

Thermal Rearrangements of *gem*-Difluorocyclopropanes

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Physical organic chemists have long taken advantage of the strain of small-ring hydrocarbons to study the mechanisms of various thermal carbon-carbon bond-breaking processes. The advantage of such systems is that *selectivity* of reaction is possible. In acyclic systems, however, much higher energies are required to induce C-C bond cleavage, with the result that *lack* of selectivity is generally the rule. Thus it has been within the context of thermal isomerization studies of small-ring systems that much of our insight into the nature of unimolecular homolytic processes has come. I would include reactions which are thought to involve sigmatropic or electrocyclic mechanisms within the definition of unimolecular homolytic processes as well as those reactions which proceed through diradical mechanisms. A general identifying feature of such "homolytic" reactions might be the lack of any polar characteristics. For example, the rates of such processes generally exhibit little, if any, solvent effects and proceed at about the same rate in the gas phase as in solution.

It is within the realm of such reactions that activation parameters are especially useful in understanding the effects of substituents on the mechanistic pathways which are involved.¹⁻³ For example, while the cleavage of a cyclopropane C-C bond requires an E_a of about 65 kcal/mol,⁴ attachment of a vinyl group to the ring allows the cleavage to occur with an E_a of 50 kcal/mol.⁵ This 15 kcal/mol incremental lowering of activation energy is entirely explainable in terms of transition-state allylic stabilization of the incipient diradical by the substituent.

As this example implies, the effect of substituents on the activation parameters for thermal rearrangements of cyclopropane and cyclobutane systems have, for the most part, been explained either in terms of that substituent's ability to stabilize (or destabilize) the incipient diradical intermediate (or the transition state for the concerted sigmatropic or electrocyclic process) or in terms of a steric effect of the substituent.

William R. Dolbier, Jr., received his B.S. degree from Stetson University and his Ph.D. with M. J. Goldstein at Cornell University in 1965. Following postdoctoral work with William Doering at Yale, he joined the faculty of the University of Florida where he is now Professor of Chemistry. His research interests center on the study of structure-reactivity relationships in thermal homolytic and pericyclic processes with an emphasis on the effect of fluorine as a substituent.

Ground-state effects, that is, effects of the substituent on the thermodynamic or kinetic stability of the starting material, have generally been considered to be relatively unimportant, and for the most part such interpretations of substituent effects have been entirely justified and have led to reasonable mechanistic conclusions. There have been attempts recently to predict and understand the thermodynamic effects of substituents on the ground state of cyclopropane, with the general conclusion being that most substituents should stabilize (i.e., diminish the strain) of a cyclopropane system.⁶ These effects are qualitatively the same as those for a substituent on ethylene but are generally less. Kinetic effects of these same substituents are much less well understood, with steric inhibition most often being invoked to explain discrepancies between thermodynamic and kinetic effects.

Fluorine as a Substituent

The effect of fluorine as a substituent is of particular interest because of its small size,⁷ and hence its lack of a significant steric effect, and because of its unique intrinsic character.⁸ The unusual properties of fluorine as a substituent derive largely from three factors. These factors are fluorine's high electronegativity, its three nonbonded electron pairs, and the fact that, as a second period element, its orbital dimensions are such that excellent overlap is possible, both in forming σ bonds and in π -conjugative interactions with contiguous carbon π systems.

The high electronegativity and effective orbital overlap combine to give rise to a very polar, very short

(1) Willcott, M. R. III; Cargle, R. L.; Sears, A. B. *Prog. Phys. Org. Chem.* **1972**, *9*, 25.

(2) Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley: New York, 1976.

(3) Benson, S. W.; O'Neal, H. E. "Kinetic Data on Gas Phase Unimolecular Reactions", *Natl. Stand. Ref. Data Series*, **1970**, NSRDS-NBS 21.

(4) Flowers, M. D.; Frey, H. M. *Proc. R. Soc. (London, Ser. A)* **1960**, *257*, 121.

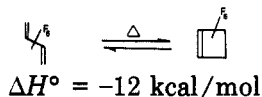
(5) (a) Flowers, M. D.; Frey, H. M. *J. Chem. Soc.* **1961**, 3547. (b) Wellington, C. A. *J. Phys. Chem.* **1962**, *66*, 1671.

(6) Dill, J. D.; Greenberg, A.; Liebman, J. F. *J. Am. Chem. Soc.* **1979**, *101*, 6814.

(7) Forster, H.; Vogtle, F. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 429.

(8) Chambers, R. D. "Fluorine in Organic Chemistry"; Wiley: New York, 1973.

C-F σ bond (1.317 relative to 1.766 for a C-Cl bond). Moreover, the bond strength of the C-F bond seems strongly dependent upon carbon's hybridization such that there is a significant thermodynamic advantage for fluorine to be bound to carbon orbitals with high p character (i.e., sp^3 orbitals). A prime example of this advantage is the modification of the cyclobutane-butadiene equilibrium, by substitution, F for H, so that the cyclobutene becomes the more stable component.⁹



This thermodynamic effect of the fluorine substituent has been rationalized as being a consequence of fluorine's high electronegativity (which should give rise to stronger bonds with less electronegative carbon orbitals) and fluorine's apparent ability to donate electrons to a conjugated π system (which would give rise to a "repulsive" antibonding interaction of fluorine's lone pairs with the π system).^{8,9} (In fact there is every indication that a *single* fluorine substituent actually stabilizes a π system¹⁰ but that geminal or vicinal difluoro substitution, or higher fluorine substitution, leads to rather large increments of thermodynamic destabilization.)¹¹

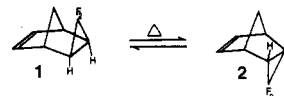
A particularly interesting consequence of fluorine's unique character as a substituent is its effect on a cyclopropane system. O'Neal and Benson were the first to comment on the unusual kinetic and thermodynamic consequences of fluorine substitution on cyclopropane.¹² While no heats of formation are available for fluorinated cyclopropanes, it was apparent from fragmentary early studies¹³ that increasing amounts of fluorine substituents on a cyclopropane ring gave rise to increasing ease of cleavage. From examination of the available data, O'Neal and Benson estimated that there is an increase of strain of 4.5–5 kcal/mol per fluorine substituent on a cyclopropane ring. They reasoned that the greater thermal reactivity of these compounds was a ground-state effect since they found no evidence of radical stabilization by fluorine substituents. Indeed, we also have obtained results which indicate that fluorine substituents provide no stabilization to a carbon radical.¹⁴

Hoffmann discussed the general effect of electron donor (and acceptor) substituents on the bond strengths of cyclopropane and concluded that a potent donor such as fluorine should weaken the bond *opposite* to the carbon bearing the substituent(s) (the C_2-C_3 bond), while the adjacent bonds should be strengthened.¹⁵ Gunter predicted a general weakening of bonds in the cyclopropane system with fluorine substitution.¹⁶ A structure determination of 1,1-difluorocyclopropane and recent theoretical calculations are consistent with Hoffmann's conclusion inasmuch as the C_1-C_2 bond is

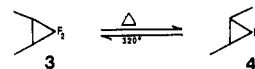
seen to be shortened (1.464 Å) and the C_2-C_3 bond lengthened (1.553 Å) relative to cyclopropane itself (1.514 Å).¹⁷

Cyclopropane Thermolyses

At the time we began our quantitative examination of the specific effects of geminal difluoro substitution on the thermal behavior of cyclopropane compounds, there had been only a small number of qualitative reports, all of which seemed to be consistent with a weakening of the C_2-C_3 bond.¹⁸ Perhaps the best example was the rapid thermal interconversion of *exo* and *endo* isomers 1 and 2 at 60 °C.^{18a}



The initial study in an effort to quantify such effects was that of the geometrical isomerization of *cis*-1,1-difluoro-2,3-dimethylcyclopropane (3).¹⁹ In order to



examine the kinetics of this and other fluorinated cyclopropane systems, it was necessary to overcome great surface effect problems. The gas-phase reactions were all carried out at 4–20 mm in well-conditioned Pyrex vessels immersed in a salt bath, the temperature of which was able to be controlled at ± 0.1 °C. In all cases the rate data at five to eight temperatures was converted, via an Arrhenius plot and least-squares treatment of the data, to the activation parameters which are presented in this Account.

A plot of the equilibrium constants for $3 \rightleftharpoons 4$ yielded a ΔH° of -0.72 ± 0.05 kcal (-3.0 kJ)/mol, which is not inconsistent with the observed -1.1 kcal (-4.6 kJ)/mol for the hydrocarbon system. The predicted longer C_2-C_3 bond in 3 and 4 would certainly diminish the interaction between the methyls in 3 and hence reduce the enthalpic difference between 3 and 4.

Of even greater significance was the modification of activation parameters induced by the presence of the geminal fluorine substituents. While Flowers and Frey had reported activation parameters [$\log A = 15.25$, $E_a = 59.4$ kcal (248.3 kJ)/mol] for the analogous hydrocarbon rearrangement,⁴ the conversion of $3 \rightarrow 4$ showed a significant diminution of activation energy [$\log A = 14.7 \pm 0.2$ and $E_a = 49.7 \pm 0.6$ kcal (207.7 kJ)/mol]. This amounts to a $\Delta\Delta G^\ddagger$ of -8.2 kcal/mol, with 3 isomerizing 1073 times faster than its hydrocarbon counterpart at 320 °C. This result, of course, is consistent with O'Neal and Benson's approximation of the increase in strain which would be expected for two fluorine substituents. However, it will be apparent as we discuss more and more systems that the incremental lowering of E_a for the rearrangement of 3 cannot be thought of as due to a "general" increase of strain, but rather seems to be indicative of a *specific* weakening of the opposite C_2-C_3 bond as predicted by Hoffmann and as foresha-

(17) (a) Perretta, A. T.; Laurie, V. W. *J. Chem. Phys.* 1975, 62, 2469. (b) Deakyns, C. A.; Allen, L. C.; Craig, N. C. *J. Am. Chem. Soc.* 1977, 99, 3895. (c) Durmaz, S.; Kollmar, H. *Ibid.* 1980, 102, 6942.

(18) (a) Jefford, C. W.; Mareda, J.; Gehret, J. C. E.; Karbengele, T.; Graham, W. D.; Gruger, U. *J. Am. Chem. Soc.* 1976, 98, 2585. (b) Sargeant, P. B. *Ibid.* 1969, 91, 3061.

(19) Dolbier, W. R., Jr.; Enoch, H. O. *J. Am. Chem. Soc.* 1977, 99, 4532.

(9) Schlag, E. W.; Peatmen, W. B. *J. Am. Chem. Soc.* 1964, 86, 1676.

(10) Abell, P. L.; Adolf, P. K. *J. Chem. Thermodyn.* 1969, 1, 333.

(11) For example, the Cope rearrangement of 1,1-difluoro-1,5-hexadiene to 3,3-difluoro-1,5-hexadiene has $\Delta G^\circ = -5$ kcal/mol. Dolbier, W. R., Jr.; Medinger, K., unpublished results.

(12) O'Neal, H. E.; Benson, S. W. *J. Phys. Chem.* 1968, 72, 1866.

(13) Mitsch, R. A.; Neuvar, E. W. *J. Phys. Chem.* 1966, 70, 546.

(14) Dolbier, W. R., Jr.; Piedrahita, C. A.; Al-Sader, B. H. *Tetrahedron Lett.* 1979, 2957.

(15) (a) Hoffmann, R.; Stohrer, W. P. *J. Am. Chem. Soc.* 1971, 93, 6941. (b) Hoffman, R. *Tetrahedron Lett.* 1970, 2907.

(16) Gunter, H. *Tetrahedron Lett.* 1970, 5173.

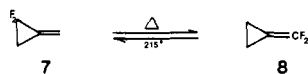
dowed by the earlier qualitative studies and the structure determination.

Observed to compete with the geometrical isomerization was a process which has proved to be a chronic parallel reaction in most thermal studies of fluorine-substituted cyclopropanes, that of CF_2 extrusion. While few kinetic studies have been reported, the extrusion of CF_2 from polyfluorocyclopropanes is a well-known reaction. It has been demonstrated that increasing the number of fluorine substituents on a cyclopropane will give rise to *dramatic* increases in rate for CF_2 extrusion. Table I summarizes the kinetic data that are available for this process.^{20,21,22}

In view of the reactivity of **5**, it is not surprising that CF_2 extrusion from **3** was not a major competing pathway, with $k_{\text{isom}}/k_{\text{extr}} = 21.3$ at 297.3 °C and 15.6 at 344.9 °C. **3**, however, did extrude CF_2 significantly faster than **5** at 320 °C, with $k_3/k_5 \approx 55$. The presence of the two methyl groups must therefore facilitate loss of CF_2 .

Methylenecyclopropane Rearrangements

In order to probe unambiguously the effect of a CF_2 group on the ability to cleave an *adjacent* C-C bond, the thermal rearrangement of 2,2-difluoromethylene-cyclopropane (**7**) was investigated.²³ Activation pa-



rameters were determined ($\log A = 13.25$ and $E_a = 38.3$ kcal (160 kJ)/mol), with the result being that the cleavage of the adjacent ($\text{C}_2\text{-C}_3$) bond is enhanced *only slightly* by the presence of the CF_2 groups. At 210 °C, **7** rearranges at a rate only 3.8 times faster than the hydrocarbon and at about the same rate as 2-methylmethylene-cyclopropane.^{24,25} Assuming that trimethylenemethane species **9** is an intermediate in this rearrangement, a lower limit for adjacent bond weakening ($\Delta\Delta G^\ddagger = -1.2$ kcal/mol) can be assigned.

Thus it would appear that the incremental "strain" of the system due to the geminal fluorine substituents and as evidenced by kinetic data on the cleavage of the cyclopropane ring cannot be described as simple thermodynamic *strain* in the usual sense. It is apparent that the kinetic effect of the CF_2 group is *much greater* on the opposite bond than it is on the adjacent bond. It should be mentioned that in view of the fact that the $\text{C}_2\text{-C}_3$ bond of **7** should be shorter than that of the hydrocarbon, it is interesting that the shorter bond of **7** is nevertheless slightly weaker.

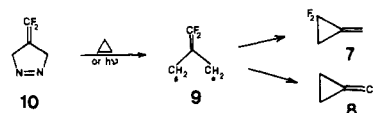
Regarding the *thermodynamic* effect of the CF_2 group, the magnitude of the equilibrium constant for $7 \rightleftharpoons 8$ is of some significance. It is generally accepted, though on rather skimpy evidence, that a vinylic CF_2 group gives rise to inherent destabilization of the olefinic system.¹⁰ We have accumulated much thermo-

Table I
 CF_2 Extrusion Reaction

cyclopropane	$\log A$	E_a , kcal (kJ)/mol	ref
1,1-difluoro-cyclopropane (5)	14.1	56.4 (236)	20
1,1,2-trifluoro-cyclopropane	14.4	50.5 (211)	20
1,1,2,2-tetrafluoro-cyclopropane (6)	15.3	48.5 (203)	20
perfluorocyclopropane	13.25	38.6 (161)	21
2-trifluoromethyl-1,1,2-trifluorocyclopropane	15.2	50.6 (212)	22

dynamic data on the effect of increasing numbers of fluorine substituents on the relative stability of an olefinic system, and there appears to be a destabilization of ~ 5 kcal (~ 21 kJ)/mol for a 1,1-difluorovinyl system.¹¹ Generally, in practice as well as theoretically, substituent effects are similar but greater for vinyl in comparison to cyclopropyl systems.⁶ Thus one would have expected **7** to be *more* stable than **8**. However, although **7** is preferred statistically 2:1 over **8**, the equilibrium lies significantly in favor of **8** with $K \approx 6.0$ at 193.4 °C and 5.1 at 235.5 °C. This amounts to a ΔH° of -1.9 kcal (-7.9 kJ)/mol. Thus geminal fluorine substituents give rise to a substantial thermodynamic destabilization of cyclopropane which is totally unpredictable in terms of what has been published regarding substituent effects in vinyl and cyclopropyl systems. It however *was* predictable on the basis of O'Neal and Benson's estimate of ~ 5 kcal/mol incremental strain per F substituent. In fact, assuming **8** to be destabilized by ~ 5 kcal/mol, one can estimate (by using the ΔH° value) that **7** is ~ 7 kcal/mol more strained than its hydrocarbon counterpart.

Since it is assumed that the interconversion of **7** to **8** proceeds via the difluorotrimethylenemethane diradical (**9**), it was of interest to compare the ratio of **7/8**



obtained when independently generated **9** was allowed to cyclize under completely *kinetically controlled* conditions. When pyrazoline **10** was induced, either thermally or photochemically in solution, to extrude N_2 , **7** and **8** were obtained in almost exactly a statistical ratio of 2:1, in contrast to the thermodynamic preference of **8**.²⁶ Thus it is safe to conclude that the cyclization transition state for $9 \rightarrow 7 + 8$ must not have enough product character to be influenced by the differences in stability of **7** and **8**.

Spiropentane Rearrangements

Another system ideally suited to probe the effect of a CF_2 group on the cleavage of the adjacent C-C bond is the 1,1-difluorospiro-pentane system. The parent hydrocarbon has been shown to rearrange to methylenecyclobutane via initial peripheral $\text{C}_1\text{-C}_2$ bond cleavage.²⁷ Therefore, 1,1-difluorospiro-pentane (**11**) might

(20) Herbert, F. P.; Kerr, J. A.; Trotman-Dickenson, A. F. *J. Chem. Soc.* 1965, 5710.

(21) Atkinson, B.; McKeagan, D. *Chem. Commun.* 1966, 189.

(22) Quero, E. D.; Ferrero, J. C.; Staricco, E. H. *Int. J. Chem. Kinet.* 1977, 9, 339.

(23) Dolbier, W. R. Jr.; Fielder, T. H., Jr. *J. Am. Chem. Soc.* 1978, 100, 5577.

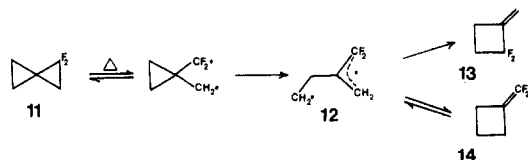
(24) Chesick, J. P. *J. Am. Chem. Soc.* 1963, 85, 2720.

(25) Slafer, W. D.; English, A. D.; Harris, D. O.; Shellhamer, D. F.; Meshishned, M. J.; Aue, D. H. *J. Am. Chem. Soc.* 1975, 97, 6638.

(26) Dolbier, W. R. Jr.; Burkholder, C. R., unpublished results.

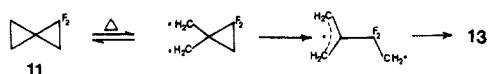
(27) (a) Gajewski, J. J. *J. Am. Chem. Soc.* 1972, 92, 3688. (b) Gilbert, J. C. *Tetrahedron* 1969, 25, 1459.

be expected to rearrange via cleavage of its C₁-C₂ bond. mechanism a



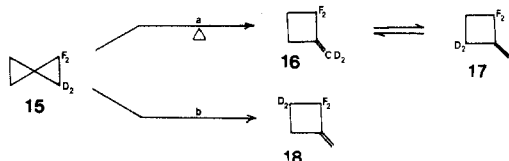
Indeed 11 *did* rearrange regioselectively to 2,2-difluoromethylenecyclobutane (13) and 1-(difluoromethylene)cyclobutane (14) (in a 9:1 ratio) in >85% yield.²⁸ The minor product 14 was found to itself rearrange rapidly under the reaction conditions to the major product 13. Conversion of 11 occurred with activation parameters ($\log A = 16.1$, $E_a = 58.0$ kcal (242 kJ)/mol) very similar to those observed for the rearrangement of spiro-pentane itself ($\log A = 15.9$, $E_a = 57.6$ kcal (241 kJ)/mol).²⁹

The regioselectivity is entirely consistent with either the mechanism depicted above (a) or that below (b). In mechanism a one would expect diradical 12 to cyclize preferentially to the product 13 with the more stable sp³-hybridized CF₂ group,³⁰ while in mechanism b one mechanism b



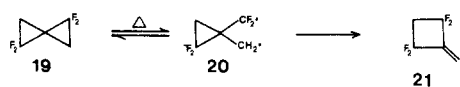
would expect the weaker C₂-C₃ bond opposite mechanism b to the CF₂ group to migrate preferentially. With the thermolysis of 11 proceeding only 1.2 times as fast as that of spiro-pentane (at 340 °C), one sees that the fluorine substituents exert little kinetic influence on the rearrangement. Hence mechanisms a and b should be competitive.

It was possible to evaluate the relative importance of the two mechanisms by examination of the thermal isomerization of the labeled species 15. Product 16 was



found to have equilibrated with 17 under the reaction conditions, and the ratio of products (16 + 17)/18 = 3:1 indicated that mechanisms a and b were indeed competitive.²⁸

Additional insight into the spiro-pentane-methylenecyclobutane conversion mechanism was provided by our investigation of tetrafluorospiro-pentane (19).³¹

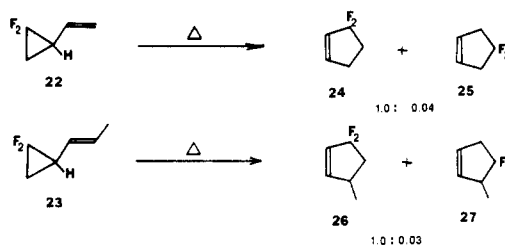


1,1,4,4-Tetrafluorospiro-pentane (19) has two identical cyclopropane rings. Hence there is no ambiguity as to which ring will cleave (as there is for 11). The reaction

again proceeds regioselectively to a single methylenecyclobutane product, 21. In this case there is a significant rate enhancement derived from the presence of the second CF₂ group. 19, with activation parameters $\log A = 14.8$, $E_a = 51.7$ kcal (216 kJ)/mol, rearranges at a rate ~10 times as fast as that of 13. This modest, but significant, rate enhancement is entirely consistent with our proposed mechanism for conversion of 19 to 21 with a preequilibrium formation of the diradical 20 followed by the kinetically significant ring expansion to 21. It is the rate of the ring-expansion step which is, of course, enhanced by the presence of the *second* CF₂ group at the 4-position. Again the regioselectivity of the reaction merely requires initial C₁-C₂ cleavage followed by ring expansion of the *weaker* C₃-C₅ bond to the CF₂ terminus.

Vinylcyclopropane Rearrangement

The thermal isomerizations of 2,2-difluorovinylcyclopropane (22)^{32a} and 2,2-difluoro-(*trans*-1-propenyl)cyclopropane (23)^{32b} both show substantial

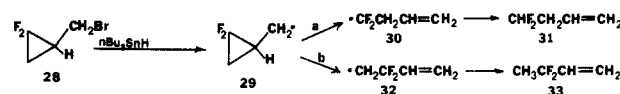


rate enhancement ($\log A = 13.7$ and $E_a = 40.3$ kcal (168 kJ)/mol for 22 and $(k_{23}/k_{22})_{200.6\text{ }^\circ\text{C}} = 2.5$), and the product distributions in each case are entirely consistent with a diradical mechanism involving preferential cleavage of the C₁-C₃ bond. The magnitude of the rate enhancement for rearrangement of 22 ($\Delta\Delta G^\ddagger = 9.6$ kcal/mol) is consistent with the earlier determination¹⁹ of the effect of *gem*-difluoro substitution on *opposite* bond cleavage of cyclopropane.

The results presented above for the pyrolysis of 22 constitute a *correction* of the original report which, because of a product isolation problem whereby 24 completely polymerized prior to spectroscopic analysis, claimed 25 to be the exclusive product.

Cyclopropylcarbinyl-Allylcarbinyl Rearrangement

Also related to the problem of the relative ease of opposite vs. adjacent bond cleavage was our study of the cyclopropylcarbinyl-allylcarbinyl radical rearrangement of the 2,2-difluorocyclopropylcarbinyl radical (29).³² Only process b, involving opposite bond



cleavage and leading exclusively to product 33, was observed. This regioselectivity of cleavage of radical

(28) Dolbier, W. R., Jr.; Al-Sader, B. H.; Sellers, S. F.; Elsheimer, S. *J. Am. Chem. Soc.* 1981, 103, 715.

(29) Flowers, M. C.; Frey, H. M. *J. Chem. Soc.* 1961, 5550.

(30) Dolbier, W. R., Jr.; Piedrahita, C. A.; Houk, K. N.; Strosier, R. W.; Gandour, R. W. *Tetrahedron Lett.* 1978, 2231.

(31) Dolbier, W. R., Jr.; Sellers, S. F.; Al-Sader, B. H.; Fielder, T. H., Jr. *J. Am. Chem. Soc.* 1981, 103, 717.

(32) (a) Dolbier, W. R., Jr.; Al-Sader, B. H.; Sellers, S. F.; Koroniak, H. *J. Am. Chem. Soc.* 1981, 103, 2138. (b) Dolbier, W. R., Jr.; Sellers, S. F. *J. Am. Chem. Soc.* 1981, submitted for publication.

29 provides further clear and unambiguous corroboration of the fact that the CF_2 group preferentially enhanced homolytic cleavage of the opposite bond.

Tetrafluorocyclopropane Systems

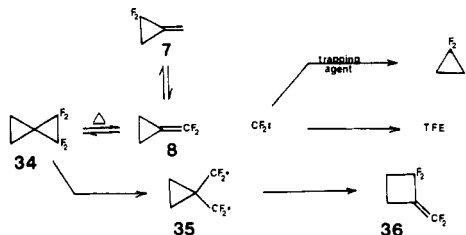
Related to the rearrangements of the difluorocyclopropanes, methylenecyclopropanes and spiropentanes are rearrangements of these same systems with two CF_2 groups in a single ring (6). A structure calculation for



6 indicated that the $\text{C}_1\text{-C}_2$ bond length should be shortened to 1.47 Å (compared to 1.514 Å for cyclopropane),³³ and there is some evidence that contiguous CF_2 groups in cyclobutanes or in nonstrained systems give rise to an especially strong C-C bond. There is, however, no way to predict the kinetic effect of two CF_2 groups in a cyclopropane ring. One can estimate, using O'Neal and Benson's criteria, that there should be an increment in strain of 18–20 kcal (75–84 kJ)/mol for 6.

In fact 6 extrudes CF_2 with activation parameters ($\log A = 15.3$, $E_a = 48.5$ kcal (203 kJ)/mol)²⁰ which are consistent with O'Neal and Benson's predictions. 6 extrudes CF_2 at a rate 1.7×10^4 times faster than that of 1,1-difluorocyclopropane (5) at 260 °C; this converts to a $\Delta\Delta G^\ddagger$ of -11.1 kcal/mol. The CF_2 extrusion reaction seems to be the only unimolecular process of 6. Since the extrusion process is likely a concerted process, the thermolysis of 6 gives us no real information about the homolytic cleavage of the $\text{CF}_2\text{-CF}_2$ bond.

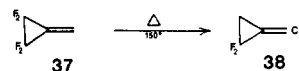
A system which does give such information is the thermal rearrangement of 1,1,2,2-tetrafluorospiro-pentane (34).³¹ While CF_2 extrusion is a major de-



composition pathway for 34, a substantial fraction (40%) of the reaction proceeds via rearrangement. The single rearrangement product, 36, is consistent with expectation if diradical 35 is the initially formed intermediate. Of even greater interest, however, is the greatly enhanced rate of rearrangement of 34 in comparison to that of difluorospiro-pentane (11) ($k_{34}/k_{11} = 140$ at 340 °C). A determination of activation parameters ($\log A = 13.75$, $E_a = 45.4$ kcal (190 kJ)/mol) indicates that this rate enhancement amounts to a $\Delta\Delta G^\ddagger = 6.0$ kcal/mol. There is no doubt, therefore, that the presence of two CF_2 groups in a cyclopropane ring gives rise to a very substantial weakening of that adjacent bond between them. In view of the probable bond shortening effect of these CF_2 groups, it would certainly appear that for fluorinated cyclopropanes bond length and bond strength are not correlatable in the sense that one has generally assumed them to be.

The rate of CF_2 extrusion ($\log A = 15.2$, $E_a = 48.6$ kcal (203 kJ)/mol) is close to that which one would expect for a tetrafluorocyclopropyl system. 34 does, in fact, extrude CF_2 at a rate nearly identical (a factor of 0.80) to that of 6 at 260 °C. The remarkable incremental kinetic destabilization exerted by the second CF_2 group can perhaps be best understood by invoking the same kind of destabilizing effect of multiple fluorine substituents on cyclopropane as they have on olefins. It is well-known that for olefins, the addition of fluorine substituents to ethylene leads to nonadditive destabilization effects. (Vinylidene fluoride and tetrafluoroethylene are estimated to be more strained than ethylene by 4 and 16 kcal/mol, respectively.)³⁴ Thus 6 and 34 might well be thought of as tetrafluoroethylene-type species.

Consistent with these conclusions as to the effect of a second CF_2 group were the results of the thermolysis of 2,2,3,3-tetrafluoromethylenecyclopropane (37).³⁵



Again the activation parameters ($\log A = 12.6$, $E_a = 29.6$ kcal (124 kJ)/mol) showed a great rate enhancement due to the second CF_2 group ($k_{37}/k_7 = 7850$ at 150 °C). The $\Delta\Delta G^\ddagger$ of -7.4 kcal/mol is not inconsistent with the 6 kcal/mol increment for the rearrangement of 34.

Because of the expected equilibrium between 37 and 38, one also was able to impute the thermodynamic effect of two CF_2 groups on the stability of 37. The fact that no 37 could be detected in equilibrium with 38 while 7 was present to the extent of 16% in equilibrium with 8 pointed to a sizable incremental thermodynamic destabilization due to the second CF_2 group. By making the reasonable assumption that the cyclopropane ring strains of 38 and 7 should be approximately the same, one can then estimate their rates of rearrangement to be the same. Thus one can estimate an equilibrium constant of 7850 for $37 \rightarrow 38$ and a $\Delta G^\circ \approx -7.5$ kcal/mol.

It again is instructive to relate these results to the ethylene-vinylidene fluoride-TFE analogy. 37 is a TFE-type molecule expected to have ~18–20 kcal/mol of "O'Neal-Benson" strain, while 38 should have 9–10 kcal/mol of such strain plus 4 kcal/mol of vinylidene fluoride strain, a total of 13–14 kcal of strain. Such an analysis predicts a ΔH° of -6–7 kcal/mol, a value nicely consistent with the facts. The very low E_a of this rearrangement, of course, precludes CF_2 extrusion from being a competitive process in the thermolysis of 37.

Conclusion

At this point in our research many general conclusions, which can be substantiated by multiple experiments, are beginning to take shape. First of all a pair of geminal fluorine substituents on cyclopropane give rise to an apparent substantial thermodynamic increase in strain in the system. The kinetic effects of the 9–10 kcal of incremental strain seem to derive largely from

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a weakening of that C-C bond which is *opposite* to the CF₂ group, while the strengths of the bonds adjacent to the CF₂ group are affected only minimally. The incorporation of a *second* pair of geminal fluorine substituents into the cyclopropane ring gives rise to a dramatic weakening of the bond *between* the two CF₂ groups.

The specific effects of geminal fluorine substituents on the thermodynamic stability and the kinetic reactivity of cyclopropane compounds as described in this

review are dramatic and completely unprecedented. A complete understanding of these effects must await further experimentation as well as careful theoretical examination.

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