Trialkali Salts of N-Acetyl-α-benzoylacetamide. Condensations with Certain Electrophilic Reagents[1]

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Condensations at the methyl group of N-acetyl-α-benzoylacetamide (1) were effected through its 1,3,5-tripotassio or trisodio salts, which were prepared from 1 and 3 molecular equiv of alkali amide in liquid ammonia. The tripotassio salt underwent alkylations with benzyl chloride and methyl iodide. The trisodio salt, which was less suitable for alkylation, underwent addition reactions with benzophenone, chalcone, anisaldehyde, p-methylbenzaldehyde, and p-chlorobenzaldehyde to produce hydroxy β-keto imides which were subsequently dehydrated to form unsaturated β-keto imides. In a similar addition reaction with p-methoxybenzophenone the unsaturated derivative was obtained directly. These reactions represent useful synthetic methods for a number of new compounds. Attempts to effect similar condensations at the methyl group of N-acetyl-α-benzoylphenylacetamide by means of 3 molecular equiv of alkali amide were unsuccessful.

A recent publication[2] concerning the formation and reactions of the trisodio salts of 1-phenyl-1,3,5-hexanetrione and 1-(*p*-methoxyphenyl)-1,3,5-hexanetrione appears to be the first report of synthetically useful trialkali salts derived from 1,3,5-tricarbonyl compounds.

We now wish to report that N-acetyl-α-benzoylacetamide (**1**), which may be regarded as a nitrogen analog of 1-phenyl-1,3,5-hexanetrione, undergoes certain condensations at its terminal methyl group through 1,3,5-tripotassio or trisodio salts **1′** (M = K or Na) which were prepared from **1** and 3 molecular equiv of potassium amide or sodium amide in liquid ammonia.

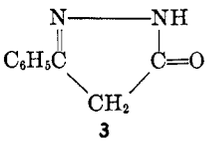
$$\underset{\mathbf{1}}{C_6H_5COCH_2CONHCOCH_3} \xrightarrow[\text{liquid } NH_3]{3MNH_2} \underset{\mathbf{1'}}{C_6H_5COCHCONCOCH_2M}$$

Thus, **1′** (M = K) underwent alkylation with benzyl chloride and methyl iodide to form **2a** and **2b** in yields of 69 and 48%, respectively.

$$\mathbf{1'},\ M = K \xrightarrow[2.\ acid]{1.\ RX} C_6H_5COCH_2CONHCOCH_2R$$

2a, R = $C_6H_5CH_2$
b, R = CH_3

Structural assignments **2a** and **2b** were based on analyses, spectral data, and chemical evidence. The infrared spectra had a strong N–H band at 3.05 μ indicating that alkylation on nitrogen had not occurred. The nmr spectra (see the Experimental Section) were characterized by the absence of resonance for acetyl methyl protons which had appeared as two singlets at 2.25 and 2.33 ppm in the spectrum of **1**.[3] Acidic hydrolysis of **2a** and **2b** afforded acetophenone and, in the case of **2a**, hydrocinnamic acid; the propionic acid presumably formed in the hydrolysis of **2b** was not isolated. The presence of an unchanged α-benzoylacetamido moiety in **2a** and **2b** was established by cyclization of both compounds with hydrazine[4] to form pyrazolone **3**. Final verification of structure **2b** was obtained by its independent synthesis from benzoylacetonitrile, propionic anhydride, and boron trifluoride diacetic acid complex (BTDA).[5]



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Attempted alkylation of tripotassio salt **1′** with benzhydryl chloride produced tetraphenylethylene, along with unchanged **1**. Evidently the tripotassio salt served as a strong base, rather than as a nucleophile, to effect self-condensation of this halide.[6] Although alkylation of tripotassio salt **1′** with benzyl chloride afforded relatively pure monobenzyl derivative **2a**, that of trisodio salt **1′** produced a mixture of products from which **2a** was isolated in only 8% yield. This is somewhat surprising since the trisodio salt of 1-phenyl-1,3,5-hexanetrione underwent alkylation in liquid ammonia with certain halides which failed to alkylate the corresponding tripotassio salt.[2] Moreover, 1,3-disodio salts of β-diketones are usually more suitable for alkylation than their dipotassio analogs.[7]

Trisodio salt **1′** underwent a carbonyl addition reaction with benzophenone to afford hydroxy β-keto imide **5** in 40% yield. When tripotassio salt **1′** was employed

$$\mathbf{1'},\ M = Na \xrightarrow{(C_6H_5)_2CO} \underset{\mathbf{4}}{C_6H_5COCHCONCOCH_2C(C_6H_5)_2} \xrightarrow{acid}$$

$$C_6H_5COCH_2CONHCOCH_2C(C_6H_5)_2 \longrightarrow$$

5

$$C_6H_5COCH_2CONHCOCH{=}C(C_6H_5)_2$$

6

in a similar reaction, the yield of **5** was only 16%. This may have been due to the fact that intermediate **4**

(1) (a) Acknowledgment is made to the donors of the Petroleum Research Fund administered by the American Chemical Society and to the Committee on Grants-in-Aid of Research of the Society of the Sigma Xi for partial support of this work. (b) Presented in part at the Southeast–Southwest Regional Meeting of the American Chemical Society, Memphis, Tenn., Dec 3, 1965.

(2) K. G. Hampton, T. M. Harris, C. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 4263 (1965).

(3) J. F. Wolfe, C. J. Eby, and C. R. Hauser, *ibid.*, **30**, 55 (1965).

(4) S. D. Work, D. R. Bryant, and C. R. Hauser, *J. Am. Chem. Soc.*, **86**, 872 (1964).

(5) See J. F. Wolfe and C. L. Mao, *J. Org. Chem.*, **31**, 3069 (1966), for a description of a similar reaction employing acetic anhydride and BTDA.

(6) R. B. Meyer and C. R. Hauser, *ibid.*, **25**, 158 (1960).

(7) K. G. Hampton, T. M. Harris, and C. R. Hauser, *ibid.*, **30**, 61 (1965).

TABLE I

CARBONYL ADDITIONS OF TRISODIO SALT 1′ WITH AROMATIC ALDEHYDES AND KETONES TO FORM HYDROXY β-KETO IMIDES

Aldehyde or ketone	Hydroxy β-keto imides	Mp, °C	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
Benzophenone	N-(β-Hydroxy-β-phenylhydrocinnamoyl)-α-benzoylacetamide (**5**)	147–148[a]	40	$C_{24}H_{21}NO_4$	74.40	5.46	3.62	74.25	5.44	3.49
Chalcone	N-(β-Hydroxy-β-styrylhydrocinnamoyl)-α-benzoylacetamide (**9**)	147–149 dec[b]	58	$C_{26}H_{23}NO_4$	75.53	5.61	3.39	75.43	5.50	3.36
Anisaldehyde	N-(β-Hydroxy-*p*-methoxyhydrocinnamoyl)-α-benzoylacetamide (**12a**)	119–120[c]	70	$C_{19}H_{19}NO_5$	66.85	5.61	4.10	66.87	5.56	4.42
p-Methylbenzaldehyde	N-(β-Hydroxy-*p*-methylhydrocinnamoyl)-α-benzoylacetamide (**12b**)	128.5–129.5[b]	56	$C_{19}H_{19}NO_4$	70.14	5.89	4.31	70.08	5.99	4.42
p-Chlorobenzaldehyde	N-(β-Hydroxy-*p*-chlorohydrocinnamoyl)-α-benzoylacetamide (**12c**)	125.5–127[a]	41	$C_{18}H_{16}ClNO_4$[d]	62.52	4.66	4.05	62.44	4.78	3.84

[a] Recrystallized from 95% ethanol. [b] Recrystallized from absolute ethanol. [c] Recrystallized from isopropyl alcohol–petroleum ether (bp 30–60°). [d] Calcd: Cl, 10.25. Found: Cl, 10.55.

TABLE II

NMR DATA FOR CARBONYL ADDITION PRODUCTS AND UNSATURATED β-KETO IMIDES[a,b]

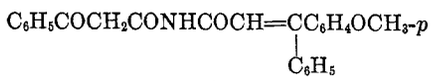
Compound	Types of hydrogen and chemical shift, δ (ppm): Enol OH	Phenyl	O— | —C=CH	PhCH=C—	Ph | =CCH=CPh	O ‖ —C—CH=C—	PhCH=CH	Free COH	O— | PhCH—	—COCH₂CO—	—COCH₂CPh	OCH₃	CH₃
5	10.72[c] 10.62[c]	7.45[d]	6.70[e]	...	...	...	...	5.98[e] 6.09[e]	...	4.25[e]	3.45[e,i] 3.55[e]	...	...
9	10.76[c] 10.50[c]	7.65[d]	6.86[e]	...	...	...	6.68[f]	...	...	4.38[e]	3.22[e,i] 3.31[e]	...	...
12a	10.84[c]	7.35[d]	...	...	...	...	...	5.35[h]	4.95[f]	4.32[e]	2.63[e,i] 2.74[e]	3.65[c]	...
12b	10.84[c]	7.41[d]	6.79[e]	...	...	...	...	5.37[h]	4.97[f]	4.31[e]	2.61[e,i] 2.73[e]	...	2.16[c]
12c	10.90[c]	7.74[d]	6.80[e]	...	...	...	...	5.60[h]	5.05[f]	4.38[e]	2.65[e,i] 2.79[e]	...	...
6	11.20[c]	7.50[d]	...	...	...	6.70[e]	...	...	...	4.31[c]	...	...	...
7	10.82[c]	7.35[d]	...	...	...	6.67[c]	...	...	...	4.30[c]	...	3.70[c]	...
11	11.00[c]	7.65[d]	...	6.31[f]	6.59[f]	6.15[c]	...	...	...	4.41[c]	...	...	...
13a	10.98[c]	7.41[d]	...	...	...	6.59[g]	...	...	...	4.42[c]	...	3.70[c]	...
13b	11.00[c]	7.38[d]	...	6.89[g]	...	6.63[g]	...	...	...	4.37[c]	...	...	2.15[c]
13c	11.02[c]	7.57[d]	...	6.89[h]	...	6.70[g]	...	...	...	4.41[c]	...	...	...

[a] The nmr spectra were obtained on a Varian Associates A-60 spectrometer using deuteriodimethyl sulfoxide as solvent and tetramethylsilane as external standard. [b] Chemical shifts are measured to the center of a singlet or multiplet. In each spectrum the peak areas were consistent with the assignments given in the above table. [c] Singlet. [d] Multiplet. [e] Singlet with shoulders. [f] Triplet with fine splitting. [g] Broad singlet with fine splitting. [h] Doublet with fine splitting. [i] These two singlets apparently arise because of different chemical shifts for the methylene hydrogens in the keto and enol forms of this compound; see ref 3.

(M = K) was less stable than the analogous trisodio salt **4** (M = Na).[8]

Structure **5** was supported by analysis (Table I) and by its nmr spectrum (Table II) which had, in addition to the appropriate aromatic bands, absorption for two pairs of methylene hydrogens at 4.25 and 3.45–3.55 ppm. In addition, **5** was dehydrated by means of *p*-toluenesulfonic acid in refluxing benzene to give unsaturated β-keto imide **6** in 94% yield. The identity of **6** was established by its nmr spectrum (Table II), which had absorption for a pair of methylene hydrogens at 4.31 and vinyl proton absorption at 6.70 ppm, and by its basic hydrolysis to form acetophenone and β-phenylcinnamic acid.

Trisodio salt **1′** underwent a similar addition reaction with *p*-methoxybenzophenone, but unsaturated β-keto imide **7**[9] rather than the expected hydroxy β-keto imide **8** was isolated from the reaction in 45% yield. Apparently **8** was formed initially and subsequently



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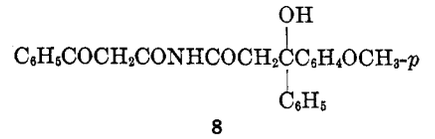

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dehydrated during work-up of the reaction mixture. The nmr spectrum of **7**, which was consistent with the assigned structure, had absorption for one pair of methylene hydrogens and a single vinyl proton at 4.30 and 6.67 ppm, respectively.

(8) That trisodio intermediate **4** was also relatively unstable was supported by the observation that in reactions of **1′** (M = Na) with benzophenone, optimum yields of adduct **5** were obtained when the reaction mixture was neutralized after 2–5 min. Neutralization after longer periods resulted in considerably lower yields of **5**, presumably because of reversion of intermediate **4** (M = Na). A similar time effect was also noted in the addition reactions of trisodio salt **1′** with *p*-methoxybenzophenone and chalcone. See E. M. Kaiser and C. R. Hauser, *J. Org. Chem.*, **31**, 3317 (1966), for a discussion of similar effects of reaction time and the metallic cation in addition reactions of benzophenone with certain dialkali salts in liquid ammonia.

(9) Although the physical properties of this compound indicated that it was a single geometric isomer, its configuration was not established.

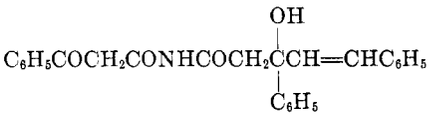
TABLE III

UNSATURATED β-KETO IMIDES DERIVED FROM CARBONYL ADDITION PRODUCTS

Addn product	Unsaturated β-keto imides	Mp, °C	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
5	N-(β-Phenylcinnamoyl)-α-benzoylacetamide (6)	138–139[a]	94	$C_{24}H_{19}NO_3$	78.03	5.18	3.79	78.22	5.13	3.94
...	N-(β-Phenyl-*p*-methoxycinnamoyl)-α-benzoylacetamide (7)	173–174[b]	47[e]	$C_{25}H_{21}NO_4$	75.17	5.30	3.51	75.33	5.23	3.42
9	N-(β-Styrylcinnamoyl)-α-benzoylacetamide (11)	171–173[c]	85	$C_{26}H_{21}NO_3$	78.97	5.35	3.54	78.73	5.45	3.41
12a	N-(*p*-Methoxycinnamoyl)-α-benzoylacetamide (13a)	171–172[d]	60	$C_{19}H_{17}NO_4$	70.57	5.30	4.33	70.45	5.13	4.48
12b	N-(*p*-Methylcinnamoyl)-α-benzoylacetamide (13b)	173–175[a]	79	$C_{19}H_{17}NO_3$	74.25	5.58	4.56	74.48	5.70	4.59
12c	N-(*p*-Chlorocinnamoyl)-α-benzoylacetamide (13c)	179–181[a]	67	$C_{18}H_{14}ClNO_3$[f]	65.96	4.31	4.27	65.79	4.22	4.12

[a] Recrystallized from 95% ethanol. [b] Recrystallized from absolute ethanol. [c] Recrystallized from ethyl acetate. [d] Recrystallized from methanol. [e] This product was obtained directly from the carbonyl addition reaction. [f] Calcd: Cl, 10.82. Found: Cl, 11.09.

When trisodio salt **1′** was allowed to react with chalcone, carbinol **9** was isolated in 58% yield. That this product was **9** and not the product (**10**) resulting from 1,4 addition of the trisodio salt to the α,β-unsaturated carbonyl system, was verified by its nmr spectrum, which was consistent with structure **9** but not with **10**, and by its acid-catalyzed dehydration to form **11**[9] in 85% yield. Structural assignment **11** was based on analysis (Table III), spectral data, and base-catalyzed hydrolysis to form acetophenone and β-styrylcinnamic acid.



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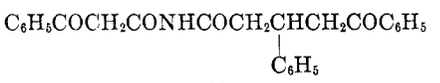

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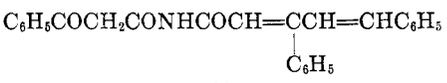

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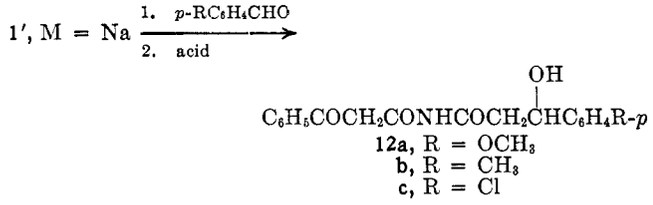
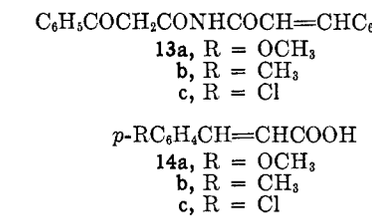
Next, reactions of trisodio salt **1′** with several aromatic aldehydes were investigated. This salt underwent addition reactions with anisaldehyde, *p*-methylbenzaldehyde, and *p*-chlorobenzaldehyde to form hydroxy β-keto imides **12a–c** in yields of 41–70%. These results are summarized in Table I. Tripotassio salt **1′** was found to be less suitable than its trisodio counterpart for these condensations.[10]



12a, R = OCH_3
b, R = CH_3
c, R = Cl

Analytical and spectral data were consistent with structural assignments **12a–c**. In particular, the nmr spectra (Table II) exhibited absorption for two pairs of methylene hydrogens at 4.31–4.38 and 2.61–2.79, as well as absorption for methinyl hydrogen at 4.95–5.95 ppm. That structural assignments **12a–c** were correct was further verified by dehydration of these compounds to form unsaturated β-keto imides **13a–c** (Table III) in yields of 60–79%.[11]



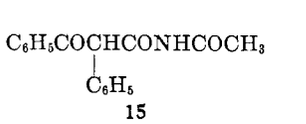
13a, R = OCH_3
b, R = CH_3
c, R = Cl

14a, R = OCH_3
b, R = CH_3
c, R = Cl

The nmr spectra (Table II) of **13a–c** had absorption for one pair of methylene hydrogens at 4.37–4.42 ppm, as well as vinyl hydrogen resonance at 6.59–6.70 ppm. The methinyl hydrogen absorption which had appeared in the spectra of **12a–c** was absent from the spectra of these compounds. Hydrolysis of **13a–c** afforded acetophenone and *para*-substituted cinnamic acids **14a–c**.

It should be mentioned that attempts to effect carboxylation[2,12] and aroylation of trialkali salts **1′** with solid carbon dioxide and methyl benzoate, respectively, failed to afford the desired terminal derivatives, starting imide **1** being largely recovered in each instance. In addition, attempts to realize condensations at the terminal methyl group of **1** with benzyl chloride and benzophenone by means of 2 molecular equiv of potassium or sodium amide were unsuccessful. Products resulting from condensation at the methylene or NH group of **1** could not be detected, and only starting materials were recovered. Apparently the dialkali salts[13] produced in these reactions are less nucleophilic than trialkali salts **1′** where removal of a weakly acidic methyl hydrogen produces a highly reactive nucleophilic site.

Finally, N-acetyl-α-benzoylphenylacetamide[5] (**15**) was apparently converted into tripotassio or trisodio salt **15′** (M = K or Na) by means of 3 molecular equiv



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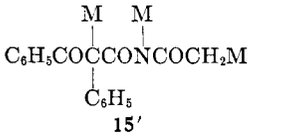

15′

(10) As in the addition reactions of trisodio salt **1′** with aromatic ketones, optimum yields of **12a–c** were obtained when the reaction mixtures were neutralized within 1–5 min after addition of the aldehyde.

(11) Apparently only one of the two possible geometric isomers of **13a–c** was isolated from the dehydrations of **12a–c**, but to which of the isomers about the double bond they correspond was not determined.

(12) T. M. Harris and C. M. Harris, *J. Org. Chem.*, **31**, 1032 (1966).

(13) Formation of these salts presumably involved metalation at the more acid methylene and NH positions of **1**.

of the appropriate alkali amide in liquid ammonia. However, in contrast to tripotassio salt **1′**, tripotassio salt **15′** failed to undergo alkylation with benzyl chloride, and attempts to effect condensation of trisodio salt **15′** with benzophenone were unsuccessful. The limited solubility of these salts in liquid ammonia may have been the major reason for these failures.

The present reactions of trialkali salts **1′** serve to emphasize the synthetic utility of such intermediates, since, with the exception of **2b** and possibly **2a**, all other compounds reported in this study would appear to be difficult to prepare in comparable yields by more conventional methods.

Experimental Section[14]

Trialkali Salts 1′ (M = K or Na).—To a stirred suspension of 0.03 mole of potassium amide, prepared from 0.03 g-atom of potassium in 300 ml of liquid ammonia[15] contained in a 500-ml, three-necked flask, was added 2.05 g (0.01 mole) of finely powdered N-acetyl-α-benzoylacetamide (**1**).[5] After 30 min, the bright yellow suspension was assumed to contain 0.01 mole of tripotassio-N-acetyl-α-benzoylacetamide (**1′**, M = K).

Similarly, addition of **1** (0.01 mole) to 0.03 mole of sodium amide, prepared from 0.03 g-atom of sodium in 300 ml of liquid ammonia,[16] produced after 30 min a bright yellow suspension which presumably contained 0.01 mole of trisodio-N-acetyl-α-benzoylacetamide (**1′**, M = Na).

Alkylations of Tripotassio Salt 1. A. Benzylation.—To a stirred suspension of tripotassio salt **1′** (0.01 mole) in 300 ml of liquid ammonia was added 4.20 g (0.033 mole) of benzyl chloride in 30 ml of anhydrous ether. After 1 hr the resulting gray suspension was neutralized by addition of excess solid ammonium chloride. The ammonia was evaporated (steam bath) as an equal volume of ether was added. A mixture of 20 ml of 12 *N* hydrochloric acid and 150 g of crushed ice was added to dissolve inorganic salts. The two layers were separated and the aqueous layer was extracted with three 100-ml portions of ether–ethyl acetate (1:1). The extracts and the original ethereal layer were combined, washed with 5% sodium bicarbonate solution, dried ($MgSO_4$), and concentrated. The residue was washed with petroleum ether (bp 30–60°) and recrystallized from ethanol to afford 2.05 g (69%) of N-(β-phenylpropionyl)-α-benzoylacetamide (**2a**) as colorless needles: mp 122–123°; infrared absorption at 3.0–3.1 (NH) and 5.8–5.9 μ (C=O); and nmr peaks ($CDCl_3$) at δ 2.90 (4 H multiplet, CH_2CH_2Ph), 4.34 (1.1 H singlet, $COCH_2CO$), 6.72 (0.45 H singlet, COCH=C), 7.58 (10 H multiplet, phenyl), 9.10 (0.5 H singlet, NH), 9.60 (0.5 H singlet, NH), and 14.0 (0.45 H singlet, C=COH).

Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.27; H, 5.75; N, 4.62.

In a similar experiment, employing trisodio salt **1′**, there was obtained 0.25 g (8%) of **2a**.

B. Methylation.—To a stirred suspension of 0.01 mole of tripotassio salt **1′** in 300 ml of liquid ammonia was added 2.83 g (0.02 mole) of methyl iodide in 40 ml of anhydrous ether. After 40 min the reaction mixture was processed in the manner described for benzylation except that the combined organic extracts were first washed with sodium thiosulfate solution until they were essentially colorless. The crude residue obtained on concentration of the solvent was recrystallized from 95% ethanol to afford 1.05 g (48%) of N-propionyl-α-benzoylacetamide (**2b**) as colorless needles: mp 117–118°; infrared absorption at 2.90–3.10 (NH) and 5.8–6.0 μ (C=O); and nmr peaks ($CDCl_3$) at δ 1.14 (3 H multiplet, CH_3C), 2.50 (2 H multiplet, $COCH_2Me$), 4.41 (1.1 H singlet, $COCH_2CO$), 6.84 (0.45 H singlet, COCH=C), 7.68 (5 H multiplet, phenyl), 9.84 (1 H singlet, NH), and 14.10 (0.45 H singlet C=COH).

Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.90; H, 6.10; N, 6.53.

C. Attempted Benzhydrylation.—To a suspension of 0.01 mole of tripotassio salt **1′** in 300 ml of liquid ammonia was added 2.3 g (0.011 mole) of benzhydryl chloride in 30 ml of dry ether. After 30 min the reaction mixture was processed in the usual manner to afford 1.30 g (69%) of tetraphenylethylene, mp 222–224° (lit.[17] mp 222–224°). A mixture melting point with an authentic sample of tetraphenylethylene was not depressed. A small amount (0.5 g) of **1** was also recovered.

Hydrolysis of Alkylation Products 2a and 2b.—A 1.48-g sample of **2a** was refluxed with 50 ml of 6 *N* hydrochloric acid for 13 hr. The reaction mixture was cooled and extracted with three 100-ml portions of ether. The combined ethereal extracts were extracted with three 50-ml portions of saturated sodium bicarbonate solution. The ethereal layer was dried ($MgSO_4$) and distilled to afford 0.35 g (58%) of acetophenone, bp 198–200° (740 mm) [lit.[18] bp 202–205° (760 mm)], which was identified by comparison of its infrared spectrum with that of an authentic sample. The sodium bicarbonate extracts were acidified with cold 12 *N* hydrochloric acid and extracted with three 50-ml portions of ether. The combined ethereal extracts were dried ($MgSO_4$) and concentrated to give 0.57 g (76%) of hydrocinnamic acid, mp 44–47° and 48–49° (lit.[19] mp 49°) after two recrystallizations from petroleum ether (bp 30–60°).

Similarly, hydrolysis of a 0.5-g sample of **2b** afforded acetophenone in 58% yield as its 2,4-dinitrophenylhydrazone, mp 240–242° dec (lit.[20] mp 238–240°).

Cyclization of 2a and 2b with Hydrazine to Form Pyrazolone 3.—A solution of 0.5 g of **2a** and 5 drops of 95% hydrazine in 25 ml of 95% ethanol was refluxed for 1 hr. The reaction mixture was added to 25 ml of water and the volume of the resulting solution was reduced to about 10 ml. The solution was cooled to precipitate 0.022 g (60%) of 3-phenylpyrazolone-5 (**3**), mp 242–244° (lit.[4] mp 242–244°). The infrared spectrum of **3** was identical with that of an authentic sample,[4] and a mixture melting point determination showed no depression.

In a similar experiment employing 1.01 g of **2b**, 10 drops of 95% hydrazine, and 50 ml of 95% ethanol, there was obtained 0.30 g (55%) of **3**.

Independent Synthesis of 2b.—A mixture of 1.0 g of benzoylacetonitrile,[21] 10 ml of BTDA,[22] and 10 ml of propionic anhydride was stirred at room temperature for 48 hr. The reaction mixture was added to a solution of 30 g of sodium acetate trihydrate in 150 ml of water and the resulting mixture was stirred at room temperature for 24 hr, neutralized with solid sodium bicarbonate to pH 5–7, and extracted with three 50-ml portions of ether–ethyl acetate (1:1). The combined extracts were dried ($MgSO_4$) and concentrated. The resulting crude product was recrystallized from 95% ethanol to afford 0.8 g (53%) of **2b**, mp 116–118°. A mixture melting point of this material and a sample of **2b** obtained from methylation of tripotassio salt **1′** was not depressed; the infrared spectra of the two samples were identical.

Condensations of Trisodio Salt 1′ with Aromatic Ketones.—To a stirred suspension of trisodio salt **1′** (0.01–0.02 mole) in 300 ml of liquid ammonia was added 0.01–0.02 mole of the appropriate ketone in 30 ml of dry ether. The reaction mixtures were stirred for 1–5 min and neutralized either directly or inversely as described below.[23]

In the condensation with benzophenone to form **5**, the ammonia was evaporated (steam bath) as an equal volume of dry ether was added. The resulting ethereal suspension was carefully poured into a mixture of 20 ml of 12 *N* hydrochloric acid and 200 g of crushed ice (inverse neutralization). The two layers were separated and the aqueous layer was extracted with three 100-ml portions of ether. The combined extracts were washed with sodium bicarbonate solution, dried ($MgSO_4$), and concentrated.

(14) Melting points were taken on a Thomas–Hoover melting point apparatus in open capillary tubes and are corrected. Analyses were performed by Galbraith Laboratories, Knoxville, Tenn., and by C. S. Menon using an F & M Model 185 C, H, and N analyzer. Infrared spectra were taken on a Beckman IR-5A spectrophotometer using the potassium bromide pellet method.

(15) See C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958).

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

(17) L. J. Durham and H. S. Mosher, *J. Am. Chem. Soc.*, **84**, 2811 (1962).

(18) R. L. Shriner and T. A. Turner, *ibid.*, **52**, 1267 (1930).

(19) T. Mitsui, H. Shiroyama, and S. Takei, *J. Agr. Chem. Soc. Japan*, **19**, 39 (1943).

(20) M. S. Newman and W. M. Edwards, *J. Am. Chem. Soc.*, **76**, 1843 (1954).

(21) C. R. Hauser and C. J. Eby, *ibid.*, **79**, 723 (1957).

(22) This reagent was obtained from the Harshaw Chemical Co., and was used without further purification.

(23) The neutralization procedures described are those which gave maximum yields of products.

In the condensation with *p*-methoxybenzophenone to form unsaturated imide **7**, the reaction mixture was cautiously poured into a solution of excess ammonium chloride in 100 ml of liquid ammonia contained in a 2-l. erlenmeyer flask (inverse neutralization).[24] The ammonia was evaporated as an equal volume of ether was added. The ethereal suspension was treated with 20 ml of 12 *N* hydrochloric acid and 150 g of crushed ice. The layers were separated and the aqueous layer was extracted with ether. The combined ethereal extracts were washed with sodium bicarbonate solution, dried ($MgSO_4$), and concentrated.

In the condensation with chalcone to form **9**, the reaction mixture was neutralized by addition of excess solid ammonium chloride (direct neutralization). The ammonia was replaced by an equal volume of ether and the resulting ethereal suspension was treated as in the condensation with *p*-methoxybenzophenone.

Yields and analytical data for hydroxy β-keto imides **5** and **9** appear in Table I. Similar information for unsaturated imide **7** may be found in Table III. Nmr data for all three of these products are given in Table II.

Dehydration of Adducts 5 and 9 to Form Unsaturated β-Keto Imides 6 and 11.—A mixture of 2.0 g of **5** in 25 ml of benzene, containing a few crystals of *p*-toluenesulfonic acid, was refluxed for 3 hr. The reaction mixture was cooled to precipitate 1.80 g of **6**.

Similarly, dehydration of a 1.0-g sample of **9** produced 0.81 g of **11**.

The crude products were collected by filtration and recrystallized from appropriate solvents. Analytical data and yields for **6** and **11** are presented in Table III. Nmr data for these products appear in Table II.

Hydrolysis of Unsaturated β-Keto Imides 6 and 11.—A 0.37-g sample of **6** was refluxed with 20 ml of 3 *N* potassium hydroxide solution for 15 hr. The reaction mixture was cooled and extracted with three 50-ml portions of ether. The ethereal extracts were combined, dried ($MgSO_4$), and distilled to give 0.06 g (50%) of acetophenone. The aqueous solution was acidified with cold 12 *N* hydrochloric acid to precipitate 0.23 g (98%) of crude β-phenylcinnamic acid, mp 145–155° and 159–161° (lit.[25] mp 162°) after two recrystallizations from 95% ethanol.

A mixture of 0.5 g of **11** and 30 ml of 6 *N* hydrochloric acid was refluxed for 28 hr. The reaction mixture was extracted with three 50-ml portions of ether. The ethereal extracts were combined, extracted with sodium bicarbonate solution, dried, ($MgSO_4$), and distilled to produce 0.10 g (66%) of acetophenone. The sodium bicarbonate extracts were combined and acidified with cold, 12 *N* hydrochloric acid. The resulting cloudy solution was extracted with ether–ethyl acetate (1:1). The extracts were dried ($MgSO_4$) and concentrated. The crude residue was recrystallized from aqueous ethanol to afford 0.28 g (88%) of β-styrylcinnamic acid, mp 140–142° (lit.[26] mp 142°).

In contrast to **6** and **11**, unsaturated β-keto imide **7** was resistant to acidic and basic hydrolysis.

Condensations of Trisodio Salt 1′ with Aromatic Aldehydes.—To a stirred suspension of 0.01 mole of trisodio salt **1′** in 300 ml of liquid ammonia was added 0.01–0.012 mole of the appropriate aldehyde in 30 ml of anhydrous ether. The resulting suspensions were stirred for 3–5 min and neutralized with ammonium chloride as described below.

In the condensation of trisodio salt **1′** with anisaldehyde to form **12a**, the reaction mixture was neutralized directly[27] and processed in the manner described for the condensation with chalcone.

In the condensations of trisodio salt **1′** with *p*-methylbenzaldehyde and *p*-chlorobenzaldehyde to form **12b** and **12c**, respectively, the reaction mixtures were neutralized inversely and processed in the same manner as that described for the condensation with *p*-methoxybenzophenone.

Crude products were recrystallized from appropriate solvents. Analytical data and yields for the addition products are presented in Table I. Nmr data are summarized in Table II.

Dehydration of Hydroxy β-Keto Imides 12a–c to Form Unsaturated β-Keto Imides 13a–c.—A mixture of 2.0 g of **12a**, 50 ml of benzene, and a few crystals of *p*-toluenesulfonic acid was refluxed for 3 hr. The reaction mixture was cooled to precipitate **13a**.

A 0.9-g sample of **12b** was dissolved in 10 ml of concentrated sulfuric acid at room temperature. After 30 min, the resulting golden orange solution was poured onto crushed ice to precipitate **13b**.

Similarly, dehydration of a 0.9-g sample of **12c** to form **13c** was effected by means of 20 ml of concentrated sulfuric acid at room temperature.

Recrystallization of the crude dehydration products from appropriate solvents afforded the pure unsaturated derivatives **13a–c** for which yields and analytical data are summarized in Table III. Principal nmr absorptions are given in Table II.

Hydrolysis of Unsaturated β-Keto Imides 13a–c.—A solution of 0.4 g of **13a** in 25 ml of 3 *N* potassium hydroxide solution was refluxed for 15 hr. The reaction mixture was extracted with ether. The combined ethereal extracts were dried ($MgSO_4$) and distilled to give 0.09 g (60%) of acetophenone. The aqueous layer was acidified to precipitate 0.13 g (59%) of *p*-methoxycinnamic acid (**14a**), mp 171–173° (lit.[28] mp 170°). A mixture melting point with an authentic sample[28] showed no depression.

Similarly, hydrolysis of a 0.4-g sample of **13c** by means of 20% sodium hydroxide solution afforded 0.1 g (68%) of acetophenone and 0.19 g of *p*-chlorocinnamic acid (**14c**), mp 248–250° (lit.[29] mp 248–250°).

A mixture of 0.5 g of **13b** and 20 ml of 6 *N* hydrochloric acid was refluxed for 36 hr. The reaction mixture was extracted with ether and the ethereal extracts were washed with sodium bicarbonate solution. The ethereal extracts afforded 0.15 g (77%) of acetophenone. The sodium bicarbonate extracts were acidified to produce 0.2 g (83%) of *p*-methylcinnamic acid (**14b**), mp 197–199° (lit.[30] mp 198–199°).

Trialkali Salts 15′ (M = K or Na).—To a stirred suspension of 0.03 mole of potassium amide in 300 ml of liquid ammonia was added 2.81 g (0.01 mole) of finely divided N-acetyl-α-benzoylphenylacetamide[5] (**15**). After 30 min the bright yellow suspension was assumed to contain 0.01 mole of tripotassio-N-acetyl-α-benzoylphenylacetamide (**15′**, M = K).

Similarly, addition of 2.81 g (0.01 mole) of **15** to 0.03 mole of sodium amide in 300 ml of liquid ammonia produced after 30 min a bright yellow suspension which presumably contained 0.01 mole of trisodio-N-acetyl-α-benzoylphenylacetamide (**15′**, M = Na).

Addition of 2.53 g (0.02 mole) of benzyl chloride in 20 ml of anhydrous ether to 0.01 mole of tripotassio salt **15′** in 300 ml of liquid ammonia produced no apparent color change even after 2 hr.[31] Neutralization of the reaction mixture followed by the usual isolation procedure afforded recovered **15** in 72% yield.

Addition of 2.20 g (0.012 mole) of benzophenone in 20 ml of anhydrous ether to 0.01 mole of trisodio salt **15′** in 300 ml of liquid ammonia, followed by inverse neutralization of the reaction mixture with ammonium chloride, resulted in recovery of 82% of **15**.

Registry No.—**2a**, 10300-06-8; **2b**, 10300-07-9; **5**, 10300-08-0; **6**, 10316-12-8; **7**, 10300-09-1; **9**, 10300-10-4; **11**, 10300-11-5; **12a**, 10300-12-6; **12b**, 10300-13-7; **12c**, 10316-13-9; **13a**, 10300-14-8; **13b**, 10300-15-9; **13c**, 10300-16-0.

(24) Direct neutralization of the reaction mixture with solid ammonium chloride led to recovery of starting materials.

(25) H. Rupe and E. Busolt, *Ber.*, **40**, 4537 (1907).

(26) R. J. Light, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **26**, 1344 (1961).

(27) Inverse neutralization of this reaction mixture resulted in isolation of unsaturated β-keto imide **13a** rather than hydroxy derivative **12a**.

(28) E. Knoevengel, *Ber.*, **31**, 2606 (1898).

(29) J. K. Kochi, *J. Am. Chem. Soc.*, **78**, 1228 (1956).

(30) R. Stoermer, F. Grimm, and E. Laage, *Ber.*, **50**, 980 (1917).

(31) That conversion of **15** to its tripotassio salt **15′** was essentially complete was indicated by the absence of the transient purple color associated with stilbene formation, a reaction which occurs rapidly in the presence of amide ion in liquid ammonia. See C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Brodhag, *J. Am. Chem. Soc.*, **78**, 1653 (1956).