cleavage, and is only about one-tenth or less of the rate of dehydration of the isomer 1-(*p*-methoxyphenyl)-1-hydroxy-3-pentanone. This fact, coupled with the facile dehydration of 4-(*p*-methoxyphenyl)-4-hydroxy-2-butanone (III), makes it clear that the structural course of the aldol type condensation (the Claisen-Schmidt condensation) is determined in the latter stages of the reaction.

In contrast, the acid-catalyzed condensation of anisaldehyde and methyl ethyl ketone gave results[3,4] consistent *only* with the conclusion that the structure of the product is determined by the condensation step itself. Particularly pertinent is the observation that III undergoes dehydration more rapidly than V. Analogously, 1-(*p*-methoxyphenyl)-1-hydroxy-3-pentanone should undergo similar rapid dehydration were it formed during the course of the acid-catalyzed reaction. However, Noyce and Snyder[3,4] excluded the formation of 1-(*p*-methoxyphenyl)-1-hydroxy-3-pentanone in their kinetic investigations.

The conclusions presented in this paper are therefore in complete accord with the deductions of Stiles and Wolf[20] and supplement their observations with additional quantitative information.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF MICHIGAN]

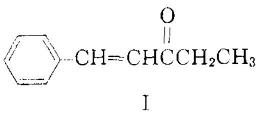
Catalyst Selectivity in the Reactions of Unsymmetrical Ketones; Reaction of Butanone with Benzaldehyde and *p*-Nitrobenzaldehyde

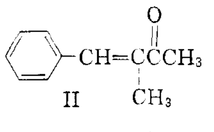
BY MARTIN STILES, DANIEL WOLF AND GWYN V. HUDSON

RECEIVED AUGUST 11, 1958

The hydroxy ketone intermediates III and IV from the reaction between benzaldehyde and butanone have been prepared by the Schöpf method. Treatment of either the straight-chain isomer III or the branched isomer IV with dilute alkali produced the straight-chain unsaturated ketone I. Treatment of III and IV with acid afforded I and II, respectively, with no evidence of rearrangement. The reaction between *p*-nitrobenzaldehyde and butanone in alkali yielded three hydroxy ketones (V, VIa and VIb) indicating that both methyl and methylene positions were attacked to a comparable extent. These results support a mechanism for the alkaline condensation in which the dehydration of the intermediate hydroxy ketones is a slow step and thus responsible for the exclusive formation of I. The formation of II in acid results from selectivity at the addition step (2) of the reaction.

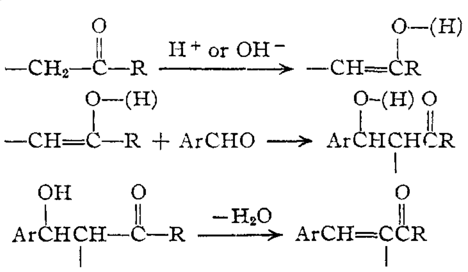
The replacement of hydrogen atoms adjacent to a carbonyl group normally proceeds through enolization and is therefore frequently catalyzed by either acidic or basic reagents. An unsymmetrical dialkyl ketone may allow substitution at either of two positions which differ in the extent of substitution already present. Much investigation has been directed at determining the position of attack upon such unsymmetrical ketones, and several important reactions have been encountered in which acidic reagents favor attack at the more substituted, and basic reagents at the less substituted, of two α-carbons. Thus butanone undergoes bromination predominantly at the methyl group in alkali and at the methylene group in acid[1]; it is acylated by boron trifluoride–acetic anhydride largely at the methylene group and by sodium ethoxide–ethyl acetate at the methyl group[2]; and it reacts with benzaldehyde to give exclusively 1-phenyl-1-penten-3-one (I) when dilute sodium hydroxide is used as catalyst and exclusively 3-methyl-4-phenyl-3-buten-2-one (II) with hydrogen chloride as catalyst.[3]


I


II

Since enolization is the rate-controlling step in the bromination of ketones at moderate catalyst concentrations,[4] it may be concluded that the first of these examples of catalyst selectivity is due to rate differences at the enolization step, acid favoring formation of the more highly branched enol and base preferentially removing the primary hydrogens. However, most other substitution reactions in which such catalyst selectivity is observed require much more vigorous conditions, and the selectivity must be due to other causes. We have chosen to examine in detail the reaction of butanone with aromatic aldehydes, with the aim of understanding those factors which are responsible for the catalyst selectivity.

The generally accepted reaction sequence for the aldehyde–ketone condensation is



$$-CH_2-\overset{\overset{O}{\|}}{C}-R \xrightarrow{H^+ \text{ or } OH^-} -CH=\overset{\overset{O-(H)}{|}}{C}R \qquad (1)$$

$$-CH=\overset{\overset{O-(H)}{|}}{C}-R + ArCHO \longrightarrow Ar\overset{\overset{O-(H)}{|}}{C}H\underset{|}{C}H\overset{\overset{O}{\|}}{C}R \qquad (2)$$

$$Ar\overset{\overset{OH}{|}}{C}H\underset{|}{C}H-\overset{\overset{O}{\|}}{C}-R \xrightarrow{-H_2O} ArCH=\underset{|}{\overset{\overset{O}{\|}}{C}}\!CR \qquad (3)$$

Although kinetic data had not been reported for the acid-catalyzed condensation[5] it was clear that the conditions under which it is usually car-

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[1] H. M. E. Cardwell and A. E. H. Kilner, *J. Chem. Soc.*, 2430 (1951); H. M. E. Cardwell, *ibid.*, 2442 (1951).

[2] C. R. Hauser, F. W. Swanson and J. T. Adams, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 59.

[3] (a) C. Harries and G. H. Müller, *Ber.*, **35**, 966 (1902); (b) J. D. Gettler and L. P. Hammett, THIS JOURNAL, **65**, 1824 (1943); (c) for a summary of many reactions between butanone and aldehydes see H. Haeussler and C. Brugger, *Ber.*, **77**, 152 (1944–1946).

[4] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 96–97.

[5] Such data for this reaction and related ones have now been presented; D. S. Noyce and L. R. Snyder, THIS JOURNAL, **80**, 4033, 4324 (1958).

ried out (anhydrous hydrogen chloride) are far more drastic than would be necessary for either enolization (1) or dehydration (3), and that (2) must therefore be rate-determining

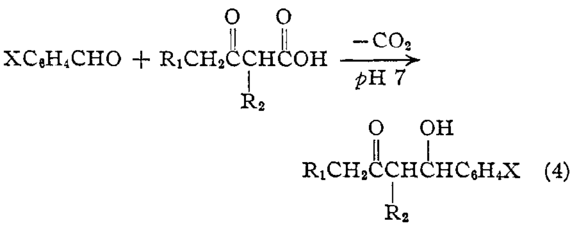
Gettler and Hammett[3b] studied the kinetics of the base-catalyzed (Claisen–Schmidt) reaction between butanone and benzaldehyde and found it to be first order in each reactant. They postulated that the second step was the rate-determining one. The assumption that (3) is a slow step is also compatible with the kinetic results, but this possibility has been generally overlooked or discounted.[6]

If dehydration were involved in the rate-determining process in alkaline reaction, a fundamental difference between the acid- and base-catalyzed condensations would thus exist, and might be related to the catalyst selectivity. This suggestion receives some support from the fact that this selectivity has been observed only among aromatic aldehydes, which produce unsaturated products, and is not apparent from examination of the results of condensation of butanone with aliphatic aldehydes.[3c]

The present report concerns a study of aldehyde–ketone condensation from two different approaches: (1) preparation of the intermediate hydroxy ketones III and IV and examination of their behavior under both basic and acidic conditions, and (2) base-catalyzed condensation of *p*-nitrobenzaldehyde with butanone, a reaction which stops at the hydroxy ketone stage and allows study of step 2 independently.

Results

Benzaldehyde–Butanone Condensation.—The two hydroxy ketones III and IV were prepared by reaction of benzaldehyde with the appropriate β-keto acid (equation 4), a method used by Schöpf and Thierfelder[7] in the case of acetoacetic acid. Both products were liquids and IV undoubtedly was



$$XC_6H_4CHO + R_1CH_2\overset{O}{\overset{\|}{C}}\underset{R_2}{\underset{|}{C}H}\overset{O}{\overset{\|}{C}}OH \xrightarrow[pH\ 7]{-CO_2} R_1CH_2\overset{O}{\overset{\|}{C}}\underset{R_2}{\underset{|}{C}H}\overset{OH}{\overset{|}{C}H}C_6H_4X \quad (4)$$

III, $X = H, R_1 = CH_3, R_2 = H$
IV, $X = H, R_1 = H, R_2 = CH_3$
V, $X = p\text{-}NO_2, R_1 = CH_3, R_2 = H$
VI, $X = p\text{-}NO_2, R_1 = H, R_2 = CH_3$

a mixture of the two diastereoisomers. These two hydroxy ketones III and IV had not been reported previously as pure compounds, although a mixture of the two was obtained by reaction between benzaldehyde and methyl ethyl ketone at 0–5°.[8]

The behavior of III and IV toward 1% sodium hydroxide is illustrated in Fig. 1. The straight chain isomer III (upper curve) eventually was converted to the unsaturated ketone I (63% by ultraviolet spectroscopy; 43% crystalline material isolated; this difference is typical of the losses sustained in crystallizing both I and II, which melt below 40°), but during the early stages of the reaction considerable benzaldehyde appeared in the mixture. Identical treatment of the branched-chain isomer IV converted it in similar yield to the *straight-chain unsaturated ketone* I. In this case the formation of benzaldehyde was faster and more extensive, and the formation of unsaturated ketone I slower at the outset, but after 6 hours the reaction mixtures from III and IV apparently were identical. In neither case was any of the branched unsaturated ketone II detectable in the reaction mixture or in the mother liquors from the crystallization of the straight-chain isomer I.

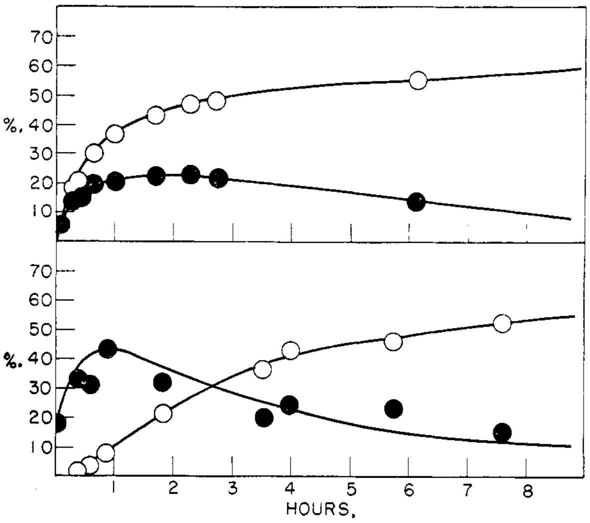


Fig. 1.—Percentage yield, as a function of time, of benzaldehyde (●) and 1-phenyl-1-penten-3-one (○) in the treatment of 1-phenylpentan-1-ol-3-one (III) (upper curves) and 4-phenyl-3-methylbutan-4-ol-2-one, (IV) (lower curves) with 0.25 M sodium hydroxide at 27 ± 1°.

An examination of the behavior of very dilute solutions of the hydroxy ketones in methanolic sodium hydroxide is informative. Under these conditions benzaldehyde and methyl ethyl ketone do not react; hence any decomposition of the hydroxy ketones in a reverse aldol reaction is irreversible. It was found that the straight-chain hydroxy ketone III underwent simultaneous dehydration to unsaturated ketone I and decomposition to benzaldehyde. The branched hydroxy ketone IV, on the other hand, underwent exclusive decomposition to benzaldehyde and methyl ethyl ketone.

Rate constants for the dehydration and reverse aldol decomposition of III and IV in 90% aqueous methanol at 25° are given in Table I. The cleavage of IV was measured by following the appearance of the benzaldehyde absorption at 250 mμ. The determination of $(k_2 + k_5)$ in the reaction of III was made both at 250 and at 286 mμ, the two methods giving almost identical results. Since both cleavage and dehydration reactions were cleanly first order, the ratio k_2/k_5 could be determined from the spectral analysis of the solution for

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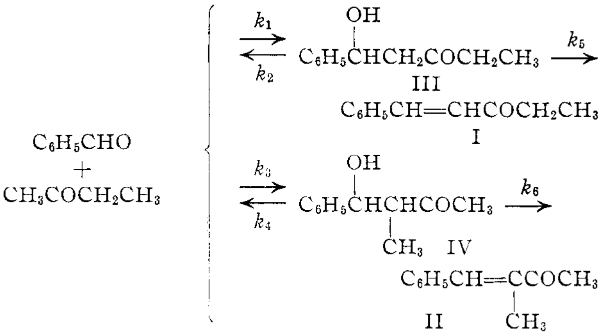
[6] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 683; E. Coombs and D. P. Evans, *J. Chem. Soc.*, 1295 (1940); however, see L. F. Fieser and M. Fieser, "Introduction to Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1957, p. 450.

[7] C. Schöpf and K. Thierfelder, *Ann.*, **518**, 127 (1935).

[8] H. Midorikawa, *Bull. Chem. Soc. Japan*, **27**, 131 (1954).



benzaldehyde and unsaturated ketone I after more than ten half-lives. The dehydration and cleavage of the straight-chain hydroxy ketone in base occur at very nearly the same rate and the ratio k_2/k_5 appears to be insensitive to base concentration.

TABLE I

DEHYDRATION AND CLEAVAGE OF HYDROXY KETONES IN 90% AQUEOUS METHANOL AT 25.0°

Compound	10^4 concn.[a]	$[OH^-]$[a]	10^5k_2[b]	10^5k_5[b]	$10^4k_2/[OH^-]$	$10^4k_5/[OH^-]$
III	1.87	0.030	2.23	2.19	7.43	7.30
	1.74	.050	3.95	3.88	7.90	7.76
	1.87	.050	3.94	3.86	7.88	7.72
	1.74	.100	8.28	8.12	8.28	8.12
	1.74	.100	8.44	8.27	8.44	8.27
				Av.	7.99	7.83
			10^5k_4		$10^4k_4/[OH^-]$	
IV	1.83	0.0050	5.68		114	
	1.83	.0050	5.92		118	
	1.83	.010	11.1		111	
	1.83	.010	11.1		111	
	1.83	.030	33.2		111	
	1.83	.030	31.6		105	
				Av.	112	

[a] Moles per liter. [b] Sec.$^{-1}$.

The measured rate of the alkaline condensation of benzaldehyde and methyl ethyl ketone must therefore be a function of all three rate constants k_1, k_2 and k_5. The rate of dehydration of the branched hydroxy ketone, k_6, is negligibly small compared to k_4; hence under Claisen–Schmidt conditions the compound is in equilibrium with benzaldehyde and methyl ethyl ketone, and thereby rapidly convertible to the much more readily dehydrated straight-chain isomer. That the branched hydroxy ketone IV is in fact formed during the Claisen–Schmidt reaction, though only in a transient side equilibrium, can be concluded from the results of Midorikawa[8] at low temperatures and from the condensation of *p*-nitrobenzaldehyde (*vide infra*).

Treatment of III with dilute (1%) sulfuric acid in methanol, conditions too mild to effect any significant condensation of benzaldehyde and butanone, converted it to I in 33% yield as determined by the isolation of crystalline material. The infrared spectrum of the residual oil indicated that it was also largely I, and failed to disclose any II. Similar acid treatment of the branched hydroxy ketone IV produced a low yield of II along with a large quantity of benzaldehyde. Noyce and Reed[9] have similarly observed that the *p*-methoxy analog of IV undergoes cleavage as well as dehydration in acid and that the homolog which lacks branching next to the carbonyl is dehydrated much faster than the branched compound. These results indicate that dehydration cannot play any determining role in the preferential formation of II in the acid-catalyzed condensation reaction.

The conclusion which can be drawn from these experiments concerning the catalyst selectivity in the benzaldehyde–butanone condensation may be summarized as follows. In the alkaline condensation both hydroxy ketones are formed in an easily reversible reaction. The dehydration is therefore the process which determines the identity of the product, and the straight-chain isomer I is produced exclusively, chiefly because k_5 is much greater than k_6. In strong acid these β-hydroxy ketones are rapidly dehydrated. The process which determines the product under these conditions is therefore the irreversible addition step, and II is formed in preference to I because k_3 is much larger than k_1. Noyce and Reed[9] have been led to the same conclusions independently.

It seems likely that IV is formed more rapidly than III in base as well as in acid, but its more rapid reversal ($k_4 > k_2$) serves to make its equilibrium concentration nearly the same as that of III.

p-Nitrobenzaldehyde–Butanone Condensation.—The condensation of *p*-nitrobenzaldehyde with butanone in sulfuric acid has been reported to give the unsaturated ketone corresponding to attack at the methylene group.[10] The base-catalyzed condensation has not been reported, although acetone reacts with *p*-nitrobenzaldehyde to give the hydroxy ketone under the usual dilute alkaline conditions.[11] We have found that this aldehyde reacts readily with butanone in 1% sodium hydroxide to give nearly quantitative yields of a mixture of hydroxy ketones. A clean separation of this mixture has not been achieved, but chromatography on silica gel[12] led to the isolation of three different hydroxy ketones, m.p. 91°, 94° and 61°. The first of these could be obtained by crystallization of the crude product. It was identical with the product of reaction of propionylacetic acid with *p*-nitrobenzaldehyde (equation 4) and therefore represents the product of condensation at the methyl group V. The hydroxy ketone melting at 94° (VIa) could be obtained easily by chromatography, being the most strongly adsorbed of the three. The 61° material VIb was found in intermediate fractions and was very difficult to crystallize. Both VIa and VIb were more readily obtained from the reaction of *p*-nitrobenzaldehyde and α-methylacetoacetic acid (equation 4).

Each of the three hydroxy ketones was dehydrated by *p*-toluenesulfonic acid in benzene without skeletal rearrangement. Thus V gave the straight-chain unsaturated compound VII, m.p. 108-110°,

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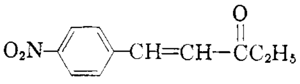
[9] D. S. Noyce and W. L. Reed, THIS JOURNAL, **81**, 618 620, 624 (1959).

[10] G. Heller, H. Lauth and A. Buchwaldt, *Ber.*, **55**, 483 (1922).

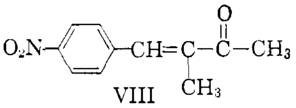
[11] A. Baeyer and P. Becker, *ibid.*, **16**, 1968 (1883).

[12] The advice of Dr. Howard E. Zimmerman concerning this separation is gratefully acknowledged.

and both VIa and VIb gave exclusively the branched isomer VIII, m.p. 92-93°.[13] These observations made it possible to analyze the mixture from the *p*-nitrobenzaldehyde–butanone condensation rather precisely for the ratio of methyl- to methylene-condensation product (V/VI). Dehydration of the crude mixture and infrared analysis of the resulting mixture of unsaturated ketones revealed 50% VII and 45% VIII, along with 5% of unidentified material, possibly higher condensation products. These results agree roughly with the crude analysis based upon chromatography of the hydroxy ketones, which indicated that the three products V, VIa and VIb appeared in approximately a 3:2:2 ratio.



VII



VIII

These results strongly support the conclusions reached in the study of the benzaldehyde–butanone system, *i.e.*, that butanone combines with aromatic aldehydes at both methyl and methylene positions in alkali, and that the exclusive formation of the straight-chain benzylidene compounds is a result of large rate differences at the dehydration stage.

It has been noted that cinnamaldehyde and *p*-methoxycinnamaldehyde condense with butanone preferentially at the methylene position in both acid and alkali.[3c] It seems likely that the intermediate hydroxy ketones in these cases are dehydrated so readily that the final step no longer plays the determining role, and in alkali, as in acid, rate of condensation is the determining factor.

Although furfural was reported[14] to condense with butanone at the methylene group in alkali, more recent work[15] has shown that condensation at the methyl group predominates when the reaction is carried out under conditions which lead to the unsaturated ketone. The branched unsaturated ketone can be obtained in this instance by stopping the reaction at the hydroxy ketone stage and dehydrating the product with acetic anhydride. These observations are easily reconciled with the mechanism proposed here.

At the present time no stereochemical assignments can be reported for the isomers of VI. It also remains to be determined whether the ratio of these isomers from the Schöpf reaction (equation 4) results from an equilibrium or a kinetically controlled process. The fact that the ratio of VIa to VIb appears to be smaller from this reaction than from the butanone condensation suggests that equilibrium between the diastereoisomers may not be reached in the former process.

Experimental[16]

1-Phenyl-1-penten-3-one (I) was prepared as described previously.[3a] The pure product melted at 38° (reported[3b] 38.0°); $\lambda_{\max}^{\mathrm{MeOH}}$ 286 (log ϵ 4.37), 225 (4.01, shoulder), 220 (4.04).

3-Methyl-4-phenyl-3-buten-2-one (II), prepared as described previously,[3a] melted at 38–40° (reported[3b] 38.1°); $\lambda_{\max}^{\mathrm{MeOH}}$ 278 (log ϵ 4.30), 224–226 (3.9, shoulder), 220 (3.96).

Ethyl 2-Methyl-3-ketobutanoate.—Two hundred ml. of pyrrolidine[17a] (Eastman Kodak practical) was added slowly to a mixture of 250 g. (1.92 moles) of acetoacetic ester and 100 ml. of benzene. After the exothermic reaction had subsided the benzene and excess pyrrolidine were removed under reduced pressure. The residue was treated with 410 g. (2.88 moles) of methyl iodide on the steam-bath for 10 min. Water (400 ml.) was added, the mixture was refluxed for 20 min., and the organic layer was taken up in ether. The ether solution was washed with aqueous sodium thiosulfate and with water, dried over Drierite, and freed of solvent. The residue was distilled at reduced pressure to yield 188 g. (68%) of colorless liquid, b.p. 93–95° (33 mm.) (reported[17b] 75–76° (15 mm.)), n^{20}D 1.4189.

Ethyl propionylmalonate was prepared from ethyl ethoxymagnesiomalonate and propionyl chloride essentially as described by Lund[18] except that purification through the copper salt was omitted. The compound distilled at 98–100° (2.7 mm.) (reported[19] 129–131° (18 mm.)).

Ethyl 3-ketopentanoate was prepared from 200 g. of ethyl propionylmalonate as described by Brandstrom.[20] The fraction boiling at 65–71° at 7.0–3.6 mm. was fractionated through a Podbielniak column to yield 54.6 g. (41%) of colorless liquid, b.p. 87–90° (17 mm.); reported[21] 88–93° (17 mm.).

1-Phenylpentan-1-ol-3-one (III).—Fifteen grams of ethyl 3-ketopentanoate was mixed with 1.5 l. of 0.10 *M* NaOH. After 6 hr. at 25° the solution was neutralized with dilute hydrochloric acid, 100 ml. of 0.1 *M* phosphate buffer (*p*H 7) was added, and the solution was freed from air by bubbling nitrogen through it for 5 min. Freshly distilled benzaldehyde (3.0 g.) was added and the mixture was allowed to stand for 4 weeks at room temperature. Extraction of 2 such reaction mixtures with ether furnished an oil which was distilled under reduced pressure to yield 3.5 g. (35%) of colorless liquid, b.p. 113° (0.9 mm.). The products of several similar runs were combined and redistilled through a 10-cm. vacuum-jacketed Vigreux column to furnish the sample, b.p. 93° (0.18 mm.), n^{26}D 1.5241, used in subsequent experiments.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.14; H, 7.92. Found: C, 74.18; H, 8.04.

Reaction times of less than 4 weeks furnished smaller yields, as did the use of aqueous alcohol as solvent.

3-Methyl-4-phenylbutan-4-ol-2-one (IV) was prepared from 20 g. of ethyl 2-methyl-3-ketobutanoate and 3.0 g. of benzaldehyde as in the previously described experiment except that only 1 hr. was required for the hydrolysis of the keto ester. The yield of product from two such batches, b.p. 102° (0.7 mm.), was 2.2 g. (22%). Products from several similar runs were combined and distilled through a 10-cm. vacuum-jacketed Vigreux column to yield a sample, b.p. 102° (0.7 mm.), n^{25}D 1.5224, used in subsequent experiments.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.14; H, 7.92. Found: C, 73.63, 73.75; H, 7.63, 7.60.

The *p*-nitrophenylhydrazone, prepared in the usual manner,[22] melted at 208–209°.

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[13] We are indebted to Dr. J. H. Burckhalter for samples of VII and VIII, the melting points and infrared spectra of which agreed completely with our samples. The original report [J. H. Burckhalter and S. H. Johnson, THIS JOURNAL, **73**, 4835 (1951)] gave the melting point of VIII as 109°; ref. 10 reports 95–96°

[14] I. Kasiwagi, *Bull. Chem. Soc. Japan*, **2**, 310 (1927).

[15] H. Midorikawa, *ibid.*, **26**, 460 (1953); **27**, 149 (1954).

[16] (a) Microanalyses by Spang Microanalytical Laboratory, Ann Arbor, Mich.; (b) melting points are uncorrected.

[17] (a) The use of pyrrolidine instead of the less reactive diethylamine [H. M. E. Cardwell, *J. Chem. Soc.*, 719 (1949)] in the alkylation of β-keto esters was suggested to us by Dr. Robert E. Ireland of these laboratories; (b) K. Folkers and H. Adkins, THIS JOURNAL, **53**, 1416 (1931).

[18] H. Lund, *Ber.*, **67**, 937 (1934).

[19] K. von Auwers and H. Jacobsen, *Ann.*, **426**, 219 (1922).

[20] A. Brandstrom, *Acta Chem. Scand.*, **5**, 820 (1951).

[21] D. S. Breslow, E. Baumgarten and C. R. Hauser, THIS JOURNAL, **66**, 1286 (1944).

[22] R. L. Shriner, R. C. Fuson and D. Y. Curtin, "Systematic Identification of Organic Compounds," 4th ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 219.

Anal. Calcd. for $C_{17}H_{19}N_3O_3$: C, 65.14; H, 6.11; N, 13.41. Found: C, 65.28, 65.34; H, 5.89, 5.81; N, 13.41, 13.39.

Dehydration in Alkali. (a).—One gram of 1-phenyl-1-pentanol-3-one (III) was shaken for 7 days with 0.45 g. of methyl ethyl ketone, 15 ml. of H_2O and 0.6 ml. of 10% sodium hydroxide. The mixture was poured into 25 ml. of water and extracted with 25 ml. of petroleum ether, then with 25 ml. of 1:1 ether–petroleum ether. The extracts were washed twice with water, dried over Drierite, and freed of solvent, whereupon the residue (0.722 g.) crystallized. Washing with a small quantity of cold petroleum ether left 0.388 g. (43.2%) of colorless crystals, m.p. 37–39°. A mixture of this material and I melted at 37.5–39.5°. The compound liquefied upon admixture with II.

The petroleum ether washings were evaporated to an oil which crystallized at −80°, but isolation of further crystalline materials was not accomplished. The infrared spectrum of the oil showed it to be principally I (*e.g.*, 780, 1400 and 1010 cm.$^{-1}$).

(b).—The base-catalyzed dehydration of 1.00 g. of 3-methyl-4-phenylbutan-4-ol-3-one (IV) was carried out exactly as described in (a). The crude crystalline product weighed 0.685 g. After washing with cold petroleum ether there was obtained 0.273 g. (30.5%) of colorless crystals, m.p. 38–40°. The mixture with the product in (a) melted at 37–39°. The oily residue from the petroleum ether washings exhibited an infrared spectrum identical with that of the oil in (a), the absence of II again being demonstrated.

Dehydration of III in Acid.—The straight-chain hydroxy ketone III (0.808 g.) was dissolved in 10 ml. of methanol and 0.10 ml. of concd. sulfuric acid was added. After 18 hr. standing at room temperature the solution was diluted with 40 ml. of water and extracted with petroleum ether (30–60°). The organic layer was washed with water, dried and evaporated to 0.526 g. of oil, which crystallized from petroleum ether to yield 0.240 g. (33.1%) of colorless crystals, m.p. 36–38°, mixed m.p. with I, 37–39°. The mother liquor was evaporated to an oil the infrared spectrum of which indicated it to be largely I and to contain no detectable II.

Dehydration of IV in Acid.—The branched-chain hydroxy ketone IV (0.756 g.) was treated with 10 ml. of methanol and 0.50 ml. of concd. sulfuric acid at room temperature for 20 hr. At this time the ultraviolet spectrum of a diluted aliquot indicated the yield of unsaturated ketone II to be 43%. After a further 2 hr. at 50–60° the spectrum indicated the solution to contain 48% of the theoretical quantity of unsaturated ketone II. The reaction mixture was then worked up as before to yield an oil (0.428 g.) which was surprisingly fluid and smelled strongly of benzaldehyde. The oil crystallized from petroleum ether to yield 0.064 g. (9.4%) of crystals, m.p. 35–36°, mixed m.p. with II, 35–37°. The sample liquefied upon admixture with a sample of I.

Rate Measurements.—The data of Fig. 1 were obtained as follows. Small samples (25–40 mg.) of the hydroxy ketone III or IV were weighed into glass-stoppered tubes, and 0.5 ml. of 0.25 *N* sodium hydroxide solution was added to each one. The tubes were immediately placed in a mechanical shaker and agitated vigorously at room temperature (27 ± 1°). Individual tubes were removed periodically and diluted to 50 ml. with methanol. After a further twenty-fold dilution with methanol the concentrations of benzaldehyde and unsaturated ketone were determined from the ultraviolet absorption.

The data of Table I were obtained by periodic measurement of the optical density at 250 mμ (for compound IV) and 286 mμ (for compound III) of solutions of the hydroxy ketones at 25.0 ± 0.1°. The solutions were prepared by adding 10 ml. of an aqueous solution, made by mixing 1 *M* NaOH and 1 *M* NaCl in suitable proportions, to the hydroxy ketone contained in *ca.* 80 ml. of methanol, and diluting quickly to 100 ml. with more methanol.

1-(*p*-Nitrophenyl)-pentan-1-ol-3-one (V).—The hydrolysis of 15 g. (0.104 mole) of ethyl 3-ketopentanoate was allowed to proceed in 400 ml. of 50% aqueous ethanol containing 6.0 g. of NaOH for 12 hr. The reaction of the resulting keto acid with 4.0 g. (0.0265 mole) of *p*-nitrobenzaldehyde was carried out as described for benzaldehyde except that the solvent was 50% aqueous ethanol instead of water and the reaction time was only 4 days. The residue from the ether extraction of the reaction mixture crystallized from ethanol to yield 3.6 g. (61%) of nearly colorless crystals, m.p. 89–91°. A mixture of this compound and the hydroxy ketone which crystallized from the *p*-nitrobenzaldehyde–methyl ethyl ketone reaction melted at 89–91°.

Diastereoisomers of 4-(*p*-Nitrophenyl)-3-methylbutan-4-ol-2-one (VIa and VIb).—The hydrolysis of 20 g. (0.139 mole) of ethyl 2-methyl-3-ketobutanoate in 400 ml. of 50% aqueous ethanol for 2.5 hr. was followed by reaction of the resulting keto acid with 4.0 g. (0.0265 mole) of *p*-nitrobenzaldehyde as in the previously described experiment except that the reaction time was 23 days. The yield of crystals (VIa), m.p. 93–94°, was 2.5 g. (42%).

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.28. Found: C, 59.15; H, 5.83; N, 6.30.

A subsequent reaction mixture was chromatographed on silica gel to yield unreacted *p*-nitrobenzaldehyde (19%) and, in the 15% ether–85% benzene eluate, a 23% yield of a different isomer (VIb), m.p. 61–62°, followed by a 42% yield of VIa. The low-melting isomer was recrystallized from benzene–petroleum ether.

Anal. Calcd. for $C_{11}H_{13}O_4N$: C, 59.19; H, 5.87. Found: C, 59.29; H, 5.93.

Condensation of *p*-Nitrobenzaldehyde with Butanone.—Treatment of 7.0 g. of *p*-nitrobenzaldehyde with 100 ml. of butanone and 6.0 ml. of 1% NaOH at 0° for 30 min., followed by 30 min. at room temperature, pouring into 100 ml. of water, extraction with ether, and evaporation of the dried ether solution, gave 8.1 g. of a light oil. Upon standing for several days the oil deposited 0.340 g. of nearly colorless crystals, m.p. 87–90°. Recrystallization from alcohol and from benzene–petroleum ether furnished the analytical sample of compound V, m.p. 91–92°.

Anal. Calcd. for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.28. Found: C, 59.00, 59.15; H, 5.63, 5.78; N, 6.32, 6.25.

In a similar experiment using 3.5 g. (0.0232 mole) of the aldehyde, the crude condensation product weighed 4.3 g. One gram of this oil was adsorbed on a column of silica gel. Elution with benzene–ether mixtures afforded *p*-nitrobenzaldehyde (0.024 g.), then a wide band (0.593 g.) consisting of crystalline V in the first fractions and oily mixtures of V and VIb in later ones, and finally 0.234 g. of VIa. Infrared examination of the mixed fractions allowed an estimation of the ratio of V, VIa and VIb to be approximately 3:2:2.

A 1.38-g. portion of the above mixture was treated with 0.125 g. of *p*-toluenesulfonic acid in 40 ml. of benzene on the steam-bath for one hour. The crude mixture of unsaturated ketones was analyzed for VII and VIII by infrared analysis (chloroform solution) using the bands at 885, 980 and 1000 cm.$^{-1}$. The result (50% VII, 45% VIII) is probably more accurate than could be determined from the chromatographic separation of the hydroxy ketones.

Dehydration of V.—The straight-chain hydroxy ketone V (0.304 g., 0.00136 mole) was treated with 0.050 g. of *p*-toluenesulfonic acid in 10 ml. of benzene on the steam-bath for 40 min. After washing with aqueous bicarbonate, the solution was dried and evaporated to produce 0.261 g. of a light yellow solid which was recrystallized from alcohol to yield 0.238 g. (85%) of yellow crystals, m.p. 108–110°. A mixed melting point with a sample of 1-(*p*-nitrophenyl)-pent-1-en-3-one[13] (VII) was undepressed.

Dehydration of VIa and VIb.—The branched isomer VIa which melted at 94° (0.319 g., 0.00143 mole) was dehydrated as in the case of V. The yield of light buff fibrous needles, m.p. 91–92°, was 0.182 g. (62%). The melting point was raised to 92.5–93.5° by further recrystallization from alcohol or benzene–petroleum ether. The mixed melting point with a sample of VIII[13] was undepressed. From the 61° isomer VIb (0.0959 g., 0.00043 mole) the yield of VIII, m.p. 91–92°, by the same procedure was 0.0622 g. (71%).

Acknowledgment.—We are grateful to Dr. D. S. Noyce for making his results available to us prior to publication, and to the Research Corporation for a Frederick Gardner Cottrell Grant in support of this work.

ANN ARBOR, MICH.