CRYSTAL AND MOLECULAR STRUCTURE OF 6,6-DIMETHYL -cis-2,4-DIPHENYL-3-AZA-7-OXABICYCLO[3.3.1]NONAN-9-ONE

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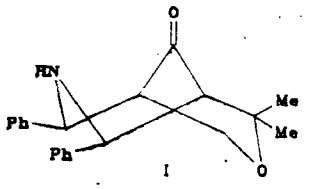
A method is presented for synthesizing 6,6-dimethyl-2,4-diphenyl-3-aza-7-oxabicyclo[3.3.1]nonan-9-one. The x-ray structure shows that the compound in the crystal exists in the chair–boat conformation with the piperidine ring in the boat form. The two phenyl substituents in the 2- and 4-positions are responsible for such a conformation.

The conformational behavior of cyclic compounds and the effect of various intramolecular interactions on it are important problems in modern stereochemistry. Bicyclic compounds, especially heteroanalogs and derivatives of bicyclo[3.3.1]nonane, are suitable models for studying these interactions. The chair–chair conformation of bicyclo[3.3.1]nonane itself is only 2.5 kcal/mole more favorable than the chair–boat [1]. Therefore, even comparatively small intramolecular interactions can cause the latter to be favored. The effect of substituents in the 2- and 4-positions on the conformational behavior was studied for a series of heteroanalogs of bicyclo[3.3.1]nonane [2-7]. However, the conformational behavior of the 3-aza-7-oxaanalogs needs more study. Therefore, an x-ray structure study of 6,6-dimethyl-2,4-diphenyl-3-aza-7-oxabicyclo[3.3.1]nonan-9-one $C_{21}H_{23}NO_2$ (I) seemed interesting.



I

The atomic coordinates of the molecule (Table 1) and the angles between certain planes (Table 2) were determined. The bond lengths and angles of bicyclo[3.3.1]nonane and the phenyl substituents have their normal values. Molecules of I in the crystal adopt the chair–boat conformation with the piperidine ring in the boat form. Atoms $N_{(3)}$ and $C_{(9)}$ are located to one side of the $C_{(1)}C_{(2)}C_{(4)}C_{(5)}$ plane (deviations of 0.686 and 0.722 Å, respectively). Atoms $O_{(7)}$ and $C_{(9)}$ are located on different sides of the $C_{(8)}C_{(1)}C_{(5)}C_{(6)}$ plane (deviations –0.621 and 0.725 Å). The distances $C_{(9)}$–$N_{(3)}$ and $C_{(9)}$–$O_{(7)}$ are 2.465(2) and 2.820(2) Å. Both phenyl substituents are equatorial in the ring in the boat conformation. Apparently the main reason that the chair–boat conformation is preferred in the studied compound is the presence in the 2- and 4-positions of the two phenyl rings. These would be axial in the alternate conformation with two chairs. The inability to place two bulky substituents in the axial positions at a distance of about 2.5 Å was also demonstrated for 2,4,6,8-tetraphenyl-3,7-disubstituted derivatives of bicyclo[3.3.1]nonane [3, 5].

EXPERIMENTAL

X-Ray Structure Analysis. The x-ray diffraction study was carried out on a DRON-2.0 diffractometer (Cu Kα radiation, graphite monochromator). A total of 2008 independent nonzero reflections were measured. Crystals are monoclinic: *a*

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TABLE 1. Atomic Coordinates (× 10^4, × 10^3 for H atoms)

Atom	x	y	z	Atom	x	y	z
$C_{(1)}$	5128(2)	−735(2)	2857(2)	$H_{(1)}$	592(2)	−60(1)	338(2)
$C_{(2)}$	5206(2)	−1427(2)	1785(2)	$H_{(2)}$	488(2)	−111(1)	94(2)
$N_{(3)}$	4466(2)	−2207(1)	1909(2)	$H_{(3)}$	448(2)	−260(2)	135(2)
$C_{(4)}$	3183(2)	−1970(1)	1730(2)	$H_{(4)}$	289(2)	−161(1)	94(2)
$C_{(5)}$	3190(2)	−1310(1)	2834(2)	$H_{(5)}$	261(2)	−160(1)	333(2)
$C_{(6)}$	2566(2)	−384(2)	2346(2)	$H_{(6.1)}$	333(2)	23(2)	413(2)
$O_{(7)}$	3285(1)	16(1)	1590(1)	$H_{(6.2)}$	197(2)	−10(2)	398(2)
$C_{(8)}$	4522(2)	147(2)	2284(2)	$H_{(6.3)}$	218(2)	80(2)	317(2)
$C_{(9)}$	4385(2)	−1149(1)	3651(2)	$H_{(7.1)}$	72(2)	−78(2)	182(2)
$O_{(10)}$	4746(1)	−1322(1)	4798(1)	$H_{(7.2)}$	98(2)	16(2)	120(2)
$C_{(11)}$	6493(2)	−1706(1)	1912(2)	$H_{(7.3)}$	131(2)	−79(2)	65(2)
$C_{(12)}$	7146(3)	−2206(2)	2952(3)	$H_{(8.1)}$	494(2)	38(1)	158(2)
$C_{(13)}$	8345(3)	−2419(2)	3086(3)	$H_{(8.2)}$	459(2)	63(1)	293(2)
$C_{(14)}$	8914(2)	−2146(2)	2203(3)	$H_{(9)}$	671(2)	−234(2)	363(3)
$C_{(15)}$	8274(3)	−1635(2)	1183(3)	$H_{(10)}$	877(3)	−279(2)	381(3)
$C_{(16)}$	7082(2)	−1440(2)	1023(2)	$H_{(11)}$	976(2)	−233(2)	235(2)
$C_{(17)}$	2471(2)	−2818(1)	1759(2)	$H_{(12)}$	869(2)	−144(2)	57(2)
$C_{(18)}$	2791(2)	−3380(2)	2833(2)	$H_{(13)}$	659(2)	−105(2)	27(2)
$C_{(19)}$	2153(3)	−4152(2)	2887(3)	$H_{(14)}$	356(2)	−318(1)	361(2)
$C_{(20)}$	1173(3)	−4378(2)	1867(4)	$H_{(15)}$	250(2)	−460(2)	370(2)
$C_{(21)}$	846(3)	−3826(2)	791(3)	$H_{(16)}$	72(2)	−499(2)	192(2)
$C_{(22)}$	1485(2)	−3037(2)	731(2)	$H_{(17)}$	5(2)	−388(2)	10(3)
$C_{(23)}$	2508(2)	213(2)	3502(3)	$H_{(18)}$	128(2)	−260(2)	−8(2)
$C_{(24)}$	1301(2)	−467(2)	1418(3)				

TABLE 2. Interplanar Angles

Angle	Deg.
$O_{(10)}C_{(1)}C_{(9)}C_{(5)}$ — $C_{(8)}C_{(1)}C_{(5)}C_{(6)}$	124.0
$O_{(10)}C_{(1)}C_{(9)}C_{(5)}$ — $C_{(1)}C_{(2)}C_{(4)}C_{(5)}$	122.8
$C_{(8)}C_{(1)}C_{(5)}C_{(6)}$ — $C_{(1)}C_{(2)}C_{(4)}C_{(5)}$	113.2
$C_{(8)}C_{(1)}C_{(5)}C_{(6)}$ — $O_{(7)}C_{(8)}C_{(6)}$	127.0
$C_{(1)}C_{(2)}C_{(4)}C_{(5)}$ — $N_{(3)}C_{(2)}C_{(4)}$	123.1

= 11.470(2), b = 14.902(2), c = 10.718(2) Å, β = 105.92(5)°, Z = 4, space group $P2_1/c$, V = 1761.7 Å^3, ρ_{calc} = 1.219 g/cm^3. The asymmetric unit contains one molecule. Calculations were performed on a BÉSM-6 computer using the Rentgen-75 program. The structure was solved by direct methods. Coordinates of all nonhydrogen atoms were found in an E-map and were refined by least squares until R = 0.10. Coordinates of 19 H atoms were found in a difference synthesis. Coordinates of the remaining 4 H atoms were assigned geometrically. The final refinement using full-matrix anisotropic (isotropic for H atoms)least squares reduced R to 0.048.

6,6-Dimethyl-2,4-diphenyl-3-aza-7-oxabicylo[3.3.1]nonan-9-one (I). A solution of 19 g (0.25 mole) ammonium acetate in 50 ml ethanol and 53 g (0.5 mole) benzaldehyde was placed in a three-necked flask fitted with a reflux condenser, mechanical stirrer, and dropping funnel. The flask was cooled in a dry ice–acetone mixture. A solution of 32 g (0.25 mole) 2,2-dimethyltetrahydropyran-4-one in 50 ml ethanol was added dropwise. The mixture was kept for 5-6 h at 78°C and then heated at 80°C for 5 h. It was then cooled. The upper layer was poured off. The lower layer was washed with water by decantation. The washed residue was dissolved in ether and converted to the hydrochloride. The salt obtained was treated with aqueous KOH and extracted with ether. The ether extract was dried with KOH. The solvent was removed. The residue was recrystallized from petroleum ether. Yield: 16.3 g (20%) compound I with mp 171-172°C.

LITERATURE CITED

1. V. S. Mastrykov, M. V. Popik, O. V. Dorofeeva, A. V. Golubinskii, L. V. Vilkov, N. A. Belikova, and N. L. Allinger, *J. Am. Chem. Soc.*, **103**, 1333 (1981).
2. T. T. Omarov, M. Zh. Buranbaev, A. I. Gubin, Kh. T. Suleimenov, and Yu. P. Gladii, *Zh. Org. Khim.*, **54**, 440 (1984).

3. H. Quast, B. Muller, E.-M. Peters, K. Peters, and H. G. von Schnering, *Chem. Ber.*, **115**, 363 (1982).
4. H. Quast and B. Muller, *Chem. Ber.*, **113**, 2959 (1980).
5. N. S. Pantaleo, D. van der Helm, K. Ramarajan, B. R. Bailey, and K. D. Berlin, *J. Org. Chem.*, **46**, 4199 (1981).
6. E. L. Eliel, M. Manoharan, D. J. Hodgson, and D. S. Eggleston, *J. Org. Chem.*, **47**, 4353 (1982).
7. R. Jeyaraman, C. B. Jawaharsingh, S. Avila, K. Ganapathy, E. L. Eliel, M. Manoharan, and S. Morris-Natschke, *J. Heterocycl. Chem.*, **19**, 449 (1982).

SYNTHESIS OF FURO[2,3-d]PYRIMIDINES CONDENSED WITH A TETRAHYDROTHIOPYRAN

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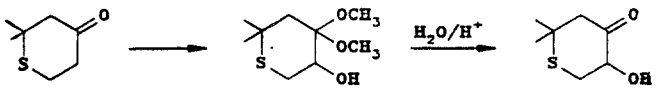
Using o-iodobenzoic acid we synthesized 5-hydroxy-2,2-dimethyltetrahydrothiopyran-4-one. From the latter we synthesized 2-amino-5,5-dimethyl-3-cyano-4,5-dihydro-7H-furo[2,3-c]thiopyran; this is a starting material for the preparation of furo[2,3-d]pyrimidine condensed with tetrahydrothiopyran and triazole rings.

In a number of condensed derivatives of 2,2-dimethyltetrahydrothiopyran-4-one we wished to find new biologically active compounds. We therefore attempted to obtain thiopyran condensed with a 2-amino-3-cyanofuran ring, and also furo[2,3-d]pyrimidines condensed with a thiopyran or triazole ring.

Data have been published on the synthesis of thiopyranes condensed with a 2-amino-3-cyanothiophene ring [1], and on their further conversions [2]. Thiopyran synthesis proceeds smoothly in one step when powdered sulfur is used [3]. For the synthesis of condensed furan derivatives ketol (III), a 5-hydroxy derivative of ketone (I), is necessary. There are efficient methods for the α-hydroxylation of ketones that use "hypervalent iodine," [iodosobenzene, o-iodosobenzoic acid (o-IBA), and idosobenzene diacetate] [4-6]. We used o-IBA to oxidize the starting ketone to ketal (II), which was then hydrolyzed to (III) in good yield.



I II III

According to the PMR spectra the hydroxy group in (II) has axial orientation.

Condensation of acyl ion (III) with malonodinitrile in the presence of an equimolar amount of diethylamine forms furo[2,3-c]thiopyran (IV). Attempts to condense o-aminonitrile (IV) with formamide and then to cyclize to furo[2,3-d]pyrimidine (VII) were unsuccessful even with boiling. To obtain (VII), 2-amino-3-cyanofuran (IV) was first converted to 2-ethoxymethyleneamino-3-cyanofuran (V). Treatment of (V) with cooled 25% ammonia in ethanol gave 2-aminomethyleneamino-3-cyanofuran (VI); boiling of (VI) in ethanolic sodium hydroxide formed furo-[2,3-d]pyrimidine (VII), which represents a new condensed heterocyclic system (see scheme on page 1171).

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