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Synthesis of novel 1,2,3-triazole based silatranes via "click silylation"

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ABSTRACT

A single step reaction for the synthesis of novel 1,2,3-triazole based silatranes (TBS)-scaffolds (**2a**–**2o**) using polyfunctionalised organotriethoxysilanes (**1a**–**1l**) as precursors is described. The synthesized silatranes are the first compounds of this type and hydrolytically more stable than their open chain analogues. The structures of **2a**–**2o** were characterized by IR, NMR (^{1}H and ^{13}C) and mass spectroscopy studies.

Introduction

"Click chemistry" has been honoured as a library of versatile spring loaded reactions that offer covalent assembly of smaller fragments to complex molecules [1–4]. Initiated by the incredible invention of Cu(I) catalysed azide-alkyne cycloaddition reaction (CuAAC), the dummy of 1,2,3-triazole moiety has emerged as a powerful heterocycle in modern chemical and pharmaceutical research [5]. Since innovation, the applications into various research fields have been wholesaled due to its reliability, specificity and biocompatibility [6].

Click reaction is one of the best choices for the design of sophisticated biomaterials requiring high levels of precision and control [7]. One of the key intermediate for the synthesis of such hybrid materials is substituted organotrialkoxysilane [8–14]. We have recently reported "click silylation" to en-cap the precursor triethoxysilanes with wide range of functional groups [15]. Therefore, permutation of click with organosilicon chemistry has resulted into a powerful strategy for the preparation of functional hybrid materials. In order to establish the utility of 1,2,3-triazole based triethoxysilane (TBTES)-linkers, they were used as precursors for the synthesis of various silatranes, that can find numerous applications in biomaterials, catalysis and sol–gel chemistry [16–18].

We herein report an interesting application of the click reaction to organosilicon chemistry with the aim to assemble a small series of well defined 1,2,3-triazole based silatrane (TBS)-scaffolds, that offers a number of imperative advantages. Primarily, this is a general method which could be readily extended to an extensive range of materials, including proteins, micelles, dye molecules and hybrid biomaterials [19–22]. Secondly, unlike triethoxysilanes, assembled TBS-scaffolds are hydrolytically more stable [23,24]. On the tertiary part, the ability of the all nitrogen atoms of 1,2,3-triazole and oxygen atoms of silatrane ring to act as a hydrogen bond acceptor even makes it more attractive in supramolecular chemistry. Therefore, TBS-scaffolds would give boost to ongoing research in the field of "click" and "organosilicon chemistry".

Materials and methods

General reaction procedure for the click silylation

To a 50.0 ml two-necked round bottom flask with alkyne function (2 mmol), azide function (2 mmol/alkyne function), $[CuBr(PPh_3)_3]$ (0.01 mmol/alkyne function), triethylamine (2.0 ml), and THF (2.0 ml) under nitrogen atmosphere and then the mixture was stirred at 60 °C for 5 h. The reaction mixture was allowed to cool, and the solvents were removed under vacuum followed by addition of hexane. The mixture was filtered and washed with 2 × 5.0 ml of hexane. The concentration of the filtrate under reduced pressure afforded the title compound in good to excellent yield.

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General procedure for the synthesis of silatranes

To the stirred solution of trisalkoxyamine (2 mmol) in toluene (50.0 ml), catalytic amount of potassium hydroxide was added, in apparatus fitted with dean stark assembly. After stirring it for 10 min, substituted triethoxysilane (2 mmol/trisalkoxyamine) was added dropwise within 2 min. The reaction mixture was then refluxed at 110 °C for 5 h. Then, the reaction mixture was allowed to cool and toluene was removed by vacuum evaporation and on slow addition of hexane (5.0 ml), white solid precipitated out. The contents were further stirred for 4 h at room temperature. The solid was filtered and washed twice with diethylether (2 × 5.0 ml) and dried under vacuum.

2a: M.pt.: 137 °C. Yield: 78%. IR (neat, cm^{-1}): 2920, 2870, 1682, 1589, 1454, 1438, 1392, 1212, 1160, 1087, 1020, 939, 847, 775, 712, 702, 655, 584, 531. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 10.41 (s, 1H), 7.76–6.97 (m, 5H), 5.25 (s, 2H), 4.28 (t, J = 6 Hz, 2H), 3.68 (t, J = 3 Hz, 6H), 2.74 (t, J = 3 Hz, 6H), 1.97–1.88 (m, 2H), 0.37–0.32 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 189.9, 160.8, 142.8, 136.0, 128.5, 122.8, 121.2, 113.2, 62.7, 57.5, 53.4, 50.9, 26.2, 13.0. MS (*m*/*z*, assignment): 459 (20.7), 458 (26.6), 457 (100), 441 (73.1), 419 (27.4), 297 (21.7), 215 (5.5), 192 (6.8), 174 (24.1), 172 (9.5), 150 (5.0). HRMS (ES^+) calcd for $C_{19}H_{26}N_4O_5Si$ $[M + K]^+$ 457.1309, found 457.1317.

2b: M.pt.: 127 °C. Yield: 78%. IR (neat, cm^{-1}): 2973, 2926, 2884, 1690, 1599, 1507, 1438, 1390, 1251, 1159, 1099, 1072, 955, 759, 605, 541. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 9.79 (s, 1H), 7.74 (d, J = 8.7 Hz, 2H), 7.56 (s, 1H), 7.03 (d, J = 8.6 Hz, 2H), 5.20 (s, 2H), 4.25 (t, J = 7.4 Hz, 2H), 3.65 (t, J = 5.8 Hz, 6H), 2.71 (t, J = 5.8 Hz, 6H), 1.94–1.83 (m, 2H), 0.30–0.25 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 195.6, 160.8, 142.8, 130.6, 122.5, 114.7, 62.7, 57.6, 53.3, 51.3, 26.2, 12.9. MS (*m*/*z*, assignment): 459 (20.7), 458 (26.6), 457 (100), 441 (73.1), 419 (27.4), 297 (21.7), 215 (5.5), 192 (6.8), 174 (24.1), 172 (9.5), 150 (5.0). HRMS (ES^+) calcd for $C_{19}H_{26}N_4O_5Si$ $[M + K]^+$ 457.1309, found 457.1315.

2c: M.pt.: 127 °C. Yield: 78%. IR (neat, cm^{-1}): 2975, 2925, 2883, 1660, 1596, 1488, 1454, 1366, 1299, 1172, 1152, 1119, 1072, 954, 770, 759, 617, 566, 530. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.67–7.60 (m, 1H), 7.60 (s, 1H), 7.42–6.95 (m, 3H), 5.23 (s, 2H), 4.28 (t, J = 7.4 Hz, 2H), 3.69 (t, J = 5.8 Hz, 6H), 2.74 (t, J = 5.8 Hz, 6H), 2.51 (s, 3H), 1.98–1.88 (m, 2H), 0.39–0.25 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 189.8, 183.0, 142.5, 133.2, 129.8, 120.5, 102.8, 65.4, 62.1, 56.9, 52.8, 50.3, 25.7, 12.6. MS (*m*/*z*, assignment): 472 (20.4), 471 (100), 455 (82.3), 433 (97.2), 391 (7.8), 279 (9.2), 215 (6.1), 174 (14.9), 150 (15.0), 132 (4.0). HRMS (ES^+) calcd for $C_{20}H_{28}N_4O_5Si$ $[M + K]^+$ 471.1466, found 471.1454.

2d: M.pt.: 96 °C. Yield: 73%. IR (neat, cm^{-1}): 2985, 2925, 2883, 1658, 1566, 1488, 1454, 1366, 1299, 1172, 1152, 1119, 1072, 954, 770, 627, 571, 535. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.83 (d, J = 8.6 Hz, 2H), 7.55 (s, 1H), 6.94 (dd, J = 8.6 Hz, 2H), 5.18 (s, 2H), 4.24 (t, J = 7.4 Hz, 2H), 3.65 (t, J = 5.7 Hz, 6H), 2.71 (t, J = 5.7 Hz, 6H), 2.46 (s, 3H), 1.91–1.86 (m, 2H), 0.32–0.26 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 189.8, 183.1, 142.6, 131.9, 130.5, 122.6, 115.3, 73.3, 62.6, 57.7, 53.4, 51.3, 26.2, 12.9. MS (*m*/*z*, assignment): 472 (20.4), 471 (100), 455 (82.3), 433 (97.2), 391 (7.8), 279 (9.2), 215 (6.1), 174 (14.9), 150 (15.0), 132 (4.0). HRMS (ES^+) calcd for $C_{20}H_{28}N_4O_5Si$ $[M + K]^+$ 471.1466, found 471.1458.

2e: M.pt.: 144 °C. Yield: 78%. IR (neat, cm^{-1}): 3132, 2945, 2868, 2823, 1656, 1597, 1535, 1435, 1350, 1218, 1034, 886, 763, 695. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.43 (s, 1H), 4.23 (t, J = 7.7 Hz, 2H), 3.69 (t, J = 5.8 Hz, 6H), 3.52 (s, 2H), 2.74 (t, J = 5.8 Hz, 6H), 2.20 (s, 6H), 1.97–1.86 (m, 2H), 0.33–0.38 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 144.6, 122.1, 56.7, 54.1, 52.1, 50.1, 45.9, 24.0, 13.2. MS (*m*/*z*, assignment): 381 (2.4), 380 (13.0), 364 (18.3), 343 (21.0), 342 (100), 206 (10.0), 174 (37.6), 172 (67.0). HRMS (ES^+) calcd for $C_{14}H_{27}N_5O_3Si$ $[M + H]^+$ 342.1961, found 342.1977.

2f: M.pt.: 137 °C. Yield: 76%. IR (neat, cm^{-1}): 3132, 2971, 2927, 2884, 1551, 1438, 1389, 1294, 1214, 1165, 1099, 1072, 954, 876, 780. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.30 (s, 1H), 4.27 (t, J = 6 Hz, 2H), 3.76 (t, J = 5.8 Hz, 6H), 2.81 (t, J = 5.8 Hz, 6H), 2.66 (t, J = 7.4 Hz, 2H), 2.0–1.92 (m, 2H), 1.72–1.63 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H), 0.47–0.38 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 147.7, 120.6, 57.6, 53.3, 51.0, 27.8, 26.4, 22.3, 13.9, 13.3. MS (*m*/*z*, assignment): 365 (15.9), 349 (34.3), 328 (41.2), 327 (100), 285 (18.5), 233 (16.5), 206 (22.7), 174 (27.9), 172 (25.4), 150 (11.7), 132 (6.5). HRMS (ES^+) calcd for $C_{14}H_{26}N_4O_3Si$ $[M + H]^+$ 327.1882, found 327.1870.

2g: M.pt.: 97 °C. Yield: 77%. IR (neat, cm^{-1}): 3370, 2930, 2874, 1735, 1577, 1485, 1414, 1271, 1183, 1120, 1096, 1034, 1010, 820, 797, 775, 671, 620, 577. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.52 (d, J = 16.8 Hz, 1H), 5.12 (s, 2H), 4.25 (t, J = 8.1 Hz, 2H), 3.69 (t, J = 5.8 Hz, 6H), 2.75 (t, J = 5.8 Hz, 6H), 2.0 (s, 3H), 1.97–1.89 (m, 2H), 0.38–0.32 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 196.1, 195.4, 126.7, 126.1, 123.7, 61.0, 57.6, 53.4, 51.1, 26.2, 13.1. MS (*m*/*z*, assignment): 396 (14.8), 395 (100), 379 (43.6), 357 (18.7), 353 (10.0), 315 (22.6), 297 (7.3), 273 (7.0), 216 (3.7), 206 (11.0), 192 (12.0), 174 (27.7). HRMS (ES^+) calcd for $C_{14}H_{24}N_4O_5Si$ $[M + K]^+$ 395.1153, found 395.1142.

2h: M.pt.: 127 °C. Yield: 76%. IR (neat, cm^{-1}): 2973, 2929, 2887, 1724, 1634, 1439, 1407, 1295, 1267, 1180, 1045, 957, 809, 782. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.58 (s, 1H), 6.37 (d, J = 17.2 Hz, 1H), 6.16-5.92 (m, 1H), 5.78 (d, J = 10.5 Hz, 1H), 5.24 (s, 2H), 4.29 (t, J = 7.1 Hz, 2H), 3.74 (t, J = 6.9 Hz, 6H), 2.80 (t, J = 6.9 Hz, 6H), 2.02–1.79 (m, 2H), 0.67–0.39 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 165.3, 142.3, 130.8, 128.1, 123.6, 58.2, 57.5, 52.1, 24.0, 18.1, 7.3.

2i: M.pt.: 204–205 °C. Yield: 73%. IR (neat, cm^{-1}): 2973, 2926, 2884, 1690, 1599, 1507, 1438, 1390, 1251, 1159, 1099, 1072, 955, 759, 605, 541. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 10.58 (s, 1H), 7.15–7.27 (m, 4H), 7.58 (s, 1H), 5.18 (s, 2H), 4.29 (t, 2H, J = 6.5 Hz), 3.65–3.73 (m, 3H), 2.13–2.46 (m, 6H), 1.78 (m, 2H), 1.02–1.19 (m, 9H), 0.32 (m, 2H). MS (*m*/*z*, assignment): 501 (21.9), 499 (17.2), 216 (8.8), 193 (9.1), 192 (100), 174 (56.7), 156 (16.9). HRMS (ES^+) calcd for $C_{22}H_{32}N_4O_5Si$ $[M + K]^+$ 499.1779, found 499.1785.

2j: M.pt.: 98 °C. Yield: 77%. IR (neat, cm^{-1}): 3133, 2944, 2866, 2824, 1655, 1535, 1435, 1350, 1218, 1034, 886, 767, 694. ^1H NMR (400 MHz, $CDCl_3$): δ_H = 7.48 (s, 1H), 4.49 (s, 2H), 4.02 (t, J = 6.9 Hz, 6H), 3.40 (d, J = 6.5 Hz, 2H), 2.86 (s, 3H), 2.63–2.54 (m, 4H), 2.34–2.03 (m, 15H), 1.38–1.11 (m, 2H), 0.60–0.40 (m, 2H). MS (*m*/*z*, assignment): 440 (28.4), 422 (26.6), 385 (13.8), 384 (68.0), 285 (21.6), 247 (40.6), 230 (62.5), 214 (99.6), 192 (100), 174 (89.7), 156 (21.6). HRMS (ES^+) calcd for $C_{17}H_{33}N_5O_3Si$ $[M + H]^+$ 384.2430, found 384.2440.

2k: M.pt.: 106 °C. Yield: 77%. IR (neat, cm^{-1}): 3134, 2970, 2927, 2884, 1551, 1438, 1389, 1294, 1214, 1165, 1099, 1072, 954, 876, 780. ^1H NMR (400 MHz, $CDCl_3$): δ_H = 7.72–7.33 (s, 1H), 4.44–4.15 (m, 1H), 3.82 (s, 2H), 3.20 (d, J = 6.5 Hz, 1H), 2.66 (s, 1H), 2.59–2.21 (m, 4H), 2.14–1.83 (m, 2H), 1.68 (d, J = 6.1 Hz, 2H), 1.18–0.91 (m, 9H), 0.66–0.24 (m, 2H). MS (*m*/*z*, assignment): 425 (13.7), 407 (100), 368 (65.5), 319 (11.9), 216 (3.9), 206 (7.7), 192 (8.4), 174 (27.7), 156 (26.4). HRMS (ES^+) calcd for $C_{17}H_{32}N_4O_3Si$ $[M + K]^+$ 407.1880, found 407.1899.

2l: M.pt.: 71 °C. Yield: 70%. IR (neat, cm^{-1}): 2926, 1599, 1437, 1346, 1214, 1178, 1080, 964, 757, 675. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.26 (dd, J = 45.8, 42.1 Hz, 1H), 3.69 (s, 5H), 2.35 (ddd, J = 30.8, 23.6, 10.7 Hz, 6H), 2.11 (d, J = 9.9 Hz, 1H), 1.21–0.83 (m, 10H).MS (*m*/*z*, assignment): 395 (41.8), 230 (6.2), 216 (14.7), 192 (100), 174 (99.8), 156 (20.7), 116 (8.2), 98 (16.3). HRMS (ES^+) calcd for $C_{15}H_{28}N_4O_4Si$ $[M + K]^+$ 395.1516, found 395.1510.

2m: M.pt.: 120 °C. Yield: 82%. IR (neat, cm^{-1}): 2928, 2873, 1718, 1570, 1450, 1397, 1091, 908, 770, 712, 612, 570, 540. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 7.77–7.81 (m, 2H), 7.61–7.65 (m, 2H), 7.58 (s, 1H), 4.90 (s, 2H), 4.23 (t, 2H, J = 6.5 Hz), 3.62–3.83 (m, 3H),

2.32–2.90 (m, 6H), 1.90 (m, 2H), 1.06–1.20 (m, 9H), 0.32–0.36 (m, 2H). MS (*m*/*z*, assignment): 542 (50.6), 524 (100), 504 (77.6), 486 (45.6), 394 (13.3), 216 (37.5), 192 (61.3), 174 (23.0), 156 (11.3), 126 (11.7). HRMS (ES^+) calcd for $C_{23}H_{31}N_5O_5Si$ $[M+K]^+$ 524.1732, found 524.1740.

2n: M.pt.: 66 °C. Yield: 73%. IR (neat, cm^{-1}): 3330, 2941, 2880, 1590, 1453, 1324, 1265, 1211, 1018, 940, 758, 617, 578. ^1H NMR (300 MHz, $CDCl_3$): $\delta_H = 7.56$ (s, 1H), 4.90 (s, 2H), 4.24 (m, 2H), 3.68 (m, 7H), 2.33 (m, 10H), 1.87 (m, 2H), 1.04 (m, 9H), 0.48 (m, 2H). MS (*m*/*z*, assignment): 482 (25.6), 464 (36.7), 427 (15.0), 426 (66.4), 230 (20.0), 214 (70.1), 192 (100), 174 (87.1), 156 (21.1). HRMS (ES^+) calcd for $C_{19}H_{35}N_5O_4Si$ $[M+K]^+$ 464.2095, found 464.2080.

2o: M.pt.: 127 °C. Yield: 79%. IR (neat, cm^{-1}): 2969, 2860, 2876, 1660, 1459, 1370, 1344, 1185, 1050, 965, 762, 692, 540. ^1H NMR (300 MHz, $CDCl_3$): $\delta_H = 7.56$ (s, 1H), 7.19 (m, 5H), 4.06–4.28 (m, 2H, $J = 6.5$ Hz), 3.70–3.78 (m, 3H), 2.07–2.42 (m, 6H), 1.83 (m, 2H), 1.01–1.18 (m, 9H), 0.46 (m, 2H). MS (*m*/*z*, assignment): 459 (11.2), 441 (14.1), 404 (7.5), 403 (23.2), 230 (12.2), 216 (15.1), 214 (65.2), 192 (100), 156 (26.4). HRMS (ES^+) calcd for $C_{20}H_{30}N_4O_3Si$ $[M + K]^+$ 441.1724, found 441.1720.

Results and discussion

General reaction

Recently, Cattoen and co-workers successfully exploited azidopropyltriethoxysilane (AzPTES) as prominent azide precursor in CuAAC for the synthesis of polyfunctionalized water-sensitive organotriethoxysilanes (TBTES-linkers) [25–27]. This method has proven to be well-suited for several functionalities such as amine, alcohol, diol, ether, and ester. In our approach, we have extended the scope of this reaction to other functional groups showing the versatility of the method. All TBTES-linkers were synthesized by using corresponding alkynes under anhydrous click condition (Scheme 1, Table 1) [28]. In all cases, CuAAC reactions proceeded smoothly to completion giving TBTES-linkers (**1a**–**1l**) in good yields and were characterized by IR, ^1H and ^{13}C NMR and Mass spectroscopy.

IR spectra

Almost all vibrational frequencies in the IR absorption spectra are well in agreement with those observed in the spectra of the usual organosilicon compounds. The IR spectra reveals that the characteristic bands of the azido group (−N═N═N, 2091 cm^{-1}) and alkyne groups (−C≡C, 3279 and 2102 cm^{-1}) are no longer present after the click reaction. The absorption band at 2091 cm^{-1} is greatly depressed for the spectra of 1,2,3-triazole incorporated compounds, which is due to the complete conversion of the azido moiety to 1,2,3-triazole ring. This indicates the high efficiency of the click reaction. The −C═C− skeletal ring vibrations are observed in the region between 1600 and 1480 cm^{-1}. The bands observed in this region are not affected appreciably by the nature of the substituent at C-4 position of the 1,2,3-triazole ring.

NMR spectra

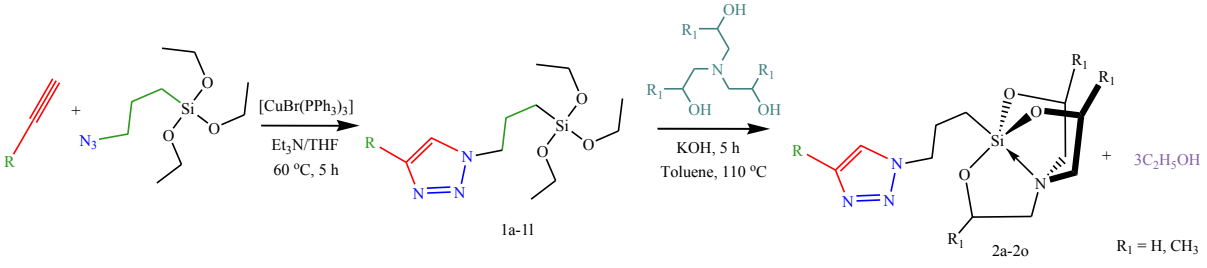
^1H NMR spectra of TBTES-linkers exhibit a triplet around $\delta \approx 1.14$ ppm and a quartet roughly at $\delta \approx 3.65$ ppm corresponding to $-CH_3$ and $-OCH_2-$ of triethoxysilyl moiety, respectively. The downfield shift of triplet of $-N_3CH_2-$ protons from $\delta = 3.19$ to $\delta \approx 4.19$–4.31 ppm signifies the C–N bond formation resulting into 1,2,3-triazole.

Our previous familiarity in the field of organosilicon chemistry prompted us to investigate the utility of TBTES-linkers for the synthesis of silatranes. Scheme 1 illustrates the general synthetic route, in which TBTES-linkers serve as precursors for the transesterification reaction with triethanolamine and trisisopropanolamine. In all cases, the reactions were carried out at 110 °C for 5 h in the presence of catalytic amount of KOH. All synthesized TBS-scaffolds, summarized in Table 1, were isolated as white solids that are insensitive to air and characterized by IR, NMR (^1H, ^{13}C), low and high resolution mass spectroscopic studies [18].

All the synthesized compounds containing silatranyl moiety possess three methylene groups in propyl chain and six methylene groups as three bridges between O and N atoms. Symmetric deformational vibrations of the silatranyl skeleton with a predominant contribution resulting from the donation of nitrogen lone pair to the vacant orbital of silicon are observed in the region of 590–579 cm^{-1}. In the ^1H NMR spectra of TBS-scaffolds (**2a**–**2h**) derived from triethanolamine, two intense triplets and the characteristic feature of $Si(OCH_2CH_2)_3N$ moiety (due to protons of $-OCH_2$, $\delta \approx 3.75$–3.78 ppm and NCH_2, $\delta \approx 2.80$–2.83 ppm). The triplets clearly distinguish silatranes from their parent compounds. In the ^{13}C NMR spectra, methylene carbon of propyl chain attached to silicon atom appears as the most shielded carbon atom which is identified at $\delta \approx 12$–13 ppm. This downfield shift of methylene carbon clearly indicates the hypervalency at silicon atom. On the other hand, the introduction of the methyl groups at the 3,7,10 positions of the silatrane cage by using trisisopropanolamine leads to the loss of C_3 symmetry, resulting into more complex NMR spectra of compounds (**2i**–**2o**) [16].

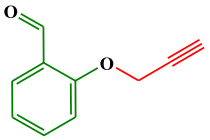
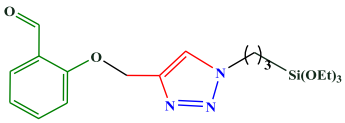
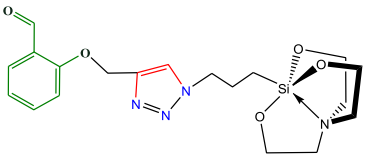
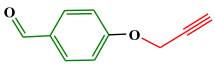
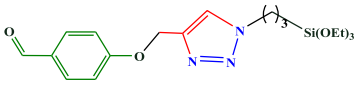
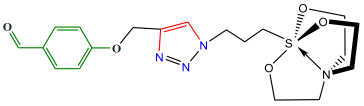
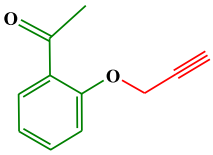
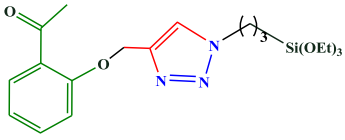
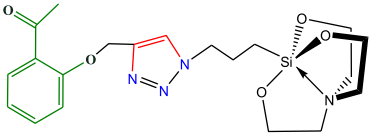
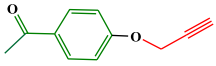
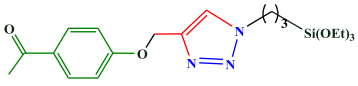
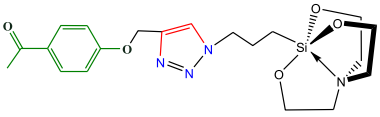
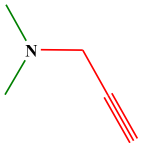
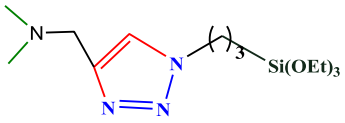
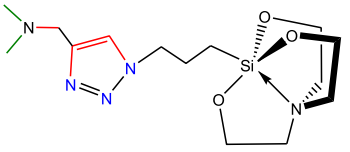
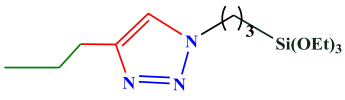
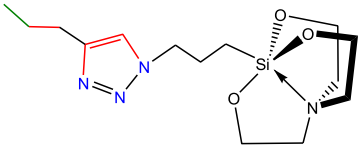
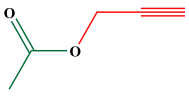
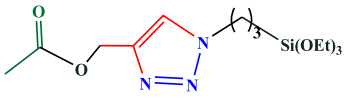
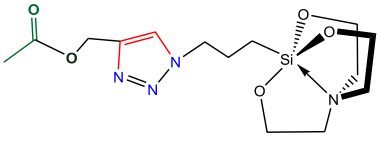
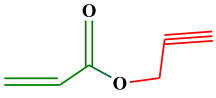
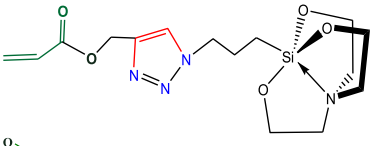
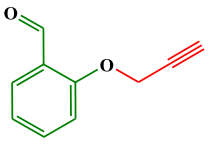
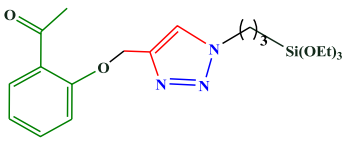
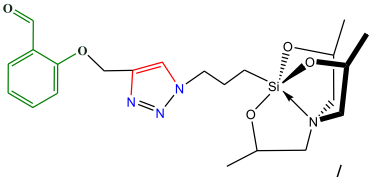
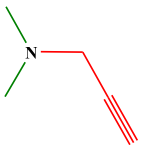
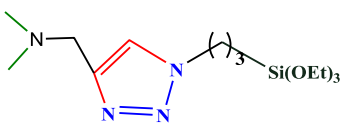
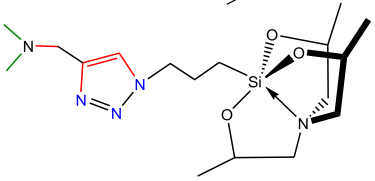
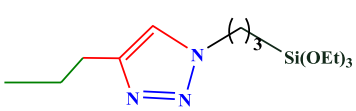
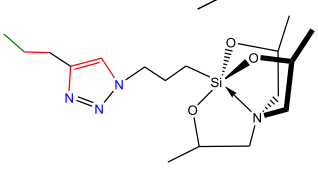
Mass spectra

The structure of all 1,2,3-triazole incorporated silatranes were confirmed by the mass spectroscopy. In the mass spectra of all compounds, $[M + H]^+$ peak appears with a very high intensity along with $[M + Na]^+$ and $[M + K]^+$ peaks. The most abundant $[M - 42]^+$ peak corresponds to exclusion of a cyclic $-OCH_2CH_2-$ arm from the silatranyl ring to form bicyclic moiety (Scheme 2).



Scheme 1. General reaction scheme for the synthesis of 1,2,3-triazole-based silatrane (TBS)-scaffolds (**2a**–**2o**).

Table 1
Synthesized 1,2,3-triazole based silatrane (TBS)-scaffolds (**2a**–**2o**).

Terminal alkynes (R)	TBTES-linkers (**1a**–**1l**)		TBS-scaffolds (**2a**–**2o**)		Yield (%)
		**1a**		**2a**	**78**
		**1b**		**2b**	**78**
		**1c**		**2c**	**78**
		**1d**		**2d**	**73**
		**1e**		**2e**	**78**
		**1f**		**2f**	**76**
		**1g**		**2g**	**77**
		**1h**		**2h**	**76**
		**1a**		**2i**	**73**
		**1e**		**2j**	**77**
		**1f**		**2k**	**77**

(*continued on next page*)

Table 1 (*continued*)

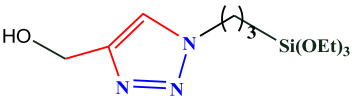
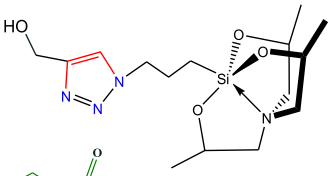
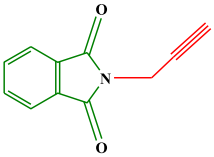
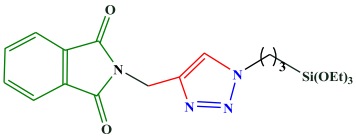
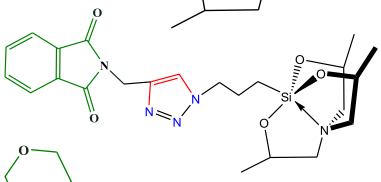
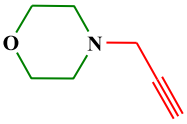
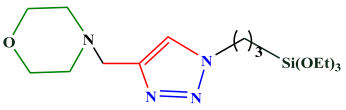
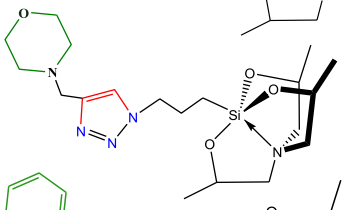
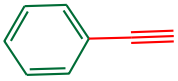
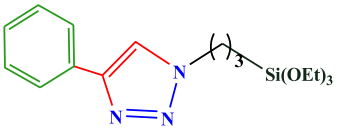
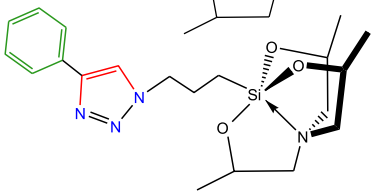
Terminal alkynes (R)	TBTES-linkers (**1a**–**1l**)	TBS-scaffolds (**2a**–**2o**)	Yield (%)
	 **1i**	 **2l**	**70**
	 **1j**	 **2m**	**82**
	 **1k**	 **2n**	**73**
	 **1l**	 **2o**	**78**

Table 2
Optimization reaction conditions for the synthesis of silatrane (**2a**).

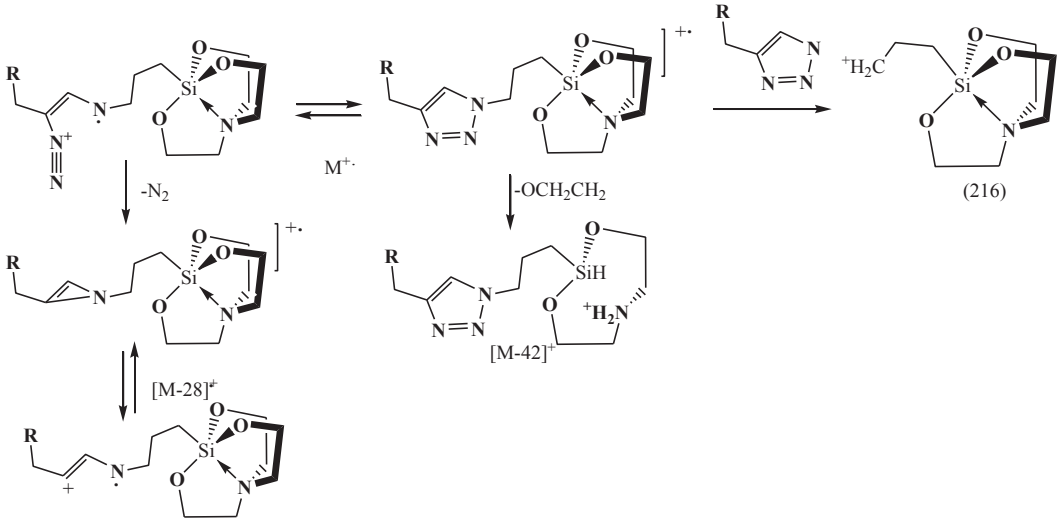
Entry	Solvent	Catalyst (mmol)	Reaction condition[a]	Reaction Duration	Yield (%)
1	Toluene	No catalyst	rt, st	5 h	0
2	Toluene	KOH (0.2)	rt, st	5 h	0
3	Toluene	KOH (0.4)	rt, st	10 h	0
4	Toluene	No catalyst	110 °C, st	5 h	20
5	**Toluene**	**KOH (0.2)**	**110 °C, st**	**5 h**	**78**
6	Toluene	KOH (0.4)	110 °C, st	5 h	77
7	Toluene	KOH (0.8)	110 °C, st	5 h	78
8	*o*-Xylene	KOH (0.2)	144 °C, st	5 h	66
9	*o*-Xylene	KOH (0.4)	144 °C, st	5 h	65
10	*o*-Xylene	KOH (0.8)	144 °C, st	5 h	62

The bold values specifies the best optimized reaction condition for the synthesis of Silatrane.
[a] rt = room temperature, st = stirring.

There is no evidence from the mass spectra of all compounds about the elimination of two $-OCH_2CH_2-$ arms from the silatranyl ring. Furthermore, a peak of prominent abundance at mass $m/z = 216$, corresponding to 1-propylsilatrane, appears in all cases [28]. This fragment results from the elimination of 1,2,3-triazole part from 1-propylsilatrane.

Optimising reaction conditions

Several reports cite silatranes as hydrolytically unstable and therefore incapable of finding applications in medicine and biology [16]. But the drastic transformation of TBTES-linkers on N-lone pair donation to form TBS-scaffolds has resulted into hydrolytically stable molecular species. The optimization of reaction conditions for the synthesis of TBS-scaffolds was also studied. It



Scheme 2. General fragmentation pattern of 1,2,3-triazole based silatrane (TBS)-scaffolds.

was found that yield decreased drastically with variation in reaction time both above and below the ideal reaction conditions. The optimization of ideal condition for the synthesis of silatrane (**2a**) in high yield and purity is as per entry 5 in Table 2. The use of KOH as catalyst has pronounced effect on yield of final product in comparison to when non-catalytic reaction was performed. In addition to this, the reaction does not occur even in the presence of KOH at room temperature leading us to enforce refluxing reaction conditions.

Conclusion

We have successfully synthesized a new series of TBS-scaffolds (**2a**–**2o**) based on the combinatorial methodology between organosilicon chemistry and click reaction. TBS-scaffolds are the first silatranes of this type, synthesized in good yield having high stability and sufficient solubility in organic solvents. This opens up the new pathways for the family of TBS-scaffolds to be used significantly in synthetic decoration of alkyne based DNA, G-quadruplex structures, peptides, proteins, oligosaccharides, and glycoconjugates of a higher level of hierarchy.

Acknowledgements

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