Negative Ion Hyperconjugation and Its Relevance to the Mechanism of E1cB Reactions. An ab Initio Study

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Some time ago I proposed that E2 and E1cB(irrev) mechanisms could be distinguished by the observation of a leaving group isotope effect or element effect in the former but not in the latter case.[1] This argument assumes that there is no weakening of the bond to the leaving group in the rate-determining proton transfer of the E1cB reaction. If, however, there is negative ion hyperconjugation in the carbanion resulting from proton abstraction, such hyperconjugation might also weaken the bond to the leaving group in the proton-transfer transition state.[2] Qualitative MO arguments and Hartree−Fock calculations (most at rather low levels) suggest that negative ion hyperconjugation can be important in carbanions of the type Y−C−C$^-$, but no high-level ab initio calculations with correlation corrections are to be found in the literature.[3−8]

In order to address this problem, three fluorine-substituted ethyl carbanions, **1**−**3**, were examined at the

$CF_2HCH_2^-$ $CF_3CH_2^-$ CF_3CFH^-
1 **2** **3**

MP2/6-31+G*//MP2/6-31+G* level. Criteria for hyperconjugation were (1) the length of the C−F bond anti to the unshared pair in the carbanion vs the conjugate acid, Δ*R*, (2) the charge on the F anti to the unshared pair in the carbanion vs the conjugate acid, Δ*Q*, and (3) the $^{18}F/^{19}F$ EIE (equilibrium isotope effect) for the F anti to the unshared pair on ionization of the conjugate acid. Each of the three quantities was also calculated for the F gauche to the unshared pair so as to allow for inductive and other nondirectional effects. Table 1 gives the results.

All three criteria point to significant weakening of the anti C−F bond, and all are of lower magnitude for the gauche than for the anti fluorines, demonstrating the expected sensitivity to conformation. In addition, hyperconjugation is greatest where the least (**1**) and least where the most (**3**) inductive stabilization of the negative charge is expected. The large changes for **1** suggest it is best regarded as an ion−dipole complex between fluoride and fluoroethylene. The next step was to determine whether hyperconjugation is also important in the proton-transfer transition state leading to the carbanion.

Table 1. Changes in Fluorine Atoms on Ionization of Fluoroethanes to Carbanions

	carbanion		
quantity[a]	$^-CH_2CF_2H$	$^-CH_2CF_3$	$^-CHFCF_3$
ΔR_{CF}(anti)	1.4120	0.1536	0.0823
ΔR_{CF}(gauche)	0.0086	0.0327	0.0261[b]
ΔQ_F(anti)[c]	−0.5068	−0.1292	−0.0840
ΔQ_F(gauche)[c]	−0.0254	−0.0403	−0.0397[b]
$^{18}F/^{19}F$ EIE(anti)	1.0246	1.0152	1.0093
$^{18}F/^{19}F$ EIE(gauche)	1.0004	1.0040	1.0028[b]

[a] Value for the carbanion − value for the conjugate acid. [b] Average of values for the two nonequivalent gauche fluorines. [c] NPA (natural population analysis) charges.

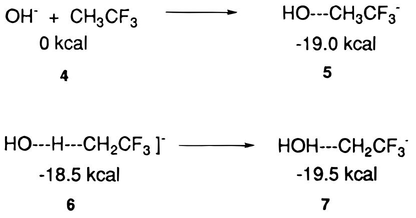

Figure 1. Stationary points in the deprotonation of 1,1,1-trifluoroethane by hydroxide ion with enthalpies relative to the reactants corrected for ZPE values and for contributions of the translational, rotational, and vibrational partition functions (frequencies scaled to 0.95).

Table 2. Isotope Effects at the Various Positions of 5−7 Relative to Reactant 4

	IE at 20 °C for species		
atom	**5**	**6**	**7**
F(anti)[a]	1.0026	1.0058	1.0102
F(gauche)[a]	1.0007	1.0022	1.0029
H(*β*-sec)[b]	1.0597	1.1462	1.2685
H(prim)[b]	1.1245	4.7076	1.1255
C(α)[c]	1.0073	1.0199	1.0334
C(*β*)[c]	1.0023	1.0158	1.0266

[a] $^{18}F/^{19}F$. [b] H/D. [c] $^{13}C/^{12}C$.

Stationary points in the reaction of hydroxide ion with 1,1,1-trifluoroethane were determined at the MP2/6-31+G*//MP2/6-31+G* level. Steps of the reaction through the proton transfer are shown in Figure 1. The product **7** is stable to elimination of a fluoride ion. In order to complete the elimination, it is necessary either to migrate the water molecule solvating the carbanion center to the anti fluorine or to introduce an additional water molecule solvating the anti fluorine. The ion−dipole complex resulting from elimination, CH_2=CF_2---FHOH$^-$, is at −19.0 kcal mol^{-1}, and the separated products, CH_2=CF_2 + FHOH$^-$, are at −14.0 kcal mol^{-1} relative to the reactants.

A full account of all the features of the reaction will be given in a paper to follow. For the present discussion, the relevant species are the ion−dipole complex **5**, proton transfer TS **6**,[9] and the proton-transfer product **7**. Calculated isotope effects at all positions of the species **5**−**7** relative to the separated reactants **4** are given in Table 2.

Isotope effects even in the ion−dipole complex **5** are not negligible but do not indicate serious bonding changes. The KIE's (kinetic isotope effects) for **6**, however, are quite substantial. The deuterium KIE for the anti proton indicates that it is close to half transferred in the TS,

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(9) A reviewer questions the reality of **6** in view of the small barrier. The potential energy barrier is 3.9 kcal and the imaginary frequency is 1187*i*, so there seems no room for doubt that it represents a real saddle point.

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Table 3. Isotope Effects at Various Positions in the anti-E2 Reaction between Hydroxide Ion and Ethyl Fluoride

	Level of IE at 20 °C	
atom	MP2/6-31+G*	MP2/6-311+G**
F[a]	1.0088	1.0072
H(α-sec)[b]	1.0512	1.0510
H(β-sec)[b]	1.1958	1.1821
H(prim)[b]	4.7114	4.5548
C(α)[c]	1.0184	1.0152
C(β)[c]	1.0188	1.0166

[a] $^{18}F/^{19}F$. [b] H/D. [c] $^{13}C/^{12}C$.

and the isotope effect for the anti fluorine is 55−60% of its value in the product **7**. To guide in the interpretation of the fluorine KIE's, it should be pointed out that the maximum KIE estimated for the cleavage of a C−F bond is 1.032 and the largest effect observed experimentally so far is below 1.03.[10,11] The carbon isotope effects for the CF_3 and the CH_3 carbons and the secondary deuterium isotope effect at the gauche hydrogen agree with the conclusion that all bond changes are a little more than half complete in **6**. This is the kind of transition structure one would expect for a *concerted* E2 but not for an E1cB mechanism!

In order to test this conclusion, KIE's in the E2 reaction between hydroxide and ethyl fluoride were calculated at MP2/6-31+G*//MP2/6-31+G* and MP2/6-311+G**//MP2/6-311+G** (Table 3).[12] Two points emerge clearly: (1) There is little qualitative difference between the KIE's in Table 3 and the corresponding KIE's in Table 2. Thus, both the E1cB and E2 reactions have similar E1cB-like transition states, with only a little more C−F cleavage in the latter than in the former. Fluorine KIE's in both reactions fall far short of the expected maximum values (*vide supra*). (2) The patterns of results at the two levels reported in Table 3 are essentially identical, the only difference being that MP2/6-311+G** gives slightly smaller values across the board. This evidence strongly suggests that MP2/6-31+G* is adequate to describe the features of both the E2 and E1cB reactions.

The E1cB reaction is clearly a stepwise reaction overall. At the same time, the proton removal step could be described as concerted in the sense that it occurs with bonding changes at both the α and β carbon atoms. There thus must be a spectrum of transition states in the proton transfer steps of E1cB reactions much like the spectrum of transition states we are accustomed to thinking of in E2 reactions. If a carbanion intermediate is well stabilized by inductive, resonance, or solvation effects, little or no weakening of the bond to the leaving group is expected in the TS for its formation. A relatively unstable carbanion, on the other hand, can arise *via* a TS that looks very much like an E2 TS. Along the spectrum of transition states, the TS thus begins to resemble an E2 TS well before the reaction goes over to the E2 mechanism. Such a spectrum is entirely consistent with the argument of Gandler and Jencks that the E1cB mechanism is transformed into the E2 mechanism when the carbanion intermediate becomes too unstable to exist and that this transformation occurs with very little change in transition state structure.[13]

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Supporting Information Available: A description of methods as well as potential energies in Hartrees and *Z*-matrices for key structures (6 pages).

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