

Complex Dibenzofurans

I. Dehydration of Polyhydroxy-*p*-terphenyls

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The synthesis of a series of polymethoxy-*p*-terphenyls, all containing methoxyl groups in the 2,2',5',2'-positions, is described. The series was suitable for a study of the structural requirements for facile acid catalysed dehydration of 2,2'-dihydroxydiphenyl derivatives with formation of dibenzofurans. A brief discussion of the dehydration experiments is presented.

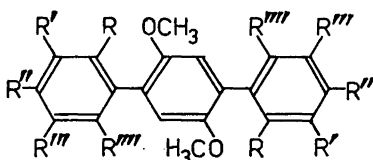
During the course of our studies on the acid catalysed polymerisation of quinones crystalline dioxidoterphenyls of still incompletely known structure were obtained in addition to large amounts of amorphous products^{1,2}, which presumably also contain dibenzofuran units. The mechanism of the formation of the trimeric and polymeric reaction products is not known, but the simplest assumption is that they are formed by dehydration of polyphenolic intermediates.

Several examples of acid catalysed dehydration of hydroxydiphenyls are known. The conversion of *o,o'*-dihydroxydiphenyl to dibenzofuran does not proceed smoothly and heating with zinc chloride is needed³. Some substituted *o,o'*-dihydroxylated diphenyls are, however, more easily dehydrated. This dehydration is frequently a source of complication when di- or polyphenol methyl ethers are demethylated with hydrobromic or hydriodic acid. Thus 2,4,2',4'-tetramethoxydiphenyl⁴ easily yields the corresponding dibenzofuran derivative and analogous reactions are reported for 2,4,2',6'-tetramethoxydiphenyl⁵, 4-methyl-2,6,2',4'-tetramethoxydiphenyl⁶, 2,2'-dimethyl-4,6,4',6'-tetramethoxydiphenyl⁷, diphenylhexamethyl ether⁸, 2,4,5,2',4',5'-hexamethoxydiphenyl⁹ and 2,5,2',5'-tetrahydroxy-4,4'-dimethoxydiphenyl¹⁰.

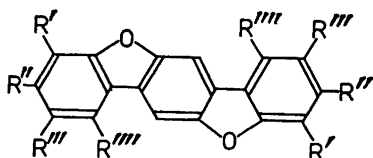
Dehydrations, effected under relatively mild conditions, are of obvious interest in relation to the formation of dibenzofuran derivatives in the acid polymerisation of *p*-benzoquinones. Apart from the above mentioned diresorcinol derivatives comparatively little (*cf.* Refs.^{2,11} dealing with hydroquinones) is known about the ease with which *o,o'*-hydroxylated di- or polyphenols undergo transformation into dibenzofurans and as a consequence this investigation was undertaken.

An ideal series of compounds for a study of the dehydration reaction would be substituted anisols, containing in the *ortho* position a 2-methoxy-, a 2,3-dimethoxy- or a 2,4-dimethoxyphenyl group, *etc.* Some unsymmetrical polymethoxydiphenyls of this type have been prepared, but they are not easily synthesised.

Our earlier experience in the transformation of trihydroquinone hexamethyl ether (III) to the dioxido-*p*-terphenyl VIIa² made the series of 2,5-disubstituted hydroquinone dimethyl ethers I–V attractive for a comparative study, especially because terphenyl derivatives are formed during the polymerisation of *p*-benzoquinones. Compounds of this type are easily prepared by the mixed Ullmann coupling of suitable mono- and diiodophenyl derivatives. The reaction products are readily separated by fractional distillation *in vacuo* followed by recrystallisation.



- I R = R' = OCH₃
 R'' = R''' = R'''' = H
 II R = R'' = OCH₃
 R' = R''' = R'''' = H
 III R = R''' = OCH₃
 R' = R'' = R'''' = H
 IV R = R'''' = OCH₃
 R' = R'' = R''' = H
 V R = R' = R'' = OCH₃
 R''' = R'''' = H



- VI R'' = OCH₃ (VIa: OH instead of OCH₃)
 R' = R''' = R'''' = H
 VII R''' = OCH₃ (VIIa: OH instead of OCH₃)
 R' = R'' = R'''' = H
 VIII R'''' = OCH₃ (VIIIa: OH instead of OCH₃)
 R' = R'' = R''' = H
 IX R' = R'' = R''' = R'''' = H

Coupling of 2,5-diiodohydroquinone dimethyl ether with 3-iodoveratrol yielded a mixture containing mainly 2,3,2',3'-tetramethoxydiphenyl and 2,3,2',5',2'',3''-hexamethoxy-*p*-terphenyl (I). Similarly 2,4,2',5',2'',4''-hexamethoxy-*p*-terphenyl (II), 2,6,2',5',2'',6''-hexamethoxy-*p*-terphenyl (IV) and 2,3,4,2',5',2'',3'',4''-octamethoxy-*p*-terphenyl (V) were synthesised employing 4-iodoresorcinol dimethyl ether, 2-iodoresorcinol dimethyl ether and 4-iodopyrogallol trimethyl ether, respectively. A ratio 1:8 of diiodohydroquinone dimethyl ether and monoiodocompound was generally used and the yields were about 40 % based on the diiodocompound. Some dehalogenation of the monoiodocompound with formation of the corresponding phenol ethers always occurred, but this is a common observation in Ullmann reactions.

With one exception the starting materials were prepared according to standard procedures as indicated in the experimental part. Kauffmann and Kieser¹² obtained 4-iodoresorcinol dimethyl ether in a rather poor yield by iodination of resorcinol dimethyl ether in alcoholic solution with iodine and mercuric oxide. Omission of the solvent raised the yield substantially (*cf.* the synthesis of 4-iodopyrogallol trimethyl ether¹⁰).

Pummerer *et al.*¹³ reported the synthesis of the diresorcylyl- and dipyrrogallylhydroquinones corresponding to II and V by condensing *p*-benzoquinone

with resorcinol and pyrogallol under acid conditions. The present author was, however, unable to confirm the results of Pummerer *et al.* On attempting to synthesise the diresorcylic derivative 2,4,2',5',2'',4''-hexahydroxy-*p*-terphenyl (demethylated II), according to Pummerer *et al.* an amorphous product, was obtained. Similar results were reported by Erdtman¹ who after methylation of this amorphous material succeeded in isolating a crystalline substance. This product was assumed to be 2,4,2',5',2'',4''-hexamethoxy-*p*-terphenyl (II), but it was not identical with compound II, obtained by the Ullmann reaction. It might perhaps be a diphenyl derivative; this problem, however, requires further investigation.

The formation of 2,4,2',5'-tetrahydroxydiphenyl by simply heating resorcinol with *p*-benzoquinone has been claimed by Pummerer *et al.*¹³ This reaction could not be reproduced either and in an attempt to repeat the synthesis of the dipyrogallylhydroquinone octaacetate (2,3,4,2',5',2'',3'',4''-octaacetoxy-*p*-terphenyl, corresponding to V), the present author obtained pyrogallol triacetate as the sole crystalline product. The m.p. of Pummerer's «octaacetate» was surprisingly low (158°). Pyrogallol triacetate melts at 165° and the slightly impure pyrogallol triacetate obtained from the reaction melted at about 160°. These results suggest that Pummerer's «octaacetate» was pyrogallol triacetate.

The dehydrations were studied in the following way. The methoxylated terphenyl was refluxed with an excess of constant boiling hydrobromic acid for three days. The phenol obtained was collected and methylated directly. The methylation product was either identical with the starting material or a substance of dioxidoterphenyl type with a high melting point and exhibiting strong fluorescence in ultra violet light.

In our earlier experiments² the trihydroquinone derivative III was converted into the corresponding dioxidoterphenyl VIIa (characterised as the dimethyl ether VII). It has now been found that the diresorcylic hydroquinone hexamethyl ethers II and IV are dehydrated to the dihydroxydioxido-*p*-terphenyls VIa and VIIIa (characterised as VI and VIII). The terphenyls I and V, containing veratrol- and pyrogallol trimethyl ether groupings, however, did not undergo ring closure.

The first step in these reactions is of course demethylation and it is interesting to note that the terphenyls II and IV, which show a pronounced aptitude for ring closure, are derivatives of *m*-dihydroxybenzene as are the diresorcinols. The latter also undergo facile dehydration as previously mentioned in this paper. Another interesting feature of these reactions is that a hydroxyl group in the 3 and 3''-positions does not facilitate the dehydration. Other cases of the same type are represented by, *e.g.*, 2,3,4,2',3',4'-hexahydroxydiphenyl¹⁴ and a tetrapyrogallol (with the diphenyl linkages in the *o*-positions to hydroxyl groups; Erdtman, unpublished results), both easily prepared by demethylation of the corresponding methyl ethers with hydrogen bromide. This problem will be the subject of a future communication.

Ullmann¹⁵ reported normal demethylation of 2,5,2',5'-tetramethoxydiphenyl, dihydroquinone dimethyl ether, with hydrobromic acid. According to our experience with trihydroquinone the 2,5,2',5'-tetrahydroxydiphenyl should undergo dehydration with formation of 2,8-dihydroxydibenzofuran.

A reinvestigation showed that dihydroquinone tetramethyl ether on prolonged refluxing with constant boiling hydrobromic acid gave 2,8-dihydroxydibenzofuran in good yield. This is also in accordance with the early findings of Nietzki *et al.*¹¹ on the dehydration of a dimethyldihydroquinone dimethyl ether, the structure of which was elucidated by Posternak *et al.*¹⁶, with concentrated hydrochloric acid.

Zinc dust distillation of the dioxido-*p*-terphenyl derivative VIa gave 2,2',5',2''-dioxido-*p*-terphenyl (IX) identical with the dioxido-*p*-terphenyl described by Schimmelschmidt¹⁷ (*cf.* Ref.²).

EXPERIMENTAL

All melting points are uncorrected

4-Iodoresorcinol dimethyl ether. Finely divided iodine (300 g) followed by freshly precipitated mercuric oxide (240 g) were added in small portions to resorcinol dimethyl ether (150 g) with vigorous stirring. Complete decolouration of the reaction mixture was awaited before each new addition of iodine. The exothermic reaction required about an hour. The hot reaction mixture was filtered with suction and the inorganic material thoroughly washed with ether. The ether was evaporated and the residue, a yellow oil, crystallised on scratching. The crude product (265 g, 92 % yield) was recrystallised from methanol. Yield 215 g, 81 %, m.p. 40–41° (lit.¹² m.p. 40°).

Ullmann reaction. General procedure. 2,5-Diiodohydroquinone dimethylether¹⁸ (3.9 g), copper bronze (35 g) and the monoiodocompound (3-iodoveratrol¹⁹, 4-iodoresorcinol dimethyl ether, 2-iodoresorcinol dimethyl ether²⁰, 21 g, or 4-iodopyrogallol trimethyl ether¹⁹, 25 g) were thoroughly mixed in a 300 ml flask and heated on a salt bath to 220–240°, when a vigorous reaction started which raised the temperature to about 300°. After some minutes the reaction mixture was allowed to cool and the organic products extracted with chloroform. The solvent was evaporated and the residue subjected to distillation *in vacuo*.

*2,3,2',5',2'',3''-Hexamethoxy-*p*-terphenyl (I).* The combined extracts from three runs yielded veratrol (3 g), 2,3,2',3'-tetramethoxydiphenyl (28 g) and a light brown thick syrup (7 g, b.p. about 300°, 0.4 mm), which crystallised on scratching with a few drops of methanol. The substance was recrystallised from *n*-butanol. M.p. 177–179°. (Found: C 69.9; H 6.5. Calc. for C₂₄H₂₆O₆: C 70.2; H 6.4.)

*2,4,2',5',2'',4''-Hexamethoxy-*p*-terphenyl (II).* The distillation *in vacuo* yielded a very small amount of resorcinol dimethyl ether, 2,4,2',4'-tetramethoxydiphenyl (8.5 g) and an oil (2.5 g, b.p. 215–265°, 1 mm), which crystallised on scratching with a few drops of methanol. The product was recrystallised from acetic anhydride and sublimed *in vacuo*. M.p. 207–209°. (Found: C 69.8; H 6.7. Calc. for C₂₄H₂₆O₆: C 70.2; H 6.4.)

*2,6,2',5',2'',6''-Hexamethoxy-*p*-terphenyl (IV).* The combined products from three runs yielded resorcinol dimethyl ether (5 g), 2,6,2',6'-tetramethoxydiphenyl (21 g) and a highboiling yellow oil (5.3 g, b.p. 240–300°, 1 mm), which crystallised on cooling. The terphenyl was recrystallised from a mixture of ligroin and benzene and was finally purified by sublimation *in vacuo*. M.p. 227–228°. (Found: C 70.0; H 6.5. Calc. for C₂₄H₂₆O₆: C 70.2; H 6.4.)

*2,3,4,2',5',2'',3'',4''-Octamethoxy-*p*-terphenyl (V).* The combined products from three runs yielded pyrogallol trimethyl ether (5 g), 2,3,4,2',3',4'-hexamethoxydiphenyl (31 g) and a dark yellow crystalline material (7 g, b.p. ca. 300°, 1 mm), which was recrystallised from ligroin. Colourless crystals, m.p. 171–172°. (Found: C 66.4; H 6.4. Calc. for C₂₈H₃₀O₈: C 66.4; H 6.4.)

Demethylation and dehydration. General procedure. The polymethoxy-*p*-terphenyl (ca. 500 mg) was refluxed with hydrobromic acid (48 %, 25 ml) in an atmosphere of carbon dioxide or nitrogen for three days. The reaction mixture was allowed to cool, diluted with water (100 ml) and filtered. The crude phenol was directly methylated in methanol suspension with an excess of dimethyl sulphate and sodium hydroxide.

4,4'-Dimethoxy-2,2',5',2"-dioxido-*p*-terphenyl (VI). 2,4,2',5',2",4"-Hexamethoxy-*p*-terphenyl (II, 590 mg) yielded a crude blue phenolic precipitate (VIa, 400 mg, m.p. ca. 345°, decomp.) which was methylated. The yield of dimethyl ether VI was almost quantitative. It was recrystallised from acetic anhydride. M.p. 290–292°. (Found: C 75.4; H 4.5. Calc. for C₂₀H₁₄O₄: C 75.5; H 4.4.)

6,6'-Dimethoxy-2,2',5',2"-dioxido-*p*-terphenyl (VIII). 2,6,2',5',2",6"-Hexamethoxy-*p*-terphenyl (IV, 560 mg) yielded a crude brown phenolic precipitate (VIIIa, 330 mg, m.p. ca. 330°, decomp.), which was converted into compound VIII in an almost quantitative yield. It was purified by recrystallisation from acetic acid and sublimation *in vacuo*. M.p. 287–289°. (Found: C 75.5; H 4.7. Calc. for C₂₀H₁₄O₄: C 75.5; H 4.4.)

Demethylation of 2,3,2',5',2",3"-hexamethoxy-*p*-terphenyl (I). This compound (570 mg) yielded a crude blue phenolic precipitate (400 mg, m.p. ca. 280°, decomp.) which was quantitatively converted to the starting material by methylation.

Demethylation of 2,3,4,2',5',2",3",4"-octamethoxy-*p*-terphenyl (V). The octamethyl ether (450 mg) yielded a crude blue phenol (350 mg, m.p. ca. 260°, decomp.), which on methylation was almost quantitatively converted to the starting material.

Demethylation and dehydration of 2,5,2',5'-tetramethoxydiphenyl. 2,5,2',5'-Tetramethoxydiphenyl¹⁵ (900 mg) was refluxed with constant boiling hydrobromic acid (30 ml) in an atmosphere of carbon dioxide for 80 h. The reaction mixture was then diluted with water (100 ml) and the slightly bluish 2,8-dihydroxydibenzofuran (400 mg) collected. M.p. 233–235°. The phenol was converted to 2,8-dimethoxydibenzofuran, m.p. 89–90°, and 2,8-diacetoxydibenzofuran, m.p. 152–154°, using standard procedures. Swislowsky²¹ reports the following melting points for these substances: 242–243°, 88–89° and 150–151°, respectively.

2,2',5',2"-Dioxido-*p*-terphenyl (IX). 4,4'-Dihydroxy-2,2',5',2"-dioxido-*p*-terphenyl (VIa, 200 mg) was thoroughly mixed with zinc dust (2 g) and heated in a test tube to red heat when a partially phenolic mixture (ca. 20 mg) of substances sublimed on the cool walls of the tube. The mixture was treated with dilute sodium hydroxide and the insoluble material sublimed *in vacuo* and recrystallised from chlorobenzene. M.p. 264–266°. Mixed melting point with an authentic sample^{2,17}, 265–266°.

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