stereomer with thionyl chloride followed by hydrolysis gives excellent yields of benzoic acid and 2-aminopyridine. Either stereomer (or their mixture) with concentrated sulfuric acid undergoes not only Beckmann rearrangement but also hydrolysis, giving, however, exclusively picolinic acid and sulfanilic acid, the latter by incidental sulfonation of the corresponding aniline.

4. On the current premise of *trans* interchange of radicals during Beckmann rearrangement, these results require for the higher-melting oxime the *anti*-phenyl configuration; for the lower-melting oxime, the *syn*-phenyl configuration.

5. The benzenesulfonate and *p*-toluenesulfonate esters of the lower-melting oxime have been prepared and shown to undergo thermal Beckmann rearrangement directly, in solvents, or even slowly on standing at ordinary temperature.

6. Treatment of the lower-melting oxime with thionyl chloride leads under specified conditions to the hydrochlorides of N-(2-pyridyl)-benzimidyl chloride or of N,N'-di-(2-pyridyl)-benzamidine. The higher-melting stereomer with thionyl chloride can be caused to give the hydrochloride of N-phenylpicolinimidyl chloride.

7. In the course of this work the *p*-nitrophenylhydrazone and both stereoisomeric 2,4-dinitrophenylhydrazones of 2-benzoylpyridine, together with the bisulfate salt of the low melting form of 2-benzoylpyridine oxime, have incidentally been characterized.

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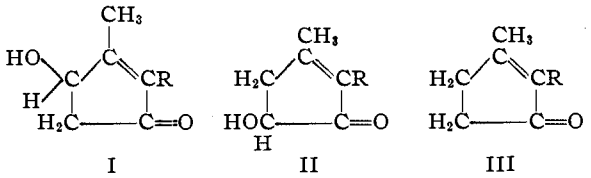
Constituents of Pyrethrum Flowers. XXII. Synthesis and Relative Toxicity of Two Isomers of Cinerin I

BY F. B. LAFORGE, NATHAN GREEN AND W. A. GERSDORFF

It has been shown that the hydroxyl group in dihydrocinerolone (Ia) and tetrahydropyrethrolone (Ib), and hence in cinerolone (Ic) and pyrethrolone (Id), occupies position 4, in the nucleus instead of position 5 as formerly accepted.



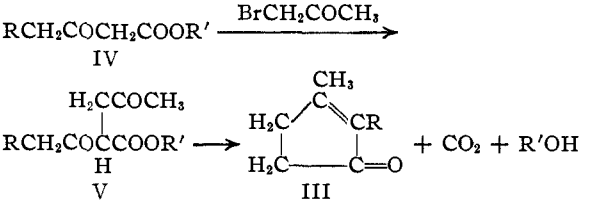
I II III

a, R = —*n*-C_4H_9
b, R = —*n*-C_5H_{11}
c, R = —$CH_2CH{=}CHCH_3$
d, R = —$CH_2CH{=}CH{-}CH{=}CH_2$
e, R = —$CH_2CH_2CH{=}CH_2$

This revision in their structures resulted from the fact that 2-butyl-5-hydroxy-3-methyl-2-cyclopentene-1-one (IIa) was not identical with dihydrocinerolone[1] and from the synthesis of the 2-butyl[2] and 2-amyl-4-hydroxy compounds[3] (Ia and Ib), identical with dihydrocinerolone and tetrahydropyrethrolone, respectively. The synthesis of the last two compounds was accomplished by the bromination of dihydrocinerone (IIIa) and tetrahydropyrethrone (IIIb) in the allylic, 4, position with N-bromosuccinimide and subsequent replacement of the bromine with hydroxyl.

Owing to the presence of an unsaturated side chain, this method is not available for a synthesis of cinerolone, where the reagent causes complete decomposition of cinerone (IIIc). Since no other method has yet been found for the introduction of hydroxyl in position 4 in cinerone itself, we have undertaken to prepare the 5-hydroxycinerone (IIc) and its analog with a 3-butenyl side chain (IIe), and have compared the toxicities of their chrysanthemum monocarboxylic acid esters with those of cinerin from natural sources and the pyrethrum standard. The results of such tests would show the effect of the transposition of the acyl group from position 4 to position 5 in the nucleus, and of the double bond from 2 to 3 in the side chain.

For the synthesis of IIc and IIe the starting compounds are cinerone (IIIc) and 2-(3-butenyl)-3-methyl-2-cyclopenten-1-one (IIIe), the syntheses of which have been described by Harper,[4] and are based on the general procedure of Hunsdiecker.[5] The steps involved are illustrated by the scheme



IV V III

For the synthesis of cinerone (IIIc) we have found it more convenient to prepare the intermediate, ethyl 3-oxo-6-octenoate, by a series of reactions different from those employed by Harper.

The reaction of crotyl chloride with ethyl acetoacetate followed by decarbethoxylation furnished

(1) LaForge and Soloway, THIS JOURNAL, **69**, 186 (1947).
(2) LaForge and Soloway, *ibid.*, **69**, 989 (1947).
(3) Dauben and Wenkert, *ibid.*, **69**, 2074 (1947).
(4) Harper, *J. Chem. Soc.*, 892 (1946).
(5) Hunsdiecker, *Ber.*, **75B**, 455 (1942).

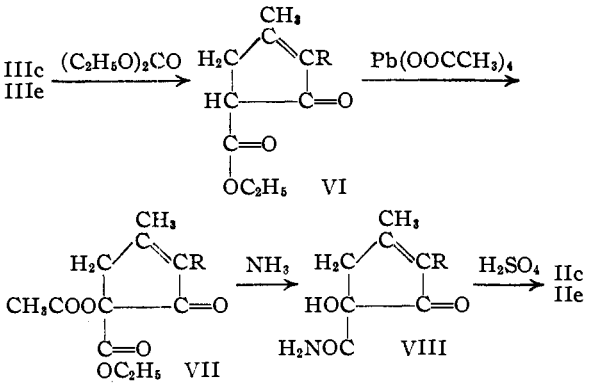
5-hepten-2-one, which was carbethoxylated on the methyl group with ethyl carbonate to IVc. Except for certain minor details the procedure from this stage on was according to the directions as published.[4]

Harper reports that the melting points of the semicarbazones and *p*-nitrophenylhydrazones of synthetic cinerone differ from the melting points of these derivatives of cinerone prepared from natural cinerolone. He believes this discrepancy may be due to geometric isomerism involving the unsaturated side chain. We have made the same comparisons and observed substantially the same divergencies. This problem is one that requires additional study and will be given further consideration in our next article.

In the synthesis of 2-(3-butenyl)-3-methyl-2-cyclopenten-1-one (IIIe), we have also deviated from the directions in the preparation of the intermediate, 5-hexenoic acid.

With 4-penten-1-ol as the initial product, the corresponding 5-hexenonitrile was prepared *via* the 5-bromo-1-pentene, which was saponified to the required acid. From this stage the steps as directed led to methyl-3-oxo-7-octenoate (IVe).

For the synthesis of 5-hydroxycinerone (IIc) and 2-(3-butenyl)-5-hydroxy-3-methyl-2-cyclopentene-1-one (IIe), we have employed the same sequence of reactions as in the synthesis of the dihydro compound,[2] which is represented by the scheme



The 5-hydroxycinerone (IIc) and its analog with the 3-butenyl side chain (IIe) are colorless, odorless liquids which reduce Fehling solution. The former yields a semicarbazone but, strangely, this derivative could not be obtained from the compound IIe, although it readily formed a 3,5-dinitrobenzoate, which in turn yielded a semicarbazone.

The 5-hydroxycinerone (IIc) and 2-(3-butenyl)-5-hydroxy-3-methyl-2-cyclopenten-1-one (IIe) yielded the corresponding chrysanthemum monocarboxylic acid esters by esterification by the method previously described,[6] and these isomers of natural cinerin I were tested for insecticidal activity.

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

From the results obtained by the method described in the Experimental Section, the chrysanthemum acid ester of the hydroxyketone IIc is about one-sixth as toxic to house flies as the pyrethrum standard and, in comparison with previous results,[7] about one-eighth as toxic as its isomer cinerin I (the ester of the hydroxyketone Ic). Thus, the transposition of the acyl group from position 4 in the nucleus to position 5 has resulted in a decrease in toxicity to one-eighth. With respect to the two compounds with the acyl group in position 5, the chrysanthemum acid ester of the hydroxyketone IIe is nearly half again as toxic as the ester of the hydroxyketone IIc; that is, the transposition of the double bond in the side chain from the 2 to the 3 position has resulted in an increase in toxicity of nearly 50%.

The presence of a double bond in the side chain is essential to high insecticidal activity, since it has already been shown that tetrahydropyrethrin I has relatively low toxicity.[7]

Experimental

5-Heptene-2-one.[8,9,10]—Three hundred and ninety grams (3 moles) of ethyl acetoacetate was added to a cold solution of 81 g. (1.5 moles) of sodium methoxide in 600 ml. of absolute methanol. After a short time 136 g. (1.5 moles) of crotyl chloride was added and the mixture was warmed on the steam-bath for one hour; the solution was then acidified with a few drops of acetic acid. The separated sodium chloride was removed by filtration and the solvent by distillation in vacuum. The excess of ethyl acetoacetate was removed at 10 mm. on a column still. The residue (256 g.) was suspended in 3200 ml. of hot water, and 250 g. of sodium hydroxide in 1800 ml. of water was added in three portions over a period of two hours, while the solution was being heated and stirred. The product was separated and the aqueous solution extracted with petroleum ether. After the solution had been dried, the solvent was removed by distillation and the residue combined with the main portion and distilled: yield 133 g. (79%); b. p. 151–154° (750 mm.); $n^{25}D$ 1.4275. The constants reported are: b. p. 151–153°, 152–155°; n_D 1.4272 (25°), 1.4292 (20°).

Ethyl 3-Oxo-6-octenoate.[10]—Fifty-eight grams (2.4 moles) of sodium hydride was covered with 300 ml. of absolute ether under nitrogen in a flask equipped with stirrer, condenser, and dropping funnel; 283 g. (2.4 moles) of ethyl carbonate was added, and 136 g. (1.2 moles) of 5-hepten-2-one was slowly dropped into the refluxing solution over a period of five hours. As the contents of the flask become thick, more ether was added. The reflux was continued for about two hours longer, and the contents of the flask was then poured into ice and water containing 150 ml. of acetic acid. The ethereal solution was washed with dilute sodium bicarbonate and saturated sodium chloride solution. After the solution had been dried with anhydrous sodium sulfate, the solvent was removed on the steam-bath, and the residue, after removal of the excess of ethyl carbonate *in vacuo*, was distilled from a modified Claisen flask. The yield was 188 g. (85%); b. p. 110–120° (10 mm.); $n^{25}D$ 1.4460.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76; OC_2H_5, 24.4. Found: C, 64.67; H, 8.80; OC_2H_5, 23.9.

Ethyl 2-Acetonyl-3-oxo-6-octenoate (Vc).—Seven and two-tenths g. (0.3 mole) of sodium hydride was covered

(7) Gersdorff, *J. Econ. Entomol.*, **40**, 878 (1948).

(8) Kimel and Cope, This Journal, **65**, 1996 (1943).

(9) Braun and Gossel, *Ber.*, **57**, 373 (1924).

(10) This preparation was made in collaboration with S. B. Soloway.

with 80 ml. of dry dioxane, and 55 g. (0.3 mole) of ethyl 3-oxo-6-octenoate in 70 ml. of the same solvent was added slowly. After all the sodium hydride had dissolved, the solution was cooled to about −25° with a Dry Ice-bath, causing separation of the sodium compound. A solution of 45 g. of bromoacetone in 50 ml. of dioxane was added at once and the reaction mixture allowed to come to room temperature. After the heat evolution had ceased, the solution was refluxed for a short time until it had become neutral. Without removal of the separated sodium bromide, most of the solvent was removed by vacuum distillation.

2-(2-Butenyl)-3-methyl-2-cyclopenten-1-one (IIIc) (Synthetic Cinerone).—The crude residue was dissolved in 1 liter of 3% sodium hydroxide solution, which was slowly heated to 70° during two hours. This temperature was maintained for another hour and then 20 ml. of sulfuric acid in 100 ml. of water was added, and the oil which had separated was heated on the steam-bath until the evolution of carbon dioxide ceased. The aqueous solution was again boiled, cooled and extracted with petroleum ether. The extract was added to the decarboxylated material, and the solution was washed with water and sodium carbonate solution and dried, and the residue distilled from a modified Claisen flask. The yield of synthetic cinerone was 20.2 g. (45%). The constants observed for the free ketone and its derivatives in comparison with those reported by Harper, are given in Table I.

TABLE I

CONSTANTS FOR SYNTHETIC (IIIc) AND NATURAL CINERONES AND SOME OF THEIR DERIVATIVES

	Substance		Observed	Reported by Harper
1	Synthetic cinerone (IIIc)	B. p.	107–113° (9 mm.)	119° (15 mm.)
		$n^{25}D$	1.4980	1.4983
2	Natural cinerone	$n^{31}D$	1.4978[11]	..
3	Semicarbazone of synthetic cinerone	M. p.	216–218°	220°
4	Semicarbazone of natural cinerone	M. p.	214–215°	..
	Mixture of 3 and 4	M. p.	209–210°	..
5	*p*-Nitrophenylhydrazone of synthetic cinerone IIIc	M. p.	155–156°	162°
6	*p*-Nitrophenylhydrazone of natural cinerone	M. p.	148°	..
	Mixture of 5 and 6	M. p.	153–155°	..

5-Bromo-1-pentene.—This compound has been described,[12,13] but the best yields were obtained by a modification of the published directions. A mixture of 133 g. (1.55 moles) of 4-penten-1-ol[14] and 35 g. (0.44 mole) of pyridine was placed in a flask equipped with a stirrer. To this mixture 174 g. (0.64 mole) of phosphorus tribromide was added dropwise over a period of about four hours, while the contents of the flask was held at about −25 to −30° in an ethanol-Dry Ice-bath. The stirrer was then replaced by a condenser, and the product was distilled with an oil-bath until no more distillate was obtained. This distillation was made with caution because the escaping vapors tend to ignite spontaneously, especially near the end of the operation. The distillate was washed twice with water and then with dilute sodium hydroxide, and was dried with calcium chloride. The yield of product boiling between 128 and 130° at atmospheric pressure was 189 g. (81.5%); $n^{25}D$ 1.4610.

(11) LaForge and Barthel, *J. Org. Chem.*, **10**, 114 (1945).

(12) Juvala, *Ber.*, **63**, 1993 (1930).

(13) Kharasch and Fuchs, *J. Org. Chem.*, **9**, 370 (1944).

(14) "Organic Syntheses," Vol. XXV, John Wiley and Sons, Inc., New York, N. Y., 1945, p. 84.

5-Hexenonitrile.—Ninety-six grams (0.61 mole) of 5-bromo-1-pentene, 49 g. (0.75 mole) of potassium cyanide, and 250 ml. of ethylene glycol were stirred at 100° for two hours. The light-brown solution was diluted with water and the separated nitrile extracted with ether.[15] The residue from the washed and dried solution was distilled at atmospheric pressure; yield 51 g. (88%); b. p. 158–162°, 54–59° (16 mm.); $n^{25}D$ 1.4268.

Anal. Calcd. for C_6H_9N: N, 14.7. Found: N, 13.9.

5-Hexenoic Acid.—One hundred and twenty-nine grams of the nitrile was refluxed with 800 ml. of 20% potassium hydroxide for eighteen hours. After the alkaline solution had been extracted with ether, it was acidified to congo red paper and the separated acid was extracted with ether. The ethereal solution was dried and the solvent removed. The yield was 138 g. (89%); b. p. 101–105° (13 mm.); $n^{25}D$ 1.4318. The constants previously reported are b. p. 107° (17 mm.)[16]; $n^{20}D$ 1.4343. The acid chloride was obtained in nearly quantitative yield by the addition of 75 g. of redistilled thionyl chloride to 48.5 g. of the acid during forty-five minutes at 0°, b. p. 45–50° (16.5 mm.).

Ethyl 2-Acetyl-3-oxo-7-octenoate.—Ten and five-tenths grams (0.44 mole) of sodium hydride was placed in a flask with stirrer, condenser, and dropping funnel, and covered with 400 ml. of dry ether; 60 g. of ethyl acetoacetate was added slowly over a period of forty-five minutes, together with more ether as the contents of the flask thickened. It was then cooled in an ice-bath, and 52 g. (0.39 mole) of the acid chloride was added during about thirty minutes. After the reaction mixture had been stirred for an additional thirty minutes, ice and water containing a sufficient quantity of sulfuric acid was added and the ethereal layer separated. After washing, drying, and removal of the solvent, the residue yielded 73.3 g. (83%) of the ester; b. p. 146–148° (17 mm.); $n^{25}D$ 1.4740. This represents an increase in yield over that reported (60%),[4] b. p. 148° (16 mm.).

Methyl 3-Oxo-7-octenoate (IVe).—This intermediate was prepared by dissolving 217 g. of ethyl 2-acetyl-3-oxo-7-octenoate (0.96 mole) in a cold solution of sodium methoxide prepared by dissolving 24 g. of sodium in 470 ml. of absolute methanol. After twenty-one hours at room temperature the pale-yellow solution was diluted with 1500 ml. of ice water containing 30 ml. of sulfuric acid. The separated oil was extracted with petroleum ether, and after the solution had been dried, the solvent was removed and the residue distilled. A fraction distilling below 114°, (16 mm.) amounting to 47 g., consisted largely of the methyl ester of 5-hexenoic acid, from which 23.7 g. of the acid was recovered by saponification, acidification and extraction, b. p. 107° (19 mm.); $n^{25}D$ 1.4321. The main distillate of b. p. 114–122° (16 mm.), $n^{25}D$ 1.4500, amounted to 110.7 g. (68% without consideration of the recovered acid).

Methyl 2-Acetonyl-3-oxo-7-octenoate (Ve).—The method of preparation was the same as the one described for Vc. The quantities employed were 55 g. of IVe (0.32 mole) in 175 ml. of dioxane, 8.2 g. of sodium hydride, and 49.5 g. of bromoacetone in 75 ml. of dioxane.

2-(3-Butenyl)-3-methyl-2-cyclopenten-1-one (IIIe).—The free ketone was obtained in the manner already described; yield, 26.7 g. (55%); b. p. 115–118° (16 mm.) $n^{25}D$ 1.4943. Harper reports b. p. 110 (13 mm.), $n^{25}D$ 1.4948. The semicarbazone melted as reported, at 188°.

2-(2-Butenyl)-5-carbethoxy-3-methyl-2-cyclopenten-1-one[10] (VIc).—Sodium hydride, 9.1 g. (0.35 mole), was covered with 100 ml. of absolute ether in a flask with stirrer and condenser, and 45 g. of ethyl carbonate was added. A solution of 28.4 g. (0.19 mole) of cinerone (IIIc) was introduced dropwise over a period of one and one-half hours, and more ether was added as the contents of the flask thickened. The reflux was continued for one hour, after which 25 ml. of acetic acid was added, followed by

(15) This is an unpublished general method for the preparation of nitriles from alkyl halides which has been employed previously in this laboratory.

(16) Linstead and Rydon, *J. Chem. Soc.*, 1996 (1934).

addition of water. The ethereal solution was separated, washed with sodium bicarbonate solution, and dried, and the solvent removed. The residue after removal of the excess of ethyl carbonate at 13 mm. was distilled on a modified Claisen flask. After a forerun of 5.8 g., the yield was 24.5 g. (58%), b. p. 110–115° (0.4 mm.).

Anal. Calcd. for $C_{13}H_{18}O_3$: OC_2H_5, 24.5. Found: OC_2H_5, 24.9.

The compound gives a blue color with ferric chloride. It was later observed that the success of this preparation depends on the particle size of the sodium hydride.[17] The compound can also be prepared by the forced sodium ethoxide condensation, which was employed in the preparation of the 3-butenyl compound (VIe).

2-(3-Butenyl)-5-carbethoxy-3-methyl-2-cyclopenten-1-one (VIe).—This compound was prepared by the forced sodium ethoxide catalyzed condensation method.[18] Sodium ethoxide was prepared by gradually adding 25 ml. of absolute ethanol to 3.2 g. (0.13 mole) of sodium hydride covered with 60 ml. of benzene in a flask equipped with stirrer and a short distilling column. After the sodium hydride had dissolved, the alcohol was removed by azeotropic distillation with continuous addition of benzene until the refractive index of the distillate corresponded to that of the pure solvent. Twenty grams (0.133 mole) of IIIe in 78 g. (0.66 mole) of ethyl carbonate was added dropwise, with stirring, over a period of one hour while about 300 ml. of distillate, which was constantly replaced by the pure solvent was being distilled off. When the refractive index of the distillate was constant, the reaction was considered complete. Ten milliliters of glacial acetic acid in 50 ml. of water was added, and the benzene solution was washed with water, sodium bicarbonate and salt solution. After removal of the solvent, the residue yielded on distillation 24.9 g. (84%) of distillate; b. p. 101–103° (0.1 mm.); $n^{25}D$ 1.4872.

Anal. Calcd. for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16; OC_2H_5, 20.2. Found: C, 69.92; H, 8.23; OC_2H_5, 19.3.

5-Acetoxy-2-(2-butenyl)-5-carbethoxy-3-methyl-2-cyclopenten-1-one (VIIIc).[10]—A solution of 13.3 g. (0.06 mole) of the carbethoxy compound in 60 ml. of glacial acetic acid was warmed to 50°, and 45 g. of red lead was added, with stirring, in small portions. The reaction was exothermic, and the temperature was held between 50 and 60°, time being allowed for the red color to disappear after each addition of reagent. When all had been added and a positive test for excess lead tetraacetate persisted for fifteen minutes, it was decomposed with a few drops of glycerol. Water was added and the reaction products were extracted with ether. After repeated washings with water and finally with sodium bicarbonate and salt solution, the solvent was removed and the residue distilled. The yield was 8.4 g. (50%); b. p. 135–140° (0.5 mm.); $n^{25}D$ 1.4865. A considerable residue remained in the flask, probably the product of addition of acetoxy groups on the side chain.

Anal. Calcd. for $C_{15}H_{20}O_5$: OC_2H_5, 16.1. Found: OC_2H_5, 15.9.

5-Acetoxy-2-(3-butenyl)-5-carbethoxy-3-methyl-2-cyclopenten-1-one (VIIe).—Twenty-three grams (0.10 mole) of VIe was dissolved in 140 ml. of glacial acetic acid, and 46 g. (0.10 mole, 100% basis) of lead tetraacetate was added in small portions to the stirred solution while the temperature was maintained at slightly below 40°. Each addition of the reagent caused a rise in temperature and the temporary appearance of a yellow color. The reaction required about one and one-quarter hours. One milliliter of glycerol was added, and about half the acetic acid was distilled off *in vacuo*. Water was added and the separated reaction products were extracted with ether. The extract was washed repeatedly with water and finally with bicarbonate and salt solution and dried. The residue was distilled from a Claisen flask. The yield was 12.6 g. (43%); b. p. 127–131° (0.2 mm.). The compound is a viscous, colorless liquid; $n^{25}D$ 1.4837.

Anal. Calcd. for $C_{15}H_{20}O_5$: OC_2H_5, 16.1. Found: OC_2H_5, 16.3.

2-(2-Butenyl)-5-carbamyl-5-hydroxy-2-cyclopenten-1-one (VIIIc).—Ten grams of VIIc was covered with 18 ml. of concentrated ammonium hydroxide and allowed to stand for three days with frequent shaking. The mass of crystals that formed was filtered from the aqueous solution and washed with water and with ether. The yield was 6 g. (80%). A part was recrystallized from water and melted at 115°.

Anal. Calcd. for $C_{11}H_{15}O_3N$: C, 63.14; H, 7.23; N, 6.70. Found: C, 63.18; H, 7.51; N, 6.61.

2-(3-Butenyl)-5-carbamyl-5-hydroxy-3-methyl-2-cyclopenten-1-one (VIIIe) was prepared in the same manner from 11.3 g. of VIIe and 25 ml. of ammonium hydroxide; yield 6.0 g. (71%), m. p. 86–87°.

Anal. Calcd. for $C_{11}H_{15}O_3N$: C, 63.14; H, 7.23; N, 6.70. Found: C, 63.15; H, 7.57; N, 6.49.

2-(2-Butenyl)-5-hydroxy-3-methyl-2-cyclopenten-1-one (IIc).—Three grams of the amide (VIIIc) was boiled for one hour with 25 ml. of 10% sulfuric acid. The amide first dissolved in the hot solution, which soon became turbid with separation of an oily phase. The product was extracted with ether and the residue distilled; yield of the hydroxy ketone 1.65 g. (70%); b. p. 93–96° (0.4 mm.); $n^{25}D$ 1.5130. The compound reduced Fehling solution strongly. The semicarbazone was prepared and after recrystallization from ethyl acetate it melted at 183–184°.

Anal. Calcd. for $C_{11}H_{17}O_2N_3$: C, 59.17; H, 7.68. Found: C, 59.21; H, 7.66.

2-(3-Butenyl)-5-hydroxy-3-methyl-2-cyclopenten-1-one (IIe) was prepared in the same manner from 6 g. of VIIIe; yield, 3.3 g. (70%); b. p. 90–92° (0.2 mm.); $n^{25}D$ 1.5130.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49; $2CH_3$, 9.4. Found: C, 71.80; H, 8.36; CH_3, 10.7.

The ketone reduces Fehling solution strongly, but no semicarbazone was obtained either by the pyridine–ethanol or the sodium acetate method, where only slow decomposition was observed.

The 3,5-dinitrobenzoyl ester was prepared in benzene solution by reaction of the acid chloride in the presence of pyridine. It was recrystallized from methanol and melted at 90°.

Anal. Calcd. for $C_{17}H_{16}O_7N_2$: C, 56.66; H, 4.48. Found: C, 56.66; H, 4.73.

The 3,5-dinitrobenzoyl ester yielded a semicarbazone in pyridine–ethanol in the form of orange-colored prisms, which was recrystallized from methanol, m. p. 176–177°.

Anal. Calcd. for $C_{18}H_{19}O_7N_5$: C, 51.88; H, 4.59. Found: C, 51.37; H, 4.83.

Preparation of Chrysanthemum Acid Esters.—The hydroxy ketones IIc and IIe were esterified with chrysanthemum monocarboxylic acid chloride in the manner already described.[6] Traces of the benzene solvent were removed in a high vacuum, and the esters, undistilled but of a high degree of purity in deodorized kerosene, were employed for the biological tests.

Relative Toxicities of Isomers of Cinerin I.—The toxicity tests were made by the Campbell turntable method[19] with adult house flies (*Musca domestica* L.) three or four days old, reared by standard procedure, as the test insects. Knockdown and mortality percentages were determined for deodorized kerosene sprays at a series of concentrations, six replications being made at each

(17) Green and LaForge, This Journal, **70**, 2287 (1948).

(18) Wallingford, Homeyer and Jones, *ibid.*, **63**, 2252 (1941).

(19) F. L. Campbell and W. N. Sullivan, *Soap*, [6] **14**, 119 (1938).

concentration with approximately 100 flies to each test.

The tests were made in two series four months apart, because of the time involved in the preparation of the compounds and the desirability of testing the compounds immediately after their preparation. The second series includes another preparation of the ester of IIc, and even though the two series of tests on this compound were made on populations of flies differing greatly in resistance, the results on relative toxicity are in good agreement. Tests at one concentration with the first preparation, which had been held in a refrigerator at 2°, were repeated in the second series, and the mortality results were in agreement with those of the second preparation.

The results in comparison with a standard pyrethrum–kerosene extract (55% of the total "pyrethrins" being pyrethrin I + cinerin I) are summarized in Table II.

TABLE II

TOXICITY OF TWO ISOMERS OF CINERIN I AS COMPARED WITH THAT OF PYRETHRUM EXTRACT

Material	Concentration, mg. per ml.	Knock-down in 25 min., %	Mortality in 1 day, %	Mean concentration causing 50% mortality, mg. per ml.	Relative toxicity, %
Series I					
Chrysanthemum ester of hydroxy ketone IIc (preparation 1)	16	100	92	6.43 ± 0.50	16.1 ± 1.7
	8	99	51		
	4	91	20		
	2	39	10		
Pyrethrum extract	4	100	92	1.03 ± 0.08	100
	2	100	71		
	1	100	50		
Series II					
Chrysanthemum ester of hydroxy ketone IIc:					
Preparation 2	16	100	56	13.6 ± 1.07	18.2 ± 1.9
	8	99	34		
	4	85	6		
Preparation 1	8	99	34		
Chrysanthemum ester of hydroxy ketone IIe	32	100	94	10.7 ± 0.85	23.0 ± 2.4
	16	100	71		
	8	99	35		
	4	60	9		
Pyrethrum extract	4	100	68	2.48 ± 0.19	100
	2	100	41		
	1	100	21		

The mortality results were plotted on log-probability paper, and the straight lines approximating the course of toxic action for each material were fitted by the method of least squares. From the equations of these lines the concentrations required to cause 50% mortality were determined. These concentrations were compared with the value obtained for the pyrethrum extract standard with the same population of flies.

For comparison of the toxicity of these isomers with cinerin I, previous results obtained with the latter compound and the same standard[7] were used in conjunction with the results in Table II.

The standard errors were obtained from an analysis of variance of the logarithms of the concentrations causing 50% mortality, the errors of concentrations being determined from those of logarithms.

The knock-down values of both the cinerin isomers derived from the hydroxyketones IIc and IIe are appreciably lower than those of the natural pyrethrins and cinerins, the knock-down caused by the isomers falling below 100% with concentrations of 8 mg. per milliliter and lower, whereas with the latter group knock-down is still complete at a concentration one-fourth of this, or lower, with flies of comparable resistance.

Summary

The synthesis of the chrysanthemum monocarboxylic acid esters of 2-(2-butenyl)-5-hydroxy-3-methyl-2-cyclopentene-1-one (5-hydroxycinerone) and of 2-(3-butenyl)-5-hydroxy-3-methyl-2-cyclopentene-1-one are described.

Results of toxicity tests on house flies (*Musca domestica* L.) are presented which show that these isomers of cinerin I possess insecticidal activity of a high order but lower than that of the natural cinerins or pyrethrins.

The ester of the 2-butenyl-4-hydroxy ketone, natural cinerin I, is about eight times as toxic as the ester of the 2-butenyl-5-hydroxy ketone. The ester of the 3-butenyl-5-hydroxy ketone is but slightly more toxic than the latter compound. The position of the ester group on the cyclopentenone nucleus is therefore of greater importance from the standpoint of insecticidal activity than the position of the double bond in the side chain.

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