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Eclipsed Conformation for Both Axial and Equatorial N−CH$_2$ Bonds in *N,N′,N″*-Tris(neopentyl)-1,3,5-triazane

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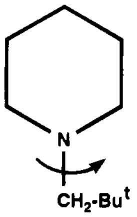
Abstract: The molecular structure of *N,N′,N″*-tris(neopentyl)-1,3,5-triazane is shown by a crystal X-ray diffraction study to have one axial and two equatorial neopentyl groups with eclipsing of both axial and equatorial exocyclic N−CH$_2$ bonds. In solution at about −130 °C both ring inversion and nitrogen inversion are slow on the NMR time scale, and 91% of molecules adopt that structure while 9% adopt the all-equatorial arrangement. The usefulness and shortcomings of molecular mechanics calculations of the structure are shown.

Introduction

There has been much interest recently[1,2,3] in compounds with a totally saturated bond which prefers to adopt an eclipsed conformation. Examples have been demonstrated from simpler and simpler systems,[2,3] albeit with bonds of a quite defined type $R^1X-YR^2R^3$ (X = CH$_2$, NH, or O; Y = CH or N) where steric repulsion of groups R along the bond disfavors staggered conformations.

Most recently, indirect NMR evidence and molecular mechanics calculations have suggested that $-YR_2R_3$ can be as simple as an unsubstituted six-membered ring so that, in *N*-neopentylpiperidine[3] **1** and *tert*-butoxycyclohexane[2h] **2**, the exocyclic bonds shown appear to be eclipsed. Because of the relatively short C−N and C−O bonds of **1** and **2**, the adjacent equatorial hydrogen atoms are suggested to be sufficient to force the *tert*-butyl group toward eclipsing, see **3** and **4**.



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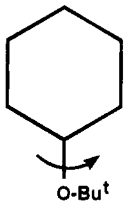

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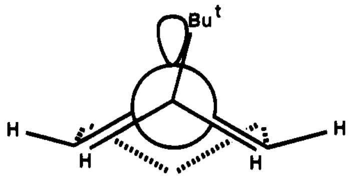

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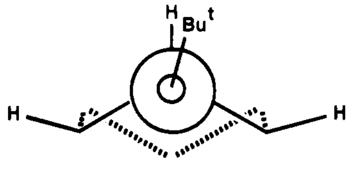

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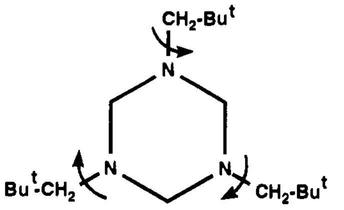
We now show directly from a crystal structure determination that 1,3,5-tris(neopentyl)-1,3,5-triazane **5** prefers a conformation with one axial and two equatorial neopentyl groups, in which both axial and equatorial N−CH$_2$Bu^t bonds are eclipsed, and we explore this molecule further by NMR studies and by molecular mechanics calculations.



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The crystal structure of **5** and a molecular mechanics calculated structure (MMX[4]) are shown in Figure 1, and some pertinent data are included in Table 1. One *N*-neopentyl group is axial and two are equatorial, the (aee) conformation, in

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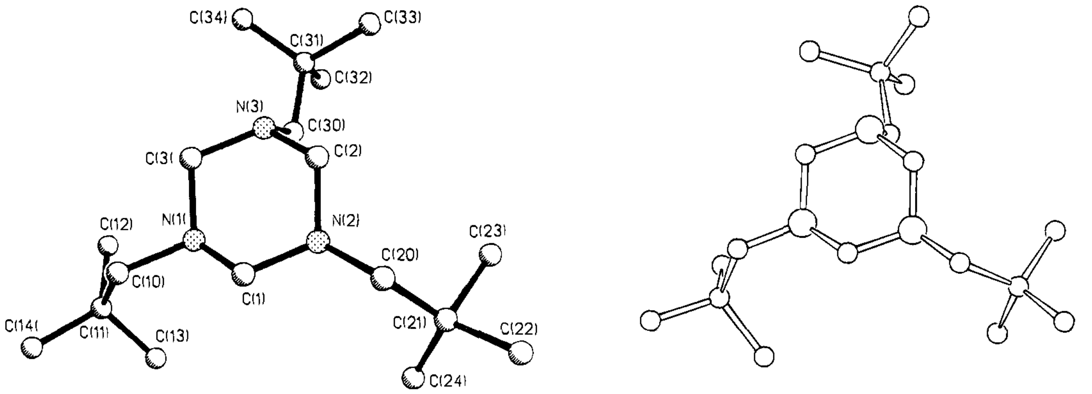

Figure 1. Structure of the most stable conformation of **5**: (left) X-ray diffraction determination of the crystal; (right) MMX calculation of the structure of the isolated molecule.

Table 1. Relative Energy (kcal mol^{-1}) of Conformations of **5** and Selected Structural Parameters Determined by X-ray Diffraction Study of the Crystal and by MM3 and MMX Calculations

	obsd	MM3	MMX
	(aee) Conformation		
rel energy[a]	0.00	0.21	0.00
torsion angles (deg)			
C_{ring}–N–*ax*C–H	4.6, 12.4	13.4, 22.6	−20.4, −28.4
C_{ring}–N–*eq*C–H	−5.8, −2.9	3.4, −6.0	12.7, 20.3
	−0.8, 6.4	4.0, −6.4	14.2, 22.9
C_{ring}–N–*ax*C–Bu^t	115.3, −119.3	101.6, −133.8	−139.4, 100.4
C_{ring}–N–*eq*C–Bu^t	117.3, −120.0	116.0, −117.9	134.4, −104.5
	122.1, −114.9	116.3, −118.7	132.2, −104.5
	(eee) Conformation[b]		
rel energy[a]	0.35	0.00	1.00
torsion angles (deg)			
C_{ring}–N–*eq*C–H	*b*	6.0, −5.6	−11.3, −19.5
		4.8, −6.6	−12.0, −20.3
		−1.2, −12.5	−13.0, −21.0
C_{ring}–N–*eq*C–Bu^t	*b*	−116.7, 116.4	−131.5, 104.5
		−117.2, 115.5	−132.2, 103.9
		−122.5, 110.4	−133.0, 103.2

[a] For the two conformations (aee or eee) as measured from the low-temperature NMR or as calculated. [b] This conformation is not found in the crystal.

Table 2. NMR Parameters[a] for **5**

	carbon-13 NMR		proton NMR	
signal	ambient	−126 °C	ambient	−126 °C
ring –CH$_2$–[b]	79.69	81.01	3.32	2.68, 3.61
		76.98		3.08, 3.36
		76.53		2.60, 3.56
side chain CH$_2$	65.19	64.77	2.12	2.69
		62.48		1.67
		65.07		1.61
tert-butyl CH$_3$	28.29	26.66	0.87	0.80
		26.98		0.82
		c		*c*
C_{quat}	34.34	33.27		
		33.18		
		33.54		

[a] At −126 °C groups have three signals at the chemical shifts quoted with fractional intensity 0.3033, 0.6066, and 0.09, respectively. [b] At −50 °C this appears as an AB quartet ($^3J \approx 10$ Hz) at $\delta = 3.11$ and 3.53. [c] Signals for the *tert*-butyl methyl group of the minor isomer could not be distinguished and are presumably overlapped by the major isomer signals. In the carbon-13 NMR at −126 °C this signal is unusually broad, and it broadens further down to the lowest temperature observed, −142 °C, in a manner quite in keeping with rotation about the *tert*-butyl–CH$_2$N bond becoming slow on the NMR time scale.[14]

keeping with previous studies of other triazanes.[5–10] The most striking feature of the structure of **5** is the torsion angles about the exocyclic N–C bonds. For both the axial and equatorial neopentyl groups the C_{ring}–N–C–H_{alpha} and C_{ring}–N–C–Bu^t angles are close to 0° and 120°, respectively, implying that the *tert*-butyl group eclipses the lone-pair, while the nitrogen–carbon bonds of the ring eclipse the carbon–hydrogen bonds of the side chain methylene group. The solid state carbon-13 NMR spectrum of **5** was recorded at room temperature and shows sets of 1:2 doublets, which corresponds with the (aee) conformation observed by X-ray diffraction.

A dynamic NMR study shows that two different conformations of compound **5** are present in solution (see Table 2). In the proton NMR below about −30 °C, the ring methylene proton NMR signal splits to an AB quartet with no associated changes in the carbon-13 NMR, indicating that ring inversion is slow on the NMR time scale while nitrogen inversion is still fast. All proton and carbon-13 signals split below about −100 °C, apparently to 2:1 pairs of signals, but below about −120 °C additional weak signals of about 9% of the total intensity become apparent as part of this second set of changes. The carbon-13 NMR spectrum at −126 °C, see Figure 2, shows these changes most clearly.

The carbon-13 chemical shifts for the major isomer fit with those in the solid state NMR confirming the (aee) conformation, while for the second conformation, all NMR signals are singlets except the AB quartet for protons of the ring methylene groups. This fits with the minor conformation having all three neopentyl groups equatorial.

Two types of conformation, (aee) 91% and (eee) 9% thus coexist, and their interconversion by nitrogen inversion and *N*-neopentyl bond rotation is slow on the NMR timescale. Full line-shape treatment of the solution NMR spectra leads to barriers to ring inversion and to nitrogen inversion/rotation of 11.0 and 6.4 kcal mol^{-1}, respectively.

Molecular mechanics calculations using the MMX program[4] and Allinger's MM3 program[11,12] agree (see Table 1) that the

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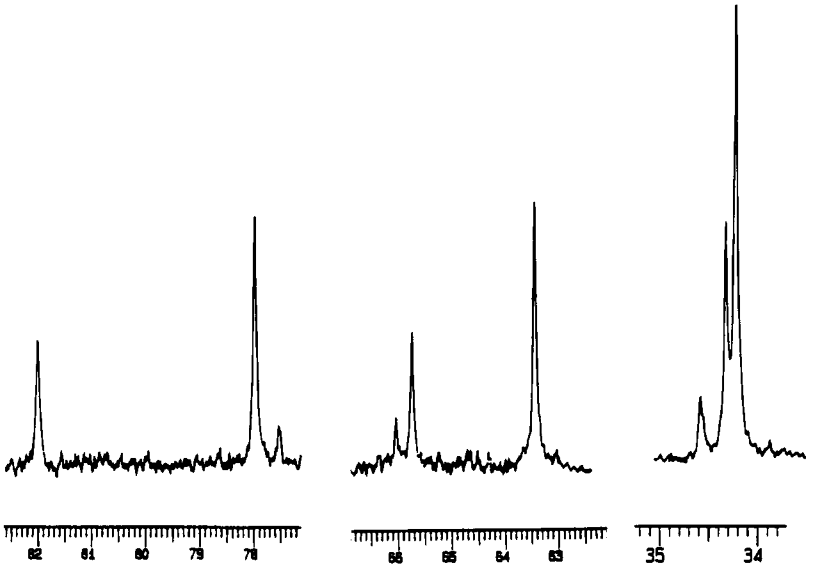

Figure 2. Sections of the carbon-13 NMR spectrum (100.5 MHz, CF_2Cl_2 solution) of **5** at −126 °C, showing 2:1 doublets for the (aee) conformation, 91%, and singlets for the (eee) conformation, 9%; (left to right) N−CH_2−N region, N−CH_2−C region, and C_{quat} region.

(aee) and (eee) conformations are the two most stable and that both have nearly eclipsed exocyclic N−CH_2 bonds whether axial or equatorial. Figure 1 shows that the MMX calculation of the (aee) conformation closely resembles the crystal structure.

The two programs disagree as to which of these two conformations is the more stable. The MM3 program suggests that the (eee) conformation is the most stable by 0.21 kcal/mol while the MMX program suggests that the (aee) conformation is more stable by 1.00 kcal/mol. Experimentally, NMR shows 9% (eee) and 30.33% of each of three degenerate (aee) conformations at −126 °C. $\Delta G°_{exp} = 0.35$ kcal/mol. The calculated conformational enthalpies' differences are thus about 0.6 kcal/mol on either side of the experimental free energy difference with MMX at least suggesting the correct relative stability. There is thus rather poor agreement, between programs and between calculated and experimental energy differences, that cannot plausibly be attributed to entropy differences between conformations.

The treatment of the lone-pair on nitrogen in calculations may be the origin of this disagreement. The MMX program[4] and MM2, a precursor[13] of MM3, treat the lone pair as a pseudoatom and so include in particular lone-pair−N−C−C and lone-pair−N−C−H torsional terms. MM3 has no such terms and so seeks to subsume any conformational preferences a lone-pair might be perceived to have, in the C−N−C−C and C−N−C−H torsional terms. Both populated conformations found for **5** confront lone pairs with eclipsing neopentyl groups, a state quite distant from any used to parametrize amine calculations. The discrepancy of the experimental and MM3-calculated conformational equilibria may reflect this problem, while shortcomings in the pseudoatom approach may explain the moderately poor MMX relative energy.

The calculations in any case provide satisfactory support for eclipsing and for the presence of the (eee) conformation which has not been observed previously in NMR studies of a range of trialkyltriazanes.[5−10] NMR studies of the dynamic processes in **3** and in a series of neopentylpiperidines and analogues with eclipsed N−C bonds will be reported fully elsewhere.

Experimental Section

Compound **3** is prepared as for similar compounds[5] by condensation of neopentylamine with formaldehyde: mp 76 °C, uncorrected. Found: C, 72.85; H, 13.31; N, 14.24. $C_{18}H_{39}N_3$ requires C, 72.72; H, 13.13; N, 14.14. Crystal data for **3**, $C_{18}H_{39}N_3$: orthorhombic $Pbn2_1$, $a = 10.002(2)$ Å, $b = 11.633(2)$ Å, $c = 18.066(2)$ Å, $V = 2102$ Å^3, $M_r = 297.26$, $Z = 4$, $d_{calc} = 0.94$ g/cm^3, $F(000) = 672$, λ(Mo Kα) = 0.710 73 Å, μ(Mo Kα) = 0.52 cm^{-1}. The structure was solved by direct methods and developed by using alternate cycles of least-squares refinement and difference-Fourier synthesis. All non-hydrogen atoms were refined anisotropically while hydrogens were placed in idealized positions (C−H 0.96 Å) and assigned a common isotropic thermal parameter ($U = 0.08$ Å^2); 2124 reflections (1899 unique) in the range $5° < 2\theta < 50°$. Three standard reflections (remeasured every 97 scans) showed a 10% loss of intensity during data collection. Data were corrected for Lorentz and polarization effects and for crystal decay. The 1257 unique data with $I > 1.5\sigma(I)$ were used, and the final least-squares refinement cycle included 189 parameters and did not shift any parameter by more than 0.35 times its standard deviation. $R = 0.0641$, $R_w = 0.0687$. Further details of the crystal structure investigation may be obtained from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, GB. Any request should be accompanied by the full literature citation for this communication.

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Supplementary Material Available: Details of the crystal structure determination of $C_{18}H_{39}N_3$ and tables of crystallographic data, atomic coordinates and equivalent isotropic displacement parameters, bond lengths and angles, anisotropic displacement parameters, and hydrogen atom coordinates and isotropic displacement parameters for $C_{18}H_{39}N_3$ (9 pages); observed and calculated structure factors (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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