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A Facile Method for Deprotection of *O*-Allylphenols

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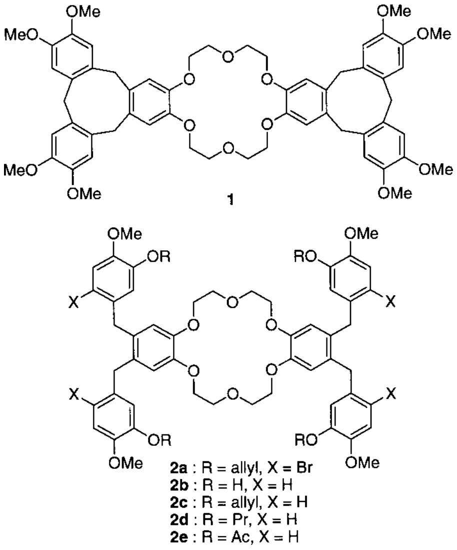
Allyl aryl ethers can be easily cleaved by the use of 10% Pd/C under the mild and basic conditions.

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 procedures(1) have been developed for one step cleavage of the group including palladium-catalyzed reaction. Among them, most of palladium catalysts used were $Pd(PPh_3)_4$ together with $NaBH_4$,(2) $LiBH_4$,(3) Bu_3SnH,(4) $PhSiH_3$,(5) morphorine,(6) $ZnCl_2$–polymethylhydrosiloxane,(7) or $TolSO_2H$.(8) Also, electrochemical cleavage using $PdCl_2$(9) and Ni(10) were appeared. As an alternative catalyst, Boss and Scheffold reported the reaction using 10% Pd/C with *p*-TsOH(11) 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(*O*-allyl-6-bromoisovanillyl)dibenzo-18-crown-6 **2a**,(13) prepared by condensation of dibenzo-18-crown-6 and 4 eq of *O*-allyl-6-bromoisovanillyl alcohol, was subjected to hydrogenolysis on 10% Pd–C(14) in 10% KOH–MeOH yielding a product **2b**(15) 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, H_2, 4 eq of Et_3N, MeOH), the ether bond was inert and the tetrapropyl derivative **2d**(13) 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)

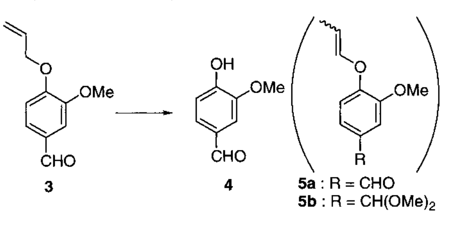
Next, we applied this procedure to various types of *O*-allylphenols **6a**—**13a** for confirmation of scope and limitation (Table 2). *O*-Allylphenols **6a**—**10a** were readily deprotected to give the corresponding phenols **6b**—**10b**, respectively, without affecting aldehyde, amide and nitro 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, isomerization(16) of allyl ethers to enol ethers followed by cleavage of them could not be excluded.



2a : R = allyl, X = Br
2b : R = H, X = H
2c : R = allyl, X = H
2d : R = Pr, X = H
2e : R = Ac, X = H

Fig. 1

Table 1. Deallylation of *O*-Allylvanillin



3 **4**
5a : R = CHO
5b : R = $CH(OMe)_2$

Entry	Conditions	Yield (%)
1	10% KOH–MeOH r.t., 24 h then reflux 24 h	0
2	10% KOH–MeOH dibenzo-18-crown-6 (1 eq) r.t., 24 h then reflux 24 h	0
3	10% Pd/C, MeOH r.t., 72 h	0
4	10% Pd/C, MeOH reflux 24 h	28[a)]
5	10% Pd/C, 10% KOH–MeOH r.t., 8 h	96
6	10% Pd/C, NaOMe (10 eq) MeOH, r.t., 5 h	54

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

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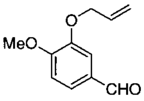
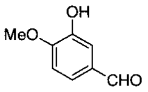
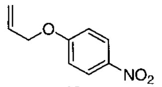
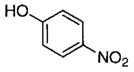
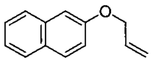
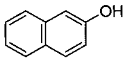
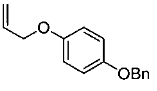
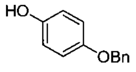
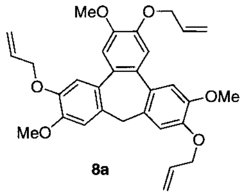
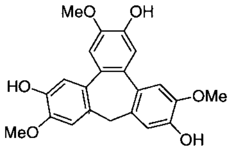
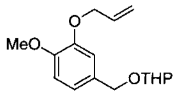
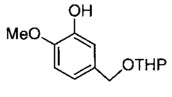
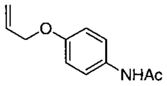
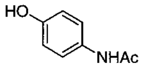
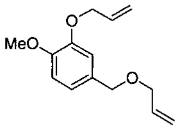
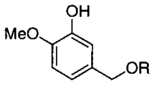
Table 2. Deallylation of Various *O*-Allylphenols[a)]

Entry	Substrate	Time (h)	Product (%)	Entry	Substrate	Time (h)	Product (%)
1	 **6a**	4	 **6b** (87%)	5	 **10a**	9	 **10b** (94%)
2	 **7a**	4	 **7b** (75%)	6	 **11a**	8	 **11b** (95%)
3	 **8a**	13	 **8b** (71%)	7	 **12a**	7	 **12b** (65%)
4	 **9a**	48	 **9b** (86%)	8	 **13a**	7	 **13b** : R = Allyl (81%) **13c** : R = Pr (10%)

a) All reaction were run using substrate (100 mg) and 10% Pd/C (20 mg) in 10% KOH–MeOH (10 ml) at r.t. under argon atmosphere.

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

1) Green T. W., Wuts P. M. G., "Protecting Groups in Organic Synthesis," 3rd ed., John Wiley & Sons, New York, 1999.
2) Beugelmans R., Bourdet S., Bigot A., Zhu J., *Tetrahedron Lett.*, **35**, 4349—4350 (1994).
3) Bois-Choussy M., Neuville L., Beugelmans R., Zhu J., *J. Org. Chem.*, **61**, 9309—9322 (1996).
4) Four P., Guibe F., *Tetrahedron Lett.*, **23**, 1825—1828 (1982).
5) Dessolin M., Guillerez M.-G., Thieriet N., Guibe F., Loffet A., *Tetrahedron Lett.*, **36**, 5741—5744 (1995).
6) Eicher T., Ott M., Speicher A., *Synthesis*, **1996**, 755—762 (1996).
7) Chandrasekhar S., Reddy C. R., Rao R. J., *Tetrahedron*, **57**, 3435—3438 (2001).
8) Honda M., Morita H., Nagakura I., *J. Org. Chem.*, **62**, 8932—8936 (1997).
9) Franco D., Panyella D., Rocamora M., Gomez M., Clinet J. C., Muller G., Dunach E., *Tetrahedron Lett.*, **40**, 5685—5688 (1999).
10) Yasuhara A., Kasano A., Sakamoto T., *J. Org. Chem.*, **64**, 4211—4213 (1999).
11) Boss R., Scheffold R., *Angew. Chem., Int. Ed.*, **15**, 558—559 (1976).
12) Hara H., Watanabe S., Yamada M., Hoshino O., *J. Chem. Soc.*, *Perkin Trans. 1*, **1996**, 741—746 (1996).
13) All new compounds were characterized by ^{1}H-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**.
16) Similar isomerization of allyl ether to enol ether was reported using Pd/C in boiling benzene; Carless H. A. J., Haywood D. J., *J. Chem. Soc. Chem. Commun.*, **1980**, 980—981 (1980).
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 H_2O 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 $MgSO_4$. The solvent was evaporated under reduced pressure to give a colorless solid (76 mg, 96%), which was identified with vanilline on the basis of ^{1}H-NMR spectroscopy and behavior on thin layer chromatography.