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

The Reaction between Quinones and Metallic Enolates. XII. Dibromo-*m*-xyloquinone and Sodium Malonic Ester[1]

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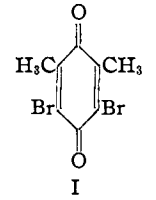
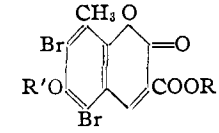
The reaction between excess sodium malonic ester and fully halogenated quinones such as chloranil leads to replacement of two *para* halogen atoms by malonic ester residues.[3] In the case of duroquinone, in which all the substituents are methyl groups, this reaction leads to a coumarin derivative, one of the methyl groups taking part in the reaction.[4] When both alkyl groups and halogen atoms are present in a fully substituted benzoquinone, the course of the reaction apparently depends upon the nature of the substituents. Thus dibromothymoquinone gives a reaction of the first type, but only one bromine atom—the one ortho to the methyl group—is replaced by a malonic ester residue[5]; 2-bromo-3-mesityl-α-naphthoquinone is inert toward sodium malonic ester, although it does react with sodium cyanoacetic ester[6]; while in the case of bromotrimethylquinone a methyl group, rather than the halogen atom, is involved in the reaction and the product is a coumarin.[7] Moreover, in this last case the bromine atom exerts a pronounced orienting effect, for of the three possible coumarins that could result, only one is formed—the one resulting from the attack of the reagent upon the methyl group meta to the bromine atom.

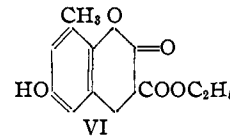
In order to explore further the factors which affect these two competing reactions, the action of sodium malonic ester upon dibromo-*m*-xyloquinone (I) has been studied. This quinone contains one more halogen atom, and one less alkyl group, than does bromotrimethylquinone. Moreover, the dibromoquinone differs from bromotrimethylquinone in that it does not contain a methyl group which is meta to a bromine atom, and it differs from dibromothymoquinone in that the bromine atoms are meta, instead of para, to each other. Hence in dibromo-*m*-xyloquinone there are different relationships between the two halogen atoms, and between the halogen atoms and the alkyl groups, from those existing in the quinones of this type which have been studied previously.

The quinone I proved to be far less tractable than bromotrimethylquinone. In alcohol or benzene, the chief solvents used previously, the reaction with sodium malonic ester produced very poor yields of metallic derivative. Use of the magnesium derivative of malonic ester in alcohol, benzene or dioxane gave even poorer results, for although fair yields of metallic derivatives were

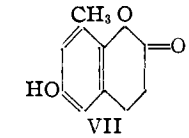


I





VI



VII

II	$R = C_2H_5$; $R' = H$	V	$R = H$; $R' = Ac$
III	$R = R' = H$	VIII	$R = H$; $R' = CH_3$
IV	$R = C_2H_5$; $R' = Ac$	XI	$R = R' = CH_3$

produced, the action of acids upon these metallic derivatives gave largely dark, non-crystallizable oils from which very little solid material could be obtained. These oils gave yellow solutions in most organic solvents and the solutions exhibited a pronounced greenish fluorescence. These results are quite at variance with those previously obtained, for the reaction between magnesium malonic ester and bromotrimethylquinone[7] leads to an excellent yield of coumarin.

By operating carefully with sodium malonic ester in dioxane the quinone I was converted into a metallic derivative which, when decomposed by acids, led to a coumarin (II). Even under the best conditions, however, the yield of coumarin was only about 50%, and although the coumarin was the only solid product that could be isolated, other reactions must have occurred because little more than 10% of the quinone could be recovered from the reaction mixture. These results show that an increase in the number of nuclear bromine atoms in a methylated-*p*-benzoquinone reduces

(1) Paper XI, THIS JOURNAL, **62**, 138 (1940).

(2) Abstracted from a Thesis by D. J. Byers, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, July, 1940.

(3) Stieglitz, *Am. Chem. J.*, **13**, 38 (1891).

(4) Smith and Dobrovolny, THIS JOURNAL, **48**, 1693 (1926).

(5) Hoffmann, *Ber.*, **34**, 1558 (1901).

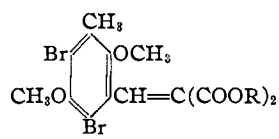
(6) Han Chiang Yuan, *J. Chinese Chem. Soc.*, **3**, 141 (1935).

(7) Smith and Johnson, THIS JOURNAL, **59**, 673 (1937).

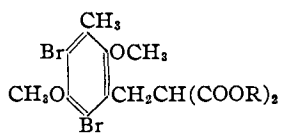
the ease with which coumarins are formed when these quinones react with the enolates of malonic ester. At the same time, there is a much greater sensitivity of the reaction to changes in the experimental conditions such as the nature of the solvent.

The coumarin II had the composition $C_{13}H_{10}O_5Br_2$, and was an ester, for when it was refluxed with hydrochloric acid in acetone the product was an acid, III. Both the ester and the acid are yellow, and both contain one hydroxyl group, for acetic anhydride converts each to the corresponding monoacetate, IV and V, respectively, which are white. Catalytic reduction of the ester II gave a colorless, bromine-free ester, $C_{13}H_{14}O_5$ (VI) resulting from hydrogenation of the double bond and simultaneous removal of both bromine atoms. The ester VI could be hydrolyzed, but the resulting acid immediately lost carbon dioxide to form the rather sensitive dihydrocoumarin VII.

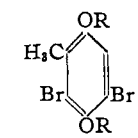
The presence of the two bromine atoms in the ester II exerted a very surprising effect upon the ease with which the coumarin ring was opened by means of alkali and methyl sulfate. Whereas the hydroxylcoumarin esters obtained from 2,3-dimethyl-4-naphthoquinone[8] and from bromotrimethylquinone[7] merely gave methyl ethers under these conditions, the coumarin ester II was readily converted into three products: the monoether (VIII) of the coumarin acid III, the diether diacid IX, and the diether diester X. When the methylation was terminated on the alkaline side, the product was a mixture of the two acids VIII and IX; when the methylation was terminated on the acid side, all three substances, VIII, IX and X were formed. The coumarin ring in II was



IX R=H
X R=CH$_3$



XII R=H
XIII R=CH$_3$

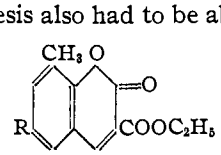


XIV R=H
XV R=CH$_3$

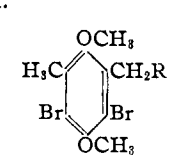
opened even more readily than that of the completely methylated analog[4] and it was possible to convert II into IX in yields as high as 71%. The acids VIII and IX were readily converted into the methyl esters XI and X, respectively. Both the acid IX and its methyl ester X gave dihydro derivatives (XII and XIII, respectively) when reduced catalytically, and in these cases the bromine was not removed from the nucleus as it was when the coumarins themselves were reduced by the same procedure.

In order to obtain definite proof of the structure of the yellow ester II, it was decided to synthesize independently either II or one of its degradation products. Since the hetero ring in II was opened so readily, the synthesis of the diether diester X or its dihydro derivative XIII appeared to offer the easiest approach. Tribromo-*m*-cresol was converted into 3,5-dibromotoluquinone and the latter was converted into the hydroquinone (XIV) and the hydroquinone dimethyl ether (XV) by the usual processes. This projected synthesis, however, had to be abandoned when it was found impossible to chloromethylate the ether XV or to introduce the aldehyde group into XIV by the Gattermann reaction—another surprising effect of the two bromine atoms.

A second synthesis, leading to the hydrocoumarin ester VI, was then undertaken. *o*-Cresol was converted, though in poor yield, into *o-hcmosalicylaldehyde* by the Reimer–Tiemann reaction. This aldehyde condensed readily with malonic ester to give 8-methyl-3-carbethoxy coumarin XVI and the coumarin, in turn, gave a good yield of a nitro derivative, presumably the 6-nitro compound XVII. Reduction of this nitrocoumarin was extremely difficult and only very small yields of the aminocoumarin XVIII were obtained. No method could be found for converting the amino coumarin XVIII into VI, however, and this synthesis also had to be abandoned.



XVI R=H
XVII R=NO$_2$
XVIII R=NH$_2$



XIX R=H
XX R=Cl

The synthesis of the diether diacid XII and from it, the diether diester XIII, was finally accomplished from dibromo-*m*-xyloquinone. This quinone was converted first into the hydroquinone and then into the hydroquinone dimethyl ether XIX. This ether was then chlorinated with sulfuryl chloride using the procedure of Kharasch

(8) Smith and Webster, THIS JOURNAL, **59**, 662 (1937).

and Brown.[9] The reagent selectively chlorinated one of the nuclear methyl groups in XIX and this reaction represents another use of this elegant method of chlorination whereby it was possible to prepare a chloromethyl derivative XX, that could not be obtained by the direct chloromethylation of XV. The product, however, was a mixture of XX (about 80%) and unchanged XIX (about 20%) which was difficult to separate without great losses. Therefore the crude reaction product was used to alkylate sodium malonic ester and the resulting ester XIII (R = C_2H_5) was hydrolyzed directly to the malonic acid XII. At this point a separation of XII from unchanged XIX was easily accomplished. The ester XIII was then prepared from the acid XII in the usual way. The specimens of acid XII and ester XIII prepared by this method were identical with those prepared by degradation of the coumarin II.

Experimental Part[10]

8-Methyl-5,7-dibromo-6-hydroxy-3-carbethoxy Coumarin (II).—Sodium (1.5 g.) was added to a solution of ethyl malonate (16 cc.) in dry dioxane (8 cc.) and the mixture was warmed occasionally until the metal dissolved, after which dry dioxane (130 cc.) was added. Dibromo-*m*-xyloquinone (20 g.) in dry dioxane (120 cc.) was added dropwise (thirty minutes) to the refluxing solution. The color became green, then brown, and after five minutes a brown solid began to separate. The mixture was refluxed for an hour longer, during which the solid turned red and the solution became very dark brown. The suspension was allowed to cool somewhat and the red solid was filtered off, suspended in acetone (100 cc.) and decomposed by addition of hydrochloric acid. Addition of water (1 liter) caused the separation of a flocculent yellow solid and a dark oil which solidified on standing overnight. The solids were removed and crystallized twice from acetone. The coumarin ester II obtained in this way formed lemon-yellow needles (5.28 g., 38%) which melted at 191–193° (decompn.). An additional 0.73 g. of product obtained from the mother liquors brought the total amount of coumarin II to 6.01 g. (44%). A portion of the product, crystallized twice more from acetone, melted at 192–193° (decompn.).

Anal. Calcd. for $C_{13}H_{10}O_5Br_2$: C, 38.44; H, 2.48. Found: C, 38.43; H, 2.44.

Dibromo-*m*-xyloquinone (1.4 g.) was recovered from the dioxane mother liquors by addition of ferric chloride.

As illustrative of the effect of different experimental conditions upon this reaction, the following may be cited. (A) Ethyl malonate (4 g.) and magnesium ethoxide (4 g.) were refluxed in dry ethanol (250 cc.) and the quinone (6 g.) was added in small portions (0.5 g. each) over a period of an hour. The suspension was refluxed for fifteen hours while a current of dry air was passed through. The chocolate-brown metallic derivative was removed and washed with ether. It weighed 10 g. The filtrates, when evaporated, left a dark oil from which no solid could be obtained. (B) Ethyl malonate (4 g.) was added to a solution of sodium (0.7 g.) in dry ethanol (35 cc.). Dry ethanol (100 cc.) saturated with the quinone (1.5 g.) was added slowly and the mixture was allowed to stand for two and one-half hours. Solid quinone (3.5 g.) was then added and the mixture was refluxed for thirty minutes. From the cooled reaction mixture, a red amorphous solid (1.3 g.) was obtained. (C) Procedure as in (A) using ethyl malonate (2 g.), magnesium ethoxide (2 g.), dry benzene (75 cc.) and a solution of quinone (6 g.) in benzene (75 cc.). The brick red solid product weighed 5.0 g. (D) Sodium (0.146 g.) and ethyl malonate (4.5 cc.) were heated until the metal dissolved. The solution was poured into dry benzene (30 cc.), and then the quinone (2.5 g.) in benzene (40 cc.) was slowly added (thirty minutes). The mixture was heated for twenty-six hours and then the red solid was removed and extracted with acetone. A dark brown, fluorescent solution resulted, and no coumarin could be obtained from it. (E) Ethyl malonate (1.4 g.) and magnesium ethoxide (0.7 g.) were refluxed in dioxane (30 cc.) for thirty minutes and then the quinone (2.5 g.) in dioxane (40 cc.) was added. After heating for sixteen hours, the solid was removed, triturated twice with ether and six times with acetone and then thoroughly extracted with acetone. The light brown metallic derivative weighed 1.27 g.

Decomposition of the metallic derivatives obtained in A, B, C, and E with diluted acid (hydrochloric or sulfuric) in alcohol, acetone, water or dioxane gave only small amounts of the coumarin ester accompanied by much dark oil and highly fluorescent (green) solutions.

8-Methyl-5,7-dibromo-6-acetoxy-3-carbethoxycoumarin (IV).—The ester II (0.5 g.) was dissolved in acetic anhydride (10 cc.). Sulfuric acid (2 drops) was added and the solution was warmed on the steam-bath for fifteen minutes. The solution was poured into water and the solid was removed and crystallized first from ethanol and then from acetone. It weighed 0.46 g. (84%) and melted at 183.5–184°.

Anal. Calcd. for $C_{15}H_{12}O_6Br_2$: C, 40.17; H, 2.70. Found: C, 40.23; H, 2.78.

8-Methyl-5,7-dibromo-6-hydroxy-3-carboxycoumarin (III).—The ester II (0.5 g.) was suspended in a mixture of acetone (25 cc.), hydrochloric acid (25 cc.) and water (25 cc.) and the mixture was refluxed for six and one-half hours. The solid was removed from the cooled suspension and crystallized several times from dioxane. It formed yellow needles (0.37 g., 82%) which melted at 260–260.5° with decomposition.

Anal. Calcd. for $C_{11}H_6O_5Br_2$: C, 34.92; H, 1.59. Found: C, 35.26; H, 2.08.

The ester II (0.40 g.) was not hydrolyzed at all after standing for a day at room temperature in 80% sulfuric acid (10 cc.), and was only partially hydrolyzed when refluxed for six hours in acetone containing 6 *N* sulfuric acid. After nine hours, however, hydrolysis occurred but the product was quite impure.

8-Methyl-5,7-dibromo-6-acetoxy-3-carboxycoumarin (V).—The acid III (0.55 g.) was acetylated as

(9) Kharasch and Brown, THIS JOURNAL, **61**, 2142 (1939).

(10) Microanalyses by E. E. Renfrew and C. O. Guss.

described for acetylation of the ester II. The product (0.51 g., 81%) was crystallized once from dilute dioxane and four times from ethanol, when it melted at 209.5–210°.

Anal. Calcd. for $C_{13}H_8O_6Br_2$: C, 37.14; H, 1.90. Found: C, 37.33; H, 2.02.

8-Methyl-6-hydroxy-3,4-dihydro-3-carbethoxycoumarin (VI).—The ester II (1.0 g.) was dissolved in ethanol (75 cc., 95%), palladium catalyst (0.5 g.)[11] was added and the mixture was shaken for six and one-half hours under hydrogen (3 atmospheres). The catalyst was removed and the solution was concentrated under reduced pressure to a small volume. Water was added until cloudiness developed, and the solution deposited white needles on standing overnight. After crystallization three times from dilute ethanol (previously boiled to remove dissolved air) the substance (0.47 g., 76%) melted at 133–134°.

Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.37; H, 5.64. Found: C, 62.40; H, 5.53.

8-Methyl-6-hydroxy-3,4-dihydrocoumarin (VII).—Acetone (2 cc.), hydrochloric acid (8 cc.) and water (8 cc.) were refluxed for ten minutes and then cooled in an atmosphere of hydrogen. The dihydro ester VI (0.5 g.) was added and the solution was refluxed under nitrogen for two hours. The cooled solution was extracted with ether and the ether was evaporated. The residue, a light brown solid (0.24 g., 67%) was crystallized three times from ethanol. It was white and melted at 149–150°.

Anal. Calcd. for $C_{10}H_{10}O_3$: C, 67.39; H, 5.66. Found: C, 67.57; H, 5.85.

Methylation of Ester, II.—The ester II (2 g.) was dissolved in dry methanol (50 cc.) and methyl sulfate (27 cc.). Aqueous sodium hydroxide (10%) was added to the hot solution in small portions, waiting for the red color to disappear before another portion of alkali was added. When a color change no longer occurred on addition of alkali, excess base (50 cc., 20%) was added and the solution was refluxed for thirty minutes. The cooled solution was extracted once with ether and the aqueous layer was acidified with dilute sulfuric acid and thoroughly extracted with ether. Evaporation of the ether left a light brown solid (1.94 g.) which was a mixture of the monobasic acid VIII and the dibasic acid IX. The mixture was dissolved in the minimum amount of methanol and set aside to cool. **8-Methyl-5,7-dibromo-6-methoxy-3-carboxycoumarin, VIII,** separated as a light brown solid (0.09 g.). It was crystallized four times from acetic acid, when it formed very pale yellow needles which melted at 206–207°.

Anal. Calcd. for $C_{12}H_8O_5Br_2$: C, 36.93; H, 2.04. Found: C, 37.22; H, 2.11.

Dilution of the methanol filtrate from VIII caused the separation of a brown powder (1.47 g., 71%), the dibasic acid IX. **2,5-Dimethoxy-3-methyl-4,6-dibromobenzalmalonic acid (IX)** was white and melted at 208–208.5° (decompn.) after crystallization from aqueous methanol.

Anal. Calcd. for $C_{13}H_{12}O_6Br_2$: C, 36.79; H, 2.86. Found: C, 36.99; H, 2.90.

8-Methyl-5,7-dibromo-6-methoxy-3-carbomethoxycoumarin (XI) was prepared by refluxing the methoxy acid VIII (0.22 g.) in methanol (40 cc.) and sulfuric acid (2 cc.) for sixty hours. The cooled solution was diluted with water, made alkaline with sodium carbonate and extracted with ether. Removal of the ether left the ester XI (0.18 g., 80%) as pale yellow needles which after crystallization twice from methanol melted at 170–171°.

Anal. Calcd. for $C_{13}H_{10}O_6Br_2$: C, 38.44; H, 2.48. Found: C, 38.53; H, 2.69.

Dimethyl 2,5-Dimethoxy-3-methyl-4,6-dibromobenzalmalonate, X.—The coumarin ester II (0.3 g.) was dissolved in hot methyl sulfate (5 cc.). Aqueous sodium hydroxide (20%) was added dropwise with shaking until the mixture was alkaline. The solution was cooled and the methylation was completed by adding alternately methyl sulfate and base. Each reagent was added three times, and the methylation was completed on the acid side. The reaction mixture was poured into water and the aqueous layer was decanted from the yellow oil. The oil was stirred with dilute ammonium hydroxide (1:4) and the orange solid was removed and crystallized twice from dil. methanol. The product then formed white needles (0.06 g.) which melted at 92–94°. The same substance, m. p. and mixed m. p. 93–94°, was obtained by refluxing the acid IX in dry methanol containing a trace of sulfuric acid.

Anal. Calcd. for $C_{15}H_{16}O_6Br_2$: C, 39.82; H, 3.54. Found: C, 39.86; H, 3.71.

2,5-Dimethoxy-3-methyl-4,6-dibromobenzylmalonic Acid (XII).—The benzalmalonic acid IX (2.0 g.) in ethanol (50 cc.) was shaken with palladium catalyst[11] for two hours under hydrogen at 38 lb. pressure. The catalyst was removed and the solution concentrated under reduced pressure to a volume of 3 cc. Water was added until cloudiness developed and the solution was set aside. The white solid (0.8 g., 40%) melted at 151–152° (decompn.) after crystallization from dilute dioxane.

Anal. Calcd. for $C_{13}H_{14}O_6Br_2$: C, 36.64; H, 3.31; neut. equiv., 213. Found: C, 36.62, 36.74; H, 3.23; 3.28; neut. equiv., 222, 224.

Dimethyl 2,5-Dimethoxy-3-methyl-4,6-dibromobenzylmalonate, XIII.—The ester X (0.5 g.) was reduced in methanol (35 cc.) using a palladium catalyst as described for the reduction of IX. The product was isolated in the same way, and after crystallization from dilute methanol it formed white needles (0.27 g., 54%) which melted at 92.5–94°. When mixed with the ester X (m. p. 92–94°) the substance melted at 79–87°. The same ester XIII, (0.45 g., 85%) m. p. and mixed m. p. 92.5–93.5° was obtained from the acid XII (0.5 g.) by the same procedure used to convert acid VIII into its ester XI.

Anal. Calcd. for $C_{15}H_{18}O_6Br_2$: C, 39.64; H, 3.99; OCH_3, 13.7. Found: C, 39.87; H, 3.66; OCH_3, 13.5.

Dimethyl Ether of Dibromo-*m*-xylohydroquinone, XIX.—The hydroquinone (11 g.) was dissolved in methanol (300 cc.) containing methyl sulfate (50 g.). To the hot solution there was added slowly and with stirring a solution of potassium hydroxide (96 g.) in methanol (400 cc.). After addition of the alkali was completed, the solution was stirred and refluxed for thirty minutes. Addition of water (1200 cc.) precipitated a solid which was removed

(11) Busch and Stove, *Ber.*, **49**, 1064 (1916).

and crystallized from ethanol. The substance (10.4 g., 87%) formed white needles which melted at 114–115.°[12]

2,5-Dimethoxy-3-methyl-4,6-dibromobenzyl Chloride, XX.—The ether XIX (6.48 g.), sulfuryl chloride (2.70 g.) and benzoyl peroxide (0.07 g.) were dissolved in dry, alcohol-free chloroform (10 cc.) and the solution was refluxed vigorously for six hours.[9] At the beginning of the reaction hydrogen chloride was evolved copiously, but after six hours, hydrogen chloride was barely detectable with ammonia. The solvent was allowed to evaporate spontaneously at room temperature. The residue (7.19 g.), a mixture of XIX and XX, could not be separated by fractional crystallization, but slow evaporation of the chloroform solution in an evaporating dish left a cake of material which consisted of a light brown amorphous material on top and white needles on the bottom. The needles (1 g., m. p. 86–90°) were removed mechanically and crystallized three times from methanol. The product then melted at 96–96.5°. For the next step, however, the crude product was used and a calculation based on the over-all yield indicated that the benzyl chloride XX had been formed in about 80% yield.

Anal. Calcd. for $C_{10}H_{11}O_2ClBr_2$: C, 33.48; H, 3.09. Found: C, 32.92; H, 3.14.

The **Benzylmalonic Acid, XII.**—Sodium (0.023 g.) was dissolved in dry ethanol (2 cc.), ethyl malonate (0.160 g.) was added and the solution was refluxed for ten minutes. To the boiling solution there was added dropwise (ten minutes) a solution of the benzyl chloride XX (0.358 g.) in dry ethanol (10 cc.). The mixture was refluxed for three hours, then aqueous sodium hydroxide (10 cc., 20%) was added and the mixture was boiled for an hour longer. The cooled mixture was diluted with water (50 cc.) and extracted twice with ether. The alkaline layer was acidified with dilute sulfuric acid and extracted three times with ether. Removal of the ether left a white powder (0.31 g., 73%) which, after crystallization from dilute dioxane melted at 152° (decompn.) alone or when mixed with a specimen of XII obtained by degradation of the coumarin II. In a similar experiment, 1.19 g. of the crude chloride as obtained from the sulfuryl chloride reaction gave 0.85 g. of the acid XII. Assuming a yield of 73% in the alkylation, then the benzyl chloride XX was formed in at least 80% yield.

Dimethyl Ester of the Benzylmalonic Acid, XIII.—The above acid (0.9 g.) was refluxed for three days in methanol (10 cc.) containing sulfuric acid (10 drops). Water (20 cc.) was added and the solution was made alkaline with sodium carbonate and extracted three times with ether. The product (0.89 g., 93%) after crystallization three times from methanol melted at 92–94°, alone or when mixed with the ester XIII prepared by degradation of the coumarin II.

***m*-Dibromotoluquinone.**—Tribromo-*m*-cresol (m. p. 82–83°)[13] (10 g.) was dissolved in acetic acid (70%, 500 cc.). The solution was heated to 70°, chromic oxide (3.2 g.) was added, and the temperature was maintained at 70–75° for ten minutes. Water (1500 cc.) was added and the yellow solid was removed and crystallized from dil. ethanol. The quinone (6.2 g., 77%) melted at 114–115° in agreement with the value in the literature.[13]

***m*-Dibromotoluhydroquinone, XIV.**—The quinone (7.0 g.) in acetic acid (30 cc.) and water (20 cc.) was refluxed with an excess of 20-mesh zinc. The colorless solution was decanted from the zinc and diluted with water. The hydroquinone (3 g., 42%) melted at 148° (decompn.) after crystallization from benzene.[14]

Dimethyl Ether, XV.—When the above hydroquinone (3 g.) in hot methanol (10 cc.) and methyl sulfate (9 cc.) reacted with potassium hydroxide (11.4 g.) in methanol (50 cc.) the methyl ether XV could be isolated by adding water and extracting with ether. Recrystallized from ethanol, it formed white needles (1.7 g., 52%) which melted at 71–72°.[15] When *m*-dibromotoluquinone in acetic acid was reduced by stannous chloride in hydrochloric acid, there was produced in excellent yield a product which melted at 143–145° (decompn.). This product, however, was not the hydroquinone XIV for when it was methylated as described above, the methyl ether melted at 60.5–61.5° and was not the ether XV. Beyond analyzing it, nothing further was done with this substance.

Anal. Calcd. for $C_9H_{10}O_2Br_2$ (XV): C, 34.85; H, 3.25. Found: C, 38.42, 38.46; H, 3.78, 3.62.

Gattermann Reaction.—Dry hydrogen chloride was passed rapidly into a stirred mixture of the hydroquinone XIV (2.82 g.), ether (50 cc.), zinc cyanide (1.75 g.) and potassium chloride (0.35 g.). After six hours, aluminum chloride (1.0 g.) was added and hydrogen chloride was passed into the mixture for three hours longer. From the reaction mixture there was isolated 0.32 g. of the hydroquinone and by addition of chromic acid to the filtrates, 1.5 g. of the quinone was obtained. No other solid material could be isolated.

Chloromethylation.—Dry hydrogen chloride was passed into a stirred mixture of the diether XV (1.55 g.), hydrochloric acid (8 cc.) and formalin (3 cc., 40%) for twenty-nine hours at 65–70°. Starting material (1.25 g.) melting at 71–72° was the only product that could be isolated.

Summary

1. The magnesium and sodium enolates of ethyl malonate have been added to dibromo-*m*-xyloquinone under a variety of conditions. The best results were obtained using the sodium enolate and dioxane as the solvent.

2. Both metallic derivatives converted the quinone into 3-carbethoxy-6-hydroxy-5,7-dibromo-8-methylcoumarin (II). Thus this quinone behaved as a pentadienol system, and the reaction involved one of the methyl groups without affecting the halogen atoms.

3. The structure of the coumarin II was proved by degradation to 2,5-dimethoxy-3-methyl-4,6-dibromobenzylmalonic acid (XII) and syn-

(12) Kohn and Feldman, *Monatsh.*, **49**, 169 (1928), report the m. p. as 116°.

(13) Claus and Hirsch, *J. prakt. Chem.*, [2] **39**, 59 (1889).

(14) Von Auwers, *Ber.*, **35**, 461 (1902), reported the m. p. as 149–150° (decompn.).

(15) Kohn and Steiner, *Monatsh.* **58**, 106 (1931), report the m. p. as 73°.

thesis of the latter from the dimethyl ether of dibromo-*m*-xylohydroquinone.

4. The chemical properties of the coumarin II and many of its derivatives have been described.

MINNEAPOLIS, MINNESOTA
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[CONTRIBUTION FROM THE UNIVERSITY OF MARYLAND]

The Structure of Phellonic Acid[1]

BY NATHAN L. DRAKE, HOMER W. CARHART AND RALPH MOZINGO

Work in this Laboratory on material isolable from cork[2] has led to a re-examination of the structure of phellonic acid, one of the saponification products of that portion of cork which is not appreciably soluble in solvents. The present paper is concerned with the degradation of phellonic acid and the synthesis of products identical in every respect with natural phellonic acid and its degradation products.

Previously, phellonic acid had been isolated by Kügler,[3] and its structure investigated in a number of laboratories,[4] with the result that phellonic acid has come to be generally regarded as an α-hydroxy acid[5] containing twenty-two carbon atoms, α-hydroxybehenic acid, $CH_3(CH_2)_{19}CHOHCO_2H$ (I).

However, more recent work in this Laboratory[6] and elsewhere[7] convinced us that phellonic acid is not a twenty-two carbon α-hydroxy acid. We have consequently re-investigated the structure of phellonic acid, and have shown by degradation and synthesis that phellonic acid and 22-hydroxytetracosanoic acid are identical in every respect.

Phellonic acid, purified to constant melting point, was shown by carbon and hydrogen analyses and by determinations of its neutral equivalent to possess the formula $C_{24}H_{48}O_3$. The acid showed no unsaturation with bromine in carbon tetrachloride or with permanganate. Phellonic acid forms an acetate, and, in the "Grignard machine,"[8] liberates methane equivalent to two active hydrogens and consumes four moles of reagent. All of this behavior corroborates the previous conclusion that phellonic acid is a saturated hydroxy acid.

It appeared logical to attempt to oxidize the hydroxyl group to a carbonyl, to prepare the oxime and subject it to Beckmann rearrangement, and to investigate the hydrolysis products of the resultant amide. We were, however, unable to isolate a pure keto acid from the products of oxidation or dehydrogenation of phellonic acid although we used various oxidizing and dehydrogenating agents. Oxidation occurred in most cases, but it either proceeded too far, or produced a mixture which was difficult to separate.

Chromic anhydride in glacial acetic acid oxidized phellonic acid to a dibasic acid, $C_{22}H_{42}O_4$, with loss of two carbon atoms. Reduction of the ester of this acid gave docosamethylene glycol, which possessed the melting point predicted from an extrapolation of the curve given by Chuit[9a] who plotted the melting points of the α,ω-polymethylene glycols up to twenty-one carbon atoms against their carbon contents. These facts, together with analytical data, including neutral equivalent determinations, and the concordance between the melting points of our acid, and its methyl ester and those of 1,20-eicosanedicarboxylic acid and its methyl ester leave no doubt concerning the structure of the acid.

When subjected to a potassium hydroxide fusion, phellonic acid is quickly and quantitatively converted into a dibasic acid. Von Schmidt,[4b] who first isolated this acid, named it "phellogenic acid" and assigned the formula $C_{21}H_{40}O_4$ (m. p. 121°). Zetsche and Bähler repeated the fusion

(1) In part from the Ph.D. dissertation of Homer W. Carhart, University of Maryland, 1939. The syntheses from sebacic acid were carried out by Ralph Mozingo.

(2) For the latest paper on this subject see Drake and Wolfe, THIS JOURNAL, **62**, 3018 (1940).

(3) Kügler, *Arch. Pharm.*, **22**, 217 (1884); *Ber.*, **17**, 213 (1884).

(4) (a) Gilson, *La Cellule*, **6**, 63 (1890); (b) Schmidt, *Monatsh.*, **25**, 277. 302 (1904); **31**, 347 (1910); (c) Scurti and Tommasi, *Gazz. chim. ital.*, **46**, pt. 2, 159 (1916); *Ann. staz. chim. agrar. sper. Roma*, II, **6**, 40. 53. 67 (1917); *ibid.*, II, **9**, 145 (1920); (d) Zega, Diss. Zürich (1924); (e) Karrer, Peyer and Zega, *Helv. Chim. Acta*, **5**, 856 (1923).

(5) (a) Zetsche and Rosenthal, *ibid.*, **10**, 346 (1927); (b) Zetsche, Cholatnikov and Scherz, *ibid.*, **11**, 272 (1928); (c) Zetsche and Sonderegger, *ibid.*, **14**, 632 (1931); (d) Zetsche and Bähler, *ibid.*, **14**, 642 (1931); (e) Zetsche and Bähler, *ibid.*, **14**, 852 (1931).

(6) Drake and Cary, unpublished work.

(7) C. T. Turner, Master's Thesis, Cornell Univ., Ithaca, N. Y., 1931.

(8) Kohler and Richtmyer, THIS JOURNAL, **52**, 3736 (1930).

(9) (a) Chuit, *Helv. Chim. Acta*, **12**, 850 (1937); (b) *ibid.*, **9**, 264 (1926).