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Synthesis of Tetrahydrofuran and Tetrahydropyran Derivatives Catalyzed by Tungstophosphoric Acid in Ionic Liquid

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Abstract: Synthesis of tetrahydrofuran and tetrahydropyran derivatives catalyzed by tungstophosphoric acid ($H_3PW_{12}O_{40}$) were conveniently performed with high yield from the corresponding unsaturated alcohols in ionic liquid. Sufuric acid (H_2SO_4), trifluoromathanesulfonic acid (TfOH) and *p*-toluenesulfonic acid (TsOH) were also explored for preparing these products in ionic liquid. The catalysts and ionic liquid can be easily recovered and reused.

Keywords: Tetrahydrofuran and tetrahydropyran derivatives, tungstophosphoric acid, ionic liquid, catalyst, synthesis.

The tetrahydrofuran and tetrahydropyran derivatives are widely found in many natural products of biological interest[1]. They are also found in many perfume and flavour[2]. The preparation of such important subunit is still a challenge for the chemists[3,4]. Heteropoly acids (HPAs) as catalysts and ionic liquid as solvent have been found widespread application in organic reactions[5,6]. To develop "green chemistry" synthetic procedures we decided to examine the heteropoly acid ($H_3PW_{12}O_{40}$) as catalyst and probe the potential of ionic liquid as a cheap and environmentally friendly solvent to synthesize tetrahydrofuran and tetrahydropyran derivatives (**Scheme 1**).

Herein we report an efficient conversion of the corresponding unsaturated alco- hols to tetrahydropyran and tetrahydrofuean derivatives catalyzed by tungstophosphoric acid ($H_3PW_{12}O_{40}$) in ionic liquid and accomplished also to use sufuric acid (H_2SO_4), trifluoromethane sulfonic acid (TfOH) and *p*-toluenesulfonic acid (*p*-TsOH) as catalysts in ionic liquid. In addition, we also explored the tungstophosphoric acid ($H_3PW_{12}O_{40}$) as a catalyst and ionic liquid can be recovered in this reaction.

For our initial studies, we examined the role of the ionic liquid on the cyclization of 6-methyl-5-hepten-2-ol as a substrate to tetrahydropyran catalyzed by various acids (**Table 1**)[7,8]. The results indicated that the yield of product was low when sufuric acid and *p*-toluenesulfonic acid were ued as catalyst (entry 1 and 2), and the yield of product was excellent when the tungstophosphoric acid and trifluoromethanesulfonic acid were

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Scheme 1

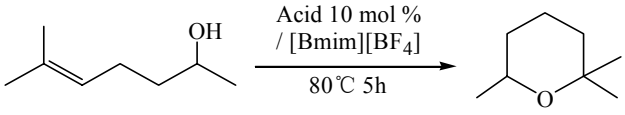


Table 1 The results catalyzed by various acids in ionic liquid[a]

Entry	Acid	Yield(%)[b]
1	H_2SO_4	50
2	*p*-TsOH	58
3	TfOH	85
4	$H_3PW_{12}O_{40}$	85

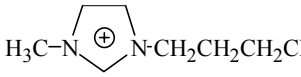
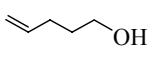
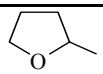
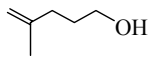
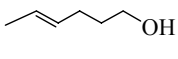
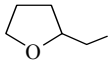
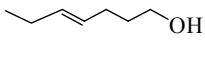
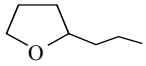
[a] The ionic liquid is  , [b] Isolated yield.

Table 2 The results of cyclization to tetrahydrofuran derivatives[a]

Entry	Substrate	Product	Yield[b]
1			88
2			81
3			75
4			69

[a] Conditions: Substrate (1 mmol), HPAs (0.1 mmol), [bmim][BF_4] (5 mL), 80℃, 5 hours.
[b] Isolated yield.

used as catalysts (entry 3 and 4). We also observed the same result when we used recovered tungstophosphoric acid, trifluoromethanesulfonic acid and ionic liquid separately in these reactions.

Then, to further extend the scope of this green chemistry procedure, we applied this method to prepare tetrahydrofuran derivertives using corresponding unsaturated alcohol as substrate catalyzed by tungstophosphoric acid in ionic liquid (**Table 2**)[9], and found that the cyclizations were also performed with high yield.

In conclusion, we have developed a green chemistry procedure for cyclizations of unsaturated alcohol, and prepared tetrahydrofuran and tetrahydropyran derivatives with high yield. The reaction was catalyzed by heteropoly acid in a cheap and environmentally friendly solvent-ionic liquid. The heteropoly acid and ionic liquid could be recycled in this reaction. Further studies aimed at expanding the scope of the heteropoly acid and ionic liquid for organic synthesis are currently underway.

References and Notes

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7. As a typical experiment, a solution of unsaturated alcohol (1 mmol), HPAs (0.1 mmol), and [bmim][BF_4] (5 mL) was stirred 80℃ for 5 hours. After cooling to ambient temperature, the solution was extracted with toluene, dried with $MgSO_4$ and purified by flash chromatography (Silica gel, hexane:EtOAc = 8:2) to give the title compound as oil. The products were analyzed by ^{1}H NMR and GC.
8. 2, 2, 6-Trimethyltetrahydropyran: ^{1}H NMR ($CDCl_3$, δ ppm) 1.21-1.28 (m, 9H), 1.36-1.41 (m, 2H), 1.52-1.61 (m, 2H), 1.66-1.71 (m, 2H), 3.71 (m, 1H); ^{13}C NMR ($CDCl_3$, δ ppm): 17.6, 22.8, 26.9, 27.3, 34.8, 38.9, 70.8, 75.1.
9. 1-Methyltetrahydrofuran: ^{1}H NMR ($CDCl_3$, δ ppm): 1.21(m, 3H), 1.67(m, 2H), 2.13(m, 2H), 3.49(m, 2H), 3.64 (m, 1H); ^{13}C NMR ($CDCl_3$, δ ppm): 15.6, 30.8, 33.4, 62.4, 66.2.

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