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# Effects of electron donation into C–F σ* orbitals: explanations, predictions and experimental tests

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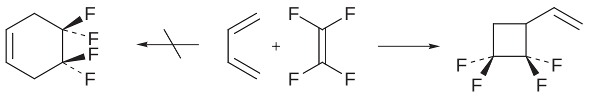
**The ability of C–F σ* orbitals to act as electron acceptors is shown to be capable of explaining and predicting a wide variety of apparently unrelated phenomena. Among these are (i) pyramidalization of fluorinated radical centers, (ii) the much weaker π-bond in tetrafluoroethylene (TFE) than in ethylene, (iii) the stepwise reaction of TFE with butadiene to form 2,2,3,3-tetrafluoro-1-vinylcyclobutane, rather than the Diels–Alder adduct, (iv) the thermodynamic favorability of replacing C–H with C–C bonds at fluorinated carbons, (v) the preference for disrotatory ring opening and closure of 1,1-difluorocyclopropanes, and (vi) the change from a triplet to a singlet ground state upon substitution of fluorines for the pair of hydrogens at C-2 of cyclopentane-1,3-diyl.**

Over the past ten years my research group at the University of Washington has been carrying out computational research on organic molecules containing geminal fluorines. The unifying principle that has emerged from our research is that C–F σ-bonds have low-lying antibonding σ* orbitals, which are capable of accepting electrons from nonbonding p-π AOs, either on the same carbon or on adjacent carbons, and also from σ- and π-bonds on adjacent carbons. We have applied this understanding to explaining otherwise puzzling results, already in the literature, and to making new predictions that we have subsequently verified experimentally.

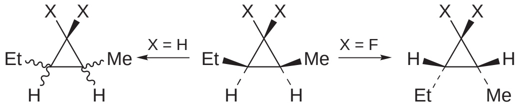
There is now good evidence, both computational[1a] and experimental,[1b] that the ability of C–F σ* orbitals to accept unshared electron pairs from adjacent carbons (negative hyperconjugation) stabilizes fluorinated carbanions. However, as will be shown in this article, the electron-accepting ability of C–F σ* orbitals is also capable of explaining and predicting a wide variety of additional and apparently unrelated phenomena. Among these are the following: (i) in contrast to methyl radical, trifluoromethyl radical is non-planar and has a high barrier to inversion;[2] (ii) tetrafluoroethylene (TFE) has a much weaker π-bond than ethylene;[3] and, (iii) unlike ethylene, TFE does not undergo a Diels–Alder reaction with butadiene but, instead, forms 2,2,3,3-tetrafluoro-1-vinylcyclobutane [eqn. (1)];[4] (iv) heats of formation show that transfer of the geminal fluorines from difluoromethane to C-2 of propane [eqn. (2)] is exothermic



(1)

$$CH_2F_2 + H_3CCH_2CH_3 \rightarrow CH_4 + H_3CCF_2CH_3 \qquad (2)$$

by 14.5 kcal mol$^{-1}$;[5] (v) although 1-ethyl-2-methylcyclopropane undergoes stereorandom ring opening and closure,[6] replacement of the geminal ring hydrogens by geminal fluorines has been both predicted[7] and found[8] to lead to a very large preference for stereomutation by coupled disrotation of the alkylated ring carbons [eqn. (3)]; and (vi) cyclopentane-1,3-diyl has a triplet ground state;[9] but, as predicted,[10] a derivative of 2,2-difluorocyclopentane-1,3-diyl appears to have a singlet ground state.[11]



(3)

In showing how these diverse phenomena can all be explained by the electron accepting ability of the σ* orbitals of C–F bonds, I will take advantage of the possibility in a review of this type of revealing the intellectual threads that connect what might otherwise appear to be a collection of unrelated research projects. This review is written from a historical perspective and describes how one research project led to another and how each contributed to our understanding of the effects of geminal fluorines on the structure, energetics, and reactivity of fluorinated alkanes, alkenes, radicals, and diradicals.

## Why do some radical centers have significant barriers to planarity?

In 1976 I taught a course on MO theory at the University of Washington. The text for the course[12] used second-order perturbation theory to explain the shapes of simple molecules. Bill Cherry, who was a graduate student in the course, saw how this theoretical framework could be used to explain the greater degree of pyramidalization and much higher barrier to inversion in phosphine, compared to ammonia, and why successive replacement of the hydrogens by fluorines in $AH_3$ molecules with seven or eight valence electrons also increases the barriers to inversion.[13,14] Subsequent conversations between Bill, his thesis adviser, Nick Epiotis, and myself resulted in the three of us coauthoring an article for *Accounts of Chemical Research* on this subject.[15]

The crucial factor in determining how favorable pyramidalization is in a planar $AH_3$ molecule is the amount of net stabilization provided by the mixing of the nonbonding $p_z$ AO ($a_2''$) on A with the antibonding $2a_1'$ MO.[13,15] These orbitals are shown in Fig. 1, which also illustrates how their mixing upon pyramidalization transforms the nonbonding $p_z$ AO in planar $AH_3$ into an MO that consists of a hybridized AO on A whose smaller lobe interacts in a bonding fashion with the three hydrogens.

According to second-order perturbation theory, the amount of net stabilization that arises from mixing between $a_2''$ and $2a_1'$ is inversely proportional to the size of the energy gap between these orbitals.[12,13,15] Therefore, in two similar $AH_3$ molecules (*e.g.* $NH_3$ and $PH_3$ or $CH_3$ and $SiH_3$), the energy lowering caused by pyramidalization and, hence, the amount of pyramidalization at the equilibrium geometry will both be larger in the molecule with the smaller energy difference between the antibonding $2a_1'$ and the nonbonding $a_2''$ orbitals.

Calculations find that planar $AH_3$ molecules have much lower-lying $2a_1'$ antibonding MOs when A is a second-row, rather than a first-row atom.[13,15] Consequently, second-order perturbation theory rationalizes the greater pyramidalization and higher barriers to inversion found in phosphines than in

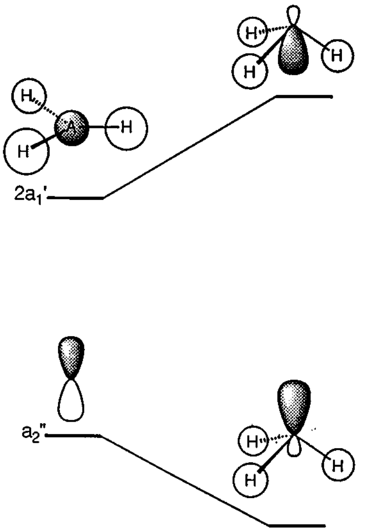


**Fig. 1** Effect of mixing the $a_2''$ nonbonding MO with the $2a_1'$ antibonding MO of planar $AH_3$ on pyramidalization

amines[16] and in silyl radicals, compared to alkyl radicals.[17] The existence of low-lying $2a_1'$ MOs in planar $PH_3$ and $SiH_3$ can be traced to the fact that, unlike the case with 2s and 2p AOs, the maximum density of a 3s AO is significantly closer to the nucleus than that of a 3p AO.[18]

Another way to lessen the energy difference between the nonbonding $a_2''$ AO on A and the antibonding $2a_1'$ MO in $AH_3$ is to replace the three hydrogens with more electronegative atoms, such as fluorines.[13,15] The reduction in the energy difference between $a_2''$ and $2a_1'$ that results from the substitution of fluorine for hydrogen makes mixing of these two orbitals by pyramidalization more energetically favorable.The physical reason that this substitution leads to pyramidalization is that, as shown in Fig. 1, the filled MO that results from mixing of these two orbitals is no longer localized just on A, but is delocalized onto the more electronegative fluorines. Experimentally, it is known that electronegative substituents increase the barriers to inversion at nitrogen[16,19] and, as noted in the Introduction, it has also been found that successive replacement of hydrogens by fluorines results in increased pyramidalizaion and higher barriers to inversion in carbon-centered radicals.[2]

## The effect of pyramidalization on the π-bond dissociation energy of tetrafluoroethylene and on the barriers to rotation in fluorinated allyl radicals

In a footnote in our 1977 paper in *Accounts* we pointed out that the favorability of pyramidalization of silyl,[17] cyclopropyl,[20] and fluoroalkyl[2] radical centers should tend to weaken the π-bonds in silenes, methylenecyclopropane, and tetrafluoroethylene (TFE), thus possibly accounting, at least in part, for the high reactivity of these compounds.[15] As illustrated in Fig. 2, if a π-bond is formed between two radical centers, one or both of which prefer a pyramidal geometry, the π-bond dissociation energy (BDE) will be less than the intrinsic strength of a π-bond formed between the planar radical centers by the amount of energy that is released by their pyramidalization. We have investigated the impact of this effect on the π BDEs of silenes,[21] disilenes,[22] methylenecyclopropane,[23] and tetrafluoroethylene (TFE).[24]

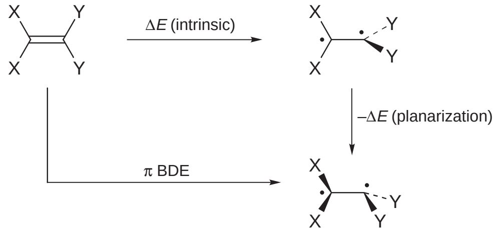


**Fig. 2** Thermocycle showing that the π BDE of an alkene is reduced from the intrinsic strength of a π-bond between the planar radical centers by the energy released by their pyramidalization

The electronegative substituents attached to each carbon in TFE have a substantial effect on reducing the π-bond strength in TFE from that in ethylene. The strength of the π-bond in ethylene can be obtained experimentally from either the kinetics of *cis–trans* isomerization of 1,2-dideuterioethylene[25] or from the thermodynamics of the reaction shown in eqn. (4).[26] Both methods give a π-bond energy of *ca.* 65 kcal $mol^{-1}$.

$$H_2C{=}CH_2 + CH_3CH_3 \rightarrow 2\ CH_3CH_2\cdot \qquad (4)$$

Obviously, the kinetics of *cis–trans* isomerization cannot be used to provide an experimental value for the π-bond energy of TFE, but the thermodynamics of the reaction in eqn. (5) with

$$F_2C{=}CF_2 + CF_2XCF_2X \rightarrow 2\ CF_2XCF_2\cdot \qquad (5)$$

X = F has been employed to yield an experimental value of 52 ± 2 kcal $mol^{-1}$ for this quantity.[3]

Computationally, either the barrier to rotation or the energy of the reaction in eqn. (5) can be used. Both types of calculations concur with experiment in finding that the π-bond in TFE is *ca.* 15 kcal $mol^{-1}$weaker than that in ethylene.[24]

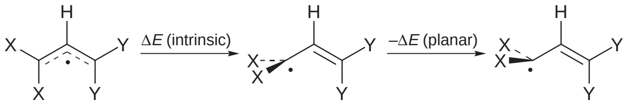
We used *ab initio* calculations to show that the lower π-bond energy in TFE, compared to ethylene, is due entirely to the energetic cost of planarizing the radical centers in TFE. The energy of 18.0 kcal $mol^{-1}$that is computed to be necessary to planarize the carbons in the singlet diradical transition state for rotation about the double bond[27] is very close to the calculated increase of 18.4 kcal $mol^{-1}$when the energy of the reaction in eqn. (5) is recomputed with the radical center in $CF_2XCF_2$ (X = H) constrained to planarity.[24] The intrinsic strength of the π-bond in TFE is actually *ca.* 3 kcal $mol^{-1}$ larger than that in ethylene.[27]

Dr Bruce Smart suggested that we investigate whether the much lower barrier to rotation that EPR experiments had found in 1,1,3,3-tetrafluoroallyl radical,[28a] compared to the unfluorinated radical,[28b,c] might have a similar explanation. We found that pyramidalization of the twisted $CF_2$ group did indeed lower the barrier to rotation in 1,1,3,3-tetrafluoroallyl radical by about 10 kcal $mol^{-1}$.[29] In the corresponding anion pyramidalization was calculated to provide so much stabilization that a $C_s$ geometry, with one $CF_2$ group pyramidalized and twisted out of conjugation, was computed to be 17 kcal $mol^{-1}$ *lower* in energy than the planar, conjugated, $C_{2v}$ structure and only 1 kcal $mol^{-1}$ higher in energy than a $C_2$ structure in which both $CF_2$ groups are pyramdalized but oriented so that they are in conjugation with the central carbon.[30]

It was known experimentally that 1,1-difluoroallyl radical does not have a particularly low barrier to $CF_2$ rotation.[28a,b] If $CF_2$ group pyramidalization were the sole reason for the low barrier to rotation found in 1,1,3,3-tetrafluoroallyl radical, one would have expected 1,1-difluoroallyl to have a similarly low barrier to rotation of the $CF_2$ group.

In agreement with experiment, our calculations found the barrier to $CF_2$ rotation to be 6.9 kcal $mol^{-1}$ higher in 1,1-difluoroallyl than in 1,1,3,3-tetrafluoroallyl. The results of our CISD calculations are summarized in Fig. 3.[27]

As shown in Fig. 3, pyramidalization of the rotated $CF_2$ group actually contributes more to lowering the barrier to rotation in 1,1-difluoroallyl than in 1,1,3,3-tetrafluoroallyl radical. The barrier to $CF_2$ rotation is higher in difluoro- than in tetrafluoroallyl radical because the intrinsic barrier to rotation of a planar $CF_2$ group is 9.7 kcal $mol^{-1}$ larger in the former than in the latter radical. The reason for the intrinsically higher barrier to planar $CF_2$ rotation in difluoroallyl is that, after $CF_2$ rotation, the $CH{=}CH_2$ π-bond that remains in difluoroallyl is about 10 kcal $mol^{-1}$ weaker than the $CH{=}CF_2$ π-bond that remains in tetrafluoroallyl. A similar difference between the intrinsic



| X | Y | ΔE (intrinsic) | ΔE (planar) |
|---|---|---|---|
| H | H | 15.4 | 0.1 |
| F | F | 12.6 | 9.9 |
| H | F | 12.3 | 0.0 |
| F | H | 22.3 | 12.7 |

**Fig. 3** Intrinsic rotation barriers and planarization energies (kcal mol$^{-1}$) calculated for allyl, difluoroallyl, and tetrafluoroallyl radicals (ref. 27). The net barriers to rotation are given by $\Delta E$ (rotation) = $\Delta E$ (intrinsic) − $\Delta E$ (planarization) − $\Delta$ZPE, where the zero-point energy corrections (kcal mol$^{-1}$) are $\Delta$ZPE = −0.9 for X = Y = H, 1.3 for X = Y = F, −0.5 for X = H, Y = F, and 1.3 for X = F, Y = H. The origin of the different signs of the $\Delta$ZPE corrections for X = H and X = F resides in the pyramidalization that occurs for X = F in the transition state for rotation (ref. 27).

π-bond energies of ethylene and 1,1-difluoroethylene (DFE) was calculated.[27] This explains why these two molecules have similar π BDEs, despite the fact that the latter contains a $CF_2$ group, pyramidalization of which is calculated to lower the intrinsic π BDE by 11.4 kcal mol$^{-1}$.

The origin of the much higher intrinsic π-bond energy in DFE than in either ethylene or TFE is the asymmetric substitution of fluorine on the π-bond in DFE. This allows much better donation of the p-π fluorine lone pairs into the π-bond in DFE than in TFE. The 14.6 ± 1.5 kcal mol$^{-1}$ exothermcity of the reaction in eqn. (6) can be viewed as a specific example of

$$H_2C{=}CH_2 + F_2C{=}CF_2 \longrightarrow 2\ F_2C{=}CH_2 \qquad (6)$$

Paulings finding that the reaction, $A_2 + B_2 \rightarrow 2\ AB$ is always exothermic and that the exothermicity increases with the elecronegativity difference between A and B.[27]

## Why does TFE not undergo a Diels–Alder reaction with butadiene?

Although the reaction of ethylene with buta-1,3-diene yields a trace of vinylcyclobutane,[31] by far the major product (99.98%) is cyclohexene, formed by a concerted Diels–Alder reaction. In contrast, as shown in eqn. (1), TFE reacts with buta-1,3-diene to give, as the only isolated product, 2,2,3,3-tetrafluoro-1-vinylcyclobutane,[4] formed *via* a stepwise mechanism involving a diradical intermediate.[32]

Although the π-bond in TFE is considerably weaker than the π-bond in ethylene,[3,27] this fact, by itself, does not explain why a transition state involving formation of a bond to just one carbon of TFE is apparently lower in energy than the transition state for a Diels–Alder reaction, in which bonds are simultaneously formed to both carbons. In fact, our calculations found that, despite the weaker π-bond in TFE, the energy difference between the reactants and the transition state for a concerted Diels–Alder reaction is nearly the same for TFE and ethylene.[33] Moreover, *syn* pyramidalization of TFE to $\phi$ = 26°, as in the transition state for its Diels–Alder reaction with butadiene, was computed to raise the energy of TFE by 5 kcal mol$^{-1}$ more than the same distortion in ethylene. Presumably, repulsions between the fluorines make pyramidalization of TFE in a *syn* fashion energetically costly, so that $CF_2$ pyramidalization in the Diels–Alder transition state does not accelerate this reaction.

The prediction that the Diels–Alder reactions of butadiene with both TFE and ethylene have approximately the same activation energy cannot be verified experimentally, because, as noted above, TFE reacts rapidly with butadiene to form a diradical intermediate. The energy of this diradical, relative to the reactants, was calculated to be *ca.* 26 kcal mol$^{-1}$ lower for TFE than for ethylene. Clearly this is why TFE, unlike ethylene, reacts with butadiene by forming just one C–C bond.

As expected, the $CF_2$ radical center is highly pyramidal ($\phi$ = 47°) in the diradical; and, of course, the $CF_2$ group at which the new C–C bond is formed also becomes non-planar. Relief of the 18 kcal mol$^{-1}$ 'strain' that is associated with having two planar $CF_2$ groups in TFE is obviously the major factor that favors the diradical pathway by 26 kcal mol$^{-1}$ in the reaction of TFE with butadiene. However, this diradical intermediate is apparently stabilized by an additional 8–10 kcal mol$^{-1}$ when it is formed from TFE than from ethylene.

We were able to show that the source of this additional stabilization of the fluorinated, over the unfluorinated, diradical is the greater strength of the C–C bond that is formed in the reaction of butadiene with TFE than with ethylene. This bond is not only stronger, but it is also 0.05 Å shorter in the fluorinated than in the unfluorinated diradical. Our calculations indicated that about 90% of the greater strength of this bond comes from the geminal pair of fluorines on the carbon to which this bond is formed.

Calculations and experimental heats of formation both show the favorability of forming C–C bonds to fluorinated carbons. For example, the reaction in eqn. (7) can be thought of as

$$H_3CCH_2CH_3 + HCF_2CH_3 \longrightarrow H_3CCH_3 + CH_3CF_2CH_3 \qquad (7)$$

replacing a hydrogen in 1,1-difluoroethane with a methyl group from propane. Without corrections for $\Delta$ZPE, we calculated this reaction to be exothermic by 8.0 kcal mol$^{-1}$ at the MP2 level of theory,[33] which is slightly larger than the value of 6.2 kcal mol$^{-1}$ obtained from experimental heats of formation.[5] An even more dramatic example is provided by the reaction in eqn. (2), in which both hydrogens in difluoromethane are replaced by methyl groups. As noted in the introduction, experimental heats of formation[5] show that this reaction is exothermic by 14.5 kcal mol$^{-1}$.

## Electron delocalization into C–F σ* orbitals in neutral molecules

One possible explanation of the preference for attachment of electronegative elements, such as fluorine[33,34*c*] and oxygen,[34] to the more highly alkylated of two carbons is that the electrons in the C–H bonds at the β carbons delocalize electrons into the low-lying C–F and C-O σ* orbitals. This would explain not only the energetics of the reactions shown in eqns. (2) and (7), but also why our calculations found that the lengths of C–F bonds increase with increasing alkylation of the carbon to which they are attached, and why the lengths of C–C bonds decrease with the addition of fluorines to one of the carbons.

It is generally accepted that electron delocalization into C–F σ* MOs stabilizes carbanions[1] and is also responsible for the anomeric effect observed when fluorine and a heteroatom with unshared π electrons are attached to the same carbon.[35] However, it is much less clear to what extent delocalization of electrons from C–H bonds into C–F σ* MOs actually is responsible for the energetic preference for attachment of alkyl groups to fluorinated carbons and the accompanying changes in bond lengths. In order to test whether delocalization of electrons into C–F σ* orbitals is of any importance in neutral molecules, we performed additional calculations.[36]

Computational evidence, supporting the delocalization of π-electrons into C–F σ* orbitals, was actually published in 1983 by Greenberg *et al.*[37] Their calculations found the reaction in eqn. (8) to be exothermic by 9.6 kcal mol$^{-1}$.

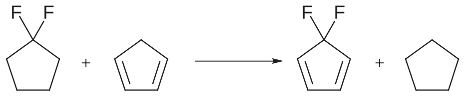
(8)

They attributed the exothermicity to electron donation from the π-bonding orbital of 3,3-difluorocyclopropene into the out-of-phase combination of C–F σ* orbitals. This interaction, which can be represented schematically by the ionic resonance structure shown in Fig. 4, confers a degree of aromaticity on 3,3-difluorocyclopropene. The calculated and observed bond

**Fig. 4** Resonance structures for 3,3-difluorocyclopropene. The ionic resonance structure schematically depicts the effect of electron donation from the π-bonding orbital into the out-of-phase combination of C–F σ* orbitals.

lengths and dipole moment of this molecule are consistent with the delocalization of electron density from the π-bond into the C–F σ* orbitals that is depicted in Fig. 4.[36]

The differences in symmetry between the HOMO and LUMO of the ethylene π-bond in cyclopropene and the butadiene π-bonds in cyclopentadiene should make hyperconjugative electron donation from the C–H bonds at C-5 of cyclopentadiene much more stabilizing than delocalization of electron density into the C–F σ* orbitals of 5,5-difluorocyclopentadiene. These hyperconjugative interactions should make cyclopentadiene somewhat aromatic and 5,5-difluorocyclopentadiene somewhat anti-aromatic. Therefore, it is not surprising that our calculations found the reaction in eqn. (9) to be endothermic by 14.1 kcal mol$^{-1}$.[36]



(9)

## Hyperconjugative delocalization into C–F σ* orbitals in 1,3-diradicals

If the C–F σ* orbitals in 1,1-difluorocyclopropene can accept electron density from the π-bonding orbital, they should certainly be able to accept electron density from the in-phase combination of non-bonding p-π AOs in 2,2-difluoropropane-1,3-diyl. Similarly, if the C–H bonds at C-5 of cyclopentadiene can donate electron density into the antibonding butadiene LUMO, they certainly ought to be able to donate electron density into the in-phase combination of non-bonding p-π AOs in propane-1,3-diyl. These hyperconjugative interactions are depicted by the resonance structures in Fig. 5.

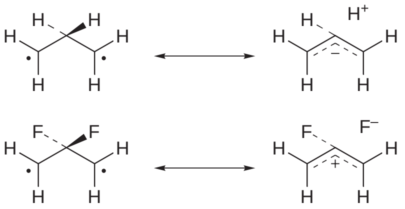


**Fig. 5** Resonance structures depicting hyperconjugative electron donation from the C–H bonds of the central CH$_2$ group into the in-phase combination of p-π AOs at C-1 and C-3 in propane-1,3-diyl and electron donation from the in-phase combination of p-π AOs at C-1 and C-3 into the C–F σ* orbitals at C-2 in 2,2-difluoropropane-1,3-diyl

Thirty years ago Hoffmann analyzed the results of his extended Hückel calculations on propane-1,3-diyl in terms of interaction of the C–H bonds at C-2 with the in-phase combination of p-π AOs at C-1 and C-3.[38] This interaction destabilizes the latter orbital, making it advantageous for the two non-bonding electrons to occupy preferentially the out-of-phase combination of p-π AOs at C-1 and C-3. This combination is the highest occupied MO (HOMO) of the allylic anion in the hyperconjugated resonance structure for propane-1,3-diyl in Fig. 5.

An orbital interaction diagram for 2,2-difluoropropane-1,3-diyl shows that the in-phase combination of p-π AOs at C-1 and C-3 is stabilized by interaction with the C–F σ* orbitals at C-2.[7,36] Therefore, the two non-bonding electrons preferentially occupy the orbital that results from this mixing. This orbital has the same symmetry as the HOMO of the allylic cation in the hyperconjugated resonance structure for 2,2-difluoropropane-1,3-diyl in Fig. 5.

The difference in the symmetry of the HOMO between propane-1,3-diyl and 2,2-difluoropropane-1,3-diyl is predicted to result in a difference in the preferred mode by which these two diradicals are formed from, and undergo closure to, the corresponding cyclopropanes. More specifically, although ring opening and ring closure are predicted to be conrotatory in cyclopropane,[38] they are predicted to be disrotatory in 1,1-difluorocyclopropane.[7,36]

The difference in the symmetry of the HOMOs between unfluorinated and fluorinated diradicals can explain some otherwise puzzling experimental results that were obtained by Dolbier and co-workers[39] and which are summarized in Fig. 6.

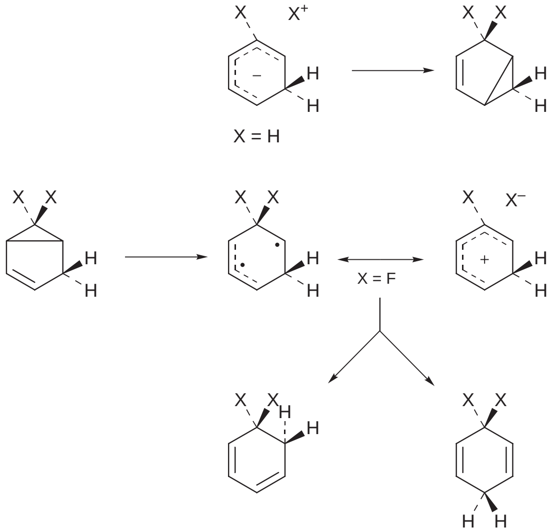


**Fig. 6** Rearrangement pathways followed by bicyclo[3.1.0]hex-2-ene and its 6,6-difluoro derivative. The hyperconjugated resonance structure shown for the diradical intermediate formed in each reaction can be used to rationalize the difference between the reaction pathways followed by the hydrocarbon and fluorocarbon (ref. 36).

Derivatives of bicyclo[3.1.0]hex-2-ene (X = H) undergo vinylcyclopropane rearrangements, presumably *via* a diradical intermediate; but Dolbier found that 6,6-difluorobicyclo-[3.1.0]hex-2-ene (X = F) gives no vinylcyclopropane rearrangement product; only the two products of hydrogen shifts in a putative diradical intermediate were detected.

The hyperconjugated resonance structures shown in Fig. 6 can readily account for the different reactions observed for X = H and X = F.[36] Hyperconjugative electron donation from the C–X bonds for X = H gives the diradical intermediate some character of a pentadienyl anion. Disrotation, which is the only stereochemically feasible mode of ring closure in the diradical, is allowed by orbital symmetry for a pentadienyl anion; but the node in the LUMO at the distal CH$_2$ group makes [1,2]-hydrogen shifts from this carbon symmetry forbidden. In contrast, for X = F, hyperconjugative electron delocalization into a C–X σ* orbital in the diradical confers on it some character of a pentadienyl cation. For such a species disrotatory ring closure is forbidden by orbital symmetry, but the symmetry of the LUMO makes [1,2]-hydrogen shifts allowed.

The hyperconjugated resonance structures for propane-1,3-diyl and 2,2-difluoropropane-1,3-diyl in Fig. 5 also allow one to predict that π-electron donation from alkyl groups at C-1 and C-3 should compete with electron donation from a filled combination of C–H bonding orbitals at C-2. In contrast, it is clear from Fig. 5 that electron donation from alkyl groups at C-1 and C-3 should enhance electron donation into the C–F σ* orbitals of the fluorocarbon. Both predictions have been confirmed by *ab initio* calculations[7,36] and are consistent with the experimental results that are discussed in the next section.

Before discussing the effect on cyclopropane stereomutations of replacing the hyperconjugatively electron-donating $CH_2$ group in propane-1,3-diyl with the electron-accepting $CF_2$ group in 2,2-difluoropropane-1,3-diyl, it is important to address the question of whether two hydrogens or two fluorines at C-2 provide more stabilization for the diradical formed by cyclopropane ring opening. After correcting eqn. (10) for the fact that the

$$H_3CCF_2CH_3 + {\cdot}H_2CCH_2CH_2{\cdot} \rightarrow {\cdot}H_2CCF_2CH_2{\cdot} + H_3CCH_2CH_3 \quad (10)$$

C–H BDE of 2,2-difluoropropane is computed to be 2.4 kcal $mol^{-1}$ larger than that of propane, the $CF_2$ group in 2,2-difluoropropane-1,3-diyl is calculated to provide 3.2 kcal $mol^{-1}$ more stabilization for this diradical than the $CH_2$ group at C-2 provides for propane-1,3-diyl.[36]

### Stereomutation of cyclopropanes and 1,1-difluorocyclopropanes

The publication of Hoffmann's 1968 paper on propane-1,3-diyl[38] inspired a huge amount of computational and experimental work on the stereomutation of cyclopropane. Our own computational efforts in this area were initially motivated less by an interest in propane-1,3-diyl *per se* than by the desire to have calculations on the hydrocarbon diradical with which we could compare our computational results on 2,2-difluoropropane-1,3-diyl.[7]

The most important results of the computational and experimental studies of the hydrocarbon diradical can be summarized as follows. (i) *Ab initio* calculations predict only a 1–2 kcal $mol^{-1}$ preference for con- over dis- and monorotation,[40] a much smaller preference than was found by Hoffmann's Extended Hückel calculations.[38] (ii) As already noted, *ab initio* calculations also predict that alkyl substituents will greatly reduce the small preference for conrotation that is computed for unsubstituted cyclopropane.[36] (iii) Presumably for this reason, experiments on the stereomutation of substituted cyclopropanes have found no preference for coupled rotation.[6,40]

For cyclopropane substituted only by deuterium, (iv) Berson and co-workers[41*a,b*] and, later, Baldwin[41*c*] reported a preference for coupled rotation in their studies of the stereomutation of [1,2-$^2H_2$]cyclopropane. (v) However, Baldwin and co-workers found no evidence for coupled rotation in their subsequent study of the stereomutation of [1,2,3-$^2H_3$, 1-$^{13}C$]cyclopropane.[41*d,e*] (vi) Calculations show that isotope effects are incapable of reconciling the results of these two experiments.[40*a,b*] (vii) The results of reaction dynamics calculations[42] are more consistent with the experimental results for [$^2H_2$]cyclopropane[41*a–c*] than for [$^2H_3$]cyclopropane.[41*d,e*]

Since the dynamics calculations predict that the coupled rotation found in [$^2H_2$]cyclopropane consists of not only orbital symmetry-allowed conrotation but also of symmetry-forbidden disrotation, the experimental results on [$^2H_2$]cyclopropane should not be taken as confirmation of Hoffmann's prediction of a preference for coupled *conrotation* in the stereomutation of cyclopropane. There is currently no method available for distinguishing between conrotation and disrotation in the experimental study of the stereomutation of [1,2-$^2H_2$]cyclopropane; so there is no known experimental technique that could disprove the mischievous conjecture of a devil's advocate who asserted that the coupled methylene rotation observed in the stereomutation of [$^2H_2$]cyclopropane consists entirely of disrotation rather than conrotation.

What a difference geminal fluorines make! As already noted, the greater ability of C–F σ* orbitals at C-2 to accept electrons in 1,3-diradicals, compared to the ability of filled C–H orbitals at C-2 to donate electrons, is calculated to make hyperconjugative stabilization of the so-called (0,0) geometry[38] of 2,2-difluoropropane-1,3-diyl larger than that of the same geometry of the hydrocarbon diradical.[36] This should make disrotation much more favorable in the stereomutation of 1,1-difluorocyclopropane than conrotation is in the stereomutation of cyclopropane. The results of *ab initio* calculations on the ring opening of the fluorocarbon show that the transition state for disrotation is, in fact, *ca.* 4 kcal $mol^{-1}$ lower in energy than the transition states for conrotation, monorotation, or cleavage of a ring bond to C-1.[7,36]

As discussed above, 2,3-dialkyl-1,1-difluorocyclopropanes are expected to show an even greater preference for disrotatory ring opening and closure than 1,1-difluorocyclopropanes. As shown in Fig. 7, the calculated preference for ring opening of 1,1-difluoro-2,3-dimethylcyclopropane to the s-*trans*,s-*trans* (0,0) geometry of 3,3-difluoropentane-2,4-diyl, over rotation of just one methylene group, to form the so-called (0,90) geometry,[38] amounts to 6.6 kcal $mol^{-1}$ when the effects of dynamic electron correlation[43] are included at the CASPT2 level.[8]

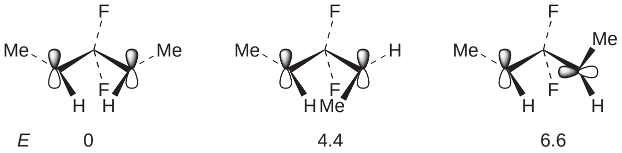


**Fig. 7** Relative CASPT2 energies (kcal $mol^{-1}$) of three conformations of 3,3-difluoropentane-2,4-diyl (ref. 8)

As also shown in Fig. 7, ring opening of 2,3-dimethyl-1,1-difluorocyclopropane to the s-*trans*,s-*cis* (0,0) geometry of 3,3-difluoropentane-2,4-diyl is calculated to be more favorable than opening to the (0,90) geometry, but only by 2.2 kcal $mol^{-1}$.[8] The very large calculated preference of *ca.* 4 kcal $mol^{-1}$ for ring opening to the s-*trans*,s-*trans*, rather than the s-*trans*,s-*cis* geometry of 3,3-difluoropentane-2,4-diyl has been shown to have its origin in the symmetry of the HOMO in this fluorinated diradical.[36]

The large predicted preference for opening of a 2,3-dialkyl-1,1-difluorocyclopropane to an s-*trans*,s-*trans*, rather than an s-*trans*,s-*cis*, geometry can be used to design an experiment to distinguish between conrotatory and disrotatory ring opening.[7,36] If, as predicted, ring opening is disrotatory, the *cis* cyclopropane stereoisomer will open to the preferred s-*trans*, s-*trans* geometry of the 1,3 diradical, whereas the *trans* cyclopropane stereoisomer must open to the s-*trans*,s-*cis* geometry. Therefore, if ring opening is, in fact, disrotatory, an optically active *cis*-2,3-dialkyl-1,1-difluorocyclopropane should racemize faster than its *trans* stereoisomer.

In collaboration with the group of Professor William Dolbier, we prepared optically active *cis*- and *trans*-2-ethyl-3-methyl-1,1-difluorocyclopropane and studied the stereomutations of these two isomers.[8] At 274.5 °C, racemization of the *cis* isomer was found to be 107 times faster than its epimerization to the *trans* isomer by any pathway that effects one-center rotation. At this temperature, racemization was also found to be favored over epimerization in the *trans* isomer, but only by a factor of 6.6. The finding that the ratio of the rate constants for racemization and epimerization is 16.2 times larger for the *cis* cyclopropane than for its *trans* isomer shows that the coupled rotation that is observed in both isomers is disrotation, as predicted.[7,36]

### Effect of electron delocalization into C–F σ* orbitals on singlet-triplet energy differences in 1,3-diradicals

Increasing the energy separation between the HOMO and LUMO in a diradical selectively stabilizes the lowest singlet state, relative to the triplet, since in the former state more than one electron can occupy the HOMO, whereas in the latter the HOMO and the LUMO are each occupied by one electron.[44] Thus, either the presence of filled σ orbitals at C-2 that are good hyperconjugative electron donors or unfilled σ* orbitals that are good hyperconjugative electron acceptors can, in principle, result in singlet ground states for derivatives of propane-1,3-diyl. Therefore, it is not surprising that, although cyclopentane-1,3-diyl has been both calculated[10,45] and found[9] to have a triplet ground state, the ground state of 2,2-difluorocyclopentane-1,3-diyl has been predicted to be a singlet (Fig. 8).[10]

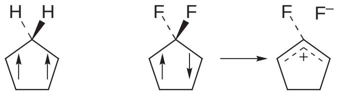
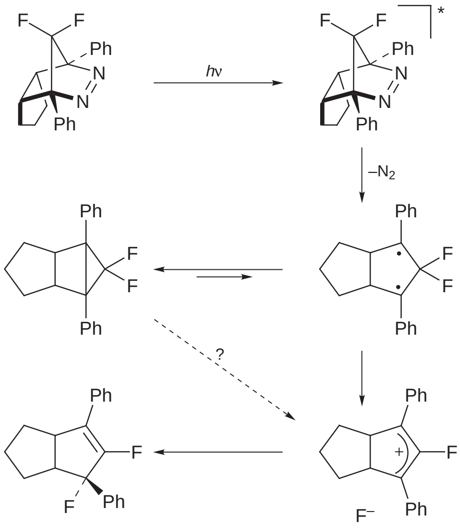


**Fig. 8** Cyclopentane-1,3-diyl is known to have a triplet ground state (ref. 9), but electron donation into the C–F σ* orbitals at C-2 is predicted to make 2,2-difluorocyclopentane-1,3-diyl a ground state singlet (ref. 10)

In order to test this prediction, we collaborated with the research groups of Professors Waldemar Adam and Jakob Wirz on the generation and study of the derivative of 1,3-diphenyl-2,2-difluorocyclopentane-1,3-diyl shown in Scheme 1.[11] As shown, the diradical was generated by flash photolysis of an azo compound. A strong absorption with $\lambda_{\max} = 530$ nm appeared with a time constant of $\tau = 8 \pm 1$ ps, and in pentane it disappeared with $\tau = 80 \pm 3$ ns. In this solvent the diradical reacts to form both the tricyclic difluoride and the bicyclic difluoroalkene. The former was observed by $^{19}$F NMR spectroscopy at low temperatures, but at room temperature it rearranges with $\tau = 225 \pm 20$ μs to the latter.



**Scheme 1**

The temperature dependence of the rate of disappearance of the diradical was measured and gave log $A = 12.8 \pm 0.4$ and $E_a = 7.8 \pm 0.5$ kcal mol$^{-1}$. These Arrhenius parameters are very different from those of log $A = 6.7$ and $E_a = 2.6$ kcal mol$^{-1}$ measured for disappearance of the hydrocarbon diradical, lacking the geminal fluorines. The fluorocarbon and hydrocarbon diradicals also differ in the rate of their reaction with $O_2$. The former cannot be trapped by oxygen, making $k_{O2} < 4 \times 10^7$ $\mathrm{M}^{-1}\mathrm{s}^{-1}$; whereas, the latter reacts with $O_2$ with a rate constant of $k_{O2} = 3\times 10^9$ $\mathrm{M}^{-1}\mathrm{s}^{-1}$.

The hydrocarbon diradical gives a triplet EPR spectrum and, like the parent cyclopentane-1,3-diyl, it appears to have a triplet ground state. This accounts for the low values of log $A$ and $E_a$ for the disappearance of the hydrocarbon diradical, since intersystem crossing to a slightly higher energy singlet state is the rate determining step. The reaction of the triplet hydrocarbon diradical with triplet oxygen is fast, because the two triplet species can give a singlet product by forming two C–O bonds in a concerted fashion.

The high $E_a$ for disappearance of the fluorocarbon diradical allowed frozen solutions of it to be studied at low temperatures. At 77 K the red color of the diradical persisted for a day, but no triplet EPR signal was detected. The conclusion that the fluorinated diradical has a singlet ground state is supported by the activation parameters for its disappearance, which are typical of those for a spin-allowed process, and the rate at which it is trapped by oxygen, which was too slow for us to measure. These experimental results[11] are consistent with our prediction that the ability of C–F σ* orbitals to accept electrons is sufficiently large to make the singlet the ground state of 2,2-difluorocyclopentane-1,3-diyls.[10]

## Future research

In the course of the theoretical studies described in the previous sections, we moved from explaining phenomena that were already known to predicting new phenomena. Prediction is the ultimate goal of any theory, and the experimental confirmation of our predictions that geminal fluorine substituents should result in disrotatory cyclopropane ring-opening and in singlet ground states for 1,3-diradicals shows that delocalization of electrons into C–F σ* orbitals is a very useful theoretical construct.

If the presence of low-lying empty σ* orbitals at C-2 can stabilize the singlet states of 1,3-diradicals, it follows that high-lying filled σ orbitals at C-2 should have the same effect. Therefore, replacement of the C–H bonds at C-2 of propane-1,3-diyl by weaker bonds to less electronegative elements, for example silicon, should also favor formation of the (0,0) geometries of such diradicals by coupled rotation of the methylene groups in the ring-opening reactions of the corresponding cyclopropanes. The hyperconjugated resonance structure for 2,2-disilylpropane-1,3-diyl in Fig. 9 allows the prediction that ring-opening to form this diradical should be conrotatory.

**Fig. 9** Hyperconjugated resonance structure for 2,2-disilylpropane-1,3-diyl

To the extent that the hyperconjugated resonance structures, like that in Fig. 9, are important, it seems likely that 2,2-disilylcyclopentane-1,3-diyls should, like 2,2-difluorocyclopentane-1,3-dilyls, have singlet ground states. However, since disrotatory closure is expected to be an orbital-symmetry forbidden reaction in 2,2-disilylcyclopentane-1,3-diyls, unlike their difluoro-substituted counterparts, they should be kinetically stabilized against ring closure.

These qualitative predictions have already survived the tests of calculations performed at levels that are deemed to provide quantitatively accurate results.[46,47] It remains to be seen if, as predicted, geminal disilylcyclopropanes will be found experimentally to undergo stereomutation by coupled conrotation[46] and whether 2,2-disilylcyclopentane-1,3-diyls will be found to have singlet ground states and appreciable kinetic barriers to ring closure.[47]

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