STRUCTURE OF 2-AMINO-5-OXO-4-*p*-TOLYL-4,5-DIHYDRO-PYRANO[3,2-*c*]CHROMENE-3-CARBONITRILE

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Keywords: 2-amino-5-oxo-4-p-tolyl-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile; scaffolds; hydrogen bond; crystal structure; direct methods.

The compound 2-amino-5-oxo-4-*p*-tolyl-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile, crystallizes in the monoclinic space group P121/c1 with the unit-cell parameters: *a*= 9.1330(7), *b*= 13.1343(9), *c*= 13.1945(8) Å, β = 91.746(4)° and *Z* = 4. 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 0.0537 for 1830 observed reflections. The molecules within the unit cell are stabilized by C-H….O, N-H…O N-H….N and C-H…..π type of hydrogen bonding.

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Introduction

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

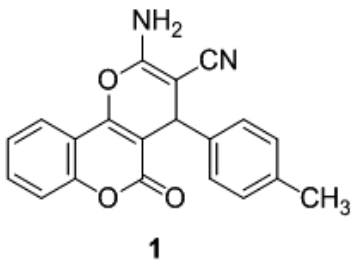

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Figure 1. The chemical structure of the compound **1**.

Experimental

Synthesis

An oven-dried screw cap test tube was charged with a magnetic stir bar, 4-methylbenzaldehyde (0.120 gm, 1 mmol), malononitrile (0.066 gm, 1.1 mmol), urea (0.007 gm, 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 20 min. After that, 4-hydroxycoumarin (0.162 gm, 1 mmol) was added to the stirred reaction mixture, and the stirring was continued for 10 hour.[5] 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 purified just by recrystallization from ethanol without carrying out column chromatography. The structure of 2-amino-5-oxo-4-(*p*-tolyl)-4,5-dihydropyrano[3,2-*c*]chromene -3-carbonitrile (**1**) was confirmed by analytical as well as spectral studies including FT-IR, ^{1}H NMR, ^{13}C NMR, and TOF-MS. Unit crystal was obtained from DMSO. 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 crystal structure of the title compound is given in Figure 2.

White solid. (0.301 gm, yield 91 %). m.p. 530-532 K. IR (KBr) ν_{max}/cm^{-1}: 3375, 3292, 3182, 3024, 2193, 1691, 1609, 1523, 1379, 1053, 916, 748, 490. ^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 7.90 (1H, d, *J* = 8.0 Hz, aromatic H), 7.70 (1H, t, *J* = 8.0 & 7.6 Hz, aromatic H), 7.48 (1H, t, *J* = 8.0 & 7.6 Hz, aromatic H), 7.46 (1H, d, *J* = 8.1 Hz, aromatic H), 7.34 (2H, s, NH_2), 7.12 (4H, m, aromatic H), 4.40 (1H, s, CH), 2.26 (3H, s, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ/ppm: 159.94, 158.33, 153.68, 152.51, 140.80, 136.71, 133.32, 129.48 (2C), 127.92 (2C), 125.09, 122.89, 119.67, 116.96, 113.37, 104.53, 58.52, 36.97, 21.03. TOF-MS: 353.0881 $[M+Na]^+$. Elemental analysis: Calcd. (%) for $C_{20}H_{14}N_2O_3$: C, 72.72; H, 4.27; N, 8.48; found: C, 72.68; H, 4.29; N, 8.52.

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X-Ray Structure determination

X-ray intensity data of 6510 reflections (of which 3100 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 1805 reflections in the θ range 3.75 to 28.42°. The intensities were measured by ω scan mode for θ ranges 3.8 to 26.00°. 1830 reflections were treated as observed ($I > 2\sigma(I)$). Data were corrected for Lorentz, polarization and absorption factors. The structure was solved by direct methods using SHELXS97.[6] All non-hydrogen atoms of the molecule were located in the best E-map. Full-matrix least-squares refinement was carried out using SHELXL97.[6] The final refinement cycles converged to an R = 0.0537 and wR (F^2) = 0. 1605 for the observed data. Residual electron densities ranged from $-0.212 < \Delta\rho < 0.262$ 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	**994051**
Crystal description	Block
Crystal size	0.30 x 0.20 x 0.20 mm
Empirical formula	$C_{20}H_{14}N_2O_3$
Formula weight	330.33
Radiation, Wavelength	Mo *K*α, 0.71073 Å
Unit cell dimensions	*a*= 9.1330(7) Å *b*= 13.1343(9) Å *c*= 13.1945(8) Å α= 90.0° β = 91.746(4)° γ= 90.0°
Crystal system, Space group	monoclinic, $P2_1/c_1$
Unit cell volume	1582.02(3)Å^3
No. of molecules per unit cell	4
Absorption coefficient	0.095 mm^{-1}
F(000)	687.9
θ range for entire data collection	3.8 <θ< 26.00
Reflections collected / unique	6510/ 3100
Reflections observed *I*>2σ(*I*))	1830
Range of indices	*h*= -10 to 11 *k*=-16 to 15 *l*= -16 to 15
No. of parameters refined	234
Final *R*-factor	0.0537
wR(*F*2)	0.1605
R_{int}	0.0331
R_{sigma}	0.0659
Goodness-of-fit	1.042
(Δ/σ)max	-0.001 for U22 O1
Final residual electron density	$-0.212 < \Delta\rho < 0.262$ eÅ^{-3}

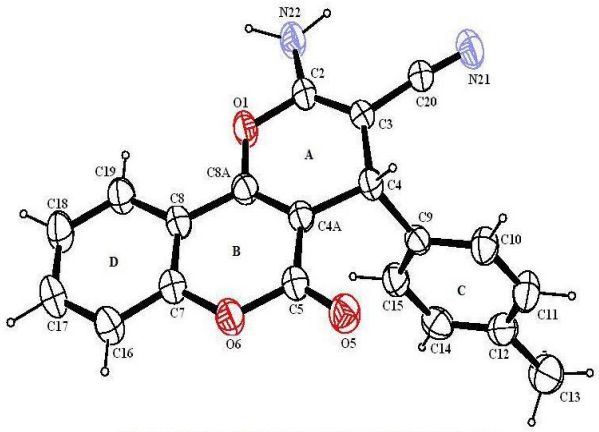

Figure 2. Ortep view of the moelcule with displacement ellipsoids drawn at the 40% probability level. H-atoms are shown as small sphere of arbitrary radii.

Result and discussions

An ORTEP[7] view of the compound with atomic labeling is shown in Figure 2. The geometry of the molecule was calculated using the WinGX[8], PARST[9] and PLATON[10] softwares. Packing view of the molecules in the unit cell viewed down the c-axis is shown in Figure 3.

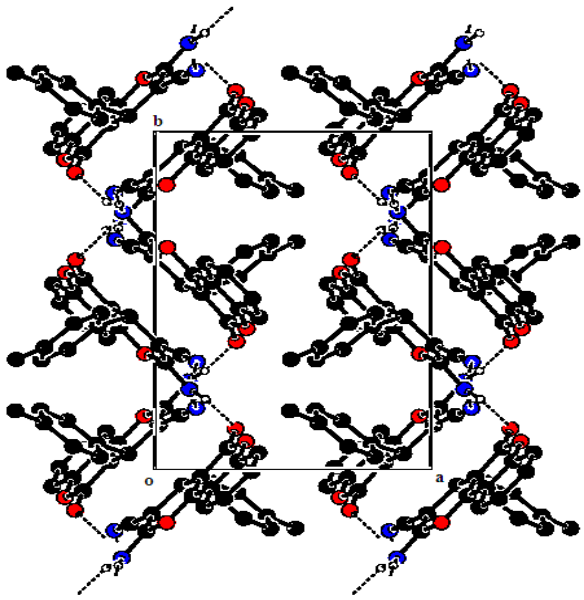

Figure 3. Packing diagram down to c-axis

The title compound comprises of four rings in which chromene moiety is fused with the pyran ring-A. Both the rings in chromene moiety (ring-B and ring-D) and pyran ring-A are almost coplanar as reflected from the small values of dihedral angle between these three rings i.e. dihedral angle between ring-A and ring-B, ring-A and ring-D and ring-B and ring-D are 1.99°(6), 1.54°(8) and 1.42°(7) respectively.

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

Bond distances(Å)		Bond angles(°)		Torsion angles(°)	
C20-N21	1.147(3)	C11-C12-C13	120.6(3)	C4A-C4-C9-C15	-137.2(2)
C5-O5	1.208(3)	C14-C12-C13	122.0(2)	C19-C8-C8A-O1	1.4(4)
C12-C13	1.515(4)	N21-C20-C3	175.5(3)	C3-C4-C9-C10	-74.3(3)
C2-N22	1.338(3)	C3-C4-C9	110.67(19)		
C20-N21	1.047(3)	C10-C9-C4	121.6(2)		
O1-C8A	1.366(3)	O6-C7-C16	117.0(2)		
C5-O6	1.381(2)	C5-C4A-C4	117.65(19)		
		O1-C8A-C8	113.9(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)]
N22 -- H16A.. N21^{i}	0.98	2.17	3.14	172(3)
N22 -- H16B.. O5^{ii}	0.99	2.00	2.98	168(3)
C10..H4..Cg1^{iii}	0.93	2.86	3.18	101.7
C17..H24..Cg4^{iv}	0.93	3.36	4.20	151.1

Symmetry codes: i. x, 1/2-y,-1/2+z; ii. 2-x,-1/2+y,1/2-z;iii. x,y,z; iv. 1-x,1-y,-z

Table 4. Geometry of π–π interactions.

CgI-CgJ	CgI…CgJ(Å)	CgI…P(Å)	α (º)	β(º)	Δ (Å)
Cg1-Cg3^{i}	3.62	3.54	1.68	12.35	0.7568

Symmetry code: i. 2-x, 1-y, -z

The plane of phenyl ring-C is nearly perpendicular to the plane of the chromene and pyran ring moieties, as the dihedral angle of ring-C with ring-A, ring-B and ring-D are 85.90º(7), 87.66º(6) and 86.36º(7) respectively. Both the phenyl rings i.e. ring-C and ring-D are almost planar with maximum deviation from planarity is observed for atoms C14 and C18 by 0.009(3)Å for both in ring-C and ring-D respectively. The atoms C20 and N21 of cyanide group and atom N22 of amine group attached to ring-A have deviations of 0.059(2)Å, 0.047(2)Å and -0.010(2)Å respectively from the least square plane of ring-A. The bond length C20-N21 is 1.147(3) (Table 2) which is comparable with the typical C_{sp} - N bond length in most of the organic carbonitriles. The C5=O5 bond length is found to be 1.208(3) which is comparable with some similar structures.[11-12] The C12-C13 bond length is 1.515(4) which is comparable to $C(sp_3)$ - C_{ar} bond length. The bond angles C11-C12-C13 and C14-C12-C13 are 120.6º(3) and 122.0º(2) respectively which are close to 120.0º as expected due to sp_2 hybridization of carbon atom C12. The bond angle C3-C20-N21 is 175.5(3)º which indicates that these three atoms are almost linear. The torsion angle C4A-C4-C9-C15 is found to be -137.2º(2). The other bond lengths and bond angles are within the expected values[13] and are comparable to related structures.[11-12]

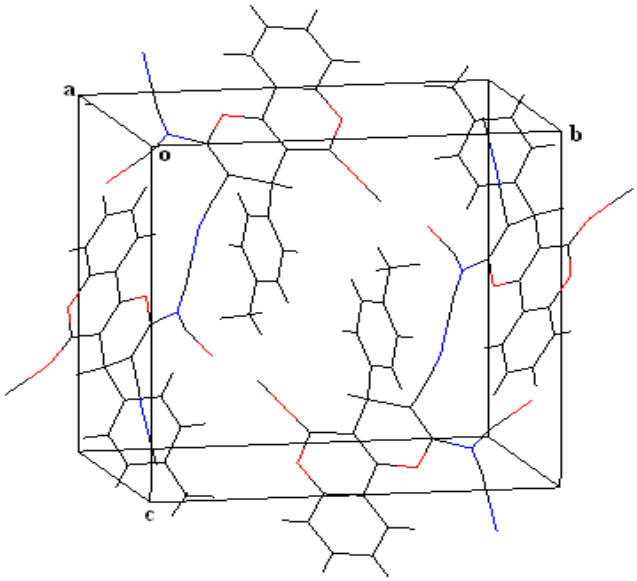

Figure 4. Stereo plot of molecules within the unit cell linked with N-H…N hydrogen bonds

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). The hydrogen atom H16B of the amine group form N22-H16B…O5 interaction with the O5 of other molecule to form double helix like structure extended parallel to b-axis as shown in Figure 3.

The other hydrogen atom H16A of amine group form N22-H16A…N21 interaction with the N21 of the neighboring molecule as represented in Figure 4. In addition to these the crystal packing is also stabilized by weak hydrogen bonds and π-π interactions (Table 4) shown in Figure 5.

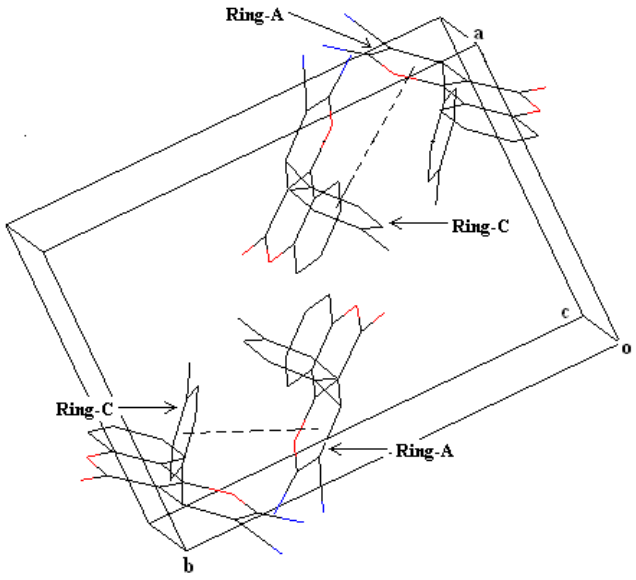

Figure 5. π–π interactions in the crystal structure

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