New method for trimethylsilylation of hydroxy-containing compounds. Synthesis of persilylated ecdysteroids and carbohydrates

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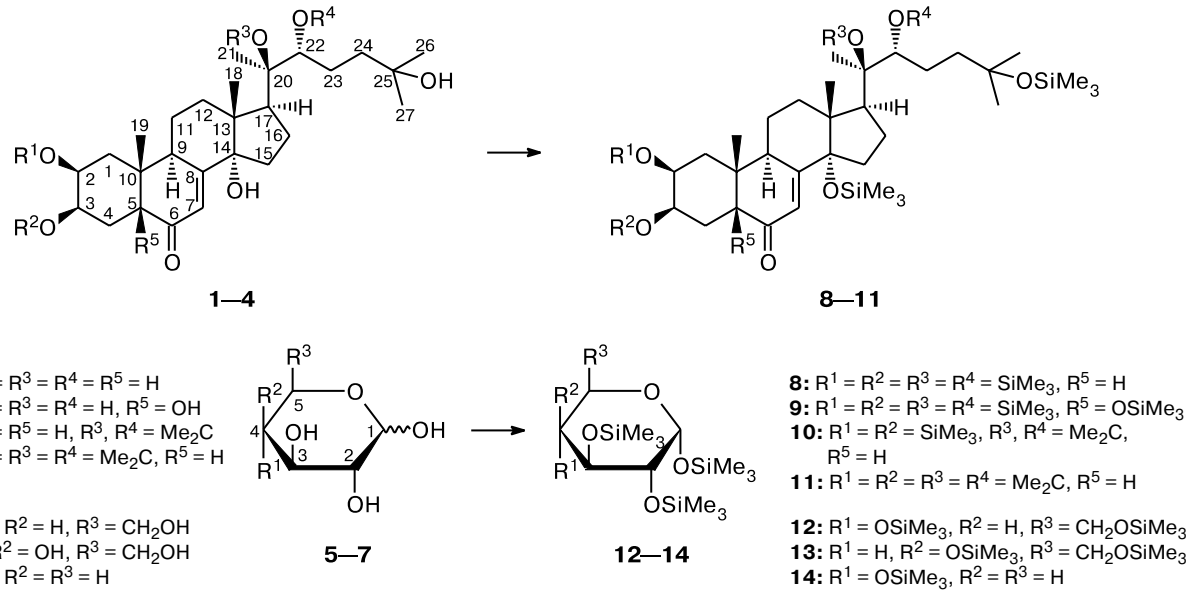
A new method was developed for trimethylsilylation of alcohols by the reactions with (trifluoromethyl)trimethylsilane in the presence of tetrabutylammonium fluoride. The reactions of ecdysteroids (20-hydroxyecdysone, its 20,22-mono- and 2,3:20,22-diacetonides, and polypodine B) and carbohydrates (D-gluco-, D-galacto-, and D-xylopyranoses) afforded the corresponding persilylated derivatives.

Key words: trimethylsilylation, (trifluoromethyl)trimethylsilane, ecdysteroids, 20-hydroxyecdysone, acetonides, polypodine B, carbohydrates, D-glucopyranose, D-galactopyranose, D-xylopyranose.

The trimethylsilyl group is widely used in organic synthesis for protecting the hydroxy groups in steroids, carbohydrates, and other alcohols.[1] A large number of procedures are available for silylation of hydroxy groups by different reagents.[2,3] Previously, we have reported the use of (trifluoromethyl)trimethylsilane (Me_3SiCF_3) catalyzed by tetrabutylammonium fluoride Bu_4NF for trimethylsilylation of the 14α-hydroxy group in ecdysteroids.[4] Further investigations demonstrated that this is a general method. In the present study, we used this procedure for exhaustive trimethylsilylation of a number of polyhydroxy compounds. These were ecdysteroids, *viz.*, 20-hydroxyecdysone (**1**), polypodine B (**2**), 20,22-acetonide of **1** (**3**), and 2,3:20,22-diacetonide of **1** (**4**), and carbohydrates, *viz.*, D-gluco- (**5**), D-galacto- (**6**), and D-xylopyranoses (**7**). Transformations of all these compounds under mild con-

Scheme 1



1: $R^1 = R^2 = R^3 = R^4 = R^5 = H$
2: $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = OH$
3: $R^1 = R^2 = R^5 = H$, R^3, $R^4 = Me_2C$
4: $R^1 = R^2 = R^3 = R^4 = Me_2C$, $R^5 = H$

5: $R^1 = OH$, $R^2 = H$, $R^3 = CH_2OH$
6: $R^1 = H$, $R^2 = OH$, $R^3 = CH_2OH$
7: $R^1 = OH$, $R^2 = R^3 = H$

8: $R^1 = R^2 = R^3 = R^4 = SiMe_3$, $R^5 = H$
9: $R^1 = R^2 = R^3 = R^4 = SiMe_3$, $R^5 = OSiMe_3$
10: $R^1 = R^2 = SiMe_3$, R^3, $R^4 = Me_2C$, $R^5 = H$
11: $R^1 = R^2 = R^3 = R^4 = Me_2C$, $R^5 = H$

12: $R^1 = OSiMe_3$, $R^2 = H$, $R^3 = CH_2OSiMe_3$
13: $R^1 = H$, $R^2 = OSiMe_3$, $R^3 = CH_2OSiMe_3$
14: $R^1 = OSiMe_3$, $R^2 = R^3 = H$

Reagents and conditions: Me_3SiCF_3 (3 equiv. per OH group of the substrate), $Bu_4N^+F^-$ (0.8 mol.%), anhydrous THF, 0 °C, 2 min (for **1**—**4**) or 30 min (for **5**—**7**).

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 10, pp. 1784—1786, October, 2002.

1066-5285/02/5110-1937 $27.00

ditions afforded the corresponding derivatives **8**—**14** in high yields (Scheme 1).

Exhaustive silylation of the hydroxy groups of ecdysteroids **1**—**4** proceeded with retention of the carbonyl group. The IR and UV spectra of ethers **8**—**11** provide evidence that the Δ^7-6-keto system of the ring B remained intact.

Trimethylsilylation of carbohydrates **5**—**7** (mixtures of the α and β anomers of the cyclic pyranose forms[5]) gave rise to the corresponding α anomers (**12**—**14**). The assignment of anomers **12**—**14** was made based on the signals for H(1) in the ^{1}H NMR spectra of these compounds.

Therefore, the Me_3SiCF_3—Bu_4NF system used previously for trifluoromethylation of carbonyl compounds[6,7] proved to be a highly efficient *O*-silylating reagent, which acts under mild conditions and performs exhaustive trimethylsilylation of complex hydroxy-containing substrates in nearly quantitative yields.

Experimental

The IR spectra were recorded on a Specord 75-IR spectrometer (in KBr pellets). The UV spectra were measured on a Specord M-40 spectrometer in $CHCl_3$. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 instrument (300.13 MHz for ^{1}H and 75 MHz for ^{13}C) in $CDCl_3$ as the solvent. The chemical shifts are given in the δ scale relative to Me_4Si (internal standard). The melting points were measured on a Boetius stage. The specific rotation was determined on a Perkin—Elmer 141 polarimeter. The TLC was carried out on SiO_2 plates (Silufol); spots were visualized by spraying with a vanilline solution in ethanol acidified with H_2SO_4.

Trimethylsilylation (general procedure). Tetrabutylammonium fluoride (0.8 mol.%) was added to a stirred mixture of the corresponding substrate (**1**—**7**) (0.5 mmol) and Me_3SiCF_3 (3.0 equiv. per OH group of the substrate) in anhydrous THF (3 mL). The reaction was completed in 3 min (for **1**—**4**) or 30 min (for **5**—**7**) (TLC control). The reaction mixture was concentrated to dryness and the residue was chromatographed on a column with SiO_2 (3 g, elution with $CHCl_3$). The corresponding derivatives **8**—**14** were prepared.

2,3,14,20,22,25-Hexakis-*O*-(trimethylsilyl)-20-hydroxyecdysone or (20*R*,22*R*)-2β,3β,14α,20,22,25-hexakis(trimethylsilyloxy)-5-cholest-7-en-6-one (8), the yield was 95%, R_f 0.91 ($CHCl_3$—MeOH, 10 : 1), m.p. 85—87 °C, $[\alpha]_D^{23}$ +34.2 (*c* 15.95, $CHCl_3$). IR (KBr), ν/cm^{-1}: 840 and 1250 (SiMe), 1664 (C=CC=O). UV ($CHCl_3$), λ_{max}/nm (ε): 241 (15240). ^{1}H NMR, δ: 0.08, 0.09, 0.10, 0.11, 0.12, and 0.13 (all s, 54 H, $SiMe_3$); 0.73 (s, 3 H, C(18)H$_3$); 0.94 (s, 3 H, C(19)H$_3$); 1.22 (s, 6 H, C(26)H$_3$, C(27)H$_3$); 1.38 (s, 3 H, C(21)H$_3$); 1.56—2.05 (m, 16 H, CH_2); 2.47—2.59 (m, 2 H, H(5), H(17)); 2.95 (m, 1 H, H(9)); 3.21 (d, 1 H, H(22), J = 8.6 Hz); 3.75 (m, 1 H, H(2)); 3.89 (br.s, 1 H, H(3), $w_{1/2}$ = 8.6); 5.83 (br.s, 1 H, H(7), $w_{1/2}$ = 6.4). ^{13}C NMR, δ: −0.05, 0.49, 1.03, 1.70, 2.62, and 2.73 (SiMe); 16.43 (C(18)); 20.70 (C(16)); 22.39 (C(11)); 24.26 (C(19)); 27.92 (C(23)); 28.19 (C(21)); 29.84 (C(26); C(27)); 30.13 (C(4)); 31.17 (C(15)); 33.19 (C(12)); 34.16 (C(9)); 36.85 (C(1)); 38.13 (C(10)); 43.93 (C(24)); 47.58 (C(17)); 48.83 (C(13)); 50.26 (C(5)); 69.19 (C(3), C(2)); 73.68 (C(25)); 80.50 (C(20)); 84.56 (C(22)); 87.61 (C(14)); 122.11 (C(7)); 164.21 (C(8)); 204.06 (C(6)).

2,3,5,14,20,22,25-Heptakis-*O*-(trimethylsilyl)polypodine B or 2,3,5,14,20,22,25-heptakis-*O*-(trimethylsilyl)-5β,20-hydroxyecdysone, or (20*R*, 22*R*)-2β,3β,5β,14α,20,22,25-heptakis(trimethylsilyloxy)-5β-cholest-7-en-6-one (9), the yield was 91%, R_f 0.83 ($CHCl_3$—MeOH, 20 : 1), m.p. 50—52 °C, $[\alpha]_D^{21}$ +50.4 (*c* 7.29, $CHCl_3$). IR (KBr), ν/cm^{-1}: 840 (SiMe), 1250 (SiMe, OCOMe), 1665 (C=CC=O). UV ($CHCl_3$), λ_{max}/nm (ε): 241 (15240). ^{1}H NMR, δ: 0.07, 0.09, 0.10, 0.12, 0.13, 0.16, and 0.17 (all s, 63 H, $SiMe_3$); 0.72 (s, 3 H, C(18)H$_3$); 1.21 (s, 9 H, C(19)H$_3$, C(26)H$_3$, C(27)H$_3$); 1.36 (s, 3 H, C(21)H$_3$); 0.86—2.35 (m, 16 H, CH_2); 2.65 (t, 1 H, H(17), J = 8.2 Hz); 3.20 (d, 1 H, H(22), J = 7.9 Hz); 3.41 (m, 1 H, H(9)); 3.74 (m, 2 H, H(2), H(3)); 5.80 (d, 1 H, H(7), J = 2.0 Hz). ^{13}C NMR, δ: −0.01, 0.48, 1.01, 1.79, 1.93, 2.63, and 2.74 (SiMe); 16.60 (C(18)); 20.07 (C(19)); 22.68 (C(16)); 27.52 (C(11)); 27.95 (C(23)); 28.11 (C(21)); 28.87 (C(15)); 29.83 (C(26)); 29.91 (C(27)); 33.19 (C(12)); 33.32 (C(1)); 40.18 (C(10)); 38.11 (C(4)); 43.87 (C(24)); 45.17 (C(9)); 47.33 (C(17)); 53.14 (C(13)); 69.82 (C(3)); 70.79 (C(2)); 73.71 (C(25)); 79.02(C(5)); 80.38 (C(20)); 84.55(C(22)); 89.13 (C(14)); 118.49 (C(7)); 166.69 (C(8)); 197.36 (C(6)).

20,22-*O*-Isopropylidene-2,3,14,25-tetrakis-*O*-(trimethylsilyl)-20-hydroxyecdysone, or (20*R*,22*R*)-20,22-isopropylidene-2β,3β,14α,25-tetrakis(trimethylsilyloxy)-5β-cholest-7-en-6-one (10), the yield was 90%, R_f 0.85 ($CHCl_3$—MeOH, 10 : 1), m.p. 54 °C, $[\alpha]_D^{22}$ +39.2 (*c* 5.49, $CHCl_3$). IR (KBr), ν/cm^{-1}: 840 and 1250 (SiMe), 1660 (C=CC=O). UV ($CHCl_3$), λ_{max}/nm (ε): 242 (11581). ^{1}H NMR, δ: 0.08, 0.10, and 0.12 (1 : 2 : 1, all s, 36 H, $SiMe_3$); 0.74 (s, 3 H, C(18)H$_3$); 0.95 (s, 3 H, C(19)H$_3$); 1.15 (s, 3 H, C(21)H$_3$); 1.24 (s, 3 H, C(26)H$_3$); 1.25 (C(27)H$_3$); 1.31 and 1.40 (both s, 6 H, C$\underline{Me}_2$); 1.46—2.14 (m, 16 H, CH, CH_2); 2.51 (dd, 1 H, H(5), ^3J = 4.0 and 12.9 Hz); 2.94 (m, 1 H, H(9)); 3.63 (m, 1 H, H(22), $w_{1/2}$ = 17.1); 3.77 (m, 1 H, H(2), $w_{1/2}$ = 18.8); 3.89 (br.s, 1 H, H(3), $w_{1/2}$ = 8.9); 5.82 (br.s, 1 H, H(7), $w_{1/2}$ = 5.4). ^{13}C NMR, δ: −0.09, 0.49, 1.82, and 2.60 (SiMe); 16.23 (C(18)); 20.62 (C(11)); 21.45 (C(16)); 21.87 (C(21)); 23.56 (C(23)); 24.26 (C(19)); 26.83 (C(27)); 28.97 and 29.35 ($\underline{C}H_3C\underline{C}H_3$); 29.86 (C(15)); 30.20 (C(26)); 31.27 (C(12)); 33.16 (C(4)); 34.10 (C(9)); 36.75 (C(1)); 38.19 (C(10)); 42.05 (C(24)); 48.81 (C(13)); 49.39 (C(17)); 50.22 (C(5)); 69.10 (C(3)); 69.16 (C(2)); 73.49 (C(25)); 81.70 (C(22)); 84.19 (C(20)); 87.83 (C(14)); 106.57 (OCO); 122.41 (C(7)).

2,3:20,22-Di-*O*-isopropylidene-14,25-bis-*O*-(trimethylsilyl)-20-hydroxyecdysone, or (20*R*,22*R*)-2,3:20,22-di-*O*-isopropylidene-14α,25-bis(trimethylsilyloxy)-5β-cholest-7-en-6-one (11), the yield was 90%, R_f 0.78 ($CHCl_3$—MeOH, 10 : 1), m.p. 48—50 °C, $[\alpha]_D^{22}$ +47.1 (*c* 4.3, $CHCl_3$). IR (KBr), ν/cm^{-1}: 835 and 1240 (SiMe), 1670 (C=CC=O). UV ($CHCl_3$), λ_{max}/nm (ε): 242 (12420). ^{1}H NMR, δ: 0.05 and 0.08 (both s, 18 H, $SiMe_3$); 0.70 (s, 3 H, C(18)H$_3$); 1.01 (s, 3 H, C(19)H$_3$); 1.11 (s, 3 H, C(21)H$_3$); 1.20 (s, 3 H, C(26)H$_3$); 1.21 (s, 3 H, C(27)H$_3$); 1.28, 1.30, 1.37, and 1.49 (all s, 12 H, C$\underline{Me}_2$); 1.25—2.05 (m, 16 H, CH_2); 2.12 (t, 1 H, H(17), J = 8.4 Hz); 2.33 (dt, 1 H, H(5), J = 5.5 and 10.6 Hz); 2.61 (m, 1 H, H(9)); 3.60 (dt, 1 H, H(22), J = 4.0 and 8.2 Hz); 4.15 (m, 1 H, H(2)); 4.22 (m, 1 H, H(3)); 5.77 (d, 1 H, H(7), ^4J = 1.9 Hz). ^{13}C NMR, δ: 1.95 and 2.44 (SiMe); 16.19 (C(18)); 21.05 (C(11)); 21.36 (C(16)); 21.71 (C(21)); 23.42 (C(23)); 23.84 (C(19)); 26.01 (C(15)); 26.16 and

26.65 ($\underline{C}H_3C\underline{C}H_3$); 28.34 (C(27)); 28.81 (C(26)); 29.16 ($\underline{C}H_3C\underline{C}H_3$); 29.34 (C(12)); 30.10 ($\underline{C}H_3C\underline{C}H_3$); 31.18 (C(4)); 36.18 (C(9)); 36.90 (C(1)); 37.14 (C(10)); 41.88 (C(24)); 49.21 (C(17)); 49.59 (C(13)); 49.94 (C(5)); 71.31 (C(3)); 72.33 (C(2)); 73.32 (C(25)); 81.53 (C(22)); 83.99 (C(20)); 87.89 (C(14)); 106.40 and 108.05 (OCO); 121.56 (C(7)); 162.86 (C(8)); 201.82 (C(6)).

1,2,3,4,6-Pentakis-*O*-(trimethylsilyl)-α-D-glucopyranose (12), the yield was 92%, R_f 0.88 ($CHCl_3$—MeOH, 5 : 1), $[\alpha]_D^{21}$ +67.8 (*c* 11.87, $CHCl_3$). ^{1}H NMR, δ: 0.10, 0.13, 0.14, and 0.17 (1 : 1 : 2 : 1, all s, 45 H, $SiMe_3$); 3.32 (dd, 1 H, H(2), $^3J_{2,1}$ = 3.1 Hz, $^3J_{2,3}$ = 9.2 Hz); 3.36—3.45 (m, 1 H, H(4)); 3.64—3.81 (m, 4 H, H(3), H(5), H(6)); 5.01 (d, 1 H, H(1), $^3J_{1,2}$ = 3.1 Hz). ^{13}C NMR, δ: –0.26, 0.17, 0.43, 0.93, and 1.26 (5 $SiMe_3$); 62.30 (C(6)); 72.46 (C(4)); 74.00 (C(2)); 72.23 (C(5)); 74.17 (C(3)); 93.89 (C(1)).

1,2,3,4,6-Pentakis-*O*-(trimethylsilyl)-α-D-galactopyranose (13), the yield was 96%, R_f 0.87 ($CHCl_3$—MeOH, 5 : 1), $[\alpha]_D^{24}$ +82.1 (*c* 9.41, $CHCl_3$). ^{1}H NMR, δ: 0.09, 0.10, 0.12, 0.13, and 0.14 (all s, 45 H, $SiMe_3$); 3.48—3.65 (m, 2 H, H(6)); 3.74—3.96 (m, 4 H, H(2), H(3), H(4), H(5)); 5.04 (d, 1 H, H(1), $^3J_{1,2}$ = 2.0 Hz). ^{13}C NMR, δ: –0.58, 0.06, 0.20, 0.37, and 0.55 (5 $SiMe_3$); 61.14 (C(6)); 69.90 (C(5)); 70.44 (C(3)); 71.07 (C(2)); 72.24 (C(4)); 94.53 (C(1)).

1,2,3,4-Tetrakis-*O*-(trimethylsilyl)-α-D-xylopyranose (14), the yield was 93%, R_f 0.85 ($CHCl_3$—MeOH, 20 : 1), $[\alpha]_D^{21}$ +44.0 (*c* 16.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$), δ: 0.12, 0.13, 0.15, and 0.16 (all s, 36 H, $SiMe_3$); 3.34 (dd, 1 H, H(2), $^3J_{2,1}$ = 3.0 Hz, $^3J_{2,3}$ = 10.0 Hz); 3.40—3.73 (m, 4 H, H(3), H(4), H(5)); 4.92 (d, 1 H, H(1), $^3J_{1,2}$ = 3.0 Hz). ^{13}C NMR, δ: 0.11, 0.25, 0.31, and 0.89 (4 $SiMe_3$); 62.24 (C(5)); 71.81 (C(4)); 74.02 (C(2)); 74.10 (C(3)); 94.17 (C(1)).

This study was financially supported by the Russian Foundation for Basic Research (Project Nos. 00-03-32811 and 02-03-06473).

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Received July 23, 2002