# Hydroxide Ion Catalyzed Reverse Aldol Type Condensation Reactions of Para-Substituted Benzoylacetaldehydes[1]

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**Abstract:** The apparent hydroxide ion catalyzed decomposition of para-substituted benzoylacetaldehydes to give para-substituted acetophenones and formate ions is characterized by rate saturation at high hydroxide ion concentrations (0.1–1 *M*); thus the order in hydroxide ion varies from 1 at low hydroxide ion concentrations to 0 at high hydroxide ion concentrations. These kinetics suggest that the critical transition state contains aldehyde hydrate monoanion and hydroxide ion or the kinetically equivalent aldehyde hydrate dianion in analogy to earlier work. A number of rate constants, including those for product-forming decomposition of aldehyde hydrate monoanion apparently catalyzed by hydroxide ion, were *calculated* from the experimental data and estimates of various equilibrium constants. For decomposition of aldehyde hydrate monoanions catalyzed by hydroxide ions, the calculated $\rho = 1$ and the deuterium solvent kinetic isotope effects $k^D/k^H = 1.1$–$1.5$ suggest that heavy atom reorganization plays a major role in product formation.

A number of enzyme catalyzed reactions involve the formation or cleavage of carbon–carbon bonds. Syntheses or degradations of β-ketoacids by carboxylyases, of β-ketols by aldehyde lyases, and of β-diketones and β-keto acids by acyl hydrolases are examples of such reactions.[2,3] The substrates for the degradation reactions differ with respect to the state of oxidation of one of the carbon atoms of the scissile bond which is β to the carbonyl group; for the examples selected these carbon atoms are at the carboxylate, carbinol, and carbonyl levels of oxidation, respectively. Of these enzymic reactions, that of acetoacetate decarboxylase is perhaps best understood.[4-9] Extensively investigated, but less well understood, are the aldolase and acyl hydrolase catalyzed reactions.[10-23]

Representative nonenzymic counterparts of the above mentioned reactions which have been studied from a mechanistic viewpoint are nonoxidative decarboxylations of β-keto acids,[14-16] dealdolization of diacetone alcohol[17-20] and of 4-phenyl-4-hydroxy-2-butanone,[21] and cleavage of β-diketones.[22] A related study involved deformoylation of 2,6-dihalobenzaldehydes in alkali.[23] No studies concerned with the electronic effects of substituents on rates and mechanisms of carbon–carbon bond cleavage reactions of β-diketones have been reported. The present work is concerned with the hydroxide ion catalyzed cleavage of para-substituted benzoylacetaldehydes to give para-substituted acetophenones and formate ions (eq 1): X = $(CH_3)_2N$ (**1**), $CH_3O$ (**2**), H (**3**), Cl (**4**), $NO_2$ (**5**).

$$p\text{-}XC_6H_4COCH_2CHO + OH^-(H_2O) \longrightarrow p\text{-}XC_6H_4COCH_3 + HCO_2^- \quad (1)$$

## Results

In basic aqueous solution the decomposition of **1–5** to give para-substituted acetophenones and formate ions obeys the kinetic law of eq 2. Thus at low concentrations of hydroxide ion wherein $K > [OH^-]$, $k_{obsd} = k[OH^-]/K$; at high concentrations of hydroxide ion wherein $[OH^-] > K$, $k_{obsd} = k$ and reverse aldol condensation is independent of hydroxide ion concentration. At intermediate concentrations of hydroxide ion, $k_{obsd}$ is dependent on a fractional order (<1, >0) of hydroxide ion (Figure 1). For reactions of **1–5** plots of $1/k_{obsd}$ vs. $1/[OH^-]$ gave as intercept $1/k$ and as slope $K/k$ from which the respective constants could be evaluated. Values of $k$'s and $K$'s are provided in Table I. The appropriate constants for reactions of **1** and **3** in potassium deuterioxide–deuterium oxide solutions are similarly listed in Table I (Figure 2). The sensitivity of $k$ and $K$ values of **1–5** toward electronic effects is given by eq 3 and 4, respectively.

$$-d[\mathbf{1\text{–}5}]/(dt[\mathbf{1\text{–}5}]) = k_{obsd} = k[OH^-]/(K + [OH^-]) \quad (2)$$

$$\log k = -(1.03 \pm 0.04)\sigma - 1.85 \quad (r = 0.997) \quad (3)$$

$$\log K = -(1.13 \pm 0.005)\sigma - 0.616 \quad (r = 0.997) \quad (4)$$

For **1–5**, plots of log $k_{obsd}$ vs. $H_-$[24] were nonlinear. Forced fitting of the data to a linear regression analysis gave slopes of 0.8 for **1** to 0.1 for **5**; compliance of the rate data with this acidity function requires a linear relationship of unit slope. A small positive salt effect was obtained for reactions of **1** in 0.4 *M* potassium hydroxide solution: ([KCl, *M*], $k_{obsd}$, $min^{-1}$) 0, 0.0126; 0.2, 0.013; 0.4, 0.0145; 0.6, 0.0161. For reactions of **1** in 3-diethylaminopropionate buffer solution, $R_3N/R_3NH^+ = 1$, 0.06, 0.12, 0.2 *M*, $\mu = 0.4$ *M* (KCl), $t = 45.6°$, $k_{obsd} = (4.18 \pm 0.27) \times 10^{-4}$ $min^{-1}$; for $R_3N/R_3NH^+ = 4$, 0.03, 0.06, 0.1 *M*, $\mu = 0.2$ *M* (KCl), $t = 48°$, $k_{obsd} = (5.78 \pm 0.31) \times 10^{-4}$ $min^{-1}$. For reactions of **1** in triethylamine buffer solution, $R_3N/R_3NH^+ = 1$, 0.06, 0.12, 0.2 *M*, $\mu = 0.2$ *M* (KCl), $t = 48°$, $k_{obsd} = (6.48 \pm 0.01) \times 10^{-4}$ $min^{-1}$.

## Discussion

On the basis of kinetics evidence, Pearson et al.[25] postulated the mechanism of Scheme I for hydrolytic cleavage of C–C bonds in suitably activated carbonyl containing compounds. The nature of the observed kinetics for a given reaction depends on which of the three steps of Scheme I is

Scheme I

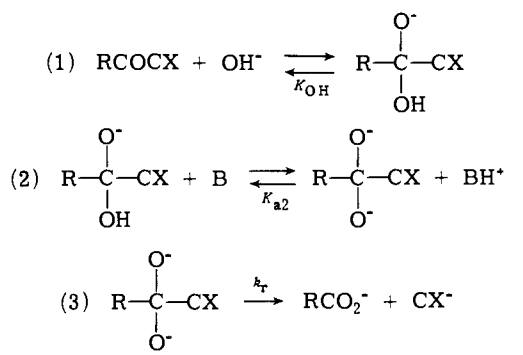


Table I. Rate Data for Reactions of Para-Substituted Benzoylacetaldehydes (1–5) in Alkaline Solution[a]

| Compd[b] | $k \times 10^3$, $min^{-1}$ | $K \times 10^2$, $M$ | No. of $k_{obsd}$ | Range of $[OH^-, OD^-]$, $M$ | $r$[e] |
|---|---|---|---|---|---|
| (1) ($N(CH_3)_2$) | 108 ± 11 | 225 ± 20 | 9 | 0.1–1.0 | 1.000 |
| | 115 ± 3[c] | 237 ± 60[c] | 6 | 0.1–1.0 | 0.999 |
| | 26 ± 0.4[d] | 53 ± 0.8[d] | 14 | 0.104–1.04 | 1.000 |
| (2) ($CH_3O$) | 26 ± 0.6 | 39.8 ± 0.9 | 6 | 0.1–1.0 | 0.999 |
| (3) (H) | 11.8 ± 0.5 | 25.9 ± 1.1 | 6 | 0.1–1.0 | 0.999 |
| | 3.6 ± 0.07[d] | 5.99 ± 0.12[d] | 9 | 0.022–1.10 | 0.988 |
| (4) (Cl) | 8.52 ± 0.42 | 14.5 ± 0.7 | 12 | 0.1–1.0 | 0.996 |
| (5) ($NO_2$) | 2.38 ± 0.4 | 3.18 ± 0.6 | 12 | 0.1–1.0 | 0.950 |
| | 2.36 ± 0.4[c] | 4.29 ± 0.7[c] | 6 | 0.1–1.0 | 0.960 |

[a] $t = 30 \pm 0.1°$, $\mu = 1.0\ M$ (KCl). [b] Unless specified, the compounds used were β-methoxyacrylophenones. [c] The compound used was the para-substituted benzoylacetaldehyde. [d] Solvent = deuterium oxide. [e] Correlation coefficient for the double reciprocal plot used to evaluate $k$ and $K$ of eq 2.

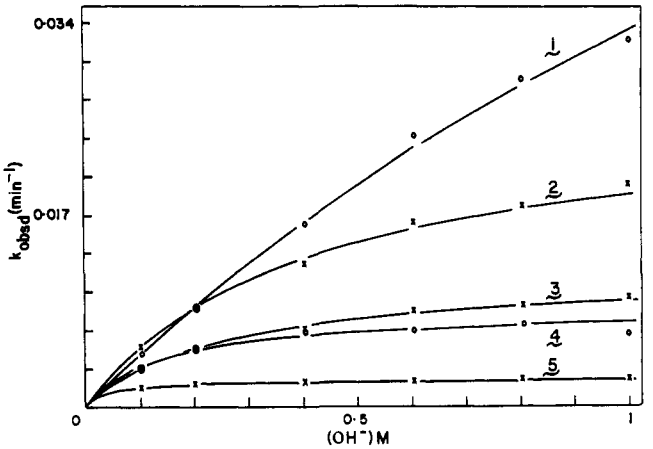



**Figure 1.** Plots of pseudo-first-order rate constants vs. the molar concentration of hydroxide ion for reactions of **1–5** to give para-substituted acetophenones. The solid lines were calculated from the constants of Table I.

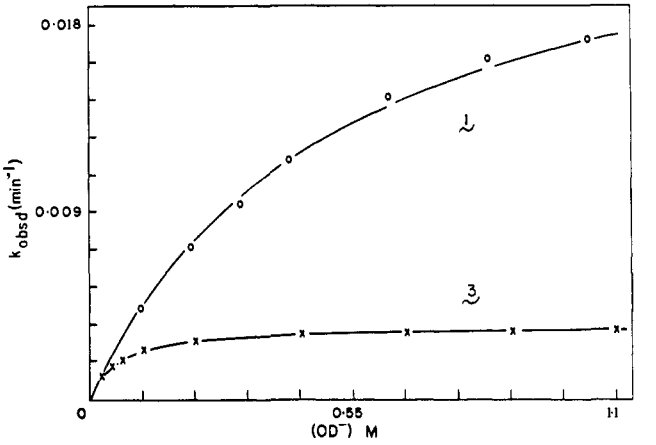



**Figure 2.** Plots of the pseudo-first-order rate constants vs. the molar concentration of deuterioxide ion for reactions of **1** and **3** to give *p*-dimethylaminoacetophenone and acetophenone, respectively. The solid lines were calculated from the constants of Table I.

rate determining. In the present study the kinetics of C–C bond cleavage are distinguished by rate saturation at high hydroxide ion concentrations. Because of the presumed low $pK_a$ of **1–5** as carbon acids, the variation in $k_{obsd}$ with $[OH^-]$ requires that chemically reactive species be the aldehyde hydrate dianion, or its kinetic equivalent, the aldehyde hydrate monoanion, and hydroxide ion. Employing the mechanism of Pearson and including the minimum pertinent equilibria, we show Scheme II wherein decomposition of aldehyde hydrate dianion is rate determining.

Equation 5 is the rate law derived for the mechanism of Scheme II for decomposition of **1–5**; $K_{OH} = K_H K_w / K_a$

$$\frac{-d[1\text{–}5]}{dt[1\text{–}5]_{total}} = k_{obsd} = \frac{k_r[OH^-]^2}{\frac{K_w^2(K_H + 1)}{K_a K_{a2}} + \frac{K_w}{K_a K_{a2}}(K_a + K_H K_i)[OH^-] + [OH^-]^2} \quad (5)$$

wherein $K_w$ is the autoprotolysis constant for water. From estimates of $K_H \simeq 1$ and $K_a \simeq 10^{-13}\ M$, which are based on values for aldehydes,[26] from $K_i = 10^{-6}\ M$,[32] and from the reasonable prediction that $K_{a2} = 10^{-15}\ M$, the value of the term $K_w^2(K_H + 1)/K_a K_{a2} \simeq 1$, $(K_w/K_a K_{a2})(K_a + K_H K_i) \simeq 10^8$, and the denominator term $\simeq 10^8\ [OH^-]$. Equation 5 then reduces to one with a first-order hydroxide ion dependence which is not in agreement with experimental results (eq 2). As well, on usual chemical grounds it is difficult to sensibly accommodate the solvent isotope effects and the Hammett $\rho$ constants for $k$'s and $K$'s of Table I to the mechanism of Scheme II.[27]

Scheme II

(1) (1–5) + $OH^-$ $\underset{K_{OH}}{\rightleftharpoons}$ $ArCOCH_2CHO_2H^-$

(2) (1–5) + $H_2O$ $\underset{K_H}{\rightleftharpoons}$ $ArCOCH_2CH(OH)_2$

(3) (1–5) $\overset{K_i}{\rightleftharpoons}$ $ArCOCHCHO^-$ + $H^+$

(4) $ArCOCH_2CH(OH)_2$ + B $\overset{K_a}{\rightleftharpoons}$ $ArCOCH_2CHO_2H^-$ + $BH^+$

(5) $ArCOCH_2CHO_2H^-$ + B $\overset{K_{a2}}{\rightleftharpoons}$ $ArCOCH_2CHO_2^{-2}$ + $BH^+$

(6) $ArCOCH_2CHO_2^{-2}$ $\xrightarrow{k_r}$ $ArCOCH_3$ + $HCO_2^-$ + $OH^-$

After considering without success a number of modifications of Scheme II which involve the dianion, or its equivalent, and preequilibria, we turned our attention to a similar mechanism based on a low steady state concentration of aldehyde hydrate monoanion (Scheme III). We believe that the concentration of the aldehyde hydrate monoanion could reasonably be quite small because of the rather high concentration of carbanion-enolate anion likely present in 0.1–1.0 $M$ potassium hydroxide solutions. If it is assumed that total substrate concentration is approximately equal to the sum of the concentrations of **1–5**, **1–5** hydrates, and **1–5** carbanion-enolates, then eq 6 can be derived for the mecha-

$$\frac{-d[1\text{–}5]}{dt[1\text{–}5]_{total}} = k_{obsd} = \frac{k_5[OH^-]^2(k_1 K_w + k_3 K_H K_w)}{A + B[OH^-] + C[OH^-]^2} \quad (6)$$

Table II. Assumed and Calculated Constants for the Mechanism of Scheme III[a]

| Compd | $K_H$ | $K_{OH}$, $M^{-1}$ | $K_a/K_w$, $M^{-1}$ | $K_i \times 10^7$, $M$ | $k_1 \times 10^{-7}$, $M^{-1}$ min$^{-1}$ | $k_2 \times 10^{-5}$, min$^{-1}$ | $k_3 \times 10^{-5}$, $M^{-1}$ min$^{-1}$ | $k_4 \times 10^{-4}$, min$^{-1}$ | $k_5 \times 10^{-5}$, $M^{-1}$ min$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 1.00 | 4.0 | 10 | 9.8 | 1.04 | 10.4 | 2 | 5 | 4.84 |
| 2 | 0.93 | 9.1 | 16 | 56 | 1.32 | 8.25 | 4 | 4.44 | 21.8 |
| 3 | 0.90 | 13.9 | 20 | 146 | 1.50 | 7.5 | 5.6 | 4.03 | 30.5 |
| 4 | 0.88 | 20.5 | 24.2 | 231 | 1.67 | 6.9 | 7.2 | 3.5 | 50 |
| 5 | 0.82 | 50 | 39 | 1160 | 2.15 | 5.5 | 15 | 3.0 | 182 |

[a] The constants were calculated from the data of Table I and assumptions described in the Discussion section. No implication of correctness of these "data" vis à vis the mechanism of Scheme III is intended. Rather, the suggestion that these "data" are possible and reasonable is intended.

Scheme III

(1) 1–5 + $H_2O \underset{K_H}{\rightleftharpoons}$ $ArCOCH_2CH(OH)_2$

(2) 1–5 $\overset{K_i}{\rightleftharpoons}$ $ArCOCHCHO^-$ + $H^+$

(3) $ArCOCH_2CH(OH)_2 \underset{k_2(H_2O)}{\overset{k_1(OH^-)}{\rightleftharpoons}} ArCOCH_2CH(OH)O^-$

(4) 1–5 + $OH^- \underset{k_4}{\overset{k_3}{\rightleftharpoons}}$ $ArCOCH_2CH(OH)O^-$

(5) $ArCOCH_2CH(OH)O^- \xrightarrow{k_5(OH^-)}$ $ArCOCH_3 + HCO_2^- + OH^-$

nism of Scheme III. The constant $A = K_w(k_2 + k_2K_H + k_4 + k_4K_H)$; the constant $B = (k_2K_iK_H + k_4K_iK_H + k_5K_w + k_5K_wK_H)$; the constant $C = k_5K_iK_H$.

For the purpose of discussion of the mechanism of Scheme III vis à vis the experimentally determined constants of Table I, the reduced form of the rate law of Scheme III, the influence of electronic effects on reactivity, and the deuterium solvent kinetic isotope effects we *calculated* the constants of Table II from the data of Table I and some assumptions which follow. For a number of aliphatic aldehydes, $K_H = 1$ and its value decreases with increasing electrophilicity of the aldehydic carbon atom.[26] For **1**, $K_H$ was assigned the value 1. The constant $K_{OH} = k_3/k_4$. For substituted benzaldehydes, the best model we found, $K_{OH}$ = 0.095–215 $M$,[31] the larger values being associated with increasing electrophilicity of the carbonyl carbon atom. We assigned the value 4 to **1**. For acetaldehyde hydrate, $K_a = 2.7 \times 10^{-14}$ $M$; for chloral hydrate, $K_a = 9.1 \times 10^{-11}$ $M$.[26] We assigned the value $10^{-13}$ $M$ to **1**. For acetylacetaldehyde, $K_i = 1.2 \times 10^{-6}$ $M$.[32] For **1–5**, we assumed $K_i$ could vary within the limits of $K_a$ values for substituted benzoic acids. From the work of Exner et al.,[33] there is a 209-fold difference in acidity between *p*-dimethylaminobenzoic acid and *p*-nitrobenzoic acid in 50% ethanol and a 245-fold difference in 80% methyl Cellosolve. Based on this work we believe a 118-fold difference in $K_i$ for **1–5** is reasonable and that $K_i = 10^{-6}$ $M$ for **1** is also a reasonable approximation of the acidity of **1**. Overall the range of values of $K_H$, $K_{OH}$, $K_a/K_w$, and $K_i$ is reasonable on the basis of the distances between reacting centers and para substituents and on the basis of the types of reactions involved in the various equilibria. The constants $k_1$, $k_2$, $k_3$, $k_4$, and $k_5$ (Table II) were calculated using the constants of Table I, the assumed values of the constants $K_H$, $K_{OH}$, $K_a/K_w = k_1/k_2$, and $K_i$, and the requirement that $k_1$ could not exceed $kK_iK_H/K_w$. Table III contains the Hammett $\rho$ constants associated with the assumed and calculated constants of Table II.

**Form of the Reduced Rate Equation.** Accepting the reasonableness of the values of the constants of Table II which pertain to the mechanism of Scheme III, the interested reader can establish that division of the numerator and the denominator by $C$ and evaluation of the constant $A/C$ (Table II) shows that $A/C \rightarrow 0$. A similar numerical analysis of $B/C$ shows that this term reduces to $(k_2 + k_4)/k_5$ and that eq 6 may be simplified to equation 7 which has the form of eq 2.[34]

Table III. $\rho$ Values for the Assumed and Calculated Constants of Table II[a]

| Constant | $\rho$ | Correlation coefficient |
|---|---|---|
| $K_H$ | −0.05 | 1.000 |
| $K_{OH}$ | 0.68 | 1.000 |
| $K_a/K_w$ | 0.37 | 1.000 |
| $K_i$ | 1.29 | 0.998 |
| $k_1$ | 0.20 | 1.000 |
| $k_2$ | −0.17 | 1.000 |
| $k_3$ | 0.54 | 1.000 |
| $k_4$ | −0.14 | 0.987 |
| $k_5$ | 0.96 | 0.996 |

[a] See footnote *a* of Table II.

$$-d[1\text{–}5]/dt[1\text{–}5]_{total} = k_{obsd} = \frac{\{(k_1 + k_3K_H)K_w/(K_iK_H)\}[OH^-]}{(k_2 + k_4)/k_5 + [OH^-]} \quad (7)$$

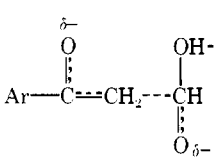
**Magnitude of the Rate Constants.** Rates of proton transfer between oxygen atoms are frequently diffusion controlled.[35] However, proton transfer from hydrogen bonded structures to hydroxide ions may occur with rate constants of $10^6$–$10^8$ $M^{-1}$ min$^{-1}$.[35,36] The $k_1$ values of Table II could reflect a proton transfer process from highly structured, hydrogen bonded **1–5**. Such intramolecular and intermolecular hydrogen bonded **1–5** could stabilize the bound hydrogen atom, change its orientation, or otherwise shield it so as to make its transfer more difficult.[35,36] The value of $k_2$ is fixed by the value of $k_1$ and $K_a/K_w$. The reaction of acetaldehyde with hydroxide ion proceeds with a rate constant of $6.8 \times 10^5$ $M^{-1}$ min$^{-1}$ at 0°.[37] The values of $k_3$ (Table II) are therefore reasonable values for attack of hydroxide ion on **1–5**. As for the $k_2$ constants, the values of $k_4$ constants are fixed, now by the values of $k_3$ and $K_{OH}$. Values of $k_5$ are those which could be associated with proton transfers from intramolecularly hydrogen bonded compounds such as dicarboxylic acids, salicylic acid, etc. (vide supra). Whether or not the values of $k_5$ are reasonable for a process involving primarily heavy atom reorganization we cannot say although electronic effects and deuterium solvent kinetic isotope effects which are discussed below support just such a process for decomposition of **1–5**.

**Electronic Effects.** For the mechanism of Scheme III and eq 7, $\rho(k) \simeq \rho k_1 - \rho K_iK_H$. From the $\rho$ values of Table III, the calculated $\rho(k) = -1.04$ which is its experimental value

(eq 3). For $\rho(K) \simeq \rho k_2 - \rho k_5$, the calculated $\rho(K) = -1.13$ which is its experimental value (eq 4). We note that the $\rho$ values of Table III all possess the correct sign, and the relative magnitudes of the $\rho$'s are reasonable for their respective reactions. The positive $\rho$ (0.96) for $k_5$ suggests that considerable negative charge is developed in the para-substituted acetophenone leaving groups which likely depart as their enolate anions. In the somewhat analogous case of the spontaneous decarboxylation of para-substituted benzoyl acetates in 50% dioxane-water, $\rho$ is 1.7.[16]

**Deuterium Solvent Kinetic Isotope Effects.** If it is assumed that $(k_1 + k_3K_H) \simeq k_1$ (Table II), then $k(H_2O)/k(D_2O) = (k_1^H/k_1^D)(K_w^H/K_w^D)(K_i^D/K_i^H)(K_H^D/K_H^H)$. The value of $(K_w^H/K_w^D) = 7.2$.[38] The value $(K_i^D/K_i^H) = 0.3$ was estimated from a Rule-LaMer plot.[39,40] The value of $(K_H^D/K_H^H) = 0.8$ was used.[26] From these data and those of Table I $(k_1^H/k_1^D) = 2.5$ for **1**, a reasonable isotope effect for proton transfer from **1** aldehyde hydrate to hydroxide ion. Similarly, for **3**, $(k_1^H/k_1^D) = 1.8$. The isotope effect on $k_2$ can be estimated from the relationship $(k_1/k_2) = (K_a/K_w)$. From a Rule-LaMer plot, $(K_a^H/K_a^D) = 4.7$ for **1** and 4.6 for **3** whence $(K_a^H/K_a^D)(K_w^D/K_w^H) = 0.65$ for **1** and 0.64 for **3**. The isotope effect $(k_2^H/k_2^D) = 2.5/0.65 = 3.9$ for **1** and $1.8/0.64 = 2.8$ for **3**. Finally, if $k_2 + k_4 \simeq k_2$ (Table II), then $(K^H/K^D) = (k_2^H/k_2^D)(k_5^D/k_5^H)$. For **1**, $k_5^H/k_5^D = 3.9/4.24 = 0.92$; for **3**, $k_5^H/k_5^D = 2.8/4.31 = 0.65$. These isotope effects on $k_5$ are not those expected for a transition state wherein rate determining proton transfer from aldehyde hydrate monoanions to hydroxide ions is taking place. Rather, they suggest that proton transfer is not rate determining, or only partially rate determining, for decomposition of **1–5** and the isotope effect is primarily a secondary isotope effect. Weak support for the noninvolvement of proton transfer in the transition state is afforded by the result that general catalysis by amines was not detected under our experimental conditions (Results section). Bunton and Shiner[42] calculated $k^H/k^D$ values for the hydroxide ion catalyzed decomposition of diacetone alcohol to acetone, a somewhat analogous reaction: for an alcoholate-like transition state $k^H/k^D = 0.89$; for an enolate-like transition state, $k^H/k^D = 0.76$. Both values are in good agreement with experimental results. Swain et al.[43] proposed for transition states involving proton transfer between oxo groups ($OH^-$, ROH) that the proton should lie in a stable potential at the transition state (solvation rule). One of several lines of support adduced for this thesis is the result that for the apparent hydroxide ion catalyzed decomposition of 2,6-dichlorobenzaldehyde hydrate monoanion to formate ion and *o*-dichlorobenzene, $k^H/k^D = 0.5$, which led them to propose for this reaction a transition state which involved heavy atom reorganization. Similarly the deuterium solvent kinetic isotope effects on $k_5$ for **1** and **3** can be rationalized on the basis that heavy atom reorganization is the rate-determining process for decomposition of **1–5**. A transition state possessing enolate ion character is certainly in keeping with $\rho(k_5) = 1$ (Table III).

In summary, the *data* appear to be internally consistent and in agreement with the proposed mechanism (Scheme III) which identifies hydroxide ions and **1–5** hydrate monoanions as major transition state components. The critical product-forming event is envisaged as heavy atom reorganization rather than as a proton transfer reaction.



## Experimental Section

**Materials.** Syntheses of **1–5** or their vinyl ether precursors were previously reported.[44] Inorganic salts were Fisher ACS grade reagents. Potassium deuterioxide (40% in deuterium oxide) and deuterium oxide (99.7%) were purchased from Diaprep, Inc. Doubly distilled water was used for kinetic runs in water.

**Apparatus.** A Gilford Model 2400 spectrophotometer was used for collection of rate data as previously described.[44]

**Kinetics.** Either para-substituted benzoylacetaldehydes or para-substituted 3-methoxyacrylophenones were used. Under the basic reaction conditions employed, acrylophenones very rapidly hydrolyze ($k_{OH} \simeq 5$–$121\ M^{-1}\ min^{-1}$) to para-substituted benzoylacetaldehydes which very slowly undergo the retroaldol type condensations reported in this study. Reactions, carried out under pseudo-first-order conditions (concentration of **1–5** ca. $10^{-4}$–$10^{-5}\ M$), were initiated by addition of a microdrop of **1–5** in methanol to 3 ml cuvettes containing potassium hydroxide or potassium deuterioxide solutions previously equilibrated to 30 ± 0.1°. Absorbance loss vs. time was monitored at the following wavelengths: 356 (**1**), 325 (**2**), 320 (**3**), 255 (**4**), and 290 nm (**5**). Pseudo-first-order rate constants were calculated from the slopes of plots of log $(OD_i - OD_\infty)/OD_t - OD_\infty)$ vs. time; first order plots were excellent, exhibiting linearity beyond three half-times. Ionic strength was maintained with KCl.

**Product Analysis.** Para-substituted benzoylacetaldehydes (**1–5**) in alkaline solution yield the corresponding para-substituted acetophenones and formate ions. The uv spectra of the products exactly resemble those of the appropriate acetophenones. The $\lambda_{max}$ of benzoic acid, *p*-methoxybenzoic acid, and *p*-nitrobenzoic acid differ markedly from those of similarly substituted acetophenones under identical conditions. These qualitative observations of product identity were quantitated as follows. A known amount of **1** was allowed to react in 0.2 *M* KOH and the final OD at 356 nm was noted. Comparison of the calculated $\epsilon = 15{,}707$ with that of 15,885 for *p*-dimethylaminoacetophenone determined under identical conditions shows that conversion of **1** to products is quantitative (98.9%). Similar experiments with **5**, $\epsilon = 15{,}633$ at 290 nm after reaction, showed a 96.8% conversion to *p*-nitroacetophenone, $\epsilon = 16{,}147$.

## References and Notes


(1) This work was supported in part by grants from the U.S. Public Health Service.
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(27) Here we attempt only to justify our estimates of the values of $K_a$, $K_{a2}$, and $K_H$, acknowledging that the justification is based on additional assumptions and inexact models; data for $\beta$-ketoaldehydes are unavailable. For $K_a$, we started with $K_a = 2.7 \times 10^{-14}$ *M* for acetaldehyde hydrate and $K_a = 9 \times 10^{-11}$ *M* for chloral hydrate[26] and attempted to estimate the effect of the benzoyl group on $K_a$ for acetaldehyde hydrate by interpolation. The electronic influence of the benzoyl group was estimated from the ionization constants for acetic acid ($K_a = 1.75 \times 10^{-5}$ *M*), trichloroacetic acid ($K_a = 0.219$ *M*), and acetoacetic acid ($K_a = 2.63 \times 10^{-4}$ *M*).[28] The last constant was corrected for substitution of methyl by phenyl, a factor of 1.44 based on $K_a = 2.18 \times 10^{-5}$ *M* for $\beta$-phenylpropionic acid and $K_a = 1.5 \times 10^{-5}$ *M* for butyric acid,[29] to give $K_a = 3.78 \times 10^{-4}$ *M* for benzoylacetic acid. For the acids, the factor $1.65 \times 10^{-3}$ was calculated for the effect of the benzoyl group. $K_a = 1.75 \times 10^{-13}$ *M* for benzoylacetaldehyde hydrate was then calculated by multiplying the factor by ($K_a$(chloral hydrate) − $K_a$(acetaldehyde hydrate)) and adding the product to $K_a$ for acetaldehyde hydrate. $K_{a2}$ data, unavailable for aldehydes, are plentiful for dicarboxylic acids and $K_a > K_{a2}$. For *o*-phthalic acid, $\Delta pK_a = 2.46$;[28] for malonic acid, $\Delta pK_a = 2.84$;[28] for *cis*-3,3-diphenylcyclopropane-1,2-dicarboxylic acid, $\Delta pK_a = 6.74$.[30] From these data and the estimated $K_a$ for benzoylacetaldehyde hydrate, $K_{a2} = 10^{-15}$ *M* seems reasonable. For $K_H$ we started with $K_H = 0.7$ for acetaldehyde hydrate and $K_H = 0.03$ for chloroacetaldehyde hydrate[26] and attempted to estimate the effect of the benzoyl group on the value for acetaldehyde hydrate by interpolation. The electronic influence of the benzoyl group was estimated as above using *K*'s for acetic acid and benzoylacetic acid and $K_a = 1.41 \times 10^{-3}$ *M* for chloroacetic acid. For the acids, the factor is 0.26. $K_H = 0.53$ for benzoylacetaldehyde hydrate was then calculated by multiplying the factor by ($K_H$(acetaldehyde) − $K_H$(chloral hydrate)) and substracting the product from $K_H$ for acetaldehyde.
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# The Strong Acid-Catalyzed Hydrogenation of Aromatics

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**Abstract:** The strong acid-catalyzed hydrogenation of benzene has been studied. It is possible to hydrogenate benzene at 50° through protonation with either HF-$TaF_5$, HF-$SbF_5$, or HBr-$AlBr_3$ and reaction of the protonated aromatic with a tertiary hydride source such as isopentane. Ultimately cyclohexane and a number of $C_5$-alkylated benzenes are formed. No hydrogenation occurs when a secondary hydride source or hydrogen is substituted for the tertiary hydride source. However, when hydrogen is used in conjunction with isopentane, it is consumed. As a result, at pressures greater than 14.6 atm $H_2$, the reduction becomes catalytic in both acid and isopentane. The function of the hydrogen is to reduce the isopentyl cations formed during the benzene reduction, thereby regenerating the isopentane and a proton. HCl-$AlCl_3$ also catalyzes the hydrogenation of benzene in the presence of a tertiary hydride source, while HF-$TiF_4$, HF-$HfF_4$, and $CF_3SO_3H$-$TaF_5$ are all inactive.

Superacids offer a novel method to hydrogenate aromatics through protonation and reaction of the resultant carbonium ion with hydrogen. However, attempts to hydrogenate the aromatics benzene[1] and hexamethylbenzene[2] using the acids HBr-$AlBr_3$ and HF-$SbF_5$, respectively, failed. On the other hand, benzene has been hydrogenated in the HF-$TaF_5$-hexane system[3] and in the HBr-$AlBr_3$-3-methylpentane system.[4] In the latter case, the observation was made that no reaction occurred in the absence of the aliphatic solvent.

We have investigated the hydrogenation of benzene in all of the above and a number of other superacids and have found that the aliphatic solvent, hydrogen, and the nature of the superacid all play a crucial role in the success of these hydrogenations. This paper presents our results which we will use to rationalize the previous work and to describe the mechanism of the reduction.

## Results and Discussion

**Aliphatic Solvent.** It is possible to hydrogenate benzene in either HF-$TaF_5$, HBr-$AlBr_3$, or HF-$SbF_5$ at 50° in the absence of hydrogen, if an aliphatic solvent capable of donating a tertiary hydride ion is present[5] (eq 1). *n*-Pentane is an excellent solvent because it does not interfere with analysis of products and because it does not undergo the extensive cracking reactions observed for higher molecular weight alkanes. By sampling the hydrocarbon phase of the two-phase systems, one can follow the course of the reaction using gas chromatography. For all of these acids, one observes that the pentane is isomerized to isopentane, and the benzene is reduced to an equilibrium mixture of cyclohexane and methylcyclopentane. When left standing over the acid, these latter products are slowly cleaved to a mixture of isohexanes. There is no evidence for the generation of hydrogen through reaction of the acid with isopentane.[2] After 10–25% of the benzene has been converted to cyclohexane, the reaction stops. Analysis, after quenching with water, indicated that large amounts of $C_5$-alkylated benzenes had formed in the acid layer. When these reductions were done in the absence of pentane, but in the presence of 35.0 atmo-