The Stereochemical Consequences of Electron Delocalization in Extended π Systems. An Interpretation of the Cis Effect Exhibited by 1,2-Disubstituted Ethylenes and Related Phenomena

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Abstract: The stereochemical consequences of electron delocalization in substituted ethylenes (e.g., 1,2-difluoroethylene), propenes, butadienes and allyl and pentadienyl anions, as well as 1,2-disubstituted ethanes, are discussed. It is shown, on the basis of simple perturbation theory, that the generally greater stability of the bent (cis or gauche) conformations of these molecules may be attributed to a previously unrecognized conjugative destabilization which is transmitted through bonds and is greater for elongated, trans conformations than for bent, cis structures. This destabilization is due to the exchange (exclusion) repulsion associated with overlap between filled orbitals. The effect is conformation dependent in extended π systems as a result of the fact that electrons delocalize preferentially in straight lines.

Organic chemists are generally well served by the concept of steric bulk.[1] Quite naturally, apparent contradictions to established trends have received considerable attention over the years. This is particularly true, of late, with respect to a variety of 1,2-disubstituted ethylenes which exhibit a thermodynamic preference for cis rather than trans substitution,[2-4] the latter incorrectly expected on the basis of steric arguments.

Several 1,2-disubstituted ethanes also contradict normal steric principles. In these cases, vicinal polar bonds are found generally to favor gauche rather than the sterically less crowded trans conformations.[5]

To explain these anomalies, the possible importance of nonbonded attraction has been proposed,[3,4] and detailed theoretical arguments have been presented which appear to justify this concept.[4] In this paper, we document the shortcomings of the steric attraction model, as it relates to ground state phenomena,[6] and propose an alternative theoretical interpretation of the relative thermodynamic stabilities of cis–trans isomers and the associated stereochemical consequences of vicinal polar bonds in ethane derivatives.

The Steric Attraction Postulate. Two types of attractive forces have been proposed. The first, termed pπ attraction, makes note of the fact that, in extended π systems, long range/partial bonding interactions may occur through-space.[4] The second, termed pσ attraction, evolves from the through-space interaction of lone pairs, which is normally repulsive in character[7] but rendered potentially attractive if interaction with an unoccupied σ* orbital of a vicinal σ bond is also possible.[4b-e]

Both types of attractive forces may be operative, for example, in *cis*-1,2-difluoroethylene, stabilizing it relative to the trans isomer. The extended π system of this molecule incorporates a lone pair on each of the fluorine atoms making it isoelectronic with the butadiene dianion. As shown by simple Hückel theory, the highest occupied molecular orbital (ψ_3) of the system is 1,4-bonding,[8] a factor which should favor the cis structure. Similarly, the fluorine lone pairs which point toward each other in the nodal plane of the π system may interact in the cis conformation giving rise to a bonding and an antibonding combination. The latter is of the proper symmetry to also interact with the unoccupied σ* orbital of the adjacent carbon–carbon bond, an interaction which might further stabilize the cis geometry.[4b-d]

A variety of theoretical and experimental data discourage confidence in the postulated long-range attractive interactions, however. Kollman[9] has recently published ab initio calculations which indicate that the geometries of AB_2 molecules (or fragments) are not determined by through-space interactions, as is alleged[4b] by the steric attraction model. Analogously, 1,3-bonding in the allyl cation, which is allowed by symmetry, has been judged to be insignificant.[10] In *cis*-1,2-difluoroethylene itself, the C═C—F angles are actually larger, not smaller, than those in the trans isomer.[11] Fluorine-fluorine attraction in the cis structure[4b] is not indicated. The predicted stabilization of the pentadienyl anion in the *Z,Z* conformation **1** by a 1,5-pπ-bonding interaction[4a] has also been disproved.[12] The all-trans *E,E* conformation **2** predominates in this system.[12a] Even acetylacetonate (**3**) adopts the *E,E* configuration preferentially despite the significant 1,3-methyl–methyl repulsion which must be present in this structure.[12c]


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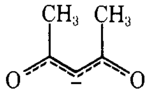

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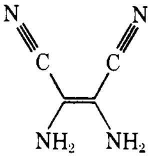

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Additionally, neither pπ nor pσ attraction can account for the strong conformational preference exhibited for diaminomaleonitrile (**4**) as opposed to its trans isomer.[13] The cyano groups themselves prefer the trans geometry,[2d] while lone pair–lone pair attraction cannot stabilize the cis structure since, in the crystal, **4** adopts a conformation having one nitrogen lone pair in conjugation with and the other in the nodal plane of the double bond.[14] Lone pair–lone pair overlap must be negligible. Similarly, x-ray analysis[15] of *cis*-hexacyanobutadiene dianion[16] indicates that the anticipated[4a] 1,4-bonding interaction in this system is in fact antibonding due to the helical structure of the dianion. The cis conformation is stabilized nevertheless![16] Clearly, alternative explanations for the cis effect exhibited by such systems must be sought.

The Stereochemical Consequences of Electron Delocalization in Extended π Systems. The concept of localized bonds in molecules is a cornerstone of modern chemistry. While this concept remains, and will continue to be, pedagogically useful, it is well recognized today that the bonding

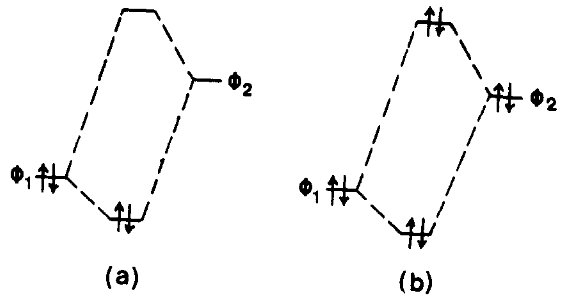


Figure 1. Interaction of p orbitals on adjacent π centers. (a) Stabilizing two electron interaction. (b) Destabilizing four electron interaction.

electrons of all organic molecules are significantly delocalized, occupying molecular rather than localized orbitals.

Conceptually, electron delocalization arises predominantly through interactions between orbitals on adjacent atoms. From this point of view, the energetic and potential stereochemical consequences associated with electron delocalization may be readily deduced by means of simple perturbation theory.[7b,g,h]

Consider, for example, two localized p orbitals (ϕ_1 and ϕ_2) on adjacent atoms in an extended π system. Interaction between them gives rise to two new, "delocalized" orbitals, a lower energy bonding ($\phi_1 + \phi_2$) and a higher energy antibonding ($\phi_1 - \phi_2$) combination (Figure 1). If ϕ_1 is doubly occupied and ϕ_2 is unoccupied, their interaction will obviously be strongly stabilizing (Figure 1a). Electron delocalization is energetically favorable in such a case. On the other hand, antibonding molecular orbitals are always more antibonding than the corresponding bonding ones are bonding.[7] If, therefore, both ϕ_1 and ϕ_2 are doubly occupied, as in Figure 1b, their interaction is energetically unfavorable. Electron delocalization involving filled orbitals is destabilizing.[7,17]

The same conclusions emerge for more extended molecular orbitals involving three or more π centers. Such orbitals may be constructed in the same manner, treating the individual vicinal interactions in a sequential, pairwise additive, fashion.[7h] Again, the antibonding molecular orbitals which evolve are destabilized more than the corresponding bonding ones are stabilized. As for the two orbital case, the net energetic effect will be determined by the specific orbital occupancies. When only bonding (or nonbonding) molecular orbitals are occupied, electron delocalization will be energetically favorable. When antibonding molecular orbitals are also occupied, such delocalization becomes energetically unfavorable.

The extent of electron delocalization due to vicinal orbital interactions and consequently the magnitude of the associated energetic effect will be directly proportional to the efficacy with which the adjacent orbitals overlap in space and inversely proportional to the energy separation between them.[7] These facts have important stereochemical implications. Clearly, if only the bonding or nonbonding molecular orbitals of an extended π system are occupied, those conformations which maximize electron delocalization will be preferentially stabilized. If, on the other hand, one or more antibonding orbitals are also occupied, those molecular conformations which minimize the associated destabilization become relatively more favorable.[7e] The relative energies of the interacting orbitals will control the magnitude of these stereochemical preferences. The closer they are in energy, the more pronounced will be the effect.

Experimentally, electron delocalization in molecules is manifested by spin-spin coupling in nuclear magnetic resonance spectra.[18] Since vicinal spin-spin interactions are typically much larger for trans than for cis configurations, electrons must delocalize preferentially through trans conformations.[18b] This fact is expressed by Eyring's comment that "electrons hate to go around corners" (i.e., electrons delocalize preferentially in straight lines) and may be interpreted quantum mechanically as a kinetic energy effect.[19] As a consequence, electron delocalization in extended π systems should be greater for elongated, trans conformations than for bent, cis geometries. Electron delocalization will, therefore, stabilize trans conformations relative to the corresponding cis structures when only bonding or nonbonding molecular orbitals are occupied.[19] Cis conformations will be stabilized (less destabilized) relative to trans when antibonding molecular orbitals are also filled. The magnitude of these effects will increase as the energy differences between the interacting orbitals decreases.

Discussion

Classical π Systems. Only bonding molecular orbitals are occupied in classical polyenes. Electron delocalization is therefore energetically favorable and is expected to stabilize planar trans configurations relative to the corresponding cis geometries,[18] such delocalization being more effective in the former. Experimentally, planar trans configurations have been demonstrated for 1,3-butadiene,[20] isoprene,[21] fluoroprene,[22] acrolein,[23] and glyoxal,[24] among others. Less extensive data are available for trienes, although both diethyl fumarate[25] and fumaronitrile[2d] are known to be more stable than their cis isomers, while calculations[26] predict the planar, all-trans geometry to be the most stable configuration of 1,3,5-hexatriene. Trans conjugation also predominates over cis in a variety of naturally occurring polyenes such as the caratenoids and vitamin A.[27] The preferential stabilization of the trans configuration of conjugated double bonds is clearly apparent.

Undoubtedly, part of the preferential stabilization of trans polyenes is steric in origin. The concurrent importance of the proposed electronic effect is corroborated, however, by a comparison of the ultraviolet spectra of cis-trans isomers. Typically, the π-π^* absorption maxima of cis polyenes occur at longer wavelengths than do those of the corresponding trans compounds.[28] This difference implies a larger excitation energy ($E = hc/\lambda$) and hence a larger π-π^* energy separation for the trans isomers. This is to be expected if electron delocalization is greater for trans configurations than for cis. As indicated in the previous section, increased delocalization stabilizes bonding and destabilizes antibonding molecular orbitals. The greater electron delocalization in trans polyenes must, therefore, lead to a larger π-π^* energy separation and hence a more stable structure relative to the corresponding cis geometries,[29] as is observed.

In contrast to the simple polyenes, the highest occupied molecular orbital of butadiene dianion is strongly antibonding. Electron delocalization is energetically unfavorable in this case. A thermodynamic preference for the cis conformation is therefore predicted, electron delocalization being minimized in this configuration. The experimental evidence on the hexacyanobutadiene dianion supports this conclusion. Despite the severe steric crowding associated with the cis structure, an equilibrium mixture of the interconvertible cis-trans isomers is comprised of approximately 25% of the cis and 75% of the trans form.[16] The cis conformation is clearly stabilized to a far greater extent than normal steric effects would predict. The stereochemical consequences of electron delocalization explain this observation.

The preferred conformation of the pentadienyl anion may be similarly understood. In this case, the highest occupied

Table I. Enthalpy Values for Cis–Trans Isomerizations of 1,2-Disubstituted Ethylenes (XHC=CHX) in the Gas Phase and the Corresponding Resonance Substituent Constants ($-\sigma_R$)

X	$-\sigma_R{}^a$	ΔH^b
OCH_3	0.61	1.45[c]
F	0.45	0.93
Cl	0.23	0.65
Br	0.19	0.32
I	0.16	0.0

[a] Reference 34. [b] Reference 2b, unless otherwise noted. [c] Reference 2c.

molecular orbital is nonbonding. Electron delocalization remains energetically favorable. A preference for an elongated, trans *E,E* configuration is therefore anticipated, a conclusion which is in accord with considerable experimental evidence.[12a]

Substituted Ethylenes. A significant, repulsive, interaction between fluorine lone pairs and the adjacent double bond of vinyl fluorides has been documented by means of photoelectron spectroscopy.[30] This interaction renders 1,2-difluoroethylene isoconjugate and isoelectronic with the butadiene dianion. Thus, the stereochemical consequences of electron delocalization anticipate that this molecule will also prefer a cis configuration, a conclusion which is again in agreement with experiment.[2b]

In the 1,2-difluoroethylene case, the proposal that electron delocalization is greater (and, hence, more energetically unfavorable) in the trans structure is supported by a variety of spectroscopic data. The much larger trans than cis fluorine–fluorine coupling constant[31a] indicates this quite clearly. Furthermore, electron delocalization in these molecules is expected to destabilize the highest occupied molecular orbital. An increase in delocalization should therefore result in a lower ionization potential as well as longer wavelength (lower energy) ultraviolet absorption. Experimentally, the ionization potential of *trans*-1,2-difluoroethylene has been reported to be 0.05 eV less[30] and its π–π^* ultraviolet absorption to be 8 nm more bathochromic[31b] than that of its cis isomer. All of these observations are clearly consistent with the concept of conjugative destabilization in molecules of this type and the stereochemical consequences associated with it.

The preference for the cis conformation in the 1,2-difluoroethylene case should, of course, be small relative to that of the butadiene dianion. As a result of the high electronegativity of fluorine, its lone pairs are quite low in energy relative to the π orbital of ethylene. The total antibonding interaction in 1,2-difluoroethylene should, therefore, be small. Decreasing the electronegativity of the terminal atoms by going from fluorine toward carbon along the first row of the periodic table raises the energy of the $p\pi$ lone pairs. Conjugation increases correspondingly and with it the net antibonding character of the system. As a result, the preference for the cis conformation should also increase. In fact, the relative stability of the cis isomer increases substantially as one goes from 1,2-difluoroethylene to the 1,2-dimethoxy derivative (see Table I).[2c]

Although diaminomaleonitrile (**4**), which we discuss in detail in the following section, is well known, to the best of our knowledge only *N,N,N′,N′*-tetraalkyl derivatives of 1,2-diaminoethylene itself have been prepared. In these cases, only the trans structures have been reported,[32] although cis–trans equilibria do not appear to have been investigated. Such molecules would not be expected to exhibit a particularly large, if any, preference for cis conformations. The antibonding interactions which they are subject to can be substantially reduced by simply rotating one of the nitrogen lone pairs into the plane of the double bond. That this is in fact the case is supported by the substantial dipole moments (~2 D) observed for the trans isomers.[32a] With the electronic effect minimized in this way, normal steric effects should come to the fore, destabilizing the cis structures much as they would in the corresponding hydrocarbon case.

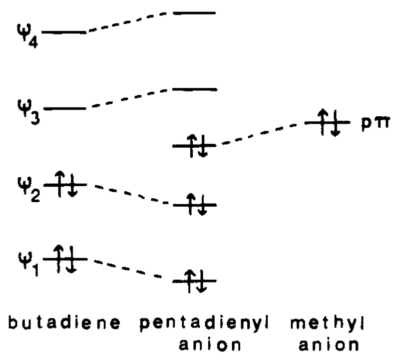


Figure 2. Union of butadiene and methyl anion to form the pentadienyl anion.

In the 1,2-dihaloethylene series, the magnitude of the $p\pi$–π interaction decreases in the order F > Cl > Br > I.[33,34] The substituent constants σ_R, which are −0.45, −0.23, −0.19, and −0.16 for fluorine, chlorine, bromine, and iodine, respectively,[34] provide a quantitative measure of this trend. Antibonding character and, consequently, the preference for the cis conformation in 1,2-dihaloethylenes should exhibit an analogous pattern. The experimental data,[2b,c] summarized in Table I along with that for the dimethoxy derivative, are consistent with this conclusion.

Substituted Butadienes. Conceptually, the pentadienyl anion is equivalent to butadiene substituted by a methyl anion. As indicated above, electron delocalization is energetically favorable in this case, and preferential stabilization of the elongated, all-trans *E,E* conformation results.

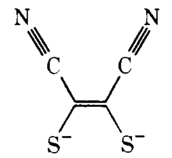
The favorability of electron delocalization in the pentadienyl anion may be visualized as resulting from a stabilizing, two electron interaction between the $p\pi$ lone pair of the "methyl anion substituent" and the lowest unoccupied molecular orbital ($\psi_3{}^*$) of butadiene (Figure 2). In this case, the corresponding destabilization associated with the four-electron interaction between $p\pi$ and ψ_2 (as well as that between $p\pi$ and ψ_1) should be less significant. The energetic effect of these interactions is, of course, a balance between the destabilization of one orbital and the slightly smaller stabilization of another (cf. Figure 1).[7] As a result, the net destabilization would be expected to be inherently smaller than the stabilization derived from the two-electron, $p\pi$–$\psi_3{}^*$, interaction.

Increasing the electronegativity of the butadiene substituent, however, lowers the $p\pi$ energy level and thus decreases the magnitude of the stabilizing $p\pi$–$\psi_3{}^*$ interaction (the $p\pi$–$\psi_3{}^*$ energy separation increases) allowing the destabilizing $p\pi$–ψ_2 and $p\pi$–ψ_1 interactions to become dominant. At some point, therefore, the net effect of electron delocalization will become energetically unfavorable and the preferred conformation of the butadiene derivative will switch from trans to cis.

This general pattern is observed experimentally. Electron delocalization involving a double bond and an alkoxy substituent ($p\pi$ ionization potential $\simeq$ 10.5 eV)[35] is strongly stabilizing.[36] In 1-alkoxybutadienes, therefore, the bonding $p\pi$–$\psi_3{}^*$ interaction is expected to dominate. Electron delocalization is thus energetically favorable and, as a result, preferential stabilization of the elongated trans conformation is anticipated. In fact, 1-ethoxybutadiene is favored over cis by approximately 1 kcal/mol.[37] In contrast, a fluorine substituent has a much higher $p\pi$ ionization potential (~16 eV)[38] and thus a much lower $p\pi$ energy level. The bonding $p\pi-\psi_3^*$ interaction in 1-fluorobutadiene is therefore minimized. Electron delocalization in this system becomes energetically unfavorable, and preferential stabilization of the cis (i.e., destabilization of the trans) conformation is expected, in agreement with observation.[39] A methyl group, on the other hand, has a "pseudo π" ionization potential of approximately 14 eV,[40] intermediate between that of the alkoxy and fluoro substituents. The net energetic effect of electron delocalization in 1,3-pentadiene is therefore expected to be relatively small (bonding and antibonding interactions will nearly balance), and no important stereochemical preferences due to electronic effects alone are anticipated. Thus, the 1 kcal/mol preference exhibited by 1,3-pentadiene for the trans conformation[41] is assumed to be largely steric in origin while, more significantly, the much less sterically encumbered crotonitrile exhibits the expected small (0.17 kcal/mol) stereochemical preference, in this case for the cis isomer.[42]

In light of these arguments and those discussed above with respect to ethylene derivatives, the preference for the cis configurations in diaminomaleonitrile (**4**)[13] and dimercaptomaleonitrile dianion (**5**)[43] as opposed to their trans isomers is easily explained. The cis structures offer two important electronic advantages. First, the energetically unfavorable electron delocalization involving the heteroatom lone pairs (cf. the butadiene dianion) is minimized by the maleonitrile conformation. As with 1,2-difluoroethylene, this point is supported by the observation that the ultraviolet spectra of both **4** and **5** are considerably hypsochromic with respect to their trans isomers.[13,43,44] Second, the energetically favorable electron delocalization involving a relatively high energy heteroatom lone pair and a trans cyano substituent (cf. the pentadienyl anion) is maximized.

Alkylation of **4** and **5** to give **6**[45] and **7**,[43] respectively, substantially reduces the bias for the cis conformation. In **6**, assuming its basic geometry is similar to that observed for **4** (see above), conjugation of the out-of-plane lone pair is sterically hindered. In **7**, the ionization potential of the sulfur substituent is increased and its symmetry (hence, overlap) diminished relative to **5**. Thus, for both the nitrogen and sulfur derivatives, alkylation serves to inhibit electron delocalization and, consequently, the associated stereochemical effects are reduced.



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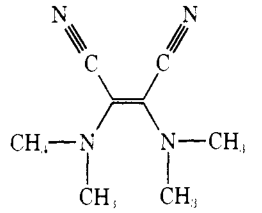

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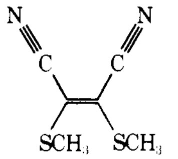

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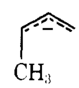
Substituted Allyl and Pentadienyl Anions. The highest occupied molecular orbitals of both allyl and pentadienyl anion are nonbonding in character and are thus much higher in energy than the π-bonding orbitals encountered in butadiene. At the same time, the lowest unoccupied molecular orbitals (LUMO's) of the anions should be higher in energy.[46] As a result, electron delocalization in donor-substituted allyl and pentadienyl anions will be dominated by the destabilizing interactions between filled orbitals. The large energy separation between the substituent donor orbital and the LUMO of the anions will render the stabilizing two-electron interaction energetically inferior.

Electron delocalization in substituted allyl and pentadienyl anions is therefore expected to be energetically unfavorable and, as a result, all donor substituents are expected to prefer bent, cis geometries with respect to the conjugated anion. Numerous investigations illustrate this point. Thus, cis conformations are favored in both 1-methylallyl (**8**)[47] and 1-methylpentadienyl (**9**)[12a,48] anion as well as the 1-methylheptatrienyl analog (**10**).[49] Similarly, the fact that base catalyzed isomerization of dodecyl allyl ether proceeds through an allyl anion intermediate followed by irreversible protonation to give dodecyl *cis*-propenyl ether as the exclusive product (eq 1)[50] suggests that 1-alkoxyallyl anions also prefer cis configurations.



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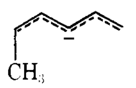

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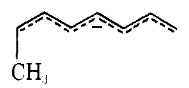

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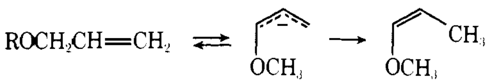
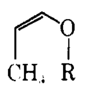


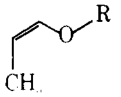
(1)

An intriguing contrast to the preference for cis conformations in substituted allyl and pentadienyl anions is provided by the corresponding cations. In these cases, of course, the LUMO's are much lower in energy, appearing in the Hückel approximation at the nonbonding energy level. Electron delocalization becomes energetically favorable in donor-substituted allyl and pentadienyl cations, being dominated by the interaction between the LUMO of the cation and the occupied substituent orbital. Elongated, trans conformations are therefore anticipated. This conclusion is consistent with the observation that allyl cations react to form trans-disubstituted olefins stereospecifically[51] and that the *cis.-cis*-1,3-dimethylallyl cation rearranges quantitatively to the trans,trans isomer in strong acid solutions.[52]

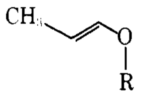
Substituted Propenes. Propenes which have donor substituents (OCH_3, F, Cl, etc.) at the 1-position are isoconjugate with the 1-methylallyl anion. Consequently, they are also expected to be subject to conjugative destabilization and a general preference for cis conformations is anticipated.[53] In this respect, the 1-alkoxypropenes (**11**) provide a particularly intriguing example. On the basis of the stereochemical effects associated with through-bond electron delocalization alone, **11a** should represent the most stable and **11d** the least stable conformation, while **11b** and **11c** should have nearly equivalent, intermediate stabilities. Conformation **11a**, of course, suffers from obvious adverse steric effects which suggests that either **11b** or **11c** should best represent the preferred conformation of 1-alkoxypropenes. Furthermore, for bulky R groups, a clear preference for **11b** should emerge since, in this conformation, the steric effect of R is minimized. This is precisely the pattern observed experimentally. As illustrated in Table II, when R is methyl, a trans-cis equilibrium constant of 1.03 has been reported, while increasing the size of R steadily shifts the equilibrium toward the cis configuration.[37] These results clearly substantiate the subtle balance between through-bond (conjugative) and through-space (steric) effects operative in these molecules.



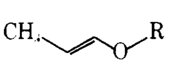
11a



11b



11c



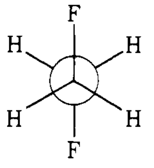
11d

Saturated Systems. Saturated molecules have bonding and antibonding molecular orbitals which closely resemble the orbitals of conjugated systems.[7h] The conjugative effects described for unsaturated molecules are, therefore,

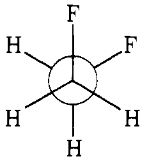
Table II. Trans–Cis Equilibrium Ratios (K) for $CH_3CH{=}CHOR$[37]

R	K
CH_3	1.03
CH_2CH_3	0.72
$CH(CH_3)_2$	0.37
$C(CH_3)_3$	0.30

also applicable to saturated ones. Thus, for example, *anti*-1,2-difluoroethane (**12a**) is subject to conjugative destabilization, an effect which is minimized in the corresponding bent, gauche conformation (**12b**).[54] Consequently, **12a** is destabilized relative to **12b**. The latter should therefore be populated to a far greater extent than would be expected on the basis of steric and dipolar effects alone, just as was the case for the analogous ethylene derivative. Experimentally, **12b** is indeed found to be more stable than **12a**.[55] In fact, a recent electron diffraction study suggests that, in the gas phase, only the gauche conformation is significantly populated.[56]



12a

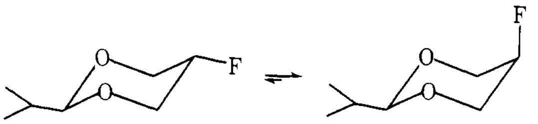


12b

In contrast, 1,2-difluorocyclopropane appears to prefer the trans configuration.[2b] In this case, the anti-clinical dihedral angle (~120–140°) between the vicinal fluorine substituents in the trans isomer should minimize electron delocalization relative to that in the eclipsed cis structure. The generally greater fluorine–fluorine coupling constants observed for cis cyclopropane derivatives[57] demonstrate this point. Once again, therefore, the conformation having minimum electron delocalization between vicinal donor substituents is found to be more stable.

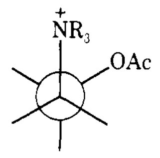
As was the case for the substituted ethylenes, the magnitude of the conjugative destabilization in saturated systems decreases, and with it, the relative stability of the gauche structure, as the donor abilities of the substituents diminish. Thus, in addition to 1,2-difluoroethane, the gauche conformation predominates in 1,2-dimethoxyethane,[58] 2-methoxyethyl acetate,[59] 2-fluoroethyl acetate,[60] and 2-fluoroethanol,[61] compounds in which both substituents are good donors. In the 1,2-dihaloethane series, on the other hand, the proportion of the gauche conformation decreases substantially as one proceeds down the periodic table,[5,55,62] paralleling the previously discussed donor abilities of the halogens themselves.

The concept of conjugative destabilization also accounts for the fact that axial fluorine is preferred over equatorial in 5-fluoro-2-isopropyl-1,3-dioxane (eq 2).[55,63] Furthermore, this proposal is consistent with the observation that the ring inversion barrier in 5,5-difluoro-1,3-dioxane is lower than that in 1,3-dioxane itself.[64] The energy of the ground state of the former should be raised by conjugative destabilization, which should, assuming that the effective through-bond conjugation is diminished in the transition state, lower its inversion barrier relative to that for the parent compound.



(2)

Finally, in view of the fact that the NMe_3^+ group has been shown to be a resonance donor,[65] the gauche conformation adopted by acetylcholine (**13**) and its analogs[66] may also be due, at least in part, to the conjugative destabilization of the trans rotamers.



13

Summary and Conclusions

When one isomer of an organic molecule is more stable than another, the first may be stabilized or the second destabilized. Previous discussions of the cis effect exhibited by the conformations of a variety of extended π systems have assumed cis stabilization, a phenomenon attributed quite naturally to steric attraction. This concept is unjustifiable in many cases, however, leaving its general validity questionable. In this paper, we have shown that the cis effect can be more adequately and consistently interpreted in terms of stereospecific trans destabilization.

Such destabilization arises from exchange (exclusion) repulsion associated with overlap between filled orbitals. It is conformation dependent due to the fact that electrons delocalize preferentially in straight lines.

These proposals are based on sound theoretical concepts and are shown to be completely consistent with a wide variety of experimental data. We conclude, therefore, that conjugative destabilization, rather than steric attraction, embodies the fundamental electronic effect which determines the preferred conformations of a wide variety of extended π systems.

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