A Convenient Route to *ortho*-Alkylated Phenols and Quinone Monoacetals

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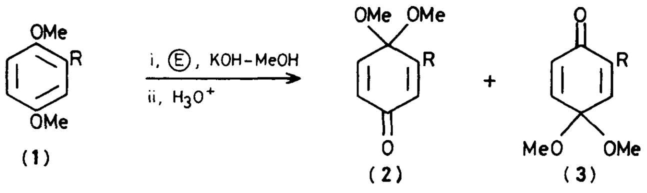
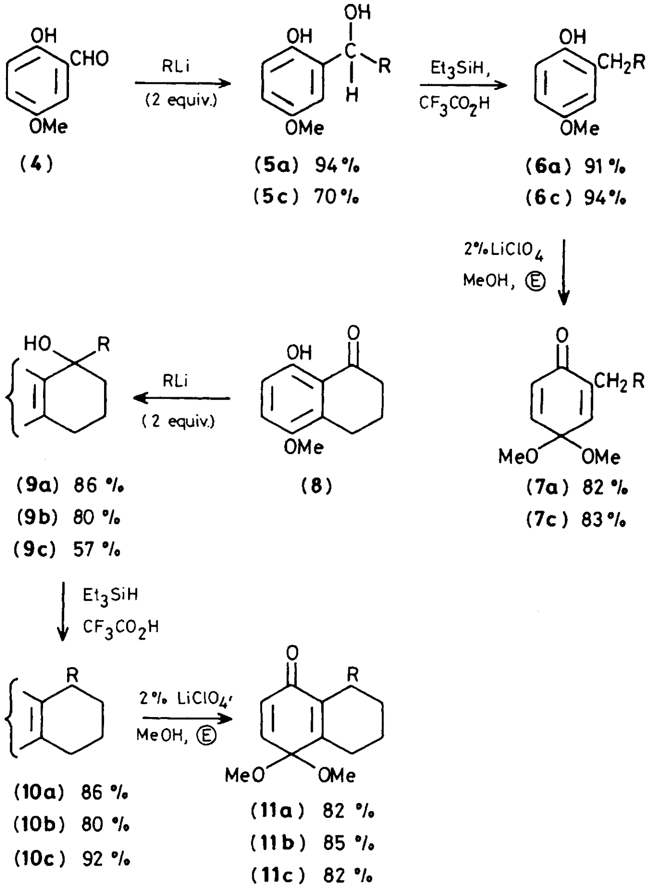
An efficient, regiospecific, convergent route to *o*-alkylated phenols and thence to quinone monoacetals involves reaction of the corresponding 2-hydroxy carbonyl derivative with alkyl-lithium reagents, followed by triethylsilane reduction and electrochemical oxidation.

Quinone monoacetals are established as valuable regiospecific quinone equivalents[1] in organic synthesis, serving as precursors to lignins,[2] various polycyclic quinone natural products,[3] indoles,[4] and isoindoles.[5] A key aspect of the synthetic utility of these intermediates is their regiospecific preparation from readily available starting materials. Quinone monoacetals of type (**2**) are conveniently prepared from regioselective hydrolysis of quinone bisacetals[1,6] [*e.g.* (**1**; R = Me) affords (**2**) (85%) and (**3**) (15%)].† However, the regioisomeric dimethylacetals of structure (**3**)† are available only from the oxidation of the corresponding phenol.[6—8] Thus, a convenient route to monoacetals of this orientation requires a general route to the respective phenol.

In principle, the required phenols can be prepared by oxidation of *p*-methoxybenzaldehydes, *i.e.* Claisen rearrangement of *p*-methoxy allyl ethers,[8] or the *o*-alkylation of *p*-methoxyphenols;[9] however, these routes are inappropriate or inconvenient for many systems. Since many *o*-hydroxybenzaldehydes[10] and 1-acyl-2,5-dimethoxyaromatic derivatives[11] are readily available, the use of these substrates for quinone monoacetal synthesis was examined. We report



Ⓔ = Electric current



a; R = Me
b; R = CH_2Me
c; R = Bu^t

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† All compounds reported herein showed i.r., ^1H n.m.r., and ^{13}C n.m.r. spectra in agreement with those of assigned structures. Except for the following compounds, the products were obtained as colourless oils: (**5a**) m.p. 70.5—72 °C; (**5c**) m.p. 102—103 °C; (**6c**) m.p. 77.5—78.5 °C; (**10c**) m.p. 91.5—93.5 °C.

herein a convergent, regiospecific, high-yield route to the above-mentioned quinone monoacetals from readily available starting materials.

The requisite *p*-methoxyphenols (**5**)† were prepared by treating commercially available (**4**) at −78 °C with two equivalents of alkyl-lithium reagent,[12a,b] followed by reduction of the resulting alcohols with triethylsilane in trifluoroacetic acid. The second class of *p*-methoxyphenols was prepared by regiospecific demethylation (BCl_3, −78 °C) of the dimethyl ether of (**8**),[11]† followed by functionalization and reduction as described above. A number of methods have been employed for the oxidation[6—8] of *p*-methoxyphenols to quinone monoacetals. While anodic oxidation of the *p*-methoxyphenol in methanol using lithium perchlorate as supporting electrolyte at a platinum anode was reported more than ten years ago,[13] it has not found general use. We observed that this constant current oxidation of the *p*-methoxyphenols not only furnished the quinone monoacetals in excellent yield without the use of toxic or expensive oxidants but also proceeds with near unit current efficiency.

This chemistry serves as a convergent method for the regiospecific synthesis of *p*-methoxyphenols and quinone monoacetals in good yields, nicely complementing existing routes. Furthermore, these compounds have the side chain oriented for intramolecular reaction with the carbonyl group of quinone monoacetals, offering considerable potential for the synthesis of fused heterocyclic and carbocyclic systems.

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