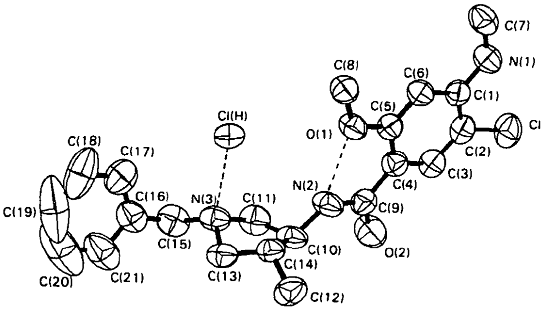

Fig. 1. Molecular structure and atom numbering.

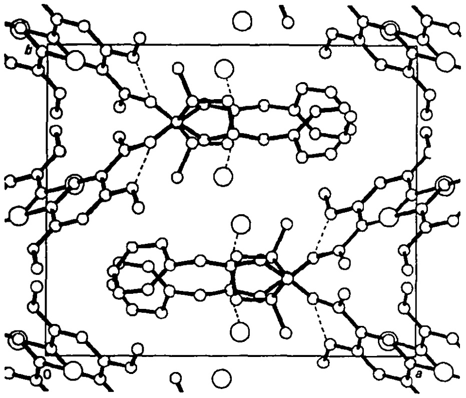

Fig. 2. Projection of the structure on the *ab* plane.

C(9) [1·492 (5) Å] are distinctly shorter than the ordinary single bond. These indicate that there is some contribution of the quinonoidal form. The benzene ring *A* [C(1)–C(6)] is almost planar with a maximum atomic deviation of 0·004 Å. The amino, methoxy and carbamoyl groups also lie on the plane.

An intramolecular hydrogen bond between the amide N(2) and methoxy O(1) results in a six-membered ring fused with the benzene ring *A*. This type of hydrogen bond is also observed in the benzamide neuroleptics we have studied and in metochlopramide (Cesario, Pascard, Moukhtari & Jung, 1981). The N(2)···O(1) length [2·635 (4) Å] is rather shorter than that of the compounds [2·662 (3)–2·716 (9) Å] in this series of studies and in metochlopramide [2·683 (6) Å]. Thus, the benzamide moiety constitutes a rigid part of the molecule by this strong hydrogen bond.

The distance between the tertiary amino N and the center of the benzene ring *A* and the deviation of the N from the mean plane of the ring *A* are used as the parameters relevant to neuroleptic activity. Comparing these values of the present compound to those of the compounds having a methyl group at the 2-position of the pyrrolidine ring, the distance, 6·91 Å, is longer than that of the free base of YM-09151-2 (6·26 Å) (Furuya *et al.*, 1982), but shorter than that of the hydrochloride of YM-09151-1 (7·25–7·5 Å) (Furuya *et al.*, 1986). On the other hand, the deviation of the present molecule, 1·75 Å, is rather greater than that of both compounds (–0·9–0·0 Å).

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*Acta Cryst.* (1986). C**42**, 1191–1194

# Nonsteroidal Antiinflammatory Drugs. IV. Structure of (±)-(2*SR*)-2-{4-[(1*RS*,2*RS*)-2-Hydroxycyclopentylmethyl]phenyl}propionic Acid

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**Abstract.** $C_{15}H_{20}O_3$, $M_r = 248{\cdot}3$, triclinic, $P\bar{1}$, $a = 21{\cdot}511\,(1)$, $b = 12{\cdot}275\,(1)$, $c = 5{\cdot}5745\,(4)$ Å, $\alpha = 103{\cdot}05\,(1)$, $\beta = 101{\cdot}59\,(1)$, $\gamma = 73{\cdot}73\,(1)°$, $V = 1361{\cdot}4\,(2)$ Å$^3$, $Z = 4$, $D_x = 1{\cdot}21$ g cm$^{-3}$, graphite-monochromated Cu $K\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 6{\cdot}8$ cm$^{-1}$, $F(000) = 536$, $T = 298$ K, final $R = 0{\cdot}068$ for 2042 reflections. The molecules form tetramers through four hydrogen bonds between the carboxyl and hydroxyl

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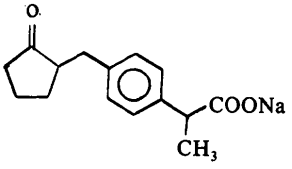
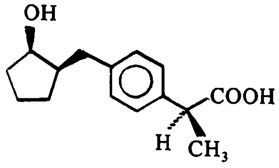
groups. The two benzene rings in the independent molecules have different rotational angles with respect to the substituent groups, but are otherwise similar. All bond lengths and bond angles are normal.

**Introduction.** Sodium (+)-2-[4-(2-oxocyclopentylmethyl)phenyl]propionate (loxoprofen sodium) (1) is a newly synthesized 2-arylpropionic acid derivative having potent antiinflammatory and analgesic activities (Terada, Naruto, Wachi, Tanaka, Iizuka & Misaka, 1984). The inhibitory studies of loxoprofen sodium for prostaglandin synthesis *in vivo* and *in vitro* suggested that loxoprofen sodium may exhibit inhibitory activity after the conversion to an active metabolite of (+)-(2*S*)-2-{4-[(1*R*,2*S*)-2-hydroxycyclopentylmethyl]-phenyl}propionic acid (Matsuda, Tanaka, Ushiyama, Ohnishi & Yamazaki, 1984). Although the title compound (2) is the steroisomer of this active metabolite of (1), poor inhibition of prostaglandin synthesis was observed. We have tried to elucidate the structure of (2) in order to gain information on structure/activity relationships.



(1)



(2)

Table 1. *Fractional atomic coordinates* (×10⁴) *and equivalent isotropic thermal parameters* (Å²), *with e.s.d.'s in parentheses*

$$B_{\rm eq} = \tfrac{1}{3}\sum_i\sum_j B_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

| | $x$ | $y$ | $z$ | $B_{\rm eq}$ |
|---|---|---|---|---|
| Molecule (I) | | | | |
| C(1) | 1552 (3) | 1035 (5) | −59 (10) | 3·3 (2) |
| C(2) | 1822 (3) | 1564 (5) | −1360 (11) | 3·6 (2) |
| C(3) | 1854 (3) | 2713 (5) | −508 (12) | 4·4 (2) |
| C(4) | 1600 (3) | 3343 (5) | 1614 (11) | 3·5 (2) |
| C(5) | 1317 (3) | 2813 (5) | 2916 (11) | 4·0 (2) |
| C(6) | 1300 (3) | 1651 (5) | 2061 (11) | 4·3 (2) |
| C(7) | 1540 (3) | −235 (5) | −937 (11) | 3·8 (2) |
| C(8) | 856 (3) | −415 (6) | −1492 (14) | 6·0 (3) |
| C(9) | 1971 (3) | −917 (5) | 1004 (11) | 3·8 (2) |
| O(10) | 1776 (2) | −1153 (4) | 2654 (8) | 5·6 (2) |
| O(11) | 2600 (2) | −1195 (4) | 758 (8) | 5·0 (2) |
| C(12) | 1661 (3) | 4579 (5) | 2483 (12) | 4·3 (2) |
| C(13) | 1027 (3) | 5470 (5) | 1771 (11) | 3·6 (2) |
| C(14) | 1135 (3) | 6655 (5) | 1796 (12) | 4·0 (2) |
| C(15) | 447 (3) | 7426 (5) | 1667 (13) | 5·1 (3) |
| C(16) | 83 (3) | 6957 (6) | 3111 (14) | 6·5 (3) |
| C(17) | 494 (3) | 5733 (6) | 3426 (13) | 5·6 (3) |
| O(18) | 1534 (2) | 6992 (3) | 4125 (8) | 4·8 (2) |
| Molecule (II) | | | | |
| C(1) | 6571 (3) | 6313 (5) | 1683 (10) | 3·0 (2) |
| C(2) | 6324 (3) | 7004 (5) | −127 (11) | 3·7 (2) |
| C(3) | 6335 (3) | 8151 (5) | 402 (11) | 4·1 (2) |
| C(4) | 6609 (3) | 8643 (5) | 2724 (11) | 3·2 (2) |
| C(5) | 6851 (3) | 7968 (5) | 4532 (10) | 3·2 (2) |
| C(6) | 6835 (3) | 6813 (5) | 4009 (10) | 3·1 (2) |
| C(7) | 6539 (3) | 5047 (5) | 1023 (11) | 3·4 (2) |
| C(8) | 5837 (3) | 4967 (6) | 904 (14) | 6·2 (3) |
| C(9) | 6999 (3) | 4351 (5) | 2860 (11) | 3·5 (2) |
| O(10) | 6835 (2) | 4140 (4) | 4627 (8) | 5·4 (2) |
| O(11) | 7604 (2) | 4021 (3) | 2373 (8) | 4·4 (2) |
| C(12) | 6659 (3) | 9888 (5) | 3224 (12) | 4·2 (2) |
| C(13) | 6012 (3) | 10775 (5) | 3608 (11) | 3·8 (2) |
| C(14) | 6053 (3) | 12030 (5) | 3860 (11) | 4·2 (2) |
| C(15) | 5401 (3) | 12713 (5) | 4688 (13) | 5·3 (3) |
| C(16) | 5236 (3) | 12007 (6) | 6302 (14) | 6·4 (3) |
| C(17) | 5726 (3) | 10819 (5) | 5936 (12) | 4·7 (2) |
| O(18) | 6588 (2) | 12253 (3) | 5762 (8) | 4·9 (2) |

**Experimental.** Colorless prisms grown by slow evaporation of a solution in mixture of ether and hexane at room temperature; approximate crystal dimensions 0·1 × 0·1 × 0·7 mm. Rigaku-Denki AFC-5 automated diffractometer, graphite-monochromated Cu $K\alpha$, 25 reflections with $30 < 2\theta < 50°$ used to determine cell parameters. No absorption correction. $2\theta_{\rm max} = 130°$, $\omega$–$2\theta$ scan, range of $hkl$: −23–24, −14–14, 0–6. No significant variation in intensities for three standard reflections. 4053 reflections measured; 2042 unique with $F \geq 3\sigma(F)$ used for structure solution and refinement, $R_{\rm int} = 0·049$. Structure solved by direct methods using *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). Block-diagonal least-squares refinement based on $F$ for non-H atoms with anisotropic thermal parameters. H-atom positions determined from difference Fourier synthesis and refined with isotropic thermal parameters. Final refinement converged at $R = 0·068$, $wR = 0·049$, $S = 0·87$; $w = 1/\sigma(F)$, $(\Delta/\sigma)_{\rm max}$ 0·05 for non-H atoms, 0·35 for H atoms. Max. peak height on final map 0·2 e Å$^{-3}$. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Calculations carried out with the *DIRECT-SEARCH* program system described by Koyama & Okada (1975).

**Discussion.** Fractional atomic coordinates and equivalent isotropic thermal parameters are given in Table 1.* The atom labelling and anisotropic thermal ellipsoids of the two independent molecules (I) and (II) are shown in Fig. 1. Bond lengths and angles are given in Table 2; they are all normal within the limits of experimental error.

The torsional angles C(2)—C(1)—C(7)—C(9) and C(1)—C(7)—C(9)—O(10) of the propionic acid side chain are 114·7 (6) and 94·9 (7)° in (I) and 162·6 (5) and 96·2 (7)° in (II), respectively. Although the values for (I) are compatible with those of 111·7 and 90·2° in naproxen (Ravikumar, Rajan, Pattabhi & Gabe, 1985),

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* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Divison as Supplementary Publication No. SUP 42970 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

one of those for (II) is very large. Recently, the large torsional angle of 144·2° has been found in a derivative of 2-methyl-2-phenylpropionic acid (Hata, Sato & Tamura, 1986), an overcrowded compound.

The cyclopentane rings of the two independent molecules adopt half-chair conformations with axial hydroxyl groups and equatorial methylphenyl groups. In (I), C(13) and C(14) are displaced by 0·23 (3) and −0·40 (3) Å from the plane through C(15)—C(16)—C(17) and in (II) C(13) is displaced by 0·41 (10) Å and C(14) by −0·28 (10) Å. The rotational angles C(3)—C(4)—C(12)—C(13) in (I) and (II) are 100·7 (7) and 76·6 (8)° and angles C(4)—C(12)—C(13)—C(14) are −160·0 (5) and −174·4 (4)°, respectively. These values make the dihedral angle between the benzene and cyclopentane rings 42·8 (3)° for (I) and 70·2 (3)° for (II). Although this non-planarity is required to avoid steric hindrance, the rotational angles are different in the two molecules.

The crystal structure of the title compound is shown in Fig. 2. The molecules form tetramers through four hydrogen bonds. The O(18) atom in (I) donates a proton to O(10$^{i}$) in the same molecule (I) and accepts another from O(11$^{ii}$) in (II) [(i) *x*, 1+*y*, *z*; (ii) 1−*x*, 1−*y*, 1−*z*]. Atom O(18$^{iii}$) in (II) also donates to O(10$^{ii}$) in the same molecule (I) and accepts from O(11$^{i}$) in a different molecule (I) [(iii) 1−*x*, 2−*y*, 1−*z*]. The lengths of these four hydrogen bonds are 2·793 (7), 2·674 (6), 2·745 (7) and 2·646 (6) Å, respectively. The geometries of the two independent molecules are very similar except for the relative orientations of the benzene rings as shown in Figs. 1 and 2. The carboxyl group forms a dihedral angle of 42·7 (3)° with the cyclopentane ring in (I) and 46·7 (3)° in (II). The benzene ring in (II) is rotated by 39·8° compared with (I) along the axis through the C(1) and C(4) atoms.

Table 2. *Bond lengths* (Å) *and bond angles* (°), *with e.s.d.'s in parentheses*

| | (I) | (II) | | (I) | (II) |
|---|---|---|---|---|---|
| C(1)—C(2) | 1·370 (10) | 1·392 (9) | C(9)—O(10) | 1·204 (9) | 1·211 (9) |
| C(1)—C(6) | 1·374 (8) | 1·386 (7) | C(9)—O(11) | 1·326 (8) | 1·314 (7) |
| C(1)—C(7) | 1·532 (8) | 1·532 (8) | C(12)—C(13) | 1·535 (7) | 1·529 (7) |
| C(2)—C(3) | 1·399 (9) | 1·378 (9) | C(13)—C(14) | 1·532 (9) | 1·540 (9) |
| C(3)—C(4) | 1·380 (8) | 1·388 (8) | C(13)—C(17) | 1·535 (10) | 1·528 (10) |
| C(4)—C(5) | 1·391 (10) | 1·378 (8) | C(14)—C(15) | 1·515 (8) | 1·519 (9) |
| C(4)—C(12) | 1·519 (8) | 1·521 (9) | C(14)—O(18) | 1·449 (7) | 1·443 (7) |
| C(5) C(6) | 1·406 (9) | 1·390 (8) | C(15)—C(16) | 1·519 (12) | 1·529 (12) |
| C(7)—C(8) | 1·510 (10) | 1·528 (9) | C(16)—C(17) | 1·543 (10) | 1·540 (8) |
| C(7)—C(9) | 1·518 (8) | 1·508 (8) | | | |

| | (I) | (II) |
|---|---|---|
| C(2)—C(1)—C(6) | 119·4 (6) | 117·8 (5) |
| C(2)—C(1)—C(7) | 120·4 (5) | 118·9 (5) |
| C(6)—C(1)—C(7) | 120·2 (6) | 123·3 (5) |
| C(1)—C(2)—C(3) | 120·3 (5) | 120·8 (5) |
| C(2)—C(3)—C(4) | 120·9 (7) | 121·1 (6) |
| C(3)—C(4)—C(5) | 118·9 (6) | 118·5 (5) |
| C(3)—C(4)—C(12) | 118·6 (6) | 120·5 (6) |
| C(5)—C(4)—C(12) | 122·5 (5) | 121·0 (5) |
| C(4)—C(5)—C(6) | 119·6 (6) | 120·4 (5) |
| C(1)—C(6)—C(5) | 120·9 (7) | 121·3 (5) |
| C(1)—C(7)—C(8) | 112·9 (5) | 109·9 (4) |
| C(1)—C(7)—C(9) | 108·5 (4) | 111·4 (4) |
| C(8)—C(7)—C(9) | 111·9 (6) | 110·6 (6) |
| C(7)—C(9)—O(10) | 124·6 (6) | 124·0 (5) |
| C(7)—C(9)—O(11) | 112·6 (6) | 112·5 (6) |
| O(10)—C(9)—O(11) | 122·7 (5) | 123·5 (5) |
| C(4)—C(12)—C(13) | 113·0 (5) | 113·8 (5) |
| C(12)—C(13)—C(14) | 113·5 (5) | 113·4 (5) |
| C(12)—C(13)—C(17) | 116·1 (6) | 116·7 (5) |
| C(14)—C(13)—C(17) | 104·1 (5) | 102·5 (5) |
| C(13)—C(14)—C(15) | 102·9 (5) | 102·2 (6) |
| C(13)—C(14)—O(18) | 108·5 (5) | 109·7 (5) |
| C(15)—C(14)—O(18) | 111·0 (4) | 110·6 (5) |
| C(14)—C(15)—C(16) | 106·0 (6) | 106·3 (5) |
| C(15)—C(16)—C(17) | 107·0 (6) | 105·9 (6) |
| C(13)—C(17)—C(16) | 104·6 (6) | 104·6 (6) |

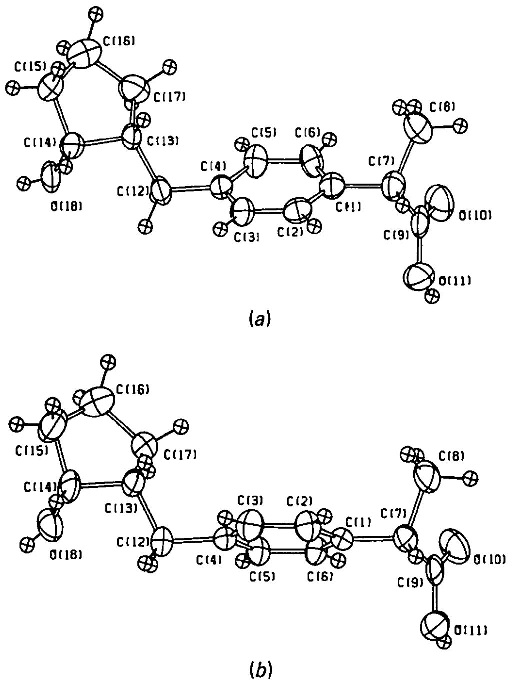

Fig. 1. *ORTEP* plots (Johnson, 1965) of the two independent molecules in the title compound with thermal ellipsoids at the 50% probability level. (*a*) Molecule (I), (*b*) Molecule (II).

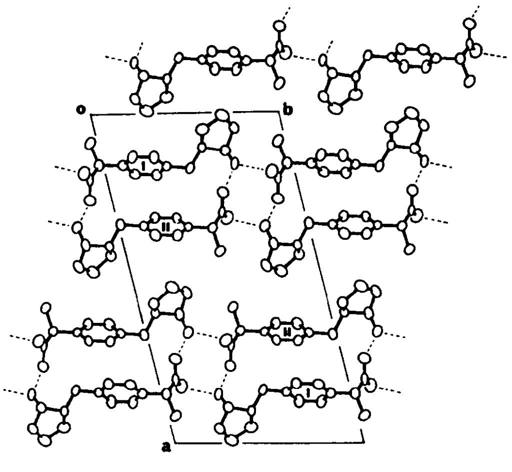

Fig. 2. Packing diagram down the *c* axis.

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# Structure of 10-[4-(Acetoxy)phenyl]-10-hydroxy-9(10*H*)-anthracenone*

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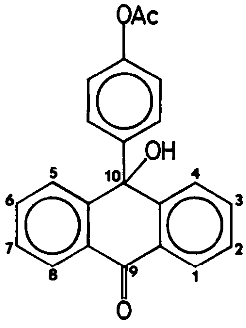
(*Received* 6 *January* 1986; *accepted* 21 *February* 1986)

**Abstract.** $C_{22}H_{16}O_4$, $M_r = 344·37$, triclinic, $P\bar{1}$, $a = 7·1485\,(3)$, $b = 9·3921\,(5)$, $c = 13·509\,(1)$ Å, $\alpha = 108·186\,(4)$, $\beta = 99·371\,(3)$, $\gamma = 95·515\,(3)°$, $V = 839·67\,(9)$ Å$^3$, $Z = 2$, $D_x = 1·362$ Mg m$^{-3}$, $\lambda(\text{Cu}\,K\alpha) = 1·54178$ Å, $\mu = 0·72$ mm$^{-1}$, $F(000) = 360$, room temperature, final $R = 0·055$ for 2722 unique observed reflections. The molecules, stacked head to tail, form dimers by hydrogen bonding between hydroxyl and carbonyl groups with distance O—H···O = 2·844 (2) Å.

**Introduction.** The structure determination of the title compound (I) forms part of an investigation of the relationship between structure and reactivity of a hydroxyl group attached to the central C(10) atom of various related compounds.



(I)

**Experimental.** Crystals pale yellow prisms (from ethanol), m.p. 554·1–555·1 K (Gronowska & Dzieleńdziak, 1982); $D_m$ not determined; space group determined by film methods to be $P1$ or $P\bar{1}$; lattice parameters refined and intensity data obtained from a crystal approx. 0·7 × 0·3 × 0·2 mm sealed in a thin-walled glass capillary and mounted in random orientation on CAD-4 diffractometer, Ni-filtered Cu $K\alpha$ radiation, $\omega/2\theta$-scan mode, scan width $(0·60 + 0·14\tan\theta)°$, horizontal aperture $(2·50 + 0·80\tan\theta)$ mm, vertical aperture 4 mm; max. $\sin\theta/\lambda = 0·6285$ Å$^{-1}$; $hkl$ range: $h = -8\rightarrow 8$, $k = -11\rightarrow 11$, $l = 0\rightarrow 16$. Three standard reflections monitored periodically showed no significant variation, 3490 reflections measured, 2724 with $I > 2\sigma(I)$ employed for structure determination. Data corrected for Lorentz and polarization factors, but not for absorption or extinction. Structure solved by direct methods with *SHELXS*84 (Sheldrick, 1984) in space group $P\bar{1}$, justified by calculated $E$ statistics; successfully refined by full-matrix least squares (Sheldrick, 1976), using 2722 reflections in last cycle (two reflections suffering seriously from extinction omitted); $\sum w(|F_o| - |F_c|)^2$ minimized, $w^{-1} = \sigma^2(F)$. Seven H atoms located from Fourier difference map, rest determined from geometrical considerations. All H atoms (methyl group as rigid group with geometrical constraints: C—H 1·08 Å, H—C—H 109·5°) refined isotropically, non-H atoms anisotropically. Final $R = 0·055$, $wR = 0·060$, $S = 3·76$. Max. $\Delta/\sigma = 0·09$ for positional and thermal parameters, and 0·7 for rotation parameters of the rigid methyl group, highest and lowest residual peaks in the final difference Fourier map +0·35 and −0·43 e Å$^{-3}$.

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* IUPAC name: 4-(9,10-dihydro-9-hydroxy-10-oxo-9-anthryl)-phenyl acetate.

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