Selective Demethylation of Di- and Tri-methoxyanthraquinones *via* Aryloxydifluoroboron Chelates. Synthesis of 4-Hydroxy-1,5-dimethoxyanthraquinone and 1,4-Dihydroxy-5-methoxyanthraquinone

Peter N. Preston,[a] **Thomas Winwick,**[a] **and John O. Morley**[b]

[a] *Department of Chemistry, Heriot-Watt University, Riccarton, Currie, Edinburgh EH14 4AS, U.K.*
[b] *I.C.I. plc, Organics Division, Blackley, Manchester M9 3DA, U.K.*

Methoxyanthraquinone derivatives react with boron trifluoride–diethyl ether to give mono- and bis-difluoroboron chelates which, in methanol, are converted into hydroxyanthraquinones; an extension of this method is described for the synthesis of 2-hydroxy-2′,4,4′-trimethoxybenzophenone.

Selective $AlCl_3$-induced demethylation is achieved in dimethoxyarenes in which an acyl function is *ortho* to a methoxy-group [*e.g.* 1,2-$(MeO)_2$,3-$(COEt)C_6H_3$, $AlCl_3$, 0 °C gives 1-MeO, 2-HO,3-$(COEt)C_6H_3$ (75%)].[1] Recently we described the transformation of dimethoxyanthracenones (**1a**, **b**) into 4-methoxy derivatives (**1c**, **d**) *via* isolatable aryloxydifluoroboron chelates [*e.g.* (**2**)].[2] A notable feature in the sequence is the selective demethylation achieved at the methoxy-group in proximity to the carbonyl function [*e.g.* (**1a**) → (**2**) → (**1e**); conditions for (**2**) → (**1e**): MeOH, 20 °C, 1 h]. We now desdescribe how isolatable mono- and bis-difluoroboron chelates derived from di- and tri-methoxyanthraquinones can be used to provide simple syntheses of hydroxymethoxyanthraquinones.

Treatment of 1,4-, 1,8-, 1,2-, and 1,5-dimethoxyanthraquinones† with $BF_3{\cdot}Et_2O$ (2—4 mol. equiv.) in benzene (for 1,4-, 1,8-, and 1,2-) or *o*-dichlorobenzene (for 1,5-) under reflux gave difluoroboron chelates‡ (>90%) akin to (**2**) [*e.g.* (**3**)]. These complexes were converted in methanol (50—60 °C, 10 min) into anthraquinone derivatives [1-OH,4-MeO[3] (93%), 1-OH,8-MeO[4] (90%), 1-OH,2-MeO[5] (93%), and 1-OH,-5-MeO[4] (92%) respectively]. These syntheses of hydroxymethoxyanthraquinones provide valuable alternatives to the

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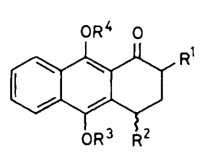
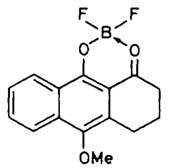
† Dimethoxyanthraquinones were prepared in high yield (80—87%) by methylation (using *p*-$MeC_6H_4SO_3Me$–Na_2CO_3–*o*-Cl_2-C_6H_4) of appropriate dihydroxyanthraquinones.

‡ Generally, the difluoroboron chelates are coloured solids [*e.g.* that from the 1,4-$(MeO)_2$-derivative is brown, m.p. 268 °C (decomp.), that from the 1,8-$(MeO)_2$-compound is red, m.p. 270 °C (decomp.), and 1,4,5-$(MeO)_3$-anthraquinone gives a red-brown mono-chelate, m.p. 286 °C (decomp.) and a blue-black bis-chelate, m.p. > 220 °C (decomp.)]. They are mostly stable in air but unstable in polar solvents. They were transformed into hydroxymethoxyanthraquinones before purification, with the exception of (**3**) which gave satisfactory analytical data [i.r. (KBr) 1670, 1615, 1580, 1560, 1522, 1453, 1285, 1252, 1052, and 750 cm^{-1}; u.v., λ_{max} ($CHCl_3$) 253, 275, and 410 nm].



	R^1	R^2	R^3	R^4
(1) a,	H	H	Me	Me
b,	Me	H	Me	Me
c,	H	MeO	Me	H
d,	Me	MeO	Me	H
e,	H	H	Me	H



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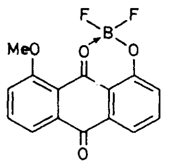

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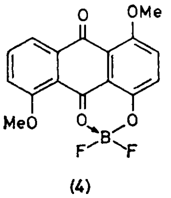

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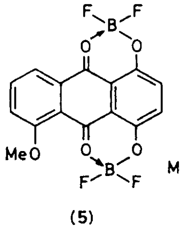

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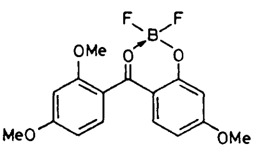

(6)

H_2SO_4-promoted demethylation of dimethoxy-derivatives[4]§ and the selective methylation of hydroxyanthraquinones by diazomethane.[6]

The selectivity of demethylation can be controlled in a subtle manner on 1,4,5-trimethoxyanthraquinone. Decomposition (MeOH, 50 °C, 10 min) of the mono-difluoroboron chelate (**4**)‡ [from 1,4,5-trimethoxyanthraquinone, $BF_3\cdot Et_2O$ (4 mol. equiv.), C_6H_6, reflux, 0.5 h, 89%] gave 4-hydroxy-1,5-dimethoxyanthraquinone (94%).[7] Treatment (MeOH, 50 °C, 10 min), though, of the bis-difluoroboron chelate (**5**)‡ [from 1,4,5-trimethoxyanthraquinone, $BF_3\cdot Et_2O$ (8 mol. equiv.), PhMe, reflux, 3 h] gave 1,4-dihydroxy-5-methoxyanthraquinone (86%). It may be noted that bis-diacetoxy(anthraquinonato)boron chelates [from 1,4,5-trihydroxyanthraquinone, $B(OAc)_3$] may form in a 1,4-chelate arrangement [*cf.* (**5**)] (thermodynamic control) or in a 1,5-manner (kinetic control).[8]

An important feature of the method is the selectivity achieved by preliminary isolation of the difluoroboron chelate. Whereas a mixure of products is obtained from $AlCl_3$-induced cleavage of 2,2′,4,4′-tetramethoxybenzophenone,[1e] the difluoroboron chelate (**6**) {from $[2,4\text{-}(MeO)_2C_6H_3]_2CO$, $BF_3\cdot Et_2O$, PhMe, reflux, 86% yield, m.p. 160—161 °C} in methanol (50 °C, 10 min) is converted into 2-hydroxy-2′,4,4′-trimethoxybenzophenone (m.p. 108—109 °C, 95% yield).

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§ In our hands the demethylation[4] of 1,5-dimethoxyanthraquinone to 1-hydroxy-5-methoxyanthraquinone (98% H_2SO_4, 100 °C, 2 h) proceeded satisfactorily (79%) but we could not repeat the recommended[4] procedure (60% H_2SO_4, 100 °C, 1.5 h) for the synthesis of 1-hydroxy-8-methoxyanthraquinone from the 1,8-dimethoxy-derivative.