Native silica nanoparticle catalyzed anti-Markovnikov addition of thiols to inactivated alkenes and alkynes: a new route to linear and vinyl thioethers

Subhash Banerjee [a], Jayanta Das [a,b], Swadeshmukul Santra [a,b,c,*]

[a] NanoScience Technology Center, University of Central Florida, 12424 Research Parkway, Suite 400, Orlando, FL 32826, USA
[b] Department of Chemistry, University of Central Florida, 4000 Central Florida Blvd., Orlando, FL 32826, USA
[c] Biomolecular Science Center, University of Central Florida, College of Medicine, 4000 Central Florida Blvd., Orlando, FL 32826, USA

ABSTRACT

A new route for the synthesis of linear and vinyl thioethers has been demonstrated using bare silica nanoparticle as catalyst at room temperature under solvent-free conditions. The catalyst can be reused up to six times without loss of catalytic activity.

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Recently, the use of nanoparticulate materials in catalysis has attracted considerable attention because of their improved efficiency under mild and environmentally benign conditions in the context of Green Chemistry.[1,2] Because of enormously large and highly reactive surface area,[3] nanoparticles (NPs) exhibit some unique properties in comparison to bulk materials. Among many other NPs, silica-based NPs have been well studied because of the following reasons: (i) silica NPs are easy to syntheses at room temperature, (ii) NP size can be easily tuned, (iii) easy adjustment of synthesis parameters leads to NPs with narrow size distribution ('monodispersed NPs'), (iv) silica NPs are stable in organic solvents, and (v) they are environmentally friendly materials. Due to these attractive features, silica NPs found wide-spread applications in the synthesis of core-shell hybrid nanomaterial for catalysis of organic reactions. Dominguez-Quintero et al. synthesized nanostructured palladium materials supported on silica for the catalytic hydrogenation of benzene, 2-hexanone, and cyclohexanone.[4] The catalytic performance of silica-coated Pt metal particles for the competitive oxidation of methane and other higher hydrocarbons with gaseous oxygen has been reported by Hori et al.[5] Corma and coworkers demonstrated Pd nanoparticles embedded in a porous sponge-like silica as a suitable catalyst for the Suzuki–Miyaura coupling of electron-rich aryl bromides.[6] Chung and co-workers[7] have applied palladium and cobalt nanoparticles immobilized on

silica for the Tsuji–Trost reaction. However, the catalytic activity of bare silica NPs in organic transformations has not been studied to the best of our knowledge. Here, we accidentally discovered inherent catalytic activity of native silica NPs. This discovery stimulated us to explore the possibility of using this very old nanomaterial as catalyst to study a few very basic chemical transformations that would demonstrate its potential.

Thioethers play important roles in biological and chemical processes[8] and also serve as useful building blocks for various organosulfur compounds.[9] Therefore, synthesis of thioethers in 'Green' and 'straight-forward' ways would have tremendous importance. Traditionally, they are synthesized by the addition of thiolate anions to olefins. The electrophilic (i.e., ionic process) addition of thiolate anion to olefin promotes Markovnikov addition,[10] whereas free-radical course leads to anti-Markovnikov adduct.[11] Most of the protic acids (e.g., H_2SO_4, $HClO_4$, and p-TSOH) and Lewis acids ($AlCl_3$, BF_3, $TiCl_4$, $SnCl_4$, $ZnCl_2$) catalysts are reported for the electrophilic additions, only a few reagents such as H-rho-zeolite[12] and benzene-reflux[13] are found to induce anti-Markovnikov products. Recently, Ranu et al.[14] have reported water-promoted addition of thiols to inactivated alkenes. Some of these procedures are associated with disadvantages such as unsatisfactory yields, long reaction times, and use of highly carcinogenic and hazardous organic solvent (such as benzene). Moreover, limited reports are available that involves styrenes, possibly due to their facile polymerization under acidic conditions.[15] The development of robust protocol (i.e., neutral catalyst) for this transformation is thus highly

* Corresponding author. Tel.: +1 407 882 2848; fax: +1 407 882 2819.
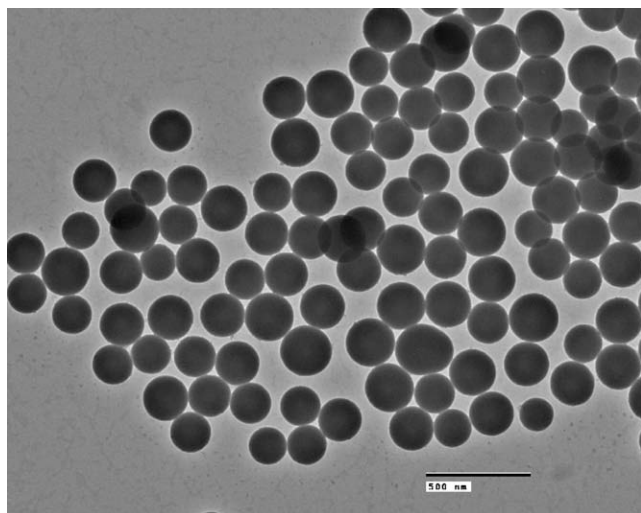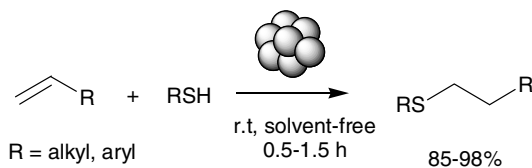E-mail address: ssantra@mail.ucf.edu (S. Santra).

Figure 1. TEM image of fresh silica NPs (before reaction).

Scheme 1. The silica NPs-catalyzed synthesis of linear thioethers is represented.

Silica NPs were synthesized using well-established Stobar method[16] that involves basic hydrolysis and condensation reaction of tetraethoxyorthosilane (TEOS) in ethanol/water (1:1) mixtures at room temperature. The silica NPs were characterized by transmission electron microscopic image (Fig. 1).

These silica NPs exhibited a marked influence in directing the anti-Markovnikov addition of thiols to different alkenes (Scheme 1).

In a simple experimental procedure,[21] olefin (1 mmol) was added to a mixture of thiol (1 mmol) and silica NPs (1 wt %), and the reaction mixture was stirred at room temperature until completion of reaction (TLC). The extraction with ethyl acetate followed by evaporation of solvents leads to the crude product in almost pure form. The results are summarized in Table 1. Both

desirable. Here, we report a simple and efficient protocol for the synthesis of linear and vinyl thioethers via anti-Markovnikov addition of thiols to alkenes and alkynes using a recyclable native silica nanoparticle catalyst at room temperature.

Table 1
Silica NP-catalyzed anti-Markovnikov addition of thiophenol to inactivated alkenes

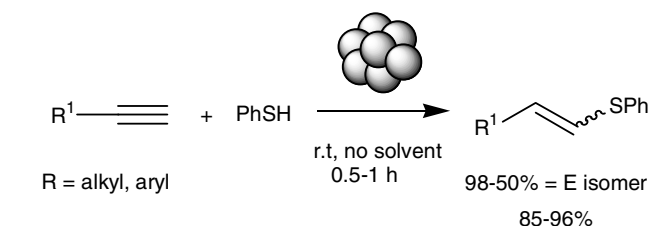| Entry	Thiol	Alkene	Product	Time (h)	Yield[a] (%)	Ref.
1	PhSH	C_4H_9 —	C_4H_9 — SPh	1.5	87	14
2	PhSH	C_6H_{13} —	C_6H_{13} — SPh	1.5	85	19
3	PhSH	(cyclohexene)	(cyclohexyl)—SPh	1.0	88	14
4	EtSH	(cyclohexene)	(cyclohexyl)—SEt	1.5	85	14
5	PhSH 2 equiv	Br —	PhS — SPh	1.0	86	19
6	PhSH	C_6H_5 —	C_6H_5 — SPh	0.5	98	14
7	PhSH	(4-methylstyrene)	(4-methylphenyl)—SPh	0.5	94	20
8	PhSH	Cl (4-chlorostyrene)	Cl — SPh	0.5	90	14
9	PhSH	MeO (4-methoxystyrene)	MeO — SPh	0.5	90	14
10	PhSH	Cl (4-chloromethylstyrene)	Cl — SPh	0.5	96	–

^a Yield refers to the pure isolated products characterized by spectroscopic (^{1}H NMR and IR) data.

the aliphatic and aromatic-substituted alkenes were made to participate in the reaction without any difficulty. All the reactions were made to proceed at room temperature to produce the thioethers in high yield (85–98%) at shorter reaction time (0.5–1.5 h). The addition of thiols to olefins is highly regioselective and anti-Markovnikov in nature. It is observed that the addition of thiols to the aromatic-substituted alkenes (Table 1, entries 6–10) is faster than that of aliphatic one (Table 1, entries 1–6). The addition of thiophenol to 1-chloromethyl-4-vinyl-benzene is highly selective (Table 1, entry 10). The reactive chloromethyl group in the molecule remained intact even after use of two equivalents of thiophenol that can be further functionalized.

We found that only 1 wt % of catalyst was sufficient to carry out the addition reaction. The reaction of thiophenols and olefin has been reported to give the Friedel Crafts product;[17] however, no such side-reaction was observed in this protocol.

Encouraged by the high reactivity and effectiveness of the catalyst for the anti-Markovnikov addition of thiols to inactivated olefins, we attempted to study the catalytic activity of silica NPs on the addition of thiols to inactivated alkynes. We have observed comparable reactivity of the catalyst on the addition of thiols to alkynes. The addition of alkyne (e.g., phenylacetylene) to a mixture of thiol (e.g., thiophenol) and catalyst (1 wt %) leads to vinyl thioethers in high yields at room temperature (Scheme 2).

The results for the addition of thiols to alkynes are represented in Table 2. Both the aliphatic- and aromatic-substituted alkynes were made to participate in this addition reaction to produce the vinyl thioethers in high yield. Here, we have also observed the 100% anti-Markovnikov addition, no Markovnikov adducts were isolated in any case. The addition of thiophenol to a hydroxyl-substituted alkyne, 2-Methyl-but-3-yn-2-ol, is highly stereoselec-

tive and it exclusively produced trans-vinyl thioether (Table 2, entry 2); on the other hand, the catalysts reported in the literature[18] were found to produce a mixture of cis and trans isomers. However, 1:1 mixture of cis and trans isomers was isolated in the case of hydrocarbon-substituted alkyne (Table 2, entry 1). Possibly, hydrogen bond formation between –OH group of 2-Methyl-but-3-yn-2-ol and silica NPs triggers addition of thiophenol from the opposite site (due to steric factor) leading to trans-isomer which was not reflected in case of hept-1-yne. Thus, silica NPs played an important role in the addition of thiophenol to alkynes.

The catalyst can be easily recovered from the reaction mixture by adding organic solvents (e.g., ethyl acetate) because the catalyst (i.e., silica NPs) is insoluble in organic solvents. The catalyst was re-used for six times without loss of any catalytic activity (Fig. 2). To determine the fate of the catalyst after reaction, we have done the TEM of the recovered silica NPs. We have not found any change in the particulate nature of the silica NPs (image is not given here).

Silica NPs play an important role in this reaction. A comparison of reactivity of different reagents for anti-Markovnikov addition of thiophenol to styrene in benzene is presented in Table 3.

The neat reactions without silica NPs are very slow, and we have observed that only about 45% of the reactions were completed even after 24 h. Possibly, silica NPs (also called silanol) promotes the reaction through hydrogen-bond formation with the sulfhydryl hydrogen of the thiol with surface hydroxyl group of silanol, and thus increases the nucleophilicity of the thiolate ion. Fur-
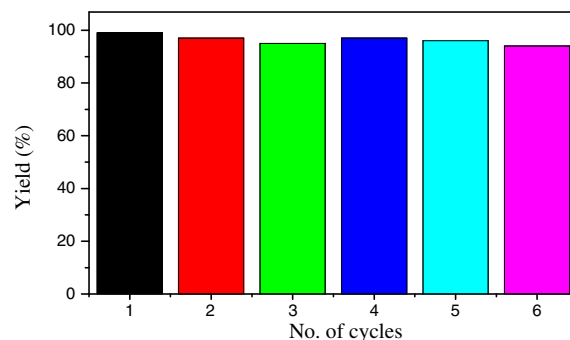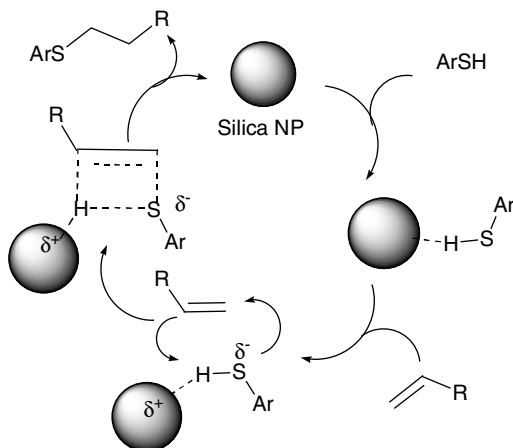
Scheme 2. The silica NPs-catalyzed synthesis of vinyl thioethers is represented.

Figure 2. The variation of yield (%) with number of recycles of the catalyst for the addition of PhSH to styrene is represented.

Table 2
Silica NP catalyzed anti-Markovnikov addition of thiophenol to alkynes

Entry	Thiol	Alkyne	Product	Time (h)	Yield[a] (%)	Ref.
1	PhSH	C_5H_{11}——≡	C_5H_{11} ⌇ SPh (E:Z = 1:1)	1.0	85	18
2	PhSH	HO—≡	HO ⌇ SPh (100% E)	1.0	85	18
3	PhSH	⬡—≡	⬡ ⌇ SPh (E:Z = 3:2)	0.5	96	18

[a] Yield refers to the pure isolated products characterized by spectroscopic (^{1}H NMR and IR) data.

Table 3
The comparison of different reagent for anti-Markovnikov of thiophenol to styrene is represented

Reagent	Reaction time/condition	Yield (%)
Benzene	24 h/rt or 10 h/Reflux	92
Neat	24 h/rt	30
Silica NPs	0.5 h/rt	98
Water	1.5 h/rt	90

Scheme 3. The proposed mechanism for the silica NPs-catalyzed addition of thiols to alkenes is represented.

ther, it may be speculated that addition of the thiolate anion to the C=C bond takes place in a concerted manner with steric factors controlling the regioselectivity leading to the anti-Markovnikov product (Scheme 3).

In conclusion, we have demonstrated the use of native silica NPs as catalyst in the anti-Markovnikov addition thiols to alkenes and alkynes for the first time. The reactions are considerably fast (0.5–1 h) and highly regioselective in nature. This present protocol offers several advantages such as (1) mild reaction conditions (room temperature), (2) high isolated yields (85–99%) of the linear and vinyl thioethers, (3) low cost, non-toxicity and recyclability of the catalyst, and (4) solvent-free reaction conditions, which meets the requirements for 'green synthesis' over existing protocols. Moreover, this is the first use of native silica NPs in organic synthesis. Certainly, this observation provides great promise toward additional useful applications.

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21. *Typical experimental procedure for the anti-Markovnikov addition of olefins to thiols* (Table 1, *entry 6*): Styrene (104 mg, 1 mmol) was added to a mixture of thiophenol (110 mg, 1 mmol) and silica NP (1 wt %) in neat condition, and the reaction mixture was stirred for 0.5 h at room temperature till completion of reaction (TLC). The extraction with ethyl acetate followed by evaporation of solvents leads to the crude product in almost pure form, which was purified by short column chromatography over silica gel (hexane–ethyl acetate, 95:5) to provide 2-phenylsulfanylethylbenzene (209 mg, 98%) as a colorless liquid. This procedure was followed for all the reactions listed in Tables 1 and 2. Except one (Table 1, entry 10) all the products known were characterized by spectroscopic ^{1}H NMR and IR) data, and these data were compared with the reported values. The unknown product (Table 1, entry 10) was characterized by IR, NMR (^{1}H and ^{13}C) spectroscopic data, and elemental analysis and was given below.Table 1, entry 10: Colorless liquid. IR (Neat): 689, 736, 823, 1024, 1089, 1265, 1438, 1479, 1514, 1582 cm^{-1}. ^{1}H NMR (CDCl$_3$, 500 MHz): δ 2.96 (t, J = 7.5 Hz, 2H), 3.19 (t, J = 7.5 Hz, 2H), 4.60 (s, 2H), 7.22–7.24 (m, 3H), 7.34–7.40(m, 6H). ^{13}C NMR: δ 34.9, 35.3, 46.2, 125.9 (2C), 126.2 (2C), 128.7, 129.1 (2C), 129.4 (2C), 135.7, 136.2, 140.5. Anal. Calcd for C$_{15}$H$_{15}$ClS: C, 68.55; H, 5.75. Found: C, 68.47; H, 5.66.