A Facile Method for Deprotection of O-Allylphenols

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Allyl aryl ethers can be easily cleaved by the use of 10% Pd/C under the mild and basic conditions.

Key words allyl aryl ethers; deprotection; palladium on carbon

Phenolic hydroxyl groups exist in various type of chemical compounds (e.g., natural products, drugs). The functional group plays a very important role for increasing biological activities in many cases. Moreover, it is introduced as a key functional group into Host compounds with interesting property for molecular recognition (e.g., calixarenes, cyclophanes). In order to synthesize such complicated compounds, protection and deprotection of the phenol group are crucial steps. Among them, the allyl group is known as one of the stable protective groups towards both acidic and basic conditions. Also allyl ethers have advantage that can be readily prepared by the reaction of a phenol with allyl halide in the presence of base. Thus, several procedures1) have been developed for one step cleavage of the group including palladium-catalyzed reaction. Among them, most of palladium catalysts used were Pd(PPh₃)₄ together with NaBH₄,2) LiBH₄,3) Bu₃SnH,4) PhSiH₃,5) morphorine,6) ZnCl₂–polymethylhydrosloxane,7) or TsOH11) under reflux conditions. In the course of synthetic studies on a series of host compounds 1 combined with a crown ether and two orthocyclophanes,12) we found a facile reaction for deprotection of O-allylphenols using 10% Pd/C in 10% KOH–MeOH at ambient temperature. Here, we describe preliminary results of mild and convenient cleavage of allyl aryl ether bond.

Tetra(3-allyl-6-bromoisoovanillyl)dibenzo-18-crown-6 2a,13) prepared by condensation of dibenzo-18-crown-6 and 4 eq of 3-allyl-6-bromoisoovanillyl alcohol, was subjected to hydrogenolysis on 10% Pd–C14) in 10% KOH–MeOH yielding a product 2b15) instead of 2c, unexpectedly. As a result, the ether 2a was suffered not only debromination but deallylation. Indeed, under weaker basic conditions (10% Pd/C, H₂, 4 eq of Et₃N, MeOH), the ether bond was inert and the tetrapropyl derivative 2d13) was obtained in 45% yield. Thus, essential conditions for this facile reaction were searched by the use of O-allylvanillin 3 as a simple substrate (Table 1). Without both Pd catalyst and base, the reaction did not occur at room temperature (entries 1 and 3). Also, crown ether part was not necessary for the reaction (entry 2). Although the reaction proceeded in the absence of KOH under reflux, the reaction was sluggish and isomerized enol ethers 5a, b were produced (entry 4).16) Eventually, it was verified to be a simple combination of reagents (10% Pd/C and 10% KOH–MeOH) (entry 5).17)

Next, we applied this procedure to various types of O-allylphenols 6a—13a for confirmation of scope and limitation (Table 2). O-Allylphenols 6a—10a were readily deprotected to give the corresponding phenols 6b—10b, respectively, without affecting aldehyde, amide and nitro groups. Deprotection of O-allylphenols 11a or 12a, bearing acid labile acetal or benzyl ether, gave the corresponding phenol 11b or 12b keeping another protective group. In the case of a diether 13a, which has two kinds of allyl ethers, allyl aryl ether bond was selectively cleaved to give the phenol 13b together with a small amount of a benzyl propyl ether 13c. Although detail mechanism of the reaction was not clear at this stage, we assumed the reaction proceeded via the formation of π-allyl complex. However, isomerization16) of allyl ethers to enol ethers followed by cleavage of them could not be excluded.

Table 1. Deallylation of O-Allylvanillin

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10% KOH–MeOH, r.t., 24 h then reflux 24 h</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10% KOH–MeOH, dibenzo-18-crown-6 (1 eq), r.t., 24 h then reflux 24 h</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>10% Pd/C, MeOH, r.t., 72 h</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>10% Pd/C, MeOH reflux 24 h</td>
<td>28*</td>
</tr>
<tr>
<td>5</td>
<td>10% Pd/C, 10% KOH–MeOH, r.t., 8 h</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>10% Pd/C, NaOMe (10 eq), MeOH, r.t., 5 h</td>
<td>54</td>
</tr>
</tbody>
</table>

*a) Starting material 3 (49%) and enol ethers 5a (9%) and 5b (5%) were also obtained.

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In conclusion, the present method for deprotection of O-allylphenol is quite useful because of its easy performance and mild conditions.

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References and Notes
13) All new compounds were characterized by 1H-NMR spectroscopy and high resolution mass spectrometry.
14) Ten percent Pd/C was purchased from Kojima Chemical Co. Ltd.
15) Tetraphenol 2b could not be extracted into organic solvent because of its high polarity. Structure of 2b was determined as the corresponding tetraacetate 2e.
17) Typical procedure for deallylation (Table 1, entry 5): To a solution of O-allylvanillin 3 (100 mg, 0.52 mmol) in 10% KOH–MeOH (10 ml) was added 10% Pd/C (20 mg). The whole mixture was stirred under an atmosphere of argon at room temperature for 9 h. After the catalyst was filtered out, the filtrate was concentrated in vacuo. An oily residue was dissolved in H2O and the mixture was washed with ether. After the aqueous layer was acidified with 1 M HCl, the mixture was extracted with AcOEt. The organic extracts were washed with brine and dried over MgSO4. The solvent was evaporated under reduced pressure to give a colorless solid (76 mg, 96%), which was identified with vanilline on the basis of 1H-NMR spectroscopy and behavior on thin layer chromatography.