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Synthesis and Structural Chacterization of Isomeric Silatranes of Unsymmetrical Alkoxysilanes via 'Click Silylation'

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Abstract. A series of new silatranes (7a-c) having azomethine and 1, 2, 3-triazole units have been synthesized from polyfunctionalised unsymmetrical alkoxysilanes (6a-c) precursors. These silatranes are the first compounds of this type and hydrolytically more stable than their open chain trialkoxysilanes analogues (6a-c). Azomethine part have wide range of applications in the field of biochemistry, medicines and in agriculture. Similarly 1, 2, 3-triazole unit also attract very much attention of researchers due to their broad spectrum of applications. The structures of 6a-c and 7a-c were characterized by infrared (FT-IR) and NMR (^{1}H and ^{13}C) spectroscopy studies. The spectral data indicates strong conformation of new synthesized compounds. These newly synthesized compounds (7a-c) bearing both azomethine and 1, 2, 3-triazole moieties can show numerous applications in the field of pharmaceutical science, agriculture and in material science in future. Herein authors are reporting the synthesis of these compounds.

Keywords: Trialkoxysilane, silatrane, click-silylation, schiff base, triazole, [Cu Br $(PPh_3)_3$].

1. Introduction

Recently, silatranes gained great interest worldwide due to specific arrangement of atom [1]. Silatranes, cyclic organosilicon ethers of tris-(2-oxyalkyl) amines or their derivatives X-Si$[OCHYCH_2]_3N$, (Y = H, CH_3), have stretch applications [2]. The immense interest of researchers in these compounds was induced by their unusual polyhedral structure [3], existence of a pantavalent X-Si-N segment, specific physical properties such as distinctive reactivity, and a wide range of biological activity [4]-[8]. Specifically azomethine (-CH=N) linkage, derived from N-amino and carbonyl compounds, have been reported in literature are an important class of ligands showing numerous biological applications[9]-[10]. 1, 2, 3-triazole is also an principal scaffold getting extensive popularity now a days due to their pharmacology importamnce [11]. Many methodologies for synthesizing triazolyl segment e have been reported in literature [12], but best results are obtained via 'click chemistry reaction' i.e. CuAAC (copper catalyzed azide alkyne cycloaddition) reaction of azide–alkyne fragments to 1, 2, 3- triazole with 98% conversion of reactants into products [13].

Herein, we report an isomeric organosilatranes series having azomethine and 1, 2, 3-triazole units via 'click-silylation' [14]. This synthetic perspective generates polyfunctionalised triethoxysilanes (PfTES), which are precursors [15] to these silatranes comprising azomethine and 1, 2, 3-triazole. From the utility point of view, these hybrid silatranes can extend their applications to a broad spectrum in the field of drug discovery, catalysis, surface coating of materials, agriculture, polymer formation, ion-detecting fluorescent probes, anti-HIV, antiviral, antimycobacterial, anticancer, activities.

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2. Experimental

2.1 General material and methods

All the synthesis was carried out under a dry nitrogen atmosphere using a glass vacuum line. The organic solvents were dried and purified according to the standard procedure [16] and stored under a dry nitrogen atmosphere. Bromotris-(triphenylphosphine) copper (I) (Aldrich), 3-chloropropyltriethoxysilane (ClPTES) (Aldrich), propargyl bromide (80 wt% solution in toluene) (Aldrich), sodium azide (SDFCL), potassium carbonate (Thomas Baker), and N, N-dimethylformamide (SDFCL) were used as supplied. Salicylaldehyde (Aldrich), 3-hydroxybenzaldehyde (SDFCL), 4-hydroxybenzaldehyde (SDFCL), were used as supplied for the synthesis of the terminal alkynes. 3-Azidopropyltriethoxysilane (AzPTES) was synthesized according to known literature procedure [17]. All the synthetic procedure for the synthesis unsymmetrical silatranes are described in Fig. 1.

2.2 Synthesis of terminal alkynes (2a-c)

The o-, m-, p- salicylaldehyde (commercially available) were alkylated with propargyl bromide (80% solution in toluene) (1.3 equiv) using DMF as solvent and K_2CO_3 (5.0 equiv) for 16 h at room temperature. The alkylated product was separated using ethyl acetate and brine. Final product was obtained in 90% yield after filtration over anhydrous magnesium sulphate and dried under vacuum.

The synthesis of different positional isomers, alkylated schiff based trialkoxysilane (3a-c), was carried out under a dry nitrogen atmosphere using a glass vacuum. To uniformly stirred solution of terminal alkyn (1.0 mmol in ethanol, the APTES (1mmol) was added and the mixture was refluxed azeotropicaly for 4 hours. The solvent was evaporated by vacuum evaporation to obtain the desired products (3a-c).

2.3 Synthesis of 3–azidopropyltriethoxysilane (AzPTES)

To the stirred solution of sodium azide (11.0 g, 169.23 mmol) in DMF (80.0 ml) 3–chloropropyltriethoxysilane (4) (10.0 g, 41.66 mmol) was added drop wise under inert dry nitrogen atmosphere. The reaction mixture was stirred at 90 ℃ for 4 h. Removal of dimethylformamide was carried out under reduced pressure. The crude mixture was then diluted with diethylether and filtered under inert atmosphere. The diethyl ether was removed under vacuum and the crude oil obtained was distilled under reduced pressure resulting into AzPTES colorless liquid. Yield: 6.20 ml, 61%, colourless oil, Empirical formula: $C_9H_{21}N_3O_3Si$ ^{1}H NMR (300 MHz, $CDCl_3$) δH = 3.74 (q, *J* = 7.0 Hz, 6H), 3.19 (t, *J* = 6.9 Hz, 2H), 1.73 – 1.51 (m, 2H), 1.16 (t, *J* = 7.0 Hz, 9H), 0.63 – 0.51 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$) δ_C = 58.2, 53.7, 22.7, 18.4, 7.8 IR (Neat, cm^{-1}): 2974, 2927, 2885, 2093, 1442, 1389, 1073, 953, 775.

2.4 Synthesis of unsymmetrical trialkoxysilane (6a-c)

Isomeric unsymmetrical trialkoxysilane (6a-c) were synthesized under a dry nitrogen atmosphere using a glass vacuum line. To a stirred solution of AzPTES (1.0 mmol) in THF, newly synthesized compounds (3a-c) (1.0 mmol), Et_3N (3.0 equiv), Cu $(PPh_3)_3Br$ (cat. amt.) and stirred for 10 h at 60 ℃. The solvent was removed under vacuum and the crude oil obtained as a desired product (6a-c).

2.5 Synthesis of silatranes (7a-c)

Isomeric silatranes (7a-c) were synthesized under a dry nitrogen atmosphere using a glass vacuum line. To a stirred solution of newly synthesized Isomeric unsymmetrical trialkoxysilane (1mmol) in toluene, triethanolamine (2 mmol/ 6a–c) was added drop wise and KOH added in a catalytic amount to the mixture. The mixture was refluxed for 6 hours and after completion of reaction was allowed to cool at room temperature. The solvent volume in mixture was reduced to 3.0 ml by vacuum evaporation and addition of 10.0 ml of n–pentane resulted into separation of slightly colored solid. The solid so obtained was stirred for 2 days, filtered and washed with 2 x 5 ml n–pentane to afford titled compounds (7a-c).

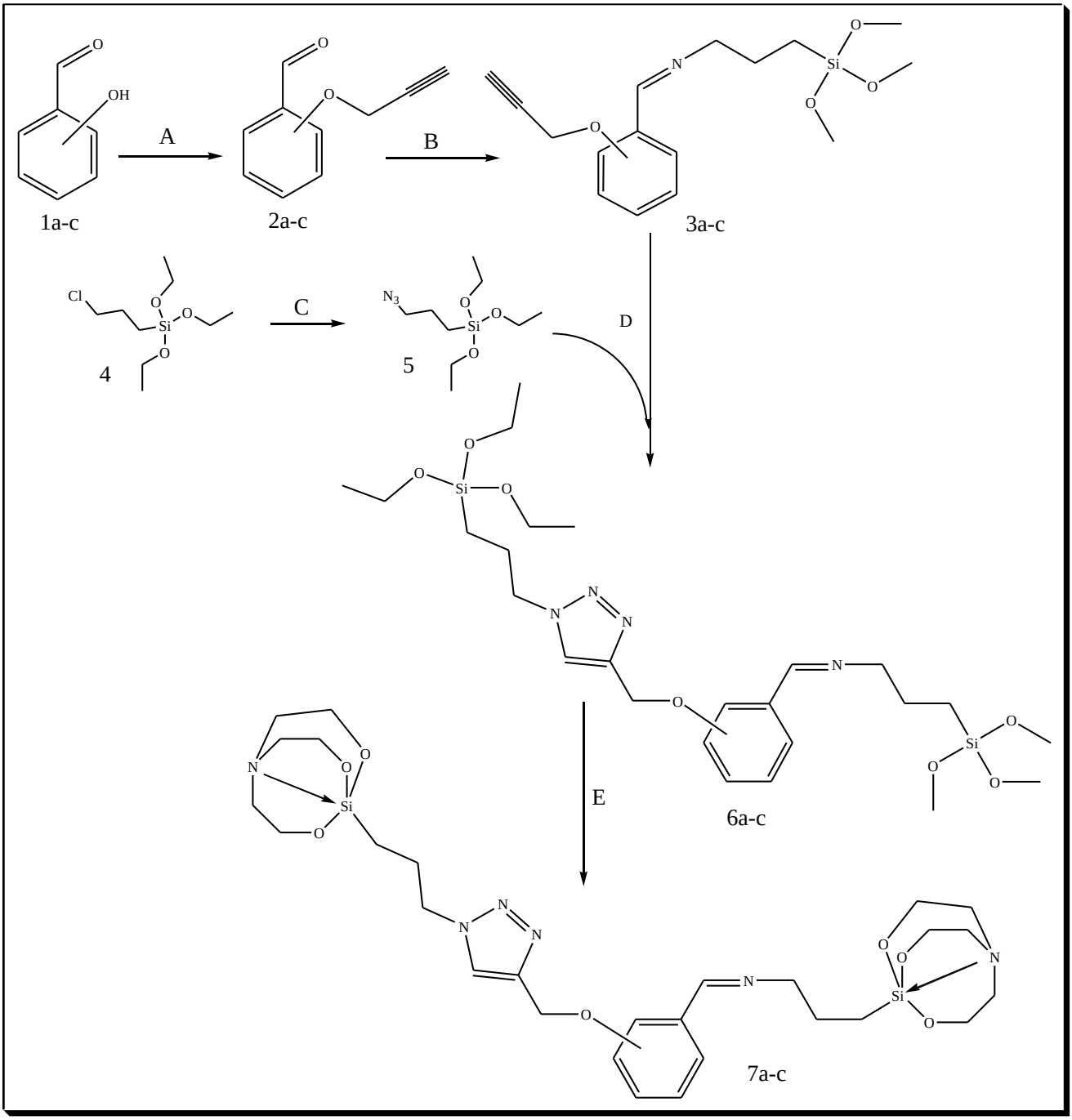

Fig. 1: General synthetic design of unsymmeterical alkoxysilanes (6a-c) and silatranes (7a-c) containing azomethine and triazoles via click-silylation reaction. Reagents and conditions: (1a-c) o-, m-, p- isomers of salicylaldehyde (A) propargyl bromide, K_2CO_3, DMF, 15 h. (B) APTES, C_2H_5OH, 4h, reflux. (C) ClPTES, sodium azide, DMF, 4 h, 80 ℃, (D) AzPTES, $Cu(PPh_3)_3Br$, Et3N, THF, 10 h, 60 ℃, (E) triethanolamine, KOH, toluene, 111 ℃, 12 h.

6a (o-isomer)

Yield 85%, pale yellow oil, ^{1}HNMR (300 MHz, $CDCl_3$, 25 ℃) δ_H = 8.21(s, 1H, CH=N), 7.65-7.05 (m 4H-Ar), 5.02 (s, 1H), 4.60 (s, 2H), 4.26 – 4.04 (t, *J* = 4.8 Hz, 2H), 3.87(s, 9H), 3.50(m, 6H), 2.45 (t, *J* = 5.8 Hz, 2H) 1.91 – 1.80 (m, 2H), 1.60 (m, 2H) 1.10 (t, *J* = 3.5 Hz, 9H), 0.38 – 0.17 (m, 4H).^{13}CNMR (300 MHz, $CDCl_3$, 25 ℃), δ_C = 148.3, 144.2, 128.9, 127.3, 121.1, 115.3, 112.8, 52.2, 50.7, 45.4, 27.3, 11.2. . IR (Neat, cm^{-1}): 2922, 2870, 1909, 1665, 1459, 1234, 1225, 1099, 1091, 915, 850,520.

6b (m-isomer)

Yield 78%, colorless oil, ^{1}HNMR (300 MHz, $CDCl_3$, 25 ℃) δ_H = 8.11(s, 1H, CH=N), 7.65-7.11 (m 4H-Ar), 5.32 (s, 1H), 4.42 (s, 2H), 4.26 – 4.04 (t, *J* = 4.8 Hz, 2H), 3.87(s, 9H), 3.50(m, 6H), 2.45 (t, *J* = 5.8 Hz, 2H) 1.91 – 1.80 (m, 2H), 1.60 (m, 2H) 1.05 (t, *J* = 4.2 Hz, 9H), 0.38 – 0.17 (m, 4H).^{13}CNMR (300 MHz, $CDCl_3$, 25 ℃), δ_C = 147.3, 143.6, 128.2, 127.3, 121.1, 116.3, 112.4, 52.1, 49.7, 45.4, 25.3, 12.2. IR (Neat, cm^{-1}): 2900, 2785, 1560, 1506, 1390, 1245, 1215, 1169, 1069, 983, 810, 735, 646.

6c (p-isomer)

Yield 90%, colorless oil, ^{1}HNMR (300 MHz, $CDCl_3$, 25 ℃) δ_H = 8.21(s, 1H, CH=N), 7.75-7.31 (m 4H-Ar), 5.30 (s, 1H), 4.42 (s, 2H), 4.26 – 4.04 (t, *J* = 4.8 Hz, 2H), 3.77(s, 9H), 3.58(m, 6H), 2.45 (t, *J* = 5.8 Hz, 2H) 1.91 – 1.80 (m, 2H), 1.60 (m, 2H) 1.22 (t, *J* = 4.2 Hz, 9H), 0.38 – 0.17 (m, 4H).^{13}CNMR (300 MHz, $CDCl_3$, 25 ℃), δ_C = 146.3, 144.6, 127.2, 126.9, 120.1, 116.3, 113.4, 53.1, 49.8, 45.4, 25.5, 13.3. IR (Neat, cm^{-1}): 3016, 2965, 1926, 1620, 1589, 1469, 1362, 1285, 1189, 1075, 958, 875, 714, 542.

7a (o- isomer)

3-(2,8,9-trioxa-5-aza-1-sila-bicyclo[3.3.3]undecan-1-yl)-N-(2-((1-(3-(2,8,9-trioxa-5-aza-1-sila-bicyclo[3.3.3]undecan-1-yl)propyl)-1H-1,2,3-triazol-4-yl)methoxy)benzylidene) propan-1-amine. Yield 90%, white solid, mpt 221-225 ℃, ^{1}HNMR (300 MHz, $CDCl_3$, 25 ℃) δ_H = 8.10(s, 1H, CH=N), 7.35-7.23 (m 4H-Ar), 5.10 (s, 1H), 4.57 (s, 2H), 4.26 – 4.04 (t, *J* = 4.8 Hz, 2H), 3.67 (t, *J* = 5.8 Hz, 12H), 2.74 (t, *J* = 5.8 Hz, 12H), 2.45 (t, *J* = 5.8 Hz, 2H) 1.91 – 1.80 (m, 2H), 1.60 (m, 2H) 0.38 – 0.17 (m, 4H).^{13}CNMR (300 MHz, $CDCl_3$, 25 ℃), δ_C = 147.3, 143.6, 128.2, 127.3, 121.1, 116.3, 112.4, 52.1, 49.7, 45.4, 25.3, 12.2. IR (Neat, cm^{-1}): 2942, 2875, 1599, 1505, 1289, 1294, 1215, 1104, 1091, 923, 877, 760.

7b (m- isomer)

3-(2,8,9-trioxa-5-aza-1-sila-bicyclo[3.3.3]undecan-1-yl)-N-(3-((1-(3-(2,8,9-trioxa-5-aza-1-sila-bicyclo[3.3.3]undecan-1-yl)propyl)-1H-1,2,3-triazol-4-yl)methoxy)benzylidene) propan-1-amine. Yield 84%, white solid, mpt 212-214 ℃, ^{1}HNMR (300 MHz, $CDCl_3$, 25 ℃) δ_H = 8.10(s, 1H, CH=N), 7.50-7.05 (m 4H-Ar), 5.10 (s, 1H), 4.57 (s, 2H), 4.26 – 4.04 (t, *J* = 4.8 Hz, 2H), 3.67 (t, *J* = 5.8 Hz, 12H), 2.74 (t, *J* = 5.8 Hz, 12H), 2.45 (t, *J* = 5.8 Hz, 2H) 1.91 – 1.80 (m, 2H), 1.60 (m, 2H) 0.38 – 0.17 (m, 4H). ^{13}CNMR (300 MHz, $CDCl_3$, 25 ℃), δ_C = 147.3, 143.6, 128.2, 127.3, 121.1, 116.3, 112.4, 52.1, 49.7, 45.4, 25.3, 12.2. IR (Neat, cm^{-1}): 2972, 2885, 1599, 1505, 1389, 1294, 1215, 1164, 1071, 953, 877, 780.

7c (p- isomer)

3-(2,8,9-trioxa-5-aza-1-sila-bicyclo[3.3.3]undecan-1-yl)-N-(4-((1-(3-(2,8,9-trioxa-5-aza-1-sila-bicyclo[3.3.3]undecan-1-yl)propyl)-1H-1,2,3-triazol-4-yl)methoxy)benzylidene) propan-1-amine. Yield 92%, white solid, mpt 189-194 ℃, ^{1}HNMR (300 MHz, $CDCl_3$, 25 ℃) δ_H = 8.10(s, 1H, CH=N), 7.35 (dd, *J* = 12.0 Hz 2H-Ar), 7.10 (dd, *J* = 15.1 Hz, 2H-Ar),5.10 (s, 1H), 4.57 (s, 2H), 4.26 – 4.04 (t, *J* = 4.8 Hz, 2H), 3.67 (t, *J* = 5.8 Hz, 12H), 2.74 (t, *J* = 5.8 Hz, 12H), 2.45 (t, *J* = 5.8 Hz, 2H) 1.91 – 1.80 (m, 2H), 1.60 (m, 2H) 0.38 – 0.17 (m, 4H). ^{13}CNMR (300 MHz, $CDCl_3$, 25 ℃), δ_C = 147.3, 143.6, 128.2, 127.3, 121.1, 116.3, 112.4, 52.1, 49.7, 45.4, 25.3, 12.2. IR (Neat, cm^{-1}): 3015, 2985, 1589, 1621, 1158, 1226, 1300, 1125, 1041, 923, 875, 750, 542.

3. Results and Discussion

In our methodology, we have widened the scope of click reaction to other functional groups giving the versatility of the method. Herein, CuAAC reactions proceeded smoothly to synthesize high yield and products formed were characterized using IR, 1H and 13C NMR spectroscopy.

IR spectra

The IR spectra predicted that the characteristic bands of the azido group (-N=N=N, 2091 cm^{-1}) and alkyn groups (CC, 3279 and 2102 cm^{-1}) are absent after the click reaction. The absorption band at 2091 cm^{-1} disappeared from the spectra of 1, 2, 3-triazole incorporated compounds. This indicates high efficiency of the click reaction.

NMR spectra

1H NMR spectra of triazoles linkers exhibit a triplet around δ_H=1.14 ppm and a quartet roughly at δ_H=3.65 ppm corresponding to -CH3 and -OCH2- of triethoxysilyl moiety, respectively. The downfield shift of triplet of $-N_3CH_2-$ protons from δ_H=3.19 to δ_H= 4.19-4.31 ppm signifies the C-N bond formation resulting into 1, 2, 3-triazole. Azomethine (-CH=N) proton appears at δ_H=8.05-8.21 ppm and –CHO proton of salicylaldehyde is absent from δ_H=9.98 ppm which confirms the schiff base formation.

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5. Conclusions

We have successfully synthesized a new series of isomeric unsymmetrical trialkoxysilane (6a-c) and their corresponding silatranes (7a-c) contain azomethine and triazoles moieties based on the combinatorial technique between organosilicon chemistry and click chemistry reaction. Silatranes (7a-c) are synthesized first time in high yield having stability and sufficient solubility in organic solvents. This opens up the new era for such silicon compounds; to be used significantly in synthetic decoration of alkyne based DNA, peptides, proteins, oligosaccharides, G-quadruplex structures, agricultural field and pharmaceutical industry.

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