Open-chain sulfones show a remarkable constancy for this distance (Hargittai, 1985*a*); its mean value is 2·484 Å with a standard deviation of 0·004 Å in a large group of substances. This result refers to free gas-phase molecules. The SO_2 geometries in crystalline sulfones are generally similar to those of the free molecules. The O···O distances, however, show a much greater variation in the crystalline phase (Hargittai, 1985*a*). The mean value of the O···O distances in some crystalline sulfones is 2·47 Å ($\sigma = 0.02$ Å). Thermal-motion corrections have not always been employed in the sample examined, therefore one has to be cautious in making conclusions.

There are only few data for cyclic sulfones and only the ethylene episulfone (thiirane 1,1-dioxide), $(CH_2)_2SO_2$, O···O distance was determined accurately, *viz.* 2·501 (3) Å, by microwave spectroscopy (Nakano, Saito & Morino, 1970).

The present result of $r_g(O\cdots O) = 2.516$ (10) Å seems to be more plausible than the 2·39 Å observed in the crystal structure. If the latter were correct, it could be a consequence of intermolecular interactions. However, in the above-mentioned sample of 35 crystalline molecules, none had an O···O distance shorter than 2·44 Å (Hargittai, 1985*a*).

The molecule is puckered both in the gas and in the crystal phase. The equilibrium structure is not necessarily different as the consequences of averaging over intramolecular motion are not the same in the two experiments.

The presence of both equatorial and axial bromine positions is indicated by the electron diffraction data. This is an interesting result that will hopefully incite spectroscopic studies of this structure. Further information on the molecular vibrations of this compound could make a more detailed analysis of the present electron diffraction data worthwhile.

The electron diffraction patterns were recorded by Mrs Mária Kolonits and we appreciate her skillful assistance. Dr Béla Rozsonai did some work on the experimental intensity curves and instructed one of us (JB) in the use of some programs.

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Nonsteroidal Antiinflammatory Drugs. I. Structure of 2-(2-Isopropyl-5-indanyl)-2-methylpropionic Acid

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Abstract. $C_{16}H_{22}O_2$, $M_r = 246.4$, monoclinic, $P2_1/c$, $a = 13.674$ (2), $b = 6.686$ (2), $c = 15.670$ (2) Å, $\beta = 92.14$ (2)°, $V = 1431.6$ (5) Å^3, $Z = 4$, $D_x = 1.14$ g cm^{-3}, graphite-monochromated Cu $K\alpha$, $\lambda = 1.5418$ Å, $\mu = 5.9$ cm^{-1}, $F(000) = 536$, $T = 298$ K, final $R = 0.074$ for 1748 reflections. The torsion angle of the 2-methyl-2-phenylpropionic acid moiety with respect to the benzene ring is larger than those of 2-phenylpropionic acid derivatives owing to the substituted methyl groups. Such a restriction in conformation may be related to the attenuation of the antiinflamatory activity.

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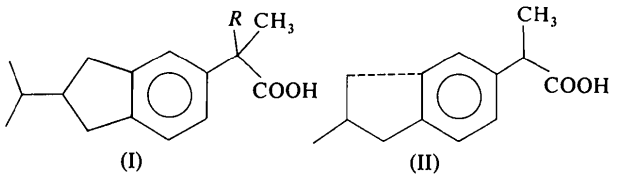
Introduction. In the course of a series of studies on non-steroidal antiinflammatory drugs, several indanylpropionic acid derivatives were synthesized, among which 2-(2-isopropyl-5-indanyl)propionic acid (I*a*) exhibited a particularly potent activity (Yoshida *et al.*, 1980). The structure of this compound includes an indan ring system that may be compatible with the structure of ibuprofen (II) if one of the methyl groups is brought close to the *ortho* position of the benzene ring, as shown in (II) by the dotted line. Methyl substitution of the 2-position of the propionic acid in (I*a*) lowers the antiinflammatory activity. To gain insight into the structure/activity relationship of this series of related compounds, the crystal structure of the title compound (I*b*) was investigated.



(I) (II)

(*a*) R=H
(*b*) R=CH_3

Experimental. Colorless prisms grown from hexane solution by slow evaporation at room temperature; approximate crystal dimensions 0·2 × 0·3 × 0·9 mm. Rigaku AFC-5 automated diffractometer, graphite-monochromated Cu $K\alpha$. Twenty reflections with $18 < 2\theta < 29°$ used to determine cell parameters. No absorption correction. $2\theta_{max} = 120°$, ω–2θ scan, range of h,k,l: 0–15, 0–7, −17–17. No significant variation in intensities for three standard reflections. 2129 reflections measured; 1750 unique with $F \geq 3\sigma(F)$ used for structure determination. Structure solved by direct methods using *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). Full-matrix least-squares refinement on F for non-H atoms with anisotropic thermal parameters. Positions of H atoms except those of isopropyl group detectable in difference Fourier synthesis and refined with isotropic thermal parameters. H atoms of isopropyl group included in refinement at idealized positions, but with parameters fixed ($B = 10·0$ Å^2). Two intense low-angle reflections (004, 012) affected by secondary extinction and excluded. Final refinement converged at $R = 0·074$, $wR = 0·054$, $S = 0·53$; $w = 1/\sigma^2(F)$. $(\Delta/\sigma)_{max}$ 0·01 for non-H atoms, 0·15 for H atoms. Max. peak height on final $\Delta\rho$ map 0·2 e Å^{-3}. Further improvement of discrepancy factor by another weighting scheme failed owing to some disorder of the five-membered ring and attached isopropyl group. 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 the anisotropic thermal ellipsoids are shown in Fig. 1. Bond lengths and angles are given in Table 2. They are all normal within the limits of experimental error except for the isopropyl group in which the thermal parameters are large and the bond lengths are short owing to some disorder.

The five-membered-ring system adopts an envelope-shape conformation with C(14) displaced by 0·16 (2) Å from the plane through the remaining four atoms, to which the isopropyl group is connected at the equatorial position.

The torsion angles C(2)–C(1)–C(7)–C(10) and C(1)–C(7)–C(10)–O(11) of the 2-methylpropionic acid side chain are 144·2 (3) and 110·0 (4)°, respectively, whereas the corresponding angles of the propionic acid derivatives are 96·4, 89·3° in ibuprofen (McConnell, 1974) and 107·5, 77·2° in flurbiprofen (Flippen & Gilardi, 1975).

* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42486 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional atomic coordinates* (×10^4) *and equivalent isotropic thermal parameters* (Å^2) *with e.s.d.'s in parentheses*

$B_{eq} = \frac{1}{3}\sum_i\sum_j B_{ij}a^*_i a^*_j \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
C(1)	2345 (2)	2532 (5)	3726 (2)	2·80 (10)
C(2)	3077 (3)	1105 (6)	3673 (2)	3·30 (11)
C(3)	4059 (2)	1678 (5)	3705 (2)	3·02 (10)
C(4)	4311 (2)	3671 (6)	3787 (2)	3·03 (11)
C(5)	3588 (3)	5097 (6)	3840 (3)	4·03 (13)
C(6)	2621 (3)	4510 (6)	3804 (2)	3·71 (12)
C(7)	1258 (2)	1976 (5)	3640 (2)	2·98 (10)
C(8)	886 (3)	2334 (7)	2720 (3)	4·21 (13)
C(9)	1057 (3)	−214 (7)	3894 (3)	4·52 (14)
C(10)	696 (2)	3304 (5)	4240 (2)	3·27 (11)
O(11)	144 (2)	4612 (4)	3986 (1)	4·81 (8)
O(12)	864 (2)	2957 (4)	5051 (2)	4·87 (9)
C(13)	4961 (3)	378 (7)	3689 (3)	4·28 (13)
C(14)	5793 (3)	1823 (7)	3655 (4)	6·80 (18)
C(15)	5410 (3)	3902 (7)	3818 (3)	3·97 (13)
C(16)	6787 (3)	1289 (7)	3822 (3)	6·87 (17)
C(17)	7570 (3)	2776 (8)	3762 (3)	7·84 (18)
C(18)	7075 (3)	−851 (7)	3725 (3)	6·29 (15)

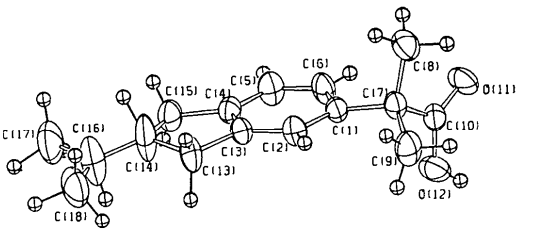


Fig. 1. *ORTEP* plot (Johnson, 1965) of the title compound with thermal ellipsoids at the 50% probability level.

The molecules form centrosymmetric dimers through hydrogen bonds between the carboxyl groups. The hydrogen-bond length of O(11)···O(12) is 2·640 (4) Å.

As the 2-methylpropionic acid side chain appears to be quite flexible in solution, the full geometric minimization by the empirical force field energy calculation using the *MM2'* program (Jaime & Ōsawa, 1983) was performed for the model compound, 2-methyl-2-phenylpropionic acid, starting from various rotamers derived by simultaneously varying the torsion angles τ_1 and τ_2, which correspond to C(2)–C(1)–C(7)–C(10) and C(1)–C(7)–C(10)–O(11) of the title compound, at intervals of 10°. The energy surface mapped as a function of τ_1 and τ_2 is shown in Fig. 2. Because of the symmetry of the benzene ring, the resulting map has a period of 180° with respect to τ_1. The twofold rotation axes also lie at $\tau_1 = 0$, $\tau_2 = 180°$ because of the two equivalent methyl groups of the 2-methylpropionic acid, resulting in four global minima. In the crystalline state of the title compound, the observed $\tau_1 = 144{\cdot}2\ (3)$ and $\tau_2 = 110{\cdot}0\ (4)°$ are not very different from the $\tau_1 = 130$ and $\tau_2 = 120°$ at the global minima denoted by *A* in Fig. 2. In order to evaluate the effect of two methyl substituents in the 2-methyl-2-phenylpropionic acid, the conformation energy calculation on 2-phenylpropionic acid, having only one methyl group, has been performed and the results show that the global minimum-energy conformation is at 120° for both τ_1 and τ_2. The torsion angle of C(2)–C(1)–C(7)–C(10) of the dimethyl derivative is larger than that of the monomethyl derivative by 10° in the global minimum-energy conformations and 37–48° in the crystalline states, owing to the hindrance of the two methyl substituents. Such a restricted conformation may be related, to some extent, to the lowering of antiinflammatory activity. The attenuation in activity may also be explained by one of the global minimum conformations being bonded to the receptor, so that the population of the bioactive conformation of the dimethyl derivative would be less than that of the monomethyl derivatives since the former possesses the four symmetrically equivalent global minima in contrast with the latter having the two global ones.

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

C(1)–C(2)	1·388 (5)	C(7)–C(9)	1·545 (6)
C(1)–C(6)	1·380 (5)	C(7)–C(10)	1·522 (5)
C(1)–C(7)	1·533 (4)	C(10)–O(11)	1·212 (4)
C(2)–C(3)	1·395 (5)	C(10)–O(12)	1·304 (5)
C(3)–C(4)	1·381 (5)	C(13)–C(14)	1·495 (6)
C(3)–C(13)	1·510 (5)	C(14)–C(15)	1·510 (6)
C(4)–C(5)	1·378 (5)	C(14)–C(16)	1·420 (6)
C(4)–C(15)	1·509 (5)	C(16)–C(17)	1·466 (6)
C(5)–C(6)	1·379 (5)	C(16)–C(18)	1·494 (7)
C(7)–C(8)	1·529 (5)		
C(2)–C(1)–C(6)	117·9 (3)	C(8)–C(7)–C(9)	109·6 (3)
C(2)–C(1)–C(7)	121·8 (3)	C(8)–C(7)–C(10)	109·5 (3)
C(6)–C(1)–C(7)	120·1 (3)	C(9)–C(7)–C(10)	107·2 (3)
C(1)–C(2)–C(3)	120·3 (3)	C(7)–C(10)–O(11)	122·7 (3)
C(2)–C(3)–C(4)	120·3 (3)	C(7)–C(10)–O(12)	115·1 (3)
C(2)–C(3)–C(13)	128·8 (3)	O(11)–C(10)–O(12)	122·2 (3)
C(4)–C(3)–C(13)	110·8 (3)	C(3)–C(13)–C(14)	104·6 (3)
C(3)–C(4)–C(5)	119·7 (3)	C(13)–C(14)–C(15)	108·6 (3)
C(3)–C(4)–C(15)	110·3 (3)	C(13)–C(14)–C(16)	123·7 (4)
C(5)–C(4)–C(15)	130·0 (4)	C(15)–C(14)–C(16)	122·4 (4)
C(4)–C(5)–C(6)	119·3 (4)	C(4)–C(15)–C(14)	104·6 (3)
C(1)–C(6)–C(5)	122·4 (4)	C(14)–C(16)–C(17)	120·9 (4)
C(1)–C(7)–C(8)	109·3 (3)	C(14)–C(16)–C(18)	118·5 (4)
C(1)–C(7)–C(9)	112·9 (3)	C(17)–C(16)–C(18)	116·6 (4)
C(1)–C(7)–C(10)	108·3 (3)		

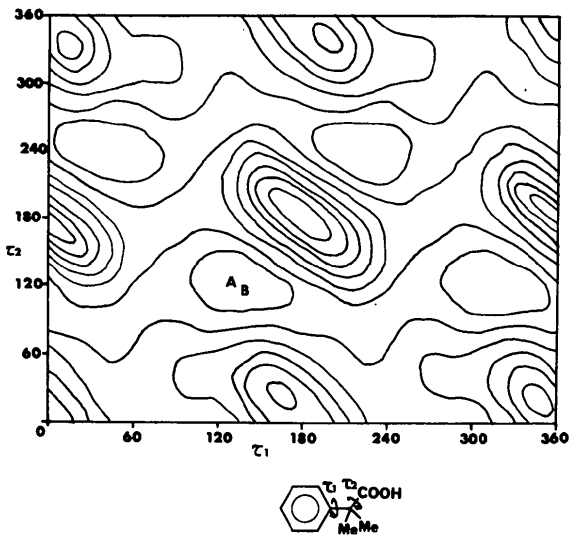


Fig. 2. *MM2'* calculated rotational energy surface for the side chain of 2-methyl-2-phenylpropionic acid. Contours are drawn at 4·2 kJ mol^{-1} intervals. The global minimum point is at *A*. The observed point of the side chain of the title compound in the crystal is at *B*.

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