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Design, Synthesis and Characterization of Novel Poly-Functionalized Siloxanes

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Abstract :

The synthesis, structural characterization and stability properties of a new family of siloxane-based poly-functionalised molecules are described. Derivatives of 1,3-dichloro-1,1,3,3-tetramethyldisiloxane have been employed as effective silylating reagent for the synthesis of functionalised siloxanes with varied functionalities. Stable bridged urea and thiourea compounds (**5-7**) with the amine tetramethylsiloxy functionality have been synthesized. To understand the properties of these polymers more thoroughly, we also synthesized the well-defined, closely related tetramethylamide functionalized disiloxane (**8-13**) and aliphatic-functionalised disiloxane model compounds **14** and **15**. It was envisaged that the bridged compounds with amide and tetramethylsiloxy functionality could be employed to prepare phenolic compounds with amide functionality. We observed that the urea compounds possessing the tetramethylsiloxy functionality were stable as compared to the amide poly-functional siloxane.

Key words: siloxanes, poly-functionalised siloxanes, isocyanate and thioisocyanate

Introduction

Organosilicon chemistry is a branch of chemistry that specializes in investigating the chemical and physical properties of organic compounds that contain silicon-carbon bonds [1]. This branch of chemistry has generated much interest due to diverse application of its products in industry and as consumer products [2, 3]. Furthermore, these compounds have been found to be good

sources of chemical diversity in drug design [4-7]. For the past thirty years there has been a dramatic development of organosilicon chemistry leading to an increasing volume of scientific data. The first organosilicon compound was made in 1863 by Friedel and Craft [8]. In clinical studies some organosilicon compounds have been identified as potential drugs [9-10]. For example, Silperisone has been identified as a neuromuscular antagonist effective for controlling muscle spasm [11] and zifrosilone functions as an acetyl-cholinesterase inhibitor for the treatment of Alzheimer's disease [12]. Phenyl containing polysiloxanes have also been identified as exhibiting estrogenic activity. The siloxane *cis*-2,6-diphenyl hexamethylcyclotetrasiloxane (cisobitan) is reported to show potent biological activity,[13] with a hormonal agonist activity comparable to that of oestradiol and at the same time giving a low acute toxicity (LD_{50} > 5000 mg/Kg) [13]. This drug of promise has been identified to be good for the treatment of prostate cancer. TAC 101 and BNP1350 are currently being developed clinically for the treatment of cancer [11,12]. From recent discoveries it has become evident that organosilicon chemistry has a future for providing chemical diversity in drug discovery [13]. Even though much has been discovered in terms of organosilicon drugs, no silicon containing drug has so far been put on the market by the Drug Standards Board in the USA or Europe, basically due to concerns about the toxicity of organosilicon compounds [13]. In recent times about seven organosilicon drugs are reported to be in human clinical drug trials and an eighth is a highly marketed agrochemical fungicide known as flusilajole [13].

1,3-Dichloro-1,1,3,3-tetramethyldisiloxane is a versatile silylating reagent which was employed to incorporate the tetramethylsiloxy functionality into selected phenols and alcohols of interest. The selected compounds have known germicidal, bactericidal, analgesic and antibiotic properties. Amide, urea and thiourea derivatives of the synthesised siloxane compounds were developed and problems associated with stability studied. The direct silylation of the phenolic compounds with 1,3-dichloro-1,1,3,3-tetramethyldisiloxane raised real issues of stability due to the generation of hydrogen chloride, which immediately catalyses the cleavage of the siloxane functionality, leading to the rupturing of the tetramethylsiloxy group. Urea and thiourea derivatives bearing the tetramethylsiloxy functionality were found to tolerate water for longer periods without cleaving the tetramethylsiloxy functionality and these compounds were successfully recrystallized in ethanol. On the contrary, some of the amide derivatives bearing the

tetramethylsiloxy functionality were less stable to water and common organic solvents. The rupturing of the tetramethylsiloxy functionality in the amide derivatives in common laboratory solvents provides a viable synthetic pathway for the synthesis of compounds requiring both amide and alcohol functionalities but cannot be synthesized using the conventional methods. Reaction time, presence of moisture and acidic conditions were found to facilitate the dimerization of the functionalised siloxane compounds synthesized. The aim of the project is to explore the synthesis and properties of new functionalised siloxanes of which some may be of potential biological interest. Herein we report synthesis and characterization of stable and pure di-arylsiloxanes, as well as aliphatic siloxanes and their derivatives, paying attention to compounds with potential bactericidal, germicidal, preservative and analogues of other compounds of potential biological importance with the aim of discovering new and potential useful chemistry. The biological activities of these compounds will be reported in near feature.

Experimental

Materials and Method

Unless stated otherwise, starting materials were purchased from commercial sources (Sigma Aldrich) and used without further purification. Pyridine was dried by refluxing over potassium hydroxide under nitrogen gas and allowed to stand over 4Å molecular sieve. Tetrahydrofuran (THF) was dried by refluxing over sodium wire and benzophenone under nitrogen gas, distilled and allowed to stand over 4Å molecular sieve. Toluene was dried with sodium wire and allowed to stand over 4Å molecular sieve. Diethyl ether was dried with sodium wire and allowed to stand over sodium wire. 1,4-Dioxane was refluxed over sodium wire and benzophenone, distilled off and allowed to stand over 4Å molecular sieve. Acetonitrile was dried with 4Å molecular sieve.

IR Spectra: The Thermo-Nicolet Avatar 370 Fourier Transform Infra-Red Spectrophotometer was used for obtaining all the Infra-Red spectra data over the range of 4000-400 cm^{-1}.

Nuclear Magnetic Resonance: The NMR spectra were determined using the Bruker FT-NMR Spectrometer at 300 and 75.5 MHz for ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra, respectively. The chemical shifts are quoted in parts per million (ppm) relative to the signal of tetramethylsilane (TMS), which was used as an external standard for proton (^{1}H NMR) and carbon-13 ($^{13}C\{^{1}H\}$ NMR).

All NMR were run in deuterated dimethyl sulphoxide (DMSO-d_6) or deuterated chloroform ($CDCl_3$-d_6) as solvent unless stated otherwise.

Mass Spectra Analysis: The mass spectra analyses were obtained at the EPSRC National Mass Spectrometry Centre, University of Swansea. The spectra obtained were either low electron impact (EI/LR), chemical impart (CI), electrospray (nanospray) ionization mass spectrometry (ES-MS) or by orbitrap spectrometry.

Melting points: These were measured using a Stuart SMP3 melting point apparatus and are uncorrected.

Kugelrohr Distillation: The Buchi GKR-51 Kugelrohr distillation kit was employed in the purification of oil and sticky solid compounds.

Gas Chromatography-Mass Spectrometry: A Finnegan Gas Chromatograph directly coupled to a Polaris Q mass spectrometer was used to carry out the chromatography. The oven was programmed from 40 ^{0}C (1 min) at 10 ^{0}C / min to 300 ^{0}C. Chromatography was performed on immobilized polydimethylsiloxane stationary phase in fused silica column (12 m x 0.2, 0.33 micro m thickness) (SGE, Milton Keynes UK). The carrier gas was helium and the flow rate was 1 ml / min.

Synthesis of siloxane compounds

1,3-Bis(diethylamino)-1,1,3,3-Tetramethyldisiloxane (2)

Diethylamine (18.4 g, 250 mmol) in anhydrous diethyl ether (200 mL) in a multi-necked round bottom flask (500 mL) equipped with reflux condenser, addition funnel, thermometer and stirrer was maintained under a positive pressure of argon and chilled in an ice water bath to maintain a temperature range of 5-10 ^{0}C. The reaction mixture was stirred and 1,3-dichloro-1,1,3,3,-tetramethyldisiloxane (10 g, 50 mmol) was added drop wise over a period of 20 minutes. After addition was complete the mixture was stirred overnight at room temperature (20 ^{0}C). A white precipitate was formed. The white solid, identified as diethylamine hydrochloride was isolated by filtration using a Buchner funnel. The filtrate was then put on a rotary evaporator and the solvent was removed under reduced pressure. Yellow oil was obtained as the crude product. The oil was further dried under vacuum to give Bis(diethylamino)-1,1,3,3-tetramethyldisiloxane as a light yellow oil (8.96 g, 89.6% yield).

^{1}H NMR (d_6-DMSO): δ 0.95 (t, 12H, 4x-C**H$_3$**), 2.8 (q, 8H, 4x**CH$_2$**), 0.00 (12H, s, -Si-C**H$_3$**). ^{13}C {^{1}H} NMR (d_6-DMSO): δ 0.0 (Si-**C**H$_3$), 16.0 (N-**C**H$_2$), 39.63 (N- CH$_2$**C**H$_3$). IR (FTIR): υ cm^{-1} 2963, 2930, 2865, 1450, 1398, 1292, 1257, 1206, 1174, 1059, 1023, 929, 790.

1,3-Bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (3)

4-Aminophenol (2.0 g, 20 mmol) in an oven-dried round-bottom flask (500 mL) equipped with distillation condenser, addition funnel, and stirrer was added toluene (50 mL) and reaction mixture was maintained under argon gas. The mixture was stirred and heated to 70 ^{0}C. 1,3-Bis(diethylamino)-1,1,3,3-tetramethyldisiloxane (2.53 g, 10 mmol) was then added drop wise over a period of twenty minutes. After addition was completed, the mixture was heated to 86 ^{0}C and stirred for 2.5 hours. The reaction mixture was then cooled to 15 ^{0}C when reaction was complete and unreacted 4-aminophenol filtered off. The filtrate was then concentrated on a rotary evaporation under reduced pressure to give a thick brown liquid, which solidified on cooling. The crude product was then recrystallized from toluene to give 1,3-bis(4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane as waxy amber-coloured solid (2.1 g, 66%); m.p.: 56-57 ^{0}C.

^{1}H NMR (DMSO-d_6): δ 7.1 (d, 2H, J = 7.8 Hz, 2x Ar-**H**), 6.8 (d, 2H, J = 8.0 Hz, 2xAr-**H**), 6.75 (d, 2H,J = 7.0 Hz, 2x Ar-**H**), 6.6 (d, 2H,J = 7.8 Hz, 2 x Ar-**H**), 3.4 (s, 3H**,** C**H$_3$), 2**.3 (s, br, 2H**,-**N**H$_2$**)**, δ 0. 00 (12H, s, -Si-**CH$_3$**). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 147.6 (Ar-**C**), 117.2 (Ar-**C**), 116.9 (Ar-**C**), 0.0 (Si-**C**H$_3$). IR (FTIR): υ cm^{-1} 1509, 1260, 1089, 1031, 904, 797, 751. MS (LTQ orbitrap): m/z = 348 (76%) ([M+H]$^{+}$), 241 (100%), = 224 (38%).

1,3-bis [4'-(3"-(4-nitrophenyl) ureido) phenoxy]-1,1,3,3-tetramethyldisiloxane (5a)

4-nitrophenyl isocyanate (1.89 g, 12 mmol) was ground to a fine powder and dissolved in toluene (50 mL) in an oven-dried round-bottomed (250 mL) and stirred under argon until the starting material had dissolved. 1,3-Bis(4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (2.0 g, 6 mmol) dissolved in toluene (50 mL) was added drop wise over a period of fifteen minutes from an addition funnel, and reaction was maintained under argon at a temperature of 75 ^{0}C for fifteen hours. A greenish yellow colour was observed at the beginning of the reaction changing to a yellow precipitate at the end of reaction. A greenish yellow solid was obtained after

evaporation of the solvent under reduced pressure. The crude product was recrystallized from ethanol to give 1,3-bis [4^{l}-(3$^{l\,l}$-(4-nitrophenyl)ureido)phenoxy]-1,1,3,3-tetramethyldisiloxane as an off-white solid powder. Yield = 2.15 g, 56%; m.p.: 289-291 ^{0}C.

^{1}H NMR (d$_6$-DMSO): δ 6.61 (d, 4H,J = 8.3 Hz, 4 x Ar-**H**), 7.13 (d, 4H, J = 8.3 Hz, 4 x Ar-**H**), 7.45 (d, 4H, J = 8.7 Hz, 4 x Ar-**H**), 7.95 (d, 4H, J = 8.7 Hz, 4 x $C_6H_4NO_2$-**H**), 8.56 (s, 2H, -N**H**CO), 9.17 (s, 2H, -N**H**CO), 0. 00 (s, 12H, -SiC**H**$_3$). ^{13}C {^{1}H} NMR (d$_6$-DMSO): δ 151.5 (**C**=O), 148.5 (Ar-**C**), 145.9, (Ar-**C**), 140.3 (Ar-**C**), 132.6 (Ar-**C**), 124.5 (Ar-**C**), 119.8 (Ar-**C**), 119.3 (Ar-**C**), 116.8 (Ar-**C**), -1.2 (Si-**C**H$_3$). IR (FTIR): υ cm^{-1} = 1641, 1612, 1591, 1556, 1509, 1343, 1273, 1262, 1230, 1079, 937, 911, 848, 835, 807, 738. MS (LTQ orbitrap): m/z = 677 ([M+H]$^{+}$, 70%), 601 (14%), 485 (37%), 391 (15%), 290 (75%), 217 (10%). HR-MS (LTQ Orbitrap) ($C_{30}H_{33}N_7O_7S_2Si_2$) [M+H]$^{+}$: Calc: m/z = 676.1769, measured: m/z = 676.1097.

1,3-Bis [4^{l}–(3$^{l\,l}$- (4-phenyl) ureido) phenoxy]-1,1,3,3-tetramethyldisiloxane (5b)

A solution of phenyl isocyanate (1.37 g, 12 mmol) in toluene (50 mL) in an oven-dried round-bottomed flask (250 mL) was stirred under argon. 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (2.0 g, 6 mmol) dissolved in toluene (30 mL) was added dropwise over a period of fifteen minutes from an addition funnel, and reaction was stirred and maintained under a pressure of argon gas for fifteen hours. A brown colour was observed at the beginning changing to a mauve slurry product at the end of reaction. An off-white solid was obtained after rotary evaporation of the solvent under reduced pressure. The crude product was recrystallized from ethanol and dried under vacuum for twelve hours to give 1,3-bis [4^{l} –(3$^{l\,l}$ - (4-phenyl) thioureido) phenoxy]-1,1,3,3-tetramethyldisiloxane **(5b)** as a white powder (2.88 g, 41.1% yield); m.p.:203-205 ^{0}C.

1H NMR (DMSO-d$_6$): δ 0. 00 (12H, s, -Si-C**H**$_3$), 6.61 (4H, d, J =**8.4** Hz, 4 x Ar-**H**), 6.72 (4H, d, J =7.2 8.6 Hz, 4 x Ar-**H**), 7.04 (4H, d, J =7.7 9.0 Hz, 4 x Ar-**H**), 7.12 (2H, d, J = **8.4** Hz, 2 x C_6H_4-**H**), 7.23 (2H, d, J = 8.09.0 Hz, 2 x C_6H_4-**H**) 8.38 (2H**,** s, -N**H**CO**),** 8.29 (2H**,** s, -N**H**CO).^{13}C NMR (DMSO-d$_6$): δ 153.4 (**C**=O), 149.2 (Ar-**C**), 140.5 (Ar-**C**), 134.6 (Ar-**C**), 129.4 (Ar-**C**), 122.3 (Ar-**C**), 120.5 (Ar-**C**), 120.4 (Ar-**C**), 118.8 (Ar-**C**), 0.0 (Si-**C**H$_3$). IR (FTIR): υ cm^{-1} = 1638, 1592, 1549, 1505, 1402.8, 1268, 1253, 1223, 1082, 952.0, 919, 839, 800, 735, 708. MS (LTQ orbitrap): m/z = 587 ([M+H]$^{+}$ 100 %), 494 (7 %), 391 (20 %), 229 (12 %), 279 (6 %). HR-

MS (LTQ Orbitrap) ($C_{30}H_{35}N_4O_5Si_2$) $[M+H]^+$: Calc: m/z = 587.2140, measured: m/z = 587.2137.

1,3-Bis [4'-(3''-(4-nitrophenyl) thioureido) phenoxy]-1,1,3,3-tetramethyldisiloxane (6)

A solution of 4-nitrophenyl isothiocyanate (2.0 g, 10 mmol) in dry toluene (50 mL) in an oven-dried round-bottomed flask (500 mL) was stirred under argon until the starting material had dissolved. 1,3-Bis(4-aminophenoxy)-1,1,3,3-tetramethyl-disiloxane (1.93 g, 5 mmol) dissolved in toluene (50 mL) was added drop wise over a period of fifteen minutes from an addition funnel, and reaction mixture was stirred and maintained under a pressure of argon for fifteen hours. A dark brown colour was observed at the beginning of the reaction changing to a greenish yellow solution at the end of reaction. A greenish yellow solid was obtained after evaporation of the solvent under reduced pressure. The crude product was recrystallized from ethanol to give 1,3-bis [4'-(3'' -(4-nitrophenyl)thioureido)phenoxy]-1,1,3,3-tetramethyldisiloxane as a yellow powder. Yield =3.12 g, 80%; m.p.: 156-159 ^{0}C.

^{1}H NMR (DMSO-d_6): δ 6.64 (d, 4H,J = 8.6 Hz, 4 x Ar-**H**), 7.12 (d, 4H,J = 8.6 Hz, 4 x Ar-**H**), 7.58 (d, 4H,J = 9.0 Hz, 4 x Ar-**H**), 7.95 (d, 4H, J = 9.0 Hz, 4x $C_6H_4NO_2$-**H**), 10.1 (br s, 4H**,**-N**H**C=S), 0. 00 (s, 12H,-SiC**H**$_3$). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 179.9 (**C**=S), 151.8 (Ar-**C**), 147.0 (Ar-**C**), 142.8 (Ar-**C**), 133.6 (Ar-**C**), 126.3 (Ar-**C**), 125.0 (Ar-**C**), 122.0 (Ar-**C**), 120.8 (Ar-**C**), 0.5 (Si-**C**H_3). IR (FTIR): υ cm^{-1} = 1594.8, 1554, 1509, 1502, 1334, 1260.9, 1223, 1178, 1108, 1063, 919, 854, 803, 750. MS (LTQ orbitrap): m/z = 709 ($[M+H]^+$, 70%), 601 (14%), 485 (37%), 391 (15%), 290 (75%), 217 (10%). HR-MS (LTQ Orbitrap) ($C_{30}H_{33}N_7O_7S_2Si_2$) $[M+H]^+$: Calc: m/z = 709.1372, measured: m/z = 709.1375.

1,3-Bis [-4'-(3''-(4-nitrophenyl)thioureido) phenoxy]-1,1,3,3-isopropyldisiloxane (7)

A solution of 4-nitrophenyl isothiocyanate (0.6 g, 10 mmol) in toluene (40 mL) in an oven-dried round-bottomed flask (500 mL) was stirred under argon until the starting material had dissolved. 1,3-bis (4-aminophenoxy)-1,1,3,3-tetraisopropyl-disiloxane (0.75 g, 5 mmol) dissolved in toluene (25 mL) was added drop wise for fifteen minutes from an addition funnel, and was maintained under a pressure of argon for 15 hours. A dark brown colour was obtained at the beginning changing to a mauve precipitate at the end of reaction. A mauve solid was obtained

after evaporation of the solvent under reduced pressure. The crude product was recrystallized from ethanol to give mauve powder. Yield = 0.97 g, 72%; m.p.: 122-125 ^{0}C.

^{1}HNMR (d_6-DMSO): δ 1.10 (s, 24H, -Si-CH **(**C**H$_3$**)$_2$), 1.02 (m, 4H,-Si-C**H(**CH_3)$_2$), 6.94 (d, 4H, J = 8.5 Hz, 4 x Ar-**H**), 7.18 (d, 4H, J = 8.6 Hz, 4 x Ar-**H**), 7.7 (4H, d, J = 9.0 Hz, 4 x Ar-**H**), 8.2 (d, 4H,J = 9.0 Hz, 4 x $C_6H_4NO_2$-**H**), 8.4 (s, br, 4H**,** -N**H**CO). ^{13}C{^{1}H} NMR (d_6-DMSO): δ 179.9 (**C**=S), 151.8 (Ar-**C**), 147.0 (Ar-**C**), 142.8, (Ar-**C**), 133.6 (Ar-**C**), 126.3 (Ar-**C**), 125.0 (Ar-**C**), 122.0 (Ar-**C**), 120.8 (Ar-**C**), 0.5 (Si-**C**H_3). IR (FTIR): υ cm^{-1} = 1595, 1554, 1509, 1502, 1334, 1261, 1223, 1178, 1108, 1063, 919, 854, 803, 750. HRMS (LTQ Orbitrap) ($C_{34}H_{40}N_6O_7S_2Si_2$) [M]$^+$: Calc: m/z = 764.1938, measured: m/z = 764.1334.

1,3-Bis [4' –(3"-(4-nitrobenzamido)phenoxy]-1,1,3,3-tetramethyldisiloxane (8)

To a solution of 1,3-bis(4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (2.11 g, 6 mmol) in a mixture of dry toluene (75 mL) and triethylamine (4.1 g, 40 mmol) in an oven-dried round-bottomed flask (250 mL) was added 4-nitrobenzoyl chloride (2.25 g, 12 mmol) and the mixture stirred under argon for twenty hours. The mixture was poured into water (200 mL) in a separating funnel and the two layers were separated. A greenish yellow solid was isolated and filtered off from the aqueous layer using Buchner funnel. The crude product was washed with diethyl ether and recrystallized from ethanol to give 1,3-bis [4'-(3"-(4-nitrobenzamido)phenoxy]-1,1,3,3-tetramethyldisiloxane (**8**) as a greenish-yellow solid. Yield = 0.6 g, 7.5%; m. p.: 205-207 ^{0}C.

^{1}H NMR (DMSO-d_6): δ 8.10 (d, 4H, J = 7.9 Hz, 4 x Ar-**H**), 7.90 (d, 4H, J = 7.9, 4 x Ar-**H**), 7.40 (d, 4H, J = 8.2 Hz, 4 x Ar-**H**), 6.6 (d, 4H, J = 8.0 Hz, 4 x Ar-**H**), 10.20 (s, 2H**,** -N**H**CO), 0. 00 (12H, s, -Si-C**H$_3$**). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 164.1 (**C**=O), 150.8 (Ar-**C**), 149.7 (Ar-**C**), 141.3 (Ar-**C**), 133.6 (Ar-**C**), 129.7 (Ar-**C**), 124.1 (Ar-**C**), 122.8 (Ar-**C**), 120.3 (Ar-**C**), 0.0 (Si-**C**H_3). IR (FTIR): υ cm^{-1} 1647, 1601, 1510, 1346, 1320, 1264, 1957, 939, 916, 870, 856, 833, 807, 719. HRMS (LTQ Orbitrap) ($C_{32}H_{34}N4O_9Si_2$) [M+H]$^+$: Calc: m/z = 647.1551, measured: m/z = 647.2064.

1,3-Bis [4'-(3"-(benzamido)phenoxy]-1,1,3,3-tetramethyldisiloxane (9)

A solution of 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (2.0 g, 6 mmol) in toluene (50 mL) in a round-bottomed flask (250 mL) was stirred under argon at room temperature.

Benzoyl chloride (1.69 g, 12 mmol) dissolved in toluene (30 mL) was added drop wise over a period of 15 minutes from an addition funnel, and reaction mixture was maintained under a pressure of argon gas. The mixture was heated on an oil-bath at 80 ^{0}C for 15 hours. A brown coloured solution was obtained at the beginning of the reaction changing to a violet precipitate at the end of reaction. The mixture was cooled to room temperature and solvent removed by rotary evaporation turning into a violet paste. The violet paste was dissolved in diethyl ether (80 mL). The mixture was washed with saturated $NaHCO_3$ (2 x 80 mL) followed by water (2 x 100 mL), dried ($MgSO_4$) and solvent removed by means of rotary evaporation under reduced pressure. An off-violet crude product was obtained and recrystallized from ethanol to give 1,3-bis[4'-(3''-(benzamido)phenoxy]-1,1,3,3-tetramethyldisiloxane **9** as off-violet solid. Yield = 1.52 g, 59%; m.p.:213-215 ^{o}C.

^{1}H NMR (DMSO-d_6): δ 0. 00 (12H, s, -Si-**C**$\mathbf{H_3}$), 7.98 (4H, d, J = 7.5 Hz, 4x Ar-**H**), 7.63-7.57 (4H, m, 4x Ar-**H**), 6.8 (4H, d, J = 8.2 Hz, 4x Ar-**H**), 9.3 (2H**,** s, -N**H**CO**),** 10.1 (2H**,** s, -N**H**CO**).** ^{13}C{^{1}H} NMR (DMSO-d_6): δ 164.85 (**C**=O), 153.6 (Ar-**C**), 135.01 (Ar-**C**), 131.2 (Ar-**C**), 130.5 (Ar-**C**), 128.2 (Ar-**C**), 127.4 (Ar-**C**), 122.2 (Ar-**C**), 114.8 (Ar-**C**), 0.0 (Si-**C**H_3). IR (FTIR): υ cm^{-1} 3328, 1649, 1610, 1538, 1510, 1436,1332, 1260, 1248, 1228, 1102, 1017, 825, 798, 779, 720. HRMS (LTQ Orbitrap) ($C_{32}H_{34}N4O_9Si_2$) $[M+H]^+$: Calc: m/z = 556.1850, measured: m/z = 556.1801.

1,3-Bis [4'-(3''-(4-chlorobenzamido)phenoxy]-1,1,3,3-tetramethyldisiloxane (**10**)

To a stirred solution of 1,3-bis(4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (1.0 g, 3 mmol) in a mixture of dry toluene (30 mL) and triethylamine (5 g, 50 mmol) in a round-bottomed flask (250 mL) under argon, was added 4-chloro-benzoyl chloride (0.98 g, 6 mmol) in toluene (30 mL) drop wise over a period of five minutes. The solution was heated on an oil-bath at 80 ^{0}C for 1 hour and then stirred overnight at 20 ^{0}C. The mixture was poured into distilled water (200 mL) in a separating funnel to dissolve the triethylamine hydrochloride formed. The aqueous layer and organic (toluene) layers were separated. A white precipitate was isolated by filtration from the aqueous layer using a Buchner funnel and washed with diethyl ether (30 mL) to give an off-white powder. The crude product was recrystallized from ethanol to give 1,3-bis [4'-(3''- (4-

chlorobenzamido)-phenoxy]-1,1,3,3-tetramethyldisiloxane **(10)** as fine white powder. Yield = 0.90 g, 25%; m.p.: 210-212 ^{0}C.

^{1}H NMR (DMSO-d_6): δ 7.72 (d, 4H, J = 7.8 Hz, 4 x Ar-**H**), 7.40 (d, 4H, J = 8.3 Hz 4 x Ar-**H**), 7.34 (d, 4H, J = 8.2 Hz, 4x Ar-**H**), 6.63 (d, 4H, J = 8.2 Hz, 4 x Ar-**H**), 9.99 (s, 2H, -N**H**CO), 0.00 (s, 12H, -SiC**H$_3$**). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 164.69 (**C**=O), 150.6 (Ar-**C**), 136.9 (Ar-**C**), 134.3 (Ar-**C**), 130.2 (Ar-**C**), 129.01 (Ar-**C**), 122.6 (Ar-**C**), 120.2 (Ar-**C**), 115.6 (Ar-**C**), 0.0 (Si-**C**H$_3$). IR (FTIR): υ cm^{-1} 2988, 2901**,** 1653, 1599, 1407, 1394,1272, 1258, 1066, 939, 906, 829, 804, 749. HRMS (LTQ Orbitrap) ($C_{30}H_{30}Cl_2N_2O_5Si_2$) $[M+H]^+$, $[M-2Cl]^+$: Calc: m/z = 626.1070 and 557.1883, Measured: m/z = 626.5410 and 557.1801 respectively.

Synthesis of 1,3-Bis [4'-(3"(-2-chlorobenzamido)-4-phenoxy]-1,1,3,3-tetramethyldisiloxane (11)

To a stirred solution of 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (2.0 g, 6 mmol) in a mixture of dry toluene (50 mL) and triethylamine (7 mL) in an oven-dried round-bottomed flask (250 mL) under argon was added 2-chloro-benzoyl chloride (1.96 g, 6 mL) dissolved in toluene (30 mL) drop wise over a period of five minutes. The reaction mixture was heated on an oil-bath at 80 ^{0}C for 1 hour and reaction mixture made to stir overnight at 20 ^{0}C. The mixture was poured into distilled water (200 mL) in a separating funnel. Two layers were separated. The aqueous layer was discarded and the organic phase (toluene layer) dried ($MgSO_4$). The solvent was removed by rotary evaporation to give a crude off-white solid. The crude product was washed with diethyl ether (30 mL) to give an off-white powder. This was recrystallized from ethanol to give 1,3-bis[4^{I}-(3$^{I\ I}$ -(2-chlorobenzamido)phenoxy]-1,1,3,3-tetramethyldisiloxane (**11**) as a fine white powder. Yield = 1.25 g, 17.4%; m.p.: 117-119.5 ^{0}C.

^{1}HNMR (DMSO-d_6): δ 7.39-7.2 (m, 12H, 6xAr-**H**), 6.5 (d, 4H, J = 8.2 Hz, 4xAr-**H**), 10.2 (s, 2H, N**H**CO), 0. 00 (s, 12H, -Si-C**H$_3$**)**.** ^{13}C {^{1}H} NMR (DMSO-d_6): δ 165.2 (**C**=O), 150.5 (Ar-**C**), 137.7 (Ar-**C**), 133.9 (Ar-**C**), 131.7 (Ar-**C**), 130.6 (Ar-**C**) ,130.3 (Ar-**C**), 129.6 (Ar-**C**), 127.9 (Ar-**C**), 121.4 (Ar-**C**), 120.4 (Ar-**C**), 0.00 (Si-**C**H$_3$). IR (FTIR): υ cm^{-1} 3683, 3665, 3645, 2988, 2901, 1653, 1510, 1271, 1258, 1069, 1052, 934, 829, 804, 749. 749. HRMS (LTQ Orbitrap) ($C_{30}H_{30}Cl_2N_2O_5Si_2$) $[M]^+$: Calc: m/z = 624.1070, measured: m/z = 624.1240.

1,3-Bis[4'-(3"-(4-phenylacetylo)-3-phenoxy]-1,1,3,3-tetramethyldisiloxane (12)

To a stirred solution of 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyl-disiloxane (1.74 g, 5 mmol) in a mixture of dry toluene (50 mL) and triethylamine (3.3 g, 30 mmol) in an oven-dried round-bottomed flask (250 mL) under argon gas was added phenylacetyl chloride (1.55 g, 10 mmol) dissolved in toluene (30 mL) drop wise over a period of fifteen minutes. The solution was made to stir for fifteen hours at room temperature. The solution caused a precipitation of a white solid. The solution was then transferred into a separating funnel and deionised water (150 mL) poured onto it. The aqueous layer and the toluene layer were separated in a separating funnel. The aqueous layer was discarded and the toluene layer was dried ($MgSO_4$) and toluene was removed by rotary evaporation under reduced pressure. Light brown oil was obtained as the crude product. The crude was further purified by Kugelrohr distillation to remove all residual toluene to give thick brown oil (**12**). Yield = 2.1 g, 35.4%.

^{1}HNMR (DMSO-d_6): δ 7.28 (d, 4H, J= 8.5, 2x Ar**H**), 6.62 (d, 4H, J= 8.5, 2xAr**H**), 7.10-7.20 (m, 10H, 5xAr**H**), 3.41 (s, 4H, 2xC**H$_2$**) 9.91 (s, 2H, -N**H**CO), 0. 00 (12H, s, -SiC**H**$_3$). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 168.5 (**C**=O), 152.6 (Ar-**C**), 136.1 (Ar-**C**), 133.7 (Ar-**C**), 130.5 (Ar-**C**), 129.5 (Ar-**C**), 129.1 (Ar-**C**), 127.6 (Ar-**C**), 115.6 (Ar-**C**), 40.2 (**C**H$_2$), 0.0 (Si-**C**H$_3$). HRMS (LTQ Orbitrap) ($C_{32}H_{36}N_2O_5Si_2$) $[M]^+$: Calc: 587.2165, measured: 587.2140.

1,3-Bis(-2-acetylsalicyloyl-4-aminophenoxy) 1,1,3,3-tetramethyldisiloxane (13)

To a stirred solution of 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyl-disiloxane (2.10 g, 6 mmol) in a mixture of dry toluene (50 mL) and triethylamine (3.3 g, 30 mmol) in a round-bottomed flask (250 mL) under argon gas was added *o*-acetylsalicyloyl chloride (2.4 g, 12 mmol) dissolved in toluene (30 mL) drop wise over a period of fifteen minutes. The solution was made to stir for fifteen hours at room temperature of 50 ^{0}C and reaction mixture was maintained under argon gas. The solution caused a precipitation of a white solid. The solution was isolated by filtration using a Buchner funnel. Deionised distilled water (100 mL) was added to the toluene layer in a separating funnel to remove residual triethylamine hydrochloride. Two layers were separated after agitation of the mixture in the separating funnel. The aqueous layer was discarded and the toluene layer dried ($MgSO_4$). The solvent was removed by rotary evaporation under reduced pressure and purified further by kugelrohr distillation to give brown oil. Yield=1.0 g, 56.7%.

^{1}HNMR (DMSO-d_6): δ 0. 00(12H, s, -Si-C**H**$_3$), (3H, s, -OC**H**$_3$), 6.93 (2H, d, J= 8.5, 2×Ar-**H**), 7.10 (2H, d, J= 7.8, 2xAr-**H**), 7.43 (1H, t, Ar-**H**), 7.67 (2H, d, J= 7.8, 2xAr-**H**), 7.80 (1H, d, Ar-**H**), 19.40 (2H, s, -N**H**CO). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 166. 5 (**C**=O), 166. 6(**C**=O), 152.6 (Ar-**C**), 136.1 (Ar-**C**), 133.7 (Ar-**C**), 130.5 (Ar-**C**), 129.5 (Ar-**C**), 129.1 (Ar-**C**), 127.6 (Ar-**C**), 115.6 (Ar-**C**), 40.2 (**C**H$_2$), 0.0 (Si-**C**H$_3$).

1,3-Bis (-*N*-pentanoyl-4-phenoxy)-1,1,3,3-tetramethyldisiloxane (14)

To a stirred solution of 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (1.74 g, 5 mmol) in a mixture of dry toluene (50 mL) and triethylamine (3.3 g, 30 mmol) in an oven-dried round-bottomed flask (250 mL) under argon was added valeroyl chloride (1.21 g, 10 mmol) dissolved in toluene (30 mL) drop wise over a period of five minutes at room temperature. The reaction mixture was stirred and maintained under argon gas for fifteen hours at 20 ^{0}C. The mixture was poured into distilled water (200 mL) in a separating funnel. Two layers were observed after agitation of the mixture in a separating funnel. The toluene layer was dried ($MgSO_4$) and the aqueous layer was discarded. Thick light brown oil was obtained after rotary evaporation of the toluene. The oil was triturated with cyclohexane and dried under vacuum for thirty six hours to give1,3-bis (pentanoyl]-1,1,3,3-tetramethyldisiloxane (**14**) as a waxy brown solid. Yield = 1.28 g, 43.4%; m.p.: 127-130 ^{0}C.

^{1}H NMR (DMSO-d_6): δ 2.2 (q, 4H, 2xC**H**$_2$), 1.5 (q, 4H, 2 x C**H**$_2$), 1.2 (q, 4H, 2 x C**H**$_2$), 0.84 (t, 6H, 3, x C**H**$_2$), 7.3 (d, 4H, 4 x Ar-**H**), 6.6 (d, 4H, 4xAr-H), 9.54 (s, 2H, -N**H**CO), 0. 00 (s, 12H,-Si-C**H**$_3$). ^{13}C{^{1}H} NMR (d_6-DMSO): δ 172.2 (**C**=O), 153.7 (Ar-**C**), 134.3 (Ar-**C**), 121.5 (Ar-**C**), 115.6 (Ar-**C**), 36.7 (**C**H$_2$), 28.1 (**C**H$_2$), 22.5 (**C**H$_2$), 14.5 (**C**H$_3$), 0.0 (Si-**C**H$_3$). IR (FTIR): υ cm^{-1} 3314**,** 1651, 1611, 1554,1516, 1451, 1420, 1382, 1256, 1254, 1194, 1105, 1028, 966, 832, 802, 717.

1,3-Bis (-2-chloropropionyl-4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (15)

A solution of 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane (2.0 g, 6 mmol) dissolved in toluene (50 mL) in an oven-dried round-bottomed flask (250 mL) was added triethylamine (4.0 g, 4.0 mmol) and stirred. 2-Propionyl chloride (1.46 g, 12 mmol) in toluene (30 mL) was added drop wise over a period of fifteen minutes from an addition funnel, and reaction was

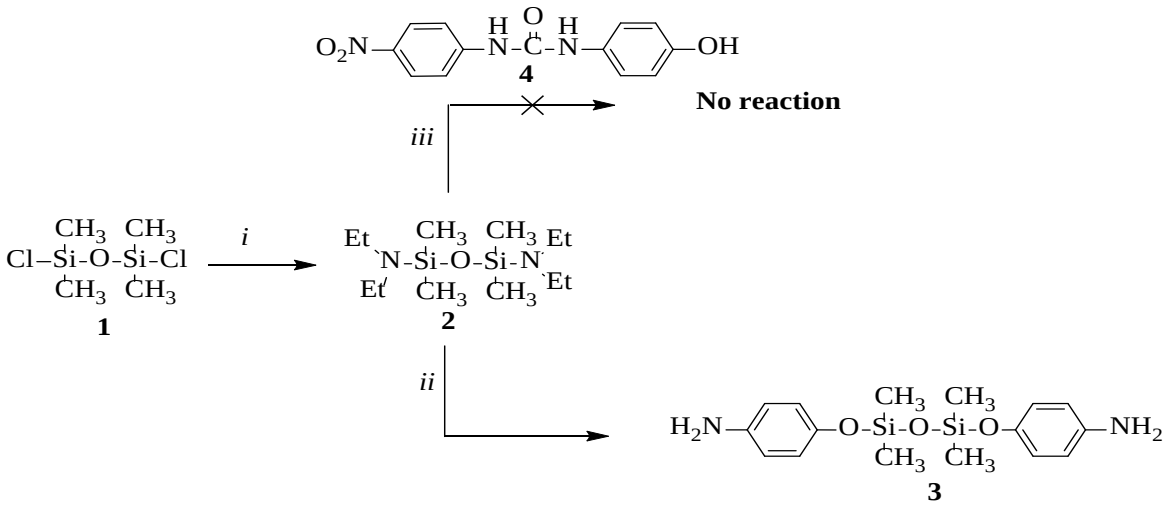
maintained under a pressure of argon gas for fifteen hours. The mixture was poured into a separating funnel, and distilled water (200 mL) was added and mixture was shaken. The aqueous and organic layers were separated. The toluene layer was dried ($MgSO_4$) and the aqueous layer discarded. Thick light brown oil was obtained after the solvent was removed by rotary evaporation under reduced pressure. The thick brown oil was left to stand for 36 hours in a minimum quantity of dry diethyl ether in a dark place and crystalline colourless crystals was obtained. This was identified as 1,3-Bis [-2-chloropropionyl-4-aminophenoxy]-1,1,3,3-tetramethyldisiloxane (**15**). Yield = 1.50 g, 28%; m.p.: 135 ^{o}C.

^{1}H NMR ($CDCl_3$-d_6): δ 8.28 (2H, s, -NHCO), 7.37 (4H, d, J = 8.5, 4xAr-H), 6.83 (4H, d, J = 8.5, 4xAr-H), 4.56 (2H, m, J = 7.0, 2xCH), 1.83 (12H, d, 4×CH_3), 0. 00 (12H, s, -Si-CH_3). ^{13}C{^{1}H} NMR ($CDCl_3$-d_6): δ 167.9 (C=O), 152.0 (Ar-C), 131.5 (Ar-C), 122.5 (Ar-C), 120.8 (Ar-C), 56.7 (CH), 23.3 (CH_3), 0.0 (Si-CH_3). IR (FTIR): υ cm^{-1} 1653, 1510, 1271, 1258, 1069, 1052, 934, 829, 804, 749. HRMS (LTQ Orbitrap) ($C_{22}H_{30}Cl_2N_2O_5Si_2$) $[M+H]^+$: Calc: m/z = 529.1070, measured: m/z = 529.2140.

Results and discussion

The title compounds were prepared *via* coupling reaction of an isocyanate and a diamino compound. The procedure for the synthesis of an intermediate diamino compound **3** was achieved by the reaction of excess diethylamine with 1,3-Dichloro-1,1,3,3-tetramethyldisiloxane to give 1,3-Bis(diethylamino)1,1,3,3-tetramethyldisiloxane **2** followed by treatment of **2** with 4-aminophenol at 86 ^{o}C (Scheme 1) [7]. Two equivalents of 4-aminophenol was reacted with 1,3-(diethylamino)-1,1,3,3-tetramethyldisiloxane (**2**) at 86 ^{0}C under inert condition. The reaction was stirred for three hours. Cooling the solution precipitated a solid, which was filtered off and identified as unreacted 4-aminophenol. The solvent was removed under vacuum to give light brown oil. The oil solidified into an amber coloured solid. The solid was recrystallized from toluene to give an amber solid in 84% yield with a melting point of 57 ^{0}C. Analysis of the solid **3** by ^{1}H NMR spectroscopy indicated the presence of four peaks in the spectrum. There were two signals in the aromatic region. A doublet at 6.5 ppm (four protons), and the other doublet at 6.35 ppm. The peak representing the amino protons was a broad singlet at 3.1 ppm (four protons). The tetramethyl-siloxy protons were observed in the alkyl region at 0.00 ppm (twelve protons). The

presence of the NH_2 protons indicated that the diamino isomer **3** had formed and not the possible dihydroxy derivative.

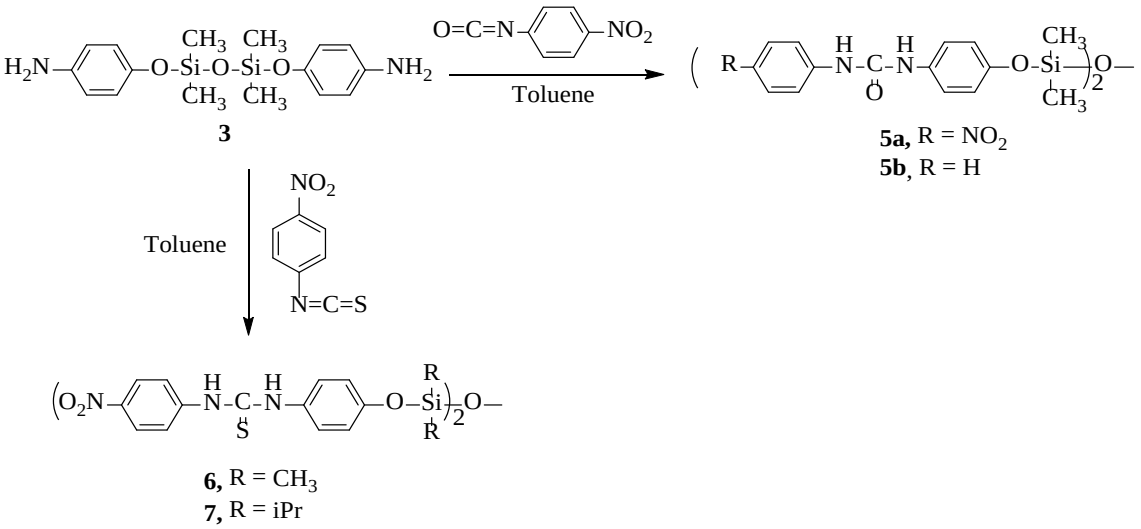


Scheme 1: Synthesis of diamino intermediate compound. Reagents: (i) Diethyl ether, exces diethylamine, 0°C (ii) Toluene, 4-aminophenol, 86°C (iii) Toluene.

The $^{13}C\{^1H\}$ NMR spectrum also supported the formation of the product **3**. Four carbons were observed in the aromatic chemical shift range and one carbon in the alkyl chemical shift range. Two quaternary carbons were observed at 147.1 and 141.1 ppm respectively. The other two aromatic carbons were observed at 121 and 116.5 ppm respectively. The tetramethylsiloxy carbons were observed at 0.00 ppm in the alkyl region. The major absorption in the infra-red spectrum was the absorption due to the disiloxane functionality. The Si-O-Si band was observed at 1089 and 1031 cm^{-1} respectively [14-18]. The Si-CH_3 band was also indicated and the band was observed at 1259 cm^{-1} [14,16-18]. A low resolution mass spectrum indicated the molecular ion $[M]^+$ at m/z = 348 (76%). A fragment at m/z = 241 (100%) equates the loss of a 4-aminophenol group and a further loss of an amino group gave a fragment at m/z = 224 (38%) which indicates the formation of desired intermediate **3**.

Subsequently, the desired products (**5-7**) were prepared by coupling of an isocyanate or thioisocyanate and the diamino compound **3** (Scheme 2). The direct synthesis of desired products **5** and **6** by reaction of two equivalents of 1,3-(diethylamino)-1,1,3,3-tetramethyldisiloxane (**2**) and N^1-(4-hydroxyphenyl)-N^2-(4-nitrophenyl)-urea (**4**) in toluene (Scheme 1) yielded undesired

yellow solid, which was analysed to be the mixture of starting materials. However, an intermediate diamine and isocyanate coupling method was adopted (Scheme 2) [19].



Scheme 2: Synthesis of diaryl disiloxanes compounds

The desired compounds were confirmed by NMR, FT-IR and mass spectrometry. The stability of the siloxane bond to water was investigated by adding two drops of D_2O into a solution of the product in DMSO-d_6 for 3, 6, 12, 24 and 48 h. The peaks observed in the ^{1}H NMR spectra were intact after 48 hours. The ^{1}H NMR analysis of the product gave a very clean spectrum with distinct peaks for all protons. The compound was successfully recrystallized from ethanol with the siloxane grouping remaining intact. The mass spectrum of 1,3-bis [4^{l} –(3 ^{l} ^{l}-(4-nitrophenyl) ureido) phenoxy]-1,1,3,3-tetramethyldisiloxane **5**, a compound with the urea functionality produced very few fragment ions. The fragment ions gave diagnostic features (see SEI, Scheme S1) which led to the confirmation of the structure of compound **5**, which has been explained in details in the supplementary material section (Scheme S1). Analysis of the ^{1}H NMR spectrum indicated the presence of two broad peaks for the –NH protons appearing at 10.1 and 9.8 ppm, respectively, and integrating to a total of four protons for compound **6.** The presence of the –NH protons was confirmed by exchange with D_2O.

Analysis of the ^{1}H NMR spectrum (Figure S2) indicated the presence of four distinct sets of doublets in the aromatic region of the spectrum giving a total of sixteen protons in the aromatic region. There were four doublets of equal intensities which integrate to give the same number of

protons. The doublet appearing at 7.95 ppm (four protons), (J = 9.0 Hz) is indicative of the protons adjacent to the nitro group. The doublet at 7.58 ppm (four protons), is indicative of the protons adjacent to the urea group, the doublet at 7.12 ppm (four protons), (J = 8.6 Hz) is indicative of the protons adjacent to the tetramethylsiloxy group and finally the doublet at 6.64 ppm (four protons), (J = 8.6 Hz). The total number of protons suggests two pairs of symmetrically *para*-substituted phenyl groups which is consistent with the proposed structure **6**.

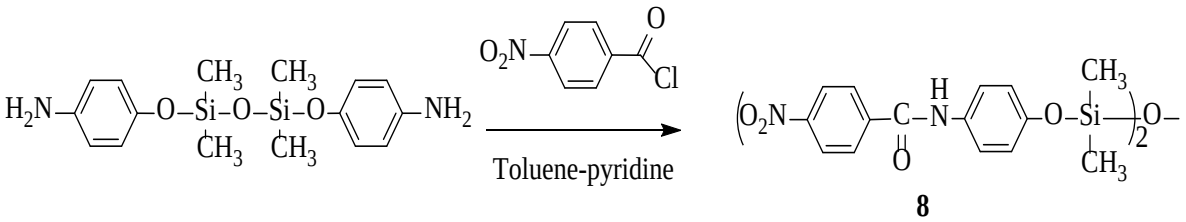
The analysis of the ^{13}C {^{1}H} NMR spectrum (~~Figure 10~~ Figure S2, Supplementary documents) indicated ten carbon environments. Eight of the ten carbons are observed in the aromatic chemical shift range of 120-151 ppm. This further proves the presence of two different sets of aromatic carbons. The signal at179.96 ppm is due to a C=S function. The quaternary carbon signal at δ 151.7 indicating a C=S group. The FT-IR band at 1509 and 1061 cm^{-1} confirms the presence of NHC=S band. The Si-CH_3 group is recognised by a strong sharp band at about 1260 cm^{-1} in addition to other strong bands observed in the range of 856-811 cm^{-1}. The Si-O-Si of siloxanes shows very strong single band of infrared at 1062 cm^{-1} [14-18]. The presence of the NH-groups is further confirmed by the exchangeable signal at 10.1 ppm in the ^{1}H NMR spectrum and the characteristic NH-stretching vibrations at 3200-3250 cm^{-1} in the infrared spectrum. Further signals indicating the presence of the nitro group appeared at 1559, 1344 cm^{-1}. Similar products were then prepared by the same method. 1,3-bis[4^{I}-(3^{II}-(4-nitrophenyl) ureido)phenoxy]-1,1,3,3-tetramethyldisiloxane **5** was synthesized by a process similar to that outlined for the isothiocyanate compound **6** (Scheme 2). 1,3-Bis (4-amino-phenoxy)-1,1,3,3-tetramethyldisiloxane **3** was reacted with two equivalents of 4-nitrophenyl isocyanate dissolved in toluene and made to stir at a temperature of 70 ^{0}C as outlined in Scheme 2.

The NMR spectrum of compound **5** was relatively simple and similar to compound **6**. Analysis of the ^{1}HNMR spectrum (Figure S1) indicated the presence of six peaks. Four of the peaks are found in the aromatic region of the spectrum. All the peaks in the aromatic region appeared as doublets with equal intensities at 7.95, 7.60, 7.12 and 6.68 ppm, respectively. Each of the peaks integrates to give a total of four protons and a grand total of sixteen protons are observed in the aromatic region. The $^{13}C\{^{1}H\}$ NMR spectrum (Figure S2) showed ten carbon environments. Low resolution electrospray mass spectroscopy, conducted in positive and negative modes led to the decomposition of the compound. The use of orbitrap spectroscopy led to the identification of

the mass of the compound. The formation of the urea and thiourea derivatives of 1,3-bis(4-amino-phenoxy)-1,1,3,3-tetramethyldisiloxane **3** has been a success. The compounds have been relatively stable in many organic solvents and water, without the rupturing of the tetramethylsiloxy functionality. Problems due to steric hindrance of bulky reagents have not been experienced.

Having successfully synthesised the amine tetramethylsiloxy functionality, amides of 1,3-bis(4-amino-phenoxy)-1,1,3,3-tetramethyldisiloxane were synthesised to facilitates the comparison of the chemistry of 1,3-bis[4'-(3 "-(4-nitrophenyl)ureido)phenoxy]-1,1,3,3-tetramethyldisiloxane (**5** or **6**) to 1,3-Bis[4'-(3"-(4-nitrobenzamido)phenoxy]1,1,3,3-tetramethyl-disiloxane (**8**) compound, as very stable urea and thiourea compounds. Amides of 1,3-bis(4-amino-phenoxy)-1,1,3,3-tetramethyldisiloxane (**8-12**) were also synthesized by reacting two equivalents of appropriate reagents eg. 4-nitrobenzoyl chloride with one equivalent of 1,3-bis(4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane in toluene-pyridine mixture according to the reaction route in scheme 3.

The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of amides compounds (**8-12**) showed the expected resonances. For example, the ^{1}H NMR spectrum of the solid product **8** was very neat and gave six distinct peaks as expected. The presence of the -NH protons was indicated as a sharp singlet at 10.20 ppm, (two protons).

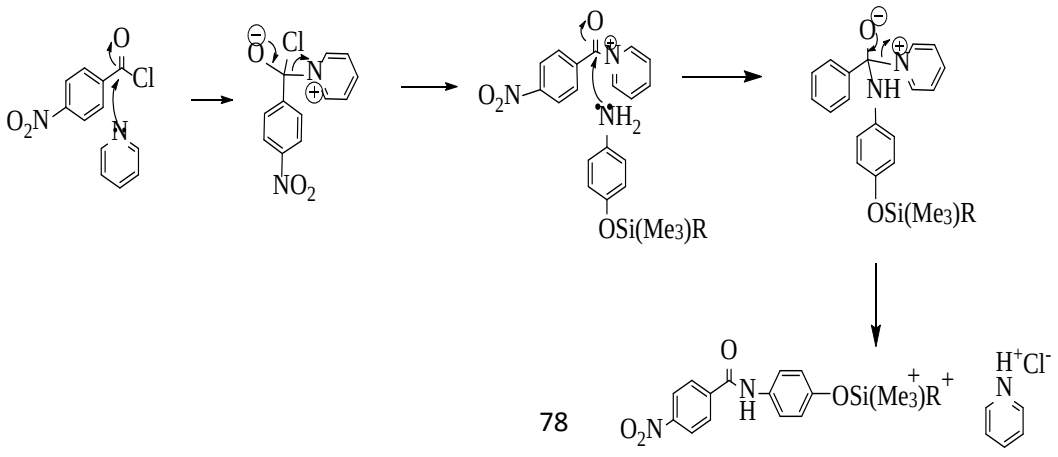


Scheme 3: Synthesis of amide of 1,3-bis(4-amino-phenoxy)-1,1,3,3-tetramethyldisiloxane.

The presence of the -NH group was also exchangeable with D_2O signal at 10.20 ppm in the ^{1}H NMR spectrum and was further confirmed by the characteristic N-H stretching vibration at 3339-2988 cm^{-1} in the IR spectrum. Four doublets of equal intensity were observed in the aromatic region of the ^{1}H NMR spectrum. The aromatic protons adjacent to the nitro group appeared as a doublet at 8.10 ppm (four protons), (J = 7.9 Hz) and the aromatic protons adjacent to the carbonyl functional group absorbed as a doublet at 7.90 ppm (four protons), (J = 7.9 Hz). These

aromatic protons were shifted more downfield due to the presence of the nitro and carbonyl groups present on the aromatic ring. The other two doublets were well spaced absorbing at 7.40 ppm (four protons), (J = 8.2 Hz) and 6.6 ppm (four protons), (J = 8.2 Hz) signifying protons adjacent to the –NH and tetramethylsiloxy groups respectively. The tetramethylsiloxy protons were observed at 0.00 ppm (twelve protons).

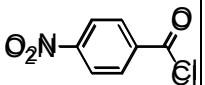
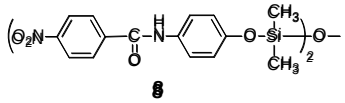
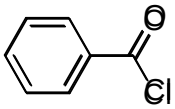
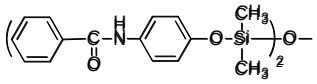
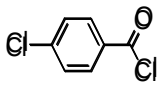
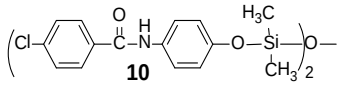
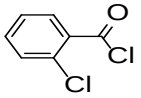
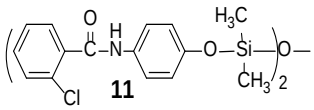
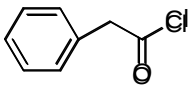
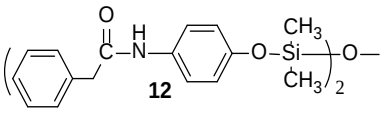
The analysis of the $^{13}C\{^{1}H\}$ NMR spectrum indicated ten carbon environments. The carbonyl signal was observed at 164 ppm (**C**=O). Eight of the ten carbons were observed in the aromatic chemical shift range of 120-151 ppm. Four quaternary carbons were observed at 151, 149.7, 141.3 and 134 ppm respectively. The other four aromatic carbons were observed at 129.7, 124.1, 122.9 and 120 ppm. The infra-red spectrum of compound **8** revealed important functional groups. The amide functional group was signified by a sharp peak at 1647 cm^{-1} (C=O bonding) [20]. The Si-CH_3 group was recognised by a strong sharp band at about 1264 cm^{-1} coupled with a peak in the fingerprint region between 807 cm^{-1} attributed to bending and rocking modes of the Si−CH_3 groups [14]. The siloxane linkage (Si-O-Si) showed up as a very strong single band of infrared at 1057 cm^{-1} [14-18]. The symmetrical ($ArNO_2$) N=O stretch was observed at 1346 cm^{-1} respectively, as well as the ($ArNO_2$) C-N stretch absorbing at 856 cm^{-1}. High resolution mass spectral data for compound **8, 9, 10** and **12** at m/z = 647.2064, 556.1801, 626.5410 and 587.2140 were further evidence that pure products were isolated. The mechanism of action for the reaction of 4-nitrobenzoyl chloride and 1,3-bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane is illustrated in Scheme 4. The mechanism of reaction was viewed as a nucleophilic attack by pyridine on the acyl chloride forming a highly electrophilic intermediate. The intermediate eventually reacted with the amine to form the amide. The pyridine acted both as a scavenger for the hydrogen chloride as well as speeding the reaction [21].

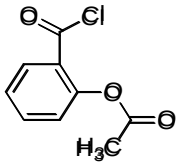
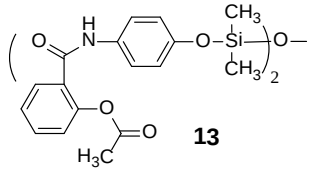
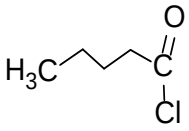
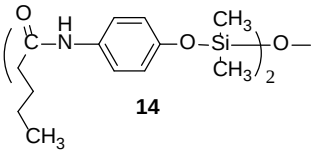
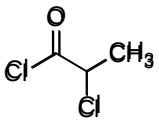
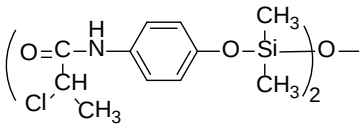


Scheme 4: Acylation of 4-nitrobenzoyl chloride with 1,3-bis(4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane

Following the successful synthesis of the amides of 1,3-bis(4-amino-phenoxy)-1,1,3,3-tetramethyldisiloxane (**8-13**) (Table 1) with compounds with phenyl functionality, the need to prepare amides with aliphatic functionality was considered in order to compare their reactivity and gain insight to their mechanism. Valeroyl chloride was chosen as the aliphatic acid chloride compound**.** The reaction route in scheme 4 was followed to synthesize the target molecule **14** and **15** (Table 1).

Table 1: 1,3-Bis (4-aminophenoxy)-1,1,3,3-tetramethyldisiloxane compounds with Amide functionality

Entry	Substrate	Product	Yield %; MP (^{0}C)
1		 **8**	75; 205
2		 **9**	59; 214
3		 **10**	25; 210
4		 **11**	17.4; 117
5		 **12**	35.4

6		 **13**	56.7
7		 **14**	43.4; 127
8		 **15**	28; 135

Conclusions

In summary, a series of poly-functionalized siloxane-based compounds, containing amine and amide pendant, compounds with known germicidal, bactericidal, analgesic and antibiotic properties with silicon-bridged moieties, have been obtained via the coupling reaction of an isocyanate and diamino compound and structurally characterized. The synthetic work has primarily involved the silylation reactions in which the 1,1,3,3-tetramethyldisiloxane functionality has been incorporated into selected reagents to obtain the targeted compounds (**5-15**). Dimerisation of the tetramethylsiloxy and tetraisopropylsiloxy functionalities has been observed in a few cases as well as the rupturing of the tetramethylsiloxy group. Therefore, the facile method of engineering poly-functionalized siloxane-based compounds, containing amine and amide pendant, may have interesting wide applications in the therapeutic application.

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