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# Microwave-assisted preparation of dialkylimidazolium tetrachloroaluminates and their use as catalysts in the solvent-free tetrahydropyranylation of alcohols and phenols

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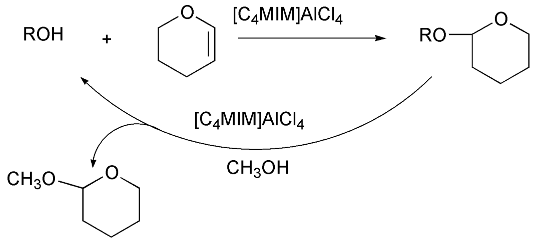
**Microwave-assisted preparation of dialkylimidazolium tetrachloroaluminates, [$C_n$MIM][$AlCl_4$] and their application as recyclable catalysts for the efficient and eco-friendly protection of alcohols as tetrahydropyranyl (THP) ethers are described. The same catalyst can also be utilized for the deprotection of THP ethers.**

Room temperature ionic liquids (RTILs) consisting of *N*-alkylimidazolium cations[1] and various anions, have received wide attention due to their potential in a variety of commercial applications such as electrochemistry,[2] heavy metal ion extraction,[3] phase transfer catalysis and polymerization,[4] and as substitutes for conventional volatile organic solvents.[5] They are polar but consist of poorly coordinating ions and provide a polar alternative for biphasic systems. Other important attributes of these ionic liquids include negligible vapor pressure, potential for recycling, compatibility with various organic compounds and organometallic catalysts,[6] and ease of separation of products from reactions.

In view of the emerging importance of the ionic liquids as reaction media[7] and our general interest in microwave-assisted chemical processes,[8,9] we decided to explore the synthesis of ionic liquids bearing tetrachloroaluminate anions using microwave (MW) irradiation under solvent-free conditions. Ionic liquids, being polar and ionic in character, couple to the MW irradiation very efficiently and consequently may be ideal microwave absorbing entities for expediting chemical manipulations. An efficient preparation of the 1,3-dialkylimidazolium halides *via* microwave heating has been described that reduces the reaction time from several hours to minutes and avoids the use of a large excess of alkyl halides/organic solvents as the reaction medium.[8] Herein, we report an efficient method for the preparation of ionic salts that involves exposing *N*, *N′*-dialkylimidazolium chloride and aluminum chloride to microwaves in an unmodified household MW oven. This solvent-free approach, again, requires only a few minutes of reaction time in contrast to several hours needed under conventional heating conditions.[10] A schematic representation for the preparation of [$C_n$MIM][$AlCl_4$] is shown in Table 1.

The tetrahydropyranyl (THP) protection and deprotection of alcohols is one of the most frequently employed methods in multi-step organic syntheses.[11] The THP ethers are attractive for the reason that they are less expensive, easy to deprotect and are stable enough to strong basic media, oxidative conditions, reduction with hydrides, and reactions involving Grignard reagents, lithium alkyls and alkylating and acylating reagents. There are several processes available in the literature for these protection–deprotection sequences[12] but most of these methods require a high catalyst to substrate ratio, have a long reaction time and involve the use of volatile organic solvents or large amounts of solid supports, which eventually result in generation of a large amount of toxic waste. Thus, there is a need for a solvent-free and catalytically efficient alternative for the protection and deprotection of hydroxy functionality as THP ether. Herein, we report an efficient solvent-free tetrahydropyranylation of alcohols and phenols catalyzed by [$C_n$MIM][$AlCl_4$] (Scheme 1).



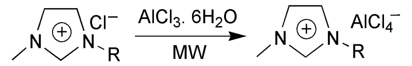
**Scheme 1**

The ionic liquids with tetrachloroaluminate anion are significant for several synthetic applications, especially Friedel-Crafts reaction where they can be good substitutes for the conventional highly toxic and corrosive reagents such as HF or $AlCl_3$, which are consumed in large quantity and consequently generate a large amount of contaminated waste. The reported methods for the preparation of these salts are time consuming[10] and we have extended our microwave heating protocol to the preparation of tetrachloroaluminates (Table 1).

A recently introduced household MW oven (Panasonic) equipped with inverter technology provides a realistic control of the microwave power to a desirable level.[8] Microwave heating provides a more uniform heating of this highly viscous medium and is also faster than the corresponding conventional heating. A mixture of alkylimidazolium chloride and aluminum chloride is mixed using a vortex mixer and heated in the MW oven when the solid aluminum chloride phase slowly disappears and the complete conversion results in a clear single phase.†

Table 1 provides the optimized reaction conditions for obtaining pure products using three N,N'-dialkylimidazolium chlorides (1-butyl-3-methylimidazolium chloride [$C_4$MIM]Cl and the corresponding hexyl [$C_6$MIM]Cl and octyl chlorides [$C_8$MIM]Cl). The NMR data of the products are in conformity with the structure. The TGA and DSC data show that all these ionic salts are pure and are free of any starting materials.

**Table 1** Preparation of [$C_n$MIM][$AlCl_4$] using microwave[a]



where R = butyl, hexyl or octyl

| Ionic liquid (3 mmol) | MW-Power (Watts) | Time (s) | Yield (%) |
|---|---|---|---|
| [$C_4$MIM]Cl | 240 | 30+30+30+30+30+30+30 | 100[b] |
| | 360 | 30+30+30+30+30+30+30 | 100 |
| | 480 | 30+15+15+15+15+15+15 | 100 |
| | 480 | 60+30+30+30+30+30+30 | 100[c] |
| [$C_6$MIM]Cl | 360 | 30+30+30+30+30+30+30 | 100 |
| | 480 | 30+15+15+15+15+15+15 | 100 |
| [$C_8$MIM]Cl | 360 | 30+30+30+30+30+30+30 | 100 |
| | 480 | 30+30+15+15+15+15+15 | 100 |

[a] $AlCl_3.6H_2O$ (3 mmol). [b] Traces of unreacted aluminum chloride found. [c] [$C_4$MIM]Cl (20 mmol, $AlCl_3.6H_2O$ (20 mmol).

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The use of these ionic liquids as recyclable catalysts has been explored in the protection and deprotection sequence for alcohols as THP-ethers using [C$_4$MIM]AlCl$_4$ as a model catalyst (Table 2). It is apparent that the MW-generated tetrachloroaluminate salts are efficient catalysts in tetrahydropyranylation of alcohols and deprotection of THP ethers and can be utilized as such without further purification. A wide variety of hydroxylated compounds were rapidly converted to the corresponding THP ethers *via* this procedure at rt. It is important to note that an acid sensitive alcohol like *tert*-butanol (entry 5, Table 2) undergoes protection as tetrahydropyranyl ether without the formation of a dehydration product. Another important feature of this method is the efficient monotetrahydropyranylation of 1,*n*-diols (entry 7, Table 2), a transformation that is difficult to accomplish *via* conventional methods. The NMR studies on the THP ethers are in conformity with the corresponding literature reports.[12]

**Table 2** Tetrahydropyranylation of alcohols in presence of [C$_4$MIM]AlCl$_4$[a,b]

| Entry | Alcohol | Time (min) | Temperature (°C) | Yields % GC (isolated) |
|---|---|---|---|---|
| 1 | 1-Hexanol | 15 | 25 | 100(95) |
| 2 | Cyclohexanol | 15 | 25 | 100(96) |
| 3 | Phenol | 10 | 25 | 100(97) |
| 4 | 2-Naphthol | 30 | 50 | 100(95) |
| 5 | *tert*-Butanol | 15 | 25 | 100(95) |
| 6 | 3-Methyl-2-buten-1-ol | 15 | 25 | 100(98) |
| 7 | 1,2-Ethanediol | 30 | 25 | 76(74) |
| 8 | Benzyl alcohol | 15 | 25 | 100(98) |
| 9 | Benzyl alcohol | 15 | 25 | 100(96)[c] |

[a] [C$_4$MIM]AlCl$_4$ (1 mmol) and 3,4-dihydropyran (110 mmol) and alcohol (100 mmol). [b] For complete detetrahydropyranylation at rt: THP ether (100 mmol), [C$_4$MIM]AlCl$_4$ (1 mmol) and methanol (800 mmol), 30 min. [c] Yield after 4 recycles.

The tetrahydropyranylation reactions with tetrachloroaluminate salts do not require absolute anhydrous conditions. The ionic liquid catalyst is recovered for further use by simply extracting the products with diethyl ether, which forms a separate layer and can be conveniently decanted off. The recycling study with ionic liquid catalyst reveals that the catalyst can be recycled without much loss of reactivity (entry 9, Table 2), which we checked up to 4 recycles. The complete deprotection of the alcohols is achieved *via* a metathesis reaction with excess methanol using the same catalyst.

In conclusion, a solvent-free MW-assisted protocol is developed for the synthesis of 1,3-dialkylimidazolium tetrachloroaluminates using an unmodified household microwave oven, a method that precludes the usage of volatile organic solvents and is relatively much faster, efficient, and eco-friendly. The general use of these ionic liquids in the protection and deprotection of alcohols is demonstrated in the tetrahydropyranylation reaction. We envisage that this method will find practical application for the protection and deprotection of alcohols in modern synthetic chemistry.

VVN is a postgraduate research participant at the National Risk Management Research Laboratory administered by the Oak Ridge Institute for Science and Education.

## Notes and references

† 1-Methylimidazole (MIM) and alkyl halides were obtained from Aldrich Chemical company and were used as such. 1,3-Dialkylimidazolium chlorides were prepared using microwave as reported earlier.[8] The NMR spectra of the samples were recorded on a Brucker 250 MHz spectrometer using D$_2$O as solvent and CD$_3$OD/CDCl$_3$ as the standards. The thermogravimetric analysis (TGA) of the samples were performed by heating from 25 to 500 °C at a rate of 10 °C min$^{-1}$ and differential scanning calorimetric analysis (DSC) was conducted from 25 to 450 °C at a heating rate of 10 °C $^{-1}$min. An unmodified household microwave (MW) oven, Panasonic NN-S740WA-1200W, was used for heating.

**[C$_4$MIM]AlCl$_4$**. In a typical method, aluminum chloride hexahydrate (3.0 mmol) and 1-butyl-3-methylimidazolium chloride (3.0 mmol) were placed in a glass test tube and mixed thoroughly on a vortex mixer. The mixture was heated in the MW oven at 360 W (30 s irradiation with 10 s mixing) until the dissolution of aluminum crystals was completed and resulted in the formation of a single phase (Table 1). The bulk temperature recorded was in the range 80 to 110 °C. The resulting ionic liquid was then dried under vacuum at 80 °C to afford [C$_4$MIM][AlCl$_4$]. The same experiment *via* conventional heating (oil bath at 90 °C for 3 h) resulted only in impure product. An experiment on a relatively large scale starting from 20 mmol of aluminum chloride hexahydrate and 20 mmol of [C$_4$MIM]Cl also afforded [C$_4$MIM]AlCl$_4$ (20.0 mmol, mp 65 °C). $^1$H NMR (250 MHz; D$_2$O), $\delta_H$: 0.72(t, CH$_3$), 1.15(m, CH$_2$), 1.81(m, CH$_2$), 3.71(s, N-CH$_3$), 4.09 (m, N-CH$_2$), 7.38(s, NCH), 7.43 (s, NCH), 8.7 (s, N(H)CN); $^{13}$C NMR $\delta_C$ 12.89 (t, CH$_2$), 19.02 (m, CH$_3$), 31.51 (m, CH$_2$), 35.86 (N-CH$_2$), 49.51(N-CH$_3$), 122.40 (NCH), 123.73 (NCH), 136.21 (N(H)CN).

**Tetrahydropyranyl ether**. In a typical procedure, benzyl alcohol (100 mmol) and 3,4-dihydro-2*H*-pyran (110 mmol) were added to [C$_4$MIM]AlCl$_4$ (1 mmol) prepared earlier and then stirred with a magnetic stirring bar. The progress of the reactions was followed using GC-MS. The disappearance of the alcohol signal in the GC determined the completion of reaction and the product was extracted with ether and filtered through a silica column (2 cm length) to remove any ionic impurities. The residual 3,4-dihydropyran and solvent were removed on a rotary evaporator followed by vacuum drying to afford THP ether (98%). In the case of diol (entry 7, Table 2), further purification was accomplished by filtering it through a short silica column (eluted with petroleum ether). For recycling studies, the ionic liquid separated after product extraction into diethyl ether, was dried and reused (entry 9, Table 2).

**Detetrahydropyranylation of THP ethers.** THP ether (100 mmol), [C$_4$MIM]AlCl$_4$ (1 mmol) and excess methanol (800 mmol) were mixed together at rt for 30 min affording complete regeneration of the alcohol. The cleavage of THP ethers and regeneration of alcohols were similarly followed by GC.

1 T. Welton, *Chem. Rev.*, 1999, **99**, 2701.

2 J. S. Wilkes, J. A. Levinsky, R. A. Wilson and C. L. Hussey, *Inorg. Chem.*, 1982, **21**, 1263.

3 A. E. Visser, R. P. Swatloski and R. D. Rogers, *Green Chemistry*, 2000, **2**, 1; A. E. Visser, R. P. Swatloski, W. M. Reichert, R. D. Rogers, R. Mayton, S. Sheff, A. Wierzbicki and J. H. Davis Jr., *Chem. Commun.*, 2001, 135.

4 A. J. Carmichael, D. M. Haddleton, S. A. F. Bon and K. R. Seddon, *Chem. Commun.*, 2000, 1237.

5 J. S. Wilkes and M. J. Zaworotko, *J. Chem. Soc., Chem. Commun.*, 1992, 965.

6 J. D. Holbrey and K. R. Seddon, *Clean Products and Processes*, 1999, **1**, 223; J. G. Huddleston, H. D. Willauer, R. P. Swatloski, A. E. Visser and R. D. Rogers, *Chem. Commun.*, 1998, 1765.

7 M. Freemantle, *Chem. Eng. News*, 1 January, 2001, p. 21; M. Freemantle, *Chem. Eng. News*, 15 May, 2000, p. 37.

8 R. S. Varma and V. V. Namboodiri, *Chem. Commun.*, 2001, 643; R. S. Varma and V. V. Namboodiri, *Pure Appl. Chem.*, 2001, **73**, 1309.

9 R. S. Varma, in *Green Chemical Syntheses and Processes,* ed. P. T. Anastas, L. G. Heine and T. C. Williamson, ACS Symposium Series 767, American Chemical Society, Washington, D.C., 2000, pp. 292–312; R. S. Varma, *J. Heterocyclic Chem.*, 1999, **35**, 1565; R. S. Varma, *Green Chemistry*, 1999, **1**, 43; R. S. Varma, *Pure Appl. Chem.*, 2001, **73**, 193.

10 J. G. Huddleston, A. E. Visser, W. M. Reichert, H. D. Willauer, G. A. Brocker and R. D. Rogers, *Green Chemistry*, 2001, **3**, 156.

11 T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 2nd edn., John Wiley & Sons, Inc., New York, 1999.

12 T. Nishiguchi, S. Fujisaki, M. Kuroda, K. Kajisaki and M. Saitoh, *J. Org. Chem.*, 1998, **63**, 8183; N. Deka and J. C. Sarma, *J. Org. Chem.*, 2001, **66**, 1947; T. C. Turek, I. Gaon, M. D. Distefano and C. L. Strick, *J. Org. Chem.*, 2001, **66**, 3256; G. A. Olah, A. Husain and B. P. Singh, *Synthesis*, 1983, 892; S. Hoyer, P. Laszlo, M. Orlovic and E. Polla, *Synthesis*, 1986, 655; B. C. Ranu and M. Saha, *J. Org. Chem.*, 1994, **59**, 8269.