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Highly selective methanesulfonic acid-catalyzed 1,3-isomerization of allylic alcohols

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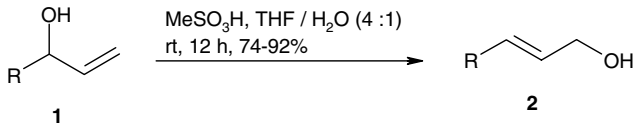
Abstract—Secondary and tertiary allylic alcohols undergo 1,3-isomerization smoothly in the presence of methanesulfonic acid under simple and efficient conditions to afford selectively the corresponding primary *E*-allylic alcohols in excellent yields.

Allylic alcohols and their derivatives are important precursors in various synthetic organic reactions.[1] The direct 1,3-allylic rearrangement of allylic alcohols is a useful reaction, because one regioisomer is often more difficult to prepare than the other, but has received little attention. Only a few methods have been reported in the literature for this transformation, such as H_2SO_4,[2] $CoCl_2$[3] and isomerization catalyzed by transition-metal oxo complexes.[4] These methods suffer from low yields and low regioselectivity. In addition, transition-metal oxo complexes are moisture-sensitive and highly expensive reagents. To overcome these problems, herein we report a new, simple, and efficient protocol for this transformation using inexpensive methanesulfonic acid (Scheme 1).

As a part of our continuing interest in the development of new synthetic methodologies, we disclose our results on the methanesulfonic acid-catalyzed *E*-selective 1,3-isomerization of allylic alcohols. To the best of our knowledge, there have been no reports on the use of methanesulfonic acid in 1,3-isomerization of allylic alcohols.



Scheme 1.

The treatment of α-vinyl benzyl alcohol **1** with methanesulfonic acid at room temperature over 12 h underwent 1,3-isomerization to afford the corresponding *E*-selective cinnamyl alcohol **2** in 91% yield.[5] Encouraged by these results, we turned our attention to substituted α-vinyl benzyl alcohols. Interestingly, a large number of substituted α-vinyl benzyl alcohols such as *p*-chloro-, *p*-bromo-, *o*-bromo-, *p*-fluoro-, *o*-fluoro-, *p*-nitro-, *p*-methoxy, and *o*-methoxy derivatives isomerized efficiently in the presence of methanesulfonic acid to afford corresponding *E*-selective substituted cinnamyl alcohols in high yields (Table 1, entries a–i). This method is equally effective for electron-rich as well as electron-deficient aromatic allylic alcohols.

We also investigated a number of aliphatic allylic alcohols and tertiary allylic alcohols (Table 1, entries j–o) in the presence of methanesulfonic acid to selectively afford the corresponding primary *E*-allylic alcohols in good yields. The products were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectroscopic data and also by comparison with authentic samples.[4a,b,6] In all cases, the reactions proceeded efficiently in high yields at ambient temperature. As a solvent, THF/H_2O (4:1) appeared to give the best results. Of the various acids investigated (Table 2), methanesulfonic acid gave the best results in terms of conversion and reaction rates. The reaction did not go to completion with triflic acid or *p*-toluenesulfonic acid, giving low yields. No reaction was observed with acetic acid or trifluoroacetic acid.

Keywords: Methanesulfonic acid; Allylic alcohols; 1,3-Isomerization; THF; Water.
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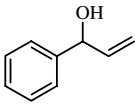
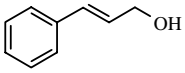
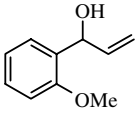
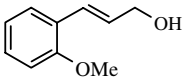
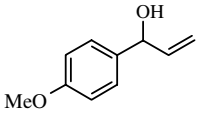
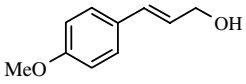
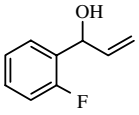
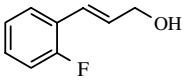
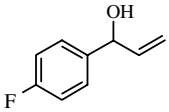
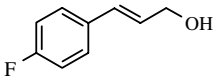
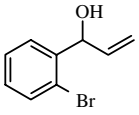
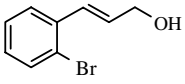
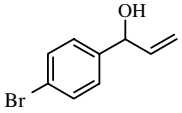
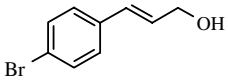
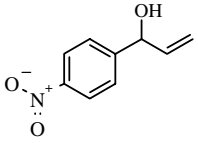
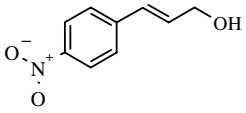
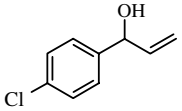
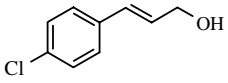
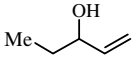
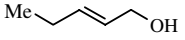
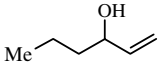
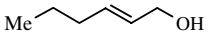
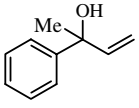
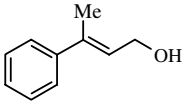
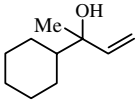
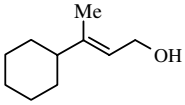
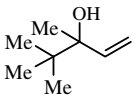
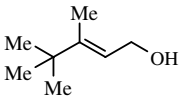
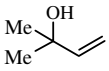
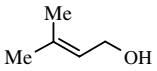
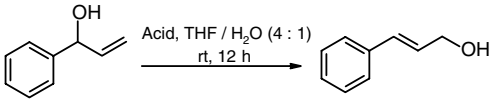
Table 1. 1,3-Isomerization of allylic alcohols via methanesulfonic acid catalysis

Entry	Substrate	Product[a]	Yield[b] (%)
a			90
b			89
c			92
d			82
e			86
f			82
g			88
h			86
i			91
j			78
k			76
l			90
m			83
n			82
o			74

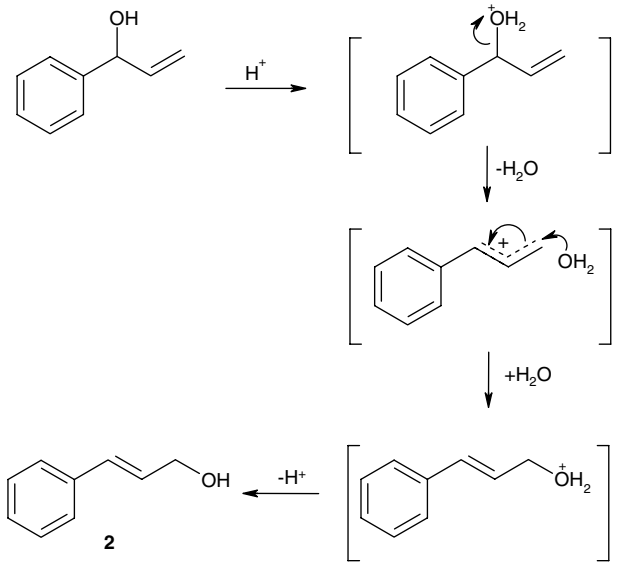
[a] All products were characterized by ^{1}H NMR, ^{13}C NMR and mass spectroscopy.
[b] Isolated yields.

Table 2. 1,3-Isomerization of allylic alcohols in the presence of different acids



Entry	Acid	Yield[a] (%) (recovered SM (%))
1	$MeSO_3H$	91 (0)
2	TfOH	65 (5)
3	$PhSO_3H$	65 (20)
4	p-$CH_3C_6H_4SO_3H$	62 (21)
5	CH_3COOH	0 (90)
6	CF_3COOH	0 (85)

[a] Isolated yields.



Scheme 2.

A possible mechanism for this reaction is depicted in Scheme 2.

In conclusion, we have developed a simple and efficient approach for 1,3-isomerization of allylic alcohols using inexpensive methanesulfonic acid as the catalyst. The notable feature of this reaction is a high regioselective conversion of secondary and tertiary allylic alcohols to primary allylic alcohols in excellent yields.

References and notes

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5. *Typical experimental procedure:* To a solution of alcohol (1.0 mmol) in THF/H_2O (4:1, 5 mL) methanesulfonic acid (2.0 mmol) was added dropwise over 5 min at rt, and stirring was continued at this temperature for 12 h. The progress of the reaction was monitored by TLC. After complete conversion, the reaction mixture was quenched with saturated $NaHCO_3$ solution (10 mL). The resulting mixture was extracted with *i*-PrOAc (3× 10 mL). The combined organic layers were washed with water and concentrated under reduced pressure. The resulting crude product was purified by column chromatography (silica gel 230–400 mesh) using a gradient mixture of *i*-PrOAc and pentane to furnish pure allylic alcohol.
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