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AN APPLICATION OF FREMY'S SALT FOR THE SYNTHESES OF POLYCYCLIC QUINONES

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A general synthetic route for the production of polycyclic quinones of the polyketide series has been reported[1]. The procedure which involves a Diels-Alder addition of a 1-methoxycyclohexa-1,3-diene to a quinone, followed by enolization, oxidation and thermal elimination of the ethano-bridge[2,3], suffers from a serious disadvantage if the intermediate quinol contains an enol ether function as this is rapidly hydrolysed to the corresponding ketone, e.g. (1) and (2) → (3) and (4) respectively. We now report a method which avoids the isolation of the quinol and is an efficient one-step conversion of the adduct into the intermediate bridged-ring quinone, (5) and (6) respectively.

An initial, unsuccessful attempt was made using DDQ which as a high potential quinone[4] might dehydrogenate the model enedione (7, R = H) to the quinone (8). Treatment of (7, R = H) with excess DDQ in benzene resulted in the production in high yield of a naphthoquinone (9, R = H, m.p. 266-268°), the structure of which was confirmed by spectral methods. Presumably, this product was obtained by an initial 1,3-fission of a C-C bond[5] followed by dehydrogenation. If this cleavage was promoted by the α-phenolic group then its methylation should render the adduct suitable for DDQ treatment, but both diazomethane in ether-methanol and methyl iodide/potassium carbonate/acetone resulted in the same rearranged methyl ether (10), m.p. 166-168°.

From our earlier work[1] this structure[+] was readily assigned on examination of its spectral properties and by the formation of the diacetate (11), m.p. 198-200°. The infrared spectrum of (10) has only one carbonyl absorption at 1716 cm^{-1} while the n.m.r. spectrum has a characteristic ABX type sub-spectrum in the cyclohexanone ring. Spin decoupling revealed that

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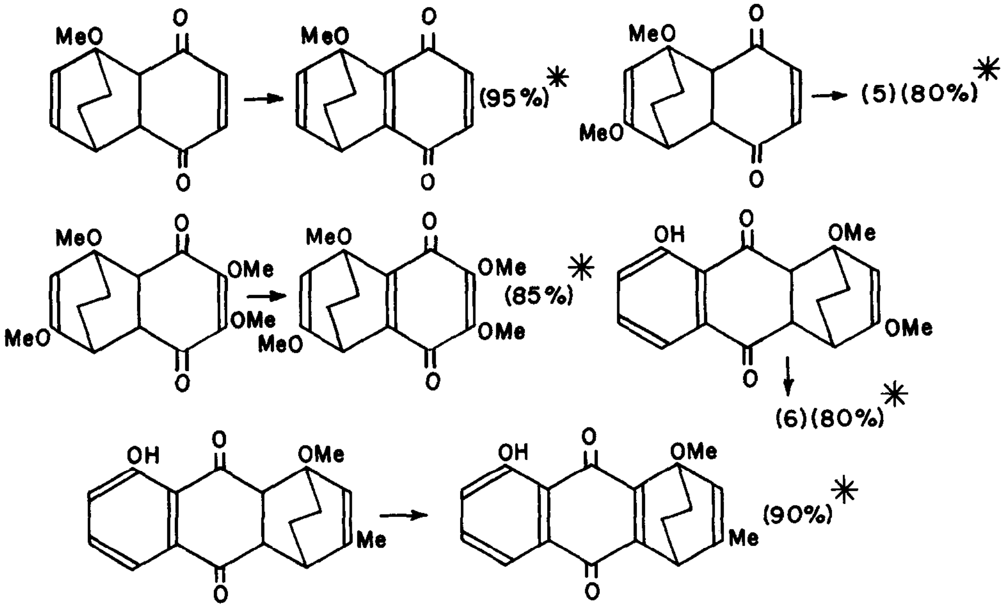
[+] The relative position of the methoxyl group has not been fully substantiated but the spectral data for (10) and (11) indicates the orientation depicted.

coupling of the X proton with the other bridgehead proton is 9.5Hz while J_{AB} is 16.5Hz.

Acetylation of the adduct (7, R = H) with acetic anhydride and pyridine produced the desired mono-acetate (7, R = Ac), m.p. 122-123°, which on treatment with DDQ yielded the rearranged acetoxynaphthoquinone (9, R = Ac), m.p. 226-228°.

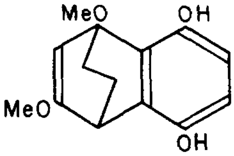
While Fremy's salt (potassium nitrosodisulphonate) has been used extensively for the production of benzoquinones from monohydric phenols[6] and to a limited extent for the dehydrogenation of some dihydroindole alkaloids[7], its potential as an oxidising agent in organic chemistry has not been fully exploited. Initial attempts to dehydrogenate the enedione acetate (7, R = Ac) with Fremy's salt resulted in the recovery of starting material; but if after its enolization (and approximately 70% saponification) with potassium hydrogen carbonate in hot methanol for ten minutes, water, sodium acetate and Fremy's salt were added, virtual quantitative yield of the desired naphthoquinone nucleus was obtained, in a 2:1 mixture of the hydroxy- and acetoxy-derivatives.

Similarly,

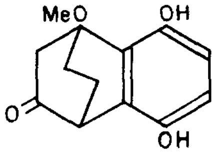


* by weight of crystalline material recovered

Thus the use of Fremy's salt for the dihydrogenation of the enedione appears to be of general applicability, but is particularly useful in avoiding hydrolysis of an enol-ether group.



(1)



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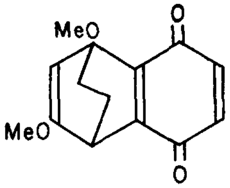
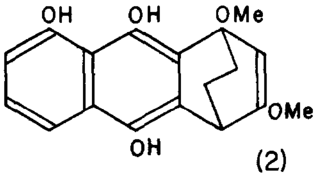
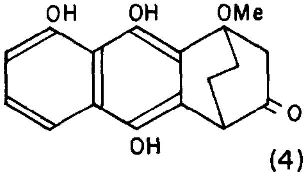


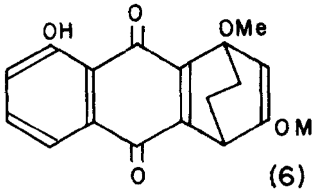
(5)



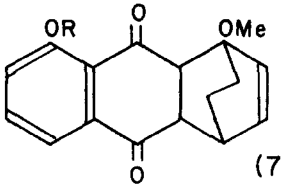
(2)



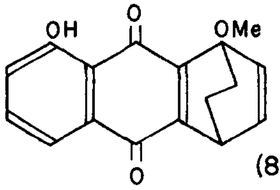
(4)



(6)



(7)



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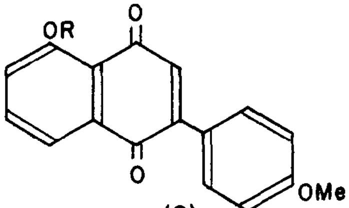
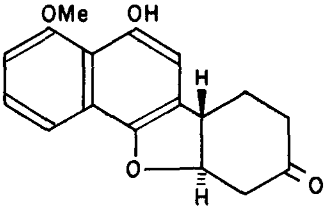
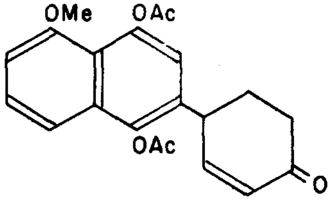


(9)



(10)



(11)

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