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REACTIONS OF ORGANOLITHIUM REAGENTS WITH *p*-BENZOQUINONES AND CYCLOHEXADIENONES. SYNTHESIS OF 4-ALKYL-4-HYDROXYCYCLOHEXA-2,5-DIEN-1-ONES AND 1,4-DIALKYLCYCLOHEXA-2,5-DIENE-1,4-DIOLS.

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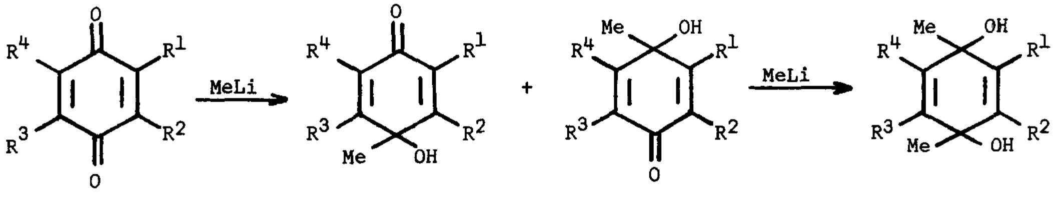
Summary: Addition of organolithium reagents to *p*-benzoquinones in ether gives the corresponding 4-alkyl-4-hydroxycyclohexa-2,5-dien-1-ones. Addition of excess of the reagent to the *p*-benzoquinones, or to the 4-alkyl-4-hydroxycyclohexa-2,5-dien-1-ones, in tetrahydrofuran, gives the corresponding dialkylcyclohexa-2,5-diene-1,4-diols.

Many attempts have been made to add various alkylmetal reagents such as RMgX,[1-3] RLi,[4,5] R_3Al,[6,7] R_2Cd[8] and R_3B[9] to benzoquinones. 1,2 Addition products, viz., 4-alkyl-4-hydroxycyclohexa-2,5-dien-1-ones and 1,4-dialkylcyclohexa-2,5-diene-1,4-diols, have been obtained only in the case of the fully substituted duroquinone.[4,5,9] The fused-ring quinones, e.g. naphthaquinone and anthraquinone, do however undergo 1,2 addition with alkylmetal reagents[11] and the unsaturated organometallic reagents lithium acetylide,[12] triallyboron,[13] and diallylzinc[14] have been added to benzoquinone to give the corresponding diadducts: 1,4-diethynylcyclohexa-2,5-diene-1,4-diol and 1,4-diallylcyclohexa-2,5-diene-1,4-diol.

We wish to report the ready synthesis of 4-hydroxy-4-methylcyclohexa-2,5-dien-1-one and 1,4-dimethylcyclohexa-2,5-diene-1,4-diol in excellent yields by the 1,2 addition of methyllithium to *p*-benzoquinone at -78 °C[15]. Phenyl, *n*-butyl- and *tert*-butyllithium also readily react with *p*-benzoquinone to give the corresponding hydroxydienones and dienediols, and methyllithium reacts with various substituted benzoquinones to give the expected dienones and dienediols (Scheme 1 and Table 1). Thus the reaction is general. For small-scale reactions (1 mmol of quinone) the best yield of either dienone or dienediol was obtained in dilute

Scheme 1



1 2 3 4

a $R^1 = R^2 = R^3 = R^4 = H$
b $R^1 = Me; R^2 = R^3 = R^4 = H$
c $R^1 = Ph; R^2 = R^3 = R^4 = H$
d $R^1 = R^2 = Me; R^3 = R^4 = H$
e $R^1 = R^3 = Me; R^2 = R^4 = H$
f $R^1 = R^4 = Me; R^2 = R^3 = H$
g $R^1 = R^2 = R^3 = Me; R^4 = H$
h $R^1 = R^2 = R^3 = R^4 = Me$

Table 1. Yields of products from reactions of *p*-benzoquinones with methyllithium.

Quinone^a	MeLi^b mmol	Ether cm^3	THF cm^3	Dienone **2** and **3**	Dienediol **4**	Hydroquinone
1*a*^{c,d}	1.5	24	0	22	18	57
1*a*^{c}	4	2	12	0	29	71
1*a*	1.5	24	0	81	3	16
1*a*	4	2	12	0	79	21
1*b*	1.5	24	0	94^e	2	4
1*b*	4	2	12	0	91	9
1*c*	1.5	24	0	94^f	3	3
1*c*	4	2	12	0	85	15
1*d*	1.5	24	0	96	2	2
1*d*	4	2	12	0	96	4
1*e*	1.5	24	0	80	7	13
1*e*	4	2	12	0	98	2
1*f*	1.5	24	0	97^g	0.5	2
1*f*	4	2	12	0	98	2
1*g*	1.5	24	0	97^h	3	0^i
1*g*	4	2	12	0	100	0^i
1*h*	1.5	24	0	98	2	0^i
1*h*	4	2	12	0	100	0^i

[a] 1 mmol
[b] Added as a solution in ether
[c] Reactions carried out at 22 °C for 5 minutes; all other reactions were done at -78 °C for 60 minutes
[d] 3% of **1***a* was unreacted
[e] 51% **2***b* and 43% **3***b*
[f] 60% **2***c* and 34% **3***c*
[g] 57% **2***f* and 40% **3***f*
[h] 45% **2***g* and 52% **3***g*
[i] None detected by pmr.

solution (25 cm^3). This minimized the formation of hydroquinone which was always obtained in addition to the desired product. Ether was found to be the best solvent for the preparation of the hydroxydienones, as the lithium salt of each hydroxydienone precipitated out of ether solution at -78 °C, reducing the chance for further reaction. Tetrahydrofuran was preferred for the preparation of dienediols as this readily dissolved the lithium salt of the hydroxydienone formed by the initial attack of the alkyllithium on the quinone, allowing the further reaction with another alkyllithium molecule to give the dienediol. Because of electrical repulsion the second alkyllithium adds to the carbonyl group from the opposite side of the ring to the OLi group resulting in predominant formation of the *cis*-diol. The largest amount (10%) of *trans*-diol was obtained in the case of *p*-benzoquinone. The diastereoisomeric dienediols *cis*- **4***a* and *trans*- **4***a* were separated by high pressure liquid chromatography and their structures established by nuclear magnetic resonance spectroscopy. *Cis*- **4***a* had mp 83 °C; ^{1}H nmr (CDCl$_3$)δ : 1.25 (s, 6, (CH_3)$_2$), 3.87 (broad s, 2, (OH)$_2$), 5.74 ppm (s, 4, C$_4H_4$);

^{13}C nmr ($CDCl_3$) δ_C: 28.4 (CH_3), 65.3 (COH), 132.6 ppm (C=C). *Trans*- **4a** had mp 159 °C; ^1H nmr ($CDCl_3$)δ : 1.28 (s, 6, $(CH_3)_2$), 2.98 (broad s, 2, $(OH)_2$), 5.98 ppm (s, 4, C_4H_4); ^{13}C nmr ($CDCl_3$) δ_C: 29.4 (CH_3), 65.3 (COH), 133.9 ppm (C=C). The *cis:trans* isomer ratios were determined from the ^1H nmr of the crude reaction products. When alkyllithium was added to the quinones an intense blue to green colour developed. The colour is attributed to the formation of the semiquinone radical anion, a likely precursor to the hydroquinone. In a small-scale experiment methyllithium solution (4 mmol, 2 cm^3) was added to *p*-benzoquinone (1 mmol) in tetrahydrofuran (24 cm^3) at -78 °C to give 81% of the dienediol and 19% of hydroquinone. Almost the same yield was obtained on a ten-fold scale, but with reduced solvent (30 cm^3), when reverse addition was used. However, when the small-scale reaction was carried out at ambient temperature (22 °C), the major product was the hydroquinone and only 29% of dienediol was obtained. For dienone formation a reduced amount of methyllithium (1.5 mmol) was added to *p*-benzoquinone (1 mmol) in ether (24 cm^3) at -78 °C: 81% dienone, 3% dienediol and 16% hydroquinone were formed. On the ten-fold scale methyllithium solution (13 mmol, 32 cm^3) was added to *p*-benzoquinone in ether (50 cm^3) at -78 °C giving an almost identical product distribution. A small-scale reaction at ambient temperature gave a poor yield of the dienone, with the hydroquinone as the major product.

Reaction of methyllithium at -78 °C with 4-hydroxy-4-methylcyclohexa-2,5-dien-1-one in tetrahydrofuran gives quantitatively 1,4-dimethylcyclohexa-2,5-diene-1,4-diol (88% *cis* and 12% *trans*). Similarly reaction with the dienone methyl ether in ether gives 4-methoxy-1,4-dimethylcyclohexa-2,5-dien-1-ol (isomer ratio = 76:24). Reactions of the hydroxydienone with phenyl-, *n*-butyl- and *tert*-butyllithium give the corresponding dienediols. This is a good method of synthesizing mixed dienediols. Wessely and coworkers have made an extensive study of the action of organometallic compounds on hydroxy- and acetoxy-dienones.[16,17] Except for the possible isolation of 4-methyl-4-phenylcyclohexa-2,5-diene-1,4-diol as an unstable intermediate from the reaction of phenyllithium with 4-acetoxy-4-methylcyclohexa-2,5-dien-1-one they only obtained aromatic compounds, although some of the phenols isolated indicated the intermediacy of dienediols.[17] More recently dienediols have been obtained from dienones substituted with bulky groups in the 2,4 and 6 positions.[18]

Hydroxydienones have previously been obtained by oxidation of phenols[19-23] and by the treatment of arylhydroxylamines with sulfuric acid.[17] These methods generally give poor yields of dienones in a mixture with other compounds and this is particularly so for dienones from compounds with unsubstituted *ortho* positions. Evans, Hoffman and Truesdale introduced an improved method of preparing·hydroxydienones which involves blocking of one carbonyl group of the quinone by reaction with trimethylsilyl cyanide, followed by reaction of the other carbonyl group with an alkyllithium or Grignard reagent.[24] The protecting group is then removed with silver fluoride. Our results show that such protection is unnecessary.

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