# Base-Catalyzed β-Elimination Reactions in Aqueous Solution. IV. Elimination from 4-(4-Substituted benzoyloxy)-2-butanones[1]

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**Abstract:** 4-(4-Substituted benzoyloxy)-2-butanones undergo general base-catalyzed elimination to give methyl vinyl ketone and 4-substituted benzoic acids. The relative insensitivity of the reaction to the nature of the leaving group, $\rho = +0.18$ for hydroxide ion catalysis, is suggestive of an E1cB mechanism wherein anion formation is rate determining or of a concerted process wherein the transition state is of the E1cB type.

General base catalysis has been established in β-elimination reactions of β-acetoxy ketones,[4] β-acetoxy thiolesters,[5] and 4-(4-substituted phenoxy)-2-butanones.[6] β-Acetoxy ketones exhibit simple E2-type kinetics and elimination likely proceeds *via* rate-determining enolization or *via* a concerted process; 4-(4-substituted phenoxy)-2-butanones exhibit complex kinetics[7] suggestive of a two-step mechanism wherein the enolate anion, or some intermediate, partitions in a kinetically detectable way between starting ketone and products. In an attempt to delineate between a mechanism involving rate-determining enolization *vs.* a concerted mechanism in simple E2 reactions of β-substituted ketones possessing good leaving groups we examined the general base catalyzed eliminations of 4-substituted benzoates from 4-(4-substituted benzoyloxy)-2-butanones (eq 1, X = $NO_2$ (**1**); Cl (**2**); H

$$4\text{-X-}C_6H_4CO_2CH_2CH_2COCH_3 + B \longrightarrow CH_2{=}CH{-}COCH_3 + 4\text{-X-}C_6H_4CO_2^- + BH^+ \quad (1)$$

(**3**); $CH_3$ (**4**); $OCH_3$ (**5**). Marked sensitivity of the reactions to the nature of the leaving group could be indicative of a concerted process wherein the transition state has appreciable E1 character; marked insensitivity of the reactions to the nature of the leaving group could be indicative of (1) an E1cB mechanism involving rate-determining enolization wherein the slow step is proton abstraction from the ketone by a base or (2) a concerted mechanism wherein the transition state has appreciable E1cB character.

## Experimental Section

**Reagents.** Inorganic reagents as well as methylamine hydrochloride were Fisher Certified ACS Grade and were used without further purification. 2-Ethoxyethylamine, dimethylaminoethanol, *p*-methoxy-, *p*-methyl-, *p*-chloro-, *p*-nitrobenzoyl chloride, methyl vinyl ketone (Aldrich), N,N,N′,N′-tetramethylethylenediamine, and benzoyl chloride (Eastman, White Label) were used as supplied. 4-Hydroxy-2-butanone (Eastman, practical grade) was fractionated on a Nester-Faust annular-Teflon spinning band column, bp 70–72° (11.2–12.5 mm) (lit.[8] 70–71° (12 mm)). Tap-distilled water was distilled through a Corning AG-la glass still.

**4-(4-Substituted benzoyloxy)-2-butanones.** To a stirred solution of the appropriate acyl chloride (0.05 mol) in 25 ml of dry methylene chloride in a dry three-necked 100-ml round-bottomed flask maintained at 5–10° was added dropwise a solution of dry distilled pyridine (4.11 g, 0.052 mol) in 15 ml of dry methylene chloride during 15 min. After stirring the mixture for 1 hr, a solution of distilled 4-hydroxy-2-butanone (4.58 g, 0.05 mol) in 15 ml of methylene chloride was added dropwise to the stirred mixture which was maintained at 5–10°. Stirring was continued at 5° for an additional hour and then at room temperature for a total of 5.5–7.5 hr (Table I). The reaction mixture was separated and washed with 50 ml of 5% HCl solution, with two 50-ml portions of saturated aqueous sodium bicarbonate, and finally with 50 ml of water. The methylene chloride extract was dried over anhydrous magnesium sulfate and the solvent was removed *in vacuo* on the rotary evaporator. The residue was crystallized from the solvents listed in Table I. Infrared and pmr spectra were consonant with the assigned structure; analytical data are provided in Table I.

**Apparatus.** A Gilford Model 2400 spectrophotometer was used to collect rate data. The temperature was maintained by circulating water at 30 ± 0.1° from a Tamson Model TE-3 water bath. pH was determined by using a Radiometer Model PHM-22 pH meter equipped with a PHA 630 scale expander using a combined glass–calomel electrode (Radiometer G.K. 2021 B). Ultraviolet scans were taken on a Beckman Model DB-G recording spectrophotometer.

**Kinetics.** Reactions were carried out under pseudo-first-order conditions at 30 ± 0.1° in aqueous solution and at a calculated ionic strength of 1.0 *M* with KCl. The primary and tertiary amines used supplied their own buffering capacity and the pH's of all solutions were determined before and after each run to ensure constancy of pH (±0.02 unit) at 30 ± 0.1°. All of the reactions were carried out in 3-ml quartz cuvettes. The cuvettes were filled, stoppered, and allowed to equilibrate for 15 min in the thermostated sample chamber. The reaction was initiated by adding one or two drops of the substrate in methanol to the cuvette from a calibrated micropipet (concentration range $2.0\text{–}3.5 \times 10^{-4}$ *M*) capped, shaken, and quickly returned to the sample chamber. Pseudo-first-order rate constants, $k_{obsd}$ were determined by multiplying the slope of plots of log $(OD_\infty - OD_0)/(OD_\infty - OD_t)$ *vs.* time by 2.303 in the case of methyl vinyl ketone formation or by multiplying the slope of plots of log $(OD_0 - OD_\infty)/(OD_t - OD_\infty)$ *vs.* time by 2.303 in the case of ester disappearance. The reactions were followed to completion to obtain $OD_\infty$ and all the pseudo-first-order plots were linear to at least 80% completion. Rates were followed by monitoring the decrease in optical density of the starting ester at the following wavelengths; **1** 260, **4** 255, **2**,**5** 245, and **3** 235 mμ. Production of methyl vinyl ketone was generally not followed due to the high absorbance of the concentrated amine solutions below 230 mμ. The formation of methyl vinyl ketone from **1**–**5** in potassium hydroxide solution was monitored at 220 mμ.

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(2) Taken in part from a thesis submitted by Cavestri in partial fulfillment of the requirements for the M.S. degree.

(3) To whom inquiries should be directed.

(4) L. R. Fedor, *J. Amer. Chem. Soc.*, **89**, 4479 (1967).

(5) L. R. Fedor, *ibid.*, **91**, 913 (1969).

(6) L. R. Fedor, H. J. Schaeffer, and W. R. Glave, to be published.

(7) Plots of $k_{obsd}$ *vs.* total amine concentration at constant pH for reactions of $4\text{-X-}C_6H_4OCH_2CH_2COCH_3$ (X = $CH_3O$, $CH_3$, H, Cl) exhibit saturation effects at high amine concentration such that the rate of elimination of 4-substituted phenoxides becomes independent of amine concentration. Under comparable conditions, $4\text{-CNC}_6H_4\text{-}OCH_2CH_2COCH_3$ undergoes simple general base catalyzed β elimination suggesting that for the good leaving group 4-cyanophenoxy, partitioning of the intermediate enolate anion is unimportant.

(8) T. White and R. N. Haward, *J. Chem. Soc.*, 25 (1943).

Table I. 4-(4-Substituted benzoyloxy)-2-butanones

| Compd | Mp,[a] °C | % yield[b] | Total reaction time, hr | Calcd % carbon | Calcd % hydrogen | Found[c] % carbon | Found[c] % hydrogen | Recryst[d] solvent |
|---|---|---|---|---|---|---|---|---|
| **1** ($NO_2$) | 76–77 | 87.5 | 5.5 | 55.70 | 4.67 | 55.56 | 4.65 | A–B |
| **2** (Cl) | 47.5–49 | 83 | 6.5 | 58.26 | 4.89 | 57.98 | 4.85 | B |
| **3** (H) | *e* | *f* | 6.5 | 68.74 | 6.29 | 68.61 | 6.34 | |
| **4** ($CH_3$) | 34–36 | 50 | 7.5 | 69.89 | 6.84 | 69.60 | 6.92 | A–B |
| **5** ($CH_3O$) | 54–56 | 75 | 7.5 | 64.85 | 6.35 | 65.35 | 6.87 | A–B |

[a] All melting points were taken on a Mel-Temp melting point apparatus and are uncorrected. [b] After one recrystallization. All microanalyses were performed by Galbraith Lab., Inc., Knoxville, Tenn. [d] A = benzene, B = cyclohexane, A–B = benzene–cyclohexane mixture. [e] Compound **3** is heat labile and was purified by rapid column chromatography with silica gel and benzene solvent. The clear oil residue was used for analysis without further purification. [f] Not determined.

Half-neutralization of the amines used gave the stated $pK_a$ (Table III) values. The hydroxide ion activity, $a_{OH}$, was determined from $K_w/a_H$ where $a_H$ is the activity of the hydrogen ion measured with the combination glass-calomel electrode and $K_w$ is the autoprotolysis constant for water, $-\log K_w = 13.833$ at 30°.[9]

**Product Analysis.** Repetitive scans of the basic reaction solutions (substrates decomposed in base) showed only the formation of methyl vinyl ketone and the appropriately substituted benzoate ions. Table II illustrates the decomposition kinetics of **1–5** by hydroxide ion. Since the rate of loss of the ester equals the rate of formation of methyl vinyl ketone, within experimental error, competing side reactions such as ester hydrolysis are unimportant. Also, there is no kinetic evidence for the existence of any intermediate.

Table II. Rate Constants for the Reaction of Hydroxide Ion with 4-(4-Substituted benzoyloxy)-2-butanones[a]

| Ester | $k_{OH}$, $M^{-1}$ min$^{-1}$ [b] | $k_{OH}$, $M^{-1}$ min$^{-1}$ [c] | Total no. of $k_{obsd}$ |
|---|---|---|---|
| **1** ($NO_2$) | 715.4 ± 34.8 | 751.4 ± 30.1 | 6 |
| **2** (Cl) | 609.0 ± 10.7 | 591.6 ± 31.7 | 6 |
| **3** (H) | 556.7 ± 17.4 | 508.1 ± 9.5 | 6 |
| **4** (Me) | 514.3 ± 28.9 | 516.8 ± 21.9 | 6 |
| **5** (MeO) | 513.5 ± 11.8 | 491.0 ± 29.8 | 6 |

[a] Obtained by following the formation of methyl vinyl ketone (220 mμ) and the disppearance of the ester (solvent $H_2O$, $t = 30 \pm 0.1°$, $\mu = 1.0$ $M$ with KCl, 0.006 $M$ KOH, pH 11.385). [b] Following the formation of methyl vinyl ketone. [c] Following the disappearance of the starting ester.

## Results

4-(4-Substituted benzoyloxy)-2-butanones (**1–5**) undergo general base catalyzed β elimination to give methyl vinyl ketone and 4-substituted benzoates (eq 1). Kinetically the reactions obey the general form of eq 2

$$-d[S]/dt = d[P]/dt = [\textstyle\sum k_2[\text{base}]][SH] \quad (2)$$

and in aqueous solutions of basic buffers at constant pH are described by eq 3.[10] Plots of $k_{obsd}$ *vs.* the

$$\text{rate}/[S] = k_{obsd} = k_2'[\text{base}]_{total} + k_{OH}K_w/a_H \quad (3)$$

concentration of total base gave as the slope the apparent second-order rate constant $k_2'$ and as the intercept the concentration dependent rate constant $k_{OH}$ $(K_w/a_H)$ (Figure 1). The true second-order rate constant $k_2$ was determined by dividing $k_2'$ by $K_a/(K_a + a_H)$, the mole fraction of total base present as free base (Table III). The rate constant $k_{OH}$ was determined from the slope of plots of intercept values (Figure 1, eq 3) *vs.* $K_w/a_H$ or from $k_{obsd}/(K_w/a_H)$ for reactions run in potassium hydroxide solutions (Table II).

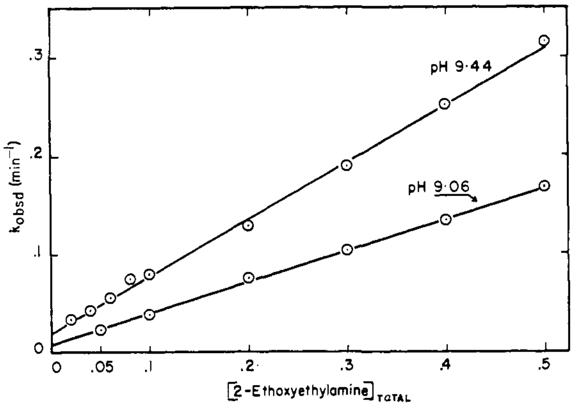

Figure 1. Least-squares plot of the pseudo-first-order rate constant $k_{obsd}$, *vs.* the total concentration of 2-ethoxyethylamine for the reactions of **3** with that amine: pH 9.44 ($r$ = 0.9990), pH 9.06 ($r$ = 0.9997), $t = 30 \pm 0.1°$, $\mu = 1.0$ with KCl. For pH 9.44, the calculated intercept (Table II) = 0.0206 min$^{-1}$; the least-squares value = 0.0200 min$^{-1}$. For pH 9.06, the calculated intercept (Table II) = 0.0086 min$^{-1}$; the least-squares value = 0.0071 min$^{-1}$.

For those reactions of **3** with bicarbonate ion and with carbonate ion in bicarbonate–carbonate buffer solutions two simultaneous equations (eq 4) were set

$$k_2' = k_{2(HCO_3^-)}[a_H/(K_a + a_H)] + k_{2(CO_3^{2-})}[K_a/(K_a + a_H)] \quad (4)$$

up for two $k_2'$ values determined at two pH values and the appropriate true second-order rate constants for the reactions of **3** with bicarbonate ion and with carbonate ion were determined. Similarly, second-order rate constants for the reactions of **1–5** with N,N,N′,N′-tetramethylethylenediamine and with N,N,N′,N′-tetramethylethylenediamine monocation were determined (Table III).[10a]

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(9) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," 2nd ed, Butterworths, London, 1959, p 544.

(10) The data for the reactions of **3** with 2-ethoxyethylamine were also treated by the equation $[k_{obsd} - k_{OH}(K_w/a_H)]/[B]_{free} = k_2 + k_{22}[B]_{free}$ using the linear regression and correlation coefficient program No. 09100–70803 with a Hewlett-Packard 9100H calculator. With the same program, $k_{OH}(K_w/a_H)$ values used in the above equation were calculated as intercepts of plots of $k_{obsd}$ *vs.* $[B]_{total}$. These values were virtually identical with those calculated from $(K_w/a_H)$ and the rate constants of Table II. The following rate constants (molar concentrations, time in minutes) were obtained (pH, $k_2$, $k_{22}$): 9.06, 1.08, 0.017; 9.07, 0.91, 0.14; 9.27, 0.93, 0.07; 9.38, 1.19, −0.16; 9.44, 1.21, −0.14; $\bar{k}_2 = 1.07 \pm 0.14$; $\bar{k}_{22} = -0.02 \pm 0.13$.

(10a) Note Added in Proof. For the reactions 1–5 with (G + H), the reported standard deviations for the apparent second-order rate constants were incorrectly transcribed. For pH 9.45, the standard

**Table III.** Rate Constants for the Reactions of 4-(4-Substituted benzoyloxy)-2-butanone Derivatives[a]

| Ester | Buffer | p$K_a$ | pH | $k_2$, $M^{-1}$ min$^{-1}$[d] | Correlation coefficient | Concn range, $M$ | No. of $k_{obsd}$ |
|---|---|---|---|---|---|---|---|
| **3** | A | 9.44 | 9.06 | 1.09 ± 0.01 | 0.9997 | 0.05–0.50 | 6 |
| **3** | A | | 9.07 | 0.96 ± 0.02 | 0.9990 | 0.05–0.50 | 6 |
| **3** | A | | 9.27 | 0.94 ± 0.01 | 0.9998 | 0.02–0.10 | 5 |
| **3** | A | | 9.38 | 1.13 ± 0.03 | 0.9981 | 0.10–0.50 | 5 |
| **3** | A | | 9.44 | 1.16 ± 0.02 | 0.9990 | 0.02–0.50 | 9 |
| **3** | B | 10.66 | 10.66 | 6.17 ± 0.20 | 0.9985 | 0.10–0.50 | 5 |
| **3** | C + D | | 9.09 | 0.122 ± 0.003[e] | 0.9994 | 0.18–0.93 | 5 |
| **3** | C + D | | 9.52 | 0.295 ± 0.018[e] | 0.9944 | 0.13–0.66 | 5 |
| **3** | C | 3.9[b] | | 0.003 | | | |
| **3** | D | 10.4[c] | | 2.55 | | | |
| **3** | E | 7.15 | 7.94 | 0.0464 ± 0.0032 | 0.9930 | 0.02–0.10 | 5 |
| **3** | F | 9.43 | 9.43 | 4.61 ± 0.35 | 0.9913 | 0.02–0.10 | 5 |
| **3** | F | | 8.95 | 5.07 ± 0.10 | 0.9994 | 0.02–0.10 | 5 |
| **3** | F | | 8.51 | 4.33 ± 0.01 | 0.9994 | 0.02–0.10 | 5 |
| **3** | G + H | | 9.45 | 4.87 ± 0.57[e] | 0.9949 | 0.02–0.10 | 5 |
| **3** | G + H | | 8.99 | 3.08 ± 0.45[e] | 0.9986 | 0.02–0.10 | 5 |
| **3** | G | 9.45 | | 8.58 ± 0.68 | | | |
| **3** | H | 6.28 | | 1.16 ± 0.11 | | | |
| **1** | F | 9.43 | 9.43 | 6.88 ± 0.18 | 0.9989 | 0.02–0.10 | 5 |
| **1** | F | | 8.95 | 5.61 ± 0.09 | 0.9996 | 0.02–0.10 | 5 |
| **1** | F | | 8.51 | 7.07 ± 0.20 | 0.9988 | 0.02–0.10 | 5 |
| **1** | G + H | | 9.45 | 5.46 ± 0.55[e] | 0.9962 | 0.02–0.10 | 5 |
| **1** | G + H | | 8.99 | 3.63 ± 0.74[e] | 0.9959 | 0.02–0.10 | 5 |
| **1** | G | 9.45 | | 9.24 ± 0.46 | | | |
| **1** | H | 6.28 | | 1.68 ± 0.10 | | | |
| **2** | F | 9.43 | 9.43 | 5.12 ± 0.06 | 0.9997 | 0.02–0.10 | 5 |
| **2** | F | | 8.95 | 5.30 ± 0.07 | 0.9997 | 0.02–0.10 | 5 |
| **2** | F | | 8.51 | 5.48 ± 0.18 | 0.9984 | 0.02–0.10 | 5 |
| **2** | G + H | | 9.45 | 5.28 ± 0.21[e] | 0.9996 | 0.02–0.10 | 5 |
| **2** | G + H | | 8.99 | 3.25 ± 0.25[e] | 0.9994 | 0.02–0.10 | 5 |
| **2** | G | 9.45 | | 9.47 ± 0.18 | | | |
| **2** | H | 6.28 | | 1.08 ± 0.03 | | | |
| **4** | F | 9.43 | 9.43 | 5.07 ± 0.07 | 0.9997 | 0.02–0.10 | 5 |
| **4** | F | | 8.95 | 5.48 ± 0.08 | 0.9997 | 0.02–0.10 | 5 |
| **4** | F | | 8.51 | 5.53 ± 0.07 | 0.9998 | 0.02–0.10 | 5 |
| **4** | G + H | | 9.45 | 4.73 ± 0.45[e] | 0.9967 | 0.02–0.10 | 5 |
| **4** | G + H | | 8.99 | 3.08 ± 0.64[e] | 0.9957 | 0.02–0.10 | 5 |
| **4** | G | 9.45 | | 8.15 ± 0.34 | | | |
| **4** | H | 6.28 | | 1.31 ± 0.11 | | | |
| **5** | F | 9.43 | 9.43 | 4.36 ± 0.09 | 0.9993 | 0.02–0.10 | 5 |
| **5** | F | | 8.95 | 3.96 ± 0.15 | 0.9979 | 0.02–0.10 | 5 |
| **5** | F | | 8.51 | 4.76 ± 0.14 | 0.9987 | 0.02–0.10 | 5 |
| **5** | G + H | | 9.45 | 4.72 ± 0.38[e] | 0.9990 | 0.02–0.10 | 5 |
| **5** | G + H | | 8.99 | 3.17 ± 0.08[e] | 0.9999 | 0.02–0.10 | 5 |
| **5** | G | 9.45 | | 7.92 ± 0.34 | | | |
| **5** | H | 6.28 | | 1.52 ± 0.09 | | | |

[a] With 2-ethoxyethylamine (A), methylamine (B), bicarbonate ion (C), carbonate ion (D), imidazole (E), dimethylaminoethanol (F), N,N,N′,N′-tetramethylethylenediamine (G), and N,N,N′,N′-tetramethylethylenediamine monocation (H) (solvent $H_2O$, $t$ = 30 ± 0.1°, $\mu$ = 1.0 $M$ with KCl). [b] D. Berg and A. Patterson, Jr., *J. Amer. Chem. Soc.*, **75**, 5179 (1953). [c] A. Albert and E. P. Sergeant, "Ionization Constants of Acids and Bases," Wiley, New York, N. Y., 1962, p 151. [d] Determined by using the program of linear regression and correlation coefficient (program No. 09100-70803) with a Hewlett-Packard 9100H calculator. [e] Slope obtained from a plot of $k_{obsd}$ *vs.* total buffer concentration.

The Hammett $\rho$ values for the reactions of **1–5** with various bases were determined from slopes of plots of log $k_2$ values *vs.* $\sigma$ values. For hydroxyl ion, $\rho = +0.18 \pm 0.02$ ($r = 0.9797$); for N,N-dimethylaminoethanol, $\rho = +0.14 \pm 0.05$ ($r = 0.8667$); for N,N,N′,N′-tetramethylethylenediamine, $\rho = +0.07 \pm 0.03$ ($r = 0.8396$).

Rate constants for the reactions of **3** with tertiary amines and hydroxide ion are related to p$K_a$ *via* eq 5.

$$\log k_2 = 0.30 \pm 0.02\text{p}K_a - 1.903 \quad (r = 0.9948) \quad (5)$$

Equation 6 (Figure 2) characterizes the hydroxide ion catalyzed elimination reactions of **1–5**, 4-(4-X-phenoxy)-2-butanones (X = $CH_3O$ (**6**), $CH_3$ (**7**), H (**8**), Cl (**9**), CN (**10**)),[6] and as well, the general base catalyzed exchange reaction for the $\alpha$-methylene protons of 4-methoxy-2-butanone (**11**) in $D_2O$ ($k_{OD}$ = 176 $M^{-1}$ min$^{-1}$).[11]

$$\log k_{OH} = -1.16 \pm 0.07\text{p}K_a + 6.25 \quad (r = 0.9823) \quad (6)$$

In calculating eq 6, the rate constant $k_{OH}$ = 130 $M^{-1}$ min$^{-1}$ for the exchange reaction was used to allow for the solvent isotope effect.[12,13] The p$K_a$ values of eq 6 are those for 4-substituted benzoyloxyacetic acids,[14] phenoxyacetic acids,[15] and methoxyacetic acid.[16] The p$K_a$ value for 4-methylben-

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deviations reported (Table III) are too high by a factor of 2; for pH 8.99, the standard deviations are too high by a factor of 3.9.

(11) L. R. Fedor, *J. Amer. Chem. Soc.*, **91**, 908 (1969).
(12) Y. Pocker, *Chem. Ind.* (London), 1383 (1959).
(13) F. A. Long, *Ann. N. Y. Acad. Sci.*, **84**, 596 (1961).
(14) C. Concilio and A. Bongini, *Ann. Chim.* (Rome), **56**, 417 (1966).
(15) N. V. Hayes and G. E. K. Branch, *J. Amer. Chem. Soc.*, **65**, 1555 (1943).
(16) M. H. Palomaa, *Ann. Acad. Sci. Fenn., Ser. A*, 4, 1 (1911); *Chem. Abstr.*, **8**, 1772 (1914).

zoyloxyacetic acid (3.07) was extrapolated from the data of Concilio and Bongini[14] *via* a plot of p$K_a$ *vs.* $\sigma$.

## Discussion

A notable feature of the elimination reactions of **1–5** is their insensitivity to the nature of the leaving group. Thus for the reactions of 4-(4-substituted benzoyloxy)-2-butanones with various bases, $\rho = 0.15$ (*vide supra*) demonstrating that these reactions are about as sensitive to substituent effects as are the ionizations of 4-substituted benzoyloxyacetic acids, $\rho = 0.16$.[14] Practically, $\rho$ reflects the effect of the 4-substituents on the acidity of the $\alpha$-methylene protons of **1–5** and $\rho$ for the elimination reactions is essentially zero.

The general base character of the reactions described herein (eq 1) requires that proton transfer from **1–5** to an acceptor base be rate determining. This taken with the low $\rho$ value suggests a concerted mechanism wherein the transition state has carbanionic or ElcB character[17] or the ElcB mechanism of eq 7 wherein

$$\mathrm{SH} \underset{k_2\mathrm{BH}^+}{\overset{k_1\mathrm{B}}{\rightleftharpoons}} \mathrm{S}^- \xrightarrow{k_3} \mathrm{P} \qquad (7)$$

$k_3 \gg k_2$. The latter mechanism is preferred for the following reasons. (1) The rates of the hydroxide ion catalyzed $\beta$-elimination reactions of **1–10** and as well the rate of the general base catalyzed *exchange reaction* in $D_2O$ of **11** constitute the LFER (linear free energy relationship) of eq 6. Conformity of all the compounds to eq 6 provides evidence for a single mechanism, *viz.*, the mechanism of eq 7 wherein $k_1$ is rate determining. In connection with eq 6 and in accord with the mechanism of eq 7, a LFER does *not* result from a plot of log $k_{OH}$ *vs.* p$K_a$ of the *leaving group.* (2) $\beta$ elimination from **6–9** catalyzed by weaker bases such as N,N-dimethylaminoethanol is characterized by saturation kinetics,[6,18] *i.e.*, **6–9**, whose reactivities toward hydroxide ion are characterized by eq 6,[19] likely undergo $\beta$ elimination *via* the mechanism of eq 7, but in N,N-dimethylaminoethanol buffer solutions, partitioning of $S^-$ is kinetically significant. (3) For **3**, $\beta = 0.30 \pm 0.02$ (eq 5); for **11**, $\beta = 0.29 \pm 0.04$ for exchange of the $\alpha$-methylene protons in $D_2O$ catalyzed by eight tertiary amines and deuterioxide ion;[19] the nearly identical values may be indicative of the same mechanism, *viz.*, that of eq 7. (4) $\rho = 0$.

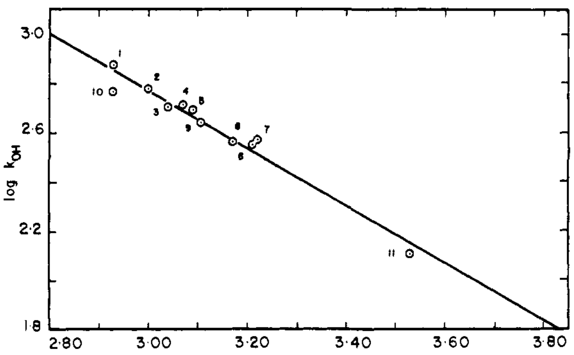

Figure 2. Plot of log $k_{OH}$ for the $\beta$ elimination reactions of **1–10** and for the H–D exchange reaction of **11** *vs.* the p$K_a$ of the appropriate 4-substituted benzoyloxyacetic acid, 4-substituted phenoxyacetic acid, and methoxyacetic acid (eq 6).

Primary and secondary amine-catalyzed dealdolization of diacetone alcohol occurs *via* unimolecular decomposition of the imine.[20] Methylamine catalyzed $\alpha$-hydrogen exchange of isobutyraldehyde-2-*d* occurs largely *via* the aldiminium ion;[21] to a lesser extent, presumably because of the less favorable equilibrium constant, general base catalysis of deuterium exchange in methoxyacetone occurs *via* the methylketimine.[22] In the present study, a term second order in amine is statistically unimportant[10] in the elimination reactions of **3** catalyzed by ethoxyethylamine and methylamine,[23] suggesting that the equilibrium concentration of 3-ketimine is too low to be kinetically significant in the general base catalyzed elimination reactions or alternatively, 3-ketimine undergoes unimolecular decomposition to products. We favor the first possibility on the basis that the rate constants for elimination from **3** catalyzed by ethoxyethylamine and by methylamine show the predicted negative deviations from eq 5.[24]

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