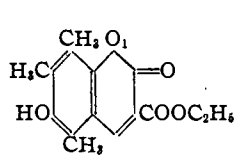


[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

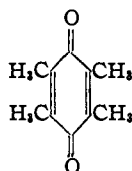
The Reaction between Methylated Quinones and Sodium Enolates. VIII. Mechanism. The Addition of Sodium Malonic Ester to a Methylene Quinone¹

BY LEE IRVIN SMITH AND JAMES W. HORNER, JR.²

In previous work from this Laboratory it has been shown that when a completely substituted quinone, such as duroquinone, reacts with metallic enolates such as sodium malonic ester, the product is a 6-hydroxycoumarin derivative (I). In this

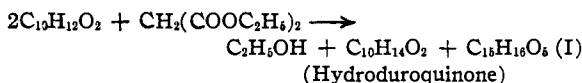


I



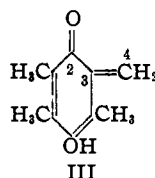
II

reaction, two molecules of the quinone are involved, one of them acting as a dehydrogenating agent, and the over-all reaction (after acidification) can be represented as

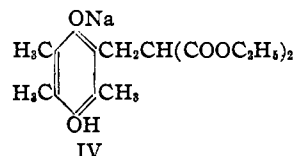


The curious feature of this reaction is the modification of one of the methyl groups of the quinone and the fact that the methylene carbon atom of the ester becomes attached to the side chain, rather than the nucleus, of the quinone. This type of reaction occurs even when one bromine atom (trimethylbromoquinone) is available for metathesis,¹ or when one of the groups is ethyl³ but the reaction fails when all four of the groups are ethyl.³

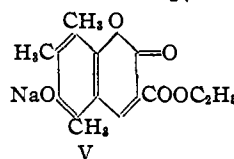
In seeking an explanation for this reaction, only two hypotheses are available: (a) the malonic ester residue becomes attached elsewhere at first, and then migrates to the methyl carbon atom; (b) the quinone itself rearranges first, in such a way that the malonic ester residue can become directly attached to the α -carbon atom in the side chain. Of these two possibilities (b) is *a priori* much the more probable and some time ago Fuson,⁴ in his paper on vinylogy, cited this reaction and suggested a mechanism for it. This mechanism involved a pentad enolization of the quinone (II) under the influence of the alkaline condensing agent to give III, in which a new conjugated sys-



III



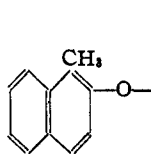
IV



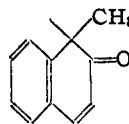
V

tem (1-4 in III) is present. The addition of sodium malonic ester to this system would produce IV, which by elimination of sodium ethoxide and dehydrogenation by a second molecule of quinone would lead finally to V, the sodium derivative of I. While it is not certain whether ring closure precedes or follows the dehydrogenation, the essential features of this mechanism have been regarded by the workers in this Laboratory as correct and the mechanism has been used with success in predicting and correlating the facts obtained from reactions between a variety of enolates and substituted quinones.

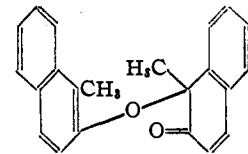
In order to obtain further evidence as to the mechanism, it was decided to study the reaction between sodium malonic ester and an ortho methylene quinone containing an unsubstituted methylene group. Pummerer and Cherbuliez⁵ have shown that the structures of the methylene quinones previously reported⁶ were incorrect, and that the dehydrogenation of, for instance, α -methyl- β -naphthol probably involved the following steps: the first product was a radical containing univalent oxygen (VI) which could rearrange into a radical containing trivalent carbon (VII).



VI



VII



VIII

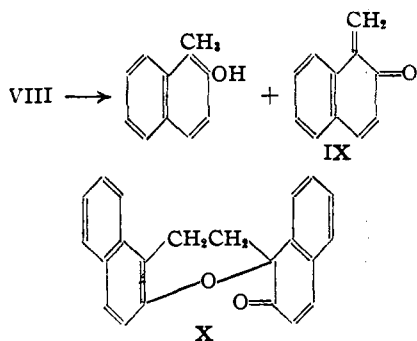
(1) Part VII, THIS JOURNAL, 59, 673 (1937).

(2) From the Ph.D. thesis of James W. Horner, Jr.

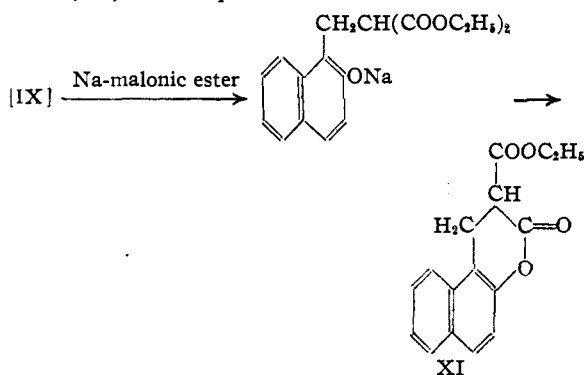
(3) J. W. Opie, unpublished work.

(4) Fuson, *Chem. Rev.*, 16, 1 (1935).(5) Pummerer and Cherbuliez, *Ber.*, 52, 1392 (1919).(6) (a) Zincke, *Ann.*, 328, 294 (1903); (b) Fries and Hubner, *Ber.*, 39, 435 (1906); (c) Fries and Kann, *Ann.*, 358, 335 (1907); (d) Zincke and Hohorst, *ibid.*, 358, 357 (1907); (e) Zincke and Klostermann, *Ber.*, 40, 679 (1907).

Although three products could be formed by the dimerization of these radicals, Pummerer and Cherbuliez regarded the dimer as VIII, composed of VI + VII. Moreover, this product VIII, when heated in xylene, cleaved by disproportionation to give one molecule of α -methyl- β -naphthol and one of the ortho methylene quinone (IX), which in turn immediately polymerized to a dimer, X.

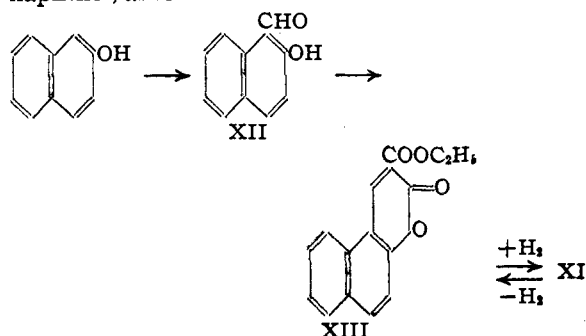


If, then, the structures of Pummerer and Cherbuliez were correct, it might be possible to "catch" the ortho methylene quinone (IX) by cleaving the dimer VIII in the presence of sodium malonic ester, provided IX would add the ester more rapidly than it would dimerize to X, and the product of the reaction between the methylene quinone and the ester should be a dihydrocoumarin derivative (XI) if the methylene quinone actually behaved as postulated for the methylene quinone form (III) of duroquinone.



When dehydro- α -methyl- β -naphthol (VIII) was warmed with sodium malonic ester in dry ethanol, the hydrocoumarin (XI) was isolated from the product. The hydrocoumarin was readily dehydrogenated to the coumarin (XIII) by ferric chloride, or even on standing in air, and the coumarin XIII was readily reduced to XI. It was not possible to isolate XI in good yield because of the great difficulty of separating it from the reac-

tion mixture containing also the naphthol, X, and XIII. The structure of the coumarin was proved by an independent synthesis, starting with β -naphthol, as follows



The results of this work show that at least one ortho methylene quinone will react with malonic ester to form a coumarin derivative, and they lend support to the hypothesis discussed above, in which an ortho methylene quinone is postulated as an intermediate in the reaction between duroquinone and sodium malonic ester. Moreover, these results lend support to the structures assigned by Pummerer and Cherbuliez to the products obtained by the dehydrogenation of α -methyl- β -naphthol, and to the arguments recently advanced by Shearing and Smiles⁷ in favor of analogous structures for the dehydro-di-(hydroxynaphthyl)-methanes. Work upon similar reactions of the dehydro compounds of the highly methylated (mononuclear) phenols is in progress, which will be discussed in a future paper.

Experimental Part

Di-(2-hydroxy-1-naphthyl)-methane.^{5b}—Commercial aqueous formaldehyde (163 cc.), β -naphthol (297 g.), and powdered sodium acetate (56.5 g.) were dissolved in ethanol (357 cc.) and allowed to stand. The temperature rose 15° in one and one-half hours and then slowly fell. After sixty-seven hours the mass of solid was crushed and filtered. The solid was washed on the filter several times with ethanol and then with methanol until the washings were colorless. The product weighed 218 g. (71%) and melted at 198–199°.

α -Methyl- β -naphthol.^{5b}—Sodium hydroxide (50 g.) and the dinaphthylmethane (50 g.) were dissolved in water (500 cc.). Zinc (30 g., analytical, 20 mesh, washed with 0.5 N hydrochloric acid, water, and 15% sodium hydroxide immediately before using) was added and the mixture was stirred and refluxed for eight hours. After standing overnight, more zinc was added and the mixture again refluxed for eight hours. At the end of this time, formaldehyde solution (10 cc.) was added and the mixture again allowed to stand overnight. This treatment—addition of zinc in the morning, refluxing for eight hours,

(7) Smiles, *J. Chem. Soc.*, 1931 (1937).

addition of formaldehyde at night, etc.—was repeated for four days more. The solution was then filtered from the zinc, the zinc was washed with sodium hydroxide solution and the washings were added to the filtrate. The alkaline solution was acidified with concentrated hydrochloric acid and the precipitate was removed and washed with water. The solid was extracted repeatedly with hot water until no further material crystallized when the extract was cooled. From the water extracts 15.5 g. (29%) of the naphthol, melting at 109–110°, was obtained.

Dehydro- α -methyl- β -naphthol (VIII).⁸—A solution prepared from sodium hydroxide (15%, 23 cc.), water (435 cc.), the naphthol (9.1 g.), and saturated aqueous sodium chloride (114 cc.) was stirred and cooled in an ice-bath while an aqueous solution of potassium ferricyanide (19.4 g. in 57 cc. of water) was added slowly. After the addition was completed, stirring was continued for two hours longer. The precipitate was removed, washed with water, and dried under reduced pressure. It was then digested with acetone (10 cc.), filtered and then crystallized from a mixture of acetone (60 cc.) and water (15 cc.). The product weighed 4.8 g. and melted at 131–132.5°. By dilution of the filtrate with water a second crop of material was obtained, but this was quite impure.

Dimeric Methylene Quinone (X).⁸—The dehydro compound VIII (0.8 g.) was refluxed for thirty hours in dry benzene (5 cc.). More benzene was added and the solution was extracted thoroughly with sodium hydroxide (15%). From the alkaline washings, 0.37 g. of α -methyl- β -naphthol was obtained; evaporation of the benzene solution left an oil (0.28 g.) which gave yellow crystals when its solution in acetone was cooled. The quinone dimer melted at 139–141°.

Ethyl 5,6-Benzo-3,4-dihydrocoumarin-3-carboxylate (XI).—The dehydronaphthol VIII (2.5 g.) in dry ethanol (5 cc.) was added to a solution of sodium (0.37 g.) in dry ethanol (10 cc.). After solution was complete, ethyl malonate (2.54 g.) in ethanol (4 cc.) was added, and the mixture was refluxed. A solid appeared within twenty minutes. More ethanol (5 cc.) was added and refluxing was continued for fifteen hours. The solid was removed, washed with iced hydrochloric acid, and crystallized from aqueous ethanol. It weighed 0.13 g. and melted at 110.5–112°.

*Anal.*⁹ Calcd. for $C_{16}H_{14}O_4$: C, 71.11; H, 5.19. Found: C, 71.21; H, 5.40.

The low yield undoubtedly was due to the complexity of the mixture, which contained the naphthol, X, XI, and XIII. The liquid filtrate from the reaction mixture, when poured into hydrochloric acid, gave a brown oil from which nothing could be isolated except the naphthol, and the same was true when the whole reaction mixture was poured into hydrochloric acid without filtering off the hydrocoumarin.

β -Hydroxy- α -naphthaldehyde was prepared from β -naphthol in 39% yield by the method of Adams and Levine.¹⁰ The product boiled at 179–180° under 22 mm., and melted at 79–81.5°.

(8) Pummerer and Cherbuliez, *Ber.*, **47**, 2969 (1914).

(9) Microanalysis by J. W. Opie.

(10) Adams and Levine, *This Journal*, **45**, 2373 (1923).

Ethyl-5,6-benzocoumarin-3-carboxylate (XIII).¹¹—The hydroxyaldehyde (23.3 g.) was dissolved in ethyl malonate (21.7 g.) on the steam-bath, and piperidine (47 drops) was added. The mixture was kept on the steam-bath for two hours and was then allowed to stand overnight. The solid was removed, washed twice with 50% ethanol, and crystallized from 95% ethanol (charcoal). The product formed yellow crystals which weighed 19.9 g. (55%) and melted at 115°.

Reduction of XIII to XI.—The coumarin ester (2 g.) was dissolved in ethanol (120 cc.), about 0.5 g. of Raney nickel catalyst¹² was added and the mixture was shaken for twelve hours with hydrogen under 40 lb. (3 atm.) pressure, then allowed to stand for thirty-three hours without shaking. The catalyst was removed, and the filtrate when cooled deposited 0.18 g. of the colorless hydrocoumarin XI. After crystallization from ethanol, the product melted at 113–114°. When mixed with a specimen of XI (m. p. 110.5–112°) prepared from the dehydronaphthol, the material melted at 111.5–114°. Dilution of the filtrate yielded 1.49 g. of less pure material which melted, after crystallization from ethanol, at 109–112°.

Dehydrogenation of XI to XIII.—The dihydrocoumarin was dissolved in alcoholic ferric chloride (ferric chloride, 28.5 g., concentrated hydrochloric acid, 4 cc., ethanol, 100 cc.) and allowed to stand in the cold. Dilution with water precipitated the coumarin quantitatively. After crystallization from ethanol, the substance formed yellow crystals which melted at 111.5–114°. When mixed with a specimen of XIII prepared from β -hydroxy- α -naphthaldehyde, the material melted at 112–115°. Mixtures of the coumarin XIII and the dihydrocoumarin XI melted quite low—usually between 80 and 95°.

Summary

1. A mechanism for the formation of coumarins from duroquinone and sodium enolates has been suggested, which involves a pentad enolization of the quinone to a methylene quinone, and addition of the enolate to the conjugated system of the latter.

2. It has now been shown that sodium malonic ester will react with an ortho methylene quinone to give a dihydrocoumarin, thus lending support to the mechanism postulated. In this case the dehydrogenation to the coumarin does not occur because, unlike duroquinone, the methylene quinone does not dehydrogenate the hydrocoumarin.

3. The results support the conclusions of Pummerer and Cherbuliez as to the structures of dehydrophenols, and they are also in accord with the recent work of Shearing and Smiles on the structures of similar compounds derived from hydroxydiphenylmethanes.

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(11) Knoevenagel and Schröter, *Ber.*, **37**, 4486 (1904).

(12) Covert and Adkins, *This Journal*, **54**, 4116 (1932).