is relayed coherence transfer to the amide proton without applying an effective pulse to the C$^{\alpha}$ proton. Following the evolution period, carbon coherence is transferred to the ^{15}N with a refocussed INEPT sequence ($^1J_{CN}$ = 11 Hz). Subsequently, the nitrogen coherence is defocussed with respect to the coupling to the amide proton and then transferred to the amide proton using a proton 90° TANGO[7] pulse which is selective for protons directly coupled to ^{15}N and does not flip α-protons. Subsequently, the proton coherence which is antiphase with respect to nitrogen is refocussed and detected during t_2 with broadband nitrogen decoupling. A purge pulse at the nitrogen frequency prior to detection converts incompletely refocussed antiphase proton magnetization into multiple quantum coherence which is not detectable.

To test this technique we have applied it to the terminally blocked tripeptide Ac-Asn-Pro-[^{15}N]Tyr-NHMe. The synthesis and characterization of this peptide has been described elsewhere.[8] The coupling constant $^3J(H^{\alpha}-H^{N})$ for Tyr 3 can readily be measured from a 1D spectrum and compared with the result of the new technique. Its value is 8.9 ± 0.2 Hz. In this sample, ^{13}C is at natural abundance. The resulting cross peak between the α-carbon (along ω_1) and the amide proton (along ω_2) of tyrosine is shown in Figure 1B. The splitting along ω_1 (140 Hz) is due to the coupling between H$^{\alpha}$ and C$^{\alpha}$, and the splitting along ω_2 of 9.7 ± 0.8 Hz is due to the coupling between H$^{\alpha}$ and H^{N}, the quantity to be measured. As expected, this is slightly larger than the value obtained from the inphase doublet in the 1D experiment. The precision of these $^3J(H^{\alpha}-H^{N})$ measurements is determined by the digital resolution of the data in the ω_2 dimension (1.6 Hz). It could even be improved by determination of the first moments (centers of mass) of the two cross peak components.

An alternative experiment with a longer sequence but fewer pulses would use C$^{\alpha}$–H^{N} long-range coherence transfer and could be called H$^{\alpha}$–C$^{\alpha}$(ω_1)–selective–H^{N}(ω_2) heteronuclear long-range COSY. An experiment symmetric to that of Figure 1A is H^{N}–N(ω_1)–C$^{\alpha}$–selective–H$^{\alpha}$(ω_2) heteronuclear RELAY. The latter sequence has the disadvantage that the cross peaks of interest are at the ω_2 position of the α-proton which sometimes overlaps with the t_1 noise of residual water. However these two experiments are complementary in the sense that overlapping cross peaks in C$^{\alpha}$–H^{N} RELAY (Figure 1A) may be resolved in the symmetric N–H$^{\alpha}$ RELAY.

The pulse sequence of Figure 1A can be easily expanded into a 3D experiment by adding a second evolution period. There are different choices: (i) After the first 90°(H) pulse a proton evolution period may be inserted. This experiment is an H$^{\alpha}$-(ω_1)–C$^{\alpha}$(ω_2)–N–H^{N}(ω_3) 3D COSY. (ii) A nitrogen evolution period could be inserted after the nitrogen magnetization has refocussed to inphase magnetization (i.e., between the delays b and c of Figure 1A); this is a H$^{\alpha}$–C$^{\alpha}$(ω_1)–N(ω_2)–H^{N}(ω_3) 3D COSY.

In all of these experiments, attention has been focussed on *intraresidue* heteronuclear coherence transfer from the α-carbon (C^{α}_i) to the amide proton (H^{N}_i) or from the amide nitrogen (N_i) to the C$^{\alpha}$ proton(H^{α}_i). By appropriate tuning of the delay b (Figure 1A), these same heteronuclear relay experiments can be used to develop *interresidue* cross peaks due to sequential connectivities C^{α}_{i-1} to H^{N}_i or H^{α}_i to N_{i+1}, as will be demonstrated in a subsequent publication.[9]

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Hyperconjugative Distortions and the Cyclopentyl Cation Structure

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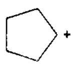
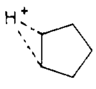
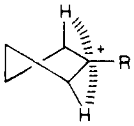
The structure of the cyclopentyl cation is intriguing. The first NMR studies of this species, one of the few secondary carbenium ions which can be observed in nonnucleophilic (superacid) media, revealed fluxional behavior.[1-4] Due to extremely rapid 1,2-hydride shifts, only one-line ^{1}H and ^{13}C NMR signals could be observed even at low temperatures in solution. Under these conditions, the energy difference between the "classical" (**1**) and the hydrogen-bridged (**2**) structures must be less than 3 kcal/mol.[5] Nevertheless early analyses of the NMR chemical shifts[1,2,6] as well as the ESCA spectrum[7] clearly showed **1** to be favored over **2**. This conclusion was confirmed by the solid-state (CPMAS) NMR observations of Myhre, Yannoni et al.[8] who were able to freeze out and observe the individual carbon signals in the solid state at 70 K. The ^{13}C resonances were broadened, but the chemical shifts (given in Table I) agreed reasonably well with earlier estimates based on static models.[2] But this data tells us nothing about the detailed geometry of **1**, which might be planar (C_{2v}) or might adopt "envelope" (C_s) or twisted (C_2) symmetries. Strong experimental evidence for the last conformation is provided by Forsyth et al.'s isotopic perturbation results on the related tertiary 1-methylcyclopentyl cation (**3**, R = CH$_3$).[9] The Boston group concluded that partial H-bridging was involved and proposed that this possibility "should be explored further in higher level calculations which would probably predict a twisted structure as the minimum energy conformation for cyclopentyl cations". We now verify this prescient suggestion.



1



2



3

Low level ab initio calculations on the cyclopentyl cation establish the planar C_{2v} form of **1** to be 2–3 kcal/mol less stable than the twisted (C_2) global minimum (Table II). No stationary

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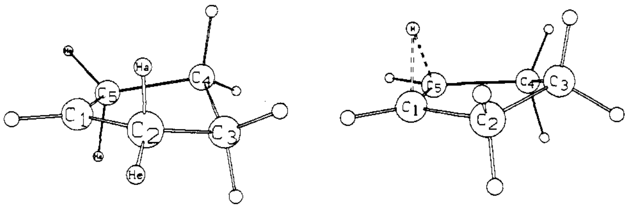
Table I. Comparisons of Experimental with Calculated (IGLO) ^{13}C Chemical Shifts (vs CH_4)[a] for Various Cyclopentyl Cation Geometries

description	point group	IGLO basis// geometry level	^{13}C			
			C(1)	C(2)	C(3)	av[b]
planar	C_{2v}	DZ//assumed[c]	401.9	64.2	18.4	113.4
		II//assumed[c]	415.4	68.2	26.9	121.1
		DZ//3-21G[d]	367.8	57.7	18.4	104.0
H-bridged	C_s	DZ//3-21G[d]	170.0	27.6	15.4	82.1
		DZ//6-31G*	167.7	28.2	13.5	81.1
		DZ//MP2/6-31G**	170.6	29.7	15.5	83.2
twisted	C_2	DZ//3-21G[d]	365.7	60.5	21.2	105.8
		DZ//6-31G*	363.3	62.3	21.3	106.1
		DZ//MP2/6-31G*	337.0	61.5	20.0	100.0
		DZ//MP2/6-31G**	332.0	62.1	19.5	99.0
experiment[e]		CPMAS/matrix[f]	320.0	71.0	28.0	103.6
		super acid (−70 °C)[g]				98.4

[a] The methane (218.3 ppm) and TMS (218.13 ppm) carbon absolute chemical shifts calculated at the DZ level differ by only 0.2 ppm. [b] Average of all carbons, corresponding to rapid equilibration. [c] Schindler data, ref 14. [d] Geometries optimized by Forsyth, D. A., private communication. [e] TMS literature values. See footnote *a*. [f] Reference 8. [g] Reference 1b.

Table II. Relative Energies, kcal/mol

level	**1** (C_2)	**1** (C_{2v})	**2** (C_s)
HF/3-21G//HF/3-21G	0.0	2.4	12.1
HF/6-31G*//HF/6-31G*	0.0	2.6	5.7
MP2/6-31G*//HF/6-31G*	0.0	3.4	0.1
MP4sdtq/6-31G*//HF/6-31G*	0.0	3.1	1.2
MP2(FU)/6-31G**//MP2(FU)/6-31G**	0.0		−0.4
MP2(FC)/6-31G**//MP2(FU)/6-31G**	0.0		−0.5
MP3/6-31G**//MP2(FU)/6-31G**	0.0		0.3
MP4sdtq/6-31G**//MP2(FU)/6-31G**	0.0		0.7
final + ZPE	0.0		0.3



1 2

Figure 1. The MP2(FU)/6-31G** optimized cyclopentyl cation structures, **1** (C_2) and **2** (C_s). Note the distortions at the C(2) and C(5) methylene groups in **1** (geometrical details are given in Table III).

point corresponding to **1** in C_s symmetry could be located. The H-shift transition structure (**2**) can be optimized readily in C_s symmetry. Due to torsional effects,[10] it adopts a boat-like conformation. Extensive earlier calculational studies on smaller carbocations demonstrated that basis sets with polarization functions on both carbon and hydrogen as well as electron correlation and zero-point energy (ZPE) corrections are needed in order to obtain reliable relative energies for species differing in structure as much as **1** and **2**.[11] Additionally, we demonstrate here the critical need to carry out optimizations by using larger basis sets at correlated levels. Specifically, an MP2(FU)/6-31G** optimization of **1**[12] brings out the partial hydrogen bridging prophesied by Forsyth's group.[9] In contrast, further optimization at this level produces relatively little change in the geometry of the *fully* H-bridged structure of **2** (these geometries are plotted in Figure 1; see Table III for comparisons of some key geometrical parameters for **1** (C_2) optimized at different levels). The relative energy summary in Table II shows the expected changes due to basis set expansion and inclusion of electron correlation. At our highest level (MP4stdq/6-31G**//MP2(FU)/6-31G**, "//" means "at the geometry of"), **1** is favored over **2** by only 0.7 kcal/mol, but this is decreased to 0.3 kcal/mol when the zero-point energy differences are taken into account. Since accumulating evidence indicates "classical" carbocations to be better solvated, but only a bit more than their bridged isomers,[5b,13b,c] our calculations agree satisfactorily with the experimental observations.

Table III. Key Geometrical Parameters for Cyclopentyl Cation **1** in Various Optimized Geometries[a]

parameter	3-21G[b]	6-31G*	MP2(FU)/ 6-31G*	MP2(FU)/ 6-31G**
C(1)–C(2)	1.463	1.457	1.439	1.437
C(2)–C(3)	1.558	1.542	1.538	1.536
C(2)–H_a	1.104	1.104	1.126	1.122
C(2)–H_e	1.083	1.084	1.094	1.088
C(1)–C(2)–H_a	103.41	101.00	97.13	95.26
C(1)–C(2)–H_e	114.27	114.45	116.66	117.19
H_a–C(2)–C(1)–C(5)	103.6	104.6	101.3	100.2

[a] Bond lengths in Å; angles in deg. [b] Geometry optimized by Forsyth, D. A., private communication.

But more information can now be obtained by comparing experimental chemical shifts with those calculated quantum mechanically. Following Schindler's demonstration[14] of the effectiveness of IGLO (individual gauge for localized orbitals) chemical shift calculations[15] on carbocations, we have been demonstrating the effectiveness of this new tool for the elucidation of structural problems.[13]

The remarkable sensitivity of chemical shifts to small but critical changes in geometry is demonstrated by the comparisons in Table I. Schindler's IGLO results for the cyclopentyl cation (**1**) were far from the experimental δ ^{13}C values, because he used an assumed, planar structure.[14] The 3-21G optimized C_{2v} form gives better, but still unsatisfactory results, especially for the carbenium ion center. No significant improvement is achieved by use of the C_2-optimized 3-21G or even the 6-31G* geometries. Correlated (MP2) geometries are needed to bring out the partial hydrogen bridging in **1** (Figure 1 and Table III). The MP2/6-31G** geometry gives IGLO results with the best agreement with experiment. The average chemical shift at this level (99.0 ppm) agrees closely with that observed experimentally (98.4 ppm) for the rapidly equilibrating cyclopentyl cation at −70 °C. In contrast, the average IGLO ^{13}C value calculated for **2** (83.2 ppm) does not agree with experiment.

The MP2/6-31G** structure of **1** reveals the methylene C(1)-C(2)-H_a and C(1)-C(2)-H_e bond angles to be very different, 95.3° and 117.2°, respectively (Table III). The axial hydrogens (at C(2) and C(5)) bend toward the carbenium ion center and partially bridge **3**. The C–H_a distances lengthen due to the strong hyperconjugative interaction.[16] Clearly, this positively charged species cannot "be adequately represented by a single Lewis structure involving only two-electron–two-center bonds",[17] either geometrically or in terms of its electronic structure (as shown by the NMR chemical shifts). As we will bring out in future papers,

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(10) See: Schleyer, P. v. R. *J. Am. Chem. Soc.* **1967**, *89*, 699–701, 701–703. Note that the 3,2-H shift in the 2-norbornyl cation is faster exo than endo (see ref 17).

(11) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: 1986; p 312.

(12) The standard theoretical levels described in ref 11 were employed as well as the CONVEX GAUSSIAN 82 and the vectorized IBM version of the GAUSSIAN 86 program.

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(15) (a) Kutzelnigg, W. *Isr. J. Chem.* **1980**, *19*, 143–200. (b) Schindler, M.; Kutzelnigg, W. *J. Chem. Phys.* **1982**, *76*, 1919–1933.

(16) The ESR spectra of cyclopentyl radicals also show marked differentiation of the β-axial and β-equatorial hydrogens and an appreciable barrier for exchange. See: Wood, D. E.; Lloyd, R. V. *J. Am. Chem. Soc.* **1977**, *99*, 8269–8273, and literature cited.

(17) Brown, H. C. *The Nonclassical Ion Problem*; with comments by Schleyer, P. v. R., Plenum Press: 1977; p 49.

very few carbocations are fully "classical" when evaluated by these sensitive criteria.

Acknowledgment. This work was supported at Erlangen by the Fonds der Chemischen Industrie, the Volkswagen-Stiftung, and the Convex Computer Corporation. We thank Professor W. Kutzelnigg and Dr. M. Schindler for the development of the IGLO program at Bochum and Dr. Schindler for the CONVEX version. We also thank Ulrich Fleischer and Professor David A. Forsyth for assistance and discussion. J. W. de M. Carneiro was the recipient of a CNPq-Brazil Doctoral Fellowship. Thanks also goes to the IBM Düsseldorf Computing Center for making available significant computing resources.

Note Added in Proof. The IR spectrum of the 1-methylcyclopentyl cation shows an intense CH stretching absorption at 2775 cm^{-1} at 77 K in an SbF_5 matrix.[18] The shift of ca. 220 cm^{-1} to lower frequencies was attributed to weakening of the CH bonds adjacent to the carbenium ion center due to hyperconjugative interactions. This is just what we have discussed above for the secondary cyclopentyl cation. Our calculations on the 1-methylcyclopentyl cation[19] and on the 2-propyl cation[13e,f] show similar features.

Registry No. Cyclopentyl cation, 25076-72-6.

Supplementary Material Available: Table of the absolute energies of the $C_5H_9^+$ species and full geometrical information in the form of Gaussian archive entries (2 pages). Ordering information is given on any current masthead page.

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Calixarene-Catalyzed Basic Hydrolysis of *p*-Nitrophenyl Dodecanoate: A Possible Change in the Mechanism from "Deshielding" to "Host-Guest"

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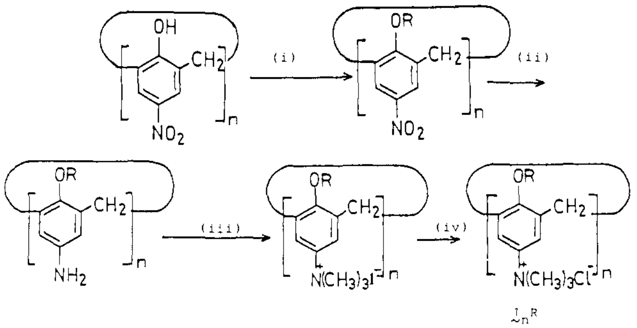
It is known that the rate constants for basic hydrolysis of *p*-nitrophenyl dodecanoate (pNPD) decrease with increasing initial ester concentration in the range of 10^{-6}–10^{-5} M.[1] It is postulated that pNPD in water forms aggregates within which the ester groups are protected from the OH^- attack, resulting in hydrolysis that is about three orders of magnitude smaller than for a short-chain monomer.[1-3] Ammonium salts of the general structure $RNMe_3^+X^-$ are capable of disrupting these aggregates; the rate constants increase with increasing salt concentrations.[1,4] A characteristic feature of this "deshielding" effect is that plots of k_{obsd} (pseudo-first-order rate constant) vs [salt] curve upward.[1,4] Menger and Venkataram[4] found that this peculiar relation between k_{obsd} and [salt] can be accommodated to a linear relationship between log k_{obsd} and [salt], which suggests that the "deshielding" process may be similar to that of solubilization phenomena (i.e., Setschenow equation).[5] The slopes ("microscopic" hydrophobicity parameters (MH): the larger, the more hydrophobic) correlate well with Hansch π values for aliphatic substituents.[6]

Recently, we have been interested in the syntheses and functionalization of water-soluble calixarenes (cyclic oligomers made up of benzene units[7,8]).[9,10] If the $RNMe_3^+X^-$ units are covalently linked as macrocyclic ring members, how do they behave for basic hydrolysis of pNPD? Calixarenes **1**$_n$R are well-suited for studies of this question.

Scheme I[a]



1_nR
(n=4, 6: R=Me, Oct)

[a] (i) RX, (ii) $N_2H_4/FeCl_3$ on activated charcoal, (iii) MeI, (iv) ion exchange.

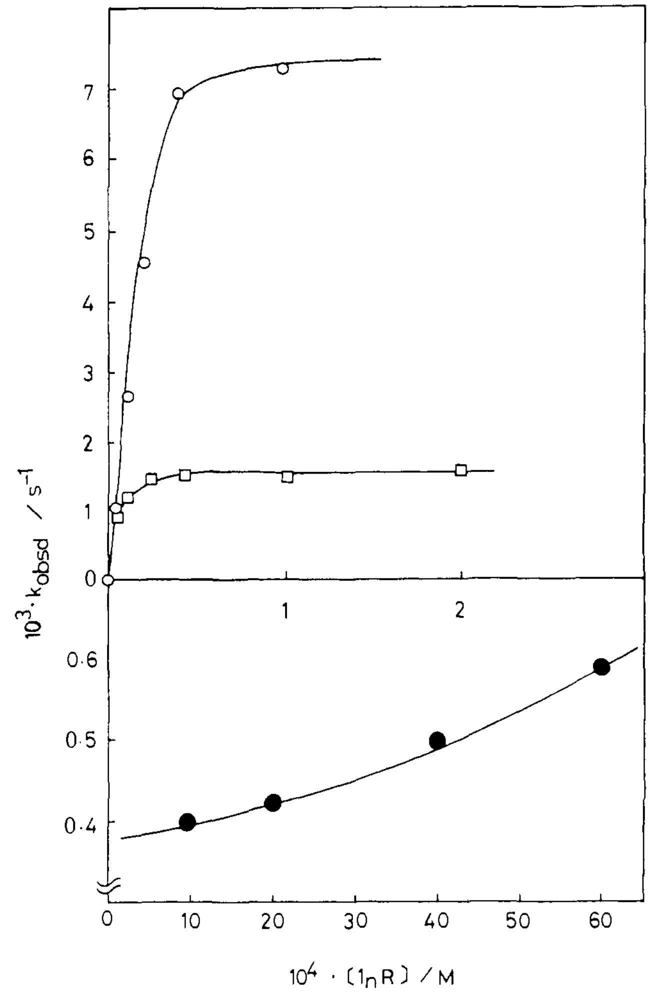


Figure 1. Plots of k_{obsd} vs [1_nR]: 30 °C, [pNPD] = 5.75 × 10^{-5} M, 0.83 vol % acetonitrile; (●) 1_4Me in 0.1 M NaOH, (□) 1_6Me, and (○) 1_6Oct at pH 8.51 with 0.1 M borate buffer, μ = 0.1 with NaCl.

1$_n$R compounds were synthesized from *p*-nitrocalixarenes[11] according to Scheme I.[12] The measurements of surface tension

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