Aza-bowls: synthesis and molecular structure of triaza-[3]-peristylane

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Abstract

A one-pot synthesis of the first aza-bowl, [3]-aza-[3]-peristylane system, from bullvalene is described. The molecular structure of this novel entity has been probed by X-ray crystallography and theoretical calculations. © 2000 Elsevier Science Ltd. All rights reserved.

We have been interested in the synthesis of a new class of molecular entities named 'hetero-bowls' which are derived through the replacement of methylene groups by hetero atoms in the well-known family of homologous polycyclic hydrocarbons known as peristylanes.[1] Besides having high C_{nv} symmetry, these hetero-bowls are endowed with two chemically distinct surfaces composed of a hydrophobic base and a hydrophilic rim, and are expected to exhibit many interesting properties like selective avidity for metal ions. As part of our endeavours in this area, we have recently reported the synthesis of several novel oxa-bowls, like tetraoxa-[4]-peristylane,[1b] pentaoxa-[5]-peristylane[1c] and seco-hexaoxa-[6]-peristylane[1d] and elucidated their molecular structure by X-ray crystallography[1b,e] and ab initio calculations.[2] These results have spurred us to extend our studies towards the synthesis of [*n*]-aza-[*n*]-peristylanes (*n*=3–6) **1**–**4** which appeared to be fascinating target structures. Herein, we report a synthesis of the first and smallest member of this aza-bowl family, the triaza-[3]-peristylane derivative **8a**, and elucidate its molecular structure by X-ray crystallography and theoretical calculations on **1**.

1   2   3   4

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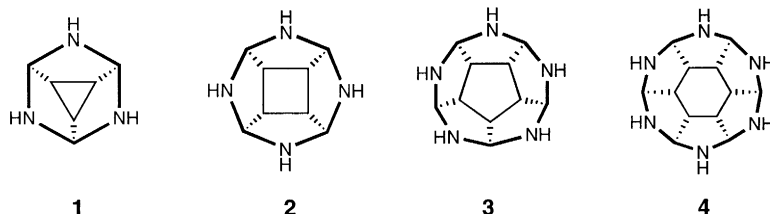
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Ozonolysis of bullvalene **5** (Scheme 1) furnished all *cis*-cyclopropane-tricarbaldehyde **6** which was immediately reacted with an excess of benzylamine to afford through threefold cascade cyclization, a stable tribenzyl derivative of triaza-[3]-peristylane **8a**, formed probably through the intermediacy of the triimine **7a**, in 70% yield. The structure of **8a** was secured on the basis of the molecular ion peak at *m/z* 393 in the mass spectrum and its simple ^{1}H NMR and seven line (only two lines from the non-benzyl portion) ^{13}C NMR spectrum.[3] Similarly, when **6** was reacted with 4-methoxybenzylamine, triaza-peristylane **8b** was obtained in 64% yield. However, attempts to prepare the parent **1** either through cyclization of **6** in the presence of ammonia or via *N*-debenzylation of **8a,b** were unsuccessful. Results with other amines like tryptamine, aniline, propyl- and butylamine were also disappointing and led to intractable products in poor yield.
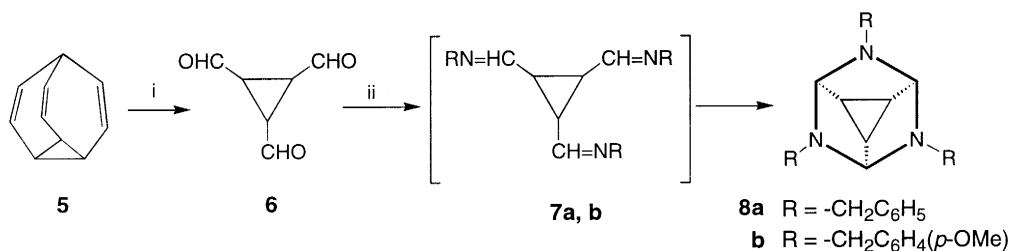
Scheme 1. Reagents: (i) O_3, DCM:MeOH (4:1), $NaHCO_3$; DMS, $-78°C$; (ii) $C_6H_5CH_2NH_2$, $CHCl_3$, rt

X-Ray analysis[4] of the needle shaped crystals of **8a** showed that the space group is P-1 with two independent molecules in the asymmetric unit. The ORTEP diagram of **8a** (Fig. 1) clearly shows the bowl-like shape of the molecule but it has C_s symmetry in the solid state (cf. C_{3v} in solution), due to different orientations of the three *N*-benzyl groups. The benzylic methylene carbons linked to two of the nitrogen atoms of the chair-shaped triaza-cyclohexane ring, which forms the rim of the bowl, are equatorial, while the third one is axial.
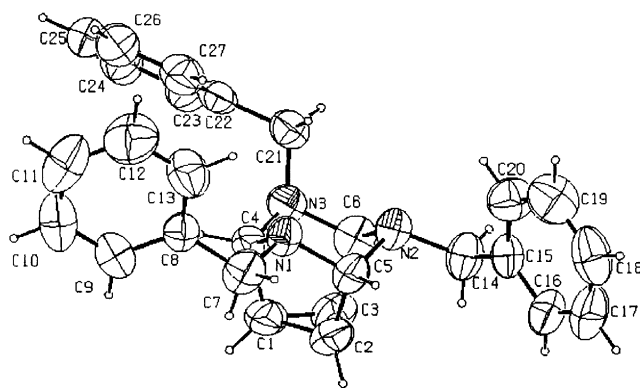

Fig. 1. ORTEP diagram of **8a**

We also carried out theoretical calculations on triaza-[3]-peristylane **1** at HF/6-31G*[6a] and B3LYP/6-31G*[6b] levels to obtain the relative energies and structural details. In relation to the peristylanes and their oxa-analogues, **1** has an additional dimension in terms of the axial versus equatorial positioning of the N–H bonds. Depending on the orientation of the N–H bonds, there are four isomers possible for triaza-[3]-peristylane, aae (**1a**, C_s), aaa (**1b**, C_{3v}), aee (**1c**, C_s) and eee (**1d**, C_{3v}), where the symbols a- and e- are used to denote the axial and the equatorial position of the N–H bonds, respectively (Fig. 2). The structures **1a–d** are shown to be minima on their potential energy surface.
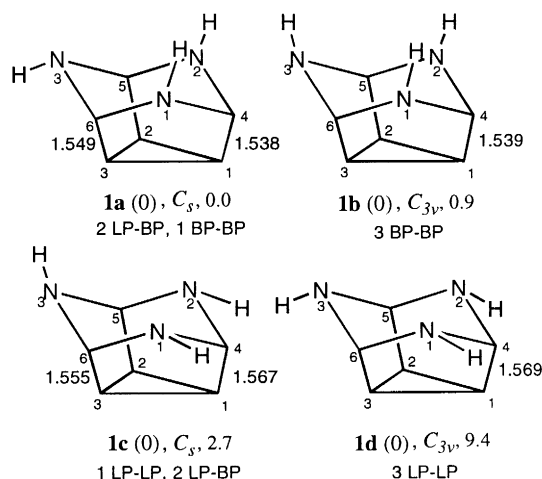
Fig. 2. Various isomers of **1**, their symmetry, relative energies (in kcal/mol) and the number of interactions

The relative energies and the geometrical parameters are recorded in Table 1. The most favorable structure among these is **1a** with two axial and one equatorial N–H bonds (aae). One of the factors that contribute to the relative energies is the decreasing magnitude of the lone pair–lone pair (LP–LP), lone pair–bond pair (LP–BP) and bond pair–bond pair (BP–BP) interactions (Fig. 3). The most unfavorable structure **1d**, has the maximum number (three) of LP–LP interactions. Structure **1c**, with just one LP–LP interaction, is the next higher energy structure from the top. The difference in energies between **1a** and **1b** is very small, these structures have no LP–LP interactions.

Table 1
Total energies (au), relative energies (kcal/mol) and important bond lengths (Å) of **1a–d**

Structure*	B3LYP/6-31G*				HF/6-31G*				Expt. Str.
	1a, C_s	1b, C_{3v}	1c, C_s	1d, C_{3v}	1a, C_s	1b, C_{3v}	1c, C_s	1d, C_{3v}	
Total Energy (au)	-398.23925	-398.23789	-398.23491	-398.22415	-395.73042	-395.72942	-395.72520	-395.71305	
Rel. Energy. (kcal/mol)	0.0	0.9	2.7	9.4	0.0	0.6	3.3	10.9	
$C_{base} - C_{base}$ (Å)	1.507,1.509	1.508	1.505,1.509	1.507	1.494,1.494 1.497	1.495	1.492,1.497	1.495	1.481,1.496 1.489
$C_{base}-C_{rim}$ (Å)	1.538,1.549	1.539	1.555,1.567	1.569	1.532,1.540 1.540	1.532	1.541, 1.555	1.556	1.533,1.530 1.525
$C_{rim}- N$ (Å)	1.471,1.483 1.490	1.482	1.471,1.481 1.487	1.478	1.455,1.465 1.471	1.464	1.456,1.463 1.468	1.460	1.456,1.476 1.480,1.484

*All the structures of Table I are minima on their potential energy surfaces.

There is practically no difference in the C_{base}–C_{base} bond length in these isomers, while the C_{base}–C_{rim} distances increase by around 0.024 Å for **1c** and **1d** compared to that of **1a** and **1b**. Negative hyperconjugative interaction, involving a lone pair (LP) of electrons and the σ* orbital of an adjacent bond, explains these variations. The extremes, **1b** and **1d**, where the C_{base}–C_{rim} distances are 1.539 Å and 1.569 Å, respectively, are a manifestation of this effect. The lengthening of this distance is due to the negative hyperconjugation, the interaction of the nitrogen LP with the σ* orbital as shown in Fig. 3. By symmetry,
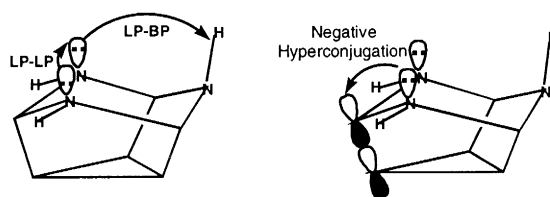
Fig. 3. Schematic diagram for the various interactions in **1**

for any such C–C bond in **1d**, there are two such lengthening interactions. On the other hand, structure **1b** has no such interaction so that the C_{base}–C_{rim} distance is short. The variations in the distances in the less symmetric structures, **1a** and **1c**, can also be explained in the same fashion. According to this, C2–C5 and C3–C6 (**1a**) should be longer than C1–C4 (1.549 Å versus 1.538 Å). Similarly, C1–C4 in **1c**, which has two negative hyperconjugation interactions, is longer than C2–C5 and C3–C6 (1.567 Å versus 1.555 Å).

While calculations show **1a** (aae) is the most favorable structure, **8a** was found to have **1c** (aee) conformation in solid state. The substituents and the various conformations of the benzyl groups do not permit direct energetic comparison. However, there is general agreement between the observed and the calculated geometric parameters, Table 1.

In conclusion, we have reported a simple synthesis of the triaza-[3]-peristylane system and examined its molecular structure computationally and by X-ray crystallography.

Acknowledgements

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3. Selected spectral data for **8a**: ^{1}H NMR (300 MHz): δ 7.33–7.19 (m, 15H), 4.17 (s, 3H), 3.63 (s, 6H), 2.84 (s, 3H); ^{13}C NMR (75 MHz, DEPT): δ 138.8 (C, 3C), 128.9 (CH, 6C), 128.1 (CH, 6C), 126.7 (CH, 3C), 82.7 (CH, 3C), 53.6 (CH$_2$, 3C), 38.1 (CH, 3C); *m/z* 393 (M$^+$); **8b**: ^{1}H NMR (300 MHz): δ 7.21 (d, 6H, *J*=8.4 Hz), 6.77 (d, 6H, *J*=8.7 Hz), 4.13 (s, 3H), 3.78 (s, 9H), 3.54 (s, 6H), 2.81 (s, 3H); ^{13}C NMR (75 MHz): δ 158.4 (C, 3C), 130.8 (C, 3C), 130.1 (CH, 6C), 113.5 (CH, 6C), 82.4 (CH, 3C), 55.2 (CH$_3$, 3C), 52.9 (CH$_2$, 3C), 38.0 (CH, 3C); *m/z* 483 (M$^+$).

4. Crystal data for **8a**: $C_{27}H_{27}N_3$, M=393.52, colorless crystals, triclinic, space group *P*-1, *a*=11.8938(18), *b*=13.498(2) and *c*=15.062(3) Å, α=82.829(17), β=81.630(16), γ=63.475(13)°, *V*=2135.7(6) Å^3, *Z*=4, D_c=1.224 Mg/m^3, *T*=293(2)K, *F*(000)=840, μ(Mo-K$_\alpha$)=0.072 mm^{-1}, crystal dimensions 0.40×0.48×0.24 mm^3. Data were collected on Enraf–Nonius MACH-3 diffractometer, graphite-monochromated Mo-K$_\alpha$ radiation (λ=0.71073 Å), by ω scan method in the range $1.69 \leq \theta \leq 24.98°$, 7486 unique reflections [R_{int}=0.00], of which 3647 had $F_o > 4\sigma(F_o)$, were used in all calculations. At final convergence $R_1[I > 2\sigma(I)]$=0.0557, wR_2=0.1746 for 541 parameters and 0 restraint, GOF=1.285, $\Delta\rho_{max}$=0.354 eÅ^{-3}, $\Delta\rho_{min}$=−0.371 eÅ^{-3}. The data were reduced using XTAL (ver. 3.4), solved by direct methods, refined by full-matrix least-squares on F^2 with the non-H atoms anisotropic and H atoms were placed in calculated positions and were allowed to ride on their parent atoms.[5]

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