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Microwave-assisted preparation of imidazolium-based tetrachloroindate(III) and their application in the tetrahydropyranylation of alcohols

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Abstract—Microwave-assisted preparation of 1-alkyl-3-methylimidazolium tetrachloroindate(III), $[Rmim][InCl_4]$ (R = methyl, ethyl, butyl, hexyl, octyl) and their application as recyclable catalysts for the efficient and eco-friendly protection of alcohols to form tetrahydropyranyl (THP) ethers are described.

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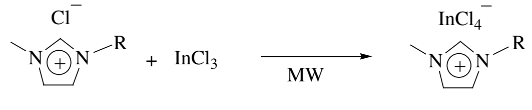
1. Introduction

Room temperature ionic liquids (RTILs), especially those based on the 1-alkyl-3-methylimidazolium cation, are attracting increasing interest as new reaction media in many organic transformations, as electrolytes for batteries and capacitors, and in separation processes, mainly because of their advantageous nonvolatile nature and their easily tunable physicochemical properties.[1] Ionic liquids have been developed for task-specific purposes, however, a large majority of those studies have focused on the use of ILs as reaction media.[2] More recently, there have been increasing efforts to utilize ILs as active catalysts for the organic synthesis.[3] Among ionic liquids in this context, we are particularly interested in the imidazolium-based RTILs containing chloroindate(III), which exhibit Lewis acid properties similar to those of chloroaluminate ILs without being reactive toward air and water, which is generally considered to be a main limitation.[4]

A recently introduced household microwave (MW) oven (Panasonic) equipped with inverter technology provides a realistic control of the microwave power to a desirable level.[5] As a part of an ongoing research program to develop solventless chemical transformations using MW,[6] herein we report expeditious preparation of 1-alkyl-3-methylimidazolium tetrachloroindate(III) compounds using MW irradiation, which are subsequently utilized in the tetrahydropyranylation of alcohols.

2. Results and discussion

Admixing equimolar amounts of indium trichloride and solid 1-butyl-3-methylimidazolium chloride, followed by MW irradiation for 30 s (15 s × 2 times) without any solvent afforded a crude mixture of liquid and small quantity of unreacted $InCl_3$, which was removed by filtration to afford colorless single phased liquid (Scheme 1). This liquid product was fully characterized as $[C_4mim][InCl_4]$ (C_4mim = 1-butyl-3-methylimidazolium) by NMR spectroscopy and TGA analysis. It was found that MW irradiation provided a more uniform heating of this viscous medium and the reaction proceeded much faster than the corresponding protocol using conventional heating. Table 1 shows the optimized reaction conditions for the preparation of the pure $[R_nmim][InCl_4]$ using five



R = methyl, ethyl, butyl, hexyl, octyl

Scheme 1.

Keywords: Microwave irradiation; Ionic liquid; Tetrahydropyranylation; Imidazolium-based tetrachloroindate.

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Table 1. Preparation of $[R_n\text{mim}][\text{InCl}_4]$ using MW[a]

Entry	Ionic liquid	Time (s)	Yield (%)
1	$[C_1\text{mim}]\text{Cl}$	15+15	93
2	$[C_2\text{mim}]\text{Cl}$	15+15	94
3	$[C_4\text{mim}]\text{Cl}$	15+15	93
4	$[C_6\text{mim}]\text{Cl}$	15+15+15+15	90
5	$[C_8\text{mim}]\text{Cl}$	15+15+15+15	89

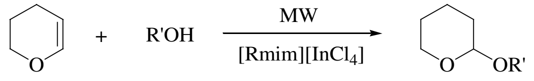
[a] Conditions: ionic liquid (5 mmol), InCl_3 (5.0 mmol), MW power (600 W).

different imidazolium halides, $[R_n\text{mim}]\text{Cl}$ (R_n = methyl (C_1), ethyl (C_2), butyl (C_4), hexyl (C_6), octyl (C_8)). The NMR spectra of the ionic liquids obtained from MW reactions are in conformity with the structure.

Tetrahydropyranylation is one of the most frequently employed methods for the protection of hydroxyl groups in multi-step organic synthesis.[7] The tetrahydropyranyl (THP) ethers are attractive because they are less expensive and are stable enough to strong basic media, oxidative conditions, reduction with hydrides, reactions involving Grignard reagents, etc. There are several processes available in the literature for the preparation of THP-ethers but majority of them have a long reaction time and involve the use of volatile organic solvents or large amounts of solid supports, which eventually leads to generation of a large amount of toxic waste. Therefore, there is a need for a solvent-free and efficient alternative for the protection of hydroxyl compounds (Scheme 2).

The tetrahydropyranylations of various alcohols were carried out using 25 mol % of $[C_4\text{mim}][\text{InCl}_4]$ as a model catalyst at 60 °C, 100 W of MW power (CEM system). As shown in Table 2, the conventional heating (60 °C, 1 h) afforded only 20% and 39% yields of corresponding THP-ethers from phenol and benzyl alcohol, respectively (entries 1 and 2). When the same reaction was conducted under MW irradiation conditions in the presence of $[C_4\text{mim}][\text{InCl}_4]$, the yields of products increased to 88% and 85% within 5 min, respectively. The protection methodology was successful for a variety of substrates with a range of functional groups, providing fairly good yields of THP-ether. However, the *o*-cresol (entry 3) produced the product in only 52% yield, probably due to the steric effect of *ortho* position of methyl group. The effect of the change of alkyl group appended to the imidazolium cation was found to be less pronounced in the activity, giving similar yields to that of model catalyst, $[C_4\text{mim}][\text{InCl}_4]$ in the tetrahydropyranylation of benzyl alcohol.

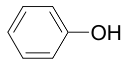
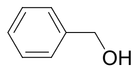
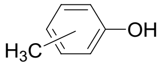
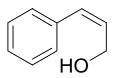
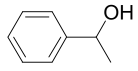
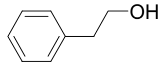
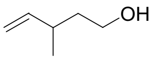
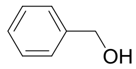
To investigate the possibility of recycling the catalyst, the $[C_4\text{mim}][\text{InCl}_4]$ is recovered for further use by simply extracting the products with diethyl ether, which forms a separate layer and can be conveniently decanted off, followed by fresh charge of reactants in the same reaction vessel. The recycling study with the ionic liquid catalyst reveals that the catalyst can be recycled several times without much loss of its reactivity (entry 8, after five cycles).



R = methyl, ethyl, butyl, hexyl, octyl

Scheme 2.

Table 2. MW-assisted tetrahydropyranylation of alcohols in the presence of $[C_4\text{mim}][\text{InCl}_4]$[a]

Entry	Alcohol	Time (min)	Yields (%) GC (isolated)
1		5	88 (82)
2		60[b] 5 60[b]	20[b] 85 (79) 39[b]
3		10 5 5	*o*: 52 *m*: 70 *p*: 72
4		5	84
5		10	77 (70)
6		5	86 (79)
7		10	65
8		5	86[c]

[a] Conditions: 3,4-dihydropyran (11 mmol), alcohol (10 mmol), $[C_4\text{mim}][\text{InCl}_4]$ (2.5 mmol).

[b] Conventional heating at 60 °C.

[c] Yield after five recycles.

3. Conclusion

In conclusion, a solvent-free MW-assisted protocol is developed for the synthesis of 1-alkyl-3-methylimidazolium tetrachloroindate(III) using an unmodified household microwave oven. The use of these ionic liquids in the MW-assisted protection of alcohols is demonstrated in the tetrahydropyranylation that precludes the use of volatile organic solvents. Furthermore, these ionic liquid catalysts can be effectively recycled, thus rendering this expeditious protection protocol more efficient and eco-friendly.

4. Preparation of [1-butyl-3-methylimidazolium][InCl_4]—general procedure

In a typical method, indium trichloride (5.0 mmol) and 1-butyl-3-methylimidazolium chloride (5 mmol) were placed in a glass test tube and mixed on a vortex mixer. The mixture was subjected to the MW irradiation at 600 W (two times for 15 s irradiation) in Panasonic household MW oven until these solid mixtures resulted in a crude mixture of liquid and a small quantity of unreacted $InCl_3$, which was filtered using a syringe filter to afford colorless single phased liquid. This liquid was fully characterized by NMR spectroscopy and TGA analysis. The bulk temperature recorded was in the range 60–80 °C. The same experiment via conventional heating (glycerol bath at 70 °C for 1 h) resulted only in 73% yield. An experiment on a relatively large scale starting from 30 mmol of indium trichloride and 30 mmol of [C_4mim]Cl afforded the same product (yield: 93%; mp: −6 °C). ^{1}H NMR (300 MHz, D_2O, 25 °C): δ 0.81 (t, ^3J(H,H) = 7.2 Hz, 3H, CH_3); 1.19 (m, 2H, CH_2); 1.72 (m, 2H, CH_2); 3.79 (s, 3H, NCH_3); 4.09 (t, ^3J(H,H) = 7.6 Hz, 2H, NCH_2); 7.30 (d, ^3J(H,H) = 1.5 Hz, 2H, $C_3H_3N_2$); 8.58 (s, 1H, $C_3H_3N_2$). ^{13}C NMR (300 MHz, D_2O, 25 °C): δ 12.6 (CH_3); 18.7 (CH_2); 31.2 (CH_2); 35.7 (NCH_3); 49.3 (NCH_2); 122.2 ($C_3H_3N_2$); 123.5 ($C_3H_3N_2$); 135.8 ($C_3H_3N_2$).

5. Tetrahydropyranyl (THP) ethers—general procedure

The experimental set-up for the MW experiment was the commercially available 'Discover Focused Microwave Synthesis System' from CEM Corporation, with a proper temperature and a pressure control.[8] In a typical procedure, a mixture of benzyl alcohol (10 mmol), 3,4-dihydro-2*H*-pyran (11 mmol), and [C_4mim][$InCl_4$] (2.5 mmol) was charged in a round-bottom glass flask (50 mL) containing a magnetic stirring bar and a reflux condenser. The flask was placed in the microwave cavity, which is designed to house a round-bottom flask. The flask was subjected to MW irradiation at 60 °C (power 100 W) for a specified period. After completion of the reaction, the flask was removed and cooled to room temperature. The progress of the reaction was followed using GC–MS and the disappearance of the signal for the starting alcohol in the GC determined the completion of reaction. The product was extracted with ether and filtered through the short silica column to remove any impurities. The residual 3,4-dihydro-2*H*-pyran and solvent were removed on a rotary evaporator followed by vacuum drying to afford THP-ether (79% yield).

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References and notes

1. For leading reviews, see: (a) Welton, T. *Chem. Rev.* **1999**, *99*, 2071; (b) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3772; (c) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667; (d) Olivier-Bourbigou, H.; Magna, L. *J. Mol. Catal. A* **2002**, *182–183*, 419; (e) Sheldon, R. *Chem. Commun.* **2001**, 2399; (f) Zhao, D.; Wu, M.; Kou, Y.; Min, E. *Catal. Today* **2002**, *74*, 157.
2. (a) Rogers, R. D.; Seddon, K. R. In *Ionic Liquids as Green Solvents: Progress and Prospects*. ACS Symposium Series 856; American Chemical Society: Washington, DC, 2003; (b) Rogers, R. D.; Seddon, K. R. *Science* **2003**, *302*, 792; (c) Kim, D. W.; Song, C. E.; Chi, D. Y. *J. Am. Chem. Soc.* **2002**, *124*, 10278; (d) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometalics* **2002**, *21*, 2866; (e) Bates, E. D.; Mayton, R. D.; Ntai, I.; Davis, J. D., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 926; (f) Adams, C. J.; Earle, M. J.; Seddon, K. R. *Chem. Commun.* **1999**, 1043; (g) Lee, H.; Kim, D. B.; Kim, S.-H.; Kim, H. S.; Kim, S. J.; Choi, D. K.; Kang, Y. S.; Won, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3053.
3. (a) Kim, H. S.; Kim, Y. J.; Lee, H.; Park, K. Y.; Lee, C.; Chin, C. S. *Angew. Chem., Int. Ed.* **2002**, *41*, 4300; (b) Kim, H. S.; Kim, Y. J.; Bae, J. Y.; Kim, S. J.; Lah, M. S.; Chin, C. S. *Organometallics* **2003**, *22*, 2498; (c) Brown, R. J. C.; Dyson, P. J.; Ellis, D. J.; Welton, T. *Chem. Commun.* **2001**, 1862; (d) Kim, H. S.; Kim, J. J.; Kim, H.; Jang, H. G. *J. Catal.* **2003**, *220*, 44; (e) Peng, J.; Deng, Y. *New J. Chem.* **2001**, *25*, 639; (f) Li, F.; Xiao, L.; Xia, C.; Hu, B. *Tetrahedron Lett.* **2004**, *45*, 8307.
4. da Silveira Neto, B. A.; Ebeling, G.; Goncalves, R. S.; Gozzo, F.; Eberlin, M. N.; Dupont, J. *Synthesis* **2004**(8), 1155.
5. (a) Varma, R. S.; Namboodiri, V. V. *Chem. Commun.* **2001**, 643; (b) Varma, R. S.; Namboodiri, V. V. *Pure Appl. Chem.* **2001**, *73*, 1309.
6. (a) Varma, R. S. In *Green Chemistry: Challenging Perspectives*; Tundo, P., Anastas, P. T., Eds.; Oxford University Press: Oxford, 2000; pp 221–244; (b) Varma, R. S. In *Green Chemical Synthesises and Processes*. Anastas, P. T., Hein, L. G., Williamson, T. C., Eds.; ACS Symposium Series 767; American Chemical Society: Washington, DC, 2001; pp 292–312; (c) Varma, R. S. *J. Heterocycl. Chem.* **1999**, *35*, 1565; (d) Varma, R. S. *Green Chem.* **1999**, *1*, 43; (e) Varma, R. S. *Advances in Green Chemistry: Chemical Syntheses Using Microwave Irradiation*; AstraZeneca Research Foundation: Bangalore, India, 2002. Free copy available on request from: azrefi@astrazeneca.com; (f) Varma, R. S. *Pure Appl. Chem.* **2001**, *73*, 1309.
7. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley & Sons Inc.: New York, 1999.
8. Kim, Y. J.; Varma, R. S. *Tetrahedron Lett.* **2004**, *45*, 7205.