

Experimental Part⁶

3,3,5,6,8,8-Hexamethylbenzo[1,2-b,4,3-b']dipyrano (I).²
 —A mixture of *o*-xylohydroquinone (1 g.), zinc chloride (0.67 g., freshly fused), and acetic acid (25 cc.) was heated until the solids dissolved. The solution was cooled, and isoprene (2 g.) in acetic acid (10 cc.) was added. The mixture was allowed to stand for one hour at room temperature, and then was boiled for one hour. Sulfuric acid (2 drops) was added and the mixture was boiled for another hour. The mixture was poured into water and the oil was taken up in petroleum ether (b. p. 60–68°). Extraction of this solution successively with aqueous sodium bicarbonate (5%), aqueous sodium hydroxide (5%), and Claisen alkali, removed no material. Evaporation of the petroleum ether left an oily solid which was crystallized from methanol. The product then weighed 1.25 g. (63%). After several crystallizations from methanol, the substance melted at 102.5–103.5°.

Anal. Calcd. for C₁₅H₂₆O₂: C, 78.79; H, 9.55.
 Found: C, 78.90; H, 9.82.

The same product was obtained in 84% yield in a duplicate of the above experiment, except that the reaction mixture was allowed to stand at room temperature for one week instead of being heated.

Silver nitrate (2.5 g.) was added to a solution of the chroman I (0.35 g., m. p. 93–101°) in dry ethanol (20 cc.), and the solution was boiled. The solution slowly acquired a yellow color; after seven hours, the solution (pale yellow) was poured into water and extracted with ether. The ether extracts were washed successively with water, aqueous sodium bicarbonate (5%), and water. Evaporation

(6) Micro analyses by Stanley T. Rolfson.

of the ether left a solid residue which, on crystallization from aqueous methanol, gave the chroman I (0.26 g.), m. p. and mixed m. p., 93–98°. Nitric acid (20 cc., 16 *N*) was added to a solution of the chroman I (150 mg.) in dry ethanol (100 cc.) and the solution was warmed on the steam-bath. After a few seconds, a red color developed; after ten minutes, the solution was poured into water and extracted with ether. The ether extracts were washed with water and dried (sodium sulfate). Removal of the ether left an orange-red oil. This was taken up in carbon tetrachloride and the solution was poured through a column of Brockmann alumina. The upper brown zone was eluted with ethanol; evaporation of the solvent left a red oil (80 mg.) which slowly dissolved in boiling petroleum ether (b. p. 60–68°) forming a yellow solution. This solution was concentrated to about 5 cc. and cooled; about 10 mg. of a dull red solid was deposited. This solid had an indefinite melting point, but it was completely liquid at 94°. No other solid could be obtained from the reaction product.

Summary

1. The double chroman I, a dipyrano-*o*-xylene, has been prepared in a pure state as a white crystalline solid melting at 102.5–103.5°. Contrary to the previous report, this substance is unattacked by action of silver nitrate in ethanol. However, the substance is attacked by action of nitric acid in ethanol, but no red *o*-quinone II could be isolated from the resulting red oil.

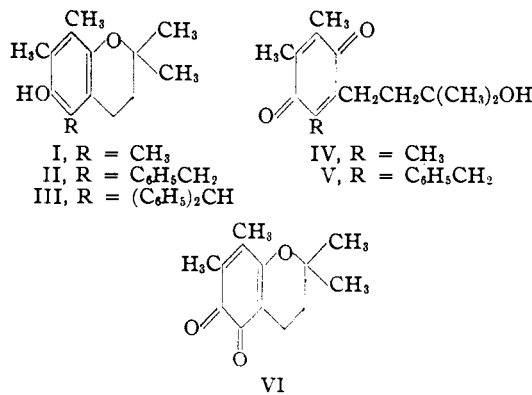
MINNEAPOLIS 14, MINNESOTA RECEIVED JUNE 2, 1944

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

Vitamin E. XLV.¹ Synthesis of 2,2,7,8-Tetramethyl-5-benzyl-6-hydroxychroman, and its Behavior upon Oxidation

BY LEE IRVIN SMITH AND ROY W. H. TESS²

It has been shown³ that oxidation of the tocopherols and other *p*-hydroxychromans and -coumarans by a wide variety of reagents produces yellow *p*-quinones; thus, the quinone IV is produced from the *p*-hydroxychroman I. These yellow *p*-quinones can be reduced to hydroquinones, and the latter can be cyclized, regenerating, in most cases, the original heterocyclic compound. When silver salts, or nitric acid under carefully controlled conditions, are used as the oxidizing agents, certain of the initial yellow quinones IV are transformed into brilliant red substances, a fact first noted by John.⁴ The study of these red compounds was continued by John and his associates^{3,5b} and by Karrer and his collaborators,⁶



but Smith, Irwin and Ungnade⁷ first showed that the red compounds were *o*-quinones, I giving VI, and that the group originally present in the 5-position (R in I) was eliminated in the transformation of I into VI. No evidence as to the mechanism of the transformation of I into VI was obtained, however, although certain general conclusions were drawn as to the effect of the nature of the group in the 2-position of the quinone IV upon the elimination of the group R.

An interesting and suggestive mechanism for

(1) (a) XLIV, *THIS JOURNAL*, **66**, 1525 (1944); (b) XLIII, **66**, 1523 (1944).

(2) Abstracted from a thesis by Roy W. H. Tess, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, March, 1944.

(3) (a) John, *Z. physiol. Chem.*, **253**, 201 (1938); (b) John, Dietzel and Emte, *ibid.*, **257**, 173 (1939); (c) Karrer, *et al.*, *Helv. Chim. Acta.*, **21**, 939 (1938); (d) Smith, Hoehm and Whitney, *THIS JOURNAL*, **62**, 1863 (1940); (e) Smith, Ruoff and Wawzonek, *J. Org. Chem.*, **6**, 236 (1941); (f) Tishler and Wendler, *THIS JOURNAL*, **63**, 1532 (1941); (g) Smith and King, *ibid.*, **65**, 441 (1943).

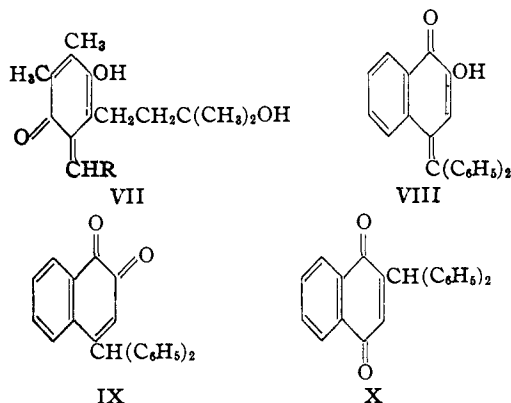
(4) John, *Z. physiol. Chem.*, **300**, 11 (1937).

(5) (a) John and Schmeil, *Ber.*, **72**, 1653 (1939); (b) John and Emte, *Z. physiol. Chem.*, **261**, 24 (1939).

(6) Karrer, Fritzsche and Escher, *Helv. Chim. Acta*, **22**, 661 (1939).

(7) Smith, Irwin and Ungnade, *THIS JOURNAL*, **61**, 2424 (1939).

formation of VI from IV is one in which the quinone IV undergoes a tautomeric change leading to the methylene quinone VII, which then, either by



cyclization followed by oxidation, or by oxidation followed by cyclization, gives the *o*-quinone VI with elimination of the unsaturated group as an oxidation product—ketone, aldehyde or acid. Tautomerism of this sort has been observed in the case of certain *o*-quinones derived from naphthalene⁵; thus, both forms, VIII and IX, of 4-benzhydryl- β -naphthoquinone have been isolated. This tautomerism is apparently realized only in the case of the *o*-naphthoquinones; the *p*-quinone X, isomeric with IX, showed no properties which would indicate the presence of any tautomeric methylene quinone.

In order to test this mechanism for the formation of the red compounds, 2,2,7,8-tetramethyl-5-benzyl-6-hydroxychroman II has been prepared, and its behavior on oxidation by action of various reagents has been studied. This chroman, m. p. 88.5–89°, when oxidized by action of ferric chloride or ceric sulfate, gave only yellow oils from which it was impossible to isolate any solids, but when silver acetate was used, the crystalline yellow *p*-quinone V, m. p. 73–74°, was isolated in 81% yield. Reduction of V by action of sodium hydrosulfite gave the corresponding hydroquinone, m. p. 133–135°, in 90% yield. Action of sulfuric acid in acetic acid converted the hydroquinone into the chroman II. However, oxidation of II by action of nitric acid in ethanol or of silver nitrate in ethanol gave only red oils from which no VI (a known substance, m. p. 109–110°) could be isolated. Blank experiments showed that the *o*-quinone VI could be separated quite efficiently by chilling in Dry Ice ethereal solutions of mixtures containing it, but this procedure failed to produce any crystals from the red oxidation products of II even when the solutions were inoculated with a crystal of VI.

John, Dietzel and Emte^{3b} obtained the red quinone VI by oxidation of IV as well as of I. It was expected, therefore, that the yellow *p*-quinone V

might give VI upon oxidation. Surprisingly, V was quite indifferent to the action of nitric acid or of silver nitrate—not a trace of red color was produced when solutions of V were boiled with silver nitrate for periods of time as long as six hours, or with nitric acid for thirty minutes. This behavior is in sharp contrast with the behavior of the chroman II, which gave red solutions in one and one-half hours by action of silver nitrate, and in fifteen minutes by action of nitric acid. It must therefore be concluded that oxidation of the chroman II does not lead to the *o*-quinone VI and, further, that although oxidation of II does lead ultimately to red oils, these red products do not arise *via* the *p*-quinone V as an intermediate. When the oxidation of II by action of nitric acid was continued beyond the time necessary to produce red solutions, the red color gradually faded, and after forty-five minutes the color of the mixture was an amber-orange. In only two of the many oxidations of II by action of nitric acid were any solids isolated: one was red and melted at 180–188°; the other was white and melted at 160.5–162.5°. Neither solid was obtained in amounts beyond a few milligrams.

Attempts were made to find evidence for the existence of VII, the tautomer of V, but without success. Action by acetyl chloride in pyridine, or of acetic anhydride and sulfuric acid, upon V produced oils; no solids could be isolated from either of these oils. The only evidence for the existence of VII was the fact that V, though insoluble in aqueous potassium hydroxide (10%), was soluble in Claisen alkali. When the solution of V in Claisen alkali was diluted and acidified, an orange solid precipitated; this had a wide range in melting point and it could not be purified by crystallization.

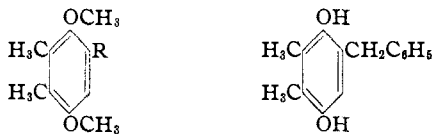
Since attempts to secure a tautomeric form of V had failed, attention was turned to other chromans analogous to II which could be transformed into *p*-quinones that might offer better chances for successful conversion into tautomeric forms. 2,2,7,8-Tetramethyl-5-benzhydryl-6-hydroxychroman, III, could not be prepared: although 2,3-dimethyl-5-benzhydrylhydroquinone was obtained without particular difficulty, conditions for successful condensation of this hydroquinone with isoprene or isoprene hydrobromide could not be found.

A consideration of previous results,^{4,5,6,7} together with those described in this and the two preceding papers¹ upon the oxidation of *p*-hydroxychromans, necessitates some modification of the general statement previously made.⁷ It may now be stated that, in this oxidation, a red *o*-quinone will result, with elimination of the group in the 5-position of the chroman, when this group is hydrogen (I, R = H) or methyl (I, α , β and γ -tocopherols). A red quinone will not result when the group in the 5-position is benzyl (II) or another chroman ring.^{1a}

(8) (a) Fieser and Hartwell, *THIS JOURNAL*, **57**, 1484 (1935); (b) Fieser and Bradsher, *ibid.*, **61**, 417 (1939); (c) Fieser and Fieser, *ibid.*, **61**, 596 (1939).

Experimental Part⁹

The two routes to 2,2,7,8-tetramethyl-5-benzyl-6-hydroxychroman (II) involved the following sequences of compounds, respectively: XI, XII, XIII, XIV, XVI; and XI, XV, XIV, XVI, followed by condensation of XVI with isoprene hydrobromide to give II.



XI, R = H XIV, R = CH₂C₆H₅
 XII, R = CHO XV, R = COC₆H₅
 XIII, R = CHOHC₆H₅ XVI

2,5-Dimethoxy-3,4-dimethylbenzaldehyde (XII).—The general procedure of Fuson, *et al.*,¹⁰ was modified in some respects. The dimethyl ether XI^b (16.6 g., 0.1 mole) was dissolved in dry tetrachloroethane (150 cc.). Zinc cyanide (23.5 g., 0.2 mole, dried in an oven) was added and the mixture was stirred vigorously at room temperature while a rapid stream of dry hydrogen chloride was introduced. After one hour, the mixture was thoroughly cooled (0°) and aluminum chloride (26.7 g., 0.2 mole) was added. Hydrogen chloride was passed into the mixture, now maintained at 60°, for two hours. More zinc cyanide (4.7 g., 0.04 mole) was added, introduction of the gas was continued for a further two hours, another portion of zinc cyanide (4.7 g., 0.04 mole) was added and introduction of the gas was continued for a further four hours. Sulfuric acid (200 cc., 2.5 *N*) was added slowly to the cooled mixture (voluminous precipitate of the aldimine salt, which was then allowed to stand overnight. The mixture was heated to the boiling point for ten minutes and then steam distilled. The solvent came over first and was collected separately; this was followed by the pale yellow aldehyde (14.6 g., m. p. 67–68°). The tetrachloroethane fraction was distilled under reduced pressure and the residue was heated to 145° in an inert atmosphere (CO₂) while the vapors were passed through a short (3") packed column. Only a few drops of material distilled below 145° (12 mm.) (b. p. of XI, 112° (15 mm.)). The residue, crystallized from dilute ethanol, gave 0.66 g. of aldehyde. The total yield of aldehyde XII was 15.3 g. (79%). A small sample, crystallized several times from dilute ethanol, melted at 67.5–68.5°.

Anal. Calcd. for C₁₁H₁₄O₂: C, 68.01; H, 7.27.
 Found: C, 68.06; H, 7.29.

The semicarbazone, prepared in the usual way and crystallized several times from dilute ethanol, softened at 205° and melted at 210–211°.

Anal. Calcd. for C₁₂H₁₇O₃N₃: C, 57.35; H, 6.82.
 Found: C, 57.1; H, 6.55.

When benzene was used as the solvent in place of tetrachloroethane, the yield of XII was only 44%.

2,5-Dimethoxy-3,4-dimethylbenzhydrol (XIII).—A solution of the aldehyde XII (18.5 g., 0.095 mole) in ether (80 cc.) was slowly added to a Grignard reagent prepared from bromobenzene (18.8 g., 0.12 mole), magnesium (2.84 g., 0.117 gram atom) and ether (20 cc.). The mixture was stirred and refluxed for forty-five minutes and was then cooled (0°) and the solid addition product was quickly filtered and washed with ether. The solid was hydrolyzed by action of sulfuric acid (5 *N*) and the resulting mixture was extracted with ether. The ether solution was washed successively with water, aqueous sodium carbonate and water, and then dried (sodium sulfate). Removal of the ether left the carbinol (23.8 g., 92%) as a clear amber, viscous oil. The substance was extremely difficult to crystallize and could be obtained as a solid only after prolonged cooling of its solution in dilute ethanol at the tem-

perature of Dry Ice. The substance then melted at 51–55°. A second form of the carbinol was obtained by crystallizing it from petroleum ether (b. p., 28–38°) at the temperature of Dry Ice. This form melted at –20°; when the resulting liquid was seeded with the higher melting form, it was slowly converted into the latter.

Anal. Calcd. for C₁₇H₂₀O₃: C, 74.97; H, 7.40.
 Found: (sample m. p. 50–55°) C, 75.2; H, 7.29.

The yield of this carbinol was much diminished when less than a 25% excess of the Grignard reagent was used: when the Grignard reagent was used in only 10% excess, the yield of XIII was only 74%.

2,3-Dimethyl-5-benzylhydroquinone Dimethyl Ether (XIV).—The carbinol XIII (23.77 g.) in ethanol (23 cc.) was reduced in a bomb in the presence of copper chromite catalyst (6 g.) with hydrogen under an initial pressure of 1920 lb. A temperature of 225° was reached in fifty minutes and after one hour at this temperature, the reduction was complete. The product was washed out of the bomb with ether, the solution was filtered, dried (sodium sulfate) and the solvents were removed under reduced pressure. The residue (20.3 g., 91%) melted at 37–39°. A sample, crystallized three times from petroleum ether (b. p. 28–38°), melted at 38.5–39°.

Anal. Calcd. for C₁₇H₂₀O₂: C, 79.65; H, 7.86.
 Found: C, 79.7; H, 7.82.

Clemmensen reduction of XIII by the procedure of Martin¹¹ gave XIV in only 4% yield.

2,3-Dimethyl-5-benzylhydroquinone (XVI).—A solution of dimethyl ether XIV (3.0 g.) in acetic acid (26 cc.) containing hydriodic acid (16 cc., sp. gr. 1.70) was boiled for thirty minutes. The mixture was poured into water and the white solid (2.67 g., 96%) m. p. 107–117°, was removed and crystallized from benzene–petroleum ether (b. p. 60–68°). The hydroquinone then melted at 118–123°. A sample crystallized several times from benzene–petroleum ether (b. p., 60–68°), melted at 124–125°.

Anal. Calcd. for C₁₅H₁₆O₂: C, 78.92; H, 7.06.
 Found: C, 79.1; H, 7.26.

The cleavage of XIV to XVI was rather extensively investigated. Action of hydrobromic acid (40%) in acetic acid¹² converted XIV into XVI in but 46% yield; action of hydrobromic acid (48%) in the same solvent¹³ produced XVI in 84% yield. All the cleavages studied in which 40% hydrobromic acid was used were accompanied by large amounts of tarry material. The stronger hydrobromic acid and hydriodic acid gave no tar at all. Several attempts were made to complete the cleavage at lower temperatures; these gave very poor yields of XVI. Action of hydrochloric acid upon XIV in a sealed tube produced only oils. Cleavage of XIV by action of anhydrous hydrogen bromide in acetic acid under pressure resulted in removal of only one of the methyl groups with the production of 2,3-dimethyl-4-acetoxy-5-benzylanisole.

The diacetate of XVI, prepared by action of acetic anhydride and a drop of sulfuric acid, and crystallized from benzene–petroleum ether (b. p. 60–68°), melted at 118–118.5° and was hygroscopic.

Anal. Calcd. for C₁₉H₂₀O₄: C, 73.06; H, 6.45.
 Found: C, 72.96; H, 6.58.

2,3-Dimethyl-5-benzylbenzoquinone.—A mixture of the hydroquinone XVI (0.5 g.), ferric sulfate (10 g.), sulfuric acid (1 cc.) and water (100 cc.) was steam distilled. The distillate (2.5 liters) was chilled and the yellow quinone (0.37 g., 75%) was removed and crystallized twice from petroleum ether (b. p. 28–38°). It then melted at 46–47°, but this product apparently contained solvent of crystallization for, when it was dried in a pistol, it liquefied and then, on cooling, solidified to a yellow solid which melted at 27–29°. This material was analyzed.

Anal. Calcd. for C₁₅H₁₄O₂: C, 79.62; H, 6.24. Found: C, 79.36; H, 6.48.

(9) Microanalyses by Stanley T. Rolfsen.

(10) Fuson, Horning, Ward, Rowland and Marsh, *THIS JOURNAL*, 64, 30 (1942).

(11) Martin, *ibid.*, 58, 1440 (1936).

(12) Smith, Wawzonek and Miller, *J. Org. Chem.*, 6, 229 (1940).

(13) Smith and Opie, *ibid.*, 6, 427 (1941).

This quinone, on reduction by action of sodium hydro-sulfite, gave the hydroquinone XVI.

2,3-Dimethyl-4-acetoxy-5-benzylanisole.—A solution of hydrogen bromide in acetic acid was prepared by passing the gas into acetic acid at 0° until the weight increased by 80%. The dimethyl ether XIV (0.53 g.) and this acid solution (6 cc.) were heated in a Carius tube at 75° for three hours and twenty-five minutes. The mixture was removed from the tube; the tube was rinsed with acetic acid, and the combined material was poured into water. The mixture, after standing for two days in a refrigerator, deposited a solid (0.30 g., 51%) which melted at 130–133°. After several crystallizations from benzene–petroleum ether (b. p. 60–68°), the substance melted at 134.5–135.5°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03; H, 7.06. Found: C, 75.71; H, 7.42.

2,3-Dimethyl-4-hydroxy-5-benzylanisole.—The above acetoxyanisole (100 mg.) was dissolved in methanol (15 cc.), hydrochloric acid (2 cc., 12 *N*) was added, and the solution was allowed to stand for eight days.¹⁴ The clear solution was evaporated under reduced pressure and the oily residue was warmed with petroleum ether (b. p. 60–68°). A small amount of the insoluble hydroquinone XVI (4 mg.) was removed, and the filtrate was evaporated. The residue was crystallized from methanol several times, when it melted at 68.5–69.5°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.57; H, 7.20.

That these anisoles have the structures assigned to them follows from the work of John and Rathmann¹⁵ who showed that action of alcohols in the presence of sulfuric acid upon trimethylhydroquinone led to monoethers and that it was the less hindered hydroxyl group, adjacent to the unsubstituted position on the benzene nucleus, which was converted into an ether group. The hydroquinone XVI, when allowed to stand in methanol containing sulfuric acid, was converted into a monomethyl ether, m. p. 68–69°, identical with the one obtained by partial cleavage of XIV. It follows that in the partial cleavage of XIV, it is the more hindered methoxyl group which is preferentially cleaved. Whether or not this behavior is general for such diethers as XIV cannot be said with certainty, for the benzyl group of XIV may exert a labilizing effect upon the ether linkage adjacent to it, an effect that might not be exerted by the methyl group in the corresponding position of the diethers of trimethylhydroquinone. Although the evidence is somewhat negative in nature, the fact that the monoether, m. p. 68–69°, could not be made to react at all with isoprene hydrobromide is in agreement with the structure assigned to this ether. The hydroquinone XVI readily reacts with isoprene hydrobromide to form a chroman; if, in the monoether, the ether group were in the more hindered 4-position, there would be no obvious reason why the ether should not also react with isoprene hydrobromide to form a chroman.

2,3-Dimethyl-5-benzoylhydroquinone Dimethyl Ether (XV).—The dimethyl ether XI (13.9 g., 0.084 mole) was dissolved in liquid sulfur dioxide (200 cc.) in a Dewar flask. Benzoyl chloride (15.7 g., 0.112 mole) was added to the red solution, and then aluminum chloride (33.6 g., 0.252 mole) was added portionwise.¹⁶ The mixture was allowed to stand for two days and was then poured over ice and acidified by addition of about one-seventh of its volume of hydrochloric acid (12 *N*). The yellow solid was removed, washed with water, dissolved in ether, and the ether solution was washed with aqueous potassium hydroxide (10%) to remove benzoic acid (4.3 g.). The ether solution was evaporated and the residue was steam distilled. Unchanged starting material (2.1 g., 0.13 mole) was recovered from the distillate (600 cc.). The residue in the flask was cooled and the solid was removed and crystallized from petroleum ether (b. p., 60–68°). The

benzyl compound weighed 13.6 g. (60%, or 71% when corrected for recovered XI) and melted at 95–99°. A sample, crystallized several times from petroleum ether (b. p. 60–68°), melted at 97.5–99°.

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.66; H, 7.00.

A solution of the ketone XV (1.35 g.) in ethanol (8 cc.) was reduced in a bomb in the presence of copper chromite catalyst (1 g.) under an initial pressure of 1900 lb. of hydrogen. The temperature of the bomb was raised to 230° (one hour) and maintained there for thirty minutes. The contents of the bomb were washed out with ether, the solution was filtered, and the solvents were evaporated. The residue of XIV (1 g., 78%) melted at 35–37°, alone or when mixed with XIV prepared from the carbinol XIII.

Attempts were made to prepare the hydroquinone XVI by other methods. Alkylation of 2,3-dimethylphenol by action of benzyl chloride upon the sodium salt in benzene¹⁷ produced a mixture from which no pure products could be isolated. Action of phenylacetyl peroxide upon 2,3-dimethylquinone¹⁸ gave an oil from which no pure product could be isolated. Likewise, action of phenylacetic acid and red lead upon 2,3-dimethylquinone in the presence of ethyl acetoacetate¹⁹ led to no pure product although the reaction was accompanied by a vigorous evolution of carbon dioxide. Benzylation of the dimethyl ether XI by action of benzyl alcohol and aluminum chloride in carbon disulfide²⁰ was unsuccessful; no reaction occurred and XI was recovered unchanged. Benzyl chloride in the presence of zinc chloride had no action upon a hot solution of 2,3-dimethylhydroquinone in ligroin; benzyl chloride and aluminum chloride in liquid sulfur dioxide likewise failed to react with this hydroquinone. Action of benzoyl chloride and aluminum chloride in liquid sulfur dioxide converted the hydroquinone into a product which appeared to be a monobenzoate.

Isoprene Hydrobromide.—This substance was prepared in 70% yield from isoprene and anhydrous hydrogen bromide by the method of Staudinger.²¹

2,2,7,8-Tetramethyl-5-benzyl-6-hydroxychroman (II).—A mixture of the hydroquinone XVI (1.75 g., 0.008 mole), isoprene hydrobromide (3.5 g., 0.024 mole), zinc chloride (1.3 g., freshly fused), and petroleum ether (35 cc., b. p. 60–68°) was boiled for forty minutes. The hot solution was decanted from the black residue, and the residue was washed with two 5-cc. portions of boiling ligroin. The combined ligroin solutions were diluted with an equal volume of ether and this solution was washed successively with water, aqueous sodium bicarbonate, and water. Evaporation of the solvent left an oily, brown solid which, when crystallized from a small volume of petroleum ether (b. p. 28–38°) yielded the chroman II (1.64 g., 72%) melting at 84–86°. A sample, crystallized several times from petroleum ether (b. p. 28–38°), melted at 83.5–89°.

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.28; H, 8.11.

Condensation of the hydroquinone XVI with isoprene according to the procedure of Smith, Ungnade, Hoehn and Wawzonek²² or of Smith and King²³ gave very poor results; only a few crystals of the chroman could be obtained by use of either procedure.

A solution of the chroman II (500 mg.) in dry methanol (30 cc.) was boiled with silver nitrate (5 g.). The color of the solution immediately became yellow, and after five minutes, it became red. After the red solution had been boiled for one hour and ten minutes, it was poured into water. The solution was extracted six times with ether, the combined extracts were washed with water and then

(17) Claisen, *Ann.*, **442**, 210 (1925).

(18) Fieser and Oxford, *This Journal*, **64**, 2060 (1942).

(19) Fieser and Chang, *ibid.*, **64**, 2043 (1942).

(20) Huston, *ibid.*, **46**, 2775 (1924).

(21) Staudinger, *Helv. Chim. Acta*, **5**, 743 (1922).

(22) Smith, Ungnade, Hoehn and Wawzonek, *J. Org. Chem.*, **4**, 311 (1939).

(23) Smith and King, *This Journal*, **63**, 1887 (1941).

(14) Baltzly and Buck, *This Journal*, **63**, 2023 (1941).

(15) John and Rathmann, *Ber.*, **73**, 995 (1940).

(16) Procedure of Ross, Percy, Brandt, Gebhardt, Mitchell and Yolles, *Ind. Eng. Chem.*, **34**, 924 (1942).

with aqueous sodium bicarbonate (5%). The bicarbonate washing was violet. Removal of the ether left a red oil from which no solid could be obtained when attempts were made to crystallize it from a variety of solvents. When ethanol was used as a solvent in a parallel experiment, it was necessary to boil the solution for one and one-half hours before the red color developed; otherwise the result was the same.

Nitric acid (200 cc., 16 *N*) was added to a solution of the chroman II in dry ethanol. The solution was boiled for twenty minutes and the resulting red liquid was poured into water. The solution was extracted seven times with ether and the combined extracts were washed successively with water, aqueous sodium bicarbonate (5%), and water. Removal of the ether left a red oil which was taken up in carbon tetrachloride and cooled. A pale yellow solid (0.07 g., m. p. 153–161°) was deposited. This, after several crystallizations from carbon tetrachloride, gave a white solid which melted at 160.5–162.5°.

Anal. Found: C, 67.47; H 6.51; mol. wt. (Rast on 1 mg. sample), 300.

The carbon tetrachloride filtrate was partially evaporated and the red solution was adsorbed on to Brockmann alumina. The upper half of the column was brown, the lower half was yellow. The brown zone was eluted with ethanol, but from the eluate, only a red uncrystallizable oil (90 mg.) resulted. When a solution of the chroman II in ethanol was boiled with nitric acid for forty-five minutes the red solution (formed within fifteen minutes) slowly became orange.

2,2,7,8-Tetramethyl-5-benzyl-6-acetoxychroman.—The chroman II (0.15 g.) was dissolved in acetic anhydride (5 cc.), a drop of sulfuric acid was added, and the solution was warmed on the steam-bath for five minutes and then poured into water. The solid was crystallized twice from petroleum ether (b. p. 28–38°); it then melted at 111–112°.

Anal. Calcd. for $C_{25}H_{28}O_3$: C, 78.07; H, 7.74. Found: C, 77.79; H, 7.38.

2,3-Dimethyl-5-benzyl-6-(3'-hydroxy-4'-methylbutyl)-benzoquinone (V).—A mixture of the chroman II (1 g.), powdered silver acetate (2 g.) and dry methanol (25 cc.) was boiled for three hours. More silver acetate (0.5 g.) was added and heating was continued for a further seven hours. Methanol (30 cc.) was added, the solution was filtered, and the filtrate was evaporated, finally under reduced pressure. The yellow residue, when crystallized from petroleum ether (b. p. 28–38°), gave the quinone V (0.85 g., 81%), melting at 67–72°. The analytical sample, prepared by crystallizing the material several times from petroleum ether (b. p. 28–38°), melted at 73–74°.

Anal. Calcd. for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 77.12; H, 8.00.

Aqueous potassium hydroxide (10%) had no effect upon the quinone V, even when gently warmed. The quinone V (150 mg.) was added to Claisen alkali (2 cc.) and the mixture was warmed on the steam-bath. The quinone dissolved, and after two minutes the solution was diluted with water. A flocculent precipitate separated but this could not be removed by filtration. The mixture was acidified with hydrochloric acid, whereupon a dull orange solid (120 mg.) slowly separated (thirty minutes). This material was removed; it had an indefinite melting point, but melted completely at 100° to a red liquid. Crystallization from a variety of solvents failed to give a pure product. This orange solid (70 mg.) was boiled with acetic anhydride (7 cc.) and fused sodium acetate (0.5 g.) for one hour and the mixture was poured into water. No solid could be isolated from the resulting oil. A solution of the quinone V (300 mg.) in dry ethanol (25 cc.) was boiled with silver nitrate (5 g.) for six hours. No red color developed. The experiment was repeated, using specially dried ethanol; again no trace of red color developed in the solution. Nitric acid (20 cc., 16 *N*) was added to a solution of the quinone V in dry ethanol and the solution was heated on the steam-bath for twenty-five minutes. No red color developed.

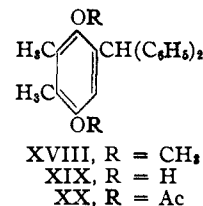
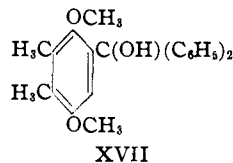
Sulfuric acid (1 drop) was added to a solution of the quinone V (100 mg.) in acetic anhydride (5 cc.). The color of solution immediately became bright red. The solution was heated on the steam-bath for ten minutes and poured into water. No solid product could be obtained from the resulting oil when attempts were made to crystallize it from various solvents. The experiment was repeated but, instead of heating the solution, it was allowed to stand overnight at room temperature. The result was the same. Acetylation of the quinone V by action of acetyl chloride in pyridine resulted in failure; no acetate could be obtained.

2,3-Dimethyl-5-benzyl-6-(3'-hydroxy-4'-methylbutyl)-benzohydroquinone.—The quinone V (200 mg.) in ether (20 cc.) was shaken with a solution of sodium hydrosulfite (1 g.) in water (20 cc.) until the yellow color disappeared (five minutes). The ether layer was removed, washed with water, and evaporated, finally under reduced pressure. The white residue (180 mg., 90%) melted at 128–130.5°; after three crystallizations from benzene-petroleum ether (b. p. 60–68°), the substance melted at 133–135°.

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 77.15; H, 8.18.

This hydroquinone (40 mg.) was dissolved in acetic acid (3 cc.), a drop of sulfuric acid was added, and the solution was allowed to stand overnight. Water (2 cc.) was added, and the solid (35 mg., 93%) was removed. It melted at 82–87°; after one recrystallization from petroleum ether it melted at 87–88.5°, alone or when mixed with a specimen of II prepared from XVI and isoprene hydrobromide.

The proposed route to 2,2,7,8-tetramethyl-5-benzyl-6-hydroxychroman (III) was patterned after the route to the benzylchroman II, and involved, in sequence, the compounds XV, XVII, XVIII and XIX.



2,5-Dimethoxy-3,4-dimethylphenyldiphenylcarbinol (XVII).—The substituted benzophenone XV (6.36 g., 0.24 mole) in ether (50 cc.) was added (ten minutes) to a Grignard reagent prepared from bromobenzene (5.5 g., 0.035 mole), magnesium (0.85 g., 0.35 gram atom) and ether (50 cc.). The mixture was refluxed for forty minutes and then the addition product was decomposed by addition of dilute sulfuric acid. The layers were separated, the aqueous layer was extracted several times with ether, and the combined ethereal solutions were washed with aqueous sodium bicarbonate (5%) and then with water. The ether was removed and steam was passed through the residue to remove biphenyl, after which the residue was cooled and the solid was removed and crystallized from petroleum ether (b. p., 60–68°). The product melted at 118–119°, and weighed 6.62 g. (81%). The analytical sample, prepared by recrystallizing this material several times, melted at 119–120°.

Anal. Calcd. for $C_{23}H_{24}O_3$: C, 79.28; H, 6.94. Found: C, 79.54; H, 6.84.

In a subsequent preparation, the carbinol XVII was obtained in a polymorphic form which melted at 129–130°. Both forms of XVII gave, on reduction, the benzhydryl compound XVIII.

2,3-Dimethyl-5-benzhydrylhydroquinone Dimethyl Ether (XVIII).—A solution of the carbinol XVII (12.87 g.) in ethanol (50 cc.) was placed in a bomb with copper chromite catalyst (2.5 g.) and subjected to the action of hydrogen under an initial pressure of 1600 lb. The bomb was heated to 200° and the temperature was maintained at this point for two hours to complete the reduction. The mixture was removed from the bomb, the bomb was washed

with ether, the combined liquids were filtered and the solvents were evaporated. The residue, crystallized from dilute ethanol, melted at 84–87°, and weighed 10.75 g. (88%). Several crystallizations from dilute ethanol gave a product which melted at 89–90.5°.

Anal. Calcd. for $C_{22}H_{24}O_2$: C, 83.10; H, 7.28. Found: C, 83.31; H, 7.16.

2,3-Dimethyl-5-benzhydrylhydroquinone (XIX).—A mixture of the dimethyl ether XVIII (4.78 g.), hydrobromic acid (48 cc., 48%), and acetic acid (66 cc.) was refluxed for two and one-half hours. The dark solution was poured into water, and the solid was removed and crystallized from benzene–petroleum ether (b. p. 30–60°) (Norit). The product (2.74 g., 63%) melted at 139–141°. A sample, recrystallized several times, melted at 142–143°.

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 83.15; H, 6.40.

Cleavage of the ether XVIII by action of hydriodic acid in acetic acid gave XIX in only 19% yield, in contrast with the excellent yield of XVI obtained from XIV by means of this procedure. Use of 40% hydrobromic acid in acetic acid also gave poor results (19%) when applied to the cleavage of XVIII. The hydroquinone XIX could not be condensed with isoprene hydrobromide or with isoprene. Four attempts were made to carry out the condensation with the hydrobromide; three in ligroin, and one in acetic acid. Condensation with isoprene was attempted twice, but no chroman was formed.

2,3-Dimethyl-5-benzhydrylhydroquinone Diacetate (XX).—Sulfuric acid (1 drop) was added to a solution of the hydroquinone XIX (120 mg.) in acetic anhydride (5 cc.). After standing for three minutes, the solution was poured into water. The solid was removed and crystallized three times from benzene–petroleum ether (b. p. 30–60°); it then melted at 185.5–186.5°.

Anal. Calcd. for $C_{26}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 77.15; H, 6.41.

Summary

1. 2,2,7,8-Tetramethyl-5-benzyl-6-hydroxychroman (II) has been prepared from 2,3-dimethylnitrobenzene.

2. This chroman has been oxidized, by action of silver nitrate, to the yellow *p*-benzoquinone V. Vigorous oxidation of the chroman

by action of silver nitrate in ethanol, or of nitric acid in the same solvent, produced red solutions but none of the red *o*-quinone VI could be isolated from these solutions.

3. Oxidation of the yellow *p*-benzoquinone V by action of silver nitrate in ethanol or of nitric acid in the same solvent did not produce the red *o*-quinone VI—indeed, did not even produce red solutions. The *p*-quinone V, therefore, is not an intermediate in the production of the red solutions by oxidation of the chroman II.

4. The only evidence obtained for the existence of a tautomeric form of the yellow *p*-quinone V was its solubility in Claisen alkali.

5. Several intermediates, leading to 2,2,7,8-tetramethyl-5-benzhydryl-6-hydroxychroman III have been prepared, but the chroman itself could not be prepared because the corresponding hydroquinone could not be condensed with isoprene or isoprene hydrobromide.

6. The results of this work have necessitated some modifications of previous statements with regard to the oxidative behavior toward silver salts and nitric acid of *p*-hydroxychromans related to the tocopherols. The oxidation always leads to yellow *p*-quinones, but the only known cases in which red *o*-quinones are formed (in amounts sufficient to isolate), with elimination of the group originally present in the 5-position of the chroman, are those in which this group is hydrogen or methyl. A benzyl group in this position is certainly not eliminated; likewise, another chroman ring attached in the 5-position is not eliminated.^{1a} Finally, some evidence has appeared that the red *o*-quinones, when they are formed, may be produced directly from the *p*-hydroxychromans, and not via the yellow *p*-quinones as intermediates.

MINNEAPOLIS 14, MINNESOTA RECEIVED JUNE 2, 1944

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Exchanges of Halogen and Hydrogen between Organic Halides and Isoparaffins in the Presence of Aluminum Halides

BY PAUL D. BARTLETT, FRANCIS E. CONDON¹ AND ABRAHAM SCHNEIDER¹

Introduction.—The experiments reported in this paper constitute part of a study of the mechanism of low-temperature paraffin alkylation. This reaction presents at the outset a mechanistic paradox. One of the strongest catalysts is aluminum chloride, which is known to be a powerful polar reagent and electron acceptor. On the other hand, the isoparaffin which is induced to react is the extreme of a non-polar and non-ionizing compound. The problem is whether the attack of a polar catalyst upon this system can have anything in common with the usual

function of this catalyst in many other organic reactions whose mechanisms are known.

Little progress has been made in resolving the complex alkylation reaction into successive steps, under the conditions of its commercial use. Usually if the reaction is interrupted at an early stage, it is found that some of the reactants have been converted into a rather complex mixture of products, while the rest remain unchanged. To circumvent this difficulty we selected for study the alkylation of isopentane with *t*-butyl chloride, catalyzed by aluminum bromide, since both aluminum bromide and *t*-butyl chloride are soluble

(1) Universal Oil Products Co. Fellows 1941–1944.