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STRAIN ENERGY EFFECT ON THE REACTIVITY OF BRIDGEHEAD HALIDES IN ELECTRON TRANSFER REACTIONS

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Abstract: We here report MNDO and AM1 calculations for halobridgehead compounds which indicate that an increase in their angular strain is accompanied by more negative reduction potentials as measured through their LUMO energies. The theoretically predicted reactivity agrees with that determined experimentally.

The dissociative or non-dissociative nature of the electron capture reaction for the compounds is estimated through the localization of the corresponding radical anion intermediates as minimum of the potential surfaces. Our calculations indicate that for bridgehead chlorides, which lead to pyramidal radicals, the electron transfer is a non-dissociative step, while for t-butyl chloride, the process is dissociative leading to a planar t-butyl radical. The presence of a substituent that lowers the LUMO of the halobridgehead compounds increases their reactivity in ET reactions. This effect is explained through an orbital mixing of the molecular orbitals involved in the ET process.

Strain energy is an important concept by which not only the properties but also the chemical reactivity of bridgehead compounds can be explained.[1]

For instance, the reactivity of bridgehead halides in nucleophilic substitution reactions that take place through a classical polar mechanism (S_N1) can be explained on these bases. These studies indicate that an increase in the strain energy difference between RH and R^+ produces a decrease in the rate constant of the solvolytic reaction.[2]

On the other hand, an S_N2 process is precluded for this type of substrates due to the steric hindrance to backside attack of the nucleophile.[3] Recently it has been proposed that the S_N2 process can be considered to take place through an electron shift or, in other words, an electron transfer (ET) accompanied by bond reorganization, that is, breaking of the R...X bond and formation of the Nu...R bond.[4] When the polar mechanisms are not favored by steric, electronic or strain factors, the ET takes place without bond reorganization.[4] This ET can occur spontaneously or through light stimulation. One of the mechanisms through which this type of reaction can take place is the radical nucleophilic substitution, or $S_{RN}1$, which has proved to be an excellent way of generating radicals.[5]

The $S_{RN}1$ mechanism has an initiation step which corresponds to the formation of the radical anion of the substrate, usually by a spontaneous (thermal) or photostimulated ET from the nucleophile (eq. 1). The radical anion of RX thus generated fragments into a radical and the anion of the leaving group (eq. 2). The radical can react with the nucleophile to give a new radical anion $(RNu)^{\cdot-}$ (eq. 3) that transfers its extra electron to the acceptor RX which continues the propagation cycle (eq. 4) (Scheme I).[5] For most haloalkanes the ET step has been considered to be dissociative and eq. 1 and 2 occur simultaneously.[6]

SCHEME I

Initiation Step $RX + Nu^- \longrightarrow (RX)^{\cdot-} + Nu^{\cdot}$ 1
Propagation Steps $(RX)^{\cdot-} \longrightarrow R^{\cdot} + X^-$ 2
$R^{\cdot} + Nu^- \longrightarrow (RNu)^{\cdot-}$ 3
$(RNu)^{\cdot-} + RX \longrightarrow RNu + (RX)^{\cdot-}$ 4

It has been shown that several halobridgehead halides react by the $S_{RN}1$ mechanism.[5c,7-9] For all the substrates studied and when bromo or iodo were the leaving groups, good yields of substitution products were obtained, while for 1-chloro derivatives only a low percentage of reaction was observed with 1-chloroadamantane (40 % of halide ion liberation in the photostimulated reaction with Ph_2P^- ion in liquid ammonia, 100 min).[7] This lack of reactivity was ascribed to a slow initiation step.[5c]

On the other hand, in the electrochemical study of 1-iodo- bridgehead compounds it has been found that the reduction potential of the substrates becomes more negative as their strain increases; however, this trend reverts beyond 1-iodobicyclo [2.2.1]heptane.[10]

In order to gain new insights into the subject, we performed a theoretical study to determine the stability of halobridgehead radical anions as well as the dependence of the reduction potential of the corresponding neutral compounds with the angular strain energy of the parent hydrocarbons. Also, we studied theoretically the 1-chlorobicyclo[2.2.2]octan-2-one due to its remarkable high reactivity in $S_{RN}1$ reactions in comparison with other chloro derivatives.[11]

PROCEDURE:

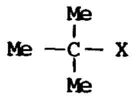
All the calculations were carried out with MNDO[12] or AM1[13] as implemented in the AMPACK package[14] without any assumptions in geometric parameters. The restricted or unrestricted version of these procedures were used depending on the electronic nature of the structure under study. The stationary points determined were proved to be so through the calculation of the corresponding Hessian matrix.

The size of the molecules of interest as well as the presence of halogen in their structures made the use of ab initio methods, including polarization functions and heavy halogen atom effect to be out of our resources.[15] On the other hand, it has been proved the goodness of MNDO and AM1 for predicting the right order of molecular orbitals eigenvalues as well as for studying the minimum energy potential surfaces of different types of reactions.

RESULTS AND DISCUSSION

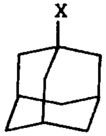
In Table I we present the MNDO and AM1 LUMO orbital energies for compounds 1-7. The LUMO eigenvalues calculated by AM1 differ from the MNDO ones by a factor that depends on the halogen involved in the calculations. These differences can be ascribed to differences in halogen atom parametrization within both procedures,[16] although with both methods the same trend is observed.

For all the compounds under study (1-7) the calculated LUMO's correspond to an antibonding σ^* C-X bond.



$$\mathrm{Me-\overset{Me}{\underset{Me}{C}}-X}$$

1



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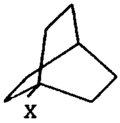

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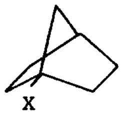

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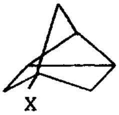

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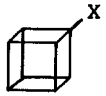

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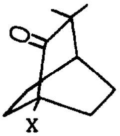


8

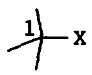
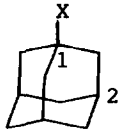
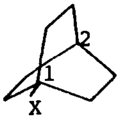
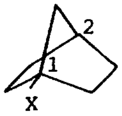
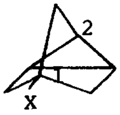
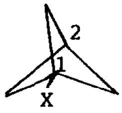
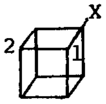
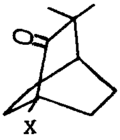
The hybridization model predicts that the smaller bond angles found in a system with angular strain should result in an increase in the p character of the strained C-C bonds and hence in an increase in the s character of the associated C-H bonds.[17,18] An empirical expression has been proposed to relate the C-H coupling constant $^1J(^{13}C\text{-H})$ to the percent s character of the bond.[19] It has also been reported that a carbon becomes more electronegative as it is subjected to more angular strain.[20]

In Table I the strain energy, the ^1J $(^{13}C\text{-H})$ bond coupling constants of the bridgehead carbon as well as its percent s character are presented for the parent hydrocarbons of the bicyclic compounds under study as well as the main results of our calculations.

It can be seen that the MNDO and AM1 LUMO eigenvalues for the halobridgehead compounds correlate perfectly well with the experimentally determined one-bond coupling constants $J(^{13}C\text{-H})$ of the bridgehead C-H bond (average $r = 0.97$) (Fig. I). The best correlations were obtained with the MNDO method. The calculations thus indicate that an increase in the angular strain, measured through the s character of the bond, is accompanied by an increase in the LUMO energy of the strained compounds. Considering the LUMO eigenvalues as a measure of the reduction potential of the RX compounds, these results lead us to propose that an increase in strain at the bridgehead carbon is accompanied by a decrease in the photostimulated outer sphere electron transfer rate for the parent RX compounds.

1-Chloroadamantane, which has been shown experimetally to have a low reactivity,[7] is calculated by MNDO to have a LUMO eigenvalue of 0.809 eV. We can thus expect that 1-chloro-

TABLE 1: Calculated LUMO Energies and Related Main Features for Halobridgehead Compounds

Compound	X	Strain RH[b,c]	LUMO Eigenvalues MNDO	LUMO Eigenvalues AM1	^1J (^{13}C-H)[a] % s[d]	R· Bond Angle Angle	R· Bond Angle MNDO	R· Bond Angle AM1
	Cl	0.0	0.638	1.375		1	119.99	119.99[e]
	Br		0.317	0.649				
	I		0.236	0.339				
	Cl	2.0	0.809	1.443	133.5 (26.7)	1	115.04	114.60
	Br		0.493	0.765		2	109.29	109.20
	I		0.380	0.444				
	Cl	7.4	0.835	1.439	134.0 (26.9)	1	115.25	114.00
	Br		0.513	0.752		2	109.17	109.80
	I		0.397	0.429				
	Cl	14.4	0.995	1.589	140.0 (28.0)	1	106.27	105.09
	Br		0.657	0.896		2	101.14	101.22
	I		0.538	0.528				
	Cl	40.0	1.043	1.570		1	106.74	104.35
	Br		0.702	0.885		2	106.89	106.63
	I		0.588	0.501				
	Cl	68.0	1.269	1.718	160.0[f] (32.0)	1	91.80	92.55
	Br		0.919	1.082	164.0[g] (33.0)	2	87.92	88.87
	I		0.820	0.662				
	Cl	154.7	1.292	1.716	154.0 (30.8)	1	93.45	88.59
	Br		0.936	1.073		2	90.35	90.30
	I		0.841	0.655				
	Cl		0.450	0.723				

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a) E. W. Della, P. T. Hine, H. K. Patney, J. Org. Chem, 42, 2940 (1977) and references cited therein; b) Franklin's group equivalents were employed in determining the energy of the strain free model; c) K. B. Wiberg, Angew. Chem. Intern. Ed. (Eng), 25, 312 (1986); d) %s character for the bridgehead C-H bond, %s = 0.2 J(^{13}C-H). e) t-Butyl radical is calculated to be planar while ab initio calculations indicated that it deviates from planarity by 22.1° see: M. Yoshimine, J. Pacansky, J. Chem. Phys., 74, 5168 (1981). f) C. G.Levy, R. L. Lichter, G. L. Nelson,Nuclear Magnetic Resonance Spectroscopy, 2nd ed.; Wiley-Interscience: New York, 1980. g) R. M. Jarret, L. Cusumano, Tet. Lett., 31, 171 (1990).

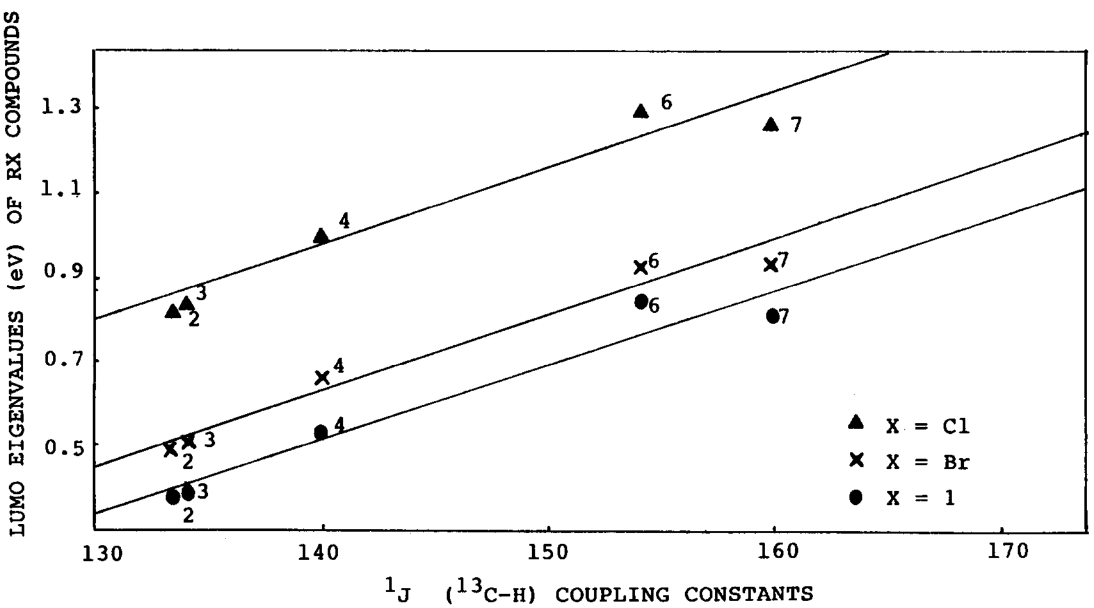


FIG. I : Plot of MNDO LUMO eigenvalues (eV) of RX compounds vs. ^1J (^{13}C - H) coupling constants of the parent hydrocarbons.

bridgehead compounds with higher LUMO's energies (higher angular strain) than 1-chloroadamantane will be unreactive toward photostimulated radical nucleophilic substitution reactions by Ph_2P^- ions in liquid ammonia. This proved experimentally to be the case.[5c]

All the bromo and iodo derivatives experimentally studied (2,3,5) and calculated to have a lower LUMO than 1-chloroadamantane gave good yields of substitution reaction, with the exception of tert-butyl halides. Elimination was the main reaction with t-butyl bromide, while an $S_{RN}1$ mechanism operated with t-butyl chloride.[21]

Another point of interest is the nature of the process of electron capture by alkyl halides, which has been proposed to be dissociative.[6] The electron capture will occur in the σ^* C-X orbital, provided there are no alternative low lying orbitals available in group R. This may lead to a potential minimum with the three-electron bond intact. Alternatively, there may be no such minimum, in such case the electron transfer process is dissociative leading to the normal products R· and X^- or to a loose complex between them. The last type of interaction has been detected by e.s.r. spectroscopy.[22]

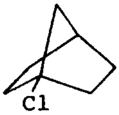
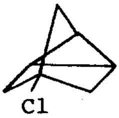
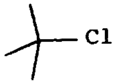
It has been proposed that σ^* radical anions are stable species whenever the radicals R· formed from them are naturally bent or pyramidal and the rehybridization energy release of R· is lower than the dissociation energy of the radical anion whereas σ^* radical anions do not exist as intermediates when the radicals formed from them are naturally planar.[23,24]

Bicyclo bridgehead radicals have a pyramidal structure and rehybridization is prevented. For this type of compounds, the radical anions will then be stable species. The radicals generated from compounds 1-6 have been calculated by AM1 and MNDO (Table I). The bond angle at the bridgehead carbon is taken as an indication of the deviation from planarity.

In order to determine the existence of the RX radical anions as minimum of the potential surface, we proceeded to calculate the radical anions of compounds 1, 4 and 5 as representatives. The calculations were carried out with the restricted and unrestricted spin version of AM1.

The radical anions derived from compounds 4 and 5 (X = Cl) were determined to be stable species through the calculations of the corresponding Force constants matrixes. In Table 2 some relevant properties for the species are presented. In the radical anions of compounds 4 and 5 there is only a small elongation of the C-Cl bond (ca. 0.3 Å) from the equilibrium distance in the neutral molecule. For the radical anion of compound 1 the calculations indicate that the potential energy minimum corresponds to a loose complex between R· and Cl^-. In the radical-anion complex the t-butyl group has a planar geometry with a C-Cl distance of 3.98 Å (Table 2). In the table is presented an analysis of the unpaired electron spin distribution.[25]

TABLE 2. AM1 UHF Spin Population and C-Cl Bond Distance in Chloro Bridgehead Radical Anions

Radical Anion	C-X Bond Distance (Å) ( )a	Atomic Orbital Spin Population C	X
	2.08 (1.74)	0.65	0.36
	2.04 (1.72)	0.60	0.38
	3.98 (1.78)	0.99	0.01

a) ()C-Cl bond distance for the equilibrium geometries of the neutral molecule state.

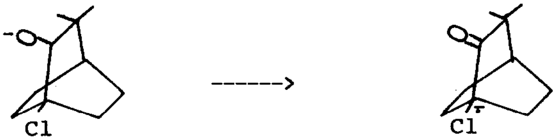
When the LUMO of the molecule does not belong to the antibonding σ* MO of the C-X bond, the situation may be different. It has been shown that the presence of a carbonyl group in carbon 2 increases dramatically the rate of $S_{RN}1$ reactions in 1-chloro bridgehead compounds. For instance, 1-chloro-3,3-dimethylbicyclo[2.2.2.]octan-2-one (8) reacts ≥ 700 faster than 1-chloroadamantane, while it is only half as reactive as 1-bromoadamantane.

The LUMO eigenvalue determined by MNDO for this compound[26] is 0.45 eV, corresponding this orbital to the π* antibonding MO of the C=O group, while the following orbital in increasing energy (0.59 eV) corresponds to the σ* antibonding MO of the C-Cl bond.

The eigenvalues of the σ* C-Cl bond of compounds 2 and 3 are quite similar (0.8 eV). The σ* C-Cl bond of compound 8 is 0.59 eV with a LUMO value of 0.45 eV. Experimentally it has been determined that compound 8 is only half as reactive as 1-bromoadamantane which has a σ*

C-Br LUMO 0.49 eV.

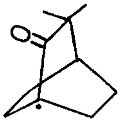
The high reactivity of compound 8 can be explained considering that it receives the electron in the π* C=O MO to form radical anion 9, which then by an intramolecular ET to the σ* C-Cl bond forms radical anion 10 (eq. 5), which fragments to give the radical 11 and the chloride ions (eq. 6). The radical 11 continues the chain propagation steps of Scheme I.



5

9 10

π* radical anion σ* radical anion

10 $\xrightarrow{\quad}$  + Cl^- 6

11

Another possibility is that the π* radical anion 9 does not actually exist. The ET reaction takes place through an orbital crossing of the σ* C-X MO which lowers its energy and the π* C=O MO which increases its energy leading directly to the σ* radical anion 10.

The calculation of 8 with an extra electron in its equilibrium geometry in fact shows that the electron is located in a wave function in which there exists an in-phase orbital mixing of the atomic orbitals of the C=O and C-Cl bonds. The σ* radical anion 10 is calculated to be the orbital isomer of lower energy by either UHF or RHF AM1. We thus conclude that the electron transfer step in 2-oxo-substituted compounds is accelerated through orbital mixing leading to the σ* C-X radical anions.

CONCLUSION: From all the results here presented we can conclude that an increase in angular strain energies correlates with an increment in LUMO eigenvalues of bridgehead halides and with a decrease in reactivity in reactions in which ET processes are involved. When there is a substituent, such as 2-oxo in 1-chlorobridgehead compounds, that has a low LUMO π* MO, it can receive the electron as an internal redox catalyst, increasing the reactivity of the substrates in spite of the strain energy.

The reaction is theoretically predicted to form a radical anion intermediate whenever the radicals formed are bent and do not have the possibility to rehybridize to a planar conformation while the reaction is a dissociative process for planar alkyl radicals, as in the case of t-butyl chloride, where a loose radical-anion complex is created.

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25. Similar results were obtained with MNDO. However, because repulsion interactions between pairs of atoms at their Van der Waals distances are overstimated in this procedure, longer bond distances were calculated with this method.
26. For the sake of simplicity the compound calculated has no methyl substituents.