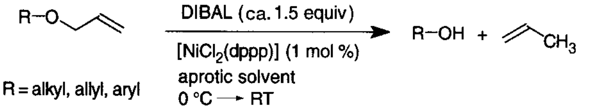
Extremely Facile and Selective Nickel-Catalyzed Allyl Ether Cleavage

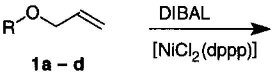
Takahiko Taniguchi and Kunio Ogasawara*

The use of an allyl ether functionality, which is stable under both acidic and basic conditions, for the protection of alcohols and phenols will become more common provided that more effective procedures for the removal of the allyl group to regenerate the hydroxyl functionality become available.[1, 2] Most generally, two strategies have been used for the removal of allyl ether groups: a two-step process in which the double bond of the allyl group is isomerized and single-step procedures employing a variety of conditions.[1] However, these methods are still less than satisfactory for practical use. We now report a simple and efficient single-step procedure for the chemoselective removal of the allyl functionality of both aliphatic and aromatic allyl ethers by treatment with a small excess of diisobutylaluminum hydride (DIBAL) in an aprotic solvent in the presence of a catalytic amount of dichloro[propane-1,3-diylbis(diphenylphosphane)nickel(II) [NiCl$_2$(dppp)].[3] Most importantly, the cleavage occurrs chemoselectively only at the allyl(2-propenyl) ether functionality with expulsion of propene even when a substituted allylic ether moiety is present in the same molecule [Eq. (a)].



(a)

The cleavage reactions of the allyl ethers of 4-methoxyphenol (**2a**), 2-phenylethanol (**2b**), (L)-menthol (**2c**), cholesterol (**2d**), and 1-adamantanol (**2e**), representatives of phenolic, primary, secondary, and tertiary allyloxy substrates, were first examined [Eq. (b), Table 1]. Thus, treatment of an



(b)

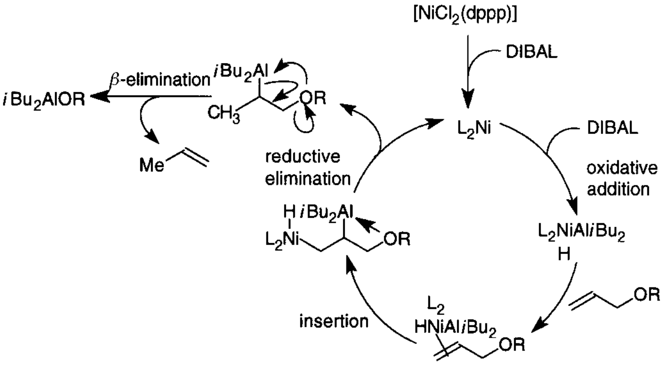
ice-cooled solution of the substrates **1a**–**e** and [NiCl$_2$(dppp)] (1 mol%) in an aprotic solvent such as diethyl ether with DIBAL in toluene (1.5 M, 1.5 equiv) afforded the deallylation products **2a**–**e** cleanly in excellent yields. Product **2a** was obtained in comparable yields in a range of solvents (Table 1, entries 2–4). The same reaction also occurred when NaBH$_4$ in THF/EtOH was used in place of DIBAL (Table 1, entry 5). Importantly, no deallylation occurred in the absence of the nickel catalyst.[4, 5] Moreover, none of the enol ether intermediates could be isolated from the reaction mixtures.

In order to clarify the reaction pathway, the reaction of the 4-methoxyphenyl ether **1a** was carried out in CDCl$_3$, and the mixture was examined directly by ^{1}H NMR (300 MHz) spectroscopy. Although the signal of the allylic methyl group could not be discerned due to overlapping signals, the signals of three olefinic protons attributable to propene[6] appeared clearly at $\delta = 5.81$ (1H, m), 5.02 (1H, brd, $J = 17.3$ Hz), and 4.93 (1H, brd, $J = 10.2$ Hz) supporting a nickel-catalyzed hydroalumination–elimination pathway[7] (Scheme 1).

Table 1. [NiCl$_2$(dppp)]-catalyzed deallylation of simple monoallyl ethers.

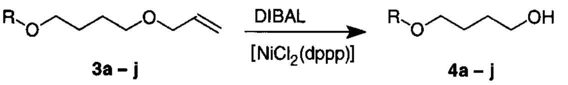
Entry	Substrate	R	Solvent	t [h]	Product	Yield [%][a]
1	**1a**	4-MeOC$_6$H$_4$	toluene[b]	2	**2a**	90
2	**1a**	4-MeOC$_6$H$_4$	CH$_2$Cl$_2$[b]	2	**2a**	86
3	**1a**	4-MeOC$_6$H$_4$	THF[b]	2	**2a**	88
4	**1a**	4-MeOC$_6$H$_4$	Et$_2$O[b]	2	**2a**	90
5	**1a**	4-MeOC$_6$H$_4$	THF/EtOH (4:1)[c]	2	**2a**	82
6	**1b**	PhCH$_2$CH$_2$	Et$_2$O[b]	2	**2b**	85
7	**1c**	(L)-menthyl	Et$_2$O[b]	3	**2c**	97
8	**1d**	cholesteryl	Et$_2$O[b]	2	**2d**	95
9	**1e**	1-adamantyl	Et$_2$O[b]	3	**2e**	80

[a] Yield after SiO$_2$ column chromatography. [b] Reaction was carried out with DIBAL (1.5 equiv) and [NiCl$_2$(dppp)] (1 mol%) at 0°C→RT. [c] Reaction was carried out with NaBH$_4$ (3.0 equiv) and [NiCl$_2$(dppp)] (4 mol%) at 0°C→RT.



Scheme 1. Proposed mechanism for the nickel-catalyzed cleavage of allyl ethers with DIBAL.

The cleavage of a series of the diether substrates **3a**–**j** having an allyl ether functionality at one end and another hydroxyl protecting group at the other end also proceeded chemoselectively at the allyl end though some cases required modified conditions [Eq. (c), Table 2]. Treatment of substrates **3a**–**g** afforded products **4a**–**g** in excellent yields,



(c)

except for the bis-allyl substrate **3d** which underwent double deallylation. Interestingly, the reaction of **3e** occurred selectively at the allyl end even though a prenyl group was located at the other end. It is also interesting to find that the cleavage occurred selectively at the allyl end of methoxymethyl (MOM) and tetrahydropyranyl (THP) ethers (**3f** and **3g**, respectively), since acetal functionalities are is known to be susceptible to DIBAL.[8, 9] Similarly, the reaction of diastereomeric furanose allyl acetals α-**5** and β-**5** gave the same

---

[*] Prof. Dr. K. Ogasawara, Dr. T. Taniguchi
Pharmaceutical Institute, Tohoku University
Aobayama, Sendai 980-8578 (Japan)
Fax: (+81)22-217-6845
E-mail: konol@mail.cc.tohoku.ac.jp

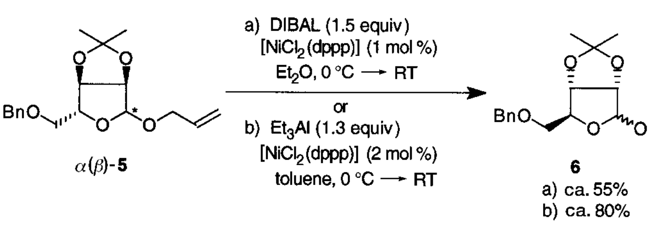
1433-7851/98/3708-1136 $ 17.50+.50/0

Table 2. [$NiCl_2$(dppp)]-catalyzed deallylation of diethers.

Entry	Substrate	R	Solvent	Product	Yield [%][a]
1	**3a**	*t*BuMe$_2$Si	Et$_2$O[b]	**4a**	92
2	**3b**	4-MeOC$_6$H$_4$	Et$_2$O[b]	**4b**	95
3	**3c**	benzyl	Et$_2$O[b]	**4c**	95
4	**3d**	allyl	Et$_2$O[b]	**4d**	51
5	**3e**	prenyl	Et$_2$O[b]	**4e**	80
6	**3f**	MOM	Et$_2$O[b]	**4f**	90
7	**3g**	THP	Et$_2$O[b]	**4g**	89
8	**3h**	acetyl	THF/EtOH (4:1)[c]	**4h**	73
9	**3i**	pivaloyl	THF/EtOH (4:1)[c]	**4i**	85
10	**3j**	benzoyl	THF/EtOH (4:1)[c]	**4j**	80

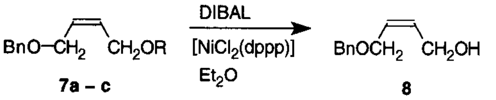
[a] Yield after SiO_2 column chromatography. [b] Reaction was carried out with DIBAL (1.5 equiv) and [$NiCl_2$(dppp)] (1 mol%) at 0 °C→RT, 2 h. [c] Reaction was carried out with $NaBH_4$ (4.0 equiv) and [$NiCl_2$(dppp)] (4 mol%) at 0 °C→RT.

hemiacetal mixture **6**, in which the the acetonide functionality is intact, by selective deallylation and spontaneous epimerization [Eq. (d)]. However, the reaction was found to proceed much better when triethylaluminum was used in place of DIBAL, because the hemiacetal functionality is more stable with the former reagent. Although ester functionalities (acetyl, pivaloyl, and benzoyl) are not incompatible with DIBAL as a reagent, when the ester substrates **3h**–**j** were treated with $NaBH_4$ in THF/EtOH the corresponding hydroxy esters **4h**–**j** were obtained in good yields (Table 2, entries 8–10).



(d)

Chemoselective cleavage of the allyl functionality was also demonstrated by the reaction of the allyl ethers of allyl alcohols [Eq. (e), Table 3]. Thus, the reaction of allyl (*Z*)-4-benzyloxy-2-butenyl ether (**7a**) occurred selectively at the nonsubstituted allyl end to give the corresponding allyl alcohol **8a** in good yield. Facile chemoselective cleavage at the nonsubstituted allyl end was also observed with the secondary allylic substrate **9** to give the secondary allylic alcohol **10** in 93% yield [Eq. (f)]. On the other hand, no reaction occurred with either prenyl and benzyl (*Z*)-4-benzyloxy-2-butenyl ethers **7b** and **7c**, respectively, under the same conditions (Table 3).

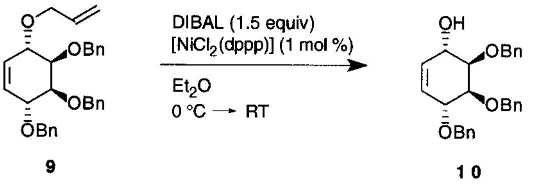


(e)

Table 3. [$NiCl_2$(dppp)]-catalyzed deallylation of diallyl ethers.

Entry	Substrate	R	*t* [h]	Product	Yield [%][a]
1	**7a**	allyl	2[b]	**8a**	71
2	**7b**	prenyl	12[b]	**8b**	0[c]
3	**7c**	benzyl	12[b]	**8c**	0[c]

[a] Yield after SiO_2 column chromatography. [b] Reaction was carried out in Et_2O with DIBAL (1.5 equiv) and [$NiCl_2$(dppp)] (1 mol%) at 0 °C→RT. [c] Starting material was recovered unchanged.



(f)

The present study offers an extremely facile and selective deallylation procedure for a variety of allyl ethers and also confirms that the reaction proceeds by nickel-catalyzed hydroalumination–elimination. Because of its simplicity and chemoselectivity, this procedure will undoubtedly extend the use of allyl groups for the protection of a variety of hydroxyl compounds.

Experimental Section

To a stirred solution of **1a** (100 mg, 0.6 mmol) and [(dppp)$NiCl_2$] (3 mg, 6 μmol) in Et_2O[10] (2 mL) under argon was added dropwise DIBAL (1.5 M in toluene, 600 μL, 0.9 mmol) at 0 °C. The mixture was stirred for 5 min at the same temperature and then for 2 h at room temperature. The mixture was diluted with Et_2O (3 mL), quenched by addition of H_2O (600 μL) and, after stirring for 1 h, dried directly over $MgSO_4$, filtered through a Celite pad, and concentrated under reduced pressure to leave the crude product, which was chromatographed on silica gel (3 g, Et_2O/hexane 1/4 v/v) to give pure **2a** (68 mg, 90%).

Received: September 26, 1997 [Z10975IE]
German version: *Angew. Chem.* **1998**, *110*, 1137–1139

Keywords: allyl ethers • aluminum • cleavage reactions • nickel • protecting groups

---

[1] For a pertinent review, see: F. Guibe, *Tetrahedron*, 1997, **53**, 13509–13556.

[2] For pertinent monographs, see: a) T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 2nd ed., Wiley, New York, **1991**; b) P. J. Kocienski, *Protective Groups*, Thieme, Stuttgart, **1994**.

[3] H. M. Colquhoun, J. Holton, D. J. Thompson, M. V. Twigg, *New Pathways for Organic Synthesis*, Plenum, New York, **1988**.

[4] K. Fischer, K. Jonas, P. Misbach, R. Stabba, G. Wilke, *Angew. Chem.* **1973**, *85*, 1002–1012; *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 943–1026.

[5] A nickel-catalyzed reductive cleavage of cyclic allyl ethers with DIBAL has been reported recently, see: M. Lautens, P. Chin, S. Ma, T. Rovis, *J. Am. Chem. Soc.* **1995**, *117*, 532–533.

[6] ^1H NMR spectrum of propene in CCl_4 (60 MHz): $\delta = 5.73$ (m, 1H), 4.97 (m, 1H), 4.88 (m, 1H), 1.72 (dt, 3H). See: A. A. Bothner-By, C. Naar-Colin, *J. Am. Chem. Soc.* **1961**, *83*, 231–236.

[7] J. Eisch in *Comprehensive Organic Synthesis, Vol. 8* (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, pp. 733–761.

[8] For a pertinent review, see: E. Winterfeldt, *Synthesis* **1975**, 617–630.

[9] For examples reported by our group, see: a) S. Takano, M. Akiyama, S. Sato, K. Ogasawara, *Chem. Lett.* **1983**, 1593–1596; b) S. Takano, M. Akiyama, K. Ogasawara, *Heterocycles* **1983**, *20*, 2237–2238; c) S. Takano, M. Akiyama, K. Ogasawara, *Chem. Pharm. Bull.* **1984**, *32*, 791–794; d) S. Takano, A. Kurotaki, Y. Sekiguchi, S. Satoh, M. Hirama, K. Ogasawara, *Synthesis* **1986**, 811–817; e) S. Takano, S. Satoh, K. Ogasawara, *J. Chem. Soc. Chem. Commun.* **1988**, 59–60.

[10] Toluene may be used in place of Et_2O; however, a stock solution of DIBAL and [$NiCl_2$(dppp)] in toluene loses its activity within a week on standing at −20 °C.