Crystal Structure of 2,4,9-Trimethylpyrido[3,2-*c*]coumarin

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The title compound, 2,4,9-trimethylpyrido[3,2-*c*]coumarin, crystallizes in the triclinic space group $P\bar{1}$ with the following unit-cell parameters: $a = 9.4892(5)$, $b = 10.4245(6)$, $c = 7.7307(4)$ Å, $\alpha = 94.556(3)$, $\beta = 120.824(3)$, $\gamma = 110.532(3)^\circ$, $Z = 2$. The crystal structure was solved by direct methods using single-crystal X-ray diffraction data, and refined by full-matrix least-squares procedures to a final R -value of 0.0411 for 1658 observed reflections. Molecules are linked into centrosymmetric dimers by means of paired C-H...O hydrogen bonds. The crystal structure is stabilized by a number of π - π stacking interactions.

(Received February 6, 2008; Accepted June 30, 2008; Published on web September 5, 2008)

Coumarins (2*H*-1-benzopyran-2-ones) are important oxygen-containing heterocyclic compounds isolated from a variety of plant sources. Owing to their diverse bioactivities viz. antibacterial, anticoagulant and antifungal *etc.*, many natural, semi-synthetic and synthetic coumarins have become an important class of molecules in drug research. Several biological activities have been claimed for compounds comprising both coumarins and coumarins fused to a pyridine ring. For instance, the coumarin nucleus is present in promising drug candidates as nonpeptidic HIV protease inhibitors, topoisomerase II and tyrosine kinase inhibitors.¹⁻³ Coumarins fused with pyridines have also been reported to possess antiallergic, anticoagulant, antidiabetic activities, and even analgesic properties,^{4,5} being characterized by a phenanthrene-like structure, as found in tetrahydrocannabinol. Owing to such interesting properties, the synthesis of pyridocoumarins has remained an active subject of interest. Considering the importance of pyridocoumarins, it was thought to be worthwhile to synthesize 2,4,9-trimethylpyrido[3,2-*c*]coumarin. Also, its crystal structure has been studied, as a part of our program on crystal structure analysis.^{6,7}

In a 100 mL round-bottom flask fitted with a water condenser and a guard tube, a solution of 6-methyl-4-hydroxy coumarin (0.004 mol) and acetyl acetone (0.004 mol) was taken in glacial acetic acid (45 mL). To this, ammonium acetate (0.04 mol) was added with stirring at room temperature. The reaction mixture was further stirred for 1 h and then refluxed in an oil bath at 140 – 150°C for 8 h. Then, the reaction mixture was allowed to come to room temperature. After it was poured into cold water

(100 mL), the crude product obtained was extracted with chloroform (3 × 30 mL). The combined chloroform extract was washed with a 10% sodium bicarbonate solution (3 × 20 mL),

Table 1 Crystal and experimental data

Empirical formula	C ₁₅ H ₁₃ NO ₂
Formula weight	239.26
Crystal description	irregular (colorless transparent)
Crystal size	0.3 × 0.2 × 0.2 mm
Wavelength	0.71073 Å
Crystal system	triclinic
Space group, Z	$P\bar{1}$, 2
Temperature	293(2)K
Unit cell dimensions	
a	9.4892(5)Å
b	10.4245(6)Å
c	7.7307(4)Å
α	94.556(3)°
β	120.824(3)°
γ	110.532(3)°
Volume (V)	582.18(5)Å ³
D_x	1.365 Mg m ⁻³
Absorption coefficient	0.091 mm ⁻¹
Reflections collected/unique	10577/2037
Reflections observed ($I > 2\sigma(I)$)	1658
$\theta_{\max}$	25.0°
No. of parameters refined	215
Final R -factor	0.0411
$wR(F^2)$	0.1220
Goodness-of-fit	1.042
$(\Delta/\sigma)_{\max}$	0.001 (for xH151)
$(\Delta\rho)_{\max}$	0.191 eÅ ⁻³
$(\Delta\rho)_{\min}$	-0.153 eÅ ⁻³
Measurement	Bruker SMART CCD area-detector diffractometer
Program system	SHELX
Structure determination	direct methods
Refinement	full-matrix least-squares on F^2
Structure drawing	ORTEP
CCDC deposition no	CCDC-664895

Fig. 1 Synthetic scheme for 2,4,9-trimethylpyrido[3,2-*c*]coumarin.

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Fig. 2 ORTEP view of the molecule with displacement ellipsoids drawn at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.

and then with water (3×20 mL). It was dried over anhydrous sodium sulfate. The removal of chloroform under a vacuum gave a solid product, which was further purified by column chromatography using silica gel and chloroform-pet ether (60 – 80) (3:7) as an eluent. Thus, 2,4,9-trimethylpyrido[3,2-*c*]coumarin was obtained as a white solid, which was recrystallized from chloroform-hexane. The synthetic scheme for the preparation of 2,4,9-trimethyl pyrido[3,2-*c*]coumarin is shown in Fig. 1.

Irregular-shaped colorless transparent crystals of the title compound were grown at room temperature from chloroform-hexane by a slow-evaporation technique. X-ray intensity data were collected at room temperature on a Bruker CCD area-detector diffractometer equipped with graphite monochromated Mo K_{α} radiation ($\lambda = 0.71073$ Å). Data were corrected for Lorentz and polarization factors. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares procedures to a final R -value of 0.0411. Hydrogen atoms were located from a difference Fourier map and refined along with all of the parameters of the non-hydrogen atoms. The crystal and experimental data are listed in Table 1. An ORTEP-3 drawing of the molecule is shown in Fig. 2. Selected bond lengths, bond angles and the geometry of hydrogen bonds are listed in Table 2.

The bond lengths and bond angles observed in the structure are comparable with those reported for other coumarin derivatives. The six C–C bond lengths in the phenyl ring lie in the range 1.370(3) – 1.398(3) Å. The double-bond character of C5–O5 is confirmed by the distance 1.199(3) Å. The bond angles, O6–C14–C7 and C10–C11–C12, at the junction of the pyrone and benzene rings are, respectively, smaller and greater than 120° . This phenomenon has also been observed in some analogous coumarins. Angular distortions about atoms C4 and C5 (Table 2) result from steric interactions between the methyl substituent at atom C4 and carbonyl oxygen O5 at atom C5 [C17...O5 = 2.784(3) Å]. There are also small angular distortions about atoms C11 and C12, which result from an intramolecular interaction between atoms C10 and N1 (Table 2). The coumarin moiety and the pyridine ring are individually planar with maximum deviations from the respective least-squares planes of $-0.022(2)$ Å for C5 and $0.015(1)$ Å for C12. The dihedral angle between the coumarin nucleus and pyridine ring is $1.83(4)^\circ$, confirming the perfect planarity of the pyrido coumarin moiety.

The supramolecular aggregation in the title compound is

Table 2 Selected bond lengths (Å), bond angles ($^\circ$) and hydrogen bonds

(i) Bond lengths				
N1 – C2	1.335(2)	C5 – O6	1.366(2)	
N1 – C12	1.340(2)	O6 – C14	1.384(2)	
C5 – O5	1.199(3)			
(ii) Bond angles				
C3 – C4 – C13	116.1(2)	C10 – C11 – C14	117.9(2)	
C3 – C4 – C17	119.9(2)	C12 – C11 – C14	118.8(2)	
C13 – C4 – C17	124.0(2)	N1 – C12 – C11	117.3(2)	
O5 – C5 – O6	116.0(2)	N1 – C12 – C13	123.6(2)	
O5 – C5 – C13	126.2(2)	C11 – C12 – C13	119.1(1)	
O6 – C5 – C13	117.8(2)	O6 – C14 – C7	116.6(2)	
C10 – C11 – C12	123.3(1)			
(iii) Hydrogen bonds				
D–H...A	D–H (Å)	D...A (Å)	H...A (Å)	D–H...A ($^\circ$)
C10–H10...N1	0.90(2)	2.841(2)	2.52(2)	101.5(14)
C7–H7...O5 ⁱ	0.95(3)	3.463(3)	2.57(3)	155.7(16)

Symmetry code: (i) $1-x, -y, -z$.

extremely simple and involves just one intermolecular hydrogen bond (Table 2). Atom C7 in the molecule at (x, y, z) acts as a hydrogen-bond donor, *via* atom H7, to carbonyl oxygen O5 in the molecule at ($1-x, -y, -z$), so forming a centrosymmetric dimer centered at ($1/2, 0, 0$). The formation of this dimer is reinforced by π - π stacking interactions involving all three rings of the molecule. There are no other direction specific interactions between the molecules; in particular, C–H... π (arene) hydrogen bonds are absent. Hence, the structure of title molecule simply consists of isolated centrosymmetric dimers.

Acknowledgements

The authors are grateful to the Head, SAIF, IIT, Madras, Chennai, for providing the intensity data-collection facility.

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