SiO₂ Nanoparticle-catalyzed Facile and Efficient One-pot Synthesis of *N*-alkyl-2,5-bis[(*E*)-2-phenylvinyl]-1,3-dioxol-4-amine Under Solvent-free Conditions

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1,3-Dioxole-4-amine derivatives have been prepared efficiently in one-pot reaction using nanosized SiO_2 as a heterogeneous catalyst. The present method does not involve any hazardous organic solvents or catalysts. The high surface-to-volume ratio of SiO_2 nanoparticle has promising features for the reaction response such as the short reaction time, good to excellent yields, easy of operation and work-up procedure, and purification of products by non-chromatographic methods.

J. Heterocyclic Chem., 00, 00 (2015).

INTRODUCTION

The efficiency of heterogeneous catalysis in organic synthesis can be improved by employing nanosized catalysts. The field of nanocatalysis has attracted the attention of researchers working in the fields of catalysis and nanoparticles, because of their high surface-tovolume ratio that increases the efficiency as well as selectivity of the catalysts [1]. Furthermore, nanocatalysis has the advantages of high atom efficiency, easy product purification, and reusability of the catalyst [2]. Clearly, the development of free nanoparticles with tunable catalytic activity is of great significance for both academia and industry [3].

Nanoparticles have also been widely used for the organic synthesis in both homogeneous and heterogeneous conditions [4]. Among the readily available catalysts, the use of silica nanoparticles has increased because of their unique properties and potential applications in various fields. The stability, high surface area, and non-toxicity made the silica nanoparticles ideal candidates for catalyst or catalyst support [5]. Furthermore, the possibility of performing multicomponent reactions under solvent-free conditions with heterogeneous catalysts like SiO₂ nanoparticles could enhance their efficiency from an economic as well as a green point of view.

The chemistry of 1,3-dioxole heterocycles has attracted much attention owing to their biological activities and their potent utility as anti-HIV (e.g., AHE) [6–8], anticancer [9,10], antidepressive, antitumor, anticonvulsant, and antipyretic agents [11,12]. Their significance is also because of applications in the treatment of cardiovascular diseases and lung cancer [13,14]. Several methods have been published on benzodioxoles [12–15], and only a few procedures for 1,3-dioxoles have been described [16].

In continuation of our work on the synthesis of 1,3-dioxole and interesting organic compounds [17], there has been a great interest in finding ways to improve reaction conditions and efficient methods. We report herein a novel method synthesis of 1,3-dioxole heterocycles using simple starting materials. To the best of our knowledge, there have been no examples of the use of SiO_2 nanoparticles for the synthesis of 1,3-dioxole derivatives through isocyanide-based reaction including aromatic aldehydes to give these compounds in one-pot reaction.

RESULTS AND DISCUSSION

The reaction of alkyl isocyanides **1** and aromatic aldehydes **2** in the presence of SiO_2 nanoparticle proceeds in one-pot under solvent-free condition, at 80°C to produce the 1,3-dioxole compounds **3** in excellent yields (Scheme 1).

The structures of the products were deduced from their elemental analyses and IR, ¹H, and ¹³CNMR spectra. The ¹H and ¹³CNMR spectra of the crude products clearly indicated the formation of the products. Any product other than **3** could not be detected by ¹HNMR spectroscopy. The mass spectra of these compounds displayed molecular ion peaks at appropriate m/z values. The run of this reaction at r.t. with SiO₂ and without for 2 h did not work. TLC and ¹H NMR spectrum of the reaction mixture indicated the formation of trace of product.

Scheme 1. SiO_2 nanoparticle catalyzed synthesis of 1,3-dioxole **3** under solvent-free conditions. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



The ¹HNMR spectrum of **3a** consisted of a *multiplet* for the cyclohexyl group (δ 1.01–2.01), a broad signal for the N—CH proton (δ 3.77–3.87), a *singlet* at δ 6.30 for the hemiacetal proton, and a *doublet* (δ 6.10, ³J_{HH}=7.5 Hz) for the N—H group in agreement with the suggested structure. The ¹H decoupled ¹³CNMR spectrum of **3a** showed 17 distinct signals in agreement with proposed structure. The characteristic signal of hemiacetal carbon was observed at δ 75.93. The olefinic C-atoms of the 1,3-dioxole ring were observed at δ 164.95 and 167.37. The ¹H and ¹³C NMR spectra of compounds **3b–i** were similar to that of **3a** except for the signals of the

 $\label{eq:sional} Table \ 1$ SiO_2 nanoparticles catalyzed synthesis of 1,3-dioxole derivatives 3a–i.



Entry	Aldehyde	Isocyanide	Product	Yields (%)
g	СІСНО	t-BuNC	H-N CI-CI-CI	95
h	H₃С−∕⊂СНО	t-BuNC	H-N O H ₃ C C CH ₃	98
i	O H	Cy-NC		94

substituted alkyl and aryl rings, which exhibited characteristic resonances with appropriate chemical shifts (all characterization data are reported in *Helv. Chem. Acta*) [17].

As shown in Table 1, we found that aromatic aldehydes containing different functional groups at different position worked well and did not show differences in the yield of products.

The proposed mechanism for the role of nano-SiO₂ as a solid acid catalyst is shown in Scheme 2. On the basis of the well-established chemistry of isocyanides [18,19] it is reasonable to assume that the reaction involves initial formation of a 1,3-dipolar intermediate between the alkyl isocyanide and aldehyde, which undergoes addition to the carbonyl group of another aldehyde molecule to give **5**. This intermediate is converted into product **3** via proton transfer.

To determine the appropriate concentration of the catalyst SiO_2 nanoparticles, we have investigated the model reaction of benzaldehyde and cyclohexyl isocyanide at



different concentrations of SiO_2 nanoparticles such as 10, 20, and 30 mol%. We found that 30 mol% of SiO_2 nanoparticles produces the best results with respect to product yield.

We have examined the recovery and reuse of the catalyst. The catalyst was recovered by a simple work-up using the filteration and reused during three consecutive runs without any apparent loss activity for the same reaction.

It is noteworthy that the yield of the product in the second and third uses was almost the same as that in the first run as has been shown in Table 2.

Figure 1 shows the broadened X-ray diffraction (XRD) analysis. The broad peak at 21.91° corresponds to the amorphous nature of silica.

The size and structure of the SiO_2 nanoparticles were also evaluated using scanning electron microscopy (SEM). According to the SEM (Fig. 2), it was observed that the silica has a nanodimension ranging from 60 to 90 nm. The SEM pictures show good agglomeration of particles of silica that is spherical in shape.

Characteristic properties of the commercially SiO₂ nanoparticles (CAB-O-SIL M5) were summarized in Table 3.

SUMMARY

We have developed a straightforward and efficient method for the preparation of 1,3-dioxole derivatives via

Table 2							
Reutilization of SiO_2 nanoparticles in the synthesis of 3a .							
Run	Fresh	1	2	3			

96

95

95

97

Yield (%)

Journal of Heterocyclic Chemistry DOI 10.1002/jhet

Table 1



Figure 1. XRD pattern of SiO_2 nanoparticles. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

one-pot reaction of alkyl isocyanides and aromatic aldehydes promoted by SiO_2 catalyst. The present method offers several advantages such as short reaction time, simple experimental procedure, and high yield of the products, and catalyst can be recycled and reused at least three times without significant loss of activity.

EXPERIMENTAL

Alkyl isocyanides, aromatic aldehydes, and solvents used in this work were obtained from *Fluka* (Buchs,

Switzerland) and used without further purification. The silica (CAB-O-SIL® M5) was purchased from Cabot Corporation. The particle size and structure of SiO₂ nanoparticles were observed by using a Seron AIF 2100 Scanning electron microscopy (SEM) operating at 25 KV. XRD pattern was taken through a Inel Equinox 3000 model with a Cu $k\alpha$ source.¹H and ¹³C NMR spectra were recorded on a *Bruker-DRX-300 Avance* instrument, in CDCl₃ using MeSi₄ as internal standard. Melting points were obtained by *Gallenkamp electrothermal-9100* apparatus; not corrected. Elemental analyses were obtained by *Heraeus-CHN-O-Rapid* analyzer. These results agreed favorably with the calculated values. Mass spectra were recorded with a *Shimadzu-QP-GC-5050* spectrometer at 70 eV; in *m/z* (%). IR spectra were recorded on *Bruker-Tensor-27* spectrophotometer.

Representative procedure for the preparation of compounds 3. To a magnetically stirred benzaldehyde (0.212 g, 2 mmol) and nano SiO₂ (30 mol.% based on aldehyde) was added cyclohexyl isocyanide (0.109 g, 1 mmol) under solvent-free condition. The reaction mixture was stirred at 80°C for 2 h. The progress of the reaction was monitored by TLC (eluent: ethyl acetate/*n*-hexane, 2:8). After completion, the reaction mixture was cooled at room temperature. Then, it was extracted with



Figure 2. SEM pictures of SiO₂ nanoparticles. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

 Table 3

 Characteristic properties of the commercially SiO₂ nanoparticles.

B.E.T. surface area	$200 \mathrm{m^2/g}$
pH (4% aqueous slurry)	3.7-4.3
Bulk density	$3.0 \text{lb/ft}^3 \text{max.}$
Loss on heating	<1.5% max.
Loss on ignition (@ 1000°C)	<2 wt. %
Specific gravity	2.2 g/cm^3
Refractive index	1.46
X-ray form	Amorphous
Oil adsorption	~350 g/100 g oil
Average particle size	60–90 nm
Assay (% SiO ₂)	>99.8

ethyl acetate (10 mL), and the catalyst was removed by filtration.

N-cyclohexyl-2,5-bis[(*E*)-2-phenylvinyl-1,3-dioxole-4-amine] (*3i*). Yield: 0.361 g (94%). White solid. IR: 3452, 3306, 3107, 1733, 1645, 1550, 1249, 1105. Anal. Calcd. for C₂₅H₂₇NO₂ (373.5): C 80.40, H 7.29, N 3.75. Found: C 79.9, H 7.3, N 3.7. ¹H-NMR: δ 1.09–2.02 (10H, m, Cy), 3.75–3.95 (1H, m, CHN), 5.88 (1H, dd, ${}^{3}J_{\rm HH}=6.6$, ${}^{4}J_{\rm HH}$ = 1.2 Hz, CH), 6.10 (1H, br s, NH), 6.36 (1H, dd, ${}^{3}J_{\rm HH} = 15.9$, ${}^{3}J_{\rm HH} = 6.6$ Hz, CH_{olefinic}), 6.59 (1H, d, ${}^{3}J_{\text{HH}} = 15.9 \,\text{Hz}, \text{ CH}_{\text{olefinic}}, 6.75 (1\text{H}, d, {}^{3}J_{\text{HH}} = 16.5 \,\text{Hz},$ CH_{olefinic}), 7.25-7.65 (10H, m, CH_{arom}), 7.84 (1H, d, ${}^{3}J_{\text{HH}} = 15.9 \,\text{Hz}, \,\text{CH}_{\text{olefinic}}.{}^{13}\text{C-NMR}: \delta 24.75, 25.41, 32.94$ (Cy), 48.22 (CHN), 74.37 (CH), 116.74 (CH_{olefinic}), 122.79 (CH_{olefinic}), 126.80, 128.26, 128.55, 128.65, 129.22, 129.75 (CH_{arom.}), 130.75 (CH_{olefinic}), 133.95 (C_{arom.}), 134.37 (CH_{olefinic}), 135.71 (C_{arom.}), 165.23, 167.15 (C=C).

Acknowledgments. This work was supported by Imam Khomeini International University Grants (project number 11454).

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