S_N2 Transition State. 5. Effect of α-Substituents on S_N2 Reactivity and the S_N2–S_N1 Borderline Problem. A Molecular Orbital Approach[1]

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Abstract: Molecular orbital (MO) theory is applied to the analysis of the S_N2 identity reaction, with various α-substituents (H, planar NH_2, planar BH_2, OH, CHO, F, and CH_3) and nucleophile leaving group pairs (H^-, NH_3, and BH_4^-). Ground states, transition states, and encounter complexes have been optimized at the 4-31G level. We find that π-interactions between an α-substituent and a π-type occupied orbital associated with the reaction coordinate axis are of major importance in governing transition-state (TS) energy and reaction rate. π-Donors in the maximum overlap ("on") conformation slow the reaction, whereas π-acceptors accelerate it. π-Donors which lack cylindrical symmetry (e.g., methoxy and hydroxy) can avoid the repulsive interaction by a 90° rotation relative to the reaction coordinate ("turning off" the interaction). Inductive electron withdrawal, when neutralized from π-effects, seems to have an accelerating influence. Four-electron repulsion in the "on" geometry of a TS with a π-donor is minimized through "Loosening" of the TS and thereby making it more "S_N1-like". Weak nucleophiles (and powerful leaving groups) also generate loose transition states with carbocationic character. The destabilizing effect of π-donors (in the on geometry) diminishes gradually with extension of the TS, until it turns to a stabilizing interaction with the developing carbocation. Thus, in terms of geometry, a distinct crossover between a tight S_N2 TS with a preferred off conformation to an S_N1-like TS with a stable on conformation is found. The diminishing rate enhancement of α-halocarbonyl compounds with decreasing nucleophilic power of the nucleophile, as well as the rate enhancement observed for *p*-nitrobenzyl chloride with powerful nucleophiles and rate retardation with neutral nucleophiles, is rationalized in terms of this analysis and the effect of the nucleophile on S_N2 TS tightness. The dependence of rate retardation by α-F on the leaving group is treated in a similar manner.

The large variety of substrates and reagents undergoing the S_N2 reaction, as well as its many applications, makes it one of the most extensively studied reactions in organic chemistry. And yet, due to its considerable complexity, some of its mechanistic aspects are not well understood. Thus, while structure–reactivity relationships in terms of the effects of variations in the nucleophile (N) or leaving group (L) on reaction rates can often (though by no means always) be adequately rationalized, the effect of substituents (Y) on the central carbon atom on S_N2 reactivity is in many cases not easy to interpret (eq 1).[2]

$$\text{N:} + \text{YCH}_2\text{–L} \rightarrow \text{N–CH}_2\text{Y} + \text{:L} \qquad (1)$$

The fact that α-halogen substituents effect a decrease in the reactivity of alkyl halides toward nucleophiles has been known for many years.[3] The effect was first systematically investigated by Hine, who found that in a series of α-substituted haloalkanes (eq 1, Y = halogen) with identical leaving groups, the deactivating power of the α-halogen decreased in the order I > Br > Cl > F $\cong$ Me.[4,5] On the other hand, it was found that α-oxygen substitution (such as in methoxy-, acetoxy-, or benzoxymethyl chlorides; Y = OR, L = Cl in eq 1) results in the *opposite* effect, namely a dramatic increase in the rate of nucleophilic displacement.[6,7] This was generally attributed to the formation of the relatively stable methoxymethyl carbocation intermediate.[6f,7] However, even under strict S_N2 conditions (KI in acetone solvent in the absence of acid catalysis), methoxymethyl chloride still reacted some 3 orders of magnitude faster than ethyl chloride.[6a–c] In fact, Jencks and co-workers concluded recently that due to the extremely short lifetimes of the oxocarbonium intermediates, substrates expected to generate these intermediates will react with nucleophiles in an enforced preassociation (i.e., concerted) mechanism.[7a,8] Furthermore, the observation that ethers are inactive toward nucleophilic attack by Grignard and organolithium reagents, whereas the corresponding acetals and ketals undergo facile reaction, is evidence for the activating effect of α-oxygen

Table I. Electronegativity of α-Substituent Elements and S_N2 Reactivity

substituent element	electronegativity[a]	S_N2 rate
H	2.1	fast
Cl	3.0	very slow
O	3.5	very fast

[a] Atomic electronegativities from ref 9.

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(5) The behavior of α-F was found to depend on the nature of the leaving group: with iodine as leaving group, α-fluoro-enhanced S_N2 reactivity relative to α-ethyl-, whereas a slight retardation was observed when Br was the leaving group.[4b]

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(7) For discussions of displacement reactions of other formaldehyde derivatives see: (a) Knier, B. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 6789. (b) Craze, G. A.; Kirby, A. J.; Osborne, R. *J. Chem. Soc., Perkin Trans. 2* **1978**, 357. (c) McClelland, R. A. *Can J. Chem.* **1975**, *53*, 2763. (d) Kirby, A. J. "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen"; Springer: Berlin, 1983; p 79.

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and the fundamental difference between oxygen and halogen substituents, under conditions which cannot be suspected to support carbocation intermediates.

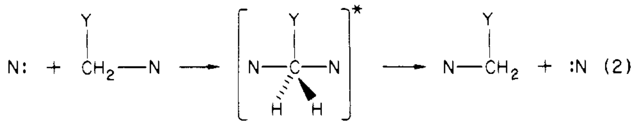
The experimental evidence thus indicates that replacement of one hydrogen atom (or more) in methyl halide by an electronegative substituent may effect two opposite results: either rate retardation or rate enhancement of the S_N2 reaction, depending on the nature of the substituent. Clearly, the order of reactivities in the series $CH_3OCH_2X > CH_3X > CH_2X_2$ cannot be accounted for on the basis of electronegativites of the substituent elements alone, as is demonstrated in Table I. The first object of the present study is to resolve this dichotomy by means of a molecular orbital (MO) analysis of the S_N2 transition state (TS). The following observations, which are associated with α-substituents at the S_N2 reaction center, will also be discussed by using this analysis.

The effect of π-acceptor substituents on the S_N2 reaction rate has been quite ambiguous. On the other hand, it has been known for decades that α-carbonyl substituents (e.g., phenacyl bromide) significantly enhance the displacement reaction rate relative to simple alkyl halides;[10] on the other hand, however, more recent evidence demonstrated that this is not generally true[11] and that the order of reactivity of $PhCOCH_2Br$ relative to $PhCH_2Br$[11a] or MeI[11b] may, in fact, be reversed. Thus, Halvorsen and Songstad have shown that the S_N2 rate ratio of $PhCOCH_2Br$ vs. MeI strongly depends on the nature of the nucleophile and ranges between 110 for the powerful anionic nucleophile Cl^- to 0.14 for the neutral triethylamine.[11b] Similar behavior was noted in the reaction of para-substituted benzyl chlorides, where a *p*-nitro group enhances the S_N2 reaction rate in the presence of powerful nucleophiles (relative to unsubstituted benzyl chloride), but it *decelerates* the reaction with weak nucleophiles.[2]

Finally, it will be shown that TS geometry and charge distribution are profoundly influenced by α-substituents, and implications on the S_N2–S_N1 borderline problem will be discussed.

Perturbational Molecular Orbital Analysis[12]

In order to account for the remarkable difference in activating effects of the halo and oxygen α-substituents, we first focus our attention on the S_N2 TS and its frontier MO's. We restrict ourselves in this discussion to the analysis of the S_N2 identity exchange (eq 2), in which the nucleophile and leaving group are equal. The simplest (hypothetical) TS is the D_{3h} CH_5^- anion,



$$N{:} + \overset{Y}{\overset{|}{CH_2}}{-}N \longrightarrow \left[N{-}\overset{Y}{\overset{|}{\underset{H\ \ H}{C}}}{-}N \right]^{*} \longrightarrow N{-}\overset{Y}{\overset{|}{CH_2}} + {:}N \quad (2)$$

with the two axial hydrogen atoms serving as the nucleophile and leaving group (in the more general case of eq 2, the TS belongs to C_{2v} symmetry). The two highest occupied MO's of this molecular structure are shown in Figure 1. The HOMO is a nonbonding orbital of σ-symmetry, with coefficients only on the nucleophile and leaving group hydrogens, while the one below is a weakly bonding, two-electron three-center MO, connecting the nucleophile and leaving group to the central carbon. It is also a σ-orbital, being cylindrically symmetric with respect to the reaction coordinate axis, but since it involves a carbon p atomic orbital, it can participate in π-overlap with substituent orbitals.[13]

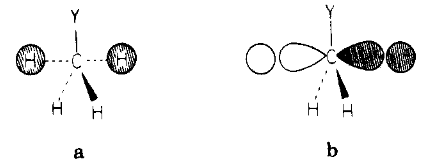


Figure 1. Highest occupied MO's of the CH_5^- TS or fragment orbitals of the CH_4 part of an α-substituted $Y-CH_4^-$ TS: (a) HOMO, (b) HOMO-1.

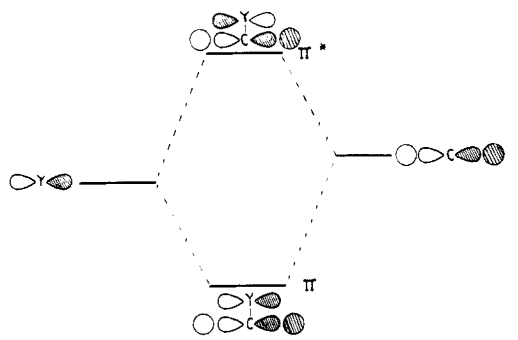
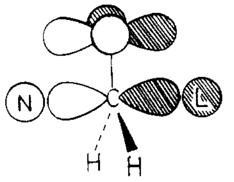


Figure 2. Schematic diagram of the π-interaction between the substituent p orbital and the HOMO-1 π-type orbital at the S_N2 TS.

Let us now examine the effect of substituting one of the equatorial hydrogen atoms of the TS by a halogen atom (eq 2, Y = X). The resulting C_{2v} TS (**1**) will have a lone-pair p orbital aligned parallel to the reaction coordinate, perfectly oriented for maximum π-overlap with the HOMO-1 MO of the unsubstituted TS fragment. The interaction between the two fragment orbitals results in the formation of two MO's, π and π*, as represented schematically in Figure 2. Since both orbitals are doubly occupied, this overlap constitutes a four electron *repulsive* π-interaction, which, in turn, causes an increase in TS energy and is responsible for the deactivating effect of the α-halo substituent.



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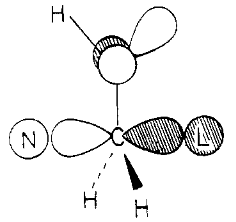

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When an oxygen substituent (e.g., methoxy, represented here for simplicity by a hydroxy group) replaces the α-hydrogen atom to form TS (**2**), the situation is quite different. The two lone pairs of electrons on oxygen occupy orbitals of different symmetries and energies. One is an in-plane, sp hybrid orbital, which is only slightly suitable for π-overlap with a neighboring p orbital, while the other oxygen fragment lone-pair orbital is essentially a pure atomic p orbital.[12c] Consequently, the extent of repulsive π-overlap with the reaction coordinate orbital will strongly depend on the conformation of the TS. When the p lone-pair orbital of oxygen is parallel to the reaction coordinate, substantial four-electron destabilization occurs, similar to the α-halo case. If, however, the OH group is rotated by 90°, as depicted in **2**, π-overlap becomes negligible and no significant destabilizing interaction can be expected. Since the alkoxy substituent is free to relax to its minimum energy conformation (i.e., the latter conformation), it

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(13) The possibility of such interaction was first suggested by Dewar[14a] and applied by Bordwell[14b] and Hine.[6b]

Table II. Substituent effect on S_N2 Activation Barrier

substituent	barrier, kcal/mol		isodesmic energy, kcal/mol[a]		on-off difference kcal/mol
	$\Delta E_{reactants}$	$\Delta E_{complex}$	$\delta E_{reactants}$	$\delta E_{complex}$[b]	
H	48.79	57.30	0.00	0.00	
NH_2(off)	44.74	59.18	−4.04	1.89	10.89
NH_2(on)	55.64	70.08	6.85	12.78	
BH_2(off)	51.64	58.61	2.85	1.31	−28.78
BH_2(on)	22.86	29.83	−25.93	−27.47	
OH(off)	41.81		−6.98		9.81
OH(on)	51.62		2.83		
CHO(off)	44.83		−3.95		−17.55
CHO(on)	27.24		−21.50		
F	44.82	64.50	−3.97	7.20	
CH_3[c]	51.42	60.51	2.63	3.22	

[a] For definitions, see text. [b] Complex structures for the nonsymmetrical CHO and OH substituents were not included, since several local (and shallow) minima could be found, and final geometries could not be determined with sufficient certainty. [c] Staggered ethane was taken as the reactant. At the TS, the two possible rotamers divided by a sixfold barrier were essentially equal in energy, differing only by 0.19 kcal/mol. The lower energy rotamer of the encounter complex was used, in which the incoming H is syn-periplanar to a methyl hydrogen.

produces no deactivating effect toward nucleophiles in the S_N2 reaction.

In the following sections, we present evidence in support of this idea that destabilizing π-interactions between α-substituents and the reaction coordinate orbitals have a major influence on S_N2 reactivity. Stabilizing (two-electron) π-interactions will also be examined, and the conditions under which they act to accelerate S_N2 reactions will be discussed.[15]

In order to test directly the effect of π-interactions upon the S_N2 TS, model substituents have been selected in which this effect can be readily isolated: planar-NH_2 and BH_2. These substituents have each a single nonbonding, pure p orbital, which is occupied by a lone pair in the former and is vacant in the latter. They offer the advantage that their π-interaction with the reaction center can be turned "on" and "off" at will, simply by rotation of the substituent plane by 90° about the C–Y bond (Y = N and B; Figure 3). In addition, several other substituents of interest have been studied.

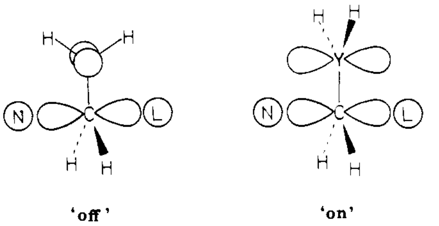

Figure 3. Conformations of S_N2 TS with planar-NH_2 and BH_2 substituents showing maximum π-overlap in the on conformation and no overlap in the off conformation.

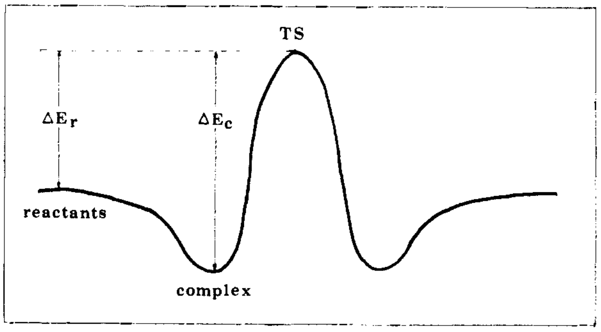

Figure 4. Potential energy profile of a gas-phase S_N2 identity exchange reaction.

SCF-MO Calculations[16]

Single-determinant, ab initio SCF–MO calculations were carried out by using the GAUSSIAN-70[17a] and GAUSSIAN-76[17b] systems of programs. Initial tests revealed that neither the minimal STO-3G[18] nor the 3-21G[19] split valence shell basis sets were sufficiently flexible to produce satisfactory optimum geometries for the negatively charged transition states. Only at the 4-31G[20] level were the calculated TS geometries close enough to those calculated previously[16] with larger basis sets. Radom has shown that geometries of anions calculated by using the 4-31G basis set agreed well with X-ray data,[21] and Wolfe and Mitchell determined the suitability of this basis set for S_N2 TS calculations after a thorough comparison with other sets and with literature data.[22] While larger basis sets with diffuse functions might be desirable, the 4-31G set seemed like the only one that would yield satisfactory results and at the same time would also be sufficiently practical. We therefore used the 4-31G basis set throughout the calculations.

Extensive geometry optimization was applied to all structures and was repeated until no further significant change (i.e., less than 0.01 Å in bond distance and less than 1° in angle, as well as less than 0.1 kcal/mol in total energy) was found in successive runs. Transition-state geometries were located by imposing equal distances between the central carbon and the (identical) nucleophile and leaving group, as well as equal bond angles (i.e., Y–C–N = Y–C–L). For most of the substituents in this study, equivalence of the L and N groups is dictated directly by the symmetry of the system (C_{2v}), and the method of optimization ensures that

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(15) π-Interactions of the type employed here are most significant in the symmetrical, identity reaction, on which the present study focuses. The extent to which this model applies in the general, nonidentity S_N2 case will be studied and reported separately. The related question of the applicability of the Marcus equation has been dealt with recently by Wolfe et al.[16p]

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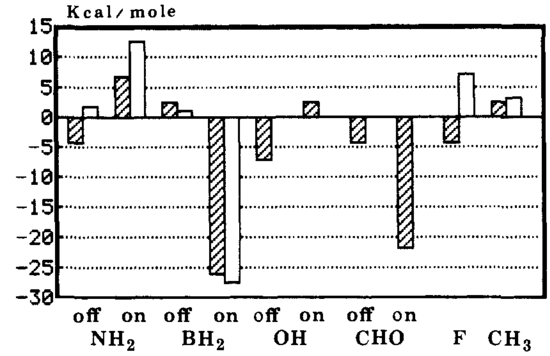


Figure 5. Substituent effect on S_N2 activation barrier relative to hydrogen (=0). Filled bars - $\delta E_{\text{reactants}}$; blank bars = $\delta E_{\text{complex}}$.

minimum-energy TS structures are found. However, for the OH and CHO groups, which lack local C_2 symmetry, this constraint may lead to geometries slightly different from the "true" saddle point transition states. Nevertheless, the results obtained with these substituents agree well with those obtained for the symmetrical model substituents, NH_2 and BH_2, and all of the conclusions rely primarily on the latter.[23]

Results and Discussion

Substituent Effect on Activation Energy. It has been demonstrated both experimentally[24] as well as by MO calculations[16] that the gas-phase S_N2 exchange proceeds via an initial encounter complex, which is stabilized relative to separate reactants, followed by activation to TS and transformation to products–complex and products, as illustrated for the identity exchange in Figure 4. This course of reaction is indeed reproduced in all the calculations. It is not quite clear which of the two barrier types shown in Figure 4 is a better representation of the actual experiment. Both types of barriers, defined by eq 3 and 4, are measured in gas-phase S_N2

$$\Delta E_{\text{complex}} = E_{\text{TS}} - E_{\text{complex}} \tag{3}$$

$$\Delta E_{\text{reactants}} = E_{\text{TS}} - E_{\text{reactants}} \tag{4}$$

reactions.[24a] For solution reactions, the solvent has a major stabilizing influence on the nucleophile and therefore the difference in the TS energy and ground-state complex (eq 3) probably better describes the reaction.[25] Both types of barriers have been calculated for the identity reaction, with hydride as the nucleophile and leaving group (eq 2, N = H^-), and are shown in Table II.

In order to examine the effect of the substituents on the barriers, the *increment* added to the activation energy due to the substituent, relative to hydrogen, is of greatest interest. This increment can be expressed in terms of the isodesmic reaction[26] energy (eq 5)

$$\text{N-YCH}_2\text{-L}^* + \text{CH}_3\text{-L} \rightarrow \text{N-CH}_3\text{-L}^* + \text{YCH}_2\text{-L} + \delta E \tag{5}$$

associated with the transfer of substituent Y from the TS structure to ground state and the simultaneous transfer of hydrogen from ground state to TS. Upon addition of N to both sides of eq 5 and proper rearrangement, (6) is obtained, which simply expresses the difference in activation energies for the substituted and unsubstituted substrate molecules, and may be replaced by (7) where

$$\text{N-YCH}_2\text{-L}^* - (\text{YCH}_2\text{L} + \text{N}) = \text{N-CH}_3\text{-L}^* - (\text{CH}_3\text{L} + \text{N}) + \delta E \tag{6}$$

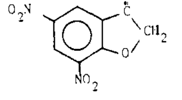
$$\delta E^{\text{Y}} = \Delta E^{\text{Y}} - \Delta E^{\text{H}} \tag{7}$$

ΔE (and consequently also δE) can be defined either as in (3) or as in (4), and δE expresses the increase in activation energy due to substituent Y relative to H. These specific changes in activation barriers associated with each substituent are listed in Table II; they were calculated by using either the reactants or complex for ground state and are represented graphically in Figure 5.

In the following discussion, the calculated results are employed to rationalize experimental results obtained in solution (and outlined in the Introduction section). Ideally, of course, one would seek to compare ab initio results with gas-phase experiments. However, gas-phase measurements of α-substituent effects on S_N2 reactions are as yet unavailable, except for alkyl substituents.[24b] These are of little interest in connection with the present problem, since no significant donor or acceptor orbitals are present on alkyl substituents. Since much of the analysis of the S_N2 TS relates to an *intramolecular* conformational change (between "on" and "off"), it may be expected that the solvent would not play an important role, since solvent effects would be similar for both rotamers.

It is evident even from a preliminary examination of Figure 5 that the PMO analysis outlined above is borne out by the calculations. Let us first analyze the results relating to activation energies with respect to free reactant molecules. There is a great difference in activation barriers for the two conformations of the NH_2 substituent, indicating that the four-electron π-interaction is of great importance. When the interaction is turned on, the substituent is strongly deactivating relative to hydrogen, whereas in the off conformation it has an activating effect. In the on conformation, this substituent serves as a model for the α-halogen group with its lone pair parallel to the reation coordinate and with its strong deactivating influence. In the off conformation, the NH_2 group resembles the α-methoxy or α-hydroxy substituents, which effectively avoid the repulsive interaction by a 90° conformational change. This analogy is also confirmed by the independent calculation for the hydroxy group: it stabilizes the TS (i.e., activates) in the off conformation and destabilizes in the on conformation.

The results for the π-acceptor substituents are also in accord with expectation, in that both π-acceptor substituents in Figure 5 (BH_2, CHO) show a dramatic activating effect relative to the unsubstituted substrate when in the on conformation, while in the off conformation they show moderate activation. In other words, the stabilizing interaction responsible for the rate enhancement observed for such substituents can only be active in the on conformation of the TS. Thus, when an α-carbonyl group is locked into a position where its π-orbital is perpendicular to the reaction coordinate at the TS, no rate enhancement can take place, as so elegantly demonstrated by Bartlett and Trachtenberg, who measured a 21 kcal/mol higher activation barrier for the reaction of KI with **3** than with **4**.[27] In **4** the α-carbonyl substituent adopts a conformation corresponding to the on arrangement at the TS (maximum overlap between the CO π-system and the reaction coordinate π-orbital), whereas in **3** the CO group is constrained to be turned off from interacting with the reaction coordinate orbitals, with a consequent huge loss in TS stabilization.



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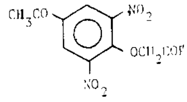

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Having demonstrated that π-interactions follow the expected trend, we now turn to σ-effects. A distinct trend emerges from

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[23] Strictly speaking, only one of the two torsional conformers (on and off) of each TS model can be a true TS, in the sense of representing the highest point in the lowest energy path for the transformation. In the mathematical sense, however, and for the sake of meaningful comparisons, *both* structures represent saddle points on a potential energy hypersurface, since the torsional coordinate is constrained and is no longer an independent variable coordinate. The higher-energy TS may be regarded as a representation of a TS for an analogous molcule in which the torsional angle is physically constrained, by means of steric effects or inclusion of the substituent in a ring.

[24] Recent gas-phase S_N2 studies: (a) Pellerite, M. J.; Brauman, J. I. *J. Am. Chem. Soc.* **1983**, *105*, 2672. (b) Caldwell, G.; Magnera, T. F.; Kebarle, P. *J. Am. Chem. Soc.* **1984**, *106*, 959. (c) Bohme, D. K.; Mackay, G. I.; Tanner, S. D. *J. Am. Chem. Soc.* **1980**, *102*, 407.

[25] Theoretical evidence supporting this energy profile for solution reaction has been published recently: Chandrasekhar, J.; Smith, S. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1984**, *106*, 3049.

[26] Hehre, W. J.; Ditchfield, R.; Radom, L.; Pople, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 4796.

[27] Bartlett, P. D.; Trachtenberg, E. N. *J. Am. Chem. Soc.* **1958**, *80*, 5808.

the results in Figure 5 and Table II, relating to barriers with respect to *reactants*. We find that substituents with electronegative central elements are *activating* relative to hydrogen, when their π-interactions are neutralized in the off conformation. Thus, NH_2, OH, and HCO in the off conformation, as well as F (for which torsion is undefined and which may be considered to be on due to its π-donor properties), are all stabilizing, whereas the electropositive substituents BH_2 (off) and methyl are slightly destabilizing relative to hydrogen. This result for the inductive effect agrees well with Bordwell's conclusions.[28] It seems consistent within the substituent elements in Figure 5 and may provide the explanation for the excessive reactivity generated by α-oxygen substituents (since the PMO model only suggests the absence of a deactivating effect for these substituents).[30]

The behavior of fluorine, on the other hand, is somewhat puzzling in this context, since as a halogen it is expected to have a deactivating effect, though not to the same extent as other halogens.[32] Hine had found that the retarding effect of an α-fluoro substituent is comparable to that of a methyl group and least of all halogens.[4,5] The slight activation reflected in the $\delta E_{\text{reactants}}$ for fluorine in Figure 5 could either result from an improper balance between σ-acceptor and π-donor properties in the basis set for this element, tending to overemphasize the former, or else it might be the result of inadequacy of the method of determination of activation energies as the difference between TS and reactants energies (eq 3). Indeed, the alternative method (eq 4) of measuring activation barriers relative to the *encounter complex* rather than free reactants yields a more satisfying result for fluorine: the activation barrier is 7.2 kcal/mol *higher* than the corresponding barrier for the unsubstituted compound (Figure 5 and Table II). Thus, it appears that $\delta E_{\text{complex}}$ provides a better description of the reaction of α-fluoro-substituted substrates in solution than does $\delta E_{\text{reactants}}$.

A comparison of the two types of S_N2 barriers seems in place. Clearly *both* methods reflect the importance of π-interactions at the TS; thus, in both, the π-donor substituents are deactivating and the π-acceptor substituents activating when in the on conformation. It is not quite obvious which of the two barrier types represents a better description of solution experiments, and it is probably reasonable to assume that the true description lies between these two barriers, depending on the nature of the solvent.[25] Therefore, trends which are consistent and common to both types of barriers may safely be regarded as real factors operating in the reaction. Thus, we conclude that π-interactions between substituents and the reaction center constitute a major factor in the S_N2 reaction and govern its rate.

A distinct *difference* between trends arising from the two barrier types is found when inductive effects are compared. Examination of $\delta E_{\text{complex}}$ values reveals that in the off conformation, when π-interactions are largely absent, no significant substituent effect can be detected (for NH_2 and BH_2); barriers for these substituents are very near that for the unsubstituted compound. This is in contrast with the activating effect of electronegative substituents which emerges from $\delta E_{\text{reactants}}$ results in Figure 5 and which has been postulated by Bordwell.[28] Since both sets of results involve the same transition states, the different trends must arise from different substituent effects on *ground states* in the two barrier types. We arrive at the conclusion that in the present system, σ (inductive) effects, whether electron withdrawing or releasing, operate much to the same extent in the encounter complex as well as in the TS, with a resulting *cancelation* of the effects on activation barriers. In line with this conclusion, the deactivating effect found for fluorine (in its $\delta E_{\text{complex}}$ barrier) may be attributed to its π-donor properties, as the σ (inductive) properties would be expected to cancel out.

Table III. Optimized Transition-State Geometries

substituent Y	$C-H_{ax}$, Å	C–Y, Å	$C-H_{eq}$, Å	$Y-C-H_{ax}$, deg	$Y-C-H_{eq}$, deg
H	1.729	1.059	1.059	90.0	120.0
NH_2(off)	1.675	1.434	1.065	91.2	122.1
NH_2(on)	1.904	1.375	1.051	101.9	120.4
BH_2(off)	1.734	1.565	1.064	94.7	122.0
BH_2(on)	1.767	1.502	1.068	82.9	122.1
OH(off)	1.612	1.434	1.058	90.2	121.1
OH(on)	1.709	1.410	1.053	94.9	116.7
			1.055[a]		122.8[a]
CHO(off)	1.657	1.510	1.062	92.5	121.2
CHO(on)	1.687	1.440	1.061	87.4	120.8
			1.061[a]		120.1[a]
F	1.588	1.421	1.060	89.6	120.2
CH3	1.718	1.522	1.059	93.8	121.3

[a] H_{eq} syn to substituent H.

Table IV. Net Mulliken Charge on Nucleophile (H_{ax}) at S_N2 TS

substituent	charge on nucleophile	substituent	charge on nucleophile
H	−0.6107	OH(off)	−0.4471
NH_2(off)	−0.5580		−0.5735[a]
NH_2(on)	−0.6938	OH(on)	−0.5907
BH_2(off)	−0.5850	F	−0.5071
BH_2(on)	−0.5478		

[a] H_{ax} syn to substituent H.

We may summarize the comparison as follows: while trends in π-interactions are strong and come through clearly in both methods of barrier measurement, σ-effects are weaker and differ between the methods; therefore, there can be little doubt concerning the validity and importance of the former, while some caution should be exercised when drawing conclusions about the latter.

Transition-State Geometry.[33] Optimum geometries found for the transition states are presented in Table III. Some of the results clearly conform to the PMO analysis, while others may seem to conflict and require interpretation. Among the former are, for instance, the $Y-C-H_{ax}$ bond angles: for π-acceptor Y substituents in the on conformation, where a stabilizing interaction develops at the TS, these angles are smaller than 90° (82.9° and 87.4° for BH_2 and CHO on, respectively), indicating that the nucleophile and leaving group *tilt toward the substituent* as to maximize overlap and stabilization. Conversely, π-donor substituents effect a tilt of the axial-H groups *away* from Y, to minimize the four-electron repulsion (101.9° and 94.9°, respectively, for NH_2 and OH in the on conformation). No such tilts are obtained with the same substituents in the off conformation, and the corresponding angles slightly exceed 90° for donors and acceptors alike, apparently reflecting some steric congestion at the substituent.

The substituent effect on the C–Y bond length is more complex. Thus, we find in Table III that the C–B distance decreases when BH_2 is turned from off to on, in accord with expectation for a stronger bond. However, turning on the destabilizing interaction associated with the NH_2 substituent is accompanied by a remarkable *shortening* of the C–N bond, in contrast with what might have been expected intuitively. This is also accompanied by a very large increase in the $C-H_{ax}$ distance, indicating a substantially "looser" TS in the on conformation for the π-donor substituent. Examination of net charges on the nucleophile (and leaving group) (Table IV) leads to an understanding of these geometrical changes.

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[28] Bordwell concluded that the inductive effect for electron-withdrawing groups is mildly rate enhancing and that rate retardation by α-sulfones is due to steric factors.[14b,29]

[29] Bordwell, F. G.; Cooper, G. D. *J. Am. Chem. Soc.* **1951**, *73*, 5184.

[30] However, the alternative possibility that under the conditions studied so far α-oyxgen substrates react substantially in an S_N1-like S_N2 mechanism (also termed "S_N2-intermediate" by Bentley and Schleyer[31]) and that the developing α-oxocarbocationic center is responsible for at least part of the observed rate enhancement cannot be ruled out without further experiments.[7a,8,16q]

[31] Bentley, T. W.; Schleyer, P. v. R. *Adv. Phys. Org. Chem.* **1977**, *14*, 1.

[32] Attempts to calculate the TS for an α-Cl substituent, CH_4Cl^-, were unsuccessful as this TS tends to decompose to $CH_4 + Cl^-$ when optimized at the 4-31G level.

[33] A different aspect of TS geometry was treated by Wolfe et al.[16p] The variation of TS geometry with changing nucleophiles was studied, whereas the present study relates to the symmetrical, identity exchange with respect to changing α-substituents.

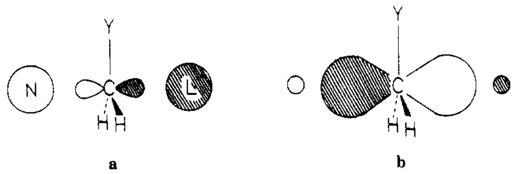


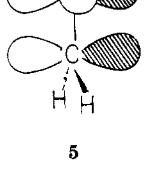
Figure 6. Effect of extension of reaction coordinate distances (TS looseness) on (a) HOMO-1 and (b) LUMO orbitals.

Table V. Substituent Effect on Methyl–Carbenium Ion Energy

substituent	TS energy, au	on–off energy difference, kcal/mol
H	-39.175 13	
NH_2(off)	-94.135 38	-71.70
NH_2(on)	-94.249 64	
BH_2(off)	-64.422 41	20.30
BH_2(on)	-64.390 06	
OH(off)	-113.958 77	-14.13
OH(on)	-113.981 29	
F	-137.895 50	

Table IV reveals that in the looser TS, charge separation is greater, such that more negative charge is concentrated on the axial groups and more positive charge on the central carbon and its equatorial substituents. Thus, the loose TS is closer in nature to a solvated carbocation and represents an "S_N1-like" S_N2 TS.[7a,8] As a result of the positive charge on the carbon, the adjacent bonds become shorter, simply due to stronger nuclear-electron attraction. This is also evidenced by the concomitant shortening of the C–H_{eq} bond (Table III). In this species, not only the nonbonding HOMO is concentrated on the N–L groups but also the HOMO-1 consists mainly of large coefficients on the axial groups, with only a minor contribution from the central carbon p orbital (Figure 6a). In order to reduce the repulsive four-electron interaction, the carbon p coefficient is minimized by way of lengthening of the reaction coordinate bonds, with a consequent decrease in π-overlap. At the same time, extension of the N–C–L distances brings about an *increase* in the carbon p coefficient in the LUMO orbital, which is the out-of-phase combination of the reaction coordinate π-like orbital, and hence stabilizing two-electron π-interaction with substituent lone pair develops (Figure 6b). Evidently the lengthening of the reaction coordinate bonds and the associated charge separation are less costly in terms of energy than the repulsive interaction in the "tight" TS. Thus, the four-electron repulsion is, in fact, translated into a combination of structural changes which represent the minimum overall energy increase.

S_N2–S_N1 Borderline Problem. It should be noted that *the very same π-interaction that is destabilizing at the S_N2 TS (with the NH_2 on substituent) stabilizes the S_N1 intermediate.* The large preference of π-donor substituents to occupy the on conformation in carbenium ions was demonstrated quantitatively in an ab initio study by Apeloig et al.[34] For the sake of comparison with our S_N2 results, we repeated some of the calculations by using the same basis set, the 4-31G set. The results are shown in Table V, and they conform to those published.[34] A striking demonstration of the importance of this interaction in stabilizing carbocations is the case of the α-hydroxymethyl ion (**5**). An attempt to optimize this species in the off structure (i.e., holding the HCH and HOC planes perpendicular to each other) resulted in a linear COH group (C_{2v} symmetry), in which the OH orbitals are rehybridized to enable π-overlap between an oxygen p orbital and the vacant carbon p orbital. Thus, the gain in energy due to this overlap is greater than the loss involved in promotion of the sp lone pair to pure p.[35]



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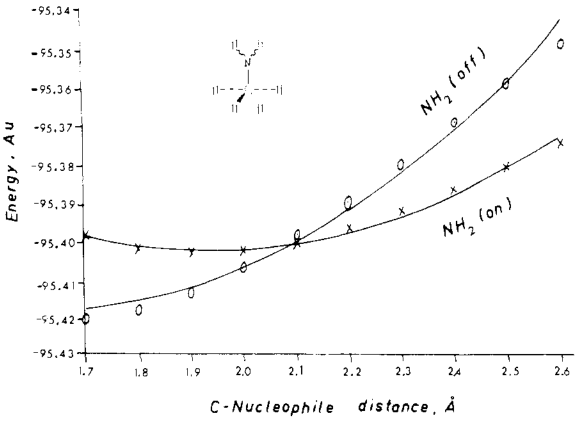

Figure 7. Effect of looseness on TS energy with NH_2 substituent in on and off conformations.

In order to investigate the gradual transformation between S_N1 and S_N2 mechanisms, one would ideally like to be able to vary the relative importance of orbital vs. charge interaction between the nucleophile and leaving group on the one hand, and the central carbon on the other. Within the framework of Klopman's equation, we consider the interaction energy to be composed of electrostatic and orbital overlap terms.[36] In the S_N2 TS, the interaction between the central carbon and the two N fragments (nucleophile and leaving group) is dominated by orbital overlap (covalent bonding). By contrast, we consider the S_N1 reaction to involve a solvated carbocation, i.e., a species in which the two N groups are held to the central carbon by electrostatic forces. Since the overlap falls off much more rapidly with the distance than does the electrostatic interaction, the latter will dominate the energy at long C–nucleophile distances, while at short distances the former term is more important.

Changing the nucleophile would be one way of affecting the balance of these interactions. However, a system which would simulate a continuous change in this balance would be more useful for the study of the S_N2–S_N1 borderline. The model we have used is a series of $CH_4NH_2^-$ structures of C_{2v} symmetry, at both the on and off conformations. The structures are generated from the optimized transition states by extension of the C–H_{ax} distances. At large C–H_{ax} distances (loose structures), the interaction energy is dominated by coulombic factors, and thus they represent S_N1-like transition states. In the region of tight TS (short C–H_{ax} distances), the structures represent S_N2 transition states dominated by overlap. While the extended structures are not true transition states in the mathematical sense, since the C–H_{ax} distances correspond to neither minimum nor maximum energies with respect to the variation of this coordinate, they do model the continuum of mechanistic types: Such structures would represent true transition states if the H_{ax} could be replaced by nucleophiles of continuously varying nucleophilic strength. In that case, the *optimized* TS structures would have gradually longer C–nucleophile distances, and the balance between charge and orbital interactions would change in a manner similar to that in the present model.

An alternative way of looking at this model is the following: A powerful nucleophile, which in the identity exchange reaction

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[34] Apeloig, Y.; Schleyer, P. v. R.; Pople, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 1291.

[35] A closely related case of a linear N–N–H arrangement in the H_2N–NH cation has been reported recently: Kost, D.; Aviram, K.; Raban, M. *Isr. J. Chem.* **1983**, *23*, 124.

[36] Klopman, G. In "Chemical Reactivity and Reaction Paths"; Klopman, G., ed.; Wiley Interscience: New York, 1974; p 55.

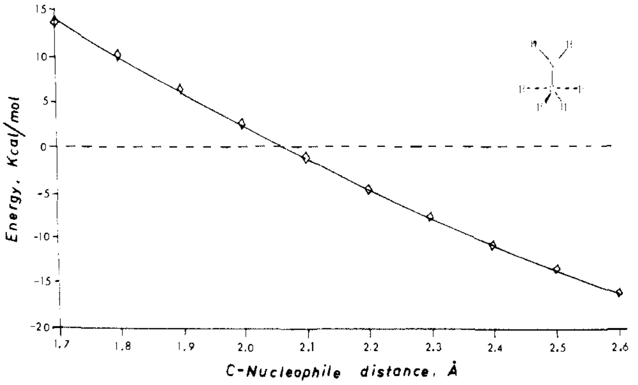

Figure 8. Difference in energy between on and off conformations of the $NH_2CH_4^-$ S_N2 TS as a function of TS looseness.

also constitutes a poor leaving group, imposes a tight S_N2 TS. A weaker nucleophile is associated with a stronger leaving group and with a looser (i.e., more S_N1-like) TS.[2h,37,38] Therefore, to a first approximation, we may consider the extended $C-H_{ax}$ bonds as representing transition states with stronger leaving groups and weaker nucleophiles. The calculated energy profiles for the on and off structures are shown in Figure 7. Both profiles acsend in energy toward looser transition states, as expected due to their departure from optimum geometry. However, the ascent of the curve describing the off conformation is significantly steeper than that for the on conformation. The latter is initially higher in energy due to the four-electron repulsion, but loosening of the TS gradually ***releases*** this interaction as the system passes from orbital control to charge control. Further extension of the reaction coordinate distances eventually turns the TS into a solvated carbocation, substantially stabilized in the on conformation relative to the other. In the borderline region, these two profiles are very close in energy, and actually a crossover between them occurs. This can best be seen in the curve representing the difference between the profiles (Figure 8), where two regions, a positive and a negative one, are found. In the positive region, four-electron repulsion dominates, and the off conformation is preferred; in the negative region, the on conformation is more stable, as two-electron bonding to the forming carbocation develops. Thus, we clearly distinguish between S_N1 and S_N2 regions along the mechanistic spectrum, with a crossover point separating them. While in terms of TS energy or activation barrier the change in the mechanism is gradual and smooth, *in terms of TS geometry, a sudden, distinct change is identified for the first time, when a 90° rotation of the substituent takes place*, as the energy difference crosses zero. At that point, the minimum energy path changes from the curve describing the NH_2-off TS to that of the NH_2-on TS (Figure 7).

Support for these ideas should also come from discrete nucleophile molecules and their transition states, rather than from the artificially extended structures. We therefore sought nucleophiles of sufficiently different nucleophilic power to demonstrate the change in preference between on and off conformations. The calculated TS energies are listed in Table VI. It is evident that by changing from the powerful hydride nucleophile to ammonia, a shift from the S_N2 to the S_N1-like region has occurred, with the on conformation now being more stable than the respective off conformation. However, it might be argued that the crossover is due to the change in the net charge on the TS (−1 with H^-; +1 with ammonia) rather than to the differences in nucleophilic strength. For this analysis to be more meaningful, the different nucleophiles should *either* be neutral or anionic. To this end, we included in Table VI the borohydride anion, in which charge distribution over five atoms is likely to moderate nucleophilic activity relative to the hydride (particularly in the absence of solvent).[39] Indeed the effect of both of the weak nucleophiles is found to be equivalent, namely, they both effect a mechanistic crossover and act as solvating agents to a stabilized carbocation in a rather loose TS. Thus, MO calculations with discrete nucleophiles lead to the same borderline phenomena as the hydride model.

Table VI. Calculated TS Energies with Different Nucleophiles

nucleophile	substituent	tot energy, au	$\delta E_{\text{reactants}}$, kcal/mol	on–off energy difference, kcal/mol
NH_3:	H	−151.534 49	0.00	
	NH_2(off)	−206.467 79	1.73	−31.11
	NH_2(on)	−206.517 37	−16.23	
	BH_2(off)	−176.741 43	4.24	−3.33
	BH_2(on)	−176.746 74	−6.80	
	F	−250.245 31	−1.81	
$BH4^{-a}$	NH_2(off)	−148.272 20		−18.74
	NH_2(on)	−148.302 08		
	BH_2(off)	−118.545 55		−10.30
	BH_2(on)	−118.561 96		

[a] The BH_4^- structure was optimized separately and kept fixed at that tetrahedral geometry (B–H bond = 1.239 Å, B–H–C axis colinear).

The borderline effects no longer relate only to geometrical changes of the TS but also to significant charge redistribution, and the question of solvent involvement should be considered again. The tight S_N2 TS is not expected to be largely affected by solvation, whereas the loose **TS** should be further stabilized by solvation of its charged particles. Therefore, we may expect the calculated curve of Figure 8 to descend in a steeper fashion in the presence of an ionizing solvent. As a result, the S_N2 region (above the zero line) would decrease and the S_N1-like region would increase, and a nucleophilic displacement with a given substrate would be more S_N1-like.

Finally, we return to the π-acceptor substituents mentioned in the Introduction section. While reduction in the nucleophile strength with a π-donor as the substituent (NH_2-on) affected TS structure and caused a mechanistic crossover, such variation with BH_2 just decreases the difference in energy between on and off conformations (Table VI, −10.30 kcal/mol with BH_4^- as nucleophile relative to −28.78 kcal/mol with hydride). Thus, for powerful nucleophiles (and poor leaving groups), the stabilization by the π-acceptor substituent in the on conformation is by far more significant than for weak nucleophiles. As a result, significantly greater rate enhancement by π-acceptor substituents would be observed for stronger nucleophiles than for weaker ones. This is precisely the observation reported by Halvorsen and Songstad,[11b] as mentioned earlier, and it provides experimental support for our MO model of the S_N2 reaction.[11c]

The behavior of p-nitrobenzyl chloride toward different nucleophiles[2] may be rationalized in similar terms: in the presence of a powerful nucleophile, a tight TS forms, and the stronger π-acceptor property of the p-nitrobenzyl vs. benzyl substituent causes the **TS** to be more stabilized and hence the reaction to proceed faster. With weak (neutral) nucleophiles, the TS is looser and more S_N1-like, with consequent development of positive charge on carbon. Since benzyl is a better π-donor than p-nitrobenzyl, it is more effective in stabilizing such a carbocationic TS, and as a result benzyl chloride reacts faster.

A change in TS tightness caused by changing nucleophiles in the previous examples resulted in different reaction rates. Such changes in TS tightness can also result from variations in the leaving group. It appears that Hine's unexpected observation[5] regrading the relative S_N2 rates of α-fluoro- and α-ethyl-substituted methyl halides may also be due to a variation in TS tightness: with iodide as the leaving group, the TS is slightly looser

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(37) Mihel, I; Knipe, J. O.; Coward, J. K.; Schowen, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 4349.

(38) Westaway, K. C.; Ali, S. F. *Can J. Chem.* **1979**, *57*, 1354.

(39) The BH_4^- is used here as a model for a charge-dispersed hydride ion and not as a reducing agent. Therefore, its geometry is kept constant, and the B–H–C axis, colinear, with no direct boron participation in the nucleophilic attack. Borohydride has been shown recently to react via cyclic transition structures when acting as a reductant: Eisenstein, O.; Schlegel, H. B.; Kayser, M. M. *J. Org. Chem.* **1982**, *47*, 2886.

than with bromide, and consequently the repulsive π-interaction in the fluoro compound is weaker, and less rate retardation is observed.[40]

Acknowledgment. We are grateful to Prof. M. Pomerantz for assistance in calculating the carbocation structures, to Dr. T. Clark for a Cyber version of GAUSSIAN-76, to Prof. M. Raban for helpful discussions, and to Prof. S. Wolfe for a copy of Mitchell's thesis.[22] Financial support from the Fund for Basic Research, administered by the Israel Academy of Sciences and Humanities, is gratefully acknowledged.

Supplementary Material Available: Optimized geometries and energies of transition states, ground-state molecules, and encounter complexes (3 pages). Ordering information is given on any current masthead page.

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[40] For an alternative view of the substituent effect on S_N2 reactivity, see: Shaik, S. S. *J. Am. Chem. Soc.* **1983**, *105*, 4359; *Prog. Phys. Org. Chem.* **1985**, *15*, 197.

Radical Cations of Bridged Bicyclo[5.1.0]octa-2,5-dienes—Open-Shell Bis-Homoaromatic Systems

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Contribution from AT&T Bell Laboratories, Murray Hill, New Jersey 07974.
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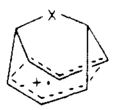
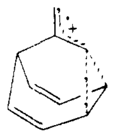
Abstract: The radical cations of a series of bridged bicyclo[5.1.0]octa-2,5-dienes have been generated by photoinduced electron transfer to strong electron acceptors (chloranil, fluoranil) in solution. Chemically induced dynamic nuclear polarization effects observed during the reactions of simple bridged systems (**1b–d,j**) indicate that the intermediates are bis-homoaromatic (BHA)



BHA

(A_2 or B_2)



VCP

a, X = $-CH{=}CH-$; **b**, X = $>CH_2$; **c**, X = $>C{=}O$; **d**, X = $>\overbrace{C-O-CH_2-CH_2-O}$; **e**, X = $>C{=}CH_2$; **f**, X = $>C{=}CHCH_3$; **g**, X = $>C{=}CHC_3H_7$; **h**, X = $>C{=}CHCl$; **i**, X = $>C{=}CHCN$; **j**, X = —

systems of B_2 symmetry. These are the first homoaromatic radical cations of any structure type. Introduction of substituted *exo*-methylene groups as bridging units (**1e–i**) leads to a composite structure type with contributions from bis-homoaromatic structures of A_2 and B_2 symmetry and/or from a vinylcyclopropane structure (VCP) with an antisymmetric singly occupied molecular orbital.

The concept of homoaromaticity was pioneered by Winstein to account for the relative stability of molecules in which the cyclic conjugation of π orbitals is interrupted by an aliphatic fragment.[1] Homoaromatic systems have attracted much attention, and particularly mono- and bis-homoaromatic cations have emerged as a well-documented class of intermediates.[2-4] There are considerably fewer, if any, examples of homoaromatic anions,[5,6] while open-shell homoaromatic systems are unknown with the sole exception of the homocyclooctatetraene radical anion.[7-9]

The concept of homoaromaticity has also been invoked to describe transition states of pericyclic reactions.[10] For example, the degenerate Cope rearrangement of a series of bridged bicyclo[5.1.0]octa-2,5-dienes, bullvalene,[11,12] barbaralane,[12] and semibullvalene,[13] can be formulated through a transition state with a bis-homoaromatic array of orbitals. In the case of semibullvalene, this array is stabilized to the extent that the degenerate Cope rearrangement is fast on the NMR time scale even at −143 °C; it requires an activation energy of only 5.5 kcal/mol.[14]

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