tion between sodiomalonic ester and ethyl 4,4-diphenyl-3-butenoate.

The preparation of the lactone of β-(α-hydroxybenzohydryl)-glutaric acid is described.

The reaction of cyclopentadienylmagnesium bromide with benzohydryl bromide has been shown to form a product in which one of the double bonds has migrated to a position of conjugation with the phenyl groups.

Diphenylacetaldehyde has been shown to yield a mixture of the stereoisomeric stilbene dichlorides upon treatment with phosphorus pentachloride.

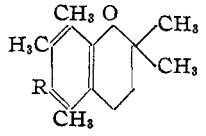
COLUMBUS, OHIO RECEIVED APRIL 25, 1940

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

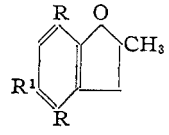
The Chemistry of Vitamin E. XXIII. A New Synthesis of 2,4,6,7-Tetramethyl-5-hydroxycoumaran and of 2-Methyl-5-hydroxycoumaran. Oxidation Products of the Tetramethylcoumaran[1]

BY LEE IRVIN SMITH, HARVEY H. HOEHN AND AMBROSE G. WHITNEY

Two reports have been published which describe experiments leading to preparation of *p*-hydroxy-chromans and -coumarans in which the introduction of the hydroxyl group para to the bridge oxygen atom constitutes the final step in the series of reactions. One of these reports[2] dealt with the conversion of chroman I into II by bromination, followed by oxidation of the Grignard reagent prepared from the bromo compound. The other report[3] dealt with the conversion of coumarans III into IV by coupling III with diazotized 2,4-dinitroaniline, reductively cleaving the azo compound to the aminocoumaran, and replacing the amino group by the hydroxyl group in the usual way via the diazonium salt. In both



I, R = H
II, R = OH



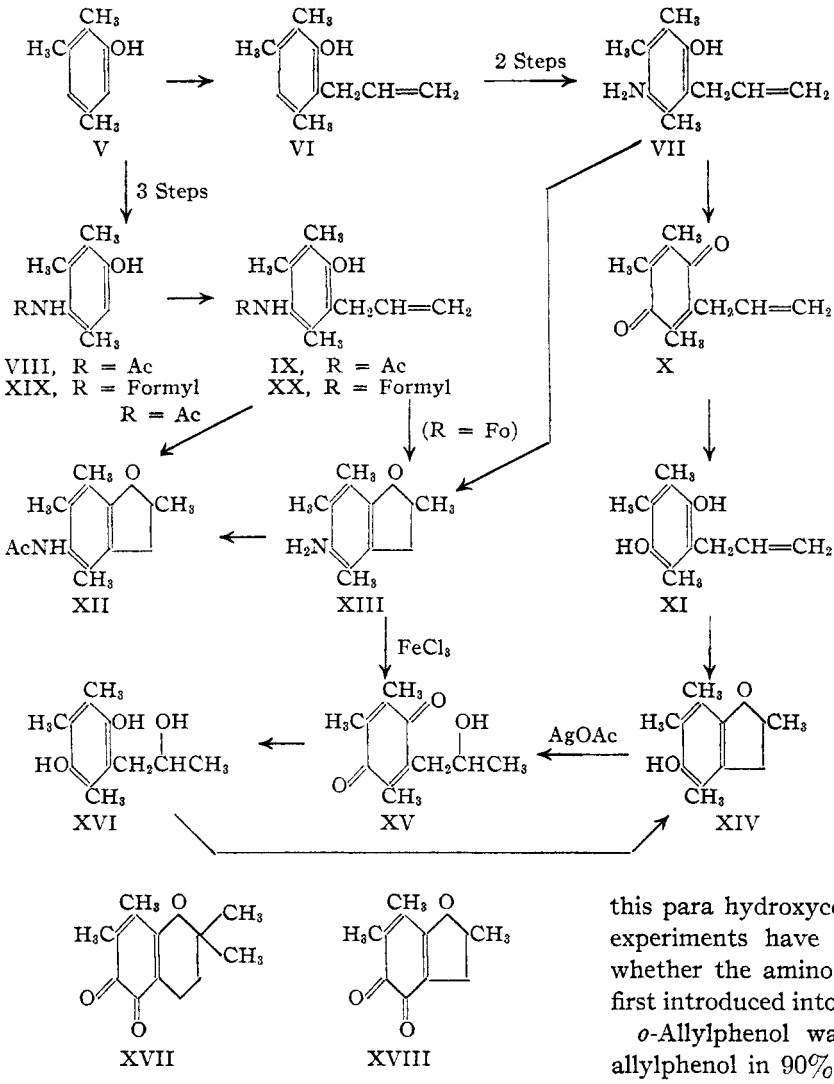
III, R = H or CH_3; R′ = H
IV, R = H or CH_3; R′ = OH

series of reactions, the over-all yields left much to be desired. Oxidation of the Grignard reagent from I gave a poor yield of II, while the aminocoumaran from III gave only poor yields of IV via the diazonium salt. Moreover, apparently only the most active diazonium salts will couple with chromans and coumarans; diazotized sulfanilic acid gave a very poor yield of azo compound from I[2] and while diazotized 2,4-dinitroaniline coupled well with III, reductive cleavage of the resulting azo compound gave a mixture of two water insoluble amines which had to be separated.[3] In the specific examples cited, this separation was successful, but for higher members of the chroman and coumaran series, in which steam distillation would probably be of little use, the separation of two basic amines might offer some difficulties.

Since diazotized sulfanilic acid couples well with phenols, a new approach to the synthesis of compounds such as II and IV has been studied in which an allylic phenol was coupled with the diazonium salt and the latter was converted into the aminophenol before the ring was closed. In the model experiments an allyl halide was used; consequently cyclization led to a coumaran. In order to be more certain that the various products would be solids (IV, R = H was reported to be a liquid[3]), 2,3,5-trimethylphenol V was used.

To avoid any para allylation, the phenol V was converted into the allylic phenol VI by rearrangement of the phenyl allyl ether.[4,5] It was found that allyl chloride could be used in preparing the phenyl allyl ether, but the reaction was more rapid, and better yields were obtained when finely powdered potassium iodide was added to the reaction mixture.[6] The allylic phenol VI coupled well with diazotized sulfanilic acid, and the azo compound, when reductively cleaved by sodium hydrosulfite, gave a good yield of the aminophenol VII. In a similar way, 4-amino-2,3,5-trimethylphenol was prepared in good yield from V. The aminophenol VII was converted to the aminocoumaran XIII by action of hydro-

(1) Paper XXII, THIS JOURNAL, **62**, 145 (1940).
(2) Smith, Hoehn and Ungnade, *J. Org. Chem.*, **4**, 351 (1939).
(3) Karrer and Fritzsche, *Helv. Chim. Acta*, **22**, 657 (1939).
(4) Hurd, THIS JOURNAL, **52**, 1702 (1930).
(5) Smith, Ungnade, Hoehn and Wawzonek, *J. Org. Chem.*, **4**, 309 (1939). In this paper, bottom of p. 309 and top of p. 310, there is an error. The directions calling for extraction by ether and subsequent washing of the ether extracts with Claisen's alkali should read *petroleum ether* instead of ether.
(6) Mauthner, *J. prakt. Chem.*, **148**, 95 (1937).



bromic acid. It was planned to synthesize XIII via the intermediates VIII, IX and XII, as shown in the chart, but while the acetaminocoumaran XII was readily synthesized in good yields, it was not found possible to remove the acetyl group from XII. The substance was recovered unchanged after the action of boiling hydrobromic acid for two hours, and no cleavage of the acetyl group resulted when XII was subjected to the action of excess methylmagnesium bromide at elevated temperatures.[7] The formyl derivatives, however, proved much more tractable and the synthesis of XIII via the intermediates XIX and XX was achieved readily.

The aminophenol VII was readily converted into the yellow quinone X; the latter was converted into the hydroquinone XI, which cyclized smoothly when subjected to the action of acids. The product of this series of reactions was the known 2,4,6,7-tetramethyl-5-hydroxycoumaran XIV. Both the aminocoumaran XIII and the hydroxycoumaran XIV, when subjected to mild oxidation, gave the same yellow quinone XV.[8] This quinone was readily reduced to the hydroquinone XVI and the latter was smoothly cyclized by acids to the hydroxy coumaran XIV.[8c]

The yields in all of these transformations were good, and it therefore appears that in this case, at least, either series of reactions—VI, VII, X, XI and XIV or XIX, XX, XIII, XV, XVI and XIV—offers a feasible method for preparation of this para hydroxycoumaran. That is, the model experiments have shown that it is immaterial whether the amino group or the allylic group is first introduced into the phenol.

o-Allylphenol was converted into *p*-amino-*o*-allylphenol in 90% yields via the azo compound derived from sulfanilic acid. This method of preparing *p*-amino-*o*-allylphenol proved to be far superior to that of Claisen,[9] which involved nitrosation of *o*-allylphenol and reduction of the nitroso phenol to the aminophenol. While the aminophenol was readily oxidized by aqueous ferric chloride, allylquinone was so thermo-labile that only a small portion of it survived ordinary steam distillation. But when a dilute solution of the hydrochloride of *p*-amino-*o*-allylphenol was slowly run into ferric chloride solution which was boiling under reduced pressure (50–60°), *o*-allylquinone was isolated from the distillate in almost quantitative yields. In the high temperature steam distillation of the quinone from ferric chloride, a

(7) Binkley, MacCorquodale, Cheney, Thayer and Doisy, THIS JOURNAL, **61**, 1613 (1939).

(8) (a) Karrer, Escher, Fritzsche, Keller, Ringier and Salomon, *Helv. Chim. Acta*, **21**, 939 (1938); (b) Karrer and Jensen, *ibid.*, **21**, 1622 (1938); (c) Karrer, Fritzsche and Escher, *ibid.*, **22**, 661 (1939).

(9) Claisen, *Ann.*, **418**, 99 (1919).

black tar formed soon after the reaction started. This tar apparently catalyzed further decomposition of the quinone, for once the tar started to form, very little quinone could be obtained. Even in the low temperature steam distillation this tar occasionally formed, and when it did, the steam distillation had to be interrupted, the flask cleaned out and the distillation continued with fresh ferric chloride solution—otherwise the yield of quinone was very small. The procedure of Karrer and Hoffmann for preparing quinones, hydrolysis of *p*-nitroso phenols by hydrogen peroxide and hydrochloric acid,[10] failed to yield this quinone when applied to *p*-nitroso-*o*-allylphenol.

An ethereal solution of the quinone was decolorized rapidly when shaken with aqueous sodium hydrosulfite, and from the ether solution allylhydroquinone was isolated in nearly quantitative yield. This hydroquinone was cyclized to 2-methyl-5-hydroxycoumaran, which, contrary to the report by Karrer and Fritzsche,[3] is a white solid which melts at 66–67°.

It has been shown that 2,2,5,7,8-pentamethyl-6-hydroxycoumaran (II) when oxidized by silver nitrate or nitric acid in methanol or ethanol, gives brilliant red solutions.[8c,11] The substance responsible for the red color has been isolated and shown to be an *o*-quinone having structure XVII.[12] Moreover, it has been shown[13] that several other substances, among them the hydroxycoumaran XIV, also give brilliant red solutions with nitric acid or silver nitrate. The red substance derived from XIV has now been isolated. It is a very sensitive *o*-quinone having structure XVIII. When first prepared, the brilliant red needles melted at 83–87°. On standing, the brilliant red color of the substance changed after two days to a dull purple; mere recrystallization of a freshly prepared specimen from benzene gave a product with a wide melting point, 83–104°, and the red melt, as it cooled, suddenly set to a *light yellow* solid which appeared white in thin layers. Although a phenazine could not be obtained, there is little doubt as to the structure of the substance, for the analysis, absorption spectrum,[12] oxidation with hydrogen peroxide and the analogy with XVII all point to the structure XVIII for this red oxidation product of XIV. The peculiar transformations of this substance will be dealt with in a later paper.

The authors acknowledge with thanks a grant from the Fluid Research Funds of the Graduate School of the University of Minnesota which aided materially in the completion of this work.

Experimental Part[14]

2,3,5-Trimethylphenyl Allyl Ether.—2,3,5-Trimethylphenol (68 g., 0.5 mole), anhydrous potassium carbonate (69.1 g., 0.5 mole), and powdered potassium iodide (83 g., 0.5 mole) were vigorously stirred while allyl chloride (40 g.) was added. After stirring and refluxing for twenty hours, the mixture was poured into water (1.5 liters). The oil was removed and the aqueous layer was thoroughly extracted with petroleum ether (b. p. 60–68°). Unchanged phenol (21 g.) was removed by extracting the combined organic layers first with 20% potassium hydroxide until the alkaline extractions remained colorless and then with Claisen's alkali. After washing the petroleum ether solution with water, it was dried over calcium chloride and the solvent was removed by distillation through a short, packed column. The fraction boiling at 100–103° under 3–4 mm. was the phenyl allyl ether. It weighed 36 g. (60%, corrected for recovered phenol).

2,3,5-Trimethyl-6-allylphenol, VI.—The above ether (42 g., 0.3 mole) was rearranged by refluxing it for fifteen minutes, during which time the temperature rose to 275°. The cooled product was diluted with petroleum ether (b. p. 60–68°) and the solution was extracted with Claisen's alkali. Acidification of the alkaline extract produced an oil which was taken up in petroleum ether, washed with water and dried over sodium sulfate. The solvent was removed and the residue was fractionated twice. The phenol VI (23 g.) boiled at 132–133° under 12 mm., and melted at 48–49°.

2,3,5-Trimethyl-6-allyl-4-aminophenol, VII.—The allylphenol VI (16 g.) was dissolved in aqueous sodium hydroxide (15 g. in 100 cc.) by warming. The solution was cooled to 5°, and into it was poured a cold diazonium solution prepared in the usual way from sulfanilic acid (21 g.). The deep red solution, after standing at room temperature for five hours, was warmed to 55° and sodium hydrosulfite (43 g.) was added. Reduction was quite rapid; after fifteen minutes the color of the mixture became light orange and a flocculent precipitate separated. The mixture was allowed to stand at room temperature for two and one-half hours, after which the precipitate was removed, taken up in benzene, and the benzene was dried. The benzene solution, on standing in the icebox, deposited the aminophenol (15 g.) which melted at 105–108°. A small sample, recrystallized twice from petroleum ether (b. p. 60–68°), melted at 110°.

Anal. Calcd. for $C_{12}H_{17}ON$: C, 75.35; H, 8.97. Found: C, 75.11; H, 9.23.

When allowed to crystallize from dry benzene or petroleum ether, the aminophenol was easily obtained white

(10) *Helv. Chim. Acta.*, **22**, 654 (1939).

(11) (a) John, Dietzel and Emte, *Z. physiol. Chem.*, **257**, 173 (1939); (b) John and Emte, *ibid.*, **261**, 24 (1939); (c) Karrer, Escher and Rentschler, *Helv. Chim. Acta*, **22**, 1287 (1939); (d) Furter and Meyer, *ibid.*, **22**, 240 (1939).

(12) Smith, Irwin and Ungnade, *Science*, **90**, 334 (1939); THIS JOURNAL, **61**, 2424 (1939).

(13) Ungnade and Smith, *J. Org. Chem.*, **4**, 397 (1939).

(14) Microanalyses by E. E. Renfrew.

and stable in air. When crystallized from alcohol, however, or from any solvent which was wet, the aminophenol rapidly turned dark in the air.

2,3,5-Trimethyl-6-allyl-1,4-benzoquinone, X.—A solution of ferric chloride (41 g.) in water (40 cc.) was added to the aminophenol (9.6 g.) in hydrochloric acid (15 cc.). The mixture was immediately steam distilled and the yellow quinone (7.1 g.) was removed from the distillate by ether extraction. After drying the ethereal solution over sodium sulfate, the solvent was removed and the residue was fractionated through a short column packed with glass helices. The quinone, a liquid, boiled at 108° under 1 mm.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.75; H, 7.42. Found: C, 75.30; H, 7.42.

2,3,5-Trimethyl-6-allylhydroquinone, XI.—The quinone (5.6 g.) in acetic acid (20 cc.) and water (6 cc.) was refluxed with zinc (20 mesh, 1 g.) for one hour. The hot solution was decanted from the zinc onto ice and the white needles were removed and dried in a vacuum desiccator. The product (5.68 g.) melted at 137–138° and was quite pure. A small sample, recrystallized from dilute acetic acid, also melted at 137–138°.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.96; H, 8.40. Found: C, 74.87; H, 8.54.

2,4,6,7-Tetramethyl-5-hydroxycoumaran, XIV.—The hydroquinone (5 g.) and pyridinium chloride (20 g.) were heated at 135° for five hours. The mixture was poured into water (about 2 l.), the solid (m. p. 120–124°) was removed and steam distilled. The white coumaran crystallized from the cooled distillate. It weighed 3.3 g. and melted at 132–133°, alone or when mixed with an authentic specimen.[6]

2,3,5-Trimethyl-6-[β-hydroxypropyl]-1,4-benzoquinone, XV.—The above coumaran (480 mg.) and silver acetate (1 g.) were refluxed in dry methanol (30 cc.) for eight hours. The cooled mixture was filtered and the solvent was removed from the filtrate by distillation. The residue, a yellow oil, solidified when cooled in a bath of ice and salt, but the solid melted below room temperature (see below).

2,3,5-Trimethyl-6-[β-acetoxypropyl]-1,4-diacetoxybenzene.—The oily quinone XV from 480 mg. of the coumaran XIV was dissolved in acetic andydride (3 cc.). Sodium acetate (freshly fused, 500 mg.) was added and the mixture was refluxed while zinc dust was added in small portions during one hour. The cooled solution was decanted from the zinc onto ice; the zinc was washed with a little warm acetic acid and the washings were decanted into the ice mixture. After the excess acetic anhydride had decomposed, the solution was extracted with ether, the ether extracts were dried over sodium sulfate and the solvent was evaporated. The residue was crystallized twice from petroleum ether (b. p. 60–68°). The product formed white cubes (150 mg.) which melted at 92–93°.[8c,15]

Anal. Calcd. for $C_{18}H_{24}O_6$: C, 64.25; H, 7.20. Found: C, 64.41; H, 7.44.

2,6,7-Trimethylcoumaran-4,5-quinone, XVIII.—The coumaran XIV (500 mg.) and silver nitrate (5 g.) were refluxed in dry ethanol (25 cc.) for twenty minutes. Oxidation began immediately, the solution quickly turning yellow and then bright red. The reaction mixture was poured into cold water (500 cc.) and the aqueous solution was thoroughly extracted with ether (about one liter of ether was necessary). The combined ether extracts were dried over sodium sulfate and the ether was removed by distillation. The residue, bright red needles suspended in an oil, was cooled and filtered. The solid (125 mg.) melted at 83–87°. Recrystallization from a mixture of benzene and petroleum ether gave red needles which softened at 90° and melted at 96–97°. Another crystallization from the same solvents gave a product which softened at 83° and which did become completely liquid at 104–105°. A well-defined melting point of this quinone was never obtained and it was apparent that the substance underwent extensive change on melting, for the red melt, on cooling, set to a light yellow solid which appeared almost white in thin layers. Changes also occurred when the substance stood in air; after one or two days the bright red color changed to a dull purple.

Anal. (Sample melting at 104–105°) Calcd. for $C_{11}H_{12}O_3$: C, 68.71; H, 6.30. Found: C, 69.03; H, 6.84.

2,3,5-Trimethyl-4-aminophenol.—The phenol V (13.6 g., 0.1 mole) was dissolved in aqueous sodium hydroxide (15 g. in 100 cc. of water) and coupled with the diazonium solution from 0.1 mole of sulfanilic acid as described for the allylic phenol above. The red solution was warmed to 50° and stirred while sodium hydrosulfite (43 g.) was added gradually, and the reduction was completed by heating the mixture to 70° for fifteen minutes. The solution was cooled and solid aminophenol was filtered off. The yield was nearly quantitative. A small portion of the aminophenol when crystallized twice from benzene, formed fine white needles which melted at 152–153° and which were stable in air.

Anal. Calcd. for $C_9H_{13}ON$: C, 71.48; H, 8.67. Found: C, 71.55; H, 9.23.

2,3,5-Trimethyl-4-acetaminophenol, VIII.—The crude aminophenol from the above experiment was dissolved in hydrochloric acid (8.2 cc.) and water (250 cc.). To the warm solution (50°) acetic anhydride (11.7 cc.) was added with stirring, followed immediately by sodium acetate (15 g.) in water (50 cc.). As the mixture was cooled and stirred, the white acetamino compound (17 g., m. p. 183°) separated. After crystallization from dilute ethanol, the substance melted at 184–185°.

Anal. Calcd. for $C_{11}H_{15}O_2N$: C, 68.35; H, 7.82. Found: C, 68.21; H, 7.89.

2,3,5-Trimethyl-4-formaminophenol, XIX.—The aminophenol (15 g., 0.1 mole) was refluxed with formic acid (25 cc., d. 1.2) for an hour. The mixture was diluted with water and the white solid (17.5 g.) was removed, dried and crystallized from petroleum ether. The white needles melted at 213°.

Anal. Calcd. for $C_{10}H_{13}O_2N$: C, 67.00; H, 7.31. Found: C, 67.35; H, 7.46.

2,3,5-Trimethyl-4-acetaminophenyl Allyl Ether.—The acetaminophenol (6.4 g.) was added to sodium ethoxide in ethanol (760 mg. sodium, 60 cc. ethanol). After solution was complete, the mixture was refluxed gently while allyl chloride (6 cc.) was added in 1-cc. portions during one and one-half hours. The reaction mixture, stirred and refluxed

(15) Karrer, Fritzsche and Escher give the m. p. as 94°.

for six hours longer, was filtered while warm and the filtrate was set aside in the icebox. The phenyl allyl ether (4 g.) separated as a solid which melted at 164°. After recrystallization from ethanol the product formed white needles which melted at 165–165.5°.

Anal. Calcd. for $C_{14}H_{19}O_2N$: C, 72.06; H, 8.21. Found: C, 71.68; H, 8.01.

2,3,5-Trimethyl-4-formaminophenyl Allyl Ether.—The formaminophenol XIX (8.95 g., 0.05 mole) was converted to the allyl ether (8.2 g.) as described above. After crystallization from ethanol, the substance formed white needles which melted at 162–162.5°.

Anal. Calcd. for $C_{13}H_{17}O_2N$: C, 71.19; H, 7.82. Found: C, 71.45; H, 7.73.

2,3,5-Trimethyl-4-acetamino-6-allylphenol, IX.—The above allyl ether (4.3 g.) was refluxed in kerosene (75 cc.) at 225° for seven hours and then allowed to stand at room temperature overnight. The crude allylphenol IX, which separated when the solution was cooled, was removed, taken up in Claisen alkali, and the alkaline solution was extracted with benzene. Acidification of the alkaline layer precipitated the phenol (4 g.) as a white solid melting at 202°. After two crystallizations from benzene the substance formed white needles which melted at 206–207°. No quinone was obtained from IX by ferric chloride oxidation.

Anal. Calcd. for $C_{14}H_{19}O_2N$: C, 72.06; H, 8.21. Found: C, 71.76; H, 8.46.

2,3,5-Trimethyl-4-formamino-6-allylphenol, XX.—The phenyl allyl ether (8.2 g.) was refluxed in kerosene (200 cc.) for two hours and the allylphenol (8.0 g.) was filtered from the cooled solution. After crystallization from benzene and petroleum ether, the substance melted at 183–184°.

Anal. Calcd. for $C_{13}H_{17}O_2N$: C, 71.19; H, 7.82. Found: C, 71.10; H, 7.65.

2,4,6,7-Tetramethyl-5-acetaminocoumaran, XII.—The allylphenol IX (4 g.) was refluxed with hydrobromic acid (40%, 50 cc.) for two hours. Water was added and the solid was removed and crystallized three times from benzene. The white solid which weighed 2.5 g. and melted at 203°, gave a negative phenol test (Folin). When mixed with the isomeric phenol IX, the substance melted at 170–190°.

Anal. Calcd. for $C_{14}H_{19}O_2N$: C, 72.06; H, 8.21. Found: C, 71.83; H, 8.55.

As the above experiment shows, the acetyl group is not removed from IX or XII by boiling for two hours with 40% hydrobromic acid. A Grignard solution was prepared from magnesium (250 mg.), ether (5 cc.) and excess methyl bromide. The ether was distilled off and replaced by dry toluene (75 cc.). The acetaminocoumaran XII (1.2 g., 0.005 mole) was added and the solution was refluxed for twenty hours. Hydrochloric acid (3 cc.) and water (20 cc.) were added and the toluene was removed by steam distillation. The residue in the distilling flask contained a solid, which was removed and crystallized twice from benzene–petroleum ether. It was the acetaminocoumaran (0.5 g.), m. p. and mixed m. p. 200–202°. The filtrate, made alkaline and extracted with ether, yielded no organic material.

2,4,6,7-Tetramethyl-5-aminocoumaran, XIII.—Trimethylallylaminophenol VII (1.91 g.) was refluxed with hydrobromic acid (40%, 20 cc.) for three hours. The cooled solution deposited the hydrobromide of the aminocoumaran. The salt was filtered off, washed with Claisen alkali and then with water. The aminocoumaran remaining on the filter, when crystallized from petroleum ether (b. p., 60–68°), formed white needles (1.05 g.) which melted at 77–78°.

Anal. Calcd. for $C_{12}H_{17}ON$: C, 75.35; H, 8.97. Found: C, 74.89; H, 8.96.

Acetylation of XIII (191 mg.) at 50° in water (2.5 cc.), and hydrochloric acid (0.08 cc.) with acetic anhydride (0.12 cc.) and sodium acetate (0.15 g. in 5 cc. of water) was immediate. The product XII weighed 210 mg. and melted at 202–203° alone or when mixed with a specimen of XII prepared from IX.

Hydrobromide.—The formaminoallylphenol XX (8.0 g.) was refluxed in hydrobromic acid (80 cc., 40%) for three hours. The hydrobromide of the aminocoumaran (8 g.) separated from the cooled solution. After several crystallizations from ethanol, the substance formed white cubes which did not melt at the boiling point of a sulfuric acid-bath.

Anal. Calcd. for $C_{12}H_{18}ONBr$: C, 52.92; H, 6.68. Found: C, 53.36; H, 7.00.

When this hydrobromide was suspended in sodium hydroxide (20%) the aminocoumaran XIII resulted quantitatively. After crystallization from petroleum ether (b. p. 28–38°) it formed white needles which melted at 77–78° alone or when mixed with a specimen prepared by cyclizing the aminophenol VII.

2,3,5-Trimethyl-6-[β-hydroxypropyl]-1,4-benzoquinone, XV.—A hot (80°) solution of the aminocoumaran hydrobromide (4.2 g., 0.015 mole) in water (50 cc.) was filtered and the filtrate was cooled to 30° by adding a little ice. A cold solution of ferric chloride (hexahydrate 8.3 g., water 10 cc., hydrochloric acid 3 cc., ice 5 g.) was added and the mixture was immediately extracted with several portions of ether (800 cc. in all). The ether extract was washed with water, dried over sodium sulfate, and the ether removed by distillation. The residual orange oil weighed 1.6 g. (50%). A portion of it, taken up in petroleum ether (b. p. 60–68°) and set aside in the icebox overnight, crystallized in yellow needles which melted at 54–55°. The literature gives 56.5° as the melting point of this substance.[8a]

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.20; H, 7.75. Found: C, 68.87; H, 7.86.

2,3,5-Trimethyl-6-[β-hydroxypropyl]-hydroquinone, XVI.—The liquid quinone XV remaining from the above oxidation of XIII and zinc (20 mesh) were refluxed for one hour in acetic acid (8 cc.) and water (2 cc.). The light yellow reaction mixture was poured over ice, but only a small amount of solid separated. The whole was extracted with benzene (once) and ether (twice) and the combined organic layers were washed with water and dried over sodium sulfate. Removal of the solvents left a red oil which was taken up in ether and shaken with aqueous sodium hydrosulfite. The ether layer was dried over sodium sulfate and the solvent was removed. The residual oil, when

crystallized from petroleum ether (b. p. 60–68°), gave white needles (450 mg.) which melted at 130–132°. A second crystallization from the same solvent gave a product which melted at 137–138°.

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.53; H, 8.63. Found: C, 68.77; H, 8.67.

The **triacetate** of this hydroquinone (see above) melted at 92–93°.

2,4,6,7 - Tetramethyl - 5 - hydroxycoumaran, XIV.—The hydroquinone XVI (560 mg.) was refluxed for one hour in acetic acid (10 cc.) containing hydrobromic acid (1 cc., 40%) and a pinch of zinc dust. The solution was poured over ice and the solid (480 mg.) was removed and crystallized from petroleum ether. It was white, and melted at 130–131° alone or when mixed with an authentic specimen.

Allyl phenyl ether (153 g.), b. p. 89° under 26 mm., was prepared in 74% yield when phenol (145 g.) in acetone (1 l.) was refluxed for eight hours with potassium carbonate (207 g.), potassium iodide (125 g.) and allyl chloride (137 g.). When the procedure of Claisen and Eisleb[16] was followed, the yield was 40%.

o-Allylphenol (108.5 g.), b. p. 93–96° under 11 mm., was prepared in 76% yield by refluxing phenyl allyl ether (143 g.) for six hours, during which time the boiling point rose from 188 to 217°.

4-Amino-2-allylphenol.—*o*-Allylphenol (20.1 g.) was dissolved in aqueous sodium hydroxide (10%, 120 cc.) and the solution was coupled at 0° with a diazonium solution prepared from sulfanilic acid (0.15 mole). After standing at room temperature for four hours, the dark red solution was reduced by adding sodium hydrosulfite (69 g.) and heating to 75° with stirring. Within a short time the red color faded and a light yellow precipitate appeared. The aminophenol (20 g., m. p. 113–114°)[9] was removed from the cooled solution. It was slightly yellow; a white product, stable in air, but melting at the same temperature, was obtained by crystallizing the crude material from benzene. Such a product cannot be obtained if alcohol–water mixtures are used for the recrystallization.

Allylquinone.—Oxidation of the hydroquinone to the quinone must be done carefully if good yields are to be obtained. The quinone must not be allowed to remain in contact with the oxidizing agent for any length of time, nor can it be steam distilled at 100° without considerable decomposition. Apparently the decomposition products catalyze further decomposition, for once any dark oil appears, most of the quinone decomposes rapidly. The following procedure, adopted after many trials, gave the best results: the aminophenol (2.29 g.) was dissolved in hydrochloric acid (4 cc.), and water was added to bring the volume of the solution to 40 cc. A solution of ferric chloride (hexahydrate, 9.3 g.) in water (500 cc.) containing hydrochloric acid (3.5 cc.) was placed in a 1-l. distilling flask fitted with a capillary, thermometer and the dropping funnel. The ferric chloride solution was rapidly boiled (47°) under reduced pressure (80 mm.) so that a good stream of condensate was obtained, and then the solution of the aminophenol was added slowly (about twenty minutes). The yellow quinone immediately distilled over as an oil (2.0 g., 87%) and was isolated from the distillate by ether extraction. The quinone was purified by vacuum distillation: b. p. 117–118° under 26 mm., 102–103° under 18 mm. Careful adherence to the procedure described above gave consistently good results; but the yield became much less whenever any dark oil separated during the oxidation. In case this happened, it was better to interrupt the process, discard the ferric chloride solution, and continue with fresh oxidizing agent. Oxidation of more than 5 g. of aminophenol in one experiment almost invariably had to be interrupted because of the separation of these tarry decomposition products.

Anal. Calcd. for $C_9H_8O_2$: C, 72.97; H, 5.40. Found: C, 72.70; H, 5.43.

***o*-Allyl-*p*-nitrosophenol** (10.5 g., m. p. 93–94°) was prepared from allylphenol (13.4 g.) by the method of Claisen,[9] who reported the substance to melt at 100–101°. When hydrogen peroxide (10 cc., 30%) was added to a mixture of the nitrosophenol (5 g.) and hydrochloric acid (75 cc.),[10] a very vigorous reaction occurred with separation of much black tarry material. Steam distillation of this mixture gave a distillate which contained only a few drops of the yellow allylquinone.

Allylhydroquinone.—The ether extract from the oxidation of 8.94 g. of *o*-allylaminophenol was shaken in a separatory funnel with a saturated aqueous solution of sodium hydrosulfite until the ether layer was only very faintly colored (about three minutes). The ether layer was washed once with water, dried, and the solvent was removed. The residual solid was crystallized twice from a mixture of benzene and petroleum ether (b. p. 60–68°). It weighed 7.0 g. (78% based upon the aminophenol taken), was white and melted at 91–92°. This hydroquinone may be purified by vacuum distillation in a current of hydrogen; b. p. 161° under 10 mm., 166–168° under 15 mm. Although the hydroquinone is a new substance, the dibenzoate and a monobenzoate have been reported.[17]

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.96; H, 6.72. Found: C, 71.78; H, 7.02.

Reduction of the quinone by zinc and acetic acid in the usual way produced much black tarry material and gave very inferior yields of hydroquinone.

Diacetate.—Allylquinone (500 mg.), zinc dust (0.5 g.), acetic anhydride (10 cc.) and freshly fused sodium acetate (0.5 g.) were refluxed for one-half hour. The solution was poured onto ice, neutralized with sodium hydroxide (5%) and extracted with ether. The ether solution was dried over sodium sulfate and the solvent evaporated. The residue, an oil, was taken up in petroleum ether (b. p. 60–68°) and chilled. Fine needles (300 mg.) of the diacetate separated. After two crystallizations from petroleum ether (b. p. 28–38°) the substance melted at 47–48°.

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.64; H, 6.03. Found: C, 66.69; H, 6.28.

2-Methyl-5-hydroxycoumaran.—Allylhydroquinone (9.0 g.) was refluxed with hydrobromic acid (35 cc., 47%) and water (25 cc.). The clear liquid soon became milky, and dioxane (20 cc.) was added to increase the solubility of the material. Refluxing was continued for one hour and the dark solution was then allowed to stand overnight. The reaction mixture was extracted with ether and the ether

(16) Claisen and Eisleb, *Ann.*, **401**, 21 (1913).

(17) Hahn and Stenner, *Z. physiol. Chem.*, **181**, 88 (1929).

layer was washed with bicarbonate solution, then with water, and dried. Removal of the solvent left an oil which, on distillation, gave 4.1 g. (51%) of the coumaran boiling at 150–154° under 14–15 mm. The distillate solidified on cooling. The solid, recrystallized three times from a mixture of benzene and petroleum ether (b. p. 60–68°), was white and melted at 66–67°. When mixed with the hydroquinone (m. p. 91–92°) the substance melted at 48–58°.

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.96; H, 6.72. Found: C, 71.96; H, 6.96.

Cyclization was not successful when the hydroquinone (3.0 g.) was heated at 135° for five hours with pyridinium chloride (12 g.). The hydroquinone (1.95 g., m. p. 86–88°, b. p. 161° under 10 mm.) was the only product isolated. Likewise unsuccessful was an attempt to cyclize the hydroquinone (1 g.) by saturating its solution in carbon tetrachloride (90 cc.) and ether (10 cc.) with dry hydrogen chloride. The only product isolated was unchanged hydroquinone. Cyclization could be brought about by refluxing the hydroquinone (13 g.) for three hours in acetic acid (40 cc.) and hydrobromic acid (20 cc., 40%) containing a little zinc dust. The mixture was poured into water and the coumaran (5.5 g., 42%) was isolated by ether extraction.

The **benzoate** and **acetate** of the coumaran were both liquids.

Summary

1. This paper contains the details of the synthesis of 2,4,6,7-tetramethyl-5-hydroxycoumaran and 2-methyl-5-hydroxycoumaran from the corresponding *o*-allylphenols. The steps in these syntheses involve diazo coupling, cleavage of the azo compound to the aminophenol, oxidation to the allylic quinone, reduction to the hydroquinone and cyclization. It is shown that the order of the different steps mentioned may be varied considerably without affecting the final yields of coumarans.

2. Both the tetramethylhydroxycoumaran and the tetramethylaminocoumaran have been oxidized to the same yellow *p*-quinone; the latter has been reduced to the hydroxyhydroquinone and cyclized, as well as oxidized to the red 2,6,7-trimethylcoumaran-4,5-quinone.

MINNEAPOLIS, MINNESOTA RECEIVED MAY 13, 1940

[JOINT CONTRIBUTION FROM THE INSTITUTE OF EXPERIMENTAL BIOLOGY OF THE UNIVERSITY OF CALIFORNIA, AND THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Chemistry of Vitamin E. XXIV.[1] The Structure of γ-Tocopherol

BY OLIVER H. EMERSON[2] AND LEE IRVIN SMITH

The isolation from cottonseed oil, palm oil and corn oil of a substance characterized by an allophanate melting at 137–140° for which the name γ-tocopherol was proposed, has been previously described.[3,4] The complete difference in the crystalline form of this allophanate from that of the slightly higher melting derivative of β-tocopherol, and the fact that the two allophanates when mixed show a distinct depression in melting point clearly indicate their non-identity. Furthermore, as the present communication reports, the *p*-nitrophenyl urethan of γ-tocopherol melts at 119–121°, while Karrer and Fritzsche[5] have reported that the corresponding derivative of β-tocopherol melts at 90°.

Oxidation of β- and γ-tocopherols[6] yielded the same lactone which Fernholz[7] had obtained from α-tocopherol, indicating that the aliphatic portions of all three tocopherols are alike. On pyrolysis γ- as well as β-tocopherol yielded trimethylhydroquinone[8,9] instead of tetramethylhydroquinone which had been obtained from α-tocopherol.[10] This indicated that β- and γ-tocopherols differ from each other only in the position of the methyl groups attached to the benzene ring.

Three "xylo-tocopherols ' or "dimethyltocols"[11] —those derived from *o*-, *m*- and *p*-xylohydroquinones are possible. That β-tocopherol is 5,8-di-

(1) XXIII, Smith, Hoehn and Whitney, THIS JOURNAL, **62**, 1863 (1940).

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(3) Emerson, Emerson, Mohammad and Evans, *J. Biol. Chem.*, **122**, 99 (1937).

(4) Emerson, Emerson and Evans, *Science*, **89**, 183 (1939).

(5) Karrer and Fritzsche, *Helv. Chim. Acta*, **22**, 260 (1939).

(6) Emerson, THIS JOURNAL, **60**, 1741 (1938).

(7) Fernholz, *ibid.*, **60**, 700 (1938).

(8) John, *Z. physiol. Chem.*, **250**, 11 (1937).

(9) Bergel, Todd and Work, *J. Chem. Soc.*, 253 (1938).

(10) Fernholz, THIS JOURNAL, **59**, 1154 (1937).

(11) Karrer and Fritzsche (*Helv. Chim. Acta*, **21**, 1234 (1938)), have proposed the name "tocol" for the tocopherol nucleus, including the methyl group, the C_{16} side chain in the 2-position of the heterocyclic ring and the hydroxyl group in the 6-position, but not including the methyl groups attached to the benzene ring. The "xylotocopherols," *o*-, *m*- and *p*-, when named in this way, become 7,8-, 5,7- and 5,8-dimethyltocols, respectively.