

A Convenient Oxidative Deprotection of Tetrahydropyranyl Ethers with Iron(III) Nitrate and Clay under Microwave Irradiation in Solvent free Conditions

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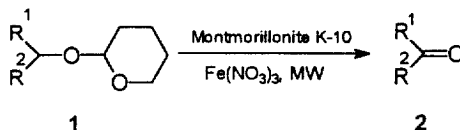
Abstract : *The efficient and environmentally benign oxidative deprotection of tetrahydropyranyl ethers using montmorillonite supported iron(III) nitrate under microwave irradiation under solvent free conditions is described.*

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The tetrahydropyranyl group is one of the most useful protective groups for alcohols in multi-step organic synthesis. ¹⁻³ Many catalysts have already been used for tetrahydropyranlation of alcohols and deprotection of tetrahydropyranyl ethers to the parent alcohols⁴ but there are only a few reports based on chromium reagents dealing with the direct oxidation of tetrahydropyranyl ethers to their carbonyl compounds.^{5,6} However, there is a serious drawback against oxidants based on chromium.⁷ They are corrosive and irritants for the skin and for sensitive parts of the body such as eyes. They are also toxic to man and to the environment. Derivatives of chromium(VI) in particular are well known carcinogens.⁸ In view of increasing environmental constraints, it has become unacceptable for industrial effluents and wastes to contain such a highly toxic transition metal. The design of new, less polluting, oxidation procedures has become a priority for the chemical industry.^{9,10}

We report here our results from work undertaken to establish an economically and environmentally acceptable protocol for oxidative deprotection of tetrahydropyranyl ethers to their corresponding carbonyl compounds. A method based on dry conditions has been developed to convert tetrahydropyranyl ethers to aldehydes and ketones by mixing iron(III) nitrate with montmorillonite K-10 and adding this mixture to the tetrahydropyranyl ether and exposing the mixture to microwave irradiation. For example upon exposure of benzyl tetrahydropyranyl ether with iron(III) nitrate supported montmorillonite K-10 to microwave irradiation, benzaldehyde was obtained in 90% yield after 1 min. The efficiency of a heterogenous system based upon iron(III) nitrate oxidation has been proved by earlier investigations.¹¹ The reaction advantages are reminiscent of those of supported reagents.¹² It should be pointed out that in the absence of the clay, the reaction was sluggish and more seriously molten ferric nitrate and or its degradation product(s) adhered to the walls of the reaction vessel forming an interactable solid mass which made the isolation of carbonyl compounds considerably more difficult and led to erratic results. Indeed when no clay was added, the conversion of **1** to **2** was only 30% under otherwise similar conditions to those described above. Clearly the clay aided the reproducibility and high activity of iron(III) nitrate. In a typical experiment montmorillonite K-10 (1 g) was mixed thoroughly with Fe(NO₃)₃ · 9H₂O (0.404 g, 1 mmol) using a pestle and mortar. This mixture was added to neat tetrahydropyranyl ether (1 mmol) in a beaker and was placed into a microwave oven (900 w). The

mixture was irradiated for the indicated time. After completion of the reaction, which was monitored by TLC or GC, the crude product was extracted with dichloromethane. GC analysis of the crude product showed that **2** were obtained in high to excellent yields. Final purification was achieved by column chromatography using hexane:ethyl acetate as eluent. (Table).



In conclusion, clay supported iron(III) nitrate mediated, solvent free, microwave thermolysis is a convenient, selective and environmentally benign direct oxidative deprotection protocol when compared to other solution phase or heterogeneous reactions. In addition by development of a continuous microwave reaction for organic synthesis^{13,14} this work may have more industrial application where the absence of solvent and low cost of the method may lead to environmental and cost advantages.

Table I. Oxidative deprotection of THP ethers with Iron(III) nitrate and clay under microwave irradiation in solvent free conditions.

Entry	Substrate	Time (sec.)	product	Yield
1	PhCH ₂ OTHP	60	PhCHO	90 ^a
2	4-MeC ₆ H ₄ CH ₂ OTHP	60	4-MeC ₆ H ₄ CHO	88 ^a
3	2-NO ₂ -5-MeC ₆ H ₃ CH ₂ OTHP	120	2-NO ₂ -5-MeC ₆ H ₃ CHO	80 ^a
4	PhCH(Me)OTHP	60	PhCOMe	80
5	Ph ₂ CHOTHP	60	PhCOPh	85
6	PhCH=CHCH ₂ OTHP	120	PhCH=CHCHO	80
7	CyclohexanoITHP	120	Cyclohexanone	88 ^a
8	2-Me-CyclohexanoITHP	120	2-Me-cyclohexanone	90 ^a
9	(-) MenthoITHP	140	(-) Menthone	87

^a Yields based on the isolation of 2,4-dinitrophenylhydrazone derivatives.

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