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REACTION OF o-BENZOQUINONE BISACETALS WITH ORGANOLITHIUMS. A NOVEL ROUTE TO SUBSTITUTED VERATROLES

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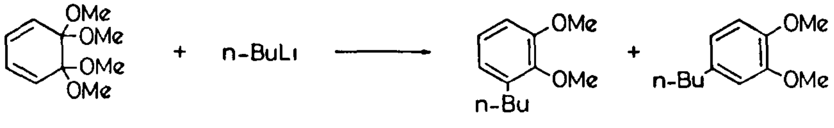
Summary: Substituted veratroles were easily obtained by the reaction of o-benzoquinone bisacetals with organolithiums.

Bisacetal of o-benzoquinone (1) is a stable equivalent of o-benzoquinone and is now available by the anodic oxidation of veratrole in alkaline methanol.[1] We have attempted to use the acetal 1 for organic synthesis and have found that the acetal 1 acts as an umpolung reagent of veratrole.[2] We describe here the synthesis of substituted veratroles by the reaction of 1 with organolithiums.

When dimethylacetal 1a was stirred with n-butyllithium (two equivalents) in diethyl ether under an argon atmosphere at -78°C for 30 min, two regioisomers of n-butylveratrole, 3a and 4a, were produced in 88% yield (3a/4a = 88/12).[4] In the other ethereal solvents, 3a was also selectively obtained (3a/4a = 91/9 in dimethoxyethane, 96/4 in tetrahydrofuran(THF)). Whereas the reaction in hexane at 0°C gave 4a as the major product (3a/4a = 41/59).

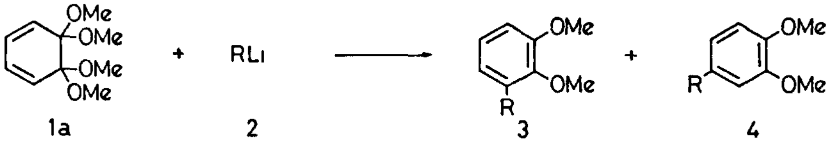


1a 3a 4a

Various reagents other than n-butyllithium were also reactive toward 1a as shown in the table. Not only primary alkyllithiums but also vinyl- and phenyllithium gave the 3-substituted isomers 3 predominantly. On the other hand, both the reactions of secondary and tertiary alkyllithium caused somewhat complicated results; disubstituted arenes 5h and 5i were obtained together with the normal 1 : 1 adducts 3 and 4. Of the products cited in the table, 3c and 3d are known as the dimethyl ethers of urushiol and laccol, respectively.

In the substitution reaction with allyllithium, eugenol methyl ether (4g) was more preferentially produced than its isomer 3g. This fact suggested that the allylic reagent adds by the way of an S_E2' mechanism. To confirm the suggestion, we examined the reaction of prenyllithium (2j). When the reagent 2j was treated with the acetal 1a in THF at -78°C for 30 min, the main product was neither 3j (5%) nor 4j (6%) but an allylic rearrangement compound 6 (b.p.

Table Reaction of o-quinone bis-dimethylacetal (1-a) with organolithiums.*



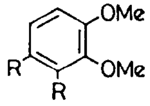
RLi	Temperature (°C)	Time (h)	Yield(%) 3	Yield(%) 4	B.p.(°C/torr) 3	B.p.(°C/torr) 4
(2b) CH_3Li	-78	1	67	9	65/2	83/6
(2c) n-$C_{15}H_{31}Li$	r.t.	16	62	13	31-34.5#	48-50#
(2d) n-$C_{17}H_{35}Li$	r.t.	16	64	11	39-43#	55-58#
(2e) $CH_3CH{=}CHLi$	r.t.	18	32	0	62/0.5	---
(2f) C_6H_5Li	-78	0.5	83	0	44.5-46#	---
(2g) $CH_2{=}CHCH_2Li$	-78**	0.5	13	46	96/4	97/2
(2h) $(CH_3)_2CHLi$@	-78	0.5	26	14	68/6	76/9
(2i) $(CH_3)_3Li$@	-78	0.5	33	41	62/0.5	92/6

* 2.0 - 2.2 equivalents of RLi were used in ether.

\# M.p. (°C)

** THF was used as a solvent.

@ As a byproduct, 3,4-disubstituted veratrole 5 was obtained.

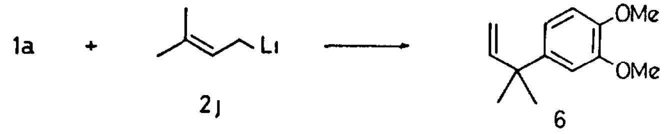


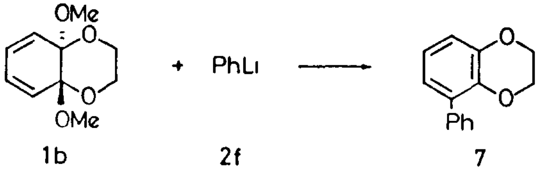
5 h: R=isopropyl (23%)

i: R=tert-butyl (11%)

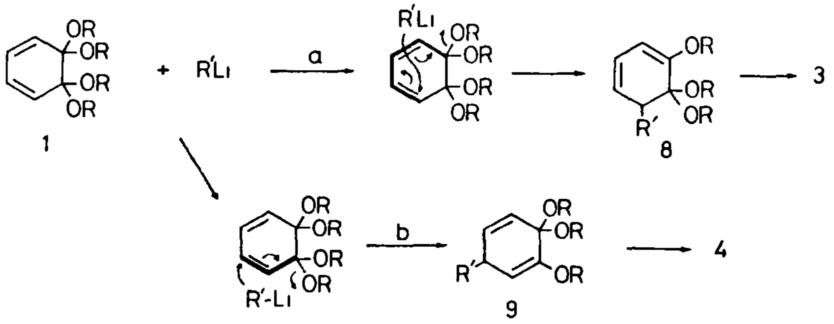
63 - 64°C/0.05torr) (72%).

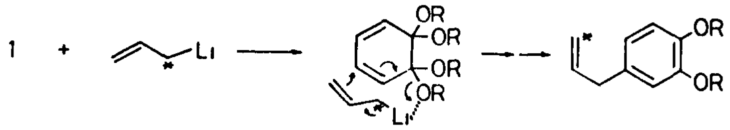
The o-quinone bisacetals other than 1a were also reactive toward organolithiums. For example, a combination of an acetal 1b with phenyllithium 2f (in ether at -78°C) gave 3-phenyl-1,2-ethylenedioxybenzene 7 in a 90% yield.





A possible mechanism of the reaction of 1 with 2 may be as following scheme. In path a, an alkyllithium adds to the terminal carbon of the dienone





acetal moiety (indicated by a thick line)after the complexation with a methoxy group of the substrate. Whereas, in path b, the lithium reagent adds to the enone acetal unit. Both reactions are conjugated addition-elimination reactions through a six-membered cyclic transition state. In the reaction of allyllithium, the terminal allylic carbon of the carbanion must add to the enone acetal system by the S_N2' mechanism. In all cases, the reaction may proceed through cyclohexadienone acetals such as 8 and 9, which lose successively an alcohol molecule to yield the substituted veratroles.

Although the organolithiums could easily undergo the substitution reaction with the acetals 1 as stated above, the other nucleophiles such as Grignard reagents and active methylene compounds gave no fruitful results. The Grignard reagents caused merely the reduction of the acetals to unsubstituted veratroles.

The results described here provide a method to introduce a carbanion into the electron-rich aromatics, veratroles, *via* *o*-quinone bisacetals.

References and Notes

(1) M. Engelhard and W. Luttke, Chem. Ber., 110, 3759 (1977).

(2) It has been known that the *p*-isomer of *o*-benzoquinone bisacetal undergoes the reaction with the nucleophiles such as alcohols, thiols, and phenols under the acidic condition.[3]

(3) B.-T. Groebel, E. Konz, H. Millaner, and R. Pistorius, Synthesis, 605 (1979).

(4) 3a:b.p. 70-70.5°/0.8torr, 4a:b.p. 57°/0.05torr(Lit.[5] 156-157°/28torr). The structures of 3a and 4a were determined by IR, Mass, and ^{1}HNMR spectral analyses. In the NMR spectrum, the coupling constants of aromatic protons were as follows; (3a) J_{ab}=8.6, J_{bc}=8.2, and J_{ac}=1.6 (err.=0.07)Hz, (4a)J_{ab}=8.6, J_{bd}=2.1, and J_{ad}=0.8 (err.=0.1)Hz.

(5) W. J. Horton and E. G Paul, J. Amer. Chem. Soc., 79, 2264 (1957).

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