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Facile and selective cleavage of allyl ethers, amines and esters using polymethylhydrosiloxane–$ZnCl_2/Pd(PPh_3)_4$☆

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Abstract—Allyl deprotection to liberate free hydroxy, amino and acid groups from the corresponding allyl ethers, amines and esters is achieved under mild conditions. The reagent combination employed for this transformation is polymethylhydrosiloxane (PMHS), $ZnCl_2$ and $Pd(PPh_3)_4$. © 2001 Elsevier Science Ltd. All rights reserved.

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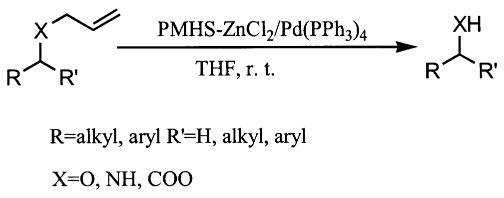
1. Introduction

The allyl group is one of the very commonly used protecting groups for various functionalities, especially alcohols, acids and less frequently for amines.[1] The most essential feature of this protective group is its stability towards both acidic and basic conditions. Removal of the allyl protecting group is commonly effected by transition metal[2]- or KO^tBu (DMSO, 100°C)[3]-catalyzed isomerization of the allyl ether to the corresponding enol ether and subsequent hydrolysis. However, KO^tBu can be used only when the substrate does not contain base sensitive functional or protecting groups. Later, several new single step procedures came into prominence, including palladium-catalyzed hydrostannolysis with Bu_3SnH,[4] $SmCl_3$-catalyzed electrochemical cleavage,[5] reductive deprotection with $Pd(PPh_3)_4/NaBH_4$,[6] a modified Kulinkovich method,[7] $AlCl_3$–*N*,*N*-dimethylaniline,[8] hydrogen activated cationic iridium complex,[9] palladium-catalyzed hydrosilanes,[10] $TiCl_3$–Mg–THF,[11] Cp_2Zr,[12] $PdCl_2/CuCl/DMF–H_2O/O_2$,[13] NBS/$h\nu$,[14] $NaBH_4/I_2$,[15] $TolSO_2H/Pd(PPh_3)_4$,[16] $I(CF_2)_6F/Zn$,[17] $BCl_3–Me_2S$,[18] DDQ,[19] $[NiCl_2(dppp)]$–DIBAL–H,[20] TMS–Cl/NaI[21] and $ZrCl_4/NaBH_4$[22] among others.[23] Recently, Bailey et al. have used *t*-BuLi[24] for selective allyl ether cleavage. Despite these available methods, there is still a need to develop new, mild and safe protocols for the general cleavage of the allyl group as the above mentioned procedures have their own limitations. A few of the reagents are expensive or pyrophoric and some are selective for a particular functional or protecting group. Our continued interest in the development of new procedures for protection–deprotection strategies[25] led us to explore the potential utility of polymethylhydrosiloxane,[26] which is particularly gaining prominence in recent times especially as a safe, economic, non-toxic, stable to air and moisture, easily handled alternative reagent in reductions.[27] Here, we wish to report a mild and extremely selective method for the cleavage of the allyl moiety from parent ethers, amines and esters using PMHS in the presence of tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$) and zinc chloride (Scheme 1).



Scheme 1.

2. Results and discussion

Initially, we envisaged that $Pd(PPh_3)_4$ alone would permit the formation of a π-allyl complex with the allyl moiety and additionally activated PMHS towards hydride transfer enabling the recovery of the parent alcohol. Unfortunately Pd(0) alone could not perform the desired transformation. Not discouraged by this finding, a few metal halides were explored as accelerators and to our satisfaction $ZnCl_2$ (previously utilized by us for activation of PMHS in reductions)[26] in combination with PMHS and $Pd(PPh_3)_4$ worked very efficiently in the cleavage of 3-phenyl-1-propanol allyl ether **1a** to afford 3-phenyl-1-propanol **2a** in 94% isolated yield (entry 1, Table 1). To rationalize this finding, a few

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Keywords: allylic protecting groups; polymethylhydrosiloxane; palladium catalysis; zinc chloride.

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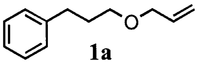
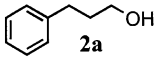
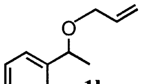
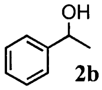
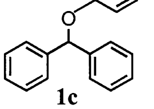
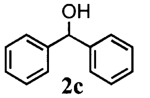
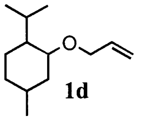
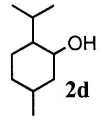
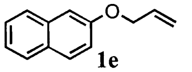
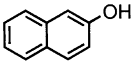
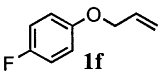
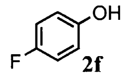
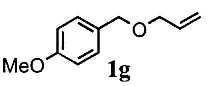
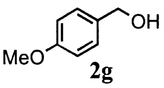
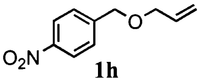
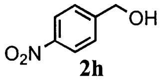
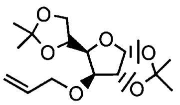
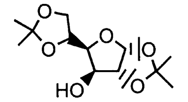
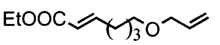
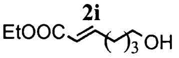
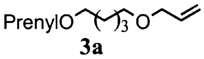
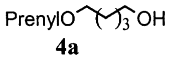
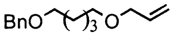
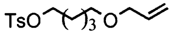
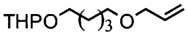
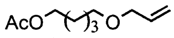
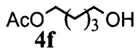
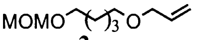
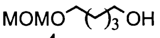
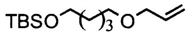
Table 1. Cleavage of allyl ethers

entry	substrate	product	yield/%
1	 **1a**	 **2a**	94
2	 **1b**	 **2b**	87
3	 **1c**	 **2c**	85
4	 **1d**	 **2d**	89
5	 **1e**	 **2e**	90
6	 **1f**	 **2f**	92
7	 **1g**	 **2g**	90
8	 **1h**	 **2h**	88
9	 **1i**	 **2i**	85
10	 **1j**	 **2j**	86

allyl ethers were prepared and subjected to the present reaction conditions. The secondary benzylic alcohol allyl ethers **1b**,**c**, alicylic secondary alcohol allyl ether **1d** and the phenolic substrates **1e**,**f** behaved well to yield the corresponding free alcohols **2b–f** in >85% yield (entries 2–6, Table 1). Also, the primary benzyl alcohol derivatives **1g** and **h** gave the parent alcohols **2g** and **h** without affecting methoxy and nitro functionalities (entries 7 and 8, Table 1). Similarly, the carbohydrate substrate **1i** produced the corresponding 1:2,5:6-di-*O*-isopropylidine-α-D-glucose **2i** in 85% yield (entry 9, Table 1). The α,β-unsaturated ester substrate **1j** also regenerated the parent alcohol **2j** in 86% yield leaving the conjugated double bond and ester functionalities intact (entry 10, Table 1). Reduction of carbonyl functionality is, however, noted as a minor limitation of this reaction.[26g]

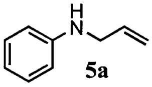
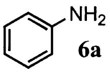
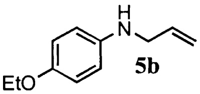
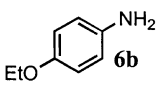
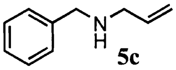
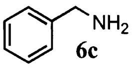
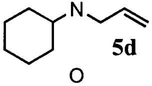
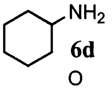
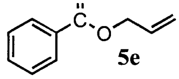
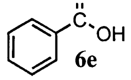
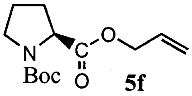
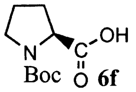
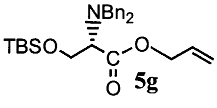
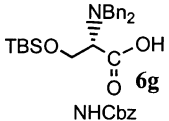
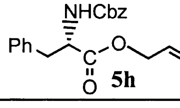
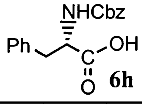
To check the compatibility and prove the mildness of the system, we have studied the cleavage of a series of 1,5-pentane diol diether substrates **3a–h** (Table 2). These substrates having allyl ether functionality at one end and a hydroxyl-protected group at the other end also underwent chemoselective deprotection at the allyl end under the same experimental conditions. Interestingly, the reaction of **3a** occurred at the allyl end even though a prenyl group was located at the other end (entry 1, Table 2). Also of interest is the finding that cleavage occurred at the allyl end of benzyl (Bn), *p*-methoxybenzyl (PMB) and tosyl (Ts) ethers (entries 2–4, Table 2). In addition, we observed that tetrahydropyranyl (THP), methoxy methyl (MOM), *tert*-butyldimethyl silyl (TBS), and acetyl (Ac) ethers (entries 5–8, Table 2) were stable to the present protocol.

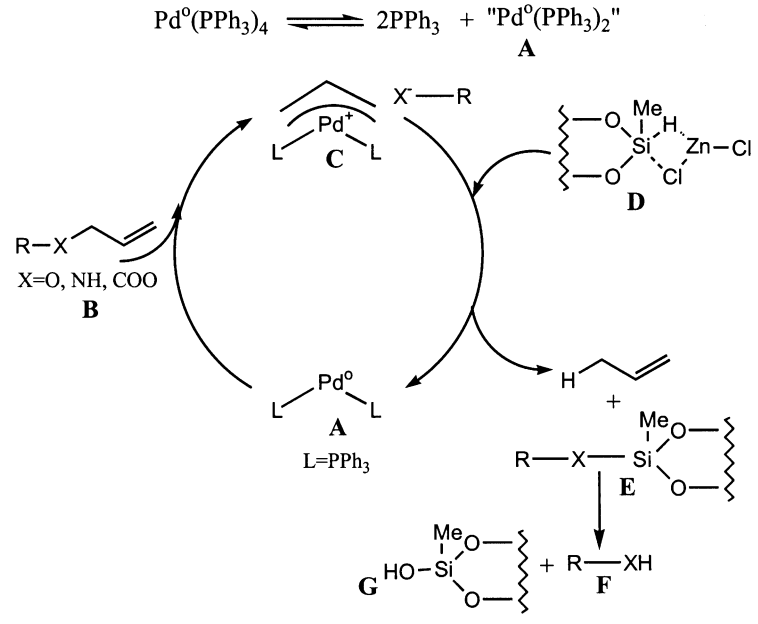
Table 2. Cleavage of allyl ethers in the presence of other ethers

entry	substrate	product	yield/%
1	 **3a**	 **4a**	92
2	 **3b**	 **4b**	90
3	 **3c**	 **4c**	87
4	 **3d**	 **4d**	92
5	 **3e**	 **4e**	85
6	 **3f**	 **4f**	89
7	 **3g**	 **4g**	85
8	 **3h**	 **4h**	90

In later studies, a few amines (entries 1–4, Table 3) and acids (entries 5–8, Table 3) were allylated and exposed to PMHS, $ZnCl_2$ and $Pd(PPh_3)_4$ to afford the corresponding amines and acids in good yields. Again, during this study, *N*-benzyl (*N*Bn), *N*-*t*-butyl carbamate (*N*Boc) and *N*-benzyl carbamate (*N*Cbz) groups were found to be stable to the reaction conditions.

Table 3. Cleavage of allyl amines and esters

entry	substrate	product	yield/%
1	 **5a**	 **6a**	90
2	 **5b**	 **6b**	88
3	 **5c**	 **6c**	92
4	 **5d**	 **6d**	89
5	 **5e**	 **6e**	87
6	 **5f**	 **6f**	85
7	 **5g**	 **6g**	87
8	 **5h**	 **6h**	85



Scheme 2.

At this time, the nature of the reaction mechanism is unclear. Allyl deprotection is probably occurring by a tentative mechanism as shown in Scheme 2. The palladium complex **A**, which is formed by ligand dissociation from tetrakis(triphenylphosphine)palladium(0),[28] reacts with allyl substrate **B** to give the π-allyl palladium(II) complex **C**. Then perhaps zinc chloride activates PMHS **D** towards hydride transfer[27i] to this π-complex affording propene **E** and deallylated product **F** along with by product **G** after workup. Clearly more work is needed to elucidate the exact mechanism.

3. Conclusion

An extremely facile and mild deallylation method is described for a variety of allyl ethers, amines and esters. The advantage of the chemoselectivity, efficiency, economy, safety and simplicity of this protocol may extend the utility of the allyl protective group in organic synthesis.

4. Experimental

4.1. General methods

Crude products were purified by column chromatography on silica gel of 60–120 mesh. ^{1}H NMR spectra were obtained in $CDCl_3$ at 200 MHz. Chemical shifts are given in ppm with respect to internal TMS, and J values are quoted in Hz. Infrared spectra were obtained neat, and only the most significant absorptions in cm^{-1} are indicated. THF was distilled over sodium–benzophenone prior to use. Polymethylhydrosiloxane (PMHS) was obtained from Fluka Chemical Company and was used as received.

4.2. General procedure for deallylation

To a stirred solution of substrate (1 mmol) in THF (8 mL) were added polymethylhydrosiloxane (120 mg, 2 mmol), tetrakis(triphenylphosphine)palladium (10 mg) and $ZnCl_2$ (25 mg). The reaction mixture was stirred at ambient temperature until completion of the reaction (monitored by TLC, generally 3–5 h). After completion of the reaction, the mixture was diluted with water (5 mL), extracted with diethyl ether (2×10 mL), washed with brine solution (8 mL) and dried (Na_2SO_4). Evaporation of the volatiles followed by column chromatography on silica gel (ethyl acetate/hexane 1:9) afforded the products in yields as indicated in Tables 1–3.

4.2.1. 5-(3-Methyl-2-butenyloxy)-1-pentanol (4a). Colorless oil; ^{1}H NMR ($CDCl_3$): δ 5.34–5.28 (m, 1H), 3.92–3.88 (d, 2H, J=7.1 Hz), 3.68–3.59 (t, 2H, J=5.7 Hz), 3.42–3.36 (m, 2H), 1.75 (s, 3H), 1.68 (s, 3H), 1.6–1.52 (m, 4H), 1.48–1.4 (m, 2H); IR (Neat): 3400, 2936, 1457, 1377, 1086 cm^{-1}; MS (*m/z*): 172 (M$^+$); Anal. calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.62; H, 11.80.

4.2.2. (2*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-2-(dibenzyl)-amino propionic acid (6g). $[\alpha]_D = -50.85$ (*c* 0.35, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.38–7.18 (m, 10H), 3.95–3.85 (m, 4H), 3.7–3.62 (d, 2H, J=3.7 Hz), 3.56–3.48 (t, 1H, J=5.6 Hz), 0.9 (s, 9H), 0.2 (s, 6H); IR (Neat): 3395, 3026, 1592, 1248, 1045, 698 cm^{-1}; MS (*m/z*): 354 (M$^+$−45); Anal. calcd for $C_{23}H_{33}NO_3Si$: C, 74.54; H, 9.25. Found: C, 74.49; H, 9.28.

4.2.3. 2a–j, 4b–h, 6a–f and h. ^{1}H NMR, IR and mass spectral data of these known compounds were identical with those of authentic samples.

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