

STUDIES ON QUINONES. XIV¹. OXIDATIVE DEMETHYLATION OF HYDROQUINONES
DIMETHYLEETHERS WITH NITRIC ACID- IMPREGNATED MANGANESE DIOXIDE

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Abstract: The oxidative cleavage of several hydroquinones dimethylethers with nitric acid- impregnated manganese dioxide, in methylene chloride solution at room temperature, gave the corresponding quinones in 76-95% yield.

The oxidative demethylation of hydroquinones dimethylethers to afford the corresponding quinone is a well known reaction in the field of synthetic quinone chemistry². This transformation, which is especially useful in the synthesis of complex quinones, has been achieved using a variety of oxidizing agents such as nitric acid³, argentic oxide⁴, and ceric ammonium nitrate⁵. More recently, pyridinium chlorocromate has been reported as a deprotecting reagent for hydroquinones silylethers⁶.

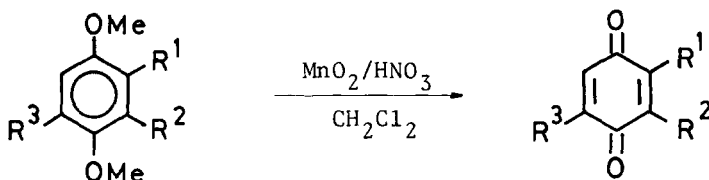
In a previous communication we described that nitric acid-impregnated manganese dioxide induces oxidative demethylation on 4-methoxyphenol and 1,4-dimethoxybenzene to give 1,4-benzoquinone in high yields⁷. Now we wish to report that this reagent can efficiently cleave substituted hydroquinones dimethylethers into the parent quinones, in this way emerging as a new and alternative reagent for oxidative demethylation.

The substrates required for our purpose were prepared by standard methods⁸. The oxidant efficiency of the impregnated reagent, which was obtained as previously reported⁷, was examined in several samples heated in a vacuum oven at 40°C by using 1,4-dimethoxybenzene as the substrate. The reactions conducted in methylene chloride solutions showed high yields in 1,4-benzoquinone (80-85%) for those samples dried for 30 and 60 minutes (weight loss ~ 15 and 30% respectively). Accordingly, oxidative demethylation of dimethylethers was carried out with the active reagent and reactions were monitored by tlc in order to determine the optimal conditions.

In a typical experiment, a mixture of 1,4-dimethoxy-2,3,5-trimethylbenzene (**5**; 1.1 mmoles), and impregnated manganese dioxide (1.77 g) in methylene chloride was shaken vigorously for 90 minutes at room temperature. The suspension was filtered (Celite) and the filter cake was washed with methylene chloride. The filtered solution was evaporated in vacuo to give a liquid residue which was purified by column chromatography on silica gel (eluant 50% benzene-petroleum ether). The isolated yield of 2,3,5-trimethyl-1,4-benzoquinone (**12**) was 76%.

In a similar manner, oxidative demethylation of hydroquinones dimethylethers **1-7** was carried out; the results are summarized in Table 1.

Table 1. Oxidative demethylation of hydroquinones dimethylethers **1-7** with acid-impregnated manganese dioxide.



Substrate	R ¹	R ²	R ³	Quinone ⁹	Yield (%) ^a
1	H	H	H	8	85
2	Me	H	H	9	77
3	Et	H	H	10	76
4	Cl	H	H	11	- ^b
5	Me	Me	Me	12	76
6	(CH=CH) ₂		H	13	95
7	CH(Ph)O-CH ₂ -CH ₂		H	14	78

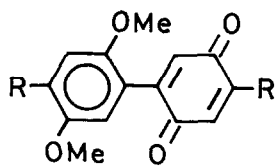
a. Established by ¹H-NMR on crude products (**8, 9, 10, 13, 14**) and on isolated compound (**12**). b. No reaction.

Interestingly, when the oxidative demethylation of **2** was done under slow shaking conditions, arylquinone **15** was obtained as the main product [39%; mp 147-149°C (ref.¹⁰ mp 150-152°C)], and small amounts of toluquinone (**9**) were detected by tlc. In addition, 1,2,4-trimethoxybenzene (**17**) under the same conditions produced arylquinone **16** as the sole product [57%; mp 150-151°C; IR(KBr): 1660, 1640 cm⁻¹; ¹H-NMR (100 MHz, CDCl₃): δ 3.80(s, 3H), 3.87(s, 3H), 3.88(s, 3H), 4.40(s, 3H), 6.05(s, 1H), 6.62(s, 1H), 6.80(s, 1H), 6.85(s, 1H)]. However,

when oxidative cleavage of **17** was attempted under vigorous shaking conditions, arylquinone **16** was formed in 24% yield whereas 5-nitro-1,2,4-trimethoxybenzene (**18**)¹⁰ was obtained as the major product [57%, mp 126-128°C (ref.¹¹ mp 128-130°C)].

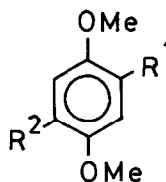
These findings and the lack of reactivity of the hydroquinone dimethyl ether **4**, which contains an electron-withdrawing group, indicate that oxidative demethylation with acid-impregnated manganese dioxide is controlled by stirring and the nature of the substituents on the substrate.

Considering that our reagent contains nitric acid, which also has oxidative demethylation properties³, we investigated the behaviour of this acid supported on a nonoxidant solid. Accordingly, we studied the reaction of 1,4-dimethoxybenzene (**1**) with nitric acid-impregnated silica gel. This new impregnated reagent was prepared by treatment of silica gel (column chromatography grade; 0.05-0.2 mm, Merck) with 4N nitric acid, according to the method used for the title reagent⁷. A mixture of 1,4-dimethoxybenzene (**1**) with the freshly prepared impregnated reagent, in methylene chloride, was shaken for five minutes at room temperature. Filtration and removal of the solvent gave 1,4-dimethoxy-2-nitrobenzene [**19**, mp 68-70°C (ref¹² mp 72°C)] in 98% yield. No trace of quinone **8** was detected by tlc or ¹H-nmr.



15. R = Me

16. R = OMe



	R ¹	R ²
17	OMe	H
18	OMe	NO ₂
19	NO ₂	H

This result implies that the oxidant nature of the support determines the oxidative cleavage properties of the nitric acid-impregnated manganese dioxide. Additional work is necessary in order to establish the mechanism of this reaction.

Further investigation on deprotection of other hydroquinones dimethyl ethers with acid-impregnated dioxide, and the potential applications of nitric acid impregnated-silica gel as a nitration agent of arenes, are currently under study.

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References and Notes

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