This article was downloaded by: [Stony Brook University] On: 26 October 2014, At: 12:40 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



### Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

### Synthesis and CuAAC Reactions of Azidoalkylethoxysilanes: Grafting CuAAC Products onto Silica Surface

Roman G. Kultyshev<sup>a</sup>, Yuji Kawanishi<sup>a</sup>, Masateru Nishioka<sup>b</sup> & Akira Miyazawa<sup>a b</sup>

<sup>a</sup> National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki, Japan

<sup>b</sup> National Institute of Advanced Industrial Science and Technology (AIST Tohoku), Nigatake, Miyagino, Sendai, Japan Published online: 27 Dec 2013.

To cite this article: Roman G. Kultyshev , Yuji Kawanishi , Masateru Nishioka & Akira Miyazawa (2014) Synthesis and CuAAC Reactions of Azidoalkylethoxysilanes: Grafting CuAAC Products onto Silica Surface, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 44:4, 556-563, DOI: <u>10.1080/00397911.2013.822514</u>

To link to this article: http://dx.doi.org/10.1080/00397911.2013.822514

#### PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing,

systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <u>http://www.tandfonline.com/page/terms-and-conditions</u>



Synthetic Communications<sup>®</sup>, 44: 556–563, 2014 Copyright © Taylor & Francis Group, LLC ISSN: 0039-7911 print/1532-2432 online DOI: 10.1080/00397911.2013.822514

#### SYNTHESIS AND CUAAC REACTIONS OF AZIDOALKYLETHOXYSILANES: GRAFTING CUAAC PRODUCTS ONTO SILICA SURFACE

# Roman G. Kultyshev,<sup>1</sup> Yuji Kawanishi,<sup>1</sup> Masateru Nishioka,<sup>2</sup> and Akira Miyazawa<sup>1,2</sup>

<sup>1</sup>National Institute of Advanced Industrial Science and Technology (AIST), Tsukuba, Ibaraki, Japan

<sup>2</sup>National Institute of Advanced Industrial Science and Technology (AIST Tohoku), Nigatake, Miyagino, Sendai, Japan

#### **GRAPHICAL ABSTRACT**



**Abstract** One-pot synthetic protocols of novel azido functionalized silane coupling agents from corresponding terminal mesylated or tosylated 1-olefins were developed. Azido groups were successfully converted to the corresponding 1,2,3-triazol ring by the copper-catalyzed azido alkyne coupling (CuAAC) reaction without alkoxysilane decomposition. The CuAAC product was readily grafted onto the silica surface in good yield.

[Supplementary materials are available for this article. Go to the publisher's online edition of Synthetic Communications<sup>®</sup> for the following free supplemental resource(s): Full experimental and spectral details.]

Keywords Azide; CuAAC reaction; silane coupling agent; surface modification

#### INTRODUCTION

Bifunctional alkylalkoxysilanes such as  $X-(CH_2)_n-Si(OR)_3$  (silane coupling agents), where X is a functional group and Si(OR<sub>3</sub>) is an anchoring group, are essential for introducing functional sites onto silica surfaces for applications in the fields of catalysis, biomedicine, and organic–inorganic hybridized materials.<sup>[1]</sup> A great deal

Received May 22, 2013.

Address correspondence to Akira Miyazawa, National Institute of Advanced Industrial Science and Technology, Nigatake, Miyagino, Sendai 983-8551, Japan. E-mail: a.miyazawa@aist.go.jp

of effort has been applied toward the development of methodologies that provide a uniform arrangement of functional groups on surfaces. In general, modifications begin with a reaction between commercially available  $X-(CH_2)_n-Si(OR)_3$  (X = halogen or amino-group) and OH-groups on a silica surface, followed by a chemical transformation of X into another functional group. However, problems can arise in this approach, even for well-known quantitative transformations, because heterogeneous reactions involving functional groups supported on silica often differ from the reactions of the functional groups in a homogeneous environment.<sup>[1c]</sup> To avoid the problems associated with poor reactivity, formation of side products, product identification, and separation of a main product from side products and/or residual catalysts, the direct reaction of silica with a silane coupling agent already bearing the required functional group would be preferred.

In this past decade, Cu(I)-catalyzed 1,3-dipolar azido-alkyne cycloadditions (CuAAC) have been developed for the stereospecific construction of 1,2,3-triazole structures. They have been widely used for introducing functional sites onto silica surfaces by reacting an azidoalkyl group pre-introduced onto the silica with an alkyne bearing functional moiety.<sup>[2a-2d]</sup> To obtain silica surfaces that present azidoalkyl groups, two general methods have been reported in the literature. One method involves grafting a halopropyl triethoxysilane onto silica, followed by displacement of the halogen with an azide group using sodium azide.<sup>[3]</sup> The second method involves the direct grafting of azidopropyltriethoxysilane onto silica.<sup>[4a-e]</sup> In these protocols, the CuAAC reaction that produces the functionalized silicas must be chosen at the last step. As mentioned, such a heterogenous organic transformations are occasionally problematic. Indeed, the generation of pure surface-modified silica requires copious washing steps with organic solvents and/or mineral acid until no metal catalyst residue is detected.<sup>[4e]</sup> Despite the great deal of interest in the azidoalkyl functionalization of silica surfaces, to the best of our knowledge, examples of azidoalkylalkoxysilane syntheses are limited. No reports have thus far described the grafting of CuAAC reaction products derived from the reactions between azidoalkylalkoxysilanes and alkynes. In part, this is because chloroalkylalkoxysilanes, the immediate precursors of azides, are generally not commercially available, with the exception of chloropropyltriethoxysilane. Their preparation from chloroalkenes via hydrosilylation requires the use of chlorosilanes followed by an additional alcoholysis step.<sup>[5]</sup> The direct reaction between triethoxysilane and allyl chloride results in reduction rather than hydrosilylation.<sup>[6]</sup> Moreover, the alkoxysilyl groups of silane coupling agents are sometimes labile to moisture, and they require careful handling during isolation and purification processes.<sup>[7]</sup> Herein, we describe a facile preparative route to azidoalkylethoxysilanes starting from the unsaturated alcohols. The utility of the method will be demonstrated by remodeling the azidoalkylethoxysilanes as new silane coupling agents containing a 1,2,3-triazole via the CuAAC reaction with several types of alkynes. The silane coupling agent obtained is readily grafted onto silica surfaces to yield functionalized silica in pure form.

#### **RESULTS AND DISCUSSION**

Commercially available 5-hexene-1-ol was chosen for a preliminary evaluation of the approach to prepare azidoalkylethoxysilanes having azido group at the one end of alkyl chain. The hydroxyl group was converted to the mesylate 1a according to the literature procedure.<sup>[8]</sup> Addition of triethoxysilane to a tetrahydrofuran (THF) solution of 1a and Karstedt's platinum-divinyltetramethyldisiloxane catalyst,<sup>[9]</sup> followed by stirring for 4 h at room temperature, resulted primarily in the desired anti-Markovnikov addition product according to the <sup>1</sup>H NMR spectrum of the brownish viscous oil obtained after removal of excess triethoxysilane and solvent in vacuo. The crude hydrosilylation product was then used directly in the substitution of mesylate for azide without purification. Sodium azide (100% excess based on 1a) and dry dimethylformamide (DMF) were added to the same pot, and the resulting suspension was stirred at room temperature for 24 h to furnish the desired pure 1-triethoxysilyl-6-azidohexane 3a in 65% isolated yield after vacuum distillation. Encouraged by this initial result, we applied the one-pot hydrosilylation-azidation protocol to ethylene glycol allylether p-tosylate<sup>[10]</sup> (1b) with several types of methylethoxysilanes. The one-pot protocol under the same conditions gave the desired azidoethoxypropyltriethoxysilane (3b), methyldiethoxysilene (3c), and dimethylethoxysilane (3d) in 63, 59, and 42% isolated yields, respectively (Scheme 1).

Initially we tested the CuI catalyst system<sup>[11]</sup> for the CuAAC reactions, because the CuI reaction can be conducted under dry conditions to avoid hydrolysis of a labile ethoxysilyl group. The CuAAC reactions of **3b** with five alkynes, namely, n-1-hexyne (4a), propynyl acetate (4b), ethynylbenzene (4c), 2-pyridinylacetylene (4d), and diphenylpropargylphosphine-borane complex<sup>[12]</sup> (4e), were carried out in the presence of CuI (10 mol%) and diisopropylethylamine (DIPEA) as a base in dry THF. In all cases the reactions proceeded smoothly to afford the corresponding coupling products after 12 h of stirring at room temperature. The <sup>1</sup>H NMR spectrum of the crude product obtained from the reaction between 3b and 4c showed only one characteristic signal of the triazole ring proton as a singlet at 7.95 ppm. This indicated that the product formed as a single isomer and the structure of 5c was determined to be 1,4-adduct with comparisons to the results reported previously.<sup>[13]</sup> The structures of other CuAAC products (5a, 5b, 5d, 5e) were determined by similar way (Scheme 2). Next, another well-known catalytic system composed of CuSO<sub>4</sub> (10 mol%) and sodium ascorbate was tested for the reaction between 3b and 4c in an aqueous reaction medium (THF-H<sub>2</sub>O).<sup>[14]</sup> This system also catalyzed the CuAAC reaction at room temperature to afford the expected product 5c as a single isomer (1,4-adduct) in 55% yield. Although the yield was slightly lower than the yield obtained by the CuI-catalyzed reaction, this result is interesting considering the compound with



Scheme 1. One-pot synthesis of azidoalkylethoxysilanes.



Scheme 2. CuAAC reactions 3a with alkynes 4a-e.

the triethoxysilyl group was tolerant to decomposition reactions under aqueous conditions.

We evaluated the following two ways to functionalize silica surfaces via the CuAAC reaction. One is a heterogenuous CuAAC reaction between the azidoalkylgrafted silica and alkynes (grafting-coupling, path A in Scheme 3) and the other is a grafting of homogeneous CuAAC product derived from the reaction between azidoalkylethoxysilane and alkyne (coupling-grafting, path B in Scheme 3). The compound 4b was chosen as the CuAAC reaction counterpart, because the strong absorption of the carbonyl streching of the ester group, which appeares around 1715 cm<sup>-1</sup>, can be used to monitor formation of coupling product. Grafting of alkoxysilanes (3b or 5b) onto silica (CARiACT Q-3, 1.9 nm of average pore size, and  $678 \text{ m}^2/\text{g}$  specific surface area) was carried out in dry toluene at  $60 \,^{\circ}\text{C}$  for 3 h (Scheme 3). After filtration, in both cases, resulting white solids were separated from the reaction mixture. A small amount of nongrafted ethoxysilanes were recovered from the filtrate. Upon copious washing with toluene and drying under vacuum, the desired functionalized silicas were obtained as clear white solids in both cases. From the elemental analysis for each material, the amount of the azido group introduced in 6 and the triazole unit introduced in 7b were estimated to be 0.57 and



Scheme 3. Grafting of ethoxysilanes onto silica surface.

0.53 mmol/g, respectively. The materials **6** and **7b** were characterized by infrared (IR) and nitrogen porosimetry. In IR spectrum of **6** showed a strong characteristic absorption corresponding to a N<sub>3</sub> stretching at  $2122 \text{ cm}^{-1}$  [Fig. 1(a)]. Compound **7b** showed a carbonyl stretching corresponding to the ester group at  $1715 \text{ cm}^{-1}$  [Fig. 1(d)]. Both modified silicas **6** and **7b** had pore-size distributions centered around 1.9 nm and specific surface areas of 444 and  $470 \text{ m}^2/\text{g}$ , respectively. For **6** and **7b**, essentially the same pore size distributions were observed without the specific surface area, and the pore volumes decreased relative to that of the parent unmodified silica. These results indicated that the major structures of **6** and **7b** did not change during the grafting process, and the observed specific surface area decrease was typical for the process of grafting to the pore walls.

The heterogeneous CuAAC reaction of **6** with **4b** was carried out by stirring **6** with a 100% excess of **4b** in the presence of CuI (10 mol%) and diisopropylethylamine (DIPEA) as a base at room temperature under the same reaction time as that used for the homogeneous CuAAC reaction between **3b** and **4b**. After workup, the white silica **7aa** obtained was characterized by IR spectroscopy. The IR spectrum of **7aa** showed the presence of both unreated azido and desired ester groups [Fig. 1(b)]. Another catalyst system composed of CuSO<sub>4</sub> and sodium ascorbate gave modified silica **7ab** in yellow color, which was originated from the catalyst residue that remained even after copious washings with toluene, acidic methanol, and water. The azido absorption corresponding starting material was also observed in the IR spectra [Fig. 1(c)]. Thus, relative to the homogeneous CuAAC reaction, the heterogeneous CuAAC reaction was very slow due to the azido group located in a sterically restricted sites that prevent to contact catalyst and alkyne. These results obviously indicate that the grafting of CuAAC products onto silica (path B, coupling-grafting protocol) is an efficient way to lead to clean surface-modified silica.

In summary, we have developed a facile preparative way for azidoalkylethoxysilanes from tosylated  $\omega$ -alkenols in a one-pot hydrosilylation-azidation. The azidoalkylethoxysilanes can be derivatized to novel silane coupling agents



Figure 1. IR spectra of surface modified silica.

561

bearing a substituted 1,2,3-triazole ring through the CuI- and CuSO<sub>4</sub>-catalyzed CuAAC reactions. The preparative protocol for the coupling–grafting process, involving a reaction between the CuAAC reaction products and silica, should be useful for preparing clean surface functionalized silicas. Further exploration of this protocol, with the goal of preparing novel organic–inorganic hybrid materials, is under way.

#### **EXPERIMENTAL**

#### General Procedure for the Synthesis of Azidoalkylethoxysilanes

To a solution of 1a (2.66 g, 14.9 mmol) and 0.20 mL of Karstedt's catalyst xylene solution (2.1 wt% of platinum, purchased from Gelest) in dry tetrahydrofuran (THF) (20 mL) was added dropwise a solution of triethoxysilane (3.1 mL, 17 mmol) in dry THF (20 mL) via syringe under an  $N_2$  atmosphere. The reaction temperature was maintained at 20 °C using a tapwater bath. The reaction mixture was stirred for an additional 2h at room temperature followed by removal of the volatiles under vacuum, which left a brownish, slightly viscous oil. Formation of the hydrosilylated intermediate and complete consumption of **1a** was confirmed by the upfield shift of the methylene protons adjacent to silicon and the disappearance of the olefinic protons of **1a** in the <sup>1</sup>H NMR measurement of the crude product. Dry DMF (40 mL) and sodium azide (1.95 g, 30 mmol) were then added to the reaction flask. After evacuation and refilling with nitrogen, the suspension was stirred at 60 °C for 12 h. The reaction mixture was filtered to remove the white solid (sodium salts and unreacted  $NaN_3$ ) followed by concentration of the filtrate in vacuo. The crude mixture was purified by vacuum distillation (trap to trap distillation) to give 1-triethoxysilyl-6-azidohexane (3a) (2.80 g, 65%) as a colorless liquid, bp  $85-87 \degree C/$ 3 torr; <sup>1</sup>H NMR  $\delta$  (400 MHz, CDCl<sub>3</sub>) 3.80 (q, J=7.1 Hz, 6H), 3.24 (t, J=7.0 Hz, 2H), 1.58 (m, 2H), 1.45–1.32 (m, 6H), 1.21 (t, J = 7.1 Hz, 9H), 0.62 (m, 2H). <sup>13</sup>C NMR  $\delta$  (100 MHz, CDCl<sub>3</sub>) 58.5, 51.6, 32.7, 28.9, 26.5, 22.8, 18.4, 10.5.  $\nu_{max}(neat)/cm^{-1}$ 2096 (N<sub>3</sub>, vs). HRMS (ESI) calcd. for C<sub>12</sub>H<sub>27</sub>N<sub>3</sub>O<sub>3</sub>SiN<sub>3</sub>Na 312.1714; found 312.1719.

Compounds **3b-d** were obtained in a similar manner. Experimental details are summarized in the Supplementary Materials.

## General Procedure for the CuAAC Coupling Reaction Between Azidoalkyltriethoxysilanes and Alkynes

1-Hexyne **4a** (82 mg, 1.0 mmol), CuI (19 mg, 0.1 mmol) in THF (5 mL), and DIPEA (129 mg, 1.0 mmol) were added to a suspension of **3b** (103 mg, 1.0 mmol), under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was evaporated, leaving a residual pale yellow oil, which was extracted with hexane (50 mL). The hexane extract was washed with water and brine several times, dried with Mg<sub>2</sub>SO<sub>4</sub>, and concentrated. The resulting hexane solution was passed through a short silica-gel column (Merck 60) using EtOAc–hexane (1/2, v/v) as an eluent to afford pure 1-[(1-triethoxysilyl-4-oxahexyl)]-4-butyl-1*H*-1,2,3-triazole 5a (357 mg, 96%) as a colorless oil. <sup>1</sup>H NMR  $\delta$  (400 MHz,

CDCl<sub>3</sub>) 7.42 (s, 1H), 4.50 (d, J = 5.2 Hz, 2H), 3.81 (q, J = 7.1 Hz, 6H), 3.77 (t, J = 5.3 Hz, 2H), 3.40 (t, J = 6.7 Hz, 2H), 2.73 (t, J = 8.0 Hz, 2H), 1.66 (m, 4H), 1.39 (sextet, J = 7.3 Hz, 2H), 1.22 (t, J = 7.1 Hz, 9H), 0.93 (t, J = 7.3 Hz, 3H), 0.60 (m, 2H). <sup>13</sup>C NMR  $\delta$  (100 MHz, CDCl<sub>3</sub>) 148.7, 122.2, 73.9, 69.4, 58.8, 50.7, 32.0, 25.8, 23.3, 22.7, 18.7, 14.2, 6.9.  $\nu_{max}(neat)/cm^{-1}$  3155, 2972, 2929, 2876, 1551. HRMS (EI) calcd. for C<sub>17</sub>H<sub>35</sub>N<sub>3</sub>O<sub>4</sub>Si 373.2397; found 373.2407.

Compounds **5b–e** were obtained in a similar manner. Experimental details are summarized in the Supplementary Materials.

# General Procedure for the Grafting of the CuAAC Products onto Silica

Silica (4.0 g), **3b** (1.0 g, 3.42 mmol), and 50 mL of dry toluene were placed in a 100-mL round-bottomed flask. The resulting suspension was heated with stirring at 60 °C for 3 h. After cooling, 4.92 g of azidoalkyl-modified silica **6** was obtained as a clear white solid by filtration under air and unreacted **3b** (218 mg, 22%) was recovered from the solution. The amount of azido groups introduced on the silica surface was estimated to be approximately 0.57 mmol/g from elemental analysis. Found C, 5.38; H, 1.57; N, 2.40.

#### **Supporting Information**

Full experimental details and <sup>1</sup>H, <sup>13</sup>C, and <sup>31</sup>P NMR spectra of new compounds can be found via the Supplementary Content section of this article's Web page.

#### ACKNOWLEDGMENTS

This work was carried out as a part of the Development of Microspace and Nanospace Reaction Environment Technology for Functional Materials Project under NEDO. The authors are grateful to R. Nagahata (AIST) and T. Yokoyama (MCPT) for the HRMS (ESI) measurement and nitrogen porosimetry analysis.

#### REFERENCES

- (a) Song, C. E.; Lee, S.-G. Chem. Rev. 2002, 103, 3495–3524; (b) Lummerstorfer, T.; Hoffman, H. J. Phys. Chem. 2004, 108, 3963–3966; (c) Gupta, A. K.; Gupta, M. Biomaterials 2005, 26, 3995–4021; (d) Hoffman, F.; Cornelius, M.; Morell, J.; Fröba, M. Angew. Chem. Int. Ed. 2006, 45, 3216–3251; (e) Li, C.; Zang, H.; Jiang, D.; Yang, Q. Chem. Commun. 2007, 547–558; (f) Minakata, S.; Komatsu, M. Chem. Rev. 2009, 109, 711–724.
- (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. Angew. Chem. Int. Ed. 2001, 40, 2004–2021;
  (b) Bock, V. D.; Hiemstra, H.; Maarseveen, J. H. J. Org. Chem. 2006, 51–68; (c) Wu, P.; Fokin, V. V. Aldrichchim. Acta 2007, 40, 7–17; (d) Moses, J. E.; Moorehouse, A. D. Chem. Rev. 2007, 36, 1249–1262.
- Patel, K.; Angelos, S.; Dichtel, W. R.; Coskun, A.; Yang, Y.-W.; Zink, J.; Stoddard, F. J. Am. Chem. Soc. 2008, 130, 2382–2383.
- (a) Ortega-Muñoz, M.; Lopez-Jaramillo, J.; Hernamdez-Mateo, F.; Santoyo-Gonzalea, F. Adv. Synth. Catal. 2006, 348, 2410–2420; (b) Guo, Z.; Lei, A.; Liang, X.; Xu, Q. Cheml

563

*Commun.* **2006**, 4512–4514; (c) Guo, Z.; Lei, A.; Zhang, Y.; Xu, Y.; Xue, X.; Zhang, F.; Liang, X. *Chem. Commun.* **2007**, 2491–2493; (d) Lv, G.; Mai, W.; Jin, R.; Gao, L. *Synlett.* **2008**, 1418–1422; (e) Nakazawa, J.; Stack, T. D. P. *J. Am. Chem. Soc.* **2008**, 130, 14360–14361.

- 5. European Patent 0050768A2, 1981; Chem. Abstr. 1982, 97, 163246.
- Chernyshev, E. A.; Belyakova, Z. L.; Knyazeva, L. K.; Pomerantseva, M. G.; Efimova, L. A. Russ. Chem. Bull. 1998, 47, 1374–1378.
- 7. Barness, Y.; Gershevitz, O.; Sekar, M.; Sukenik, C. N. Langmuir 2000, 16, 247-251.
- 8. Mori, K. Eur. J. Org. Chem. 2005, 2040-2044.
- 9. Chandra, G.; Lo, P. Y.; Hitchcock, P. B.; Lappert, M. F. Organomatallics 1987, 6, 191-192.
- 10. Umeyama, T.; Takeuchi, D.; Osakada, K. J. Organomet. Chem. 2006, 691, 5260-5266.
- 11. Tornøe, C. W.; Christensen, C.; Meldal, M. J. Org. Chem. 2002, 67, 3057-3064.
- Detz, R. J.; Heras, S. A.; de Gelder, R.; van Leeuwen, P. W. M. N.; Hiemstra, H.; Reek, J. N. H.; van Maarseveen, J. H. Org. Lett. 2006, 8, 3227–3230.
- 13. Molteni, G.; Buttero, P. D. Tetrahedron 2005, 61, 4983-4987.
- Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. Angew. Chem. Int. Ed. 2002, 41, 2596–2599.