measured rate constants place the rate of micellar exit in the time domain of the slow decay for micellized triplet radical pairs.

Acknowledgment. We thank the National Science Foundation for its generous support of this research. M.B.Z. thanks the National Science Foundation for a predoctoral research fellowship. Invaluable advice and aid from Dr. C. E. Doubleday, Jr., and Dr. E. V. Sitzmann are gratefully acknowledged.

Thermal Isomerizations of 2,2,3,3-Tetrafluorobicyclopentanes. The Kinetic Effect of Fluorine Substituents on Cyclobutane Bond Homolysis

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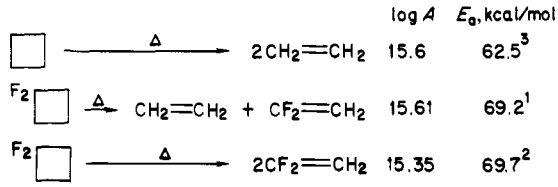
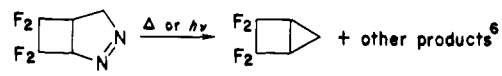
Received June 9, 1983

In 1980 Frey examined the thermal fragmentation reactions of 1,1-difluorocyclobutane and 1,1,2,2-tetrafluorocyclobutane, demonstrating that these fragmentations were significantly inhibited by the presence of the fluorine substituents.[1,2] It was not



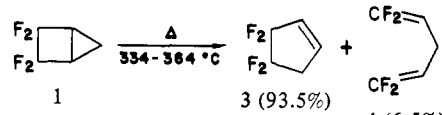
possible, however to dissect unambiguously from these results the relative ease of breaking the CH_2–CH_2 bond of each of these molecules. In view of the fact that the strength of CH_2–CH_2 bonds in cyclopropane can be drastically affected by geminal difluoro substitution, we were interested to determine if similar effects might be present in cyclobutane systems. It is well-known that perfluorocyclobutane is very much stabilized to fragmentation (E_a = 74.2 kcal/mol)[5], and as seen above in the difluoro and tetrafluoro cases, fluorine substitution definitely stablizes the cyclobutane ring to *overall* fragmentation.

The system with which we have initially tested such effects is the 2,2,3,3-tetrafluorobicyclo[2.1.0]pentane system, the parent (**1**) of which was synthesized by the thermal or photochemical deazetation of pyrazoline **2**.[6]



2 1 (Δ, 18%; *hν*, 32%)

Thermal isomerization of **1** to 3,3,4,4-tetrafluorocyclopentene (**3**) in the gas phase (10–30 torr) proceeded smoothly, following



1 3 (93.5%) 4 (6.5%)

excellent first-order kinetics with only a small amount of competitive fragmentation of **4** being observed. The Arrhenius equation was obtained by the method of least squares from a plot of the rate data in Table I: $\log k/s^{-1} = 14.9 \pm 0.4 - (54.2 \pm 1.1$ kcal/mol)$/RT \ln 10$.

Table I. Rates of Thermal Isomerization of 1 to 3

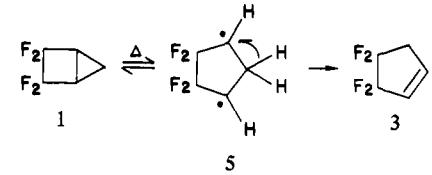
T (±0.1), °C	10^5k, s^{-1}
334.5	2.46 ± 0.01
340.0	3.95 ± 0.02
346.0	6.01 ± 0.04
352.0	8.50 ± 0.05
358.0	16.6 ± 0.2
364.5	20.9 ± 0.1

Table II. Rates of Thermal Interconversion of 6 and 7

T (±0.1), °C	10^5k_1	10^5k_{-1}
209.0	3.33	0.171
217.0	6.65	0.368
223.5	10.40	0.575
230.5	20.07	1.14
236.5	30.55	1.79
243.0	49.56	3.004

If one compares the activation parameters for conversion of **1** to **3** with those for the analogous rearrangement of the hydrocarbon system (log A = 14.6, E_a = 46.6 kcal/mol), one can see that the rearrangement of **1** is significantly inhibited (ΔE_a = 7.6 kcal/mol) relative to the hydrocarbon rearrangement.

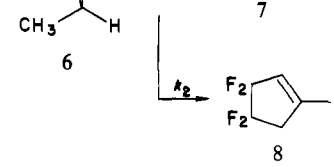
The mechanism of the rearrangement of **1** is presumed to proceed via the intermediacy of the 4,4,5,5-tetrafluorocyclopentane-1,3-diyl species (**5**).[9] A significant remaining question



1 5 3

then is whether the observed increase in activation energy is due to an increase in the C_1–C_4 bond-dissociation energy of **1** or whether it is due to a decrease in the rate of the subsequent 1,2-hydrogen shift process of diyl intermediate **5**.

In order to answer that question, the *endo*- and *exo*-5-methyl-2,2,3,3-tetrafluorobicyclo[2.1.0]pentanes **6** and **7** were



6 7 8

k_2(358.0°) = 2.68 × 10^{-4}
k(relative to 1) = 1.97

synthesized in a manner analogous to **1**, and their thermal in-

(1) Conlin, R. T.; Frey, H. M. *J. Chem. Soc., Faraday Trans. 1*, 1979, *75*, 2556.
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(8) (a) Halberstadt, M. L.; Chesick, J. P. *J. Am. Chem. Soc.* **1962**, *84*, 2688. (b) Steel, C.; Zand, C.; Hurwitz, P.; Cohen, S. G. *Ibid.* **1964**, *86*, 679.
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(10) NMR spectra (300 MHz) of **6**: ^{1}H δ 1.38 (d, J_{HH} = 6.8 Hz, 3 H), 1.76 (m, J_{HH}) = 6.9, 7.0, J_{HF} = 2.3 Hz, 1 H), 2.52 (m, J_{HH} = 7.0, J_{HF} = 9.7, 3.7 Hz, 2 H); ^{19}F ϕ 111.5 (midpoint of AB, J_{AB} = 216.1 Hz, $\Delta\nu$ = 4726.0 Hz); ^{13}C δ 11.49 (s, CH_3), 19.35 (t, J_{CF} = 3.85 Hz, C_5H), 28.18 (d, J_{CF} = 32.5 Hz, C_1H), 114.95 (t, J_{CF} = 264.15 Hz, CF_2).
(11) NMR spectra (300 MHz) of **7**: ^{1}H δ 1.1(d of t, J_{HH} = 6.2, 1.13, J_{HF} = 1.15 Hz, 3 H), 1.68 (quartet, J_{HH} = 6.3, 1.5, J_{HF} = 0.8 Hz, 1 H), 2.32 (dtd, J_{HF} = 11.8, 3.8, J_{HH} = 1.5 Hz, 2 H); ^{19}F ϕ 116.3 (midpoint of AB, J_{AB} = 210.1 Hz, $\Delta\nu$ = 4438.5 Hz, downfield F's, d, J_{FH} = 11.9 Hz); ^{13}C δ 13.86 (s, CH_3), 15.49 (t, J_{CF} = 2.7 Hz, C_5H), 29.50 (t, J_{CF} = 31.4 Hz, C_1H), 115.17 (t, J_{CF} = 274.94 Hz, CF_2).

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terconversion was examined kinetically. Equilibrium data were obtained at eight temperatures: 217.0 (18.83), 223.5 (17.99), 230.0 (17.30), 236.25 (17.06), 243.0 (16.47), 250.0 (16.08), 257.0 (15.60), and 262.5 °C (15.11), and their rates of interconversion were obtained at six temperatures (Table II).

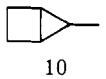
A van't Hoff plot of the equilibrium data gave a $\Delta H° = 2.38$ kcal/mol and $\Delta S = 0.95$ eu, while the Arrhenius plots of rates gave the least-squares analyses:

$$\log k_1/s^{-1} = 13.4 \pm 0.3 - (39.4 \pm 0.8 \text{ kcal/mol})/[RT \ln 10]$$

$$\log k_{-1}/s^{-1} = 13.2 \pm 0.3 - (41.8 \pm 0.8 \text{ kcal/mol})/[RT \ln 10]$$

Chesick[12] and Baldwin[13] obtained activation parameters for endo → exo isomerizations of similar hydrocarbon systems **9** and **10**. A comparison of these data with ours for **6** ⇌ **7** clearly

9



10

$\log A = 14.4$	$\log A = 15.0$
$E_a = 39.15 \pm 0.8$ kcal/mol	$E_a = 39.2 \pm 0.1$ kcal/mol

indicates that differences in activation energies for endo–exo interconversion for the three systems are insignificant. Thus it would appear that the presence of the four fluorine substituents in **6** has little effect upon the C_1–C_4 bond dissociation energy.

A necessary corrollary of such a conclusion is that the observed inhibition of cyclopentene formation observed in the isomerization of **1** must derive from an inhibition of the 1,2-hydrogen shift process of the intermediate 4,4,5,5-tetrafluorobicyclo[2.1.0]pentane-1,3-diyl species (**5**). The source of this unexpected inhibition is presently under further investigation.

Acknowledgment. The authors acknowledge with thanks the support of this research in part by the National Science Foundation.

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Dominance of the Proximity Effect of Complexation over Resonance and Inductive Effects in Directing a Metalation: Regiospecific β Lithiation of *N,N*-Diisopropylcyclohex-3-enecarboxamide and of *N,N*-Diisopropyl-2-methylpent-4-enecarboxamide

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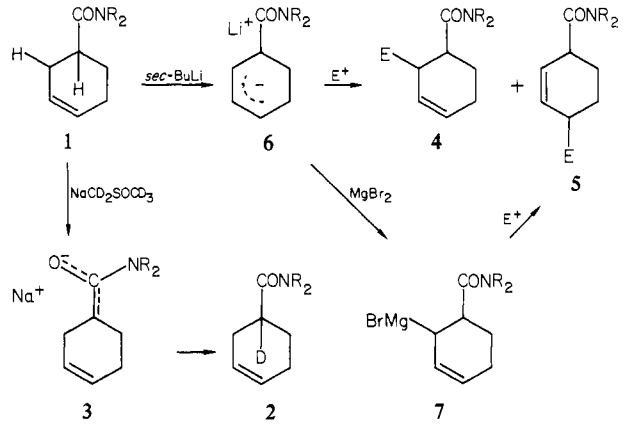
Received July 5, 1983

Complexation between a metal atom of a reagent and a functional group of a substrate usually reinforces that group's effects in subsequent chemistry. For example, recent evidence that association between a carbonyl oxygen and the lithium of an organolithium base is involved in the formation of enolates from ketones[1] and of dipole stabilized carbanions from amides[2] and formamidines[3] can be taken to suggest that resonance, inductive, and proximity effects, enhanced by complexation, are important factors in the deprotonation.[4,5] In most cases these effects are complementary and not separable. We now wish to report cases which suggest that the effect of proximity can dominate over resonance and inductive effects in directing deprotonation by a carbonyl group complexed to an organolithium.

Scheme I



1 6 4 5 3 2 7

Table I. Lithiation and Substitution of *N,N*-Diisopropylcyclohex-3-enecarboxamide (1)

reactant	electrophile	E	4[a]	5[a]
6	CH_3I	CH_3	53	18
7	CH_3I	CH_3		95
6	$(CH_3)_2CO$	$(CH_3)_2COH$	14	57
7	$(CH_3)_2CO$	$(CH_3)_2COH$		90
6	$(CH_3)_3SiCl$	$(CH_3)_3Si$	34	13
7	$(CH_3)_3SiCl$	$(CH_3)_3Si$		58
6	CH_2=$CHCH_2Br$	CH_2=$CHCH_2$	94	
7	CH_2=$CHCH_2Br$	CH_2=$CHCH_2$	18	72
6	n-$C_5H_{11}I$	n-C_5H_{11}	64	28
7	n-$C_5H_{11}I$	n-C_5H_{11}	23	68
6	D_2O	D (96% d_1)		29
7	D_2O	D (93% d_1)		94

[a] % yields of isolated analytically pure material. [b] 1.5 equiv of $MgBr_2$ in ether was added and the solution allowed to warm to ambient temperature and recooled to −78 °C before electrophile was added.

Treatment of *N,N*-diisopropylcyclohex-3-enecarboxamide (**1**) with sodium dimsylate in dimethyl-d_6 sulfoxide gives the 1-deutero isomer **2** via the expected enolate **3**. However, treatment of **1** with 1.1 equiv. of *sec*-butyllithium/tetramethylenediamine in tetrahydrofuran at −78 °C for 1 h followed by quenching with a number of electrophiles yields, after chromatographic purification, the 2- and 4-substituted products **4** and **5** (Scheme I) in the yields and ratios given in Table I.[6] The deprotonated intermediate in this sequence **6** is the result of β metalation. If the solution containing **6** is treated with magnesium bromide prior to the addition of the electrophile, the 4-substituted isomer **5** is the only product observed in four cases and predominates in the other two. Moreover, **5** is formed stereospecifically; *N,N*-diisopropyl-*trans*-4-methylcyclohex-2-enecarboxamide is obtained in 95% yield.[7]

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