

Anodic Oxidation as a General Route to Benzoquinone Bis- and Mono-acetals

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Summary Oxidation of a wide range of substituted 1,4-dimethoxybenzenes in methanolic potassium hydroxide at a platinum anode allows easy access to benzoquinone bisacetals and, by hydrolysis of the latter compounds, to the respective monoacetals.

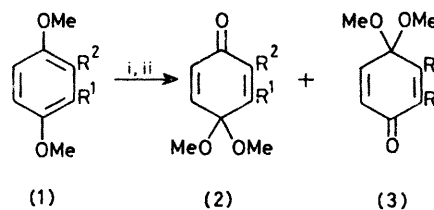
QUINONE bisacetals¹ and monoacetals² have recently found extensive use in organic synthesis. Weinberg and Belleau³ had previously reported that anodic oxidation of 1,4-dimethoxybenzene in methanolic potassium hydroxide at a platinum gauze electrode afforded the benzoquinone bisacetal in good yield. Owing to our interest in use of these groups, we investigated the generality of the anodic oxidation for substituted 1,4-dimethoxybenzenes (**1**) and the regioselectivity of the monohydrolysis of the bisacetals to monoacetals.⁴ The accessibility of the latter compounds has depended almost entirely on the availability of the requisite *p*-methoxyphenol.⁵ We report here on the generality and limitations of these two reactions. Since electrolyses in methanol-1% potassium hydroxide solution can be routinely performed on 30–50 g quantities in a single-cell apparatus without accurate potential control, we have conducted these studies under these synthetically expedient conditions;¹⁰ Table I gives the results. Whereas many substituents are quite inert to the anodic oxidation conditions (*i.e.*, Br, Me, SiMe₃, -CH₂CH=CH₂, and acetal) illustrating the general nature of the process, readily oxidized or reduced linkages [-C(O)H, -NH₂, -CH₂CH₂C(O)NH₂, -NHC(O)Me, -CH₂CO₂Me, and -CH₂CH₂CH₂OH] lower the yield of bisacetal and complicate the product mixture. However, the oxidizable

TABLE I. Anodic oxidations of 2-substituted 1,4-dimethoxybenzenes^a

Entry	1,4-Dimethoxybenzene 2-substituent	Yield bisacetal ^b /%	Current efficiency /%
1	Br (ref. 1a, c)	74	45
2	Me	80	74
3	SiMe ₃	93	39
4	(1,3-Dioxolan-2-yl)	88	34
5	CHMe(OMe)	92	43
6	CH ₂ CH=CH ₂	81	71

^a Electrolyses were performed on a 3–30 g scale essentially as described in ref. 1c. ^b Except for entry 1, all the bisacetals were oils at room temperature which were purified by distillation or recrystallization.

hydroxy and aldehyde functionalities can be protected as ethers and acetals, respectively. In general, groups having electron pairs or relatively acidic hydrogens at the benzylic positions lead to complications.†



i, Electrolysis, MeOH, KOH; ii, H₃O⁺

† Changing the solvent system and the use of a divided cell may lessen some problems associated with systems not undergoing clean oxidation. This will be studied and reported in our full manuscript.

TABLE 2. Hydrolysis of bisacetals to monoacetals

Entry	(1, R ² = H) R ¹	Yield /%	Ratio		Hydrolysis conditions ^d
			(2) (m.p./°C)	(3)	
1	Br	85	96 ^c	4 ^c	e
2	Me	76 ^a	84 ^c	16 ^c	f
3	OMe	66 ^a	>95 (62.0—64.5) ¹		g
4	SMe	60 ^b	>95 (85—86)		h
5	COPh	42	>95 (74.5—75.0)		i
6	SiMe ₃	70 ^a	44	(35—36)	56 ^c j
7	CHMe(OMe)	77 ^a	73	(34.5—35.5)	27 ^c k

^a Overall yield for electrolysis and hydrolysis. ^b Overall yield from reaction of the 2-lithiobisacetal and dimethyl disulphide followed by hydrolysis. ^c Compound is an oil. ^d Hydrolyses are conveniently monitored on a 25 ft × $\frac{1}{8}$ in column of 5% SE-30 on 60/80 Chromosorb G at column temperatures in the range 160—185 °C. ^e 2:1 acetone-2% HOAc, 4 h, room temp. ^f 4:1 acetone-2% HOAc, 0.5 h, room temp. ^g 2:1 acetone-2% HOAc, 0.75 h, room temp. ^h 1:1 acetone-2% HOAc, 0 °C, 10 min. ⁱ 30:1 wet tetrahydrofuran-CF₃CO₂H, 7 h, room temp. ^j 4:1 acetone-2% HOAc, 25 °C, 0.5 h. ^k 2:1 acetone-2% HOAc, 0.5 h, room temp. ¹ Lit. m.p. 63.5—64.5 °C (ref. 2c).

In those instances in which the anodic oxidations proceed cleanly, the yields are very high and the isolated yields usually reflect losses attendant on removing minor impurities. Thus, in studying the monohydrolysis of the bisacetals we have used the crude electrolysis product, the monoacetals being obtained in gram quantities by silica gel chromatography. The structures of the monohydrolysis products could usually be assigned from the chemical shifts and couplings of the vinyl protons in the n.m.r. spectrum. As illustrated in Table 2 many systems undergo quite selective monohydrolysis, the acetal most distant from the 2-substituent being selectively or exclusively hydrolysed. Conspicuous exceptions are entries 6 and 7. The trimethylsilyl group is especially interesting in showing virtually no selectivity in the monohydrolysis.

In summary, anodic oxidation is a conveniently available procedure for large-scale preparations of a variety of quinone bisacetals. Monohydrolysis of these bisacetals often occurs with high regioselectivity to afford synthetically valuable monoacetals.†

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† Detailed experimental procedures will be furnished upon request. All new compounds showed acceptable combustion analysis or exact mass measurement.

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³ B. Belleau and N. L. Weinberg, *J. Amer. Chem. Soc.*, 1963, **85**, 2525; For a recent discussion of anodic oxidation, see S. Ross, M. Finkelstein, and E. J. Rudd, 'Anodic Oxidation,' Academic Press, New York, 1975.

⁴ The hydrolysis of the unsubstituted benzoquinone bisacetal to its monoacetal has been noted by several groups; see ref. 2c for a compilation. The hydrolysis of 1,4-naphthoquinone bisacetals has been briefly studied: M. J. Manning, D. R. Henton, and J. S. Swenton, *Tetrahedron Letters*, 1977, 1679.

⁷ For leading references for preparations of quinone monoacetals, see G. Büchi, P. Chu, A. Hoppmann, C. Mak, and A. Pearce, *J. Org. Chem.*, 1978, **43**, 3983; A. McKillop, D. H. Perry, M. Edwards, S. Antus, L. Farkas, M. Nogradi, and E. C. Taylor, *ibid.*, 1976, **41**, 282.