peroxyoxalyl chloride in 20 ml. of pentane at 0°. After working up as in method I, 1.8 g. (54%) of ethyl *t*-butylperoxyoxalate was obtained which was identical by infrared analyses to that prepared by method I.

Anal. Calcd. for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.86; H, 7.54.

Benzyl *t*-Butylperoxyoxalate.—To 8.3 g. of *t*-butyl peroxyoxalyl chloride in 40 ml. of anhydrous ether at 0° was added dropwise over one hour a solution of 4.0 g. of benzyl alcohol and 3.0 g. of pyridine in 40 ml. of ether. After stirring at 0° for 15 minutes longer the mixture was washed with 10% sulfuric acid solution, 10% sodium carbonate solution and with water. Drying and evaporation of the ether left 5.8 g. (62%) of oily residue which crystallized on shaking. After slow recrystallization with seeding from pentane between room temperature and −25° the fine white crystals melted at 33.0–34.2° at a heating rate of 2 degrees per minute. This perester was 88.8% pure by peroxide titration. The use of an excess of the acid chloride in this preparation makes the purification of the product easier since the excess is converted to water-soluble compounds on hydrolysis.

Anal. Calcd. for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39. Found: C, 61.89; H, 6.22.

***p*-Methoxybenzyl *t*-Butylperoxyoxalate.**—*t*-Butylperoxyoxalyl chloride, 8.2 g., reacted with 3 g. of pyridine and 5.2 g. of anisyl alcohol in anhydrous ether at 0°. After working up by washing as usual, 7.7 g. (72%) of a thick oil was obtained. The compound failed to crystallize but titrated 87.4% pure. It was insoluble in pentane at room temperature, soluble in benzene and carbon tetrachloride and separated from cyclohexane as an oil when the solution was cooled.

Anal. Calcd. for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43. Found: C, 59.43; H, 6.78.

***p*-Nitrobenzyl *t*-Butylperoxyoxalate.**—*t*-Butylperoxyoxalyl chloride, 8.6 g., in 40 ml. of ether was cooled to 0° and a solution of 6.1 g. of *p*-nitrobenzyl alcohol and 3.2 g. of pyridine in about 100 ml. of ether was added over 45 minutes. After stirring at 0° for an hour and working up as usual the ether was evaporated under vacuum to leave a white solid residue. This was recrystallized from 50% pentane–ether to yield 4.5 g. (38%) of white fluffy needles with melting point 62.5–64° at a heating rate of 1 degree per minute. More perester can be recovered from the mother liquors. Peroxide titration indicated 91.4% purity. This compound was stable when rubbed with a spatula and a sample of it appeared to be stable at room temperature for over two weeks.

Anal. Calcd. for $C_{13}H_{15}O_7N$; C, 52.52; H, 5.09. Found: C, 52.38; H, 5.12.

Kinetic and Product Study Procedures.—The general procedure for kinetic and product studies was as described in Part V.

Acknowledgment.—We thank the National Science Foundation for a research grant and for a predoctoral fellowship to one of us.

CAMBRIDGE 38, MASS.

[CONTRIBUTION NO. 46 FROM THE GRADUATE DEPARTMENT OF BIOCHEMISTRY, BRANDEIS UNIVERSITY]

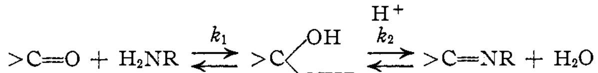
The Effect of Structure on Reactivity in Semicarbazone Formation[1]

BY BRUCE M. ANDERSON AND WILLIAM P. JENCKS

RECEIVED JULY 23, 1959

The rate and equilibrium constants for the individual steps of semicarbazone formation from a series of substituted benzaldehydes exhibit linear ρ–σ correlations: the rate and equilibrium constants of the addition step are favored by electron withdrawal and the acid-catalyzed dehydration step is favored by electron-donating substituents. The observed rate constants for semicarbazone formation at neutral *p*H are the resultant of these opposing effects and show only a slight variation with σ. At acid *p*H the rate constants increase with electron-withdrawing substituents, as expected for a shift to a rate-limiting addition step, and at an intermediate *p*H there is a break in the ρ–σ curve. Semicarbazone formation from carbonyl compounds with electron-withdrawing substituents is also subject to base catalysis, which may prove to be a useful preparative method.

In a recent study of oxime and semicarbazone formation,[2] evidence was presented in support of the reaction path



$$>C{=}O + H_2NR \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} >C\begin{matrix}OH\\NHR\end{matrix} \underset{k_{-2}}{\overset{H^+ \atop k_2}{\rightleftarrows}} >C{=}NR + H_2O$$

In the case of semicarbazone formation at neutral *p*H, the first step in the reaction is the rapid attack of the nitrogen base upon the carbonyl compound to form an intermediate addition compound. The second step is the rate-limiting, acid-catalyzed dehydration of the intermediate addition compound to form semicarbazone. Methods were described for the determination of the separate rate and equilibrium constants for these reactions. It was of interest to examine the electronic effects upon the individual steps by studying the reactions of a series of substituted benzaldehydes. The present report describes ρ–σ relationships for the individual steps in the formation of semicarbazones and a base catalysis of semicarbazone formation from benzaldehydes substituted with electron-withdrawing groups.

Experimental

Materials.—The carbonyl compounds were either redistilled under nitrogen at reduced pressure or twice recrystallized and were stored at −15°. Solutions of the carbonyl compounds in 25% ethanol containing 10^{-4} *M* ethylenediaminetetraacetic acid were made up just before use. Solutions of twice-recrystallized semicarbazide hydrochloride were neutralized with NaOH just before use. Glass-distilled water was used throughout. Solutions of semicarbazide in D_2O were prepared by dissolving semicarbazide hydrochloride in 99.8% D_2O, evaporating to dryness, and redissolving in D_2O at the desired concentration. The D_2O solutions of semicarbazide hydrochloride were neutralized with NaOD prepared by a similar procedure.

Ultraviolet measurements were made on a Beckman model DU spectrophotometer or a Zeiss model PMQ II spectrophotometer. Infrared spectra were obtained with a Perkin–Elmer model 21 spectrophotometer using KBr pellets.

Kinetic measurements were carried out spectrophotometrically as previously described.[2] All kinetic determinations were made with the concentration of semicarbazide greatly in excess of that of the carbonyl compound so that pseudo first-order kinetics were obtained. The reactions were studied in 25% ethanol (25 vol. ethanol–75 vol. water) and NaCl was used to maintain a constant ionic strength of

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[1] Presented at the 135th National Meeting of the American Chemical Society in Boston, Mass., April, 1959.

[2] W. P. Jencks, THIS JOURNAL, **81**, 475 (1959).

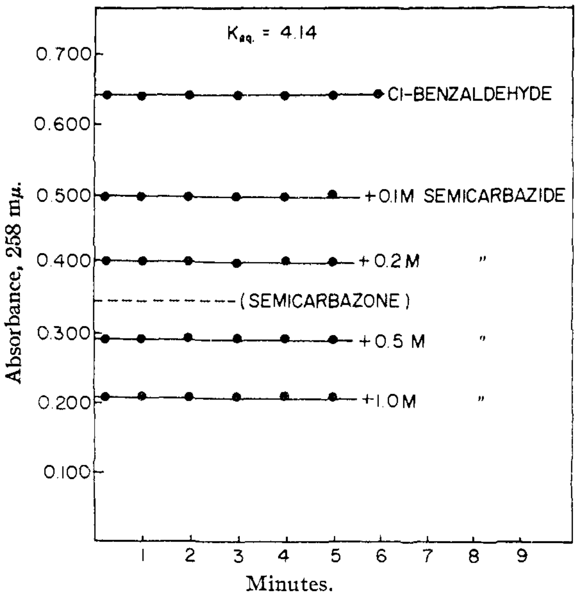

Fig. 1.—Change in absorbance of *p*-chlorobenzaldehyde after addition of increasing concentrations of semicarbazide. The reaction mixtures contained 3.33×10^{-5} *M* *p*-chlorobenzaldehyde, 0.03 *M* potassium phosphate buffer, *p*H 8.0, in 25% ethanol with constant ionic strength, 0.34, maintained with NaCl.

0.32 in reactions in which the concentration of semicarbazide was varied. A 0.01 *M* potassium phosphate buffer was used in all reaction mixtures above *p*H 6.0. Rates were followed at a wave length corresponding to the absorption maximum of the semicarbazone being studied. First-order rate constants, k_1, were calculated, using the formula $k_1 = (0.693/t_{1/2})$, from the half-times of reaction which were determined graphically from plots of the extent of the reaction, $x_\infty - x_t$, against time on semi-logarithmic graph paper. Second-order rate constants, k_2, for the acid-catalyzed dehydration step were calculated from the observed first-order rate constants and the equilibrium constants of the addition step using the formula $k_2 = k_{obs}/[H^+][\alpha]$ where α = the fraction of carbonyl compound converted to addition compound. The observed rate constants were determined at two different hydrogen ion concentrations between *p*H 6.0 and 7.0 and for two or more concentrations of semicarbazide at each *p*H. The *p*H values reported are the apparent *p*H as measured with the glass electrode of the Beckman model G *p*H meter. The ρ–σ relationships for rate and equilibrium constants were plotted by the method of least squares.

Equilibrium constants for the formation of the addition compounds of semicarbazide with a series of substituted benzaldehydes were determined by measuring the initial decrease in carbonyl absorption after the addition of semicarbazide at *p*H 8.0. No extrapolation to zero time was necessary since the subsequent dehydration of the addition compound to form semicarbazone is extremely slow at this *p*H. The fraction of the carbonyl compound converted to addition compound (α) was obtained from the fraction of the total possible decrease in carbonyl absorption (on complete conversion to addition compound) which was observed at a given semicarbazide concentration. The absorption of the addition compounds, obtained by extrapolation of the residual carbonyl absorption at high semicarbazide concentrations to infinite semicarbazide concentration, was found to be negligible at the wave lengths used for all compounds except the *m*- and *p*-nitrobenzaldehyde derivatives. Equilibrium constants were calculated from measurements in triplicate at 8–10 different semicarbazide concentrations such that 25–75% of the aldehyde was converted to addition compound, using the formula $K_{eq} = [\alpha]/[1 - \alpha][\text{base}]$. A typical experiment is shown in Fig. 1. With the addition of increasing concentrations of semicarbazide, the carbonyl absorption decreases and the absorption remains constant with time indicating that no significant dehydration to the semicarbazone is taking place. The dotted line in Fig. 1 represents the absorption at 258 mμ of an equivalent amount of *p*-chlorobenzaldehyde semicarbazone. From these data a value of 4.14 was calculated for the equilibrium constant of the addition step of the reaction of semicarbazide with *p*-chlorobenzaldehyde. In the same manner, equilibrium constants were obtained for the addition reactions of semicarbazide and a series of substituted benzaldehydes.

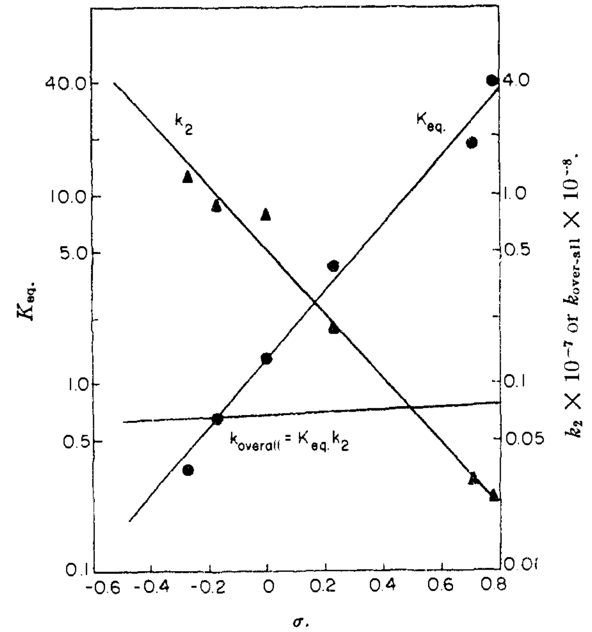

Fig. 2.—Log K_{eq}, for semicarbazide addition compound formation; log k_2, for dehydration of addition compound; and log $k_{over\text{-}all} = k_{obs}/[H^+]$, for semicarbazone formation at neutral *p*H, plotted against Hammett's σ-function.

Preparation of Semicarbazone under Alkaline Conditions.—*p*-Chlorobenzaldehyde semicarbazone was prepared from *p*-chlorobenzaldehyde in 1 *M* KOH solution containing 50% ethanol and 4-fold excess of semicarbazide. The reaction proceeds rapidly at 30° and the yield of semicarbazone is comparable to that obtained under acidic conditions. Samples of *p*-chlorobenzaldehyde semicarbazone prepared under acidic and basic conditions and recrystallized from 70% ethanol showed m.p. and mixed m.p. of 227–228° and identical infrared spectra.

Results and Discussion

The equilibrium and rate constants obtained for the individual steps of semicarbazone formation at neutral *p*H are given in Table I. The equilibrium constants for the formation of semicarbazide addition compounds show a linear logarithmic correlation with Hammett's substituent constants, σ, with a ρ value of 1.81 (Fig. 2). The semicarbazide addition compounds are therefore stabilized, relative to the starting benzaldehyde with its electron-withdrawing carbonyl group, by electron-withdrawing substituents. In contrast, the rates of acid-catalyzed dehydration, the slow step at neutral *p*H, show an almost equal and opposite ρ-value of -1.74, indicating that this step is aided by electron donation to the reaction center. Since the over-all rate of semicarbazone formation in dilute solution at neutral *p*H depends on both the equilibrium constant for addition compound formation and the rate constant for its dehydration, these two substituent effects effectively cancel each other and the observed rates show almost no variation with changing substituents (ρ = 0.07,

TABLE I

EQUILIBRIUM AND RATE CONSTANTS FOR THE INDIVIDUAL STEPS OF SEMICARBAZONE FORMATION FROM A SERIES OF SUBSTITUTED BENZALDEHYDES IN 25% ETHANOL AT 25.0°

Sub-stituent group	K_1, l. mole^{-1a}	$k_2 \times 10^{-6}$, l. mole^{-1} min.$^{-1b}$	k_1, min.$^{-1c}$	σ^d
p-CH$_3$O	0.34	12.9	0.157	−0.268
p-CH$_3$	0.62	9.1	.195	− .170
H	1.32	8.2	.304	.000
p-Cl	4.14	2.1	.347	.227
m-NO$_2$	18.3	0.31	1.02	.710
p-NO$_2$	40.1	0.24	1.50	.778

[a] K_1 = [RCH(OH)NHR']/[RCHO][H$_2$NR']. [b] $k_2 = k_{obs}/[H^+]$ (fraction as complex). [c] $k_1 = k_{obs}$ at pH 1.75 in 0.02 M semicarbazide. [d] Reference 3.

Fig. 2). A similar relationship recently has been reported by Leisten for acid-catalyzed amide hydrolysis.[4]

The ρ–σ relationship for the rates of semicarbazone formation at pH 1.75 (Fig. 3), in marked contrast to that at neutral pH, shows that in acid solution there is a significant increase in rate with electron-withdrawing substituents; the ρ-value for the observed rates under these conditions is 0.91. It has previously been suggested that the addition of semicarbazide to the carbonyl compound becomes the rate-limiting step of semicarbazone formation in acid solution, as the rate of acid-catalyzed dehydration becomes very fast and the concentration of attacking base is decreased by conversion to its conjugate acid.[2] Since substituent effects on the transition state for semicarbazide addition should be similar to those on the equilibrium constants for addition compound formation, these substituent effects are consistent with, and provide further support for, such a shift in the rate-limiting step in acid solution.

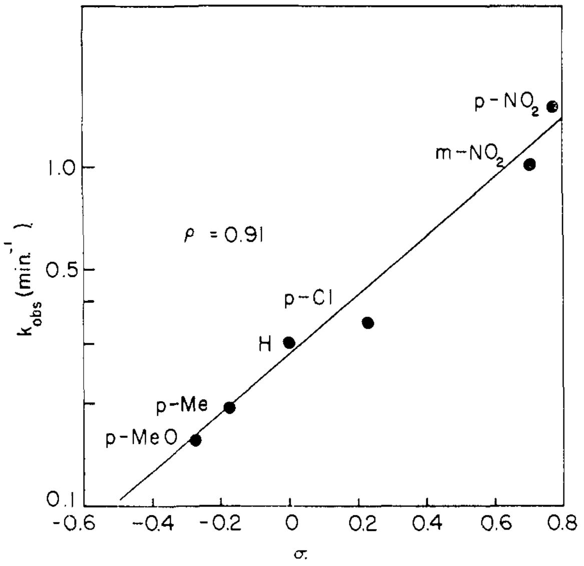

Fig. 3.—Log k_1, for semicarbazide addition compound formation at pH 1.75, plotted against Hammett's σ-function.

It has frequently been suggested that reactions with multiple mechanisms or steps may not show linear $\rho - \sigma$ relationships. These two cases should be clearly distinguished: a shift in mechanism introduces a new reaction path and results in a rate minimum in a ρ–σ plot, as is well known for a number of reactions (*cf.* ref. 5). A multi-step reaction, on the other hand, may show a ρ–σ relationship which is convex upward, resulting in a break in the curve or a rate maximum. Noyce, Bottini and Smith have reported that the rates of semicarbazone formation do not show a linear ρ–σ relationship and have interpreted their results on the basis of a balance of opposing substituent effects on the individual steps of the reaction,[6] and Santerre, *et al.*, have proposed a similar explanation for the rate maximum observed in Schiff base formation with substituted benzaldehydes.[7] The multi-step nature of a reaction alone does not result in a non-linear ρ–σ plot (Fig. 2 and ref. 4). The shift in the ρ-value for the observed rates of semicarbazone formation from 0.07 at neutral pH to 0.91 at acid pH, as the rate-limiting step of the reaction changes from dehydration to addition, suggested that at an intermediate pH a transition in the rate-limiting step might be observed at constant pH but with varying substituents. This was found to be the case at pH 3.9 (Fig. 4); a sharp break occurs in the curve at σ = 0, similar to that observed by Noyce, *et al.*[6] A shift in the rate-limiting step may also result in a maximum in the rate as a function of pH[2]; such maxima were observed for the over-all rates of semicarbazone formation from p-nitro-, p-chloro- and p-methylbenzaldehydes in 0.01 M semicarbazide between pH 3.0 and 4.0.

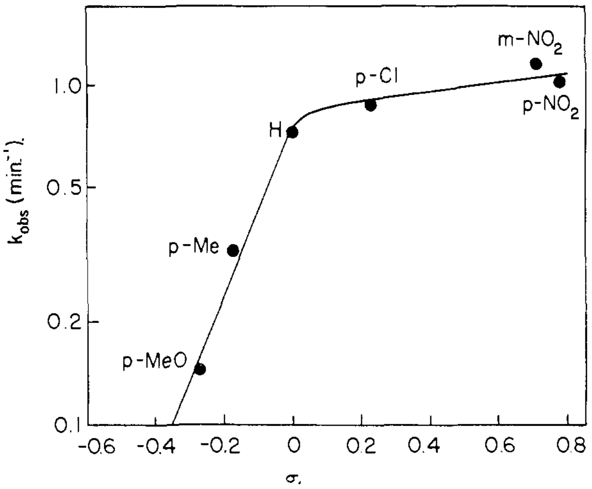

Fig. 4.—Log k_{obs}, for semicarbazone formation at pH 3.9, plotted against Hammett's σ-function.

A number of carbonyl reactions with structural requirements similar to the addition step of semicarbazone formation show similar substituent effects. Previously reported values of ρ for such reactions include 2.33 for the rate of cyanohydrin formation, 2.23 for basic ester hydrolysis, −1.49 for cyanohydrin dissociation equilibrium and 1.60

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[3] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

[4] J. A. Leisten, *J. Chem. Soc.*, 765 (1959).

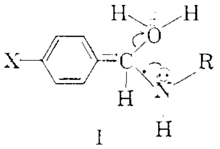
[5] H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953).

[6] D. S. Noyce, A. T. Bottini and S. G. Smith, *J. Org. Chem.*, **23**, 752 (1958).

[7] G. M. Santerre, C. J. Hansrote, Jr., and T. I. Crowell, THIS JOURNAL, **80**, 1254 (1958), and references therein.

for reduction of substituted acetophenones[5]; these may be compared to the values of 1.81 and 0.91 reported here for the equilibrium and rate constants, respectively, for semicarbazide addition compound formation. The relatively small value for the latter reaction suggests that the measured rate at *p*H 1.75 includes a significant component of an acid-catalyzed reaction which, like other acid-catalyzed reactions, is relatively insensitive to substituent effects. The steeper slope of that part of the ρ–σ plot which represents rate-limiting addition at *p*H 3.9 (Fig. 4) and the known specific and general acid catalysis of the addition of semicarbazide to furfural[2] support this interpretation.

Although the acid-catalyzed dehydration reaction may be regarded as an electrophilic side-chain reaction, plots of the rates of this step against substituent constants for reactions in which electron donation to the reaction center by resonance is important[8] did not give more satisfactory results; the deviations shown in Fig. 2, in fact, are in the opposite direction from those which would be expected if such resonance were important. This suggests that in the dehydration step electron donation from the benzene ring is transmitted principally by inductive effects and that electron donation from nitrogen to the developing double bond is of overriding importance (I).



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The rate and equilibrium constants for semicarbazone formation from *p*-chlorobenzaldehyde in water and in deuterium oxide are compared in Table II. There is no apparent deuterium isotope effect on the equilibrium constant for the formation of the addition compound. The rate constants for the acid-catalyzed dehydration step were determined in phosphate buffers and were calculated using the value of 3.62 for the ratio $K_{H_2PO_4^-}/K_{D_2PO_4^-}$ obtained by Rule and LaMer.[9] Although the observed rates at a given buffer composition are faster in H_2O than in D_2O, this is due to the greater acid strength of the phosphate buffer in H_2O, and when corrected for this effect the rate constants are some twofold greater in D_2O. Such an increase in rate in deuterium oxide is typical of a specific acid-catalyzed reaction,[10] but does not rule out the possibility of an additional general acid-catalyzed reaction path. A small contribution of such a reaction path is, in fact, suggested by a 33% increase in the observed reaction rate, from 0.042 to 0.056 min.$^{-1}$, as the concentration of phosphate buffer, *p*H 7.0, was increased from 0.01 to 0.10 *M* at a constant ionic strength of 0.40. The absence of a rate decrease in deuterium oxide as well as the *p*H–rate profile in the neutral region suggest that the primary source of electrons for expulsion of water is the free electron pair of the nitrogen atom and that little or no breaking of the N–H bond has occurred in the transition state I.

TABLE II

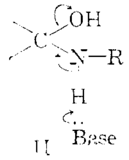
DEUTERIUM ISOTOPE EFFECTS ON THE RATE AND EQUILIBRIUM CONSTANTS OF SEMICARBAZONE FORMATION FROM *p*-CHLOROBENZALDEHYDE

	H_2O	97.8% D_2O	k_{H_2O}/k_{D_2O}
$K_{eq.}$ l. mole^{-1}	3.86	3.94	0.98
$k_{over-all}$, min.$^{-1a}$	0.408	0.211	1.97
k_2, l. mole^{-1} min.$^{-1b}$	2.37×10^6	4.47×10^6	0.53

[a] Determined in a 0.02 *M* potassium phosphate buffer, *p*H 6.0 in water, containing 0.05 *M* semicarbazide and KCl to maintain an ionic strength of 0.34. These reactions were run in triplicate. [b] Calculated from the over-all rate constants and the ratio of acid dissociation constants, $K_{H_2PO_4^-}/K_{D_2PO_4^-} = 3.62$ (ref. 9).

Price and Hammett,[11] Craft and Lester,[12] and Fitzpatrick and Gettler[13] have shown that variations of the observed rates of semicarbazone and oxime formation in a series of carbonyl compounds reflect large differences in the entropies as well as the enthalpies of activation, and Cross and Fugassi[14] have shown that although the over-all rates of semicarbazone formation from a series of substituted acetophenones show a relatively small increase with electron-withdrawing substituents, this is the resultant of opposing larger substituent effects on the enthalpies, which increase with increasing electron withdrawal, and on the entropies of the reaction. Since the enthalpy of an addition reaction to the carbonyl group would be expected to decrease with electron-withdrawing substituents,[15] it is probable that this enthalpy change is due to the dehydration step and that the compensating change in entropy reflects principally the equilibrium formation of addition compound. It will clearly be of great interest to determine the effects of substituents on these thermodynamic parameters for the individual steps of reactions of this kind.

Base-catalyzed Semicarbazone Formation.—Although semicarbazone formation is not generally considered to be a base-catalyzed reaction, it might be expected that a molecule of base could remove a proton from the nitrogen atom of the addition compound and effect the dehydration



II

step by expulsion of hydroxide ion; an indication of such a base-catalyzed dehydration was found by Conant and Bartlett in the reaction of cyclohexanone.[16] Such a base-catalyzed reaction would be

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[8] (a) Y. Okamoto and H. C. Brown, *J. Org. Chem.*, **22**, 485 (1957); (b) H. C. Brown and Y. Okamoto, THIS JOURNAL, **80**, 4979 (1958); (c) D. E. Pearson, J. F. Baxter and J. C. Martin, *J. Org. Chem.*, **17**, 1511 (1952); (d) J. K. Kochi and G. S. Hammond, THIS JOURNAL, **75**, 3445 (1953); (e) N. C. Deno and W. L. Evans, *ibid.*, **79**, 5804 (1957).

[9] C. K. Rule and V. K. LaMer, *ibid.*, **60**, 1974 (1938).

[10] K. B. Wiberg, *Chem. Revs.*, **55**, 713 (1955).

[11] F. P. Price and L. P. Hammett, THIS JOURNAL, **63**, 2387 (1941).

[12] M. J. Craft and C. T. Lester, *ibid.*, **73**, 1127 (1951).

[13] F. W. Fitzpatrick and J. D. Gettler, *ibid.*, **78**, 530 (1956).

[14] R. P. Cross and P. Fugassi, *ibid.*, **71**, 223 (1949).

[15] (a) G. E. K. Branch and A. C. Nixon, *ibid.*, **58**, 2499 (1936); (b) I. Meloche and K. J. Laidler, *ibid.*, **73**, 1712 (1951); (c) E. Berliner and L. H. Altschul, *ibid.*, **74**, 4110 (1952); (d) E. W. Timm and C. N. Hinshelwood, *J. Chem. Soc.*, 862 (1938).

[16] J. B. Conant and P. D. Bartlett, THIS JOURNAL, **54**, 2881 (1932).

facilitated by the higher equilibrium concentration of addition compound formed from benzaldehydes with electron-withdrawing substituents, and might also be aided by an easier proton removal from such addition compounds. Although no base-catalyzed reaction was detectable readily with *p*-methyl- and *p*-methoxybenzaldehydes, the rate constants for semicarbazone formation from benzaldehyde and *p*-nitro-, *m*-nitro- and *p*-chlorobenzaldehydes were found to be greater at *p*H 12 than at 10. The rate of *p*-chlorobenzaldehyde semicarbazone formation was examined between *p*H 10 and 13 and found to be proportional to the concentration of hydroxide ion in this *p*H range (Fig. 5). The rates for the reactions of *p*-chlorobenzaldehyde with hydroxylamine and methoxyamine were determined and are shown in the same figure for comparison. Equilibrium constants for addition compound formation with *p*-chlorobenzaldehyde were found to be 21.7, 9.11 and 4.14 l. mole^{-1} for hydroxylamine, methoxyamine and semicarbazide, respectively. The rates shown in Fig. 5 are corrected for the equilibrium concentration of addition compound and represent the rate of base-catalyzed dehydration of the respective addition compounds. The apparent second-order rate constants for the reactions of hydroxide ion with the addition compounds of hydroxylamine, methoxyamine and semicarbazide are 7770, 153 and 5.44 l. mole^{-1} min.$^{-1}$, respectively (calculated from the apparent *p*H and assuming $K_W = 10^{-14}$). These differences may in part reflect steric effects; it is possible that the relatively rapid reaction of the hydroxylamine compound may also reflect a particularly favorable path for proton removal from the oxygen atom followed by an intramolecular proton shift from nitrogen to oxygen or assistance to nitrogen ionization or hydroxyl expulsion by the hydroxyl hydrogen atom, acting as an intramolecular general acid catalyst.

Baddeley and Topping have reported in a preliminary communication[17] that *d*-carvone exhibits neutral and base-catalyzed[18] reactions with hydroxylamine, but not with O-benzylhydroxylamine, and suggest that the neutral reaction between *d*-carvone and hydroxylamine represents an oxygen attack upon the carbonyl compound, by hydroxylamine in the zwitterion form. In the case of *p*-chlorobenzaldehyde, base-catalyzed reactions have been demonstrated with both hydroxylamine and methoxyamine (Fig. 5) and neutral reactions of carbonyl compounds with methoxyamine have been previously reported.[2] The apparent inability of O-benzylhydroxylamine to react with *d*-carvone may represent a steric interaction rather than the necessity of a zwitterion attack.

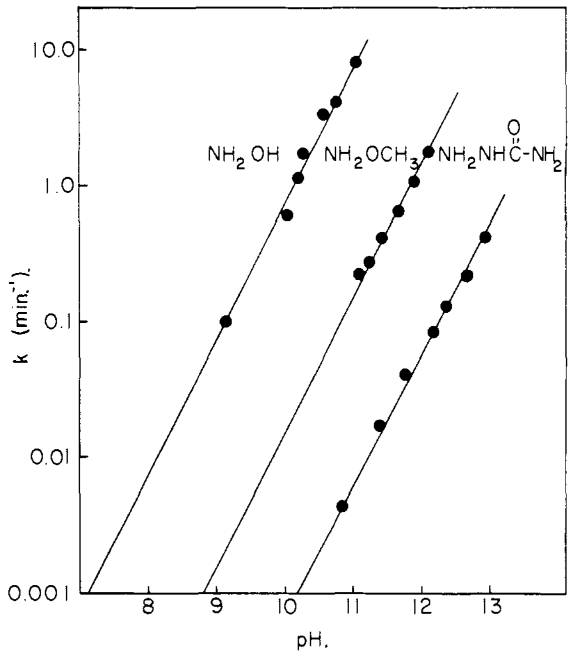

Fig. 5.—Log *k*, for the base-catalyzed dehydration of addition compounds of *p*-chlorobenzaldehyde with NH_2OH, NH_2OCH_3 and $NH_2NHCONH_2$ in 25% ethanol at 25°, plotted as a function of *p*H; $k = k_{obs}$/(fraction of carbonyl compound as addition compound).

The preparation of derivatives of carbonyl compounds with strongly electron-withdrawing substituents, such as the fluorocarbon ketones,[19] may be difficult because of the slow rate of dehydration of the addition compound under the acid conditions ordinarily used for such reactions. The base-catalyzed reaction may represent a useful preparative method for such compounds. To test this possibility and identify the product of the base-catalyzed reaction, *p*-chlorobenzaldehyde semicarbazone was prepared under basic conditions and found to give the same yield, melting point and infrared spectrum as the product of the acid-catalyzed reaction.

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WALTHAM, MASS.

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(17) G. Baddeley and R. M. Topping, *Chemistry & Industry*, 1693 (1958).

(18) E. Barrett and A. Lapworth, *J. Chem. Soc.*, **93**, 85 (1908).

(19) J. H. Simons, W. T. Black and R. F. Clark, THIS JOURNAL, **75**, 5621 (1953).