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Oxidation by Chemical Manganese Dioxide. Part 1. Facile Oxidation of Benzylic Alcohols in Hexane†

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An inexpensive, stable, commercially available reagent, chemical manganese dioxide, can be used for the oxidation of a wide variety of benzylic alcohols and the C—C bond cleavage of aromatic diols in hexane under relatively mild conditions.

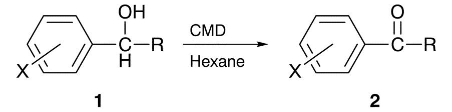
Recent development in organic synthesis owes its success, in part, to the use of potent, selective oxidizing reagents such as manganese salts.[1,2] The usefulness of active manganese dioxide (AMD),[3,4] manganese(III) acetate[5] and various manganates and permanganates[6] for a broad range of synthetic reactions has been reviewed.[1–6] Among the widely used manganese reagents, AMD enjoys from a practical point of view, remarkable advantages over others, *e.g.*, the reactions can be performed in aprotic solvents, *viz.* under neutral and water-free conditions, being therefore applicable to acid or base labile, or hydrolytically unstable compounds, and the products can easily be separated from manganese salts by filtration. However, it is well known that the preparation of AMD is time-consuming and also that the activity of AMD depends strongly on the preparation procedures and the posttreatments of the resultant oxides.[7] Instead of AMD, we have used a new reagent, chemical manganese dioxide (CMD) which has been industrially produced mainly as a battery component[8] and is now available as an inexpensive, stable laboratory reagent,[9] for the oxidation of benzylic alcohols.

Reactions were carried out simply by refluxing a heterogeneous mixture of an alcohol and CMD in hexane under an inert atmosphere. As the reaction proceeded dark muddy precipitates gradually appeared and adhered to the walls of the reaction vessel, making the work-up of the product troublesome. This phenomenon was assumed to be due to the formation of water, eqn. (1),[7] and it was therefore considered expedient to use an absorbent to trap water.

$$R^1R^2CH\text{—}OH + Mn^{IV}O_2 \longrightarrow R^1R^2C\text{=}O + Mn^{II}O + H_2O \quad (1)$$

Attempted oxidations of benzhydrol **1w** with 5 equivalents of CMD in the presence of predried molecular sieves (MS), anhydrous Na_2SO_4, $MgSO_4$, and K_2CO_3 ran smoothly to 100% conversion within 1 h and furnished benzophenone **2w** quantitatively in every case, but the work-ups of the last three reactions again suffered from the formation of muddy precipitates. On the contrary, the work-up in the reaction with MS was accomplished without difficulty.

The CMD/MS system has been favourably applied to the oxidation of benzylic alcohols **1a**–**x** (Scheme 1), affording the corresponding aldehydes or ketones in excellent (>90%) to quantitative yields. The sulfide moiety in **1k** was resistant to CMD, and the hydrolytically labile methylenedioxy linkage in **1l** survived, giving piperonal **2l**, an important fragrance and a synthetic precursor of Dopa, in quasi-quantitative yield. It is particularly interesting that there is no appreciable dependence of the reactivity of *p*-substituted benzyl alcohols **1d**–**g**,**j**,**k** and 1-phenylethanols **1p**–**s**,**v** on the electronic properties of the substituents, but that oxidations of *o*-substituted benzylic alcohols **1b**,**h**,**n**,**t** were much slower than those of *m*- (**1c**,**i**,**o**,**u**) and *p*-isomers (**1d**,**j**,**p**,**v**), suggesting that the steric environment around the hydroxyl groups played an important role in determining the reactivity of alcohols. A similar steric influence on the reactivity of benzylic alcohols has been reported in AMD oxidations.[10] Moreover, the CMD/MS system was useful for cleavage of aromatic glycols **3** (Scheme 2), giving **4** in essentially quantitative yield in each case.



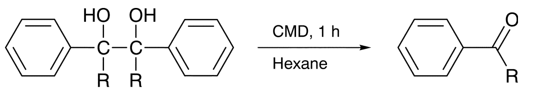
1 **2**

a X = H, R = H; 3 h
b X = 2-MeO, R = H; 6 h
c X = 3-MeO, R = H; 2 h
d X = 4-MeO, R = H; 2 h
e X = 4-Me, R = H; 2 h
f X = 4-Cl, R = H; 2 h
g X = 4-Br, R = H; 2 h
h X = 2-NO_2, R = H; 6 h
i X = 3-NO_2, R = H; 2 h
j X = 4-NO_2, R = H; 2 h
k X = 4-MeS, R = H; 2 h
l X = 3,4-OCH_2O, R = H; 2 h

m X = H, R = Me; 3 h
n X = 2-MeO, R = Me; 12 h
o X = 3-MeO, R = Me; 1 h
p X = 4-MeO, R = H; 1 h
q X = 4-Me, R = Me; 3 h
r X = 4-Cl, R = Me; 3 h
s X = 4-Br, R = Me; 1 h
t X = 2-NO_2, R = Me; 12 h
u X = 3-NO_2, R = Me; 1 h
v X = 4-NO_2, R = Me; 1 h
w X = H, R = Ph; 1 h
x X = H, R = PhCO; 15 h

Scheme 1

In short, the CMD/MS system can be successfully used for the oxidation of benzylic alcohols in hexane, providing a substitute for conventional AMD procedures.[3,4]



3 R = H or Ph **4**

Scheme 2

Experimental

General.—Commercial CMD (Wako), benzylic alcohols **1a**–**m**, **1w**–**x**, and glycols **3** were used as received. Molecular sieves 4A powder (Aldrich), anhydrous Na_2SO_4, $MgSO_4$, and K_2CO_3 were oven-dried. 1-Phenylethanols **1n**–**v** were prepared by reduction of the parent acetophenones with our *in situ* generated alumina-supported $NaBH_4$ reagent.[11] Hexane was dried, distilled, and stored over molecular sieves. Mps were determined on a Yanagimoto MP-S3 melting point apparatus and are uncorrected. Analytical GLC was performed on a Shimadzu GC-14B instrument with a 2 m × 5 mm diameter glass column packed with 5% PEG-20M

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on Chromosorb WAW-DMCS and interfaced with a Shimadzu Chromatopac C-R6A integrator, with temperature programming.

Typical Oxidation Procedure.—Benzhydrol **1w** (1 mmol; 0.184 g), predried MS (0.5 g), hexane (10 ml), and CMD (5 mmol; 0.435 g) were mixed in a 30 ml round-bottom flask. After flushing the flask with dry argon, the resultant mixture was vigorously stirred for 1 h under gentle reflux. After cooling to room temperature, the solvent was decanted and the residual precipitates were thoroughly washed with dry diethyl ether by decantation (5 × 10 ml). Removal of the combined solvent gave satisfactorily pure (^{1}H NMR, GC, and TLC) benzophenone **2w** quantitatively (0.181 g; mp 48–49 °C, lit.[12] 48.5–49 °C).

The other alcohols and diols (1 mmol) were similarly oxidized by using CMD (5 mmol, except for **1x**, 10 mmol), for given times (see Scheme 1) determined on the basis of their reactivities and the product yields. Products thus obtained were known compounds identified by spectroscopic comparisons (^{1}H NMR and IR) with authentic commercial samples and/or physical (either mp or bp) comparisons with literature data.[12] A large-scale oxidation of **1w** (30 mmol) using CMD (150 mmol), MS (4 g), and hexane (40 ml) was also successful, affording, after 1 h reaction followed by usual work-up (ether washing, 5 × 30 ml), **2w** in 98% yield.

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