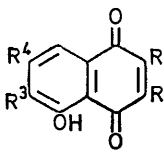
Mass Spectra of Derivatives of 5-Hydroxy-1,4-naphthoquinone (Juglone)

By **Theodore L. Folk, Harjit Singh,** and **Paul J. Scheuer,*** Department of Chemistry, University of Hawaii, Honolulu HI 96822

The mass spectra of ten derivatives of 5-hydroxy-1,4-naphthoquinone (juglone) have been investigated. The additional functions were acetyl, hydroxy, and in one case, ethyl. The fragmentation patterns of these compounds appear to follow previously noted generalizations for fragmentation of related naphthoquinones.

IN 1966 Moore *et al.* reported the isolation of some thirty quinone pigments from the sea urchins *Echinothrix diadema* Linn. and *E. calamaris* Pallis.[1] One pigment was a derivative of benzoquinone. All others were substituted 1,4-naphthoquinones, derived either from 5,8-dihydroxy-1,4-naphthoquinone (naphthazarin) or from 5-hydroxy-1,4-naphthoquinone (juglone). Singh *et al.*[2] subsequently synthesized several of these naturally occurring juglone derivatives, as well as some that had not been isolated previously. Almost without exception, the quantities of individual crystalline pigments that were isolated ranged between 1 and 20 mg, thus severely limiting the choice of tools for structural elucidation. Mass spectrometry, therefore, contributed substantially to the solution of these problems.

Mass spectrometry of a variety of naphthoquinone derivatives has received considerable attention. However, aside from a few compounds in the early work by Bowie *et al.*[3] and a few complex juglones that were treated by Becher *et al.*[4] and by Gough and Sutherland [5] no systematic study of juglone derivatives appears to have been made. This report details the behaviour under electron impact of ten substituted juglones (1)—(10), whose additional functional groups are acetyl, hydroxy, and in one case ethyl.



(1) $R^1 = R^2 = R^4 = H, R^3 = Ac$
(2) $R^1 = OH, R^2 = R^4 = H, R^3 = Ac$
(3) $R^1 = R^4 = H, R^2 = OH, R^3 = Ac$
(4) $R^1 = OH, R^2 = Ac, R^3 = R^4 = H$
(5) $R^1 = Ac, R^2 = OH, R^3 = R^4 = H$
(6) $R^1 = R^2 = OH, R^3 = Ac, R^4 = H$
(7) $R^1 = R^2 = OH, R^3 = Et, R^4 = H$
(8) $R^1 = R^4 = OH, R^2 = R^3 = H$
(9) $R^1 = R^3 = H, R^2 = R^4 = OH$
(10) $R^1 = R^2 = OH, R^3 = R^4 = H$

RESULTS AND DISCUSSION

Becher and his co-workers[4] elaborated a set of generalizations for the decomposition modes of acetylnaphthoquinones, which may be used to advantage in the interpretation of the mass spectra of derivatives of acetyljuglone. Under electron impact the acetyl function directs fragmentation of the molecule, taking precedence over hydroxy- and methoxy-groups. Loss of either methyl or keten can occur from the molecular ion if the acetyl group is on C-2 of a quinonoid ring which is unsubstituted at C-3. Subsequent expulsions of CO and acetylene from both initial fragments lead to a highly characteristic double pattern. When, however, there is a vicinal hydroxy-group, hydrogen bonding between 2-hydroxy and 3-acetyl groups favours the elimination of CO, which is then followed by loss of a methyl radical to form a very stable $M - 43$ fragment. In addition, water and/or keten can be lost from the $M -$ CO species. When the acetyl group is attached to an aromatic ring, it first loses a methyl group, which is followed by elimination of CO. Loss of keten from the molecular ion is much less pronounced in comparison with the 3-unsubstituted 2-acetylnaphthoquinones.[4]

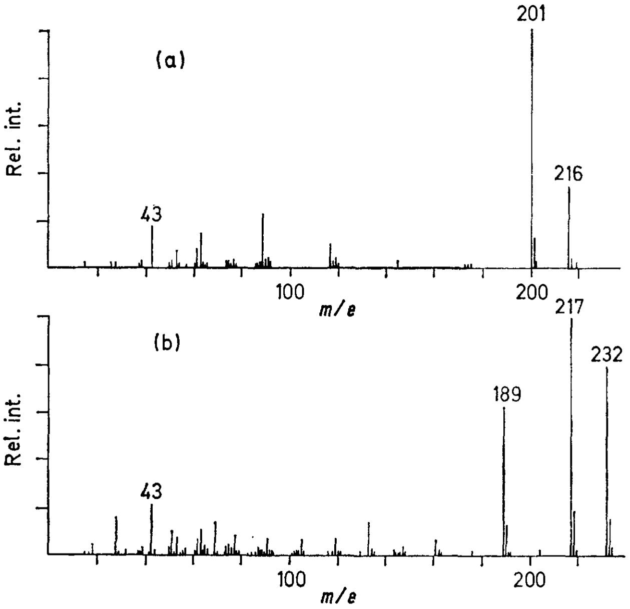


FIGURE 1 Mass spectrum of (a) 6-acetyljuglone (1) and (b) 6-acetyl-2-hydroxyjuglone (2)

As may be seen in Figure 1(a), the molecular ion of 6-acetyljuglone (1) initially loses a methyl radical (*m/e* 201), followed by the loss of carbon monoxide (*m/e* 173). As would be expected when the acetyl group is in the

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[1] R. E. Moore, H. Singh, and P. J. Scheuer, *J. Org. Chem.*, 1966, **31**, 3645.

[2] H. Singh, T. L. Folk, and P. J. Scheuer, *Tetrahedron*, 1969, **25**, 5301.

[3] J. H. Bowie, D. H. Cameron, and D. H. Williams, *J. Amer. Chem. Soc.*, 1965, **87**, 5094.

[4] D. Becher, C. Djerassi, R. E. Moore, H. Singh, and P. J. Scheuer, *J. Org. Chem.*, 1966, **31**, 3650.

[5] J. H. Gough and M. D. Sutherland, *Austral. J. Chem.*, 1970, **23** 1839.

aromatic ring, the contribution from *m/e* 43 is large. There is no opportunity for hydrogen bonding between the 6-acetyl and the 5-hydroxy-groups because of the extremely strong hydrogen bonding that exists between the 5-hydroxy and the 4-quinonoid carbonyl functions.

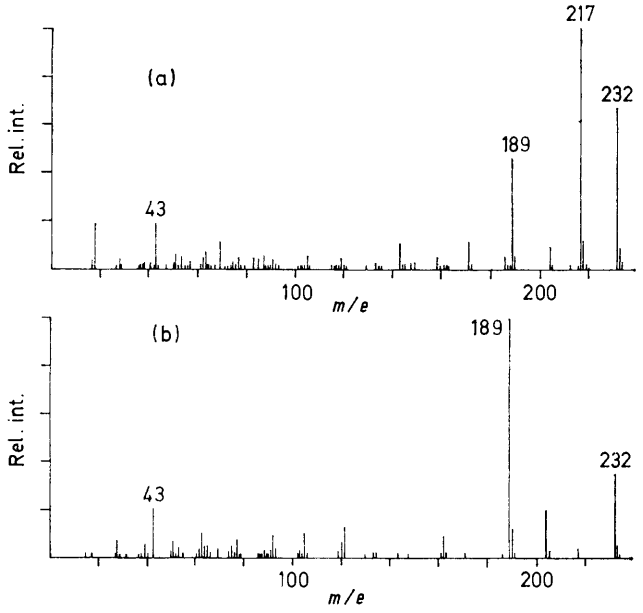


FIGURE 2 Mass spectrum of (a) 6-acetyl-3-hydroxyjuglone (3) and (b) 3-acetyl-2-hydroxyjuglone (4)

Two fragmentation routes [Figure 1(b)] can be traced for 6-acetyl-2-hydroxyjuglone (2). A minor route begins with the loss of CO which is followed by loss of a methyl radical. The main route starts with initial loss of methyl to give the base peak (*m/e* 217), followed by expulsion of CO. We also observe a respectable *m/e* 69 fragment, characteristic of all naphthoquinone derivatives containing the (OCCCO) unit, as has been noted by Bowie *et al.*[3]

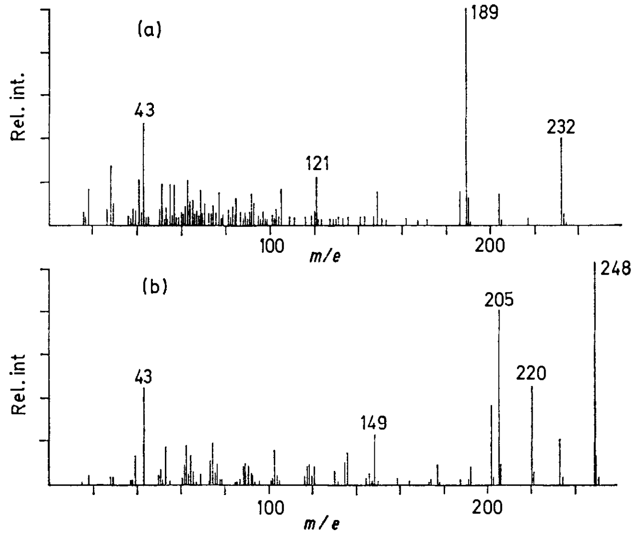


FIGURE 3 Mass spectrum of (a) 2-acetyl-3-hydroxyjuglone (5) and (b) 6-acetyl-2,3-dihydroxyjuglone (6)

The initial fragmentation routes for 6-acetyl-3-hydroxyjuglone (3) [Figure 2(a)] are identical with those of the 2-hydroxy-derivative. However, further disintegration is seen for (3) which is not noted for 6-acetyl-2-hydroxyjuglone (2). Following loss of CO from the molecular ion, either methyl or H_2O may be lost. If H_2O is lost, a fragment (*m/e* 186) is formed which can lose C_2H_3O to give an ion with *m/e* 143 or lose CO to give an ion with *m/e* 158. Likewise, the fragment with *m/e* 189 loses water to give an ion with *m/e* 171, a process that is not noted for the 2-hydroxy-derivative. The fragment with *m/e* 171 loses another CO to give an ion with *m/e* 143 also. The presence of both (OCCCO) and acetyl groups is indicated by the *m/e* 69 and 43 peaks, though both of these are slightly diminished.

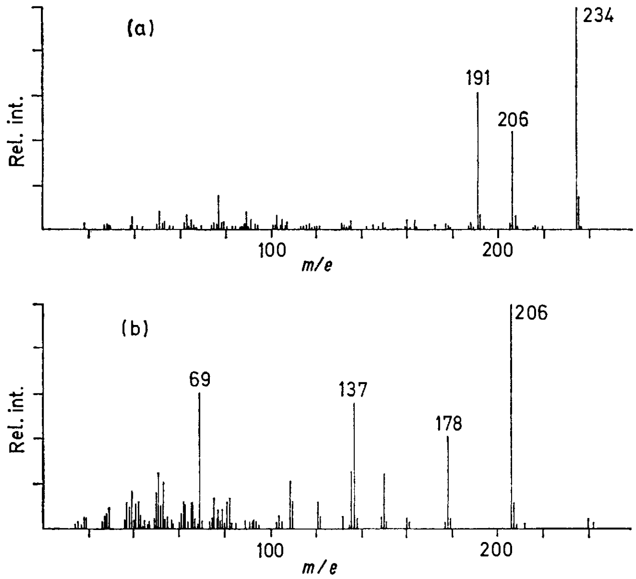


FIGURE 4 Mass spectrum of (a) 2,3-dihydroxy-6-ethyljuglone (7) and (b) 2,7-dihydroxyjuglone (8)

The fragmentation pattern of 3-acetyl-2-hydroxyjuglone (4) [Figure 2(b)] is completely different from those of the preceding compounds now that the acetyl group is on the quinonoid ring and hydrogen-bonded to a vicinal hydroxy-group. The initial loss of methyl is now negligible, whereas loss of CO followed by loss of methyl gives the base peak (*m/e* 189). Loss of water from the ion with *m/e* 204 is quite small, but can be an indication of the vicinal nature of the hydroxy and acetyl groups. Loss of keten from the ion with *m/e* 204 gives rise to the fragment of *m/e* 162, which could account for the small *m/e* 69 peak.

The fragmentation pattern of 2-acetyl-3-hydroxyjuglone (5) [Figure 3(a)] is very nearly the same as that of 3-acetyl-2-hydroxyjuglone. There is, however, increased intensity of the *m/e* 186 (204 — H_2O) and 43 peaks, and the appearance of an ion with *m/e* 149, which has not been explained.

The base peak of 6-acetyl-2,3-dihydroxyjuglone (6) [Figure 3(b)] is also the molecular ion and two distinct routes of fragmentation of about equal occurrence are present. Loss of a methyl radical followed by expulsion of a CO molecule can be traced to give a fragment with *m/e* 205; alternately, loss of CO (*m/e* 220) followed by elimination of a methyl radical also leads to this peak. It is interesting to note that there is a substantial peak for the loss of water (*m/e* 202) after initial loss of CO. Loss of water is usually indicative of an acetyl group that is hydrogen-bonded to a vicinal hydroxy-group. After initial expulsion of CO the geometry of the system could be appreciably changed so as to weaken the bonding between the *peri*-hydroxy-group and what was the quinonoid carbonyl. This would in turn allow some substantial hydrogen bonding with the acetyl group. However, there is still a substantial *m/e* 43 peak.

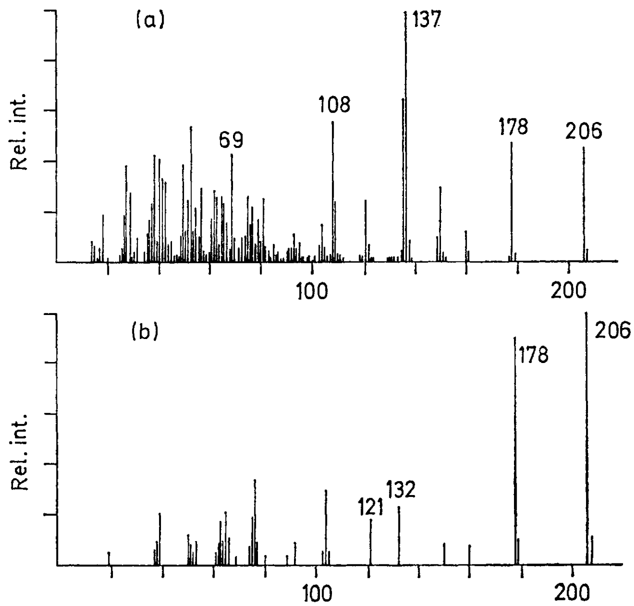


FIGURE 5 Mass spectrum of (a) 3,7-dihydroxyjuglone (9) and (b) 2,3-dihydroxyjuglone (10)

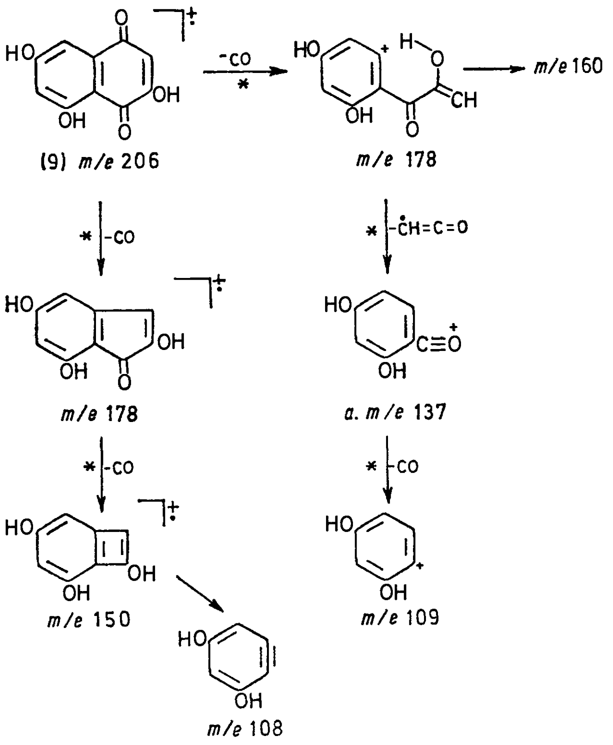
Whether this rationalization is valid in this specific case or not, there is an apparent successful competition by the 3-hydroxy-group with the acetyl group for direction of the fragmentation. This competition between the acetyl and 3-hydroxy-groups, though less significant, can be noted for several compounds previously discussed.

Loss of CO from 6-acetyl-3-hydroxyjuglone (3) is followed by loss of water. Expulsion of water is also noted following the initial losses of CO and methyl. These losses of water are not noted for the 2-hydroxy-derivative (2). The loss of water following the initial elimination of CO from 3-acetyl-2-hydroxyjuglone (4) is negligible, whereas the analogous loss of water for 2-acetyl-3-hydroxyjuglone (5) is 15% of the base peak.

Analysis of the mass spectral data of spinochrome G (6-acetyl-2,3,7-trihydroxyjuglone [5]) appears to give more evidence of the fragmentation directing influence of the 3-hydroxy-group. In fact, except for mass differences due to the addition of the 7-hydroxy-group, the spectrum is very similar to that of 6-acetyl-2,3-dihydroxyjuglone (6). Conversely, Becher *et al.*[4] used 6-acetyl-2,7-dihydroxyjuglone as one of the reference compounds on which they based their generalizations for the fragmentations of acetylnaphthoquinones. The initial loss of CO was small and the subsequent elimination of water was minor.

The main fragmentation route of 2,3-dihydroxy-6-ethyljuglone (7) [Figure 4(a)] begins with expulsion of carbon monoxide (*m/e* 206) followed by loss of a methyl radical (*m/e* 191) and successive CO molecules.

The fragmentation patterns for 2,7-dihydroxyjuglone (8) [Figure (4b)] and 3,7-dihydroxyjuglone (9) [Figure 5(a); Scheme 1] are essentially the same except for intensity differences in many of the peaks. The base peak for the 2,7-derivative is the molecular ion while that of the 3,7-isomer is fragment *a*(*m/e* 137). The peak at *m/e* 137 is highly characteristic of a hydrogen rearrangement fragment and is probably the base peak for (9) because of the greater stability of *a* as compared to *b*.

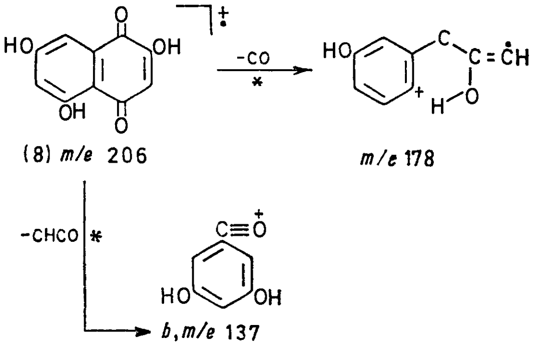


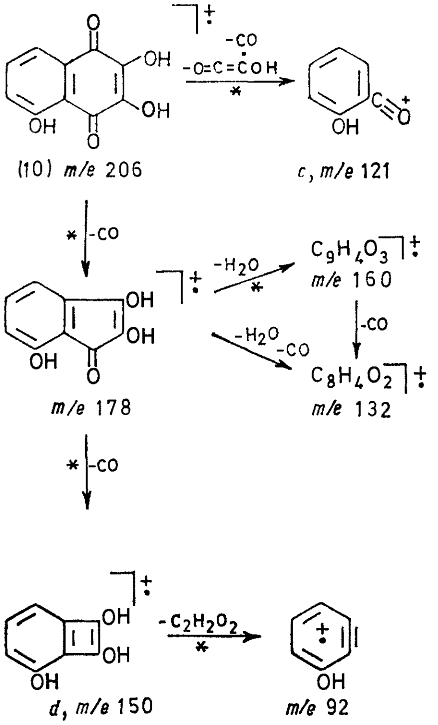
SCHEME 1

The spectra also show large peaks at *m/e* 69 indicating the presence of an (OCCCO) group. The fragment at *m/e* 160 from loss of CO followed by loss of water is somewhat larger for (9) than for (8).

The fragmentation pattern of 2,3-dihydroxyjuglone (10) [Figure 5(b); Scheme 2] is much the same as for the other two isomers (8) and (9) when adjustments are made for the presence of both hydroxy-groups in the quinonoid ring. Whereas after initial loss of CO the 2,7- and 3,7-isomers lose CH=C=O during a hydrogen rearrangement to give peaks at *m/e* 137, the 2,3-dihydroxy-derivative instead loses CO and HOC=C=O in one step to give *c* (*m/e* 121). There is no large peak for *m/e* 69, which is reasonable since such a pathway would be a poor competitor with the stabilization that can be achieved by simultaneous loss of CO and the C_2HO_2 radical. As noted in the mass spectrum of 3,7-dihydroxyjuglone (9), the ion with *m/e* 160 (*M* — CO — H_2O) is larger in the spectrum of (10) than in that of the 2,7-isomer. The fragment with *m/e* 132, not observed in (8) or (9), is formed *via* a pathway involving loss of two CO molecules and of water. Successive loss of two CO molecules, substantiated by metastable peaks at *m/e* 154 and 126, leads to fragment *d* (*m/e* 150).

None of the above ten juglone derivatives show marked deviation from the fragmentation patterns anticipated on the basis of the earlier work. We did, however, note an additional interpretive tool for distinguishing between 2- and 3-hydroxy-substituted juglone derivatives, compounds that cannot readily be differentiated otherwise. The 3-hydroxy-substituted acetyljuglones showed increased initial expulsion of CO followed by loss of water. The increased intensities for fragments arising from loss of water were also documented for 2,3- and 3,7-dihydroxyjuglone as compared to the 2,7-isomer. Since Becher *et al.*[4] had studied only a few complex juglone derivatives, this work fills a gap in the literature of organic mass spectrometry.





SCHEME 2

EXPERIMENTAL

Mass spectra were recorded on an Hitachi–Perkin-Elmer RMU-6D mass spectrometer at 70 eV ionizing voltage. The chamber temperatures were in the range 190—225°. Physical and chemical properties of the compounds were reported previously.[2]

We are grateful to Sr. M. R. Brennan for determining the spectra.

[3/684 *Received, 2nd April,* 1973]