A variety of hydroxy compounds add to 3,4-dihydro-2H-pyran in the presence of catalytic amounts of H–Y zeolite to afford the corresponding tetrahydropanyl ethers in excellent yields.

In recent years, there has been a tremendous upsurge of interest in various chemical transformations mediated by zeolites. Their characteristic features such as shape selectivity, thermal stability and unique varying acidic and basic properties have made them versatile catalysts for a wide range of reactions. Recently, we have reported the thioacetalization of various carbonyl compounds by 1,2-ethanethiol,4 ethanethiol and 1,3-propanediethiol using H–Y zeolite (Si/Al = 2.43).5 In continuation, we have extended the unprecedented use of H–Y zeolite for the protection of hydroxy compounds with a relatively bulkier protecting agent, e.g., 3,4-dihydro-2H-pyran (DHP), and this report describes the successful completion of our objective.

Tetrahydropanyl ethers are synthetically useful as hydroxy protecting groups and are important building blocks for the synthesis of primary alcohols,6 allylic alcohols7 and alkyl halides.8 Due to the outstanding stability of tetrahydropanyl ethers under a variety of reaction conditions,9 such as basic media, reduction with hydride, oxidation, and reactions involving Grignard reagents, lithium alkyls, alkylating and acylating reagents, 3,4-dihydro-2H-pyran is still the reagent of choice for hydroxy group protection in peptide, nucleotide, carbohydrate and steroid chemistry.10

A number of methods employed for tetrahydropanylation include the use of protic acids, e.g., hydrochloric acid11 and p-toluenesulfonic acid,12 Lewis acids, e.g., boron trifluoride – diethyl ether complex,13 pyridinium p-toluenesulfonate (PPTS),14 bis(trimethylsilyl)sulfate15 and ion-exchange resins.16 More recently, 2,3-dichloro-5,6-dicyano-p-benzoquinone,17 Nafion-H catalyst,18 montmorillonite clay K-10,19 poly(4-vinylpyridine) as the p-toluenesulfonate19 and hydrochloride20 have been developed for this purpose. However, many of these methods have several limitations: expensive reagents, tedious workup procedure, strongly acidic media and high temperature. Consequently, there is need to develop alternative reagents for this reaction.

Now we report that H–Y zeolite21 serves as an excellent catalyst for tetrahydropanylation of alcohols (Scheme).

![Scheme](https://example.com/scheme.png)

**Table.** THP-ethers 3a–m Prepared

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Reaction Time (h)</th>
<th>Yield* of 3 (%)</th>
<th>Molecular Formula or bp (°C)/Torr</th>
<th>Literature bp (°C)/Torr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a hexanol</td>
<td>3a</td>
<td>1.5</td>
<td>85</td>
<td>130/25</td>
<td>94/3,23</td>
</tr>
<tr>
<td>1b 2-methylpropanol</td>
<td>3b</td>
<td>2</td>
<td>95</td>
<td>58–59/10</td>
<td>109/100,24</td>
</tr>
<tr>
<td>1c 2-butanol</td>
<td>3c</td>
<td>90</td>
<td>95</td>
<td>83/25</td>
<td>80–85/25,25,15</td>
</tr>
<tr>
<td>1d tert-butyl alcohol</td>
<td>3d</td>
<td>95</td>
<td>55/10</td>
<td>76–77/25</td>
<td>75/22,16</td>
</tr>
<tr>
<td>1e allyl alcohol</td>
<td>3e</td>
<td>80</td>
<td>54–58/13,25, 54–56/10,23</td>
<td>76–79/25,5, 72–73/12,27</td>
<td></td>
</tr>
<tr>
<td>1f propargyl alcohol</td>
<td>3f</td>
<td>95</td>
<td>57–58/8,13, 150–157/25, 25,15</td>
<td>79–80/13,20</td>
<td></td>
</tr>
<tr>
<td>1g cyclohexanol</td>
<td>3g</td>
<td>90</td>
<td>70</td>
<td>152–153/25</td>
<td>105/5,20, 105/4,15, 107/3,28</td>
</tr>
<tr>
<td>1h phenol</td>
<td>3h</td>
<td>65*</td>
<td>90</td>
<td>90–91/5</td>
<td>51/0.07,29</td>
</tr>
<tr>
<td>1i benzyl alcohol</td>
<td>3i</td>
<td>70</td>
<td>125/10</td>
<td>105/2,10</td>
<td>88/3,20</td>
</tr>
<tr>
<td>1j tetrahydrofurfuryl alcohol</td>
<td>3j</td>
<td>85</td>
<td>130/5</td>
<td>88/2,15</td>
<td>88/2,16</td>
</tr>
<tr>
<td>1k furfuryl alcohol</td>
<td>3k</td>
<td>5*</td>
<td>100/5</td>
<td>C17H35O6 (330.367)</td>
<td></td>
</tr>
<tr>
<td>1l (-)-menthol</td>
<td>3l</td>
<td>70</td>
<td>105–107/0.4,15, 120–125/4,15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1m 2,3-O-isopropyliden-1-threitol</td>
<td>3m</td>
<td>10*</td>
<td>60*</td>
<td>C17H35O6 (330.367)</td>
<td></td>
</tr>
</tbody>
</table>

*a All products were characterized by their IR, 1H NMR and mass spectroscopic data.

*b Completion of the reaction was monitored by GC analysis (column OV-101) and/or TLC.

*c Unoptimized yields of isolated pure products.

*d The equivalent amount (by weight) of zeolite with respect to hydroxy compound was used in order to get maximum conversion, e.g., 83% for 1h, 82% for 1i, 40% for 1l and 60% for 1m by GC.

*e Yields based on starting material consumed.

*f Viscous distillate liquid purified by silica gel column chromatography, satisfactory microanalysis obtained for 3m.

**IR (neat): v = 1450 (s); 1380 (s); 1360 (s); 1270 (s); 1210 (s) cm⁻¹.

**1H NMR (CDCl₃/TMS): 6 = 1.24 (s, 6H), 1.37–2.38 (m, 12H), 3.28–3.71 (m, 5H), 3.72–4.14 (m, 5H), 4.52–4.7 (brs, 1H), 4.72–5.06 (brs, 1H).

**MS: m/z = 160 (M⁺–2DHP, 13%), 145 (25%), 130 (6%), 115 (21%), 85 (100%), 75 (72%), 61 (67%), 56 (46%).
Thus, when a variety of alcohols were treated with 3,4-dihydro-2H-pyranyl in the presence of catalytic amounts of H–Y zeolite, the corresponding THP-ethers were obtained in excellent yields. The results are compiled in the Table. The reaction conditions are particularly mild and the workup procedure is exceedingly simple and reduced to a mere filtration. The zeolite is recovered unchanged and can be reactivated for reuse by heating it at 500 °C in the presence of air.

The present procedure for tetrahydropyranylation is quite general as a wide range of hydroxy compounds such as primary, secondary, tertiary, allylic, acetylenic and polyfunctional can be protected with dihydropyran under mild conditions. It should be pointed out that many of the conventional catalysts and most commonly used p-toluenesulfonic acids for tetrahydropyranylation are still undesirable for highly acid-sensitive alcohols. However, H–Y zeolite was found effective for alcohols possessing acid labile functionalities, e.g., allylic, acetylenic and ketal hydroxy compounds. Thus, in these cases, isomerization of double or triple bonds and cleavage of ketal could not be observed under the reaction conditions and the resulting ethers were isolated as the only product. However, reaction of dihydropyran with bulky substrates e.g., 1b–i, 11–m was slower and the completion of reaction could not be achieved even with additional amount of zeolite catalyst or with excess DHP (Table). Other zeolites such as H-ZSM-5 and molecular sieves 4Å or 5Å failed to accomplish the above transformations. However, H-mordenite gave the desired products in low yields after prolonged stirring compared to H–Y zeolite. The observed efficient performance of H–Y zeolite may be attributed to its large pore opening (0.74 nm), three dimensional channel system and higher concentration of acid sites.22 Strongly acidic resin catalysts such as Nafion-H18 and Amberlyst A-1516 with excess of dihydropyran are reported to produce polymeric byproducts and consequently low yields of resulting THP-ethers were obtained, whereas the present method did not yield any polymeric byproducts of dihydropyran.

In summary, from commercially available H–Y zeolite, we have established a facile heterogeneous catalytic method for tetrahydropyranylation of a variety of alcohols under mild conditions. In addition, the heterogeneous catalytic method is advantageous in respect of easy separation, higher and consistent yield and recyclability of the catalyst. Thus, the present catalytic method should serve as a useful addition to synthetic organic chemistry.

Prior to use, zeolite was calcined at 500 °C in the presence of air. The dihydropyran and alcohols used for reaction were freshly distilled. Boiling points were uncorrected. The IR spectra were recorded on a Perkin-Elmer Model 683 spectrophotometer and 1H NMR spectra with a Bruker AC200 NMR spectrometer. The chemical shifts are reported in parts per million (δ) with TMS as internal standard. The mass spectra were recorded on a Finnigan MAT-1020-B-70-eV mass spectrometer.

**Tetrahydroxyranyl Ethers 3α–m: General Procedure:**

To a solution of the hydroxy compound (30 mol%) in hexane (30 mL) were added successively H–Y zeolite (0.5 equiv by weight with respect to the hydroxy compound) and 3,4-dihydro-2H-pyranyl (37.5 mmol) and the mixture was refluxed with stirring for the specified period of time (Table). The progress of reaction was monitored by TLC followed by GLC analysis (column OV-101). After the reaction was complete, the zeolite was filtered off and washed with hexane (2 × 20 mL). The solvent was evaporated to afford the product which was further purified by distillation or column chromatography.

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* NCL Communication No. 5765.


(23) The unit cell composition of H–Y zeolite is H$_5$Si$_9$O$_{23}$ (AlO$_2$)$_{58.9}$ (SiO$_2$)$_{123.1}$ OH$_{38.4}$.


