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Highly efficient and chemoselective cleavage of prenyl ethers using $ZrCl_4/NaBH_4$☆

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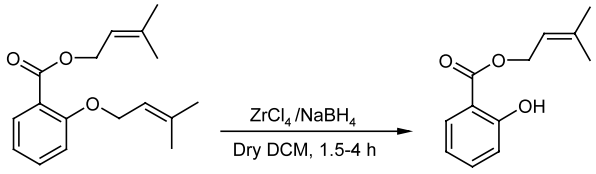
Abstract—An efficient and chemoselective deprotection of prenyl ethers of phenols and alcohols with $ZrCl_4/NaBH_4$ in DCM was achieved in high yields. The selectivity of prenyl ether deprotection is well demonstrated by carrying out the reaction in the presence of several other ether and ester functionalities.

Protection of hydroxyl and acid groups plays an important role in organic synthesis.[1] Selective deprotection of a particular functionality in the synthesis of complex natural products having a multitude of functionalities is often a challenging task for organic chemists. The allyl group has been used frequently for protecting various functionalities especially alcohols and phenols due to its stability towards acidic and basic conditions. Several methods are available for the deprotection of the allyl group and these have been reviewed.[2] Currently much attention has been given to the 2-methylbut-2-enyl (prenyl) group as protection for phenols and acids. Recently a few methods have been developed for the cleavage of prenyl ethers under different conditions which include $TiCl_4$–$n$$Bu_4NI$,[3] I_2[4] and DDQ.[5] In addition two more methods are known in the literature for the deprotection of prenyl esters, these are I_2 in cyclohexane[6] and $CeCl_3 \cdot 7H_2O/NaI$.[7]

However, many of these methods have limited synthetic scope due to lack of selectivity. Moreover, the yields of deprotection of prenyl ethers in substrates containing a carbonyl functional group in the position *para* to the ether are very low, and some of the above methods require cumbersome experimental procedures.

Herein, we wish to report $ZrCl_4/NaBH_4$ as an efficient reagent[8] for the selective removal of prenyl ether groups (Scheme 1) over a wide range of other functional groups. The cleavage was effected by $ZrCl_4/NaBH_4$ in DCM at room temperature and the reaction is clean and complete within 1.5–4 h.[9]



1a 2a

Scheme 1.

The deprotection of prenyl ethers was achieved in high yields with high chemoselectivity. The results are tabulated in Table 1, which clearly show the chemoselectivity in the deprotection of prenyl ethers. This is the first report of selective deprotection of prenyl ethers in the presence of prenyl esters.

In summary, the present methodology offers attractive features such as high chemoselectivity, high yields and simple reaction conditions. It may find extensive applications in organic synthesis where the selective deprotection of prenyl ethers is required.[9]

Acknowledgements

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Keywords: deprotection; prenyl ethers; zirconium tetrachloride; sodium borohydride.

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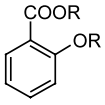
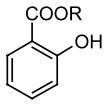
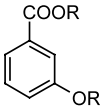
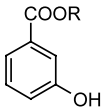
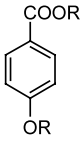
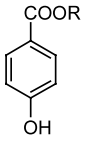
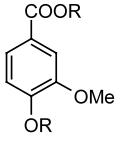
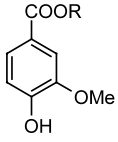
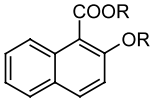
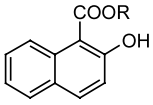
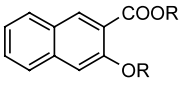
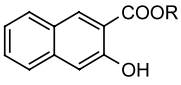
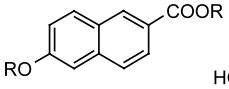
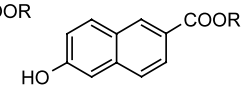
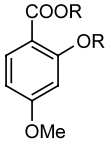
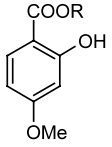
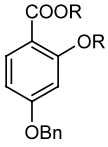
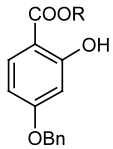
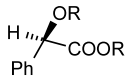
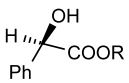
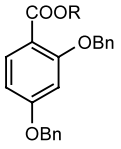
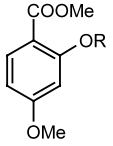
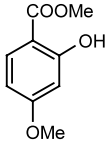
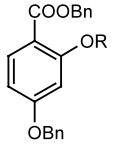
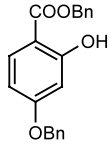
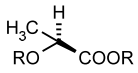
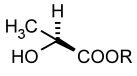
Table 1. Selective cleavage of prenyl ethers catalyzed by $ZrCl_4/NaBH_4$

Entry	Substrate **1**	Product[a] **2**	Time(h)	%Yield [b]
a			1.5	96
b			2	70
c			2	75
d			2.5	80
e			2	92
f			2	94
g			3	80
h			2.5	90
i			2.5	92
j			3.5	76

R = 2-Methylbut-2-enyl.

Table 1. (*Continued*)

Entry	Substrate **1**	Product [a] **2**	Time(h)	%yield [b]
k		——	10	-----
l			3	72
m			2.5	75
n			4	70

[a] All the products were characterized by ^{1}H NMR and mass spectroscopy.
[b] Isolated and unoptimized yields.
R = 2-Methylbut-2-enyl.

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9. *Typical experimental procedure*: $ZrCl_4$ (0.085 g, 0.364 mmol, 1 equiv.) was placed into a two necked round bottom flask equipped with a magnetic bead, and dry DCM (5 ml) was syringed into the flask. The contents were cooled to 0°C and $NaBH_4$ (0.054 g, 1.45 mmol, 4 equiv.) was added to the solution. The substrate (0.1 g, 0.364 mmol, 1 equiv., entry 1) in DCM (5 ml) was then added at the same temperature. After the complete addition the ice bath was removed and the contents brought to room temperature. The progress of the reaction was monitored by TLC which clearly indicated the disappearance of the starting material. After completion of the reaction, the reaction mixture was quenched with cold water (10 ml) and diluted with DCM (20 ml). The organic layer was separated and dried with anhydrous Na_2SO_4. The solvent was removed under vacuum and the product was purified by column chromatography on silica gel (60–120) to give pure product in 96% yield (entry 1, 2a).
Compound **1e**: ^{1}H NMR ($CDCl_3$, 200 MHz): 1.68 (br s, 12H, 4×CH_3), 4.60 (d, 2H, J=7 Hz, $\underline{CH_2}$-CH), 4.90 (d, 2H, J=7 Hz, $\underline{CH_2}$-CH), 5.28–5.38 (br t, 2H, 2 CH_2-$\underline{CH}$), 7.2–7.48 (m, 3H), 7.62–7.82 (m, 3H). Mass: m/z 324.

Compound **2e**: ^{1}H NMR ($CDCl_3$, 200 MHz): 1.64 (br s, 6H, 2×CH_3), 5.02 (d, 2H, $J=7$ Hz, $\underline{CH_2}$-CH), 5.58 (t, 1H, 7.0 Hz, CH_2-$\underline{CH}$), 7.18 (d, 1H, $J=8$ Hz), 7.32–7.38 (m, 1H), 7.42–7.58 (m, 1H), 7.72 (d, 1H, $J=8$ Hz), 7.92 (d, 1H, $J=8$ Hz), 8.80 (d, 1H, $J=8$ Hz), 12.38 (s, 1H, OH). Mass: m/z 256.

Compound **1d**: ^{1}H NMR ($CDCl_3$, 200 MHz): 1.64 (br s, 12H, 4×CH_3), 3.90 (s, 3H, OMe), 4.60 (d, 2H, $J=7$ Hz, $\underline{CH_2}$-CH), 4.78 (d, 2H, $J=7$ Hz, $\underline{CH_2}$-CH), 5.38–5.46 (br t, 2H, 2 CH_2- $\underline{CH}$), 6.82 (d, 1H, $J=10$ Hz), 7.46 (s, 1H), 7.62 (d, 1H, $J=8$ Hz). Mass: m/z 304.

Compound **1i**: ^{1}H NMR ($CDCl_3$, 200 MHz): 1.64 (br s, 12H, 4×CH_3), 3.98 (d, 2H, $J=7$ Hz, $\underline{CH_2}$-CH), 4.52 (d, 2H, $J=7$ Hz, $\underline{CH_2}$-CH), 5.32 (s, 2H, -OCH_2), 5.4–5.60 (b t, 2H, 2 CH_2-$\underline{CH}$), 6.38–6.48 (m, 2H), 7.24–7.48 (m, 5H), 7.80 (d, 1H, $J=8$ Hz). Mass: m/z 380.