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QUINONES AND QUINONE METHIDES—V

FURTHER REARRANGEMENTS OF THE DIMER FROM 5-METHOXY-2-(4-METHOXYPHENYLMETHYL)-1,4-BENZOQUINONE

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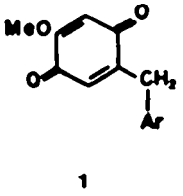
Abstract—In strongly acid solutions the dimer 3 dissociates to the quinone 1 and quinone methide 2 which recombine with elimination of *p*-methoxybenzyl alcohol to form the xanthylium salt 9a. With zinc and acetic acid 3 yields isomeric meso- and dl-ethylenediquinol derivatives 14a. Sodium borohydride reduction of 3 yields an alcoholic quinol 25a which rapidly reoxidizes to the spiro-tetrahydrofuran derivative 24a. Possible mechanisms which may be involved in the formation of these rearranged products are discussed.

In the preceeding paper[1] it was reported that in pyridine the benzyl-quinone 1 tautomerizes to an intermediate *ortho*-quinone methide 2 which then dimerizes to yield products 3, 4, 5 and 6. The dimers 4, 5 and 6 are formed by the rearrangement of 3 in basic media via the intermediate quinol 7. During the structural investigation of the dimer 3 it was observed that it undergoes further unusual rearrangements when treated with acids or acidic reducing agents. These rearrangements which appear to result from initial dissociation of 3 into the *ortho*-quinone methide 2, are described in this communication. A rearrangement which occurs upon borohydride reduction of 3 is also reported.

Reaction of 3 *with acids.* On silicic acid tlc, 3 is readily detected by formation of a bright red spot on exposure to HCl fumes. The red product was isolated by warming a solution of 3 in acetic acid with conc. hydrochloric acid. The chloride which separated crystallized



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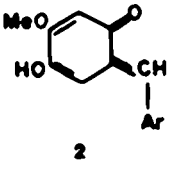

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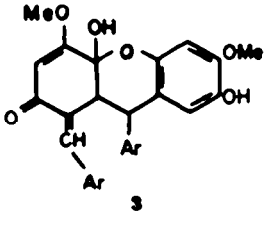

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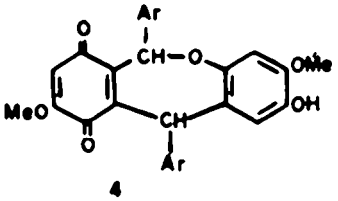

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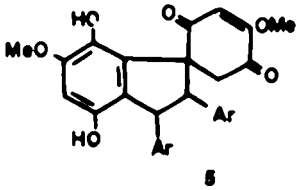

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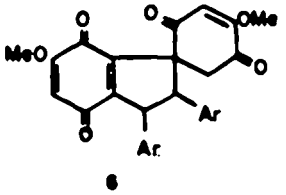

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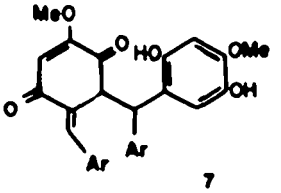

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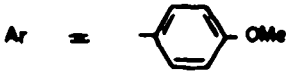
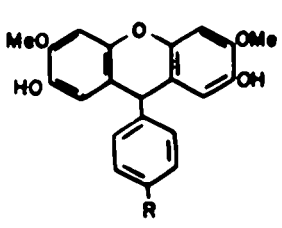


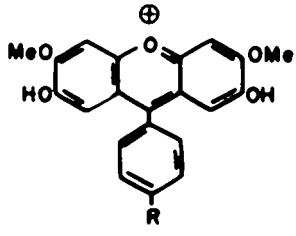
from aqueous perchloric acid to give orange-red needles of a perchlorate, $C_{22}H_{19}O_6.ClO_4$. With sodium borohydride the perchlorate was reduced to a colorless phenol, $C_{22}H_{20}O_6$, whose PMR spectrum showed the presence of only three OMe groups as singlets at δ3.74(3 H) and δ3.85(6 H), a methine proton as a singlet at δ4.99, and two OH groups as a singlet at δ5.34. Four aromatic protons appeared as 2 H singlets at δ6.53 and δ6.59, and the four aromatic protons of a *single* *p*-methoxyphenyl ring as doublets at δ6.77 and δ7.06. The symmetry of the two phenolic aromatic rings was confirmed by the formation of a diacetate in which the protons of the two acetyl groups appeared as a 6 H singlet at δ2.22. On the basis of these data the phenol is the 5 - (4 - methoxyphenyl) - xanthen derivative **8a**, and the red perchlorate is the corresponding xanthylium salt **9a**.

Some insight into the reaction sequence leading to the elimination of a *p*-methoxyphenyl group was provided by repeating the reaction in methanol with only a trace of HCl. TLC then showed the presence of xanthylium salt **9a** and traces of the hydroquinone **10a**. The major products, however, were *p*-methoxybenzaldehyde (isolated as its crystalline dimedone product) and a colorless bisquinol, which was readily isolated as its crystalline tetraacetate, $C_{22}H_{18}O_3(OCOCH_3)_4$ (m.p. 178–179°). The bisquinol contains only three OMe groups. In the PMR spectrum of its tetraacetate the protons of the four acetoxyl groups appeared as singlets at δ2.07(6 H) and δ2.24(6 H), three OMe groups as a singlet at δ3.80(9 H), and a methine group as a singlet at δ5.47. Four aromatic protons occurred as singlets at δ6.51(2 H) and δ6.73(2 H), and the four aromatic protons of a *p*-methoxyphenyl ring as doublets at δ6.81(2 H) and δ6.97(2 H). The chemical shift of the methine proton indicates its attachment to three aromatic rings as in **11b**.

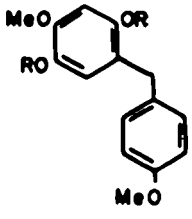
The formation of the hydroquinone **10a** and the bisquinol **11a** from **3** in acid solutions involves at least two reduction reactions. However, tlc showed the absence in the reaction mixture of dimer oxidation products such as **12**, **6**, **4** which would be expected if either **3** acts as a reductant or its previously described rearrangement products (**5** and the quinol precursor of **4**) are partially formed in the acid reaction and then function as reducing agents. The formation of *p*-methoxybenzaldehyde, on the other hand, indicates that the reductant in the reaction is the eliminated *p*-methoxybenzyl alcohol. The reaction sequence proposed in Scheme 1 suggests that in acid solutions **3** dissociates via the quinol **7** into the quinone **1** and quinone methide **2**. Recombination of **1** and **2** with elimination of *p*-methoxybenzyl alcohol yields an intermediate quinhy-



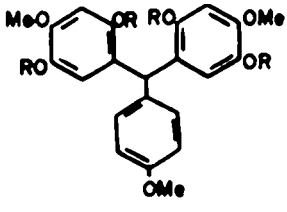
8a: R = OMe
b: R = H



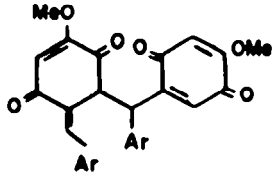
9a: R = OMe
b: R = H



10a: R = H
b: R = $COCH_3$



11a: R = H
b: R = $COCH_3$



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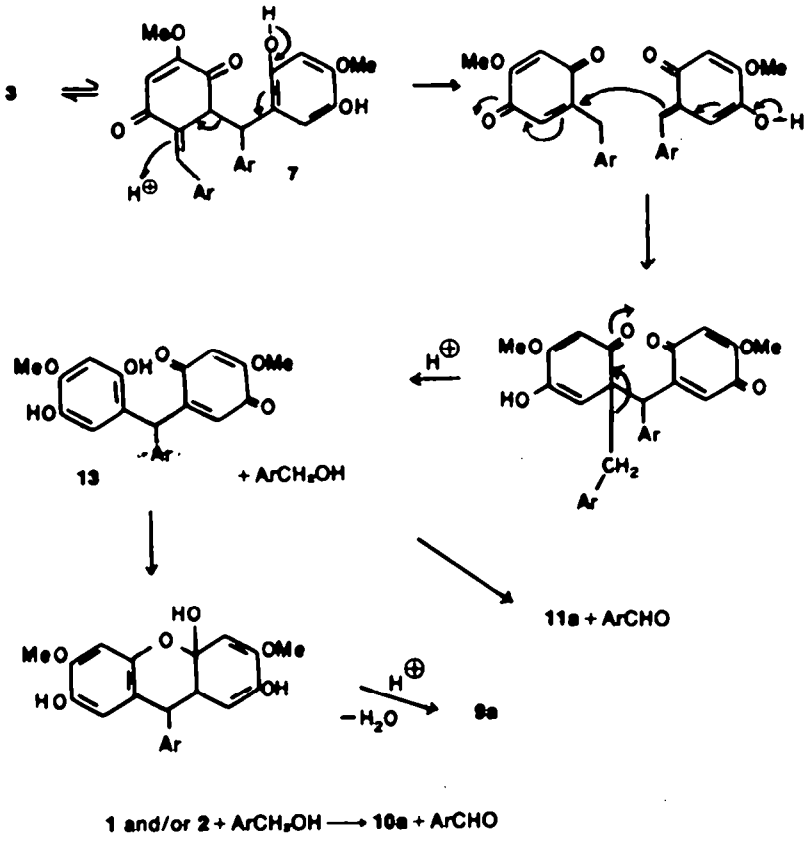
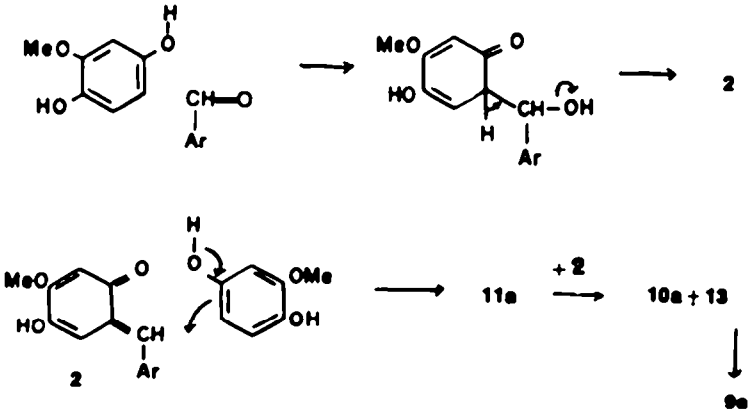


Scheme 1.

drone 13, which partly cyclizes to the xanthylium salt 9a and is partly reduced by the *p*-methoxybenzyl alcohol to the bisquinol 11a. An analogous reduction of 1 and/or 2 by *p*-methoxybenzyl alcohol accounts for the formation of traces of the hydroquinone 10a.

In the course of this investigation the xanthylium salt 9a and the bisquinol 11a were synthesized without recourse to dimer 3 by an interesting condensation of *p*-methoxybenzaldehyde with methoxyhydroquinone. It is well known that dihydric phenols, e.g. resorcinol condense with aromatic aldehydes in acid solutions to give cyclic tetramers derived from four molecules of the aldehyde and four molecules of the phenol.[2,3] However, when methoxyhydroquinone is briefly warmed with *p*-methoxybenzaldehyde in aqueous formic acid, the major product is the bisquinol 11a (isolated as the tetraacetate 11b). With longer reaction times the yield of 11a markedly decreases with formation of the xanthylium salt 9a and hydroquinone 10a, both of which are readily crystallized from the reaction mixture in good yields. Benzaldehyde condenses similarly with methoxyhydroquinone to give 9b, identified by its sodium borohydride reduction to the xanthen 8b. The formation of these products indicates that the condensation of methoxyhydroquinone and *p*-methoxybenzaldehyde (Scheme 2) involves initial formation of the *ortho*-



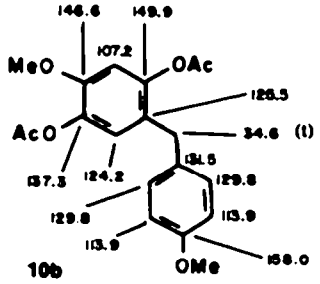
Scheme 2.

quinone methide 2, which in part reacts with more methoxyhydroquinone to form the bisquinol 11a. Redox reaction between 11a and 2 leads to the hydroquinone 10a and the quinhydrone 13 which cyclizes to 9a.

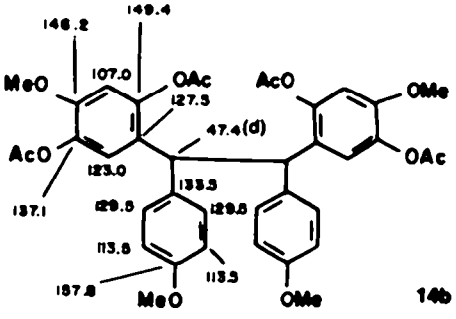
Reductive acetylation of 3. With acetic anhydride, zinc dust and sodium acetate dimer 3 gave traces of the diacetate 10b and good yields of a colorless, crystalline product, shown by tlc and PMR to be a mixture (about 3:1) of two similar tetraacetates, $C_{30}H_{26}O_4$ $(OCOCH_3)_4$, m.p. 257° (minor product) and m.p. 183° (major product). Methylation of the tetraacetates (with replacement of acetoxyl groups) gave the corresponding octa-O-methyl compounds, m.p. 148–149° and 216°, respectively, while alkaline hydrolysis in the presence of sodium dithionite gave the bisquionols, $C_{30}H_{30}O_8$, which reformed the original tetraacetates upon acetylation.

The PMR spectrum of the tetraacetate, m.p. 257° indicated molecular symmetry, the four acetoxyl groups appearing as two singlets at δ2.20(6 H) and δ2.25(6 H), the four OMe's as two singlets at δ3.71(6 H) and δ3.74(6 H), and two doubly benzylic methine groups as a singlet at δ4.52(2 H). Four aromatic protons appear as singlets at δ6.56(2 H) and δ6.98(2 H), while the aromatic protons of the two *p*-methoxyphenyl rings appear as doublets at δ6.60(4 H) and δ6.76(4 H). The PMR spectrum of the lower melting acetate is similar except that the 2 H singlet of the two methine protons shifts downfield to δ4.61. These data indicate that the two acetates are meso- and dl-forms of the ethylenediquinol derivative 14b, the specific stereochemical assignment being unknown. In agreement with the symmetrical structure 14b the ^{13}C NMR spectra of the two tetraacetates are very similar and both show only 19 signals, eleven of which are due to CH groups. These chemical shifts can be assigned with little ambiguity by comparison with the shifts of the model hydroquinone diacetate 10b. Assignments (for the lower melting tetraacetate) are shown in 14b.

As expected, the reduction of 3 with zinc and acetic acid is similar to the reductive acetylation reaction, the hydroquinone 10a and a crystalline mixture of the ethylenediquinol derivatives 14a being obtained.



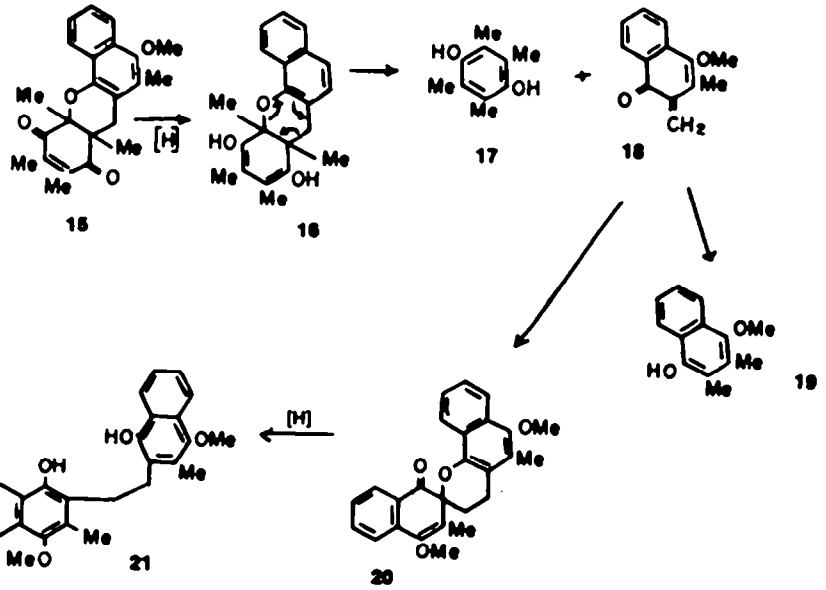
10b

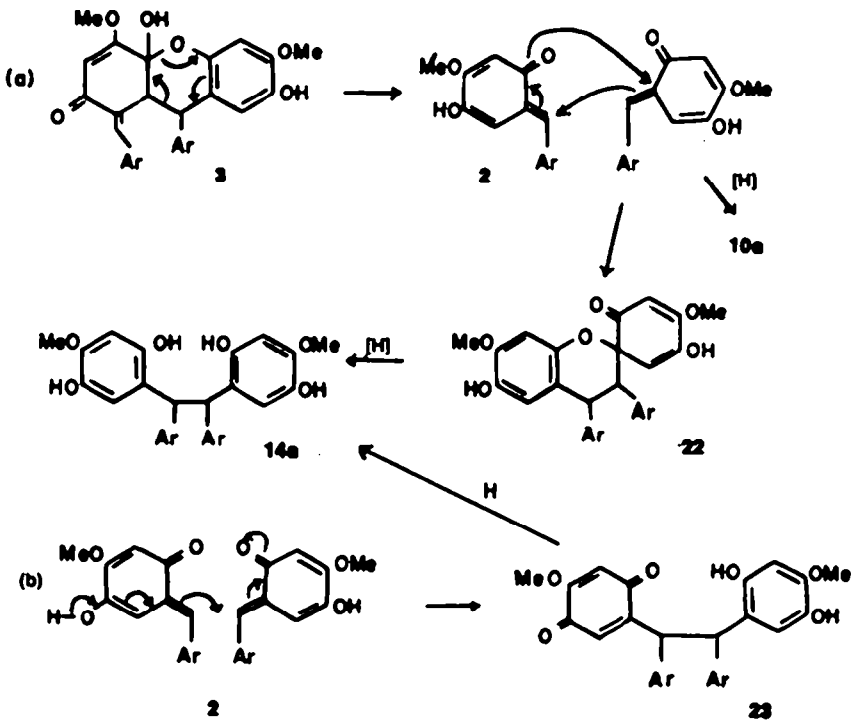


14b

The reaction of 3 with acidic reducing agents is similar to a novel method for generating *ortho*-quinone methides recently described by Dean and Matkin.[4] These authors reported that reduction of the xanthen 15 with zinc and acetic acid yields the phenols 17 and 19 and the ethylene diquinol derivative 21; the reaction involved initial reduction of the enedione of 15, followed by a retro-Diels–Alder reaction of the product 16 to form quinol 17 and quinone methide 18. 18 was partly reduced to the quinol derivative 19 and partly dimerized to the spiran 20, reduction of which led to 21.

The reduction products formed from 3 in acid media can be accounted for by a similar process except that initial reduction is not required for dissociation into the *ortho*-quinone methide 2. 2 is partly reduced to the

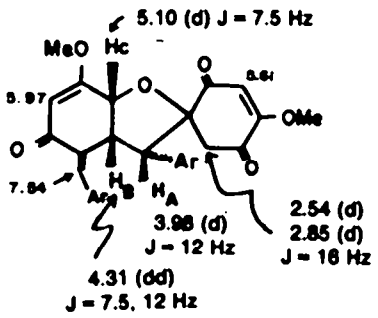




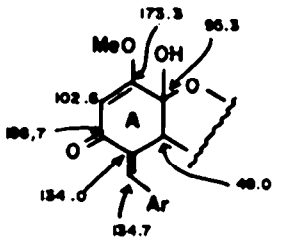
Scheme 3.

hydroquinone 10a, and partly dimerized to an intermediate spiran 22 which is then reduced to 14a (Scheme 3a). An alternative dimerization mechanism which appears entirely reasonable (Scheme 3b) involves Michael-type addition of two molecules of the quinone methide 2 to give the quinhydrone 23.

Sodium borohydride reduction of 3. Dimer 3 is rapidly reduced by sodium borohydride in methanol to a mixture of 14a (in trace amounts) and a new quinol which rapidly reduces ammoniacal silver nitrate. This quinol could not be isolated and purified directly by crystallization because of its susceptibility to oxidation. When solutions of the quinol in methanol are allowed to stand exposed to air it is converted into two isomeric, colorless oxidation products, $C_{28}H_{28}O_6$, m.p. 254–255° (major product) and m.p. 243–245° (minor product), both of which can be



24a



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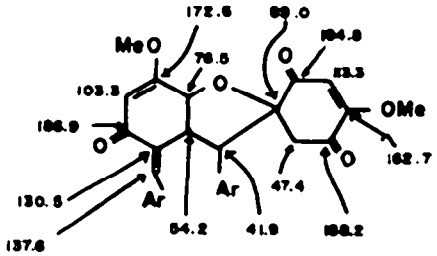
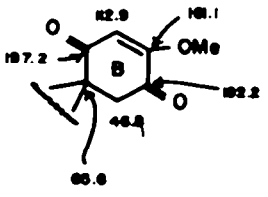


24b



5 (DIACETATE)

crystallized. Better yields of the oxidation products can be obtained by oxidation of the quinol in acetone with silver oxide. These oxidation products do not form acetates, and their IR, PMR and ^{13}C NMR spectra reveal the presence of (A) and (B) rings similar to the (A) ring of 3 and the (B) ring of the spirocyclohexene derivatives 5, 6 respectively. On the basis of these spectra the oxidation products have been identified as two stereoisomers of the spiro-tetrahydrofuran derivative 24.

In accord with structure 24 the IR spectrum of the major oxidation product shows multiple CO absorption bands at 1620, 1655, 1680, 1710 cm^{-1}, and its PMR spectrum shows the presence of a methylene group adjacent to CO as geminally coupled doublets (J = 16 Hz) at δ2.54(1 H) and δ2.85(1 H). Three olefinic protons occur as singlets at δ5.61, 5.97, 7.54. A methine proton appears as a doublet (J = 12 Hz) at δ3.98, coupled to a methine proton at δ4.31 (dd, J = 7.5, 12 Hz) which is in turn coupled to a methine proton at δ5.10 (d, J = 7.5 Hz). Assignment of these proton signals is shown in 24a. The rigidity of the A ring caused by its one endocyclic and two exocyclic double bonds necessitates a *cis* ring fusion with the heterocyclic 5-membered C ring and causes near eclipsing of H_C and H_B. The large geminal coupling (J_{AB} = 12 Hz) between H_B and H_A suggests that they are arranged *cis* to one another and models show them to be nearly eclipsed. The three protons thus lie on one side of the plane of the C ring.

The coupling constants observed for the minor isomer of 24a are the same although the chemical shifts of some of protons are different (Experimental). This suggests that the two isomers differ by the configuration at the asymmetric spiro C atom but the data do not provide a basis for assigning a specific configuration to either isomer.

Structure 24 was further confirmed by the ^{13}C NMR spectrum of the major oxidation product, significant carbon chemical shifts being assigned as indicated in 24b. The A and B ring carbon signals of 24b agree quite closely with the signals of the corresponding carbons in the A ring of 3 and the spiran B ring of the diacetate of dimer 5. As expected the spiran ring junction C atom in 24b, which is linked to O, shifts downfield to δ9.0, compared with the shift (65.6) of the corresponding C in 5.

Although, as previously mentioned, the quinol formed by borohydride reduction of 3 could not be purified directly because of its ease of oxidation to 24, it readily yielded stable, crystalline diacetyl and triacetyl derivatives. Furthermore, on methylation it gave a di-O-Me derivative which, on acetylation, formed a monoacetate, indicating that the reduction product contains two phenolic and one alcoholic OH groups. Spectral analysis of these acetyl and Me derivatives established structure 25a for the reduction product. For example, the IR spectrum of the di-O-methylmonoacetyl derivative has CO absorption bands at 1745, 1655 cm^{-1}, and the PMR spectrum shows the presence of alcoholic OAc (singlet at δ1.50) and six OMe groups. The methine H_A proton occurs as a doublet at δ4.76, coupled to the H_B methine proton at δ4.98, which is in turn coupled to the H_C proton at δ6.00. The latter proton appears as a double doublet due to allylic coupling with the olefinic H_D proton at δ5.50. These and other proton assignments are indicated in 25e. The PMR spectrum of the dimethyl derivative 25c is similar to that of its monoacetate 25e except that the alcoholic proton H_C undergoes an expected upfield shift to δ4.82 where its signal overlaps those of the H_A and H_B protons.

The formation of 25a from 3 involves reduction of the tautomeric quinol 7. Oxidation of 25a to an intermediate quinone, followed by an intramolecular Michael-type addition of the alcoholic OH to the quinone system accounts for the formation of the spiran 24 (Scheme 4).

EXPERIMENTAL

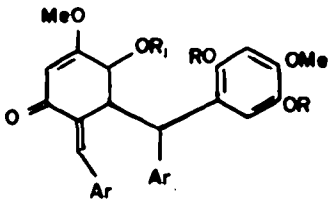
All m.ps are uncorrected. PMR spectra were determined in $CDCl_3$ with TMS as internal standard on a modified Varian HA-100 instrument. ^{13}C NMR spectra were determined on a PFT-100 Spectrophotometer in $CDCl_3$ with TMS as internal reference. IR data were obtained in mineral oil on a Perkin–Elmer model 237B grating IR spectrophotometer.

Reaction of methoxyhydroquinone and p-methoxybenzaldehyde

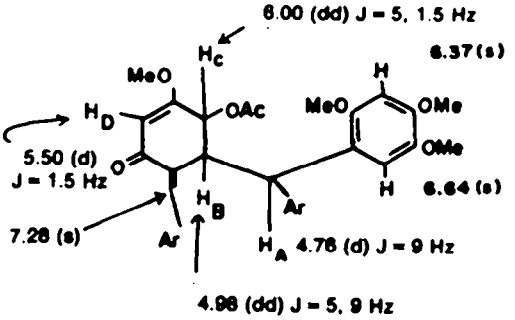
(a) A soln of methoxyhydroquinone (7 g) and *p*-methoxybenzaldehyde (3.4 g) in formic acid (25 ml) and water (25 ml) was heated on a steam-bath for 24 hr, diluted with 10% aqueous perchloric acid (200 ml) and ether (100 ml) and cooled. The crystalline orange-colored salt was collected (4.25 g) and recrystallized from AcOH–10% aq perchloric acid to give 9a as orange-red needles, m.p. 265–267°. (Found: C, 55.1; H, 4.22. $C_{22}H_{19}O_{10}Cl$ requires: C, 55.2; H, 4.00%); PMR spectrum (CF_3CO_2H): δ4.14, 3 H, s; δ4.34, 6 H, s; δ7.38, 2 H, d, J = 9 Hz; δ7.48, 2 H, s; δ7.60, 2 H, d, J = 9 Hz; δ7.67, 2 H, s.

After separation of the xanthylium salt the ether layer was separated from the filtrate, dried and evaporated. The residue was dissolved in warm benzene. On cooling colorless crystals separated (2.05 g). Recrystallized from aqueous MeOH and from benzene 10 was obtained as colorless needles, m.p. 114°, identical (tlc, m.m.p., PMR spectrum) with authentic material. The product formed a *diacetate*, m.p. 83–84°, identical with authentic 10b.

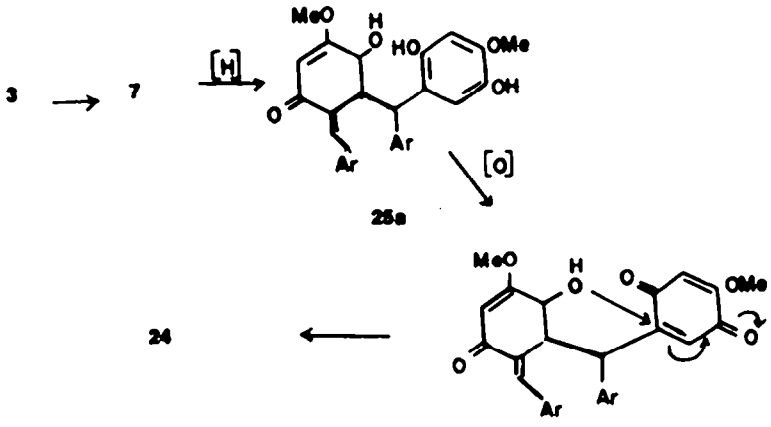
(b) A soln of methoxyhydroquinone (2.80 g) and *p*-methoxybenzaldehyde (1.36 g) in formic acid (10 ml) and water (5 ml) was heated for 2 hr on a steam-bath, diluted with 10% HCl aq (50 ml)



25a: R = R₁ = H
b: R = $COCH_3$, R₁ = H
c: R = R₁ = $COCH_3$
d: R = Me, R₁ = H
e: R = Me, R₁ = $COCH_3$



25e



Scheme 4.

and ether (50 ml) and cooled. The chloride 9a, which separated as orange needles, was filtered (0.70 g). The ether layer was separated from the aqueous filtrate, dried and evaporated. TLC on silicic acid showed the presence of major amounts of a low R_f phenolic compound which rapidly reduced ammoniacal $AgNO_3$. This was isolated as its tetraacetate by warming the crude product with Ac_2O (10 ml) and pyridine (1 ml). The gummy acetate, obtained on adding water, crystallized from MeOH. Recrystallized from Me_2CO–MeOH the *tetraacetate* 11b separated as colorless needles, m.p. 178–179° (1.54 g). (Found: C, 63.6; H, 5.28. $C_{30}H_{30}O_{11}$ requires: C, 63.6; H, 5.34%).

3,7 - *Dihydroxy* - 2,8 - *dimethoxy* - 5 - (4 - *methoxyphenyl)xanthen* 8a. $NaBH_4$ (0.4 g) was added to a suspension of 9a (1.0 g) in MeOH (15 ml). After 1 min the colorless soln was diluted with 1% $NaHSO_3$aq (100 ml) and the solid was collected. Recrystallized from MeOH containing a drop of AcOH 8a was obtained as cream-colored needles, m.p. 195–197° (dec) (0.70 g). (Found: C, 69.6; H, 5.27. $C_{22}H_{20}O_6$ requires: C, 69.5; H, 5.30%).

With Ac_2O and pyridine 8a formed a *diacetate*, colorless, glistening needles from Me_2CO–MeOH, m.p. 200–201°. (Found: C, 67.4; H, 5.28. $C_{26}H_{24}O_8$ requires: 67.2; H, 5.21%); PMR spectrum: δ2.22, 6 H, s; δ3.77, 3 H, s; δ3.83, 6 H, s; δ5.06, 1 H, s; δ6.60, 2 H, s; δ6.70, 2 H, s; δ6.81, 2 H, d, J = 9 Hz; δ7.08, 2 H, d, J = 9 Hz.

3,7 - *Dihydroxy* - 2,8 - *dimethoxy* - 5 - *phenylxanthylium perchlorate* 9b. A soln of 2-methoxyhydroquinone (1.4 g) and benzaldehyde (1.06 g) in 30% AcOH aq (30 ml) containing malonic acid (3.0 g) was heated under reflux for 48 hr, diluted with water (100 ml) and washed with ether. Conc. HCl (30 ml) was added to the aqueous layer whereupon the xanthylium chloride precipated. Recrystallized from glacial AcOH in 5% aqueous perchloric acid the *xanthylium perchlorate* 9b separated as orange needles, m.p. 268–269° (1.45 g). (Found; C, 56.2; H, 3.80. $C_{21}H_{17}O_9Cl$ requires: C, 56.2; H, 3.82%).

$NaBH_4$ (0.4 g) was added to a suspension of 9b (0.9 g) in MeOH (15 ml). After 3 min water was added and the solid product was crystallized from MeOH.

3,7 - *Dihydroxy* - 2,8 - *dimethoxy* - 5 - *phenylxanthen* 8b separated as colorless needles, m.p. 196–198° (dec, 0.61 g). (Found: C, 72.0; H, 5.12; MeO, 17.7. $C_{21}H_{20}O_5$ requires: C, 72.0; H, 5.18, 2 MeO, 17.7%). The *diacetate* of 8b crystallized from $CHCl_3$–MeOH as colorless needles, m.p. 224°. (Found: C, 69.1; H, 5.04; MeO, 14.1; CH_3CO, 20.0. $C_{25}H_{24}O_7$ requires: C, 69.1; H, 5.10; 2 MeO, 14.3; 2 CH_3CO, 19.8%); PMR spectrum: δ2.21, 6 H, s; δ3.82, 6 H, s; δ5.89, 1 H, s; δ 6.59, 2 H, s; δ6.69, 2 H, s; δ 7.06–δ7.40, 5 H, m.

Reaction of dimer 3 *with hydrochloric acid*

(a) Mixture of dimer 3 (6.0 g), 9% HCl (60 ml) and AcOH (60 ml) was heated to boiling for 2 min, diluted with conc. HCl (60 ml) and allowed to stand for 24 hr. The orange-red powder was collected (1.9 g) and the filtrate treated with more conc. HCl (60 ml) to produce a second crop of salt (1.1 g). Dissolved in hot AcOH containing 0.5% conc. HCl the crude xanthylium salt recrystallized as dark orange fine needles, m.p. 300–315°. The sharper melting perchlorate salt was prepared by recrystallization from AcOH 10% aqueous perchloric acid and separated as orange-red needles, m.p. 265–267°. The PMR spectrum, m.p. and m.m.p. were identical to those of 9a (*vide supra*). Reduction of the xanthylium salt with $NABH_4$ in MeOH gave after acetylation a diacetate identical (m.p., m.m.p., PMR spectrum) with the diacetate of 8a described above.

(b) A soln of the dimer 3 (1.0 g) in THF (15 ml) and MeOH (15 ml) containing a drop of 36% HCl was concentrated to 15 ml, heated under reflux for 3 hr, and evaporated. The residue was extracted with warm benzene, leaving an insoluble residue which was acetylated by warming with Ac_2O and pyridine. The acetate crystallized from Me_2CO–MeOH to give 11b, m.p. 178–179° (0.63 g). (Found: C, 63.7; H, 5.42. $C_{30}H_{30}O_{11}$ requires: C, 63.6; H, 5.34%). This product was identical (tlc, m.m.p., NMR spectrum) with the tetraacetate obtained by reaction of methoxyhydroquinone with *p*-methoxybenzaldehyde.

Tlc of the benzene soluble fraction of the reaction products showed the presence of 10a and of a compound which formed a 2,4-DNP derivative and had R_f values identical to those of *p*-methoxybenzaldehyde. The benzene soln was evaporated to a gum which was extracted with boiling 50% petroleum ether–ether. The residue remaining after evaporation of the solvents was refluxed for 15 min with dimedone (600 mg) in EtOH–water 1:1 (8 ml) containing a drop of 5% ethanolic KOH. Addition of excess of water precipitated a solid which crystallized from MeOH–water to give colorless needles, m.p. 141–143° (148 mg). This material was identical (tlc, m.p., m.m.p.) with the authentic dimedone condensation product prepared from *p*-methoxybenzaldehyde.

Reductive acetylation of 3. A mixture of dimer 3 (3.0 g), anhyd NaOAc (4.0 g), Zn dust (4.0 g) and Ac_2O (20 ml) was heated briefly to boiling and then on a steam-bath for 10 min. The filtered soln was diluted with water and allowed to stand until the oily product solidified. The product crystallized from Me_2CO–MeOH to give colorless needles (1.8 g). These crystals melt over a wide range (170–235°) and tlc and the PMR spectrum indicate the presence of two acetates in an approximate ratio of 3:1. TLC of the MeOH filtrate from the crystalline product showed the presence among other unidentified products of trace amounts of 10b.

The crystalline product (1.8 g) was heated to boiling with benzene (20 ml) and the undissolved residue (0.62 g; m.p. 253–255°) was collected. This was recrystallized from THF–MeOH to give the pure *tetraacetate* 14b as colorless needles, m.p. 257°. (Found: C, 66.4; H, 5.65. $C_{30}H_{30}O_{12}$ requires: C, 66.5; H, 5.58%); A soln of this tetraacetate (0.15 g) in Me_2CO (15 ml) and MeOH (5 ml) was heated under reflux with Me_2SO_4 (2.0 ml) and K_2CO_3 (4 g) for 3 hr, concentrated, and diluted in water. The solid product was recrystallized from Me_2CO–MeOH to give a *tetra-O-methyl derivative of* 14a as colorless, glistening plates, m.p. 148–149°

(0.11 g). (Found: C, 71.0; H, 6.67. $C_{34}H_{38}O_9$ requires: C, 71.1; H, 6.67%); PMR spectrum: δ3.68, 6 H, s; δ3.71, 6 H, s; δ3.74, 6 H, s; δ3.76, 6 H, s; δ5.15, 2 H, s; δ6.32, 2 H, s; δ6.64, 4 H, d, J = 9 Hz; δ6.90, 2 H, s; δ7.13, 4 H, d, J = 9 Hz. A soln of the tetraacetate (0.50 g) in THF (20 ml) and MeOH (20 ml) was treated at b.p. with 10% NaOHaq (15 ml) containing sodium dithionite (2 g). After 30 min water was added and the soln acidified. The crystalline product was recrystallized from wet Me_2CO–MeOH to give the *diquinonol* 14a as almost colorless prisms, m.p. 237–238° (dec; 0.19 g). (Found: C, 67.1; H, 5.69. $C_{30}H_{30}O_8 \cdot H_2O$ requires: C, 67.1; H, 6.01%). The diquinol was reacetylated with Ac_2O and pyridine. The tetraacetate 14b, m.p. and m.m.p. 257°, was obtained.

The benzene soln from which the crude tetraacetate (m.p. 257°) had been filtered, was concentrated and diluted with skelly solve F to give colorless needles, m.p. 178–182° (1.0 g). Tlc and PMR spectrum of this product showed the presence of traces of the higher melting acetate which could not be removed by repeated recrystallization. The product was hydrolyzed by warming the soln in Me_2CO (30 ml) and MeOH (30 ml) with 10% NaOHaq (15 ml) containing sodium dithionite (2 g). After 10 min the soln was diluted with water and acidified. The solid product was repeatedly recrystallized from THF–MeOH and from Me_2CO to give an isomer of the diquinol 14a as cream-colored microprisms, m.p. 256–258° (0.52 g). (Found: C, 69.3; H, 5.85. $C_{30}H_{30}O_8$ requires: C, 69.5; H, 5.83%). Acetylation of the diquinol (0.4 g) with warm pyridine (2.0 ml) and Ac_2O (1.0 ml) gave an isomer of 14b, hygroscopic colorless needles from Me_2CO–MeOH, m.p. 183–184°. (Found: C, 64.9; H, 5.79. $C_{38}H_{38}O_{12} \cdot H_2O$ requires: C, 65.2; H, 5.72%); PMR spectrum: δ2.20, 6 H, s; δ2.25, 6 H, s; δ3.71, 12 H, s; δ4.61, 2 H, s; δ6.50, 2 H, s; δ6.65, 4 H, d, J = 9 Hz; δ6.84, 2 H, s; δ6.91, 4 H, d, J = 9 Hz. MS: 642 (0.4) ($M^+ - C_2H_2O$, −2 H), 600 (0.8) ($M^+ - 2\ C_2H_2O$, −2 H), 598 (0.8) ($M^+ - 2\ C_2H_2O$, −4 H), 556 (2.7) ($M^+ - 3\ C_2H_2O$, −4 H), 514 (2.97) ($M^+ - 4\ C_2H_2O$, −4 H), 343 (75) ($M^+/2$), 301 (100), 259 (59), 257 (37), 243 (12), 227 (27). Benzoylation of the diquinol gave a *tetrabenzoate*, colorless needles from THF–MeOH m.p. 246–247°. (Found: C, 74.4; H, 4.87. $C_{58}H_{46}O_{12}$ requires: C, 74.5; H, 4.96%); PMR spectrum: δ3.70, 6 H, s; δ3.75, 6 H, s; δ4.80, 2 H, s; δ6.63, 2 H, s; δ6.68, 4 H, d, J = 8 Hz; δ6.96, 4 H, d, J = 8 Hz; δ6.99, 2 H, s; δ7.38–δ7.76, 12 H, m; δ8.00–δ8.22, 8 H, m. Methylation of the tetraacetate (m.p. 183–184°) (0.5 g) in Me_2CO–MeOH as described for the tetraacetate (m.p. 257°) gave a tetra-O-Me derivative of 14a, colorless, glistening plates from Me_2CO–MeOH, m.p. 216° (0.31 g). (Found: C, 70.9; H, 6.56. $C_{34}H_{38}O_8$ requires: C, 71.0; H, 6.67%); PMR spectrum: δ3.62; 6 H, s; δ3.69, 6 H, s; δ3.76, 6 H, s; δ3.78, 6 H, s; δ5.17, 2 H, s; δ6.33, 2 H, s; δ6.62, 4 H, d, J = 9 Hz; δ6.89, 2 H, s; δ7.12, 4 H, d, J = 9 Hz.

Reaction of 3 *with zinc and acetic acid.* A mixture of the dimer 3 (1.0 g), Zn dust (3 g) and glacial AcOH (5 ml) was heated briefly to boiling and then on a steam-bath for 15 min. The filtered soln was added to excess of water. The off-white ppt was dissolved in Me_2CO, diluted with MeOH and concentrated until cream-colored crystals separated (m.p. 235–255°; 0.19 g). Tlc showed that the product was a mixture of the two diquinols 14a. On acetylation with Ac_2O and pyridine the product formed a mixture of acetates, m.p. 170–230°, identical (tlc, PMR spectrum) with the mixed tetraacetates obtained by reductive acetylation of the dimer. The MeOH filtrate from the crystalline diquinols was evaporated and the residue extracted with ether. Tlc of the ether soln showed the presence of 10a. This was isolated as its diacetate by acetylation of the ether soluble fraction and crystallization of the product from MeOH. 10b was obtained as colorless needles, (0.06 g) m.p. 84°, identical (m.m.p., tlc, PMR spectrum) with an authentic specimen.

Reduction of dimer 3 *with sodium borohydride*

(a) A suspension of dimer 3 (5.0 g) in MeOH (125 ml) was stirred with three portions of $NaBH_4$ (0.6 g each) added at 10 min intervals. The resulting clear yellow soln was diluted with water (700 ml) containing AcOH (8 ml) causing precipitation of a pale yellow solid which was collected and dried *in vacuo* (4.5 g). Because this material was so easily oxidized when in soln it was not possible to obtain a pure sample by recrystallization; chemical modifications described below gave stable pure derivatives.

(b) *Acetylation.* A mixture of the crude reduction product (600 mg), Ac_2O (4 ml) and pyridine (6 drops) was warmed on the steam-bath for 5 min and diluted with water (60 ml). The crude product was comprised of two compounds (tlc) which were separated by crystallization. The triacetate 25c was isolated by crystallization from Me_2CO–MeOH as colorless needles m.p. 153–154° (340 mg). (Found: C, 66.8; H, 5.67. $C_{36}H_{36}O_{11}$ requires: C, 67.1; H, 5.63%); PMR spectrum: δ1.70, 3 H, s; δ2.24, 3 H, s; δ2.29, 3 H, s; δ3.68, 3 H, s; δ3.72, 3 H, s; δ3.79, 3 H, s; δ3.88, 3 H, s; δ4.55, 1 H, d, J = 9.5 Hz; δ4.76, 1 H, dd, J = 5, 9.5 Hz; δ5.59, 1 H, d, J = 1.5 Hz; δ6.09, 1 H, dd, J = 1.5, 5 Hz; δ6.50–6.60, 4 H, m; δ6.63, 1 H, s; δ6.81, 1 H, s; δ6.95, 2 H, d, J = 9 Hz; δ7.24, 1 H, s; δ7.25, 2 H, d, J = 9 Hz.

The filtrate from the triacetate was evaporated to dryness, dissolved in benzene and cyclohexane added, causing separation of colorless needles of a diacetate, 25b, m.p. 132–133° (190 mg). (Found: C, 66.7; H, 5.99. $C_{34}H_{34}O_{10}$. 1/2 CH_3OH requires: C, 67.0; H, 5.87%) PMR spectrum: δ2.29, 6 H, s; δ2.79, 1 H, d, J = 6.5 Hz (OH); δ3.44, 1.5 H, s (CH_3OH); δ3.72, 9 H, s; δ3.85, 3 H, s; δ4.37, 1 H, d, J = 8.5 Hz; δ4.65, 1 H, dd, J = 5.5, 8.5 Hz; δ4.96, 1 H, ddd, J = 1.5, 5.5, 6.5 Hz; δ5.48, 1 H, d, J = 1.5 Hz; δ6.52, 1 H, s; δ6.59, 2 H, d, J = 9 Hz; δ6.82, 2 H, d, J = 8 Hz; δ6.84, 2 H, d, J = 8 Hz; δ7.09, 1 H, s; δ7.12, 2 H, d, J = 9 Hz; δ7.33, 1 H, s.

(c) *Methylation.* A soln of the crude reduction product (600 mg) in Me_2CO (100 ml) was refluxed for 12 hr with Me_2SO_4 (2.5 ml) and K_2CO_3 (5 g). The residue remaining after removal of solvents was stirred for 1 hr with water (125 ml) then collected and crystallized from Me_2OC–MeOH to give colorless crystals of 25d m.p. 207–208°. (Found: C, 70.2; H, 6.28. $C_{35}H_{34}O_9$ requires: C, 70.3; H, 6.27%); PMR spectrum: δ2.57, 1 H, d, J = 6 Hz (OH); δ3.71, 3 H, s; δ3.74, 9 H, s; δ3.84, 3 H, s; δ3.86, 3 H, s; δ4.60–5.10, 3 H, m; δ5.40, 1 H, d, J = 1.5 Hz; δ6.43, 1 H, s; δ6.62, 2 H, d, J = 9 Hz; δ6.76, 1 H, s; δ6.86, 2 H, d, J = 9 Hz; δ6.95, 2 H, d, J = 9 Hz; δ7.19, 2 H, d, J = 9 Hz; δ7.36, 1 H, s. Warmed with Ac_2O–pyridine for 1 hr the dimethyl ether formed colorless crystalline 25e m.p. 168°. (Found: C, 69.2; H, 6.21. $C_{34}H_{36}O_9$ requires: C, 69.4; H, 6.16%).

(d) *Oxidative cyclization.* A soln of the crude reduction product (2 g) in Me_2CO (100 ml) was refluxed with Ag_2O until tlc showed no spots which reduced ammoniacal $AgNO_3$ (20 min). The filtered mixture showed two major spots on tlc. Repeated crystallization from Me_2CO–MeOH gave the major product, an isomer of 24a, as colorless fine needles, m.p. 254–255°. (Found: C, 69.6; H, 5.45. $C_{30}H_{28}O_8$ requires: C, 69.8; H, 5.46%).

The minor isomer could not be isolated by concentration of the filtrates of the major isomer, since the crystal crops which formed were comprised of equal amounts of both isomers. However, when these mixed crops were boiled briefly with Me_2CO, the undissolved material was comprised primarily of the minor isomer. Repetition of this procedure a number of times followed by recrystallization from Me_2CO–MeOH gave the pure minor isomer of 24a as colorless prisms, m.p. 243–245° (85 mg). (Found: C, 69.8; H, 5.61. $C_{30}H_{28}O_8$ requires: C, 69.8; H, 5.46%); PMR spectrum: δ2.92, 1 H, d, J = 16.5 Hz; δ3.22, 1 H, d, J = 16.5 Hz; δ3.28, 3 H, s; δ3.32, 1 H, d, J = 12 Hz; δ3.62, 3 H, s; δ3.82, 3 H, s; δ3.83, 3 H, s; δ4.89, 1 H, dd, J = 8.5, 12 Hz; δ5.27, 1 H, d, J = 8.5 Hz; δ5.39, 1 H, s; δ5.58, 1 H, s; δ6.32, 4 H, s; δ6.79, 2 H, d, J = 9 Hz; δ6.99, 2 H, d, J = 9 Hz; δ7.47, 1 H, s.

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REFERENCES

[1]L. Jurd, J. N. Roitman and R. Y. Wong, *Tetrahedron* 35, 1041 (1979).
[2]H. Erdtman and S. Hogberg, *Tetrahedron Letters* 1679 (1968).
[3]K. J. Palmer, R. Y. Wong, L. Jurd and K. Stevens, *Acta Cryst.* B32, 847 (1976).
[4]F. M. Dean and D. A. Matkin, *J. Chem. Soc.* Perkin I, 2289 (1977).