Anal. Calcd. for $C_{11}H_{11}N_2OCl$ (222.67): C, 59.33: H, 4.98; N, 12.58; Cl, 15.92. Found: C, 59.65; H, 5.05; N, 13.47, 13.07; Cl, 16.15.

The major portion of the benzene filtrate was evaporated to a small volume. Addition of petroleum ether (b.p. 40–75°) caused precipitation of a pink solid (1.04 g.), m.p. ~80–140°. Recrystallization from ethanol–water, with charcoal, and from benzene–petroleum ether (b.p. 40–75°) did not appreciably purify the product. Vacuum sublimation at 200° (0.5 mm.) yielded a white solid, m.p. 147–157°, which, judging from its melting point, was still a mixture.

3,3′-Benzylidene-2,2′-dimethyl-5,5′-dinitrodiindole (XIIb).[3]—2-Methyl-5-nitroindole (1.00 g., 0.00567 mole) and benzaldehyde (1.50 g., 0.014 mole) were warmed together on a steam bath for 2 hr. The resulting solid mass was then recrystallized from methanol–water, yielding a yellow solid (0.72 g., 58%), m.p. 295–298° dec., reported m.p. 291°[4]; λ_{max} mμ (log ε) in 95% ethanol: 276 (4.57), 335 (4.20); ν_{NH} 3460 mw, 3360 m, ν_{NO_2} 1516 m, 1331 vs cm.$^{-1}$ in Nujol.

2,2′-Dimethyl-5,5′-dinitro-3,3′-methylenediindole (XIIa).[3] **A. From Reaction with Paraformaldehyde.**—Paraformaldehyde (1.7 g., 0.057 mole CH_2O) and concentrated hydrochloric acid (2 drops) were added to a solution of 2-methyl-5-nitroindole (5.7 g., 0.0323 mole) in methanol (50 cc.). The solution was refluxed for 3 hr. and a yellow-orange solid precipitated. Water was then added, and the yellow-orange solid (6.4 g.) was recrystallized from acetone–water, yielding an orangish yellow solid (5.9 g., 100%), m.p. 348–354° dec. (darkens at 270°); λ_{max} mμ (log ε) in 95% ethanol: 275 (4.60), 335 (4.20); ν_{NH} 3360 s, ν_{NO_2} 1503 m, 1332 vs cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{19}H_{16}N_4O_4$ (365.36): C, 62.63; H, 4.43; N, 15.38. Found: C, 62.51; H, 4.61; N, 15.04.

B. From Reaction with Formalin.—By the procedure of von Walther and Clemen,[4] a solution of 2-methyl-5-nitroindole (1.00 g., 0.00567 mole) and formalin (0.45 g. of 37% CH_2O, 0.0055 mole) in absolute ethanol (30 cc.) was refluxed for 0.5 hr. Filtration of the hot solution separated the yellow-orange solid precipitate (0.06 g., 3%), m.p. 348–354° dec., reported m.p. 131°.[4]

The cooled filtrate yielded unchanged 2-methyl-5-nitroindole (0.81 g., 81%), m.p. 175–176°, which gave no depression in mixture melting point with starting material.

2-Methyl-5-nitrogramine (XIII).[3]—A solution of 2-methyl-5-nitroindole (0.95 g., 0.00539 mole) in acetic acid (20 cc.) was added dropwise, with stirring, to a solution of formalin (0.50 g. of 37% CH_2O, 0.0062 mole) and dimethylamine (0.90 g. of aqueous 25% solution, 0.0050 mole) in acetic acid (15 cc.) at 0° over a period of 30 min. The mixture, in which an orange solid had precipitated, was stirred at 0° for an additional 30 min., then at room temperature for 45 min., and finally at 100° for 15 min. The acetic acid was neutralized to pH 7 with aqueous 20% potassium hydroxide solution, and the mixture was filtered, giving **2,2′-dimethyl-5,5′-dinitro-3,3′-methylenediindole** (XIIa) as an orange-yellow solid (0.50 g., 51%). Recrystallization from acetone gave a sample, m.p. 348–354° dec., having an infrared spectrum in Nujol identical with that of the sample prepared from the formaldehyde reaction.

The aqueous filtrate was basified to pH 10 with aqueous 20% potassium hydroxide solution and extracted with ether. The ether extract was treated with charcoal, dried over anhydrous sodium sulfate, and evaporated to a small volume. Addition of petroleum ether (b.p. 40–75°) caused precipitation of **2-methyl-5-nitrogramine** (XIII) as yellow crystals (0.21 g., 18% from dimethylamine), m.p. 173–175°; λ_{max} mμ (log ε) in 95% ethanol: 267 (4.23), 331 (3.87); ν_{NH} no well defined peaks except for a weak peak in Nujol at 2700 cm.$^{-1}$, with a broad tailing out of absorption toward lower frequencies, ν_{NO_2} 1527 m, 1333 s in Nujol, 1338 cm.$^{-1}$ in chloroform.

Anal. Calcd. for $C_{12}H_{15}N_3O_2$ (233.26): C, 61.78; H, 6.48; N, 18.02. Found: C, 61.71; H, 6.69; N, 17.96.

Equilibration of the sample with deuterium oxide in homogeneous methanol solution produced a sample containing, in addition to the weak peak at 2690, three broad medium weak peaks at 2340, 2190, and 2060 cm.$^{-1}$ attributed to the ND group, and also minor changes elsewhere in the infrared spectrum in Nujol.[14b]

Reaction of 2-Methyl-5-nitroindole with Nitroethylene.[3]—A solution of 2-methyl-5-nitroindole (2.3 g., 0.0130 mole) and nitroethylene[31] (7.0 g., 0.096 mole) in benzene (20 cc.) was kept at room temperature for 12 hr. The liquids were distilled under reduced pressure (0.7 mm.) and the residue was dissolved in acetone, producing a dark brown solution. Two treatments with liberal amounts of charcoal did not appreciably diminish the color of the solution. Addition of successive portions of petroleum ether (b.p. 40–75°) caused separation first of a quantity of dark brown tar, then a large amount of an amorphous tan solid, and finally a *1:2 adduct*, believed to be **3-(2,4-dinitro-1-butyl)-2-methyl-5-nitroindole** (XIV), as a bright yellow crystalline solid (0.35 g., 8%), m.p. 215–217°; λ_{max} mμ (log ε) in 95% ethanol: 271 (4.32), 330 (4.09); ν_{NH} 3400 s in potassium bromide and Nujol, ν_{NO_2} 1546 s, 1506 m, 1327 s in potassium bromide, 1545 s, 1510 m, 1330 s cm.$^{-1}$ in Nujol.

Anal. Calcd. for $C_{13}H_{14}N_4O_6$ (322.27): C, 48.45; H, 4.38; N, 17.39. Found: C, 49.52, 49.31; H, 4.61, 4.80; N, 16.88.

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(31) (a) G. D. Buckley and C. W. Scaife, *J. Chem. Soc.*, 1471 (1947); (b) W. E. Noland, *Org. Syn.*, **41**, 67 (1961).

Acylation *vs.* Conjugate Addition of Dipotassio β-Diketones with Cinnamic Esters. Synthesis of Unsaturated 1,3,5-Triketones and *t*-Butyl 5,7-Dioxoalkanoates[1]

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The dipotassio salts of benzoylacetone and certain related β-diketones, prepared by means of two molecular equivalents of potassium amide in liquid ammonia, were acylated with phenyl cinnamate to form unsaturated 1,3,5-triketones. These products were cyclized by means of sulfuric acid to give unsaturated 4-pyrones. Several dipotassio-β-diketones were condensed with *t*-butyl cinnamate to afford the conjugate addition products, certain of which were cleaved to produce appropriate derivatives. Methyl cinnamate exhibited, toward dipotassiobenzoylacetone, both acylation and conjugate addition. Studies were made on the influence of variations in the molecular ratios of β-diketone to ester on the yields of triketones from acylations of certain β-diketones with phenyl cinnamate and with phenyl and methyl benzoates.

Recently such β-diketones as benzoyl- and acetylacetones were shown to undergo alkylation,[2,3] acylation,[2,4,5] and the aldol type condensation[2,6] at their terminal methyl group through their dicarbanions, which were prepared by means of two molecular equivalents of an alkali amide (equation 1).

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(1) Supported by Army Research Office (Durham) and by the National Institutes of Health.

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

(3) R. B. Meyer and C. R. Hauser, *J. Org. Chem.*, **25**, 158 (1960).

(4) R. J. Light and C. R. Hauser, *ibid.*, **25**, 538 (1960).

(5) S. D. Work and C. R. Hauser, *ibid.*, **28**, 725 (1963).

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

TABLE I

ACYLATIONS OF β-DIKETONES WITH PHENYL CINNAMATE BY POTASSIUM AMIDE TO FORM 1,3,5-TRIKETONES

β-Diketone	Moles	Moles of KNH_2	Moles of ester	Reaction time, hr.	1,3,5-Triketones[a]	M.p.,[b] °C.	Yield,[c] %
Benzoylacetone	0.08	0.16	0.027	1.5	1,7-Diphenyl-6-heptene-1,3,5-trione (IVa)[d]	127.5–129.5	55[e]
Anisoylacetone	.075	.15	.025	3	1-(*p*-Methoxyphenyl)-7-phenyl-6-heptene-1,3,5-trione (IVb)[d]	145–147	54
Acetylacetone	.11	.22	.037	5	8-Phenyl-7-octene-2,4,6-trione (IVc)[d]	117–118	40[f]
2-Acetylcyclohexanone	.10	.20	.05	2	1-(2-Oxocyclohexyl)-5-phenyl-4-pentene-1,3-dione (IVd)[g]	123–125	41

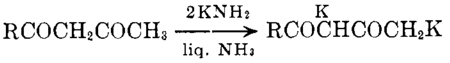
[a] These triketones were obtained as golden yellow crystals; they gave greenish brown enol tests with ethanolic ferric chloride. [b] These melting points were obtained with analytical samples; the melting points of the products on which the yields were based were slightly lower. [c] These yields were based on the ester. [d] Recrystallized from 95% ethanol. [e] The yield was only 40% when the molecular proportions of β-diketone, potassium amide, and ester were 2:4:1. [f] The yield was only 25% when the molecular proportions of β-diketone, potassium amide, and ester were 2:4:1. [g] Recrystallized from petroleum ether.

TABLE II

INFRARED AND ULTRAVIOLET SPECTRA AND ANALYSES FOR 1,3,5-TRIKETONES

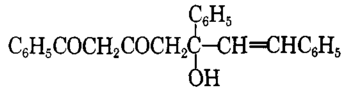
	Infrared spectra[a,b,c]		Ultraviolet spectra[a]		Empirical	Analyses[a]			
						Carbon		Hydrogen	
Triketone	μ	μ	λ_{max} mμ	log ε	formula	Calcd.	Found	Calcd.	Found
IVa	6.17	6.35	402	4.65	$C_{19}H_{16}O_3$	78.06	78.06	5.52	5.44
IVb	6.17	6.34	412	4.62	$C_{20}H_{18}O_4$	74.52	74.75	5.63	5.57
IVc	6.12	6.30	365	4.37	$C_{14}H_{14}O_3$	75.53	75.64	6.71	6.94
VI	6.15	6.33	332	4.44	$C_{17}H_{18}O_3$	73.02	72.85	6.13	5.81

[a] See ref. 12. [b] Absorption bands in the enol–chelate region from 5.5 μ to 6.5 μ. [c] All recorded infrared bands are strong.



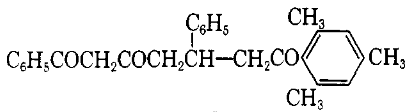
$$\mathrm{RCOCH_2COCH_3} \xrightarrow[\text{liq. NH}_3]{2\mathrm{KNH_2}} \mathrm{RCO\overset{K}{C}HCOCH_2K} \qquad (1)$$

I



$$\mathrm{C_6H_5COCH_2COCH_2\overset{C_6H_5}{\underset{OH}{C}}{-}CH{=}CHC_6H_5}$$

II



III

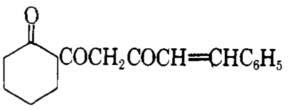
Dipotassiobenzoylacetone (I, R = C_6H_5) was observed to undergo the aldol reaction even with chalcone to form II, although it underwent conjugate addition with 2′,4′,6′-trimethylchalcone to give III.[7]

In the present investigation a study was made of the acylation and conjugate addition of dialkali β-diketones with cinnamic esters. An initial experiment with dipotassio salt I (R = C_6H_5) and methyl cinnamate afforded both the acylation and conjugate addition products. Since phenyl esters undergo alkaline hydrolysis more rapidly than corresponding methyl esters[8] whereas *t*-butyl esters undergo alkaline hydrolysis much more slowly,[8] phenyl cinnamate was chosen for the acylation reaction and *t*-butyl cinnamate for the conjugate addition. Actually acylation was observed to the exclusion of conjugate addition with the phenyl ester, and conjugate addition to the exclusion of acylation with the *t*-butyl ester. However, the phenyl ester afforded not only the desired unsaturated 1,3,5-triketone, but also cinnamic acid.

Acylations.—The dipotassio salts of benzoyl-, anisoyl-, and acetylacetones (see equation 1) were acylated with phenyl cinnamate to form unsaturated 1,3,5-triketones IVa, IVb, and IVc, respectively. Similarly dipotassio-2-acetylcyclohexanone was acylated with this ester to give V. The results are summarized in Tables I and II.

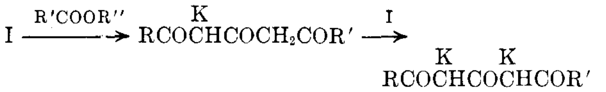
$\mathrm{RCOCH_2COCH_2COCH{=}CHC_6H_5}$

IVa, R = C_6H_5
b, R = $C_6H_4OCH_3$-p
c, R = CH_3



V

In earlier studies,[2,4] it was assumed that the β-diketone was converted quantitatively to its dipotassio salt (equation 1) and that two molecular equivalents of this salt were involved in the reaction with the aromatic methyl ester (equation 2).



$$\mathrm{I} \xrightarrow{\mathrm{R'COOR''}} \mathrm{RCO\overset{K}{C}HCOCH_2COR'} \xrightarrow{\mathrm{I}} \mathrm{RCO\overset{K}{C}HCO\overset{K}{C}HCOR'} \qquad (2)$$

In the present study, better yields of triketones IVa and IVc were obtained when the molecular ratio of the β-diketone to phenyl cinnamate was 3:1 than when it was 2:1 (see Table I). Moreover, an appreciable yield (17%) of cinnamic acid also was isolated in the former reaction under conditions that did not appear to effect hydrolysis of the phenyl cinnamate (see Experimental). A more thorough study of the influence of ratios of reactants on yields in related benzoylations is described subsequently.

The assigned structures of the triketones were consistent with their color (golden yellow) and with the color of their enol tests, which were different from those of the starting β-diketones. The structures were supported by analyses and by absorption spectra (see Table II). Their infrared spectra showed not only medium to strong bands in the 6.1–6.4-μ region similar to those observed for 1,3,5-triketones prepared previously,[2–5] but also a medium intensity band at approximately 10.2 μ which is characteristic of a *trans* double

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

[8] See L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 211.

TABLE III

CYCLIZATION OF 1,3,5-TRIKETONES TO FORM 4-PYRONES

Triketone	Pyrone[a]	Recrystallization solvent	M.p.,[b] °C.	Yield, %
IVa	2-Phenyl-6-styryl-4*H*-pyran-4-one (VIIIa)	Ethanol-water	108–109	85
IVb	2-(*p*-Methoxyphenyl)-6-styryl-4*H*-pyran-4-one (VIIIb)	Hexane-chloroform	135–137	88[c]
VI	Cyclohexeno[*b*]-6-styryl-4*H*-pyran-4-one (IX)	Hexane	124.8–125.5	76[d]

[a] All of the pyrones gave negative enol tests. [b] Melting points given are those for analytical samples. [c] The product on which this yield is based melted at 125–130°. [d] The product on which this yield is based melted at 120–123°.

TABLE IV

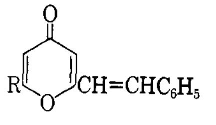
INFRARED AND ULTRAVIOLET SPECTRA AND ANALYSES FOR 4-PYRONES

	Infrared spectra[a,b,c]			Ultraviolet spectra[a]			Analyses[a]			
							Carbon		Hydrogen	
Pyrone	μ	μ	μ	λ_{max}, mμ	log ε	Empirical formula	Calcd.	Found	Calcd.	Found
VIIIa	6.05 s	6.25 m		274, 330	4.46, 4.45	$C_{19}H_{14}O_2$	83.20	82.86	5.15	4.99
VIIIb	6.06 s	6.15 s	6.22 s	290, 325	4.49, 4.39	$C_{20}H_{16}O_3$	78.93	78.58	5.30	5.27
IX	6.04 s	6.13 s	6.22 s	319	4.49	$C_{17}H_{16}O_2$	74.05	74.08	6.22	6.41

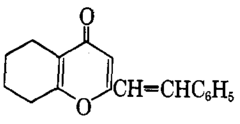
[a] See ref. 12. [b] s, strong; m, medium. [c] Absorption bands found in the region from 5.5–6.5 μ.

bond conjugated with a carbonyl grouping.[9] The ultraviolet and visible spectra of the present triketones differed from those of the previously prepared triketones in showing a large bathochromic shift ascribed to the presence of the styryl group. For example, triketones IVa and IVb exhibited absorption maxima at 402 and 412 mμ, respectively.

The structures of the triketones IVa, IVb, and VI were confirmed by cyclization by means of cold sulfuric acid to form 4-pyrones VIIIa, VIIIb, and IX, in yields of 85, 88, and 76%, respectively. The results are summarized in Tables III and IV.



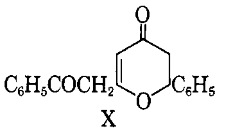
VIIIa, R = C_6H_5
b, R = $C_6H_4OCH_3$-*p*



IX

The structures of these 4-pyrones were supported by analyses, and by infrared and ultraviolet absorption spectra (see Table IV). These spectra are similar to those for 4-pyrones obtained on cyclization of aroylation[2,4] and acylation[5] products of dialkali salts of β-diketones. As expected, the infrared spectra of the present unsaturated pyrones show, besides the usual bands, a band for the carbon–carbon double bond at approximately 10.3 μ, which is somewhat shifted beyond that generally observed for this group.[1] The ultraviolet spectra of the present pyrones have absorption maxima at somewhat longer wave length than corresponding pyrones lacking the styryl double bond.

There was a possibility that cyclization might have involved the carbon–carbon double bond to form, for example, the dihydropyrone X. However, this structure is inconsistent with the analysis and properties of the product isolated (see preceding).



X

In view of the increased yields of triketones IVa and IVc obtained on increasing the molecular ratios of the β-diketones to phenyl cinnamate (see preceding), it seemed of interest to ascertain whether such an effect would be observed also in the benzoylation of acetylacetone and benzoylacetone with phenyl and methyl benzoates, which might be regarded as model systems. These aroylations would afford triketones XIa and XIb, which have been prepared previously[2,4] in yields of 53–60% and 58–62%, respectively, employing 2:1 ratios of dipotassio salts I (R = CH_3 and C_6H_5) to methyl benzoate. The present results, in which the yield of not only triketones XIa,b, but also in some cases that of benzoic acid was determined, are summarized in Table V.

$RCOCH_2COCH_2COC_6H_5$ XIa, R = CH_3
b, R = C_6H_5

TABLE V

YIELDS OF TRIKETONES XIa,b AND BENZOIC ACID FROM VARIOUS MOLECULAR RATIOS OF DIPOTASSIO SALTS I AND BENZOIC ESTERS

Salt I, R	Benzoate ester	Ratio salt I:ester	Triketone yield, %[a]	Benzoic acid, %[b]
CH_3	Phenyl	1:1	XIa, 0	50
CH_3	Phenyl	2:1	XIa, 35	45
CH_3	Phenyl	3:1	XIa, 58	23
CH_3	Phenyl	4:1	XIa, 80	10
C_6H_5	Phenyl	1:1	XIb, 19[c,d]	. .
CH_3	Methyl	1:1	XIa, 62[c]	20[e]
CH_3	Methyl	2:1	XIa, 62	22
CH_3	Methyl	2.2:1	XIa, 74, 85	20, 9
CH_3	Methyl	3:1	XIa, 80, 87	. ., 8
C_6H_5	Methyl	1:1	XIb, 64[c]	. .
C_6H_5	Methyl	2:1	XIb, 58–62[f]	. .
C_6H_5	Methyl	2.2:1	XIb, 76, 77	. .
C_6H_5	Methyl	3:1	XIb, 73	. .

[a] Yield of fairly pure triketone based on the presumed stoichiometric 2:1 ratio. [b] Yield based on ester; in certain experiments some benzamide also was isolated. [c] The per cent conversion of ester to triketone would be only half this amount. [d] Another product also was obtained (see Experimental). [e] Methyl benzoate (42%) was recovered. [f] Ref. 2 and 4.

Table V shows that, in the acylation of dipotassio acetylacetone with phenyl benzoate, the relative yield of triketone XIa increased and that of benzoic acid decreased as the molecular ratio was increased. Rather

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[9] See L. J. Bellamy, "Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 45.

TABLE VI

CONJUGATE ADDITION OF β-DIKETONES TO *t*-BUTYL CINNAMATE BY POTASSIUM AMIDE TO FORM *t*-BUTYL 5,7-DIOXOALKANOATES

β-Diketone	Conjugate addition product[a]	Recrystallization solvent	M.p., °C.	Yield, %
Benzoylacetone	*t*-Butyl 5,7-dioxo-3,7-diphenylheptanoate (XIIa)	Ethanol	92–93[b]	70
Anisoylacetone	*t*-Butyl 5,7-dioxo-7-(*p*-methoxyphenyl)-3-phenylheptanoate (XIIb)	Hexane	69–70.5	40
Acetylacetone	*t*-Butyl 5,7-dioxo-3-phenyloctanoate (XIIc)	Ethanol–water	47–48.5	40

[a] Enol tests for these compounds all produced bright red solutions. [b] The melting point on which the yield was based was 88–92°.

TABLE VII

INFRARED SPECTRA AND ANALYSES OF CONJUGATE ADDITION PRODUCTS

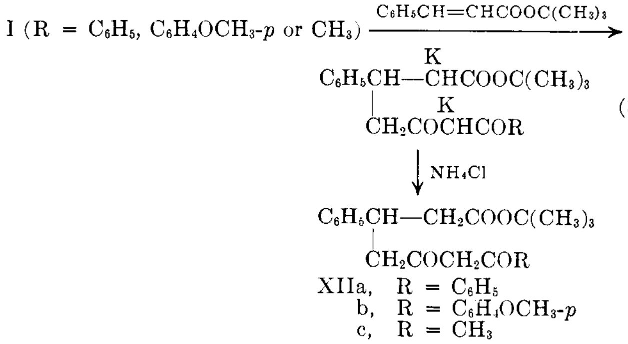
Conjugate addition product	Infrared spectra[a,b] μ	Infrared spectra[a,b] μ	Empirical formula	Analyses[a] Carbon Calcd.	Analyses[a] Carbon Found	Analyses[a] Hydrogen Calcd.	Analyses[a] Hydrogen Found
XIIa	5.82	6.24	$C_{23}H_{26}O_4$	75.38	75.41	7.15	7.11
XIIb	5.80	6.20	$C_{24}H_{28}O_5$	72.70	72.79	7.14	7.14
XIIc	5.80	6.15	$C_{18}H_{24}O_4$	71.02	71.52	7.95	8.00

[a] See ref. 12. [b] All recorded bands are strong.

surprisingly, the experiment in which the molecular ratio of these reagents was 1:1 afforded much benzoic acid but apparently none of triketone XIa. However, the corresponding experiment with dipotassio benzoylacetone gave triketone XIb in low yield. These results suggest that in aroylations employing phenyl esters O-benzoyl derivatives of the β-diketones may be intermediates, although other explanations are conceivable.

Table V further indicates that with methyl esters substantially better yields of triketones XIa,b are obtained with a 2.2:1 ratio of dipotassio salt I to methyl benzoate than with the previously employed stoichiometric 2:1 ratio. This improvement in yield may reflect only the scavenging of moisture by the excess dicarbanion, since the use of a 3:1 ratio does not provide further improvement. These results lend support to the pathway described by equations 1 and 2.

Conjugate Addition.—The dipotassio salts of benzoyl-, anisoyl-, and acetylacetones (see equation 1) underwent conjugate addition with *t*-butyl cinnamate to form the *t*-butyl 5,7-dioxoalkanoates XIIa, XIIb, and XIIc, respectively (equation 3). The results are summarized in Tables VI and VII.

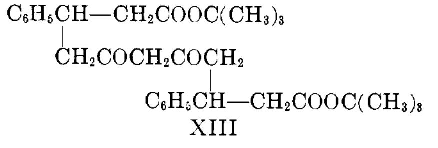


$$\text{I }(R = C_6H_5,\ C_6H_4OCH_3\text{-}p \text{ or } CH_3) \xrightarrow{C_6H_5CH=CHCOOC(CH_3)_3} \begin{array}{l} \quad\ K \\ C_6H_5CH{-}CHCOOC(CH_3)_3 \\ |\qquad\ \ K \\ CH_2COCHCOR \end{array} \quad (3)$$

$$\xrightarrow{NH_4Cl} \begin{array}{l} C_6H_5CH{-}CH_2COOC(CH_3)_3 \\ | \\ CH_2COCH_2COR \end{array}$$

XIIa, R = C_6H_5
b, R = $C_6H_4OCH_3$-*p*
c, R = CH_3

In accordance with equation 3, the first two dipotassio salts I were treated with molecular equivalents of the ester to form XIIa and XIIb in yields of 70 and 40%, respectively. However, molecular equivalents of dipotassio salt I (R = CH_3) and the ester afforded a mixture of products. On the assumption that the initial conjugate addition product XIIc underwent further conjugate addition with the ester to form XIII, three molecular equivalents of I (R = CH_3) were treated with one of the ester. These conditions afforded XIIc in 40% yield along with another compound, the analysis of which was consistent with XIII (4%). If the latter product is indeed XIII, it might be obtained in better yield under appropriate conditions.



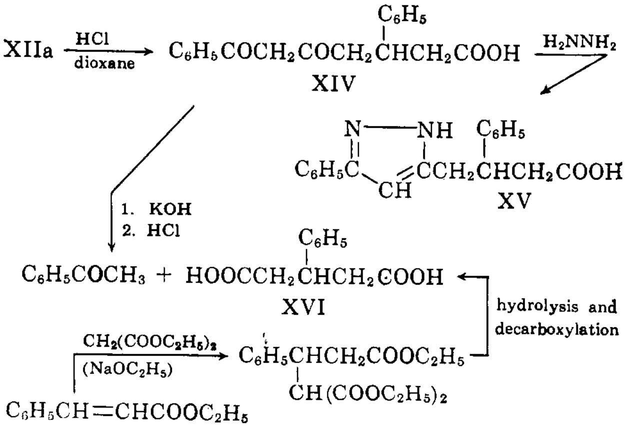
$$\begin{array}{l} C_6H_5CH{-}CH_2COOC(CH_3)_3 \\ | \\ CH_2COCH_2COCH_2 \\ \qquad\qquad\qquad | \\ \qquad\qquad C_6H_5CH{-}CH_2COOC(CH_3)_3 \end{array}$$

XIII

The structure of products XIIa–c were supported by analyses and infrared spectra, which showed bands characteristic of the β-diketone grouping in addition to a strong absorption in the ester carbonyl region (see Table VII).

The structure of the conjugate addition product XIIa was established by cleavage to the corresponding carboxylic acid XIV, which was not only converted to its pyrazole XV, but was also further cleaved to acetophenone and diacid XVI. The latter acid was independently synthesized by a known method[10] (Scheme A). The steps in this scheme were realized in good to excellent yields.

SCHEME A



The base-catalyzed cleavage of XIV in the direction indicated in Scheme A was expected from a consideration of data obtained in earlier studies of cleavage reactions of compounds with similar structures.[11]

(10) A. Michael, *Am. Chem. J.*, **9**, 115 (1887).

(11) W. M. Kutz and H. Adkins, *J. Am. Chem. Soc.*, **52**, 4036 (1930).

The structure of XIIb was established by base-catalyzed cleavage to form *p*-methoxyacetophenone and β-phenylglutaric acid (XVI) (equation 4). Diacid XVI was independently synthesized as indicated in Scheme A.

$$\text{XIIb} \xrightarrow[\text{C}_2\text{H}_5\text{OH, H}_2\text{O}]{\text{KOH}} p\text{-CH}_3\text{OC}_6\text{H}_4\text{COCH}_3 + \text{XVI} \qquad (4)$$

Experimental[12]

Reactions of Dipotassiobenzoylacetone with Methyl Cinnamate.—To a stirred solution of dipotassiobenzoylacetone,[2,4] prepared from 0.088 mole of benzoylacetone and 0.176 mole of potassium amide in 500 ml. of liquid ammonia, was added 7.17 g. (0.044 mole) of methyl cinnamate in 100 ml. of dry ether. After 0.5 hr., 11 g. of ammonium chloride was added and the ammonia replaced by ether. The resulting ethereal suspension was shaken with 200 ml. of 0.1 *N* hydrochloric acid and the two layers were separated. The ethereal layer was washed with water and dried over anhydrous magnesium sulfate. After filtering, the solvent was removed to leave a yellow solid, which was dissolved in 150 ml. of 95% ethanol. The resulting solution was cooled slowly to precipitate 1.3 g. (10%) of triketone IVa, m.p. 127.5–129.5° (for analysis and other data, see Table II).

The ethanol filtrate obtained on filtering product IVa was distilled to give about 5 g. of recovered benzoylacetone. The residue (7.5 g.) was recrystallized from 95% ethanol to give 5.3 g. (38%) of methyl 5,7-dioxo-3,7-diphenylheptanoate, m.p. 97–98°, and melting at 102.5–103° after four more recrystallizations from 95% ethanol. Its infrared spectrum showed bands at 5.75 and 6.20 μ. It gave a reddish brown enol test with ethanolic ferric chloride.

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.22. Found: C, 74.08; H, 6.41.

Acylations of Dipotassio β-Diketones with Phenyl Cinnamate to Form 1,3,5-Triketones (Tables I and II).—To a stirred solution of the dipotassio-β-diketone,[2,4] prepared from the appropriate β-diketone and potassium amide in 400–500 ml. of liquid ammonia, was added, during 10 min., a solution of phenyl cinnamate[13] in 20–50 ml. of dry ether, and the reaction mixture was stirred for 1.5–5 hr. (see Table I). The ammonia was removed on the steam bath as an equal volume of ether was gradually added. The resulting suspension was neutralized by addition of 20 ml. of glacial acetic acid in ether, followed by 200 ml. of aqueous 0.1 *N* hydrochloric acid (stirred). After shaking, the two layers were separated. The ethereal layer was washed with water, then extracted with saturated sodium bicarbonate solution, and washed again with water. The ethereal solution was dried over anhydrous magnesium sulfate and filtered. The solvent was removed under reduced pressure from the ethereal filtrate and the resulting residue was recrystallized generally from 95% ethanol. In the case of triketone VI, the crude product was dissolved in methanol, and the solution cooled in a Dry Ice–acetone bath. The resulting precipitate was filtered, dried, and recrystallized from petroleum ether (b.p. 30–60°) with cooling.

The sodium bicarbonate extracts of the reaction product from dipotassiobenzoylacetone (I, R = C_6H_5) and phenyl cinnamate were acidified to precipitate cinnamic acid (17%), which was identified by the mixture melting point method. In some experiments in which the molecular ratio of β-diketone (acetylacetone) to phenyl cinnamate was 2:1, a considerably higher yield (50–60%) of cinnamic acid was obtained. A blank experiment showed that no isolable amount of cinnamic acid is produced from phenyl cinnamate under the work-up conditions described earlier (phenyl cinnamate was recovered in 96% yield).

Cyclizations of 1,3,5-Triketones to Form 4-Pyrones (Tables III and IV).—A 1-g. sample of the triketone was dissolved in 30 ml. of concentrated sulfuric acid at 0°. After swirling for 20 min. at this temperature, the solution was poured into ice–water. The resulting precipitate was filtered and washed several times with water. The pyrones were recrystallized from appropriate solvents (see Table III). Pyrone IX was washed directly from filter paper with methanol and reprecipitated from the methanol solution by addition of water. After drying it was recrystallized from hexane.

Effect of Variation in Ratio of Acetylacetone to Benzoic Esters on Yields of Triketone XIa (Table V).—Essentially the only variant in these experiments was the ratio of β-diketone to ester. To a stirred solution of the appropriate amount of dipotassio salt I (R = CH_3), prepared from acetylacetone and two molecular equivalents of potassium amide in 400–500 ml. of liquid ammonia, was added, during 10 min., 0.03 mole of the phenyl or methyl benzoate in 50 ml. of dry ether. After stirring for 1 hr., the liquid ammonia was replaced by ether, and the resulting suspension was neutralized with acetic acid, followed by dilute hydrochloric acid. The layers were separated. The ethereal layer was washed with water and extracted with saturated sodium bicarbonate solutions. The triketone XIa was isolated from the ethereal solution, being recrystallized from ethanol. The benzoic acid was isolated from the sodium bicarbonate extracts.

In an experiment with molecular equivalents of acetylacetone and phenyl benzoate, almost a quantitative yield of phenol was detected by vapor phase chromatography. In certain other experiments with phenyl benzoate, potassium benzoate was isolated by filtering the ether insoluble salts. After dissolving these salts in a small quantity of water and acidifying the resulting solution, benzoic acid was collected by filtration.

Effect of Variation in Ratio of Benzoylacetone to Benzoic Esters on Yields of Triketone XIb (Table V).—To a stirred solution of dipotassio salt I (R = C_6H_5), prepared from benzoylacetone and two molecular equivalents of potassium amide in 500 ml. of liquid ammonia, was added 0.05 mole of methyl or phenyl benzoate in 50 ml. of ether. After stirring 30 min., excess ammonium chloride was added and the ammonia was evaporated. The residue was taken up in ether and cold, dilute hydrochloric acid. The layers were separated and the aqueous layer extracted with additional ether. The ethereal solutions were combined and dried over sodium sulfate. The solvent was evaporated and triketone XIb was obtained by recrystallization of the residue from ethanol.

In the experiment involving a 3:1 ratio of dipotassio benzoylacetone to methyl benzoate, 95% of the benzoylacetone that had not been converted to XIb was recovered by distillation of the recrystallization liquors. In the experiment involving phenyl benzoate, a substantial amount of an unidentified enolic compound, m.p. 135–137°, was obtained in addition to triketone XIb.

Conjugate Addition of Dipotassio Salts to *t*-Butyl Cinnamate (Tables VI and VII). (A) Reactions of Salts of I, R = C_6H_5 and $C_6H_4OCH_3$-*p*.—To a stirred solution of dipotassiobenzoylacetone, prepared from 0.055 mole of benzoylacetone and 0.11 mole of potassium amide in 400 ml. of liquid ammonia, was added 11.32 g. (0.055 mole) of *t*-butyl cinnamate[14] dissolved in 75 ml. of dry ether. After stirring for 40 min., 16 g. (0.3 mole) of ammonium chloride was added, and the ammonia was evaporated (steam bath) as an equal volume of ether was added. The resulting ethereal suspension was shaken with 200 ml. of 0.1 *N* hydrochloric acid and the two layers were separated. The ethereal layer was washed with water and dried over anhydrous magnesium sulfate. After filtering, the solvent was removed *in vacuo*, and the resulting residue was recrystallized from ethanol to give 14 g. (71%) of XIIa, m.p. 88–92°.

Similarly, dipotassioanisoylacetone, prepared from 0.063 mole of anisoylacetone and 0.126 mole of potassium amide in 500 ml. of liquid ammonia, was treated with 12.0 g. (0.063 mole) of *t*-butyl cinnamate in 50 ml. of ether. After 30 min., the reaction mixture was poured into 10 g. of ammonium chloride in 300 ml. of liquid ammonia and the ammonia was replaced by ether. The resulting ethereal suspension was worked up as described before to give 21 g. of light red oil. This oil was dissolved in 50 ml. of 95% ethanol and the solution cooled to precipitate 14 g. of solid, m.p. 56–65°. Recrystallization from hexane afforded 10 g. (40%) of XIIb (light green), m.p. 69–71°. Further recrystallization from hexane afforded white product, m.p. 69–70.5°.

(B) **Reaction of Salt I, R = CH_3.**—To a stirred solution of dipotassioacetylacetone prepared from 0.11 mole of acetylacetone

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[12] Melting points were taken on a Mel-Temp capillary melting point apparatus. Infrared spectra were determined with a Perkin-Elmer Infracord or Model 21 spectrophotometer by the potassium bromide pellet method. Ultraviolet spectra were determined with a Cary Model 14 recording spectrophotometer using 95% ethanol solutions with a 1-cm. sample cell. Elemental analyses were by Dr. Ing. A. Schoeller Mikro-Labor, Kronach, West Germany.

[13] This ester was prepared as described in "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 714.

[14] B. Abramovitch, J. C. Shivers, B. E. Hudson, and C. R. Hauser, *J. Am. Chem. Soc.*, **65**, 986 (1943).

and 0.22 mole of potassium amide, in 500 ml. of liquid ammonia, was added during 40 min., 8.9 g. (0.04 mole) of *t*-butyl cinnamate in 100 ml. of dry ether. After 20 min., 15 g. of ammonium chloride was added and the ammonia replaced by ether. The resulting ethereal suspension was shaken with 300 ml. of water and the two layers were separated. The ethereal layer was washed with water, then extracted with saturated sodium bicarbonate solution, and washed again with water. After drying over anhydrous magnesium sulfate and filtering, the solvent was removed *in vacuo* to leave 9.8 g. of light red oil. Trituration of this oil with hexane left a small amount of suspended solid, which was removed by filtration (later text). The oil was recovered by evaporation of the hexane filtrate and dissolved in 200 ml. of 95% ethanol. Water was added dropwise to the solution to produce, initially, some red oil that was removed, and, finally, slight cloudiness. After standing several days, there was obtained a fluffy precipitate, which was removed by filtration and to give 5.6 g. (40%) of XIIc, m.p. 47–48.5° (see Table VI).

The solid that was removed from the hexane suspension mentioned earlier was recrystallized from hexane to give crystals, m.p. 114–115°, the analysis of which fitted XIII (4%).

Anal. Calcd. for $C_{31}H_{40}O_6$: C, 73.20; H, 7.93. Found: C, 73.22; H, 7.78.

The infrared spectrum of this product was essentially identical with that of XIIc (see Table VII), though the relative intensity of the β-diketone absorption compared to that of the carbonyl band was lower for the former compound.

Cleavage of Conjugate Addition Product XIIa.—A solution of 3 g. of XIIa in 60 ml. of freshly purified dioxane[15] containing 1.4 ml. of concentrated hydrochloric acid was refluxed for 4 hr. After cooling, the mixture was shaken with ether and water, and the two layers were separated. The ethereal layer was extracted with several small quantities of saturated sodium bicarbonate solution and the combined bicarbonate extract was acidified carefully with dilute hydrochloric acid. The acid solution was extracted several times with ether and the combined ethereal extract was evaporated *in vacuo*. The residue was recrystallized from ethanol–water to give 1.2 g. (72%; this yield is corrected as a large quantity of unchanged XIIa was recovered) of diketo acid XIV, 5,7-dioxo-3,7-diphenylheptanoic acid, m.p. 148.5–149°. This acid gave a bright red enol test with ethanolic ferric chloride. Its infrared spectrum showed a broad band at 3.45 μ and strong bands at 5.87 and 6.20 μ.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 73.24; H, 5.77.

The pyrazole XV was prepared by dropwise addition of excess hydrazine to a solution of 0.2 g. of XIV in 30 ml. of 95% ethanol, the resulting solution being gently heated on the steam bath for 1 hr. After cooling, water was added, followed by dilute hydrochloric acid until the solution became cloudy. On standing, there was obtained 0.19 g. (96%) of the white crystalline product XV, m.p. 155.5–157°. It gave a negative enol test. Its infrared spectrum showed bands at 3.05 and 5.87 μ, but no absorption in the region 6.1–6.3 μ.

Anal. Calcd. for $C_{19}H_{18}O_2N_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.74; H, 5.88; N, 9.38.

Further cleavage of acid XIV was accomplished by heating a solution of 0.5 g. of it in 100 ml. of 0.1 *N* potassium hydroxide in 50% ethanol-water on the steam bath for 11 hr. After cooling, the mixture was shaken with ether and water, and the two layers were separated. The ethereal layer was dried over anhydrous magnesium sulfate. After filtering, most of the solvent was removed *in vacuo*. A vapor phase chromatogram of a sample of the remaining solution exhibited one peak, the retention time of which corresponded to that of authentic acetophenone. This ketone was isolated as its 2,4-dinitrophenylhydrazone (0.26 g., 54%), which, after recrystallization from ethanol-ethyl acetate, melted at 249–250° (lit.[16] m.p. 250°).

The alkaline layer containing the cleavage product (see text) was acidified and the acidic solution then extracted with ether. The solvent was removed from the ethereal extract and the residue was recrystallized from benzene to give 0.3 g. (90%) of β-phenylglutaric acid (mVI), m.p. 139.5–140.5°. This melting point was not depressed on admixture with an authentic sample of this diacid prepared as described previously.[10] The infrared spectra of the two samples of XVI were identical.

Cleavage of Conjugate Addition Product XIIb.—A solution of 0.5 g. of XIIb in 100 ml. of 50% ethanol containing 0.6 g. of potassium hydroxide was heated on the steam bath for 4 hr. After cooling, the solution was shaken with water and ether, and the two layers were separated. Most of the solvent was removed from the ethereal layer *in vacuo*. A vapor phase chromatogram on a sample of the remaining solution exhibited a peak, the retention time of which corresponded to that of *p*-methoxyacetophenone. This ketone was isolated as its 2,4-dinitrophenylhydrazone (0.28 g., 67%), m.p. 225–226° (lit.[17] m.p. 226–227°).

The alkaline layer containing cleavage product XVI (see text) was acidified with dilute hydrochloric acid and the acidic solution was then extracted with ether. The solvent was removed from the ether extract and the residue was recrystallized from benzene to give 0.28 g. (58%) of β-phenylglutaric acid (XVI), m.p. 135–138°. Its infrared spectrum was identical with that of authentic XVI.

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[15] See L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1957, p. 284.

[16] See R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., p. 317.

[17] E. Buchta and G. Schaeffer, *Ann.*, **597**, 129 (1955).

The Stereochemistry of the Neber Rearrangement

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The Neber reaction with the tosyl esters of either *syn-p*-methoxybenzyl *p*-nitrobenzyl ketoxime or *anti-p*-methoxybenzyl *p*-nitrobenzyl ketoxime produced essentially the same mixture of α-amino ketones in which the major product, after acetylation, was 1-acetamido-3-*p*-methoxyphenyl-1-*p*-nitrophenyl-2-propanone. The composition of the by-product, either ethyl *p*-nitrophenylacetate or ethyl *p*-methoxyphenylacetate, from a competing Beckmann rearrangement in each of the reaction mixtures provided evidence that the two stereoisomeric oxime tosylates were not interconverted prior to the Neber rearrangement. Consequently, the major product from the Neber rearrangement is determined by the relative acidities of the α protons and not by the stereochemistry of the oxime or by the insertion of an electron-deficient nitrogen species into a C–H bond.

Previous studies of the Neber rearrangement of an oxime tosylate (*e.g.*, **1b** or **2b**) to an α-amino ketone (*e.g.*, **5a** or **6a**)[2] have not provided an unambiguous answer to the questions of what influence the stereochemistry of the oxime function and the electronic influence of substituents play in determining the structure of the product. From these studies, two general mechanistic paths appeared possible. Either the reaction is initiated by removal of an α proton followed (or accompanied) by loss of the tosyloxy group (*e.g.*, **1** → **7** or **1** →

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[1] Massachusetts Institute of Technology Solar Energy Fellow, 1961–1962; Fellow of the U. S. Rubber Co. Post Graduate Foundation in Physical and Engineering Sciences, 1960–1961.

[2] (a) D. J. Cram and M. J. Hatch, *J. Am. Chem. Soc.*, **75**, 33 (1953); (b) M. J. Hatch and D. J. Cram, *ibid.*, **75**, 38 (1953); (c) H. O. House and W. F. Berkowitz, *J. Org. Chem.*, **28**, 307 (1963).