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REGIOSPECIFIC ADDITION OF METHOXYCYCLOHEXA-1,3-DIENES TO 2-METHOXY-1,4-BENZOQUINONE. APPLICATION TO THE SYNTHESIS OF 3-METHOXY-7-METHYLJUGLONE AND α-CARYOPTERONE.

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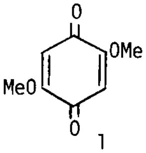
Nucleophilic attack on 1,4-benzoquinone leads in general to 2,5-disubstituted 1,4-benzoquinones[1]. For example, the action of methanol on benzoquinone, in the presence of zinc chloride, gives 2,5-dimethoxy-1,4-benzoquinone (1)[2]. This implies that the methoxyl substituent in the intermediate quinone (2) directs the second methanol molecule to attack at a position "para" to it on the quinone nucleus.

Diels-Alder addition of methoxycyclohexa-1,3-diene (3) to quinone (2) could formally take place to give either of the two adducts (5) or (6), but that (5) should be favoured to the exclusion of (6) might be anticipated on inspection of (4), a resonance contributor to diene (3).

On heating quinone (2)[3] and diene (3)[4] under reflux in benzene, only one adduct was isolated (60%)[5]. That this was (5)† and not (6) was demonstrated as follows. The adduct was enolised (potassium t-butoxide/THF) and the intermediate quinol was oxidised (Ag_2O) to the quinone (7)†. This was heated, with loss of ethylene, to give the naphthaquinone (8)†, which was converted into species (9) with 1% aqueous sodium hydroxide; the yield of this latter compound from adduct (5) was virtually quantitative. Compound (9) was demethylated (BBr_3) and the crude product acetylated to afford the diacetate (10), m.p. 136° (lit. m.p. 137°)[6]. The



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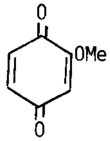

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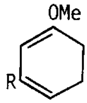
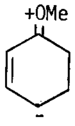


3, R=H
12, R=Me



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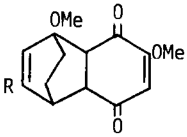
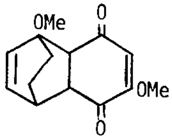


5, R=H
13, R=Me



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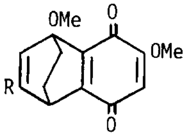
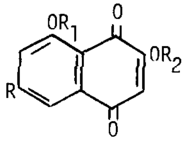


7, R=H
14, R=Me

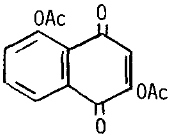
diacetate (11), which would have arisen from alternative adduct (6), has lit. m.p. 152°[6].

The adduct (13)[†] between 1-methoxy-3-methylcyclohexa-1,3-diene (12) and quinone (2) was similarly converted via compound (14)[†] into the quinone (15)[†]. This was selectively O-demethylated (BCl_3) to give 3-methoxy-7-methyljuglone (16)[†], identical with an authentic sample[7].

Subjection of quinone (9) to a Hooker reaction with 3-methylbutanal afforded the product (17)[†], which was cyclised with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to the chromene quinone (18)[†]. This was demethylated with boron tribromide to give α-caryopterone (19)[†], identical with the natural pigment[8].



8, R=H, R_1=R_2=Me
9, R=R_2=H, R_1=Me
10, R=H, R_1=R_2=COMe
15, R=R_1=R_2=Me
16, R=R_2=Me, R_1=H



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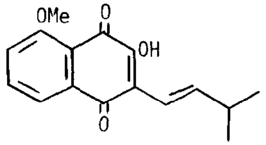
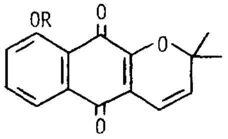


17



18, R=Me
19, R=H

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[†] All new compounds gave satisfactory elemental analyses and spectroscopic data.