Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Organocatalysis

Enantioselective kinetic resolution of cyclic chiral *trans*-1,2-diols**

*Christian E. Müller, Lukas Wanka, Kevin Jewell, and Peter R. Schreiner**

Supporting Information

Contents

[*] Dipl.-Chem. C. E. Müller, Dr. L. Wanka, K. Jewell, Prof. Dr. P. R. Schreiner
Institute of Organic Chemistry
Justus-Liebig University
Heinrich-Buff-Ring 58, 35392 Giessen, Germany
Fax: (+)49-641-9934309
E-mail: prs@org.chemie.uni-giessen.de
Homepage: www.chemie.uni-giessen.de

[**] This work was supported by the Deutsche Forschungsgemeinschaft (SPP1179).

1. General remarks

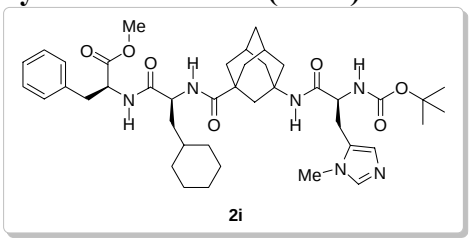
Unless otherwise noted, chemicals were purchased from Acros Organics, Alfa Aesar, Aldrich, Lancaster, Merck, Novabiochem or Fluka at the highest purity grade available and were used without further purifications. All solvents were distilled prior to use. Toluene, CH_3CN, CH_2Cl_2 and $CHCl_3$ were distilled from appropriate drying agents prior to use and stored under argon atmosphere. α-Trifluorotoluene, anhydrous was purchased from Sigma-Aldrich in 99.9% purity. Acetic anhydride was distilled prior to use and stored in a Schlenk tube. All catalytic reactions were carried out under an argon atmosphere employing oven- and flame-dried glassware. Column chromatography was conducted using J.T. Baker silica gel (0.063 – 0.200 mm) or, for flash column chromatography, Merck silica gel 60 (0.040 – 0.063 mm), respectively. TLC R_f values are reported. ^1H and ^{13}C NMR spectra were recorded on Bruker AV600, AV400 or AV200 spectrometers, respectively, using TMS as the internal standard with chemical shifts given in ppm relative to TMS or the respective solvent residual peaks. Infrared spectra were recorded on a Bruker IFS25 spectrometer. MS / HRMS were recorded on a Finnigan MAT95 sectorfield spectrometer; ESI mass spectra on a Finnigan LCQDuo spectrometer using methanol/acetic acid solutions of the respective compounds. High resolution ESI mass spectrometry was performed on a Thermo Scientific LTQ FT Ultra hybrid mass spectrometer using methanol/water solutions of the respective compounds. Optical rotation was measured by using a Jasco P-2000 polarimeter. Elemental analyses were measured using a Carlo Erba 1106 CHN analyzer. GC analyses were performed by using Hewlett Packard 5890 and Carlo Erba 2900 gas chromatographs. The analytical HPLC was accomplished by using a Spectra SP 8700 system and the preparative HPLC by using a Knauer system (Knauer Differential-Refractometer, Knauer HPLC Pump 64, Knauer 2151 Variable Wavelength Monitor).

2. Synthesis of peptides 2a-2l and Miller peptides 3a + 3b via solid phase peptide synthesis

Peptide Synthesis:

For the peptide screenings of Figure 1 the peptides **2a-2l** and **3a** + **3b** were synthesized using standard solid phase strategy on solid support using commercially available Fmoc-Phe-Wang polystyrene resin using the automated synthesizer platform ASW 1000 (Chemspeed). Double Couplings were performed using 2 equiv. of amino acid, 2 equiv. of HBTU, 2 equiv. of HOBt, and 4 equiv. Hünig's base in DMF, for 1h. For L-(π-Me)-His double couplings were performed using 1.5 equiv. of amino acid, 2 equiv. of HBTU, 2 equiv. of HOBt, and 4 equiv. Hünig's base in DMF, for 2 h. Double deprotections were performed using 25% piperidine in DMF for 25 min. Peptides were cleaved from solid support using a mixture of MeOH: THF: Et_3N (9:1:1) shaking 2 times for 2 d. A representative procedure for the solid-phase synthesis of peptide **2i** is given below. Some peptides were synthesized in a larger batch (0.3 mmol or 0.6 mmol) by manual SPPS synthesis using the same methology and were then characterized completely.

Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OMe (2i):

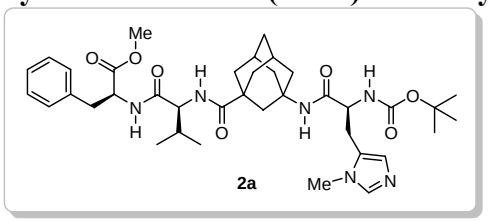


2i

The tetramer was synthesized on solid support using commercially available Wang polystyrene resin endcapped and preloaded with Fmoc-protected L-phenylalanine (0.405 g, 0.74 mmol/g, 0.3 mmol). Fmoc cleavage was performed by shaking the resin twice in 25% piperidine in DMF (v/v). The resin was washed 5 times each with DMF, dichloromethane, and DMF. Chain elongation with Fmoc-L-Cha-OH was performed by a double coupling procedure (1 h shaking per coupling step) using Fmoc-L-Cha-OH (0.237 g, 0.6 mmol), HBTU (0.228 g, 0.6 mmol), HOBt·H_2O (0.092 g, 0.6 mmol), and DIPEA (0.155 g, 204.1 µL, 1.2 mmol) per coupling step (2:2:2:4 equiv., respectively). After washing and cleavage of the Fmoc-protective group as described above, the peptide was elongated using Fmoc-^{A}Gly-OH (0.250 g, 0.6 mmol), HBTU, HOBt, and DIPEA in the same stoichiometric ratio as given above. After washing and cleavage of the Fmoc-protective group as described above, the peptide was elongated using again a double coupling strategy (2h shaking per coupling) Boc-L-(π-Me)-His-OH (0.121 g, 0.45 mmol) , HBTU (0.228 g, 0.6 mmol), HOBt (0.092 g, 0.6 mmol), and DIPEA (0.155 g, 204.1 µL, 1.2 mmol) per coupling step (1.5:2:2:4 equiv., respectively). After washing (5 times each with DMF, dichloromethane, and diethylether), the tetramer was cleaved from the resin by shaking two times for 2 days with methanol, triethylamine and THF (9:1:1, v/v). The resin was filtered off and washed several times with THF. The collected solutions were concentrated and the residue was purified by HPLC (eluent: TBME/CH_3OH 85:15, 6 ml/min.; UV-detector λ = 254 nm, E_{max} = 2.56; refractometer; column l = 250 mm, d = 8 mm, LiChrosorb Diol (7 µm, Merck); retention time (**2i**) = 10.43 minutes. The peptide was characterized by ESI-MS, HR-ESI-MS, NMR, IR and EA.

^{1}H NMR (600 MHz, $CDCl_3$): δ/ppm = 7.35 [s, 1 H, C*H*-Imidazole (His)]; 7.24 – 7.15 [m, 3 H, H_{Ar} (Phe)]; 7.05 – 7.01 [m, 2 H, H_{Ar} (Phe)]; 6.79 [s, 1 H, C*H*-Imidazole (His)]; 6.44 [d, J = 7.8 Hz, 1 H, N*H* (Phe)]; 5.91 [d, J = 7.9 Hz, 1 H, N*H* (Cha)]; 5.68 [s, 1 H, N*H* (^{A}Gly)]; 5.09 [d, J = 8.3 Hz, 1 H, N*H* (His)]; 4.78 – 4.70 [m, 1 H, H_α (Phe)]; 4.41 – 4.30 [m, 1 H, H_α (Cha)]; 4.13 – 4.03 [m, 1 H, H_α (His)]; 3.64 (s, 3 H, OCH_3); 3.54 (s, 3 H, NCH_3); 3.09 – 2.98 [m, 2 H, H_β (Phe)]; 2.98 – 2.88 [m, 2 H, H_β (His)]; 2.13 (m, 2 H, adamantane); 1.93 – 1.80 (m, 6 H, adamantane + Cha); 1.71 – 1.51 (m, 12 H, adamantane + Cha); 1.40 – 1.36 (m, 1 H, Cha); 1.37 [s, 9 H, C(CH_3)$_3$]; 1.23 – 1.00 (m, 4 H, Cha); 0.92 – 0.69 (m, 2 H, Cha).
^{13}C NMR (150 MHz, $CDCl_3$): δ/ppm = 176.3 (C=O); 171.9 (C=O); 171.6 (C=O); 169.7 (C=O); 155.4 (C=O); 138.3; 135.7; 129.2; 128.6; 128.2; 127.2; 127.2; 80.5; 54.4; 53.2; 52.3; 50.7; 42.5; 42.1; 40.3; 40.3; 39.5; 38.2; 38.0; 37.8; 35.1; 34.2; 33.5; 32.7; 31.5; 29.1; 29.1; 28.3; 26.8; 26.3; 26.1; 26.1;
IR (KBr): $\tilde{\nu}$ /cm^{-1} = 3427; 2921; 2853; 2912; 1746; 1661; 1510; 1518; 1450; 1366; 1280 1249; 1169.
MS:
ESI: m/z = 761.5 $[M+H]^+$ (calc. m/z = 761.5); m/z = 783.4 $[M+Na]^+$ (calc. m/z = 783.4); m/z = 1521.3 $[2M+H]^+$ (calc. m/z = 1521.9); m/z = 1543.3 $[2M+Na]^+$ (calc. m/z = 1543.9).
HR-ESI: m/z = 761.45963 $[M+H]^+$ (calc. m/z = 761.45963).
Elem. Anal.: $C_{32}H_{43}N_5O_6$ calc. C 66.29; H 7.95; N 11.04; found C 64.45; H 7.75; N 10.33.

Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Val-L-Phe-OMe (2a):

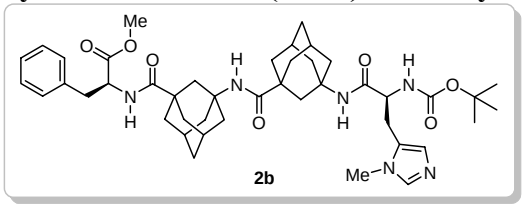


2a

Solid support: Fmoc-L-Phe Wang Resin (0.811 g, 0.74 mmol/g, 0.6 mmol). 1. Coupling: Double coupling: Fmoc-L-Val (0.407 g, 1.2 mmol) in 2.4 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.501 g, 1.2 mmol) in 2.4 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.242 g, 0.9 mmol) in 2.4 mL DMF for 2h each coupling step. The crude product was purified by preparative HPLC (eluent: TBME/CH_3OH 90:10; UV-detector λ = 254 nm, E_{max} = 2.56; refractometer; column l = 250 mm, d = 8 mm, LiChrosorb Diol (7 µm, Merck); retention time (**2a**) = 6.54 minutes. The peptide was characterized by ESI-MS, NMR, IR and EA.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.45 [s, 1 H, H_{Ar}, C*H* (His)]; 7.31 – 7.22 [m, 3 H, H_{Ar} (Phe)]; 7.10 [d, 2 H, J = 6.4 Hz, H_{Ar} (Phe)]; 6.85 [s, 1 H, H_{Ar}, C*H* (His)]; 6.52 [d, 1 H, J = 7.6 Hz, N*H* (Phe)]; 6.22 [d, 1 H, J = 8.4 Hz, N*H* (Val)]; 5.88 [s, 1 H, N*H* (^{A}Gly)]; 5.25 [d, 1 H, J = 8.0 Hz, N*H* (His)]; 4.84 [q, 1 H, J = 6.7 Hz, $H_α$ (Phe)]; 4.27 – 4.23 [m, 1 H, $H_α$ (Val)]; 4.18 – 4.17 [m, 1 H, $H_α$ (His)]; 3.71 (s, 3 H, OCH_3); 3.60 (s, 3 H, NCH_3); 3.15 – 3.05 [m, 2 H, $H_β$ (Phe)]; 3.01 – 2.98 [m, 2 H, $H_β$ (His)]; 2.20 – 1.56 (m, 14 H, adamantane); 2.12 – 2.07 [m, 1 H, $H_β$ (Val)]; 1.43 (s, 9 H, C(CH_3)$_3$); 0.89 [t, 6 H , J = 6.2 Hz, $H_γ$ (Val)].
^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 176.3 (C=O); 171.7 (C=O); 170.9 (C=O); 169.7 (C=O), 155.4 (C=O); 138.3; 135.6; 129.2; 128.7; 128.3; 127.2; 127.2; 80.4; 77.2; 57.8; 54.5; 53.2; 52.3; 52.3; 42.7; 42.3; 40.3; 42.2; 38.3; 38.2; 37.8; 35.2; 31.5; 31.2; 29.1; 28.3; 26.8;19.1; 18.1.
ESI-MS: *m/z* = 707.4 $[M+H]^+$ (calc. *m/z* = 707.4); *m/z* = 729.3 $[M+Na]^+$ (calc. *m/z* = 729.4); *m/z* = 1413.0 $[2M+H]^+$ (calc. *m/z* = 1413.8); *m/z* = 1435.0 $[2M+Na]^+$ (calc. *m/z* = 1435.8).
IR (KBr): $\tilde{\nu}$ /cm^{-1} = 3422; 3323; 2917; 1748; 1654; 1540; 1507; 1367; 1168.
Elem. Anal.: $C_{38}H_{54}N_6O_7$: calc. C 64.57; H 7.70; N 11.89; found: C 63.31; H 7.71; N 11.47.

Synthesis of Boc-L-(π-Me)-His-^{A}Gly-^{A}Gly-L-Phe-OMe (2b):

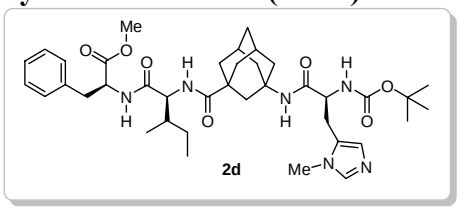


2b

Solid support: Fmoc-L-Phe Wang Resin (0.405 g, 0.74 mmol/g, 0.3 mmol). 1. Coupling: Double coupling: Fmoc-^{A}Gly (0.250 g, 0.6 mmol) in 1.2 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.250 g, 0.6 mmol) in 1.2 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.121 g, 0.45 mmol) in 1.2 mL DMF for 2h each coupling step. The crude product was purified by flash chromatography eluting with dichloromethane/methanol (90:10) R_f(**2b**) = 0.35. The peptide was characterized by ESI-MS and NMR.
^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.51 (s, 1 H); 7.31 – 7.22 (m, 4 H, H_{Ar}); 7.09 (m, 2 H, H_{Ar}); 6.85 (s, 1 H); 6.12 (d, 1 H, J = 8.0 Hz); 5.89 (s, 1 H); 5.29 (s, 1 H); 5.25 (d, 1 H, J = 7.6 Hz, $H_α$); 4.84 (m, 1 H, $H_α$); 3.72 (s, 3 H, OCH_3); 3.59 (s, 3 H, NCH_3); 3.18 – 2.99 [m, 4 H, $H_β$ (His) + $H_β$ (Phe)]; 2.19 – 1.62 (m, 28 H, adamantane); 1.44 (s, 9 H, C(CH_3)$_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 176.1 (C=O); 175.7 (C=O); 172.2 (C=O); 169.7 (C=O), 155.4 (C=O); 138.2; 136.0; 135.9; 129.3; 128.6; 128.1; 127.3; 127.1; 80.5; 77.3; 72.0; 54.4; 53.4; 52.9; 52.5; 52.3; 51.7 42.9; 42.6; 42.6; 42.5; 42.2; 40.5; 40.4; 38.3; 38.3; 38.2; 38.1; 38.0; 37.8; 35.3; 35.2; 35.1; 31.5; 29.2; 29.0; 28.3; 26.8.
ESI-MS: m/z = 785.5 $[M+H]^+$ (calc. m/z = 785.5); m/z = 807.5 $[M+Na]^+$ (calc. m/z = 807.5); m/z = 1570.3 $[2M+H]^+$ (calc. m/z = 1569.9); m/z = 1592.3 $[2M+Na]^+$ (calc. m/z = 1591.9).

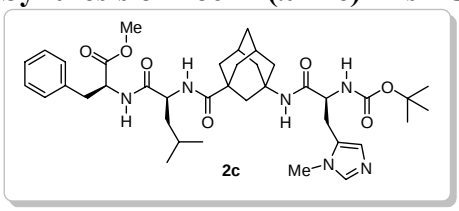
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Ile-L-Phe-OMe (2d):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-L-Ile (0.071 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 721.5 $[M+H]^+$ (calc. m/z = 721.4); m/z = 743.4 $[M+Na]^+$ (calc. m/z = 743.4); m/z = 1463.1 $[2M+Na]^+$ (calc. m/z = 1463.8).

Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Leu-L-Phe-OMe (2c):

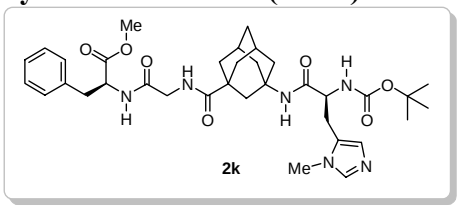


Solid support: Fmoc-L-Phe Wang Resin (0.405 g, 0.74 mmol/g, 0.3 mmol). 1. Coupling: Double coupling: Fmoc-L-Leu (0.212 g, 0.6 mmol) in 1.2 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.250 g, 0.6 mmol) in 1.2 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.121 g, 0.45 mmol) in 1.2 mL DMF for 2h each coupling step. The crude product was purified by preparative HPLC (eluent: TBME/CH_3OH 90:10; UV-detector λ = 254 nm, E_{max} = 2.56; refractometer; column l = 250 mm, d = 8 mm, LiChrosorb Diol (7µm, Merck); retention time (**2c**) = 7.97 minutes. The peptide was characterized by ESI-MS, NMR, IR and EA.

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.35 [s, 1 H, C*H*-Imidazole (His)]; 7.24 – 7.15 [m, 3 H, H_{Ar} (Phe)]; 7.06 – 7.02 [m, 2 H, H_{Ar} (Phe)]; 6.78 [s, 1 H, C*H*-Imidazole (His)]; 6.44 [d, J = 7.6 Hz, 1 H, N*H* (Phe)]; 5.92 [d, J = 7.9 Hz, 1 H, N*H* (Leu)]; 5.68 [s, 1 H, N*H* (^{A}Gly)]; 5.09 [d, J = 8.2 Hz, 1 H, N*H* (His)]; 4.76 – 4.71 [m, 1 H, H_α (Phe)]; 4.37 – 4.32 [m, 1 H, H_α (Leu)]; 4.13 – 4.03 [m, 1 H, H_α (His)]; 3.65 (s, 3 H, OCH_3); 3.52 (s, 3 H, NCH_3); 3.09 – 2.93 [m, 2 H, H_β (Phe)]; 2.94 – 2.90 [m, 2 H, H_β (His)]; 2.12 (s, 2 H, adamantane); 1.94 – 1.82 (m, 6 H, adamantane); 1.66 – 1.44 [m, 9 H, adamantane + H_β, H_γ (Leu)]; 1.40 [s, 9 H, C(CH_3)$_3$]; 0.85 – 0.81 [m, 6 H, H_γ (Leu)].
^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 176.4 (C=O); 171.8 (C=O); 171.7 (C=O); 169.7 (C=O); 155.5 (C=O); 138.3; 135.7; 129.2; 128.6; 128.2; 127.2; 127.2; 80.5; 54.4; 53.2; 52.3;

51.3; 42.5; 42.1; 41.0; 40.4; 40.3; 39.2; 38.0; 37.8; 35.1; 31.5; 29.7; 29.1; 28.3; 26.8; 25.8; 22.9; 22.2.
IR (KBr): $\tilde{\nu}$ /cm^{-1} = 3426; 3327; 2954; 2915; 2856; 1745; 1665; 1512; 1454; 1367; 1277; 1248; 1168.
MS:
ESI: m/z = 721.5 $[M+H]^+$ (calc. m/z = 721.4); m/z = 743.4 $[M+Na]^+$ (calc. m/z = 743.4); m/z = 1463.2 $[2M+Na]^+$ (calc. m/z = 1463.8).

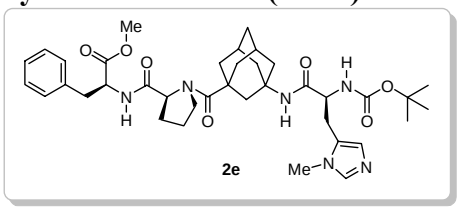
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-Gly-L-Phe-OMe (2k):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-Gly (0.060 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 665.4 $[M+H]^+$ (calc. m/z = 665.4); m/z = 687.3 $[M+Na]^+$ (calc. m/z = 687.3); m/z = 1329.2 $[2M+H]^+$ (calc. m/z = 1329.7); m/z = 1351.2 $[2M+Na]^+$ (calc. m/z = 1351.7)

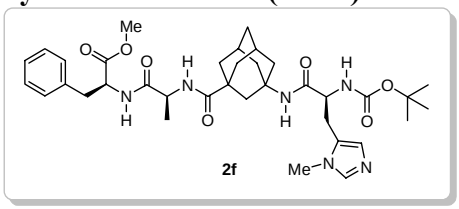
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Pro-L-Phe-OMe (2e):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-L-Pro (0.068 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 705.5 $[M+H]^+$ (calc. m/z = 705.4); m/z = 727.4 $[M+Na]^+$ (calc. m/z = 727.4); m/z = 1431.1 $[2M+Na]^+$ (calc. m/z = 1431.8).

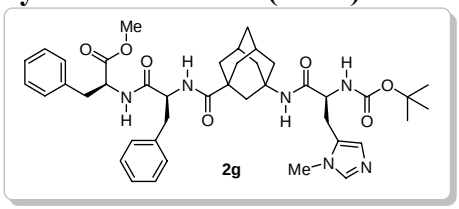
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Ala-L-Phe-OMe (2f):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-L-Ala (0.062 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 679.4 $[M+H]^+$ (calc. m/z = 679.4); m/z = 701.3 $[M+Na]^+$ (calc. m/z = 701.4); m/z = 1379.1 $[2M+Na]^+$ (calc. m/z = 1379.7).

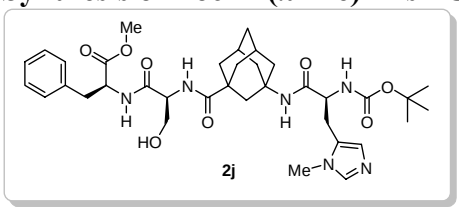
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Phe-L-Phe-OMe (2g):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-L-Phe (0.078 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 755.5 $[M+H]^+$ (calc. m/z = 755.4); m/z = 777.4 $[M+Na]^+$ (calc. m/z = 777.4); m/z = 1531.1 $[2M+Na]^+$ (calc. m/z = 1531.8).

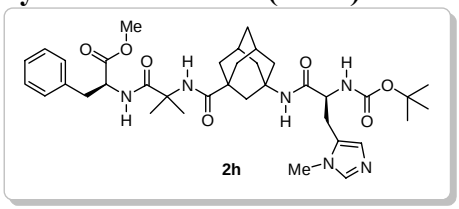
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Ser-L-Phe-OMe (2j):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-L-Ser (0.066 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 695.5 $[M+H]^+$ (calc. m/z = 695.4); m/z = 717.4 $[M+Na]^+$ (calc. m/z = 717.4); m/z = 1411.1 $[2M+Na]^+$ (calc. m/z = 1411.7).

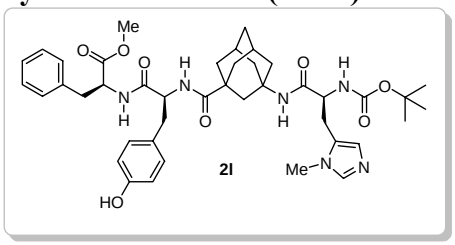
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-Aib-L-Phe-OMe (2h):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-AiB (0.65 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 693.4 $[M+H]^+$ (calc. m/z = 693.4); m/z = 715.3 $[M+Na]^+$ (calc. m/z = 715.4); m/z = 1407.1 $[2M+Na]^+$ (calc. m/z = 1407.8).

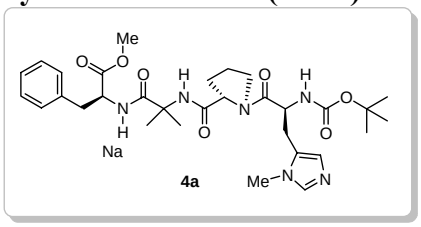
Synthesis of Boc-L-(π-Me)-His-^{A}Gly-L-Tyr-L-Phe-OMe (2l):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-L-Tyr (0.081 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-^{A}Gly (0.084 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 771.5 $[M+H]^+$ (calc. m/z = 771.4); m/z = 793.4 $[M+Na]^+$ (calc. m/z = 793.4); m/z = 1541.1 $[2M+H]^+$ (calc. m/z = 1541.8); m/z = 1563.2 $[2M+Na]^+$ (calc. m/z = 1563.8)

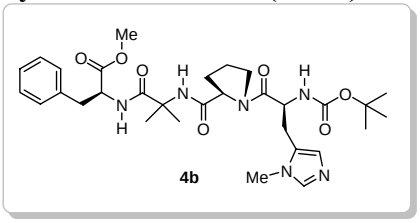
Synthesis of Boc-L-(π-Me)-His-L-Pro-AiB-L-Phe-OMe (3a):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-AiB (0.065 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-L-Pro (0.068 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 613.3 $[M+H]^+$ (calc. m/z = 612.3); m/z = 635.3 $[M+Na]^+$ (calc. m/z = 635.3)

Synthesis of Boc-L-(π-Me)-His-D-Pro-AiB-L-Phe-OMe (3b):



Solid support: Fmoc-L-Phe Wang Resin (0.135 g, 0.74 mmol/g, 0.1 mmol). 1. Coupling: Double coupling: Fmoc-AiB (0.065 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 2. Coupling: Double coupling: Fmoc-D-Pro (0.068 g, 0.2 mmol) in 0.8 mL DMF for 1h each coupling step. 3. Coupling: Double coupling: Boc-L-(π-Me)-His (0.040 g, 0.15 mmol) in 0.8 mL DMF for 2h each coupling step. The peptide was characterized by ESI-MS and tested as catalyst directly after resin cleavage without further purifications.

ESI: m/z = 613.3 $[M+H]^+$ (calc. m/z = 612.3); m/z = 635.3 $[M+Na]^+$ (calc. m/z = 635.3)

3. Availability of the racemic starting materials: *Trans*-cyclopentane-1,2-diol ((±)-1b), *trans*-cyclohexane-1,2-diol ((±)-1a), *trans*-cycloheptane-1,2-diol ((±)-1c), *trans*-cyclooctane-1,2-diol ((±)-1d)

Racemic *trans*-cyclopentane-1,2-diol ((±)-**1b**) was purchased from Aldrich (97% purity) and used without further purification. Racemic *trans*-cyclohexane-1,2-diol ((±)-**1a**) was purchased from Acros Organics (98% purity). *Trans*-cycloheptane-1,2-diol ((±)-**1c**) was synthesized according to the method of the *Organikum*[1] using freshly distilled cycloheptene (purchased from Aldrich, 92% purity), formic acid, H_2O_2 followed by a saponification with aq. NaOH. *Trans*-cyclooctane-1,2-diol ((±)-**1d**) was synthesized via epoxide opening of cyclooctaneoxide (purchased from Alfa Aesar, 99% purity) in water with p-toluenesulfonicacid.

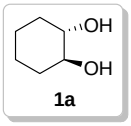
[1] Autorenkollektiv. *Organikum*: *Organisch-chemisches Grundpraktikum*, 19th ed.; Deutscher Verlag der Wissenschaften: Leipzig, **1993**.

4. Description of the catalyst screenings (2a-2l and 3a+3b) of Figure 1 with *trans*-cyclohexane-1,2-diol ((±)-1a)

Description of Standard Conditions for Catalyst Screening

The conditions for the kinetic resolutions (catalyst screening) of *trans*-cyclohexane-1,2-diol ((±)-**1a**) are given by the following experimental protocol. All peptides were used as catalysts directly after resin cleavage without further purification. Catalyst **2a** (2.7 mg, 0.00375 mmol) and diol (±)-**1a** (43.6 mg, 0.375 mmol) were dissolved in 0.85 mL of dry $CHCl_3$ and 2.25 mL of dry toluene were added to produce a clear solution at room temperature. The reaction mixture was cooled to –20 °C and 21.2 µL (0.0375 mmol, 0.1 equivalents of acetic anhydride) of a solution of 100 µL acetic anhydride in 500 µL toluene (cooled to –20 °C) was then added with an Eppendorf Pipette and allowed to stir for 15 h at –20 °C. The reaction mixture was quenched with methanol and directly analyzed by chiral GC-analysis.

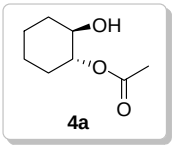
Data for diol 1a:



Diol (±)**-1a** was purchased from Acros Organics at the highest purity grade available and was used without further purifications.

Assay of enantiomeric purity.
Enantiomers of diol **1a** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Macherey Nagel).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 140 °C isothermal
Retention Times: R_1 = 10.9 min; R_2 = 11.5 min

Data for monoacetate 4a:



Assay of enantiomeric purity.
Enantiomers of monoacetate **4a** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Macherey Nagel).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 140 °C isothermal
Retention Times: R_1 = 9.3 min; R_2 = 9.6 min

Proof of GC retention times:

Racemic *trans*-cyclohexane-1,2-diol ((±)**-1a**) (0.345 g, 3.0 mmol) was treated with acetic anhydride (371 µL, 4 mmol) in the presence of *N,N*-dimethylaminopyridine (0.073 g, 0.6 mmol) in 20 mL dichloromethane and the resulting solution was stirred for 3 h at room temperature (25 °C). Dichloromethane was then removed *in vacuo*, and the monoacylated product ((±)**-4a)** was purified by silica flash gel chromatography (EtOAc, R_f (**4a**) = 0.42). Isolated racemic ((±)**-4a)** was characterized and then subjected to the GC assay described above to proof the origin of the GC signals.

Analytical data of the monoacylated product ((±)**-4a**) were identical with those reported in literature.[2-4]

[2] C. Fang, T. Ogawa, H. Suemune, K. Sakai, *Tetrahedron*: *Asymmetry* **1991**, *2*, 389-398.
[3] A. Sevin and J.-M. Cense, *Bull. Chem. Soc. Fr*. **1974**, 918.
[4] V. Bódai, O. Orovecz, G. Szakács, L. Novák and L. Poppe, *Tetrahedron*: *Asymmetry* **2003**, *14*, 2605-2612.

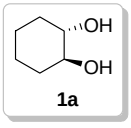
entry	*cat.*	*e.r. of 4a [ee (%)]*	*e.r. of 1a [ee (%)]*	*conversion (%)*
1	12	84.7 : 15.3 [69.4]	46.4 : 53.6 [7.2]	9.4
2	19	67.1 : 32.9 [34.2]	48.4 : 51.6 [3.2]	8.6
3	20	86.2 : 13.8 [72.4]	45.6 : 54.4 [8.8]	10.8
4	21	86.3 : 13.7 [72.6]	46.8 : 53.2 [6.4]	8.1
5	22	75.1 : 24.9 [50.2]	48.7 : 51.3 [2.6]	4.9
6	23	79.7 : 20.3 [59.4]	48.5 : 51.5 [3.0]	4.8
7	24	81.2 : 18.8 [62.4]	48.4 : 51.6 [3.2]	4.9
8	25	71.2 : 28.8 [42.4]	49.1 : 50.9 [1.8]	4.1
9	26	87.5 : 12.5 [75.0]	46.6 : 53.4 [6.8]	8.3
10	27	72.2 : 27.8 [44.4]	48.2 : 51.8 [3.6]	7.5
11	28	69.7 : 30.3 [39.4]	49.0 : 51.0 [2.0]	4.8
12	29	73.1 : 26.9 [46.2]	49.3 : 50.7 [1.4]	2.8
13	5	56.6 : 43.4 [13.2]	49.7 : 50.3 [0.6]	4.4
14	6	58.0 : 42.0 [16.0]	49.8 : 50.2 [0.4]	2.4

5. Description of the catalytic experiments of Table 1 with *trans*-cyclopentane-1,2-diol ((±)-**1b**), *trans*-cyclohexane-1,2-diol ((±)-**1a**), *trans*-cycloheptane-1,2-diol ((±)-**1c**) and *trans*-cyclooctane-1,2-diol ((±)-**1d**)

Description of Standard Conditions for Catalytic Runs

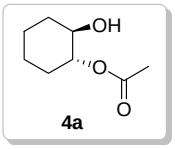
The conditions for the kinetic resolutions of *trans*-cyclopentane-1,2-diol ((±)-**1b**), *trans*-cyclohexane-1,2-diol ((±)-**1a**), *trans*-cycloheptane-1,2-diol ((±)-**1c**) and *trans*-cyclooctane-1,2-diol ((±)-**1d**) are given exemplary by the following experimental protocol. Catalyst **2i** (1.9 mg, 0.0025 mmol) was dissolved in 500 µL of dry toluene. 100 µL of this catalyst solution (0.0005 mmol, 2 mol%) were added to a clear solution of *trans*-cyclohexane-1,2-diol ((±)-**1a**) (2.9 mg, 0.025 mmol) in 4.65 mL dry toluene. The reaction mixture was cooled to –20 °C and 25 µL (0.1325 mmol, 5.3 equivalents of acetic anhydride) of a solution of 100 µL acetic anhydride in 100 µL toluene (cooled to –20 °C) was then added with an Eppendorf Pipette and allowed to stir at –20 °C. After the reaction the reaction mixture was quenched with methanol and directly analyzed by chiral GC-analysis.

Data for diol 1a:



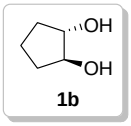
See chapter 4.

Data for monoacetate 4a:



See chapter 4.

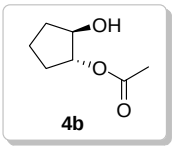
Data for diol 1b:



Diol (±)-**1b** was purchased from Aldrich at the highest purity grade available and was used without further purifications.

Assay of enantiomeric purity.
Enantiomers of diol **1b** were separated by chiral GC employing a 30 m FS-Lipodex D column (Macherey Nagel).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 100 °C – 160 °C, 2°C/min
Retention Times: R_1 = 21.89 min; R_2 = 22.32 min

Data for monoacetate 4b:



Assay of enantiomeric purity.
Enantiomers of monoacetate **4b** were separated by chiral GC employing a 30 m Chiraldex G-TA column (Astech).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 100 °C – 155 °C, 2°C/min
Retention Times: R_1 = 12.93 min; R_2 = 14.17 min

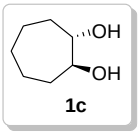
Proof of GC retention times:

Racemic *trans*-cyclopentane-1,2-diol ((±)-**1b**) (0.306 g, 3.0 mmol) was treated with acetic anhydride (371 µL, 4 mmol) in the presence of *N,N*-dimethylaminopyridine (0.073 g, 0.6 mmol) in 20 mL dichloromethane and the resulting solution was stirred for 3 h at room temperature (25 °C). Dichloromethane was then removed *in vacuo*, and the monoacylated product ((±)-**4b** was purified by silica flash gel chromatography (EtOAc, R_f ((±)-**4b**) = 0.53). Isolated racemic (±)-**4b** was characterized and then subjected to the GC assay described above to proof the origin of the GC signals.

Analytical data of the monoacylated product (±)-**4b** were identical to those reported in literature.[2-4]

[2] C. Fang, T. Ogawa, H. Suemune, K. Sakai, *Tetrahedron*: *Asymmetry* **1991**, *2*, 389-398.
[3] A. Sevin and J.-M. Cense, *Bull. Chem. Soc. Fr.* **1974**, 918.
[4] V. Bódai, O. Orovecz, G. Szakács, L. Novák, L. Poppe, *Tetrahedron*: *Asymmetry* **2003**, *14*, 2605-2612.

Data for diol (1c):



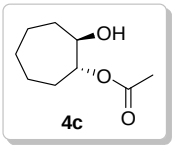
Diol (±)-**1c** was synthesized according to the method of the *Organikum*[1] (see chapter 3). Analytical data of the diol (±)-**1c** were identical with those reported in literature.[5]

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 3.37 – 3.36 (m, 2 H); 2.67 (bs, 2 H, OH); 1.87 – 1.77 (m, 2 H); 1.59 – 1.57 (m, 2 H); 1.49 – 1.39 (m, 6 H).
^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 77.9; 32.4; 26.4; 22.1.

[1] Autorenkollektiv. *Organikum*: *Organisch-chemisches Grundpraktikum*, 19th ed.; Deutscher Verlag der Wissenschaften: Leipzig, **1993**.
[5] L. N. Owen, G. S. Saharia, *J. Chem. Soc.* **1953**, 2582.

Assay of enantiomeric purity.
Enantiomers of diol **1c** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Macherey Nagel).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 100 °C – 180 °C, 2°C/min
Retention Times: R_1 = 27.24 min; R_2 = 27.73 min

Data for monoacetate (4c):



Assay of enantiomeric purity.
Enantiomers of monoacetate **4c** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Macherey Nagel).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 100 °C – 180 °C, 2°C/min
Retention Times: R_1 = 23.97 min; R_2 = 24.20 min

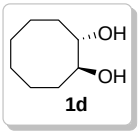
Proof of GC retention times:

Racemic *trans*-cycloheptane-1,2-diol ((±)-**1c**) (0.391 g, 3.0 mmol) was treated with acetic anhydride (371 µL, 4 mmol) in the presence of *N,N*-dimethylaminopyridine (0.073 g, 0.6 mmol) in 20 mL dichloromethane and the resulting solution was stirred for 3 h at room temperature (25 °C). Dichloromethane was then removed *in vacuo*, and the monoacylated product (±)-**4c** was purified by silica flash gel chromatography (EtOAc, R_f ((±)-**4c**) = 0.49). Isolated racemic (±)-**4c** analytically characterized and then subjected to the GC assay described above to proof the origin of the GC signals.

Analytical data of the monoacylated product ((±)-**4c**) were identical to those reported in literature.[4]

[4] V. Bódai, O. Orovecz, G. Szakács, L. Novák and L. Poppe, *Tetrahedron*: *Asymmetry* **2003**, *14*, 2605-2612.

Data for diol (1d):



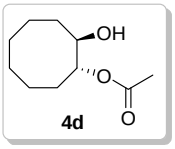
Diol ((±)-**1d**) was synthesized according to the method mentioned in chapter 3. Analytical data of the diol ((±)-**1d**) were identical to those reported in literature.[6]

^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 3.55 – 3.49 (m, 2 H); 2.64 (bs, 2 H, OH); 1.83 – 1.76 (m, 2 H); 1.67 – 1.58 (m, 4 H); 1.55 – 1.40 (m, 6 H).
^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 76.2; 31.9; 26.2; 23.7.

[6] A. C. Cope, S. W. Fenton, C. F. Spencer, *J. Am. Chem. Soc.* **1952**, *74*, 5884.

Assay of enantiomeric purity.
Enantiomers of diol **1d** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Macherey Nagel).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 160 °C isothermal
Retention Times: R_1 = 13.24 min; R_2 = 13.50 min

Data for monoacetate (4d):



Assay of enantiomeric purity.
Enantiomers of monoacetate **4d** were separated by chiral GC employing a 30 m Chiraldex G-TA column (Astech).
T (Injector + Detector) = 250°C
Splitflow = 80 mL/min
Precolumn pressure = 0.8 bar
Conditions: 100 °C – 180 °C, 2°C/min
Retention Times: R_1 = 25.63 min; R_2 = 26.31

Proof of GC retention times:

Racemic *trans*-cyclooctane-1,2-diol ((±)-**1d**) (0.433 g, 3.0 mmol) was treated with acetic anhydride (371 µL, 4 mmol) in the presence of *N,N*-dimethylaminopyridine (0.073 g, 0.6 mmol) in 20 mL dichloromethane and the resulting solution was stirred for 3 h at room

temperature (25 °C). Dichloromethane was then removed *in vacuo*, and the monoacylated product ((±)-**4d**) was purified by silica flash gel chromatography (EtOAc, R_f ((±)-**4d**) = 0.50). Isolated racemic ((±)-**4d**) was characterized and then subjected to the GC assay described above to proof the origin of the GC signals.

Analytical data of the monoacylated product ((±)-**4d**) were identical to those reported in literature.[4,7]

[4] V. Bódai, O. Orovecz, G. Szakács, L. Novák and L. Poppe, *Tetrahedron*: *Asymmetry* **2003**, *14*, 2605-2612.

[7] G. H. Posner, D. Z. Rogers, *J. Am. Chem. Soc*. **1977**, *99*, 8208-8214.

6. Kinetic resolution of *trans*-cyclohexane-1,2-diol ((±)-1a) with peptide catalyst 2i under variation of the solvent

For reaction conditions: See chapter 5

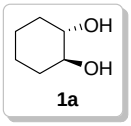
entry	*solvent*	*time (h)*	*e.r. of 4a [ee (%)]*	*e.r. of 1a [ee (%)]*	*conversion (%)*	*s-value*
1	CH_3CN	48	70.4 : 29.6 [40.8]	48.9 : 51.1 [2.2]	5.1	2.4
2	CH_2Cl_2	24	88.4 : 11.6 [76.8]	38.2 : 61.8 [23.6]	23.5	9.6
3	trifluormethylbenzene	4	87.7 : 12.3 [75.4]	39.6 : 62.4 [22.8]	23.2	8.9

7. Description of the preparative experiments with *trans*-cyclohexane-1,2-diol ((±)-1a), *trans*-cycloheptane-1,2-diol ((±)-1c) and *trans*-cyclooctane-1,2-diol ((±)-1d)

Values in red for the 1 mmol batch:

The conditions for the preparative kinetic resolution of the cyclic diols are given exemplary by the following experimental protocol. Catalyst **2i** [3.3 mg, 0.0043 mmol, 1 mol% (7.6 mg, 0.01 mmol, 1 mol%)] and diol (±)-**1a** [50 mg, 0.43 mmol (116.2 mg, 1 mmol)] were dissolved in 80 mL (185 mL) of dry toluene to produce a clear solution. The reaction mixture was cooled to 0 °C and 0.215 mL (2.28 mmol, 5.3 equivalents) [0.5 mL (5.3 mmol, 5.3 equivalents)] acetic anhydride (cooled to 0 °C) was then added and allowed to stir for 4 h 30 (4 h) min at 0 °C. The reaction mixture was quenched with 10 mL methanol and then filtered using 37 g (40 g) silica gel suspended with EtOAc to remove the catalyst and acetic acid (the silica gel was washed with EtOAc). After the filtration the solvents were removed under reduced pressure. The crude product was directly purified by silica gel column chromatography. Eluting with EtOAc afforded 33.9 mg (0.214 mmol, 50.0%) [86.7 mg (0.548 mmol, 54.8%)] of monoacetate **4a** (R_f = 0.47) and 19.4 mg (0.167 mmol, 38.8%) [42.6 mg (0.367 mmol, 36.7%)] of diol **1a** (R_f = 0.20). The products were then directly characterized by chiral GC analysis and NMR.

Data for diol (1a):

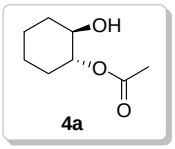


1a

$[\alpha]_D^{24} = +40.8\ ^\circ$ (0.55 g/100 mL; $CHCl_3$)

See chapter 4.

Data for monoacetate (4a):



4a

$[\alpha]_D^{24} = -37.3\ ^\circ$ (1.59 g/100 mL; $CHCl_3$)

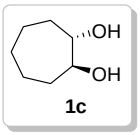
See chapter 4.

Kinetic resolution of *trans*-cycloheptane-1,2-diol ((±)-1c):

Batch: Diol (±)-**1c** (56 mg, 0.43 mmol)
Yields: 36.8 mg (0.214 mmol, 49.8%) of monoacetate **4c** ($R_f = 0.50$)
22.0 mg (0.169 mmol, 39.3%) of diol **1c** ($R_f = 0.25$)

Batch: Diol (±)-**1c** (130.2 mg, 1 mmol)
Yields: 91.0 mg (0.528 mmol, 52.8%) of monoacetate **4c** ($R_f = 0.50$)
53.6 mg (0.412 mmol, 41.2%) of diol **1c** ($R_f = 0.25$)

Data for diol (1c):

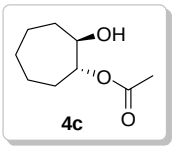


1c

$[\alpha]_D^{24} = +10.1\ ^\circ$ (0.81g/100mL; $CHCl_3$)

See chapter 5.

Data for monoacetate (4c):



4c

$[\alpha]_D^{25} = -5.7\ ^\circ$ (1.7g/100mL; $CHCl_3$)

$[\alpha]_D^{23} = -19.5\ ^\circ$ (1.5g/100mL; CH_3CN)

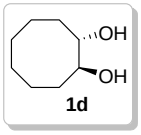
See chapter 5.

Kinetic resolution of *trans*-cyclooctane-1,2-diol ((±)-1d):

Batch: Diol (±)-**1d** (62 mg, 0.43 mmol)
Yields: 39.6 mg (0.213 mmol, 49.5%) of monoacetate **4d** ($R_f = 0.50$)
24.6 mg (0.171 mmol, 39.3%) of diol **1d** ($R_f = 0.30$)

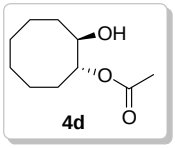
Batch: Diol (±)-**1d** (144.2 mg, 1 mmol)
Yields: 88.7 mg (0.476 mmol, 47.6%) of monoacetate **4d** ($R_f = 0.50$)
62.7 mg (0.435 mmol, 43.5%) of diol **1d** ($R_f = 0.30$)

Data for diol (1d):



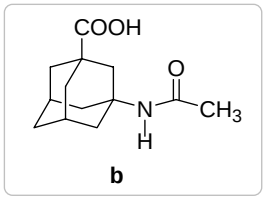
$[\alpha]_D^{25} = +15.3\ ^\circ$ (1.2g/100mL; $CHCl_3$)
See chapter 5.

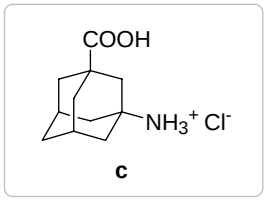
Data for monoacetate (4d):

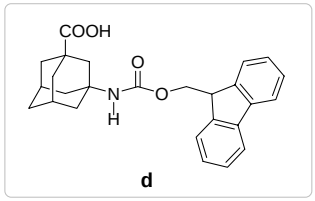


$[\alpha]_D^{25} = -33.6\ ^\circ$ (1.9g/100mL; $CHCl_3$)
$[\alpha]_D^{23} = -30.9\ ^\circ$ (1.8g/100mL; CH_3CN)
See chapter 5.

8. Synthesis of Fmoc-^{A}Gly d via Acetamide b and Hydrochloride c







Analytical data and preparative details of the synthesis of **b**, **c**, **d** can be found in literature.[8]

[8] L. Wanka, C. Cabrele, M. Vanejews, P. R. Schreiner, *Eur. J. Org. Chem.*, **2007**, 1474-1490.

9. Determination of conversions and S-values

Conversions and S-values were calculated according to the method of Kagan.[9]

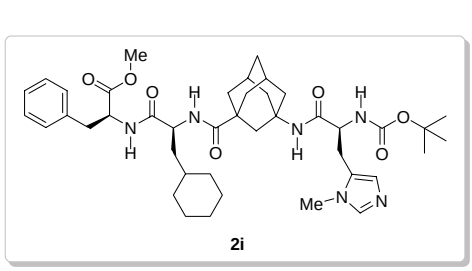
$$C = \frac{ee}{ee + ee'} \cdot 100 \qquad S = \frac{\ln[1 - C(1 + ee')]}{\ln[1 - C(1 - ee')]} = \frac{\ln[(1 - C)(1 - ee)]}{\ln[(1 - C)(1 + ee)]}$$

ee = enantiomeric excess measured for the educt
ee' = enantiomeric excess measured for the product
C = conversion

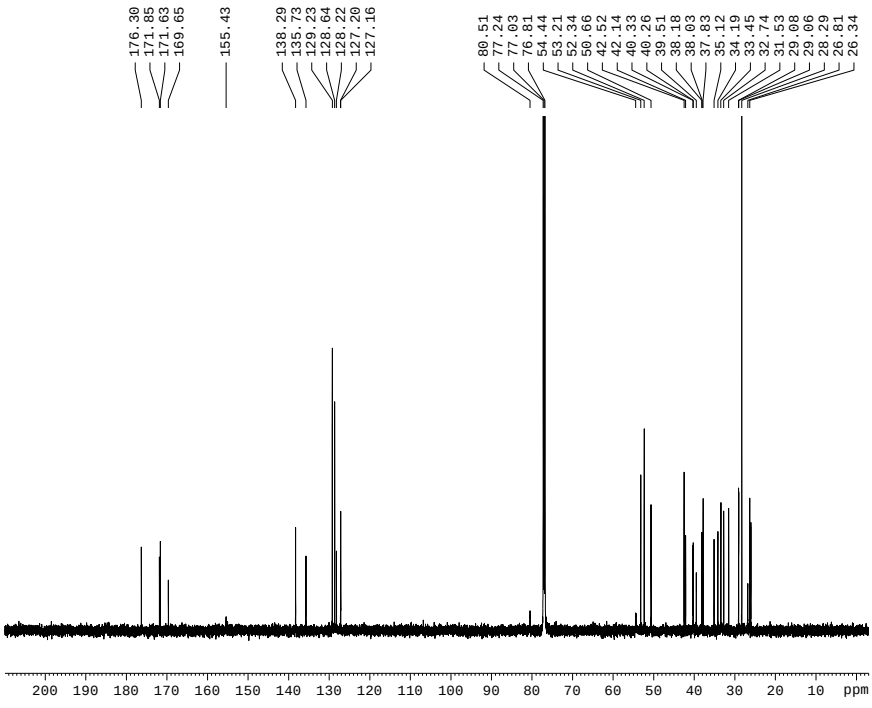
[9] H. B. Kagan, J. C. Fiaud, *Top. Stereochem.* **1988**, *18*, 249 – 330.

10. Spectra

Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OMe (2i):

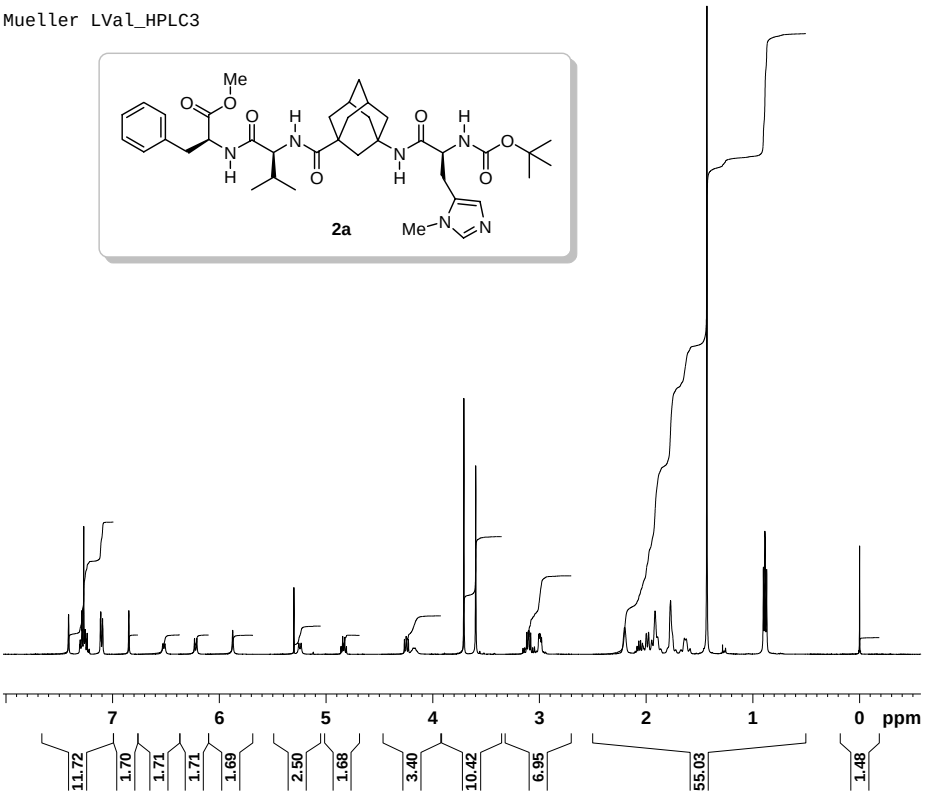



```
Current Data Parameters
NAME        CMNov08-2007
EXPNO                 40
PROCNO                 1

F2 - Acquisition Parameters
Date_           20071109
Time                7.01
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           12335.526 Hz
FIDRES         0.188225 Hz
AQ             2.6564426 sec
RG                  322
DW               40.533 usec
DE                6.50 usec
TE                296.4 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                12.50 usec
PL1               -2.00 dB
SFO1         600.1937064 MHz

F2 - Processing parameters
SI                 32768
SF            600.1900518 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                  1.00
```

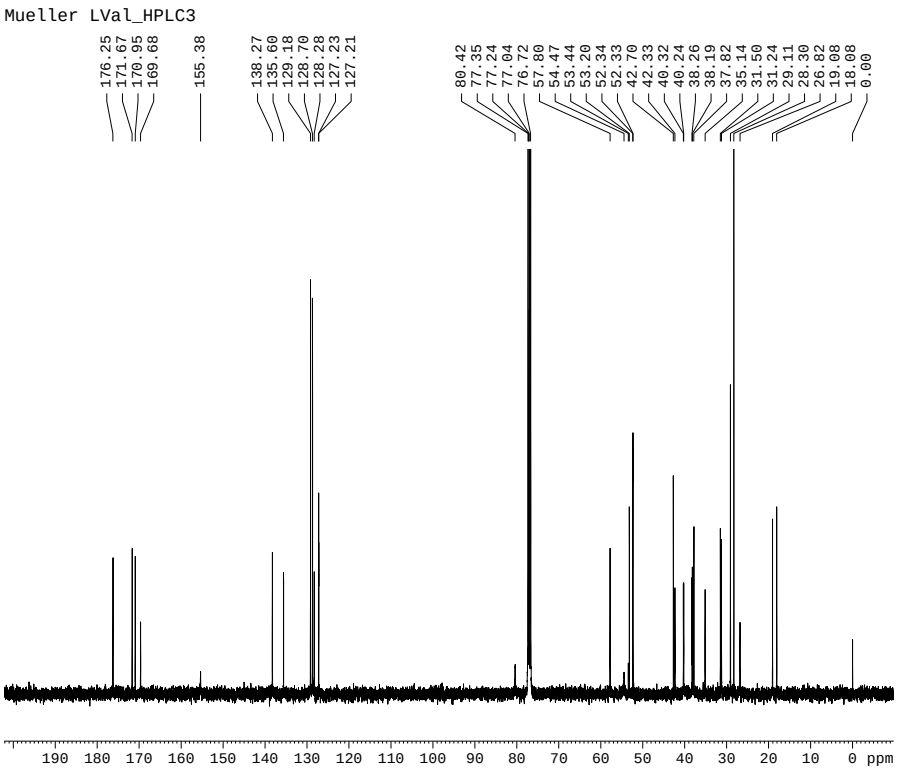



```
Current Data Parameters
NAME        CMNov08-2007
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20071109
Time               10.15
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 2048
DS                    4
SWH           36057.691 Hz
FIDRES         0.550197 Hz
AQ             0.9088159 sec
RG                  2050
DW               13.867 usec
DE                6.50 usec
TE                296.9 K
D1            2.00000000 sec
d11           0.03000000 sec
DELTA         1.89999998 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                9.50 usec
PL1               2.00 dB
SFO1         150.9329873 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             77.00 usec
PL12              14.00 dB
PL13              20.00 dB
PL2               -2.00 dB
SFO2         600.1924008 MHz

F2 - Processing parameters
SI                 32768
SF            150.9178960 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                  1.40
```

Boc-L-(π-Me)-His-^{A}Gly-L-Val-L-Phe-OMe (2a):

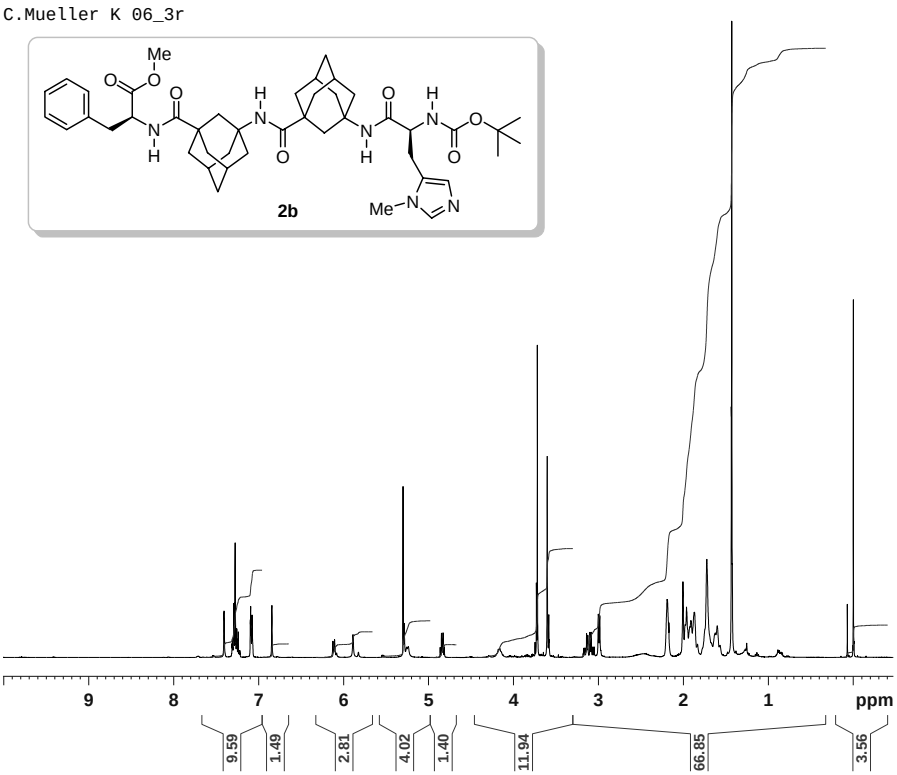



```
Current Data Parameters
NAME       CMMar15-2007
EXPNO               163
PROCNO                1

F2 - Acquisition Parameters
Date_          20070317
Time               2.45
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9846387 sec
RG                  80.6
DW                60.800 usec
DE                 6.00 usec
TE                295.7 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.00 usec
PL1                -2.50 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300049 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

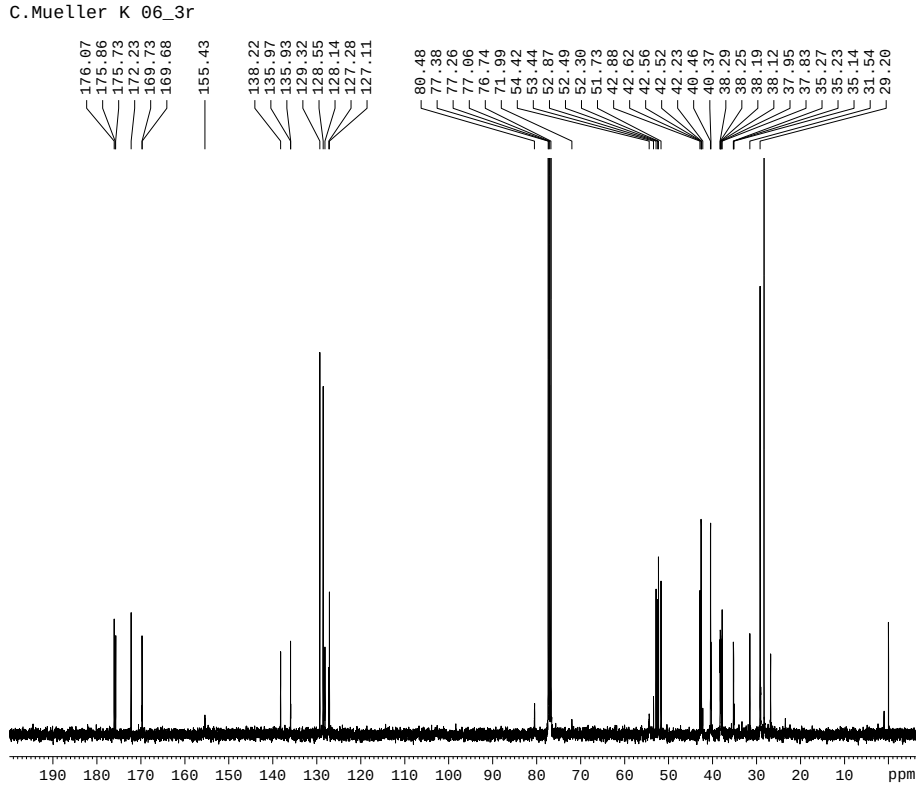



```
Current Data Parameters
NAME       CMMar15-2007
EXPNO               162
PROCNO                1

F2 - Acquisition Parameters
Date_          20070316
Time               7.37
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ             1.3631988 sec
RG                  2050
DW                20.800 usec
DE                 6.00 usec
TE                296.6 K
D1           2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                 8.80 usec
PL1               -2.60 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             80.00 usec
PL2               -1.80 dB
PL12              13.30 dB
PL13              25.00 dB
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127692 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

Boc-L-(π-Me)-His-^{A}Gly-^{A}Gly -L-Phe-OMe (2b):




```
Current Data Parameters
NAME       CMJun20-2006
EXPNO                60
PROCNO                1

F2 - Acquisition Parameters
Date_           20060620
Time               17.58
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ             3.9846387 sec
RG                    64
DW                60.800 usec
DE                 6.00 usec
TE                297.4 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                14.00 usec
PL1               -2.50 dB
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF           400.1300024 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.00
```




```
Current Data Parameters
NAME       CMJun20-2006
EXPNO                61
PROCNO                1

F2 - Acquisition Parameters
Date_           20060620
Time               18.59
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ             1.3631988 sec
RG                  2050
DW                20.800 usec
DE                 6.00 usec
TE                298.5 K
D1           2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                 8.80 usec
PL1               -2.60 dB
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2               -1.80 dB
PL12               13.30 dB
PL13               25.00 dB
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6127670 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                 1.40
```

Boc-L-(π-Me)-His-^{A}Gly-L-Leu-L-Phe-OMe (2c):