sequent heating at 90–100° had no effect. Addition of benzoyl peroxide or ammonium persulfate to aqueous emulsions of the esters had a similar result. Several attempts to copolymerize diethylaminoethyl and ethyl acrylates (weight ratio 1:10) in ethyl acetate solution and in aqueous emulsion, with benzoyl peroxide and ammonium persulfate, respectively, as catalysts, resulted in discoloration of the monomer but no appreciable polymerization. Diethyl- and dibutylaminoethyl acrylates were sealed in glass tubes and heated at 90° for one week without visible change. The tubes were than irradiated with ultraviolet light. Viscous, liquid polymers were thus formed.

No polymerization occurred when a 10% aqueous solution of the acetate of diethylaminoethyl acrylate containing 1% of benzoyl peroxide was refluxed for twenty-four hours. A 10% aqueous solution of the acrylate (salt) of diethylaminoethyl acrylate containing 0.06% (based on ester) of ammonium persulfate was placed in sunlight. After a few hours it polymerized vigorously, the entire solution being converted to a soft, pasty solid. This was soluble in water, from which it could be precipitated by sodium chloride. A sample of the polymer which had been precipitated from dilute hydrochloric acid and then from water was analyzed: N, found 2.95% (calcd. 5.75%).

A 1% aqueous solution of morpholinoethyl polyacrylate (prepared from polymer formed spontaneously while in the refrigerator) was added to a 1% aqueous solution of polyacrylic acid. A voluminous precipitate formed instantly. When dried it was hard and brittle.

Summary

The acrylic esters of eight alcohols containing tertiary amino groups were prepared by the alcoholysis of methyl or ethyl acrylate.

All attempts to polymerize the esters with benzoyl peroxide, ammonium persulfate or heat, whether in bulk, in solution or in aqueous emulsion, were failures. Ultraviolet light was effective in promoting polymerization.

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[CONTRIBUTION FROM THE BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, AGRICULTURAL RESEARCH ADMINISTRATION, U. S. DEPARTMENT OF AGRICULTURE]

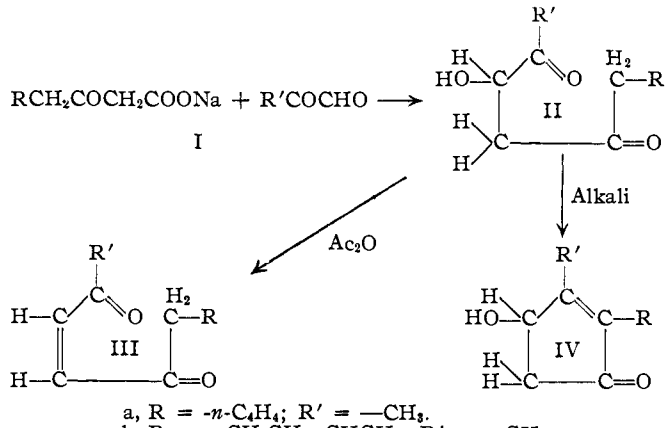
Constituents of Pyrethrum Flowers. XXIII. Cinerolone and the Synthesis of Related Cyclopentenolones[1]

BY MILTON S. SCHECHTER, NATHAN GREEN AND F. B. LAFORGE

Of the two substituted cyclopentenolones, pyrethrolone and cinerolone, the chrysanthemum acid esters of which constitute the principal insecticidal constituents of pyrethrum flowers, cinerolone, 2-(2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one, possesses the simplest structure. When it is re-esterified with *d-trans*-chrysanthemum monocarboxylic acid, the resulting cinerin I has been shown to be of about the same order of toxicity[2] as pyrethrin I, and it has the added advantage of decidedly greater stability. For these reasons cinerolone has been given first consideration from the standpoint of synthesis.

In previous articles[3,4] the synthesis of 2-*n*-butyl-4-hydroxy-3-methyl-2-cyclopenten-1-one (*dl*-dihydrocinerolone) and the corresponding 2-*n*-amyl compound (*dl*-tetrahydropyrethrolone) has been described. The method employed consisted in the introduction of bromine in the 4-position of dihydrocinerone and tetrahydropyrethrone, respectively, by the agency of N-bromosuccinimide and the replacement of the halogen by hydroxyl. This method failed[5] when the side chain was unsaturated, as it is in cinerone and pyrethrone.

It has been shown[6] that 3-methyl-2-cyclopentenones with a side chain in position 2 are readily obtained by the cyclization of 1,4-diketones con-



a, R = -*n*-C_4H_4; R′ = $-CH_3$.
b, R = $-CH_2CH{=}CHCH_3$; R′ = $-CH_3$.
c, R = $-CH_2CH{=}CH_2$; R′ = $-CH_3$.
d, R = $-CH_2C(CH_3){=}CH_2$; R′ = $-CH_3$.
e, R = $-CH_2CH_2CH{=}CH_2$; R′ = $-CH_3$.
f, R = $-CH_2CH{=}C(CH_3)_2$; R′ = $-CH_3$.
g, R = $-H$; R′ = $-CH_3$.
h, R = $-CH_2CH{=}CH_2$; R′ = $-C_6H_5$.

taining a $-CH_2-$ group in the 5-position. If 2-hydroxy-1,4-diketones also having a $-CH_2-$ group in the 5-position could be prepared, they might be expected to cyclize with the elimination of a molecule of water to 2,3-disubstituted-4-hydroxy-2-cyclopenten-1-ones. It will be shown that this

(1) A communication to the Editor on this subject appeared in THIS JOURNAL, **71**, 1517 (1949), and an article in *Agr. Chemicals*, **4**, [6], 57 (1949). This article not copyrighted.

(2) Gersdorff, *J. Econ. Entom.*, **40**, 878 (1947).

(3) Soloway and LaForge, THIS JOURNAL, **69**, 979 (1947).

(4) Dauben and Wenkert, *ibid.*, **69**, 2074 (1947).

(5) LaForge, Green and Gersdorff, *ibid.*, **70**, 3707 (1948).

(6) Hunsdiecker, *Ber.*, **75B**, 455 (1942); see also Blaise, *Compt. rend.*, **158**, 708 (1914).

route can, in fact, be used to prepare a variety of substituted cyclopentenolones.

Only two 2-hydroxy-1,4-diketones appear to have been described in the literature—3-hydroxy-2,5-hexanedione ($CH_3COCHOHCH_2COCH_3$) and 2-hydroxy-1-phenyl-1,4-pentanedione ($C_6H_5COCHOHCH_2COCH_3$)—the chemistry and biochemistry of which have been extensively studied by Henze and colleagues.[7] They were obtained by the aldol condensation of methylglyoxal (pyruvaldehyde) and phenylglyoxal, respectively, with sodium acetoacetate in faintly alkaline aqueous solution at room temperature. In addition, Shaffer, Friedemann, and co-workers,[8] who were also interested in antiketogenesis, investigated the reaction of a number of aldehydes, glyoxal, etc., on alkali acetoacetate both with and without the addition of peroxide, but they failed to isolate or characterize the reaction products.

Henze represented his reaction as proceeding *via* an intermediate condensation product containing a carboxyl group (as the sodium salt), which had to be decarboxylated by warming with acid in order to produce the hydroxydiketone. We have found that the decarboxylation proceeds spontaneously under the conditions of the reaction, the final product being the hydroxydiketone, which can be extracted directly from the alkaline reaction mixture. We have also shown that the reaction can be carried out under acidic conditions, in which case carbon dioxide is liberated instead of being converted to alkali bicarbonate.

Hunsdiecker and Blaise[6] specified that a $-CH_2-$ group in the 5-position of 1,4-diketones is an essential condition for their cyclization to cyclopentenones, and that hence a compound such as acetonylacetone cannot be cyclized. This rule probably holds true in the case of 2-hydroxy-1,4-diketones, since we were unable to cyclize Henze's ketol, 3-hydroxy-2,5-hexanedione (IIg).

Preparation of 2-Hydroxy-1,4-diketones (Formula II).—Convenient methods for the preparation of saturated and unsaturated β-keto esters with a $-CH_2-$ group in the γ-position are described elsewhere[9,10] and in this article. With these esters as starting materials, a number of 2-hydroxy-1,4-diketones of the general formula II have now been prepared by the condensation of pyruvaldehyde with the alkali salts of the β-keto acids of formula I.. Also, 2-hydroxy-1-phenyl-7-octene-1,4-dione (IIh), has been prepared by the condensation of phenylglyoxal with the potassium salt of Ic.

Although the reactions can be carried out under acid conditions, we have generally prepared the hydroxydiketones by the reaction of a substituted glyoxal, R'COCHO, with a faintly alkaline aqueous solution of an alkali salt of a β-keto acid, RCH_2COCH_2COOH, in substantially equimolecular proportions, the final solution being adjusted so that it is near *p*H 8. It is inadvisable to have the solution too alkaline or too acidic. If it is too alkaline, some of the substituted glyoxal may dismutate to a hydroxy acid, whereas, if it is too acidic, some of the β-keto acid may decompose; in either case, the yield of desired product will be lowered. In order to carry out the reaction under acid conditions, buffers may be used or acid may be added as the reaction proceeds. Provided that the reaction is not made too acidic nor too alkaline at first, the *p*H will tend to adjust itself to a suitable value because of the production of alkali bicarbonate. The reactions are practically complete in about six hours at room temperature but they may be allowed to proceed for a day or two. In general, the hydroxydiketones were isolated in about 50–75% yields by extraction with ether and distillation *in vacuo*.

With the exception of 2-hydroxy-1-phenyl-7-octene-1,4-dione, IIh, which is a colorless, crystalline solid, all of the hydroxydiketones are practically colorless liquids. They all reduce Fehling solution rapidly in the cold.

Attempts to prepare acetates by treatment with acetic anhydride and sodium acetate led instead to the formation of anhydro compounds of formula III. The anhydro compounds form disemicarbazones almost instantaneously upon treatment with semicarbazide hydrochloride in pyridine–ethanol solution. In contrast to this behavior, the hydroxydiketones form semicarbazone derivatives very slowly. However, the semicarbazone derivatives of the hydroxydiketones are identical with those from the corresponding anhydro compounds as shown by analysis and mixed melting point behavior. Furthermore, these semicarbazones show dimorphism when recrystallized from different solvents, ethanol usually giving a higher melting form than acetic acid. We were not able to obtain the simple disemicarbazones of our hydroxydiketones; in every case dehydration occurred. The possibility of pyrazoline formation as noted by Henze[7g] is not excluded.

It is interesting to note that the formation of the hydroxydiketones from pyruvaldehyde and salts of β-keto acids takes place under what is considered to be physiological conditions and there is a possibility that the synthesis of pyrethrolone and cinerolone may proceed via a similar mechanism in the pyrethrum plant. In fact, there is a strong resemblance between this reaction and the elegant "physiological" synthesis of tropinone by Schöpf and Lehmann.[11]

(7) (a) Henze, *Z. physiol. Chem.*, **189**, 121 (1930); (b) **195**, 248 (1931); (c) **198**, 82 (1931); (d) **200**, 232 (1931); (e) **232**, 117 (1935); (f) **232**, 123 (1935); (g) Henze and Müller, *ibid.*, **193**, 88 (1930); (h) **200**, 101 (1931); (i) **214**, 281 (1933); (j) Stöhr and Henze, *ibid.*, **206**, 1 (1932); (k) **212**, 111 (1932); (l) Stöhr, *ibid.*, **235**, 265 (1935); (m) **240**, 23 (1936); (n) Henze and Stöhr, *Wien. klin. Wochschr.*, **50**, 721 (1937).

(8) Shaffer and Friedemann, *J. Biol. Chem.*, **61**, 585 (1924); Friedemann, *Proc. Soc. Expil. Biol. Med.*, **23**, 370 (1926); and other articles mentioned in these references.

(9) Soloway and LaForge, THIS JOURNAL, **69**, 2677 (1947).

(10) Green and LaForge, *ibid.*, **70**, 2287 (1948).

(11) Schöpf and Lehmann, *Ann.*, **518**, 1 (1935); see also Schöpf and Arnold, *ibid.*, **558**, 109 (1947), and Schöpf and Thierfelder, *ibid.*, **518**, 127 (1935).

Cyclization of 2-Hydroxy-1,4-diketones (II) to 4-Hydroxycyclopentenones (IV).—The cyclization is accomplished by agitation of the hydroxydiketones with aqueous alkali at room temperature yielding the substituted cyclopentenolones. Employing about 10–20 volumes of 1 to 10% sodium hydroxide solution for several hours, yields of about 50–65% were obtained. The distilled products are practically colorless oils except IVh, which is crystalline. When pure, they do not reduce Fehling solution in the cold but only on warming.

Among the cyclopentenolones prepared, the one of formula IVb, obtained by the cyclization of the hydroxydiketone IIb, merits special consideration because it corresponds to the structure assigned to cinerolone.[12] The synthetic 2-(2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVb) was characterized by the preparation of the semicarbazone, acetate semicarbazone and the 3,5-dinitrobenzoate. The corresponding derivatives prepared from natural *dl*-cinerolone, with the exception of the semicarbazone, have melting points near those derived from the synthetic cyclopentenolone. In each case, however, mixed melting points of the corresponding derivatives from the two sources showed very definite depressions leaving no doubt as to their non-identity (see Table I).

Catalytic hydrogenation of the synthetic compound IVb furnished as the major product 2-butyl-4-hydroxy-3-methyl-2-cyclopenten-1-one (*dl*-dihydrocinerolone) identical with the compound (IVa) obtained by direct synthesis. The identity of the hydrogenated compound with compound IVa and also with *dl*-dihydrocinerolone prepared by the hydrogenation of *dl*-cinerolone from the natural source, has been established by mixed melting point determinations of the corresponding semicarbazones, the 3,5-dinitrobenzoates, and the 2,4-dinitrophenylhydrazones. The identity of the semicarbazones was further confirmed by a comparison of their X-ray diffraction patterns.

The possibility that the crotyl halide and hence all of the subsequent intermediates employed in the synthesis of 2-(2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVb), contained any considerable amount of the methyl vinyl carbinyl isomer due to an allylic rearrangement[13] has been excluded by the hydrogenation result. The only remaining explanation for the difference between this synthetic cyclopentenolone (IVb) and natural *dl*-cinerolone seems to be that of *cis–trans* isomerism. Harper[14] has also attributed the lack of identity of synthetic 2-(2-butenyl)-3-methyl-2-cyclopenten-1-one with cinerone obtained from natural cinerolone to geometric isomerism. In addition to isomerism due to the allylic rearrangement, crotyl halides may exist as mixtures of *cis* and *trans* isomers but there is scant information on this point.[15] However, it is probable that crotyl halides exist predominantly in the *trans* form, and that hence our synthetic product (IVb) has a *trans* configuration at the double bond in the side chain, whereas natural cinerolone is probably the *cis* isomer.

All of the substituted cyclopentenolones described in this article have been esterified[16] with natural *d-trans*-chrysanthemum monocarboxylic acid yielding esters analogous to cinerin I. In addition, two of them, IVb and IVc, have been esterified with synthetic *dl-cis-* and *dl-trans*-chrysanthemum monocarboxylic acids.[17]

Most of these esters exhibited a high order of insecticidal activity, with associated knock-down and paralytic effects characteristic of pyrethrum extracts. Some of them (those of IVc and IVd) exceeded the reference test standard (pyrethrin I + cinerin I 50%, pyrethrin II + cinerin II 50%) in their toxic action against house flies when tested by the turntable method.[18] Natural *d-trans*-chrysanthemum monocarboxylic acid yielded esters more toxic than the synthetic *dl-cis–trans* mixture.

The processes for the preparation of these substituted cyclopentenolones utilize starting materials which are readily available commercially. Although the yields are fair, they undoubtedly could be increased by systematic study. Campbell and Harper[19] have recently improved the synthesis of chrysanthemum monocarboxylic acid and it is possible that other acids may be found that might replace it in the synthesis of insecticidally active esters. A technical synthesis of insecticides of the pyrethrum type now seems to have been brought within the realm of possibility.

Experimental

All melting points are corrected.

α-Alkenyl Acetoacetic Esters

Ethyl α-Allylacetoacetate.[20]—A solution of sodium ethoxide prepared by dissolving 46 g. (2 moles) of sodium in 700 ml. of absolute ethanol was cooled to 15° and 286 g. (2.2 moles) of ethyl acetoacetate was added to the stirred solution. After one-half hour 153 g. (2 moles) of allyl chloride was added at once, and the stirring was continued for a short time. The reaction was then allowed to proceed overnight, and completed by refluxing for one hour. After the sodium chloride had been removed by filtration, and most of the ethanol by distillation, the reaction product was distilled and a fraction collected between 85 and 105° (15 mm.), yield of crude product 250–300 g. The purity as calculated from ethoxyl determinations was found to range from 75–90%. This fraction, which contained some unreacted ethyl acetoacetate, was generally employed for the preparation of 5-hexen-2-one (allyl acetone). Pure ethyl α-allyl acetoacetate obtained by

(12) LaForge and Soloway, THIS JOURNAL, **69**, 2932 (1947).

(13) Winstein and Young, *ibid.*, **58**, 104 (1936).

(14) Harper, *J. Chem. Soc.*, 892 (1946).

(15) Van Dormael, *Bull. soc. chim. Belg.*, **52**, 100 (1943); Young and Andrews, THIS JOURNAL, **66**, 421 (1944); Hatch, Gordon and Russ, *ibid.*, **70**, 1093 (1948). In a recent private communication, Prof. Hatch has informed use of the successful preparation of *cis*-crotyl chloride; Hatch and Nesbitt, THIS JOURNAL, in press.

(16) LaForge and Barthel, *J. Org. Chem.*, **12**, 199 (1947).

(17) We are indebted to Dr. S. H. Harper for samples of the synthetic *dl-cis* and *dl-trans* acids.

(18) Gersdorff, *J. Econ. Entom.*, **42**, 532 (1949).

(19) Campbell and Harper, *J. Chem. Soc.*, 283 (1945).

(20) Philippi, *Monatsh.*, **51**, 278 (1929).

careful fractionation through a packed column distilled at 96-97° (14 mm.), $n^{26}D$ 1.4365.

Anal. Calcd. for $C_9H_{14}O_3$: OC_2H_5, 26.5. Found: OC_2H_5, 26.8.

Ethyl α-Crotylacetoacetate.[5]—The method employed was essentially the same as in the previous preparation, the proportions in a typical experiment being 260 g. (2 moles) of ethyl acetoacetate, 23 g. of sodium (1 mole) dissolved in 600 ml. of absolute methanol and 135 g. (1 mole) of crotyl bromide that had been fractionated through a glass helix-packed column, b. p. 106-109° (765 mm.), $n^{25}D$ 1.4786, d^{25}_4 1.3357. The constants reported[13] for crotyl bromide are b. p. 107° (760 mm.), $n^{25}D$ 1.4795, d^{25}_4 1.3335.

The excess of the solvent and the ethyl acetoacetate were removed by vacuum distillation and the 203 g. of residue was employed for the preparation of 5-hepten-2-one, any ester exchange which might have occurred being of no importance.

Ethyl α-methallylacetoacetate was prepared by the same procedure from 286 g. (2.2 moles) of ethyl acetoacetate, 46 g. (2 moles) of sodium dissolved in 600 ml. of absolute ethanol, and 181 g. (2 moles) of methallyl chloride. After removal of the solvent and the excess of ethyl acetoacetate, the residue was distilled and the fraction b. p. 98-112° (15 mm.) collected, $n^{26}D$ 1.4408; yield 280 g. (77%).

Anal. Calcd. for $C_{10}H_{16}O_3$: OC_2H_5, 24.4. Found: OC_2H_5, 24.0.

Methyl Alkenyl Ketones

5-Hexen-2-one (Allyl Acetone).[21]—Three hundred grams of crude ethyl α-allylacetoacetate (92% pure) was added to an aqueous solution of 112 g. of potassium hydroxide (100% basis) in 1 l. of water at 0° and the suspension was stirred until all but a small residue had dissolved. The solution was then kept in the refrigerator for three days. After the small amount of undissolved oil had been removed with petroleum ether, 60 ml. of sulfuric acid in 100 ml. of water was added to the aqueous solution in a flask equipped with a water condenser and the flask was heated on the steam-bath until no more carbon dioxide evolved. The separated oil was removed and the aqueous solution, after saturation with sodium chloride, was extracted with petroleum ether. The extract was combined with the separated oil, and the solution was washed with dilute alkali and with saturated salt solution. After drying the solution over potassium carbonate and removing the solvent, the residue was distilled; yield 93 g. (60% based on 92% ester, 48% based on the allyl chloride), b. p. 127-132° (760 mm.).

By the same procedure 170 g. (1 mole) of the pure ester yielded 83 g. (85%) of allyl acetone, b. p. 127-132° (760 mm.), $n^{27}D$ 1.4170.

5-Hepten-2-one (Crotyl Acetone).[5,21b].—Two hundred and three grams of crude ethyl α-crotylacetoacetate dissolved in 1 l. of a cold aqueous solution of 73 g. of potassium hydroxide (100% basis) after three days in the refrigerator furnished crude crotyl acetone on decarboxylation and isolation in the manner described for allyl acetone. Fractionation through a concentric tube column gave a forerun of 2.4 g., b. p. 148-151°, and 90.2 g. (81% overall yield based on crotyl bromide) of the desired product, b. p. 151-154° at 770 mm., $n^{25}D$ 1.4280.

5-Methyl-5-hexen-2-one (Methallyl Acetone).[21b]—This compound was prepared by saponification of 280 g. (1.52 moles) of ethyl α-methallylacetoacetate with 96 g. (1.71 moles) of potassium hydroxide (100% basis) in 650 ml. of water for four days in the refrigerator. The ketone was obtained in the usual manner. Fractionation gave 15 g. of forerun and 117 g. (69% yield) of the desired product, b. p. 142-154° at 760 mm., 90% of which distilled at 145-150°, $n^{27}D$ 1.4278. The **semicarbazone** was prepared, m. p. 136-137°.

Anal.[22] Calcd. for $C_8H_{14}ON_3$: N, 24.83. Found: N, 24.98.

Ethyl Esters of 3-Oxo-alkenoic Acids

The preparation of ethyl β-oxocaprylate and of ethyl 3-oxo-6-octenoate by carbethoxylation of 2-heptanone and 5-hepten-2-one, respectively, by the agency of sodium hydride has been described in previous articles.[5,9] By the same procedure the following esters have been prepared.

Ethyl 3-Oxo-6-heptenoate.—The proportions of the reactants were 90 g. (0.92 mole) of 5-hexen-2-one (allyl acetone), 44 g. (1.84 moles) of sodium hydride, and 218 g. (1.84 moles) of ethyl carbonate: yield 120 g. (77%), b. p. 107-111° (14 mm.), $n^{28}D$ 1.4393.

Anal. Calcd. for $C_9H_{14}O_3$: OC_2H_5, 26.5. Found: OC_2H_5, 25.8.

This ester has also been prepared by the forced condensation method. Ethyl carbonate, 350 g. (3 moles), and commercial sodium methylate, 30 g. (0.55 mole), were placed in a 2-l. flask equipped with a dropping funnel, a thermometer, a stirrer having a lubricated rubber seal, and a short column surmounted with a total reflux take-off head. Employing a vacuum of about 100 mm., 49 g. (0.5 mole) of allyl acetone was added dropwise over a period of three hours while about 100 ml. of distillate was collected using a take-off ratio of about 1 to 4. The temperature of the bath was about 90° and of the vapor about 62°. Two 50-ml. portions of ethyl carbonate were added at intervals of one hour during the distillation. A part of the remaining ethyl carbonate was distilled off; the solution was cooled and acidified with a slight excess of glacial acetic acid. Water was then added and the produced isolated in the usual manner to yield 60.7 g. (70.6%).

Ethyl 6-Methyl-3-oxo-6-heptenoate.—One hundred and twelve grams (1.04 moles) of 5-methyl-5-hexen-2-one (methallyl acetone), 50 g. (2.08 moles) of sodium hydride, and 248 g. (2.1 moles) of ethyl carbonate were employed in one experiment: yield 134 g. (70%), b. p. 119-125° (16 mm.), $n^{27}D$ 1.4468.

Anal. Calcd. for $C_{10}H_{16}O_3$: OC_2H_5, 24.4. Found: OC_2H_5, 24.1.

Ethyl 7-Methyl-3-oxo-6-octenoate.—This compound was obtained from 126 g. (1 mole) of 6-methyl-5-hepten-2-one,[23] 48 g. (2 moles) of sodium hydride, and 236 g. (2 moles) of ethyl carbonate: yield 141 g. (71%), b. p. 135-136° (15 mm.), $n^{25}D$ 1.4519.

Anal. Calcd. for $C_{11}H_{18}O_3$: OC_2H_5, 22.7. Found: OC_2H_5, 23.2.

The refractive indices of some of these β-keto esters were observed to change on standing due to a shift of the keto-enol ratio.

β-Keto Acids

β-Oxocaprylic Acid (Ia).—This acid was prepared by the method of Locquin,[24] m. p. 75-76° (dec.).

3-Oxo-6-octenoic Acid (Ib).—Twenty-eight grams of the ethyl ester was saponified for three days at about 5° with 100 ml. of 10% aqueous potassium hydroxide. Upon acidification to congo red with hydrochloric acid the free acid was obtained in crystalline form, m. p. (air dried) 71-72° (dec.). This acid and the previous one, Ia, are stable for months in the refrigerator but slowly decompose at room temperature with the liberation of carbon dioxide.

Anal. Calcd. for $C_8H_{12}O_3$: mol. wt., 156. Found: mol. wt. (titration), 160.

3-Oxo-6-heptenoic Acid (Ic).—This compound was prepared in the same manner but isolated as an oil. It is crystalline when cooled with dry ice, but melts with slow decomposition on warming to room temperature.

2-Hydroxy-1,4-diketones of Formula II

The general procedures used in the preparation of the

(21) (a) Hibbert and Timm, THIS JOURNAL, 45, 2438 (1923); (b) Kimel and Cope, *ibid.*, 65, 1992 (1943).

(22) Microanalyses by Oakwold Laboratories, Alexandria, Va.

(23) Hey and Morris, *J. Chem. Soc.*, 48 (1948); Verley, *Bull. soc. chim.*, 17, 176 (1899).

(24) Locquin, *Bull. soc. chim.*, [3], 31, 597 (1904).

hydroxydiketones will be outlined, and supplementary details will be described for each experiment when necessary.

In **Procedure A** the β-keto acid was isolated, stored in a desiccator in the refrigerator until ready to be used, and then mixed with ice-cold water and exactly neutralized with cold 10% sodium hydroxide solution. The pyruvaldehyde prepared by a modification of the method of Riley[25a,b] usually dissolved in a little water, was added, and the alkalinity adjusted to approximately *p*H 8. It is immaterial whether or not the pyruvaldehyde has polymerized on storage in the refrigerator, for either it dissociates on standing in dilute aqueous solution[25b] or else the equilibrium shifts to the monomer as it reacts. If the reaction medium is too alkaline, some of the substituted glyoxal may be converted to a hydroxy acid before it can react with the salt of the β-keto acid. In those cases where the hydroxydiketones are difficultly soluble, the reaction mixture turns cloudy in about two hours, and during several more hours the oily reaction product separates almost completely. The hydroxydiketones of lower molecular weight may separate partially or not at all, depending on their solubility and the volume of the reaction mixture. In these cases the solution was saturated with sodium chloride before extraction. After about sixteen hours to several days the reaction mixture was extracted with peroxide-free ether. The ether solution was washed with saturated salt solution, and after drying over sodium sulfate the solvent was removed and the residue distilled in high vacuum. There was little or no forerun, but a fraction, not further investigated, having a considerably higher boiling point than the desired compound was present in all the preparations.

Procedure B was the same as A except that the β-keto ester was saponified with a slight excess of a 5 to 20% potassium hydroxide solution for several days in the refrigerator. The excess alkali was neutralized with dilute sulfuric acid, the pyruvaldehyde solution added, and the alkalinity finally adjusted to approximately *p*H 8.

Procedure C was the same as procedure B except that, instead of neutralizing the alkaline solution of the β-keto acid with dilute sulfuric acid, the solution was saturated with carbon dioxide employing a porous disperser. The excess alkali was thereby converted to bicarbonate, giving a suitable *p*H, and the pyruvaldehyde solution could be added without further adjustment of the alkalinity.

3-Hydroxy-2,5-decanedione (IIa). (Procedure A).— Thirty grams (0.19 mole) of β-oxocaprylic acid, Ia, mixed with 50 ml. of cold water in a glass-stoppered flask was kept cold in an ice-bath and titrated with 10% sodium hydroxide solution until just alkaline to phenolphthalein. The stoppered flask was shaken vigorously near the end of the titration. Eighteen grams of pyruvaldehyde (87.6% assay[26]) (0.22 mole) was added and rinsed in with a little water. The alkalinity of the reaction mixture was adjusted to approximately *p*H 8 by the careful addition of a little 10% sodium hydroxide solution. The total volume of the reaction mixture was 200 ml. After about two hours at room temperature the solution turned milky and the oily reaction product rose to the surface. By placing the solution in a graduated cylinder the progress of the reaction could be measured by noting the increase in volume of the oil layer. After two days the reaction mixture was still faintly alkaline. It was extracted several times with ether, the extracts were combined and washed several times with saturated sodium chloride solution and, after drying over anhydrous sodium sulfate, the ether was distilled off leaving a residue of 32 g. of yellow oil which was distilled *in vacuo*. After a small forerun the main fraction was collected at 89–95° (0.05 mm.), most of it distilling at 93–95°, $n^{25}D$ 1.4514, yield 23 g. (65%). There was also a higher boiling fraction, b. p. 150–155° at 0.15 mm., which was not investigated. After redistillation, the 3-hydroxy-2,5-decanedione, $n^{25}D$ 1.4508, d^{25}_4 0.9967, was analyzed.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.48; H, 9.74; *MR*D, 49.93. Found: C, 64.10; H, 9.56; *MR*D, 50.29.

An aliquot of the reaction mixture, after it had been extracted with ether, was titrated for sodium bicarbonate, using 1 *N* sulfuric acid solution and methyl orange indicator, the solution being boiled near the end of the titration. The theoretical amount of sodium bicarbonate was found.

A similar experiment was performed with 10.2 g. (0.065 mole) of β-oxocaprylic acid and 18.1 g. (0.065 mole) of pyruvaldehyde-sodium bisulfite compound[27] (instead of pyruvaldehyde) with final adjustment of the alkalinity to approximately *p*H 8. After standing for two days very little oil separated. The reaction mixture was acidified to congo red with dilute sulfuric acid (1:4) and heated for fifteen minutes on the steam-bath under a reflux condenser in order to decompose any bisulfite addition compounds. The product was isolated as usual by extraction with ether and distillation *in vacuo*, giving only a 19% yield of 3-hydroxy-2,5-decanedione.

Another experiment was performed with commercially available pyruvaldehyde.[28] Procedure B was used. Ninety-nine grams (0.53 mole) of ethyl β-oxocaprylate was mixed with 195 ml. of an ice-cold solution containing 39 g. of potassium hydroxide (86% assay) (0.60 mole). After standing for three days in the refrigerator, the excess alkali was approximately neutralized by the slow addition of dilute sulfuric acid (1:4). One hundred and forty grams of commercial pyruvaldehyde (30%) (0.58 mole) was added, and the solution was adjusted to approximately *p*H 7.5 to 8 by the addition of 10% potassium hydroxide solution. The total volume of the reaction mixture was 537 ml. In ninety minutes the reaction product began to separate as an oil. After four hours 104 ml. had separated, after which there was no further increase. The product was isolated in the usual manner by extraction with ether and distillation to yield, after a small forerun, 50.9 g. (52%), b. p. 105–110° at 0.4 mm., $n^{25}D$ 1.4532. Redistillation gave 41.7 g., b. p. 90–98° at 0.05 mm., $n^{25}D$ 1.4528.

To illustrate that these reactions can be run under acidic conditions, a solution of sodium β-oxocaprylate (0.05 mole) was mixed with a slight excess of pyruvaldehyde in the presence of a buffer consisting of a solution of citric acid (0.1 mole) partially neutralized with sodium hydroxide. The initial *p*H of the reaction mixture was 4.9. The reaction was allowed to proceed for twenty-four hours during which time carbon dioxide was evolved and the reaction product separated as an oil, the final *p*H being 5.1. Extraction and distillation as usual yielded 5.5 g. (59%) of 3-hydroxy-2,5-decanedione.

Sometimes, after several weeks, the formation of crystals in some preparations of 3-hydroxy-2,5-decanedione was noticed. The crystals were filtered off and recrystallized from petroleum ether (b. p. 60–70°) to give colorless plates, m. p. 91–91.5°.

Anal.[22] Calcd. for $C_{20}H_{34}O_5$: C, 67.76; H, 9.67. Found: C, 68.26, 68.24; H, 9.66, 9.61.

Derivatives of 3-Hydroxy-2,5-decanedione (IIa)

The **anhydrodisemicarbazone** was prepared by treatment of IIa with a 50% excess of semicarbazide hydrochloride in pyridine–ethanol. The reaction required several days for completion, as did all the analogous derivatives described later. The anhydrodisemicarbazone was filtered off, washed, and dried, and after recrystallization from acetic acid was colorless, m. p. 224–225° (dec.).[29]

(25) (a) Riley, Morley and Friend, *J. Chem. Soc.*, 1875 (1932); (b) Moulds and Riley, *ibid.*, 621 (1938).

(26) Friedemann, *J. Biol. Chem.*, **73**, 331 (1927); Simon and Neuberg, *Biochem. Z.*, **232**, 479 (1931).

(27) Neuberg, *ibid.*, **255**, 1 (1932).

(28) This product was supplied as an approximate 30% aqueous solution. It contained formaldehyde, acidic substances, and other unknown impurities.

(29) The melting point behavior of many of the semicarbazone derivatives reported in this article was variable. Differences of as much as 5° were sometimes observed, depending on the rate of heating and the temperature at which the capillaries were inserted in the

Anal. Calcd. for $C_{12}H_{22}O_2N_6$: C, 51.04; H, 7.86. Found: C, 50.62; H, 7.65.

It was found to be identical with the disemicarbazone of 3-decene-2,5-dione described below. The analysis indicated that water had been eliminated. Hence the compound may be a pyrazoline derivative, as suggested by Henze[7g] for the analogous derivative of his ketol.

3,5-Dinitrobenzoate.—This derivative was obtained by using 3,5-dinitrobenzoyl chloride in benzene in the presence of pyridine. After isolation in the usual manner, the ester crystallized when kept in the refrigerator for several days and was recrystallized several times from methanol, m. p. 67–68°. The compound was unstable on storage.

Anal. Calcd. for $C_{17}H_{20}O_8N_2$: C, 53.68; H, 5.30. Found: C, 53.53; H, 5.00.

The 2,4-dinitrophenylhydrazone derivative was prepared by refluxing the hydroxydiketone for thirty minutes with an excess of 2,4-dinitrophenylhydrazine in ethanol acidified with concentrated hydrochloric acid. The compound was filtered off, washed with ethanol, dried and recrystallized from chloroform (other solvents were not as satisfactory) giving red crystals, m. p. 226–227°.

3-Decene-2,5-dione (IIIa).—To IIa was added twice its weight of acetic anhydride plus a little anhydrous sodium acetate. The following day the solution was warmed at 100° for ten minutes and the excess acetic anhydride removed under reduced pressure. The residue was dissolved in ether and washed with water, dilute sodium bicarbonate solution, and saturated sodium chloride solution. After the ether solution was dried over anhydrous sodium sulfate, the solvent was evaporated. The residue (practically theoretical yield) crystallized on standing and was recrystallized from low-boiling petroleum ether to give pale yellow crystals, m. p. 52–53°.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.27, 70.86, 71.40; H, 9.44, 9.40, 9.33.

The compound (IIIa) reacted almost immediately with semicarbazide hydrochloride in pyridine-ethanol to give a yellow **disemicarbazone**, which was filtered off, washed with water and ethanol, and dried, m. p. 228–229° (dec.). This derivative was obtained in two forms. Recrystallization by solution in a large volume of boiling 95% ethanol and concentration gave one form, yellow, m. p. 228–229° (dec.).

Anal. Calcd. for $C_{12}H_{22}O_2N_6$: C, 51.04; H, 7.86. Found: C, 51.39; H, 7,94.

Recrystallization from acetic acid gave another form, colorless, m. p. 224–225° (dec.). The mixed melting point[29] of either form with the anhydrodisemicarbazone obtained from 3-hydroxy-2,5-decanedione (m. p. 224–225° dec.) was 224–225° (dec.) in each instance, indicating that the semicarbazone derivatives from the two sources are identical and that the lower melting form is the more stable one.

3-Hydroxy-8-decene-2,5-dione (IIb).—Procedure A was used. From 50.4 g. (0.27 mole) of 3-oxo-6-octenoic acid, Ib, and 29.5 g. of pyruvaldehyde (90% assay) (0.37 mole), the time of reaction being three days and the total volume 290 ml., 44.7 g. (75%) of distilled product, b. p. 97–100° at 0.1 mm., $n^{25}D$ 1.4679, was obtained.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 64.75; H, 8.79.

The **anhydrodisemicarbazone** was prepared and recrystallized from acetic acid, giving a yellow product, m. p. 227–228° (dec.).

bath. Some of the differences in the values given in the literature may be due to this factor in addition to the usual thermometer inaccuracies. Where comparisons and mixed-melting-point determinations were made, the capillaries containing the individual samples and the mixture were placed adjacent to the thermometer and all three run at the same time in a modified type of Hershberg apparatus. It was found that results were more reproducible when the capillaries were inserted in the bath about 10–15° below the expected melting point and the temperature raised about 10° per minute.

Anal. Calcd. for $C_{12}H_{20}O_2N_6$: C, 51.41; H, 7.19. Found: C, 51.47; H, 7.02.

3,8-Decadiene-2,5-dione (IIIb).—This compound was prepared from IIb in the same manner as IIIa. Recrystallization from low-boiling petroleum ether gave pale yellow crystals, m. p. 52–53°.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.74; H, 8.35.

3-Hydroxy-8-nonene-2,5-dione (IIc).—Procedure A was used, starting with 50 g. (0.35 mole) of 3-oxo-6-heptenoic acid and 32.2 g. of pyruvaldehyde (90% assay) (0.40 mole). The time of reaction was three days and the total volume 270 ml.; 35 g. (58%) of distilled product, b. p. 85–90° (mostly 86–89°) at 0.07 mm., $n^{25}D$ 1.4657, was obtained.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 62.82; H, 8.05.

There was also a higher boiling fraction, 5.2 g., b. p. 142–152° at 0.5 mm., $n^{25}D$ 1.4977, which was not investigated.

The **anhydrodisemicarbazone** of IIc was prepared and recrystallized from acetic acid, giving a yellow compound, m. p. 228–229° (dec.), identical with the disemicarbazone of 3,8-nonadiene-2,5-dione described below.

Anal. Calcd. for $C_{11}H_{18}O_2N_6$: C, 49.61; H, 6.81. Found: C, 49.65; H, 6.85.

3,8-Nonadiene-2,5-dione (IIIc).—This compound was prepared from IIc in the same manner as the other analogs. The oily product crystallized in the refrigerator but melted on warming to room temperature.

Its **disemicarbazone** was obtained in two forms. By solution in a large volume of boiling 95% ethanol and concentration, a bright yellow compound was obtained, m. p. 231–232° (dec.). Recrystallization from acetic acid gave the bright yellow lower-melting form, m. p. 228–229° (dec.). A mixed melting point of the latter with the anhydrodisemicarbazone of IIc was 228–229° (dec., no depression).

An experiment to determine the feasibility of using pyruvaldehyde diethyl acetal as a source of the pyruvaldehyde proceeded satisfactorily. Seventeen and a half grams (0.12 mole) of pyruvaldehyde diethyl acetal was refluxed for one hour with 1.6 g. of concentrated sulfuric acid in 60 ml. of water. The solution was cooled in an ice-bath and neutralized by the slow addition of about 3 g. of sodium bicarbonate. Procedure C was used. Starting with 17 g. (0.10 mole) of ethyl 3-oxo-6-heptenoate, saponified in the usual manner with 7.1 g. of potassium hydroxide (87.5% assay) (0.11 mole) in 80 ml. of water, and the hydrolyzed pyruvaldehyde diethyl acetal solution, after two days, 10.6 g. (62%) of distilled product (IIc), $n^{25}D$ 1.4660, was obtained. Pyruvaldehyde diisopropyl acetal[30] was also used successfully in a similar manner.

3-Hydroxy-8-methyl-8-nonene-2,5-dione (IId).—Procedure C was used. From 44 g. (0.24 mole) of ethyl 6-methyl-3-oxo-6-heptenoate and 24 g. of pyruvaldehyde (76% assay) (0.25 mole), the time of reaction being twenty-four hours and the total volume 254 ml., 25.7 g. (58%) of distilled product, b. p. 98–102° at 0.3 mm., $n^{25}D$ 1.4687, was obtained.

Anal.[22] Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.28; H, 8.38.

The **anhydrodisemicarbazone** was prepared in the usual manner and when recrystallized from acetic acid was bright yellow, m. p. 225–226° (dec.).

Anal.[22] Calcd. for $C_{12}H_{20}O_2N_6$: C, 51.41; H, 7.19. Found: C, 50.76; H, 6.80.

3-Hydroxy-9-decene-2,5-dione (IIe).—Procedure C was used. Starting with 50 g. (0.27 mole) of methyl 3-oxo-7-octenoate,[14] and 32.2 g. of pyruvaldehyde (72.4% assay) (0.32 mole), the time of reaction being sixteen hours and

(30) Guest, MacDowell and McNamee, U. S. Patent 2,421,559 (1947).

the total volume 255 ml., 38.4 g. (77%) of distilled product, b. p. 94–97° at 0.2 mm., $n^{25}D$ 1.4675, was obtained.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.01; H, 8.52.

The **anhydrodisemicarbazone** was prepared in the usual manner. It was obtained in two forms, m. p. 214–215° (dec.) from acetic acid, and m. p. 220–221° (dec.) from 95% ethanol, both of which were pale yellow. The latter form was analyzed.

Anal. Calcd. for $C_{12}H_{20}O_2N_6$: C, 51.41; H, 7.19. Found: C, 51.70; H, 6.98.

The **3,5-dinitrobenzoate** was prepared and recrystallized from ether plus low-boiling petroleum ether to give the pale yellow crystalline ester, m. p. 60–61°. The derivative is unstable on storage.

3,9-Decadiene-2,5-dione (IIIe).—This compound was prepared by treating IIe in the same manner as the other analogs. The oily product crystallized in the refrigerator but melted on warming to room temperature. The **disemicarbazone** occurred as a low-melting form, m. p. 214–215° (dec.), when recrystallized from acetic acid and as a high-melting form, m. p. 220–221°, when recrystallized from 95% ethanol, both of which were pale yellow. A mixed melting point of the latter with the high-melting form of the anhydrodisemicarbazone of 3-hydroxy-9-decene-2,5-dione, IIe, was 220–221° (dec., no depression).

3-Hydroxy-9-methyl-8-decene-2,5-dione (IIIf).—Procedure C was used. Starting with 47.5 g. (0.24 mole) of ethyl 7-methyl-3-oxo-6-octenoate and 25 g. of pyruvaldehyde (76% assay) (0.26 mole), the time of reaction being one day and the total volume 300 ml., 32.2 g. (68%) of distilled product, b. p. 106–109° at 0.5 mm., $n^{25}D$ 1.4715, was obtained.

Anal.[22] Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.80; H, 8.75.

The **anhydrodisemicarbazone** was prepared and recrystallized from acetic acid, m. p. 238–239° (dec.).

3-Hydroxy-2,5-hexanedione (Henze's Ketol, IIg).—Procedure C was used, starting 65 g. (0.50 mole) of ethyl acetoacetate and 41.4 g. of pyruvaldehyde (88.6% assay) (0.51 mole). After three days the solution was saturated with sodium chloride (no separation of oil) and extracted with ether in a continuous extractor. It was not necessary to acidify and heat the solution as Henze[7a,g,h,i] specified; therefore, decarboxylation must have taken place spontaneously during the reaction as in the other analogous reactions described in this article. The ether was distilled off and the residue dried by refluxing with benzene by use of a Dean-Stark trap. The benzene was removed with a water pump and the residue distilled in high vacuum. The yield of distilled product was 24.1 g. (37%), b. p. 62–67° (mostly 65–67°) at 0.5 mm., $n^{25}D$ 1.4497.

2-Hydroxy-1-phenyl-7-octene-1,4-dione (IIh).—Procedure B was used. Since phenylglyoxal hydrate is not readily soluble in water, the reaction mixture was shaken for five hours and then allowed to stand overnight. Starting with 28 g. (0.16 mole) of ethyl 3-oxo-6-heptenoate and 22.5 g. (0.17 mole) of phenylglyoxal hydrate,[31] m. p. 83–84°, the total volume of reaction mixture being 210 ml., 23.3 g. (68%) of distilled product, b. p. 154–157° at 0.8 mm., was obtained.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 71.71; H, 6.74.

A small amount was cooled in dry ice to obtain seeds, and then the main product was recrystallized from ether plus low-boiling petroleum ether, filtered, and washed with low-boiling petroleum ether, to give colorless crystals, m. p. 38.5–39°.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.56; H, 6.85.

Cyclopentenolones (Formula IV)

General Procedure for Cyclizing 2-Hydroxy-1,4-diketones to Cyclopentenolones.—The hydroxydiketone was placed in a glass-stoppered Erlenmeyer flask or bottle, and 10 to 20 volumes of 1 to 10% sodium hydroxide solution were added. Although other alkaline cyclizing agents, such as potassium hydroxide, barium hydroxide and piperidine, can be used, sodium hydroxide was found to give uniformly good yields and was generally employed. The air was displaced with nitrogen and the slightly lubricated stopper inserted. (If further precautions against oxidation are desired, boiled water may be used in making up the alkali solution, and a small amount of hydroquinone may be added to the reaction mixture.) It was then shaken for one to four hours on a shaking machine, occasionally somewhat longer. The reaction mixture turned yellow as soon as the alkali was added and usually became darker as the reaction proceeded. After extraction with peroxide-free ether (in the case of the lower molecular weight cyclopentenolones, after saturation with salt), the extract was washed several times with saturated salt solution and after drying over sodium sulfate the solvent was removed and the residue distilled in high vacuum. Sometimes there was a small forerun. In each case, as in the distillation of the hydroxydiketones, there was a fraction, not further investigated, boiling considerably higher than the desired compound.

2-Butyl-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVa, Synthetic *dl*-Dihydrocinerolone).—Fourteen grams of IIa was shaken overnight with 140 ml. of 2% sodium hydroxide solution. By the general procedure, 8.0 g. (63%) of the distilled product, b. p. 110–113° at 0.07 mm., $n^{25}D$ 1.4920, was obtained. The compound was purified by regeneration from the semicarbazone, b. p. 111–113° at 0.2 mm., $n^{25}D$ 1.4945 (literature values[3] are $n^{22}D$ 1.4958 and $n^{25}D$ 1.4955).

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.10; H, 9.64.

The **semicarbazone** was prepared in pyridine–ethanol and recrystallized from methanol–ethyl acetate, m. p. 199–200° (dec.).

Anal. Calcd. for $C_{11}H_{19}O_2N_3$: C, 58.64; H, 8.50. Found: C, 58.79; H, 8.29.

A sample of *dl*-dihydrocinerolone semicarbazone prepared from natural *dl*-cinerolone had a melting point of 195–196° on our thermometer[29] instead of 185° as previously reported.[3] It probably was slightly impure, but the amount available was too small to purify further. A mixed melting point[29] of this semicarbazone with that of the synthetic dihydrocinerolone, IVa (m. p. 199–200°, dec.), was 195–196° (dec., no depression).

The **3,5-dinitrobenzoate** of IVa was prepared in benzene in the presence of pyridine and was recrystallized from methanol, m. p. 111.5–112°.

Anal. Calcd. for $C_{17}H_{18}O_7N_2$: C, 56.35; H, 5.01. Found: C, 56.27; H, 4.81.

The mixed melting point with the 3,5-dinitrobenzoate[3] *dl*-dihydrocinerolone from the natural source was 111.5–112°.

The **2,4-dinitrophenylhydrazone** of IVa was prepared and recrystallized from 95% ethanol, m. p. 140.5–141.5°.

2-(2-Butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVb).—Instead of shaking as in the general procedure, the reaction was carried out with stirring. To 500 ml. of a 1% sodium hydroxide solution in a nitrogen-swept flask fitted with a Hershberg stirrer and dropping funnel, 25 g. of IIb was added over a period of thirty minutes. Stirring was continued for another hour, after which the reaction was worked up as usual. Fourteen grams (62%) of distilled product, b. p. 110–114° at 0.15 mm., $n^{25}D$ 1.5143, was obtained.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.75; H, 8.40.

The **semicarbazone** was prepared in pyridine–ethanol and recrystallized from methanol–ethyl acetate, m. p. 222–223° (dec.).

Anal. Calcd. for $C_{11}H_{17}O_2N_3$: C, 59.17; H, 7.68. Found: C, 59.29; H, 7.51.

The **acetate semicarbazone** was obtained by first acetyl-

(31) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 509.

ating the cyclopentenolone and then preparing the semicarbazone of the acetate. Recrystallized from ethyl acetate, it melted at 155-155.5° (without dec.).

Anal. Calcd. for $C_{13}H_{19}O_3N_3$: C, 58.85; H, 7.22. Found: C, 58.70; H, 7.16.

The **3,5-dinitrobenzoate** was prepared and recrystallized from 95% ethanol, m. p. 125-126°.

Anal. Calcd. for $C_{17}H_{16}O_7N_2$: C, 56.66; H, 4.48. Found: C, 56.16; H, 4.53.

A comparison of synthetic 2-(2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVb), the natural product *dl*-cinerolone, and their derivatives is presented in Table I. The very definite depressions of the mixed melting points of the corresponding derivatives leaves no doubt as to their non-identity.

The **3,5-dinitrobenzoate** (not previously reported) of natural *dl*-cinerolone was prepared and recrystallized from methanol, m. p. 119.5-121.5°.

Anal. Calcd. for $C_{17}H_{16}O_7N_2$: C, 56.66; H, 4.48. Found: C, 57.26; H, 4.86.

TABLE I

MELTING POINTS OF SYNTHETIC AND NATURAL *dl*-2-(2-BUTENYL)-4-HYDROXY-3-METHYL-2-CYCLOPENTEN-1-ONES AND THEIR DERIVATIVES

	n_D	Semicarbazone, m. p., °C. (dec.)	Acetate semicarbazone, m. p., °C.	3,5-Dinitrobenzoate, m. p., °C.
Synthetic[a]	1.5143 (25°)	222-223	155-155.5	125-126
Natural[b]	1.5240 (28°)	199-200	151-152	.....
Natural[a]	.....	196-197	154-156	119.5-121.5
Natural + synthetic[a]	.....	192-193	143-149	100-108

[a] Melting points taken on our thermometer.[29] [b] Literature values [LaForge and Barthel, *J. Org. Chem.*, 10, 106, 114 (1945)].

Hydrogenation of Synthetic 2-(2-Butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVb).—Three and one-half grams of IVb in ethanol was hydrogenated with Adams platinum oxide catalyst until 570 ml. of hydrogen at normal temperature and pressure (20% excess over that required to saturate one double bond) was absorbed. After filtration from the catalyst, 3.25 g. of crude semicarbazone, m. p. 191-192° (dec.), was prepared directly from the concentrated solution. Recrystallization from ethanol gave 2.65 g., m. p. 197-198° (dec.).

From 2.0 g. of the recrystallized semicarbazone 1.4 g. of 2-butyl-4-hydroxy-3-methyl-2-cyclopenten-1-one was regenerated, b. p. 109-110° at 0.2 mm., $n^{25}D$ 1.4927.

When the semicarbazone, 3,5-dinitrobenzoate and 2,4-dinitrophenylhydrazone of the hydrogenated compound were mixed with the corresponding derivatives of 2-butyl-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVa), there was no depression of the melting points.[29] Mixed melting points of the semicarbazone and 3,5-dinitrobenzoate with the corresponding derivatives of *dl*-dihydrocinerolone from the natural source also did not show any depression.

The semicarbazones of IVa and of hydrogenated IVb showed the same X-ray diffraction patterns.[32] These patterns agreed with that of *dl*-dihydrocinerolone semicarbazone from the natural source except for moderate shifts in some of the lines attributable to impurities in solid solution in the latter sample. The X-ray diffraction patterns of the three semicarbazone derivatives, therefore, further confirmed their identity.

2-Allyl-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVc).—Twenty-five grams of IIc was shaken for one hour with 200 ml. of 10% sodium hydroxide solution. By the general procedure 13.3 g. (59%) of distilled product, b. p. 100-103° at 0.15 mm., $n^{25}D$ 1.5141, was obtained.

(32) Grateful acknowledgment is made to E. L. Gooden of this Bureau for the X-ray diffraction data.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 70.23; H, 8.07.

The **semicarbazone** was prepared and recrystallized from methanol-ethyl acetate, m. p. 213-214° (dec.).

Anal. Calcd. for $C_{10}H_{15}O_2N_3$: C, 57.40; H, 7.23. Found: C, 57.90; H, 7.22.

The **3,5-dinitrobenzoate** was prepared and recrystallized from 95% ethanol, m. p. 129-130°.

Anal. Calcd. for $C_{16}H_{14}O_7N_2$: C, 55.49; H, 4.07. Found: C, 55.86; H, 4.21.

4-Hydroxy-3-methyl-2-(2-methylallyl)-2-cyclopenten-1-one (IVd).—Treatment of 31.6 g. of IId with 640 ml. of 2% sodium hydroxide solution for three hours by the general procedure yielded 18.9 g. (66%) of distilled compound, b. p. 115-120° at 0.3 mm., $n^{25}D$ 1.5113. Purification by regeneration from the semicarbazone gave a product, b. p. 112-114° at 0.3 mm., $n^{25}D$ 1.5120.

Anal.[22] Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.48; H, 8.18.

The **semicarbazone** was prepared and recrystallized from methanol-ethyl acetate, m. p. 213-214° (dec.).

Anal.[22] Calcd. for $C_{11}H_{17}O_2N_3$: C, 59.17; H, 7.68. Found: C, 59.29; H, 7.53.

2-(3-Butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IVe).—This compound was prepared in the same manner as IVb. Fifteen grams of IIe dissolved in a little 95% ethanol was dropped into 225 ml. of 2% sodium hydroxide solution during forty-five minutes with stirring, in a nitrogen-swept flask. Stirring was continued for a total of three hours, after which the reaction was worked up as usual. The yield was 6.4 g. (47%) of distilled product, b. p. 109-113° at 0.2 mm., $n^{25}D$ 1.5089.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.88; H, 8.35.

The **semicarbazone** was prepared and recrystallized from methanol-ethyl acetate, m. p. 195-196° (dec.).

Anal. Calcd. for $C_{11}H_{17}O_2N_3$: C, 59.17; H, 7.68. Found: C, 58.78; H, 7.60.

The **acetate semicarbazone** of IVe was prepared by acetylating the cyclopentenolone and then preparing the semicarbazone of the acetate. When recrystallized from ethanol plus a little water, it melted at 136-138° (without dec.).

Anal. Calcd. for $C_{13}H_{19}O_3N_3$: C, 58.85; H, 7.22. Found: C, 58.80; H, 7.26.

The **3,5-dinitrobenzoate** was prepared. Several recrystallizations from ethanol and from benzene-petroleum ether failed to raise the melting point above 109-112°.

Anal. Calcd. for $C_{17}H_{16}O_7N_2$: C, 56.66; H, 4.48. Found: C, 57.22; H, 4.82.

4-Hydroxy-3-methyl-2-(3-methyl-2-butenyl)-2-cyclopenten-1-one (IVf).—Treatment of 25 g. of IIf in the presence of 0.2 g. of hydroquinone with 375 ml. of 2% sodium hydroxide solution for four hours by the general procedure yielded 13.0 g. (57%) of distilled compound, b. p. 116-119° at 0.3 mm., $n^{25}D$ 1.5100.

Anal.[22] Calcd. for $C_{11}H_{16}O_2$: C, 73.29; H, 8.95. Found: C, 73.44; H, 8.71.

The **semicarbazone** was prepared and recrystallized from methanol-ethyl acetate, m. p. 222-223° (dec.).

Anal.[22] Calcd. for $C_{12}H_{19}O_2N_3$: N, 17.70. Found: N, 17.84.

2-Allyl-4-hydroxy-3-phenyl-2-cyclopenten-1-one (IVh).—Treatment of 15 g. of IIh with 225 ml. of 2% sodium hydroxide solution for four hours according to the general procedure yielded 7.0 g. (51%) of distilled compound, b. p. 153-156° at 0.6 mm., $n^{25}D$ 1.5975. When purified by regeneration from the semicarbazone, it crystallized. Recrystallization from benzene-petroleum ether gave colorless crystals, m. p. 97.5-98.5°.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.49; H, 6.56.

The semicarbazone recrystallized from acetic acid melted at 212–213° (dec.).

Anal. Calcd. for $C_{15}H_{17}O_2N_3$: C, 66.40; H, 6.32. Found: C, 66.43; H, 6.37.

Attempted Cyclization of Henze's Ketol, 3-Hydroxy-2,5-hexanedione.—Fifteen grams of II g. was dissolved in 300 ml. of 2% sodium hydroxide solution with the addition of 0.1 g. of hydroquinone. The flask was filled with nitrogen and allowed to stand for four hours. After saturation with sodium chloride, the reaction mixture was extracted with ether in a continuous extractor for twenty-four hours. The ether was distilled off and the residue dried by refluxing with benzene by use of a Dean-Stark trap. The benzene was removed with a water pump, and the residue fractionated in a high vacuum to give three fractions as follows: (1) 0.90 g., b. p. 39–41° at 0.3 mm., $n^{25}D$ 1.4387; (2) 0.65 g., b. p. 92–103° at 0.3 mm., $n^{25}D$ 1.5104; (3) 1.75 g., b. p. 118–128° at 0.3 mm., $n^{25}D$ 1.5342. Only fraction (1) gave a semicarbazone (it precipitated immediately), but the amount was too small to characterize. It was evident from the distillation that the reaction was not clear cut and that cyclization had not taken place. By analogy with the other cyclopentenolones, which have a little higher boiling point than the respective hydroxydiketones from which they are prepared, the cyclized product from 3-hydroxy-2,5-hexanedione, if any were formed, would have an estimated boiling point in the region of 70–85° at 0.3 mm. No such fraction was obtained. If any cyclized product were formed, its detection would require a more rigorous search. The degradation of Henze's ketol by alkali apparently leads to a complex mixture of products.

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Summary

The reaction between substituted glyoxals of the type R'COCHO and salts of substituted acetoacetic acids of the type RCH_2COCH_2COOH, yields 2-hydroxy-1,4-diketones, which cyclize upon treatment with alkali to 2,3-disubstituted-4-hydroxy-2-cyclopenten-1-ones. The chrysanthemum monocarboxylic acid esters of certain of these cyclopentenolones exceed the pyrethrins in insecticidal activity to house flies.

Synthetic 2-(2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one appears to be a geometric isomer of natural *dl*-cinerolone.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TULANE UNIVERSITY]

The Nitration of 1,1,1-Trichloro-2,2-bis-(*p*-methoxyphenyl)-ethane

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1,1,1 - Trichloro - 2,2 - bis - (*p* - methoxyphenyl)-ethane (methoxychlor) has recently become available commercially because of its favorable properties as an insecticide. We have investigated the nitration of methoxychlor because of the usefulness of this reaction as a route to various derivatives whose biological properties are of interest. We were primarily interested in the possible activity of methoxychlor derivatives, particularly the amino derivatives, as anti-tubercular chemotherapeutic agents in view of the observation reported by Kirkwood and Phillips[1] of the high anti-tubercular activity *in vitro* of 1,1,1 - trichloro - 2,2 - bis - (*p* - aminophenyl)-ethane and 1,1-dichloro-2,2-bis-(*p*-aminophenyl)-ethylene.

Nitration of methoxychlor (I in Fig. 1) with concentrated nitric acid in glacial acetic acid solution produced a dinitro derivative. This dinitro compound was shown to be 1,1,1-trichloro-2,2-bis-(3-nitro-4-methoxyphenyl)-ethane (II in Fig. 1) by the methods indicated below.

Treatment of the dinitro derivative II with alcoholic base effected dehydrohalogenation to 1,1 - dichloro - 2,2 - bis - (3 - nitro - 4 - methoxyphenyl)-ethylene (III). Oxidation of this compound with chromic anhydride in glacial acetic acid gave 3,3'-dinitro-4,4'-dimethoxybenzophenone (VII). This ketone has been reported by several workers[2] and its melting point reported as 205°,[2a] 193°,[2d] 190°[2c] and 189–190°.[2b] Our product VII reached a maximum melting point of 187–187.5°[3] after a total of eight recrystallizations from a variety of solvents.

Conclusive proof of the structure of II was given by two independent methods. The first of these was by the condensation of chloral hydrate and *o*-nitroanisole to a product identical with II, indicating that the nitro groups in II were ortho to the methoxyl groups. In addition the nitration product (VI) of DDT (V), shown by Backeberg and Morris[4] to be 1,1,1-trichloro-2,2-bis-(3-nitro-4-chlorophenyl)-ethane, on treatment with alcoholic sodium methoxide caused dehydrohalogenation and replacement of the para chlorine atoms by methoxyl groups giving a product identical with III.

Reduction of the nitro groups in III gave the corresponding diamine, 1,1-dichloro-2,2-bis-(3-amino-4-methoxyphenyl)-ethylene, IV.

Preliminary *in vitro* tests were carried out on compounds II, III and IV by the Parke, Davis

(1) Kirkwood and Phillips, THIS JOURNAL, **69**, 934 (1947).

(2) (a) Consonno, *Gazz. chim. ital.*, **34**, 376, 381 (1904); (b) van Alphen, *Rec. trav. chim.*, **49**, 153 (1930); (c) Quelet, *Compt. rend.*, **196**, 1411 (1933); (d) Matsumura, THIS JOURNAL, **57**, 128 (1935).

(3) All melting points are uncorrected and determined with a Fisher–Johns apparatus.

(4) Backeberg and Morris, *J. Chem. Soc.*, 803 (1945).