N2	1.2203 (3)	0.3911 (2)	0.4725 (2)	0.0251 (6)
C1	1.2955 (3)	0.23311	0.4740 (2)	0.0189 (6)
C2	1.3267 (3)	0.1542 (2)	0.5389 (2)	0.0195 (6)
C3	1.3228 (3)	0.1465 (2)	0.6614 (2)	0.0181 (6)
C4	1.2849 (3)	0.2215 (2)	0.7227 (2)	0.0156 (5)
C5	1.2533 (3)	0.3026 (2)	0.6615 (2)	0.0167 (6)
C6	1.2602 (3)	0.3060 (2)	0.5391 (2)	0.0189 (6)
C7	1.2673 (3)	0.2111 (2)	0.8522 (2)	0.0174 (6)
O22	1.1016 (2)	0.2578 (2)	1.0873 (2)	0.0238 (5)

Table 2. *Geometric parameters* (Å, °)

O7—C9	1.366 (3)	C18—C19	1.505 (4)
O7—C14	1.429 (4)	C20—C21	1.497 (3)
O8—C15	1.426 (3)	O1—N1	1.228 (3)
O8—C16	1.436 (3)	O2—N1	1.225 (4)
O9—C17	1.426 (4)	O3—C7	1.215 (4)
O9—C18	1.423 (4)	O4—C7	1.314 (4)
O10—C19	1.434 (3)	O5—N2	1.226 (4)
O10—C20	1.431 (3)	O6—N2	1.223 (3)
O11—C10	1.364 (3)	N1—C2	1.475 (4)
O11—C21	1.432 (4)	N2—C6	1.470 (4)
C8—C9	1.383 (3)	C1—C2	1.379 (3)
C8—C13	1.406 (3)	C1—C6	1.382 (3)
C9—C10	1.404 (4)	C2—C3	1.384 (3)
C10—C11	1.390 (3)	C3—C4	1.389 (4)
C11—C12	1.406 (3)	C4—C5	1.388 (4)
C12—C13	1.369 (4)	C4—C7	1.499 (3)
C14—C15	1.500 (3)	C5—C6	1.386 (3)
C16—C17	1.509 (4)		
C9—O7—C14	118.0 (2)	O11—C21—C20	106.3 (2)
C15—O8—C16	112.2 (2)	O1—N1—O2	124.3 (3)
C17—O9—C18	112.8 (2)	O1—N1—C2	117.6 (3)
C19—O10—C20	112.0 (2)	O2—N1—C2	118.1 (2)
C10—O11—C21	117.9 (2)	O5—N2—O6	124.1 (3)
C9—C8—C13	119.2 (3)	O5—N2—C6	117.6 (2)
O7—C9—C8	125.2 (3)	O6—N2—C6	118.3 (3)
O7—C9—C10	114.3 (2)	C2—C1—C6	115.8 (2)
C8—C9—C10	120.5 (2)	N1—C2—C1	118.6 (2)
O11—C10—C9	114.5 (2)	N1—C2—C3	118.2 (3)
O11—C10—C11	125.6 (3)	C1—C2—C3	123.2 (2)
C9—C10—C11	119.8 (2)	C2—C3—C4	118.9 (3)
C10—C11—C12	119.5 (3)	C3—C4—C5	120.1 (2)
C11—C12—C13	120.3 (2)	C3—C4—C7	118.3 (2)
C8—C13—C12	120.7 (2)	C5—C4—C7	121.5 (2)
O7—C14—C15	105.4 (2)	C4—C5—C6	118.3 (3)
O8—C15—C14	109.5 (2)	N2—C6—C1	117.7 (2)
O8—C16—C17	113.3 (2)	N2—C6—C5	118.5 (2)
O9—C17—C16	107.9 (2)	C1—C6—C5	123.7 (3)
O9—C18—C19	107.7 (2)	O3—C7—O4	125.2 (2)
O10—C19—C18	111.9 (2)	O3—C7—C4	121.5 (2)
O10—C20—C21	110.2 (2)	O4—C7—C4	113.3 (2)

Crystals of the title compound [m.p. 373.0 (5) K] were prepared by slow evaporation of a mixture of 3,5-dinitrobenzoic acid and benzo-15-crown-5 (0.0002 *M*) (1:1) in ethanol (5 ml) at 298 K.

All non-H atoms in the structure were found by direct methods and refined anisotropically. The H-atom positions were located from $\Delta\rho$ syntheses and all parameters were refined individually. The absolute structure is arbitrarily chosen. Inversion of the structure yields insignificant differences in the *R* value.

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71034 (22 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HA1021]

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Structure of (*S*)-(+)-Ibuprofen

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Abstract

(*S*)-(+)-Ibuprofen, α-methyl-4-(2-methylpropyl)-benzeneacetic acid, crystallizes with two molecules in the asymmetric unit to form a cyclic hydrogen-bonded dimer. Within the dimer each molecule shows subtle conformational differences *via* rotations about the acetic C(1)—C(2) and C(10)—C(11) bonds. Bond distances and angles for (*S*)-(+)-ibuprofen are in close agreement with those found for the structure of the racemic compound [McConnell (1974). *Cryst. Struct. Commun.* **3**, 73–75].

Comment

The properties of enantiomers and their mixtures are relevant to the study of molecular recognition in biological systems, and to acute drug toxicity. At the molecular level, asymmetry often underlies the specificity of only one member of an enantiomeric pair for

its bio target and hence the asymmetric centre plays a key role in determining the clinical efficacy of the compound.

We have already reported an investigation of the lattice energy and crystal shape of racemic ibuprofen (Bunyan, Shankland & Sheen, 1991) and now our attention turns to crystals of the single enantiomer.

(*S*)-(+)-Ibuprofen crystallizes with two molecules per asymmetric unit to form a cyclic hydrogen-bonded dimer (Fig. 1); each molecule adopts an *S* configuration. This contrasts to racemic ibuprofen where the dimer is formed by hydrogen bonds across a centre of inversion (space group $P2_1/c$), one molecule being *R* and the other *S*. Within the (*S*)-(+) dimer each molecule displays subtle conformational differences effected by two rotations. In the first instance, a rotation of 180° about the C(1)—C(2) bond by the carboxylic acid group, and secondly, a rotation of 60° by the isobutyl group about the C(10)—C(11) bond. Hence in one molecule of the dimer the C(3) methyl lies adjacent to the carbonyl O atom and in the other half of the dimer it is adjacent to the hydroxyl O atom. The second rotation confers a different arrangement of the isobutyl methyls with respect to C(3) – in one half of the dimer they are both on the same side, whereas in the other they lie on opposite sides of the molecule. It is probable that these two rotations are brought about by, in the first case, the requirement to form an acid dimer (in a space group devoid of a centre of symmetry) and, in the second case, the need to avoid steric interactions primarily between adjacent isobutyl groups of neighbouring molecules.

This type of free rotation may be a necessary prerequisite for crystallization of certain molecules in asymmetric space groups. In racemic ibuprofen the necessity to use space-group symmetry leads to a more open lattice with lesser steric interactions.

Bond lengths and angles are similar to those of (*R*,*S*)-ibuprofen, the largest deviation occurring at the C(11)—C(12) bond. The propionic acids are interlinked to form a cyclic hydrogen-bonded dimer with O(1*A*)···O(2*B*) and O(1*B*)···O(2*A*) distances of 2.66 (1) and 2.64 (1) Å, respectively. A final difference Fourier synthesis revealed the positions of two peaks in the expected vicinity of the missing hydroxyl protons; however, quality and paucity of data did not allow these positions to be refined.

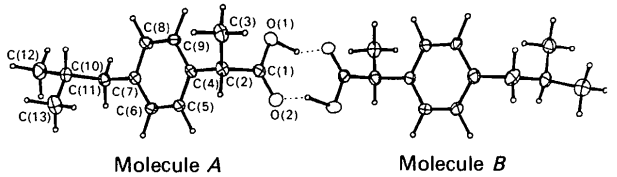

Fig. 1. A perspective view (Johnson, 1976; Mallinson & Muir, 1987) of the cyclic dimer formation between (*S*)-(+)-ibuprofen molecules.

Experimental

Crystal data

$C_{13}H_{18}O_2$
M_r = 206.3
Monoclinic
$P2_1$
a = 12.462 (3) Å
b = 8.035 (3) Å
c = 13.539 (4) Å
β = 112.89 (3)°
V = 1248.8 Å^3
Z = 4
D_x = 1.10 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 25 reflections
θ = 12–15°
T = 291 K
Needle
0.5 × 0.5 × 0.2 mm
Colourless
Crystal source: from methanol

Data collection

CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: none
2911 measured reflections
2911 independent reflections
1259 observed reflections [$I > 3.0\sigma(I)$]
θ_{max} = 27°
h = 0 → 15
k = 0 → 10
l = −17 → 17
2 standard reflections
frequency: 120 min
intensity variation: <5%

Refinement

Refinement on F
Final R = 0.056
wR = 0.067
S = 3.09
1259 reflections
271 parameters
H-atom parameters not refined
$w = 1/\sigma^2(F_o)$
$(\Delta/\sigma)_{max}$ = 0.22
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2)

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

	x	y	z	U_{eq}
O(1*A*)	−0.9649 (5)	−0.9020 (10)	−0.7762 (4)	0.093
O(2*A*)	−1.0849 (4)	−0.7330	−0.8958 (4)	0.076
C(1*A*)	−0.9875 (7)	−0.7597 (13)	−0.8305 (6)	0.068
C(2*A*)	−0.8907 (6)	−0.6410 (12)	−0.8011 (6)	0.077
C(3*A*)	−0.9005 (7)	−0.5283 (13)	−0.8955 (6)	0.092
C(4*A*)	−0.8838 (6)	−0.5465 (12)	−0.6991 (6)	0.063
C(5*A*)	−0.9503 (7)	−0.4072 (13)	−0.7049 (6)	0.073
C(6*A*)	−0.9468 (6)	−0.3258 (12)	−0.6166 (6)	0.066
C(7*A*)	−0.8766 (7)	−0.3801 (12)	−0.5159 (7)	0.075
C(8*A*)	−0.8111 (7)	−0.5229 (13)	−0.5092 (6)	0.082
C(9*A*)	−0.8140 (7)	−0.6038 (13)	−0.6016 (6)	0.079
C(10*A*)	−0.8637 (7)	−0.2878 (15)	−0.4112 (6)	0.092
C(11*A*)	−0.7653 (7)	−0.1641 (12)	−0.3729 (5)	0.076
C(12*A*)	−0.7429 (7)	−0.0998 (15)	−0.2646 (6)	0.105
C(13*A*)	−0.7843 (7)	−0.0218 (13)	−0.4485 (7)	0.090
O(1*B*)	−0.2680 (4)	0.0713 (9)	0.0491 (4)	0.075
O(2*B*)	−0.1496 (5)	−0.1000 (8)	0.1688 (4)	0.087
C(1*B*)	−0.2439 (7)	−0.0699 (12)	0.1008 (6)	0.061
C(2*B*)	−0.3420 (6)	−0.1968 (12)	0.0675 (5)	0.068
C(3*B*)	−0.4567 (6)	−0.1145 (13)	0.0514 (6)	0.094
C(4*B*)	−0.3400 (6)	−0.2878 (11)	−0.0325 (5)	0.058

C(5B)	−0.2668 (6)	−0.4213 (11)	−0.0168 (5)	0.059
C(6B)	−0.2623 (6)	−0.5106 (11)	−0.1041 (5)	0.060
C(7B)	−0.3324 (6)	−0.4670 (11)	−0.2057 (6)	0.058
C(8B)	−0.4058 (7)	−0.3294 (12)	−0.2216 (6)	0.070
C(9B)	−0.4088 (6)	−0.2404 (11)	−0.1353 (5)	0.062
C(10B)	−0.3372 (6)	−0.5633 (11)	−0.3051 (5)	0.066
C(11B)	−0.4390 (7)	−0.6831 (12)	−0.3517 (6)	0.074
C(12B)	−0.4338 (10)	−0.8180 (15)	−0.2766 (8)	0.122
C(13B)	−0.4477 (8)	−0.7513 (13)	−0.4568 (6)	0.107

Table 2. *Geometric parameters* (Å, °)

O(1A)—C(1A)	1.329 (13)	O(2A)—C(1A)	1.211 (10)
C(1A)—C(2A)	1.466 (13)	C(2A)—C(3A)	1.533 (13)
C(2A)—C(4A)	1.549 (12)	C(4A)—C(5A)	1.376 (13)
C(4A)—C(9A)	1.348 (11)	C(5A)—C(6A)	1.347 (12)
C(6A)—C(7A)	1.374 (12)	C(7A)—C(8A)	1.390 (14)
C(7A)—C(10A)	1.552 (12)	C(8A)—C(9A)	1.398 (12)
C(10A)—C(11A)	1.505 (14)	C(11A)—C(12A)	1.476 (11)
C(11A)—C(13A)	1.491 (13)	O(1B)—C(1B)	1.306 (11)
O(2B)—C(1B)	1.202 (10)	C(1B)—C(2B)	1.520 (12)
C(2B)—C(3B)	1.512 (12)	C(2B)—C(4B)	1.548 (10)
C(4B)—C(5B)	1.370 (12)	C(4B)—C(9B)	1.374 (10)
C(5B)—C(6B)	1.402 (10)	C(6B)—C(7B)	1.358 (10)
C(7B)—C(8B)	1.397 (12)	C(7B)—C(10B)	1.533 (11)
C(8B)—C(9B)	1.382 (11)	C(10B)—C(11B)	1.521 (12)
C(11B)—C(12B)	1.470 (15)	C(11B)—C(13B)	1.489 (11)
O(1A)—C(1A)—O(2A)	119.5 (8)	O(1A)—C(1A)—C(2A)	115.7 (8)
O(2A)—C(1A)—C(2A)	124.6 (9)	C(1A)—C(2A)—C(3A)	111.6 (7)
C(1A)—C(2A)—C(4A)	108.4 (7)	C(3A)—C(2A)—C(4A)	114.4 (8)
C(2A)—C(4A)—C(5A)	121.6 (7)	C(2A)—C(4A)—C(9A)	119.7 (8)
C(5A)—C(4A)—C(9A)	118.6 (8)	C(4A)—C(5A)—C(6A)	122.2 (8)
C(5A)—C(6A)—C(7A)	120.9 (9)	C(6A)—C(7A)—C(8A)	117.3 (8)
C(6A)—C(7A)—C(10A)	123.7 (9)	C(8A)—C(7A)—C(10A)	119.0 (8)
C(7A)—C(8A)—C(9A)	121.0 (8)	C(4A)—C(9A)—C(8A)	120.0 (9)
C(7A)—C(10A)—C(11A)	114.3 (7)	C(10A)—C(11A)—C(12A)	112.8 (7)
C(10A)—C(11A)—C(13A)	112.3 (7)	C(12A)—C(11A)—C(13A)	109.4 (9)
O(1B)—C(1B)—O(2B)	122.6 (8)	O(1B)—C(1B)—C(2B)	115.7 (7)
O(2B)—C(1B)—C(2B)	121.7 (8)	C(1B)—C(2B)—C(3B)	110.8 (8)
C(1B)—C(2B)—C(4B)	106.9 (6)	C(3B)—C(2B)—C(4B)	114.6 (6)
C(2B)—C(4B)—C(5B)	118.0 (6)	C(2B)—C(4B)—C(9B)	122.7 (8)
C(5B)—C(4B)—C(9B)	119.3 (7)	C(4B)—C(5B)—C(6B)	120.8 (7)
C(5B)—C(6B)—C(7B)	120.1 (8)	C(6B)—C(7B)—C(8B)	119.0 (7)
C(6B)—C(7B)—C(10B)	123.3 (8)	C(8B)—C(7B)—C(10B)	117.7 (7)
C(7B)—C(8B)—C(9B)	120.7 (7)	C(4B)—C(9B)—C(8B)	120.1 (8)
C(7B)—C(10B)—C(11B)	115.2 (6)	C(10B)—C(11B)—C(12B)	112.0 (7)
C(10B)—C(11B)—C(13B)	111.6 (7)	C(12B)—C(11B)—C(13B)	110.9 (9)

The structure was solved by direct methods with *MITHRIL* (Gilmore, 1984). Full-matrix least-squares refinement of coordinates and anisotropic thermal parameters was performed for all non-H atoms. All calculations were made on a MicroVAX 3600 using the Glasgow *GX* package (Mallinson & Muir, 1985).

(*S*)-(+)-Ibuprofen was kindly supplied by Boots Chemicals, Nottingham, England.

Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, and bond distances and angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 71015 (12 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: AL1030]

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Synthesis and Structure of New Families of Potential Antitumor or Antiviral Agents. I. 4b,6a,10b,10c-Tetrahydrobenzo[3,4]-cyclobuta[1,2-*a*]biphenylene-4b,6a-diyl Diacetate

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Abstract

The bent triphenylene derivative 4b,6a,10b,10c-tetrahydrobenzo[3,4]cyclobuta[1,2-*a*]biphenylene-4b,6a-diyl diacetate was prepared during the course of research into the synthesis of aromatic polycyclic derivatives showing antitumor or antiviral activity, and its structure determined by X-ray diffraction. The two benzocyclobutene groups are *anti* across the central cyclohexene ring; the acetoxy groups are *anti* to each other and *cis* to the benzocyclobutene groups. The geometry of the pentacyclic system is discussed and the factors determining the orientation of the acetoxy substituents are considered. The results of the refinements on F and F^2 are compared.

Comment

As a continuation of our program aimed at the synthesis of aromatic polycyclic derivatives with biological activ-