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An ab Initio Investigation of the Stabilization of Selected β-substituted Ethyl Cations and α-substituted Methyl Cations

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Conclusions

Changes in PA as R is homologated in *n*-alkyl RMeNNMeR are approximately the same as changes in vIP. R homologation (mainly from R) stabilizes one NH^+ about the same as two R's stabilize the two half-positive $N^{\bullet+}$ of the cation radical as Aue and co-workers previously showed it does for amines.[6b] Cyclization of the alkyl groups in rings, which changes the lone-pair, lone-pair hybridization and rotational angle, causes much larger effects on vIP than on PA. The changes in gas-phase $D(N^+–H)$ in cyclic hydrazines **8–16** correlate highly with changes in acetonitrile solution $E^{\circ\prime}$ values, suggesting that both are principally determined by changes in hydrazine cation-radical stabilization. Changes in solvation energy as the alkyl groups are changed for both proton transfer in water and for electron transfer in acetonitrile prove to be nearly linear with the gas-phase "alkyl group inductive" parameter *n*(eff). This behavior is not consistent with important specific solvation with the nitrogen lone pairs in the neutral form or with the formally positive nitrogens in the cationic forms for either equilibrium for these rather hindered compounds, even in water. It is also not consistent with the nitrogens actually bearing the positive charge present on the molecules. The positive charge is dispersed onto the alkyl substituents, and approach of solvent near the nitrogens is not required.

Experimental Section

Compound preparation[1b] and the NBS pulsed high-pressure mass spectrometric system[16] have been previously described. Proton-transfer equilibria were studied at 0.1 to 1% hydrazine concentration in methanol as a carrier gas, which produces $CH_3OH_2^+$ as a proton source upon ionization, at 550 K (277 °C). Errors in equilibria measured are estimated to be approximately 0.02 eV (0.5 kcal/mol). Hydrazine pK_a values were measured by titration of 2–4 mM solutions of the hydrazine in dearated, triply distilled water thermostated at 25.0 °C and containing 0.1 M tetraethylammonium perchlorate as supporting electrolyte, using 10% perchloric acid solutions. **10** was studied as the hydrochloride salt, and titrated with 10% NaOH. pK_a values were determined from the inflection point of pH (measured by an Orion Instruments Model 811) versus volume of titrant added plots,[17] and the error is estimated at no more than 0.05 pK unit.

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An ab Initio Investigation of the Stabilization of Selected *β*-Substituted Ethyl Cations and *α*-Substituted Methyl Cations

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Abstract: In this study, we calculate the stabilization of *β*-substituted ethyl cations (R = H, Li, BeH, BH_2, CH_3, NH_2, OH, F, Na, MgH, AlH_2, SiH_3, PH_2, SH, Cl) and *α*-substituted methyl cations (R = H, Li, CH_3, NH_2, OH, F, Na, SiH_3, PH_2, SH, Cl) in order to obtain a relationship between the nature of the substituent and the degree of stabilization of the cation. Results show that the stabilization energy is related to the electronegativity of the *β* substituents, but not the *α* substituents. The rotational barrier of the *β*-substituted ethyl cation is linearly related to the Mulliken population of the 2p(C+) orbital. We found that the stabilization energy is linearly related to the ionization potential of the *α*- and PLA *β*-substituted radicals, and the HOMO energies of the PLA *β*-substituted radical are linearly related to the corresponding ionization potentials. Trends in the stabilization by second- and third-row substituents are discussed.

A wide variety of theoretical results have been presented which examine substituent effects in carbocation systems.[1-14] Simple theoretical models have been studied as a means of interpreting experimental results obtained for larger, more complex carbocations. As a result, a relatively clear qualitative picture has emerged of the factors that can affect the stability of carbocations.[12]

One way of assessing the stability of a carbocation is to use an isodesmic reaction such as eq 1, where SE+ (SE+ is the

$$RCH_2CH_2^+ + HCH_2CH_3 \xrightarrow{SE+} RCH_2CH_3 + HCH_2CH_2^+ \quad (1)$$

"stabilization" energy of the cation) is defined as ΔE.[12] (Here we use a *β*-substituted ethyl cation as an example; an analogous equation would be used for methyl cations.) When SE+ is greater than zero the cation $RCH_2CH_2^+$ is more stable than the corresponding unsubstituted one, $HCH_2CH_2^+$. It has been determined that two distinct types of substituents are capable of stabilizing the cation center. The first consists of substituents more electropositive than H (e.g., BeH, BH_2, AlH_2) that can act as *σ*-donors and *π*-acceptors. For the case of carbocations the *π*-acceptor function is of less importance than for radicals or carbanions.[12]

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* Author to whom correspondence should be addressed.

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The second group consists of species more electronegative than H (e.g., NH_2, OH, Cl) that can act as σ-acceptors and π-donors. In either case some amount of stabilization is generally expected.

However, more detailed studies have revealed that trends can be complicated by the competition of other factors with the simple electronegativity difference. For α-substituted methyl cations electronegativity differences would predict that the stabilization by first-row electropositive substituents would increase in the order $BH_2 < BeH < Li$. In geometries where hyperconjugation (see below and ref 12) with the formally empty 2p(C+) orbital is symmetry forbidden this trend is borne out. However, in geometries where the BH bonds of BH_2 can overlap the 2p(C+) orbital, thus allowing for possible hyperconjugation, one finds a reversal in stabilization energies in the above series, that is $BeH < BH_2 < Li$.[12] In addition, differences in stabilization by first- and second-row substituents may be not solely related to electronegativity differences and may involve such factors as the relative sizes of substituent orbitals and changes in bond lengths.

In the present paper our goal is to quantitatively systematize the calculated stabilization energies in first- and second-row β-substituted ethyl cations (R = H, Li, BeH, BH_2, CH_3, NH_2, OH, F, Na, MgH, AlH_2, SiH_3, PH_2, SH, Cl) and α-substituted methyl cations (R = H, Li, CH_3, NH_2, OH, F, Na, SiH_3, PH_2, SH, Cl). The objective is to obtain a relationship between the nature of the substituent and the degree of stabilization of the cation. In particular, we will examine the correlation between the stabilization energy of the cation and (a) the electronegativity of the substituent, (b) the Mulliken population of the formally empty atomic orbital on the α-carbon, and (c) the ionization potential of the corresponding radical. Other studies along these lines should be noted. Spitznagel et al.[15] have examined the relationship between electronegativity of a substituent and the stabilization of methyl anions. They found essentially linear relationships between stabilization energy and electronegativity for the two different classes of substituents discussed above, with differing slopes for the two classes. Rodriquez and Hopkinson[13] have obtained a linear relationship between the π-population on the cationic carbon and the stabilization energy in α-substituted ethyl cations. Hopkinson and Lien[8] have also compared the stabilization for a given substituent in the series CX^+, CHX^+, and CH_2X^+ and found that the greatest stabilization is obtained for CX^+, with the stabilization decreasing as H's are added to the cation center.

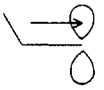
Methods

Restricted Hartree–Fock (RHF) wave functions were used for the cations and neutral molecules. Restricted open-shell Hartree–Fock (ROHF) wave functions were used for the radicals examined. All calculations were done with the program GAMESS.[16] The geometries of the α-substituted species were optimized with a 6-31G** basis set[17] (d functions on all heavy atoms, p functions on all hydrogens). The geometries of the β-substituted cations, radicals, and neutral molecules were optimized with a 6-31G* basis set[17] (d orbitals included on all non-hydrogen atoms). The hydrogen p functions were not included in the calculation for the ethyl cations for computational simplicity. Their removal is expected to have only a minor effect on the calculated geometries and energies. β-Substituted cations were studied in both the PLA and PER conformations (see below), but the geometry of the PER was not optimized because of the potential formation of a non-classical bridged structure.[18] Instead, the bond lengths from the optimized PLA conformation were used to construct the PER cation, with a tetrahedral (109.47°) arrangement about the β-carbon and a trigonal planar (120°) arrangement at the α-carbon. A single energy calculation was performed on the PER cation.

Results and Discussion

In what follows we make frequent use of the terms "induction" and "hyperconjugation". Before proceeding to our results we establish operational definitions for these quantities.

Qualitatively, hyperconjugation can be described as an energy lowering that results from the through-space delocalization of electrons (**1**), and induction can be taken as an energy lowering resulting from through-bond delocalization of electrons (**2**). These definitions have been used by other workers.[1-4]



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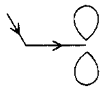

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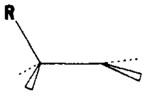
The magnitude of induction varies with the bond length but not the bond angle. The magnitude of hyperconjugation, on the other hand, depends on both bond angle and the dihedral angle between the vacant α-center p orbital relative to the R–C(β) bond. In the carbocation systems, hyperconjugation is at a maximum when the bond that is donating electrons is alligned with the formally empty 2p(C+) orbital on the cationic center. Conversely, minimum hyperconjugation occurs when the bond and the atomic orbital are orthogonal.

In studies of β-substituted ethyl cations by Apeloig et al.,[3] two configurations of the ethyl cation were examined (**3** and **4**), perpendicular (PER) and planar (PLA), respectively.



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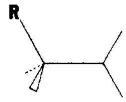

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One expects that hyperconjugation with the R–C bond occurs in the PER conformation but does not occur in the PLA conformation. The Mulliken populations (that is, the relative electron populations) of the 2p(C+) orbitals reported by Apeloig et al.[3] support this prediction. The 2p(C+) populations in the PLA orientation were fairly constant, while the populations in the PER orientations decreased as R became more electronegative.

In the results below we report the relative stabilization energy (SE+) of each cation. These values were obtained from the isodesmic reactions 1 and 2. SE+ is the stability of the cation

$$RCH_2^+ + HCH_3 \xrightarrow{SE+} RCH_3 + HCH_2^+ \qquad (2)$$

relative to the unsubstituted methyl or ethyl cation (in the same conformation). The rotational barrier, that is, the energy difference PLA − PER,[3,5] is a useful value for β-substituted cations. As the bond lengths are kept the same in the PLA and PER calculations, we assume that the stabilization energy due to induction is cancelled out in the rotational barrier. Following Apeloig et al.[3] we take this rotational barrier as a measure of the stabilization of the cation due to hyperconjugation with the R–C bond, since, as noted above, hyperconjugation with the R–C bond can occur in the PER conformation but not the PLA conformation.

Turning to our results, we have used three basic schemes to systematize the trends in the stabilization energies. We relate the calculated stabilization energies to (a) substituent electronegativity, (b) relative Mulliken populations in the 2p(C+) orbitals in the PER and PLA orientations, and (c) the ionization potentials (IP) of the corresponding radicals. These factors are examined in order below.

Electronegativity and Stabilization. The relationship between electronegativity and stabilization energy can be examined quantitatively by rewriting (1) as

$$\begin{tikzcd}
RCH_2CH_2^+ + HCH_2CH_3 \arrow[r, "SE+"] \arrow[d, "\Delta E_1"] & RCH_2CH_3 + HCH_2CH_2^+ \arrow[d, "\Delta E_3"] \\
R\bullet\ \bullet CH_2CH_2^+ + H\bullet\ \bullet CH_2CH_3 \arrow[r, "\Delta E_2"] & R\bullet\ \bullet CH_2CH_3 + H\bullet\ \bullet CH_2CH_2^+
\end{tikzcd} \qquad (3)$$

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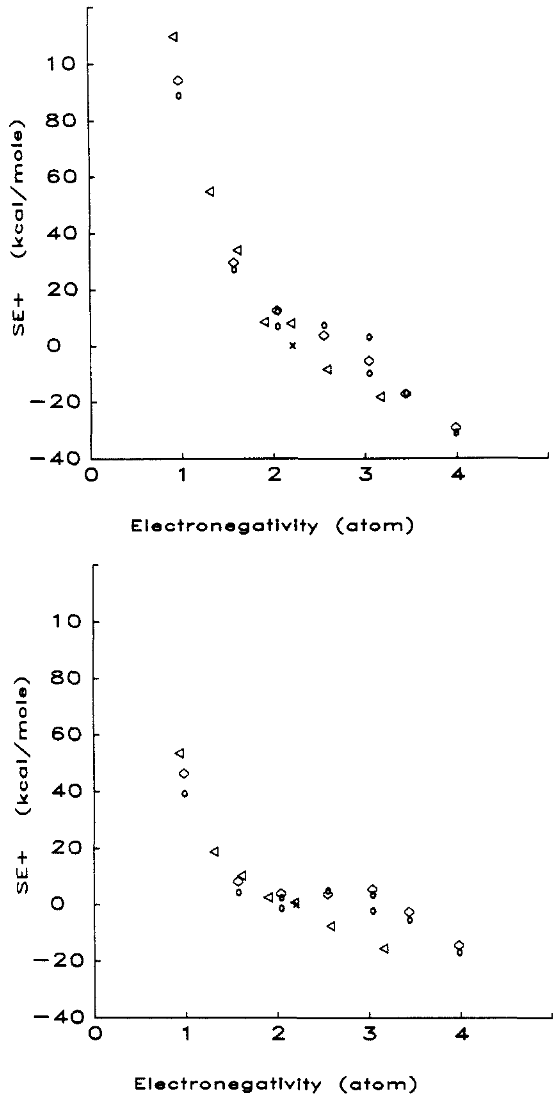

Figure 1. (a) Stabilization energy (kcal/mol) of PER β-substituted ethyl cations versus Pauling electronegativity of the non-hydrogen atom of the substituent: X = hydrogen substituent; ◇ = second-row substituents; Δ = third-row substituents; O = Apeloig et al.[3] second-row data, 4-31G basis set. (b) Stabilization energy (kcal/mol) of PLA β-substituted ethyl cations versus Pauling electronegativity of the non-hydrogen atom of the substituent.

Since ΔE_2 is zero, the stabilization energy is the difference of the dissociation energies ΔE_1 and ΔE_3. That is

$$SE_\beta + = D(\text{R-CH}_2\text{CH}_2{}^+) + D(\text{H-CH}_2\text{CH}_3) - D(\text{R-CH}_2\text{CH}_3) - D(\text{H-CH}_2\text{CH}_2{}^+) \quad (4)$$

Similarly for (2)

$$SE_\alpha + = D(\text{R-CH}_2{}^+) + D(\text{H-CH}_3) - D(\text{R-CH}_3) - D(\text{H-CH}_2{}^+) \quad (5)$$

From Pauling's definition of electronegativity

$$D_{AB} = a(\chi_A - \chi_B)^2 + (D_{AA} + D_{BB})/2 \quad (6)$$

for the neutral molecule, where D_{IJ} is the dissociation energy of the I–J bond, "a" is a constant, and χ_I is the electronegativity of element I. If this is generalized slightly to replace the electronegativities of the elements by the electronegativities of functional groups, and (6) is assumed to hold for ions, then (6) may be substituted into (4) and (5) and the results may be written as

$$SE_\beta + /2a = (\chi_R - \chi_H)(\chi_{\bullet CH_2CH_2{}^+} - \chi_{\bullet CH_2CH_3}) \quad (7)$$

$$SE_\alpha + /2a = (\chi_R - \chi_H)(\chi_{\bullet CH_2{}^+} - \chi_{\bullet CH_3}) \quad (8)$$

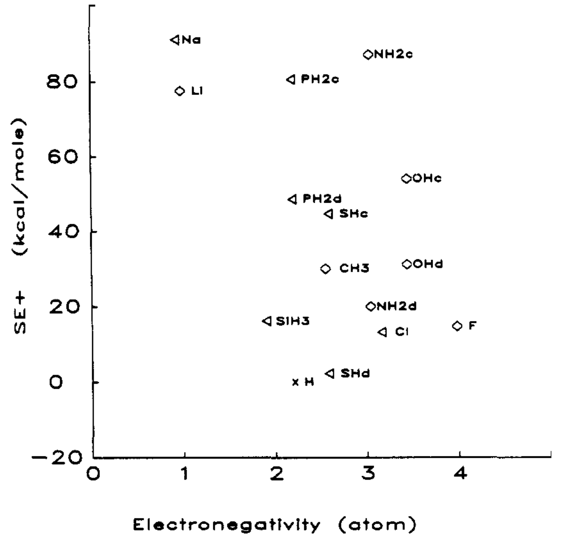

Figure 2. Stabilization energy (kcal/mol) of α-substituted methyl cations versus Pauling electronegativity of the non-hydrogen atom of the substituent.

These equations show that the SE+ would be a linear function of χ_R in this extension of the Pauling model. Interestingly, in the original Pauling model $\chi_{\bullet CH_2CH_2{}^+}$ and $\chi_{\bullet CH_2CH_3}$ could be replaced by χ_C and no dependence of SE+ on χ_R would be expected.

Geometry optimizations and energy calculations were performed on the β- and α-substituted cations and neutral molecules (Tables I and II). A plot of stabilization energy of the PER and PLA β-substituted cations against electronegativity was made to test the proposed relationship (Figure 1, a and b). Because electronegativities of the polyatomic substituents (i.e., AlH_2, SiH_3, etc.) were not available, the Pauling electronegativities of the non-hydrogen atom of the substituent (Al, Si, etc.) were used. It is seen that while electronegativity and SE+ are related, the relation is not linear, unlike the findings of a similar study for carbanion systems.[15] It might be argued that since the electronegativities of the polyatomic systems are unknown, the approximate values used are the cause of the nonlinearity. We can, however, use the results from the atomic substituents (R = H, Li, Na, Cl) to examine this question. From parts a and b of Figure 1 it can be seen that the relation between SE+ and the electronegativity of just these atomic substituents is not linear. Thus, while Pauling's electronegativity is clearly correlated with the SE+, the relationship to bond energies is not as simple as we assumed in applying (6). The quadratic dependence in Figure 1a,b suggests that the parameter "a" would need to be different for ions and for neutral molecules (and probably for α- and β-substituents).

A similar plot was made for the α-substituted cations (Figure 2) and shows no relationship between the stabilization of the cation and the electronegativity of the substituent. In the α-substituted case, where R is bonded to the carbon with the formally empty 2p(C+) orbital, varying numbers of lone pairs and R–H bonds can overlap with the 2p(C+) orbital as R is changed. The several possible electron donation sources are varied with R, not all of which are related to the electronegativity of R, and the result leads to no apparent correlation of the stabilization energy with the electronegativity of R.

Mulliken Population and Stabilization. The stabilization of the cation is expected to increase in conjunction with the donation of electrons to the α-carbon. A measure of electron donation can be obtained by examining the Mulliken population of the 2p(C+) orbital. The population in the 2p(C+) orbital due to inductive effects should be independent of conformation. Since it is expected that hyperconjugation with the R–C bond occurs in the PER conformation, but not in the PLA conformation, the extra population in the PER conformation should be directly related to the extent of hyperconjugation.

Another property reflecting the degree of hyperconjugation is the rotational barrier. Thus there should exist a relationship

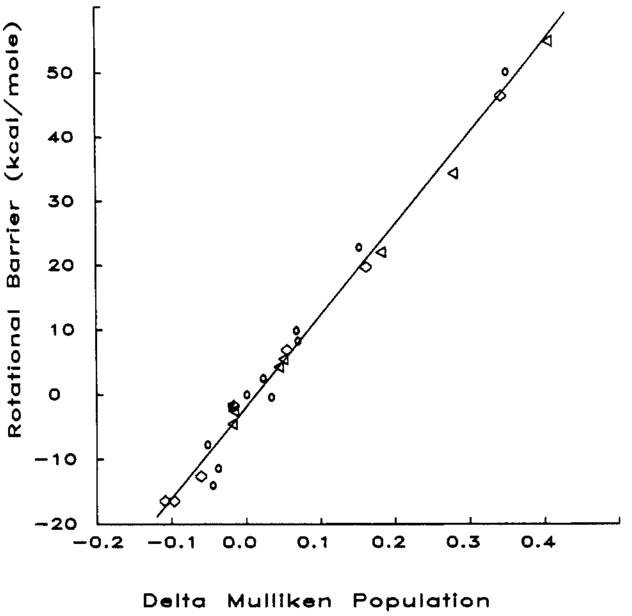

Figure 3. Rotational barrier (kcal/mol) of β-substituted ethyl cations versus the difference in Mulliken populations, PER − PLA.

between the extra electron density and the rotational barrier, as both are reflections of hyperconjugation with the R–C bond. In particular, we expect an increase in both the rotational barriers and the extra Mulliken populations as R becomes less electronegative and the R–C bond electrons are more easily delocalized.

Mulliken populations of atoms and individual orbitals were calculated with GAMESS (Table III). Mulliken populations are basis set dependent, but they are useful when calculations are compared within a given basis set. Since two p and a set of d basis functions were included on the α-carbons in the calculations, the Mulliken population listed is the electron population of all the basis functions on the α-carbon which are of a″ symmetry relative to the local CH_2 plane (i.e., both p_π basis functions plus similarly oriented d orbitals—$p_y + d_{xy} + d_{yz}$ for the PER cation and $p_z + d_{xz} + d_{yz}$ for the PLA cation). Figure 3 shows that the relation between extra Mulliken population and rotational barrier is, in fact, linear.

Ionization Potential and Stabilization. The third approach to relating the substituent and the degree of stabilization of the cation is to examine the ionization potentials of the radicals. We may rewrite the isodesmic reaction 1 as

$$\begin{tikzcd} e^- + RCH_2CH_2^+ + HCH_2CH_3 \arrow[r, "SE+"] \arrow[d, "-IP_{RCH_2CH_2\bullet}"] & RCH_2CH_3 + HCH_2CH_2^+ + e^- \arrow[d, "-IP_{HCH_2CH_2\bullet}"] \\ RCH_2CH_2\bullet + HCH_2CH_3 \arrow[r, "SE\bullet"] & RCH_2CH_3 + HCH_2CH_2\bullet \end{tikzcd}$$ (9)

It can be seen that the stabilization energy of the cation is the difference of the ionization potentials of the substituted and unsubstituted radicals, plus the stabilization energy of the substituted radical (SE•). That is

$$SE+ = SE\bullet + (IP_{HCH_2CH_2\bullet} - IP_{RCH_2CH_2\bullet}) \quad (10)$$

A similar result follows for the SE+ of the α-substituted cations. If SE• were small (that is, the energy needed to add a methyl hydrogen is about the same for the substituted and unsubstituted radicals), then there should be a direct linear relation between $IP_{RCH_2CH_2\bullet}$ and the stabilization energy (SE+). In fact, previous results exist for methyl cations that indicate that SE• is significantly smaller than SE+.[12,20]

The stabilization energy is plotted against the ionization potential of the radical for both α- and PLA β-substituted species in Figures 4 and 5. Ionization potentials were taken as the SCF energy difference between the geometry optimized radical and cation of interest. (It should be noted that due to differences in the number of electrons between the radical and the cation we expect an underestimation of the IP using this procedure. However, we expect the error to be of similar magnitude for all the compounds examined, and thus use the calculated quantity as an approximation to the actual IP.) We find that SE• is much smaller than SE+ (Tables I and II), and as a result we obtain a linear relation between stabilization energy and IP of the radical.

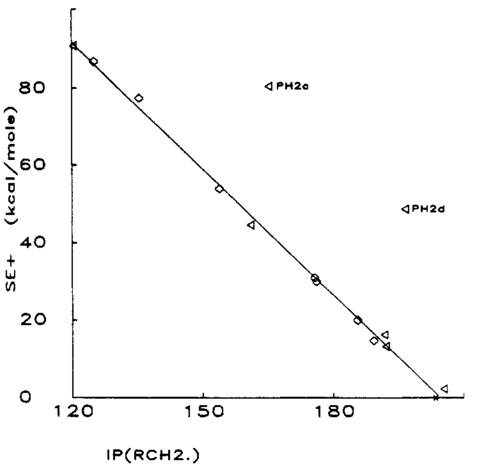

Figure 4. Stabilization energy (kcal/mol) of α-substituted methyl cations versus ionization potential of the corresponding radicals (kcal/mol).

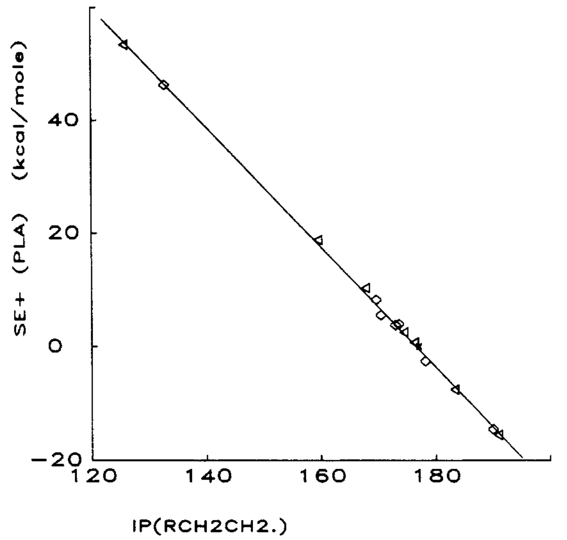

Figure 5. Stabilization energy (kcal/mol) of PLA β-substituted ethyl cations versus ionization potential of the corresponding radicals (kcal/mol).

In Figure 4 the two conformations of the PH_2 substituted cations present obvious deviations from the near-linear plot. These α-substituted cations in both planar and twisted configurations are unusually stabilized, by means other than the simple induction and hyperconjugation apparent in the other cations. The planar cation is nearly C_{2v} in symmetry and our results indicate that the phosphorus atom has donated electrons to form a double bond with the carbon. In the twisted conformation, the PH_2 hydrogens have bent back so that the HPC bond angle is almost 90°. Although symmetry constrained, the cation is moving toward a $PHCH_3^+$ configuration, and is stabilized from the partial transfer of hydrogens from phosphorus to the carbon. In fact, a significantly lower energy is obtained in the symmetry unconstrained case, where the stable minimum is found to be $^+PHCH_3$. Similar results were obtained by Pople et al.[7] in a study of first-row electropositive substituents.

Ionization Potential and Koopmans' Theorem. To further investigate the causes of the relationship between stabilization energy

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Table I. β-Ethyl Stabilization[a]

molecule[b]	$-E$ (hartree)	χ[c]	SE+[d]	SE·[d]	$IP_{RCH_2CH_2\cdot}$[d]	ΔIP[d]
$H-CH_2CH_2^+$ (PLA)	78.3102	2.2	0.0		177.0	0.0
$H-CH_2CH_2^+$ (PER)	78.3074		0.0			
$H-CH_2CH_2^\bullet$	78.5922			0.0		
$H-CH_2CH_3$	79.2288					
$Li-CH_2CH_2^+$ (PLA)	85.1963	1.0	46.3		132.8	44.2
$Li-CH_2CH_2^+$ (PER)	85.2699		94.2			
$Li-CH_2CH_2^\bullet$	85.4079			2.1		
$Li-CH_2CH_3$	86.0411					
$BeH-CH_2CH_2^+$ (PLA)	92.9331	1.6	8.2		169.7	7.3
$BeH-CH_2CH_2^+$ (PER)	92.9645		29.6			
$BeH-CH_2CH_2^\bullet$	93.2035			0.9		
$BeH-CH_2CH_3$	93.8386					
$BH_2-CH_2CH_2^+$ (PLA)	103.5489	2.0	3.9		173.6	3.4
$BH_2-CH_2CH_2^+$ (PER)	103.5600		12.6			
$BH_2-CH_2CH_2^\bullet$	103.8256			0.6		
$BH_2-CH_2CH_3$	104.4612					
$CH_3-CH_2CH_2^+$ (PLA)	117.3511	2.6	3.8		173.0	4.0
$CH_3-CH_2CH_2^+$ (PER)	117.3484		3.8			
$CH_3-CH_2CH_2^\bullet$	117.6268			-0.2		
$CH_3-CH_2CH_3$	118.2636					
$NH_2-CH_2CH_2^+$ (PLA)	133.3344	3.0	5.5		170.5	6.5
$NH_2-CH_2CH_2^+$ (PER)	133.3143		-5.4			
$NH_2-CH_2CH_2^\bullet$	133.6061			-1.0		
$NH_2-CH_2CH_3$	134.2442					
$OH-CH_2CH_2^+$ (PLA)	153.1530	3.4	-2.6		178.2	-1.2
$OH-CH_2CH_2^+$ (PER)	153.1269		-17.2			
$OH-CH_2CH_2^\bullet$	153.4370			-1.4		
$OH-CH_2CH_3$	154.0757					
$F-CH_2CH_2^+$ (PLA)	177.1355	4.0	-14.5		190.0	-13.0
$F-CH_2CH_2^+$ (PER)	177.1094		-29.2			
$F-CH_2CH_2^\bullet$	177.4383			-1.5		
$F-CH_2CH_3$	178.0772					
$Na-CH_2CH_2^+$ (PLA)	239.5933	0.9	53.4		125.8	51.2
$Na-CH_2CH_2^+$ (PER)	239.6799		109.5			
$Na-CH_2CH_2^\bullet$	239.7937			2.2		
$Na-CH_2CH_3$	240.4268					
$MgH-CH_2CH_2^+$ (PLA)	277.8923	1.3	18.8		159.6	17.4
$MgH-CH_2CH_2^+$ (PER)	277.9468		54.7			
$MgH-CH_2CH_2^\bullet$	278.1466			1.4		
$MgH-CH_2CH_3$	278.7809					
$AlH_2-CH_2CH_2^+$ (PLA)	320.7893	1.6	10.2		167.8	9.1
$AlH_2-CH_2CH_2^+$ (PER)	320.8244		34.0			
$AlH_2-CH_2CH_2^\bullet$	321.0568			1.1		
$AlH_2-CH_2CH_3$	321.6915					
$SiH_3-CH_2CH_2^+$ (PLA)	368.3873	1.9	2.5		174.5	2.5
$SiH_3-CH_2CH_2^+$ (PER)	368.3941		8.5			
$SiH_3-CH_2CH_2^\bullet$	368.6654			0.0		
$SiH_3-CH_2CH_3$	369.3018					
$PH_2-CH_2CH_2^+$ (PLA)	419.5985	2.2	0.7		176.3	0.6
$PH_2-CH_2CH_2^+$ (PER)	419.6072		7.9			
$PH_2-CH_2CH_2^\bullet$	419.8795			0.0		
$PH_2-CH_2CH_3$	420.5159					
$SH-CH_2CH_2^+$ (PLA)	475.8051	2.6	-7.6		183.3	-6.3
$SH-CH_2CH_2^+$ (PER)	475.8010		-8.4			
$SH-CH_2CH_2^\bullet$	476.0971			-1.3		
$SH-CH_2CH_3$	476.7357					
$Cl-CH_2CH_2^+$ (PLA)	537.1882	3.2	-15.5		190.9	-13.9
$Cl-CH_2CH_2^+$ (PER)	537.1810		-18.3			
$Cl-CH_2CH_2^\bullet$	537.4924			-1.6		
$Cl-CH_2CH_3$	538.1315					

[a] Calculations were performed with a 6-31G* basis set. [b] All molecules are C_s symmetry. [c] Reference 19. [d] kcal/mol.

and the IP of the radical, we examine the Koopmans' ionization potentials of the molecules.

Koopmans' theorem states that the orbital energy of the highest occupied molecular orbital can be taken as an approximation to the ionization potential of an atom or molecule. In effect, one uses the molecular orbitals of the neutral molecule to approximate the wave function of the ion. The orbital energies for the β-substituted radicals are compared with the calculated ionization potentials in Figure 6 and are seen to follow the same trend. This result sheds light on the origin of the stabilization energy of the cation.

One can envision two extremes. In the first, no inductive or hyperconjugative effects are operative in the radical. One might easily imagine this to be the case, due to the small stabilization energies obtained in the radicals. In this case the variation of the ionization potential with R would arise from delocalization effects

Table II. α-Methyl Stabilization[a]

molecule	$-E$ (hartree)	χ[b]	SE+[c]	SE·[c]	$IP_{RCH_2\cdot}$[c]	ΔIP[c]
$H-CH_2^+$	39.2363	2.2	0.0		203.3	0.0
$H-CH_2^\cdot$	39.5603			0.0		
$H-CH_3$	40.2017					
$Li-CH_2^+$	46.1785	1.0	77.5		135.4	67.9
$Li-CH_2^\cdot$	46.3943			9.6		
$Li-CH_3$	47.0204					
$CH_3-CH_2^+$	78.3206	2.5	30.0		176.2	27.0
$CH_3-CH_2^\cdot$	78.6015			2.9		
CH_3-CH_3	79.2382					
$NH_2-CH_2^{+\,d}$	94.3947	3.0	86.8		125.0	78.2
$NH_2-CH_2^\cdot$	94.5940			8.5		
NH_2-CH_3	95.2219					
$NH_2-CH_2^{+\,e}$	94.2884	3.0	20.0		185.6	17.7
$NH_2-CH_2^\cdot$	94.5842			2.4		
$OH-CH_2^{+\,d}$	114.1672	3.4	53.9		153.9	49.4
$OH-CH_2^\cdot$	114.4124			4.4		
$OH-CH_3$	115.0467					
$OH-CH_2^{+\,e}$	114.1308	3.4	31.0		175.8	27.5
$OH-CH_2^\cdot$	114.4110			3.6		
$F-CH_2^+$	138.0978	4.0	14.7		189.3	14.0
$F-CH_2^\cdot$	138.3994			0.7		
$F-CH_3$	139.0397					
$Na-CH_2^+$	200.5847	0.9	90.8		120.3	83.0
$Na-CH_2^\cdot$	200.7764			7.8		
$Na-CH_3$	201.4054					
$SiH_3-CH_2^+$	329.3410	1.9	16.2		191.7	11.6
$SiH_3-CH_2^\cdot$	329.6465			4.5		
SiH_3-CH_3	330.2807					
$PH_2-CH_2^{+\,d}$	380.5970	2.2	80.5		165.3	38.0
$PH_2-CH_2^\cdot$	380.8604			42.5		
PH_2-CH_3	381.4342					
$PH_2-CH_2^{+\,e}$	380.5461	2.2	48.6		196.6	6.6
$PH_2-CH_2^\cdot$	380.8595			41.9		
$SH-CH_2^{+\,d}$	436.8147	2.6	44.6		161.1	42.2
$SH-CH_2^\cdot$	437.0714			2.4		
$SH-CH_3$	437.7090					
$SH-CH_2^{+\,e}$	436.7472	2.6	2.2		205.4	-2.1
$SH-CH_2^\cdot$	437.0745			4.3		
$Cl-CH_2^+$	498.1536	3.2	13.2		192.0	11.3
$Cl-CH_2^\cdot$	498.4595			1.9		
$Cl-CH_3$	499.0979					

[a] Calculations were performed with a 6-31G** basis set. [b] Reference 19. [c] kcal/mol. [d] A plane through the R–C bond bisects CH_2 and the substituent is symmetric about the plane. [e] The substituent is rotated about the R–C bond by 90° and optimized.

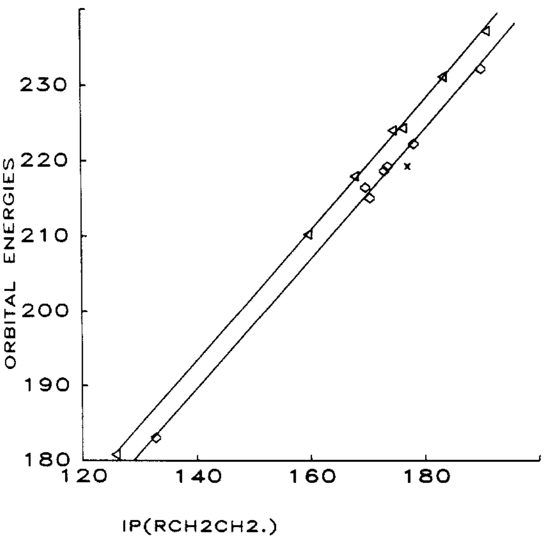

Figure 6. HOMO energies (kcal/mol) versus Δ(SCF) ionization potentials (kcal/mol).

Table III. Mulliken Populations of 2p(C+) Orbitals (β-Ethyl Cations)

substituent	rotational barrier[a]	Mulliken pop. (p + d) PER	PLA	ΔMulliken pop. (PER–PLA)
H	−1.8	0.13	0.15	−0.02
Li	46.2	0.57	0.23	0.34
BeH	19.7	0.33	0.17	0.16
BH_2	6.9	0.20	0.15	0.06
CH_3	−1.7	0.15	0.16	−0.02
NH_2	−12.6	0.08	0.14	−0.06
OH	−16.4	0.05	0.16	−0.11
F	−16.4	0.05	0.14	−0.10
Na	54.4	0.65	0.24	0.41
MgH	34.2	0.47	0.19	0.28
AlH_2	22.0	0.35	0.17	0.18
SiH_3	4.3	0.21	0.16	0.04
PH_2	5.5	0.21	0.16	0.05
SH	−2.5	0.15	0.17	−0.02
Cl	−4.5	0.12	0.14	−0.02

[a] kcal/mol.

after ionization and one would predict that the Koopmans' ionization potential would not vary significantly with R. The second extreme is that significant hyperconjugative and inductive effects occur in the radical, lowering the orbital energy of the R–C and C–H bonds and raising the energy of the singly occupied orbital. Thus the major charge readjustments would have already occurred in the radical. In this case the Koopmans' theorem ionization potential would approximate the Δ(SCF) ionization potential. Figure 6 shows that the relaxation effects are 40–50 kcal/mol (i.e., $IP_{\Delta SCF}$ is 40–50 kcal less than $IP_{Koopmans}$), but are independent of the substituents, so that the second extreme is more nearly the actual situation.

It is interesting to note that the observed small value of SE· (and it's small variation with R) implies that the increase in energy of the radical HOMO and the decrease in energy due to hyperconjugation and induction of the R–C and C–H bonds must be largely offsetting. This provides an interesting example of a system where the HOMO energy is unrelated to the overall molecular stability.

Finally, the results presented here shed light on the ambiguity in the literature[7,21,22] in comparisons of stabilization energies of SiH_3 versus CH_3 in α-substituted methyl cations or β-substituted ethyl cations. For substituents in the β position the present results indicate that there is no significant difference between first- and second-row stabilization energies beyond that expected from electronegativity differences. However, for α-substituted methyl cations there is no clearly defined relation between electronegativity and stabilization energy, since one has inductive effects (sensitive to electronegativity) and hyperconjugative effects with the R–H bond and R lone pairs (sensitive to R–C bond length). If one concludes that the alkali metals demonstrate that the inductive stabilization in α-substituted cations decreases with increasing electronegativity of R, then the greater stability of CH_3 over SiH_3 must be attributed to better hyperconjugation with the C–H bonds due to the shorter C–C bond length.

Conclusions

In conclusion, we have attempted to quantitatively systematize the stabilization energies of two types of cations, the β-substituted ethyl cation and the α-substituted methyl cation. The major results obtained are the following: (1) although there is a qualitative relationship between electronegativity and stabilization energy, it is found to be nonlinear, (2) a strong linear relation exists between the rotational barrier and the Mulliken population in the formally empty 2p(C+) orbital, and (3) the stabilization energy in the cation is strongly correlated with the IP of its corresponding radical. The relationship between the radical IP and the stabi-

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lization energy is a result of the small values of the stabilization energies in the radicals. However, in comparison with Koopmans' IP estimates it is seen that hyperconjugative and inductive effects are still operative in the radicals, but that they destabilize the singly occupied HOMO of the radical to a larger extent than they stabilize the lower lying orbitals.

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Conformational Analysis of the Pyrrolizidine Alkaloid Senecionine Using Molecular Mechanics

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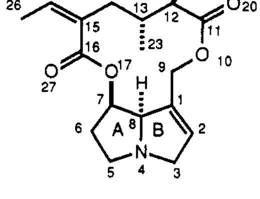
Abstract: A molecular mechanics (MM) program is used to identify low-energy conformations of the pyrrolizidine alkaloid (PA) senecionine. Ab initio calculations on hydroxyacetic acid were carried out in order to develop new MM parameters for α-hydroxy esters. Potential conformations of the macrocyclic ring of senecionine were systematically generated and minimized. Analysis of the resulting data indicates that several conformations should be readily accessible in solution at room temperature. This is in contrast to the solid state, where a number of related PA's show nearly identical conformations. The influence of MM parameter choice and the role of hydrogen bonding are also discussed.

The pyrrolizidine alkaloids (PA's) are a diverse family of plant metabolites containing the 4-azabicyclo[3.3.0]octane or closely related ring system.[1] Many of these alkaloids are potent hepatotoxins,[2] carcinogens, and mutagens[3] and have been shown to represent a serious environmental threat to human and animal health.[4] The problem is particularly acute in geographical regions where livestock ingest significant quantities of PA's from plant sources such as *Senecio* species, since these alkaloids can pass through the food chain.[5]

As a result of our synthetic investigation of the PA's[6] we became interested in conformational aspects of members of the group that contain a dicarboxylic (necic) ester spanning the pyrrolizidine nucleus. In particular, we were intrigued by reports that a number of macrolactone PA's related to senecionine (**1**) exhibited nearly identical conformations in the solid phase.[7] The structures of these PA's are shown in Figure 1. This fact was especially surprising in light of the variety of functional groups present in the 12-membered macrocyclic diester portion of these molecules. In order to gain insight into this remarkable conformational homogeneity we undertook a molecular mechanics study of senecionine. We report herein the results of this investigation which suggest that, in solution, senecionine should exist in several conformations of nearly equal energy.



1, Senecionine

Results and Discussion

Computational Methods. Early investigations into conformational aspects of this family of alkaloids recognized that the pyrrolizidine nucleus could exist in either an exo-buckled or endo-buckled conformation.[8] In most cases, including the systems of interest to us, the exo-buckled geometry was predominant due to diminished steric interactions present in this conformer (Figure

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