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REACTIONS OF HYDROXYQUINONES WITH DIMETHYL SULFOXIDE-ACETIC ANHYDRIDE

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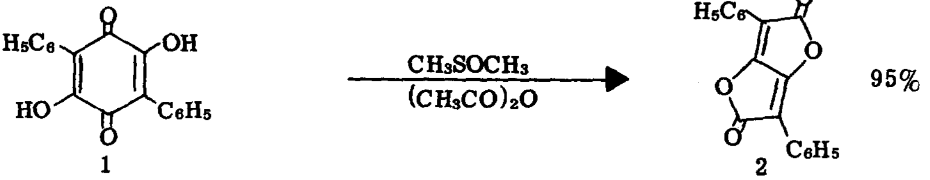
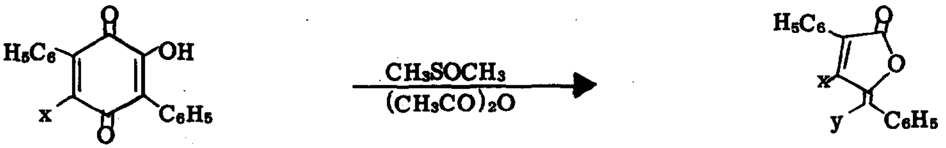
Hydroxyquinones react with dimethyl sulfoxide-acetic anhydride[1] resulting in either oxidative rearrangement to γ-lactones or in the formation of sulfonium ylids. The reaction products depend upon the nuclear substitution pattern; hydroxyquinones with phenyl substituents adjacent to the hydroxyl group rearrange while those quinones in which the corresponding position is unsubstituted give ylids.

The oxidative rearrangement finds significant synthetic utility in the one step conversion of polyporic acid, 1, to pulvinic acid dilactone, 2, in 95% isolated yield. This transformation was accomplished by reacting the hydroxyquinone, 1, with a solution of acetic anhydride-dimethyl sulfoxide (1:2) at 60° for 15 minutes. The dilactone, 2,[2] precipitated from the reaction solution in high purity in over 90% yield.[3]



To gain some insight into the mechanism of this rearrangement (Scheme I) three additional 2-hydroxy-3-phenyl-1,4-benzoquinones, 3, 4, 5, were subjected to the reaction conditions. These quinones, which are substituted at the 5-position with a substituent other than a hydroxyl group, react with decarbonylation and rearrangement giving the γ-arylidene-$\Delta^{\alpha,\beta}$-butenolides, 6, 7, 8, in 40 - 70% yields.[4]

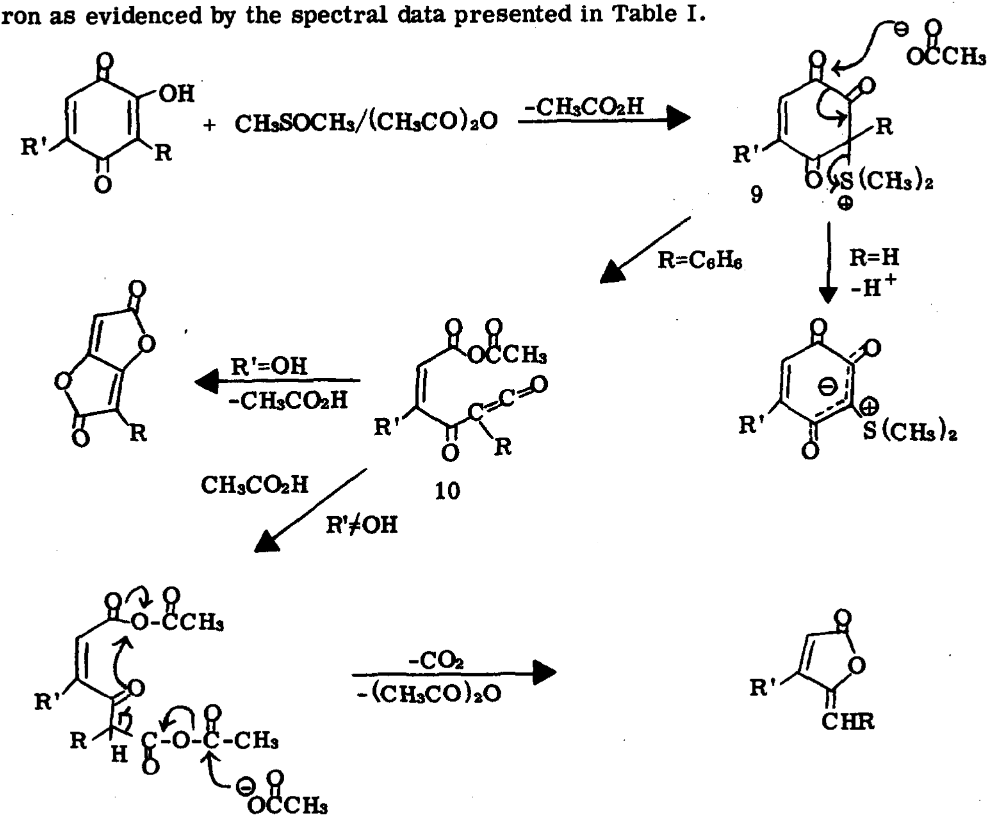
Formation of the butenolides, 2, 6, 7, 8, is consistent with the proposed mechanism (Scheme I). The dilactone, 2, could be formed via the ketene intermediate, 10, which reacts intramolecularly with the hydroxyl group originally at C-5 followed by alcoholysis of the anhydride linkage to form the dilactone structure. For those compounds in which the C-5 hydroxyl



3 x = Cl
4 x = H
5 x = OCH_3

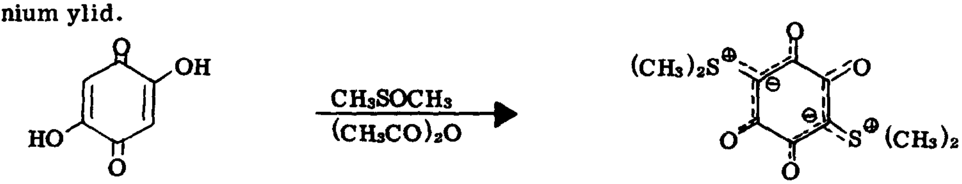
6 x = Cl, y = H
7a x = H, y = H
7b x = H, y = D
8 x = OCH_3, y = H

group is missing, 3, 4, 5, the ketene, 10, is converted to a β-ketoanhydride by addition of acetic acid. Decarboxylation and ring closure initiated by acetate ion then gives the observed products, 6, 7a, 8. The ketene intermediate, 10, is also in agreement with the observed product, *7b, obtained in low yield when the quinone, 4, was reacted with 5% D_2O in dimethyl sul*foxide-acetic anhydride.[5] Under these conditions the γ-arylidene vinyl proton was replaced by a deuteron as evidenced by the spectral data presented in Table I.



Scheme I

The mechanism (Scheme I) is in agreement with the observed formation of ylids when hydroxyquinones which are *unsubstituted at the position (s) adjacent to the hydroxyl group (s)* are subjected to the oxidative conditions. These ylids are visualized as arising from the sulfonium salt intermediate, **9**, which loses the acidic ring proton[6] before rearrangement to the ketene, **10**. An interesting example of this reaction is the 90% conversion of 2, 5-dihydroxy-1, 4-benzoquinone, **11**, to 2, 5-dioxy-3, 6-*bis* (dimethylsulfonium)-benzoquinone-*bis*-betaine, **12** , the first example of a disulfonium ylid.



11 12

The reactions presented here illustrate a mild oxidative method for the modifications of quinone nuclei, transformations which may have a number of biosynthetic analogies.[7] These reactions also suggest a general synthetic method for the conversion of quinones to a variety of ring systems found in natural products. Hydroxyquinones having structural variations containing substituents capable of addition to the ketene intermediate are currently under investigation

i.e.,

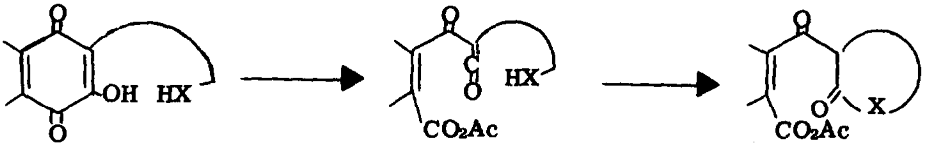


TABLE I[8,9]

Physical Properties of New Compounds

Compound	Mp, °C	Ir, cm^{-1} (mujol)	Nmr, ppm	Mass Spectra
6	146-147	1770 1645 1585	6.40 (1) s, 7.2 - 7.5 (10) m 7.6 - 8.0 (DMSO-d_6)	282 (M^+) (100), 191 (40), 118 (36), 90 (38)
7b[10]			8.27 (1) s 7.3 - 8.1 (10) m (DMSO-d_6)	249 (M^+) (100), 193 (20), 119 (30), 91 (33)
12	>300	1560 1495 1250	3.25 s (TFA)	260 (M^+) (11), 94 (52) 62 (100)

ACKNOWLEDGEMENT

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REFERENCES

1. A mixture of dimethyl sulfoxide-acetic anhydride has recently been uniquely employed by J. D. Albright and L. Goldman, J. Am. Chem. Soc., 89, 2416 (1967) for the oxidation of alcohols having α-protons to the corresponding carbonyl compounds.
2. R. L. Frank, G. R. Clark and J. N. Coker, ibid., 72, 1824 (1950) observed the conversion of polyporic acid to pulvinic acid dilactone in 28% yield by lead tetraacetate oxidation.
3. Either anhydrous or reagent grade dimethyl sulfoxide can be employed without significant change in the reaction.
4. These compounds did not precipitate from the reaction solution. They were isolated from a methylene chloride extract of the reaction solution after it had been poured into water and treated with sodium carbonate.
5. The large amount of D_2O does retard the overall reaction. However, the only product detected in addition to the unreacted quinone, 4, was the deuterated butenolide, 7b.
6. F. Ramirez, D. Rhum and C. P. Smith, Tetrahedron, Vol. 21, 1941 (1965) have determined the first and second ionization constants for the phosphonium ylid analogous in structure to 12 and found these to be -3.55 and ca. -0.4 respectively in H_2O-HCl.
7. P. Bernfeld "Biogenesis of Natural Compounds," Macmillan Company, New York, 1963.
8. Compounds 2, 7, and 8 are known compounds which were identical to those reported here. See respectively, ref. 2, J. Thiele, H. Rossner, Ann., 306, 219 (1904), and F. Kogl, ibid., 465, 256 (1928).
9. C, H-analysis of all compounds are in agreement with their formulation.
10. The deuterated butenolide, 7b, showed identical spectral properties to 7a except for the absence of the arylidene vinyl proton absorption at 6.42 ppm in the nmr and the molecular weight of 249 compared to 248 for 7a.