Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 46 (2005) 2259–2262

Tetrahedron Letters

A chemoselective deprotection of trimethylsilyl acetylenes catalyzed by silver salts

Alban Orsini, Aurélien Vitérisi, Anne Bodlenner, Jean-Marc Weibel and Patrick Pale*

Laboratoire de synthèse et réactivité organique, associé au CNRS, Institut Le Bel, Université L. Pasteur, 67000 Strasbourg, France

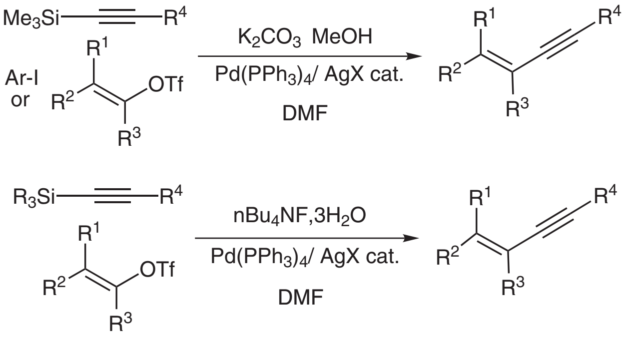
Received 24 December 2004; revised 31 January 2005; accepted 2 February 2005

Abstract—Trimethylsilyl acetylenes can be selectively deprotected in the presence of a catalytic amount of silver salts. $AgNO_3$ and AgOTf proved to be the most effective catalyst in a mixture of methanol, water and dichloromethane. Other functional groups, and especially silyl ethers, are not affected in these conditions.

© 2005 Elsevier Ltd. All rights reserved.

Silyl derivatives are widely used as protecting groups for various functions, mainly hydroxylated ones.[1,2] Due to their increasing use as building blocks for organic based materials, alkynes have seen a tremendous surge in their chemistry.[3,4] Among other aspects, the protection and deprotection of terminal alkynes is becoming an important issue, especially when selectivity is involved.[2c] Classically, such alkynes are protected by silyl groups, which are removed by fluoride ions in various conditions.[5] However, no selectivity with other silyl protecting groups can be achieved in these deprotection conditions. Deprotection with excess of mild bases is usually selective for the less bulky silyl groups (trimethylsilyl TMS or triethylsilyl TES).[2c,5,6]

Facing such issues while working on the preparation of conjugated enynes for natural products and organic materials synthesis,[7] we came up with Pd/Ag-catalyzed cross-coupling procedures selective for 1-trimethylsilyl-1-alkynes[8] and for any 1-trialkylsilyl-1-alkynes[9] (Scheme 1).

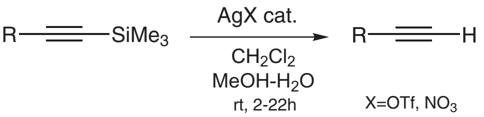


Scheme 1.

While deciphering the mechanism of these new coupling reactions, we observed the key role played by silver ions[10] This led us to investigate further the protiodesilylation of silylated alkynes using silver salts as deprotecting reagents. To the best of our knowledge, only a few reports described the use of silver nitrate as a desilylating agent. However, it has to be used in excess (up to 10 equiv) and usually required the presence of excess potassium cyanide[11a] or pyridine.[11b]

We found that some silver salts are indeed able to efficiently and selectively catalyze the deprotection of 1-trimethylsilyl-1-alkynes (Scheme 2) and we present here our preliminary results.

Based on our own experience concerning silver alkynes and some of our recent results,[8–10] we reasoned that in

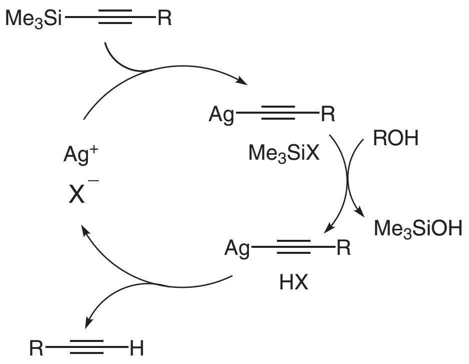


Scheme 2.

Keywords: Trimethylsilyl acetylenes; Deprotection; Silver; Catalysis.

* Corresponding author. Tel./fax: +33 390 241 517; e-mail: ppale@chimie.u-strasbg.fr

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.02.017



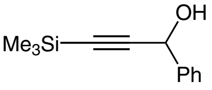
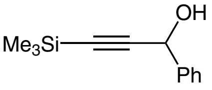
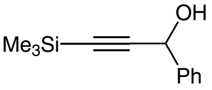
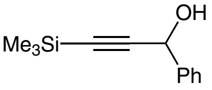
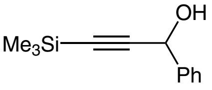
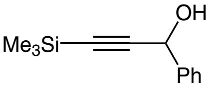
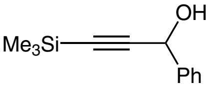
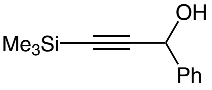
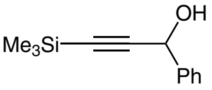
Scheme 3. Mechanistic hypothesis for a Ag-catalyzed deprotection of 1-trimethylsilyl-1-alkynes.

order to achieve deprotection, the silver counter-ion (X^- in Scheme 3) of the introduced silver salt must be nucleophilic enough to attack the silicon atom upon silver activation. This would lead to cleavage of the C–Si bond and to the in situ formation of an alkynyl silver and a silyl-X species. In protic solvents, the latter would be hydrolyzed leading to a better proton source, strong enough to hydrolyze the alkynyl silver species. Silver ion would thus be released, allowing for a catalytic cycle to take place (Scheme 3).

In order to check the above assumptions, we looked at the behavior of silver chloride, iodide, nitrate, triflate, and tetrafluoroborate toward 3-trimethylsilyl-2-phenyl propynol[12] **1a**. Since silver salts and silver acetylides are not readily soluble in alcohol or water, we selected various combinations of protic and aprotic solvents for the deprotection of 1-trimethylsilyl-1-alkynes (Table 1).

We were pleased to observe the formation of the expected terminal alkyne, 2-phenyl propynol **2a** but, as

Table 1. Deprotection of 3-trimethylsilyl-2-phenyl propynol **1a** in the presence of various silver salts in various conditions

	1-TMS-1-Alkyne	Ag salt[a]	Solvent	Time (h)	Yield[b]
1	 **1a**	$AgNO_3$	Me_2CO H_2O (1 equiv)	30	50
2	 **1a**	$AgNO_3$	MeOH 9 H_2O 1	30	30
3	 **1a**	$AgNO_3$	Me_2CO 9 H_2O 1	22	76
4	 **1a**	$AgNO_3$	MeOH 4 H_2O 1 CH_2Cl_2 7	16	79
5	 **1a**	AgCl	MeOH 4 H_2O 1 CH_2Cl_2 7	40	5
6	 **1a**	AgI	MeOH 4 H_2O 1 CH_2Cl_2 7	40	3
7	 **1a**	$AgBF_4$	MeOH 4 H_2O 1 CH_2Cl_2 7	40	3
8	 **1a**	AgOTf	MeOH 4 H_2O 1 CH_2Cl_2 7	2.5	86
9	 **1a**	—	MeOH 4 H_2O 1 CH_2Cl_2 7	50	0

[a] 0.1 equiv.

[b] Yield of isolated pure product.

expected, yields were dramatically influenced by the nature of both the silver catalyst used (Table 1, entries 4–8) and the solvents used (Table 1, entries 1–4).

In mixtures of methanol and water or acetone and water, a white precipitate formed upon addition of silver nitrate. TLC monitoring showed the clean but slow disappearance of the starting material to the benefit of **2a** (entries 1–2). With enough acetone mixed to water, the reaction mixture appeared cloudy but the reaction was faster and the deprotected alkyne was recovered in good yield (entry 3). A homogeneous reaction mixture could eventually be achieved using a mixture of dichloromethane, methanol, and water, 7–4–1, respectively. In this mixture, the deprotection reaction was over after several hours (entry 4). These results probably reflected the solubility of the alkynyl silver, which should be in situ formed. Indeed, the presence of silver ion is critical since no reaction was observed without silver salt whatever the conditions (e.g., entry 9).

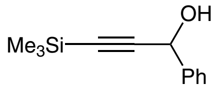
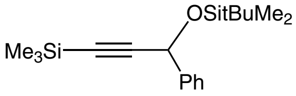
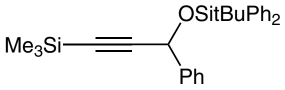
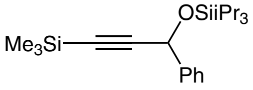
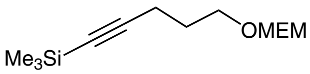
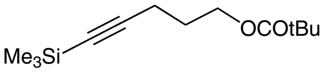
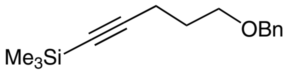
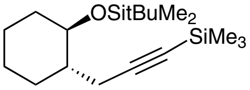
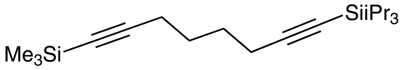
In order to study the scope of this new deprotection method, various representative trimethylsilylated alkynes **1b–d**, **3d–g**, **5b**, **7b** bearing various protecting groups were then prepared by conventional methods[12,13] and submitted to the above conditions. The expected terminal alkynes **2b–d**, **4e–g**, **6b**, **8b** were obtained in good to excellent yields (Table 2). As with **1a**, the reaction proved to be more rapid when catalyzed by silver triflate than by silver nitrate.

Acetal, ester, and benzyl protecting groups proved to be perfectly compatible with this method, as demonstrated by the selective reaction of the pivalate of 5-trimethylsilylpent-4-ynol **3e**, its methylethoxymethyl **3f** and benzyl analogs **3g** (Table 2, entries 8–13).

More interestingly, this method proved to be selective toward other silyl protecting groups. Indeed, 3-trimethylsilyl-2-phenyl propynols O-protected either with *tert*-butyldimethylsilyl, *tert*-butyldiphenylsilyl, or tri*iso*propylsilyl group, **1b**,**c**,**d**, were cleanly and selectively deprotected at the acetylenic end (entries 3–7). A similar behavior was observed with **5b** (entry 14).

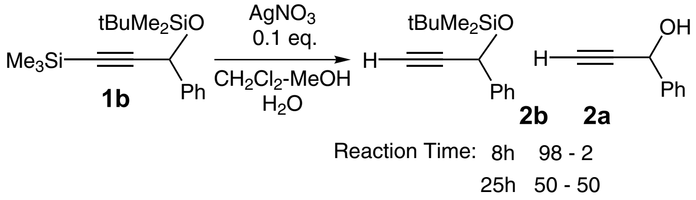
The *O*-*tert*-butyldimethylsilyl group proved however sensitive to these conditions after prolonged contact within the reaction mixture, while bulkier silyl protecting goups (TBDPS, TIPS) remained unaffected. Indeed, the deprotection of **1b** was perfectly selective for the TMS group up to 7 h but then the O-TBDMS group started to be removed and was half deprotected after

Table 2. Deprotection of various 1-trimethylsilyl-1-alkynes: reaction performed with 0.1 equiv of silver salt in a 7-4-1 mixture of CH_2Cl_2–MeOH–H_2O

	1-TMS Alkyne		Catalyst	Time (h)	Yield (%)[a]
1	**1a**		$AgNO_3$	16	79
2			AgOTf	2.5	86
3	**1b**		$AgNO_3$	7.5	88
4			AgOTf	4	97
5	**1c**		$AgNO_3$	2.5	91
6	**1d**		$AgNO_3$	22	96
7			AgOTf	7.5	98[b]
8	**3e**		$AgNO_3$	20	95
9			AgOTf	9	98
10	**3f**		$AgNO_3$	22	92
11			AgOTf	8	95
12	**3g**		$AgNO_3$	22	76
13			AgOTf	8	97
14	**5b**		$AgNO_3$	5.5	96[b]
15			AgOTf	5.5	91[b]
16	**7d**		$AgNO_3$	23	93[b]
17			AgOTf	7	95

[a] Yield of isolated pure product.

[b] Yield relative to conversion, some starting material being recovered.



Scheme 4. Selectivity of the deprotection of **1b**.

16 h in the presence of 0.1 equiv of silver nitrate (Scheme 4).

Interestingly enough, a complete selectivity was achieved with a diyne protected with two different silyl groups (entries 16–17). Indeed, the TMS group of **7d** was removed in the presence of 0.1 equiv of silver nitrate or triflate, while the TIPS group remained unaffected. Again, silver triflate induced a faster reaction than the nitrate (entry 17 vs 16).

In conclusion, we demonstrated here that 1-trimethylsilyl-1-alkynes can be selectively deprotected in the presence of catalytic amounts of silver nitrate or triflate. Various other protecting groups are fully compatible with this new method. Interestingly, other silylated functions are not affected by this process. Further works in this area are now in progress.

Supplementary material

Typical procedure for the deprotection of 1-trimethylsilyl-1-alkynes catalyzed by silver nitrate or triflate: To a solution of 1-trimethylsilyl-1-alkyne (1 equiv) in a premixed mixture of acetone–water–dichloromethane (4:1:7; 20 mL/mmol) was added silver nitrate or silver triflate (0.1 equiv). The resulting mixture was then stirred at room temperature. Once the starting materials disappeared, an aqueous saturated solution of ammonium chloride (5 mL/mmol) was added. The resulting mixture was then extracted three times with dichloromethane (5 mL/mmol). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by silica gel column chromatography yielding the corresponding pure 1-alkyne.

Acknowledgements

The authors thank the CNRS for financial support. A.B. thanks the ‘Ministère de l’Education Nationale et de la Recherche’ for a PhD fellowship. We also thank a referee for pointing out additional references in Ref. 11.

References and notes

1. (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991; (b) Kocienski, P. *Protecting Groups*, 3d ed.; Thieme: Weinheim, 2003.
2. (a) Lalonde, M.; Chan, T. H. *Synthesis* **1985**, 818–845; (b) Crouch, R. D.; Nelson, T. D. *Synthesis* **1996**, 1031–1069; (c) Crouch, R. D. *Tetrahedron* **2004**, *60*, 5833–5871.
3. (a) Caroll, R. L.; Forman, C. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 4378–4400; (b) Iwamura, H.; Matsuda, K. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, 1995; pp 385–414; (c) Young, J. K.; Moore, J. S. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, 1995; pp 416–442; (d) Diederich, T. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, 1995; pp 443–471.
4. (a) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 402–428; (b) Zhao, Y.; Campbell, K.; Tykwinski, R. R. *J. Org. Chem.* **2002**, *67*, 336–344; (c) Spreiter, R.; Bosshard, C.; Knöpfle, G.; Tykwinski, R. R.; Schreiber, M.; Diederich, F. *J. Phys. Chem. B* **1998**, *102*, 29–32; (d) Schwab, P. F. H.; Noll, B. C.; Michl, J. *J. Org. Chem.* **2002**, *67*, 5476–5485; (f) Zhao, D.; Moore, J. S. *J. Org. Chem.* **2002**, *67*, 3548–3554.
5. Colvin, E. W. *Silicon Reagent in Organic Synthesis*; Academic: London, 1988.
6. Benkouider, A.; Pale, P. *J. Chem. Res. (S)* **1999**, 104–105.
7. (a) Bertus, P.; Pale, P. *Tetrahedron Lett.* **1996**, *37*, 2019–2022; (b) Bertus, P.; Pale, P. *Tetrahedron Lett.* **1997**, *38*, 8193–8196; (c) Bertus, P.; Pale, P. *J. Organomet. Chem.* **1998**, *567*, 173–180; (d) Halbes, U.; Pale, P. *J. Organomet. Chem.* **2003**, *687*, 420–424.
8. Halbes, U.; Pale, P. *Tetrahedron Lett.* **2002**, *43*, 2039–2042.
9. (a) Halbes, U.; Bertus, P.; Pale, P. *Tetrahedron Lett.* **2001**, *42*, 8641–8644; (b) Halbes, U.; Pale, P. *Eur. J. Org. Chem.* **2002**, 2039–2042.
10. (a) Dillinger, S.; Bertus, P.; Pale, P. *Org. Lett.* **2001**, *3*, 1661–1664; (b) Halbes, U.; Bertus, P.; Pale, P., in preparation.
11. (a) Schmidt, H. M.; Arens, J. F. *Rec. Trav. Chim. Pays-Bas* **1967**, *86*, 1138–1142, and for recent exemples; Banfi, L.; Guanti, G. *Eur. J. Org. Chem.* **2002**, 3745–3755; Nazaré, M.; Waldmann, H. *Chem: Eur. J.* **2001**, *7*, 3363–3376; (b) Carreira, E. M.; Du Bois, J. *J. Am. Chem. Soc.* **1995**, *117*, 8106–8125; Clive, D. L. J.; Bo, Y.; Selvakumar, N.; McDonald, R.; Santarserio, B. D. *Tetrahedron* **1999**, *55*, 3277–3290; Clive, D. L. J.; Bo, Y.; Tao, Y.; Daigneault, S.; Wu, Y.-J.; Meignan, G. *J. Am. Chem. Soc.* **1998**, *120*, 10332–10349.
12. Cossy, J.; Pale, P. *Tetrahedron Lett.* **1987**, *28*, 6039–6040.
13. (a) Brandsma, L. *Preparative Acetylenic Chemistry*, 2nd ed.; Elsevier: Amsterdam, 1988; (b) Winterfeldt, E. In *Modern Synthetic Methods*; Scheffold, R., Ed.; VCH: Weinheim, 1992; Vol. 6, pp 103–226.