Condensations at the Terminal Methyl Group of Anilino Derivatives of Benzoylacetone and Acetylacetone through Their Dialkali Salts in Liquid Ammonia[1]

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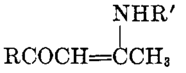
Condensations at the terminal methyl group of anilino-type derivatives of benzoylacetone were effected through their dipotassio or disodio salts, which were prepared by means of 2 mole equiv of the alkali amide in liquid ammonia. These condensations involved carbonyl addition with benzophenone, benzoylation with methyl benzoate, and alkylation with benzyl chloride. The aldol products were dehydrated, and one of the benzoylation products was cyclized to an iminopyrone. Similarly, condensations were effected at the acetyl methyl group of the aniline derivative of acetylacetone through its dipotassio salt. The benzoylation product was cyclized to form an N-phenylpyridone. These reactions furnish useful methods of synthesis. However, attempts to effect corresponding condensations at the terminal methyl group of the methylamine derivatives of benzoylacetone and acetylacetone were unsuccessful.

Since condensations at the terminal methyl group of β-diketones of type 1 can be effected through the dialkali salts,[2] it seemed possible that such condensations might similarly be accomplished at the terminal methyl group of the primary amine derivatives 2a or 2b[3] of these β-diketones through the dialkali salts. This was realized when R′ of 2a was phenyl or a substituted phenyl group, but not when R′ was methyl.

$\mathrm{RCOCH_2COCH_3}$

1



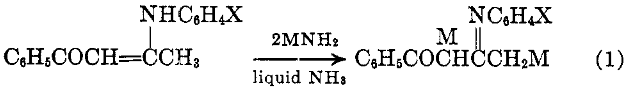
$\mathrm{RCOCH{=}\overset{NHR'}{\overset{|}{C}}CH_3}$

2a

$\mathrm{RCOCH_2\overset{NR}{\overset{\|}{C}}CH_3}$

2b

First, a study was made of the four anilino-type derivatives of benzoylacetone, 3a–d,[4] which were converted to their dipotassio or disodio salts 3′a–d[5] by means of 2 mole equiv of alkali amide in liquid ammonia (eq 1). Evidently, these dialkali salts are yellow and the intermediate monoalkali salts olive (see Experimental Section).



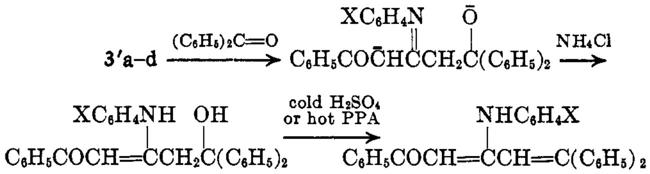
$$\mathrm{C_6H_5COCH{=}\overset{NHC_6H_4X}{\overset{|}{C}}CH_3 \xrightarrow[\text{liquid NH}_3]{2MNH_2} C_6H_5CO\overset{M}{\overset{|}{C}}H\overset{NC_6H_4X}{\overset{\|}{C}}CH_2M} \qquad (1)$$

3a, X = H
b, X = $\mathrm{OCH_3}$-*p*
c, X = Cl-*p*
d, X = Cl-*o*

3′a, X = H; M = K
b, X = $\mathrm{OCH_3}$-*p*; M = K
c, X = Cl-*p*; M = K
d, X = Cl-*o*; M = Na

Carbonyl additions of dialkali salts 3′a–d were effected with benzophenone to form hydroxy-β-ketoenamines 4a–d, which were dehydrated by means of sulfuric acid or polyphosphoric acid (PPA) to give unsaturated β-ketoenamines 5a–d, respectively (Scheme I).

SCHEME I



$$\mathrm{3'a\text{–}d \xrightarrow{(C_6H_5)_2C{=}O} C_6H_5CO\bar{C}H\overset{XC_6H_4N}{\overset{\|}{C}}CH_2\overset{\bar{O}}{\overset{|}{C}}(C_6H_5)_2 \xrightarrow{NH_4Cl}}$$

$$\mathrm{C_6H_5COCH{=}\overset{XC_6H_4NH}{\overset{|}{C}}CH_2\overset{OH}{\overset{|}{C}}(C_6H_5)_2 \xrightarrow{\text{cold } H_2SO_4 \text{ or hot PPA}} C_6H_5COCH{=}\overset{NHC_6H_4X}{\overset{|}{C}}CH{=}C(C_6H_5)_2}$$

4a, X = H
b, X = $\mathrm{OCH_3}$-*p*
c, X = Cl-*p*
d, X = Cl-*o*

5a, X = H
b, X = $\mathrm{OCH_3}$-*p*
c, X = Cl-*p*
d, X = Cl-*o*

These results are summarized in Tables I and II. To minimize possible reversion in the carbonyl additions, the reaction mixtures were neutralized inversely. Although the hydroxyketoenamine 4d was obtained in 82% yield with disodio salt 3′d, none of 4d was isolated in the corresponding reaction with the dipotassio salt of 3d, and starting materials were recovered; apparently reversion occurred more readily with the dipotassio salt.[6]

The structures of the hydroxyketoenamines 4a–d were supported not only by their dehydrations but also by their infrared spectra which showed strong hydroxyl bands at 2.95 μ. This band was absent in the spectra of the starting ketoenamines 3a–d and in the dehydration products 5a–d; the latter compounds showed characteristic bands (see Table II).

Incidentally, aldol product 4a underwent cleavage in refluxing decalin to form ketoenamine 3a and benzophenone.

Benzoylations of dipotassio salts 3′a,b were effected with methyl benzoate in the presence of potassium amide[7] to form 1,5-diketoenamines 6a,b in yields of 50 and 35%, respectively; 6b was cyclized to give iminopyrone 7 in 50% yield (Scheme II).

Structures 6a,b were supported not only by the cyclization (for 6b) but also by their infrared spectra, which showed carbonyl absorption near 5.95 μ (not present in the starting ketoenamines 3a,b) and absorption similar to that of 3a,b. The structure of iminopyrone 7 was supported by infrared and ultraviolet spectra (see Experimental Section).

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[1] This investigation was supported by Public Health Service Research Grant No. CA 04455-07 from the National Cancer Institute.

[2] See especially (a) C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958); (b) R. J. Light and C. R. Hauser, *J. Org. Chem.*, **25**, 538 (1960); (c) R. J. Light and C. R. Hauser, *ibid.*, **26**, 1716 (1961); (d) K. G. Hampton, T. M. Harris, and C. R. Hauser, *ibid.*, **30**, 61 (1965).

[3] Infrared studies have indicated that such compounds are ketoenamines (**2a**) rather than ketoimines (**2b**): N. H. Cromwell, R. D. Babson, and C. E. Harris, *J. Am. Chem. Soc.*, **65**, 312 (1943); N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank, and D. J. Wallace, *ibid.*, **71**, 3337 (1949).

[4] For evidence that the anilino derivatives of benzoylacetone have structure **3a–d**, not the possible isomeric structures where the nitrogen is attached to the carbon adjacent to the phenyl group, see (a) C. Beyer, *Chem. Ber.*, **20**, 1770 (1887); (b) R. H. Baker and A. H. Schlesinger, *J. Am. Chem. Soc.*, **68**, 2009 (1946).

[5] As in the earlier studies of the dialkali salts of β-diketones,[2] only the dicarbanion resonance form will be indicated, even though other resonance forms may contribute more to the structure of the dianion.

[6] A similar observation has recently been made in the carbonyl addition reaction of dialkaliphenylacetamides with benzophenone: see E. M. Kaiser and C. R. Hauser, *Chem. Ind.* (London), 1299 (1965).

[7] For analogous acylations of β-ketoaldehydes, see T. M. Harris, S. Boatman, and C. R. Hauser, *J. Am. Chem. Soc.*, **87**, 3186 (1965).

TABLE I.—CARBONYL ADDITIONS OF DIALKALI SALTS **3′a–d** WITH BENZOPHENONE TO FORM HYDROXY-β-KETOENAMINES **4a–d**

Dialkali salt	Metallic cation	Hydroxy-β-ketoenamines	Mp, °C	Yield, %	Infrared spectrum, μ	Empirical formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
3′a	K	1,5,5-Triphenyl-3-anilino-5-hydroxy-2-penten-1-one (**4a**)	140–142	80[a]	6.30, 6.50, 6.92, 7.86, 2.95	$C_{29}H_{25}NO_2$	83.02	6.01	3.34	83.08	6.22	3.09
3′b	K	1,5,5-Triphenyl-3-(*p*-methoxyanilino)-5-hydroxy-2-penten-1-one (**4b**)	169–170	80[a]	6.26, 6.35, 6.65, 7.83, 8.05, 2.95	$C_{30}H_{27}NO_3$	80.15	6.05	3.12	80.27	6.28	3.23
3′c	K	1,5,5-Triphenyl-3-(*p*-chloroanilino)-5-hydroxy-2-penten-1-one (**4c**)	181–182	60[a]	6.21, 6.35, 6.94, 7.62, 7.90, 2.95	$C_{29}H_{24}ClNO_2$	76.73	5.33	3.09	76.55	5.39	3.12
3′d	Na	1,5,5-Triphenyl-3-(*o*-chloroanilino)-5-hydroxy-2-penten-1-one (**4d**)	128–129	82[b]	6.20, 6.40, 6.74, 7.85, 2.95	$C_{29}H_{24}ClNO_2$	76.73	5.33	3.09	76.21	5.37	3.13

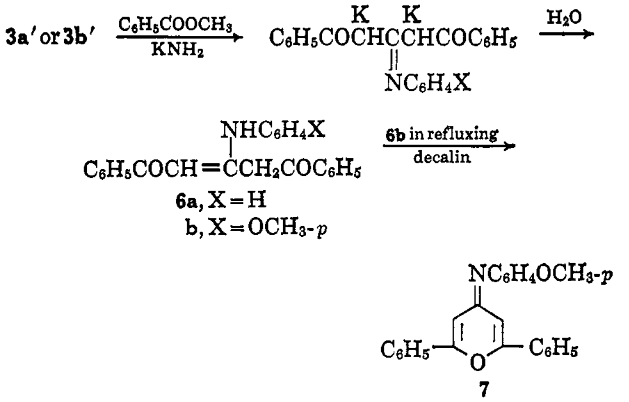
[a] Recrystallized from 95% ethanol. [b] Recrystallized from methanol.

TABLE II.—DEHYDRATIONS OF HYDROXY-β-KETOENAMINES **4a–d** BY ACIDS TO FORM UNSATURATED β-KETOENAMINES **5a–d**

Hydroxy-β-ketoenamine	Acid	Unsatd β-ketoenamines	Mp, °C	Yield, %	Infrared spectrum, μ	Empirical formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
4a	H_2SO_4	1,5,5-Triphenyl-3-anilino-2,4-pentadien-1-one (**5a**)	230–232	96[a]	6.22, 6.35, 6.48, 7.58, 7.94	$C_{29}H_{23}NO$	86.75	5.77	3.49	86.70	5.69	3.37
4b	H_2SO_4	1,5,5-Triphenyl-3-(*p*-methoxyanilino)-2,4-pentadien-1-one (**5b**)	197–198	93[a]	6.21, 6.32, 6.48, 6.67, 7.55, 7.80	$C_{30}H_{25}NO_2$	83.50	5.84	3.25	83.34	5.97	3.44
4c	PPA	1,5,5-Triphenyl-3-(*p*-chloroanilino)-2,4-pentadien-1-one (**5c**)	224–225	50[b,c]	6.21, 6.35, 6.46, 6.95, 7.63, 7.89	$C_{29}H_{22}ClNO$	79.90	5.09	3.21	79.90	5.17	3.35
4d	PPA	1,5,5-Triphenyl-3-(*o*-chloroanilino)-2,4-pentadien-1-one (**5d**)	214–215	50[a,c]	6.23, 6.48, 6.75, 7.62, 7.88	$C_{29}H_{22}ClNO$	79.90	5.09	3.21	79.68	5.27	3.13

[a] Recrystallized from 95% ethanol. [b] Recrystallized from methanol. [c] The yield was only about 20% when the dehydration was effected with sulfuric acid (see Experimental Section).

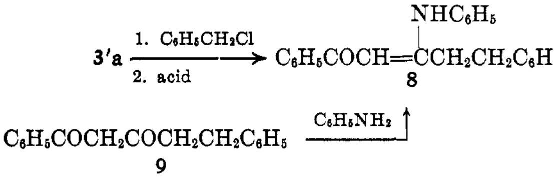
SCHEME II



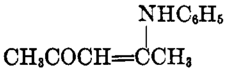
β-Ketoenamines **3a,b** were also benzoylated with methyl benzoate by means of sodium hydride in refluxing 1,2-dimethoxyethane, but the yields of **6a,b** were somewhat lower than those obtained with potassium amide. Similar aroylations of β-diketones have recently been realized in better yields with sodium hydride than with alkali amides.[8]

Alkylation of dipotassio salt **3′a** was effected with benzyl chloride to form **8** in 63% yield; **8** was independently synthesized in 70% yield from β-diketone **9** and aniline, which is a new example of the common method of preparation of such compounds[4a] (Scheme III). Structure **8** was further supported by its nmr spectrum, which showed a collapsed A_2B_2 system centered at 2.62 ppm for four methylene hydrogens, a sharp singlet at 5.58 ppm for one vinyl hydrogen, several peaks between 6.50 and 7.67 ppm for 15 aromatic hydrogens, and a broad singlet at 12.32 ppm for the hydrogen on nitrogen; peak area ratios for the various types of hydrogens were, respectively, 3.8:1: 14.7:1 (calculated 4:1:15:1).

SCHEME III



Next, a study was made of the aniline derivative (**10**) of acetylacetone, which might afford either or both dipotassio salts **10a** and/or **10b** with 2 mole equiv of potassium amide in liquid ammonia.


$CH_3COCH{=}\overset{NHC_6H_5}{C}CH_3$

10


$KCH_2COCH\overset{K\;\;NC_6H_5}{C}CH_3$

10a


$CH_3COCH\overset{K\;\;NC_6H_5}{C}CH_2K$

10b

Actually, only dipotassio salt **10a** appeared to be formed. Thus, benzoylation with methyl benzoate in the presence of potassium amide[7] afforded 1,3-diketoenamine **11** in 25% yield. None of the isomeric 1,5-diketoenamine **12**, which might have arisen from dipotassio salt **10b**, was isolated.

The 1,3-diketoenamine structure **11** was indicated by a positive enol test like that of benzoylacetone; this would not have been expected had the product been

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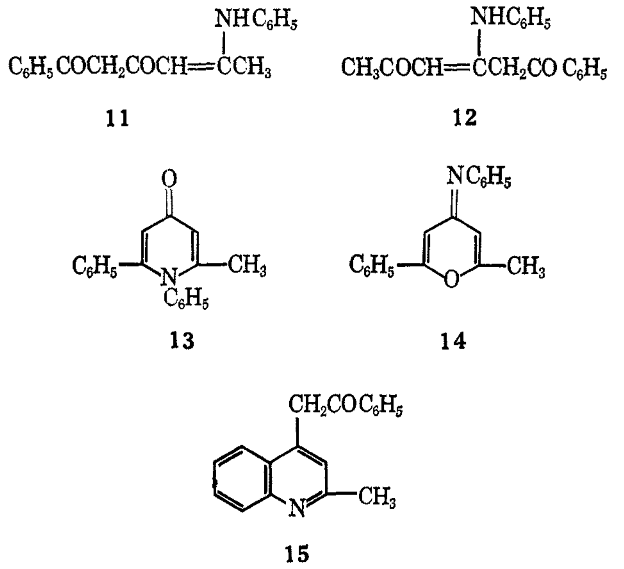
[8] M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 1007 (1965).

the 1,5-diketoenamine **12**, since the 1,5-diketoenamine **6a** failed to give this test. Moreover, like the 1,3-diketone, the product was soluble in dilute sodium hydroxide, whereas **12** would probably not have been soluble since **6a** was not. Structure **11** was further supported by cyclization by means of hot polyphosphoric acid to produce N-phenylpyridone **13** in 94% yield; structure **13** was supported by infrared and ultraviolet spectra (see Experimental Section). Had the benzoyl derivative been **12**, cyclization should have yielded the iminopyrone **14** or its hydrolysis product, 2-methyl-6-phenyl-4-pyrone, neither of which was isolated. Evidently, the cyclic product was not a possible quinoline derivative such as **15**, which might have been produced from **11**.

SCHEME I



Also, β-ketoenamine **10** was benzoylated with methyl benzoate by means of sodium hydride in 1,2-dimethoxyethane to form **11** in 23% yield.

Alkylation and carbonyl addition of dipotassio salt **10a** were effected with benzyl chloride and benzophenone to afford presumably **16** and **17** in yields of 40 and 45%, respectively.


$C_6H_5CH_2CH_2COCH{=}\overset{NHC_6H_5}{C}CH_3$

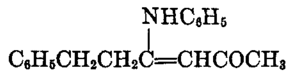
16


$(C_6H_5)_2\overset{HO}{C}CH_2COCH{=}\overset{NHC_6H_5}{C}CH_3$

17

$C_6H_5CH_2CH_2COCH_2COCH_3$

18

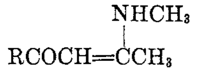

$C_6H_5CH_2CH_2\overset{NHC_6H_5}{C}{=}CHCOCH_3$

19

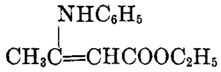
Although treatment of benzoylacetone and β-diketone **9** with aniline afford exclusively β-ketoenamines **3a**[4] and **8**, respectively, treatment of β-diketone **18** with aniline produced a mixture of β-ketoenamine **16** and presumably **19** in a ratio of 2:1, but **19** was not characterized. The structure of hydroxy ketoenamine **17** was supported by its infrared spectrum, which showed hydroxyl absorption at 2.90 μ.

It is of interest that β-ketoenamine **10** undergoes condensations at the acetyl methyl group rather than at the other methyl group, which would correspond to the position at which secondary ionization occurred in β-ketoenamine **3a**. That a possible tripotassio salt was not involved was indicated by treatment of **10** with 3 mol equiv of potassium amide in liquid ammonia, followed by two of benzyl chloride; this afforded benzyl derivative **16** and much stilbene, which arose through self-condensation of the halide. Presumably, **16** was produced by alkylation of dipotassio salt **10a**, and the stilbene by reaction of halide with excess alkali amide.[9]

In contrast to anilino derivatives **3a-d** and **10**, the methylamine derivatives of benzoylacetone and acetylacetone **20a,b** and the aniline derivative of ethyl acetoacetate **21** were evidently not converted sufficiently to dipotassio salts by 2 mol equiv of potassium amide in liquid ammonia for successful terminal condensations. Thus, treatment of these compounds with the alkali amide followed by benzyl chloride afforded only stilbene (from the halide),[9] and **20a,b** and **21** were recovered. Also, treatment of **20a** and **21** with the alkali amide followed by benzophenone failed to yield an isolable amount of adduct, and the starting compounds were recovered.


$RCOCH{=}\overset{NHCH_3}{C}CH_3$

20a, R = C_6H_5
b, R = CH_3


$CH_3\overset{NHC_6H_5}{C}{=}CHCOOC_2H_5$

21

Discussion

In view of the failure of the methylamine derivatives (**20a, b**) of the β-diketones to afford suitable dialkali salts, success with the anilino derivatives **3a-d** may be ascribed to resonance stabilization of the intermediate monoanions involving the aromatic ring; this permits sufficient secondary ionization of the intermediate monoanion by alkali amide to form a dianion satisfactory for condensation.

Although corresponding terminal condensations of dialkali β-diketones followed by reactions with aniline can be employed to prepare ketoenamine **8** (see Scheme III) and diketoenamine **11**[10] in equally good or better yield, the other products described above could probably not be synthesized satisfactorily by this method. *E.g.*, reactions of hydroxy diketone **22**[2c] and of 1,3,5-triketone **23**[2b] with aniline might involve not only the appropriate carbonyl group to give hydroxyketoenamine **4a** and diketoenamine **6a**, respectively, but also the other carbonyl group to afford the isomeric products; moreover, **22** might undergo cleavage or dehydration under the conditions required. As mentioned above, reaction of β-diketone **18** with aniline yielded a mixture of the isomeric ketoenamines.


$C_6H_5COCH_2COCH_2\overset{OH}{C}(C_6H_5)_2$

22

$C_6H_5COCH_2COCH_2COC_6H_5$

23

Diketoenamine **6a** has previously[11] been prepared from 1,5-diphenyl-2,3-pentadiene-1,5-dione and aniline, but the present method appears preferable.

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[9] See C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Brodhag, *J. Am. Chem. Soc.*, **78**, 1653 (1956).

[10] This compound has been obtained in 75% yield from 1-phenyl-1,3,5-hexanetrione and aniline; the details will be published later in connection with a study now in progress on the reactions of 1,3,5-triketones with primary amines and related compounds.

[11] F. Gaudemar, *Compt. Rend.*, **242**, 2471 (1956).

The present method could probably be extended considerably since it should be satisfactory not only with other aromatic ketones (or aldehydes), aromatic esters, and various alkyl or aralkyl halides, but also with other anilino-type β-ketoenamines.

It should be mentioned that, although the acid catalyzed cyclization of diketoenamine **11** did not involve the aniline ring to form quinoline **15**, such a cyclization could presumably be realized with certain of the other new compounds described above since this type of reaction is known to occur with the starting ketoenamine **10** and similar compounds.[12]

Experimental Section[13]

β-Ketoenamines 3a–d.—Compounds **3a–c** were prepared from benzoylacetone and aniline or substituted aniline by the general method of Beyer.[3a]

1-Phenyl-3-anilino-2-buten-1-one (**3a**), mp 108–109°, lit.[4a] mp 110°, and 1-phenyl-3-(*p*-methoxyanilino)-2-buten-1-one (**3b**), mp 106–108°, lit.[14] mp 107–108°, were obtained in yields of 72 and 81%, respectively. The infrared spectra of **3a,b** showed bands at 6.22, 6.27, and 6.36 μ. The nmr spectrum of **3a** exhibited a singlet at 2.18 ppm for three methyl hydrogens, a singlet at 5.98 ppm for one vinyl hydrogen, several peaks between 7.12 and 8.14 ppm for 10 aromatic hydrogens, and one broad peak at 12.25 ppm for the hydrogen on nitrogen.

1-Phenyl-3-(*p*-chloroanilino)-2-buten-1-one (**3c**) was obtained in 65% yield; it melted at 128–129° after recrystallization from methanol. The infrared spectrum showed bands at 6.15, 6.50, and 7.50 μ.

Anal. Calcd for $C_{16}H_{14}ClNO$: C, 70.72; H, 5.19; N, 5.15. Found: C, 70.77; H, 5.24; N, 5.16.

1-Phenyl-3-(*o*-chloroanilino)-2-buten-1-one (**3d**) was prepared by refluxing 0.25 mole of benzoylacetone and 0.26 mole of *o*-chloroaniline with 0.1 g of *p*-toluene sulfonic acid in benzene for 18 hr using a water separator. The benzene solution was concentrated and cooled; the precipitate was collected, washed with cold hexane, and recrystallized from methanol to afford 67.7 g (68%) of **3d**, mp 98–99°. The infrared spectrum showed bands at 6.23, 6.37, 7.60, and 7.80 μ.

Anal. Calcd for $C_{16}H_{14}ClNO$: C, 70.72; H, 5.19; N, 5.15. Found: C, 70.77; H, 5.22; N, 5.14.

Conversion of β-Ketoenamines 3a–d to Dialkali Salts 3'a–d. A. By Potassium Amide.—To a stirred solution of 0.108 mole of potassium amide, prepared from 0.108 g-atom of potassium in 300 ml of commercial, anhydrous liquid ammonia,[2a] was added 0.05 mole of a β-ketoenamine (**3a–d**) to produce an olive solution which changed to a yellow suspension of the dialkali salt within 10–20 min. After stirring for 1 hr, the suspensions, which were assumed to contain 0.05 mole of the dipotassio salt, were employed in condensations as described below in the following sections.

A similar color change was observed when a solution of potassium amide in liquid ammonia was added to a stirred suspension of β-ketoenamine **3a** in liquid ammonia (inverse addition). The first few drops of the alkali amide produced a bright greenish yellow color which deepened to an olive solution by the time half of the base had been added. After the addition of the remaining base, a fine yellow solid began to form and continued to form until a thick yellow suspension resulted. This apparently did not thicken further after 20 min.

B. By Sodium Amide.—Disodio salt **3'd** was prepared similarly from 0.05 mole of **3d** and 0.108 mole of sodium amide[15] in liquid ammonia and used as described below. Its color was olive.

Carbonyl Additions of Dialkali Salts 3'a–d with Benzophenone to Form Hydroxy-β-ketoenamines 4a–d.—In Table I are summarized yields, melting points, infrared spectra, and analyses of products **4a–d**. Details of the reactions are given below.

A. Reaction of Dipotassio Salts to Form 4a–c.—To stirred suspensions of 0.05 mole of dipotassio salts **3'a–c** in 600 ml of liquid ammonia was added 0.05 mole of finely divided solid benzophenone. After 1 hr, the thick yellow suspensions were poured into excess ammonium chloride in liquid ammonia. The ammonia was evaporated on the steam bath, and ether and water were added. Since the products were only slightly soluble in ether, the suspensions were filtered and the solids washed with ether. The ether layers, dried and evaporated, afforded an additional 1–3 g of the products. In all three cases the combined solids were recrystallized from 95% ethanol to afford yellow crystals of **4a–c**.

When the dipotassio salt of β-ketoenamine **3d**[16] was treated similarly with benzophenone, the starting ketoenamine **3d** and benzophenone were largely recovered from the ether layer of the reaction mixture neutralized inversely 5, 10, 30, or 60 min after the ketone was added.

Cleavage of carbonyl addition product **4a** occurred on refluxing a 1.0-g sample of it with decalin for 30 min. The solution was cooled and 20 ml of petroleum ether was added. The solid was collected and washed with petroleum ether (bp 30–60°) to give 0.75 g (75%) of **3a**, mp 104–107° (mixture melting point undepressed). Benzophenone was also observed.

B. Reaction of Disodio Salt 3'd to Form 4d.—This reaction was carried out as described above under A except that an ethereal solution of benzophenone was used. The reaction mixture was poured into excess ammonium chloride in liquid ammonia after 5 min. Since **4d** was soluble in ether, the ethereal solution of the reaction product was evaporated (without filtration), and the residue was recrystallized from methanol.

Dehydrations of Hydroxy-β-ketoenamines 4a–d to Form 5a–d.—In Table II are summarized yields, melting points, infrared spectra, and analyses of products **5a–d**. Details of the reactions are given below.

A. With Sulfuric Acid.—Samples (2.0 g) of **4a–d** were dissolved in 20 ml of cold, concentrated sulfuric acid. After 15–20 min, the solutions were poured over ice. The resulting solids were collected, washed with water, sodium bicarbonate solution and water, and recrystallized from ethanol to afford yellow-orange crystals of **5a–d**. In the reactions of **4c,d**, unidentified products were also obtained; these may have resulted from sulfonation of the anilino ring.

B. With Polyphosphoric Acid.—Samples (2.0 g) of **4c,d** were heated on the steam bath with 20 g of polyphosphoric acid for 10 min. The solutions were then cooled and diluted with ice and water. The resulting solids were collected and purified as described above under A.

Benzoylations of Dipotassio Salts 3'a,b to Form 6a,b.—To a stirred suspension of 0.05 mole of **3'a** and 0.05 mole of potassium amide (prepared from 0.05 mole of **3a** and 0.15 mole of potassium amide) in liquid ammonia was added 0.1 mole of methyl benzoate in ether. After 3 hr, the ammonia was replaced by ether, and ether, ice, and water were added carefully. The ether layer[17] was dried and evaporated. The solid residue was refluxed with 200 ml of hexane and the solvent decanted; this process was repeated five times. The residual solid (1.8 g) was benzamide (determined by mixture melting point with an authentic sample). The combined hexane solution was concentrated and cooled. The resulting precipitate was collected and recrystallized from hexane to afford 8.5 g (50%) of 1,5-diphenyl-3-anilino-2-pentene-1,5-dione (**6a**, light beige crystals): mp 120–122°, lit.[11] mp 125°. The infrared spectrum showed bands at 5.98, 6.23, 6.28, 6.35, and 7.86 μ. The nmr spectrum exhibited a singlet at 4.03 ppm for two methylene hydrogens, a singlet at 5.92 ppm for one vinyl hydrogen, two complex groups between 7.00 and 8.10 ppm for 15

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[12] See R. C. Elderfield, "Heterocyclic Compounds," Vol. 4, John Wiley and Sons, Inc., New York, N. Y., 1952, p 36.

[13] Melting points, which were taken on a Mel-Temp capillary melting point apparatus, and boiling points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 137 or 237 Infracord with potassium bromide pellets or carbon tetrachloride solutions of the solids and neat samples of the liquid on sodium chloride plates. Nmr spectra were obtained with a Varian A-60 spectrometer using tetramethylsilane as an external reference and carbon tetrachloride as solvent. Ultraviolet spectra were obtained with a Cary 14 recording spectrophotometer, using 10^{-4} *M* solutions in 95% ethanol. Elemental analyses were by Janssen Pharmaceutica, Beerse, Belgium, and by Triangle Chemical Laboratories, Chapel Hill, N. C.

[14] W. Koenigs and F. Meinberg, *Chem. Ber.*, **28**, 1045 (1895).

[15] See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 122 (1954).

[16] That the conversion of **3d** to its dipotassio salt by the alkali amide was essentially complete was indicated by failure to obtain stilbene on treatment of the reaction mixture with benzyl chloride.[9] Some of the benzylation product was evidently produced, but it was not isolated.

[17] Apparently, water is a strong enough acid to liberate the neutral diketoenamines **6a,b**, because acidification of the water layer required only a little acid and afforded very little product.

aromatic hydrogens, and a broad peak at 13.12 for the hydrogen on nitrogen.

Anal. Calcd for $C_{23}H_{19}NO_2$: C, 80.91; H, 5.61; N, 4.10. Found: C, 80.67; H, 5.48; N, 4.37.

Diketoenamine **6a** gave a negative enol test (no color) with ethanolic ferric chloride. After heating a sample of **6a** with 50% sulfuric acid on the steam bath for 10 min, a green enol test was obtained similar to that observed with the corresponding 1,3,5-triketone.[2a] However, much of **6a** was recovered after this treatment.

Similarly, dianion **3′b** (0.05 mole) was benzoylated to afford 6.0 g (35%) of 1,5-diphenyl-3-(*p*-methoxyanilino)-2-pentene-1,5-dione (**6b**, light beige crystals), mp 129–130°; it gave no enol test with alcoholic ferric chloride. The infrared spectrum showed bands at 5.95, 6.23, 6.33, 7.79, and 8.05 μ

Anal. Calcd for $C_{24}H_{21}NO_3$: C, 77.61; H, 5.70; N, 3.77. Found: C, 77.31; H, 5.74; N, 3.97.

Cyclization of **6b** was accomplished by refluxing a 1.0-g sample of it with 25 ml of decalin for 1 hr. The suspension was cooled to room temperature and filtered. To the filtrate was added with stirring 150 ml of hexane, and the resulting orange mixture was centrifuged. The solid was recrystallized from ethanol to afford 0.45 g (50%) of 1,4-dihydro-4-(*p*-methoxyphenyl)-imino-4-pyranone (**7**, orange crystals), mp 186–187°. The infrared spectrum showed strong bands at 6.00, 6.61, and 8.00 μ. The ultraviolet spectrum exhibited maxima at 353 mμ (log ε 4.15), 285 (4.58), and 253 (4.55).

Anal. Calcd for $C_{24}H_{19}NO_2$: C, 81.56; H, 5.42; N, 3.96. Found: C, 81.54; H, 5.64; N, 4.05.

Benzoylation of β-Ketoenamines 3a,b by Sodium Hydride.—To a stirred suspension of 0.20 mole of sodium hydride[18] in 200 ml of 1,2-dimethoxyethane (monoglyme) was added 0.05 mole of **3a** or **3b**. After hydrogen evolution ceased (about 3 hr), 0.05 mole of methyl benzoate in monoglyme was added. After hydrogen evolution again ceased (*ca.* 6 hr), 5 ml of ethanol was gradually added to decompose excess sodium hydride, and the monoglyme suspension was concentrated under reduced pressure. Water and ether were added, and the water layer was extracted twice with ether. The combined ether layers were worked up as described under A to afford **6a** and **6b** in yields of 40 and 30%, respectively (mixture melting points with above samples were undepressed).

Benzylation of Dipotassio Salt 3′a to Form 8.—To a stirred suspension of 0.05 mole of **3′a** was added 0.06 mole of benzyl chloride in ether. After 1 hr, excess ammonium chloride was added, and the ethereal solution was dried and evaporated. The residue was recrystallized from methanol to give 1,5-diphenyl-3-anilino-2-penten-1-one (**8**, white crystals), mp 57–60° and 63–65° after further recrystallization, yield 62%. The infrared spectrum showed bands at 6.28, 6.34, 7.62, and 7.85 μ.

Anal. Calcd for $C_{23}H_{21}NO$: C, 84.37; H, 6.46; N, 4.28. Found: C, 84.40; H, 6.45; N, 4.27.

Independent synthesis of **8** was accomplished by heating an equimolar mixture of 1,5-diphenyl-1,3-pentanedione (**9**)[2a] and aniline at 150° for 3 hr. The cooled product was recrystallized from methanol to give **8**, mp 64–65°, in 70% yield. A mixture melting point of the two samples was undepressed, and their infrared spectra were identical.

4-Anilino-3-penten-2-one (10).—This ketoenamine was prepared by heating a mixture of 0.4 mole of acetylacetone and 0.4 mole of aniline on the steam bath for 6 hr. After adding water, the product was extracted with methylene chloride; the extract was dried and evaporated. The residue was distilled to afford **10**, bp 148–151° at 8 mm, in 70% yield; on standing it solidified, mp 49–51°, lit.[4a] mp 51–53°. The infrared spectrum showed bands at 6.18, 6.27, 6.36, and 7.87 μ. The nmr spectrum exhibited two singlets for six methyl hydrogens at 1.83 and 1.89 ppm, a singlet for one vinyl hydrogen at 4.86 ppm, several peaks for five aromatic hydrogens between 6.58 and 7.17 ppm, and a broad peak for the hydrogen on nitrogen at 11.74 ppm.

Conversion of β-Ketoenamine 10 to Dipotassio Salt 10a.—To a stirred solution of 0.108 mole of potassium amide prepared from 0.108 g-atom of potassium in liquid ammonia was added 0.05 mole of **10**. After 1 hr, the green solution was assumed to contian 0.05 mole of dipotassio salt **10a**.

Benzoylation of Dipotassio Salt 10a to Form 11.—Benzoylation of **10a** was carried out in the presence of potassium amide as described above for that of dianion **3′a,b**, but the work-up was modified as follows.[19] After addition of ether, ice, and water, the water layer was acidified by addition of cold 6 *M* hydrochloric acid in the presence of ether. The water layer was extracted twice more with ether, and the three ethereal fractions were combined, dried, and evaporated. The solid residue was recrystallized from hexane–absolute ethanol to give 1-phenyl-5-anilino-4-hexene-1,3-dione (**11**, yellow crystals), mp 96–98°, in 25% yield. The product gave a brown enol test with alcoholic ferric chloride. The infrared spectrum showed bands at 6.22, 6.38, 6.74, and 7.84 μ.

Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.22; H, 6.18; N, 5.16.

Cyclization of diketoenamine **11** was effected by heating a 5-g sample of it with polyphosphoric acid on the steam bath for 1.5 hr. The solution was diluted with ice and water. The cold solution was made basic with concentrated ammonia. The resulting precipitate was collected and recrystallized from ethanol–water to give 4.1 g (94%) of 1,2-diphenyl-6-methyl-4-pyridone (**13**, white crystals), mp 241–242°. The infrared spectrum showed bands at 6.10, 6.40, 6.74, and 7.40 μ. The ultraviolet spectrum exhibited maxima at 268 mμ (log ε 4.39), 241 (4.18), and 207 (4.40).

Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.67; H, 5.87; N, 5.45.

Pyridone **13** was recovered unchanged after treatment with concentrated sulfuric acid at room temperature for 10 min, followed by dilution with ice and neutralization with concentrated ammonia.

Benzoylation of β-Ketoenamine 10 by Sodium Hydride.—This reaction was effected essentially as described above for those of β-ketoenamines **3a,b**, employing the modification of the work-up described in the benzoylation of dipotassio salt **10a**.

Benzylation of Dipotassio Salt 10a.—Benzylation of **10a** was carried out as was the benzylation of dipotassio salt **3′a**. The resulting oil was distilled to afford recovered starting material **10** (50%), bp 110–114 at 0.5 mm, and presumably 6-phenyl-2-anilino-2-hexen-3-one (**16**), bp 176–178° at 0.5 mm in 36% yield; vpc of this product showed a single peak. The infrared spectrum showed bands at 6.20, 6.29, 6.39, and 7.86 μ.

Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.24. Found: C, 81.42; H, 7.09; N, 5.47.

An equimolar mixture of β-diketone **18** and aniline was heated at 165° for 1.5 hr and cooled. The resulting oil was distilled to afford a mixture, bp 174–178° at 0.5 mm, which consisted of **16** (identified by vpc) and presumably isomeric **19** in the ratio of 2:1 (by vpc).

Carbonyl Addition of Dipotassio Salt 10a to Benzophenone.—This reaction was carried out as above for **3′a–c**. Evaporation of the ether solution of the product and recrystallization of the solid residue from methanol afforded presumably 1,1-diphenyl-5-anilino-1-hydroxy-4-hexen-3-one (**17**, white crystals), mp 144–145°, in 45% yield. The infrared spectrum showed bands at 6.23, 6.28, 6.43, 7.42, 7.98, and 2.95 μ.

Anal. Calcd for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.48; N, 3.91. Found: C, 80.74; H, 6.24; N, 3.84.

Attempted Condensations of β-Ketoenamines 20a,[20] 20b,[21] and Crotonate 21.[22]—To solutions of 0.1 mole of potassium amide (prepared from 0.1 g-atom of potassium) in liquid ammonia was added 0.05 mole of **20a,b**, or **21**. After 1 hr, 0.05 mole of benzyl chloride was added to produce an immediate violet color, which persisted throughout the addition. After 0.5 hr, the reaction mixtures were neutralized with ammonium chloride and worked up to give recovered starting materials and stilbene (identified by vpc). Only very small vpc peaks of unidentified products were observed.

Similarly, β-ketoenamine **20a** and crotonate **21** were treated with potassium amide in liquid ammonia, followed by benzophenone. The reaction mixtures were neutralized inversely with ammonium chloride, and worked up to give recovered starting materials (by vpc). Only very small peaks of unidentified products were observed.

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[18] This reagent was obtained as an approximately 50% dispersion in mineral oil from Metal Hydrides, Inc., Beverly, Mass.

[19] This modification was employed because water is not a strong enough acid to liberate neutral diketoenamine **11** (*cf.* footnote 17).

[20] C. Beyer, *Chem. Ber.*, **24**, 1669 (1891).

[21] E. Knoevenagel and W. Ruschhaupt, *ibid.*, **31**, 1030 (1898).

[22] G. A. Reynolds and C. R. Hauser, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 615.