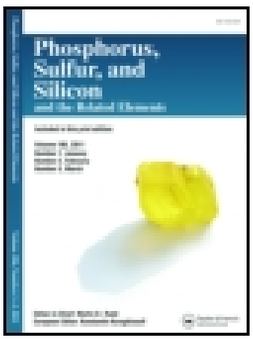


Taylor & Francis
Taylor & Francis Group

Phosphorus, Sulfur, and Silicon and the Related Elements

ISSN: 1042-6507 (Print) 1563-5325 (Online) Journal homepage: https://www.tandfonline.com/loi/gpss20

Modification of polyhedral oligomeric silsesquioxane derivatives with heck reaction as possible new bio-hybrid materials

Omer Tahir Gunkara

To cite this article: Omer Tahir Gunkara (2019): Modification of polyhedral oligomeric silsesquioxane derivatives with heck reaction as possible new bio-hybrid materials, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI: 10.1080/10426507.2019.1576678

To link to this article: https://doi.org/10.1080/10426507.2019.1576678

PHOSPHORUS, SULFUR, AND SILICON AND THE RELATED ELEMENTS
https://doi.org/10.1080/10426507.2019.1576678

Modification of polyhedral oligomeric silsesquioxane derivatives with heck reaction as possible new bio-hybrid materials

Omer Tahir Gunkara

Faculty of Science and Arts Chemistry Department, Yildiz Technical University, Istanbul, Turkey

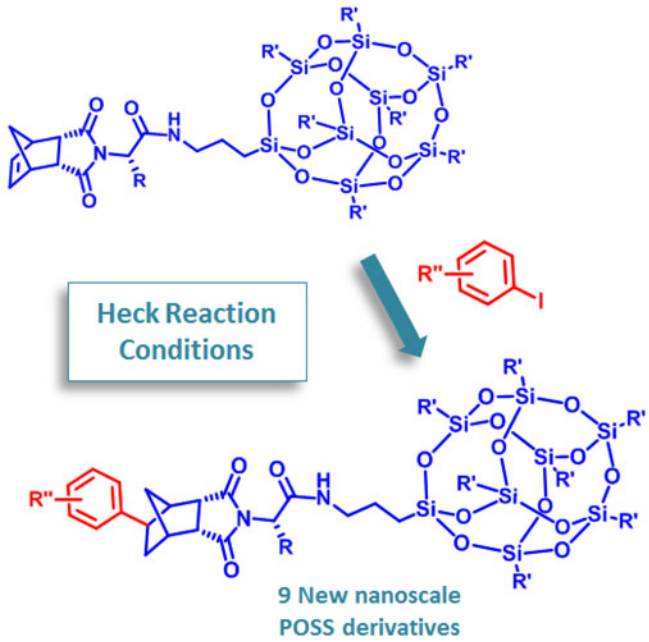
ABSTRACT

The regioselective synthesis of Polyhedral oligomeric silsesquioxane (POSS)-based norbornyl imide derivatives through palladium catalyzed Heck coupling reaction was reported on an effective synthetic method to organic–inorganic bio-hybrids serving as advanced materials. The reaction of POSS-based imide derivatives with various aryl iodides catalyzed by palladium acetate in the presence of triethyl amine, as the base, in DMF afforded the products in moderate yields. All new POSS derivatives were structurally characterized by FTIR, ^{1}H, ^{13}C NMR, HRMS and GC/MS analyses.

ARTICLE HISTORY
Received 13 November 2018
Accepted 28 January 2019

KEYWORDS
Bio-hybrid material; Heck reaction; hydroarylation reaction; polyhedral oligomeric silsesquioxane (POSS)

GRAPHICAL ABSTRACT



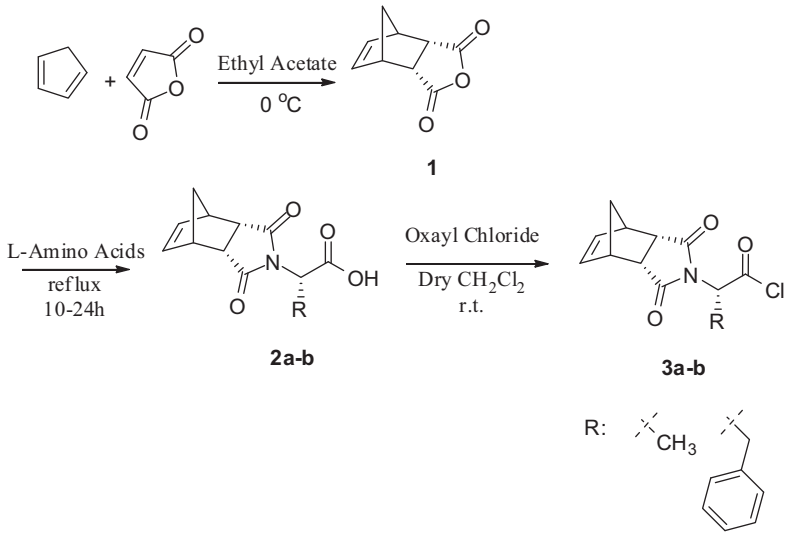
Introduction

Polyhedral oligomeric silsesquioxanes (POSS) are characterized by their unusual chemical skeleton, which has attract attention from scientists of various disciplines.[1–3]

POSS materials have an enormous potential as a building block for several materials, and their applications can be found in the areas of coordination, catalysis, and bio-material chemistry.

POSS are completely defined molecules of unusual 3D nanoscale dimensions and hybrid organic–inorganic materials, and also they are odorless, nonvolatile and eco-friendly.[4] Its chemical structure is in between silica (SiO_2) and silicones (R_2SiO).[5–7] The POSS molecule consists of a cubic Si–O core that is surrounded by 8 different substrates, one in each corner of the cubic form.[5,7] Each silicon atom is bonded to three oxygen atoms by siloxane bonds (Si–O–Si), and one carbon silicon bond (Si–C) that may be

CONTACT Omer Tahir Gunkara gunkara@yildiz.edu.tr Faculty of Science and Arts Chemistry Department, Yildiz Technical University, Davutpasa Campus, Esenler, Istanbul, 34220, Turkey.
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/gpss.
Supplemental data for this article can be accessed on the publisher's website.



Scheme 1. Synthesis of compounds **2a–b** and **3a–b**.

unreactive or reactive, thus presenting the POSS structures coherent with biological and polymeric systems.

The mechanical properties of these materials lie between those of conventional glasses and highly crosslinked rubbers. The matchless characteristics of POSS nanostructures offers a various application an enormous potential in a wide range of areas for bio-medical sciences, such as tissue engineering scaffolds, biomedical devices, dental applications, drug delivery systems and biological sensors.[8–14]

The mono- or multi-functional POSS nanostructures could be obtained through reaction of their reactive organic functional substrates.

It is possible to prepare various unique POSS nanostructures by changing the functional groups and size on the silsesquioxane and that increases the compatibility of POSS with many polymers.[15]

Great numbers of hybrid materials such as polymeric nanocomposites with POSS structure have been developed.[16–24]

Recently, unusual POSS nanomaterials have attracted the increasing interest of scientists to investigate the property-structure relationship of such polymer nanocomposites. As nanoscale building blocks, POSS and their analogs have been investigated for their self-assembly behavior at the nanoscale.[7,25–33]

Previous studies show that, dispersion of micro or nanoscale inorganic nanoparticles in polymers have been shown to improve crack resistance of scaffolds.[34–38]

In the light of this information, in this paper new nano-POSS-derivatives have been developed as possible bio-hybrid materials.

The reductive Heck reaction of POSS analogs might be considered the most direct synthetic approach for preparing novel POSS derivatives and possible use as bio-hybrid material,[39] which is being potently investigated in medical science.[8]

POSS-based structures have got ability to be incorporated into a great variety of biocompatible polymers make POSS nanostructure an attractive material for a versatile array of applications in medicine. The nanostructured new POSS derivatives can mimic the toughening mechanism of natural materials to dissipate energy. For example, there is no single existing material possesses all the necessary properties required in an ideal bone graft, the approach has been to develop a three dimensional, porous composite of new POSS nanomaterial that is biodegradable and bioactive.

Results and discussion

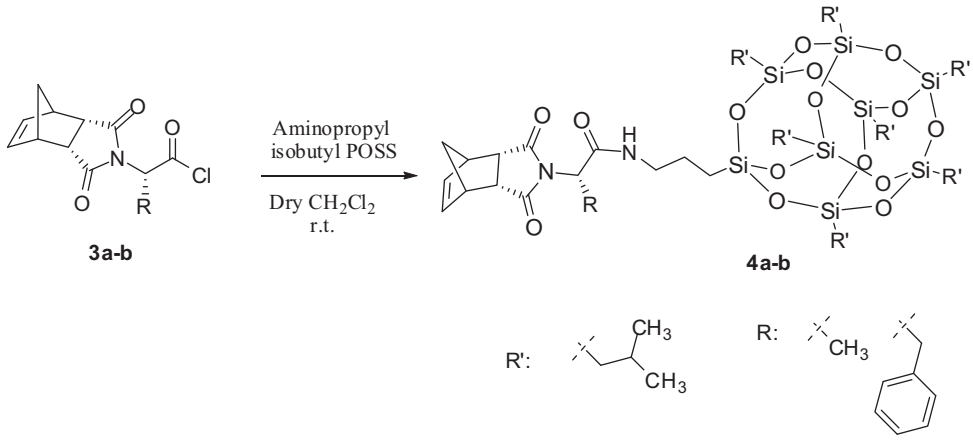
For this approach, bicyclo-[2.2.1]hept-5-ene-*endo*,*endo*-2,3-di-carboxylic anhydride (endic anhydride) **1** was obtained from the reaction between maleic anhydride and freshly distilled cyclopentadiene with a known procedure.[40] The Diels-Alder reaction was performed at 0°C in ethyl acetate.

Optically active norbornenylimide substituted amino acids **2a–b** were prepared from **1** with L-amino acids (L-alanine or L-phenyl alanine), using a known procedure [41] (Scheme 1).

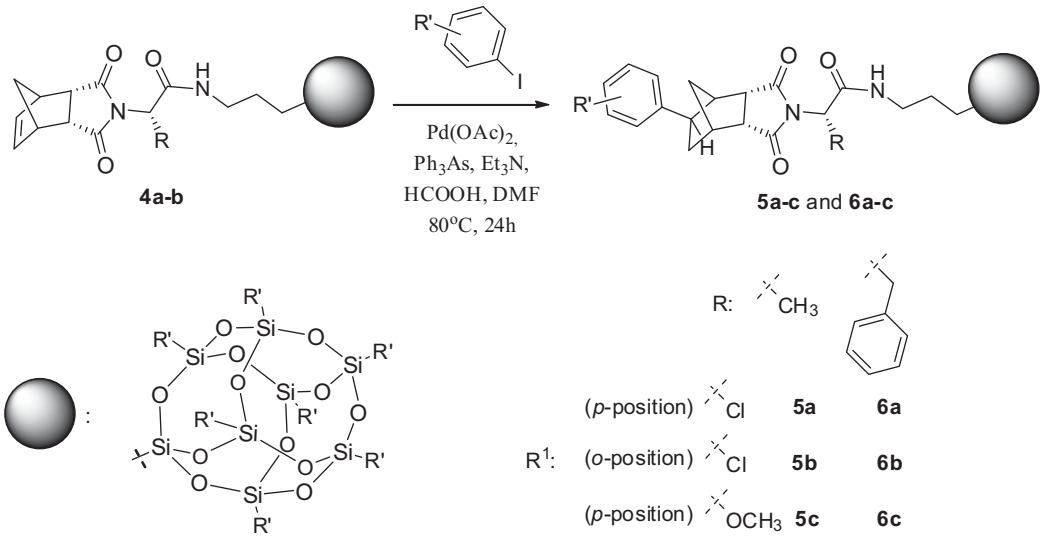
Treatment of compounds **2a-b** with oxalyl chloride in dry dichloromethane gave the 2-(4-azabicyclo[2.2.1]hept-8-ene-3-*endo*,5-*endo*-dicarboximide-4-yl) propionyl chloride (**3a**) and 2-(4-Azabicyclo[2.2.1]hept-8-ene-3-*endo*,5-*endo*-dicarboximide-4-yl)-3-phenyl propionyl chloride (**3b**) in 95and 94% yields, respectively [42] (Scheme 1). The reactions were performed at room temperature in dry CH_2Cl_2.

Treatment of the aminopropyl isobutyl POSS with the acyl chloride derivatives (**3a-b**) in dry dichloromethane at room temperature under nitrogen atmosphere afforded the condensation amide products (**4a-b**) in 80 and 79 yields, respectively (Scheme 2).[42]

In order to optimize the reductive Heck reaction conditions, the reaction of *N*-[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-Azabicyclo[2.2.1]hept-8-ene-3-*endo*, 5-*endo*-dicarboximide-4-yl) propanamide **4a** with p-1-chloro-4-iodobenzene was selected as a model system. Based on our previous studies,[43–48] the reaction was run on a 1 mmol scale using 2.5 mol% of $Pd(OAc)_2$, 0.11 mmol As_3P as a



Scheme 2. Synthesis of compounds **4a–b**.



Scheme 3. Synthesis of compounds **5a–c** and **6a–c**.

ligand, 3.5 equiv. of base and 3 mmol formic acid in 3 mL DMF under an anhydrous and inert atmosphere for 24 h, which yielded the product **5a** in a 65% reaction yield (Scheme 3). The same reaction was also run on a 1 mmol scale, 0.11 mmol Ph_3P as a ligand, and DMSO as solvent under an anhydrous and inert atmosphere for 24 h, which yielded the product **5a** in a 35% reaction yield.

As a result, 2.5 mol% of $Pd(OAc)_2$ in the presence of the Et_3N as the base, As_3P as a ligand, and formic acid in DMF at 80°C for 24 h were found to be the best reaction conditions to give **5a**.

With the optimized conditions in hand, reactions of **4a** with 1-chloro-4-iodobenzene, 1-chloro-2-iodobenzene and 4-iodoanisole under reductive Heck conditions gave the pure products **5a–c**, after chromatographic separation on silica gel as single diastereomers in in 65, 50 and 55% yields, respectively (Scheme 3).

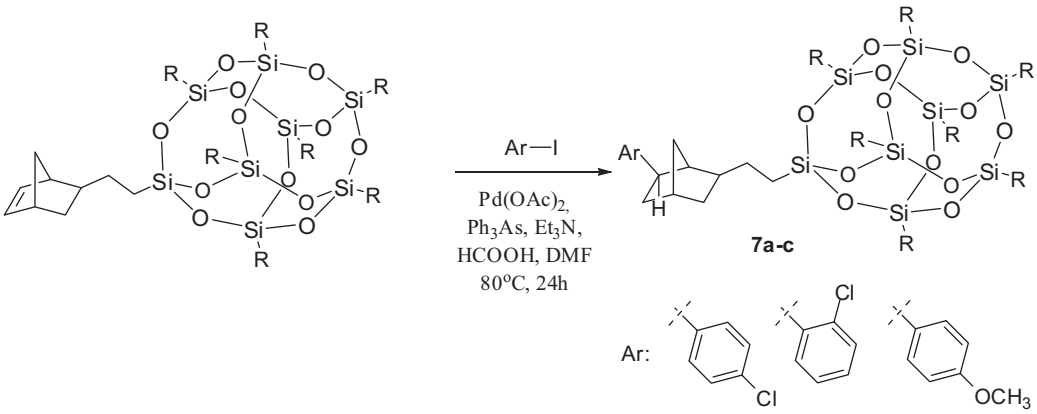
The same Heck arylation conditions were successfully applied to the reactions of *N*-[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-azabicyclo[2.2.1]hept-8-ene-3-*endo*,5-*endo*-dicarboximide-4-yl)-3-phenyl propanamide **(4b)** with 1-chloro-4-iodobenzene, 1-chloro-2-iodobenzene and 4-iodoanisole to obtain the new *exo*-arylated POSS derivatives **6a–c** in good yields after chromatographic separation (Scheme 3).

The spectroscopic data of POSS derivatives **5a–c** and **6a–c** are given in detail in the Experimental part. All newly synthesized POSS derivatives confirmed on the basis of their spectroscopic data. For compounds **5a–c** and **6a–c** the LC-MSMS/Qtof spectra displayed the correct molecular ion peaks (M^+.) in accordance with the proposed structures.

IR spectra of the hydroarylation derivatives showed strong absorption bands due to the stretching vibrations of the POSS cage group Si–O–Si bonds in the expected areas. Structured nanomaterials are usually associated with unique mechanical and biological properties although the newly synthesized six compounds showed similar FTIR absorption bands corresponding to the same POSS nano-cage groups.

The reductive Heck reactions were found to be completely stereoselective, giving only the *exo* arylation products in moderate to good yields.

The stereochemistry of the products was investigated from their ^{1}H-NMR spectra including diagnostic spin–spin interactions. The *exo*-position of the C-5 substituent was confirmed by the fact that *endo*-H_5 proton showed no significant interaction with H_7 proton but did show a cross-



Scheme 4. Synthesis of compounds **7a–c.**

Table 1. Characterization data of newly prepared compounds.

Entry	Substituent	Appearance	Yield %	m. p. °C
5a	4-chlorophenyl	White solid	65	122–124
5b	2-chlorophenyl	White solid	50	108–110
5c	4-methoxyphenyl	Colorless oil	55	–
6a	4-chlorophenyl	White solid	45	131–133.5
6b	2-chlorophenyl	Colorless oil	52	–
6c	4-methoxyphenyl	Colorless oil	48	–
7a	4-chlorophenyl	White solid	55	90–92
7b	2-chlorophenyl	Colorless oil	50	–
7c	4-methoxyphenyl	Colorless oil	60	–

peak because of W-coupling to H_8-syn. The geminal protons on C_8 were identified by vicinal coupling to H_7 and W-coupling to H_{3a}-*exo*, respectively. And also, the ^{13}C-NMR and HRMS spectral data were confirmed the suggested structures and the HRMS spectra of all new products showed the expected molecular ion peaks.

And also shown in Scheme 5, for 1-chloro-4-iodobenzene, 1-chloro-2-iodobenzene and 4-iodoanisole the reductive Heck-hydrogenation process afforded **7a**, **7b** and **7c**, via Norbornenylethyl isobutyl POSS, in 55, 50 and 60% yields, respectively (Scheme 4).

In the ^{1}H-NMR spectra, the compound **7a** gave a doublet at 7.51 ppm and a doublet at 7.56 ppm due to its four aromatic protons. Similarly, the compound **7c** gave doublet at 7.53 ppm and at 7.58 ppm due to its four aromatic protons at the p-substituted aromatic ring. The compound **7b** gave multiplet at 7.52 due to its four aromatic protons at the o-substituted aromatic ring.

And also the characteristic data of products **7a-c** are given in detail in the Experimental part.

7a, **7b** and **7c** have been characterized by FTIR, ^{1}H, ^{13}C NMR and TOF/Qtof analyses. Their ^{1}H NMR spectra exhibited all the signals of the suggested structures.

Characterization data of newly prepared compounds are summarized in Table 1.

Experimental

General

All Heck reactions were carried out in flame-dried Schlenk tubes and run under an atmosphere of dry nitrogen. The solvents were dried by known techniques. Aminopropyl isobutyl POSS and Norbornenylethyl isobutyl POSS were purchased from Hybrid Plastic, L-alanine and L-phenyl alanine were purchased from Alfa Aesar. Aryl halides and other reagents were commercially available and used without further purification. Thin-layer chromatography (TLC) on silica gel GF 254 was used to control reaction progress. Gallenkamp digital thermometer was used to determine melting points of all solid compounds. IR spectra were recorded on a Perkin Elmer FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were obtained with a Bruker Avance III-500 MHz NMR system. Chemical shifts were reported in parts per million (ppm) with respect to internal standard TMS. Mass spectral studies were performed on an Agilent 6890N/5973 GC/IMSD system and high-resolution mass spectra were recorded on an Agilent G6530B TOF/Qtof Mass spectrometer. All crude products were purified with Teledyne Isco CombiFlash Rf 200 system and RediSep Rf Gold Silica columns. The Supplementary Materials contains sample ^{1}H and ^{13}C NMR spectra and HRMS scans from products **5**, **6** and **7**. (Figures S1–S36).

General procedure for the synthesis of norbornyl imide acyl chloride derivatives (3a–b)

A solution of oxalyl chloride (254 mg, 2.00 mmol) in dry dichloromethane (5 mL) was added dropwise L-amino acid derivatives (**2a–c**) (1.00 mmol) in dry dichloromethane (5 mL) at room temperature under nitrogen atmosphere. The reaction mixture was stirred at room temperature. After the TLC control, the reaction mixture was concentrated and the the leftover residue was washed with diethyl ether. Acyl chloride derivatives (**3a–b**) were obtained in almost quantitative yields.[42]

General procedure for the synthesis of POSS-based amide derivatives (4a–b)

A solution of norbonyl imide acyl chloride derivatives (**3a–b**) (1.00 mmol) in dry dichloromethane (5 mL) was added to solution of aminopropyl isobutyl POSS (874.58 mg, 1.00 mmol) in dry dichloromethane (5 mL) at room temperature under nitrogen atmosphere. The reaction mixture was stirred for 10–24h (depending on TLC monitor) at

room temperature. The reaction mixture was concentrated under reduced pressure, the crude product was subsequently purified through combiflash chromatography to yield the desired products.[42]

General procedure for heck reaction of POSS derivatives (5a–c, 6a–c and 7a–c)

A solution of $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) and Ph_3As (33.7 mg, 0.11 mmol) in dry DMF (5 mL) was stirred in a flame-dried Schlenk tube under nitrogen atmosphere at 80 °C for 15 min to form the catalyst complex. Then, aryl iodide (1.5 mmol), alkene (**4a**, **4b** or, Norbornenylethyl isobutyl POSS respectively; 1 mmol), Et_3N (354 mg, 3.5 mmol), and formic acid (138 mg, 3 mmol) were added. The reaction mixture was stirred at 80 °C for 24 h. The progress of the reaction was monitored using TLC. After completion of the reaction, brine (50 mL) was added, and the mixture was extracted with ethyl acetate, dried over Na_2SO_4 and concentrated. The crude product purified by column chromatography.

N-[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-Azabicyclo[2.2.1]hept-8-(4-chlorophenyl)-3-endo,5-endo-dicarboximide-4-yl) propanamide (5a)

White solid. mp 122–124 °C; Yield 65%. IR ν cm^{-1} 3340 (amide NH), 2953 and 2870 (Aliphatic C–H), 1704 (C = O), 1537 (Si–O–Si), 1463, 1381 and 1085 (Si–O–R), 740. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.61 (14H, dd, *J* = 3.40; 7.25, 7xCH_2-Si); 0.82-0.86 (2H, m, CH_2); 0.96 (42H, d, *J* = 6.62, 14xCH_3); 0.99 (3H, d, *J* = 6.62, CH_3); 1.25–1.30 (4H, m, H_{10a}, H_{10s}, CH_2); 1.58 (1H, m, CH); 1.62 (2H, t, *J* = 7.25, CH_2); 1.81–1.90 (7 H, m, 7xCH); 2.96 (1H, t, *J* = 6.00, H_1); 3.17–3.36 (5H, m, *N*-CH_2, H_{9n}, H_{8n}, H_7); 4.76 (1H, q, *J* = 7.25; 14.50, CH); 5.73 (1H, dt, *J* = 5.65; 25.37, NH); 7.52 (2H, d, *J* = 2.50, ArH); 7.54 (2H, d, *J* = 1.91, ArH). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 9.4 (CH_2); 14.4 (CH_3); 14.7 (CH); 22.4 (CH_2); 22.5 (7xCH_2); 22.8 (CH_2); 23.8 (7xCH_3); 23.9 (7xCH_3); 25.6 (7xCH); 36.4 (CH_2); 42.0 (CH); 42.3 (CH_2); 43.9 (CH); 44.4 (CH); 45.7 (CH); 46.4 (CH); 124.3 (Cq); 128.3 (CAr); 128.4 (CAr); 132.0 (2xCAr); 155.6 (Cq); 167.7 (C = O); 175.6 (C = O); 176.3 (C = O). HRMS: - Found, m/z: 1205.3805 $[M^+ + H]$. $C_{49}H_{87}ClN_2O_{15}Si_8$ Calculated, m/z: 1204.3920 $[M]^+$.

N-[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-Azabicyclo[2.2.1]hept-8-(2-chlorophenyl)-3-endo,5-endo-dicarboximide-4-yl) propanamide (5b)

White solid. mp 108–110 °C; Yield 50%. IR ν cm^{-1} 2953, 2930, 2906 and 2870 (Aliphatic C–H), 1690 (C = O), 1524 (Si–O–Si), 1463, 1398, 1382, 1083 (Si–O–R), 808. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.62 (14H, dd, *J* = 3.46; 7.25, 7xCH_2-Si); 0.83–0.88 (2H, m, CH_2); 0.97 (42H, d, *J* = 6.61, 14xCH_3); 1.00 (3H, d, *J* = 6.61, CH_3); 1.26–1.33 (4H, m, H_{10a}, H_{10s}, CH_2); 1.59 (1H, m, CH); 1.63 (2H, t, *J* = 7.50, CH_2); 1.82-1.90 (7H, m, 7xCH); 2.97 (1H, t, *J* = 5.90, H_1); 3.18-3.36 (5H, m, *N*-CH_2, H_{9n}, H_{8n}, H_7); 4.77 (1H, q, *J* = 7.3; 14.0, CH); 5.75 (1H, dt, *J* = 5.67; 28.37, NH); 7.57 (4H, m, ArH). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 9.3 (CH_2); 14.4 (CH_3); 14.6 (CH); 22.4 (CH_2); 22.5 (7xCH_2); 22.8 (CH_2); 23.8 (7xCH_3); 23.9 (7xCH_3); 25.6 (7xCH); 36.4 (CH_2); 41.9 (CH); 42.3 (CH_2); 43.9 (CH); 45.7 (CH); 46.9 (CH); 49.2 (CH); 127.4 (Cq); 128.3 (CAr); 128.4 (CAr); 131.0 (Car); 132.1 (CAr); 155.9 (Cq); 167.8 (C = O); 175.8 (C = O); 176.2 (C = O). HRMS: - Found, m/z: 1205.3800 $[M^+ + H]$. $C_{49}H_{87}ClN_2O_{15}Si_8$ Calculated, m/z: 1204.3920 $[M]^+$.

N-[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-Azabicyclo[2.2.1]hept-8-(4-methoxyphenyl)-3-endo,5-endo-dicarboximide-4-yl) propanamide (5c)

Colorless oil; Yield 55%. IR ν cm^{-1} 3301 (NH) 2952, 2926, 2906 and 2869 (Aliphatic C–H), 1699 (C = O), 1551 (Si–O–Si), 1498, 1383, 1084 (Si–O–R), 740. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.63 (14H, dd, *J* = 3.4; 7.3, 7xCH_2-Si); 0.83–0.90 (2H, m, CH_2); 0.97 (42H, d, *J* = 6.62, 14xCH_3); 1.02 (3H, d, *J* = 6.62, CH_3); 1.28-1.32 (2H, m, H_{10a}, H_{10s},); 1.56 (1H, d, *J* = 10.4, CH); 1.65 (4H, m, 2xCH_2); 1.82-1.92 (7 H, m, 7xCH); 2.97 (1 H, m, H_1); 3.17-3.40 (5H, m, *N*-CH_2, H_{9n}, H_{8n}, H_7); 3.78 (3H, s, OCH_3); 4.75 (1H, q, *J* = 7.2; 14.5, CH); 5.76 (1H, dt, *J* = 5.7; 25.0, NH); 7.52 (4H, dd, *J* = 2.4; 5.4, ArH). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 9.3 (CH_2); 14.4 (CH_3); 14.6 (CH); 22.5 (7xCH_2); 22.8 (CH_2); 23.8 (7xCH_3); 23.9 (7xCH_3); 25.7 (7xCH); 36.4 (2xCH_2); 41.9 (CH); 42.3 (CH_2); 43.9 (CH); 45.7 (CH); 46.9 (CH); 49.2 (CH); 54.9 (OCH_3); 124.3 (Cq); 128.3 (CAr); 128.4 (CAr); 132.0 (2xCAr); 155.9 (Cq); 167.7 (C = O); 175.6 (C = O); 175.8 (C = O). HRMS: - Found, m/z: 1200.4508 $[M^+ + H]$. $C_{50}H_{90}N_2O_{16}Si_8$ Calculated, m/z: 1199.4478 $[M]^+$.

N-[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-Azabicyclo[2.2.1]hept-8-(4-chlorophenyl)-3-endo,5-endo-dicarboximide-4-yl)-3-phenyl propanamide (6a)

White solid; mp 131–133.5 °C; Yield: 45%. IR ν cm^{-1} 3307 (N–H), 2953 and 2869 (Aliphatic C–H), 1705 (C = O), 1541 (Si–O–Si), 1463, 1399, 1228, 1086 (Si–O–R), 836, 740. ^{1}H NMR (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 0.56–0.58 (2H, m, CH_2); 0.61 (14H, t, *J* = 6.93, 7xCH_2-Si); 0.82–0.90 (2H, m, CH_2); 0.95 (42H, dd, *J* = 3.2; 6.6, 14xCH_3); 1.43 (2H, m, CH_2); 1.57–1.65 (3H, m, H_{10a}, H_{10s}, CH); 1.86 (7H, pent, *J* = 6.6, 7xCH); 2.73 (1H, dd, *J* = 4.7; 19.9, H_1); 3.02–3.11 (3H, m, CH_2, H_7); 3.21–3.31 (2H, m, *N*-CH_2); 3.37–3.42 (1H, m, CH); 3.54 (1H, dd, *J* = 12.0; 14.2, H_{8n}), 4.05 (1H, m, CH); 5.94 (1H, m, NH), 6.92 (1H, t, *J* = 7.3, ArH); 7.15 (3H, dd, *J* = 7.9; 15.4, ArH); 7.26 (1 H, d, *J* = 6.0, ArH); 7.36 (1H, d, *J* = 8.51, ArH); 7.43 (1H, d, *J* = 8.51, ArH); 7.52 (2H, dd, *J* = 5.04; 8.27, ArH). ^{13}C NMR (125 MHz, $CDCl_3$), δ, ppm: 9.4 (CH_2); 22.5 (7xCH_2); 22.8 (2xCH_2); 23.9 (7xCH); 23.9

(7xCH$_3$); 25.7 (7xCH$_3$); 34.2 (CH$_2$); 36.0 (CH$_2$); 41.6 (CH); 42.4 (CH$_2$); 43.8 (CH); 45.2 (CH); 46.4 (CH); 51.5 (CH); 55.4 (CH); 124.4 (Cq); 127.8 (CAr); 128.2 (CAr); 128.3 (CAr); 128.7 (CAr); 128.9 (CAr); 129.0 (2xCAr); 132.0 (CAr); 132.1 (CAr); 135.9 (Cq); 155.6 (Cq); 176.0 (C=O); 176.3 (C=O). 176.6 (C=O). HRMS: - Found, m/z: 1281.4223 [M$^+$+H]. $C_{55}H_{91}ClN_2O_{15}Si_8$ Calculated, m/z: 1280.4233 [M]$^+$.

N-*[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-Azabicyclo[2.2.1]hept-8-(2-chlorophenyl)-3-endo,5-endo-dicarboximide-4-yl)-3-phenyl propanamide (6b)*

Colorless oil; Yield: 52%. IR ν cm^{-1} 2953 (Aliphatic C–H), 1702 (C=O), 1541 (Si–O–Si), 1463, 1399, 1382, 1089 (Si–O–R), 836, 740. ^{1}H NMR (500 MHz, CDCl$_3$), δ, ppm (*J*, Hz): 0.57–0.59 (2H, m, CH$_2$); 0.62 (14H, t, *J* = 6.8, 7xCH$_2$-Si); 0.83–0.91 (2H, m, CH$_2$); 0.96 (42H, dd, *J* = 3.1; 6.5, 14xCH$_3$); 1.44 (2H, m, CH$_2$); 1.58–1.65 (3H, m, H$_{10a}$, H$_{10s}$, CH); 1.87 (7H, pent, *J* = 6.5, 7xCH); 2.74 (1H, dd, *J* = 4.7; 19.9, H$_1$); 3.03-3.09 (3H, m, CH$_2$, H$_7$); 3.22–3.33 (2H, m, *N*-CH$_2$); 3.39-3.43 (1H, m, H$_{9n}$); 3.55 (1H, m, H$_{8n}$), 4.12 (1H, m, CH); 5.96 (1H, m, NH), 7.11 (1H, t, *J* = 7.3, ArH); 7.17 (3H, dd, *J* = 7.9; 15.5, ArH); 7.28 (1H, d, *J* = 6.0, ArH); 7.44 (2H, m, ArH); 7.52 (2H, m, ArH). ^{13}C NMR (125 MHz, CDCl$_3$), δ, ppm: 9.4 (CH$_2$); 22.3 (7xCH$_2$); 22.9 (2xCH$_2$); 23.7 (7xCH); 23.9 (7xCH$_3$); 25.8 (7xCH$_3$); 34.0 (CH$_2$); 36.0 (CH$_2$); 41.5 (CH); 42.4 (CH$_2$); 44.2 (CH); 45.2 (CH); 46.7 (CH); 51.9 (CH); 55.9 (CH); 127.1 (Cq); 127.8 (CAr); 128.2 (CAr); 128.3 (CAr); 128.8 (CAr); 128.9 (CAr); 129.0 (2xCAr); 132.0 (CAr); 132.1 (CAr); 135.9 (Cq); 155.4 (Cq); 176.0 (C=O); 176.3 (C=O). 176.7 (C=O). HRMS: - Found, m/z: 1281.4253 [M$^+$+H]. $C_{55}H_{91}ClN_2O_{15}Si_8$ Calculated, m/z: 1280.4233 [M]$^+$.

N-*[3-(isobutylpolyhedral oligomeric silsesquioxanyl)propyl]-2-(4-Azabicyclo[2.2.1]hept-8-(4-methoxyphenyl)-3-endo,5-endo-dicarboximide-4-yl)-3-phenyl propanamide (6c)*

Colorless oil; Yield: 48%. IR ν cm^{-1} 3057 (Aroomatic C–H), 2952, 2908 and 2867 (Aliphatic C–H), 1707 (C=O), 1598 (Si–O–Si), 1464, 1450, 1382, 1077 (Si–O–R), 778, 739. ^{1}H NMR (500 MHz, CDCl$_3$), δ, ppm (*J*, Hz): 0.55–0.59 (2H, m, CH$_2$); 0.62 (14H, t, *J* = 7.0, 7xCH$_2$-Si); 0.82–0.90 (2H, m, CH$_2$); 0.99 (42H, dd, *J* = 3.15; 6.62, 14xCH$_3$); 1.43 (2H, m, CH$_2$); 1.63–1.67 (3H, m, H$_{10a}$, H$_{10s}$, CH); 1.88 (7H, pent, *J* = 6.5, 7xCH); 2.80 (1H, dd, *J* = 4.6; 19.7, H$_1$); 3.02–3.10 (3H, m, CH$_2$, H$_7$); 3.23–3.31 (2H, m, *N*-CH$_2$); 3.42–3.44 (1H, m, H$_{9n}$); 3.58 3.80 (3H, s, OCH$_3$); (1H, m, CH), 4.08 (1H, m, CH), 5.95 (1H, m, NH), 6.94 (1H, t, *J* = 7.25, ArH); 7.15 (3 H, m, ArH); 7.28 (1H, d, *J* = 6.0, ArH); 7.39 (3H, m, ArH); 7.54 (2H, m, ArH). ^{13}C NMR (125 MHz, CDCl$_3$), δ, ppm: 9.5 (CH$_2$); 22.5 (7xCH$_2$); 23.0 (2xCH$_2$); 23.9 (7xCH); 24.0 (7xCH$_3$); 26.0 (7xCH$_3$); 34.3 (CH$_2$); 36.2 (CH$_2$); 41.6 (CH); 42.5 (CH$_2$); 44.0 (CH); 45.3 (CH); 46.6 (CH); 51.6 (CH); 52.1 (CH); 55.9 (CH$_3$); 127.4 (Cq); 128.0 (CAr); 128.4 (CAr); 128.5 (CAr); 128.8 (CAr); 129.0 (CAr); 129.2 (2xCAr); 132.1 (CAr); 132.2 (CAr); 136.0 (Cq); 155.7 (Cq); 176.1 (C=O); 176.4 (C=O). 176.8 (C=O). HRMS: - Found, m/z: 1276.4751 [M$^+$+H]. $C_{56}H_{94}N_2O_{16}Si_8$ Calculated, m/z: 1275.4753 [M]$^+$.

2 -(2-isobutyl POSS-ethyl)-5-(4-chlorophenyl) bicyclo[2.2.1]heptane (7a)

White solid. m.p.: 90–92 °C. Yield: 55%. IR: ν cm^{-1} 2953, 2926, 2869 (Aliphatic CH), 1590 (Si–O–Si), 1464, 1382, 1365, 1087 (Si–O–R). ^{1}H NMR (500 MHz, CDCl$_3$), δ, ppm (*J*, Hz): 0.59 (16H, dt, *J* = *1.9; 6.9*, CH$_2$-Si); 0.81-0.87 (2H, m, CH$_2$); 0.95 (42 H, dt, *J* = *2.1*; *6.6*, CH$_3$); 1.24 (1H, m, CH); 1.38-1.57 (6H, m, CH$_2$); 1.83 (7H, hept, *J* = *4.09*, CH); 2.42 (1H, brs, CH); 2.63 (1H, brs CH); 3.38 (1H, m, CH); 7.51 (2H, d, *J* = *8.82*, HAr); 7.56 (2H, d, *J* = *8.82*, HAr). ^{13}C NMR (125 MHz, CDCl$_3$), δ, ppm: 11.1 (CH$_2$); 22.5 (7xCH$_2$); 23.9 (7xCH$_3$); 24.0 (7xCH$_3$); 25.4 (CH$_2$); 25.7 (7xCH); 33.7 (2xCH$_2$); 34.7 (CH$_2$); 39.3 (CH); 40.3 (CH); 45.9 (CH); 57.1 (CH); 123.9 (Cq); 128.2 (2xCar); 131.9 (2xCar); 156.2 (Cq). HRMS: - Found, m/z: 1051.3581 [M$^+$+H]. $C_{43}H_{81}ClO_{12}Si_8$. Calculated, m/z: 1050.3541 [M$^+$].

2 -(2-isobutyl POSS-ethyl)-5-(2-chlorophenyl) bicyclo[2.2.1]heptane (7b)

Colorless oil. Yield: 50%. IR: ν cm^{-1} 3058 (Aromatic C–H), 2952, 2909, 2887 (Aliphatic CH), 1580 (Si–O–Si), 1464, 1382, 1365, 1076 and 1047 (Si–O–R). ^{1}H NMR (500 MHz, CDCl$_3$), δ, ppm (*J*, Hz): 0.62 (16H, dt, *J* = *2.2; 6.8*, CH$_2$-Si); 0.80 (2H, m, CH$_2$); 0.97 (42H, dt, *J* = *2.2; 6.7*, CH$_3$); 1.23 (1H, d, *J* = *10.4*, CH$_2$); 1.41–1.46 (6H, m, CH$_2$); 1.87 (7 H, hept, *J* = *6.8*, CH); 2.43 (1H, brs, CH); 2.64 (1H, brs CH); 3.41 (1H, m, CH); 7.52 (4H, m, HAr). ^{13}C NMR (125 MHz, CDCl$_3$), δ, ppm: ^{13}C NMR (125 MHz, CDCl$_3$), δ, ppm: 11.1 (CH$_2$); 22.5 (7xCH$_2$); 23.8 (7xCH$_3$); 23.9 (7xCH$_3$); 25.4 (CH$_2$); 25.7 (7xCH); 33.7 (2xCH$_2$); 34.7 (CH$_2$); 39.2 (CH); 40.2 (CH); 45.9 (CH); 57.0 (CH); 128.2 (Car); 128.4 (Cq); 130.2 (Car); 131.9 (Car); 133.3 (Car); 148.1 (Cq).HRMS: - Found, m/z: 1051.3550 [M$^+$+H]. $C_{44}H_{81}ClO_{12}Si_8$. Calculated, m/z: 1050.3541 [M$^+$].

2 -(2-isobutyl POSS-ethyl)-5-(4-methoxyphenyl) bicyclo[2.2.1]heptane (7c)

Colorless oil. Yield: 60%. IR: ν cm^{-1} 3057 (Aromatic C–H), 2952, 2908, 2867 (Aliphatic CH), 1579 (Si–O–Si), 1464, 1382, 1365, 1087 (Si–O–R). ^{1}H NMR (500 MHz, CDCl$_3$), δ, ppm (*J*, Hz): 0.61 (16H, dt, *J* = *2.20; 6.93*, CH$_2$-Si); 0.85 (2H, m, CH$_2$); 0.97 (42H, dt, *J* = *2.20*; 6.5, CH$_3$); 1.26 (1H, d, *J* = *10.5*, CH$_2$); 1.37-1.45 (6H, m, CH$_2$); 1.84 (7H, hept, *J* = *6.5*, CH); 2.44 (1H, brs, CH); 2.65 (1H, brs CH); 3.40 (1 H, m, CH); 3.85 (3H, s, OCH$_3$); 7.53 (2H, d, *J* = *7.8*, HAr); 7.58 (2H, d, *J* = *7.8*, HAr). ^{13}C NMR (125 MHz, CDCl$_3$), δ, ppm: 11.1 (CH$_2$); 22.5 (7xCH$_2$); 23.8 (7xCH$_3$); 23.9 (7xCH$_3$); 25.4 (CH$_2$); 25.8 (7xCH); 33.7 (2xCH$_2$); 34.7 (CH$_2$); 39.3 (CH); 40.3 (CH); 45.9 (CH); 57.1 (CH); 128.3

(2xCar); 128.4 (Cq); 131.9 (2xCar); 156.2 (Cq). HRMS: -Found, m/z: 1046.3955 [M^++H]. $C_{44}H_{84}O_{13}Si_8$. Calculated, m/z: 1045.4100 [M^+].

Conclusions

The novel area of nano-medicine will continue to revolutionize current medical application. The matchless properties of POSS and its ability to be incorporated into a wide range of biocompatible polymers make POSS nanostructure an attractive material for a versatile array of applications in medical practice.

In conclusion, efficient synthetic strategy for the preparation of new 9 POSS norbornenyl derivatives has been reported. The palladium catalyzed hydroarylation of the easily accessible novel POSS-based derivatives (**5a–c**, **6a–c** and **7a–c**) has been proven to be a stereo-selective and moderate-yield method for the preparation of aryl and heteroaryl POSS derivatives.

Newly designed POSS nanoscales have been synthesized via reductive Heck reactions with three different aryl iodides. Different aryl iodides were selected to change POSS nano-cages behaviors in different polymer matrix. Monofunctional POSS compounds can be prepared by addition of a chloro- or alkoxysilane to a corner-truncated cube species R_7–Si_7O_9. With this information, 1-chloro-2-iodobenzene and 1-chloro-4-iodobenzene were selected as coupling reagents. In future application, their behavior in polymer matrix will be investigated.

The flexible arm of POSS cages was changed with this method and they are expected to exhibit both the advantages of organic and inorganic materials.

These newly synthesized POSS-based derivatives should have the potential to show several biological activities due to their chemical structures. The structures of the novel derivatives were characterized by their spectroscopic data such as FTIR, ^{1}H NMR, ^{13}C NMR and LC-MSMS/QTOF analyses.

Acknowledgements

The author expresses his grateful thanks to Prof.Dr. Nuket OCAL and thanks to Yildiz Technical University Scientific Research Projects Coordination Department for financial support of this work (2015-01-02-GEP03).

ORCID

Omer Tahir Gunkara http://orcid.org/0000-0003-3528-5045

References

[1] Hartmann-Thompson, C. *Applications of Polyhedral Oligomeric Silsesquioxanes*; Springer: Dordrecht, The Netherlands, **2011**, p. 420.

[2] Polyhedral oligomeric silsesquioxanes: From early and strategic development through to materials application. In Hartmann-Thompson C.; Markovic, E.; Constantopolous, K.; Matisons, J. G. (eds) *Applications of Polyhedral Oligomeric Silsesquioxanes. Advances in Silicon Science*, **2011**; Springer, Dordrecht, Vol. *3*, pp. 1–46.

[3] Donnio, B.; Guillon, D.; Harada, A.; Hashidzume, A.; Jaeger, W.; Janowski, B.; Kudaibergenov, S.; Laschewsky, A.; Njuguna, J.; Pielichowski, J. *Supramolecular Polymers Polymeric Betains Oligomers. Springer: Berlin, Germany*, **2006**; vol. *201*, pp. 225–296.

[4] Hui, Z.; Qun, Y.; Jianwei, X. Polyhedral Oligomeric Silsesquioxane-based Hybrid Materials and Their Applications. *Mater. Chem. Front.* **2017**, *1*, 212–230. DOI: 10.1039/c6qm00062b.

[5] Scott, D. W. Thermal Rearrangement of Branched-Chain Methylpolysiloxanes. *J. Am. Chem. Soc.* **1946**, *68*, 356–358. DOI: 10.1021/ja01207a003.

[6] Jianjun, D.; Joseph, T. P.; John, R. H.; Catherine, E, F.-C.; Brent, D. V.; R. E. Polyhedral Oligomeric Silsesquioxanes, A. A New Class of Amphiphiles at the Air/Water Interface. *J. Am. Chem. Soc.* **2002**, *124*, 15194–15195. DOI: 10.1021/ja027860v.

[7] Cordes, D. B.; Paul, D.; Lickiss, P. D.; Rataboul, F. Recent Developments in the Chemistry of Cubic Polyhedral Oligosilsesquioxanes. *Chem. Rev.* **2010**, *110*, 2081–2173. DOI: 10.1021/cr900201r.

[8] Ghanbari, H.; Cousins, B. G.; Seifalian, A. M. A Nanocage for Nanomedicine: Polyhedral Oligomeric Silsesquioxane (POSS). *Macromol. Rapid Commun.* **2011**, *32*, 1032–1046. DOI: 10.1002/marc.201100126.

[9] John, Ł.; Malik, M.; Janeta, M.; Szafert, S. First Step towards a Model System of the Drug Delivery Network Based on amide-POSS Nanocarriers. *RSC Adv.* **2017**, *7*, 8394–8401. DOI: 10.1039/C6RA26330E.

[10] John, L.; Janeta, M.; Szafert, S. Synthesis of Cubic Spherosilicates for Self-assembled Organic-inorganic Biohybrids Based on Functionalized Methacrylates. *New J. Chem.* **2018**, *42*, 39–47. DOI: 10.1039/C7NJ02533E.

[11] Janeta, M.; John, L.; Ejfler, J.; Lis, T.; Szafert, S. Multifunctional imine-POSS as Uncommon 3D Nanobuilding Blocks for Supramolecular Hybrid Materials: Synthesis, structural Characterization, and Properties. *Dalton Trans.* **2016**, *45*, 12312–12321. DOI: 10.1039/C6DT02134D.

[12] Janeta, M.; John, L.; Ejfler, J.; Szafert, S. High-yield Synthesis of Amido-functionalized Polyoctahedral Oligomeric Silsesquioxanes by Using Acyl Chlorides. *Chem. Eur. J.* **2014**, *20*, 15966–15974. DOI: 10.1002/chem.201404153.

[13] John, Ł. Selected Developments and Medical Applications of Organic–Inorganic Hybrid Biomaterials Based on Functionalized Spherosilicates. *Mater. Sci. Eng. C* **2018**, *88*, 172–181. DOI: 10.1016/j.msec.2018.02.007.

[14] Kannan, R. Y.; Salacinski, H. J.; Butler, P. E.; Seifalian, A. M. Polyhedral Oligomeric Silsesquioxane Nanocomposites: The Next Generation Material for Biomedical Applications. *Acc. Chem. Res.* **2005**, *38*, 879–884. DOI: 10.1021/ar050055b.

[15] Kuo, S.-W.; Chang, F.-C. POSS Related Polymer Nanocomposites. *Prog. Polym. Sci.* **2011**, *36*, 1649–1696. DOI: 10.1016/j.progpolymsci.2011.05.002.

[16] Liu, Y. R.; Huang, Y. D.; Liu, L. Thermal Stability of POSS/methylsilicone Nanocomposites. *Compos. Sci. Technol.* **2007**, *67*, 2864–2876. DOI: 10.1016/j.compscitech.2007.01.023.

[17] Lewicki, J. P.; Patel, M.; Morrell, P.; Liggat, J.; Murphy, J.; Pethrick, R. The Stability of Polysiloxanes Incorporating Nanoscale Physical Property Modifiers. *Sci. Technol. Adv. Mater.* **2008**, *9*, 024403. DOI: 10.1088/1468-6996/9/2/024403.

[18] Zhang, H. X.; Lee, H. Y.; Shin, Y. J.; Lee, D. H.; Noh, S. K. Effect of 3rd Monomer Addition on Styrene/styryl-polyhedral Oligomeric Silsesquioxane (POSS) Copolymerization. *Macromol. Res.* **2009**, *17*, 352–355. DOI: 10.1007/BF03218874.

[19] Kwon, Y.; Kim, K. H. Synthesis of Norbornene Block Copolymers Containing Polyhedral Oligomeric Silsesquioxane by Sequential Ring-opening Metathesis Polymerization. *Macromol. Res.* **2006**, *14*, 424–429. DOI: 10.1007/BF03219105.

[20] Feng, Y.; Jia, Y.; Guang, S. Y.; Xu, H. Y. Study on Thermal Enhancement Mechanism of POSS-containing Hybrid Nanocomposites and Relationship between Thermal Properties and Their Molecular Structure. *J. Appl. Polym. Sci.* **2010**, *115*, 2212–2220. DOI: 10.1002/app.31319.

[21] Feng, Y.; Jia, Y.; Xu, H. Y. Preparation and Thermal Properties of Hybrid Nanocomposites of Poly(methyl Methacrylate)/Octavinyl Polyhedral Oligomeric Silsesquioxane Blends. *J. Appl. Polym. Sci.* **2009**, *111*, 2684–2690. DOI: 10.1002/app.29240.

[22] Ma, X.-M.; Wang, B.; Zhang, M.-X.; Min, F.-F.; He, J. Synthesis and Thermal Characterizations of Pmma Nanocomposite Functionalized by Polyhedral Oligomeric Silsesquioxane. *Phosphorus, Sulfur Silicon Relat. Elem.* **2013**, *188*, 1819–1826. DOI: 10.1080/10426507.2013.788001.

[23] Mohamed, G. M.; Hsu, K. C.; Hong, J. L.; Kuo, S.-W. Unexpected Fluorescence from Maleimide-containing Polyhedral Oligomeric Silsesquioxanes: nanoparticle and Sequence Distribution Analyses of Polystyrene-based Alternating Copolymers. *Polym. Chem.* **2016**, *7*, 135–145. DOI: 10.1039/C5PY01537E.

[24] Mohamed, M. G.; Jheng, Y.-R.; Yeh, S.-L.; Chen, T.; Kuo, S.-W. Unusual Emission of Polystyrene-Based Alternating Copolymers Incorporating Aminobutyl Maleimide Fluorophore-Containing Polyhedral Oligomeric Silsesquioxane Nanoparticles. *Polymers* **2017**, *9*, 103. DOI: 10.3390/polym9030103.

[25] Zhang, W.; Muller, A. H. E. Architecture, self-assembly and Properties of Well-defined Hybrid Polymers Based on Polyhedral Oligomeric Silsequioxane (POSS). *Prog. Polym. Sci.* **2013**, *38*, 1121–1162. DOI: 10.1016/j.progpolymsci.2013.03.002.

[26] Zhang, Q.; He, H.; Xi, K.; Huang, X.; Yu, X.; Jia, X. Synthesis of N-Phenylaminomethyl POSS and Its Utilization in Polyurethane. *Macromolecules* **2011**, *44*, 550–557. DOI: 10.1021/ma101825j.

[27] Chen, P.; Huang, X.; Zhang, Q.; Xi, K.; Jia, X. Hybrid Networks Based on Poly (styrene-co-maleic Anhydride) and N-phenylaminomethyl POSS. *Polymer* **2013**, *54*, 1091–1097. DOI: 10.1016/j.polymer.2012.12.047.

[28] Milliman, H. W.; Boris, D.; Schiraldi, D. A. Experimental Determination of Hansen Solubility Parameters for Select POSS and Polymer Compounds as a Guide to POSS–Polymer Interaction Potentials. *Macromolecules* **2012**, *45*, 1931–1936. DOI: 10.1021/ma202685j.

[29] Raftopoulos, K. N.; Koutsoumpis, S.; Jancia, M.; Lewicki, J. P.; Kyriakos, K.; Mason, H. E.; Harley, S. J.; Hebda, E.; Papadakis, C. M.; Pielichowski, K.; Pissis, P. Reduced Phase Separation and Slowing of Dynamics in Polyurethanes with Three-Dimensional POSS-Based Cross-Linking Moieties. *Macromolecules* **2015**, *48*, 1429–1441. DOI: 10.1021/ma5023132.

[30] Jiang, S. D.; Tang, G.; Bai, Z. M.; Wang, Y. Y.; Hu, Y.; Song, L. Surface Functionalization of MoS_2 with POSS for Enhancing Thermal, flame-retardant and Mechanical Properties in PVA Composites. *RSC Adv.* **2014**, *4*, 3253–3262. DOI: 10.1039/C3RA45911J.

[31] Chua, M. L.; Shao, L.; Low, B. T.; Xiao, Y.; Chung, T. S.; Chua, M. L.; Shao, L.; Low, B. T.; Xiao, Y.; Chung, T. S. Polyetheramine–polyhedral Oligomeric Silsesquioxane Organic–inorganic Hybrid Membranes for CO_2/H_2 and CO_2/N_2 Separation. *J. Membr. Sci.* **2011**, *385*, 40–48. DOI: 10.1016/j.memsci.2011.09.008.

[32] Le, N. L.; Wang, Y.; Chung, T. S. Pebax/POSS Mixed Matrix Membranes for Ethanol Recovery from Aqueous Solutions via Pervaporation. *J. Membr. Sci.* **2011**, *379*, 174–183. DOI: 10.1016/j.memsci.2011.05.060.

[33] Mohamed, G. M.; Kuo, S.-W. Functional Silica and Carbon Nanocomposites Based on Polybenzoxazines. *Macromol. Chem. Phys.* **2019**, *220*, 1800306. DOI: 10.1002/macp.201800306.

[34] Porter, B. D.; Oldham, J. B.; He, S. L.; Zobitz, M. E.; Payne, R. G.; An, K. N.; Currier, B. L.; Mikos, A. G.; Yaszemski, M. J. Mechanical Properties of a Biodegradable Bone Regeneration Scaffold. *J. Biomech. Eng.* **2000**, *122*, 286–288. DOI: 10.1115/1.429659.

[35] Wang, Q.; Mynar, J. L.; Yoshida, M.; Lee, E.; Lee, M.; Okuro, K.; Kinbara, K.; Aida, T. High-water-content Mouldable Hydrogels by Mixing Clay and a Dendritic Molecular Binder. *Nature* **2010**, *463*, 339–343. DOI: 10.1038/nature08693.

[36] Haraguchi, K.; Takehisa, T. Nanocomposite Hydrogels: A Unique Organiceinorganic Network Structure with Extraordinary Mechanical, Optical, and Swelling/de-swelling Properties. *Adv. Mater.* **2002**, *14*, 1120–1124. DOI: 10.1002/1521-4095(20020816)14:16<1120::AID-ADMA1120>3.0.CO;2-9.

[37] Blaker, J. J.; Maquet, V.; Jerome, R.; Boccaccini, A. R.; Nazhat, S. N. Mechanical Properties of Highly Porous PDLLA/Bioglass Composite Foams as Scaffolds for Bone Tissue Engineering. *Acta Biomater.* **2005**, *1*, 643–652. DOI: 10.1016/j.actbio.2005.07.003.

[38] Lu, H. H.; El-Amin, S. F.; Scott, K. D.; Laurencin, C. T. Three-dimensional, bioactive, biodegradable, polymerebioactive Glass Composite Scaffolds with Improved Mechanical Properties Support Collagen Synthesis and Mineralization of Human Osteoblast-like Cells in Vitro. *J. Biomed. Mater. Res. A* **2003**, *64A*, 465–474. DOI: 10.1002/jbm.a.10399.

[39] Zhou, X.; Sahai, N.; Qi, L.; Mankoci, S.; Zhao, W. Biomimetic and Nanostructured Hybrid Bioactive Glass. *Biomaterials* **2015**, *50*, 1–9. DOI: 10.1016/j.biomaterials.2015.01.024.

[40] Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Ishihara, Y.; Maruyama, K. Lewis Acid Mediated Reactions of Organocopper Reagents. Entrainment in the Conjugate Addition to α,β-Unsaturated Ketones, esters, and Acids via the $RCu{\cdot}BF_3$ System. *J. Org. Chem.* **1982**, *47*, 119–126. DOI: 10.1021/jo00340a02.

[41] Frady, G. A.; Michael, G. G.; Ashraf, G. Design and Synthesis of Novel Chiral Dirhodium(II) Carboxylate Complexes for Asymmetric Cyclopropanation Reactions. *Chem. Eur. J.* **2016**, *22*, 3447–3461. . DOI: 10.1002/chem.201504817.

[42] Ersoy, E. B.; Gunkara, O. T.; Ocal, N. Synthesis of New Polyhedral Oligomeric Silsesquioxane Derivatives as Some Possible Antimicrobial Agents. *Phosphorus, Sulfur Silicon Relat. Elem.* **2018**, *in press*, DOI: 10.1080/10426507.2018.1539721.

[43] Goksu, G.; Gul, M.; Ocal, N.; Kaufmann, D. E. Hydroarylation of Bicyclic, unsaturated Dicarboximides: Access to Aryl-Substituted, Bridged Perhydroisoindoles. *Tetrahedron Lett.* **2008**, *49*, 2685–2688. DOI: 10.1016/j.tetlet.2008.02.171.

[44] Namyslo, J. C.; Storsberg, J.; Klinge, J.; Gartner, C.; Yao, M. L.; Ocal, N.; Kaufmann, D. E. The Hydroarylation Reaction—Scope and Limitations. *Molecules* **2010**, *15*, 3402–3410. DOI: 10.3390/molecules15053402.

[45] Gunkara, O. T.; Kulu, I.; Ocal, N.; Kaufmann, D. E. Synthesis of Arylated Norbornyl Amino Acid Esters. *Monatsh. Chem.* **2010**, *141*, 1237–1243. DOI: 10.1007/s00706-010-0384-3.

[46] Gunkara, O. T.; Sucu, B. O.; Ocal, N.; Kaufmann, D. E. Synthesis of New Aryl(hetaryl)-Substituted Tandospirone Analogues with Potential Anxiolytic Activity via Reductive Heck Type Hydroarylations. *Chem. Pap* **2013**, *67*, 643–649. DOI: 10.2478/s11696-013-0338-4.

[47] Gul, M.; Kulu, I.; Gunkara, O. T.; Ocal, N. Reductive Heck Reactions and [3 + 2] cycloadditions of Unsaturated N,N'-bistricyclic Imides. *Acta Chim. Slov.* **2013**, *60*, 87–94.

[48] Albayrak, F.; Gunkara, O. T.; Ersoy, E. B.; Ocal, N.; Kaufmann, D. E. Synthesis of New N-norbornylimide Substituted Amide Derivatives, their Reductive Heck and Domino Heck Reactions. *Arkivoc* **2017**, *2017*, (*v*), 244–256. DOI: 10.24820/ark.5550190.p010.304.