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Microwave Thermolysis IV: Selective Deprotection of MPM Ethers using Clay Supported Ammonium Nitrate "Clayan" in Dry Media

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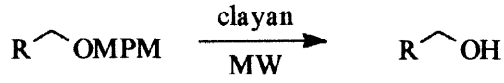
Abstract : Selective deprotection of (4-methoxyphenyl)-methyl (MPM) ethers using clay supported ammonium nitrate under microwave irradiation is described. The use of expensive reagents and problems associated with slurry reactions are avoided.

Protection and deprotection of alcohols have been given considerable attention in recent years not only because of their fundamental importance but also as to their role in multistep synthesis.[1] In the realm of hydroxyl protecting groups, the methoxyphenyl methyl (MPM) ether has often been used because of its stability towards acid, alkali and a number of other reagents. Thus their deprotection into the parent hydroxyl group has increased importance.[1] There are various methods[2] for the selective deprotection of MPM ethers, but all use excess of solvent and some of them employ heavy metal containing reagents[3] which are not ideal from an environment point of view. The non-metallic oxidative reagent DDQ[4a] (or DDQ/$FeCl_3$[4b]) is most popularly used for deprotection but it is very expensive. In this context there is still scope to devise a method with environmental consciousness using inexpensive reagents. Recently, more emphasis has been given to environmental protection.[5] In this direction solid supported reagents[6] alone or in combination with microwaves[7] have made tremendous progress. Earlier we have demonstrated clay supported NH_4NO_3 as a dethioacetalization reagent.[8] In continuation of our work, herein we wish to report "clayan" as a selective deprotection reagent for MPM ethers under solvent free conditions using microwave irradiation.

Scheme



R = alkyl, aryl, silyl ether, acetate, ester, double or triple bond or benzyl ether.

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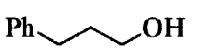
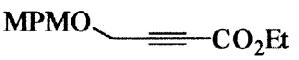
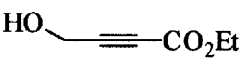
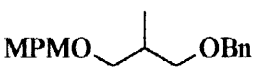
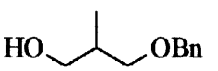
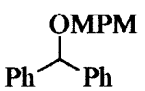
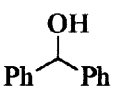
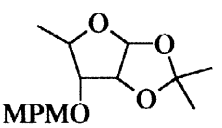
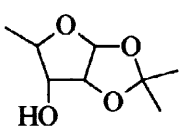
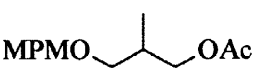
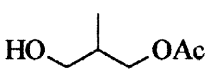
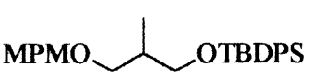
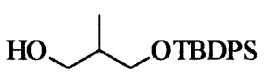
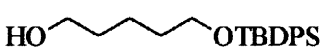
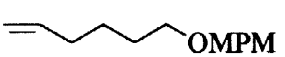
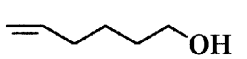
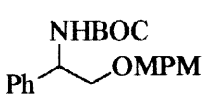
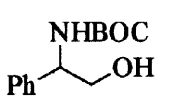
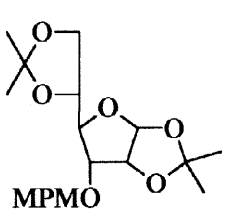
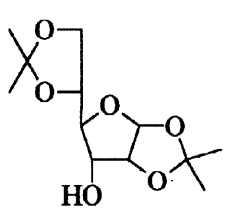
Table-1 : Deprotection of MPM ethers

entry	Substrate	Products	Time (min.)	Yield[a]
1.	$H_3C-(CH_2)_3-CH_2-OMPM$	$H_3C-(CH_2)_3-CH_2-OH$	3	86
2.	$Br-(CH_2)_9-CH_2-OMPM$	$Br-(CH_2)_9-CH_2-OH$	3	86
3.			3	85
4.			2.5	81
5.			3	88
6.			3	87
7.			2.5	84
8.			2.5	82
9.			2.5	80
10.			2.5	81
11.			3	80
12.			2.5	78
13.			3	70*

All the products exhibited physical nd spectral (NMR, IR & Mass) properties in accord with the assigned structures

* 10% deprotection of 5,6-acetonide was obtained.

Initially the reaction was carried out using clayan (1:7, substrate : ammonium nitrate in reagent) in refluxing benzene (12 h) but the reaction remained incomplete. Then we subjected this solid phase reaction mixture to microwave irradiation and found that the reaction was completed within few minutes.

In a typical experiment, MPM protected substrate (3 mmol) is mixed with clay supported ammonium nitrate "clayan"[9] (21 mmol of ammonium nitrate in reagent). The mixture is transferred into a test tube and subjected to microwave irradiation in a microwave oven (BPL make, Hi Powder) for a stipulated time (see table). After completion of the reaction (followed by tlc), it is extracted with CH_2Cl_2 (3 x 20 ml). Solvent is removed under reduced pressure. The products are obtained by column chromatography using hexane : ethyl acetate (70:30) as eluent. We have noticed that the reaction remained incomplete with ratios of 1:2, 1:4, 1:6 of substrate to clayan reagent.

The selectivity of the present method can be demonstrated by the survival of other protected groups like esters, silyl ethers, acetonides, BOC, acetate and benzyl ether under the same reaction conditions. Similarly, a double or triple bond elsewhere in the substrate remains unaffected. However, the THP ether is cleaved under similar reaction conditions. It is important to note that in spite of compatable yields, the present method has advantages over existing methods, like easy preparation of reagent, rapid reaction and solvent free conditions.

In conclusion, we have demonstrated a selective, simple and alternative method for the deprotection of MPM ethers. The use of an inexpensive oxidising reagent and non solvent reaction conditions makes the procedure more economic and eco-friendly. The scope of "clayan" reagent for the deprotection of other protecting groups is under investigation.

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9. Preparation of Clay Supported Ammonium Nitrate "Clayan" : To a solution of ammonium nitrate (5 g) in distillted water (70 ml) was added montmorillonite K 10 (Aldrich Chemicals Co.) (5 g) in portions at room temperature and the suspension stirred for 1 h. Water is removed using a rotary evaporator at 50-60°C under reduced pressure and the resulting moist solid was dried under vacuum at 40°C for 2 h. and the powdery reagent stored in a stoppered bottle.