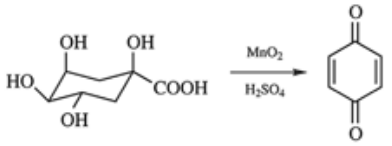
Kirk-Othmer Encyclopedia of Chemical Technology.

QUINONES

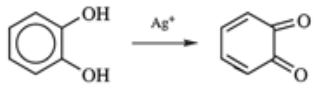
1. Introduction

A quinone is defined as a cross-conjugated system of two α, β-unsaturated carbonyl groups, usually in a cyclohexane ring. In 1838, quinic acid [36413-60-2] (**1**) was oxidized to 1,4-benzoquinone (**2**) with manganese dioxide (eq. 1) (1). This starting material gave us the generic name quinone.



(1) (2) (1)

The isomeric form, 1,2- benzoquinone (**3**) was prepared from catechol (1,2-benzenediol) using silver ion as the oxidant (eq. 2) (2).



(3) (2)

Synthesis by oxidation remains the first choice for commercial and laboratory preparation of quinones (3). Compounds related to (**3**) must be prepared using mild conditions because of their great sensitivity to both electrophiles and nucleophiles (4).

The simple, descriptive name quinone has been abandoned by *Chemical Abstracts*, which now uses 2,5-cyclohexadiene-1,4-dione for (**2**) and 3,5-cyclohexadiene-1,2-dione for (**3**). The use of quinone nomenclature remains universal among publishing organic chemists and will be used in this article. Several examples of quinone synomyms are given in Table 1 and analogous, but more complicated, structures are presented in Fig. 1.

Quinonoid compounds and their chemistry have been thoroughly reviewed (5,6). Quinone addition and substitution chemistry were reviewed in 1993 (7). The quinone system in natural products continues to promote extensive research and the literature has been summarized (8,9). The *meta*-quinone problem has also been treated (10).

The close electrochemical relationship of the simple quinones, (**2**) and (**3**) with hydroquinone (1,4-benzenediol) (**4**) and catechol (1,2-benzenediol) (**5**) respectively, has proven useful in ways extending beyond

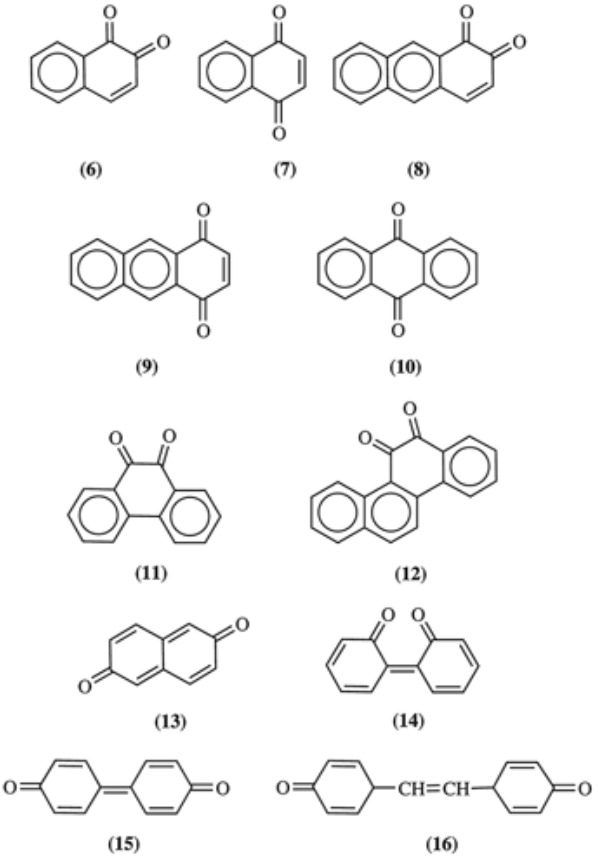
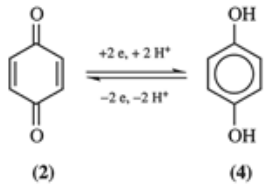


Fig. 1. Quinones of polynuclear hydrocarbons: (**6**) 1,2-naphthoquinone [524-42-5]; (**7**) 1,4-naphthoquinone [130-15-4]; (**8**) 1,2-anthraquinone [655-04-9]; (**9**) 1,4-anthraquinone [635-12-1]; (**10**) 9,10-anthraquinone [84-65-1]; (**11**) 9,10-phenanthraquinone [84-11-7]; (**12**) 5,6-chrysenequinone (5,6-dihydrochrysene-5,6-dione) [2051-10-7]; (**13**) 2,6-naphthoquinone [613-20-7]; (**14**) 2,2′-diphenoquinone [59869-78-2]; (**15**) 4,4′-diphenoquinone [494-72-4]; (**16**) 4,4′-stilbenequinone (stilbene-4,4′-dione) [3457-53-2].

their being an attractive synthetic route (eqs. 3, 4).



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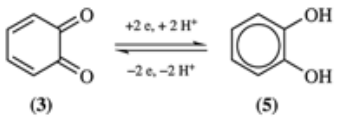


(4)

Table 1. Quinone Nomenclature

Common name	CAS Registry Number	Synonym	Structure number
1,4-benzoquinone	[106-51-4]	*p*-benzoquinone	**2**
1,2-benzoquinone	[583-63-1]	*o*-benzoquinone	**3**
1,4-naphthoquinone	[130-15-4]	α-naphthoquinone	**7**
4,4′-diphenoquinone[a]	[492-72-4]	diphenoquinone	**15**
o-chloranil[b]	[2435-53-2]	tetrachloro-*o*-quinone	**20**
p-chloranil[c]	[118-75-2]	tetrachloro-*p*-quinone	**21**
2,3-dichloro-5,6-dicyano-1,4-benzoquinone[d]	[84-58-2]	DDQ	**22**

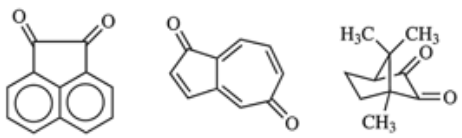
[a] [Bis-2,5-cyclohexadien-1-ylidene]-4,4′-dione; 4-(4-oxo-2,5-cyclohexadiene-1-ylidene)-2,5-cyclohexadien-1-one is also used.
[b] 3,4,5,6-Tetrachloro-3,5-cyclohexadiene-1,2-dione.
[c] 2,3,5,6-Tetrachloro-2,5-cyclohexadiene-1,4-dione.
[d] 4,5-Dichloro-3,6-dioxo-1,4-cyclohexadiene-1,2-dicarbonitrile.

Photographic developers and dye syntheses often involve (**4**) or its derivatives (11). Biochemists have found much interest in the interaction of mercaptans and amino acids with various compounds related to (**3**).

Concern for the environment and the need to explore renewable natural resources has prompted the exploration of biosynthetic routes and green chemistry. Using bacterial enzymes to convert D-glucose [50-99-7] to either 1,2- or 1,4-benzenediol allows an entry to benign quinone syntheses (12,13). Solvents are also playing an important role in this fundamentally new approach. Supercritical carbon dioxide combined with ordinary solvents, such as acetonitrile, allowed the efficient conversion of 2,6-di-*tert*-butylphenol to 2,6-di-*tert*-butyl-1,4-benzoquinone [719-22-2], (14). A similar catalytic oxidation was carried out in an ionic liquid (15). Using molecular oxygen and a catalytic amount of copper(II) chloride, it was possible to obtain an 86% yield of 2,3,5-trimethyl-1,4-benzoquinone [935-92-2] from the corresponding phenol.

The cross-conjugated system of two α,β-unsaturated carbonyl groups of both 1,2- and 1,4-quinones occurs in many polynuclear hydrocarbons as illustrated in Fig. 1. The carbonyl groups may be located in different rings, but they occupy positions corresponding to the 1,2- or 1,4-orientation of monocyclic quinones.

There is a rich literature of non-benzenoid quinones, such as acenaphthenequinone (1,2-acenaphthylenedione) [82-86-0] (**17**) (16,17). The more extensive chemistry of quinines derived from azulene such as 1,5-azuloquinone [74424-63-8] (**18**) has also been reviewed (18). A few compounds with no apparent relationship to quinones continue to be misnamed, eg, camphorquinone [465-29-2] (2,3-camphandione) (**19**) (19).



(17) (18) (19)

Table 2. Physical Properties of Selected Quinones

Name	CAS Registry number	Structure number	Color	Melting point, °C
1,4-benzoquinone	[106-51-4]	**2**	yellow	113, 116
1,2-benzoquinone	[583-63-1]	**3**	red	60–70 dec
1,2-naphthoquinone	[524-42-5]	**6**	yellow red-orange	145–147
1,4-naphthoquinone	[130-15-4]	**7**	bright yellow	125, 128.5
3,4,5,6-tetrachloro-1,2-benzoquinone	[2435-53-2]	**20**	orange-red	133, 122–7
2,3,5,6-tetrachloro-1,4-benzoquinone	[118-75-2]	**21**	yellow	290, 294
2,3-dichloro-5,6-dicyano-1,4-benzoquinone	[84-58-2]	**22**	bright yellow	290, 294
2-chloro-1,4-benzoquinone	[695-99-8]	**23**	yellow-red	57
2,5-dichloro-1,4-benzoquinone	[615-93-0]	**24**	pale yellow	161–162
2,5-dimethyl-1,4-benzoquinone	[137-97-9]	**25**	yellow	125
2-methyl-1,4-benzoquinone	[553-97-9]	**26**	yellow	69
3-chloro-1,2-naphthoquinone	[18099-99-5]	**27**	red	172 dec
2,3-dichloro-1,4-naphthoquinone	[177-80-6]	**28**	yellow	193, 195
2-methyl-1,4-naphthoquinone	[58-27-5]	**29**	yellow	105–107

	Structure	Crystalline	Solubility	
	number	form	Soluble	Insoluble
	2	monoclinic prisms	alcohol, ether	water, pentane
	3	plates or prisms	ether, benzene	pentane
	6	needles	water, alcohol	ligroin
	7	needles	alcohol, benzene	water, ligroin
	20			
	21	monoclinic prisms	ether	water, ligroin
	22	plates		
	23	rhombic-hexagonal	water, alcohol	
	24	monoclinic prisms	ether,chloroform	water, alcohol
	25		ether, alcohol	water, alcohol
	26	plates or needles	ether, alcohol	water
	27	needles	alcohol, benzene	water
	28	needles	benzene, chloroform	water, alcohol
	29	needles	ether, benzene	water, alcohol

2. Physical Properties

Simple quinones have two notable physical properties: odor and color. The 1,4-benzo- and 1,4-naphthoquinones and many of their derivatives have high vapor pressures and pungent, irritating odors. The single ring compounds are often found as constituents of insects' chemical defense against predators. In general, the 1,2-quinones are vibrant in color, ranging from orange to red, whereas the 1,4-quinones are usually lighter, ie, yellow to orange.

Selected physical data for various quinones are given in Table 2 (20). References 21,22,23 greatly expand the range of data treated. Spectral and redox data are given in Table 3. Structures for Tables 2 and 3 are found in Figure 2, if not already used.

2.1. Chemical Properties

The quinones have excellent redox properties; thus, they are important oxidants in laboratory and biological synthons. The presence of an extensive array of conjugated systems, especially the α,β-unsaturated carbonyl

Table 3. Spectral [Ultraviolet (uv)] Data and Redox Potentials for Selected Quinones[a]

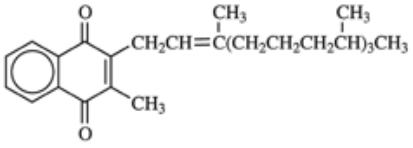
Structure number	λ_{max}, nm(ε)[c]	$-E_{1/2}$[b], V	
		E_1	E_2
3	385 (1585)[d]	0.31	0.90
20	430 (1995)	0.1	−0.71
2	243	0.51	1.14
23	251 (7740)	0.34	0.92
24	271 (5710)	0.18	0.81
22	238 (11,950)[e]	−0.51	−0.30
25	251 (11,650)	0.67	1.27
26	246 (13,804)[f]	0.58	1.10
21	286 (12,600)	−0.01	0.71
6	248 (20,400)	0.56	1.02
27	246 (20,417)[g]	0.71	1.25
7	279, 252, 246	−0.67	−1.05[h]
28	253, 249, 244[i]	0.77	1.28

[a] See Fig. 2; Ref. 20.
[b] 25°C,SCE, CH_3CN, 0.1 *N* $(C_2H_5)_4NClO_4$.
[c] Solvent is CH_3OH unless otherwise noted; usually several solvents are given in the works cited.
[d] Ether.
[e] Ref. 24.
[f] Ethanol.
[g] CH_3CN.
[h] Propylene carbonate.
[i] Cyclohexane.

arrangement, allows the quinones to participate in a variety of reactions. Characteristic of quinone chemistry are nucleophilic addition and substitution; electrophilic, radical, and cycloaddition reactions; photochemistry; and normal and unusual carbonyl chemistry.

2.2. Biochemical Reactions

The quinones in biological systems play varied and important roles (25,26). In insects, they are used for defense purposes, and the vitamin K family members, eg, vitamin K_1 [11104-38-4] (**30**) and vitamin K_2 [11032-49-8] (**31**) which are based on 2-methyl-1,4-naphthoquinone, are blood-clotting agents.



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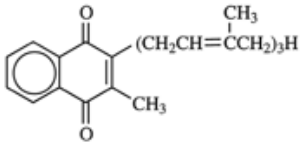


(31)

Two groups of substituted 1,4-benzoquinones are associated with photosynthetic and respiratory pathways; the plastoquinones, eg, plastoquinone [4299-57-4] (**32**) and the ubiquinones, eg, ubiquinone [1339-63-5] (**33**) are involved in these processes. Although they are found in all living tissue and are central to life itself, a vast amount remains to be learned about their biological roles.

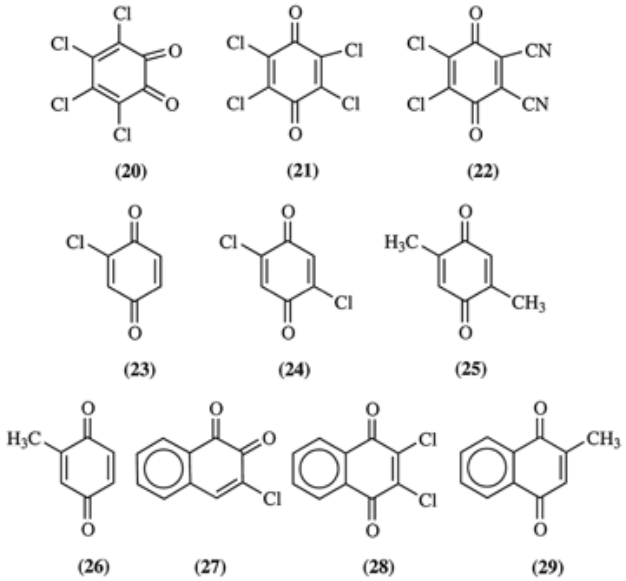
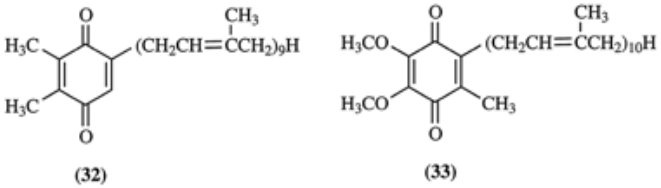
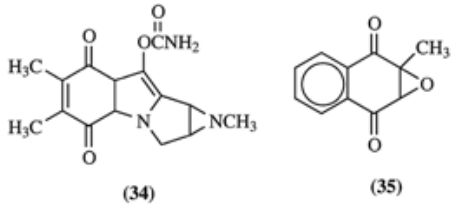
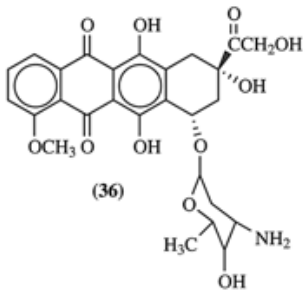


Fig. 2. Selected quinones for which property data are given in Tables 2 and 3.



Quinones of various degrees of complexity have antibiotic, antimicrobial, and anticancer activity, eg, aziridinomitosene [80594-63-8] (**34**) (−)-2-methyl-1,4-naphthoquinone 2,3-epoxide [61840-91-3] (**35**) and doxorubicin, [23214-92-8] (adriamycin) (**36**). All of these natural and synthetic materials have stimulated extensive research in preparative chemistry (9).



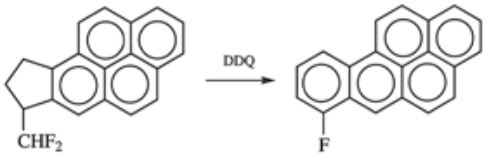


(36)

Interest in the use of quinones as oxidants has not been restricted to biosynthetic and biochemical problems. Since the 1960s, the literature of quinone oxidation and dehydrogenation chemistry has grown enormously (27,28). The most widely used oxidants have been 1,4-benzoquinone (**2**) (oxidation potential, 711 mV), *p*-chloranil (**21**) (742 mV), and DDQ (**22**) (∼1000 mV). Low cost, availability, stability, and high oxidation potential characterize these reagents. Although the oxidation potential is of primary importance, it can be outweighed by other considerations. For example, 2,3,5,6-tetracyano-1,4-benzoquinone [4032-03-5] has been prepared, but its high reactivity and moisture sensitivity have greatly restricted its application. Because the 1,2-quinones tend to undergo Diels-Alder dimerization easily, only *o*-chloranil (**20**) has been used extensively. More complex quinones have been used, eg, 2,5-dibromo-6-isopropyl-3-methyl-1,4-benzoquinone [29096-93-3] has found specific applications. By contrast anthraquinone (**10**) is important industrially, but rarely used in the synthetic laboratory.

2.3. Dehydrogenation

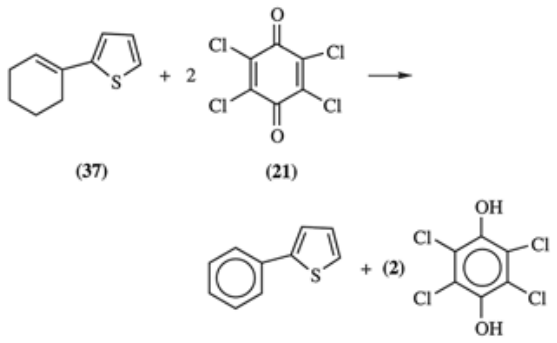
The oldest, and still important synthetic use of quinones is in the removal of hydrogen, especially for aromatization. This method has often been applied to the preparation of polycyclic aromatic compounds, and may be accompanied by unexpected ring expansion (29), eg, in the conversion of 7-difluoromethyl-8,9-dihydro-7(*H*)-cyclopenta[*a*]pyrene [71511-38-1] to 7-fluorobenzo[*a*]pyrene [72297-03-1] (eq. 5).



(5)

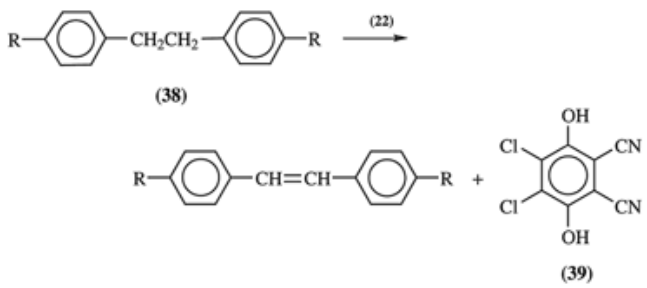
8 QUINONES

Excellent evidence of the gentle nature of quinones as oxidants in the presence of the thiophene ring is given for compound (**37**) (eq. 6) (30).



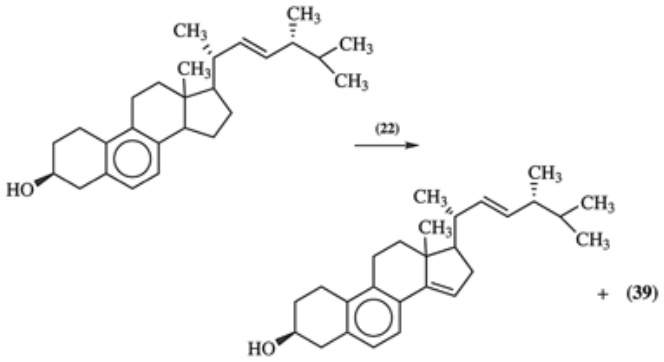
(6)

The powerful accelerating effect of electron-donating substituents in dehydrogenation reactions is illustrated in a reaction of DDQ (**22**) with substituted bibenzyls (**38**) where the yield is 10% when R = H, but 85% when R = OCH_3 (eq. 7) (31,32).



(7)

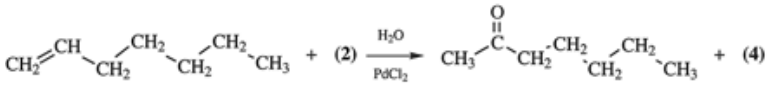
Quinones are used extensively in the dehydrogenation of steroidal ketones (31,32). Such reactions are marked by high yield and selectivity. Generally, the results with nonsteroidal ketones are disappointing (33). A spectacular example of selective dehydrogenation in a steroid ring system (eq. 8) has been attributed to stereoelectronic effects (34). Several related steroids also show this chemistry. An extensive review containing many additional examples and a mechanistic discussion has been presented (35).



(8)

2.4. Oxidation

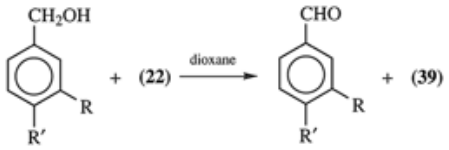
The use of 1,4-benzoquinone in combination with palladium(II) chloride converts terminal alkenes to alkyl methyl ketones in very high yield (eq. 9) (36). The quinone appears to reoxidize the palladium.



(9)

Although saturated alcohols are sufficiently stable toward quinones to be used as solvents for these oxidation reactions, benzylic and allylic alcohols are often readily converted to the corresponding carbonyl compounds (eq. 10) (37). Typical yields and substituents are as follows:

R	R′	% Yield
H	CH_3	93
OH	H	83
OH	OCH_3	97



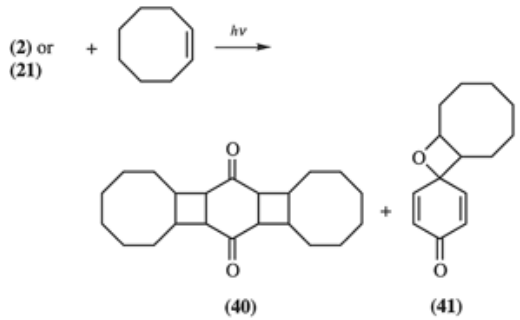
(10)

2.5. Photochemical Reactions

Increased knowledge of the centrality of quinone chemistry in photosynthesis has stimulated renewed interest in their photochemical behavior. Synthetically interesting work has centered on the 1,4-quinones and the two reaction types most frequently observed, ie, [2 + 2] cycloaddition and hydrogen abstraction. Excellent reviews of these reactions, along with mechanistic discussion, have appeared (38,39).

2.6. Cycloadditions

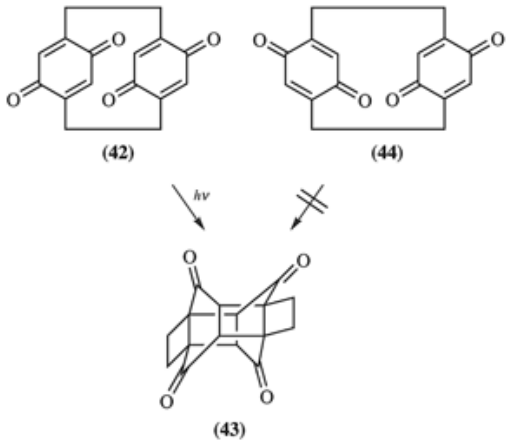
The products of [2 + 2] cycloaddition are usually of the cyclobutane type, eg, (**40**) [80328-12-7], or spirooxetane type, eg, (**41**) [137378-86-0] (eq. 11).



(11)

The product distribution appears to depend on the radiation used for quinone excitation, the structure of the quinone, and the quinone/alkene ratio. In the example cited, 1,4-benzoquinone gives only the spirooxetane, whereas chloranil gives both products in amounts related to the ratio of starting materials (40,41).

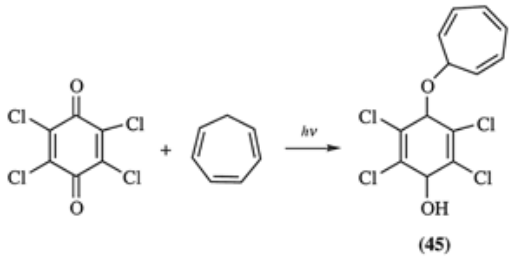
A delicate stereochemical balance is clear in the high yield photocyclization of one cyclophane configuration (**42**) to a cage compound (**43**), whereas its spatial relative (**44**) leads only to higher molecular weight product (eq. 12) (42).



(12)

2.7. Hydrogen Abstraction

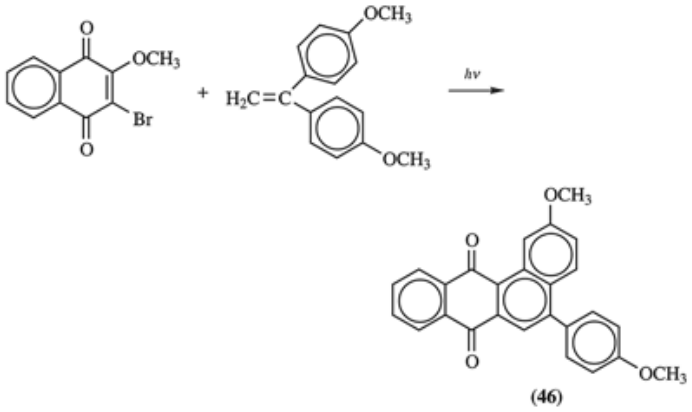
These important reactions have been carried out using a variety of substrates. In general, the reactions involve the removal of hydrogen either directly as a hydrogen atom or indirectly by electron transfer followed by proton transfer. The products are derived from ground-state reactions. For example, *p*-chloroanil probably reacts with cycloheptatrienyl radicals to produce the ether (**45**) (eq. 13) (43). This chemistry contrasts with the ground-state reaction in which DDQ produces tropylium quinolate in 91% yield (44).



(13)

The synthesis of the highly carcinogenic polycyclic hydrocarbons, eg, (**46**) [72735-91-2], may be affected by photocycloaddition of 2-bromo-3-methoxy-1,4-naphthoquinone [26037-61-6] with 1,1-diarylethylenes such

as 1,1-bis(*p*-methoxyphenyl)ethene (eq. 14) (45).



(46)

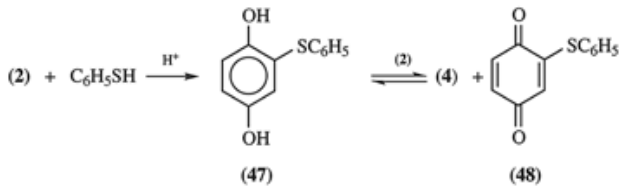
(14)

Although the yields are variable and isomeric products are obtained using unsymmetrical ethenes, the reaction conditions are mild and show promise of stereoselectivity.

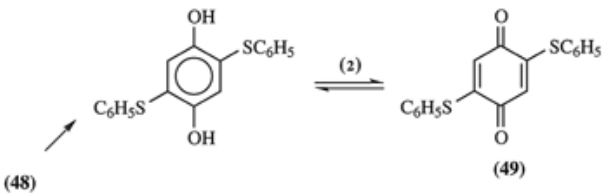
The role of rose bengal and other sensitizer dyes in the photodimerization of 2-acetyl-1,4-benzoquinone [1125-55-9] involves electron transfer, but not singlet oxygen (46).

2.8. Addition Reactions

The addition of nucleophiles to quinones is often an acid-catalyzed, Michael-type reductive process (7,47,48). The addition of benzenethiol to 1,4-benzoquinone was studied by A. Michael for a better understanding of valence in organic chemistry (eqs. 15 and 16) (49). The presence of the reduced product thiophenylhydroquinone (**47**), the cross-oxidation product 2-thiophenyl-1,4-benzoquinone [18232-03-6] (**48**), and multiple addition products, such as 2,5-bis(thiophenyl)-1,4-benzoquinone [17058-53-6] (**49**) and 2,6-bis(thiophenyl)-1,4-benzoquinone [121194-11-4] (**50**), is typical of many such transformations.



(47) (48)



(48) (49)

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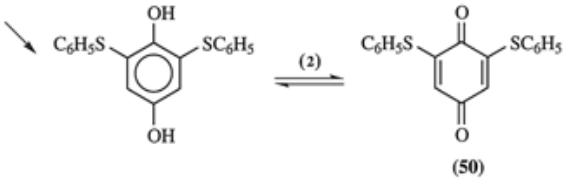
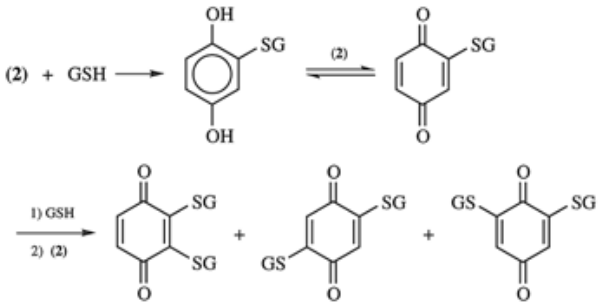


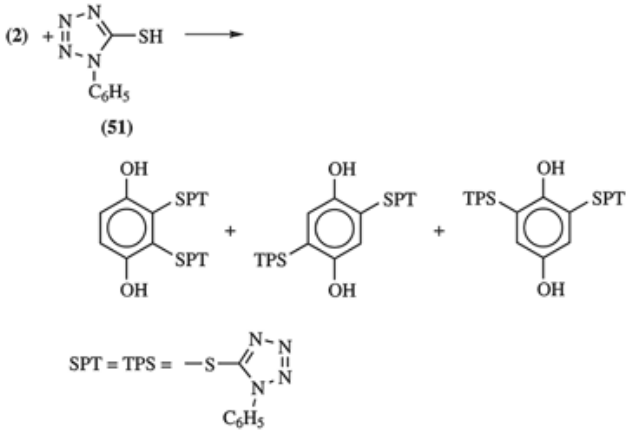
(16)

Recognition of the thiol group's key role in biochemistry has led to studies of 1,4-benzoquinone with glutathione, a tripeptide γ-Glu·Cys·Gly (GSH). The cross-oxidation of the initial addition product by excess quinone leads, under physiological conditions, to all three isomeric products (eq. 17) (50).



(17)

The acidic thiol 1-phenyl-5-mercaptotetrazole (HSPT)(**51**) also yields all three expected products when its initial hydroquinone product is further oxidized (51). With this nucleophile the reduced hydroquinone products are formed and cross-oxidation by (**2**) does not occur to any measurable extent (eq. 18).

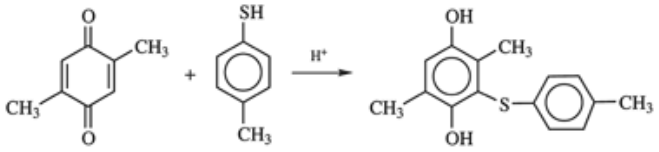


(18)

The complications of subsequent cross-oxidation and further addition depend on both electronic and steric considerations. Thiols and amines generally promote cross-oxidation and tend to be oriented in the 2,5-positions of the resulting quinonoid product; eg, the electron-donating phenyl sulfide linkage makes the hydroquinone product susceptible to oxidation by the quinone starting material as illustrated by the reaction of (**2**) and benzenethiol. The 2,5-bis(phenylthio)-1,4-benzoquinone (**49**) predominates for electronic reasons,

but an appreciable amount of the 2,6-isomer (**50**) is also obtained. Electron-withdrawing substituents, eg, arylsulfonyl, effectively prevent further oxidation.

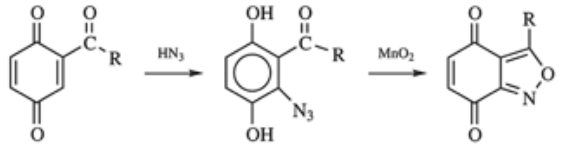
The importance of steric effects in determining the oxidation state of the product can be illustrated by a thioether linkage, eg, (**52**). If a methyl group is forced to be adjacent to the sulfur bond, the planarity required for efficient electron donation by unshared electrons is prevented and oxidation is not observed (eq. 19) (52). Similar chemistry takes place in the addition of organic nitrogen and oxygen nucleophiles as well as inorganic anions.



(52) (19)

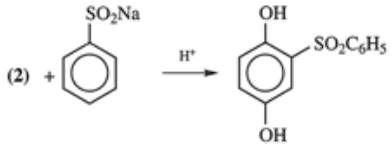
The azide anion, often in hydrazoic acid, adds in good yield, and when strong electron-withdrawing groups are present, shows the normal 2,3-orientation (**53**) (eq. 20) (53). The intermediates are useful for further synthetic goals like conversion to heterocyclic products, eg, (**54**). The yields for various R groups are as follows:

R	Yield of **53**, %	Yield of **54**, %
H	66	52
CH_3	92	76
OCH_3	89	



(53) (54) (20)

The most extensive mechanistic studies of quinone Michael addition chemistry involve the arylsulfinic acids, which yield reduced product (eq. 21) (54). The sulfones produced in such reactions

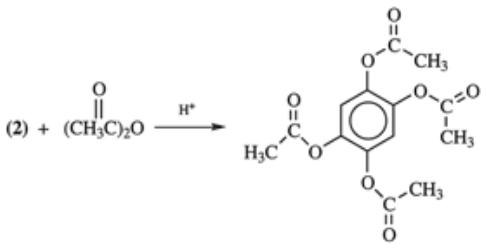


(21)

have been examined electrochemically (52) and kinetically (55). The influence of substitutents in the quinone has also been studied (56).

The influence of solvent and acidity on the ratio of 2,5- to 2,6-product has been studied for 2-methyl-1,4-benzoquinone (**26**) and benzenesulfonic acid (57). The ratio can be made to favor either product by controlling the concentration of protonated or hydrogen-bonded quinone. This reaction has also been studied in ionic-liquids and shows somewhat different yield patterns (58).

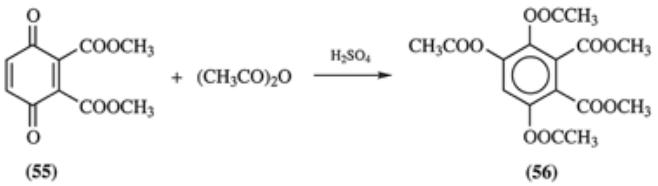
An especially interesting case of oxygen addition to quinonoid systems involves acidic treatment with acetic anhydride, which produces both addition and esterification (eq. 22). This Thiele-Winter acetoxylation has been used extensively for synthesis, structure proof, isolation, and purification (59).



(22)

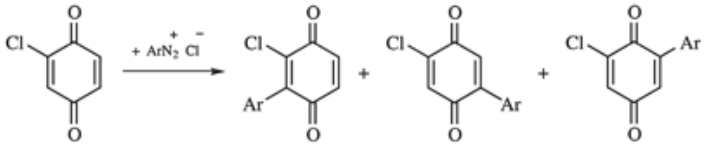
The kinetics and mechanism of acetoxylation have been described (60). Although the acetylium ion is an electrophile, extensive studies of electronic effects show a definite relationship to nucleophilic-addition chemistry (61).

In seeking a synthetic route to an antibiotic antitumor agent, the Thiele-Winter synthon, with 2,3-bis(methoxycarbonyl)-1,4-benzoquinone [77220-15-6] (**55**) was used to introduce a required third oxygen linkage (62). A 67% yield of (**56**) was obtained (eq. 23).



(23)

Electrophilic addition to quinones, eg, the reaction of 2-chloro-1,4-benzoquinone (**23**) with diazonium salts, represents a marked contrast with acetoxylation in product distribution (eq. 24) (63).

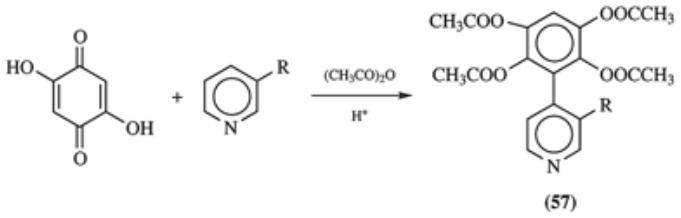


(24)

Phenyldiazonium chloride ($Ar = C_6H_5$) yields 8% 2,3-substitution [80632-59-3], 75% 2,5-substitution [39171-11-4], and 17% 2,6-substitution [80632-60-6]. For *p*-chlorophenyldiazonium chloride, the pattern is 28% 2,3-substitution [80632-61-7], 35% 2,5-substitution [62120-48-3], and 37% 2,6-substitution [80954-64-9]. For *p*-nitrophenyldiazonium chloride, the pattern is 41% 2,3-substitution [80632-62-8], 19% 2,5-substitution [80632-63-9], and 40% 2,6-substitution [80954-64-9]. Noteworthy is the presence of all three isomeric products, and the product ratio dependence on the aryl substituent. The reaction of 2-methyl-1,4-benzoquinone (**26**) with a wide variety of diazonium salts produces only the 2,5-isomer (64).

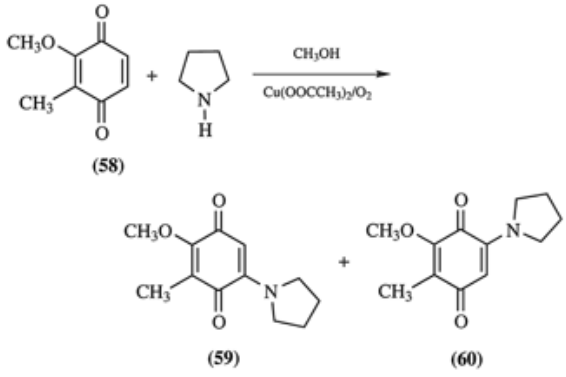
The development of the tandem reaction sequence in quinone chemistry is opening up interesting new possibilities. In seeking elegant syntheses of complex molecules, careful orchestration of transformations has become essential. The use of the Thiele-Winter reaction in tandem with arylation gives good yields of pharmacologically interesting heterocycles, such as (**57**) from 2,5-dihydroxy-1,4-benzoquinone [615-94-1] and pyridines,

where R = H or CH_3 (eq. 25) (65).



(57) (25)

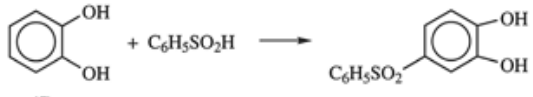
The quinones undergo Michael addition with nitrogen nucleophiles in much the same fashion as sulfur (66). Interest in quinones that contain heterocyclic nitrogen has prompted a detailed study of the addition of pyrrolidine to unsymmetrical benzoquinones such as 2-methoxy-3-methyl-1,4-benzoquinone [2207-57-0] (**58**) where high regioselectivity has been observed (67). The yields are 93% of (**59**) [77357-35-8] and 5% of (**60**) [77357-36-9] (eq. 26).



(58)

(59) (60) (26)

Information on nucleophilic-addition chemistry of quinones and various mechanistic rationalizations have been discussed, and molecular orbital calculations have been proposed as more definitive approaches for explanation and prediction (68). The synthetic techniques of *in situ* generation of the quinone and utilization of quinone monoacetals avoid the problems of instability, sequential addition, and poor regiospecificity, which often occur in quinone addition reactions. For example, although 1,2-benzoquinones react in much the same fashion as the 1,4-benzoquinones, their lower stability makes *in situ* generation advisable. A number of nascent quinone reactions such as eq. 27 have been reviewed (69).

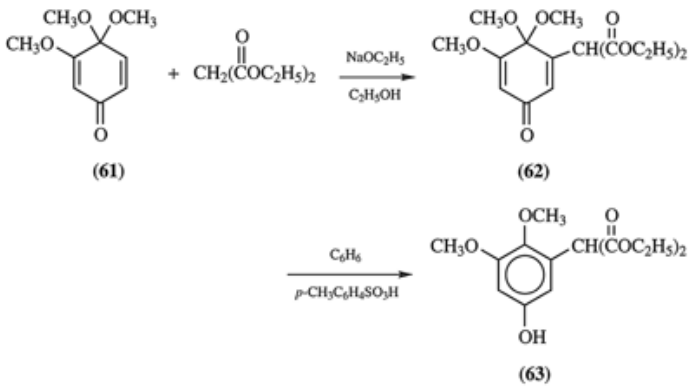


(5) (27)

Of special importance is the complex problem of nitrogen addition as related to the drug dopamine where even model compounds lead to extremely complex chemistry and difficult analytical problems (70).

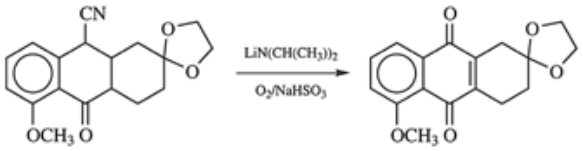
Quinone monoacetals, such as 2-methoxybenzoquinone monoacetal [64701-03-7] (**61**) show regiospecific addition of active methylene compounds (eq. 28) (71), yielding 83% (**62**) and 63% (**63**) on reaction with ethyl

malonate.



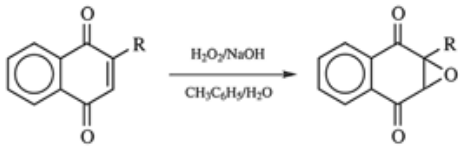
(28)

An interesting conversion of keto nitriles, eg, (**64**) to quinones has been reported (eq. 29) and shows excellent regiospecificity when combined with a preceding cyclization step (72).



(29)

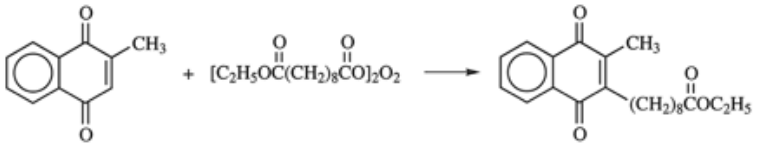
The synthesis of optically active epoxy-1,4-naphthoquinones using benzylquininium chloride as the chiral catalyst under phase-transfer conditions has been reported (73). 2-Methyl-1,4-naphthoquinone (R = CH_3) (**29**) yields 70% of levorotatory (**35**) (eq. 30). 2-Cyclohexyl-1,4-naphthoquinone [34987-31-0] yields 85% of (+)-2-cyclohexyl-1,4-naphthoquinone-2,3-epoxide [73377-78-3]. 2-Phenyl-1,4-naphthoquinone [2348-77-8] yields 92% (−)-2-phenyl-1,4-naphthoquinone-2,3-epoxide [73377-82-9].



(30)

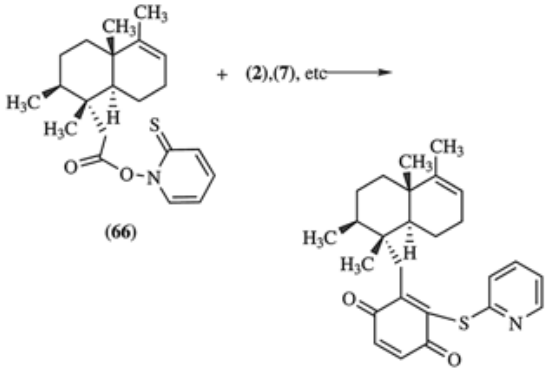
The reaction is characteristic of the usual Michael addition of hydroperoxide anion, yielding enantiomeric excesses of up to 45%. Reactions of quinones with radicals have been explored, and alkylation with diacyl peroxides constitutes an important synthetic tool (74). Although there are limitations, an impressive range of substituents can be introduced in good yield; examples include alkyl chains ending with functional groups, eg,

50% yield of (**65**) [80632-67-3] (eq. 31) (75,76).



(29) (65) (31)

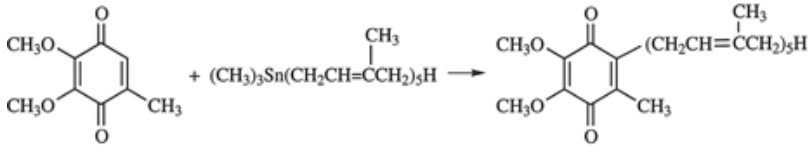
The synthesis of quinone sesquiterpenes has been achieved through a regioselective radical addition reaction (eq. 32) (77). The



(66) (32)

process depends upon the photochemical decarboxylation of a thiocarbonyl derivative (**66**). The utility of the method was demonstrated through the synthesis of several natural products containing various *trans*-decalin ring systems.

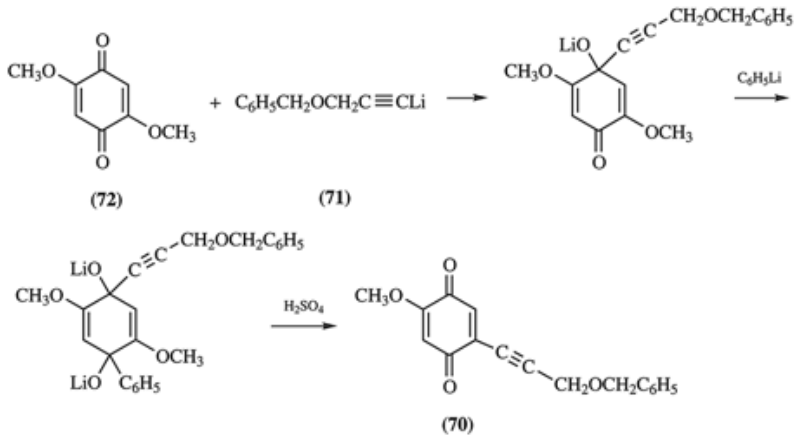
The importance of quinones with unsaturated side chains in respiratory, photosynthetic, blood-clotting, and oxidative phosphorylation processes has stimulated much research in synthetic methods. Polyisoprenyltin reagents, eg, (**67**) converts 2,3-dimethoxy-5-methyl-1,4-benzquinone [605-94-7] (**68**) to 94% (**69**) [4370-61-0] (eq. 33) (78,79,80).



(68) (67) (69) (33)

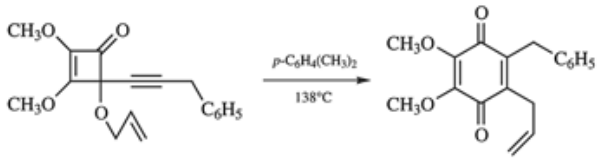
A selective method for preparing unsymmetrical 2-alkynyl-5-alkyl- or aryl-1,4-benzoquinones, eg, 60% yield of (**70**) [64080-65-5], involves the sequential introduction of lithium salts, eg, (**71**) (eq. 34) (81). Because the lithium reagents are generated *in situ* and the intermediates are not isolated, the transformations are

showing great promise as pro-drugs (82,83).



(34)

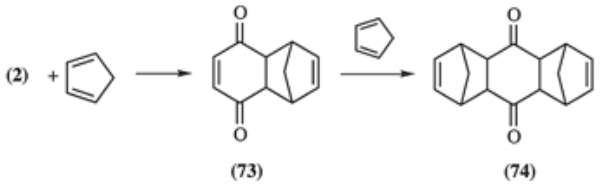
Cyclobutenones, ketenes and, alkynes have been shown to undergo rearrangement to a variety of highly substituted quinones (eq. 35) (84,85,86)



(35)

This chemistry has been combined with tin compounds to produce stannylquinones directly. These intermediates undergo smooth palladium-catalyzed coupling with aryl and heteroaryl iodides (87).

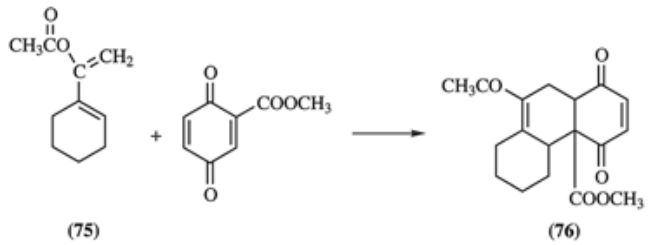
The synthesis of natural products containing quinonoid structure has led to intensive and extensive study of the classic diene synthesis (88). The Diels-Alder cycloaddition of quinonoid dienophiles has been reported for a wide range of dienes (89,90,91). Reaction of (**2**) with cyclopentadiene yields (**73**) [1200-89-1] and (**74**) [5439-22-5] (eq. 36). The analogous 1,3-cyclohexadiene adducts have been the subject of ^{13}C nmr and X-ray studies, which indicate the endo-anti-endo stereostructure (92).



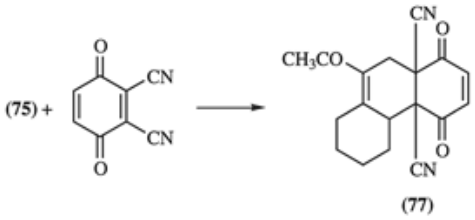
(36)

Unsymmetrical dienes in this synthesis are often capable of high regioselectivity (eqs. 37 and 38) (93). Reaction of (**75**) with 2-methoxycarbonyl-1,4-benzoquinone [3958-79-0] yields 97% of (**76**) [80328-15-0]. Reaction

of (**75**) with 2,3-dicyano-1,4-benzoquinone [4622-04-2] yields 58% of (**77**) [80328-16-1].

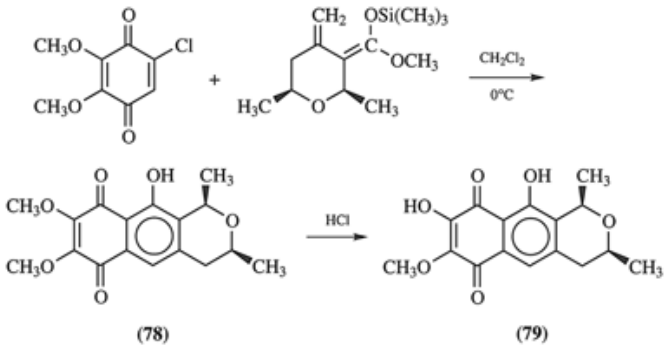


(75) (76) (37)



(77) (38)

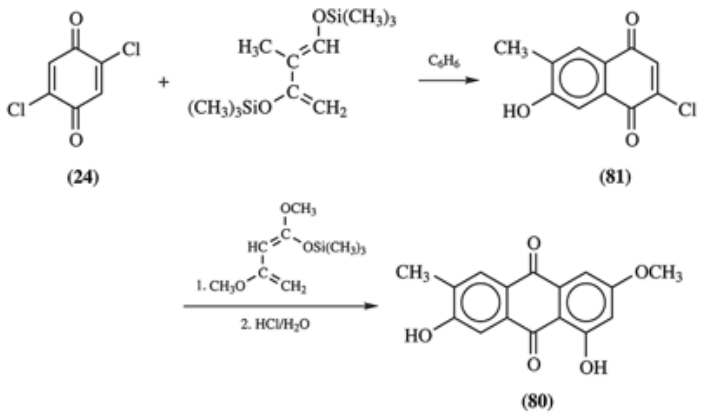
The importance of both electronic and steric effects is clear in cycloadditions as in cross-oxidations; an example is a heterocyclic modification leading to the thermodynamically less stable natural form of juglone derivatives such as ventiloquinones *H* [124917-64-2] (**78**) and *I* [124917-65-3] (**79**) (eq. 39) (94). The yields are 97% (**78**) from 5-chloro-2,3-dimethoxy-1,4-benzoquinone [30839-34-0] and 100% (**79**) upon hydrolysis.



(78) (79) (39)

Sequential applications of these methods yield naturally occurring anthraquinones, eg, macrosporin [22225-67-8] (**80**) in 83% yield from 2-chloro-6-methyl-7-hydroxy-1,4-naphthoquinone [76665-67-3] (**81**) which

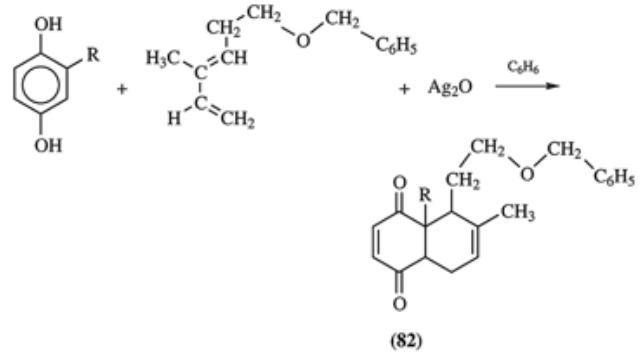
is produced in 78% yield from (**24**) (eq. 40) (95).



(24) (81) (80)

(40)

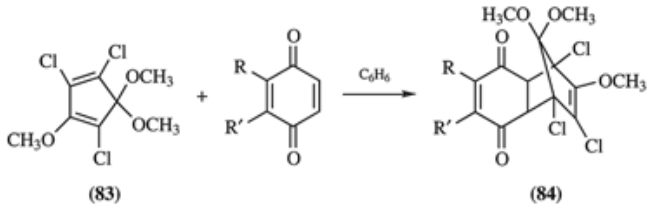
The problems associated with predicting regioselectivity in quinone Diels-Alder chemistry have been studied, and a mechanistic model based on frontier molecular orbital theory proposed (96). In certain cases of poor regioselectivity, eg, 2-methoxy-5-methyl-1,4-benzoquinone with alkyl-substituted dienes, the use of Lewis acid catalysts is effective (97). Especially sensitive quinones can be generated *in situ* and the diene adducts, eg, (**82**) can be obtained in excellent yield (98). For R = methoxycarbonyl, carboxaldehyde, and acetyl (eq. 41), the yields are 95, 97, and 100%, respectively.



(82)

(41)

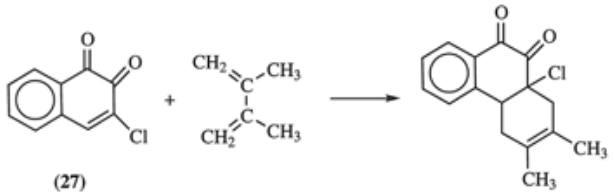
The potentially important 3,5,5-trialkoxy-1,2,4-trichlorocyclopentadienes, eg, (**83**) react with 1,4-benzoquinone (R = R′ = H) (**2**) and 1,4-naphthoquinone (R,R′ close the ring) (**7**) (99). For (**2**) (eq. 42) the yield is 95% of (**84**); for (**7**) 60%.



(83) (84)

(42)

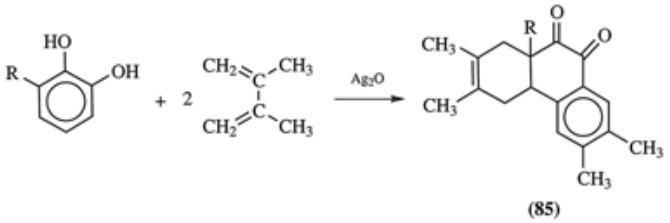
Typical diene reactions of 1,2-quinones are also well known (eq. 43) (100).



(27)

(43)

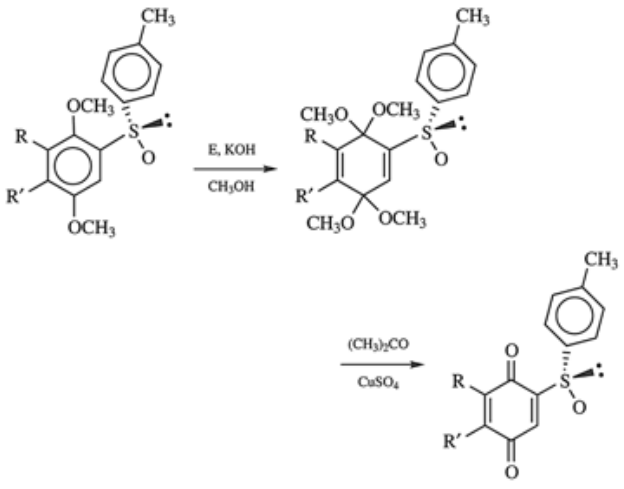
A wide variety of substituents, eg, CH_3O, Br, CN, CH_3OOC, and NO_2, have been investigated, and the products described (101). The Diels-Alder reactions of 1,2-benzoquinones generated *in situ* have also been reported (102). For R = acetyl, 51% of (**85**) [67984-83-2] has been reported; for R = benzoyl, 65% of (**85**) [67984-84-3] (eq. 44).



(85)

(44)

The search for enantiomerically selective synthetic pathways to drugs and natural products has produced a powerful tool in 2-*p*-tolylsulfinlyquinones (103). Their preparation through anodic oxidation of 1,4-dimethoxy aromatics followed by hydrolysis of the bisketals allows the preparation of either monoketal isomer as well as the quinone (eq. 45).

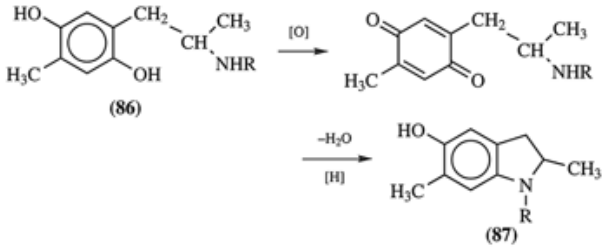


(45)

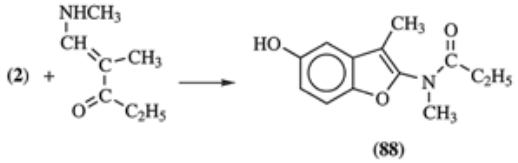
These quinones have shown great promise in promoting diastereoselectivity in the Diels-Alder synthesis under both thermal and Lewis acid conditions (104). Lewis acid mediated Diels-Alder chemistry has been applied in the synthesis of polycyclic quinonoid antibiotics (105).

The synthesis of 2-styryl-1,4-benzoquinones showed them to be very reactive towards Diels-Alder dimerization (106). These compounds undergo selective thermal and photochemical reactions to produce oligomers. The study of their chemistry appear to shed light on the degradation of important photoelectric materials (107).

The formation of heterocycles derived from quinones is an important synthetic technique. The reaction may be intramolecular, eg, the reaction of (**86**) (eq. 46). Either nitrogen products, eg, (**87**) (yields of 85–91% for R = H, CH_3, and C_6H_5) or oxygen products (**88**) (eq. 47) are obtained (108,109). Reactions with enamines have been especially important.

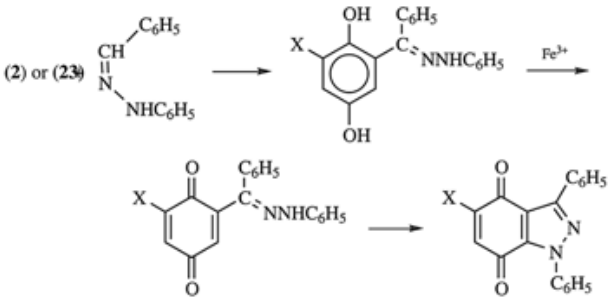


(46)



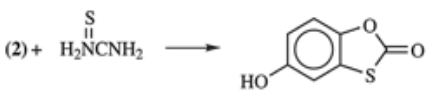
(47)

An aza-Nenitizescu reaction has been reported from the reaction of benzaldehyde phenylhydrazone with 1,4-benzoquinone (**2**) and its 2-chloro derivative (**23**) (eq. 48) (110). While the yields are rather poor, a new approach to interesting heterocyclic systems is offered.



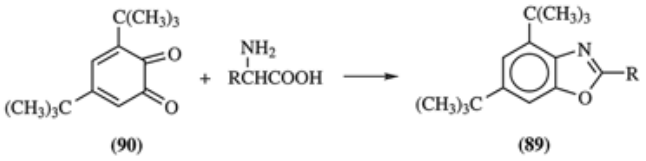
(48)

The addition of thioureas to 1,4-benzoquinone is an excellent preparation of 5-hydroxy-1,3-benzoxathiol-2-one (92% in eq. 49) (111). Monosubstituted 1,4-benzoquinones gave good yields and high regioselectivity, eg, 2-phenyl-1,4-benzoquinone produced 93% of the 6-phenyl product.



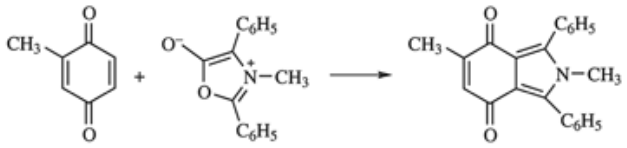
(49)

A useful synthesis of benzoxazoles (**89**) was developed in an attempt to oxidize an antibiotic α-amino acid with 3,5-di-*tert*-butyl-1,2-benzoquinone [3383-21-9] (**90**) (112). Yields of (**89**) are 80% for $R = CH_3$ and 32% for $R = CH_2C_6H_5$ (eq. 50).



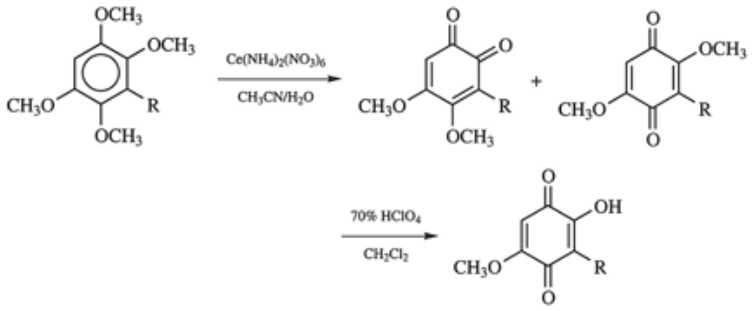
(90) (89) (50)

A general method for the preparation of 2*H*-isoindol-4,7-diones (**91**) [72726-02-4] involves 1,3-dipolar addition of oxazolium-5-oxides (sydnones) (**92**) to 2-methyl-1,4-benzoquinone (113). Yield of (**91**) (eq. 51) is 37%.



(26) (92) (91) (51)

Several novel synthetic approaches to the synthesis of naturally occurring quinones have been reported and should be developed more broadly. After successfully alkylating 1,2,4,5-tetramethoxybenzene the precursors to several naturally occurring quinones were oxidized with ceric ammonium nitrate (eq. 52) (114).

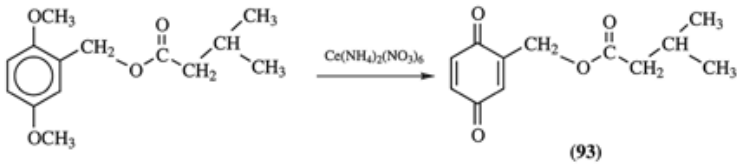


(52)

The initial mixture of 1,2- and 1,4-benzoquinones was smoothly converted to the desired, and selectively demethylated product in yields of 70–76%.

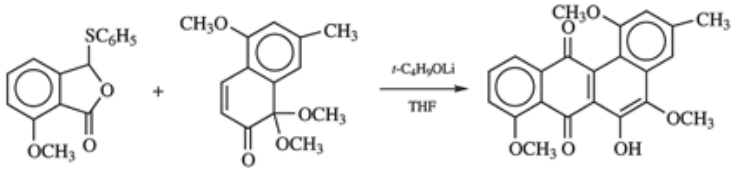
This same oxidizing agent converts dimethoxybenzenes attached to β-lactams to the corresponding quinones in moderate to excellent yields (115).

The sex pheromone of the German cockroach, commonly called blattellaquinone (**93**) was also synthesized using ceric ammonium nitrate (eq. 53) (116)



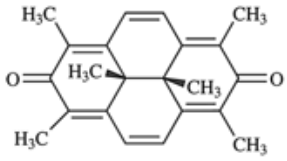
(93) (53)

An efficient total synthesis of a polycyclic compound exhibiting significant anticancer activity was realized in 72% yield from an *ortho*-quinone monoketal and phthalide sulfide (eq. 54) (117).



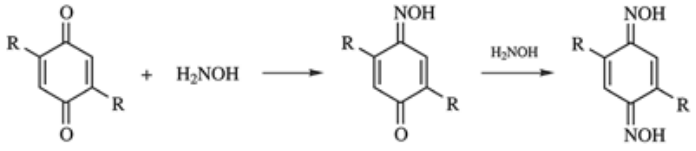
THF = tetrahydrofuran (54)

Ceric ammonium nitrate was used to prepare an extended quinonoid system in a study of a dihydropyrene 14 π-electron system (**94**) (118).

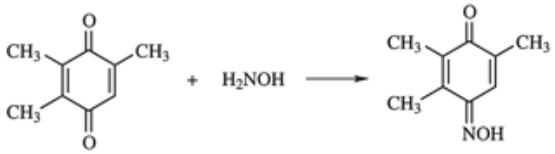


(**94**)

The formation of oximes of the quinones is strongly influenced by ring substitution (eqs. 55 and 56). The mono and dioximes form if at least one position adjacent to the carbonyl group is unsubstituted (119), eg, in the case of (**2**) (R = H) and (**25**) (R = CH_3).



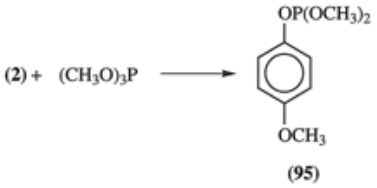
(**2**),(**25**) (55)



(56)

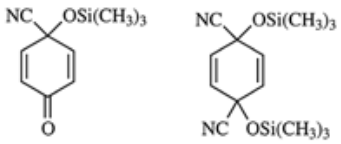
Unlike simple, unhindered carbonyl compounds, the quinones do not yield bisulfite addition products, but undergo ring addition. Another significant carbonyl reaction is the addition of tertiary phosphites under anhydrous conditions (eq. 57) (120). The ester product (**95**) is easily hydrolyzed, and the overall sequence

produces excellent yields of hydroquinone monoethers.



(95) (57)

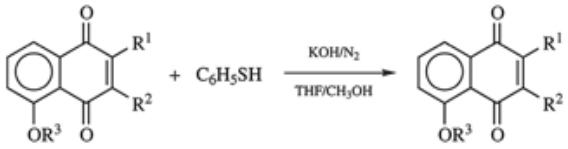
The valuable addition of cyanotrimethylsilane, $(CH_3)_3SiCN$, to 1,4-benzoquinone can be controlled using specific catalysts (121). Hydroxyapatite in CH_2Cl_2 at 0°C for 5 h gives 74% of (**96**) whereas using Fe^{3+} ion-exchange montmorillonite in the same solvent at 0°C for 1.5 h gives 91% of (**97**).



(96) (97)

2.9. Nucleophilic Substitution Reactions

Many of the transformations realized through Michael additions to quinones can also be achieved using nucleophilic substitution chemistry. In some instances the stereoselectivity can be markedly improved in this fashion (122), eg, in the reaction of benzenethiol with esters ($R^3 = CH_3C{=}O$) and ethers ($R^3 = CH_3$) of 1,4-naphthoquinones (eq. 58).

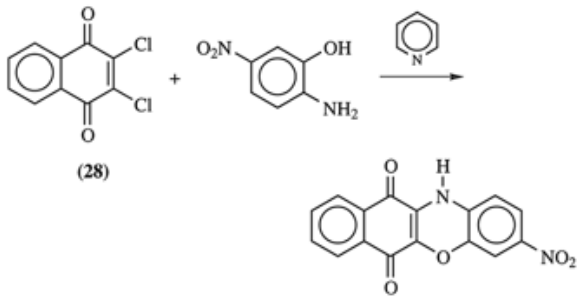


(58)

2-Bromo-5-acetyloxy-1,4-naphthoquinone [77189-69-6], $R^1 = Br$, yields 75% of 2-thiophenyl-5-acetyloxy-1,4-naphthoquinone [71700-93-1], $R^1 = SC_6H_5$. 3-Bromo-5-methoxy-1,4-naphthoquinone [69833-10-9], $R^2 = Br$, yields 82% of 3-thiophenyl-5-methoxy-1,4-naphthoquinone [112740-62-2] $R^2 = SC_6H_5$.

The nitrogen substitution chemistry of 2,3-dichloro-1,4-naphthoquinone (**28**) has been widely employed (123). Although the product mixtures are sometimes complex, many examples illustrate the excellent results

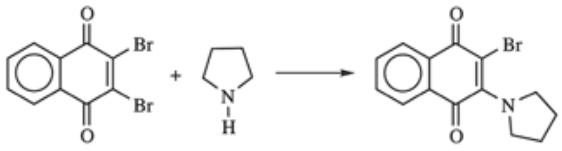
possible in specific instances; eg, 3-nitro-12*H*-benzo[*b*]phenoxazine-6,11-dione [75197-88-5] (eq. 59).



(28)

(59)

Analogous chemistry with 2,3-dibromo-1,4-naphthoquinone [13243-65-7] (**98**) has been used in the synthesis of mitomycin antibiotics; eg, (**99**) (eq. 60) (124).

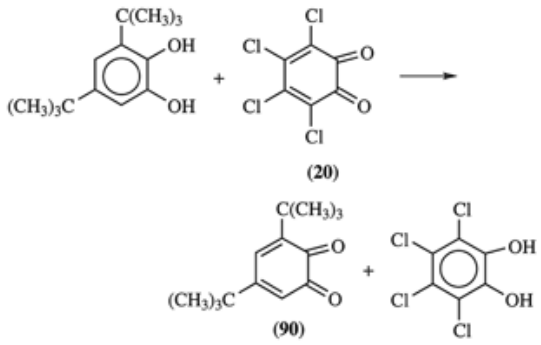


(98) (99)

(60)

3. Syntheses

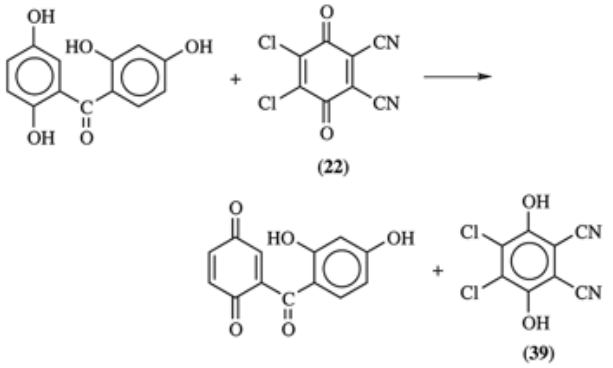
Syntheses of quinones often involve oxidation, since this is the only completely general method (125). Thus, in several instances, quinones are the reagents of choice for the preparation of other quinones. Oxidation has been especially useful with catechols and hydroquinones as starting materials (eqs. 61 and 62) (27,28). The preparative utility of these reactions depends largely on the relative oxidation potentials of the quinones (126,127).



(20)

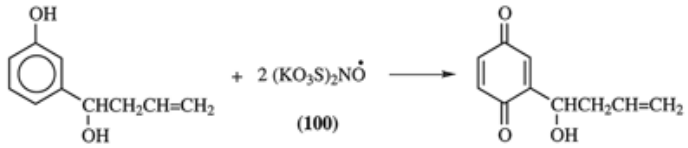
(90)

(61)



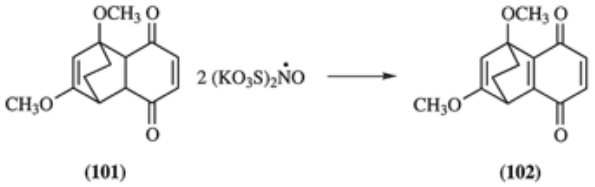
(62)

For the preparation of ≤10 g of a quinone, the oxidation of a phenol with Fremy's salt (**100**) in the Teuber reaction is the method of choice (eq. 63) (128). A wide range of phenols has been



(63)

used, including some with 4-substituents. The latter usually produce 1,2-benzoquinones, but the 4-chloro-, and 4-*tert*-butyl groups can be eliminated, resulting in 1,4-benzoquinones. The yield for simple phenols is frequently in excess of 70%, and some complex phenols show highly selective oxidation. With an occasional exception, substituents and side chains are not attacked by Fremy's salt (129,130). The extraordinary delicacy and selectivity possible is illustrated by a conversion, (**101**) [58785-57-2] to (**102**) [58785-59-4], achieved only with Fremy's salt (eq. 64) (131).

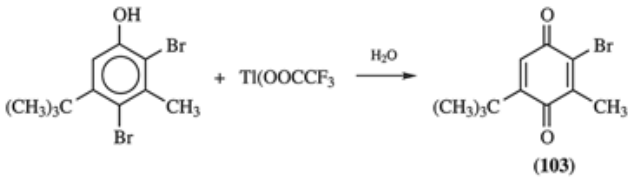


(64)

It has been shown that *p*-hydroxy-*N,N*-dimethylbenzylamines react smoothly with Fremy's salt to give 1,4-benzoquinones in high yield (132).

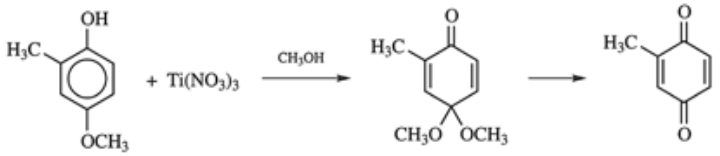
In small-scale syntheses, a wide variety of oxidants have been employed in the preparation of quinones from phenols. Of these reagents, chromic acid, ferric ion, and silver oxide show outstanding usefulness in the oxidation of hydroquinones. Thallium(III) trifluoroacetate converts 4-halo- or 4-*tert*-butylphenols to 1,4-benzoquinones in high yield (133); eg, 2-bromo-3-methyl-5-*tert*-butyl-1,4-benzoquinone [25441-20-3] (**103**) has

been made by this route (eq. 65).

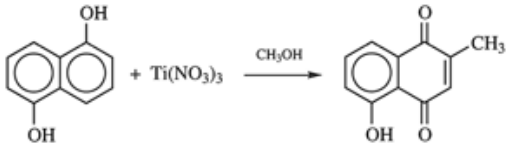


(103) (65)

Thallium trinitrate oxidizes naphthols and hydroquinone monoethers, respectively, to quinones and 4,4-dialkoxycyclohexa-2,5-diones, eg, 4,4-dimetmethoxyoxy-2-methyl-2,5-cyclohexadienone [57197-11-2] (eq. 66) (**104**) (134,135). The yield of (**104**) is 89%. Because the monoketal is easily converted to the quinone, the yield of 5-hydroxy-1,4-naphthoquinone [481-39-0] is 64% (eq. 67).

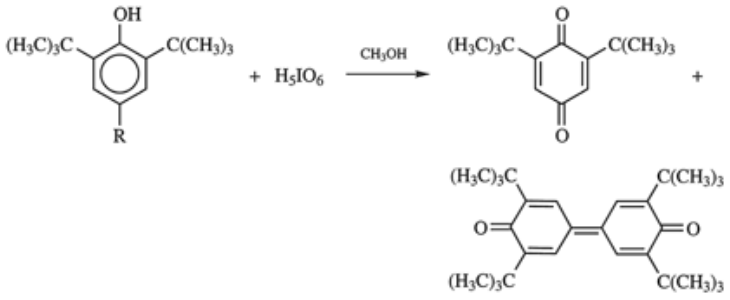


(104) (26) (66)



(67)

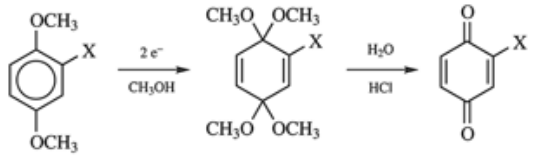
The oxidation of 4-bromophenols to quinones can also be accomplished with periodic acid (136). A detailed study of this reagent with sterically hindered phenols provided insight about the quinonoid product (eq. 68) (137). The highest yield of 2,6-di-*tert*-butyl-1,4-benzoquinone [719-22-2] occurs when $R = OCH_3$. The stilbene structure [2411-18-9] is obtained in highest yield for R = H.



(68)

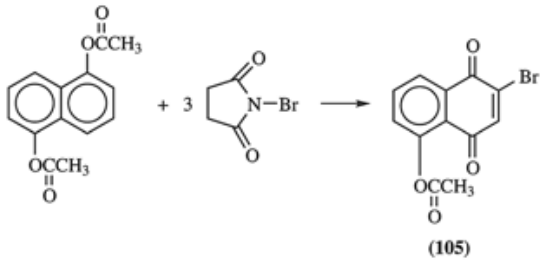
The anodic oxidation of hydroquinone ethers to quinone ketals yields synthetically useful intermediates that can be hydrolyzed to quinones at the desired stage of a sequence (83). The yields of intermediate diketals

are 83% for chlorine and 75% for bromine (eq. 69).



(69)

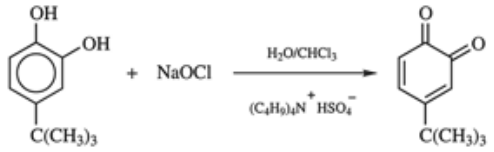
Derivatives of the natural product juglone (**105**) [77189-69-6], eg, have been obtained in 90% yield in a single reaction involving halogenation and oxidation by *N*-bromosuccinimide (NBS) (eq. 70) (138).



(105)

(70)

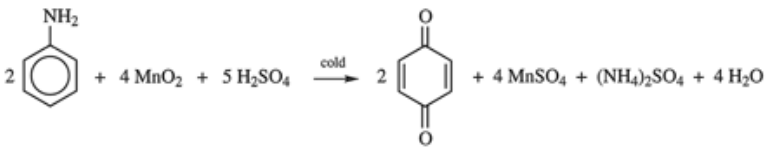
The dimethyl ethers of hydroquinones and 1,4-naphthalenediols can be oxidized with silver(II) oxide or ceric ammonium nitrate. Aqueous sodium hypochlorite under phase transfer has also produced efficient conversion of catechols and hydroquinones to 1,2- and 1,4-benzoquinones (139), eg, 4-*tert*-butyl-1,2-benzoquinone [1129-21-1] in 92% yield (eq. 71).



(71)

4. Manufacture

With the exceptions of 1,4-benzoquinone and 9,10-anthraquinone, quinones are not produced on a large scale, but a few of these are commercially available. The 2005 prices of selected quinones are listed in Table 4. Most of the compounds are prepared by the methods described herein. The few large-scale preparations involve oxidation of aniline (eq. 72), phenol (eq. 73), or aminonaphthols, eg, (**106**) from which (**6**) is obtained in 93% yield (eq. 74).

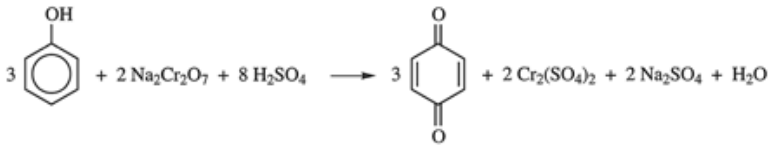


(72)

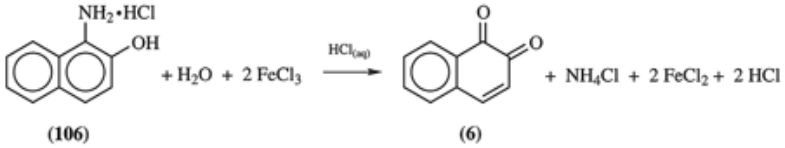
Table 4. Commercially Available Quinones

Quinone	Structure number	Price in 2005, $	
		ARCOS[a]	Aldrich[b]
1,4-benzoquinone	**2**	67.80/kg	70.50/kg
1,2-naphthoquinone	**8**	195.20/25 g	75.10/5 g
1,4-naphthoquinone	**9**	55.80/500 g	64.80/500 g
2-methyl-1,4-benzoquinone	**28**	59.00/100 g	63.60/100 g
p-chloranil	**23**	101.40/500 g	75.50/100 g
o-chloranil	**22**	56.10/25 g	30.40/5 g
2,3-dichloro-5,5-dicyano-1,4-benzoquinone	**24**	204.20/100 g	212.40/100 g
2,3-dichloro-1,4-naphthoquinone	**30**	32.20/250 g	16.00/100 g
9,10-anthraquinone	**12**	88.30/kg	42.10/250 g

[a]Ref. 140.
[b]Ref. 19.



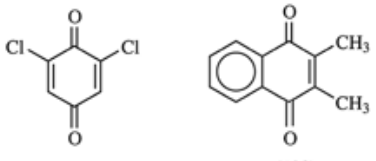
(73)



(106) (6)

(74)

In the case of 1,4-benzoquinone, the product is steam-distilled, chilled, and obtained in high yield and purity. Direct oxidation of the appropriate unoxygenated hydrocarbon has been described for a large number of ring systems, but is generally utilized only for the polynuclear quinones without side chains. A representative sample of quinone uses is given in Table 5.



(107) (108)

5. Health and Safety Factors

Because of the high vapor pressure of the simple quinones and their penetrating odor, adequate ventilation must be provided in areas where these quinones are handled or stored. Quinone vapor can harm the eyes, and a limit of 0.1 ppm of 1,4-benzoquinone in air has been recommended. Quinones in either solid or solution form can cause severe local damage to the skin and mucous membranes. Swallowing benzoquinones may be fatal; the LD_{50} in rat is 130 mg/kg orally and 0.25 mg/kg intravenously. There is insufficient data concerning quinones and cancer. The higher quinones are less of a problem because of their decreased volatility (141,142,143,144).

Table 5. Uses of Selected Quinones

Quinone	Structure number	Use
1,4-benzoquinone	**2**	oxidant, amino acid determination
2-chloro-, 2,5-dichloro-, and 2,6-dichloro-1,4-benzoquinone	**23**, **24**, **107**[a]	bactericides
2,3-dichloro-5,5-dicyano-1,4-benzoquinone	**22**	oxidation and dehydrogenation
2-methyl and 2,3-dimethyl-1,4-naphthoquinone	**29**, **108**[b]	vitamin K substitute antihemorrhagic agent

[a]CAS Registry Number [697-91-6].
[b]CAS Registry Number [2197-57-1].

BIBLIOGRAPHY

"Quinones" in *ECT* 1st ed., Vol. 11, pp. 410–424, by J. R. Thirtle, Eastman Kodak Company; in *ECT* 2nd ed., Vol. 16, pp. 899–913, by J. R. Thirtle, Eastman Kodak Company; in *ECT* 3rd ed., Vol. 19, pp. 572–606, by K. T. Finley, State University College at Brockport; in *ECT* 4th ed., Vol. 20, pp. 799–830, by K. T. Finley, State University College of New York, Brockport; "Quinones" in *ECT* (online), posting date: December 4, 2000, by K. T. Finley, State University College of New York, Brockport.

Cited Publications

1. A. Woskressenski, *Justus Liebigs Ann. Chem.* **27**, 268 (1838).
2. Willstätter and Pfannenstiel, *Chem. Ber.* **37**, 4744 (1904).
3. J. Cason, *Org. Reactions* **4**, 305 (1948).
4. R. H. Thomson, in Ref. 5, pp. 123–124.
5. S. Patai, ed., *The Chemistry of Quinonoid Compounds*, Wiley, New York, 1974.
6. S. Patai and Z. Rappoport, eds., *The Chemistry of Quinonoid Compounds*, Vol. 2, Wiley, New York, 1988.
7. K. T. Finley, in S. Patai, ed., *Supplement E: The Chemistry of Hydroxyl, Ether and Peroxide Groups*, Vol. 2, Wiley, New York, 1993, pp. 1027–1134.
8. R. H. Thomson, *Naturally Occurring Quinones*, 3rd ed., Chapman & Hall, London, 1987.
9. R. H. Thomson, in J. ApSimon, ed., *The Total Synthesis of Natural Products*, Vol. 8, Wiley, New York, 1992.
10. J. A. Berson, in Ref. 6, pp. 455–536.
11. H. H. Szmant, *Organic Building Blocks of the Chemical Industry*, Wiley, New York, 1989, Chapt. 9.
12. K. M. Draths and J. W. Frost, *J. Am. Chem. Soc.* **113**, 9361 (1991).
13. K. M. Draths, T. L. Ward, and J. W. Frost, *J. Am. Chem. Soc.* **114**, 9725 (1992).

14. M. Wei and co-workers, *J. Am. Chem. Soc.* **124**, 2513 (2002).
15. H. Sun, K. Harms, and J. Sundermeyer, *J. Am. Chem. Soc.* **126**, 9550 (2004).
16. T. A. Turney, in Ref. 5, pp. 857–876.
17. H. N. C. Wong, T-L. Chan, and T.-Y. Luh, in Ref. 6, pp. 1501–1563.
18. L. T. Scott, in Ref. 6, pp. 1385–1417.
19. *Aldrich Catalog Handbook of Fine Chemicals 2005–2006*, Milwaukee, WI.
20. D. R. Lide, ed., *Handbook of Chemistry & Physics*, 84th ed., CRC Press, New York, 2003–2004; J. G. Grasselli and W. M. Ritchey, eds., *Atlas of Spectral Data and Physical Constants for Organic Compounds*, 2nd ed., CRC Press, Cleveland, Ohio, 1975; L. Meites and P. Zuman, eds., *CRC Handbook Series in Electrochemistry*, Vols. 1–4, CRC Press, Boca Raton, Flor., 1980 J. P. Phillips and co-workers, *Organic Electronic Spectral Data*, Vol. 15, Wiley-Interscience, New York, 1973.
21. S. Berger and A. Rieker, in Ref. 5, pp. 163–229.
22. S. Berger, P. Hertl and A. Rieker, in Ref. 6, pp. 29–86.
23. J. Q. Chambers, in Ref. 5, pp. 770–785.
24. P. W. D. Mitchell, *Can. J. Chem.* **41**, 550 (1963).
25. R. Bentley and I. M. Campbell in Ref. 5, pp. 683–736.
26. H. Inouye and E. Leistner in Ref. 6, pp. 1293–1349.
27. H.-D. Becker, in Ref. 5, pp. 335–423.
28. H.-D. Becker and A. B. Turner, in Ref. 6, pp. 1351–1384.
29. M. S. Newman, V. K. Khanna, and K. Kanakarajan, *J. Am. Chem. Soc.* **101**, 6788 (1979).
30. A. I. Kosak and co-workers, *J. Am. Chem. Soc.* **76**, 4450 (1954).
31. E. J. Agnello and G. D. Laubach, *J. Am. Chem. Soc.* **82**, 4293 (1960).
32. D. Burn, D. N. Kirk, and V. Petrov, *Proc. Chem. Soc.* 14 (1960).
33. E. A. Braude, A. G. Brook, and R. P. Linstead, *J. Chem. Soc.*, 3569 (1954).
34. W. Brown and A. B. Turner, *J. Chem. Soc. C*, 2057 (1971).
35. J. W. A. Findlay and A. B. Turner, *Organic Syntheses*, Vol. 49, Wiley, New York, 1973, pp. 428–431.
36. U. S. Pat. 3,365,499 (Jan. 23, 1968), W. H. Clement and C. M. Selwitz (to Gulf Research Development Co.).
37. H.-D. Becker, A. Björk, and E. Adler, *J. Org. Chem.* **45**, 1596 (1980).
38. J. M. Bruce, in Ref. 5, pp. 465–538.
39. K. Maruyama and A. Osuka, in Ref. 6, pp. 759–878.
40. D. Bryce-Smith, A. Gilbert, and M. G. Johnson, *J. Chem. Soc. C*, 383 (1967).
41. D. Bryce-Smith and A. Gilbert, *Tetrahedron Lett.*, 3471 (1964).
42. H. Irngartinger and co-workers, *Angew. Chem. Int. Ed. Engl.* **13**, 674 (1974).
43. G. O. Schenck and co-workers, *Angew. Chem. Int. Ed. Engl.* **1**, 516 (1964).
44. D. H. Reid and co-workers, *Tetrahedron Lett.*, 530 (1961).
45. M. Maruyama, T. Otsuki, and K. Mitsui, *J. Org. Chem.* **45**, 1424 (1980).
46. K. Maruyama and N. Narita, *J. Org. Chem.* **45**, 1421 (1980).
47. K. T. Finley, in Ref. 5, pp. 877–1144.
48. K. T. Finley, in Ref. 6, pp. 537–717.
49. A. Michael, *J. Prakt. Chem.* **79**, 418 (1909) and **82**, 306 (1910).
50. S. S. Lau and co-workers, *Mol. Pharmacol.* **34**, 829 (1988).
51. H. S. Wilgus and co-workers, *J. Org. Chem.* **29**, 594 (1964).
52. E. R. Brown, K. T. Finley, and R. L. Reeves, *J. Org. Chem.* **36**, 2849 (1971).
53. R. Cassis and co-workers, *Synth. Commun.* **17**, 1077 (1987).
54. O. Hinsberg, *Chem. Ber.* **27**, 3259 (1894) and **28**, 1315 (1895).
55. Y. Ogata, Y. Sawaki, and M. Isone, *Tetrahedron* **25**, 2715 (1969) and **26**, 731 (1970).
56. J. M. Bruce and P. Lloyd-Williams, *J. Chem. Soc. Perkin Trans. 1*, 2877 (1992).
57. D. E. Allgeier and co-workers, *J. Org. Chem.* **68**, 4988 (2003).
58. J. S. Yadav and co-workers, *Synthesis*, 1849 (2004).
59. J. F. W. McOmie and J. M. Blatchly, *Organic Reactions*, Vol. 19, Wiley, New York, 1972, pp. 199–277.
60. H. A. E. Mackenzie and E. R. S. Winter, *Trans. Faraday Soc.* **44**, 159 (1948).
61. H. S. Wilgus and J. W. Gates, Jr., *Can. J. Chem.* **45**, 1975 (1967).

62. K. A. Parker, D. M. Spero, and K. A. Koziski, *J. Org. Chem.* **52**, 183 (1987).
63. J. F. Bagli and P. L'Ecuyer, *Can J. Chem.* **39**, 1037 (1961).
64. P. Brassard and P. L'Ecuyer, *Can. J. Chem.* **37**, 1505 (1959).
65. N. Farfán, E. Ortega, and R. Contreras, *J. Heterocycl. Chem.* **23**, 1609 (1986).
66. M. L. Iskander, H. A. A. Medien, and S. Nashed, *Microchem. J.* **36**, 368 (1987) and **39**, 43 (1989).
67. J. R. Luly and H. Rapoport, *J. Org. Chem.* **46**, 2745 (1981).
68. M. D. Rozeboom, I-M. Tegmo-Larsson, and K. N. Houk, *J. Org. Chem.* **46**, 2338 (1981).
69. W. H. Wanzlick, in W. Foerst, ed., *Newer Methods of Preparative Organic Chemistry*, Vol. IV, Academic, New York, 1968, pp. 139–154.
70. M. K. Manthey, S. G. Pyne, and R. J. W. Truscott, *Aust. J. Chem.* **42**, 365 (1989).
71. K. A. Parker and S-K. Kang, *J. Org. Chem.* **45**, 1218 (1980).
72. K. A. Parker and J. Kallmerten, *J. Org. Chem.* **45**, 2620 (1980).
73. H. Pluim and H. Wynberg, *J. Org. Chem.* **45**, 2498 (1980).
74. L. F. Fieser and A. E. Oxford, *J. Am. Chem. Soc.* **64**, 2060 (1942).
75. L. F. Fieser and R. B. Turner, *J. Am. Chem. Soc.* **69**, 2338 (1947).
76. D. H. R. Barton, D. Bridow, and S. Z. Zard, *Tetrahedron* **43**, 5307 (1987).
77. T. Ling and co-workers, *J. Am. Chem. Soc.* **124**, 12261 (2002).
78. K. Maruyama and Y. Naruta, *J. Org. Chem.* **43**, 3796 (1978).
79. Y. Naruta, *J. Org. Chem.* **45**, 4097 (1980).
80. Y. Naruta, *J. Am. Chem. Soc.* **102**, 3774 (1980).
81. H. W. Moore, Y-L. L. Sing, and R. S. Sidhu, *J. Org. Chem.* **45**, 5057 (1980).
82. K. F. West and H. Moore, *J. Org. Chem.* **47**, 3591 (1982).
83. H. W. Moore and co-workers, *J. Org. Chem.* **52**, 2537 (1987).
84. J. O. Karlsson and co-workers, *J. Am. Chem. Soc.* **107**, 3392 (1985).
85. S. T. Perri and co-workers, *J. Org. Chem.* **51**, 3068 (1986).
86. S. T. Perri and H. W. Moore, *J. Am. Chem. Soc.* **112**, 1897 (1990).
87. L. S. Liebeskind and S. W. Riesinger, *J. Org. Chem.* **58**, 408 (1993).
88. K. T. Finley, in Ref. 7, pp. 1063–1091.
89. W. Albrecht, *Justus Liebigs Ann. Chem.* **348**, 31 (1906).
90. O. Diels and K. Alder, *Justus Liebigs Ann. Chem.* **460**, 98 (1928).
91. O. Diels and co-workers, *Chem. Ber.* **62**, 2337 (1929).
92. R. K. Hill and co-workers, *J. Org. Chem.* **45**, 1593 (1980).
93. M. F. Ansell, B. W. Nash, and D. A. Wilson, *J. Chem. Soc.*, 3006 (1963).
94. M. Blouin, M.-C. Béland, and P. Brassard, *J. Org. Chem.* **55**, 1466 (1990).
95. C. Brisson and P. Brassard, *J. Org. Chem.* **46**, 1810 (1981).
96. I.-M. Tegmo-Larsson, M. D. Rozeboom, and K. N. Houk, *Tetrahedron Lett.* **22**, 2043 (1981).
97. J. S. Tou and W. Reusch, *J. Org. Chem.* **45**, 5012 (1980).
98. G. A. Kraus and M. J. Taschner, *J. Org. Chem.* **45**, 1174 (1980).
99. U. O'Connor and W. Rosen, *J. Org. Chem.* **45**, 1824 (1980).
100. M. F. Ansell and R. A. Murray, *Chem. Commun.*, 1111 (1969).
101. M. F. Ansell and R. A. Murray, *J. Chem. Soc. C*, 1429 (1971).
102. R. Al-hamdang and B. Ali, *Chem. Commun.*, 397 (1978).
103. M. C. Carreño and co-workers, *Tetrahedron* **47**, 605 (1991).
104. M. C. Carreño and co-workers, *J. Org. Chem.* **61**, 503 (1996).
105. J. Motoyoshiya and co-workers, *Synthesis*, 2099 (2004).
106. I. Brehm and H. Meier, *Eur. J. Org. Chem.*, 3307 (2001).
107. I. Brehm, S. Hinneschiedt, and H. Meier, *Eur. J. Org. Chem.*, 3162 (2002).
108. U. Kuckländer and co-workers, *Chem. Ber.* **120**, 1791 (1987).
109. U. Kuckländer and K. Kuna, *Chem. Ber.* **120**, 1601 (1987).
110. V. M. Lyubchauskaya, L. M. Alekseeva, and V. G. Granik, *Tetrahedron* **53**, 15005 (1997).
111. P. T. S. Lau and M. Kestner, *J. Org. Chem.* **33**, 4426 (1968).
112. M. C. Zwan and co-workers, *J. Org. Chem.* **43**, 509 (1978).

113. J. A. Myers and co-workers, *J. Org. Chem.* **45**, 1202 (1980).
114. S. Poigny, M. Guyot, and M. Samadi, *Tetrahedron* **54**, 14791 (1998).
115. B. Alcaide, P. Amendros, and N. R. Salgado, *Tetrahedron Lett.* **42**, 1503 (2001).
116. S. Nojima and co-workers, *Science* **307**, 114 (2005).
117. F. M. Hauser, W. A. Dorsch, and D. Mal, *Org. Lett.* **4**, 2237 (2002).
118. G. J. Bodwell and co-workers, *Eur. J. Org. Chem.*, 243 (2002).
119. F. Kehrmann, *Chem. Ber.* **21**, 3315 (1888).
120. F. Ramirez and S. Dershowitz, *J. Am. Chem. Soc.* **81**, 587 (1959).
121. M. Onaka and co-workers, *Chem. Lett.*, 1393 (1989).
122. S. Laugraud and co-workers, *J. Org. Chem.* **53**, 1557 (1988).
123. N. L. Agarwal and W. Schäfer, *J. Org. Chem.* **45**, 2155 and 5139 (1980).
124. S. N. Failing and H. Rapoport, *J. Org. Chem.* **45**, 1260 (1980).
125. Y. Naruta and K. Maruyama, in Ref. 6, p. 242.
126. M. F. Ansell and co-workers, *J. Chem. Soc. C*, 1401 (1971).
127. R. C. Ellis, W. B. Whalley, and K. Ball, *Chem. Commun.* 803 (1967).
128. H. Zimmer, D. C. Lankin, and S. W. Horgan, *Chem. Rev.* **71**, 229 (1971).
129. O. Dann and H.-J. Zeller, *Chem. Ber.* **93**, 2829 (1960).
130. J. M. Bruce, D. Creed, and K. Dawes, *J. Chem. Soc. C*, 2244 (1971).
131. V. H. Powell, *Tetrahedron Lett.*, 3463 (1970).
132. J. M. Saá and co-workers, *J. Org. Chem.* **53**, 4263 (1988).
133. A. McKillop, B. P. Swann, and E. C. Taylor, *Tetrahedron* **26**, 4031 (1970).
134. A. McKillop and co-workers, *J. Org. Chem.* **41**, 282 (1976).
135. D. J. Crouse and co-workers, *J. Org. Chem.* **46**, 1814 (1981).
136. P. T. Perumal and M. V. Bhatt, *Synthesis*, 205 (1979).
137. H.-D. Becker and K. Gustafsson, *J. Org. Chem.* **44**, 428 (1979).
138. S. W. Heinzman and J. R. Grunwell, *Tetrahedron Lett.*, 4305 (1980).
139. F. Ishii and K. Kishi, *Synthesis*, 706 (1980).
140. *ARCOS Chemical Catalog, 2004–2005*, Fisher Scientific Co., Pittsburgh, Pa.
141. *The Sigma-Aldrich Library of Regulatory and Safety Data*, Aldrich Chemical Co., Milwaukee, Wiss., 1993, Vol. 2.
142. *Toxic and Hazardous Industrial Chemicals Safety Manual*, The International Technical Information Institute, Tokyo, 1989.
143. R. J. Lewis, Sr., ed., *Sax's Dangerous Properties of Industrial Materials*, 11th ed., Wiley-Interscience, New York, 2004, Vol. III, p. 2855.
144. R. J. Lewis, Sr., ed., *Hazardous Chemical Desk Reference*, 5th ed., Wiley-Interscience, New York, 2002, p. 1013. The literature has been reviewed through March, 2005.

General References

145. S. Patai, ed., *The Chemistry of Quinonoid Compounds*, Wiley, New York, 1974.
146. S. Patai and Z. Rappoport, eds., *The Chemistry of Quinonoid Compounds*, Vol. 2, Wiley, New York, 1988.
147. K. T. Finley, in S. Patai, ed., *Supplement E: The Chemistry of Hydroxyl, Ether and Peroxide Groups*, Vol. 2, Wiley, New York, 1993, pp. 1027–1134.

148. R. H. Thomson, *Naturally Occurring Quinones*, 3rd ed., Chapman & Hall, London, 1987.
149. R. H. Thomson, in J. ApSimon, ed., *The Total Synthesis of Natural Products*, Vol. 8, Wiley, New York, 1992.

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