

Oxygenophilic Organoaluminium-promoted 1,4-Addition of Organolithium Reagents to Quinone Monoacetals

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Complexation of quinone monoacetals with methylaluminium bis-(2,6-di-*t*-butyl-4-methylphenoxide), followed by addition of organolithium reagents, gives products from 1,4-addition of the organolithium reagent to the quinone monoacetal.

Quinone monoacetals serve as useful quinone equivalents^{1,2} since they undergo 1,2-additions with a variety of organolithium species, 1,4-additions with soft nucleophiles, and annelation reactions with 1,4-dipole equivalents. However, there is no general method for 1,4-addition of simple alkyl and aryl groups to quinone monoacetals.³⁻⁵ Reduction of the quinone monoacetal to the corresponding *p*-methoxyphenol by dimethylcuprate³ and some Grignard reagents⁴ precludes standard conjugate reaction conditions for 1,4-addition of alkyl groups to quinone monoacetals.⁵ Yamamoto *et al.*⁶ reported an interesting method for effecting 1,4-addition of alkyl and aryl organolithium reagents to certain cyclic enones.

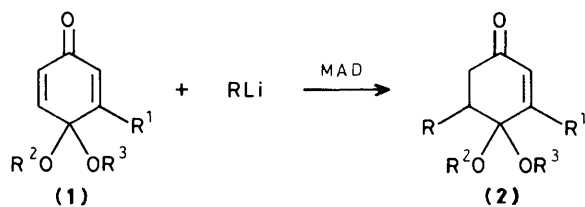
We report here that this synthetic method serves as the first general method for 1,4-addition of organolithium reagents to quinone monoacetals.

Addition of 4,4-dimethoxycyclohexa-2,5-dienone (**1**) to a toluene solution of methylaluminium bis-(2,6-di-*t*-butyl-4-methylphenoxide) (MAD)⁶ at -78°C gave a bright purple solution which faded to light yellow upon dropwise addition of phenyl-lithium. Addition of water to the mixture at -78°C , removal of the aluminium salts by filtration, and chromatography on silica gel gave a white solid (78%) assigned structure (**2a**); i.r. 1690 cm^{-1} ; $^1\text{H n.m.r. } \delta$ 7.25 (s, 5 H), 6.93 (d of d, *J* 10 and 0.8 Hz, 1 H), 6.15 (d, *J* 10 Hz, 1 H), 3.7 (m, 1 H),

Table 1. 1,4-Addition of organolithium reagents to quinone monoacetals (Scheme 1).^a

Entry	R ¹	R ²	R ³	RLi (equiv.)	Product	% Yield
1	H	Me	Me	PhLi (1.0)	(2a)	78 ^b
2	H	Me	Me	Me ₃ SiC≡CLi (2.4)	(2b)	86 ^b
3	H	Me	Me	[CH ₂] ₃ S ₂ CHLi ^g (1.5)	(2c)	70 ^b
4	H	Me	Me	MeLi (1.5)	(2d)	24 ^c
5	H	Me	Me	Bu ⁿ Li (1.5)	(2e)	42 ^{c,d}
6	Me	Me	Me	PhLi (1.7)	(2f)	54 ^{b,e,f}
7	Cl	Me	Me	PhLi (1.7)	(2g)	50 ^c
8	H	Me	SiBu ^t Me ₂	PhLi (1.2)	(2h)	80 ^e
9	H	-CH ₂ CH ₂ -		Bu ⁿ Li (1.0)	(2i)	18 ^c
10	H	-CH ₂ CH ₂ -		Bu ⁿ Li (1.0)	(2h)	35 ^c

^a The organolithium was added to a complex formed from the quinone monoacetal (1 equiv.), 2,6-di-*t*-butyl-4-methylphenol (4 equiv.), and trimethylaluminium (2 equiv.). ^b No 1,2-addition product was detected. ^c Other uncharacterized products were formed. ^d Mixture of 1,4-addition product and phenol isolated. Pure 1,4-addition product isolated by silica gel chromatography after reaction of phenols with Bu^tMe₂SiCl. ^e Mixture of stereoisomers formed which were not separated. ^f The product from addition of PhLi to the 3-position was obtained in *ca.* 27% yield. ^g 1,3-Dithianyl-lithium.



Scheme 1

3.21 (s, 3H), 3.19 (s, 3H), and 2.8 (m, 2H); ^{13}C n.m.r. δ 198.0, 148.4, 139.1, 131.2, 128.9, 128.2, 126.9, 98.0, 49.4, 48.9, 48.5, and 43.0.

Table 1 lists the results from organolithium reactions with quinone monoacetals (Scheme 1) performed essentially as just described. Phenyl-, trimethylsilylethynyl-, and 1,3-dithianyl-lithium gave good yields of the respective 1,4-addition product (entries 1–3). Entry 2 represents the first high-yield 1,4-addition of an acetylenic lithium reagent to a cyclic enone. Although methyl- and n-butyl-lithium gave only modest yields of the respective 1,4-addition products, this does serve as the only method for affecting this conversion. The chemoselectivity of the 1,4-addition to 3-substituted quinone monoacetals was less than expected: the 3-methyl compound (entry 6) gave a mixture of 1,4-addition products and the 3-chloro compound (entry 7) gave only 50% yield of product.

The 1,4-addition of phenyl-lithium proceeded in good yield with the mixed quinone acetal⁷ (entry 8), but the ethylene derivative (entries 9 and 10) offers no advantage over the more readily available dimethyl compound. In fact, the ethylene acetal of benzoquinone appears to give poorer yields in the reaction. The conversion of these 1,4-adducts into the respective phenols by elimination of methanol has not been extensively studied; however, heating (2c) with toluene-*p*-sulphonic acid in dry tetrahydrofuran gave the corresponding phenol in 85% yield.

This comprises the first method for the 1,4-addition of simple alkyl and aryl groups to quinone monoacetals. It is

especially interesting that this procedure⁶ was successful for 1,4-additions to (1) since only 1,2-addition was reported for organolithium additions to cyclohexenone, 4-*t*-butylcyclohexenone, and benzylideneacetone, ketones having relatively unhindered carbonyl groups.⁶ Furthermore, 1,4-additions could not be effected with alkynyl-lithium reagents in the earlier work.⁶ Finally, the acetal oxygen atoms of (1) are at least as basic as a carbonyl oxygen,⁸ and complexation of MAD with the acetal oxygen atoms could have complicated the chemistry. The results reported herein for quinone monoacetals indicate that this chemistry may be useful for effecting similar 1,4-additions with other reactive enones.[†]

We thank the National Institutes of Health for support.

Received, 10th May 1988; Com. 8/01831F

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[†] All new compounds showed spectroscopic properties and exact mass measurements in agreement with the assigned structures. All products were colourless liquids except the following: (2a), m.p. 57.5–58.5 °C; (2c), m.p. 133–134 °C; the phenol derived from (2c), m.p. 121–122 °C.