Because of the relatively low amount of dipentene formed (approximately 2%) quantities of *cis*- and *trans*-ocimene can be prepared as described and can be distilled pure. (See Fig. 1 for a comparison of the vapor phase chromatographic curves of the dehydration and pyrolysis.)

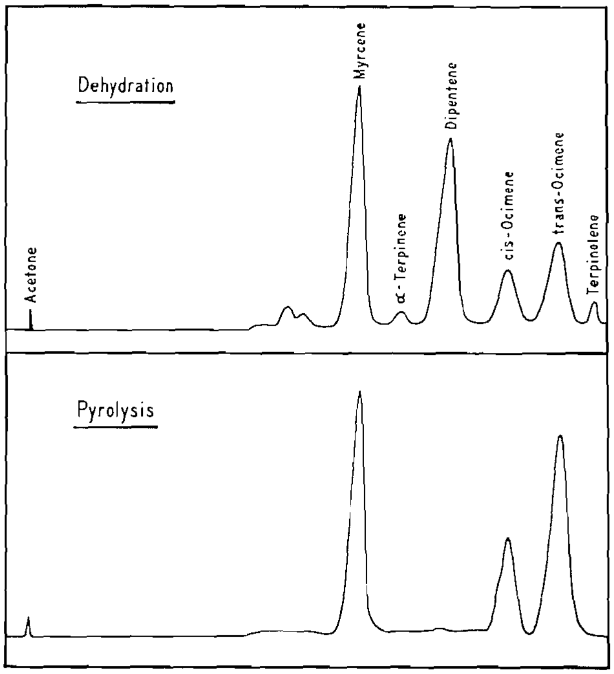

FIG. 1. Gas–liquid chromatographic comparison of the elimination reactions.

Dehydration of Linalool

A mixture of 175 g $KHSO_4$ (analytical grade) and 3 000 g linalool (99% pure as indicated by vapor phase chromatography) was heated and stirred at 128–160 °C liquid temperature, under a vacuum of 150 mm Hg, in a flask fitted with a thermometer, stirrer, and 6 inch distillation column. In this manner, 2 715 g of oil and 278 g of water were collected. The oil was fractionated via a 28 inch P.P. column; the ocimene-rich section, b.p. 70–72 °C at 60 mm Hg, n_D^{20} 1.478, amounted to 773 g and had the analysis shown in Table I.

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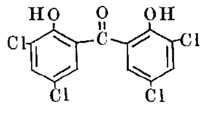
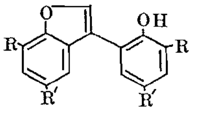
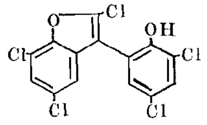
SYNTHESIS OF CHLORINATED 2-(3-BENZOFURANYL)PHENOLS

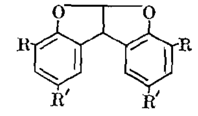
E. C. M. COXWORTH

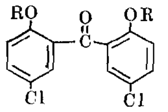
An interest in *o*-hydroxybenzophenones prompted us to repeat the reaction of β,β-dichloro-α,α-bis(3,5-dichloro-2-hydroxyphenyl)ethane with potassium hydroxide in refluxing methanol, which was reported by Riemschneider and his co-workers (1) to yield 2,2′-dihydroxy-3,3′,5,5′-tetrachlorobenzophenone (I). The product we obtained (A) conformed with that of Riemschneider with respect to melting point and the melting points of its acetate and its methyl ether. However, the analytical and spectroscopic data led us to conclude that the product A is actually 2-(5,7-dichloro-3-benzofuranyl)-4,6-dichlorophenol (II*a*).

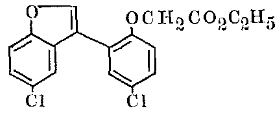

I


II*a* R=R′=Cl
II*b* R=H, R′=Cl


III


IV*a* R=R′=Cl
IV*b* R=H, R′=Cl


V*a* R=$CH_2CO_2C_2H_5$
V*b* R=CH_2CO_2H


VI

The following evidence led us to the conclusion that A has structure II*a* and not structure I.

(*i*) The analytical data for the experimental product A and its acetate and methyl ether are in good agreement with those for II*a* and its derivatives; they do not agree with those for I and its derivatives. Riemschneider and his co-workers (1) found a percentage chlorine for A close to the calculated value for I, but since II*a* has a similar percentage chlorine, this analytical data will not distinguish between the two structures.

(*ii*) The nuclear magnetic resonance spectrum of the acetate of A had peaks at 7.89 τ (singlet, 3H), 2.61 τ (doublet, 2H), 2.49 τ (triplet, 2H), and 2.22 τ (singlet, 1H). On the basis of the acetate of structure II*a* these peaks may be assigned, respectively, to an acetate CH_3, benzene H's, benzene H's, and the H on the α-carbon of the furan ring. The diacetate of structure I would be expected to show peaks for six acetate H's and four benzene H's, and no other peaks.

(*iii*) The ultraviolet spectrum of A showed λ_{max} 296, 287, and 253 mμ, but there was no absorption in the region 325–450 mμ where *o*-hydroxybenzophenones have been reported (2) to show a strong absorption maximum. In corroboration of this, a sample of 5,5′-dichloro-2,2′-dihydroxybenzophenone (3) had λ_{max} 344, 259, and 223 mμ. (Attempts to synthesize 2,2′-dihydroxy-3,3′,5,5′-tetrachlorobenzophenone by the unambiguous route (3) used to synthesize 5,5′-dichloro-2,2′-dihydroxybenzophenone were not successful.)

(*iv*) The infrared spectrum of A had absorption bands at 1 610 and 1 582 cm^{-1} but only of medium intensity, and a sharp band in the OH stretching region at 3 500 cm^{-1} suggestive of an unchelated phenolic hydroxyl group. In contrast, 5,5′-dichloro-2,2′-dihydroxybenzophenone had an intense, broad band at 1 630 – 1 615 cm^{-1} (both the position and intensity being typical of chelated *o*-hydroxyphenyl ketones (4)), and a broad hydroxyl peak at 3 340 cm^{-1}.

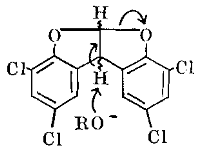
When the literature was now checked for references concerning the synthesis of 2-(3-benzofuranyl)phenols, it was found that Riemschneider and Lange (5) had reported recently that treatment of α,α-bis(3,5-dichloro-2-hydroxyphenyl)-β,β,β-trichloroethane with refluxing aqueous potassium hydroxide gave the potassium salt of 4,6-dichloro-2-(2,5,7-trichloro-3-benzofuranyl)phenol (III). However, in their report, no mention was made of previous reactions of this kind.

One other relevant synthesis of 2-(3-benzofuranyl)phenols was noted. Dischendorfer (6) had reported that treatment of the inner acetal of bis(2-hydroxy-1-naphthyl)acetaldehyde with hot alcoholic sodium hydroxide, or with acetic acid containing hydrochloric acid, gave 4-(2-hydroxy-1-naphthyl)naphtho[2′,1′,2,3]furan. Now, in the original paper which prompted our investigation, Riemschneider (1) had reported that the phenolic product A mentioned previously could also be obtained by treatment of the inner acetal of bis(3,5-dichloro-2-hydroxyphenyl)acetaldehyde (IV*a*) with either hot alcoholic potassium hydroxide or hot 10% sulfuric acid. Our proposal that the phenolic product A has the structure II*a* thus makes the reactions of the acetal IV*a* with acid or base analogous to the reactions described by Dischendorfer (6). The inner acetal IV*a* was obtained by treating β,β-dichloro-α,α-bis(3,5-dichloro-2-hydroxyphenyl)ethane with cold alcoholic potassium hydroxide (1). The acetal may thus be considered a possible intermediate in the reaction of this dichloroethane compound with hot alcoholic potassium hydroxide, which leads directly to II*a*.

Since II*a* could not be prepared by the unambiguous route of Moshfegh *et al.* (3), it was of interest to determine the effect of hot alcoholic potassium hydroxide on the known acetal IV*b* (1), since the product from this reaction could be compared directly with the available 5,5′-dichloro-2,2′-dihydroxybenzophenone. The benzophenone was not obtained from this reaction; the product (B) which was obtained is considered to be the benzofuranyl phenol II*b*, on the basis of analytical and spectroscopic data (see Experimental section). The structure of II*b* was proven by the independent synthesis of the carbethoxymethyl ether in the following fashion, the method of approach being modelled on the work of Johnson and Robertson (7):

The reaction of 5,5′-dichloro-2,2′-dihydroxybenzophenone (3) with ethyl bromoacetate gave the diester V*a*, which was converted readily into the diacid V*b*. Ring closure of V*b* was effected by heating the diacid in acetic anhydride containing sodium acetate. The crude product from the ring closure, apparently a mixture of anhydride and acid (ν 1 850 and 1 780 cm^{-1}, with a prominent shoulder at 1 750 cm^{-1}), was converted directly into the desired ethyl ester by refluxing in ethylene chloride containing ethanol and a trace of toluenesulfonic acid. The ethyl ester VI so obtained was identical (by mixed melting point and infrared spectrum) with the product obtained by treating the experimental product B with ethyl bromoacetate.

The reactions of acetals such as IV*a* with acids to yield enol ethers, of which II*a* would be a special type, are well known (10). However, the reactions of acetals with bases, as exemplified by the transformation IV*a* → II*a* (as the potassium salt), seems more unusual, since acetals are generally considered not to react with bases. Some ethers have been reported to undergo E2-type elimination reactions in the presence of strong bases such as NaPh in aprotic solvents (11), but the types of base and solvent are quite different from the reagents employed in the reactions under consideration here. It is suggested that a possible mechanism for these base–acetal reactions is a normal E2 elimination process, which would be favored in this type of acetal by the following characteristics: the considerable acidity of the β-hydrogen, the stabilization of the incipient double bond by the benzofuran system being formed, the ease of accommodation of the negative charge on the leaving phenoxide ion, and the favorable geometry. By analogy to the physostigmine ring system (12), the ring fusion between the two dihydrofuran rings in acetals such as IV*a* is probably *cis*. Thus the β-hydrogen and the acetal oxygen would be in a *trans* relationship to each other, favorable for an E2 elimination to occur.



Further work on the reaction of these types of acetals with base is in progress. This will include attempts to distinguish between the E2 elimination process and the alternative E1*cb* process.

EXPERIMENTAL

The infrared spectra were all recorded as Nujol mulls. The ultraviolet spectra were measured in methanol. The nuclear magnetic resonance spectra were all taken in carbon tetrachloride, with tetramethylsilane as internal standard. Melting points are uncorrected.

Reaction of β,β-Dichloro-α,α-bis(3,5-dichloro-2-hydroxyphenyl)ethane with Potassium Hydroxide in Refluxing Methanol

This reaction was carried out as described by the previous authors (1). The product obtained (A) had m.p. 185–187° (reported (1) m.p. 185–186°).

Anal. Calcd. for $C_{13}H_6Cl_4O_3$ (I): C, 44.40; H, 1.72. Calcd. for $C_{14}H_6Cl_4O_2$ (II*a*): C, 48.31; H, 1.73. Found: C, 48.16; H, 1.83.

The acetate of A had m.p. 128.5–130.5° (reported (1) m.p. 126°).

Anal. Calcd. for $C_{17}H_{10}Cl_4O_5$ (diacetate of I): C, 46.9; H, 2.31; mol. wt. 436. Calcd. for $C_{16}H_8Cl_4O_3$ (acetate of II*a*): C, 49.26; H, 2.06; mol. wt. 390. Found: C, 49.37; H, 2.21; mol. wt. 402.

The methyl ether of A had m.p. 107.5–108.5° (reported (1) m.p. 107°).

Anal. Calcd. for $C_{15}H_{10}Cl_4O_3$ (dimethyl ether of I): C, 47.4; H, 2.65. Calcd. for $C_{15}H_8Cl_4O_2$ (methyl ether of II*a*): C, 49.8, H, 2.22. Found: C, 49.6; H, 2.40.

The nuclear magnetic resonance spectrum of the methyl ether of A showed peaks at 6.40 τ (singlet, 3H), 2.57 τ (multiplet, 3H), 2.41 τ (doublet, 1H), and 1.97 τ (singlet, 1H). On the basis of the methyl ether of II*a*, these peaks were assigned, respectively, to a methoxy CH_3, benzene H's, a benzene H, and the H on the α-carbon of the furan ring.

Reaction of the Inner Acetal IVb with Potassium Hydroxide (Preparation of B)

The inner acetal IV*b* was prepared as described by previous authors (1). The acetal (0.584 g) in ethylene glycol (9.0 g) containing potassium hydroxide (1 g) was heated at 100–115° for 3 h with occasional swirling. The resultant clear yellow solution was cooled and diluted with water (30 ml), and the solution was filtered. The filtrate was acidified with hydrochloric acid and the resultant oil extracted with benzene. The benzene solution was washed three times with water, and then film evaporated to remove benzene and moisture. The residue was a viscous oil (0.586 g) that crystallized to a product of m.p. 80–92°. Recrystallization from *n*-hexane gave prisms, m.p. 89–91°, but further crystallizations from *n*-hexane gave needles, m.p. 109.5–110° (B). The compound had the following ultraviolet spectrum: λ_{max} 293 (ε 8 200), 285 (ε 7 400), 260 (ε 12 800), 254 (ε 15 000), 248 (ε 14 950), and 242 mμ (ε 15 800); λ_{min} 289 (ε 6 900), 278 (ε 6 490), 259 (ε 12 300), 252 (ε 13 800), and 246 mμ (ε 14 000). The general shape of this spectrum was similar to that of the spectrum of II*a*. The infrared spectrum showed peaks at 1 619, 1 600, 1 580, and 3 520 cm^{-1}, all of medium intensity.

Anal. Calcd. for $C_{14}H_8O_2Cl_2$ (II*b*): C, 60.23; H, 2.88. Found: C, 60.46; H, 3.13.

The acetate was prepared by refluxing product B for 3 h in acetic anhydride containing sodium acetate. The acetate of B had m.p. 119–120°; the nuclear magnetic resonance spectrum of the acetate had peaks at 8.04 τ (singlet, 3H), 2.41–2.98 τ (multiplet, 6H), and 2.31 τ (singlet, 1H), assigned, respectively, on the basis of the acetate of II*b*, to an acetate CH_3, benzene H's, and the H on the α-carbon of the furan ring.

Anal. Calcd. for $C_{16}H_{10}O_3Cl_2$ (acetate of II*b*): C, 59.8; H, 3.14. Found: C, 59.6; H, 3.16.

The carbethoxymethyl ether of B was prepared by the same method as was used to prepare V*a*. The product had m.p. 132–133°, mixed m.p. with authentic VI 131.5–133.5°. The infrared spectrum was identical with that of VI.

5,5′-Dichloro-2,2′-dihydroxybenzophenone

The procedures and relative molar quantities of reagents that were used were according to the method of Moshfegh *et al.* (3). However, the methyl ether was used instead of the ethyl ether as a protecting group. Thus, 5,5′-dichloro-2,2′-dihydroxydiphenylmethane was converted into 5,5′-dichloro-2,2′-dimethoxydiphenylmethane (8), which was oxidized to 5,5′-dichloro-2,2′-dimethoxybenzophenone (9). The dimethoxybenzophenone was demethylated to give the desired 5,5′-dichloro-2,2′-dihydroxybenzophenone, m.p. 151.5–153.5° (reported (2) m.p. 152–155°); λ_{max} 344, 259, and 223 mμ; λ_{min} 290 and 245 mμ.

5,5′-Dichloro-2,2′-dihydroxybenzophenone, Bis(carbethoxymethyl Ether) (Va)

In 100 ml dry acetone were placed 5,5′-dichloro-2,2′-dihydroxybenzophenone (2.69 g, 0.0095 mole), ethyl bromoacetate (5.0 g, 0.030 mole), and freshly ground anhydrous potassium carbonate (8.3 g, 0.060 mole). The mixture was refluxed, with the exclusion of atmospheric moisture, for 5 h. The reaction mixture was cooled and filtered, and the filtrate was film evaporated to remove the acetone. The residue from the film evaporation was dissolved in diethyl ether (40 ml) and filtered to remove the insoluble material; the insoluble material was washed with diethyl ether (10 ml). The combined filtrates were film evaporated to remove the solvents. The gummy residue from the film evaporation was stirred with *n*-hexane (20 ml) to yield a white solid, which was removed by filtration, washed with *n*-hexane, and dried to yield 3.14 g (73.5%) of V*a*, m.p. 86.5–87.5°. Recrystallization from *n*-hexane gave colorless plates, m.p. 88.5–89.5°, ν 1 770 and 1 675 cm^{-1}.

Anal. Calcd. for $C_{21}H_{20}Cl_2O_7$: C, 55.39; H, 4.42. Found: C, 55.30; H, 4.47.

5,5′-Dichloro-2,2′-dihydroxybenzophenone, Bis(carboxymethyl Ether) (Vb)

The diester V*a* (2.63 g, 0.0058 mole) was refluxed for 45 min in a mixture of ethanol (100 ml) and water (70 ml) containing potassium hydroxide (4.5 g). The solution was then film evaporated to remove most of the ethanol. After removal of the ethanol the solution was cooled, filtered, and extracted once with diethyl ether. The aqueous layer was then acidified with dilute hydrochloric acid to precipitate the product as a white solid. The product was removed by filtration, washed with water, and dried to yield 2.14 g (93%) of V*b*, m.p. 217–218°, ν 1 752 (intense shoulder at 1 729) and 1 684 cm^{-1}. Recrystallization from ethanol–water gave material of m.p. 218–221°.

Anal. Calcd. for $C_{17}H_{12}Cl_2O_7$: C, 51.14; H, 3.03. Found (crude product): C, 51.34; H, 3.37.

Ring Closure of Vb and Preparation of 2-(5-Chloro-3-benzofuranyl)-4-chlorophenol Carbethoxymethyl Ether (VI)

The diacid V*b* (2.03 g, 0.0051 mole), acetic anhydride (20 ml), and fused sodium acetate (5.0 g) were mixed, and the mixture was then refluxed (bath temperature 150–155°) for 50 min. After the reaction mixture was cooled, it was poured into water (200 ml) and stirred for 2 h. The white precipitate so formed was removed by filtration, washed with water, and dried. This material (1.86 g) had m.p. 85–98°; ν 1 850 and 1 780 (anhydride) with a prominent shoulder at 1 750 (acid), and 1 619 and 1 576 cm^{-1}, no bands between 1 750 – 1 620 cm^{-1}. The product was partially soluble in dilute sodium hydroxide.

The crude product (0.45 g) was dissolved in ethylene dichloride (10 ml) containing ethanol (1.3 ml) and toluenesulfonic acid (30 mg), and the solution refluxed for 6 h. The solution was cooled, diluted with chloroform, washed with water and then sodium bicarbonate, and dried over sodium sulfate. Film evaporation left a crystalline product, 0.41 g, m.p. 125–131°. Recrystallization from *n*-hexane gave VI, m.p. 132–133°; ν 1 759, 1 618, and 1 572 cm^{-1}.

Anal. Calcd. for $C_{18}H_{14}Cl_2O_4$ (VI): C, 59.19; H, 3.86. Found: C, 58.96; H, 3.98.

ACKNOWLEDGMENTS

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