

Carbonyl and Thiocarbonyl Compounds. XI (1).
 Synthesis of Halogenated Benzodioxoles by the Action of Tetrahalo-*o*-Benzoquinones
 on Benzophenone Hydrazones and Their Cleavage by Nucleophilic Reagents

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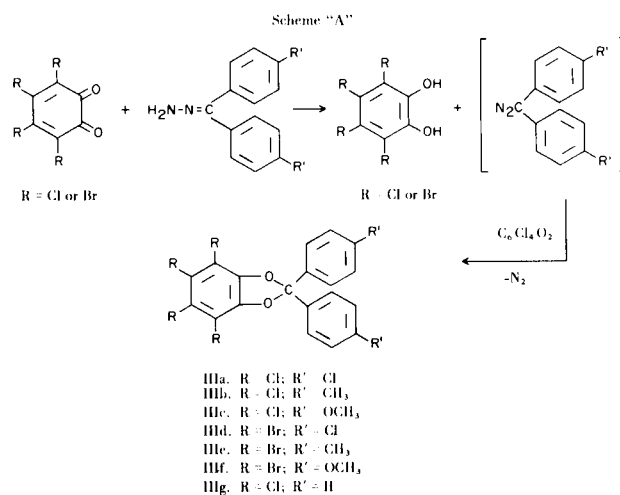
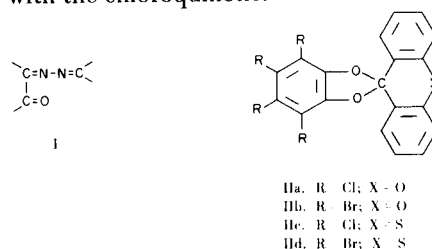
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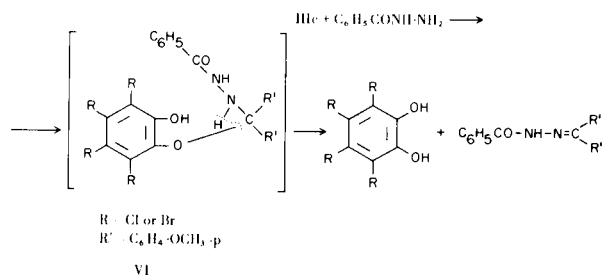
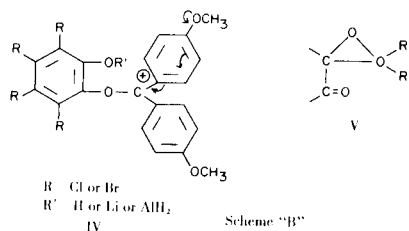
p,p'-Dichloro-, *p,p'*-dimethyl- and *p,p'*-dimethoxybenzophenone hydrazones react with tetrachloro- and tetrabromo-*o*-benzoquinone to give directly the halogenated benzodioxoles (IIIa-IIIf), respectively, together with the corresponding tetrahalocatechol. Cleavage of the dioxole ring by nucleophilic reagents depends markedly on the nature of the substituents. The dimethoxyderivatives (IIIc) and (IIIf) proved to be unusually reactive toward cleavage by dilute mineral acids, lithium aluminum hydride, hydrazines and malonitrile, whereas the dichloro analog behaves normally and is not cleaved under the same conditions.

It is known that *o*-quinones normally give quinone-azines of the type I when allowed to react with keto-hydrazones (3,4). In previous publications we have reported a new reaction between tetrahalo-*o*-benzoquinones and keto-hydrazones leading to the formation of halogenated benzodioxoles. Thus, it has been shown that tetrachloro and tetrabromo-*o*-benzoquinones react with xanthone (5) and thioxanthone (6) hydrazones, at room temperature to give IIa-IId, respectively. A similar reaction took place between the quinones and benzoxanthone hydrazones (7,8). Meanwhile, it has been found that benzophenone hydrazone is mainly oxidized to diphenylketazine by tetrachloro- or tetrabromo-*o*-quinone under similar conditions, possibly through the intermediate formation of an unstable tetrazone (9).

In the present investigation it is found that *p,p'*-dichloro-, *p,p'*-dimethyl- and *p,p'*-dimethoxybenzophenone hydrazones react with tetrachloro-*o*-benzoquinone in dry ether at room temperature or slightly warm solutions, affording the benzodioxoles (IIIa-IIIc) respectively, together with tetrachlorocatechol. In the case of the dimethoxy-hydrazone, the cyclic ether is produced in almost quantitative yield, whereas in the cases of the methyl and the chloro derivatives, the corresponding ketazines are also produced at the expense of the cyclic ether formation. The yield of the ketazine in the latter case is, however, greater than in the case of the dimethyl compound. The reactions with tetrabromo-*o*-benzo-

quinone leading to the cyclic ethers (IIId-IIIf) run parallel to those with the chloroquinone.





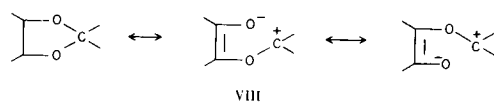
The constitution of the dioxoles obtained is based on analytical data, lack of color, and on the fact that they could be produced also by the reaction of the corresponding diaryldiazomethane on the appropriate quinone (10). *p,p'*-Dichlorodiphenyldiazomethane could be successfully prepared in a pure crystalline state for the first time by the base catalyzed oxidation of *p,p'*-dichlorobenzophenone hydrazone with yellow mercuric oxide at lower temperature, (11), a method which was also adopted for the preparation of the dimethyl and dimethoxy derivatives.

It is assumed that the direct formation of the cyclic ethers by the interaction of the haloquinones with the hydrazones, in contrast to benzophenone hydrazone itself, takes place through dehydrogenation of the latter by the high potential quinone producing the corresponding diazoalkane. This diazoalkane reacts further with another molecule of the quinone yielding the product together with the corresponding tetrahalocatechol as shown in Scheme "A". In the case of di-*p*-anisilyldiazomethane, the cyclic ether formation is enhanced by the presence of the strong electron donating methoxyl groups which increase the electron density on the diazocarbon. In contrast, the electron withdrawing chlorine atom has a retarding effect and a more pronounced ketazine formation takes place. Similar substituents effects have been observed by Hancock *et al.*, (13) during their studies on the kinetics of the reaction of benzoic acid with diphenyldiazomethane. They found that the rate of ester formation is markedly increased in the case of dianisilyldiazomethane, whereas

it is very small in the case of the dichloro derivative.

It is also observed that the reaction of the foregoing dioxoles with nucleophilic reagents is mainly dependent on the nature of substituents on the diphenylmethane residue. Thus, it is found that the dioxole ring in the dimethoxy derivative (IIIc) is cleaved with unusual ease by these reagents whereas the unsubstituted (IIIg) and the dichloro (IIIa) compounds, behave normally (14), and resist cleavage under similar conditions. Compound IIIc undergoes reductive cleavage by lithium aluminum hydride under very mild conditions giving di-*p*-anisylmethane and tetrachlorocatechol in excellent yield. It is readily hydrolyzed by dilute mineral acids to give *p,p'*-dimethoxybenzophenone. In these respects IIIc behaves like the xanthenic compounds (II) (15) and it is assumed that the reaction proceeds through the formation of a carbonium ion intermediate as a result of the initial attack of a positive ion such as Li^+ or AlH_2^+ in the case of reductive cleavage, or H^+ in the case of acid hydrolysis (*cf.* IV). The carbonium ion is stabilized by resonance with the *p*-methoxyphenyl residue involving an unshared electron pair on the oxygen of the methoxyl group, thus facilitating cleavage.

Compound IIIc reacts readily with hydrazones in absolute ethanol to give the corresponding dimethoxybenzophenone hydrazones through cleavage of the dioxole ring and the formation of an open chain ether as an intermediate (*cf.* Scheme "B" in the case of benzoyl hydrazine) which gives the hydrazone through a β -elimination process (*cf.* 16). In the case of the reaction with hydrazine hydrate, dimethoxybenzophenone azine is produced. This is possibly due to the interaction between the first formed hydrazone and another molecule of IIIc. This view is supported by the fact that the azine is obtained in excellent yield when *p,p'*-dimethoxybenzophenone hydrazone is allowed to react with IIIc. In the case of phenyl and benzoyl hydrazine, dimethoxybenzophenone phenyl and benzoyl hydrazones are produced, respectively. Compound IIIc is also found to be quite reactive toward cleavage by malononitrile affording the unsaturated dinitrile (VII). In this connection it might be assumed that the methylene ether is a resonance hybrid of various structures (*cf.* VIII) and cleavage proceeds through the nucleophilic attack of the active hydrogen compound.



The ease of cleavage of IIIc may be due to the fact that the carbonium ion is stabilized by resonance with the unshared electron pair on the oxygen of the methoxy

TABLE I

Ketohydrazone	<i>o</i> -Benzoquinone derivative	Product	M.P. °C	Formula	Calcd.	Found (c)
<i>p,p'</i> -Dichlorobenzophenone	Tetrachloro-	IIIa	174° (b)	C ₁₉ H ₈ Cl ₆ O ₂	C, 47.40; H, 1.66; Cl, 44.28.	C, 47.85; H, 1.45; Cl, 43.9.
<i>p,p'</i> -Dichlorobenzophenone	Tetrabromo-	III d	172° (b)	C ₁₉ H ₈ Br ₄ Cl ₂ O ₂	C, 34.59; H, 1.21; Br-Cl, 59.33.	C, 34.51; H, 1.40; Br-Cl, 58.38.
<i>p,p'</i> -Dimethylbenzophenone	Tetrachloro-	IIIb	142°	C ₂₁ H ₁₄ Cl ₄ O ₂	C, 57.27 H, 3.18; Cl, 32.27.	C, 57.29; H, 3.21; Cl, 32.14.
<i>p,p'</i> -Dimethylbenzophenone	Tetrabromo-	IIIe	170°	C ₂₁ H ₁₄ Br ₄ O ₂	C, 40.77; H, 2.26; Br, 51.77.	C, 41.37; H, 2.29; Br, 50.88.
<i>p,p'</i> -Dimethoxybenzophenone	Tetrachloro-	IIIc	216° (a)	C ₂₁ H ₁₄ Cl ₄ O ₄	C, 53.38; H, 2.96; Cl, 30.08.	C, 54.22; H, 3.17; Cl, 29.42.
<i>p,p'</i> -Dimethoxybenzophenone	Tetrabromo-	III f	220°	C ₂₁ H ₁₄ Br ₄ O ₄	C, 38.76; H, 2.15; Br, 49.23.	C, 39.30; H, 2.14; Br, 48.70.

(a) Schonberg and Frese gave m.p. 217-219° (19). (b) M.p. undepressed when admixed with authentic sample (5). (c) In some cases, slightly higher carbon values are found, probably due to difficulties in analyzing these relatively unstable polyhalo-compounds.

TABLE II

Diazomethane Derivative	<i>o</i> -Benzoquinone Derivative	Product
di- <i>p</i> -tolyl	tetrachloro-	IIIb
di- <i>p</i> -tolyl	tetrabromo-	IIIe
di- <i>p</i> -anisyl	tetrachloro-	IIIc
di- <i>p</i> -anisyl	tetrabromo-	III f
di- <i>p</i> -chlorophenyl	tetrachloro-	IIIa
di- <i>p</i> -chlorophenyl	tetrabromo-	III d

group. In the case of the dimethyl derivative (IIIb), resonance stabilization is less pronounced and accordingly cleavage takes place less readily.

Authentic *p,p'*-dimethoxydiphenylmethylenemalonitrile (VII) is prepared, in excellent yield, by condensing *p,p'*-dimethoxythiobenzophenone with malonitrile. *p,p'*-Dimethoxydiphenylmethane is prepared by the reaction of the ketone with lithium aluminum hydride in an ether-benzene mixture. The reduction proceeds smoothly within a few hours and does not require such drastic conditions as have been described previously (17).

EXPERIMENTAL (18)

Reaction of Ketohydrazone with Tetrachloro- and Tetrabromo-*o*-benzoquinone. General Procedure.

The hydrazone (0.01 mole) was added portionwise to the solution of the quinone (0.02 mole) in dry ether. A vigorous reaction took place after each addition. When all the hydrazone had been added, the reaction mixture was slightly warmed for a few minutes on the water bath and left to cool. The separated crystalline product was filtered off and washed with ether. The solid obtained was extracted with warm acetone and the extract was concentrated and left to cool to give the ketazine (in the case of *p,p'*-dimethoxybenzophenone hydrazone, no azine was isolated). The residue which remained after acetone extraction was recrystallized from the same solvent to give the benzodioxoles as colorless crystals.

The main ethereal mother liquor was evaporated to dryness under reduced pressure, and the residue was extracted with methanol. The alcoholic extract was poured onto ice-cold water and acidified with dilute hydrochloric acid. The white precipitate obtained was filtered off, washed with water, dried, dissolved in acetic anhydride (10 ml.), and refluxed for 30 minutes. The

reaction mixture was left to cool, poured onto ice and left overnight. The separated solid was filtered off, and recrystallized from methanol to give the diacetate of the tetrahalocatechol. Data for the benzodioxoles obtained are shown in Table I.

Action of Diazoalkanes on Tetrachloro- and Tetrabromo-*o*-benzoquinone. General Procedure.

The quinone (0.01 mole) was added in portions to a dry ethereal solution of the diazoalkane (0.015 mole). A virgous reaction with evolution of gas occurred after each addition. When all the quinone had been added, the reaction mixture was left for 30 minutes at room temperature when a crystalline solid separated out. This was filtered off, washed with ether and recrystallized from acetone. The methylenedioxy derivatives IIIb, IIIe, IIIc, IIIf, IIIa, and IIId were obtained as colorless crystals in almost quantitative yields. Results of the experiments are shown in Table II.

Preparation of bis-(*p*-chlorophenyldiazomethane)

p,p'-Dichlorobenzophenone hydrazone (4 g.), yellow mercuric oxide (7 g.), and anhydrous sodium sulphate (1 g.) were ground together in a dry mortar and transferred to a dry 100 ml. round bottom flask containing 50 ml. dry ether. One milliliter of a freshly prepared saturated solution of potassium hydroxide in absolute ethanol was added while shaking the mixture for two minutes. The mixture was then stirred for an additional 30 minutes at room temperature. The violet ethereal solution was filtered off and the residue was washed with dry ether. The combined ethereal solutions were concentrated under reduced pressure in the cold, when crystals of the diazo compound separated out. These were recrystallized from petroleum ether (40-60°) in violet crystals, m.p. 106°.

Anal. Calcd. for $C_{13}H_8Cl_2N_2$: C, 59.31; H, 3.04; Cl, 26.90; N, 10.75. Found: C, 59.58; H, 3.18; Cl, 26.42; N, 10.79.

Hydrolysis of IIIc.

To a suspension of IIIc (0.5 g.) in dioxane (5 ml.), concentrated hydrochloric acid (1 ml.) was added and the reaction mixture was refluxed for three hours, left to cool and then poured onto ice. The precipitate was filtered off, washed with water, dried, extracted with cold methanol and the extract was concentrated and cooled. The separated crystals were filtered off, dissolved in acetic anhydride (20 ml.), refluxed for 30 minutes, left to cool and poured onto ice. The solid separated was recrystallized from methanol and proved to be the diacetate of tetrachlorocatechol (m.p. and mixed m.p.). The residue left after extraction with methanol was recrystallized from the same solvent to give *p,p'*-dimethoxybenzophenone.

Preparation of *p,p'*-Dimethoxydiphenylmethane.

A solution of *p,p'*-dimethoxybenzophenone (2 g.) in dry benzene (25 ml.) was added dropwise to a suspension of lithium aluminum hydride (2 g.) in dry ether (50 ml.). When all the solution had been added, the reaction mixture was refluxed for six hours on the water bath, and left to cool. It was decomposed with alcohol, then with dilute hydrochloric acid, and extracted repeatedly with ether. The combined ethereal extracts were washed with water, dried over anhydrous sodium sulfate, and the ethereal solution was concentrated to a small bulk. The separated solid was recrystallized from petroleum ether (40-60°) to give *p,p'*-dimethoxydiphenylmethane as colorless crystals, m.p. 48-50° (17); yield 1.4 g.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.58; H, 7.03.

Reaction of IIIc with Lithium Aluminum Hydride.

The reaction was carried out as described above using two grams of IIIc. After decomposing the reaction mixture with alcohol and hydrochloric acid, it was extracted with ether. The ethereal extract was dried over anhydrous sodium sulfate, concentrated and left to cool. The separated solid was filtered off and recrystallized from petroleum ether (40-60°) to give *p,p'*-dimethoxydiphenylmethane, yield 0.6 g.

The ethereal mother liquor was evaporated to dryness, extracted with methanol and the extract poured onto ice and acidified with hydrochloric acid. The solid separated was dried and added to acetic anhydride and the mixture refluxed for 30 minutes, then poured onto ice. The solid which separated was recrystallized from methanol and proved to be the diacetate of tetrachlorocatechol (m.p. and mixed m.p.).

Preparation of *p,p'*-Dimethoxydiphenylmethylene Malononitrile (VII).

A mixture of *p,p'*-dimethoxythiobenzophenone (1 g.), malononitrile (1 g.) and yellow mercuric oxide (1 g.) in absolute alcohol (20 ml.) was refluxed for six hours in a nitrogen atmosphere. The solution was filtered while hot and left to cool. The separated yellow crystalline product was filtered off and recrystallized from acetone to give VII as straw yellow crystals, m.p. 152-154°, yield 1.1 g.

Anal. Calcd. for $C_{18}H_{14}N_2O_2$: C, 74.48; H, 4.86; N, 9.65. Found: C, 74.32; H, 4.97; N, 9.85.

Reaction of IIIc with Malononitrile.

A mixture of IIIc (2 g.) and malononitrile (1 g.) in *n*-butyl alcohol (10 ml.) was heated under reflux for 6 hours. The solution was filtered while hot and left to cool. The separated product was filtered off, recrystallized from acetone to give VII, yield (0.9 g.). Tetrachlorocatechol, identified as its diacetate, was isolated from the mother liquor as described before.

Reaction of IIIc with Hydrazine Hydrate.

To a suspension of IIIc (1 g.) in *n*-butyl alcohol (10 ml.), 0.5 ml. of hydrazine hydrate (99-100%) was added and the reaction mixture refluxed for 6 hours. The solution was filtered hot, concentrated and cooled. The separated solid was filtered off and recrystallized from acetone to give *p,p'*-dimethoxybenzophenone azine, m.p. 182° (undepressed when admixed with an authentic sample) (20). Tetrachlorocatechol was isolated from the mother liquor as described before.

Preparation of *p,p'*-Dimethoxybenzophenone Benzoylhydrazone.

A mixture of *p,p'*-dimethoxybenzophenone (1.2 g.) and benzoylhydrazine (0.6 g.) was heated at 170° for 3 hours. The reaction mixture was cooled and extracted with boiling methanol. The extract was concentrated and cooled. The separated product was filtered off and recrystallized from methanol as colorless crystals, m.p. 193-195°, yield 0.65 g.

Anal. Calcd. for $C_{22}H_{20}O_3N_2$: C, 73.31; H, 5.59; N, 7.77. Found: C, 73.65; H, 5.60; N, 7.14.

Reaction of IIIc with Benzoylhydrazine.

The reaction was carried out as in the case of hydrazine hydrate using 2 g. of the cyclic ether and 1 g. of the hydrazine. The reaction mixture was filtered hot, concentrated and a crystalline product separated out when cooled. It was filtered off, extracted with warm methanol and the extract was concentrated and left to cool. The straw yellow crystals separated proved to be *p,p'*-

dimethoxybenzophenone azine (0.2 g.). The alcohol insoluble residue was dissolved in the least amount of boiling methanol and left to cool. The colorless crystals separated, (1.2 g.) proved to be benzophenone benzoylhydrazone (m.p. and mixed m.p.). Tetrachlorocatechol, identified as its diacetate, was isolated from the mother liquor as described above.

Reaction of IIIc with Phenylhydrazine.

The reaction was carried out as before and after hot filtration, concentration and cooling, dimethoxybenzophenone phenylhydrazone was obtained as colorless crystals m.p. 115-116° (undepressed when admixed with an authentic sample prepared by fusing *p,p'*-dimethoxybenzophenone with phenylhydrazine at 150° for three hours). Schnackenberg and Scholl (21) reported m.p. 123-124°.

Anal. Calcd. for C₂₁H₂₀N₂O₂: C, 75.88; H, 6.07; N, 8.43. Found: C, 76.14; H, 6.01; N, 8.80.

Tetrachlorocatechol, identified as its diacetate, was isolated from the mother liquor as described above.

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- (10) It is known that diazoalkanes react with *o*-quinones to give either methylenedioxy compounds or ethylene oxides (12a). Infrared spectra of the product obtained do not show absorption characteristic of the CO group, thus excluding ethylene oxide structure. Diazomethane and diphenyldiazomethane react with tetrachloro-*o*-quinone to give methylenedioxy compounds (12b).
- (11) This diazo compound has been usually used without recrystallization and no analytical data were given to assess its purity (13).
- (12a) cf. B. Eistert in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, 1948, p. 513.
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