyrazol-5-one undergoes tautomerization to afford a corresponding *enol via* proton transfer reaction. The compound crystallizes in the triclinic space group $P\bar{1}$ with the following unit-cell parameters: a = 11.1593(3)Å, b = 11.2247(3)Å, c = 14.1140(4)Å, α = 73.333(3)°, β = 88.286(2)°, γ = 82.767(2)°, Z = 2. The crystal structure was solved by direct methods and refined by full-matrix least-squares procedures to a final R-value of 0.0405 for 4611 observed reflections. The dihedral angles between the mean planes through the phenyl ring and the pyrazole ring are: 28.04(5)°, 47.38(5)° and 49.32(6)° for molecules I, IIA, IIB, respectively. The crystal structure is stabilized by intermolecular N–H···N, O–H···O, O–H···N, C–H···O and C–H···π hydrogen bonds.

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Pyrazoles are a class of heterocyclic compounds whose members exhibit a wide range of interesting biological properties *viz.* antibacterial,[1] insecticidal,[2] anticancer,[3] anti-HIV,[4] herbicidal[5] and anti-inflammatory[6] *etc.* and are quite useful to the pharmaceutical industry for new drug formulations. The biological properties of pyrazole derivatives have propitiated the development of synthesis methods for these, and also for precursors and analogous compounds. Considering the importance of pyrazole derivatives, it was thought to be worthwhile to synthesize a compound incorporating a pyrazole moiety. The compound has been synthesized by a mixture of methyl-isobutylacetate (0.01 mol) and phenylhydrazine (0.01 mol) in methanol (10 mL). In this reaction mixture, two drops of acetic acid were added and the solution was refluxed for 5 h. After completion of the reaction, the solvent was removed under vacuum, and the resulting solid was crystallized from methanol to afford crystals of suitable size for X-ray work. This compound undergoes tautomerism by proton transfer between

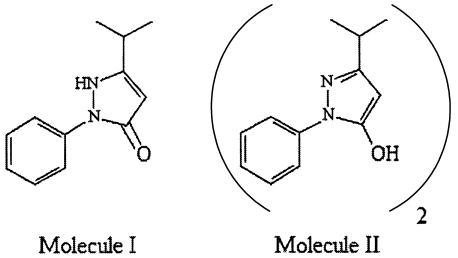

Fig. 1 Chemical structure of 1-phenyl-3-(propan-2-yl)-1,2-dihydro-pyrazol-5-one (molecule I) and 1-phenyl-3-(propan-2-yl)-1*H*-pyrazol-5-ol (molecule II).

Table 1 Crystal and experimental data

Chemical formula: $C_{12}H_{14}N_2O{\cdot}2C_{12}H_{14}N_2O$	
Formula weight = 606.76	
T = 293 K	
Crystal system: triclinic	Space group: $P\bar{1}$
a = 11.1593(3)Å	α = 73.333(3)°
b = 11.2247(3)Å	β = 88.286(2)°
c = 14.1140(4)Å	γ = 82.767(2)°
V = 1680.13(8)Å^3	Z = 2
D_x = 1.199 g/cm^3	D_m (floatation) = not measured
Radiation: Mo K_α (λ = 0.71073 Å)	
μ(Mo K_α) = 0.078 mm^{-1}	F(0 0 0) = 648
Crystal size = 0.3 × 0.2 × 0.1 mm^3	
No. of reflections collected = 23149	
No. of independent reflections = 5862	
θ range for data collection: 3.44 to 24.99°	
Data/Restraints/Parameters = 5862/0/542	
Goodness-of-fit on F^2 = 1.016	
R indices [$I > 2\sigma(I)$]: $R1$ = 0.0405, $wR2$ = 0.0966	
R indices (all data): $R1$ = 0.0556, $wR2$ = 0.1044	
$(\Delta/\sigma)_{max}$ = 0.001 for y H83	
$(\Delta\rho)_{max}$ = 0.194 eÅ^{-3}	$(\Delta\rho)_{min}$ = –0.188 eÅ^{-3}
Measurement: *X'calibur system—Oxford diffraction make*,	
Programs system: SHELXL-97, Crysalis *RED*	
Structure determination: SHELXS-97	
CCDC deposition number: 824525	

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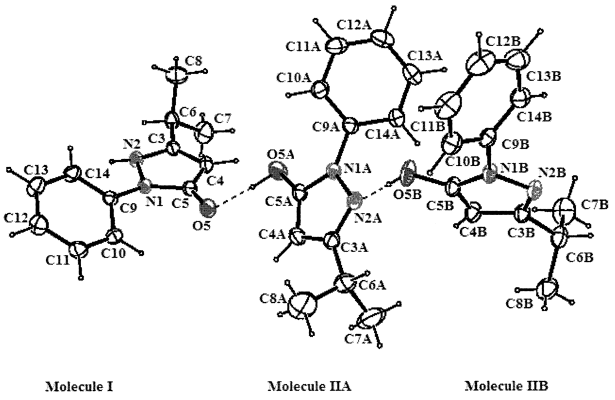

Fig. 2 *ORTEP* view of the molecules, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms are shown as small spheres of arbitrary radii.

the hydroxyl O atom and the N2 atom forming two tautomers, *keto* form (molecule I) and *enol* form (molecule II) (Fig. 1), and the two different tautomeric forms of the same molecule cocrystallized in a 1:2 ratio.

The crystallographic data are summarized in Table 1.

An ORTEP view of all the three molecules[8] [molecule I (*keto* form); molecule IIA and IIB (*enol* form with two independent molecules in the asymmetric unit)] is shown in Fig. 2. Selected bond lengths, bond angles and torsion angles are given in Table 2. When compound I undergoes tautomerisation during crystallization to afford corresponding *enol* via proton transfer reaction, an appreciable decrease in the N2–C3 and C4–C5 distance is observed [N2–C3 = 1.346(2)Å *versus* N2A–C3A = 1.326(2)Å; N2B–C3B = 1.327(2)Å and C4–C5 = 1.411(2)Å *versus* C4A–C5A = 1.368(2)Å; C4B–C5B = 1.368(2)Å]. A concomitant increase in the C3–C4 and C5–O5 distance has also been observed [C3–C4 = 1.366(2)Å *versus* C3A–C4A = 1.397(2)Å; C3B–C4B = 1.399(2)Å and C5–O5 = 1.261(2)Å *versus* C5A–O5A = 1.326(2)Å; C5B–O5B = 1.325(2)Å]. Hence the above-mentioned C–C, C–N, and C–O bond lengths (Table 2) help to establish the *keto* form of molecule I and the *enol* form of molecule IIA and molecule IIB, respectively. In addition, the magnitude of planarity for the molecules in *keto* and *enol* forms is different. The pyrazole and the phenyl rings are inclined at an angle of 28.04(5)° in molecule I, 47.38(5)° in molecule IIA and 49.32(6)° in molecule IIB.

The six C–C bond lengths in the phenyl ring lie in the range 1.378(2)Å – 1.386(2)Å, molecule I; 1.370(3)Å – 1.387(2)Å, molecule IIA; 1.371(3)Å – 1.390(3)Å, molecule IIB. The pyrazole ring and the phenyl ring are individually planar with maximum deviations from the respective least-squares planes of: –0.023(1)Å for C5 and –0.008(2)Å for C14 (molecule I); –0.004(2)Å for C3A and –0.008(2)Å for C14A (molecule IIA); 0.006(1)Å for C3B and 0.011(2)Å for C14B (molecule IIB). Both intrá- and intermolecular hydrogen bonds are found in the crystal structures of the tautomers. The two tautomers are connected *via* intermolecular N–H···N, O–H···O, O–H···N and C–H···O hydrogen bonds. Despite the rich availability of aryl rings, there are no aromatic π-π stacking interactions in the structure. However, C–H···π hydrogen bonds are present. Details of N–H···N, O–H···O, O–H···N, C–H···O and C–H···π hydrogen bonds are given in Table 3S.

Table 2 Selected bond lengths (Å), bond angles (°) and torsion angles (°) for non hydrogen atoms (e.s.d.'s are given in parentheses)

	Molecule I	Molecule IIA	Molecule IIB
N1-N2	1.382(1)	1.377(1)	1.384(1)
N2- C3	1.346(2)	1.326(2)	1.327(2)
C3-C4	1.366(2)	1.397(2)	1.399(2)
C4-C5	1.411(2)	1.368(2)	1.368(2)
N1- C5	1.387(2)	1.358(2)	1.352(2)
C5 -O5	1.261(2)	1.326(2)	1.325(2)
C3- N2- N1	108.4(1)	105.6(1)	104.7(1)
C5 -N1 -N2	108.6(1)	110.3(1)	110.8(1)
C5 -N1 -C9	130.0(1)	129.3(1)	127.0(1)
N2 -N1 -C9	119.6(1)	120.3(1)	121.1(1)
O5 -C5 -N1	122.4(1)	119.1(1)	118.8(1)
N1 -C5 -C4	105.5(1)	107.3(1)	107.4(1)
N2 -C3 -C4	108.9(1)	110.9(1)	111.5(1)
N2 -C3 -C6	119.1(1)	120.2(1)	121.2(1)
C5 -N1 - C9 -C10	-38.0(2)	49.2(2)	54.7(2)
N2 - N1 - C9 - C10	159.0(1)	-133.7(1)	-138.1(1)
N2 - N1 - C9 - C14	-19.8(2)	45.8(2)	42.8(2)
C4 - C3 - C6 - C7	-82.4(2)	75.0(2)	69.2(2)
N2 - C3 - C6 - C8	-142.3(2)	128.9(2)	125.4(2)

In conclusion, a crystal structure of a pyrazole derivative has been determined by X-ray crystallographic techniques. Two different tautomeric forms are found in the solid state, and these are hydrogen bonded to one another.

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References

1. A. Tanitame, Y. Oyamada, and K. Ofuji, *J. Med. Chem.*, **2004**, *47*, 3693.
2. Y. Kondo, T. Kiji, M. Noguchi, and Y. Manabe, Jpn. Kokai Tokkyo Koho JP 08, 311, 036, Chem Abstr., **1997**, *126*, 89367r.
3. D. Berta, E. Felder, A. Valpetti, and M. Villa, PCT Int. Appl. WO 02 62804 (Cl.CO7D498/04; Chem Abstr., **2002**, *137*, 169517g.
4. S. D. Bhardwaj and V. S. Jolly, *Oriental J. Chem.*, **1996**, *12(2)*, 185 (Eng.); Chem. Abstr. **1997**, *126*, 1442174.
5. Siddal, T. Lyman, B. Zaltan, and G. Gail, PCT Int. Appl. WO 98, 52, 926, Chem Abstr., **1999**, *130*, 25068u.
6. A. Kumar, R. S. Verma, and B. P. Jagu, *J. Ind. Chem. Soc.*, **1990**, *67*, 120.
7. G. M. Sheldrick, *Acta Cryst.*, **2008**, *A64*, 112.
8. L. J. Farrugia, *J. Appl. Cryst.*, **1997**, *30*, 565.