

seem to be quite frequent, difficulties in the determination of molecular weights may be encountered. Nevertheless, the results obtained by Ardenne and his group combined with ours seem to indicate that negative ion mass spectrometry *using low-energy electrons, but employing operating conditions where ion-molecule reactions are minimized*, may lead to results useful for molecular weight and structure determination of organic compounds. Further research in this direction is certainly warranted.

Experimental

This investigation was carried out using a standard Atlas CH-4 mass spectrometer equipped with an AN4 ion source fitted with a tungsten ribbon filament. All

the spectra were determined with an ionizing current of 40 μ a. and an ionizing energy of 70 e.v. (except for Figure 1a). The polarity of the collector ion lens was reversed to increase sensitivity and the electron multiplier was run at 2 kv. The source and sample reservoirs were maintained at a temperature of 80°. All the spectra were obtained with a source pressure between 1×10^{-7} and 5×10^{-7} mm. The mass of the individual peaks was determined using the "Masscontactor" of the instrument rather than the mass marker, which can only be employed for positive ion spectra.

Acknowledgment. The authors gratefully acknowledge the assistance of Dr. W. H. Nickels of Atlas Werke, Bremen, for his help in the initial stages of this study.

Condensations of Carbonyl Compounds at the γ -Position of β -Ketoaldehydes by Means of Potassium Amide or Sodium Hydride¹

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Contribution from the Department of Chemistry, Duke University, Durham, North Carolina. Received February 25, 1965

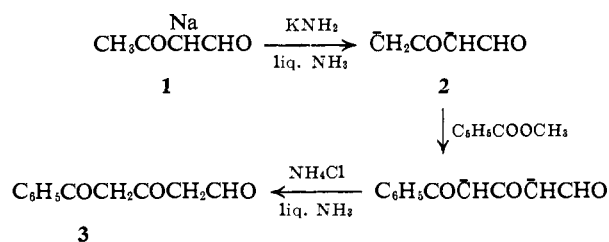
Condensations of carbonyl compounds at the γ -positions of β -ketoaldehydes were effected through the dicarbanions, which were prepared by means of potassium amide in liquid ammonia. The dicarbanions were aroylated with methyl benzoate and condensed with benzophenone and with chalcone in aldol-type and conjugate additions, respectively. γ -Aroylations of β -ketoaldehydes were also effected by means of sodium hydride. These three types of γ -condensations complement the earlier reported γ -alkylations and extend considerably the usefulness of β -ketoaldehyde dicarbanions in synthesis.

Previous papers have described alkylations at the γ -methyl,² γ -methylene,³ and γ -methinyl groups of β -ketoaldehydes with alkyl halides. This novel mode of alkylation was effected through the β -ketoaldehyde dicarbanions, which were prepared by means of potassium amide in liquid ammonia.

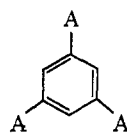
The present paper describes some examples of three other types of condensations at the γ -methyl or γ -methylene groups of appropriate β -ketoaldehydes with carbonyl compounds. Also another γ -alkylation is described.

γ -Aroylations. Four β -ketoaldehyde dicarbanions were prepared and aroylated with methyl benzoate. The simplest dicarbanion (2) was prepared from mono-

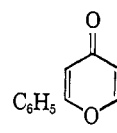
sodioacetoacetaldehyde (1)⁴ and 1 molecular equiv. of potassium amide in liquid ammonia and benzoylated with 0.5 molecular equiv. of the ester to form diketoaldehyde 3 in 52% yield. Similar aroylations of β -diketone dicarbanions have been effected previously.⁵



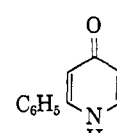
As might be expected, diketoaldehyde 3 readily underwent self-condensation, apparently to form 4. This reaction occurred in low (4%) yield even during the preparation (isolation) of 3, and in good yield on refluxing an ethereal solution of 3. Interestingly, this intermolecular reaction predominated over pyrone formation on treatment of 3 with sulfuric acid, 4 and 5 being obtained in yields of 67 and 25%, respectively. Similar treatment of a 1,3,5-triketone affords exclusively



4, A = COCH₂COC₆H₅



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(1) This investigation was supported by Public Health Service Research Grant No. USPHS CA 04455-06 and by National Science Foundation Research Grant No. NSF GP 2274.

(2) T. M. Harris, S. Boatman, and C. R. Hauser, *J. Am. Chem. Soc.*, **85**, 3273 (1963).

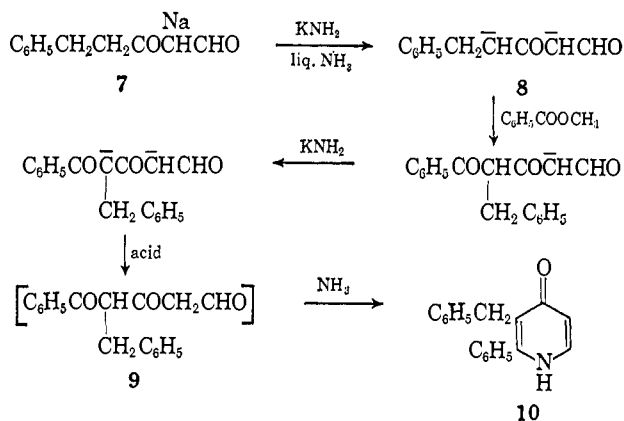
(3) S. Boatman, T. M. Harris, and C. R. Hauser, *ibid.*, **87**, 82 (1965).

(4) This sodio β -ketoaldehyde is readily prepared by acylation of acetone with ethyl formate by means of sodium methoxide; see R. P. Mariella, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 210.

the corresponding 4-pyrone.⁵ Also **3** was cyclized with ammonia to form pyridone **6** in good yield.

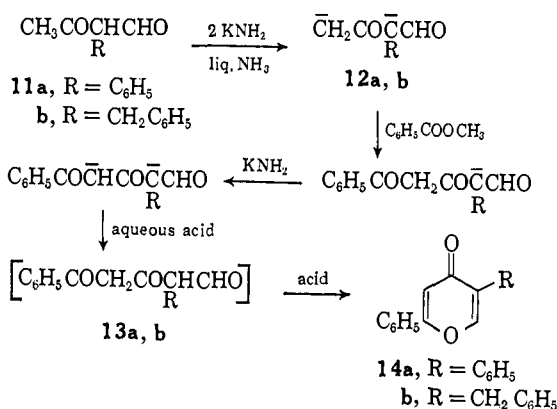
The structures of **3** and **4** were supported by analyses and infrared spectra, which showed carbonyl absorption at 6.05 and 6.13 μ , respectively. Pyrone **5** and pyridone **6** were known compounds; the infrared spectrum of **5** showed carbonyl absorption at 6.03 μ .

Another β -ketoaldehyde dicarbanion, **8**, was prepared from potassium amide and monosodio salt **7** (obtained by benzylation of **2**) and benzoylated in the presence of potassium amide⁶ to form diketoaldehyde **9**, which was isolated as pyridone **10** in 72% yield.



The structure of pyridone **10** was supported by analysis and absorption spectra. The infrared spectrum showed strong absorption at 6.18 μ , and the ultraviolet spectrum showed absorption at 268 m μ (log ϵ 4.01). These values are consistent with those obtained for other 4-pyridones.⁵

Two other β -ketoaldehyde dicarbanions, **12a** and **b**, were prepared from β -ketoaldehydes **11a** and **b** and benzoylated in the presence of potassium amide⁶ to give, on acidification, pyrones **14a** and **b** in yields of 50 and 60%, respectively. Diketoaldehydes **13a** and **b** presumably were intermediates. Another possible route to the pyrones would involve O-benzoylation at the less nucleophilic oxygen of dianions **12a** and **b** and cyclization of the resulting enol esters $\text{CH}_3\text{COCR}=\text{CHOCOC}_6\text{H}_5$, but this seems less likely.



Apparently diketoaldehydes **13a** and **b** were converted to pyrones **14a** and **b** even by cold, dilute hydrochloric acid, which was employed to neutralize the reaction mixtures. Generally such cyclizations have

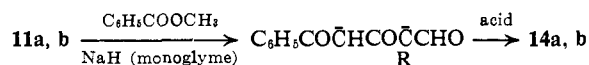
(5) See R. J. Light and C. R. Hauser, *J. Org. Chem.*, **25**, 538 (1960).

(6) For similar aroylations of β -diketone dicarbanions in the presence of alkali amide see ref. 5.

been effected by cold, concentrated sulfuric acid.⁵ The intermediate ketoaldehyde **13a** may have been obtained as an oil in another experiment in which the liquid ammonia reaction mixture was neutralized with ammonium chloride (see Experimental).

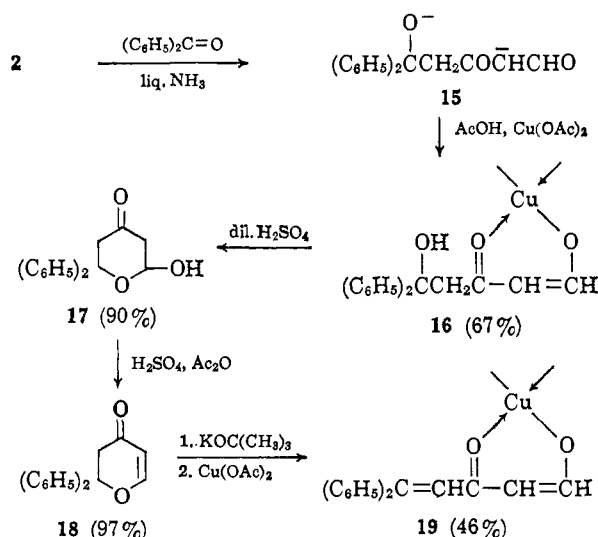
The structures of pyrones **14a** and **b** were supported by analysis and by infrared and ultraviolet spectra, which showed bands at 6.06 and 6.10 μ and maxima at 259 m μ (log ϵ 3.72) and 273 m μ (log ϵ 3.64), respectively. These values are consistent with spectral data obtained previously for 4-pyrones.⁵

The γ -benzoylations of β -ketoaldehydes **11a** and **b** were also effected with methyl benzoate by means of sodium hydride in refluxing 1,2-dimethoxyethane (monoglyme) to form, on acidification of the reaction mixtures, 4-pyrones **14a** and **b** in yields of 53 and 61%, respectively.



This method, which may be preferred by some workers, may not involve the intermediate formation of β -ketoaldehyde dicarbanions **12a** and **b**, as analogous dicarbanions appear not to be formed in γ -benzoylations of β -diketones (for example, that of benzoylacetone).⁷

γ -Carbonyl Addition. Dicarbanion **2** (see previous section) underwent an addition reaction with benzophenone to form adduct **15**, which was isolated as its copper chelate **16**. Chelate **16** was decomposed with dilute acid to give hemiacetal **17**, which could be dehydrated under more vigorous conditions to afford dihydropyrone **18**; **18** was converted to chelate **19**. The yields in each of these reactions is given in the following chart.

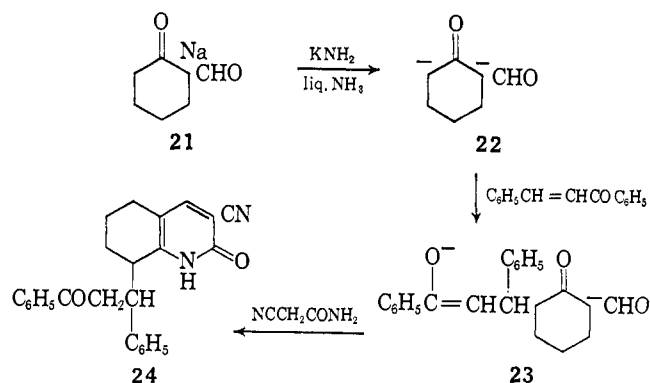


The structures of compounds **16**–**19** were supported by analyses and absorption spectra. The infrared spectra of chelate **16** and hemiacetal **17** showed strong absorption at 6.27 and 5.85 and hydroxyl absorption at 2.95 and 2.98 μ , respectively. The ultraviolet spectrum of **17** showed a maximum at 258 m μ (log ϵ 2.88). The infrared spectra of dihydropyrone **18** and chelate **19** exhibited strong absorption at 6.00 and 6.35 μ ,

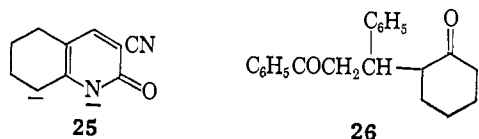
(7) M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, to be published.

respectively. The ultraviolet spectrum of **18** exhibited a maximum at 263 m μ (log ϵ 4.06), which is near that (267 m μ (log ϵ 3.92)) of the related 2-methyl-6,6-diphenyl-5,6-dihydro-4-pyrone reported previously.⁸

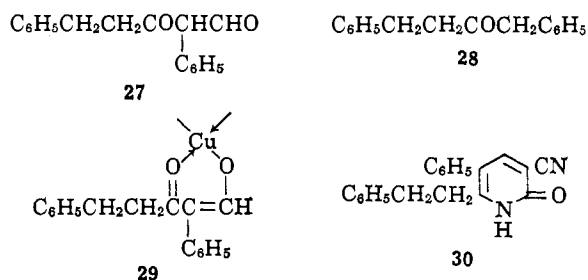
γ -Conjugate Addition. Dicarbanion **22** was prepared from monosodio salt **21** and condensed with chalcone to form conjugate adduct **23**, which was isolated as its cyanopyridone **24** in 63% yield.



Structure **24** was supported by analysis and absorption spectra. The infrared spectrum showed a band at 6.06 with a distinct side peak at 5.94 μ , indicating a carbonyl besides that of the ring amide. Structure **24** was confirmed by independent synthesis from dianion **25** and chalcone; **25** was prepared from the corresponding cyanopyridone and 2 molecular equiv. of potassium amide in liquid ammonia.⁹ Also, intermediate adduct **23** was deformylated to form diketone **26**, which is known.



γ -Alkylation. Dicarbanion **12a** (see section on γ -arylations) was alkylated with benzyl chloride to form **27** in 42% yield; the corresponding alkylation of dicarbanion **12b** was described previously.² Ketoaldehyde **27** was deformylated with alkali to afford ketone **28**, which was independently synthesized from di- β -phenylethylcadmium and phenylacetyl chloride. As might be expected, base-catalyzed formylation of **28** yielded **27**. Ketoaldehyde **27** was also converted to chelate **29** and was cyclized with cyanoacetamide to form **30**.



(8) R. J. Light and C. R. Hauser, *J. Org. Chem.*, **26**, 1716 (1961).

(9) The details of this reaction as well as related condensations will be published shortly.

Discussion

The carbonyl condensations illustrated above may be quite general. Thus, not only should other β -ketoaldehyde dicarbanions undergo such condensations, but other aromatic esters, aromatic ketones or aldehydes, and certain α,β -unsaturated carbonyl compounds should also be suitable for aryations, carbonyl additions, and conjugate additions, respectively. Extension of the method to aliphatic esters and ketones appears possible by the use of dilithio salts of the β -ketoaldehydes.^{8,10}

Experimental¹¹

Benzoylation of Acetoacetaldehyde Dicarbanion 2. Dicarbanion **2** was prepared from 15.12 g. (0.14 mole) of sodioacetoacetaldehyde (**1**)⁴ and 0.149 mole of potassium amide (from 5.8 g. or 0.15 g.-atom of potassium) in 800 ml. of commercial, anhydrous, liquid ammonia (stirred for 1 hr.).² To the stirred solution of **2** (0.14 mole) was added 9.52 g. (0.07 mole) of methyl benzoate, and the ammonia was allowed to evaporate. Ether and cold water were added. The water layer was separated, acidified with cold hydrochloric acid, and extracted with ether. The ethereal solution was dried and evaporated under reduced pressure. The residue crystallized on readdition of a small amount of ether; the mixture was filtered to give 6.9 g. (52%) of diketone **3**, m.p. 85–87° (some sintering at 83°). Further washing with small amounts of ether raised the melting point to 87–89°. The compound gave a red-brown enol test with ethanolic ferric chloride.

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{O}_3$: C, 69.46; H, 5.30. Found: C, 69.80; H, 5.30.

Concentration of the mother liquors from above afforded presumed trimer **4** (see below), as light yellow needles that melted over a wide range up to 190°. Recrystallization from ethanol gave m.p. 215–217°.

When an ethereal solution of **3** was refluxed or even allowed to stand at room temperature, these light yellow needles, m.p. 216–217°, apparently the trimeric self-condensation product **4**, gradually precipitated. Recrystallization from ethanol raised the melting point to 217–218°. This compound gave a yellow-brown enol test.

Anal. Calcd. for $\text{C}_{33}\text{H}_{24}\text{O}_6$: C, 76.73; H, 4.68. Found: C, 77.00; H, 4.98.

A sample (2.5 g.) of diketone **3** was dissolved in 25 g. of concentrated sulfuric acid at 0° and stirred for 10 min. The solution was poured onto 500 g. of ice, and the resulting suspension was extracted with ether. The ethereal extract was dried and evaporated to afford 1.5 g. (67%) of trimeric self-condensation product **4**, m.p. 215–216°. The aqueous layer was neutralized with sodium carbonate and extracted with ether. The ethereal extract was evaporated to leave 0.55 g. (25%) of 2-phenyl-4-pyrone (**5**), m.p. 101–102 and 102–103°.

(10) See S. D. Work and C. R. Hauser, *J. Org. Chem.*, **28**, 725 (1963).

(11) Melting points (taken on a Mel-Temp capillary melting point apparatus) and boiling points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 237 Infracord with potassium bromide pellets of solids and with neat samples of liquids on sodium chloride plates. Ultraviolet spectra were obtained with a Cary Model 14 recording spectrophotometer, using approximately 10^{-4} M solutions in 95% ethanol. Elemental analyses were by Dr. Ing. A. Schoeller, Mikro-Labor, Kronach, West Germany, and by Galbraith Laboratories, Knoxville, Tenn. Molecular weight determinations were also by Galbraith Laboratories.

after recrystallization from aqueous ethanol (lit.¹² m.p. 104°).

A sample of diketoaldehyde **3** dissolved in ethanolic ammonia was heated on a steam bath. After evaporation of the solvent, the residual oil was treated with ether to give in good yield 2-phenyl-4-pyridone (**6**), m.p. 153–157° (when heated slowly). Treatment with charcoal and recrystallization from water raised the m.p. to 156–157° (lit.¹² m.p. 155°). Rapid heating caused a preliminary liquefaction at about 80° followed by resolidification at about 130°. Borsche and Peter¹² have reported that crystallization of the pyridone from water afforded the hemihydrate, which decomposed on heating.

Monosodio Salt of 5-Phenyl-1,3-pentanedione (7). Sodioacetoacetaldehyde⁴ was added with stirring to 0.33 mole of potassium amide (from 12.87 g., 0.33 g.-atom of potassium) in 800 ml. of liquid ammonia. After 0.5 hr., 41.75 g. (0.33 mole) of benzyl chloride was added dropwise, and the mixture was stirred for 1 hr. The ammonia was allowed to evaporate, and anhydrous ether was added. The thick slurry was filtered, and the filter cake was washed well with anhydrous ether, care being taken to protect it from atmospheric moisture. The cake was broken up as finely as possible and dried *in vacuo* at 70° to give 70 g. (80%) of a mixture of salt **7** and potassium chloride, which was stored in a tightly capped bottle. A solution of 3.0 g. of the salt mixture in water was treated with saturated cupric acetate solution containing 1.3 ml. of acetic acid to precipitate the blue chelate, which was collected, washed thoroughly with water, dried, and recrystallized from methanol to give 1.9 g. (76% overall yield) of the chelate, m.p. 174–176° (lit.² m.p. 176–178°). On this basis, 1 g. of the salt mixture contained 0.0033 mole of salt **7**.

Conversion of Salt 7 to Dianion 8 and Benzoylation. To a stirred solution of 0.108 mole of potassium amide (from 4.2 g., 0.108 g.-atom of potassium) in 700 ml. of liquid ammonia was added 16.8 g. of the salt mixture (0.05 mole of the sodio salt **7**) prepared above. After 1 hr., 6.9 g. (0.051 mole) of methyl benzoate in 25 ml. of anhydrous ether was added, and the mixture was stirred until all the ammonia had evaporated, ether having been added gradually. Ice and water were added to dissolve the salts, and the layers were separated. The aqueous solution was acidified with 6 *M* hydrochloric acid and extracted with ether. The ethereal solution was dried with anhydrous magnesium sulfate and evaporated. The residual oil, which presumably contained diketoaldehyde **9**, failed to crystallize. It was dissolved in absolute ethanol and treated with liquid ammonia, and the solution was evaporated to dryness. This procedure was repeated twice to give, after recrystallization from ethanol, 8.5 g. (72%) of pyridone **10**, m.p. 247–248°.

Anal. Calcd. for C₁₈H₁₃NO: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.78; H, 5.91; N, 5.40.

Benzoylation of α -Phenyl- and α -Benzylacetoacetaldehyde. A. By Means of Potassium Amide. To a solution of 0.15 mole of potassium amide (from 5.9 g. or 0.15 g.-atom of potassium) in 800 ml. of liquid ammonia was added a solution of 8.1 g. (0.05 mole) of α -

phenylacetoacetaldehyde (**11a**) in 50 ml. of anhydrous tetrahydrofuran. After 1 hr., formation of the dicarbanion was considered complete and 6.8 g. (0.05 mole) of methyl benzoate in 10 ml. of tetrahydrofuran was added. The reaction mixture was stirred for 6 hr. and the ammonia was allowed to evaporate; the tetrahydrofuran was removed under reduced pressure and ice, water, and ether were added. The aqueous layer was separated, acidified with 6 *M* hydrochloric acid, and extracted with ether. The ethereal solution was dried with anhydrous magnesium sulfate and evaporated. The partially crystalline residue was recrystallized from ethanol to afford 6.4 g. (50%) of 2,5-diphenyl-4-pyrone (**14a**), m.p. 151–152°.

Anal. Calcd. for C₁₇H₁₂O₂: C, 82.24; H, 4.87; mol. wt., 248. Found: C, 82.40; H, 5.02; mol. wt., 280.

This product failed to give an enol test with ethanolic ferric chloride and was recovered unchanged after treatment with cold, concentrated sulfuric acid. Since the crude product produced an enol test, it evidently contained diketoaldehyde **13a** and/or the starting ketoaldehyde **11a**.

The γ -benzoylation of **11a** was repeated but, before evaporation of the liquid ammonia, the reaction mixture was neutralized with 10.8 g. (0.2 mole) of ammonium chloride. The ammonia was then removed, and water and ether were added. The organic layer was dried and evaporated. The residual oil, which presumably contained diketoaldehyde **13a**, failed to crystallize; it was stirred with cold, concentrated sulfuric acid for 10 min., and the mixture was poured onto ice. The solid was collected and recrystallized from ethanol to give 6.4 g. (50%) of pyrone **14a**, m.p. 150–152°, identified by mixture melting point with a sample obtained as described above. Also, the infrared spectra of the two samples were identical.

The γ -benzoylation of α -benzylacetoacetaldehyde (11b) was effected similarly employing 0.15 mole of potassium amide and 0.05 mole each of **11b** and methyl benzoate and acidifying the aqueous solution of the reaction product with hydrochloric acid (see above). There was obtained 8.4 g. (64%) of 2-phenyl-5-benzyl-4-pyrone (**14b**), m.p. 131–132°.

Anal. Calcd. for C₁₈H₁₄O₂: C, 82.42; H, 5.38; mol. wt., 262. Found: C, 82.47; H, 5.31; mol. wt., 282.

B. By Means of Sodium Hydride. To 7.2 g. (0.15 mole) of commercial sodium hydride¹³ in 100 ml. of monoglyme purged with nitrogen was added 8.1 g. (0.05 mole) of α -phenylacetoacetaldehyde (**11a**) in 50 ml. of anhydrous 1,2-dimethoxyethane (monoglyme). The mixture was stirred and refluxed. When hydrogen ceased to be evolved (about 3 hr.) a solution of 6.8 g. (0.05 mole) of methyl benzoate in 10 ml. of monoglyme was added dropwise. The stirring and refluxing were continued until additional hydrogen ceased to be evolved. The solvent was removed under reduced pressure, and a little alcohol was added cautiously to destroy any remaining sodium hydride. Water, ice, and ether were added. The organic layer, dried and evaporated, gave a partially crystalline residue, which was recrystallized from ethanol to af-

(12) W. Borsche and W. Peter, *Ann.*, **453**, 148 (1927).

(13) This reagent was obtained as an approximately 50% dispersion in mineral oil from Metal Hydrides, Inc., Beverly, Mass.

ford 6.6 g. (53%) of 2,5-diphenyl-4-pyrone (**14a**), m.p. 150–152°.

The γ -benzoylation of α -benzylacetoacetaldehyde (**11b**) was effected similarly to give 61% of **14b**, m.p. 130–132°.

These products were shown to be identical with pyrones **14a,b** obtained by means of potassium amide under (A) by mixture melting points and by comparison of infrared spectra.

γ -Carbonyl Addition of Acetoacetaldehyde Dicarbanion (**2**) to Benzophenone. To a stirred solution of 0.067 mole of potassium amide (from 2.6 g., 0.067 g.-atom of potassium) in 300 ml. of liquid ammonia was added 7.03 g. (0.065 mole) of sodioacetoacetaldehyde.⁴ After stirring for 45 min., 12.2 g. (0.067 mole) of benzophenone was added. The reaction mixture was stirred for 4 hr. while ether was added, and the ammonia was evaporated. The hygroscopic condensation product was rapidly collected by filtration and washed with anhydrous ether; it was added immediately to a saturated, aqueous solution of copper acetate which had been acidified with 9.0 g. of acetic acid. The light blue copper chelate, which formed at once, was collected, washed with water and with ethanol, and dried. The yield of the crude chelate of 6,6-diphenyl-6-hydroxy-1,3-pentanedione (**16**) was 13.1 g. (67%), m.p. 176–177°. Two recrystallizations from chloroform and ethanol raised the melting point to 177–178°.

Anal. Calcd. for $C_{34}H_{30}CuO_6$: C, 68.27; H, 5.06; Cu, 10.62. Found: C, 68.17; H, 5.10; Cu, 10.79.

Chelate 16 (5.0 g.) was stirred with a mixture of 10 g. of sulfuric acid, 100 ml. of water, and 250 ml. of ether for 1 hr. at room temperature. The ether layer was separated and dried over anhydrous magnesium sulfate. The solvent was removed *in vacuo* to leave 4.4 g. of crystalline residue. Recrystallization from 50% aqueous ethanol gave 4.0 g. of 2-hydroxy-6-phenyltetrahydro-4-pyrone (**17**), m.p. 116–118°. Additional recrystallization from this solvent mixture did not raise the melting point, but recrystallization from ether-hexane raised the melting point to 123–124°. The product failed to give an enol test with ethanolic ferric chloride.

Anal. Calcd. for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.00; H, 6.00.

Treatment of tetrahydropyrone 17 with hot aqueous sodium hydroxide caused initial solution followed rapidly by formation of benzophenone, which was identified as its 2,4-dinitrophenylhydrazone.

Tetrahydropyrone 17 (6.0 g.) was heated on a steam bath for 15 min. with 20 ml. of acetic anhydride containing 1 drop of sulfuric acid. Then 0.1 g. of sodium carbonate was added, and the acetic anhydride and acetic acid were removed under reduced pressure. The residue was filtered and washed with water to give 5.4 g. of 2,2-diphenyl-2,3-dihydro-4-pyrone (**18**), m.p. 108–111°. Recrystallization from ethanol raised the melting point to 114.5–115.5°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.55; H, 5.48.

Dihydropyrone 18 (1.0 g. or 0.004 mole) was stirred for 1 hr. at room temperature with 0.004 mole of potas-

sium *t*-butoxide (prepared from 0.16 g. of potassium) in 20 ml. of *t*-butyl alcohol. The solution was added to excess aqueous cupric acetate solution. The precipitate was removed by filtration and recrystallized from ethanol to give the yellow-green chelate of unsaturated β -ketoaldehyde **19**, m.p. 181–182°, in 57% yield.

Anal. Calcd. for $C_{34}H_{26}O_4Cu$: C, 72.64; H, 4.66; Cu, 11.31. Found: C, 72.68, H, 4.82; Cu, 11.57.

γ -Conjugate Addition of 2-Formylcyclohexanone Dianion (**22**) to Chalcone. To a stirred solution of 0.11 mole of potassium amide (from 4.3 g., 0.11 g.-atom of potassium) in 700 ml. of liquid ammonia was added 14.8 g. (0.1 mole) of sodio-2-formylcyclohexanone (**21**) followed after 1.5 hr. by 22.9 g. (0.11 mole) of chalcone. After 1 hr., the ammonia was allowed to evaporate. Ether, ice, and water were added and the layers were separated. The basic aqueous layer was adjusted to pH 8 with acetic acid, and excess cyanoacetamide was added. The mixture was refluxed for 2 hr., cooled, acidified with 6 *M* hydrochloric acid, cooled again in an ice bath for 2 hr., and filtered. The solid was washed with water, dried *in vacuo*, and recrystallized from acetic acid to give 25 g. (67%) of cyanopyridone **24**, m.p. 261–263°.

Anal. Calcd. for $C_{25}H_{22}N_2O_2$: C, 78.51; H, 5.80; N, 5.33. Found: C, 78.44; H, 5.71; N, 5.34.

This product was recovered unchanged after treatment with cold, concentrated sulfuric acid for 10 min., followed by water.

The γ -conjugate addition of dianion **22** with chalcone was repeated, except that the basic aqueous solution of the product was treated with sodium hydroxide and heated on a steam bath to remove dissolved ether; after 48 hr., the solid which had separated was collected and recrystallized from ethanol to afford 14.3 g. (47%) of diketone **26**, m.p. 139–141° (lit.¹⁵ mp. 149°). The infrared spectrum showed carbonyl bands at 5.83 and 5.93 μ .

Anal. Calcd. for $C_{21}H_{22}O_2$: C, 82.32; H, 7.24. Found: C, 82.09; H, 7.03.

The dioxime, recrystallized from ethanol, melted at 183–185° (lit.¹⁵ m.p. 186°).

Independent synthesis of cyanopyridone 24 was accomplished from dianion **25** and chalcone.⁹ The product melted at 259–260°, undepressed on admixture with a sample of **24** prepared as described above. Also the infrared spectra of the two samples were identical.

γ -Benzoylation of Dicarbanion **12a**. This alkylation was effected essentially as described recently² for dicarbanion **12b**. Dicarbanion **12a** was prepared from 0.2 mole of potassium amide and 0.1 mole of α -phenylacetoacetaldehyde and treated with 0.36 mole of benzyl chloride. There was obtained 10.6 g. (42%) of 2,5-diphenyl-1,3-pentanedione (**27**), b.p. 155–158° at 0.8 mm. The product solidified on standing and, after recrystallization from hexane, melted at 45–46°. Its infrared spectrum showed an enol band at 6.19 μ . A sample gave a violet enol test with ethanolic ferric chloride.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.14; H, 6.66. Found: C, 80.00; H, 6.57.

(15) C. F. H. Allen and H. R. Sallans, *Can. J. Research*, 9, 574 (1933).

A sample of **27** was treated with copper acetate solution to give the green copper chelate **29**, m.p. 138–139° after three recrystallizations from ethanol. Its infrared spectrum showed an enol band at 6.28 μ .

Anal. Calcd. for $C_{34}H_{30}CuO_4$: C, 71.95; H, 5.34; Cu, 11.22. Found: C, 71.84; H, 5.71; Cu, 10.90.

A sample of **27** was heated on a steam bath with cyanoacetamide and aqueous sodium carbonate for 2 hr. The mixture was cooled and acidified with acetic acid. The precipitate was collected and recrystallized from ethanol to give 5-phenyl-6-(β -phenylethyl)-3-cyano-2(1)-pyridone (**30**) in 50% yield; its melting point was 285–286° after three recrystallizations from ethanol. The infrared spectrum of the pyridone showed an amide band at 6.03 μ .

Anal. Calcd. for $C_{20}H_{16}N_2O$: C, 79.97; H, 5.36; N, 9.32. Found: C, 79.72; H, 5.19; N, 9.21.

A sample of **27** was deformylated with hot sodium hydroxide solution to form 1,4-diphenyl-2-butanone (**28**), which was isolated in 87% yield as its semicarbazone, m.p. 127–128° after recrystallization from 75% ethanol (lit.¹⁶ m.p. 129–130°).

Ketone **28** was independently synthesized from di- β -phenylethylcadmium and phenylacetyl chloride. The cadmium reagent was prepared by treating a cooled solution of the Grignard reagent of 0.22 mole of β -

phenylethyl bromide in ether with 0.109 mole of finely powdered, dried cadmium chloride. The suspension was refluxed until there was no Gilman test and the ether replaced by benzene. The suspension was heated to reflux and 15.5 g. (0.1 mole) of phenylacetyl chloride was added as rapidly as possible. The mixture was stirred under reflux for 3 hr., then stirred for 8 hr. at room temperature. The complex was decomposed with 50% sulfuric acid and ice. The benzene layer, combined with two benzene extracts of the aqueous layer, was washed with water, 5% aqueous sodium carbonate, and saturated aqueous sodium chloride, dried over anhydrous magnesium sulfate, and evaporated. The residue was distilled under reduced pressure to give 15.5 g. (70%) of ketone **28**, b.p. 157–158° at 7 mm. The semicarbazone, recrystallized from 75% ethanol, melted at 130–131°, undepressed on admixture with a sample of the semicarbazone of ketone **28** obtained on deformylation of **27**.

Ketone **28** (10.0 g., 0.04 mole) was formylated with 3.5 g. (0.047 mole) of ethyl formate by means of sodium ethoxide (prepared from 1 g., 0.044 g.-atom of sodium) in 50 ml. of absolute ethanol (stirred for 12 hr.). The reaction mixture was worked up to give 5 g. (50%) of crude β -ketoaldehyde **27**, which was isolated as its green copper chelate **29**, m.p. 137–138°, undepressed on admixture with a sample of the chelate prepared as described above. The infrared spectra of the two samples were identical.

(16) A. Y. Berlin and Y. V. Markova, *Zh. Obshch. Khim.*, **18**, 1791 (1948).

Trifluoroacetanilide. pK_a and Alkaline Hydrolysis Kinetics

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The rate of hydrolysis of trifluoroacetanilide levels off at high pH. This occurs at a pH well above the pK_a of the anilide and is therefore not due, as previously suggested, to formation of an unreactive anion. In fact, the rate data indicate that an anionic species of the substrate is reactive, giving hydrolysis products in a reaction first order in this species and in hydroxide. This reaction predominates at high pH. Its rate approaches a limiting value as pH is increased, accounting for the observed leveling off in hydrolysis rate. It is proposed that this leveling off is due to a limitation imposed by the rate of formation of the reactive anionic species. The hydrolysis rates and their salt effects are in agreement with this explanation. The hydrolysis is catalyzed by mono-, di-, and triethanolamine and morpholine buffers. The last gives nonlinear dependence of rate on buffer concentration.

Trifluoroacetanilide ($C_8H_8NHCOCF_3$) hydrolyzes in alkaline solutions to give aniline and trifluoroacetate ion. Hydrolysis rates in 0.006–0.557 *M* sodium hy-

droxide were measured by Biechler and Taft.¹ The pseudo-first-order rate constant increases with pH but not linearly. Rather, it approaches a limiting value. This behavior was attributed to dissociation of the nitrogen proton to give an unreactive anion.¹ A pK_a value of 11.9 (25°) for the anilide was calculated from the rate data. This interpretation of the data is apparently incorrect, for it has now been found by spectrophotometry that pK_a for trifluoroacetanilide is 9.5 at 25°. The ultraviolet absorption spectrum of the anilide shows a pronounced change with pH in the vicinity of 9.5. There is no change with pH in the higher pH region within which the hydrolysis rate levels off. This paper presents additional rate data, extending to pH values below the pK_a of the anilide. It also suggests a mechanism to explain the rate data.

Results

The log hydroxide concentration–log rate profile for the hydrolysis of trifluoroacetanilide in water con-

(1) S. S. Biechler and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 4927 (1957).