

β -D-Glucose, α,α -Trehalose, and β -Cellobiose Azoates.—Adsorbent, silicic acid; solvent, chloroform with 0.2% alcohol; column, 27 mm. diameter. From 75 mg. of each derivative was obtained a top band of 81.6 mg., $[\alpha]^{25}_{D_{438}} 116^\circ$, corresponding to $[\alpha]^{25}_{D_{438}} 105^\circ$ for β -cellobiose azoate. A second band of 63 mg., $[\alpha]^{25}_{D_{438}} 178^\circ$, corresponding to $[\alpha]^{25}_{D_{438}} 210^\circ$ for α,α -trehalose azoate. A third band of 59.7 mg., $[\alpha]^{25}_{D_{438}} -33^\circ$, corresponding to $[\alpha]^{25}_{D_{438}} -50^\circ$ for β -D-glucose azoate. These separations represent a purity of at least 85-90%.

β -L-Arabinose, β -D-Glucose, α,α -Trehalose, and β -Cellobiose Azoates.—Adsorbent, silicic acid; solvent, chloroform with 0.1% alcohol; column, 40 mm. diameter and developed for twelve hours. One hundred and fifty milligrams of each derivative was used and four bands obtained. The top band which was not displaced was 11 cm. wide from which was eluted 152.7 mg., $[\alpha]^{25}_{D_{438}} 109^\circ$, corresponding to $[\alpha]^{25}_{D_{438}} 105^\circ$ for β -cellobiose azoate. The eluted material was sparingly soluble in chloroform as is β -cellobiose azoate. A second band 2 cm. in width was separated from the first band by 1 cm. and was intensely colored. The second band gave on elution 136.0 mg., $[\alpha]^{25}_{D_{438}} 199^\circ$, corresponding to $[\alpha]^{25}_{D_{438}} 210^\circ$ for α,α -trehalose azoate. The eluted material was a glassy amorphous solid which is characteristic of α,α -trehalose azoate after evaporation of a chloroform solution in which it is extremely soluble. There was 15 cm. between the second and third bands. The third band was 10 cm. wide from which was eluted 138.0 mg., $[\alpha]^{25}_{D_{438}} 13^\circ$, corre-

sponding to $[\alpha]^{25}_{D_{438}} -50^\circ$ for β -D-glucose azoate. The eluted material was typical of β -D-glucose azoate in appearance and solubility. The fourth band was 7 cm. below the third and was 10 cm. wide. It gave on elution 130.4 mg., $[\alpha]^{25}_{D_{438}} 721^\circ$, corresponding to $[\alpha]^{25}_{D_{438}} 750^\circ$ for β -L-arabinose azoate. The eluted material formed the golden crystals typical of β -L-arabinose azoate. The purity of band three was calculated as 92.5%, assuming β -L-arabinose azoate as the impurity. The purity of band four was calculated as 96.25%, assuming β -D-glucose azoate as the impurity.

Acknowledgment is made of funds received from the Corn Products Refining Company which made possible this investigation.

Summary

1. The method of preparation, purification and analysis of the azoyl derivatives of sugars has been modified and several new sugar azoates have been prepared.

2. Chromatographic adsorption separations have been carried out with closely related compounds as well as with several new types of azoyl derivatives. One separation involving four sugar derivatives was accomplished.

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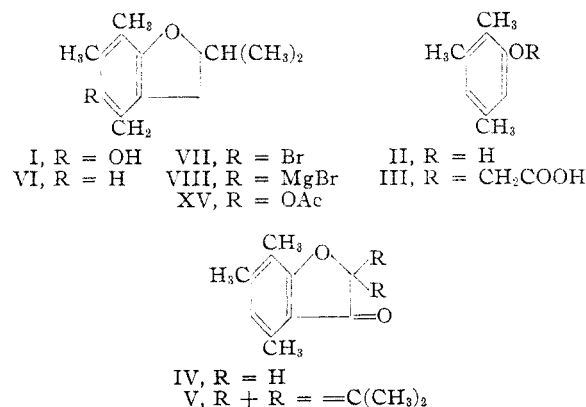
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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Polyalkylbenzenes. XXXIII.¹ 4,6,7-Trimethylcoumaran-3-one and its Conversion into 2-Isopropyl-4,6,7-trimethyl-5-hydroxycoumaran

By LEE IRVIN SMITH, JOHN A. KING, WILLA IRWIN GUSS AND JOSEPH NICHOLS

In a previous paper² there was described a successful synthesis of 2-isopropyl-4,6,7-trimethyl-5-hydroxycoumaran (I), a substance of interest in connection with the chemistry of vitamin E. Previous to this successful synthesis, experiments had been started with a view to a synthesis of 2-isopropyl-4,6,7-trimethylcoumaran (VI) by means of a series of reactions in which, as a first step, 2,3,5-trimethylphenol (II) was to be converted into 2,3,5-trimethylphenoxyacetic acid (III). The latter was then to be cyclized to 4,6,7-trimethylcoumaran-3-one (IV). Condensation of IV with acetone would give 2-isopropylidene-4,6,7-trimethylcoumaran-3-one (V), which by reduction under the proper conditions could be transformed into VI. The reactions apparently proceeded normally, but the properties of the substance supposed to be V were so unusual that for some



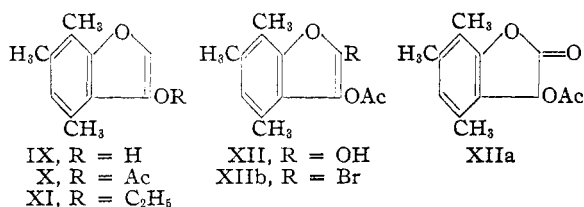
time it was believed the substance could not possibly have this structure. However, later work showed that the substance actually had this structure; it was possible, though difficult, to reduce V to VI. The coumaran VI was identified by transforming it into the known hydroxycoumaran I, via

(1) XXXII, THIS JOURNAL, 65, 202 (1943).

(2) Smith and King, *ibid.*, 65, 441 (1943).

the bromo derivative VII, by oxidation of the Grignard reagent VIII.

Condensation of ethyl bromoacetate with the sodium salt of II gave ethyl 2,3,5-trimethylphenoxyacetate which was not isolated but was hydrolyzed to the phenoxyacetic acid III, m. p. 130–131°. When a solution of III in 95% sulfuric acid was heated to 90–95°, there resulted a good yield of a white substance $C_{11}H_{12}O_2$ which melted at 90.5–91.5°.

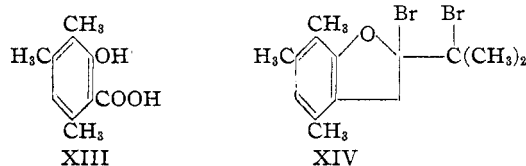


This material IV could not be converted into a 2,4-dinitrophenylhydrazone; instead, when it reacted with 2,4-dinitrophenylhydrazine, the product was a salt, $C_{17}H_{18}O_6N_4$. It thus appeared that IV reacted in the enolic form, and that the structure of the hetero-ring must be represented as a hydroxycoumarone, IX. In agreement with this structure, IV was converted into an enol acetate X, $C_{18}H_{14}O_3$, by action of acetic anhydride, and into an enol ethyl ether XI, $C_{18}H_{16}O_2$, by action of ethanol and zinc chloride. The enol acetate X combined readily with bromine, and no hydrogen bromide was evolved. The first product was apparently a very sensitive one; during the isolation and purification, the solution of it was washed with sodium bisulfite and the material isolated was a bromine-free compound, XII, $C_{18}H_{14}O_4$, which was likewise an enol acetate. Such a result was in harmony with the enol structure for the acetate X, and difficult to interpret on the basis of any other structure. The initial reaction involved direct addition of bromine to the double bond in X; this was followed by elimination of hydrobromic acid to give XIIb, and the latter was converted into XII by hydrolysis. This substance XII was not investigated further; tautomerism is of course possible and likely, but no experiments were performed to determine whether the substance existed partly as XIIa.

All of the data so far were consistent with structure IV for the coumaranone, although the data did serve to show clearly the strongly enolic and acidic properties of the substance. True coumaran-3-ones contain a reactive methylene group,

and many years ago it was shown⁴ that these substances could be condensed with aromatic aldehydes to give products such as 2-benzalcoumaran-3-ones. Lately Shriner and his students⁵ have studied this condensation and have found that aliphatic aldehydes and ketones may also undergo the reaction under favorable experimental conditions. Thus, 6-methoxycoumaran-3-one condensed with most aldehydes and ketones to give the 2,2'-bis-derivatives, but with acetone and cyclohexanone, this coumaranone reacted mole for mole and gave 2-alkylidene derivatives. These substances in turn could be reduced either to the 2-alkylcoumaranones or to the 2-alkylcoumarans, depending upon the nature of the catalyst employed to bring about the hydrogenation.

The coumaranone IV reacted smoothly with acetone in the presence of ethanol and zinc chloride to give a nicely crystalline product melting at 90–91° and having the composition $C_{14}H_{16}O_2$ required by structure V. Ozonolysis of V followed



by oxidative decomposition of the ozonide with hydrogen peroxide, gave a crystalline acid, XIII, $C_{10}H_{12}O_3$, which melted at 181–182°, gave a strongly positive phenol test (Folin-Denis), and which was identified as 2,4,5-trimethyl-6-hydroxybenzoic acid.⁶ The coumaranone V re-

(4) (a) v. Auwers and Pohl, *Ann.*, **405**, 243 (1914); (b) *Ber.*, **48**, 85 (1915).

(5) (a) Shriner and Damschroder, *THIS JOURNAL*, **60**, 894 (1938); (b) Shriner and Anderson, *ibid.*, **60**, 1415 (1938); Shriner and Witte, *ibid.*, **61**, 2328 (1939); **63**, 1108 (1941).

(6) Four trimethylsalicylic acids are possible; two derived from pseudocumene, and two derived from hemimellitene, but only the first two of these have been reported. A compound supposed to be 2,4,5-trimethyl-6-hydroxybenzoic acid (XIII) was prepared by fusion of durenol with alkali in the presence of air, and it was reported to melt at 148°. The acid was decarboxylated to a phenol which melted at 85–88°, and which was regarded as 2,3,5-trimethylphenol since this phenol was known and reported by Edler^{7b} to melt at 93°. But a mixed melting point determination was not made. The other trimethylsalicylic acid derived from pseudocumene, 2,3,5-trimethyl-6-hydroxybenzoic acid, was prepared by a Kolbe synthesis from 2,4,5-trimethylphenol⁸ and reported to melt at 181°. It appeared, then, that the acid XIII, m. p. 181–182°, was 2,3,5-trimethyl-6-hydroxybenzoic acid. If so, a migration of a methyl group had occurred when III was cyclized to IV by action of sulfuric acid. Many Jacobsen reactions are known, but so far none have been observed in which either of the two groups in IV, an ether linkage and an oxygenated carbon atom (carbonyl or enol), is attached to an aromatic nucleus. Krohn's synthesis was therefore repeated; no difficulty was experienced in obtaining a salicylic acid which melted at 179–181°, but a mixture of this acid and XIII melted at 160–169°. Barring polymorphism, it therefore followed either that Jacobsen had not actually prepared the acid XIII, or else XIII was a derivative of

(3) Kruber and Schmitt, *Ber.*, **64**, 2270 (1931), report 128°.

acted with bromine to give a white dibromide, XIV, $C_{14}H_{16}O_2Br_2$, which melted at 127–128° with decomposition.

Catalytic hydrogenation of V gave products which varied greatly depending upon the conditions used for the reduction. In absolute alcohol, with a palladium catalyst on calcium carbonate, and under moderate (40 lb.) pressures of hydrogen, V was converted into an oil which boiled at 146–147° (15 mm.) and which had the composition $C_{14}H_{18}O_2$, a dihydro derivative of V. Under high pressures (2600 lb.) of hydrogen, at 175° for fifty minutes, and in the presence of Raney nickel catalyst, this same oil was obtained. This oil failed to react with carbonyl reagents or with reagents for the hydroxyl group, and it thus appeared that this product could not be one of the simple dihydro derivatives of V, *i. e.*, the unsaturated alcohol, the saturated ketone, or its enol. However, when the coumaranone V was subjected to hydrogenation under more drastic conditions (3000 lb., four hours at 200° in the presence of Raney nickel), there was obtained, in 50% yield, a solid which melted at 38–39° and which had the composition required by the coumaran VI. The oil obtained under milder conditions of reduction was apparently a mixture of VI and intermediate reduction products between V and VI; the oil gave a positive Folin test, as did IV, whereas the solid VI gave a negative Folin test.

Bromination of VI gave the monobromo derivative VII; this was converted into the Grignard reagent VIII by the entrainment procedure in which a secondary aliphatic halide, cyclohexyl bromide, was used; and the Grignard reagent was oxidized, in the presence of the secondary aliphatic Grignard reagent,¹⁰ to the hydroxy coumaran I, in 34% yield. The coumaran I prepared this way melted at 119–120°; the acetate XV melted at 76–77°. This coumaran and its acetate, as prepared in the previous study,² melted at 114–116° and 72–73°, respectively, and

hemimellitene. To decide this point, the acid XIII was decarboxylated. The product melted at 87–89°, and when mixed with authentic 2,3,5-trimethylphenol (m. p. 95°), the substance melted at 88–94°. Hence the acid XIII is a derivative of pseudocumene, and since it differs from Krohn's acid, structure XIII must be correct for it. Jacobsen's acid from durenol was either a polymorphic form of XIII, or else was a meta hydroxy acid, in which case his phenol was 2,3,6-trimethylphenol. This phenol, however, has been reported to melt at 62°.⁹

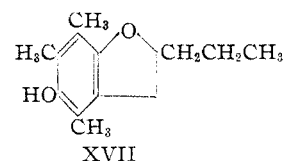
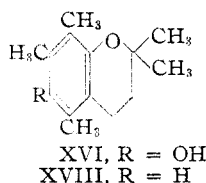
(7) (a) Jacobsen and Schnapauff, *Ber.*, **18**, 2841 (1885); (b) Eder, *ibid.*, **18**, 830 (1885).

(8) Krohn, *ibid.*, **21**, 884 (1888).

(9) Morgan and Pettet, *J. Chem. Soc.*, 418 (1934).

(10) Ivanoff, *Bull. soc. chim.*, [4] **39**, 47 (1926); see also Kharasch and Reynolds, *This Journal*, **65**, 501 (1943).

the mixed melting points lay in each case between the two sets of individual melting points. However, the mixed melting points of isomers in this series frequently show only slight depressions. Because of this, and because the drastic conditions used for reduction of V might possibly have caused a rearrangement, it was considered necessary to prove that this specimen of the coumaran I was not the isomeric *n*-propylcoumaran XVII. The other possibility, the chroman XVI, was excluded because it melts at 94–94.5°¹¹; I melts at 119–120°.



Moreover, the chroman XVIII melts at 41–42°¹²; the coumaran VI melts at 38–39°; and a mixture of the two was a liquid at room temperature.

The *n*-propyl isomer XVII of I was prepared by the method of Smith and Kaiser.¹³ The sodium enolate of dibutylmethane was added to trimethylquinone, and the crude reaction product was cyclized, by action of hydrochloric acid, to 2-propyl-4,6,7-trimethyl-5-hydroxycoumarone. Reduction of this coumarone gave XVII, which melted at 96–97° alone and at 89–92° when mixed with I.

It followed, therefore, that the reduction of V had produced the coumaran VI and that no rearrangement had occurred in any of the steps leading from II to VI. The method outlined here for synthesis from IV of coumarans such as VI may be of general application; the two (methyl) groups attached to the α -carbon atom in the side chain may be varied at will merely by varying the ketone which is condensed with IV. Moreover, when combined with the elegant procedure of Ivanoff¹⁰ for introduction of the hydroxyl group, this series of reactions constitutes a good method for preparation of 5-hydroxycoumarans such as I—a method of synthesis which not only supplements that of Smith and King² but which has the advantage that it avoids the troublesome preparation of the symmetrical diacylmethane, a necessary feature of the synthesis of Smith and King.

(11) Smith, Hoehn and Ungnade, *J. Org. Chem.*, **4**, 351 (1939).

(12) Smith, Ungnade, Hoehn and Wawzonek, *ibid.*, **4**, 314 (1939).

(13) Smith and Kaiser, *This Journal*, **62**, 133 (1940); see also ref. 2.

Experimental Part¹⁴

2,3,5-Trimethylphenoxyacetic Acid (III).—A mixture of 2,3,5-trimethylphenol (68 g., 0.5 mole), potassium carbonate (69 g., 0.5 mole), ethyl bromoacetate (92 g., 0.55 mole), and acetone (150 cc.) was stirred and refluxed for seventy-two hours. Water (200 cc.) was added, the acetone was removed by distillation, and the cooled residue was extracted with three 100-cc. portions of ether. The ether extracts were combined, the solvent was removed, and the residual ester of III was refluxed for twenty-four hours with a solution of sodium ethoxide in dry alcohol (sodium 10 g., alcohol, 175 cc.). Water (200 cc.) was added, the mixture was acidified with hydrochloric acid (congo red), and the alcohol was removed by distillation. The oil in the residue solidified on cooling; the solid was removed and crystallized from benzene. This material melted at 100–125° and contained some unchanged phenol. The solid was boiled with a saturated solution of sodium carbonate, the hot solution was filtered, and the cooled filtrate was acidified with hydrochloric acid. The white solid was removed, dried, and crystallized from benzene. It formed long white needles (68.3 g., 70.5%) which melted at 130–131°. ^{14a}

4,6,7-Trimethylcoumaran-3-one (IV).—The phenoxyacetic acid III (11.0 g., 0.057 mole) was covered with sulfuric acid (150 cc.) and warmed on the steam-bath until the temperature of the mixture reached 90–95°. The cherry-red solution was poured into ice (1 kg.) and water (2 l.); the solid was removed, washed thoroughly with water and dried. After crystallization from petroleum ether (b. p. 60–68°) the substance formed white needles (8.7 g., 86%) which melted at 90.5–91.5°.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 75.00; H, 6.82. Found: C, 75.07; H, 6.71.

A solution of the above coumaranone (1 g.) in dry alcohol (5 cc.) was added to a solution of 2,4-dinitrophenylhydrazine (1 g.) in sulfuric acid (2 cc.) which had been diluted with dry alcohol (15 cc.). A red precipitate formed at once; this was removed, washed with cold alcohol, and recrystallized first from a chloroform-alcohol mixture and then from an acetone-alcohol mixture. The substance melted at 231° with decomposition.

Anal. Calcd. for $C_{17}H_{16}O_6N_4$ (phenylhydrazine): C, 57.30; H, 4.49. Calcd. for $C_{17}H_{18}O_6N_4$ (salt): C, 54.54; H, 4.81. Found: C, 55.15; H, 4.65.

4,6,7-Trimethyl-3-ethoxycoumarone (XI).—Powdered zinc chloride (30 g., freshly fused) was added to a solution of the coumaranone IV (2.0 g.) in dry alcohol (50 cc.). An exothermic reaction occurred immediately; after this subsided, the mixture was poured into water (200 cc.) and extracted with two 50-cc. portions of ether. Removal of the ether left a yellow crystalline residue which was recrystallized from dilute alcohol. It then melted at 86–88°. A mixture of XI and IV melted below 80°; a mixture of XI and V melted below 70°.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 76.47; H, 7.84. Found: C, 76.77; H, 6.85.

(14) Microanalysis by E. E. Renfrew, E. M. Schultz, C. H. Stratton and Stanley Rolfson.

(14a) Ref. 3, the recorded m. p. is 128°.

4,6,7-Trimethyl-3-acetoxycoumarone (X).—The coumaranone IV (2.0 g.) was suspended in acetic anhydride (10 cc.). A drop of sulfuric acid was added; the solid immediately dissolved and heat was evolved. The solution was at once poured over ice (100 g.) and the mixture was allowed to stand until the ice melted. The solid was removed and crystallized first from dilute acetic acid (1:1) and then twice from dilute alcohol. It then melted at 88–89°, and gave a negative Folin-Denis test. A mixture of X and IV melted below 78°.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 71.56; H, 6.42. Found: C, 71.62; H, 6.46.

4,6,7-Trimethyl-3-acetoxyisocoumaranone (XII or XIIa).—A solution (5%) of bromine in carbon tetrachloride was slowly added to a stirred solution of the enol acetate X (0.2 g.) in carbon tetrachloride (15 cc.) until the bromine color persisted. The solution was immediately washed with saturated bisulfite and dried (calcium chloride). The solvent was removed, and the residual yellow oil solidified when it was cooled. After recrystallization from a mixture of chloroform and petroleum ether (b. p. 90–100°), the substance formed light yellow needles which melted at 127.5–128.5°.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 66.66; H, 5.98. Found: C, 66.15; H, 6.15.

2-Isopropylidene-4,6,7-trimethylcoumaran-3-one (V).—A solution of the coumarone IV (8.4 g., 0.048 mole) in dry alcohol (100 cc.) was added slowly to a refluxing suspension of powdered zinc chloride (67 g., 0.5 mole, freshly fused) in acetone (60 g., 1.0 mole). The mixture was refluxed for nineteen hours, after which 100 cc. of liquid was removed by distillation and the residue was poured into ice (200 g.) and water (600 cc.). The solid was removed and crystallized from dry alcohol. The light yellow needles weighed 9.2 g. (89%) and melted at 90.5–91.5°. A mixture of V and XI melted below 70°; a mixture of V and IV melted at 65–80°.

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.78; H, 7.41. Found: C, 77.72, 77.41; H, 7.08, 7.68.

Substance V gave a negative Folin-Denis test, and all attempts to prepare from it any carbonyl derivatives—phenylhydrazones, 2,4-dinitrophenylhydrazones, oxime, or semicarbazones—were unsuccessful.

2-Isopropyl-4,6,7-trimethylcoumaran (VI).—The coumaranone V (8 g.) in dry ethanol (20 cc.) was subjected to the action of hydrogen under 3000 lb. at 200° for four hours in the presence of Raney nickel catalyst. The cooled mixture was filtered and the solvent was removed by distillation. The residual light yellow oil solidified when it was cooled; the yield of crude product was nearly quantitative. The material was recrystallized three times from ethanol. There resulted 3.8 g. (50%) of a white solid which melted at 36–37°; further crystallization from ethanol ultimately gave a product which melted at 38–39°. When mixed with the chroman XVIII (m. p. 41–42°), the substance liquefied at once at room temperature. The coumaran VI gave a negative Folin-Denis test.

Anal. Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.21; H, 9.73.

When the coumaranone V was reduced under less drastic conditions, mixtures resulted and the product was an oil.

The coumaranone V (12 g.) in dry ethanol (100 cc.) was refluxed with Raney nickel (2 g.) for four hours. The solution was decanted into a hydrogenation bomb, fresh catalyst (2 g.) was added, and the mixture was subjected to the action of hydrogen under 2600 lb. at 185° for two hours. After the mixture was processed as described above, the residual yellow oil was distilled. It boiled at 138–150° (10 mm.) and the distillate weighed 10 g. Redistillation gave 8.1 g. of oil boiling at 141–144° (13 mm.). This oil gave a positive Folin–Denis test. It solidified at 0°, but the solid melted below room temperature. The oil was dissolved in ether (30 cc.) and the ethereal solution was extracted twice with sodium hydroxide (25 cc., 10%). No material could be recovered from the alkaline extracts. The ether was removed, and the residual oil was distilled. It boiled for the most part at 145° (15 mm.). A middle and an end fraction were analyzed.

Anal. Fraction 1. Found: C, 79.15; H, 9.38. Fraction 2. Found: C, 79.68; H, 8.68. Calcd. for a mixture of 50% VI and 50% of a dihydro derivative: C, 79.63; H, 9.06. Calcd. for a mixture of 50% VI and 50% of a tetrahydro derivative: C, 79.31; H, 9.51.

The oil gave no semicarbazone or oxime, nor could an acetate or benzoate be prepared. The oil (2.8 g.) dissolved when it was warmed with a solution of sodium acetate (3 g.) in aqueous ethanol (60%, 15 cc.) on the steam-bath for thirty minutes. When the solution was cooled and diluted with water (5 cc.), it deposited 1.4 g. (50%) of the white coumaran VI which melted at 28–30°. These experiments showed that reduction of V to VI required rather drastic conditions for completion, but that even when the reduction was incomplete, the product contained a considerable amount of VI.

2,4,5-Trimethyl-6-hydroxybenzoic Acid (XIII).—The coumaranone V (2.5 g.) was dissolved in ethyl bromide (60 cc.) and the solution was subjected for fifteen minutes to the action of a rapid current of ozonized oxygen (5% ozone) at 25°. The solution was poured into water (200 cc.) containing hydrogen peroxide (20 cc., 30%), and the mixture was warmed on the steam-bath to remove ethyl bromide. The residual solution was cooled, made alkaline with potassium hydroxide (10%) and extracted with ether (extract discarded). The aqueous solution was acidified with hydrochloric acid and the solid (1.5 g., m. p. 144–147°) was removed and crystallized from chloroform. This product (m. p. 168–174° dec.) was dissolved in sodium carbonate solution, reprecipitated with hydrochloric acid and crystallized from chloroform. It then melted at 181–182° with decomposition. The substance gave a strongly positive test for a phenol (Folin–Denis).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.66; H, 6.66; mol. wt., 180. Found: C, 66.58; H, 6.88; mol. wt. (Rast), 179.

Some of the above acid XIII was decarboxylated by heating it repeatedly in an open capillary tube until the substance melted without evolution of gas. The product melted at 87–89°; when mixed with an approximately equal amount of 2,3,5-trimethylphenol (m. p., 95°), the substance melted at 88–94°.

3,4,5-Trimethyl-6-hydroxybenzoic Acid.—Sodium (small pieces, 0.575 g., 0.025 mole) was added to a well-stirred

solution of 2,4,5-trimethylphenol (pseudocumenol-5, 3.4 g., 0.025 mole) in dry ether (60 cc.) and contained in a flask equipped with a reflux condenser surmounted by a calcium chloride guard tube. After the reaction was complete, dry benzene (50 cc.) was added and the sodium phenoxide was filtered and dried for two hours in an oven at 75°. The dry phenoxide (3.49 g., 88.5%) and solid carbon dioxide (15 g.) were placed in a small steel bomb and heated at 250° for two and one-half hours. The material was washed out of the bomb with hot water, the mixture was filtered and the filtrate was acidified with hydrochloric acid. The solid was removed and stirred with warm (50°) saturated potassium carbonate solution. The solution was filtered and the filtrate was acidified with hydrochloric acid. The solid (m. p. 177–179°) was removed and crystallized from chloroform. It then weighed 1.0 g. (25%) and melted at 181° with some decomposition. A mixture of this acid and XIII melted at 160–169°.

2-Bromo-2-[dimethylbromocarbonyl]-4,6,7-trimethylcoumaran-3-one (XIV).—A solution of bromine in carbon tetrachloride (5%) was added dropwise to a solution of the coumaranone V (250 mg.) in carbon tetrachloride (5 cc.). Evolution of hydrogen bromide began when 6 cc. of the bromine solution had been added; at this point the solution was immediately washed with saturated aqueous bisulfite. The colorless organic layer was washed with water and the solvent was removed. The pale yellow, oily residue solidified when it was triturated with a little alcohol. The solid (300 mg.) was removed and crystallized three times from dilute alcohol. It then formed short white needles which melted at 127–128° with decomposition.

Anal. Calcd. for $C_{14}H_{16}O_2Br_2$: C, 44.68; H, 4.26. Found: C, 44.97; H, 4.84.

5-Bromo-2-isopropyl-4,6,7-trimethylcoumaran (VII).—The coumaran VI (0.5 g., 0.0025 mole) was dissolved in carbon tetrachloride (10 cc.) and bromine (0.44 g., 0.00275 mole) was added dropwise. The solvent was removed under reduced pressure and the residue of white solid, after crystallization from ethanol, melted at 65–66° and weighed 0.55 g. (80%).

Anal. Calcd. for $C_{14}H_{18}OBr$: C, 59.37; H, 6.76. Found: C, 59.30; H, 6.85.

2-Isopropyl-4,6,7-trimethyl-5-hydroxycoumaran (I).—A solution of the bromo compound VII (1.5 g., 0.0053 mole), cyclohexyl bromide (1 g., 0.0061 mole), and ethyl bromide (0.7 g., 0.0064 mole) in dry ether (30 cc.) was added dropwise and with stirring to magnesium ribbon (0.6 g., 0.025 gram atom) moistened with a little ethyl bromide (0.3 g., 0.0028 mole), and the mixture was refluxed for two hours. The mixture was cooled (–15°) and a stream of dry oxygen (washed with potassium hydroxide solution and dried with sulfuric acid) was passed through it for one hour. The greenish-yellow product was acidified with dilute hydrochloric acid and extracted with ether. The ether layer was washed with water, dried (sodium sulfate) and the solvent was removed. The residue, after crystallization from petroleum ether (b. p. 28–38°), was white, weighed 0.4 g. (34%), and melted at 119°. When mixed with a specimen of I (m. p. 113–114°) prepared by the method of Smith and King, the substance melted at 114–116°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.09; H, 8.93.

The substance formed an acetate (XV) which melted at 76–77°; when this acetate was mixed with an impure specimen of XV (m. p. 67–71°) prepared by Smith and King, it melted at 69–73°.

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.24; H, 8.45. Found: C, 72.87; H, 8.24.

Dibutylmethane was prepared by the method of Morgan and Thomason¹⁵ and purified via the blue copper compound, m. p. 145–150°. The yield of purified diketone was 18.6 g. (16.6%) from 450 g. of ethyl butyrate and 62 g. of methyl propyl ketone. The diketone was a colorless oil which boiled at 85–86° (11 mm.).¹⁶

2-Propyl-4,6,7-trimethyl-5-hydroxycoumarone.—Dibutylmethane (18.5 g., 0.12 mole) was added dropwise and with stirring to a cooled (ice-bath) solution of sodium (2.7 g., 0.12 gram atom) in dry ethanol (50 cc.). A solution of trimethylquinone (17.5 g., 0.12 mole) in dry ethanol (50 cc.) was then slowly (one hour) added to the cooled and stirred solution of the enolate. The dark brown reaction mixture was then stirred at room temperature for one hour, after which it was cooled in an ice-bath and acidified (litmus) by dropwise addition of hydrochloric acid. The mixture was poured into water (200 cc.) and extracted with ether. The ether extract was washed with water, dried (sodium sulfate), and the solvent was removed. The residual red oil was refluxed with hydrochloric acid (300 cc.) and ethanol (15 cc.) for three hours. The mixture was then diluted with water and distilled with steam. The white solid in the distillate was removed and crystallized from aqueous ethanol. It then weighed 4.1 g. (16%) and melted at 88–89°.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.06; H, 8.25. Found: C, 77.03; H, 8.03.

2-Propyl-4,6,7-trimethyl-5-hydroxycoumaran (XVII).—The above coumarone (1.4 g.) in dry ethanol (20 cc.) was subjected to the action of hydrogen under 1300 lb. at 135° for one hour in the presence of Raney nickel catalyst (2 g.). After removal of catalyst and solvent, the residual

white solid was crystallized from petroleum ether (b. p. 28–38°). It weighed 1 g. (71%) and melted at 96–97°. When mixed with the coumarone, it melted at 85–87°; when mixed with the isomeric isopropylcoumaran I (m. p. 119–120°), it melted at 89–92°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.09. Found: C, 76.38; H, 9.27.

Summary

1. Cyclization of 2,3,5-trimethylphenoxyacetic acid by action of sulfuric acid produces 4,6,7-trimethylcoumaran-3-one IV.

2. This coumaranone, IV, exists in the enolic form IX which is an acid strong enough to form a salt with 2,4-dinitrophenylhydrazine. No carbonyl derivatives of IV could be prepared, but IV is converted with ease into an enol acetate X and an enol ethyl ether XI.

3. Condensation of IV with acetone occurs readily, and the product is the corresponding 2-alkylidenecoumaranone V. Although V is reduced with considerable difficulty, the final product, obtained under rather drastic conditions, is 2-isopropyl-4,6,7-trimethylcoumaran VI. The structure of this coumaran was proved by converting it, via the bromo derivative VII, into the known 2-isopropyl-4,6,7-trimethyl-5-hydroxycoumaran I. This conversion was accomplished by oxidation of the Grignard reagent from VII by the procedure of Ivanoff.

4. The sequence of reactions leading from IV to VI and thence to I may possibly be of general utility for synthesis of 5-hydroxy-2-*s*-carbinylcoumarans.

5. The 2,4,5-trimethyl-6-hydroxybenzoic acid, m. p. 148°, reported by Jacobsen and Schnapauff, probably does not have this structure.

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(15) Morgan and Thomason, *J. Chem. Soc.*, **125**, 756 (1924).

(16) Leroide, *Ann. chim.*, [9] **16**, 394 (1921), gives the b. p. as 96–98° (21 mm.).