Structural Study of 3-Methyl-2,4-diphenyl-3-azabicyclo[3.3.1]nonan-9β-ol

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The infrared spectra in several media and the crystal structure of 3-methyl-2,4-diphenyl-3-azabicyclo[3.3.1]-nonan-9β-ol (**I**) (Scheme I) have been determined, in order to complete the structural study described for the title compound from the ^1H and ^{13}C nmr data [1]. The bicyclic system adopts a flattened chair-chair conformation in which the cyclohexane ring is more flattened. The methyl and phenyl groups are in equatorial positions and the OH group in an axial position with respect to the piperidine ring.

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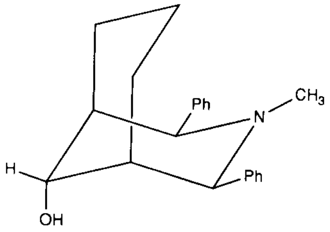
Introduction.

In a previous paper [1] we reported the ^1H and ^{13}C nmr study of 3-methyl-2,4-diphenyl-3-azabicyclo[3.3.1]nonan-9β-ol (**I**). Along the same lines we report in this paper the ir data and the crystal structure of compound **I** with the objective to determine its preferred conformation in the solid state. A comparison between the preferred conformation of **I** in solution and in the solid state is also reported.

Scheme I



Compound I

Results and Discussion.

The main crystallographic data and the structure determination conditions are given in Table 1. Table 2 shows the atomic parameters. Also given in Tables 3 and 4 are bond lengths, bond and torsion angles in which some hydrogen atoms are involved. Figure 1 shows a view of the molecule and numbering used in the crystallographic study. Figure 2 displays a view of the asymmetric unit, and Figure 3 shows a view of the packing of the molecules in the unit cell.

Table 1

Experimental Data and Structure Refinement Procedures

Crystal data	
Formula:	**$C_{21}H_{25}NO$**
Symmetry:	**Triclinic, P-1**
Unit cell dimensions:	**a = 11.11(1)Å, b = 13.048(9)Å, c = 13.483(8)Å α = 73.10(5)°, β = 78.81(5)°, γ = 84.00(6)°**
Packing: V(Å)^3, Z:	**1.832(3), 4**
Dc(g•cm^{-3}), M, F(000):	**1.114, 307.44, 664**
μ(Mo,Kα)(cm^{-1}):	**0.63**
Experimental data	
Technique:	**Four circle diffractometer: Enraf-Nonius CAD-4 Bisecting geometry Graphite oriented monochromator: Mo, Kα,ω/2θ scans**
Scanning range for θ:	**2 < θ < 25**
Numbers of reflections	
Measured:	**6433**
Observed:	**2467 (4σ (I) criterion)**
Range of hkl:	**0, 13; -15, 15; -16, 16**
Absorption:	**No correction applied**
Standard reflections:	**Two reflections every 120 minutes Variation: no**
Solution and refinement	
Solution:	**Direct methods [2,3]**
Refinement:	**L.S. on Fobs**
Number of variables:	**494**
H atoms:	**Difference Fourier synthesis exception H of the methyl groups**
Final shift/error:	**0.19**
ω-scheme:	**$\omega = 4Fo^2 / [\sigma(Fo)^2]^2$**
Final ΔF peaks:	**0.42e/Å^3**
Final R and Rw:	**0.086, 0.089**
Computer and programs:	**Microvax II, Structure Determination Package Enraf-Nonius [4]**
Scattering factors:	**Int. Tables for X-Ray Crystallography [5]**

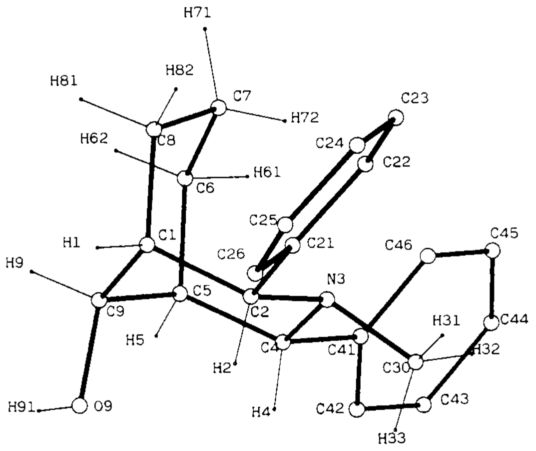


Figure 1

The molecular structure has two crystallographically independent molecules in the asymmetric unit (**A** and **B**, Figure 2), and they present only small differences. Hereafter the data for comparison corresponds to the average value of both molecules. As it is shown, the compound crystallizes with a molecule of methanol.

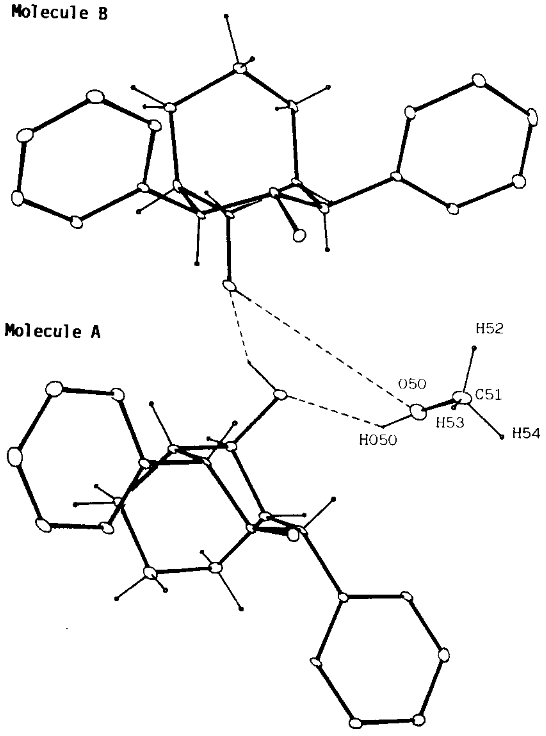


Figure 2

Table 2

Positional Parameters and Estimated Standard Deviations

		Molecule A				Molecule B		
Atom	x	y	z	B(Å^2) [a]	x	y	z	B(Å^2) [a]
C1	0.0849(6)	0.4537(5)	0.2330(5)	3.1(2)	0.0485(6)	0.0823(6)	0.6971(5)	3.5(2)
C2	0.2234(6)	0.4622(5)	0.1919(5)	2.8(2)	0.1746(6)	0.0978(5)	0.6183(5)	3.2(2)
N3	0.2797(5)	0.3649(4)	0.1629(4)	2.4(1)	0.2591(5)	0.1574(4)	0.6491(4)	3.0(1)
C4	0.2476(6)	0.2668(5)	0.2470(5)	3.0(2)	0.2012(6)	0.2563(5)	0.6749(5)	3.2(2)
C5	0.1118(6)	0.2585(5)	0.2899(5)	3.3(2)	0.0771(6)	0.2401(5)	0.7504(5)	3.2(2)
C6	0.0318(7)	0.2485(6)	0.2118(6)	4.2(2)	0.0801(7)	0.1714(6)	0.8635(5)	3.8(2)
C7	0.0330(6)	0.3476(6)	0.1172(6)	4.3(2)	0.1240(7)	0.0560(6)	0.8698(5)	3.9(2)
C8	0.0078(6)	0.4504(6)	0.1522(6)	4.0(2)	0.0585(6)	0.0064(6)	0.8060(6)	4.1(2)
C9	0.0591(6)	0.3576(6)	0.3277(5)	3.5(2)	-0.0087(6)	0.1919(6)	0.7030(5)	3.5(2)
O9	0.1182(5)	0.3674(4)	0.4094(4)	4.3(1)	-0.0282(5)	0.2561(4)	0.6005(4)	4.2(1)
C21	0.2480(6)	0.5637(5)	0.1030(5)	3.0(2)	0.2318(6)	-0.0102(5)	0.6079(5)	3.2(2)
C22	0.2606(6)	0.5673(6)	-0.0040(5)	3.6(2)	0.3244(7)	-0.0630(6)	0.6594(5)	3.7(2)
C23	0.2760(6)	0.6632(6)	-0.0799(5)	3.7(2)	0.3715(7)	-0.1624(6)	0.6490(6)	5.0(2)
C24	0.2778(7)	0.7573(6)	-0.0568(6)	4.1(2)	0.3211(8)	-0.2093(6)	0.5883(6)	5.6(2)
C25	0.2650(7)	0.7548(6)	0.0480(6)	4.6(2)	0.2296(8)	-0.1598(6)	0.5386(6)	5.0(2)
C26	0.2508(7)	0.6583(6)	0.1258(5)	3.6(2)	0.1837(7)	-0.0597(6)	0.5473(6)	4.3(2)
C30	0.4119(7)	0.3725(6)	0.1394(6)	3.8(2)	0.3631(7)	0.1883(6)	0.5604(5)	4.0(2)
C41	0.2986(7)	0.1683(5)	0.2116(5)	3.3(2)	0.2871(6)	0.3057(5)	0.7201(5)	3.4(2)
C42	0.3290(8)	0.0772(6)	0.2849(6)	4.5(2)	0.2773(7)	0.4163(6)	0.7059(6)	4.3(2)
C43	0.3718(9)	-0.0145(7)	0.2567(7)	6.5(3)	0.3485(8)	0.4611(6)	0.7524(6)	5.2(2)
C44	0.3771(9)	-0.0187(7)	0.1549(7)	6.8(3)	0.4268(7)	0.4010(6)	0.8141(6)	5.3(2)
C45	0.3446(8)	0.0701(7)	0.0842(6)	5.7(2)	0.4379(7)	0.2925(6)	0.8273(6)	4.7(2)
C46	0.3049(7)	0.1623(6)	0.1114(6)	4.6(2)	0.3666(7)	0.2466(6)	0.7818(6)	4.1(2)

[a] Starred atoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: $(4/3)x[a^2xB_{1,1} + b^2 \times B_{2,2} + c^2 x B_{3,3} + ab(\cos\gamma) \times B_{1,2} + ac (\cos\beta) \times B_{1,3} + bc (\cos\alpha) \times B_{2,3}]$.

Table 3

Selected Bond Distances (Å)

Bond	Molecule A	Molecule B	Bond	Molecule A	Molecule B
C1-C2	1.534(9)	1.577(9)	O9-H91	0.95(5)	1.12(5)
C1-C8	1.52(1)	1.532(9)	C21-C22	1.41(1)	1.37(1)
C1-C9	1.513(8)	1.52(1)	C21-C26	1.36(1)	1.39(1)
C2-N3	1.478(9)	1.47(1)	C22-C23	1.370(9)	1.38(1)
C2-C21	1.514(8)	1.52(1)	C23-C24	1.35(1)	1.38(1)
N3-C4	1.465(7)	1.483(9)	C24-C25	1.38(1)	1.33(1)
N3-C30	1.448(9)	1.486(8)	C25-C26	1.386(9)	1.38(1)
C4-C5	1.510(9)	1.541(9)	C41-C42	1.367(9)	1.40(1)
C4-C41	1.52(1)	1.51(1)	C41-C46	1.36(1)	1.35(1)
C5-C6	1.54(1)	1.532(9)	C42-C43	1.37(1)	1.37(1)
C5-C9	1.54(1)	1.52(1)	C43-C44	1.38(1)	1.35(1)
C6-C7	1.53(1)	1.52(1)	C44-C45	1.34(1)	1.37(1)
C7-C8	1.53(1)	1.53(1)	C45-C46	1.36(1)	1.37(1)
C9-O9	1.43(1)	1.437(8)			

In both cases (**A** and **B**), there is a pseudo-mirror plane, passing through N3, C7, C9, O9 and C30 atoms. The methyl group is attached to the nitrogen atom in the equatorial position with respect to the piperidinol ring.

Both six membered rings have a distorted chair conformation, flattened at the C9 atoms. Such distortion increases the N3–C9 and C7–C9 nonbonded distances from the ideal chair value of 2.52 Å to 2.951 Å and 2.957 Å respectively, in this compound.

The displacement of N3 and C9 from the plane defined by C1, C2, C4 and C5 are 0.568 Å and 0.756 Å respectively, and C7 and C9 from plane C5, C6, C8 and C1 are 0.582 Å and 0.786 Å. These values show that the C9 atom is less deviated from the value corresponding to an ideal chair than N3 and C7 atoms (ideal chair: 0.73 Å).

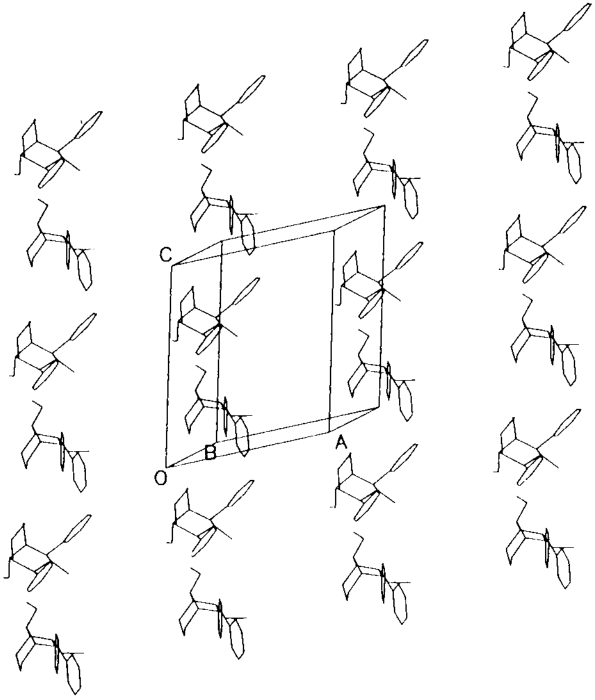


Figure 3

The OH group is in an axial position with respect to the piperidinol ring.

The angles between the pseudo-mirror plane and the phenyl group are 99.57° and 78.82° and the angle between both phenyl groups is 21.63°.

The two independent molecules are linked by three hydrogen bonds between **A**, **B** and the methanol of crystallization, their geometry is given in Table 5.

Infrared Spectra.

The ir spectra were recorded on a Perkin-Elmer 599B Spectrophotometer in the solid state (potassium bromide) and in deuteriochloroform solution (0.06 *M*) using 0.2 mm sodium chloride cells; spectra for very dilute carbon tetrachloride solutions in the 3600-2500 cm^{-1} region were taken with 4 cm quartz cells. Indene and polystyrene were used for instrument calibration and the reported wave numbers are estimated to be accurate to within ±4 cm^{-1}.

In the OH stretching region, the infrared spectrum in the solid phase showed a medium complex absorption band with a maximum at about 3480 cm^{-1}. This frequency is higher than in the case of the exo derivative (3365 cm^{-1}) [1] indicating a weaker hydrogen bond in the present case as a consequence of the bonding of a methanol molecule to both independent molecules in the asymmetric unit (see X-ray data). In the infrared spectrum of the crystalline solid the presence of methanol can be deduced from the shoulder at about 3570 cm^{-1}. Upon dilution in carbon

Table 4

Selected Bond Angles (°)

Bonds	Molecule A	Molecule B	Bond	Molecule A	Molecule B
C2-C1-C8	115.3(3)	113.9(6)	C1-C9-O9	109.4(6)	110.0(6)
C2-C1-C9	111.1(5)	108.8(5)	C5-C9-O9	111.2(5)	113.6(6)
C8-C1-C9	109.0(6)	112.2(6)	C9-O9-H91	88.0(4)	112.0(3)
C1-C2-N3	112.0(6)	112.1(6)	C2-C21-C22	123.2(7)	123.1(7)
C1-C2-C21	110.4(5)	110.0(5)	C2-C21-C26	119.4(7)	118.3(6)
N3-C2-C21	112.8(5)	111.6(6)	C22-C21-C26	117.3(6)	118.5(7)
C2-N3-C4	112.1(5)	113.5(5)	C21-C22-C23	119.9(8)	120.8(8)
C2-N3-C30	108.7(5)	108.4(6)	C22-C23-C24	122.7(7)	119.0(7)
C4-N3-C30	109.7(5)	108.2(4)	C23-C24-C25	117.9(6)	121.2(8)
N3-C4-C5	114.5(5)	114.2(5)	C24-C25-C26	120.3(8)	120.1(9)
N3-C4-C41	110.7(5)	110.9(6)	C21-C26-C25	122.0(8)	120.4(7)
C5-C4-C41	110.3(6)	109.2(5)	C4-C41-C42	119.0(6)	118.9(6)
C4-C5-C6	115.2(6)	116.8(6)	C4-C41-C46	123.1(6)	122.9(6)
C4-C5-C9	110.8(6)	108.5(6)	C42-C41-C46	117.6(7)	118.0(8)
C6-C5-C9	106.6(6)	108.9(5)	C41-C42-C43	120.8(7)	119.5(7)
C5-C6-C7	112.7(6)	112.8(7)	C42-C43-C44	120.5(7)	121.8(7)
C6-C7-C8	111.2(7)	112.6(7)	C43-C44-C45	118.2(8)	118.9(9)
C1-C8-C7	112.7(6)	112.3(6)	C44-C45-C46	121.4(8)	119.8(7)
C1-C9-C5	106.0(6)	106.6(5)	C41-C46-C45	121.4(7)	121.9(7)

Table 4 (Continued)

Selected Torsional Angles (°)

Bonds	Molecule A	Molecule B	Bond	Molecule A	Molecule B
H1-C1-C2-H2	61.65(4.7)	47.07(4.6)	H71-C7-C8-H82	-62.46(4.5)	157.27(32)
H1-C1-C8-H81	-57.22(4.5)	-43.59(3.4)	H72-C7-C8-H81	166.85(4.6)	59.18(3.4)
H1-C1-C8-H82	54.74(4.5)	-49.10(3.4)	H72-C7-C8-H82	55.52(4.8)	56.90(3.3)
H1-C1-C9-H9	57.21(4.7)	65.03(4.2)	H4-C4-C5-H5	-56.95(4.8)	-49.71(4.5)
H5-C5-C6-H61	-60.85(4.0)	-66.70(3.1)	C2-C1-C9-O9	59.52(0.7)	59.22(0.7)
H5-C5-C6-H62	63.96(4.5)	62.63(3.1)	C6-C5-C9-O9	173.57(0.5)	174.07(0.6)
H5-C5-C9-H9	-60.21(4.6)	-70.74(4.4)	C1-C9-O9-H91	167.18(3.3)	168.5(3.0)
H61-C6-C7-H71	77.95(4.3)	-40.01(3.5)	H9-C9-O9-H91	46.46(4.7)	56.25(4.4)
H61-C6-C7-H72	-50.17(4.7)	75.86(3.6)	C30-N3-C4-C5	171.07(0.5)	168.68(0.5)
H62-C6-C7-H71	-45.30(4.6)	-171.43(3.5)	C30-N3-C4-C41	-63.48(0.7)	-67.44(0.6)
H62-C6-C7-H72	-173.42(4.9)	-55.55(3.5)	N3-C4-C41-C42	150.39(0.7)	151.56(0.6)
H71-C7-C8-H81	48.88(4.3)	159.56(3.2)	N3-C4-C41-C46	-36.23(0.9)	-34.27(0.9)

Table 5

Interatomic Distances (Å) and Angles (°) in the Hydrogen Bonds

a b c	ab	bc	ac	abc
O9A-H91A...O9B	0.949	2.009	2.840	145.7
O50-HO50...O9A	1.216	1.634	2.790	156.8
O9A-H91B...O50	1.120	1.623	2.720	163.4

tetrachloride the broad absorption disappeared and only a sharp band at 3625 cm^{-1} was observed, which is assigned to free O-H groups. In deuteriochloroform solution the band was shifted towards 3610 cm^{-1}. The steric impediment of the phenyl rings excludes any O-H...N bonding which could be observed.

NMR Spectra.

In our previous paper from the ^{1}H and ^{13}C nmr data [1] we concluded that 3-methyl-2,4-diphenyl-3-azabicyclo[3.3.1]nonan-9β-ol adopts in deuteriochloroform and perdeuteriobenzene solutions a flattened chair-chair conformation in which the cyclohexane ring is more flattened with the phenyl groups in a preferred conformation in which $H2(4)_{ax}$ (Figure 1) are near coplanar with the phenyl groups.

Hence, good agreement of the preferred conformation of 3-methyl-2,4-diphenyl-3-azabicyclo[3.3.1]nonan-9β-ol in deuteriochloroform and perdeuteriobenzene solutions is observed.

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