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Microwave-assisted preparation of 1-butyl-3-methylimidazolium tetrachlorogallate and its catalytic use in acetal formation under mild conditions

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Abstract—1-Butyl-3-methylimidazolium tetrachlorogallate, [bmim][$GaCl_4$], prepared via microwave-assisted protocol, is found to be an active catalyst for the efficient acetalization of aldehydes under mild conditions.

1. Introduction

Acetalization is one of the most widely used methods for protecting carbonyl compounds during multistep synthesis in organic, medicinal, and drug chemistry.[1] Besides their use as protecting groups, acetals have found many applications such as in fragrances, in cosmetics, as food additives, in detergents, and in polymer chemistry.[2] They are usually obtained by treatment of aldehydes with alcohol and/or corresponding orthoformate in the presence of a protic acid catalyst. Some of these methods employ *p*-toluenesulfonic acid (PTSA),[3a] Me_3-SiOTf,[3b] BF_3/etherate,[3c] $FeCl_3$,[3d] and dry HCl.[3e] However, the use of toxic and corrosive materials and the production of large volumes of salt waste during neutralization of the acids render these processes cumbersome with respect to both industrial and environmental viewpoints. Accordingly, there have been numerous efforts to overcome the drawbacks by using solid acid catalysts such as polymer-bound metal complexes,[4a] titanium cation-exchanged montmorillonite,[4b] Ru(III),[4c,d] Co(III),[4e] and In(III) trichloride[4f] for the acetal formation. However, most of these catalyst systems are used at elevated temperatures or for longer reaction times. Notable among these has been SO_3H-functionalized silica that shows significant improvement in the catalytic activity under nearly neutral conditions.[5]

There have been increasing efforts to utilize room temperature ionic liquids (RTILs) as active catalysts and/or green reaction media for organic synthesis.[6–8] Although an acid functionalized 'task-specific' IL system for the title reaction provided high catalytic performance, there are still disadvantages in using a large amount of these ILs to achieve optimum yields.[8f] Recently, indium(III) and gallium(III) compounds have gained widespread application as efficient Lewis acid catalysts for various important organic synthetic transformations.[9] During the course of our study on preparation of the indium- and gallium-based RTILs and their use, both as solvent and as a catalyst for organic synthesis,[10] we have found that imidazolium-based organogallate as well as organoindate afforded improved catalytic performance on the acetal formation.

In this letter, we describe an improved preparation of imidazolium-based organogallate, [bmim][$GaCl_4$] (bmim = 1-butyl-3-methylimidazolium) and its use as an active catalyst system that offers improved catalytic activity for the acetalization of various aldehydes to generate products in high yields at room temperature.

Ionic liquids were synthesized using microwave (MW) irradiation under solvent-free conditions.[11] Admixing equimolar amounts of $InCl_3$ or $GaCl_3$ with 1-butyl-3-methylimidazolium chloride, [bmim]Cl, followed by

Keywords: Microwave irradition; Tetrachlorogallate ionic liquid; Aldehyde; Acetal formation.
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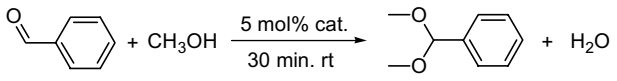
Table 1. Acetalization of benzaldehyde with various catalysts[a]



Entry	Catalyst	Yield[b] (%)
1	$InCl_3$	40
2	$GaCl_3$	55
3	[bmim][$InCl_4$]	70
4	[bmim][$GaCl_4$]	81

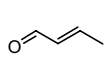
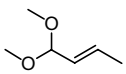
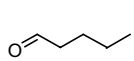
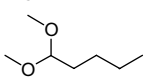
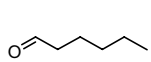
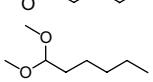
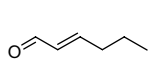
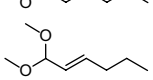
[a] Conditions: benzaldehyde 5.66 mmol, catalyst 0.28 mmol (5 mol %), rt for 30 min, bmim = 1-butyl-3-methylimidazolium.
[b] Isolated yield.

MW irradiation for 30 s (15 s × 2 times) afforded pure ionic liquid compounds. The NMR spectra of the ionic liquids obtained from MW reactions were in conformity with the structure.

Initial exploratory acetalization reactions were performed using benzaldehyde with methanol in the presence of $InCl_3$ or $GaCl_3$ at room temperature for 30 min. However, these reactions afforded corresponding acetals only in 40% and 55% yield, respectively (Table 1, entries 1 and 2). This prompted us to investigate further the use of [bmim][$InCl_4$] and [bmim][$GaCl_4$]. We envisaged that the incorporation of imidazolium into the indium(III) or gallium(III) chlorides would facilitate the transformation reaction since imidazolium cation can act as an intermediate–stabilizer during catalysis.[8a,b,10b] Indeed, the yields increased to 70% and 81%, respectively, when [bmim][$InCl_4$] and [bmim][$GaCl_4$] were used as catalyst (Table 1, entries 3 and 4).

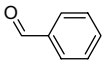
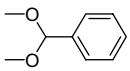
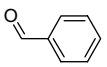
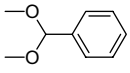
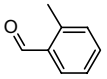
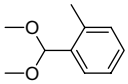
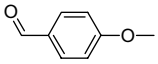
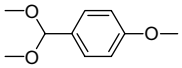
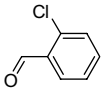
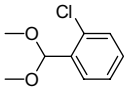
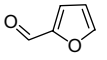
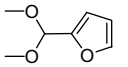
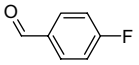
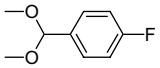
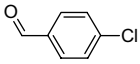
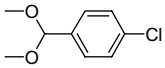
The acetalization of various aliphatic aldehydes were carried out using 5 mol % of [bmim][$GaCl_4$] as a model catalyst at room temperature for 30 min. As shown in Table 2, acetaldehyde and propionaldehyde were converted to corresponding acetals quantitatively.

Table 2. Acetalization of various aliphatic aldehydes using [bmim][$GaCl_4$][a]

Entry	Substrate	Product	Yield[b] (%)
1			97
2			98
3			55
4			88
5			78
6			51

[a] Conditions: substrate 5.66 mmol, [bmim][$GaCl_4$] 0.28 mmol (5 mol %), rt for 30 min.
[b] Isolated yield.

Table 3. Acetalization of various aromatic aldehydes using [bmim][$GaCl_4$][a]

Entry	Substrate	Product	Yield[b] (%)
1			81
2[c]			80
3			58
4			72
5			81
6			78
7			79
8			79

[a] Conditions: substrate 5.66 mmol, [bmim][$GaCl_4$] 0.28 mmol (5 mol %), rt for 30 min.
[b] Isolated yield.
[c] Yield after five recycles.

Likewise, crotonaldehyde, *n*-valeraldehyde, *n*-hexanal, and *trans*-2-hexanal were transformed to the respective acetals in 51–88% yields. The protection methodology was equally successful for a variety of aromatic aldehydes, providing moderate to good yields of corresponding acetals (Table 3). However, the *o*-tolualdehyde (entry 3) produced the product in only 58% yield, probably due to the steric hindrance. The ketones, for example, cyclohexanone derivatives afforded 67–70% yields under same reaction conditions (data not shown).

To investigate the possibility of recycling the catalyst, the [bmim][$GaCl_4$] was recovered for further use by simply extracting the products with diethyl ether, which formed a separate layer and was conveniently decanted off, followed by fresh charge of reactants in the same reaction vessel. The recycling study with the ionic liquid catalyst revealed that the catalyst could be recycled several times without much loss of its reactivity (Table 3, entry 2, after five cycles).

In conclusion, a mild, simple, efficient, and eco-friendly protocol has been developed for the protection of aldehydes as acetals in the presence of imidazolium-based organogallate that provides good to high yields.

2. Preparation of [1-butyl-3-methylimidazolium]-[$GaCl_4$]—general microwave-assisted procedure

In a typical method, gallium trichloride (5.0 mmol) and 1-butyl-3-methylimidazolium chloride (5.1 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 a crude mixture of the liquid and a small quantity of unreacted $GaCl_3$ remained, which was filtered using a syringe filter to afford colorless single phased liquid. This product was fully characterized by NMR spectroscopy. (Yield: 94%) Anal. Calcd for $C_8H_{15}Cl_4GaN_2$: C, 27.39; H, 4.31; N, 7.99. Found: C, 27.46; H, 4.34; N, 8.02. ^{1}H NMR (300 MHz, DMSO-d_6, 25 °C): δ 9.12 (s, 1H, imidazolium ring); 7.76 (s, 1H, imidazolium ring); 7.70 (s, 1H, imidazolium ring); 4.16 (t, $J = 7.1$, H, –NCH_2R); 3.85 (s, 3H, –NCH_3); 1.77 (m, 2H, –CH_2–); 1.25 (m, 2H, –CH_2–); 0.91 (t, $J = 7.0$, 3H, –CH_3). ^{13}C{^{1}H} NMR (75 MHz, DMSO-d_6, 25 °C): δ 136.5, 123.6, 122.2 (imidazolium ring); 48.5 (–NCH$_2$R); 35.7 (–NCH$_3$); 31.3 (–CH$_2$–); 18.7 (–CH$_2$–); 13.2 (–CH$_3$).

3. Acetalization—general procedure

In a typical procedure, methanolic solution (1.0 mL) of benzaldehyde (5.66 mmol) was placed in a round-bottomed glass flask (25 mL) and [bmim][$GaCl_4$] (0.28 mmol) was added. The reaction mixture was stirred at room temperature for 30 min. After completion of the reaction (TLC monitoring), the product was extracted with ether and filtered through the short silica column to remove any impurities, followed by vacuum drying to afford pure dimethylacetal (81% yield).

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