

6,6'-Bis(1,5-diazabicyclo[3.1.0]hexane)

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The interaction of 1,3-diaminopropane with glyoxal and NaOCl in water at pH 9.5–10.5 afforded the previously unknown 6,6'-bis(1,5-diazabicyclo[3.1.0]hexane). According to X-ray diffraction data, both bicyclic fragments of the title compound adopt a boat conformation.

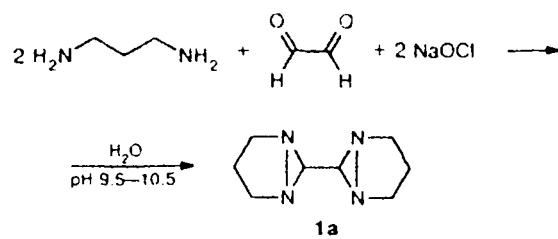
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Previously, based on the analysis of the ^1H and ^{13}C NMR spectra and the data of the MO perturbation theory, it has been suggested that 1,5-diazabicyclo[3.1.0]hexanes adopt predominantly a boat conformation.^{1–3} However, these suggestions must be taken as tentative but not conclusively proved in the absence of X-ray diffraction data on at least several crystal structures of the most typical representatives of this series. At the same time, the agreement between the spectral characteristics, such as the spin-spin coupling constants for protons of the bicycle and the chemical shifts of the C(3) and C(6) atoms in the structural analogs, and the proposed conformations can serve as evidence for the validity of indirect methods used previously^{1–3} for establishing the structures of these compounds. All known representatives of 1,5-diazabicyclo[3.1.0]hexanes are low-boiling liquids, which does not allow one to study them by X-ray diffraction analysis.

In this work, we improved a known procedure^{4,5} by optimizing pH of the reaction medium in analogy to a procedure reported previously⁶ and used this procedure for preparing the previously unknown 6,6'-bis(1,5-diazabicyclo[3.1.0]hexane) (**1a**) (Scheme 1), which is the

first representative of 1,5-diazabicyclo[3.1.0]hexanes that exists in the solid state under standard conditions.

Scheme 1



The structure of molecule **1a** was unambiguously established by X-ray diffraction analysis (Fig. 1). In the crystal, two independent molecules occupy special positions, *viz.*, crystallographic centers of symmetry located on the C(6)–C(6') bonds. The bond lengths and bond angles in the two independent molecules differ only slightly.

The pyrazolidine ring of the bicyclic fragment in molecule **1a** adopts a flattened envelope conformation.

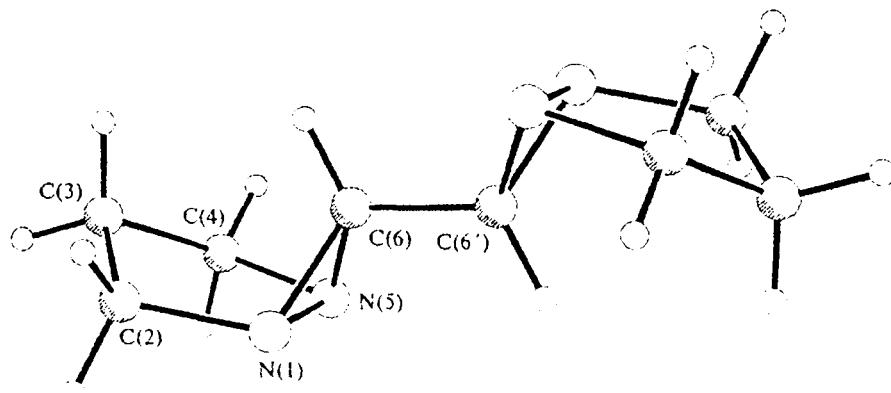
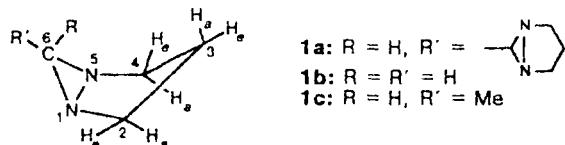


Fig. 1. Overall view of molecule **1a**.

Table 1. Chemical shifts of the C(3) and C(6) atoms in the ^{13}C NMR spectra and selected spin-spin coupling constants (Hz) of 1,5-diazabicyclo[3.1.0]hexanes



Compound	δ		$^2J_{\text{HH}}$			$^3J_{\text{HH}}$		
	C(3)	C(6)	2(4)ae	2(4)a3e	2(4)e3a	(4)e3e		
1a^a	20.5	55.6	-12.0	7.9	8.7	1.3		
1b^b	20.4	47.0	-12.1	8.2	8.5	1.4		
1c^b	22.2	52.3	-12.0	8.3	8.1	2.0		

^a The boat conformation established in the present work.

^b The boat conformation proposed in Refs. 1-3.

The C(3) atom deviates from the plane (to within 0.002 Å) through the remaining four atoms, *viz.*, N(1), C(2), C(4), and N(5), by 0.40 Å. The C(6) atom deviates from the above-mentioned plane by 1.17 Å. The overall conformation of the ring can be described as a boat. The geometric parameters of the two independent molecules differ insignificantly.

The spectral characteristics of compounds **1b** and **1c** (the closest structural analogs of compound **1a**) (Table 1) used in the conformational analysis¹⁻³ of 1,5-diazabicyclo[3.1.0]hexanes are close to the corresponding characteristics of **1a**, which counts in favor of the assumption that compounds **1b** and **1c** have a boat-like conformation.

Experimental

The IR spectra were recorded on a UR-20 spectrometer as KBr pellets (ν/cm^{-1}). The NMR spectra were measured on Bruker WM-250 (^1H , 250 MHz) and Bruker AM-300 (^{13}C ,

75.5 MHz) spectrometers in CDCl_3 in the δ scale relative to Me_4Si as the internal standard. TLC was performed on Silufol UV-254 plates; spots were visualized with I_2 vapor and independently by spraying the TLC plates with a solution of diphenylamine in acetone followed by heating of the plate (a 9 : 1 CHCl_3 —MeOH mixture was used as the eluent). The pH of the medium was monitored using an EV-74 ionometer.

Synthesis of 6,6'-bis(1,5-diazabicyclo[3.1.0]hexane) (1a).

NaOH (8.0 g, 0.2 mol) was added to a solution of 1,3-diaminopropane dihydrochloride (15 g, 0.1 mol) in water (100 mL), and then a 36% aqueous solution of glyoxal (6.3 mL, 0.05 mol) was added at 0–10 °C. At 0–5 °C, a solution of NaOCl (0.1 mol) in water (36 mL) was added dropwise to the reaction mixture at a rate such that the pH of the mixture remained within 9.5–10.5. The reaction mixture was kept at 0–5 °C for 24 h and then at 20 °C for 24 h, pH being maintained equal to 9.5–10.5 by adding an aqueous NaOH solution. The yield was determined by iodometric titration (76%). The reaction mixture was saturated with NaCl and extracted with CHCl_3 (3×100 mL). The extract was dried with K_2CO_3 , and the solvent was evaporated. Product **1a** was isolated by preparative chromatography on silica gel L 40/100 μm (CHCl_3 , which was twice washed with equal volumes of a 25% aqueous solution of ammonia, was used as the eluent). Compound **1a** was obtained in a yield of 5.1 g (61%), m.p. 215 °C (with decomp.), R_f 0.42 (CHCl_3). ^1H NMR, δ : 1.54 (m, 1 H, $\text{H}_a(3)$, $^2J_{ae} = -13.1$ Hz, $^3J_{ae} = 8.7$ Hz, $^3J_{aa} = 11.1$ Hz); 1.69 (m, 1 H, $\text{H}_e(3)$, $^2J_{ea} = -13.1$ Hz, $^3J_{ea} = 7.9$ Hz, $^3J_{ee} = 1.3$ Hz); 2.01 (br.s., 1 H, $\text{H}(6)$); 2.88 (m, 1 H, $\text{H}_a(2)$ or $\text{H}_a(4)$, for J , see Table 1); 3.32 (m, 1 H, $\text{H}_e(2)$ or $\text{H}_e(4)$, $^4J_{(H_eH_e)(6)} = 0.5$ Hz; other J are given in Table 1). ^{13}C NMR, δ : 20.5 (t, C(3), $^1J = 133$ Hz); 50.4 (t, C(2) or C(4), $^1J = 143$ Hz); 55.6 (d, C(6), $^1J = 165$ Hz). Found (%): C, 57.6; H, 8.4; N, 33.7. $\text{C}_8\text{H}_{14}\text{N}_4$. Calculated (%): C, 57.8; H, 8.4; N, 33.8. IR, ν/cm^{-1} : 710, 790, 860, 970, 1020, 1210, 1250, 1310, 1460, 2890, 2950.

X-ray diffraction study of compound 1a. X-ray diffraction data were collected on an automated four-circle Siemens P3 diffractometer (Mo-K α radiation, graphite monochromator, 0/20 scanning technique, $2\theta < 58^\circ$, at -120 °C). Crystals are monoclinic: $a = 9.075(1)$, $b = 9.235(2)$, $c = 11.146(2)$ Å, $\beta = 111.61(1)^\circ$, $V = 868.5(3)$ Å 3 , mol. weight 166.23, space group $P2_1/c$, $Z = 4$, $d_{\text{calc}} = 1.271$ g cm $^{-3}$, $F(000) = 360$, $\mu = 0.83$ cm $^{-1}$. A total of 2187 reflections were measured of which

Table 2. Atomic coordinates ($\times 10^4$ Å) and isotropic equivalent thermal parameters ($\times 10^3/\text{\AA}^2$) in the structure of **1a**

Atom	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq}	Atom	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq}
N(1)	5168(2)	760(1)	6627(1)	43(1)	H(22)	606(2)	189(2)	827(2)	75(6)
C(2)	6425(2)	1669(2)	7550(2)	58(1)	H(31)	685(2)	386(2)	743(2)	68(5)
C(3)	6596(2)	3033(2)	6854(2)	56(1)	H(32)	740(2)	292(2)	649(2)	64(5)
C(4)	4984(2)	3181(2)	5787(2)	51(1)	H(41)	427(2)	374(2)	608(2)	61(5)
N(5)	4246(1)	1725(1)	5498(1)	41(1)	H(42)	497(2)	358(2)	496(2)	64(5)
C(6)	5359(2)	649(1)	5396(1)	35(1)	H(6)	636(2)	97(2)	534(2)	41(4)
N(1A)	9703(1)	875(1)	6431(1)	41(1)	H(21A)	1149(2)	75(2)	816(2)	51(4)
C(2A)	10850(2)	1523(2)	7630(1)	44(1)	H(22A)	1020(2)	194(2)	811(2)	59(5)
C(3A)	11800(2)	2668(2)	7266(1)	47(1)	H(31A)	1274(2)	223(2)	720(2)	60(5)
C(4A)	10666(2)	3138(2)	5943(2)	53(1)	H(32A)	1207(2)	345(2)	786(2)	55(4)
N(5A)	9562(1)	1929(1)	5350(1)	43(1)	H(41A)	1123(2)	339(2)	539(2)	64(5)
C(6A)	10403(2)	572(1)	5481(1)	34(1)	H(42A)	1000(2)	393(2)	600(2)	70(5)
H(21)*	739(2)	113(2)	786(2)	73(6)	H(6A)	1152(2)	60(1)	572(1)	35(3)

* The coordinates ($\times 10^3$ Å) and isotropic thermal parameters ($\times 10^3/\text{\AA}^2$) are given for the hydrogen atoms. The hydrogen atoms have numbers equal to those of the carbon atoms to which the hydrogen atoms are attached.

Table 3. Bond lengths (*d*) and bond angles (ω) in the structure of **1a**

Bond	<i>d</i> /Å	Angle	ω /deg	Angle	ω /deg
N(1)—C(6)	1.449(2)	C(6)—N(1)—C(2)	111.6(1)	C(6A)—N(1A)—C(2A)	112.7(1)
N(1)—C(2)	1.483(2)	C(6)—N(1)—N(5)	58.50(8)	C(6A)—N(1A)—N(5A)	58.32(8)
N(1)—N(5)	1.517(2)	C(2)—N(1)—N(5)	107.0(1)	C(2A)—N(1A)—N(5A)	106.4(1)
C(2)—C(3)	1.518(3)	N(1)—C(2)—C(3)	108.2(1)	N(1A)—C(2A)—C(3A)	108.7(1)
C(3)—C(4)	1.514(3)	C(4)—C(3)—C(2)	103.0(1)	C(2A)—C(3A)—C(4A)	102.2(1)
C(4)—N(5)	1.484(2)	N(5)—C(4)—C(3)	108.6(1)	N(5A)—C(4A)—C(3A)	108.8(1)
N(5)—C(6)	1.451(2)	N(6)—N(5)—C(4)	111.5(1)	C(6A)—N(5A)—C(4A)	111.3(1)
C(6)—C(6)*	1.488(2)	C(6)—N(5)—N(1)	58.39(8)	C(6A)—N(5A)—N(1A)	58.46(7)
N(1A)—C(6A)	1.449(2)	C(4)—N(5)—N(1)	106.6(1)	C(4A)—N(5A)—N(1A)	106.5(1)
N(1A)—C(2A)	1.484(2)	N(1)—C(6)—N(5)	63.11(8)	N(5A)—C(6A)—N(1A)	63.21(8)
N(1A)—N(5A)	1.517(2)	N(1)—C(6)—C(6)*	116.1(1)	N(5A)—C(6A)—C(6A)**	116.1(1)
C(2A)—C(3A)	1.511(2)	N(5)—C(6)—C(6)*	115.6(1)	N(1A)—C(6A)—C(6A)**	115.6(1)
C(3A)—C(4A)	1.518(2)				
C(4A)—N(5A)	1.483(2)				
N(5A)—C(6A)	1.446(2)				
C(6A)—C(6A)**	1.491(2)				

* The atom is generated from the basis atom by the symmetry transformation $-x + 1, -y, -z + 1$. ** The atom is generated from the basis atom by the symmetry transformation $-x + 1, -y, -z + 2$.

2041 independent reflections were used in calculations and refinement.

The structure was solved by the direct method and refined by the full-matrix least-squares method in the anisotropic-isotropic approximation based on F^2 . The positions of the hydrogen atoms were located from difference electron density syntheses and refined isotropically. The final values of the *R* factors were as follows: $wR_2 = 0.1320$, GOOF = 1.029 using all reflections ($R_I = 0.0419$ using 1521 reflections with $I > 2\sigma(I)$). All calculations were carried out on an IBM PC/AT computer using the SHELXTL PLUS program package (version 5). The atomic coordinates and thermal parameters are given in Table 2. The bond lengths and bond angles are listed in Table 3.

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