Dimethyl Sulfoxide–Acetic Anhydride Oxidative Rearrangements of Hydroxyterphenylquinones. A Possible Biosynthetic Model[1]

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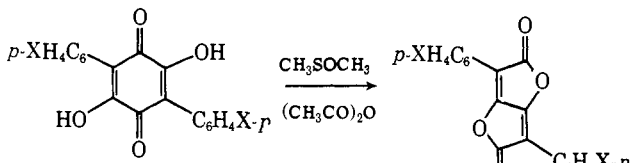
Abstract: Dimethyl sulfoxide–acetic anhydride oxidation of the 2,5-dihydroxy-3,6-diaryl-1,4-benzoquinones **1**, **2**, and **3** gives good to excellent yields of, respectively, the ring-contracted dilactones **4**, **5**, and **6**. The monohydroxyterphenylquinones **9**, **10**, and **11** also undergo ring contraction when subjected to these oxidation conditions giving, respectively, the butenolides **13**, **14**, and **15**. Hydroxyquinones which are unsubstituted at the position(s) adjacent to the hydroxyl group, *i.e.*, **21**, **22**, **23**, and **24**, give the corresponding sulfonium ylides, **25**, **26**, **27**, and **28**. The mechanism of these transformations as well as their significance as a possible biosynthetic model are also discussed.

The biosynthetic conversion of the naturally occurring terphenylquinone, polyporic acid (**1**), to pulvinic



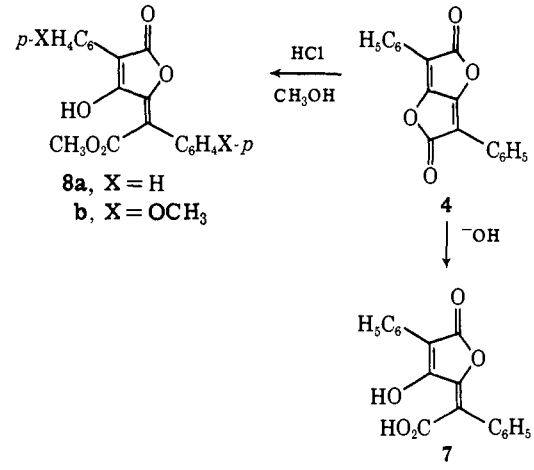
1, X = H
2, X = OH
3, X = OCH_3

4, X = H
5, X = OH
6, X = OCH_3

acid dilactone (**4**) has been established.[2] New and efficient nonenzymatic conditions for this oxidative rearrangement have now been developed and the results are reported here.[3]

The above transformations are conveniently accomplished *in vitro* in good to excellent yields by treating the respective hydroxyquinones with a solution of dimethyl sulfoxide–acetic anhydride[4] (2:1) at 60° for approximately 15 min. Under these reaction conditions polyporic acid (**1**) is converted to pulvinic dilactone (**4**) in 95% yield, and the dilactone **5** is obtained in 55% yield from atromentin (**2**). It is interesting to note that the major product of the atromentin reaction is 4,4′-dihydroxypulvinic dilactone (**5**) and not the diacetate of **5** which is a minor product (<10%). It is surprising, in fact, that the dilactone **5** is formed at all in reasonable yield since phenols readily react with dimethyl sulfoxide–acetic anhydride to give thiomethoxy methylation of the aromatic ring.[5] No such products were isolated here. It was, however, observed that the reaction proceeds much smoother when the 4,4′-phenolic hydroxyl groups in **2** are protected. For example, 2,5-bis(*p*-methoxyphenyl)-3,6-dihydroxy-1,4-benzoquinone (**3**)[6] reacts with dimethyl sulfoxide–acetic anhydride giving 4,4′-dimethoxypulvinic dilactone (**6**)[7] in over 90% isolated yield. This product, like that obtained from polyporic acid, precipitates from the reaction solution after only a few minutes of reaction time.

The dilactones **4**, **5**, and **6** are known compounds and their spectral and/or physical properties are in agreement with those reported.[7-9] In addition, pulvinic dilactone (**4**) was converted to pulvinic acid (**7**)[9]

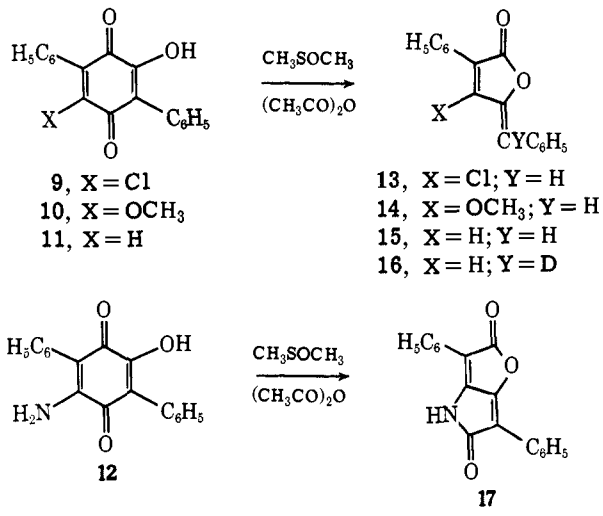


8a, X = H
b, X = OCH_3

and vulpinic acid (**8a**)[9] upon, respectively, base hydrolysis and hydrolysis with methanolic HCl. These two naturally occurring tetronic acids, **7** and **8a**, were identical in all respects with those synthesized by an alternate method which has been previously reported.[10] Atromentin dilactone (**5**) was identical with a sample prepared in low yield by the reaction of atromentin with acidic hydrogen peroxide.[6a] The diacetate derivative showed the same melting point as that reported by Kögl and Becker,[6a] and its ir spectrum was identical with that reported by Beaumont, Edwards, and Elsworthy.[8] The lactone **6** was converted to 4,4′-dimethoxyvulpinic acid (**8b**)[7a,b] by the action of alcoholic KOH.

(1) Based upon the Ph.D. Dissertation of R. J. Wikholm.
(2) W. S. G. Maass and A. C. Neish, *Can. J. Bot.*, **45**, 59 (1967). For these authors' most recent views on the biosynthesis of pulvinic acid derivatives see W. S. G. Maass, *Phytochemistry*, 9, 2477 (1970).
(3) A preliminary account of this work has been reported: H. W. Moore and R. J. Wikholm, *Tetrahedron Lett.*, 5049 (1968).
(4) J. D. Albright and L. Goldman have utilized this reagent as a convenient method for the oxidation of alcohols to carbonyl compounds (*J. Amer. Chem. Soc.*, **89**, 2416 (1967)).
(5) Y. Hayaski and R. Oda, *J. Org. Chem.*, **32**, 457 (1967); P. Claus, *Monatsh Chem.*, **99**, 1034 (1968).
(6) (a) F. Kögl and H. Becker, *Justus Liebigs Ann. Chem.*, **465**, 211 (1928); (b) B. F. Cain, *J. Chem. Soc.*, 356 (1963).
(7) (a) F. Kögl, *Justus Liebigs Ann. Chem.*, **465**, 243 (1928); (b) S. C. Agarwal and T. R. Seshadri, *Indian J. Chem.*, **2**, 17 (1964).
(8) P. C. Beaumont, R. L. Edwards, and G. C. Elsworthy, *J. Chem. Soc. C*, 2968 (1968).
(9) R. L. Frank, G. R. Clark, and J. N. Coker, *J. Amer. Chem. Soc.*, **72**, 1824 (1950).
(10) H. W. Moore, H. R. Shelden, D. W. Deters, and R. J. Wikholm, *ibid.*, **92**, 1675 (1970).

To gain some insight into the mechanism of this rearrangement, four additional 2-hydroxy-3,6-diphenyl-1,4-benzoquinones (**9**–**12**) were subjected to the oxida-



9, X = Cl
10, X = OCH_3
11, X = H

13, X = Cl; Y = H
14, X = OCH_3; Y = H
15, X = H; Y = H
16, X = H; Y = D

12

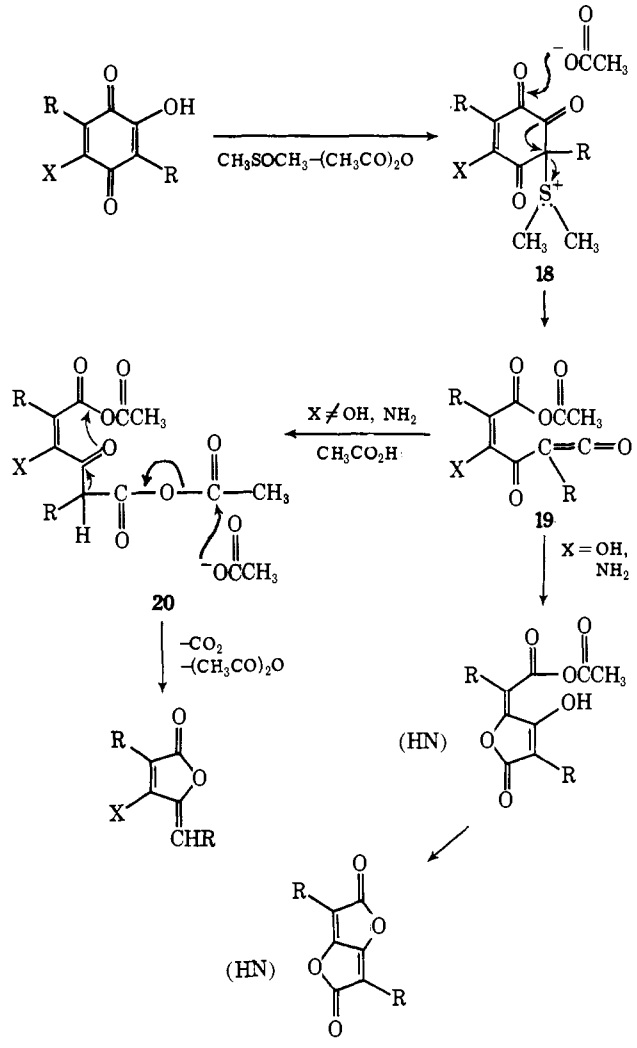
17

tive conditions. Three of these quinones, **9**, **10** and **11**, which are substituted at the 5 position with a substituent other than a hydroxyl group, react with decarbonylation and rearrangement giving the γ-arylidine-$\Delta^{\alpha,\beta}$-butenolides **13**–**15** in 60–70% yield. The oxidation of 2-hydroxy-5-amino-3,6-diphenyl-1,4-benzoquinone (**12**) presented a more complex reaction giving a mixture of products. However, the interesting lactone–lactam **17** was isolated in 30% yield by column chromatography on silica gel.

The structures of the previously unreported compounds, **13**, **16**, and **17**, are in complete accord with their observed spectral data (see Experimental Section). They show characteristic ir and nmr absorptions and mass spectral fragmentation patterns and molecular ions in strict agreement with their proposed formulations.

The mechanism for the oxidative rearrangements reported here is envisaged as depicted below (Scheme I). The key intermediate in these transformations is the ketene **19**. The dilactones **4**, **5**, and **6** and the lactone–lactam **17** are viewed as arising from this ketene intermediate, **19**, by intramolecular addition of the protic substituent (OH or NH_2) originally at the quinone C-5 position to the ketene functionality, followed by alcoholysis of the anhydride linkage to form the bicyclic structures. For those quinones in which the protic C-5 substituent is missing, **9**, **10**, and **11**, the ketene **19** can be converted to the β-keto anhydride **20** by addition of acetic acid. Decarboxylation and subsequent ring closure initiated by acetate ion could then give the observed γ-arylidine-$\Delta^{\alpha,\beta}$-butenolides **13**, **14**, and **15**. The ketene intermediate, **19**, is also in agreement with the observed product, **16**, obtained in low yield when the quinone **11** was reacted with 5% D_2O in dimethyl sulfoxide–acetic anhydride. Under these conditions, the γ-arylidine vinyl proton was replaced by a deuteron as evidenced by nmr and mass spectral analysis of the product. The large amount of D_2O in this reaction does retard the reaction. However, the only product in addition to unreacted quinone was the deuterated butenolide **16**. Unfortunately, no direct unambiguous evidence for the existence of the ketene

Scheme I



intermediate was obtained. For example, when polyporic acid was subjected to the oxidation conditions in the presence of varying amounts of *tert*-butyl alcohol, only the dilactone **4** or no reaction at all (high concentration of alcohol) was observed.

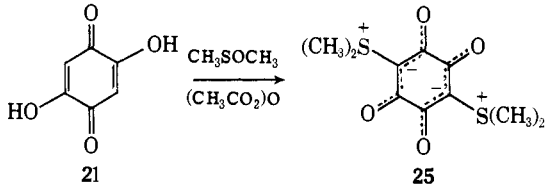
The proposed sulfonium salts, **18**, were not isolated or detected. However, products consistent with their existence were formed in high yield when hydroxyquinones which are unsubstituted at the position adjacent to the hydroxyl group were subjected to the oxidation conditions. 2,5-Dihydroxy- (**21**), 2-hydroxy-5-phenyl- (**22**), and 2-hydroxy-5-methyl-1,4-benzoquinone (**23**) and 2-hydroxy-1,4-naphthoquinone (**24**) all readily reacted with dimethyl sulfoxide–acetic anhydride to give, respectively, the sulfonium ylides **25**, **26**, **27**, and **28**. These ylides are visualized as arising from the sulfonium salt intermediate, **18**, which loses the acidic ring proton[11] to give the ylides.[12]

Recently, in an experiment prompted by the present work, Beaumont and Edwards[13] have utilized this ylide

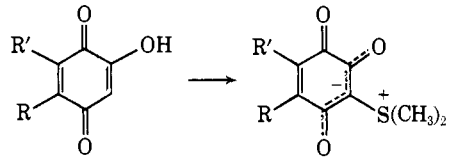
(11) F. Ramirez, D. Rhum, and C. P. Smith (*Tetrahedron*, 21, 1941 (1965)) have determined the first and second ionization constants for the phosphonium ylide analogous in structure to **25** and found these to be −3.55 and *ca.* −0.4, respectively, in H_2O–HCl.

(12) The ylide **28** was independently prepared in the manner reported here by R. Gompper and H. Euchner, *Chem. Ber.*, 99, 527 (1966). Compound **25** has also been reported since the completion of this work: K. Y. Z. Cheng and C. C. Cheng, *J Med. Chem.*, 13, 264 (1970), and ref 13.

(13) P. C. Beaumont and R. L. Edwards, *J. Chem. Soc. C*, 1000 (1971).



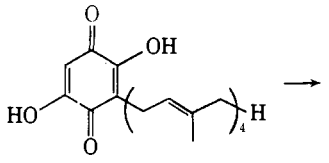
21 25



22, 26, R = C_6H_5; R′ = H
23, 27, R = CH_3; R′ = H

24, 28, R′ = 

formation as a diagnostic reaction in the structure proof of the naturally occurring dihydroxyquinone, bovinone (**29**). The fact that this natural product has



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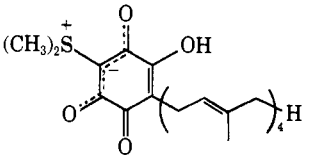

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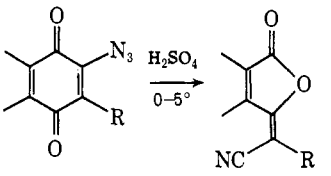
an unsubstituted position adjacent to one of the hydroxyl groups was evidenced by the fact that the ylide **30** was formed upon reaction of **28** with dimethyl sulfoxide–acetic anhydride. It is interesting to note that these workers observed the formation of bright yellow compound which slowly converted to the ylide and suggested that the initial compound was the corresponding sulfonium salt.

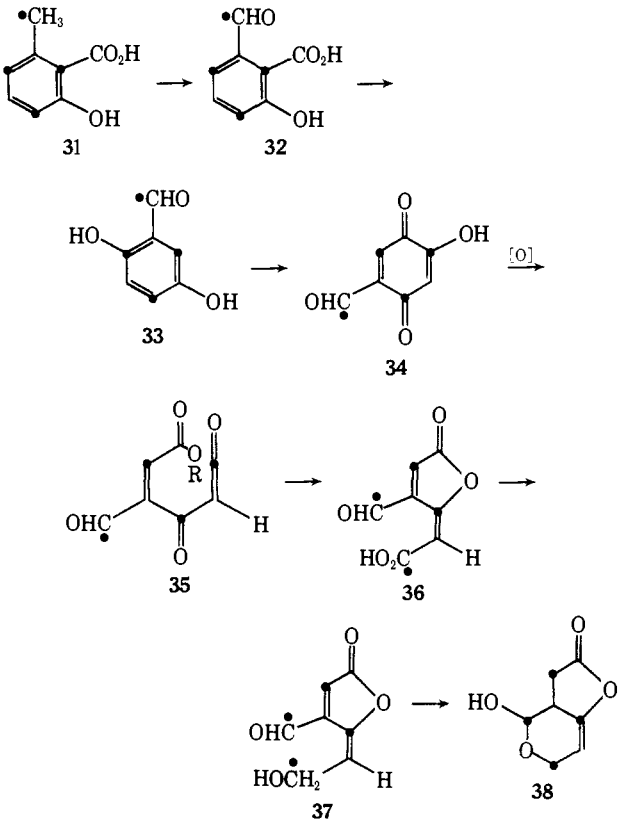
The scope of the dimethyl sulfoxide–acetic anhydride oxidative rearrangement of hydroxyquinones has not been extensively probed. However, in the few examples that were investigated in attempts to extend this reaction beyond the 2,5-diaryl-3-hydroxy-1,4-benzoquinones the results were disappointing. Hydroxyquinones with alkyl groups adjacent to the hydroxyl were surprisingly inert to this rearrangement. Thus, 2,5-dimethyl-3-hydroxy- and 2,5-di-*tert*-butyl-3-hydroxy-1,4-benzoquinone failed to undergo oxidative cleavage even under prolonged reaction conditions. In each case, the only product observed was corresponding acylated hydroxyquinone. Even more surprising was the fact that 2-hydroxy-3-phenyl- and 2-hydroxy-3-*p*-methoxyphenyl-1,4-naphthoquinone failed to undergo oxidative rearrangements. Prolonged heating (90°) of these quinones under the oxidative conditions gave only a small amount of the corresponding acetates. The starting quinones could be recovered in 85–90% yield.

The oxidative rearrangements of 2,5-diaryl-3-hydroxy-1,4-benzoquinones reported here do provide a convenient synthetic route to the corresponding butenolide ring systems. The only other method of general synthetic utility for the transformation of benzoquinones to γ-alkylidene (or arylidene)-$\Delta^{\alpha,\beta}$-butenolides is the stereospecific acid-catalyzed rearrangement of azido-1,4-benzoquinones,[10] *i.e.*



It should also be mentioned that lead tetraacetate oxidation of polyporic acid gives the dilactone **4** in low yield.[9] Also, acidic hydrogen peroxide oxidation of **2** gives 4,4′-dihydroxypulvinic dilactone **5** in moderate yield but failed in the case of polyporic acid.[6,9]

The results of this study of the reactions of hydroquinones with dimethyl sulfoxide–acetic anhydride provide an efficient *in vitro* pathway from the terphenylquinones to the pulvinic acid derivatives, a sequence possibly paralleling the biosynthetic pathway. The ubiquity of hydroxyquinones in nature[14] as well as phenolic compounds[15] which may be oxidized to hydroxyquinones suggests a number of possible biosynthetic schemes involving analogous oxidative cleavages of quinone nuclei. Tenuazonic acid,[16] penicillic acid,[17]

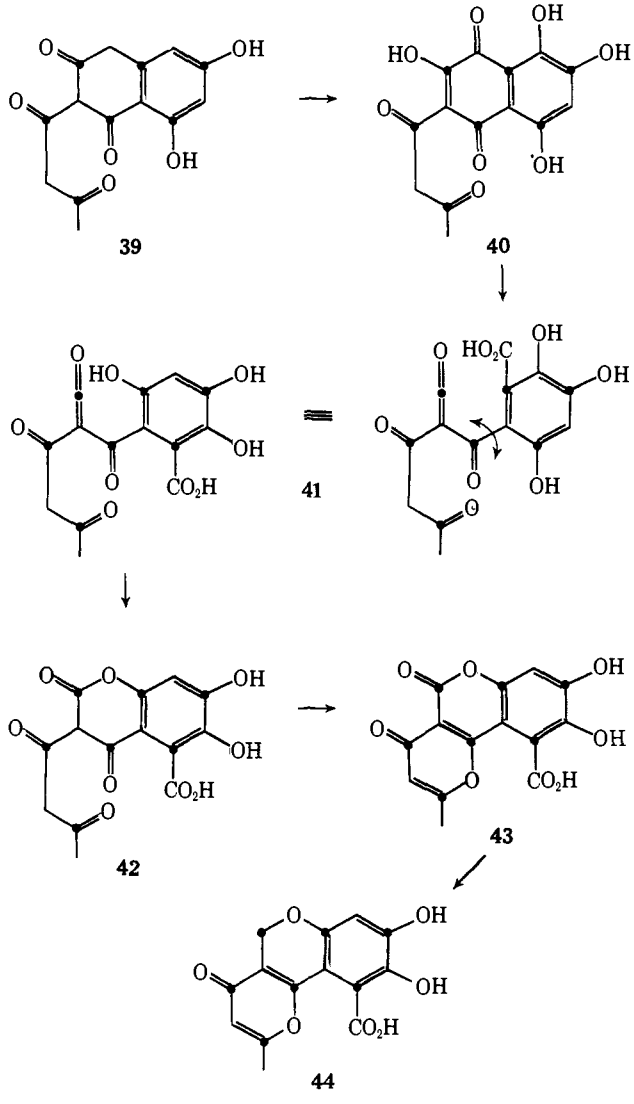


31 32 33 34 35 36 37 38

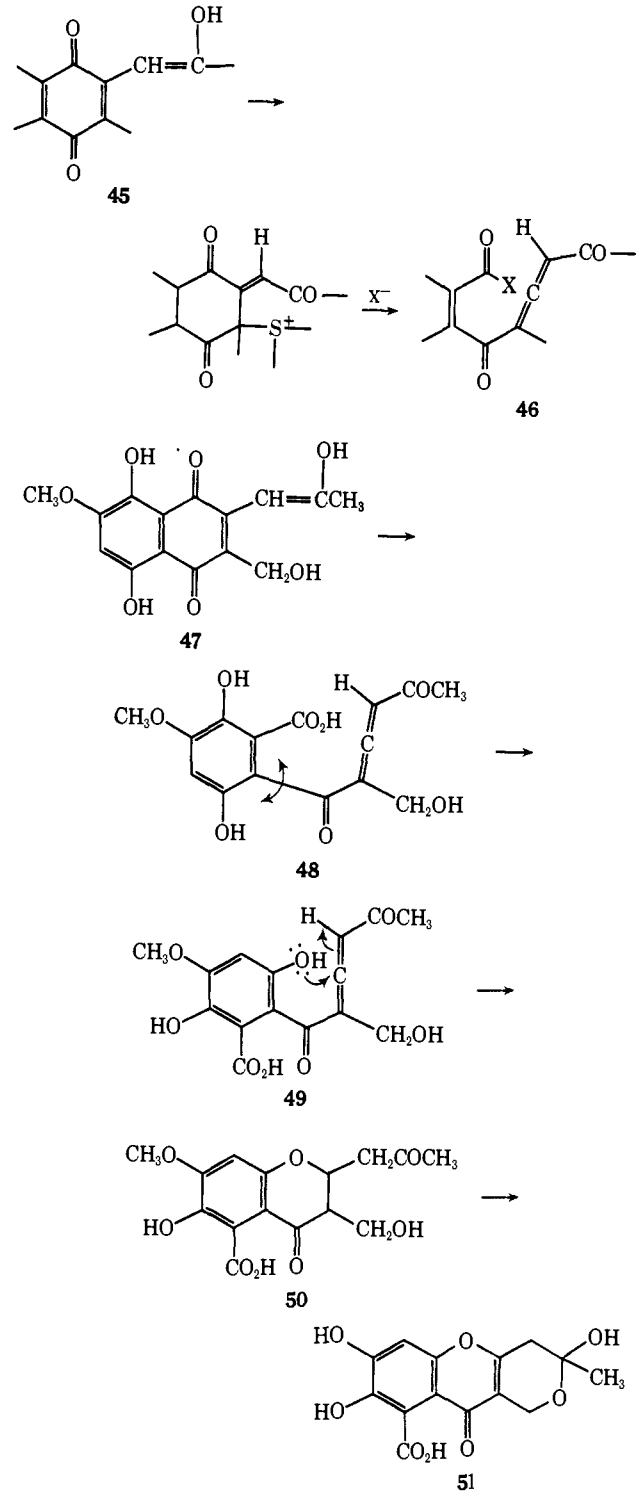
(14) R. H. Thomson, "Naturally Occurring Quinones," Academic Press, London and New York, 1971.
(15) W. D. Ollis, Ed., "Chemistry of Natural Phenolic Compounds," Pergamon Press, London, 1961.
(16) J. H. Richards and J. B. Hendrickson, "The Biosynthesis of Steroids, Terpenes and Acetogenins," W. A. Benjamin, New York, N. Y., 1964, pp 165–166.
(17) Reference 16, pp 166–167.

patulin,[18] citromycetin,[19] aflatoxin B,[20] brevifolin, and brevifolincarboxylic acid,[21] to mention only a few, can all be viewed as arising from ketene intermediates which could be formed *via* oxidative cleavage of hydroxyquinone precursors. Biosynthetic studies on several of the above compounds have been reported[17-20] and their labeling pattern, starting from radioactive precursors, has been established. The proposed oxidative cleavage of hydroxyquinone precursors can adequately explain these labeling results. This proposal is uniquely illustrated below for the biosynthetic conversion of 6-methylsalicylic acid (**31**) to patulin (**38**).

Another example is the following proposed conversion of the acetate-derived intermediate **39** to citromycetin (**44**) *via* the ketene **41**.



Extension of these concepts to vinylogous hydroxyquinones, **45**, would lead to allene intermediates, **46**. An interesting speculative application of a possible allene biosynthetic intermediate in nature arises in the biosynthesis of fulvic acid (**51**) from the quinone fusarubin (**47**). Fulvic acid, citromycetin, and fusarubin are metabolites of similar mold species and their biosynthesis by various polyacetate cyclizations has been suggested.[22] The notion that fulvic acid arises from



fusarubin *via* cleavage of the latters' quinone ring giving an allene intermediate, **48**, seems plausible.

The aforementioned biosynthetic examples are indeed speculative but consistent with the available published data. They provide possible examples of what may be a general *in vivo* oxidative pathway for the conversion of certain hydroxyquinones and other ketoenols to cumulene intermediates.

(18) Reference 16, pp 167-168.
(19) Reference 16, p 148.
(20) M. Biollaz, G. Büchi, and G. Miline, *J. Amer. Chem. Soc.*, 92, 1035 (1970).
(21) Reference 16, p 96.
(22) A. J. Birch, R. J. English, R. A. Massy-Westripp, M. Slayton, and H. Smith, *J. Chem. Soc.*, 365 (1958).

Experimental Section[23]

2,5-Dihydroxy-3,6-diphenyl-1,4-benzoquinone (Polyporic Acid) (1). A solution of 3.0 g (0.01 mol) of 2-chloro-5-hydroxy-3,6-diphenyl-1,4-benzoquinone (**9**),[10] in 100 ml of dimethyl sulfoxide, was treated with 6 ml of 50% aqueous sodium hydroxide. The red solution immediately became deep purple upon addition of the base. The reaction mixture was allowed to stand for 15 min at room temperature and then 200 ml of water was added. This purple solution was then acidified with concentrated hydrochloric acid which resulted in the precipitation of polyporic acid. The quinone was collected by filtration and recrystallized from dioxane to give the bright orange dioxane complex previously noted by Cain.[24] The dioxane was removed *in vacuo* to give 2.6 g (87% yield) of polyporic acid, mp 303–305° (lit.[25] 305°). A diacetate derivative, prepared in acetic anhydride and pyridine, has mp 214–215° (lit.[25] 215°).

2-Azido-5-hydroxy-3,6-diphenyl-1,4-benzoquinone. To a solution of 2.7 g (9 mmol) of 2-chloro-5-hydroxy-3,6-diphenyl-1,4-benzoquinone (**9**) in 250 ml of ethanol, 75 ml of dimethylformamide, and 10 ml of acetic acid was added a solution of 1.95 g of sodium azide in *ca.* 10 ml of water. The reaction mixture was allowed to stand at room temperature for 2 hr and then poured into 200 ml of water. The precipitated reddish brown azidoquinone[10] was collected by filtration and weighed 2.5 g after drying (90% yield). The above procedure gave the azidoquinone in greater purity than the previously reported synthesis.[10]

2-Amino-5-hydroxy-3,6-diphenyl-1,4-benzoquinone (12). 2-Azido-5-hydroxy-3,6-diphenyl-1,4-benzoquinone was reduced smoothly by hydrogen (30 lb/in.^{2}) over platinum oxide catalyst (50 mg/2.0 g of quinone) in 95% ethanol (10% solution) over 6 hr. The colorless reaction mixture was refluxed about 0.5 hr and concentrated. After cooling, the solution was filtered and the residue was taken up in boiling dioxane, filtered to remove the catalyst, and allowed to cool. The aminoquinone separated as an orange complex with dioxane. Drying *in vacuo* gave the aminoquinone (**12**) which melted at 323–325° with sintering at 315°. Satisfactory analysis could not be obtained on this material after four recrystallizations from dioxane: ir spectrum (Nujol) 3450, 3300, 3160 (s), 1565 (s) cm^{-1}.

2,5-Bis(*p*-methoxyphenyl)-3,6-dihydroxy-1,4-benzoquinone (Atromentin Dimethyl Ether) (3). 2,5-Dichloro-1,4-benzoquinone was arylated with *p*-methoxybenzenediazonium acetate as described by Cain:[24] ir (Nujol) 1680, 1615, 1255, 1175, 1030 cm^{-1}. Hydrolysis of the 2,5-bis(*p*-methoxyphenyl)-3,6-dichloro-1,4-benzoquinone with aqueous NaOH in methanol (reflux) by the method of Thomas[26] gave on acidification atromentin dimethyl ether (**3**):[6] ir (Nujol) 3300, 1650 (sh), 1615 (s), 1250, 1030 cm^{-1}.

2,5-Bis(*p*-hydroxyphenyl)-3,6-dihydroxy-1,4-benzoquinone (Atromentin) (2). Atromentin dimethyl ether was reductively demethylated by the procedure of Kögl, *et al.*[7] Thus, 1.0 g of atromentin dimethyl ether (**3**) was suspended in 35 ml of glacial acetic acid and 20 ml of hydriodic acid (47%). After refluxing for 1 hr the reaction mixture was colorless and a yellowish appearing precipitate was filtered off. The hydrequinone thus obtained was dissolved by warming in 50 ml of NaOH. After 15 min, acidification with acetic acid gave the brown quinone, atromentin (**2**): ir (Nujol) 3310 (b), 1690, 1610, 1245, 990 cm^{-1}. The tetraacetate derivative of atromentin was prepared in acetic anhydride and a drop of concentrated H_2SO_4 and after recrystallization from acetic acid had mp 241–242° (lit.[7] 242°): ir (Nujol) 1780, 1755, 1670, 1195, 1175 cm^{-1}; nmr ($DCCl_3$) δ 2.22 (s, 3 H), 2.30 (s, 3 H), 7.26 (m, 5 H).

Pulvinic Acid Dilactone (4). The hot reaction mixture containing 2,5-dihydroxy-3,6-diphenyl-1,4-benzoquinone (polyporic acid) (**1**) (0.70 g) in 10 ml of dimethyl sulfoxide–acetic anhydride (2:1) deposited a yellow precipitate after heating on a steam bath for *ca.* 10 min. The precipitate was filtered off giving pulvinic acid dilactone in yields greater than 90%. The yield is essentially quantitative if the solvent is removed *in vacuo* and the residue crystallized from benzene. The dilactone was recrystallized from chloroform and had mp 221–222° (lit.[9] 220–221): ir (Nujol) 1815, 1660 cm^{-1} (identical with published spectrum[9]); mass spectrum *m/e* (rel intensity), 290 (M^+) (100%) (identical with published spectrum[27]); uv ($\lambda_{max}^{dioxane}$) 376 nm (log ϵ 4.48), 235 (4.28).

The pulvinic acid dilactone was converted to pulvinic acid (**7**) by the procedure of Frank, *et al.*,[9] yielding the yellow orange acid with mp 216–217° (lit.[9] 216–217°): ir (Nujol) 3170, 1760, 1680, 1590 cm^{-1} (identical with published spectrum[9]).

Vulpinic acid (**8**) was obtained from pulvinic acid dilactone as described by Frank:[9] mp 146–147° (lit.[9] 145–146°); ir (Nujol) 1770, 1680, 1615 cm^{-1} (identical with published spectrum[9]); nmr ($CDCl_3$) δ 3.84 (s, 3 H), 7.2–7.6 and 8.0–8.3 (m, 10 H).

4,4′-Dihydroxypulvinic Acid Dilactone (5). Atromentin (**2**) (0.65 g; 2 mmol) was dissolved in 5 ml of dimethyl sulfoxide and 2 ml of acetic anhydride by warming on the steam bath. After heating for *ca.* 15 min the solvent was removed *in vacuo*. The residue was suspended in a little acetic acid and filtered giving 0.35 g of a brick red material (54% crude yield), the ir spectrum of which was identical with that of atromentin dilactone (**5**) prepared by the hydrogen peroxide method of Kögl and Becker.[6] Tlc analysis (silica gel, CH_2Cl_2) of the filtrate indicated the dilactone as the main component with only a trace of material having the same R_f value as the diacetate derivative of the authentic dilactone. There was no sign of the tetraacetate derivative of atromentin by tlc analysis. The solvent was removed *in vacuo* and the residue was treated with acetic anhydride and a drop of concentrated sulfuric acid. After heating on the steam bath for a few minutes the acetylation mixture was cooled and the yellow precipitate was filtered off. Recrystallization from acetic acid gave the 4,4′-diacetoxypulvinic acid dilactone, mp 270–271° (lit.[6a] 271°). The melting point and ir spectrum of this compound were identical with that of an authentic sample (*vide infra*).[6a]

4,4′-Dihydroxypulvinic Acid Dilactone (Peroxide Oxidation) (5). The procedure of Kögl and Becker[6] was followed. Thus, 0.5 g of atromentin was dissolved in 70 ml of hot glacial acetic acid. Three drops of 0.1 *N* HCl and 5 ml of 3% H_2O_2 (1 ml of 30% H_2O_2 diluted to 10 ml) were added. After standing for *ca.* 15 min the yellow precipitate was filtered giving the rearranged dilactone (**5**). Variations from the above procedure gave little or none of the dilactone: ir (Nujol) 3490 (br), 1818, 1785, 1650, 1600, 1585, 1505, 1230, 1155 cm^{-1}; uv $\lambda_{max}^{dioxane}$ 402 nm (log ϵ 4.30), 247 (4.26).

4,4′-Diacetoxypulvinic Acid Dilactone. The diacetate derivative of 4,4′-dihydroxypulvinic acid dilactone (**5**) was prepared by heating in acetic anhydride and a drop of concentrated H_2SO_4 and cooling. The diacetate was recrystallized from acetic acid and had mp 270–271° (lit.[6] 271°): ir (Nujol) 1825, 1755, 1660, 1200, 1155 cm^{-1}.

4,4′-Dimethoxypulvinic Acid Dilactone (6). 2,5-Bis(*p*-methoxyphenyl)-3,6-dihydroxy-1,4-benzoquinone (**3**) (0.50 g) was dissolved in 6 ml of DMSO and 4 ml of acetic anhydride upon warming on the steam bath. After *ca.* 2 min a yellow precipitate appeared; the reaction mixture was cooled and 0.45 g (90% yield) of the yellow dilactone was filtered off and washed with a little cold methanol: mp 272–273° (lit.[7] 268.5°); ir (Nujol) 1815, 1805, 1780, 1650, 1600, 1260, 1160 cm^{-1}; uv $\lambda_{max}^{dioxane}$ 412 nm (log ϵ 4.43), 247 (4.38).

The dilactone isolated above was converted to the substituted vulpinic acid by the method of Kögl.[7] Thus, 0.13 g of the dilactone was dissolved in 10 ml of methanol and acidified with 6 *N* HCl. The bright red orange precipitate was filtered off and recrystallized from methanol: mp 177–178° (lit.[7] 174.5°); ir (Nujol) 2700 (broad), 1765, 1680, 1600, 1580, 1245, 1190, 1185 cm^{-1}; nmr ($CDCl_3$) δ 3.87 (s, 6 H), 3.92 (s, 3 H), 6.9–7.5 and 8.1–8.3 (m, 13.7 (s, 10 H).

General Procedure for Conversion of Arylhydroxybenzoquinones to γ-Arylidene-$\Delta^{\alpha,\beta}$-butenolides. Between 1 and 2 g of the arylhydroxybenzoquinone was dissolved in a mixture of 6 ml of dimethyl sulfoxide and 4 ml of acetic anhydride. The reaction mixture was heated on a steam bath with the temperature remaining *ca.* 70–75°. In some cases, the rearranged product precipitated from the hot

(23) Melting points were determined with a Thomas Hoover capillary melting point apparatus, and are uncorrected. Infrared (ir) spectra of new compounds were obtained on a Perkin-Elmer Model 521 spectrophotometer. A Perkin-Elmer Model 137 was used for routine analysis and comparison. Ultraviolet–visible spectra were determined on a Cary 14 spectrophotometer. Nuclear magnetic resonance (nmr) spectra were recorded using a Varian A56/60 spectrometer. Chemical shifts are reported on the δ scale from TMS as internal standard. Gas–liquid partition chromatography (glc) was used where feasible for determining reaction progress and for collection of analytical samples. An F&M Model 700 with a flame ionization detector and a Varian-Aerograph 93A with a thermal conductivity detector were utilized with the temperature and column listed. Mass spectra were obtained from West Coast Technical Service, San Gabriel, Calif., using a Hitachi-Perkin-Elmer RMU-6D mass spectrometer at 70 eV. Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

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reaction mixture and was filtered off upon cooling. With most of the quinones studied no precipitate appeared and after *ca.* 1 hr the reaction mixture was poured into water (300 ml) and sufficient sodium carbonate was added to make the solution basic to litmus. The basic solution was extracted with methylene chloride or chloroform and the organic layer was dried (Na_2SO_4) and the solvent removed leaving a dark oil which was taken up in hot alcohol. Upon cooling, the crystalline butenolide was obtained. Acidifying the aqueous layer and extracting with chloroform failed to produce acidic products. An alternative work-up which provided greater yields was to remove the solvent *in vacuo* overnight. The dark oil thus obtained could be taken up in hot alcohol or chromatographed on silica gel. Nuclear magnetic resonance analysis of the crude reaction mixture failed to indicate the presence of more than one isomer.

β-Chloro-α-phenyl-γ-arylidene-$\Delta^{\alpha,\beta}$-butenolide (13). The most efficient isolation of the butenolide product from 2-chloro-5-hydroxy-3,6-diphenyl-1,4-benzoquinone (**9**) was through removal of the solvent *in vacuo* and dissolving the dark residue in hot alcohol. Upon cooling, the chlorobutenolide **13** was obtained in 65% yield. The red oil obtained from the extraction procedure eventually solidifies giving the same product in *ca.* 60% yield. Recrystallization from alcohol gave yellow needles with mp 146–147.5°: ir (Nujol) 1765, 1645, 1580 cm^{-1}; nmr ($CDCl_3$) δ 6.40 (s, 1 H), 7.2–8.0 (m, 10 H); mass spectrum *m/e* (R.A., relative abundance) 282 (M^+) (100%), 254 (4), 219 (10), 191 (40), 136 (10), 118 (36), 90 (38), uv $\lambda_{max}^{95\%\ EtOH}$ 358 nm (log ε 4.57).

Anal. Calcd for $C_{17}H_{12}O_2Cl$: C, 72.22; H, 3.92; Cl, 12.54. Found: C, 72.18; H, 3.73; Cl, 12.52.

β-Methoxy-α-phenyl-γ-arylidene-$\Delta^{\alpha,\beta}$-butenolide (14). 2,5-Diphenyl-3-hydroxy-6-methoxy-1,4-benzoquinone (**10**) was prepared by reaction of 3-chloro-2,5-diphenyl-6-hydroxy-1,4-benzoquinone with sodium methoxide as described by Cain.[24] Reaction of the hydroxyquinone with DMSO–acetic anhydride gave the butenolide (**14**) in *ca.* 60% yield by either the extraction work-up or solvent removal method. The waxy material was recrystallized from methanol giving beautiful pale yellow needles with mp 103–104° (lit.[28] 104–105°): ir (nujol) 1760, 1630 cm^{-1}; nmr ($CDCl_3$) δ 3.78 (s, 3 H), 6.28 (s, 1 H), 7.0–8.0 (m, 10 H); mass spectrum *m/e* (R.A.) 278 (M^+) (100%), 235 (6), 207 (10), 191 (9), 179 (23), 177 (10), 145 (13), 132 (20), 118 (23), 90 (29), 89 (64); uv $\lambda_{max}^{95\%\ EtOH}$ 328 nm (log ε 4.51), 224 (4.13).

α-Phenyl-γ-arylidene-$\Delta^{\alpha,\beta}$-butenolide (15). 2,5-Diphenyl-3-hydroxy-1,4-benzoquinone was prepared by Thiele acetylation of 2,5-diphenyl-1,4-benzoquinone as described by Cain,[24] mp 245–246° (lit.[24] 226–227° and 236–237°[29]). After reaction of the quinone with DMSO–acetic anhydride at *ca.* 75° for 1 hr, the solvent was removed *in vacuo* and the dark residue taken up in benzene and chromatographed on a column of silica gel. This procedure gave the yellow butenolide in yields up to 60%. Matetial after recrystallization from ethanol had mp 141–142° (lit.[30] 141–142°): ir (Nujol) 1760, 1650, 1590 cm^{-1}; nmr (DMSO) δ 6.42 (s, 1 H), 7.3–8.1 (m, 10 H), 8.26 (s, 1 H); ($CDCl_3$) 6.05 (s, 1 H), 7.58 (s, 1 H), 7.2–7.5, 7.7–8.1 (m, 10 H); mass spectrum *m/e* (R.A.) 248 (M^+) (100%), 220 (8), 192 (24), 191 (17), 119 (52), 102 (23), 90 (68), 89 (30); uv $\lambda_{max}^{95\%\ EtOH}$ 362 nm (log ε 4.62).

Rearrangement of 11 in the Presence of D_2O. α-Phenyl-γ-(arylidene-d_1)-$\Delta^{\alpha,\beta}$-butenolide (16). When the reaction of 2,5-diphenyl-3-hydroxy-1,4-benzoquinone (**11**) with DMSO–acetic anhydride was repeated including *ca.* 5% D_2O in the reaction mixture, the extraction procedure yielded a brown crystalline material in low yield along with recovered hydroxyquinone. Recrystallization of this brown material from alcohol (charcoal) gave the deuterated butenolide **16**: mp 140–142°; ir (Nujol) identical with that of **15**; nmr (DMSO) δ 7.3–8.1 (m, 10 H), 8.26 (s, 1 H); mass spectrum *m/e* (R.A.) 249 (M^+) (100%), 221 (8), 193 (20), 192 (16), 119 (30), 102 (13), 91 (33), 90 (20).

3,6-Diphenyl-4*H*-furo[3,2-*b*]pyrrole-2,5-dione (17). 2-Amino-6-hydroxy-3,5-diphenyl-1,4-benzoquinone (**12**) (0.9 g) was dissolved in 10 ml of dimethyl sulfoxide with warming. To the warm solution was added 4 ml of acetic anhydride and the reaction mixture was heated on a steam bath. After *ca.* 5 min the initially purple reaction mixture was dark green and the odor of dimethyl sulfide was noted. After heating on the steam bath for an additional 20 min the reaction mixture was poured into 50 ml of cold water, a few drops of concentrated HCl was added, and the mixture was extracted with three 100-ml portions of CH_2Cl_2. The organic layer was dried (Na_2SO_4) and the solvent was removed *in vacuo*. The residue was chromatographed on a column of silica gel. Elution with petroleum ether–benzene (50:50) removed a brown oil which crystallized upon the addition of ether. The bright yellow crystals of **17** had mp 291–292°. No suitable solvent was found for recrystallization of this material. The analytical sample was obtained directly from the column: ir (Nujol) 3160, 1790, 1710, 1640 cm^{-1}; nmr (DMSO-d_6) 7.3–8.1 (m), 3.4 ppm (very broad probably due to exchange with solvent); mass spectrum *m/e* (R.A.) 290 (22%), 289 (100), 260 (9), 205 (10), 145 (32), 144 (12), 118 (12), 117 (10), 116 (12), 90 (12), 89 (55), 63 (12); m* 94 (144 → 116), 68.5 (116 → 89), 181 (232 → 205), 233.5 (289 → 260). *Anal.* Calcd for $C_{18}H_{11}NO_3$: C, 74.73; H, 3.83; N, 4.84. Found: C, 73.74; H, 3.87; N, 4.89.

Elution of the column with benzene–ether (50:50) removed a brown oil which again crystallized upon addition of ether. The yellow crystals turned red upon melting at 164–168° and gas evolution was noted. Insufficient material was obtained for complete characterization: mass spectrum *m/e* (R.A.) 250 (1%), 122 (10), 105 (17), 94 (10), 79 (24), 78 (100), 77 (31), 63 (32), 52 (20), 51 (23), 50 (18), 39 (13); ir (Nujol) 1735, 1715, 1650 cm^{-1}.

2,5-Bis(dimethylsulfonium)-3,6-dioxy-1,4-benzoquinone Bisbetaine (25). A mixture of 14 ml of dimethyl sulfoxide and 6 ml of acetic anhydride was added to 1.5 g of 2,5-dihydroxy-1,4-benzoquinone (**21**) (Eastman practical) and the reaction mixture was heated on a steam bath. After *ca.* 15 min the yellow product precipitated from the dark brown reaction mixture. The precipitate was collected by filtration, washed with a little cold methanol, and dried, giving 2.3 g (83% yield) of the yellow, crystalline diylide:[12] mp >310°; ir (Nujol) 1560, 1250 cm^{-1}; nmr (CF_3CO_2H) δ 3.25 ppm (s); mass spectrum *m/e* (R.A.) 260 (M^+) (5), 94 (52), 79 (27), 62 (100), 61 (96), 47 (99), 46 (94), 45 (98), 44 (100), 35 (78); uv-visible (95% EtOH) λ_{max} (log ε) 278 nm (4.39), 293 (4.40), 304 (4.35), 365 (2.65). *Anal.* Calcd for $C_{10}H_{12}O_4S_2$: C, 46.13; H, 4.65; S, 24.63. Found: C, 46.15; H, 4.66; S, 24.60.

2-Dimethylsulfonium-3-oxy-1,4-naphthoquinone Betaine (28). To 1 g of 2-hydroxynaphthoquinone (**24**) (Eastman) was added a mixture of 5 ml of acetic anhydride and 10 ml of dimethyl sulfoxide. After heating *ca.* 30 min on a steam bath a yellowish precipitate was observed. From the cooled reaction mixture was obtained 1.2 g (90% yield) of yellow crystals which were washed with methanol. The ylide melted with decomposition around 255–260°: ir (Nujol) 1670 (w), 1605 (m), 1585 (s), 1540 (vs) cm^{-1}; nmr (CF_3CO_2H) δ 3.42 ppm (s), 7.8–8.5 (m); mass spectrum *m/e* (R.A.) 234 (M^+) (33%), 220 (57), 173 (100), 159 (37), 104 (78), 76 (83), 62 (100), 61 (62), 47 (98), 46 (70), 45 (85), 44 (50), 35 (50). This compound was independently synthesized by Gompper and Euchner.[12] *Anal.* Calcd for $C_{12}H_{10}O_3S$: C, 61.52; H, 4.30; S, 13.69. Found: C, 61.37; H, 4.29; S, 13.79.

3-Dimethylsulfonium-2-oxy-5-phenyl-1,4-benzoquinone Betaine (26). 2-Hydroxy-5-phenyl-1,4-benzoquinone (**22**) (1.5 g) was allowed to react with a mixture of 5 ml of acetic anhydride and 10 ml of dimethyl sulfoxide with heating on a steam bath for 1 hr. After cooling the reaction mixture was poured into 100 ml of cold water; the solution was made basic with 10% Na_2CO_3 and extracted with CH_2Cl_2. The organic layer was dried and the solvent removed leaving a dark red oil. The residue was chromatographed on a column of silica gel. Elution with petroleum ether–benzene (50:50) removed a yellow oil which smelled like DMSO and dimethyl sulfide. Elution with $CHCl_3$ removed a red oil which solidified upon standing overnight. The waxy solid was leached with a benzene–chloroform mixture (50:50) and beautiful orange crystals were collected: yield *ca.* 2 g (10% theor); ir (Nujol) 1670 (m), 1630 (w), 1615 (w), 1599 (w), 1565 (vs) cm^{-1}; nmr ($CDCl_3$) δ 3.07 (s), 6.73 (s), 7.41 (b); mass spectrum *m/e* (R.A.) 260 (M^+), (30%), 199 (65), 102 (55), 62 (100).

Anal. Calcd for $C_{14}H_{12}O_8S$: C, 64.59; H, 4.65; S, 12.32. Found: C, 64.70; H, 4.65; S, 12.31.

3-Dimethylsulfonium-5-methyl-2-oxy-1,4-benzoquinone Betaine (27). 4-Hydroxy-2,5-toluquinone[31] (1 g) was warmed in a mixture of 5 ml of acetic anhydride and 10 ml of dimethyl sulfoxide for 1 hr. The reaction mixture was poured into cold water and the aqueous solution was made basic to litmus with 10% Na_2CO_3. The mixture

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was extracted with $CHCl_3$ and the organic layer was dried and the solvent removed. The residual red oil deposited orange crystals upon standing. The ylide could be recrystallized from $CHCl_3$ and decomposed at 185°: yield *ca.* 0.2 g (15% theor); ir (Nujol) 1680 (w), 1630 (w), 1565 (s) cm^{-1}; nmr ($CDCl_3$) δ 2.07 (d, J = 1.5 Hz), 6.54 (m), 3.07 (s) ppm; mass spectrum *m/e* (R.A.) 198 (M^+) (17%), 137 (53), 62 (100), 44 (34).

3-Chloro-2,5-di-*tert*-butyl-1,4-benzoquinone. Chlorine was bubbled through a stirred suspension of 25 g (0.11 mol 1) of 2,5-di-*tert*-butyl-1,4-benzoquinone (Eastman, practical) in 250 ml of glacial acetic acid for *ca.* 0.5 hr. After stirring for an additional 2 hr, a slightly yellow precipitate was filtered off (14.8 g). The reaction mixture was poured into 1 l. of water and the resulting precipitate was recrystallized from alcohol (13.6 g); total yield was 28.4 g (86%). The dichloro adduct had mp 127–128°:[32] ir (Nujol) 1700, 1600 cm^{-1}; nmr ($CDCl_3$) δ 1.28 (s, 9 H), 1.37 (s, 9 H), 4.75 (s, 1 H), 6.47 (s, 1 H).

Dehydrohalogenation was accomplished by treating a suspension of 22 g (0.078 mol) of the dichloro adduct in 250 ml of ether with a solution of 5.7 g (0.077 mol) of diethylamine in 20 ml of ether. The ether solution was washed with water, dried, and evaporated giving 19 g (98%) of 3-chloro-2,5-di-*tert*-butyl-1,4-benzoquinone. The quinone is an oil and may be purified by distillation at reduced pressure (bp 98–102° (0.05 mm)): ir (neat) 1680, 1660 cm^{-1}; nmr ($CDCl_3$) δ 1.30 (s, 9 H), 1.46 (s, 9 H), 6.59 (s, 1 H).[32]

3-Azido-2,5-di-*tert*-butyl-1,4-benzoquinone. A solution of 5.1 g (0.02 mol) of the 3-chloro-2,5-di-*tert*-butyl-1,4-benzoquinone in 100 ml of methanol was cooled to 5° in an ice bath. A solution of 3.9 g (0.06 mol) of sodium azide in *ca.* 10 ml of water was added slowly with stirring. The reaction is conveniently followed by glc (SE-30, 175°). After about 2 hr, <5% chloroquinone remained, and the solvent was removed *in vacuo* (T < 35°) leaving a yellow orange precipitate which was slurried in *ca.* 50 ml of 70% EtOH, cooled to 5°, and filtered giving 2.2 g (42% yield) of the azidoquinone: mp 50–55° (melting with gas evolution); ir (Nujol) 2115 (s), 1670 (s), 1650 (s), 1555, 1380, 1370, 1300, 905 cm^{-1}; nmr ($CDCl_3$) δ 1.27 (s, 9 H), 1.37 (s, 9 H), 6.42 (s, 1 H); $\lambda_{max}^{95\%\ EtOH}$ 402 nm (log ϵ 3.56), 272 (4.24), 248 (4.25), 205 (4.62).

3-Amino-2,5-di-*tert*-butyl-1,4-benzoquinone. A solution of 3.5 g of the azidoquinone in *ca.* 300 ml of methanol containing *ca.* 50 mg of PtO_2 was shaken under hydrogen (30 lb/in.^{2}) for 10 hr at room temperature. The clear solution became dark red on filtering and was concentrated to *ca.* 100 ml, water was added to the cloud point, and the aminoquinone was allowed to crystallize. Filtration gave 2.5 g of the dark red quinone. A second crop of 0.3 g was obtained upon cooling. Recrystallization from methanol–water gave 2.7 g (86% yield) of material with mp 108–109°: ir (Nujol) 3490 (m), 3368 (s), 1670 (m), 1640 (m), 1570 (vs), 1560 (vs), 1330 (s) cm^{-1}; nmr ($CDCl_3$) δ 1.23 (s, 9 H), 1.40 (s, 9 H), 6.35 (s, 1 H); mass spectrum *m/e* (R.A.) 235 (M^+) (53%), 220 (94), 164 (100), 192 (25), 57 (40), 41 (42); m* 206 (235 → 220), 122.2 (220 → 164). This compound was recently prepared by an alternate route.[33] *Anal.* Calcd for $C_{11}H_{21}NO_2$: C, 71.45; H, 9.00; N, 5.95. Found: C, 71.38; H, 8.91; N, 5.94.

3-Hydroxy-2,5-di-*tert*-butyl-1,4-benzoquinone. 3-Amino-2,5-di-*tert*-butyl-1,4-benzoquinone (2.0 g, 8.5 mmol) was dissolved in 10 ml of glacial acetic acid and 2 ml of water. Cupric acetate monohydrate (2.0 g, 10 mmol) was added to the above solution and the reaction mixture was kept at 70°. The reaction is conveniently followed by tlc (silica gel–CH_2Cl_2). After *ca.* 4 hr no aminoquinone remained and the reaction mixture was poured into water and the resulting yellow precipitate was collected and recrystallized from acetic acid–water. The recrystallized hydroxyquinone weighed 1.5 g (75% yield) and had mp 78–79°. An analytical sample was obtained by preparative glc (SE-30, 175°): ir (Nujol) 3370, 1665, 1645, 1610, 1180 cm^{-1}; nmr ($CDCl_3$) δ 1.26 (s, 9 H), 1.36 (s, 9 H), 6.38 (s, 1 H), 7.63 (s, 1 H) (disappears on shaking with D_2O); mass spectrum *m/e* (R.A.) 236 (M^+) (78%), 221 (100), 193 (35), 179 (41), 97 (33), 57 (44), 43 (35); m* 207 (236 → 221), 145 (221 → 179). *Anal.* Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.20; H, 8.39.

3-Hydroxy-2,5-di-*tert*-butyl-1,4-benzoquinone was recently isolated in an impure state by Hewgill and Lee[34] who reported ir and nmr data for a yellow gum in agreement with the above results. The original synthesis of the hydroxyquinone employed cupric chloride instead of cupric acetate, but the hydroxyquinone was not itself stable under the reaction conditions.[35] Cupric acetate is thus the reagent of choice for the hydrolysis reaction.

2,5-Dimethyl-3-hydroxy-1,4-benzoquinone. This quinone was prepared according to the method of Fieser and Ardao.[36]

2-Hydroxy-3-phenyl-1,4-naphthoquinone. This quinone was prepared according to the method reported by Soliman and West.[37]

2-Hydroxy-3-*p*-methoxyphenyl-1,4-naphthoquinone. This quinone was prepared by the method reported by Neunhoeffer and Weise.[38]

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