2-*n*-Tridecyl-4,6,7-trimethyl-5-hydroxycoumaron (IX, R = *n*-$C_{13}H_{27}$).—The diketone VIII (560 mg.) was warmed on the steam-bath for one hour with aqueous sodium hydroxide (1 *N*, 20 cc.) in an atmosphere of nitrogen. (When air was allowed to come into contact with the reaction mixture, the product was a red oil which could not be crystallized.) The cooled mixture was acidified with hydrochloric acid and then steam-distilled. From the distillate there was obtained 51 mg. (20%) of 2-methyl-4,6,7-trimethyl-5-hydroxycoumaron (IX, R = CH_3), m. p. and mixed m. p., 136–137°. The residual oil in the distillation flask solidified on cooling; it was removed and crystallized from methanol, when it weighed 260 mg. (54%) and melted at 101–102°. The analytical sample, crystallized from methanol, melted at 102–104°.

Anal. Calcd. for $C_{24}H_{38}O_2$: C, 80.39; H, 10.68. Found: C, 80.41; H, 11.04.

The absorption spectrum in the ultraviolet is shown in Fig. 1. The diketone VIII (430 mg.) was recovered unchanged after 500 mg. of it was boiled with hydrochloric acid (10 cc.) and ethanol (2 cc.) for seven hours; likewise, action of hydrogen chloride in refluxing acetic acid (10 cc.) for one hour upon the diketone (500 mg.) did not bring about ring closure; the recovery of diketone was 275 mg.

2-*n*-Tridecyl-4,6,7-trimethyl-5-hydroxycoumaran (X, R = *n*-$C_{13}H_{27}$).—The coumaron IX (75 mg.) in acetic acid (10 cc.) was shaken with hydrogen at 46° and under a pressure of 20 lb. for four hours in the presence of a palladium–charcoal catalyst. The solvent was removed under reduced pressure at 40°; the residue was dissolved in methanol and the catalyst was removed by centrifugation. The solution, when concentrated and cooled, deposited a white solid melting at 93–94°. When mixed with the coumaran (m. p. 102–104°), the substance also melted at 93–94°.

Anal. Calcd. for $C_{24}H_{40}O_2$: C, 79.94; H, 11.18. Found: C, 79.76; H, 11.22.

The absorption spectrum in the ultraviolet is shown in Fig. 2. The coumaron IX (360 mg.) in dry ethanol (10 cc.) was heated on the steam-bath for fifteen minutes with Raney nickel catalyst. The catalyst was removed, fresh catalyst was added, and the mixture was subjected to the action of hydrogen for one hour at 125° and 1600 lb. The product weighed 230 mg. and melted at 101–103°. This material, subjected to the same conditions as before, but at 140°, gave a product which melted at 97–99°, alone or when mixed with known IX. The absorption spectrum in the ultraviolet indicated that no reduction had occurred.

Summary

1. The coumaran 2-(6′,10′,14′-trimethyl-2′-pentadecyl) - 4,6,7 - trimethyl - 5 - hydroxycoumaran, I, an isomer of α-tocopherol, II, has been synthesized. The coumaran has been characterized by its absorption spectrum, by conversion into an allophanate melting at 176–180° and by the absorption spectrum of the latter. Although I differs from II only in the size of the hetero ring, I has only about 5% as much vitamin E activity as II.

2. The synthesis of Smith and King, whereby 2-isopropyl-5-hydroxycoumaran and homologs are produced, has been modified in such a way that the more accessible unsymmetrical acetylacylmethanes may be used instead of the symmetrical diketones. When the R of the acyl group has a relatively high molecular weight, the coumaron with the higher alkyl group is formed exclusively or in preponderant amounts; if two coumarons are formed, the simple one may be removed from the reaction product by steam distillation. In this way, 2-*n*-tridecyl-4,6,7-trimethyl-5-hydroxycoumaron (IX) R = *n*-$C_{13}H_{27}$, has been prepared and separated from 2,4,6,7-tetramethyl-5-hydroxycoumaron (IX, R = CH_3), formed in the same reaction. The coumaron IX (R = *n*-$C_{13}H_{27}$) has been reduced to the corresponding coumaran X (R = *n*-$C_{13}H_{27}$).

3. The absorption spectra of a number of intermediates in the above syntheses have been determined.

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Preparation and Cyclization of Certain Insecticidally Active α-Acetyl-δ-keto Esters

BY HERMAN WACHS AND OSCAR F. HEDENBURG

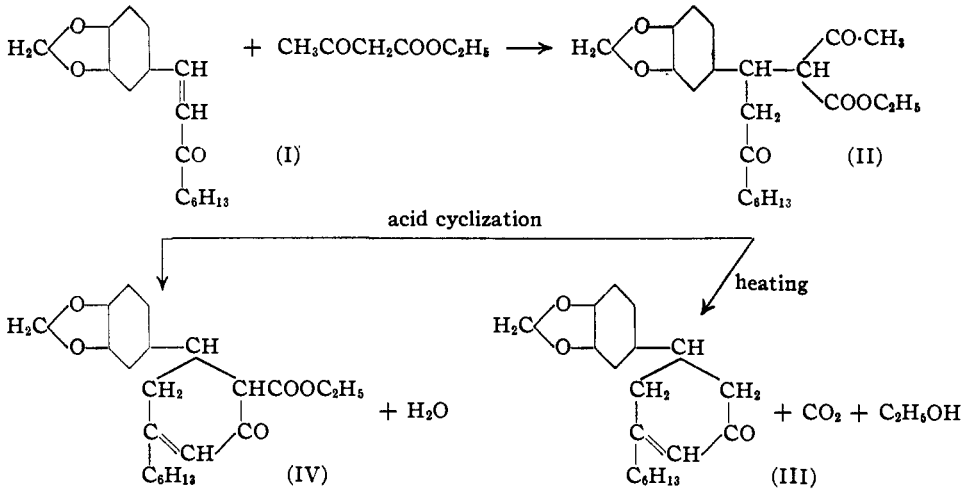
The condensation of ethyl acetoacetate with hexyl 3,4-methylenedioxystyryl ketone[1] at room temperature yields a mixture having high insecticidal activity. When allowed to crystallize, 3-hexyl - 5 - (3,4 - methylenedioxyphenyl) - 2 - cyclohexene-1-one (III) is obtained, which has been found to have the same insecticidal activity as the original mixture or the remaining mother liquor. This mother liquor contains resinous material and approximately 50% of 3-hexyl-5-(3,4-methylenedioxyphenyl) - 6 - carbethoxy - 2 - cyclohexene - 1 - one (IV). Proceeding on the assumption that the resinous portion was of little activity, it appeared desirable to devise a method by which the above ester (IV) could be obtained as the main product. The present paper describes the procedure developed to accomplish this purpose. This procedure also made it possible to obtain esters other than ethyl esters and to compare their relative effectiveness. The work was expanded to include compounds containing the furfuryl group in the 3 position of the cyclohexenone ring.

It was assumed that a Michael addition[2] takes place intermediate to the formation of the cyclohexenone ring. Taking advantage of the fact that such addition reactions are reversible,[3] by employing a large excess of ethyl acetoacetate and by

(1) Hedenburg and Wachs, THIS JOURNAL, **70**, 2216 (1948).

(2) Michael, *J. prakt. Chem.*, **35**, 351 (1887).

(3) Ingold and Powell, *J. Chem. Soc.*, 1976–82 (1921).



working at a temperature of +5° we obtained α-acetyl-β-(3,4-methylenedioxyphenyl)-δ-ketoethyl undecylate (II) from hexyl 3,4-methylenedioxystyryl ketone (I), in a yield of 65%. Compound (II) was a white crystalline solid melting at 149°; above its melting point it yielded ethyl alcohol, carbon dioxide and the cyclohexenone (III) in stoichiometric proportions.

When compound (II) was refluxed in benzene solution in the presence of a small quantity of toluene sulfonic acid or trichloroacetic acid, until no more water would distil over with the benzene, one molecular equivalent of water collected in the water trap, indicating that cyclization had taken place with a minimum of decomposition of the ester group. Only traces of liberated carbon dioxide were observed. The product was a light-colored, viscous liquid, which dissolved in most of the common organic solvents; it would not crystallize on cooling to −30° and could not be distilled *in vacuo* without decomposition; the saponification value indicated the presence of more than 90% of ester. On saponification, partial resinification occurred, but it was possible to isolate a good yield of crystals, which were identical with the decarboxylated cyclohexenone (III).

Hexyl 3,4-methylendioxystyryl ketone was also condensed with butyl, octyl, benzyl and allyl acetoacetates in an analogous manner and the corresponding α-acetyl-δ-keto esters were obtained in pure form. Upon cyclization by the aid of trichloroacetic or toluene sulfonic acid, the resulting allyl and butyl compounds had an insecticidal activity equal to that of the ethyl compound; the octyl and benzyl compounds were definitely inferior.

By the condensation of furfural with methyl isobutyl ketone, furylidene isobutyl ketone was prepared. It was condensed with ethyl acetoacetate and with butyl acetoacetate at 5° and the α-acetyl-δ-keto esters were isolated and purified. Upon cyclization the insecticidal activity was found to be poor.

The Table I summarizes certain characteristics of the products.

TABLE I

PROPERTIES OF SUBSTITUTED α-ACETYL-δ-KETO ESTERS

Ketone used	Aceto-acetate used	Melting point of α-acetyl-δ-keto ester, °C.	Formula	Carbon % Calcd.	Carbon % Found	Hydrogen % Calcd.	Hydrogen % Found
Hexyl-	Ethyl	149	$C_{22}H_{30}O_6$	67.67	67.92	7.75	7.55
3,4-me-	Allyl	134	$C_{21}H_{26}O_6$	68.64	68.41	7.51	7.30
thylene	Butyl	131	$C_{24}H_{34}O_6$	68.87	68.69	8.19	8.01
dioxy-	Octyl	133	$C_{28}H_{42}O_6$	70.85	70.67	8.92	8.62
styryl	Benzyl	138	$C_{27}H_{30}O_6$	71.71	71.81	7.12	7.34
Furylidene	Ethyl	116	$C_{17}H_{24}O_6$	66.28	66.41	7.84	7.51
isobutyl	Butyl	98	$C_{19}H_{28}O_6$	67.84	67.96	8.39	8.77

Experimental

α-Acetyl-β-3,4-methylenedioxyphenyl-δ-keto-ethyl Undecylate (II).—Metallic sodium (5.7 g., 0.25 mole) was dissolved in 150 cc. of anhydrous ethyl alcohol, 97 g. of ethyl acetoacetate was added, the solution cooled to 5° and, during one hour, a solution of 65 g. (0.25 mole) of hexyl 3,4-methylendioxystyryl ketone in 65 g. of benzene was added under agitation. The temperature was kept at 5 to 7° during the addition. The mixture was then agitated for an additional two hours and allowed to stand overnight at a temperature of 5 to 7°. It was neutralized with dilute hydrochloric acid under cooling, then warmed on the steam-bath to allow the benzene solution of the reaction product to separate. The benzene solution was drawn off and allowed to crystallize in an ice-box. The crystals were filtered off and washed with benzene. The dry crystals weighed 252 g. After recrystallization from benzene they melted at 149°.

Cyclization of (II).—A solution of 25 g. of (II) in 75 g. of benzene was refluxed in the presence of 1.5 g. of trichloroacetic acid or toluenesulfonic acid until no more water would distil over. The residue in the flask was neutralized with sodium carbonate solution, the benzene solution dried and filtered, the solvent distilled and the product dried *in vacuo*. It was a light colored viscous oil, the saponification value indicating about 90% of the ester, IV.

Furylidenemethyl Isobutyl Ketone.—Methyl isobutyl ketone (60 g.) was dissolved in 96 g. of methanol, 15 g. of a 20% aqueous solution of sodium hydroxide was added, and to this mixture 57.5 g. of freshly distilled furfural was added over a period of 0.5 hour under agitation at a temperature of 18 to 20°. The agitation was continued for two hours at the same temperature. The mixture was allowed to stand overnight. Water, 100 cc., and 100 cc. of benzene were added and the mixture neutralized with acetic acid. The benzene solution was separated, the solvent removed, and the remainder distilled *in vacuo*.

The final product distilled at 108° at 1.4 mm. It was a yellowish oil which darkened rather rapidly.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.12; H, 7.92. Found: C, 73.97; H, 7.84.

The melting points and the analyses of other α-acetyl-δ-keto esters, similarly prepared, are given in Table I. In each case, saponification indicated about 90% of the cyclic ester in the crude cyclized product.

Summary

The preparation of 3,4-methylenedioxyphenyl substituted α-acetyl-δ-keto esters in pure form and in good yield is outlined. A method of their cyclization which yields cyclohexenone esters of high insecticidal activity with a minimum of splitting of the ester group is described.

Furyl substituted α-acetyl-δ-keto esters were prepared and cyclized to cyclohexenone esters and were found to be of much lower insecticidal activity than the 3,4-methylenedioxyphenyl substituted products.

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Synthetic and Degradative Studies in the Isoquinoline Series. III

BY V. BRUCKNER, G. FODOR, J. KOVÁCS AND J. KISS

In previous communications[1,2] the structure of different 1,3-dimethyl-6,7-dialkoxy- and aralkoxyisoquinolines (Ia-If), of 1-benzyl-3-methyl-6,7-methylenedioxyisoquinoline (II), synthesized by us,[3,4] was established by exhaustive methylation followed by oxidation. In all cases investigated by us, degradation gives rise either to metahemipinic acid (IIIa), or to hydrastic acid (IIIb). To complete our first paper,[1] the structure of 1,3-dimethyl-6,7-methylenedioxyisoquinoline[5] (Ig) is now ascertained, by preparing it from the 6,7-dihydroxy derivative Ia of known structure.[1] Ring closure of α-(3,4-disubstituted phenyl)-β-acylaminopropanols to the isoquinolines takes place, consequently, in all cases studied by us in *m,p*-position to the alkoxy groups, to form 6,7-disubstituted 3-methylisoquinolines, independently of the substituents.

Pfeiffer, *et al.*,[6] obtained from brasiline a compound and suggested for its structure IV 1-(2′-hydroxy-4′-methoxyphenyl)-3-methyl-6,7-dimethoxyisoquinoline by analogy with the structure of the compound obtained by them from hematoxyline. They attempted to confirm its constitution by synthesis from α-(3,4-dimethoxyphenyl)-β-(2′-carbethoxy-oxy-4′-methoxybenzoylamino)-propanol. Ring closure yielded only a small amount of an oily phenolic isoquinoline; its picrate was, however, not identical with that of the compound obtained from brasiline. Ring closure of the amorphous α-(3,4-dimethoxyphenyl)-β-(2′,4′-dimethoxybenzoylamino)-propanol led to a crystalline isoquinoline isomer, but which was not identical with the methyl ether of the compound from brasiline. Therefore they assign structure V, 1-(2′-hydroxy-4′-methoxyphenyl)-3-methyl-7,8-dimethoxyisoquinoline, to the synthetic isoquinoline.

The present work was undertaken to synthesize through crystalline, well-defined intermediates the same phenolic isoquinoline whose picrate was described by Pfeiffer, *et al.*[6] As the structure of this synthetic compound and of its isomer have not been confirmed by degradation, it seemed desirable to carry out the oxidative degradation of the former.

We started with the stereoisomeric α-(3,4-dimethoxyphenyl)-β-aminopropanols. One of these (m. p. 128°) was prepared according to Bruckner[5]; another (m. p. 138°) according to Iwamoto and Hartung.[7] 2-Benzyloxy-4-methoxybenzoic acid was prepared from β-resorcylic acid *via* methyl 2-hydroxy-4-methoxybenzoate and methyl 2-benzyloxy-4-methoxybenzoate. On condensation of 2-benzyloxy-4-methoxybenzoyl chloride with the aminopropanol (m. p. 138°) the amide VI is formed; on ring closure it yielded smoothly the corresponding isoquinoline derivative (benzyl ether of IV). The stereoisomeric aminopropanol gave on a similar treatment the identical isoquinoline. The benzyloxyisoquinoline derivative afforded on hydrogenolysis (Pd charcoal) the crystalline hydroxyisoquinoline IV in nearly quantitative yield. Its picrate shows m. p. 275°; its methyl ether prepared by diazomethane, m. p. 144°; its methyl ether picrate, m. p. 231–232°. The same data are recorded by Pfeiffer, *et al.*[6], for the compound formulated by them as V (*cf.* table of m. p.'s), they are consequently identical, whereas the product obtained from brasiline is different.

As a degradative approach to the structure of this phenolic isoquinoline we have chosen the oxidation with alkaline permanganate. Metahemipinic acid alone could be detected as a fragment, identified by its m. p., analysis and conversion into its ethylimide (m. p. 228°). For the synthetic hydroxyisoquinoline derivative the structure 1-

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