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Brönsted acidic ionic liquid ([Hmim][HSO_4]) as a green, efficient and reusable catalyst for the tetrahydropyranylation of alcohols

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ABSTRACT

A simple and mild method for tetrahydropyranylation of alcohols is reported at room temperature using a catalytic amount of 3-methylimidazolinium hydrogensulfate ([Hmim]HSO_4) as a green, efficient and reusable catalyst. Using solvent-free conditions, non-toxic and inexpensive materials, modest and clean work-up, short reaction times and high yields of the products are the advantages of this method.

Keywords*: Brönsted acidic ionic liquids, Catalyst, Tetrahydropyranylation, Alcohols.*

1. Introduction

Recently, ionic liquids have gained recognition as environmentally benign alternatives to more volatile organic solvents and functional materials in many fields because of their interesting properties such as broad liquid range, negligible vapor pressure, high thermal stability and good solvating ability for a vast range of substrates and catalysts [1-7]. Our specific interest in ionic liquids is its design ability, thus giving us the ability to manipulate the structure (with respect to the organic cation and inorganic anion) and consequently, their properties. Apart from this, they exhibit acidic properties [8-9]. Brönsted acidic ionic liquids have been successfully applied to a variety of reactions including esterification of carboxylic acids [10], protection and deprotection of aldehydes and ketons [11-12], cleavage of ethers [13], oxidation [14], iodination of alcohols [15], acetylation of alcohols [16], preparation of azides from alcohols [17], and synthesis of organic compounds [18].
Tetrahydropyran (THP) is an attractive protecting group that is often used for the protection of alcohols and phenols due to their ease of preparation and stability under a wide variety of reaction conditions such as hydrides, alkylating reagents, Grignard reagents and organometallic reagents [19-20]. There are several known methods for the tetrahydropyranylation and depyranylation of alcohols. The most commonly used reagents that can catalyze the protection and deprotection of both transformations are pyridinium *p*-toluenesulfonate (PPTS) [21], pyridinium chloride [22], acetonyltriphenylphosphonium bromide [23], I_2 [24], $ZrCl_4$ [25], tetra-butylammonium tribromide [26], $Fe(ClO_4)_3$ [27], $K_5CoW_{12}O_4.3H_2O$ [28], benzyltriphenyl phosphonium-tribromide [29], $PdCl_2(CH_3CN)_2$ [30], trichloroisocyanuric acid [31], silica sulfuric acid [32], $La(NO_3)_3.6H_2O$ [33], aqueous zinc tetra- fluoroborate [34], $AlCl_3.6H_2O$ [35], and *N*, *N*′-Dibromo-*N*, *N*′-1,2-ethanediylbis(benzene sulfonamide) (BNBBS) [36].
However, in most cases, these procedures suffer from one or more disadvantages such as stringent conditions, elevated reaction temperatures, longer reaction times, and expensive reagents. Thus, there is a need for a mild, fast and catalytically efficient alternative for the protection of hydroxyl groups as THP ethers.

2. Experimental

The yields refer to isolated pure products. The products were characterized by comparison of their spectral data (^{1}H NMR, IR) and melting and boiling points with authentic samples (authentic samples prepared by reported methods) [37-39]. All ^{1}H NMR spectra were recorded at 400 MHz in $CDCl_3$ relative to TMS (0.00 ppm) on a Bruker, Avance 500 instrument (Rheinstetten, Germany) and Varian 400 NMR. All of the reactions were carried out in a hood with strong ventilation. IR spectra were recorded on Shimadzu 435 IR spectrophotometer. Spectra of solids were carried out using KBr pellets.

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2.1. Preparation of 3-methylimidazolium hydrogensulfate ([Hmim]HSO$_4$)

3-methylimidazolium hydrogensulfate ([Hmim]HSO$_4$) was prepared according to our previous work [5]. 1-Methylimidazole (0.82 g, 0.01 mol) was placed in a two-necked flask with magnetic stirrer and was cooled to 0 ºC. Then 10mL of acetonitrile was added to the reaction mixture, and sulfuric acid (0.98 g, 0.01 mol) was added slowly under stirring. The mixture was stirred for 30 min, and the acetonitrile was removed by simple decanting to afford the ionic liquid in quantitative yields.

2.2. Tetrahydropyranylation of benzyl alcohol: A Typical Procedure

A mixture of benzyl alcohol (1mmol, 0.108 g), 3,4-dihydro-2*H*-pyran (1.2 mmol, 0.1 g) and 3-methylimidazolinium hydrogen sulfate (0.25 mmol, 0.045 g) was ground with a pistol. The completion of the reaction was monitored by TLC (EtOAc: cyclohexane (20:80) or GC. After the reaction was completed, resulting product was isolated by straightforward extraction with dichloromethane and washed with water. The organic layer was dried with Na_2SO_4 and evaporated under reduced pressure. The resulting residue was purified by flash chromatography on SiO_2 (eluent EtOAC-cyclohexane, 20:80) to give 0.188 g (98%) of pure product.

The selected spectral data

2-(phenylmethoxy)tetrahydro-2*H*-pyran (Table 1, entry 1): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.50-1.90 (m, 6 H), 3.48-3.52 (m, 1 H), 3.87-3.90 (m, 1 H), 4.43 (d, *J* = 11.6 Hz, 1 H), 4.69-4.71 (m, 1 H), 4.79 (d, *J* = 12.0 Hz, 1 H) 7.25-7.34 (m, 5 H).

2-(4-methoxybenzyloxy)tetrahydro-2*H*-pyran (Table 1, entry 4): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.40-1.91 (m, 6 H), 3.49-3.51 (m, 1 H), 3.76 (s, 3 H), 3.89-3.91 (m, 1 H), 4.42 (d, *J* = 11.6 Hz, 1 H), 4.68-4.70 (m, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 7.28 (d, *J* = 8.6 Hz, 2 H).

2-(4-chlorobenzyloxy)tetrahydro-2*H*-pyran (Table 1, entry 9): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.53–1.87 (m, 6 H), 3.50–3.56 (m, 1 H), 3.85–3.91 (m, 1 H), 4.44 (d, *J* = 12.2 Hz, 1 H), 4.66–4.68 (m, 1 H), 4.71 (d, *J* = 12 Hz, 1 H), 7.23 (d, *J* = 8.8 Hz, 2 H), 7.46 (d, *J* = 8.8 Hz, 2 H).

2-(2-nitrobenzyloxy)tetrahydro-2*H*-pyran (Table 1, entry 10): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.43-1.99 (m, 6 H), 3.51-3.53 (m, 1 H), 3.88-3.90 (m, 1 H), 4.74-4.76 (m, 1 H), 4.89 (d, *J* = 15.8 Hz, 1 H), 5.15 (d, *J* = 15.6 Hz, 1 H), 7.40 (t, *J* = 7.4 Hz, 1 H), 7.63 (t, *J* = 7.4 Hz, 1 H), 7.80 (d, *J* = 7.6 Hz, 1 H), 8.05 (d, *J* = 8.0 Hz, 1 H).

2-(4-nitrobenzyloxy)tetrahydro-2*H*-pyran (Table 1, entry 12): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.52–1.92 (m, 6 H), 3.51–3.59 (m, 1 H), 3.86–3.92 (m, 1 H), 4.61 (d, *J* = 13.6 Hz, 1 H), 4.73–4.74 (m, 1 H), 4.89 (d, *J* = 13.2 Hz, 1 H), 7.53 (d, *J* = 9.2, 2 H), 8.20 (d, *J* = 8.8 Hz, 2 H).

2-(1-phenylethoxy)tetrahydro-2*H*-pyran (Table 1, entry 13): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.40-1.98 (m, 9 H), 3.49-3.51 (m, 1 H), 3.97-3.99 (m, 1 H), 4.38-4.40 (m, 1 H), 4.89-4.91 (m, 1 H), 7.29-7.31 (m, 5 H).

2-(benzhydryloxy)tetrahydro-2*H*-pyran (Table 1, entry 14): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.51–1.62 (m, 4 H), 1.63–1.75 (m, 1 H), 1.82–2.05 (m, 1 H), 3.45–3.56 (m, 1 H), 3.88-3.90 (m, 1 H), 4.62–4.73 (m, 1 H), 5.81 (s, 1 H), 7.18–7.38 (m, 10 H).

(*E*)-2-(3-phenylallyloxy)tetrahydro-2*H*-pyran (Table 1, entry 16): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.50-1.86 (m, 6 H), 3.49-3.51 (m, 1 H), 3.89-3.91 (m, 1 H), 4.14-4.16 (m, 1 H), 4.38-4.39 (m, 1 H), 4.68-4.70 (m, 1 H), 6.29-6.31 (m, 1 H), 6.60 (d, *J* = 16 Hz, 1 H), 7.15-7.40 (m, 5 H).

2-phenoxytetrahydro-2*H*-pyran (Table 1, entry 17): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.55-2.09 (m, 6 H), 3.60-3.66 (m, l H), 3.92-3.99 (m, l H), 5.45 (t, *J* = 3.3, l H), 7.10 (d, *J* = 9.0 Hz, 2 H), 7.23-7.33 (m, 3 H).

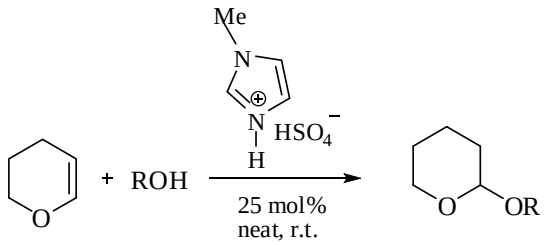
2-(2-phenylethoxy)tetrahydro-2*H*-pyran (Table 1, entry 18): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.45-1.83 (m, 6 H), 2.90 (t, *J* = 7.2 Hz, 2 H), 3.40-3.47 (m, 1 H), 3.61 (dt, *J* = 7.2, *J* = 4.0, 10.0 Hz, 1 H), 3.73-3.75 (m, 1 H), 3.94 (dt, *J* = 7.6, 5.2, 9.6 Hz, 1 H), 4.60 (t, *J* = 3.5 Hz, 1 H), 7.18-7.30 (m, 5 H).

2-(3-phenylpropoxy)tetrahydro-2*H*-pyran (Table 1, entry 19): ^{1}H NMR (400 MHz, $CDCl_3$ ppm) δ: 1.48-1.96 (m, 8 H), 2.68-2.70 (m, 2 H), 3.35-3.49 (m, 2 H), 3.72-3.85 (m, 2 H), 4.55-4.57 (m, 1 H), 7.22-7.24 (m, 5 H).

3. Results and discussion

In continuation of our recent investigations on the organic synthesis [40], and applications of the ionic liquids in chemical reactions [2-8], in this paper we disclose that 3-methylimidazolinium hydrogensulfate ([Hmim]HSO$_4$), as a Brönsted acidic ionic liquid, can be used as a green and efficient catalyst for tetrahydropyranylation of alcohols at room temperature (Scheme1).

The investigation of the reaction conditions for the protection of benzyl alcohol with DHP using [Hmim]HSO$_4$ demonstrated that 0.25 mmol of the catalyst and 1.2 mmol of DHP at room temperature was optimal for the desired tetrahydropyranylation. The results of the reactions of a diverse range of alcohols are collected in Table 1. The data reported show that 3-methylimidazolinium hydrogensulfate can affect tetrahydropyranylation of alcohols in good to excellent yields. Primary benzylic alcohols with electron-donating and electron-withdrawing groups were tetrahydropyranylated in the presence of 0.25 mmol of catalyst and the corresponding tetrahydropyranyl ethers were obtained in good to excellent yields (Table 1, entries 1-12). 1-phenylethanol, benzhydrol and 4-chloro benzhydrol as three model compounds for secondary benzylic alcohols, were satisfactorily subjected to tetrahydropyranylation as well (Table 1, entries 13-15). Moreover,



Scheme 1. An efficient, green, and fast procedure for the tetrahydropyranylation of alcohols**.**

tetrahydropyranylation of saturated alcohols was carried out in the presence of catalytic amount of [Hmim]HSO_4 at room temperature in high yields (Table 1, entries 18-20).

In order to illustrate the catalytic activity of [Hmim]HSO_4, we compared our results for the tetrahydropyranylation of benzyl alcohol with the best of the well-known data from literature (Table 2). As shown in Table 2, [Hmim][HSO_4] can act as an effective catalyst with respect to reaction times, yields and simplified conditions of the obtained products. Finally, the reusability of the catalyst was also investigated so that after each run, the aqueous phase was collected and washed with CH_2Cl_2 to remove organic impurities. Then water was evaporated and the catalyst was dried at 65 °C under reduced pressure for 2 h. It was found that the catalyst could be employed three times, although its activity gradually decreased Table 2 (entry 1).

4. Conclusion

In comparison with other previously reported methods, we have developed a simple and efficient method for tetrahydropyranylation of alcohols at room temperature using [Hmim]HSO_4 as a green, efficient and reusable catalyst. The mild reaction conditions, short reaction times, good to high yields are the advantages of this method.

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Table 1. Tetrahydropyranylation of alcohols in the presence of 3-methylimidazolinium hydrogensulfate[a]

Entry	Substrate	Product	Time (min)	Yield (%)[b]
1	$PhCH_2OH$	$PhCH_2OTHP$	2	98
2	2-$OMeC_6H_4CH_2OH$	2-$OMeC_6H_4CH_2OTHP$	2	95
3	3-$OMeC_6H_4CH_2OH$	3-$OMeC_6H_4CH_2OTHP$	2	90
4	4-$OMeC_6H_4CH_2OH$	4-$OMeC_6H_4CH_2OTHP$	1	97
5	3,4-$(OMe)_2C_6H_4CH_2OH$	3,4-$(OMe)_2C_6H_4CH_2OTHP$	3	92
6	4-$MeC_6H_4CH_2OH$	4-$MeC_6H_4CH_2OTHP$	2	96
7	2-$ClC_6H_4CH_2OH$	2-$ClC_6H_4CH_2OTHP$	2	95
8	3-$ClC_6H_4CH_2OH$	3-$ClC_6H_4CH_2OTHP$	3	93
9	4-$ClC_6H_4CH_2OH$	4-$ClC_6H_4CH_2OTHP$	2	95
10	2-$NO_2C_6H_4CH_2OH$	2-$NO_2C_6H_4CH_2OTHP$	3	80
11	3-$NO_2C_6H_4CH_2OH$	3-$NO_2C_6H_4CH_2OTHP$	3	87
12	4-$NO_2C_6H_4CH_2OH$	4-$NO_2C_6H_4CH_2OTHP$	3	85
13	$C_6H_4CHOHCH_3$	$C_6H_4CHOTHPCH_3$	3	92
14	PhCHOHPh	PhCHOTHPPh	5	95
15	4-$ClC_6H_4CHOHPh$	4-$ClC_6H_4CHOTHPPh$	5	95
16	Ph-CH=CH-CH_2OH	Ph-CH=CH-CH_2OTHP	5	80
17	PhOH	PhOH	10	40
18	$PhCH_2CH_2OH$	$PhCH_2CH_2OTHP$	2	95
19	$Ph(CH_2)_3OH$	$Ph(CH_2)_3OTHP$	2	90
20	$Ph(CH_2)_4OH$	$Ph(CH_2)_4OTHP$	3	90

[a]The reaction was carried out at room temperature under solvent–free conditions and the molar ratio of alcohol/ DHP/ IL was 1:1.2:0.25.
[b]Yields based on the isolated pure products after chromatography and confirmed by comparison with authentic samples (TLC, GC, IR, and NMR).

Table 2. Comparison of the activity of various catalysts in the tetrahydropyranylation of benzyl alcohol.

Entry	Catalyst	Conditions	DHP: Cat	Time (min)	Yield (%)	Ref
1	$[Hmim]HSO_4$ (first run) (2nd run) (3nd run)	Solvent-free, r.t.	1.2: 0.25	2 4 6	98 90 86	This work
2	TBATB	CH_2Cl_2, r.t.	5.5:0.1	60	85	26
3	$La(NO_3)_3.6H_2O$	Solvent-free, r.t.	1:0.1	150	93	33
4	$Fe(ClO_4)_3$	Et_2O	5:0.15	90	98	27
5	BNBBS	CH_2Cl_2, r.t.	1.2:0.01	110	89	36
6	$PdCl_2(CH_3CN)_2$	THF, r.t.	1.1:0.1	60	72	30

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