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## Structure of 2-(6-Bromo-3-methyl-4-oxo-4*H*-1-benzopyran-2-yl)-1-(2-oxocyclopentyl)-1-phenylethane

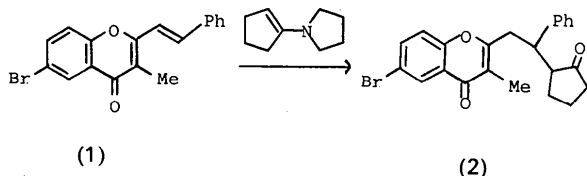
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**Abstract.**  $C_{23}H_{21}BrO_3$ ,  $M_r = 425.32$ , monoclinic,  $P2_1/c$ ,  $a = 10.656(2)$ ,  $b = 12.167(2)$ ,  $c = 15.508(2)$  Å,  $\beta = 98.42(1)^\circ$ ,  $V = 1988.9(1.0)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_x = 1.420$  g cm<sup>-3</sup>,  $\lambda(\text{Mo } K\alpha) = 0.71073$  Å,  $\mu = 20.63$  cm<sup>-1</sup>,  $F(000) = 872$ ,  $T = 295$  K,  $R = 0.041$ ,  $wR = 0.039$  for 1630 reflections. This work unambiguously establishes the position of the 2-oxocyclopentyl group in the molecule.

**Introduction.** The addition of cyclopentanone-pyrrolidine enamine to (*E*)-6-bromo-3-methyl-4-oxo-2-styryl-4*H*-1-benzopyran (1) gave a nitrogen-free crystalline product, which from <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy (Letcher & Yue, 1992) was shown to be 2-(6-bromo-3-methyl-4-oxo-4*H*-1-benzopyran-2-yl)-1-phenylethane with a 2-oxocyclopentyl substituent attached at either the 1- or 2-position of ethane. In order to determine the exact position of the substituent, the structure of the product was determined by a single-crystal X-ray analysis; the structure has been found to be that represented by (2).



**Experimental.** The title compound (2) was obtained in 50% yield from the reaction between (1) and cyclopentanone-pyrrolidine enamine, and was crystallized from 95% ethanol.

A colourless crystal of dimensions 0.15 × 0.25 × 0.2 mm was selected for intensity measurement on an

Enraf-Nonius CAD-4 diffractometer, with graphite-monochromated Mo  $K\alpha$  radiation, and scintillation counter. Cell parameters were determined by least squares from setting angles of 25 reflections ( $10 < 2\theta < 16^\circ$ ), measured on the diffractometer. The intensities of 6611 reflections ( $2\theta_{\text{max}} = 48^\circ$ ), in the range  $-12 \leq h \leq 12$ ,  $0 \leq k \leq 13$ ,  $-17 \leq l \leq 17$ , were measured using the  $\omega$ - $2\theta$  scan,  $\omega$ -scan angle  $(0.75 + 0.344 \tan \theta)^\circ$  at  $0.92$ – $5.49$  min<sup>-1</sup>, extended 25% on each side for background measurement. Three standard reflections measured every 2 h showed no decay. Systematic absences indicated  $P2_1/c$  and this was confirmed in the structure solution. The intensity data were corrected for Lorentz and polarization effects only. After equivalent reflections were averaged, the 6611 measured data gave 3280 independent reflections, of which 1630 reflections with  $I > 1.0\sigma(I)$ , where  $\sigma^2(I) = S + 4(B1 + B2)$ ,  $S = \text{scan}$ ,  $B1$  and  $B2$

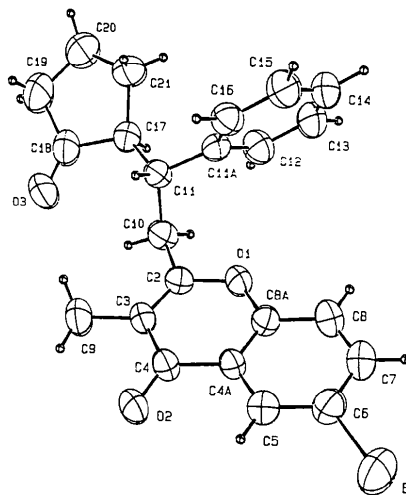


Fig. 1. ORTEP (Johnson, 1976) drawing of the molecule (2) with numbering of atoms.

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Table 1. Fractional coordinates and equivalent isotropic thermal parameters ( $\text{\AA}^2$ )
$$B_{\text{eq}} = (8\pi^2/3) \sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$$

	x	y	z	$B_{\text{eq}}$
Br	-0.07010 (5)	0.13697 (5)	0.12817 (3)	7.04 (1)
O1	0.2766 (2)	0.1750 (2)	-0.1418 (2)	4.26 (7)
O2	0.4368 (2)	0.1532 (3)	-0.1116 (2)	5.12 (8)
O3	0.7517 (3)	0.1141 (3)	-0.1997 (2)	7.9 (1)
C2	0.4058 (4)	0.1708 (3)	-0.1197 (3)	3.7 (1)
C3	0.4634 (4)	0.1619 (3)	-0.0366 (3)	4.0 (1)
C4A	0.2513 (3)	0.1537 (3)	0.0089 (2)	3.48 (9)
C4	0.3889 (4)	0.1549 (3)	0.0337 (3)	3.9 (1)
C5	0.1690 (4)	0.1428 (4)	0.0704 (3)	4.3 (1)
C6	0.0404 (4)	0.1466 (4)	0.0433 (3)	4.6 (1)
C7	-0.0101 (4)	0.1564 (4)	-0.0441 (3)	5.4 (1)
C8A	0.2008 (4)	0.1640 (3)	-0.0783 (3)	3.6 (1)
C8	0.0692 (4)	0.1653 (4)	-0.1054 (3)	5.1 (1)
C9	0.6058 (4)	0.1585 (4)	-0.0128 (3)	5.8 (1)
C10	0.4687 (4)	0.1791 (3)	-0.1995 (3)	4.1 (1)
C11A	0.3477 (4)	0.0285 (3)	-0.2904 (2)	3.62 (9)
C11	0.4766 (3)	0.0677 (3)	-0.2460 (2)	3.7 (1)
C12	0.2718 (4)	0.0950 (4)	-0.3487 (3)	4.7 (1)
C13	0.1568 (4)	0.0568 (4)	-0.3922 (3)	5.4 (1)
C14	0.1182 (4)	-0.0489 (4)	-0.3781 (3)	5.5 (1)
C15	0.1923 (4)	-0.1160 (4)	-0.3203 (3)	5.3 (1)
C16	0.3070 (4)	-0.0768 (4)	-0.2759 (3)	4.3 (1)
C17	0.5717 (3)	0.0764 (4)	-0.3121 (3)	4.1 (1)
C18	0.7102 (4)	0.0780 (4)	-0.2696 (3)	5.3 (1)
C19	0.7887 (4)	0.0195 (5)	-0.3290 (3)	8.1 (2)
C20	0.6976 (4)	-0.0107 (5)	-0.4100 (3)	7.1 (1)
C21	0.5692 (4)	-0.0180 (4)	-0.3770 (3)	5.8 (1)

= background counts, were considered observed.  $R_{\text{int}} = 0.026$  for observed reflections and 0.060 for all reflections. The structure was solved by direct methods (*MULTAN*11/82; Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1982) and refined by full-matrix least squares (on  $F$ ) with atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV) using the *SDP* programs (Enraf-Nonius, 1985) on a Micro-VAX II computer. The H atoms, in calculated positions, were not refined. Convergence for 244 variables by least-squares method with  $w = 4F_o^2/\sigma^2(F_o^2)$ , where  $\sigma(F_o^2) = [\sigma^2(I) + (0.04F_o^2)^2]^{1/2}$ , and reflections with  $I < 1.0\sigma(I)$  given negative weights, was reached at  $R = 0.041$ ,  $wR = 0.039$  and  $S = 1.043$  for 1630 reflections.  $(\Delta/\sigma)_{\text{max}} = 0.01$ . A final difference Fourier map was featureless, with maximum positive and negative peaks of 0.35 and  $0.37 \text{ e \AA}^{-3}$  respectively.

**Discussion.** An *ORTEP* drawing (Johnson, 1976) of the molecule is shown in Fig. 1. The fractional coordinates are listed in Table 1.\* Bond lengths,

\* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, bond distances and angles involving H atoms, torsion angles, root-mean-square amplitudes of thermal vibration and least-squares-planes data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55022 (29 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Bond lengths ( $\text{\AA}$ ), bond angles ( $^\circ$ ) and selected torsion angles ( $^\circ$ )

Br—C6	1.894 (4)	C8A—C8	1.404 (5)
O1—C2	1.370 (4)	C10—C11	1.543 (6)
O1—C8A	1.368 (5)	C11A—C11	1.520 (6)
O2—C4	1.241 (4)	C11A—C12	1.384 (5)
O3—C18	1.194 (5)	C11A—C16	1.380 (6)
C2—C3	1.348 (5)	C11—C17	1.547 (6)
C2—C10	1.496 (6)	C12—C13	1.389 (6)
C3—C4	1.443 (6)	C13—C14	1.377 (7)
C3—C9	1.508 (5)	C14—C15	1.374 (7)
C4A—C4	1.461 (6)	C15—C16	1.397 (5)
C4A—C5	1.393 (6)	C17—C18	1.526 (5)
C4A—C8A	1.386 (6)	C17—C21	1.525 (6)
C5—C6	1.374 (5)	C18—C19	1.509 (7)
C6—C7	1.389 (6)	C19—C20	1.516 (6)
C7—C8	1.366 (6)	C20—C21	1.532 (6)
C2—O1—C8A	119.6 (3)	C2—C10—C11	113.0 (3)
O1—C2—C3	122.8 (4)	C11—C11A—C12	121.0 (4)
O1—C2—C10	110.3 (3)	C11—C11A—C16	120.1 (3)
C3—C2—C10	126.9 (4)	C12—C11A—C16	118.8 (3)
C2—C3—C4	120.2 (3)	C10—C11—C11A	112.3 (3)
C2—C3—C9	122.5 (4)	C10—C11—C17	109.6 (3)
C4—C3—C9	117.3 (3)	C11A—C11—C17	111.0 (3)
C4—C4A—C5	122.0 (3)	C11A—C12—C13	120.7 (5)
C4—C4A—C8A	119.2 (3)	C12—C13—C14	119.9 (4)
C5—C4A—C8A	118.9 (3)	C13—C14—C15	120.2 (4)
O2—C4—C3	122.9 (3)	C14—C15—C16	119.7 (4)
O2—C4—C4A	120.6 (4)	C11A—C16—C15	120.7 (4)
C3—C4—C4A	116.4 (3)	C11—C17—C18	113.7 (3)
C4A—C5—C6	119.2 (4)	C11—C17—C21	115.9 (3)
Br—C6—C5	118.7 (4)	C18—C17—C21	102.5 (3)
Br—C6—C7	119.5 (4)	O3—C18—C17	127.1 (4)
C5—C6—C7	121.8 (5)	O3—C18—C19	124.3 (4)
C6—C7—C8	119.8 (4)	C17—C18—C19	108.6 (4)
O1—C8A—C4A	121.7 (3)	C18—C19—C20	106.0 (4)
O1—C8A—C8	116.9 (3)	C19—C20—C21	103.4 (4)
C4A—C8A—C8	121.4 (4)	C17—C21—C20	104.3 (4)
C7—C8—C8A	118.9 (4)		
O1—C2—C10—C11	-83.5 (4)	C11A—C11—C17—C18	-161.0 (4)
C3—C2—C10—C11	97.3 (5)	C11A—C11—C17—C21	-42.5 (5)
C2—C10—C11—C11A	70.8 (4)	C11—C17—C18—O3	-30.8 (7)
C2—C10—C11A—C17	-165.3 (3)	C11—C17—C18—C19	146.0 (4)
C12—C11—C11A—C10	53.6 (5)	C21—C17—C18—O3	-156.7 (5)
C12—C11—C11A—C17	-69.5 (5)	C21—C17—C18—C19	20.1 (5)
C16—C11—C11A—C10	-129.4 (4)	C11—C17—C21—C20	-160.4 (4)
C16—C11—C11A—C17	107.5 (4)	C18—C17—C21—C20	-36.0 (4)
C10—C11—C17—C18	74.4 (5)	C18—C19—C20—C21	-25.6 (6)
C10—C11—C17—C21	-167.2 (3)	C19—C20—C21—C17	38.8 (5)

bond angles and selected torsion angles are given in Table 2. All five  $\text{C}(sp^3)\text{—C}(sp^3)$  bonds have different environments and their lengths range from 1.516 (7) to 1.547 (6)  $\text{\AA}$ . The average of the bond angles at the  $\text{C}(sp^3)$  atoms (C10 and C11) is  $111.6^\circ$  and the average of the bond angles involving a  $\text{C}(sp^3)$  atom inside the oxocyclopentyl ring is  $104.1^\circ$ , while the C17—C18—C19 angle is  $108.6(4)^\circ$ . The dihedral angle between the phenyl ring and the planar portion of the oxocyclopentyl ring is  $81.1^\circ$ . Across the substituted ethane, the torsion angles C2—C10—C11—C11A and C2—C10—C11—C17 are  $70.8(4)$  and  $-165.3(3)^\circ$  respectively. Intermolecular contacts between non-H atoms less than 3.5  $\text{\AA}$  include O3...C7 (at  $1+x, y, z$ ) of 3.28  $\text{\AA}$ , O3...C15 (at  $1-x, \frac{1}{2}+y, -\frac{1}{2}-z$ ) of 3.34  $\text{\AA}$ , Br...C15 (at  $x, y, z$ ) of 3.43  $\text{\AA}$  and O2...C11 (at  $1-x, y, z$ ) of 3.44  $\text{\AA}$ .

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## Structure of 1-[(Benzyloxycarbonyl)amino]cyclopropane-1-carbohydroxamic Acid\*

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**Abstract.** C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub> (Z-Ac<sub>3</sub>c-NHOH, Z = benzyloxycarbonyl, Ac<sub>3</sub>c = 1-amino-1-cyclopropanecarboxylic acid, NHOH = hydroxamic acid), *M<sub>r</sub>* = 250.25, monoclinic, *P*2<sub>1</sub>/*n*, *a* = 25.010 (2), *b* = 6.144 (1), *c* = 8.169 (1) Å, β = 93.30 (2)°, *V* = 1253.2 (3) Å<sup>3</sup>, *Z* = 4, *D<sub>m</sub>* = 1.32, *D<sub>x</sub>* = 1.326 g cm<sup>-3</sup>, λ(Mo *K*α) = 0.71069 Å, μ = 0.943 cm<sup>-1</sup>, *F*(000) = 528.0, *T* = 298 K, final *R* value for 1807 [*I* ≥ 2.5σ(*I*)] reflections is 0.053. The conformation of the urethane —CONH— bond is unusual (*cis*). The Ac<sub>3</sub>c amino-acid residue is folded and the set of backbone torsion angles falls in the uncommon *B* ('bridge') region of the energy map. The conformation of the R—C(=O)—NHOH moiety is synperiplanar.

**Introduction.** During the past few years it has become increasingly apparent that C<sup>α,α</sup>-disubstituted glycines may be exploited to design analogs of bioactive peptides with restricted conformational flexibility (Toniole & Benedetti, 1988). In this connection, a distinct conformational preference of the 1-amino-1-cyclopropanecarboxylic acid (Ac<sub>3</sub>c) residue for the *B* ('bridge') region of the energy map (Zimmerman, Pottle, Némethy & Scheraga, 1977) was observed (Benedetti, Di Blasio, Pavone, Pedone, Santini, Crisma, Valle & Toniolo, 1989).

Electrophilic cyclopropane-containing compounds, including Ac<sub>3</sub>c peptides, have been found to be latent irreversible inhibitors of chemotherapeutically significant metalloproteinases (Breckenridge & Suckling, 1986; Suckling 1986, 1988). The potential utility of Z-Ac<sub>3</sub>c-OH as an enzyme inhibitor has been

enhanced by synthesizing its hydroxamic acid derivative. It has been shown that amino-acid and peptide hydroxamates are potent inhibitors (Nishino & Powers, 1978) and bind to metalloproteinases with the —NHOH group complexed to the metal (Holmes & Matthews, 1981).

**Experimental.** Colourless crystals of Z-Ac<sub>3</sub>c-NHOH were obtained from an acetone/petroleum ether solution by slow evaporation. X-ray diffraction data were collected on a Philips PW 1100 four-circle diffractometer with the θ/2θ scan mode (scan width 1.0°, scan speed 0.02° s<sup>-1</sup>) and Mo *K*α radiation (graphite monochromated). The crystal had approximate dimensions 0.2 × 0.2 × 0.3 mm. Unit-cell parameters were determined from least-squares refinement of 25 reflections with 15 ≤ θ ≤ 28°. Data were collected to a maximum 2θ = 56° and for -33 ≤ *h* ≤ 32, 0 ≤ *k* ≤ 8, 0 ≤ *l* ≤ 10. Three standard reflections were measured every 180 min. 3021 independent reflections were obtained, 1807 with *I* ≥ 2.5σ(*I*). *R*<sub>int</sub> for 188 equivalent reflections was 0.015. Intensities were corrected for Lorentz and polarization effects, but not for absorption. The structure was solved by direct methods using *MULTAN78* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). Anisotropic refinement based on *F* was carried out by conventional least-squares procedures with unit weights. The scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). The H atoms were localized in the difference Fourier maps and isotropically refined in the last least-squares cycle. For all calculations the *SHELX76* (Sheldrick, 1976) program was used. The final *R* value was 0.053. *S* = 1.14. (Δ/σ)<sub>max</sub> in the final refinement cycle for non-H atoms was 0.025.

\* Linear Oligopeptides. 258. Part 257: Valle, Formaggio, Crisma, Toniolo, Boesten, Polinelli, Schoemaker & Kamphuis (1992).

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