1,2,6-Trimethyl-3,5-nonamethylenepyridinium perchlorate. Crystal structure and molecular mechanics calculations for *ansa*-[9]-*meta*-cyclophanes

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Abstract

The nonamethylene bridge of the title compound shows high conformational mobility and an asymmetric structure in the crystal. Molecular mechanics (MM+) calculations reproduced well the crystal structure, which has the lowest energy conformation.

Keywords: 1,2,6-Trimethyl-3,5-nonamethylenepyridinium, crystal structure, ansa-[9]-meta-cyclophanes

Introduction

The crystal molecular structure of medium and large cyclophanic rings is an interesting subject which complements the information gained on the structure in solution by dynamic NMR methods. The low temperature NMR study of heterocyclic [9]cyclophanes has revealed a rapid ring flipping with an energy barrier $\Delta G\ddagger$ between 8.9 and 9.8 kcal/mol.[1] In order to gain insight on the crystal structure of the nonamethylene bridge we analysed the structure of the title compound (**3**) by X-ray crystallography. Furthermore, we performed molecular mechanics calculations using the MM+ force field, which is adequately parameterised for cycloalkanes within the HyperChem® package,[2] in order to obtain more information on such [9]*meta*-cyclophanes annulated to related heterocycles. The calculations show that several conformations of the *ansa* bridge are within 1.5 kcal/mol of the lowest energy structure which corresponds to the one encountered in the crystal.

Results and Discussion

Compounds **1-3** were previously synthesized and analysed by dynamic ^{1}H-NMR techniques in the temperature range between +20°C and -90°C in CD_2Cl_2.[1] The various conformations involved in the bridge flipping revealed by the NMR spectra were presented and discussed. The three compounds were the pyrylium perchlorate (**1**, X = O$^+$), obtained by diacetylation of cyclododecene by acetic anhydride and 70% perchloric acid,[3] the corresponding pyridine (**2**, X = N) and *N*-methylpyridinium perchlorate (**3**, X = N-Me$^+$) formed from the pyrylium salt **1** and ammonia and methylamine, respectively. The last compound is the topic of the present paper.
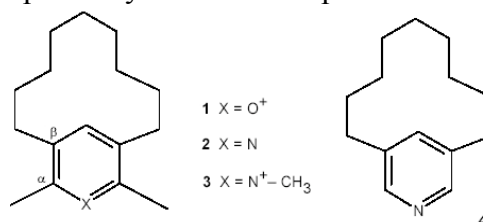

Figure 1 presents an ORTEP plot of the molecular structure of **3** in the crystal. The perchlorate anion is disordered in the crystal, and multiple orientations had to be taken into account for solving the structure. Only one of the orientations is shown in Figure 1. Figure 2 presents a different orientation of the molecule together with the unit cell and the different orientations of the distorted perchlorate anion.
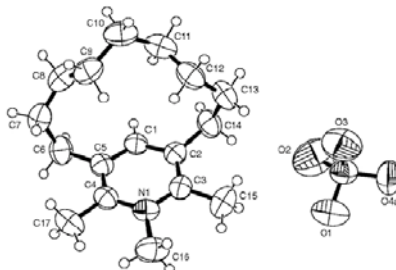
Figure 1. ORTEP plot of **3** in the crystal with atom numbering. Only the most populated orientation of the distorted perchlorate anion is shown. Note the relatively large thermal ellipsoids of the methylenic carbons in the ansa-bridge, of the three-methyl carbons and of the oxygen atoms in comparison to the relatively rigid pyridinium ring atoms.
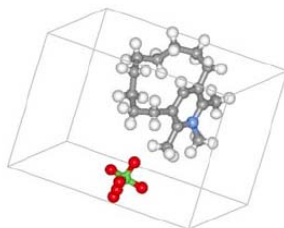
Figure 2. A different orientation of **3** for visualizing the conformation of the ansa-nonamethylene bridge.

Table 1. Atomic coordinates for non-hydrogen atoms with standard e.s.d.'s in parentheses and the equivalent isotropic displacement coefficients (Å^2)

Atom	x	y	z	Ueq
C1	0.7446(4)	0.6242(2)	0.5568(2)	0.0537(8)
C2	0.6029(4)	0.6032(2)	0.5331(2)	0.0541(8)
C3	0.4927(4)	0.6392(3)	0.5864(2)	0.0586(8)
N1	0.5280(3)	0.6872(2)	0.6632(2)	0.0570(7)
C4	0.6678(4)	0.6999(3)	0.6912(2)	0.0568(8)
C5	0.7802(3)	0.6704(2)	0.6361(2)	0.0564(8)
C6	0.9384(4)	0.6804(3)	0.6620(3)	0.0755(10)
C7	0.9946(4)	0.5874(4)	0.7153(3)	0.0804(11)
C8	0.9968(4)	0.4846(4)	0.6650(3)	0.0853(12)
C9	0.8719(5)	0.4125(3)	0.6843(3)	0.0764(11)
C10	0.8542(5)	0.3230(3)	0.6176(3)	0.0822(12)
C11	0.7718(5)	0.3524(3)	0.5358(3)	0.0794(11)
C12	0.6096(5)	0.3710(3)	0.5506(2)	0.0734(11)
C13	0.5283(5)	0.4241(3)	0.4741(3)	0.0820(12)
C14	0.5752(5)	0.5354(3)	0.4526(2)	0.0707(10)
C15	0.3348(4)	0.6256(4)	0.5632(3)	0.0863(13)
C16	0.4083(5)	0.7289(3)	0.7183(3)	0.0836(12)
C17	0.6922(5)	0.7440(3)	0.7803(3)	0.0829(12)
Cl1	0.08209(10)	0.51088(7)	0.36700(6)	0.0725(3)
O1	0.0407(4)	0.5937(3)	0.4224(2)	0.1120(12)
O2	0.2245(5)	0.5389(4)	0.3412(3)	0.156(2)
O3	0.0949(6)	0.4166(2)	0.4126(3)	0.1257(13)
O4A	-0.0519(13)	0.4960(14)	0.3151(12)	0.147(5)
O4B	0.0749(32)	0.5136(21)	0.2709(14)	0.118(9)
O4C	0.0104(13)	0.5074(14)	0.2930(10)	0.058(4)

   The final atomic coordinates for non-hydrogen atoms are given in Table 1. Selected bond lengths and angles are given in Table 2. There are no intermolecular distances shorter than van der Waals contacts. Interestingly, the structure is asymmetric as evidenced by the torsion angles of the nonamethylene bridge, which are listed in Table 3.

   We could reproduce the structure by performing energy minimizations with MM+ molecular mechanics within the HyperChem® package. The force field is adequately parameterized and the lowest energy conformation was indeed the one encountered in the crystal. However, by a combination of molecular dynamics and repeated energy minimization, several other conformations could be found. These were situated within less than 1.5 kcal/mol higher in energy. Table 3 presents the relative energies and the torsion angles of the Nonamethylene Bridge for the corresponding pyridine devoid of the 2,6- (α-methyl groups 4 Also given in Table

3 are the torsion angles of the nonamethylene bridge encountered in the crystal of **3**. The next lowest energy conformation **4b**, which is also asymmetric, is only 0.5 kcal/mol higher in energy than the one, which mimics the crystal structure **4a**. The next two conformations have a C_2 symmetry axis passing through C1 and C10. These four structures are presented in Figure 3. Other conformations of the nonamethylenic chain, all higher in energy, were also encountered as stable minima.

Table 2. Selected bond lengths (Å) and angles (°)

C1-C2	1.375(5)	C2 C1 C5	122.4(3)	O4C Cl1 O3	116.4(8)
C1-C5	1.385(4)	C3 C2 C1	118.2(3)	O4C Cl1 O2	103.5(7)
C2-C3	1.376(5)	C3 C2 C14	123.0(3)	O3 Cl1 O2	106.3(3)
C2-C14	1.524(5)	C1 C2 C14	118.7(3)	O4C Cl1 O1	114.2(8)
C3-N1	1.361(4)	N1 C3 C2	119.0(3)	O3 Cl1 O1	111.7(2)
C3-C15	1.500(5)	N1 C3 C15	119.0(3)	O2 Cl1 O1	103.1(3)
N1-C4	1.361(4)	C2 C3 C15	122.0(3)	O4C Cl1 O4B	27.8(9)
N1-C16	1.482(4)	C4 N1 C3	123.2(3)	O3 Cl1 O4B	121.5(11)
C4-C5	1.381(5)	C4 N1 C16	118.4(3)	O2 Cl1 O4B	75.9(11)
C4-C17	1.489(5)	C3 N1 C16	118.4(3)	O1 Cl1 O4B	124.8(11)
C5-C6	1.509(5)	N1 C4 C5	118.6(3)	O4C Cl1 O4A	27.4(8)
C6-C7	1.528(6)	N1 C4 C17	118.2(3)	O3 Cl1 O4A	103.1(7)
C7-C8	1.519(6)	C5 C4 C17	123.2(3)	O2 Cl1 O4A	130.9(7)
C8-C9	1.498(6)	C4 C5 C1	118.2(3)	O1 Cl1 O4A	101.3(7)
C9-C10	1.538(6)	C4 C5 C6	122.3(3)	O4B Cl1 O4A	55.2(10)
C10-C11	1.507(6)	C1 C5 C6	119.4(3)	Cl1 O2 O4B	53.5(6)
C11-C12	1.522(7)	C5 C6 C7	113.5(3)	O4C O4A O4B	2.9(23)
C12-C13	1.543(6)	C8 C7 C6	113.9(3)	O4C O4A Cl1	62.5(17)
C13-C14	1.520(5)	C9 C8 C7	114.9(4)	O4B O4A Cl1	62.2(12)
Cl1-O1	1.406(3)	C8 C9 C10	114.0(4)	O4C O4B O4A	2.9(22)
Cl1-O2	1.409(5)	C11 C10 C9	114.6(3)	O4C O4B Cl1	63.0(18)
Cl1-O3	1.395(3)	C10 C11 C12	113.9(3)	O4A O4B Cl1	62.7(12)
Cl1-O4B	1.470(2)	C11 C12 C13	115.3(3)	O4C O4B O2	113.1(25)
Cl1-O4A	1.474(13)	C14 C13 C12	115.9(3)	O4A O4B O2	113.1(18)
Cl1-O4C	1.308(12)	C2 C14 C13	113.8(3)	Cl1 O4B O2	50.5(9)
				O4A O4C O4B	174.2(45)
				O4A O4C Cl1	90.0(23)
				O4B O4C Cl1	89.2(23)

Table 3. MM+ Energies and torsion angles (°) of the bridge in the crystal structure of **3** with e.s.d.'s in parentheses and in the calculated pyridinophanes **4**

MM+ Energy (kcal/mol)		C1C2C14C13 C2C14C13C12		C14C13C12C11 C13C12C11C10		C12C11C10C9 C11C10C9C8		C10C9C8C7 C9C8C7C6		C8C7C6C5 C7C6C5C1	
3	X-ray	104.3(4)	-41.3(5)	-64.5(5)	167.2(3)	-70.3(5)	-83.0(5)	165.5(3)	-100.6(4)	65.0(5)	-91.3(4)
4a	22.04	108.4	-36.8	-63.9	166.6	-73.1	-82.6	167.5	-97.6	58.8	-90.6
4b	22.58	57.4	55.1	-143.8	68.1	66.0	-179.9	63.7	78.2	62.0	-55.4
4c	23.28	97.4	-44.0	-68.1	167.6	-89.5	89.5	-167.7	68.1	44.0	-97.3
4d	23.45	53.5	68.6	-64.3	-61.1	162.7	-162.6	61.1	64.2	-68.7	-53.4
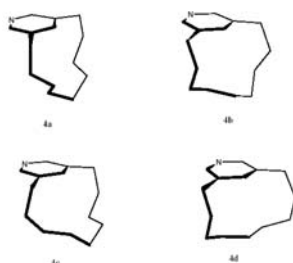
Figure 3. Minimized geometries of [9]3,5-pyridinophane.

The calculations indicate a high conformational mobility of the chain, which is also reflected by the thermal ellipsoids of the crystal structure. The same great mobility was encountered previously in the crystal structure of (*E*)-(–)-2-cyclododecenyl camphanate, which is also loosely packed.[4] However, the torsion angles are quite different in this case due to the *trans* double bond, which is a different structural element as compared to our *meta*-cyclophanic unit.

Experimental Section

The pyrylium salt with a nonamethylene bridge[3] was reacted with an excess of an ethanol solution of methylamine to give in 71% isolated yield the colorless microcrystals of pyridinium salt **3** with a melting point of 229 °C (dec.).[1] Crystals suitable for the X-ray analysis were grown by slowly diffusing diethyl ether into a saturated chloroform solution of **3**. The crystal was mounted on a Nonius diffractometer. Details of the crystal structure determination and solution refinement:[5-8] colourless prism with dimensions 0.525 × 0.5 × 0.275 mm, M = 345.87, orthorhombic, $P2_12_12_1$, a = 9.166(1), b = 12.759(3), c = 15.260(2) Å, $\alpha = \beta = \gamma$ = 90°, V = 1784.6(5) Å^3, Z = 4, T = 296(2) K, ρ_{calc} = 1.287, $F(000)$ = 744, μ = 0.230 cm^{-1}, λ = 0.71093 Å, source = MoKα, 2495 total independent reflections measured, 2305 reflections observed with $I \geq 2\sigma(I)$, no. of parameters refined = 226, R = 0.0501, goodness of fit = 1.129.

Conclusions

It is interesting to note that crystal packing effects do not enforce a conformation of the nonamethylene bridge different from the one that lies lowest in energy according to our MM+ calculations, though other conformations are within less than 1.5 kcal/mol, well within the span of such crystal lattice effects. Furthermore, in accord with the earlier published results from D-NMR spectra in CD_2Cl_2 solution where quite tight ion pairing should be encountered, there were no significant differences in the barrier height encountered for the neutral pyridine **2** and the salts **1** and **3**. Therefore, the dynamic processes involve flipping of the *meta*-cyclophanic ring relative to the *ansa*-bridge (or *vice versa*) without involvement the perchlorate counterions. „Hula hoop" or „cord skipping" motions do not appear to be involved, since these dynamic processes are likely to require higher barriers in the ionic compounds than would be encountered in **2**.

Acknowledgements

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