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Homotropenylium Cation: Structure, Stability, and Magnetic Properties

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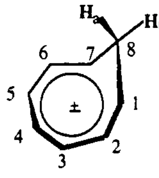
Abstract: The equilibrium geometry of the homotropenylium cation (**1**) and its planar form (**5**) have been calculated at the MP2/6-31G(d) level of theory. The potential surface of **1** in the direction of the 1,7 coordinate R(1,7) has been explored by MP2 and MP4(SDQ) calculations. In addition, ^{13}C NMR chemical shifts, ^{1}H chemical shifts, and the magnetic susceptibility of **1** have been determined for a continuous change from $R(1,7) = 1.5$ to $R(1,7) = 2.5$ Å using IGLO/6-31G(d,p). All calculations performed predict a single minimum potential curve for **1** with the minimum being located at 2.03 Å. At this distance, there is a maximum equalization of positive charge and bond lengths in the seven-membered ring C1-C7, which indicates efficient 6π electron delocalization involving through-space 1,7 interactions. Electron delocalization is also responsible that ^{13}C chemical shifts in the ring become similar for **1** and that both the magnetic susceptibility and the shift difference between endo and exo proton at C8 reach maximum values. Using **5** as an appropriate reference state, the relative values of magnetic, geometric, and energetic properties of **1** establish its homoaromatic character.

1. Introduction

The homotropenylium cation, $C_8H_9^+$ (**1**), has been considered as the prototype of a homoaromatic system[1] ever since it was first synthesized.[2,3] Recently, Haddon has reported second- and third-order Møller–Plesset (MP2 and MP3) perturbation calculations on **1**, which showed that there is only one energy minimum on the potential energy surface along the coordinate represented by the 1,7 distance.[4] The minimum energy structure of **1** possesses an elongated homoaromatic 1,7 "bond" of about 1.9 Å. In earlier ab initio studies a double minimum potential was found, which suggested the existence of two valence tautomers, one with a short 1,7 distance of about 1.6 Å and one with a long 1,7 distance of about 2.3 Å.[5] The first valence tautomer (**1a**) was described to be homoaromatic while the latter (**1b**) seemed to be the "normal" cyclooctatrienylium cation. The existence of two valence tautomers of **1** as well as their electronic characterization seemed to be in accordance with MO theory[1,6] and the description of homoaromaticity in terms of properties of the calculated electron density distribution.[7] Even further support was provided by Childs and co-workers[8,9] who, in an elegant piece of experimental work, succeeded in synthesizing the derivatives **2** and **3** of the two valence tautomers.



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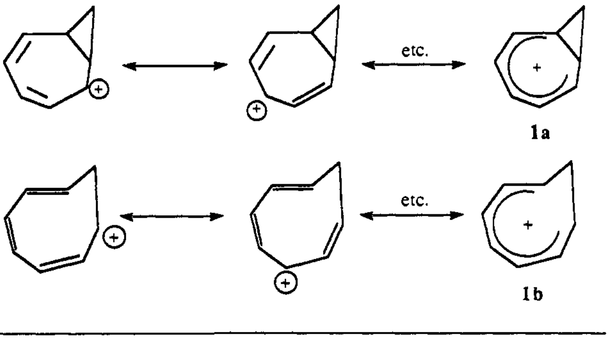

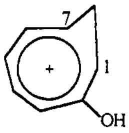

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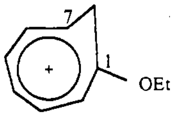

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In view of the experimental work Haddons recent results are difficult to accept. But they are understandable in view of the shortcomings of the Hartree–Fock (HF) approach used in the earlier ab initio investigations of **1**. If one considers the rearrangement **1a** → **1b**, both structures can be reasonably well-described at the HF level provided a sufficiently large basis set is used.[10] More problematic is a balanced description of the intermediate range where the 1,7 bond of **1a** is stretched and finally broken. HF is known to overestimate destabilization due to bond stretching, and, therefore, it is clear that upon rearranging **1a** to **1b**, the energy will first raise and lead to a barrier between **1a** and **1b** due to the basic deficiencies of the HF method. Hence, the double minimum potential of **1** obtained at the HF level is an artifact of the HF approach.

MP2 and MP3 include correlation corrections by considering double excited configurations.[11] Accordingly, they can describe structures with stretched or dissolved bonds much better than HF. By stabilizing intermediate structures below the energy of **1a** and **1b**, the double minimum potential changes to a single minimum potential at the MP2 (MP3) level of theory. The question,

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(10) A DZ+P basis set is a prerequisite for the correct description of any bicyclic system containing the cyclopropane entity. A minimal basis set is not sufficient in this respect.

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however, is whether the MP calculations reported by Haddon[4] come close to the true solution of the problem.

There are two reasons that make it difficult to answer this question. First, Haddon calculated MP2 (MP3) energies using HF geometries. However, HF and MP2 geometries may differ considerably.[12] This is already reflected by the equilibrium geometries of closed shell molecules calculated at the MP2 or MP3 level. Bond lengths are in general longer, bond angles smaller than those computed at the HF level.[12] Since there is a significant coupling between the 1,7 distance and the other internal coordinates of **1**, it is easy to foresee that MP2 will lead to a different equilibrium geometry of **1** than the one obtained at the HF level. Because of computational reasons, geometry optimization at the MP level was not considered by Haddon, and, therefore, the HF equilibrium geometry he reports is an important, but not conclusive prediction for the true equilibrium geometry of **1**.

Secondly, MP2 and, to a lesser extent, also MP3 are known to overestimate the stability of structures with stretched bonds or biradical nature,[13] i.e., structures as they should occur in the intermediate range of 1,7 distances ($1.7 < R(1,7) < 2.3$ Å) in **1**. Accordingly, MP2 leads to an artificial stabilization of these structures which can only be corrected if higher order correlation effects are included. The best way to do this would be by a coupled cluster method,[14] but in view of the size of **1** a computationally less demanding method must be used, for example, MP4 with single (S), double (D), and quadruple (Q) excitations (MP4(SDQ)).[15] By the S excitations orbital relaxation effects and by the Q excitations pair,pair correlation effects are accounted for. Furthermore, the overestimation of the stability of structures with stretched bonds is corrected by a coupling of D with Q excitations.[12,13]

On the basis of these considerations it is desirable to explore the potential energy surface of **1** along the 1,7 reaction coordinate by (a) carrying out MP2 geometry optimizations and (b) doing in addition MP4(SDQ) calculations thus describing **1** with a better correlation method. Apart from this it is helpful to determine the structure of **1** in an independent way. For this purpose, its magnetic properties can be used. It is possible to calculate NMR chemical shifts and magnetic susceptibility for all geometries investigated along the 1,7 reaction coordinate. It can be predicted that for one of the geometries considered the calculated magnetic properties will coincide with the corresponding experimental values of **1**. Since magnetic properties can be calculated with sufficient accuracy[16] and since magnetic properties are known to depend on the geometrical parameters of a molecule, a coincidence between calculated and experimental values of magnetic properties will positively identify the equilibrium geometry of **1**.

Hence, we report in this work a two-pronged approach to reliably determine the equilibrium geometry of **1** as well as the shape of the potential energy surface along the 1,7 reaction coordinate by first calculating its magnetic properties using HF and the IGLO (individual gauge for localized orbitals) method[16] and, then, by directly determining the structure of **1** by MP2 and MP4(SDQ) calculations. With the results obtained in this way we will investigate the following questions. (1) Is the $C_8H_9^+$ ion **1** the prototype of an homoaromatic system, and, if so, how can its homoaromaticity be described? (2) Which properties, in particular which magnetic properties, reflect the homoaromatic character of **1**? (3) Do theoretical results help to explain experimental observations made in connection with homotropenylium cations?

In section 2 we will briefly describe the computational methods used in this study. In section 3, calculated magnetic properties of **1** will be discussed. Geometry, energy, and the potential surface of **1** are investigated in section 4. Finally, in section 5 the potential homoaromaticity of **1** is considered.

Table I. Comparison of Experimental and IGLO ^{13}C NMR Chemical Shifts Calculated with Various Basis Sets at the Corresponding HF Geometries[a]

molecule	6-31G	6-31G(d)	6-31G(d,p)	6-311G(d,p)	exptl
TMS	3.6	4.4	3.1		7.0
$\underline{C}H_3CN$	9.5	6.8	5.0	3.2	7.4
C_2H_6	5.9	7.8	7.1	11.9	14.2
CH_3NH_2	22.9	27.5	26.2	32.7	36.8
$(\underline{C}H_3)_2CO$	33.4	30.9	29.4	30.2	37.1
CH_3OH	43.3	49.3	47.1	51.2	58.5
C_2H_2	88.3	82.1	76.8	77.2	77.9
HCN	138.6	120.3	115.2	114.3	113.0
$CH_3\underline{C}N$	143.8	125.4	122.0	121.8	121.3
C_2H_4	141.0	127.4	123.9	130.7	130.6
CO_2	154.6	123.9	123.9	132.7	136.3
C_6H_6	143.9	135.8	131.5	137.5	137.9
$(CH_3)_2\underline{C}O$	232.1	201.7	197.2	199.3	208.2
Δ	12.6	5.7	5.7	3.3	

[a] All chemical shifts in ppm relative to CH_4. For molecules with more than one ^{13}C chemical shift the C atom in question is underlined. Δ is the mean deviation.

2. Computational Methods

In this work the 6-31G(d) and 6-31G(d,p) basis sets[17] have been used as a compromise between calculational accuracy and economy. These basis sets are known to lead to reasonable energies and geometries both at the HF and MP2 level of theory.[18] However, they may be insufficient to calculate magnetic properties. To clarify this question, we have done test calculations with the IGLO method by Kutzelnigg and Schindler.[16] Kutzelnigg and co-workers have designed special basis sets of triple- and quadruple-ζ character to obtain reliable NMR chemical shifts for molecules, for which the geometry is experimentally known.[19,20] However, in those cases where no structural information is available, a basis set designed for the calculation of magnetic properties may not be useful for geometry optimizations. Also, for large molecules a geometry optimization with triple- or quadruple-ζ basis sets is often not feasible. Therefore, we have tested various split valence basis sets using ab initio rather than experimental geometries. Results are given in Table I.

They show that a consistent calculation of molecular geometries and magnetic properties at the HF/6-31G(d) and HF/6-31G(d,p) level is sufficient to get ^{13}C chemical shifts with an accuracy of 6 ppm. As far as geometries are concerned this has been known before,[18] but for the calculation of ^{13}C chemical shifts this was less obvious. It helps to reduce calculational costs by substituting the more costly triple-ζ basis of Schindler and Kutzelnigg[19] by standard 6-31G(d) and 6-31G(d,p) basis sets. Of course, a triple-ζ basis will always improve agreement between experimental and calculated ^{13}C chemical shifts. This is clearly reflected by the 6-311G(d,p) values in Table I and amply documented in the literature.[20] On the other hand, further cost reduction by using a DZ basis such as 6-31G is not advisable since it leads already to an uncertainty of 13 ppm thus reflecting the fact that polarization functions are essential for the calculation of NMR chemical shifts with the IGLO method.

Because of the results obtained for the test molecules in Table I, we have exclusively used the 6-31G(d,p) basis in this and in other work on ^{13}C chemical shifts. Results in general show that the accuracy of IGLO/6-31G(d,p) calculations can be improved by the use of better equilibrium geometries. Hence, if MP2 or any other correlation corrected ab initio method leads to better than HF geometries, this will show up in the accuracy of the IGLO/6-31G(d,p) values of ^{13}C chemical shifts. Finally, a caveat is necessary with regard to the calculation of other chemical shifts at this level of theory. Proton chemical shifts should be calculated with 6-31G(d,p) rather than 6-31G(d). However, in general it is difficult to reproduce experimental ^1H chemical shifts since they strongly depend on environmental effects. As for other nuclei such as ^{17}O, ^{19}F, or ^{31}P, test calculations clearly show that a DZ+P basis is not sufficient in these cases.[21]

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[12] See, e.g.: Gauss, J.; Cremer, D. *Adv. Quant. Chem.*, in press.

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Table II. Calculated Magnetic Properties of 1 in Dependence of the 1,7 Distance: IGLO/6-31G(d,p)//HF/6-31G(d) Calculations

$R(1,7)$	δC_1	δC_2	δC_3	δC_4	δC_8	Δ	$\delta H_a-\delta H_b$	$-\chi$
1.450	28.8	191.0	123.3	193.4	3.3	47.9	4.0	75.1
1.500	32.7	189.2	125.6	189.5	10.2	44.0	4.6	78.7
1.550	38.4	186.7	126.4	184.6	16.9	40.1	5.3	82.0
1.600	45.4	183.5	127.3	179.4	22.3	35.7	5.8	85.3
1.664	56.0	178.1	129.2	172.4	27.6	29.7	6.5	89.3
1.800	82.6	163.8	135.5	158.2	32.8	16.4	7.3	95.4
1.900	102.5	152.3	141.9	149.4	33.1	7.5	7.4	97.1
2.000	117.3	147.4	150.9	143.8	33.3	6.0	7.1	96.1
2.100	130.9	141.2	160.3	139.6	31.4	11.1	6.4	92.9
2.200	141.4	137.2	168.4	136.4	29.7	16.7	5.6	89.4
2.285	148.0	135.0	174.1	134.2	28.5	20.2	5.1	86.4
2.300	148.9	134.7	175.0	133.9	28.3	20.7	5.0	85.9
2.400	154.3	133.2	180.4	131.7	27.4	23.8	4.3	82.7
2.500	158.0	132.3	184.7	129.7	26.9	26.1	3.7	79.8
planar	162.4	119.9	196.6	121.6	32.5	32.3	0	52.9
exptl	122.2	153.7	143.2	144.7	43.7	0	5.8	72±2

[a] ^{13}C and ^{1}H chemical shifts relative to TMS in ppm. Δ is the mean deviation of the calculated ^{13}C chemical shifts in the ring C_1–C_7 from the experimental values. H_a is endo, H_b is exo positioned. The molecular susceptibility χ is given in 10^{-6} cm^3/mol, the distance R in Å. [b] Minima on the HF/6-31G(d) potential energy surface of 1. [c] Experimental ^{13}C, ^{1}H, and χ values from refs 26, 27, and 28.

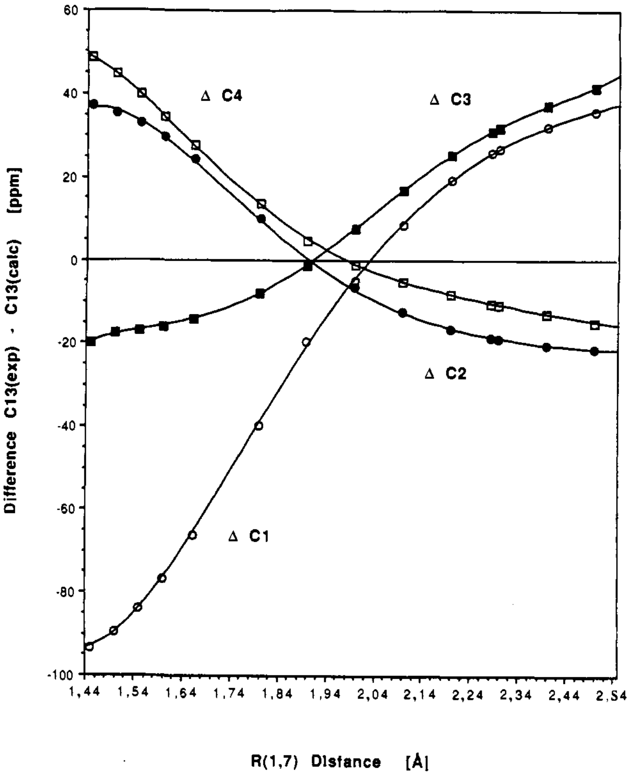

Figure 1. Difference Δ between experimental and calculated IGLO/6-31G(d,p)//HF/6-31G(d) ^{13}C NMR chemical shifts of 1 as a function of the 1,7 distance. All values in ppm.

To carry out IGLO calculations, the original program by Kutzelnigg, Schindler, and van Wüllen[22] has been adopted to the ab initio package COLOGNE[23] which allows analytical gradient calculations for MPn methods up to $n = 4$.[24,25] Hence, it was possible to combine calculations of equilibrium geometries with IGLO calculations in a routine way.

3. Magnetic Properties of the Homotropenylium Cation

HF/6-31G(d) calculations of the equilibrium geometry of 1 and various other structures of 1 along the 1,7 coordinate fully confirm Haddon's results obtained with the same basis but using five 3d rather than six 3d functions.[4] The global minimum is found at $R(1,7) = 2.285$ Å and a local minimum at $R(1,7) = 1.664$ Å. The corresponding values of ref 4 are 2.290 and 1.660 Å, respectively. The energy difference between the two minima is 4.1 kcal/mol in agreement with Haddons value. In view of the X-ray crystal structures obtained for 2 and 3 by Childs and co-workers,[8,9] these results seem to be in agreement with the available knowledge on the experimental data on homotropenylium cations.

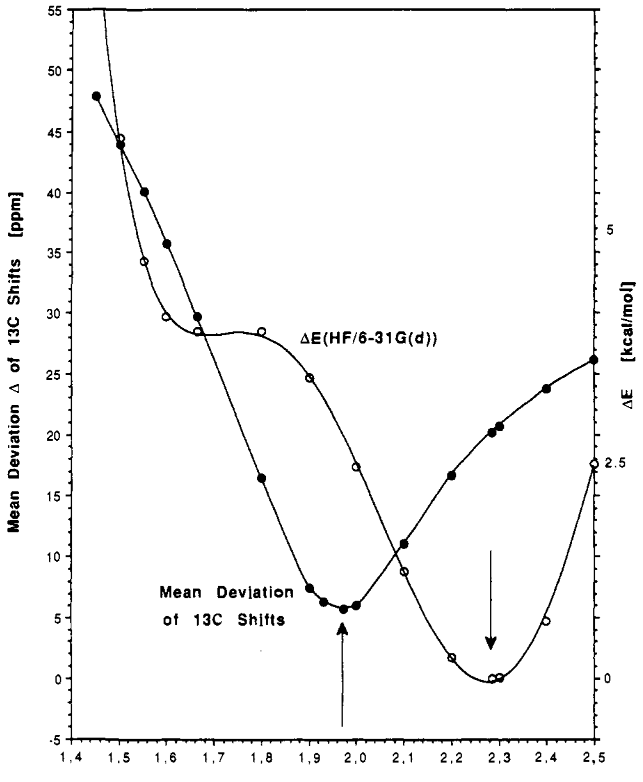

Figure 2. Determination of the equilibrium value of the 1,7 distance of 1 by HF/6-31G(d) calculations and IGLO/6-31G(d,p) calculations. The minimum of the mean deviation of the calculated IGLO ^{13}C chemical shifts defines the equilibrium value of $R(1,7)$ (see upward directed arrow).

In Table II, experimental and calculated magnetic properties of 1 are compared, in particular, ^{13}C chemical shifts, the magnetic susceptibility χ, and the difference $\delta H_a-\delta H_b$ between the ^{1}H chemical shifts of the endo proton H_a and the exo proton H_b at C8. The experimental ^{13}C chemical shifts[26] do not agree with chemical shifts calculated for the two HF/6-31G(d) minima structures or for any of the structures close to the minima. Mean

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(22) Kutzelnigg, W.; Schindler, M.; van Wüllen, C. IGLO, University of Bochum, 1989.

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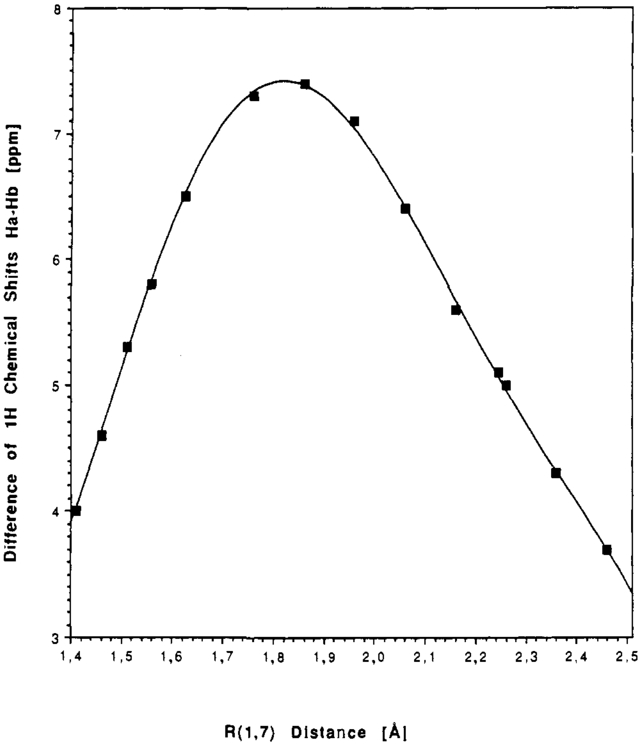

Figure 3. IGLO/6-31G(d,p) difference δH_a–δH_b (H_a endo, H_b exo) of **1** as a function of the distance $R(1,7)$.

deviations are as large as 40 ppm, thus exceeding normal IGL/6-31G(d,p) errors (see Table I) by a factor of 6 and more. Clearly, the calculated ^{13}C chemical shifts suggest that neither **1a** nor **1b** are representing the true equilibrium structure of **1**.

In Figure 1, deviations Δ of calculated ^{13}C chemical shifts for atoms C1–C7 are plotted in dependence of the distance $R(1,7)$. All curves intersect between 1.9 and 2.0 Å, the zero line corresponding to experimental ^{13}C values. In this region of $R(1,7)$, the best agreement between IGLO and experimental ^{13}C chemical shifts for **1** is found. This is revealed by the calculated mean deviations listed in Table II and plotted in Figure 2. The smallest mean deviation (indicated by an arrow in Figure 2) is 6 ppm and is found for $R(1,7)$ = 1.97 Å. Hence, with the 6-31G(d,p) basis we obtain for **1** a similarly good agreement between experimental and theoretical values as observed for the test molecules of Table I. However, this implies that the potential energy surface of **1** in the direction of the $R(1,7)$ coordinate possesses a single minimum rather than the double minimum calculated with HF/6-31G(d) (see Figure 2).

A direct comparison of experimental and computed ^{1}H NMR chemical shifts is problematic since the former depend strongly on temperature, solvent, and other environmental effects.[27] The magnetic susceptibility χ[28] is normally overestimated by IGLO.[29] For DZ basis sets discrepancies are as large as 20%. Hence, both δH_a–δH_b and χ are not parameters that allow a reliable determination of $R(1,7)$. On the other hand, these quantities should be sensitive to electron delocalization in the potential ring C1–C7. If for a particular $R(1,7)$ value between 1.5 and 2.5 Å homoaromatic 6π delocalization becomes a maximum, then this will lead to a large exaltation of χ as well as large diamagnetic shielding of the endo proton H_a and, therefore, to a large difference δH_a–δH_b.

In Figures 3 and 4 the difference δH_a–δH_b and the magnetic susceptibility χ are given in dependence of $R(1,7)$. Both quantities adopt maximal values at $R(1,7)$ distances close to 1.9 Å suggesting that for this 1,7 distance (homoaromatic) 6π delocalization is strong. Although it is not clear at all whether 6π delocalization will substantially increase the stability of **1** (see below), one might argue that delocalization of π electrons in the seven-membered ring should be strongest in the equilibrium of **1**. Then, the location of the maximum of both the difference δH_a–δH_b and χ provides further support to the prediction that the equilibrium structure of **1** is characterized by a 1,7 distance close to 1.9 Å.

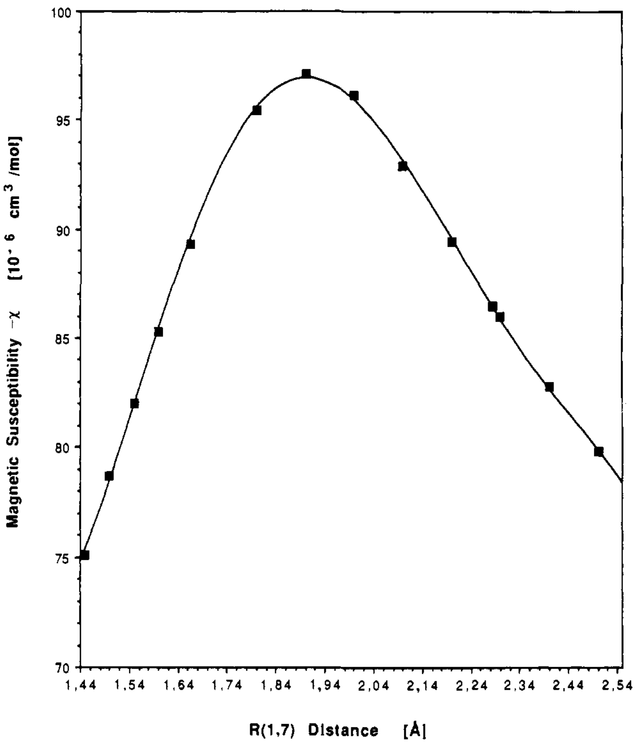

Figure 4. IGLO/6-31G(d,p) magnetic susceptibility $-\chi$ of **1** as a function of the distance $R(1,7)$.

In conclusion, the calculated magnetic properties of **1** suggest that (a) the homotropenylium cation possesses a single minimum potential energy surface along the 1,7 coordinate (Figures 1–4); (b) the preferred 1,7 distance is probably close to 1.9 or 2.0 Å; (c) 6π electron delocalization at this $R(1,7)$ value increases the difference δH_a–δH_b and the magnetic susceptibility χ to maximum values.

4. Equilibrium Geometry and Potential Energy Surface

In Table III, MP*n* energies for various values of $R(1,7)$ are given. MP*n*/6-31G(d) (*n* = 2, 3, 4) calculations for **1** lead to only one minimum in the direction of the 1,7 coordinate. This has been proven in three different ways. First, the equilibrium geometry of **1** has directly been calculated at the MP2/6-31G(d) level of theory. Then, these calculations have been repeated for five fixed values of the 1,7 distance in the range of 1.6–2.4 Å. In this way, the potential energy hypersurface of **1** has been explored in the direction of the 1,7 coordinate. Finally, MP3 and MP4(SDQ)/6-31G(d) calculations have been carried out at the MP2/6-31G(d) geometries to give the MP3 and MP4(SDQ) potential energy curve for the 1,7 distance.

Figure 5 shows the calculated MP2/6-31G(d) equilibrium geometry of **1**. The equilibrium structure possesses a 1,7 distance of 1.906 Å in agreement with the predictions derived from the calculated magnetic properties. Inspection of the geometrical parameters reveals that with a 1,7 distance of 1.906 Å there is almost complete bond equalization in the seven-membered ring. The CC bond lengths vary between 1.396 and 1.404 Å with an average CC bond length (without C1–C7) of 1.399 Å. This differs significantly from the corresponding HF geometries which predict bond alternation between 1.35 and 1.41 Å (compare with Table IV).

The geometrical parameters of the C1C7C8 unit are close to that of a hypothetical valence isomer predicted by HF/6-31G(d)

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[27] Winstein, S.; Kaesz, H. D.; Kreiter, C. G.; Friedrich, E. C. *J. Am. Chem. Soc.* **1965**, *87*, 3267.

[28] Dauben, H. J.; Wilson, J. D.; Laity, J. L. In *Nonbenzoid Aromatics*; Snyder, J. P., Ed.; Academic Press: New York, 1967; Vol. 2, p 167.

[29] See, e.g.: ref 20, chapter 3.12.

Table III. Calculated Energies in Dependence of the $R(1,7)$ Distance[a]

$R(1,7)$	HF//HF	MP2//HF	$R(1,7)$	MP2//MP2	MP3//MP2	MP4//MP2
1.50	6.36	14.37	1.664	3.78	2.71	2.36
1.60	4.26	6.46				
1.664	4.07	5.07	1.782	0.91	0.85	0.93
1.80	4.07	0.89				
1.90	3.53	0	1.901	0	0.04	0.22
2.00	2.48	0.66				
2.10	1.26	2.29	2.138	2.29	0.15	0.15
2.20	0.25	4.40				
2.285	0	6.46	2.375	7.89	2.41	2.40
2.30	0.01	6.87				
2.40	0.68	9.83	2.675	36.82	27.61	25.08
2.50	2.51	13.46				
energy	−307.8898	−308.93903		−308.94079	−308.93680	−308.94573
R_{min}	2.285	1.900		1.901	1.985	2.031

[a] $R(1,7)$ in Å, relative energies in kcal/mol, absolute energies in hartree. Basis: 6-31G(d).

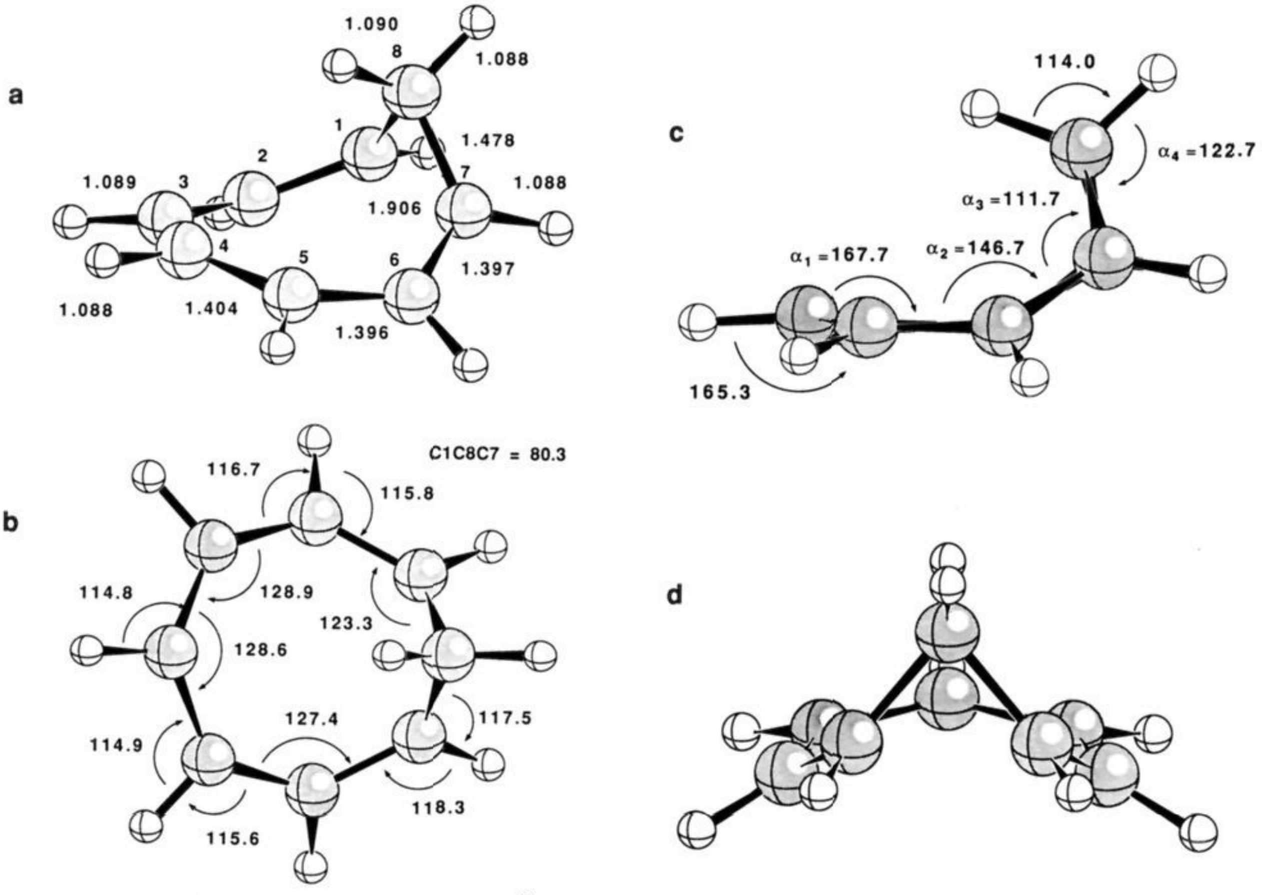

Figure 5. MP2/6-31G(d) geometry of **1**: (a) bond lengths in Å, (b) bond angles in deg, (c) side view, folding angles in deg, and (d) view along the symmetry plane.

at a 1,7 distance of 1.664 Å. The bond C1C8 is relatively short (1.478 Å), and the HCH angle is widened to 114° similar to the HCH angle in cyclopropane (114.7°[30]). Most interesting, however, is the fact that the CH_2 bridge is bent inward by 23° (see Figure 5c). In this way the endo H atom takes a position about 2.2 Å above the center of the seven-membered ring. The H atoms at the periphery of the ring are slightly bent downward away from the bridge (see Figure 5d).

In Figure 6, the MP2, MP3, and MP4(SDQ) potential curves in the direction of the 1,7 coordinate are shown. They all possess just one minimum which moves from 1.901 (MP2) to 1.985 (MP3) and 2.031 Å (MP4(SDQ), see Table III) when improving correlation corrections at the MP level. Hence, the most reliable prediction for the equilibrium value of the 1,7 distance in the

Table IV. Selected Geometrical Parameters of the Homotropenylium Cation (**1**) and Its Planar Form **4**[a]

parameter	HF 1[b]	HF 1[c]	HF 4	MP2 1	MP2 4
$R(1,7)$	2.285	1.664	2.685	1.906	2.675
$R(1,2)$	1.353	1.428	1.340	1.397	1.363
$R(2,3)$	1.413	1.368	1.433	1.396	1.425
$R(3,4)$	1.390	1.400	1.382	1.404	1.392
$R(1,8)$	1.494	1.481	1.498	1.478	1.496
α_1	166.9	172.0	180	167.7	180
α_2	145.5	155.2	180	146.7	180
α_3	116.1	110.4	180	111.7	180
α_4	124.7	121.5	128.2	122.7	128.8
HCH	109.7	115.3	103.3	114.0	102.5

[a] Bond lengths in Å, angles in deg. The folding angles α are defined in Figure 5c. [b] Global minimum with long 1,7 distance. [c] Local minimum with short 1,7 distance.

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[30] Kasai, D. H.; Myers, R. J.; Eggers, D. F.; Wiberg, K. B. *J. Chem. Phys.* **1959**, *30*, 512.

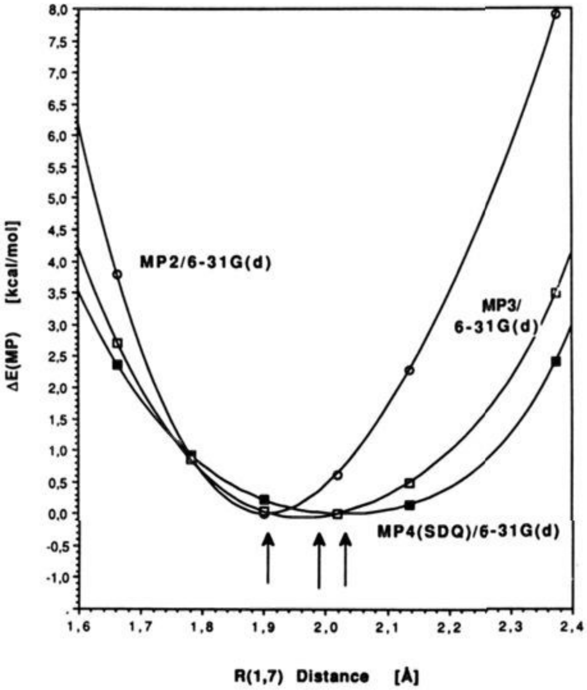


Figure 6. MP2, MP3, and MP4(SDQ) potential energy surface of **1** along the coordinate $R(1,7)$. For each MP level used, the position of the minimum is indicated by an arrow.

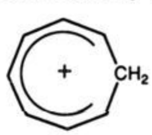
homotropenylium cation is 2.03 Å.

Another feature, which becomes apparent from Figure 6, is the flatness of the potential curve in the region between 1.5 and 2.5 Å, which has also been observed by Haddon.[4] At MP4-(SDQ)/6-31G(d) a change in the equilibrium value of $R(1,7)$ by ±0.4 Å leads to an energy change of just 3.5 kcal/mol! The corresponding (harmonic) force constant is just 0.2 mdyn/Å (0.7 mdyn/Å at MP2).

The MP2 geometry of **1** has been used to recalculate the ^{13}C NMR chemical shifts. In addition, chemical shifts have been calculated for the geometry with the optimum MP4(SDQ) 1,7 distance. Results of these calculations are shown in Figure 7. They reveal that a better account of the molecular geometry leads to a better agreement between calculated and observed ^{13}C chemical shifts. Noteworthy is the improvement of the chemical shift value for atoms C1 and C7 when the MP4 1,7 distance is used. Since this shift value is probably most sensitive to a correct description of 1,7 interactions at the actual 1,7 distance, we conclude that MP4 provides the best account of this geometrical parameter.

5. Homotropenylium Cation: The Homoaromatic Prototype?

To assess the homoaromatic character of a given molecule, an appropriate reference state has to be defined. In experimental chemistry this is normally the most difficult part since it requires finding of another compound that differs from the target molecule just with regard to the electronic feature to be investigated but otherwise possesses identical properties. Such a reference molecule normally does not exist, and, therefore, all kinds of assumptions have to be made that make a reliable assessment of the electronic property in question problematic. In quantum chemistry this problem is less severe. For example, if the homoaromatic character of **1** has to be investigated, a natural choice of the reference system will be the planar form **4**. In **4**, the π orbitals are perpendicular to the ring plane, and, therefore, any significant π-π overlap between atoms C1 and C7 is excluded. Form **4** does not benefit from 6π electron delocalization in the seven-membered ring even though it possesses the same C framework as **1**.



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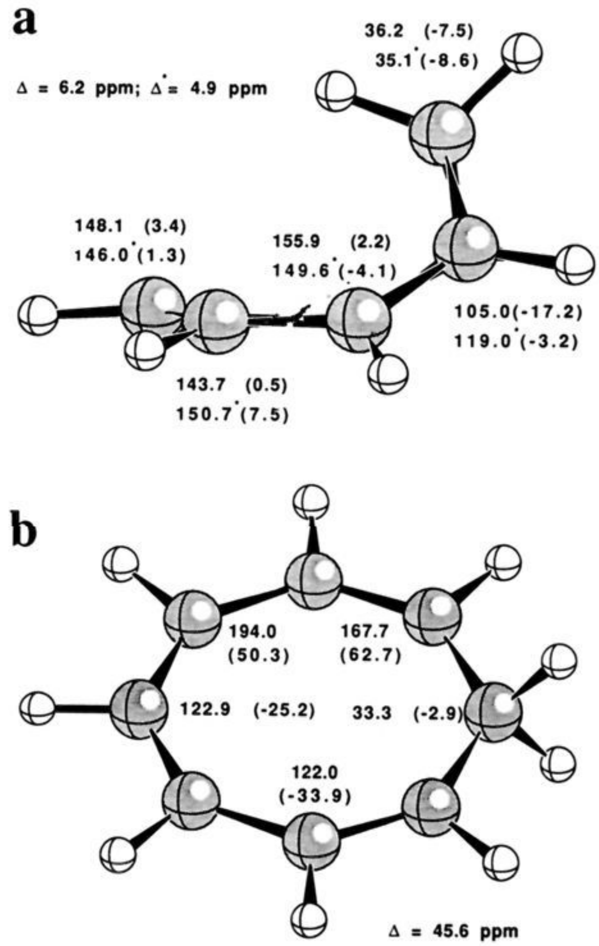

Figure 7. IGLO/6-31G(d,p)//MP2/6-31G(d) ^{13}C NMR chemical shifts for (a) **1** and (b) **4**. Starred values correspond to the MP4(SDQ) value of $R(1,7)$. Values in parentheses give the deviation (a) from the experimental ^{13}C chemical shifts and (b) from the values of **1**. In each case the mean deviation Δ is given. All values in ppm are relative to TMS.

There is another reason why **4** is a good choice of a reference state. It has been shown that **1** can undergo ring inversion, probably by passing through the planar form **4**. The free enthalpy of activation has been found to be 22.3 kcal/mol.[31] By calculating the energy of **4**, another check on the reliability of the methods used in this work can be made.

In Figure 8 the calculated MP2/6-31G(d) equilibrium geometry of the planar form **4** is given. Apart from the necessary widening of the internal CCC angles, there is stronger bond alternation in **4** than in **1**. Bonds C1C2 and C6C7 possess more double bond character, and bonds C2C3 and C5C6 possess more single bond character while C3C4C5 resembles an allylic unit. Hence, **4** represents a normal cyclotrienyl cation structure (see also HF/6-31G(d) geometry in Table IV).

At the HF/6-31G(d) level, **4** is a transition state with one negative eigen value of the Hessian matrix. Its energy relative to **1** is 18.9 (HF/6-31G(d)), 36.8 (MP2/6-31G(d)), and 24.8 kcal/mol (MP4(SDQ)/6-31G(d)), respectively. To compare the theoretical barrier values with the experimental free enthalpy of activation for ring inversion, $\Delta G^{\ddagger} = 22.3$ kcal/mol,[31] we have calculated HF/6-31G(d) zero point energies (ZPE) for **1** (98.5 kcal/mol) and **4** (98.2 kcal/mol) as well as the activation entropy $\Delta S^{\ddagger}$ (−1.8 eu) for ring inversion. Since both ΔZPE and $\Delta S^{\ddagger}$ are

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(31) Winst S.; Kreiter, C. G.; Brauman, J. I. *J. Am. Chem. Soc.* **1966**, *88*, 2047.

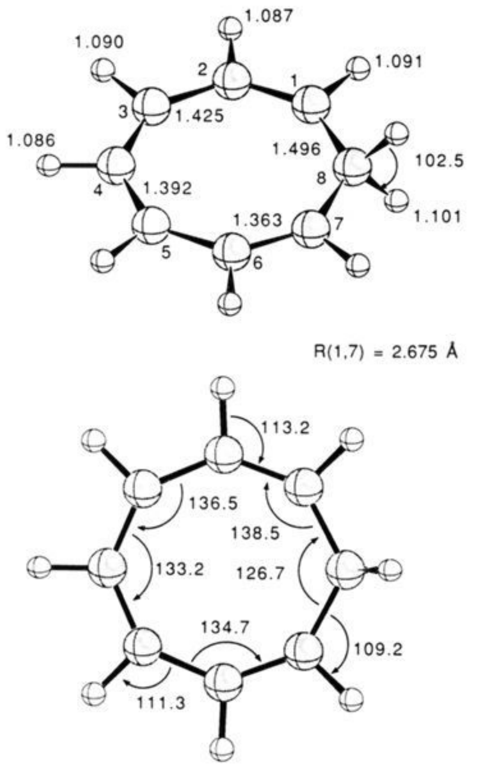

Figure 8. MP2/6-31(d) geometry of the planar form **4**: bond lengths in Å and angles in deg.

rather small, corrections to $\Delta E^{\ddagger}$ at T = 300 K are just 0.2 kcal/mol, i.e., it is reasonable to compare calculated and experimental barrier directly. Obviously, MP4(SDQ) provides the best account of the barrier to inversion.

In Figure 7b, ^{13}C NMR chemical shifts of the planar form are given. They clearly deviate from those of **1** (mean deviation Δ = 45.6 ppm) alternating in the seven-membered ring between 122 and 194 ppm. This is indicative of a similar alternation of the positive charge and the CC bond lengths in **4**. At the same time, the magnetic susceptibility (51.8 × 10^{-6} cm^3/mol) adopts its lowest value, namely 45 ppm below that of **1**.

Utilizing the planar form **4** as a reference state, the properties of **1** clearly define its homoaromatic character. 1. ^{13}C chemical shifts in the seven-membered ring of **1** are equalized by 40%. 2. The same equalization can be found for CC bond lengths in the C1–C7 unit. The calculated bond orders are close to 1.5 with a variation of less than 2%. 3. The magnetic susceptibility adopts a maximum value for **1**, which is about 80% larger than that of **4**. 4. The difference between the chemical shifts of the CH_2 protons also adopts a maximum value.

All these properties characterize **1** as a cyclic system with substantial electron delocalization. However, electron delocalization is only possible if there are 1,7 through-space interactions. This does not imply that there is a real CC bond between atoms C1 and C7. Cremer and Kraka[32] have given two conditions for the existence of a covalent bond between two atoms A and B. (1) Atoms A and B have to be connected by a path of maximum electron density. The existence of such a maximum electron density path implies a (3,–1) saddle point $\mathbf{r}_b$ of the electron density distribution $\rho(\mathbf{r})$ as well as a zero-flux surface between A and B (necessary condition). (2) The local energy density $H(\mathbf{r}_b)$ has to be smaller than zero (sufficient condition).

Analysis of the MP2 response density distribution $\rho^{MP2}(\mathbf{r})$[13] shows that both criteria are not fulfilled in the case of atoms C1 and C7, i.e., there is no bond C1C7. But lack of a bond C1C7 does not exclude electron delocalization in the unit C1–C7 of **1**. Electron delocalization can also be established by strong through-space interactions (and orbital overlap) between C1 and C7. Delocalization of an aromatic ensemble of electrons caused by through-space interactions is the essence of homoaromaticity.[1] In this way, **1** is clearly homoaromatic. The same conclusion has been reached by Haddon[4] on the basis of orbital overlap criteria.

It is desirable to determine the homoaromatic stabilization energy. This cannot be done by taking the energy difference between **1** and **4** since this is dominated by changes in strain energy, which are difficult to quantify.[33] An alternative way is to assess the homoaromatic stabilization energy from the 1,7 potential given in Figure 6. The MP4(SDQ) potential, which certainly is the most reliable one at present, is rather flat with a curvature at the equilibrium point that corresponds to a 1,7 stretching force constant of 0.2 mdyn/Å. For comparison, the stretching force constant of the CC bridge in bicyclobutane is 3.45 mdyn/Å.[34] Assuming a linear dependence of the CC bond energy[35] on the CC stretching force constant, a value of 0.2 mdyn/Å suggests a stabilizing 1,7 interaction energy of just 4 kcal/mol. This is exactly the energy needed to either stretch or reduce the 1,7 distance to such an extent that a CC bond develops and valence structure **1a** is reached or that the through-space interactions are lowered to the level they adopt in valence structure **1b**. Furthermore, a homoaromatic stabilization energy of 4 kcal/mol sets the increase in strain energy when going from **1** to **4** equal to 18 kcal/mol. This is reasonable in view of observed activation enthalpies for cyclooctatetraenes.[36]

6. Conclusion

*The homotropenylium cation **1** is the prototype of an homoaromatic compound.* This becomes obvious from the calculated magnetic, geometric, and energetic properties. In line with previous expectations,[4] the "homoaromatic" 1,7 distance is within being 2.03 Å close to 2 Å. This is the result of a calculation of the potential energy surface in the direction of the 1,7 coordinate using the highly correlated MP4(SDQ) method. The curvature of the potential curve at the 1,7 equilibrium distance is extremely flat (stretching force constant k(C1C7) = 0.2 mdyn/Å). As a consequence, homoaromaticity in the case of **1** implies a relatively small stabilization energy of about 4 kcal/mol, probably a large amplitude vibration along the 1,7 coordinate, and a fast adjustment to perturbations in the form of substituents or strong environmental effects.

The chemical relevance of our calculational results is 2-fold. First, our results indicate that measuring of the homoaromatic character of **1** by experimental means is difficult and requires sensitive detecting antennas. Hence, NMR spectroscopy is probably the best method to investigate the homoaromatic character of **1**. Thermodynamic measurements to directly determine the homoaromatic character of **1** are probably the most difficult ones. This, of course, has also to do with the definition of an appropriate reference state (see above).

Secondly, substituents that either stabilize or destabilize positive charge will immediately change the 1,7 distance to much shorter or much longer values.[4] This is an immediate consequence of the potential curve given in Figure 6. Childs and co-workers[8,9] actually used this principle long before the exact potential curve was known. Future work has to show whether perturbations due to the substituents completely destroy the homoaromatic character of **1** and/or lead to a double minimum potential function. It is easy

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(33) For a discussion of this problem, see: Kraka, E.; Cremer, D. In *Molecular Structure and Energetics, Structure and Reactivity*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: New York, 1988, Vol. 7, p 65.

(34) Wiberg, K. B.; Peters, K. S. *Spectrochim. Acta* **1977**, *34A*, 261.

(35) The CC bond energy in cyclopropane has been calculated to be 71 kcal/mol. See: Cremer, D.; Gauss, J. *J. Am. Chem. Soc.* **1986**, *108*, 7467.

(36) For cyclooctatetraene (COT) values of 12–15 kcal/mol have been given. See, e.g.: Gardlik, J. M.; Paquette, L. A.; Gleiter, R. *J. Am. Chem. Soc.* **1979**, *101*, 1619. The increase in strain energy for **4** will be higher than that of planar COT because of the inclusion of a sp^3 hybridized C atom in the ring.

to foresee that it will be difficult to synthesize a derivative of **1** that still possesses the same properties as **1**.

Acknowledgment. We thank Prof. Kutzelnigg, Dr. Fleischer, and C. van Wüllen for fruitful discussions about and assistance with the IGLO program. This work was supported by the Swedish Natural Science Research Council (NFR). All calculations were done on the CRAY XMP/48 of the Nationellt Superdatorcentrum (NSC), Linköping, Sweden. We thank the NSC for a generous allotment of computer time.

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Molecular Dynamics with Dimethyl Sulfoxide as a Solvent. Conformation of a Cyclic Hexapeptide

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Abstract: Molecular dynamics simulations including dimethyl sulfoxide (DMSO) as solvent are reported. Simulations of the pure solvent produce good agreement with the X-ray diffraction data of liquid DMSO. Simulations of the cyclic hexapeptide *cyclo*[-D-Ala-Phe^2-Val-Lys-Trp-Phe^6-] in the presence of DMSO have been carried out. The conformation of the peptide in DMSO has been well refined from NMR studies and is used as a model system. The solvent forms hydrogen bonds with backbone amide protons and the Lys side chain. However, besides this small amount of ordering close to the peptide, the solvent is randomly distributed. The radial distribution of the solvent atoms quickly approaches that of pure DMSO. The effects of the solvent on the conformational preferences of the cyclic hexapeptide are discussed.

During the last few years, the importance of molecular dynamics simulations[1-4] in the structure determination of peptides has steadily increased.[5-10] The simulations have for the most part been limited to in vacuo or incorporating water as a solvent. However, many peptides of interest are not highly soluble in water and have been studied experimentally in organic solvents such as dimethyl sulfoxide (DMSO) or chloroform ($CHCl_3$). It is of course desirable to carry out the calculations under similar conditions (i.e. same solvent) as the experimental results were obtained.

In addition, computer simulations with solvents other than water will allow for greater insight into the role of environmental factors (solvent effects) on conformation. The conformational changes induced from varying the polarity, viscosity, and ability to form hydrogen bonds can be better understood from computer simulations involving models of these different solvents.

We have reported the use of carbon tetrachloride (CCl_4) in computer simulations of a cyclic undecapeptide, cyclosporin A.[11] A comparison of molecular dynamics simulations in vacuo and in water and CCl_4 illustrated the effects of solvent on the dynamics of the molecule, conformation of side chains, and formation of hydrogen bonds.

Here we report molecular dynamics simulations with DMSO as a solvent. In a recent publication, Rao and Singh used DMSO in a series of simulations investigating the solvation of cations and anions.[12] The use of the potential parameters of these authors within the GROMOS force field[13] reproduced the structure of the solvent as determined from X-ray diffraction.[14] The solvent was then utilized in molecular dynamics simulations of a model cyclic hexapeptide.[15] The solvation of the peptide and the conformational influences of the solvent are discussed.

Methods

The molecular dynamics simulations were carried out using the GROMOS program.[13] For the parameters of DMSO, new atom types were defined for the S, O, and methyl group (CH_3) for which the united atom approach was utilized. Jorgensen has shown for methanol that using the united atom approach or including all of the atoms of the methyl group produces very similar results.[16] A similar approach was used in our simulations of cyclosporin A; the CCl_4 was simulated as a Lennard-Jones solvent using a united atom.[11] For the bond lengths and angles of DMSO the equilibrium values were taken from the structure determined from microwave spectroscopy;[17] the force constants were taken from a study of a series of cyclic sulfoxides from Allinger and Kao.[18] The charges of the atoms and nonbonded (Lennard-Jones) parameters were taken from Rao and Singh.[12]

The molecular dynamics simulations of the pure solvent were carried out for 80 ps (following a 30-ps equilibration period) using a step size of 2 fs with the application of SHAKE. A cube of volume 2.45×10^4 Å^3 containing 208 DMSO molecules was used with periodic boundary conditions and a nonbonded cutoff distance of 15 Å. The temperature and pressure were maintained at 500 K and 1 atm by the weak coupling technique.[19] A temperature relaxation time of 0.1 ps (0.01 ps during the equilibration) and an isothermal compressibility of 8.719×10^{-4} (kJ mol^{-1} nm^{-3})$^{-1}$ were used. A simulation at 300 K produced identical results. The radial distribution function was calculated following standard procedures.[20,21]

To examine the effects of the organic solvent on peptide conformation, a simulation of a model hexapeptide, cyclo[-D-Ala^1-Phe^2-Val^3-Lys^4-

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