X-RAY STUDIES OF 2-AMINO-4-ISOPROPYL-5-OXO-4,5-DIHYDROPYRANO[3,2-*c*]CHROMENE-3-CARBONITRILE

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Keywords: 2-amino-4-isopropyl-5-oxo-4,5-dihydropyrano[3,2-*C*]chromene-3-carbonitrile, X-ray structure, space group, direct methods, π-π interactions.

The title compound, 2-amino-4-isopropyl-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile ($C_{16}H_{14}N_2O_3$) is synthesized *via* one-pot multi-component reaction (MCR) at room temperature using commercially available urea as inexpensive and environmentally benign organo catalyst and crystallizes in the triclinic space group P -1 with the unit-cell parameters: a = 7.8231(4), b = 8.0622(4), c = 12.3038(5) Å, α = 99.443(4)º, β = 102.419(4)º, γ = 109.907(4)º and Z = 2. The crystal structure was solved by direct methods using single-crystal X-ray diffraction data collected at room temperature and refined by full-matrix least-squares procedures to a final R-value of 0.0405 for 2118 observed reflections. The packing of molecules within the unit cell is stabilized by N-H…O and N-H…N type of intermolecular hydrogen interactions. In addition C-H…π and π-π interactions are also observed in the crystal structure.

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Introduction

4*H*-Pyran-annulated heterocyclic scaffolds represent a "*privileged*" structural motif well distributed in naturally occurring compounds[1] with a broad spectrum of significant biological activities.[2] Synthetic 2-amino-3-cyano-4*H*-pyrans have been evaluated to possess potent anticancer,[3] antibacterial,[4] antifungal,[5] and anti-rheumatic[6] properties. In this communication, we wish to report the crystal structure of a 4*H*-pyran-annulated heterocyclic compound, namely 2-amino-4-isopropyl-5-oxo-4,5-dihydropyrano[3,2-*c*] chromene-3-carbonitrile which is synthesized *via* one-pot multi-component reaction (MCR) at room temperature using commercially available urea as inexpensive and environmentally benign organocatalyst. The structure of the title compound was elucidated by spectral methods and XRD studies.

Experimental

An oven-dried screw cap test tube was charged with a magnetic stir bar, isobutyraldehyde (0.072 g, 1 mmol), malononitrile (0.066 g, 1.1 mmol), urea (0.007 g, 10 mol % as organo-catalyst), and EtOH:H_2O (1:1 v/v; 4 ml) in a sequential manner; the reaction mixture was then stirred vigorously at room temperature for about 30 min. After that, 4-hydroxycoumarin (0.162 g, 1 mmol) was added to the stirred reaction mixture, and the stirring was continued for 10 h.[7] The progress of the reaction was monitored by TLC. On completion of the reaction, a solid mass precipitated out that was filtered off followed by washing with aqueous ethanol to obtain crude product which was then purified just by recrystallization from ethanol without using column chromatography. White solid. (0.240 gm, yield 85 %). m.p. 524-526 K. IR (KBr) ν_{max}/cm^{-1}: 3379, 3308, 3198, 2962, 2189, 1707, 1666, 1605, 1383, 1317, 1261, 1178, 1061, 960, 754. ^{1}H NMR (400 MHz, DMSO-*d*6) δ/ppm: 7.81 (1H, d, J = 7.6 Hz, , aromatic H), 7.69 (1H, t, J = 7.2 Hz, aromatic H), 7.46 (2H, d, J = 8.0 Hz, , aromatic H), 7.38 (2H, s, NH_2), 3.31 (1H, d, J = 2.8 Hz, C*H*), 2.00 (1H, m, C*H*), 1.01 (3H, d, J = 6.8 Hz, CH_3), 0.69 (3H, d, J = 6.4 Hz, CH_3). ^{13}C NMR (100 MHz, DMSO-*d*6) δ/ppm: 161.21, 160.48, 154.95, 152.46, 133.12, 125.00, 122.53, 121.08, 116.94, 113.38, 105.25, 51.88, 37.53, 33.18, 20.57, 16.89. TOF-MS: 305.0887 $[M+Na]^+$. Elemental analysis: Calcd. (%) for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92; found: C, 68.03; H, 4.98; N, 9.94.

The structure of 2-amino-4-isopropyl-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile was confirmed by analytical as well as spectral studies including FT-IR, ^{1}H NMR, ^{13}C NMR, and TOF-MS. Single crystals were obtained from DMSO as a solvent. For crystallization 50 mg of compound dissolved in 5 ml DMSO and left for several days at ambient temperature which yielded white block shaped crystals. The chemical structure of title compound is shown in Figure 1.

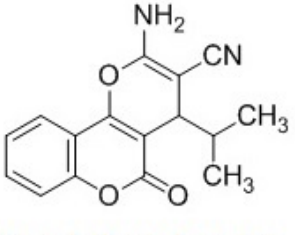

Figure 1. Chemical structure of 2-amino-4-isopropyl-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile

X-Ray Structure determination

X-ray intensity data of 11113 reflections (of which 2695 unique) were collected on *X'calibur* CCD area-detector diffractometer equipped with graphite monochromated MoKα radiation (λ = 0.71073 Å). The crystal used for data collection was of dimensions 0.30 x 0.20 x 0.20 mm. The cell dimensions were determined by least-squares fit of angular settings of 5360 reflections in the θ range 3.50° to 28.97°**.** The intensities were measured by ω scan mode for θ ranges 3.51° to 25.99°. 2118 reflections were treated as observed (I > 2σ(I)). Data were corrected for Lorentz, polarization and absorption factors. The structure was solved by direct methods using SHELXS97.[8] All non-hydrogen atoms of the molecule were located in the best E-map. Full-matrix least-squares refinement was carried out using SHELXL97.[8] The final refinement cycles converged to an R = 0.0405 and wR (F^2) = 0.1007 for the observed data. Residual electron densities ranged from -0.161 < Δρ < 0.179 eÅ^{-3}. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4). The crystallographic data are summarized in Table 1.

Table 1. Crystal data and other experimental details

CCDC Number	**1409950**
Crystal description	Block
Crystal size	0.30 x 0.20 x 0.20 mm
Empirical formula	$C_{16}H_{14}N_2O_3$
Formula weight	282.29
Radiation, Wavelength	MoK_α, 0.71073 Å
Unit cell dimensions	a= 7.8231(4) Å
	b= 8.0622(4) Å
	c= 12.3038(5) Å
	α= 99.443(4)°
	β = 102.419(4)°
	γ= 109.907(4)°
Crystal system, Space group	triclinic , *P-1*
Unit cell volume	688.37(6) Å^3
No. of molecules per unit cell, Z	2
Absorption coefficient	0.096 mm^{-1}
F(000)	296
θ range for entire data collection	3.50 <θ< 28.97
Reflections collected / unique	11113/ 2695
Reflections observed I > 2σ(I))	2118
Range of indices	h= -9 to 9
	k= -9 to 9
	l= -15 to 15
No. of parameters refined	192
Final R-factor	0.0405
$wR(F2)$	0.1007
R_{int}	0.0287
R_σ	0.0236
Goodness-of-fit	1.038
Final residual electron density	-0.161 < Δρ < 0.179 eÅ^{-3}

Result and discussions

An ORTEP [9] view of the compound with atomic labeling is shown in Figure 2. The geometry of the molecule was calculated using the WinGX, [10] PARST[11] and PLATON[12] software.

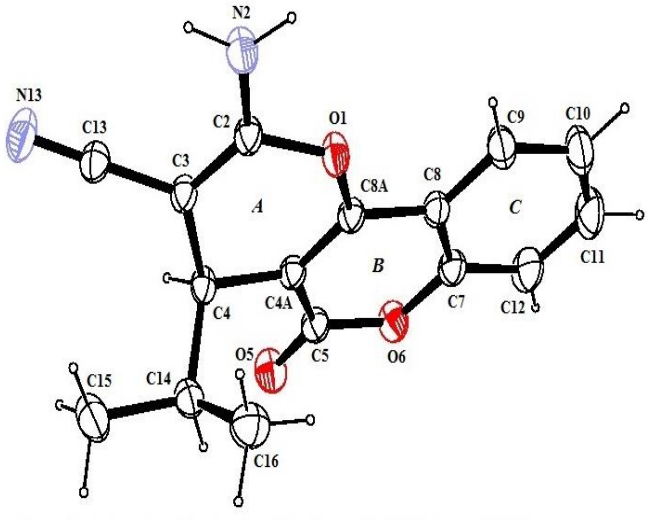

Figure 2. ORTEP view of the molecule with displacement ellipsoids drawn at 40%. H atoms are shown as small spheres of arbitrary radii.

The title compound comprises of three rings in which two are pyran rings (*A* and *B*) and third is phenyl ring (*C*). The pyran ring *A* deviates significantly from planarity and adopts boat conformation with best mirror plane passing through atoms O1 and C4 with asymmetry parameter ΔC_S(O1) = 1.297 and bisecting the bonds C2-C3 and C4A-C8A with asymmetry parameter ΔC_S(C2-C3) = 6.915. The pyran ring *B* and phenyl ring *C* are nearly planar with maximum deviation from planarity is observed for atom C5 by -0.0263 Å in pyran ring *B* and atom C7 by -0.0080 Å in phenyl ring *C* respectively. The pyran ring *B* makes the dihedral angle of 6.00(4)° and 2.13(5)° with the pyran ring *A* and phenyl ring *C* respectively, reflect that all these three rings are nearly coplanar. The mean plane of isopropyl group makes the dihedral angle of 56.75(9)° with pyran ring *A* which reflects that mean plane of isopropyl group deviate significantly from the mean plane of pyran ring *A*. The bond distances O1-C2, O1-C8A, O6-C5 and O6-C7 are 1.3749(16), 1.3648(16), 1.3754(17) and 1.3767(18) Å respectively which are close to each other and agree well with the corresponding values in the related structure. [13] The bond distances C5-O5 and C13-N13 are 1.2072(17) Å and 1.1420(18) Å confirm their respective double and triple bond character and are close to literature values.[14] The bond angles C16-C14-C4, C15-C14-C4 and C16-C14-C15 about the C14 atom of isopropyl group are 112.39(12)°, 111.24(13)° and 110.76(14)° respectively and deviate slightly above the ideal value of 109.5°. The bond angle N13-C13-C3 has the value 179.36(19)°, confirm the linear character of carbonitrile group. Some important bond distances and bond angles are listed in the Table 2. The dihedral angle N2-C2-C3-C13 with value 5.7(3)° reflects that the amino and carbonitrile groups are nearly coplanar. The torsion angle C13-C3-C4-C14 with value -78.28(17)° implies that the carbonitrile and isopropyl group deviate significantly from each other. All other values of torsion angles are reasonable and some important torsion angles are listed in the Table 2.

Analysis of the crystal packing of title compound shows the presence of intermolecular N-H…N and N-H…O hydrogen bonds in the structure [Table 3].

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

Bond distances(Å)		**Bond angles(°)**		**Torsion angles(°)**	
O1-C2	1.3749(16)	C16-C14-C15	110.76(14)	N2-C2-C3-C13	5.7(3)
O1-C8A	1.3648(16)	C16-C14-C4	112.39(12)	C13-C3-C4-C14	-78.28(17)
C5-O6	1.3754(17)	C15-C14-C4	111.24(13)	C8A-C4A-C5-O5	-176.69(15)
O6-C7	1.3767(18)	O5-C5-O6	116.55(13)	C4A-C4-C14-C16	59.26(16)
C5-O5	1.2072(17)	O5-C5-C4A	125.42(13)	C3-C4-C14-C15	62.64(16)
C13-N13	1.1420(18)	N13-C13-C3	179.36(19)	C4-C4A-C8A-O1	-4.1(2)
C4-C14	1.549(2)	C8A-O1-C2	118.11(11)	C5-C4A-C8A-C8	-1.9(2)
C2-N2	1.3334(18)	C5-O6-C7	122.01(11)	O6-C7-C8-C8A	3.2(2)

Table 3. Geometry of intermolecular hydrogen bonds

D-H…A	**D-H (Å)**	**H…A (Å)**	**D…A (Å)**	**θ[D-H…A (º)]**
N1-H2A..N13^{i}	0.86	2.22	3.064(2)	166
N2-H2B-O5^{ii}	0.86	2.18	3.018(2)	165
C4-H4-*Cg3*^{iii}	0.98	3.12	3.760(2)	124.32

where *Cg*3 represent the centre of gravity of phenyl ring *C*, symmetry codes: i. -x+1,-y+1,-z+1; ii. x+1, y, z; iii. -x, -y+1/2,-z

Table 4. Geometry of π-π interaction

CgI-CgJ	***CgI...CgJ (Å)***	***CgI...P (Å)***	**α(º)**	**β(º)**	**Δ(Å)**
Cg2-Cg2^{i}	3.5077(8)	3.483	0.00	6.75	0.416

where *Cg2* represent the centre of gravity of pyran ring *B;* symmetry codes: i. -x, -y+1,-z

Both the hydrogen atoms of amino group are involved in hydrogen bonds with N-H…O interactions link the molecules to form chain like structure and these parallel chains are linked together with N-H…N hydrogen interactions. Further the N-H….N interactions are responsible for the formation of dimmers as shown in Figure 3.

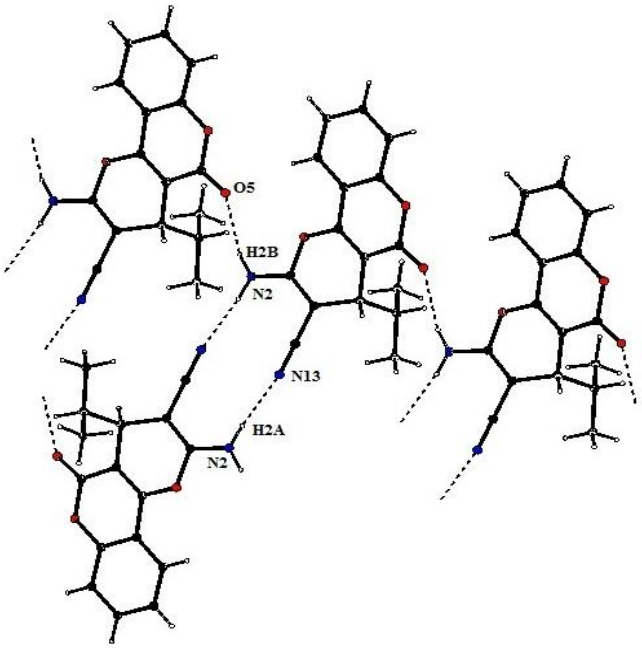

Figure 3. Partial view of intermolecular hydrogen interactions between the molecules.

In addition C-H…π interactions are also observed in the crystal structure. The geometry of these intermolecular hydrogen interactions is given in Table 3. Crystal structure is further stabilized by aromatic π-π stacking interactions and their geometry is given in Table 4.

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