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Chiral Pyrrolidine Bridged Polyhedral Oligomeric Silsesquioxanes as Heterogeneous Catalysts for Asymmetric Michael Additions

Torsak Luanphaisarnnont[1] · **Sasikarn Hanprasit**[1] · **Vetiga Somjit**[1] · **Vuthichai Ervithayasuporn**[1]

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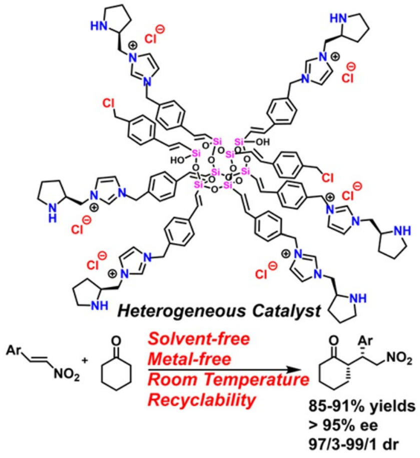
Abstract

A chiral pyrrolidine bridged polyhedral oligomeric silsesquioxane (SQ) was synthesized, characterized, and used as an effective heterogeneous catalyst. The synthesis involves two simple steps: nucleophilic substitution between benzylchloride functionalized SQ and imidazoyl pyrrolidine carboxylate and subsequent deprotection. The catalyst was isolated by simple filtration. The SQ-supported chiral pyrrolidine catalyst was used as a heterogeneous catalyst in an asymmetric Michael addition into nitrostyrenes under room temperature and neat condition, giving the product in excellent yields (85–91%), diastereoselectivities (up to 99:1) and enantioselectivities (95–98%). The catalyst can be recycled by a simple filtration without a significant loss in its reactivity and selectivity.

Graphical Abstract



Keywords Silsesquioxane · POSS · Asymmetric catalysis · Michael reaction · Heterogeneous catalysis

1 Introduction

Development of efficient catalysis for organic transformations has been among major challenges in chemistry [1]. The use of inorganic support for heterogeneous catalysis has gained attention over organic materials due to their outstanding mechanical and thermal stabilities [2]. Although silica gel has been the most widely used support for chiral catalysts [3–5], recent research investigations have shown that an ordered nanostructure of mesoporous silica can also be used

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✉ Vuthichai Ervithayasuporn
vuthichai.erv@mahidol.ac.th; maldiniandg@hotmail.com

[1] Department of Chemistry, Center of Excellence for Innovation in Chemistry (PERCH-CIC), and Center for Inorganic and Materials Chemistry, Faculty of Science, Mahidol University, 272 Rama VI Road, Ratchathewi District, Bangkok 10400, Thailand

as a support for catalyst, exhibiting high catalytic activities in both symmetric and asymmetric organic reactions [6–12]. Polyhedral oligomeric silsesquioxanes (POSS) or cage-like silsesquioxanes (SQ) with a well-defined nanostructure, composed of a silica (Si–O) core with the highest organic functionalities [13–15], have also been studied and used as sensors [16], electronic materials [17], and alternative catalyst supports [18–20]. Recent works showed that SQ could be applied in C–C bond coupling reactions [21–23], oxidations [24], multicomponent coupling reactions [25], carbon dioxide fixation reactions [26], and polymerizations [27, 28]. Despite many reports on the use of SQ as a catalyst support, the development of SQ-supported chiral catalysts for heterogeneous asymmetric reactions has been limited. An organorhodium-functionalized SQ, which was used as a bifunctional heterogeneous catalyst for an asymmetric transfer hydrogenation of aromatic ketones, has been reported [29]. To the best of our knowledge, there is no report on the use of chiral SQ as a heterogeneous catalyst in asymmetric C–C bond forming reactions.

Catalytic asymmetric Michael reactions are one of the most important and useful asymmetric C–C bond forming reactions [30, 31]. Many chiral pyrrolidine catalysts have been developed for asymmetric homogeneous Michael addition into nitrostyrenes [32, 33]. Developments of heterogeneous catalysts by attachment of chiral pyrrolidines on modified organic and inorganic materials have also been studied [34–39]. However, a chiral heterogeneous pyrrolidine-modified SQ catalyst has not been well investigated. Herein, a chiral pyrrolidine bridged polyhedral oligomeric SQ was synthesized, characterized, and used as a heterogeneous catalyst for asymmetric Michael additions of cyclohexanones into nitrostyrenes. Furthermore, the chiral pyrrolidine loading of SQ catalyst were determined to be much greater than any previous silicon-based materials.

2 Experimental

2.1 Chemicals and Instruments

Di-*tert*-butyl dicarbonate was purchased from Tokyo Chemical Industry, while imidazole, L-proline, *trans*-β-nitrostyrene, *trans*-4-methoxy-β-nitrostyrene, *trans*-4-fluoro-β-nitrostyrene, *trans*-4-chloro-β-nitrostyrene, and anhydrous toluene were purchased from Sigma Aldrich and used without additional purification. The commercial grades of ethyl acetate, methylene chloride, methanol and hexane were further distilled. Precoated silica gel 60 F254 plates and silica gel (No. 60) used for chromatography were purchased from Merck & Co., Inc.

The FT-IR spectra were collected using an attenuated total reflectance technique with Bruker model Alpha spectrometer. HPLC analysis was performed on Waters 2695 Separation Modules with Waters 2487 Dual λ Absorbance Detector using a Chiralpak AD-H column purchased from Daicel Chemical Industries, Ltd.

The ^{13}C and ^{29}Si CP/MAS NMR spectra were acquired at 60 MHz frequency with AVANCE 300 MHz Digital NMR Spectrometer (Bruker Biospin; DPX-300). A 7 mm triple resonance probe, a sample spinning rate of 5 kHz with a contact time of 2 ms, and pulse delay of 5 s were used. The pulses and the spectra were calibrated using commercially available samples of 2,2-dimethyl-2-silapentan-5-sulfonate, glycine and adamantine, for ^{29}Si and ^{13}C, respectively. Fourier transform nuclear magnetic resonance spectra in solution phase were obtained by using a Bruker-Ascend™ 400 and Bruker-AV 500 high-resolution magnetic resonance spectrometers for ^{1}H (400 MHz) and (500 MHz) nuclei, respectively. Powder X-ray diffraction was performed by Bruker D8 Advance with a monochromatic Cu K_{α} radiation at $\lambda = 0.154$ nm. Applied voltage and current were used at 40 kV and 30 mA, respectively. The mode of recorded system was operated with $2\theta = 5.00–40.00$ (scan rate = 0.005° s^{-1}). Thermogravimetric analyses (TGA) were performed on a TG 209F3 instrument in Al_2O_3 pans and carried out under oxygenated atmosphere on heating at 10 °C/min in a range of 35 and 800 °C.

2.2 Preparation of Catalysts

2.2.1 Synthesis of SQ-Supported Chiral Pyrrolidine Procatalyst (2)

Under argon atmosphere, octa(4-(chloromethyl)styryl)octasilsesquioxane [40, 41] (0.30 g, 0.18 mmol) and *tert*-butyl (*S*)-2-((1*H*-imidazol-1-yl)methyl)pyrrolidine-1-carboxylate [42] (1.13 g, 4.52 mmol) were mixed in 4 mL of dried toluene. The solution was kept at 70 °C and stirred for 24 h. The precipitate was filtered and washed with CH_2Cl_2, methanol, and ethyl ether, respectively, and dried under vacuum. The Boc-protected SQ-supported product was obtained as a pale yellow solid (0.51 g, 0.135 mmol, 75% yield). Procatalyst **2** was further quantified through CHN microanalysis and found to be 2.14 mmol/g of pyrrolidine-based imidazolium cation based on nitrogen percentage. ^{29}Si CP/MAS NMR: δ − 67.89, − 77.43 ppm; ^{13}C CP/MAS NMR: δ 154.8, 148.0, 136.9, 129.9, 127.4, 123.0, 79.4, 56.9, 52.4, 46.8, 28.4, 23.4 ppm.

2.2.2 Synthesis of SQ-Supported Chiral Pyrrolidine Catalyst (3)

The Boc-protected SQ-supported catalyst **2** (0.51 g, 0.135 mmol) was deprotected using 5 M HCl in ethanol (10 mL) with vigorously stirring at room temperature for 4 h. The reaction was subsequently neutralized with NEt_3 (3 mL). The reaction was filtered, and the solid catalyst was washed with ethanol and ethyl ether and dried under vacuum at room temperature to afford the desired product as a solid (0.39 g, 0.129 mmol, 96% yield). Catalyst **3** was further quantified through CHN microanalysis and found to be 2.28 mmol/g of pyrrolidine-based imidazolium cation based on nitrogen percentage. ^{29}Si CP/MAS NMR: δ − 59.92, − 68.14, − 78.03 ppm; ^{13}C CP/MAS NMR: δ 147.8, 136.8, 127.8, 123.0, 58.4, 52.7, 46.6, 28.8, 24.1, 21.6 ppm.

2.3 Catalytic Testing for Asymmetric Michael Addition

The SQ-supported catalyst **3** (7.5 mg, 0.0029 mmol), nitrostyrene (75 mg, 0.5 mmol), and cyclohexanone (0.4 mL) were added to a reaction flask. The reaction was stirred at room temperature for 24 h. The reaction mixture was filtered and washed with ethyl acetate. The combined filtrate was concentrated. Flash column chromatography (hexanes/ethyl acetate = 3:1) provided the *γ*-nitroketone as a solid.

3 Result and Discussion

3.1 Preparation of Catalysts

The synthesis approach for SQ-supported (*S*)-1-((pyrrolidin-2-yl)methyl)-1*H*-imidazolium chloride, the SQ-supported catalyst (**3**), was depicted in Scheme 1. Firstly, SQ-supported (*S*)-1-((1-(*tert*-butoxycarbonyl)pyrrolidin-2-yl)methyl)-1*H*-imidazolium chloride, the SQ-supported procatalyst (**2**), can be synthesized from a substitution reaction between octa(4-(chloromethyl)styryl)octasilsesquioxane (**1**) [40, 41] and *tert*-butyl (*S*)-2-((1*H*-imidazol-1-yl)methyl)pyrrolidine-1-carboxylate [42] under thermal activation in 75% yield, subsequently followed by a Boc deprotection under acidic condition to obtain SQ-supported catalyst **3** in 96% yield. It

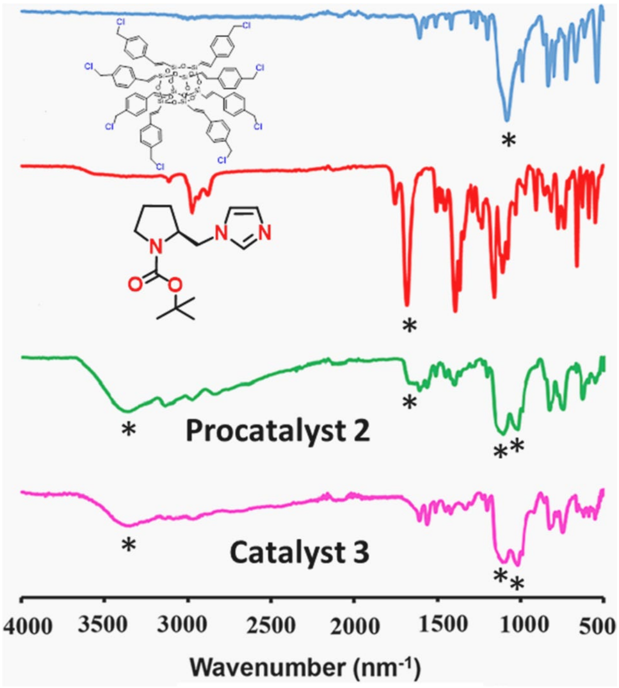
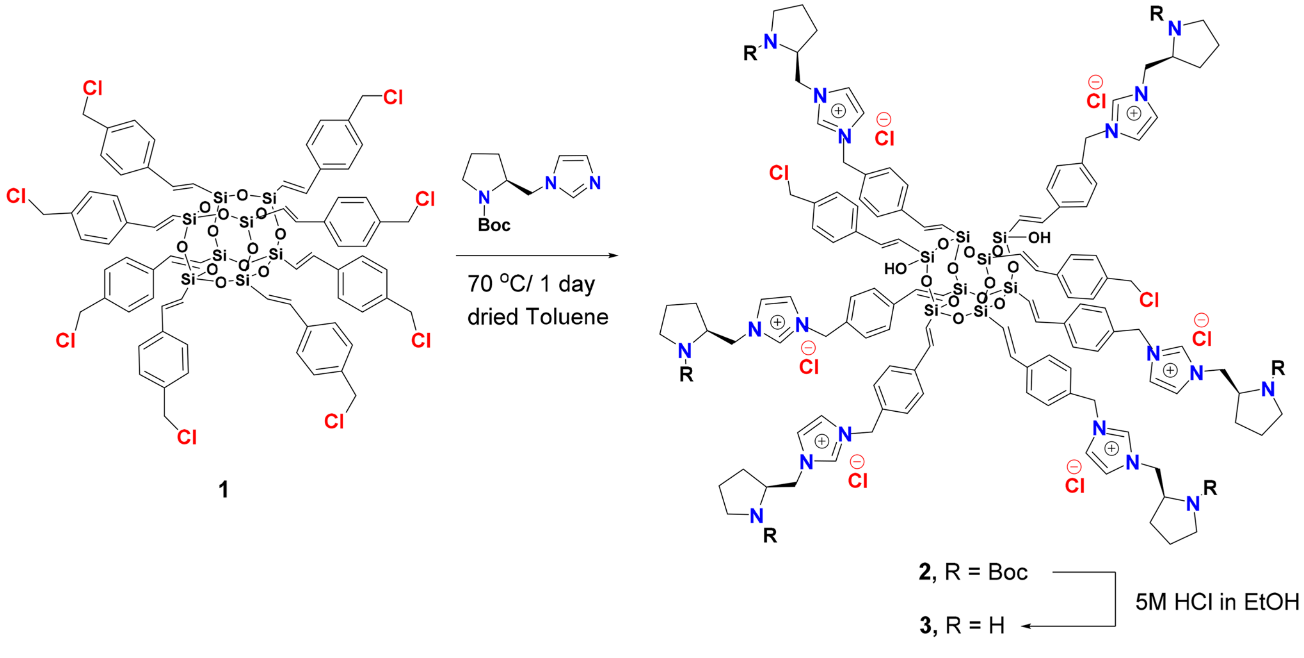


Fig. 1 IR spectra of starting materials, procatalyst **2**, and catalyst **3**



Scheme 1 Synthesis of a chiral pyrrolidine bridged polyhedral oligomeric SQ, the SQ supported catalyst (**3**)

is noteworthy that the syntheses of the procatalyst **2** and the catalyst **3** require no templating reagents and the isolation processes involve only a simple filtration because of their insolubility in organic and aqueous solvents.

3.2 Catalyst Characterizations

The formations of procatalyst **2** and the catalyst **3** were confirmed by IR, NMR, TGA, XRD, and CHN methods. The FT-IR spectra of **2** as shown in Fig. 1 showed a key C=O stretching vibration band at 1683 cm^{-1} corresponding to the presence of Boc–pyrrolidine moieties. This absorption band is absent in the IR spectra of **3** (Fig. 1), confirming the removal of Boc protecting group. Both **2** and **3** also exhibited overlapped C–N stretching vibrations of pyrrolidine rings at 1150 cm^{-1}among two distinct asymmetrical Si–O–Si stretching vibrations at 1100 and 1020 cm^{-1} arising for more disordered polyhedral SQ cages, which differ from a perfect T_8 cage of **1** with a very strong broad band at 1030 cm^{-1} [43]. The presence of a broad O–H band (3000–3700 cm^{-1}) can be assigned to SiOH units, which also confirmed the presence of some cage-degradation resulting in open siliceous structures with silanols groups such as T^1 [R-Si(OSi)$_1$(OH)$_2$] and T^2 [R-Si(OSi)$_2$(OH)]. These disordered cages from partial cage opening could be explained by the strong nucleophilicity of the *sp*^{2} nitrogen on the imidazole, which increased the chance of the cleavage of Si–O bonds at a SQ core [44].

The NMR results (Fig. 2) also agreed well with the IR spectra. To confirm a successful substitution of substituted imidazole on **1**, ^{13}C CP/MAS NMR spectrum of **2** (Fig. 2a)

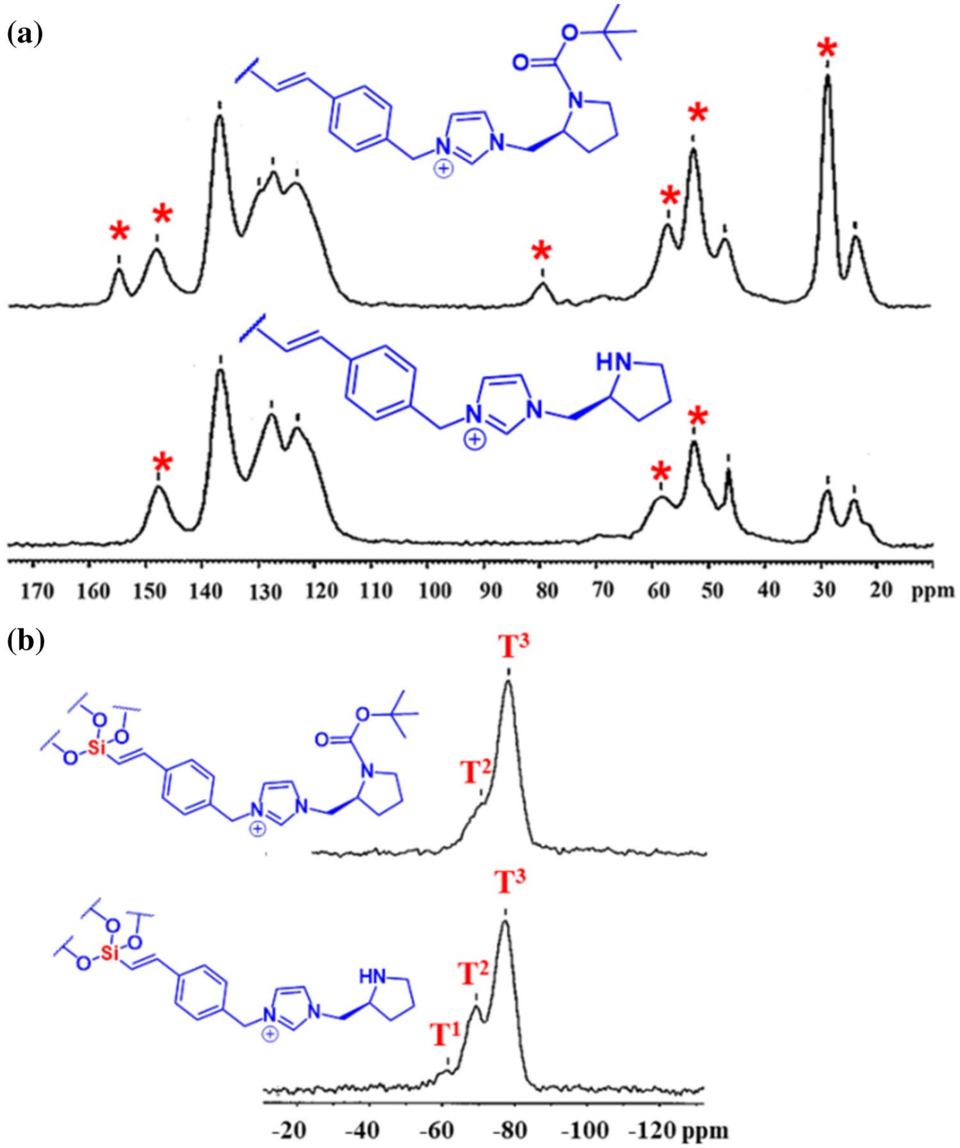


Fig. 2 **a** ^{13}C and **b** ^{29}Si CP/MAS NMR spectra of procatalyst **2** and catalyst **3**

exhibited two key signal sets corresponding to imidazolium (148.0 ppm) and Boc–pyrrolidine rings (154.8, 79.4, 56.9, 52.4, and 28.4 ppm). The absence of the signals at 154.8, 79.4, and 28.4 ppm in the ^{13}C CP/MAS NMR spectrum of **3** (Fig. 2a) confirmed the complete removal of the Boc protecting group. The ^{29}Si CP/MAS NMR spectra were used to probe into the core structures of **2** and **3** (Fig. 2b). The signals of catalyst **3** at − 77, −68, and − 59 ppm corresponded to the T^3 [R-Si(OSi)$_3$] and some partially cage-opening silsesquioxanes (T^2 and T^1), respectively.

TGA of **2** and **3** (Fig. 3) confirmed the existence of the hydrophilic imidazolium and silanol moieties, which can strongly absorb moisture, on both materials. The TGA curves showed 5% weight loss between 25 and 120 °C; therefore, the reformulated ceramic yields of **2** and **3** were 13.7 and 17.9 wt%, respectively, versus the calculated values of 14.9 and 18.3 wt%, respectively. The derivative weight loss of **2** (Fig. 3) showed an additional peak at 150–215 °C confirmed the degradation of Boc groups on **2**. This peak was absent in the curve of **3** (Fig. 3).

According to the XRD spectra of **2** and **3** in Fig. 4, both materials exhibited an amorphous nature with a key characteristic reflection at $2\theta = 21.0°$, which can be converted to a 4.22 Å of *d*-value. This value indicated the existence of a SQ (Si–O–Si) cage [27]. When compared with that of the SQ-supported procatalyst **2**, the reflection of the SQ catalyst **3** was shifted from $2\theta = 7.3°–8.5°$, and the *d*-spacing is decreased to about 1.70 Å. This shift confirmed a successful removal of the Boc protecting group on **2**. In order to confirm the number of active sites of pyrrolidine-based imidazole on SQ, catalyst **3** was simply quantified through CHN microanalysis. Its carbon-to-nitrogen (C:N) mass ratio was found to be 6.09, compared to a calculated value of 5.95 for the SQ with six chiral pyrrolidine rings. This result suggested that the number of active chiral pyrrolidine rings on the SQ core in **3** is approximately 6.

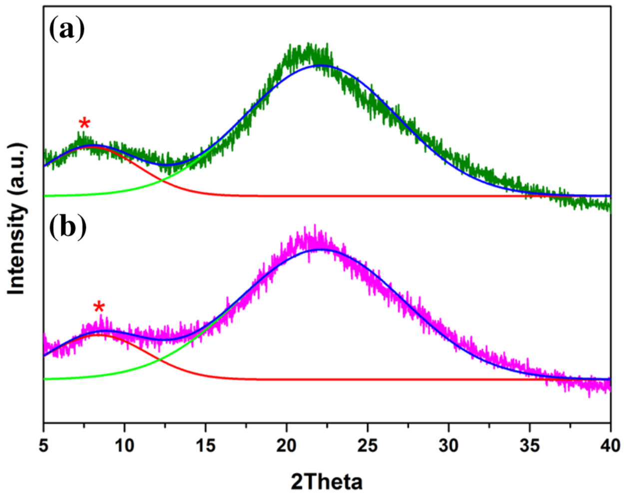


Fig. 4 XRD spectra of **a** procatalyst **2** and **b** catalyst **3**

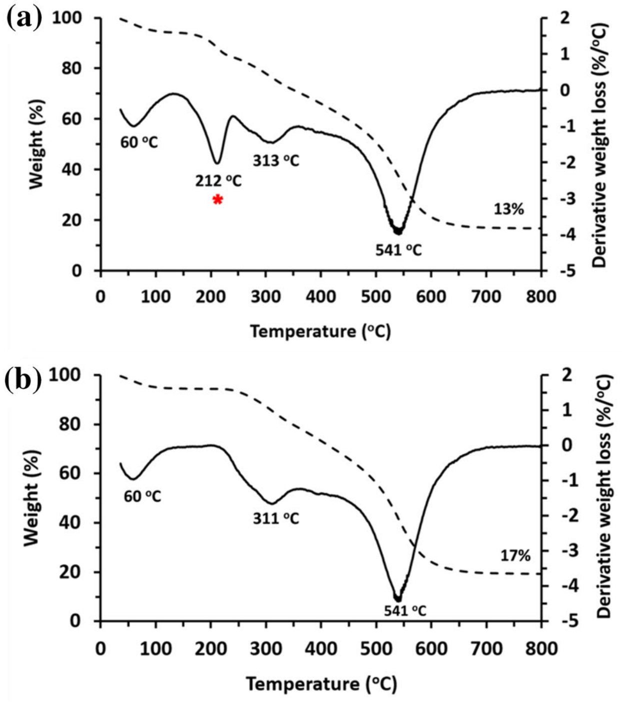
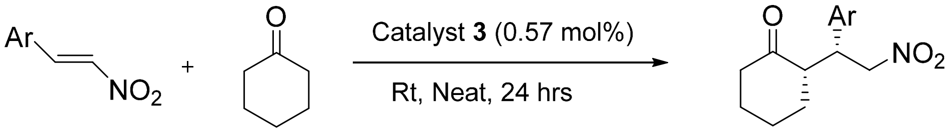


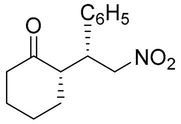
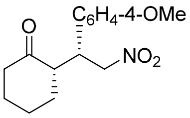
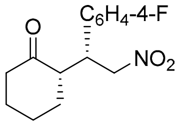
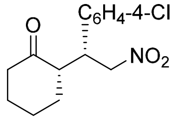
Fig. 3 TGA and derivative weight loss curves of **a** procatalyst **2** and **b** catalyst **3**

3.3 Catalytic Testing for Asymmetric Michael Addition

To test for the effectiveness and efficiency of the SQ scaffold as a support for chiral catalysts, the SQ-supported chiral catalyst **3** was used in an asymmetric Michael addition reaction of cyclohexanone into nitroolefins (Table 1). The amount of catalyst **3** is 0.57 mol%, which is approximately equal to 3.4 mol% active chiral pyrrolidine rings. Both electron-rich and electron-poor nitrostyrenes work well in the reaction, giving the corresponding products in excellent yields, diastereoselectivities and enantioselectivities. The slightly lower yield of electron-rich substrate may be due to the lower electrophilicity of the substrate. The high yields and selectivities were similar to those obtained from the homogeneous catalysis [32] and silica–gel-supported catalyst [35], suggesting that the SQ core did not interfere with the active chiral pyrrolidine ring. It is noteworthy that the SQ-supported catalyst was more efficient at catalyzing the reaction, yielding similar yields and selectivities even with a lower amount of the active chiral pyrrolidine rings and a shorter reaction time. When compared with the homogeneous catalyst, the SQ-supported catalyst was also easier to

Table 1 Asymmetric Michael additions of cyclohexanone catalyzed by the SQ-supported chiral catalyst **3**



Entry[a]	Product	Yield[b] (%)	dr[c]	ee[d] (%)
1		90	98:2	98
2		85	97:3	97
3		90	99:1	97
4		91	99:1	95

[a] Nitroolefin (0.5 mmol), cyclohexanone (0.4 mL) and **3** (0.57 mol%) under neat reaction condition at room temperature for 24 h

[b] Isolated yields

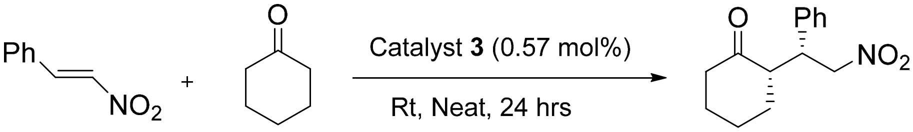
[c] Diastereomeric ratio, dr (syn:anti), determined by ^{1}H NMR spectroscopy of the crude product

[d] Determined by HPLC using a Chiralpak AD-H column

handle with a simple filtration to separate the catalyst from the reaction mixture and without need for solvents.

The recyclability of the SQ-supported catalyst **3** was investigated by subjecting it into a new reaction for multiple cycles (Table 2). The catalyst can be used for at least four cycles with a minimal loss in yields and selectivities. This result showed the high robustness of the SQ as a catalyst support. To further study the durability of the SQ-supported catalyst **3**, a leaching test and a filtration test were performed, and their results suggested that no catalytically active species leached out form the SQ-supported catalyst **3** during the reaction. A preliminary study on the basic kinetic behavior of the catalyst was performed by monitoring the product yield at different times (Fig. S5). The formation of the product plateaued after around 24 h. The turnover number of the catalyst after 24 h could be calculated to be approximately 158. A further kinetic investigation to study the detailed behavior of the SQ-supported catalyst, particularly at the beginning of the reaction, is currently being investigated.

Table 2 Recycling experiments of the catalyst **3**



Cycle	Yield (%)	dr	ee (%)
1	90	98:2	98
2	88	98:2	97
3	89	98:2	98
4	85	97:3	95

4 Conclusion

The chiral pyrrolidine bridged cage-like SQ catalyst was synthesized and characterized. The catalyst was used to effectively and efficiently catalyze the Michael addition reactions of cyclohexanone into nitroolefins with excellent yields and selectivities at room temperature. The catalyst could be recycled by a simple filtration with a minimal loss in the yields and selectivities, which confirms the effectiveness and robustness of the SQ core as a heterogeneous scaffold for chiral catalysts. Further applications of SQ cage as a support for other chiral catalysts is undergoing and will be reported in due course.

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References

1. Beller M, Renken A, van Santen RA (2012) Catalysis: from principles to applications. Wiley, Weinheim
2. Liu H, Zheng S, Nie K (2005) Macromolecules 38:5088
3. Soai K, Watanabe M, Yamamoto A (1990) J Org Chem 55:4832
4. Heckel A, Seebach D (2000) Angew Chem Int Ed 39:163
5. Fraile JM, Mayoral JA, Serrano J, Pericas MA, Sola L, Castellnou D (2003) Org Lett 5:4333
6. Kawasaki T, Araki Y, Hatase K, Suzuki K, Matsumoto A, Yokoi T, Kubota Y, Tatsumi T, Soai K (2015) Chem Commun 51:8742
7. Cheng T, Zhao Q, Zhang D, Liu G (2015) Green Chem 17:2100
8. del Pozo C, Corma A, Iglesias M, Sánchez F (2011) Green Chem 13:2471
9. Croissant JG, Cattoën X, Durand JO, Man MWC, Khashab NM (2016) Nanoscale 8:19945
10. Hosseini HG, Doustkhah E, Kirillova MV, Rostamnia S, Mahmoudi G, Kirillov A (2017) Appl Catal A 548:96
11. Rostamnia S, Gholipour B, Hossenini HG (2016) Process Saf Environ Prot 100:74
12. Rostamia S, Hossieni HG, Doustkhah E (2015) J Organomet Chem 791:18
13. Cordes DB, Lickiss PD, Rataboul F (2010) Chem Rev 110:2081
14. Hanprasit S, Tungkijanansin N, Prompawilai A, Eangpayung S, Ervithayasuporn V (2016) Dalton Trans 45:16117
15. Chimjarn S, Kunthom R, Chancharone P, Sodkhomkhum R, Sangtrirutnugul P, Ervithayasuporn V (2015) Dalton Trans 44:916
16. Chanmungkalakul S, Ervithayasuporn V, Hanprasit S, Masik M, Prigyai N, Kiatkamjornwong S (2017) Chem Commun 53:12108
17. Ervithayasuporn V, Abe J, Wang X, Matsushima T, Murata H, Kawakami Y (2010) Tetrahedron 66:9348
18. Zheng W, Lu C, Yang G, Chen Z, Nie J (2015) Catal Commun 62:34
19. Moreau JJE, Vellutini L, Man MWC, Bied C (2003) Chem Eur J 9:1594
20. Duchateau R (2002) Chem Rev 102:3525
21. Bivona LA, Giacalone F, Carbonell E, Gruttadauria M, Aprile C (2016) ChemCatChem 8:1685
22. Zhang C, Leng Y, Jiang P, Lu D (2016) RSC Adv 6:57183
23. Mohapatra S, Chaiprasert T, Sodkhomkhum R, Kunthom R, Hanprasit S, Sangtrirutnugul P, Ervithayasuporn V (2016) ChemistrySelect 1:5353
24. Sangtrirutnugul P, Chaiprasert T, Hunsiri W, Jitjaroendee T, Songkhum P, Laohhasurayotin K, Osotchan T, Ervithayasuporn V (2017) ACS Appl Mater Interfaces 9:12812
25. Safaei-Ghomi J, Nazemzadesh SH, Shahbazi-Alavi H (2016) Appl Organomet Chem 30:911
26. Bivona LA, Fichera O, Fusaro L, Giacalone F, Buaki-Sogo M, Gruttaduaria M, Aprile C (2015) Catal Sci Technol 5:5000
27. Kunthom R, Jaroentomeechai T, Ervithayasuporn V (2017) Polymer 108:173
28. Pochwala M, Bialek M, Franczyk A, Marciniec B, Czaja K (2016) Eur Polym J 79:121
29. Tang S, Jin R, Zhang H, Yao H, Zhuang J, Liu G, Li H (2012) Chem Commun 48:6286
30. Berner OM, Tedeschi L, Enders D (2002) Eur J Org Chem 2002:1877
31. Almasi D, Alonson DA, Najera C (2007) Tetrahedron: Asymmetry 18:299
32. Ishii T, Fujioka S, Sekiguchi Y, Kotsuki H (2004) J Am Chem Soc 126:9558
33. Reyes-Rangel G, Vargas-Caporali J, Juaristi E (2017) Tetrahedron 73:4707

34. Du J, Shuai B, Tao M, Wang G, Zhang W (2016) Green Chem 18:2625
35. Li P, Wang L, Zhang Y, Wang G (2008) Tetrahedron 64:7633
36. Luo S, Mi X, Zhang L, Liu S, Xu H, Cheng JP (2006) Angew Chem Int Ed 45:3093
37. Tian J, Zhang C, Qi X, Yan X, Li Y, Chen L (2015) Catal Sci Technol 5:724
38. Qi X, Tian J, Li Y, Chen L, Yan X (2015) Catal Commun 71:70
39. Liu J, Li P, Zhang Y, Ren K, Wang L, Wang G (2010) Chirality 22:432
40. Harrison PG, Hall C (1997) Main Group Met Chem 20:515
41. Cheng G, Vautravers NR, Morris RE, Cole-Hamilton DJ (2008) Org Biomol Chem 6:4662
42. Wang L, Tang R, Yang H (2013) J Korean Chem Soc 57:591
43. Fina A, Tabuani D, Carniato F, Frache A, Boccaleri E, Camino G (2006) Thermochim Acta 440:36
44. Jaroentomeechai T, Yingsukkamol PK, Phurat C, Somsook E, Osotchan T, Ervithayasuporn V (2012) Inorg Chem 51:12266