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STRUCTURE OF 2,6-DIMETHOXY- AND DIBENZYLOXYQUINONE-ACETONE ADDUCTS AND BEHAVIOUR OF RELATED QUINONES

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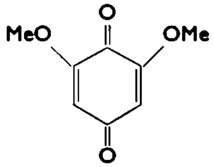
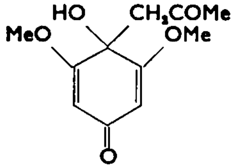
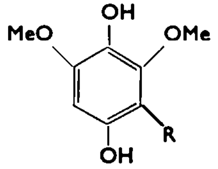
Abstract—The properties of dimethoxyquinone-acetone adduct conclusively prove that it involves addition on the carbonyl group of the quinone at 1-position. It forms two acetates, one, a direct monoacetate and the other, a diacetate derived from a transformation product of the adduct. Since the two methoxyl groups do not sterically deactivate the carbonyl group in position 1, the extent of this effect has been examined by taking 2,6-dibenzyloxyquinone as a suitable example. This is also found to form an adduct involving addition of acetone on the 1-carbonyl group proving thereby that steric factors are not important in this reaction. A number of other quinones have also been studied. They do not form adducts, but undergo various changes such as polymerization or reduction.

THE addition of acetone to 2,6-dimethoxyquinone (I) yields a sweet water-soluble product[1,2] with the following characteristics: (i) It has no phenolic hydroxyl group and (ii) gives two carbonyl absorptions in the IR spectrum, one corresponding to an isolated aliphatic carbonyl (acetonyl group) and the other to a conjugated carbonyl group. These two properties are sufficient to show that there has been 1,2-addition of acetone on one of the quinone carbonyl groups (see II) and no 1,4-addition, since in the latter case the product (III) would be phenolic and have only one carbonyl function; (iii) the readiness with which the reverse reaction takes place yielding acetone is also in agreement with the 1,2-addition; (iv) further, reduction of the adduct yields a phenol showing only one carbonyl absorption in the IR corresponding to the acetonyl group and this confirms the above conclusions and further shows that the addition has taken place on the 1-carbonyl group and that the adduct has the structure II.


I


II


III; R = CH_2COMe
IV; R = H
V; R = COMe

In spite of all the data, Singh and Singh[3] have expressed the opinion that it was not conclusively proved that 1,4-addition (structure III) is ruled out. They do not explain how the 1,4-addition can be compatible with points (i), (ii) and (iii), but regarding (iv) they mention that a compound with structure III can undergo reduction with zinc and acetic acid. In support of this view they have recapitulated the reduction of the

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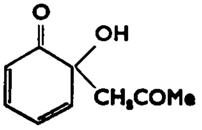
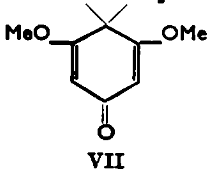
[1] K. Aghoramurthy, K. V. Rao and T. R. Seshadri, *Proc. Indian Acad. Sci.* **37A**, 798 (1953).
[2] K. Aghoramurthy, M. G. Sarngadharan and T. R. Seshadri, *J. Indian. Chem. Soc.* **39**, 439 (1962).
[3] Gurbaksh Singh and Sujan Singh, *Indian J. Chem.* **2**, 374 (1964).

following compounds: (i) methyl 3,4,5-trimethoxycinnamate to 3,5-dimethoxyphenylpropanol using sodium and alcohol,[4] (ii) methyl 3,4,5-trimethoxybenzoate to methyl 3,5-dimethoxybenzoate with sodium and liquid ammonia[5] and (iii) phloroglucinol to resorcinol with sodium borohydride;[6] but the examples selected and the conditions employed have no analogy to structure III. Further, 2,6-dimethoxyquinol (IV) and 2,5-dihydroxy-4,6-dimethoxyacetophenone (V) which are closely analogous to structure III cannot be reduced with zinc and acetic acid and, therefore, the reduction reaction cannot be explained by structure III. Structure II, however, can since it contains a tertiary alcoholic group in an allylic position. Closely analogous cases where zinc and acetic acid reduction has been employed successfully in the past are 9,10-diaryl-9,10-dihydroxy-9,10-dihydroanthracene and its substitution products[7] and acetone adducts of *ortho* quinones e.g. VI.[8]

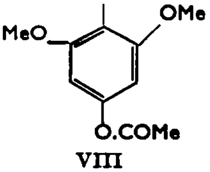


VI

Singh and Singh studied the acetate obtained by boiling the quinone-acetone adduct with acetic anhydride and sodium acetate. They found it to be a diacetate which perhaps supported the 1,4-adduct structure (III), but further study of its reactions and the NMR spectrum showed that it is a transformation product derived from the 1,2-adduct structure (II). After our earlier report, it has been noted that the acetate does not yield acetone on hydrolysis, thus indicating that the quinone-acetone adduct is not regenerated. Further investigations of the acetylation with acetic anhydride and pyridine at *low temperature* shows that an acetate m.p. 111–113° is produced which is fairly soluble in water and agrees with the monoacetate of the adduct in C, H and acetyl values and in the IR gives an ester band (1751 cm^{-1}) corresponding to the acetate of an alcohol and two ketone bands (1709 and 1667 cm^{-1}). On hydrolysis it gives acetone. It is therefore, the monoacetate of the 1,2-adduct (II). Acetylation using acetic anhydride and sodium acetate brings about dehydration and acetic anhydride addition as suggested by Singh and Singh but instead of two IR carbonyl bands as recorded by them there are three: 1770 cm^{-1} corresponding to a phenol acetate, 1745 cm^{-1} corresponding to an alcohol acetate and 1724 cm^{-1} corresponding to the ketone carbonyl. The compound gives the same C and H values as the monoacetate (VII), but has two acetoxyl groups and is therefore a diacetate (VIII).



VII



VIII

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[4] D. Nasipuri, R. Roy and U. Rakshit, *J. Indian Chem. Soc.* **37**, 369 (1960).

[5] O. L. Chapman and P. Fitton, *J. Amer. Chem. Soc.* **85**, 41 (1963).

[6] G. I. Fray, *Tetrahedron* **3**, 316 (1958).

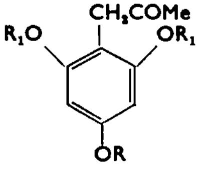
[7] C. K. Ingold, *J. Chem. Soc.* 3080 (1926).

[8] R. Magnusson, *Acta Chem. Scand.* **18**, 421 (1964).

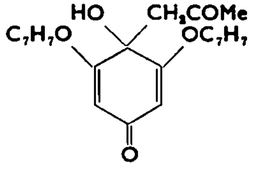
We originally recorded[1] that the dinitrophenylhydrazone of the adduct is soluble in alkali and may be recovered unchanged. Singh and Singh used this solubility as support for the 1,4-addition, but later recorded that the alkali-solubility is due to dehydration and isomeric change into a phenolic product and that the original dinitrophenylhydrazone is not recovered on acidification. It has now been confirmed that the dinitrophenylhydrazone is recovered on acidifying the alkaline solution. 2,4-Dinitrophenylhydrazones are generally soluble in aqueous alkali, e.g., acetone dinitrophenylhydrazone; this property is used in paper chromatography by spraying with aqueous alkali.[9]

Thus the evidence (i to iv) provided earlier[1,2] eliminates the 1,4-adduct structure (III) and establishes the 1,2-adduct structure (II). Later studies involving reactions of the acetate and the NMR spectra further confirm this. This formulation of the adduct means that the two methoxyl groups do not sterically obstruct the addition of acetone on the carbonyl group between them. The only directing influence is the electromeric deactivation of the 4-carbonyl group by the two methoxyl groups. Recently 2,6-dibenzyloxyquinone has been studied in order to test the influence of bulkier but similar *ortho* substituents on the course of the above addition. It has been found that an adduct is formed with acetone and its constitution has been worked out on lines similar to those used for the constitution of the 2,6-dimethoxyquinone-acetone adduct.[2] The IR spectrum of the adduct shows the following absorptions: (1) 3344 cm^{-1} corresponding to an alcoholic hydroxyl group, (2) 1721 cm^{-1} indicating the presence of an aliphatic carbonyl group, (3) 1664 cm^{-1} showing the presence of a quinonoid carbonyl and (4) 1600 cm^{-1} with an inflexion at 1608 cm^{-1} corresponding to the benzene rings and the quinone double bonds.

Reduction of the adduct with zinc and acetic acid yields 2,6-dibenzyloxy-4-hydroxyphenylacetone (IX) which gives the vanillin-hydrochloric acid colour reaction[10] characteristic of a phloroglucinol system. The IR spectrum of IX shows an hydroxyl absorption at 3236 cm^{-1} and a carbonyl absorption at 1704 cm^{-1} (see Ref. 2 for the explanation for the low frequencies). It was further characterized by debenzylation followed by methylation to 2,4,6-trimethoxyphenylacetone (X) which was earlier obtained in connection with our work on the constitution of 2,6-dimethoxyquinone-acetone adduct. The two samples were identical in all respects. All these results show that the acetone adduct of 2,6-dibenzyloxyquinone has the structure XI. The addition of acetone on the 1-carbonyl group in 2,6-dibenzyloxyquinone shows that the steric inhibition of the 1-carbonyl group due to two benzyloxy groups is again not important and that the electromeric deactivation of the 4-carbonyl group is the controlling factor in the reaction.



IX; R = H; R$_1$ = C$_7$H$_7$
X; R = R$_1$ = CH$_3$

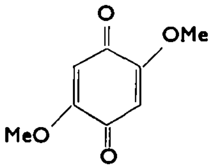


XI

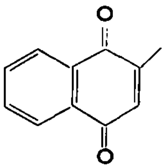
[9] C.-C. Liang, *Biochem. J.* **82**, 429 (1962).

[10] [a] A. L. Kursanov, *Biokhimiya* **6**, 128 (1941); [b] W. E. Hillis and A. Carle, *Austr. J. Chem.* **13**, 390 (1960).

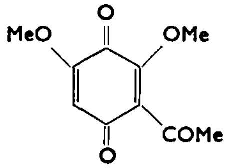
Other typical 1,4-quinones such as 2,5-dimethoxyquinone (XII), lawsone methyl ether (XIII) and 2-acetyl-3,5-dimethoxybenzoquinone (XIV) do not react with acetone and potassium carbonate. In each case nearly 90% of the quinone was recovered unchanged; the remainder undergoing polymerization. The separation of the quinone from the polymeric resins was achieved by chromatography of the reaction mixture on a column of alumina. 2,6-Dimethylbenzoquinone (XV) and 1,4-naphthoquinone (XVI) undergo complete polymerization, no adduct being obtained and no quinone being recovered. *p*-Benzoquinone does not yield an adduct but is partly reduced to hydroquinone and partly polymerized. A similar behaviour for benzoquinone has been reported by Rao *et al.* who obtained quinol dimethyl ether and quinol dibenzoate by treating benzoquinone in alkaline medium with dimethyl sulphate and benzoyl chloride respectively.[11]



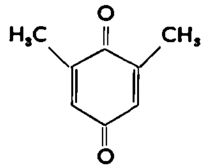
XII



XIII; R = OMe
XVI; R = H



XIV



XV

EXPERIMENTAL

Diacetate derived from 2,6-dimethoxyquinone-acetone adduct. This diacetate was prepared using our earlier procedure.[1] It had the following IR absorptions (nujol) in the carbonyl region: 1770, 1745 and 1724 cm^{-1}. (Found: $COCH_3$, 29·8. $C_{11}H_{12}O_3(OCOCH_3)_2$ requires: $COCH_3$, 27·7%.)

Monoacetate of 2,6-dimethoxyquinone-acetone adduct. The adduct (0·5 g) was dissolved in the cold in a mixture of acetic anhydride (4 ml) and pyridine (1 ml) and the solution kept at room temp for 30 hr. It was then poured into excess of pet. ether (60–80°) yielding a turbid solution which was decanted from a small quantity of a brown semisolid that settled and after cooling in the refrigerator the monoacetate separated as dull white needles. These were recrystallized from benzene–pet. ether as colourless needles, m.p. 111–113°. (Found: C, 57·9; H, 6·2; $COCH_3$, 13·3. $C_{11}H_{12}O_4$ $(OCOCH_3)$ requires: C, 58·2; H, 6·0; $COCH_3$, 16·0%.) Its IR spectrum has the following peaks in the double bond region: 1751, 1709, 1667, 1616 and 1608 cm^{-1}.

2,4-*Dinitrophenylhydrazone of the adduct.* The 2,4-Dinitrophenylhydrazone was prepared as earlier.[1] (Found: C, 50·4; H, 4·6. $C_{17}H_{18}N_4O_8$ requires: C, 50·2; H, 4·4%.) It dissolved in 1% NaOHaq giving a transient green colour changing into brown with excess alkali. The compound was reprecipitated on addition of HCl and after crystallization had the same analytical values, m.p. and identical chromatographic behaviour both on paper and on thin layer (silica gel G with ethyl acetate as the irrigating solvent).

Preparation of the quinones. 2,6-Dibenzyloxybenzoquinone was prepared by the oxidation of 1,2,3-tribenzyloxybenzene according to the method of Clarke and Robertson.[12] 1,4-Naphthoquinone

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[11] G. S. K. Rao, K. V. Rao and T. R. Seshadri, *Proc. Indian Acad. Sci.* **27A**, 245 (1948).

[12] J. R. Clarke and A. Robertson, *J. Chem. Soc.* 302 (1949).

was obtained by the oxidation of 1,4-aminonaphthol hydrochloride.[13] 3,5-Dimethylphenol was oxidized to 2,6-dimethylbenzoquinone using potassium nitrosodisulphonate.[14] Lawsone methyl ether was prepared using the method of Fieser[15] and 2,5-dimethoxyquinone according to the method of Knoevenagel and Bückel.[16]

2-Acetyl-3,5-dimethoxyquinone is a new compound. 2,5-Dihydroxy-4,6-dimethoxyacetophenone has been prepared by the nuclear oxidation of phloracetophenone-2,4-dimethyl ether following the method of Sastry and Seshadri.[17] The quinol (1·0 g) in benzene (100 ml) was shaken at room temp with freshly prepared Ag_2O (from 15 g $AgNO_3$) for 3 hr. The residue from the orange yellow solution was repeatedly washed with benzene and the filtrate and washings combined and evaporated. The residue crystallized from benzene–light petroleum yielding the quinone as shining orange plates (0·7 g), m.p. 98–99°. (Found: C, 57·3; H, 5·1. $C_{10}H_{10}O_5$ requires: C, 57·1; H, 4·8%.)

Reaction with acetone. The reaction of quinones with acetone was carried out following our earlier procedure[1] and the crude reaction products chromatographed in acetone on a column of basic alumina to remove the polymeric resins.

Reaction with 2,6-*dibenzyloxyquinone.* A solution of 2,6-debenzyloxyquinone (5·0 g) in acetone (100 ml) was refluxed with K_2CO_3 (5·0 g) for 3 hr. The solvent was removed from the acetone solution and the residue treated with pet. ether. The solid which separated was crystallized from benzene. The adduct was obtained as pale brown needles (4·0 g), m.p. 126–127°. A sample was dissolved in acetone and the solution chromatographed on alumina. The colourless acetone eluate was concentrated and the residue recrystallized from benzene–pet. ether as fine colourless needles having the same m.p. as the above sample. (Found: C, 72·6; H, 6·1. $C_{23}H_{22}O_5$ requires: C, 73·0; H, 5·8%.) It gave a positive iodoform reaction. Its IR spectrum (nujol) showed the following characteristic absorptions in the hydroxyl and the double bond regions: 3344, 1721, 1664, 1608 (sh.) and 1600 cm^{-1}.

2,6-*Dibenzyloxy-4-hydroxyphenylacetone.* A solution of the adduct (1·0 g) in glacial acetic acid (15 ml) was shaken vigorously with Zn dust (6·0 g) at room temp for 1 hr. The excess Zn was filtered off and washed with warm glacial acetic acid. The combined filtrate and washings were distilled under red. press and water added to the residue. The solid which separated on cooling the mixture in the refrigerator was collected and dried. On crystallization from benzene–pet. ether (charcoal) it was obtained as fine colourless needles (0·85 g), m.p. 120–121°; the m.p. was depressed on admixture with a sample of the adduct. It was insoluble in water but readily dissolved in NaOHaq. It gave a purple colour with vanillin and HCl and no ferric reaction. It gave a positive iodoform reaction. (Found: C, 75·8; H, 6·4. $C_{23}H_{22}O_4$ requires: C, 76·2; H, 6·1%.) The IR spectrum (nujol) in the hydroxyl and double bond regions contained the following peaks: 3236, 1704 and 1616 cm^{-1}.

2,4,6-*Trimethoxyphenylacetone.* 2,6-Dibenzyloxy-4-hydroxyphenylacetone (0·3 g) in ethyl acetate (25 ml) was stirred in an atmosphere of H_2 in the presence of Pd–C (0·2 g) until there was no more absorption of H_2. The catalyst was then filtered off and washed with ethyl acetate. The filtrate and washings were combined and the solvent evaporated yielding a sticky mass which could not be solidified but gave a deep red colour with vanillin and HCl.

The above compound was methylated with excess dimethyl suphate (0·5 ml) and anhydrous K_2CO_3 (1·0 g) in dry acetone (15 ml) during 5 hr. The solvent was removed from the mixture and water added to the residue. The solution was made strongly alkaline with NaOH and then extracted with $CHCl_3$ (5 × 15 ml). The dried $CHCl_3$-extract was distilled and the residue treated with pet. ether and left in the refrigerator overnight. The solid which separated was crystallized from $CHCl_3$–pet. ether as colourless prisms, m.p. 88°. A mixed m.p. with an authentic sample[3] of 2,4,6-trimethoxyphenylacetone was undepressed.

Reaction with 2,5-*dimethoxybenzoquinone, lawsone methyl ether and* 2-*acetyl*-3,5-*dimethoxybenzoquinone.* When the above quinones were treated with acetone and K_2CO_3 as described the starting materials in the main were recovered unchanged. When the K_2CO_3 was filtered off and the brown filtrates purified by chromatography on alumina, the quinones were recovered (90%). The minor

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[13] L. F. Fieser, in *Organic Synthesis* (Edited by Gilman and Blatt) Coll. Vol. 1, p. 383. J. Wiley, New York (1958).

[14] H.-J. Teuber and W. Rau, *Chem. Ber.* **86**, 1036 (1953).

[15] L. F. Fieser, *J. Amer. Chem. Soc.* **70**, 3165 (1948).

[16] E. Knoevenagel and C. Bückel, *Ber. Dtsch. Chem. Ges.* **34**, 3993 (1901).

[17] V. D. N. Sastry and T. R. Seshadri, *Proc. Indian Acad. Sci.* **23A**, 262 (1946).

amounts of the polymeric resins formed in each case remained as dark brown bands at the top of the column.

Reaction with 1,4-*naphthoquinone and* 2,6-*dimethylbenzoquinone*. Treatment of the above quinones with acetone and K_2CO_3 for 4 hr resulted in complete polymerization. In each case the reaction mixture after removal of K_2CO_3 and evaporation of the solvent gave a dark brown sticky residue which could not be purified by crystallization. When chromatographed in the usual way the material was completely absorbed on the top of the column.

Reaction with p-*benzoquinone*. A solution of *p*-benzoquinone (5·0 g) in acetone (100 ml) was refluxed with anhydrous K_2CO_3 (5·0 g) for 4 hr. On evaporation of the solvent from the filtrate, a dark brown semisolid was obtained. This was redissolved in acetone and the solution passed through a column of alumina. The colourless eluate was concentrated and cooled yielding clusters of colourless needles (2·0 g), m.p. 172–173°, identified as hydroquinone. The acetate prepared with acetic anhydride and pyridine melted at 124° alone and on admixture with an authentic sample of quinol diacetate.