

## Reactions between Quinones and Carbonyl Compounds Catalysed by Aluminium Oxide

### Part III \*. Conversion of 2-Acetyl-*o*-quinols into 2-Acetylphenols and 2-Methylbenzofurans

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A number of alkyl- and/or alkoxy-substituted 2-acetyl-*o*-quinols (6-acetyl-6-hydroxy-2,4-cyclohexadienones) were reduced to 2-acetylphenols with zinc and acetic acid. To elucidate the position of the substituents, some 2-acetylphenols were oxidised to quinones with potassium nitrosodisulfonate.

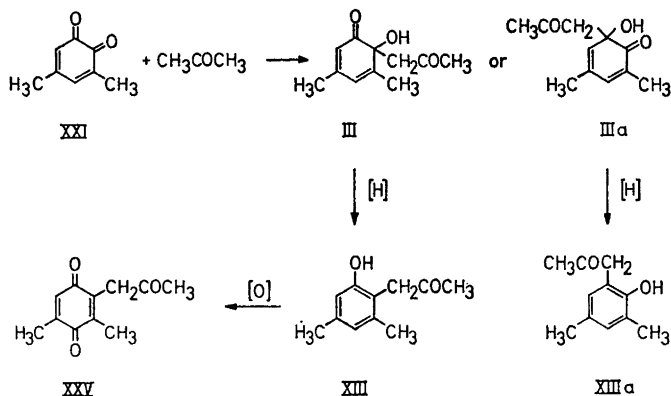
Reduction of 2-acetyl-*o*-quinols with zinc and hydrochloric acid or with sulfur dioxide gives 2-methylbenzofurans.

In a previous paper in this series<sup>1</sup> some examples were described of the addition of acetone to *o*-benzoquinones at room temperature in the presence of activated aluminium oxide. The reaction was shown to be a nucleophilic addition of acetone to one of the carbonyl groups of the quinone with formation of a 2-acetyl-*o*-benzoquinol.

Of the *o*-quinones used as starting materials, the unsubstituted *o*-benzoquinone and the symmetrically substituted 4,5-dimethyl-*o*-benzoquinone could give only one 2-acetyl-*o*-quinol (I and II). The other *o*-quinones were unsymmetrically substituted and could, formally, give two isomeric 2-acetyl-*o*-quinols. However, from the latter *o*-quinones, too, only one of the two possible isomers was obtained. The structure of the *o*-quinols formed was elucidated in most cases by reduction of the acetyl-*o*-quinol and treatment of the 2-acetylphenol obtained with potassium nitrosodisulfonate. The formation of *p*-benzoquinones in this reaction showed that the 2-acetylphenols had an unsubstituted 4-position and thus demonstrated the structure of the 2-acetyl-*o*-quinols. This is illustrated for 3,5-dimethyl-*o*-benzoquinone (XXI).

The *o*-quinol obtained on addition of acetone to this *o*-quinone could have structures III or IIIa, and the 2-acetylphenol formed on reduction of the *o*-quinol could be expected to have structures XIII or XIIIa. Nitrosodisul-

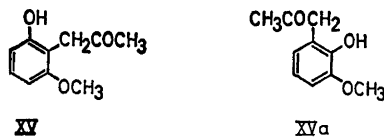
\* Part II: see Ref<sup>1</sup>.



fonate converted the acetylphenol rapidly to the corresponding *p*-benzoquinone (XXV) showing that the acetylphenol had structure XIII and thus that the 2-acetyl-*o*-quinol had structure III.

In the same way the 2-acetylquinols IV and VI–IX, which like III were derived from unsymmetrically substituted *o*-quinones, could be reduced to 2-acetylphenols which were oxidised to *p*-benzoquinones with nitrosodisulfonate (see below).

The structure of the *o*-quinol V obtained by addition of acetone to 3-methoxy-*o*-benzoquinone could not be deduced from the ability of the reduction product XV to react with nitrosodisulfonate since the isomeric *o*-quinol would also give a phenol with a free *p*-position. The correctness of the structure given for V was shown by its ultraviolet absorption spectrum which was practically the same as that of the *o*-quinol VI.<sup>1</sup> The structure of the quinol VI follows from its reduction to a phenol (XVI) with a free *p*-position.



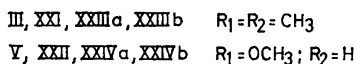
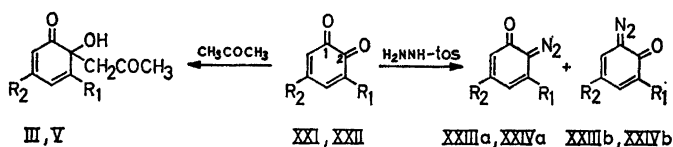
Further support for structure V is the very slow consumption of periodate by the phenol XV obtained from it. The isomeric *o*-quinol on reduction would have given a guaiacol type phenol (XVa) which would have reacted almost instantaneously with periodate to give 3-acetyl-*o*-quinone by oxidative demethylation.<sup>2</sup>

As already mentioned in a preceding paper,<sup>1</sup> the di-*tert*-butylquinol X on reduction gave a phenol which on oxidation with nitrosodisulfonate was slowly converted to an *o*-quinone with simultaneous loss of a *tert*-butyl group. As will be shown in a forthcoming communication,<sup>3</sup> this reaction indicates that the phenol is 2-acetyl-4,6-di-*tert*-butylphenol (XX).

The selective orientation of the addition of acetone to the *o*-quinones which was found in all cases, can be explained<sup>1</sup> as a consequence of the inductive or mesomeric effects of the substituents. These effects make one of the carbon

atoms of the two carbonyl groups less positive than the other and therefore less reactive for nucleophilic attack by the acetyl anion.

It is of interest to compare this selectivity with that in the reaction between *o*-benzoquinones and tosyl hydrazide to give *o*-quinone diazides, recently described by Horner and Dürckheimer.<sup>4</sup> Most of the unsymmetrically substituted *o*-quinones they investigated gave both possible *o*-quinone diazides. The *o*-quinones substituted in the 4-position gave predominantly the product whose formation would be expected to be favoured by the electronic effects of the substituents on the carbonyl groups. Substituents in 3-positions, however, affected the orientation primarily by steric hindrance of the carbonyl group closest to them. Thus 3-methoxy-*o*-quinone (XXII) for example gave a 32–37 % yield of a diazide mixture containing 70–90 % of the isomer XXIVb but only 10–30 % of the isomer XXIVa although the latter should be favoured since C<sub>1</sub> should be deactivated for nucleophilic attack by the mesomeric effect of the methoxyl group. The analogous situation in 3,5-dimethyl-*o*-quinone (XXI) gave a diazide mixture containing about 93 % of isomer XXIIIb and only 7 % of XXIIIa.



As was mentioned above, only the *o*-quinol V was isolated from the product of addition of acetone to 3-methoxy-*o*-quinone (XXII), and the corresponding reaction with 3,5-dimethyl-*o*-quinone (XXI) gave only the *o*-quinol III. Similarly, *o*-quinones with a substituent in the 4-position gave in this reaction only the *o*-quinol expected from the effect of the substituents on the carbonyl groups.

It thus appears that the acetone addition is more selective in orientation and that in general it is not affected by steric effects. Horner and Dürckheimer,<sup>4</sup> however, considered that this reaction would also give both possible isomers and that a more careful examination of the reaction mixture would give evidence of the occurrence of steric effects.

Since it was not inconceivable that an isomeric *o*-quinol could have been lost in the working up previously used, attempts were made using modified methods to detect any such isomers in the following three cases. After reaction of the *o*-quinones with acetone (in the presence of alumina) the reaction mixture was treated directly with zinc and acetic acid without attempting to isolate the often unstable *o*-quinols.

The acetylphenol product obtained in this way from 4-*tert*-butyl-*o*-quinone was separated from byproducts by extraction with sodium bisulfite. After distillation, the carbonyl fraction recovered from the bisulfite extract was gas chromatographically homogeneous and its melting point was only

slightly lower than that of the recrystallised 2-acetyl-5-*tert*-butylphenol (XIX). This result is further evidence that the *o*-quinol isomeric to IX is not formed in the acetone addition.

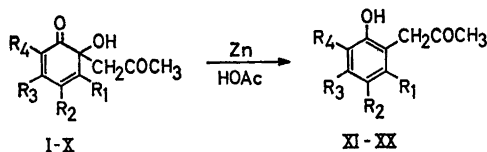
Similarly, 3-methoxy-*o*-quinone (XXII), after treatment with acetone/ $\text{Al}_2\text{O}_3$ , reduction with zinc and acetic acid and fractionation with bisulfite gave a product which on recrystallisation gave 84 % by weight of pure 2-acetyl-3-methoxyphenol (XV). Similar treatment of 3,5-dimethyl-*o*-quinone (XXI) but without the bisulfite extraction gave a crude phenol product that on recrystallisation gave 2-acetyl-3,5-dimethylphenol (XIII) in 65 % yield calculated on the crude product. In neither case could any isomeric acetylphenol be detected. Although it cannot be entirely excluded that such an isomer was present in the mother liquors from the recrystallisation, the yields of the pure acetylphenols XIII and XV show that if any isomeric *o*-quinol was formed the amounts must have been small. Thus under no circumstances can the steric effect of the 3-substituents have had any dominant influence in the acetone addition as in the tosyl hydrazide reaction.

Steric hindrance in the addition of acetone has however already been observed<sup>1</sup> in the single case of 3,5-di-*tert*-butyl-*o*-quinone. This quinone is the only one of the 3-substituted-*o*-quinones investigated so far where the acetyl anion added to carbon atom 1, forming the *o*-quinol X, instead of to carbon atom 2, clearly as a consequence of hindrance by the 3-substituent.

## 2-Acetylphenols and 2-methylbenzofurans

The reduction of 2-methyl-*o*-benzoquinols to phenols has previously been carried out with zinc and hydrochloric acid<sup>5</sup> and with sulfur dioxide<sup>6</sup> but treatment of 2-acetyl-*o*-benzoquinols with these reducing agents gave non-phenolic products (see below). The expected phenols (XI—XX) were, however, obtained by reduction with zinc and acetic acid.

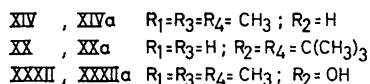
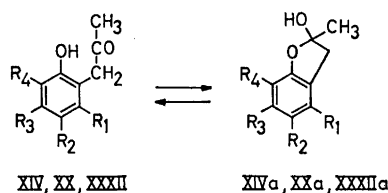
As mentioned previously,<sup>1</sup> some 2-acetyl-*o*-quinols, *e.g.* II and IX, were not stable after isolation and rapidly gave dimers. In these cases the reaction



- |             |   |
|-------------|---|
| I, XI       | R <sub>1</sub> =R <sub>2</sub> =R <sub>3</sub> =R <sub>4</sub> =H   |
| II, XII     | R <sub>1</sub> =R <sub>4</sub> =H; R <sub>2</sub> =R <sub>3</sub> =CH <sub>3</sub>                                |
| III, XIII   | R <sub>1</sub> =R <sub>3</sub> =CH <sub>3</sub> ; R <sub>2</sub> =R <sub>4</sub> =H                               |
| IV, XIV     | R <sub>1</sub> =R <sub>3</sub> =R <sub>4</sub> =CH <sub>3</sub> ; R <sub>2</sub> =H                               |
| V, XV       | R <sub>1</sub> =OCH <sub>3</sub> ; R <sub>2</sub> =R <sub>3</sub> =R <sub>4</sub> =H                              |
| VI, XVI     | R <sub>1</sub> =OCH <sub>3</sub> ; R <sub>2</sub> =R <sub>4</sub> =H; R <sub>3</sub> =CH <sub>3</sub>             |
| VII, XVII   | R <sub>1</sub> =R <sub>2</sub> =R <sub>4</sub> =H; R <sub>3</sub> =OCH <sub>3</sub>                               |
| VIII, XVIII | R <sub>1</sub> =R <sub>2</sub> =R <sub>4</sub> =H; R <sub>3</sub> =OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> |
| IX, XIX     | R <sub>1</sub> =R <sub>2</sub> =R <sub>4</sub> =H; R <sub>3</sub> =C(CH <sub>3</sub> ) <sub>3</sub>               |
| X, XX       | R <sub>1</sub> =R <sub>3</sub> =H; R <sub>2</sub> =R <sub>4</sub> =C(CH <sub>3</sub> ) <sub>3</sub>               |

solution obtained on treatment of the *o*-quinone with acetone and alumina was reduced directly with zinc and acetic acid.

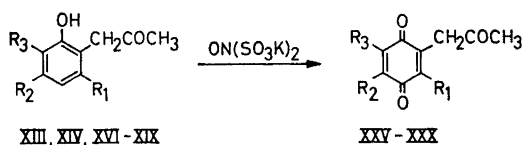
While the infrared spectra of the 2-acetylphenols XI—XIII and XV—XIX in KBr showed, as expected, strong carbonyl bands in the 1698—1718  $\text{cm}^{-1}$  region, this band was absent from the products which from their preparation were expected to have structures XIV and XX. The first of these two products, however, gave a strong carbonyl band (1693  $\text{cm}^{-1}$ ) when run as a melt (m.p. 60°); the crystals formed on cooling the melt no longer showed the carbonyl band. A solution of this compound in carbon tetrachloride also showed a strong carbonyl band (1699  $\text{cm}^{-1}$ ). The product with the expected structure XX gave in carbon tetrachloride solution a carbonyl band (1709  $\text{cm}^{-1}$ ) which increased in intensity during the first 20 min after it dissolved. The solutions of both products gave starting material on evaporation. The simplest explanation of this phenomenon is that the compounds in the crystalline state are the cyclic hemiketals XIVa and XXa which in melts or in solution are in equilibrium with



the open forms XIV and XX. Both products ionise as phenols in dilute alkali and react as ketones with phenylhydrazine. It has not, however, been possible to obtain any functional derivative of the cyclic hemiketal forms XIVa and XXa. Treatment with methanolic hydrochloric acid which might possibly have led to methylation of the free (hemiketal) hydroxyl groups in XIVa and XXa gave instead the benzofurans XXXV and XXXIX. Likewise, treatment with acetic anhydride and perchloric acid, a mixture that is suitable for acetylation of *tert*-hydroxyl groups,<sup>7</sup> gave, not the acetate of XIVa, but an acylated benzofuran.<sup>8</sup>

Like the phenolic ketones XIV and XX, the hydroquinone ketone XXXII in the solid state was found to have the hemiketal structure (XXXIIa). Compounds XIV, XX, and XXXII, unlike the other nine acetylphenols described here (XI—XIII, XV—XIX, and XXXI), all have an alkyl substituent in the 6-position. This substituent thus seems to favour ketalisation. Similar cyclisations have been described by several authors,<sup>9–11</sup> while the reverse process, the conversion of a 2-hydroxy-2,3-dihydrobenzofuran to the corresponding phenolic ketone has been observed by Spetz.<sup>12</sup>

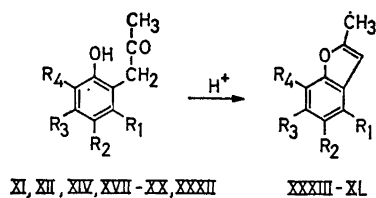
Oxidation of the 2-acetylphenols XIII, XIV, and XVI—XIX with nitrosodisulfonate by the method of Teuber and Rau<sup>13</sup> led to the yellow 2-acetyl-*p*-benzoquinones XXV—XXX. The 2-acetyl-3-methoxy-5-me-



XIII, XXV	R <sub>1</sub> = R <sub>2</sub> = CH <sub>3</sub> ; R <sub>3</sub> = H
XIV, XXVI	R <sub>1</sub> = R <sub>2</sub> = R <sub>3</sub> = CH <sub>3</sub>
XVI, XXVII	R <sub>1</sub> = OCH <sub>3</sub> ; R <sub>2</sub> = CH <sub>3</sub> ; R <sub>3</sub> = H
XVII, XXVIII	R <sub>1</sub> = R <sub>3</sub> = H; R <sub>2</sub> = OCH <sub>3</sub>
XVIII, XXIX	R <sub>1</sub> = R <sub>3</sub> = H; R <sub>2</sub> = OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>
XIX, XXX	R <sub>1</sub> = R <sub>3</sub> = H; R <sub>2</sub> = C(CH <sub>3</sub> ) <sub>3</sub>

thyl-*p*-benzoquinone (XXVII), which was obtained as an oil, was characterised by reduction to the crystalline 2-acetyl-3-methoxy-5-methylhydroquinone (XXXI). Similar reduction of 2-acetyl-3,5,6-trimethyl-*p*-benzoquinone (XXVI) gave the cyclic hemiketal form of the hydroquinone ketone XXXII, *i.e.* 2,4,6,7-tetramethyl-2,5-dihydroxy-2,3-dihydrobenzofuran (XXXIIa) which in turn, on treatment with hydrochloric acid gave 2,4,6,7-tetramethyl-5-hydroxybenzofuran (XL). The same benzofuran (XL) was obtained by Smith and McMullen<sup>14</sup> by reaction of 2,3,5-trimethyl-*p*-benzoquinone with sodium acetoacetic ester followed by ketonic hydrolysis of the product.

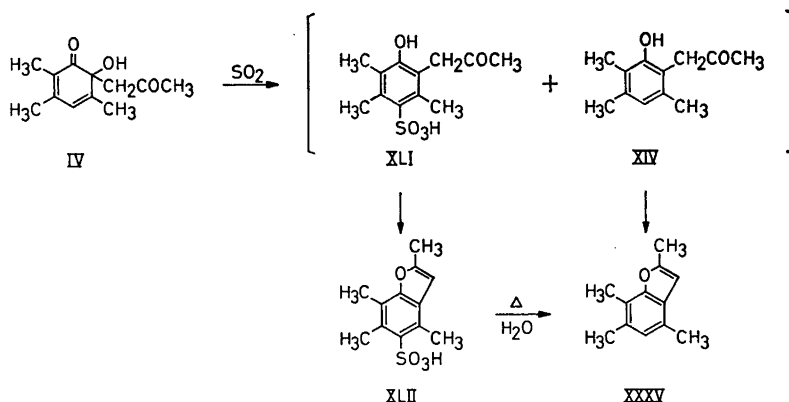
Dehydration of XXXIIa to the benzofuran XL occurred spontaneously though slowly in ethanolic solution even in the absence of hydrochloric acid. Dehydration of the two similar cyclic hemiketals XIVa and XXa, which in solution are in equilibrium with the corresponding ketophenols XIV and XX, occurred only after adding mineral acid to give the benzofurans XXXV and XXXIX. The acetylphenols XI, XII, XVI, XVIII, and XIX were converted



XI, XXXIII	R <sub>1</sub> = R <sub>2</sub> = R <sub>3</sub> = R <sub>4</sub> = H
XII, XXXIV	R <sub>1</sub> = R <sub>4</sub> = H; R <sub>2</sub> = R <sub>3</sub> = CH <sub>3</sub>
XIV, XXXV	R <sub>1</sub> = R <sub>3</sub> = R <sub>4</sub> = CH <sub>3</sub> ; R <sub>2</sub> = H
XVI, XXXVI	R <sub>1</sub> = OCH <sub>3</sub> ; R <sub>2</sub> = R <sub>4</sub> = H; R <sub>3</sub> = CH <sub>3</sub>
XVIII, XXXVII	R <sub>1</sub> = R <sub>2</sub> = R <sub>4</sub> = H; R <sub>3</sub> = OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>
XIX, XXXVIII	R <sub>1</sub> = R <sub>2</sub> = R <sub>4</sub> = H; R <sub>3</sub> = C(CH <sub>3</sub> ) <sub>3</sub>
XX, XXXIX	R <sub>1</sub> = R <sub>3</sub> = H; R <sub>2</sub> = R <sub>4</sub> = C(CH <sub>3</sub> ) <sub>3</sub>
XXXII, XL	R <sub>1</sub> = R <sub>3</sub> = R <sub>4</sub> = CH <sub>3</sub> ; R <sub>2</sub> = OH

to the corresponding benzofurans XXXIII, XXXIV, XXXVI—XXXVIII in the presence of mineral acid; clearly in these cases the intermediate cyclization must also be catalysed by an increased hydrogen ion concentration.

Sulfur dioxide in aqueous solution has previously been used to reduce both *p*-benzoquinols<sup>15</sup> and a 2-methyl-*o*-benzoquinol<sup>6</sup> to phenols. In attempts to apply this method to 2-acetyl-3,5,6-trimethyl-*o*-benzoquinol (IV), a sulfur-containing acid was obtained together with 2,4,6,7-tetramethylbenzofuran (XXXV). The ultraviolet spectrum of the sulfur-containing acid was rather similar to that of 2,4,6,7-tetramethylbenzofuran (XXXV) and 5-hydroxy-2,4,6,7-tetramethylbenzofuran (XL) and it can therefore be presumed to be a tetramethylbenzofuransulfonic acid. The composition of the product, C<sub>12</sub>H<sub>14</sub>O<sub>4</sub>S, was consistent with this. Hydrolytic desulfonation gave 2,4,6,7-tetramethylbenzofuran (XXXV) and the sulfonic acid group must therefore



be in the 3 or 5 position. Of the two possible sulfonic acid derivatives of this benzofuran, the 5-sulfonic acid (XLII) appears to be the more probable since its formation can be explained plausibly. It can be assumed that on treatment of the *o*-quinol IV with aqueous sulfur dioxide, sulfurous acid will add to form the phenolsulfonic acid XLI in competition with the reduction to the phenol XIV. The formation of XLI is reminiscent of the addition of benzenesulfonic acid to *o*-quinolacetates described by Kotlan and Wessely.<sup>16</sup> In the present case however the "initial" 1,4 or 1,6 addition of sulfurous acid to the conjugated system will be followed by migration of the sulfonic acid residue. It is moreover known<sup>17</sup> that treatment of *p*-benzoquinone with aqueous sulfur dioxide solution gives about 20 % yield of the hydroquinonesulfonic acid in addition to the hydroquinone. The formation of the final reaction products XXXV and XLII from the postulated intermediates XIV and XLI is easily understood as the result of proton catalysis. In fact the isolated phenol XIV (or its cyclohemiketal XIVa) was readily converted into the benzofuran XXXV when treated with aqueous sulfur dioxide.

#### EXPERIMENTAL

Analyses were done by Alfred Bernhardt, Mülheim, Germany.

Infrared spectra were taken as KBr discs unless otherwise specified. Molecular weight determinations were done in ethanol with a Mechrolab Vapor Pressure Osmometer Model

301. The preparation of the *o*-benzoquinols I–X, 2-acetylphenol (XI) and 2-methylbenzofuran (XXXIII) has been described previously.<sup>1</sup>

*General procedure for the preparation of 2-acetylphenols.* (A) *From isolated 2-acetyl-*o*-benzoquinols.* A solution of the *o*-quinol in 20 % acetic acid (5–10 ml per 100 mg of the *o*-quinol) was shaken with zinc dust (1–2 g per 10 ml of solution) until the solution was colourless or in the cases where the *o*-quinol was colourless, for 5 min. The solution was diluted with an equal volume of water and extracted with ether. The extract was washed with water and with sodium bicarbonate solution, dried over sodium sulfate and evaporated to give the crude 2-acetylphenol.

(B) *From *o*-quinones without isolation of the 2-acetyl-*o*-benzoquinols.* A solution of the *o*-benzoquinone in acetone was shaken with aluminium oxide at room temperature as described in Ref.<sup>1</sup> The solution was decanted and the alumina was washed with acetone. Acetic acid (5 ml per g of quinone) and zinc dust (5 g per g of quinone) were added to the combined solutions and the mixture was shaken until it was colourless. After filtering the acetone was removed under reduced pressure and the residue was taken up in ether and washed with water and then with sodium carbonate solution. The ether solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated and the product was purified as described for the individual substances.

*2-Acetyl-4,5-dimethylphenol (XII).* A solution of 4,5-dimethyl-*o*-benzoquinone (4.0 g) in acetone (200 ml) was shaken with alumina (100 g) for 30 min. The filtered solution was then treated with zinc and acetic acid as described above under method B. The crude product obtained was dissolved in 25 % ethanol. After cooling to –20° it gave slightly brown, rhombic plates, m.p. 68–70° (1.20 g, 23 %). Sublimation (10<sup>-2</sup> mm Hg, bath temperature 80°) gave a colourless product, m.p. 71–72°. (Found: C 74.07; H 7.75. Calc. for C<sub>11</sub>H<sub>14</sub>O<sub>2</sub>: C 74.13; H 7.92). Infrared bands (cm<sup>-1</sup>): 1711 (CO) and 3400 (OH).

*2-Acetyl-3,5-dimethylphenol (XIII).* 3,5-Dimethyl-*o*-benzoquinone (XXI, 2.8 g) in acetone (70 ml) was shaken with alumina (42 g) for 30 min and the solution was then treated with zinc and acetic acid by method B. The crude reduction product (1.0 g) was recrystallised from hexane, needles, m.p. 108–109° (0.65 g, 18 %). (Found: C 73.86; H 8.15. Calc. for C<sub>11</sub>H<sub>14</sub>O<sub>2</sub>: C 74.13; H 7.92). Infrared bands (cm<sup>-1</sup>): 1702 (CO) and 3330 (OH).

*2-Acetyl-3,5,6-trimethylphenol (XIV) and 2-hydroxy-2,4,6,7-tetramethyl-2,3-dihydrobenzofuran (XIVa).* 2-Acetyl-3,5,6-trimethyl-*o*-benzoquinol (IV, 400 mg) was treated according to method A. Recrystallisation of the crude product, m.p. 50–55° (358 mg), from hexane gave needles, m.p. 59–60° (260 mg). (Found: C 74.66; H 8.48. Calc. for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>: C 74.96; H 8.39).

The substance was soluble in alkali. The infrared spectrum in KBr showed a hydroxyl band at 3280 cm<sup>-1</sup> but only slight diffuse absorption around 1700 cm<sup>-1</sup> (XIVa). A melt obtained on heating between KBr plates showed a strong carbonyl band at 1693 cm<sup>-1</sup> (XIV), whereas the crystalline solid formed after cooling the melt again exhibited only slight diffuse absorption near 1700 cm<sup>-1</sup>. A carbon tetrachloride solution of the substance showed a strong carbonyl band (1699 cm<sup>-1</sup>).

The phenylhydrazone of XIV was obtained as a precipitate on treatment of XIV in acetic acid with phenylhydrazine and was recrystallised from ethanol/water, plates, m.p. 147–148°. (Found: N 9.77. Calc. for C<sub>18</sub>H<sub>22</sub>N<sub>2</sub>O: N 9.92).

*2-Acetyl-3-methoxyphenol (XV).* (a) 2-Acetyl-3-methoxy-*o*-benzoquinol (V, 221 mg) was treated according to method A and the product (190 mg) was recrystallised from water, needles, m.p. 75–76° (149 mg). (Found: C 66.55; H 6.84; OCH<sub>3</sub> 17.37. Calc. for C<sub>10</sub>H<sub>12</sub>O<sub>3</sub>: C 66.65; H 6.71; OCH<sub>3</sub> 17.22). Infrared bands (cm<sup>-1</sup>): 1712 (CO) and 3230 (OH).

The substance, dissolved in water, was oxidised only very slowly by sodium periodate. This is characteristic for *m*-alkoxyphenols while *o*- and *p*-alkoxyphenols are oxidised almost instantaneously.<sup>2</sup>

(b) 3-Methoxy-*o*-benzoquinone (XXII, 6.0 g), acetone (240 ml) and alumina (120 g) were shaken until the initially dark red solution had turned a light red (1 h). After reduction with zinc and acetic acid according to method B the reaction product was distilled (0.1 mm Hg, bath temperature 100°). The oily distillate crystallised from a small amount of ether, irregularly shaped crystals, m.p. 73–75°, no depression with XV obtained by method a (1.6 g, 20 %).



(c) 3-Methoxy-*o*-benzoquinone (3.0 g), acetone (120 ml) and alumina (60 g) were shaken as in (b). The ether solution obtained after treatment with zinc and acetic acid was extracted with 1 N NaOH solution (50 ml). The alkaline solution was neutralised with carbon dioxide and extracted with ether. The extract was evaporated and the residue extracted with 20 % sodium bisulfite solution. The product obtained after decomposition with sodium carbonate and ether extraction was distilled (0.1 mm Hg, bath temp. 100°). The distillate crystallised on inoculation. Recrystallisation of 270 mg of the product from aqueous ethanol gave 227 mg (84 % of the distillate) of XV, m.p. 73–75°.

*2-Acetyl-3-methoxy-5-methylphenol (XVI)*. Reduction of 2-acetyl-3-methoxy-5-methyl-*o*-benzoquinol (VI, 639 mg) by method A gave the phenol (571 mg) which was recrystallised from water, prisms, m.p. 85–86°. (Found: C 68.32; H 7.30; OCH<sub>3</sub> 15.95; MW 192. Calc. for C<sub>11</sub>H<sub>14</sub>O<sub>3</sub>: C 68.02; H 7.26; OCH<sub>3</sub> 15.98; MW 194.22). Infrared bands (cm<sup>-1</sup>): 1702 (CO) and 3370 (OH).

*2-Acetyl-5-methoxyphenol (XVII)* was obtained on reduction of 2-acetyl-5-methoxy-*o*-benzoquinol (VII, 300 mg) by method A. The crystalline crude product (284 mg) was purified by sublimation (10<sup>-2</sup> mm Hg, bath temp. 70°, yield 260 mg, m.p. 63–65°) followed by recrystallisation from water, prisms, m.p. 65–66°. (Found: C 66.97; H 6.83; OCH<sub>3</sub> 17.03. Calc. for C<sub>10</sub>H<sub>12</sub>O<sub>3</sub>: C 66.65; H 6.71; OCH<sub>3</sub> 17.22). Infrared bands (cm<sup>-1</sup>): 3440 (OH) and 1713 (CO).

The substance, dissolved in water, consumed sodium periodate only slowly, which is to be expected for a *m*-methoxyphenol.<sup>2</sup>

*2-Acetyl-5-benzyloxyphenol (XVIII)* was prepared by reduction of 2-acetyl-5-benzyloxy-*o*-benzoquinol (VIII, 600 mg) by method A. The crude product (575 mg) was recrystallised three times from hexane, plates, m.p. 107–108°. (Found: C 75.07; H 6.37; MW 271. Calc. for C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>: C 74.98; H 6.29; MW 256.29). Infrared bands (cm<sup>-1</sup>): 1698 (CO) and 3290 (OH).

*2-Acetyl-5-tert-butylphenol (XIX)*. 4-*tert*-Butyl-*o*-benzoquinone (27 g), acetone (500 ml) and alumina (300 g, activity 3) were shaken until the solution was a light yellow (30 min). The mixture was treated according to method B and the reduced product was then shaken with saturated sodium bisulfite solution (100 ml) for 2 h. The bisulfite adduct was filtered off and washed with ether to remove the accompanying oil. The adduct was decomposed with sodium carbonate solution and the oil formed was distilled (0.01 mm Hg, 120–130°). The distillate was gas-chromatographically pure (2 m apiezon column, helium, 175°) and crystallised completely on inoculating with material obtained by crystallising an earlier preparation from hexane. The product, m.p. 51–55°, was recrystallised from hexane, clumps of prisms, 5.6 g (17 %), m.p. 55–56°. (Found: C 75.44; H 8.66. Calc. for C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>: C 75.69; H 8.80). Infrared bands (cm<sup>-1</sup>): 1701 (CO) and 3340 (OH).

*2-Acetyl-4,6-di-tert-butylphenol (XX) and 2-hydroxy-2-methyl-5,7-di-tert-butyl-2,3-dihydrobenzofuran XXa*. 2-Acetyl-4,6-di-*tert*-butyl-*o*-benzoquinol (X, 5.7 g) was reduced with zinc (25 g) and acetic acid (75 ml). The filtered solution was diluted with water (1 l.) and the precipitate was filtered off. After 5 reprecipitations from methanol-water at room temperature it was obtained as needles, m.p. 124–126° (3.4 g) (Found: C 77.72; H 9.81. Calc. for C<sub>17</sub>H<sub>26</sub>O<sub>2</sub>: C 77.81; H 9.99). In KBr the substance showed an OH band at 3310 cm<sup>-1</sup> but only slight, diffuse absorption near 1700 cm<sup>-1</sup> (XXa). In carbon tetrachloride it gave a strong carbonyl band at 1709 cm<sup>-1</sup> (XX), which increased in intensity during the first 20 min after it was dissolved. Evaporation of the carbon tetrachloride solution gave starting material. The ultraviolet spectrum in ethanol showed a broad peak at 280–286 mμ (log ε 3.44), displaced to 291 mμ (log ε 3.54) in 0.5 N NaOH in 95 % ethanol. The compound in this respect resembled 2-methyl-4,6-di-*tert*-butylphenol.<sup>18</sup>

The phenylhydrazone of XX was obtained as a precipitate on treatment of XXa in glacial acetic acid with phenylhydrazine. It was recrystallised from aqueous ethanol as rods, m.p. 128–130°. (Found: N 7.72. Calc. for C<sub>23</sub>H<sub>32</sub>ON<sub>2</sub>: N 7.95).

*2-Acetyl-3,5-dimethyl-p-benzoquinone (XXV)*. 2-Acetyl-3,5-dimethylphenol (XIII, 100 mg) in ether (5 ml) was shaken with a solution of potassium nitrosodisulfonate (1 g) in water (100 ml) and 0.15 M KH<sub>2</sub>PO<sub>4</sub> (5 ml). After 15 min the reaction mixture was extracted with ether and the extract was dried over sodium sulfate and evaporated. Recrystallisation of the residue (95 mg) from hexane gave yellow needles, m.p. 54–55° (60 mg, 56 %). (Found: C 68.70; H 6.38. Calc. for C<sub>11</sub>H<sub>14</sub>O<sub>3</sub>: C 68.73; H 6.29), λ<sub>max</sub><sup>EtOH</sup> 255 mμ (log ε 4.22) and 333 mμ (log ε 2.66).

*2-Acetyl-3,5,6-trimethyl-p-benzoquinone (XXVI)*. Oxidation of 2-acetyl-3,5,6-trimethylphenol (XIV, 104 mg) as described in the previous experiment and crystallisation of the crude product (95 mg) from hexane gave yellow plates, m.p. 74–75° (62 mg, 56 %). (Found: C 70.26; H 6.74. Calc. for C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>: C 69.88; H 6.84),  $\lambda_{\max}^{\text{EtOH}}$  259 m $\mu$  (log  $\epsilon$  4.28) and 335 m $\mu$  (log  $\epsilon$  2.50).

*2-Acetyl-3-methoxy-5-methyl-p-benzoquinone (XXVII)*. A solution of 2-acetyl-3-methoxy-5-methylphenol (XVI, 580 mg) in water (150 ml) was added to a solution of potassium nitrosodisulfonate (4 g) in water (300 ml) and 0.15 M KH<sub>2</sub>PO<sub>4</sub> (20 ml). The mixture was extracted after 30 min with chloroform and the extract evaporated to give a red oil (340 mg). This was distilled (0.5 mm, bath temp. 60°) giving an orange oil. (Found: C 63.11; H 5.36. Calc. for C<sub>11</sub>H<sub>14</sub>O<sub>4</sub>: C 63.45; H 5.81).

*2-Acetyl-5-methoxy-p-benzoquinone (XXVIII)*. A solution of 2-acetyl-5-methoxyphenol (XVII, 200 mg) in water (25 ml) was mixed with a solution of potassium nitrosodisulfonate (2 g) in water (100 ml) and 1 N sodium acetate (5 ml). After 30 min the mixture was extracted with ether, the ethereal solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. The oily residue (110 mg) in ether solution at –80° gave yellow-brown needles, m.p. 76–78° (80 mg, 37 %). (Found: C 61.58; H 5.23; OCH<sub>3</sub> 15.91. Calc. for C<sub>10</sub>H<sub>10</sub>O<sub>4</sub>: C 61.85; H 5.19; OCH<sub>3</sub> 15.98),  $\lambda_{\max}^{\text{EtOH}}$  259 m $\mu$  (log  $\epsilon$  3.96) and 360 m $\mu$  (log  $\epsilon$  2.88).

*2-Acetyl-5-benzoyloxy-p-benzoquinone (XXIX)*. A solution of 2-acetyl-5-benzoyloxyphenol (XVIII, 100 mg) in water (350 ml) was added to a solution of potassium nitrosodisulfonate (1 g) in water (100 ml) and 0.15 M KH<sub>2</sub>PO<sub>4</sub> (10 ml). After 30 min the mixture was extracted with ether. The product obtained on evaporation of the ethereal solution was a brown oil (40 mg) which gave yellow-brown needles from ether, m.p. 97° (10 mg). (Found: C 70.47; H 5.19. Calc. for C<sub>18</sub>H<sub>14</sub>O<sub>4</sub>: C 71.10; H 5.22).

*2-Acetyl-5-tert-butyl-p-benzoquinone (XXX)*. 2-Acetyl-5-tert-butylphenol (XIX, 1.00 g) in acetone (100 ml) was mixed with a solution of potassium nitrosodisulfonate (2.5 g) in water (200 ml) and 0.15 M KH<sub>2</sub>PO<sub>4</sub> (5 ml). After 15 min the mixture was extracted with ether and the ethereal solution was evaporated and the residue obtained was extracted with light petroleum. The extract, after adding a few drops of ether and cooling, gave yellow crystals which were sublimed (0.1 mm, bath temp. 50°), m.p. 63–65° (230 mg). (Found: C 71.33; H 7.34. Calc. for C<sub>13</sub>H<sub>16</sub>O<sub>3</sub>: C 70.88; H 7.32).

*2-Acetyl-3-methoxy-5-methylhydroquinone (XXXI)*. 2-Acetyl-3-methoxy-5-methyl-*p*-benzoquinone (XXVII, 100 mg) was reduced with zinc and 20 % acetic acid. After dilution with water the reaction mixture was extracted with ether and the extract was washed with sodium bicarbonate solution, dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated. Recrystallisation of the residue from benzene gave irregular plates, m.p. 121–122°. (Found: C 63.28; H 6.84. Calc. for C<sub>11</sub>H<sub>14</sub>O<sub>4</sub>: C 62.84; H 6.71). Infrared bands (cm<sup>-1</sup>): 1708 (CO) and 3380 (OH). The substance gave a yellowish brown colour with ferric chloride.

*2,5-Dihydroxy-2,4,6,7-tetramethyl-2,3-dihydrobenzofuran (XXXIIa)*. Reduction of 2-acetyl-3,5,6-trimethyl-*p*-benzoquinone (XXVI, 0.32 g) with zinc and 5 % acetic acid gave a crystalline crude product (0.30 g) which after recrystallisation from ligroin (b.p. 80–120°) and from isopropyl ether gave irregular plates, m.p. 125–126°. (Found: C 69.32; H 7.59. Calc. for C<sub>12</sub>H<sub>16</sub>O<sub>3</sub>: C 69.21; H 7.75). Infrared band at 3390 cm<sup>-1</sup> (OH) but no absorption near 1700 cm<sup>-1</sup>.

*2,5,6-Trimethylbenzofuran (XXXIV)*. 2-Acetyl-4,5-dimethylphenol (XII, 280 mg) was dissolved in 5 N hydrochloric acid (100 ml). After 24 h the precipitate was filtered off, sublimed (bath temp 50°, 20 mm Hg) and recrystallised from aqueous methanol, irregular needles (140 mg), m.p. 53–54°. (Found: C 82.26; H 7.66. Calc. for C<sub>11</sub>H<sub>12</sub>O: C 82.46; H 7.55).

*2,4,6,7-Tetramethylbenzofuran (XXXV)*. (a) 2-Acetyl-3,5,6-trimethyl-*o*-benzoquinone (IV, 500 mg) was treated with zinc and 5 N hydrochloric acid. The product obtained by extraction of the reaction solution with ether and evaporation (395 mg) was sublimed twice (2 mm Hg, bath temp. 50°), plates, m.p. 39.5–40.5° (338 mg, 81 %). (Found: C 82.76; H 7.95. Calc. for C<sub>12</sub>H<sub>14</sub>O: C 82.72; H 8.10).

(b) 2-Acetyl-3,5,6-trimethylphenol (XIV) was dissolved in 1 N methanolic hydrochloric acid. After 2 h the solution was diluted with water and extracted with ether. The extract gave the benzofuran in 96 % yield.

*Picric acid complex.* Substance XXXV (100 mg) in ethanol (2 ml) was mixed with a saturated aqueous solution (5 ml) of picric acid. The precipitate was recrystallised from methanol, orange rods, m.p. 94–96°. (Found: N 10.44. Calc. for  $C_{18}H_{17}N_3O_8$ : N 10.42).

*2,6-Dimethyl-4-methoxybenzofuran (XXXVI).* (a) 2-Acetyl-3-methoxy-5-methyl-*o*-benzoquinol (VI, 523 mg) was treated with zinc and 5 N hydrochloric acid. The product obtained by ether extraction (427 mg) was sublimed (0.2 mm Hg, bath temp. 60°) and recrystallised from ethanol/water, plates, m.p. 58–59° (340 mg, 77 %). (Found: C 75.04; H 6.88. Calc. for  $C_{11}H_{12}O_2$ : C 74.98; H 6.87).

(b) The same substance (XXXVI) was obtained on dissolving 2-acetyl-3-methoxy-5-methylphenol (XVI) in 5 N hydrochloric acid and then extracting the solution with ether. Yield 93 %.

*2-Methyl-6-benzyloxybenzofuran (XXXVII).* 2-Acetyl-5-benzyloxyphenol (XVIII, 100 mg) in methanol (5 ml) and conc. hydrochloric acid (2 drops) was heated to boiling for a few minutes. The precipitate obtained on cooling and diluting with water was sublimed (0.5 mm Hg, bath temp. 80°), m.p. 60–61° (60 mg). (Found: C 80.19; H 5.80. Calc. for  $C_{18}H_{14}O_2$ : C 80.65; H 5.92).

*2-Methyl-6-tert-butylbenzofuran (XXXVIII).* 2-Acetyl-5-*tert*-butylphenol (XIX, 500 mg) in methanol (5 ml) and conc. hydrochloric acid (1 ml) was heated to boiling and then diluted with water. Extraction with ether gave an oil which was distilled (0.5 mm Hg, bath temp. 65°) giving a colourless mobile oil (390 mg), b.p. 253°/749 mm Hg,  $n_D^{25}$  1.5345. (Found: C 83.49; H 8.56. Calc. for  $C_{13}H_{16}O$ : C 82.93; H 8.57).

*2-Methyl-5,7-di-tert-butylbenzofuran (XXXIX).* 2-Acetyl-4,6-di-*tert*-butyl-*o*-benzoquinol (X, 1 g) in methanol (20 ml) and conc. hydrochloric acid (2 ml) was shaken with zinc dust until the solution was colourless. The mixture was diluted with water (100 ml) and extracted with ether (50 ml). The ether phase, after washing with sodium bicarbonate solution, gave an oil which was distilled (0.4 mm Hg, bath temp. 85°). The distillate was a pale yellow oil (0.8 g), b.p. 275°/751 mm Hg,  $n_D^{25}$  1.5162. (Found: C 83.49; H 9.65. Calc. for  $C_{17}H_{24}O$ : C 83.55; H 9.90).

The same product was also obtained from 2-acetyl-4,6-di-*tert*-butylphenol (XX) on warming with methanolic hydrochloric acid.

*5-Hydroxy-2,4,6,7-tetramethylbenzofuran (XL).* 2-Acetyl-3,5,6-trimethyl-*p*-benzoquinone (XXVI, 145 mg) was shaken with zinc in dilute hydrochloric acid (10 ml) until the solution was colourless. The product obtained on extraction with ether and evapora-

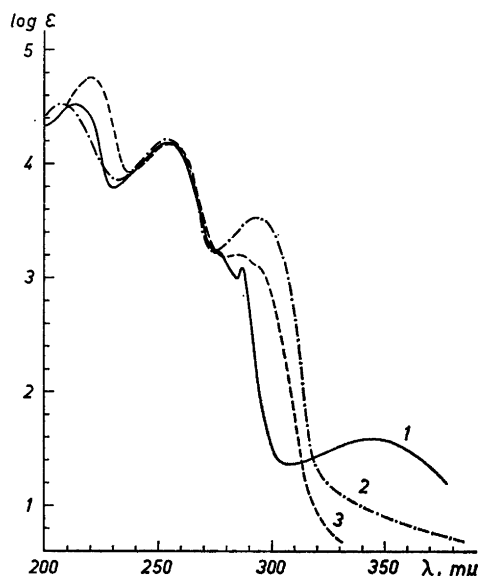


Fig. 1. Absorption spectra. 1. 2,4,6,7-Tetramethylbenzofuran (XXXV). 2. 5-Hydroxy-2,4,6,7-tetramethylbenzofuran (XL). 3. 2,4,6,7-Tetramethylbenzofuran-5 $\beta$ -sulfonic acid (XLII). Solvent: 95 % Ethanol.

tion (120 mg) was recrystallised from hexane, needles, m.p. 137–138°. Smith and McMullen<sup>9</sup> give 138–139°.

*Sulfur dioxide treatment of 2-acetonyl-3,5,6-trimethyl-o-benzoquinol (IV).* A solution of the quinol IV (2.06 g) in water (300 ml) was treated with a stream of sulfur dioxide for 4 h. After standing overnight the solution was filtered and extracted with ether. The precipitate (0.08 g) and the residue from the ether extract (0.35 g) were sublimed giving 2,4,6,7-tetramethylbenzofuran (XXXV), m.p. and mixed m.p. 39–40° (0.27 g, 16%). The filtrate was evaporated under reduced pressure and the residue (2.48 g) was extracted with ether. Evaporation of the ethereal solution and crystallisation of the oil from isopropyl ether gave 2,4,6,7-tetramethylbenzofuran-5?-sulfonic acid (XLII), plates, m.p. 96° (decomp.), (0.94 g). The ultraviolet spectrum is shown in Fig. 1. On drying in high vacuum over P<sub>2</sub>O<sub>5</sub> at room temperature the substance lost 13% of its weight (calc. for 2 H<sub>2</sub>O: 12%). The dried substance slowly discoloured. (Found: C 55.90; H 5.56; S 11.96; equiv. wt. 262. Calc. for C<sub>12</sub>H<sub>14</sub>O<sub>4</sub>S: C 56.67; H. 5.55; S 12.61; equiv. wt. 254.30).

The sodium salt was obtained as a precipitate when the acid (XLII) was mixed with 5 N NaOH. Recrystallisation from ethanol gave prisms, m.p. 260° (decomp.). The compound gave only a very small amount of phenolic material in a potassium hydroxide melt.

*2,4,6,7-Tetramethylbenzofuran (XXXV) from 2,4,6,7-tetramethylbenzofuran-5?-sulfonic acid (XLII).* The air-dried sulfonic acid (XLII, 50 mg) was heated rapidly in a sublimation apparatus to 200°. The sublimate obtained after resublimation (7 mg) was identified as 2,4,6,7-tetramethylbenzofuran (XXXV) by melting point and mixed melting point.

*Sulfur dioxide treatment of 2-acetonyl-3,5,6-trimethylphenol (XIV) (or its cyclohemiketal XIVa).* Treatment of an aqueous solution (50 ml) of the phenol XIV (100 mg) with a stream of sulfur dioxide rapidly gave a precipitate. This was identified as 2,4,6,7-tetramethylbenzofuran (XXXV) by melting point and mixed melting point.

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