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DIRECT FACILE TETRAHYDROFURANYLATION OF ALCOHOLS IN p-TsCl/NaH/THF SYSTEM

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ABSTRACT: Several alcohols were converted in excellent yields into their 2-tetrahydrofuranyl-ethers in the presence of p-TsCl and NaH in THF under mild conditions. A radical process was proposed.

The protection of hydroxyl group as tetrahydrofuranyl ethers has been well used in organic synthesis. More recently, tetrahydrofuranylation of alcohols by using ceric ammonium nitrate and (Bu₄N)₂S₂O₈ were reported, both involved the radical processes.
Free radical reactions mediated by the arenesulfonyl radicals have been well investigated\textsuperscript{4-9}. The addition of the arenesulfonyl radicals to carbon-carbon double bond is always the first step in these reactions. The arenesulfonyl radicals can be generated from arenesulfonyl chloride by employing the dibenzoyl peroxide\textsuperscript{5}, AlBN\textsuperscript{6} as the catalyst or under irradiation\textsuperscript{7}. The $p$-toluenesulfonyl radical generated from sodium $p$-toluenesulfinate in aqueous acetic acid is also investigated\textsuperscript{8,9}. We report here the facile tetrahydrofuranylation of several alcohols in the $p$-TsCl/NaH/THF system under very mild conditions (Scheme 1). A radical process just like the reactions under (Bu$_4$N)$_2$S$_2$O$_8$\textsuperscript{3} is proposed. Therefore, the tetrahydrofuranylation of alcohols is assumed to undergo through coupling of the tetrahydrofuran-2-yl radical and the alkoxy radical\textsuperscript{3}, which are generated by the $p$-toluenesulfonyl radical\textsuperscript{4}. The $p$-toluenesulfonyl radical appears to be produced by the disproportionation of the $p$-toluenesulphinic acid\textsuperscript{9}, and the $p$-TsCl/NaH/THF system we used here might generate the $p$-toluenesulphinic acid just as the $p$-TsNa/aq. HOAc system did\textsuperscript{8,9}. It's the first time, to our knowledge, to use the $p$-TsCl/NaH as a useful radical source in organic solvent. The results obtained are summerized in Table 1.

The long chain saturated primary alcohols (Run 1-3) and the secondary cyclohexanol were converted into their THF-ethers in excellent yields, only a
Table 1.

<table>
<thead>
<tr>
<th>Run</th>
<th>ROH</th>
<th>Product</th>
<th>Yield(^a)(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HO(CH_2)_1(CHO_2)_10(CH_2)_1OH</td>
<td>(\overset{\text{O}}{\text{O}}(\text{CH}_2)_1(\text{CHO})_10(\text{CH}_2)_1\overset{\text{O}}{\text{O}}))</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>CH_3(CH_2)_1OH</td>
<td>(\text{CH}_3(\text{CH}_2)_1\overset{\text{O}}{\text{O}})</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>BrCH_2(CH_2)_1OH</td>
<td>(\text{BrCH}_2(\text{CH}_2)_1\overset{\text{O}}{\text{O}})</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>(\text{O}^{})</td>
<td>(\text{O}^{})</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>Cholesterol</td>
<td>(\text{O}^{})</td>
<td>43</td>
</tr>
<tr>
<td>6</td>
<td>CH_2-CH(CH_2)_3OH</td>
<td>complex</td>
<td>/</td>
</tr>
<tr>
<td>7</td>
<td>BnOH</td>
<td>BnOTs</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>HOCH_2CH_2OH</td>
<td>TsOCH_2CH_2OTs</td>
<td>95</td>
</tr>
</tbody>
</table>

a. isolated yield

Little amount of tosylated products (\(<5\%\)) were detected. The carbon-carbon double bond showed sensitive under this reaction conditions (Run 5-6). While employing the cholesterol as alcohol, only 43\% of its THF-ether was obtained. Moreover, the 10-undecen-1-ol gave a complex reaction and no tetrahydrofuranylated product was detected. When the alcohols bearing active hydroxyl groups were used (Run 7-8), only the tosylated products were isolated and no tetrahydrofuranylated products were detected. Finally, the \(p\)-TsCl could be replaced by MsCl or 2,4,6-triisopropylbenzenesulfonyl chloride in the reaction.

**EXPERIMENTAL**

IR spectra were obtained on a Shimadzu IR-440 spectrometer. \(^1\)H NMR spectra were recorded on a Varian EM-360A or a AM-300 spectrometer with...
tetramethylsilane as external reference. Mass spectra were measured on a HP 5989A mass spectrometer.

**General procedure:**

1-Undecanol (50mg, 0.27mmol) was added to a stirred solution of \(p\)-TsCl (150mg, 0.77mmol) and NaH (50mg, 1.67mmol) in dry THF at room temperature. After being stirred overnight, the reaction mixture was poured into water and extracted with CHCl₃. The organic layer washed with water, dried with anhydrous Na₂SO₄ was then filtered, concentrated, and the residue was chromatographed on a silica gel column with petroleum-ether/ethyl acetate (20:1) as the eluant.

1: \(^1\)H NMR (CD₃COCD₃): \(\delta\) 5.06 (2H, d, \(J = 4.98\) Hz), 3.78 (4H, t, \(J = 6.00\) Hz), 3.58 (2H, m), 3.32 (2H, m), 2.20 (4H, m), 1.84 (8H, m), 1.59 (4H, m), 1.48 (8H, m), 1.32 (24H, m); Ms (m/z): 982 (M⁺), 912 (M⁺-70), 843 (44, M⁺-2x70), 71 (100); IR (KBr, cm⁻¹): 1450, 1180, 1040.

2: \(^1\)H NMR (CDCl₃): \(\delta\) 5.10 (1H, dd, \(J = 1.89, 4.12\) Hz), 3.90 (2H, m), 3.65 (2H, m), 3.38 (2H, m), 1.89 (4H, m), 1.57 (2H, m), 1.30 (18H, m), 0.89 (3H, t, \(J = 4.46\) Hz); Ms (m/z): 257 (18, M⁺+1), 71 (100); IR (film, cm⁻¹): 1460, 1040.

3: \(^1\)H NMR (CDCl₃): \(\delta\) 5.10 (1H, dd, \(J = 4.12, 2.23\) Hz), 3.87 (1H, m), 3.65 (1H, m), 3.41 (2H, t, \(J = 6.79\) Hz), 3.36 (2H, t, \(J = 6.79\) Hz), 1.87 (4H, m), 1.57 (4H, m), 1.44 (2H, m), 1.28 (12H, s); Ms (m/z): 323 (14, M⁺+1), 321 (16, M⁺+1), 71 (100); IR (film, cm⁻¹): 1460, 1040.
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4: $^1$H NMR (CDCl$_3$): $\delta$ 5.29 (1H, m), 3.87 (2H, m), 3.54 (1H, m), 1.88 (4H, m), 1.24 (4H, m); Ms (m/z): 171 (11, M$^+$+1), 71 (100); IR (film, cm$^{-1}$): 1450, 1040.

5: $^1$H NMR (CDCl$_3$): $\delta$ 5.35 (1H, s), 5.29 (1H, d, $J = 4.22$ Hz), 3.89 (2H, m), 3.46 (1H, m), 2.31-0.70 (4H); Ms (m/z): 386 (3, M$^+$-70), 71 (100); IR (KBr, cm$^{-1}$): 1450, 1040.

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REFERENCES:


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