

Structure and Absolute Configuration of (–)-(3*R*)-5,7-Dimethoxy-3,9-dihydro-4′-eucomnaliny *p*-Bromobenzoate:* an Uncommon Case

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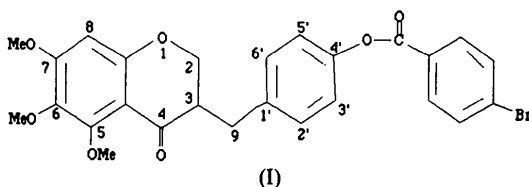
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Abstract. $C_{26}H_{23}BrO_7$, $M_r = 527.38$, triclinic, $P1$, $a = 8.066$ (1), $b = 11.044$ (2), $c = 15.518$ (4) Å, $\alpha = 112.39$ (2), $\beta = 76.40$ (2), $\gamma = 110.34$ (1)°, $V = 1190$ (1) Å³, $Z = 2$, $D_x = 1.47$ Mg m⁻³, $\lambda(\text{Cu } K\alpha) = 1.5418$ Å, $\mu = 2.73$ mm⁻¹, $F(000) = 540$, room temperature, final $R = 0.056$ for 3517 independent observed reflections and 361 parameters. The two independent molecules in the unit cell form an arrangement which is centrosymmetrical except for a few atoms around the chiral centre. The absolute configuration has been assigned on the grounds of the anomalous dispersion effect of some selected enantiomer-sensitive Friedel pairs.

Introduction. A series of homoisoflavanones with the 3-benzylchroman-4-one skeleton have been isolated from *Muscari* species (Barone, Corsaro, Lanzetta & Parrilli, 1988, and references quoted therein). Application of the chiral exciton coupling method (Harada & Nakanishi, 1983) to proper derivatives allowed the *R* configuration to be assigned to the chiral center C(3) (Adinolfi, Barone, Corsaro, Mangoni, Lanzetta & Parrilli, 1988). In order to check this result by the crystallographic Bijvoet method and, in addition, to achieve an insight into the conformational abilities of this molecular framework, a suitable bromo derivative of one of the isolated molecules, *i.e.* the title compound (I), has been prepared and crystallized.



Experimental. *Primary data collection for structure determination.* Plate-shaped crystals were grown

* Alternative name: *p*-{[(3*R*)-5,6,7-trimethoxy-4-oxochroman-3-yl]methyl}phenyl *p*-bromobenzoate.

from methanol. A crystal of dimensions $0.12 \times 0.3 \times 0.6$ mm was used for data collection on an Enraf-Nonius CAD-4 diffractometer. Its longest edge was approximately aligned with the φ axis. Ni-filtered Cu $K\alpha$ radiation was used. Cell dimensions were determined by a least-squares procedure applied to the setting angles of 24 reflections in the θ range $23 \leq \theta \leq 28^\circ$. Out of the ~ 5000 independent reflections measured by the ω/θ -scan technique with $\theta \leq 76^\circ$, $-10 \leq h \leq 10$, $-13 \leq k \leq 13$, $-19 \leq l \leq 0$, 3517 having $I_o > 3\sigma(I_o)$ were taken as observed. Three monitoring reflections showed intensity variations less than 2%. Lp correction applied, absorption ignored. The structure determination has been carried out by direct methods using MULTAN78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). Full-matrix least squares minimized $\sum w(\Delta F)^2$, $w = 1/\sigma^2(F)$. H atoms at their calculated stereochemical positions were included in structure factor calculations with isotropic thermal factors derived from those of the carrier atoms, but not refined. 361 parameters included overall scale factor, positional and anisotropic thermal parameters of the non-H atoms. Final $R = 0.056$, $wR = 0.080$, $S = 1.88$. Final $\Delta/\sigma(\text{max.}) = 0.04$. Apart from six positive satellite peaks ranging from 0.53 to 0.74 e Å⁻³, located symmetrically around the Br atoms, all other peaks in the final difference electron density map were less than 0.4 e Å⁻³.

Secondary data collection for absolute configuration determination. On the basis of the structure factor calculation, 50 enantiomer-sensitive Friedel pairs were measured several times on the CAD-4 diffractometer using Mo $K\alpha$ radiation ($\lambda = 0.7107$ Å, $\mu = 1.75$ mm⁻¹). The measurement of each reflection hkl at 2θ , ω , χ and φ was immediately followed by that of the anti-reflection $-h-k-l$ at -2θ , $\omega - 2\theta$, χ and φ . The various measurements were merged. Their disagreement, in terms of F , was 5% or less.

Atomic scattering factors and anomalous-dispersion corrections were taken from *International Tables*

for *X-ray Crystallography* (1974). All calculations were performed by the Enraf-Nonius (1979) system of programs (*SDP*) on a PDP 11/34 computer of the Centro di Metodologie Chimico-fisiche dell'Università di Napoli.*

Discussion. The calculated density was consistent with two molecules in the triclinic unit cell. The *E*-map, calculated from the best phase set produced by *MULTAN78*, showed two molecules in *quasi* centrosymmetrical arrangement (Fig. 1). All non-H atoms, except a few located around the chiral centers, were easily detected. They were correlated by a pseudo symmetry center at $x = 0.5, y = 0.5, z = 0.5$, exactly within a few times the standard deviations of atomic positions. The doubt that the compound had formed a racemic crystal of space group $P\bar{1}$ was ruled out by the observation that a solution obtained by dissolving a few crystals in CHCl₃ showed at the polarimeter a significant levorotatory optical activity. A following accurate scrutiny of the difference Fourier map allowed us to locate unambiguously the remaining non-H atoms.

The parameters for the two molecules, including the H atoms, were then refined independently by least squares. Nevertheless, the resulting molecular geometries were irregular and correlation coefficients between homologous parameters of the corresponding atoms in the two molecules, except C(2) and C(3), were as high as 0.6–0.8. The refinement was then repeated imposing a symmetry center between the molecules with the exclusion of the two fragments O(1)C(2)C(3)C(4)O(2)C(14) which were refined independently. The final values of the agreement indices were $R = 0.056$ and $wR = 0.080$. Table 1 lists the final parameters of the atoms of the molecule hereinafter indicated as *A*, together with those of the atoms independently refined, of the other molecule (molecule *B*). Atoms of molecule *B* are marked with an asterisk.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52001 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

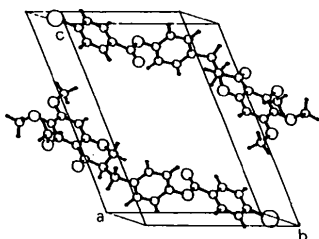


Fig. 1. Projection of the crystal structure down *a*.

Table 1. Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic thermal parameters ($\text{\AA}^2 \times 10$) of the non-H atoms with e.s.d.'s in parentheses

$$B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i a_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq}
Br	-59 (1)	8260.9 (7)	350.6 (6)	74.9 (2)
O(1)	2168 (5)	-216 (4)	3835 (3)	51 (1)
O(2)	6590 (6)	-1440 (5)	2478 (4)	94 (1)
O(3)	5958 (4)	-2977 (3)	3591 (3)	47 (1)
O(4)	3976 (5)	-3533 (3)	5153 (3)	54 (1)
O(5)	1247 (5)	-2523 (4)	6009 (3)	55 (1)
O(6)	3657 (5)	4315 (3)	1272 (3)	54 (1)
O(7)	1432 (9)	4317 (5)	2421 (4)	86 (2)
C(2)	3584 (7)	533 (6)	3305 (4)	57 (2)
C(3)	4570 (9)	-264 (6)	2563 (5)	62 (2)
C(4)	5275 (8)	-1107 (6)	2926 (5)	50 (2)
C(5)	4602 (6)	-2386 (4)	4036 (3)	39 (1)
C(6)	3575 (6)	-2714 (5)	4794 (3)	42 (1)
C(7)	2125 (7)	-2177 (5)	5249 (4)	42 (1)
C(8)	1706 (6)	-1360 (5)	4891 (4)	41 (1)
C(9)	2752 (6)	-1045 (4)	4124 (4)	39 (1)
C(10)	4259 (6)	-1500 (4)	3681 (3)	38 (1)
C(11)	7543 (7)	-2344 (6)	4032 (4)	53 (1)
C(12)	2848 (11)	-4905 (6)	4905 (6)	80 (2)
C(13)	-141 (11)	-1913 (7)	6537 (6)	59 (2)
C(14)	5906 (9)	540 (6)	1991 (6)	56 (2)
C(15)	5412 (7)	1527 (5)	1760 (4)	43 (1)
C(16)	4204 (9)	1097 (5)	1129 (4)	50 (1)
C(17)	3618 (9)	2021 (6)	980 (4)	53 (1)
C(18)	4189 (7)	3381 (5)	1487 (4)	44 (1)
C(19)	5388 (9)	3843 (5)	2115 (5)	53 (1)
C(20)	5992 (9)	2898 (6)	2243 (5)	51 (2)
C(21)	2229 (9)	4685 (6)	1776 (4)	52 (2)
C(22)	1742 (7)	5571 (5)	1412 (4)	45 (1)
C(23)	250 (9)	6015 (7)	1865 (5)	64 (2)
C(24)	-306 (8)	6804 (6)	1559 (4)	64 (1)
C(25)	657 (8)	7159 (6)	795 (5)	51 (1)
C(26)	2126 (8)	6755 (6)	350 (4)	58 (1)
C(27)	2701 (8)	5978 (5)	667 (4)	56 (1)
O(1*)	7756 (4)	10276 (3)	6195 (3)	45 (1)
O(2*)	3001 (6)	11124 (4)	7374 (3)	59 (1)
C(2*)	6981 (7)	10260 (6)	7127 (4)	44 (1)
C(3*)	4955 (7)	9820 (5)	7206 (4)	45 (1)
C(4*)	4413 (7)	10882 (5)	7040 (4)	43 (1)
C(14*)	3932 (7)	9565 (5)	8104 (4)	44 (1)

* Atoms of molecule *B*.

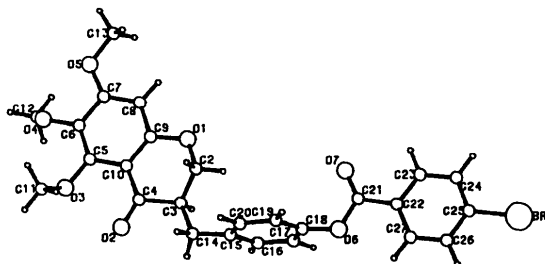
Table 2 presents bond lengths and angles. They fall in the expected ranges for the molecular moiety refined under the centrosymmetry constraint. Otherwise, geometric parameters, chemically equivalent in the two molecules and involving the atoms surrounding the chiral centers, show relevant discrepancies, much larger than their e.s.d.'s. This result is a clear effect of the too drastic refinement scheme, which transfers an excess of errors to the freely refined moiety. A perspective view of molecule *A* with the atom-labelling is scheme shown in Fig. 2.

The crystal packing (Fig. 1) does not show intermolecular contacts between non-H atoms shorter than 3.3 Å.

Molecular conformation. Excluding the methyl groups, all other non-H atoms of both molecules are roughly spread out on three planes. They are: the mean plane of the chromanone fused ring (I), the mean plane of the phenyl ring C(14)C(15)C(16)-C(17)C(18)C(19)C(20)O(6) (II) and the main plane of the *p*-bromobenzoate group (III). Plane II is approximately perpendicular to planes I and III, which are nearly coincident.

Table 2. Bond lengths (Å) and relevant valence angles (°) with their e.s.d.'s in parentheses

O(1)—C(2)	1.444 (9)	O(1*)—C(2*)	1.439 (8)
O(1)—C(9)	1.406 (7)	O(1*)—C(9*)	1.338 (6)
C(2)—C(3)	1.420 (10)	C(2*)—C(3*)	1.523 (9)
C(3)—C(14)	1.491 (13)	C(3*)—C(14*)	1.516 (11)
C(3)—C(4)	1.557 (11)	C(3*)—C(4*)	1.507 (10)
C(4)—O(2)	1.214 (10)	C(4*)—O(2*)	1.211 (9)
C(4)—C(10)	1.387 (10)	C(4*)—C(10*)	1.541 (9)
C(10)—C(9)	1.404 (6)	C(17)—C(18)	1.370 (8)
C(10)—C(5)	1.417 (6)	C(18)—C(19)	1.366 (8)
C(5)—O(3)	1.377 (5)	C(19)—C(20)	1.387 (7)
O(3)—C(11)	1.421 (6)	O(20)—C(15)	1.372 (7)
C(5)—C(6)	1.363 (7)	C(18)—O(6)	1.413 (5)
C(6)—O(4)	1.380 (5)	O(6)—C(21)	1.329 (6)
O(4)—C(12)	1.426 (7)	C(21)—O(7)	1.186 (7)
C(6)—C(7)	1.412 (7)	C(21)—C(22)	1.490 (7)
C(7)—O(5)	1.342 (6)	C(22)—C(23)	1.390 (7)
O(5)—C(13)	1.432 (7)	C(23)—C(24)	1.368 (8)
C(7)—C(8)	1.386 (6)	C(24)—C(25)	1.369 (9)
C(8)—C(9)	1.374 (7)	C(25)—C(26)	1.352 (8)
C(14)—C(15)	1.464 (11)	C(26)—C(27)	1.377 (7)
C(15)—C(16)	1.380 (7)	C(27)—C(22)	1.369 (8)
C(16)—C(17)	1.373 (7)	C(25)—Br	1.899 (5)
O(1)—C(2)—C(3)	115.2 (8)	O(1*)—C(2*)—C(3*)	111.0 (7)
C(2)—C(3)—C(4)	110.8 (8)	C(2*)—C(3*)—C(4*)	107.5 (7)
C(3)—C(4)—C(10)	116.9 (8)	C(3*)—C(4*)—C(10*)	112.9 (7)
C(4)—C(10)—C(9)	119.7 (7)	C(4*)—C(10*)—C(9*)	120.5 (7)
C(10)—C(9)—O(1)	123.6 (6)	C(10*)—C(9*)—O(1*)	120.8 (7)
C(9)—O(1)—C(2)	111.9 (6)	C(9*)—O(1*)—C(2*)	115.5 (6)
C(2)—C(3)—C(14)	112.6 (9)	C(2*)—C(3*)—C(14*)	117.6 (7)
C(3)—C(14)—C(15)	118.9 (9)	C(3*)—C(14*)—C(15*)	107.1 (7)
C(3)—C(4)—O(2)	116.7 (9)	C(3*)—C(4*)—O(2*)	123.0 (8)
O(2)—C(4)—C(10)	126.2 (9)	O(2*)—C(4*)—C(10*)	123.8 (8)
C(9)—C(10)—C(5)	116.0 (6)	C(5)—O(3)—C(11)	114.6 (6)
C(10)—C(5)—C(6)	121.5 (7)	C(5)—C(6)—O(4)	120.6 (7)
C(5)—C(6)—C(7)	120.6 (7)	O(4)—C(6)—C(7)	118.8 (7)
C(6)—C(7)—C(8)	119.2 (7)	C(6)—O(4)—C(12)	113.6 (7)
C(7)—C(8)—C(9)	119.4 (7)	C(6)—C(7)—O(5)	115.6 (7)
C(8)—C(9)—C(10)	123.2 (7)	O(5)—C(7)—C(8)	125.2 (8)
C(10)—C(5)—O(3)	119.8 (6)	C(7)—O(5)—C(13)	117.5 (8)
O(3)—C(5)—C(6)	118.6 (6)		

Fig. 2. Perspective view of molecule *A* showing the atom-labelling scheme.

The most interesting conformational features are those concerning the flexibility of the dihydro- γ -pyrone, which allows the homochiral molecules *A* and *B* to pack in such a way that about 94% of the electronic density is in a centrosymmetrical arrangement. Fig. 3 shows in (a) and (b) the conformations of the dihydro- γ -pyrone ring in molecules *A* and *B* respectively, and in (c) the dihydro- γ -pyrone ring as obtained by inversion of the molecule *A* through the pseudo center of symmetry.

The comparison of the figures shows how the conformational changes between molecules *A* and *B* are essentially limited to atoms C(2) and C(3) which together with the attached H atoms are also the only

atoms responsible for departure from the exact centrosymmetrical arrangement. In molecule *A* the dihydro- γ -pyrone ring displays a nearly regular sofa conformation with C(2) at the flap, 0.457 (8) Å out of the plane of the chromanone ring.

The values of the ring-puckering parameters according to Cremer & Pople (1975) for the sequence O(1)—C(2)—C(3)—C(4)—C(10)—C(9) are: Q (puckering amplitude) = 0.407 (8) Å, $\theta = 128.7 (9)^\circ$, $\varphi = 250 (1)^\circ$. In molecule *B* the dihydro- γ -pyrone ring is more distorted and displays a conformation intermediate between sofa and half-chair, in which C(2*) and C(3*) have the largest out-of-plane amplitudes, 0.582 (6) and 0.291 (6) Å respectively. For the same sequence, the ring puckering parameters have the following values: $Q = 0.533 (8) \text{ \AA}$, $\theta = 118.8 (9)^\circ$, $\varphi = 257 (1)^\circ$. In both molecules the H atom linked to C(3) is in the axial position.

Absolute configuration. As most atoms of the structure are in a centrosymmetrical arrangement, the anomalous-dispersion effects are expected to be tiny. Nevertheless, structure factors, calculated at the end of refinement, showed a sufficient number of enantiomer-sensitive Friedel pairs with values of $\Delta F^c = |F_{hkl}^c| - |F_{-h-k-l}^c|$ quite larger than the standard deviations of the corresponding observed amplitudes. 50 enantiomer-sensitive Friedel pairs have been re-measured using Mo radiation in order to reduce the absorption errors.

Table 3 shows the results for the 20 most sensitive ones. Atomic coordinates of Table 1, which correspond to *R* chirality for C(3), were used in calculating the structure factors. The full agreement between observed ΔF^o and calculated ΔF^c , which holds even for the Friedel pairs not included in Table 3, gives convincing evidence of the correctness of the

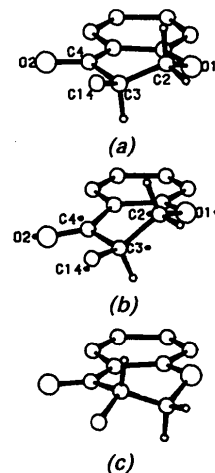
Fig. 3. (a) The heterocycle ring in molecule *A*, (b) in molecule *B* and (c) that obtained by inversion of molecule *A* through the pseudo symmetry centre.

Table 3. *Effects of anomalous dispersion of Mo K α radiation measured on selected Friedel pairs*

$\Delta F^o = |F_h^o| - |F_{-h}^o|$ is the difference between the observed structure factors for the Friedel pair; $\Delta F^c = |F_h^c| - |F_{-h}^c|$ is the corresponding difference between the structure factors calculated from the coordinates of Table 1. The terms of anomalous dispersion used for the C atom and Mo radiation are $f' = 0.002$, $f'' = 0.002$.

<i>h</i>	<i>k</i>	<i>l</i>	θ	ΔF^o	ΔF^c
4	-4	9	14.2	10.6 (7)	9.2
-6	5	-6	16.3	-7.4 (8)	-6.8
2	-1	6	8.9	9.7 (4)	9.9
-1	4	6	13.9	4.3 (8)	3.9
-2	-1	-5	9.6	-9.7 (4)	-12.9
2	0	5	8.5	6.4 (4)	6.2
-3	0	-5	10.2	9.0 (8)	8.5
-2	-3	4	10.3	-7.2 (6)	-7.1
2	2	-4	9.2	11.1 (4)	9.3
2	0	-4	8.4	4.8 (6)	6.9
1	-1	-4	7.3	-13.8 (4)	-14.7
2	-3	-4	10.7	-4.3 (7)	-7.2
0	4	3	10.6	-9.4 (8)	-12.2
-1	-3	-3	9.5	-14.9 (6)	-13.1
2	-6	3	11.2	4.7 (6)	9.9
3	3	-2	11.8	6.3 (4)	5.2
-2	0	2	6.4	-5.7 (3)	-4.7
2	-4	-2	10.1	10.7 (6)	10.9
1	-3	1	6.8	18.5 (4)	17.0
4	5	-1	17.2	5.1 (11)	4.8

assumed *R* chirality at C(3). This result, moreover, agrees with that obtained by the chiral exciton coupling method (Adinolfi *et al.*, 1988).

Finally, it is worth noting that, apart from the formal difference in the chirality symbol (*R* instead of *S*), the title compound is stereochemically congruent, in conformation and configuration of the

dihydro- γ -pyrone ring, with Eucomol, a natural compound with the same heterocycle system, in which a hydroxyl group replaces the H atom at C(3) (Weber, Heller & Tamm, 1977).

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Structure of *N*,2-Dibenzoylthioacetamide

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Abstract. C₁₆H₁₃NO₂S, *M_r* = 283.35, monoclinic, *C*2/*c*, *a* = 28.40 (2), *b* = 3.927 (3), *c* = 24.25 (2) Å, β = 90.12 (6)°, *V* = 2705 (3) Å³, *Z* = 8, *D_x* = 1.39 g cm⁻³, $\lambda(\text{Mo } K\alpha)$ = 0.71073 Å, μ = 2.28 cm⁻¹,

F(000) = 1184, *T* = 143 K, *R* = 0.054 for 2407 observed reflections. The molecule exists as a keto-thio keto-enol tautomer with enolization of the O atom in the 2-acylthioacetamide fragment. The con-