Electrochemical Oxidations of Benzo[*b*]thiophens: A Simple Route to Benzo[*b*]thiophen-4,7-quinone Bis- and Mono-acetals

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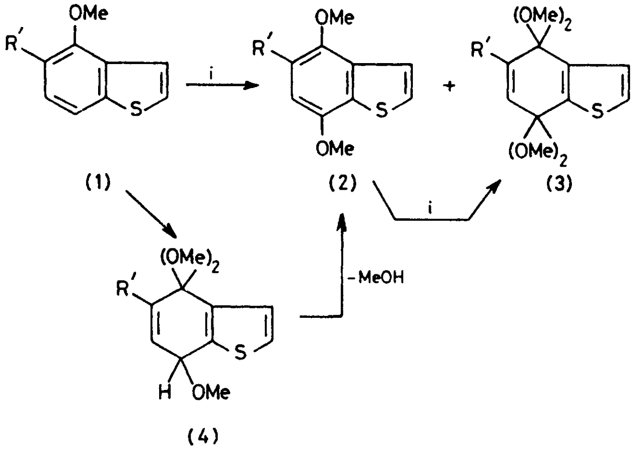
Summary Anodic oxidation of 4-methoxybenzo[*b*]thiophens is temperature dependent, proceeding at elevated temperature *via* a four-electron process to give benzo[*b*]thiophen-4,7-quinone bisacetals in excellent yield.

Recent interest in a naturally derived 5,6-disubstituted benzo[*b*]thiophen-4,7-quinone[1] and the absence of a simple route to this substituted quinone[2] system inspired anodic oxidation studies of the conveniently available 4-methoxybenzo[*b*]thiophens.[3] Electrochemical oxidation[4] of these latter compounds could afford a direct route to the quinone bisacetals and thence to their monoacetals, facilitating a regiospecific synthesis of the required 5,6-disubstituted derivatives. We report here the first anodic oxidation studies of benzo[*b*]thiophens, the temperature dependence of the products, and the utility of these reactions for preparation of the 4,7-quinones and their bis- and monoacetals.

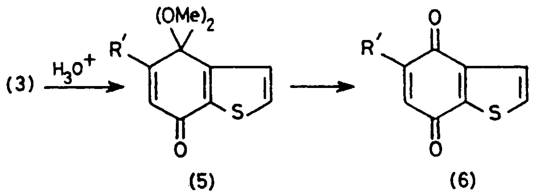
Anodic oxidation of (**1a**) in 1% methanolic potassium hydroxide (Pt gauze anode, Pt sheet cathode)[5] in a single-cell apparatus at 20 °C afforded (**2a**) (21%) and (**3a**) (36%) on work-up (Scheme). Interestingly, the (**2a**):(**3a**) ratio was markedly temperature dependent. At *ca.* −30 °C, (**2a**) predominated [(**2a**):(**3a**) = 46:16], and in refluxing methanol, the reaction showed an isosbestic point (247 nm) with (**3a**) being formed exclusively (78% isolated yield). This remarkable temperature effect represents a 'one-pot' four-electron oxidation of (**1a**) to the protected quinone in high yield.



a; R' = H
b; R' = Br
c; R' = Me

Scheme. i, electrolysis, KOH–MeOH.

Similarly, (**1b**) was electrolysed in a divided cell using 1% methanolic potassium hydroxide to afford (**3b**) in 60% recrystallized yield (light petroleum). The yield for this particular reaction was markedly improved (79% by direct crystallization) when the solvent was 1% methanolic sodium methoxide. The 5-methyl compound (**1c**) was reluctant to undergo the four-electron oxidation even in refluxing methanol. However, when (**1c**) was electrolysed, the crude electrolysis mixture concentrated at *ca.* 50 °C, and this material further electrolysed in 1% methanolic potassium hydroxide, (**3c**) was obtained in 85% yield. Furthermore, careful work-up of the anodic oxidation of (**1c**) afforded an oil (> 95% pure) which is assigned as (**4c**) on the basis of its n.m.r. spectrum: δ 7·11 (ABq, *J* 5 Hz, Δν 17 Hz, 2H), 6·08 (sym. m, 1H), 5·00 (sym. m, 1H), 3·10 (s, 3H), 2·90 (s, 3H), 2·85 (s, 3H), and 1·80 (t, *J* 1·5 Hz, 3H). These results, together with the temperature dependence of the product ratio observed for (**1a**), suggest that the overall four-electron oxidation derives from a two-electron oxidation to yield (**4**) followed by loss of methanol to afford (**2**), and further oxidation of (**2**) to (**3**). (A temperature dependence of an initial substitution *vs.* addition process could also be involved.)



The bisacetals (**3a**—**c**) were hydrolysed to their respective quinones† in high isolated yield (78, 77, and 95%, respectively), while under milder conditions (1:1:1 acetone–acetic acid–water, *ca.* 25 °C, 15 min) monohydrolysis occurred. Thus, (**3b**) and (**3c**) afforded (**5b**) (92%) and (**5c**) (95%) regiospecifically, while (**3a**) was hydrolysed with little regioselectivity to a mixture of monoacetals (94%, ratio 59:41). The structural assignments for (**5b**) and (**5c**) were made on the basis of the n.m.r. splitting of the tertiary hydrogen of the alcohols obtained from sodium borohydride reduction[6] of the respective monoacetals.‡

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† Hydrolysis to quinones: (**6a**) (1:15:15 trifluoroacetic acid–acetone–water, 25 °C, 0·5 h); (**6b**) and (**6c**) (1:1 acetone–6 N hydrochloric acid, 45 °C, 0·5 h).

‡ All new compounds gave acceptable combustion analyses or exact mass measurements: m.p.s are: (**1a**), oil; (**1b**), 53—54 °C; (**1c**), oil; (**2a**), 90·5—92 °C; (**2c**), 56—57 °C; (**3a**), 45—46 °C; (**3b**), 118—119 °C; (**3c**), 86—87 °C; (**5b**), 102—103 °C; (**5c**), 85—86 °C; (**6a**), 128—130 °C (lit.[2b] 130—131 °C); (**6b**), 114—117 °C; (**6c**), 115—117 °C (lit.[2a] 120—121 °C).

The electrochemical oxidation of these 4-methoxybenzo[*b*]thiophens serves as a high-yield route to the related quinones and the bis- and mono-acetals, circumventing conventional multistep methods.

We thank the National Science Foundation for support.

(*Received*, 18*th September* 1979; *Com.* 1007.)

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