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Nano-colloidal silica-tethered polyhedral oligomeric silsesquioxanes with eight branches of 3-aminopropyltriethoxysilane as high-performance catalyst for the preparation of bis-thiazolidinones under ultrasonic conditions

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Abstract: We report a class of organic–inorganic hybrid material based on nano-colloidal silica-tethered polyhedral oligomeric silsesquioxanes with eight branches of 3-aminopropyltriethoxysilane [nano-colloidal silica@APTPOSS (a series of polyhedral oligomeric silsesquioxanes with eight branches of 3-aminopropyltriethoxysilane)]. It was characterized by ^{1}H NMR spectroscopy, dynamic light scattering, scanning electron microscope, energy dispersive spectroscopy and thermogravimetric analysis. An easy and rapid method for the synthesis of bis-thiazolidinones has been presented by one-pot pseudo-five-component reaction of benzaldehydes, ethylenediamine and 2-mercaptoacetic acid using nano-colloidal silica@APTPOSS. The reusability of the catalyst and little catalyst loading, excellent yields, short reaction times, using the sonochemical procedure as a green process and an alternative energy source are some benefits of this method.

Keywords: nanocatalyst; one-pot reaction; organic–inorganic hybrid; thiazolidinones; ultrasonic conditions.

1 Introduction

Thiazolidinones represent biological properties such as anticancer [1], anti-virus [2], antibacterial [3], antituberculous therapy [4] and anti-AIDS [5] activities. These activities make them attractive targets in organic synthesis. Hence, seeking easy and brief techniques for the preparation of thiazolidinones is a significant subject. Among the thiazolidine derivatives, bis-thiazolidinones have received substantial attention because of their biological activities [6, 7]. Recently, syntheses of bis-thiazolidinones have been reported using catalysts such as zeolite [8], $HClO_4$–SiO_2 [9], ChCl (choline chloride)/urea-based ionic liquid [10], $ZnCl_2$ [11] and nano-$CdZr_4(PO_4)_6$ [12]. Despite these advances, there remains need to search for new ways for an efficient, high yield, and mild approach to achieve these syntheses.

Recently, performing one-pot reactions with a nanocatalyst under ultrasonic irradiation has been given much attention [13, 14]. The ultrasound approach offers several advantages including higher yields, enhanced reaction rates, milder reaction conditions, and waste minimization compared with traditional methods and thus saving money and energy [15, 16]. The ultrasound approach decreases times, and increases yields of products by creating the activation energy in micro surroundings [17, 18]. The cavitation process generates high temperature and pressure in the micro surroundings, which causes a disturbed current in the liquid and elevated mass transfer [19, 20].

Recently, several nanocatalysts have been utilized for the preparation of organic compounds under ultrasonic conditions [21, 22]. The surface of nanoparticles (NPs) can be modified through loading with desirable functionalities such as polyhedral oligomeric silsesquioxanes (POSS). Silsesquioxane is an organosilicon compound with the chemical formula $[RSiO_{3/2}]_n$ (R = H, alkyl, vinyl, aryl, alkoxy), including an inorganic core of oxygen and silicon of size ~0.45 nm in diameter [23, 24]. In continuation of our work on the synthesis of NPs [25–28], a series of polyhedral oligomeric silsesquioxanes with eight branches of 3-aminopropyltriethoxysilane (APTPOSS) has been anchored on the surface of colloidal silica NPs. In the current study, we investigated an easy and rapid method for the synthesis of bis-thiazolidinones by a one-pot pseudo-five-component reaction of benzaldehydes, ethylenediamine and 2-mercaptoacetic acid using nano-colloidal silica@APTPOSS as a reusable catalyst under ultrasonic conditions (Scheme 1).

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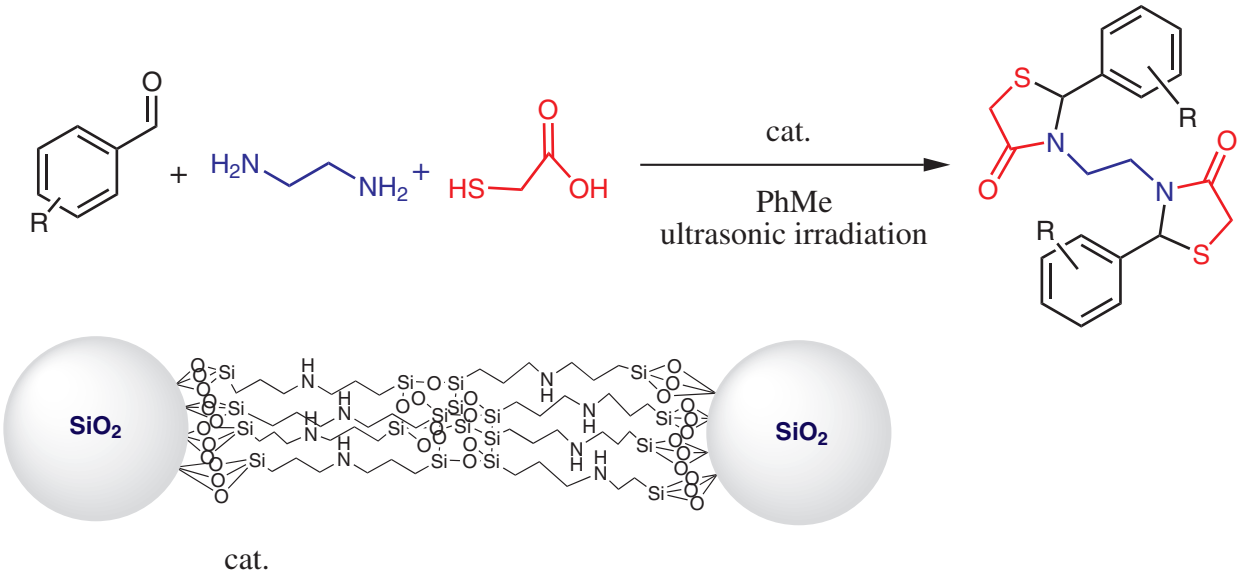


Scheme 1: Synthesis of bis-thiazolidinones using nano-colloidal silica@APTPOSS.

2 Results and discussion

The preparation steps of nano-colloidal silica-tethered polyhedral oligomeric silsesquioxanes with eight branches of 3-aminopropyltriethoxysilane have been described in Scheme 2. In the first step, octakis(3-chloropropyl)octasilsesquioxane (Cl-POSS) is synthesized by the hydrolysis of 3-chloropropyltrimethoxysilane under acidic conditions. Afterwards, the reaction of 3-aminopropyltriethoxysilane with Cl-POSS yields APTPOSS. Then, the reaction of nano-colloidal silica with APTPOSS affords nano-colloidal silica@APTPOSS.

Figure S1 (see Supplementary Information) shows the ^{1}H NMR spectra for the Cl-POSS in $CDCl_3$. The NMR spectra of Cl-POSS are consistent with expectation.

Figure 1 shows the field emission scanning electron microscope (FE-SEM) image of nano-colloidal silica@APTPOSS (nanocatalyst). The SEM image reveals the particle to have diameters in the nanometer range. The results show that nano-colloidal silica@APTPOSS was obtained with a particle diameter in the range of 10–85 nm.

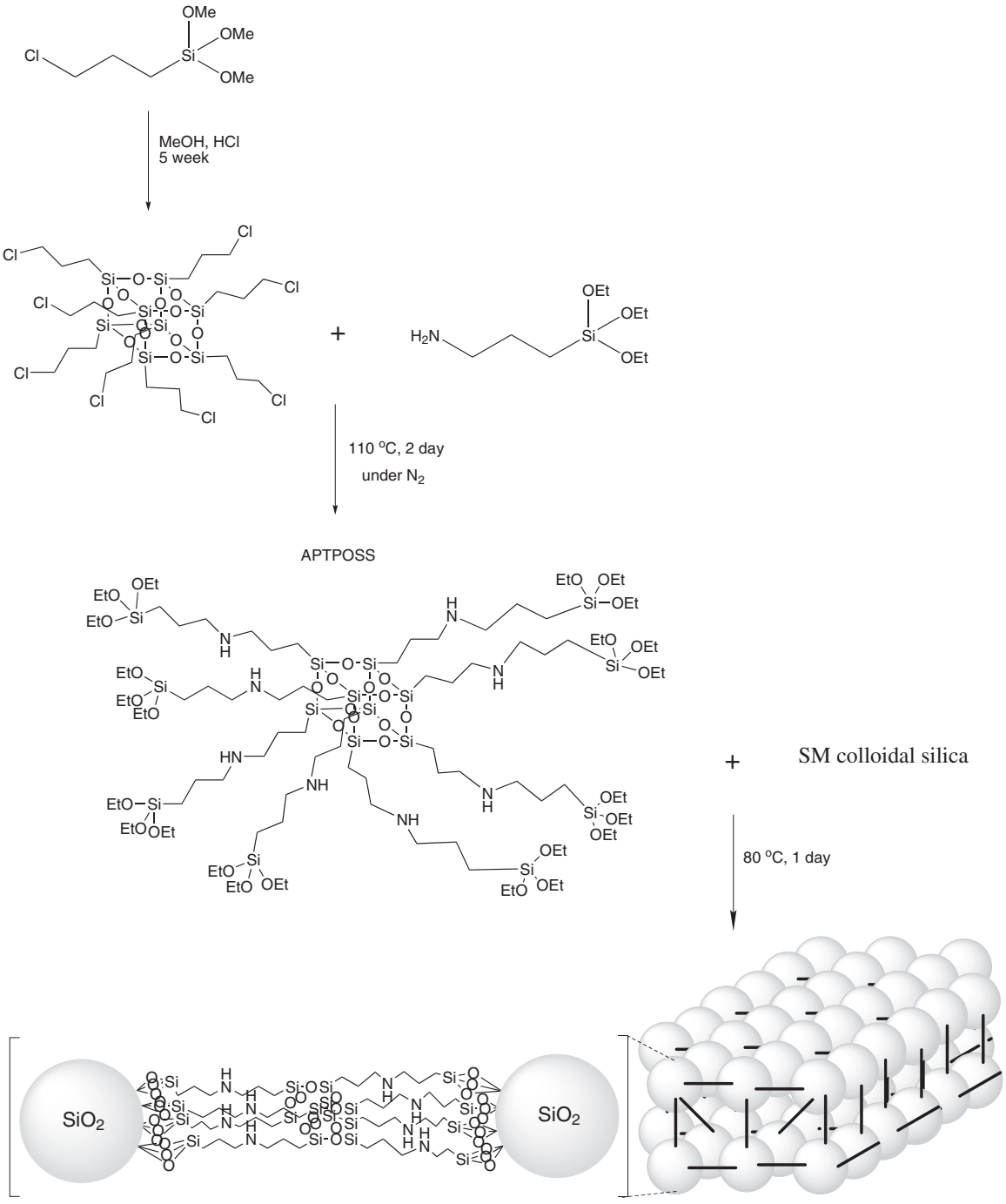
APTPOSS and silica@APTPOSS were analyzed using energy dispersive spectroscopy (EDS) (Fig. 2). EDS confirmed the presence of C, N, O and Si in the compounds, and the higher intensity of the Si peak compared with the C peak in the nanocatalyst indicates that SiO_2 is loaded with ATPPOSS.

Thermogravimetric analysis (TGA) evaluates the thermal stability of the nano-colloidal silica-tethered APTPOSS (Fig. S2; Supplementary Information). The curve shows a weight loss of temperatures below 210°C related to the desorption of physically adsorbed water, while a weight loss at the temperature from 210 to 560°C could be due to the decomposition of the organic spacer attaching to the silica NPs. Thus, the nano-catalyst was stable up to 210°C.

In order to study the size distribution of the nanocatalyst, dynamic light scattering (DLS) measurements of the NPs were performed (Fig. 3). This size distribution centers around 19.6 nm.

Initially, we explored and optimized different reaction parameters for the synthesis of bis-thiazolidinones by the three-component reaction of 4-chlorobenzaldehyde (2 mmol), ethylenediamine (1 mmol) and 2-mercaptoacetic acid (2 mmol) in diverse solvents. Yields were determined for the model reaction in the presence of various catalysts such as nano-CeO_2, nano-SnO, nano-Fe_3O_4, APTPOSS and nano-colloidal silica@APTPOSS. The best results were obtained under ultrasonic conditions (40 W) in toluene, and it was found that the reaction gave satisfying results in the presence of nano-colloidal silica@APTPOSS at 6 mg, which gave excellent yields of products (Table 1). When the reaction was carried out under reflux conditions, it gave low yields of products and took longer reaction times, while when the same reaction was carried out under ultrasonic irradiation, good yields of products in short reaction times were obtained.

With these hopeful results in hand, we turned to investigate the scope of the reaction using various aromatic aldehydes as substrates under the optimized reaction conditions. The results show that the present catalytic method is extensible to a wide diversity of substrates to create a variety-oriented library of bis-thiazolidinones (Table 2).



Scheme 2: Preparation routes of nano-colloidal silica@APTPOSS.

Owing to the presence of 2 and 2′ equivalent stereogenic centers, bis-thiazolidinones can be obtained as *rac*. 2R,2′R/2S,2′S and 2R,2′S-*meso* isomers. After workup, the crude mixture of isomers was separated by silica gel column chromatography (diethyl ether/petroleum ether in variable ratio mixtures). In general, *meso* isomers eluted more slowly than corresponding racemates. The *racemate* isomer **4f** was obtained in higher yields than *meso* isomer **4f** (85% for the *rac*. isomer **4f** and 15% for the *meso* isomer **4f**). The ^{1}H NMR spectra of the compounds **4a–4j** displayed a doublet of doublets at δ 3.80–3.95 ppm due to the methylene proton HA at C-5 (-CO-C**HA**HB-S) because of its interaction with the geminal proton HB at C-5 (-CO-CHA**HB**-S) and the proton at the chiral C-2 (S-C**H**Ar-N), and a doublet of doublets at δ 3.50–3.75 ppm due to the methylene proton HB at C-5 (-CO-CHA**HB**-S) because of its

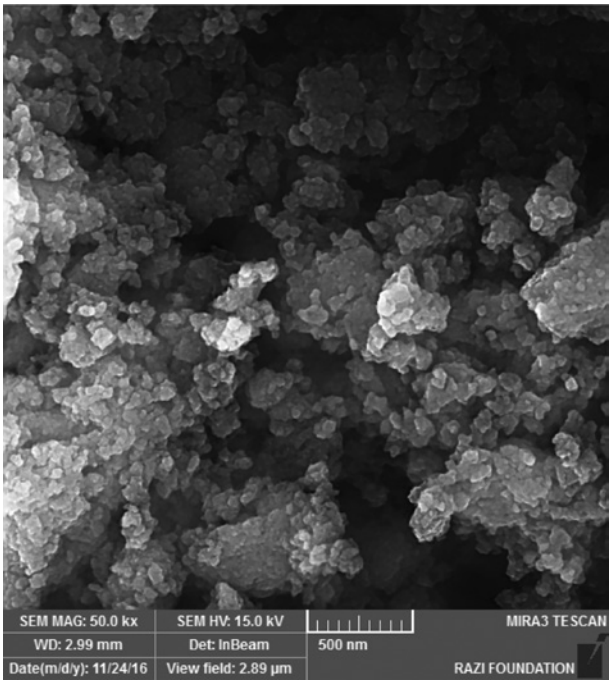


Fig. 1: FE-SEM image of nano-colloidal silica@APTPOSS.

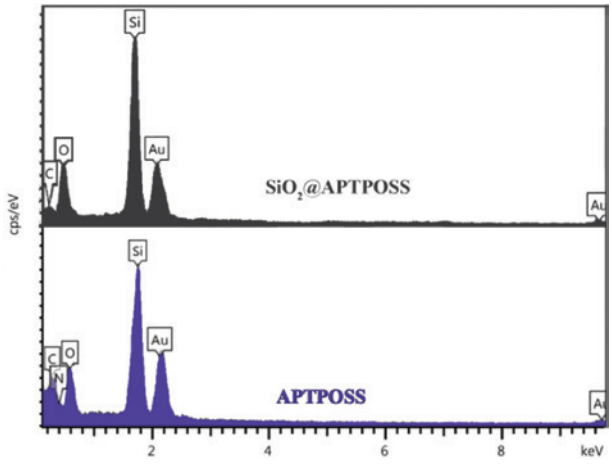


Fig. 2: Energy-dispersive spectroscopy (EDS) for APTPOSS and nano-colloidal silica@APTPOSS.

interaction with the geminal proton HA (-CO-C**HA**HB-S) and a diastereotopic proton Ha (-N-C**Ha**Hb-CHaCHb-N-) of the ethylene fragment. This last proton Ha (-N-C**Ha**Hb-CHaCHb-N-) displayed a doublet of doublets or a multiplet at δ 2.50–2.85 ppm because of its interaction with the geminal proton Hb (-N-CHa**Hb**-CHaCHb-N-) and the proton HB (-CO-CHA**HB**-S) at C-5. The Hb proton (-N-CHa**Hb**-CHaCHb-N-) at the aliphatic chain suffered the anisotropic effect from the near amide group or aryl substituents and it went to down field at δ 3.35–4.0 ppm appearing overlapped with HB or HA (-CO-C**HAHB**-S) as a multiplet. These germinal protons of each methylene group reside in magnetic non-equivalent environments [29, 30].

We also checked the reusability of nano-colloidal silica@APTPOSS as an efficient catalyst; its reusability was achieved by the reaction of *p*-Cl-benzaldehyde (2 mmol), ethylenediamine (1 mmol), 2-mercaptoacetic acid (2 mmol) and 6 mg of nano-colloidal silica@APTPOSS under optimized conditions. After completion of the reaction, the catalyst was washed with water and acetone and was used with new substrates under the same conditions. The results showed that the nano-colloidal silica@APTPOSS can be reused several times (yields 96–93%) in Fig. S3 (Supplementary Information).

A probable mechanism for the synthesis of bis-thiazolidine derivatives using nano-colloidal silica@APTPOSS is shown in Scheme 3. The N–H groups distributed on the surface of nano-colloidal silica@APTPOSS activate the C=O groups of the substrates and intermediates through hydrogen bonding. A proposed mechanism is outlined via primary imine intermediate formation followed by attack of the sulfur atoms of the 2-mercaptoacetic acid on the activated imine groups followed by intramolecular cyclization with the elimination of H_2O giving rise to the cyclized product bis-thiazolidines [29, 30]. In this mechanism nano-colloidal silica@APTPOSS acts as a highly efficient and green catalyst activating the C=O, C=N groups for better reaction with nucleophiles through hydrogen bonding [25, 31, 32].

3 Conclusions

In conclusion, we demonstrated an efficient method for the synthesis of bis-thiazolidinones using nano-colloidal silica-tethered polyhedral oligomeric silsesquioxanes with eight branches of 3-aminopropyltriethoxysilane as a high-performance catalyst under ultrasonic conditions. The advantages of this method are the use of a superior catalyst, recoverability of the catalyst, little catalyst loading, low reaction times, a simple procedure, high atom economy and excellent yields.

4 Experimental section

All organic materials were purchased commercially from Sigma-Aldrich and Merck and were used without further purification. FT-IR spectra were recorded with KBr pellets using a Magna-IR spectrometer 550 Nicolet. NMR spectra were recorded on a Bruker 400 MHz spectrometer with [D_6] dimethyl sulfoxide (DMSO) and $CDCl_3$ as solvent and tetramethylsilane as an internal standard. CHN compositions

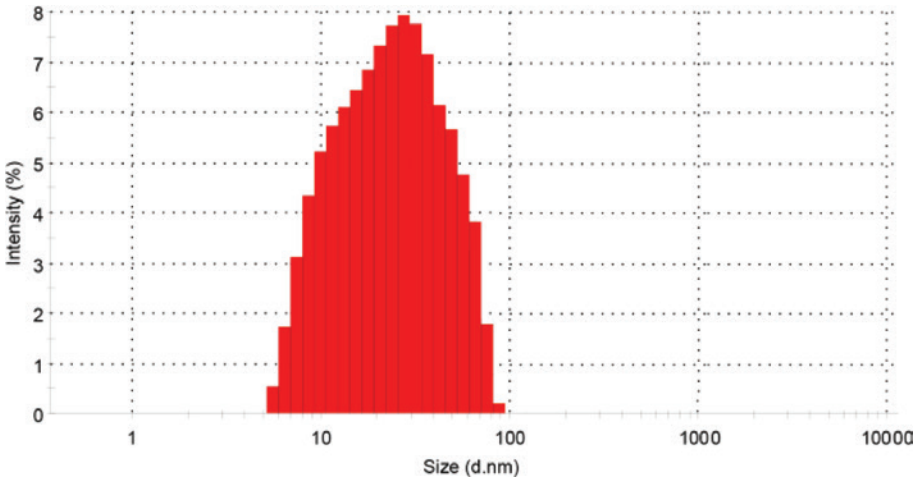


Fig. 3: DLS of nano-colloidal silica@APTPOSS.

Table 1: The influence of diverse catalysts and reaction conditions on the model reaction.[a]

Entry	Solvent	Catalyst (mg)	Time (min)	Yield (%)[b]
1	Toluene (reflux)	No catalyst	300	<10
2	DMF (reflux)	CeO_2 NPs (20)	240	34
3	Toluene (reflux)	CeO_2 NPs (20)	240	37
4	Toluene (reflux)	SnO NPs (20)	240	39
5	Toluene (reflux)	Fe_3O_4 MNPs (10)	240	30
6	Toluene (reflux)	Fe_3O_4 MNPs (20)	240	30
7	Toluene (reflux)	APTPOSS (10)	140	45
8	DMF (reflux)	Nano-colloidal silica@APTPOSS (10)	120	69
9	EtOH (reflux)	Nano-colloidal silica@APTPOSS (10)	120	50
10	CH_3CN (reflux)	Nano-colloidal silica@APTPOSS (10)	120	58
11	Toluene (reflux)	Nano-colloidal silica@APTPOSS (6)	120	72
12	Toluene (reflux)	Nano-colloidal silica@APTPOSS (10)	120	76
13	Toluene (reflux)	Nano-colloidal silica@APTPOSS (14)	120	76
14	Toluene (US)[c]	Nano-colloidal silica@APTPOSS (4)	15	92
15	Toluene (US)[c]	Nano-colloidal silica@APTPOSS (6)	15	96
16	Toluene (US)[c]	Nano-colloidal silica@APTPOSS (8)	15	96
17	Toluene (US)[c]	–	20	34

[a]4-Chlorobenzaldehyde (2 mmol), ethylenediamine(1 mmol), 2-mercaptoacetic acid (2 mmol); [b]isolated yields; [c]ultrasonic irradiation (40 W).

were measured by a Carlo ERBA Model EA 1108 analyzer. The TGA curves are recorded using a V5.1A DUPONT 2000. To investigate the morphology and particle size of the synthesis structures, NPs, FE-SEM images and EDS spectrum of the products were visualized by a Sigma ZEISS, Oxford Instruments Field Emission Scanning Electron Microscope.

4.1 Preparation of Cl-POSS

3-Chloropropyltrimethoxysilane (80 g) was added to a stirred mixture of methanol (1800 mL) and concentrated hydrochloric acid (90 mL). The reaction mixture was stirred for 5 weeks at room temperature. Then the resultant solution was filtered and dried to give a white solid in 42% yield. – Analysis for $C_{24}H_{48}Cl_8O_{12}Si_8$ (1036.9): calcd. C 27.80, H 4.67; found C 27.74, H 4.60. – IR (KBr): $\nu = 2953, 1439, 1104, 810\ cm^{-1}$. – ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.81 (m, 2H), 1.88 (m, 2H), 3.54 (m, 2H).

4.2 Preparation of Octakis[3-(3-aminopropyltriethoxysilane)propyl]octasilsesquioxane (APTPOSS)

Two millimoles (2.07 g) of Cl-POSS was added in 20 mmol (4.43 g) of 3-aminopropyltriethoxysilane and was

Table 2: Preparation of bis-thiazolidinones using nano-colloidal silica@APTPOSS under ultrasonic irradiation.

Entry	Aldehyde	Product	Time (min)	Yield (%)[a]	M.p. (°C)	M.p. (°C)	[ref.]
1	4-Cl–C_6H_4	**4a**	15	96	280–282	285–288	[29]
2	2-Cl–C_6H_4	**4b**	20	90	208–209	210–211	[29]
3	C_6H_5	**4c**	15	90	155–157	152–155	[9]
4	4-NO_2–C_6H_4	**4d**	15	94	164–166	164–166	[12]
5	3-NO_2–C_6H_4	**4e**	20	89	222–224	222–224	[12]
6	Pyridin-2-yl	**4f**	20	88	170–172	167–169	[30]
7	Pyridin-3-yl	**4g**	20	86	195–197	198–200	[30]
8	Pyridin-4-yl	**4h**	20	84	221–223	224–225	[30]
9	4-CH_3–C_6H_4	**4i**	15	81	158–160	158–160	[12]
10	4-Isopropyl–C_6H_4	**4j**	25	75	163–165	163–165	[12]

[a]Isolated yields.

transferred to a round-bottom flask under N_2 atmosphere. The mixture was heated in an oil bath at 110°C for 2 days. After the reaction was complete, the mixture was cooled to room temperature and the mixture was filtered and washed with acetone and methanol to wash the additional reactants. Finally, the resultant pale brown precipitates were dried in a vacuum oven at 70°C for 12 h. – Analysis for $C_{96}H_{224}N_8O_{36}Si_{16}$ (2516): calcd. C 45.82, H 8.97, N 4.45; found C 45.56, H 8.67, N 4.32. – IR (KBr): ν = 2924, 1633, 1112, 1025 cm^{-1}.

4.3 Preparation of nano-colloidal silica@APTPOSS

In a typical procedure, 0.3 mL of colloidal silica NPs (LUDOX SM colloidal silica 30 wt.% suspensions in H_2O) was diluted in 2 mL of deionized water. After that 0.6 g of APTPOSS was dispersed in 3 mL of deionized water by ultrasonic vibration for 15 min. Then the suspension was added slowly during 1 h to the above solution. The mixture was kept at 80°C for 1 day (Scheme 2). Finally, the nano-colloidal silica-attached APTPOSS was separated by centrifugation and washed with acetone and ethanol for several times; then, the mixture was dried in vacuum at 50°C.

4.4 General procedure for the preparation of bis-thiazolidinones

A mixture of aldehydes (2 mmol), ethylenediamine (1 mmol), 2-mercaptoacetic acid (2 mmol) and 6 mg of nano-colloidal silica@APTPOSS in PhMe (20 mL) was sonicated at 40 W power. After completion of the reaction (monitored by thin-layer chromatography), the solvent was evaporated under reduced pressure and ethyl acetate was added. The catalyst was insoluble in ethyl acetate, and it could be recycled by centrifuging. The crude mixture of isomers was separated by silica gel column chromatography (diethyl ether-petroleum ether in variable ratio mixtures). In general, *meso* isomers eluted more slowly than corresponding racemates. The *racemate* isomers were obtained in higher yields than *meso* isomers. The yields of the racemate isomers are presented in Table 2.

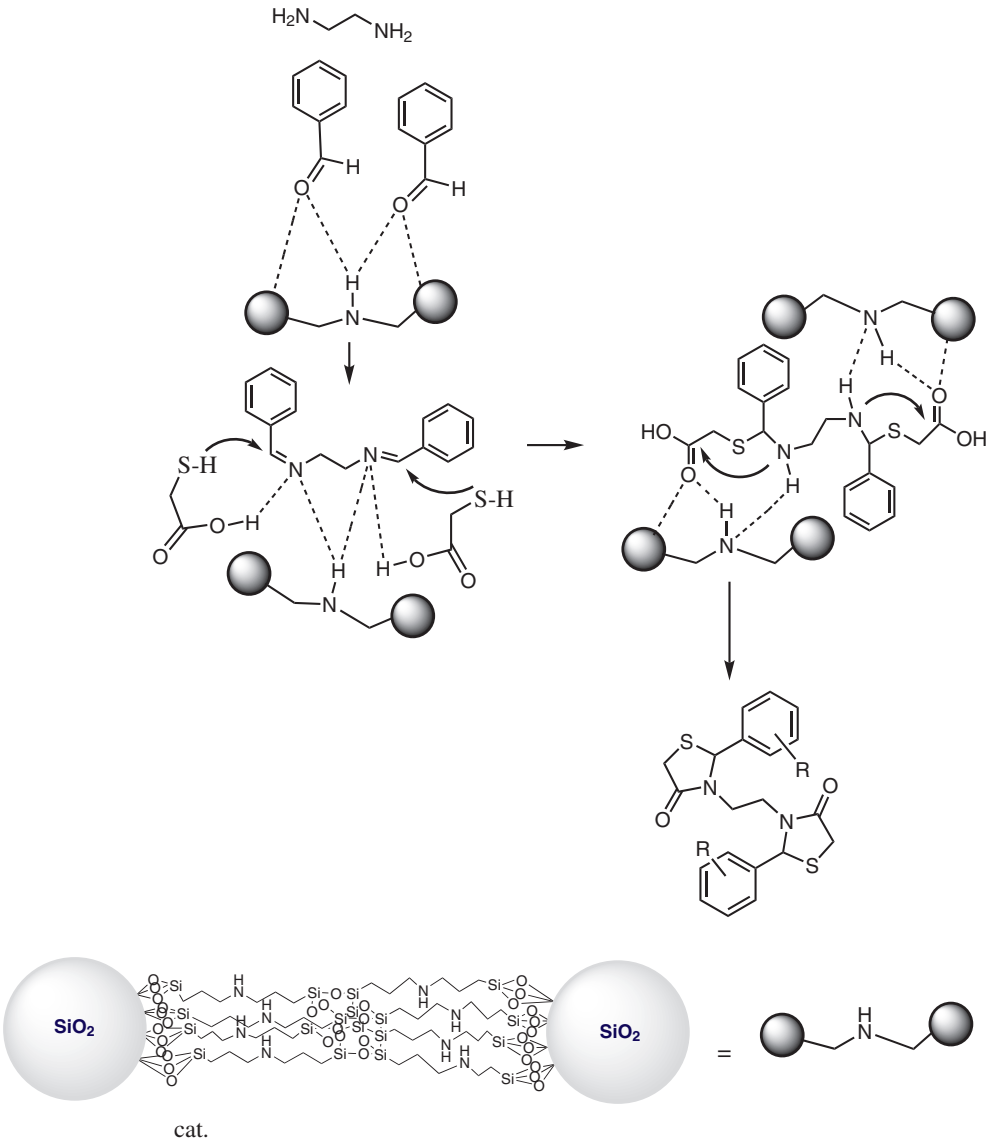
4.5 Spectral data of products

4.5.1 3,3′-(Ethane-1,2-diyl)bis(2-(4-chlorophenyl) thiazolidin-4-one) (4a) [29]

White solid, yield: 96%, m.p.: 280–282°C. – IR (KBr): ν = 2941, 1661 cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.51–2.57 (m, 2H), 3.39–3.44 (m, 2H), 3.51 (d, J = 15 Hz, 2H), 3.71 (dd, J = 1.7, 15 Hz, 2H), 5.55 (d, J = 1.4 Hz, 2H), 7.24 (d, J = 7 Hz, 4H), 7.34 (d, J = 7 Hz, 4H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 31.7, 40.2, 62.9, 128.2, 130.5, 131.4, 141.2, 170.8. – Analysis for $C_{20}H_{18}Cl_2N_2O_2S_2$: calcd. C 52.98, H 4.00, N 6.18, S 14.14; found C 52.73, H 4.23, N 6.19, S 14.03.

4.5.2 3,3′-(Ethane-1,2-diyl)bis(2-(2-chlorophenyl) thiazolidin-4-one) (4b) [29]

White solid, yield: 90%, m.p.: 208–209°C. – IR (KBr): ν = 2938, 1663 cm^{-1}. – ^{1}H NMR (400 MHz, [D_6]DMSO): δ (ppm) = 2.48–2.53 (m, 2H), 3.34–3.4 (m, 2H), 3.43–3.49 (m,2H), 3.67 (dd, J = 1.6, 16 Hz, 2H), 5.58 (d, J = 1.4 Hz, 2H), 7.19–7.25 (m, 6H), 7.27 (dd, J = 2, 5 Hz, 2H). – ^{13}C NMR (100 MHz, [D_6]DMSO): δ (ppm) = 31.7, 39.5, 62.2,



Scheme 3: Probable mechanism for the formation of bis-thiazolidinones.

124.4, 125.3, 126.4, 128.1, 128.9, 135.1, 170.8. – Analysis for $C_{20}H_{18}Cl_2N_2O_2S_2$: calcd. C 52.98, H 4.00, N 6.18, S 14.14; found C 53.83, H 4.11, N 6.09, S 14.05.

4.5.3 3,3′-(Ethane-1,2-diyl)bis(2-phenylthiazolidin-4-one) (4c) [9]

White solid, yield: 90%, m.p.: 155–157°C. – IR (KBr): ν = 2923, 1660 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ (ppm) = 2.52–2.58 (m, 2H), 3.41–3.47 (m, 2H), 3.52 (d, J = 16 Hz, 2H), 3.72 (dd, J = 1.8, 16 Hz, 2H), 5.59 (d, J = 1.6 Hz, 2H), 7.19–7.33 (m, 10H). – ^{13}C NMR (100 MHz, [D_6]DMSO): δ (ppm) = 32.3, 41.2, 62.8, 127.1, 127.3, 128.6, 140.4, 171.4. – Analysis for $C_{20}H_{20}N_2O_2S_2$: calcd. C 62.47, H 5.24, N 7.29, S 16.68; found C 62.35, H 5.17, N 7.18, S 16.57.

4.5.4 3,3′-(Ethane-1,2-diyl)bis(2-(4-nitrophenyl) thiazolidin-4-one) (4d) [12]

Yellow Solid, yield: 94%, m.p.: 164–166°C. – IR (KBr): ν = 2935, 1670, 1521 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.77–2.81 (m, 2H), 3.53–3.6 (m, 2H), 3.67–3.73 (m, 2H), 3.92 (dd, J = 1.9, 16 Hz, 2H), 5.55 (d, J = 1.9 Hz, 2H), 7.24 (d, J = 8 Hz, 4H), 7.36 (d, J = 8 Hz, 4H). – ^{13}C NMR (100 MHz,

$CDCl_3$): δ (ppm) = 32.7, 41.6, 63.4, 123.9, 130.1, 147.2, 150.2, 171.6. – Analysis for $C_{20}H_{18}N_4O_6S_2$: calcd. C 50.62, H 3.82, N 11.81, S 13.51; found C 50.52, H 3.75, N 11.67, S 13.47.

4.5.5 3,3′-(Ethane-1,2-diyl)bis(2-(3-nitrophenyl) thiazolidin-4-one) (4e) [12]

Cream solid, yield: 89%, m.p.: 222–224°C. – IR (KBr): ν = 2932, 1663, 1516 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ (ppm) = 2.63–2.69 (m, 2H), 3.53–3.59 (m, 2H), 3.62–3.68 (m, 2H), 3.88 (dd, J = 1.7, 15 Hz, 2H), 5.95 (d, J = 1.9 Hz, 2H), 7.53–7.72 (m, 4H), 8.01–8.09 (m, 4H). – ^{13}C NMR (100 MHz, [D_6] DMSO): δ (ppm) = 32.4, 41.4, 63.1, 126.2, 129.4, 130.8, 134.1, 143.9, 148.4, 171.5. – Analysis for $C_{20}H_{18}N_4O_6S_2$: calcd. C 50.62, H 3.82, N 11.81, S 13.51; found C 50.53, H 3.67, N 11.78, S 13.42.

4.5.6 3,3′-(Ethane-1,2-diyl)bis(2-(pyridin-2-yl) thiazolidin-4-one) (4f) [30]

Cream solid, yield: 88%, m.p.: 170–172°C. – IR (KBr): ν = 2937, 1674 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.66 (dd, J = 8, 18 Hz, 2H), 3.53–3.59 (m, 2H), 3.73–3.8 (m, 2H), 3.9 (dd, J = 8, 18 Hz, 2H), 5.81 (d, J = 1.2 Hz, 2H), 7.17 (dd, J = 5, 8 Hz, 2H), 7.2 (d, J = 10 Hz, 2H), 7.62 (ddd, J = 2, 8, 10 Hz, 2H), 8.49 (d, J = 5 Hz, 2H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 32.9, 40.1, 63.3, 121.1, 123.5, 138.1, 150.5, 158.4, 171.5. – Analysis for $C_{18}H_{18}N_4O_2S_2$: calcd. C 55.94, H 4.69, N 14.50, S 16.59; found C 55.83, H 4.75, N 14.40, S 16.77.

4.5.7 3,3′-(Ethane-1,2-diyl)bis(2-(pyridin-3-yl) thiazolidin-4-one) (4g) [30]

White solid, yield: 86%, m.p.: 195–197°C. – IR (KBr): ν = 2931, 1668 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ (ppm) = 2.68 (dd, J = 6 Hz, 15, 2H), 3.49 (dd, J = 6, 15 Hz, 2H), 3.62 (d, J = 16 Hz, 2H), 3.9 (dd, J = 1.9, 16 Hz, 2H), 5.78 (d, J = 1.7 Hz, 2H), 7.35–7.41 (m, 2H), 7.75–7.81 (m, 2H), 8.51–8.58 (m, 4H). – ^{13}C NMR (100 MHz, [D_6]DMSO): δ (ppm) = 32.1, 39.6, 61.4, 130.2, 134.8, 135.1, 148.5, 150.2, 171.1. – Analysis for $C_{18}H_{18}N_4O_2S_2$: calcd. C 55.94, H 4.69, N 14.50, S 16.59; found C 55.81, H 4.74, N 14.40, S 16.65.

4.5.8 3,3′-(Ethane-1,2-diyl)bis(2-(pyridin-4-yl) thiazolidin-4-one) (4h) [30]

White solid, yield: 84%, m.p.: 221–223°C. – IR (KBr): ν = 2934, 1667 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO): δ (ppm) = 2.66 (dd, J = 6, 15 Hz, 2H), 3.56–3.63 (m, 4H), 3.82 (dd, J = 1.6, 16 Hz, 2H), 5.72 (d, J = 1.4 Hz, 2H), 7.31 (d, J = 5 Hz, 4H), 8.51 (d, J = 5 Hz, 4H); ^{13}C NMR (100 MHz, [D_6] DMSO): δ (ppm) = 32.2, 40.3, 61.7, 121.1, 148.7, 149.8, 171.4. – Analysis for $C_{18}H_{18}N_4O_2S_2$: calcd. C 55.94, H 4.69, N 14.50, S 16.59; found C 55.93, H 4.74, N 14.53, S 16.53.

4.5.9 3,3′-(Ethane-1,2-diyl)bis(2-(p-tolyl)thiazolidin-4-one) (4i) [12]

White solid, yield: 81%, m.p.: 158–160°C. – IR (KBr): ν = 2929, 1669 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 2.28 (s, 6H), 2.68–2.75 (m, 2H), 3.53–3.61 (m, 4H), 3.67 (dd, J = 1.8, 16 Hz, 2H), 5.46 (d, J = 1.5 Hz, 2H), 7.11 (s, 8H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 20.8, 32.1, 39.5, 63.2, 126.7, 129.3, 135.3, 138.9, 171.1. – Analysis for $C_{22}H_{24}N_2O_2S_2$: calcd. C 64.05, H 5.86, N 6.79, S 15.54; found C 63.91, H 5.94, N 6.88, S 15.38.

4.5.10 3,3′-(Ethane-1,2-diyl)bis(2-(4-isopropylphenyl) thiazolidin-4-one) (4j) [12]

White solid, yield: 75%, m.p.: 163–165°C. – IR (KBr): ν = 2955, 1661 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.17 (d, J = 7 Hz, 12H), 2.69–2.78 (m, 2H), 2.8–2.89 (m, 2H), 3.55–3.64 (m, 4H), 3.68 (dd, J = 1.8, 16 Hz, 2H), 5.48 (d, J = 1.4 Hz, 2H), 7.13 (d, J = 8 Hz, 4H), 7.16 (d, J = 8 Hz, 4H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 23.4, 32.2, 33.4, 39.6, 63.1, 126.67, 126.75, 135.6, 149.8, 171.1. – Analysis for $C_{26}H_{32}N_2O_2S_2$: calcd. C 66.63, H 6.88, N 5.98, S 13.68; found C 66.46, H 6.79, N 6.05, S 13.53.

5 Supplementary information

NMR spectra of the products and other supporting data associated with this article can be found in the online version (https://doi.org/10.1515/znb-2017-0091).

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