Synthesis of Callyberynes A-B, Polyacetylenic Hydrocarbons from Marine Sponges

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Supporting Information

Experimental Section: General details.

All reactions were carried out under argon atmosphere with magnetic stirring. The solvents were purified and dried using standard procedures. All reagents were purchased and used without further purifications. NMR spectra were determined on a Bruker WM-250, Bruker AMX-300 or Varian Inova-400 instruments using CDCl₃ or C₆D₆ as solvents with tetramethylsilane as internal standard. Mass spectra were measured on a Hewlett-Packard 59970-G/MS or Micromass Autospec spectrometers. Column chromatographies were made on silica gel 230-400 mesh (flash) from Merck.

Hexane-1,6-dial (9).

To a vigorously stirred suspension of chromatographic grade silica gel (105 g, 1.75 mmol) in CH₂Cl₂ (500 mL) was added an aqueous solution of NaIO₄ (0.65 M, 105 mL, 68.2 mmol), dropwise, whence a flaky suspension was formed. *Trans*-cyclohexanediol (6.08 g, 52.3 mmol) in CH₂Cl₂ (200 mL) was then added, and the reaction was stirred for 24 h. The mixture was filtered on a sintered glass, and the silica gel was thoroughly washed with CH₂Cl₂. Evaporation of the solvent afforded the title compound (5.91 g) as a colorless oil in quantitative yield. No further purification was necessary.

¹H-RMN (250.13 MHz, CDCl₃): δ 1.65 (4H, t, *J* = 6.9 Hz, 2H₃+2H₄), 2.4-2.5 (4H, m, 2H₂+2H₅), 9.76 (2H, t, *J* = 1.4 Hz, H₁+H₆).

¹³C-RMN (75.47 MHz, CDCl₃): δ 21.5 (2xCH₂), 43.6 (2xCH₂), 201.6 (2xCH).

MS (EI) *m/z* (%): 115 (100), 114 (M⁺, 31), 113 (85), 85 (41), 57 (67), 56 (12).

IR (Csl): ν 1723 (C=O).

1,1,8,8-Tetrabromoocta-1,7-diene (10).

To a solution of Ph_3P (12.0 g, 45.6 mmol) in CH_2Cl_2 (34 mL), cooled in an ice-water bath, was slowly added CBr_4 (7.56 g, 22.8 mmol) in CH_2Cl_2 (15 mL) at a rate to maintain the reaction temperature below 15°C . A solution of hexane-1,6-dial (**9**) (1.0 g, 8.77 mmol) and Et_3N (2.44 mL, 17.54 mmol) in CH_2Cl_2 (10 mL) was added dropwise at 0°C . After stirring for 35 min at this temperature, the reaction was warmed to rt for 1 h. The mixture was poured into hexane (20 mL) and filtered through Celite. The solid was washed with hexane (3 x 20 mL) and the filtrate was concentrated under reduced pressure. Hexane was added (20 mL) and the mixture was filtered again. The filtrate was concentrated and purified by column chromatography (hexane) to give the title compound as a colorless oil (3.03 g, 81 % yield).

^1H -RMN (250.13 MHz, CDCl_3): δ 1.4-1.5 (4H, m, $2\text{H}_4+2\text{H}_5$), 2.1-2.3 (4H, m, $2\text{H}_3+2\text{H}_6$), 6.38 (2H, t, $J = 7.4$ Hz, H_2+H_7).

^{13}C -RMN (62.90 MHz, CDCl_3): δ 27.1 ($2\times\text{CH}_2$), 32.6 ($2\times\text{CH}_2$), 89.1 ($2\times\text{C}$), 138.2 ($2\times\text{CH}$).

MS (Cl^+) m/z (%): 430 (1), 428 (3), 426 (4), 424 (3), 422 (M^+ , 1), 349 (3), 347 (11), 345 (13), 343 (6), 267 (34), 265 (66), 263 (36), 201 (39), 199 (80), 187 (24), 185 (100), 183 (79).

HRMS: calculated for $\text{C}_8\text{H}_{10}\text{Br}_4$: 421.7516; found: 421.7512.

(1Z,7Z)-1,8-Dibromoocta-1,7-diene (4).

A mixture of PPh_3 (0.19 g, 0.71 mmol) and Pd(OAc)_2 (0.04 g, 0.18 mmol) in dry CH_2Cl_2 (30 mL) was stirred at rt for 15 min to generate a light, yellow solution. 1,1,8,8-tetrabromoocta-1,7-diene (**10**) (0.95 g, 2.23 mmol) in CH_2Cl_2 (5 mL) and Bu_3SnH (2.2 mL, 2.42 g, 8.30 mmol) were added successively, and the mixture was stirred at rt for 2 h. After the reaction was completed, it was diluted with ether (30 mL) and washed with water (3 x 50 mL) and brine (3 x 50 mL). The ethereal extract was dried over Na_2SO_4 and the solvent removed under reduced pressure. The residue was purified by column chromatography (hexane) to give the title compound as a colorless oil (0.48 g, 81 % yield).

^1H -RMN (300.08 MHz, C_6D_6): δ 1.0-1.1 (4H, m, $2\text{H}_4+2\text{H}_5$), 2.0-2.1 (4H, m, $2\text{H}_3+2\text{H}_6$), 5.57 (2H, c, $J = 6.9$ Hz, H_2+H_7), 5.93 (2H, d, $J = 6.9$ Hz, H_1+H_8).

^{13}C -RMN (75.47 MHz, CDCl_3): δ 27.4 ($2\times\text{CH}_2$), 29.3 ($2\times\text{CH}_2$), 107.8 ($2\times\text{CH}$), 134.4 ($2\times\text{CH}$).

MS (Cl^+) m/z (%): 267 (6), 265 (12), 263 (M^+ , 6), 201 (50), 199 (100), 197 (52).

HRMS: calculated for $\text{C}_8\text{H}_{12}\text{Br}_2$: 266.8276; found: 266.8268.

Octa-2,7-diyn-1-ol (12).

To a solution of hepta-1,6-diyne (**11**) (2.0 mL, 1.62 g, 17.6 mmol) in THF (22 mL), cooled at -78°C , was added $n\text{BuLi}$ (1.6 M in hexane, 8.45 mL, 13.52 mmol). After stirring for 1 h at this temperature, HMPA (9.5 mL) was added. The mixture was stirring for 15 min and then paraformaldehyde (0.41 g, 13.5 mmol) was also added and the reaction was stirring for 19 h at rt. The mixture was diluted with ether (20 mL) and hydrolyzed with saturated aqueous solutions of NH_4Cl (40 mL), NaHCO_3 (2 x 40 mL) and brine (2 x 40 mL). The organic phase was dried and the solvent was removed in vacuo. Flash chromatography (hexane/ethyl acetate 70:30) of the residue afforded 1.05 g (64 % yield) of the title compound as a colorless oil, together with 0.07 g (3 % yield) of nona-2,7-diyn-1,9-diol (**13**).

^1H -RMN (250.13 MHz, CDCl_3): δ 1.73 (2H, q, $J = 7.0$ Hz, 2H_5), 1.96 (1H, t, $J = 2.7$ Hz, H_8), 2.2-2.4 (4H, m, $2\text{H}_4+2\text{H}_6$), 4.20 (2H, m, 2H_1).

^{13}C -RMN (75.47 MHz, CDCl_3): δ 17.5 (CH_2), 17.7 (CH_2), 27.4 (CH_2), 51.3 (CH_2), 68.9 (CH), 79.0 (C), 83.4 (C), 85.2 (C).

MS (Cl^+) m/z (%): 123 (MH^+ , 40), 107 (49), 105 (97), 79 (100).

HRMS: calculated for $\text{C}_8\text{H}_{10}\text{O}$: 123.0810; found: 123.0810.

IR (Csl): ν 3294 ($\equiv\text{C-H}$; O-H), 2253, 2116 ($\text{C}\equiv\text{C}$).

Nona-2,7-diyne-1,9-diol (13).

^1H -RMN (300.13 MHz, CDCl_3): δ 1.71 (2H, q, J = 6.9 Hz, 2H_5), 1.81 (2H, broad s, 2xOH), 2.34 (4H, t, J = 6.9 Hz, $2\text{H}_4+2\text{H}_6$), 4.24 (4H, s, $2\text{H}_1+2\text{H}_9$).

^{13}C -RMN (75.47 MHz, CDCl_3): δ 17.9 (2xCH_2), 27.3 (CH_2), 51.3 (2xCH_2), 79.0 (2xC), 85.3 (2xC).

MS (Cl^+) m/z (%): 133 ($\text{MH}^+-\text{H}_2\text{O}$, 12), 115 (5), 105 (65), 91 (100).

HRMS: calculated for $\text{C}_9\text{H}_9\text{O}$ ($\text{MH}^+-\text{H}_2\text{O}$): 133.0653; found: 133.0654.

IR (Csl): ν 3332 (O-H), 2224 ($\text{C}\equiv\text{C}$).

10-Triisopropylsilyldeca-2,7,9-triyn-1-ol (15).

To mixture of Pd_2dba_3 (0.036 g, 0.04 mmol), CuI (0.007 g, 0.04 mmol) and Lil (0.03 g, 0.23 mmol) in degassed DMSO (3 mL), cooled at 0 °C, was added dropwise a solution of octa-2,7-diyne-1-ol (**12**) (0.17 g, 1.4 mmol) and 2-iodo-1-triisopropylsilylacetylene (**14**) (0.15 g, 0.49 mmol) in DMSO (3 mL). After stirring for 5 min at 0 °C, Et_3N (0.390 mL, 2.81 mmol) was added and the reaction was stirred for 14 h at rt. The mixture was diluted with Et_2O (15 mL) and washed with saturated NH_4Cl aqueous solution (10 mL). The organic phase was separated and the aqueous phase was extracted with Et_2O (3 x 15 mL). The combined organic phases were extracted with

saturated aqueous solutions of NH_4Cl (2 x 30 mL), $\text{Na}_2\text{S}_2\text{O}_3$ (2 x 30 mL) and NaCl (2 x 30 mL) and dried over Na_2SO_4 . After removal of the solvent, the residue was purified by flash chromatography (hexane/ethyl acetate 80:20) to yield the title compound (0.14 g, 95 % yield) as a yellow oil.

^1H -RMN (250.13 MHz, CDCl_3): δ 1.07 (21H, m, TIPS), 1.74 (2H, q, $J = 6.9$ Hz, 2H_5), 2.3-2.4 (4H, m, $2\text{H}_4 + 2\text{H}_6$), 4.25 (2H, s, 2H_1).

^{13}C -RMN (75.47 MHz, CDCl_3): δ 11.3 (3xCH, TIPS), 17.9 (CH_2), 18.3 (CH_2), 18.5 (6x CH_3 , TIPS), 27.1 (CH_2), 50.9 (CH_2), 66.4 (C), 77.4 (C), 79.3 (C), 80.2 (C), 84.5 (C), 89.8 (C).

MS (Cl^+) m/z (%): 303 (MH^+ , 18), 285 (46), 259 (34), 243 (40), 157 (100).

HRMS: calculated for $\text{C}_{19}\text{H}_{31}\text{OSi}$: 303.2144; found: 303.2148.

IR (Csl): ν 3310 (O-H), 2104 ($\text{C}\equiv\text{C}$).

10-Triisopropylsilyldeca-2,7,9-triyn-1-al (**16**).

A solution of alcohol **15** (0.70 g, 2.30 mmol) in dry CH_2Cl_2 (40 mL) was added to a stirred suspension of the Dess-Martin periodinane (2.21 g, 5.21 mmol) and NaHCO_3 (0.44 g, 5.21 mmol) in CH_2Cl_2 (10 mL). After stirring for 24 h, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and filtered through Celite. The solvent was removed in vacuo and the crude was purified by flash chromatography (hexane/ethyl acetate 75:25) to afford the title compound (0.62 g, 89 % yield) as a yellow oil.

^1H -RMN (250.13 MHz, CDCl_3): δ 1.07 (21H, m, TIPS), 1.84 (2H, q, $J = 6.9$ Hz, 2H_5), 2.45 (2H, t, $J = 6.9$ Hz, 2H_6), 2.57 (2H, t, $J = 6.9$ Hz, 2H_4), 9.18 (1H, s, CHO).

^{13}C -RMN (62.90 MHz, CDCl_3): δ 11.2 (3xCH, TIPS), 18.2 (CH_2), 18.4 (CH_2), 18.5 (6x CH_3 , TIPS), 26.1 (CH_2), 67.1 (C), 77.2 (C), 81.1 (C), 82.1 (C), 89.6 (C), 97.3 (C), 177.0 (CH, CHO).

MS (Cl^+) m/z (%): 302 (MH^+ , 30), 301 (M^+ , 100), 285 (16), 257 (79), 157 (54).

HRMS: calculated for $\text{C}_{16}\text{H}_{21}\text{OSi}$ (M-iPr): 257.1362; found: 257.1364.

IR (Csl): ν 2737 ($\text{C}=\text{O}$), 2225, 2104 ($\text{C}\equiv\text{C}$).

1,1-Dibromo-11-triisopropylsilylundec-1-ene-3,8,10-triyn (17).

Following the same procedure described for **10**, reaction of 10-triisopropylsilyldeca-2,7,9-triyn-1-ol (**16**) (0.65 g, 2.16 mmol) with PPh₃ (1.42 g, 5.40 mmol) and CBr₄ (1.47 g, 4.43 mmol) in Et₃N (0.6 mL, 4.35 mmol) and CH₂Cl₂ (35 mL) afforded the title compound (0.98 g, 99 % yield) as a yellow oil.

¹H-RMN (250.13 MHz, CDCl₃): δ 1.07 (21H, m, TIPS), 1.80 (2H, q, *J* = 6.9 Hz, 2H₆), 2.4-2.5 (4H, m, 2H₅+2H₇), 6.52 (1H, t, *J* = 2.0 Hz, H₂).

¹³C-RMN (75.47 MHz, CDCl₃): δ 11.4 (3xCH, TIPS), 18.5 (CH₂), 18.6 (6xCH₃, TIPS), 19.1 (CH₂), 26.9 (CH₂), 66.6 (C), 77.2 (C), 78.6 (C), 80.4 (C), 89.8 (C), 97.5 (C), 100.7 (C), 119.6 (CH).

MS (CI⁺) *m/z* (%): 459 (1), 457 (3), 455 (MH⁺, 3), 454 (M⁺, 1), 415 (12), 413 (24), 411 (11), 335 (11), 333 (13), 157 (67), 28 (100).

HRMS: calculated for C₂₀H₂₈Br₂Si: 454.0327; found: 454.0323.

IR (Csl): ν 2223, 2105 (C≡C).

1-Triisopropylsilylundeca-1,3,8,10-tetrayne (7).

EtMgBr (1M in THF, 9.60 mL, 9.60 mmol) was added dropwise to a cooled solution of dibromoalkene **17** (1.45 g, 3.17 mmol) in THF (100 mL) as a rate to maintain the reaction mixture at 0°C. After stirring for 6 h, saturated aqueous solution of NH₄Cl (100 mL) was added and the mixture was extracted with Et₂O (2 x 100 mL). The

organic layer was washed with saturated aqueous solution of NaHCO_3 (3 x 150 mL) and brine (2 x 150 mL), dried and concentrated. The residue was purified by flash chromatography (hexane) to afford the title compound (0.78 g, 83 % yield) as a yellow oil.

^1H -RMN (250.13 MHz, CDCl_3): δ 1.08 (21H, m, TIPS), 1.78 (2H, q, J = 6.8 Hz, 2H_6), 1.98 (1H, s, H_{11}), 2.42 (4H, t, J = 6.8 Hz, $2\text{H}_5+2\text{H}_7$).

^{13}C -RMN (75.47 MHz, CDCl_3): δ 11.3 (3xCH, TIPS), 18.2 (CH_2), 18.4 (CH_2), 18.5 (6x CH_3 , TIPS), 26.6 (CH_2), 64.9 (CH), 65.6 (C), 66.8 (C), 68.2 (C), 76.8 (C), 76.9 (C), 80.7 (C), 89.7 (C).

MS (EI^+) m/z (%): 296 (M^+ , 6), 253 (37), 211 (69), 183 (100), 169 (40).

HRMS: calculated for $\text{C}_{20}\text{H}_{28}\text{Si}$: 296.1960; found: 296.1960.

IR (Csl): ν 3310 ($\equiv\text{C-H}$), 2144 ($\text{C}\equiv\text{C}$).

6-Iodo-5-hexyn-1-ol (18).

To a solution of 5-hexyn-1-ol (1 mL, 0.89 g, 9.07 mmol) in MeOH (10 mL) was added an aqueous solution (2 mL) of KOH (1.27 g, 22.7 mmol) and the mixture was stirred for 10 min at 0 °C. Iodine (2.53 g, 9.98 mmol) was added in one portion and the mixture was then warmed to rt. After being stirring for 3 h, the mixture was diluted with H_2O (15 mL) and the aqueous layer was extracted with Et_2O (3 x 25 mL). The combined organic layers were concentrated to give a residue which was dissolved in CH_2Cl_2 (15 mL) and washed with saturated aqueous solutions of $\text{Na}_2\text{S}_2\text{O}_3$ (15 mL) and NaCl (15 mL). Purification by flash-chromatography (CH_2Cl_2 /ethyl acetate 90:10) afforded the title compound (1.23 g, 61 % yield) as a yellow oil.

^1H -RMN (250.13 MHz, CDCl_3): δ 1.5-1.7 (4H, m, $2\text{H}_2 + 2\text{H}_3$), 2.41 (2H, t, J = 6.8 Hz, 2H_4), 3.70 (2H, t, J = 6.1 Hz, 2H_1).

^{13}C -RMN (75.46 MHz, CDCl_3): δ -6.2 (C-I), 20.5 (CH_2), 24.7 (CH_2), 31.5 (CH_2), 61.8 (CH_2), 94.1 (C).

MS (CI^+) m/z (%): 225 (MH^+ , 3), 207 (2), 97 (57), 80 (100), 79 (92).

HRMS: calculated for $\text{C}_6\text{H}_{10}\text{OI}$: 224.9776; found: 224.9784.

IR (Csl): ν 3343 (O-H), 2183 ($\text{C}\equiv\text{C}$).

8-Trimethylsilylocta-5,7-diyn-1-ol (**20**).

To a solution of trimethylsilylacetylene (0.50 mL, 0.34 g, 3.51 mmol) and 6-iodo-5-hexyn-1-ol (**18**) (0.30 g, 1.34 mmol) in degassed piperidine (2 mL), cooled at 0 °C, was added CuCl (0.01 g, 0.14 mol) and the mixture was stirred at rt for 30 min. Saturated NH₄Cl aqueous solution (6 mL) was added and the reaction mixture was extracted with Et₂O (3 x 10 mL). Combined organic layers were washed with brine (2 x 25 mL), dried over Na₂SO₄ and concentrated. Purification by flash chromatography (CH₂Cl₂/ethyl acetate 95:5) gave the title compound (0.22 g, 87 % yield) as a yellow oil.

¹H-RMN (250.13 MHz, CDCl₃): δ 0.15 (9H, s, TMS), 1.6-1.7 (4H, m, 2H₂ + 2H₃), 2.01 (1H, broad s, OH), 2.30 (2H, t, *J* = 6.6 Hz, 2H₄), 3.61 (2H, t, *J* = 6.0 Hz, 2H₁).

¹³C-RMN (62.90 MHz, CDCl₃): δ -0.4 (3xCH₃, TMS), 18.9 (CH₂), 24.3 (CH₂), 31.5 (CH₂), 62.0 (CH₂), 65.7 (C), 79.6 (C), 83.1 (C), 88.3 (C).

MS (Cl⁺) *m/z* (%): 195 (MH⁺, 20), 177 (20), 161 (17), 105 (79), 73 (100).

HRMS: calculated for C₁₁H₁₉OSi: 195.1204; found: 195.1205.

IR (Csl): ν 3339 (O-H), 2225, 2108 (C≡C).

8-Trimethylsilylocta-5,7-diyn-1-ol (20).

Following the same procedure as for **16**, treatment of 8-trimethylsilylocta-5,7-diyn-1-ol (**20**) (0.50 g, 2.57 mmol) with the Dess-Martin periodinane (2.18 g, 5.14 mmol) in CH_2Cl_2 (30 mL) afforded, after 2 h, the title compound (0.42 g, 84 % yield) as a yellow oil.

^1H -RMN (300.07 MHz, CDCl_3): δ 0.18 (9H, s, TMS), 1.85 (2H, q, $J = 6.9$ Hz, 2H_3), 2.36 (2H, t, $J = 6.9$ Hz, 2H_4), 2.61 (2H, dt, $J = 6.9, 0.9$ Hz, 2H_2), 9.79 (1H, t, $J = 0.9$ Hz, H_1).

^{13}C -RMN (62.90 MHz, CDCl_3): δ -0.5 ($3\times\text{CH}_3$, TMS), 18.4 (CH_2), 20.4 (CH_2), 42.4 (CH_2), 66.3 (C), 78.3 (C), 83.5 (C), 88.0 (C), 201.3 (CH).

MS (Cl^+) m/z (%): 193 (MH^+ , 91), 177 (100), 149 (6).

HRMS: calculated for $\text{C}_{11}\text{H}_{17}\text{OSi}$: 193.1049; found: 193.1048.

IR (Csl): ν 2727 (C=O), 2225, 2108 ($\text{C}\equiv\text{C}$).

(1Z)-1-Iodo-9-trimethylsilylnon-1-ene-6,8-diyne (22).

To a suspension of iodomethyltriphenyl phosphonium iodide (2.88 g, 5.43 mmol) in THF (30 mL) was slowly added 5 mL of a 1M solution of sodium hexamethyldisilazane in THF. After stirring for 10 min, the solution was cooled at -78°C and HMPA (4 mL) and a solution of aldehyde **21** (0.95 g, 4.94 mmol) in THF (10 mL) were added. The cold bath was removed, and stirring was continued for 1 h. The mixture was washed with H_2O (60 mL) and brine (2 x 30 mL), dried (Na_2SO_4) and concentrated. After purification by flash chromatography (hexane) the title compound (1.03 g, 66 % yield) was obtained as a colorless oil. *Z/E* ratio, as determined by ^1H -NMR, was 9/1.

^1H -RMN (250.13 MHz, CDCl_3): δ 0.16 (9H, s, TMS), 1.6-1.7 (2H, m, 2H_4), 2.2-2.3 (4H, m, $2\text{H}_3 + 2\text{H}_5$), 6.1-6.2 (1H, m, H_2), 6.25 (1H, dt, $J = 7.3, 1.3$ Hz, H_1).

^{13}C -RMN (62.90 MHz, CDCl_3): δ -0.4 ($3\times\text{CH}_3$, TMS), 18.7 (CH_2), 26.4 (CH_2), 33.7 (CH_2), 66.0 (C), 79.1 (C), 83.2 (C), 83.6 (CH), 88.3 (C), 139.7 (CH).

MS (Cl^+) m/z (%): 317 (MH^+ , 2), 316 (M^+ , 6), 301 (61), 190 (62), 175 (38), 160 (2), 145 (20), 117 (26), 73 (100).

HRMS: calculated for $C_{12}H_{17}Si$: 316.0144; found: 316.0150.

IR (Csl): ν 2225, 2107 ($C\equiv C$).

(3Z)-1-Triisopropylsilyl-11-trimethylsilylundec-3-ene-1,8,10-triyn (24).

A mixture of (*Z*)-iodo-9-trimethylsilylnon-1-ene-6,8-diyne (**22**) (0.25 g, 0.79 mmol), triisopropylsilylacetylene (0.55 mL, 0.45 g, 2.48 mmol), $PdCl_2(PPh_3)_2$ (0.06 g, 0.09 mmol) and CuI (0.02 g, 0.1 mmol) in degassed piperidine (8 mL) was stirred at rt for 4 h. Et_2O (15 mL) was added and the resulting solution was washed with saturated NH_4Cl aqueous solution (2 x 20 mL) and brine (2 x 20 mL), dried over Na_2SO_4 and concentrated. Purification by flash chromatography (hexane/ethyl acetate 95:5) gave the title compound (0.20 g, 70 % yield) as a yellow oil.

1H -RMN (250.13 MHz, $CDCl_3$): δ 0.18 (9H, s, TMS), 1.08 (21H, m, TIPS), 1.66 (2H, q, $J = 7.4$ Hz, $2H_6$), 2.29 (2H, t, $J = 7.4$ Hz, $2H_7$), 2.43 (2H, c, $J = 7.4$ Hz, $2H_5$), 5.56 (1H, d, $J = 10.8$ Hz, H_3), 5.91 (1H, dt, $J = 10.8, 7.4$ Hz, H_4).

^{13}C -RMN (75.47 MHz, $CDCl_3$): δ -0.2 (3x CH_3 , TMS), 11.4 (3xCH, TIPS), 18.7 (6x CH_3 , TIPS), 19.0 (CH_2), 27.5 (CH_2), 29.6 (CH_2), 65.8 (C), 79.4 (C), 83.1 (C), 88.4 (C), 95.5 (C), 103.3 (C), 110.8 (CH), 142.9 (CH).

MS (Cl^+) m/z (%): 371 (MH^+ , 7), 355 (14), 327 (43), 313 (31), 285 (67), 157 (100).

HRMS: calculated for $C_{23}H_{39}Si_2$: 371.2593; found: 371.2596.

IR (Csl): ν 2226, 2146, 2109 ($C\equiv C$).

(3Z)-1-Triisopropylsilylundec-3-ene-1,8,10-triyn (8).

To a solution of **24** (0.26 g, 0.7 mmol) in a 1:1 mixture MeOH/THF (12 mL) was added K_2CO_3 (0.37 g, 2.68 mmol) and the reaction was stirred for 30 min. The mixture was diluted with a solution 1:2 EtOH/ H_2O (12 mL) and the organic layer was washed with H_2O (20 mL) and brine (2 x 20 mL), dried and concentrated. Purification by flash chromatography (hexane/ethyl acetate 98:2) afforded the title compound (0.20 g, 95 % yield) as a yellow oil.

^1H -RMN (250.13 MHz, CDCl_3): δ 1.08 (21H, s, TIPS), 1.68 (2H, q, $J = 7.3$ Hz, 2H_6), 1.96 (1H, s, H_{11}), 2.28 (2H, t, $J = 7.3$ Hz, 2H_7), 2.44 (2H, dt, $J = 7.7, 7.3$ Hz, 2H_5), 5.56 (1H, d, $J = 11.1$ Hz, H_3), 5.92 (1H, dt, $J = 11.1, 7.7$ Hz, H_4)

^{13}C -RMN (62.90 MHz, CDCl_3): δ 11.2 (3xCH, TIPS), 18.6 (6xCH₃, TIPS), 18.7 (CH₂), 27.3 (CH₂), 29.5 (CH₂), 64.6 (CH), 65.0 (C), 68.4 (C), 77.8 (C), 95.6 (C), 103.3 (C), 110.9 (CH), 143.0 (CH).

MS (Cl^+) m/z (%): 299 (MH^+ , 4), 298 (M^+ , 2), 255 (68), 213 (91), 157 (100).

HRMS: calculated for $\text{C}_{20}\text{H}_{31}\text{Si}$: 299.2195; found: 299.2198.

IR (Csl): ν 3311 ($\equiv\text{C-H}$), 2227, 2146 ($\text{C}\equiv\text{C}$).

(1Z,7Z)-1-Bromo-10-[(3'-cyanopropyl)dimethylsilyl]deca-1,7-dien-9-yne (6).

To a solution of dibromide **4** (0.32 g, 1.19 mmol) in degassed benzene (10 mL) were added, successively, $\text{PdCl}_2(\text{PPh}_3)_2$ (0.11 g, 0.15 mmol), CuI (0.029 g, 0.15 mmol) and $n\text{BuNH}_2$ (0.66 mL, 0.49 g, 6.65 mmol) and the mixture was stirred for 10 min. A solution of (3'-cyanopropyl)dimethylsilylacetylene (**5**) (0.09 g, 0.59 mmol) in benzene (2 mL) was added dropwise from an automatic syringe ($\Phi = 12$ mm, $v = 1$ mL/h) and the reaction mixture was stirred for 5 h more. Saturated aqueous solution of NH_4Cl (15 mL) was added and the organic phase was

washed with brine (3 x 10 mL), dried and concentrated. Flash chromatography (hexane/ethyl acetate 90:10) afforded the title compound (0.15 g, 77 % yield) as a yellow oil, together with a small amount of the dicoupling product (3Z,9Z)-1,12-bis-[(3'-cyanopropyl)dimethylsilyl]dodeca-3,9-diene-1,11-diyne (**25**) (0.01 g, 8 % yield).

^1H -RMN (250.13 MHz, C_6D_6): δ 0.06 (6H, s, SiMe_2), 0.3-0.4 (2H, m, 2H_1), 1.2-1.3 (6H, m, $2\text{H}_4+2\text{H}_5+2\text{H}_2$), 1.50 (2H, t, $J = 6.9$ Hz, 2H_3), 2.0-2.1 (2H, m, 2H_3), 2.2-2.3 (2H, m, 2H_6), 5.44 (1H, d, $J = 10.9$ Hz, H_8), 5.6-5.7 (2H, m, H_2+H_7), 5.84 (1H, d, $J = 6.9$ Hz, H_1).

^{13}C -RMN (75.47 MHz, CDCl_3): δ -2.0 ($2\times\text{CH}_3$, SiMe_2), 15.5 (CH_2), 20.2 (CH_2), 20.4 (CH_2), 27.3 (CH_2), 27.8 (CH_2), 29.1(CH_2), 29.8 (CH_2), 96.2 (C), 103.0 (C), 107.6 (CH), 109.0 (CH), 119.4 (CN), 134.4 (CH), 145.2 (CH).

MS (Cl^+) m/z (%): 340 (1), 338 (MH^+ , 1), 337 (M^+ , <1), 324 (4), 322 (4), 258 (1), 126 (100).

HRMS: calculated for $\text{C}_{16}\text{H}_{24}\text{NSiBr}$: 337.0861; found: 337.0859.

IR: 2246 ($\text{C}\equiv\text{N}$), 2147 ($\text{C}\equiv\text{C}$).

(3Z,9Z)-1,12-Bis-[(3'-cyanopropyl)dimethylsilyl]dodeca-3,9-diene-1,11-diyne (**25**).

^1H -RMN (399.97 MHz, C_6D_6): δ 0.17 (12H, s, $2\text{Me}_2\text{Si}$), 0.7-0.8 (4H, m, 4H_1), 1.4-1.5 (4H, m, $2\text{H}_6+2\text{H}_7$), 1.7-1.8 (4H, m, 4H_2), 2.2-2.3 (4H, m, $2\text{H}_5+2\text{H}_8$), 2.37 (4H, t, $J = 7.0$ Hz, 4H_3), 5.45 (2H, dt, $J = 10.9, 1.4$ Hz, H_3+H_{10}), 5.95 (2H, dt, $J = 10.9, 6.5$ Hz, H_4+H_{11}).

^{13}C -RMN (100.58 MHz, CDCl_3): δ -1.8 ($4\times\text{CH}_3$), 15.7 ($2\times\text{CH}_2$), 20.4 ($2\times\text{CH}_2$), 20.6 ($2\times\text{CH}_2$), 28.2 ($2\times\text{CH}_2$), 30.2 ($2\times\text{CH}_2$), 96.4 ($2\times\text{C}$), 103.3 ($2\times\text{C}$), 109.1 ($2\times\text{CH}$), 119.6 ($2\times\text{CN}$), 145.6 ($2\times\text{CH}$).

MS (Cl^+) m/z (%): 409 (MH^+ , 4), 408 (M^+ , <1), 393 (4), 340 (3), 279 (4), 127 (57), 126 (100), 96 (27).

HRMS: calculated for $\text{C}_{24}\text{H}_{36}\text{N}_2\text{Si}_2$: 408.2417; found: 408.2420.

IR (CsI): ν 2245 ($\text{C}\equiv\text{N}$), 2146 ($\text{C}\equiv\text{C}$).

(3Z,9Z)-1-[(3'-Cyanopropyl)dimethylsilyl]-21-triisopropylsilylheneicosa-3,9,diene-1,11,13,18,20-pentayne (26).

Following the same procedure as described for **24**, treatment of vinyl bromide **6** (0.14 g, 0.42 mmol), alkyne **7** (0.25 g, 0.84 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (0.03 g, 0.04 mmol) and CuI (0.008 g, 0.04 mmol) in degassed pyrrolidine (4 mL) for 2 h afforded, after purification by flash chromatography (hexane/ethyl acetate 90:10), the title compound (0.17 g, 74 % yield) as a brown oil.

$^1\text{H-NMR}$ (300.08 MHz, CDCl_3): δ 0.22 (6H, s, Me_2Si), 0.8-0.9 (2H, m, 2H_1), 1.09 (21H, s, TIPS), 1.4-1.5 (4H, m, $2\text{H}_6+2\text{H}_7$), 1.7-1.8 (4H, m, $2\text{H}_{16}+2\text{H}_2$), 2.3-2.5 (10H, m, $2\text{H}_5+2\text{H}_8+2\text{H}_{15}+2\text{H}_{17}+2\text{H}_3$), 5.49 (2H, d, $J = 10.8$ Hz, H_3+H_{10}), 5.98 (1H, dt, $J = 10.8, 7.5$ Hz), 6.05 (1H, dt, $J = 10.8, 7.5$ Hz).

$^{13}\text{C-NMR}$ (75.47 MHz, CDCl_3): δ -1.6 ($2\times\text{CH}_3$, Me_2Si), 11.4 ($3\times\text{CH}$, TIPS), 15.9 (CH_2), 18.5 (CH_2), 18.7 ($6\times\text{CH}_3$, TIPS), 18.9 (CH_2), 20.6 (CH_2), 20.7 (CH_2), 26.9 (CH_2), 28.2 (CH_2), 28.4 (CH_2), 30.3 (CH_2), 30.6 (CH_2), 66.1 (C), 66.7 (C), 72.4 (C), 77.1 (C), 77.9 (C), 80.6 (C), 83.1 (C), 89.7 (C), 96.4 (C), 103.3 (C), 108.1 (CH), 109.1 (CH), 119.6 (CN), 145.5 (CH), 147.5 (CH).

MS (Cl^+) m/z (%): 554 (MH^+ , 3), 510 (3), 279 (6), 167 (22), 149 (70), 126 (100).

HRMS: calculated for $\text{C}_{36}\text{H}_{52}\text{NSi}_2$: 554.3638; found: 554.3641.

IR (CsI): ν 2244 ($\text{C}\equiv\text{N}$), 2224, 2147, 2104 ($\text{C}\equiv\text{C}$).

(3Z,9Z)-Heneicosa-3,9-diene-1,11,13,18,20-pentayne [Callyberyne A, Callypentayne] (2).

To a solution of **26** (0.06 g, 0.11 mmol) in THF (1 mL) was added TBAF (1.0 M solution in THF, 0.36 mL, 0.36 mmol) and the reaction was stirred at rt for 30 min. The mixture was diluted with Et₂O (3 mL), washed with brine (3 x 5 mL), dried and concentrated. Purification by flash chromatography (hexane/ethyl acetate 95:5) gave the title compound (0.025 g, 93 % yield) as a yellow oil.

¹H-RMN (300.13 MHz, CDCl₃): δ 1.4-1.5 (4H, m, 2H₆+2H₇), 1.78 (2H, q, J = 6.9 Hz, 2H₁₆), 1.98 (1H, s, H₂₁), 2.3-2.5 (8H, m, 2H₅+2H₈+2H₁₅+2H₁₇), 3.08 (1H, d, J = 1.7 Hz, H₁), 5.4-5.5 (2H, m, H₃+H₁₀), 5.99 (1H, dt, J = 10.8, 7.5 Hz), 6.04 (1H, dt, J = 10.8, 7.5 Hz).

¹³C-RMN (75.47 MHz, CDCl₃): δ 18.2 (CH₂), 18.7 (CH₂), 26.7 (CH₂), 28.1 (CH₂), 28.2 (CH₂), 30.0 (CH₂), 30.5 (CH₂), 64.9 (CH), 65.5 (C), 66.2 (C), 68.2 (C), 72.5 (C), 76.9 (C), 77.9 (C), 80.4 (C), 81.3 (CH), 82.9 (C), 108.2 (CH), 108.3 (CH), 145.7 (CH), 147.7 (CH).

MS (Cl⁺) m/z (%): 273 (MH⁺, 4), 272 (M⁺, 5), 229 (67), 215 (75), 203 (71), 165 (66), 28 (100).

HRMS: calculated for C₂₁H₂₁: 273.1643; found: 273.1634.

IR (Csl): ν 3296 ($\equiv\text{C-H}$), 2226 (C $\equiv$ C).

(3Z,12Z,18Z)-21-[(3'-Cyanopropyl)dimethylsilyl]-1-triisopropylsilylheneicosa-3,12,18-triene-1,7,9,20-tetrayne (27).

Following the same procedure as for **24**, treatment of **6** (0.06 g, 0.18 mmol), **8** (0.11 g, 0.37 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (0.014 g, 0.02 mmol) and CuI (0.004 g, 0.02 mmol) in degassed pyrrolidine (4 mL) for 1 h afforded, after purification by flash chromatography (hexane/ethyl acetate 98:2), the title compound (0.07 g, 68 % yield) as a yellow oil.

^1H -RMN (300.06 MHz, CDCl_3): δ 0.22 (6H, s, Me_2Si), 0.7-0.8 (2H, m, 2H_1), 1.09 (21H, s, TIPS), 1.4-1.5 (4H, m, $2\text{H}_{15}+2\text{H}_{16}$), 1.70 (2H, q, $J = 7.3$ Hz, 2H_6), 1.8-1.9 (2H, m, 2H_2), 2.3-2.5 (10H, m, $2\text{H}_3+2\text{H}_5+2\text{H}_7+2\text{H}_{14}+2\text{H}_{17}$), 5.48 (2H, d, $J = 10.3$ Hz, $\text{H}_{12}+\text{H}_{19}$), 5.55 (1H, d, $J = 11.0$ Hz, H_3), 5.9-6.1 (3H, m, $\text{H}_4+\text{H}_{13}+\text{H}_{18}$).

^{13}C -RMN (75.47 MHz, CDCl_3): δ -1.2 ($2\times\text{CH}_3$, Me_2Si), 11.8 ($3\times\text{CH}$, TIPS), 16.3 (CH_2), 19.1 ($6\times\text{CH}_3$, TIPS), 19.8 (CH_2), 20.9 (CH_2), 21.2 (CH_2), 28.1 (CH_2), 28.6 (CH_2), 29.0 (CH_2), 30.0 (CH_2), 30.1 (CH_2), 31.0 (CH_2), 65.9 (C), 72.5 (C), 78.7 (C), 84.6 (C), 95.8 (C), 96.8 (C), 103.7 ($2\times\text{C}$), 108.7 (CH), 109.5 (CH), 111.0 (CH), 120.0 (CN), 143.4 (CH), 145.9 (CH), 147.5 (CH).

MS (Cl^+) m/z (%): 557 (MH^+ , 1), 556 (M^+ , 3), 512 (4), 279 (7), 167 (19), 149 (57), 126 (96), 29 (100).

HRMS: calculated for $\text{C}_{36}\text{H}_{54}\text{NSi}_2$: 556.3795; found: 556.3803.

IR (Csl): ν 2245 ($\text{C}\equiv\text{N}$), 2146 ($\text{C}\equiv\text{C}$).

(3Z,12Z,18Z)-Heneicosa-3,12,18-triene-1,8,10,20-tetrayne [Callyberyne B] (3).

Following the same procedure as for **2**, treatment of a solution of **27** (0.05 g, 0.09 mmol) in THF (1 ML) with TBAF (1M in THF, 0.36 mL, 0.36 mmol) for 25 min gave, after purification by flash chromatography (hexane/ethyl acetate 95:5), the title compound (0.022 g, 90 %) as a colorless oil.

^1H -RMN (250.13 MHz, CDCl_3): δ 1.4-1.5 (4H, m, $2\text{H}_{15}+2\text{H}_{16}$), 1.65 (2H, q, $J = 7.3$ Hz, 2H_6), 2.3-2.5 (8H, m, $2\text{H}_5+2\text{H}_7+2\text{H}_{14}+2\text{H}_{17}$), 3.09 (2H, t, $J = 2.8$ Hz, H_1+H_{21}), 5.4-5.5 (3H, m, $\text{H}_3+\text{H}_{12}+\text{H}_{19}$), 6.0-6.1 (3H, m, $\text{H}_4+\text{H}_{13}+\text{H}_{18}$).

^{13}C -RMN (100.58 MHz, CDCl_3): δ 19.2 (CH_2), 27.4 (CH_2), 28.1 (CH_2), 28.2 (CH_2), 29.4 (CH_2), 30.0 (CH_2), 30.4 (CH_2), 65.6 (C), 72.2 (C), 78.2 (C), 80.1 (C), 80.4 (C), 81.3 (CH), 81.8 (CH), 84.2 (C), 108.2 (CH), 108.3 (CH), 109.3 (CH), 144.2 (CH), 145.7 (CH), 147.4 (CH).

MS (Cl^+) m/z (%): 275 (MH^+ , 3), 181 (50), 179 (77), 156 (21), 155 (72), 92 (16), 91 (100), 79 (88).

HRMS: calculated for $\text{C}_{21}\text{H}_{23}$: 275.1800; found: 275.1794.

IR (CsI): ν 3294 ($\equiv\text{C-H}$), 2233, 2146 ($\text{C}\equiv\text{C}$).