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A NOVEL SYNTHESIS OF 4-CHLORO-4-METHYLCYCLOHEXA-2,5-DIENONE AND 4,4-DIMETHOXYCYCLOHEXA-2,5-DIENONE.

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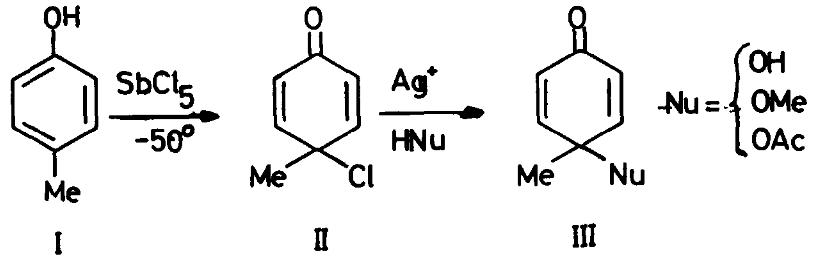
The oxidation of phenols to give coupled or substituted products is of considerable current interests. Unless all reactive positions are blocked (as in 2,4,6-trialkylphenols) oxidative substitution of phenols (halogenation, methoxylation, etc.) normally leads to other aromatic compounds. A few cases are known [1,2,3,4,5] where cyclohexadienone derivatives are formed. These dienones are reactive and polyfunctional and should be useful as intermediates for the synthesis of complex molecules Nevertheless, little effort has been made to prepare such compounds and little is known about their chemistry We therefore report a novel and simple synthesis and some reactions of 4-chloro-4-methylcyclohexa-2,5-dienone (II) and 4,4-dimethoxycyclohexa-2,5-dienone (V).

Chlorination of p-alkylated phenols with the traditional chlorinating agents usually gives o-chlorophenols (4-chlorodienones are formed in low yield on reaction of 3,4-xylenol[2,3] or phenolic steroids[4,5] with chlorinating agents like tert-butylhypochlorite or N-chloro succinimide in a polar medium). We have now found that p-alkylphenols can be monochlorinated to the corresponding 4-chloro-4-alkyl-cyclohexadienone derivatives in very high yield by treatment with an excess of antimony pentachloride in cold dichloromethane. For example, slow addition of a cold (-50^{o}) solution of p-cresol (9.0 g, 0.083 mol) in dichloromethane (250 ml) to a cold (-70^{o}) solution of $SbCl_5$ (60 ml, 0 47 mol) in dichloromethane (150 ml) resulted in the formation of a brownish precipitate. This was stirred for 10 min at -60^{o}. Cold methanol was then added until the precipitate had dissolved completely (50 ml) The reaction mixture was poured into water (200 ml) and the resulting mixture was filtered and extracted with dichloromethane (3x150 ml). The combined dichloromethane extract was washed with a phosphate buffer (pH 6, 2x150 ml). Evaporation of the dichloromethane gave a yellow oil which was purified by filtration through a silica column (50 g, dichloromethane eluent). Yield 10.9 g (92 %) of a light green oil, $Bp._{0\ 2mm}30^{o}$, identified as 4-chloro-4-methyl-cyclohexa-2,5-dienone (II) by its NMR ($CDCl_3$, TMS) δ 1.85 (s, 3H), 6.16 ($d_{J=}$10 Hz' 2H), 6.97 ($d_{J=10\ Hz}$, 2H), IR(film) ν3060, 1716,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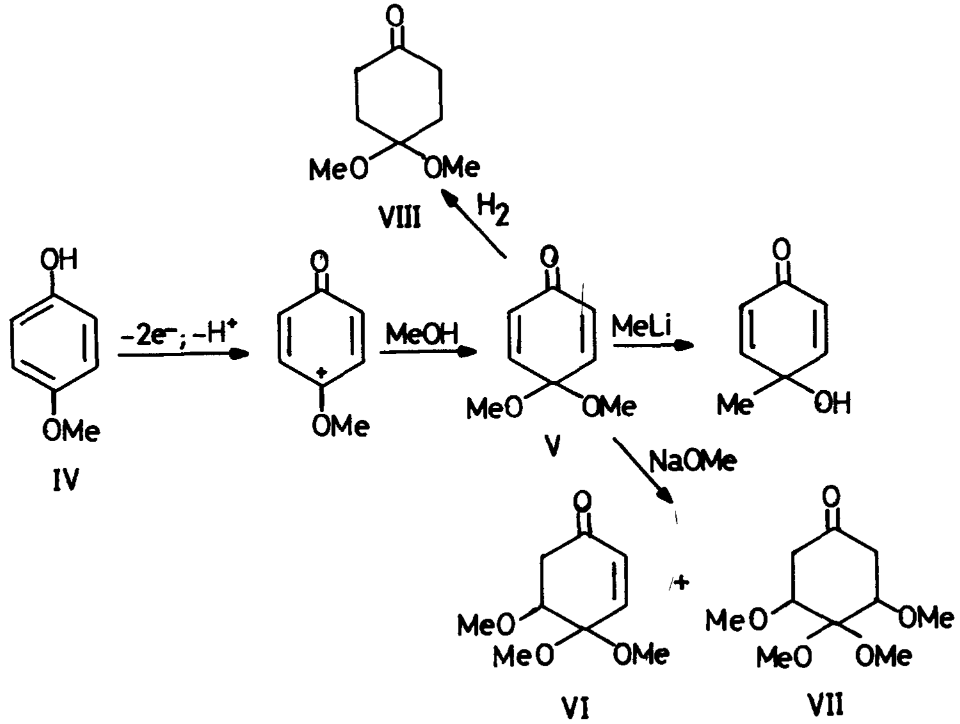
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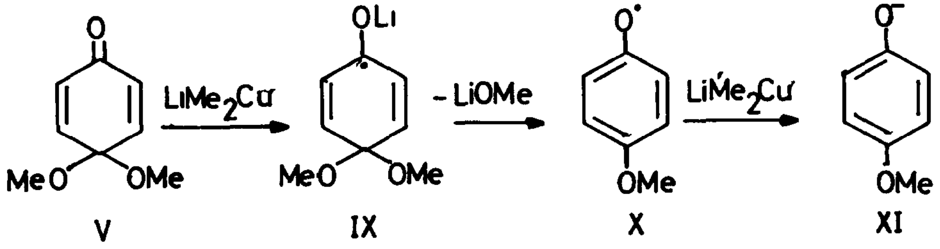
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1675, 1640 cm^{-1}, and its molecular weight (142) from the mass spectrum). The temperature and the amount of $SbCl_5$ used are critical At room temperature, the reaction gives a mixture of chlorinated phenols regardless of the amount of $SbCl_5$ while the use of one equivalent of $SbCl_5$ at low temperature (-60°), in the same way as described above, results in the formation of dimers, trimers, etc. of the phenol (but no chlorination).

The chlorodienone (II) readily gives a series of dienones (III)[7] by silver-induced solvolysis[8]. These and other reactions of II are presently being studied.

A second synthetically useful dienone that offers a route to III is 4,4-dimethoxycyclohexa-2,5-dienone (V). This has been prepared previously from p-methoxyphenol (IV) in 65 % yield by oxidation with cerium(IV) in methanol[6] and by hydrolysis of p-benzoquinone-bis-(dimethyl)-ketal[9]. It was synthesised in the following way p-Methoxyphenol (10 g) dissolved in methanol (60 ml) containing lithium perchlorate (4 g) was subjected to constant current (500 mA) electrolysis[7] on a platinum anode (50 cm^2) in an open water-cooled vessel. The cathode was a tungsten wire (diameter 0.5 mm). The electrolysis mixture was stirred magnetically The oxidation was monitored by NMR. When 95-100 % of the starting material had been consumed (this requires about 3 6 Faradays/mol[10], corresponding to an electrolysis time of 930 min) the electrolysis mixture was poured into a phosphate buffer (pH 6, 300 ml). Extraction with dichloromethane (3x150 ml) followed by evaporation at reduced pressure (the temperature of the heating bath should not exceed 30°) afforded almost pure V (12 1 g, 97 % yield) Further purification can be achieved by filtration through deactivated alumina (dichloromethane eluent) or by distillation at reduced pressure but decomposition of the dienone reduces the yield to 85 %. The purified product has Bp.$_{0.7mm}$70-73°, NMR (CDCl$_3$), TMS) δ 3.41 (s, 6H), 6 30 (d$_{J=11\ Hz}$, 2H), 6 92 (d$_J$=11 Hz, 2H), and was identical with V prepared as described in the literature[6]

Catalytic hydrogenation of V with tris(triphenylphosphine)-rhodium chloride as catalyst affords 4,4-dimethoxycyclohexanone (VIII) in 64 % yield, Bp.$_{12mm}$100°, NMR (CDCl$_3$, TMS) δ 1.87-2.57 (m, 8H), 3.18 (s, 6H). Reaction of V with methyllithium in ether at -70° gave, after hydrolytic workup, 4-hydroxy-4-methylcyclohexa-2,5-dienone[1] (III, Nu=OH) in 88 % yield Treatment of V with sodium methoxide in methanol results in the formation of a mixture of 4,4,5-trimethoxycyclohex-2-enone (VI) and 3,4,4,5-tetramethoxycyclohexanone (VII) Addition of V to lithium dimethylcopper[11] in ether at -70° did not afford the **expected** 1,4-addition product. Instead, reduction occurred and p-methoxyphenol was obtained. This finding supports the suggestion[11] that the initial step in the reaction of the lithium dimethylcopper reagent with α,β-unsaturated ketones is an electron transfer to give the radical anion (IX) of the ketone. In this particular case the radical anion of (V) presumably eliminates lithium methoxide with formation of the phenoxy radical (X) which by further reduction affords the phenoxide ion (XI).

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