bons and olefins, other than those expected from the type II reactions, constituted less than 0.1% of the yield of the expected type II olefins. In cases where the photolyses were conducted in the absence of nitric oxide the major products observed were those expected from the free-radical reactions of the alkyl groups of the ester, with some contribution from smaller alkyl radicals. Products from the reactions of free radicals with nitric oxide did not undergo subsequent decomposition to produce olefins. Although a detailed study of the mechanisms of these free-radical reactions was not made, it could be estimated that the type II olefins accounted for approximately 1 to 10% of the hydrocarbon products. Hydrocarbon products were analyzed using a 30 ft, 0.25 in. o.d.

column parked with 20% squalane on 60–80 mesh Chromosorb P, operated at ambient temperature and a helium flow of 70 cm³/min.

Open Shell Interactions, Nonbonded Attraction, and Aromaticity. Implications for Regiochemistry

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Abstract: Molecules and transition state complexes can be constructed, in theory, from union of component fragments. Whenever one of these fragments has an open shell electronic configuration, there is a strong one-electron bias toward cis regioselectivity. This simple theoretical analysis can be used to rationalize unexpected chemical phenomena such as the greater stability of the cis relative to the trans isomer of various olefins, the gauche effect in conformational analysis, and the cis regioselectivity of cycloadditions.

Nonbonded interactions of substituents have been traditionally regarded as repulsive in nature[1] although a large body of experimental evidence seemed to indicate that in many instances such interactions can be attractive in nature. Some of this evidence is tabulated in Table I. In the last few years, some novel ideas regarding the nature of long range, or, nonbonded, interactions[2] have been discussed in the literature. Specifically, Woodward and Hoffmann[3] examined the effect of secondary attractive interactions on regioselection as part of their original formulation of the stereochemistry of pericyclic reactions. Hoffmann and Olofson[4] showed subsequently that nonbonded interactions which obtain in conjugated molecules and ions are important structural consequences, and Lowe[5] extended these ideas to problems in conformational analysis. Recently, Hoffmann[6] and his coworkers discussed the concept of steric attraction with particular reference to organic reactions and we showed that through bond and through space orbital interactions can lead to nonbonded attraction in various types of organic molecules and reactions.[7] In this paper, we have adopted a composite

molecule approach in order to elucidate the electronic factors which lead to nonbonded attraction in molecules and transition states. We consider the case of an open shell molecule or fragment[8] interacting with an open or closed shell molecule or fragment to form a product which arises from union of the two molecules or fragments. We shall examine the regioselectivity[9] of such processes and develop a general regioselection rule as a result of a simple theoretical analysis.

Theory

We shall illustrate our approach by considering typical reactions of *cis*-difluoroethylene in its various open shell forms: (1) *cis*-difluoroethylene (CS) + excited *cis*-difluoroethylene (OS); (2) *cis*-difluoroethylene (CS) + *cis*-difluoroethylene cation radical (OS); (3) *cis*-difluoroethylene (CS) + *cis*-difluoroethylene anion radical (OS); (4) excited *cis*-difluoroethylene (OS) + *cis*-difluoroethylene cation radical (OS); (5) excited *cis*-difluoroethylene (OS) + *cis*-difluoroethylene anion radical (OS); (6) *cis*-difluoroethylene cation radical (OS) + *cis*-difluoroethylene cation radical (OS); (7) *cis*-difluoroethylene cation radical (OS) + *cis*-difluoroethylene anion radical (OS); (8) *cis*-difluoroethylene anion radical (OS) + *cis*-difluoroethylene anion radical (OS). Cases 1, 2, and 3 are typical reactions of a ground state, closed shell molecule and an open shell molecule, while cases 4, 5, 6, and 7 are typical reactions between two open shell molecules. The notation CS, in parentheses, stands for closed shell and the notation OS, also in parentheses, stands for open shell.

We first consider a typical closed shell–open shell case such as the reaction of excited *cis*-difluoroethylene and

(1) M. S. Newman, Ed., "Steric Effects in Organic Chemistry," Wiley, New York, N. Y., 1956.

(2) The term nonbonded interaction usually denotes the combined internuclear and interelectronic interaction of two systems. In this paper, we are concerned with the interelectronic component of nonbonded interactions since the variation of the internuclear term is almost always intuitively obvious.

(3) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, Weinheim/Bergstr., Germany, 1970.

(4) R. Hoffmann and R. A. Olofson, *J. Amer. Chem. Soc.*, **88**, 943 (1966).

(5) J. P. Lowe, *J. Amer. Chem. Soc.*, **92**, 3799 (1970); J. P. Lowe, *Science*, 179, 527 (1973).

(6) R. Hoffmann, C. C. Levin, and R. A. Moss, *J. Amer. Chem. Soc.*, **95**, 629 (1973).

(7) N. D. Epiotis and W. Cherry, *Chem. Commun.*, 278 (1973); N. D. Epiotis, *J. Amer. Chem. Soc.*, **95**, 3087 (1973); N. D. Epiotis, D. Bjorkquist, L. Bjorkquist, and S. Sarkanen, *J. Amer. Chem. Soc.*, **95**, 7558 (1973).
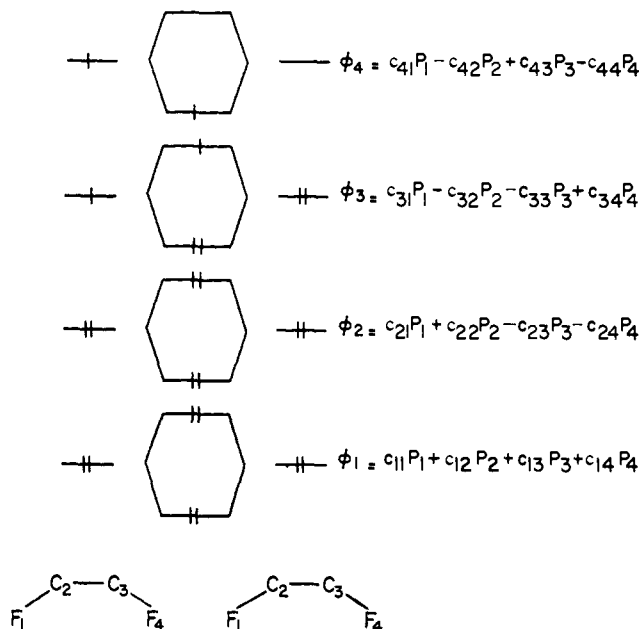
(8) In a closed shell molecule all electrons are paired, while in an open shell molecule they are not.

(9) The term regioselectivity refers to the orientational preference in the union of two molecules.

$$\phi_4 = c_{41}P_1 - c_{42}P_2 + c_{43}P_3 - c_{44}P_4$$

$$\phi_3 = c_{31}P_1 - c_{32}P_2 - c_{33}P_3 + c_{34}P_4$$

$$\phi_2 = c_{21}P_1 + c_{22}P_2 - c_{23}P_3 - c_{24}P_4$$

$$\phi_1 = c_{11}P_1 + c_{12}P_2 + c_{13}P_3 + c_{14}P_4$$

Figure 1. Dominant π MO interactions accompanying the union of an excited and a ground state cis-difluoroethylene.

ground state cis-difluoroethylene to form a cyclobutane adduct. The two regiochemical modes of union are shown below. The interaction diagram[10] shown in
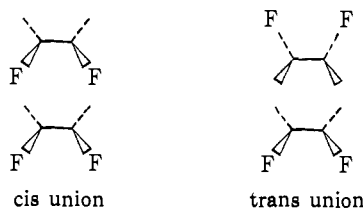

cis union   trans union

Figure 1 displays the principal orbital interactions involved in the union of the two molecules. The stabilization energies which arise from the nonbonded interactions of the fluorines are

$$SE(cis) = (c_{31}^2 + c_{34}^2 + c_{41}^2 + c_{44}^2)\gamma_{FF} \qquad \gamma_{FF} > 0$$

$$SE(trans) = 0 \qquad \gamma_{FF}' = 0$$

where $c_{\mu\nu}$ = coefficient of the νth atomic orbital of the μth MO and γ = resonance integral.

Stabilization is large for cis union and zero for trans union because the resonance integrals γ_{FF} and γ_{FF}' are proportional to the overlap integrals S_{FF} and S_{FF}', respectively,[11] and S_{FF} is appreciable while S_{FF}' is nearly zero. The attractive nonbonded interaction of the fluorines in the case of cis union can be easily visualized by sketching the two principal orbital interactions involved in this reaction. Our analysis can be repeated for cases 2 and 3 and the general conclusion is reached that in all open shell–closed shell cases union of the reactants will be favored to occur in a cis manner on

(10) The use of interaction diagrams has been repeatedly discussed in the literature. For example, see (a) L. Salem, J. Amer. Chem. Soc., 90, 543 (1968); (b) K. Fukui and H. Fujimoto in "Mechanisms of Molecular Migrations," Vol. 2, B. S. Thygarajan, Ed., Interscience, New York, N. Y., 1969, pp 117–190; (c) N. D. Epiotis, J. Amer. Chem. Soc., 94, 1924 (1972).

(11) For a discussion of this and related approximations, one should consult S. P. McGlynn, L. G. Vanquickenborne, M. Kinoshita, and D. G. Carroll, "Introduction to Applied Quantum Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1972, Chapter 4.

Table I. Relative Stability of the Geometric Isomers of XHC=CHY Olefins

X, Y	$\Delta H°$, cal/mol[t]	K_{eq}[t]	Ref
F, F (g)	928 ± 29	0.401–0.582	a, b
Cl, Cl (g)	650 ± 70	0.577–0.683	a, c, d
Br, Br (g)	0 ± 130		a, e
I, I (g)	0 ± 200		a, f
Br, Br (l)	320 ± 200		a, g
I, I (l)	−1550 ± 1000	0.681 ± 0.792	h, i
F, Cl (g)	780 ± 20	0.485–0.669	a, j
Me, Cl		0.316	k
Me, Br		0.471	l
Me, OMe	−910 ± 50	0.408	m
		1.033	n
		1.210	o
Me, OEt	−370 ± 20	0.234	m
		0.722	n
Me, O-i-Bu	−430 ± 50	0.699	n
Me, O-i-Pr	+560 ± 40	0.368	n
Me, O-t-Bu	+680 ± 130	0.296	n
Me, OPh		0.538	p
OMe, OMe (l)	1549 ± 19	0.150–0.338	q
(g)	1445 ± 54	0.210–0.410	q
OEt, OEt (l)		0.25	n
Cl, OEt	+660 ± 130	0.221	n
Me, CN (g)		0.754	k, r
Cl, CN		0.449	k
F, CH=CH₂		0.613	s
Cl, CH=CH₂		0.428	s

^{a} F. L. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967. ^{b} E. B. Whipple, W. E. Stewart, G. S. Reddy, and J. H. Goldstein, J. Chem. Phys., 34, 2136 (1961). ^{c} R. E. Wood and D. P. Stevenson, J. Amer. Chem. Soc., 63, 1650 (1941). ^{d} D. V. Gardner and D. E. McGreer, Can. J. Chem., 48, 2104 (1970). ^{e} R. M. Noyes and R. G. Dickinson, J. Amer. Chem. Soc., 65, 1427 (1943). ^{f} S. Furuyama, D. M. Golden, and S. W. Benson, J. Phys. Chem., 72, 3204 (1968). ^{g} A. R. Olson and W. Maroney, J. Amer. Chem. Soc., 56, 1320 (1934). ^{h} R. M. Noyes, R. G. Dickinson, and V. Schomaker, J. Amer. Chem. Soc., 67, 1319 (1945). ^{i} S. F. Miller, A. Weber, and F. F. Cleveland, J. Chem. Phys., 23, 44 (1955). ^{j} N. C. Craig, Y. S. Lo, L. G. Piper, and J. C. Wheeler, J. Phys. Chem., 74, 1712 (1970). ^{k} J. W. Crump, J. Org. Chem., 28, 953 (1963). ^{l} K. E. Harwell and L. F. Hatch, J. Amer. Chem. Soc., 77, 1682 (1955). ^{m} P. Salomaa and P. Nissi, Acta Chem. Scand., 21, 1386 (1967). ^{n} T. Okuyama, T. Fueno, and J. Furukawa, Tetrahedron, 25, 5409 (1969). ^{o} S. J. Rhoads, J. K. Chattopadhyay, and E. E. Waali, J. Org. Chem., 35, 3352 (1970). ^{p} C. C. Price and W. H. Snyder, J. Amer. Chem. Soc., 83, 1773 (1961). ^{q} J. T. Waldron and W. H. Snyder, J. Amer. Chem. Soc., 95, 5491 (1973). ^{r} J. N. Butler and R. D. McAlpine, Can. J. Chem., 41, 2487 (1963). ^{s} H. G. Viehe, Angew. Chem., 75, 793 (1963). ^{t} A positive enthalpy and an equilibrium constant less than unity mean that the cis isomer is more stable relative to the trans.
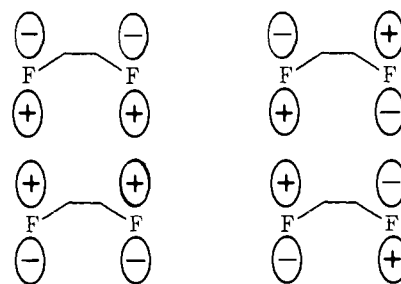
account of nonbonded attractive interactions of the substituents located adjacent to the union sites.

We now consider a typical open shell–open shell case such as the reaction of excited cis difluoroethylene and the cis difluoroethylene radical cation. Again, the two regiochemical modes of union are cis and trans and the interaction diagram shown in Figure 2 displays the
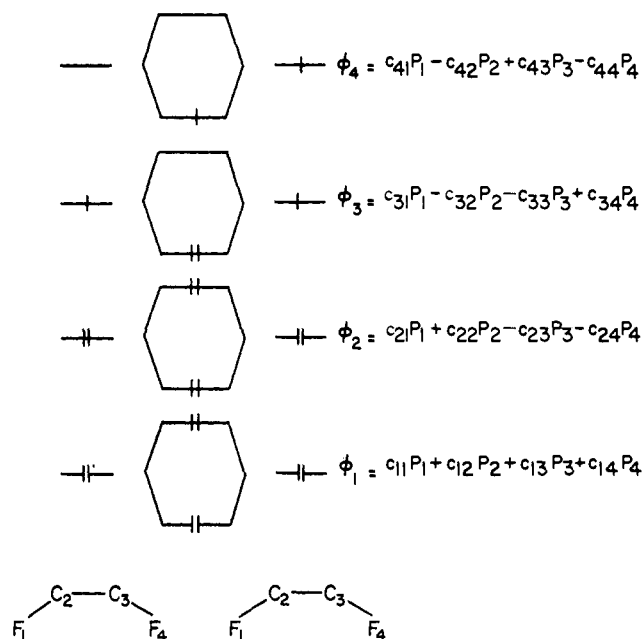
$$\phi_4 = c_{41}P_1 - c_{42}P_2 + c_{43}P_3 - c_{44}P_4$$

$$\phi_3 = c_{31}P_1 - c_{32}P_2 - c_{33}P_3 + c_{34}P_4$$

$$\phi_2 = c_{21}P_1 + c_{22}P_2 - c_{23}P_3 - c_{24}P_4$$

$$\phi_1 = c_{11}P_1 + c_{12}P_2 + c_{13}P_3 + c_{14}P_4$$

Figure 2. Dominant π MO interactions accompanying the union of excited *cis*-difluoroethylene and *cis*-difluoroethylene radical cation.

principal orbital interactions involved in the union of the two molecules. The stabilization energies for cis and trans union due to nonbonded interactions are given below.

$$SE(cis) = (2c_{31}^2 + 2c_{34}^2 + c_{41}^2 + c_{44}^2)\gamma_{FF} \qquad \gamma_{FF} > 0$$

$$SE(trans) = 0 \qquad \gamma_{FF}' = 0$$

The situation is very similar to the situation encountered in the case of the reaction of an open shell and a closed shell molecule. Our analysis can be repeated for cases 5, 6, 7, and 8 and the general conclusion is reached that in all open shell–open shell cases union of the reactants will be favored to occur in a cis manner on account of secondary nonbonded attractive interactions of the substituents located adjacent to the union sites. The general principle which emerges from this discussion can be simply stated: *the interaction of an open shell molecule or fragment with either a closed or open shell molecule or fragment leads to a bias toward cis regioselectivity.*[13,14] As we shall see in a subsequent section, inclusion of overlap in the theoretical treatment does not basically alter this general principle which merely becomes the consequence of the fundamental result of perturbation theory (overlap included) that the interaction between two MO's or AO's can be attractive when total occupancy is 1, 2, or 3 electrons and repulsive when it is 4. We shall now examine chemical examples of various types which illustrate this general principle.

Orientation of Nonpolar Thermal Cycloadditions

The 2 + 2 thermal cyclodimerization of an olefin is a typical example of a nonpolar cycloaddition involving

(12) C. M. Sharts and J. D. Roberts, *Org. React.*, **12**, 1 (1962).
(13) Of course, when the two systems get too close together (presumably less than their van der Waals radii) these considerations cease to be valid as internuclear repulsion comes to dominate.
(14) In the course of a seminar presented by one of the authors, Professor Saul Wolfe suggested that this theory be baptized the "bi cycle" theory (*bias* for *cyclic* structures).
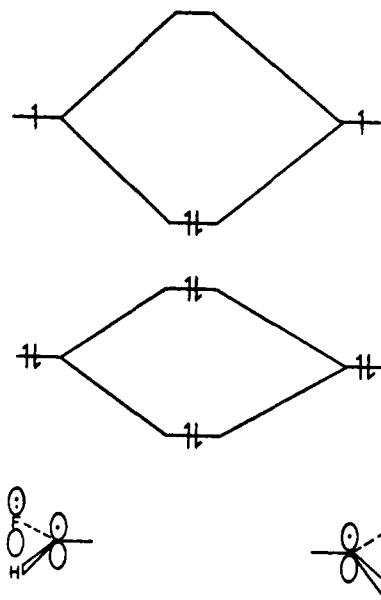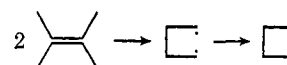

Figure 3. Dominant π MO interactions obtaining in the union of the FHC– radical fragments.

$4n$ electrons. This reaction is probably nonconcerted and occurs *via* the intermediacy of diradicals.[12]

The regiochemistry of the reaction depends on the manner in which the two radical ends of the intermediate unite to form the final product. This latter process is a typical case of open shell–open shell interaction. It is instructive to consider the general case of union of two radical centers which are located at the two ends of a hydrocarbon chain. The possible modes of internal union of such a diradical are shown below

cis union   trans union
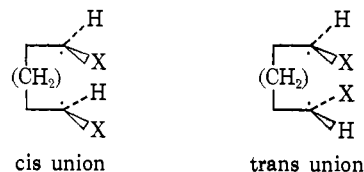
and it is assumed that X is a heteroatom carrying a p_z lone pair. The appropriate interaction diagram for the union of the two radical centers is shown in Figure 3. The stabilization energy equations for cis and trans union of the radical centers are

$$SE(cis) = 2c_{22}^2\gamma_{xx} \qquad \gamma_{xx} > 0$$

$$SE(trans) \simeq 0 \qquad \gamma_{xx}' \simeq 0$$

In this case, the stabilization energy term due to nonbonded interaction of the two heteroatoms is large for cis union and near zero for trans union. In summary, we find that 2 + 2 thermal dimerizations proceeding *via* diradical intermediates can be cis regioselective. These reactions involve open shell–open shell interactions and we have seen that, in general, open shell–open shell or open shell–closed shell interactions lead to cis regioselection.

In the space below we provide a pertinent example drawn from the literature.[15] However, the reader is

(15) E. Vogel, *Angew. Chem.*, **71**, 386 (1959); *Justus Liebigs Ann. Chem.*, **615**, 1 (1959).
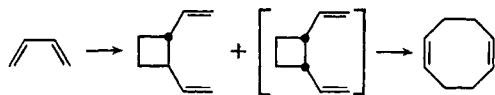
reminded that there could be extreme cases where dipole–dipole or steric repulsions, which are not taken into account by this simple treatment, can reverse the preference for cis union.

Orientation of Nonpolar Photochemical Cycloadditions

The 2 + 2 photodimerization of an olefin is a typical case of nonpolar photocycloaddition involving $4n$ electrons. This reaction is an example of an open shell–closed shell interaction of the type which we considered in some detail in the general theoretical section. It is expected to occur with 2s + 2s stereochemistry in accordance with the Woodward–Hoffmann rules and cis regiochemistry according to the analysis provided in this work. Experimental results which indicate that cis union is favored in such reactions are given below.[16,17] The syn photodimerizations of uracil,

major   minor

major   minor
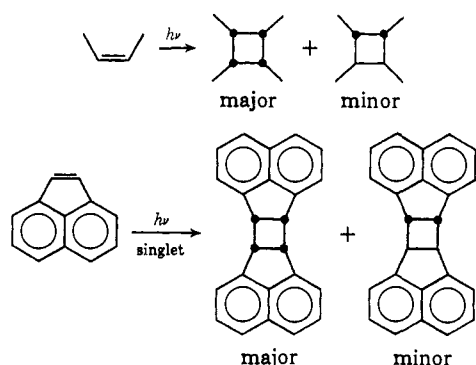
thymine, and most of their derivatives are further examples of the regioselection rule and have been discussed in recent reviews.[18] Again, we note that dipole–dipole and steric repulsion effects can reverse the cis regioselectivity in certain cases. Finally, we note that the reactions cited above are the most likely singlet reactions. In the case of triplet photodimerizations, the secondary stabilization of cis union can be counteracted by several spin-related effects, and simple generalizations might not be possible.[19]

Nonpolar 4 + 2 photocycloadditions could proceed *via* diradical intermediate because the concerted mechanism is rendered unfavorable by the 4s + 2a geometry of a union. Unfortunately, such reactions are difficult to study because the 4 + 2 pathway is dominated by the 2 + 2 pathway which is favored to proceed in a 2s + 2s concerted manner. Nonetheless, stepwise 4 + 2 photocycloadditions can be analyzed in a manner similar to that for stepwise 2 + 2 or 4 + 2 thermal cycloadditions. Future research may provide us with examples of cis regioselection in stepwise 4 + 2 nonpolar photocycloadditions.

(16) H. Yamazaki and R. J. Cvetanovic, *J. Amer. Chem. Soc.*, 91, 520 (1969).

(17) R. Livingston and K. S. Wei, *J. Phys. Chem.*, 71, 541 (1967); D. O. Cowan and R. I. Drisko, *Tetrahedron Lett.*, 1255 (1967).

(18) D. J. Trecker in "Organic Photochemistry," Vol. 2, O. L. Chapman, Ed., Marcel Dekker, New York, N. Y., 1969.

(19) On the other hand, if spin–orbit coupling is of appreciable magnitude the stabilization might in effect be similar for singlet and triplet reactions.

Geometric Isomerism

The relative stability of the cis and trans isomers of various types of olefins cannot be predicted on the basis of intuitive ideas. In fact, the greater stability of the cis isomer of many olefins constitutes a puzzling phenomenon and a very important theoretical problem. We shall treat the problem of geometric isomerism within the framework of the general analysis of open shell–open shell interactions.

We first consider the relative stability of the cis and trans isomers of molecules of the type shown below.

$$XHC{=}CHX$$
I
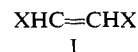
It is assumed that X is a heteroatom which carries, in the most general case, three lone pairs, one in a p_z, one in a p_x, and one in an s atomic orbital. Fluorine is a typical example of such a heteroatom. The assignment of a lone pair to a p_x rather than a p_y atomic orbital is made on the basis of simple theoretical considerations. Specifically, the sp^2 hybrid orbital[20] of the ethylenic carbon which is utilized to form the σ bond with the heteroatom has primary p_y character, as an inspection of the eigenvectors reveals.

$$\phi_{sp^2} = \frac{1}{\sqrt{3}}\left(s + \frac{\sqrt{2}}{2}p_x + \frac{\sqrt{6}}{2}p_y\right)$$

The Cartesian coordinate system is shown below.
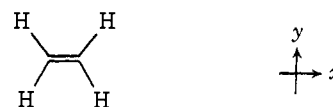
The hybrid sp^2 orbital overlaps more strongly with the p_y rather than the p_x atomic orbital of the heteroatom. For example, in the case of fluoroethylenes, the following overlap integrals are calculated between an olefinic carbon and the p_x and p_y atomic orbitals of the fluorine atom which is attached on the olefinic carbon.[21]

$$\langle\phi_{sp^2}|F_{p_x}\rangle = 0.174$$

$$\langle\phi_{sp^2}|F_{p_y}\rangle = 0.295$$

Hence, the σ bond between the olefinic carbon and the heteroatom involves primarily, *though not exclusively*, the p_y atomic orbital of the heteroatom. The validity of this assumption is further substantiated by a theoretical analysis of the σ nonbonded interactions between ethylenic ligands.[22] In theory, molecules like I can be constructed from union of two XHC: diradical fragments.
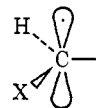
The π system of this formal diradical is isoconjugate to the π system of the ethylene anion radical. Union of

(20) The quantum mechanical description of hybrid orbitals can be found in most quantum chemistry books. For example, see W. Kauzmann, "Quantum Chemistry," Academic Press, New York, N. Y., 1957.

(21) The necessary overlap integrals between individual atomic orbitals were obtained from semiempirical INDO calculations of fluoroethylenes where standard bond lengths and bond angles were used. The argument does not change if the calculations are done for the experimentally deduced geometries.

(22) N. D. Epiotis, submitted for publication.

two such formal diradicals constitutes a typical case of open shell–open shell interaction. One can have cis or trans union, and the interaction diagram which shows the principal π orbital interactions involved in the union of the two formal diradicals is identical with the one drawn for the union of two actual radicals in Figure 3. The stabilization energies for cis and trans union due to nonbonded interaction of the two fluorines (X = F) are

$$SE(cis) = 2c_{22}{}^2\gamma_{FF} \qquad \gamma_{FF} > 0$$

$$SE(trans) = 0 \qquad \gamma_{FF} = 0$$

Once again, we arrive at the conclusion that nonbonded interactions will favor cis union. In the union of two C–X fragments, increasing electronegativity of X results in greater localization of the p_z lone pair of X and smaller nonbonded attraction since the coefficient c_{22} tends to zero. One can analyze the σ orbital interactions in the same manner and arrive at the same conclusions as above.

The relationship between nonbonded attraction and bond order is an important one and can be easily understood by reference to the simple open shell–open shell interaction case involving union of two XHC: formal diradicals to form XHC=CHX. The bond order between the p_z lone pairs of the two heteroatoms can be calculated from the π MO's of XHC=CHX, which are, in general, the following.

$$\phi_1 = l_{11}p_1 + l_{12}p_2 + l_{13}p_3 + l_{14}p_4$$

$$\phi_2 = l_{21}p_1 + l_{22}p_2 - l_{23}p_3 - l_{24}p_4$$

$$\phi_3 = l_{31}p_1 - l_{32}p_2 - l_{33}p_3 + l_{34}p_4$$

$$\phi_4 = l_{41}p_1 - l_{42}p_2 + l_{43}p_3 - l_{44}p_4$$

The bond order between the two p_z lone pairs is

$$P(p_1,p_4) = 2(l_{11}l_{14} - l_{21}l_{24} + l_{31}l_{34})$$

Now, the stabilization resulting from the nonbonded interaction of the two X heteroatoms is given by the following expression, as we have seen before.

$$SE(nonbonded) = 2c_{22}c_{22}\gamma_{FF}$$

In the bond-order expression, the first two terms in parentheses tend to cancel each other and ultimately the bond order and the stabilization energy are directly proportional to one another.

$$c_{22}c_{22} \simeq l_{31}l_{34}$$

$$e.g., SE(nonbonded) \simeq P(p_1,p_4)$$

In other words, a positive long range bond order reflects a stabilizing interaction which is readily identifiable if one thinks of molecules or transition state complexes as composite systems arising from union of two fragments, one being an open shell and the other an open or closed shell fragment. Naturally, a similar analysis can be given for the interaction between p_x and s lone pairs. In this work, we shall restrict our attention to the $p_z - p_z$ long range bond orders since they can be interpreted in a straightforward way. On the other hand, the interpretation of the $p_x - p_x$ and s $-$ s long range bond orders requires more caution since one does not deal with "pure" lone pairs but rather with partially delocalized ones.

The relative energies of the geometric isomers of representative XHC=CHX molecules as well as the long range bond orders of the cis isomers have been calculated by the CNDO/2 method and the results are shown in Table II. A number of trends are revealed.

Table II. CNDO/2 Calculations of the Geometric Isomers of XCH=CHX Molecules[a]

Molecule	X–X π bond order (cis isomer)	X–X δ bond order (cis isomer)	$E_{trans} - E_{cis}$,[b] kcal/mol
cis-FCH=CHF	0.0441		+0.250
cis-CH₃OCH=CHOCH₃	0.0597		+0.412
cis-H₂NCH=CHNH₂	0.0797		+0.669
cis-ClCH=CHCl	0.0287	0.0036 (d_{z^2})	+2.449
		0.0150 (d_{x-z})	
		0.0341 (d_{y-z})	
cis-CH₃SCH=CHSCH₃	0.0311	0.0045 (d_{z^2})	+4.868
		0.0166 (d_{x-z})	
		0.0380 (d_{y-z})	

[a] In all cases standard bond lengths and bond angles were used. [b] A positive number indicates that the cis isomer is more stable than the trans.

(a) While the cis isomer is always the more stable, the energy difference between the cis and the trans isomers increases as the $p_z - p_z$ bond order between two second or third period heteroatoms increases.

(b) The assignment of four atomic orbital basis functions to F, O, and N in these calculations (one s + three p) allows for π bonding between vicinal second period heteroatom substituents. However, there may be both π and δ bonding in the case of third period heteroatom substituents, since Cl and S are assigned nine atomic orbital basis functions (one s + three p + five d). The results in Table I clearly show that δ bonding contributes substantially to the greater stability of the cis isomer of XHC=CHX molecules, where X is a third period heteroatom. However, this latter effect may well be an artifact of the calculations, since it is known that the CNDO/2 procedures overemphasize the participation of d orbitals in bonding.

In summary, our analysis strongly indicates that the greater stability of the cis isomer in molecules like I is due to long range interactions and their energetic consequences. Thus, XHC=CHX molecules are most correctly depicted in the manner shown below.

$$X\text{-----}X$$

Typical experimental results which are in accordance with our expectations are listed in Table I.

We next consider the relative stability of the cis and trans isomers of molecules of the type shown below.

XHC=CHCH=Y   XHC=CHC≡Y
     II   III

The two regiochemical modes of union are cis and trans and the theoretical construction of a type II molecule from formal diradical fragments is shown via the interaction diagram of Figure 4. Unlike the previous cases, we are not dealing any more with a dominant first-order stabilizing interaction between identical MO's. In particular, there are more than one principal orbital interacting to be considered. Thus, the singly occupied
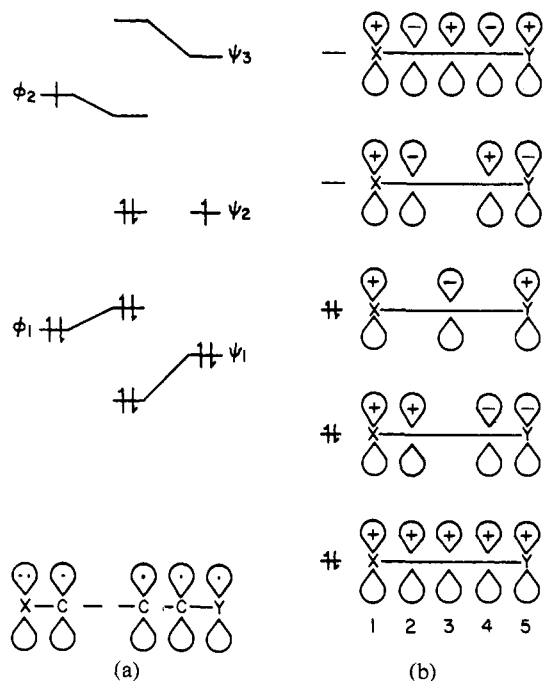
Figure 4. (a) Interaction diagram for the union of XHĊ– and (Y = CH)HĊ– radical fragments where only π MO interactions are considered; (b) π MO's of the pentadienyl system.

ϕ_2 orbital interacts mostly with the unoccupied ψ_3 orbital, but the singly occupied ϕ_2 orbital interacts appreciably with both the doubly occupied ϕ_1 and the singly occupied ϕ_2 orbitals. As a result, the stabilization energy for the union of the two formal diradicals cannot be written in a single form. On the other hand, one can determine that in molecules like II there are two electrons which occupy a MO which is bonding between atoms 1 and 5 and between 1 and 4, two electrons which occupy a MO which is antibonding between atoms 1 and 5 and between 1 and 4, and, finally, two electrons which occupy a MO which is bonding between atoms 1 and 5 but nonbonding between 1 and 4. Hence, it is expected that the π bond order between atoms 1 and 5 will be strongly positive and the π bond order between atoms 1 and 4 will be weakly negative or positive, e.g., the net π bond order between X and the vinylic group C=Y is predicted to be positive and their nonbonded interaction attractive. Now, in molecules of type II the 1–4 and 1–5 overlaps are not the same and depend on the conformation of the vinylic group. As we have seen, the net π bond order between the heteroatom X and the vinylic group is predicted to be positive, but this can arise from a small negative 1–4 π bond order and a large positive 1–5 π bond order. In such a case, one has to use π overlap populations rather than π bond orders in order to assess the type of nonbonded interaction between X and CH=Y or C=Y. In molecules of type II, there are two possible conformational isomers. Calculations
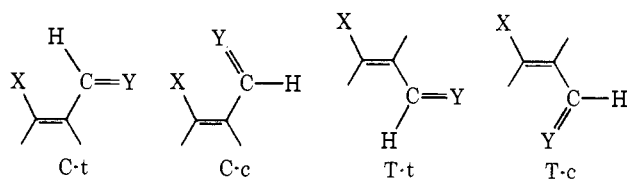
show that in the C-t geometry, the π overlap population between X and CHO is negative and their interaction

repulsive because the 1–4 π bond order is small and negative and the overlap appreciable, while the 1–5 π bond order is larger and positive but the overlap is nearly zero. On the other hand in the C-c geometry the π overlap population between X and CHO is positive and their interaction attractive. This arises because the 1–4 π bond order is small and negative and the 1–5 π bond order larger and positive, while the 1–5 overlap is larger than the 1–4 overlap. Hence, the C-c conformer is expected to be more stable than the C-t conformer.

The relative stability of the T-t and C-c isomers is predictable on the basis of the same electronic considerations which apply to butadiene conformational isomerism; e.g., an antibonding 2–5 interaction favors the T-t over the T-c conformer. In these cases, there is no possibility for nonbonded attraction between the two ligands of the olefinic bond.

In short, our analysis indicates that there will be a one-electron bias favoring T-t over C-t and C-c over C-t. We should emphasize that in type II molecules conventional internuclear as well as interelectronic repulsion (a two-electron effect) between the two ligands can become more important than one-electron nonbonded interactions. Thus, in such cases, the relative stability of conformational and geometric isomers will primarily be determined by the steric repulsive effects which the organic chemist is well aware of.

The linearity of the C=Y group assures that conformational complications do not obtain in type III molecules where combined σ and π nonbonded attraction will tend to stabilize the cis relative to the trans isomer. Experimental results which are in accord with these considerations are given in Table I.

Finally, we consider the relative stability of the cis and trans isomers of molecules of the type shown below.

$$Y=CHHC=CHHC=Y \qquad Y\equiv CHC=CHC\equiv Y$$
$$\text{IV} \qquad\qquad \text{V}$$

Again, it is assumed that Y is a heteroatom and that molecules like IV and V can be constructed from union of two formal diradical fragments. Once more, we are dealing with a typical open shell–open shell interaction. The interaction diagram of Figure 5 leads to the conclusion that cis union will be stabilized relative to trans union, e.g., there will be a net positive bond order between the two olefinic ligands. In type IV molecules the situation is complicated by the possibility of conformational isomerism and it becomes necessary to use overlap populations as the indices of nonbonded interactions. These indicate that nonbonded interactions favor C-cc over C-tc and C-tt and T-tt over T-ct and T-cc. Once more, internuclear and interelectronic repulsion may dominate one-electron nonbonded inter-
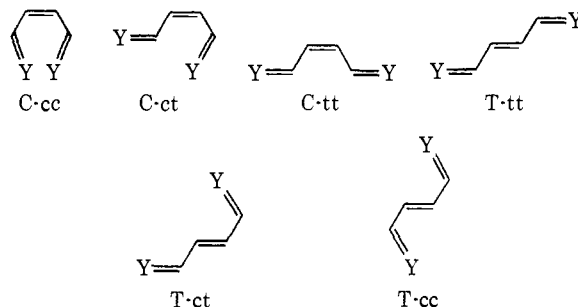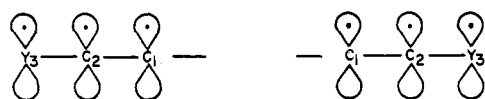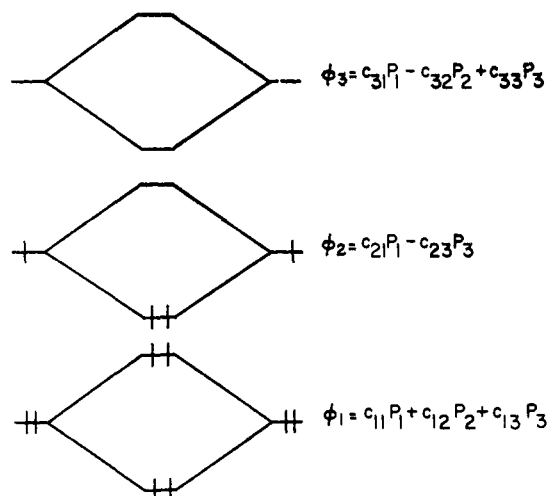
Figure 5. Interaction diagram for the union of two (Y=CH)-HĊ- radical fragments where only π MO interactions are considered.

actions and conventional steric repulsive effects may be primarily responsible for the relative stability of conformational and geometric isomers.

Conformational complications do not obtain in type V molecules were combined π and σ nonbonded attractive interactions will tend to stabilize the cis relative to the trans isomer.

Conformational Isomerism

In the last few years, the origin of the "gauche effect" has become the topic of numerous theoretical and experimental investigations.[23] In terms of our simple approach, the "gauche effect" is nothing else than an additional example of the consequences of open shell–open shell interactions.

We consider the general case of conformational isomerism in molecules of the type shown below.

$$XCH_2CH_2X$$

These molecules can be constructed from union of two formal radicals.

We assume that X has a p_z, a p_x, and an s lone pair. The σ system of the formal radical will be defined as the one which involves the atomic orbitals of X and C in the xy plane. Interaction of the σ systems of the two formal radicals is expected to lead to preference for syn rather than anti union. The analysis is similar to the one given for the interaction involved in the case of union of two actual radical centers. The π system of the formal radical involves a methylene group conjugated with the Xp_z lone pair, e.g., a four-electron three-center system isoconjugate to the allyl anion.

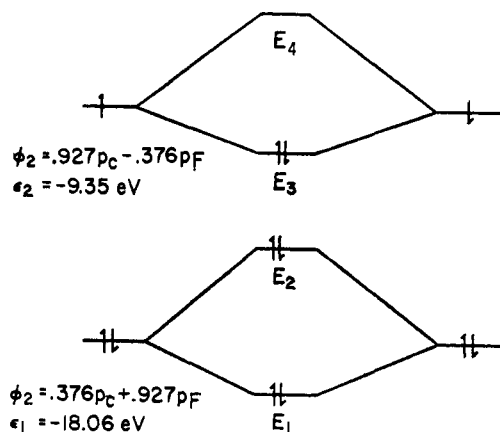(23) S. Wolfe, *Accounts Chem. Res.*, **5**, 102 (1972).

Figure 6. Interaction diagram for the union of two FHĊ- fragments with inclusion of overlap. The MO eigenvectors have been obtained from Hückel calculations and the MO energies have been derived by reference to the experimental ionization potential and the Hückel calculations. Only π MO interactions are considered.

Now, the stabilization arising from the interaction of the open shell σ systems, of the formal radicals is first order in energy and first order in overlap, while the stabilization arising from the interaction of the closed shell π systems of the formal radicals is second order in energy and second order in overlap. Since overlap is smaller than unity, the first-order effect will dominate the second-order effect and the relative stabilization for syn and anti unions will be determined principally by the interactions of the open shell σ systems of the two formal radicals which favors syn over anti union; e.g., there is a one electron effect which favors the syn conformer. On the other hand, interelectronic and internuclear repulsion, which is not taken into account by our simple approach, will be maximal for the syn conformation and minimal for the anti conformation. There is a compromise between the two opposing effects and the net result is preference for the gauche form. Of course, the important feature here is that conventional steric repulsion is counteracted by attraction which can be traced back to an open shell–open shell interaction.

Discussion

The approach taken in this work is a simple one-electron approach with neglect of overlap. Hence, it is important to discuss the effect of inclusion of overlap on the results of our analysis. If overlap is included, one-, two-, or three-electron stabilization will be antagonized by four-electron destabilization and one has to assess the relative importance of the two types of interactions in order to draw definitive conclusions. As we shall see, general principles indicate that two-electron stabilization by far outweighs four-electron destabilization and neglect of overlap is a fully justified simplication of the analysis.

We shall consider the union of two π systems of two formal HFC: diradicals to form the π system of *cis*-difluoroethylene. The appropriate interaction diagram is shown in Figure 6. If overlap is included, and only first-order interactions are considered, the energies of the three occupied levels of *cis*-difluoroethylene are given by the expressions

$$E_1 = \frac{\epsilon_1 + H_{11'}}{1 + S_{11'}}, \quad E_2 = \frac{\epsilon_1 - H_{11'}}{1 - S_{11'}}, \quad E_3 = \frac{\epsilon_2 + H_{22'}}{1 + S_{22'}}$$

where

$$H_{11'} = \langle \phi_1 | H | \phi_1' \rangle \qquad H_{22'} = \langle \phi_2 | H | \phi_2' \rangle$$

$$S_{11'} = \langle \phi_1 | \phi_1' \rangle \qquad S_{22'} = \langle \phi_2 | \phi_2' \rangle$$

Now, if the usual approximation of setting the resonance integral proportional to the overlap integral is made, we can write

$$H_{11'} = kS_{11}, \; H_{22'} = kS_{22'}, \; k = -39.69 \text{ eV}$$

Simple algebra leads to the conclusion that the result of the four-electron $\phi_1 - \phi_1'$ interaction is destabilization given by the expression

$$\Delta E_{cis}^4 = (\epsilon_1 - k)[4S_{11'}^2/(1 - S_{11'}^2)]$$

Similarly, the result of the two-electron $\phi_2 - \phi_2'$ interaction is stabilization given by the expression

$$\Delta E_{cis}^2 = (k - \epsilon_2)[2S_{22'}/(1 + S_{22'})]$$

Now, we can expand the molecular orbital overlap integrals into atomic orbital overlap integrals. The values of the latter overlap integrals can be obtained from semiempirical calculations of cis-difluoroethylene. As a result, one can evaluate $S_{11'}$ and $S_{22'}$ quantitatively. These rather simple calculations are illustrated below.

$$S_{11'} = \langle (0.376p_C + 0.927p_F) | (0.376p_C + $$
$$0.927p_F) \rangle = (0.376)^2 S_{CC} + (0.927)^2 S_{FF} + $$
$$2(0.376)(0.927)S_{CF} = 0.0463$$

$$S_{22'} = \langle (0.927p_C - 0.376p_F) | (0.927p_C - $$
$$0.376p_F) \rangle = (0.927)^2 S_{CC} + (0.376)^2 S_{FF} - $$
$$2(0.376)(0.927)S_{CF} = 0.2240$$

Finally, ϵ_2 can be taken to be roughly equal to the ionization potential of the fluoromethyl radical and ϵ_1 to lie lower than ϵ_2 by an amount set equal to the energy difference between ϵ_1 and ϵ_2 as computed from Hückel MO theory. The input data are

$$\epsilon_1 = -18.06 \text{ eV} \qquad \epsilon_2 = -9.35 \text{ eV}$$

After the substitutions are made, it is found that

$$\Delta E_{cis}^4 = +0.182 \text{ eV} \qquad \Delta E_{cis}^2 = -11.105 \text{ eV}$$

The same type of analysis can be carried out for trans union of the two diradical fragments. In such a case, the only difference is that the atomic overlap integrals S_{FF} are taken equal to zero. The results are given below.

$$\Delta E_{trans}^4 = +0.182 \text{ eV} \qquad \Delta E_{trans}^2 = -11.100 \text{ eV}$$

It can be seen that the four-electron destabilization is a small number and constant for cis and trans union.[24] On the other hand, the two-electron stabilization is a large number and different for cis and trans due to the fact that the trans union does not enjoy the attractive interaction between the two fluorines, a situation which materializes in the case of cis union. Furthermore, the calculation reveals that cis union is stabilized relative to trans union by 100 cal/mol, compared with the experimentally determined 928 cal/mol. This analysis reveals

(24) The numerical values are rounded off to a third decimal point. If higher accuracy is imposed ΔE_{cis} is more negative than ΔE_{trans}^2 by roughly 100 cal and ΔE_{cis}^4 is more positive than ΔE_{trans}^4 by roughly 1 cal.

that neglect of overlap cannot alter our general qualitative conclusions as long as two-electron stabilization competes with four-electron destabilization. This occurs because *the four-electron destabilization is a function of the square of overlap, while two-electron stabilization is a simple function of overlap.*[25] However, from the explicit calculations of $S_{11'}$ and $S_{22'}$, it is also clear that ΔE^2 is proportional to S_{FF} with a coefficient $2 \times (0.376)^2$ and ΔE^4 is proportional to S_{FF}^2 with a coefficient (0.927).[4] In other words, there is a *smaller* coefficient-dependent effect which tends to accentuate the importance of four-electron destabilization.

Finally, we wish to emphasize that this analysis of the preferred geometry of 1,2-difluoroethylene reveals that the electronic factor which stabilizes the cis over the trans geometry is small. As a congenial referee pointed out, there is a delicate balance but the numbers should ultimately favor cis over trans.

The expressions for the energy change accompanying the interaction of two degenerate levels occupied by one and three electrons are given below. In cases

$$\Delta E^2 = (k - \epsilon)S/(1 + S)$$

$$\Delta E^3 = S(k - \epsilon)(1 - 3S)/(1 - S^2)$$

involving π interactions, S is generally smaller than 0.33 and both one-electron and three-electron interactions are stabilizing. In such cases, two-electron interaction leads to large stabilization, one- and three-electron interactions lead to modest stabilization, and four-electron interaction leads to destabilization. Similar conclusions are reached when $p\sigma$ overlap in *reactant-like* transition states is considered.

Open Shell Interactions, Aromaticity, and Nonbonded Attraction

In this work, we have seen that whenever two open shell fragments unite to form a transition state or molecule there are stabilizing interactions which favor cis union. We have further seen that inclusion of overlap renders a two-electron interaction strongly stabilizing, a three- and one-electron interaction weakly stabilizing, and a four-electron interaction destabilizing. Hence, we can have two general situations arising in the union of two open shell fragments.

(a) Situations where a two-electron or a one-electron plus a three-electron stabilizing interaction competes with four-electron destabilization. Here, stabilization is expected to dominate destabilization.

(b) Situations where a one-electron or a three-electron stabilizing interaction competes with four-electron destabilization. Here, there may be a delicate balance between stabilization and destabilization.

Situations of the first type, where two-electron stabilization leads to cis preference, arose from union of two open shell fragments containing $2n + 1$ electrons to yield a composite ground state system containing $2(2n + 1) = 4n + 2$ electrons. Typical examples are the union of two formal diradicals to form substituted ethylenes. In other words, the greater stability of the cis isomer of a variety of olefins is due to nonbonded attraction which is the theoretical justification of the $4n + 2$ aromaticity rule for ground state systems; e.g., systems with $4n + 2$ electrons are more stable in a cyclic than in a noncyclic geometry in their ground state.

(25) This point has been adequately emphasized by L. Salem, ref 10.

Additionally, situations of the first type where one-electron plus three-electron stabilizations lead to cis preference arise from the union of an excited and a ground state molecule each having $2n$ electrons to yield a composite excited state system containing $2(2n) = 4n$ electrons. Typical examples are the photocyclo-additions of olefins. Here, cis preference is due to non-bonded attraction which is a theoretical justification of the $4n$ aromaticity rule for excited state systems; e.g., systems with $4n$ electrons are more stable in a cyclic geometry in their excited state.

Situations of the second type, where there is a fine balance between stabilization and destabilization, arise in the union of a $2n + 1$ (or $2n - 1$) and a $2n$ electron system to yield a $4n + 1$ (or $4n - 1$) composite ground state system. Typical examples are the thermal cyclo-addition of an olefin and its corresponding radical anion (or cation). The fact that there is no empirical rule for predicting the regiochemistry of $4n + 1$ or $4n - 1$ electron systems simply reflects the fine balance of attractions and repulsions which theoretically obtain if overlap is included.[26]

In short, we want to emphasize that the experimental observation that in many systems the more crowded structure is preferred can be interpreted by the concept of nonbonded attraction which is directly linked with the idea of aromaticity, an idea which has always been in the mainstream of organic chemical thinking. Table I shows that olefins bearing substituents whch are not sufficiently bulky to introduce conventional coulombic repulsion are more stable in their cis geometry. In all these examples the two substituents (heteroatoms or unsaturated groups) directly attached to the double bond contain 4π electrons; e.g., these molecules are effective 6π-electron systems. Extension of these ideas to conformational problems can be very useful. Thus, methyl vinyl ether, a 6π-electron system, has been found to have a preferred cisoid conformation,[27] a prediction which can be arrived at simply by counting electrons.

Conclusion

We have shown that nonbonded attraction can be a consequence of the interaction of two open shell systems. This approach is different from but equivalent to the approach we took in analyzing the importance of nonbonded attraction between lone pairs and unsaturated bonds. We have further shown that these ideas are intimately tied up with the idea of aromaticity when overlap is included in the analysis. In the subsequent paper we shall see that this composite molecule approach leads to interesting predictions about the difference in structure and reactivity between geometric isomers. The internal consistency of these models and their success to correlate a large number of experimental facts leads us to believe that nonbonded attraction is a significant factor, but, obviously, not the only factor, in determining the geometric preference of molecules and transition states. However, we would like to draw attention to the following two points.

(1) The results of the CNDO/2 and INDO semiempirical calculations should only be given qualitative significance. These procedures do not adequately represent interelectronic repulsion and they may tend to favor crowded structures. Furthermore, these calculations tend to overemphasize the importance of d orbitals for third period elements. Thus, the significantly greater stability of cis olefins bearing third period heteroatom substituents revealed by the CNDO/2 calculations may be a basis set dependent effect. Obviously, *ab initio* calculations coupled with studies of basis set dependence will be necessary in order to resolve these questions.

(2) Our analysis of nonbonded attraction reveals that this factor can be important in determining chemical behavior. A plausible alternative is that van der Waals attraction could also account for the same effects. In other words, we are confronted with the possibility that correlation energy could have important chemical consequences. The resolution of this dilemma is obviously extremely difficult, if not impossible, because there is no simple way of evaluating quantitatively the nonbonded attraction electronic factor and comparing it with the correlation energy correction. Nonetheless, it will be interesting to see at least whether the greater stability of cis olefins is reproduced by near Hartree–Fock *ab initio* calculations. At this point, it is not unrealistic to expect that the greater stability of cis olefins can be traced to the Hartree–Fock solution rather than to correlation energy. The fact that *ab initio* calculations have been fairly successful in the prediction of the stereochemistry of small molecules and in the calculation of rotation and inversion barriers seems to favor this viewpoint.[28]

Finally, some cautionary remarks are in order. First, exceptions to the cis regioselectivity rule in the case of open shell–open shell or open shell–closed shell interactions can naturally arise when conventional steric repulsive effects become imporant. Second, one should use good judgment in applying these ideas to organic systems of interest. For example, the Cope rearrangement transition state can be formulated as the interaction between two allyl radicals. One might have expected that this open shell–open shell interaction would lead to preference for a boat rather than a chair transition state conformation. A careful consideration of

the problem indicates that there is no secondary stabilization possible, because the singly occupied allyl orbitals of the formal allyl radicals have a node through the central carbon which is not directly involved in the reaction. The preferred transition state conformation is the chair form and this preference can be taken to reflect the absence of nonbonded attraction between the middle carbons of the formal allyl radicals.

(26) L. Salem, in press.
(27) P. Cahill, L. P. Gold, and N. L. Owen, *J. Chem. Phys.*, **48**, 1620 (1968).
(28) J. M. Lehn in "Conformational Analysis," G. Chiurdoglou, Ed., Academic Press, New York, N. Y., 1971, p 129.

Appendix

In this work, we have used CNDO/2 and INDO SCF-MO calculations in order to illustrate qualitatively several theoretical points. The computations were carried out on a CDC-6400 computer utilizing a computer program which is essentially identical with the one of Pople and Dobosh described in ref 29. In all cases, standard bond lengths and bond angles were used. In one case, the π MO's of the FHC– fragment were determined by a simple Hückel MO calculation with the following input parameters: $H_{FF} = \alpha + 2.1\beta$, $H_{CC} = \alpha$, $H_{CF} = 1.25\beta$, $\alpha = 0$, $\beta = -2.88$ eV.

(29) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N. Y., 1970.

Semiempirical MC-SCF Theory. I. Closed Shell Ground State Molecules

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Abstract: A new semiempirical molecular orbital theory, based on the zero differential overlap approximation, is presented. In this theory the dissociation error of the conventional Hartree-Fock model is corrected through the use of the multi-configuration self-consistent-field (MC-SCF) approach. The specific configurations chosen in the MC-SCF ansatz introduce intraorbital correlation only, thus keeping the number of configurations small but yielding wave functions which permit proper dissociation into molecular fragments. An additional benefit is that for the presented model the variational solution of the orbital equations results in localized "chemical" orbitals. A set of atomic parameters for this model has been determined *via* least-squares fitting for the atoms C, H, O, and N. The model is applied to the calculation of molecular geometries, force constants, and heats of atomization of closed shell ground state molecules containing these atoms, giving results in good agreement with known experimental data.

This paper is the first in a series involving the development of a semiempirical method for the calculation of molecular systems of sufficient accuracy to be of chemical usefulness. To this end we feel the theory should be able to give reliable estimates of molecular geometries, heats of atomization, and force constants, as well as describing adequately bond formation and dissociation. If these objectives can be achieved, we then feel that we would have a quantum mechanical model useful for the study of a variety of reaction mechanisms. This should lead us to the prediction of transition species and selection of reaction paths.

Given these general expectations, the theory should be designed to make its interpretation on the basis of traditional chemical intuition as easy as possible. Since a semiempirical theory is built up from the standpoint that we know something about chemistry, it seems reasonable to expect that its output should lead to interpretation of chemical problems in those terms. For example, we believe that the bonding in molecules essentially involves the valence electrons, so we can then use a theory which treats the valence electrons explicitly and freezes the inner electrons as cores around the atomic nuclei. Furthermore, since we like to picture electrons as forming bond pairs between atoms, a theory which localizes electrons in this manner makes it convenient for the description of what is happening to reacting molecules in terms of these bonding electrons.

Pople's original development of the CNDO[1] semiempirical method was designed to be an approximation to a full LCAO-SCF minimal basis set calculation.

That is, he designed the theory to reproduce a specific type of quantum mechanical calculation and not experimental data. However, the literature contains a number of proposals for modifying the theory to achieve agreement with various types of experimental information.[2] Dewar was one of the first to recognize the need for developing a method for general chemical usefulness. His MINDO[3] procedure has been for the most part successful. However, the parameterization seems unnecessarily complicated in that the resonance integrals and core-core repulsions are treated with bond-dependent parameters. Another rather successful method has been developed by Fischer and Kollmar.[4] Their theory remains uncomplicated requiring essentially a reparameterization of Pople's CNDO/2 method, but it has not been extended beyond hydrocarbons. A number of other modifications have been suggested but they do not appear to be applicable in meeting our general objectives. In particular, since all these theories are based on the HF model, they are afflicted with the well-known HF dissociation error; *i.e.*, if a bond is broken, the molecular fragments do not dissociate into their respective electronic ground states in the restricted HF model.

In this first paper we have attempted to keep the basic

(1) J. A. Pople and G. A. Segal, *J. Chem. Phys.*, **44**, 3289 (1966); **43**, S129 (1965).

(2) (a) K. B. Wiberg, *J. Amer. Chem. Soc.*, **90**, 59 (1968); (b) J. M. Sichel and M. A. Whitehead, *Theor. Chim. Acta*, 11, 220, 254, 263 (1968); (c) J. Del Bene and H. H. Jaffe, *J. Chem. Phys.*, **48**, 4050 (1968); **49**, 1221 (1968).

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(4) H. Fischer and H. Kollmar, *Theor. Chim. Acta*, 13, 213 (1969).