Figure 2. Correlation between pair energy and cosphere diameter. Same code as Figure 1.

$$K_s = \alpha/(1 - \alpha) = \exp(-E_s/kT) \qquad (4)$$

where E_s is the energy difference between a pair in the states $r = a$ and $r = R$. Combining (3) and (4) gives for the overall pairing constant $K = (1 - \gamma)/c\gamma^2f^2$

$$K = K_R(1 + K_s) = K_R \exp(-E_s/kT) \qquad (5)$$

showing that K depends not only on D but also on the system-specific parameters R and E_s: $K = F(D,R,E_s)$.

Define $G(R,E_s)$, a surface in the (G, R, E_s) 3-space, by dividing out the term in K which depends on long-range Coulomb forces:

$$G = K \exp(-\beta/R) = (4\pi N R^3/3000) \exp(-E_s/kT) \quad (6)$$

The steps in the formation of contact pairs from $r = R$ pairs involve ion–solvent site interchanges; therefore E_s depends both on short-range ion–solvent interactions as well as on cation–anion interaction at $r = a$. The cosphere diameter R depends on dipole moment, polarizability, size and shape of solvent molecules, and ionic charge and size. For a given electrolyte, a plot of E_s/kT against R is the trace on the $G(R,E_s)$ surface of the part of K which depends on short range parameters characteristic of the solvent. Figure 2 is the $E_s/kT - R$ plot for potassium iodide in the various solvents listed in the caption of Figure 1. In contrast to Figure 1, where the K-D points are scattered over the plane, the points in Figure 2 cluster around a single curve. This correlation between the parameters E_s and R for such a variety of solvents suggests that (2) presents a realistic model for electrolytic solutions.

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Thermal Isomerization of 2,2-Difluoromethylenecyclopropane

Sir:

The effect of a fluorine substituent on the thermodynamic stability of a cyclopropane ring is not quantitatively well understood at present. Our earlier study of the geometrical isomerization of 1,1-difluoro-2,3-dimethylcyclopropane indicated that *gem*-difluoro substituents weaken cyclopropane to cleavage by ~9 kcal/mol.[1] However, the only previous work which shed light on the *overall* thermodynamic effect of fluorine on a cyclopropane ring was that of Oth and Merényi, who examined the NMR spectra of monosubstituted bullvalenes. They found that *all* substituents including fluorine prefer *not* to be cyclopropane bound in the bullvalene equilibrium.[2,3] Benson and O'Neal expressed their interpretation of the available thermochemical data in 1968 by suggesting that each fluorine substituent increases the strain of cyclopropane by ~5 kcal/mol.[4] This estimate is certainly consistent with our above-mentioned isomerization studies.

Hoffmann has examined the problem theoretically and predicted that all cyclopropane ring bonds would be weakened by fluorine substitution.[5] This prediction was brought into question by microwave spectral studies of 1,1-difluorocyclopropane which indicated that, while the C_2-C_3 bond was indeed substantially lengthened with respect to cyclopropane itself, the C_1-C_2 bonds were shortened and thus expected to be stronger.[6]

We would now like to present preliminary experimental kinetic and thermodynamic results on the thermal unimolecular isomerization of 2,2-difluoromethylenecyclopropane (**1**) to difluoromethylenecyclopropane (**2**). These results provide
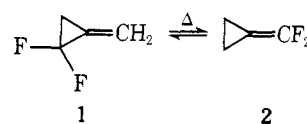
the first experimental support for Hoffmann's prediction that not only the bond opposite to the fluorine-substituted carbon, but also those adjacent to the substituted carbon itself, in this case the C_2-C_3 bond of **1**, are weakened. This study also provides the first quantitative evaluation of the relative thermodynamic stability of cyclopropane-bound fluorine vs. vinylic fluorine.

2,2-Difluoromethylenecyclopropane (**1**) was synthesized by the thermal decomposition of hexafluoropropylene oxide in the presence of an excess of allene.[7] It was characterized by an ^{1}H NMR spectrum (100 MHz, DCCl$_3$) (δ 1.84–2.06 (m, 2 H), 5.58–5.78 (m, 1 H), and 5.92–6.1 (m, 1 H)) and an ^{19}F NMR spectrum (100 MHz, DCCl$_3$) (δ 53.0 (m) (relative to TFA)). **1** was found to rearrange smoothly thermally to difluoromethylenecyclopropane (**2**) which was characterized by an ^{1}H NMR absorption of δ 1.28–1.52 (t, $J = 2$ Hz) and by a ^{19}F NMR absorption at δ 9.13 (p, $J = 4$ Hz). The reaction was found to follow good, reversible first-order kinetics. Equilibrium constants were obtained at six temperatures (see Table I), and a plot of ln K vs. $1/T$ yielded a ΔH for the isomerization of -1.9 ± 0.1 kcal/mol. Rate constants were also obtained at six temperatures (see Table II), and an Arrhenius plot of this data gave a good straight line with the frequency factor and energy of activation being calculated by the method of least squares.

$$\log A = 13.25 \pm 0.2 \qquad E_a = 38.3 \pm 0.4 \text{ kcal/mol}$$

2-Methylmethylenecyclopropane (**3**) has been shown to rearrange to ethylidenecyclopropane with log $A = 14.26$ and $E_a = 40.4$ kcal/mol,[9] 2,2-dimethylmethylenecyclopropane (**4**)

Table I. Equilibrium Constants for **1 ⇌ 2**

Temp, °C	193.4	201.7	209.7	217.9	226.5	235.5
K	6.04	5.89	5.63	5.48	5.32	5.10

Table II. Rate Constants for **1 → 2**

Temp, °C	193.4	201.7	209.7	217.9	226.5	235.5
$10^5 k_1$, s^{-1}	2.13	4.44	8.79	17.4	31.6	66.2

analogously rearranges with an estimated $E_a = 41.0$ kcal/mol (assuming $\log A = 14.26$),[10] and 2,2,3,3-tetradeuteriomethylenecyclopropane (**5**) undergoes degenerate isomerization with an estimated $E_a = 41.6$ kcal/mol.[11,12] It is thus apparent that the isomerization of **1** is *enhanced* substantially by the presence of the fluorine substituents. (Calculated relative rates of isomerization of **1, 3, 4,** and **5** at 210 °C are 3.8, 3.5, 2.3 and 1.0, respectively.) Much recent theoretical and experimental work on the structure of methylenecyclopropane and fluorinated cyclopropanes has appeared.[6,13-15] If the perturbation effects on cyclopropane of the fluorine substituents and of the methylene group are additive,[14] and it seems that they should be, then one would predict a *higher* activation energy for rearrangement of **1** than for methylenecyclopropane itself. The apparent incompatibility of our results with expectation (on the basis of the microwave data) might be able to be rationalized if a fluorine substituent were to stabilize a radical site.[16] However, that data which exists points neither to stabilization nor destabilization of a radical site by fluorine.[4,18] It does appear that the effect of fluorine substituents on a cyclopropane should not, thermochemically, be thought of as a simple "strain" effect,[4] since the various C–C bonds seem to be affected to different extents, with the opposite bond appearing to be more dramatically affected.

The preference of **2**, with vinylic CF_2 over **1** in the equilibrium was foreshadowed by the fluorobullvalene work.[2,3] The deleterious thermodynamic effect of fluorine on a vinylic site is fairly well documented. While tetrafluoroethylene is enhanced in its addition and dimerization reactions by ~16 kcal/mol[18,20] over those of ethylene, the heats of hydrogenation of trifluoroethylene and 1,1-difluoroethylene reflect smaller degrees of enhanced reactivity, i.e., 8 and 4 kcal/mol, respectively.[21] Butadiene–cyclobutene equilibria also indicate a nonlinear relationship between numbers of fluorine substituents and π-bond reactivity.[22,23]

Additional systematic equilibrium studies are needed to gain a firm quantitative insight into the incremental thermodynamic effect of fluorine substitution on double bonds. From our study we can unambiguously state that a vinylic *gem*-difluoro group is 1.9 kcal/mol more stable than a CF_2 group which is incorporated into a cyclopropane ring.

Interestingly, the analogous 2,2-dichloromethylenecyclopropane has been examined and shown to rearrange virtually quantitatively to dichloromethylenecyclopropane, indicating a much greater propensity for chlorine to exist in the vinylic position.[24] Uncertainties relating to both kinetic and thermodynamic effects of cyclopropyl-, vinyl-, and alkyl-bound fluorine still are prevalent. Further research is in progress to elucidate such effects.

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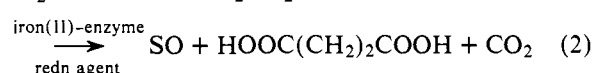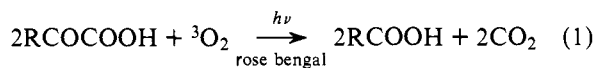*Department of Chemistry, University of Florida*
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Dioxygen Fixation. Oxene Transfer in the Reaction of Singlet Dioxygen with α-Keto Acids

Sir:

The mechanism of dioxygen activation in iron-containing oxygenases such as cytochrome P-450 has been discussed in terms of an oxenoid intermediate.[1-5] Some chemical systems function apparently as oxenoid oxygen transfer agents, notably pyridine N-oxide,[6] the oxidant from low temperature ozonation of alkynes,[7] and iodosobenzene.[8]

We report now that the $^1O_2$ oxidative decarboxylation of α-keto acids (eq 1)[9] proceeds via an intermediate which is capable of oxygen transfer to unsaturated substrates. This result also enables us to suggest a role for the hitherto unexplained function played by α-ketoglutarate in α-ketoglutarate dependent oxygenases[10,11] (eq 2).

$$2RCOCOOH + {}^3O_2 \xrightarrow[\text{rose bengal}]{h\nu} 2RCOOH + 2CO_2 \quad (1)$$

$$S + {}^3O_2 + HOOCCOCH_2CH_2COOH$$
$$\xrightarrow[\text{redn agent}]{\text{iron(II)-enzyme}} SO + HOOC(CH_2)_2COOH + CO_2 \quad (2)$$

A central point in the reaction presented in eq 1 is the role of dioxygen. It has been shown that α-ketoglutaric acid upon irradiation in the presence of methylene blue, but in the absence of dioxygen, undergoes decarboxylation.[12] Furthermore, the α-ketoglutaric acid can undergo photodecarboxylation.[13,22] Also superoxide anion-radical formation from the sensitizer may occur:

$$D + \text{sens} \rightarrow D_{ox} + \text{sens}^- \cdot \xrightarrow{O_2} O_2^- \cdot + \text{sens}$$
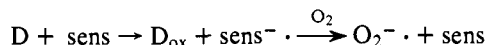
The basic question is whether the reaction in eq 1 is a reaction of singlet dioxygen. Accordingly we generated singlet dioxygen