THE CRYSTAL AND MOLECULAR STRUCTURE OF (1R*,3S*,4R*,6S*)-1,4-DIMETHYL-3,6-DIPHENYL-2,5,7--TRIOXABICYCLO[2,2,1]HEPTANE

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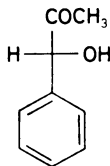[b] Department of Organic Chemistry,
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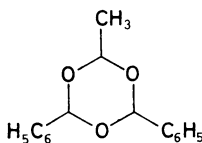
The structure of 1,4-dimethyl-3,6-diphenyl-2,5,7-trioxabicyclo[2,2,1]heptane was solved by direct methods and anisotropically refined to a final R value 0·023 for 648 observed reflections ($I > 3\sigma(I)$) and 133 refined parameters. The symmetry of the structure corresponds to the $P2_12_12$ space group with lattice parameters $a = 16·857(2)$, $b = 8·756(1)$, $c = 5·245(1)$ Å. The unit cell contains two formula units. The molecule under study possesses twofold rotation axis, which passes through the O2 atom. The molecular structure found from X-ray data corresponds to ^{1}H and ^{13}C NMR spectroscopic results. Further IR spectrum and optical rotation value are included.
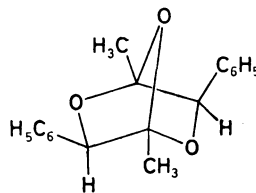
(R)-(−)-1-Hydroxy-1-phenyl-2-propanone (*I*) can be obtained easily from an industrially produced solution of Neuberg's ketol[1−3]. Upon distillation of the crude isolate[4] another crystalline compound is formed in the distillation residue. Ježo[5] has proposed this compound to be 4-methyl-2,6-diphenyl-1,3,5-trioxane (*II*). How-

ever, ^{1}H and ^{13}C NMR spectra measured later did not correspond with this proposed structure but with the structure[6] of 1,4-dimethyl-3,6-diphenyl-2,5,7-trioxabicyclo-[2,2,1]heptane (*III*). According to the NMR analyses, *III* contains a quaternary

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carbon and a single methine-proton which appears as a singlet in the ^{1}H NMR spectrum. Compound *III* shows optical activity and has not been previously described in the literature. It is formed by the condensation of two molecules of *I* followed by dehydration thus forming the bicyclic product. Similar compounds produced from acyloins have been studied[7]. After our study of models we can conclude that the most likely structure of *III* has the both phenyl groups in *exo* positions with the corresponding relative configuration (1R*,3S*,4R*,6S*). The determination of the structure of 1,4-dimethyl-3,6-diphenyl-2,5,7-trioxabicyclo[2,2,1]heptane by X-ray diffraction proved this conclusion and provided the salient geometrical features of this molecule.

EXPERIMENTAL

An industrially produced solution of Neuberg's ketol in butylacetate (276 g containing 0·94 mol of *I*; produced by Research Institute for Antibiotics and Biotransformations at Roztoky near Prague[2,3]) was dissolved in 1 000 ml of ether and extracted with saturated sodium carbonate (2 × 150 ml) and washed with water (5 × 200 ml). The organic layer was separated and stirred in a round bottom flask eqipped with a mechanical stirrer and ice-water cooling bath (0°C). The solution of 130 g (0·68 mol) of sodium bisulfite in 350 ml of water was added dropwise over one hour. The mixture was stirred for additional two hours and the precipitated adduct was filtered off and washed with ether. The white solid was then dissolved in 600 ml of water and sodium hydrogen carbonate was added in portions until the evolution of carbon dioxide ceased. The mixture was saturated with sodium chloride and extracted with ether (7 × 150 ml). The combined ether extracts were dried over anhydrous sodium sulfate and the solvent was removed under vacuum. The residue was subjected to fractional distillation under vacuum to provide 89·2 g (63%) of *I* as a yellow liquid, b.p. 72—74°C/33 Pa, $[\alpha]_D^{20} = -164\cdot7°$ (*c* 2·2; ethanol). Ref.[4]: b.p. 124—5°C/1·6 kPa, $[\alpha]_D^{20} = -181\cdot9°$ (*c* 2·0; ethanol). ^{1}H NMR spectrum (100 MHz): 2·03 s, 3 H; 4·29 sb, 1 H; 5·02 s, 1 H; 7·29 m, 5 H. For $C_9H_{10}O_2$ (150·2) calculated 71·97% C, 6·71% H; found 72·1% C, 6·76% H.

During the distillation the contents of the distilling pot slowly crystallized. The recovered solid was recrystallized twice from ethanol to provide 9·5 g of *III* as white needles, m.p. 150·0 to 150·5°C, $[\alpha]_D^{20} = -9\cdot2°$ (*c* 5·8; chloroform). Ref.[5]: m.p. 149·5—150·0°C. For $C_{18}H_{18}O_3$ (282·3) calculated: 76·59% C, 6·41% H; found 76·62% C, 6·30% H. ^{1}H NMR spectrum (100 MHz): 1·42 s, 6 H (3 × H3, 3 × H3^i); 4·95 s, 2 H (H1, H1^i); 7·32 m, 10 H (H5—H9, H5^i—H9^i). ^{13}C NMR spectrum (25·14 MHz): 15·2 (C3, C3^i); 87·0 (C1, C1^i); 109·7 (C2, C2^i); 127·3 (C5, C7, C9, C5^i, C7^i, C9^i); 128·3 (C6, C8, C6^i, C8^i); 138·7 (C4, C4^i). IR spectrum (cm^{-1}): 835 w, 895 m, 1 000 vs, 1 100 w, 1 165 s, 1 250 m, melting point was determined on a Boetius apparatus and is uncorrected. Optical rotations were measured on a Zeiss Opton LEP A2 polarimeter. NMR spectra were obtained with a Tesla BS-567 instrument in deuteriochloroform using tetramethylsilane as an internal standard, chemical shifts are in ppm (δ-scale). IR spectrum was recorded on a Perkin–Elmer 325 spectrometer in chloroform.

Crystal Structure Determination

Orthorombic, space group $P2_12_12$, $a = 16\cdot857(2)$, $b = 8\cdot756(1)$, $c = 5\cdot245(1)$ Å, $V = 774\cdot1(2)$ Å^3, $Z = 2$, $\varrho_o = 1\cdot18(1)$, $\varrho_c = 1\cdot21$ g cm^{-3}, $\mu = 0\cdot08$ mm^{-1}, $F(000) = 300$.

The density of the crystals studied was determined by the flotation method in a diiodomethane /toluene mixture at room temperature. The single crystal with the dimensions of $0.30 \times 0.15 \times 0.10$ mm was measured on an Enraf–Nonius CAD4 diffractometer. Graphite-monochromated MoK_{α} radiation ($\lambda = 0.71073$ Å) was employed and the measurement was carried out at the temperature of $22°C$. The lattice parameters were refined from a set of 21 reflections (Θ range $16.5—19.5°$). A total of 4 808 intensities were measured in the range $-19 \leq h \leq 19, -10 \leq k \leq 10, -5 \leq l \leq 5$ including Friedel pairs. During the data collection ($\omega–2\Theta$ mode, scan rate $2.06—16.48°$ min^{-1}) two standard reflections (0, 2, 0 and 0, 1, 3) monitored after every 120 min showed the intensity loss of 1%. Averaging of the equivalent reflections, except Friedel pairs, yielded 1 130 intensities. ($R_{int} = 0.019$). The absorption correction was ignored. The structure was solved by direct methods and the coordinates of all the H atoms were found from the electron density difference synthesis. On the basis of the $I > 3\sigma(I)$ condition, only 648 reflections (including Friedel pairs) were considered as observed and used for the full-matrix least-squares efinement. The function minimized was $\sum w(|F_o| - |F_c|)^2$ and scale factor, positional and

TABLE I

The final coordinates ($.10^4$) for non-H atoms. Isotropic equivalent displacement parameter is defined as $B_{eq} = \frac{4}{3}\sum_i\sum_j B_{ij}a_ia_j$

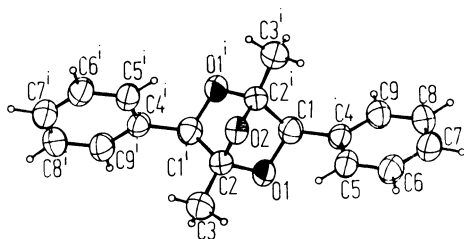| Atom	x	y	z	B_{eq}, Å^2
O1	491·0(7)	3 737(2)	503(3)	4·99(3)
O2	0	5 000	3 847(4)	4·19(4)
C1	824(1)	5 238(2)	429(4)	4·36(5)
C2	−212(1)	3 884(2)	2 009(4)	4·32(5)
C3	−432(1)	2 389(3)	3 185(6)	7·01(7)
C4	1 662(1)	5 253(2)	1 430(5)	4·03(5)
C5	1 868(1)	4 402(3)	3 543(6)	4·96(6)
C6	2 638(1)	4 432(3)	4 497(5)	5·41(6)
C7	3 198(1)	5 329(3)	3 315(6)	5·84(6)
C8	3 004(1)	6 181(3)	1 228(6)	5·89(6)
C9	2 230(1)	6 148(3)	270(5)	5·20(6)

FIG. 1

View of the molecule of 1,4-dimethyl-3,6-di-phenyl-2,5,7-trioxabicyclo[2,2,1]heptane. Thermal ellipsoids are drawn at the 50% probability level

anisotropic thermal parameters of non-H atoms and positional and isotropic thermal parameters of H atoms were refined (a total of 133 parameters). The final weighting scheme had the form[8] $w = 4F_o^2/(\sigma F_o^2)^2$. In the last refinement cycle the maximal value of (Δ/σ) was 0·03. Refinement yielded the $R = 0.023$, $wR = 0.026$ and $S = 0.623$ values. The maximum and minimum heights in the final $\Delta\varrho$ map were 0·10 and -0.11 e Å^{-3}. Determination of the absolute configuration based on the refinement of the η parameter[9] using all 2 785 observed intensities (selected from a set of 4 808 reflections) was unsuccesful as assumed before — see a non-spherical shape of the crystal studied, using molybden radiation and no heavy atom present in the structure. Programs used: SHELXS — 86 ref.[10] and SDP ref.[8]; EC 1033 and PDP 11/73 computers.

RESULTS AND DISCUSSION

Table I lists the final positional and thermal parameters of non-H atoms.* **Fig.** 1 depicts a perspective view of the molecule with atom numbering. The interatomic

TABLE II

The interatomic distances (Å) and angles (°). Symmetry code i: $\bar{x}$, $1 - y$, z

Bond	Bond length	Bond	Bond length
O1–C1	1·430(2)	C2–C1^i	1·531(2)
O1–C2	1·429(2)	C4–C5	1·380(4)
O2–C2	1·418(3)	C4–C9	1·379(3)
O2–C2^i	1·418(1)	C5–C6	1·391(3)
C1–C4	1·506(3)	C6–C7	1·376(3)
C1–C2^i	1·531(2)	C7–C8	1·364(4)
C2–C3	1·495(3)	C8–C9	1·399(3)

Atoms	Angle	Atoms	Angle
C1–O1–C2	104·9(1)	C3–C2–C1^i	119·7(2)
C2–O2–C2^i	94·3(2)	C1–C4–C5	120·8(2)
O1–C1–C4	111·5(2)	C1–C4–C9	120·1(2)
O1–C1–C2^i	100·5(1)	C5–C4–C9	119·1(2)
C4–C1–C2^i	116·1(2)	C4–C5–C6	121·0(2)
O1–C2–O2	103·3(1)	C5–C6–C7	119·2(2)
O1–C2–C3	110·8(2)	C6–C7–C8	120·6(2)
O1–C2–C1^i	107·8(2)	C7–C8–C9	120·0(2)
O2–C2–C3	112·7(2)	C4–C9–C8	120·1(2)
O2–C2–C1^i	101·1(1)		

*   Tables of F_o, F_c and H atom positions are available on request from the authors.

distances and angles are given in Table II. The optimal least-squares planes fitted through the atoms in the molecule are summarized in Table III.

TABLE III

The optimal least-squares planes fitted through the atoms in the molecule. Each plane is defined as $AX + BY + CZ - D = 0$

Atoms	Deviation, Å	Atoms	Deviation, Å
	Plane I[a]		Plane II[b]
C1*	0·019(2)	C1*	−0·004(2)
O1*	−0·019(1)	O1*	0·004(1)
C1^i*	0·019(2)	C2*	−0·003(2)
C1^i*	−0·019(1)	C2^i*	0·002(1)
C2	−0·809(2)	O2	−0·798(2)
O2	−1·773(2)		
C2^i	−0·809(2)		
	Plane III[c]		
C4*	0·001(2)	C7*	0·0003(30)
C5*	−0·001(2)	C8*	−0·0004(30)
C6*	0·0004(20)	C9*	−0·001(2)

^{a} A = 0, B = 0, C = −1, D = −0·2447, χ^2 = 233; ^{b} A = −0·5256, B = 0·1945, C = −0·8282, D = −0·0213, χ^2 = 12; ^{c} A = 0·2463, B = −0·7655, C = −0·5945, D = −3·2783, χ^2 = 1. The planes are fitted only through the atoms designated by an asterisk.
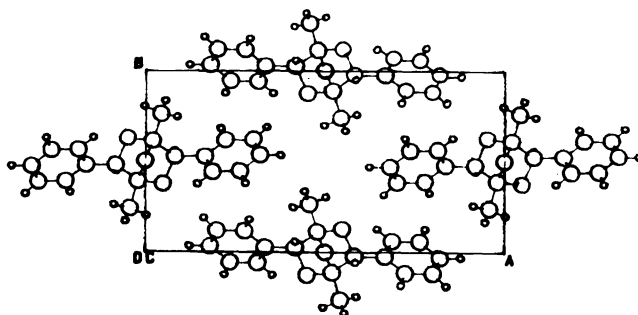

Fig. 2
Packing diagram

The molecule studied possesses twofold rotation axes, which passes through the O2 atom. The O2 atom is surrounded by the six-membered ring of the C1, O1, C2, C1^i, O1^i and C2^i atoms, where i: $\bar{x}$, $1 - y$, z. The least-square plane may be fitted through the C1, O1, C1^i and O1^i atoms from which the O2 atom is displaced by $-1.773(2)$ Å. Both C2 and C2^i atoms also protrude below this plane $(-0.809(2)$ Å$)$. If the O2 atom is included in rings, then the molecule contains two five-membered ones (C1, O1, C2, O2, C2^i and C1^i, O1^i, C2^i, O2, C2). The C1, O1, C2, C2^i and C1^i, O1^i, C2^i, C2 form two planes which are tilted by $68.17(6)°$. The dihedral angle between the phenyl planes (C4, C5, C6, C7, C8, C9 and the equivalent i-set) is $107.05(5)°$. The bond lengths and bond angles for the phenyl rings are unexceptional. The C1, O1, C2, C2^i and C1^i, O1^i, C2^i, C2 planes tilt from that of the corresponding phenyl ring by $77.64(7)°$ and $53.52(8)°$ respectively. The molecular structure of *III* corresponds to the structure suggested from a study of models with the relative configuration $(1R*,3S*,4R*,6S*)$ — see nomenclature of organic compounds[11].

As can be seen from packing diagram (Fig. 2), no hydrogen bond contacts were found in the structure. The molecules are obviously interconnected by the van der Waals forces only.

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