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“One-Step” Alkynylation of Adamantyl Iodide with Silver(I) Acetylides

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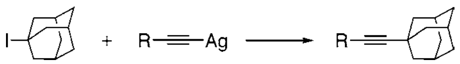
ABSTRACT

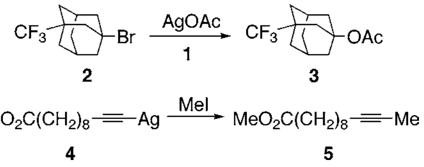


Silver(I) acetylides allow one-step alkynylation of adamantyl iodide in yields ranging from 25 to 68%.

Organosilver(I) compounds have found little application to organic synthesis, as many are unstable to air and water and decompose to the corresponding organic dimer and metallic silver.[1] An exception to this rule is the acetylide class, which generally lacks the aforementioned properties and is readily synthesized.[2] Surprisingly, investigations into this class are limited to a handful of synthetic applications (i.e., addition to aldehydes,[3] ketones,[3] acid chlorides,[2,4] pyridines,[5] and nucleosides[6]). A role in elucidating palladium−silver carbonate mediated processes has also been reported.[7]

Considering that silver(I) salts, such as AgOAc (**1**), have been used for converting adamantyl halides (e.g., **2**) to the corresponding acetates[8] (**3**) and that silver(I) acetylides react readily with methyl iodide to give methylated acetylenes[9] (Scheme 1), we reasoned that silver(I) acetylides (e.g., **4**) may well facilitate alkynylation at a tertiary center (Scheme 1).[10] Not surprisingly, this type of C−C bond connection is poorly represented in the chemical literature.[11]

Scheme 1



Preliminary investigations concentrated on reacting silver(I) phenylacetylide **6** with adamantyl bromide **7**. The choice of solvent was found to be crucial as silver(I) acetylides are notoriously insoluble and require strongly coordinating aprotic solvents [e.g., dimethyl sulfoxide (DMSO), hexamethylphosphoramide (HMPA), and pyridine].[12] Reactions

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(1) (a) Bähr, G.; Burba, P. In Houben-Weyl, *Methoden der Organische Chemie*; Müller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1970; Vol. 13/1, p 774. (b) Van Koten, G.; Noltes, J. G. In *Comprehensive Organometallic Chemistry*; Wilkinson, Stone, Abel, Eds.; Pergamon: New York, 1982; Vol. 2, p 709. (c) *Comprehensive Organometallic Chemistry II*; Pergamon: New York, 1982−1994; Vol. 3, p 71. (d) Gmelin Handbuch, Der Anorganischen Chemie, 8. Auflage Teil B5.

(2) Davis, R. B.; Scheiber, D. H. *J. Am. Chem. Soc.* **1956**, *78*, 1675−1678.

(3) Shahi, S. P.; Koide, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 2525−2527.

(4) (a) Inanaga, J.; Katsuki, T.; Takimoto, S.; Ouchida, S.; Inoue, K.; Nakano, A.; Okukado, N.; Yamaguchi, M. *Chem. Lett.* **1979**, 1021−1024. (b) Yerino, L. V.; Osborn, M. E.; Mariano, P. S. *Tetrahedron* **1982**, *38*, 1579−1591.

(5) (a) Nishiwaki, N.; Minakata, S.; Komatsu, M.; Ohshiro, Y. *Chem. Lett.* **1989**, 773−776. (b) Agawa, T.; Miller, S. I. *J. Am. Chem. Soc.* **1961**, *83*, 449−453.

(6) (a) De Las Heras, F. G.; Tam, S. Y.-K.; Klein, R. S.; Fox, J. J. *J. Org. Chem.* **1976**, *41*, 84−90. (b) Albrecht, H. P.; Repke, D. B.; Moffatt, J. G. *J. Org. Chem.* **1974**, *39*, 2176−2182.

(7) Dillinger, S.; Bertus, P.; Pale, P. *Org. Lett.* **2001**, *3*, 1661−1664.

(8) Duddeck, H.; Spitzer, M.; Bolte, G. *Liebigs Ann. Chem.* **1985**, 545−554.

(9) Isabelle, M. E.; Leitch, L. C. *Can. J. Chem.* **1958**, *36*, 440−448.

(10) For a two-step alkynylation of adamantane, see: Broxterman, Q. B.; Hogeveen, H.; Kingma, R. F. *Tetrahedron Lett.* **1986**, *27*, 1055−1058.

(11) For one-step alkynylation of adamantane, see: (a) Capozzi, G.; Ottaná, R.; Romeo, G.; Marcuzzi, F. *Gazz. Chim. Ital.* **1985**, *115*, 311−314 and references therein. (b) Xiang, J.; Fuchs, P. L. *Tetrahedron Lett.* **1998**, *39*, 8597−8600 and references therein. (c) Negishi, E.-i.; Baba, S. *J. Am. Chem. Soc.* **1975**, *97*, 7385−7387

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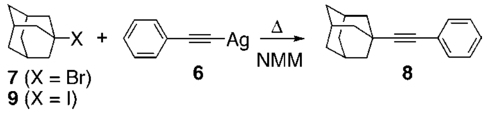
using either DMSO or HMPA as the solvent led mostly to gross mixtures, but reaction with pyridine as the solvent at 100 °C gave after prolonged (24−48 h) reaction times low yields of the desired product[13] (**8**) (Scheme 2).

Scheme 2



When adamantyl bromide **7** was substituted with adamantyl iodide **9** the rate of reaction increased, as expected,[14] and the yield rose to 35%. Although these results were promising, it was evident from GC/MS data that silver(I) phenylacetylide **6** was undergoing many side reactions with the solvent (pyridine). However, attempts to prevent these side reactions with related solvents, such as lutidine and picoline, failed to increase the yield of the product **8**. The use of triethylamine and tetramethyl ethylenediamine as solvent gave no product, but *N*-methylmorpholine (NMM) increased the yield of **8** to 68%. Interestingly, triphenylphosphine silver(I) phenylacetylide,[15] gave no improvement.

A range of silver(I) arylacetylides were then screened utilizing the optimized conditions (entries 1−6, Table 1), which afforded the corresponding adamantane in isolated yields ranging from 25 to 68%. Surprisingly, however, silver(I) 4-dimethylaminophenylacetylide preferred to undergo electrophilic aromatic substitution[16] (entry 7).

Aliphatic and silylated silver(I) acetylides were also found to react with adamantyl iodide under these conditions (entries 1−4, Table 2) but the yields were found to be lower in these cases as compared to the phenylacetylides.

The addition of silver(I) acetylides to adamantyl halides is thought to proceed through an $S_{RN}1$ mechanism. There is precedent for such a process in the substitution of alkyl halides with low reactivity toward nucleophiles, including bridgehead halides.[18,20,21] Further, silver salts have been used previously to generate adamantyl radicals.[19] Experimentally, this is supported by the observation of adamantane, a significant by-product of the $S_{RN}1$ process,[22] when analyzing the reaction mixtures using GC/MS. While a carbocationic mechanism may be envisaged,[11c,17] it cannot account for the formation of adamantane or the lack of reaction of adamantyl iodide with copper(I) phenylacetylide.[23,24]

Table 1. One-Step Alkynylation of Adamantyl Iodide with Silver(I) Phenylacetylides (NMM, Reflux)

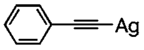
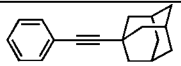
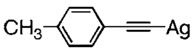
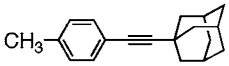
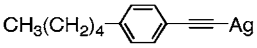
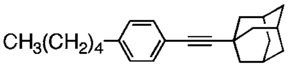
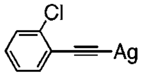
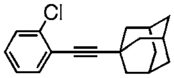
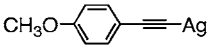
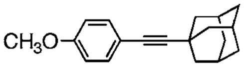
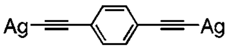
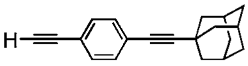
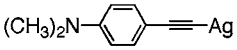
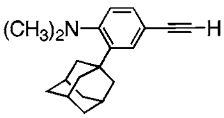
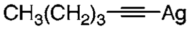
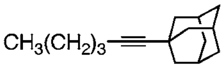
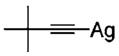
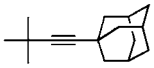
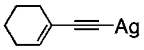
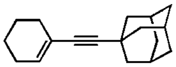
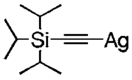
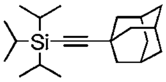
Entry	Reactant	Product [Yields (%)]
1		 68
2		 27
3		 57
4		 62
5		 51
6		 40
7		 20

Table 2. One-Step Alkynylation of Adamantyl Iodide with Silver(I) Acetylides (NMM, Reflux)

Entry	Reactant	Product [Yield(%)]
1		 29
2		 42^a
3		 25^a
4		 25

[a] Reaction conducted at 150−170 °C (pressure vessel).

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(12) Protic solvents were not examined as these undergo solvolysis with the halogenated substrate.

(13) Raine, A. L.; Williams, C. M.; Bernhardt, P. V. *Acta Crystallogr.* **2002**, *E58*, o1439−o1440.

(14) Goh, S. H.; Goh, L. Y. *J. Chem. Soc., Dalton Trans.* **1980**, 1641−1645.

(15) Bruce, M. I.; Humphrey, M. G.; Matisons, J. G.; Roy, S. K.; Swincer, A. G. *Aust. J. Chem.* **1984**, *37*, 1955−1961.

(16) Arylation of adamantyl halides is known: Bräse, S.; Waegell, B.; de Meijere, A. *Synthesis* **1998**, 148−152 and references therein.

(17) Kitano, Y.; Chiba, K.; Tada, M. *Synthesis* **2001**, 437−443.

(18) Rossi, R. A.; Pierini, A. B.; Peñéñrory, A. B. *Chem. Rev.* **2003**, *103*, 71−168.

(19) Testaferri, L.; Tieico, M.; Tingoli, M.; Fiorentino, M.; Troisi, L. *J. Chem. Soc., Chem. Commun.* **1978**, 93−94.

(20) (a) Ohno, M.; Shimizu, K.; Ishizaki, K.; Sasaki, T.; Eguchi, S. *J. Org. Chem.* **1988**, *53*, 729−733. (b) Molle, G.; Dubois, J. E.; Bauer, P. *Can. J. Chem.* **1987**, *65*, 2428−2433. (c) Osawa, E.; Majerski, Z.; Schleyer, P. von R. *J. Org. Chem.* **1971**, *36*, 205−207.

(21) Baldwin, J. E.; Adlington, R. M.; Birch, D. J.; Crawford, J. A.; Sweeney, J. B. *J. Chem. Soc., Chem. Commun.* **1986**, 1339−1340.

In conclusion, a novel carbon−carbon bond forming protocol is reported for direct one-step alkynylation of the adamantyl ring system. Unfortunately, this procedure is not applicable to substrates that can easily eliminate HI for example, *tert*-butyl iodide.

Acknowledgment. We thank the University of Queensland for financial support.

Supporting Information Available: Representative experimental procedure, characterization data, and copies of ^{1}H and ^{13}C NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) (a) Palacios, S. M.; Santiago, A. N.; Rossi, R. A. *J. Org. Chem.* **1984**, *49*, 4609−4613. (b) Borosky, G. L.; Pierini, A. B.; Rossi, R. A. *J. Org. Chem.* **1990**, *55*, 3705−3707. (c) Camps, P.; Lukach, A. E.; Rossi, R. A. *J. Org. Chem.* **2001**, *66*, 5366−5373.

(23) (a) Royer, E. C.; Barral, M. C.; Moreno, V.; Santos, A. *J. Inorg. Nucl. Chem.* **1981**, *43*, 705−709. (b) Aleksanyan, V. T.; Garbuzova, I. A.; Gol'ding, I. R.; Sladkov, A. M. *Spectrochim. Acta* **1975**, *31A*, 517−524.

(24) Reaction of copper(I) phenylacetylide with adamantyl iodide affords less than 5% coupled product.