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Synthesis of polyfunctional triethoxysilanes by 'click silylation'

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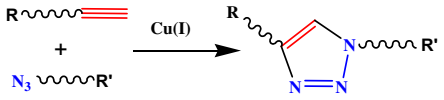
ABSTRACT

The copper-catalyzed 'click silylation' has been exploited for the chemical modification of γ-azidopropyltriethoxysilane (AzPTES) with a wide range of terminal alkynes (**1a**–**1v**) in a one-pot operation. The novel 1,2,3-triazole-triethoxysilane derivatives (**2a**–**2v**) were synthesized by this procedure and comprehensively characterized by IR spectra, ^1H and ^{13}C NMR, and HRMS studies.

The extension of the functional group versatility in organotriethoxysilanes (OTES) has made it a flexible building block in organic synthesis.[1,2] The OTES are key modules for the synthesis of well designed organic–inorganic hybrid materials[3] having potential applications such as biosensors,[4] surface group modifiers,[5] and supported catalysts.[6] The syntheses of OTES with enhanced properties require the functionalization of triethoxysilyl moiety with various challenging substrates. This has been achieved either through an organometallic route[7] or by the hydrosilylation[8] of olefins or dienes thus leading to complicated mixtures which considerably affects isolation of products. Thus purification process requires skillful techniques such as distillation or crystallization[9] to avoid hydrolytic decomposition of triethoxysilanes. Therefore, a revolutionary method is required to override these purification steps to conventional total synthesis.

Initiated by Sharpless[10] and co-workers, 'click chemistry' is well known for its flexibility[11] and is a valuable technique that has become a simple solution for long known challenges.[12] The research in this field is booming with the use of copper-catalyzed azide alkyne cycloaddition reaction (CuAAC) (Scheme 1), that allows a safe and selective post functionalization over other synthetic routes. This cross-coupling reaction has come up as an important addition to the usual synthetic methodologies for the synthesis of OTES. The integration of triethoxysilanes with heterocyclic triazole can extend its physical, chemical, and mechanical properties, and can provide a robust route for drug discovery,[13] polymer chemistry,[14] and sol-gel processes.[15]



Scheme 1. General reaction scheme for CuAAC.

The restricted research on 1,2,3-triazole based OTES is primarily due to their hygroscopic nature. As a part of our ongoing work, we herein report the synthesis of OTES substituted with various terminal polyfunctionalized molecular entities[16] via 1,2,3-triazole linkage, that have made it a flagship reaction of the click chemistry. The quest for the synthesis of polyfunctional OTES under milder reaction conditions has been exploited by the use of Cu(I) and is gaining wide popularity under the term 'click-silylation'.[17]

Inspired by the pioneering work of Cattoen and co-workers.[1,17] on click silylation, the cycloaddition of alkyne functionalities has been carried out with 3-azidopropyltriethoxysilane (AzPTES) to obtain products having importance, well documented in research fields. This methodology is based on $[CuBr(PPh_3)_3]$-THF/Et_3N system, under strict anhydrous conditions for the synthesis of hybrid silica precursors. Terminal alkyne functionalities (Table 1) such as N-heterocycle, aniline, ether, acrylate, acetate, Schiff base, aldehyde, and the ketone group were synthesized (Scheme 2) following the procedure[18] described in the literature and have been found to be in harmony with click strategy.

The CuAAC reaction between these terminal alkynes and AzPTES afforded polyfunctionalized triethoxysilanes (PfTES) in high yield with upto 95% conversion (Scheme 3, Table 2). IR, NMR

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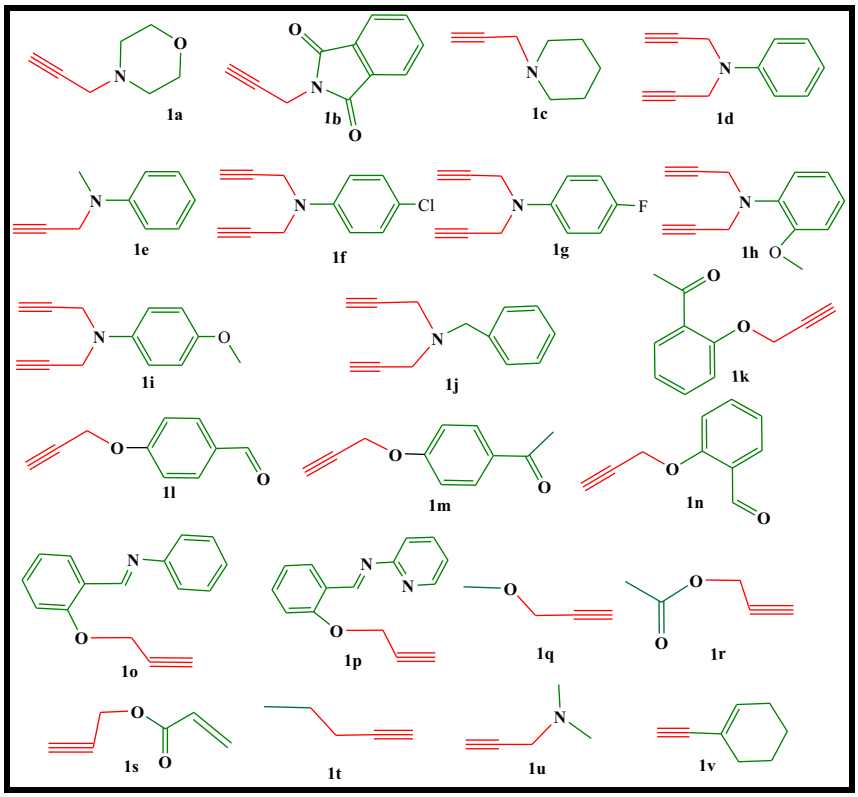
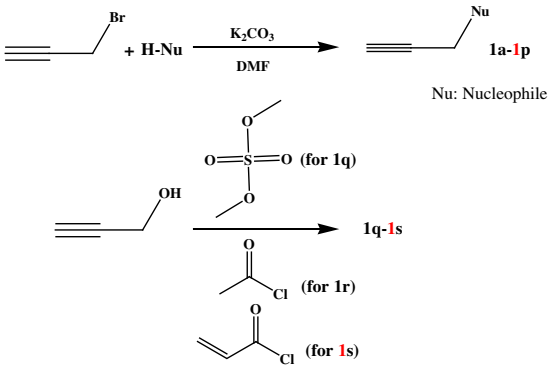
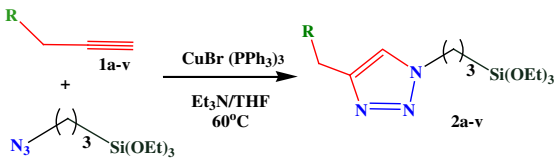
Table 1
Clickable terminal alkynes (**1a–1v**)





Scheme 2. Synthesis of terminal alkynes from propargyl bromide and propargyl alcohol.

(^{1}H, ^{13}C), and High Resolution Mass spectroscopic details provide a handful of information for the complete structure elucidation of PfTES. The downfield shift of triplet due to $-N_3CH_2-$ protons from $\delta = 3.19$ to $\delta = 4.19–4.31$ ppm signifies the C–N bond formation resulting in triazole (Fig. 1). The sharing of two free π bonded electrons of terminal alkyne to form a conjugated heterocycle drastically changes the chemical shift from $\delta = 2.0$ to $\delta = 7.12–7.58$ ppm. The parallel shifting of the peaks has been observed in ^{13}C NMR spectra as well. FT-IR spectroscopic data (Fig. 2) show absorption due to N_3 functionality existing in uncyclized silane at 2096 cm^{-1} whereas upon cyclization this peak disappears. The blank region between 2140–2100 cm^{-1} and the distinctive bands around 1650 cm^{-1} point out to the successful cycloaddition of two molecular entities.



Scheme 3. General reaction scheme for the synthesis of polyfunctional triethoxysilanes.

To determine the scope of this methodology, AzPTES was derivatized with N-heterocycles such as morpholine, piperidine, and phthalimide which have maintained the interest of researchers through decades of historical development of organic synthesis.[19–21] So, 1:1 mixture of the N-heterocycle (**1a–1c**) and AzPTES was totted up in the beginning to obtain the functionalized compounds (**2a–2c**) with desired moiety. The cycloaddition proceeded smoothly under standard condition at 60 °C for 5 h to give a small series of N-heterocyclic derivatives in excellent yield. Furthermore, the aniline derivatives[22] could be selectively functionalized as this silylation method has proven to be very helpful to explore the triazole substitution in material chemistry. Therefore, compounds (**1d–1i**) were chosen as the starting material for the synthesis of bulky aniline derivatives (**2d–2i**) in outstanding yield. The use of benzylamine[23] in bacterial degradation encouraged us to link this functionality (**1j**) with sol-gel precursors for the synthesis of bio-inspired materials (**2j**).

Click silylation also proved to be an effective route to immobilize aldehyde and ketone functionality on to silica supports, as it would play important role for protease inhibition.[24] The potent antimalarial activity of precursor compounds (**1k–1n**), on