Table V

	GLC retention time, min		composition, %	
	Carbowax 20M[a]	Silicone DC 550[b]	58 °C[c]	3 °C[c,d]
6-OH-1	124	159	33	46
1-OH-1	136	172	67	52

[a] 6 mm × 6 m, 145 °C. He 17.5 kg/cm². [b] 6 mm × 9 m, 165 °C. He 16 kg/cm². [c] Temperature of bromination reaction. [d] 2% of an unknown component having a retention time of 148 min on Carbowax 20M also was present.

$-$ CH$_3$, 80%), 147 (16%), 133 (33%), 91 (59%), 79 (79%). Anal. ($C_{13}H_{20}$) C, H.

Hydroxyethanoadamantanes. The monobromide mixtures were hydrolyzed by the method of Geluk and Schlatmann.[51] The crystalline, mixed bromide (3.4 g), obtained by heating 1 with liquid bromine, was heated in 5 mL of 0.69 N HCl and 4 mL of dimethylformamide at 105 °C with stirring for 0.5 h. After the solution was cooled, the reaction mixture was diluted with 30 mL of water and the pasty precipitates were pressed onto a porcelain plate overnight. Sublimation in vacuo gave 1.9 g (crude yield 76%) of glassy crystals; IR 3320 cm^{-1} (br). This mixture, as well as that obtained similarly from the product of bromination at 3 °C consists of 6-OH-1 and 1-OH-1.

The alcohols were separated by preparative GLC under the conditions specified in Table V. Poor separation necessitated repeated passes in order to obtain satisfactory purity.

6-OH-1: glass transition temperature (T_g) ~140 °C; mp ~210 °C; high-dilution IR (CCl$_4$) 3622, 3608 cm^{-1}; ^{1}H NMR (Eu(fod)$_3$[25] was used) δ 1.94 (d, J = 3 Hz, 2 H), 1.93 (m, 4 H), 1.8–1.5 (m, 9 H), 1.41 (d, J = 12 Hz, 1 H), 1.19 (d, J = 12 Hz, 1 H), 0.8 (br s, OH); mass spectrum, m/e 178 (M$^+$, 68%), 160 (M$^+$ − 18, 95%), 108 (86%), 107 (72%), 95 (base peak). Anal. ($C_{12}H_{18}O$) C, H.

1-OH-1: T_g ~140 °C; mp ~230 °C; high dilution IR (CCl$_4$) 3606 cm^{-1}; ^{1}H NMR δ 2.1–1.0 (m); mass spectrum, m/e 178 (M$^+$, 15%), 95 (base peak). Anal. ($C_{12}H_{18}O$), C, H.

6-Bromoethanoadamantane from 6-OH-1. A suspension of 33.5 mg of purifed and well-pulverized 6-OH-1 in 4 mL of 47% hydrobromic acid was sealed in a test tube and heated at 100 °C for 2 h with occasional shaking. The reaction mixture was poured into water and extracted with ether. The combined ether solution was washed with water, dried with calcium chloride, and evaporated. The solid residue remaining was sublimed in vacuo to give 37.5 mg (83%) of white, ill-formed crystals, mp 127–130 °C; ^{1}H NMR δ 2.56 (d, J = 2 Hz, 2 H), 2.5–1.2 (m with a prominent peak at 1.80); mass spectrum m/e 161 (M$^+$ − Br). Anal. ($C_{12}H_{17}Br$) C, H, Br.

1-Bromoethanoadamantane from 1-OH-1 was prepared as above from 92.5 mg of 1-OH-1. The pure bromide (88.9 mg, 66.5%) melted at 121–125 °C; its mass spectrum was superimposable with that of 6-Br-1. Anal. ($C_{12}H_{17}Br$) C, H, Br.

6-Methylethanoadamantane from 6-Br-1. Pure 6-Br-1 (128 mg) was treated with methyl Grignard reagent as described above. The product (76 mg, 80%) had the same GLC retention time and ^{1}H NMR spectrum as the sample of 6-Me-1 described above.

1-Methylethanoadamantane from 1-Br-1. The reaction was carried out on 3 mg of 1-Br-1. The product had the same GLC retention time as the sample of 1-Me-1 obtained previously.

Acknowledgment. This project was initiated at Princeton University under support by the National Institutes of Health. We thank Professor E. Wenkert and Dr. P. M. Wovkulich, University of Houston, for preliminary measurements of ^{13}C NMR spectra. Calculations were performed at the Computing Center, Hokkaido University, and at the Regionales Rechenzentrum, Erlangen. Financial support by Grant-in-Aid for Developmental Scientific Research No. 385212 from the Ministry of Education, Science and Culture at Sapporo and by the Fonds der Chemischen Industrie at Erlangen is gratefully acknowledged.

Registry No. 1, 15002-90-1; 1-Br-1, 72708-40-8; 2-Br-1, 72708-41-9; 6-Br-1, 72708-42-0; 8-Br-1, 72708-43-1; 1-OH-1, 72708-44-2; 6-OH-1, 72725-70-3; 1-Me-1, 72708-45-3; 2-Me-1, 72708-46-4; 6-Me-1, 72708-47-5; 1-cation-1, 72708-48-6; 2-cation-1, 72708-49-7; 6-cation-1, 72708-50-0; 8-cation-1, 72708-51-1; 2, 18326-54-0; 1-Br-3, 30545-17-6; 4-Br-3, 30545-30-3; 6, 38773-02-3; 7, 72708-52-2; 1-bromoadamantane, 768-90-1; adamantyl 1-cation, 19740-18-2; 2-methyl-2-hydroxyadamantane, 702-98-7.

(51) Geluk, H. W.; Schlatmann, J. L. M. A. *Tetrahedron* 1968, 24, 5361.

Base-Catalyzed Deuterium Exchange of 6,6-Dimethylfulvene[1]

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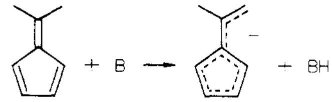
Received August 23, 1979

The kinetics of the deuterium exchange of 6,6-dimethylfulvene have been studied in the presence of sodium methoxide–methanol-*d* and potassium *tert*-butoxide–*tert*-butyl alcohol-*d*. The rate of disappearance of undeuterated starting material was followed by mass spectral measurements. The rate of introduction of deuterium into the methyl groups and into the ring was followed by ^{1}H NMR. The rates of methyl exchange and ring exchange were of the same order of magnitude. The reaction of *tert*-butyl alcohol-*d* was speeded by addition of cryptate (4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane). The occurrence of methyl exchange establishes a deprotonation mechanism (Scheme I) in both solvents. The greater rate in *tert*-butyl alcohol-*d* than in methanol-*d* is evidence that an addition–elimination mechanism for ring exchange is not important in *tert*-butyl alcohol-*d* solution, but its importance in methanol-*d* cannot be proven or disproven.

To better understand the preferred positions of reaction of mesomeric species, we earlier studied the protonation of the anion **2** produced by deprotonation of 6,6-dimethylfulvene (**1**).[2,3] Anion **2** was generated almost



1 2 (1)

quantitatively by reaction of **1** with potassium *tert*-but-

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[1] Supported in part by National Science Foundation Grant No. CHE 76-23337. Part 21 in the series "Structural Effects on Rates and Equilibria". For part 20 see: Hine, J.; Green, L. R.; Meng, P. C., Jr.; Thiagarajan, V. *J. Org. Chem.* 1976, 41, 3343-9.

0022-3263/80/1945-0991$01.00/0

Table I. Kinetics of Alkoxide Ion Catalyzed Deuteration of 6,6-Dimethylfulvene (1) As Followed by Mass Spectral Measurements[a]

[base], M	base	[1], M	$10^4 k_a$, s^{-1}	$10^4 \sigma$,[b] s^{-1}	$10^3 k_s$,[c] M^{-1} s^{-1}	y[d]
0.134	MeONa	0.095	8.3	0.4	6.2	2.0 (2.0)
0.134	MeONa	0.095	8.2	0.1	6.0	2.0 (2.3)
0.0706	MeONa	0.174	3.8	0.3	5.4	1.6[e]
0.0706	MeONa	0.210	4.5	0.1	6.4	1.6[e]
0.0706	MeONa	0.246	4.0	0.2	5.7	1.4[e]
0.0146	MeONa	0.104	1.04	0.04	7.1	1.5 (2.2)
0.215	*t*-BuOK	0.201	500	30	230	0.4 (0.0)
0.215	*t*-BuOK	0.201	640	20	300	0.0 (0.8)
0.0912	*t*-BuOK	0.205	480	80	530	0.2 (0.0)
0.127	*t*-BuOK[f]	0.178	2500	100	2000	0.5 (0.6)
0.0711	*t*-BuOK[f]	0.108	1900	200	2700	0.8 (0.6)
0.0312	*t*-BuOK[f]	0.270	760	70	2430	0.6 (1.2)
0.0312	*t*-BuOK[f]	0.270	560	20	1800	0.8 (0.8)
0.0312	*t*-BuOK[f]	0.287	550	60	1750	0.7 (0.7)

[a] At 35 °C in ROD, where RONa or ROK is the base used. About half as much benzene as dimethylfulvene was present as an NMR reference. [b] Estimated standard derivation (see Appendix). [c] Second-order rate constant obtained by dividing k_a by the base concentration. [d] Calculated from f_1 values by using eq 4. The parenthesized values were calculated from f_2 values as indicated in the Appendix for those runs in which the reaction was carried far enough to give f_2 values larger than 0.04. [e] Since the amount of dideuterated species (f_2) never reached 0.025, no y value was calculated from the f_2 data. [f] Cryptate (4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane) added in the same concentration as the *t*-BuOK.

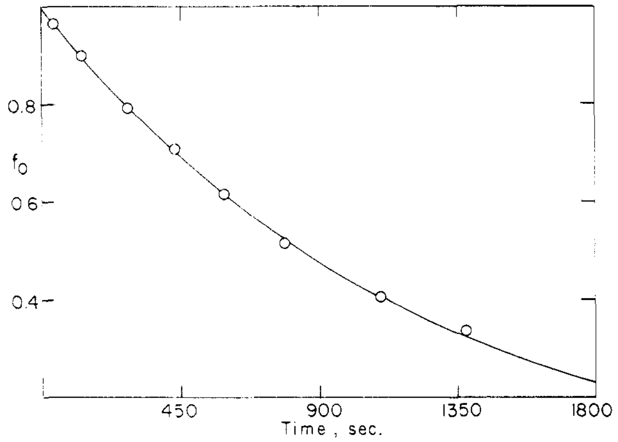
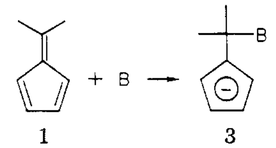


Figure 1. Plot of fraction of 6,6-dimethylfulvene (1) that is undeuterated vs. time for 0.095 M 1 and 0.134 M sodium methoxide in methanol-*d* at 35 °C. The line is based on eq 3 and the *k* value 8.2 × 10^{-4} s^{-1}.

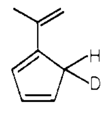
oxide in diglyme [bis(2-methoxyethyl) ether] to give a solution that was quenched with aqueous acid. We now seek to learn more about the effect of the medium on the position of protonation of 2 and about the possibility of forming the alternative carbanion 3, by *addition* to 1.



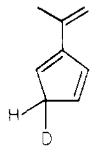
1 3 (2)

Carbanions like 2 have been generated by reactions of fulvenes with (triphenylmethyl)sodium[4] and sodamide,[5] as well as potassium *tert*-butoxide. The nucleophilic reagents lithium aluminum hydride,[5,6,8] methyllithium,[5,7,8] and phenyllithium[5,7,8] all give carbanions like 3.

We have now studied the alkoxide ion catalyzed deuterium exchange of 1 in methanol-*d* and *tert*-butyl alcohol-*d* solution. Exchange can involve the deuteronation of 2 to give 1-*d* directly or to give 4-*d* or 5-*d*, which are

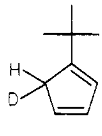


4-*d*

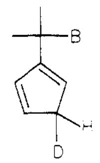


5-*d*

known[2,3] to be much less stable than 1-*d* and would therefore rapidly be transformed to 1-*d* or 1-d_2 under the reaction conditions. Alternatively, 3 could be deuteronated to give 6-*d* or 7-*d*, which would rapidly be transformed to 3 or 3-*d*.



6-*d*



7-*d*

Results

When 1 was treated with sodium methoxide in methanol-*d* or potassium *tert*-butoxide in *tert*-butyl alcohol-*d*, mass spectral measurements showed that deuterium was taken up. The relative amounts of the various deuterated species present were calculated from parent peak intensities, neglecting isotope effects on the efficiency of formation and cleavage of the parent peaks. (Fragmentation was not extensive at 15 eV, where the mass spectra were run; the parent peaks were larger than any other peaks in the spectrum.) The kinetics of exchange were studied at 35 °C. First-order rate constants for the disappearance of undeuterated 1 were calculated by a nonlinear least-squares fit to eq 3, in which f_0 is the fraction of 1 undeuterated at time t and f_{00} is the fraction at zero time (essentially 1.0). (Under the reaction conditions the equilibrium fraction of undeuterated 1 is essentially zero.)

$$f_0 = f_{00} e^{-kt} \tag{3}$$

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(2) Hine, J.; Knight, D. B. *J. Org. Chem.* **1970**, *35*, 3946-9.

(3) Knight, D. B.; Hartless, R. L.; Jarvis, D. A. *J. Org. Chem.* **1972**, *37*, 688-92.

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(6) Ziegler, K.; Gellet, H. G.; Martin, H.; Nagel, K.; Schneider, J. *Justus Liebigs Ann. Chem.* **1954**, *589*, 91-121.

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Scheme I

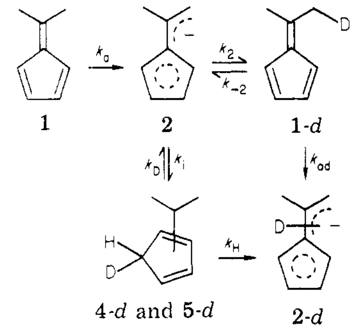


Figure 1 shows a kinetic plot in a run using 0.095 M 1 and 0.134 M sodium methoxide in methanol-*d*. The results obtained in methanol-*d* are summarized in Table I, including second-order rate constants obtained by dividing *k* by the base concentration. Also shown are the somewhat less reproducible rate constants obtained by using potassium *tert*-butoxide in *tert*-butyl alcohol-*d* in the presence and absence of "cryptate" (4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane).

The kinetics of formation of monodeuterated **1** may be based on Scheme I, in which the mixture of **4**-*d* and **5**-*d* is treated as a single species. The carbanions are assumed to combine only with deuterium rather than protium. Thus, any reactant that becomes **2**-*d* cannot become **1**-*d*. The derivation shown in the Appendix gives eq 4, in which

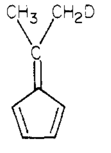
$$f_1 = \frac{k_a f_{00}}{(k_a - C)(y + 1)} (e^{-Ct} - e^{-k_a t}) \tag{4}$$

y and *C* are defined in eq 5 and 6 and f_1 is the fraction of reactant that is monodeuterated at time *t*. Since k_{ad} is

$$y = \frac{k_i k_H}{k_2(k_H + k_D)} \tag{5}$$

$$C = \frac{k_{-2} y}{y + 1} + k_{ad} \tag{6}$$

the rate constant for deprotonating **1**-*d*, it would be equal to $5k_a/6$ if only a statistical effect were allowed for.



1-*d*

However, two of the protons that may be removed are subject to an α secondary deuterium kinetic isotope effect, and three of them are subject to a γ secondary deuterium kinetic isotope effect. We have found reports of only a few secondary isotope effects on formation of sp^2-hybridized carbanions. Bordwell and Boyle have noted α effects, expressed as k^H/k^D ratios, of around 1.15 per deuterium for carbanion formation by phenylnitromethane[9] and have referred to values of 1.18 for nitroethane[10] and 1.15 for toluene.[11] On the other hand, values ranging from 0.99 to 1.09 have been found for cyclopentanone and 3-pentanone.[12] We therefore assume that the α effect is in the range 1.00–1.15 and, neglecting the γ effect, the k_{ad} is in the range $0.72k_a$–$0.83k_a$. Since k_{-2} is the rate constant for removal of deuterium from **1**-*d*, its value may be obtained by dividing k_a by a statistical factor of 6 and allowing for a primary kinetic isotope effect. We conservatively assume that for the primary isotope effect, k^H/k^D will be in the range 1–20. This puts k_{-2} in the range $0.008k_a$–$0.167k_a$. Since the *y* values we obtain are in the range 0–2, the resulting *C* values are in the range $0.72k_a$–$0.94k_a$ or $(0.83 \pm 0.11)k_a$. In Table I are *y* values calculated by a nonlinear least-squares method using $C = 0.83k_a$. With $C = 0.94k_a$ larger *y* values and with $C = 0.72k_a$ smaller *y* values are obtained, but the difference is only about 0.1 in the runs that were carried furthest to completion and less than that in the other runs; there was little difference in the precision of the fit of the data. This precision is illustrated in Figure 2 for a run using sodium methoxide in methanol-*d*.

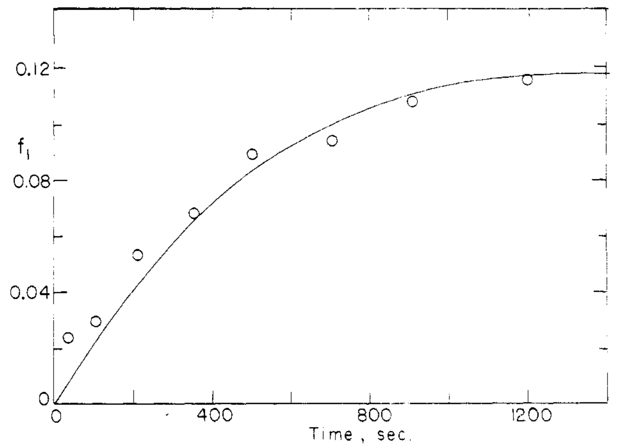
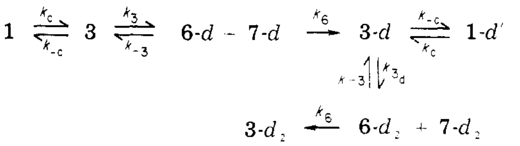


Figure 2. Plot of fraction of 6,6-dimethylfulvene (**1**) that is monodeuterated vs. time for 0.095 M **1** and 0.134 M sodium methoxide in methanol-*d* at 35 °C. The line is based on eq 4, a *C* value of $0.83k_a$, a *y* value of 2.0, and a k_a value of 8.3×10^{-4} s^{-1}.

Scheme II



A more approximate relationship derived in the Appendix permits the calculation of *y* from f_2, the fraction of dideuterated reactant present at a given time. These values, which are also listed in Table I, are in fair agreement with those calculated from eq 4.

Although Scheme I, based on intermediate **2**, fits the data described so far, Scheme II, based on intermediate **3**, may also be capable of fitting it.

The derivation in the Appendix, which neglects secondary isotope effects and treats each of the pairs **6**-*d* and **7**-*d* and **6**-d_2 and **7**-d_2 as an individual species, gives eq 7,

$$f_1 = \frac{k_{obsd} f_{00}}{(k_{obsd} - Z)(r + 1)} (e^{-Zt} - e^{-k_{obsd} t}) \tag{7}$$

with the definitions shown in eq 8–11.

$$Z = \frac{(k_{3_d}/k_3 + r/q)k_{obsd}}{r + 1} \tag{8}$$

$$r = qk_{3_d}/k_{-c} \tag{9}$$

$$q = k_6/(k_6 + k_{-3}) \tag{10}$$

$$k_{obsd} = pqk_c$$

$$p = k_3/(k_3 + k_{-c}) \tag{11}$$

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[9] Bordwell, F. G.; Boyle, W. J., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 3447–52.

[10] Bell, R. P.; Goodall, D. M. *Proc. R. Soc. London, Ser. A* **1966**, *294*, 273–97.

[11] Streitwieser, A., Jr.; Van Sickle, D. E. *J. Am. Chem. Soc.* **1962**, *84*, 254–8.

[12] Zeigler, J. P. Ph.D. Dissertation, The Ohio State University, Columbus, OH, 1978, pp 74–5.

Table II. Kinetics of Alkoxide Ion Catalyzed Deuteration of 6,6-Dimethylfulvene (1) As Followed by ^{1}H NMR[a]

[base], M	base	[1], M	$10^3 \times (6k_M)$,[b] s^{-1}	$10^3 \times (4k_R)$,[c] s^{-1}
1.012	NaOMe	0.588	4.3	*d*
0.860	NaOMe	0.682	4.6	8.0
0.416	NaOMe	0.802	5.1	7.7
0.384	*t*-BuOK	0.919	19	32
0.194	*t*-BuOK	0.828	19	23
0.206	*t*-BuOK	1.119	10	7.6
0.057	*t*-BuOK	1.549	14[e]	9.2[e]
0.022	*t*-BuOK	1.228	5.7[e]	3.9[e]
0.024	*t*-BuOK	1.339	13[e]	16[e]

[a] At 39 °C in ROD, where RONa or ROK is the base used, and benzene is added as an NMR reference unless otherwise stated. [b] Rate constant for exchange of methyl protons. [c] Rate constant for exchange of ring protons. [d] The area of the ring-proton peak could not be measured because of interference by the ROH peak. [e] At 37 °C.

Comparison with eq 4, in which k_a is the value of k_{obsd} according to Scheme I, shows that eq 7 is the same as eq 4 except that C has been replaced by Z and y by r. As shown in the Appendix, if the primary deuterium kinetic isotope effect k_6/k_{-3} is around 6, the value of Z will be near the value of 0.83 used for C in eq 4 in calculating y values for Table I. Hence, Scheme II is also capable of fitting the mass spectral kinetic data, and if Scheme II is correct, the y values in Table I should be interpreted as r values (eq 9). Simultaneous reaction by both schemes should also be capable of fitting the data.

Kinetic studies were also made by using ^{1}H NMR measurements in the alcoholic reaction solutions. Individual species could not be identified, but the areas of the methyl peak at δ 2.2 and the peaks for the ring protons near δ 6.5 showed how much deuterium had been taken up at these two parts of the molecule. Benzene was present in the reaction solutions as an NMR reference compound. Absorption by the ROH formed in the reaction interfered with measurement of the area of the ring-proton peak and in a few runs made it impossible. In order to obtain fairly reliable results, we had to use much higher concentrations of 1 than needed for the mass spectral studies. Also, the reactions had to be followed much further than in the mass spectral runs, which dealt with only the d_0, d_1, and d_2 species specifically. For this reason, allowance had to be made for the fact that deuteration is significantly incomplete at equilibrium. We could not achieve a useful sophisticated kinetic analysis of the NMR data, which were considerably less reproducible (especially the ring-proton areas) than the mass spectral data. Exchange at the methyl groups and in the ring were simply treated (separately) as first-order approaches to equilibrium. First-order rate constants were obtained from eq 12, in which R, R_∞,

$$R = R_\infty - (R_\infty - R_0)e^{-kt} \qquad (12)$$

and R_0 are the ratios of the methyl or ring peak area to that of the benzene peak at times t, infinity, and zero, respectively. Nonlinear least-squares fits to experimental t and R values gave optimum values of R_∞, R_0, and k. Typical data were plotted in Figure 3, and the kinetic results are summarized in Table II. For reasons described in the next section, values of $6k_M$ (for methyl exchange) and $4k_R$ (for ring exchange) are listed.

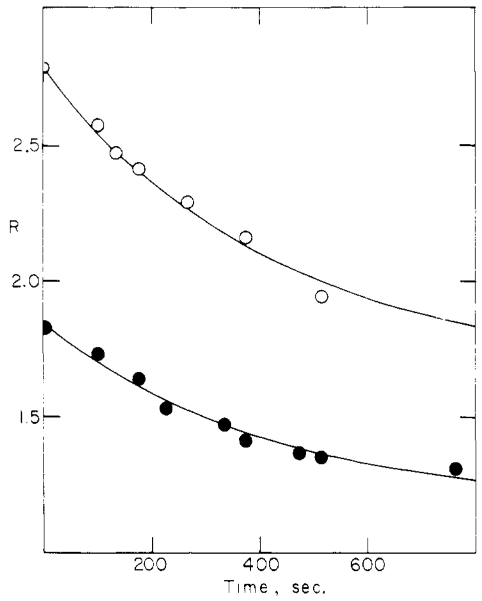

Figure 3. Plot of ratios (R) of peak areas to peak area for benzene reference for 1.55 M 6,6-dimethylfulvene and 0.057 M potassium *tert*-butoxide in *tert*-butyl alcohol-*d*. The open circles are for methyl peak areas and the solid circles for ring peak areas. The lines are based on eq 12 with k values of 0.00235 and 0.00230, respectively.

Discussion

Rate Constants. As explained in the Appendix the uncertainties in the rate constants in Tables I and II are probably several times as large as the calculated standard deviations.

The rate constants for exchange of total protium in Table II are not directly comparable to the rate constants for exchange of the first protium atom in Table I. First there are statistical effects. If exchange took place only at methyl and each successful attack by base simply replaced one protium atom of 1 by deuterium (as would be the case in Scheme I if k_i were zero), the k_a of Table I and eq 4 would be equal to $6k_M$. Similarly, if exchange took place only on the ring and involved only one protium at a time (as would essentially by the case in Scheme II if the 6 and 7 species were formed at equal rates and k_{-c} were much larger than k_3), k_a would be equal to $4k_R$. On the other hand, if every successful attack by base exchanged all the ring protium atoms (as would be the case in Scheme II if k_3 were much larger than k_{-c}), k_a would be equal to k_R. Many of the other possible relative magnitudes of rate constants in Schemes I and II do not even lead to clearly first-order kinetics. Because the mass spectral observations show that exchange takes place much more nearly in a one-at-a-time fashion rather than all at once, the values in Table II are of $6k_M$ and $4k_R$. Nevertheless, in the case of k_R, where exchange of more than one hydrogen at a time probably occurs to at least some extent, the value $4k_R$ must be somewhat too large for direct comparison with k_M and k_a. Additional complications in comparing the rate constants in Table II with those in Table I arise from the extensive reversibility that occurs during the NMR runs, the medium effects that must result from the higher concentrations of reactants (15% and up, by volume) in the NMR runs, and the 2–4 °C higher temperature at which the NMR runs were carried out.

The data in Table I show that up to base concentrations of around 0.13 M the rate of exchange of 1 in methanolic sodium methoxide or with potassium *tert*-butoxide in the presence of cryptate is approximately proportional to the base concentration. The data in the two tables show that the rate increases much more slowly than the base concentration in the presence of potassium *tert*-butoxide without cryptate or in the presence of methanolic sodium methoxide at concentrations above 0.4 M. This suggests that the more highly aggregated forms of the bases are less reactive than are more dissociated forms. If the bases were largely ion pairs and the reactions arose only from the dissociated alkoxide anions, the rate would be proportional to the square root of the total base concentration. In view of the considerable uncertainty in the data, it is possible that some such relationship is approximately true. In any case the powerful catalytic effect of cryptate is strong evidence for the much greater reactivity of free *tert*-butoxide ions.

If the acidity of 1 were great enough that 2 was formed in amounts comparable to that of either potassium *tert*-butoxide or 1, the rate constant for exchange would increase less rapidly than the increasing base concentration. In the extreme case where essentially all the 1 is transformed to 2 by excess potassium *tert*-butoxide, the reaction simply becomes first order in 2 and further increases in the base concentration would not increase the rate. (The quenching used in following the mass spectral kinetics would transform 2 to 1 rather than 1-*d*.) Experimentally, it was observed that addition of potassium *tert*-butoxide to 1 immediately gave a red-brown color resembling that formed when potassium *tert*-butoxide was added to 1 in diglyme. No such color was formed in the methanol-*d* runs. Hence, it is possible that some complications of this type may be occurring in the *tert*-butyl alcohol-*d* runs. However, the acidity of 1 does not appear to be great enough that most of the limiting reagent is transformed to 2 in *tert*-butyl alcohol solution. This should give large enough concentrations of 2 for its ^{1}H NMR spectrum to be observable, but this spectrum was sought and not found in the runs in which the kinetics were followed by NMR measurements. The smallness of the increase in k_a that accompanies an increase in potassium *tert*-butoxide concentration from 0.0912 to 0.215 M in the absence of cryptate (Table I) cannot result from the transformation of practically all the 1 to 2 because 0.0912 M potassium *tert*-butoxide cannot transform practically all of the 0.205 M 1 to 2 and because if the 1 were practically all transformed to 2 in these runs, there would be no reason why increasing the effective basicity of the solutions by adding cryptate should increase the rate as much as it is seen to be increased in some of the other runs in Table I.

Table III. Reactivities toward Alkali Metal Alkoxides in Alcohol

reaction	temp, °C	$k_{t\text{-BuOK}}{}^a/k_{\text{MeONa}}$	$k_{t\text{-BuOK}}{}^a/k_{\text{EtONa}}$
p-$O_2NC_6H_4NH_2$ ⇌ p-$O_2NC_6H_4NH^-$	20-30	$3 \times 10^{6\ b}$	$4 \times 10^{4\ c}$
$PicCH_3$ ⇌ $PicCH_2^{-\ d}$	25-30	$\sim 1.8 \times 10^{4\ e,f}$	$\sim 120^{e,f}$
$PhCH_2CH(Me)CN$ racemization	25	$4 \times 10^{6\ g}$	
$CH_2I_2 \rightarrow CD_2I_2$	36	7000^h	
$CH_2Br_2 \rightarrow CD_2Br_2$	36	4900^h	
$(PhS)_2CDCH_3 \rightarrow (PhS)_2CHCH_3$	158	370^i	110^i
$PicCH_3 \rightarrow PicCH_2^{-\ d}$	25	$380^{f,j}$	60^j
$PhCOCH_2T \rightarrow PhCOCH_3$	25	90^k	13^k
$(p\text{-}O_2NC_6H_4)_2CH_2 \rightarrow (p\text{-}O_2NC_6H_4)_2CH^-$	20		$0.24^{f,l}$
$PicH$ ⇌ $PicH\text{-}OR^{-\ d,m}$	25	$>1700^{f,n}$	$>12^{f,n}$
$PicCH_3$ ⇌ $PicCH_3\text{-}OR^{-\ d,o}$	25-30		$\sim 80^{o,p}$
$PicH \rightarrow PicH\text{-}OR^{-\ d,m}$	25	$5^{f,n}$	$0.77^{f,n}$
$PicCH_3 \rightarrow PicCH_3\text{-}OR^{-\ d,m}$	25-30		$\sim 0.7^{o,p}$
o-$O_2NC_6H_4F \rightarrow o$-$O_2NC_6H_4OR$	31	11^q	
p-$O_2NC_6H_4F \rightarrow p$-$O_2NC_6H_4OR$	31	0.3^q	
$CH_3Br \rightarrow CH_3OR$	40	$3.6^{r,s}$	
$C_2H_5Br \rightarrow C_2H_5OR$	40	$0.48^{r,s}$	

[a] Ratio of equilibrium constants for those reactions written as reversible; ratio of rate constants for the other reactions. The *t*-BuOK, MeONa, and EtONa reactions were run in *t*-BuOH, MeOH, and EtOH, respectively, unless otherwise noted. Where data were available over a range of base concentrations, data were chosen for concentrations near the more dilute concentrations shown in Table I. [b] This refers to about 0.1 M alkoxides. It is based on the ratio of [A$^-$]/[HA] of 6.02 reported for *p*-nitroaniline in 0.0955 M *t*-BuOK[13] and on the pK value 21.67 for *p*-nitroaniline and the H_M value of 15.94 for 0.1 M MeONa in methanol.[14] [c] This is obtained from the value of $k_{t\text{-BuOK}}/k_{\text{MeONa}}$ shown for this reaction and the difference of 1.91 between H_- in methanol and H_- at the same base concentration in ethanol.[15] [d] Pic is the picryl (2,4,6-trinitrophenyl) group. [e] Uncertain by about a factor of 5, largely because of uncertainty in the *tert*-butoxide value, which was obtained at 30 °C.[16] The methoxide and ethoxide values[17] are at 25 °C. [f] *t*-BuONa used. [g] Reference 18. [h] Reactions carried out in ROD.[19] [i] Reference 20. [j] References 16 and 17. [k] Reference 21. [l] Reference 22. [m] Meisenheimer-complex formation. [n] Reference 23. [o] This was thought to be Meisenheimer-complex formation, but the authors were not sure. [p] The ethoxide value[17] is uncertain by a factor of 2, and the *tert*-butoxide value is perhaps even less certain.[16] [q] Reaction of ~0.4 M *t*-BuOK and 0.24 M MeOK.[24] [r] The cations used with *tert*-butoxide and ethoxide ions were not stated.[25] [s] Reference 26.

Reaction Mechanism. The rate constants in Table II show no case in which the rate constant for ring exchange ($4k_R$) is as much as twice as large as that for methyl exchange ($6k_M$). Since methyl exchange can occur only via Scheme I, reaction by this scheme must be important in both methanol and *tert*-butyl alcohol. Whether reaction via Scheme II is also important is less obvious; Scheme I can explain both methyl exchange and ring exchange. The increased reaction rates seen upon going from the methanol to the *tert*-butyl alcohol reactions give evidence on this point. This increase in reactivity will be interpreted in terms of the illustrative literature data[13-26] in Table III, which also lists some relative reactivities toward sodium ethoxide in ethanol. The first nine reactions in Table III are proton transfers. The largest $\Delta\Delta G$ values are for the first two reactions, which are equilibrium processes, and for the next three reactions,[27] for which the intrinsic

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(27) Note that since a 370-fold rate effect at 158 °C corresponds to a $\Delta\Delta G^{\ddagger}$ value of 5.1 kcal/mol and a 4900-fold effect at 36 °C to 5.2 kcal/mol, the rate effects in the fourth and fifth reactions are essentially equal.

barriers (in the Marcus treatment) would be expected to be small. Nitriles are known to have small barriers to α deprotonation[28,29] probably because the resulting carbanions do not have a strong tendency to be planar.[30] The fourth, fifth, and sixth reactions should yield pyramidal carbanions and, hence, should have small barriers. In uphill reactions (as these are expected to be) with small barriers, equilibrium differences are often strongly reflected in rate differences. The best models for the transformation of 1 to 2 that we have found are the formations of carbanions from acetophenone, 2,4,6-trinitrotoluene, and bis(*p*-nitrophenyl)methane. In these reactions the carbon from which hydrogen is removed should become planar, and the negative charge should be delocalized onto other atoms. The values of $k_{t\text{-BuOK}}/k_{\text{MeONa}}$ shown for acetophenone and trinitrotoluene are in or near the range (30–100) that may be calculated for 1 (not counting the runs in which cryptate was used) from the data in Table I. Judging from the $k_{t\text{-BuOK}}/k_{\text{EtONa}}$ ratio shown, the $k_{t\text{-BuOK}}/k_{\text{MeONa}}$ ratio for bis(*p*-nitrophenyl)methane may be too small to be near this range. However, among the imperfections in this model is the much greater steric shielding of the protons that are removed, a factor that should decrease the ratio.

The last eight reactions in Table III are bond formations by the alkoxide ions to carbon. We could find no data on a reaction in which the alkoxide ions were shown to form bonds to an sp^2-hybridized tertiary carbon atom to give a bis tertiary ether like **3**. The $k_{t\text{-BuOK}}/k_{\text{MeONa}}$ and $k_{t\text{-BuOK}}/k_{\text{EtONa}}$ values are largest in the first two of these reactions, the only two equilibrium processes. However, the only rate process for which the ratio is larger than 5 is the reaction of *o*-nitrofluorobenzene, which has been shown (by the relative insensitivity of the rate, relative to that of the para isomer, to added crown ether) to be greatly complicated by coordination of the potassium cation to several atoms near the reaction center, when the reaction is carried out in *tert*-butyl alcohol.[22] The $k_{t\text{-BuOK}}/k_{\text{MeONa}}$ ratio of 5 is for the formation of a secondary–tertiary ether. Like any such ether it has a conformer available in which much of the bulk of the tertiary butyl group is near the hydrogen atom on the carbon atom to which oxygen becomes bonded. Bis tertiary ethers have no such conformers available. Even after allowing for 2.0 kcal/mol of gauche interactions, di-*tert*-butyl ether was found to be specifically strained by 7.8 kcal/mol; allowance for 1.5 kcal/mol of gauche interactions overestimated the stability of isopropyl *tert*-butyl ether by 0.4 kcal/mol.[31] The last two entries in Table III illustrate the sensitivity of the ratios to steric effects.

For the preceding reasons, we feel that if Scheme II were important in both alcohols and if k_c were rate determining, the $k_{t\text{-BuOK}}/k_{\text{MeONa}}$ ratios would be much smaller than those we have found. We further feel that if **3**, a bis tertiary ether, were formed at equilibrium and k_3 (involving protonation by a very weak acid in the case of *tert*-butyl alcohol) were rate determining, smaller ratios would also be observed. Furthermore, it is known that for proton-transfer equilibria, such as the first reaction in Table III, *and* for equilibrium coordination to carbon, as in the formation of Meisenheimer complexes,[14] the concentration equilibrium constants increase *more* rapidly than the alkali metal alkoxide concentration does. This contrasts with our reaction, where the exchange rate increases more slowly than the base concentration [as is also the case with carbanion formation from bis(*p*-nitrophenyl)methane].[22] Hence, we feel that exchange via **3** may be neglected in the faster solvent, *tert*-butyl alcohol.

If our conclusion that Scheme II may be neglected in *tert*-butyl alcohol solution is correct, then ring exchange of **1** in *tert*-butyl alcohol must proceed by Scheme I. Scheme I requires that ring exchange occurs only when methyl exchange occurs also; that is, ring exchange can occur only when at least two hydrogen atoms are exchanged at once. The fact that ring exchange is seen in Table II to be comparable in rate to methyl exchange in *tert*-butyl alcohol solution requires that k_i in Scheme I be comparable to k_2. Since y is equal to $(k_i/k_2)k_H/(k_H + k_D)$ and $k_H/(k_H + k_D)$ should be in the range 0.5–0.95, y would not be expected to be smaller than about 0.5 in *tert*-butyl alcohol solution. In Table I the y values obtained in *tert*-butyl alcohol (without cryptate) average only about 0.2. This value is smaller than expected, but there are several possible explanations for this fact other than significant contributions from Scheme II. First, the values of y obtained in *tert*-butyl alcohol-*d* are less reliable than those obtained in methanol-*d* (note the variations in Table I) because the reactions in *tert*-butyl alcohol-*d* are so fast. Second, the k_R values in Table II are less reliable than the k_M values because the ring protons absorb so near the hydroxylic proton. Third, there is a systematic error that causes all our calculated y values to be a little smaller than the real ones. This comes from our neglect of reaction of the intermediate carbanions with protonated alcohol. If Scheme I is followed to give **4**-*d* or **5**-*d* and then ring-deuterated **2**-*d* and the **2**-*d* abstracts a proton rather than a deuteron from the solvent, it can give ring exchange without methyl exchange. If the primary kinetic isotope effect, k_H/k_D, is 6, the 3% *t*-BuOH present in our solvent at half reaction would lead to about 16% of **2**-*d* combining with protium rather than deuterium. A rigorous treatment of this complication is beyond us, but rough calculations indicate that this will cause y to be too small by about 0.1. All in all, we feel that the reactivity argument, based on the data in Table III, for Scheme I in the *tert*-butyl alcohol-*d* reaction is probably correct and that the imperfect agreement of the y values and the relative magnitudes of the k_M and k_R values result from the errors just described.

Experimental Section

Reagents. 6,6-Dimethylfulvene was prepared as described previously.[2,3] The methyl alcohol-*d* and *tert*-butyl alcohol-*d* used contained about 0.29 and 1.7% protio alcohol, respectively. Sodium methoxide and potassium *tert*-butoxide solutions were prepared under nitrogen. Dimethylfulvene solutions were prepared in a glovebox under argon. In the runs where cryptate was used, 1 mol was used per mol of potassium *tert*-butoxide.

Mass Spectral Kinetics. In an illustrative run at zero time 0.50 mL of 1.48 M sodium methoxide in methanol-*d* at 35 °C was added to 10.0 mL of 0.221 M 6,6-dimethylfulvene in methanol-*d* at 35 °C. At recorded times a 1-mL aliquot was removed by syringe and quenched by injection through a septum stopper into 2 mL of 10% acetic acid in water and 1 mL of ether in a 5 mL vial. The vial was shaken and water added to raise the ether layer into the neck of the vial, from which most of it was withdrawn by syringe. Most of the ether was then removed in a stream of nitrogen and the residue stored in a freezer until it was analyzed. All operations were carried out under nitrogen. Mass spectral peak heights, obtained at 15 eV, for the parent and p − 1 peaks, in the range 105–116 daltons, were corrected for natural-abundance ^{13}C and deuterium and p − 1 fragmentation to determine how much deuterium had been introduced by exchange. The same extent of p − 1 fragmentation observed with unexchanged di-

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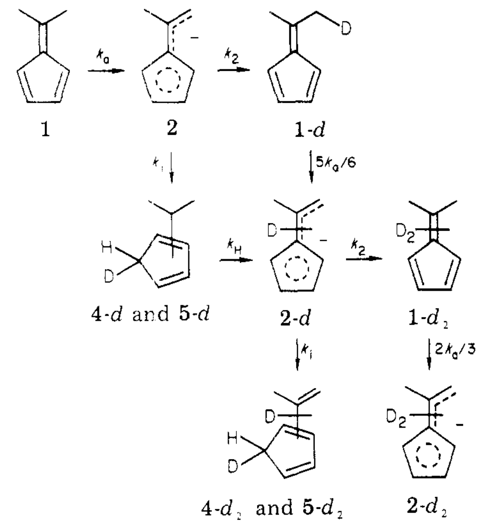
Scheme III



methylfulvene (10.0%) was assumed to occur with all the deuterated species, an approximation that is probably fairly good because we were only using the fractions of undeuterated, monodeuterated, and dideuterated materials in our data analysis.

^{1}H NMR Kinetics. In an illustrative run 0.1171 g of 6,6-dimethylfulvene and 0.0429 g of benzene were weighed into a septum-stoppered NMR tube containing only nitrogen. The NMR spectrum was taken and integrated on an EM-360 60 spectrometer at 39 °C or on a T-60 spectrometer at 37 °C. At zero time 1.0 mL of 1.178 M sodium methoxide in methanol-d was added with shaking, and the spectrum was integrated repeatedly until the relative peak heights no longer changed.

Appendix

Derivation of Eq 4. If the mixture of 4-d and 5-d in Scheme I is considered to be a species, whose concentration will be denoted as g, the steady-state assumption for g gives eq 101, when solved for g. The steady-state assumption for **2** is eq 102. Substitution from eq 101 and solution for [**2**] gives eq 103. If y is defined by eq 104, [**2**] may be expressed as shown in eq 105. The rate equation for **1**-d is eq 106. Substitution from eq 105 gives eq 107, which may be rearranged to give eq 108. The definition of C in eq 109 then gives eq 110.

$$g = \frac{k_i[2]}{k_D + k_H} \qquad (101)$$

$$k_a[1] + k_D g + k_{-2}[1\text{-}d] = (k_2 + k_i)[2] \qquad (102)$$

$$[2] = (k_a[1] + k_{-2}[1\text{-}d]) \Big/ \left(k_2 + \frac{k_i k_H}{k_D + k_H} \right) \qquad (103)$$

$$y = \frac{k_i k_H}{k_2(k_D + k_H)} \qquad (104)$$

$$[2] = \frac{k_a[1] + k_{-2}[1\text{-}d]}{k_2(y + 1)} \qquad (105)$$

$$\frac{\mathrm{d}[1\text{-}d]}{\mathrm{d}t} = k_2[2] - (k_{-2} + k_{ad})[1\text{-}d] \qquad (106)$$

$$\frac{\mathrm{d}[1\text{-}d]}{\mathrm{d}t} = \frac{k_a[1] + k_{-2}[1\text{-}d]}{y + 1} - (k_{-2} + k_{ad})[1\text{-}d] \qquad (107)$$

$$\frac{\mathrm{d}[1\text{-}d]}{\mathrm{d}t} + \left(\frac{k_{-2}y}{y + 1} + k_{ad} \right)[1\text{-}d] = \frac{k_a[1]}{y + 1} \qquad (108)$$

$$C = \frac{k_{-2}y}{y + 1} + k_{ad} \qquad (109)$$

$$\frac{\mathrm{d}[1\text{-}d]}{\mathrm{d}t} + C[1\text{-}d] = \frac{k_a[1]}{y + 1} \qquad (110)$$

If we divide by the total concentration of dimethylfulvene in all states of deuteration, eq 110 becomes eq 111, in which f_0 is the fraction that is undeuterated, and f_1 is the fraction monodeuterated. The rate equation for disappearance of [**1**] gives eq 112, in which f_{00}, the value of f_0 at zero time, is essentially equal to 1.0. Substitution into eq 111 gives eq 113. Integration gives eq 114, which can be checked by integration and manipulation to give eq 115. Substitution from eq 114 gives eq 116, which may be rearranged to eq 113.

$$\frac{\mathrm{d}f_1}{\mathrm{d}t} + Cf_1 = \frac{k_a f_0}{y + 1} \qquad (111)$$

$$f_0 = f_{00}e^{-k_a t} \qquad (112)$$

$$\frac{\mathrm{d}f_1}{\mathrm{d}t} + Cf_1 = \frac{k_a f_{00} e^{-k_a t}}{y + 1} \qquad (113)$$

$$f_1 = \frac{k_a f_{00}}{(k_a - C)(y + 1)}(e^{-Ct} - e^{-k_a t}) \qquad (114)$$

$$\frac{\mathrm{d}f_1}{\mathrm{d}t} = \frac{-k_a f_{00}}{(k_a - C)(y + 1)}(Ce^{-Ct} - Ce^{-k_a t} + Ce^{-k_a t} - k_a e^{-k_a t}) \qquad (115)$$

$$\frac{\mathrm{d}f_1}{\mathrm{d}t} = -Cf_1 - \frac{k_a f_{00}}{(k_a - C)(y + 1)}(C - k_a)e^{-k_a t} \qquad (116)$$

Calculation of y from f_2 Values. In order to use the extent of dideuteration of **1** to calculate y values, we must expand Scheme I. However, we could not treat any such scheme unless it was also simplified. The primary kinetic isotope effects are assumed to be large enough that species such as **4**-d and **5**-d will always lose protium instead of deuterium when attacked by base. Thus k_D in Scheme I is neglected relative to k_H, and k_{-2} is neglected relative to k_{ad}. The next exchange step is treated analogously and secondary deuterium isotope effects are neglected so that k_{ad} is simply equal to $5k_a/6$ (as a result of statistical effects). These and analogous assumptions give Scheme III. The steady-state assumption for **2** gives eq 117, and the steady-state assumption for **2**-d gives eq 118 and then eq 119. The rate equation for [**1**-d] is eq 120 and then eq 121. When k_D is neglected compared to k_H, y becomes k_i/k_2 (see eq 5) so that eq 121 may be written as eq 122.

$$[2] = \frac{k_a[1]}{k_i + k_2} \qquad (117)$$

$$k_i[2] + 5k_a[1\text{-}d]/6 = (k_i + k_2)[2\text{-}d] \qquad (118)$$

$$[2\text{-}d] = \frac{k_i k_a[1]}{(k_i + k_2)^2} + \frac{5k_a[1\text{-}d]}{6(k_i + k_2)} \qquad (119)$$

$$\frac{\mathrm{d}[1\text{-}d]}{\mathrm{d}t} = k_2[2] - \frac{5k_a[1\text{-}d]}{6} \qquad (120)$$

$$\frac{\mathrm{d}[1\text{-}d]}{\mathrm{d}t} = \frac{k_a k_2[1]}{k_i + k_2} - \frac{5k_a[1\text{-}d]}{6} \qquad (121)$$

$$\frac{\mathrm{d}[1\text{-}d]}{\mathrm{d}t} = \frac{k_a[1]}{y + 1} - \frac{5k_a[1\text{-}d]}{6} \qquad (122)$$

This is analogous to eq 110 with C equal to $5k_a/6$. The C resulting from the more rigorous derivation in the preceding section and defined by eq 109 was evaluated in the main body of this paper as $(0.83 \pm 0.11)k_a$. Apparently there has been some cancellation of errors in the present less rigorous treatment. Further treatment of eq 122 gives eq 114 with y and C having the new meaning just described.

The rate equation for 1-d_2 is eq 123, into which eq 119

$$\frac{\mathrm{d}[1\text{-}d_2]}{\mathrm{d}t} = k_2[2\text{-}d] = \frac{2k_a[1\text{-}d_2]}{3} \tag{123}$$

may be substituted to give eq 124, which is equivalent to eq 125. Substituting from eq 112 and 114 gives eq 126.

$$\frac{\mathrm{d}[1\text{-}d_2]}{\mathrm{d}t} = \frac{k_i k_a k_2[1]}{(k_i + k_2)^2} + \frac{5k_a k_2[1\text{-}d]}{6(k_i + k_2)} - \frac{2k_a[1\text{-}d_2]}{3} \tag{124}$$

$$\frac{\mathrm{d}f_2}{\mathrm{d}t} = \frac{k_a y f_0}{(y+1)^2} + \frac{5k_a f_1}{6(y+1)} - \frac{2k_a f_2}{3} \tag{125}$$

$$\frac{\mathrm{d}f_2}{\mathrm{d}t} = \frac{k_a y f_{00}}{(y+1)^2}e^{-k_a t} + \frac{5k_a^2 f_{00}}{6(k_a - C)(y+1)^2}(e^{-Ct} - e^{-k_a t}) - \frac{2k_a f_2}{3} \tag{126}$$

The present definition of C (as $5k_a/6$) permits transformation to eq 127. Rearrangement and multiplication by

$$\frac{\mathrm{d}f_2}{\mathrm{d}t} = \frac{k_a f_{00}(y-5)}{(y+1)^2}e^{-k_a t} + \frac{5k_a f_{00}}{(y+1)^2}e^{-Ct} - \frac{2k_a f_2}{3} \tag{127}$$

the integrating factor $e^{2k_a t/3}$ gives eq 128. This equation

$$\left(\frac{\mathrm{d}f_2}{\mathrm{d}t} + \frac{2k_a f_2}{3}\right)e^{2k_a t/3} = \frac{k_a f_{00}(y-5)}{(y+1)^2}e^{-k_a t/3} + \frac{5k_a f_{00}}{(y+1)^2}e^{-k_a t/6} \tag{128}$$

is exact and can be integrated and rearranged to give eq 129, in which Z is the integration constant. When $t = 0$,

$$f_2 = \frac{3f_{00}(5-y)}{(y+1)^2}e^{-k_a t} - \frac{30f_{00}}{(y+1)^2}e^{-5k_a t/6} + Ze^{-2k_a t/3} \tag{129}$$

$f_2 = f_{20}$, and eq 130 results. In our runs, f_{20} is essentially

$$Z = f_{20} + \frac{3f_{00}(y+5)}{(y+1)^2} \tag{130}$$

zero, and eq 129 becomes eq 131.

$$f_2 = \frac{3f_{00}}{(y+1)^2}[(5-y)e^{-k_a t} - 10e^{-5k_a t/6} + (5+y)e^{-2k_a t/3}] \tag{131}$$

Statistical Treatment of Data. Let us denote the variance–covariance matrix for a set of parameters as $\mathbf{M}_X$, which is defined in eq 132, where σ_{X_1} is the standard deviation of the first parameter (X_1) and ρ_{12} is the covariance of parameters 1 and 2. The equation shows that there are m parameters. Then $\mathbf{M}_X$ may be calculated, in the case of a nonlinear least-squares treatment, from eq 133, where

$$\mathrm{M}_X = \begin{vmatrix} \sigma_{X_1}{}^2 & \sigma_{X_1}\sigma_{X_2}\rho_{12} \cdots & \sigma_{X_1}\sigma_{X_m}\rho_{1m} \\ \sigma_{X_1}\sigma_{X_2}\rho_{12} & \sigma_{X_2}{}^2 & \vdots \\ \sigma_{X_1}\sigma_{X_m}\rho_{1m} & \cdots\cdots\cdots & \sigma_{X_m}{}^2 \end{vmatrix} \tag{132}$$

$$\mathbf{M}_X = (\mathbf{A}'\mathbf{M}_f\mathbf{A})^{-1} \tag{133}$$

$\mathbf{A}$ is the Jacobian matrix, $\mathbf{A}'$ is its transpose, and $\mathbf{M}_f$ is the variance–covariance matrix for the experimental observables.[32] That is, if there are n difference observables (C_1 through C_n), then $\mathbf{A}$ is defined in eq 134 and $\mathbf{M}_f$ in eq 135.

$$\mathrm{A} = \begin{vmatrix} \dfrac{\partial C_1}{\partial X_1} & \dfrac{\partial C_1}{\partial X_2} & \cdot\ \dfrac{\partial C_1}{\partial X_m} \\ \dfrac{\partial C_2}{\partial X_1} & \dfrac{\partial C_2}{\partial X_2} \cdots & \vdots \\ \dfrac{\partial C_n}{\partial X_1} \cdots\cdots & \vdots & \dfrac{\partial C_n}{\partial X_m} \end{vmatrix} \tag{134}$$

$$\mathrm{M}_f = \begin{vmatrix} \sigma_{C_1}{}^2 & \sigma_{C_1}\rho_{12} \cdots \sigma_{C_1}\sigma_{C_n}\rho_{1n} \\ \sigma_{C_1}\sigma_{C_2}\rho_{12} & \sigma_{C_2}{}^2 \quad \vdots \\ \sigma_{C_1}\sigma_{C_n}\rho_{1n} & \sigma_{C_n}{}^2 \end{vmatrix} \tag{135}$$

To use eq 133, the elements of the matrix $\mathbf{M}_f$ must be available. They were not in the present case and commonly are not. In such a case, if $\mathbf{M}_f$ is known within a scale factor, that is, if eq 136 holds, where $\mathbf{N}$ is known but σ^2

$$\mathbf{M}_f = \sigma^2\mathbf{N} \tag{136}$$

is unknown, $\mathbf{M}_X$ may still be estimated fairly reliably. We have assumed that the standard deviation of all the observables are the same in a given run. With this standard deviation, σ, all the diagonal elements of $\mathbf{N}$ become 1. Not having any reasonable basis for values of the correlation coefficients (p's), we took them all to be zero; that is, we set $\mathbf{N}$ equal to the unit matrix. This is just the Gauss method of least squares, which is commonly used. However, the neglect of the correlation coefficients appears to lead to particularly large errors where $\mathbf{M}_X$ is calculated. The estimated standard deviations of the parameters are considerably smaller than they would be if the correlation coefficients were known. This is believed to be the principal reason why rate constants calculated from pairs of runs under very similar conditions agree with each other much more poorly than would be expected from the standard deviations calculated from data obtained within given runs.

Registry No. 1, 2175-91-9; 1-d, 72610-65-2; 1-d_2, 72611-69-9.

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[32] Hamilton, W. C. "Statistics in Physical Science"; Ronald Press: New York, 1964; Sections 4-1 and 5-3.