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STABLE ORTHO- AND PARA-NAPHTHAQUINONE METHIDES

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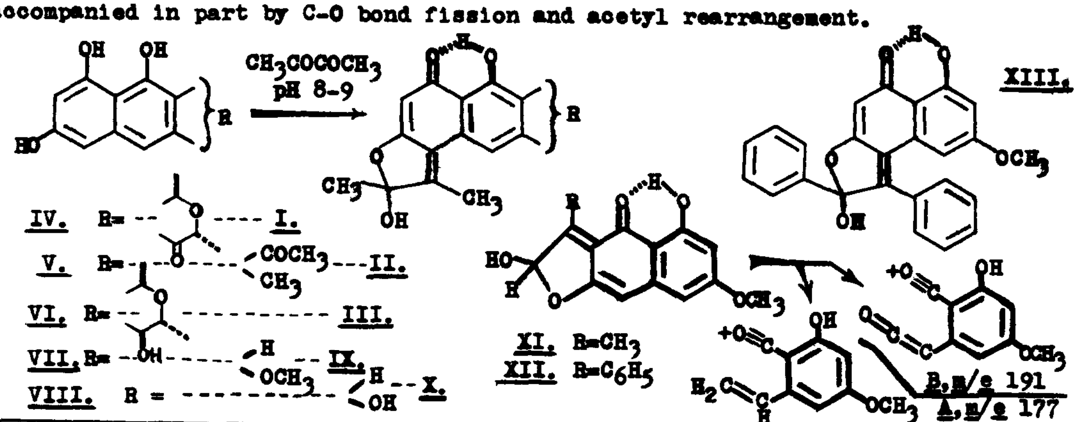
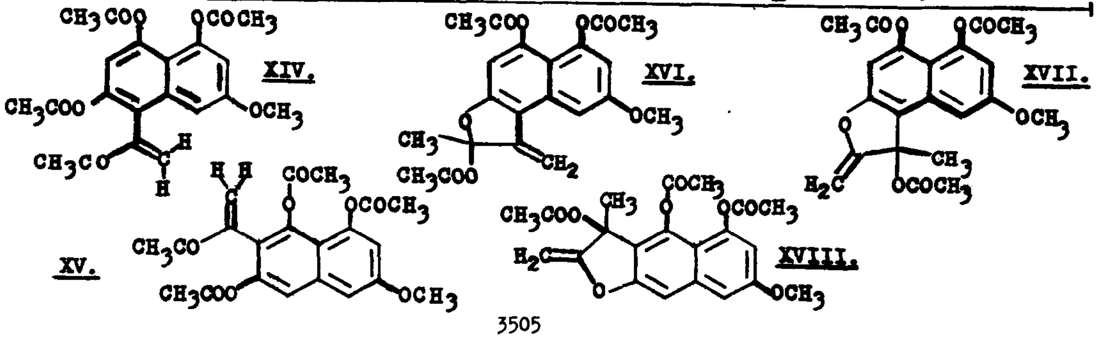
In the preceding communication (1), we have described the isolation and characterization of some unusual quinone methides (I,II,III) related to three 1,3,8-trihydroxynaphthalene derivatives (IV,V,VI) which are present as their 8-glucosides in the insect *Aphis nerii* Fonscolombe. These methides could be synthesized by the facile condensation of the naphthalene-triols with biacetyl in weakly alkaline medium, and were stable to light, air, silica or Florisil chromatography, aqueous sodium dithionite, strong acids, and moderately strong bases. Under mild acetylation conditions they suffered re-aromatization, accompanied in part by C-O bond fission and acetyl rearrangement.





The rather unusual stability of these quinone methides (2) may be ascribed to the small energy difference between naphtharesorcinols and monoenolized dioxotetralins (3), and to the juglone-type stabilizing influence of the hydrogen-bonded peri-phenol. It was of considerable interest to try to prepare model compounds in this series, both to delimit the scope of the condensation and to study the detailed physical and chemical properties of the products.

A priori, it might be expected that 1,3,8-trihydroxynaphthalenes in general would condense with α-dicarbonyl compounds to give products of type I-III. In support of this, synthetic 1,3,8-trihydroxy-6-methoxynaphthalene, VII [from $MgI_2 \cdot Et_2O$ demethylation (4) of 1,3-dihydroxy-6,8-dimethoxynaphthalene (5)], condensed smoothly with biacetyl in the presence of Florisil or triethylamine to give methide IX, dec. 213-215°, whose IR, UV (λ_{max}^{EtOH} 223,273,310,425 nm), and NMR (Fig. 1) characteristics corresponded very well with those observed for I-III. An unexpected lesser product of this condensation was the stable ortho-quinone methide XI, m.p. 144-147°, which had IR and NMR spectra very similar to those of IX (Fig. 2), but very different electronic and mass spectra. Only a single strong band appeared at 267 nm in the UV; strong absorptions at 418 and 510 nm imparted a deep wine-red color to the compound, which demonstrated very long-wavelength fluorescence (appearing nearly black on the blue TLC plate under UV light). Two characteristic peaks appeared in the mass spectrum of XI at m/e 177 (A) and 191 (B), absent from the spectrum of IX.

Acetylation of IX gave a more polar product XIV, m.p. 163-164° (NMR spectrum, Fig. 3), and an inseparable mixture of the less polar triacetates XVI and XVII, whose NMR spectrum (Fig. 5) greatly aided the interpretation of the nature of the analogous mixture from I (1). From the ortho-methide XI were obtained the polar triacetate XV (non-crystalline; NMR spectrum, Fig. 4), and a predominant vinyl ether XVIII, m.p. 172-175° (NMR spectrum, Fig. 6), resulting from 1,4-addition of acetic acid across the methide system.

Similarly, 1,3,6,8-tetrahydroxynaphthalene (VIII), a minor product of the $MgI_2 \cdot Et_2O$ demethylation above, condensed smoothly with biacetyl to give methide X, dec. 225-228°, whose spectral characteristics fully supported its formulation as shown. The trihydroxynaphthalene VII could also be condensed with benzil, under forcing conditions, to give the para-methide XIII, dec. 246-249°, λ_{max}^{EtOH}

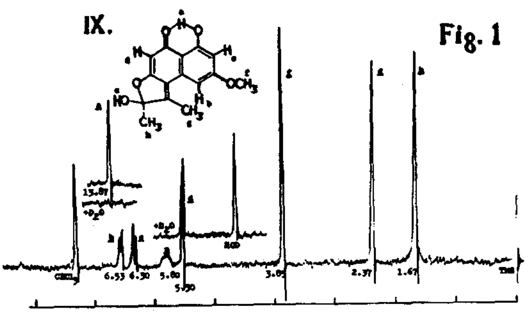

IX.

Fig. 1

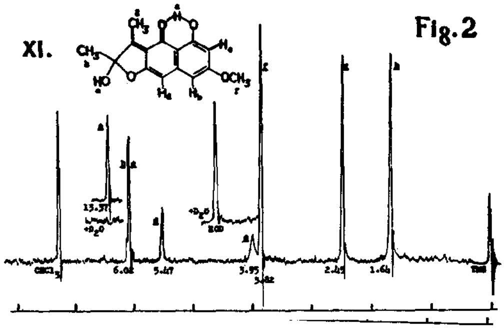

XI.

Fig. 2

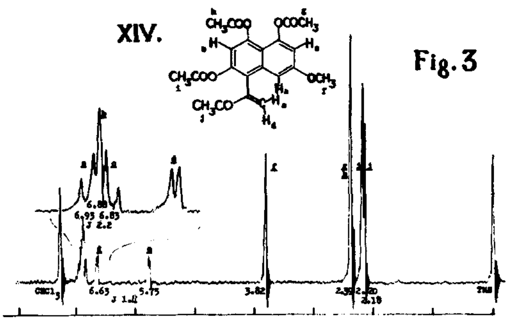

XIV.

Fig. 3

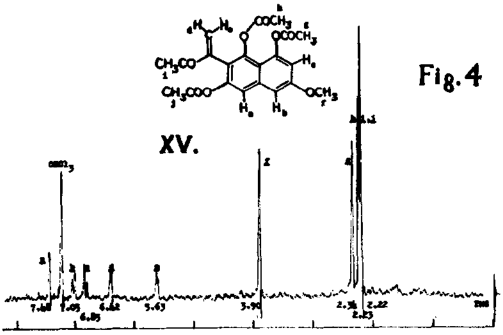

XV.

Fig. 4

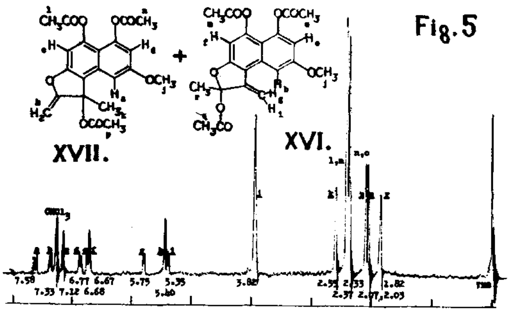

XVII. + XVI.

Fig. 5

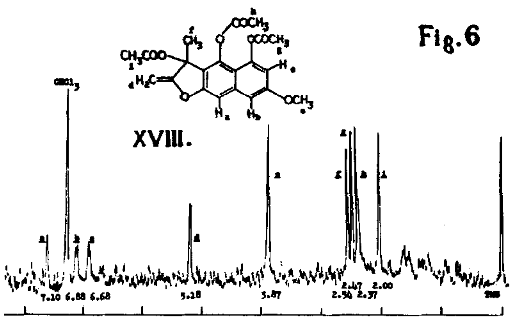

XVIII.

Fig. 6

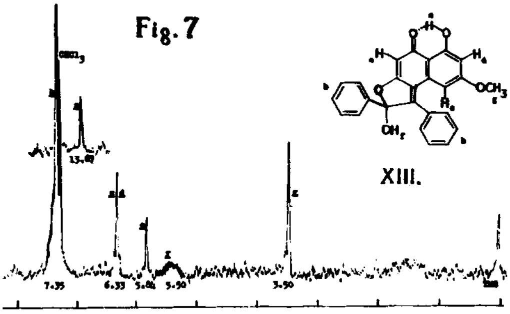


Fig. 7

XIII.

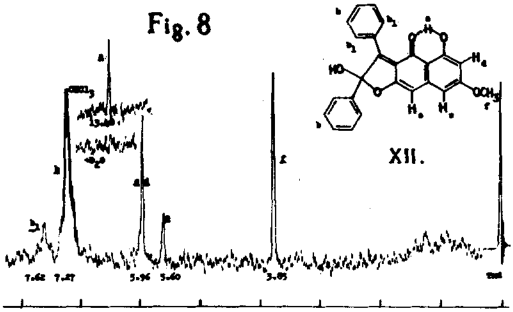


Fig. 8

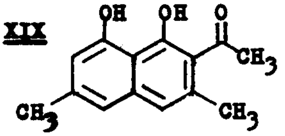
XII.

270,325,437 nm; and the *ortho*-methide XII, m.p. 130-135°, λ_{max}^{EtOH} 255,413,524 nm (see NMR spectra, Figs. 7 and 8). The two *ortho*-quinone methides XI and XII were considerably less stable than the *para*-isomers IX and XIII, being slowly oxidized upon exposure to air and smoothly reduced by aqueous sodium dithionite at 80° to give material (not isolated) with UV absorption similar to that of the parent VII.

Attempted condensations with pyruvaldehyde, glyoxal, or methyl pyruvate gave no quinone methides, even under forcing conditions. The two aldehydic dicarbonyl compounds apparently polymerized rapidly under the reaction conditions, and the keto-ester probably lacked the activation necessary for the condensation.

Although 1,3- and 1,8-dihydroxynaphthalenes are also quite active towards oxidation and condensation (3), naphthoresorcinol and Collie's naphthalene XIX (6) gave no red-fluorescent products even when heated with biacetyl on Florisil or alumina for extended periods; only starting material and polymeric decomposition products could be recovered. Likewise, all attempts to form methides from 1,3-dihydroxy-8-methoxynaphthalenes failed; the *peri*-hydroxyl, which stabilizes the products, is apparently also necessary to facilitate the initial condensation.

XIX



Further experiments on the chemistry of these singular methides [XI and XII are among the very few *ortho*-quinone methides to be isolated in crystalline state (7)] will be presented in a complete paper.

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