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Structure of 4-Cyclohexyl-3,4-dihydro-2-hydroxy-2-methyl-2*H*,5*H*-pyrano-[3,2-*c*][1]benzopyran-5-one

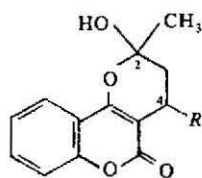
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Abstract. $C_{19}H_{22}O_4$, monoclinic, $P2_1/c$, $a = 2.515$ (2), $b = 17.472$ (3), $c = 7.489$ (1) Å, $\beta = 90.40$ (1)°. The structure was solved by direct methods. The cyclohexyl group is pseudo-equatorial and *trans* to the axial hydroxyl; the dihydropyran ring is a half-chair distorted towards the *d,e*-diplanar conformation. Hydrogen bonding between the coumarin carbonyl and the hydroxyl groups at an O...O distance of 2.834 (4) Å is found. In $CDCl_3$ solution, this compound exists predominantly in the open-chain keto form.

Introduction. Michael-type addition of 4-alkyl- or 4-rylbut-3-en-2-ones to 4-hydroxycoumarin produces 3-substituted 4-hydroxycoumarins that may exist as cyclic hemiketals (Ikawa, Stahmann & Link, 1944). Each isomer is diastereomeric, and the configuration of the molecule in the crystal will depend on the steric interactions between the substituents on the dihydropyran (hemiketal) ring. Substituents at the 2 and 4 positions have the largest interactions. The 2-hydroxyl or alkoxy group normally prefers the axial conformation, related to the anomeric effect. The 4-pseudo-axial substituent will therefore have a short axial contact while a 4-pseudo-equatorial substituent is close to the coumarin carbonyl oxygen. Previously, (1) was found to induce distortions in the dihydropyran ring relative to (2) in both 4 placements (Valente, Santarsiero & Schomaker, 1979). The present contribution extends this series to $R =$ cyclohexyl, (3), a substituent envisioned to be larger than methyl, and describes the conformation of the distorted dihydropyran ring obtained in the crystal, and the structure in solution revealed by nuclear magnetic resonance.



- (1) $R = CH_3$
 (2) $R = C_6H_5$
 (3) $R = C_6H_{11}$

Colorless rods of (3) crystallize from ethyl acetate or ethane solutions. After a preliminary photographic

study of several crystals which established the space group as $P2_1/c$ ($h0l$ absent for l odd, $0k0$ absent for k odd), an individual $0.156 \times 0.063 \times 0.469$ mm was mounted along the long crystal axis. Cell constants were measured from 12 reflections ($2\theta > 30^\circ$) and 2385 reflections were observed on a Picker FACS-I automated diffractometer with quartz-monochromatized $Mo K\alpha$ radiation ($\lambda = 0.70926$ Å). Of these, 1621 exceeded $1.5\sigma(I)$ and were used in the final refinement stages. The structure was discovered with *MULTAN* (Main, 1978), and refined by full-matrix least-squares calculations until the model, represented by anisotropic and isotropic U 's associated with the non-hydrogen and hydrogen-atom positions respectively, converged at $R = 0.055$; goodness-of-fit = 1.8. No absorption or extinction corrections were applied to the data. The atom positions appear in Table 1.*

In $CDCl_3$, the 1H and ^{13}C magnetic resonance spectra of (3) (HA-100 spectrometer) and its methyl ketal, (3a), formed by treatment of (3) with methanol and acid, were recorded and show that for (3) a mixture of one cyclic diastereomeric hemiketal and the open form is present. By integration, the open form represents 75% of the mixture. The spectra of (3a) indicate that it is the *trans* diastereomer.

Discussion. An ellipsoid plot (Johnson, 1965) of the structure is given in Fig. 1 together with the numbering scheme which is based on the coumarin heterocycle. The cyclohexyl group is pseudo-equatorial on the dihydropyran ring and *trans* to the axial hydroxyl group. The dihydropyran ring has a half-chair conformation distorted towards the *d,e*-diplanar form (Valente, Santarsiero & Schomaker, 1979). Relevant torsion angles are shown in Fig. 2. Both methylenes C(16) and C(20), bound to C(15), are plainly disposed

* Lists of structure factors, thermal parameters and bond lengths and angles, and the tabulated spectra have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34561 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Atom positions ($\times 10^4$, for H $\times 10^3$) with e.s.d.'s in parentheses

	x	y	z		x	y	z
O(1)	-4736 (2)	2536 (2)	4987 (4)	H(31)	-340 (4)	110 (3)	46 (6)
O(2)	-3026 (2)	2818 (2)	5029 (4)	H(51)	-637 (4)	42 (3)	269 (6)
O(3)	-3520 (3)	612 (2)	368 (4)	H(61)	-812 (4)	92 (3)	290 (6)
O(4)	-4409 (2)	416 (2)	2793 (4)	H(71)	-822 (4)	214 (3)	420 (6)
C(2)	-3719 (3)	2323 (2)	4725 (5)	H(81)	-665 (5)	286 (3)	521 (8)
C(3)	-3547 (3)	1550 (2)	4140 (5)	H(111)	-221 (3)	162 (2)	299 (5)
C(4)	-4438 (3)	1106 (2)	3574 (5)	H(121)	-180 (4)	31 (3)	290 (5)
C(5)	-6460 (4)	923 (3)	3153 (6)	H(122)	-246 (3)	16 (2)	448 (6)
C(6)	-7458 (4)	1223 (3)	3314 (6)	H(141)	-420 (3)	-70 (2)	79 (5)
C(7)	-7534 (4)	1935 (3)	4072 (7)	H(142)	-357 (4)	-90 (3)	276 (6)
C(8)	-6624 (4)	2372 (3)	4671 (6)	H(143)	-290 (4)	-77 (2)	107 (6)
C(9)	-5624 (3)	2074 (2)	4469 (5)	H(151)	-154 (3)	201 (3)	584 (5)
C(10)	-5517 (3)	1356 (2)	3743 (5)	H(161)	-171 (4)	45 (3)	718 (7)
C(11)	-2411 (3)	1295 (2)	3964 (5)	H(162)	-247 (4)	118 (3)	755 (5)
C(12)	-2448 (4)	451 (3)	3382 (6)	H(171)	-97 (5)	185 (3)	926 (7)
C(13)	-3446 (3)	237 (2)	2028 (6)	H(172)	-107 (4)	104 (3)	1011 (7)
C(14)	-3542 (4)	-611 (3)	1637 (7)	H(181)	32 (4)	51 (3)	858 (7)
C(15)	-1537 (3)	1444 (3)	5671 (6)	H(182)	81 (5)	129 (3)	973 (8)
C(16)	-1749 (4)	1044 (3)	7378 (6)	H(191)	40 (4)	208 (3)	705 (7)
C(17)	-895 (5)	1270 (4)	9021 (7)	H(192)	118 (5)	134 (3)	681 (5)
C(18)	251 (5)	1104 (4)	8697 (8)	H(201)	-34 (4)	66 (3)	506 (6)
C(19)	456 (4)	1476 (4)	6972 (8)	H(202)	-26 (3)	147 (3)	417 (6)
C(20)	-401 (4)	1251 (3)	5337 (7)				

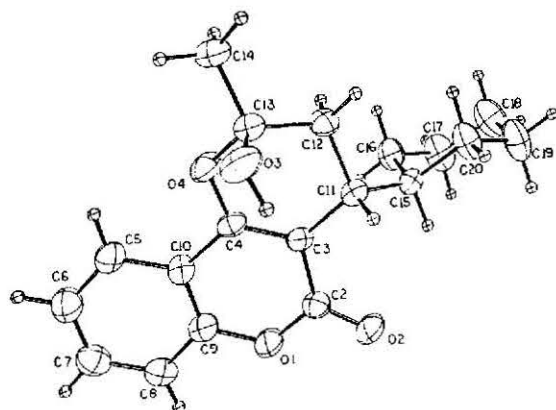
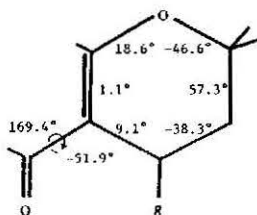


Fig. 1. An ellipsoid plot of (3) with the numbering scheme.

Fig. 2. Selected torsion angles for (3); e.s.d.'s are about 0.5° .

away from the carbonyl oxygen. The cyclohexyl group is accommodated as though it were an isopropyl group, and thus only small conformational differences between the dihydropyran rings of (3) and the *trans* (1) methyl ketal are seen.

Carbonyl and hydroxyl groups are intermolecularly hydrogen bonded along the *c* glide at an O...O distance of 2.834 (4) Å. The H on O(3) is antiperiplanar to the methyl C(14) and therefore disposed over the dihydropyran ring. This is in contrast to the more common conformation in which the substituent on O(3) is antiperiplanar to C(12) (Valente, Trager & Jensen, 1975; Valente, Lingafelter, Porter & Trager, 1977) and therefore directed away from the ring (McConnell, Schwartz & Stevens, 1979). The most obvious effect of this arrangement is the widening of O(3)-C(13)-C(12) to $113.4(4)^\circ$ and the closing of O(3)-C(13)-C(14) to $107.4(4)^\circ$ over the representative values of 109 and 112° respectively for the H antiperiplanar to C(12) (Valente, Santarsiero & Schomaker, 1979).

The solution spectra of (3) show that the open-chain keto form predominates, representing a continuation of the trend correlating decreased stability of the hemiketals with increasing bulk of the 4 substituent on the ring. The hemiketal diastereomer that constitutes the minor portion of (3) in solution is most likely the *trans* isomer, as in the crystal. This is suggested by the formation of the *trans* methyl ketal, (3a), as the product of methylation.

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