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$Mn(OAc)_3$—an efficient oxidant for regeneration of DDQ: deprotection of *p*-methoxy benzyl ethers[†]

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Abstract

$Mn(OAc)_3$ has been successfully developed as a new oxidant for the regeneration of DDQ from HDDQ. This DDQ regeneration technique, making use of 3 equiv. of $Mn(OAc)_3$–DDQ (10 mol%), was applied to the deprotection of *p*-methoxy benzyl (PMB) ethers. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: oxidative regeneration; deprotection; manganese triacetate; catalytic; 2,3-dichloro-5,6-dicyanoquinone.

Quinones[1] of high oxidation potential are versatile reagents; DDQ, particularly with its oxidation ability and relative stability, is one of the most used reagents to perform several organic transformations such as dehydrogenation,[2] oxidation of allylic and benzylic alcohols[3] and ethers, oxidative removal of Cr,[4] Fe,[5] Mn[6] arene complexes, etc. DDQ[7] also has been used for the deprotection[8] of several protecting groups from alcohols such as allyl, *p*-methoxy benzyl (PMB) and di-methoxy benzyl (DMB) groups. Of the several reagents available for removal of the PMB group, DDQ has a prominent place, since the reaction conditions are nearly neutral. However, the two main problems associated with DDQ are the cost and difficulty of removing HDDQ, the by-product. To circumvent both these problems 'regeneration' of DDQ is an interesting alternative, which resulted in the development of reagents such as $HClO_4$, HIO_4,[9] HNO_3[10] and $FeCl_3$,[11] most of which are acidic, and are hence incompatible with acid sensitive functional groups. Since DDQ is an expensive reagent, used in stoichiometric quantities and removal of the resulting HDDQ is cumbersome, it is essential to develop mild and efficient methods for regeneration of DDQ. Herein, we report $Mn(OAc)_3$ (3 equiv.) as a mild oxidant for the regeneration of DDQ and demonstrate the usefulness of reagent system for the deprotection of PMB ethers (Eq. (1)).

$$\text{ROPMB} \xrightarrow[\text{(10 mol\%) DDQ, CH}_2\text{Cl}_2\text{, rt}]{\text{3 equiv. Mn(OAc)}_3} \text{ROH} \qquad (1)$$

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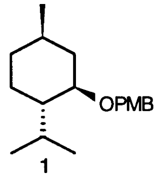
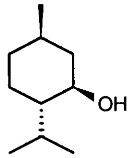
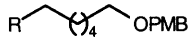
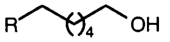
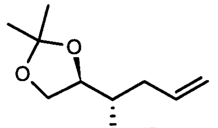
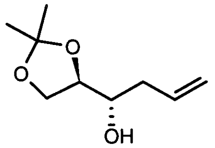
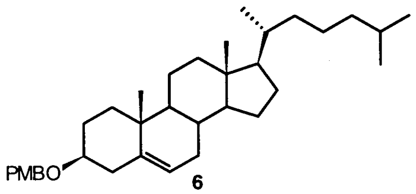
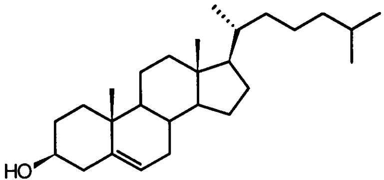
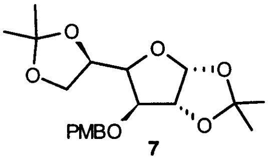
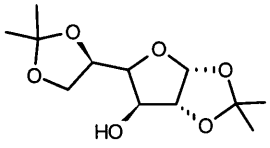
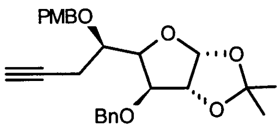
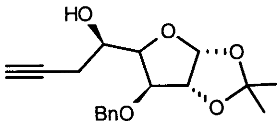
Mild and selective protocols for unmasking protecting groups play a prominent role in the synthesis of complex natural products. PMB ethers are one of the protecting groups which are usually removed oxidatively by DDQ.[8] $Mn(OAc)_3$,[12] is a powerful and neutral one electron oxidant which was chosen as an oxidant in the present study for the regeneration of DDQ from HDDQ, thereby avoiding the use of DDQ in stoichiometric quantity.

Accordingly, PMB ether **1** (entry 1; Table 1) was treated with 10 mol% of DDQ–3 equiv. $Mn(OAc)_3$ in CH_2Cl_2 at room temperature to afford **1a** in 75% yield, whose optical integrity was intact. The study was then extended to PMB ethers **2**, **3** and **4** having TBS, THP and benzoyl

Table 1
$Mn(OAc)_3$–DDQ mediated deprotection of PMB ethers

Entry No.	Starting materials	Time(h)	Products (isolated yields)
1.	 **1**	8.5	 **1a** (75%)
			
2.	**2** R = OTBS	9	**2a** R = OTBS (83%)
3.	**3** R = OTHP	10	**3a** R = OTHP (90%)
4.	**4** R = OBz	10	**4a** R = OBz (79%)
5.	 **5**	10.5	 **5a** (86%)
6.	 **6**	6	 **6a** (71%)
7.	 **7**	12.5	 **7a** (81%)
8.	 **8**	24	 **8a** (61%)

protective groups (entries 2, 3 and 4) to give the alcohols **2a** (83%), **3a** (90%) and **4a** (79%), respectively. These examples demonstrated that acid sensitive groups TBS and THP, as well as base sensitive benzoyl groups are completely compatible with the present conditions. Homoallylic ether **5** (entry 5) and steroidal ether **6** (entry 6) gave the expected alcohols **5a** (86%) and **6a** (71%) in 10.5 and 6 h, respectively. Further, treatment of sugar ether **7** (entry 7) and propargylic ether **8** (entry 8) afforded the respective alcohols **7a** (81%) and **8a** (61%). All the products formed were characterised from the spectroscopic data.

The plausible mechanism[12] for the regeneration of DDQ from HDDQ is shown in the Fig. 1. Accordingly, electrons transfer from the Mn(III) complex **B** by the loss of Mn(II) results in the formation of quinone.

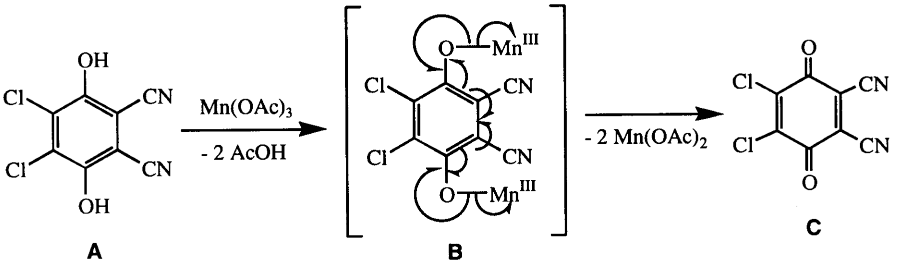


Figure 1.

Thus, the present study demonstrated an efficient use of $Mn(OAc)_3$ as an oxidant for the 'regeneration' of DDQ which is used in 10 mol% for the removal of PMB ethers. The reaction conditions are: (a) compatible with both acid and base sensitive groups, (b) optical integrity is retained and (c) homoallylic and propargylic systems were unaffected. Thus, the present protocol demonstrating the use of $Mn(OAc)_3$–DDQ for the removal of PMB ethers of aliphatic, terpenoidal, steroidal and sugar substrates, should find use in organic synthesis. The use of the $Mn(OAc)_3$–DDQ reagent system for other synthetic transformations is in progress.

Typical experimental procedure: A mixture of **1** (0.276 g, 1 mmol), $Mn(OAc)_3 \cdot 2H_2O$ (0.804 g, 3 mmol) and DDQ (0.022 g, 0.1 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 8.5 h. The reaction mixture was treated with aq. $NaHCO_3$ solution (10 mL) and the organic layer was separated. It was washed with water (2×10 mL), brine (10 mL), dried (Na_2SO_4), evaporated and the residue purified by column chromatography (Silica gel, 1:10 ethyl acetate:petroleum ether) to afford **1a** (0.117 g) in 75% yield as a solid, whose spectroscopic data was comparable with a known compound.

Spectral data for selected compounds: (^1H NMR, 200 MHz, $CDCl_3$, TMS):
1: $[\alpha]_D$ −20.86 (*c* 1.5, $CHCl_3$); δ 0.8 (d, 3H, *J* 3.48 Hz), 0.85–1.10 (m, 11H), 1.57–1.70 (m, 2H), 1.90–2.01 (m, 1H), 2.10–2.25 (m, 1H), 3.4 (dt, 1H, *J* 5.18, 2.07 Hz), 3.80 (s, 3H), 4.45 (s, 2H), 6.85 (d, 2H, *J* 4.41 Hz), 7.25 (d, 2H, *J* 4.41 Hz); EIMS: *m*/*z* 276 (M^+); HRMS: calc. for $C_{18}H_{28}O_2$: 276.208930, observed: 276.207990; **8a**: $[\alpha]_D$ −94.86 (*c* 1.5, $CHCl_3$); δ 1.28 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.94 (m, 1H, H-8), 2.45–2.60 (m, 1H, H-6), 2.67–2.80 (m, 1H, H-6), 3.90–4.10 (m, 3H, H-3, H-4 and H-5), 4.50–4.75 (m, 3H, H-2 and CH_2Ar), 5.89 (d, 1H, *J* 5.1 Hz, H-1), 7.35 (s, 5H, ArH); EIMS: *m*/*z* 317 (M^+−1).

Acknowledgements

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