column chromatography as described by Huisgen[10]) were calibrated *vs.* the standard.

Registry No.—2-Diazobenzophenone tetrafluoroborate, 14319-50-7; 2-(*o*-diazobenzoyl)naphthalene tetrafluoroborate, 14319-51-8; *p*-bromobenzenediazonium tetrafluoroborate, 14319-52-9.

Catalysis of α-Hydrogen Exchange. VII. Isobutyraldehyde-2-*d* Exchange in the Presence of Primary Amine Salts and Pyridine Buffers[1]

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The dedeuteration of isobutyraldehyde-2-*d* has been studied in the presence of pyridine buffers and the hydrochlorides of ten different primary amines. The principal term in the kinetic equation has the form $k[\mathrm{Me_2CDCHO}][\mathrm{C_5H_5N}][\mathrm{RNH_3^+}]$ and is believed to be due to the rate-controlling attack of pyridine on N-isobutylidenealkylammonium ions present in equilibrium with aldehyde and alkylammonium ions. With $\mathrm{RNH_3^+}$ such that R is primary, the catalytic efficiency tends to increase with increasing acidity (decreasing basicity of $\mathrm{RNH_2}$), but isopropyl- and *t*-butylammonium ions are less reactive than would be expected from their acidities. The effect of the structure of R on the reactivity is discussed in terms of the hybridization of and the charge on the nitrogen atom to which R is attached in the alkylammonium ion, the imine, and the transition state of the rate-controlling step and also in terms of steric factors.

In previous papers in his series the dedeuteration of isobutyraldehyde-2-*d* catalyzed by tertiary amines and oxygen bases has been studied[3] and evidence has been described that catalysis of this dedeuteration by methylammonium ions involves the intermediate formation of the conjugate acid of N-isobutylidenemethylamine, which is then attacked by base to give an enamine in the rate-controlling step of the reaction.[1b,4,5] In order to learn more about the effect of structure on reactivity in deuterium exchange *via* the iminium ion mechanism, we have studied the catalytic action of other amine hydrochlorides in the presence of pyridine buffers.

Results

The rate of loss of deuterium from isobutyraldehyde-2-*d* was followed by nmr measurements of the type used previously. Within any given run the reaction was found to obey the first-order rate equation (eq 1) where AD represents isobutyraldehyde-2-*d*.

$$-\frac{\mathrm{d[AD]}}{\mathrm{d}t} = k_\mathrm{p}[\mathrm{AD}] \qquad (1)$$

SCHEME I

$$\mathrm{Me_2CDCHO + B \xrightarrow{k_B} Me_2C{=}CHO^- + BD}$$

$$\mathrm{RNH_3^+ \overset{K_{RNH_3}}{\rightleftharpoons} RNH_2 + H^+}$$

$$\mathrm{Me_2CDCHO + RNH_2 \overset{K}{\rightleftharpoons} Me_2CDCH{=}NR + H_2O}$$

$$\mathrm{Me_2CDCH{=}NR + H^+ \overset{1/K_{IH}}{\rightleftharpoons} Me_2CDCH{=}NHR^+}$$

$$\mathrm{Me_2CDCH{=}NHR^+ + B \xrightarrow{k_B'} Me_2C{=}CHNHR + BD}$$

If the reaction mechanism given in Scheme I is operative and equilibrium between aldehyde and iminium ion is established rapidly relative to the deuterium exchange reaction, so that the steps governed by k_B and k_B' are rate controlling, then the first-order rate constants k_p obtained in individual runs may be expressed as in eq 2,[1b,3-5] where K is the equilibrium constant for the formation of the imine from aldehyde and amine, $K_\mathrm{RNH_3}$ is the acidity constant of the ammonium ion, K_IH is the acidity constant of the iminium ion, k_B is the rate constant for the attack of a given base on the deuterioaldehyde, and k_B' is the rate constant for the attack of the same base on the deuterioiminium ion. Unless otherwise stated, the rate and equilibrium constants used are not the "true" values based on the concentration of free aldehyde but are apparent constants based on the total concentration of aldehyde (free and hydrated).

$$k_\mathrm{p} = \sum_i k_{\mathrm{B}_i}[\mathrm{B_i}] + \frac{KK_\mathrm{RNH_3}[\mathrm{RNH_3^+}]}{K_\mathrm{IH}} \sum_i k_{\mathrm{B_i}}'[\mathrm{B_i}] \qquad (2)$$

In the current studies the bases in the solutions were pyridine, water, hydroxide ions, amine (the conjugate base of the ammonium salt used), isobutyrate ions (from isobutyric acid present as an impurity in the aldehyde used), and imine. It has already been shown that a plot of the logarithms of the rate constants for the attack of various bases on isobutyraldehyde-2-*d* *vs.* the logarithms of the rate constants for the attack of the same bases on the N-methyliminium ion of isobutyraldehyde-2-*d* gives a fairly straight line.[1b] We have assumed that one iminium ion will resemble another at least as much as either resembles an aldehyde and therefore that the relative reactivities of bases toward the iminium ions derived from isobutyraldehyde and any of the primary ammonium ions investigated will be about the same as toward the N-methyliminium ion. On the basis of this assumption and previous observations,[1b,3-5] it may be shown that catalysis by water, hydroxide ions, imine, and

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(1) (a) This investigation was supported in part by Public Health Service Grants 06829 MCB and AM 10378 from the National Institute of Arthritis and Metabolic Diseases. (b) For the preceding paper in this series, see J. Hine, J. Mulders, J. G. Houston, and J. P. Idoux, *J. Org. Chem.*, **32**, 2205 (1967).

(2) To whom all correspondence should be addressed: The Ohio State University, Columbus, Ohio 43210.

(3) J. Hine, J. G. Houston, J. H. Jensen, and J. Mulders, *J. Am. Chem. Soc.*, **87**, 5050 (1965).

(4) J. Hine, B. C. Menon, J. H. Jensen, and J. Mulders, *ibid.*, **88**, 3367 (1966).

(5) J. Hine, F. C. Kokesh, K. G. Hampton, and J. Mulders, *ibid.*, **89**, 1205 (1967).

TABLE I

DEUTERIUM EXCHANGE OF Me_2CDCHO IN THE PRESENCE OF PRIMARY AMINE HYDROCHLORIDES AND PYRIDINE BUFFERS AT 35° [a]

M	RNH_3^+	[Py]	$[PyH^+]$	10^6k_p, sec^{-1}	10^6k_{cor}, sec^{-1}	$10^6k_{cor}/[RNH_3^+]$
0.155	$EtNH_3^+$	0.206	0.282	5.86[b]	4.21	27.2
0.361	$EtNH_3^+$	0.226	0.262	12.9[b]	11.1	30.7
0.210	n-$PrNH_3^+$	0.226	0.262	13.3[b]	11.5	54.8
0.210	n-$PrNH_3^+$	0.475	0.175	27.5[b]	23.7	113
0.233	n-$BuNH_3^+$	0.226	0.262	16.3[b]	14.5	62.2
0.233	n-$BuNH_3^+$	0.475	0.175	33.3[b]	29.5	127
0.261	n-$BuNH_3^+$	0.079	0.262	6.13	5.49	21.0
0.325	n-$BuNH_3^+$	0.280	0.175	24.0	21.8	67.1
0.161	i-$PrNH_3^+$	0.206	0.282	2.85[b]	1.20	7.45
0.269	i-$PrNH_3^+$	0.206	0.282	3.57[b]	1.92	7.14
0.235	t-$BuNH_3^+$	0.525	0.175	6.50	2.34	9.96
0.327	t-$BuNH_3^+$	0.280	0.175	4.22	1.99	6.09
0.325	c-$C_3H_5NH_3^+$	0.280	0.175	120	118	363
0.325	c-$C_3H_5NH_3^+$	0.525	0.175	242	238	732
0.124	$MeOCH_2CH_2NH_3^+$	0.206	0.282	18.5[b]	16.9	136
0.310	$MeOCH_2CH_2NH_3^+$	0.206	0.282	44.7[b]	43.1	139
0.283	$MeO(CH_2)_3NH_3^+$	0.082	0.113	9.84[b]	9.17	32.4
0.283	$MeO(CH_2)_3NH_3^+$	0.206	0.282	25.2[b]	23.5	83.0
0.328	$EtOCOCH_2NH_3^+$	0.280	0.175	196	194	591
0.341	$EtOCOCH_2NH_3^+$	0.280	0.093	191[c]	189	554
0.686	$EtOCOCH_2NH_3^+$	0.280	0.093	385[c]	382	557
0.341	$EtOCOCH_2NH_3^+$	0.400	0.133	256[c]	252	739
0.686	$EtOCOCH_2NH_3^+$	0.400	0.133	523[c]	520	758
0.341	$EtOCOCH_2NH_3^+$	0.525	0.175	325[c]	321	941
0.686	$EtOCOCH_2NH_3^+$	0.525	0.175	672[c]	668	974
0.317	p-$O_2NC_6H_4CH_2NH_3^+$	0.280	0.175	213	211	666
0.317	p-$O_2NC_6H_4CH_2NH_3^+$	0.525	0.175	398	394	1243

[a] $[Me_2CDCHO]_0$ is 0.383 M unless otherwise noted. [b] $[Me_2CDCHO]_0$ is 0.319 M. [c] $[Me_2CDCHO]_0$ is 0.122 M.

isobutyrate ions should be negligible under the conditions used in our kinetic runs.

With the neglect of these four bases, eq 2 may be written in the form given by eq 3, where k_{cor} is defined

$$\frac{k_{cor}}{[RNH_3^+]} = \frac{k_a K_{RNH_3}}{[H^+]} + \frac{KK_{RNH_3}}{K_{IH}}\left(k_{Py}'[Py] + \frac{k_a' K_{RNH_3}[RNH_3^+]}{[H^+]}\right) \quad (3)$$

as $k_p - k_{Py}[Py]$, the subscript a refers to the amine RNH_2, and Py refers to pyridine.

In the presence of methylammonium chloride and pyridine buffers, reaction due to attack of free methylamine on the aldehyde or N-methyliminium ion never contributed more than 0.2% to the over-all reaction rate.[1b] It therefore seems unlikely that catalysis by the free amine will be significant in any of the present reactions in which we use the salt of a primary amine whose basicity is near that of methylamine. On going to less basic amines the fraction of amine salt present as free amine will increase by 10-fold for every 10-fold decrease in amine basicity (over the range of basicities we have studied). Since the Brønsted β for the reaction studied is only about 0.5, the catalytic activity of the amine will decrease by only about $\sqrt{10}$-fold for every 10-fold decrease in basicity. Therefore the increasing concentration factor will outweigh the decreasing reactivity so that the extent of catalysis by free amine should increase with decreasing basicity of the amine. We have therefore sought evidence for such catalysis with the ethyl ester of glycine, the weakest base of the primary amines we have studied. Since most of the reaction, under the conditions we have used, proceeds through the iminium ion, catalysis due to the free amine will appear largely in the k_a' term of eq 3. According to this equation, the value of $k_{cor}/[RNH_3^+]$ at a given pH and pyridine concentration should be a constant if the k_a' term is negligible, but it should increase with increasing concentration of amine salt if the k_a' term is significant.

The results in Table I show that in the presence of 3:1 pyridine–pyridine hydrochloride buffers with three different concentrations, an increase in the concentration of glycine ethyl ester hydrochloride from 0.341 to 0.686 M results in increases of 3.5, 2.6, and 0.5% in $k_{cor}/[RNH_3^+]$. Although these results suggest a slight contribution from a k_a' term, the observed increases are no larger than the uncertainty in the rate constants. Therefore catalysis by the free amine was neglected in this case and also in the case of all the other amine salts studied, where such catalysis should comprise an even smaller fraction of the over-all reaction. Equation 3 is thereby reduced to eq 4.

$$\frac{k_{cor}}{[RNH_3^+]} = \frac{KK_{RNH_3}k_{Py}'[Py]}{K_{IH}} \quad (4)$$

Discussion

According to eq 4, division of the entries in the last column of Table I by the concentration of pyridine should yield a value of $KK_{RNH_3}k_{Py}'/K_{IH}$ for the amine salt in question. In Table II the average values thus obtained and the average deviations from them are listed, with the value obtained previously[1b] for methylammonium ions. These values are rate constants for exchange *via* the iminium ion mechanism (the last four steps of Scheme I, with the last step rate controlling). In order to see if there is a relationship between these over-all rate constants and the electron-withdrawing power of R, log $(KK_{RNH_3}k_{Py}'/K_{IH})$ was plotted against log K_{RNH_3}, as shown in Figure 1.

TABLE II
KINETIC CONSTANTS FOR VARIOUS PRIMARY AMMONIUM IONS

Ion	$10^6KK_{RNH_3}k_{Py}'/K_{IH}$	K	$10^{11}K_{RNH_3}$[a]	k_{Py}'/K_{IH}
$MeNH_3^+$	170[b]	4950[c]	4.90[d]	710
$EtNH_3^+$	134 ± 3	3490[c]	4.90[d]	780
n-$PrNH_3^+$	240 ± 3	4180[c]	6.14[d]	940
n-$BuNH_3^+$	262 ± 12	4030[c]	5.75[d]	1130
i-$PrNH_3^+$	35.4 ± 0.9	1840[c]	6.20[c]	310
t-$BuNH_3^+$	20.4 ± 1.4	199[c]	4.50[d]	2280
c-$C_3H_5NH_3^+$	1340 ± 60		125[e]	
$MeOCH_2CH_2NH_3^+$	668 ± 8	2020[f]	91[f]	360
$MeO(CH_2)_3NH_3^+$	399 ± 4	3550[f]	14.3[f]	790
$EtOCOCH_2NH_3^+$	1920 ± 90		3800[g]	
p-$O_2NC_6H_4CH_2NH_3^+$	2370 ± 10		612[f]	

[a] At 35° and zero ionic strength. [b] Data from ref 1b. [c] Data from ref 7. [d] Calculated as described in ref 7. [e] Determined in the present investigation. [f] Data from ref 8. [g] Calculated from the value at 25° [h] and Perrin's method of temperature correction.[i] [h] D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworth and Co., Ltd., London, 1965, p 384. [i] D. D. Perrin, *Australian J. Chem.*, **17**, 484 (1964).

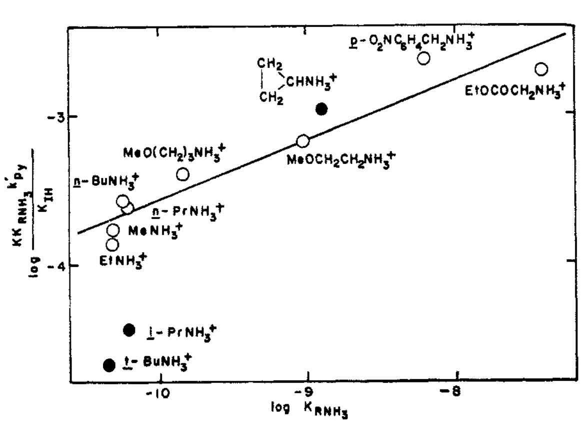
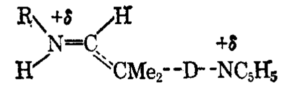


Figure 1.—Log–log plot of over-all rate constants for catalysis of dedeuteration of isobutyraldehyde-2-*d* *via* the iminium ion mechanism by RNH_3^+ *vs.* the acidity constants of RNH_3^+: ○, primary R.

The line shown is the best straight line through the points for which R is primary, as calculated by the method of least squares. The average deviation of the points from the line is 0.11 and the slope of the line is 0.40. The positive slope shows that the rate is increased by electron-withdrawing substituents in R and hence that the group to which R is attached in the reactant is more electron withdrawing than the group to which it is attached in the transition state. In the reactant, R is attached to NH_3^+. The transition state has a structure of type A in which R is attached to a



$$\overset{+\delta}{R-N}(H)=C(H)\text{-}CMe_2\cdots D\cdots \overset{+\delta}{NC_5H_5}$$

A

nitrogen atom with only a partial positive charge on it but with hybridization near sp^2, a factor that would make it more electron withdrawing than an sp^3-hybridized nitrogen atom. Apparently the decreased positive charge on the transition-state nitrogen atom more than offsets its increased sp^2 character. Inasmuch as the Taft ρ^* constant for the acidity of primary ammonium ions is 3.14,[6] the slope 0.40 of the line in Figure 1 corresponds to a ρ^* value of (0.40)(3.14) or 1.26.

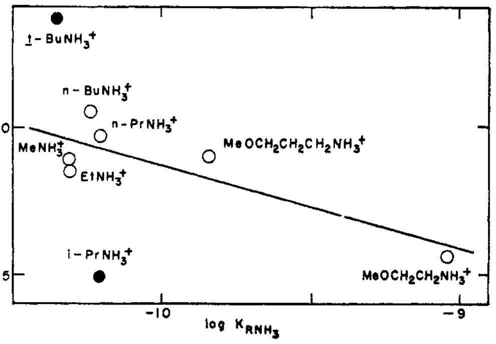
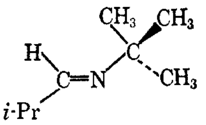


Figure 2.—Plot of log (k_{Py}'/K_{IH}) *vs.* log K_{RNH_3}: ○, primary R.

The points for isopropyl- and *t*-butylammonium ions lie considerably below the line for primary ammonium ions. We believe that this is because the catalytic activity of these ions is decreased by steric effects.

It would be desirable to learn the effect of structure on reactivity in each of the four individual steps of the reaction whose over-all rate constants we are considering. The first step is just the action of ammonium ions as acids, which has been discussed frequently, and the second step is imine formation, which is discussed elsewhere,[7,8] but no data are available on the third step, the action of isobutyraldimines as bases. Nevertheless for eight of the primary ammonium ions studied it is possible to divide $KK_{RNH_3}k_{Py}'/K_{IH}$ by KK_{RNH_3} to obtain values of k_{Py}/K_{IH}. k_{Py}'/K_{IH} is the rate constant for dedeuteration of the imine *via* its conjugate acid, *i.e.*, the rate constant for the combined last two steps of Scheme I. These values are plotted against log K_{RNH_3} in Figure 2 and the points for ions with primary R groups are found to deviate by an average of 0.07 from the least-squares line, whose slope is -0.28, corresponding to a ρ^* value of -0.88. Apparently the partially positive, largely sp^2-hybridized nitrogen to which R is attached in the transition state is more electron withdrawing than the imine nitrogen to which R is attached in the reactant.

The large reactivity of the *t*-butyl compound, relative to compounds with primary R groups and about the same basicity, may well be due to relief of the strain caused by repulsions between the carbimino hydrogen atom and the nearby methyl group that is eclipsed with the carbon–nitrogen double bond. Evidence for such



$$(i\text{-}Pr)(H)C=N-C(CH_3)_3$$

strain was found in the effect of structure on the equilibrium constants for the formation of isobutyraldimines and on the nmr spectra of these imines.[7] The lengthening of the carbon–nitrogen double bond to a single bond that accompanies the dedeuteration of the iminium ion will certainly tend to decrease this strain and there may be other changes in molecular geometry that also have effect. Such a relief of strain should not be important in any other case since none of the other imines would exist to a significant extent in a conformation that placed an alkyl group so near the carbimino hydrogen atom. The deviation of the point for isopropylam-

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(6) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **79**, 5441 (1957).

(7) J. Hine and C. Y. Yeh, *ibid.*, **89**, 2669 (1967).

(8) C. Y. Yeh, unpublished experiments.

monium ions from the line for primary R groups is probably due to some type of steric effect, but we have no convincing detailed explanation for this deviation or for the smaller deviations by the other points.

Experimental Section

The kinetics of the dedeuteration of isobutyraldehyde-2-*d* were studied by nmr measurements of the type described previously, in which the reactions were stopped by the addition of hydrochloric acid and the reaction mixtures extracted with chloroform.[3-5]

In order to learn whether any significant amount of isobutyraldehyde was present in the form of imine or iminium ion rather than aldehyde or aldehyde hydrate, measurements were made on glycine ethyl ester hydrochloride, the most strongly acidic amine salt used and therefore the one for which the largest fraction of free amine will be present (at a given pH) to transform aldehyde to imine. An acetate buffer was used to give a pH of 5.7, as basic as the most basic of the kinetic reaction solutions. The presence of the glycine ethyl ester hydrochloride in various concentrations up to 0.34 *M* in 0.122 *M* solutions of isobutyraldehyde was found to have no detectable effect on the absorbance at the 2850-A aldehyde maximum (at which the hydrochloride absorbs negligibly). It was therefore concluded that less than 1% of the aldehyde was transformed to the imine or iminium ion (neither of which should absorb significantly at 2850 A) under these conditions.

p*K* Measurements.—Potentiometric measurements at 35° were made as described previously[3-5] to determine that pK_a for *p*-nitrobenzylammonium chloride is 8.240 and 8.260 at ionic strengths 0.0029 and 0.0050 *M* and pK_a for cyclopropylammonium chloride is 8.911, 8.914, and 8.944 at ionic strengths 0.034, 0.049, and 0.164 *M*. Values extrapolated to zero ionic strength are 8.21 and 8.90, respectively.

Registry No.—Isobutyraldehyde-2-*d*, 4303-51-9.

Acknowledgment.—We wish to acknowledge our indebtedness to the National Science Foundation for grants that permitted the purchase of the nmr spectrometers used in this investigation.

Electron Spin Resonance Studies of Substituent Effects. II. Diaryl Nitroxides[1]

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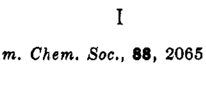
Six *para* and four *meta* symmetrically substituted diaryl nitroxides were formed by photolysis of the corresponding nitroso compounds. The nitrogen hyperfine splitting constants (hfsc's) give a good correlation with σ, but for substituents which withdraw electrons strongly by resonance a better correlation is obtained with σ^-. Substituent effects on hfscs were surveyed for a variety of aromatic radicals. Charged radicals appear to be more sensitive to substituent than uncharged radicals. Almost all results indicate that in radical systems the *p*-F substituent has a slight electron-supplying effect.

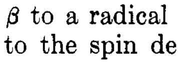
Electron spin resonance spectroscopy offers a convenient method of measuring substituent effects on electron density, for the hyperfine splitting constant (hfsc) of a nucleus is related to unpaired electron densities. Since the Hammett σ constant is interpreted as a measure of the substituent effect on electron density at an atom,[3] it is desirable to learn if the substituent effect on nuclear hfscs in aromatic free radicals relates in any manner to the σ constant. Recently, it was found that methyl hfsc's in *meta*- and *para*-substituted 1-phenyl-1,2-propanesemidiones give a correlation with σ constants derived from the ionization of benzoic acids.[1] Sixteen substituents of the twenty-one studied were found to be "well behaved;" *i.e.*, they give an excellent correlation with σ constants. These were *m*-CN, *m*-CF_3, *m*-Br, *m*-Cl, *p*-Br, *p*-Cl, *m*-OCH_3, *p*-H, *m*-CH_3, *m*-NH_2, *p*-CH_3, *p*-$C(CH_3)_3$, *p*-NH_2, and *m*-O^-. The five "ill-behaved" substituents were *p*-CN, *p*-CF_3, *p*-Ph, *p*-F, and *p*-$N(CH_3)_2$. Here we present results in another system.

Of primary concern is the recognition of conditions where the properties of a free radical will follow a Hammett relationship. In radicals of the type I,

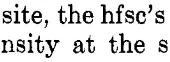


I

it is found that both electron-withdrawing and electron-supplying groups decrease the nitrogen hfsc, A^N.[4] The criterion for determining whether an aromatic radical will follow a Hammett relationship has been stated by Walter[4] as follows. For a functional group F with a substituent X, if resonance structures can be drawn with an unpaired electron (II) and an unshared



II



III

electron pair (III) on the atom *para* to the site of substitution, then the system will exhibit Hammett behavior.

Even if electron distribution within a system follows a Hammett relationship, however, in radicals this fact must be detected by measuring a nuclear hfsc. For protons α or β to a radical site, the hfsc's are directly proportional to the spin density at the site,[5] but for nuclei which supply orbitals to the π system, the hfsc is also a function of the spin density at the adjoining atoms.[6] For an atom X attached to three other atoms Y_1, Y_2, and Y_3, the hfsc is given by expression IV

$$A^{X} = Q_{X}^{X}\rho_{X} + \sum_{i=1}^{3} Q_{X}^{Y_i}\rho_{Y_i}$$

IV

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[1] E. T. Strom, *J. Am. Chem. Soc.*, **88**, 2065 (1966), is to be considered part I of the series.

[2] Author to whom inquiries should be sent at the Mobil Oil Corp., Field Research Laboratory, Dallas, Texas 75221.

[3] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp 186–194.

[4] R. I. Walter, *J. Am. Chem. Soc.*, **88**, 1923 (1966).

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[6] M. Karplus and G. K. Fraenkel, *J. Chem. Phys.*, **35**, 1312 (1961).