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Cellulose-SO_3H as a recyclable catalyst for the synthesis of tetrahydropyranols via Prins cyclization

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ABSTRACT

Tetrahydropyranols are prepared in good yields and with high *cis*-selectivity by means of the Prins cyclization using cellulose-sulfonic acid under mild reaction conditions. This is the first report on the preparation of tetrahydropyranols using epoxides and homoallylic alcohols via Prins cyclization.

The Prins cyclization is an important reaction to generate a large number of tetrahydropyran derivatives, usually with net addition of an external nucleophile to the resulting carbocation.[1–3] This approach has been successfully employed to the synthesis of complex natural products.[4,5] In particular, tetrahydropyran-4-ols are important building blocks for many biologically active natural products (Fig. 1).[6] Therefore, there is a continuing interest in the development of improved methods for the synthesis of tetrahydropyran-4-ols. Only a few methods are reported for the synthesis of tetrahydropyranols.[7] However, many of these classical methods often involve the use of expensive reagents, high temperatures, extended reaction times, strongly acidic conditions, and also produce mixtures of products. Furthermore, to the best of our knowledge, there have been no examples on the preparation of tetrahydropyranols from epoxides and homoallylic alcohols via the Prins cyclization.

Recently, the use of heterogeneous catalysts has received considerable attention in organic synthesis as powerful catalysts,[8] because of mild reaction conditions, simple experimental procedures, and minimal waste disposal.[9]

Very recently, cellulose-SO_3H has been introduced as a biodegradable heterogeneous solid acid catalyst for the synthesis of quinolines (Friedlander synthesis), α-amino nitriles, aryl-14*H*-dibenzo[*a.j*]xanthenes, tetrahydroquinolines, and functionalized pyrrolidines.[10] However, there are no reports on the use of cellulose-SO_3H for the preparation of tetrahydropyran-4-ols under mild reaction conditions.

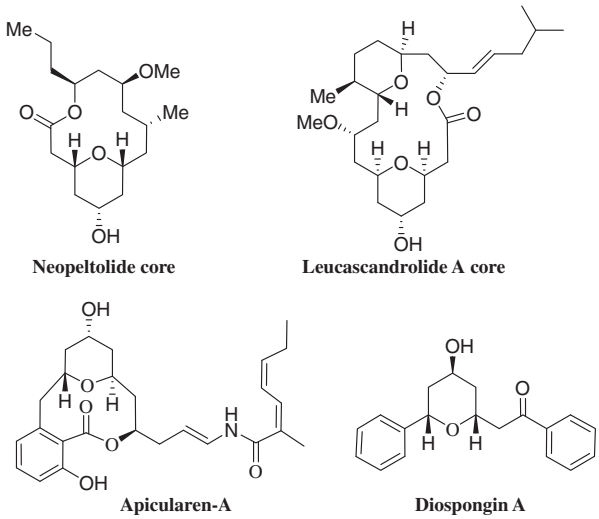

Figure 1. Examples of some natural products bearing tetrahydropyranol skeleton.

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Table 1
Cellulose-SO_3H catalyzed synthesis of tetrahydropyran-4-ols

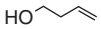
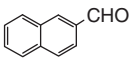
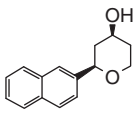
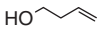
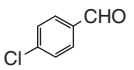
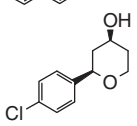
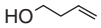
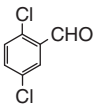
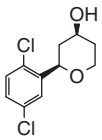
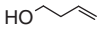
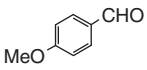
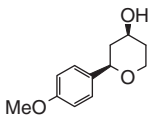
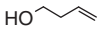
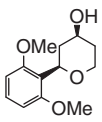
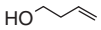
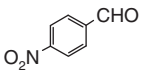
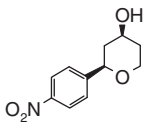
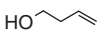
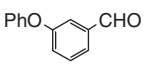
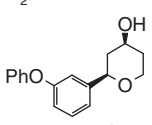
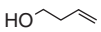
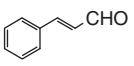
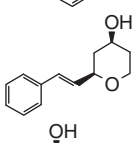
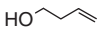
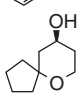
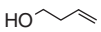
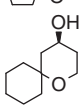
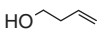
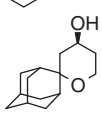
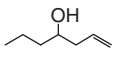
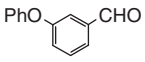
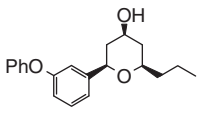
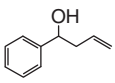
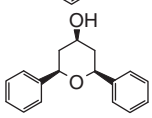
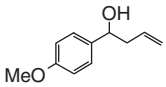
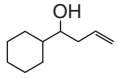
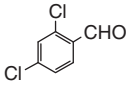
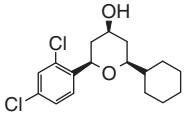
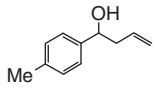
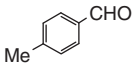
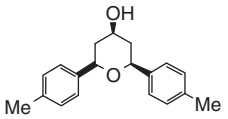
Entry	Alcohols (**2**)	Carbonyl compounds (**1**)	Pyranols[a] (**3**)	Time (min)	Yield[b] (%)
a				60	86
b				65	83
c				75	80
d				90	76
e				100	73
f				120	75
g				90	81
h				90	82
i				140	70
j				140	73
k				150	70
l				90	86
m				90	88
n				90	83
o				90	85

Table 1 (*continued*)

Entry	Alcohols (**2**)	Carbonyl compounds (**1**)	Pyranols[a] (**3**)	Time (min)	Yield[b] (%)
p				90	80
q				100	85

[a] All products were characterized by ^{1}H NMR, ^{13}C NMR, IR and mass spectrometry.
[b] Yield refers to pure products after chromatography.

Table 2
Cellulose-SO_3H catalyzed synthesis of 4-hydroxy tetrahydropyrans with epoxides

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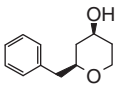
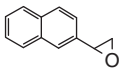
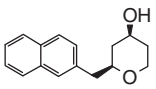
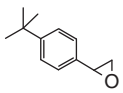
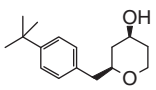
a				55	86
b				60	79
c				50	84
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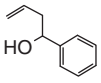
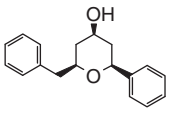
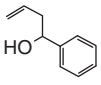
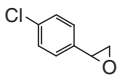
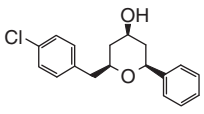
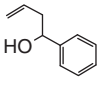
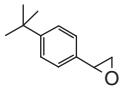
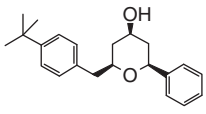
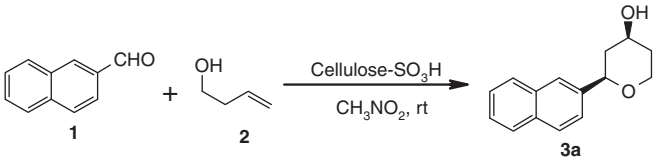
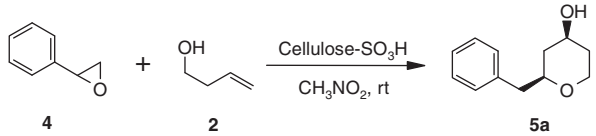
e				60	85
f				75	83
g				65	79

[a] All products were characterized by ^{1}H NMR, ^{13}C NMR, IR and mass spectrometry.
[b] Yield refers to pure products after chromatography.



Scheme 1. Preparation of 2-naphthyl tetrahydropyran-4-ol.



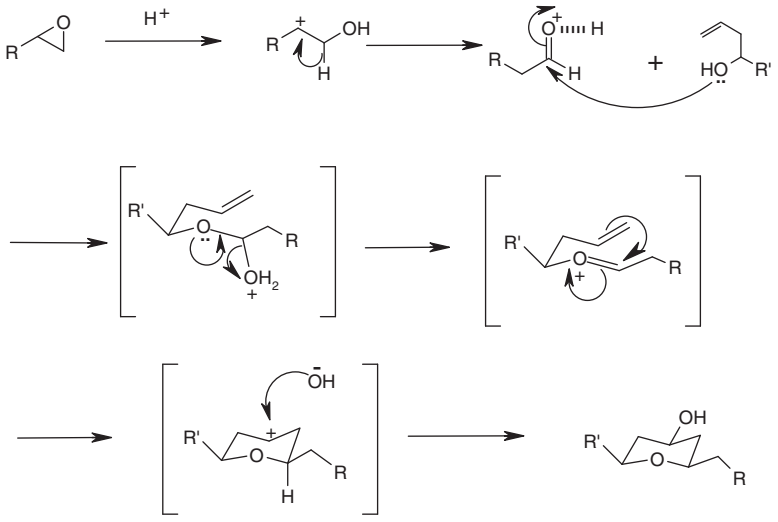
Scheme 2. Preparation of 2-benzyltetrahydropyran-4-ol.

We herein report a novel method for the synthesis of tetrahydropyranols from homoallylic alcohols and carbonyl compounds by means of the Prins cyclization using cellulose-SO_3H under mild conditions. Accordingly, treatment of 2-naphthaldehyde (**1**) with

Table 3
Recycling of cellulose-SO_3H for the preparation of **3a**

Cycle	Yield[a] (%)
1	86
2	85
3	85
4	83
5	84
6	83
7	80
8	80

[a] Isolated yield after chromatography.



Scheme 3. A plausible reaction mechanism.

3-buten-1-ol (**2**) in the presence of cellulose-SO_3H in nitromethane at room temperature over 60 min gave the 2-naphthyl tetrahydropyran-4-ol **3a** in 86% yield with all *cis*-selectivity (Scheme 1, Table 1).

Next, the reaction was carried out with various aromatic aldehydes. Interestingly, the corresponding 2-aryl tetrahyropyran-4-ols were obtained in good yields (Table 1, entries b–g). It is noteworthy to highlight that simple aromatic and moderately activated aldehydes gave higher yields compared to strongly activated or deactivated aldehydes. Notably, acid sensitive *trans*-cinnamaldehyde also gave the corresponding *trans*-2-styryltetrahydropyran-4-ol in 82% yield (Table 1, entry h). This reaction was also successful with cyclic ketones such as cyclopentanone, cyclohexanone, and 2-adamantanone to give the spirocyclic-tetrahydropyran-4-ols in good yields (Table 1, entries i–k).

This method also works well with substituted homoallylic alcohols such as hept-1-en-4-ol, 1-phenylbuten-1-ol, 1-(4-methoxyphenyl)-3-buten-1-ol, 1-cyclohexylbut-3-en-1-ol, and 1-(4-methylphenyl)-3-buten-1-ol (Table 1, entries l–q) under identical reaction conditions. The scope and generality of this process is illustrated in Table 1.[11]

The above results prompted us to investigate the reactivity of epoxides with homoallylic alcohols in Prins cyclization. Interestingly, styrene oxide (**4**) underwent a smooth rearrangement on the surface of cellulose-SO_3H to give the phenyl acetaldehyde which was subsequently reacted with 3-buten-1-ol (**2**) to furnish *cis*-2-benzyl-tetrahydropyran-4-ol (Table 2, entry a, Scheme 2).

Similarly, other epoxides such as 2-(naphthalene-2-yl)oxirane, 2-(4-tert-butylphenyl)oxirane, 2-methyloxirane, and 2-(4-chlorophenyl)oxiranes (Table 2, entries b–g) also participated well in this reaction. In all the cases, the reactions proceeded well at room temperature with high *cis*-selectivity.

In the absence of cellulose-SO_3H, no Prins cyclization was observed even under refluxing nitromethane. As solvent, nitromethane gave the best results. In most cases, the reactions were clean and the products were obtained at room temperature in high yields and selectivity as determined from the NMR spectra of the crude products. It is important to mention that the catalyst could be recycled eight times without significant of loss of activity (Table 3).

In all cases, *cis*-isomer was obtained exclusively and the structure of which was confirmed by NOE experiments. Mechanistically, the reaction proceeds via the rearrangement of epoxide to the corresponding aldehyde which subsequently reacts with homoallylic alcohol to give the hemi-acetal followed by Prins cyclization (Scheme 3).

A rationale for the *cis*-selectivity could be explained by assuming the formation of an (*E*)-oxocarbenium ion via a chair-like transition state, which has an increased stability relative to the open oxocarbenium ion due to delocalization. The optimal geometry for this delocalization places the hydrogen atom at C4 in a pseudo-axial position, which favors equatorial attack of the nucleophile.[12]

In summary, we have developed an efficient protocol for the preparation of 2-aryl- or 2-alkyl tetrahydropyran-4-ols via Prins cyclization using cellulose-SO_3H as a novel recyclable catalyst. The use of cellulose-SO_3H makes this method simple, convenient, and economically viable for large scale synthesis.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.10.015.

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11. *General procedure*: A mixture of carbonyl compound or epoxide (1 mmol), homoallylic alcohol (1 mmol), and cellulose-SO_3H (70 mg) in nitromethane (5 mL) was stirred at room temperature for a specified time (Tables 1 and 2). After completion of the reaction, as indicated by TLC, the catalyst was removed by filteration and the resulting filtrate was dried over Na_2SO_4 and concentrated under vacuum. The product was purified by silica gel column chromatography (70:30, hexane/ethyl acetate) to afford the pure tetrahydropyran-4-ol. The products thus obtained were characterized by IR, NMR, and mass spectroscopy. The spectral data were found to be consistent with authentic samples.[7]
Compound **3h**: (*E*)-2-styryl-tetrahydro-2*H*-pyran-4-ol: IR (KBr): ν 3387, 2924, 2853, 1601, 1449, 1203, 1138, 1074, 967, 747 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.15–7.42 (m, 5H), 6.55 (dd, 1H, J = 1.5, 15.8 Hz) 6.14 (dd, 1H, J = 6.0, 15.8 Hz), 4.04–411 (m, 1H), 3.77–3.95 (m, 2H), 3.42–3.51 (m, 1H), 2.02–2.10 (m, 1H), 1.86–1.93 (m, 1H), 1.32–1.61 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.5, 130.4, 129.3, 128.4, 127.6, 126.4, 76.4, 67.8, 65.8, 41.4, 35.2. LC–MS: m/z: (M^+) 204. HRMS calcd for $C_{13}H_{16}O_2$: 204.1150. Found: 204.1156.
Compound **5a**: 2-benzyltetrahydro-2*H*-pyran-4-ol: IR (KBr): ν 3414, 2924, 1603, 1493, 1249, 1067, 755, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.15–7.33 (m, 5H) 3.99 (dd, 1H, J = 4.0, 11.7 Hz) 3.52–3.78 (m, 1H) 3.29–3.48 (m, 2H) 2.62–2.94 (m, 2H), 1.80–1.92 (m, 2H) 1.41–1.54 (m, 1H), 1.18–1.33 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.0, 129.2, 128.2, 127.8, 77.0, 67.9, 65.8, 42.5, 40.7, 35.5. LC–MS: m/z: (M^+) 192. HRMS calcd for $C_{12}H_{16}O_2$: 192.1150. Found: 192.1148.
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