CARBONYL AND THIOCARBONYL COMPOUNDS

I *a.* REACTION OF 9-DIAZOXANTHENE WITH *o*-QUINONES

b. THE DIRECT PREPARATION OF HALOGENATED CYCLIC ETHERS FROM CERTAIN THIONES AND THEIR MOLLUSCICIDAL ACTIVITY[1]

NAZIH LATIF AND IBRAHIM FATHY

ABSTRACT

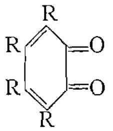
The preparation and properties of 9-diazoxanthene are described. It reacts with tetrachloro- and tetrabromo-*o*-benzoquinone, 4-triphenylmethyl-1,2-benzoquinone, and phenanthraquinone to give the cyclic ethers III*a*, III*b*, IV, and V respectively. The action of hydrochloric acid – dioxane solution on the products is stressed.

Tetrachloro- and tetrabromo-*o*-benzoquinone react with xanthione forming the halogenated cyclic ethers III*a* and III*b* respectively. A 1,2-benzopyran derivative IX is obtained by the action of tetrachloro-*o*-quinone on coumarin-2-thione. IX is toxic to *Biomphalaria boissi* snails in high dilution.

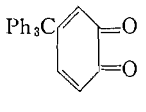
Reaction of 9-Diazoxanthene with o-Quinones

The reactions of diazomethane and diphenyldiazomethane with *o*-quinones have been described by various authors (1). Schönberg and Latif (2) investigated the action of 9-diazofluorene on *o*-quinones and found that it reacts readily with *o*-benzoquinone and β-naphthoquinone derivatives to give methylenedioxy derivatives in good yield, but it fails to react with phenanthraquinone under the same conditions.

9-Diazoxanthene has not been described before. It could be prepared by the oxidation of xanthone hydrazone with mercuric oxide in the presence of alkali at room temperature. However, microanalysis could not be carried out, since the substance decomposes at room temperature with the formation of the ketazine. In contrast to diazofluorene, it reacts readily with phenanthraquinone to give the cyclic ether V. It also reacts, but more vigorously, with tetrachloro- I*a*, and tetrabromo-*o*-benzoquinone I*b*, and 4-triphenylmethyl-1,2-benzoquinone II, to give, in excellent yield, the analogous products III*a*, III*b*, and IV, respectively, according to scheme A (2).



I*a*; R = Cl
I*b*; R = Br



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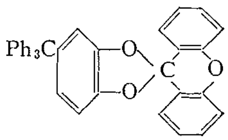

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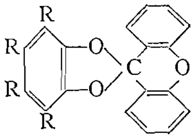
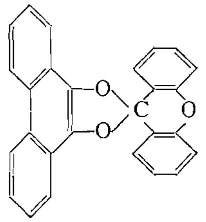


III*a*; R = Cl
III*b*; R = Br



V

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Contribution from the Organic Chemistry Department, National Research Centre, Dokki, Cairo, Egypt, U.A.R.

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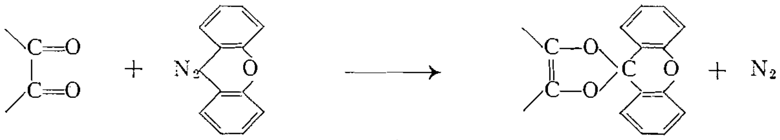


A

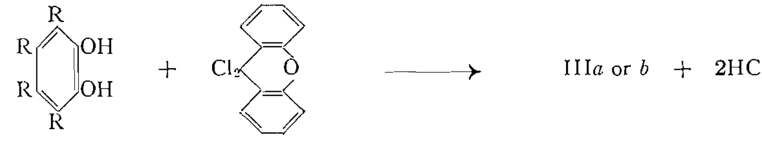
The constitution of the products formed is based on the following facts:

(*a*) they are colorless or nearly so,

(*b*) they are readily hydrolyzed by acids, and

(*c*) III*a* and III*b* can be obtained by the reaction between 9,9-dichloroxanthene and the corresponding tetrahalogenocatechol according to scheme B.

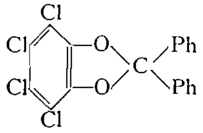
The identity of the products obtained from reactions A and B is established by analysis, melting point and mixed melting point, and by their identical infrared spectra.



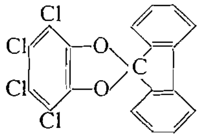
R = Cl or Br

B

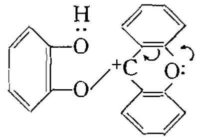
It is observed that all the cyclic ethers obtained in this reaction are readily and quantitatively cleaved by hydrochloric acid in dioxane; for example, when III*a* or III*b* are boiled for 30 minutes with a mixture of concentrated hydrochloric acid and dioxane (1:5), xanthone and the corresponding catechol are obtained in quantitative yield. In the case of V, xanthone and phenanthraquinone are obtained after air oxidation. This is rather remarkable as the analogous products VI and VII obtained by the action of diphenyl- (3) and diphenylene-diazomethane (2) on tetrachloro-*o*-quinone are not similarly attacked. This may be explained by assuming that the proton attacks first the ethereal oxygen atom and this is followed by the heterolytic fission of the C–O bond, to give a carbonium ion which is stabilized by resonance with the unshared electron pair of the oxygen of the xanthyl residue (4) (cf. VIII for III*a*). However, it is observed that these products are not appreciably cleaved by concentrated sulphuric acid at room temperature, as usually happens with the other methylenedioxy derivatives obtained by the action of diazomethanes on *o*-quinones. This may be attributed to the formation of an oxonium salt which is rather stable under the conditions of the experiment, a property generally shown by xanthenes.



VI



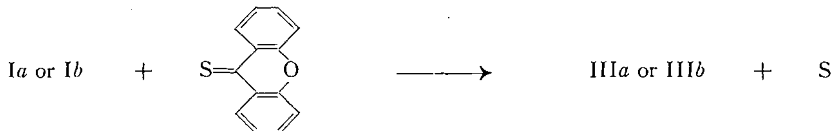
VII



VIII

The Direct Preparation of Halogenated Cyclic Ethers from Certain Thiones

Several reactions of thioketones have been described (5), but it is believed that nothing is mentioned about the action of *o*-quinones on cyclic thiones. It is found that the high potential quinones, tetrachloro- and tetrabromo-*o*-benzoquinone, react with xanthione in dry benzene at room temperature with the formation of III*a* and III*b*, respectively, according to scheme C.

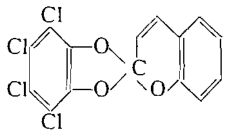


C

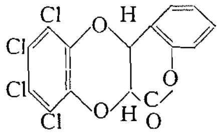
However, the reaction is slow at room temperature, but is remarkably accelerated by heat. Thus when I*a* and xanthione are boiled in dry benzene for 1 hour, an 80% yield of III*a* is obtained, whereas, at room temperature, a 75% yield is reached only after 5 days. The reaction of I*b* with xanthione is affected by temperature in almost a similar way. III*a* can also be obtained by heating I*a* and xanthione without a solvent in a carbon dioxide atmosphere.

The identity of the compounds obtained in this reaction with those obtained by either reaction A or B is established by analysis, melting point and mixed melting point, and by similar infrared spectra.

It is found also that tetrachloro-*o*-quinone reacts similarly with coumarin-2-thione in boiling benzene with the formation of a 1,2-benzopyran derivative IX in good yield. The constitution of the product obtained is based on analogy, as well as on the fact that it is colorless and easily hydrolyzed by hydrochloric acid in dioxane to coumarin and tetrachlorocatechol. The absence of sulphur and of the characteristic frequency band of a *d*-lactone (1755 cm^{-1} nujol) (6) shown by coumarin excludes structure X of a 1,4-dioxane, which may result by the addition of the quinone to the double bond of the lactone ring. Addition of *o*-quinones to the double bond in ethylenes, benzofurans, isocoumarins, etc. is well known. However, it is reported that coumarin fails to react with phenathraquinone (7).



IX



X

The Molluscicidal Activity of Halogenated Cyclic Ethers

Halawani and Latif (8) found that halogenated *o*-benzoquinone and benzodioxole derivatives are toxic to *Biomphalaria boissi* snails—the intermediate host of *Schistosoma mansoni* in Egypt—in high dilutions. The toxicity of the above-mentioned halogenated cyclic ethers has been investigated. It is found that IX kills the snails in concentrations as low as 20 p.p.m. in water during a 24-hour-exposure period to the drug followed by a 72-hour-observation period in fresh water. III*a*, III*b*, IV, and V could not be tested, since they are almost insoluble in the solvents usually used for the test. Details of these experiments will be published separately.

EXPERIMENTAL

Melting points are not corrected. Microanalyses were carried out by A. Bernhardt, Germany.

Preparation of 9-diazoxanthene.—Xanthone hydrazone (4 g), mercuric oxide (7 g), and anhydrous sodium sulphate (1 g) were ground together in a dry mortar, and transferred to a dry 100-ml R.B.F. guarded with a calcium chloride tube and containing 50 ml dry ether. One milliliter of a freshly prepared saturated solution of potassium hydroxide in absolute alcohol was added while shaking the mixture for 2 minutes at room temperature (20° C), then stirring for 30 minutes at 10°. The green ethereal solution was filtered off and the residue washed with dry ether. The combined ethereal solutions were concentrated under reduced pressure in the cold, when green crystals of 9-diazoxanthene separated, and filtered. The compound is soluble in most organic solvents in the cold, melts with decomposition at about 60° C (red melt), and turns orange-red when left at room temperature for a few hours.

Xanthone ketazine.—9-Diazoxanthene (0.1 g) was left in a watch glass exposed to air for 24 hours. The orange-red crystals formed were washed with ether and recrystallized from benzene when xanthone ketazine was obtained (m.p. 285° not depressed when admixed with an authentic sample prepared according to Schönberg and Stolpp (9)).

Reaction of tetrachloro-o-quinone with 9-diazoxanthene.—Tetrachloro-*o*-quinone (10) (0.8 g) was added slowly to a dry ethereal solution of diazoxanthene (1.1 g). A vigorous reaction with evolution of gas took place and after a few seconds a yellowish crystalline solid separated. On recrystallization from xylene 9,9-(tetrachloro-*o*-phenylenedioxy) xanthene III*a* separated in colorless crystals,* m.p. 286° (yield almost quantitative). It is difficultly soluble in cold alcohol, acetone, or benzene. Calc. for $C_{19}H_8O_3Cl_4$: C, 53.52; H, 1.87; Cl, 33.3. Found: C, 53.43; H, 2.17; Cl, 32.87%. It dissolves in concentrated sulphuric acid with a deep yellow color and when the solution was kept overnight at room temperature (20° C) and then poured into ice, above 75% of the substance was recovered unchanged.

Hydrolysis of IIIa.—To a solution of concentrated hydrochloric acid (sp. gr. 1.19) (1 ml) in dioxane (5 ml) was added III*a* (0.15 g), the mixture boiled for 30 minutes, and then left to cool. It was then poured into ice and the colorless precipitate formed was filtered, dried, and dissolved in the least amount of boiling methyl alcohol and left to cool. The colorless crystals separated proved to be xanthone (m.p. and mixed m.p. 174°). On addition of dilute hydrochloric acid to the mother liquor a white precipitate was formed. After filtering, drying, and refluxing with acetic anhydride for 30 minutes, the mixture was left to cool, and then poured into ice. The solid formed was recrystallized from methyl alcohol and proved to be the diacetyl derivative of tetrachlorocatechol (melting point and mixed melting point). Using methyl alcohol instead of dioxane, hydrolysis was partial and about 50% of the substance was recovered unchanged.

Reaction between tetrachlorocatechol and 9,9-dichloroxanthene.—Tetrachlorocatechol (0.1 mole) and 9,9-dichloroxanthene (0.1 mole from thionyl chloride and xanthone) were heated together in a test tube protected from moisture at 150° (oil bath) for 1 hour. The reaction mixture was left to cool, washed several times with acetone, and recrystallized from xylene when III*a* was obtained (m.p. 286° undepressed when admixed with an authentic sample prepared by the action of diazoxanthene on tetrachloro-*o*-quinone) (yield about 80%). The product and the authentic sample have identical infrared spectra. Calc. for $C_{19}H_8O_3Cl_4$: C, 53.52; H, 1.87; Cl, 33.3. Found: C, 54.32; H, 2.08; Cl, 32.6%.

Reaction of tetrabromo-o-quinone with 9-diazoxanthene.—Tetrabromo-*o*-quinone (11) (1 g) was added to a crude ethereal solution of diazoxanthene (from 2 g of xanthone hydrazone). A vigorous reaction took place with evolution of gas and the immediate separation of a yellowish deposit. This was filtered off, washed with boiling acetone,

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**In a parallel experiment carried out using the crude ethereal solution obtained from the oxidation of xanthone hydrazone as described above, instead of diazoxanthene crystals, the same yield of IIIa was obtained. In the coming experiments this crude ethereal solution will be generally used.*

and recrystallized from xylene (using charcoal) when 9,9-(tetrabromo-*o*-phenylenedioxy) xanthene III*b* separated in almost colorless crystals, m.p. 280° (decomp.). Yield almost quantitative. The compound dissolves in concentrated sulphuric acid with a yellow color and most of it was recovered unchanged when poured into ice as in the case of the chloro-analogue. Calc. for $C_{19}H_8O_3Br_4$: C, 37.74; H, 1.32; Br, 52.98. Found: C, 37.68; H, 1.75; Br, 53.24%. When III*b* was boiled with concentrated hydrochloric acid – dioxane as in the case of the chloro-analogue, xanthone and tetrabromocatechol (identified as its diacetyl derivative) were obtained.

Reaction of tetrabromocatechol with 9,9-dichloroxanthene.—Tetrabromocatechol (4 g) and dichloroxanthene (from 2 g of xanthone and thionyl chloride) were dissolved in dry benzene (20 ml), and a few drops of piperidine added. The mixture was refluxed for 3 hours, concentrated, and left to cool. The solid separated was washed with boiling acetone and recrystallized from xylene (using charcoal) when III*b* was obtained in colorless crystals, m.p. 280° (decomp.). Its infrared spectrum is identical with that of the product obtained from diazoxanthene.

Reaction of 4-triphenylmethyl-1,2-benzoquinone with 9-diazoxanthene.—The quinone (12) (1.2 g) was added in very small portions to a crude ethereal solution of diazoxanthene (from 2 g of xanthone hydrazone). A new portion was only added when the reaction from a previous addition had subsided. After all the quinone was added, the reaction mixture was left for 2 hours at room temperature with occasional shaking. The color of the quinone disappeared and a colorless solid was formed. This was recrystallized from xylene when 9,9-(4-triphenylmethyl-*o*-phenylenedioxy) xanthene IV was obtained in colorless crystals, m.p. 264° (yield about 60%). Calc. for $C_{38}H_{26}O_3$: C, 86.01; H, 4.94. Found: C, 86.45; H, 5.28%.

Reaction of phenanthraquinone with 9-diazoxanthene.—The quinone (0.5 g) was added in very small portions to a crude ethereal solution of diazoxanthene (from 2 g xanthone hydrazone) with mild stirring at 37°. When all the quinone had been added, stirring of the reaction mixture was continued for 2 hours. The yellowish solid formed was washed several times with boiling acetone and recrystallized from xylene when (V) was obtained in almost colorless crystals, m.p. 298°. It is insoluble in most organic solvents and gives a deep yellow color with concentrated sulphuric acid. Calc. for $C_{27}H_{16}O_3$: C, 83.5; H, 4.15. Found: C, 84.1; H, 4.35%. V (0.2 g) was refluxed with hydrochloric acid – dioxane solution as above, the reaction mixture was left to cool and then poured into ice. The yellowish solid formed was filtered off using the pump and suction was allowed to continue for 1 hour to facilitate air oxidation. The product was then pressed on a porous plate and recrystallized from benzene. The resulting orange crystals proved to be phenanthraquinone (melting point and mixed melting point). It gives olive green color with concentrated sulphuric acid.

Reaction of tetrachloro-o-quinone with xanthione.—Method "a". The quinone (2.4 g) and xanthione (2.2 g) in dry benzene (15 ml) were refluxed together for 1 hour on the water bath. The red color of the quinone disappeared and the solution became dark brown; it was left to cool. The crystalline solid formed was filtered off and the mother liquor concentrated to obtain another crop of crystalline solid.* The whole crude reaction product was washed with acetone several times and recrystallized from xylene in colorless crystals which proved to be III*a* (m.p. 286° undepressed when admixed with an authentic sample prepared in the above experiments. The product and the authentic sample have

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**When the mother liquor was evaporated to dryness under reduced pressure and the residue heated in a carbon dioxide atmosphere at 150° (oil bath) for 1 hour, sulphur collected on the cooler parts of the reaction vessel. Xanthione is stable when heated alone under the same conditions.*

identical infrared spectra.). Yield above 80%. Calc. for $C_{19}H_8O_3Cl_4$: C, 53.52; H, 1.87; Cl, 33.3. Found: C, 53.51; H, 2.07; Cl, 33.04%. *Method "b"*. Tetrachloro-*o*-quinone (0.61 g) and xanthione (0.5 g) were mixed together in a dry test tube protected from moisture. The mixture was heated for 2 hours at 200° (oil bath) while passing carbon dioxide, and then left to cool. The solid mass obtained was ground well, washed with acetone, and recrystallized from xylene (using charcoal) when III*a* was obtained in colorless crystals, m.p. 286° (yield about 50%).

Reaction of tetrabromo-o-quinone with xanthione.—The quinone (1 g) and xanthione (0.5 g) in dry benzene (20 ml) were refluxed together for 1 hour on the water bath. The reaction mixture became dark brown, and yellowish crystals separated. These were filtered off, and the filtrate concentrated and left to cool when another crop of crystals was obtained. The combined crude product was washed with boiling acetone and recrystallized from xylene (using charcoal) when III*b* was obtained in almost colorless crystals, m.p. 280° (decomp.). Its infrared spectrum is identical with that of the products obtained by reactions A and B.

When the quinone and the thione in dry benzene were kept at room temperature in a carbon dioxide atmosphere for 3 days about 75% yield of III*b* separated.

Reaction of tetrachloro-o-quinone with coumarin-2-thione.—The quinone (1.2 g) and the thione (0.8 g) in dry benzene (10 ml) were refluxed for 3 hours. The reaction mixture was filtered while hot, concentrated, and left to cool. The crystals that separated were washed with acetone and recrystallized from benzene when 2,2-(tetrachloro-*o*-phenylenedioxy) benzopyran IX was obtained in colorless crystals, m.p. 214° C. It is soluble in hot acetone, benzene, and chloroform, difficultly soluble in alcohol. Calc. for $C_{15}H_6O_3Cl_4$: C, 47.87; H, 1.59; Cl, 37.7. Found: C, 47.88; H, 1.64; Cl, 37.38%.

Hydrolysis of IX.—IX (0.2 g) was refluxed with a solution of hydrochloric acid in dioxane as usual. The reaction mixture was then poured into ice and filtered and the filtrate left to concentrate slowly at room temperature. The separated colorless crystals were recrystallized from petroleum ether (30–50°) and proved to be coumarin (melting point and mixed melting point). Diluted hydrochloric acid was added to the mother liquor and the white solid obtained was filtered off, dried, and refluxed with acetic anhydride when the diacetyl derivative of tetrachlorocatechol was obtained.

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