Supplementary Material (ESI) for Chemical Communications

Configurationally Stable Propeller-like Triarylphosphine and Triarylphosphine Oxide

Áron Pintér,[a] Gebhard Haberhauer,*[a] Isabella Hyla-Kryspin[b] and Stefan Grimme*[b]

[a] *Institut für Organische Chemie, Fachbereich Chemie, Universität Duisburg-Essen, Universitätsstraße 5, D-45117 Essen, Germany*

[b] *Organisch-Chemisches Institut, Westfälische Wilhelms-Universität, Corrensstrasse 40, D-48149 Münster, Germany*

Supporting Information

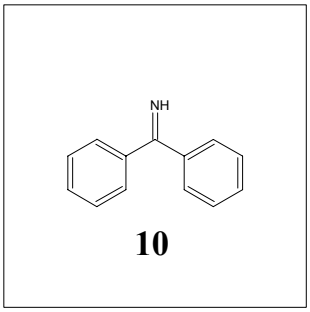
General remarks: Unless otherwise indicated, all reagents and solvents were purchased from commercial distributors and used without further purification. THF and diethyl ether were dried over sodium/benzophenone, DCM (dichloromethane) and acetonitrile were dried over CaH_2 and purified by distillation prior to use. Solvents (petroleum ether, ethyl acetate, dichloromethane, methanol) used for preparative liquid chromatography were of technical grade and used after distillation in a rotary evaporator. Benzophenone imine[1], glycine benzyl ester tosylate[2], benzyl N-(diphenylmethylene)glycinate[3], phthalimido acetic acid[4] and phthalimido acetyl chloride[4] were prepared according to reported procedures.

Moisture sensitive reactions were carried out in oven-dried (120 °C) glassware under an argon atmosphere using classical Schlenk-technique. Transfer of anhydrous solvents or mixtures were accomplished with the standard syringe/septum method. Reactions were monitored by TLC analysis with silica gel 60 F254 thin layer plates. Visualization of TLC zones was performed by irradiation with short-wave (254 nm) UV-emitting mercury lamp in a viewing cabinet or by dipping the developed TLC plate in 20% ethanolic solution of phosphomolybdic acid hydrate followed by drying it with a hot air gun at 300 °C. Flash chromatography was carried out on silica gel 60 (230-400 mesh). ^{1}H- and ^{13}C-NMR spectra were measured with Bruker Avance DRX 500 and DMX 300 spectrometers. All chemical shifts are given in ppm relative to TMS and were referenced to the solvent residual peaks. High resolution mass spectra were recorded with a Bruker BioTOF III Instrument. Infrared spectra were measured with a Varian 3100 FT-IR Excalibur Series spectrometer. UV-VIS spectra were recorded with a Varian Cary 300 spectrophotometer. Circular dichroism spectra were recorded with a Jasco J-815 CD-spectrophotometer. Elemental microanalyses were performed by the microanalytical laboratory of the Ruprecht-Karls University of Heidelberg.

Abbreviations: Boc: *tert*-butoxycarbonyl; Z: benzyloxycarbonyl; PhtN: phthalimido; Bn: benzyl; Val: valine; DCM: dichloromethane; DMF: N,N-dimethylformamide; EtOAc: ethyl acetate; MeOH: methanol; PE: petroleum ether; THF: tetrahydrofurane; NMM: N-methylmorpholine; PyBOP: **(**benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate

Benzophenone imine (10)

A dry three-necked round-bottom flask was equipped with a mechanical stirrer, a reflux condenser and a dropping funnel. Magnesium turnings (14.42 g, 600.0 mmol) were placed in the flask, activated with some iodine crystals (0.600 g) and finally covered with dry diethyl ether (200 mL). The stirring was switched on, and a solution of bromobenzene (94.206 g, 600.0 mmol) in diethyl ether (150 mL) was added within 80-90 minutes while maintaining a gentle reflux of the mixture upon heating. The reaction was allowed to stir at boiling temperature for further 2 hours, then a solution of benzonitrile (61.872 g, 600.0 mmol) in diethyl ether (100 mL) was added dropwise. After the addition was complete the mixture was stirred under reflux for further 8 hours. Then the heating bath was removed, and methanol (144 mL, 3560 mmol) was dropped cautiously to the mixture, while an intensive heat formation was observed. This slurry was stirred for further 2 hours, then filtered, and the filter cake was immediately washed two times with ethyl acetate (300 mL). The filtrate and the washings were mixed and evaporated to give a slightly brownish oil. Purification of this raw material was accomplished by distillation in high vacuum and provided **10** (86.12 g, 79.2%) as a light yellowish liquid. bp.: 116-125 °C at 1.0-1.3 mbar. TLC: R_f=0.45 (PE-EtOAc 4:1). ^{1}H-NMR (300 MHz, $CDCl_3$): δ= 9.07 (br s, 1H, *Ph_2C=N**H***), 7.58 (dd, 4H, $^3J_1$=8.0Hz, $^3J_2$=1.8Hz, Ph *C**H***-2,6), 7.52-7.38 (m, 6H, Ph *C**H***-3,4,5) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 178.2 (q, *Ph_2**C**=NH*), 139.2 (q, Ph ***C***-1), 130.2 (t, Ph ***C**H*-4), 128.3 (t, Ph ***C**H*-2,6), 128.2 (t, Ph ***C**H*-3,5) ppm. IR (KBr): ν = 3254, 3059, 3027, 1601, 1568, 1489, 1447, 1364, 1196, 1151, 1073, 1029, 931, 892, 789, 762, 720, 697, 670, 623 cm^{-1}. UV-VIS (CH_2Cl_2, c=0.132 mg/ml): λ_{max} (log ε) = 240 (4.13), 280 (3.34) nm. MS (EI+): m/z (%) = 181.2 $[M]^+$, 180.2, 152.2, 104.2, 77.1, 51.1; EA $C_{13}H_{11}N$ (181.23): calcd. C 86.15, H 6.12, N, 7.73; found C 85.92, H 6.13, N 7.72.

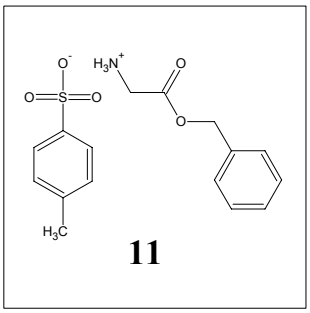


10

Glycine benzyl ester 4-toluenesulfonate (11)

In a three-necked round-bottom flask were placed glycine (15.01 g, 200.0 mmol), 4-toluenesulfonic acid monohydrate (39.95 g, 210.0 mmol), benzyl alcohol (43.26 g, 400.0 mmol) and toluene (200 mL). The flask was equipped with a stirring bar, a Dean-Stark trap and a reflux condenser and then immersed in an oil-bath. The mixture was heated to reflux temperature and the reaction was driven to completion by azeotropic removal of water over a period of 6 hours. Finally, the mixture was cooled to room temperature and diluted with diethyl ether (400 ml) to induce precipitation. The product was collected by filtration, washed two times with ether (200 mL), and dried in an oven at 75°C to yield 64.98 g (96.3%) of **11** as a white powder. TLC: R_f = 0.83 (DCM-MeOH 1:1).

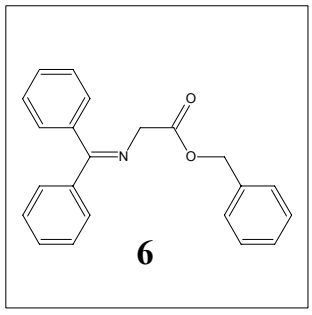
^{1}H-NMR (300 MHz, DMSO-d6): δ = 8.24 (br s, 3H, *N**H**$_3^+$*), 7.49 (d, 2H, J=7.75Hz, Ts *C**H***-2,6), 7.39 (m, 5H, Ph *C**H***-2,3,4,5,6), 7.12 (d, 2H, J=7.75Hz, Ts *C**H***-3,5), 5.23 (s, 2H, *CO_2C**H**$_2$Ph*), 3.89 (s, 2H, *C**H**$_2CO_2Bn$*), 2,28 (s, 3H, Ts *C**H**$_3$*) ppm. ^{13}C-NMR (75 MHz, DMSO-d6): δ = 167.5 (q, ***C**O$_2$Bn*), 145.4 (q, TsOH ***C***-1), 137.7 (q, TsOH ***C***-4), 135.2 (q, Ph ***C***-1), 128.4 (t, Ph ***C**H*-3,5), 128.3 (t, Ph ***C**H*-4), 128.2 (t, TsOH ***C**H*-3,5), 128.1 (t, TsOH ***C**H*-2,6), 125.4 (t, Ph ***C**H*-2,6), 66.8 (s, *CO_2**C**H$_2$Ph*), 20.7 (p, ***C**H$_3$*) ppm. IR (KBr): ν = 3438, 3036, 1752, 1600, 1524, 1498, 1454, 1417, 1373, 1185, 1126, 1037, 1012, 907, 814, 728, 688, 620, 568, 511 cm^{-1}. UV-VIS (MeOH, c=0.080 mg/ml): λ_{max} (log ε) = 210 (4.25), 250 (2.93), 262 (3.67) nm. MS (ESI+): m/z (%) = 165.9 (100) $[C_9H_{12}NO_2]^+$, 197.9 (48) $[C_9H_{12}NO_2$+MeOH$]^+$, 243.9 (10), 331.1 (14), 503.2 (20); EA $C_{16}H_{19}NO_5S$ (337.391): calcd. C 56.96, H 5.68, N 4.15; found C 56.75, H 5.65, N 4.22.



11

_N_-Diphenylmethylene-glycine benzyl ester (6)

To a stirred slurry of glycine benzylester 4-toluenesulfonate (67.48 g, 200.0 mmol) in DCM (400 mL) was added benzophenone imine (36.25 g, 200.0 mmol) in DCM (200 mL) over a period of 15 minutes, and then the mixture was stirred for 24 hours at ambient temperature. The resulting white milky mixture was thoroughly extracted with water (300 mL) and filtered through a glass funnel to remove precipitated solid material. The organic layer of the clear, biphasic filtrate was separated, extracted with water (100 mL) and brine (100 mL), then dried over $MgSO_4$, filtered and evaporated. The solidified row product was grinded and stirred in petroleum ether (200 mL) for a half hour, then filtered and dried to obtain compound **6** (52.70 g, 80.0%) as a white powder. TLC: R_f = 0.63 (PE-EtOAc 3:1).

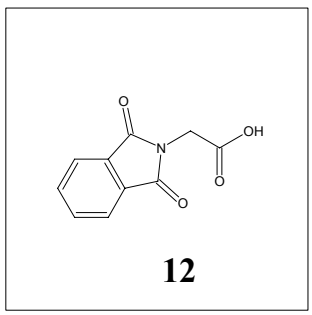


6

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.81 (dd, 1H, J_1=8.1Hz, J_2=1.5Hz), 7.67 (dd, 2H, J_1=8.1Hz, J_2=1.5Hz), 7.50 (dd, 1H, J_1=6.0Hz, J_2=1.5Hz), 7.44 (d, 2H, J=6.6Hz), 7.35 (d, 2H, J=6.6Hz), 7.35 (s, 5H), 7.17 (d, 1H, J=6.6Hz), 7.15 (d, 1H, J=6.6Hz), 5.20 (s, 2H, *$CO_2C\mathbf{H}_2Ph$*), 4.27 (s, 2H, *$C\mathbf{H}_2CO_2Bn$*) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 172.0 (q, *$Ph_2\mathbf{C}$=N*), 170.4 (q, *$\mathbf{C}O_2Bn$*), 139.1 (q), 135.9 (q), 135.7 (q), 130.5 (t), 128.8 (t), 128.75 (t, 2x), 128.65 (t, 2x), 128.5 (t, 2x), 128.3 (t, 2x), 128.2 (t, 2x), 128.0 (t), 127.6 (t, 2x), 66.5 (s, *$CO_2\mathbf{C}H_2Ph$*), 55.6 (s, *$\mathbf{C}H_2CO_2Bn$*) ppm. IR (KBr): ν = 3432, 3060, 2955, 2900, 2870, 1960, 1894, 1829, 1748, 1624, 1596, 1444, 1386, 1351, 1313, 1288, 1220, 1177, 1054, 958, 918, 908, 780, 758, 706, 696, 583 cm^{-1}. UV-VIS (CH_2Cl_2, c=0.012 mg/ml): λ_{max} (log ε) = 250 (4.164) nm. HRMS (ESI+) Exact mass calculated for $[C_{22}H_{20}NO_2]^+$: 330.1489, found: 330.1498.; EA $C_{22}H_{19}NO_2$ (329.392): calcd. C 80.22, H 5.81, N 4.25; found C 80.12, H 5.82, N 4.25.

Phthalimido acetic Acid (12)

In a three-necked round-bottom flask were placed glycine (22.52 g, 300.0 mmol), phthalic anhydride (44.44 g, 300.0 mmol), triethyl amine (3.036 g, 30.0 mmol) and toluene (180 mL). The flask was equipped with a stirring bar, a Dean-Stark trap and a reflux condenser. The mixture was heated to reflux temperature and stirred for further 6 hours with azeotropic removal of water. After completion of the reaction the solvent was removed in a rotary evaporator. The resulting white solid was taken up in water (450 mL) and the mixture was acidified by adding conc. hydrochloric acid (6.0 mL, 66.0 mmol). The product was collected by filtration, washed with water (2x 30 mL) and dried to yield 60.87 g (98.9%) of **12** as a white powder. TLC: R_f = 0.12 (PE-EtOAc 2:1).



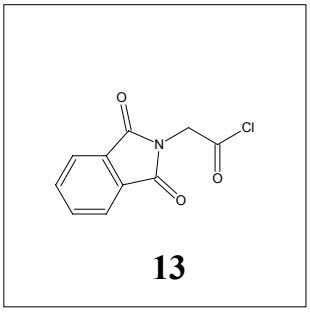
12

^{1}H-NMR (300 MHz, DMSO-d6): δ = 12.80 (br s, 1H, *$CO_2\mathbf{H}$*), 7.95-7.85 (m, 4H, PhtN *$C\mathbf{H}$*-2,3,4,5), 4.32 (s, 2H, *$C\mathbf{H}_2CO_2H$*) ppm. ^{13}C-NMR (75 MHz, DMSO-d6): δ = 168.7 (q, *$\mathbf{C}O_2H$*), 167.1 (q, 2x PhtN *$\mathbf{C}O$*), 134.7 (t, PhtN *$\mathbf{C}H$*-3,4), 131.3 (q, PhtN *$\mathbf{C}$*-1,6) 123.3 (t, PhtN *$\mathbf{C}H$*-2,5), 38.8 (s, *$\mathbf{C}H_2CO_2H$*) ppm. IR (KBr): ν = 3433, 2935, 1773, 1724, 1616, 1469, 1418, 1391, 1319, 1248, 1195, 1119, 1087, 957, 800, 738, 715, 623, 563, 531 cm^{-1}. UV-VIS (CH_2Cl_2, c=0.147 mg/ml): λ_{max} (log ε) = 234 (4.08), 240 (3.97), 294 (3.22) nm. MS (EI+): m/z (%) = 205.0 (5) $[M]^+$, 165.0 (100) $[M-40u]^+$; EA $C_{10}H_7NO_4$ (205.167): calcd. C 58.54, H 3.44, N 6.83; found C 58.30, H 3.51, N 6.87.

Phtalimido acetyl chloride (13)

In a round-bottom flask were placed phthalimidoacetic acid (41.03 g, 200.0 mmol) and chloroform (40 mL), then thionyl chloride (20.0 mL, 275.0 mmol) was cautiously added. The flask was equipped with a reflux condenser, flushed with argon, and the mixture was stirred at reflux temperature for 3 hours, to obtain a light yellowish, clear solution. Then solvent and

excess of thionyl chloride were removed under argon atmosphere in a rotary evaporator to obtain 43.92 g (98.2%) of the acid chloride **13** as a slightly grey-brownish solid.

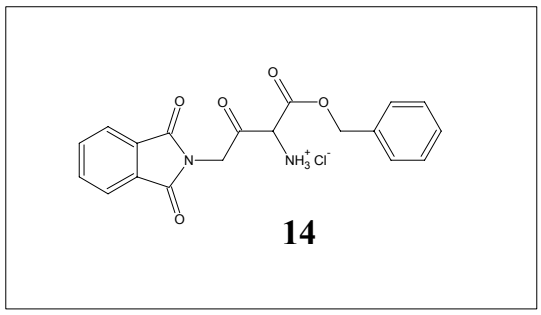


13

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.94-7.88 (m, 2H, PhtN *C**H***-2,5), 7.82-7.74 (m, 2H, PhtN *C**H***-3,4), 4.82 (s, 2H, *C**H**$_2$COCl*) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 169.1 (q, ***C**OCl*) 166.6 (q, 2x PhtN ***C**O*), 134.6 (t, PhtN ***C**H*-3,4), 131.6 (q, PhtN ***C***-1,6), 124,0 (t, PhtN ***C**H*-2,5), 47.6 (p, ***C**H$_2$COCl*) ppm. IR (KBr): ν = 3422, 2979, 2936, 1804, 1774, 1722, 1468, 1418, 1313, 1195, 1117, 1088, 998, 957, 937, 736, 715, 609, 531, 521 cm^{-1}. UV-VIS (CH_2Cl_2, c=0.137 mg/ml): λ_{max} (log ε) = 240 (3.98), 296 (3.29), 306 (3.21) nm. MS (EI+): m/z (%) = 223.0 (1) $[M]^+$, 160.0 (100) $[M-63u]^+$; $C_{10}H_6ClNO_3$ (223.613): calcd. C 53.71, H 2.70, N 6.26; found C 53.86, H 2.81, N 6.29.

Benzyl-2-amino-3-oxo-4-phthalimidobutanoate hydrochloride (14) (a modified general procedure of [5])

A solution of KO^{t}Bu (11.22 g, 100.0 mmol) in dry THF (200 mL) was cooled under argon to -60 °C, and a solution of N-(diphenylmethylene)glycine benzyl ester (32.94 g, 100.0 mmol) in THF (200 mL) was added dropwise while maintaining an inner temperature below -50 °C. After addition was completed (15 minutes) the resulting orange mixture was stirred for further 30 minutes at -60 to -50 °C, then transferred by a long, flexible double-tipped needle to a pre-cooled solution of phthalimido acetyl chloride (22.36 g, 200.0 mmol) in dry THF (200 mL) at -60 °C being stirred vigorously by a mechanical stirrer. After completion of the addition (30 minutes) the mixture was stirred further 60 minutes at -60 to -50 °C, then quenched by rapidly adding 2M aqueous HCl solution (100 mL), and stirred at room temperature for 2 hours. Then all solvents were removed by evaporation, the resulting solid was dried in vacuo, then broken up and stirred with DCM (100 mL) for half an hour to obtain a fine suspension. After filtration the white solid was washed on the glass funnel with DCM (2x 100 mL) then with ice-cold 2M HCl (100 mL) to remove KCl and dried in vacuo to yield 16.70 g (71.6%) of the hydrochloride salt **14** as a white powder.

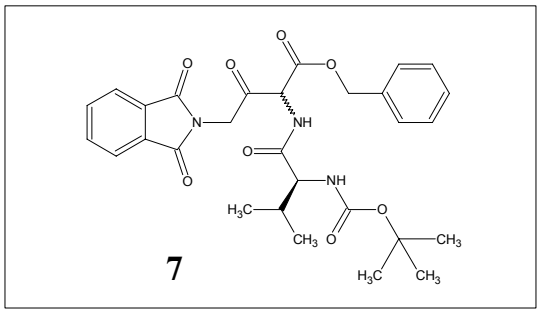


14

^{1}H-NMR (500 MHz, DMSO-d6): δ = 9.21 (br s, 3H, *N**H**$_3^+$*), 7.95-7.92 (m, 2H, PhtN *C**H***-2,5), 7.92-7.88 (m, 2H, PhtN *C**H***-3,4), 7.52 (d, 2H, J=7.0Hz, Bn *C**H***-2,6), 7.43-7.37 (m, 3H, Bn *C**H***-3,4,5), 5.84 (s, 1H, *C**H**NH$_3^+$*), 5.41 (d, 1H, J^2=12.3Hz, Bn *C**H**$_2$*), 5.32 (d, 1H, J^2=12.3Hz, Bn *C**H**$_2$*), 4.99 (d, 1H, J^2=18.9Hz *PhtNC**H**$_2$CO*), 4.94 (d, 1H, J^2=18.9Hz *PhtNC**H**$_2$CO*) ppm. ^{13}C-NMR (125.7 MHz, DMSO-d6): δ = 193.2 (q, *PhtNCH$_2$**C**O*), 166.9 (q, 2x PhtN ***C**O*), 162.9 (q, ***C**O$_2$Bn*), 134.8 (t, PhtN ***C**H*-3,4), 134.4 (q, Bn ***C***-1), 131.2 (q, PhtN ***C***-1,6), 128.46, (t, Bn *C**H***-4), 128.43 (t, Bn ***C**H*-3,5), 128.3 (t, Bn ***C**H*-2,6), 123.4 (t, PhtN ***C**H*-2,5), 68.5 (s, Bn ***C**H$_2$*), 59.5 (t, ***C**HNH$_3^+$*), 45.3 (s, *PhtN**C**H$_2$CO*) ppm. IR (KBr): ν = 3474, 3319, 3170, 3125, 3087, 3065, 3031, 2970, 2887, 2818, 2779, 2663, 2593, 1957, 1777, 1761, 1741, 1721, 1578, 1525, 1501, 1468, 1419, 1377, 1329, 1266, 1233, 1196, 1171, 1146, 1103, 1048, 1012, 947, 907, 882, 854, 820, 803, 753, 735, 713, 697, 618 cm^{-1}. UV-VIS (MeOH, c=0.0058 mg/ml): λ_{max} (log ε) = 218 (4.46), 239 (3.88), 268 (4.03) nm. HRMS (ESI+) Exact mass calculated for $[C_{19}H_{17}N_2O_5]^+$: 353.1132, found: 353.1108.; EA $C_{19}H_{17}ClN_2O_5$ (388.802): calcd. C 58.69, H 4.41, N 7.21; found C 58.44, H 4.58, N 7.00.

Benzyl 2-(R/S)-[(S)-(2-[*tert*-butoxycarbonyl]amino-3-methyl)butanoyl]amino-3-oxo-4-phthalimidobutanoate (7)

In a round-bottomed flask equipped with a mechanical stirrer (S)-Boc-valine (13.04 g, 60.0 mmol) was dissolved in dry THF (120 mL) and N-methylmorpholine (6.069 g, 60.0 mmol) was added. The solution was cooled to -30 °C and a solution of isobutyl chloroformate (8.195 g, 60.0 mmol) in THF (30 mL) was added while the inner temperature was maintained at -30 °C.[6] After 60 minutes ketoamine **14** (23.33 g, 60.0 mmol) was added in one portion followed by a solution of NMM (6.069 g, 60.0 mmol) in THF (30 mL) over a period of 30 minutes. Stirring was continued for 3 hours at -30 °C then the mixture was allowed to warm up to room temperature in further 2 hours. The solvent was evaporated and the residue was taken up in water (300 mL) and DCM (300 mL). The mixture was thoroughly shaken, the layers were separated, then the aqueous layer was further extracted with DCM (2x 100 mL). The collected organic layers were washed with 1M $KHSO_4$ (50 mL), conc. $NaHCO_3$ (50 mL) and brine (50 mL), then dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of the crude product was accomplished by chromatography on silica gel (DCM-EtOAc 95:5 → 70:30) to yield 21.51 g (65.0%) of **7** as a 1:1 mixture of two diastereomers as a white powder. TLC: R_f = 0.70 (DCM-EtOAc 3:1).

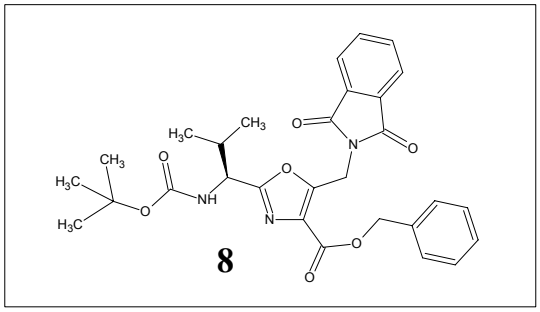


7

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.86 (dd, 2H, J_1=5.3Hz, J_2=3.0Hz, PhtN *C**H***-2,5), 7.73 (dd, 2H, J_1=5.3Hz, J_2=3.0Hz, PhtN *C**H***-3,4), 7.41-7.33 (m, 5H, Z *C**H***-2,3,4,5,6), 7.15-7.11 (2x d, 1H, J=5.5Hz, amide *N**H***), 5.51-5.47 (2x d, 1H, J=6.8Hz, BOC *N**H***), 5.34-5.24 (2x dd, 2H, *CO_2C**H_2***Ph), 5.01 (br s, 1H, *NHC**H**CO_2Bn*), 4.89-4.82 (2x d, 1H, J=18.1Hz, *PhtNC**H_2***), 4.76-4.69 (2x d, 1H, J=18.1Hz, *PhtNC**H_2***), 4.08 (br s, 1H, Val α-*C**H***), 2.23-2.13 (m, 1H, Val β-*C**H***), 1.43-1.42 (2x s, 9H, BOC *C**H_3***), 0.95 (dd, 3H, J_1=6.8Hz, J_2=2.3Hz, Val *C**H_3***), 0.89 (dd, 3H, J_1=6.8Hz, J_2=2.3Hz, Val *C**H_3***) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 193.76 (q, *PhtNCH_2**CO***), 193.67 (q, *PhtNCH_2**CO***), 171.6 (q, amide ***CO***), 167.13 (q, 2x PhtN ***CO***), 167.10 (q, 2x PhtN ***CO***), 164.9 (q, ***CO_2**Bn*), 155.8 (q, BOC ***CO***), 134.8 (q, Bn ***C***-1), 134.22 (t, PhtN ***CH***-3,4), 134.20 (t, PhtN ***CH***-3,4), 132.0 (q, PhtN ***C***-1,6), 128.81 (t, Bn ***CH***), 128.74 (t, Bn ***CH***), 128.72 (t, Bn ***CH***), 123.6 (t, PhtN ***CH***-2,5), 80.19 (q, BOC ***C**$(CH_3)_3$*), 80.16 (q, BOC ***C**$(CH_3)_3$*), 68.93 (s, Bn ***CH_2***), 68.90 (s, Bn ***CH_2***), 60.68 (t, *NH**CH**CO_2Bn*), 60.66 (t, *NH**CH**CO_2Bn*), 59.51 (t, Val α-***CH***), 59.47 (t, Val α-***CH***), 45.28 (s, *PhtN**CH_2***), 45.20 (s, *PhtN**CH_2***), 30.75 (t, Val α-***CH***), 28.25 (p, BOC ***CH_3***), 19.2 (p, Val ***CH_3***), 19.1 (p, Val ***CH_3***), 17.4 (p, Val ***CH_3***), 17.3 (p, Val ***CH_3***) ppm. IR (KBr): ν = 3420, 2969, 1722, 1500, 1468, 1416, 1392, 1261, 1166, 1111, 948, 716, 698, 531 cm^{-1}. UV-VIS (MeOH, c=0.0069 mg/ml): λ_{max} (log ε) = 219 (4.76), 239 (4.08), 279 (3.65) nm. HRMS (ESI+) Exact mass calculated for $[C_{29}H_{34}N_3O_8]^+$: 552.2340, found: 552.2316. EA $C_{29}H_{33}N_3O_8$ (551.5877): calcd. C 63.15, H 6.03, N 7.62; found C 64.32, H 5.65, N 7.62.

2-[(S)-1-(*tert*-butoxycarbonyl)amino-2-methylpropyl]-4-benzyloxycarbonyl-5-(phthalimidomethyl)oxazole (8)

A solution of ketoamide **7** (5.516 g, 10.0 mmol) in dry DCM (50 mL) was cooled to -10 to -5 °C, then a solution of hexachloroethane (4.735 g, 20.0 mmol) and triphenylphosphine (2.885 g, 11.0 mmol) in DCM (50 mL) was added followed by triethylamine (10.12 g, 100 mmol) in DCM (25 mL).[7] After completion of addition the cooling bath was removed, and the mixture was stirred for a week. The volatiles were then removed at reduced pressure leaving a viscous, tacky material, which was subjected to column chromatography on silica gel (DCM-EtOAc 95:5 → 75:25) to give 2.775 g (52.0 %) of **8** as a white solid. TLC: R_f = 0.80 (DCM-EtOAc 3:1).

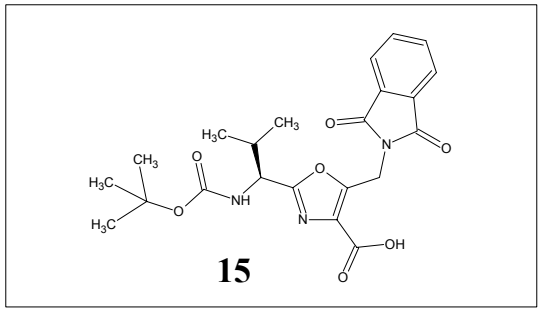


8

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.87 (dd, 2H, J_1=5.3Hz, J_2=3.0Hz, PhtN *C**H***-2,5), 7.75 (dd, 2H, J_1=5.3Hz, J_2=3.0Hz, PhtN *C**H***-3,4), 7.46 (dd, 2H, J_1=8.3Hz, J_2=2.3Hz, Bn *C**H***-3,5), 7.38-7.31 (m, 3H, Bn *C**H***-2,4,6), 5.43 (d, 1H, J=12.3Hz, Bn *C**H**$_2$*), 5.38 (d, 1H, J=12.3Hz, Bn *C**H**$_2$*), 5.26 (d, 1H, J=9.1Hz, BOC *N**H***), 5.21 (d, 2H, J=5.3Hz, *PhtNC**H**$_2$*), 4.69 (dd, 1H, J_1=9.1Hz, J_2=5.3Hz, Val α-*C**H***), 2.14-2.03 (m, 1H, J=6.8Hz, Val β-*C**H***), 1.38 (s, 9H, BOC *C**H**$_3$*), 0.84 (d, 6H, J=6.8Hz, Val *C**H**$_3$*) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.1 (q, 2x PhtN ***C**O***), 163.4 (q, oxazole ***C***-5), 161.2 (q, ***C**O$_2$Bn*), 155.3 (q, oxazole ***C***-2),151.9 (q, BOC ***C**O***), 135.4 (q, oxazole ***C***-4), 134.3 (t, PhtN ***C**H***-3,4), 131.8 (q, Bn ***C***-1), 128.8 (q, PhtN ***C***-1,6), 128.6 (t, Bn ***C**H***-2,6), 128.55 (t, Bn ***C**H***-3,5), 128.4 (t, Bn ***C**H***-4), 123.6 (t, PhtN ***C**H***-2,5), 79.9 (q, BOC ***C**(CH$_3$)$_3$*), 67.1 (s, Bn ***C**H$_2$*), 54.0 (t, Val α-***C**H***), 32.9 (t, Val β-***C**H***), 32.9 (s, *PhtN**C**H$_2$*), 28.2 (p, BOC ***C**H$_3$*), 18.5 (p, Val ***C**H$_3$*), 17.7 (p, Val ***C**H$_3$*) ppm. IR (KBr): ν = 3395, 2972, 1775, 1718, 1616, 1499, 1468, 1456, 1421, 1392, 1367, 1248, 1172, 1115, 1068, 941, 753, 715, 699, 530 cm^{-1}. UV-VIS (CH_2Cl_2, c=0.077 mg/ml): λ_{max} (log ε) = 294 (3.33) nm. HRMS (ESI+) Exact mass calculated for $[C_{29}H_{32}N_3O_7]^+$: 534.2235, found: 534.2229. EA $C_{29}H_{31}N_3O_7$ (533.5725): calcd. C 65.28, H 5.86, N 7.88; found C 64.81, H 5.84, N 7.76.

2-[(S)-1-(*tert*-Butoxycarbonyl)amino-2-methylpropyl]-5-(phthalimidomethyl)oxazole-4-carboxylic acid (15)

Oxazole ester **14** (10.67 g, 20.0 mmol) in methanol (200 mL) was hydrogenated at room temperature and atmospheric pressure using Pearlman's catalyst (0.200 g, 20% $Pd(OH)_2$ on charcoal). The reaction was monitored by TLC, and on completion (3 h) the catalyst was filtered off and washed with several portions of methanol. The solvent was then removed in vacuo to obtain 8.683 g (97.9%) of **15** as a white solid.

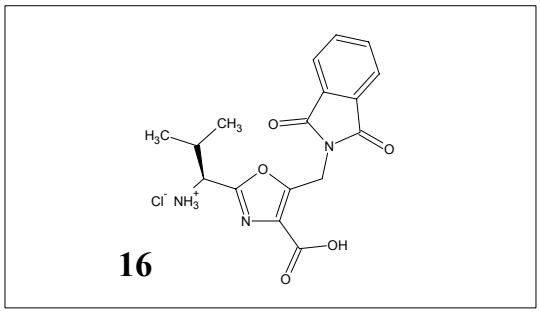


15

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.70 (br s, 1H, *C**O$_2$H***), 7.87 (dd, 2H, J_1=5.3Hz, J_2=3.0Hz, PhtN *C**H***-2,5), 7.74 (dd, 2H, J_1=5.3Hz, J_2=3.0Hz, PhtN *C**H***-3,4), 6.16 (d, 1H, J=9.8Hz, BOC *N**H***), 5.28 (s, 2H, *PhtNC**H**$_2$*), 4.71 (dd, 1H, J_1=9.8Hz, J_2=6.8Hz, Val α-*C**H***), 2.16-2.05 (m, 1H, J=6.8Hz, Val β-*C**H***), 1.37 (s, 9H, BOC *C**H**$_3$*), 0.86 (t, 6H, J=6.8Hz, Val *C**H**$_3$*) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.1 (q, 2x PhtN ***C**O***), 164.5 (q, oxazole ***C***-5), 163.8 (q, ***C**O$_2$H*), 155.7 (q, oxazole ***C***-2), 152.9 (q, BOC ***C**O***), 134.3 (t, PhtN ***C**H***-3,4), 131.8 (q, PhtN ***C***-1,6), 128.3 (q, oxazole ***C***-4), 123.6 (t, PhtN ***C**H***-2,5), 79.8 (q, BOC ***C**(CH$_3$)$_3$*), 54.3 (t, Val α-***C**H***), 32.9 (s, *PhtN**C**H$_2$*), 32.8 (t, Val β-***C**H***), 28.2 (p, BOC ***C**H$_3$*), 18.6 (p, Val ***C**H$_3$*), 18.0 (p, Val ***C**H$_3$*) ppm. IR (KBr): ν = 3387, 2973, 2935, 1776, 1726, 1617, 1514, 1468, 1420, 1393, 1368, 1307, 1247, 1171, 1116, 1070, 1015, 941, 715, 530 cm^{-1}. UV-VIS (CH_2Cl_2, c=0.072 mg/ml): λ_{max} (log ε) = 240 (4.259), 296 (3.22) nm. HRMS (ESI+) Exact mass calculated for $[C_{22}H_{26}N_3O_7]^+$: 444.1765, found: 444.1773. EA $C_{22}H_{25}N_3O_7$ (443.4498): calcd. C 59.59, H 5.68, N 9.48; found C 59.23, H 5.70, N 9.29.

2-[(S)-1-amino-2-methylpropyl]-5-(phthalimidomethyl)oxazole-4-carboxylic acid hydrochloride (16)

To a solution of HCl in EtOAc (15%, 30 mL) oxazole carboxylic acid **15** (6.652 g, 15.0 mmol) was added, and the mixture was stirred for 2 hours at ambient temperature. The volatiles were then removed in vacuo to provide 5.589 g (98.1 %) of the hydrochloride salt **15** as a white powder, which was used in the next step without further purification.

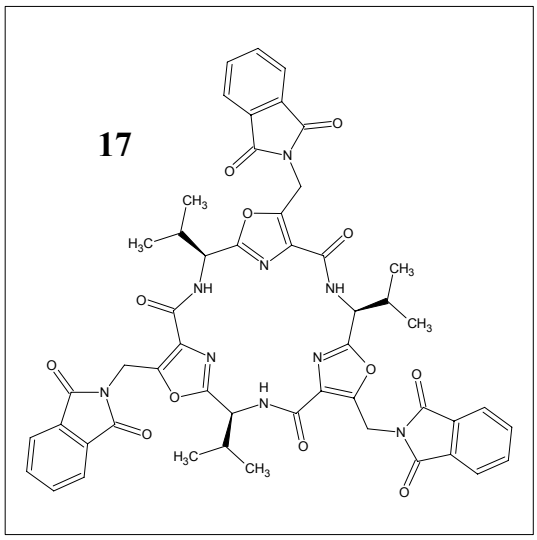


16

^{1}H-NMR (300 MHz, DMSO-d6): δ = 8.98 (br s, 4H, *CO$_2$**H*** und *N**H**$_3^+$*), 7.94-7.86 (m, 4H, PhtN *C**H***-2,3,4,5), 5.20 (s, 2H, *PhtNC**H**$_2$*), 4.36 (d, 1H, J=6.8Hz, Val α-*C**H***), 2.28-2.16 (m, 1H, J=6.8Hz, Val β-*C**H***), 0.92 (d, 3H, J=6.8Hz, Val *C**H**$_3$*), 0.78 (d, 3H, J=6.8Hz, Val *C**H**$_3$*) ppm. ^{13}C-NMR (75 MHz, DMSO-d6): δ = 166.9 (q, oxazole ***C***-5), 161.9 (q, 2x PhtN ***CO***), 158.4 (q, *CO$_2$**H***), 152.7 (q, oxazole ***C***-2), 134.7 (q, oxazole ***C***-4), 131.3 (t, PhtN *C**H***-3,4), 129.0 (q, PhtN ***C***-1,6), 123.3 (t, PhtN *C**H***-2,5), 52.6 (t, Val α-*C**H***), 32.7 (t, Val β-*C**H***), 30.5 (s, *PhtNCH$_2$*), 18.4 (p, Val *C**H**$_3$*), 17.0 (p, Val *C**H**$_3$*) ppm. IR (KBr): ν = 3420, 2967, 1775, 1718, 1613, 1511, 1468, 1421, 1394, 1245, 1190, 1118, 1068, 941, 828, 793, 715, 648, 607, 531 cm^{-1}. UV-VIS (MeOH, c=0.060 mg/ml): λ_{max} (log ε) = 220 (4.63), 240 (4.18), 290 (4.29) nm. HRMS (ESI+) Exact mass calculated for $[C_{17}H_{18}N_3O_5]^+$: 344.1269, found: 344.1297. EA $C_{17}H_{18}ClN_3O_5$ (379.795): calcd. C 53.76, H 4.78, N 11.06; found C 53.20, H 5.17, N 10.05.

(4*S*,11*S*,18*S*)-Tris(1-methylethyl)-7,14,21-tris(phthalimidomethyl)-2,9,16-trioxo-3,10,17,22,23,24-hexaaza-6,13,20-trioxatetracyclo[17.2.1.1^{5,8}.1^{12,15}]tetracosa-1(21),5(23),7,12(24),14,19(22)-hexaene (17)

To a solution of **16** (1.717 g, 5.0 mmol) in dry DMF (125 mL) were added PyBOP (3.903 g, 7.5 mmol) and ^{i}Pr$_2$NEt (4.201 g, 32.5 mmol) under argon atmosphere at 0 to 5 °C. After 15 minutes the cooling bath was removed and stirring was continued at room temperature for further 72 hours. The solvent was then evaporated in vacuo, and purification of the product was performed by flash chromatography on silica gel (DCM-EtOAc-MeOH 75:25:0 → 75:25:3) to yield 0.514 g (31.6 %) of **17** as a light yellowish powder. TLC: R_f = 0.50 (DCM-EtOAc 3:1).

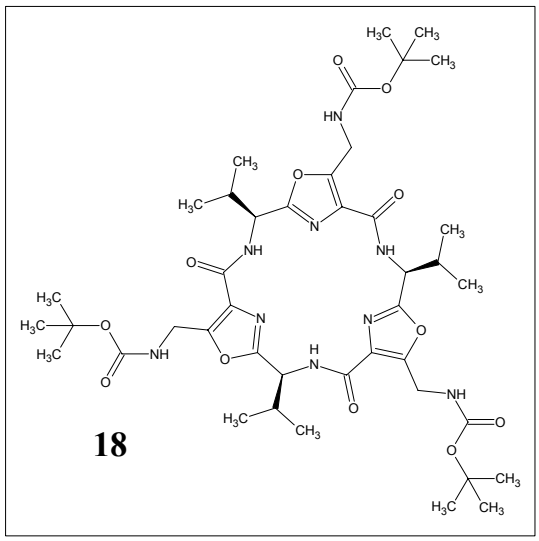

17

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.11 (d, 1H, J=8.0Hz, amide *N**H***), 7.86 (dd, 2H, J_1=5.6Hz, J_2=3.1Hz, PhtN *C**H***-2,5), 7.73 (dd, 2H, J_1=5.6Hz, J_2=3.1Hz, PhtN *C**H***-3,4), 5.36 (d, 1H, ^{2}J=16.4Hz, *PhtNC**H**$_2$*), 5.23 (d, 1H, ^{2}J=16.4Hz, *PhtNC**H**$_2$*), 5.01 (dd, 1H, J_1=7.8Hz, J_2=5.0Hz, Val α-*C**H***), 2.30-2.19 (m, 1H, J=6.6Hz, Val β-*C**H***), 0.95 (t, 6H, J=6.6Hz, Val *C**H**$_3$*) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 167.1 (q, 2x PhtN ***CO***), 161.9 (q, oxazole ***C***-2), 159.8 (q, ***CONH***), 149.4 (q, oxazole ***C***-5), 134.2 (t, PhtN *C**H***-3,4), 131.8 (q, PhtN ***C***-1,6), 130.1 (q, oxazole ***C***-4), 123.5 (t, PhtN *C**H***-2,5), 52.9 (t, Val α-*C**H***), 33.5 (s, *PhtNC**H**$_2$*), 32.5 (t, Val β-*C**H***), 18.2 (p, Val *C**H**$_3$*), 18.1 (p, Val *C**H**$_3$*) ppm. IR (KBr): ν = 3390, 2966, 2933, 2876, 1776, 1722, 1683, 1637, 1576, 1524, 1468, 1423, 1391, 1197, 1087, 943, 903, 787, 753, 714, 611, 531 cm^{-1}. UV-VIS (MeOH, c=0.0034 mg/ml): λ_{max} (log ε) = 220 (5.189), 294 (3.790)

nm. CD (MeOH, c=0.0034 mg/ml): λ (Δε [$dm^3mol^{-1}cm^{-1}$]) = 201 (+16.4), 211 (0.0), 220 (-31.2) nm. HRMS (ESI+) Exact mass calculated for $[C_{51}H_{46}N_9O_{12}]^+$: 976.3266, found: 976.3293.

(4*S*,11*S*,18*S*)-Tris(1-methylethyl)-7,14,21-tris[(*tert*-butoxycarbonyl)aminomethyl]-2,9,16-trioxo-3,10,17,22,23,24-hexaaza-6,13,20-trioxatetracyclo[17.2.1.1^{5,8}.1^{12,15}]tetracosa-1(21),5(23),7,12(24),14,19(22)-hexaene (18)

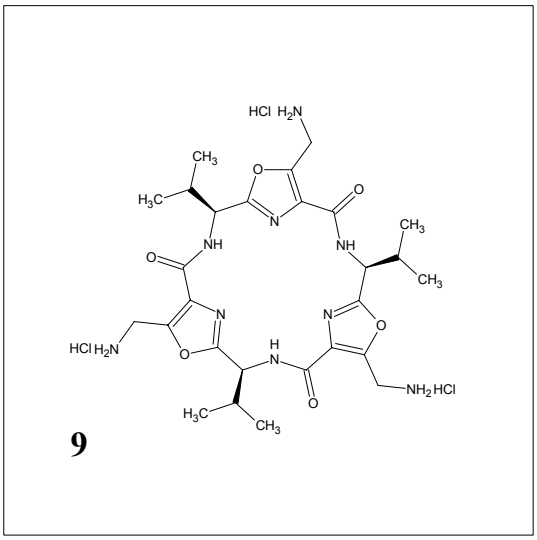
To a solution of **17** (0.195 g, 0.20 mmol) in a 2:2:1 mixture of DCM, THF and EtOH (50 mL) hydrazine monohydrate (0.501 g, 10.0 mmol) was added at room temperature, and the mixture was stirred for further 24 hours. The resulting suspension was cooled to 0 to 5 °C, and a solution of di-*tert*-butyldicarbonate (5.456 g, 25.0 mmol) in DCM (25 mL) was slowly added. After completion of addition the resulting solution was stirred without cooling for further 3 hours. Then solvents were evaporated in vacuo, and column chromatography of the residue on silica gel (DCM-EtOAc-MeOH 75:25:0 → 75:25:4) yielded 0.164 g (92.3%) of **18** as a colorless glassy solid. TLC: R_f = 0.70 (DCM-EtOAc-MeOH 75:25:3).



^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.14 (d, 1H, J=7.9Hz, *CON**H***), 5.82 (br s, 1H, *BocN**H**CH$_2$*), 5.03 (dd, 1H, J_1=7.9Hz, J_2=4.7Hz, Val α-*C**H***), 4.63 (dd, 1H, J_1=16.4Hz, J_2=6.6Hz, *BocNHC**H**$_2$*), 4.55 (dd, 1H, J_1=16.4Hz, J_2=5.7Hz, *BocNHC**H**$_2$*), 2.33-2.26 (m, 1H, J=6.9Hz, Val β-*C**H***), 1.38 (s, Boc *C(C**H**$_3$)$_3$*), 1.02 (d, J=6.9Hz, Val *C**H**$_3$*), 0.97 (d, J=6.9Hz, Val *C**H**$_3$*) ppm. ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ = 161.20 (q, oxazole ***C***-2), 160.4 (q, ***C**ONH*), 155.5 (q, Boc ***C**O*), 153.7 (q, oxazole ***C***-5), 129.6 (q, oxazole ***C***-4), 79.7 (q, Boc ***C**(CH$_3$)$_3$*), 53.0 (t, Val α-***C**H*), 35.4 (s, *BocNH**C**H$_2$*), 33.4 (t, Val β-***C**H*), 28.2 (p, Boc *C(**C**H$_3$)$_3$*), 18.2 (t, 2x Val ***C**H$_3$*) ppm. UV-VIS (MeOH, c=0.0116 mg/ml): λ_{max} (log ε) = 223 (4.545), 297 (2.608) nm. CD (MeOH, c=0.0116 mg/ml): λ (Δε [$dm^3mol^{-1}cm^{-1}$]) = 207 (+13.3), 217 (0.0), 231 (-28.9) nm. HRMS (ESI+) Exact mass calculated for $[C_{42}H_{64}N_9O_{12}]^+$: 886.4669, found: 886.4722.

(4*S*,11*S*,18*S*)-Tris(1-methylethyl)-7,14,21-tris(aminomethyl)-2,9,16-trioxo-3,10,17,22,23,24-hexaaza-6,13,20-trioxatetracyclo[17.2.1.1^{5,8}.1^{12,15}]tetracosa-1(21),5(23),7,12(24),14,19(22)-hexaene hydrochloride (9)

Scaffold **18** (0.133 g, 0.15 mmol) was treated with HCl/EtOAc solution (15%, 30 mL) at room temperature for 2 hours. Volatiles were then removed in a rotary evaporator and the resulting white solid was dried in vacuo in order to completely remove traces of acetic acid. Yield: 0.104 g (quant.).

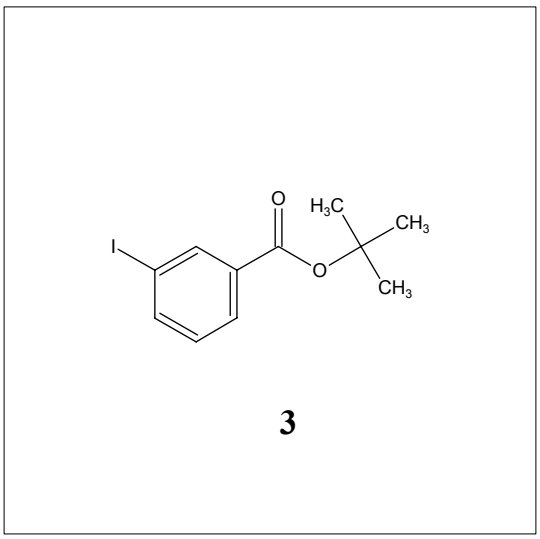


9

^{1}H-NMR (500 MHz, MeOH-d4): δ = 8.54 (d, 1H, J=7.9Hz, Amid *N**H***), 5.24-5.21 (m 1H, Val α-*C**H***), 4.60 (s, 1H, *C**H**$_2$NH$_3^+$*), 2.45-2.38 (m, 1H, Val β-*C**H***), 1.09 (d, 3H, J=6.9Hz, Val *C**H**$_3$*), 1.06 (d, 3H, J=6.9Hz, Val *C**H**$_3$*) ppm. ^{13}C-NMR (125.7 MHz, MeOH-d4): δ = 164.4 (q, oxazole ***C***-2), 161.7 (q, ***C**ONH*), 149.6 (q, oxazole ***C***-5), 133.2 (q, oxazole ***C***-4), 54.7 (t, Val α-***C**H*), 34.9 (s, *C**H**$_2$NH$_3^+$*), 34.8 (t, Val β-***C**H*), 18.9 (p, Val ***C**H$_3$*), 18.5 (p, Val ***C**H$_3$*) ppm. IR (KBr): ν = 3438, 3380, 2967, 2877, 2607, 1661, 1579, 1540, 1474, 1446, 1410, 1373, 1326, 1295, 1275, 1252, 1216, 1200, 1160, 1128, 1079, 1021, 982, 939, 902, 822, 784, 775, 725, 644, 614 cm^{-1}. UV-VIS (MeOH, c=0.0053 mg/ml): λ_{max} (log ε) = 221 (4.661) nm. CD (MeOH, c=0.0053 mg/ml): λ (Δε [dm^{3}mol^{-1}cm^{-1}]) = 208 (+24.2), 218 (0.0), 232 (-48.6) nm. HRMS (ESI+) Exact mass calculated for $[C_{27}H_{40}N_9O_6]^+$: 608.2916, found: 608.2885.

***Tert*-butyl-3-iodobenzoate (3)**

To a suspension of 3-iodobenzoic acid (9.921 g, 40.0 mmol) in dry DCM (50 mL) at room temperature under argon atmosphere a solution of 4-dimethylamino pyridine (1.222 g, 10.0 mmol) in DCM (10 mL) and then a solution of di-*tert*-butyldicarbonate (10.91 g, 50.0 mmol) in DCM (20 mL) were added. Stirring of the resulting clear mixture was continued for further 18 hours. The mixture was then diluted with DCM (400 mL) and extracted with water (100 mL) and with 1M HCl (100 mL). The organic layer was separated, dried over $MgSO_4$, filtered and concentrated in vacuo. Flash chromatography of the residue on silica gel (PE-EtOAc 90:10) afforded 8.005 g (65.8%) of **3** as a colorless, clear liquid. TLC: R_f = 0.62 (PE-EtOAc 90:10).



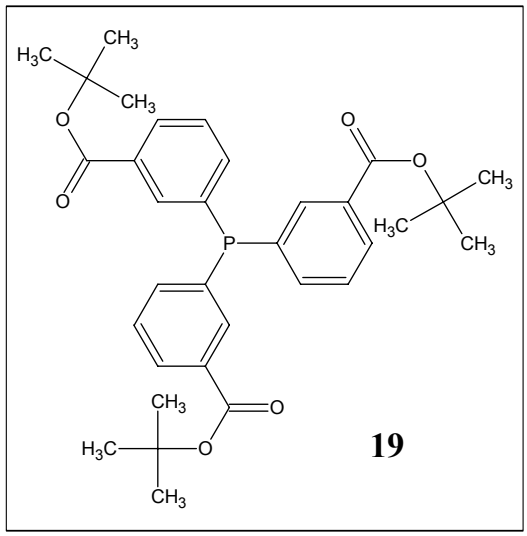
3

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.30 (s, 1H, Ar *C**H***-2), 7.94 (d, 1H, J=7.9Hz, Ar *C**H***-6), 7.84 (d, 1H, J=7.9Hz, Ar *C**H***-4), 7.15 (t, 1H, J=7.9Hz, Ar *C**H***-5), 1.59 (s, 9H, *CO$_2$C(C**H**$_3$)$_3$*) ppm. ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ = 164.1 (q, ***C**O$_2$C(CH$_3$)$_3$*), 141.1 (t, Ar ***C**H*-4), 138.3 (t, Ar ***C**H*-2), 133.9 (q, Ar ***C***-1), 129.8 (t, Ar ***C**H*-6), 128.6 (t, Ar ***C**H*-5), 93.7 (q, Ar ***C***-3), 81.6 (q, *CO$_2$**C**(CH$_3$)$_3$*), 28.1 (p, *CO$_2$C(**C**H$_3$)$_3$*) ppm. IR (KBr-Film): ν = 3415, 3063, 2977, 2931, 1715, 1565, 1472, 1458, 1416, 1393, 1368, 1299, 1256, 1162, 1123, 1099, 1081, 1061,1036, 998, 924, 902, 873, 849, 810, 745, 707, 694, 674, 646 cm^{-1}. UV-VIS (MeOH, c=0.0074 mg/ml): λ_{max} (log ε) = 219 (4.434), 287 (2.951), 292 (2.924) nm. MS (EI+): m/z (%)=: 304 (22) $[M]^+$, 248 (100), 231 (46), 203 (13), 76 (22), 57 (50).

Tris-[3-(*tert*-butoxycarbonyl)phenyl]phosphine (19)

A solution of *tert*-butyl-3-iodobenzoate (6.082 g, 20.0 mmol) in dry THF (75 mL) under argon atmosphere was cooled to -25 °C, and isopropylmagnesium chloride solution 2.0M in Diethyl ether (10.5 mL, 21.0 mmol) was slowly added thereto with rapid stirring. After stirring for 30 minutes at -25 °C, a solution of phosphorus tribromide (1.760 g, 6.5 mmol) in

dry THF (75 mL) was added dropwise, and the mixture was stirred for further 30 minutes at -25 °C. Then the cooling-bath was removed, and the reaction mixture was let to warm up to room temperature. Solvent was evaporated in vacuo, and the residual material was subjected to column chromatography on silica gel (PE-EtOAc 90:10 → 60:40) to give 1.415 g (38.7 %) of **19** as a white powder. TLC: R_f = 0.37 (PE-EtOAc 90:10).

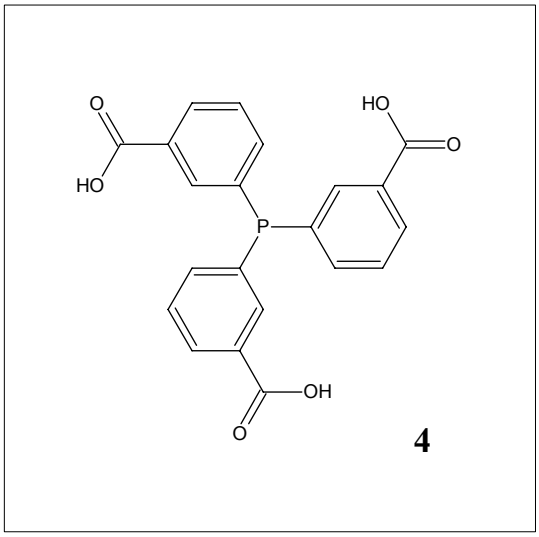


19

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.00-7.97 (m, 1H, Ar ***CH***-4), 7.96-7.94 (m, 1H, Ar ***CH***-2), 7.43-7.39 (m, 2H, Ar ***CH***-5,6), 1.53 (s, 9H, $CO_2C(\mathbf{CH_3})_3$) ppm. ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ = 165.2 (q, $\mathbf{C}O_2C(CH_3)_3$), 137.4 (t, Ar ***CH***-6, d, $J^{C,P}$ =16.8Hz), 136.6 (q, Ar ***C***-1, d, $J^{C,P}$ =12.1Hz), 134.7 (t, Ar ***CH***-2, d, $J^{C,P}$ =23.3Hz), 132.4 (q, Ar ***C***-3, d, $J^{C,P}$ =7.5Hz), 130.1 (t, Ar ***CH***-4, s), 128.6 (t, Ar ***CH***-5, d, $J^{C,P}$ =5.6Hz), 81.2 (q, $CO_2\mathbf{C}(CH_3)_3$), 28.1 (s, $CO_2C(\mathbf{CH_3})_3$) ppm. ^{31}P-NMR (202.3 MHz, $CDCl_3$): δ = -6.25 ppm. IR (KBr-Film): ν = 3404, 3058, 3002, 2977, 2932, 2819, 2721, 2589, 2412, 2143, 1985, 1927, 1846, 1708, 1593, 1570, 1477, 1458, 1412, 1393,1369, 1305, 1258, 1165, 1134, 1038, 999, 934, 912, 887, 850, 824, 773, 752, 687, 660, 558, 529 cm^{-1}. UV-VIS (MeOH, c=0.0079 mg/ml): λ_{max} (log ε) = 228 (4.679), 283 (3.751) nm. HRMS (ESI+) Exact mass calculated for $[C_{33}H_{40}O_6P]^+$: 563.2557, found: 563.2561. EA $C_{33}H_{39}O_6P$ (562.6329): calcd. C 70.45, H 6.99; found C 70.04, H 7.25.

Tris-[3-carboxyphenyl]phosphine (4)

Tert-butyl ester **19** (1.125 g, 2.0 mmol) was treated with HCl/EtOAc solution (15%, 50 mL) at room temperature. After stirring for 24 hours the solvent was evaporated and the substrate was dried in vacuo to obtain 0.773 g (98.0 %) of **4** as a white powder. TLC: R_f = 0.15 (DCM-EtOAc-MeOH 75:25:10).



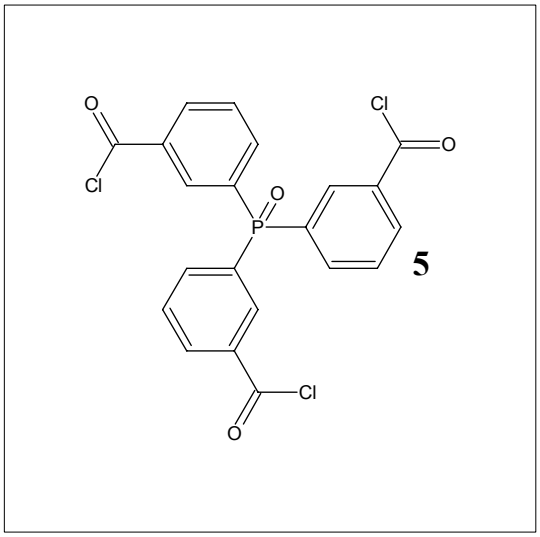
4

^{1}H-NMR (500 MHz, DMSO-d6): δ = 13.14 (br s, 3H, $CO_2\mathbf{H}$), 8.00 (dt, 3H, J_1=7.6Hz, J_2=1.3Hz, Ar ***CH***-2), 7.79 (dt, 3H, J_1=7.6Hz, J_2=1.3Hz, Ar ***CH***-4), 7.59 (td, 3H, J_1=7.6Hz, J_2=1.3Hz, Ar ***CH***-6), 7.53 (tt, 3H, J_1=7.6Hz, J_2=1.3Hz, Ar ***CH***-5) ppm. ^{13}C-NMR (125.7 MHz, DMSO-d6): δ = 166.7 (q, $\mathbf{C}O_2H$), 137.5 (q, d, $J^{C,P}$=20.5Hz, Ar ***C***-1), 136.35 (t, d, $J^{C,P}$=13.1Hz, Ar ***CH***-2), 133.6 (t, d, $J^{C,P}$=20.5Hz, Ar ***CH***-6), 131.3 (q, d, $J^{C,P}$=6.5Hz, Ar ***C***-3), 130.2 (t, s, Ar ***CH***-4), 129.4 (t, d, $J^{C,P}$=7.5Hz, Ar ***CH***-5) ppm. ^{31}P-NMR (202.3 MHz, DMSO-d6): δ = -6.98 ppm. IR (KBr-Film): ν = 3004, 2980, 2882, 2836, 2714, 2666, 2554, 1695, 1592, 1576, 1476, 1431, 1407, 1301, 1265, 1170, 1140, 1107, 1075, 998, 931, 845, 816, 746, 718, 684, 654 cm^{-1}. HRMS (ESI+) Exact mass calculated for $[C_{21}H_{16}O_6P]^+$: 395.0679, found: 395.0691.

Tris-[3-chlorophenyl]phosphine oxide (5)

Carboxylic acid **4** (0.039 g, 0.10 mmol) was stirred in refluxing thionyl chloride (5 mL) under argon atmosphere for 3 hours. The resulting clear solution was evaporated to dryness in vacuo to give 0.044 g (quant.) of **5** as a light yellowish glassy solid. Note: this substrate may be kept at 0 to 5 °C under argon for weeks, but we used it as soon as possible for the next synthetic operation.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.40 (d, 1H, J=12.6Hz, Ar *C**H***-2), 8.36 (d, 1H, J=7.9Hz, Ar *C**H***-4), 8.00 (dd, 1H, J_1=11.1Hz, J_2=7.7Hz, Ar *C**H***-6), 7.74 (t, 1H, J=6.3Hz, Ar *C**H***-5) ppm. ^{13}C-NMR (125.7 MHz, $CDCl_3$): δ =167.4 (q, ***C**OCl*), 138.0 (t, d, J=10.3Hz, Ar ***C**H*-6), 135.3 (t, d, J=2.3Hz, Ar ***C**H*-4), 134.17 (t, d, J=11.2Hz, Ar ***C**H*-2), 134.15 (q, d, J=12.1Hz, Ar ***C***-3), 132.4 (q, d, J=105.5Hz, Ar ***C***-1), 130.0 (t, d, J=12.1Hz, Ar ***C**H*-5) ^{31}P-NMR (202.3 MHz, $CDCl_3$): δ = 25.20 ppm.



5

Phosphine oxide propeller 1b

To a slurry of scaffold **9** (0.0695 g, 0.10 mmol) in dry DCM (30 mL) a 0.50 M stock solution of **5** in DCM (240 µL, 0.12 mmol) was added at 0 to 5 °C followed by the slow addition of a 1.00 M stock solution of Et_3N in dry DCM (1000 µL, 1.00 mmol). The cooling-bath was then removed, and the mixture was stirred for further 16 hours at ambient temperature. Solvent was removed in a rotary evaporator in vacuo, and purification of the product was performed by liquid chromatography on silica gel (DCM-EtOAc-MeOH 75:25:0 → 75:25:15) to yield 0.024 g (25.5%) of **1b** as a colorless solid.

TLC: R_f = 0.45 (DCM-EtOAc-MeOH 75:25:15).

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 8.20 (ddt, 1H, $J_1^{H,P}$=11.35Hz, J_2=7.3Hz, J_3=1.6Hz, Ar *C**H***-4), 7.68 (dq, 1H, J_1=7.6Hz, J_2=1.6Hz, Ar *C**H***-6), 7.65 (td, 1H, J_1=7.6Hz, J_2=2.5Hz, Ar *C**H***-5), 7.54 (d, 1H, J=10.4Hz, *CON**H***), 7.02 (dd, 1H, J_1=9.1Hz, J_2=3.5Hz, *ArCON**H**CH$_2$*), 6.82 (dt, 1H, J_1=13.6Hz, J_2=1.6Hz, Ar *C**H***-2), 5.03 (dd, 1H, J_1=10.4, J_2=7.9Hz, Val α-*C**H***), 4.89 (dd, 1H, J_1=15.1Hz, J_2=9.1Hz, *CONHC**H**$_2$*), 4.35 (dd, 1H, J_1=15.1Hz, J_2=3.8Hz, *CONHC**H**$_2$*), 2.10-2.03 (m, J=6.9Hz, 1H, Val β-*C**H***), 1.10 (d, 3H, J=6.9Hz, Val *C**H**$_3$*), 1.01 (d, 3H, J=6.9Hz, Val *C**H**$_3$*) ppm.

^{13}C-NMR (125.7 MHz, $CDCl_3$): δ = 168.35 (q, Ar***C**ONHCH$_2$*), 162.95 (q, ***C**ONH*), 161.25 (q, oxazole ***C***-2), 154.35 (q, oxazole ***C***-5), 135.34 (q, Ar ***C***-1), 135.27 (t / d, $J^{C,P}$=8.4Hz, Ar ***C**H*-4), 134.27 (t / d, $J^{C,P}$=14.0Hz, Ar ***C**H*-2), 132.65 (q / d, $J^{C,P}$=106.4Hz, Ar ***C***-3), 130.59 (q, oxazole ***C***-4), 129.57 (t / d, $J^{C,P}$=2.8Hz, Ar ***C**H*-6), 129.46 (t / d, $J^{C,P}$=11.2Hz, Ar ***C**H*-5), 52.6 (t, Val α-***C**H*), 34.4 (s, *CONHC**H**$_2$*), 33.8 (t, Val β-***C**H$_3$*), 18.94 (p, Val ***C**H$_3$*), 18.65 (p, Val ***C**H$_3$*) ppm.

^{31}P-NMR (202.3 MHz, $CDCl_3$): δ = 34.1 (s) ppm.

UV-VIS (Acetonitrile, c=0.188 mg/ml): λ_{max} (log ε) = 200 (5.120)

CD (Acetonitrile, c=0.188 mg/ml): λ (Δε [$dm^3mol^{-1}cm^{-1}$]) = 186 (+54.8), 196 (0.0), 206 (-117.2), 228 (0.0), 234 (26.0), 249 (17.0), 257 (0.0), 264 (-6.8), 281 (-5.9)

HRMS (ESI+) Exact mass calculated for $[C_{48}H_{49}N_9O_{10}P]^+$: 942.3345, found: 942.3340.

Phosphine propeller 1a

In a glass NMR-Tube trichlorosilane (50 mg, 0.50 mmol) was added to a solution of phosphine oxide **1b** (3.5 mg, 0.0037 mmol) in C_6D_6 (0.8 mL), and the sample was immersed in an oil-bath maintained at 85-90 °C under argon atmosphere for 4 hours. The completeness of the reaction was verified by ^{31}P-NMR measurement. The solution was then diluted with DCM (2 mL), passed through a small column filled with silica gel (10 g) and eluted with DCM-MeOH 100/1 → 100/15 to yield 2.7 mg **1a** (78%) as a colorless solid.

TLC: R_f = 0.52 (DCM-EtOAc-MeOH 75:25:5).

^{1}H-NMR (500 MHz, C_6D_6): δ = 7.62 (d, 1H, J=10.1Hz, *CON**H***), 7.36 (tdd, 1H, J_1=8.5Hz, J_2=1.9Hz, J_3=1.3Hz, Ar *C**H***-4), 7.09-7.04 (m, 3H, Ar *C**H***-2,6 and *ArCON**H***), 6.83 (td, 1H, J_1=7.6Hz, J_2=1.9Hz, Ar *C**H***-5), 5.12 (dd, 1H, J_1=9.8Hz, J_2=7.6Hz, Val α-*C**H***), 4.95 (dd, 1H, J_1=15.1Hz, J_2=9.8Hz, *CONHC**H**$_2$*), 4.03 (dd, 1H, J_1=15.1Hz, J_2=3.5Hz, *CONHC**H**$_2$*), 1.79-1.72 (m, 1H, J=6.9Hz, Val β-*C**H***), 0.91 (d, 3H, J=6.9Hz, Val *C**H**$_3$*), 0.76 (d, 3H, J=6.9Hz, Val *C**H**$_3$*) ppm.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.72-7.67 (m, 1H), 7.53 (d, 1H, J=10.4Hz, *CON**H***), 7.45 (d, 2H, J=3.8Hz), 7.02 (dd, 1H, J_1=9.3Hz, J_2=3.6Hz. *ArCON**H***), 6.76 (br d, 1H, J=3.8Hz), 5.05 (dd, 1H, J_1=10.4, J_2=7.9Hz, Val α-*C**H***), 4.93 (dd, 1H, J_1=15.1Hz, J_2=9.1Hz, *CONHC**H**$_2$*), 4.32 (dd, 1H, J_1=15.1Hz, J_2=3.8Hz, *CONHC**H**$_2$*), 2.11-2.03 (m, J=6.6Hz, 1H, Val β-*C**H***), 1.10 (d, 3H, J=6.6Hz, Val *C**H**$_3$*), 1.00 (d, 3H, J=6.6Hz, Val *C**H**$_3$*)

^{13}C-NMR (125.7 MHz, C_6D_6): δ = 168.6 (q, Ar*C**O**NHCH$_2$*), 163.0 (q, oxazole ***C***-2), 161.5 (q, *C**O**NH*), 155.2 (q, oxazole ***C***-5), 137.2, 136.9, 136.8, 136.6, 136.5, 132.9, 130.3 (q, oxazole ***C***-4), 125.8, 55.7 (t, Val α-*C**H***), 34.9 (s, *CONHC**H**$_2$*), 34.06 (t, Val β-*C**H**$_3$*), 18.81 (p, Val *C**H**$_3$*), 18.54 (p, Val *C**H**$_3$*) ppm.

^{31}P-NMR (202.3 MHz, C_6D_6): δ = -5.34 ppm.

^{31}P-NMR (202.3 MHz, $CDCl_3$): δ = -2.37 ppm.

HRMS (ESI+) Exact mass calculated for $[C_{48}H_{49}N_9O_9P]^+$: 926.3385, found: 926.3423.

Figure 1: Molecular structures of the energetically preferred conformer **(*P1*)-1a** and **(*P1*)-1b** calculated at the BP86/TZVP level; all hydrogen atoms have been omitted for clarity.

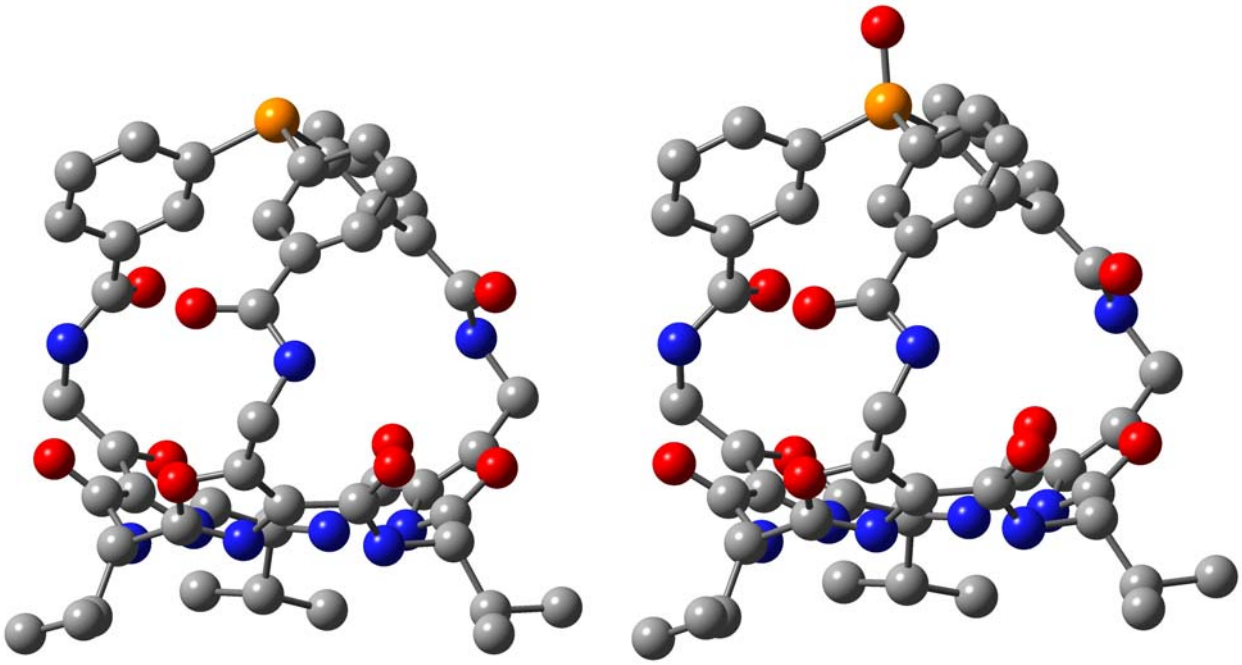
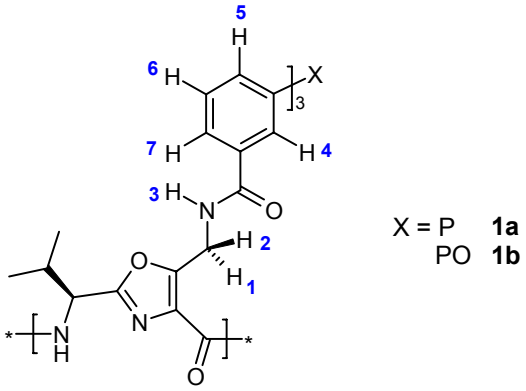


Figure 2. Numbering of hydrogen atoms of **1**.



X = P **1a**
PO **1b**

Table 1. Atomic distances and dihedral angles of **1b** obtained from NMR-experiments and calculated values of atomic distances and dihedral angles for conformers *P1*, *P2*, *M1* and *M2* of **1b** by BP86/TZVP.

	distance [Å]					dihedral angle [°]	
	H1-H3	H2-H3	H3-H4	H3-H7	H4-H5	H1-C-N-H3	H2-C-N-H3
1b$_{observed}$	2.3	3.3	3.0	2.1	3.0	43 or 120	168
(***P1***)-**1b**$_{calculated}$	2.38	2.97	4.24	2.48	3.31	49.9	168.1
(***P2***)-**1b**$_{calculated}$	2.94	2.70	2.12	4.40	3.63	153.2	89.4
(***M1***)-**1b**$_{calculated}$	2.46	2.97	1.99	4.48	3.61	52.3	171.4
(***M2***)-**1b**$_{calculated}$	2.98	2.41	4.34	2.24	4.13	163.6	45.6

Table 2. Dihedral angles of **1a** obtained from NMR-experiment and calculated values of dihedral angles for conformers *P1*, *P2*, *M1* and *M2* of **1a** by BP86/TZVP.

	dihedral angle [°]	
	H1-C-N-H3	H2-C-N-H3
1a$_{observed}$	43 or 120	168
(***P1***)-**1a**$_{calculated}$	51.4	169.7
(***P2***)-**1a**$_{calculated}$	147.6	95.0
(***M1***)-**1a**$_{calculated}$	53.3	172.4
(***M2***)-**1a**$_{calculated}$	178.3	60.4

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