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PREPARATION AND BEHAVIOR OF SIMPLE QUINONE METHIDES

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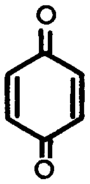
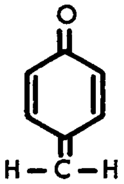
METHYLENE cyclohexadienones, or quinone methides, e.g., the simplest member II, are of considerable theoretical interest in the same context with benzoquinone (I) and *p*-xylylene[1,2] (III).


I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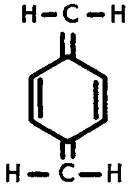
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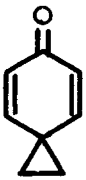
IV

Therefore, they have been the subject of numerous investigations and discussions extending over many years.[3] Certain substituted methides,

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[1] M. Diatkina and J. Syrkin, *Acta Physicochim. URSS* **21**, 23, 921 (1946); C. A. Coulson, D. P. Craig, A. Maccoll, and A. Pullman, *Discuss. Faraday Soc.* **2**, 36 (1947); A. Pullman, G. Berthier, and B. Pullman, *Bull. Soc. Chim France* **15**, 450 (1948).

[2] L. A. Errede and M. Szwarc, *Quart. Revs.* **12**, 301 (1958).

[3] See R. W. Martin *The Chemistry of Phenolic Resins*, p. 139, Wiley, N. Y. (1956); and K. Hultzsch, *Chemie der Phenolharze*, p. 63, Springer, Berlin (1950).

such as 10-methylene anthrone,[4] are well-authenticated compounds. With fewer substituents on the ring, the methides become much less stable, and attempts to isolate the simpler ones, such as the 2,6-dimethyl compound, have led only to dimeric products.[5] With the 2,6-di-t-butyl compound, stable products have resulted only when the methylene group was further substituted.[6] The recently reported o-quinone methide,[7] was unstable even at high dilution at room temperature.

By the general spectroscopic approach employed previously in the study of spiro[2,5]octa-1,4-diene-3-one (IV),[8] it has been possible to study the preparation and behavior of the relatively simple and quite unstable quinone methides in dilute solution. The results obtained are very instructive, and we present some of them in the present communication.

We have observed that dilute solutions of quinone methides may be prepared from either the corresponding benzyl halide or the parent phenol. Thus, 2,6-dimethyl-4-methylene-2,5-cyclohexadienone (VI) is obtained in 10^{-5} to 10^{-3} M solution from treatment of a hydrocarbon solution of 3,5-dimethyl-4-hydroxybenzyl chloride (Va) with a base, such as triethylamine. Analogously, 2,6-di-t-butyl-4-methylene-2,5-cyclohexadienone may be obtained from the appropriate benzyl bromide.[9]

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[4] E.g., H. Heymann and L. Trowbridge, J. Am. Chem. Soc. 72, 84 (1950).

[5] K. Fries and E. Brandes, Ann. 542, 48 (1939); H. von Euler, E. Adler, J. O. Cedwall, and O. Törngren, Arkiv. Kem. Mineral Geol. 15A, No. 11 (1942).

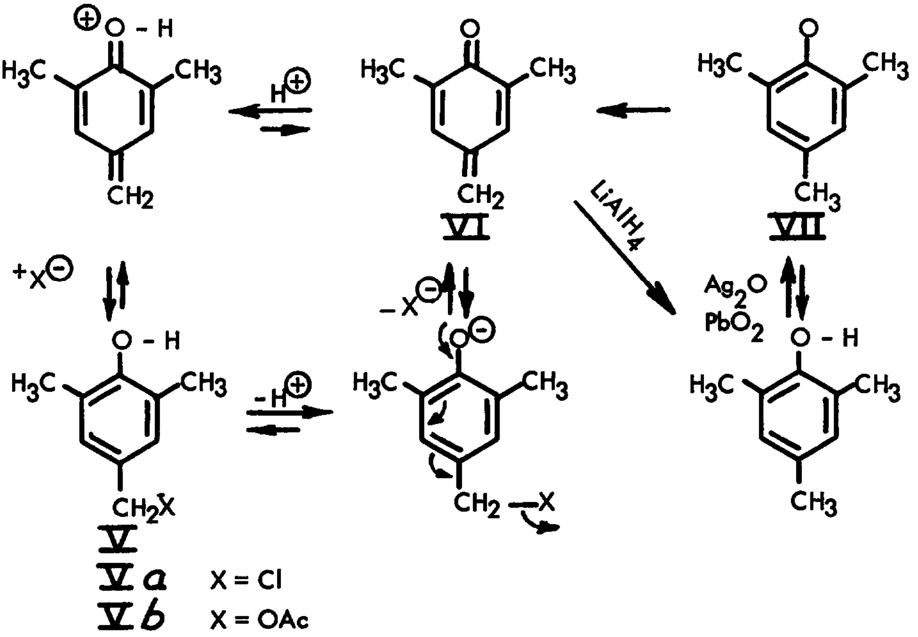
[6] C. D. Cook and B. E. Norcross, J. Am. Chem. Soc. 78, 3797 (1956). Ibid. 81, 1176 (1959).

[7] P. D. Gardner, H. Sarrafizadeh R., and R. L. Brandon, Ibid. 81, 5515 (1959).

[8] S. Winstein and R. Baird, Ibid. 79, 756, 4238 (1957).

[9] C. D. Cook, N. G. Nash, and H. R. Flanagan, Ibid. 77, 1783 (1955).

Alternatively, the quinone methide VI was obtained by shaking a solution of mesitol with silver oxide. Analogously, the 2,6-di-t-butyl analog was obtained from oxidation of the parent phenol with lead dioxide.



The formation of quinone methides by oxidation of the corresponding phenols presumably proceeds through aryloxy radicals, e.g., VII. In reporting on the behavior of such radicals, Cook and Norcross[6] have described a second order disproportionation of the 2,6-di-t-butyl-4-isopropylphenoxy radical to the corresponding phenol and quinone methide. On the other hand, Bennett[10] has reported first order decay of the corresponding 4-methyl and 4-ethyl analogs. Under the present conditions, with excess metal oxide, it is not clear how aryloxy radical is converted to quinone methide.

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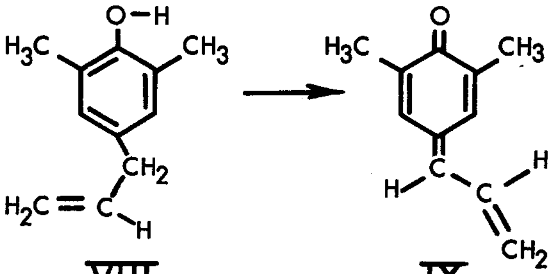
[10] J. E. Bennett, *Nature* **186**, 385 (1960).

An interesting extension of the oxidation method of producing quinone methides involves 2,6-dimethyl-4-allylphenol (VIII). Treatment of the latter compound with silver oxide yields a material whose properties are consistent with the quinone methide structure IX.



VIII IX

The structure of the quinone methides is clear from their ultraviolet and infrared spectra. Thus, in isooctane solution, the quinone methide VI has an intense band at 283 mµ (ϵ = 29,000). Also, it has bands at 6.15 and 6.07 µ ascribed to the conjugated carbonyl group,[11] and bands at 1.626, 2.079 and 2.140 µ, attributable to terminal methylene.[12] The ultraviolet spectra of several quinone methides are summarized in Table I, which shows that the effect of solvent or of substituents on the methylene group of the quinone methide changes the position of the intense, long wave length ultraviolet bands in the expected direction.

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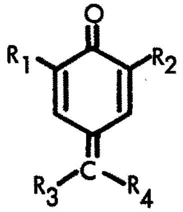
[11] G. M. Coppinger and J. W. Campbell, Ibid. 75, 734 (1953); M. S. Kharasch and B. S. Joshi, J. Org. Chem. 22, 1435 (1957).

[12] R. F. Goddu, Anal. Chem. 29, 1790 (1957).

Table I Ultraviolet Spectra of Quinone Methides



				Isooctane		MeOH
R_1	R_2	R_3	R_4	$\lambda_{MAX.}$	Log ϵ	$\lambda_{MAX.}$
CH_3[a,b]	CH_3	H	H	283	4.46	ca. 290
CH_3[b]	CH_3	H	CH_3	297	4.40	ca. 312
CH_3[b]	CH_3	H	CH_2=CH	329	4.62	338
t-Bu[b]	CH_3	H	H	285	4.35	290
t-Bu[a,c]	t-Bu	H	H	285	4.45	289
t-Bu[b,d]	t-Bu	H	CH_3	299	4.42	303
t-Bu[d]	t-Bu	CH_3	CH_3	314	4.40	322

[a-d] Prepared by: [a] Et_3N method; [b] Ag_2O method; [c] PbO_2 method; [d] Alkaline ferricyanide method[6]

The stability of the simple quinone methides in inert solvents appears to be a function of concentration. Thus, the quinone methide VI is stable for days at room temperature at a concentration of 10^{-5} $\underline{M}$ in inert solvents. As the concentration is increased, the disappearance of methide becomes more rapid, so that a 10^{-2} $\underline{M}$ solution was more than 60% reacted in 140 minutes at room temperature. The reaction products are primarily dimeric materials.[5] The 2,6-di-t-butyl analog of VI is more stable than VI at 10^{-2} $\underline{M}$ concentration in isooctane, only about 2% having reacted in 72 hours. Even here, we have so far been unsuccessful in attempts to isolate the pure material by evaporation of the solvent at reduced pressure. This procedure yields a mixture of products no longer having the spectrum of quinone methide. The only compound clearly identified was 3,5,3',5'-tetra-t-butylstilbene-4,4'-quinone.[13] It is obvious that the stability of the quinone methides toward tail-to-tail dimerization is increased enormously by methyl groups on the terminal methylene. Thus, 2,6-di-t-butyl-4-ethenyl quinone methide,[6] with one such methyl group, is an easily isolable compound, and 2,6-di-t-butyl isopropenyl quinone methide[6] is stable for days at room temperature in the solid state.

The same dimeric products formed from quinone methides have also been formulated as arising from aryloxy radicals, either by rearrangement to benzyl radicals and dimerization of these[9] or by way of a complex between two of the aryloxy radicals which yield the final products.[14] Thus the present observation that quinone methides are converted to dimeric species has implications for the whole question of the mechanism of formation of dimeric materials during oxidation of phenols.

Toward lithium aluminum hydride, hydrogen chloride and various hydroxylic species, the quinone methide VI shows the expected behavior. Lithium aluminum hydride yields mesitol and the other species give rise to the appropriate benzyl derivative V from 1,6-addition. These reactions were demonstrated spectroscopically, the yields being essentially quantitative, and the products from reactions with methanol, acetic acid, and lithium aluminum hydride were isolated and found identical with authentic specimens. The chemical behavior of the quinone methide VI from oxidation of mesitol confirmed that it was essentially

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[13] C. D. Cook, J. Org. Chem., **18**, 261 (1953).

[14] J. K. Becconsall, S. Clough, and G. Scott, Proc. Chem. Soc., 308 (1959).

quantitatively the p-methide. No more than 2-3% of the ortho-isomer could have been present.

The high order of reactivity of the simple quinone methides is demonstrated by the rate of their reactions with methanol. The rate constant for reaction of the quinone methide VI in neutral methanol at 25°, followed spectrophotometrically at 290 mμ, is 4.0×10^{-2} sec.$^{-1}$, the half-life of VI being 17 seconds. Thus, the quinone methide VI reacts with methanol approximately 100 times as fast as spiro[2,5]octa-1,4-diene-3-one[8] (IV). As summarized in Table II, reactivity toward methanol is only slightly reduced by methyl substitution in the methylene group of the quinone methide. On the other hand, 2,6-t-butyl groups exert a profound rate-retarding effect.

TABLE II

Rate Constants for Reaction
of Quinone Methides in Methanol at 25.0°C.
(R_1, R_2, R_3, R_4 as in Table I)

R_1	R_2	R_3	R_4	k (sec.$^{-1}$)
CH_3	CH_3	H	H	4.0×10^{-2}
CH_3	CH_3	H	CH_3	3.1×10^{-2} (23°)
CH_3	t-Bu	H	H	3.8×10^{-3}
t-Bu	t-Bu	H	H	9.4×10^{-5}
t-Bu	t-Bu	H	CH_3	5.5×10^{-5}
t-Bu	t-Bu	CH_3	CH_3	2.5×10^{-5}

It is interesting that every instance we have examined of a nucleophilic substitution reaction of a p-hydroxybenzyl derivative V proceeds by way of the quinone methide VI as an intermediate. Examples are the hydrolysis of the chloride Va or its reaction with sodium acetate in acetic acid to produce the benzyl acetate Vb. Even attempted basic saponification of the benzyl acetate Vb produced the quinone methide intermediate.