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Crystal structure and spectroscopy of 4-N-benzylaminocoumarin

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The structure of 4-N-benzylaminocoumarin ($C_{16}H_{13}NO_2$) has been determined by X-ray diffraction and the Ft-ir, ^{1}H- and ^{13}C-nmr spectra of the compound were recorded. Crystals of the compound are monoclinic, space group $P2_1/c$, with cell dimensions $a = 8.077(2)$, $b = 14.598(4)$, $c = 10.890(3)$ Å, and $\beta = 97.76(3)°$. The Ft-ir and nmr spectra indicate that the nitrogen atom is in the amino form in solution. The crystal structure is consistent with this observation, but the C(3)–C(4) double bond is clearly delocalized to include the lone pair on the nitrogen atom.

KEY WORDS: X-ray diffraction, Ft-ir-, ^{1}H-, ^{13}C-nmr spectra.

Introduction

Coumarins represent a wide class of compounds including many naturally occurring compounds with antibacterial and antifungal activity. In the course of our investigations of the reactions of amines with 4-hydroxycoumarins, the title compound, 4-N-benzylamino-2H-benzopyran-2-one was synthesized through condensation of 4-hydroxycoumarin with benzylamine. This derivative could be readily purified without the use of chromatographic methods. This is significant because chromatographic methods as applied to these compounds have been found to result in a large degree of product degradation. A thorough investigation of the compound was undertaken in the hope of gaining insight into the properties and characteristics of this compound and of related 4-N substituted coumarins.

Experimental

Synthesis

4-N-Hydroxycoumarin (1.5 g) and benzylamine (25 ml) were heated at 180°C for 1 hr. The reaction mixture was allowed to cool to room temperature and was poured with constant stirring into 3 M HCl (250 ml). The resulting suspension was stirred for 30 min. The precipitate was isolated by filtration, washed with water, and recrystallized from methanol, affording the title compound in 65% yield.

General characterization

The melting point was determined by a Fisher-Johns melting point apparatus and is uncorrected. Elemental analysis was performed at Guelph Chemical Laboratories, Guelph, Ontario, Canada.

Spectroscopy

Infrared spectra were acquired on a Perkin Elmer FT Infrared Spectrophotometer. A Bruker QNP 200 spectrometer was used to acquire the nmr spectra, with DMSO-d_6 as solvent and internal reference. Chemical shifts are reported in parts per million from the central reference peak of the solvent (DMSO 40.4 and 2.49 ppm for ^{13}C and ^{1}H-nmr respectively) and are corrected to TMS ($\delta = 0.0$ ppm). Proton assignments were based on 2D-heteronuclear shift correlation, DEPT multiplicity analysis, and comparison to known compounds. Confirmation of these assignments was obtained from INADEQUATE nmr, performed by Bruker Spectrospin Canada.

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Crystallography

Crystals of the compound were colorless and block shaped. A sample of dimensions 0.48 × 0.32 × 0.20 mm was chosen. From precession photographs the crystal was found to be monoclinic, $P2_1/c$. The cell constants were determined from a least-squares fit to the positions of 44 reflections in the range $26 < 2\theta < 40$. Values found using Mo $K\alpha$ radiation ($\lambda = 0.71073$ Å) were $a = 8.077(2)$, $b = 14.598(4)$, $c = 10.890(3)$ Å, $\beta = 97.76(3)°$, $V = 1272.1(9)$ Å^3, $Z = 4$, μ(Mo $K\alpha$) $= 0.94$ cm^{-1}, $M_r = 251.28$, $D_x = 1.31$ g cm^{-3}, $D_m = 1.31(1)$ g cm^{-3}.

The integrated intensities of 2249 reflections were collected to $2\theta = 50°$ at 220(5) K. No decay was observed in the intensities of the three standard reflections. Of the reflections observed, 1605 showed $I > 2\sigma(I)$, and were used in the structure determination. The structure was solved by direct methods. The first electron-density Fourier map showed the positions of all nonhydrogen atoms and five of the hydrogen atoms. The position of the remaining eight hydrogen atoms were found from a difference map. The structure was refined by full-matrix least squares using the XTAL 2.4 software package[1] to a final $R = 0.046$, $R_w = 0.041$, based on refinement of F. The weights were the reciprocal of the variances, σ^2 (F), where $\sigma(F)$ was calculated from the counting statistics of the individual reflection with a contribution added to account for the excess scatter in the standard reflections. The maximum value of Δ/σ for the least-squares variables in the last cycle of refinement was 0.15, and the maximum residual electron density was -0.29e Å^{-3}.

Results

Melting point: 243–244°C.

Elemental analysis: Calculated (%) C 76.46; H 5.22; N 5.58: Found (%) C 76.62; H 5.61; N 5.66.

Ft-ir (KBr disk, cm^{-1}): 3320 (N-H stretch); 1660-1680 and 1550-1570 (associated with substituted α-pyrone ring).

^{1}H-nmr (δ(DMSO), ppm): 8.39 (t, 1 NH-(H(1))); 8.15 (d, 1 aromatic H (H(5))); 7.60 (t, 1 aromatic H (H(7))); 7.20–7.30 (m, 2 aromatic H (H(6), H(8))); 5.11 (s, 1 =CH— (H(3))); 4.56 (d, 2 —CH— (H(101), H(102))).

^{13}C-nmr (δ(DMSO), ppm): 161.5 (C(2)); 153.1 (C(4), C(9)); 137.8 (C(11)); 132.0 (C(7)); 128.6 (C(13), C(15)); 127.1 (C(12), C(16)); 127.0 (C(14)); 123.5 (C(6)); 122.5 (C(5)); 117.0 (C(8)); 114.5 (C(10)); 82.5 (C(3)); 45.5 (C(1)).

The fractional atomic coordinates and equivalent isotropic temperature factors for the nonhydrogen atoms and the isotropic temperature factors for the hydrogen atoms are given in Tables 1 and 2, respectively. Figure 1 shows a stereo view of the molecule with atomic numbering. The bond lengths are given in Table 3 and the interatomic angles of the molecule are given in Table 4.

Table 1. Fractional atomic coordinates and equivalent isotropic temperature factors ($\times 10^2$) for nonhydrogen atoms, with esd's in parentheses

Atom	x	y	z	U_{eq}[a]
C(1)	0.6076(5)	0.1928(2)	0.4108(3)	3.8(2)
C(2)	0.4910(4)	−0.0775(2)	0.2736(3)	3.8(2)
C(3)	0.5282(4)	0.0120(2)	0.3164(3)	3.6(2)
C(4)	0.4736(4)	0.0882(2)	0.2499(3)	3.3(2)
C(5)	0.3064(5)	0.1470(2)	0.0515(3)	4.1(2)
C(6)	0.2079(5)	0.1283(3)	−0.0591(4)	5.0(2)
C(7)	0.1714(5)	0.0385(3)	−0.0928(4)	5.2(3)
C(8)	0.2313(5)	−0.0323(3)	−0.0183(3)	4.7(2)
C(9)	0.3308(4)	−0.0130(2)	0.0925(3)	3.6(2)
C(10)	0.3702(4)	0.0757(2)	0.1304(3)	3.2(2)
C(11)	0.7914(4)	0.1689(2)	0.4179(3)	3.6(2)
C(12)	0.8813(5)	0.1471(3)	0.5315(4)	5.4(3)
C(13)	1.0500(6)	0.1259(3)	0.5405(5)	6.9(3)
C(14)	1.1277(6)	0.1251(3)	0.4374(5)	6.3(3)
C(15)	1.0399(6)	0.1464(3)	0.3246(4)	6.1(3)
C(16)	0.8721(5)	0.1691(3)	0.3146(4)	4.9(2)
N(1)	0.5099(4)	0.1737(2)	0.2911(3)	3.7(2)
O(1)	0.3875(3)	−0.0877(1)	0.1626(2)	4.2(1)
O(2)	0.5407(3)	−0.1492(1)	0.3242(2)	4.6(1)

[a] $U_{eq} = \frac{1}{3} \Sigma_j a_i^* a_j^* a_i \cdot a_j U_{ij}$

Table 2. Fractional atomic coordinates and isotropic temperature factors ($\times 10^2$) for hydrogen atoms, with esd's in parentheses

Atom	x	y	z	U_{iso}
H(1)	0.481(4)	0.222(2)	0.248(3)	4(1)
H(3)	0.595(3)	0.016(2)	0.392(2)	1(1)
H(5)	0.328(4)	0.212(2)	0.077(3)	4(1)
H(6)	0.166(4)	0.184(2)	−0.114(3)	7(1)
H(7)	0.098(4)	0.025(2)	−0.172(3)	6(1)
H(8)	0.209(4)	−0.092(2)	−0.040(3)	4(1)
H(101)	0.587(3)	0.262(2)	0.431(2)	4(1)
H(102)	0.557(3)	0.163(2)	0.476(3)	4(1)
H(12)	0.825(4)	0.151(2)	0.605(3)	8(1)
H(13)	1.11(4)	0.110(3)	0.621(3)	9(1)
H(14)	1.24(5)	0.101(3)	0.439(3)	10(2)
H(15)	1.08(4)	0.154(2)	0.249(3)	8(1)
H(16)	0.809(4)	0.193(2)	0.237(3)	5(1)

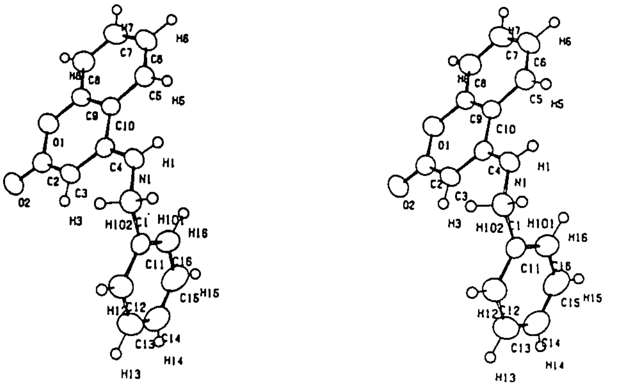

Fig. 1. Stereo view of the molecule with atom labelling.

Table 4. Interatomic bond angles (°) with esd's in parentheses

C(2)-C(3)-C(4)	122.7(3)	C(3)-C(4)-C(10)	118.4(3)
C(4)-C(10)-C(5)	124.9(3)	C(4)-C(10)-C(9)	117.7(3)
C(10)-C(5)-C(6)	120.6(3)	C(5)-C(6)-C(7)	120.1(3)
C(6)-C(7)-C(8)	120.4(3)	C(7)-C(8)-C(9)	119.1(3)
C(8)-C(9)-C(10)	122.2(3)	C(1)-C(11)-C(12)	119.4(3)
C(11)-C(12)-C(13)	120.4(4)	C(12)-C(13)-C(14)	120.2(4)
C(13)-C(14)-C(15)	119.9(4)	C(14)-C(15)-C(16)	120.5(4)
C(15)-C(16)-C(11)	120.2(4)	C(16)-C(11)-C(1)	121.8(3)
C(8)-C(9)-O(1)	115.7(3)	C(10)-C(9)-O(1)	122.1(3)
C(3)-C(2)-O(1)	117.9(3)	C(3)-C(2)-O(2)	127.0(3)
C(2)-O(1)-C(9)	121.1(2)	O(1)-C(2)-O(2)	115.1(3)
C(3)-C(4)-N(1)	122.6(3)	C(10)-C(4)-N(1)	119.1(3)
C(11)-C(1)-N(1)	114.2(3)	C(1)-N(1)-C(4)	122.9(3)

The amine hydrogen atom is hydrogen bonded to an O(2) atom of a neighbouring molecule related to the first by the 2_1 screw axis to form infinite chains running in the ***b*** and $-$***b*** directions. The hydrogen bond geometry is defined by [N(1)· · ·(2)] = 2.878(4) Å, [N(1)-H(1)] = 0.86(3) Å, [H(1)O· · ·O(2)] = 2.04(3) Å.

Discussion

The molecule contains two planes consisting of the benzyl group and the amino coumarin moiety with C(1) being a member of both planes and forming the linkage between them. The angle between the plane fitted to the benzene portion of the benzopyranone system and the plane fitted to the benzene portion of the benzyl group is 84.4(1)°, and the torsional angle C(4)-N(4)-C(1)-C(11) is 70.8(4)°. The rings themselves are planar within the esd's of the atoms. Some of the atoms of the pyranone ring are slightly removed from the plane of the adjoining benzene ring. In particular, C(2) and O(2) are 0.047(6) and 0.123(9) Å out of plane.

The length of the C(4)-N(4) bond is 1.345(4) Å. This bond length is much shorter than a normal Csp_3-Nsp_2 single bond at 1.454(11) Å. The uncertainties for the bond lengths, as given in the brackets, are taken directly from Allen *et al.*[2] and are estimates of the standard deviation of the bond lengths in the sample from which the average bond length is calculated. The standard deviation of the average bond length itself would be assumed to be smaller, but is not given because the average may not involve truly equivalent populations of bond lengths. Nevertheless, the values quoted here may be assumed to represent an upper limit of the standard deviation of the mean, which would be implied by the first canonical form shown in Fig. 2, and is midway between a Csp_2-Nsp_2 bond length (1.339(16) Å) and a $C_{aromatic}$-Nsp_2 bond length (1.355(20) Å).[1]

The bond lengths to C(4) substituents in other four-substituted coumarins also tend to fall in a range suggesting that the atom C(4) can be considered as being in an intermediate state between being part of an aromatic ring and being an sp_2 carbon atom.

Fig. 2. Important canonical forms.

Table 3. Bond distances (Å) with esd's

C(2)-C(3)	1.406(5)	C(6)-C(7)	1.385(6)	C(12)-C(13)	1.387(6)
C(3)-C(4)	1.367(4)	C(7)-C(8)	1.367(5)	C(13)-C(14)	1.359(7)
C(4)-C(10)	1.460(4)	C(8)-C(9)	1.385(5)	C(14)-C(15)	1.389(6)
C(10)-C(5)	1.402(5)	C(1)-C(11)	1.516(5)	C(15)-C(16)	1.385(6)
C(5)-C(6)	1.378(5)	C(11)-C(12)	1.384(5)	C(16)-C(11)	1.374(5)
C(2)-O(1)	1.382(4)	C(9)-O(1)	1.374(4)	C(2)-O(2)	1.227(4)
C(1)-N(1)	1.457(4)	C(4)-N(1)	1.345(4)	N(1)-H(1)	0.86(3)

The C(2)–C(3) bond length at 1.406(5) Å is shorter than its value in most coumarins (e.g., 1.448(5) Å in unsubstituted coumarin.[3] The C(3)–C(4) bond length at 1.367(4) Å is longer than its value in most coumarins (e.g., 1.344(5) Å in unsubstituted coumarin.[2] These observations suggest that the lone pair electrons of the atom N(4) are delocalized over the ring system to an extent greater than in four-substituted coumarins not involving nitrogen, resulting from the contribution of the second resonance form shown in Fig. 2. Presumably this reflects the combined effect of the nitrogen lone pair and the relatively low electronegativity of nitrogen. This is further confirmed by the C(3)–C(4)–N(4)–C(1) torsional angle which is 178.8(5).

The second canonical form in Fig. 2 should also be manifested by a longer C(2)–O(2) bond. The C(2)–O(2) bond length at 1.227(4) Å is indeed longer than that in other four-substituted coumarins and the value of 1.204(4) Å in coumarin itself. The atom O(2) is the acceptor for a hydrogen bond from an N(1) atom on a neighboring molecule. From very accurate results on similar molecules with different hydrogen bonding networks, we conclude that the effect of the hydrogen bonding will account for 0.010(2) Å of this difference,[4] the rest arising from the delocalization of the nitrogen lone-pair electrons into the π system.

The synthesis of this compound produced only one coumarin derivative. Most syntheses produce a mixture from which it is difficult to separate a specific compound by crystallization. These results suggest that the reason may involve crystallization from solvent containing hydrogen-bonded chains or aggregates of similar molecules.

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