THREE-DIMENSIONAL STRUCTURES AND SPECTRA OF 2,6- AND 2,8-DIETHYL-2,4,6,8-TETRAAZABICYCLO[3.3.0]OCTANE-3,7-DIONES

É. B. Shamuratov, A. S. Batsanov, Yu. T. Struchkov,
A. Yu. Tsivadze, M. G. Tsintsadze, L. I. Khmel'nitskii,
Yu. A. Simonov, A. A. Dvorkin, O. V. Lebedev,
and T. B. Markova

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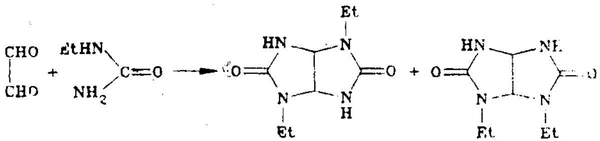
Isomeric 2,6- and 2,8-diethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-diones were obtained by the reaction of glyoxal with ethylurea, and their crystal structures and IR, Raman, and PMR spectra were studied.

Derivatives of bicyclic bisurea, or 2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione (TABOD), are of interest in view of the psychotropic activity that some of them display [1]. These compounds have been subjected to structural studies in complexes with metal salts [2-5].

In the present research we isolated in pure form the isomeric 2,6-diethyl-TABOD (I) and 2,8-diethyl-TABOD (II), which are formed simultaneously in the reaction



I II

Isomeric I and II actually have identical R_f values in thin-layer chromatography (using the most diverse eluents). Their separation by fractional crystallization from various solvents was also ineffective. In the case of slow evaporation of an aqueous solution of a mixture of isomers I and II they precipitate simultaneously in the form of colorless crystals with different physical appearances (II was obtained in the form of fine rhombic plates, while I was obtained in the form of compact crystals resembling sucrose), which makes it possible to separate them manually.

The structures of I and II were established by PMR spectroscopy, by converting them to the corresponding N-methylated products by the action of $NaNH_2$ in liquid ammonia and CH_3I [6], and by x-ray diffraction analysis.*

The I molecule has C_2 crystallographic symmetry (Fig. 1a); two crystallographically independent A and B molecules, the geometrical parameters of which are similar, whereas noncrystallographic C_s symmetry is basically adhered to in each of the molecules, were discovered in the II structure (the average values are presented in Fig. 1b).

Let us note that the I molecule is chiral; noncentrosymmetric crystals of both enantiomers (SS and RR) are formed from the racemic solution. The absolute configuration of the investigated sample was not established objectively and was arbitrarily assumed to be S [with respect to the $C_{(1)}$ atom]. On the other hand, achiral isomer II gives centrosymmetric crystals.

The geometry of the bicyclic fragment in the I and II molecules is similar to that observed in complexes of 2,4,6,8-tetramethyl-TABOD (mebicar) with the composition $Co(NCS)_2(H_2O)(C_8H_{14}N_4O_2)$ [4] and in a complex with a I molecule as a ligand with the composition $ZnCl_2(H_2O)(C_8H_{14}N_4O_2)$ (III) [5]. The five-membered rings are planar with an accuracy of up to 0.02 Å in the I molecule and up to 0.03 Å in the II molecule [except for the

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*See [7] for a preliminary communication regarding the crystal structure of I.

A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow 117813. N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow 117813. Institute of Applied Physics, Moldavian SSR, Kishinev 277028. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 937-941, July, 1991. Original article submitted August 18, 1989; revision submitted July 17, 1990.

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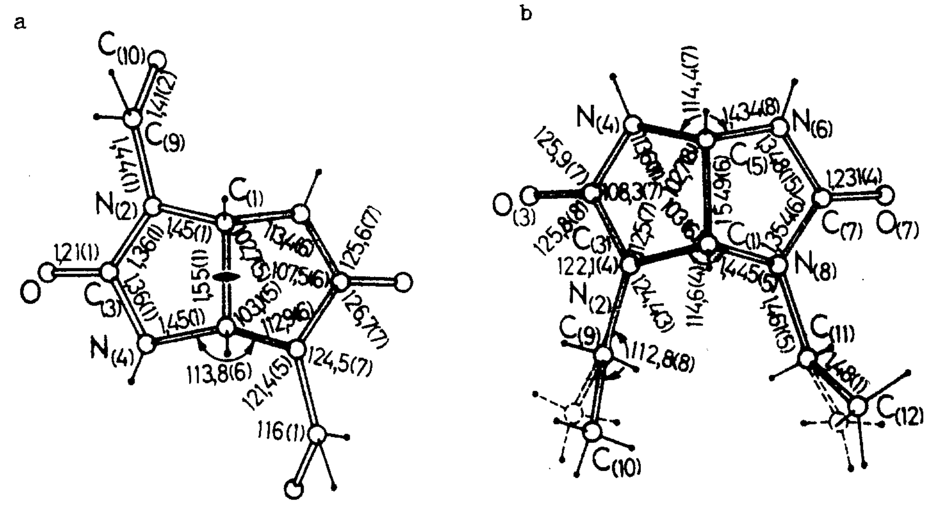

Fig. 1. Structures of I (a) and II (b). The bond lengths (*l*, Å) and bond angles (ω, deg) are presented. The average *l* and ω values are given for the two independent II molecules; the orientations of the Et groups in the A (unbroken lines) and B (broken lines) molecules are shown.

TABLE 1. Hydrogen Bonds in the I and II Structures

Compound	D—H...A bond	d, Å			∠DHA°
		D—H	H···A	D···A	
I	$N_{(4)}—H_{(4)}\cdots O$*	0,75(6)	2,14(6)	2,88(1)	165(6)
II	$N_{(4A)}—H_{(4A)}\cdots O_{(3A)}$**	0,75(3)	2,17(3)	2,812(5)	169(6)
	$N_{(6A)}—H_{(6A)}\cdots O_{(7B)}$	0,86(4)	2,08(4)	2,890(5)	158(3)
	$N_{(4B)}—H_{(4B)}\cdots O_{(3B)}$***	0,77(3)	2,12(3)	2,892(4)	173(3)
	$N_{(6B)}—H_{(6B)}\cdots O_{(3A)}$**	0,80(4)	1,96(4)	2,837(5)	162(4)

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*The atoms associated with basis transformations with 1/2 − x, 1/2 + y, and 1/4 − z symmetry.

**The atoms associated with basis transformations with 1 − x, −y, and 1 − z symmetry.

***The atoms associated with basis transformations with 2 − x, −y, and 1 − z symmetry.

$C_{(1)}C_{(5)}N_{(6)}C_{(7)}N_{(8)}$ ring of the B molecule, which has an envelope conformation with 0.10 Å bending of the $N_{(6)}$ atom]. They have cis fusion in the form of a "slightly open book" forming dihedral angles of 121° (I), 119° (II, A), and 126° (II, B). The nitrogen atoms participate by means of their unshared electron pairs in conjugation with the CO groups and have a flattened geometry, and the N—C(Et) bonds are therefore almost coplanar with respect to the rings. The C—C bonds of the ethyl groups have different orientations in the I and II molecules: in the I isomer they are directed inside the "slightly open book", whereas in the II isomer they are directed outside it [i.e., in the same direction as the $H_{(1)}$ and $H_{(5)}$ atoms]; the conformation is less symmetrical in the A molecule than in the B molecule [torsion angle $C_{(3)}N_{(2)}C_{(9)}C_{(10)}$ 90.7° and torsion angle $C_{(7)}N_{(8)}C_{(11)}C_{(12)}$ −123.8° in A, as compared with −100.2° and 98.0°, respectively, in the B molecule]. These differences are evidently due to packing effects, since in the III complex the conformation of ligand I is closer to that found in isomer II than in the noncoordinated I molecule.

The systems of hydrogen bonds in structures I and II (Table 1) differ. In the I crystal the molecules are joined together in helical chains around the 4_1 axes, and since each molecule participates in two helixes (associated with the 2 axis), the molecules are joined together in a three-dimensional network. In the II crystal the molecules form centrosymmetric A—A′ and B—B′ dimers joined together in a ribbon in the [100] direction parallel to the (010) plane.

TABLE 2. IR Spectra of I and II

Compound	Vibrational frequencies, cm^{-1}													
	ν_{NH}	ν_{CH}	ν_{CO}	$\nu_{CN\ am}$	δ_{CH_3}	δ_{CH_2}	ω_{CH_2}	$\nu_{(CH)CH}$	δ_{CH_3}; ρ_{CH_2}	ν_{CC}	ν ring	ρ_{CH_2}	r_{NCO}	δ_{NCN}
I	3294 br., 3120	3000, 2985, 2949, 2888	1694 sh, 1670, 1645 sh	1500, 1453, 1387	1443, 1359	1326	1261, 1242	1196	1090, 975	1037	893, 860	738, 683	625	477
II	3300 br., 3125	2988, 2898, 2830	1702, 1635 sh	1502	1475 sh., 1394, 1372	1296 sh., 1227	1258	1125	1085, 1073	980, 902	838, 794	675	633, 604	497, 485, 440

TABLE 3. Raman Spectra of I and II

Compound	Vibrational frequencies, cm^{-1}														
	ν_{NH}	ν_{CH}	ν_{CO}	$\nu_{CN\ am}$	δ_{CH_3}	δ_{CH_2}	ω_{CH_2}	$\delta_{CH_{CH}}$	δ_{CH_3}; ρ_{CH_2}	ν_{CC}	ν_{ring}	ρ_{CH_2}	r_{NCO}	δ_{NCN}	Other frequencies
I	3200	2976, 2947, 2883	1710 sh, 1665	1460, 1380	1445, 1330		1270, 1190		1090, 973		915, 790		627	506, 440, 390, 345	
II	3285	2965, 2936, 2878	1684, 1666	1453, 1367	1367	1337, 1296	1255	1169	1080, 1023	980	908, 893	782, 753	627, 598	431, 348	304, 207

TABLE 4. Coordinates of the Nonhydrogen Atoms in Structure I (·104)

Atom	x	y	z	Atom	x	y	z
O	1766(1)	2859(8)	1776(2)	$N_{(4)}$	3019(11)	6193(9)	1831(2)
$C_{(1)}$	2156(11)	6854(1)	2762(2)	$C_{(9)}$	546(23)	3343(2)	2930(4)
$N_{(2)}$	1698(9)	4758(9)	2581(2)	$C_{(10)}$	1697(29)	2288(2)	3344(5)
$C_{(3)}$	2112(12)	4439(1)	2032(2)				

TABLE 5. Coordinates of the Nonhydrogen Atoms in Structure II (·10^4)

Atom	Molecule A			Molecule B		
	x	y	z	x	y	z
$O_{(3)}$	3780(2)	448(3)	4960(2)	1020(2)	473(3)	3783(2)
$O_{(7)}$	2321(2)	−980(3)	591(2)	5632(2)	−840(3)	2113(2)
$C_{(1)}$	2828(3)	1480(4)	2406(3)	7514(3)	1496(4)	2740(3)
$N_{(2)}$	2768(2)	1250(4)	3363(2)	8457(2)	1240(3)	2702(2)
$C_{(3)}$	3622(3)	714(4)	4071(3)	9142(3)	730(4)	3596(3)
$N_{(4)}$	4258(2)	536(4)	3648(2)	8700(2)	558(4)	4220(2)
$C_{(5)}$	3884(3)	985(4)	2611(3)	7673(3)	969(4)	3802(3)
$N_{(6)}$	3678(2)	16(4)	1858(3)	6963(2)	−67(4)	3549(2)
$C_{(7)}$	2684(3)	−175(4)	1266(3)	6351(3)	−113(4)	2522(3)
$N_{(8)}$	2178(2)	689(3)	1559(2)	6684(2)	734(3)	2039(2)
$C_{(9)}$	2010(3)	1817(5)	3640(3)	8743(3)	1752(5)	1930(3)
$C_{(10)}$	2179(6)	3186(6)	3884(6)	8824(6)	3148(6)	1960(6)
$C_{(11)}$	1086(3)	766(5)	1072(4)	6164(3)	944(5)	931(3)
$C_{(12)}$	697(4)	2051(5)	647(4)	5506(5)	2068(6)	678(5)

In the PMR spectrum of isomer I the $H_{(1)}$ and $H_{(5)}$ protons give a singlet with δ 6.0 ppm, while for isomer II they give an AB system with δ 5.54 ppm (A) and 5.71 ppm (B) (J_{AB} = 8.9 Hz).

The IR and Raman spectra of I and II (Tables 2 and 3) show the greatest differences in the region of the ν_{CO} frequencies (1600-1800 cm^{-1}). The IR spectrum of isomer II contains an intense band at ≈ 1702 cm^{-1} with an inflection on the low-frequency side at ≈ 1675 cm^{-1}, while in the spectrum of isomer I the relative intensities of the low- and high-frequency components of the doublet change inversely. In the Raman spectrum of isomer II one observes a distinct doublet at 1666 and 1648 cm^{-1} with a more intense low-frequency component; in the case of isomer I only the latter component was clearly revealed, and the high-frequency component appears in the form of an inflection at ≈ 1702 cm^{-1}. These differences can be explained by restructuring of the system of hydrogen bonds. In the I crystal each oxygen atom is an acceptor in one N—H···O bond (all such bonds in this structure are symmetrically equivalent), while in the II structure the $O_{(3A)}$ atom accepts two bonds, the $O_{(3B)}$ and $O_{(7B)}$ atoms accept one each, and the $O_{(7A)}$ atom does not participate in hydrogen bonds; this nonequivalence intensifies the splitting of the ν_{CO} bands.

On the other hand, the ν_{NH} bands in the IR spectra of isomers I and II (a broad and intense high-frequency band and a weak low-frequency band) are virtually identical, since the functions of the NH groups in the hydrogen bonds remain almost unchanged. We did not find an appreciable difference in the IR spectra of isomers I and II in the ν_{CH} region (2700-3000 cm^{-1}), although there are differences in the Raman spectra. Individual differences are also observed in other regions of the IR and Raman spectra. In general, the spectra of isomer II contain more bands than the spectra of isomer I; this can be explained by the lower symmetry of the II molecule.

EXPERIMENTAL

2,8-Diethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione (II, $C_8H_{14}N_4O_2$). An 8.8-g (0.1 mole) sample of ethylurea was added to 6 ml (0.05 mole) of a 38% aqueous solution of glyoxal, and the mixture was acidified to pH 1-2 with concentrated HCl and heated for 1 h on a boiling-water bath. It was then cooled, and the precipitated I was removed by filtration, washed with the minimum amount of ice water, and air dried to give 3.6 g of a product with mp 286-288°C (from water). Evaporation of the residual solution to half its original volume precipitated 5.4 g of a mixture of isomers I and II. Slow evaporation of an aqueous solution of the latter gave large crystals of isomers I and II, which were sorted out manually and recrystallized twice from water to give II with mp 239-241°C. The presence of admixtures of one isomer in the other lowered the melting points.

The x-ray diffraction experiments were carried out with RÉD-4 (for I) and Hilger—Watts (for II) automatic four-circle diffractometers at room temperature (Mo K_α emission). The crystals of isomer I were tetragonal and had the following parameters: a = 6.461(2), c = 24.039(9) Å, V = 1003.6 Å^3, space group $P4_12_12$, Z = 4 ($C_8H_{14}N_4O_2$), d_{meas} = 1.32 g/cm^3 (with a pycnometer), d_{calc} = 1.312 g/cm^3. The crystals of isomer II were monoclinic and had the following parameters: a = 14.768(2), c = 14.451(2) Å, β = 115.55(1)°, space group $P2_1/c$, Z = 8, d_{calc} = 1.30 g/cm^3.

For I we measured the intensities of 463 independent reflections with $I \geq 3\sigma$ (ω scanning, $2\theta \leq 50°$), while for II we measured the intensities of 1561 reflections with $I \geq 2\sigma$ ($\theta/2\theta$ scanning, $2\theta \leq 44°$). Both structures were decoded by the direct method and were refined by the method of least squares within the anisotropic approximation [within the isotropic approximation for the H atoms; the H atoms were not revealed for isomer I because of the strong thermal vibrations of the $C_{(10)}$ atom, which has B_{eq} = 13.5 Å^2] up to R = 0.067 (I) and R = 0.051 and R_w = 0.044 (II). The absolute configuration of structure I was not determined. The coordinates of the atoms are presented in Tables 4 and 5.

The IR absorption spectra (400-4000 cm^{-1}) were recorded with a UR-20 spectrometer (the samples were triturated with mineral and fluorinated oils and hexachlorobutadiene). The Raman spectra were obtained with a Spex RAMALOG-4 spectrometer (the samples were contained in glass capillaries, the recording was carried out using the "90°" irradiation scheme, the emission source was a Spectra Physics argon laser, and λ = 4880 and 5145 Å).

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