Hydrogenation of this product in methanol in the presence of Adams catalyst was complete in ten minutes. The 3-propyl-4-hydroxyveratrole so obtained melted at 92–93° after recrystallization from dilute methanol.

*Anal.* Calcd. for $C_{11}H_{16}O_3$: C, 67.33; H, 8.21. Found: C, 67.30; H, 8.42.

**6-Allyloxyveratric Acid.**—This acid was obtained from the methyl ester (12.6 g.) by refluxing for one and one-half hours with 500 cc. of potassium hydroxide (5%); wt. 10.2 g.; m. p. 123.5–124° after recrystallization from dilute acetic acid.

*Anal.* Calcd. for $C_{12}H_{14}O_5$: C, 60.48; H, 5.92 Found: C, 60.76; H, 6.03.

**4-Hydroxy-5-allylveratrole.**—Nine grams of 6-allyloxyveratric acid was refluxed for one hour with dimethylaniline (9.0 g.). A quantitative amount of carbon dioxide was liberated. The reaction mixture was taken up in benzene and the dimethylaniline removed by extraction with hydrochloric acid. Removal of the benzene afforded a residue which distilled at 143–145° (2 mm.): wt. 6.7 g. This product solidified in the receiver; m. p. 38–41°.

*Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26 Found: C, 67.60; H, 7.51.

**4-Hydroxy-5-propylveratrole.**—This product was obtained by catalytic reduction of 4-hydroxy-5-allylveratrole (1.5 g.) in methanol (10 cc.) by the use of Adams catalyst (10 mg.), m. p. 70.5–72°.

*Anal.* Calcd. for $C_{11}H_{16}O_3$: C, 67.35; H, 8.21. Found: C, 67.87; H, 8.01.

**Methyl 3-Propyl-4-methoxysalicylate.**—Catalytic hydrogenation of methyl 3-allyl-4-methoxysalicylate[5] (106 g.) dissolved in warm methanol (150 cc.) was brought about quantitatively in twenty-five minutes in the presence of Adams catalyst (300 mg.); m. p. 58–59° after crystallization from dilute methanol.

*Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 64.33; H, 7.19. Found: C, 64.23; H, 7.45.

Saponification of the ester (45 g.) with potassium hydroxide (400 cc., 10%) and ethanol (50 cc.) gave 3-propyl-4-methoxysalicylic acid (33.3 g.); m. p. 168–170° (dec.).

*Anal.* Calcd. for $C_{11}H_{14}O_4$: C, 62.90; H, 6.71. Found: C, 62.68; H, 6.85.

**2,5-Dihydroxy-3-propyl-4-methoxybenzoic Acid.**—Twenty-one grams of 3-propyl-4-methoxysalicylic acid was dissolved in aqueous sodium hydroxide (10 g. in 80 cc.). To this was added simultaneously (a), a solution of sodium hydroxide (20 g. in 60 cc.), and (b), a warm aqueous solution of potassium persulfate (34 g. in 400 cc.) over a period of forty minutes. The color of the solution changed from light amber to permanganate purple. After forty-two hours the solution was acidified to congo red and extracted three times with ether to remove unchanged starting material. The aqueous solution was treated with concentrated hydrochloric acid (30 cc.) and heated to boiling. The product precipitated on cooling and was recrystallized from benzene; wt. 6.0 g. (56% based on starting material used); m. p. 164.5–165.5°.

*Anal.* Calcd. for $C_{11}H_{14}O_5$: C, 58.45; H, 6.24. Found: C, 58.31; H, 6.34.

When this acid was treated with diazomethane in ether there was obtained a crude ester which on saponification gave 5-propyl-6-hydroxyveratric acid; m. p. 114.5–116.5°. This sample was identical with that obtained by an independent route as described above.

## Summary

It has been shown that isomeric pairs of 3,4- and 4,5-disubstituted veratroles can be readily prepared from a common intermediate by means of the Claisen rearrangement of phenyl allyl ethers.

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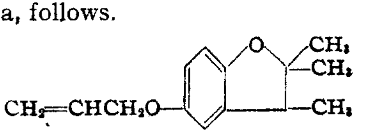
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

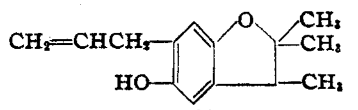
# The Rearrangement of Phenyl Allyl Ethers. IX. 2,2,3-Trimethyl-5-allyloxycoumaran[1]

BY WALTER M. LAUER AND EDGAR E. RENFREW[2]

The thermal rearrangement of 2,2,3-trimethyl-5-allyloxycoumaran, V, yields 2,2,3-trimethyl-5-hydroxy-6-allylcoumaran, Va. This finding is in accord with predictions based on the Mills–Nixon effect. Evidence for the structures assigned to the allyl ether, V, and to its rearrangement product, Va, follows.

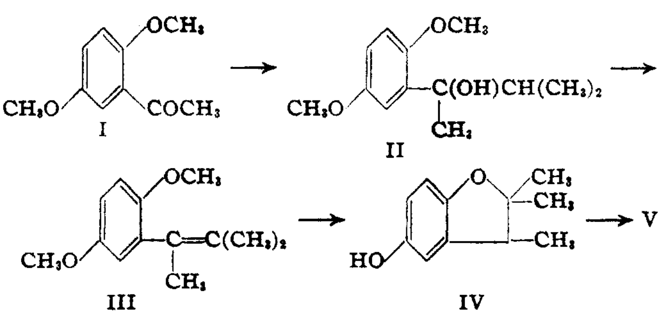


V



Va

The synthesis of 2,2,3-trimethyl-5-allyloxycoumaran was accomplished in a manner similar to that described[3] for the preparation of 2,2,3-trimethylcoumaran. The starting point for the present synthesis was 2,5-dimethoxyacetophenone, I, and the following outline shows the transformations which were involved in the synthesis of the allyl ether, V.



The rearrangement of V was carried out in an atmosphere of nitrogen at a temperature of 215–

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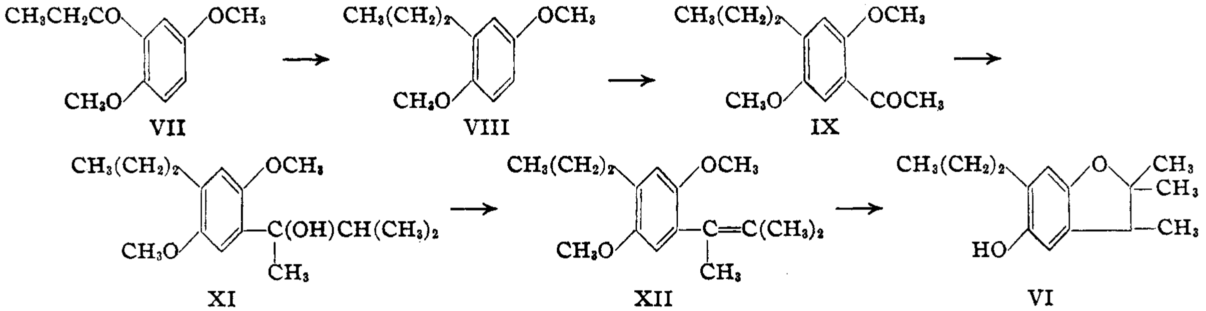
[1] Paper VIII, THIS JOURNAL, 65, 289 (1943).

[2] Abstract of Ph.D. Thesis submitted in February, 1944.

[3] Lauer and Moe, THIS JOURNAL, 65, 291 (1943).

225°. The rearrangement product, Va, was hydrogenated and the resulting 2,2,3-trimethyl-5-hydroxy-6-propylcoumaran, VI, was compared with a specimen which was obtained by means of the series of reactions outlined below. Melting point and appropriate mixed melting point determinations of the two samples of VI and of their *p*-nitrobenzoates served to establish their identity.



Compound IX, 2,5-dimethoxy-4-propylacetophenone, was demethylated. The completely demethylated product, 2,5-dihydroxy-4-propylacetophenone, X, has been described by Cruickshank and Robinson.[4] These investigators assigned the acetyl group in compound IX to the position indicated, since it has been found by Baker and Lothian[5] that 2,6-disubstituted acetophenones will not yield semicarbazones by the usual procedures. This finding has been extended by Cruickshank and Robinson to include the action of 2,4-dinitrophenylhydrazine on compounds such as 2,5-dihydroxy-6-propylacetophenone. Since demethylation of IX led to a product which readily yielded a 2,4-dinitrophenylhydrazone, 2,5-dimethoxy-6-propylacetophenone was eliminated as a likely structure. The next step in the present synthesis supplies additional evidence of the correctness of structure IX, for it is improbable that addition of the Grignard reagent to give an 84% yield of the tertiary alcohol would occur in the case of a 2,6-disubstituted acetophenone.

## Experimental

**2,5-Dimethoxyacetophenone, I** (b. p. 141–146° at 10 mm., m. p. 19–21°) was prepared from the dimethyl ether of hydroquinone, acetic anhydride and aluminum chloride, using nitromethane as the solvent. The melting points of the oxime (106–108°), the semicarbazone (182–183.5°) and the 2,4-dinitrophenylhydrazone (169–170°) agreed with the recorded values. Treatment of the 2,5-dimethoxyacetophenone with hydrobromic acid (48%) and acetic acid yielded quinacetophenone (m. p. 202°).

**Methyl-isopropyl-(2,5-dimethoxyphenyl)-carbinol (II).**—To an ether solution (200 ml.) of isopropylmagnesium bromide (0.36 mole) contained in a flask equipped with a mechanical stirrer, a dropping funnel and a reflux condenser, 2,5-dimethoxyacetophenone (58.2 g., 0.33 mole) was added dropwise over a period of two hours. The reaction mixture was then poured onto crushed ice (300 g.) and water (225 ml.) containing a small amount of hydrochloric acid. The solution was extracted with ether. The ether extract (dried over sodium sulfate) was distilled under reduced pressure. A viscous yellow product (65.2 g., 90%, b. p. 124–128° at 4 mm.) was obtained.

*Anal.* Calcd. for $C_{13}H_{20}O_3$: C, 69.6; H, 8.9. Found: C, 69.6; H, 8.2.

**α,β,β-Trimethyl-2,5-dimethoxystyrene (III).**—The carbinol (35.0 g., 0.156 mole) was dehydrated by slowly distilling (at 12 mm.) in the presence of a small amount of iodine. The distillate, dissolved in ether, was washed with aqueous sodium bisulfite. The ether solution, dried over sodium sulfate, yielded the dehydration product (24.3 g., 75%, b. p. 123–126° at 11 mm.).

*Anal.* Calcd. for $C_{13}H_{18}O_2$: C, 75.7; H, 8.9. Found: C, 75.7, 75.7; H, 9.5, 9.4.

Oxidation of this substituted styrene using chromic acid in dilute acetic acid, yielded 2,5-dimethoxyacetophenone, which was identified by means of its semicarbazone (m. p. 180–182°, mixed m. p. 181–183°).

**2,2,3-Trimethyl-5-hydroxycoumaran (IV).**—A mixture of α,β,β-trimethyl-2,5-dimethoxystyrene (24.3 g.), acetic acid (240 ml.) and hydrobromic acid (144 g., 48%) was boiled for one and one-half hours. The solution (claret) was then poured into ice water (750 ml.). The oil, which separated, was extracted with ether and the combined ether extracts were neutralized with aqueous sodium carbonate. The ether extract, dried with sodium sulfate, yielded a viscous oil upon distillation under reduced pressure (b. p. 156–162° at 16 mm.). After standing for a few minutes, crystallization began and at the end of an hour the entire product had solidified. Crystallization from petroleum ether (low boiling) gave a product (16.5 g., 78%, m. p. 75°) which was completely soluble in dilute potassium hydroxide and which showed a negative ferric chloride test in water or alcohol.

*Anal.* Calcd. for $C_{11}H_{14}O_2$: C, 74.1; H, 7.8. Found: C, 74.1; H, 7.7.

**2,2,3-Trimethyl-5-allyloxycoumaran (V).**—A mixture of 2,2,3-trimethyl-5-hydroxycoumaran (10.0 g., 0.056 mole), allyl bromide (7.1 g., 0.060 mole), finely powdered anhydrous potassium carbonate (8.0 g., 0.060 mole) and acetone (75 ml.) was boiled (mechanical stirring) under reflux for eight hours. After cooling, water (100 ml.) was added to the reaction mixture. The combined ether extracts, after washing with aqueous sodium hydroxide and water, yielded a colorless liquid distillate (11.1 g., 91%, b. p. 152–157° at 17 mm.).

*Anal.* Calcd. for $C_{14}H_{18}O_2$: C, 77.1; H, 8.3. Found: C, 77.1; H, 8.4.

**The thermal rearrangement of V** (0.96 g.) was accomplished in a Pyrex test-tube and under an atmosphere of nitrogen. The test-tube was heated to 215–225° by means of a metal bath and this temperature was maintained for four hours. The reaction mixture was a golden-orange viscous oil, which on distillation *in vacuo* yielded a product (0.79 g.), soluble in dilute aqueous potassium hydroxide.

*Anal.* Calcd. for $C_{14}H_{18}O_2$: C, 77.1; H, 8.3. Found: C, 76.8; H, 8.1.

**Reduction of the rearrangement product** (0.78 g.) to give 2,2,3-trimethyl-5-hydroxy-6-propylcoumaran (VI) was carried out in the presence of a platinum oxide catalyst

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[4] Cruickshank and Robinson, *J. Chem. Soc.*, 2064 (1938).

[5] Baker and Lothian, *ibid.*, 274 (1936).

and methanol (30 ml.). After removal of the catalyst and the methanol, an amber oil remained. The addition of petroleum ether (20 ml., b. p. 45–60°) followed by cooling to −20° gave a colorless solid (0.38 g., m. p. 62–65°).

*Anal.* Calcd. for $C_{14}H_{20}O_2$: C, 76.4; H, 9.1. Found: C, 76.5; H, 9.0.

The *p*-nitrobenzoate of 2,2,3-trimethyl-5-hydroxy-6-propylcoumaran (m. p. 109–111°) was prepared as follows. A mixture of 2,2,3-trimethyl-5-hydroxy-6-propylcoumaran (0.80 g.), anhydrous pyridine (3 ml.) and *p*-nitrobenzoyl chloride (0.75 g.) was heated for a short time and then poured into water (10 ml.). The precipitated oil was washed with aqueous sodium carbonate (5%), after which the oil solidified. The solid (0.47 g.), crystallized several times from ethanol, melted at 109–111°.

**2,5-Dimethoxypropiophenone, VII** (b. p. 165–172° at 19 mm., 2,4-dinitrophenylhydrazone m. p. 122–123°) was converted to 2,5-dimethoxy-1-propylbenzene, VIII (b. p. 132–140° at 21 mm.), by treatment of VII with amalgamated zinc in the presence of hydrochloric acid. Nitration of VIII yielded 2,5-dimethoxy-4-nitro-1-propylbenzene (m. p. 63–64°; reported 64°).[6]

**2,5-Dimethoxy-4-propylacetophenone, IX** (m. p. 39–40°), was prepared by means of a Friedel–Crafts reaction using 2,5-dimethoxy-1-propylbenzene (82 g., 0.45 mole), aluminum chloride (133 g., 1 mole), acetic anhydride (46.5 g., 0.45 mole) and carbon disulfide (250 ml.). The product (75 g., b. p. 171–179 at 22 mm.) which was isolated gave a blue-green color with ferric chloride in alcohol solution, indicating that some demethylation had occurred. An ether solution of the product was therefore extracted repeatedly with aqueous potassium hydroxide. (This base soluble material is described under the heading, 2-hydroxy-4-propyl-5-methoxyacetophenone.) After this extraction with alkali, the ether solution yielded IX.

*Anal.* Calcd. for $C_{13}H_{18}O_3$: C, 70.2; H, 8.1. Found: C, 69.9; H, 8.0.

The 2,4-dinitrophenylhydrazone of IX, crystallized from ethanol, melted at 142–143°.

*Anal.* Calcd. for $C_{19}H_{22}N_4O_6$: C, 56.8; H, 5.5. Found: C, 56.9; H, 5.7.

**2-Hydroxy-4-propyl-5-methoxyacetophenone** (b. p. 149–155° at 13 mm.) was obtained from the aforementioned alkali extraction described in the preparation of IX. This ketone was transformed to the red 2,4-dinitrophenylhydrazone (m. p. 184–185°).

*Anal.* Calcd. for $C_{18}H_{20}N_4O_6$: C, 55.6; H, 5.2. Found: C, 55.4; H, 5.0.

**2-Acetoxy-4-propyl-5-methoxyacetophenone** (m. p. 74–75°) was prepared from the corresponding 2-hydroxy compound by acetylation with acetic anhydride.

*Anal.* Calcd. for $C_{14}H_{18}O_4$: C, 67.2; H, 7.2. Found: C, 67.4; H, 7.1.

**2,5-Dihydroxy-4-propylacetopehnone, X,** was obtained from the corresponding dimethyl ether IX, by boiling IX for two hours with a mixture of acetic and hydrobromic acids. After cooling, the solution was diluted with water and then extracted with ether. The combined ether extracts were washed with aqueous sodium bicarbonate and water. The dried ether solution was then concentrated and petroleum ether was added. On standing in the refrigerator, crystals appeared. Recrystallization from aqueous methanol gave colorless platelets, m. p. 92.5–94° (reported 85°).[7]

*Anal.* Calcd. for $C_{11}H_{14}O_3$: C, 68.1; H, 7.2. Found: C, 68.3; H, 7.3.

The 2,4-dinitrophenylhydrazone of X, m. p. 215–216°, was prepared and analyzed. This compound has been reported by Cruickshank and Robinson to melt at 216°, but no analysis was reported.

*Anal.* Calcd. for $C_{17}H_{18}N_4O_6$: C, 54.6; H, 4.8. Found: C, 55.0; H, 4.5.

**(2,5-Dimethoxy-4-propylphenyl)-methylisopropylcarbinol, XI.**—Magnesium (4.8 g., 0.20 g. atom) and ether (10–15 ml.) were placed in a flask (500 ml.) equipped with a stirrer, reflux condenser and a dropping funnel. A small amount of isopropyl bromide was then added and as soon as reaction began, more ether (100–120 ml.) and isopropyl bromide (24.6 g., 0.20 mole) were added. A solution of 2,5-dimethoxy-4-propylacetophenone (16.8 g., 0.075 mole) in ether (25 ml.) was added dropwise. The reaction mixture was stirred and boiled for one hour and then poured onto crushed ice (150 g.) and aqueous ammonium chloride (50 g.). The ether layer was removed and the aqueous solution extracted five times with ether. The combined ether extracts were washed with water and dried. The residual golden viscous oil was distilled using a packed column and the carbinol, XI (16.9 g., 84%; b. p. 148–154° at 6 mm.) was obtained.

*Anal.* Calcd. for $C_{16}H_{26}O_3$: C, 72.3; H, 9.8. Found: C, 72.5; H, 9.6.

**α,β,β-Trimethyl-2,5-dimethoxy-4-propylstyrene, XII.**—The carbinol XI was dehydrated by heating with a small amount of iodine. The mixture turned dark and when the bath temperature reached 130–140° vigorous boiling took place; at 150–160° drops of water appeared in the air condenser. The temperature was finally raised to 180°. After cooling, the reaction mixture was subjected to reduced pressure for fifteen minutes. Distillation then yielded a clear mobile liquid (b. p. 132–135° at 5 mm.).

*Anal.* Calcd. for $C_{16}H_{24}O$: C, 77.4; H, 9.8. Found: C, 76.6; H, 9.6.

**2,2,3-Trimethyl-5-hydroxy-6-propylcoumaran, VI.**—In a flask (50 ml.) connected to a reflux condenser was placed α,β,β-trimethyl-2,5-dimethoxy-4-propylstyrene, XII (1.5 g.), hydrobromic acid (15 ml., 48%) and acetic acid (15 ml.). The reaction mixture was boiled for five hours and then allowed to cool. Water was then added (total volume of reaction mixture 250 ml.) and the resultant solution was extracted with chloroform. The chloroform extract was concentrated and a small amount of petroleum ether was then added. Crystals were deposited after several days in the refrigerator. Recrystallization from petroleum ether yielded a product melting at 62–65°.. A mixed melting point with the reduced thermal rearrangement product of V was 62–65°.

The *p*-nitrobenzoate of this synthesized hydroxycoumaran was prepared. This ester, after crystallization from alcohol melted at 111–112°.

*Anal.* Calcd. for $C_{21}H_{23}O_5$: C, 68.2; H, 6.3. Found: C, 67.9; H, 6.5.

The ester derived from the reduced rearrangement product melted at 109–111°; a mixed melting point of the two samples of ester remained unchanged.

## Summary

The thermal rearrangement of 2,2,3-trimethyl-5-allyloxycoumaran yields 2,2,3-trimethyl-5-hydroxy-6-allylcoumaran. Evidence in support of these structures is described.

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(6) Thoms, *Ber.*, **36**, 857 (1903).

(7) Cruickshank and Robinson, *J. Chem. Soc.*, 2064 (1938).