A Conformational Analysis of the Spirocyclic Quaternary Ammonium Cation $[(CH_2)_4N(CH_2)_4]^+$ in its Bromide and Picrate Salts

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High-yield syntheses of the bromide (**1a**) and picrate salts (**1b**) of the 5-azonia-spiro[4]nonane cation $[(CH_2)_4N(CH_2)_4]^+$ are reported. In the single crystal X-ray diffraction analyses of the two salts the spirocyclic quaternary ammonium cations have their five-membered rings in envelop and twist conformations modified by packing forces. The conformation found experimentally for **1a** has C_2-symmetry as predicted for the gas phase by quantum-chemical calculations (RI-DFT, RI-MP2), but the five-membered rings are intermediate between the expected envelop and the twist form. For **1b**, both of the two independent cations can be described as a combination of rings in an envelop and a twist conformation. According to the NMR spectra, in solution the cations are highly flexible and pseudosymmetrical (point group D_{2d}).

Key words: Conformational Analysis, Spirocyclic Ammonium Salts, 5-Azoniaspirononane Cation, Heterospirononanes

Introduction

Cyclopentane $(CH_2)_5$ and the related heterocycles $(CH_2)_4EH_2$ (E = C, Si, Ge, B^-, N^+, P^+ *etc.*, **A**, **B**) show a delicate equilibrium of conformations, which can be assigned to either envelop or twist geometries [1]. In spiro[4,4]nonane and its analogues with the heteroatom in the spiro-position (**C**, **D**), *i.e.* where two of these units share a common carbon or other Group III-V heteroatom, respectively, the same conformational alternatives are valid for both rings which leads to an even larger conformational variety [2].

A　　**B**　　**C**　　**D**
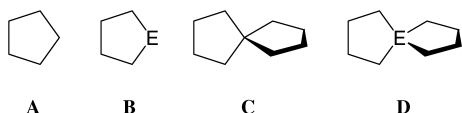
In the context of preparative studies in organophosphorus chemistry we have recently investigated the structures of several spirocyclic quaternary phosphonium salts based on the 5-phosphonia-spiro[4,4]-nonane cation (**D**, E = P^+) [3]. This study has now been extended to the corresponding spirocyclic *ammonium* salts (**D**, E = N^+), the structure of which had not previously been investigated.

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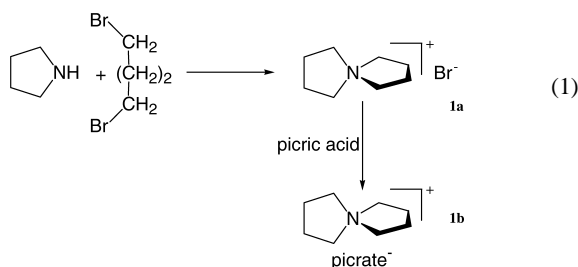
Results and Discussion

Quaternary ammonium salts with the cation $[(CH_2)_4N(CH_2)_4]^+$ were first prepared by v. Braun (in 1916, [4]) and later by Blicke *et al.* (in 1954, [5]) and others [6]. These authors have demonstrated that pyrrolidine can be quaternized with 1,4-dibromo-butane in alkaline aqueous solution to give the bromide salt **1a**. This preparation has now been slightly modified to give acceptable yields (86%) [eq. (1)].

The product is soluble in water and in most polar organic solvents and highly hygroscopic, but insoluble in solvents of low polarity. Even short exposure to humid air leads to the formation of a viscous yellow oil. From solutions of **1a** in dry methanol the picrate **1b** can be precipitated on addition of picric acid. This salt is not hygroscopic and insoluble in water, alcohols
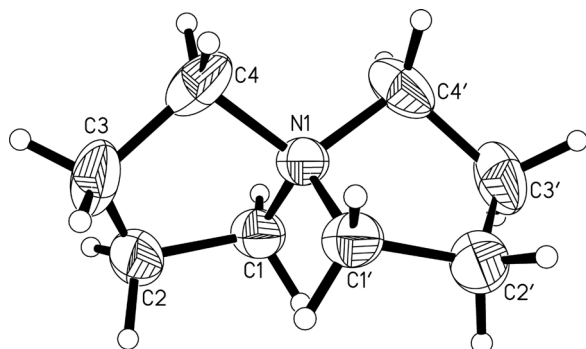
Fig. 1. Structure of the spirocyclic ammonium cation in crystals of the bromide salt **1a** (ORTEP, 50% probability ellipsoids; hydrogen atoms with arbitrary radii) with atomic numbering. Selected bond lengths [Å] and angles [°]: N1-C1 1.474(7), N1-C4 1.512(6), C1-C2 1.523(8), C2-C3 1.447(12), C3-C4 1.559(10); C1-N1-C1' 109.2(6), C4-N1-C4' 110.7(6), C1-N1-C4 105.5(4), C1-N1-C4' 113.1(3); N1-C1-C2 102.0(6), C1-C2-C3 110.5(9), C2-C3-C4 104.2(5), N1-C4-C3 100.8(5).

and non-polar organic solvents, but soluble in chloroform, dichloromethane and acetonitrile. It appears that the spirocyclic cations are sufficiently flexible to establish an efficiently space-filling structure with less compact anions such as picrate. The bromide salt **1a** has recently been used as a reagent for the precipitation of other organic anions [7]. It appears therefore that it shows advantages in crystallization and crystal growth over more rigid cations like $[Ph_4P]^+$.

The salts **1a** and **1b** have been characterized by elemental analysis, mass spectrometry and NMR spectroscopy. The ^{1}H and ^{13}C resonances for the cation are virtually identical in both cases indicating electrolytic dissociation in the solvents employed (CDCl$_3$, CD$_2$Cl$_2$ or D$_3$CCN). The cations show equivalent CH$_2$ groups for the α- and β-positions suggesting a high flexibility of the five-membered rings in solution leading to an (average) D_{2d} symmetry. The resonances of the picrate anion of **1b** show no anomalies (Experimental Section).

Crystals of the bromide **1a** as obtained from acetonitrile solution upon addition of diethyl ether at 20 °C are trigonal, space group $P321$ with $Z = 3$ formula units in the unit cell. The cation has C_2 symmetry with the twofold axis passing through the nitrogen atom and bisecting the angles C1-N1-C1' and C4-N1-C4' (Fig. 1). The conformation of each of the two equivalent five-membered rings is intermediate between the envelop and twist reference models, but closer to the latter. The projection chosen for Fig. 2 reveals that the twist axis
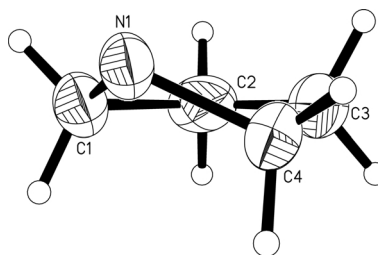

Fig. 2. Projection of the asymmetric unit of the spirocyclic ammonium cation in crystals of the bromide salt **1a** along the twist axis (ORTEP, 50% probability ellipsoids, hydrogen atoms with arbitrary radii) with atomic numbering.

passes through C2 and through the center of the N1-C4 bond, while the envelop is generated by a folding along the C1–C4 line (Fig. 1).

Crystals of the picrate **1b** as obtained from chloroform solution upon addition of diethyl ether at 20 °C are monoclinic, space group $P2_1$, with $Z = 4$ formula units in the unit cell. The asymmetric unit contains two formula units, the cations of which have very similar geometries (Fig. 3).

Each of the two cations features a combination of five-membered rings in the envelop and twist conformation. The geometry of the rings N1-C15-C16-C17-C18 and N2-C21-C22-C23-C24 approaches the standard envelop conformation with the nitrogen atoms folded away from the plane of the carbon atoms, while the other two rings approach the standard twist conformation (with C12-C13-C14 and C26-C27-C28 as the reference planes). Details are given in the captions to Fig. 3.

The picrate anions are stacked in the crystals with a plane-to-plane distance of *ca.* 3.4 Å (Fig. 4). The nitro groups in *ortho* position relative to the phenolate oxygen atom are twisted disrotatorily out of the ring plane, while the nitro group in the *para* position is virtually coplanar with the reference plane. This conformation confirms previous findings [8].

With regard to the structure of the analogous phosphonium cations [3], the geometry of the title ammonium cations differs by small endocyclic C-N-C angles in the range 102.38(8) – 105.5(4)°, as compared to the range of 95.7(6) – 97.9(5)° for the C-P-C angles. The complementary exocyclic angles are therefore larger for the phosphonium cations [C-P-C: 112.0(7) – 119.58(6)°] than for the ammonium cations [C-N-C: 109.2(6) – 113.6(2)°]. All N-C bonds [1.474(7) – 1.514(3) Å] are shorter than the P-C bonds [1.773(8) – 1.8145(12) Å] as required by the differ-
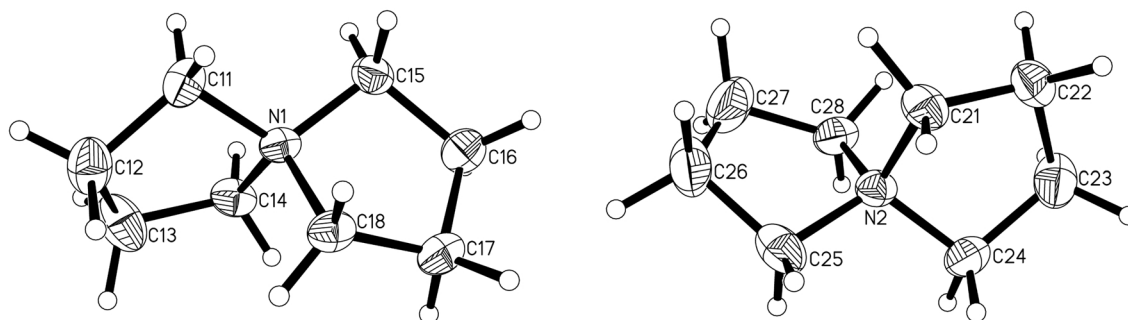
Fig. 3. The two independent spirocyclic ammonium cations in crystals of the picrate salt **1b** (ORTEP, 50% probability ellipsoids, hydrogen atoms with arbitrary radii) with atomic numbering. Selected bond lengths [Å] and angles [°] of the cations: N1-C11 1.499(3), N1-C14 1.517(3), N1-C15 1.509(3), N1-C18 1.509(3); N2-C21 1.509(3), N2-C24 1.508(3), N2-C25 1.497(3), N1-C28 1.514(3); C11-C12 1.518(4), C12-C13 1.542(4), C13-C14 1.531(4); C15-C16 1.517(4), C16-C17 1.548(4), C17-C18 1.519(4); C21-C22 1.519(4), C22-C23 1.544(4), C23-C24 1.529(4); C25-C26 1.530(5), C26-C27 1.535(6), C27-C28 1.511(4). C11-N1-C15 113.38(18), C11-N1-C14 103.3(2), C11-N1-C18 113.3(2), C14-N1-C15 113.3(2), C14-N1-C18 110.7(2), C15-N1-C18 103.1(2); C21-N2-C24 102.4(2), C21-N2-C25 113.6(2), C21-N2-C28 111.5(2), C24-N2-C25 113.5(2), C24-N2-C28 112.6(2), C25-N2-C28 103.5(2).
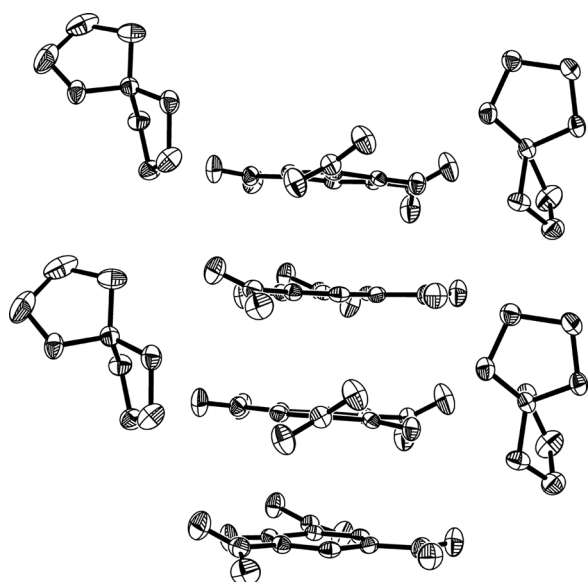

Fig. 4. Stacking of the picrate anions (central column) in crystals of the picrate salt **1b** (ORTEP, 50% probability ellipsoids, hydrogen atoms omitted).

ence in the colvalent radii of nitrogen and phosphorus [*ca.* 0.30 Å]. All C-C bonds and all C-C-C angles in **1a** and **1b** are similar to the gas phase data of cyclopentane [1d] and X-ray data of its substituted derivatives [2b, 9].

The experimental structural data for the title cations are in good agreement with the results of quantum-chemical calculations (RI-DFT and RI-MP2). The theoretical data call for endocyclic C-N-C angles in the range between 102.4 and 105.1° and exocyclic C-N-C angles in the range between 111.0 and 118.6° depending on the conformational model (envelop / twist) and the computational method (DFT / MP). In the gas phase, the spirocyclic ammonium cation has an energy-minimum geometry of C_2 symmetry with both rings in an envelop conformation. A second conformation of D_2 symmetry is *ca.* 13 kJmol^{-1} higher in energy (Fig. 5). It therefore appears that the conformations of lower symmetry observed in the crystals are strongly influenced by packing forces. Details of the computational results have been documented elsewhere together with data for the spirocyclic compounds of type **D** with E = C, Si, P$^+$, or B$^-$ [10].

Experimental Section

Preparations

5-Azonia-spiro[4.4]nonane bromide, (**1a**)

A mixture of pyrrolidine (71.0 g, 1 mol), 1,4-dibromobutane (135.9 g, 1 mol) and a solution of potassium hydroxide (56.0 g, 1 mol) in water (760 ml) is heated under reflux for 2 h. Subsequently, most of the water and remaining other volatiles are removed by vacuum distillation. The residue is filtered and KOH is added to the filtrate until two liquid phases are formed which are separated. The lower phase is taken up with chloroform and dried over anhydrous magnesium sulfate. The mixture is filtered and the product (**1a**) precipitated from the filtrate by addition of diethyl ether. The colourless, hygroscopic solid is filtered off, washed with diethyl ether and dried in a vacuum. (Single crystals can be grown from acetonitrile / diethyl ether [2:1,
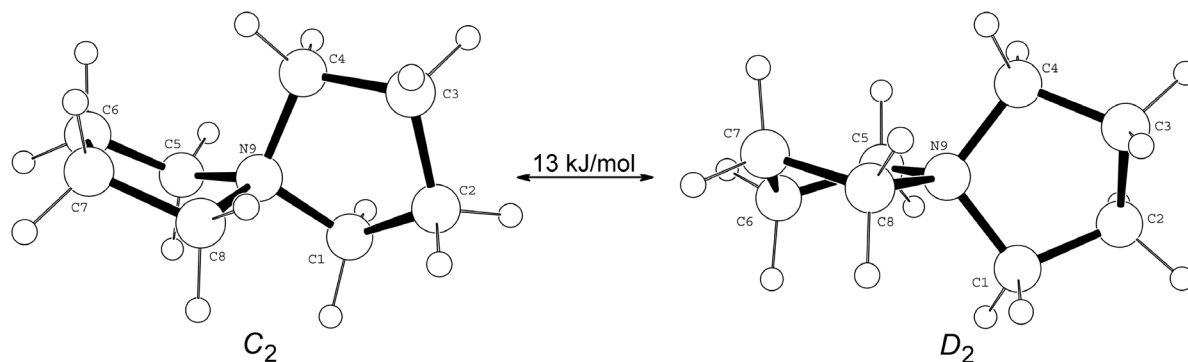
Fig. 5. Calculated energy minimum geometries of the spirocyclic ammonium cation $[(CH_2)_4N(CH_2)_4]^+$ (RI-MP2/SV(P)). The conformation with C_2 symmetry is lower in energy by 13 kJmol^{-1} than the D_2 conformation. (The atomic numbering is different from that used in the crystal structure determination.)

v/v]). 177.3 g (86% yield), m.p. 273 °C. NMR (CDCl$_3$, 20 °C), ^{1}H: 2.22 (m, CH$_2$, 8H) and 3.79 (m, CH$_2$N, 8H), AA'BB'. ^{13}C{^{1}H}: 22.11 (s, CH$_2$), 62.92 (s, CH$_2$N). MS (FAB): *m/z* 126.1 (100%) [N(CH$_2$)$_8$]$^+$. Elemental analysis for C$_8$H$_{16}$NBr (206.13): calcd. C 46.62, H 7.82, N 6.80, Br 38.76; found C 47.04, H 7.92, N 6.96, Br 37.87.

*5-Azonia-spiro[4.4]nonane picrate, (*1b*)*

A solution of picric acid (2.5 g, 11 mmol) in 10 ml of ethanol is added to a solution of compound **1a** (1.0 g, 5.0 mmol) in ethanol (10 ml). Immediately a yellow solid precipitates which is filtered off, washed with ethanol and redissolved in chloroform. Careful layering of this solution with diethyl ether induces the formation of single crystals of the product **1b**, which are not hygroscopic. 1.63 g (92% yield), m.p. 230 °C with decomposition. ^{1}H NMR (CD$_2$Cl$_2$, 20°C): 2.26 (m, CH$_2$, 8H), 3.79 (m, CH$_2$N, 8H,), AA'BB'; 8.76 (s, CH, 2H). ^{13}C{^{1}H} NMR (acetone-d$_6$, 20 °C): 22.87 (s, CH$_2$), 63.68 (s, CH$_2$N), 125.85 (s, C3), 143.48 (s, C2), 162.21 (s, C1), C4 not detected. MS (FAB): *m/z* 126.1 (100%) [N(CH$_2$)$_8$]$^+$. Elemental analysis for C$_{14}$H$_{18}$N$_4$O$_7$ (354.32): calcd. C 47.46, H 5.08, N 15.82; found C 46.80, H 5.21, N 15.27%.

Crystal structure determinations

Specimens of suitable quality and size of compounds **1a** and **1b** were mounted on the ends of quartz fibers in inert perfluoropolyalkylether and used for intensity data collection on a DIP2020 diffractometer, employing graphite-monochromated Mo-K$_\alpha$ radiation. The structures were solved by a combination of direct methods (SHELXS-97) and difference-Fourier syntheses and refined by full matrix least-squares calculations on F^2 (SHELXL-97) [11]. The thermal motion was treated anisotropically for all non-hydrogen atoms. The hydrogen atoms of **1a** were calculated in ideal positions and allowed to ride on their parent atoms with fixed isotropic contributions. Further information

Table 1. Crystal data, data collection, and structure refinement of the compounds **1a** and **1b**.

	1a	1b
Empirical formula	C$_8$H$_{16}$NBr	C$_{14}$H$_{18}$N$_4$O$_7$
M	618.38	354.32
Crystal system	trigonal	monoclinic
Space group	$P321$	$P2_1$
a/Å	11.7729(1)	7.0170(1)
b/Å	a	11.1590(2)
c/Å	5.8447(1)	20.4295(5)
β/°	90	97.2986(8)
V/Å^3	701.55(1)	1586.72(5)
ρ_{calc}/g cm^{-3}	1.464	1.483
Z	3	4
F(000)	318	744
μ(Mo-K$_\alpha$) (cm^{-1})	43.28	1.21
T/K	143	143
Refls. measured	19858	40658
Refls. unique	1010	6270
	[$R_{int} = 0.041$]	[$R_{int} = 0.049$]
Refined parameters /restraints	48 / 0	596 / 1
$R1[I \geq 2\sigma(I)]$	0.0395	0.0431
$wR2^a$	0.0975	0.1031
Weighting scheme	$A = 0.0303$	$a = 0.0403$
	$B = 2.0240$	$b = 0.5017$
σ_{fin}(max/min)/eÅ^{-3}	0.939 / −0.604	0.428 / −0.207

on crystal data, data collection and structure refinement are summarized in Table 1. Absorption correction was carried out for **1a** using DELABS as part of the PLATON suite of programs [12], for **1b** no absorption correction was applied. Displacement parameters and tables of interatomic distances and angles have been deposited with the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. The data are available on request quoting CCDC-229982 and 229981.

Quantum-chemical calculations

All calculations were carried out with the TURBOMOLE package of programs (version 5.3, 5.4 and 5.6) on the

RI-MP2 and RI-DFT level of theory [13]. RI-MP2 designates a second order Møller-Plesset calculation using the Resolution-of-the-Identity method [14], RI-DFT the density functional method with the Resolution-of-the-Identity approach of the Coulomb interactions [15]. For numerical integrations the "standard lattice" m3 was employed as implemented in TURBOMOLE. Basis sets were of the SV(P) (double zeta quality, split level, with a polarization function P for non-hydrogen atoms), TZVP (triple zeta basis set with a polarization function for all atoms) and TZVPP type (cc-pVTZ) [16].

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