750 mg. of the pyrimidine (m.p. 258°) was heated for 15 hours with 50 ml. of phosphoryl chloride and worked up by the general method described above (using ether extraction), there was obtained by sublimation at 120° and 0.03 mm. a compound with a proportion of chlorine higher than that of the starting amide. The colorless needles melted at 168–170°.

Anal. Calcd. for $C_9H_{12}Cl_2N_4O$: C, 41.1; H, 4.6; Cl, 27.0. Found: C, 40.9; H, 4.5; Cl, 26.0.

(b) **With Phosphoryl Chloride Containing Phosphorus Pentachloride.**—Treatment of the starting material (750 mg.) with 50 ml. of phosphoryl chloride containing 10 g. of phosphorus pentachloride under the same conditions again failed to give the desired oxazolopyrimidine but gave a small quantity of product with an even lower carbon analysis, giving a strong qualitative test for chlorine.

Anal. Calcd. for $C_9H_{11}Cl_3N_4$: C, 38.4; H, 3.9. Found: C, 37.4; H, 3.4.

(c) **With Phosphoryl Chloride Containing Water.**—When 350 mg. of starting material was heated for 90 minutes with 4 ml. of phosphoryl chloride to which had been added 0.65 ml. of water and worked up as above, there was obtained 150 mg. of a product which sublimed in needles at 90–130° (0.03 mm.), m.p. 107–108°. The oxazolopyrimidine was not obtained in a completely pure state, being accompanied by a substance richer in chlorine from which complete separation was not achieved. Nevertheless the ultraviolet absorption spectrum and analysis indicated the probability of its presence as the major component of the mixture.

Anal. Calcd. for $C_9H_{11}ClN_4O$: C, 47.7; H, 4.9; Cl, 15.7. Found: C, 46.5; H, 4.9; Cl, 16.2.

Ultraviolet Absorption Spectra.—Ultraviolet absorption spectra were determined using the Beckman model DU spectrophotometer, in aqueous solutions at a concentration of 10 mg. per l. (unless otherwise indicated) in 0.1 *N* hydrochloric acid and in a Sørensen glycine–sodium hydroxide buffer at *p*H 11.

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Constituents of Pyrethrum Flowers. XXIV. Synthetic *dl-cis*-Cinerolone and Other Cyclopentenolones[1,2]

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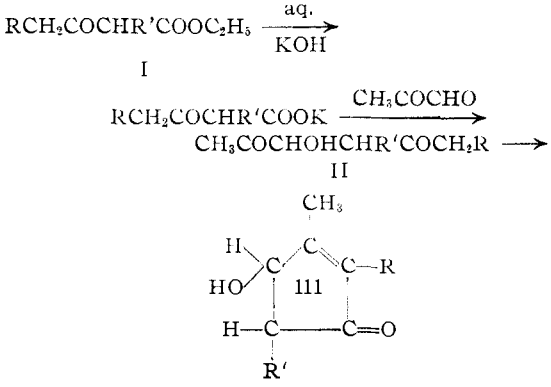
A general synthesis of cyclopentenolones previously described has been extended to the preparation of some new ones with chlorine-containing side chains. A synthesis of *dl-cis*-cinerolone identical with the product from the natural source is also presented.

The general procedure originated by Schechter, *et al.*,[2] for the synthesis of cyclopentenolones analogous to cinerolone and pyrethrolone has made possible the preparation of completely synthetic, highly potent insecticidal esters of the pyrethrin type.[3] The ester considered to be most practical from the standpoint of both technical production and entomological results, *dl*-2-allyl-4-hydroxy-3-methyl-2-cyclopenten-1-one esterified with a mixture of *cis*- and *trans-dl*-chrysanthemum monocarboxylic acids, for which the name allethrin has been adopted, is now being produced commercially.[4] It seems to be relatively safe on the basis of pharmacological results,[5] its properties in this respect being in marked contrast to the toxic chlorine- or phosphorus-containing insecticides, such as DDT, chlordane, parathion, etc.

As with most biologically active compounds, it is of interest to effect changes in the structure of an active compound with the hope of producing a more potent one or to learn something about the effect of structure on activity. Since the pyrethrin-like compounds are esters, it is possible to make changes in either the acid or the cyclopentenolone moieties.

This article describes a number of new cyclopentenolones which are analogs of cinerolone. They were prepared by the same general procedure as described previously,[2] which consists in the condensation of pyruvaldehyde with a salt of a β-keto acid obtained by saponification of a β-keto ester (I) and cyclization of the resulting hydroxydiketone (II) to a cyclopentenolone (III) in the presence of alkali.



R′ = H except in e; c, R = $-CH_2CH{=}CClCH_3$
a, R = $-CH_2CH{=}CHCl$; d, R = $-CH_2C{\equiv}CCH_3$
b, R = $-CH_2CCl{=}CH_2$; e, R and R′ = $-CH_2CH{=}CH_2$

In our previous article,[2] the synthesis of 2-(2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one was described and it was stated that this synthetic product was probably the *trans* isomer because of the *trans* configuration of the crotyl bromide used as a starting material. Furthermore, a comparison of derivatives with those of natural

(1) Presented before the Division of Organic Chemistry at the A.C.S. Meeting in Chicago, Illinois, on September 5, 1950.

(2) For XXIII see M. S. Schechter, N. Green and F. B. LaForge, THIS JOURNAL, **71**, 3165 (1949).

(3) Anon., *Chem. Eng. News*, **27**, 1942 (1949); M. S. Schechter, N. Green and F. B. La Forge, *Agr. Chemicals*, [6] **4**, 57 (1949).

(4) Anon., *ibid.*, [4] **5**, 75 (1950).

(5) D. F. Starr, P. Ferguson and T. N. Salmon, *Soap and Sanit. Chem.*, [3] **26**, 139 (1950); C. P. Carpenter, C. S. Weil, U. C. Pozzani and H. F. Smyth, *Arch. Ind. Hyg. Occupational Med.*, **2**, 420 (1950).

dl-cinerolone showed the two to be different; hence natural cinerolone was presumed to be the *cis* isomer. This has been proved beyond a doubt by the work of Cupples,[6] who compared the infrared spectra of synthetic 2-(*trans*-2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one and natural cinerolone.

The synthesis of *dl-cis*-cinerolone by the condensation of sodium 3-oxo-*cis*-6-octenoate with pyruvaldehyde and cyclization of the resulting hydroxydiketone to the cyclopentenolone employing the general procedure developed by us for these last two steps has been reported by Crombie and Harper.[7] However, they acidified and heated the reaction products after the condensation of pyruvaldehyde with β-keto acids, whereas we have shown that this is not necessary, decarboxylation taking place spontaneously during the reaction even in neutral or faintly alkaline solution.[8] This observation of decarboxylation during the condensation of aldehydes with β-keto acids had also been made by Schöpf[9] in his work on the synthesis of natural compounds under physiological conditions.

We have independently synthesized *dl-cis*-cinerolone. Whereas Crombie and Harper[7] introduced the *cis* double bond by catalytic reduction of a triple bond in one of the early stages of their fourteen-step synthesis, we have preferred to retain the triple bond until the last step and then to reduce it catalytically to the *cis* double bond.[10] By this procedure we avoid the possibility of rearrangements or isomerizations in any of the steps of the synthesis. We chose this route because, in addition to the preparation of synthetic *cis*-cinerolone, we also desired to obtain a cyclopentenolone having an acetylenic bond in the side chain to determine the effect of this change in structure on entomological results for its ester with chrysanthemum monocarboxylic acid. Thus, we attained both objectives with a single synthesis.

The synthetic *dl-cis*-cinerolone was shown to be identical with natural *dl*-cinerolone by mixture melting point determinations with three derivatives—the semicarbazone, the acetate semicarbazone and the 3,5-dinitrobenzoate.

Experimental

Many of the intermediates described in this article, particularly the chlorinated ones, were somewhat more difficult than usual to obtain pure and a few were employed without being completely purified in order to avoid polymerization or oxidation. The primary objective of the work was to obtain enough of the final products for entomological testing with the intention of reinvestigating any product of outstanding toxicity. Insecticide tests with house flies by W. A. Gersdorff and N. Mitlin[11] indicate none of the chrysanthemum monocarboxylic acid esters of these new cyclopentenolones to be better than allethrin.

3-Chloro-2-buten-1-ol.[12]—To a solution of 106 g. (1.0 mole) of anhydrous sodium carbonate in 890 ml. of water containing 1 g. of hydroquinone was added 125 g. (1.0 mole) of 1,3-dichloro-2-butene.[13] After refluxing for five hours with stirring, the reaction mixture was saturated with sodium chloride, cooled, and extracted several times with ether. The ether extracts were combined and dried over sodium sulfate, the solvent was removed, and the residue fractionated, yielding 82 g. (77%), distilling at 90–93° (50 mm.), $n^{25}D$ 1.4650.

2-Butyn-1-ol.[12]—To a refluxing solution of 118 g. of 85% potassium hydroxide (1.79 moles) in 138 ml. of water, 171 g. (1.61 moles) of 3-chloro-2-buten-1-ol was added during a period of one-half hour. Stirring and refluxing were continued for two hours more. After standing overnight, the reaction mixture was saturated with carbon dioxide, heated to reflux temperature, cooled and extracted several times with ether. The ether extracts were combined and dried over sodium sulfate, the solvent was distilled off, and the residue fractionated, yielding 83.7 g. (75%), which boiled at 82–92° (95 mm.), $n^{25}D$ 1.453. This procedure eliminated the troublesome extractions employed by Hatch and Nesbitt[12]; the use of potassium hydroxide instead of sodium hydroxide seems to be advantageous because of the subsequent salting-out effect of the potassium chloride and potassium carbonate which is produced.

2-Butyn-1-ol and 3-chloro-2-buten-1-ol have more recently been prepared by Hatch and Hudson,[14] Hatch and Chiola[15] and by Crombie, *et al.*[10]

1-Chloro-2-butyne.—One hundred and two grams (1.46 moles) of 2-butyn-1-ol and 26 g. of pyridine were placed in a three-necked flask equipped with a mercury-sealed stirrer, thermometer and dropping funnel. After cooling to −10°, 82 g. (0.60 mole) of phosphorus trichloride was slowly adding during a period of one hour. A slurry of crystals formed, which dissolved when warmed to room temperature. The reaction mixture was warmed to about 90–100° for a short time, whereupon a reaction took place with the formation of two layers. The upper layer was separated in a separatory funnel, filtered through a plug of cotton moistened with low-boiling petroleum ether and distilled, yielding 49.5 g., b.p. 104–106° (760 mm.), and an additional 34.6 g., b.p. about 55° (35 mm.). These fractions were combined, dissolved in low-boiling petroleum ether, and then washed with ice-water. After drying with calcium chloride, the solvent was removed and the residue distilled, the purified product boiling at 104–106° (760 mm.), 71.5 g. (55% yield), $n^{25}D$ 1.4570.[16]

α-Substituted Acetoacetic Esters

2-Acetyl-5-chloro-4-pentenoic Acid, Ethyl Ester [Ethyl α-(3-Chloroallyl)-acetoacetate].—Eleven and one-half grams (0.5 mole) of sodium was dissolved in 200 ml. of absolute ethanol. After cooling, 71.5 g. (0.55 mole) of ethyl acetoacetate was added with stirring, followed by 55.5 g. (0.5 mole) of 1,3-dichloro-1-propene.[17] After standing 16 hours at room temperature, the reaction mixture was refluxed for

(6) H. L. Cupples, THIS JOURNAL, **72**, 4522 (1950).

(7) L. Crombie and S. H. Harper, *Nature*, **164**, 534 (1949); *J. Chem. Soc.*, 1152 (1950). Although we had previously prepared *dl-trans*-cinerolone,[2] these authors made no reference to our data and table showing the non-identity of *dl-trans*-cinerolone with natural *dl-cis*-cinerolone.

(8) *Cf.* L. Crombie, A. J. B. Edgar, S. H. Harper, M. W. Lowe and D. J. Thompson, *ibid.*, 3552 (1950), who still maintain that acidification and warming gives better yields.

(9) C. Schöpf and co-workers, *Ang. Chem.*, **50**, 779 (1937); THIS JOURNAL, **72**, 2816 (1950).

(10) L. Crombie, S. H. Harper, R. E. Stedman and D. Thompson, *J. Chem. Soc.*, 2445 (1951), have, since the submission of the present article, described a new synthesis of *dl-cis*-cinerolone involving fewer steps than the one by Crombie and Harper.[7]

(11) W. A. Gersdorff and N. Mitlin, *J. Econ. Ent.*, **44**, 70 (1951).

(12) This preparation is a modification of the one described by L. F. Hatch and S. S. Nesbitt, THIS JOURNAL, **72**, 727 (1950). The authors wish to thank L. F. Hatch for having sent them the manuscript of his article before its publication.

(13) From E. I. du Pont de Nemours & Co.; sample used after a simple distillation, b.p. 127–129°, $n^{25}D$ 1.4697. According to L. F. Hatch and S. G. Ballin, *ibid.*, **71**, 1039, 1041 (1949), only the low-boiling isomer, b.p. 127–129°, $n^{25}D$ 1.4695, is present in commercial samples.

(14) L. F. Hatch and P. S. Hudson, *ibid.*, **72**, 2505 (1950).

(15) L. F. Hatch and V. Chiola, *ibid.*, **73**, 360 (1951).

(16) C. D. Hurd and F. L. Cohen, *ibid.*, **53**, 1068 (1931), give b.p. 81–84°. Hatch and Chiola[14] and Crombie, *et al.*,[10] have recently described preparations of 1-chloro-2-butyne, b.p. 102° and 101–103°, respectively, and have indicated that Hurd and Cohen's product was probably an azeotrope with water.

(17) From Shell Development Co.; sample used after a simple distillation without separation of the *cis* and *trans* isomers. It boiled at 109–111°, $n^{25}D$ 1.4700, indicating that the sample consisted of the *trans* isomer predominantly. See L. F. Hatch and R. H. Perry, *ibid.*, **71**, 3262 (1949), and other pertinent references given therein.

TABLE I

γ-SUBSTITUTED ACETOACETIC ESTERS

Ester	Yield, %	Boiling range °C.	Mm.	$n^{25}D$	Formula	Ethoxyl, % Calcd.	Ethoxyl, % Found	Chlorine, % Calcd.	Chlorine, % Found
Ia, Ethyl 7-chloro-3-oxo-6-heptenoate	76	90–100	0.2	1.464	$C_9H_{13}O_3Cl$	22.0	21.5[a]	..	..
Ib, Ethyl 6-chloro-3-oxo-6-heptenoate	27.5	85–95	0.2	1.462	$C_9H_{13}O_3Cl$	..	..	17.3	17.7
Ic, Ethyl 7-chloro-3-oxo-6-octenoate	71	87–90	0.15	1.464	$C_{10}H_{15}O_3Cl$	20.6	20.7	16.2	15.7
Id, Ethyl 3-oxo-6-octynoate	63	77–83	0.1	1.458	$C_{10}H_{14}O_3$	24.7	24.6[b]	..	..
Ie, Ethyl 2-allyl-3-oxo-6-heptenoate	75	130–137	18	1.452	$C_{12}H_{18}O_3$	21.4	21.4	..	..

[a] Analysis performed on redistilled sample, b.p. 92–93° (0.5 mm.), $n^{25}D$ 1.4664. [b] Analysis performed on a middle cut.

four hours with stirring, and after being cooled was neutralized with a little acetic acid. The sodium chloride was filtered off and the filtrate submitted to vacuum distillation, yielding 47.6 g. (46.6%) of product boiling at 88–92° (1.0 mm.), $n^{25}D$ 1.4622.

Anal. Calcd. for $C_{19}H_{13}O_3Cl$: OC_2H_5, 22.0; Cl, 17.3. Found: OC_2H_5, 22.1; Cl, 16.8.

Since a commercial *cis–trans* mixture of 1,3-dichloropropenes was employed as a starting material without separation of the isomers, compound IIIa and its intermediates are possibly mixtures of *cis* and *trans* isomers.

2-Acetyl-4-chloro-4-pentenoic Acid, Ethyl Ester [Ethyl α-(2-Chloroallyl)-acetoacetate].—This ester was prepared employing 2,3-dichloro-1-propene[18] to alkylate ethyl acetoacetate in 20.8% yield; b.p. 118–120° (15 mm.), $n^{25}D$ 1.4530.

Anal. Calcd. for $C_{19}H_{13}O_3Cl$: OC_2H_5, 22.0; Cl, 17.3. Found: OC_2H_5, 22.5; Cl, 17.7.

2-Acetyl-5-chloro-4-hexenoic Acid, Ethyl Ester [Ethyl α-(3-Chloro-2-butenyl)-acetoacetate].—1,3-Dichloro-2-butene[12] was used to alkylate ethyl acetoacetate. The fraction boiling at 95–112° (0.5 mm.), $n^{25}D$ 1.461 (76% yield) was collected. A small portion was redistilled and found to boil at 80–84° (0.05 mm.), $n^{25}D$ 1.4605.

Anal. Calcd. for $C_{20}H_{15}O_3Cl$: OC_2H_5, 20.6. Found: OC_2H_5, 20.0.

2-Acetyl-4-hexynoic Acid, Ethyl Ester [Ethyl α-(2-Butynyl)-acetoacetate].—This ester was prepared from 8.4 g. (0.37 mole) of sodium, 125 ml. of absolute ethanol, 50 g. (0.39 mole) of ethyl acetoacetate and 31 g. (0.35 mole) of 1-chloro-2-butyne. The yield of product boiling at 128–138° (15 mm.), $n^{25}D$ 1.453, was 40.6 g. (64%).

Anal. Calcd. for $C_{10}H_{14}O_3$: OC_2H_5, 24.7. Found: OC_2H_5, 24.6.

Ketones

6-Chloro-5-hexen-2-one.—To an ice-cold solution of 100 g. (1.5 moles) of potassium hydroxide (85%) in 1.2 l. of water was added 247 g. (1.2 moles) of ethyl 2-acetyl-5-chloro-4-pentenoate with stirring. After the solution had stood in the refrigerator at about 5° for five days, sulfuric acid (1:1) was added until the solution was acid to congo red paper. It was refluxed a short time until evolution of carbon dioxide ceased, then cooled and extracted several times with ether. The ether extracts were combined, washed with dilute alkali and saturated salt solution, and then dried over sodium sulfate. The solvent was removed and the residue distilled, yielding 115 g. (72%), boiling at 80–93° (17 mm.). A portion was redistilled to obtain a purer sample, b.p. 80.5–81.0° (16.5 mm.), $n^{25}D$ 1.4540.

Anal. Calcd. for C_6H_9OCl: Cl, 26.8. Found: Cl, 26.3.

Its **semicarbazone** melted at 123–124°.[19]

Anal.[20] Calcd. for $C_7H_{12}OClN_3$: Cl, 18.7. Found: Cl, 18.6.

5-Chloro-5-hexen-2-one.—This ketone was prepared from ethyl 2-acetyl-4-chloro-4-pentenoate in 37% yield, the fraction boiling at 72–82° (17 mm.), $n^{25}D$ 1.448, being collected.

Its **semicarbazone** melted at 139–140°.

Anal.[20] Calcd. for $C_7H_{12}OClN_3$: N, 22.1. Found: N, 21.9.

6-Chloro-5-hepten-2-one.—This ketone was prepared employing 50 g. (1.25 moles) of sodium hydroxide dissolved in 330 ml. of water and 244 g. (1.12 moles) of ethyl 2-acetyl-5-chloro-4-hexenoate. The yield was 137 g. (83%), b.p. 88–90° (15 mm.), $n^{25}D$ 1.4571.

Anal. Calcd. for $C_7H_{11}OCl$: Cl, 24.2. Found: Cl, 23.6.

Its **semicarbazone** melted at 137–138°.

Anal. Calcd. for $C_8H_{14}OClN_3$: Cl, 17.4. Found: Cl, 17.0.

5-Heptyn-2-one.—This ketone was prepared employing 15.3 g. (0.23 mole) of 85% potassium hydroxide dissolved in 150 ml. of water and 40.6 g. (0.22 mole) of ethyl 2-acetyl-4-hexynoate. The yield was 17 g. (69%), b.p. 75–77° (18 mm.), $n^{25}D$ 1.4472. A middle cut was taken for analysis. This compound has since been prepared by Crombie, *et al.*[10]

Anal. Calcd. for $C_7H_{10}O$: C, 76.3; H, 9.1. Found: C, 75.6; H, 9.3.

Its **semicarbazone** was prepared, m.p. 175–176°.

Anal.[21] Calcd. for $C_8H_{13}ON_3$: C, 57.46; H, 7.84. Found: C, 57.14; H, 7.85.

γ-Substituted Acetoacetic Esters

The γ-substituted acetoacetic esters listed in Table I were prepared by the general procedure described by LaForge and co-workers,[22] except for compound Ie, which was prepared as follows:

2-Allyl-3-oxo-6-heptenoic Acid, Ethyl Ester (Ie).—Six and four-tenths grams (0.28 mole) of sodium was dissolved in 170 ml. of absolute ethanol, the solution was cooled, and 50 g. (0.29 mole) of ethyl 3-oxo-6-heptenoate[2] added during five minutes, followed by the addition of 24 g. (0.31 mole) of allyl chloride with stirring. After standing overnight, the reaction mixture was refluxed for four hours with stirring. The sodium chloride was filtered off and the filtrate was submitted to distillation, the alcohol being removed as a forerun. The physical constants of the product are given in Table I.

Hydroxydiketones

8-Chloro-3-hydroxy-8-nonene-2,5-dione (IIb).—Sixteen grams of ethyl 6-chloro-3-oxo-6-heptenoate (0.078 mole) was dissolved in 50 ml. of ice-cold potassium hydroxide solution containing 5.9 g. of 85% potassium hydroxide. After standing four days at 5°, the solution was saturated with carbon dioxide. Fifteen grams (0.086 mole) of pyruvaldehyde diisopropyl acetal was refluxed with 15 ml. of 2% sulfuric acid, with stirring until homogeneous and then 20 minutes more (about two hours total). The solution was cooled in an ice-bath, neutralized by the gradual addition of sodium bicarbonate, and then added to the solution of saponified ester described above. After standing for one day at room temperature, the reaction mixture was extracted with ether, the ether extract was washed with saturated salt solution and dried over anhydrous sodium sulfate, and the solvent was removed. Distillation in high vacuum yielded 7.6 g. (48%) of product, boiling at 110–114° (0.2 mm.), $n^{25}D$ 1.4853. Another lot was prepared but polymerized on distillation.

9-Chloro-3-hydroxy-8-nonene-2,5-dione (IIa).—This hydroxydiketone was prepared in the same manner. From 40.9 g. of ethyl 7-chloro-3-oxo-6-heptenoate, 31.5 g. of crude product was obtained. Distillation of a few grams gave a pale yellow distillate, b.p. 113–116° (0.2 mm.), $n^{25}D$ 1.4905, which, however, darkened and polymerized in a few hours; hence the crude product was employed for cyclization to the cyclopentenolone, as described later.

Its **anhydrodisemicarbazone** melted at 203–204° (dec.).

(18) From Shell Development Co.; sample used after a simple distillation, b.p. 93–94°, $n^{25}D$ 1.4578.

(19) All melting points are corrected.

(20) Analysis by Oakwold Laboratories, Alexandria, Virginia.

(21) Analysis by J. S. Ard and F. W. Guay, Bureau of Agricultural and Industrial Chemistry.

(22) S. B. Soloway and F. B. LaForge, THIS JOURNAL, **69**, 2677 (1947); N. Green and F. B. LaForge, *ibid.*, **70**, 2287 (1948).

Anal.[20] Calcd. for $C_9H_{17}O_2N_6Cl$: N, 30.37. Found: N, 30.28.

9-Chloro-3-hydroxy-8-decene-2,5-dione (IIc).—This compound was prepared in a similar fashion from 40 g. (0.18 mole) of ethyl 7-chloro-3-oxo-6-octenoate and 35.1 g. (0.20 mole) of pyruvaldehyde diisopropyl acetal. The yield was 25.8 g. (64.5%), b.p. 134–137° (0.5 mm.), $n^{25}D$ 1.487. A middle cut used for analysis had $n^{25}D$ 1.4894.

Anal. Calcd. for $C_{10}H_{15}O_3Cl$: Cl, 16.2. Found: Cl, 16.3.

4-Allyl-3-hydroxy-8-nonene-2,5-dione (IIe).—This compound was prepared by the procedure described for IIb from 21.0 g. (0.1 mole) of ethyl 2-allyl-3-oxo-6-heptenoate. After saponification with aqueous alkali in the refrigerator for several days, 5.5 g. of oil that was floating on the surface was removed. This oil may have contained some unsaponified ester and some ethyl 2,2-diallyl-3-oxo-6-heptenoate. The alkaline solution was neutralized with carbon dioxide and mixed with pyruvaldehyde obtained by the acid hydrolysis and subsequent neutralization of 14.2 g. (0.082 mole) of pyruvaldehyde diisopropyl acetal. Working up the reaction mixture in the usual manner gave 4.6 g. (30% yield on the basis of 15.5 g. of ethyl 2-allyl-3-oxo-6-heptenoate actually utilized) of product boiling at 110–120° (0.2 mm.), $n^{25}D$ 1.479. Because of the possibility of oxidation or polymerization, it was immediately cyclized to the cyclopentenolone (IIIe).

3-Hydroxy-8-decyne-2,5-dione (IId).—This compound was prepared by the general procedure for hydroxy diketones from 17.9 g. (0.098 mole) of ethyl 6-octynoate and 19.0 g. (0.11 mole) of pyruvaldehyde diisopropyl acetal. The yield of product boiling at 110–115° (0.1 mm.), $n^{25}D$ 1.4812, was 11.5 g. (64.5%).

Anal.[21] Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.63; H, 7.76.

Its **anhydrodisemicarbazone** recrystallized from acetic acid melted at 226–227° (dec.).

Anal.[21] Calcd. for $C_{12}H_{18}O_2N_6$: C, 51.78; H, 6.52. Found: C, 51.65; H, 6.63.

Cyclopentenolones

An improvement on the procedure of Schechter, *et al.*,[2] for cyclizing hydroxy diketones is as follows:

The hydroxy diketone, either pure or crude and undistilled, is slowly dropped into about 10 to 15 volumes of cold (about 10°) 2% sodium hydroxide solution containing a small amount of hydroquinone during a period of about one hour with stirring, the air in the vessel having first been displaced by nitrogen. After being stirred for another hour and a half to two hours at room temperature, the solution is saturated with sodium chloride and extracted several times with ether. The ether extracts are combined, washed several times with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The solvent is then removed and the cyclopentenolone distilled in high vacuum. This procedure causes the cyclization to take place at high dilution, thus decreasing the chances for bimolecular side reactions.

2-(3-Chloroallyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IIIa).—This compound was prepared by the cyclization of 28 g. of crude IIa. There was obtained 11 g. of product, b.p. 136–138° (0.1 mm.), $n^{25}D$ 1.5342.

Anal.[20] Calcd. for $C_9H_{11}O_2Cl$: C, 57.92; H, 5.94; Cl, 19.00. Found: C, 58.10; H, 5.82; Cl, 18.86.

Its **semicarbazone** melted at 204–205° (dec.).

Anal.[20] Calcd. for $C_{10}H_{14}O_2N_3Cl$: N, 17.98. Found: N, 17.72.

2-(2-Chloroallyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IIIb).—Seven grams of IIb was cyclized by agitation with 2% sodium hydroxide solution by the improved procedure described above. The yield of product boiling at 120–125° (0.2 mm.) was 4.15 g. (22%), $n^{25}D$ 1.5297.

Anal. Calcd. for $C_9H_{11}O_2Cl$: Cl, 19.0. Found: Cl, 18.6.

Its **semicarbazone** melted at 214–214.5° (dec.).

Anal. Calcd. for $C_{10}H_{14}O_2N_3Cl$: C, 49.28; H, 5.79. Found: C, 49.52; H, 5.98.

2-(3-Chloro-2-butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IIIc).—This cyclopentenolone was prepared by cyclizing 24.2 g. of IIc. The yield of product boiling at 130–142° (0.2 mm.), $n^{25}D$ 1.521, was 9.6 g. (43%). Because the distillate had an acidic reaction, it was dissolved in ether, washed with sodium bicarbonate solution and dried over anhydrous sodium sulfate. The solvent was removed and the residue distilled to give a fraction boiling at 135–139° (0.2 mm.), $n^{25}D$ 1.5267.

Anal.[20] Calcd. for $C_{10}H_{13}O_2Cl$: Cl, 17.7. Found: Cl, 17.4.

Its **semicarbazone** melted at 220–221° (dec.).

Anal.[20] Calcd. for $C_{11}H_{16}O_2N_3Cl$: N, 16.96. Found: N, 16.44.

2,5-Diallyl-4-hydroxy-3-methyl-2-cyclopenten-1-one (IIIe).—This compound was obtained by cyclization of 4.6 g. of IIe by agitation in a nitrogen atmosphere for two hours with 50 ml. of 2% sodium hydroxide solution containing a small amount of hydroquinone. The yield of product, b.p. 112–114° (0.1 mm.), $n^{25}D$ 1.5114, was 2.2 g. (52%).[23]

Its **semicarbazone** melted at 226–227° (dec.).

Anal.[21] Calcd. for $C_{13}H_{19}O_2N_3$: C, 62.63; H, 7.68. Found: C, 62.41; H, 7.76.

2-(2-Butynyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IIId).—This cyclopentenolone was prepared in the same manner as described for the other compounds of this type. From 10.7 g. (0.059 mole) of IId there was obtained 6.15 g. (63.8%) of product, boiling range 124–129° (0.1 mm.), $n^{25}D$ 1.516. After purification by regeneration from the semicarbazone, it boiled at 125–127° (0.15 mm.), $n^{25}D$ 1.5302.[22]

Its **semicarbazone** melted at 245–246° (dec.).

Anal.[19] Calcd. for $C_{11}H_{17}O_2N_3$: N, 18.82. Found: N, 18.87.

2-(*cis*-2-Butenyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (Synthetic *dl-cis*-cinerolone) (III, R = *cis*-2-butenyl, R′ = H).—To 2.4 g. of palladium–calcium carbonate catalyst,[24] 0.8 ml. of quinoline was added, followed by 12 ml. of ethyl acetate. The catalyst was then reduced with hydrogen at atmospheric pressure in a catalytic hydrogenation apparatus. An ethyl acetate solution of 9.45 g. of 2-(2-butynyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one (IIId) was added and the hydrogenation continued until one molecular equivalent of hydrogen was absorbed. The total time required was about a half-hour, the hydrogenation being about 95% complete in the first 15 minutes.[25] The solution was then filtered, the solvent removed, and the residue converted to the semicarbazone in ethanol–pyridine–water solution. The next day the semicarbazone was filtered off, washed with water and cold ethanol, and then dried to yield 9.55 g. of the semicarbazone derivative of synthetic *dl-cis*-cinerolone, m.p. 202–203° (dec.). Recrystallization from ethyl acetate gave the pure semicarbazone, m.p. 205–206° (dec.).

Seven and five-tenths grams of the semicarbazone was hydrolyzed by shaking at 100° for 45 minutes with 27 g. of potassium acid sulfate, 50 ml. of water and 40 ml. of toluene. The toluene solution was separated, washed with sodium bicarbonate solution, and the solvent removed *in vacuo*. The residue was distilled from a small Claisen flask to give 3.8 g. of the pure cyclopentenolone, b.p. 113–114° (0.1 mm.), $n^{25}D$ 1.5168.

The **3,5-dinitrobenzoate** melted at 124–125°.

Anal.[21] Calcd. for $C_{17}H_{16}O_7N_2$: C, 56.66; H, 4.48. Found: C, 56.55; H, 4.68.

(23) Combustion analyses for this compound, even on a middle cut of redistilled sample, gave values about 1% low for carbon, probably due to slight oxidation. However, the semicarbazone derivative gave good analytical values.

(24) J. Houben, "Die Methoden der Organischen Chemie," 3rd ed., 1925, Vol. 2, p. 360.

(25) Other experiments showed that the rate of hydrogenation can be varied at will by adjusting the proportion of quinoline to catalyst. If the addition of quinoline is omitted, the hydrogenation is extremely rapid and tends to continue past the absorption of one equivalent of hydrogen. In the presence of quinoline the hydrogenation is slower and it is easier to stop at the desired point of one equivalent. In fact, the hydrogenation slows down to such a degree near the end that it is difficult to hydrogenate beyond one equivalent of hydrogen per triple bond without taking an excessively long time. A palladium–charcoal catalyst treated with quinoline has been used very successfully for the partial hydrogenation of an acetylene bond by O. Isler, *et al.*, *Helv. Chim. Acta*, **30**, 1911 (1947), in their work on the synthesis of vitamin A.

TABLE II

COMPARISON OF SYNTHETIC AND NATURAL *dl-cis*-CINEROLONE AND THEIR DERIVATIVES

Source	$n^{t}D$	t, °C.	Boiling point °C.	Mm.	Semicarbazone m.p., °C. (dec.)	Acetate semicarbazone m.p., °C.	3,5-Dinitrobenzoate
Synthetic[a]	1.5168	25	113–114	0.1	205–206	150–151	124–125
Natural[a]	1.5190	25	118–122	.4	201–202	150.5–151.5	121–123.5
Synthetic[6]	1.5100	25	102–105	.05	197–199	147–148	.....
Synthetic[9]	1.513	20	116–130	.2	199–201	.....	.....
Natural[24]	1.5240	28	.....	..	199–200	151–152	.....
Natural[a] + synthetic[a]	....	..	.....	..	203–204	150–151	122.5–124.5

[a] This article.

The synthetic *cis*-cinerolone was further characterized by the preparation of the acetate, which boiled at 102–107° (0.3 mm.), $n^{25}D$ 1.4937, and this was converted to the **acetate semicarbazone**, m.p. 150–151° (from methanol–ethyl acetate).

Anal.[20] Calcd. for $C_{13}H_{19}O_3N_3$: N, 15.84. Found: N, 15.22.

Natural *dl*-cinerolone.—This compound and a number of its derivatives were prepared again for purposes of comparison.

Four grams of natural *dl*-cinerolone semicarbazone,[26] m.p. 201–202° (dec.), was hydrolyzed as described above for the synthetic *cis*-cinerolone and the free cyclopentenolone was found to boil at 118–122° (0.4 mm.), $n^{25}D$ 1.5190, yield 2.3 g.

The **3,5-dinitrobenzoate**, after two recrystallizations from methanol, melted at 121–123.5°.[2]

The **acetate semicarbazone** was prepared and found to melt at 150.5–151.5°.

A comparison of synthetic and natural *dl-cis*-cinerolone and their derivatives is given in Table II. Mixture melting points of corresponding derivatives of the synthetic and natural products gave no depressions.

BELTSVILLE, MARYLAND

(26) F. B. La Forge and W. F. Barthel, *J. Org. Chem.*, **10**, 106, 114 (1945).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of the 2-Pyridone and α-Bromoacrylic Acid Adduct and its Derivatives

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Evidence is presented which requires reinterpretation of the structure and reactions previously attributed to the reaction product of 2-pyridone and α-bromoacrylic acid.[1] The product proved to be 2-carboxy-2,3-dihydroöxazolo[2,3-a]pyridinium bromide. New syntheses and reactions of 2-H-pyrido[1,2-a]pyrimidin-2-ones (2-keto-1,4a-diazonaphthalenes) are described.

The structure and reactions of the compound obtained when 2-pyridone and α-bromoacrylic acid are heated together were discussed previously.[1] Largely on the basis of infrared spectra, structures were assigned. It was later pointed out to one of us by Dr. Robert W. Holley of the New York State Agricultural Experiment Station that the structure of one of the compounds suggested as a β-lactam was almost certainly incorrect because its reactions did not coincide with those of previously known compounds of this type. As a consequence, the structures of many of the other compounds reported were probably erroneous. A restudy of these substances has now been made and evidence is presented in this paper which requires the following complete reinterpretation of the reactions and structures of the molecules involved.

When 2-pyridone reacted with α-bromoacrylic acid, the expected product[1] (I) was not obtained. Instead, cyclization occurred and 2-carboxy-2,3-dihydroöxazolo[2,3-a]pyridinium bromide (II) was formed. Reduction of II with hydrogen and platinum oxide yielded 1-piperidinelactic acid hydrobromide (III), the structure of which was proved by synthesis from 1-piperidineacetaldehyde cyanohydrin (IV).

When II was heated with dilute sodium hydroxide, the oxazolinium ring was cleaved and the salt of 2-oxo-1(2H)-pyridinelactic acid (V) resulted. The same compound (V) was also formed when 2-pyridone reacted with glycidic acid.

In quite analogous fashion, treatment of II with aqueous ammonia gave 2-imino-1(2H)-pyridinelactic acid (VI). Compound VI liberated ammonia when heated with dilute alkali and V was obtained.

When VI was treated with ethanolic or aqueous hydrogen bromide at room temperature, a remarkably facile ring-closure reaction occurred and 3,4-dihydro-3-hydroxy-2H-pyrido[1,2-a]pyrimidin-2-one hydrobromide (VII) was obtained. When aqueous ammonia was added to an aqueous solution of VII and the resulting solution was evaporated to dryness under reduced pressure on a water-bath, an equally remarkable ring-opening reaction occurred and VI was reformed.

When the present work was begun, structures other than that given were considered possible for the compound now designated as VII. However, the discussion in this paper will be confined to VII since the experimental facts have established it as correct. With the structure of compound VII proved, the structures assigned to compounds II, V and VI become unequivocal and those previously suggested become untenable.[1]

It is pertinent first to point out that in compound

(1) R. Adams and V. V. Jones, THIS JOURNAL, **71**, 3826 (1949).