Crystal Structure of 4-Ethoxycoumarin

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The crystal structure of 4-ethoxycoumarin, which has antimicrobial activity, has been determined. The molecule has a planar conformation with a deviation of 0.014(2) Å from the best plane, defined by the chromone moiety. The coplanar ethoxy group is connected with a *trans* conformation. The angles around the C3 atom give the ethoxy group a tilt to the C4 direction. There is a type of intermolecular-hydrogen bond between the O3 atom of the ethoxy group and the hydrogen of the phenyl ring.

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Coumarin derivatives have a variety of potent bioactivities, such as warfarin and trioxsalen being used clinically for curing platelet coagulation and leucoderma, respectively.¹⁻³ One of the coumarin derivatives, the title compound, (I), 4-ethoxy-2H-chromen-2-one, is considered to play an important role for antimicrobial activity,⁴ but the biological properties are still incompletely understood. In this study, an X-ray analysis of (I) was undertaken in order to determine the inherent conformation.

4-Ethoxycoumarin was purchased from Tokyo Chemical Industry Co. Ltd. Plate-like colorless crystals were obtained from a methanol-chloroform mixture solution with a vapor diffusion method at room temperature. A crystal with a size of 0.4 × 0.2 × 0.05 mm was used for diffraction experiments. The crystal and experimental data are given in Table 1. The

structure of (I) was solved by direct methods using the program Sir88,⁵ and refined by full-matrix least-squares. Non-hydrogen atoms were refined anisotropically. All of the hydrogen atoms were located in a difference-Fourier map, and refined isotropically. The atomic parameters for the non-hydrogen

Fig. 1 Chemical structure of (I).

Table 1 Crystal and experimental data

Formula: C₁₁H₁₀O₃
Formula weight = 190.20
Crystal system: monoclinic
Space group: *P*₂₁/*a* *Z* = 4
a = 8.7672(6) Å
b = 15.6026(7) Å
c = 7.5687(6) Å
β = 112.245(6)°
V = 958.3(1) Å³
*D*_x = 1.318 g/cm³
No. of reflections used = 1979
2 θ _{max} = 147.9° with Cu K α
R = 0.039
(Δ / σ)_{max} = 0.0007
($\Delta\rho$)_{max} = 0.20 e Å⁻³
($\Delta\rho$)_{min} = -0.16 e Å⁻³
Measurement: Enraf-Nonius CAD4-Turbo
Program system: Rigaku teXsan
Structure determination: Sir88
Refinement: full-matrix

Table 2 Atomic coordinates and equivalent isotropic thermal parameters (*B*_{eq})

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq}
O1	0.3500 (1)	0.64101 (6)	0.1049 (2)	4.58 (2)
O2	0.0848 (1)	0.62569 (7)	0.0371 (2)	6.51 (3)
O3	0.4483 (1)	0.39477 (6)	0.3114 (1)	4.50 (2)
C1	0.2188 (2)	0.59197 (9)	0.1033 (2)	4.51 (3)
C2	0.2525 (2)	0.50666 (9)	0.1786 (2)	4.23 (3)
C3	0.4060 (2)	0.47413 (8)	0.2442 (2)	3.72 (3)
C4	0.7058 (2)	0.49755 (10)	0.3033 (2)	4.52 (3)
C5	0.8263 (2)	0.5506 (1)	0.2893 (2)	5.10 (4)
C6	0.7876 (2)	0.6326 (1)	0.2166 (2)	4.92 (3)
C7	0.6286 (2)	0.66257 (10)	0.1567 (2)	4.43 (3)
C8	0.5073 (2)	0.60855 (8)	0.1695 (2)	3.79 (3)
C9	0.5427 (1)	0.52595 (8)	0.2418 (2)	3.68 (3)
C10	0.3181 (2)	0.33798 (9)	0.3130 (2)	4.86 (3)
C11	0.3946 (3)	0.2525 (1)	0.3796 (4)	6.97 (6)

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$$B_{eq} = (4/3)\sum_i \sum_j \beta_{ij}(\mathbf{a}_i \cdot \mathbf{a}_j).$$

Fig. 2 ORTEP-3 drawing representing heavy atoms as 50% probability ellipsoids and H atoms as circles of arbitrary size.

Table 3 Selected bond lengths (Å), bond angles (°) and torsion angles (°)

Bond lengths		Bond lengths	
	(Å)		(Å)
O1 - C1	1.378(2)	O1 - C8	1.374(2)
O2 - C1	1.209(2)	O3 - C3	1.337(2)
O3 - C10	1.449(2)	C1 - C2	1.434(2)
C2 - C3	1.345(2)	C3 - C9	1.451(2)
C8 - C9	1.389(2)	C10 - C11	1.493(2)
Bond angles		Bond angles	
	(°)		(°)
C1 - O1 - C8	121.4(1)	C3 - O3 - C10	117.6(1)
O1 - C1 - O2	116.0(1)	O1 - C1 - C2	117.8(1)
O2 - C1 - C2	126.2(1)	C1 - C2 - C3	121.6(1)
O3 - C3 - C2	125.8(1)	O3 - C3 - C9	114.1(1)
C2 - C3 - C9	120.1(1)	O1 - C8 - C7	116.3(1)
O1 - C8 - C9	121.8(1)	C3 - C9 - C8	117.4(1)
O3 - C10 - C11	107.1(2)		
Torsion angles		Torsion angles	
	(°)		(°)
O2-C1-O1-C8	-177.4(1)	O2-C1-C2-C3	178.1(2)
O3-C3-C2-C1	-177.9(1)	O3-C3-C9-C8	178.5(1)
C10-O3-C3-C2	0.5(2)	C10-O3-C3-C9	-178.1(1)
C11-C10-O3-C3	175.7(1)		

atoms are listed in Table 2. All calculations were carried out with the program package teXsan.⁶

An ORTEP-3⁷ drawing of (I) together with the atomic numbering is shown in Fig. 2. Selected bond lengths, bond angles and torsion angles are given in Table 3. The molecule has a planar conformation with a deviation of 0.014(2) Å from the best plane, defined by two six-member rings, which make a dihedral angle of 1.74(5)°. Electron localization was found at the short C2-C3 bond with a length of 1.345(2) Å. The coplanar ethoxy group has a *trans*-conformation. The wide-angle of C2-C3-O3 and the narrow-angle of O3-C3-C9 give the ethoxy group a tilt to the C4 direction.

In the crystal structure, the flat chromone moieties are stacked opposed to each other along the *c*-axis. Between stacked molecules, π - π and CH- π interactions are found [Cg1...Cg2(2 - *x*, -*y*, -*z*) = 3.6280(8) Å, C10-H...Cg2(-*x*, -*y*, 1 - *z*) = 3.648(4) Å and $\angle$ C10-H...Cg2 = 146(2)°, where Cg1 and Cg2 are the centers of gravity of pyran and phenyl rings, respectively]. The crystal structure is also stabilized by three weak-intermolecular hydrogen-bonds [C7-H...O2 (*x* + 1/2, 3/2 - *y*, *z*) = 3.409(2) Å, $\angle$ C7-H...O2 = 162(2)°; C10-H...O2 (-*x*, 1 - *y*, -*z*) = 3.569(2) Å, $\angle$ C10-H...O2 = 144(2)°; and C2-H...O2 (-*x*, 1 - *y*, -*z*) = 3.467(2) Å, $\angle$ C2-H...O2 = 148(2)°].

There is no significant intermolecular-interaction, which gives the ethoxy group a tilt to the C4 direction, except for the weak intramolecular-interaction [C4-H...O3 = 2.789(2) Å, $\angle$ C4-H...C3

= 100(1)°]. The tendency of the O3 atom approaching to the hydrogen of phenyl ring is found not in the 4-alkyl coumarin derivatives, but rather in a various types of 4-hydroxy or 4-alkoxy coumarin derivatives from Cambridge Structure Database.⁸ Thus, we consider that the O3 atom accepts the hydrogen of the phenyl ring as a type of intramolecular-hydrogen bond.

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