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Microwave Thermolysis V: A Rapid and Selective Method for the Cleavage of THP Ethers, Acetals and Acetonides Using Clay Supported Ammonium Nitrate "Clayan" in Dry Media

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MICROWAVE THERMOLYSIS V : A RAPID AND SELECTIVE METHOD FOR THE CLEAVAGE OF THP ETHERS, ACETALS AND ACETONIDES USING CLAY SUPPORTED AMMONIUM NITRATE "CLAYAN" IN DRY MEDIA.

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Abstract: The deprotection of a variety of tetrahydropyranyl ethers (THP), acetonides and acetals into their parent compounds using clay supported ammonium nitrate " Clayan" under microwave irradiation is described. The eco-friendly nature of the reagent and non solvent conditions are the important features of the procedure.

Protection and the subsequent deprotection of a functional group is almost inevitable in organic synthesis. The large repertoire of protecting groups available for the hydroxyl functionality [1] exemplifies its sensitivity. The protection of mono and 1,2 dihydroxyls as THP ethers and isopropylidene acetals respectively are done routinely in organic synthesis because of their ease of formation and stability to various conditions. Also, the shielding of carbonyls

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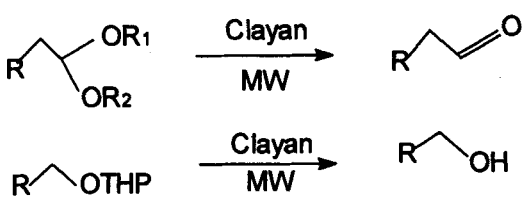
from nuclephilic attack is usual practice in multi-step organic synthesis to exploit its electrophilic properties. So the selective deprotection to their parent corbonyl or hydroxyl group has got importance in organic synthesis. The protection for carbonyls is served by a relatively small class of protecting groups and of those cyclic and acyclic acetals have proved to be more serviceable.[1] The general methods employed for the cleavage of acetals involves aqueous reaction media acidified with mineral acids or non aqueous medium acidified with organic acids.[2] Few methods utilising wet silica gel,[3] phosphorous triiodide,[4] titanium (IV) chloride,[5] boran trifloride-iodide ion [6]and cerium(III) chloride,[7] have also been reported for deprotection of acetals. But most of these procedures suffer from some drawbacks: lack of selectivity, unsatisfactory yields, toxic and expensive reagents and formation of considerable amounts of side products. These limitations prompted us to investigate a method, which proceeds selectively under environmentally benign conditions. Recently our group has developed a mild protection and deprotection method of THP ethers with NH_4Cl [8] under neutral conditions.

Reagents impregnated on mineral solid supports are efficient in solvent free conditions under microwave irradiation [9,10,11] and has attained importance because of their enhanced reactivity, selectivity and ease of manipulation.

During the course of our study in the area of supported reagent and particularly in the exploitation of oxidative capability of "Clayan"[12] for the

cleavage of various protective groups, we have observed that the THP ethers are susceptible to "Clayan". In this communication we wish to report the cleavage of THP ethers, acetonides and acetals using Clayan under microwave irradiation in solvent free conditions (scheme).

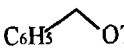
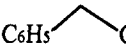
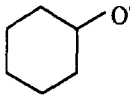
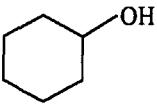
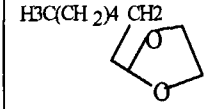
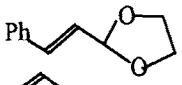
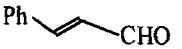
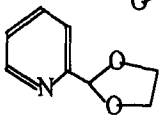
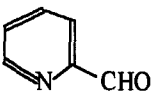
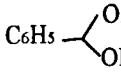
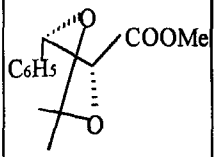
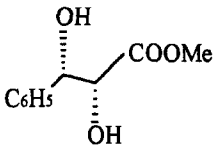
Scheme



R = Alkyl, Aryl; $R_1 = R_2$ = Et, Et, $-CH_2-CH_2-$; Clayan = Clay supported ammonium nitrate.

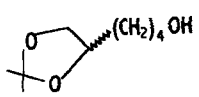
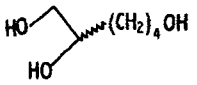
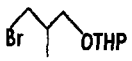
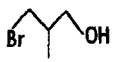
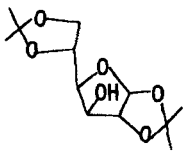
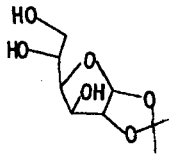
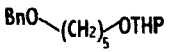
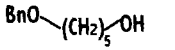
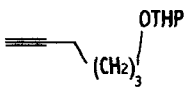
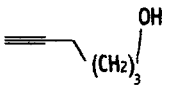
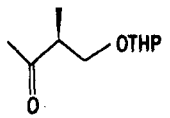
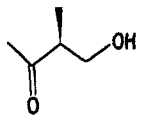
We have investigated different substrate / reagent ratios and found that 1: 4 for acetonides and 1:5 for the THP ether is suitable for the successful cleavage. Further, it is noticed that the reaction remains incomplete when a solvent (benzene) is used, even with higher ratios of reagent (1:7), at higher temperature (70 ^{0}C) and longer reaction times (8 hours). But the reaction proceeds efficiently with microwave activation within a few minutes. The results are summarised in Table **1** and **2**. The selectivity of the procedure is demonstrated by the deprotection of THP ethers in the presence of other groups like esters and benzyl ethers. It is also observed that a olefin or acetylene functionality remains unaffected. The importance of the method can be strengthen by the selective

Table 1: Cleavage of THP ethers,acetals,acetonides by"Clayan"

Entry No	THP ether (or) Acetals(or) Acetonides	Time (min)	Product	Yield[a]	mp or (bp) ^0C /Torr	
					Found[b]	Lit[13]
1.		3		90	206	205
2.		3		89	161.5	161
3.	$C_6H_5(CH_2)_3OTHP$	3	$C_6H_5(CH_2)_2CH_2OH$	83	$(118)/_{12}$	$(119)/_{12}$
4.	$HO(CH_2)_4OTHP$	2.5	$HO(CH_2)_4OH$	89	$(120)/_{10}$	$(120)/_{10}$
5.	Cholesterol-THP	2.5	Cholesterol	76	149	148.5
6.		3.0	$H_3C(CH_2)_5CHO$	90	152.8	153
7.		3.0		89	$(121)/_{10}$	$(120)/_{10}$
8.		3.0		86	180	181
9.		3.5	C_6H_5CHO	86	178.6	178
10.		2.5		70	95[c]	94

a: All the products exhibited physical and spectral (NMR, IR and m/e) properties in accordance with the assigned structures. b) Unless specified under parenthesis the boiling points are measured at 760 mm of Hg. c) conformed as an acid.

Table 2 : Deprotection of acetals, THP ethers & acetonides by "Clayan"

Entry No	THP ethers (or) Acetals (or) Acetonides	Product	Time (min)	Yield (%)	mp or (bp) ^{0} C/Torr	
					Found	Lit [13]
1.			3	83	(179.5)/$_5$	(178)/$_5$
2.			3	86	(74)/$_9$	(73)/$_9$
3.			3	78	161	159
4.			3.5	84	(142)/$_{0.4}$	(140)/$_{0.4}$
5.			3.5	86	(75)/$_{15}$	(74)/$_{15}$
6.			2.5	87	(93)/$_{15}$	(93)/$_{15}$

a: All the products exhibited physical and spectral (NMR, IR and m/e) properties in accordance with the assigned structures. b) Unless specified under parenthesis the boiling points are measured at 760 mm of Hg.

deprotection of an acetonide (Table **2**, entry 3) which can find application in carbohydrate chemistry.

In conclusion, the present procedure for the cleavage of THP ethers, acetals and acetonides is efficient and convenient which has advantages over the existing methods and shows the selectivity towards esters, acetate and benzyl ethers. The inexpensive reagent and solvent free conditions are additional features of the procedure.

EXPERIMENTAL

Boiling points and melting points are uncorrected. Melting points were recorded on Buchi R535 apparatus. All the starting materials are commercially available and used without further purification. OTHP ethers, acetals and acetonides were prepared following the literature procedure.[1,14] The reagent[12b] "Clayan" was prepared by the impregnation of ammonium nitrate on Montmorillonite-K10, which was purchased from Aldrich Chemical Limited. IR spectra were recorded on IR Nicole 740 FT IR spectrometer, 1H NMR spectra were recorded on FT (200 Gemini) spectrometer. Mass spectra were recorded on either Micromass 7070h or Finnigan Mat 1020 B mass spectrometer operating at 70 eV. Thin layer chromatography was done on precoated silica gel 60f 254 (0.5 mm) glass plates.

CAUTION : *These procedures worked safely in our hands. But as the nitrates are dangerous compounds, appropriate precautions are recommended*

for the reaction at elevated temperature. We suggest that the microwave oven be operated in multiples of shorter reaction times (1 min) because of the possible higher localised temperature.

General Procedure for the deprotection : In a typical procedure, substrate (1 mmol) is mixed with clay supported ammonium nitrate "Clayan" (640 mg, 4 mmol of ammonium nitrate in reagent) in solid state. It is transferred into a test tube and subjected to microwave irradiation (BPL make, BMO 700T, 650W, operating at a frequency 2450 MHz.). Reaction is monitored by tlc (Hexane: Ethyl acetate 80:20). After completion of the reaction, it is extracted with dichloromethane (3 x 20mL). Evaporation of the solvent gives the parent compound in good yield. Further, the products are purified by passing through a short column of neutral alumina using hexane: ethylacetate, (90:10) as an eluent.

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