A tetraspiro nonacyclic compound by condensation of 1,1-bis(aminomethyl)cyclohexane with formaldehyde

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1,1-Bis(aminomethyl)cyclohexane condenses with formaldehyde to precipitate a polymer, which upon heating is readily isomerized to the nonacyclic compound tetraspiro[tetrakis(cyclohexane)-1,5′′′′:1′,11′′′′:1′′, 17′′′′:1′′′,23′′′′-[1,3,7,9,13,15,19,21]octaazapentacyclo[19.3.1.1³,⁷.1⁹,¹³. 1¹⁵,¹⁹]octacosane 1, whose structure has been determined by X-ray analysis and ¹³C NMR spectroscopy.

The term 'strict covalent self assembly' has been defined as 'completely reversible reactions leading to products that are stable at thermodynamic equilibrium'.[1] Condensation of amines with formaldehyde to give multicyclic structures satisfies this criterion if all rings of the structure can obtain a geometry derivable from the diamond lattice. The earliest example is the formation from propane-1,3-diamine and formaldehyde of a pentacyclic octaaza compound, whose central ring is 16-membered.[2] In this laboratory it was shown that it can have two conformations, both of the diamond lattice type.[3] Subsequently, the corresponding product from 2,2-dimethylpropane-1,3-diamine and formaldehyde was also prepared and shown to exist only in the more symmetric (D_{2d}) of the two conformations.[4]

If each *gem*-dimethyl group is replaced by a spiro-linked pentamethylene chain, the resulting compound **1** would have four terminal cyclohexane rings (**C**) with high conformational mobility, while the central 16-ring (**A**) with its four laterally fused 6-rings (**B**) would remain rigid. A very special NMR spectroscopic situation can be predicted from the symmetry properties of the expected diamond lattice conformation of **1** as drawn in Fig. 1. The central part (**A** + 4**B**) has two 'vertical' planes of symmetry passing through atoms *b* and *d*, and two 'horizontal' two-fold axes passing through atoms *a*. At room temperature the terminal rings **C** will flip rapidly between the two chair forms to produce by averaging the NMR spectrum of the apparent 'planar' rings, and the molecular D_{2d} symmetry is not destroyed. When the flipping becomes slow at low temperature, the ¹³C signal from carbons *c* will split into two, having very different shifts due to the upfield *gauche* interaction when carbons *f* are on the same side of the symmetry plane. The ¹³C signals of atoms *f* themselves will however remain

unchanged since they will get the same interaction with carbons *c* on either side. Interestingly then, what is going on in ring **C** is not observed in its own spectrum but by 'remote sensing' in the spectrum of ring **B**.

A modest signal splitting should be expected also for the more distant 'corner' atoms *a* on the two-fold axes, each interacting weakly with two **C** rings. Assuming that the choice of frozen conformation is independent in each *C* ring, three situations are possible for each *a* carbon: the two neighbouring **C** chairs can either both be in the closest position, or one in the closest and one in the distant position (and *vice versa*), or both can be in their distant position. Statistically, this results in the splitting of the ¹³C NMR signal of carbon *a* into a triplet with 1:2:1 intensity.

An analysis in terms of possible species (conformers) can be carried out by looking down on a square projection of ring **A**. Each chair can be oriented clockwise (+) or counterclockwise (−), and if chirality is disregarded, four conformers are possible (Fig. 2). Of these, the conformer ++− −, drawn in full in Fig. 1, was chosen for clarity. The conformer found in the crystal structure is +++− (*vide infra*). The conclusion above that a 1:2:1 triplet should be expected statistically for carbon *a* in ring **A** is based on the assumption of equal populations of all four conformers.

Compound **1** was prepared as follows: malonodinitrile and 1,5-dibromopentane gave 1,1-dicyanocyclohexane (mp 63 °C, 65%), which by catalytic hydrogenation (W₂-Raney nickel, NH₃ saturated EtOH, 80 atm., 70 °C) yielded 1,1-bis(amino-
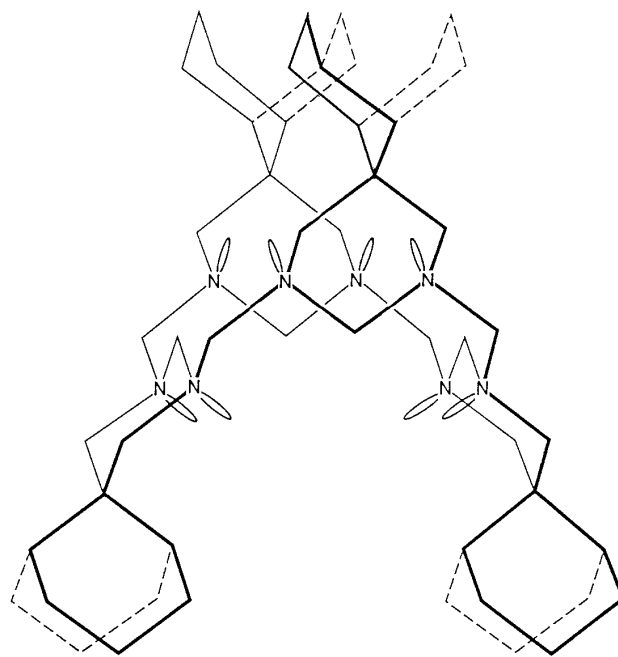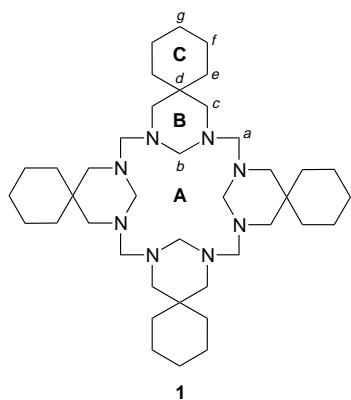

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Fig. 1 The postulated conformation of compound **1**. Both possible chair positions for each **C** ring are shown.
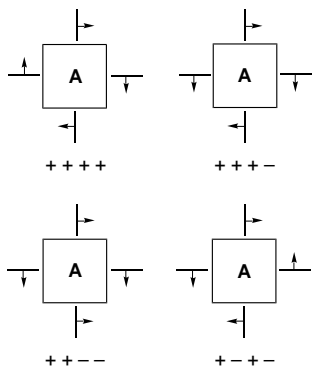
Fig. 2 The four possible arrangements of rings **C**. The sign (+) represents a clockwise oriented **C** ring and (−) represents a counterclockwise oriented **C** ring.
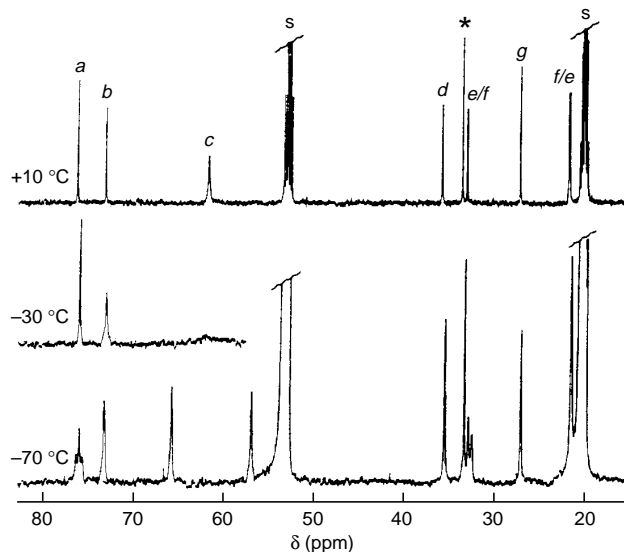

Fig. 3 125 MHz ^{13}C NMR spectra of **1** in [^{2}H$_8$]toluene–CD$_2$Cl$_2$ (1:1) at 10, −30 and −70 °C
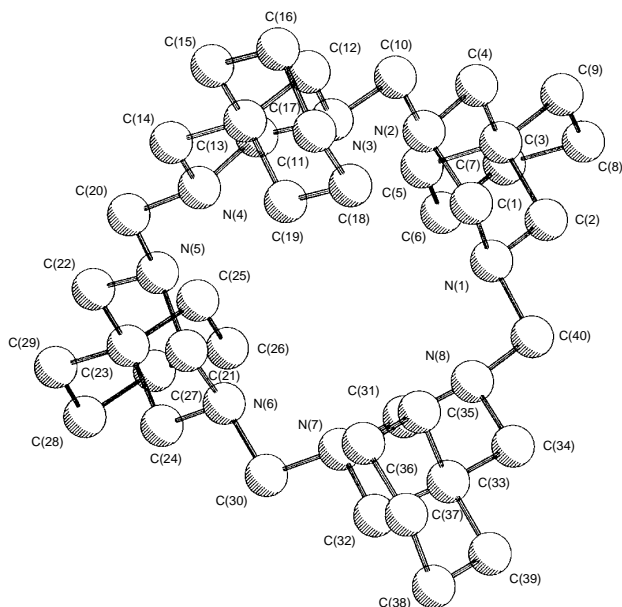

Fig. 4 PLUTO plot of **1**

higher barriers, and while at 110 °C clear exchange broadening had started, T_c could not be reached.

The X-ray analysis† of the crystal (Fig. 4) revealed that the unit cell contains four molecules all having the same +++− conformation, possibly chosen to obtain the efficient packing needed to explain the observed unusual hardness of the crystals. The molecules are arranged as two enantiomeric pairs; only one molecule of the pair is shown, the other having disorder in one of the **C** rings due to a 20% population of the +−+− conformer.

Footnote

References

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methyl)cyclohexane as a viscous liquid (80%). Aqueous formaldehyde was dropped into a cooled aqueous solution (*ca.* 0 °C) of this diamine (ratio 2:1), causing immediate precipitation of a polymer. The polymer was heated for a few minutes in refluxing dioxane to give compound **1** (mp 215 °C, 100%). It is soluble in most organic solvents and crystallizes from dioxane, CH$_2$Cl$_2$ or toluene, giving extremely hard crystals; MS (EI, 70 eV) *m/z* 664 (M$^+$), 499 (3/4 M + 1), 333 (1/2 M + 1), 167 (1/4 M + 1), 137, 124, 95, 67, 42; ^{13}C NMR (125 MHz in CD$_2$Cl$_2$, 300 K): δ 76.7 (C$_a$), 73.5 (C$_b$), 62.1 (C$_c$), 36.2 (C$_d$), 33.6 (C$_{e/f}$), 27.6 (C$_g$), 22.2 (C$_{f/e}$).

The ^{13}C NMR signals at δ 33.6 and 22.2 (Fig. 3) represent two inner and two outer *e* and *f* carbons, but the splitting is barely visible. After lowering the temperature, the predicted broadening and splitting of the carbon *c* signal at δ 62.1 into a widely separated doublet takes place, while the carbon *a* signal at δ 76.7 splits into a narrow triplet.

The flipping process (or geminal CH$_2$ exchange) of ring **C** could in principle be determined directly by ^{1}H NMR spectroscopy, but this is prevented in practice by complex coupling. Full geminal site exchange of the remaining CH$_2$ groups in ring **A** and **B** would require the passage of much