The Methylcyclobutyl Cation. A Simple sp^3-Hybridized Carbocation?

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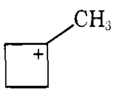
Abstract: From the observation of very low temperature line broadening in the NMR spectrum of the methylcyclobutyl cation **1**, one is forced into a major reinterpretation regarding the structure of this ion. Contrary to the latest literature interpretation, the methylcyclobutyl cation is not in a populated equilibrium with the α-methylcyclopropylcarbinyl cation. In order to rationalize the very unusual $^{13}C^+$ chemical shift in **1**, we consider the possibility of sp^3 hybridization for this cation center. This possibility is examined by considering four additional criteria which might allow one to distinguish sp^2- and sp^3-hybridized carbonium ions: (1) comparisons of the NMR spectra of **1** with spectra of other substituted cyclobutyl cations which are shown to be normal sp^2-hybridized cations; (2) comparisons of ^1H–^1H coupling in **1** with coupling of this type in known sp^2-hybridized cations; (3) comparisons of ^{13}C–^{13}C coupling constants in **1** and in analogous five- and six-membered rings; and (4) comparison of ^+C–CH_3 ^1H chemical shifts in **1** and in sp^2-hybridized model compounds. The possibility of an sp^3-hybridized carbonium ion structure for **1** is considered in light of previous solvolysis results and previous molecular orbital calculations.

The methylcyclobutyl cation **1** is an unpretentious carbonium ion, reasonably well known to those in the trade, but by no means a glamour species of textbooks or of graduate student proposals. Solvolysis studies on suitable systems **2**, e.g., X = Cl, show rates which are abnormally slow compared to larger cycloalkyl ring analogues[1] and this has been attributed to the ring strain (I-strain) involved in the sp^2-hybridized cation. In solvolysis work, the ion **1** has been generally regarded as σ-delocalized, i.e., structure **3**.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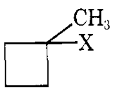
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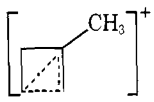
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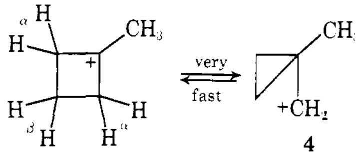
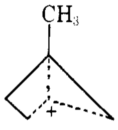
Saunders and Rosenfeld,[2] in 1970, were the first to prepare the observable ion *1*. The ^1H NMR spectrum of this ion (or ions) showed only a single peak for the α and β CH_2 protons and this averaging was attributed to a rapid equilibrium of the methylcyclobutyl cation **1** and the α-methylcyclopropylcarbinyl cation **4**, the equilibrium favoring the cyclobutyl cation.



1 4

Olah and co-workers, in 1972,[3] reported the ^{13}C NMR chemical shifts for "1" and noted, as now expected, that the α and β carbons appeared as a single peak of area three. However, these authors rejected the methylcyclobutyl structure and suggested that the ^{13}C NMR data fitted best a 2-methyl-$C_{2,3}$-cyclopropylcarbonium ion **5**. Equilibration of **5** was assumed to "involve" the methylcyclobutyl cation in order to average all the methylene groups. Very recently, Olah, Hehre, et al.[4] have used an ab initio MO method to calculate the geometry (planar) and the expected ^{13}C carbonium ion center chemical shift (δ 335 ppm) for a methylcyclobutyl cation. On this basis, the ^{13}C NMR spectrum of "1" is now attributed to a very rapid equilibrium of the methylcyclobutyl cation **1** and three degenerate σ-delocalized α-methylcyclopropylcarbinyl cations **4**, similar to the original Saunders and Rosenfeld proposal. However, the ions **1** and **4** are postulated to make about equal contributions to the actual averaged spectrum since the observed quaternary carbon ^{13}C shift is about halfway between that expected for the carbonium ion center in **1** and the corresponding saturated carbon in **4**.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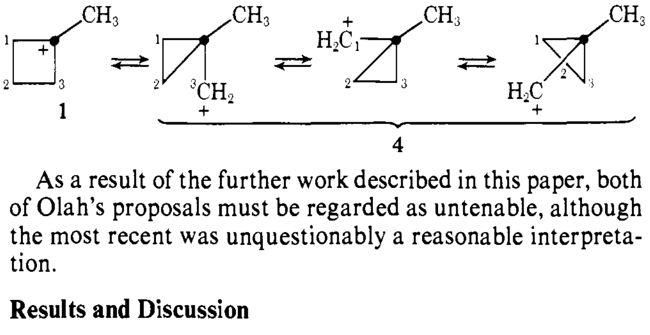

1 4

As a result of the further work described in this paper, both of Olah's proposals must be regarded as untenable, although the most recent was unquestionably a reasonable interpretation.

Results and Discussion

Observation of Line Broadening in the Spectrum (^1H and ^{13}C) for the Methylcyclobutyl Cation 1. Previous workers[2-4] have based interpretations of the structure of **1** on ^1H and ^{13}C NMR spectra showing completely averaged α and β carbons and hydrogens. However, on cooling to low temperatures, both ^1H and ^{13}C spectra show typical intermediate exchange line broadening and finally decoalesce into separate peaks at very low temperatures. The behavior of the ^{13}C NMR spectrum of **1** is shown in Figure 1, where some representative temperatures are shown. Figure 1 also shows the matching computer calculated curves. The genuinely surprising feature of these spectra is that *only* the ring carbons are affected, these finally separating into a two-carbon area peak (α carbons) at δ 71.7 and a single β carbon peak at δ −3.0. Similar results are observed for the 1-*n*-propylcyclobutyl cation **6**. These results absolutely preclude there being *any measurable* amount of the α-methylcyclopropylcarbinyl cations **4** in equilibrium with **1**, i.e., the spectrum is simply that of **1**.[5] The ^1H NMR spectrum of **1** shows similar features. Below −130 °C, the averaged methylene peak broadens, reaches a maximum at *ca.* −146 °C, and finally decoalesces into distinctly separate α and β CH_2 peaks at −158 °C (see Table I for positions). During this process, the methyl peak remains unaffected (except for viscosity broadening).

The preceding observations can be succinctly summarized in a free-energy diagram (Figure 2). The 5.8 kcal/mol $\Delta G^{\ddagger}$ barrier at −100 °C is based on the calculated rate ($k = 2.2 \times 10^5\ s^{-1}$) for the

Table I. ^{13}C and ^{1}H NMR Chemical Shifts[a]

Ion	C^+	C_α	C_β	C_γ	Methyl	Additional
Protonated cyclobutanone	252.6	45.7	11.2			
Protonated cyclopentanone	259.5	41.8	23.6			
Protonated cyclohexanone	251.1	40.8	28.1	23.0		
1	162.0	71.1	−3		25.1	
		(5.41)	(7.30)[b]		(7.13)	
6	165.2	46.3 (av)			13.2	
						39.8 ($\alpha'CH_2$)
						19.2 ($\beta'CH_2$)
7	336.7	63.0	25.8			
8 (−128 °C)	329.4	57.5	23.8	20.7	43.5	
11	297.1	49.9	16.3			55.5 (CH_2)
		42.4				54.4 (CH)
12	298.3	49.5	25.6			53.4 (CH, CH_2)
		44.2				
16	287.3 (C)	56.5	26.2			
	139.7 (CH)	48.3	25.8			
	172.1 (CH_2)					(1.93–2.27, 3 H, complex m)
		(6.27, 4 H)	(7.78, 4 H)			

[a] Chemical shifts are given in parts per million from external Me_4Si. ^{1}H chemical shifts are in parentheses. [b] Position determined by interpolation, since the peak coincides with the methyl peak.

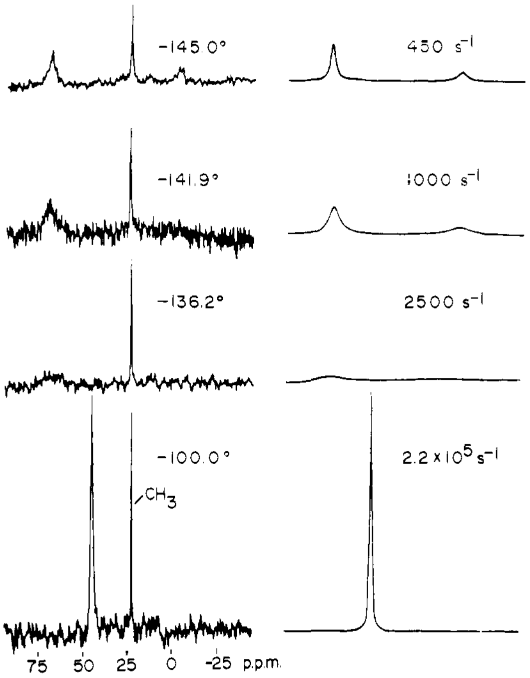


Figure 1. Left: Some selected temperatures showing the observed ^{13}C NMR line broadening in **1**. Right: The computer calculated matching curves generating the corresponding rate constants for the exchange process $\mathbf{1} \rightleftarrows [\mathbf{4}]$.

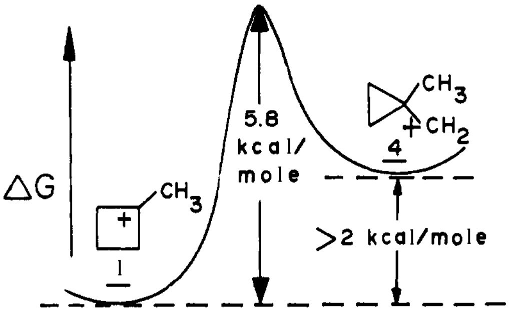


Figure 2. Potential energy diagram for methylcyclobutyl cation 1-α-methylcyclopropylcarbinyl cation **4** interconversion. At −100 °C, the maximum population of **4** is certainly less than 0.5% and this ion makes no detectable contribution to the observed NMR peaks.

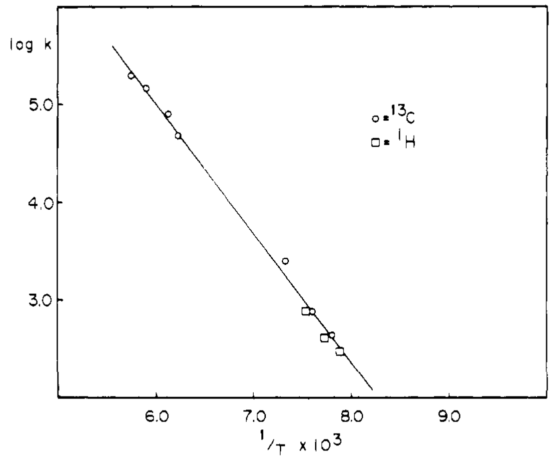


Figure 3. Arrhenius plot of log k for the reaction $\mathbf{1} \rightleftarrows [\mathbf{4}]$ vs. $1/T$.

$$\mathbf{1} \overset{k}{\rightleftarrows} [\mathbf{4}]$$

exchange[7] at this temperature. A complete line-shape analysis of all spectra (^{1}H and ^{13}C) yields rate constants over a 55 °C range. The resulting Arrhenius plot (Figure 3) yields $\Delta H^{\ddagger} = 6.0 \pm 0.1$ kcal/mol, $\Delta S^{\ddagger} = 1 \pm 1$ eu (−100 °C). In Figure 2, the >2 Kcal/mol separation of **1** and **4** is based on two complementary "nonobservations".

1. There is no shift of the $^{13}C^+$ peak with temperature changes. This carbon would exchange with the quaternary α carbon peak of **4**, which can be estimated from Olah's results[3] on the parent cyclopropylcarbinyl cation to resonate at ca. δ 100 ppm. Boltzmann distribution calculations show that as little as 0.5% of **4** would have led to an easily measurable shift of the "averaged" peak (except in the unlikely event that $K = 4/1 = 1$).

2. Calculations show that as little as 0.5% of **4** would have led to an easily observable line broadening of this "if averaged" peak in the coalescence temperature range previously referred to (see Figure 1).

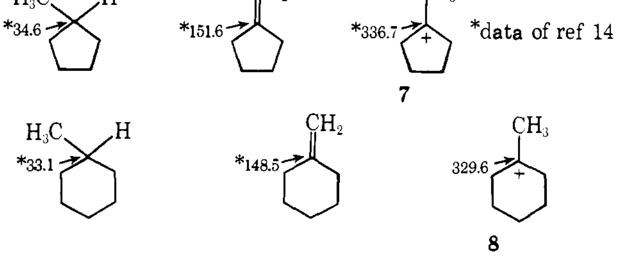
The Figure 2 free-energy diagram illustrates very well the incredibly small barriers associated with some carbonium ion rearrangements. The 5.8 kcal/mol barrier represents the smallest barrier yet "frozen out". However, the reverse barrier, [4] → **1**, must be even smaller (<3.8 kcal/mol). This $\Delta G^{\ddagger}$ value adequately explains why solvolyses of the α-methylcyclopropylcarbinyl system yield methylcyclobutyl products,[1] i.e., under solvolysis conditions also, the rearrangement of **4** is so fast that it exceeds the nucleophile capture rate. The observation of an exceedingly rapid equilibrium between **1** and **4** effectively removes the need to postulate σ-delocalized structures for **1** (i.e., structure **3**).

How Does One Rationalize the Observed NMR Peaks with the Methylcyclobutyl Cation Structure? Saunders and Rosenfeld[2] have shown that the proton chemical shifts are more or less reasonable for a methylcyclobutyl cation structure. Basically, it is the widely abnormal position of the $^{13}C^+$ peak which has caused Olah[3,4] to suggest first a cyclopropylcarbinyl structure **5** and later an equilibrating system of approximately equal parts of **1** and **4**. Just how abnormal this chemical shift is can be seen in Figure 4, where various tertiary alkyl cation $^{13}C^+$ chemical shifts are placed in perspective with Me_4Si.

We believe that the observed spectrum is unquestionably that of a fully developed cation since exactly the same spectrum is obtained in several different strong acid media, e.g., 1-methylcyclobutanol-1:1 SbF_5-FSO_3M-SO_2ClF or 1-chloro-1-methylcyclobutane-SbF_5-SO_2F_2-SO_2ClF. Furthermore, the previously noted independence of chemical shifts to temperature changes also argues against an equilibrium of a cation and a covalent neutral species.

When a chemical shift for a particular atom is at an abnormally high field, one tends to automatically look for a charge delocalization explanation. This should result in other chemical shifts which are abnormally low. This argument has been used by Olah[18] and ourselves[9] to rationalize the relatively modest higher field position of the $^{13}C^+$ peak in 2-methyl-2-norbornyl cations (see Figure 4). In this case, the exo-H_6 proton resonance is found at an abnormally low position.[10] There is, however, *little evidence for any very abnormally low field peaks* in either the ^1H or ^{13}C NMR spectrum of **1**.[11]

Under these circumstances, let us therefore assume that there is *no unusual charge delocalization* in **1**, but let us suppose instead that the ion might be sp^3 hybridized. Chemical shifts in ^{13}C NMR spectroscopy can be broadly grouped depending on the hybridization of the carbon,[12] although this valence bond description provides no particularly useful insights into the theoretical reasons for these changing chemical shifts. Additionally, in carbonium ions, there is a large downfield shift for a carbon peak in going from a neutral carbon to a formally +1 carbon.[13] In a "normal" tertiary ion, the observed $^{13}C^+$ value of ca. δ 330 ppm, compared to ca. δ 30 ppm for the saturated hydrocarbon, can be crudely rationalized as the sum of two downfield-shift terms, a hybridization change $sp^3 \rightarrow sp^2$ and the $0 \rightarrow +1$ charge effect. The following chemical shift comparisons roughly illustrate this:



*data of ref 14

7

8

sp³ hybridization
0 charge

sp² hybridization
0 charge

sp² hybridization
+1 charge

But for the cyclobutyl case, the best agreement with experiment would be obtained by only applying the charge deshielding correction.

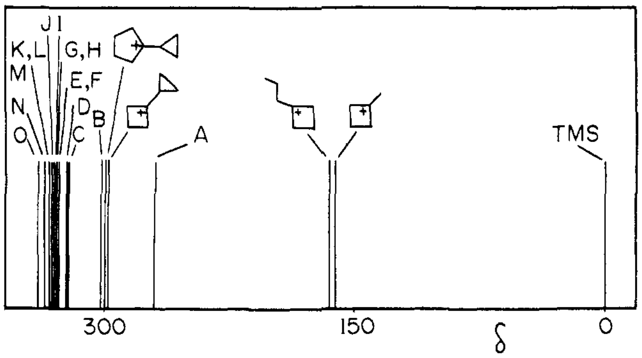
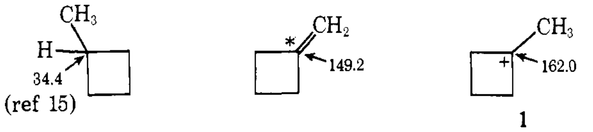


Figure 4. A ^{13}C NMR perspective showing the "normal" $^{13}C^+$ chemical shift range for representative tertiary ions and the position of this peak in alkylcyclobutyl cations, both series relative to Me_4Si. The letters refer to the following ions with literature references in brackets. A = 2-methyl-2-norbornyl [D. P. Kelly, G. R. Underwood, and P. F. Barron, *J. Am. Chem. Soc.*, **98**, 3106 (1976)], B = 1-adamantyl, C = 2-methyl-2-bicyclo [2.1.1] hexyl [G. A. Olah, G. Liang, and S. P. Jindal, *J. Am. Chem. Soc.*, **98**, 2508 (1976)], D = 2-methyladamantyl [G. A. Olah, G. Liang, and G. D. Mateescu, *J. Org. Chem.*, **39**, 3750 (1974)], E = 1-*n*-propylcyclohexyl, F = *n*-butylcyclohexyl, G = methylcyclononyl, H = 1-methylcyclohexyl, I = *tert*-butyl [G. A. Olah and A. M. White, *J. Am. Chem. Soc.*, **91**, 5801 (1969)], J = *n*-propylcycloheptyl, K = ethylcyclooctyl, L = methylcyclooctyl, M = *tert*-amyl (see under I), N = methylcyclopentyl, O = ethylcyclopentyl. We have remeasured some known ions in order to have a consistent set of data. The remainder are unpublished.



1

sp³ hybridized
0 charge

sp² hybridized
0 charge

sp³ hybridized?
+1 charge

The preceding analysis is rather simple-minded in the sense that ^{13}C chemical shifts are not completely understood and it may be possible that the large chemical shift observations are being caused by rather trivial structural variations in **1**. Obviously, further experiments are needed, and we have considered four additional arguments which can be related to the question of the cation hybridization in **1**.

Other Evidence Which Might Distinguish sp^2- vs. sp^3-Hybridized Cations. 1. Perhaps the most dramatic evidence that cyclobutyl cations *can be perfectly normal*, i.e., in C^+ chemical shifts, comes from a comparison of carbon chemical shifts for this ring carbon in cases where conjugative delocalization obviously requires sp^2 hybridization. The comparison is made to cyclopentyl and cyclohexyl cations where we have no doubt of universal sp^2 hybridization in either system (see Chart I).

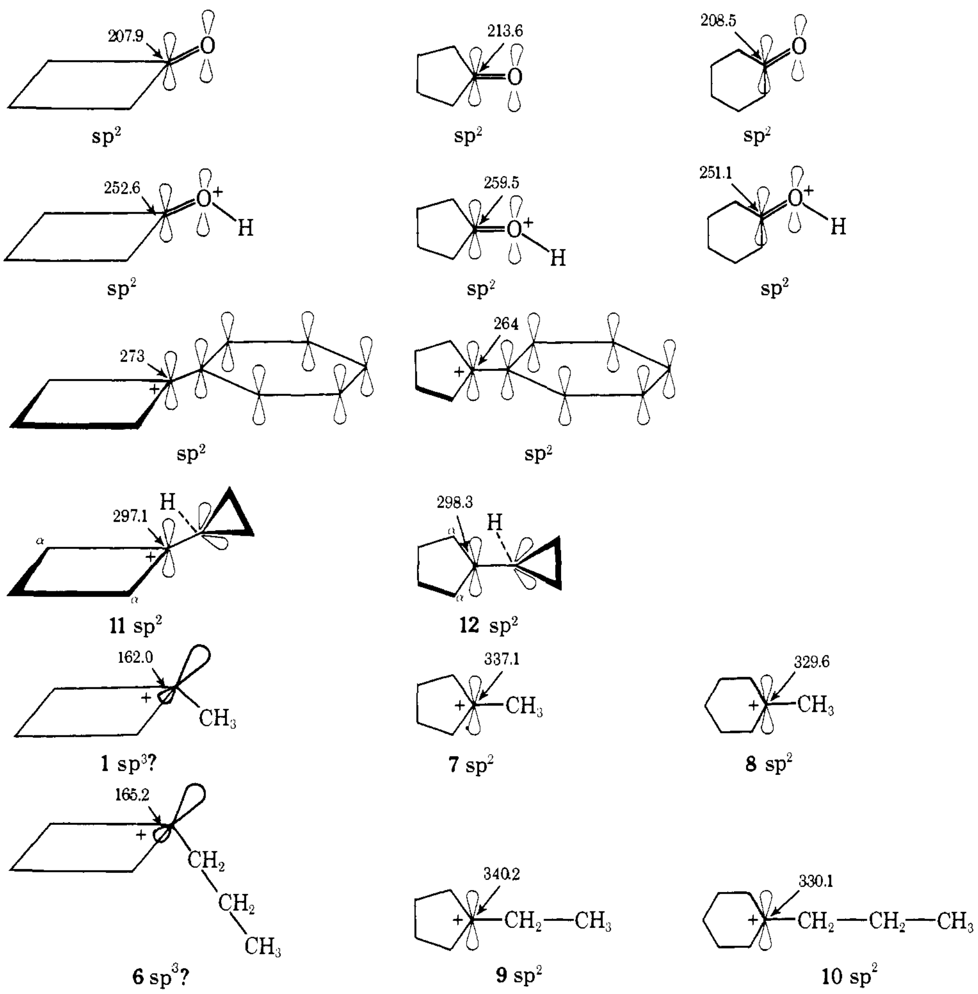
These comparisons find a close parallel in the hybridization change between ammonia (sp^3) and acetamide (sp^2), the latter change because only this hybridization allows one to delocalize the nitrogen lone pair. An equivalent situation occurs in alkyl carbanions (sp^3) and enolates (sp^2).

sp³

sp²

2. Relatively large ^1H-^1H four-bond coupling has been noted in tertiary carbonium ions. For example, in the methylcyclopentyl cation **7**, this value is 4.0 Hz.[17] In an sp^3-hybridized situation, this hyperconjugatively transferred coupling should be severely reduced. Saunders and Rosenfeld[2] report an averaged coupling constant between the α and β methylenes in **1**, and the methyl, of 0.9 Hz. Assuming that the β CH_2

Chart I



Comments

data of ref 16

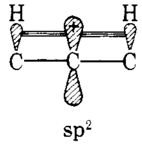
see Table I for chemical shifts of remaining carbons

data of ref 3

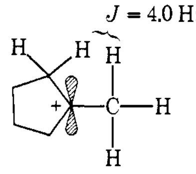
These cations have the expected bisected conformation in both cases, i.e., α CH_2 ring carbons are nonequivalent. See Table I for all chemical shifts.

The methylcyclobutyl cation is thus not unique. Other simple alkyl substituents show similar behavior.

coupling is small, the estimated static coupling for α CH_2-CH_3 is 1.3 Hz, in qualitative agreement with a hybridization change in **1.** One has, however, to be careful in this interpretation since the dihedral angle of the coupling hydrogens may be quite different in the two rings.



sp²



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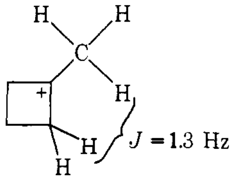
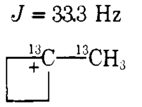


1

3. There are, of course, no direct one-bond $^{13}C^+$-^1H coupling constants in a tertiary carbonium ion. However, ^{13}C-^{13}C coupling constants have also been nicely correlated with the hybridization type of both carbons, varying from the sp-sp value of 150-180 Hz to 30-40 Hz in sp^3-sp^3.[18] Olah and Westerman[19] have shown that the sp^2-sp^3 value is lower in cations than in neutral molecules, but also that the general hybridization relationship holds reasonably well. We have applied this general hybridization criterion by comparing the $^{13}C^+$-$^{13}CH_3$ coupling constants in four-, five-, and six-membered rings. The corresponding sp^3-sp^3 values in the alcohols are also shown. The 33.3 Hz found in **1** is well within the 30-40-Hz range for sp^3-sp^3 hybridization and is also less than the corresponding alcohol value, as expected. However, the $J_{sp^2\text{-}sp^3}$ values for **7** and **8** are virtually identical with that found for **1.** Simply on the basis of analogy, this coupling constant-hybridization criterion supports an sp^2 hybridization for **1.** We have also measured $J_{C^{13}\text{-}H_3^1}$ coupling constants accurately. As expected for constant hybridization, these are very similar in **1, 7,** and **8,** 133.2, 131.7, and 131.6 Hz, respectively. The three-bond ^{13}C (methyl)-^1H (α-methylene) coupling is quite small in all of the ions as evidenced by the sharp lines observed for the ^{13}C (methyl) quartet (line width at half-height 5-14 Hz).



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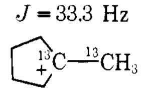

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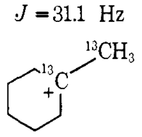

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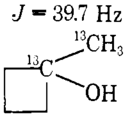

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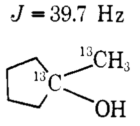

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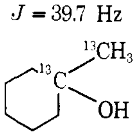

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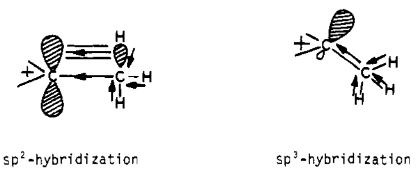
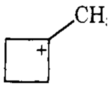
4. The chemical shift of protons β to an sp^2-hybridized carbonium ion center are deshielded by a combination of direct hyperconjugative overlap and inductive withdrawal through the bonds. Although this combination should operate for both ring CH_2 and the ^+C-CH_3 protons, the latter chemical shifts



are probably best for comparison purposes since they should be free of any special ring effects. For an sp^3-hybridized cation, we expect to see mainly the inductive mode. The following comparisons can be made: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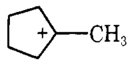
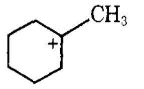
1


τ 6.02(17)
7


τ 6.05(20)
8

The methyl chemical shift in **1** is indeed at abnormally high field so that this criterion is at least consistent with sp^3 hybridization. There are, however, $^+C-CH_3$ chemical shifts in 2-methyl-2-norbornyl cations which come close to the value in **1**.[21]

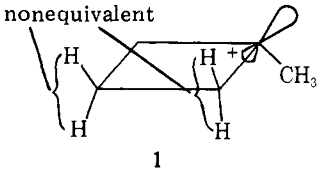
Overall it seems to us that the additional evidence, particularly number 1, supports the idea that the methylcyclobutyl cation is unusual in more ways than just the C^+ chemical shift.

Energy Relationships between sp^2- and sp^3-Hybridized Carbonium Ions. Most elementary organic texts[22] accept the universality of the planar carbonium ion hypothesis and this is of course supported by a considerable body of experimental and theoretical evidence. If one were to look for exceptions to this hypothesis, the methylcyclobutyl cation would look at first sight to be a reasonable choice since the ca. 90° ring angle (or less depending on ring puckering) should be more comfortable within sp^3 hybridization. However, calculations by Schleyer and co-workers[23] show just the opposite. Repulsion between bonding electrons at the cation center is the dominant factor in making carbonium ions planar and this repulsion is increased in going to a tetrahedral geometry (and even more so when one angle is small).

The postulate of a tetrahedral methylcyclobutyl cation is also clearly at odds with ab initio MO calculations on **1**, which are reported to minimize to a planar trigonal structure.[4] However, the estimate of δ 335 ppm for the $^{13}C^+$ center in this trigonal ion seems to us to be quite consistent, since this value is almost equal to the sp^2 methylcyclopentyl value. In all cases where we believe we have definite sp^2 hybridization in the cyclobutyl system (see Table I), the corresponding cyclopentyl value is almost identical. If however, the methylcyclobutyl cation is a planar sp^2-hybridized cation, then the calculated value for the $^{13}C^+$ chemical shift in this ion (δ 335) must rank as one of the worst ever agreements with experiment (the error would be ca. 173 ppm).

It seems clear to us that the theoretical results simply *do not* favor sp^3-hybridized carbonium ions. However, based on their ability to calculate ^{13}C chemical shifts, one should not regard the theoretical calculations as completely definitive.

An sp^3-hybridized structure for **1** also implies that the α and β geminal CH_2 protons should be nonequivalent (with or without ring puckering). Unfortunately, one has to cool the ion to about −158 °C in order to freeze out the methylcyclobutyl structure (see previous Results) and at this temperature, it is impossible to obtain sufficient resolution of the spectrum to check this point. Both α CH_2 protons are contained within the same very broad peak and the β CH_2 protons are obscured by the methyl protons.



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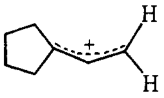
It also seems probable that sp^3- and sp^2-hybridized methylcyclobutyl cations would be distinct entities, the latter necessarily present in undetectably small amounts. Thus, the lack of temperature dependence of the $^{13}C^+$ chemical shift implies no populated equilibrium with an sp^2-hybridized form. In the sp^2-hybridized 1-cyclopropylcyclobutyl cation **11** case, this ion is extraordinarily sensitive, ring opening to the cyclopentylallyl structure **16** occurring at about −100 °C ($t_{1/2}$ = 600 s at −93.5 °C, $\delta G^{\ddagger}$ = 12.7 kcal/mol). It seems at least possible that this cyclopropyl ring opening might occur via a relatively low energy sp^3-hybridized intermediate where charge delocalization to the β-cyclopropyl position was considerably reduced, hence making these more susceptible to electrophilic attack (and ring opening).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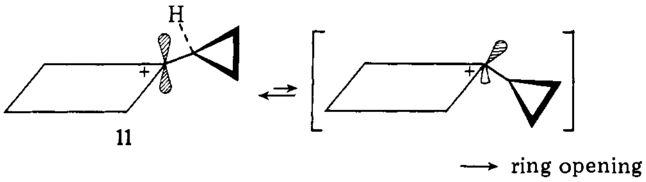
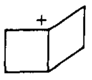


Relevance of Observable Ion Work to Previous Solvolysis Data on Methylcyclobutyl Cation. The very fact that an ion might prefer sp^3 hybridization is also an admission that the ion is relatively unstable, since, all things being equal, sp^2 hybridization is much preferred. The slow solvolysis rate of this system is therefore consistent with I-strain raising the energy of the sp^2-hybridized ion above that for the less strained but otherwise intrinsically less stable sp^3-hybridized form. It may be noted in this connection that the 1-phenylcyclobutyl system behaves much more normally in solvolyses,[24] just as this ion itself seems relatively "normal".

Sunko et al.[1d] have also reported that the solvolysis β-deuterium isotope effect in **1** (CD_3 vs. CH_3), assumed to be of a hyperconjugative origin,[25] is much smaller than normal (k_H/k_D = 1.068 ± 0.045). This is attributed to a σ-delocalization in **1** (i.e., structure **3**) but it seems to us that sp^3 hybridization of the cation would also decrease k_H/k_D by decreasing the hyperconjugative interaction.

Conclusions

The methylcyclobutyl cation has been shown to not be in a populated equilibrium with the α-methylcyclopropylcarbinyl cation. This fact alone necessitates a major reinterpretation of the NMR spectrum. We believe that the methylcyclobutyl cation should be rescued from relative obscurity and at least considered as a possible candidate for the simplest example of an observable sp^3-hybridized carbonium ion. There is simply no point, however, in trying to be dogmatic about interpretations such as those discussed here. Other explanations cannot be ruled out and it should be noted that theoretical evidence certainly does not support such an idea. Perhaps the most useful result of this work will be to force an examination of the utility of ^{13}C chemical shifts in making deductions concerning the electron delocalization in carbonium ions. In this regard, we believe that it might be useful to attempt to prepare cations of relatively fixed sp^3 geometry. The most relevant cases to this work would be **17** and **18**. However, cations types such as **19**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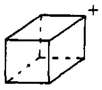
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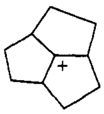
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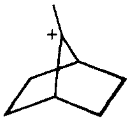
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and **20** have shown unusual solvolytic behavior[23] and it would also be interesting to obtain their ^{13}C NMR spectrum.

Experimental Section

Preparation of Ions. The described ions were prepared either from the corresponding alcohol or chloride.

The alcohol (150–200 mg) was dissolved in $CFCl_3$ (0.4 mL) and added slowly to a solution of 1:1 SbF_5–FSO_3H (1.5 mL) in SO_2ClF (2.5 mL) cooled to −115 °C. Ions which were more sensitive to temperature were obtained by using the chloride as precursor. The chloride (150–200 mg) was dissolved in $CFCl_3$ (0.4 mL) and added slowly to a solution of SbF_5 (0.75 mL) in SO_2ClF/SO_2F_2 (2 mL/1–2 mL). In these cases the ions were prepared at a temperature lower than −135 °C (methylcyclopentane–liquid nitrogen slush). The protonated ketones were obtained by adding a solution of the cycloalkanone (200 mg) in $CFCl_3$ (0.4 mL) to FSO_3H (3 mL) cooled to −78 °C.

NMR Spectroscopy. ^{13}C NMR spectra were recorded on a Bruker WH-90 spectrometer equipped with a Nicolet B-NC12 computer, a broad band decoupler, and a variable temperature probe. The temperature was measured by inserting a tube filled with 4 mL of silicone oil and containing a thermocouple into the probe. The reported values were obtained by averaging the readings before and after the accumulation of spectra. Spectra recorded during temperature variations larger than 1 °C were discarded.

The field/frequency stabilization of the spectrometer was obtained by locking on the ^{19}F NMR signal of SO_2ClF, $CFCl_3$, or FSO_3H. Some precursors were measured in $CDCl_3$, in which cases the ^{2}H NMR signal was used. All chemical shifts reported are referenced to external Me_4Si and are accurate to ±1 Hz. This same error also applies to ^{13}C coupling constants. Typically 4000–8000 transients were necessary to obtain satisfactory spectra. The flip angle was 40° (8 μs). Usually no delay time was allowed between the transients. The coupling constants J_{C-H} were measured on ^{13}C enriched material. For ^{1}H NMR spectra, the same lock materials were used; spectra are referenced to the same standard.

1-Methylcyclobutanol, 1-methylcyclopentanol, and 1-methylcyclohexanol were prepared from the commercially available ketones by Grignard reaction. ^{13}C NMR spectra of the distilled materials were recorded. 1-Methylcyclobutanol ($CDCl_3$): 72.8, 37.6, 26.8, 11.6 ppm. 1-Methylcyclopentanol ($CDCl_3$): 79.7, 41.1, 28.0, 23.8 ppm. 1-Methylcyclohexanol ($CDCl_3$): 69.7, 39.4, 29.4, 25.5, 22.6 ppm.[26]

^{13}C-Enriched 1-methylcycloalkanols were also obtained by Grignard reaction, using 90% labeled methyl iodide (Merck Sharp and Dohme). Reactions were carried out on 5.6 mmol of cycloalkanone and 7 mmol of methyl iodide. The reaction products were not distilled, as ^{13}C NMR spectroscopy revealed only minor impurities. 1-Methylcyclobutanol: J_{CC} = 39.7, J_{CH} = 125.0 Hz. 1-Methylcyclopentanol: J_{CC} = 39.7, J_{CH} = 125.5 Hz. 1-Methylcyclohexanol: J_{CC} = 39.7, J_{CH} = 125.1 Hz.

1-Cyclopropylcyclobutanol and 1-cyclopropylcyclopentanol were obtained by reaction of the corresponding ketones with cyclopropyllithium. A solution of 5 g of cyclopropyl bromide in 10 mL of ether was added to 7 g of lithium (containing 1% Na). The mixture was allowed to react for 1 h. Unreacted lithium was then removed and the solution was cooled to 0 °C. A solution of 2.0 g of cycloalkanone in 10 mL of ether was added slowly and the solution was then allowed to warm to room temperature for 20 min. The reaction mixture was then poured onto ice and extracted with ether, and the ether layer was dried with $MgSO_4$. The excess solvent was removed and the crude reaction material was distilled under vacuum. 1-Cyclopropylcyclobutanol: 57–58 °C (10 mm).[27] 1-Cyclopropylcyclopentanol: 67–68 °C (10 mm). Anal. Calcd for $C_8H_{14}O$: C, 76.15; H, 11.1. Found: C, 75.3; H, 10.5. ^{13}CNMR 1-cyclopropylcyclobutanol ($CFCl_3$), 75.1, 34.9, 19.5, 12.8, 1.1 ppm; 1-cyclopropylcyclopentanol ($CFCl_3$), 81.8, 39.2, 24.3, 20.4, 1.6 ppm.

1-Chloro-1-cyclopropylcyclobutane was obtained by reacting equimolar amounts of 1-cyclopropylcyclobutanol and PCl_5 in $CFCl_3$ solution at −20 °C. After 90 min, the solution was decanted and filtered through glass wool. The excess $CFCl_3$ was evaporated by a nitrogen stream. The product obtained was nearly pure and was used without further purification: ^{13}CNMR ($CFCl_3$) 72.4, 37.1, 21.9, 16.5, 4.2 ppm.

1-Chloro-1-methylcyclobutane was obtained by adding HCl to methylenecyclobutane following the procedure of Brown and Borkowski.[1a] The chloride obtained was used without further purification: ^{13}CNMR ($CDCl_3$) 65.7, 40.0, 30.4, 15.0 ppm.

Acknowledgment. We thank the National Research Council of Canada for generous financial support.

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(2) M. Saunders and J. Rosenfeld, *J. Am. Chem. Soc.*, **92**, 2548 (1970).

(3) G. A. Olah, C. L. Jeuell, D. P. Kelly, and R. D. Porter, *J. Am. Chem. Soc.*, **94**, 146 (1972).

(4) G. A. Olah, R. J. Spear, P. C. Hiberty, and W. J. Hehre, *J. Am. Chem. Soc.*, **98**, 7470 (1976).

(5) Perhaps this statement is overly dogmatic since, strictly speaking, one has only proof that the ion is not a mixture of **1** and **4**. Why not assign the structure as **4**, as originally proposed by Olah?[3] This would require that the $-^{+}CH_2$ carbon in **4** resonate at δ would be true of the $-^{+}CH_2$ protons. Evidence from solvolysis[1] clearly favors a lower energy for the methylcyclobutyl cation and there is often an excellent correlation between observable ions and solvolysis intermediates.[6] Finally, molecular orbital calculations place **1** at a lower energy than **4**.[4] One could argue (with, however, no evidence) that a second equilibrium exists between 1 and an α-methylcyclopropylcarbinyl species in which the β carbons are not equivalent, perhaps something like **5**. In this case, one could still expect to see temperature dependent chemical shifts unless, very fortuitously, K = 1. This is too improbable to warrant much further consideration.

(6) T. S. Sorensen, *Acc. Chem. Res.*, **9**, 257 (1976).

(7) The exchange matrix is either

$$\left|{}_{1/2}{}^{1/2}\right|$$

or

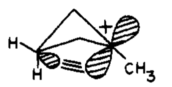
$$\left|{}_{2/3}{}^{2/3}\right|$$

The latter implies that the degenerate rearrangements in **4** are faster than the **1** ⇄ [**4**] rate. The form of the line broadening is identical in either case and using either one makes very little difference (ca. 0.1 kcal/mol) to the reported $\Delta G^{\ddagger}$ value. We have arbitrarily used the former.

(8) G. A. Olah, J. R. DeMember, C. Y. Lui, and R. D. Porter, *J. Am. Chem. Soc.*, **93**, 1442 (1971).

(9) R. Haseltine, N. Wong, T. S. Sorensen, and A. J. Jones, *Can. J. Chem.*, **53**, 1891 (1975).

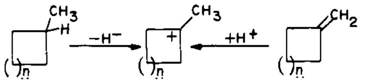
(10) The most tempting analogy of this type for **1** would be a 1,3-delocalization of the following type (i). This would perhaps help to rationalize the extremely



i

high field "cyclopropane-like" position of the β carbon in **1**. However, there is no accompanying evidence in **1** that the β hydrogens are particularly deshielded.

(11) One very approximate way to test the whole molecule for charge delocalization (into both H and C atoms) is to simply sum the chemical shift values for all atoms. These can then be compared to the summed values for neutral hypothetical progenitors, i.e.



When we do this for the series n = 1, 2, and 3, leaving out the offending C^+ shifts, we find no compensating lower field trends in the cyclobutyl system compared to the other two. In fact, just the opposite occurs. At best, one can find a slightly lower chemical shift for the α carbons in **1**, compared to the five- and six-membered rings.

(12) E. Breitmaier and W. Voelter, "^{13}C NMR Spectroscopy", Verlag Chemie, Weinheim/Bergstr., Germany, 1974, p 71.

(13) In the π-charge density expression of Spiesecke and Schneider, a value of ca. 160 ppm/π electron was deduced: H. Spiesecke and W. G. Schneider, *Tetrahedron Lett.*, 468 (1961).

(15) S. Berger, F. R. Kreissl, D. M. Grant, and J. D. Roberts, *J. Am. Chem. Soc.*, **97**, 1805 (1975). We thank Professor Roberts for kindly providing these unpublished data.

(16) F. J. Weigert and J. D. Roberts, *J. Am. Chem. Soc.*, **92**, 1347 (1970).

(17) G. A. Olah, J. M. Bollinger, C. A. Cupas, and J. Lukas, *J. Am. Chem. Soc.*, **89**, 2692 (1967).

(18) Reference 12, p 103.

(19) G. A. Olah and P. W. Westerman, *J. Am. Chem. Soc.*, **96**, 2229 (1974).
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(22) A good historical discussion can be found in E. L. Eliel, "Stereochemistry of Carbon Compounds", McGraw-Hill, New York, N.Y., 1962, pp 372–380.
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(26) Y. Senda, J. Ishiyama, and S. Imaizumi, *Tetrahedron*, **31**, 1601 (1975).
(27) M. Hanack and H. Eggensperger, *Tetrahedron Lett.*, 1975 (1963).

Carboxylate Anion Stabilization of a Developing Carbonium Ion in Acetal Hydrolysis. Hydrolysis of Phthalaldehydic Acid Acetals

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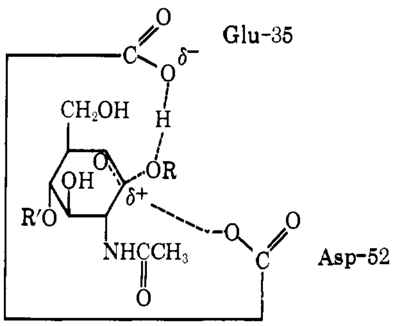
Abstract: The rates of phenol release from a series of 2- and 4-carboxybenzaldehyde methyl substituted phenyl acetals and their corresponding methyl esters have been measured in 50% dioxane-H_2O (v/v) at 30 °C ($\mu = 0.5$ M). With the ester acetals, the second-order rate constant for hydronium ion catalysis decreases as electron withdrawal in the leaving group increases ($\rho = -0.5$), and general acid catalysis is observed. The corresponding carboxylic acid acetals give pH-rate constant profiles showing hydronium ion catalysis of the reaction of the un-ionized species and a faster reaction which is either hydronium ion catalyzed reaction of the anionic species or the kinetically equivalent intramolecular general acid catalysis. The latter possibility is supported by a positive ρ value (+0.3) and by the absence of buffer acid catalysis in the reactions of any of the 2-carboxyl substituted acetals. Rate enhancements for carboxyl group participation are of the order of 10^2–10^3 in comparison with the respective methyl esters. A pH-independent reaction is observed at high pH with the 3,5-dichlorophenyl acetals. This reaction is a unimolecular decomposition to a stabilized carbonium ion, and proceeds 100 times faster with the ortho carboxyl substituted acetal than with the para carboxyl substituted compound. Thus, carboxylate anion stabilization of a developing carbonium ion has been unambiguously demonstrated and shown to be capable of generating significant rate enhancements, but only in reactions where there is a relatively large amount of C–O bond breaking in the transition state. The implications of these results for lysozyme-catalyzed reactions are discussed.

The complete amino acid sequence of the glycosidic enzyme lysozyme has been determined.[1,2] Also, the three-dimensional structure of the enzyme has been elucidated by x-ray crystallographic analysis at 2 Å resolution.[3,4] Carboxyl groups from glutamic acid-35 and aspartic acid-52 are located at the active site. A number of mechanisms have been suggested for lysozyme, all of which involve general acid catalysis by glutamic acid-35.[5] The mechanism which has received the most attention and support utilizes general acid catalysis by Glu-35 and electrostatic stabilization of the developing glycosyl carbonium ion by the Asp-52 carboxylate anion (I).[4,5]



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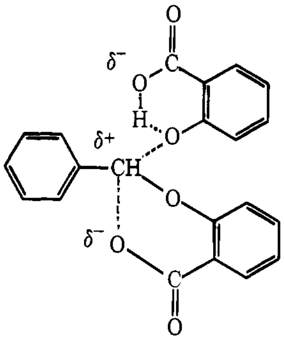
General acid catalysis by buffer acids has been observed in the hydrolysis of a number of simple acetals,[6–10] and the structural features in the acetal that will facilitate such catalysis have been determined.[11,12] Intramolecular general acid catalysis by a neighboring carboxyl group will give rise to rate enhancements of 10^5–10^6 in hydrolysis of salicylic acid acetals.[13] Benzaldehyde disalicyl acetal, in which there are two properly positioned carboxyl groups, has a bell-shaped pH-rate constant profile for release of salicylic acid and displays a rate enhancement of 3×10^9 in comparison with hydrolysis of the corresponding dimethyl ester.[14] Thus, the mechanism for the reactive monoanionic species (II) could be formally analogous to that suggested for lysozyme. The product of the reaction is the stable acylal. However, it was shown by placing one of the carboxyl groups in the para position that the maximum contribution of the second carboxyl to the rate enhancement could be no more than a factor of 50. Intramolecular general acid catalysis by a carboxyl group has also been suggested in hydrolysis of 2,3-(phenylmethylenedioxy)benzoic acid,[15] 2-carboxyphenyl β-D-glucoside,[16] and 2-methoxymethoxybenzoic acid,[16] although the mechanism for hydrolysis of the latter compound is in dispute,[17,18] No evidence was found for electrostatic participation by a second carboxyl in hydrolysis of



II