Crystal Structure of 4-Acetoxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-2H-1-benzopyran-2-one

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The title compound, 4-acetoxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-2H-1-benzopyran-2-one, $C_{21}H_{17}NO_7$, crystallized in the monoclinic system, space group $P2_1/a$, with cell constants $a = 9.5505(13)\text{\AA}$, $b = 11.9546(11)\text{\AA}$, $c = 16.336(2)\text{\AA}$, $\beta = 97.497(12)^\circ$, $V = 1849.2(4)\text{\AA}^3$ and $Z = 4$. The compound crystallized in the open-chain *keto* form and had only one asymmetric center at C 15.

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4-Hydroxycoumarin derivatives are of interest because of their physiological, photodynamic, anticoagulant, spasmolytic, bacteriostatic, and rodenticidal activities. Some coumarin derivatives are known for their antibiotic and antifungal activities. They are also used as analytical reagents. The most widely used antithrombotic in USA and Canada is racemic sodium warfarin. It is possible to obtain compounds with good biological activity, but with lower toxicity and fewer side effects, by chemical modifications of the warfarin structure.

The title compound, 4-acetoxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-2H-1-benzopyran-2-one, was synthesized from 4'-nitrobenzylideneacetone and 4-hydroxycoumarin, and the next step was treating 4-hydroxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-2H-1-benzopyran-2-one with acetic acid anhydride.

The structure of the synthesized compound was proven by IR, $^1\text{H-NMR}$ and mass-spectral analyses. Acute toxicity studies of the compound were performed on mice by oral and intraperitoneal administration. The investigated compound showed a lower acute toxicity and a higher anticoagulant activity than Warfarin.¹

The crystal structure of the compound was determined using the single-crystal X-ray diffraction method. Data collection of this compound was done at 173(2)K using graphite monochromator Mo- K_α ($\lambda = 0.71073\text{\AA}$) radiation on an ENRAF NONIUS four-circle diffractometer. Complete data

collection parameters and details of the structure solution and refinement are given in Table 1. Further details on the crystal structure investigation are available free of charge at www.ccdc.ac.uk/conts/retrieving.html or deposit@ccdc.cam.ac.uk.

The unit cell was determined and refined using the CAD4-EXPRESS program. The space group was determined using the check-hkl and was performed with the PLATON/ABS PSI program.² The structure was solved with direct methods by

Table 1 Crystal and experimental data

Empirical formula	$C_{21}H_{17}NO_7$
Formula weight	395.36
Temperature	173(2)K
Wavelength	0.71073 $\text{\AA}$ /Mo K_α
Crystal system/Space group	Monoclinic, $P2_1/a$
Unit cell dimensions	$a = 9.5505(13)\text{\AA}$; $b = 11.9546(11)\text{\AA}$; $\beta = 97.497(12)^\circ$; $c = 16.336(2)\text{\AA}$;
Volume	1849.2(4) $\text{\AA}^3$
Z	4
Density (calculated)	1.420 Mg/m^3
Absorption coefficient	0.108 mm^{-1}
$F(0\ 0\ 0)$	824
Crystal size	0.65 $\times$ 0.15 $\times$ 0.10 mm
θ range for data collection [$^\circ$]	3.13 to 26.96 deg.
Index ranges	$-12 \leq h \leq 10$, $-15 \leq k \leq 15$, $-20 \leq l \leq 20$
Reflections collected	26333
Independent reflections	3956 [$R_{\text{int}} = 0.0883$]
Reflections observed	2815
Criterion for observation	$> 2\sigma(I)$
Absorption correction	None
Measurement method	Phi-Scans
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3956/0/330
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0644$, $wR2 = 0.1252$
Goodness-of-fit on F^2	1.130
Final R indices (all) $R1/wR2$	0.0993/0.1388
Largest diff. peak and hole	0.221 and $-0.177\text{ e.\AA}^{-3}$
CCDC	652259

Fig. 1 Chemical structure of 4-acetoxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-2H-1-benzopyran-2-one.

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Fig. 2 DIAMOND drawing (50% probability level).

SHELXS97 and refined by SHELXL97.³ The structure was refined by least-square methods based on F^2 . All non-hydrogen atoms were fully refined in the calculated position. The hydrogen atoms were taken from the electron density map and refined isotropically. Plots of the molecular structure were made using the DIAMOND program (CRYSTAL IMPACT GbR, Bonn, Germany).⁴

Colorless prismatic crystals, suitable for X-ray diffraction analysis, were grown by slow evaporation of an ethyl acetate solution. Crystallographic data for the investigated compound are listed in Table 1. The solid-state structure is shown in Fig. 2.

The title compound, 4-acetoxy-3-[1-(4-nitrophenyl)-3-oxobutyl]-2H-1-benzopyran-2-one, is a structural analogue of Warfarin. X-ray crystal structure analyses showed that this compound crystallized in the monoclinic system, space group $P2_1/a$. An examination of the bond lengths revealed that the atoms retained the character expected for an open-side chain (*keto*) compound. The O11-C10 bond length of 1.389(3) Å is close to that of the phenolic C-O bond. Moreover, the bond lengths between C26-C27 and between C27-C29 are 1.515(4) and 1.505(4) Å, respectively, close to the expected values for C-C bonds adjacent to carbonyl groups. In the structure of the investigated compound there is no bond between C27 and O11. Within the coumarin system, the length of the double bond C9-C10, 1.347(3) Å is suitable for a C=C bond conjugated to a carbonyl, and the adjacent C8-C9 bond of 1.468(3) Å is slightly shorter than expected because of resonance. Two near disposed planarities of the coumarin ring system and the aromatic nucleus formed an angle between C9-C15-C20 of 107.3(2)°. The compound crystallized in the open-chain *keto* form and had only one asymmetric center at C15. No hemiketal ring was formed in the investigated compound.

Table 2 Atomic coordinates and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$). [$U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor]

Atom	x	y	z	$U(\text{eq})$
C 1	0.2765 (3)	0.1478 (2)	0.4938 (2)	35 (1)
C 2	0.3284 (3)	0.1747 (2)	0.4213 (2)	42 (1)
C 3	0.4713 (3)	0.1704(2)	0.4159 (2)	44 (1)
C 4	0.5662 (3)	0.1405 (2)	0.4834 (2)	39 (1)
C 5	0.5147 (3)	0.1180 (2)	0.5576 (2)	32 (1)
C 6	0.3707 (2)	0.1198 (2)	0.5643 (1)	29 (1)
O 7	0.6125 (2)	0.0918 (1)	0.6239 (1)	35 (1)
C 8	0.5746 (2)	0.0637 (2)	0.6997 (2)	33 (1)
C 9	0.4244 (2)	0.0689 (2)	0.7102 (1)	27 (1)
C 10	0.3295 (2)	0.0945 (2)	0.6445 (1)	26 (1)
O 11	0.1885 (2)	0.1073 (1)	0.6553 (1)	30 (1)
C 12	0.0929 (2)	0.0286 (2)	0.6188 (2)	32 (1)
C 13	-0.0513 (3)	0.0585 (4)	0.6378 (2)	55 (1)
O 14	0.1261 (2)	-0.0468 (2)	0.5777 (1)	37 (1)
C 15	0.3865 (3)	0.0554 (2)	0.7972 (2)	31 (1)
O 16	0.6694 (2)	0.0383 (2)	0.7527 (1)	44 (1)
C 20	0.4513 (2)	0.1542 (2)	0.8481 (1)	31 (1)
C 21	0.3977 (3)	0.2611 (2)	0.8300 (2)	35 (1)
C 22	0.4595 (3)	0.3548 (2)	0.8687 (2)	39 (1)
C 23	0.5766 (3)	0.3394 (2)	0.9271 (2)	37 (1)
C 24	0.6306 (3)	0.2354 (2)	0.9486 (2)	39 (1)
C 25	0.5668 (3)	0.1425 (2)	0.9089 (2)	37 (1)
C 26	0.4250 (3)	-0.0599 (2)	0.8353 (2)	39 (1)
C 27	0.3341 (3)	-0.1548 (2)	0.7965 (2)	43 (1)
O 28	0.2238 (2)	-0.1376 (2)	0.7523 (1)	57 (1)
C 29	0.3881 (5)	-0.2714 (3)	0.8159 (2)	61 (1)
N 30	0.6496 (3)	0.4382 (2)	0.9661 (2)	52 (1)
O 31	0.7450 (3)	0.4219 (2)	1.0227 (2)	80 (1)
O 32	0.6123 (3)	0.5313 (2)	0.9406 (1)	66 (1)

Savell *et al.*⁵ established that the substance analogous of Sythrom crystallized in the triclinic system, space group $P1$. It formed an intramolecular hemiketal and possessed two asymmetrical C atoms.

Obviously, the substitution of a hydrogen atom in the phenol hydroxyl group at C-4 of the coumarin fragment did not allow the formation of an intramolecular hemiketal.

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