New Highly Strained Adamantanophanes

R. Lemmerz,[a] M. Nieger[b] and F. Vögtle*[a]

[a] Institut für Organische Chemie und Biochemie der Universität Bonn, and [b] Anorganisch Chemisches Institut der Universität Bonn, Gerhard-Domagk-Str. 1, 53121 Bonn, Germany

Syntheses and X-ray crystal structures of the adamantanoparacyclophane 1 and the adamantanopyridinophane 2, as well as ^{1}H NMR absorption at extremely high field (δ −4.08), unusual conformational behaviour and dienophile addition to the benzene ring of 1 are reported.

Clamped aromatic compounds such as [n]- and [m.n]-cyclophanes have been of considerable interest both theoretically and practically in recent years.[1-3] In this context, we report the syntheses and structures of the new 'araliphanes'[4,5] [2.2](1,3)adamantanoparacyclophane 1 and [2.2](1,3)adamantano-2,6-pyridinophane 2. This new family of compounds consists of molecules in which one arene unit (e.g. phenylene or pyridinediyl) and one characteristic alicyclic building block (e.g. adamantanediyl) are clamped by ethano bridges. Compounds 1 and 2 prove to possess highly deformed skeletons
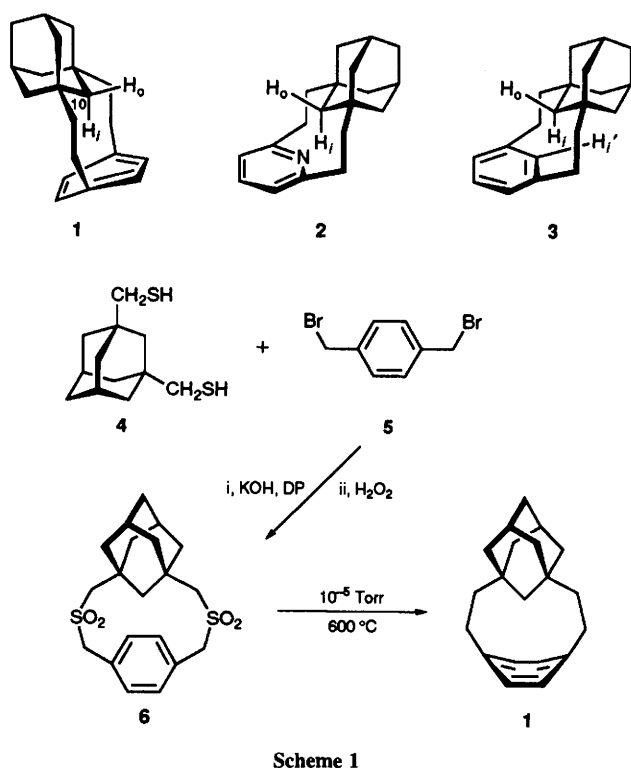
and exhibit extraordinary spectroscopic properties and chemical reactivity.

The bridgehead bond angles of adamantane, clamped in the 1- and 3-positions, are similar to those of the meta-phenylene unit.[4] Thus, the adamantanoparacyclophane 1 is an alicyclic analogue of [2.2]metaparacyclophane[6] with similar geometry. At the same time, 1 is structurally related to [7]paracyclophane[3] with additional clamps in the aliphatic bridge. A corresponding consideration establishes the adamantano-2,6-pyridinophane 2 to be in a link position between [2.2](2,6)

pyridinometacyclophane[7] and [7](2,6)pyridinophane.[8] The first example of an adamantanophane, [2.2](1,3)adamantano-metacyclophane 3, was published in 1990 and is the *meta*-connected counterpart of 1.[5]

The synthesis of the new araliphanes follows the dithia[3.3]cyclophane route with subsequent oxidation and sulfone pyrolysis.[9] The starting material for the preparation of 1 (9% yield from 4, m.p. 95 °C) and 2 (11% yield from 4, m.p. 89 °C) is 1,3-bis(mercaptomethyl)adamantane 4 which is treated with the dihalides 5 and 2,6-bis(chloromethyl)pyridine[10], respectively. (Scheme 1).

The X-ray structure† of 1 reveals that its benzene ring is boat shaped (Fig. 1). The *para*-carbon atoms, connected to the CH_2 groups, are lifted out of the plane of the other four carbon atoms by as much as 19.0° while the benzylic CH_2 carbons

Scheme 1

atoms are turned out of the same plane by 32.4° (average values). These distortions even exceed the angle deviations reported for [2.2]metaparacyclophane[6] and 3-carboxy[7]-paracyclophane.[11] Clamped arenes with a seven-membered bridge are usually regarded as reference compounds for high angle strain.[3]

The strain energies of these related molecules have been estimated by calculating heats of formation by semiempirical methods‡ and referring them to Benson's standard group increments.[12] The araliphane 1 exhibits the highest ring strain of these molecules according to this. It follows that stiffening of a unit, the bridging para-phenylene, and as a result concentrating the deformation on this, increases strain energy.

A conformational flipping gives rise to the temperature dependence of the 400 MHz ^1H NMR spectrum of 1. The energy barrier for this ring inversion process amounts to 40 kJ mol^{-1} (T_c −50 °C, CD_2Cl_2) and is much lower than the corresponding barrier for [2.2]metaparacyclophane (86 kJ mol^{-1}, T_c 140 °C).[3] At room temperature the inner and outer proton at position 10 (H_i and H_o) form a sharp singlet at unusually high field (δ −2.35).

At −65 °C two separated signals for the protons at C-10 appear. The axial H_i, apparently deeply intruded into the π-cloud, absorbs at even higher field (δ −4.08), the equatorial H_o being less shielded (δ −1.01). This is an upfield shift of 5.9 ppm for the axial H_i, compared to the corresponding hydrogen in unsubstituted adamantane at δ 1.78, and represents the
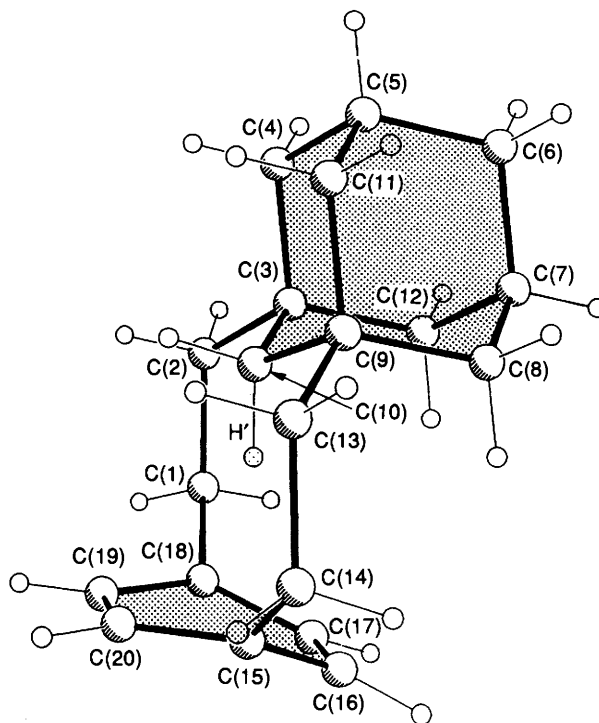
Fig. 1 X-Ray crystal structure of 1 with numbering scheme
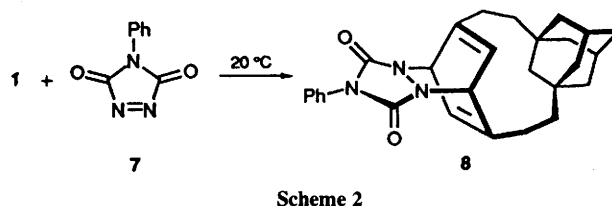
Scheme 2
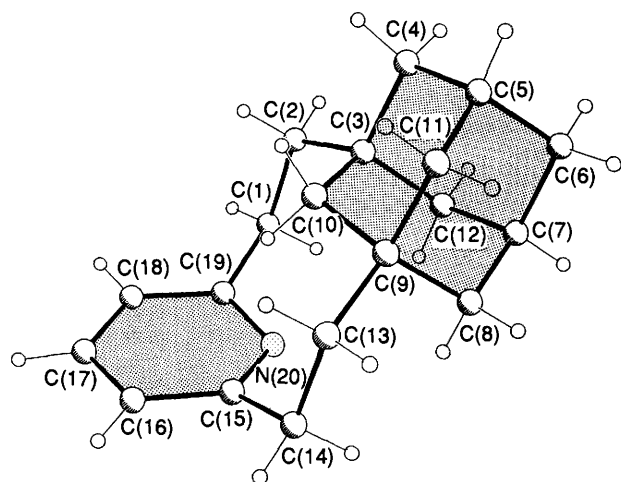
Fig. 2 A perspective view of the crystal structure of 2

Table 1 Calculated heats of formation (ΔH_f°/kJ mol^{-1}) and strain energies (E_s/kJ mol^{-1})

Strained molecule	$\Delta_f H^\circ$	E_s
[2.2](1,3)Adamantanoparacyclophane 1	90.3	145
[2.2]Metaparacyclophane	230.5	106
[7]Paracyclophane	49.5	90

for [2.2](2,6)pyridinometacyclophane ($\Delta_c G^\ddagger > 113$ kJ mol^{-1}; no coalescence at 200 °C).[7]

The results demonstrate that replacing *meta*-phenylene units in strained cyclophanes by adamantane leads to araliphanes with interesting properties on account of an increased distortion of aromatic rings like benzene and pyridine (and even adamantane).

largest negative δ value due to the proximity of a hydrogen atom to the centre of a benzene ring known to us. The crystal structure of 1 reveals a distance of only 184 pm from the axial H_i to the centre of the benzene ring.

The adamantanophane 1 reacts readily with *N*-phenyl-1,2,4-triazoline-3,5-dione (TAD) 7 to yield the Diels–Alder adduct 8 (Scheme 2) whose X-ray structure has also been determined.[13]

According to the X-ray analysis,† 2 also has a boat-shaped aromatic ring (Fig. 2). The 'out-of-plane' deformation of the pyridine nitrogen atom is 11.6°; the opposite carbon atom (C-17) of the pyridine ring is bent out of the central plane by 4.5°.

The adamantane skeleton is significantly distorted in the pyridinophane molecule 2. Bond angles C-10–C-3–C-4 and C-11–C-9–C-10 are remarkably compressed to 99.9 and 100.1°, and the angles C-2–C-3–C-4 and C-13–C-9–C-11 are stretched to 118.1 and 118.7°. These angle deformations are a result of the close proximity of the pyridine nitrogen to C-10 of the adamantane unit. The C–N distance is only 268 pm, causing a flattening of the 'cyclohexane ring' formed by C-10–C-3–C-12–C-7–C-8 and C-9. Distortions of the adamantane skeleton of comparable magnitude were observed in the case of 3 (100.4 and 117.7° are average values).[5]

The 250 MHz ^{1}H NMR spectrum of 2 shows a coalescence of the signals for the intraannular adamantane protons H_i and H_o at C-10 at 45 °C (δ −0.25 and 0.35 at room temperature, CDCl$_3$). The resulting energy barrier (62 kJ mol^{-1}) for this ring inversion is much smaller than the corresponding value

References

1 C. W. Bird, *Tetrahedron*, 1992, **48**, 335.
2 S. Grimme, *J. Am. Chem. Soc.*, 1992, **114**, 10542.
3 F. Vögtle, *Cyclophane Chemistry*, Wiley, Chichester, 1993; *Cyclophan-Chemie*, Teubner, Stuttgart, 1990.
4 J. Dohm, M. Nieger, K. Rissanen and F. Vögtle, *Chem. Ber.*, 1991, **124**, 915.
5 F. Vögtle, J. Dohm and K. Rissanen, *Angew. Chem.*, 1990, **102**, 943; *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 902.
6 A. Renault, C. Cohen-Addad, J. Lajzerowic-Bonneteau, J. P. Dutasta and M. J. Crisp, *Acta Crystallogr., Sect. B*, 1987, **43**, 480.
7 J. R. Fletcher and I. O. Sutherland, *Chem. Commun.*, 1969, 1504.
8 S. Fujima and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 2827.
9 J. Dohm and F. Vögtle, *Top. Curr. Chem.*, 1992, **161**, 69.
10 N. Furukawa, S. Ogawa and T. Kawai, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1833.
11 N. L. Allinger, T. J. Walter and M. G. Newton, *J. Am. Chem. Soc.*, 1974, **96**, 4588.
12 S. W. Benson, *Thermochemical Kinetics*, Wiley, New York, 1976; cf. Y. Tobe, A. Takemura, M. Jimbo, T. Takahashi, K. Kibiro and K. Kakiuchi, *J. Am. Chem. Soc.*, 1992, **114**, 3479.
13 M. Nieger, R. Lemmerz and F. Vögtle, unpublished work.
14 J. J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 209, 211; *J. Comput. Aided Mol. Design*, 1990, **4**, 1.
15 N. Walker and D. Stuart, *Acta Crystallogr., Sect. A.*, 1983, **39**, 158.