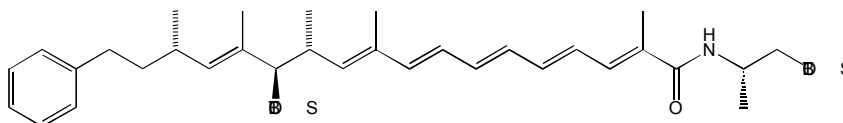


135.21; 142.37; 142.75; 143.96; 144.52; 152.40; 193.50; HRMS calc'd for C₃₂H₄₈O₂Si: 492.3424; found 492,3437.

Amide **14**

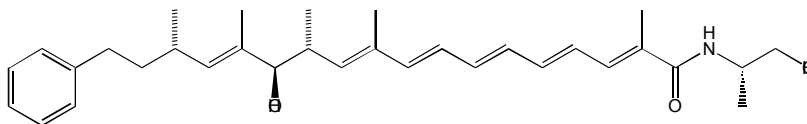


To a solution of diisopropylethylamine (24 μ L, 168 μ mol) in THF (2 mL) cooled to 0°C was added n-butyllithium (114 μ L, 1.48 M in hexane, 169 μ mol). After 15 min at this temperature [1-(2-*tert*-butyldimethylsilyloxy-1-methyl-ethylcarbamoyl)-ethyl]-phosphonic acid diethyl-ester **4** (44 mg, 112 μ mol) in THF (1 mL) was added dropwise. After another 15 min a solution of the tetraenal **3** (25 mg, 51 μ mol) in THF (0.5 mL) was added. The reaction mixture was stirred at 0°C for 30 min under complete exclusion of light. Silica gel (0.5 g) was added and the solvent was distilled off. Flash chromatography (pentane/*tert*-butyl methyl ether 1:1) provided amide **14** (28 mg, 76 %) as a yellow oil. ¹H-NMR (300 MHz, CDCl₃): δ = 7.25 (m_c, 2 H), 7.14 (m_c, 3 H), 6.98 (dd, J = 10.7 and 1.5 Hz, 1 H), 6.29-6.50 (m, 4 H), 6.18 (dd, J = 15.1 and 9.9 Hz, 1 H), 6.03 (d, J = 7.7 Hz, 1 H), 5.38 (d, J = 9.2 Hz, 1 H), 5.07 (d, J = 9.4 Hz, 1 H), 4.08-4.21 (m, 1 H), 3.67 (d, J = 7.7 Hz, 1 H), 3.64 (dd, J = 10.0 and 4.1 Hz, 1 H), 3.56 (dd, J = 9.9 and 2.9 Hz, 1 H), 2.37-2.73 (m, 4 H), 1.94 (d, J = 0.7 Hz, 3 H), 1.76 (d, J = 1.1 Hz, 3 H), 1.54 (d, J = 1.4 Hz, 3 H), 1.46-1.66 (m, 2 H), 1.18 (d, J = 6.8 Hz, 3 H), 0.93 (d, J = 6.4 Hz, 3 H), 0.90 (s, 9 H), 0.85 (d, J = 6.9 Hz, 3 H), 0.71 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H), -0.07 (s, 3 H), -0.07 (s, 3H), the signal of the amide-proton wasn't resolved; ¹³C-NMR (50 MHz, CDCl₃): δ = -5.48 (2 C), -4.94, -4.58, 11.40, 12.86, 12.92, 17.51, 17.59, 18.00, 18.07, 20.75, 25.76 (3 C), 25.85 (3 C), 31.85, 34.06, 37.63, 39.54, 46.45, 65.93, 83.57, 126.41, 126.89, 127.57, 129.08 (2 C), 129.11 (2 C), 131.94, 133.76, 134.47, 134.60, 134.77, 136.19, 137.45, 139.32, 140.38, 141.05, 143.62, 168.85.

Some peaks could be assigned to the C-6/C-7 – *Z* – isomer:

δ = 6.74 (d, J = 15.0 Hz, 0.1 H), 6.60 (dd, J = 15.0, and 11.0 Hz, 0.1 H).

Phenalamide A₂ **1b**



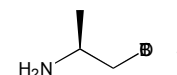
To a solution of amide **14** (10 mg, 14 μ mol) in acetonitrile (0.5 mL) was added hydrofluoric acid (0.1 mL) at 0°C. The reaction mixture was stirred under complete exclusion of light and monitored by TLC. After 3 h saturated aqueous NaHCO₃ (2 mL) was added. The phases were separated and the aqueous phase was extracted with CH₂Cl₂ (3 x 3 mL). The combined organic phases were dried (MgSO₄) and the solvent was distilled off. The crude product was purified by chromatography on reversed-phase silica gel (methanol/water 9:1) to give 6 mg (86 %) of Phenalamide A₂ **1b**. ¹H-NMR (500 MHz, CD₃OD): δ = 7.22 (t, J = 7.5 Hz, 2 H), 7.12 (m, 3 H), 6.92 (d, J = 8.9 Hz, 1 H), 6.51-6.59 (m, 2 H), 6.36-6.43 (m, 3 H), 6.25-6.30 (m, 1 H), 5.53 (d, J = 9.6 Hz, 1 H), 5.20 (d, J = 9.2 Hz, 1 H), 4.01-4.06 (m, 1 H), 3.76 (d, J = 7.6 Hz, 1 H), 3.51 (ddd, J = 16.8, 11.3, and 5.6 Hz, 2 H), 2.72-2.79 (m, 1 H), 2.60 (ddd, J = 14.3, 8.9, and 4.6 Hz, 1 H), 2.48-2.54 (m, 1 H), 2.39-2.45 (m, 1 H), 1.97 (s, 3 H), 1.82 (s, 3 H), 1.62-1.69 (m, 1 H), 1.60 (s, 3 H), 1.47-1.55 (m, 1 H), 1.25 (d, J = 6.8 Hz, 3 H), 0.97 (d, J = 6.6 Hz, 3 H), 0.93 (d, J = 6.8 Hz, 3 H), the signals of the NH and the OH protons weren't

34.97, 38.03, 40.82, 66.14, 83.56, 126.65, 127.72, 128.13, 129.29 (2 C), 129.33 (2 C), 130.72, 132.78, 135.14, 135.24, 135.32, 136.32, 137.76, 139.42, 139.91, 141.00, 143.94, 171.82, one signal was obscured by the solvent peak. HRMS calc'd for C₃₂H₄₅NO₃: 491,3399, found: 491,3410.

Some peaks could be assigned to the C-6/C-7 – Z – isomer Phenalamide A₁ **1a**:

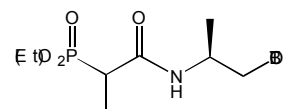
δ = 7.08 (dd, J = 15.0, and 11.1 Hz, 0.2 H), 7.00 (d, J = 12.2 Hz, 0.2 H), 6.74 (dd, J = 15.5, and 10.0 Hz, 0.2 H), 6.15 (m, 0.4 H).

O-*tert*-butyldimethylsilyl-alaninol **7**



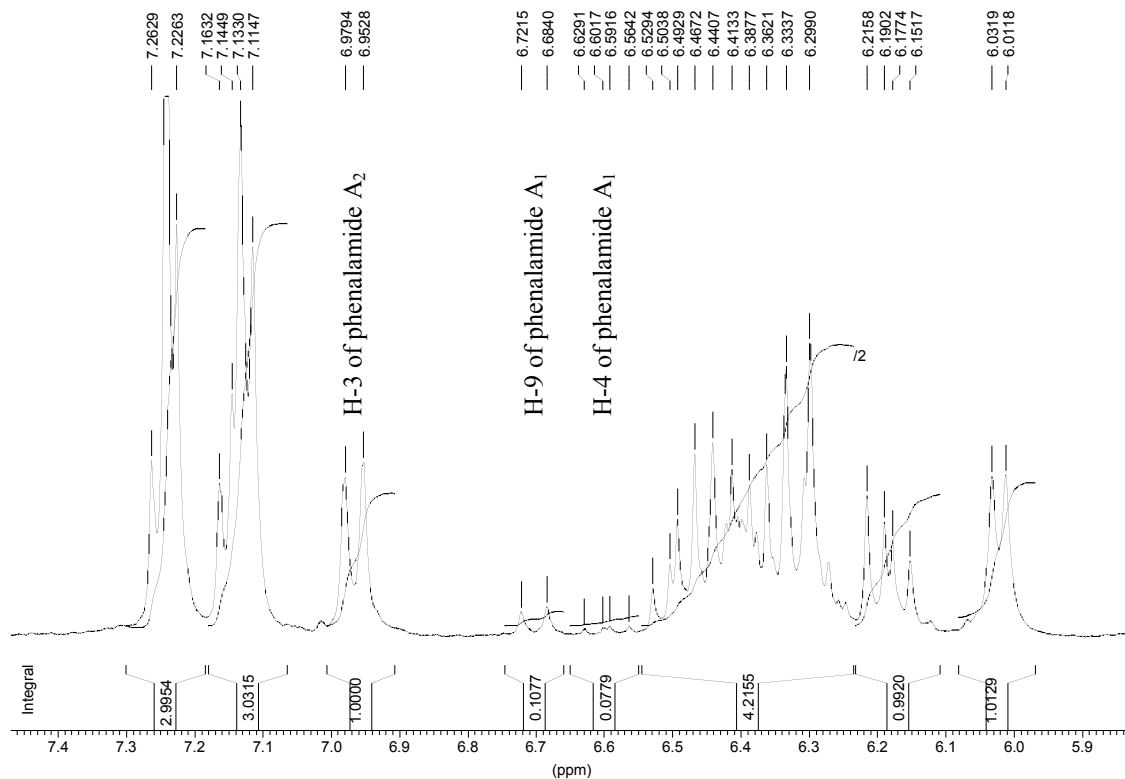
A solution of *tert*-butyldimethylchlorosilane (9.04 g, 60 mmol) in Hexane (10 mL) was added by a syringe pump to a cooled (0°C) solution of alaninol (3.76 g, 50 mmol) and imidazole (4.08 g, 60 mmol) in CH₂Cl₂ (30 mL). After 18 h at room temperature saturated aqueous NaHCO₃ (75 mL) was added. The phases were separated and the aqueous phase was extracted with CH₂Cl₂ (4 x 30 mL). The combined organic phases were dried (MgSO₄) and the solvent was distilled off. Distillation of the residue provided *O*-*tert*-butyldimethylsilyl-alaninol **7** (8.71 g, 92 %) as a colorless liquid. Bp: 67°C (11 mbar); ¹H-NMR (500 MHz, CDCl₃): δ = 0.01 (s, 6 H), 0.85 (s, 9 H), 0.96 (d, J = 6.5 Hz, 3 H), 2.91 (quind, J = 6.7 and 4.3 Hz, 1 H), 3.22 (dd, J = 9.7 and 7.4 Hz, 1 H), 3.46 (dd, J = 9.6 and 4.2 Hz, 1 H); ¹³C-NMR (50 MHz, CDCl₃): δ = -5.03, -5.00, 18.15, 19.58, 26.26 (3 C), 48.90, 70.11; HRMS calc'd for C₉H₂₃NOSi: 189,1549, found: 189,1536.

Phosphonate **4**



Carbonyldiimidazole (4.20 g, 20 mmol) was added in small portions at 0°C to a solution of 2-diethylphosphonopropionic acid (4.20 g, 20 mmol) in CH₂Cl₂ (20 mL). The reaction mixture was stirred at 0°C for 30 min, washed with water (10 mL), dried (MgSO₄) and concentrated. The crude imidazolide (4.50 g, 17.1 mmol) was dissolved in CH₂Cl₂ (34 mL) and *O*-*tert*-butyldimethylsilyl-alaninol (3.25 g, 17.1 mmol) in CH₂Cl₂ (17 mL) was added dropwise at 0°C. After 30 min at 0°C the reaction mixture was quenched with saturated aqueous NH₄Cl solution (30 mL). The phases were separated and the aqueous phase was extracted with CH₂Cl₂ (2 x 20 mL). The combined organic phases were dried (MgSO₄) and the solvent was distilled off. Flash chromatography (*tert*-butyl methyl ether) provided phosphonate **4** (5.26 g, 81 %) as a colorless oil. ¹H-NMR (200 MHz, CDCl₃): δ = 6.63 (broad t, J = 9.1 Hz, 1 H), 4.06 (mc, 5 H), 3.49 (d, J = 4.0 Hz, 2 H), 2.75 (dq, J = 22.5, 7.3, and 3.3 Hz, 1 H), 1.34 (ddd, J = 17.8, 7.3, and 2.5 Hz, 3 H), 1.26 (td, J = 7.2 and 2.0 Hz, 6 H), 1.09 (d, J = 6.5 Hz, 3 H), 0.83 (s, 9 H), 0.01 (s, 6 H); ¹³C-NMR (50 MHz, CDCl₃): δ = -5.16 (2 C), 11.68 (d, J_{CP} = 6.2 Hz), 12.23 (d, J_{CP} = 6.2 Hz), 16.70 (d, J = 5.8 Hz), 17.43 (d, J = 4.5 Hz), 18.59 (s), 26.16 (s, 3 C), 38.70 (d), 41.31 (d), 47.27 (s), 62.88 (t, J = 6.8 Hz), 66.18 (d), 167.60 (d, J = 1.8 Hz); Calc'd for C₁₆H₃₆NO₅PSi: C, 50,37; H, 9,51; N, 3,67; found: C, 50,34; H, 9,30; N, 3,86.

Olefinic part of the spectrum of amide **14**.



Olefinic part of the spectrum of a 4 : 1 mixture of phenalamide **A₂** **1b** and phenalamide **A₁** **1a**.

