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

O1—C3	1.439 (3)	C9—C10	1.526 (4)
O2—C4	1.432 (4)	C9—C11	1.530 (4)
O3—C9	1.488 (4)	C10—C14	1.535 (4)
O3—C15	1.361 (3)	C11—C12	1.533 (4)
O4—C15	1.192 (4)	C12—C13	1.547 (4)
O5—C16	1.197 (4)	C12—C15	1.524 (4)
O6—C16	1.310 (3)	C12—C16	1.504 (4)
O6—C17	1.466 (4)	O*w*—HO*wa*	0.86 (4)
C1—C2	1.530 (4)	O*w*—HO*wb*	0.95 (4)
C1—C10	1.539 (4)	O1—HO1	0.93 (4)
C2—C3	1.517 (4)	O2—HO2	1.08 (4)
C3—C4	1.513 (4)	O1—O2^{i}	2.738 (3)
C4—C5	1.540 (4)	O2—O*w*	2.640 (3)
C5—C6	1.509 (4)	O*w*—O1^{ii}	2.813 (3)
C5—C10	1.556 (4)	O*w*—O1^{iii}	2.827 (3)
C6—C7	1.318 (4)	HO1—O2^{i}	1.89 (4)
C7—C8	1.496 (4)	HO2—O*w*	1.56 (4)
C8—C9	1.533 (4)	HO*wa*—O1^{ii}	1.96 (4)
C8—C13	1.561 (4)	HO*wb*—O1^{iii}	1.89 (4)
C9—O3—C15	106.8 (2)	C1—C10—C5	109.4 (2)
C16—O6—C17	115.8 (3)	C1—C10—C9	109.9 (2)
C2—C1—C10	113.3 (2)	C1—C10—C14	110.3 (2)
C1—C2—C3	109.7 (2)	C5—C10—C9	105.9 (2)
O1—C3—C2	112.2 (2)	C5—C10—C14	111.9 (2)
O1—C3—C4	110.4 (2)	C9—C10—C14	109.3 (2)
C2—C3—C4	111.3 (2)	C9—C11—C12	93.5 (2)
O2—C4—C3	108.2 (2)	C11—C12—C13	101.5 (2)
O2—C4—C5	112.2 (2)	C11—C12—C15	99.7 (2)
C3—C4—C5	110.6 (2)	C11—C12—C16	116.3 (3)
C4—C5—C6	109.0 (2)	C13—C12—C15	105.0 (2)
C4—C5—C10	113.9 (2)	C13—C12—C16	119.4 (2)
C6—C5—C10	112.7 (2)	C15—C12—C16	112.5 (2)
C5—C6—C7	125.5 (3)	C8—C13—C12	102.5 (2)
C6—C7—C8	123.1 (3)	O3—C15—O4	123.2 (3)
C7—C8—C9	109.5 (2)	O3—C15—C12	106.7 (2)
C7—C8—C13	115.0 (3)	O4—C15—C12	130.0 (3)
C9—C8—C13	102.6 (2)	O5—C16—O6	123.6 (3)
O3—C9—C8	105.2 (2)	O5—C16—C12	123.4 (3)
O3—C9—C10	109.4 (2)	O6—C16—C12	113.0 (3)
O3—C9—C11	100.7 (2)	O1—HO1—O2^{i}	151 (3)
C8—C9—C10	117.1 (2)	O2—HO2—O*w*	175 (4)
C8—C9—C11	102.9 (2)	O*w*—HO*wa*—O1^{ii}	172 (3)
C10—C9—C11	119.5 (3)	O*w*—HO*wb*—O1^{iii}	169 (4)

Symmetry code: (i) $1 - x, 1 - y, 1 - z$; (ii) $\frac{1}{2} + x, \frac{1}{2} - y, z$; (iii) $\frac{1}{2} - x, y - \frac{1}{2}, 1 - z$.

The structure was solved by the application of direct methods and refined using full-matrix least squares on *F*. H-atom positional parameters were calculated for all C—H, and hydroxyl H atoms were located by difference Fourier map. Their positional and thermal parameters were refined except for the C17 H atoms for which positions were fixed; the thermal motion was very large at this position.

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 71119 (12 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: CD1039]

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Structures of *N*-Benzyl- and *N*-Cyclohexylmethyl-(4-diphenylacetoxy)piperidines

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Abstract

The crystal structures of *N*-benzyl-4-(diphenylacetoxy)piperidine methobromide (I) and hydrobromide (II) and *N*-(cyclohexylmethyl)-4-(diphenylacetoxy)piperidine hydrochloride (III) were determined. Cations of (I) [*N*-benzyl-4-(diphenylacetoxy)-*N*-methylpiperidinium] and (II) [*N*-benzyl-4-(diphenylacetoxy)piperidinium] adopt similar U-shaped conformations with the benzene ring of the benzyl moiety approaching the diphenylacetate group, while the cation of (III) [*N*-cyclohexylmethyl-4-(diphenylacetoxy)piperidinium] adopts a completely different (stretched) conformation. Compounds (I)–(III) are much less active at muscarinic M_2 receptors than at M_3 receptors but there is

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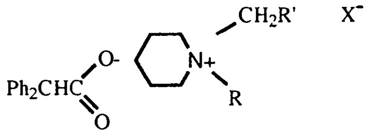
no simple correlation between biological selectivity and crystal structure. This may be because selectivity depends on steric hindrance: the molecules do not fit the receptors, particularly M_2 receptors, as well as might be expected, and the energy differences represented by different conformations are small compared with other factors which determine, and limit, binding.

Comment

4-(Diphenylacetoxy)-*N*-methylpiperidine (4DAMP) methosalts are of biological interest because they block muscarine-sensitive acetylcholine receptors in ileum [classified as M_3 (Watson & Abbott, 1991)] more than ten times as strongly as they block M_2 receptors in atria (Barlow, Berry, Glenton, Nikolaou & Soh, 1976). The crystal structure of 4DAMP methiodide (IV) was reported by Barlow, Howard, Johnson & Sanders (1987) along with that of hyoscine methiodide, which is more potent than (IV) but less selective. Recently it has been found (Barlow *et al.*, 1992) that 4DAMP benzyl bromide (I), in which an *N*-methyl group in (IV) is replaced by *N*-benzyl, is as selective as 4DAMP methobromide, even though it is much weaker, and that the tertiary base [benzyl 'fourdapine' HBr (II)] has even greater selectivity. This has only about 5% of the affinity of (IV) for M_3 receptors but less than 1% of its affinity for M_2 receptors, so has more than fiftyfold selectivity. Other aralkyl fourdapines are also selective (Barlow & Veale, 1990) but an aromatic group is not essential and the selectivity of the cyclohexylmethyl compound (III) is comparable with that of benzylfourdapine (Barlow & Veale, 1992).



R' = Ph, X = Br, R = Me (I), H (II)
R = H, R' = cyclo-C_6H_{11}, X = Cl (III)
R = Me, R' = H, X = I (IV)

These compounds are all antagonists whose activity depends only on their ability to fit the receptors. We have studied the X-ray crystal structures of the salts (I)–(III) to see if their conformation gives any clue to their biological selectivity.

The crystal structure of (I) (Fig. 1) consists of discrete ions, while those of (II) and (III) (Figs. 2 and 3) contain ionic pairs, linked by N—H···Br or N—H···Cl hydrogen bonds. The N···Br and N···Cl distances therein (3.20 and 3.04 Å) are shorter than the sums of van der Waals radii [3.40 and 3.30 Å

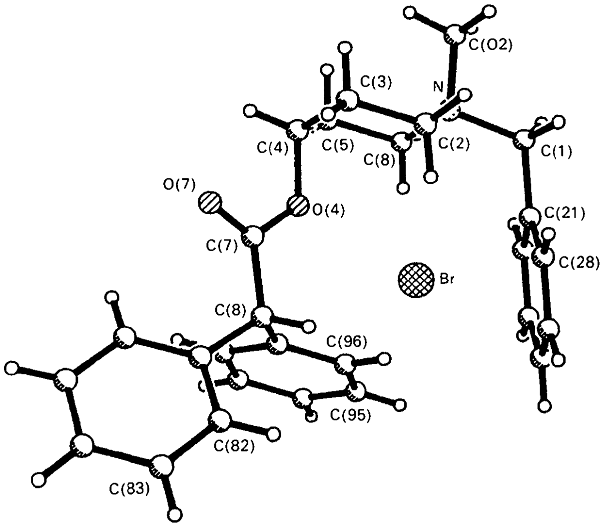


Fig. 1. Molecular structure of *N*-benzyl-4-(diphenylacetoxy)piperidine methobromide (I) and the atomic numbering scheme.

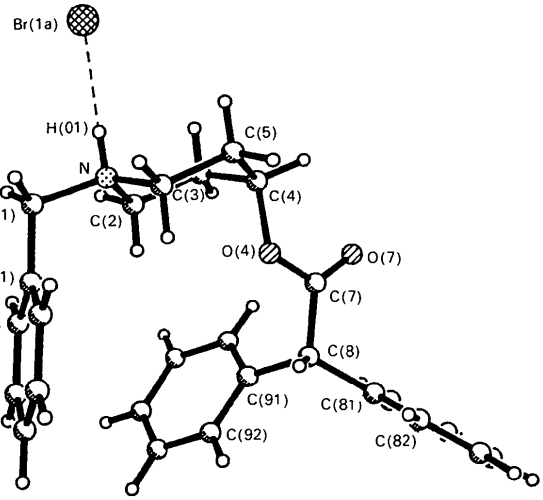


Fig. 2. Molecular structure of *N*-benzyl-4-(diphenylacetoxy)piperidine hydrobromide (II) and the atomic numbering scheme.

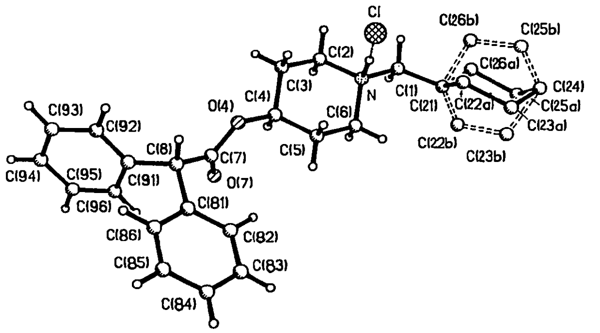


Fig. 3. Molecular structure of *N*-(cyclohexylmethyl)-4-(diphenylacetoxy)piperidine hydrochloride (III) and the atomic numbering scheme.

(Bondi, 1964)] and than the average distances for the corresponding types of hydrogen bonds [3.37 and 3.23 Å, respectively (Pimentel & McClellan, 1971; Kuleshova & Zorkii, 1981)], thus indicating rather strong bonding. This is also confirmed by H-atom positions, though poorly determined in (III) [N—H 0.90, H···Br 2.31 Å in (II); N—H 1.19, H···Cl 1.86 Å in (III)], and the form of thermal displacement ellipsoids of the halogen atoms, elongated perpendicularly to the hydrogen-bond direction.

Cations of (I) and (II) have similar U-shaped conformations (Fig. 4). Both contain diphenylacetate and benzyl groups in *cis* positions with respect to the piperidine ring. The latter adopts a chair conformation with the O(4) atom axial and the C(1) atom equatorial. However, the phenyl ring of the benzyl group is turned towards the diphenylacetate group (see torsion angles listed in Table 3).

In (III), diphenylacetate and cyclohexylmethyl substituents are in *trans* positions with respect to the piperidine ring (also adopting a chair conformation) and both are in equatorial orientation. The diphenylacetate group is rather symmetrical with respect to the piperidine moiety, unlike the cyclohexyl group [the C(1)—C(21) bond being almost *trans* to C(2)—N]. The cyclohexyl ring is disordered over two orientations, differing by a rotation around the C(1)—C(21) bond of *ca* 78°, and in both cases adopts a chair conformation. However, the *B* orientation is unlikely to occur within the contacting molecules, as it should provide too short C···C distances of 3.20–3.35 Å. Thus (III) as a whole has a stretched conformation, similar to that found in (IV), and quite different from (I) and (II).

There is no simple correlation between molecular conformation and selectivity. Compounds (II) and (III) have similar selectivity but different conformations. There are some similarities, *e.g.* the intramolecular N···O(7) distances in (I)–(III) are 5.23, 5.37 and 5.43 Å, respectively, but the N···O(4) distances are 3.48, 3.43 and 4.20 Å; the general difference in shape can be seen in Figs. 3 and 4. What is remarkable is that selectivity is accompanied by low affinity: replacing *N*-methyl in (IV) by *N*-benzyl lowers affinity more than twentyfold. As a tenfold change in affinity corresponds to a change in the free-energy of binding of 5.9 kJ mol^{-1}, changes resulting from differences in conformation are likely to be much smaller than the other changes in binding which must occur in the process of fitting the receptor. It seems clear that in the part of the receptor which interacts with the charged N atom [probably the aspartic acid residue number 105 in the sequence (Hulme, Birdsall & Buckley, 1990)] there is less space in M_2 receptors than in M_3 receptors. If the compounds were selective because they fitted M_3 receptors particularly well, the preferred conformations should be important, but these compounds are selective not because they fit M_3 receptors well but because they fit M_2 receptors badly.

Note added in proof: Recent work (Caulfield *et al.*, 1993) suggests that the selectivity observed may not be due to differences in fit but to some other cause, such as hydrolysis of the compounds during experiments on atria.

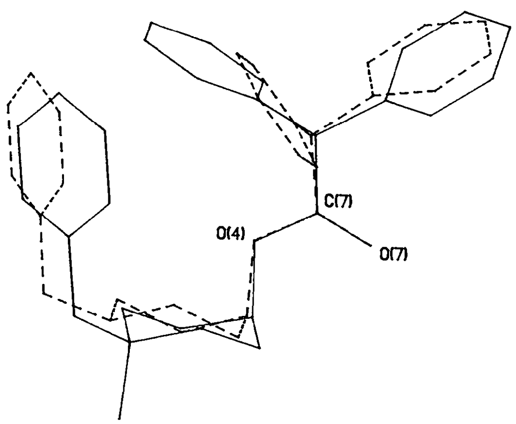


Fig. 4. Crystallographic fitting of the cations (I) (solid) and (II) (dashed). H atoms are omitted for clarity.

Experimental

Compound (I)

Crystal data

$C_{27}H_{30}NO_2^+.Br^-$
$M_r = 480.4$
Orthorhombic
$P2_12_12_1$
$a = 8.906$ (3) Å
$b = 9.826$ (3) Å
$c = 28.039$ (8) Å
$V = 2454$ (1) Å^3
$Z = 4$
$D_x = 1.30$ Mg m^{-3}

Mo $K\alpha$ radiation
$\lambda = 0.71069$ Å
Cell parameters from 18 reflections
$\theta = 13$–$22°$
$\mu = 1.68$ mm^{-1}
$T = 293$ K
Needle
0.58 × 0.16 × 0.16 mm
Colourless

Data collection

Siemens *R3m/V* diffractometer
Wyckoff (limited ω) scans
Absorption correction: empirical
$T_{\min} = 0.833$, $T_{\max} = 0.881$
1863 measured reflections
1863 independent reflections

1138 observed reflections [$I > 2\sigma(I)$]
$\theta_{\max} = 40°$
$h = 0 \rightarrow 9$
$k = 0 \rightarrow 10$
$l = 0 \rightarrow 27$
2 standard reflections monitored every 150 reflections
intensity variation: 1.7%

Refinement

Refinement on F
Final $R = 0.078$
$wR = 0.068$

$(\Delta/\sigma)_{\max} = 0.001$
$\Delta\rho_{\max} = 0.56$ e Å^{-3}
$\Delta\rho_{\min} = -0.45$ e Å^{-3}

S = 1.49
1138 reflections
139 parameters
$w = [\sigma^2(F) + 0.0005F^2]^{-1}$

Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Compound (II)

Crystal data

$C_{26}H_{28}NO_2^+.Br^-$
M_r = 466.4
Triclinic
$P\bar{1}$
a = 7.052 (2) Å
b = 12.159 (1) Å
c = 13.858 (3) Å
α = 94.12 (1)°
β = 90.96 (2)°
γ = 94.06 (2)°
V = 1182.0 (4) Å^3
Z = 2

D_x = 1.31 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 15 reflections
θ = 16–27°
μ = 1.74 mm^{-1}
T = 293 K
Needle
0.45 × 0.10 × 0.05 mm
Colourless

Data collection

Siemens $R3m/V$ diffractometer
Wyckoff (limited ω) scans
Absorption correction: empirical
$T_{\min}$ = 0.524, $T_{\max}$ = 0.996
4512 measured reflections
4149 independent reflections
3102 observed reflections [$I > 2\sigma(I)$]

$R_{\rm int}$ = 0.017
$\theta_{\max}$ = 50°
$h = -8 \rightarrow 8$
$k = -14 \rightarrow 14$
$l = 0 \rightarrow 16$
2 standard reflections monitored every 200 reflections intensity variation: 0.8%

Refinement

Refinement on F
Final R = 0.031
wR = 0.040
S = 1.00
3102 reflections
323 parameters
$w = [\sigma^2(F) + 0.00082F^2]^{-1}$

$(\Delta/\sigma)_{\max}$ = 0.025
$\Delta\rho_{\max}$ = 0.33 e Å^{-3}
$\Delta\rho_{\min}$ = −0.23 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Compound (III)

Crystal data

$C_{26}H_{34}NO_2^+.Cl^-$
M_r = 428
Monoclinic
$P2_1/n$
a = 5.833 (3) Å
b = 35.11 (2) Å
c = 11.828 (6) Å
β = 101.31 (4)°
V = 2376 (2) Å^3
Z = 4
D_x = 1.20 Mg m^{-3}

Mo $K\alpha$ radiation
λ = 0.71069 Å
Cell parameters from 26 reflections
θ = 14–24°
μ = 0.182 mm^{-1}
T = 293 K
Plate
0.5 × 0.2 × 0.06 mm
Colourless

Data collection

Siemens $R3m/V$ diffractometer
Wyckoff (limited ω) scans
Absorption correction: none
2901 measured reflections
2548 independent reflections
1737 observed reflections [$I > 2\sigma(I)$]

$R_{\rm int}$ = 0.034
$\theta_{\max}$ = 45°
$h = -5 \rightarrow 5$
$k = 0 \rightarrow 37$
$l = 0 \rightarrow 12$
2 standard reflections monitored every 100 reflections intensity variation: 1.3%

Refinement

Refinement on F
Final R = 0.078
wR = 0.090
S = 2.61
1737 reflections
267 parameters
$w = [\sigma^2(F) + 0.0004F^2]^{-1}$

$(\Delta/\sigma)_{\max}$ = 0.084
$\Delta\rho_{\max}$ = 0.41 e Å^{-3}
$\Delta\rho_{\min}$ = −0.26 e Å^{-3}
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

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

$U_{\rm eq}$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U_{\rm eq}$
(I)				
Br	0.6764 (2)	0.6417 (2)	0.9252 (1)	0.092 (1)
N	0.1146 (13)	0.5824 (12)	0.9591 (4)	0.042 (5)
O(4)	0.3513 (11)	0.3353 (10)	0.9115 (3)	0.053 (4)
O(7)	0.5499 (13)	0.2290 (13)	0.9410 (4)	0.090 (6)
C(02)	0.0210 (16)	0.5745 (15)	1.0034 (5)	0.053 (6)
C(1)	0.0852 (16)	0.7222 (15)	0.9377 (5)	0.051 (6)
C(2)	0.2793 (15)	0.5721 (15)	0.9717 (5)	0.040 (6)
C(3)	0.3213 (18)	0.4331 (16)	0.9897 (5)	0.053 (6)
C(4)	0.2732 (16)	0.3183 (17)	0.9570 (5)	0.044 (6)
C(5)	0.1108 (17)	0.3329 (14)	0.9428 (5)	0.042 (6)
C(6)	0.0705 (15)	0.4740 (13)	0.9246 (5)	0.039 (5)
C(7)	0.4884 (21)	0.2861 (16)	0.9082 (6)	0.052 (7)
C(21)	0.1524 (12)	0.7484 (10)	0.8882 (3)	0.062 (2)
C(22)	0.0686	0.7221	0.8472	0.062 (2)
C(23)	0.1309	0.7457	0.8023	0.062 (2)
C(24)	0.2771	0.7955	0.7984	0.062 (2)
C(25)	0.3609	0.8217	0.8394	0.062 (2)
C(26)	0.2986	0.7981	0.8843	0.062 (2)
C(91)	0.4643 (9)	0.3133 (11)	0.8201 (3)	0.059 (2)
C(92)	0.4288	0.1881	0.7995	0.059 (2)
C(93)	0.3407	0.1832	0.7584	0.059 (2)
C(94)	0.2882	0.3035	0.7379	0.059 (2)
C(95)	0.3237	0.4287	0.7585	0.059 (2)
C(96)	0.4118	0.4336	0.7996	0.059 (2)
C(8)	0.5686 (14)	0.3217 (12)	0.8623 (4)	0.037 (5)
C(81)	0.7148 (9)	0.2464 (11)	0.8549 (3)	0.070 (2)
C(82)	0.8342	0.3186	0.8349	0.070 (2)
C(83)	0.9700	0.2529	0.8257	0.070 (2)
C(84)	0.9864	0.1151	0.8365	0.070 (2)
C(85)	0.8671	0.0430	0.8565	0.070 (2)
C(86)	0.7313	0.1087	0.8657	0.070 (2)
(II)				
Br(1)	0.2535 (1)	0.1452 (1)	0.0484 (1)	0.051 (1)
N	0.7241 (3)	0.0905 (2)	0.8650 (2)	0.039 (1)
O(4)	0.6617 (3)	0.1118 (1)	0.6211 (1)	0.043 (1)
O(7)	0.7554 (3)	0.0401 (2)	0.4776 (1)	0.055 (1)
C(1)	0.7591 (5)	0.1753 (2)	0.9500 (2)	0.043 (1)
C(21)	0.7753 (4)	0.2927 (2)	0.9221 (2)	0.045 (1)
C(22)	0.6161 (5)	0.3525 (3)	0.9181 (2)	0.059 (1)
C(23)	0.6351 (6)	0.4612 (3)	0.8944 (3)	0.076 (2)
C(24)	0.8095 (7)	0.5104 (3)	0.8753 (3)	0.079 (2)
C(25)	0.9668 (6)	0.4525 (3)	0.8795 (3)	0.079 (2)
C(26)	0.9520 (5)	0.3433 (3)	0.9034 (2)	0.060 (1)
C(2)	0.8844 (4)	0.0900 (3)	0.7957 (2)	0.047 (1)
C(3)	0.8477 (5)	−0.0013 (3)	0.7163 (2)	0.053 (1)
C(4)	0.6576 (5)	0.0057 (2)	0.6646 (2)	0.049 (1)
C(5)	0.4982 (5)	0.0069 (3)	0.7361 (2)	0.051 (1)

C(6)	0.5347 (4)	0.0989 (3)	0.8154 (2)	0.042 (1)
C(7)	0.7241 (4)	0.1182 (2)	0.5310 (2)	0.038 (1)
C(8)	0.7531 (4)	0.2387 (2)	0.5101 (2)	0.037 (1)
C(81)	0.7326 (4)	0.2565 (2)	0.4029 (2)	0.041 (1)
C(82)	0.5621 (5)	0.2900 (3)	0.3685 (2)	0.056 (1)
C(83)	0.5393 (6)	0.3067 (3)	0.2707 (3)	0.072 (1)
C(84)	0.6839 (7)	0.2893 (3)	0.2086 (2)	0.073 (2)
C(85)	0.8529 (6)	0.2559 (3)	0.2417 (2)	0.068 (1)
C(86)	0.8770 (5)	0.2393 (2)	0.3396 (2)	0.054 (1)
C(91)	0.9403 (4)	0.2866 (2)	0.5571 (2)	0.040 (1)
C(92)	0.9595 (5)	0.3967 (3)	0.5899 (2)	0.060 (1)
C(93)	1.1285 (6)	0.4419 (3)	0.6341 (3)	0.080 (2)
C(94)	1.2766 (6)	0.3777 (4)	0.6478 (3)	0.081 (2)
C(95)	1.2597 (5)	0.2684 (3)	0.6162 (3)	0.070 (1)
C(96)	1.0934 (4)	0.2222 (3)	0.5696 (2)	0.053 (1)
(III)				
Cl	0.1511 (3)	0.2559 (1)	0.5477 (1)	0.071 (1)
O(4)	0.4784 (8)	0.1528 (1)	0.3461 (4)	0.057 (2)
O(7)	0.7398 (11)	0.1362 (2)	0.2424 (5)	0.091 (3)
N	0.3527 (9)	0.2705 (1)	0.3333 (4)	0.043 (2)
C(1)	0.3239 (12)	0.3112 (2)	0.2960 (6)	0.058 (3)
C(2)	0.2016 (12)	0.2452 (2)	0.2456 (5)	0.053 (3)
C(3)	0.2166 (12)	0.2045 (2)	0.2837 (6)	0.054 (3)
C(4)	0.4693 (12)	0.1913 (2)	0.2997 (6)	0.052 (3)
C(5)	0.6213 (11)	0.2160 (2)	0.3858 (6)	0.056 (3)
C(6)	0.6037 (11)	0.2573 (2)	0.3500 (6)	0.053 (3)
C(7)	0.6292 (14)	0.1288 (2)	0.3133 (7)	0.056 (3)
C(8)	0.6407 (13)	0.0919 (2)	0.3812 (6)	0.058 (3)
C(21)	0.4680 (16)	0.3403 (2)	0.3712 (6)	0.077 (4)
C(22*A*)	0.4692 (20)	0.3395 (3)	0.4918 (10)	0.082 (3)
C(22*B*)	0.6943 (61)	0.3482 (9)	0.3871 (27)	0.069 (9)
C(23*A*)	0.6487 (20)	0.3719 (3)	0.5551 (10)	0.083 (3)
C(23*B*)	0.7878 (70)	0.3789 (11)	0.4845 (34)	0.108 (13)
C(24)	0.5710 (22)	0.4123 (3)	0.4971 (9)	0.115 (5)
C(25*A*)	0.5814 (22)	0.4120 (3)	0.3792 (11)	0.097 (4)
C(25*B*)	0.3263 (66)	0.4015 (10)	0.4784 (30)	0.086 (11)
C(26*A*)	0.3986 (20)	0.3803 (3)	0.3127 (10)	0.081 (3)
C(26*B*)	0.2439 (57)	0.3717 (9)	0.3728 (27)	0.074 (9)
C(81)	0.8719 (14)	0.0884 (2)	0.4655 (6)	0.056 (3)
C(82)	1.0217 (17)	0.1186 (3)	0.4919 (7)	0.073 (4)
C(83)	1.2272 (16)	0.1144 (3)	0.5704 (7)	0.081 (4)
C(84)	1.2791 (17)	0.0798 (3)	0.6242 (7)	0.088 (4)
C(85)	1.1314 (20)	0.0498 (3)	0.5990 (8)	0.093 (5)
C(86)	0.9293 (17)	0.0543 (2)	0.5207 (7)	0.079 (4)
C(91)	0.5893 (14)	0.0583 (2)	0.3013 (6)	0.057 (3)
C(92)	0.3980 (16)	0.0361 (3)	0.3043 (8)	0.080 (4)
C(93)	0.3511 (18)	0.0045 (3)	0.2305 (10)	0.099 (5)
C(94)	0.4982 (22)	−0.0044 (3)	0.1563 (8)	0.089 (5)
C(95)	0.6817 (18)	0.0179 (3)	0.1543 (7)	0.076 (4)
C(96)	0.7295 (14)	0.0486 (2)	0.2256 (7)	0.062 (3)

Table 2. *Bond distances* (Å) *and angles* (°)

	(I)	(II)	(III)
N—C(2)	1.51 (2)	1.495 (4)	1.510 (8)
N—C(02)	1.50 (2)	—	—
N—C(6)	1.49 (2)	1.504 (4)	1.511 (8)
C(2)—C(3)	1.50 (2)	1.511 (4)	1.50 (1)
C(3)—C(4)	1.52 (2)	1.519 (5)	1.52 (1)
C(4)—C(5)	1.51 (2)	1.511 (5)	1.491 (9)
C(5)—C(6)	1.52 (2)	1.516 (4)	1.506 (9)
N—C(1)	1.52 (2)	1.514 (3)	1.497 (8)
C(4)—O(4)	1.46 (2)	1.462 (3)	1.458 (8)
O(4)—C(7)	1.32 (2)	1.337 (3)	1.33 (1)
C(7)—O(7)	1.21 (2)	1.197 (3)	1.18 (1)
C(7)—C(8)	1.51 (2)	1.514 (4)	1.52 (1)
C(1)—C(21)	1.53 (2)	1.503 (4)	1.50 (1)
C(8)—C(81)	1.51 (2)	1.523 (4)	1.52 (1)
C(8)—C(91)	1.51 (1)	1.521 (4)	1.51 (1)
C(2)—N—C(6)	111 (1)	112.5 (2)	109.3 (5)
C(2)—N—C(1)	109 (1)	113.1 (2)	110.1 (4)
C(6)—N—C(1)	110 (1)	112.4 (2)	112.5 (5)
C(2)—N—C(02)	110 (1)	—	—
C(6)—N—C(02)	111 (1)	—	—
C(1)—N—C(02)	106 (1)	—	—
N—C(1)—C(21)	116 (1)	113.8 (2)	117.3 (5)
N—C(2)—C(3)	112 (1)	110.7 (2)	111.3 (5)
C(2)—C(3)—C(4)	114 (1)	112.0 (3)	109.1 (6)
C(3)—C(4)—C(5)	111 (1)	110.7 (2)	109.8 (6)
C(3)—C(4)—O(4)	108 (1)	107.8 (2)	107.0 (6)
C(5)—C(4)—O(4)	103 (1)	106.1 (2)	108.1 (5)
C(4)—C(5)—C(6)	114 (1)	111.5 (2)	111.7 (5)
N—C(6)—C(5)	112 (1)	110.7 (2)	110.1 (5)
C(4)—O(4)—C(7)	117 (1)	119.1 (2)	117.0 (6)
O(4)—C(7)—O(7)	123 (2)	124.4 (2)	123.6 (7)
O(4)—C(7)—C(8)	114 (1)	109.0 (2)	110.3 (7)
O(7)—C(7)—C(8)	123 (2)	126.6 (2)	126.0 (7)
C(7)—C(8)—C(81)	114 (1)	112.8 (2)	111.0 (6)
C(7)—C(8)—C(91)	111 (1)	108.7 (2)	110.7 (6)
C(81)—C(8)—C(91)	113 (1)	114.5 (2)	113.0 (6)

Table 3. *Selected torsion angles* (°)

	(I)	(II)	(III)
C(2)—N—C(1)—C(21)	69.6	63.6	−178.0
C(6)—N—C(1)—C(21)	−52.2	−65.1	−55.9
C(3)—C(4)—O(4)—C(7)	84.0	90.1	145.8
C(5)—C(4)—O(4)—C(7)	−158.7	−151.4	−96.0
C(4)—O(4)—C(7)—C(8)	−173.2	−168.5	172.3
O(4)—C(7)—C(8)—C(81)	−170.3	−153.1	−109.3
O(4)—C(7)—C(8)—C(91)	−40.3	78.8	124.4
C(7)—C(8)—C(81)—C(82)	−141.2	99.2	13.1
C(7)—C(8)—C(91)—C(92)	−79.5	−148.9	−117.4

The structures were solved by direct methods and refined by full-matrix least squares using *SHELXTL-Plus* (Sheldrick, 1987). Absorption corrections were applied using 264 ψ scans of nine reflections for (I) and 222 ψ scans of seven reflections for (II). For (I), the phenyl rings were refined with a rigid-body model, other non-H atoms were refined in anisotropic approximation, and all H atoms were included as fixed contributions in calculated positions. The absolute configuration was not determined. For (II), all non-H atoms were refined in anisotropic approximation, phenyl-H atoms were included with a riding model, and other H atoms were refined independently with isotropic thermal parameters. For (III), difference Fourier maps revealed disorder of the cyclohexyl ring over two orientations, with atoms C(22), C(23), C(25) and C(26) occupying two positions, denoted *A* and *B*, each with occupancy factors of 0.75 and 0.25, respectively, while the positions of the atoms C(21) and C(24) coincided for both orientations. All ordered non-H atoms were refined with anisotropic thermal parameters and disordered non-H atoms in isotropic approximation. All ordered H atoms were located from a difference Fourier map and included in the refinement with a riding model, while disordered H atoms were neglected.

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55930 (48 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: HA0113]

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(*R*)-2-Hydroxy-3-iodo-2-methylpropyl 4-Nitrobenzenesulfonate

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Abstract

The global minimum conformation, as computed by *PCMODEL* [Gajewski & Gilbert (1992). Serena Software, Bloomington, IN, USA], of the title compound agrees with that observed in the crystal. In the crystal, the torsion angles I—CH$_2$—C—CH$_2$O, ICH$_2$—C—CH$_2$—O, C—CH$_2$—O—S and CH$_2$—O—S—C are −57.7 (4), −61.7 (4), 171.2 (2) and −73.0 (3)°, respectively. Weak intermolecular hydrogen bonding connects $\mathrm{O_{O-H}}$ and $\mathrm{O_{S=O}}$ with an O···O distance of 2.927 (4) Å and an angle about the H atom of 165 (4)°.

Comment

As part of an effort to synthesize chiral enzyme inhibitors, we prepared the title compound by reaction of (*S*)-(1-methyloxiranyl)methyl 4-nitrobenzenesulfonate with sodium iodide in acetic acid at 273 K. We undertook the determination of the solid-state conformation of the title compound so as to compare it to those conformations predicted in molecular modeling studies.

PCMODEL (Gajewski & Gilbert, 1992) was used to calculate the 81 possible staggered conformations of the four-torsion-angle sequence IC—C—C—O—SO$_2$Ar (where Ar is the aryl ring). For the global minimum these torsion angles are −58.9, −55.2, 169.3 and −83.6°, respectively. In the crystal they are −57.7 (4), −61.7 (4), 171.2 (2) and −73.0 (3)°, respectively. In this conformation, the I atom is on top of the benzene ring with nearly equal distances between the I atom and six C atoms of the benzene ring. The intramolecular distance [4.083 (2) Å] between I and the centroid of the aryl ring is almost equal to the sum (3.90 Å) of the van der Waals radius of I and the thickness of the benzene ring (Wheland, 1960).

With respect to bond distances and angles, *PCMODEL* agrees approximately with the X-ray determination. Notable exceptions are the C1—C2, C7—C8 and C8—C9 bond lengths and the C7—C8—C9 and O5—N—O6 bond angles, as well as many values of the SO$_3$ group. The X-ray results reveal that the O2—C3 bond is 0.049 Å longer than the O1—C2 bond, which is consistent with OSO$_2$Ar being a better leaving group than the OH group (Allen & Kirby, 1984; Jones, Dölle, Kirby & Parker, 1992; Jones, Kirby & Parker, 1992; Jones, Schmidt-Bäse, Edwards & Kirby, 1992; Kirby, Parker & Raithby, 1992). Molecules are linked in chains along **b** by weak intermolecular hydrogen bonds involving $\mathrm{O_{O-H}}$ and $\mathrm{O_{S=O}}$. The O1···O3 distance is 2.927 (4) Å and the O···H—O angle is 165 (4)°.

A search of the Cambridge Structural Database (Allen, Kennard & Taylor, 1983) reveals one related structure, 7-*exo*-isopropenylbicyclo[4.1.0]hept-7-

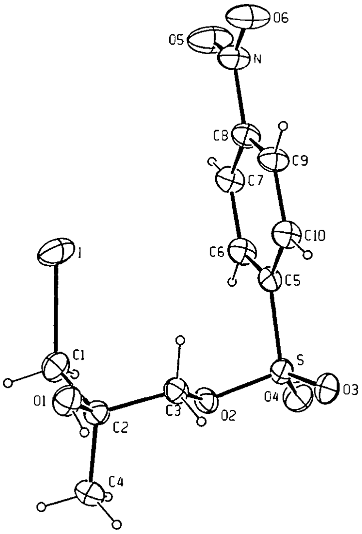

Fig. 1. Numbering scheme with thermal ellipsoids drawn at the 30% probability level. H atoms are drawn as circles of arbitrary radii.

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