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HNO_3/Silica gel supported CAN; oxidative deprotection of benzylic tetrahydropyranyl ethers under solvent-free conditions using microwaves

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Benzylic tetrahydropyranyl ethers are rapidly and selectively oxidised to the corresponding carbonyl compounds by HNO_3/ silica gel supported cerium ammonium nitrate (CAN) under solvent free conditions using microwave.

Keywords: CAN, oxidative deprotection, THP ethers

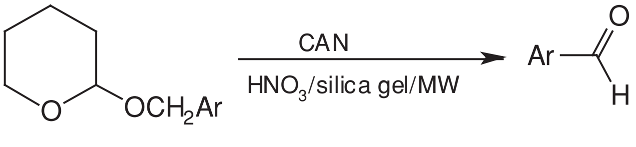
The protection–deprotection of alcohol functionalities is of paramount importance in organic chemistry as testified by the plethora of imaginative reagents and methods that have been devised to accomplish this key functional interconversion.[1] Although several methods have been appeared in the literature concerning the deprotection of tetrahydropyranyl (THP) ethers,[2] there are only few reports dealing with the direct oxidation of THP ethers to the corresponding carbonyl compounds.[3] Consequently, there is a demand to develop and introduce more selective and milder methods and reagents for this transformation.

During the past few years, cerium ammonium nitrate (CAN) has become a synthetic reagent and a catalyst of growing importance.[4] It has recently been used for the protection of THP and THF ethers under neutral conditions.[2]

The use of supported reagents has attracted much attention, because of improved selectivity, reactivity and associated ease of manipulation.[5] Since polar reactants adsorbed on the surfaces of various minerals carriers absorb microwave energy, a variety of reagents supported on such surfaces can be utilised for the enhancement of organic reactions using a simple microwave oven.[6] Recently, microwave-enhanced chemical reactions, especially on inorganic solid supports and under solvent-free conditions,[7] have attracted much attention. They offer several advantages over conventional homogeneous and heterogeneous reactions with respect to high reaction rates and yields.

In continuation of our recent work on microwave-assisted reactions under solvent-free conditions,[8] we report here our results for a solvent free microwave protocol that leads to a facile selective oxidative deprotection of benzylic THP ethers using CAN.

A series of experiments was performed to identify the best solid support and to optimise the ideal amounts of CAN for oxidative cleavage of THP ethers under microwave irradiation.



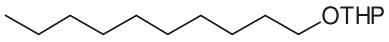
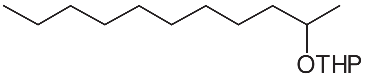
Scheme 1

First, the effect of supports on the oxidative deprotection of benzyltetrahydropyranyl ether using one equivalent of CAN was examined on various inorganic supports such as zeolite HY, clay, alumina and silica gel under microwave irradiation. TLC analyses showed the best support is silica gel, regarding the production of considerable amount of benzaldehyde. However, TLC showed some deprotected benzyl alcohol and unreacted THP ether. Addition of two equivalents of CAN did not improve the reaction. Interestingly, when a drop of nitric acid was added to the silica gel thus giving what we shall call 'nitric acid supported onto silica gel', (HNO_3/silica gel), benzyl THP ether was quntitatively converted to benzaldehyde using two equivalents of CAN under microwave irradiation in a very short reaction time. Under these conditions substituted benzylic THP ethers successfully underwent oxidative deprotection affording the corresponding benzaldehyde in excellent yields.

In these reactions no noticeable over-oxidation to carboxylic acids, even with an excess of CAN and longer reaction time, was observed.

In conrast, primary and secondary aliphatic and even secondary benzylic THP ethers are not oxidatively deprotected to their corresponding aldehydes and ketones with high efficiency under the same reaction conditions (Table 1, entries 7–9). This observation suggested a possible chemoselective oxidative deprotection of primary benzylic THP ethers in the presence of other THP ethers and even non-benzylic alcohols.

Table 1 Oxidative deprotection of THP ethers with CAN supported on HNO_3/silica gel

Entry	Substrate	Time/min	Product	[a]Yield/%
1	$PhCH_2OTHP$	6	$PhCHO$	90
2	m-O_2N-$C_6H_4CH_2OTHP$	4	m–O_2N–C_6H_4CHO	91
3	p-$O_2NC_6H_4CH_2OTHP$	4	p–$O_2NC_6H_4CHO$	92
4	p-Me-$C_6H_4CH_2OTHP$	5	p–Me–C_6H_4CHO	90
5	2-O_2N-5-Me-$C_6H_3CH_2OTHP$	5	2–O_2N–5-Me–C_6H_3CHO	90
6	PhCH(Me)OTHP	10	PhCO(Me)	trace
7	CyclohexanolTHP	10	–	–
8		10	–	–
9		10	–	–

[a]Yields refer to isolated products.

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Indeed, this procedure proved to be exceptionally chemoselective; the reaction of a 1:1 mixture of benzyl THP ether and 1-phenyl ethyl THP ether using 2 equiv. of CAN resulted benzaldehyde and 1-phenylethanol, with virtually no ketone (entry 6).

In conclusion, CAN, supported onto HNO_3/silica gel, under microwave irradiation in a solventless system is a convenient, selective, and environmentally benign protocol for oxidative deprotection of benzylic THP ethers.

Experimental

CAN, alcohols and silica gel were purchased and used as received. THP ethers were synthesised according to known procedures.[8] All products are known and their physical data were compared with those of authentic samples and found to be identical.

General procedure for the oxidative deprotection of benzylic THP ethers: In a beaker, to silica gel (1 g), a drop of conc. HNO_3 was added and mixed thoroughly using (Teflon coated) magnet stirring. To this HNO_3/ silica gel, cerium ammonium nitrate (CAN) (2 mmol) and neat THP ether (1 mmol) were added and mixed thoroughly. The beaker was placed in a household microwave oven and irradiated. The progress of reaction was monitored by TLC using hexane : EtOAc 8 : 2 as eluent. After the completion of reaction the product was extracted into CH_2Cl_2 then the solvent was removed and the residue was chromatographed on a silica gel column using hexane : EtOAc 8 : 2 to afford the corresponding aldehyde.

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