Dipyrrylmethenes.—Dipyrrylmethenes XVII,[16] XVIII,[17] XX,[18] XXIII,[9] XXII,[19] XXIV,[9] XXVI,[20] XXVII,[20] and XXVIII[21] are previously reported compounds. It appears that methenes XIX and XXI have not yet been recorded in the literature. Methene XXV has been prepared previously but was obtained by an alternative condensation reaction for use in the present study.

2-(5-Carboxy-3-ethyl-4-methyl-2-pyrrolyl)methylene-3-ethyl-4-methyl-2*H*-pyrrolenine-5-carboxylic Acid, Diethyl Ester (XIX).—This methene was prepared *via* the brominative oxidation of the corresponding methane (XI) in carbon tetrachloride solution, a method used successfully by Brunings and Corwin[20] for the preparation of a number of related methenes. The methane (750 mg.) was dissolved in carbon tetrachloride (50 ml.) and a solution of 0.105 ml. of bromine in the same solvent was then added. The resulting methene hydrobromide failed to separate as a solid even upon addition of hexane, so after subsequent addition of chloroform to dissolve a small amount of separated brownish viscous oil, the product was converted to its free base by treatment with 2-(dimethylamino)ethanol. The resulting solution was washed once rapidly with water and then evaporated to dryness *in vacuo* to give the orange free base. After repeated recrystallization from hexane, the product melted sharply at 112.5°.

Anal. Calcd. for $C_{21}H_{28}N_2O_4$: C, 67.72; H, 7.58; N, 7.52. Found: C, 67.73, 67.61; H, 7.57, 7.69; N, 7.71, 7.64.

2-(4-Chloro-3,5-dimethyl-2-pyrrolyl)methylene-4-chloro-3,5-dimethyl-2*H*-pyrrolenine (XXI).[22]—The corresponding 4,4′-free methene base (XXII) (200 mg.) was dissolved in glacial acetic acid (2.0 ml.). Sulfuryl chloride (0.20 ml.) was then added all at once with vigorous stirring. The red hydrochloride which separated almost immediately was collected by filtration, washed with ether, then converted to the crude free base in chloroform solution by shaking with calcium hydroxide. After filtration through a short alumina column to remove calcium salts and other impurities, the filtrate was evaporated to dryness. The residue was then chromatographed on alumina in benzene solution, followed by recrystallization from methanol: m.p. 160–162.5° (dec.).

Anal. Calcd. for $C_{13}H_{14}N_2Cl_2$: C, 58.00; H, 5.24; N, 10.41. Found: C, 57.97, 57.89; H, 4.89, 5.01; N, 10.14, 10.29.

2-(4-Ethyl-3,5-dimethyl-2-pyrrolyl)methylene-3,5-dimethyl-2*H*-pyrrolenine-4-carboxylic Acid, Ethyl Ester (XXV).—This compound has been previously prepared[15] *via* the acid-catalyzed condensation of 4-ethyl-3,5-dimethyl-2-pyrrolecarboxaldehyde with ethyl 2,4-dimethyl-3-pyrrolecarboxylate. We have obtained the same methene from a condensation of ethyl 5-formyl-2,4-dimethyl-3-pyrrolecarboxylate with 3-ethyl-2,4-dimethylpyrrole.

Anal. Calcd. for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 71.77, 71.98; H, 7.85, 7.77; N, 9.14, 9.28.

Spectroscopic Measurements.—The spectra were obtained with a Perkin–Elmer Model 21 Infrared spectrometer equipped with a calcium fluoride prism. The slit program was 955. The substances were dissolved in carbon tetrachloride to give solutions of 0.02*M* or less. The cell thickness varied from 1 to 5 cm., depending upon the concentration. Substances containing hydrogen-bonded N—H groups were run at different concentrations. The extinction coefficients of these compounds were found to be constant. The concentrations and cell thicknesses were adjusted so that the optical density at the absorption maximum was in the range of 0.3 to 0.7.

(16) A. H. Corwin and K. W. Doak, *J. Am. Chem. Soc.*, **77**, 464 (1955).
(17) A. H. Corwin and P. Viohl, *ibid.*, **66**, 1137 (1944).
(18) H. Fischer, P. Halbig, and G. Walach, *Ann.*, **452**, 268 (1927).
(19) H. Fischer and W. Zerweck, *Ber.*, **56**, 526 (1923).
(20) K. J. Brunings and A. H. Corwin, *J. Am. Chem. Soc.*, **66**, 337 (1944).
(21) H. Fischer and W. Zerweck, *Ber.*, **55**, 1947 (1922).
(22) The authors wish to thank Jimmie G. Tolar for his assistance in the preparation of this compound.

Acylations of Dilithio β-Diketones with Aliphatic Esters to Form 1,3,5-Triketones. Cyclizations to 4-Pyrones and 4-Pyridones

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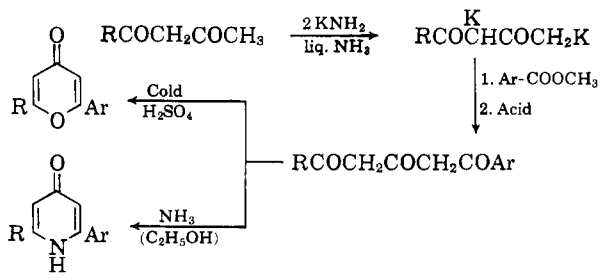
Although dipotassiobenzoylacetone appeared to ionize the α-hydrogen of ethyl acetate, dilithio β-diketones underwent acylations with this and other aliphatic esters to form the corresponding 1,3,5-triketones. Certain of the triketones were prepared from two different combinations of β-diketones and esters. These products were converted by cyclizations to corresponding 2,6-disubstituted 4-pyrones and 4-pyridones. These reactions, together with related ones described previously, furnish convenient, general methods for the synthesis of these three types of compounds.

Recently,[2,3] such β-diketones as acetyl- and benzoylacetones were aroylated at the terminal methyl group with aromatic esters through their dipotassio salts to form the corresponding 1,3,5-triketones, which were cyclized to give pyrones and pyridones (Scheme A).[4]



Scheme A

However, dipotassiobenzoylacetone failed to undergo acylation with phenyl propionate under similar conditions.[3] Since the starting β-diketone was recovered, ionization of the α-hydrogen of the ester was assumed to have occurred.[3]

We likewise recovered benzoylacetone after treatment of its dipotassio and disodio salts with ethyl acetate, no triketone being isolated. Since dilithiobenzoylacetone, but not dipotassiobenzoylacetone underwent an aldol type condensation with acetophenone,[5,6] it seemed possible that the dilithio salt might similarly undergo acylation with ethyl acetate and higher aliphatic esters. This has been realized. Thus, dilithio-

(1) National Science Foundation Cooperative Graduate Fellow (1959–1962).
(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 dianions of the intermediate dialkali salts are represented as dicarbanions, although other resonance forms may contribute more to the structure of the molecule.
(5) R. J. Light and C. R. Hauser, *J. Org. Chem.*, **26**, 1716 (1961).
(6) For other examples of such a metallic cation effect involving carbanions and acetophenone, see W. R. Dunnavant and C. R. Hauser, *ibid.*, **25**, 503 (1960); C. R. Hauser and W. R. Dunnavant, *ibid.*, **25**, 1296 (1960); W. I. O'Sullivan, F. W. Swamer, W. J. Humphlett, and C. R. Hauser, *ibid.* **26**, 2306 (1961).

TABLE I

YIELDS OF 1,3,5-TRIKETONES FROM β-DIKETONES AND ESTERS BY MEANS OF LITHIUM AMIDE

β-Diketone	Ester	1,3,5-Triketone	M.p. or b.p.,[a] °C.	Pressure, mm.	Yield, %[b] After 5 min.[e]	Yield, %[b] After 1 hr.[e]
Benzoylacetone	Ethyl acetate	1-Phenyl-1,3,5-hexanetrione (Ia)	105–107[c,d]	...	45 (66)[f]	40 (62)[f]
Benzoylacetone	Methyl propionate	1-Phenyl-1,3,5-heptanetrione (Ib)	115[g,h]	0.08	42 (79)[f]	45 (91)[f]
Benzoylacetone	Methyl isobutyrate	1-Phenyl-6-methyl-1,3,5-heptanetrione (Ic)	129[g]	0.2	43 (88)[f]	35 (64)[f]
Benzoylacetone	Methyl decanoate	1-Phenyl-1,3,5-tetradecanetrione (Id)	58–58.5[i,j]	...	...	40
Acetylacetone	Ethyl acetate	2,4,6-Heptanetrione (Ie)	85–89[k]	6.0	45 (59)[f]	...
Acetylacetone	Methyl propionate	2,4,6-Octanetrione (If)	70[l]	1.5	50	...
2-Acetylcyclohexanone	Ethyl acetate	1-(2-Oxocyclohexyl)-1,3-butanedione (II)	115.5–116[m,n]	...	...	24

[a] Melting points and boiling points given are for analytical samples in the cases of new compounds. [b] Yields are based on the β-diketones. The melting point or boiling point range for the product from which the yield was determined was usually slightly greater than that given in the table. [c] Recrystallized from isopropyl alcohol. [d] Reported m.p. 107–108°[2] and 106–107°; ref. 12, p. 1283. [e] Time allowed for condensation after addition of the ester and before replacement of the ammonia by ether (see Experimental). [f] Yield based on the amount of β-diketone used minus that recovered. [g] Obtained as a yellow liquid that decomposed after a few weeks. [h] Crystallized on cooling to give yellow needles, m.p. 35.5–37.5°. [i] Recrystallized from methanol. [j] Obtained as a very pale yellow solid. [k] Reported b.p. 121° at 10 mm.; J. N. Collie and A. Reilly, *J. Chem. Soc.*, **121**, 1984 (1922). The colorless distillate rapidly solidified to glassy, colorless plates, m.p. 42–44°. Reported m.p. 49°; ref. 13, p. 277. [l] Obtained as a colorless liquid which turned yellow within a few hours. [m] Recrystallized from acetone. [n] White solid.

TABLE II

INFRARED SPECTRA, ENOL TESTS, AND ANALYSES FOR 1,3,5-TRIKETONES

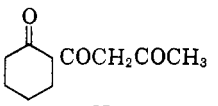
Triketone	Infrared spectra[a,b] μ	μ	μ	Enol test[c]	Empirical formula	Analyses,[a] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Ia	6.24, 6.37[d]			Reddish brown	...	...	...	...	...
Ib[e]	5.81, 6.25, 6.37			Reddish brown	$C_{13}H_{14}O_3$	71.54	71.82	6.47	6.49
Ic	5.83, 6.10, 6.35			Reddish brown	$C_{14}H_{16}O_3$	72.42	72.76	6.95	6.79
Id	6.19, 6.37[f,g]			Brown	$C_{20}H_{28}O_3$	75.98	75.89	8.92	9.02
Ie	5.82, 6.28			Reddish brown	...	...	...	...	...
If	5.82, 6.28			Reddish brown	$C_8H_{12}O_3$	61.52	61.00[h]	7.75	7.63
II	6.18, 6.30			Deep purple	$C_{10}H_{14}O_3$	65.91	65.98	7.75	7.72

[a] Ref. 17. [b] Absorption bands found in the enol–chelate region from 5.5 μ to 6.5 μ. [c] Color produced with ethanolic ferric chloride. [d] Same as reported in ref. 3. [e] The liquid form of triketone Ib was used. See footnotes *g* and *h*, Table I. [f] Shoulder. [g] Exhibited an exceptionally strong chelated hydroxyl band at 3.38 μ; see ref. 11. [h] See footnote *l*, Table I.

benzoylacetone was acylated with appropriate aliphatic esters to form triketones Ia–d.[7] Also, dilithioacetylacetone and dilithio-2-acetylcyclohexanone were acylated with appropriate aliphatic esters to form triketones Ie–f and II, respectively. The results are summarized in Tables I and II.

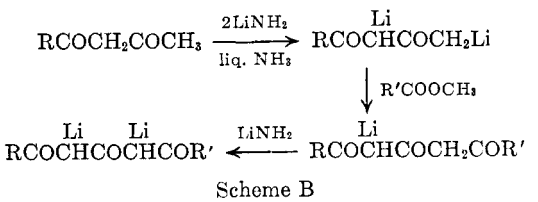
$RCOCH_2COCH_2COR'$

Ia. R = C_6H_5, R′ = CH_3
b. R = C_6H_5, R′ = C_2H_5
c. R = C_6H_5, R′ = i-C_3H_7
d. R = C_6H_5, R′ = n-C_9H_{19}
e. R = CH_3, R′ = CH_3
f. R = CH_3, R′ = C_2H_5



II

The general procedure for effecting these acylations involved addition of the β-diketone to three molecular equivalents of lithium amide in liquid ammonia, followed by two equivalents of the ester.[8] The yield of triketone was based on the β-diketone. Although only two equivalents of lithium amide are required to produce the dilithio β-diketone, an extra equivalent was employed to convert the monolithio triketone formed in the acylation to its dilithio salt (Scheme B). If the extra equivalent were not used, the final acid–base reaction in Scheme B would be effected by part of the dilithio β-diketone to regenerate the corresponding amount of β-diketone (as its monolithio salt). Because the extra equivalent of base may react with the ester to some extent (see below), an extra equivalent of ester was used over that required in the acylation (see Scheme B).



Scheme B

Table I shows that the yields of the triketones were 40–50% based on the β-diketone, except that of triketone II which was only 24%. The yields based on the β-diketone used minus that recovered, which are given in parentheses, were usually much higher. Certain of the yields were slightly better when the reaction mixture was worked up after five minutes than after one hour (see Table I).

Some of the acylations were accompanied by appreciable attack of the amide ion on the carbonyl group of

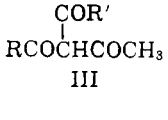
(7) A preliminary experiment with dilithiobenzoylacetone and ethyl acetate was performed in this laboratory by R. J. Light.

(8) These proportions of reactants correspond to the use of one molecular equivalent of ketone to two each of alkali amide and ester in the related synthesis of β-diketones when the yield is to be based on the ketone. See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **VIII**, 62, 114 (1954).

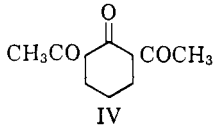
the ester to form the corresponding amide or imide, but these side-reaction products were readily separated from the triketones (see Experimental).

The acetylation of benzoylacetone with ethyl acetate was effected not only using the proportions of reactants given above, but also employing two molecular equivalents of lithium amide to one of the β-diketone and one-half of the ester.[9] The yield of the resulting triketone Ia was 42% based on the ester, which is about the same as that (40–45%) based on the β-diketone obtained in the general procedure. The earlier aroylations of dipotassio β-diketones[2,3] were generally effected employing the procedure in which the yield was based on the ester. For example, the benzoylation of dipotassioacetylacetone under these conditions afforded triketone Ia in 53–60% yield, which is somewhat higher than that (42%) obtained in the acetylation of dilithiobenzoylacetone with ethyl acetate under similar conditions. Since methyl benzoate has no α-hydrogen, the lower yield of Ia obtained in the latter experiment may indicate that even dilithiobenzoylacetone ionizes the α-hydrogen of ethyl acetate to some extent.

That the acylation products of benzoyl- and acetylacetones were the terminal methyl derivatives Ia–f, and not the methylene derivatives III, was established by cyclizations to 4-pyrones and 4-pyridones, since III could not have undergone these cyclizations (see next two sections). Similarly, the structure of the acylation product of 2-acetylcyclohexanone was established as II by cyclization. This showed that it was neither the methylene derivative corresponding to III nor the possible ring-methylene derivative IV which should not be expected to cyclize readily for steric reasons.



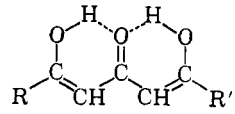
III



IV

Although some of IV might have been formed and remained undetected in the present work, evidence has been obtained previously that the similar alkylation of 2-acetylcyclohexanone with benzyl chloride affords only the corresponding terminal methyl derivative.[10]

Table II shows that all the triketones studied exhibit bands (medium to strong) in 6.1–6.5-μ region similar to bands observed for the previous aroylation products and indicative of an enol–chelate structure such as V.[3] However, triketones Ib, Ic, Ie, and If also exhibited weak bands in the 5.81–5.83-μ region characteristic of a free carbonyl group. It should be pointed out that the spectra of these four triketones (liquids) were determined neat using sodium chloride plates, while the spectra of triketones Ia, Id, and II, as well as the earlier aroylation products (crystalline solids), were determined by the potassium bromide pellet method.[3,17] Therefore, differences in the infrared spectra might be anticipated. Even triketone Ia exhibited a weak band at 5.82 μ when its infrared spectrum was determined in solution in carbon tetrachloride. Only

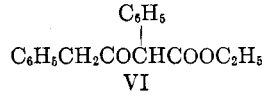


V

triketone Id exhibited a chelated hydroxyl band (strong), this band appearing at 3.38 μ.[11]

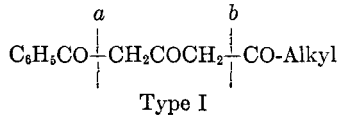
While the enol tests obtained for the triketones with ethanolic ferric chloride (see Table II) were different from those observed for the starting β-diketones, the colors of certain of them were difficult to reproduce. Thus, triketone Ia has given a reddish brown color when reasonable care has been taken in purification, but a green color when rigorously purified.[3] This may have been due to the presence of trace amounts of the starting β-diketones, which give cherry-red enol tests.

Whereas ethyl acetate and higher, purely aliphatic esters served as satisfactory acylating agents, ethyl phenylacetate, which has a relatively reactive α-hydrogen, failed to condense with dilithiobenzoylacetone. Instead, the self-condensation product of the ester (VI) was obtained, and benzoylacetone was recovered.



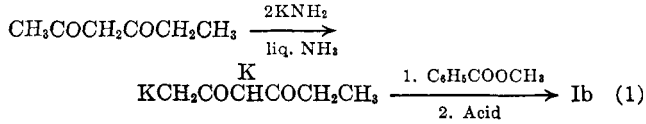
VI

The present acylations with aliphatic esters extend considerably the generality of the method of synthesis for 1,3,5-triketones from esters and β-diketones, which previously had been limited to aroylations.[2,3] For the synthesis of unsymmetrical, straight-chain triketones of type I, two different combinations of esters and β-diketones are possible depending on whether the molecule is to be put together at *a* or *b*.



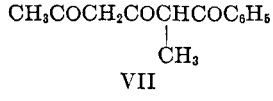
Type I

Actually triketone Ia has been put together at *a* and at *b* by benzoylation of acetylacetone and acetylation of benzoylacetone as indicated in Schemes A and B, respectively. Also, triketone Ib was put together not only at *b* by propionylation of benzoylacetone (see Scheme B), but also at *a* by benzoylation of propionylacetone (equation 1).



(1)

Although the yield of Ib by the latter method was only 37% based on the β-diketone, the product isolated appeared not to be contaminated with an appreciable amount of the isomeric, methylene derivative VII.



VII

This was indicated by comparison of the product and its corresponding 4-pyridone with authentic samples of Ib (prepared above by the propionylation of benzoylace-

(9) These proportions of reactants correspond to the use of one molecular equivalent each of alkali amide and ketone to one-half equivalent of ester in the related synthesis of β-diketones when the yield is to be based on the ester. See reference in footnote 8.

(10) T. M. Harris and C. R. Hauser, *J. Am. Chem. Soc.*, **81**, 1160 (1959).

(11) See L. J. Bellamy, "Infrared Spectra of Complex Molecules," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 96.

TABLE III

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

Triketone	Pyrone	M.p.,[a] °C.	Yield, %[b]
Ia	2-Methyl-6-phenyl-4*H*-pyran-4-one (VIIIa)	84–85[c]	86
Ib	2-Ethyl-6-phenyl-4*H*-pyran-4-one (VIIIb)	58–58.5	46
Ic	2-(2-Propyl)-6-phenyl-4*H*-pyran-4-one (VIIIc)	49–50	81
Id	2-(*n*-Nonyl)-6-phenyl-4*H*-pyran-4-one (VIIId)	51.5–52	93
Ie	2,6-Dimethyl-4*H*-pyran-4-one (VIIIe)	132–134[d]	34
II	Cyclohexeno[*b*]-6-methyl-4*H*-pyran-4-one (IX)	96–96.5	80

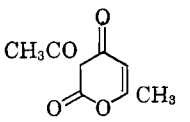
[a] Melting points given are for analytical samples in the cases of new compounds. All the pyrones were recrystallized satisfactorily from *n*-hexane. [b] The melting point range for the product from which the yield was determined was usually slightly greater than that given in the table. [c] Reported m.p. 85–87°; ref. 3. [d] Reported m.p. 132°; ref. 13, p. 273.

cold, concentrated sulfuric acid to give 4-pyrones VIIIa–e and IX, respectively. The results are summarized in Tables III and IV.

Table III shows that the yields of four of the 4-pyrones were excellent (80–93%). The yields of the other two pyrones probably could be improved.

The structures of the 4-pyrones were supported by analyses and by infrared and ultraviolet absorption spectra (see Table IV). These spectra were similar to those reported for the 4-pyrones obtained on cyclization of the aroylation products of dipotassio β-diketones.[3]

This method of synthesis of 2,6-disubstituted 4-pyrones through cyclizations of 1,3,5-triketones appears more convenient than most of the earlier methods, except that for pyrone VIIIe which may be obtained in



(3)

TABLE IV

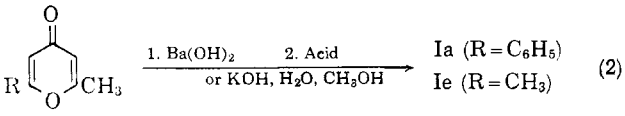
INFRARED AND ULTRAVIOLET SPECTRA AND ANALYSES FOR 4-PYRONES

Pyrone	Infrared spectra[a-c] μ	μ	μ	Ultraviolet spectra[a] λ_{max}, mμ	log ε	Empirical formula	Analyses,[a] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
VIIIa	6.00 s, 6.21 s[d]			272[e]	4.31[e]	...	...	...	...	...
VIIIb	6.08 s, 6.21 m, 6.29 m			273	4.32	$C_{13}H_{12}O_2$	77.98	77.99	6.04	6.05
VIIIc	6.04 s, 6.40 w			273	4.29	$C_{14}H_{14}O_2$	78.48	78.26	6.59	6.52
VIIId	6.05 s, 6.18 m			272	4.31	$C_{20}H_{26}O_2$	80.49	80.75	8.79	8.53
VIIIe	6.00 s, 6.25 s			248	4.20	...	...	...	...	...
IX	6.02 s, 6.27 s			252	4.15	$C_{10}H_{11}O_2$	73.14	72.94	7.36	7.44

[a] Ref. 17. [b] s = strong, m = medium, w = weak. [c] Absorption bands found in the region from 5.5 to 6.5 μ. [d] Reported bands at 6.00 and 6.19 μ; ref. 3. [e] Same as reported in ref. 3.

tone) and its corresponding 4-pyridone (Xb) (see Tables I and V and Experimental).

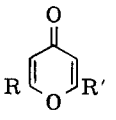
The present acylations at the terminal methyl group of β-diketones to form 1,3,5-triketones appear more convenient than the base-catalysed ring-opening of 4-pyrones, which has been employed previously for the syntheses of triketones Ia and Ie (equation 2).[12–14]

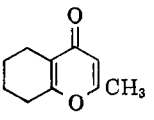


(2)

In fact, except in special cases, the 2,6-disubstituted 4-pyrones are themselves prepared more conveniently by cyclization of 1,3,5-triketones than by earlier methods, as discussed in the next section.

Cyclizations of 1,3,5-Triketones to Form 4-Pyrones.—Triketones Ia–e and II were cyclized by means of





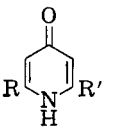
IX

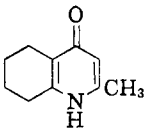
V. IIa. R = C_6H_5, R′ = CH_3
b. R = C_6H_5, R′ = C_2H_5
c. R = C_6H_5, R′ = *i*-C_3H_7
d. R = C_6H_5, R′ = *n*-C_9H_{19}
e. R = CH_3, R′ = CH_3

(12) S. Ruheman, *J. Chem. Soc.*, **93**, 1281 (1908).
(13) F. Feist, *Ann.*, **257**, 276 (1890).
(14) K. Balenović and R. Munk, *Arch. Kem.*, **18**, 41 (1946); *Chem. Abstr.*, **42** 2926a (1948).

good yield from commercially available dehydroacetic acid (equation 3).[15] Of the pyrones studied the only other one prepared previously was VIIIa.[3]

Cyclizations of 1,3,5-Triketones with Ammonia to Form 4-Pyridones.—Triketones Ia–f and II were cyclized with ammonia in ethanol to form 4-pyridones Xa–f and XI, respectively. The results are summarized in Tables V and VI.





XI

Xa. R = C_6H_5, R′ = CH_3
b. R = C_6H_5, R′ = C_2H_5
c. R = C_6H_5, R′ = *i*-C_3H_7
d. R = C_6H_5, R′ = *n*-C_9H_{19}
e. R = CH_3, R′ = CH_3
f. R = CH_3, R′ = C_2H_5

Table V shows that the yields of the 4-pyridones were 72–99%. Their structures were supported by analyses and by infrared and ultraviolet absorption spectra (see Table VI). These spectra were similar to those reported for the 4-pyridones obtained on cyclizations of the aroylation products of dipotassio β-diketones.[3] However, pyridones Xd, Xe, and XI failed to show clear-cut infrared bands in the 6.30–6.38-μ region, which were present in the spectra of the corresponding pyridones from the aroylations.[3]

This method of synthesis of 2,6-disubstituted 4-pyridones through cyclization of 1,3,5-triketones seems

(15) J. N. Collie, *J. Chem. Soc.*, **59**, 619 (1891).

TABLE V

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

Triketone	Pyridone	Recrystallization solvent	M.p.,[a] °C.	Yield,[b] %
Ia	2-Methyl-6-phenyl-4-(1*H*)-pyridone (Xa)	Acetone	174–176[c]	99
Ib	2-Ethyl-6-phenyl-4-(1*H*)-pyridone (Xb)	Acetone	154–155	72
Ic	2-(2-Propyl)-6-phenyl-4-(1*H*)-pyridone (Xc)	Ether[d]	117–118	84
Id	2-(*n*-Nonyl)-6-phenyl-4-(1*H*)-pyridone (Xd)	Acetone–water	88–89	72
Ie	2,6-Dimethyl-4-(1*H*)-pyridone (Xe)	Ethanol–acetone	231–232[e]	99
If	2-Ethyl-6-methyl-4-(1*H*)-pyridone (Xf)	Acetone	118–119	81
II	Cyclohexeno[*b*]-6-methyl-4-(1*H*)-pyridone (XI)	1,4-Dioxane	241–243 dec.	99

[a] Melting points given are for analytical samples in the cases of new compounds. [b] The melting point range for the product from which the yield was determined was usually slightly greater than that given in the table. [c] Reported m.p. 175–177° recrystallized from hot water.[3] [d] See Experimental. [e] Reported m.p. 227.5–229°; C. F. Rassweiler and R. Adams, *J. Am. Chem. Soc.*, **46**, 2763 (1924).

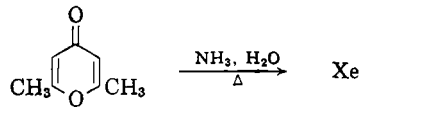
TABLE VI

INFRARED AND ULTRAVIOLET SPECTRA AND ANALYSES FOR 4-PYRIDONES

Pyridone	Infrared spectra[a-c] μ	μ	μ	Ultraviolet spectra[a] λmax mμ	log ε	Empirical formula	Analyses,[a] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
Xa	6.16 s,	6.34 m,	6.58 s[d]	239[e]	4.42[e]	...	...	...	...	...	...	...
Xb	6.20 s,	6.38 m,	6.68 s	238	4.38	$C_{13}H_{13}NO$	78.32	77.98	6.57	6.36	7.03	6.96
Xc	6.18 s,	6.27 m,	6.57 w	238	4.39	$C_{14}H_{15}NO$	78.84	78.65	7.09	7.32	6.57	6.51
Xd	6.23 s,	6.65 s		238	4.45	$C_{20}H_{27}NO$	80.76	80.89	9.15	8.93	4.71	4.72
Xe	6.20 s,	6.75 s		257	4.16	...	...	...	...	...	...	...
Xf	6.18 s,	6.35 m,	6.64 s	257	4.21	$C_8H_{11}NO$	70.04	69.56	8.08	8.11	10.21	10.16
XI	6.17 s,	6.64 s		263	4.20	$C_{10}H_{13}NO$	73.59	73.52	8.03	8.12	...	...

[a] Ref. 17. [b] s = strong, m = medium, w = weak. [c] Absorption bands found in the region from 5.5 to 6.8 μ. [d] Reported bands at 6.16 μ, 6.34 μ, 6.55 μ; ref. 3. [e] Reported ultraviolet spectrum: λ_{max} = 238 μ; log ε = 4.40; ref. 3.

more convenient than methods involving reactions of 4-pyrones with ammonia or ammonia derivatives, which have been employed previously to prepare Xe (equation 4)[16] and other 4-pyridones.[3] Of the pyridones studied in the present work the only other one prepared previously was Xa.



(4)

Experimental[17]

Acylations of β-Diketones with Aliphatic Esters to Form 1,3,5-Triketones.—In Table I are summarized the yields of 1,3,5-triketones obtained using three molecular equivalents of lithium amide to one of β-diketone and two of ester. Procedures are described below.

(A) Acylations of Benzoylacetone.—To a stirred suspension of 0.15 mole of lithium amide[18] in 500 ml. of commercial, anhydrous liquid ammonia was added 8.1 g. (0.05 mole) of benzoylacetone dissolved in 50 ml. of anhydrous ether to produce a yellowish green mixture of dilithiobenzoylacetone and lithium amide. After stirring for 1 hr., a solution of 0.1 mole of the appropriate ester in 50 ml. of anhydrous ether was added during 1–2 min. in certain experiments and for 1 hr. in certain others (see Table I), and the ammonia then was evaporated as an equal volume of anhydrous ether was added. The resulting ethereal suspension was poured, with stirring, into a slight excess of cold, dilute acetic acid. After shaking thoroughly, the two layers were separated, care being taken that the aqueous layer was weakly acidic. The ether layer was combined with an ethereal extract of the aqueous phase and washed with saturated sodium bicarbonate solution, followed by saturated sodium chloride solution. The ethereal solution was dried over anhydrous magnesium sulfate and the solvent removed. The crude residues were worked up as described below.

In the preparation of triketones Ia and Ib, the unchanged ester and benzoylacetone were removed from the crude residues by fractional distillation *in vacuo*.[19] The remaining residue in the former preparation was recrystallized to give Ia, and that in the latter was distilled to give Ib. A sample of triketone Ia was shown to be identical with a sample of this compound prepared by the benzoylation of acetylacetone[2,3] by comparison of infrared spectra and by the mixed melting point method.

In the preparation of triketone Ic the crude residue was boiled with hexane on a steam bath and the mixture filtered. The solvent was removed from the filtrate, and the residue was fractionated *in vacuo* to give β-diketone and triketone. The solid on the funnel was identified as diisobutyramide (0.45 g., 6%), m.p. 174–175.5° and 175.5–176° after recrystallization from ethanol–hexane; reported m.p. 174°.[20]

Anal. Calcd. for $C_8H_{15}NO_2$ (diisobutyramide): C, 61.16; H, 9.62; N, 8.92. Found: C, 61.00; H, 9.34; N, 8.95.

In the preparation of triketone Id the crude residue was fractionally crystallized from hexane to give, first, 4.65 g. (27%) of decanoamide, m.p. 91–93.5°, and, second, triketone Id. Recrystallization of the amide from hexane raised the melting point to 98–98.5°, reported m.p. 98°.[21]

Anal. Calcd. for $C_{10}H_{21}NO$ (decanoamide): C, 70.12; H, 12.36; N, 8.18. Found: C, 70.51; H, 12.34; N, 8.40.

(B) Acylations of Acetylacetone.—To a stirred suspension of 0.3 mole of lithium amide in 500 ml. of anhydrous liquid ammonia was added 10.0 g. (0.1 mole) of acetylacetone in 50 ml. of anhydrous ether[22] to produce a grayish white mixture of dilithioacetylacetone and lithium amide. After stirring for 1 hr., a solution of 0.2 mole of the ester in 75 ml. of anhydrous ether was added during 1–2 min. The resulting reaction mixture was stirred for 5 min. or 1 hr. (see Table I) and then worked up as

(16) Z. H. Skraup and J. Priglinger, *Monatsh.*, **31**, 367 (1910).

(17) Melting points were taken on a Mel-Temp capillary melting point apparatus. Infrared spectra were determined with a Perkin–Elmer Infracord by the potassium bromide pellet method for solids and by using sodium chloride plates for liquids. Ultraviolet spectra were determined with a Cary Model 14 recording spectrophotometer using 2 × 10^{-5} *M* solutions in 95% ethanol with a 1-cm. sample cell. Elemental analyses were by Dr. Ing. A. Schoeller, Mikro-Labor, Kronach, West Germany.

(18) See W. R. Dunnavant and C. R. Hauser, *J. Org. Chem.*, **25**, 503 (1960).

(19) During the distillation the condenser was heated with a heat lamp to prevent solidification of the benzoylacetone.

(20) A. W. Hofmann, *Ber.*, **15**, 981 (1882).

(21) See ref. 20, p. 984.

(22) The ammonium salt which forms when acetylacetone comes in contact with liquid ammonia (see ref. 2 and 3) was broken loose from the neck of the flask periodically with a spatula.

described above under A to give crude product residues. The unchanged esters and acetylacetone were removed from the crude residues by fractional distillation, and the remaining product residues were fractionated *in vacuo* to give triketones Ie and If.

The pot residue remaining after the fractionation of triketone If was recrystallized from ethanol–hexane to give about 0.2 g. (1–2%) of dipropionamide, m.p. 155–155.5°, reported m.p. 152–153°.[23]

Anal. Calcd. for $C_6H_{11}NO_2$ (dipropionamide): C, 55.78%; H, 8.54%. Found: C, 55.87%; H, 8.77%.

(C) Acetylation of 2-Acetylcyclohexanone.—To a stirred suspension of 0.3 mole of lithium amide was added 14.0 g. (0.1 mole) of 2-acetylcyclohexanone[24] in 75 ml. of anhydrous ether to produce a grayish white mixture of dilithio-2-acetylcyclohexanone and lithium amide. After stirring for 1 hr., a solution of 17.6 g. (0.2 mole) of ethyl acetate in 75 ml. of anhydrous ether was added during 1–2 min. The resulting reaction mixture was stirred for 1 hr., and then worked up as described under A to give crude residue, which was recrystallized directly to give triketone II.

Benzoylation of Propionylacetone.—Propionylacetone was prepared by alkylating disodioacetylacetone with methyl iodide in liquid ammonia.[25] The product boiled at 68–70° at 36 mm.[26]

A solution of 11.4 g. (0.1 mole) of propionylacetone in 100 ml. of anhydrous ether was added to a stirred suspension of 0.3 mole of lithium amide in 600 ml. of liquid ammonia to give a grayish-white mixture of dilithiopropionylacetone and lithium amide. After stirring for 30 min., a solution of 27.2 g. (0.2 mole) of methyl benzoate in 75 ml. of anhydrous ether was added, and the stirring continued for 30 min. The reaction mixture was worked up essentially as described above for the propionylation of benzoylacetone to give 8 0 g. (37% or 49% based on the β-diketone used minus that recovered) of triketone Ib, b.p. 117–119° at 0.1 mm., which agrees with the boiling point of this compound prepared by the method described above (see Table I).

A 1.66-g. sample of this product was cyclized with ammonia in ethanol (see below) to give 1.06 g. (70%) of pyridone Xb, m.p 152–153°. This melting point was not depressed on admixture of this product with a sample of Xb prepared as described below, and the infrared spectra of the two samples were identical (see Tables V and VI).

Cyclizations of 1,3,5-Triketones with Sulfuric Acid to Form 4-Pyrones (Tables III and IV).—A 1-g. sample of the triketone was dissolved in 10 ml. of concentrated sulfuric acid at 0°. After swirling for 10 min. at this temperature, the solution was poured into ice–water and worked up by one of the procedures described below.

In the cyclization of triketone Ia the solid hydrate which precipitated[5] was filtered and shaken in a separatory funnel with hot hexane and saturated sodium bicarbonate solution. The layers were separated. Cooling of the hexane solution precipitated pyrone VIIIa. A mixed melting point of VIIIa with authentic 2-methyl-6-phenyl-4*H*-pyran-4-one[3] showed no depression, and the infrared spectra of the two compounds were identical.

In the cyclizations of triketones Ib–d the cold, aqueous solution was extracted with ether. The extract was washed with water, followed by saturated sodium bicarbonate solution, and dried over anhydrous magnesium sulfate. The solvent was removed and the residue recrystallized from an appropriate solvent (Table III).

In the cyclizations of triketones Ie–f and II the cold, aqueous solution was first neutralized with saturated sodium bicarbonate solution, then extracted with ether and worked up as described above in the cyclizations of triketones Ib–d.

Cyclizations of 1,3,5-Triketones with Ammonia to Form 4-Pyridones (Tables V and VI).—To 1 g. of the triketone dissolved in 50 ml. of absolute ethanol in a 125-ml. erlenmeyer flask was added commercial, anhydrous liquid ammonia until the flask became cold. The solution was evaporated to dryness on a steam bath, and the entire process was repeated with the residue. The pyridone was isolated by one of the procedures described below.

Pyridones Xa and XI were isolated by direct recrystallization of the residue from an appropriate solvent (Table V).

Pyridones Xb and Xe were isolated by washing the residues with ether and hexane, respectively to remove impurities before recrystallization from an appropriate solvent (Table V).

In the preparation of pyridone Xc the residue was an oil which solidified on treatment with ether–hexane accompanied by cooling and scratching. Attempts to recrystallize Xc from various solvents gave oils. The product was finally purified by dissolving the oil in absolute ethanol, filtering to remove any solid impurities, evaporating to dryness, and washing the remaining, crushed solid several times with ether (see footnote *d*, Table V).

In the preparation of pyridone Xd the residue was first crystallized from ether–petroleum ether (b.p. 30–60°) and then recrystallized from acetone–water.

In the cyclization of triketone If crude pyridone Xf precipitated during the second treatment with absolute ethanol and liquid ammonia. The solid was filtered, placed overnight in a vacuum desiccator at 1 mm., and recrystallized from acetone after treatment with Norite.

(23) R. Otto and J. Troeger, *Ber.*, **23**, 759 (1890).

(24) For the preparation of this β-diketone see reference in footnote 8, p. 131.

(25) The details of this method will be published soon by K. G. Hampton, T. M. Harris, and C. R. Hauser. Similar alkylations have been described previously; see ref. 2 and R. B. Meyer and C. R. Hauser, *J. Org. Chem.*, **25**, 158 (1960).

(26) For other methods for preparing this compound see reference in footnote 8, pp. 122–124.

Synthesis of Some Spirobarbiturates

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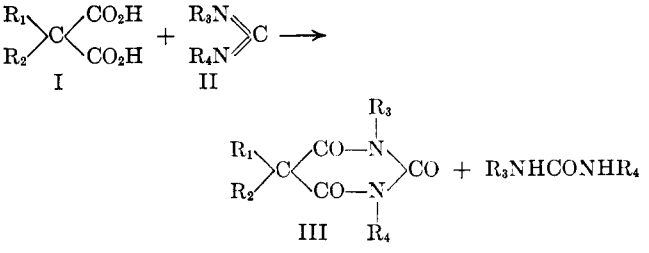
The synthesis of several spirobarbiturates by a recent new method is described. Some electronic and steric factors affecting this synthesis are discussed.

Recently, a new method was described[2] for the synthesis of barbituric acids (III) which involves the reaction between malonic acid (I) and carbodiimides (II). The scope of this reaction has now been extended by the preparation of spirobarbiturates—a class of compounds known for their interesting physiological activity.[3]



The reaction of 1,1-cyclobutanedicarboxylic acid and 1,1-cyclopentanedicarboxylic acid with different carbo-

(1) National Science Foundation Undergraduate Research Participant.

(2) A. K. Bose and S. Garratt, (a) *J. Am. Chem. Soc.*, **84**, 1318 (1962); (b) *Tetrahedron*, in press.

(3) A. Burger, "Medicinal Chemistry," Vol. IV, Interscience Publishers, Inc., New York, N. Y., 1951, p. 129.