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Efficient Role of Ionic Liquid (bmim)HSO_4 as Novel Catalyst for Monotetrahydropyranylation of Diols and Tetrahydropyranylation of Alcohols

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Efficient Role of Ionic Liquid (bmim)HSO_4 as Novel Catalyst for Monotetrahydropyranylation of Diols and Tetrahydropyranylation of Alcohols

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Abstract: A simple procedure for the monotetrahydropyranylation of diols and alcohols, in excellent to moderate yields, has been reported using a catalytic amount of the acidic ionic liquid, 1-butyl-3-methylimidazolium hydrogensulphate (bmim)HSO_4 under microwave and ultrasonic irradiation. Results have been compared with those obtained by reactions in the absence of these energies, and effectiveness of the recycled ionic liquid has also been studied.

Keywords: Ionic liquid, microwave irradiation, monotetrahydropyranylation, selective, solvent-free, tetrahydropyranylation, ultrasound

Room-temperature ionic liquids[1] have gained great impetus as attractive, promising, and green media or catalysts for various organic syntheses.[2] This popularity arises because of their unique properties such as negligible vapor pressure, thermal stability, recyclability, immiscibility with nonpolar organic solvents, catalytic efficiency, and use in biphasic systems. In fact, their high polarity makes them excellent media to facilitate microwave-assisted organic reactions.[3]

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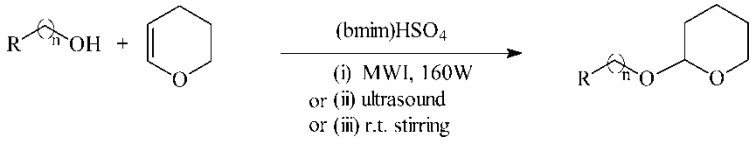
The prevalence of alcoholic groups in many multifunctional natural and pharmaceutical products makes their protection an essential prerequisite for many synthetic endeavors. Of the many protective reagents available for such a conversion, 3,4-dihydro-2*H*-pyran (DHP) has proven to be very efficient,[4] more so because the resultant tetrahydropyranyl (THP) ether is easily prepared, inexpensive, easy to deprotect, and stable in strong basic media.

Several methods are available for the protection of alcohols as THP ethers;[5] very few, however, report the selective monoprotection of 1,n diols as THP ethers. More recently, acidic ion exchange resins/metallic sulphate supported on silica gel[6] and microwave energy in combination with iodine[7] have been used to carry out the monoprotection of different diols. Ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate [(bmim)PF_6] has also been reported in conjunction with indium trichloride[8] for the protection of alcoholic group. Most of the methods require long reaction times, tedious reaction setup, difficult separation, and a large amount of solid support, leading to waste-disposal problems.

The acidic ionic liquid 1-butyl-3-methylimidazolium hydrogensulphate (bmim)HSO_4 has yet not been explored[9] in organic reactions to a great extent even though it holds great potential because of its Bronsted acidity[10] and highly polar nature, which augments absorption of microwave energy. In continuation of our endeavor for the utilization of greener technologies, such as microwave (MW) and ultrasound (US), for assisting organic synthesis[11] and ongoing work on the use of (bmim)HSO_4 in organic reactions,[12] we report herein its use for the tetrahydropyranylation of different alcohols and selective monotetrahydropyranylation of 1,n diols under solvent-free or biphasic conditions using microwave and ultrasonic energies. In all the reactions carried out, the separation of the ionic liquid was very effective and convenient by simply extracting the reaction mixture with diethyl ether or separating the hexane layer; the residue thus obtained contained the ionic liquid.

Protection of alcohols as THP ethers (Scheme 1) was carried by mixing equimolar amounts of alcohol, DHP, and a catalytic amount of ionic liquid (which was easily prepared under microwave irradiation[12]) followed by exposure to microwave radiations (160 W) for 1.5 to 2 min, ultrasound energy for 5 to 7 min, or stirring at room temperature up to 60 min to yield the pure ethers in excellent to quantitative yields without the need for further purification. The products were characterized by ^{1}H NMR

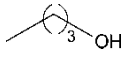
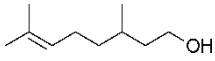
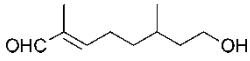
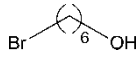
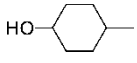
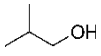
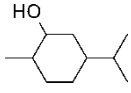
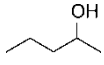
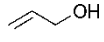
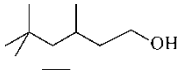
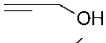
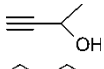
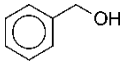
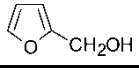


Scheme 1.

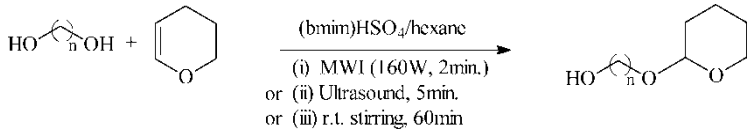
spectroscopy, which showed the absence of unreacted alcohol. Results obtained are given in Table 1.

When diols were subjected to similar reaction conditions (i.e., mixing equimolar amounts of alcohol, DHP, and a catalytic amount of ionic liquid)

Table 1. Tetrahydropyranylation of different alcohols using (bmim)HSO_4

		Microwave		Ultrasound		Stirring	
Sr. no.	Reactant	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
1		1.5	98	5	97	25	92
2		1.5	89	5	81	45	78
3		1.5	84	5	82	45	80
4		2	94	6	92	60	90
5		2	93	7	92	60	90
6		2	96	6	96	60	82
7		2	88	6	86	60	89
8		2	75	6	71	60	62
9		2	86	6	85	60	74
10		2	90	6	92	60	74
11		2	90	6	90	45	90
12		1.5	98	5	98	45	95
13		2	89	6	90	60	89
14		2	76	6	74	60	71
15		1.5	92	6	92	60	90
16		1.5	89	5	90	45	90

Note: All the compounds were characterized on the basis of ^{1}H NMR and IR spectral data, which were found to be consistent with that reported in literature. [^{1}H NMR and IR data of product 1 is reported in Ref. 16(i)].



Scheme 2.

followed by exposure to microwave/ultrasonic energies (Method 1), selectivity up to 75% of monoether was obtained.

However, when the reaction was conducted under biphasic conditions (Scheme 2), using hexane as the upper nonpolar layer, excellent selectivity (~90%) was achieved. Results have been tabulated (Table 2). Understandably, diols have greater miscibility in the lower (ionic liquid) phase and on conversion to monotetrahydropyranyl ether, pass into the hexane layer, minimizing formation of ditetrahydropyranyl ether and at the same time facilitating the recovery of monotetrahydropyranyl ether from the hexane layer.

For the microwave-assisted reactions, different conditions were studied for optimization of results. It was found that output power of microwaves of more than 320 W resulted in charring of the reaction mixture whereas irradiation at 320 W led to a decrease in the activity of the recycled ionic liquid with no further increase in the yields. The power output of choice was thus set at 160 W. In the case of reactions conducted ultrasonically and by stirring, further increase in the time beyond that reported did not result in any appreciable increase in the yield of the products.

In the case of 3,7-dimethyloctane-1,6-diol (entry 5, Table 2), solventless conditions (Method 1) provided moderate yields and biphasic conditions (Method 2) gave good yields of monoether of the corresponding primary hydroxyl group.

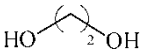
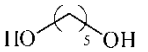
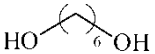
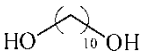
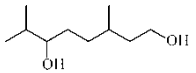
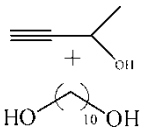
The effectiveness of recycled ionic liquid was studied in the experiments relating to tetrahydropyranylation of 1-butanol. We were able to recycle the ionic liquid once under microwave irradiation, seven times under ultrasonic conditions, and at least nine times under conditions of stirring (Fig. 1) to obtain minimum yields up to 50%.

It was observed that experiments under microwave irradiation gave the best yields, but led to decomposition of the ionic liquid, resulting in only 50% yield of the protected alcohol from the first recycled crop of ionic liquid. Under conditions of stirring at room temperature, the time taken to carry out the reaction was much longer as compared with those assisted by microwave or ultrasonic energies.

The reaction seems to progress via the normal acid-catalyzed pathway brought about by the highly acidic nature of the ionic liquid.

In conclusion, a new method has been projected for the solvent-free convenient and simple protection of alcohols as tetrahydropyranyl ethers in excellent yields and the monoprotection of diols with high selectivity

Table 2. Monotetrahydropyranylation of different diols using acidic ionic liquid (bmim)HSO_4

		Microwave, yield (%) of ether(s)				Ultrasound, yield (%) of ether(s)				Stirring, yield (%) of ether(s)			
		Method 1[a]		Method 2[b]		Method 1[a]		Method 2[b]		Method 1[a]		Method 2[b]	
Sr. no.	Reactant	Mono	Di	Mono	Di	Mono	Di	Mono	Di	Mono	Di	Mono	Di
1		69	25	86	4	66	25	85	7	66	29	84	10
2		68	23	89	5	65	23	86	8	65	30	88	7
3		75	15	97	—	72	18	88	5	68	25	85	8
4		72	18	98	—	68	18	87	7	65	28	86	8
5		55	20	75	12	52	25	70	15	50	32	60	18
6		70	20	92	4	68	22	80	18	64	30	72	25

Note: All the compounds were characterized on the basis of ^{1}H NMR and IR spectral data, which were found to be consistent with that reported in literature. [^{1}H NMR and IR data of product 3 is reported in Ref. 16(ii)].

[a]Percentage yields of reactions executed via Method 1 after purification by column chromatography.

[b]Percentage yields of reactions executed via Method 2 after purification by column chromatography.

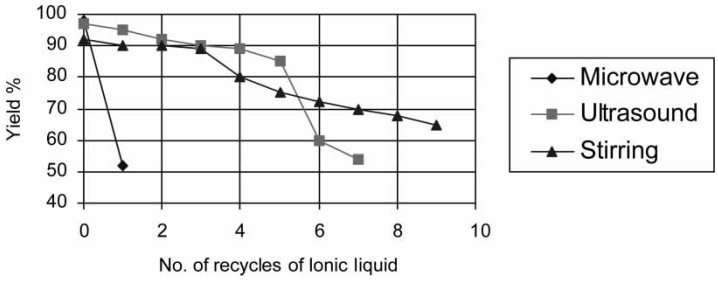


Figure 1. Comparison of yields from recycled Ionic liquid.

via the use of recyclable and catalytic amount of ionic liquid (bmim)HSO_4, which does not require any additives. The notable features of the method are its operational simplicity, ease of preparation of catalyst, lability with which the ionic liquid can be removed from the reaction mixture without contamination, and reduced reaction time and waste products.

General Procedure for Tetrahydropyranylation of Alcohols

Microwave Irradiation

A mixture of alcohol (3 mmol), DHP (3 mmol), and (bmim)HSO_4 (0.1 g, 0.42 mmol) was put in a 10-mL conical flask, covered with a watch glass, and exposed to MW radiations (160 W) in a domestic microwave oven [LGMS-194A (800 W)] for the specified time. The mixture was cooled and extracted with ether (2×10 mL), and the combined ethereal layer was passed through a short pad of silica. Evaporation of solvent under reduced pressure afforded pure protected alcohol (Table 1).

Sonication

The previously mentioned reaction mixture was exposed to ultrasonic waves using a Branson [B-2200 EI, (60 W, 47 kHz)] ultrasonic cleaning bath for the requisite time followed by workup to yield the pure product (Table 1).

Stirring

The reaction mixture previously mentioned was put in a round-bottomed flask and stirred at room temperature. On completion of the reaction, as monitored by TLC, the usual workup was carried out to yield the pure product (Table 1).

General Procedure for Monotetrahydropyranylation of Diols

Method 1: Solvent-Free Conditions

Microwave irradiation. A mixture of 1,n diol (3 mmol), DHP (3 mmol), and (bmim)HSO_4 (0.1 g, 0.42 mmol) in a 10-mL conical was covered with a watch glass and irradiated at 160 W for 2 min. The mixture was cooled and extracted with diethyl ether (2 × 10 mL); combined organic extracts were concentrated in vacuo and the resultant mixture of products was separated via column chromatography. The diether was obtained on eluting with hexane and monoether with 2% ethylacetate in hexane (Table 2).

Sonication. The reaction mixture was sonicated for 5 min and worked up as before. Results are given in Table 2.

Stirring. The reaction mixture was stirred at room temperature for 1 h and worked up as mentioned to yield mono and diethers (Table 2).

Method 2: Biphasic Conditions

Microwave irradiation. To a mixture of 1,n diol (3 mmol) and DHP (3 mmol) in a 10-mL conical was added (bmim)HSO_4 (0.2 g, 0.85 mmol) and hexane (1 mL). The conical was covered with a watch glass and irradiated at 160 W for the time specified. On cooling, the hexane layer was decanted, the remaining ionic liquid was extracted with ether (2 × 10 mL), and the combined organic layer was evaporated in vacuo to yield the crude product, which was purified by column chromatography using 2% ethyl acetate in hexane as eluent to furnish the pure monoprotected alcohol in excellent yield (Table 2).

Sonication. The reaction mixture was sonicated for the time specified and worked up as before to yield (after column purification) the pure product (Table 2).

Stirring. The mixture was stirred at room temperature and, on completion of reaction, as monitored by TLC, the pure product was obtained after usual workup and column purification (Table 2).

Recycling of Ionic Liquid

Residual ionic liquid obtained after the workup was stirred with diethyl ether (10 mL) for 15 min, and the ethereal layer was decanted. The ionic liquid was dried under reduced pressure and refrigerated under nitrogen for further use.

^{1}H NMR and IR Data of Selected Compounds

IR spectra were recorded on a Perkin-Elmer R X 1 FT-IR spectrophotometer, and ^{1}H NMR spectra were recorded on a FT JEOL 300-MHz spectrometer

with $CDCl_3$ and CCl_4 as solvent. Chemical shift is reported as ppm downfield from Me_4Si.

2-Butoxy-tetrahydro-pyran (product 1, Table 1)

^{1}H NMR: δ 4.54 (s, 1H), 3.42–3.48 (m, 4H), 1.66–1.82 (m, 6H), 1.26–1.45 (m, 4H), 0.98 (t, 3H). IR (neat) ν: 2941, 2860, 1466, 1353, 1121, 1138 cm^{-1}.

6-(Tetrahydro-pyran-2-yloxy)-hexan-1-ol (product 3, Table-2)

^{1}H NMR: δ 4.47 (s, 1H), 3.44–3.69 (m, 6H), 3.24 (s, 1H) D_2O exchangeable, 1.61–1.78 (m, 6H), 1.32–1.49 (m, 8H). IR (neat) ν: 3422, 2938, 2860, 1466, 1353, 1121, 1138 cm^{-1}.

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