

On caustic fusion of I, 2,4-dihydroxybenzophenone, benzoic acid, and 4,6-dihydroxyisophthalic acid were obtained. Thus the structure of I is undoubtedly that of 4,6-bis(3-phenylphthalidyl)resorcinol, belonging to a class of compounds for which the name of diphthalein is suggested.

Orndorff and Murray⁴ obtained two phthaleins in the reaction of 2-(4-hydroxybenzoyl)benzoic acid with resorcinol, which they believed to be isomers. Two phthaleins were also obtained in this laboratory from II and hydroquinone and from II and pyrogallol. It is quite possible that on reinvestigation one of each pair of compounds will be found to be a diphthalein.

Experimental Section⁵

Preparation of I. A. From II and Resorcinol.—To a solution of II, prepared from 45.2 g of *o*-benzoylbenzoic acid and 30 g of thionyl chloride, in 250 ml of benzene was added 11.0 g of powdered resorcinol. The suspension was heated to 80–85° for 4 hr. A fine, gray precipitate formed with the evolution of HCl. The mixture was filtered the next day and the cake washed with 50 ml of benzene and with six portions of 60 ml of ethanol, leaving 40.5–43.1 g (77–82%) of I, mp 278–290°.

B. From II and III.—To II, prepared from 22.6 g of *o*-benzoylbenzoic acid and 15 g of thionyl chloride, in 170 ml of benzene, was added 31.8 g of III,³ mp 199–200°. The mixture was slowly heated to 80°, yielding 49.4 g (94%) of I, mp 290–292°.

I (1 g) required 650 ml of acetic acid or 2 l. of ethanol for recrystallization. The crystals from acetic acid sintered with gas evolution at 227–235°, solidified, and remelted at 292–294°.

Crystals from acetic acid, dried at 20–25°, were analyzed. *Anal.* Calcd for C₃₄H₂₂O₆·CH₃COOH·H₂O: C, 71.46; H, 4.67. Found: C, 71.26; H, 5.03.

After being dried under vacuum at 230–235°, I was again analyzed. *Anal.* Calcd for C₃₄H₂₂O₆: C, 77.56; H, 4.21. Found: C, 77.20; H, 4.14.

A solution of 16 mg of I in 50 ml of 0.1 *N* sodium hydroxide is of strong reddish orange color.

Alkaline Degradation of I. A.—A solution of 10 g of I in 30 ml of 2.5 *N* sodium hydroxide was kept for 3 weeks over nitrogen, then acidified, yielding 5.19 g of *o*-benzoylbenzoic acid and 1.3 g of resorcinol.

B.—A solution of 10 g of I in 100 ml of 0.1 *N* sodium hydroxide was refluxed for 30 min, yielding 5.9 g of *o*-benzoylbenzoic acid and 1.1 g of resorcinol.

C.—I (10 g) was added to 50 g of molten potassium hydroxide at 240–245°. The melt was stirred for 10 min, then cooled, and dissolved in water. The solution yielded 4.77 g of benzoic acid, 0.67 g of 2,4-dihydroxybenzophenone (mp 142–143°), and two nonsublimable acids, which were separated from each other by fractional crystallization from 50% acetic acid. One melted at

236.2–237.3° dec and the other at 298–300° dec. The latter proved to be 4,6-dihydroxyisophthalic acid, which when treated with diazomethane yielded the dimethyl 4,6-dimethoxyisophthalate, mp 145.0–147.5°, after sublimation under high vacuum and subsequent crystallization from methanol, and did not depress the melting point of authentic dimethyl 4,6-dimethoxyisophthalate,⁶ mp 147.8–148.3°.

Diacetyl Derivative of I.—A mixture of 2.63 g of I, 10 ml of acetic acid, 5 ml of acetic anhydride, and 1 drop of concentrated sulfuric acid was refluxed for 1 hr. The mixture was poured on ice and the precipitate crystallized from ethanol (1 g in 100 ml). This diacetyl derivative melted at 253.0–256.3° (lit.¹ mp 245°). *Anal.* Calcd for C₃₈H₂₆O₈: C, 74.74; H, 4.29; mol wt, 611; 2CH₃CO, 14.1. Found: C, 74.64; H, 4.24; mol wt, 606 ± 28 (Rast); CH₃CO, 13.8 (lit.¹ C, 74.9, H, 4.3).

Dr. David N. Kendall reported on the infrared spectrum of compound I, scanned as Nujol and hexachlorobutadiene mulls: "An absorption band is observed at 893 cm⁻¹, which is believed to arise from 1,2,4,5-tetrasubstituted benzene. Monosubstituted benzene absorptions are present at 695 and 749 cm⁻¹ and *ortho*-disubstituted benzene absorption at 765 cm⁻¹. Compound I shows ketone carbonyl absorption of a γ -lactone with α,β -unsaturation at 1721 cm⁻¹; aromatic hydroxyl at 3205, 1383, and 1292 cm⁻¹; aromatic C=C at 1610, 1597, 1517, and 1490 cm⁻¹; and C–O–C of the C–O–C=O grouping at 1259 cm⁻¹. The infrared spectra of I and the known compound III are very similar in the 5000–1250-cm⁻¹ region."

Registry No.—I, 15791-04-5.

(6) F. v. Hemmelmayr, *Monatsh. Chem.*, **38**, 87 (1917); E. Spaeth, *et al.*, *Ber.*, **64**, 2211 (1931).

The Acetate-Catalyzed Enolization of 2-Butanone

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Recently, several papers have appeared on the relative rates of enolization at the two sites of simple unsymmetrical ketones, studied by deuterium exchange and nmr techniques.^{1–8} Generally, the results obtained by different workers are in agreement, but our results¹ and those of Rappe,^{4,5} on the enolization of 2-butanone differ in two important respects. We find that the relative rates for base-catalyzed enolization at the methylene and α -methyl positions are *different* for different bases and that the rate of exchange in the absence of catalyst is negligible. Rappe finds the relative rates *the same* for different bases and an appreciable rate for the so-called uncatalyzed reaction. Because of this, we have recently studied the uncatalyzed and acetate-catalyzed reactions again and have re-determined the acetate catalysis constants using the buffer method suggested by Bell.⁹ Our previous method involved the extraction of catalytic constants for acetate from over-all rate data by an extrapolation technique.¹

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(9) R. P. Bell and P. Jones, *J. Chem. Soc.*, **88** (1953).

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(5) All melting points are corrected.

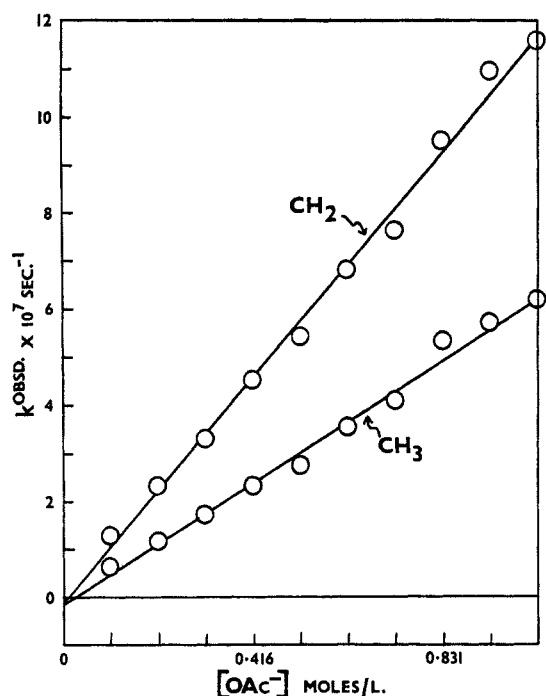


Figure 1.—Plot of observed pseudo-first-order rate constants against acetate concentration for H-D exchange of 2-butanone; buffer ratio 0.0936.

The observed rate constant for reaction in acetate buffers can be represented as a sum of terms (eq 1).

$$k^{\text{obsd}} = k_o + k_{\text{D}_2\text{O}^+}[\text{D}_2\text{O}^+] + k_{\text{OD}^-}[\text{OD}^-] + \frac{k_A[\text{DOAc}]}{k_A[\text{DOAc}] + k_p[\text{OAc}^-] + k_p[\text{DOAc}][\text{OAc}^-]} \quad (1)$$

In a buffer solution, the pD and hence $[\text{D}_2\text{O}^+]$ and $[\text{OD}^-]$ remain constant upon dilution. Consequently, as $[\text{DOAc}]$ and $[\text{OAc}^-]$ are varied at constant buffer ratio, the first three terms in eq 1 remain constant. Writing $r = \text{buffer ratio} = [\text{DOAc}]/[\text{OAc}^-]$, and assuming k_p to be small⁹ in comparison with k_A and k_B , eq 1 reduces to eq 2.

$$k^{\text{obsd}} = k' + (k_A r + k_B)[\text{OAc}^-] \quad (2)$$

If k_p is negligible, as assumed, a plot of k^{obsd} vs. $[\text{OAc}^-]$ will be linear, with slope $(k_A r + k_B)$ and intercept k' . The acetic acid concentration was kept low to emphasize the base-catalyzed reaction, and, because k_A is smaller than k_B ,⁸ the important contributor to the slope was expected to be k_B . However, both k_A and k_B can be obtained in principle by varying the buffer ratio r , and this was done. If k_p is not negligible, relative to the other terms, curved plots should result.

Our results, obtained as described in the Experimental Section, are given in Table I, and k^{obsd} vs. $[\text{OAc}^-]$ for one buffer ratio is plotted in Figure 1.

The catalytic constants for acetate at 54.8°, obtained from the slopes of the graphs, are given in Table II.

The errors involved in kinetic measurements by nmr are not low. In common with Bothner-By and Sun⁷ we found individual integrations varying by as much as 10%, and as the integral areas decrease the error in them increases. Nevertheless, we feel that we can draw the following conclusions with a high degree of confidence.

1. The plots are straight lines. Therefore, there is no detectable contribution from the product term $[\text{OAc}^-][\text{DOAc}]$.

TABLE I
PSEUDO-FIRST-ORDER RATE CONSTANTS FOR H-D EXCHANGE OF 2-BUTANONE IN DEUTERIUM OXIDE ACETATE BUFFER AT 54.8°

Buffer ratio, HA/A ⁻	Acetate concn, M	$k^{\text{obsd}} \times 10^7 \text{ sec}^{-1}$	
		CH ₂	CH ₃
0.0936	1.039	11.60 ± 0.29	6.22 ± 0.09
0.0936	0.935	10.97 ± 0.30	5.74 ± 0.11
0.0936	0.831	9.54 ± 0.20	5.37 ± 0.11
0.0936	0.727	7.67 ± 0.19	4.10 ± 0.05
0.0936	0.623	6.82 ± 0.15	3.55 ± 0.06
0.0936	0.520	5.46 ± 0.10	2.78 ± 0.04
0.0936	0.416	4.58 ± 0.11	2.36 ± 0.03
0.0936	0.312	3.31 ± 0.08	1.72 ± 0.02
0.0936	0.208	2.37 ± 0.07	1.20 ± 0.02
0.0936	0.104	1.31 ± 0.07	0.65 ± 0.04
0.0469	1.039	11.52 ± 0.35	6.09 ± 0.14
0.0469	0.935	9.53 ± 0.18	5.19 ± 0.10
0.0469	0.831	11.03 ± 0.33	4.79 ± 0.14
0.0469	0.727	9.35 ± 0.61	4.27 ± 0.15
0.0469	0.623	6.56 ± 0.18	3.57 ± 0.05
0.0469	0.520	5.97 ± 0.60	3.47 ± 0.10
0.0469	0.416	4.23 ± 0.11	2.20 ± 0.03
0.0469	0.312	3.37 ± 0.09	1.76 ± 0.03
0.0469	0.208	2.15 ± 0.08	1.23 ± 0.02
0.0469	0.104	1.31 ± 0.18	0.36 ± 0.15

TABLE II
ACETATE CATALYSIS CONSTANTS k_B , AT 54.8°, FOR THE H-D EXCHANGE OF 2-BUTANONE

Buffer ratio	$k_B \times 10^7 \text{ l. m}^{-1} \text{ sec}^{-1}$		Ratio	
	CH ₂ ^a	CH ₃ ^a	$k_{\text{CH}_2}/k_{\text{CH}_3}$ ^a	$2k_{\text{CH}_2}/3k_{\text{CH}_3}$ ^b
0.0936	11.40 ± 0.31	6.19 ± 0.22	1.84 ± 0.12	1.23 ± 0.08
0.0469	11.54 ± 0.88	5.88 ± 0.23	1.96 ± 0.23	1.31 ± 0.15
Average	11.47 ± 0.59	6.03 ± 0.22	1.90 ± 0.17	1.27 ± 0.11
Previous results ^c	11.8 ± 0.5	5.47 ± 0.70	2.16 ± 0.36	1.44 ± 0.24

^a Reactivity is defined on the *per hydrogen* basis, as was done previously.¹ ^b Relative reactivity on the *per group* basis. These ratios are labeled K_D by Rappe.⁴ ^c See ref 1.

2. Within the limits of experimental error the plots go through the origin. Therefore, under our conditions, catalysis by D_2O , D_3O^+ , or OD^- is not detectable relative to catalysis by OAc^- .

3. The catalytic constants for acetate at 54.8° are the same, within the limits of experimental error, as those previously obtained by our extrapolation technique¹ (see Table II).

4. The results for the two buffer ratios are the same, within the limits of error (Table II). This means that catalysis by acetic acid (the term $k_A[\text{DOAc}]$) is negligible relative to acetate catalysis and that the slopes of the graphs (Figure 1) may be taken to represent acetate catalysis alone.

For comparison purposes, the ratio $k_{\text{CH}_2}/k_{\text{CH}_3}$ for deuterioxide catalysis was also measured at 54.8°. Two measurements gave for $k_{\text{CH}_2}/k_{\text{CH}_3}$ 0.88 ± 0.05 and 0.84 ± 0.08 . These values are very different from the rate ratio for acetate catalysis (1.9) measured at the same temperature. Also, on comparison with the value of about 1.0 previously obtained for catalysis by OD^- at 0°, it appears that the activation energy for exchange at the methyl group exceeds that for exchange at the methylene group, at least for deuterioxide catalysis. Work is currently under way to obtain activation parameters for both processes accurately.

In order to try to obtain values for the rate constants of the uncatalyzed reaction, a sample of 2-butanone in

0.1 M NaCl-D₂O was maintained at 54.8° and integrated with the others. After 2 months no sign of exchange was observed—the nmr peaks were still sharp and unsplit,^{10,11} and the integral values were unchanged from the original. We were, therefore, unable to obtain rate constants for the uncatalyzed reaction. This contrasts with Rappe's findings,^{4,5} which were that, after "several months" at 30°, exchange could be observed. After 2 months at nearly double this temperature we could observe none. This finding is in accord with our previous estimate¹ that the uncatalyzed reaction would contribute 1% or less to the total reaction at 60°, with acetate concentrations in D₂O of 0.1 M or more. In support also is Hine's recent estimate⁸ that the uncatalyzed deuteration of methoxyacetone would contribute a maximum value of 0.2% of the total to base-catalyzed reaction rates, under a wide variety of conditions. It is likely that a high rate of "uncatalyzed exchange," where observed, is really the result of catalysis by unrecognized impurities.

We believe that this work firmly establishes the dependence of relative catalytic constants ($k_{\text{CH}_2}/k_{\text{CH}_3}$), for deuterium exchange into 2-butanone, on the nature of the catalyzing base. Such dependence was to be expected, since enolization is closely analogous to bimolecular elimination, in which product ratios depend on the base employed.¹² The relative importance of the steric requirements of the base and of its strength is not completely understood at this time.¹²

Experimental Section

Reagent grade chemicals were used; acetic acid and 2-butanone being redistilled before use. Sodium acetate was dried at 160° to obtain the anhydrous material. D₂O was used as supplied by the Columbia Organic Chemicals Co. Stock reagent solutions, made up gravimetrically, were two sodium acetate-acetic acid buffer solutions in D₂O, with buffer ratios of 0.0936 and 0.0469; the acetate concentration in each case being about 1.1 M. Aliquots of these solutions were then diluted with a solution of sodium chloride in D₂O of equivalent molarity. By this procedure ten solutions with acetate concentrations varying between about 1.1 and 0.11 M, at a constant buffer ratio of 0.0936 and a constant ionic strength of about 1, were obtained, as well as ten similar solutions at a buffer ratio of 0.0469. Addition of 0.1 ml of 2-butanone to 1 ml of the above solutions resulted in a 2-butanone concentration of 1.18 M, an ionic strength of 1.04, and the acetate concentrations shown in Table I. After mixing, the solutions were sealed into standard nmr tubes which had been cleaned with chromic acid, thoroughly rinsed, and dried.

Samples were immersed in a thermostat at 54.8°, together with a sample containing 2-butanone and 1.04 M sodium chloride, but no acetate. Integrations were performed every 1 or 2 days as necessary, after quenching exchange by chilling the tube with ice. Reaction outside the bath was negligible, and time outside the bath was not counted.

Exchange was followed to at least one half-life by integrating the signals from the 1 and 3 positions, using the β -methyl group as internal standard, on a Varian A-60 instrument.^{1,11} Each sample was integrated six times and an average was taken.

The integral from the β -methyl group was taken as internal standard and the areas for the 1 and 3 positions were converted into the average number of hydrogen atoms per molecule remaining at these positions. On plotting the logarithms of these numbers against time, good straight lines were obtained even for exchanges followed to over two half-lives. Each graph contained at least 15 points. A linear least-squares program for

(10) Splitting of the nmr peaks was taken to be a more reliable indication of initial deuterium substitution than change in the integral values. See ref 11 for splitting patterns resulting from varying amounts of substitution.

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the IBM 7040 computer was used to obtain pseudo-first-order rate constants and their standard deviations, and, from these figures, acetate catalysis constants.

For the study of deuterioxide catalysis at 54.8°, a deuterioxide concentration of 1.962×10^{-3} M was used. The probe temperature was set, using the variable-temperature controller, at $54.8 \pm 0.5^\circ$, and the deuterioxide solution was equilibrated to that temperature by leaving it in the probe for a few minutes. Butanone at the same temperature was then added, after which the tube was shaken and replaced in the probe. Integrations were performed every 150 sec over a 90-min period, which was about one half-life under the reaction conditions. The signal from the nonexchanging β -methyl group was used to normalize integrals (I_t) as described above, and best fits to the equation $\log I_t = k^{\text{obsd}}t/2.303$ were computed.

Registry No.—2-Butanone, 78-93-3.

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Conformational Analysis of the Carbon-Oxygen Bond of Alcohols Using J_{HCOH}

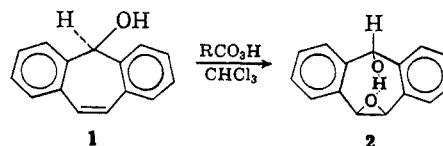
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Since the report that J_{HCOH}^1 can often be determined in DMSO solution², several papers³⁻⁶ have appeared in which a conformational dependence is invoked for J_{HCOH} similar in qualitative form to that observed for J_{HCHH} .^{7,8} Unfortunately, it is difficult to restrict rotation about the C-O bond of an alcohol, so that values of $J_{\text{HCOH}}^{\text{trans}}$ and $J_{\text{HCOH}}^{\text{cis}}$ have not been available, thus precluding corroboration and quantitative application of this potentially useful conformational probe. We have, quite fortuitously,⁹ synthesized an alcohol in which the pertinent rotation is restricted by strong internal hydrogen bond formation and from which a value can be obtained for $J_{\text{HCOH}}^{\text{trans}}$.

Epoxidation of 1 by *m*-chloroperbenzoic acid yields 2; the nmr (CDCl₃) spectrum showed signals at τ



2.75 (m, 8 H, aromatics), 4.65 (d, 1 H, $J = 12.5$ cps, carbinol methine), 5.20 (d, 1 H, $J = 12.5$ cps, hydroxyl), 5.59 (s, 2 H, methines adjacent to epoxide function). The infrared spectrum has a single,

(1) *I.e.*, the nmr coupling constant of a hydroxyl proton with a vicinal carbinol proton.

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(6) R. J. Ouellette, D. L. Marks and D. Miller *ibid.*, **89**, 913 (1967).

(7) M. Karplus *ibid.*, **85**, 2870 (1963).

(8) Similar conformational dependencies have been found for J_{HCCCH} (G. J. Karabatsos, C. E. Orzech, Jr., and N. Hsi, *ibid.*, **88**, 1817 (1966)) and J_{HCCF} (K. L. Williamson, Y. Li, F. H. Hall, and S. Swager, *ibid.*, **88**, 5679 (1966)).

(9) N. L. Bauld and Y. S. Rim, *ibid.*, **89**, 179 (1967).