$$\underset{\text{I}}{C_6H_5C(CF_3)_2OH} \xrightarrow[\text{slow}]{\text{KOH}} \underset{\text{II}}{C_6H_5COCF_3} \xrightarrow[\text{very fast}]{\text{KOH}} C_6H_5COOK + CF_3H$$

completely on contact with base in the cold. In the absence of excess alkali, *i.e.*, upon pyrolysis of the potassium salt of I, compound II was actually isolated in poor yield.

$$\begin{tikzcd} C_6H_5C(CF_3)_2OK \arrow[r, "\Delta"] & \text{II} + CF_3^- + K^+ \arrow[d, "-F^-"] \\ & :CF_2 \end{tikzcd}$$

The alkaline hydrolysis of the analogous (2-hydroxy-1,1,3,3-tetrafluoro-1,3-dichloro-2-propyl)arenes was studied only briefly and appears to proceed through a more complex path than that of the hexafluoro analogs owing to the hydrolytic instability of a *gem*-difluoromethyl group on a carbon bearing another substituent.[4] The yields of carboxylic acids were relatively poorer with the tertiary alcohols containing CF_2Cl groups (Table I) than with those containing CF_3 groups (Table II).

Experimental

Typical Hydrolysis Procedure.—The following procedure, describing the hydrolysis of I, was used for the preparation of all of the acids listed in Tables I–III.

A mixture of 4.88 g. (0.02 mole) of I, 11.2 g. (0.20 mole) of potassium hydroxide, and 20 ml. of diethylene glycol was heated at reflux (about 175°) for 3 hr. The cooled reaction mixture was acidified with concentrated hydrochloric acid. It was then made alkaline with 10% sodium bicarbonate solution and filtered to remove silica. The filtrate yielded, upon acidification, 2.20 g. of benzoic acid, m.p. 121–122°, corresponding to 90% yield.

For the identification of fluoroform as one of the reaction products, the reaction flask was equipped with a gas inlet tube and an outlet tube connected to a cold trap immersed in liquid air. The reaction was carried out as described above except that a positive pressure of helium gas was maintained over the system to avoid condensation of atmospheric gases into the cold trap. The liquid in the cold trap was identified as CHF_3 by its boiling point, −82°,[5] and by comparison of its infrared spectrum with that of an authentic sample.

Pyrolysis of the Potassium Salt of I.—The dried salt (5.64 g., 0.02 mole) and 5.64 g. of potassium chloride was heated in a 50-ml. round-bottom flask connected horizontally to a water-cooled condenser connected to a receiver cooled in Dry Ice–acetone. As the sample was heated, vapors were evolved and condensed in the traps and in the receiver. The condensed liquid was identified by its boiling point (150–152°[6]), by comparison of its infrared spectrum with that of an authentic sample, and by gas chromatographic analysis of synthetic mixtures of the collected sample with authentic samples of trifluoroacetophenone.

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(4) See (a) G. C. Stoner, U. S. Patent 2,761,875 (1956); (b) ref. 3, p. 203.

(5) A. L. Henne, *J. Am. Chem. Soc.*, **59**, 1200 (1937).

(6) T. F. McGrath and R. Levine, *ibid.*, **77**, 3656 (1955).

Aroylations at the Methyl Group of Benzoylacetone and Related β-Diketones with Esters to Form 1,3,5-Triketones by Sodium Hydride. Other Terminal Condensations[1]

Marion L. Miles, Thomas M. Harris, and Charles R. Hauser

Department of Chemistry, Duke University, Durham, North Carolina

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Terminal aroylations of benzoylacetone and certain related β-diketones were effected with sodium hydride in appreciably higher per cent conversions of the β-diketones and esters to the 1,3,5-triketones than has previously been observed with potassium amide. The mechanism of the reaction appears not to involve the intermediate formation of the β-diketone dicarbanion, which was the reactive intermediate with the alkali amide. Twofold terminal aroylations of acetone were effected with sodium hydride to form some new symmetrical 1,3,5-triketones, certain of which were cyclized to 4-pyrones and one to a 4-pyridone. Although sodium hydride is superior for aroylations, it was found not to be so satisfactory as potassium amide for certain other types of condensations.

Aroylation at the methyl group of a β-diketone such as benzoylacetone or acetylacetone to form a 1,3,5-triketone has previously been effected by means of potassium amide in liquid ammonia. This was accomplished by converting the β-diketone to its dicarbanion I with 2 molecular equiv. of the base and then adding 0.5 molecular equiv. of an aromatic ester (Scheme I).[2,3]

Typical 1,3,5-triketones that have been obtained on acidification of the reaction mixtures were IVa–e.[2,3] The related hydroxy β-diketone V has been prepared similarly by benzoylation of *o*-hydroxyacetophenone.[3]

Although the per cent conversion of ester to triketone was generally good, for example 62% in the synthesis of triketone IVa,[4] the per cent conversion of the β-diketone to IVa was only half this value, as half of dicarbanion I was neutralized in the last step (II to III, Scheme I); in this acid–base reaction, the corresponding amount of β-diketone was regenerated as its monoanion. The use of an extra equivalent of

Scheme I

$$\begin{tikzcd} & RCOCH_2COCH_3 \arrow[r, "2KNH_2", "\text{liq. }NH_3"'] & \underset{\text{I}}{RCO\breve{C}HCO\breve{C}H_2} \arrow[d, "ArCOOCH_3"] \\ & \underset{\text{III}}{RCO\breve{C}HCO\breve{C}HCOAr} & \underset{\text{II}}{RCO\breve{C}HCOCH_2COAr} \arrow[l, "\text{I}"'] \end{tikzcd}$$

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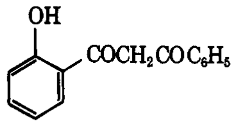
(1) This investigation was supported by National Science Foundation Grant 2274 and by Public Health Service Research Grant CA 04455-06 from the National Cancer Institute.

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

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

(4) The use of 2.2–3.0 molecular equiv. of I to 1 of the ester has recently been observed to increase the per cent conversion of the ester to IVa to 80%, but the per cent conversion of β-diketone was still only 40%: F. B. Kirby, T. M. Harris, and C. R. Hauser, *ibid.*, **28**, 2266 (1963).



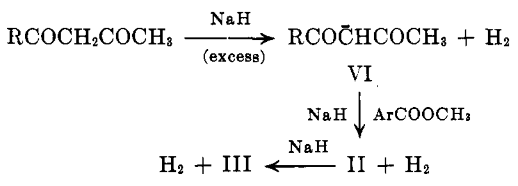
V

$RCOCH_2COCH_2COAr$
IVa, R = C_6H_5; Ar = C_6H_5
b, R = C_6H_5; Ar = $C_6H_4OCH_3$-*p*
c, R = C_6H_5; Ar = C_6H_4Cl-*p*
d, R = C_6H_5; Ar = 3-pyridyl
e, R = CH_3; Ar = C_6H_5

potassium amide to convert II to III (Ar = C_6H_5) was not satisfactory as the alkali amide reacted mainly with the ester to form benzamide.[3]

Such aroylations have now been accomplished more efficiently with respect to the β-diketone and even to the ester by means of sodium hydride in refluxing 1,2-dimethoxyethane (monoglyme). Because sodium hydride is a strong base that is relatively inert toward aromatic esters,[5] this reagent is suitable for effecting not only the condensation step but also the last step (II to III). The over-all reaction evidently requires 3 molecular equiv. of sodium hydride (see Scheme II) but 4 or 5 equiv. were usually employed to ensure maximum conversion of the β-diketone and ester to triketone. The general procedure involved, initially, addition of the β-diketone to the reagent followed by the ester but, later, addition of a mixture of the β-diketone and ester to the reagent. The latter procedure is more convenient; although it was employed in only three cases, it should be generally applicable.

SCHEME II



$$\begin{tikzcd}
RCOCH_2COCH_3 \arrow[r, "NaH", "\text{(excess)}"'] & RCO\bar{C}HCOCH_3 + H_2 \\
& VI \arrow[d, "NaH"', "ArCOOCH_3"] \\
H_2 + III & II + H_2 \arrow[l, "NaH"']
\end{tikzcd}$$

In Table I are summarized the yields of triketone IVb obtained on varying the proportions of reactants and reaction periods, and in Table II are given the yields of triketones IVa–e and V realized under one set of conditions in each case. Also in Table II are listed for comparison the yields of the triketones based on the esters reported for the potassium amide method.[2,3]

Table I shows that the yield of triketone IVb was 92% employing an excess of the ester and reagent, and 85% using molecular equivalents of the ester and β-diketone. The 92% conversion of the β-diketone to IVb is much higher than that (*ca.* 30%) observed with potassium amide,[3] and the 85% conversion of the ester to IVb is somewhat greater than that (61%) with the alkali amide.[3]

TABLE I

INFLUENCE OF CONDITIONS ON YIELDS OF TRIKETONE IVb FROM METHYL ANISATE, BENZOYLACETONE, AND SODIUM HYDRIDE IN REFLUXING MONOGLYME (85°)

Mol. equiv., ester:β-diketone:reagent	Reaction period, hr.	Yield, %
1:1:4	4	68
1:1:4	8	85
1.5:1:5	4	81
1.5:1:5	6	91 (92)[a]
2:1:5	4	92

[a] A mixture of benzoylacetone and methyl anisate was added to the reagent.

Table II shows that the per cent conversions of the appropriate β-diketones to all six of the triketones were considerably higher with sodium hydride than with potassium amide, the values for which would be only half those given in the last column of the table. Also the per cent conversions of the appropriate esters to triketones IVb and V (see Tables I and II) were somewhat better with sodium hydride than with potassium amide. However, the per cent conversion of methyl benzoate to triketone IVe was about the same with the two reagents. In this benzoylation, excess ester and reagent were avoided to minimize further terminal benzoylation of IVe to form the 1,3,5,7-tetraketone, which has been reported recently.[6]

From these results it may be concluded that sodium hydride is generally superior to potassium amide for such aroylations though, because of a shorter reaction period,[7] the latter reagent might sometimes be preferred.

Incidentally, the benzoylation of benzoylacetone was also effected with sodium hydride in refluxing tetrahydrofuran (4 hr.); the yield of IVa was 67%, which is somewhat lower than that (87%) obtained in monoglyme under similar conditions (see Table II).

Consideration of Mechanism.—In contrast to potassium amide with which dicarbanion I is the reactive intermediate (see Scheme I), excess sodium hydride appears to convert the β-diketone only to its monocarbanion VI. This was indicated by the evolution of only 1 molecular equiv. of hydrogen on addition of benzoylacetone or acetylacetone to 4 molecular equiv. of sodium hydride in refluxing monoglyme; however, 2 molecular equiv. more of hydrogen was evolved on subsequent addition of methyl benzoate (Table III). Apparently the presence of the ester caused ionizations of a methyl hydrogen of the β-diketone monocarbanion VI and of a methylene hydrogen of the triketone monocarbanion II to form the triketone dicarbanion II (Scheme II).

The mechanism of the aroylation step appears not to involve gradual ionization of a methyl hydrogen of monoanion VI by sodium hydride to form dicarbanion I which condenses with the ester, as equilibration of I with molecular hydrogen seems unlikely and relatively rapid condensation of I with the ester would not be in agreement with the favorable effect of excess ester on the rate of the reaction (see Table I). However, gradual secondary ionization of VI by sodium methoxide, which is a by-product of the condensation, might possibly form dicarbanion I in equilibrium with methanol so that I could condense with the ester in a rate-controlling step. Only a catalytic amount of sodium methoxide should be required as it would be regenerated by the action of sodium hydride on the methanol. A catalytic amount of this base might even have been produced initially from methanol impurities in the ester.

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[5] See F. W. Swamer and C. R. Hauser, *J. Am. Chem. Soc.*, **68**, 2647 (1946).

[6] M. L. Miles, T. M. Harris, and C. R. Hauser, *ibid.*, **85**, 3884 (1963).

[7] Whereas 4–8 hr. appear to be required for maximum yield of IVb with sodium hydride (see Table I), only about 2 hr. are probably required with potassium amide (see ref. 3).

TABLE II

YIELDS OF VARIOUS TRIKETONES FROM ESTERS (A), β-DIKETONES (B), AND SODIUM HYDRIDE (C) IN REFLUXING MONOGLYME (85°)

β-Diketone[a]	Methyl esters	Mol. equiv., A:B:C	Reaction period, hr.	Triketone	Yield,[b] %	M.p., °C.	Lit.[c] m.p., °C.	KNH₂ method yield, %
Benzoylacetone	Benzoate	1.2:1:4	3.0	IVa	87	106–109	106–110	62[c] (80)[d]
Benzoylacetone	Anisate	1.5:1:5	6.0	IVb	92	121–122	121–122	61[c]
Benzoylacetone	*p*-Chlorobenzoate	1.2:1:4	5.5	IVc	78	105–106.5	106–107.5	47[c]
Benzoylacetone	Nicotinate[e]	1.2:1:4	5.5	IVd	69	96–97.5	90–91	40[c]
Acetylacetone	Benzoate	1:1:3	2.0	IVe	54	101–102	105–109	53[c] (60)[f]
o-Hydroxyacetophenone[g]	Benzoate	1:1:4	2.0	V	62[h]	121.5–122	119–120	14[c]

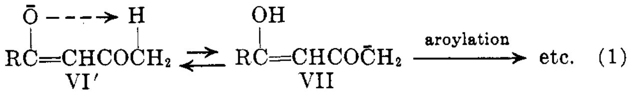
[a] All reactions were carried out using 0.05 mole of β-diketone except where noted. [b] The melting points of the products on which the yields were based were slightly lower than recorded values. [c] Ref. 3. [d] Ref. 4. [e] Ethyl ester. [f] Ref. 2. [g] *o*-Hydroxyacetophenone (0.1 mole) was used. [h] When the reaction period was 20 min., the yield was 59%. When the molecular equivalents of A:B:C were 1:2:4 and the reaction period was 2 hr., the yield was only 45%.

TABLE III

HYDROGEN EVOLVED ON ADDITION OF β-DIKETONES TO EXCESS SODIUM HYDRIDE IN REFLUXING MONOGLYME AND ON SUBSEQUENT ADDITION OF METHYL BENZOATE

	H₂ on addition of β-diketone			H₂ on subsequent addition of ester			
	Calcd. for 1 mol. equiv., l.	Found, l.	% of theory	Calcd. for 2 mol. equiv., l.	Found, l.	% of theory	Time, hr.
Acetylacetone	2.60	2.54	98				
Benzoylacetone	1.32	1.36	103	2.64	2.54	96	4
Benzoylacetone	1.12	1.40	93	2.24	2.24	100	4

Another possible mechanism for the aroylation step would be intramolecular equilibration of β-diketone monoanion VI′ with terminal monoanion VII which undergoes aroylation (eq. 1); resonance form VI′ rather than VI is shown below to indicate a six-atom cyclic mechanism. Possible aroylation of VI (or VI′) should be more reversible than that of VII.

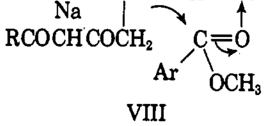


$$\underset{\text{VI}'}{\mathrm{R\overset{\overset{\bar{O}}{|}}{C}{=}CHCO\overset{\overset{H}{|}}{C}H_2}} \rightleftarrows \underset{\text{VII}}{\mathrm{R\overset{\overset{OH}{|}}{C}{=}CHCO\bar{C}H_2}} \xrightarrow{\text{aroylation}} \text{etc.} \quad (1)$$

A third possible mechanism would involve intermolecular proton exchange between two molecules of monoanion VI to form, in equilibrium, dicarbanion I which undergoes aroylation (eq. 2).

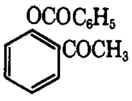
$$2\text{VI} \rightleftarrows \mathrm{RCOCH_2COCH_3} + \text{I} \xrightarrow{\text{aroylation}} \text{etc.} \quad (2)$$

A fourth possible mechanism would be an intermolecular process involving monoanion VI (or VI′), ester, and sodium hydride as indicated in VIII. Such a process might occur at the surface of the sodium hydride. A further study of the mechanism of the reaction is contemplated.

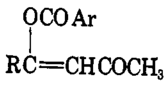


VIII

It should be mentioned that, although the benzoylation of *o*-hydroxyacetophenone might involve the intermediate formation of enol benzoate IX which rearranges,[8] the other aroylations appear not to proceed through enol esters X, as such enol esters having vinyl hydrogen have been reported to undergo β-elimination with bases to afford acetylenic products.[9]



IX

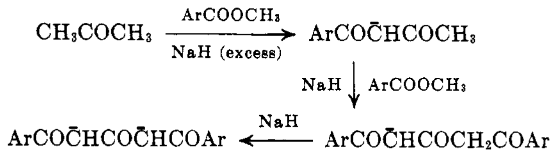


$$\mathrm{R\overset{\overset{OCOAr}{|}}{C}{=}CHCOCH_3}$$

X

Twofold Aroylation of Acetone.—Since acetone has previously[10] been benzoylated with methyl benzoate by sodium hydride and the resulting benzoylacetone is now further benzoylated by this reagent, it seemed possible to effect the twofold process in a single experiment.[11] This was realized. Presumably, the β-diketone monoanion and triketone monoanion are intermediates (Scheme III).

SCHEME III



$$\begin{tikzcd}
\mathrm{CH_3COCH_3} \arrow[r, "\mathrm{ArCOOCH_3}", "\mathrm{NaH\ (excess)}"'] & \mathrm{ArCO\bar{C}HCOCH_3} \arrow[d, "\mathrm{ArCOOCH_3}", "\mathrm{NaH}"'] \\
\mathrm{ArCO\bar{C}HCO\bar{C}HCOAr} & \mathrm{ArCO\bar{C}HCOCH_2COAr} \arrow[l, "\mathrm{NaH}"']
\end{tikzcd}$$

This twofold aroylation afforded symmetrical 1,3,5-triketones XIa–d in yields of 25–82% (Table IV). The yields for the latter two aroylations could probably be improved since no attempt was made to find optimum reaction conditions. This method should be quite general.

$\mathrm{ArCOCH_2COCH_2COAr}$
XIa, Ar = C_6H_5
b, Ar = $C_6H_4OCH_3$-*p*
c, Ar = C_6H_4Cl-*p*
d, Ar = 3-pyridyl

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[8] Rearrangement of enol benzoate IX by bases to form V is known: J. E. Gowan and T. S. Wheeler, *J. Chem. Soc.*, 1925 (1950).

[9] G. Nakaminami, *Bull. Chem. Soc. Japan*, **35**, 1629 (1962).

[10] F. W. Swamer and C. R. Hauser, *J. Am. Chem. Soc.*, **72**, 1352 (1950).

[11] Such a twofold aroylation of acetone in a single experiment seems unfeasible with potassium amide, since excess of this reagent would react with the ester to form the aroylamide.

TABLE IV

TWOFOLD AROYLATION OF ACETONE WITH ESTERS BY SODIUM HYDRIDE IN REFLUXING MONOGLYME TO FORM SYMMETRICAL 1,3,5-TRIKETONES

Methyl esters	Triketones	M.p., °C.	Yield, %
Benzoate	1,5-Diphenyl-1,3,5-pentanetrione (XIa)	106–110[a]	82
Anisate	1,5-Di(*p*-methoxyphenyl)-1,3,5-pentanetrione (XIb)[b]	126–128.5	77
p-Chlorobenzoate	1,5-Di(*p*-chlorophenyl)-1,3,5-pentanetrione (XIc)[c]	156–158	47
3-Pyridyl[d]	1,5-Di(3-pyridyl)-1,3,5-pentanetrione (XId)	149–150	25

[a] Lit. m.p. 106–110°; see ref. 3. [b] Samples were converted to 4-pyrone XIIa and 4-pyridone XIII in yields of 76 and 22%, respectively. [c] A sample was converted to 4-pyrone XIIb in 92% yield. [d] Ethyl ester.

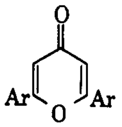
TABLE V

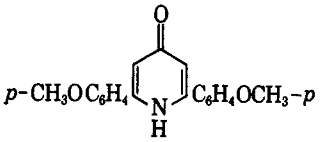
INFRARED SPECTRA AND ANALYSES OF SYMMETRICAL TRIKETONES, 4-PYRONES, AND 4-PYRIDONE

Compd.	Infrared spectra,[a,b] μ			Formula	Carbon, %		Hydrogen, %	
					Calcd.	Found	Calcd.	Found
XIb	6.15 s	6.27 s	6.38 s	$C_{19}H_{18}O_5$	69.93	70.15	5.56	5.38
XIc	6.25 s	6.38 s		$C_{17}H_{12}Cl_2O_3$[c]	60.91	61.16	3.61	3.53
XId	6.23 s	6.37 s		$C_{15}H_{12}N_2O_3$[d]	67.11	67.12	4.51	4.47
XIIa[e]	6.08 s	6.22 m	6.40 w	$C_{19}H_{16}O_4$	74.04	74.12	5.23	5.13
XIIb[f]	6.00 s	6.10 m	6.21 m	$C_{17}H_{10}Cl_2O_2$[g]	64.37	64.17	3.18	3.09
XIII[h]	6.20 s	6.36 m	6.53 s	$C_{19}H_{17}NO_3$[i]	74.25	74.08	5.58	5.61

[a] s = strong, m = medium, w = weak. [b] Absorption bands found in the region of 5.5 to 6.6 μ. [c] *Anal.* Calcd. for $C_{17}H_{12}ClO_3$: Cl, 21.16. Found: 21.21. [d] *Anal.* Calcd. for $C_{15}H_{12}N_2O_3$: N, 10.44. Found: 10.45. [e] M.p. 194–195°, recrystallized from 95% ethanol. [f] M.p. 236–237°, recrystallized from 95% ethanol. [g] *Anal.* Calcd. for $C_{17}H_{10}Cl_2O_2$: Cl, 22.36. Found: 22.12. [h] Sample melted at 274–275° after trituration with hot benzene. [i] *Anal.* Calcd. for $C_{19}H_{17}NO_3$: N, 4.56. Found: 4.30.

Triketones XIb and XIc were cyclized with cold sulfuric acid to form 4-pyrones XIIa and XIIb, respectively; also triketone XIb was cyclized with alcoholic ammonia to give 4-pyridone XIII (see notes *b* and *c*, Table IV). With the exception of triketone XIa, these compounds appear to be new; their infrared data and analyses are given in Table V.

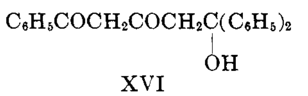

XIIa, Ar = $C_6H_4OCH_3$-*p*
b, Ar = C_6H_4Cl-*p*


XIII

Other Types of Terminal Condensations.—Although sodium hydride in refluxing monoglyme is preferable to an alkali amide in liquid ammonia for terminal aroylations of β-diketones, the latter reagent is superior for certain other types of terminal condensations. Examples of such reactions that have been effected in good yields by an alkali amide through the β-diketone dicarbanion I (see Scheme I) are carbonation, benzylation, and an aldol-type condensation to form XIV,[2] XV,[12] and XVI,[13] respectively. The last product was dehydrated with sulfuric acid to give XVII.[13]

$C_6H_5COCH_2COCH_2COOH$
XIV

$CH_3COCH_2COCH_2CH_2C_6H_5$
XV


$$C_6H_5COCH_2COCH_2\underset{\displaystyle OH}{\underset{|}{C}}(C_6H_5)_2$$
XVI

$C_6H_5COCH_2COCH{=}C(C_6H_5)_2$
XVII

In contrast, carbonation of benzoylacetone by means of sodium hydride failed, and benzylation of acetylacetone with benzyl chloride by this reagent afforded XV in only low yields (usually 6–10%). Moreover, XV was obtained contaminated with the isomeric 3-benzyl derivative along with higher boiling material (see Experimental). These results are not surprising since excess sodium hydride in refluxing monoglyme initially converts β-diketones only to their monocarbanions VI (see Scheme II).

The aldol-type condensation of benzoylacetone with benzophenone was realized by means of sodium hydride but the hydroxy β-diketone XVI was not isolated; instead the unsaturated β-diketone XVII was obtained in 52% yield. Similarly benzoylacetone was condensed with benzaldehyde and anisaldehyde to form the corresponding unsaturated β-diketones, though the latter product was generally difficult to purify (see Experimental).

It should be pointed out that, when the unsaturated β-diketone is the desired product from the aldol-type condensation, the direct sodium hydride procedure might be preferred in certain cases to that employing potassium amide with which two steps are involved.[13]

Experimental[14]

Anisoylation of Benzoylacetone to Form Triketone IVb.—The yields of this triketone obtained on varying the proportions of the reactants and reaction periods are summarized in Table I. In these experiments, 0.05 mole of benzoylacetone was used; the moles of methyl anisate and sodium hydride can be calculated from the proportions given in Table I. Since the reagent consisted of an approximately 50% dispersion of sodium hydride in mineral oil,[15] approximately twice the weight indicated by the moles given in Table I was used. The experimental procedure is described below.

To a stirred slurry of sodium hydride in 100 ml. of 1,2-dimethoxyethane (monoglyme) at reflux, under dry nitrogen, was added a solution of 0.05 mole of benzoylacetone in 50 ml. of monoglyme, followed, after 45 min., by a solution of methyl anisate in 50 ml. of monoglyme. The reaction mixture was refluxed for 4–8 hr. Most of the solvent was then removed under reduced pressure and the pasty residue was cooled to 0° in an ice–water bath. Diethyl ether (150 ml.) was added. After

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(12) K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **28**, 1946 (1963).

(13) R. J. Light and C. R. Hauser, *ibid.*, **26**, 1716 (1961).

(14) All melting points were taken on a Thomas-Hoover Uni-Melt apparatus and are corrected. The infrared spectra were determined on a Perkin-Elmer Infracord, Model 137, using the potassium bromide pellet method. Elemental analyses were by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

(15) Obtained from Metal Hydrides, Inc., Beverly, Mass.

stirring the mixture for a few minutes, 100 ml. of cold water was added; initially, the water was added dropwise until the excess sodium hydride was destroyed. The two layers were separated. The ethereal layer was extracted with two 100-ml. portions of cold water and then with 100 ml. of cold 1% aqueous sodium hydroxide. The extracts were combined with the original aqueous layer and then poured onto a mixture of 40–50 ml. of 12 *N* hydrochloric acid and 200 g. of crushed ice. The resulting precipitate was collected on a funnel, washed with water, and recrystallized from 95% ethanol to give triketone IVb, m.p. 121–122°

In one experiment, a solution of 0.05 mole of benzoylacetone and 0.075 mole of methyl anisate in 100 ml. of monoglyme was added to a slurry of 0.25 mole of sodium hydride in 100 ml. of monoglyme at reflux. After refluxing for 6 hr., the reaction mixture was worked up as described above to give 13.6 g. (92%) of triketone IVb, m.p. 121–122°.

Various Aroylations of β-Diketones to Form 1,3,5-Triketones.—These reactions were carried out essentially as described above for the anisoylation of benzoylacetone employing the proportions of reactants and reaction periods indicated in Table II; the yields of the triketones and their melting points are also given in Table II. The triketones were isolated as described below.

In the preparations of triketones IVa, IVc, IVe, and V, acidification of the alkaline solutions of the products produced oily mixtures, which were extracted with ether. The ethereal extracts were dried over anhydrous sodium sulfate and solvent was removed. The residues were recrystallized from 95% ethanol to give the triketones.

In the preparation of triketone IVd, acidification of the alkaline solutions of the product afforded an ether-insoluble salt in the acid solution, and solid sodium bicarbonate was added to adjust the solution to pH 8. The free base, triketone IVd, was then extracted into ether from which it was recovered and recrystallized from 95% ethanol.

Triketones IVa and IVc were also prepared in equally good yields by adding a solution of benzoylacetone and the appropriate ester in monoglyme to the refluxing reagent.

Measurement of Hydrogen Evolution.—In a 500-ml. two-necked flask equipped with a tightly fitting addition funnel (with a pressure-equalizing side arm) and an efficient reflux condenser was placed 50 ml. of monoglyme and 0.25 mole of sodium hydride. The upper end of the condenser was fitted with a gas take-off which was connected to an American Meter Co. wet-test meter filled with water. The system was flushed with dry nitrogen, and a solution of 0.05 mole of benzoylacetone in 25 ml. of monoglyme was placed in the addition funnel. The system was closed, and the flask was placed on the steam bath. When thermal equilibrium was established, an initial reading was taken on the test meter. The solution of β-diketone was then added during 10–12 min. After the solution had been added, readings were taken periodically until the hydrogen evolution ceased. This required about 2 hr., though almost all of the hydrogen was evolved within 20–30 min. The system was opened, and a solution of 0.074 mole of methyl benzoate in 50 ml. of monoglyme was placed in the addition funnel. The apparatus was closed, equilibrium was established, an initial reading was taken, and the ester solution was added during a period of 5–10 min. Readings were then taken periodically until gas evolution was no longer detectable. The values were corrected for temperature, pressures, and water vapor pressure. The results from the hydrogen evolution studies are summarized in Table III.

Twofold Aroylations of Acetone to Form 1,3,5-Triketones.—Under a dry nitrogen atmosphere, a solution of 0.05 mole of acetone and 0.15 mole of ester in 100 ml. of monoglyme was added to a stirred suspension of 0.25 mole of sodium hydride in 100 ml. of monoglyme at reflux. The reaction mixture was refluxed for 6 hr., and then worked up as described above for the anisoylation of benzoylacetone. Triketones XIa and XIb were isolated as described for IVa, and triketone XId as described for IVd. The disodio salt of triketone XIc was insoluble in both water and ether and was conveniently separated from the starting diketone by filtration. This salt was treated with cold dilute (6 *N*) hydrochloric acid, and the triketone was isolated by filtration and recrystallization from 95% ethanol.

The 4-pyrone and 4-pyridone derivatives of the corresponding triketones were prepared by procedures described previously.[3]

The results are summarized in Tables IV and V.

Attempted Carbonation of Benzoylacetone.—A mixture of 0.05 mole of benzoylacetone and 0.25 mole of sodium hydride in 150 ml. of monoglyme was refluxed under dry nitrogen for 45 min. Most of the solvent was then removed. The remaining mixture was cooled and 150 ml. of dry ether was added. The resulting slurry was poured onto 800 g. of finely crushed solid carbon dioxide, and the reaction mixture was worked up essentially as described previously[2] for the carbonation of benzoylacetone by means of potassium amide. There was recovered 7.3 g. (91%) of the original β-diketone, m.p. 55–57°. None of acid XIV was found.

Benzylation of Acetylacetone.—To a stirred refluxing slurry of 0.3 mole of sodium hydride in 100 ml. of monoglyme was added a solution of 0.1 mole of acetylacetone in 100 ml. of monoglyme. After 45 min., 0.13 mole of benzyl chloride in 100 ml. of monoglyme was added, and the resulting mixture was refluxed for 24 hr. Most (*ca.* 250 ml.) of the solvent was removed under reduced pressure. The remaining mixture was cooled to 0°, and 150 ml. of ether and 100 ml. of cold water were added. The layers were separated. The organic layer was extracted with three 100-ml. portions of water. The aqueous extracts were combined and poured onto a mixture of ice and 35 ml. of 12 *N* hydrochloric acid. The resulting mixture was extracted with ether. The ethereal extract was dried over anhydrous sodium sulfate, and the solvent was evaporated to leave 14 g. of an oily residue. To a 2-g. aliquot of this residue was added 0.08 g. of biphenyl (as an internal standard). A sample of this aliquot was chromatographed at 230° on a F and M vapor phase chromatograph, Model 500, using a 5-ft. Carbowax 20M on Chromosorb P column. The chromatogram showed peaks corresponding to the terminal benzylation product, 6-phenyl-2,4-hexanedione (XV), and 3-benzyl-2,4-pentanedione along with starting materials. Also there was a very broad unidentified peak which had a considerably longer retention time. By using the internal standard method, the calculated yield of XV was 7% and that of 3-benzyl-2,4-pentanedione was approximately 5%. Similar results were obtained in other experiments, the yield of XV being 6–10%.

Adol-Type Condensation. A. With Benzophenone.—To a refluxing slurry of 0.2 mole of sodium hydride and 100 ml. of monoglyme was added 0.1 mole of benzoylacetone in 100 ml. of monoglyme followed immediately by a solution of 0.1 mole of benzophenone also in 100 ml. of monoglyme. The resulting mixture was refluxed for 10 hr. Most of the solvent was removed under reduced pressure. The pasty residue was cooled to 0°, and 150 ml. of ether and 100 ml. of cold water were added. The ethereal layer was separated, washed with water, and dried over anhydrous sodium sulfate, and the solvent was removed. The solid residue was stirred with 40 ml. of 6 *N* hydrochloric acid. The resulting slurry was extracted with four 150-ml. portions of ether. The extracts were combined and dried over anhydrous sodium sulfate. The solvent was removed. The solid residue was washed with 100 ml. of cold pentane and then recrystallized from *n*-hexane to give 17 g. (52%) of β-phenylcinnamoylacetophenone, m.p. 96–97.5° (lit. m.p. 97–98°).[13] This product was identified by comparison of its infrared spectrum with that of an authentic sample and by the mixture melting point method.

B. With Aromatic Aldehydes.—To a refluxing slurry of 0.1 mole of sodium hydride in 100 ml. of monoglyme was added 0.05 mole of benzoylacetone in 25 ml. of monoglyme. After refluxing the mixture for 45 min., a solution of 0.05 mole of benzaldehyde in 25 ml. of monoglyme was added. The reaction mixture was refluxed for 20 min., and then worked up essentially as described above in the experiment with benzophenone. There was obtained, after recrystallization from 95% ethanol, 4.1 g. (33%) of cinnamoylacetophenone, m.p. 105.5–108° (lit. m.p. 110–111).[2]

Similarly, benzoylacetone was condensed with anisaldehyde to afford, in one experiment, 7.2 g. (51%) of *p*-methoxycinnamoylacetophenone, m.p. 124.5–126° (lit. m.p. 129–130.5)[3]. However, in three other experiments, the product melted at 116–120°. A thin layer chromatogram of this material, using silica gel G (E. Merck, A. G.) as the stationary phase and developing with a solution of benzene–chloroform (90:10), indicated that the desired product was contaminated with at least one other component. Recrystallization and column chromatography of this material failed to afford the pure product.