Condensations at the Terminal Methyl Group of 1,3,5-Triketones by Means of Sodamide in Liquid Ammonia[1a]

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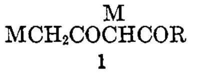
Several types of condensations at the terminal methyl group of 1-phenyl-1,3,5-hexanetrione or its *p*-methoxy analog were effected by means of 3 molecular equiv. of sodamide in liquid ammonia or ether. These reactions include alkylations, carbonyl addition reactions (aldol type), benzoylation, and carbonation. Several of the products were converted to pyrones and/or pyridones Attempts to effect terminal condensations by means of potassium amide or lithium amide were unsuccessful.

Several types of condensations at the terminal methyl group of acetylacetone or benzoylacetone have previously been effected by means of 2 molecular equiv. of an alkali amide in liquid ammonia, which converts the β-diketone to its dialkali salt **1**. These reactions include alkylations,[2] aroylations,[2,3] carbonation,[2] and carbonyl additions (aldol type).[4] For example, aroylation of **1** ($R = CH_3$) with methyl benzoate affords 1,3,5-triketone **2a**.



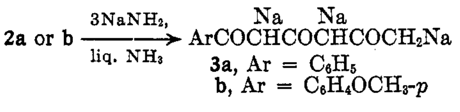
$$MCH_2CO\overset{M}{C}HCOR$$

1

$$ArCOCH_2COCH_2COCH_3$$

2a, $Ar = C_6H_5$
b, $Ar = C_6H_4OCH_3\text{-}p$

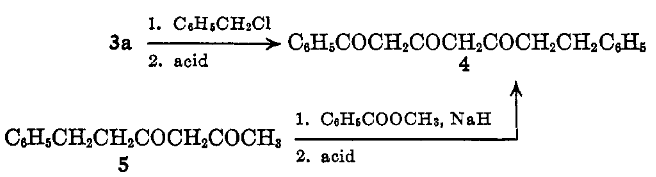
Similar condensations at the terminal methyl group of triketones **2a** and **b** have now been accomplished by means of 3 molecular equiv. of sodamide in liquid ammonia, which presumably converted the triketone to its trisodio salt **3a** or **b** or an equivalent structure.[5]



$$\textbf{2a or b} \xrightarrow[\text{liq. } NH_3]{3NaNH_2} ArCO\overset{Na}{C}HCO\overset{Na}{C}HCOCH_2Na$$

3a, $Ar = C_6H_5$
b, $Ar = C_6H_4OCH_3\text{-}p$

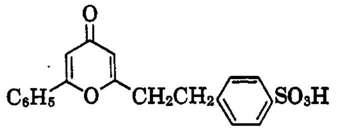
Trisodio salt **3a** underwent alkylation with benzyl chloride to form **4** in 63% yield. Also **4** was synthesized independently by benzoylation of β-diketone **5** by means of sodium hydride.[6] That benzylation of **3a** and benzoylation of **5** had occurred at the terminal methyl positions was supported by the disappearance of the methyl resonances in the n.m.r. spectra, which were identical for the products from the two reactions.



$$\textbf{3a} \xrightarrow[\text{2. acid}]{\text{1. } C_6H_5CH_2Cl} C_6H_5COCH_2COCH_2COCH_2CH_2C_6H_5 \ (\textbf{4})$$

$$C_6H_5CH_2CH_2COCH_2COCH_3 \ (\textbf{5}) \xrightarrow[\text{2. acid}]{\text{1. } C_6H_5COOCH_3,\ NaH} \textbf{4}$$

Treatment of triketone **4** with cold, concentrated sulfuric acid afforded pyrone sulfonic acid **6**, rather than the expected pyrone **7**. With these reaction conditons, triketone **4** (or pyrone **7**) underwent sulfonation, presumably on the benzyl ring to give pyrone sulfonic acid **6**. N.m.r. and infrared spectra indicated *para* substitution of the benzene ring. Sulfonation products have not been observed previously from cyclizations of aromatic triketones, such as **2a** and 1,5-diphenyl-1,3,5-pentanetrione, where the aromatic rings are deactivated toward electrophilic substitution. Pyrone **7** was prepared conveniently and in excellent yield through the use of anhydrous, liquid hydrogen fluoride as the cyclizing agent.



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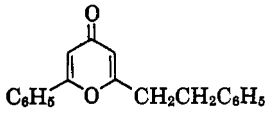

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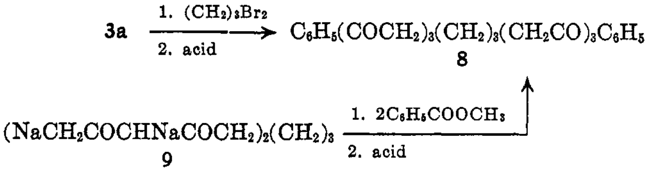
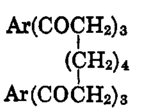
Trisodio salt **3a** underwent twofold alkylations with 1,3-dibromopropane to form bis-1,3,5-triketone **8** which was independently synthesized by dibenzoylation of tetrasodio bis-β-diketone **9** as described recently.[8]



$$\textbf{3a} \xrightarrow[\text{2. acid}]{\text{1. } (CH_2)_3Br_2} C_6H_5(COCH_2)_3(CH_2)_3(CH_2CO)_3C_6H_5 \ (\textbf{8})$$

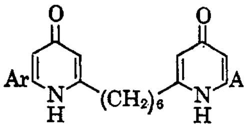
$$(NaCH_2COCHNaCOCH_2)_2(CH_2)_3 \ (\textbf{9}) \xrightarrow[\text{2. acid}]{\text{1. } 2C_6H_5COOCH_3} \textbf{8}$$

Similarly, trisodio salts **3a** and **b** underwent twofold alkylations with 1,4-dibromobutane to give bis(triketones) **10a** and **b** in yields of 53 and 46%, respectively. These 1,3,5-triketones were cyclized with ethanolic ammonia to afford bispyridones **11a** and **b** in yields of 65 and 70%, respectively.



$$\begin{array}{c} Ar(COCH_2)_3 \\ | \\ (CH_2)_4 \\ | \\ Ar(COCH_2)_3 \end{array}$$

10a, $Ar = C_6H_5$
b, $Ar = C_6H_4OCH_3\text{-}p$



11a, $Ar = C_6H_5$
b, $Ar = C_6H_4OCH_3\text{-}p$

Trisodio salts **3a** and **b** underwent addition reactions (aldol type) with benzophenone to form adducts **12a** and **b** in yields of 62 and 41%, respectively.

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[1] (a) Supported at Duke University by the Army Research Office (Durham), and at Vanderbilt University by the Research Corporation and the U. S. Public Health Service (1-R01-GM12848-01). (b) To whom inquiries should be addressed: Vanderbilt University.

[2] (a) C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958); (b) K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 61 (1965).

[3] R. J. Light and C. R. Hauser, *ibid.*, **25**, 538 (1960).

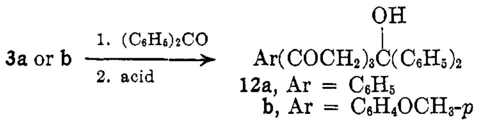
[4] R. J. Light and C. R. Hauser, *ibid.*, **26**, 1716 (1961).

[5] This was discovered independently at Duke and Vanderbilt Universities. Preliminary experiments on deuteration at the latter university has indicated that trisodio salt **3a** is formed to the extent of at least 60%; the details of this and related results on the mechanism will be published later.

[6] Although several aroylations of β-diketones have recently been effected by means of sodium hydride in 1,2-dimethoxyethane,[7] this is the first example involving a simple, unsymmetrical β-diketone such as **5**, with which aroylation at the 5-methylene group was possible. For an example of an aroylation involving a bis-β-diketone by means of this reagent, see ref. 8. The mechanism of aroylation of β-diketones by sodium hydride is currently under investigation by M. L. Miles (private communication).

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

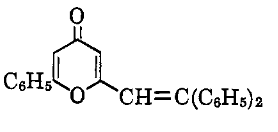
[8] K. G. Hampton and C. R. Hauser, *ibid.*, **30**, 2934 (1965).



$$\text{3a or b} \xrightarrow[\text{2. acid}]{\text{1. }(C_6H_5)_2CO} Ar(COCH_2)_3\overset{OH}{\overset{|}{C}}(C_6H_5)_2$$

12a, Ar = C_6H_5
b, Ar = $C_6H_4OCH_3$-*p*

Adduct **12a** was cyclized by means of sulfuric acid or methanolic hydrochloric acid to give the unsaturated pyrone **13** in 62–69% yields. Adducts **12a** and **b** were cyclized with ethanolic ammonia to afford hydroxypyridones **14a** and **b** in yields of 84 and 53%, respectively.



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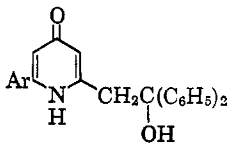
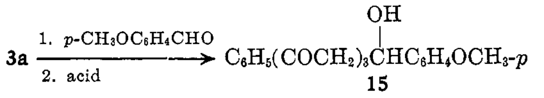


14a, Ar = C_6H_5
b, Ar = $C_6H_4OCH_3$-*p*

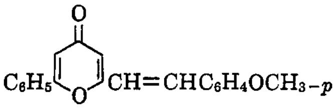
Similarly, trisodio salt **3a** underwent an addition reaction with anisaldehyde to form adduct **15** in 45% yield.



$$\mathbf{3a} \xrightarrow[\text{2. acid}]{\text{1. } p\text{-}CH_3OC_6H_4CHO} C_6H_5(COCH_2)_3\overset{OH}{\overset{|}{C}}HC_6H_4OCH_3\text{-}p$$

15

Adduct **15** was cyclized by acid to give unsaturated pyrone **16** and with ammonia to afford hydroxypyridone **17** in yields of 78 and 83%, respectively.



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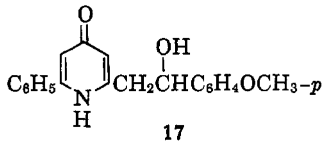

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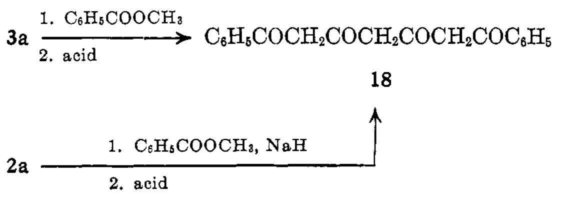
Trisodio salt **3a** underwent aroylation with methyl benzoate to form tetraketone **18** in 12% yield. Structure **18** was established by independent synthesis by the sodium hydride–1,2-dimethoxyethane method.[9]



$$\mathbf{3a} \xrightarrow[\text{2. acid}]{\text{1. } C_6H_5COOCH_3} C_6H_5COCH_2COCH_2COCH_2COC_6H_5$$

18

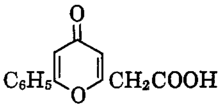
$$\mathbf{2a} \xrightarrow[\text{2. acid}]{\text{1. } C_6H_5COOCH_3,\ NaH} \mathbf{18}$$

Although the sodium hydride method appears not to involve the intermediate formation of trisodio salt **3a**,[10] it affords **18** in better yield (52%)[9] than the sodamide method which involves intermediate **3a**. However, the sodium hydride method would probably not be suitable for the other types of condensations described above, as it has not been satisfactory for alkylations and addition reactions of β-diketones.[7]

Finally, terminal carbonation of **2a** was effected in 38% yield by addition of Dry Ice to the reaction mixture containing **3a** after having replaced the ammonia by ether. The resulting triketo acid **19** was a crystalline solid that underwent decarboxylation at its melting point. Treatment of **19** with anhydrous, liquid hydrogen fluoride afforded pyrone carboxylic acid **20**. Decarboxylation of **20** occurred at its melting point, pyrone **21** being formed.

$C_6H_5COCH_2COCH_2COCH_2COOH$

19



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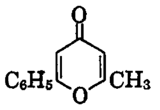

21

It should be mentioned that attempts to effect such terminal condensations of triketone **2a** with 1,4-dibromobutane, benzophenone, methyl benzoate, and carbon dioxide by means of 3 molecular equiv. of potassium amide were unsuccessful. In addition, an attempt to effect benzophenone condensation by means of lithium amide failed. This failure of both lithium amide and potassium amide to afford terminal condensations of **2a** is surprising, since these alkali amides are as suitable as sodamide for the preparation of the dianions of β-diketones. Some differences have been observed in the reactivities of these different dialkali metal salts of β-diketones,[2b,4,11] but these differences are small in comparison with the metallic cation effects observed here. This matter is the subject of further investigation.

One other triketone, 2,4,6-heptanetrione, was investigated. Benzylation and carbonation were both unsuccessfully tried by means of sodamide and potassium amide. With both bases heavy precipitation occurred when the triketone was added to the reaction mixture.

The present method employing sodamide, although apparently not completely general, can probably be extended to at least some other triketones. In addition, terminal condensations with many other alkyl halides and carbonyl compounds should also be feasible.

Experimental Section[12]

1,3,5-Triketones 2a and b.—1-Phenyl-1,3,5-hexanetrione (**2a**) was prepared from 0.4 mole each of acetylacetone and methyl benzoate and 1.3 mole of sodium hydride[13] in 300 ml. of 1,2-dimethoxyethane essentially as described previously[7] on a 0.5-mole scale; the yield was 55–60%.

1-(*p*-Methoxyphenyl)-1,3,5-hexanetrione (**2b**) was synthesized similarly from acetylacetone and methyl anisate and recrystallized from 95% ethanol. The product melted at 85–86°; yield, 72%.

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[9] M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Am. Chem. Soc.*, **85**, 3884 (1963).

[10] Treatment of triketone **2a** with excess sodium hydride in refluxing 1,2-dimethoxyethane causes evolution of only two molecular equivalents of hydrogen, not three equivalents as would be required for formation of trisodio salt **3a**. The detail of this result together with consideration of the mechanism will be published later.

[11] S. D. Work and C. R. Hauser, *J. Org. Chem.*, **28**, 725 (1963).

[12] Melting points were taken on a Thomas–Hoover melting point apparatus in open capillary tubes and are corrected. Analyses were by Galbraith Laboratories, Knoxville, Tenn., Triangle Chemical Laboratories, Inc., Chapel Hill, N. C., and Janssen Pharmaceutica, Beerse, Belgium. N.m.r. spectra were obtained with 10–20% solutions in deuteriochloroform with tetramethylsilane as internal standard using a Varian A-60 spectrometer. The area measurements were made with respect to the area of the phenyl absorption. Infrared spectra were obtained with a Perkin-Elmer Model 137 Infracord using the potassium bromide pellet method for solids. The ultraviolet spectra were determined with a Cary Model 14 recording spectrophotometer using 2 × 10^{-5} *M* solutions in methanol with a 1-cm. cell.

[13] Obtained as approximately 50% dispersion in mineral oil from Metal Hydrides, Inc., Beverly, Mass.

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.45; H, 6.19.

Trisodio Triketones 3a and b.—In a typical experiment, 0.05 mole of solid triketone **2a** or **2b** was added from an erlenmeyer flask through Gooch tubing to a stirred suspension of 0.15 mole of sodamide[14] in 600–700 ml. of commercial, anhydrous liquid ammonia; the last portions of the triketone in the flask and tubing were washed into the reaction mixture with anhydrous ether. An alternative procedure was to add the triketone as an ethereal suspension. After 20–50 min., the resulting trisodio salt **3a** or **3b** was employed as described below.

Benzylation of Trisodio Salt 3a to Form 4.—A suspension of **3a** and sodamide was prepared in 700 ml. of liquid ammonia from 0.025 mole of triketone **2a** and 0.13 mole of sodamide.[15] After 20 min., 12.6 g. (0.10 mole) of benzyl chloride was added to the stirred suspension. The ammonia was evaporated after 30 min. and ether was added. Ice and water were added, the aqueous layer was separated, and the ethereal solution was extracted with water. The combined aqueous solution was acidified with hydrochloric acid and extracted with ether. The ethereal solution was dried over magnesium sulfate and evaporated The residue was taken up in hot hexane, filtered, and cooled to −20° to afford 4.6 g. (63%) of 1,7-diphenyl-1,3,5-heptanetrione (**4**), yellow crystals, m.p. 46–51°. Column chromatography on silica gel raised the melting point to 50.5–53°. The elution solvent was 20:80 benzene–hexane.

The n.m.r. spectrum of the product showed no indication of a terminal methyl group; methyl resonance in the starting triketone **2a** appeared at 2.0–2.3 p.p.m. Triketone **4** existed as a mixture of enol forms in deuteriochloroform solution.

Independent synthesis of 4 was accomplished by refluxing a mixture of 9.5 g. (0.05 mole) of 6-phenyl-2,4-hexanedione, 10.0 g. (0.074 mole) of methyl benzoate, and 10.0 g. (0.22 mole) of sodium hydride[13] in 400 ml. of tetrahydrofuran for 6 hr. The tetrahydrofuran was evaporated under reduced pressure, ether was added, and the mixture was extracted with water. The aqueous extract was acidified and extracted with ether. The ethereal solution was washed with dilute sodium bicarbonate solution, dried, and evaporated. The residue was dissolved in hot hexane containing a small amount of benzene and cooled to −20° to afford 8.9 g. (61%) of **4**, m.p. 46–50° and 50–52.5° after two recrystallizations from hexane.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.26; H, 6.03.

The n.m.r. spectrum of the product showed no indication of a methyl group; methyl resonance in the original β-diketone appeared at 1.9 p.p.m.

The infrared and n.m.r. spectra of the triketone prepared by the sodamide and the sodium hydride routes were identical. The mixture melting point was undepressed, but it was found that certain mixtures with 1-phenyl-1,3,5-hexanetrione also melted without depression.

Cyclization of Triketone 4. A. By Sulfuric Acid.—A mixture of 1.0 g. of triketone **4** and 22.0 g. of concentrated sulfuric acid was stirred at 0° until solution was complete. The mixture was warmed to room temperature and poured onto ice. The resulting white precipitate was separated by filtration and dissolved in dilute, aqueous sodium bicarbonate. The solution was washed with ether and carefully neutralized with hydrochloric acid to afford 1.0 g. (78%) of the pyrone sulfonic acid **6**, which lost water of hydration at about 150° and decomposed at 250°. Two recrystallizations from ethanol raised the decomposition point to 285–287° (uncor., taken on a Mel-Temp).

Anal. Calcd. for $C_{19}H_{18}O_6S$: C, 60.95; H, 4.84. Found: C, 60.89; H, 5.14.

The infrared spectrum indicated *para* substitution of one ring (823 cm.$^{-1}$) as well as strong pyrone (1650 cm.$^{-1}$) and sulfonic acid (1225 cm.$^{-1}$) absorption. The n.m.r. spectrum determined in 5% sodium deuterioxide in deuterium oxide solution (external tetramethylsilane) contained AB doublets centered at 7.1 and 7.8 p.p.m. (J = 8.0 c.p.s., *para*-disubstituted phenyl), a singlet at 7.2 p.p.m. (monosubstituted phenyl), two slightly coupled absorptions at 6.1 and 6.4 p.p.m. (pyrone hydrogens), and a large broadened absorption at 2.6 p.p.m. ($-CH_2CH_2-$). Initially, the areas of the peaks were consistent with the structure assignment. However, on standing for a few minutes, the area of the peak at 2.6 p.p.m. decreased in size, apparently because of deuterium exchange of the methylene group adjacent to the pyrone ring.

B. Hydrogen Fluoride.—To 0.713 g. of triketone **4** in a polyethylene bottle was added approximately 10 ml. of anhydrous liquid hydrogen fluoride. The solution was stirred until the hydrogen fluoride had completely evaporated (12 hr.). The residue was treated with aqueous sodium bicarbonate and ether. The ethereal solution was dried and evaporated to leave a crystalline residue (0.603 g., 90%) of 2-phenyl-6-(2-phenylethyl)-4H-pyran-4-one (**7**), m.p. 80.5–84.5 and 85–86.5° after two recrystallizations from hexane.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.80; H, 5.86.

The infrared spectrum showed a strong pyrone band at 1650 cm.$^{-1}$. The n.m.r. spectrum was consistent with the assignment; the resonance peak for $-CH_2CH_2-$ was a broadened singlet at 2.97 p.p.m., and the pyrone hydrogens appearing at 6.17 and 6.70 p.p.m. were coupled by 2.1 c.p.s.

Twofold Alkylation of Trisodio Salt 3a with 1,3-Dibromopropane to Form Bis(triketone) 8.—To a stirred suspension of **3a** prepared from 0.05 mole of **2a** and 0.15 mole of sodamide in 600 ml. of liquid ammonia was added, over 15 min., 5.05 g. (0.025 mole) of 1,3-dibromopropane in 20 ml. of anhydrous ether. After 1 hr. the ammonia was evaporated on the steam bath as 300 ml. of dry ether was added. The ethereal suspension was cooled (ice bath), and a mixture of 100 g. of ice and 30 ml. of cold, concentrated hydrochloric acid was added with stirring. The two layers were separated. The ethereal layer (which was combined with three ethereal extracts of the aqueous layer) was evaporated. The residue was recrystallized from methanol to afford 3 g. (27%) of 1,15-diphenyl-1,3,5,11,13,15-pentadecanehexaone (**8**), m.p. 84–85°, undepressed on admixture with a sample of **8** prepared as described recently.[8]

Twofold Alkylations of Trisodio Salts 3a and b with 1,4-Dibromobutane to Form Bis(triketones) 10a and b.—To a stirred suspension of **3a** prepared from 0.05 mole of **2a** and 0.15 mole of sodamide was added 5.4 g. (0.025 mole) of 1,4-dibromobutane as described above for **8**. After the ammonia had evaporated and the ethereal suspension had been acidified, the resulting precipitate was removed by filtration. The ethereal layer of the filtrate (which was combined with three ethereal extracts of the aqueous layer) was evaporated, and the residue was combined with the precipitate. The mixture was recrystallized from benzene to afford 6.15 g. (53%) of 1,16-diphenyl-1,3,5,12,14,16-hexadecanehexaone (**10a**), m.p. 115.5–116.5°.

Anal. Calcd. for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.62; H, 6.68.

Similarly, twofold alkylation of **3b** was effected. The product was recrystallized from benzene to afford 6.05 g. (46%) of 1,-16-(*p*-methoxyphenyl)-1,3,5,12,14,16-hexadecanehexaone (**10b**), m.p. 120–121°.

Anal. Calcd. for $C_{30}H_{34}O_8$: C, 68.95; H, 6.56. Found: C, 68.90; H, 6.57.

Cyclization of Bis(triketone) 10a and b with Ammonia to Form Bispyridones 11a and b.—Bis(triketone) **10a** (1 g.) was treated with absolute ethanol and liquid ammonia by the procedure described recently[8] to afford 0.6 g. (65%) of hexamethylenebis-2-[6-phenyl-4(1H)-pyridone] (**11a**), m.p. 247–248°. The ultraviolet spectrum showed λ_{max} 239 mμ (log ϵ 4.69).

Anal. Calcd. for $C_{28}H_{28}N_2O_2$: C, 79.21; H, 6.65; N, 6.60. Found: C, 79.18; H, 6.65; N, 6.51.

Similarly, 2 g. of **10b** afforded 1.3 g. (70%) of hexamethylenebis-2-[6-*p*-methoxyphenyl-4(1H)-pyridone] (**11b**), m.p. 300–301° (uncor., taken on a Mel-Temp). The ultraviolet spectrum showed λ_{max} 240 mμ (log ϵ 4.80).

Anal. Calcd. for $C_{30}H_{32}N_2O_4$: N, 5.78. Found: N, 5.74.

Addition Reactions of Trisodio Salts 3a and b with Benzophenone of Form Adducts 12a and b.—To a stirred suspension of **3a** prepared from 0.05 mole of **2a** and 0.15 mole of sodamide in 600 ml. of liquid ammonia was added, over 5 min., 9.1 g. (0.05 mole) of benzophenone in 50 ml. of anhydrous ether. After 1 hr., the reaction mixture was poured into a solution of 15 g. of ammonium chloride in 200 ml. of liquid ammonia. The ammonia was evaporated on the steam bath as 250 ml. of ether was added. The resulting ethereal suspension was cooled in ice, and a mixture of ice and hydrochloric acid was added. The ethereal layer was separated, and the aqueous layer was extracted three times with ether. The combined ethereal solution was evaporated under re-

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

[15] Excess sodamide was used to favor more complete formation of **3a**. Although stilbene may have been a by-product, it was readily separated from triketone **4**.

duced pressure. The residue was recrystallized from methanol to afford 11.9 g. (62%) of 7-hydroxy-1,7,7-triphenyl-1,3,5-heptanetrione (**12a**) m.p. 85–86°. The infrared spectrum showed a peak at 2.80 μ for the hydroxyl group.[16]

Anal. Calcd. for $C_{25}H_{22}O_4$: C, 77.70; H, 5.74. Found: C, 77.44; H, 5.49.

Similarly, **3b** was condensed with benzophenone to afford 8.6 g. (41%) of 7-hydroxy-1-(*p*-methoxyphenyl)-7,7-diphenyl-1,3,5-heptanetrione (**12b**), m.p. 120–121°. The infrared spectrum showed a peak at 2.95 μ for the hydroxyl group.[16]

Anal. Calcd. for $C_{26}H_{24}O_5$: C, 74.98; H, 5.81. Found: C, 74.74; H, 5.76.

Cyclization of Adduct 12a to Form Pyrone 13.—A mixture of 1 g. of **12a**, 25 ml. of methanol, and 3 ml. of concentrated hydrochloric acid was refluxed for 3.5 hr. The reaction mixture was cooled and filtered, and the precipitate was recrystallized from aqueous ethanol to afford 0.63 g. (69%) of 2-phenyl-6-(β-phenylstyryl)-4H-pyran-4-one (**13**), m.p. 133.5–135°.

Anal. Calcd. for $C_{25}H_{18}O_2$: C, 85.69; H, 5.18. Found: C, 85.50; H, 5.23.

A mixture of 1 g. of **12a** and 10 ml. of concentrated sulfuric acid was stirred at 0° for 45 min. The resulting solution was poured into ice and the resulting precipitate was collected by filtration. The solid was recrystallized from methanol to afford 0.56 g. (62%) of **13**, m.p. 133–135°. The mixture melting point with **13** prepared as described above was undepressed.

Cyclizations of Adducts 12a and b with Ammonia to Form Pyridones 14a and b.—Adduct **12a** (1 g.) was cyclized with ammonia by the procedure described recently[8] to afford 0.80 g. (84%) of 2-phenyl-6-(2,2-diphenyl-2-hydroxyethyl)-4(1H)-pyridone (**14a**), m.p. 205.5–206°. The ultraviolet spectrum showed λ_{max} 242 mμ (log ε 4.38).

Anal. Calcd. for $C_{25}H_{21}NO_2$: C, 81.72; H, 5.76; N, 3.81. Found: C, 81.89; H, 5.87; N, 4.02.

Similarly, 2 g. of **12b** afforded 1.0 g. (53%) of 2-(*p*-methoxyphenyl)-6-(2,2-diphenyl-2-hydroxyethyl)-4(1H)-pyridone (**14b**), m.p. 211.5–212.5°. The ultraviolet spectrum of **14b** showed λ_{max} 254 mμ (log ε 4.37).

Anal. Calcd. for $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83. Found: C, 78.58; H, 5.95.

Addition Reaction of Trisodio Salt 3a with Anisaldehyde to Form Adduct 15.—To a suspension of 0.05 mole of **3a** in 600 ml. of liquid ammonia was added, over 15 min., 6.8 g. (0.05 mole) of anisaldehyde in 30 ml. of ether. The reaction mixture was worked up as described above for the reaction of **3a** and benzophenone. The product was recrystallized from methanol to afford 7.6 g. (45%) of 7-hydroxy-1-phenyl-7-(*p*-methoxyphenyl)-1,3,5-heptanetrione (**15**), m.p. 87–88°. The infrared spectrum showed a peak at 2.95 μ for the hydroxyl group.[16]

Anal. Calcd. for $C_{20}H_{20}O_5$: C, 70.06; H, 6.01. Found: C, 70.29; H, 6.17.

Cyclization of Adduct 15 to Pyrone 16 and Pyridone 17.—A mixture of 1 g. of **15**, 25 ml. of methanol, and 3 ml. of concentrated hydrochloric acid was refluxed for 2 hr. and cooled, and the precipitate was collected by filtration. The solid was recrystallized from ethanol–water to afford 0.70 g. (78%) of 2-phenyl-6-(*p*-methoxystyryl)-4H-pyran-4-one (**16**), m.p. 148–149°.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.78; H, 5.26.

Adduct **15** (1 g.) was treated with absolute ethanol and liquid ammonia by the procedure described recently[8] to afford 0.8 g. (83%) of 2-phenyl-6-[2-(*p*-methoxyphenyl)-2-hydroxyethyl]-4-(1H)-pyridone (**17**), m.p. 191–192°. The ultraviolet spectrum showed λ_{max} 238 mμ (log ε 4.42).

Benzoylation of Trisodio Salt 3a to Form Tetraketone 17.—A suspension of **3a** and sodamide in 700 ml. of liquid ammonia was prepared from 0.02 mole of triketone **2a** and 0.10 mole of sodamide. The mixture was stirred 1 hr., the ammonia was replaced by ether, and 13.6 g. (0.10 mole) of methyl benzoate was added. After 4 hr. at reflux, the mixture was treated with 200 ml. of cold water. The mixture was filtered and the precipitate was neutralized with dilute hydrochloric acid. The resulting suspension was extracted with ether, and the ethereal solution was dried, stripped, and recrystallized from ethanol to afford, after a hot hexane wash, 0.208 g. of 1,7-diphenyl-1,3,5,7-heptanetetraone (**18**), yellow crystals, m.p. 91–92.5°. The n.m.r. spectrum indicated that the product was free from contamination by starting triketone.

From the original aqueous solution above was recovered, on acidification, a large amount of starting triketone as well as a small amount of tetraketone. The tetraketone was partially separated by recrystallization from ethanol. A fraction was obtained (0.499 g., m.p. 94–97°) which contained 0.151 g. of tetraketone as determined from the n.m.r. spectrum. The total tetraketone formed in the reaction was 0.359 g. or 12% based on the probable stoichiometry of 2 moles of triketone affording 1 mole of tetraketone. The mixture melting point with **18** prepared as described previously[9] was undepressed.

Carbonation of Trisodio Salt 3a to Form 19.—Trianion **3a** was prepared in 300 ml. of liquid ammonia from 5.1 g. (0.025 mole) of **2a** and 0.17 mole of sodamide. The ammonia was rapidly removed on the steam bath while anhydrous ether was added to maintain the original reaction volume. The ethereal suspension was poured over crushed Dry Ice in a 2-l. erlenmeyer flask and allowed to stand for 2 hr. with occasional stirring. After the Dry Ice had evaporated, the reaction mixture was added to a mixture of ice and hydrochloric acid. The ether layer was separated and extracted several times with cold, 5% aqueous sodium bicarbonate. The combined sodium bicarbonate extract was acidified immediately, and the resulting solid was extracted into ether. The ethereal solution was dried over magnesium sulfate and concentrated to a small volume under reduced pressure. Hexane was added and the solution was cooled to −20° to afford 1.5 g. of 7-phenyl-3,5,7-trioxoheptanoic acid (**19**), yellow crystals, m.p. 98–99°, with decarboxylation at the melting point. Concentration of the filtrate yielded an additional 0.9 g. of **19**, m.p. 92–95° dec. The combined yield was 38%. Further recrystallization of the first crop did not increase the melting point.

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.87. Found: C, 63.14; H, 5.14.

Cyclization of Triketo Acid 19 to Form Pyrone 20.—To 1.5 g. of triketo acid **19** in a polyethylene flask was added 25 ml. of anhydrous, liquid hydrogen fluoride. The resulting homogeneous solution was allowed to stand 16 hr. at room temperature, during which time the hydrogen fluoride evaporated. After storage over sodium hydroxide in a desiccator to remove traces of hydrogen fluoride, the colorless solid residue of (6-phenyl-4H-pyran-4-on-2-yl)acetic acid (**20**), m.p. 113.5–114.5° dec., weighed 1.4 g. (~100%). The analytical sample, m.p. 115–115.5° dec., was prepared by precipitation from dilute sodium bicarbonate solution.

Anal. Calcd. for $C_{13}H_{10}O_4$: C, 67.82; H, 4.38. Found: C, 67.98; H, 4.34.

The infrared spectrum showed bands at 2800–2500 broad (COOH), 1710 (COOH), and 1645 cm.$^{-1}$ (pyrone).

Pyrone **20** (0.31 g.) was decarboxylated by heating at 115° for 1 hr. to yield 0.25 g. (~100%) of 2-methyl-6-phenyl-4H-pyran-4-one (**21**), m.p. 77–78°. Recrystallization from hexane raised the melting point to 83–84°. The melting point was undepressed upon admixture of **21** with an authentic sample of the pyrone.[3] The infrared spectra of the two samples were identical.

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(16) See L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 95.