Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supplementary Information

Enantioselective conjugate addition to nitroolefins catalysed by helical peptides with a single remote stereogenic centre.

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Table of Contents

1. General Information

All reactions were carried out in oven-dried glassware under an atmosphere of nitrogen using standard anhydrous techniques. Anhydrous tetrahydrofuran, acetonitrile, dichloromethane, acetone and *N*,*N*-dimethylformamide were purchased from Sigma-Aldrich. Petroleum ether refers to the fraction of light petroleum ether boiling between 40 and 60 °C. All other solvents and commercially available reagents were used as received without further purification All products were concentrated on a rotary evaporator followed by connection to a high vacuum system to remove any residual solvent.

Analytical thin-layer chromatography (TLC) was performed using pre-coated plates (Macherey-Nagel Polygram SIL G/UV254). Visualisation was achieved by way of UV light (at 254 nm) and staining with potassium permanganate. Stained TLC plates were heated for visualization. Preparative chromatography (flash) was performed on normal phase silica gel (Merck 60H, 40-60 nm, 230–300 mesh).

Nuclear Magnetic Resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on Bruker Ultrashield 400 MHz and 500 MHz spectrometers in deuterated solvents. All NMR characterisation experiments were performed at 25 °C and 1 atm unless otherwise stated. Chemical shifts (δ) are quoted in parts per million (ppm) relative to the specified deuterated solvent. Spectra were calibrated using the residual solvent peaks for $CDCl_3$ (δH: 7.26 ppm; δC: 77.16 ppm), CD_2Cl_2 (δH: 5.32 ppm; δC: 53.84 ppm) and $(CD_3)_2SO$ (δH: 2.50 ppm; δC: 39.52 ppm) as appropriate. Coupling constants (J) are quoted in Hz and are rounded to the nearest 0.1 Hz. Splitting patterns are abbreviated to: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) or some combination thereof. Assignments of the peaks were made based on chemical shifts, coupling constants, COSY, NOESY, HSQC and HMBC data.

High resolution spectrometry experiments (HR-MS) were recorded by staff at the University of Manchester. Electrospray (ES) spectra were recorded on a Waters Platform II. High-resolution mass spectra (HRMS) were recorded on a Thermo Finnigan MAT95XP and are accurate to ±0.001 Da.

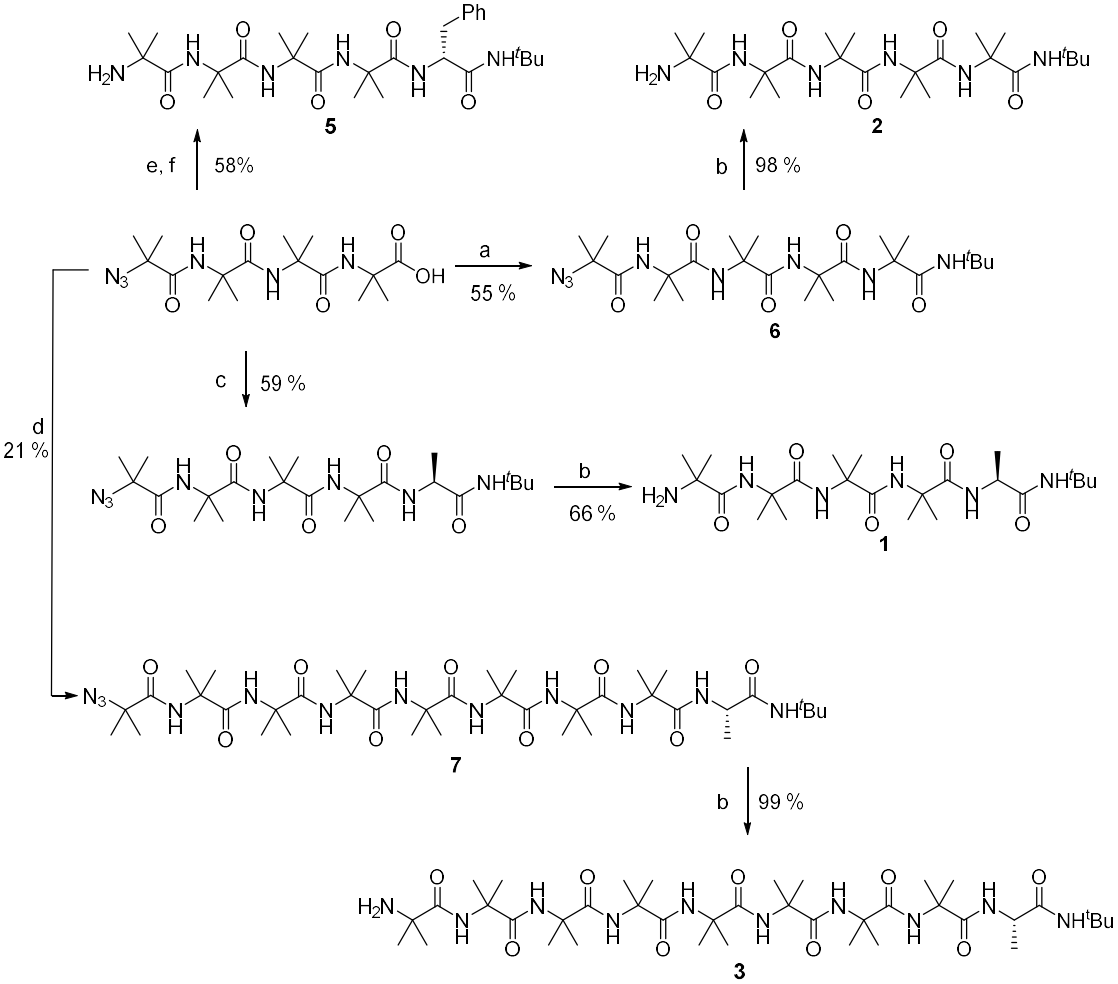
Melting points were measured on a Stuart SMP10 melting point apparatus and are uncorrected.

Circular Dichroism (CD) measurements were performed at 25 °C on a Chirascan qCD applied photophysics spectrometer, using a high precision 1 mm light path quartz cell Hellma Analytics, with the solvent and concentration stated.

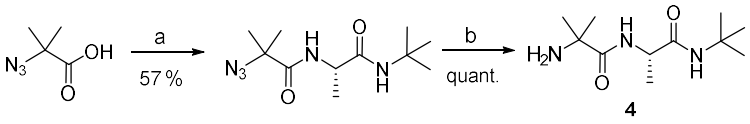
Infrared spectra were recorded on a Perkin Elmer Spectrum Two FT-IR spectrometer with samples applied as neat films. Absorptions maxima (ν_{max}) of interest are quoted in wavenumbers as ν in cm^{-1} for the most intense bands.

The following abbreviations have been used: Aib = aminoisobutyric acid, L-Alanine = L-Ala, DIPEA = *N*,*N*-diisopropylethylamine, EDC·HCl = *N*-(3-dimethylaminopropyl)-1-*N'*- ethylcarbodiimide, EtOAc = ethyl acetate, EtOH = ethanol, DMF = *N*,*N*-dimethylformamide, DCM = dichloromethane, Et_2O = diethylether, HOBt = 1-hydroxybenzotriazole, MeOH = methanol, THF = tetrahydrofuran, NEt_3 = triethylamine, TLC = thin layer chromatography.

2. General synthetic schemes



Scheme S1. Synthesis of foldamers **1**-**3**. a) EDC.HCl (1.5 equiv.), DIPEA (1.5 equiv.), CH_2Cl_2, 20 °C, 4h., then AibNH^{t}Bu (1 equiv.), CH_3CN, 82 ℃, 3 days; b) Pd/C, EtOH, H_2, 20 ℃, 1 day; c) EDC.HCl (1.5 equiv.), DIPEA (1.5 equiv.), CH_2Cl_2, 20 ℃, 4h., then (L-Ala)NH^{t}Bu (1 equiv.), CH_3CN, 82 ℃, 3 days; d) EDC.HCl (1.5 equiv.), DIPEA (1.5 equiv.), CH_2Cl_2, 20 ℃, 4h., then Aib$_4$(L-Ala)NH^{t}Bu **1** (1 equiv.), CH_3CN, 82 ℃, 7 days; e) HOBt (1.3 equiv.), EDC.HCl (1.1 equiv.), DIPEA (2.1 equiv.), CH_2Cl_2, 20 °C, 0.5 h., then (L-Phe)NH^{t}Bu (1 equiv.), 20 °C, CH_2Cl_2, 2 days; f. Pd/C, EtOH, H_2, 20 °C, 2 days.

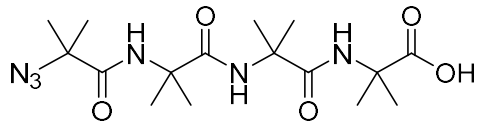


Scheme S2. Synthesis of peptide **4**. a) EDC.HCl (1.5 equiv.), HOBt (0.1 equiv.), DIPEA (1.5 equiv.), CH_2Cl_2, 20 °C, 30 min., then (L-Ala)NH^{t}Bu (1 equiv.), 3 days; b) Pd/C, EtOH, H_2, 20 °C, 1 day.

3. Experimental procedures and characterisation data

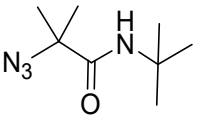
3.1. Synthesis of peptides

3.1.1 N_3Aib_4OH



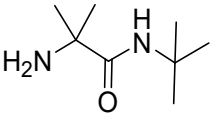
To a solution of $N_3Aib_4O^tBu$[1] (700 mg, 1.59 mmol) in dichloromethane (4 mL) was added trifluoroacetic acid (0.6 mL) and the mixture was stirred for 5h at ambient temperature. After completion of the reaction (monitored by TLC) the reaction mixture was concentrated under reduced pressure to yield $N_3Aib_4CO_2H$ as a white solid (610 mg, quantitative). Analytical data agree with previously reported data.[2] **^{1}H NMR** (400 MHz, DMSO) δ 7.85 (s, 1H, N*H*), 7.46 (s, 1H, N*H*), 7.26 (s, 1H, N*H*), 1.45 (s, 6H, (CH_3)$_2$C), 1.35 (s, 6H, (CH_3)$_2$C), 1.34 (s, 6H, (CH_3)$_2$C), 1.29 (s, 6H, (CH_3)$_2$C). **^{13}C NMR** (101 MHz, DMSO) δ 175.6 (*C*=O), 173.3 (*C*=O), 172.6 (*C*=O), 171.9 (*C*=O), 63.6 (*C*(CH$_3$)$_2$), 56.4 (*C*(CH$_3$)$_2$), 55.6 (*C*(CH$_3$)$_2$), 54.8 (*C*(CH$_3$)$_2$), 24.7 (2C, (*C*H$_3$)$_2$C), 24.5 (2C, (*C*H$_3$)$_2$C), 24.4 (2C, (*C*H$_3$)$_2$C), 23.9 (2C, (*C*H$_3$)$_2$C). **^{1}H-NMR** (400 MHz, $CDCl_3$) δ 7.37 (bs, 1H, N*H*), 6.92 (s, 1H, N*H*), 6.27 (s, 1H, N*H*), 1.57 (s, 6H, (CH_3)$_2$C), 1.53 (s, 6H, (CH_3)$_2$C), 1.49 (s, 6H, (CH_3)$_2$C), 1.46 (s, 6H, (CH_3)$_2$C). **^{13}C-NMR** (101 MHz, $CDCl_3$) δ 177.4 (*C*=O), 174.9 (*C*=O), 174.3 (*C*=O), 173.3 (*C*=O), 64.0 (*C*(CH$_3$)$_2$), 57.2 (*C*(CH$_3$)$_2$), 57.1 (*C*(CH$_3$)$_2$), 57.1 (*C*(CH$_3$)$_2$), 25.1 (2C, (*C*H$_3$)$_2$C), 24.9 (2C, (*C*H$_3$)$_2$C), 24.8 (2C, (*C*H$_3$)$_2$C), 24.4 (2C, (*C*H$_3$)$_2$C).

3.1.2 N_3AibNH^tBu



To a solution of N_3AibOH (1.22 g, 9.5 mmol) in dry dichloromethane (20 mL) was added EDC·HCl (1.81 g, 9.5 mmol) then HOBt (1.27 g, 9.5 mmol) and $^tBuNH_2$ (2 g, 28.3 mmol). The mixture was stirred at 20 °C for 16 h then concentrated under vacuum. The residue was dissolved in ethyl acetate then washed with aqueous 10% $KHSO_4$ solution, then with aqueous $NaHCO_3$ solution, then with water. The organic layer was dried (Na_2SO_4), filtered, concentrated under vacuum to yield the product (1.21 g, 54%) as a colourless liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.27 (s, 1H, N*H*), 1.46 (s, 6H, (CH_3)$_2$C), 1.32 (s, 9H, (CH_3)$_3$C); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4 (*C*=O), 64.5 (*C*(CH$_3$)$_3$), 51.1 (*C*(CH$_3$)$_2$), 28.6 (3C, (*C*H$_3$)$_3$C), 24.5 (2C, (*C*H$_3$)$_2$C). **HR – MS** (ESI, positive ion mode) – *m/z* for $[C_8H_{16}N_4ONa]^+$ 207.1216, found 207.1205.

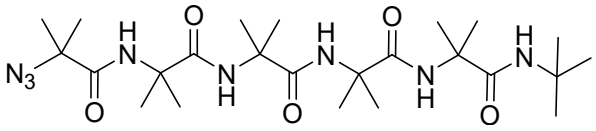
3.1.3. $AibNH^tBu$



To a solution of N_3AibNH^tBu (1.21 g, 6.6 mmol) in ethanol (120 mL) degassed with nitrogen was added palladium on carbon then the mixture was placed under a hydrogen atmosphere (vacuum/hydrogen cycle) and stirred vigorously at 20 °C for 16h. At the completion of the reaction (monitored by TLC,

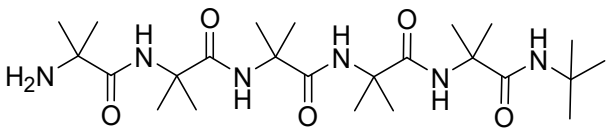
eluent dichloromethane methanol 9:1) the mixture was placed in nitrogen atmosphere (vacuum nitrogen cycle) then filtered through a Celite® plug, the Celite® was further rinsed with methanol and the organic layer was concentrated under vacuum to yield the product as a pale yellow solid (950 mg, 91%). Analytical data agree with data reported in literature.[3] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (s, 1H, N*H*tBu), 1.52 (bs, 2H, NH_2), 1.25 (s, 9H, (CH_3)$_3$C), 1.24 (s, 6H, (CH_3)$_2$C); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.8 (*C*=O), 54.9 (C), 50.0 (C), 29.2 (2C, (*C*H_3)$_2$C), 28.6 (3C, (*C*H_3)$_3$C). **HR – MS** (ESI, positive ion mode) – *m/z* for $[C_8H_{19}N_2O]^+$ 159.1492, found 159.1486.

3.1.4. $N_3Aib_5NH^tBu$, 6



To a solution of N_3Aib_4OH (382 mg, 1 mmol) in dry dichloromethane (8 mL) was added EDC·HCl (288 mg, 1.5 mmol), diisopropylethylamine (0.26 mL, 1.5 mmol) and the mixture was stirred at 20 °C for 4 h. After concentration under vacuum, the residue was dissolved in ethyl acetate (10 mL), the resulting organic phase was washed with aqueous solution of $KHSO_4$ (5%) (2 × 6 mL), brine (2 × 6 mL), dried over $MgSO_4$, filtered and concentrated. The resulting azlactone was dissolved in dry acetonitrile (5 mL) and AibNH^{t}Bu (158 mg, 1 mmol) was added. The mixture was heated at 80 °C for 3 days. At 20 °C, the mixture was concentrated under vacuum, the residue was dissolved in dichloromethane, the organic phase was washed with aqueous solution of $KHSO_4$ (5%), aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered and concentrated. Purification by chromatography on silica (eluent dichloromethane methanol 95:5, top spot R_f 0.8) yielded the product (283 mg, 55%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (s, 1H, N*H*), 7.24 (s, 1H, N*H*), 6.80 (s, 1H, N*H*), 6.33 (s, 1H, N*H*), 1.48 (s, 6H, (CH_3)$_2$C), 1.43 (s, 6H(CH_3)$_2$C), 1.42 (6H, (CH_3)$_2$C)), 1.40 (s, 6H, (CH_3)$_2$C), 1.36 (s, 6H, (CH_3)$_2$C), 1.31 (s, 9H, (CH_3)$_3$C). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.7 (*C*=O), 173.7 (*C*=O), 173.7 (*C*=O), 173.4 (*C*=O), 173.1 (*C*=O), 63.8 (*C*), 57.1 (*C*), 56.9 (*C*), 56.9 (*C*), 56.7 (*C*), 50.7 (*C*), 28.7 (3C, (CH_3)$_3$C), 25.6 (2C, (CH_3)$_2$C), 25.1 (2C, (CH_3)$_2$C), 25.0 (2C, (CH_3)$_2$C), 24.7 (2C, (CH_3)$_2$C), 24.2 (2C, (CH_3)$_2$C). **HR – MS** (ESI, positive ion mode) – *m/z* for $[C_{24}H_{44}N_8O_5Na]^+$ 547.3327, found 547.3306.

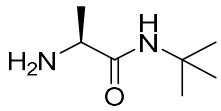
3.1.5. $(Aib)_5NH^tBu$, Peptide 2



To a degassed solution of N_3Aib_5NHtBu **6** (280 mg, 0.535 mmol) in ethanol (30 mL) was added palladium on carbon, the mixture was placed under hydrogen atmosphere (vacuum then hydrogen) and stirred at 20 °C for 1 day. The completion of the reaction was monitored by TLC on silica (eluent dichloromethane: methanol 95:5, ninhydrin stain). The mixture was filtered through Celite® plug, the Celite® was rinsed with methanol then the collected organic phase was concentrated under vacuum to yield the product as a white solid (259 mg, 98%). **^{1}H NMR** (400 MHz, CD_3OD) δ 1.41 – 1.38 (m, 18H, 3 × (CH_3)$_2$C), 1.34 (s, 6H, (CH_3)$_2$C), 1.32 (s, 15H, (CH_3)$_3$C), (CH_3)$_2$C)). **^{13}C NMR** (101 MHz, CD_3OD) δ

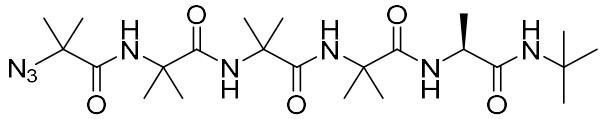
177.8 (*C*=O), 175.6 (*C*=O), 175.2 (*C*=O), 175.2 (*C*=O), 175.1 (*C*=O), 56.9 (*C*), 56.5 (*C*), 56.2 (*C*), 56.1 (*C*), 54.6 (*C*), 50.8 (*C*), 27.7 ((*C*H$_3$)$_3$C), 26.6 ((*C*H$_3$)$_2$C), 24.6 (*C*H$_3$)$_2$C), 24.2 (*C*H$_3$)$_2$C), 24.0 (*C*H$_3$)$_2$C), 23.6 (*C*H$_3$)$_2$C). **HR – MS** (ESI, positive ion mode) – *m/z* for [$C_{24}H_{46}N_6O_5Na$]$^+$ 521.3422, found 521.3401.

3.1.6. (L-Ala)NH*t*Bu



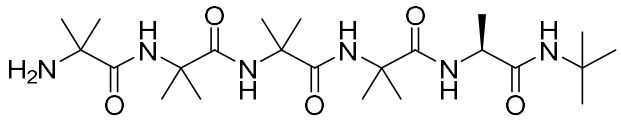
To a solution of Z-(L-Ala)NH*t*Bu[4a] (1.87 g, 6.72 mmol) in ethanol (100 mL) was added palladium on carbon (5% w/w) and the mixture was placed under hydrogen atmosphere (vacuum nitrogen purge then vacuum hydrogen). The resulting mixture was stirred vigorously for 24h at 20 C until completion of the reaction (monitored by TLC). The reaction was placed under nitrogen atmosphere, filtered on Celite®. The resulting organic phase was concentrated to afford quantitative yield of product (968 mg, quantitative) that was used with no further purification. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.08 (s, 1H, N*H*t*Bu*), 3.30 (q, *J* = 6.9 Hz, 1H, C*H*CH$_3$), 1.65 (bs, 2H, N*H*$_2$), 1.28 (s, 9H, (C*H*$_3$)$_3$C), 1.23 (d, *J* = 6.9 Hz, 3H, C*H*$_3$CH). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.9 (*C*=O), 51.2 (*C*H), 50.3 (*C*), 28.7 (3C, (*C*H$_3$)$_3$C), 21.8 (*C*H$_3$CH). **HR – MS** (ESI, positive ion mode) – m/z for [$C_7H_{16}N_2ONa$]$^+$ 167.1155, found 167.1150.

3.1.7. N_3Aib_4(L-Ala)NH^{t}Bu



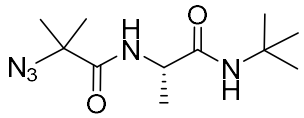
To a solution of N_3Aib_4OH (318 mg, 0.83 mmol) in dry dichloromethane (5 mL) was added EDC·HCl (239 mg, 1.24 mmol), DIPEA (0.220 mL, 1.24 mmol) and the mixture was stirred at 20 °C for 4 hours. After concentration under reduced pressure, the residue was dissolved in ethyl acetate (5 mL) and washed with aqueous $KHSO_4$ 5 mol% (2 × 3 mL), then with brine (3 mL). The organic phase was dried (Na_2SO_4), filtered and concentrated under reduced pressure and the residue was dissolved in dry acetonitrile (5 mL). L-AlaNH^{t}Bu (119 mg, 0.83 mmol) was added, and the mixture was stirred at 80 °C for 3 days. Upon completion of the reaction, the mixture was concentrated under reduced pressure and the residue was purified by chromatography on silica (eluent dichloromethane methanol 95:5) to afford the product (249 mg, 0.49 mmol, 59%). Analytical data agree with previously reported data.[5] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.5 Hz, 1H, N*H*$_{Ala}$), 7.30 (s, 2H, 2 × N*H*), 6.76 (s, 1H, N*H*), 6.74 (s, 1H, N*H*), 4.18 (p, *J* = 7.1 Hz, 1H, C*H*CH$_3$Ala), 1.50 (s, 3H, C*H*$_3$C), 1.48 (s, 3H, C*H*$_3$C), 1.46 (s, 3H, C*H*$_3$C), 1.43 (s, 3H, C*H*$_3$C), 1.42 – 1.35 (m, 12H, 4 × C*H*$_3$C), 1.32 (s, 3H, C*H*$_3$C), 1.30 (s, 9H, (C*H*$_3$)$_3$C). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.7 (*C*=O), 174.2 (*C*=O), 174.1 (*C*=O), 173.1 (*C*=O), 172.6 (*C*=O$_{Ala}$), 63.8 (*C*$_{Aib}$N$_3$), 56.9 (*C*$_{Aib}$), 56.9 (*C*$_{Aib}$), 56.7 (*C*$_{Aib}$), 50.9 (*C*(CH$_3$)$_3$), 50.3 (*C*HCH$_3$), 28.6 (3C, (*C*H$_3$)$_3$C), 27.2 (*C*H$_3$C), 27.0 (*C*H$_3$C), 25.9 (*C*H$_3$C), 24.3 (*C*H$_3$C), 24.1 (*C*H$_3$C), 23.5 (*C*H$_3$C), 23.1 (*C*H$_3$C), 23.0 (*C*H$_3$C), 17.3 (*C*H$_3$C). **HR – MS** (ESI, positive ion mode) – m/z for [$C_{35}H_{57}N_9F_6O_4SiNa$]$^+$ 832.4099, found 832.4080.

3.1.8. $(Aib)_4$(L-Ala)NH*t*Bu, Peptide 1



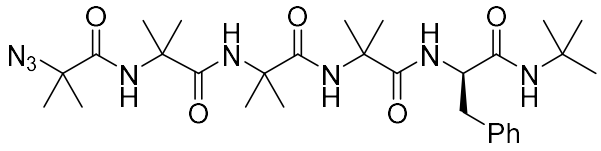
To a solution of N_3Aib_4(L-Ala)NH*t*Bu (249 mg, 0.48 mmol) in ethanol (20 mL) was added palladium on carbon 5% w/w and the mixture was placed under hydrogen atmosphere (vacuum nitrogen purge then vacuum hydrogen). The mixture was stirred vigorously at 20 °C for 24 h until completion of the reaction (monitored by TLC). The reaction was placed back under nitrogen atmosphere then filtered on Celite® and the organic phase was concentrated under reduced pressure to afford a residue that was purified by chromatography on silica (eluent dichloromethane methanol 95:) to afford the product (155 mg, 0.32 mmol, 66%) as a white solid. **^{1}H NMR** (400 MHz, Acetone) δ 8.53 (s, 1H, N*H*), 7.97 (s, 1H, N*H*), 7.81 (d, *J* = 6.9 Hz, 1H, N*H*CH), 7.55 (s, 1H, N*H*), 7.06 (s, 1H, N*H*), 4.19 – 4.01 (m, 1H, C*H*CH_3), 1.72 (s, 3H, C*H*$_3$C), 1.68 (s, 3H, C*H*$_3$C), 1.56 – 1.38 (m, 21H, 6 × C*H*$_3$C, C*H*$_3$CH), 1.33 (s, 9H, (C*H*$_3$)$_3$C). **^{13}C NMR** (101 MHz, Acetone d6) δ 175.5 (*C*=O), 175.4 (*C*=O), 175.4 (*C*=O), 174.0 (*C*=O), 173.6 (*C*=OCH_{Ala}), 57.8 (*C*$(CH_3)_2$), 57.6 (*C*$(CH_3)_2$), 57.5 (*C*$(CH_3)_2$), 57.3 (*C*$(CH_3)_2$), 51.3 (*C*$(CH_3)_3$), 51.1 (*C*$HCH_{3\ Ala}$), 29.0 (3C, (*C*$H_3)_3$C), 27.6 (*C*H_3C), 27.1 (*C*H_3C), 26.2 (*C*H_3C), 25.2 (*C*H_3C), 25.1 (*C*H_3C), 23.7 (*C*H_3C), 23.6 (*C*H_3C), 23.5 (*C*H_3C), 17.9 (*C*H_3CH). **HR – MS** (ESI, positive ion mode) – m/z for $[C_{23}H_{44}O_5N_6Na]^+$ 507.3265, found 507.3251.

3.1.9. N_3Aib(L-Ala)NH*t*Bu



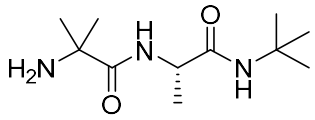
To N_3AibOH (160 mg, 1.24 mmol) dissolved in dichloromethane (5 mL) were added EDC·HCl (356 mg, 1.86 mmol, 1.5 equiv), diisopropylethylamine (0.32 mL, 1.86 mmol, 1.5 equiv) then HOBt (16 mg, 0.18 mmol, 0.1 equiv). The mixture was stirred at 20 °C for 30 minutes after which L-AlaNH*t*Bu (107 mg, 0.74 mmol) was added, and the mixture was stirred at 20 °C for 3 days. The mixture was washed with aqueous HCl 1M, then with aqueous saturated solution of $NaHCO_3$, then with brine. The organic phase was dried (Na_2SO_4), concentrated and purified by chromatography on silica (eluent petroleum ether ethyl acetate 7 :2) to afford the product (178 mg, 57%) as an oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 7.8 Hz, 1H, N*H*), 6.13 (s, 1H, N*H*), 4.31 (p, *J* = 6.8 Hz, 1H, C*H*$_{Ala}$), 1.51 (s, 3H, C*H*$_{3Aib}$), 1.50 (s, 3H, C*H*$_{3Aib}$), 1.35 – 1.30 (m, 12H, (C*H*$_3)_3$C, C*H*$_{3Ala}$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.2 (*C*=O$_{Aib}$), 171.0 (*C*=O$_{Ala}$), 64.1 (*C*$(CH_3)_2$), 51.4 (*C*$(CH_3)_3$), 49.4 (*C*H_{Ala}), 28.8 (3C, (*C*$H_3)_3$C), 24.6 (*C*H_{3Aib}), 24.5 (*C*H_{3Aib}), 18.6 (*C*H_{3Ala}). **HR – MS** (ESI, positive ion mode) – m/z for $[C_{11}H_{21}O_2N_5Na]^+$ 278.1587, found 278.1573.

3.1.10. N_3Aib_4(D-Phe)NH^{t}Bu



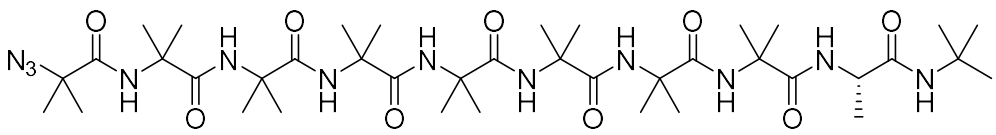
This compound was prepared following a procedure from Diemer *et al.*[5] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.7 Hz, 1H, C*H*$_{Ph}$), 7.26 (s, 1H, N*H*), 7.24 – 7.18 (m, 2H, 2 × C*H*$_{Ph}$), 7.15 – 7.07 (m, 2H, 2 × C*H*$_{Ph}$), 7.07 – 7.02 (m, 1H, N*H*$_{Phe}$), 6.91 (s, 1H, N*H*), 6.41 (s, 1H, N*H*), 4.45 (ddd, *J* = 11.9, 8.6, 3.1 Hz, 1H, PhCH$_2$C*H*), 3.53 (dd, *J* = 14.5, 3.1 Hz, 1H, PhC*H*$_2$CH), 2.83 (dd, *J* = 14.5, 12.0 Hz, 1H, PhC*H*$_2$CH), 1.46 (m, 3H, C*H*$_{3Aib}$), 1.45 (s, 3H, C*H*$_{3Aib}$), 1.41 (m, 3H, C*H*$_{3Aib}$), 1.40 (m, 6H, 2 × C*H*$_{3Aib}$), 1.38 (m, 3H, C*H*$_{3Aib}$), 1.34 (s, 9H, (C*H*$_3$)$_3$C), 1.28 (s, 3H, C*H*$_{3Aib}$), 1.07 (s, 3H, C*H*$_{3Aib}$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.9 (*C*=O), 173.9 (*C*=O), 173.7 (*C*=O), 173.2 (*C*=O), 171.2 (*C*=O), 139.0 (*C*$_{Ph}$), 129.2 (2 × *C*H$_{Ph}$), 128.1 (2 × *C*H$_{Ph}$), 126.2 (*C*H$_{Ph}$), 63.9 (*C*(CH$_3$)$_3$)), 57.2 (*C*$_{Aib}$), 57.0 (*C*$_{Aib}$), 56.7 (*C*$_{Aib}$), 55.7 (*C*H), 51.3 (*C*$_{Aib}$), 37.2 (*C*H$_2$), 28.8 ((*C*H$_3$)$_3$C), 27.4 (*C*H$_{3Aib}$), 26.9 (*C*H$_{3Aib}$), 26.5 (*C*H$_{3Aib}$), 24.4 (*C*H$_{3Aib}$), 24.2 (*C*H$_{3Aib}$), 23.4 (*C*H$_{3Aib}$), 23.3 (*C*H$_{3Aib}$), 23.3 (*C*H$_{3Aib}$). Analytical data agree with those reported in literature.

3.1.11. Aib(L-Ala)NHtBu, Peptide 4



To a solution of N_3Aib(L-Ala)NH^{t}Bu (150 mg, 0.588 mmol) in ethanol (5 mL) was added palladium on carbon (10% w/w), the flask was placed under nitrogen atmosphere then under hydrogen atmosphere (vacuum/gas cycle) and stirred at 20 °C for 24 h. At completion of the reaction (monitored by thin layer chromatography, $KMnO_4$ stain) the mixture was filtered through Celite® pad, concentrated and the residue was purified by chromatography on silica (eluent petroleum spirit ethyl acetate 7:3) to afford the product as an oil (135 mg, quantitative). **^{1}H NMR** (400 MHz, CD_3OD) δ 4.29 (q, *J* = 7.1 Hz, 1H, C*H*CH$_3$), 1.65 (s, 3H, C*H*$_3$C$_{Aib}$), 1.63 (s, 3H, C*H*$_3$C$_{Aib}$), 1.35 (d, *J* = 7.2 Hz, 3H, C*H*$_3$CH$_{Ala}$), 1.31 (s, 9H, (C*H*$_3$)$_3$C). **^{13}C NMR** (101 MHz, CD_3OD) δ 173.9 (*C*=O$_{Ala}$), 172.8 (*C*=O$_{Aib}$), 58.2 (*C*(CH$_3$)$_{2Aib}$), 52.0 (*C*(CH$_3$)$_3$), 51.3 (*C*H$_{Ala}$), 28.9 ((*C*H$_3$)$_3$C), 24.2 (*C*H$_3$C$_{Aib}$), 24.1 (*C*H$_3$C$_{Aib}$), 18.2 (*C*H$_{3Ala}$). **HR – MS** (ESI, positive ion mode) – m/z for $[C_{11}H_{23}O_2N_3Na]^+$ 252.1682, found 252.1671.

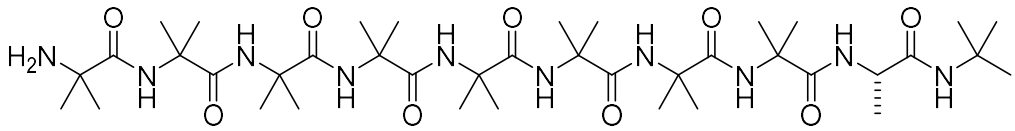
3.1.12. N_3Aib_8(L-Ala)NH^{t}Bu, Peptide 7



N_3Aib$_4$OH (174 mg, 0.45 mmol) and EDC•HCl (129.7 mg, 0.67 mmol) were dissolved in dry CH_2Cl_2 (7 mL/mmol) and the solution was stirred for 4 hours at room temperature. The organic phase was washed with saturated $NaHCO_3$ (2 ×10 mL) and brine (10 mL), then dried over $MgSO_4$, filtered and concentrated

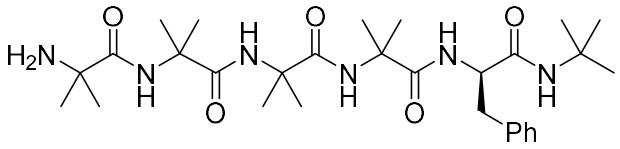
under reduced pressure to yield white crystalline crude azlactone (150 mg). Azlactone (150 mg) and Aib_4(L-Ala)NH^{t}Bu **1** (119 mg, 0.24 mmol) were dissolved in acetonitrile (10 ml) and the mixture was heated and reflux at 82 ℃ for 7 days. The mixture was concentrated under reduced pressure, the crude product was purified by flash chromatography (SiO_2, DCM/MeOH 9:1) to obtain N_3Aib_8(L-Ala)NH^{t}Bu **7** with traces of N_3Aib_4OH. The solid was further recrystallized in acetonitrile to yield pure N_3Aib_8(L-Ala)NHtBu **7** (47 mg, 21%) as a white powder. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (t, *J* = 3.9 Hz, 2H, 2 × N*H*), 7.69 (s, 1H, N*H*), 7.66 (s, 1H, N*H*), 7.55 (s, 1H, N*H*), 7.53 (s, 1H, N*H*), 7.25 (s, 1H, N*H*), 6.93 (s, 1H, N*H*), 6.70 (s, 1H, N*H*), 4.27 (p, *J* = 7.3 Hz, 1H, CH_{Ala}), 1.57 (s, 3H, CH_{3Aib}), 1.55 (s, 3H, CH_{3Aib}), 1.53 (s, 3H, CH_{3Aib}), 1.50 (m, 9H, 3 × CH_{3Aib}), 1.45 (m, 30H, 10 × CH_3), 1.38 (s, 12H, 4 × CH_{3Aib}). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.3 (*C*=O), 175.9 (*C*=O), 175.9 (*C*=O), 175.8 (*C*=O), 175.4 (*C*=O), 174.7 (*C*=O), 174.0 (*C*=O), 173.4 (*C*=O), 173.3 (*C*=O), 64.0 (*C*N_3), 57.1 (C_{Aib}), 57.0 (C_{Aib}), 56.9 (C_{Aib}), 56.9 (C_{Aib}), 56.8 (C_{Aib}), 56.7 (C_{Aib}), 56.7 (C_{Aib}), 51.3 (C_{tBu}), 50.5 (*C*H$_{Ala}$), 28.9 (3C, (*C*H$_3$)$_3$C), 27.6 (*C*H$_{3Aib}$), 27.1 (*C*H$_{3Aib}$), 27.1 (*C*H$_{3Aib}$), 26.9 (2C, 2 × *C*H$_{3Aib}$), 26.8 (*C*H$_{3Aib}$), 26.1 (*C*H$_{3Aib}$), 24.5 (*C*H$_{3Aib}$), 24.3 (*C*H$_{3Aib}$), 23.6 (*C*H$_{3Aib}$), 23.6 (*C*H$_{3Aib}$), 23.3 (*C*H$_{3Aib}$), 23.2 (*C*H$_{3Aib}$), 23.1 (3C, 3 × *C*H$_{3Aib}$), 17.5 (*C*H$_{3Ala}$). **HR – MS** (ESI, positive ion mode) – m/z for $[C_{39}H_{70}O_9N_{12}Na]^+$ 873.5281, found 873.5274. **MP**: 271 ℃-274 ℃.

3.1.13. (Aib)$_8$(L-Ala)NH^{t}Bu, Peptide 3



N_3Aib_8(L-Ala)NH^{t}Bu **7** (127 mg, 0.15 mmol) was dissolved in MeOH (25 mL). Pd/C (55 mg, 10%) was slowly added into the solution, degassed with nitrogen, and the mixture was stirred under H_2 atmosphere for 3 days (the consumption of starting material was monitored ^{1}H NMR). The mixture was then filtered through Celite®, which was washed thoroughly with MeOH to prevent loss of product due to solubility. The filtrate was concentrated and dried under reduced pressure to obtain the compound as white powder (121 mg, 99%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (s, 1H, N*H*), 7.86 (s, 1H, N*H*), 7.72 (m, 2H, 2 × N*H*), 7.65 (m, 2H, 2 × N*H*), 7.53 (s, 1H, N*H*), 6.89 (s, 1H, N*H*), 6.42 (s, 1H, N*H*), 4.28 (p, *J* = 7.4 Hz, 1H, CH_{Ala}), 1.60 – 1.33 (m, 60H). **^{1}H NMR** (500 MHz, DMSO) δ 9.54 (s, 1H, N*H*), 8.00 (m, 2H, 2 × N*H*), 7.79 (m, 3H, 3 × N*H*), 7.65 – 7.28 (m, 2H, NH_{Ala}, N*H*), 6.82 (s, 1H, N*H*), 4.09 (s, 2H, NH_2), 4.02 – 3.86 (m, 1H, C*H*CH$_3$), 1.66 – 0.91 (m, 60H, 20 × CH_3). **^{13}C NMR** (126 MHz, DMSO) δ 178.1 (*C*=O), 176.3 (*C*=O), 175.8 (*C*=O), 175.6 (*C*=O), 175.6 (*C*=O), 174.8 (*C*=O), 173.8 (*C*=O), 171.7 (*C*=O), 161.3 (*C*=O$_{Ala}$), 56.5 – 55.0 (9C, C_{tBu}, 8 × *C*(CH$_3$)$_{2Aib}$), 49.6 (*C*H$_{Ala}$), 28.5 (3C, (*C*H$_3$)$_3$C), 26.8 (*C*H$_3$), 26.2 – 25.2 (7C, 7 × *C*H$_3$), 24.9 (*C*H$_3$), 23.8-23.0 (7C, 7 × *C*H$_3$), 17.2 (*C*H$_{3Ala}$). **HR – MS** (ESI, positive ion mode) – m/z for $[C_{39}H_{72}O_9N_{10}Na]^+$ 847.5376, found 847.5381. **MP**: 279 - 287 ℃.

3.1.14. (Aib)$_4$(D-Phe)NH^{t}Bu, Peptide 5



This compound was prepared following a procedure from Diemer *et al*.[5] To a solution of H_2NAib$_4$(D-Phe)NH^{t}Bu (0.312 g, 0.53 mmol) in ethanol (30 mL) degassed with nitrogen was added palladium on carbon then the mixture was placed under hydrogen atmosphere (vacuum/hydrogen cycle) and stirred vigorously at 20 °C for 16 h. At the completion of the reaction (monitored by TLC, eluent dichloromethane methanol 9:1) the mixture was placed in nitrogen atmosphere (vacuum/nitrogen cycle) then filtered through a Celite® plug, the Celite® was further rinsed with methanol and the organic layer was concentrated under vacuum to yield the product as a pale yellow solid (282 mg, 0.5 mmol, 95%). **^{1}H NMR** (400 MHz, CD_3OD_SPE) δ 7.82 (d, *J* = 8.1 Hz, 1H, N*H*$_{Phe}$), 7.50 (s, 1H, N*H*), 7.30 (s, 1H, N*H*), 7.26 (d, *J* = 7.0 Hz, 2H, 2 × C*H*$_{Ph}$), 7.17 (t, *J* = 7.4 Hz, 2H, 2 × C*H*$_{Ph}$), 7.10 (t, *J* = 7.2 Hz, 1H, C*H*$_{Ph}$), 4.36 (ddd, *J* = 11.6, 8.0, 3.8 Hz, 1H, C*H*$_{Phe}$), 3.38 – 3.32 (m, 1H, C*H*$_{2Phe}$), 2.91 (dd, *J* = 14.4, 11.2 Hz, 1H, C*H*$_{2Phe}$), 1.63 (s, 3H, C*H*$_{3Aib}$), 1.57 (s, 3H, C*H*$_{3Aib}$), 1.47 (s, 3H, C*H*$_{3Aib}$), 1.45 (s, 3H, C*H*$_{3Aib}$), 1.43 (s, 3H, C*H*$_{3Aib}$), 1.40 (s, 3H, C*H*$_{3Aib}$), 1.37 (s, 3H, C*H*$_{3Aib}$), 1.34 (s, 9H, (C*H*$_3$)$_3$C), 1.21 (s, 3H, C*H*$_{3Aib}$). **^{13}C NMR** (126 MHz, DMSO) δ 177.7 (*C*=O), 176.3 (*C*=O), 176.2 (*C*=O), 173.9 (*C*=O), 173.2 (*C*=O), 139.6 (*C*), 129.9 (2 × *C*H$_{Ph}$), 129.2 (2 × *C*H$_{Ph}$), 127.4 (*C*H$_{Ph}$), 58.4 (*C*$_{Aib}$), 58.1 (*C*$_{Aib}$), 58.0 (*C*$_{Aib}$), 57.8 (*C*$_{Aib}$), 57.4 (*C*H$_{Phe}$), 52.6 (*C*(CH$_3$)$_3$), 38.0 (*C*H$_2$Ph), 29.0 (3C, (*C*H$_3$)$_3$C), 27.1 (*C*H$_{3Aib}$), 26.7 (*C*H$_{3Aib}$), 26.1 (*C*H$_{3Aib}$), 24.5 (*C*H$_{3Aib}$), 24.4 (*C*H$_{3Aib}$), 24.1 (*C*H$_{3Aib}$), 24.1 (*C*H$_{3Aib}$), 23.7 (*C*H$_{3Aib}$). **HR – MS** (ESI, positive ion mode) – m/z for $[C_{29}H_{48}N_6O_5Na]^+$ 583.3578, found 583.3586. **HRMS** (ESI negative ion mode) – m/z for $[C_{29}H_{47}N_6O_5]^-$ 559.3613, found: 559.3641. **MP** 178-181 °C.

3.2. Procedures for catalysed conjugate additions, listed by product.

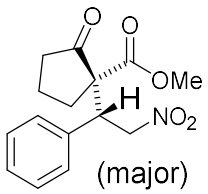
General procedure: In a dry NMR tube, the Michael acceptor (0.077 mmol, 1 equivalent), the nucleophile (3.5 equivalents), and the catalyst (0.0156 mmol, 20 mol%) were dissolved (when appropriate) in $CDCl_3$ pre-dried over K_2CO_3 (0.5 mL). The NMR tube was sealed and shaken, then was stored at the appropriate temperature and reaction time. ^{1}H NMR spectra were recorded over time to monitor the conversion of reaction. On completion of the reaction, the solvent was removed under reduced pressure, the residue was purified by chromatography on silica to afford the product. Diastereoselectivities were determined by ^{1}H NMR spectroscopy, the enantiomeric excesses were determined by HPLC using chiral columns. Where no solvent was used for the reaction, the reaction NMR tube was stored at 0 °C for 6 days without solvent then $CDCl_3$ was added for NMR analysis.

3.2.1. 1-Methyl-1-(2-nitro-1-phenylethyl)-2 -oxocyclopentane-1-carboxylate, 10

Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), 1-methyl-2-oxocyclopentanecarboxylate **9** (0.032 mL, 0.273 mmol, 3.5 equiv.), and the catalyst (either Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), Aib(L-Ala)NH^{t}Bu **4** (3 mg, 0.0156 mmol, 0.2 equiv.), Aib_4(D-Phe)NH^{t}Bu **5** (8.7 mg, 0.0156 mmol, 0.2 equiv.), Aib_8(L-Ala)NH^{t}Bu **3** (13 mg, 0.0156 mmol, 0.2 equiv.) or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)), to afford a colourless liquid after chromatography on silica (eluent: petroleum ether: ethyl acetate 9:1). NMR spectroscopic data are consistent with the reported data in the literature.[6] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.19 (m, 3H, 3 × C*H*$_{Ph}$), 7.19 – 7.15 (m, 2H, 2 × C*H*$_{Ph}$), 5.27 – 5.14 (m, 0.02H, C*H*$_{2\ dia2}$), 5.10 (dd, *J* = 13.7, 3.9 Hz, 2H, C*H*$_{2\ dia1}$), 4.94 (dd, *J* = 13.7, 10.9 Hz, 0.96H, CH$_{dia1}$), 4.76 (dd, *J* = 13.5, 3.6 Hz, 0.03 H, C*H*$_{dia2}$), 4.13 (dd, *J* = 11.1, 3.6 Hz, 0.04H, C*H*$_{dia2}$), 4.01 (dd, *J* = 11.0, 3.9 Hz, 0.96H, C*H*$_{dia1}$), 3.67 (s, OC*H*$_3$), 1.52 (d, *J* = 2.6 Hz, 2H), 1.52 – 1.38 (m, 4H). **LRMS** (ESI, positive ion mode) – m/z for $[M+K]^+$ 314.3.

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu **1**, $CDCl_3$ (0.5 mL), 20 °C: 21 mg (0.076 mmol, 98%).



(major)

Diastereomeric ratio (determined by integration of ^{1}H NMR signals): 96:4.

Diastereomeric ratio (determined by integration of chiral HPLC peaks): 92:8.

HPLC Chiralcel OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 9.064 mins (2S, 3S), t_{minor} = 12.85 mins (2R, 3R), *e.e.* = 54%; major diastereomer: t_{major} = 10.39 mins (2R, 3S), t_{minor} (2S, 3R) = 15.35 mins, *e.e.*= 58%. Analytical HPLC retention times are consistent with previously reported values.[7] The relative configuration of the product was assigned to be 2R, 3S by comparison with literature HPLC data.[8]

- With Aib_4(L-Ala)NH^{t}Bu **1**, $CDCl_3$ (0.5 mL), 40 °C: 20 mg (0.074 mmol, 94%).

Diastereomeric ratio (determined by integration of ^{1}H NMR signals): 91:9.

HPLC Chiralcel OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 9.064 mins (2S, 3S), t_{minor} = 12.85 mins (2R, 3R), *e.e.* = 9%; major diastereomer: t_{major} = 10.39 mins (2R, 3S), t_{minor} (2S, 3R) = 15.35 mins, *e.e.*= 23%. The relative configuration of the product was assigned to be 2R, 3S by comparison with literature HPLC data.[8]

- With $^{t}BuNH_2$, $CDCl_3$ (0.5 mL), 20 °C: 20 mg (0.073 mmol, 88%).

Diastereomeric ratio (determined by integration of ^1H NMR signals): 68:32.

Diastereomeric ratio (determined by integration of chiral HPLC peaks): 68:32.

HPLC OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t= 9.035 mins (2S, 3S), t= 12.973 mins (2R, 3R); major diastereomer: t = 10.579 mins (2S, 3R), t = 15.629 mins (2R, 3S). The relative configuration of the product was assigned by comparison with literature HPLC data.[8]

- With Aib_4(L-Ala)NH*t*Bu **1**, no solvent, 0 °C: 20 mg (0.073 mmol, 93%).

Diastereomeric ratio (determined by integration of ^1H NMR signals): 90:10.

HPLC OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 8.026 mins (2S, 3S), t_{minor} = 11.443 mins (2R, 3R), *e.e.*= 14%; major diastereomer: t_{major} = 9.275 mins (2R, 3S), t_{minor} = 12.41 mins (2S, 3R), *e.e.* = 69%; The relative configuration of the product was assigned to be 2R, 3S by comparison with literature HPLC data.[8]

- With Aib_4(D-Phe)NH*t*Bu **5**, $CDCl_3$ (0.5 mL), 25 °C: 19 mg (0.072 mmol, 94%).

Diastereomeric ratio (determined by integration of ^1H NMR signals): 90:10.

HPLC OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{minor} = 9.3 mins (2R, 3S), t_{major} = 13.724 mins (2S, 3R), *e.e.* = 42%; minor diastereomer: t_{minorr} = 8.195 mins (2S, 3S), t_{major} = 10.83 mins (2R, 3R), *e.e.* = 1%. The relative configuration of the product was assigned to be (2S, 3R) by comparison with literature HPLC data.[8]

Time course of evolution of enantiomeric excess over reaction time (the product had limited solubility in the HPLC eluent, which led to *d.r.* measurements by HPLC differing from the *d.r.* values measured by ^1H NMR (diastereomers totally soluble in $CDCl_3$)), OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm;

Day 1: major diastereoisomer *e.e.*: 54%, minor diastereomer *e.e.* not readable. (*d.r.* 96:4 determined by ^1H NMR integration of signals at 4.06 ppm amd 4.18 ppm).

Day 2: major diastereoisomer *e.e.*: 57%, minor diastereoisomer *e.e.*: 12% (*d.r.* 92:8).

Day 3: major diastereoisomer *e.e.*: 59%, minor diastereoisomer *e.e.*: 11% (*d.r.* 90:10).

Day 5: major diastereoisomer *e.e.*: 60%, minor diastereoisomer *e.e.*: 13% (*d.r.* 90:10).

- With H_2N^tBu, no solvent, 0 °C: 18 mg (0.064 mmol, 83%).

Diastereomeric ratio (determined by integration of ^1H NMR signals): 59:41.

- With Aib(L-Ala)NH^tBu **4**, no solvent, 0 °C: 19 mg (0.069 mmol, 88%).

Diastereomeric ratio (determined by integration of ^1H NMR signals): 82:18.

HPLC OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 10.439 mins (2S 3R), t_{minor} = 14.667 mins (2R 3S), *e.e.* = 0%; major diastereomer: t_{major} = 8.845 mins (2S, 3S), t_{minor} = 13.395 mins (2R, 3R), *e.e.* = 1%.

- With Aib_8(L-Ala)NH^tBu **3**, $CDCl_3$, 20 °C: 20 mg (0.073 mmol, 93%).

Diastereomeric ratio (determined by integration of ^1H NMR signals): 88:12.

HPLC OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 8.34 min (2S, 3R), t_{minor} = 11.9 mins ((2R, 3S), *e.e.* = 19%; major diastereomer: t_{major} = 9.67 min (2S, 3S), t_{minor} = 13.04 mins (2R, 3R), *e.e.*= 5%.

- With Aib_5NH^tBu **2** at 20 °C in $CDCl_3$: 21 mg (0.074 mmol, 83%).

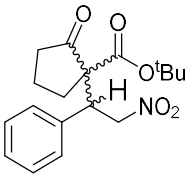
Diastereomeric ratio (determined by integration of ^1H NMR signals): 95:5.

3.2.2. 1-*tert*-Butyl-1-(2-nitro-1-phenylethyl)-2 -oxocyclopentane-1-carboxylate, 13a

Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), 1-ter-butyl-2-oxocyclopentanecarboxylate **13** (0.05 mL, 0.273 mmol, 3.5 equiv.), and the catalyst (either Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.) or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)) to afford a colourless liquid after chromatography on silica (eluent: petroleum ether: ethyl acetate 9:1). NMR spectroscopic data are consistent with the reported data in the literature.[9]

Catalysts, reaction conditions, yields:

- With H_2N^tBu, $CDCl_3$ (0.5 mL), 20 °C: 11 mg (0.031 mmol, 43%).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.19 (m, 5H, 5 x CH_{Ph}), 5.32 (dd, *J* = 13.4, 11.2 Hz, 0.13 H, CH_{dia1}), 5.16 (dd, *J* = 13.4, 3.8 Hz, 0.87 H, CH_{dia2}), 4.97 (dd, *J* = 13.4, 11.2 Hz, 0.87 H, CH_{dia2}), 4.83 dd, *J* = 13.4, 3.3 Hz, 0.13 H, CH_{dia1}), 4.13 (dd, *J* = 11.1, 3.3 Hz, 0.13 H, CH_{dia1}), 4.03 (dd, *J* = 11.1, 3.7 Hz, 0.87 H, CH_{dia2}), 2.40-2.21 (m, 2H), 2.02 – 1.74 (m, 4H), 1.46 (s, 1.17H, (CH_3)$_3$C$_{dia1}$), 1.44 (s, 7.83H, (CH_3)$_3$C$_{dia2}$).

Diastereomeric ratio (determined by integration of ^{1}H NMR signals): 87:13.

HPLC Chiralcel OD-H column, hexane/*i*-PrOH (97/3), flow rate 0.5 mL/min, 220 nm; minor diastereomer: t = 17.4 mins, t = 19.4 mins, major diastereomer: t = 22.3 mins, t = 23.9 mins. The same mixture of major diastereomers have been reported,[10] conditions to afford the opposite mixture of major diastereoisomers were also reported.[9]

- With Aib_4(L-Ala)NH^{t}Bu **1**, $CDCl_3$ (0.5 mL), 20 °C 13 mg (0.039 mmol, 50%).

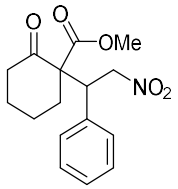
Diastereomeric ratio (determined by integration of ^{1}H NMR signals): 78:22.

HPLC Chiralcel OD-H column, hexane/*i*-PrOH (97/3), flow rate 0.5 mL/min, 220 nm; minor diastereomer: t_{minor} = 17.4 mins, t_{major} = 19.4 mins. ee = 5%, major diastereomer: t_{minor} = 22.3 mins, t_{major} = 23.9 mins, ee = 17%.

- With Aib_4(L-Ala)NH^{t}Bu **1**, no solvent, 0 °C.

Diatereomeric ratio (determined by integration of ^{1}H NMR signals): 80:20. **HPLC** Chiralcel OD-H column, hexane/*i*-PrOH (97/3), flow rate 0.5 mL/min, 220 nm; minor diastereomer: t_{minor} = 17.4 mins, t_{major} = 19.4 mins, e.e. = 2%, major diastereomer: t_{minor} = 22.3 mins, t_{major} = 23.9 mins, e.e. = 27%.

3.2.3. (−)-Methyl (S)-1-((R)-2-nitro-1-phenylethyl)-2-oxocyclohexane-1-carboxylate, 15a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), 1-methyl-2-oxocyclohexanecarboxylate **15** (0.035 mL, 0.273 mmol, 3.5 equiv.), and the catalyst (either Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent petroleum ether: ethyl acetate 9:1) provided the compound as a colourless oil. NMR spectroscopic data are consistent with the reported data in the literature.[11]

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, $CDCl_3$ (0.5 mL), 20 °C: 20 mg (0.062 mmol, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.21 (m, 3H), 7.12-7.07 (m, 2H), 5.09 (dd, *J* = 13.1, 10.7 Hz, 0.08H, CH_{dia1}), 5.03 (dd, *J* = 13.4, 3.4 Hz, 0.92H, CH_{dia2}), 4.76 (dd, *J* = 13.4, 11.3 Hz, 1H, C*H*), 4.09 (dd, *J* = 10.7, 3.1 Hz, 0.08H, CH_{dia1}), 3.98 (dd, *J* = 11.3, 3.2 Hz, 0.92H, CH_{dia2}), 3.72 (s, 2.88H, C$H_{3\ dia2}$), 3.66 (s, 0.12H, C$H_{3\ dia1}$), 2.57-2.39 (m, 2H), 2.14-1.98 (m, 2H), 1.77-1.45 (m, 4H) ppm. **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 343.2.

Diastereomeric ratio 92:8 (determined by ^{1}H NMR integration of dd signals at 4.98 ppm and 5.05 ppm). The relative configuration was assigned by comparison with literature data.[12]

HPLC Chiralpak IC column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 17.1 mins (1S, 2R), t_{minor} = 19.7 mins (1R, 2S), *e.e.* = 16%; minor diastereomer: t_{major} = 15.7 mins, t_{minor} = 22.3 mins ee = 5%.

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 21.3 mg (0.067 mmol, 85%).

Diastereomeric ratio 83:17 (determined by ^{1}H NMR integration of dd signals at 4.98 ppm and 5.05 ppm, and dd at 3.93 ppm and 4.09 ppm).

HPLC Chiralpak IC column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t = 17.1 mins (1S, 2R), t = 19.6 mins (1R, 2S); minor diastereomer: t = 15.7 mins, t = 22.4 mins.

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, no solvent, 0 °C: 21 mg (0.065 mmol, 84%)

Diastereomeric ratio 94:6 (determined by integration of ^{1}H NMR dd signals at 4.98 ppm and 5.05 ppm, and dd at 3.93 ppm and 4.09 ppm).

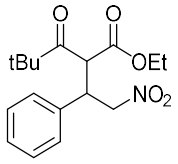
HPLC Chiralpak IC column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 18.7 mins (1S, 2R), t_{minor} = 22.1 mins (1R, 2S), *e.e.*= 17%; minor diastereomer: t_{major} = 17.2 mins, t_{minor} = 25.6 mins, *e.e.*= 16%.

- With $^{t}BuNH_2$ catalyst, no solvent, 0 °C.

Diastereomeric ratio 91:9 (termined by integration of ^{1}H NMR dd signals at 4.98 ppm and 5.05 ppm, and dd at 3.93 ppm and 4.09 ppm).

HPLC Chiralpak IC column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t = 17.1 mins, t = 19.6 mins; minor diastereomer: t = 15.7 mins, t = 22.4 mins.

3.2.4. Ethyl 4,4-dimethyl-2-(2-nitro-1-phenylethyl)-3-oxopentanoate, 20a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), ethyl pivaloylacetate **20** (0.048 mL, 0.273 mmol), and the catalyst (either Aib_4-(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent petroleum ether: ethyl acetate 9:1) provided the compound as a white solid that degrades over time.

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, $CDCl_3$ (0.5 mL), 20 °C: 21 mg (0.065 mmol, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.18 (m, 3H, 3 x C*H*$_{Ph}$), , 7.18 – 7.12 (m, 2H, 2 x C*H*$_{Ph}$), 4.87 – 4.72 (dd, *J* = 13.0, 4.2 Hz, 1.87H, C*H*$_2$NO$_{2\ dia2\ maj}$), 4.59 (dd, *J* = 13.0, 4.2 Hz, 0.12H, C*H*$_2$NO$_{2\ dia1}$), 4.30-4.19 (m, 2H, 2 x C*H*), 4.29 – 4.05 (m, 1.81H, C*H*$_2$CH$_{3\ dia2\ maj}$), 3.87 (d, *J* = 7.1 Hz, 0.2H, C*H*$_2$CH$_{3\ dia1}$), 1.20 (t, 3H, *J* = 7.1 Hz, C*H*$_3$), 0.83 (s, 9H, (C*H*$_3$)$_3$C). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.6 (*C*=O $_{dia1\ min}$), 207.2 (*C*=O $_{dia2\ maj}$), 167.5 (*C*O$_2$Et $_{dia2}$), 167.2 (*C*O$_2$Et $_{dia1}$), 137.1 (*C*$_{Ph\ dia2}$), 136.3 (*C*$_{Ph\ dia1}$), 129.0 (2C, 2 x *C*H$_{Ph\ dia2}$), 129.0 (2C, 2 x *C*H$_{Ph\ dia1}$), 128.4 (2C, 2 x *C*H$_{Ph}$), 128.36 (*C*H$_{Phpara}$), 77.3 (*C*H$_2$NO$_2$), 62.2 (*C*H$_2$CH$_{3\ dia2}$), 62.0 (*C*H$_2$ CH$_{3\ dia1}$), 56.4 (*C*H $_{dia1}$), 56.3 (*C*H $_{dia2}$), 45.8 (*C*(CH$_3$)$_{3\ dia1}$), 45.6 (*C*(CH$_3$)$_{3\ dia2}$), 44.0 (*C*H $_{dia1}$), 43.7 (*C*H $_{dia2}$), 26.3 (3C, (CH$_3$)$_3$C $_{dia1}$), 26.0 ((CH$_3$)$_3$C $_{dia2}$), 14.1 (*C*H$_{3\ dia2}$), 13.8 (*C*H$_{3\ dia1}$). **LR-MS** (ESI, positive ion mode) – m/z for [M + Na]$^+$ found at 344.2. **HRMS** (ESI) $C_{17}H_{23}NO_5$+Na$^+$ calculated 344.1468, measured 344.1486.

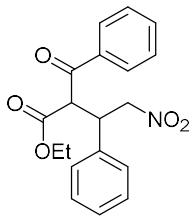
Diastereomeric ratio 95:5 (determined by integration of ^{1}H NMR signals at 4.85 ppm and 4.59 ppm, 4.29 ppm and 3.87 ppm on the mixture of diastereomers purified by chromatography, as overlap of signals with remaining starting material was observed before chromatography).

HPLC Chiralcel AD-H column, hexane/i-PrOH (98:2), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 26.2 mins, t_{minor} = 31.1 mins, *e.e.*= 46%; minor diastereomer: t_{major} = 23.6 mins, t_{minor} = 36.2 mins.

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 14 mg (0.044 mmol, 56%).

Diastereomeric ratio 91:9 (determined by integration of ^{1}H NMR signals at 4.85 ppm and 4.59 ppm, 4.29 ppm and 3.87 ppm, after chromatography (overlap of signals with remaining starting material before chromatography)).

3.2.5. Ethyl 2-benzoyl-4-nitro-3-phenylbutanoate, 21a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), ethyl 3-oxo-3-phenylpropionate **21** (0.048 mL, 0.273 mmol), and the catalyst (either Aib$_4$-(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent petroleum ether: ethyl acetate 9:1) provided the compound as a white solid. NMR spectroscopic data are consistent with the reported data in the literature.[11]

Catalysts, reaction conditions, yields:

- With Aib$_4$(L-Ala)NH^{t}Bu catalyst **1**, $CDCl_3$ (0.5 mL), 20 °C: 25 mg (0.073 mmol, 94%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 - 7.91 (m, 2H, CH_{Ph}), 7.59 – 7.49 (m, 3H), 7.48 – 7.35 (m, 5H), 4.99 – 4.87 (m, 1.7H, C$H_{2\ dia1}$, C$H_{\ dia1}$), 4.82 – 4.71 (m, 1.28H, C$H_{2\ dia2}$, C$H_{\ dia2}$), 4.52 – 4.39 (m, 1H, C$H_{\ dia}$), 4.18 (q, J=7.1 Hz, 0.8H, OCH$_{2\ dia2}$), 3.83 (q, *J* = 7.1 Hz, 1..2H, OCH$_{2\ dia1}$), 1.13 (t, *J* = 7.1 Hz, 1.35H, CH$_{3\ dia2}$), 0.85 (t, *J* = 7.1 Hz, 1.65 H, CH$_{3\ dia1}$). **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 364.5.

Diastereomeric ratio: 55:45 (determined by integration of ^{1}H NMR signals at 1.13 ppm and 0.85 ppm).

HPLC Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 17.9 mins, t_{minor} = 31.0 mins, *e.e.*= 8%; minor diastereomer: t_{major} = 13.2 mins, t_{minor} = 15.9 mins, *e.e.* = 9%.

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 26 mg (0.078 mmol, 100%).

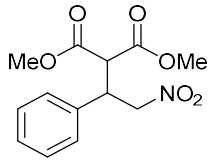
Diastereomeric ratio: 1:1 (determined by integration of ^{1}H NMR signals at 1.13 ppm and 0.85 ppm).

HPLC Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t = 17.8 mins, t = 30.9 mins; minor diastereomer: t = 13.2 mins, t = 15.6 mins.

- With no catalyst, $CDCl_3$ (0.5 mL), 20 °C: 1.3 mg (0.004 mmol, 5%).

Diastereomeric ratio: 58:42 (determined by integration of ^{1}H NMR signals at 1.13 ppm and 0.85 ppm).

3.2.6. Dimethyl 2-(2-nitro-1-phenylethyl)malonate, 17a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), dimethyl malonate **17** (0.033 mL, 0.273 mmol, 3.5 equiv.), and the catalyst (either Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent petroleum ether: ethyl acetate 9:1) provided the compound as a colourless liquid. NMR spectroscopic data are consistent with those reported in literature.[12]

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, $CDCl_3$ (0.5 mL), 20 °C: 20 mg (0.071 mmol, 91%).

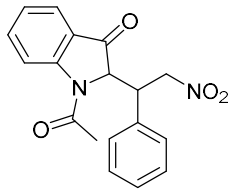
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35– 7.26 (m, 3H, 3 x C*H*$_{Ph}$), 7.24-7.20 (m, 2H, 2 x C*H*$_{Ph}$), 4.95 – 4.84 (m, 2H, C*H*$_2$NO$_2$), 4.24 (td, *J* = 8.9, 5.3 Hz, 1H, C*H*), 3.86 (d, *J* = 9.1 Hz, 1H, C*H*), 3.75 (s, 3H, OC*H*$_3$), 3.55 (s, 3H, OC*H*$_3$). **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 304.3.

HPLC Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; t_{major} = 15.7 min, t_{minor} = 24.5 min, *e.e.*= 0%.

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 19 mg (0.067 mmol, 86%).

HPLC Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; t = 15.7 min, t = 24.6 min.

3.2.7. 1-Acetyl-2-(2-nitro-1-phenylethyl)indolin-3-one, 16a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), 1-acetylindolin-3-one **16** (48 mg, 0.273 mmol, 3.5 equiv.), and the catalyst (either Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent dichloromethane: ethyl acetate 8:2) provided the compound as an orange solid. NMR data are consistent with data in the literature.[13]

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, $CDCl_3$ (0.5 mL), 20 °C: 18 mg (0.055 mmol, 71%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.46 (m, 1.3H, C*H*$_{Ph}$), 7.46 – 7.38 (m, 1.3H, C*H*$_{Ph}$), 7.11-6.97 (m, 4.5H, C*H*$_{Ph}$), 6.97-6.90 (m, 1.9H, C*H*$_{Ph}$), 5.80-4.30 (m, 4H, C*H*$_2$NO$_2$, C*H*, C*H*), 2.53 (s, 2.55H, C*H*$_{20a\ dia1}$), 2.48 (s, 0.42H, C*H*$_{20a\ dia2}$). **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 347.2.

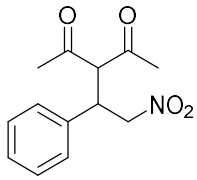
Diastereomeric ratio: 85:15 (determined by integration of ^{1}H NMR signals at 2.53 ppm and 2.48 ppm).

HPLC Chiralcel AS column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; t_{major} = 18.9 min, t_{minor} = 25.2 min, *e.e.*= 18%.

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 20 mg (0.062 mmol, 79%).

Diastereomeric ratio: 85:15 (determined by integration of ^{1}H NMR signals at 2.53 ppm and 2.48 ppm).

3.2.8 3-(2-Nitro-1-phenylethyl)pentane-2,4-dione, 18a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), acetylacetone **18** (0.028 mL, 0.273 mmol, 3.5 equiv.), and the catalyst (either Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent dichloromethane: ethyl acetate 8:2) provided the compound as a colourless liquid. Spectroscopic data is consistent with the data in the literature.[11]

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu **1** in $CDCl_3$, 20 °C: 13 mg (0.053 mmol, 67%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 3H, 3 x C*H*$_{Ph}$), 7.20 – 7.16 (m, 2H, 2 x C*H*$_{Ph}$), 4.68 – 4.58 (m, 2H, C*H*$_2$NO$_2$), 4.37 (d, *J* = 10.8 Hz, 1H, C*H*), 4.25 (dd, *J* = 6.9, 4.1 Hz, 1H,), 4.22 (dd, *J* = 6.8, 4.0 Hz, 1H, C*H*), 2.29 (s, 3H, C*H*$_3$), 1.94 (s, 3H, C*H*$_3$). **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 272.3.

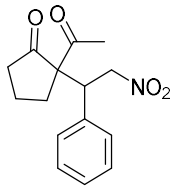
HPLC Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t_{major} = 11.2 min, t_{minor} = 15.0 min, *e.e.*= 23%. The absolute stereochemistry was assigned as (R) by comparison of the retention time of HPLC with the literature data.[14]

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 14 mg (0.064 mmol, 76%).

HPLC Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t = 6.9 min, t = 8.7 min.

- With no catalyst, $CDCl_3$ (0.5 mL), 20 °C: 5.1 mg (0.023 mmol, 28%).

3.2.9. 2-Acetyl-2-(2-nitro-1-phenylethyl)cyclopentan-1-one, 14a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), 2-acetylcyclopentanone **14** (0.033 mL, 0.273 mmol, 3.5 equiv.), the catalyst Aib_4(L-Ala)NH*t*Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent petroleum ether: ethyl acetate 8:2) provided the compound as a white solid. NMR spectroscopic data are consistent with the reported data in the literature.[15]

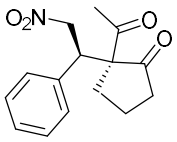
Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH*t*Bu catalyst **1**, $CDCl_3$ (0.5 mL), 20 °C: 15 mg (0.055 mmol, 70%).

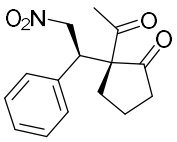
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.20 (m, 4.7H, C*H*$_{Ph}$), 7.17 – 7.13 (m, 0.3H, C*H*$_{Ph\ dia2}$), 4.99 (dd, *J* = 13.1, 11.0 Hz, 0.17H, C*H*), 4.84 (dd, *J* = 13.6, 11.5 Hz, 0.83 H, C*H*), 4.58 (dd, *J* = 13.6, 3.9 Hz, 0.17H), 4.51 (dd, *J* = 13.6, 3.9 Hz, 0.83 Hz, C*H*), 4.34 (dd, *J* = 11.5, 3.9 Hz, 0.80H, C*H*), 4.28 – 4.20 (m, 0.17H, CH), 2.61 – 2.52 (m, 0.83H, C*H*), 2.50 – 2.35 (m, 0.3H), 2.34 (s, 2.57H, Me$_{dia1}$), 2.19 (s, 0.7H, Me$_{dia2}$); 2.23 – 2.15 (m, 0.3H), 2.02 – 1.92 (m, 1H), 1.79 – 1.64 (m, 2.64H); 1.45 – 1.36 (m, 1.64H). **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 298.2.

Diastereomeric ratio 84:16 (determined by integration of ^{1}H NMR signals at 5.02 ppm (dd) and 4.86 ppm (dd), at 4.58 ppm (dd) and 4.50 (dd), 4.38 (dd) and 4.28 ppm (dd)).

HPLC Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t_{major} = 18.9 min, t_{minor} = 25.2 min, *e.e.*18%, minor diastereomer t_{major} 43.8 min, t_{minor} 60 min. The major distereoisomers have been attributed by comparison with literature data.[18]



major diastereomer



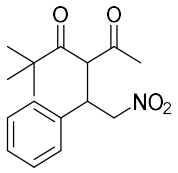
minor diastereomer

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 16 mg (0.058 mmol, 75%).

Diastereomeric ratio: 53:47 (determined by integration of ^{1}H NMR signals at 5.02 ppm (dd) and 4.86 ppm (dd), at 4.58 ppm (dd) and 4.50 (dd), 4.38 (dd) and 4.28 ppm (dd).

HPLC Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t = 19.4 min, t = 21.7 min; minor diastereomer t = 43.8 min, t = 60 min.

3.2.10. 5,5-Dimethyl-3-(2-nitro-1-phenylethyl)hexane-2,4-dione, 19a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (12 mg, 0.078 mmol, 1 equiv.), 5,5-dimethylhexane-2,4-dione **19** (0.032 mL, 0.273 mmol, 3.5 equiv.), and the catalyst Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent petroleum ether: ethyl acetate 9:1) provided the compound as a colourless liquid. NMR spectroscopic data are consistent with the reported data in the literature.[16]

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, in $CDCl_3$ at 20 °C: 18 mg (0.062 mmol, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.16 (m, 5H), 4.77 (dd, *J* = 13.3, 10.1 Hz, 0.77H, CH_{dia1}), 4.68 - 4.47 (m, 1.5 H, C*H*), 4.41 (d, *J* = 10.5 Hz, 0.75H, C*H*), 4.35 – 4.26 (m, 1H, C*H*), 2.24 (s, 2.35, Me_{dia1}), 1.91 (s, 0.65H, Me_{dia2}), 1.13 (s, 1.89H, (CH_3)$_3$C$_{dia2}$), 0.83 (s, 7.1H, (CH_3)$_3$C$_{dia1}$). **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 314.4.

Diastereomeric ratio: 79:21 (determined by integration of ^{1}H NMR signals at 2.24 ppm (s) and 1.91 ppm (s), at 1.13 ppm (s) and 0.83 ppm (s).

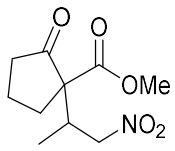
HPLC Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 9.232 mins , t_{minor} = 16.2 mins, *e.e.* = 44%; major diastereomer: t_{major} = 13.207 mins, t_{minor} = 22.302 mins, ee = 52%.

- With ^{t}BuNH$_2$ catalyst, 20 °C: 19 mg (0.065 mmol, 84%).

Diastereomeric ratio: 77:23 (determined by integration of ^{1}H NMR signals at 2.24 ppm (s) and 1.91 ppm (s), at 1.13 ppm (s) and 0.83 ppm (s).

HPLC Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t = 9.232 mins , t = 16.2 mins; major diastereomer: t = 13.207 mins, t = 22.302 mins.

3.2.11. 1-Methyl-1-(1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 12a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-1-nitropropene **12** (7 mg, 0.078 mmol, 1 equiv.), 1-methyl-2-oxocyclopentanecarboxylate **9** (0.032 mL, 0.273 mmol, 3.5 equiv.), and the catalyst Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), or ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.)). Purification on silica (eluent: petroleum ether: ethyl acetate 8:2) provided the compound as a white solid. The products tends to degrade.

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, no solvent, 0 °C: 14 mg (0.062 mmol, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.85 (dd, *J* = 12.8, 3.8 Hz, 0.84H, C*H*$_2$NO$_2$), 4.48 (dd, *J* = 12.8, 3.9 Hz, 0.16H, C*H*$_2$NO$_2$), 4.27 (dd, *J* = 12.8, 9.7 Hz, 0.85H, C*H*$_2$NO$_2$), 4.15 (dd, *J* = 12.8, 3.9 Hz, 0.15H, C*H*$_2$NO$_2$), 3.66 (s, 3H, OMe), 2.97 (C*H*CH$_3$), 2.54 – 1.73 (m, 6H, 3 x C*H*$_2$), 1.02 (d, *J* = 6.9 Hz, 0.33H, C*H*$_3$), 0.99 (d, *J* = 6.8 Hz, 2.66H, C*H*$_3$). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 212.4 (*C*=O), 169.9 (*C*=Oester), 78.2 (*C*H$_2$NO$_2$), 62.0 (*C*), 53.0 (*C*H$_3$O), 38.4 (*C*H$_2$), 35.7 (*C*H), 30.8 (*C*H$_2$), 21.1 (*C*H$_2$), 13.9 (*C*H$_3$CH). **HRMS** (ESI, positive ion mode) $C_{10}H_{15}NO_5$+Na$^+$ calculated 252.0842, measured 252.0845.

Diastereomeric ratio: 89:11 (determined by integration of ^{1}H NMR signals at 4.25 ppm and 4.09 ppm, and signals at 0.99 ppm and 1.02 ppm).

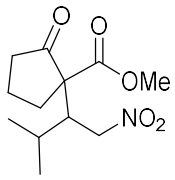
HPLC Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 10.995 mins, t_{minor} = 15.285 mins, *e.e.*= 28%; minor diastereomer: t_{major} = 11.938 mins, t_{minor} = 14.455 mins, *e.e.*= 18%.

- With ^{t}BuNH$_2$ catalyst, 0 °C, no solvent: 18 mg (0.078 mmol, 100%).

Diastereomeric ratio: 89:11 (determined by integration of ^{1}H NMR signals at 4.25 ppm and 4.09 ppm) and confirmed by integration of HPLC signals.

HPLC Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 0.7 mL/min, 220 nm; major diastereomer; t = 10.991 mins, t = 15.163 mins; minor diastereomer: t = 11.895 mins, t = 14.339 mins.

3.2.12. Methyl 1-(3-methyl-1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 11a



Following the general procedure for conjugate additions, the title compound was prepared from *(E)*-3-methyl-1-nitropropene **11** (9 mg, 0.078 mmol, 1 equiv.), 1-methyl-2-oxocyclopentanecarboxylate **9** (0.032 mL, 0.273 mmol, 3.5 equiv.), and either of the catalysts Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.), ^{t}BuNH$_2$ (0.0016 mL, 0.0156 mmol, 0.2 equiv.). Purification on silica (eluent: petroleum ether: ethyl acetate 8:2) provided the compound. Spectroscopic data is consistent with the reported data in the literature.[17] With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, $CDCl_3$, 20 °C: 16 mg (0.062 mmol, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (dd, *J* = 15.1, 4.1 Hz, 1H, CH_2NO_2), 4.44 (dd, *J* = 15.1, 6.2 Hz, 1H, CH_2NO_2), 3.64 (s, 3H, OMe), 2.48 - 1.74 (m, 8H), 0.88 (d, *J* = 7.1 Hz, 3H, CH_{3iPr}), 0.80 (d, *J* = 6.9 Hz, 3H, CH_{3iPr}). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 212.8 (*C*=O$_{dia1\ minor}$), 212.4 (*C*=O$_{dia2\ major}$), 169.9 (*C*=O$_{ester\ dia2\ major}$), 169.8 (*C*=O$_{ester\ dia1\ minor}$), 73.3 (*C*H_2NO_2), 62.3 (*C*), 52.5 (*C*H_3O), 45.4 (*C*H*C*H_2NO_2), 38.2 (*C*H_2), 32.3 (*C*H_2), 28.8 (*C*H(CH_3)$_2$), 22.6 (*C*H_3CH), 19.3 (*C*H_2), 17.9 (*C*H_3CH). **LR-MS** (ESI, positive ion mode) – m/z for $[M + Na]^+$ found at 280.2. **HRMS** (ESI, positive ion mode) $C_{12}H_{19}NO_5$+Na^+ calculated 280.1155, measured 280.1163.

Catalysts, reaction conditions, yields:

- With Aib_4(L-Ala)NH^{t}Bu catalyst **1**, $CDCl_3$ (0.5 mL), 20 °C: 16 mg (0.062 mmol, 80%).

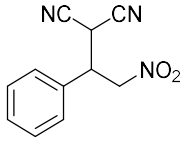
Diastereomeric ratio: 99:1 (determined by integration of ^{1}H NMR signals).

HPLC Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 10.149 mins, t_{minor} = 11.281 mins, *e.e.* = 10%; minor diastereomer: t_{major} = 10.873 mins, t_{minor} = 13.7901 mins, *e.e.*= 0%. Diastereomeric ratio by integration of HPLC signals = 98:2.

- With ^{t}BuNH$_2$ catalyst, $CDCl_3$ (0.5 mL), 20 °C: 15 mg (0.058 mmol, 75%).

Diastereomeric ratio: 98:2 (determined by integration of ^{1}H NMR signals).

3.2.13. 2-(2-Nitro-1-phenylethyl)malononitrile, 22a



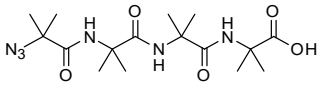
The title compound was prepared from *(E)*-(2-nitrovinyl)benzene **8** (7 mg, 0.078 mmol, 1 equiv.), malonitrile **22** (18 mg, 0.273 mmol, 3.5 equiv.), and Aib_4(L-Ala)NH^{t}Bu **1** (8 mg, 0.0156 mmol, 0.2 equiv.). Purification on silica (eluent: petroleum ether: ethyl acetate 8:2) provided the compound (16 mg, 100%) as a white solid. Spectroscopic data is consistent with the reported data in the literature.[18] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 – 7.44 (m, 3H, 3 x C*H*$_{Ph}$), 7.39-7.33 (m, 2H, 2 x C*H*$_{Ph}$), 4.99 (dd, *J* = 14.3, 8.0 Hz, 1H, C*H*$_2$NO$_2$), 4.91 (dd, *J* = 14.3, 6.2 Hz, 1H, C*H*$_2$NO$_2$), 4.43 (d, *J* = 6.0 Hz, 1H, C*H*), 4.08 (dt, *J* = 8.0, 6.1 Hz, C*H*). **HPLC** Chiralpak AD-H column, hexane/i-PrOH (90:10), flow rate 0.6 mL/min, 254 nm; Enantiomers: t_{major} = 23.2 mins, t_{minor} = 26.9 mins, ***e.e.*** = 2%.

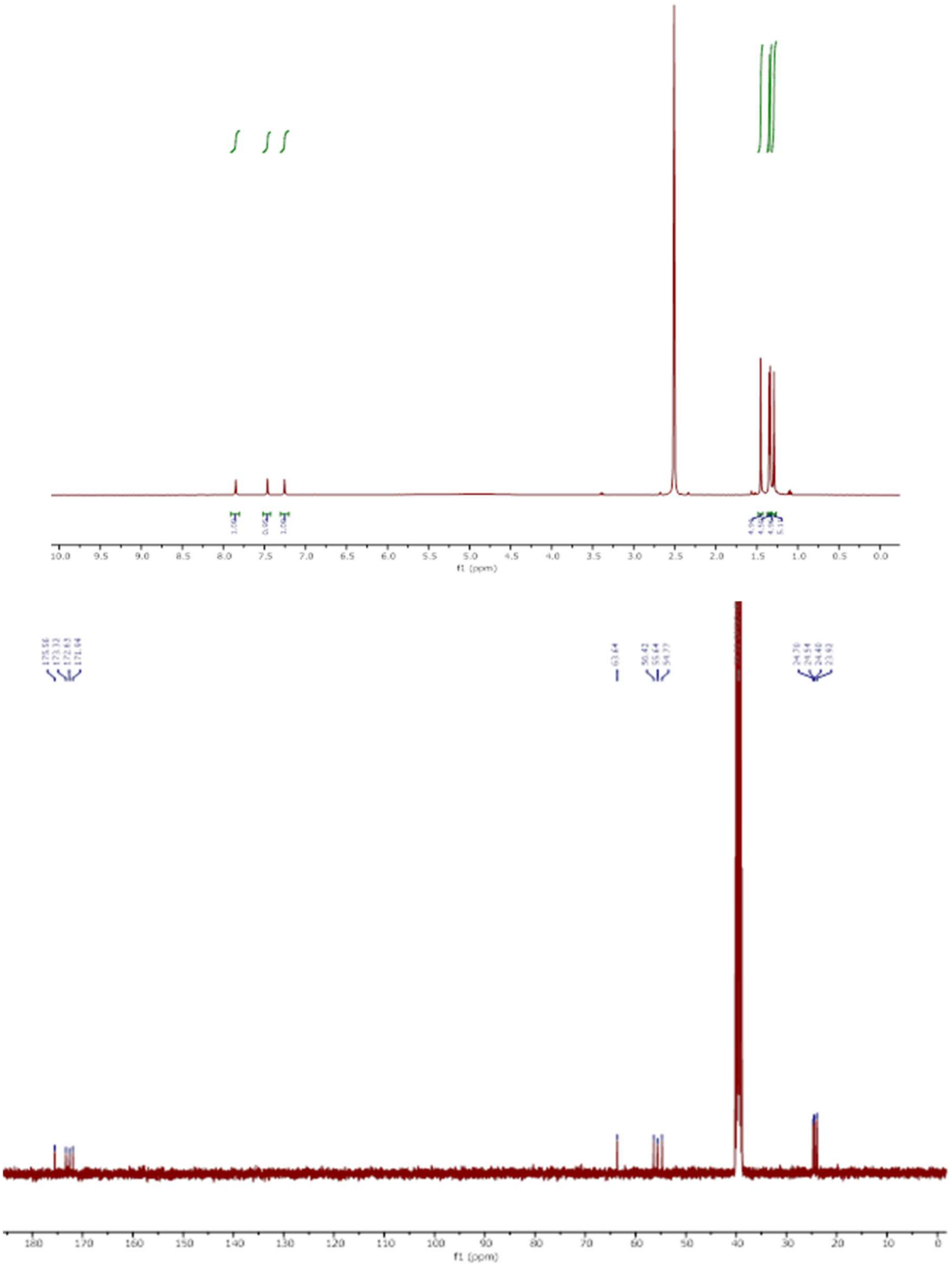
Without catalyst: a solution of *(E)*-(2-nitrovinyl)benzene **8** (7 mg, 0.078 mmol, 1 equiv.) and malonitrile **22** (18 mg, 0.273 mmol, 3.5 equiv.) in $CDCl_3$ (0.4 mL) was analysed over time by ^{1}H NMR spectroscopy, showing no conversion after 6 days at ambient temperature.

4. NMR spectra of synthesised compounds

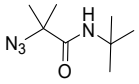
4.1. Spectra for characterisation of peptides

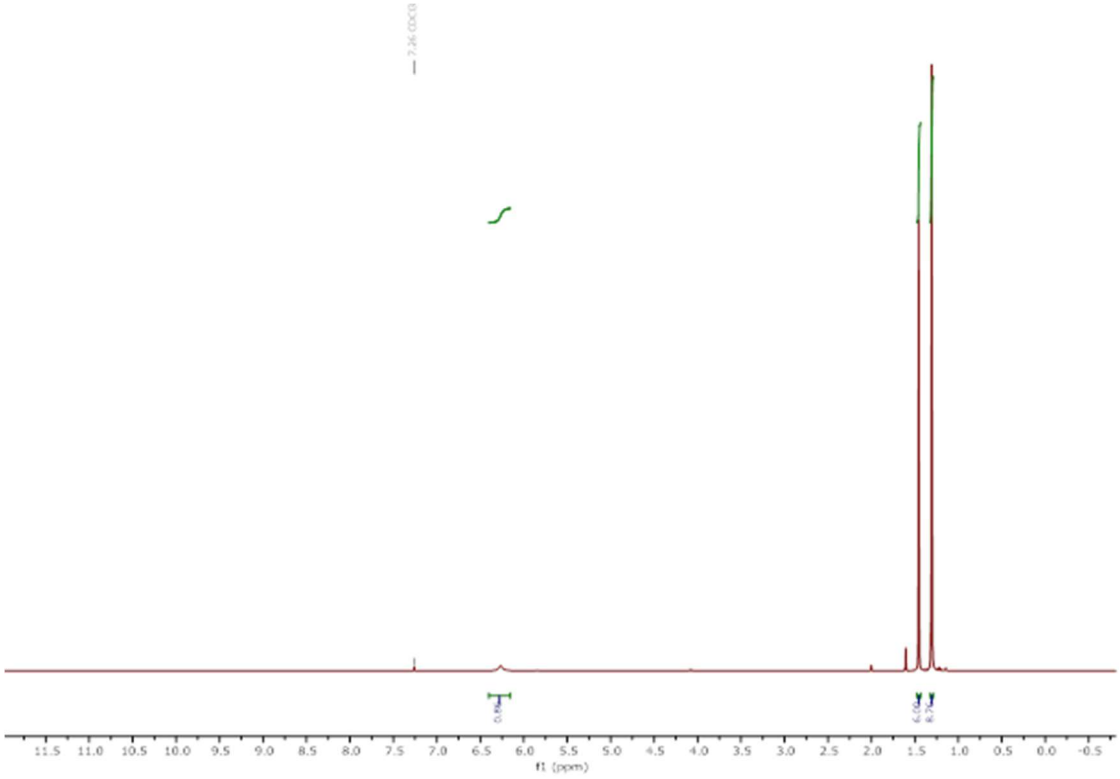
N_3Aib_4OH (in DMSO d_6)

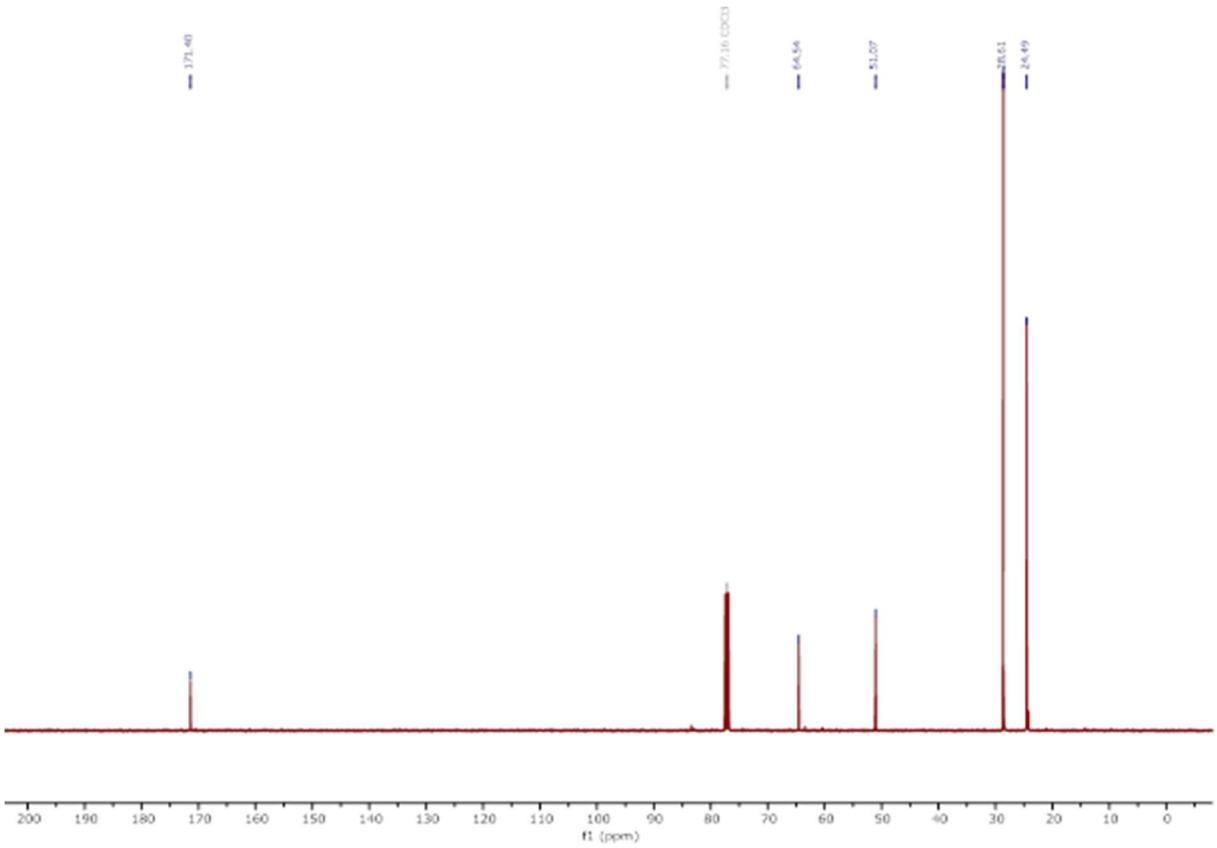




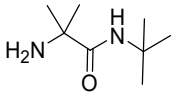
N_3AibNH^{t}Bu (in $CDCl_3$)

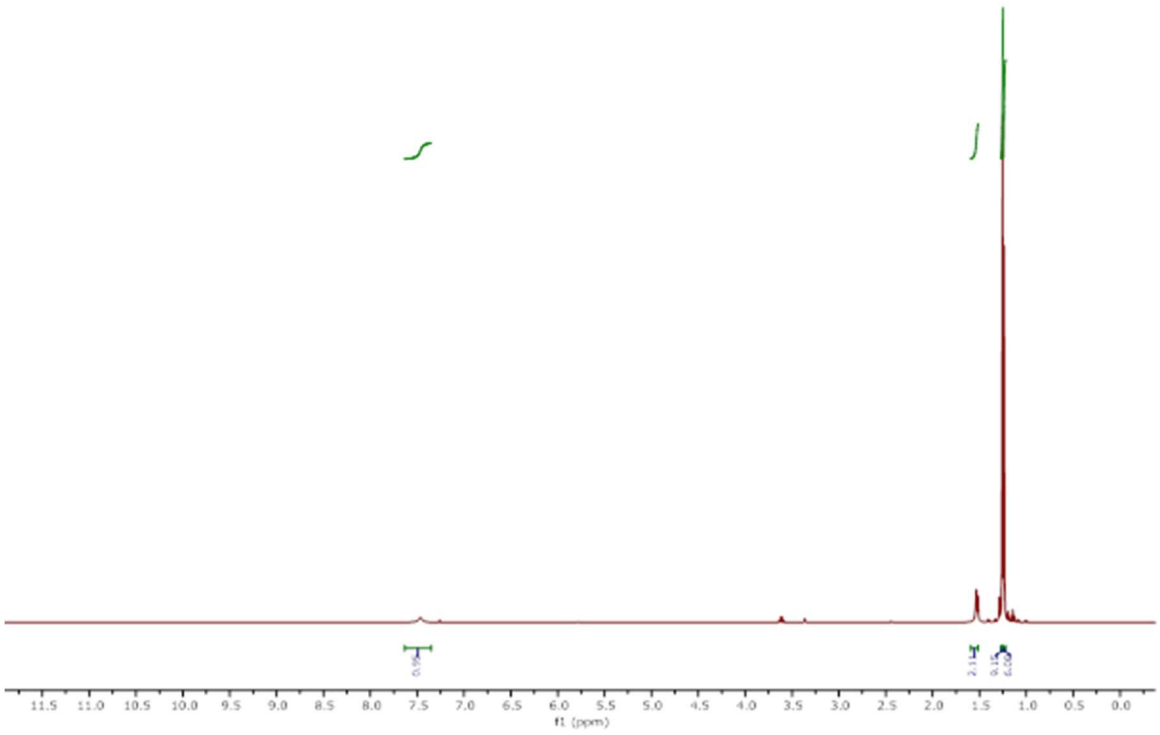


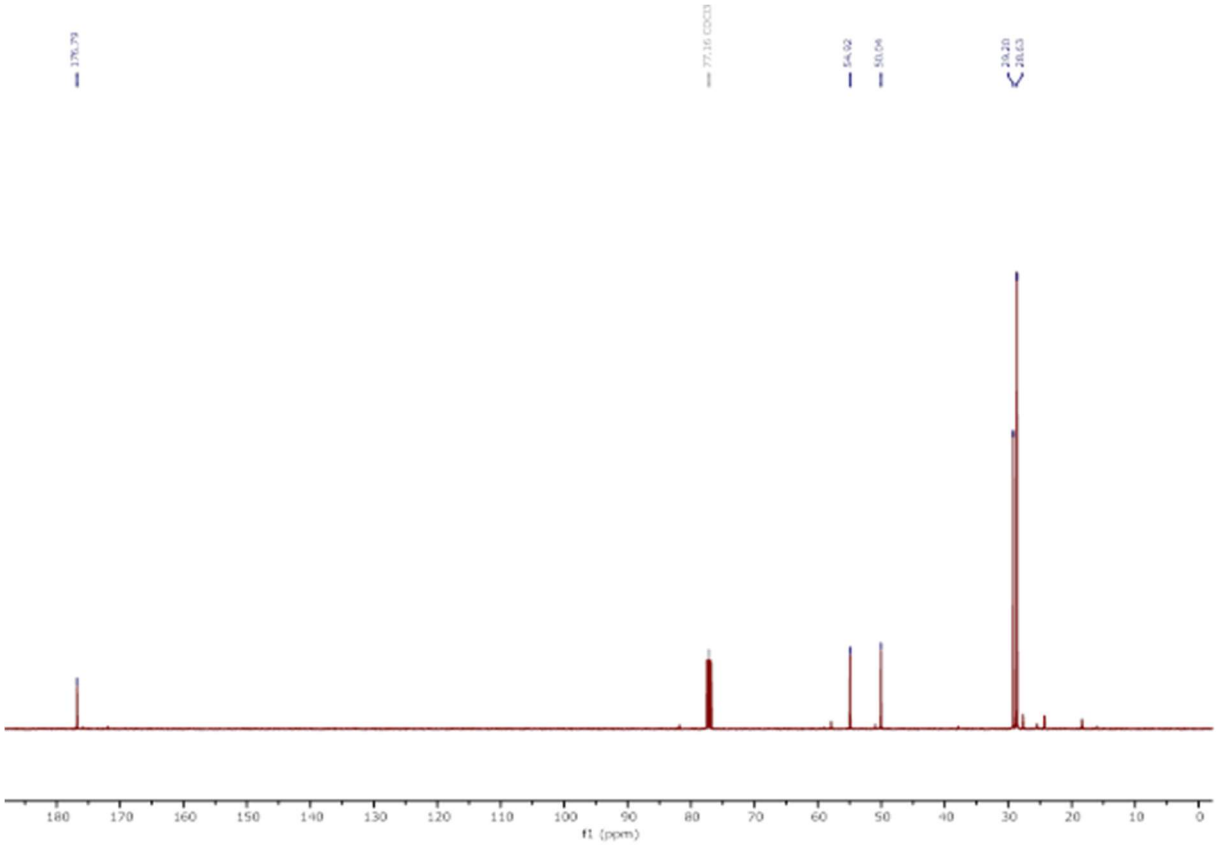




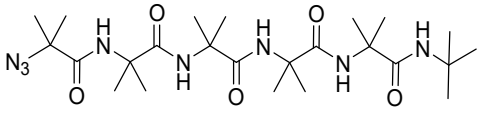
AibNH^{t}Bu (in $CDCl_3$)

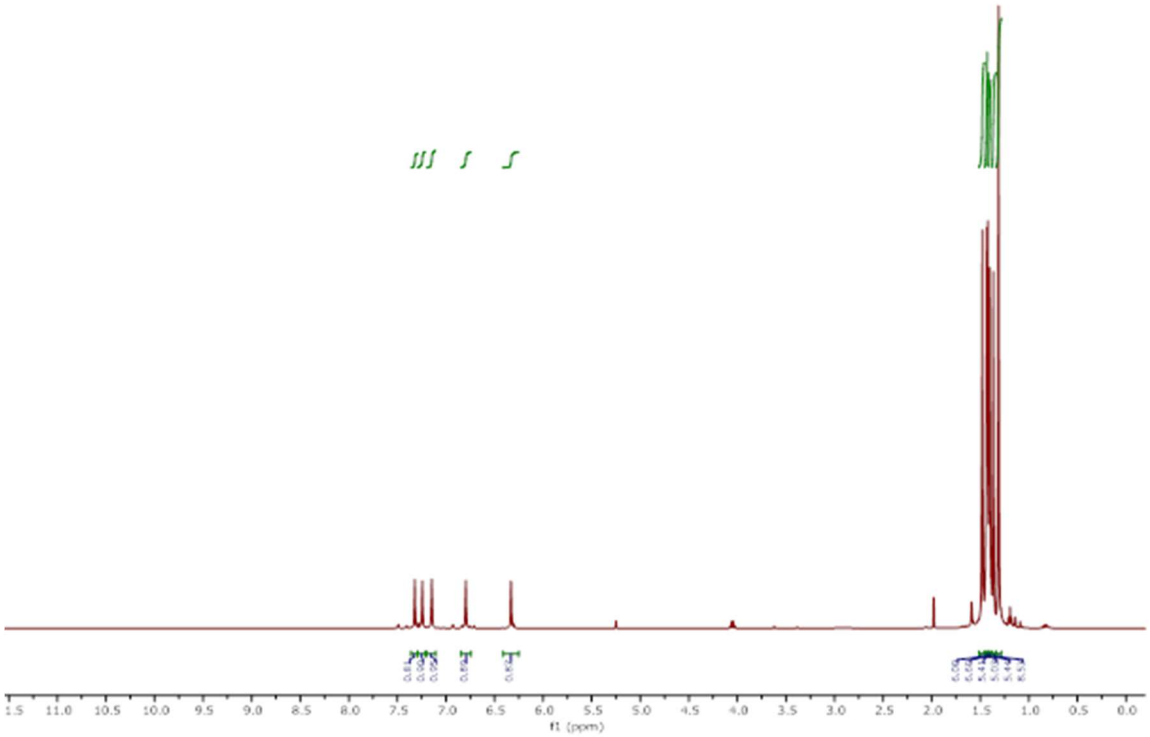


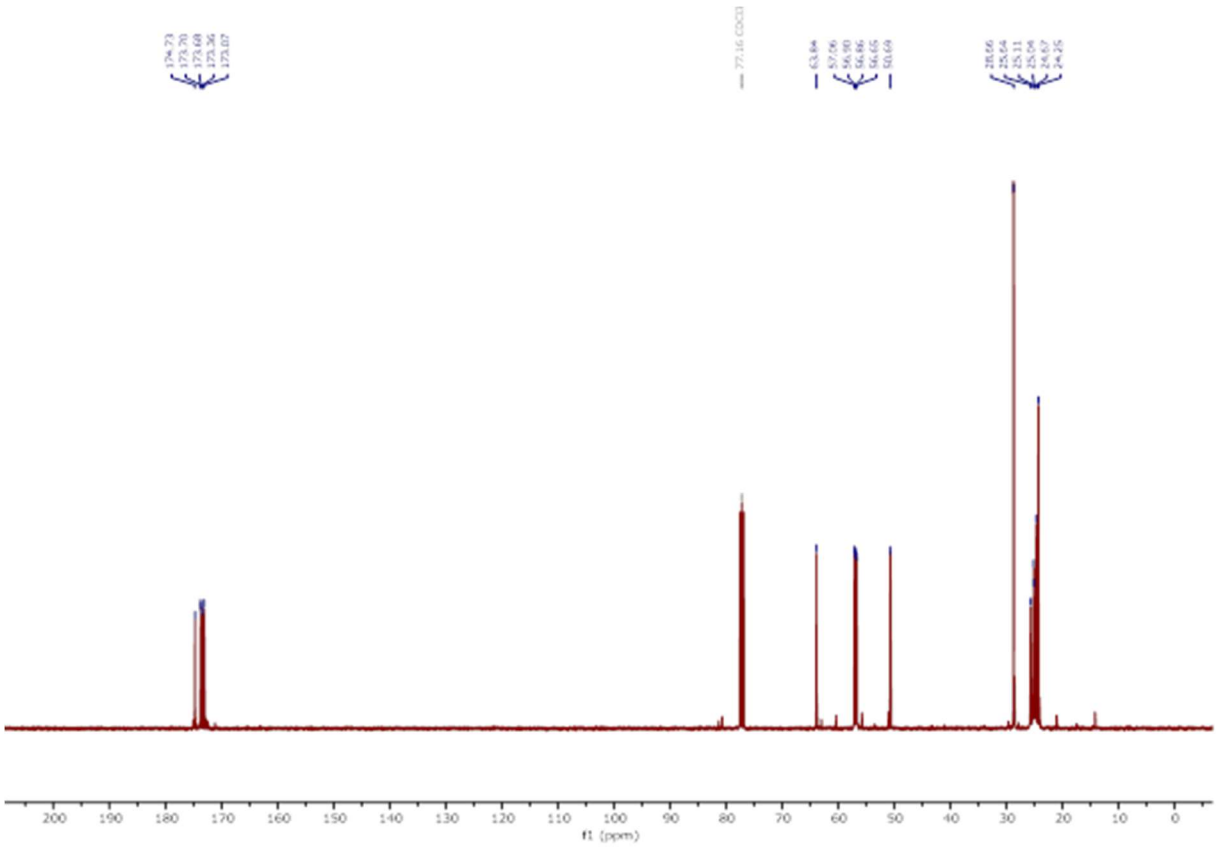




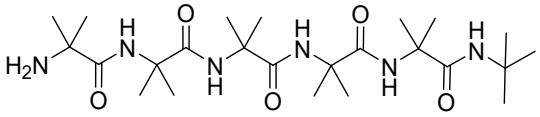
$N_3Aib_5NH^tBu$, 6 (in $CDCl_3$)

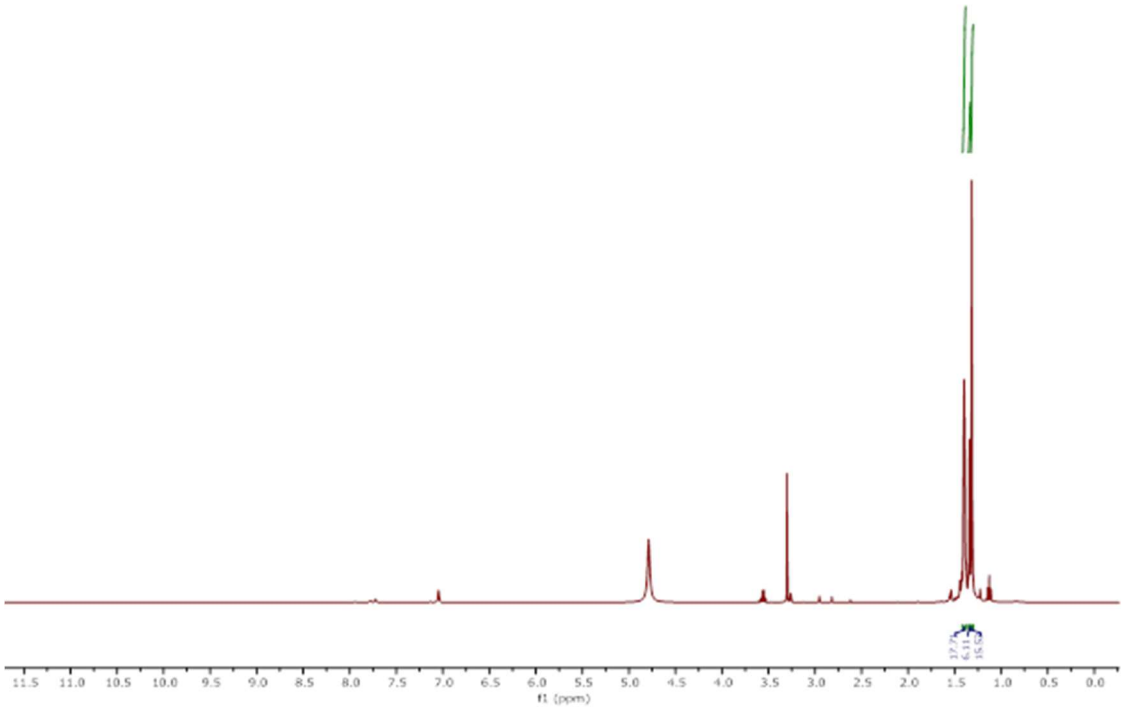


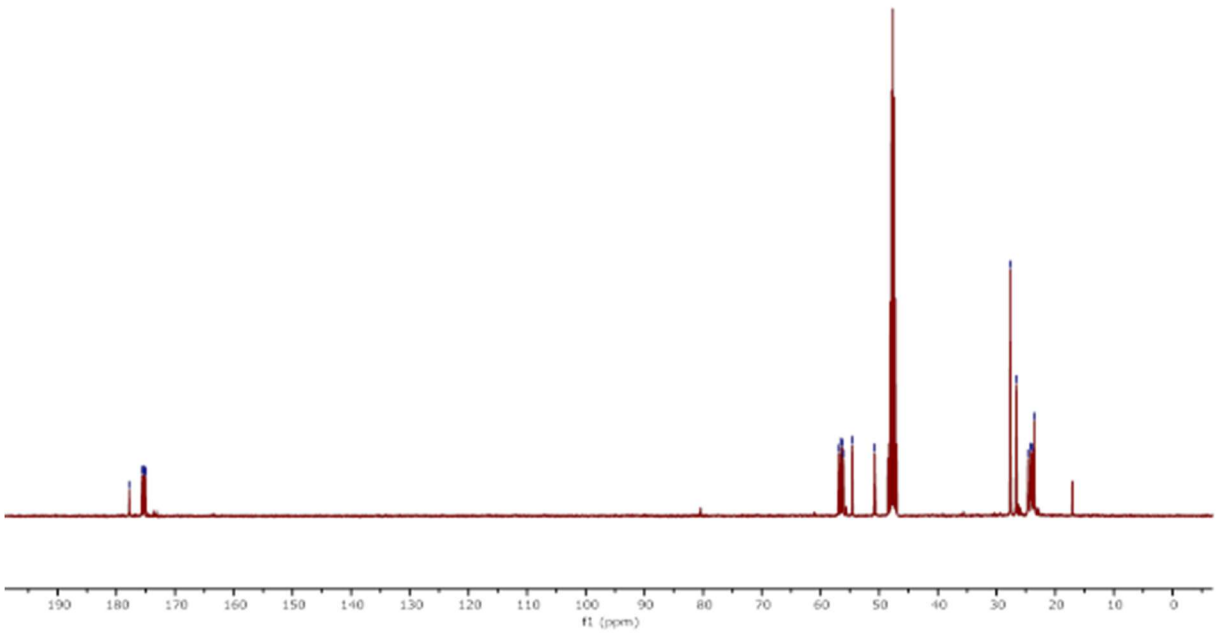




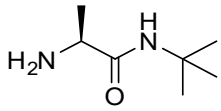
Aib$_5$NH^{t}Bu, 2 (in CD_3OD)

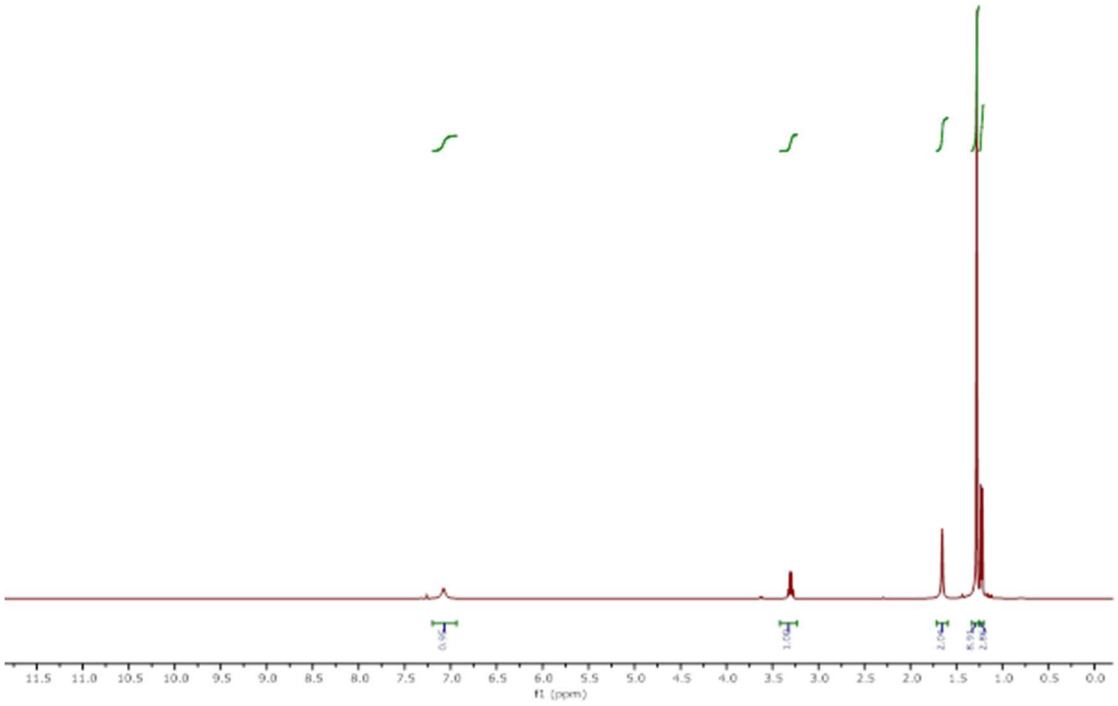


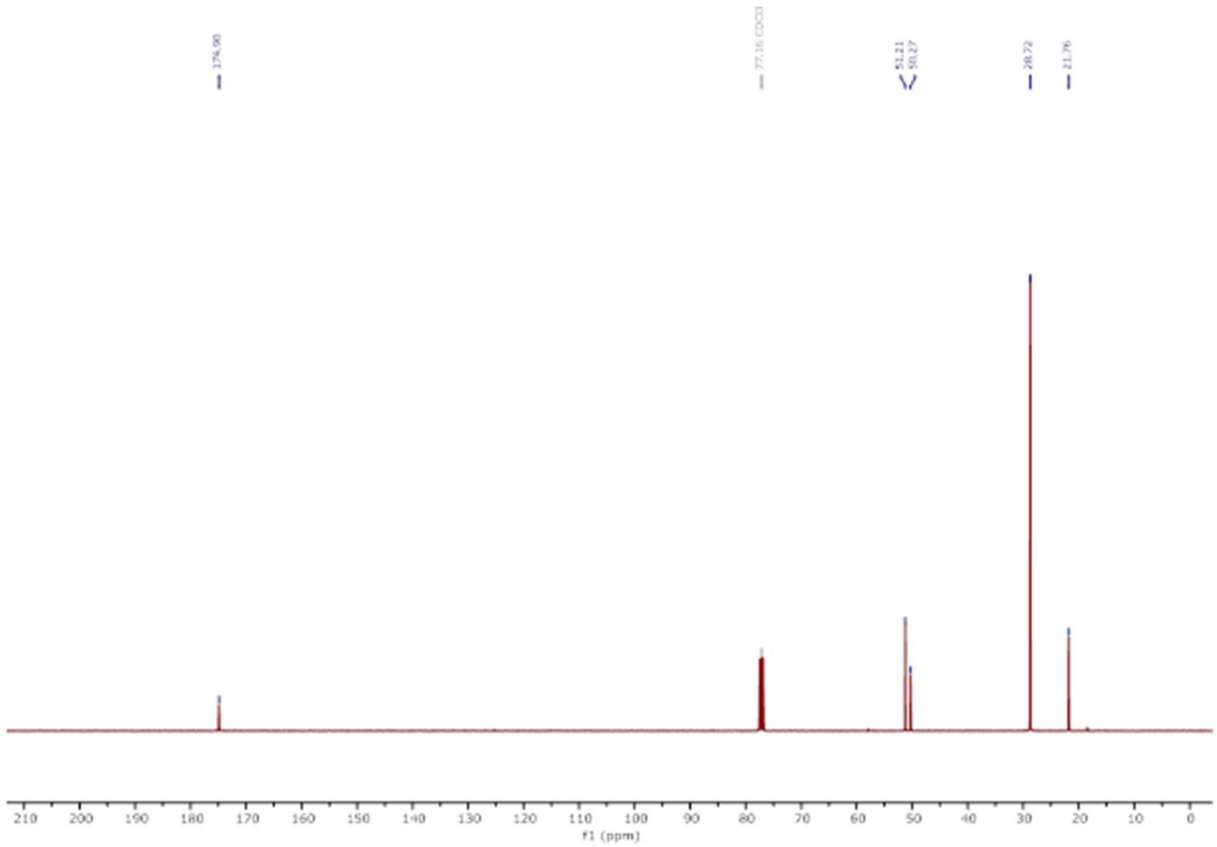




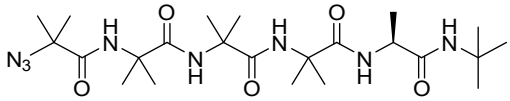
(L-Ala)NH*t*Bu (in $CDCl_3$)

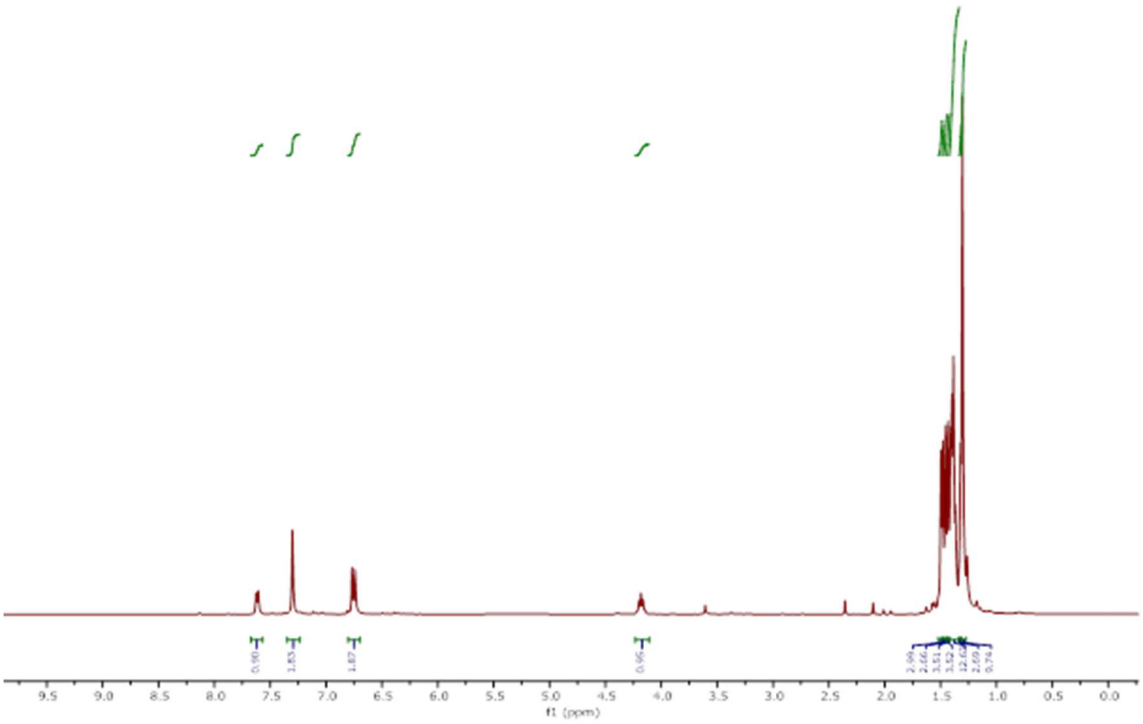


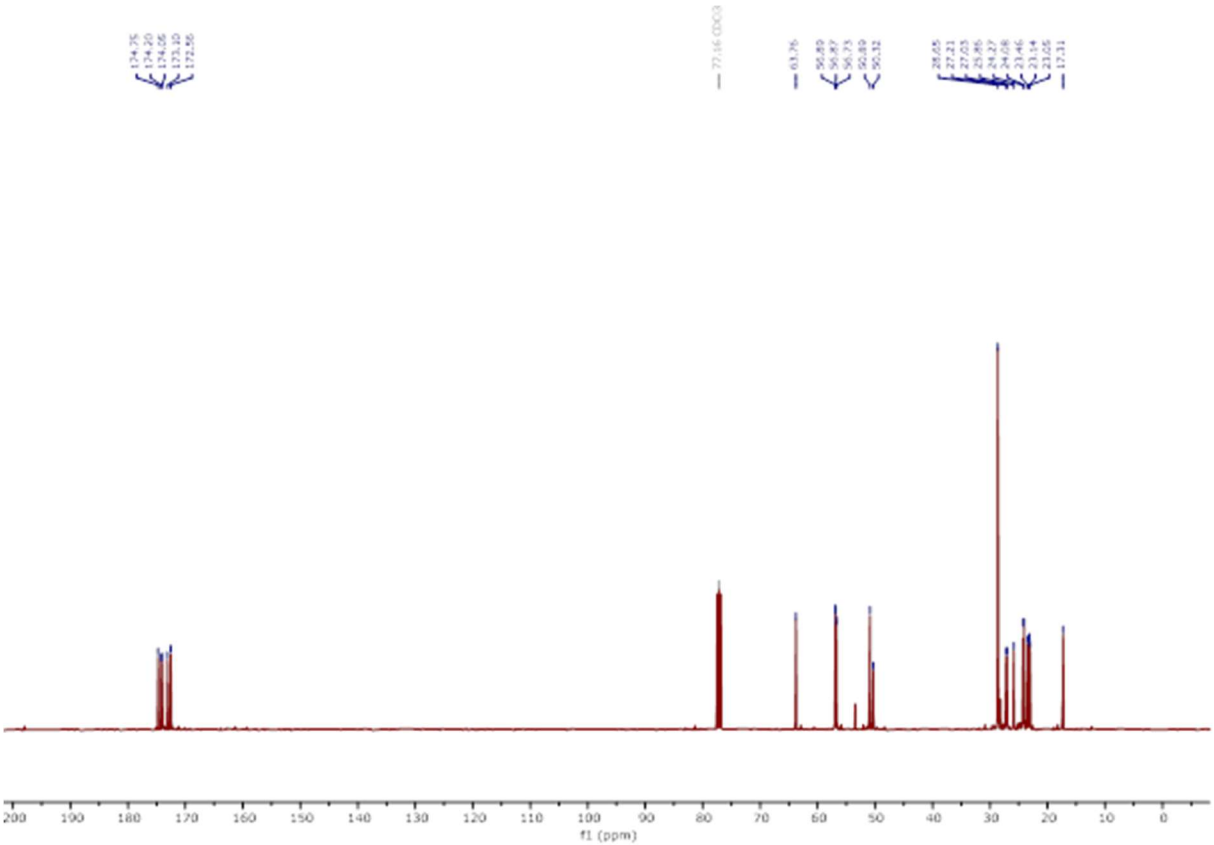




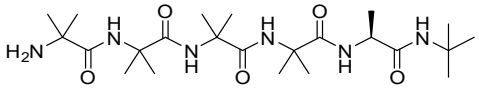
$N_3Aib_4(L\text{-}Ala)NH^tBu$ (in $CDCl_3$)

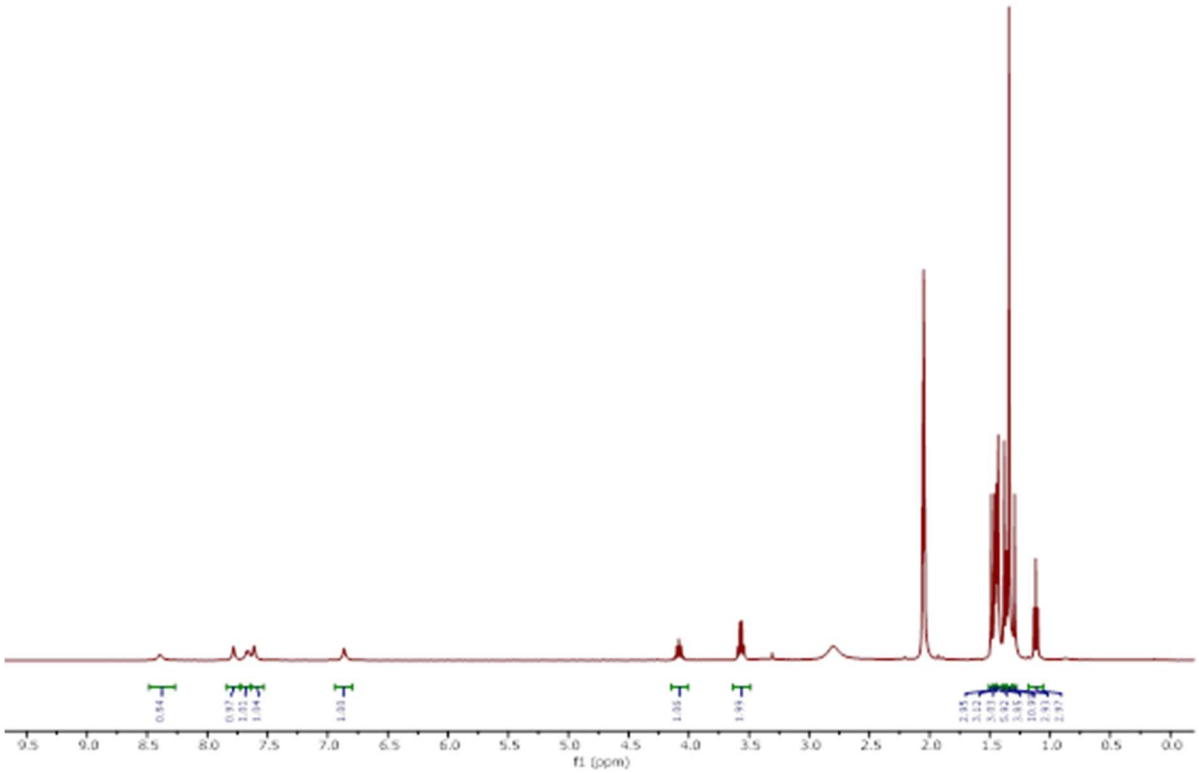


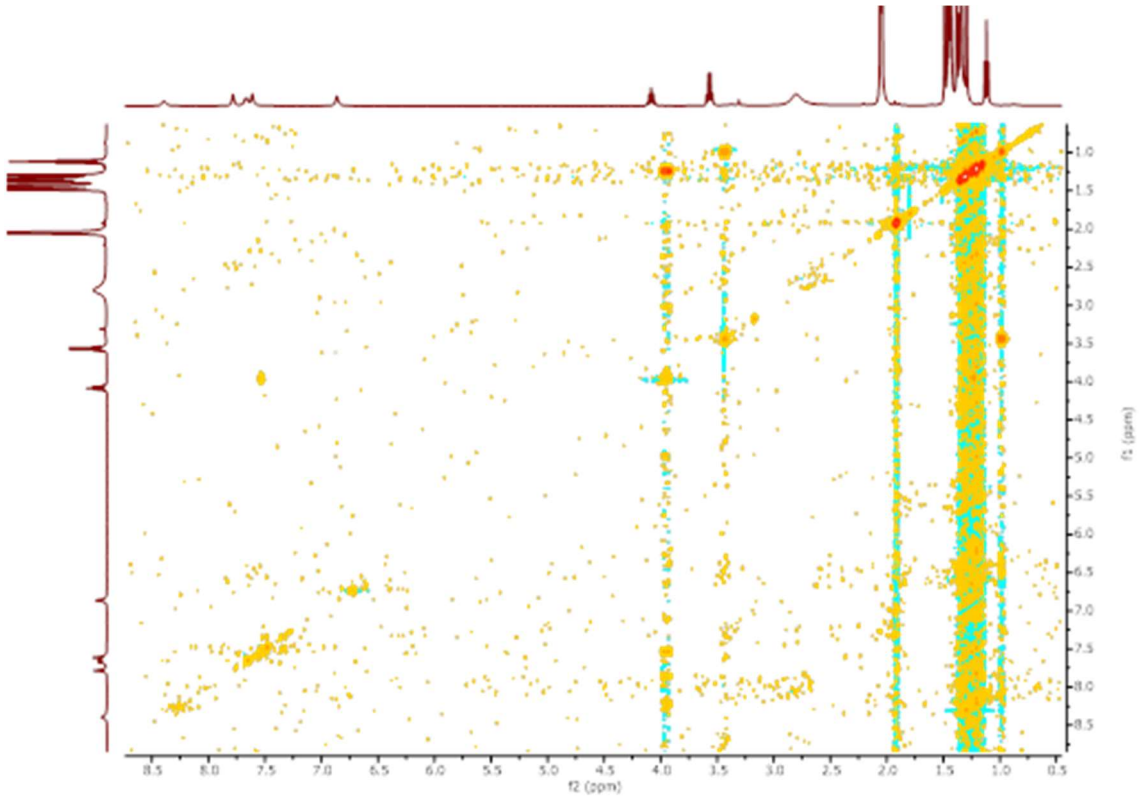


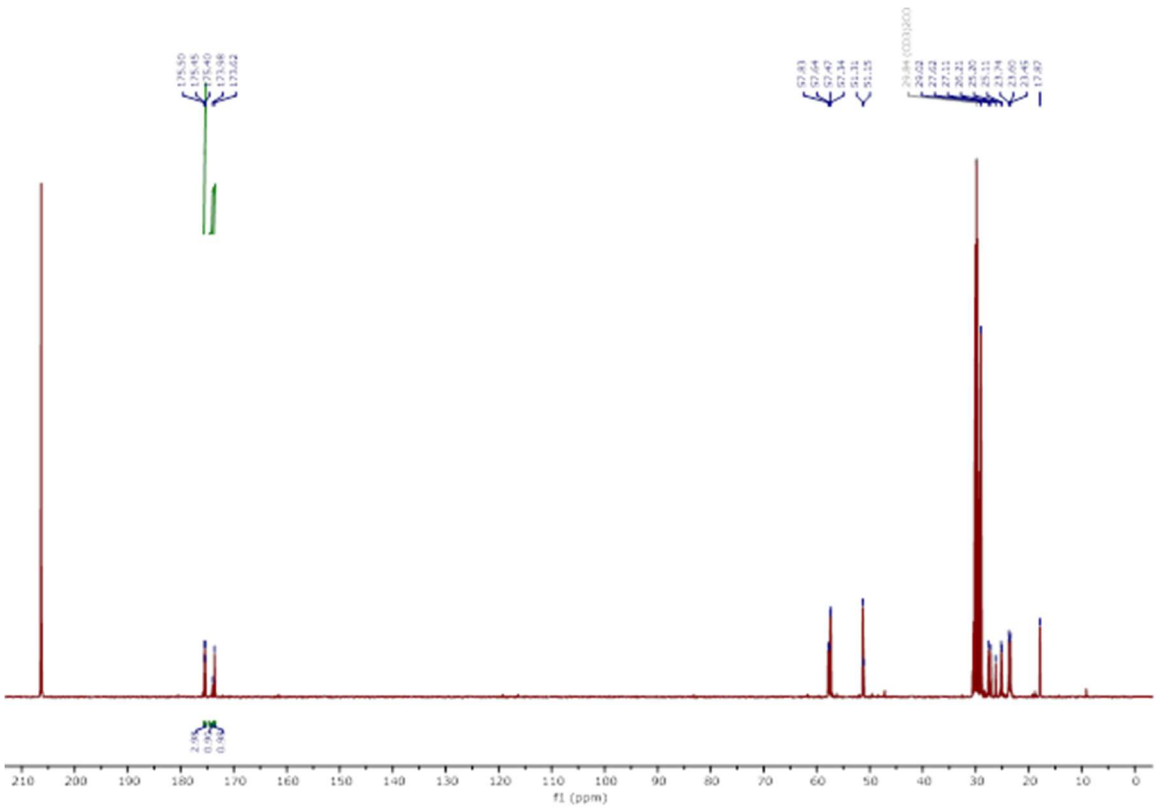


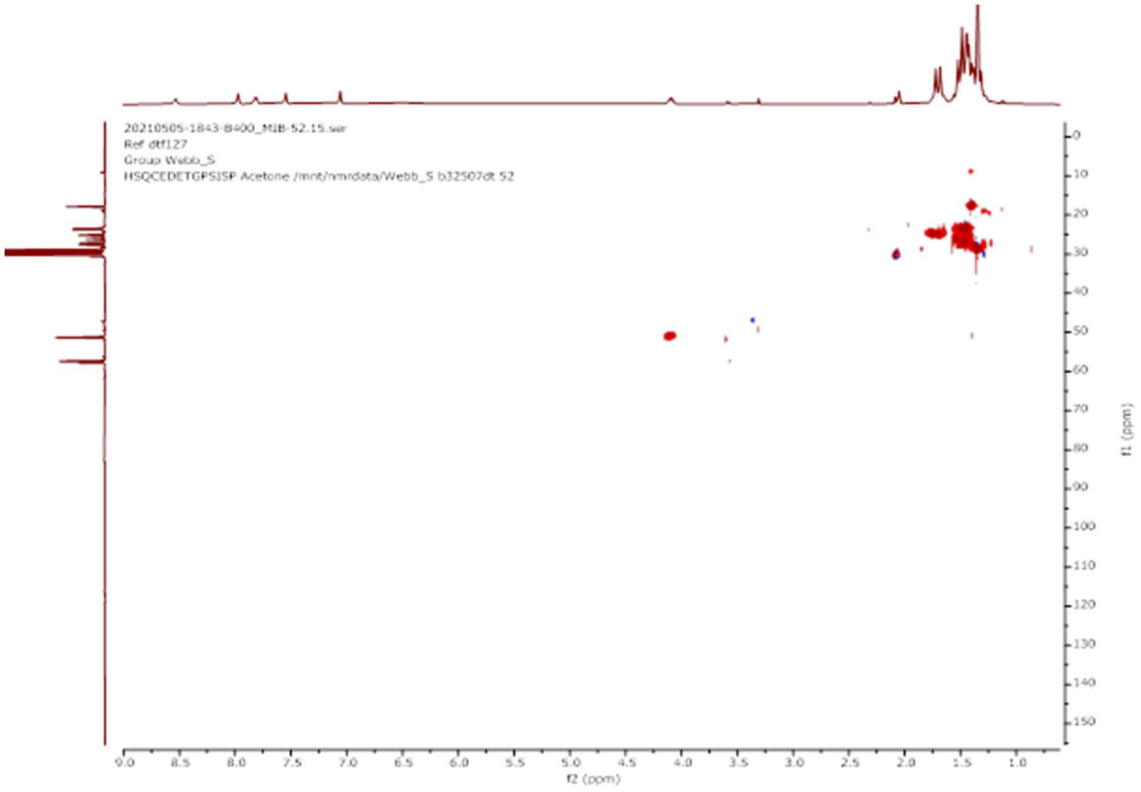
Aib$_4$(L-Ala)NH*t*Bu, foldamer 1 (in acetone d6)








f1 (ppm)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Group Webb_S
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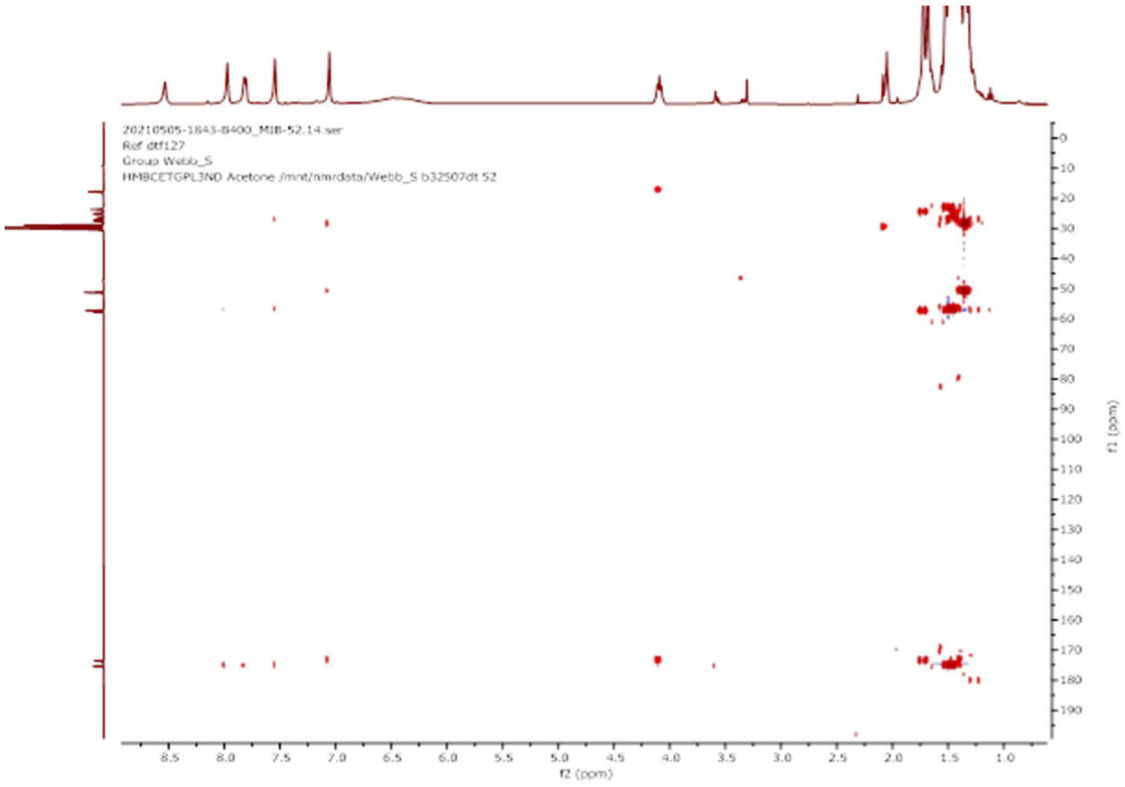
f2 (ppm)
f1 (ppm)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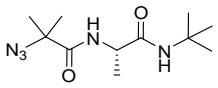
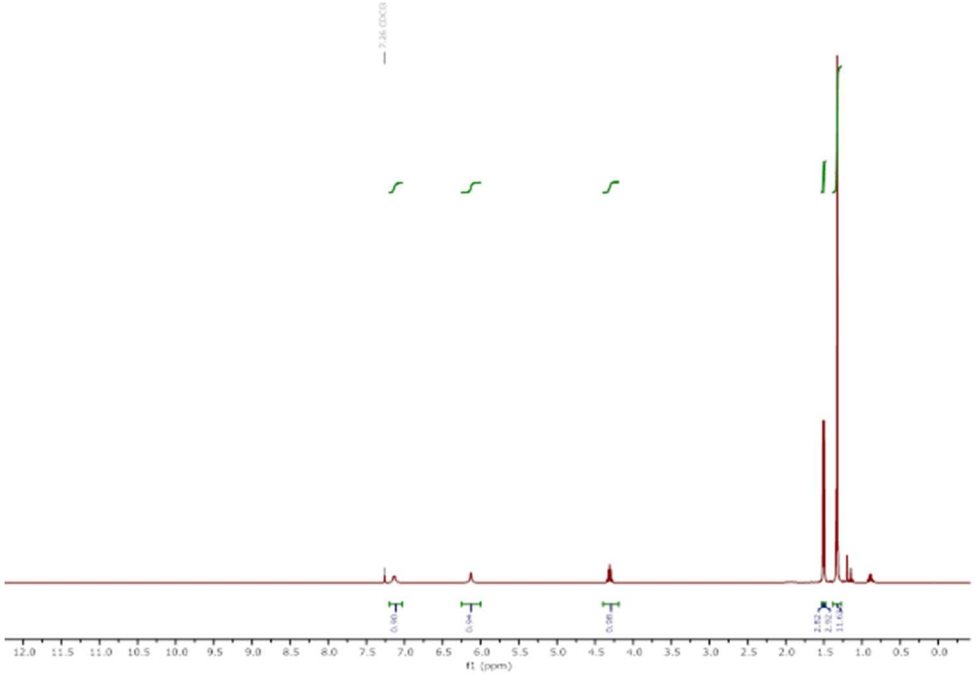
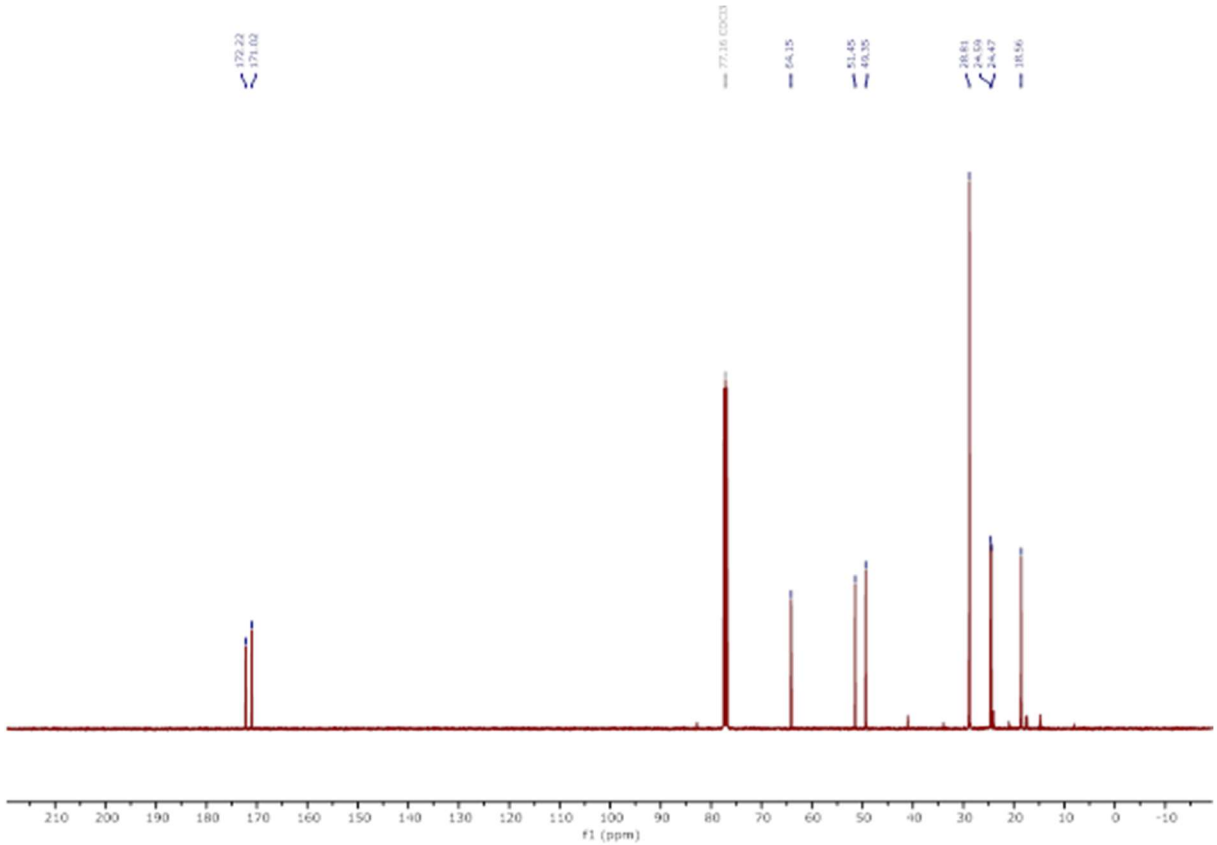
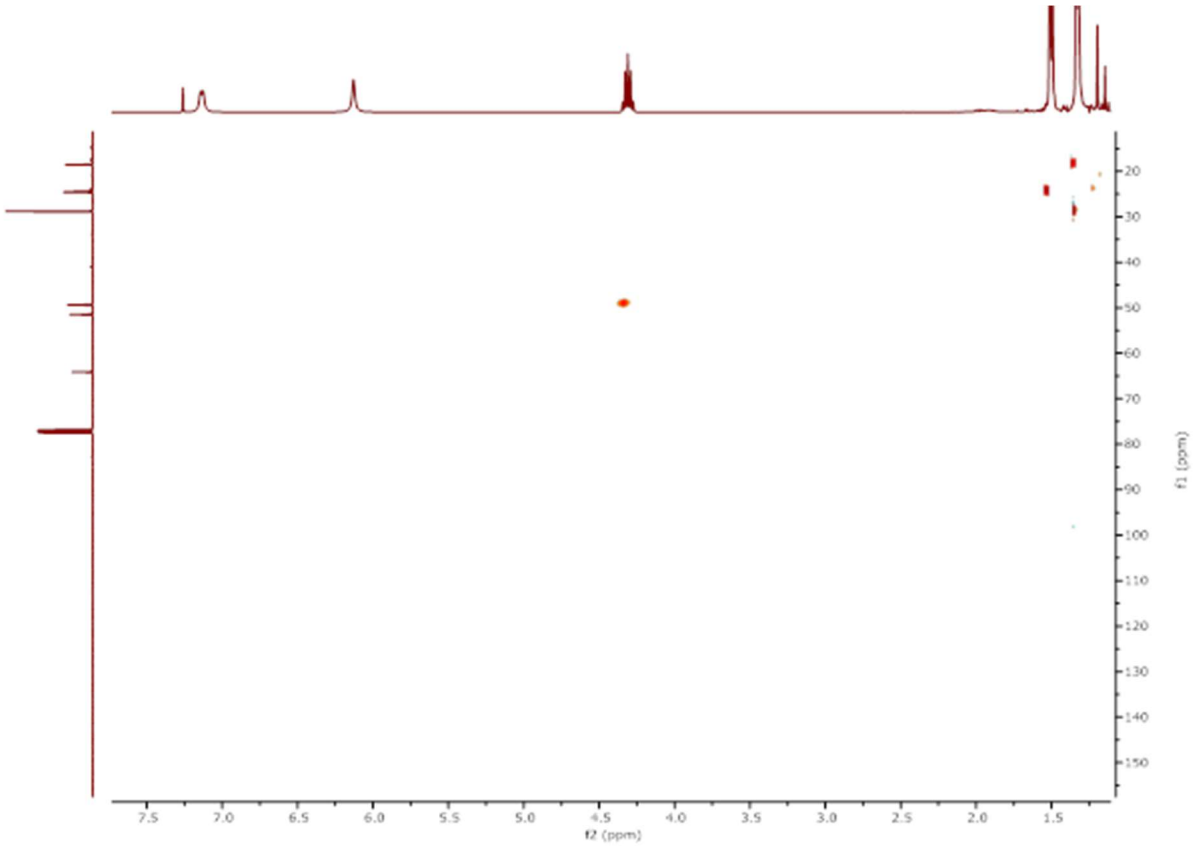
f1 (ppm)

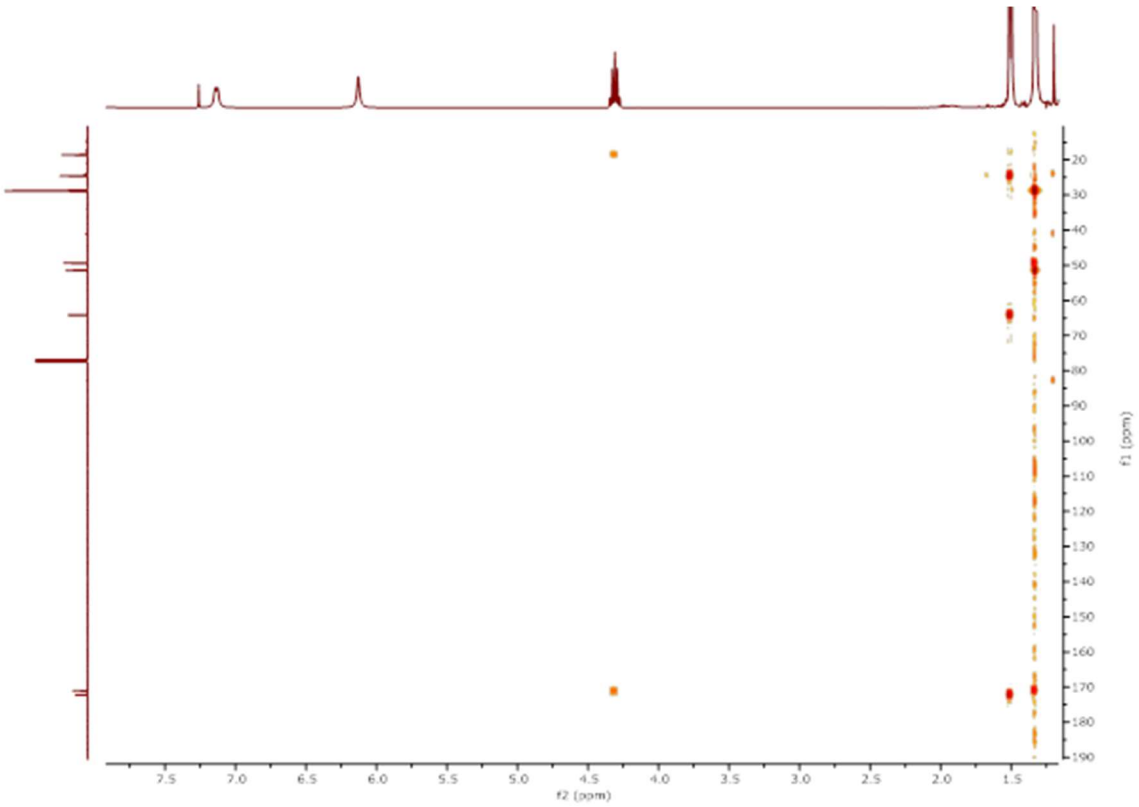
N_3Aib(L-Ala)NH^{t}Bu (in $CDCl_3$)



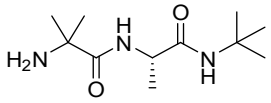


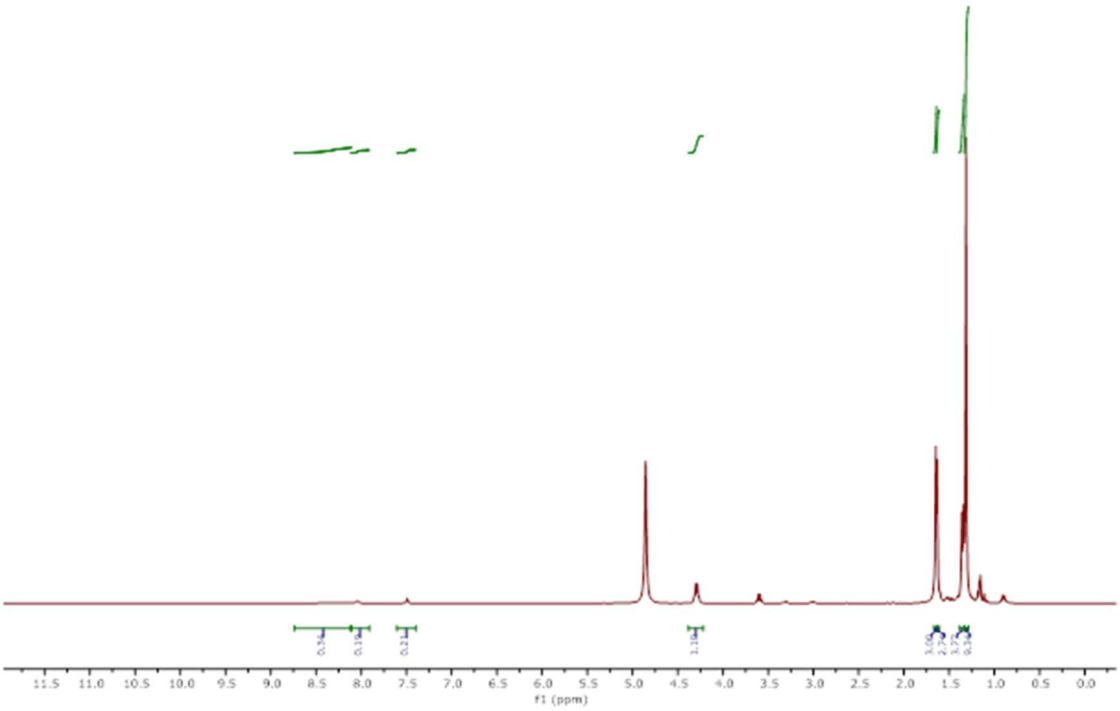


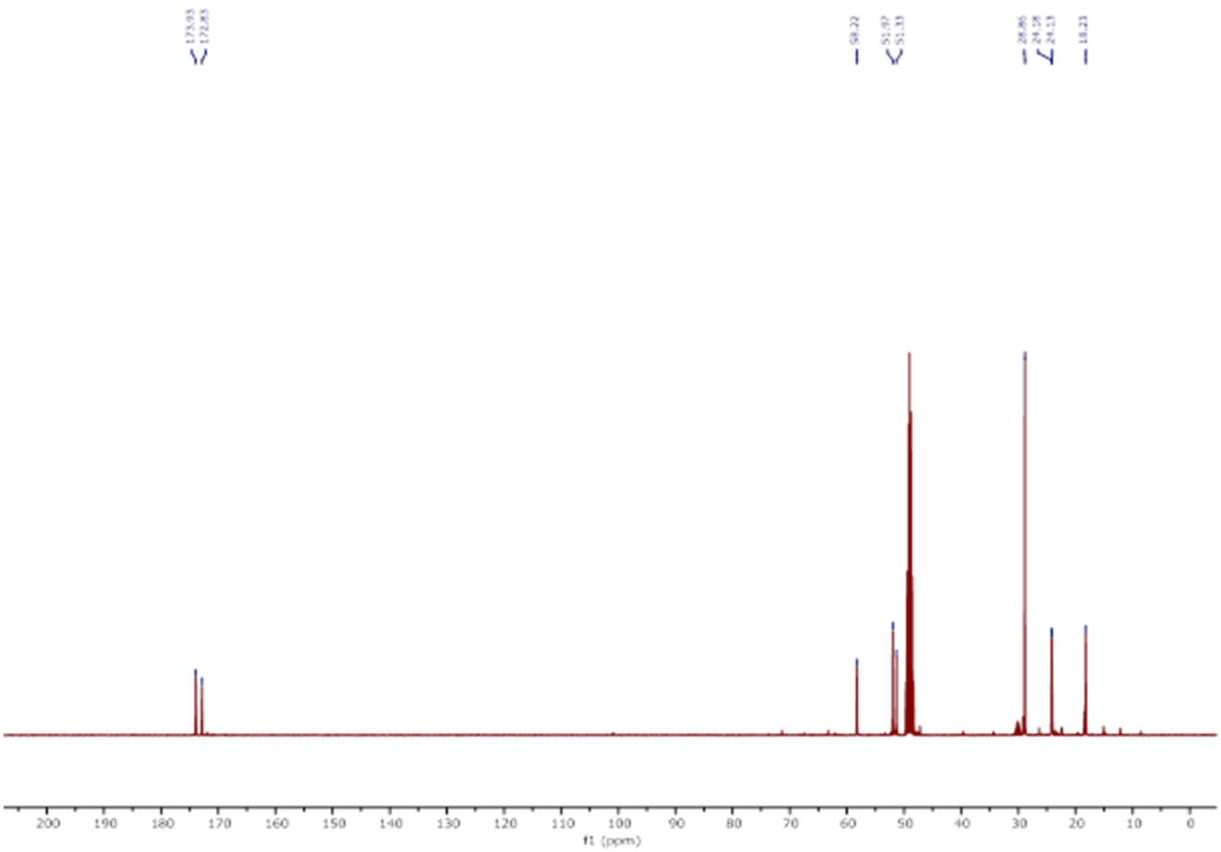

f2 (ppm)
f1 (ppm)


f2 (ppm)
f1 (ppm)

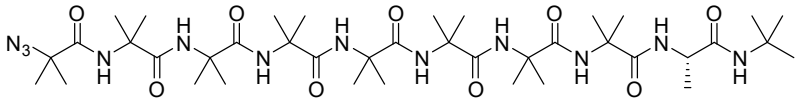
Aib(L-Ala)NH^{t}Bu, 4 (in CD_3OD)

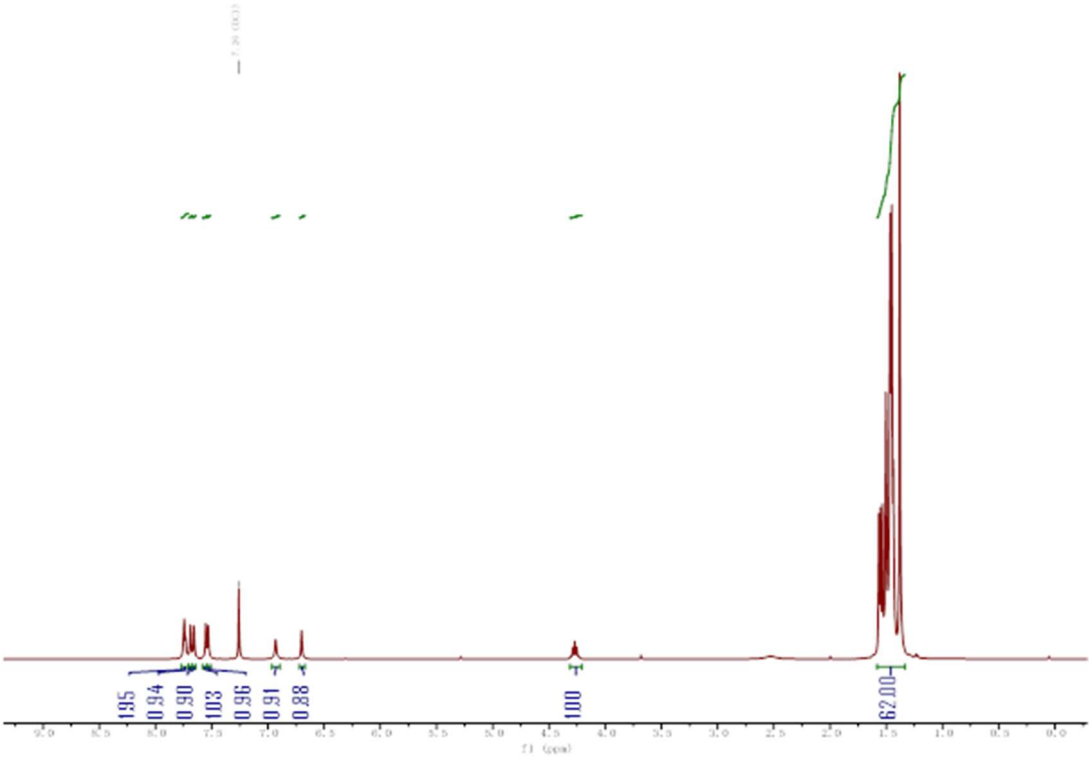


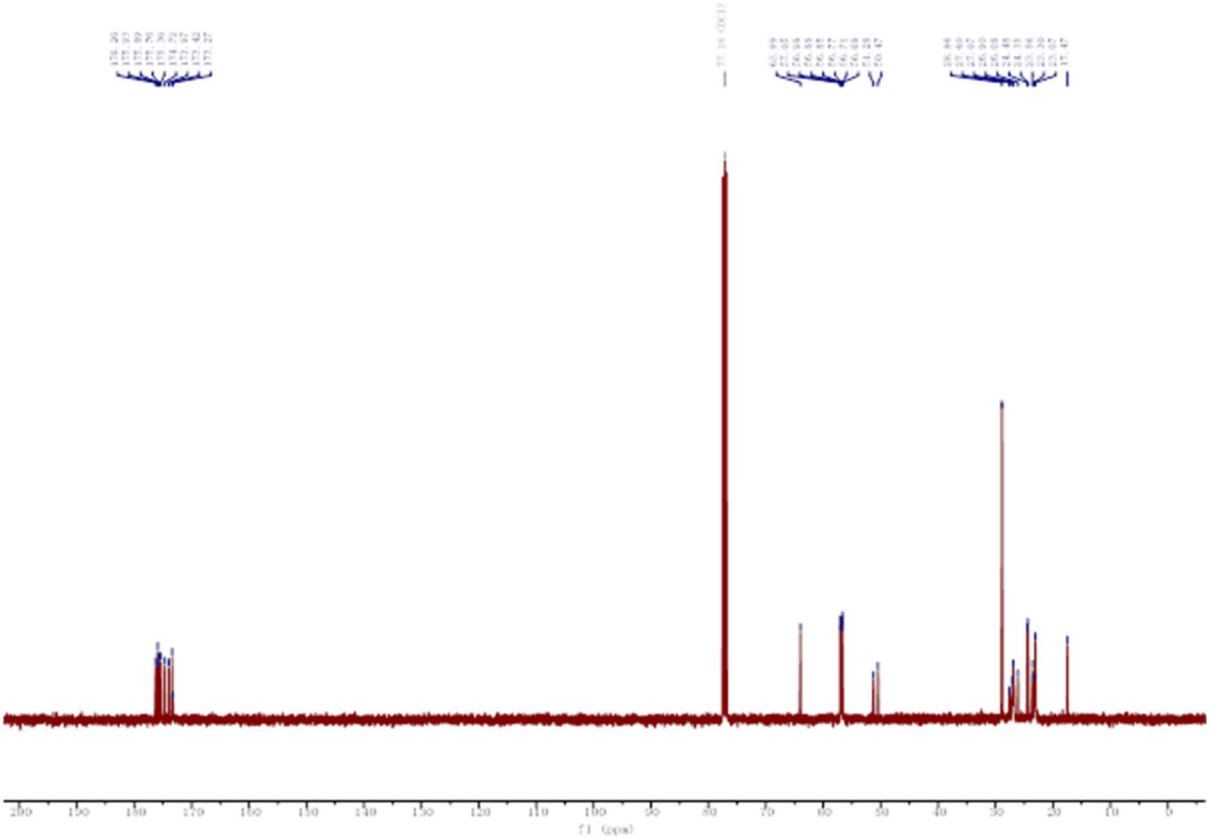




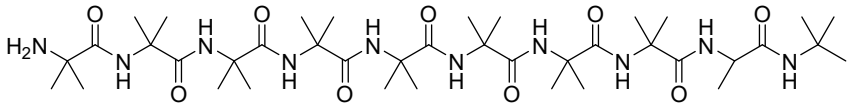
N_3Aib_8(L-Ala)NH^tBu, peptide 7 (in $CDCl_3$)



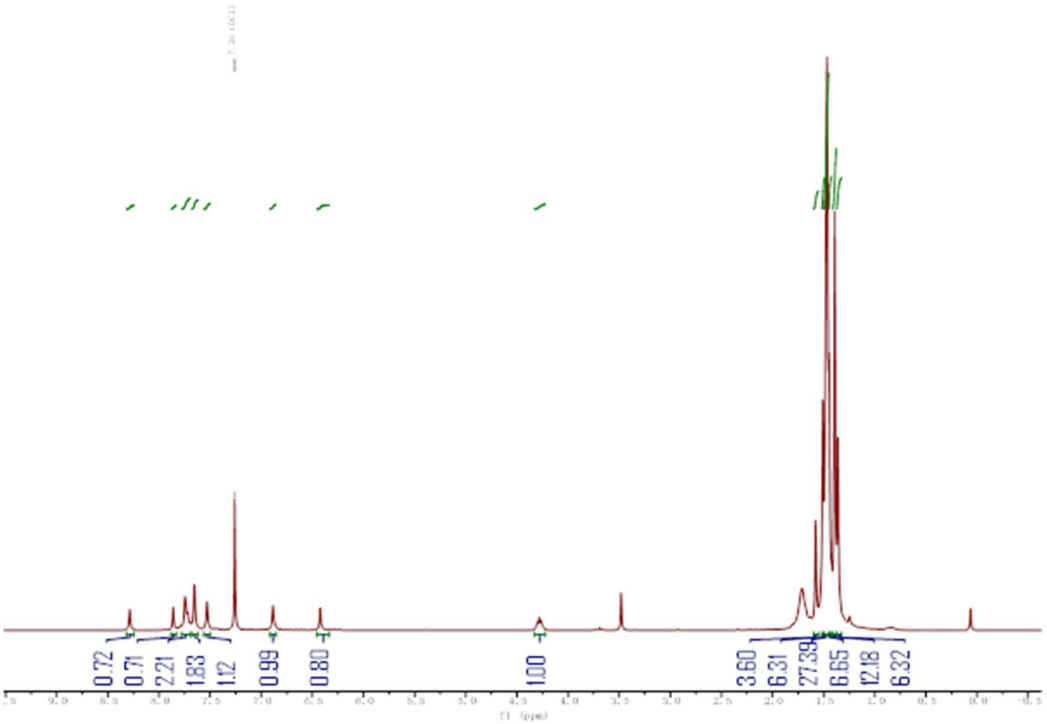




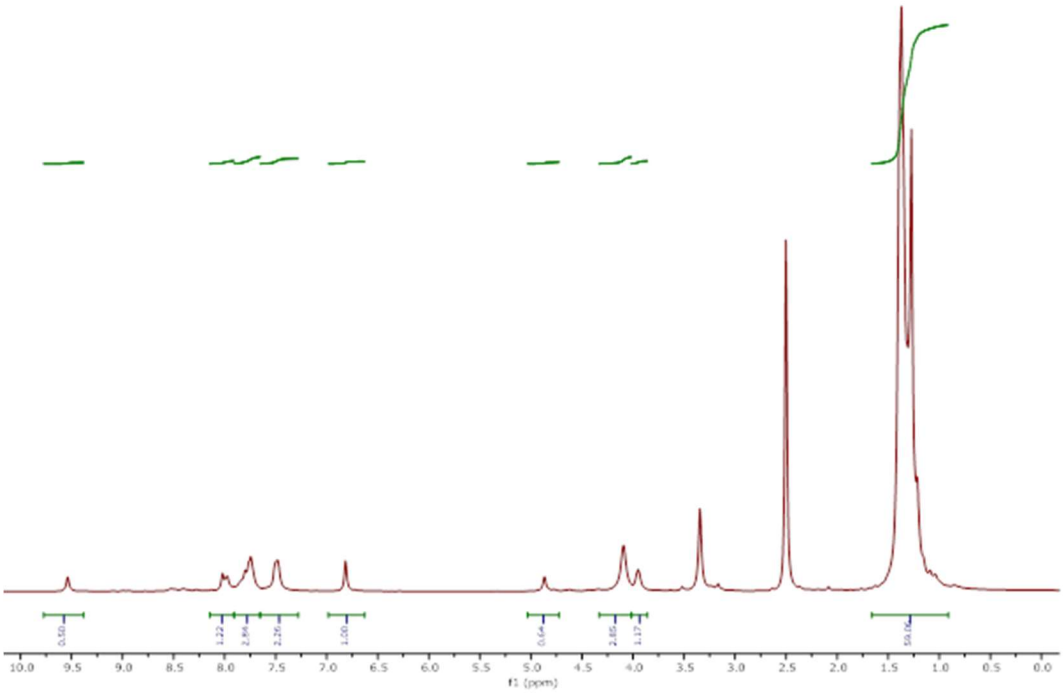
Aib$_8$(L-Ala)NH^{t}Bu, Peptide 3

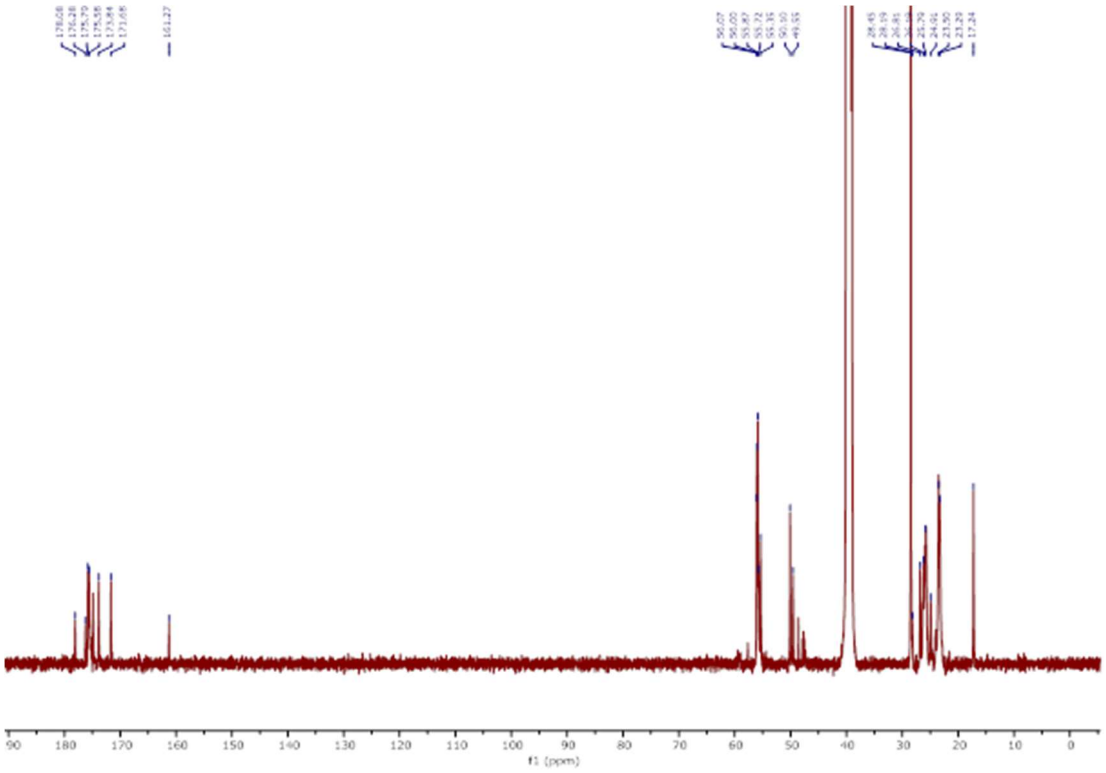


In $CDCl_3$

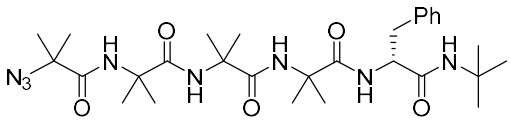


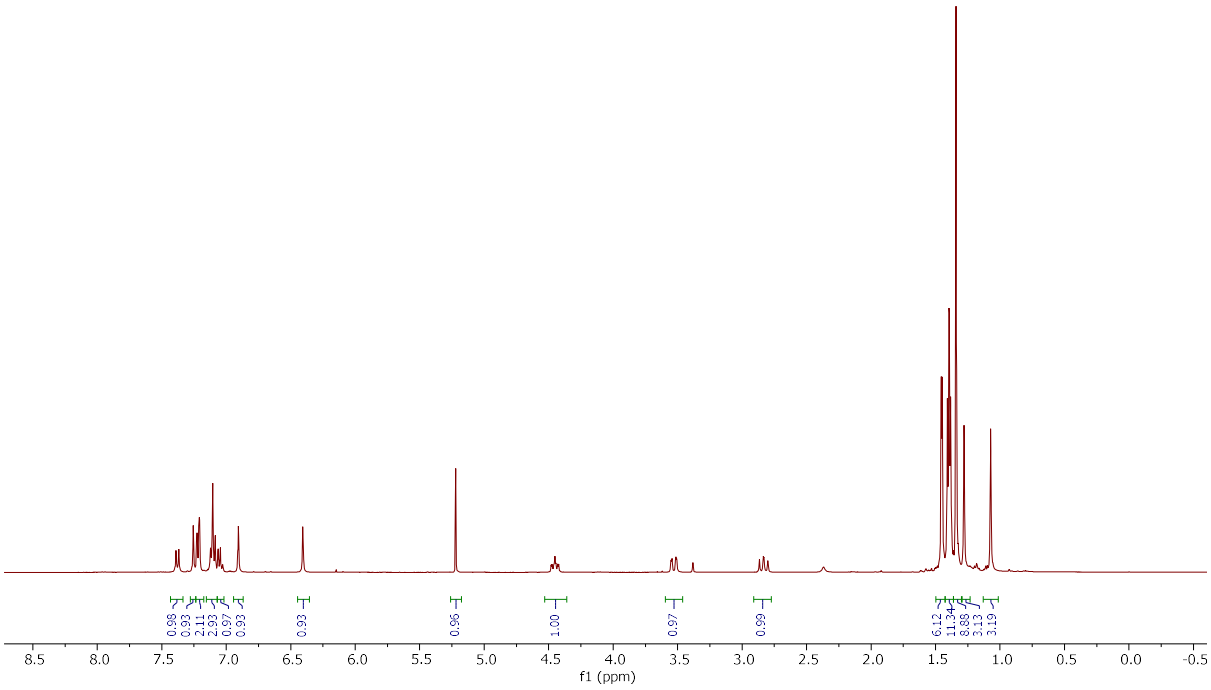
In DMSO d6

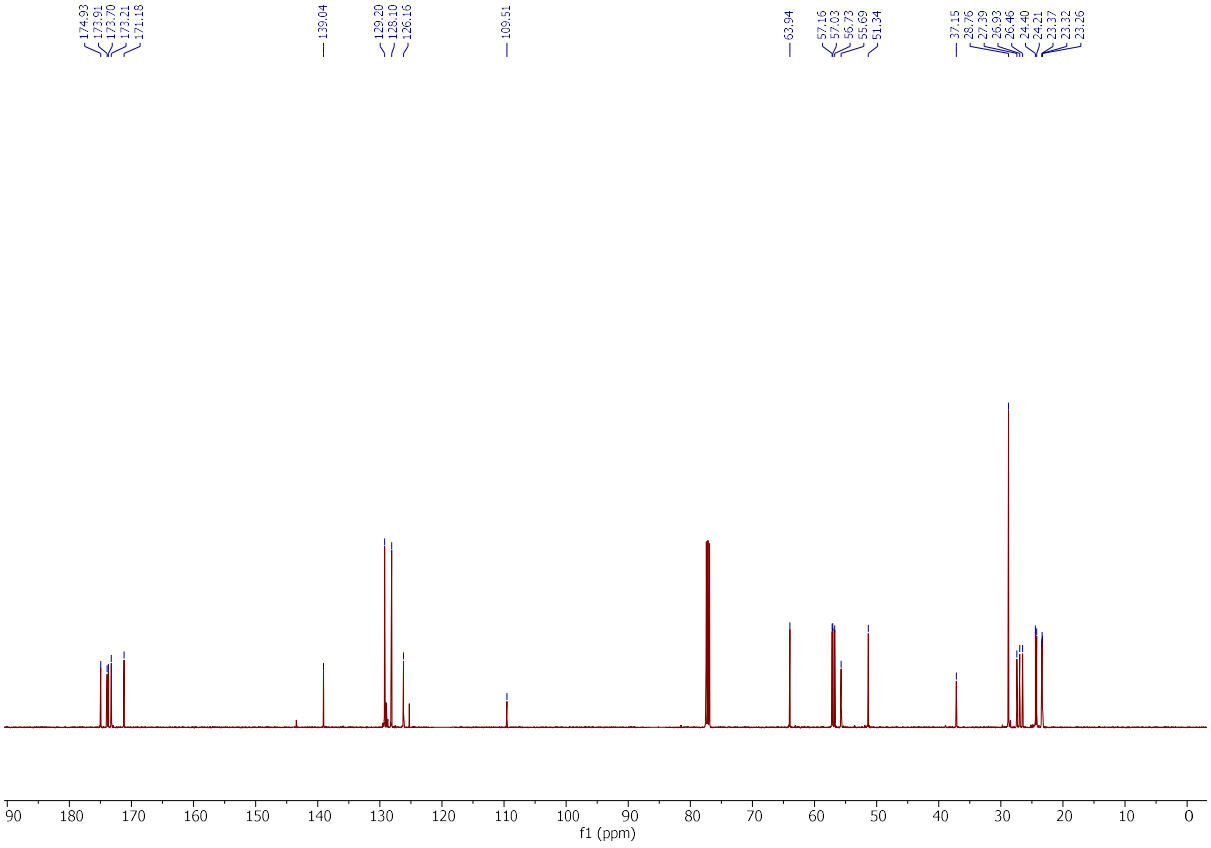



178.68
176.28
175.79
175.58
173.84
171.66
161.27
56.07
56.00
55.87
55.72
55.35
50.10
49.55
28.45
28.19
26.81
25.29
24.91
23.55
23.29
17.24
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

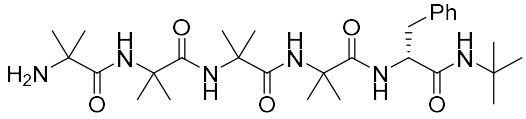
N_3Aib_4(D-Phe)NH^{t}Bu (in $CDCl_3$)

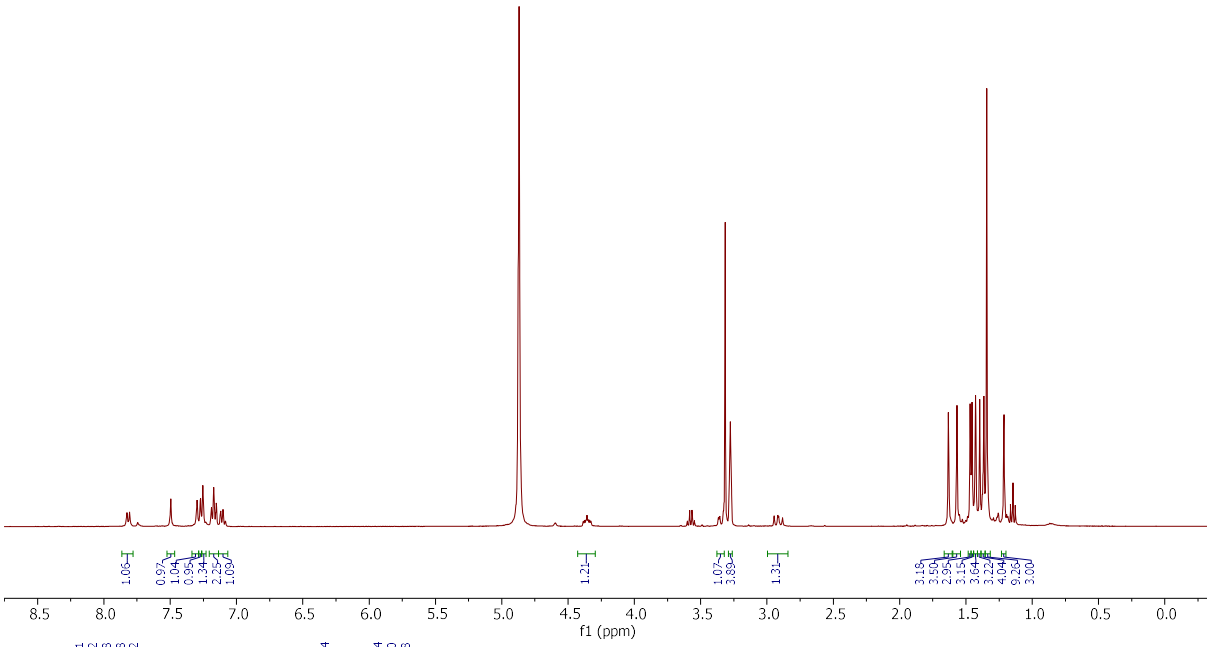


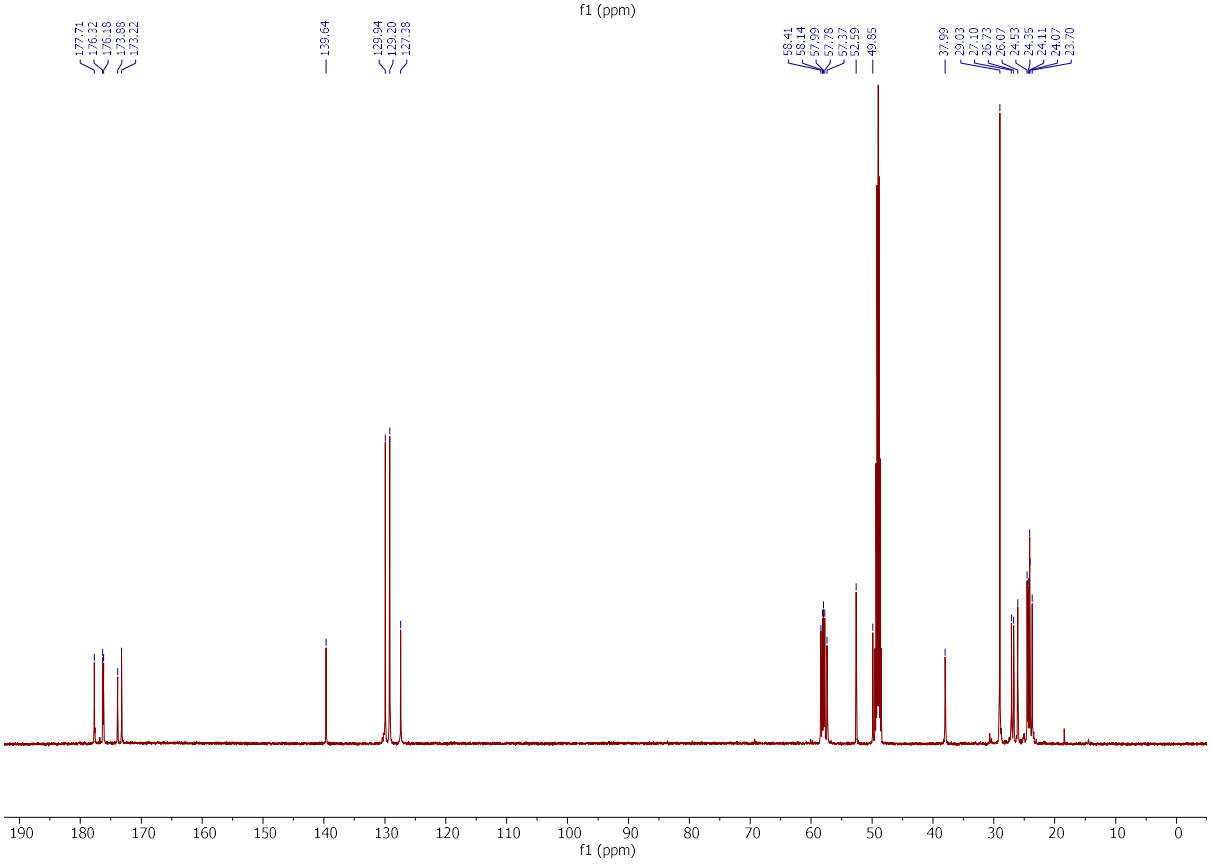




Aib$_4$(D-Phe)NH^{t}Bu, Peptide 5 (in CDCl$_3$)

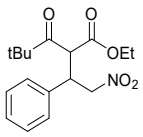


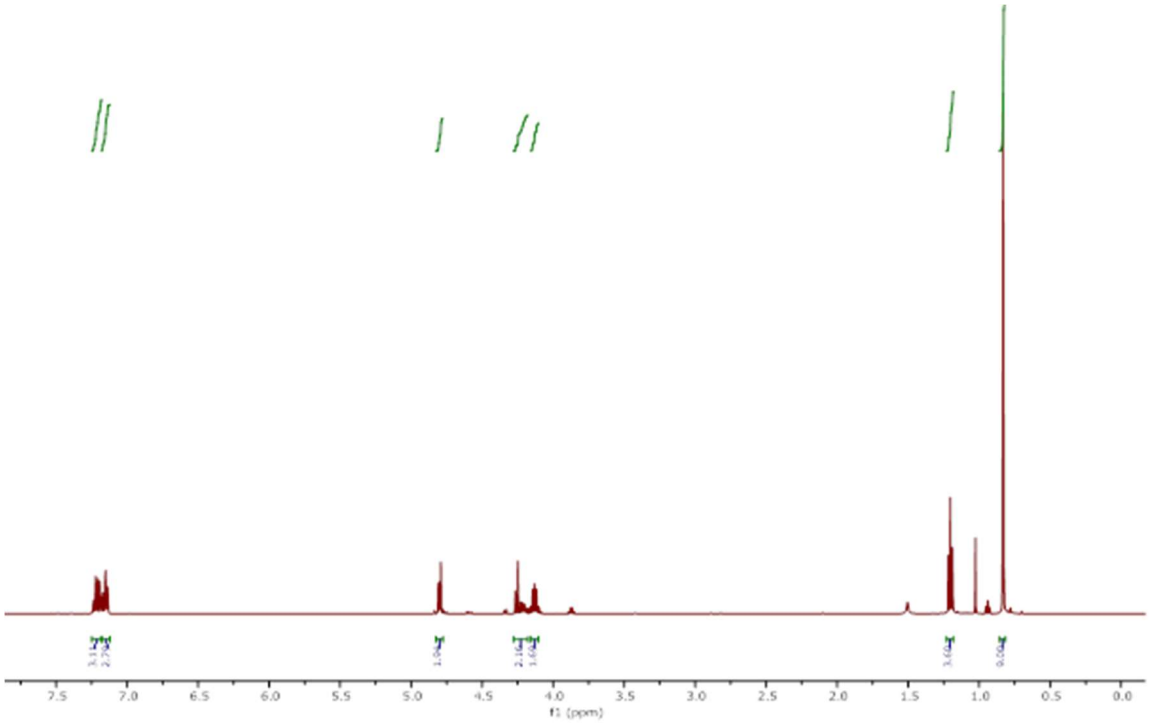


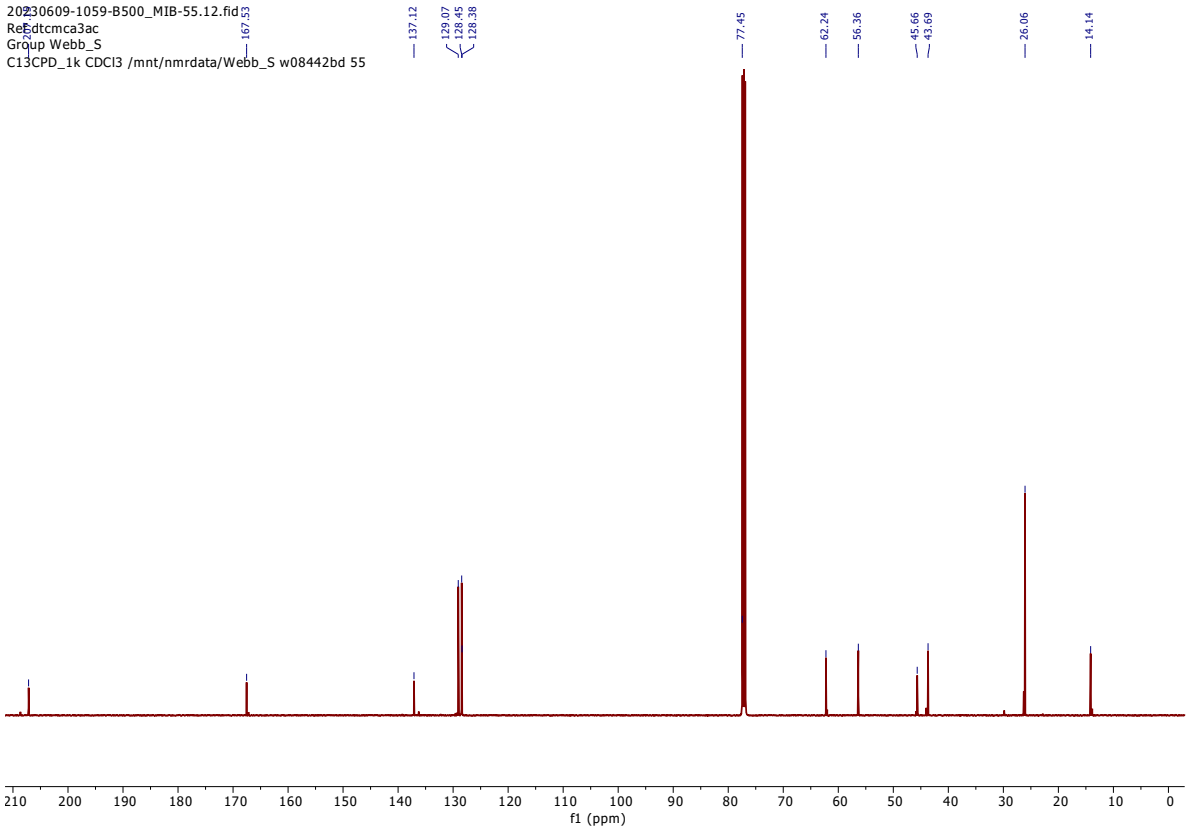


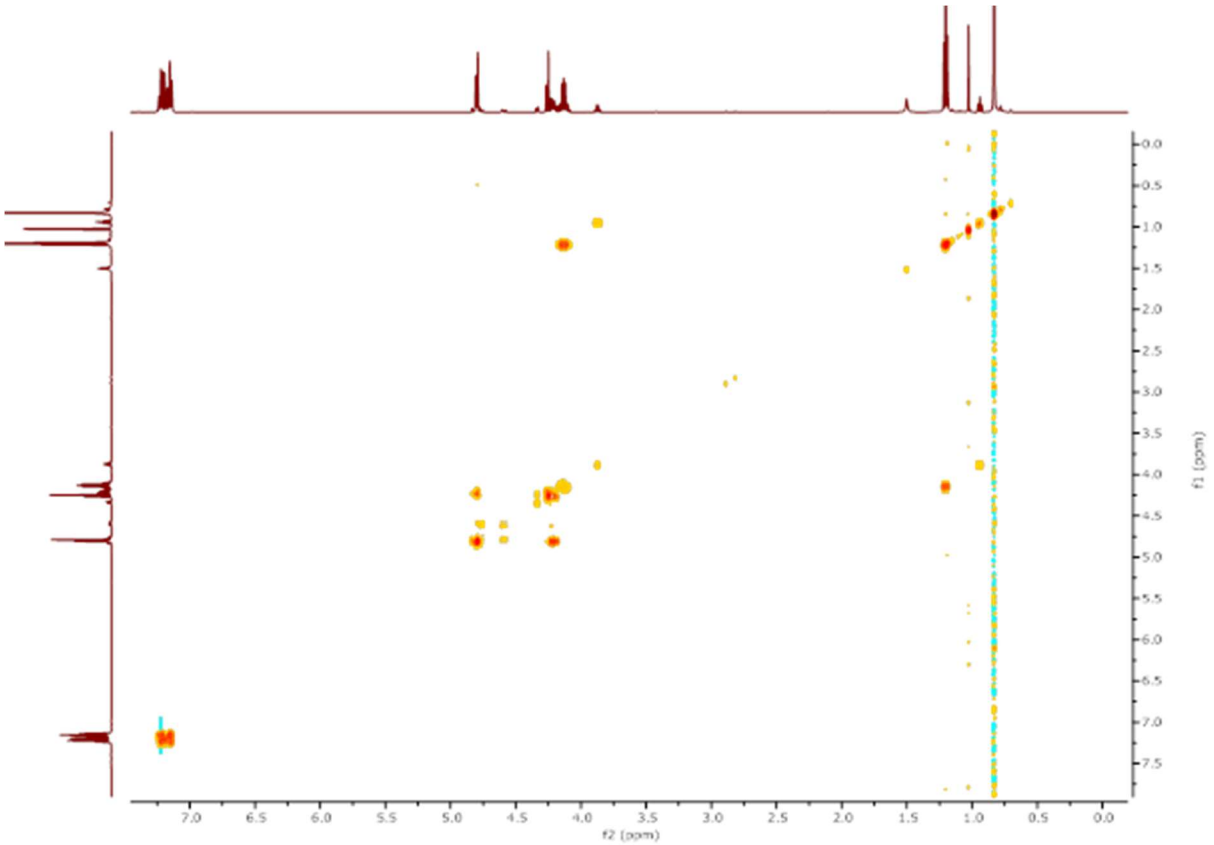
4.2. Spectra of products from catalysis

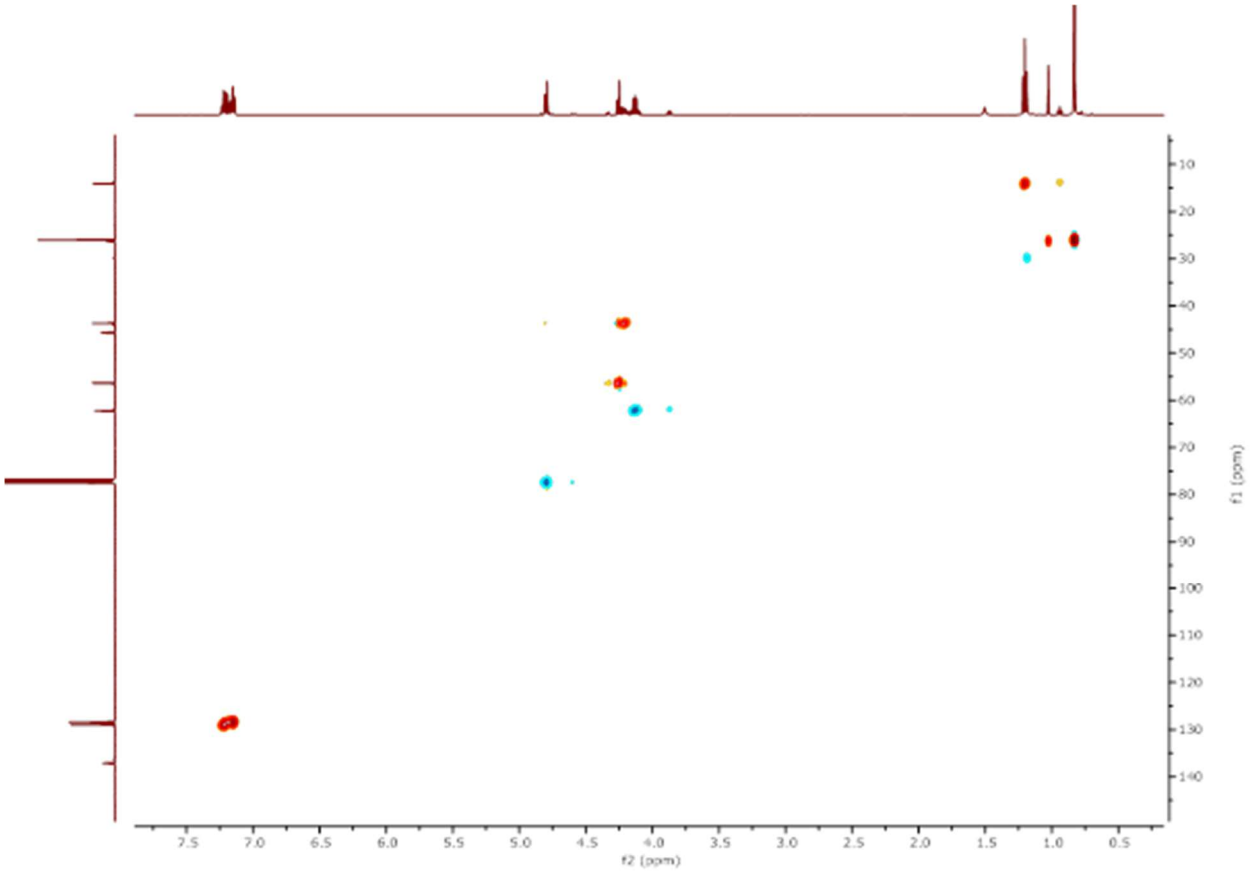
Ethyl 4,4-dimethyl-2-(2-nitro-1-phenylethyl)-3-oxopentanoate, 20a (in $CDCl_3$)

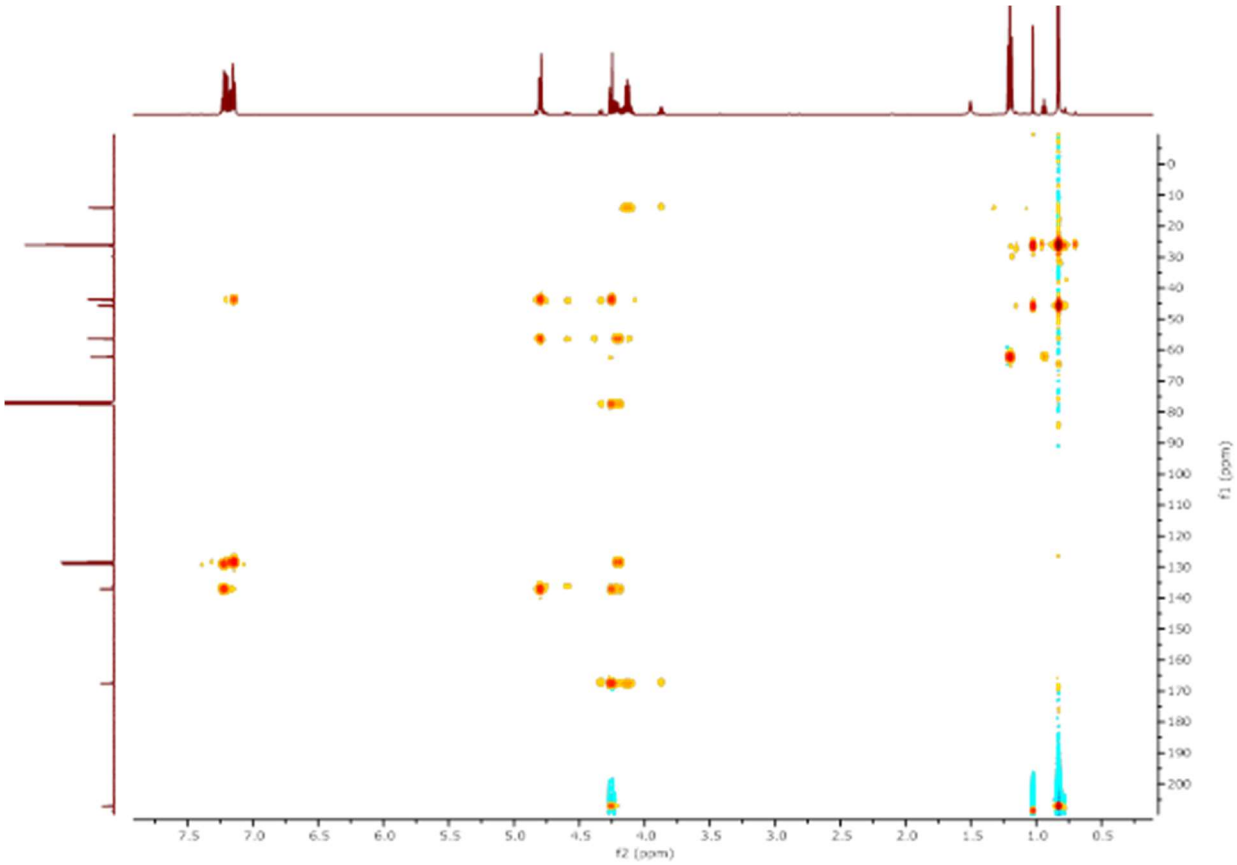




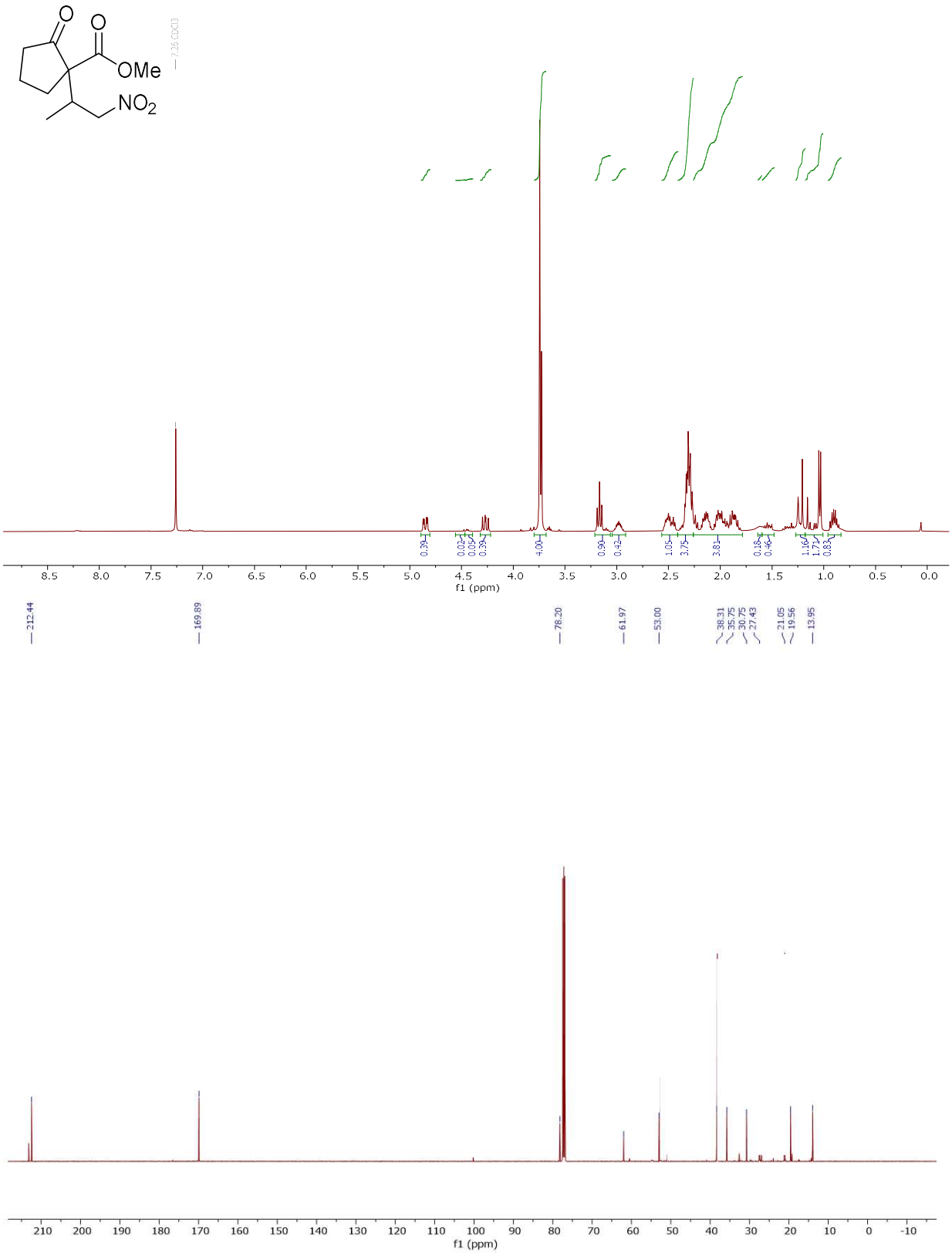



f2 (ppm)
f1 (ppm)

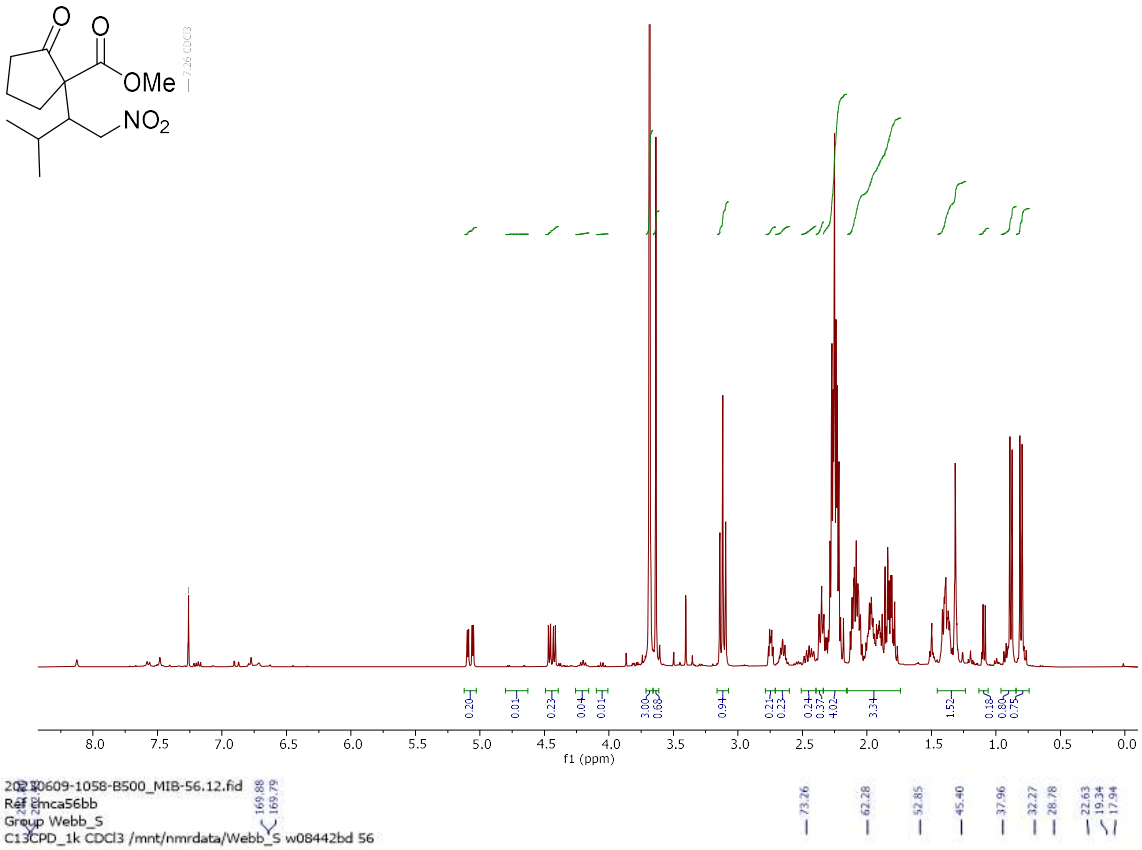

f2 (ppm)
f1 (ppm)

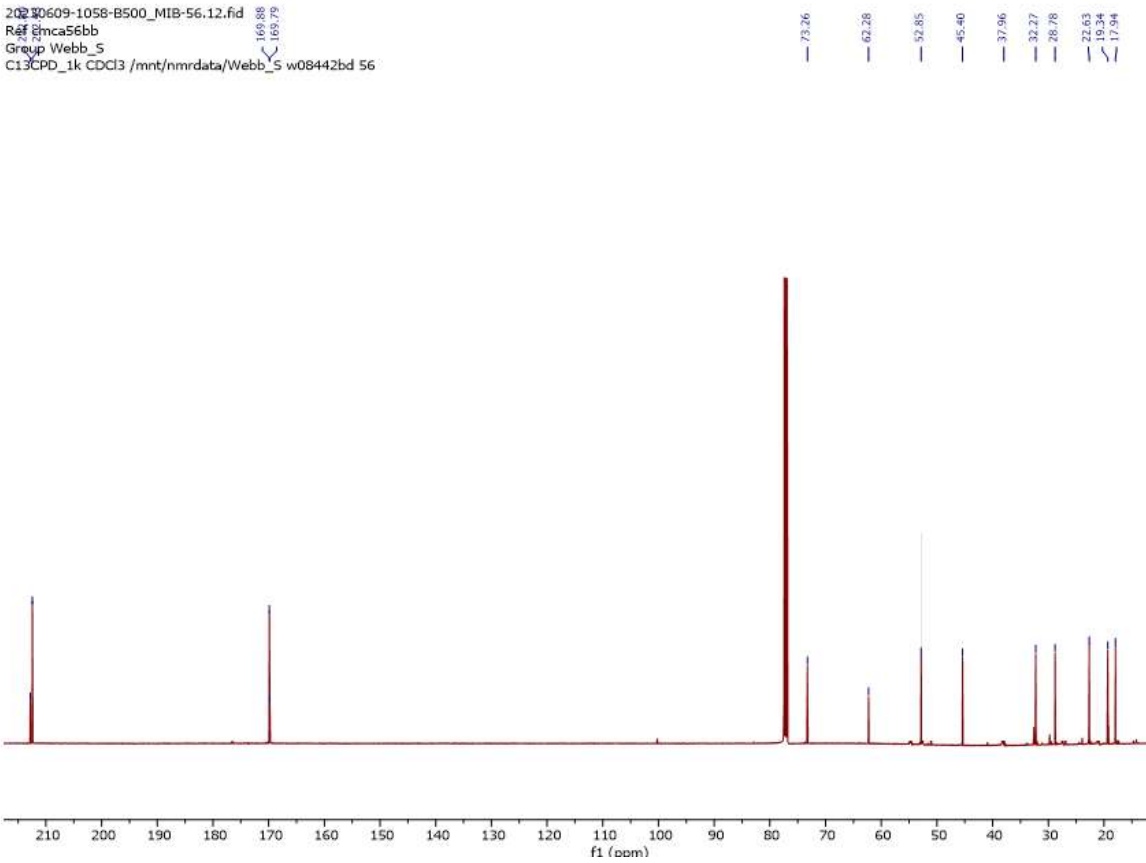

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f2 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
f1 (ppm)

1-Methyl-1-(1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 12a (in $CDCl_3$)



Methyl 1-(3-methyl-1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 11a (in $CDCl_3$)





5. Circular dichroism spectra of peptides 1, 2 and 3

Circular Dichroism (CD) measurements were performed at 25 °C on a Chirascan qCD applied photophysics spectrometer, using a high precision 1 mm light path quartz cell Hellma Analytics, with the solvent and concentration stated.

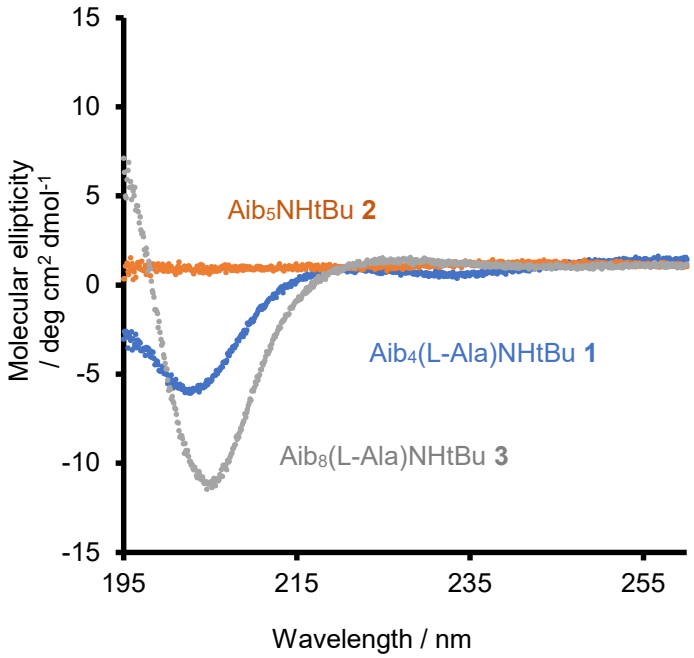


Figure S1. Circular dichroism spectra at 25 °C of Aib_4(L-Ala)NHtBu **1** (0.258 mM, blue trace), Aib_5NHtBu **2** (0.251 mM, orange trace), Aib_8(L-Ala)NHtBu **3** (0.260 mM, grey trace) in methanol.

Circular Dichroism (CD) measurements show a negative band at the diagnostic wavelength of 205 nm for peptides Aib_4-L-AlaNHtBu **1** and Aib_8-L-AlaNHtBu **3**, which is consistent with an excess of *P* 3_{10} helicity.[4] This signal is stronger for the longer peptide **3**, commensurate with the increased number of residues in this peptide. The achiral peptide Aib_5NHtBu **2** gave no CD signal as expected.

6. NMR spectra of crude reaction mixtures for measurement of diastereomeric ratios

6.1. 1-Methyl-1-(2-nitro-1-phenylethyl)-2 oxocyclopentane-1-carboxylate, 10

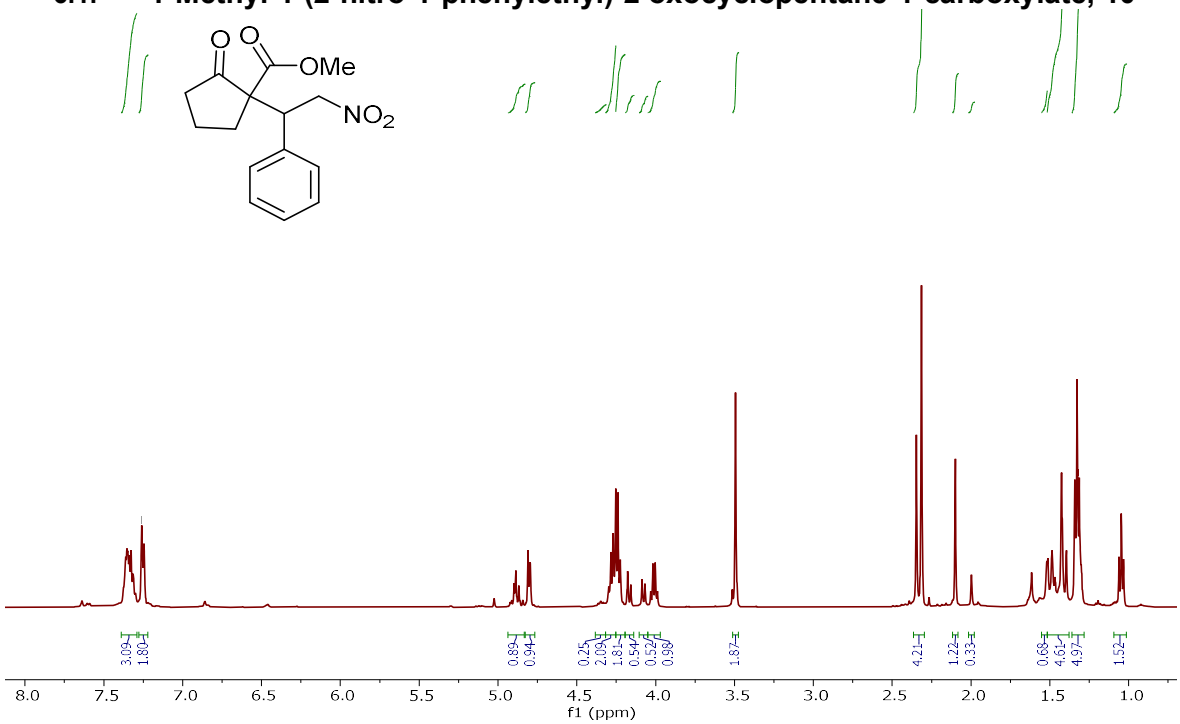


Figure S2. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 96:4).

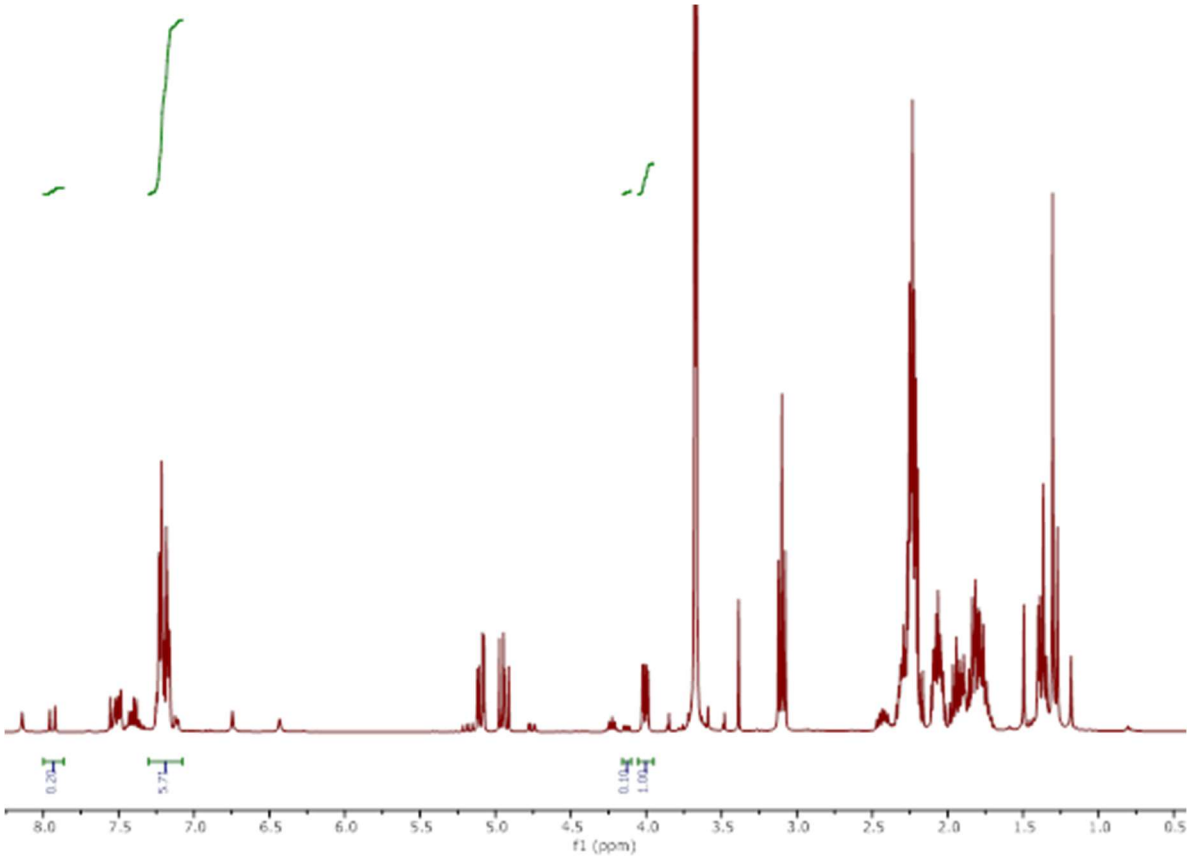


Figure S3. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 40 °C in $CDCl_3$ (diastereomeric ratio: 91:9).

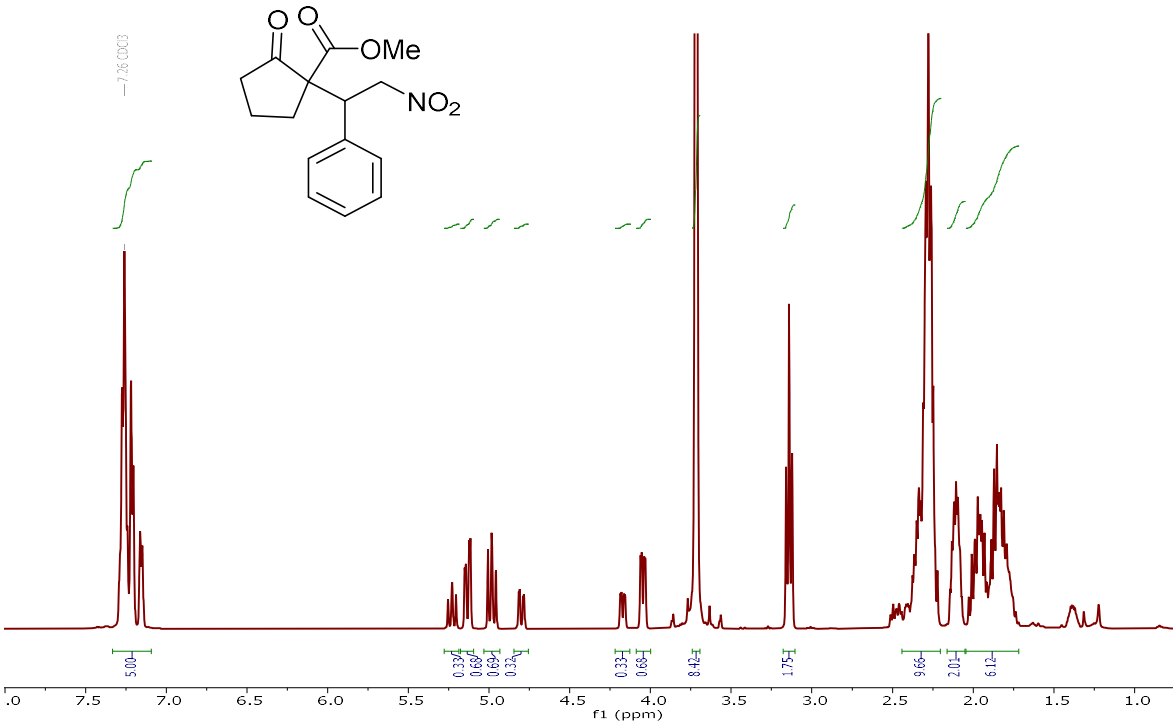


Figure S4. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with $^{t}BuNH_2$ at 20 °C in $CDCl_3$ (diastereomeric ratio: 68:32).

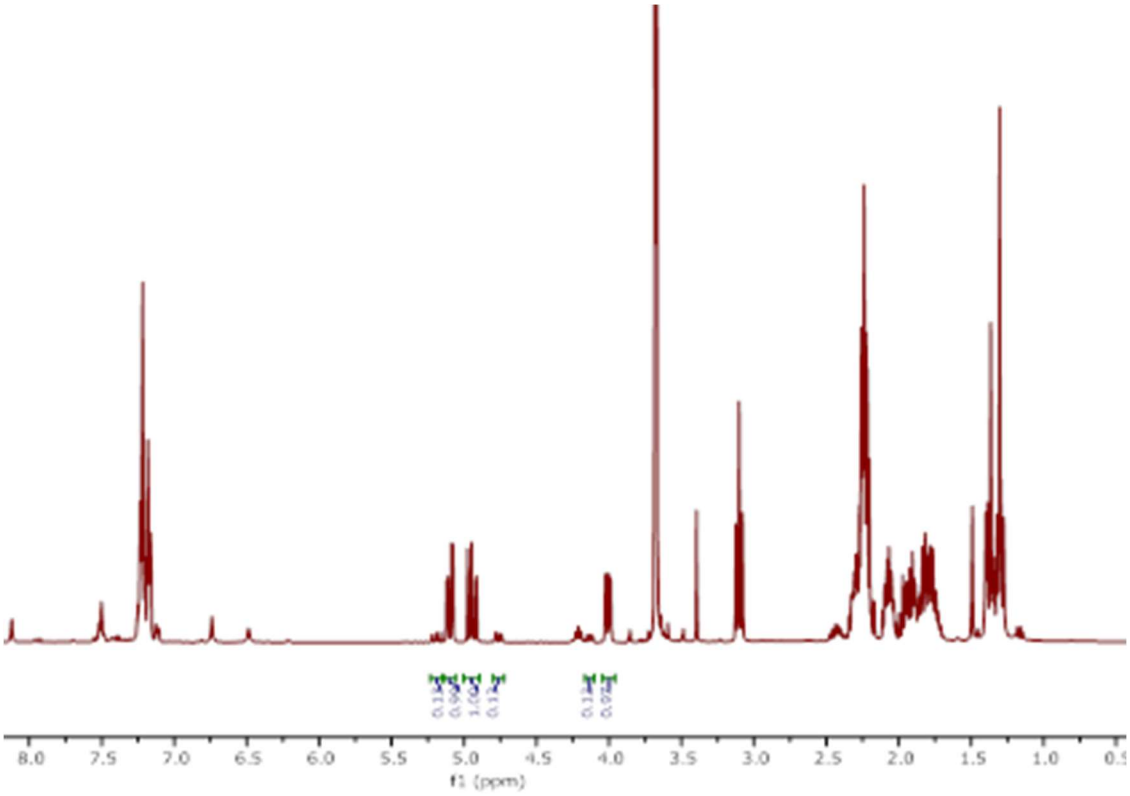


Figure S5. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with Aib_4(L-Ala)NHtBu **1** at 0 °C without solvent (diastereomeric ratio: 90:10).

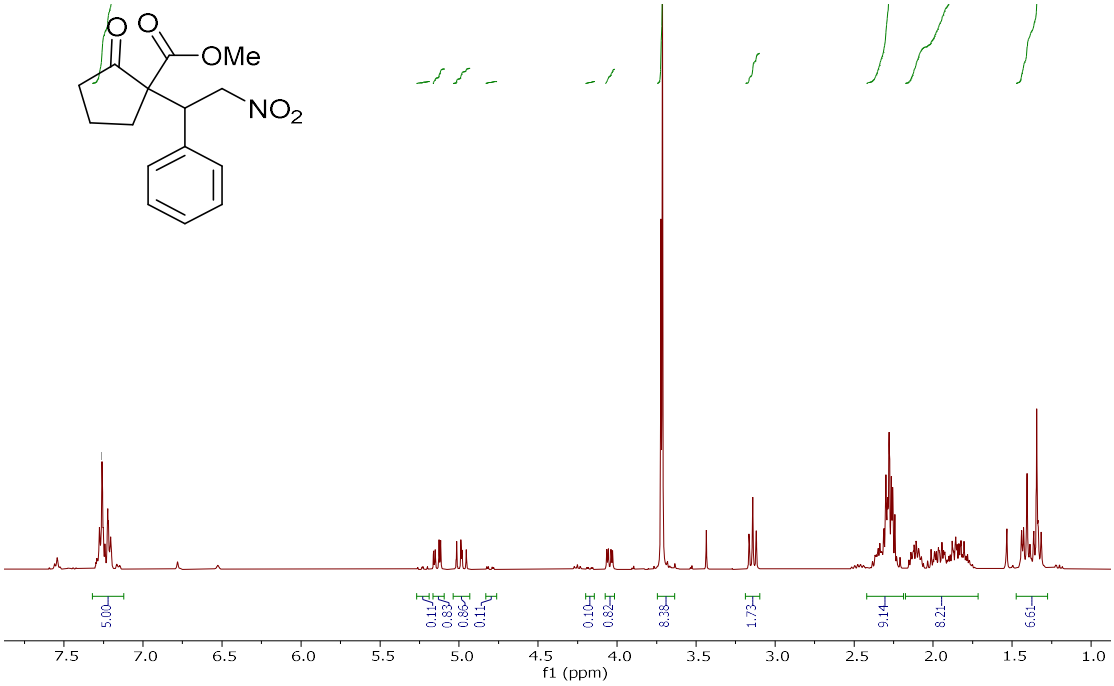


Figure S6. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with $^{t}BuNH_2$ at 0 °C without solvent (diastereomeric ratio: 59:41).

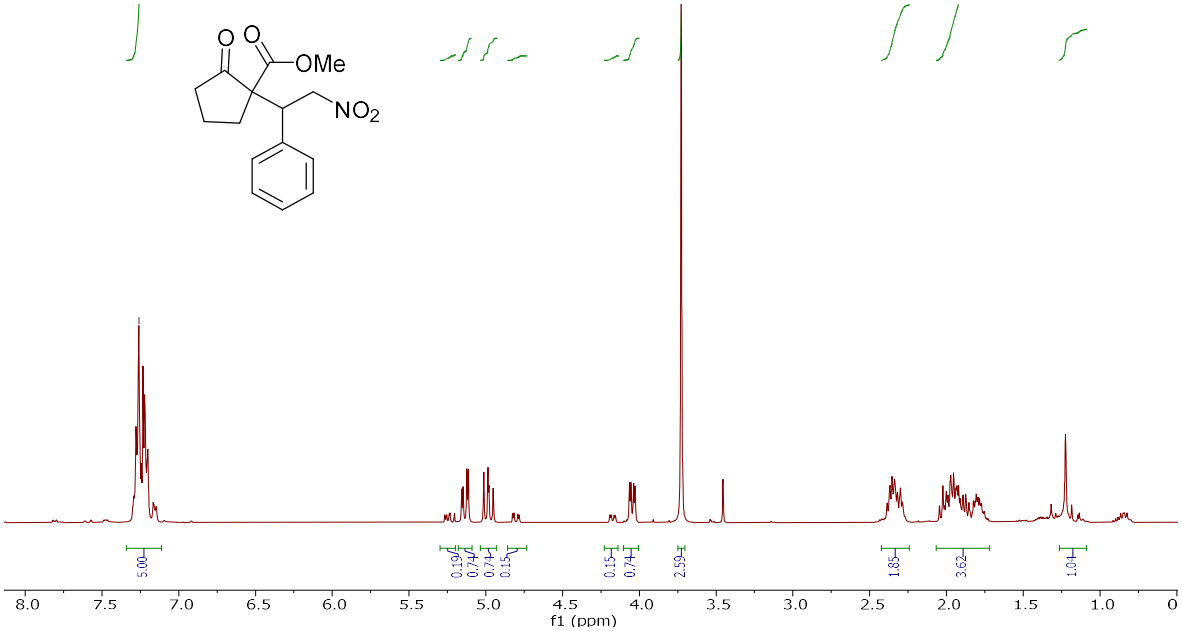


Figure S7. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with Aib(L-Ala)NH^{t}Bu **4** at 0 °C without solvent (diastereomeric ratio: 82:18).

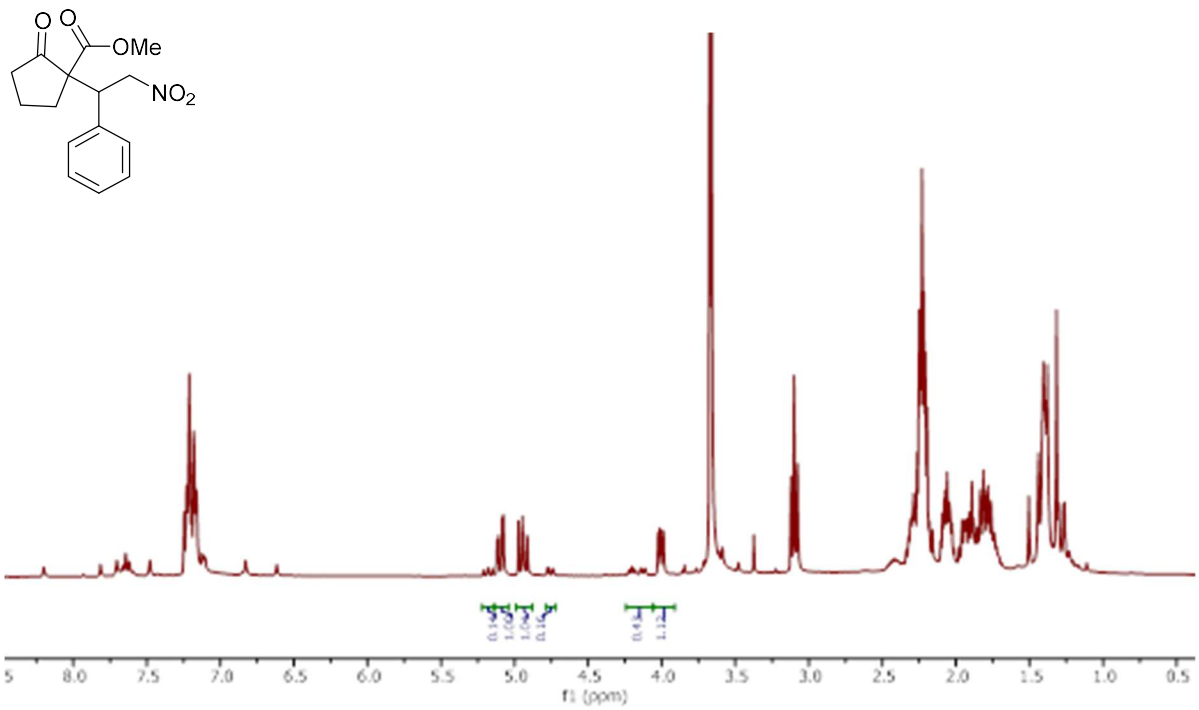


Figure S8. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with Aib_8(L-Ala)NH^{t}Bu **3** at 20 °C in $CDCl_3$ (diastereomeric ratio: 88:12).

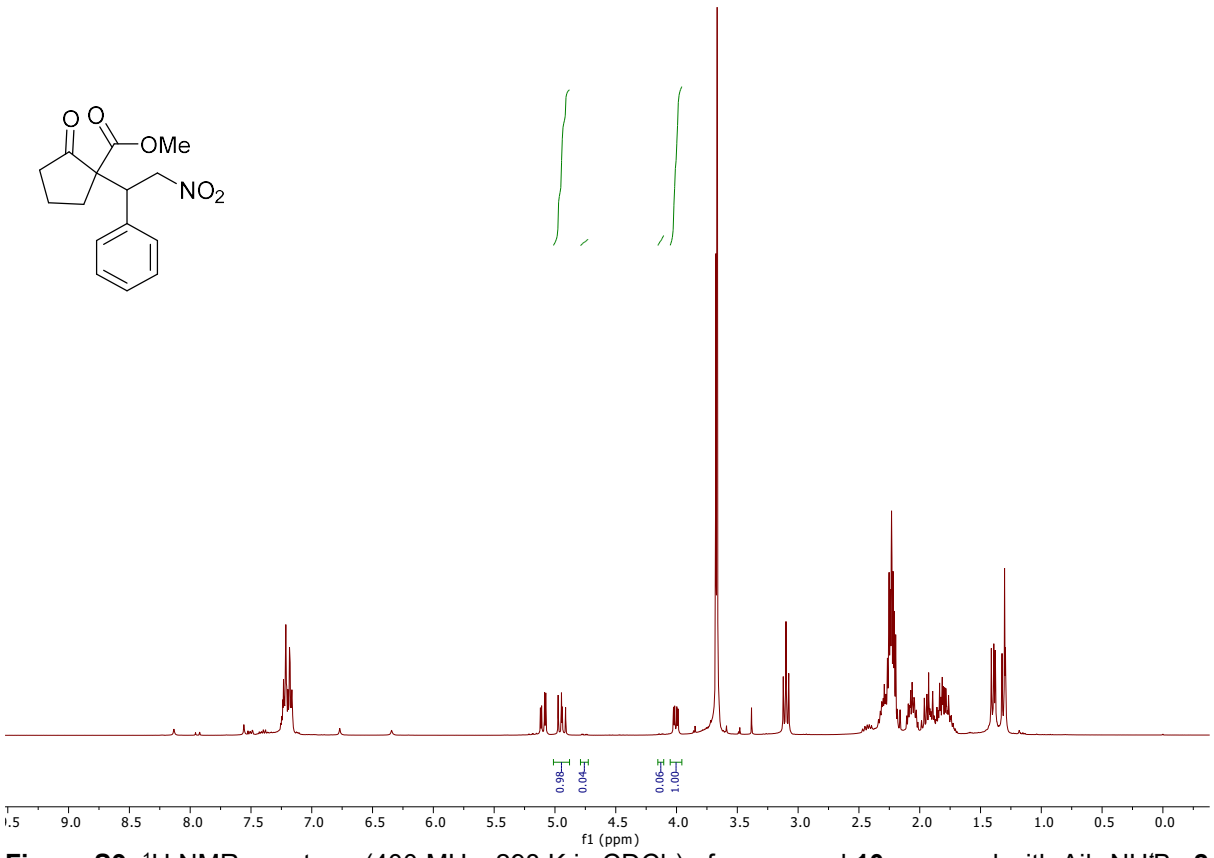


Figure S9. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with Aib_5NH^{t}Bu **2** at 20 °C in $CDCl_3$ (diastereomeric ratio: 95:5).

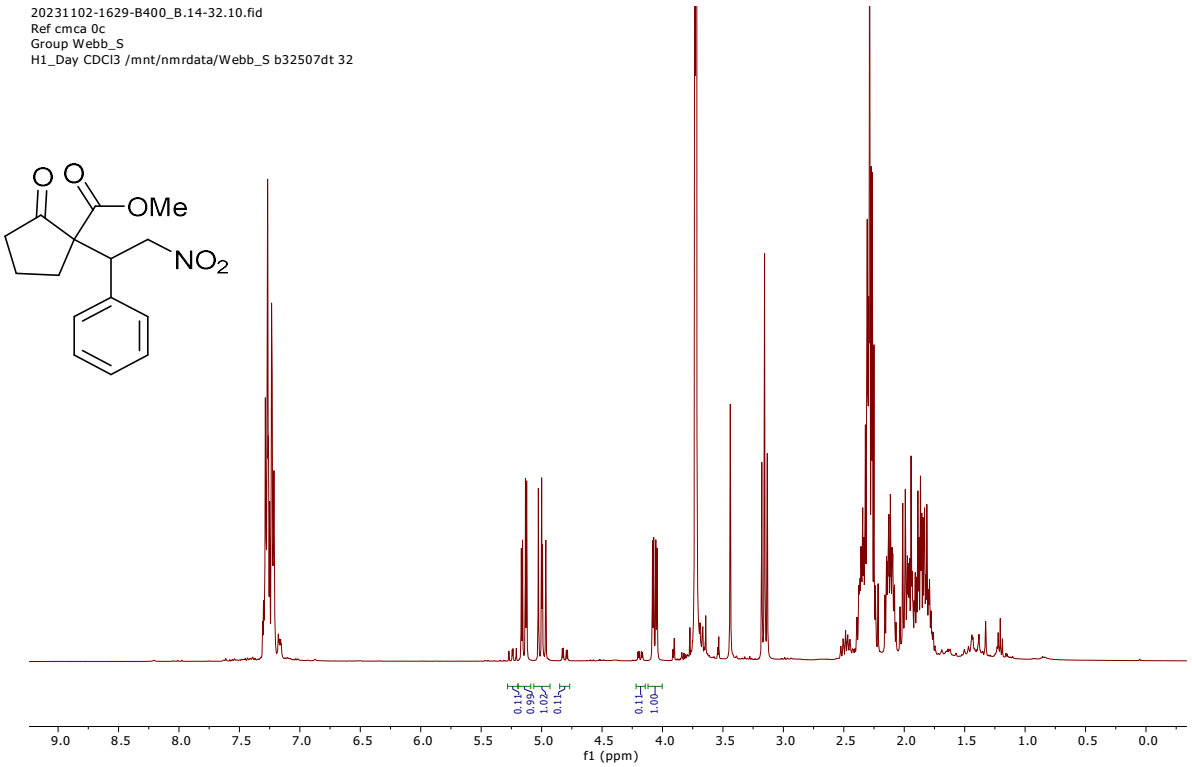
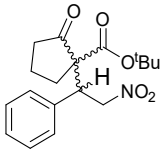


Figure S10. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **10** prepared with Aib_4(D-Phe)NH^tBu **5** at 25 °C in $CDCl_3$ (diastereomeric ratio: 9:1).

6.2. 1-tert-Butyl-1-(2-nitro-1-phenylethyl)-2 -oxocyclopentane-1-carboxylate, 13



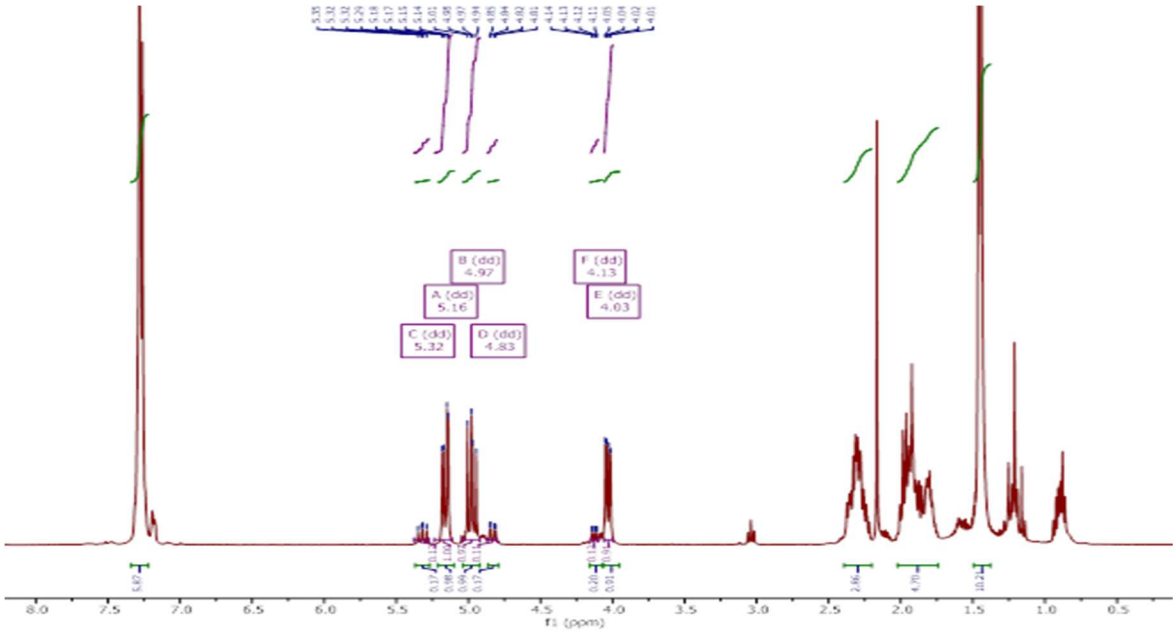


Figure S11. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **13** prepared with H_2N^tBu at 20 °C in $CDCl_3$ (diastereomeric ratio: 87:13).

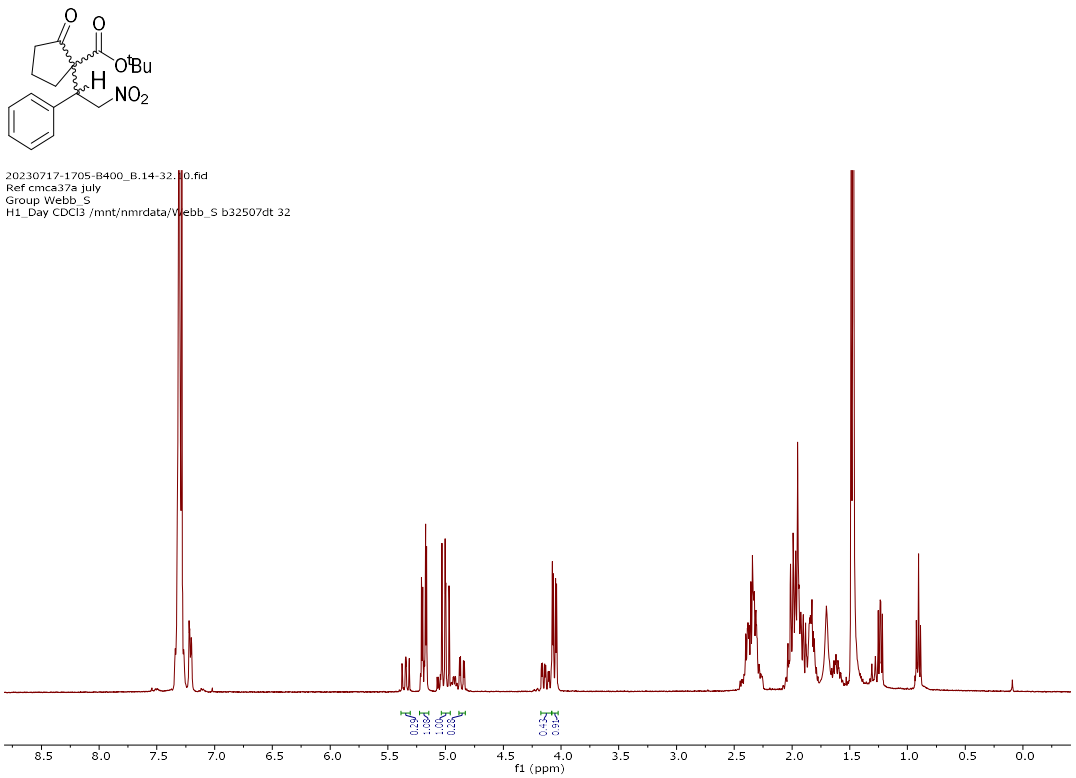


Figure S12. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **13** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 78:22).

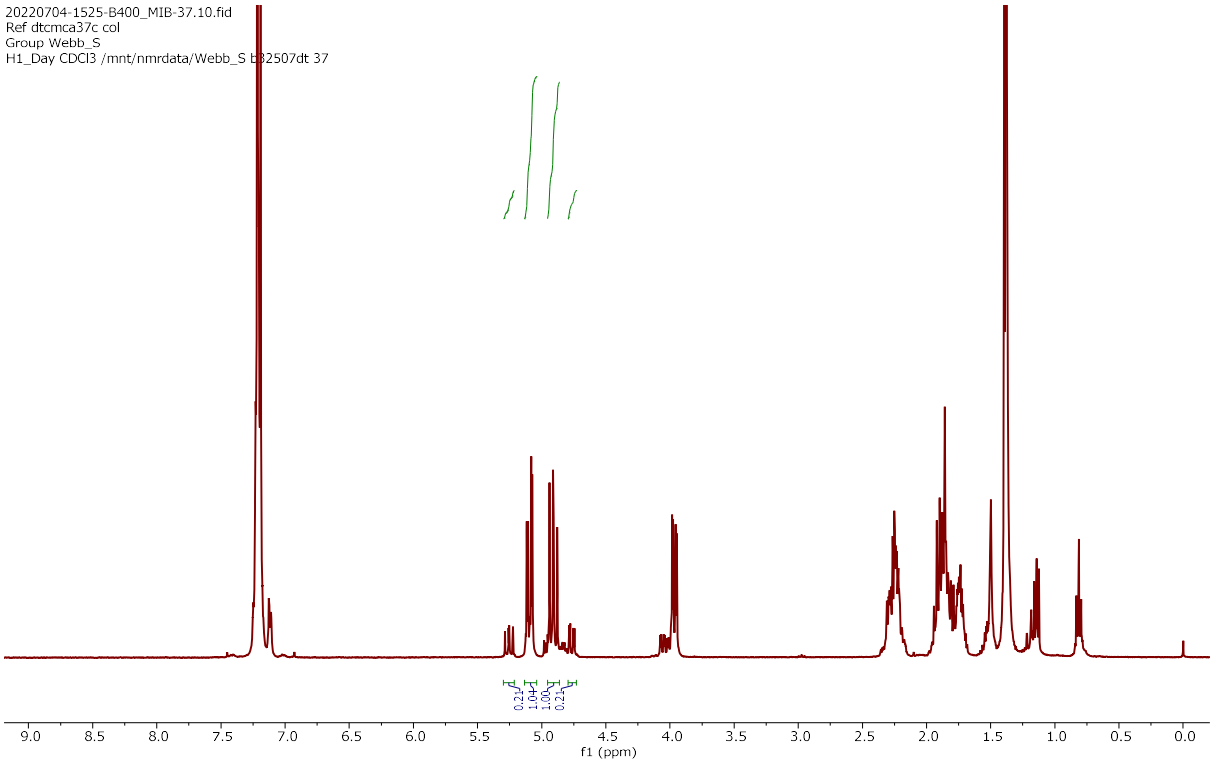


Figure S13. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **13** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 0 °C, no solvent (diastereomeric ratio: 80:20).

6.3. Methyl 1-(2-nitro-1-phenylethyl)-2-oxocyclohexane-1-carboxylate, 15

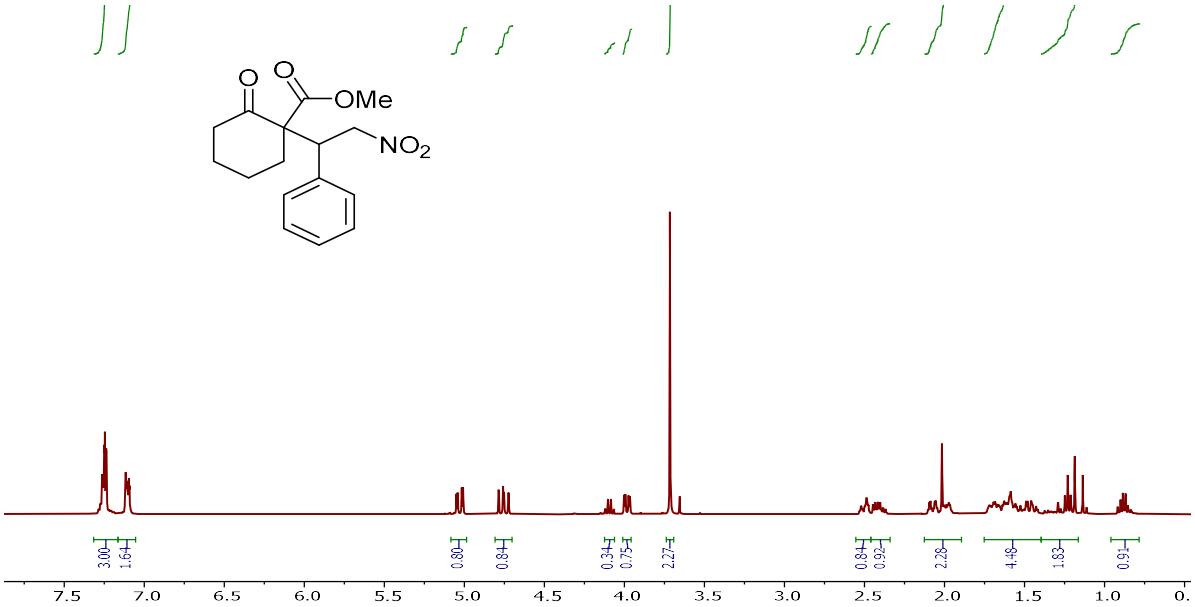


Figure S14. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **15** prepared with Aib_4(L-Ala)NH^tBu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 92:8).

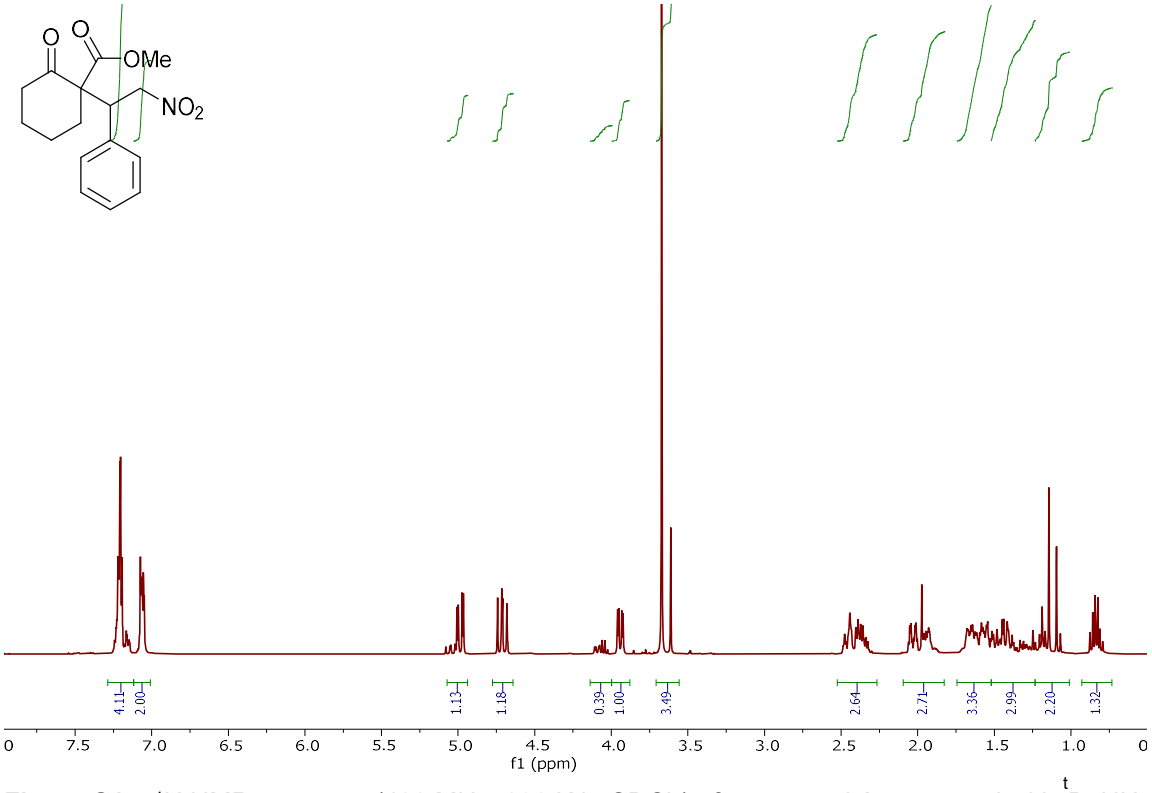


Figure S15. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **15** prepared with $^tBuNH_2$ at 20 °C in $CDCl_3$ (diastereomeric ratio: 83:17).

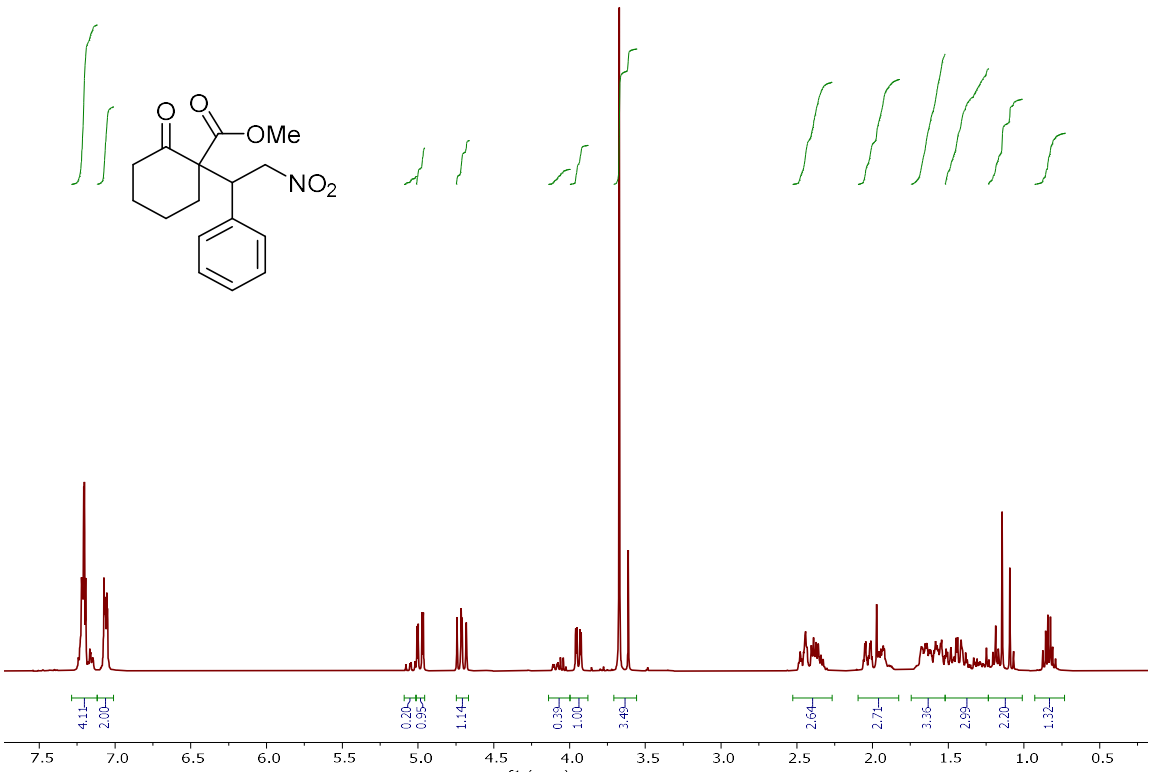


Figure S16. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **15** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 0 °C with no solvent (diastereomeric ratio: 94:6).

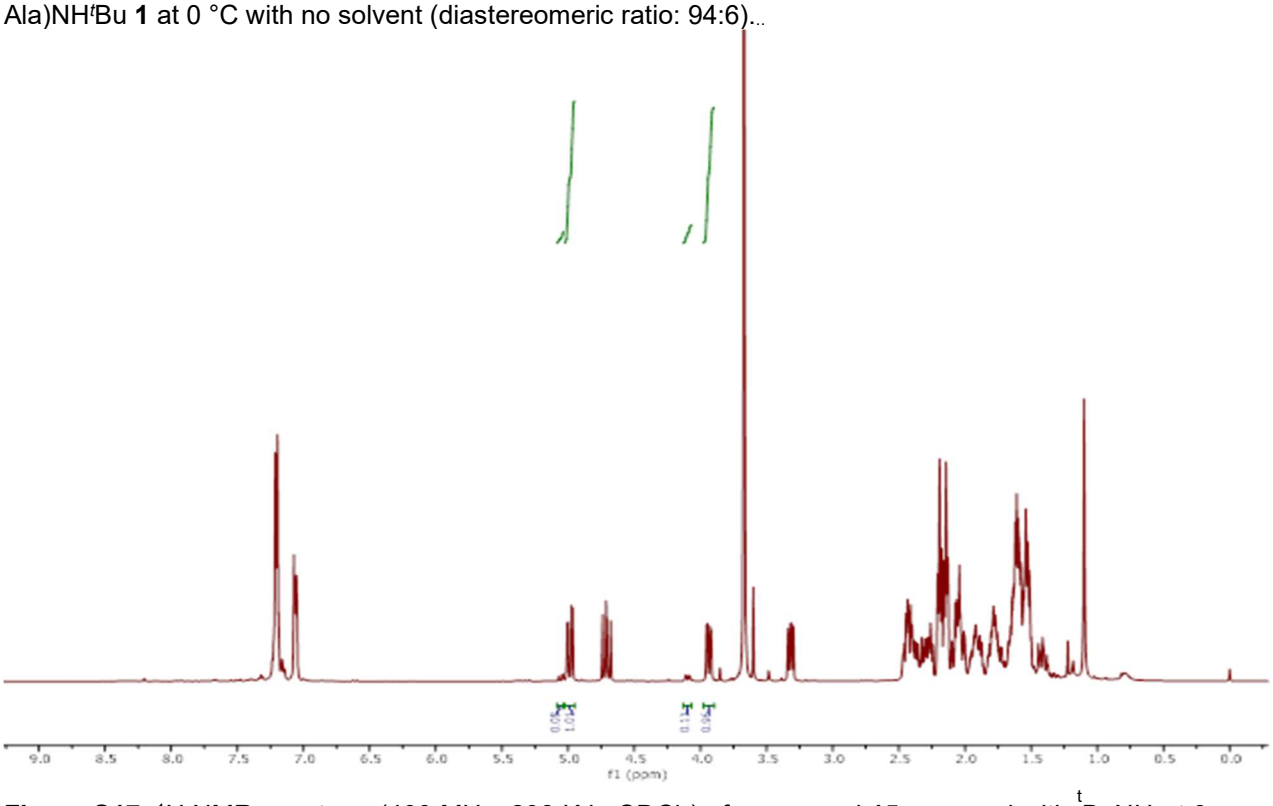


Figure S17. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **15** prepared with ^{t}BuNH$_2$ at 0 °C without solvent (diastereomeric ratio: 91:9).

6.4. Ethyl 4,4-dimethyl-2-(2-nitro-1-phenylethyl)-3-oxopentanoate, 20a

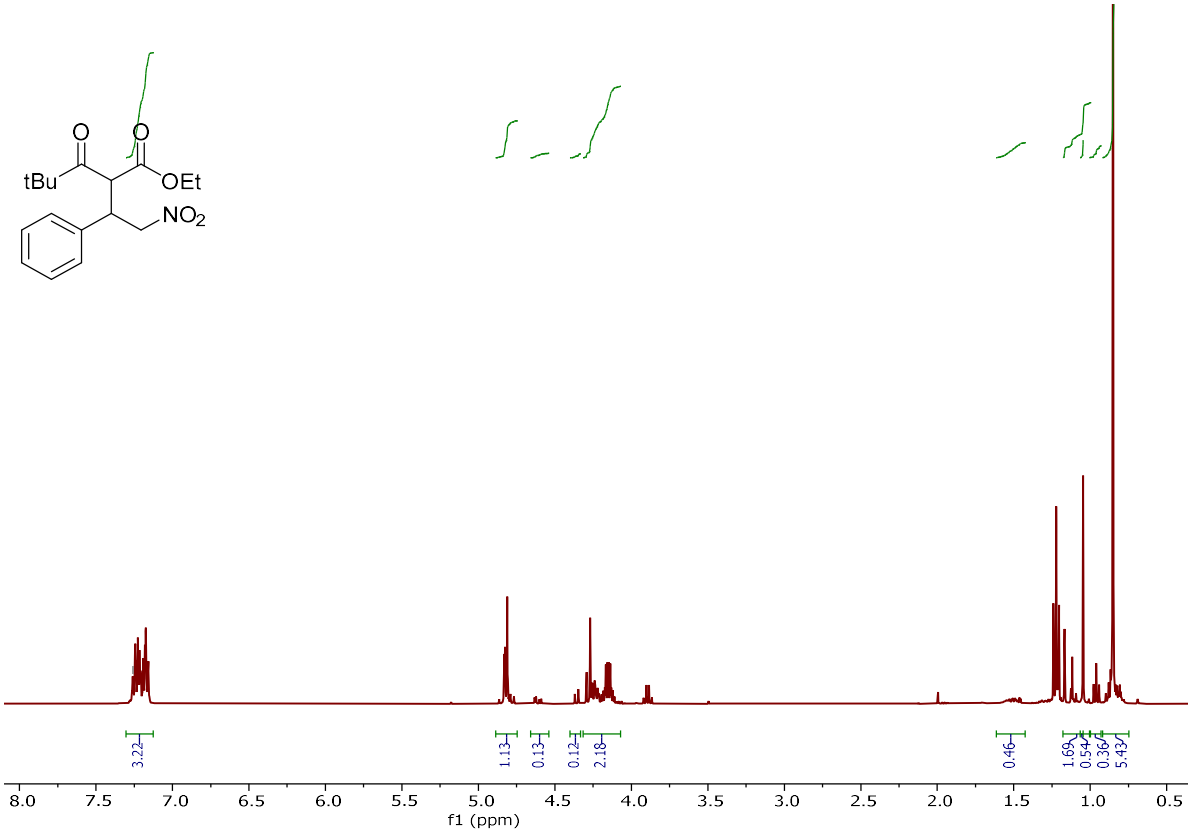


Figure S18. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **20a** prepared with Aib$_4$(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 95:5).

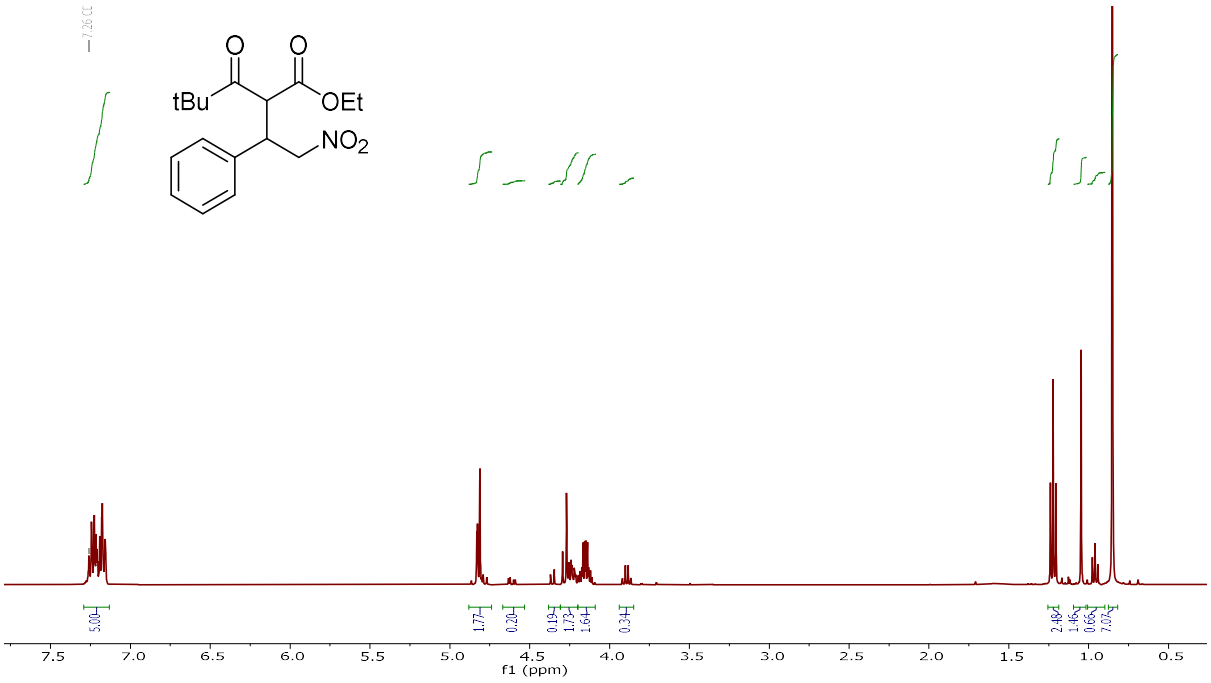


Figure S19. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **20a** prepared with ^{t}BuNH$_2$ at 20 °C in $CDCl_3$ (diastereomeric ratio: 91:9).

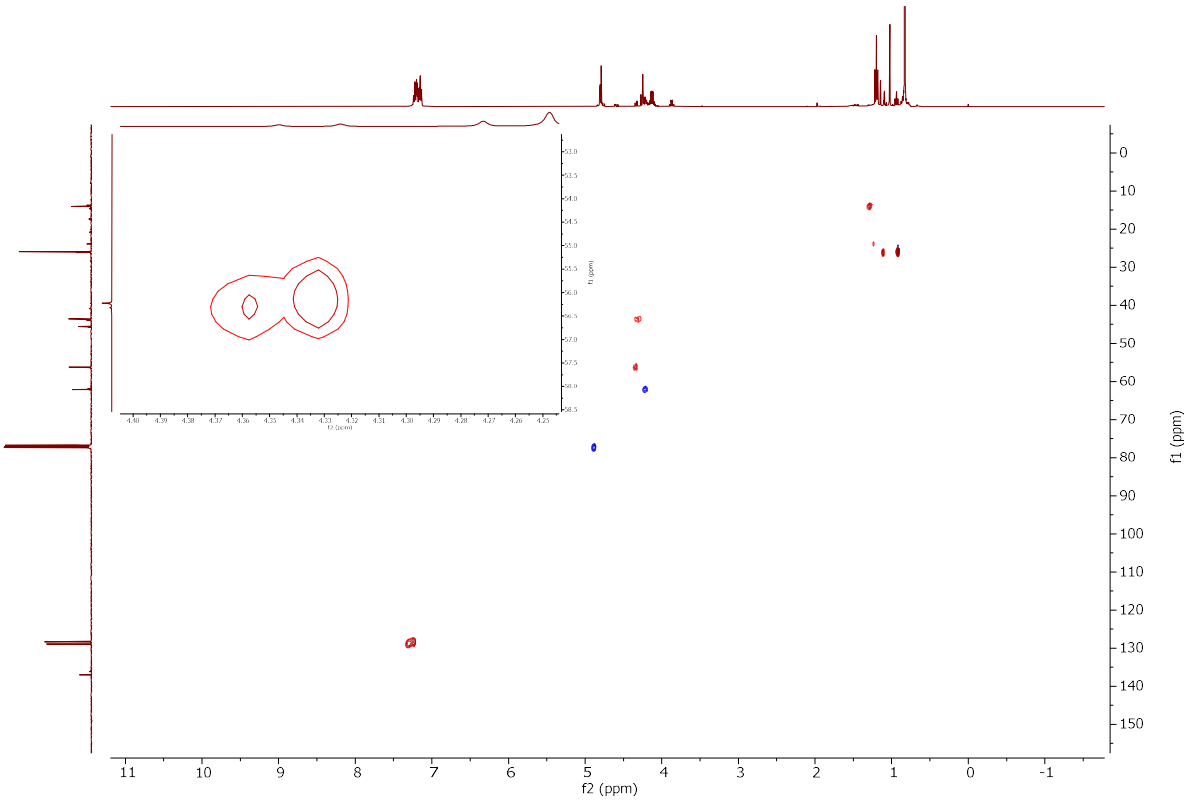


Figure S19. ^{1}H ^{13}C HSQC NMR spectrum of compound **20a** in $CDCl_3$.

6.5. Ethyl 2-benzoyl-4-nitro-3-phenylbutanoate, 21a

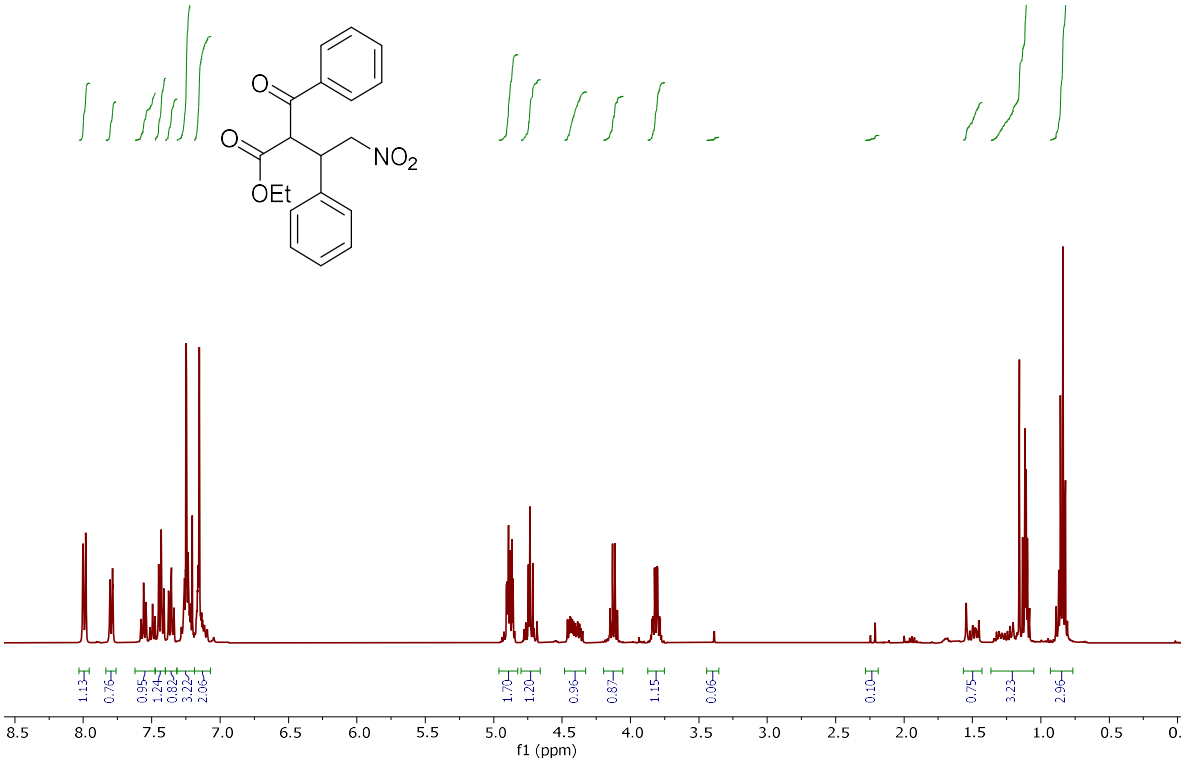


Figure S21. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **21a** prepared with Aib_4(L-Ala)NH^tBu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 55:45).

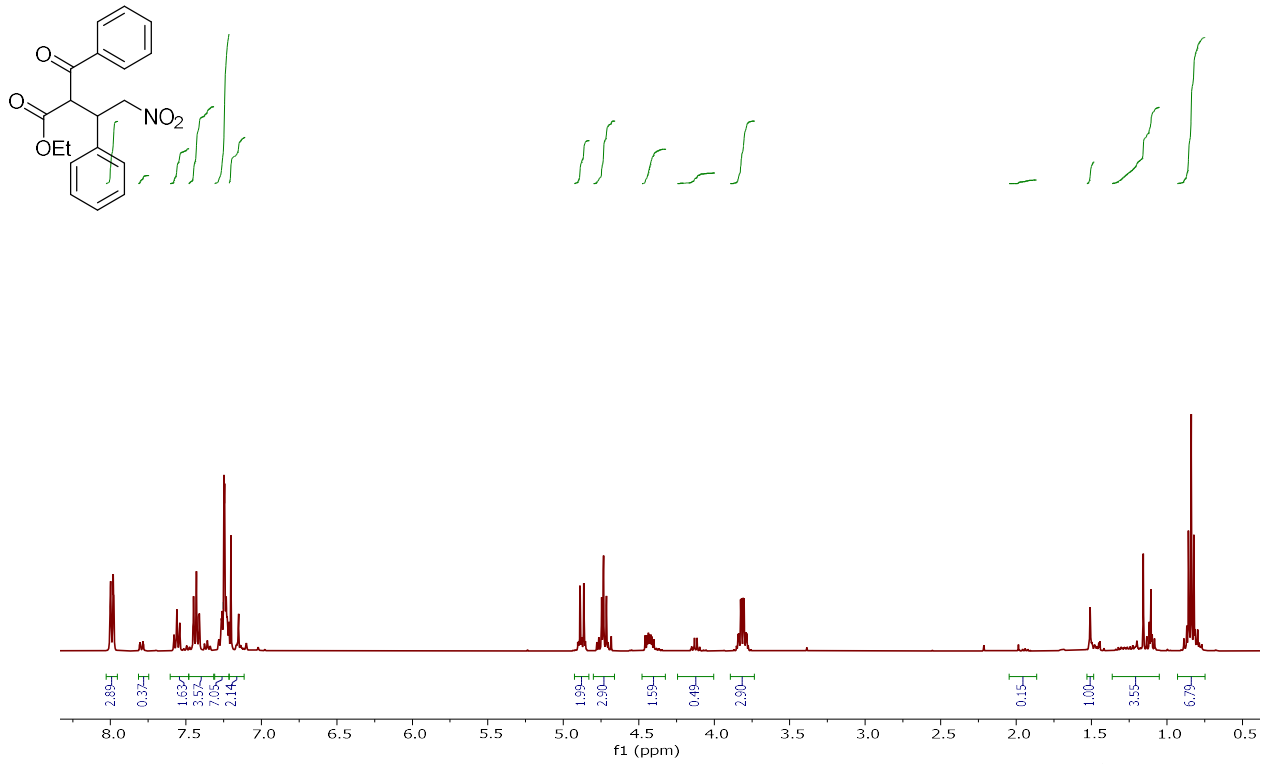


Figure S22. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **21a** prepared with $^{t}BuNH_2$ at 20 °C in $CDCl_3$ (diastereomeric ratio: 50:50).

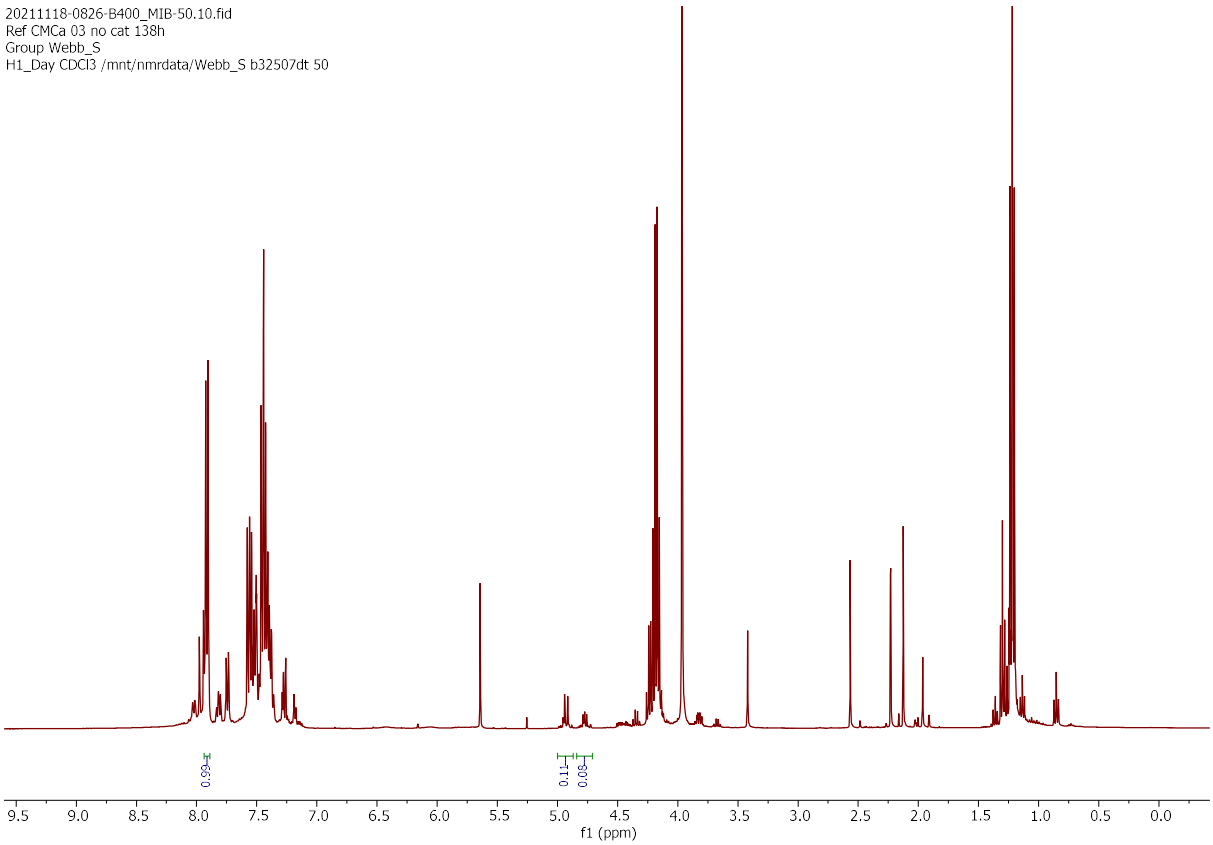


Figure S23. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **21a** prepared with no catalyst at 20 °C in $CDCl_3$ (diastereomeric ratio: 58:42).

6.6. Dimethyl 2-(2-nitro-1-phenylethyl)malonate, 17a

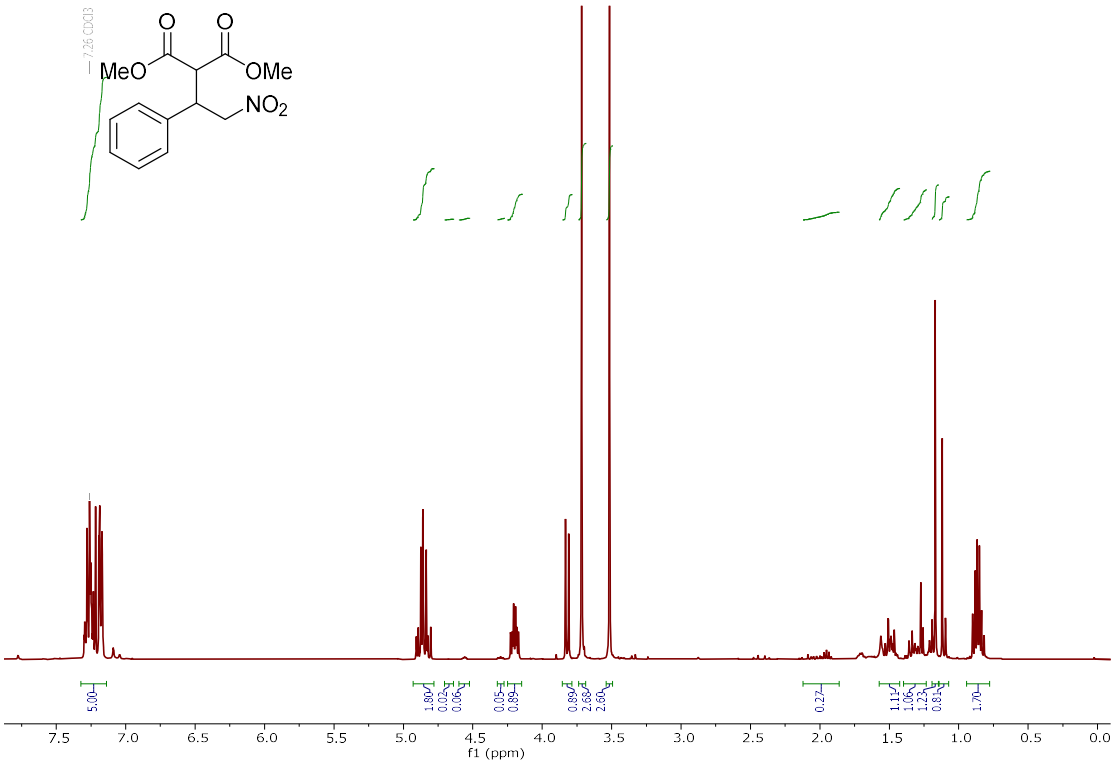


Figure S24. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **17a** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$.

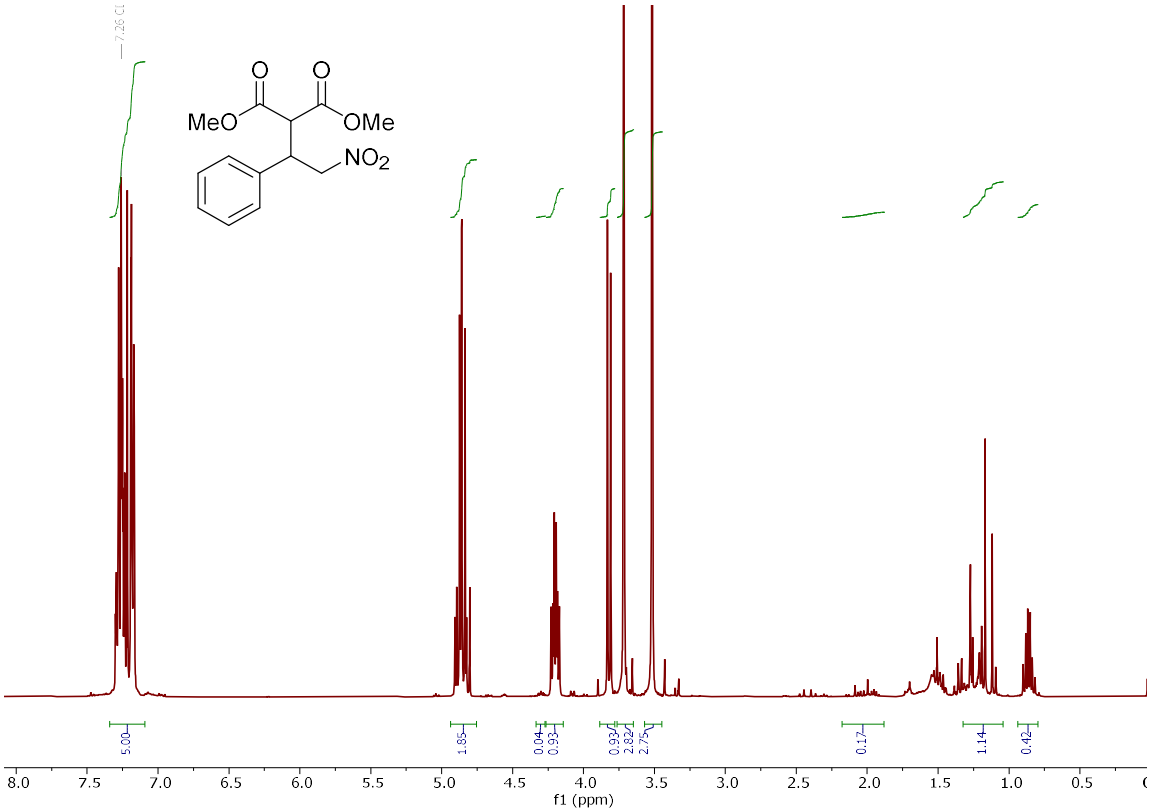


Figure S25. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **17a** prepared with $^{t}BuNH_2$ at 20 °C in $CDCl_3$

6.7. 1-Acetyl-2-(2-nitro-1-phenylethyl)indolin-3-one, 16a

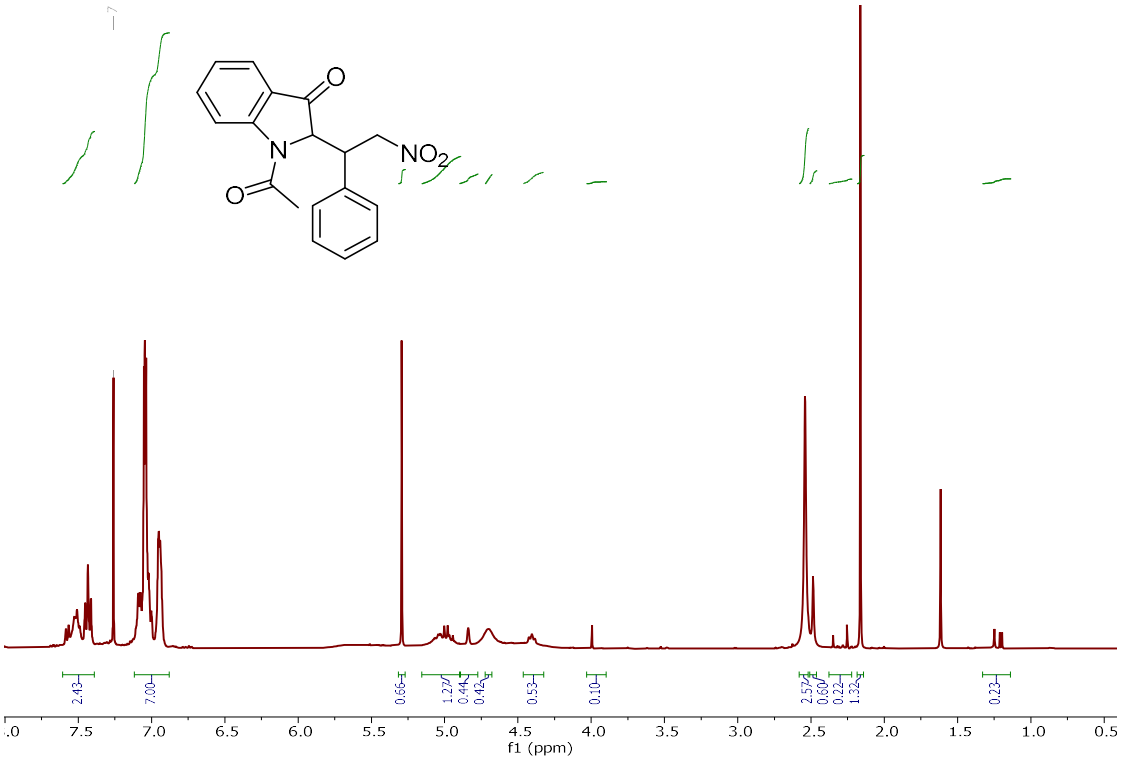


Figure S26. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **16a** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 85:15).

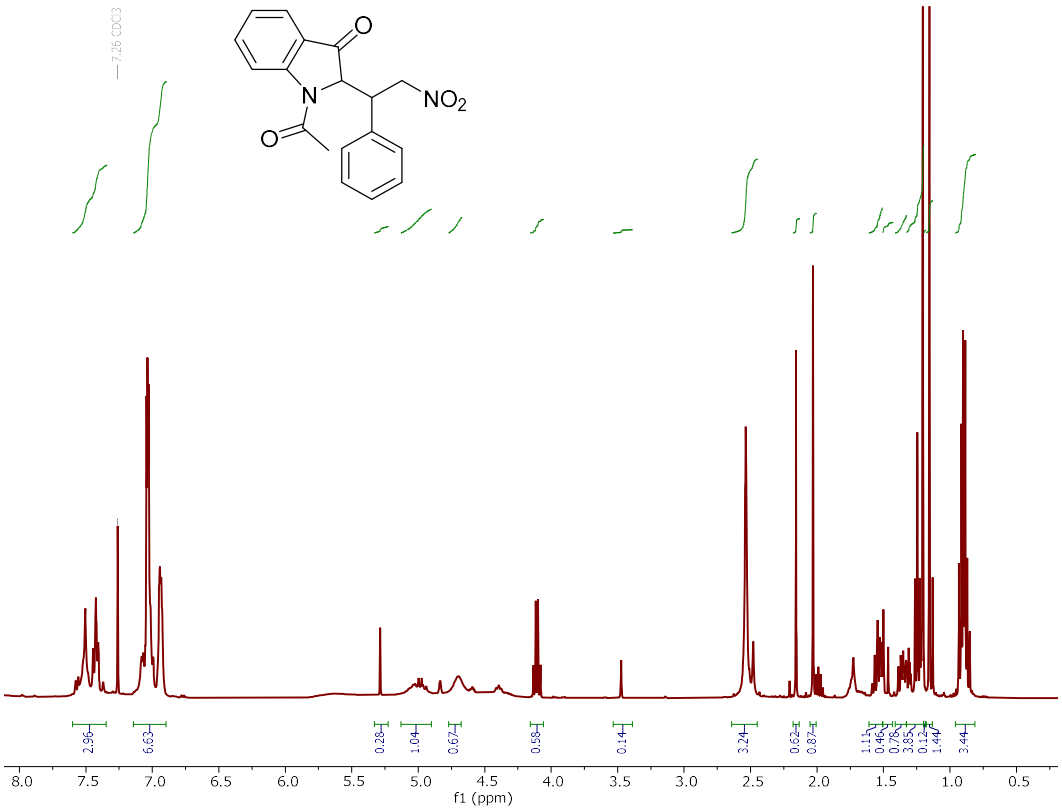


Figure S27. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **16a** prepared with $^{t}BuNH_2$ at 20 °C in $CDCl_3$ (diastereomeric ratio: 85:15).

6.8. 3-(2-Nitro-1-phenylethyl)pentane-2,4-dione, 18a

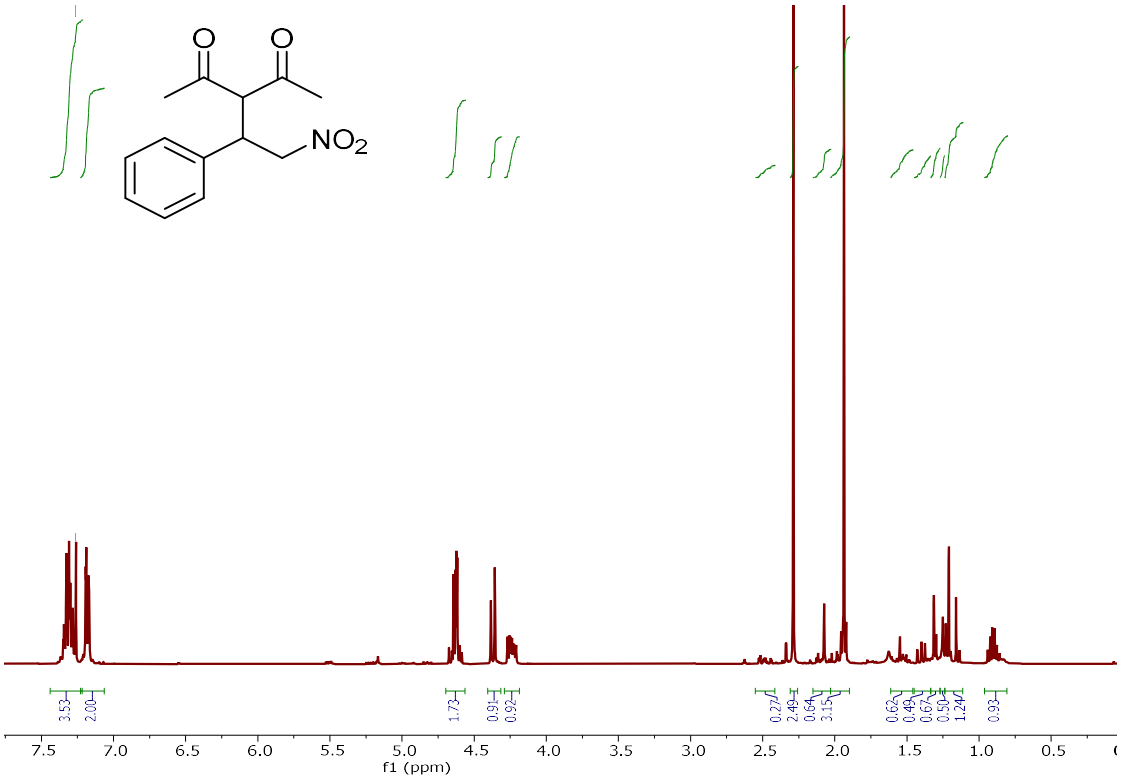


Figure S28. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **18a** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$.

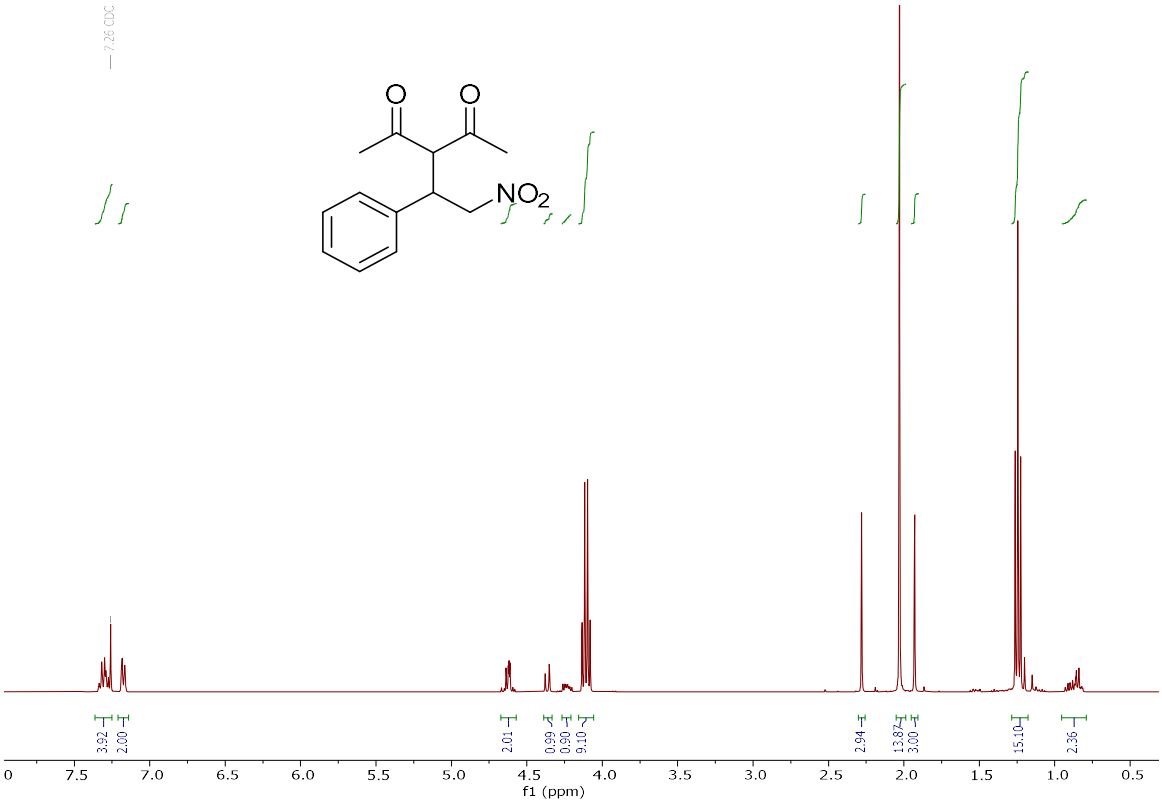


Figure S29. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **18a** prepared with $^{t}BuNH_2$ at 20 °C in $CDCl_3$

6.9. 2-Acetyl-2-(2-nitro-1-phenylethyl)cyclopentan-1-one, 14a

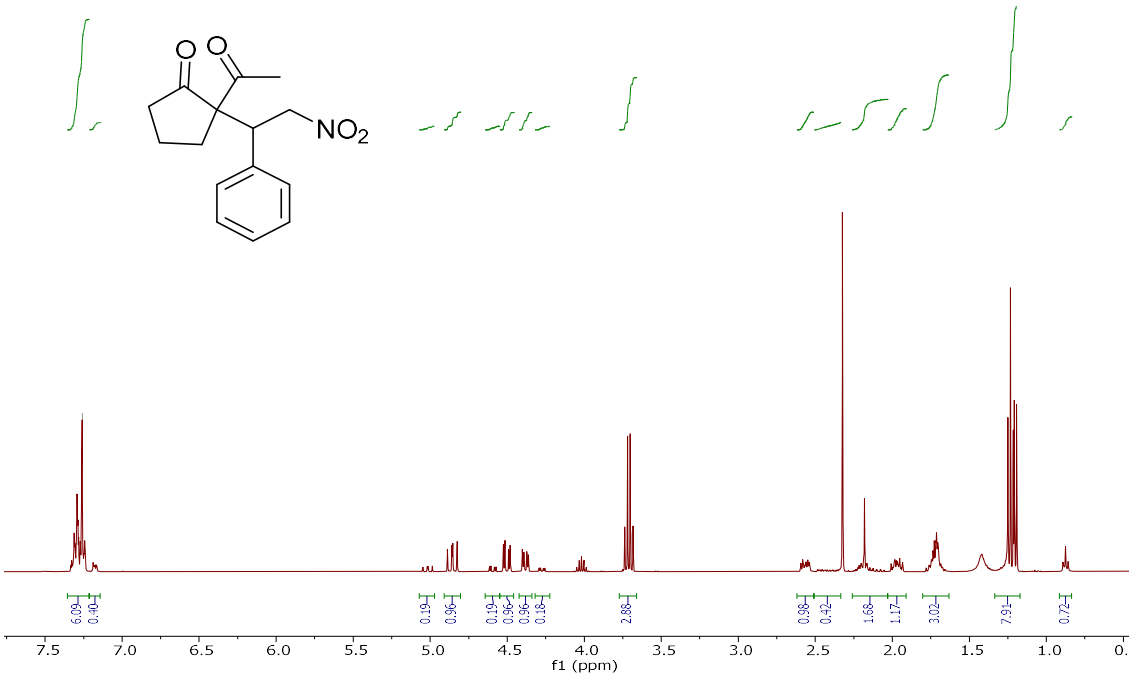


Figure S30. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **14a** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 84:16).

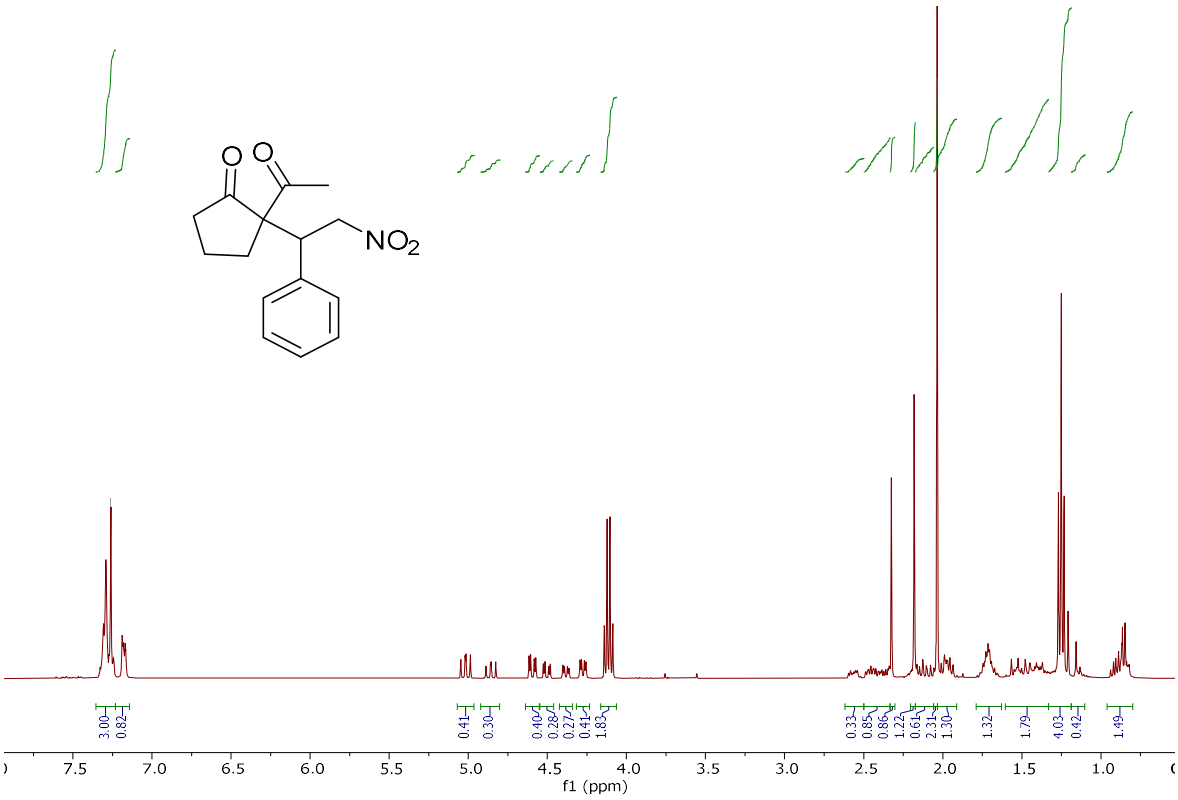


Figure S31. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **14a** prepared with $^{t}BuNH_2$ at 20 °C in $CDCl_3$ (diastereomeric ratio: 53:47).

6.10. 5,5-Dimethyl-3-(2-nitro-1-phenylethyl)hexane-2,4-dione, 19a

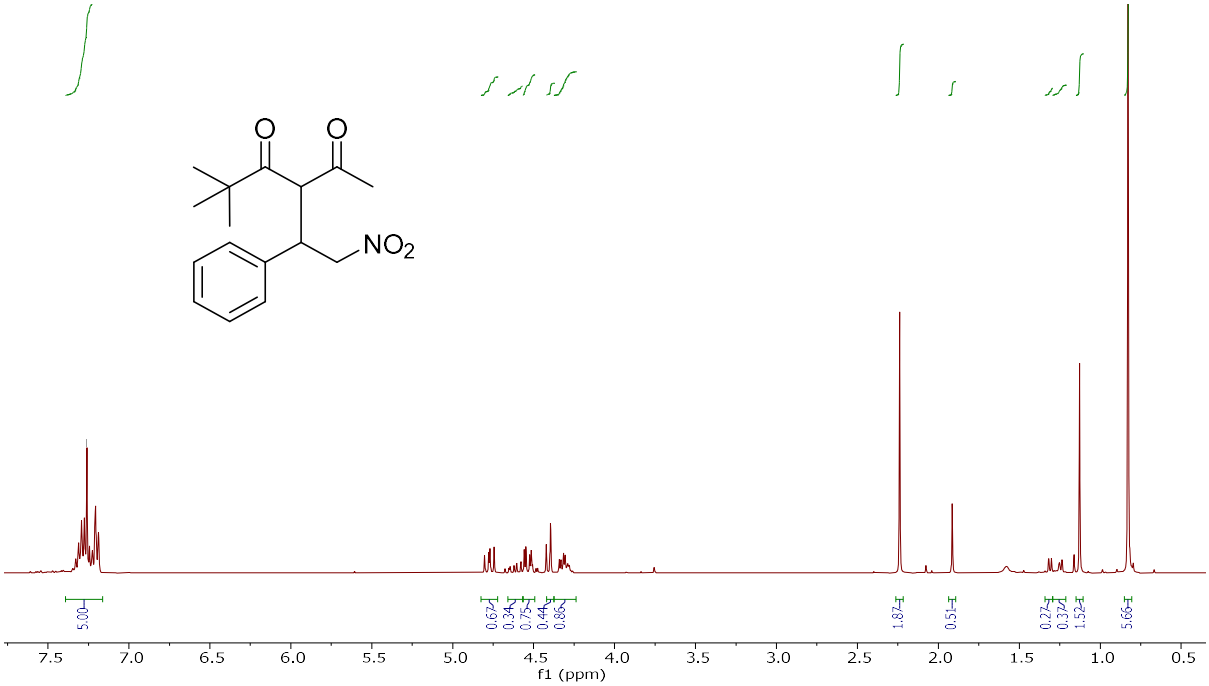


Figure S32. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **19a** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$ (diastereomeric ratio: 79:21).

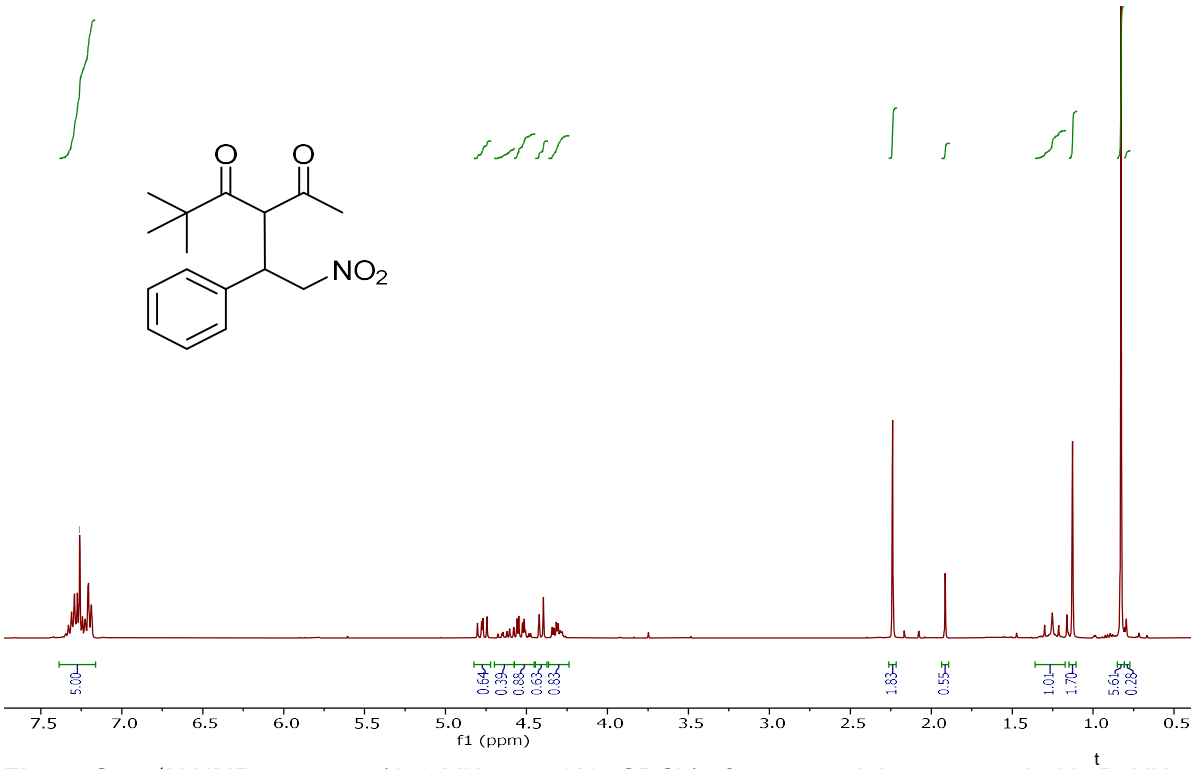


Figure S33. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **19a** prepared with $^{t}BuNH_2$ at 20 °C in $CDCl_3$ (diastereomeric ratio: 77:23).

6.11. 1-Methyl-1-(1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 12a

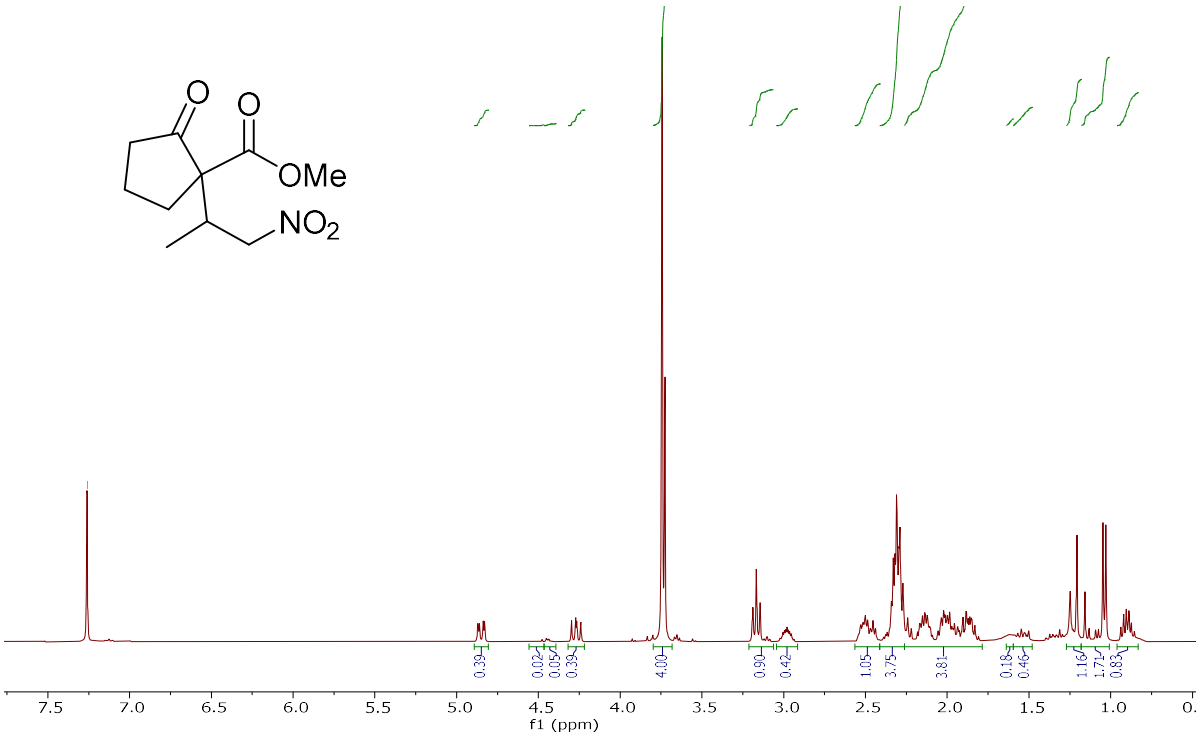


Figure S34. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **12a** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 0 °C without solvent (diastereomeric ratio: 89:11).

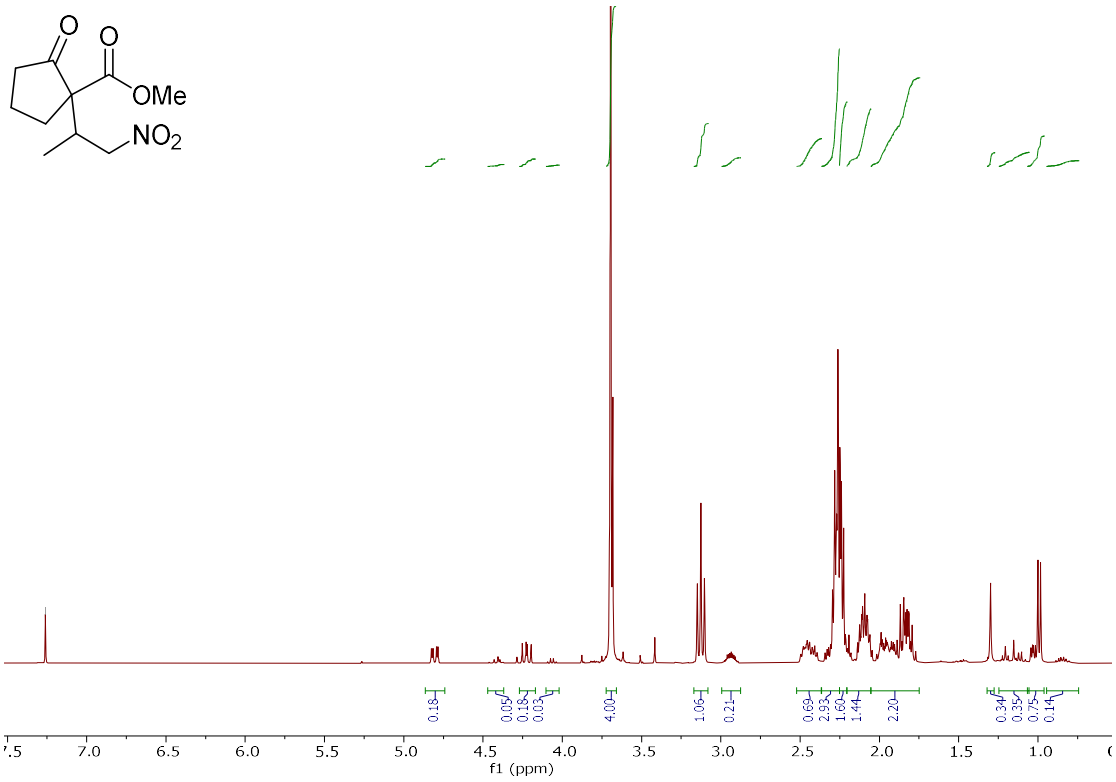


Figure S35. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **12a** prepared with $^{t}BuNH_2$ at 0 °C without solvent (diastereomeric ratio: 89:11).

6.12. Methyl 1-(3-methyl-1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 11a

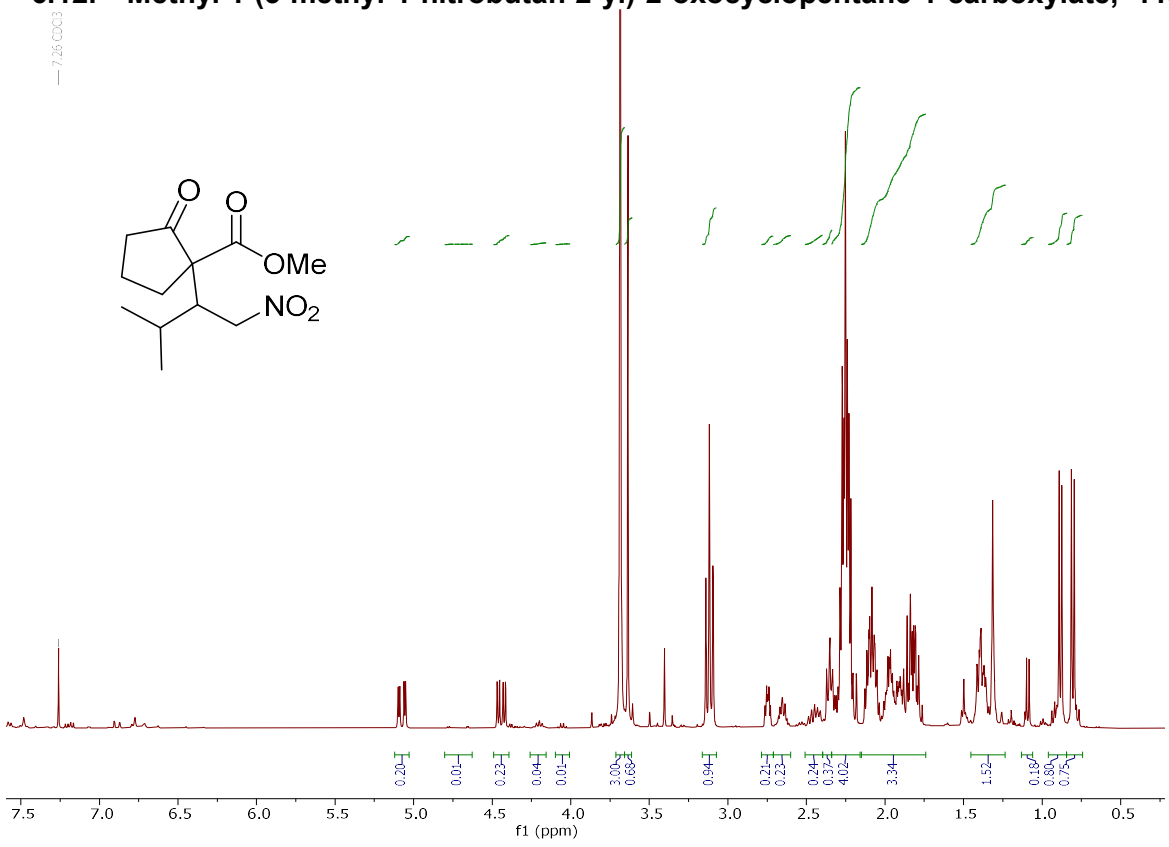


Figure S36. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **11a** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 0 °C without solvent (diastereomeric ratio: 99:1).

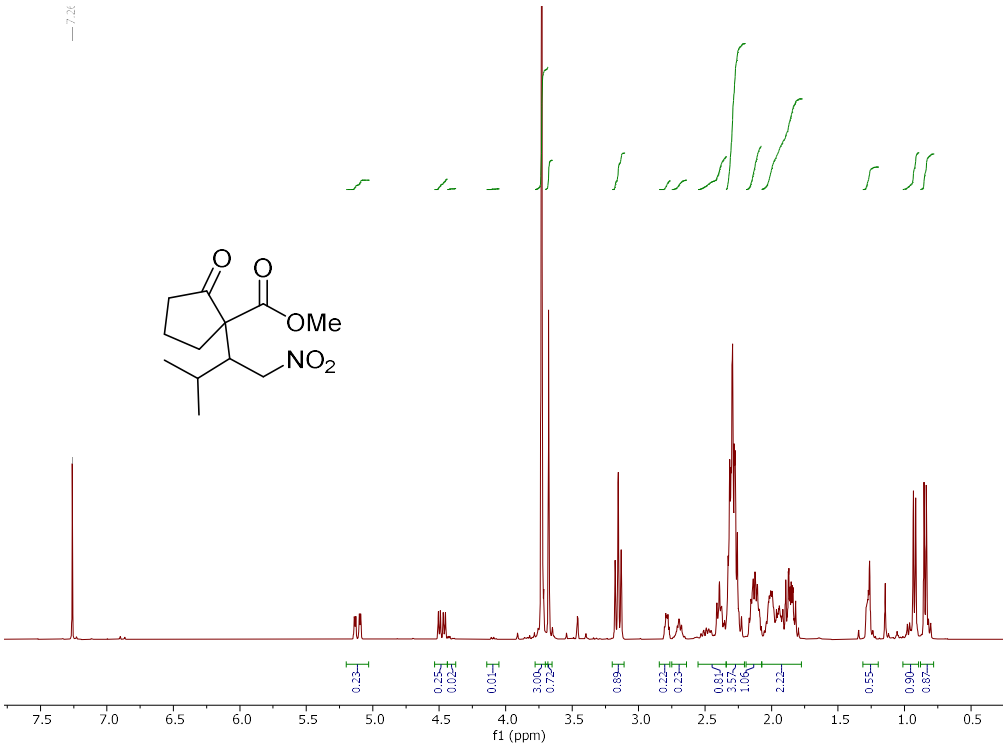


Figure S37. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of compound **11a** prepared with $^{t}BuNH_2$ at 0 °C without solvent (diastereomeric ratio: 98:2).

6.13. 2-(2-Nitro-1-phenylethyl)malononitrile 22

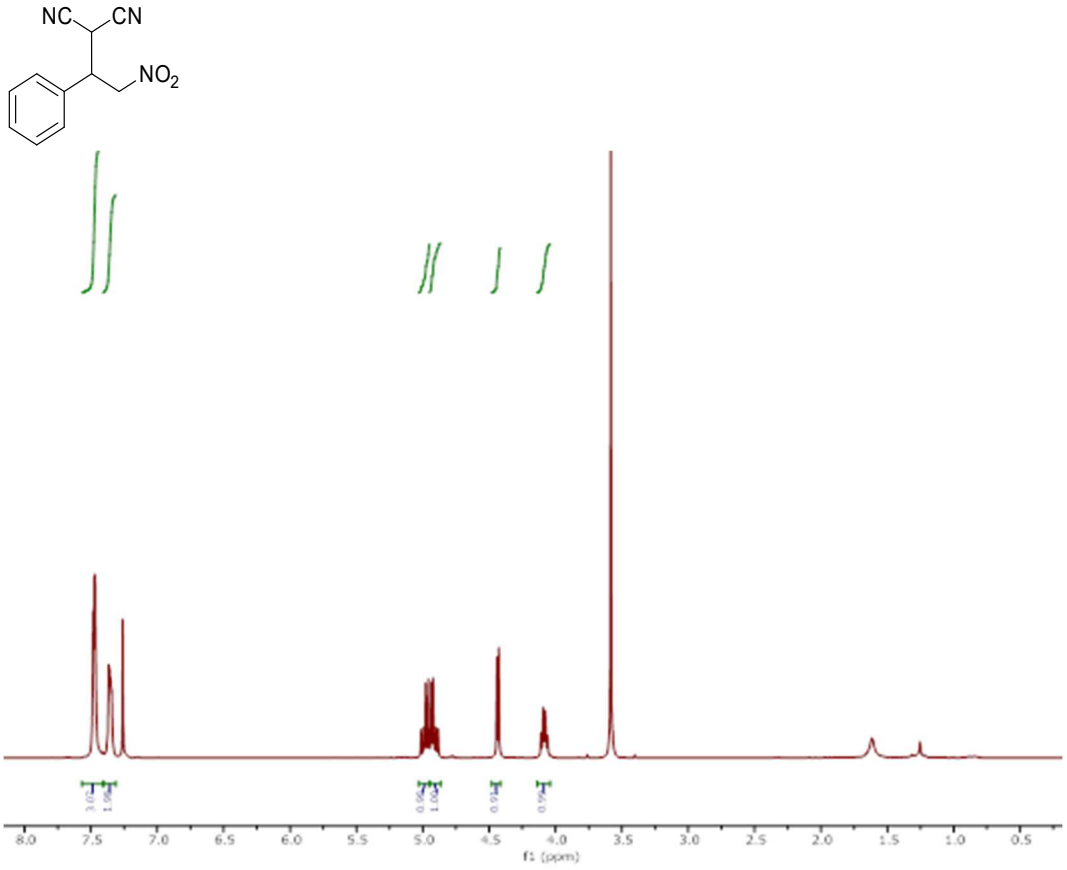


Figure S38. ^{1}H NMR spectrum (400 MHz, 298 K in $CDCl_3$) of 2-(2-nitro-1-phenylethyl)malononitrile **22** prepared with Aib_4(L-Ala)NH^{t}Bu **1** at 20 °C in $CDCl_3$.

7. Control experiments

7.1. Assessment of imine formation

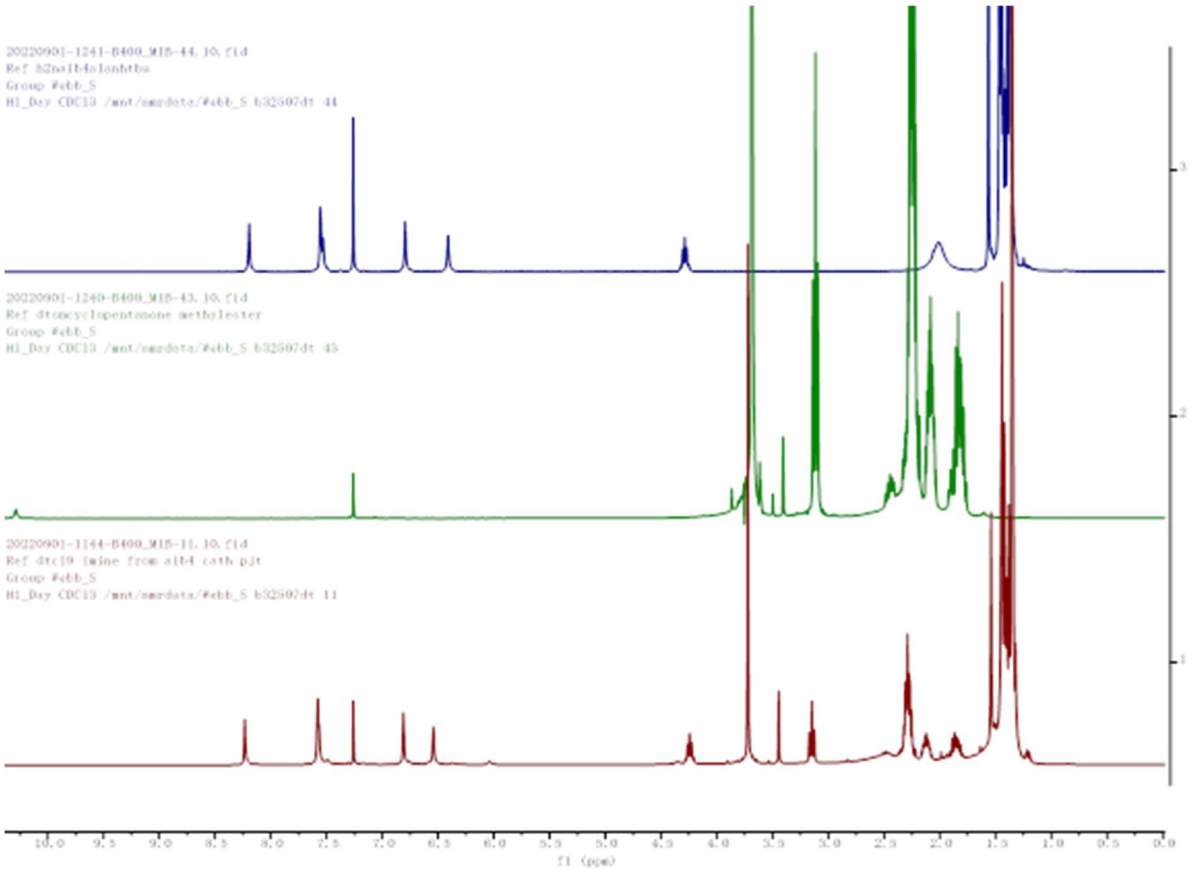
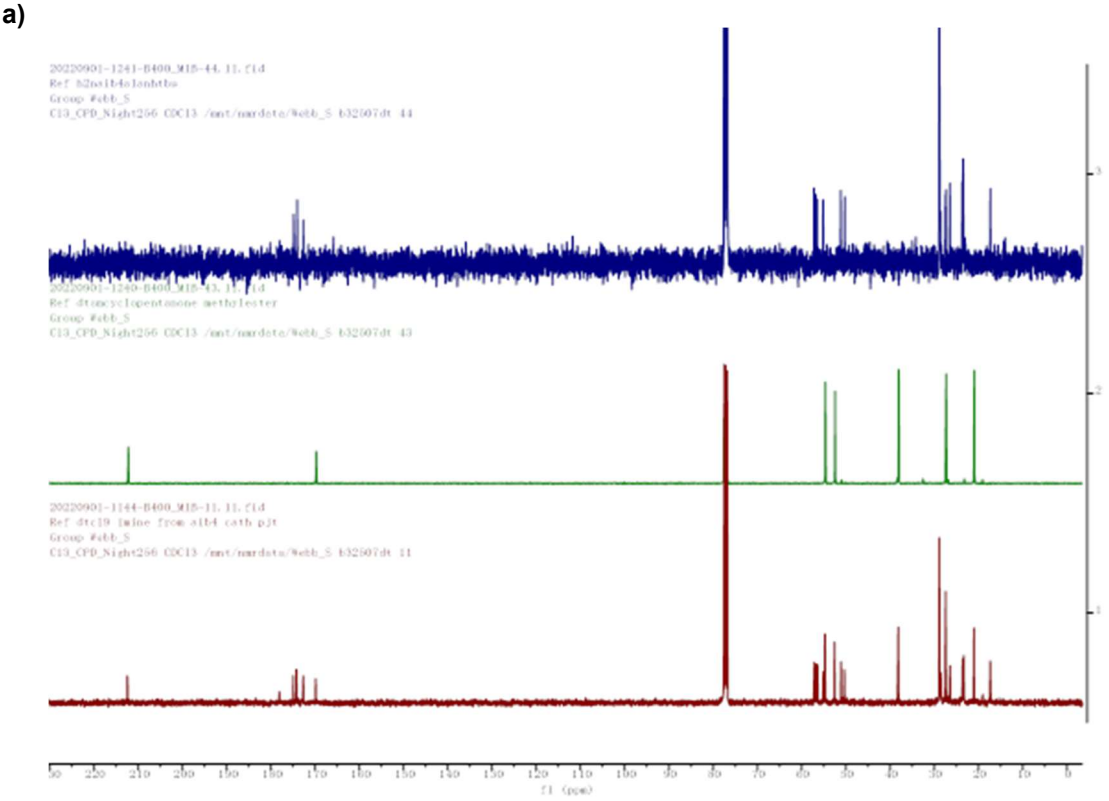
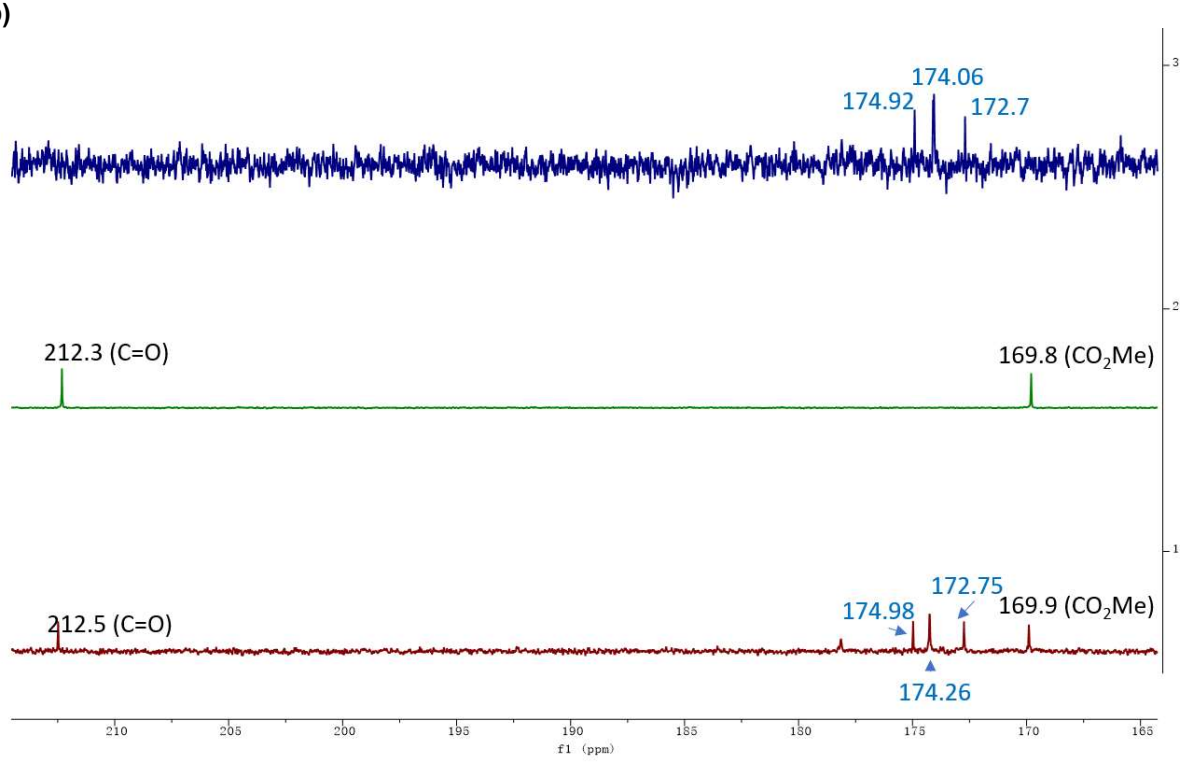


Figure S39. Overlay of ^{1}H NMR spectra (25 °C in $CDCl_3$) of (in blue) Aib_4(L-Ala)NH^tBu **1**, (in green) 1-methyl-2-oxocyclopentanecarboxylate **9**, (in brown) a **1:1 mixture of** Aib_4(L-Ala)NH^tBu **1** and 1-methyl-2-oxocyclopentanecarboxylate **9** after one week in the presence of 4 Å molecular sieves. The spectra indicate no variation of chemical shifts that would indicate the formation of imine.

a)



b)


174.06
174.92
172.7
212.3 (C=O)
169.8 (CO2Me)
172.75
174.98
169.9 (CO2Me)
212.5 (C=O)
174.26
f1 (ppm)

c)

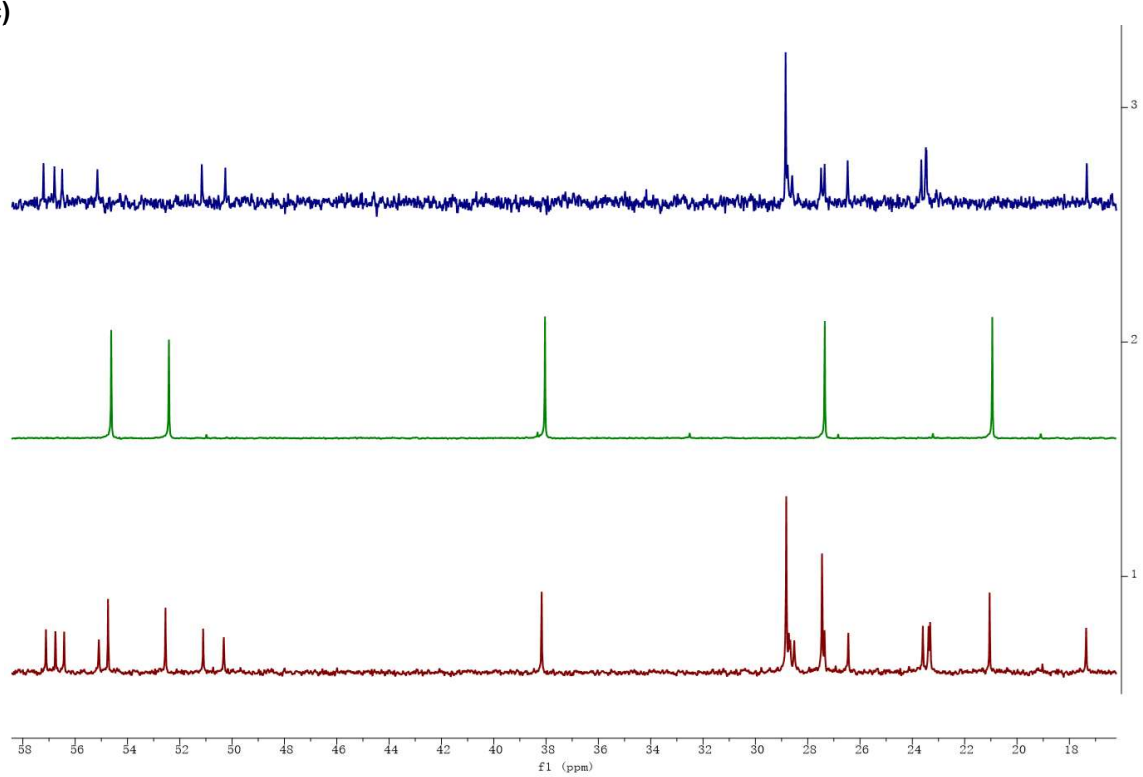


Figure S40. a) overlay of ^{13}C NMR spectra (25 °C in $CDCl_3$) of (in blue) Aib_4(L-Ala)NH^tBu **1**, (in green) 1-methyl-2-oxocyclopentanecarboxylate **9**, and (in brown) a **1:1 mixture of** Aib_4(L-Ala)NH^tBu **1** and 1-methyl-2-oxocyclopentanecarboxylate **9** after one week in the presence of 4 Å molecular sieves. b) Zoom on the region [220-165 ppm], c) Zoom on the region [60-0 ppm]. The spectra indicate no variation of chemical shifts that would indicate the formation of imine.

7.2. Binding of β-nitrostyrene to $N_3Aib_5NH^tBu$ 6 in $CDCl_3$

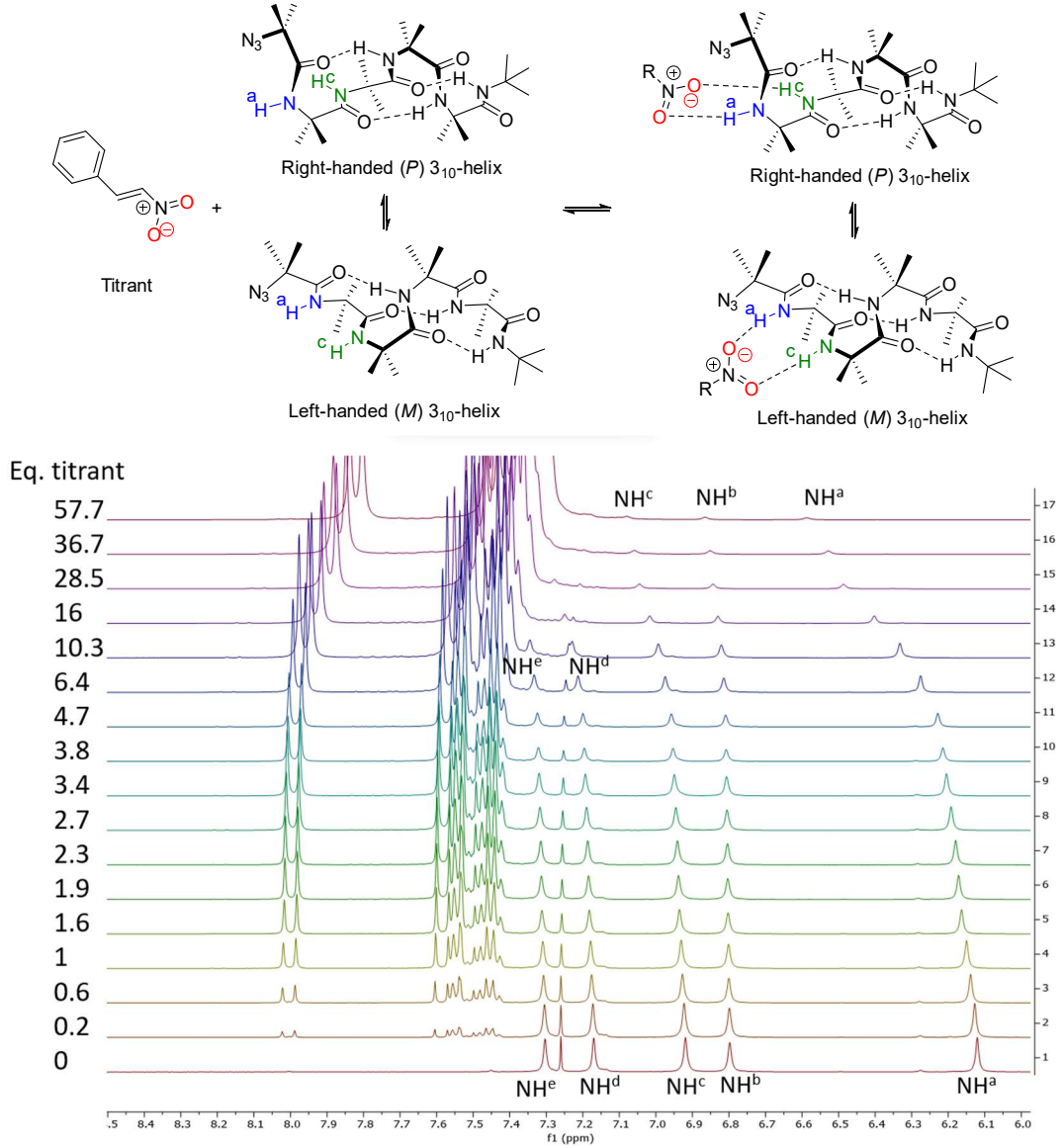


Figure S41. Overlay of ^{1}H NMR spectra of a) $N_3Aib_5NH^tBu$ **6** (29.1 mM in $CDCl_3$ at 25 °C) in the presence of *(E)*-(2-nitrovinyl)benzene) **8** (from 0 to 57 equivalents) - region between 6 ppm and 8.4 ppm. Addition of nitroalkene induces downfield shifts of NH signals (CIS (ppm) at 57 equivalents of *(E)*-(2-nitrovinyl)benzene **8**: NH^a=0.47, NH^b= 0.07, NH^c= 0.16, NH^d= 0.16, NH^e= 0.09).

Table S1: Titration of $N_3Aib_5NH^tBu$ **6** (29.1 mM in $CDCl_3$ at 25 °C) with*(E)*-(2-nitrovinyl)benzene) **8** (from 0 to 57 equivalents) - variation of the ^1H NMR chemical shift values (ppm) of NH^a, NH^b, NH^c upon addition of the titrant. CIS (ppm) at 57 equivalents of ligand added: NH^a=0.47, NH^b= 0.07, NH^c= 0.16, NH^d= 0.16, NH^e= 0.09).

G/H equivalent total	NH^a (ppm)	NH^b (ppm)	NH^c (ppm)
0	6.12	6.798	6.919
0.22	6.127	6.798	6.922
0.6	6.14	6.8	6.927
1.03	6.15	6.802	6.93
1.57	6.165	6.8025	6.936
1.89	6.171	6.803	6.938
2.3	6.18	6.804	6.946
2.76	6.191	6.805	6.946
3.39	6.205	6.807	6.95
3.76	6.215	6.807	6.953
4.64	6.23	6.809	6.958
6.4	6.275	6.814	6.975
10.31	6.332	6.82	6.994
16	6.403	6.83	7.01
28.5	6.485	6.843	7.045
36.7	6.53	6.852	7.06
57.7	6.59	6.865	7.08

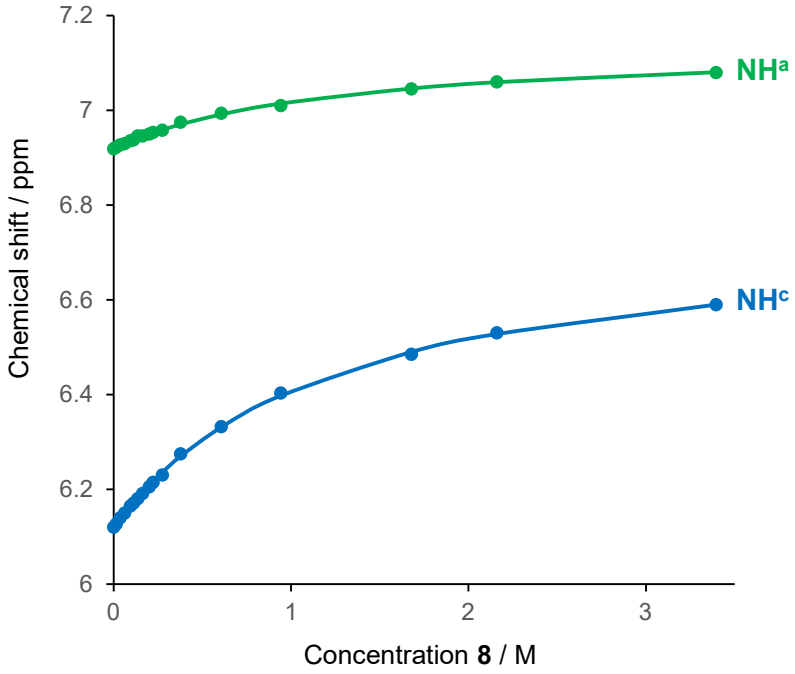
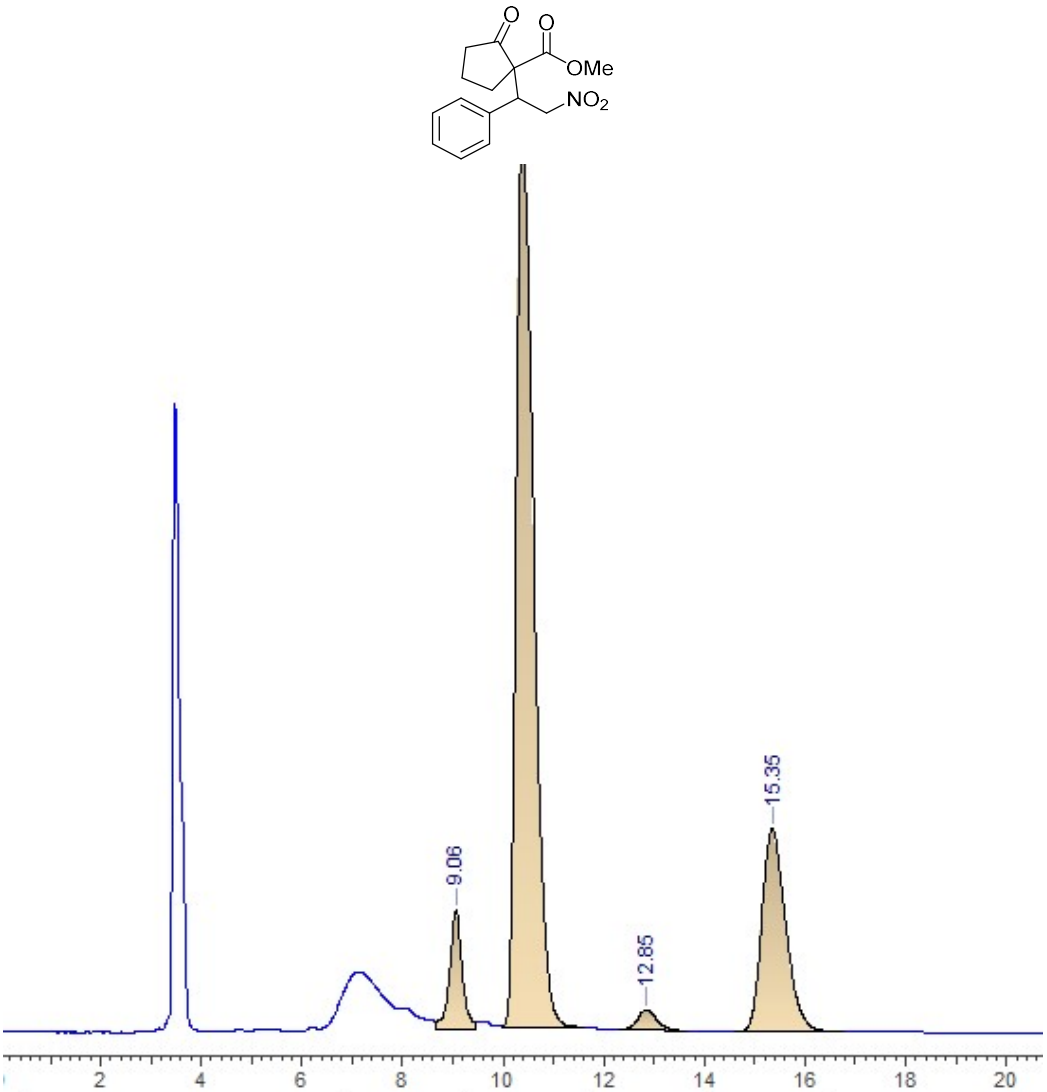


Figure S42. Titration of $N_3Aib_5NH^tBu$ **6** (29.1 mM in $CDCl_3$ at 25 °C) with*(E)*-(2-nitrovinyl)benzene **8** (from 0 to 3.4 molL^{-1}). Plot shows the variation of the ^{1}H NMR chemical shift values (ppm) of the exposed NH groups, NH^a and NH^c, upon addition of the titrant. These NHs experience the greatest change in chemical shift upon addition of **8**: CIS (ppm) at 57 equivalents of ligand added: NH^a=0.47, NH^b= 0.07, NH^c= 0.16, NH^d= 0.16, NH^e= 0.09). Curve fits shown (K = 0.84 M^{-1}) obtained from the fitting to a 1:1 binding model with http://app.supramolecular.org/bindfit/.[19]

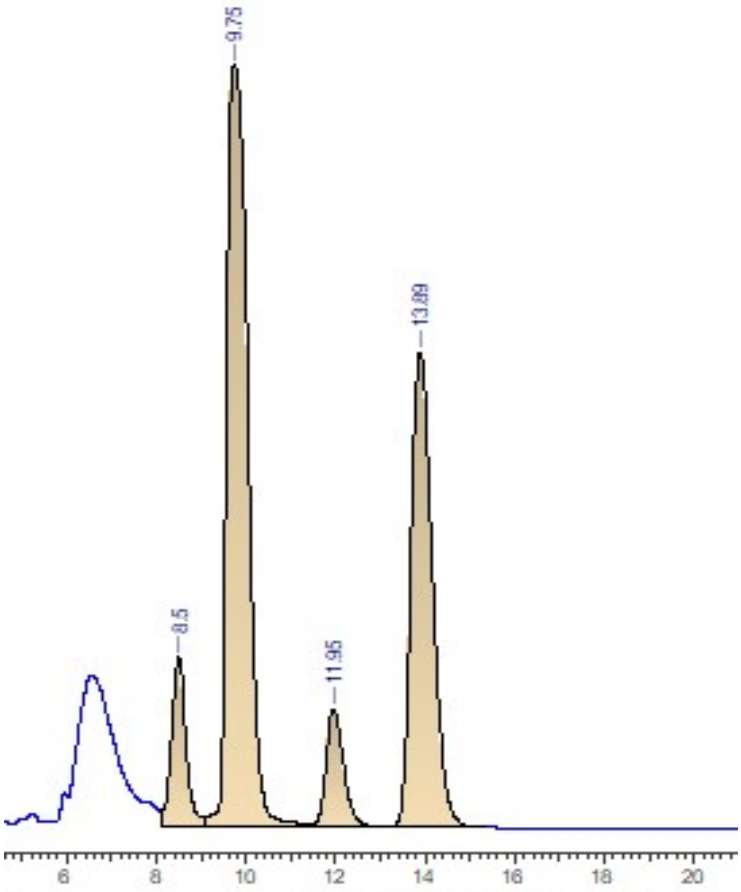
8. HPLC chromatograms of Michael adducts for the measurement of enantiomeric excess

8.1. 1-Methyl-1-(2-nitro-1-phenylethyl)-2 oxocyclopentane-1-carboxylate, 10



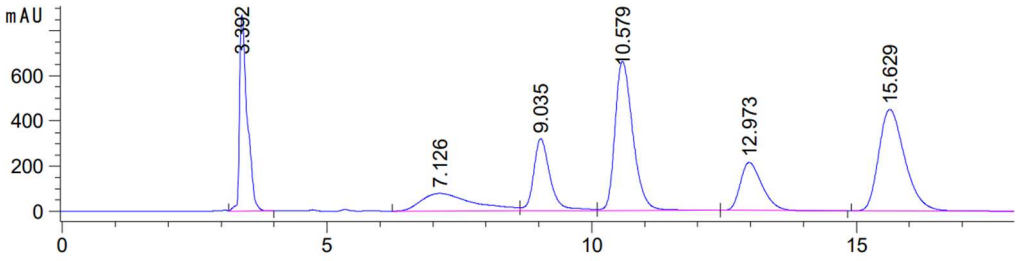
	Name	tR	Peak Area (Y units*ms)	Area Percent	Width
	unknown	9.06	3056356.250	6.568	0.416
	unknown	10.39	32772604.00	70.423	0.660
	unknown	12.85	792730.750	1.703	0.707
	unknown	15.35	9915289.000	21.306	0.859

Figure S43. Reaction conditions: catalyst Aib_4(L-Ala)NH^{t}Bu **1**, $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 9.064 mins, t_{minor} = 12.85 mins, *e.e.* = 54%; major diastereomer: t_{major} = 10.39 mins, t_{minor} = 15.35 mins, *e.e.*= 58%. Diastereomeric ratio: 92:8.



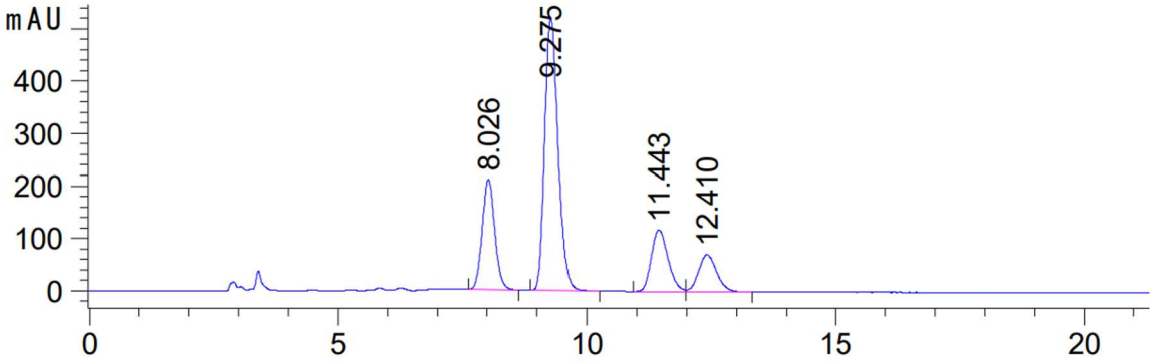
	tR	Peak Area (Y units*ms)	Area Percent	Width
MM	8.50	8724505.000	8.069	0.561
MM	9.75	56472812.000	52.230	0.875
MM	11.95	7396322.000	6.841	0.713
MM	13.89	35530184.000	32.861	0.876

Figure S44. Reaction conditions: catalyst Aib_4(L-Ala)NH^tBu **1**, $CDCl_3$, 40 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 9.064 mins, t_{minor} = 12.85 mins, *e.e.* = 23%; major diastereomer: t_{major} = 10.39 mins, t_{minor} = 15.35 mins, *e.e.*= 9%.



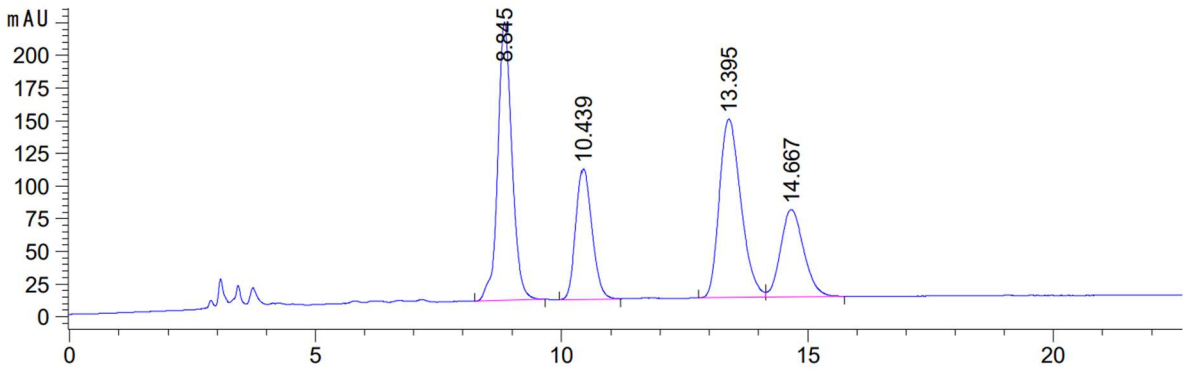
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.392	VB	0.1502	8802.76563	868.83661	15.1020
2	7.126	BV	0.9606	5380.70410	78.40569	9.2311
3	9.035	VV	0.3274	6984.83398	321.64108	11.9831
4	10.579	VB	0.3603	1.55669e4	662.21722	26.7064
5	12.973	BB	0.4392	6129.98730	214.60922	10.5166
6	15.629	BB	0.5292	1.54237e4	448.47263	26.4608

Figure S45. Reaction conditions: catalyst H_2N^tBu, $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t = 9.035 mins, t = 12.973 mins; major diastereomer: t = 10.579 mins, t = 15.629 mins. Diastereomeric ratio: 61:39.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.026	BB	0.2664	3636.19385	209.57092	20.4373
2	9.275	BB	0.2885	9644.15527	519.73334	54.2053
3	11.443	BV	0.3562	2735.08447	118.11505	15.3726
4	12.410	VB	0.3934	1776.47449	70.63925	9.9847

Figure S46. Reaction conditions: catalyst Aib_4(L-Ala)NH^tBu **1**, no solvent, 0 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 9.275 mins, t_{minor} = 12.41 mins, *e.e.* = 69%; minor diastereomer: t_{major} = 8.026 mins, t_{minor} = 11.443 mins, *e.e.*= 14%.



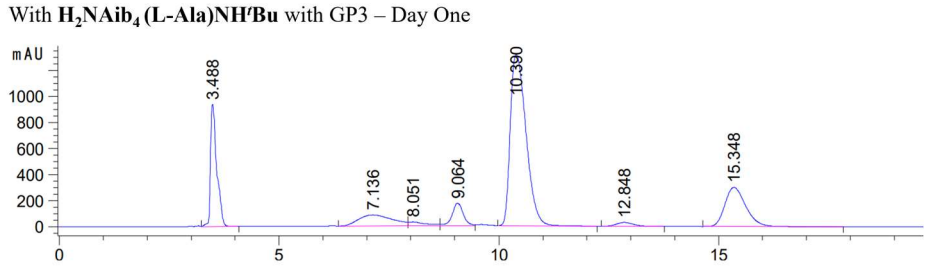
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.845	BB	0.3079	4269.00732	212.96359	23.6033
2	10.439	BB	0.3458	2205.07300	99.78053	12.1918
3	13.395	BV	0.4765	4174.33545	136.60164	23.0798
4	14.667	VB	0.4938	2188.09692	66.86594	12.0980

Figure S47. Reaction conditions: catalyst Aib(L-Ala)NH*t*Bu **4**, no solvent, 0 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 8.845 mins, t_{minor} = 13.395 mins, *e.e.* = 1%; minor diastereomer: t_{major} = 10.439 mins, t_{minor} = 14.667 mins, *e.e.* = 0%. Diastereomeric ratio: 66:34.

Time course

Reaction condition: catalyst Aib_4(L-Ala)NH^tBu **1**, no solvent, 0 °C.

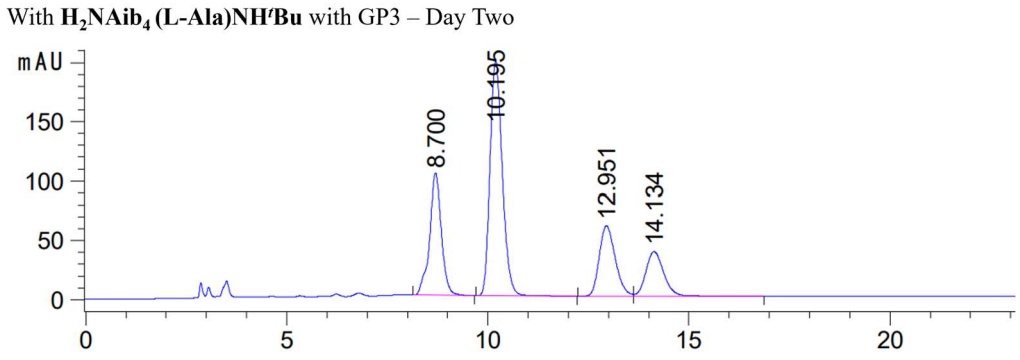
Day 1



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.488	VB	0.1477	9300.36328	937.62109	15.1983
2	7.136	BV	0.8143	4592.83594	85.01044	7.5054
3	8.051	VV	0.3788	830.05957	30.00118	1.3565
4	9.064	VV	0.2520	2936.61743	174.81396	4.7989
5	10.390	BB	0.3920	3.27775e4	1318.43567	53.5638
6	12.848	BB	0.4212	795.62738	29.64086	1.3002
7	15.348	BB	0.5088	9960.44043	301.97281	16.2770

Figure S48. Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 9.064 mins, t_{minor} = 12.848 mins, *e.e.* = 54%; major diastereomer: t_{major} = 10.39 mins, t_{minor} = 15.348 mins, *e.e.*= 54%. Diastereomeric ratio: 92:8.

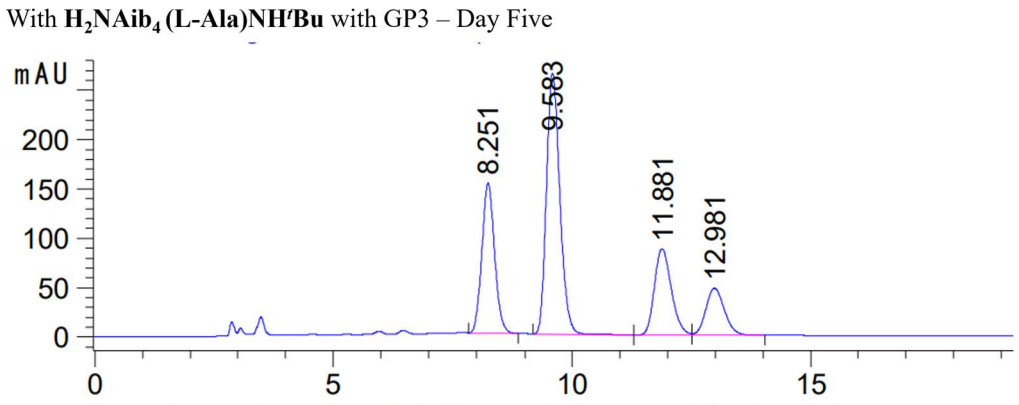
Day 2



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.700	BB	0.3217	2103.71313	101.52834	23.0311
2	10.195	BB	0.3474	4224.30615	196.00615	46.2469
3	12.951	BV	0.4361	1647.00012	59.28714	18.0311
4	14.134	VB	0.4878	1159.21863	37.59124	12.6909

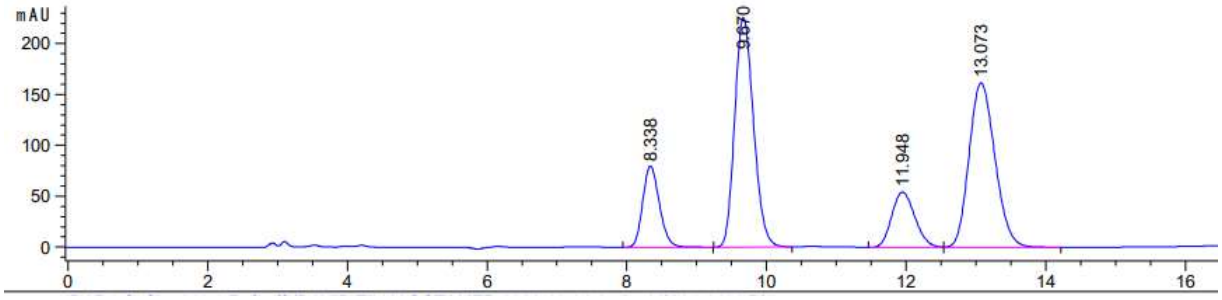
Figure S49. Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 10.195 mins, t_{minor} = 14.134 mins, *e.e.* = 57%; minor diastereomer: t_{major} = 8.7 mins, t_{minor} = 12.95 mins, *e.e.* = 12%.

Day 5



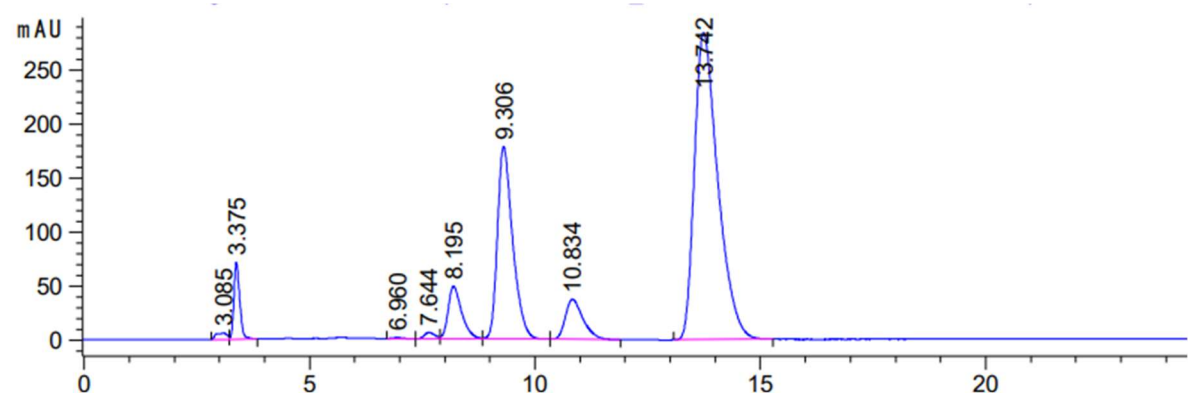
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.251	BB	0.2817	2809.74463	152.00626	24.6198
2	9.583	BB	0.3038	5164.00244	264.49216	45.2485
3	11.881	BV	0.3836	2158.10693	87.53486	18.9100
4	12.981	VB	0.4176	1280.68689	47.64676	11.2218

Figure S50. Reaction conditions: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, no solvent, 0 °C. Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 9.58 mins, t_{minor} = 1298 mins, *e.e.* = 60%; minor diastereomer: t_{major} = 8.25 mins, t_{minor} = 11.88 mins, *e.e.* = 14%.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.131	VB	0.0949	10.30577	1.64972	2.1093
2	8.308	BB	0.2727	73.57645	4.23445	15.0592
3	9.667	BB	0.2876	168.65501	9.21112	34.5192
4	11.941	BB	0.3237	50.37441	2.29850	10.3103
5	13.075	BB	0.3981	185.67105	7.12376	38.0020
Totals :				488.58270	24.51755	

Figure S51. Reaction conditions: catalyst Aib$_8$(L-Ala)NH^{t}Bu **3**, $CDCl_3$, 20 °C. Chiralcel OD-H column, hexane/*i*-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 8.34 min (2S, 3R), t_{minor} = 11.9 mins ((2R, 3S), *e.e.* = 19%; major diastereomer: t_{major} = 9.67 min (2S, 3S), t_{minor} = 13.04 mins (2R, 3R), *e.e.*= 5%

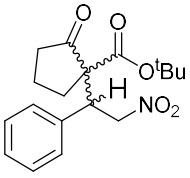


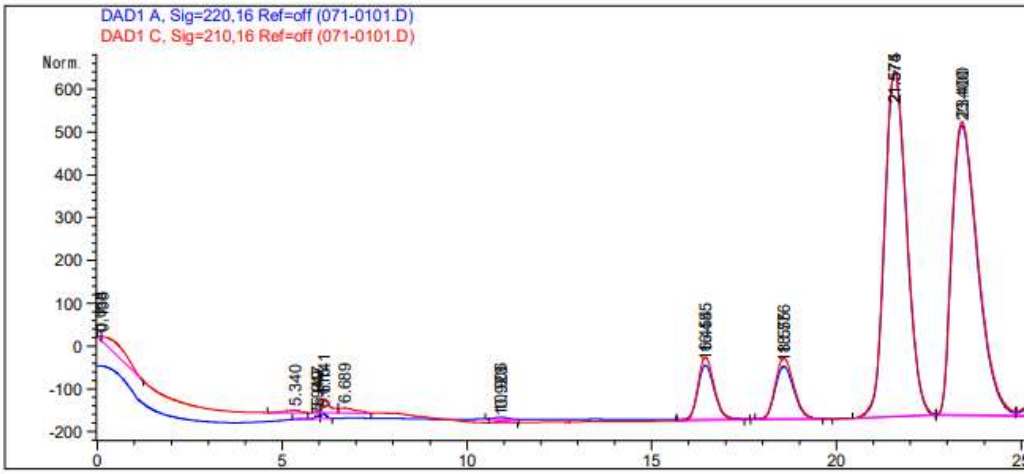
Signal 1: DAD1 A, Sig=220,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.085	BV	0.2156	105.43161	6.22438	0.6075
2	3.375	VB	0.1297	635.74939	71.52097	3.6633
3	6.960	BB	0.2064	18.04180	1.12913	0.1040
4	7.644	BV	0.2294	100.46589	6.12474	0.5789
5	8.195	VV	0.3189	1027.62061	48.94929	5.9213
6	9.306	VB	0.3518	4182.21631	178.20201	24.0987
7	10.834	BB	0.4063	1004.74091	37.05973	5.7895
8	13.742	BB	0.5420	1.02803e4	284.21118	59.2368

Figure S52. Reaction conditions: catalyst Aib_4(L-Phe)NH^tBu **5**, $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{minor} = 9.3 mins, t_{major} = 13.724 mins, *e.e.* = 42%; minor diastereomer: t_{minorr} = 8.195 mins, t_{major} = 10.83 mins, *e.e.* = 1%.

8.2. 1-*tert*-Butyl-1-(2-nitro-1-phenylethyl)-2 -oxocyclopentane-1-carboxylate, 13

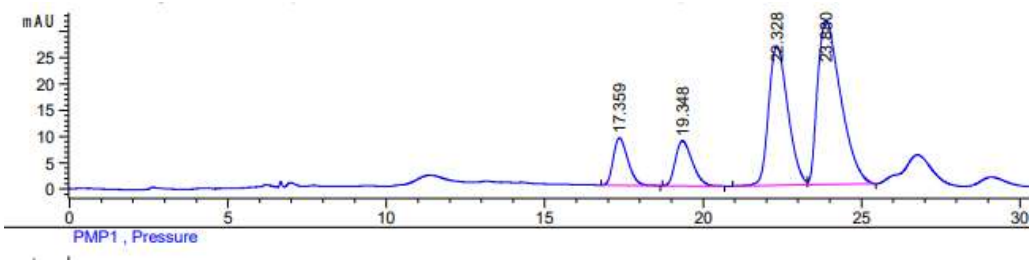




Signal 1: DAD1 A, Sig=220,16 Ref=off

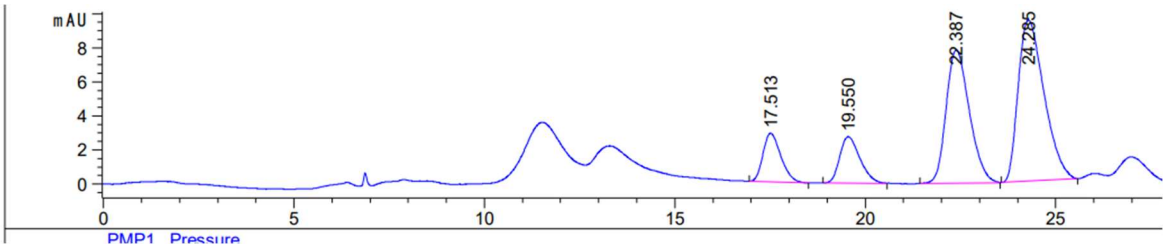
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.949	BV	0.1625	44.86659	4.01010	0.0955
2	6.115	VB	0.1135	63.54049	7.92464	0.1353
3	10.906	BB	0.3390	62.41798	2.85606	0.1329
4	16.454	BB	0.4784	2197.37012	71.93296	4.6775
5	18.575	BB	0.5534	2451.57251	69.86110	5.2186
6	21.575	BB	0.6454	1.89571e4	461.34674	40.3533
7	23.400	BV	0.7532	1.87499e4	387.01233	39.9121

Figure S53. Reaction conditions: catalyst H_2N^tBu, in $CDCl_3$, 20 °C. **HPLC** Chiralpak OD-H column, hexane/i-PrOH (97:3), flow rate 0.5 mL/min, 220 nm; minor diastereomer: t_r = 17.4 mins, t_r = 19.4 mins, major diastereomer: tr = 22.3 mins, t_r = 23.9 mins.



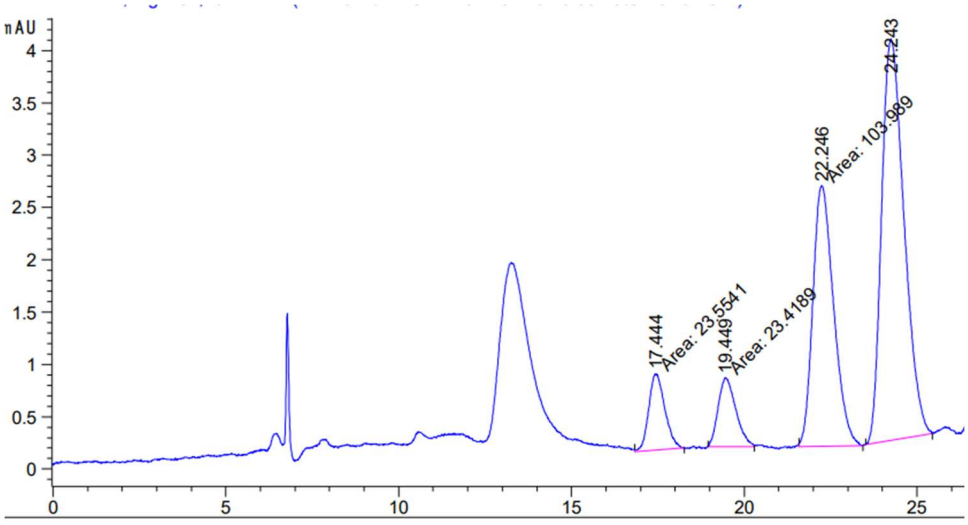
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.359	BB	0.4811	286.63654	9.01072	8.6453
2	19.348	BB	0.5548	315.70673	8.55034	9.5221
3	22.328	BV	0.6461	1121.40771	26.58702	33.8230
4	23.880	VB	0.7771	1591.76550	31.20705	48.0096

Figure S54. Reaction conditions: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, $CDCl_3$ (0.5 mL), 20 °C. **HPLC** Chiralcel OD-H column, hexane/*i*-PrOH (97/3), flow rate 0.5 mL/min, 220 nm; minor diastereomer: t_r = 17.4 mins, t_r = 19.4 mins. ee = 5%, major diastereomer: tr = 22.3 mins, t_r = 23.9 mins, ee = 17%.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.513	BB	0.4565	92.78078	2.85987	9.5488
2	19.550	BB	0.4882	99.54309	2.72518	10.2447
3	22.387	BB	0.6354	332.12558	7.82159	34.1816
4	24.285	BB	0.6809	447.20148	9.47078	46.0249
Totals :				971.65093	22.87742	

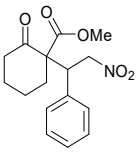
Figure S55. Reaction conditions: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, $CDCl_3$ (0.5 mL), 20 °C – repeat (for error evaluation). **HPLC** Chiralcel OD-H column, hexane/*i*-PrOH (97/3), flow rate 0.5 mL/min, 220 nm; minor diastereomer: t_r = 17.4 mins, t_r = 19.4 mins. ee = 4%, major diastereomer: tr = 22.3 mins, t_r = 23.9 mins, ee = 15%.

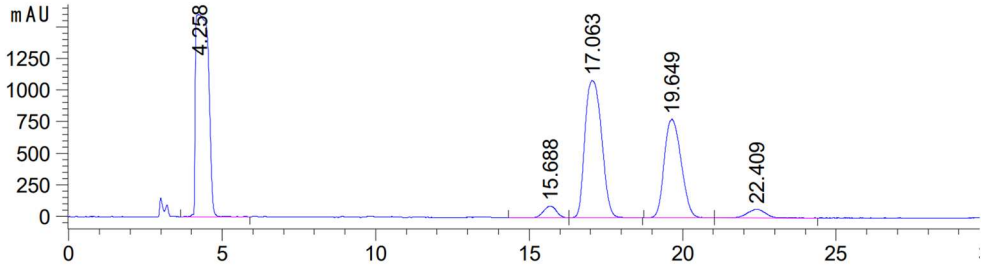


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.444	MM	0.5385	23.55407	7.28992e-1	7.2670
2	19.449	MM	0.5925	23.41892	6.58806e-1	7.2253
3	22.246	MM	0.6963	103.98937	2.48901	32.0833
4	24.243	BB	0.5987	173.16032	3.83562	53.4243
Totals :				324.12269	7.71243	

Figure S56. Reaction conditions: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, no solvent, 0 °C. **HPLC** Chiralcel OD-H column, hexane/*i*-PrOH (97/3), flow rate 0.5 mL/min, 220 nm; minor diastereomer: t_r = 17.4 mins, t_r = 19.4 mins. *e.e.* = 2%, major diastereomer: tr = 22.3 mins, t_r = 23.9 mins, *e.e.*= 27%. **Diastereomeric ratio**: 85:15.

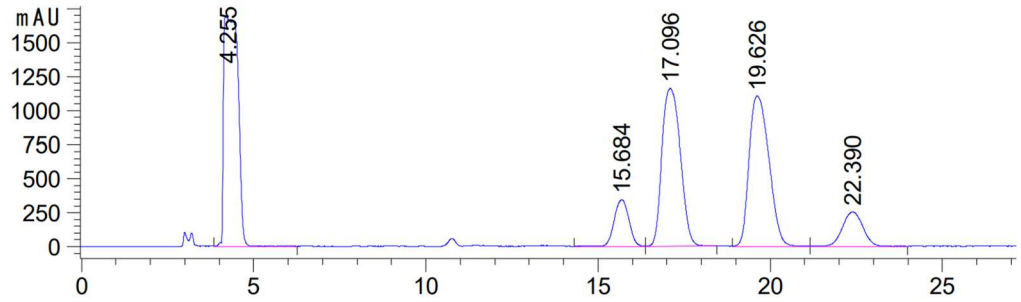
8.3. Methyl 1-(2-nitro-1-phenylethyl)-2-oxocyclohexane-1-carboxylate, 15a





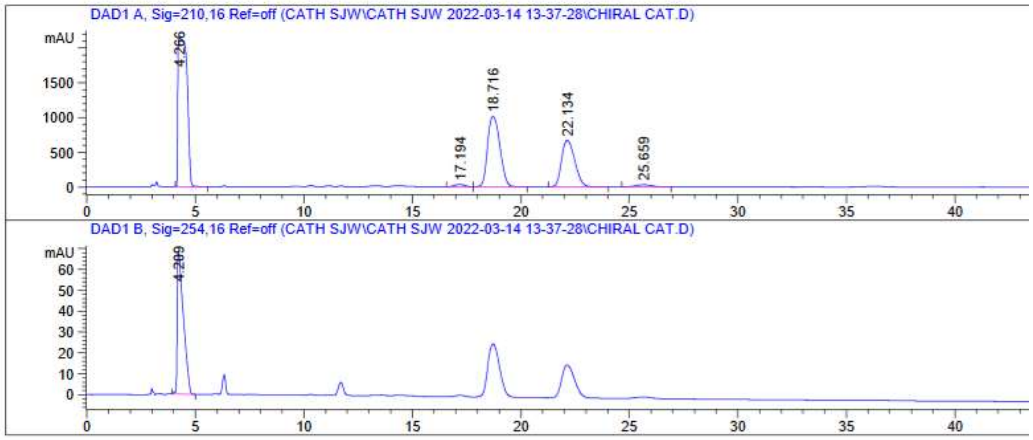
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.258	VV	0.4805	4.66787e4	1618.33997	37.8399
2	15.688	BV	0.4778	2753.14307	91.82237	2.2318
3	17.063	VB	0.6182	4.09806e4	1081.26013	33.2208
4	19.649	BV	0.6102	2.99376e4	775.86700	24.2688
5	22.409	VB	0.7080	3008.32935	68.01954	2.4387

Figure S57. Reaction conditions: catalyst Aib_4(L-Ala)NH^tBu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralpak IC column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 17.1 mins, t_{minor} = 19.7 mins, *e.e.* =16%; minor diastereomer: t_{major} = 5%.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.255	VV	0.3876	4.92232e4	1690.94702	31.2523
2	15.684	BV	0.4776	1.02404e4	341.73993	6.5017
3	17.096	VB	0.6111	4.32067e4	1158.54272	27.4324
4	19.626	BV	0.6615	4.43080e4	1100.95679	28.1316
5	22.390	VB	0.6777	1.05243e4	252.80075	6.6820

Figure S58. Reaction conditions: catalyst $NH_2{}^tBu$, in $CDCl_3$, 20 °C. **HPLC** Chiralpak IC column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t = 17.1 mins, t = 19.6 mins, minor diastereomer: t = 15.7 mins, t = 22.4 mins.

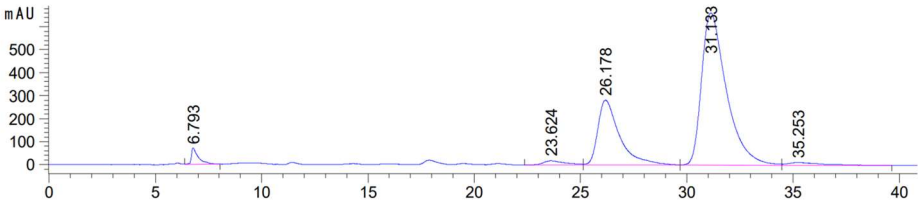


Signal 1: DAD1 A, Sig=210,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.266	VB	0.3746	6.27741e4	2137.93066	46.9560
2	17.194	BV	0.5021	1116.36609	34.81301	0.8351
3	18.716	VB	0.6328	4.00182e4	1013.11237	29.9342
4	22.134	BB	0.6713	2.82451e4	670.74158	21.1278
5	25.659	BB	0.6130	1533.32886	31.11259	1.1470
Totals :				1.33687e5	3887.71021	

Figure S59. Reaction conditions: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, no solvent, 0 °C. **HPLC** Chiralpak IC column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 18.7 mins, t_{minor} = 22.1 mins, *e.e.*= 17%; minor diastereomer: t_{major} = 17.2 mins, t_{minor} = 25.6 mins, *e.e.*= 16%.

8.4. Ethyl 4,4-dimethyl-2-(2-nitro-1-phenylethyl)-3-oxopentanoate, 20a



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.793	VB	0.3288	1691.34583	70.26266	2.1609
2	23.624	BV	0.9888	1259.38489	18.07749	1.6090
3	26.178	VB	1.0344	2.00490e4	283.05215	25.6146
4	31.133	BV	1.2204	5.38252e4	662.09711	68.7671
5	35.253	VB	1.5329	1446.84009	12.01530	1.8485

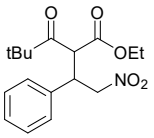
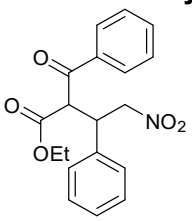
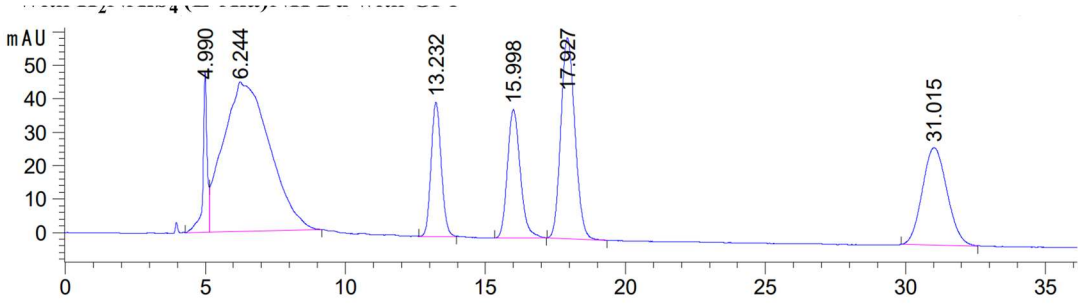


Figure S58. Reaction condition: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralcel AD-H column, hexane/i-PrOH (98:2), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 26.2 mins, t_{minor} = 31.1 mins, *e.e.*= 46%; minor diastereomer: t_{major} = 23.6 mins, t_{minor} = 36.2 mins.

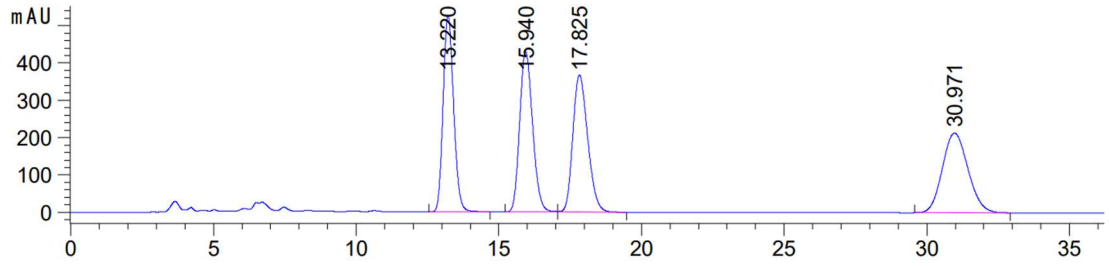
8.5. Ethyl 2-benzoyl-4-nitro-3-phenylbutanoate, 21a





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.990	BV	0.1480	499.70837	47.76864	4.2361
2	6.244	VB	1.3852	5166.08887	44.80368	43.7936
3	13.232	BB	0.3881	1010.60095	40.08469	8.5670
4	15.998	BB	0.4883	1225.17920	38.39627	10.3860
5	17.927	BB	0.5423	2102.26270	60.07494	17.8212
6	31.015	BB	0.7528	1792.60193	29.17669	15.1961

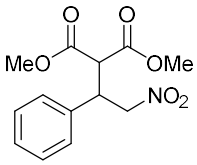
Figure S61. Reaction condition: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t_{major} = 17.9 mins, t_{minor} = 31.0 mins, *e.e.*= 8%; minor diastereomer: t_{major} = 13.2 mins, t_{minor} = 15.9 mins, *e.e.* = 9%.

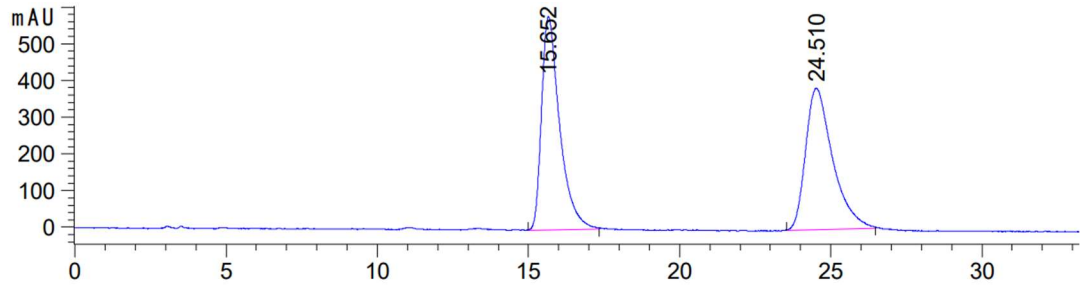


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.220	BB	0.3992	1.34888e4	526.04871	25.1996
2	15.940	BB	0.4883	1.34950e4	429.79816	25.2113
3	17.825	BB	0.5631	1.32236e4	366.35770	24.7042
4	30.971	BB	0.9359	1.33202e4	213.50677	24.8848

Figure S62. Reaction conditions: catalyst H_2N^tBu, in $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; major diastereomer: t = 17.8 mins, t = 30.9 mins, minor diastereomer: t = 13.2 mins, t = 15.6 mins.

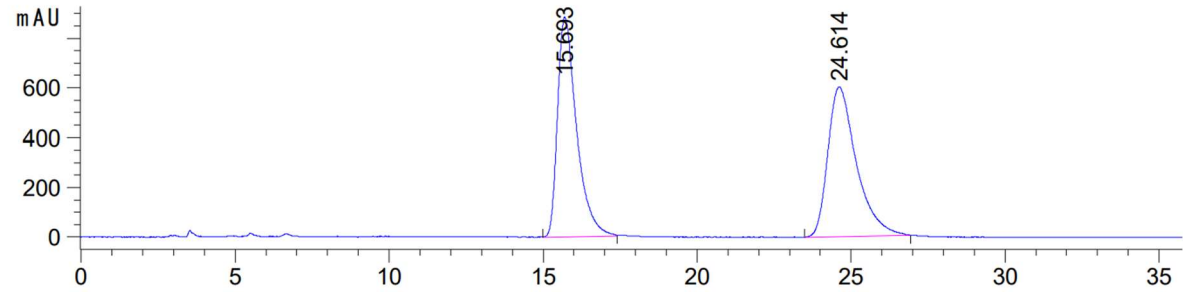
8.6. Dimethyl 2-(2-nitro-1-phenylethyl)malonate, 17a





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.652	BV	0.5315	2.41834e4	581.19061	50.0253
2	24.510	VV	0.7490	2.41590e4	386.63766	49.9747

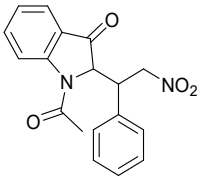
Figure S63. Reaction conditions: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; t_{major} = 15.7 min, t_{minor} = 24.5 min, *e.e.*= 0%.

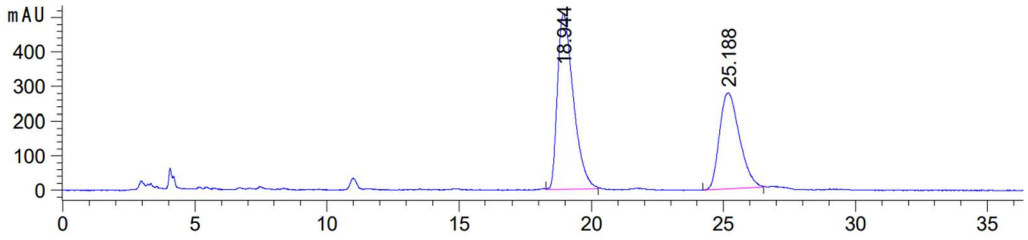


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.693	BV	0.5612	3.78734e4	885.13757	49.2310
2	24.614	VV	0.7616	3.90566e4	603.02698	50.7690

Figure S64. Reaction condition: catalyst H_2N^tBu, in $CDCl_3$, 20 °C. **HPLC** Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 210 nm; t = 15.7 min, t = 24.6 min.

8.7. 1-Acetyl-2-(2-nitro-1-phenylethyl)indolin-3-one, 16a

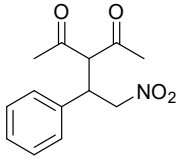


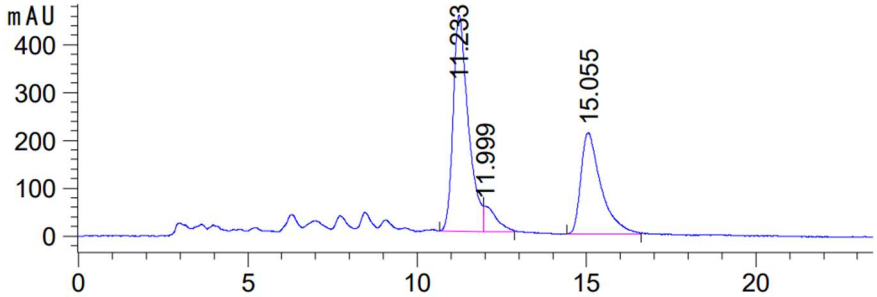


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.944	VV	0.5373	2.13035e4	507.99451	59.1795
2	25.188	BV	0.6486	1.46946e4	277.14786	40.8205

Figure S65. Reaction condition: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralcel AS column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; t_{major} = 18.9 min, t_{minor} = 25.2 min, *e.e.*= 18%.

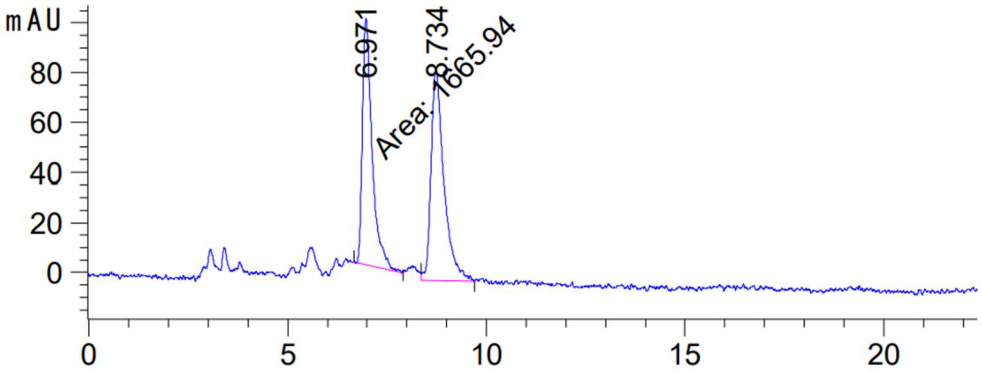
8.8. 3-(2-Nitro-1-phenylethyl)pentane-2,4-dione, 18a





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.233	BV	0.4310	1.41456e4	452.12363	58.1743
2	11.999	VV	0.3113	1381.24365	53.13335	5.6804
3	15.055	VV	0.5204	8789.06250	212.57156	36.1453

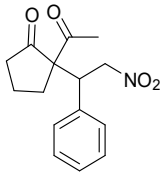
Figure S66. Reaction condition: catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t_{major} = 11.2 min, t_{minor} = 15.0 min, *e.e.*= 23%.

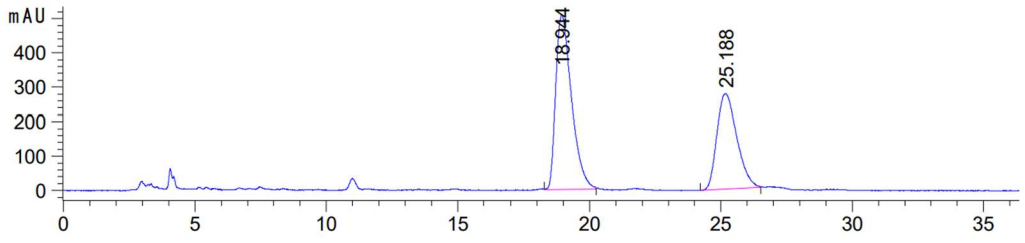


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.971	MM	0.2787	1665.93701	99.64111	46.6706
2	8.734	VB	0.3449	1903.62671	83.82983	53.3294

Figure S67. Reaction conditions: catalyst H_2N^tBu, in $CDCl_3$, 20 °C. **HPLC** Chiralcel AD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t = 6.9 min, t = 8.7 min.

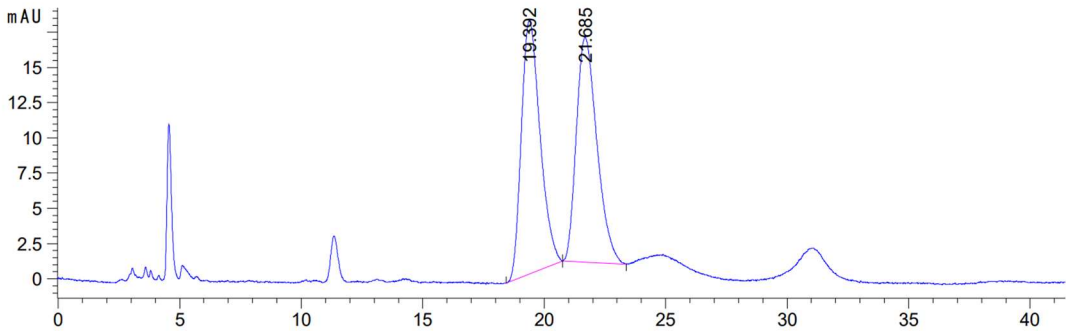
8.9. 2-Acetyl-2-(2-nitro-1-phenylethyl)cyclopentan-1-one, 14a





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.944	VV	0.5373	2.13035e4	507.99451	59.1795
2	25.188	BV	0.6486	1.46946e4	277.14786	40.8205

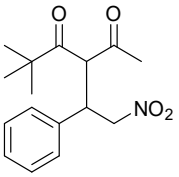
Figure S68. Reaction conditions: catalyst Aib_4(L-Ala)NH^tBu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t_{major} = 18.9 min, t_{minor} = 25.2 min, *e.e.*= 18%.

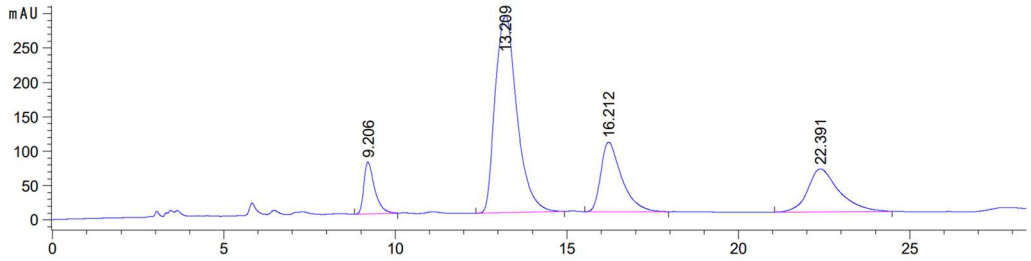


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.392	BB	0.6799	965.58246	17.99945	50.5981
2	21.685	BB	0.7568	942.75378	16.01568	49.4019

Figure S69. Reaction condition: catalyst H_2N^tBu, in $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; t = 19.4 min, t = 21.7 min.

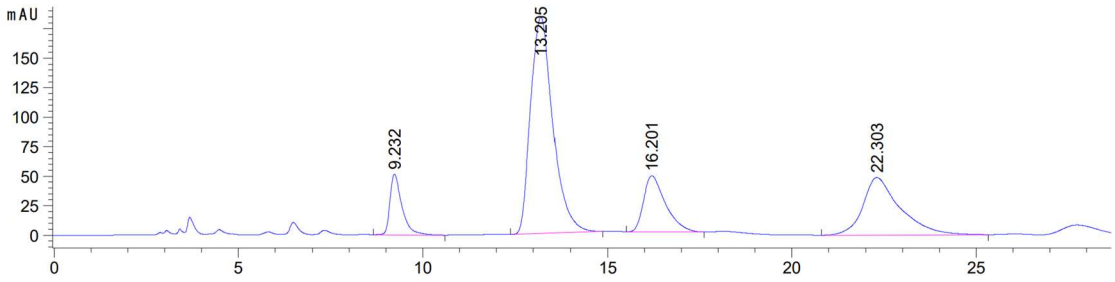
8.10. 5,5-Dimethyl-3-(2-nitro-1-phenylethyl)hexane-2,4-dione, 19a





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.206	BB	0.3244	1635.14441	74.99040	7.3739
2	13.209	BB	0.6721	1.23294e4	286.47159	55.6007
3	16.212	BB	0.6192	4259.72705	101.17147	19.2097
4	22.391	BB	0.8888	3950.61255	62.38694	17.8157

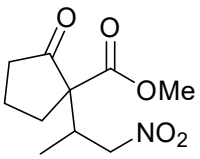
Figure S70. Reaction condition: catalyst Aib_4(L-Ala)NH^{t}Bu **1**, in $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t_{major} = 9.232 mins , t_{minor} = 16.2 mins, *e.e.* = 44%; major diastereomer: t_{major} = 13.207 mins, t_{minor} = 22.302 mins, ee = 52%.

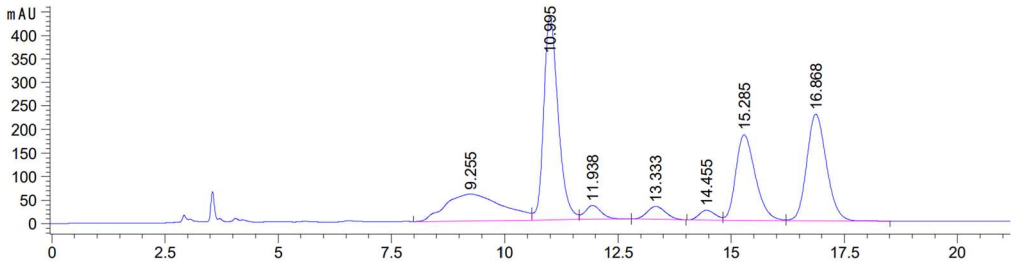


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.232	BB	0.3340	1165.37036	51.50134	8.1993
2	13.205	BB	0.6539	7671.77148	183.45686	53.9769
3	16.201	BB	0.6103	1959.03064	47.59002	13.7833
4	22.303	BB	0.9869	3416.89819	48.67791	24.0405

Figure S71. Reaction condition: catalyst H_2N^tBu, in $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (80:20), flow rate 1.0 mL/min, 220 nm; minor diastereomer: t = 9.232 mins , t = 16.2 mins; major diastereomer: t = 13.207 mins, t = 22.302 mins.

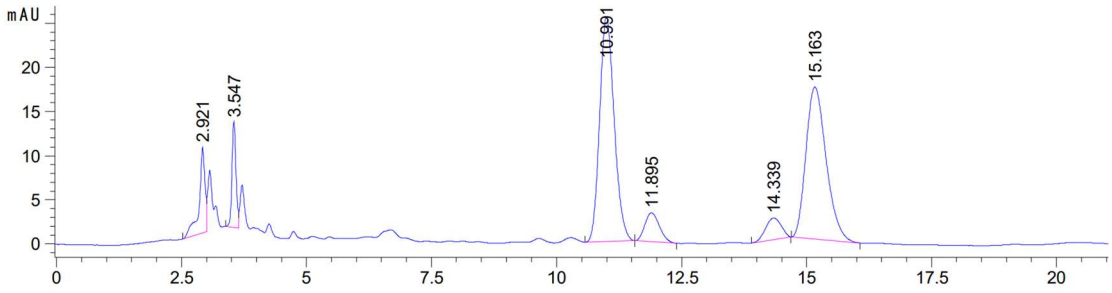
8.11. 1-Methyl-1-(1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 12a





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.255	BV	1.1552	4946.97363	57.07482	17.0957
2	10.995	VV	0.3409	9607.12598	432.88849	33.2002
3	11.938	VB	0.3726	744.08978	29.87447	2.5714
4	13.333	BB	0.4432	785.20392	27.65633	2.7135
5	14.455	BV	0.3885	515.25299	20.83973	1.7806
6	15.285	VV	0.4642	5474.33691	182.39278	18.9182
7	16.868	VB	0.4724	6863.96582	225.97897	23.7204

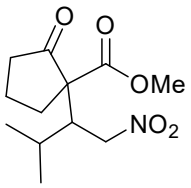
Figure S72. Reaction conditions catalyst Aib$_4$(L-Ala)NH^{t}Bu **1**, no solvent, 0 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 10.995 mins , t_{minor} = 15.285 mins, *e.e.* = 28%; minor diastereomer: t_{major} = 11.938 mins, t_{minor} = 14.455 mins, , *e.e.* = 18%.

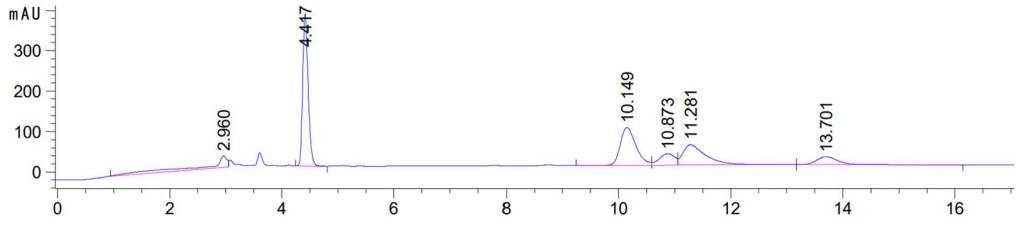


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.921	BV	0.1143	79.80574	9.67340	6.3047
2	3.547	BV	0.0848	66.25494	11.92255	5.2342
3	10.991	BB	0.3144	515.25055	25.43126	40.7050
4	11.895	BB	0.3099	67.11102	3.29125	5.3018
5	14.339	BB	0.3394	53.18807	2.46801	4.2019
6	15.163	BB	0.4305	484.20581	17.19888	38.2525

Figure S73. Reaction condition: catalyst H$_2$N^{t}Bu, no solvent, 0 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (90:10), flow rate 1.0 mL/min, 220 nm; major diastereomer; t = 10.991 mins, t = 15.163 mins, *e.e.*= 0%; minor diastereomer: t = 11.895 mins, t = 14.339 mins, *e.e.*= 0%.

8.12. Methyl 1-(3-methyl-1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 11a

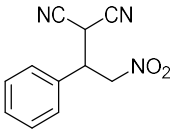


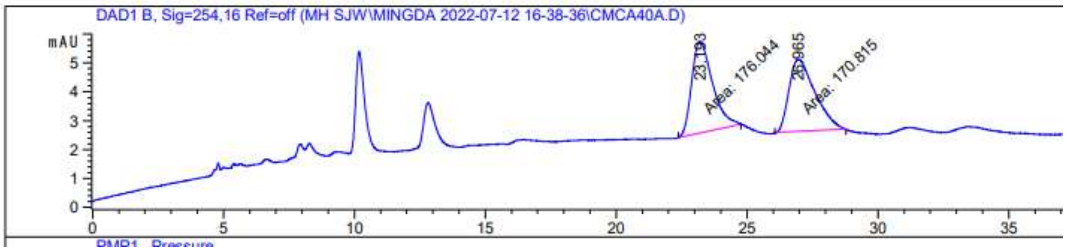


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.960	BV	0.3181	718.39954	28.30911	9.3460
2	4.417	VB	0.1029	2554.91748	377.84766	33.2383
3	10.149	BV	0.2987	1830.36353	94.21140	23.8122
4	10.873	VV	0.2967	544.95923	28.54989	7.0897
5	11.281	VB	0.4189	1484.88977	50.81455	19.3177
6	13.701	BB	0.4238	553.14282	19.68775	7.1961

Figure S74. Reaction condition: catalyst Aib_4(L-Ala)NH^tBu **1**, $CDCl_3$, 20 °C. **HPLC** Chiralcel OD-H column, hexane/i-PrOH (92:8), flow rate 1.0 mL/min, 220 nm; major diastereomer: t_{major} = 10.149 mins, t_{minor} = 11.281 mins, *e.e.* = 10%, minor diastereomer: t = 10.87 mins, t = 13.7 mins, *e.e.* = 0%.

8.13. 2-(2-Nitro-1-phenylethyl)malononitrile 22a





Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.193	MM	0.9225	176.04356	3.18044	50.7537
2	26.965	MM	1.1417	170.81523	2.49365	49.2463
Totals :				346.85880	5.67408	

Figure S75. Reaction condition: catalyst Aib_4(L-Ala)NH^{t}Bu **1**, $CDCl_3$, 20 °C. **HPLC** Chiralpak AD-H column, hexane/i-PrOH (90:10), flow rate 0.6 mL/min, 254 nm; Enantiomers: t_{major} = 23.2 mins, t_{minor} = 26.9 mins, *e.e.* = 2%.

9. Time course of conjugate addition reactions monitored by ^{1}H NMR spectroscopy

9.1. 1-Methyl-1-(2-nitro-1-phenylethyl)-2 oxocyclopentane-1-carboxylate, 10

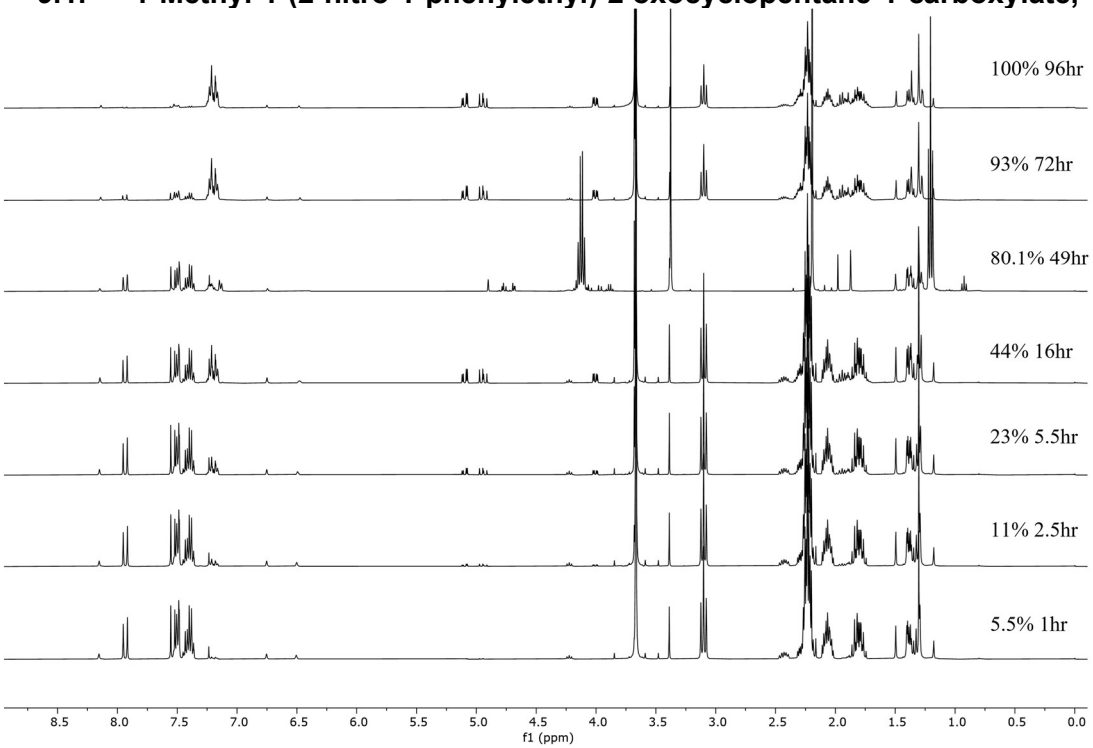


Figure S76: overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 1-methyl-2-oxocyclopentanecarboxylate **9** (3.5 equiv.) and Aib_4(L-Ala)NH^{t}Bu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **10**.

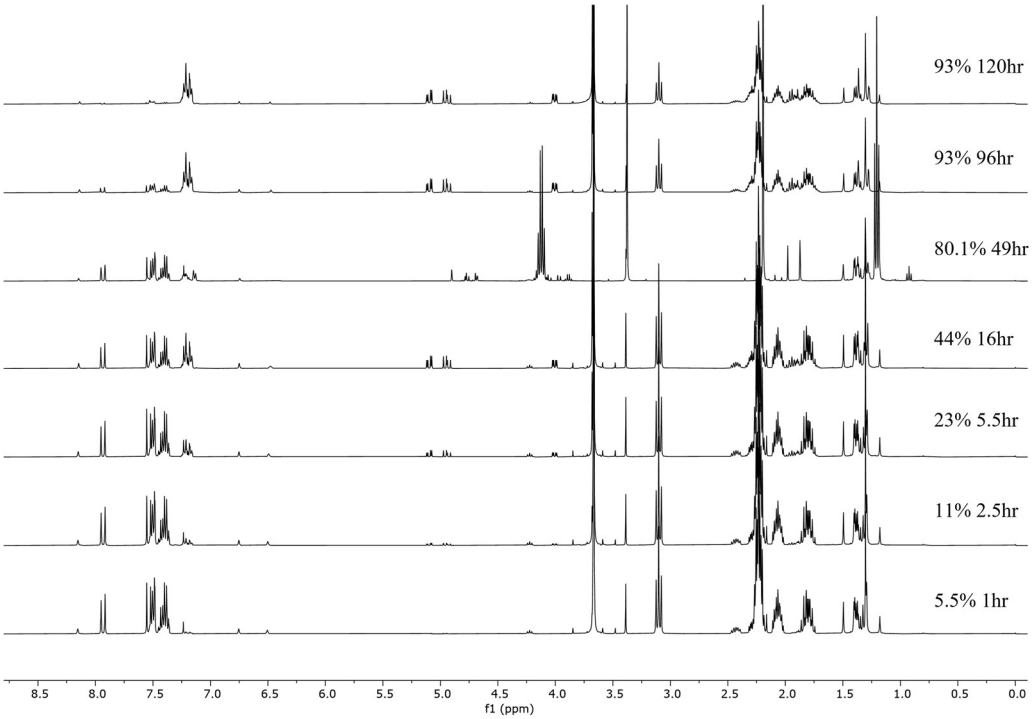


Figure S77: overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 1-methyl-2-oxocyclopentanecarboxylate **9** (3.5 equiv.) and Aib_4(L-Ala)NH^{t}Bu **1** (0.2 equiv.) at 0 °C without solvent, forming compound **10**.

9.2. Methyl 1-(2-nitro-1-phenylethyl)-2-oxocyclohexane-1-carboxylate, 15a

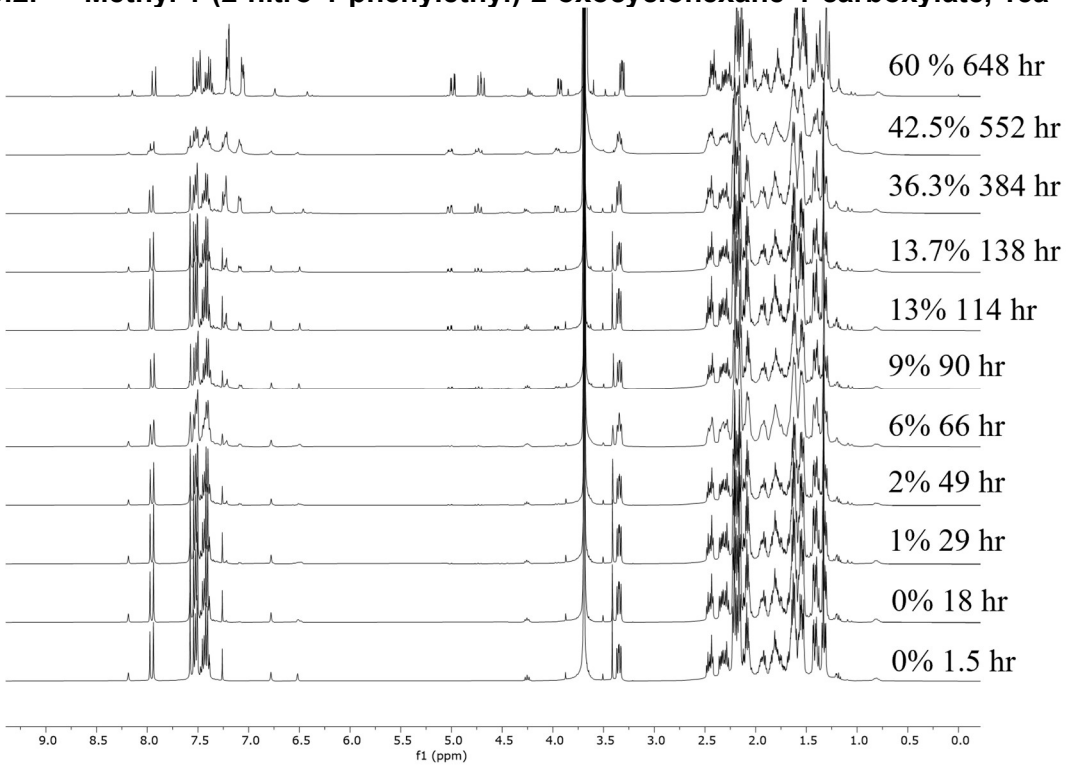


Figure S78: overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 1-methyl-2-oxocyclohexanecarboxylate **15** (3.5 equiv.) and Aib_4(L-Ala)NH^{t}Bu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **15a**.

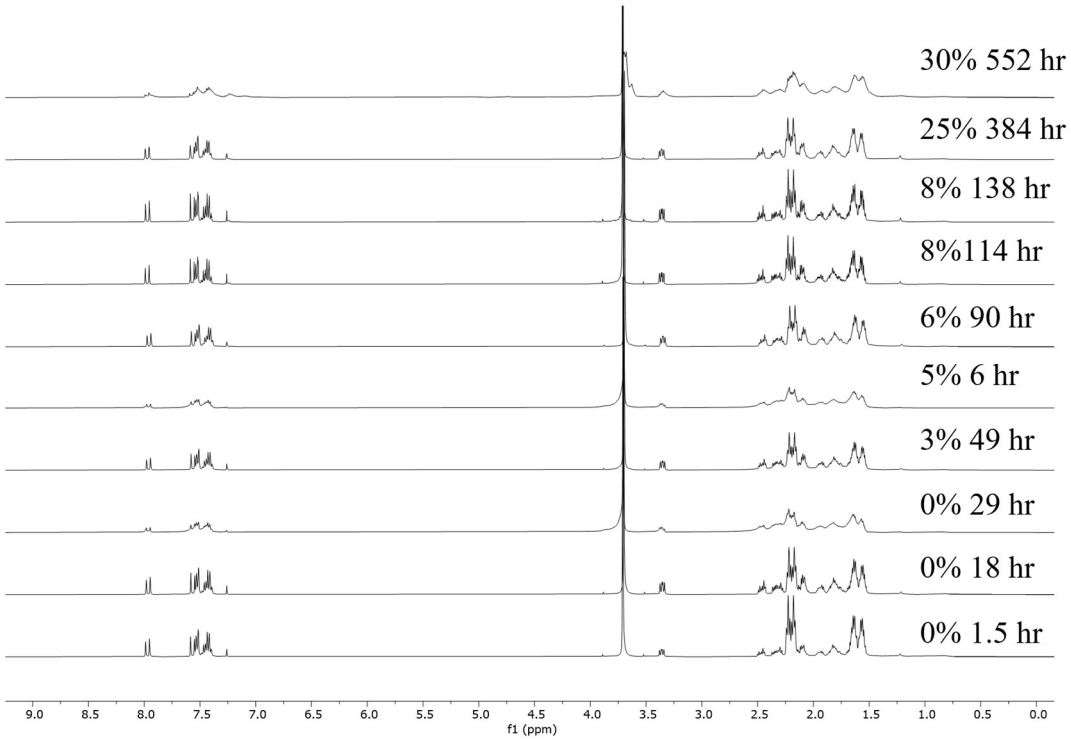


Figure S79: overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.) and 1-methyl-2-oxocyclohexanecarboxylate **15** (3.5 equiv.) in $CDCl_3$ at 20 °C (no catalyst), forming compound **15a**.

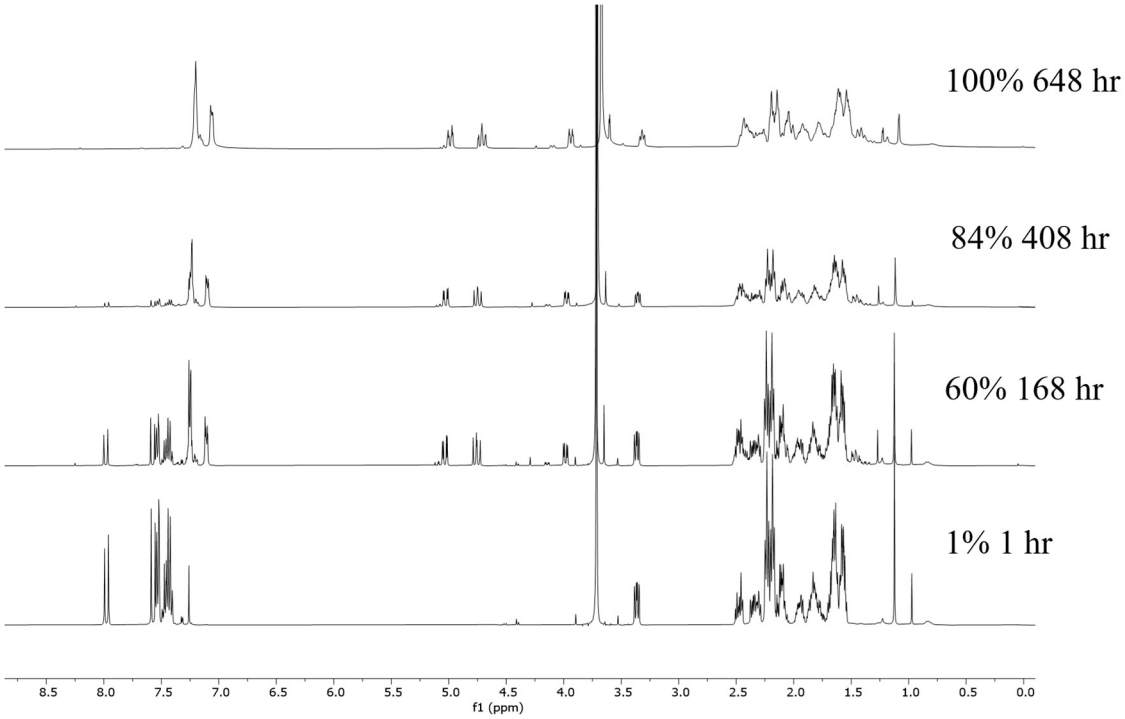


Figure S80: overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 1-methyl-2-oxocyclohexanecarboxylate **15** (3.5 equiv.) and H_2N^tBu (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **15a**.

9.3. Ethyl 4,4-dimethyl-2-(2-nitro-1-phenylethyl)-3-oxopentanoate, 20a

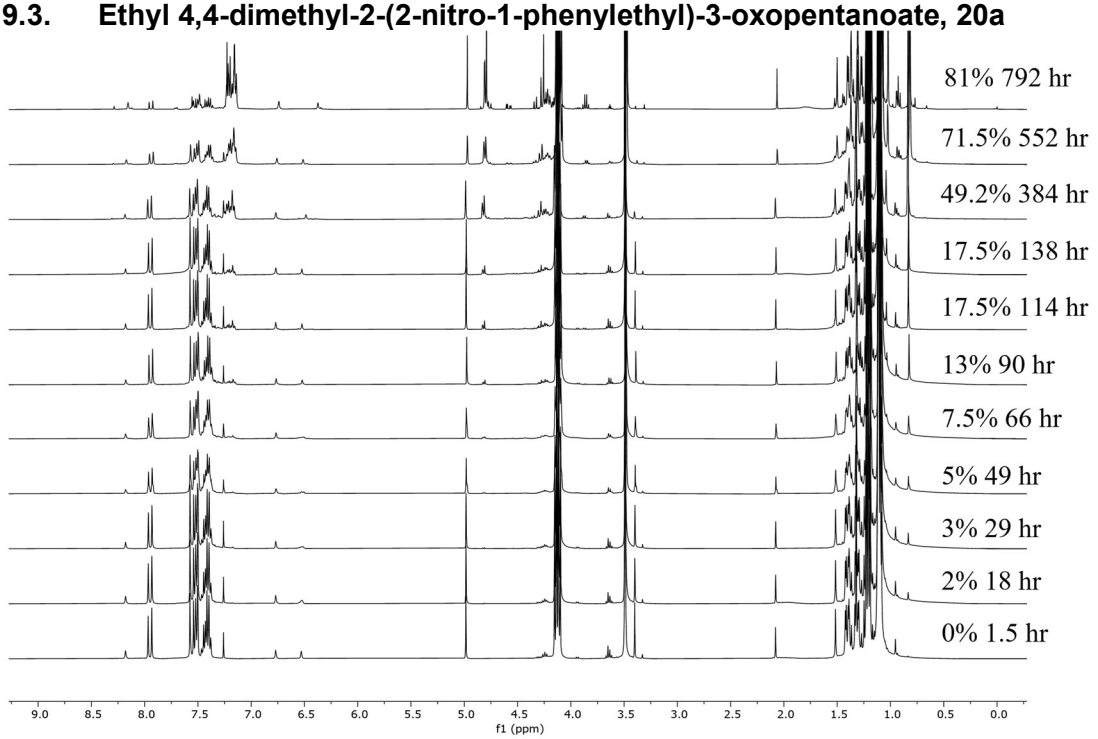


Figure S81: overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), ethyl pivaloylacetate **20** (3.5 equiv.) and Aib_4(L-Ala)NH^tBu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **20a**.

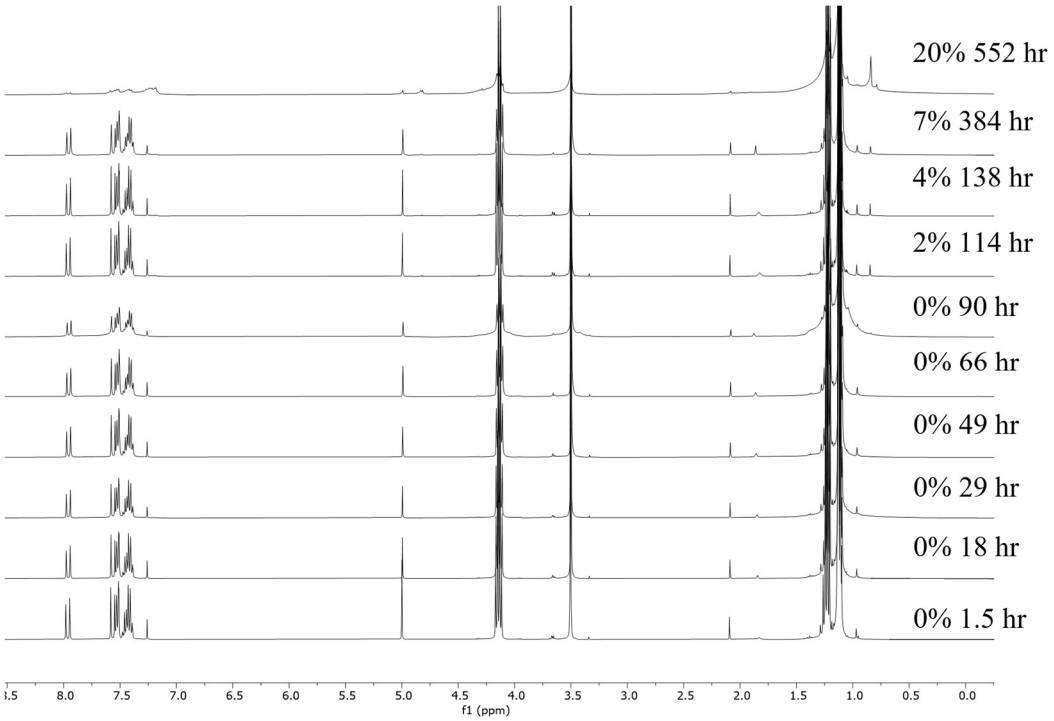


Figure S82. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), ethyl pivaloylacetate **20** (3.5 euiv.) in $CDCl_3$ at 20 °C (no catalyst), forming compound **20a**.

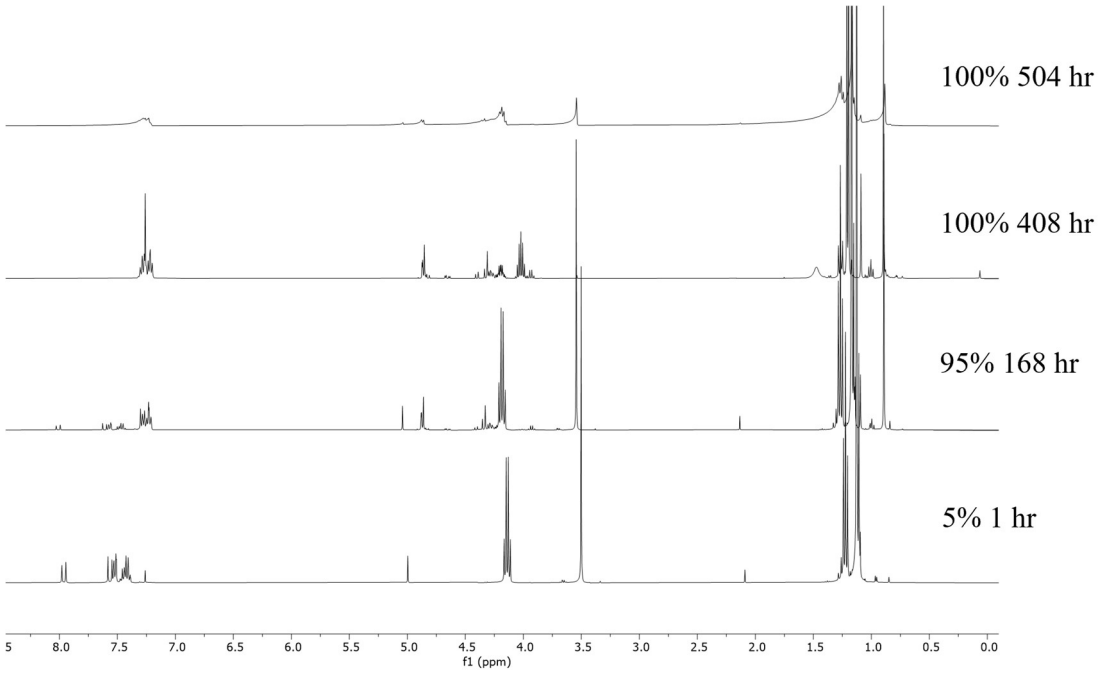


Figure S83. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), ethyl pivaloylacetate **20** (3.5 equiv.) and H_2N^tBu (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **20a**.

9.4. Ethyl 2-benzoyl-4-nitro-3-phenylbutanoate, 21a

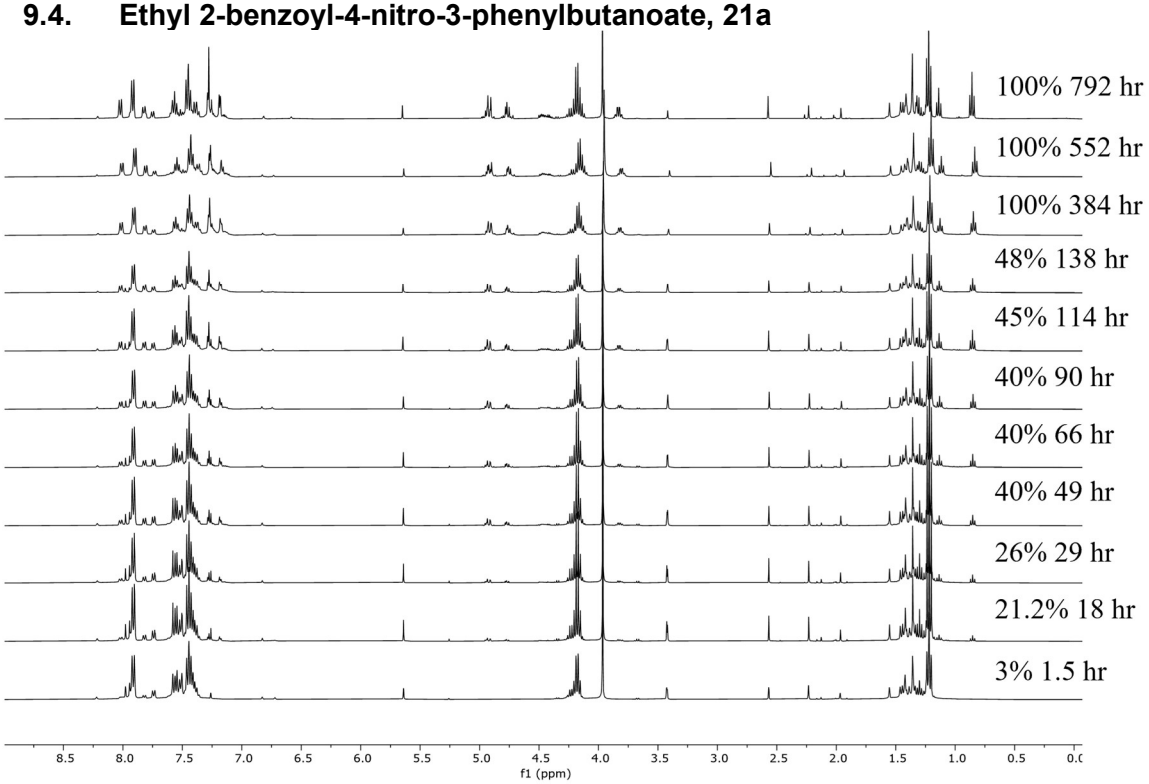


Figure S84. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), ethyl 3-oxo-3-phenylpropionate **21** (3.5 equiv.) and Aib_4(L-Ala)NH^{t}Bu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **21a**.

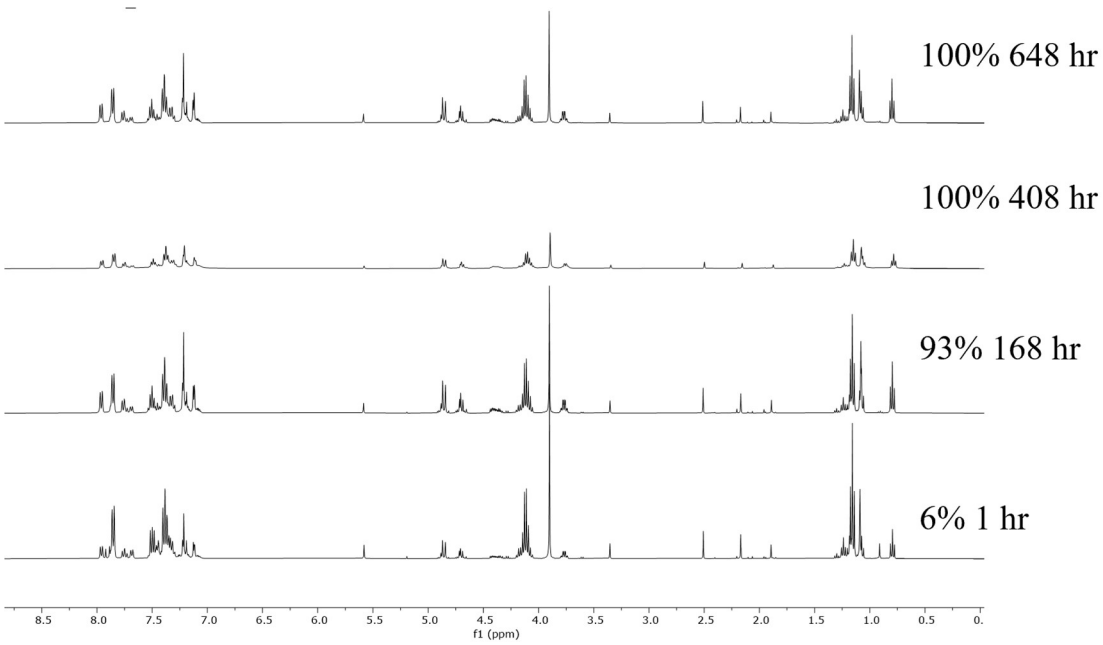


Figure S85. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), ethyl 3-oxo-3-phenylpropionate **21** (3.5 equiv.) and H_2N^tBu (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **21a**.

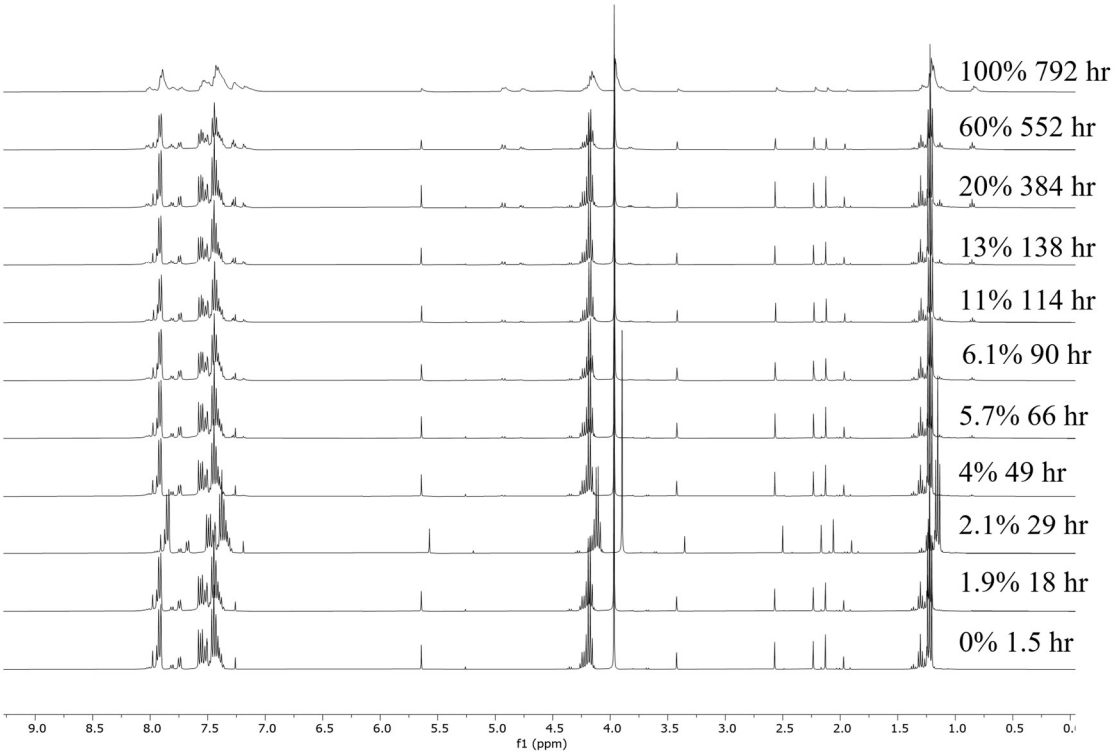


Figure S86. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.) and ethyl 3-oxo-3-phenylpropionate **21** (3.5 equiv.) (no catalyst) in $CDCl_3$ at 20 °C, forming compound **21a**.

9.5. Dimethyl 2-(2-nitro-1-phenylethyl)malonate, 17a

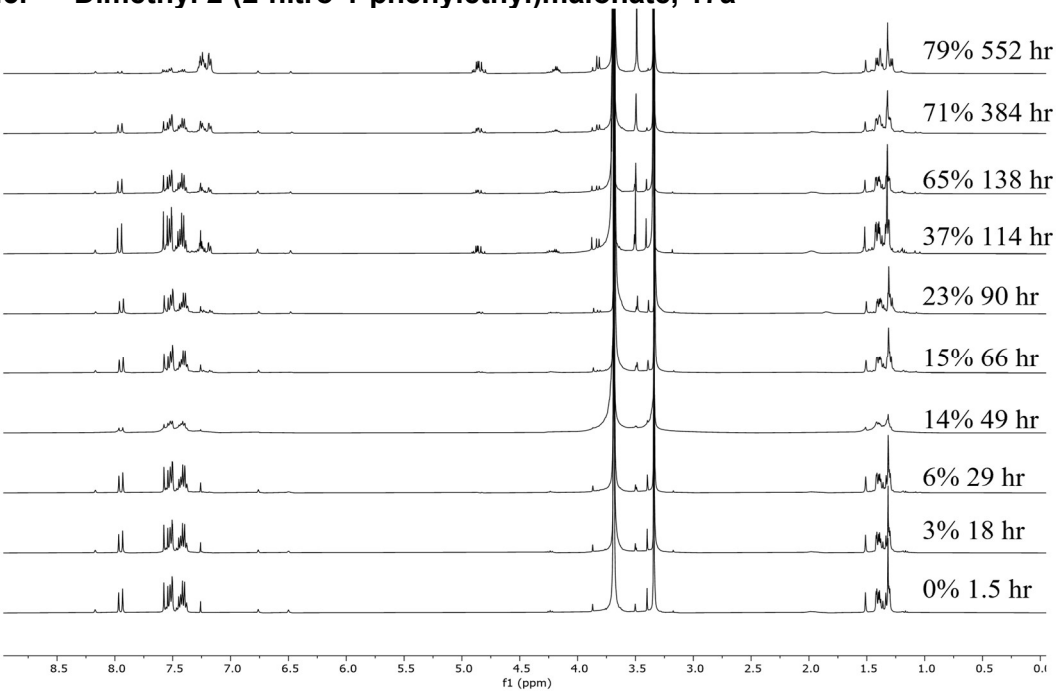


Figure S87. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), dimethyl malonate **17** (3.5 equiv.) and Aib_4(L-Ala)NH^{t}Bu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **17a**.

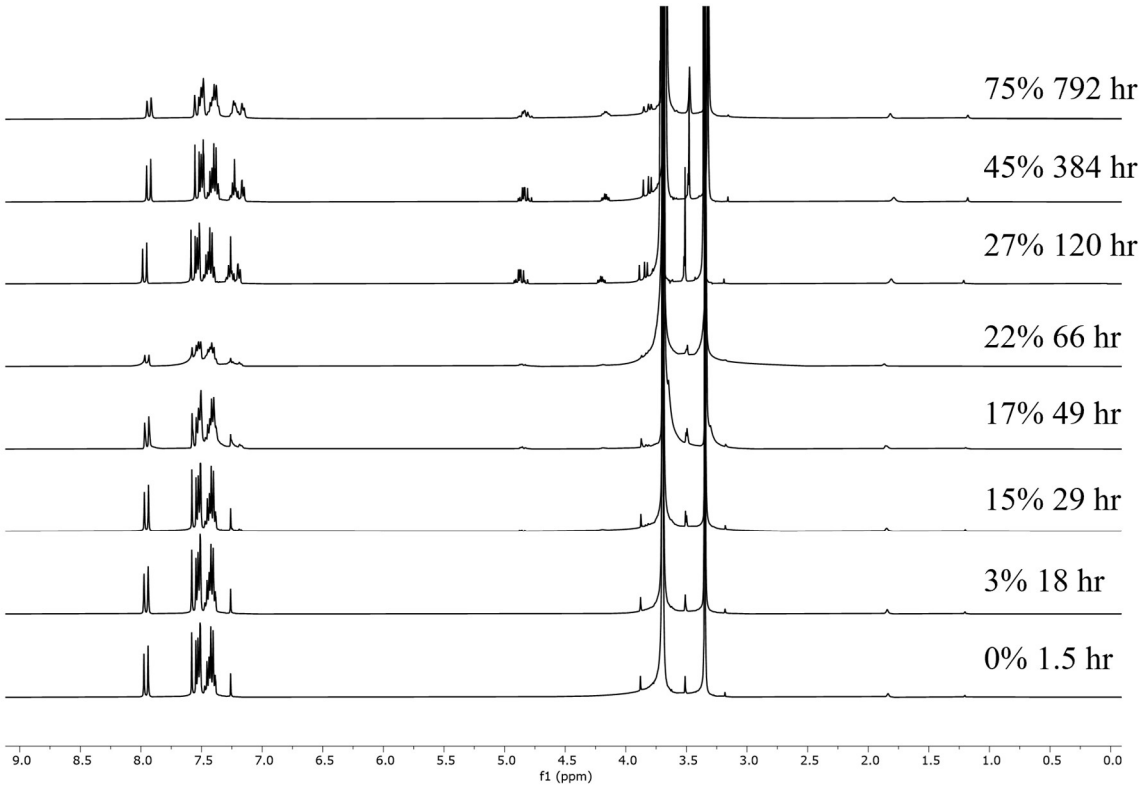


Figure S88. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.) and dimethyl malonate **17** (3.5 equiv.) (no catalyst) in $CDCl_3$ at 20 °C, forming compound **17a**.

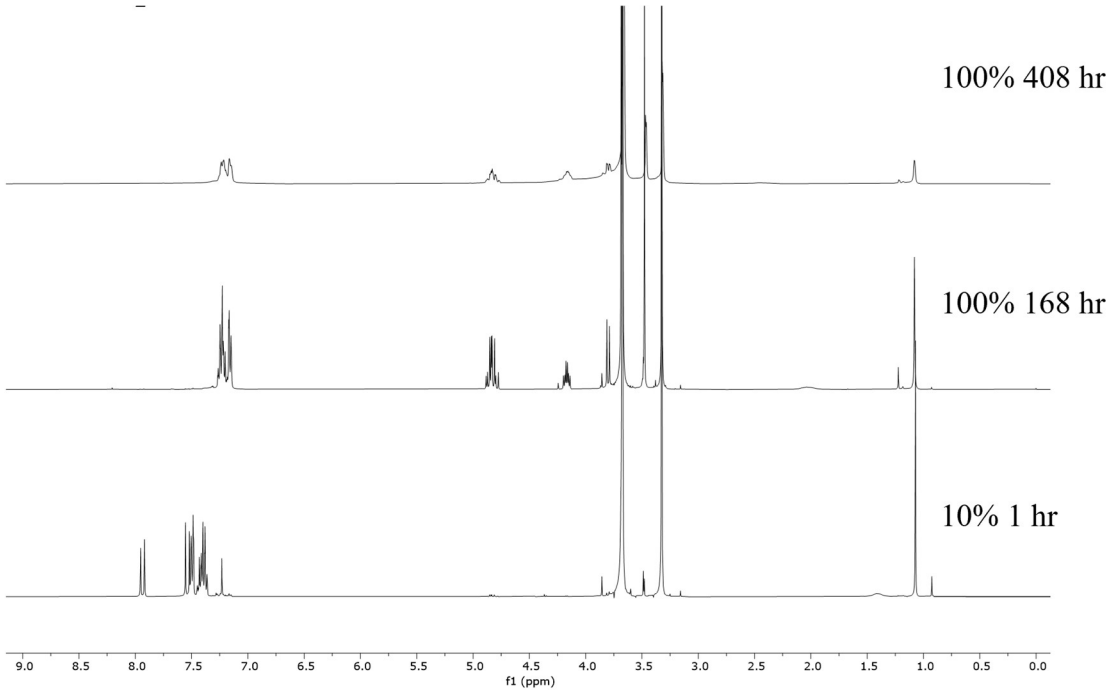


Figure S89. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), dimethyl malonate **17** (3.5 equiv.) and H_2N^tBu (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **17a**.

9.6. 1-Acetyl-2-(2-nitro-1-phenylethyl)indolin-3-one, 16a

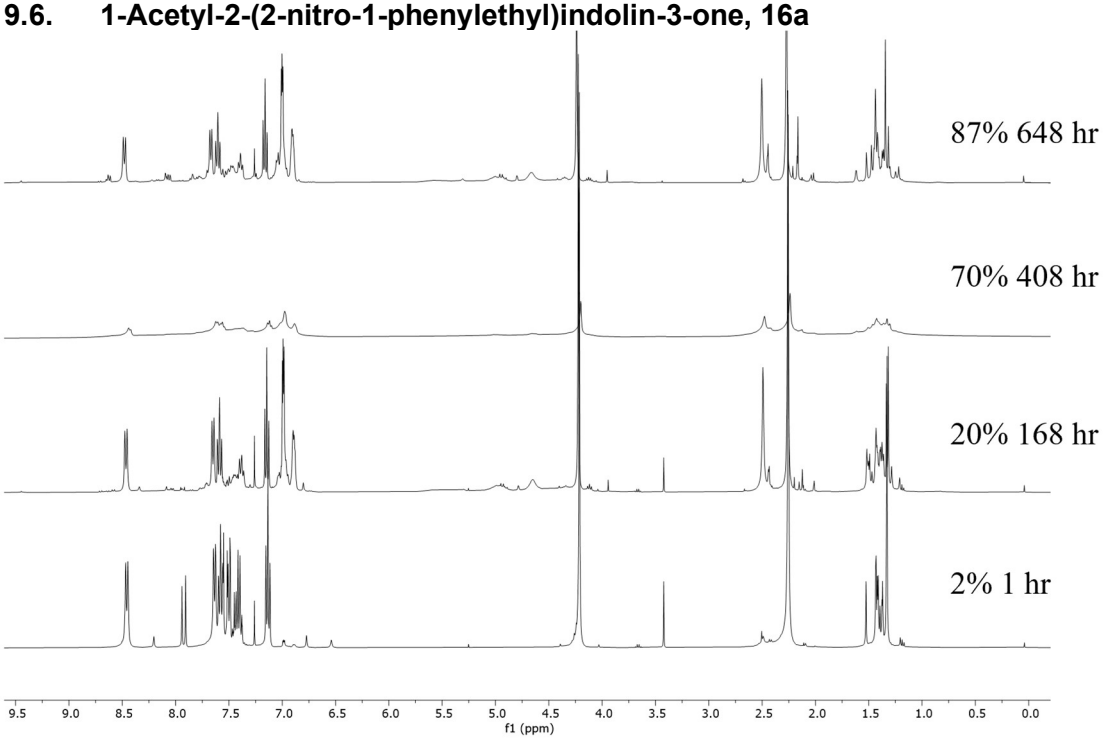


Figure S90. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 1-acetylindolin-3-one **16** (3.5 equiv.) and Aib_4(L-Ala)NH^{t}Bu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **16a**.

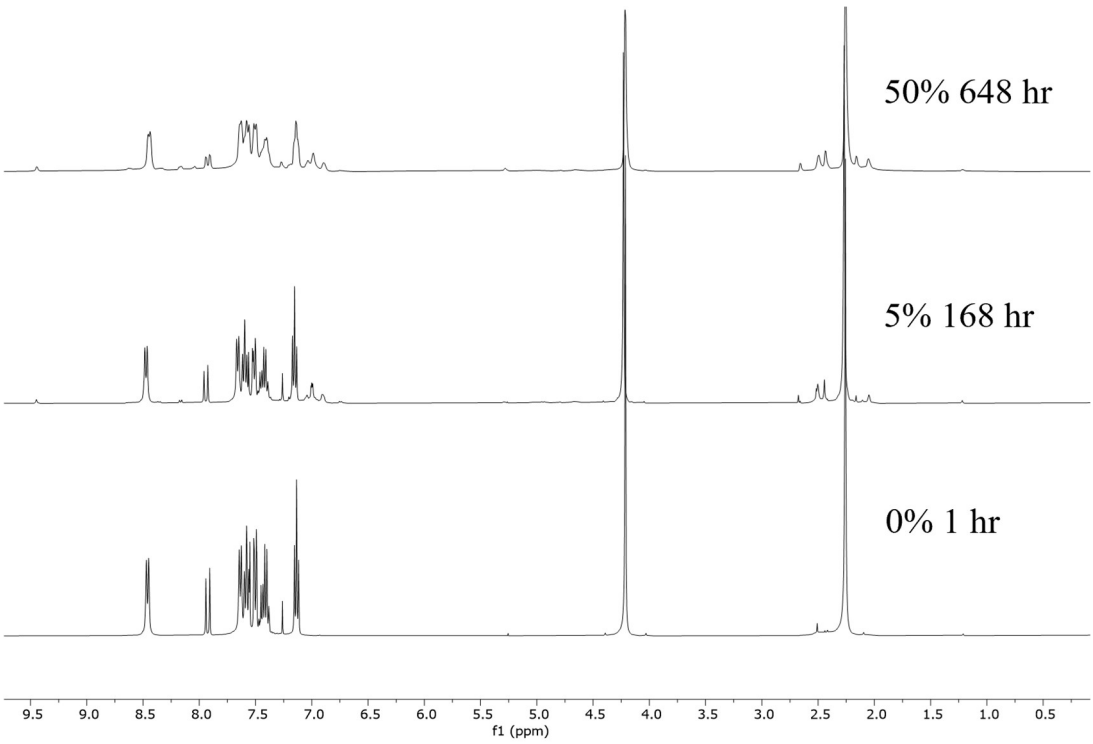


Figure S91. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.) and 1-acetylindolin-3-one **16** (3.5 equiv.) (no catalyst) in $CDCl_3$ at 20 °C, forming compound **16a**.

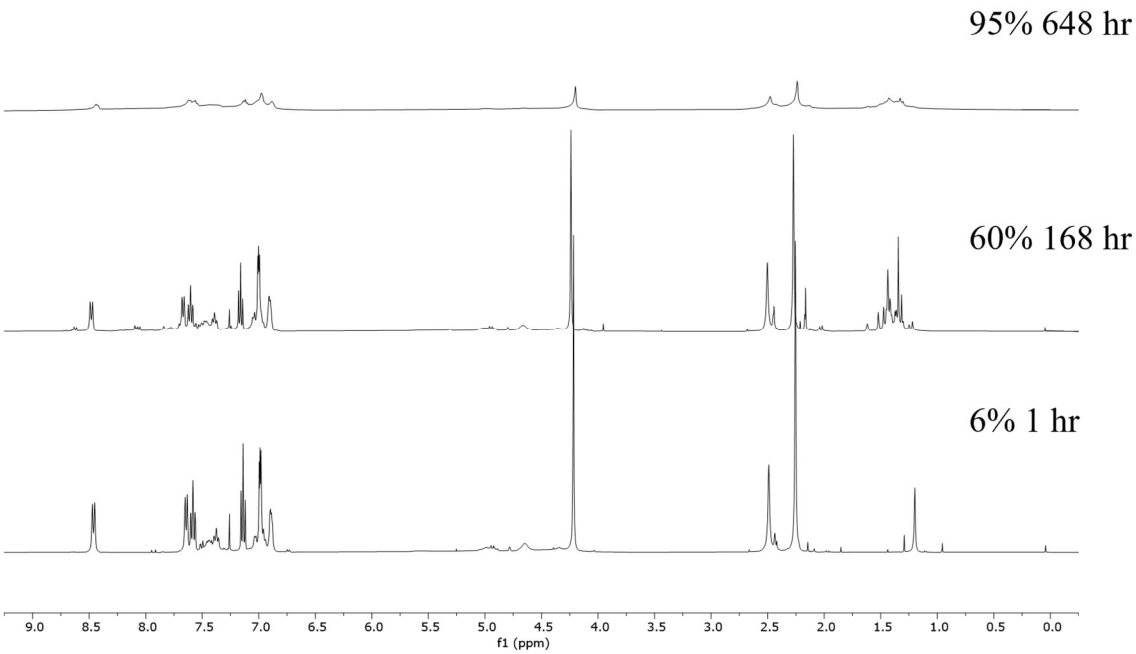


Figure S92. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 1-acetylindolin-3-one **16** (3.5 equiv.) and H_2N^tBu (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **16a**.

9.7. 3-(2-Nitro-1-phenylethyl)pentane-2,4-dione, 18a

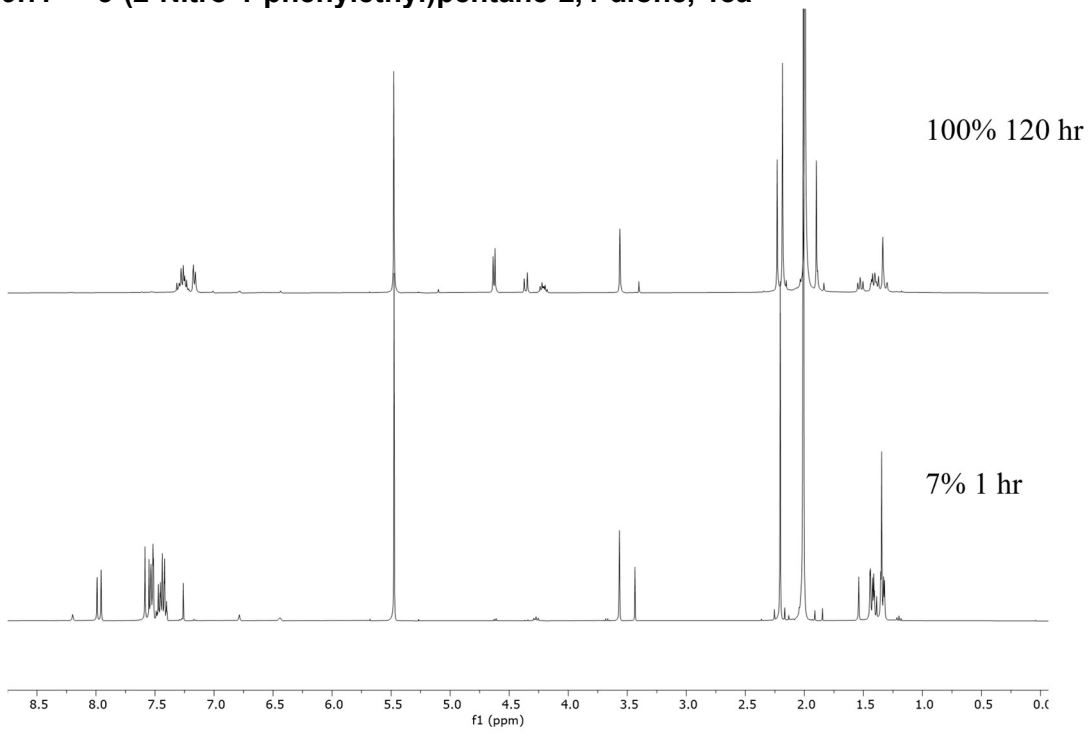


Figure S93. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), acetylacetone **18** (3.5 equiv.) and Aib_4(L-Ala)NH^tBu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **18a**.

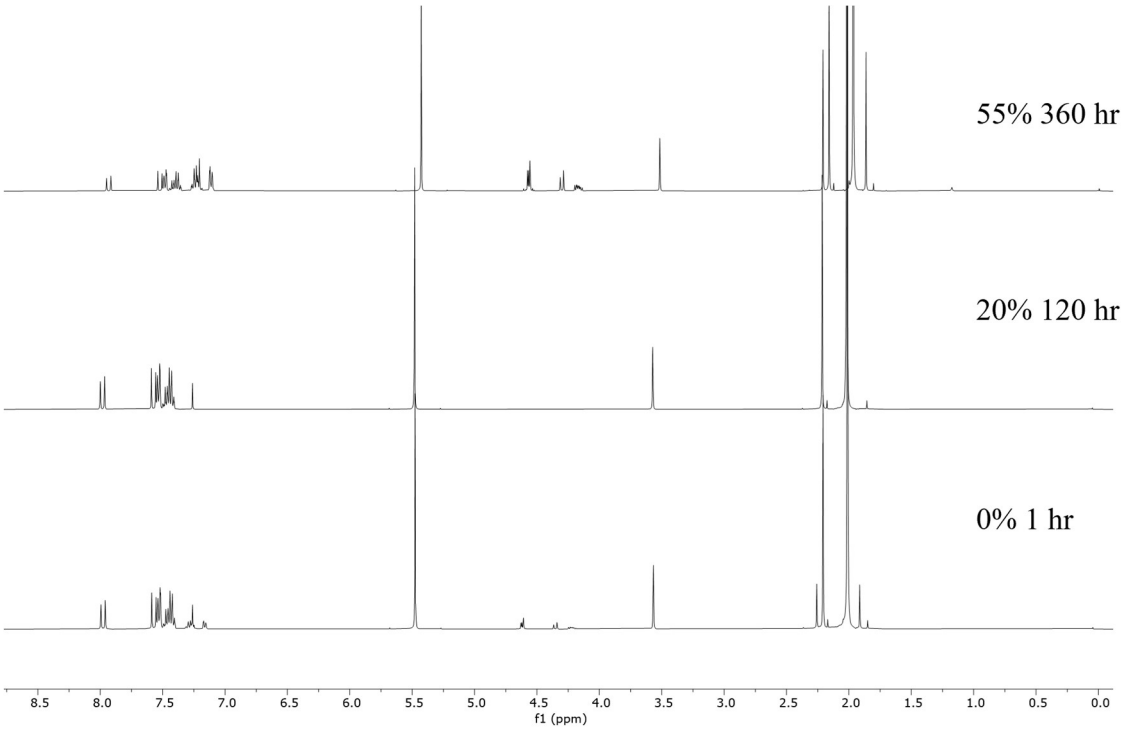


Figure S94. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.) and acetylacetone **18** (3.5 equiv.) (no catalyst) in $CDCl_3$ at 20 °C, forming compound **18a**.

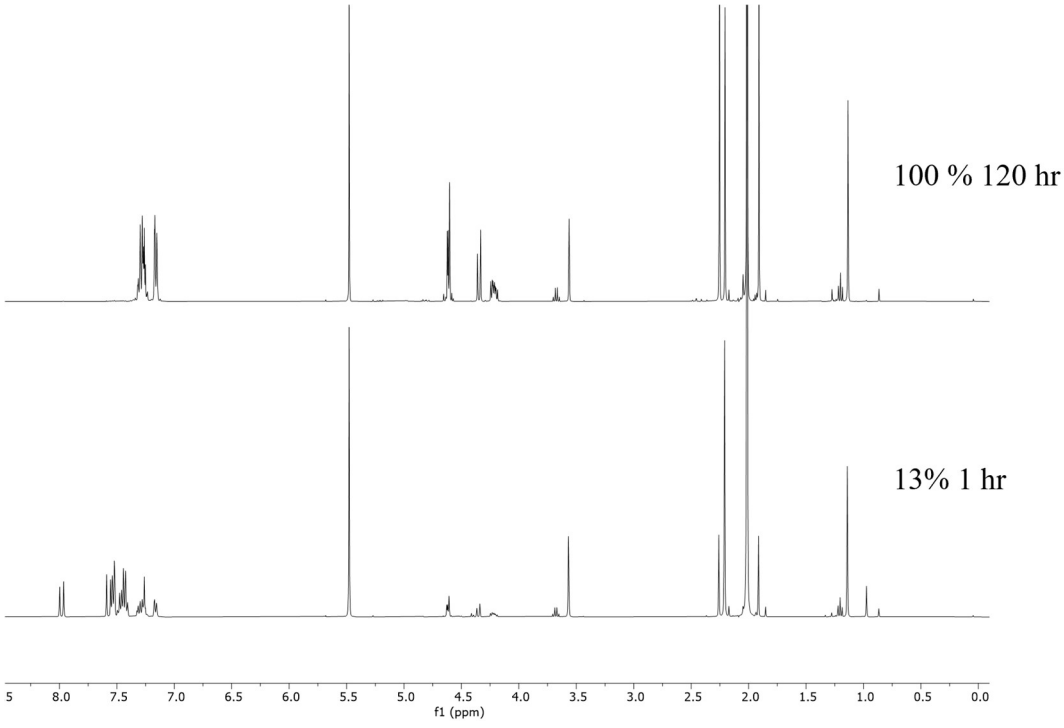


Figure S95. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), acetylacetone **18** (3.5 equiv.) and H_2N^tBu (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **18a**.

9.8. 2-Acetyl-2-(2-nitro-1-phenylethyl)cyclopentan-1-one, 14a

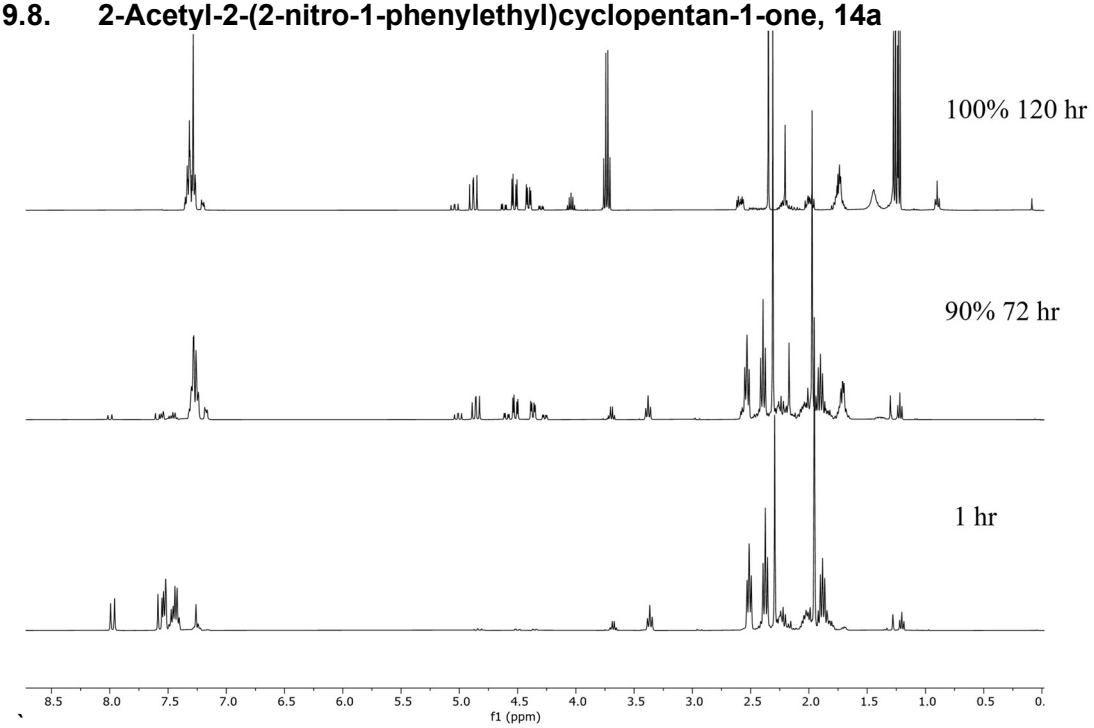


Figure S96. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 2-acetylcyclopentanone **14** (3.5 equiv.) and Aib_4(L-Ala)NH^{t}Bu **1** (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **14a**.

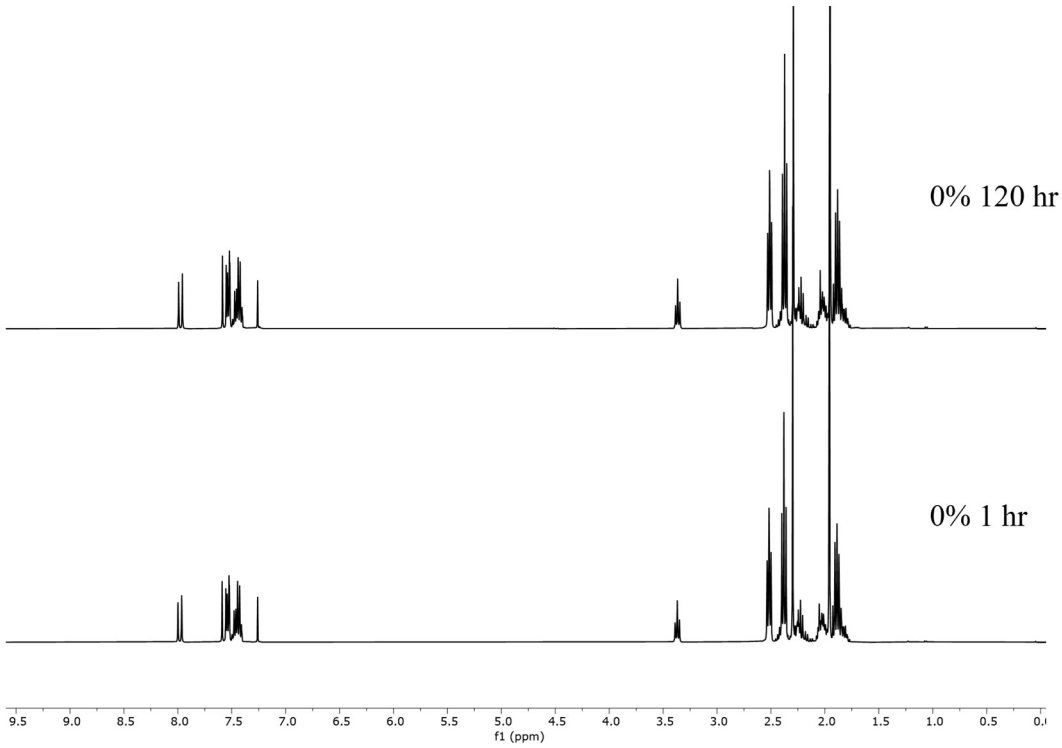


Figure S97. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.) and 2-acetylcyclopentanone **14** (3.5 equiv.) (no catalyst) in $CDCl_3$ at 20 °C, forming compound **14a**.

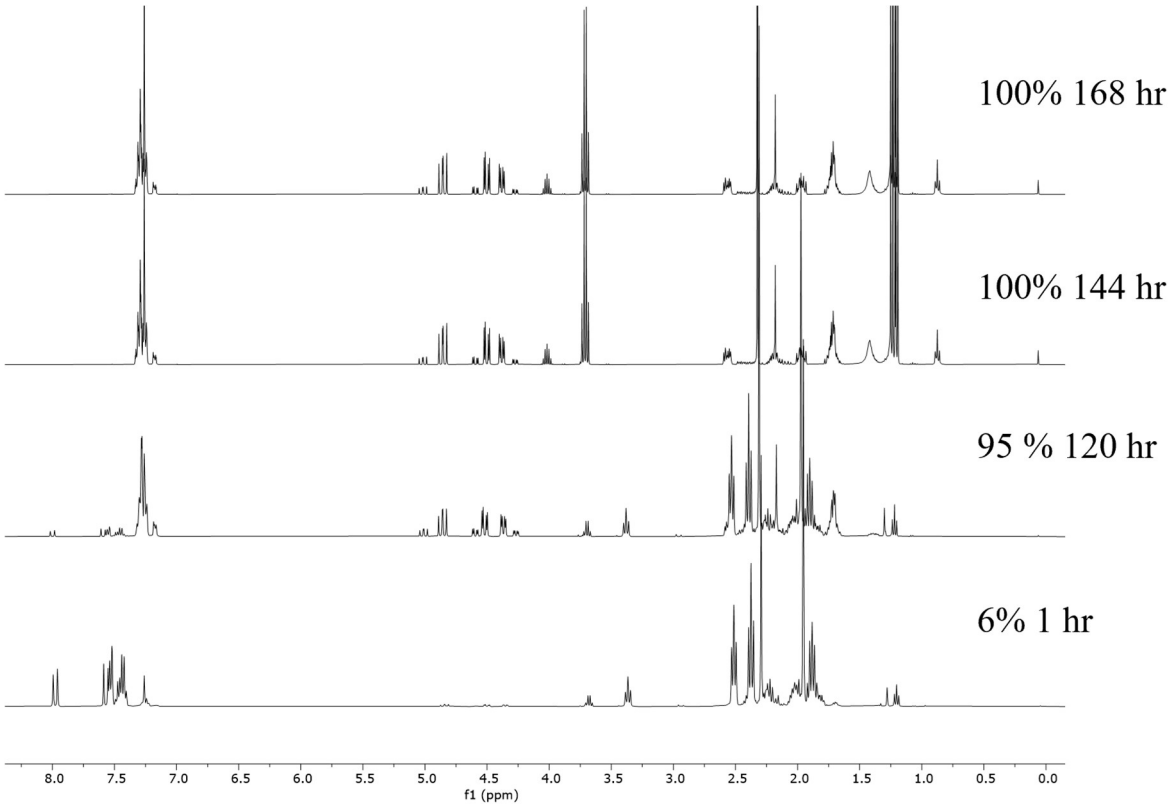


Figure S98. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 2-acetylcyclopentanone **14** (3.5 equiv.) and H_2N^tBu (0.2 equiv.) in $CDCl_3$ at 20 °C, forming compound **14a**.

9.9. 5,5-Dimethyl-3-(2-nitro-1-phenylethyl)hexane-2,4-dione, 19a

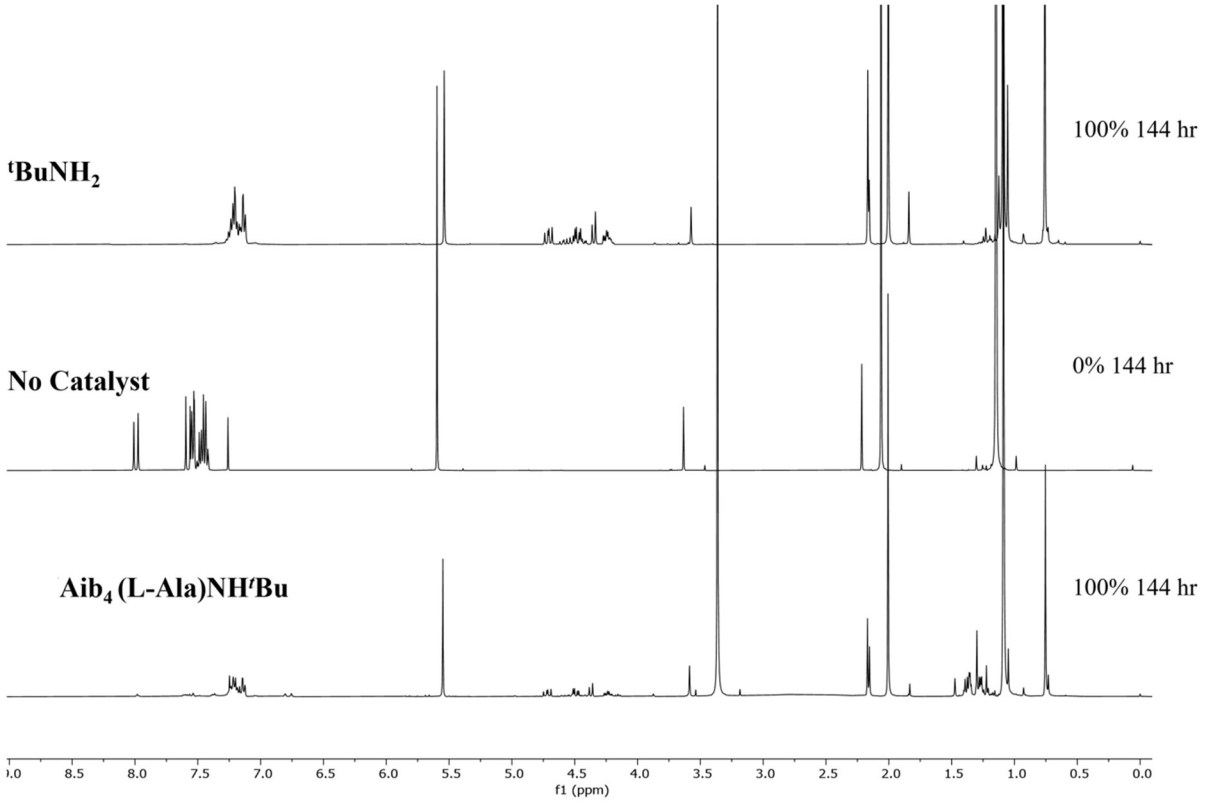


Figure S99. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 5,5-dimethylhexane-2,4-dione **19** (3.5 equiv.) and either H_2N^tBu (0.2 equiv.), or no catalyst, or Aib_4(L-Ala)NH^tBu **1** (0.2 equiv.), at 20 °C in $CDCl_3$ after 144 hours of reaction, forming compound **19a**.

9.10. 1-*tert*-Butyl-1-(2-nitro-1-phenylethyl)-2 -oxocyclopentane-1-carboxylate, 13a

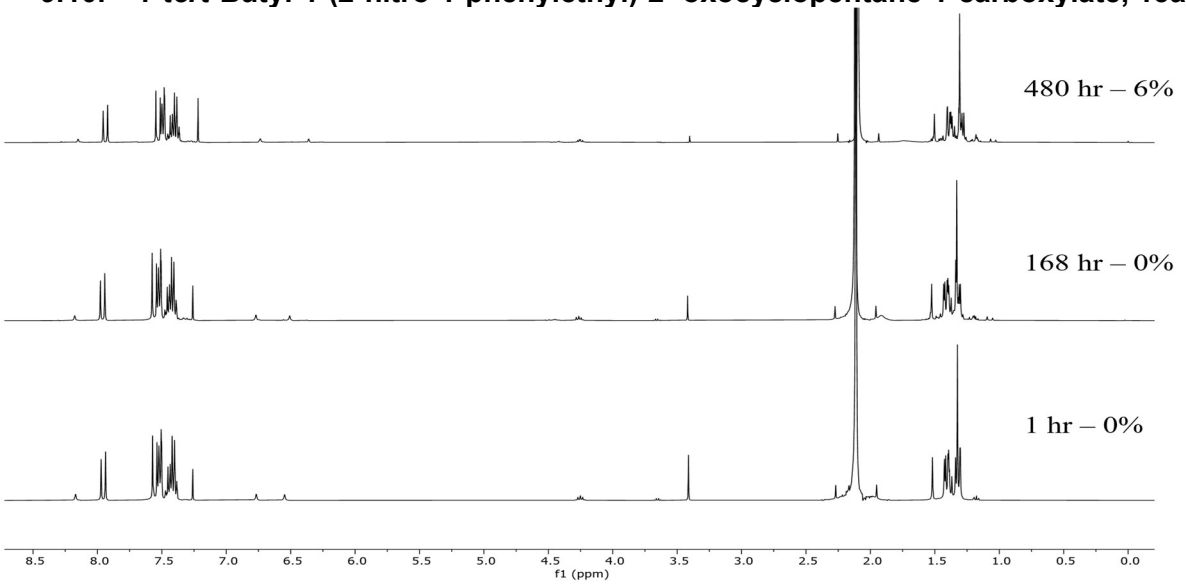


Figure S100. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.), 1-terbutyl-2-oxocyclopentanecarboxylate **13** (3.5 equiv.), and Aib_4(L-Ala)NH^tBu **1** (0.2 equiv) in $CDCl_3$ at 20 °C, forming compound **13a**.

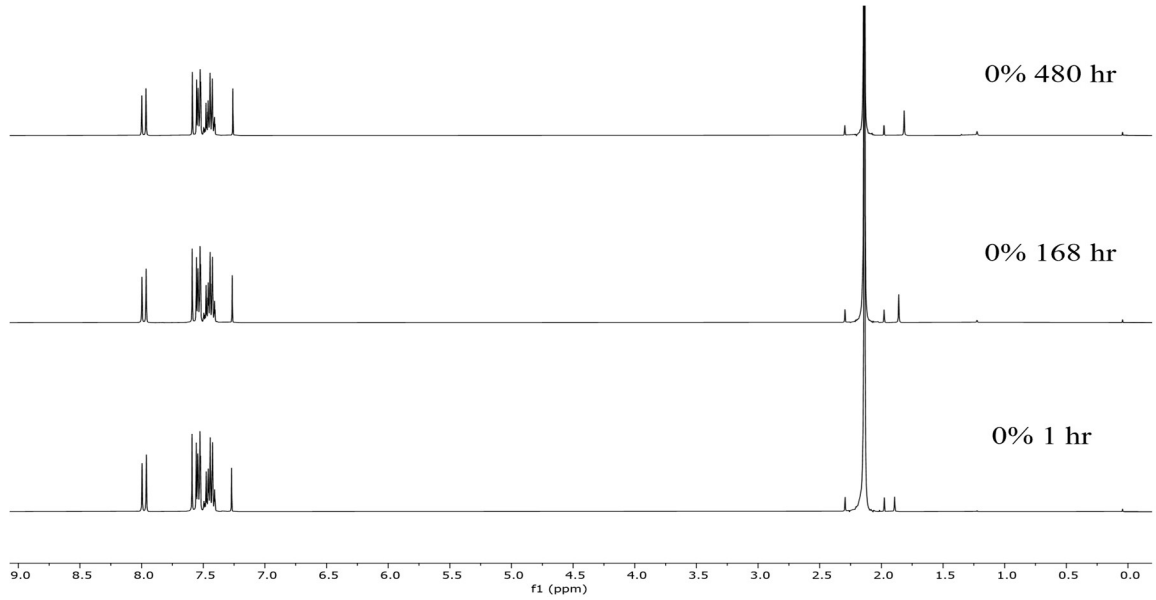


Figure S101. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) for the time course of reaction between *(E)*-(2-nitrovinyl)benzene **8** (1 equiv.) and 1-terbutyl-2-oxocyclopentanecarboxylate **13** (3.5 equiv.) (no catalyst) in $CDCl_3$ at 20 °C, forming compound **13a**.

9.11. 1-Methyl-1-(1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 12a

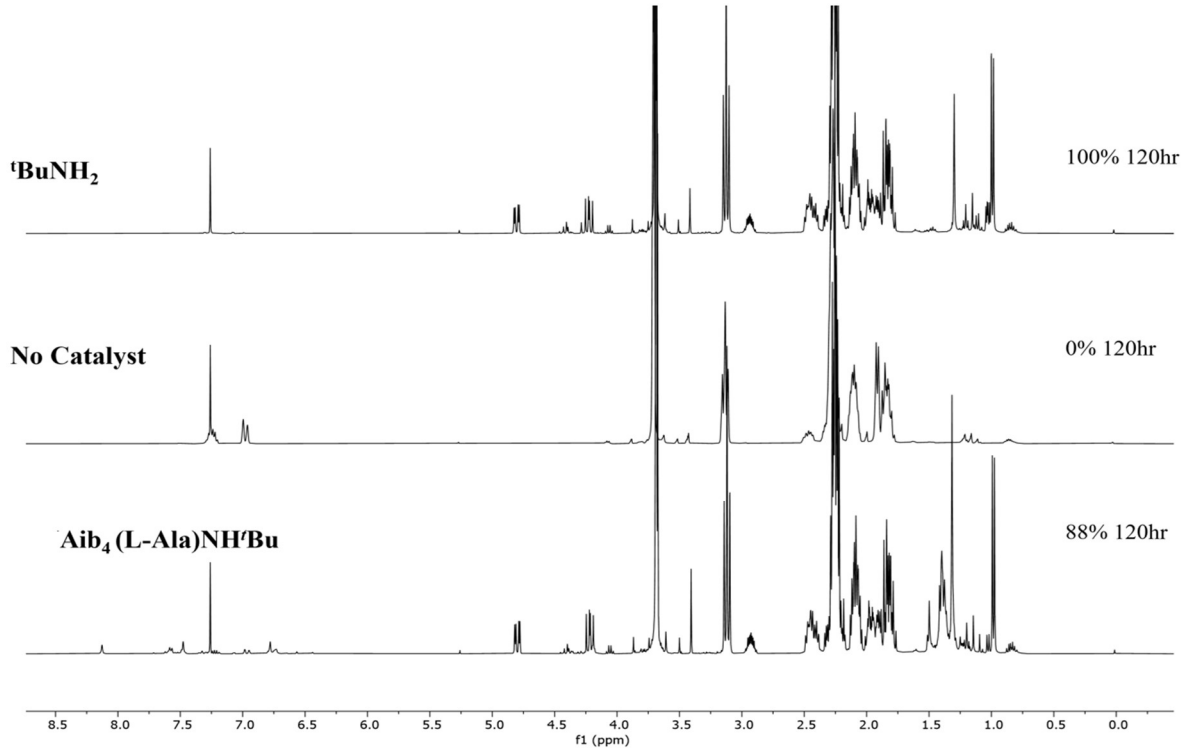


Figure S102. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) of reaction between *(E)*-1-nitropropene **12** (1 equiv.), 1-methyl-2-oxocyclopentanecarboxylate **9** (3.5 equiv.) and either H_2N^tBu (0.2 equiv.), or no catalyst, or Aib_4(L-Ala)NH^tBu ***1*** (0.2 equiv.), at 20 °C in $CDCl_3$ after 120 hours of reaction, forming compound **12a**.

9.12. Methyl 1-(3-methyl-1-nitrobutan-2-yl)-2-oxocyclopentane-1-carboxylate, 11a

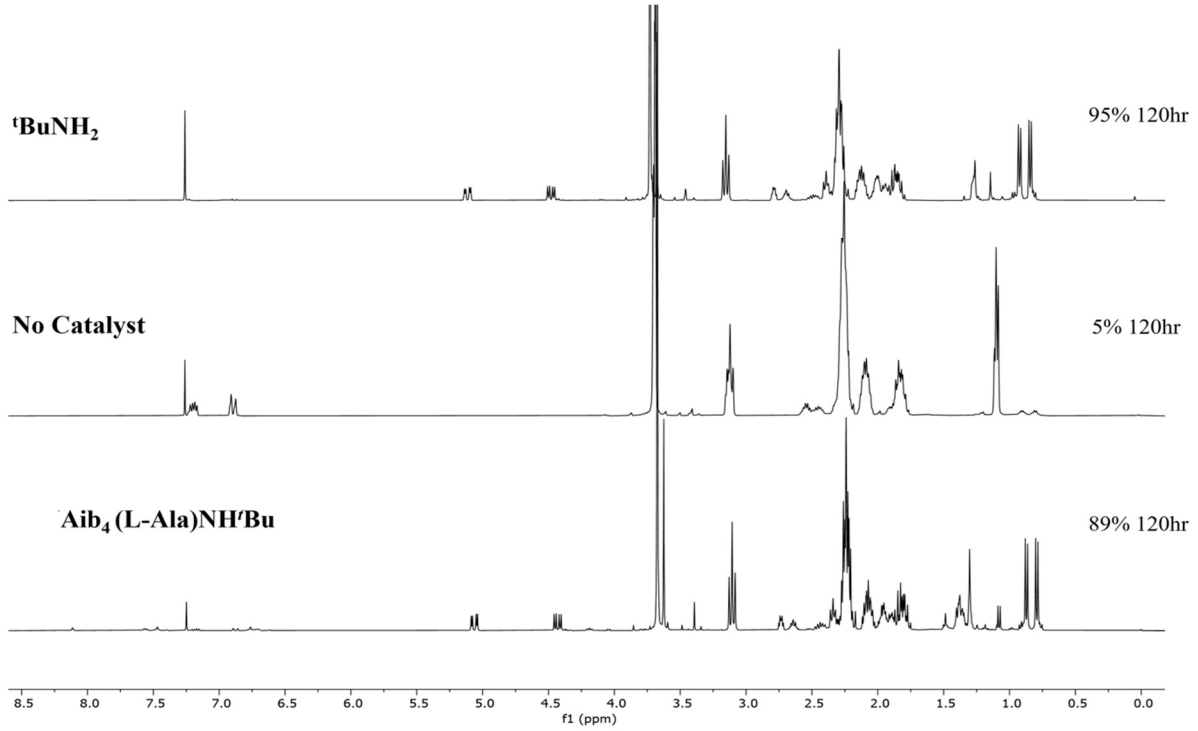


Figure S103. Overlay of ^{1}H NMR spectra (in $CDCl_3$ at 20 °C) of reaction between *(E)*-3-methyl-1-nitropropene **11** (1 equiv.), 1-methyl-2-oxocyclopentanecarboxylate **9** (3.5 equiv.) and either H_2N^tBu (0.2 equiv.), or no catalyst, or Aib_4(L-Ala)NH^tBu **1** (0.2 equiv.), at 20 °C in $CDCl_3$ after 120 hours of reaction, forming compound **11a**.

9.13. 2-(2-Nitro-1-phenylethyl)malononitrile, 22a

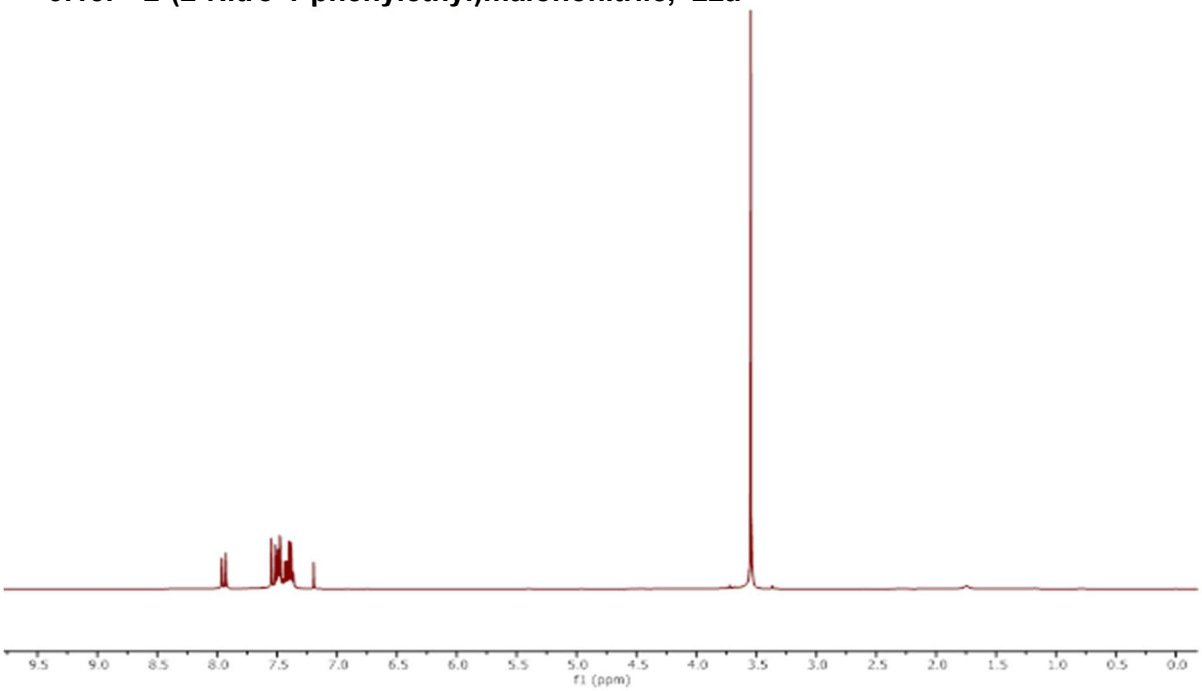


Figure S104. ^{1}H NMR spectrum of a mixture of *(E)*-(2-nitrovinyl)benzene **8** and malonitrile **22** in $CDCl_3$ at 20 °C after 6 days, showing no conversion.

10. Summary of stereoselective outcomes from organocatalysed conjugate additions

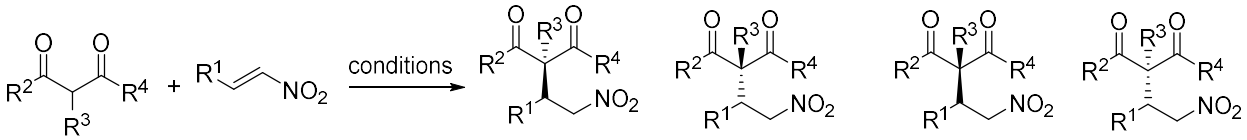
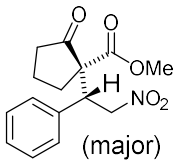
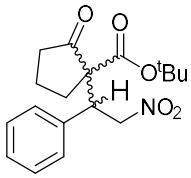
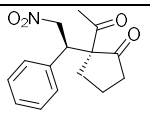
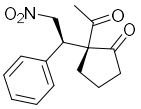
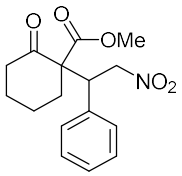
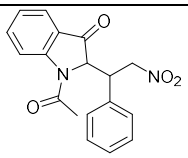
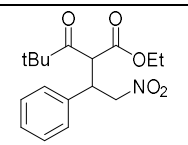
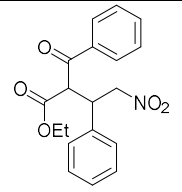
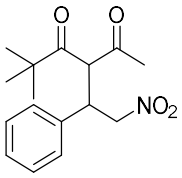
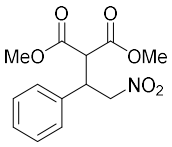
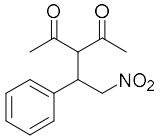
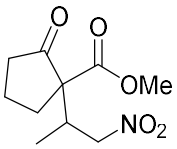
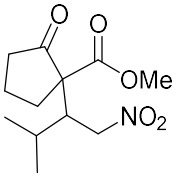
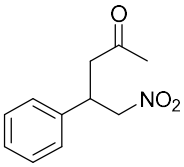
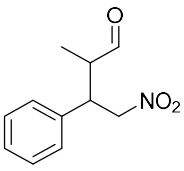
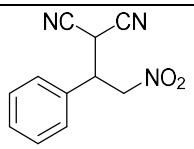


Table S2 Michael adducts isolated:

Entry	Michael Adduct [a]	Catalyst	Isolated Yield (%) [b]	Time (days)	Conv. (%) [c]	*d.r.* [d]	*e.e.* [e] (%)
1	 (major) 2R,3S **10** [f]	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	98	5	100	96:4	54/58
		Aib_4(L-Ala)NH^{t}Bu **1** 40 °C, $CDCl_3$	94	2.5	100	91:9	23/9
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	88	1	100	68:32	-
		No Catalyst 20 °C, $CDCl_3$	30 reaction not as clean as when amine is present	6	58	77:23	-
		N_3Aib_5NH^{t}Bu **6** 20 °C, $CDCl_3$	10	6	26	65:35	-
		Aib_4(L-Ala)NH^{t}Bu **1** 0 °C, no solvent	93	2.5	100	90:10	69/14
		^{t}BuNH$_2$ 0 °C, no solvent	85	1	100	59:41	-
		Aib(L-Ala)NH^{t}Bu **4** 0 °C, no solvent	88	4	100	82:18	1/0
		Aib_8(L-Ala)NH^{t}Bu **3** 20 °C, $CDCl_3$	93	5	100	88:12	5/19
		Aib_4(D-Phe)NH^{t}Bu **5** 20 °C, $CDCl_3$	94	8	100	90:10	-42/-1
2	 **13a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	50	8	100	81:19	17/5
		Aib_4(L-Ala)NH^{t}Bu **1** 0 °C, no solvent	51	10	100	85:15	27/2
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	43	8	100	87:13	-

3	 major diastereomer  minor diastereomer **14a** [f]	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	70	5	100	86:14	18/-
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	75	5	100	53:47	-
		No catalyst 20 °C, $CDCl_3$	-	5	0	-	-
4	 **15a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	80	25	100	92:8	16/5
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	85	17	100	83:17	-
		No catalyst 20 °C, $CDCl_3$	-	18	0	-	-
		Aib_4(L-Ala)NH^{t}Bu **1** 0 °C, no solvent	84	5	100	94:6	17/16
		^{t}BuNH$_2$ 0 °C, no solvent	83	4	100	91:9	-
5	 **16a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	71	25	87	85:15	18/-
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	79	25	95	85:15	-
		No catalyst 20 °C, $CDCl_3$	-	25	0	-	-
6	 **20a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	84	23	100	95:5	46/-
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	56	10	100	91:9	-
		No catalyst 20 °C, $CDCl_3$	-	23	0	-	-
7	 **21a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	94	15	100	55:45	8/9
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	100	7	100	50:50	-
		No catalyst 20 °C, $CDCl_3$	5	23	10	58:42	-

8	 **19a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	79	5	100	79:21	52/44
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	84	5	100	77:23	-
		No catalyst 20 °C, $CDCl_3$	-	6	0	-	-
9	 **17a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	91	23	100	-	0
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	86	7	100	-	0
		No catalyst 20 °C, $CDCl_3$	-	23	28	-	-
10	 **18a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	67	5	100	-	23/-
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	76	1	100	-	-
		No catalyst 20 °C, $CDCl_3$	28	15	55	-	-
11	 **12a**	Aib_4(L-Ala)NH^{t}Bu **1** 0 °C, no solvent	80	5	88	89:11	28/18
		^{t}BuNH$_2$ 0 °C, no solvent	100	5	100	89:11	-
		No catalyst 20 °C, $CDCl_3$	0	5	0	-	-
12	 **11a**	Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	80	4	89	99:1	10/-
		^{t}BuNH$_2$ 20 °C, $CDCl_3$	75	4	95	98:2	-
		No catalyst 20 °C, $CDCl_3$	-	4	5	-	-
13		Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	-	20	0	-	-
14		Aib_4(L-Ala)NH^{t}Bu **1** 20 °C, $CDCl_3$	-	20	0	-	-

15	 **22a**	Aib_4(L-Ala)NH^tBu **1** 20 °C, $CDCl_3$	100	1.5	100	-	2

a) General procedure: in a dry NMR tube, the Michael acceptor (0.077 mmol, 1 equivalent, 0.156 M in $CDCl_3$), the nucleophile (3.5 equivalents), and the catalyst (0.0156 mmol, 20 mol%) (where appropriate) were dissolved (where appropriate) in $CDCl_3$ pre-dried over K_2CO_3 (0.5 mL). The NMR tube was sealed and shaken, then was stored at the appropriate temperature and reaction time. ^{1}H NMR spectra were recorded over time to monitor the conversion of reaction. On completion of the reaction, the solvent was removed under reduced pressure, the residue was purified by chromatography on silica to afford the product. b) Isolated yields after chromatography on silica. c) Conversion determined by integration of the appropriate ^{1}H NMR signals on the crude reaction mixture. d) Ratio of diastereomers (*d.r.*) measured by integration of the appropriate ^{1}H NMR signals on the crude reaction mixture. e) Enantiomeric excess (*e.e.*) were measured by integration of signals using chiral stationary phase HPLC on the purified product. f) Configuration of products was deduced by comparison with previous data of literature.

11. Crystal data and structure refinement of peptide 1

Single crystals suitable for X-ray diffraction analysis were grown by slow evaporation of an acetonitrile solution containing the foldamer. Data were collected on a dual source Rigaku FR-X rotating anode diffractometer using CuKα wavelength radiation (λ = 1.54184) at a temperature of 100 K. The data were reduced for each component using CrysAlisPro 1.71.40.14d obtaining a 0.2/0.8 proportion. Absorption correction was performed using empirical methods (SCALE3 ABSPACK) based upon symmetry-equivalent reflections combined with measurements at different azimuthal angles.10 The structure was solved and refined against F 2 using Shelx implemented through Olex2. 11 Hydrogen atoms were placed in the calculated positions and assigned fixed thermal parameters. All the non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located geometrically and refined using a riding model. Disorder was modelled by setting the sum of the parts to 1 and refining the occupancies, restraints and constraints were applied to maintain sensible thermal and geometric parameters.

CCDC 2281755 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk)

Table S3: Crystal data and structure refinement for s6125r.

Identification code	s6125r
Empirical formula	$C_{23}H_{46}N_6O_6$
Formula weight	502.66
Temperature/K	99.99(14)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	11.6820(2)
b/Å	16.3850(3)
c/Å	15.2184(3)
α/°	90
β/°	103.063(2)
γ/°	90
Volume/Å^3	2837.57(9)
Z	4
ρ_{calc}g/cm^3	1.177
μ/mm^{-1}	0.699
F(000)	1096.0
Crystal size/mm^3	0.11 × 0.08 × 0.02
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	5.962 to 152.876
Index ranges	-14 ≤ h ≤ 14, -20 ≤ k ≤ 20, -18 ≤ l ≤ 18
Reflections collected	72133
Independent reflections	11450 [R_{int} = 0.0643, R_{sigma} = 0.0402]
Data/restraints/parameters	11450/1/655
Goodness-of-fit on F^2	1.060
Final R indexes [I>=2σ (I)]	R_1 = 0.0384, wR_2 = 0.0912
Final R indexes [all data]	R_1 = 0.0485, wR_2 = 0.0972
Largest diff. peak/hole / e Å^{-3}	0.24/-0.23
Flack parameter	-0.05(8)

Table S4: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for s6125r. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	2158.5(15)	4847.6(12)	2881.5(12)	27.2(4)
O17	-1546.2(16)	4582.2(13)	3694.9(13)	34.0(5)
O19	1527.4(17)	5663.8(14)	5934.4(12)	35.3(5)
O29	4168.6(18)	6351.3(13)	3470.5(13)	33.9(4)
O32	2948.5(16)	3858.3(12)	4940.3(12)	27.9(4)
N3	4083.0(19)	4537.0(14)	3088.7(14)	25.4(5)
N6	3760.2(19)	5081.6(13)	4749.5(14)	22.7(4)
N9	1405.8(18)	5362.4(14)	4476.3(13)	22.9(4)
N12	165.1(19)	3921.8(14)	4253.6(15)	28.7(5)
N23	4349(2)	5930.2(16)	2097.8(15)	30.7(5)
N27	6487(3)	6669.7(18)	2252(2)	46.7(7)
C2	3113(2)	4937.6(17)	2675.5(16)	25.2(6)
C4	4072(2)	3932.1(17)	3793.7(17)	25.0(5)
C5	3522(2)	4289.6(16)	4540.6(17)	23.7(5)
C7	3361(2)	5500.6(17)	5479.3(16)	25.0(5)
C8	2013(2)	5495.1(17)	5313.2(16)	25.0(5)
C10	134(2)	5417.7(17)	4214.7(17)	24.9(5)
C11	-483(2)	4593.3(17)	4024.5(16)	25.1(5)
C13	-276(3)	3072.4(18)	4128(2)	32.3(6)
C14	-1217(3)	2931(2)	4662(3)	48.3(9)
C15	-765(3)	2910(2)	3135(2)	50.2(9)
C16	764(3)	2519(2)	4491(3)	48.8(9)
C18	-220(2)	5992.4(18)	3417.3(18)	31.6(6)
C20	3732(3)	6391.8(18)	5466.9(19)	31.7(6)
C21	3901(2)	5122.9(19)	6391.4(18)	30.9(6)
C22	3221(2)	5498.8(19)	1888.7(18)	29.9(6)
C24	4732(2)	6334.7(18)	2872.9(19)	30.2(6)
C25	5910(3)	6783.7(19)	3004(2)	35.1(7)
C26	5663(3)	7689(2)	3089(3)	55.7(10)
C28	6696(3)	6464(3)	3872(2)	51.7(9)
C30	2219(3)	6112(2)	1703(2)	36.6(7)
C31	3198(3)	4961(2)	1062.8(18)	37.3(7)
C33	3403(3)	3168.2(19)	3398(2)	34.7(7)
C34	5345(2)	3714.5(18)	4226.2(19)	30.9(6)
O35	7828.8(17)	6246.9(12)	9737.2(12)	29.2(4)
O58	8839.7(17)	3662.8(12)	8500.7(13)	32.8(4)
O61	7152.1(16)	5243.2(13)	7728.1(12)	30.9(4)
O64	3388.4(17)	5508.1(14)	8817.7(14)	36.6(5)
O66	6156.6(17)	4726.5(14)	10677.1(12)	36.5(5)
N1	11394(2)	3194.5(19)	7613.7(19)	47.3(7)
N37	8661.5(19)	5005.7(14)	9706.9(14)	25.5(5)
N40	6324.2(19)	4682.3(14)	9231.9(14)	25.2(5)
N43	5129(2)	6169.9(14)	9025.2(15)	28.9(5)
N49	9116(2)	5441.8(15)	8033.0(14)	27.8(5)

Table S4: Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for s6125r. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
N52	9295(2)	3958.6(16)	7177.9(15)	31.3(5)
C36	8454(2)	5783.4(16)	9419.5(17)	25.1(5)
C38	8121(2)	4653.1(17)	10408.4(16)	25.9(5)
C39	6773(2)	4704.7(18)	10117.1(17)	27.1(6)
C41	5079(2)	4693.3(17)	8800.5(17)	27.2(5)
C42	4467(2)	5498.1(18)	8903.2(17)	27.6(6)
C44	4664(3)	7005.1(18)	8998(2)	33.5(6)
C45	3862(4)	7177(2)	8082(2)	52.1(9)
C46	5725(3)	7572(2)	9134(2)	40.2(7)
C47	4023(3)	7129(2)	9758(2)	44.7(8)
C48	9107(3)	6078.1(18)	8703.6(19)	29.3(6)
C50	8120(2)	5074.6(18)	7584.4(17)	27.8(6)
C51	8249(2)	4453.8(19)	6855.1(18)	31.1(6)
C53	9537(2)	3615.0(17)	8000.0(18)	28.6(6)
C54	10706(3)	3180.7(19)	8311(2)	33.5(6)
C55	11361(3)	3598(2)	9177(2)	37.1(7)
C57	10455(3)	2302(2)	8514(3)	48.3(8)
C59	7162(3)	3907(2)	6624(2)	40.4(7)
C60	8400(3)	4935(2)	6031.1(19)	39.1(7)
C62	10384(3)	6249(2)	9183(2)	37.1(7)
C63	8521(3)	6845(2)	8249(2)	40.3(7)
C65	4408(3)	3973.6(19)	9055.3(19)	34.7(6)
C67	8577(3)	5079.4(19)	11305.1(18)	32.3(6)
C68	8450(3)	3749.4(18)	10497.9(19)	32.6(6)
O69	1388.3(18)	5128.2(15)	7596.1(14)	44.0(6)
O70	6270.7(18)	4495.4(17)	2496.8(14)	49.6(7)

Table S5: Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for s6125r. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	18.5(9)	42.3(11)	21.2(8)	-3.3(8)	5.2(7)	-2.9(8)
O17	20.0(10)	46.0(12)	34.1(10)	-4.7(9)	2.4(8)	1.6(9)
O19	26.0(10)	59.2(13)	21.0(9)	-2.6(9)	5.9(8)	10.0(9)
O29	31.6(11)	38.3(11)	34.3(10)	-0.9(9)	12.8(9)	-3.8(9)
O32	25.1(10)	31.9(10)	28.5(9)	1.8(8)	9.5(8)	-1.2(8)
N3	17.6(11)	36.8(13)	23.3(10)	-2.2(9)	7.4(9)	-0.1(9)
N6	20.2(11)	28.0(11)	21.0(10)	-4.6(9)	6.8(8)	-1.3(9)
N9	16.8(10)	34.7(12)	17.8(10)	-0.9(8)	5.0(8)	3.0(9)
N12	18.7(11)	31.9(12)	34.7(12)	1.6(10)	4.2(9)	-2.6(9)
N23	24.3(12)	44.0(14)	25.4(11)	2.3(10)	8.9(9)	-4.0(10)
N27	45.6(17)	49.5(17)	51.4(17)	-5.2(13)	24.2(14)	-6.7(13)
C2	20.6(13)	37.0(15)	17.8(11)	-4.3(10)	4.0(10)	-0.5(11)
C4	23.1(14)	28.7(13)	24.1(12)	-1.6(10)	7.1(10)	0.8(10)
C5	17.1(13)	30.6(14)	22.8(12)	-0.7(10)	2.7(10)	1.2(10)
C7	21.2(13)	34.2(14)	19.7(12)	-4.7(10)	4.6(10)	1.5(11)
C8	24.2(13)	30.6(14)	20.9(12)	1.0(10)	6.3(10)	5.0(11)
C10	16.9(13)	34.3(14)	23.6(12)	-0.6(11)	4.8(10)	1.9(10)
C11	17.1(13)	39.3(16)	19.3(11)	-1.2(11)	4.9(10)	2.5(11)
C13	23.4(15)	32.7(15)	40.8(16)	-1.5(12)	7.4(12)	-3.8(12)
C14	41(2)	40.7(19)	69(2)	-5.7(16)	25.8(18)	-14.9(15)
C15	51(2)	45(2)	51(2)	-14.8(16)	4.0(17)	3.3(16)
C16	33.7(18)	32.4(17)	79(3)	11.6(16)	10.3(17)	-2.3(14)
C18	27.4(15)	39.1(15)	26.5(13)	3.2(11)	2.6(11)	4.9(12)
C20	31.3(15)	33.9(15)	29.7(14)	-8.1(11)	6.5(11)	-2.0(12)
C21	26.4(14)	41.6(16)	22.5(12)	-3.5(11)	1.1(11)	5.8(12)
C22	19.5(13)	46.1(17)	24.0(13)	1.2(12)	4.5(10)	-2.9(12)
C24	24.9(14)	33.3(15)	32.2(14)	4.8(11)	6.3(11)	-0.6(12)
C25	28.3(16)	39.5(16)	39.3(16)	-5.0(13)	11.0(13)	-6.7(12)
C26	53(2)	41.0(19)	82(3)	-7.7(18)	35(2)	-10.8(16)
C28	31.6(18)	75(3)	44.5(18)	-13.8(18)	1.0(14)	-4.7(17)
C30	27.0(15)	49.8(19)	31.6(15)	8.7(13)	3.6(12)	1.7(13)
C31	31.1(16)	59(2)	21.8(13)	-2.9(13)	6.6(11)	-5.4(14)
C33	35.4(17)	34.3(16)	36.5(16)	-8.4(12)	12.4(13)	-3.9(13)
C34	26.4(15)	34.6(15)	32.2(14)	0.2(12)	7.6(12)	6.8(12)
O35	26.8(10)	33.8(11)	27.7(9)	-0.3(8)	7.6(8)	0.3(8)
O58	28.8(11)	41.2(12)	30.3(10)	2.9(8)	10.5(8)	1.2(8)
O61	20.3(10)	49.7(12)	23.4(9)	5.2(8)	6.4(7)	2.8(8)
O64	21.2(10)	50.2(13)	36.4(11)	-0.8(9)	2.5(8)	-2.5(9)
O66	22.9(10)	64.5(14)	23.0(9)	3.3(9)	7.1(8)	-2.3(9)
N1	42.4(16)	54.3(17)	52.9(17)	-11.2(14)	27.2(14)	2.3(13)
N37	22.3(11)	32.0(12)	23.6(10)	4.0(9)	8.4(9)	1.7(9)
N40	22.4(11)	33.5(12)	19.1(10)	0.5(9)	3.3(8)	-3.1(9)
N43	23.8(12)	31.7(13)	31.4(12)	-0.6(9)	6.8(9)	1.0(9)

Table S5: Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for s6125r. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N49	20.9(12)	39.1(13)	24.3(11)	2.0(10)	6.8(9)	-0.5(10)
N52	23.1(12)	48.9(15)	22.6(11)	-0.6(10)	6.8(9)	2.0(10)
C36	22.0(13)	31.2(15)	21.6(12)	1.9(10)	4.1(10)	-1.5(11)
C38	22.8(13)	34.1(14)	21.6(12)	4.1(11)	6.3(10)	-2.4(11)
C39	23.5(14)	35.3(14)	23.0(12)	2.0(11)	6.2(10)	-4.0(11)
C41	23.0(13)	35.1(14)	21.9(12)	-0.5(11)	1.9(10)	-5.2(11)
C42	25.1(14)	35.7(15)	21.2(12)	2.8(11)	3.6(10)	-1.8(12)
C44	31.5(16)	32.4(16)	36.2(15)	-0.6(12)	7.1(12)	3.9(12)
C45	61(2)	41.2(19)	45.0(19)	5.4(15)	-8.1(17)	7.4(17)
C46	40.6(18)	33.2(16)	49.6(19)	-4.1(13)	16.4(15)	-0.4(13)
C47	39.6(19)	44.4(19)	54(2)	-8.2(15)	18.6(16)	2.2(14)
C48	27.5(15)	33.8(15)	27.6(13)	4.3(11)	8.2(11)	-0.4(11)
C50	21.5(14)	42.5(16)	19.0(12)	6.3(11)	3.9(10)	0.8(12)
C51	22.0(14)	49.6(18)	20.3(12)	0.4(11)	1.7(10)	0.3(12)
C53	25.2(14)	34.4(15)	26.1(13)	-1.5(11)	5.5(11)	-0.4(11)
C54	29.7(16)	38.6(16)	32.7(15)	-2.5(12)	8.2(12)	5.9(12)
C55	29.3(16)	48.8(18)	31.6(15)	-0.4(13)	3.6(12)	3.2(13)
C57	53(2)	33.7(17)	58(2)	-2.1(15)	12.5(17)	5.3(15)
C59	25.8(16)	61(2)	32.1(15)	-6.9(15)	2.2(12)	-2.9(14)
C60	35.1(17)	61(2)	22.0(13)	2.1(13)	8.0(12)	2.4(14)
C62	30.3(16)	47.3(18)	35.5(15)	-2.4(13)	11.3(13)	-10.9(14)
C63	46.4(19)	36.1(17)	42.5(17)	13.5(13)	18.5(15)	3.0(14)
C65	30.8(15)	39.4(16)	31.8(14)	2.1(12)	2.8(12)	-8.9(12)
C67	28.1(15)	47.0(17)	21.4(13)	2.7(12)	4.5(11)	-4.1(13)
C68	30.5(15)	40.2(17)	28.3(14)	8.3(12)	9.4(11)	-0.2(12)
O69	25.9(11)	72.8(16)	32.2(11)	6.6(10)	4.6(9)	-9.6(10)
O70	19.5(10)	105(2)	25.6(10)	0.5(11)	6.7(8)	2.5(11)

Table S6: Bond Lengths for s6125r.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C2	1.233(3)	O35	C36	1.226(3)
O17	C11	1.230(3)	O58	C53	1.238(3)
O19	C8	1.238(3)	O61	C50	1.231(3)
O29	C24	1.238(3)	O64	C42	1.237(3)
O32	C5	1.226(3)	O66	C39	1.234(3)
N3	C2	1.337(3)	N1	C54	1.469(4)
N3	C4	1.463(3)	N37	C36	1.351(3)
N6	C5	1.350(3)	N37	C38	1.475(3)
N6	C7	1.469(3)	N40	C39	1.331(3)
N9	C8	1.328(3)	N40	C41	1.454(3)
N9	C10	1.451(3)	N43	C42	1.334(4)
N12	C11	1.337(4)	N43	C44	1.470(4)
N12	C13	1.481(4)	N49	C48	1.461(4)
N23	C22	1.465(4)	N49	C50	1.350(4)
N23	C24	1.339(4)	N52	C51	1.457(4)
N27	C25	1.465(4)	N52	C53	1.342(4)
C2	C22	1.537(4)	C36	C48	1.543(4)
C4	C5	1.542(3)	C38	C39	1.539(4)
C4	C33	1.526(4)	C38	C67	1.518(4)
C4	C34	1.527(4)	C38	C68	1.528(4)
C7	C8	1.537(4)	C41	C42	1.525(4)
C7	C20	1.525(4)	C41	C65	1.514(4)
C7	C21	1.520(4)	C44	C45	1.520(4)
C10	C11	1.528(4)	C44	C46	1.525(4)
C10	C18	1.518(4)	C44	C47	1.527(4)
C13	C14	1.526(4)	C48	C62	1.531(4)
C13	C15	1.513(5)	C48	C63	1.521(4)
C13	C16	1.516(4)	C50	C51	1.538(4)
C22	C30	1.521(4)	C51	C59	1.529(4)
C22	C31	1.530(4)	C51	C60	1.525(4)
C24	C25	1.533(4)	C53	C54	1.517(4)
C25	C26	1.522(5)	C54	C55	1.527(4)
C25	C28	1.521(5)	C54	C57	1.514(5)

Table S6 Bond Angles for s6125r.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C2	N3	C4	122.0(2)	C36	N37	C38	121.9(2)
C5	N6	C7	122.9(2)	C39	N40	C41	125.6(2)
C8	N9	C10	123.0(2)	C42	N43	C44	124.4(2)
C11	N12	C13	125.4(2)	C50	N49	C48	122.0(2)
C24	N23	C22	122.4(2)	C53	N52	C51	122.1(2)
O1	C2	N3	122.7(2)	O35	C36	N37	122.4(2)
O1	C2	C22	120.5(2)	O35	C36	C48	121.2(2)
N3	C2	C22	116.7(2)	N37	C36	C48	116.3(2)
N3	C4	C5	111.0(2)	N37	C38	C39	110.3(2)
N3	C4	C33	110.8(2)	N37	C38	C67	110.5(2)
N3	C4	C34	107.7(2)	N37	C38	C68	107.7(2)
C33	C4	C5	110.0(2)	C67	C38	C39	111.2(2)
C33	C4	C34	109.9(2)	C67	C38	C68	109.6(2)
C34	C4	C5	107.4(2)	C68	C38	C39	107.4(2)
O32	C5	N6	122.9(2)	O66	C39	N40	122.8(2)
O32	C5	C4	120.8(2)	O66	C39	C38	121.4(2)
N6	C5	C4	116.2(2)	N40	C39	C38	115.7(2)
N6	C7	C8	111.2(2)	N40	C41	C42	114.1(2)
N6	C7	C20	107.3(2)	N40	C41	C65	113.4(2)
N6	C7	C21	111.3(2)	C65	C41	C42	111.4(2)
C20	C7	C8	106.7(2)	O64	C42	N43	123.3(3)
C21	C7	C8	110.2(2)	O64	C42	C41	119.4(3)
C21	C7	C20	109.9(2)	N43	C42	C41	117.2(2)
O19	C8	N9	122.1(2)	N43	C44	C45	110.3(3)
O19	C8	C7	120.1(2)	N43	C44	C46	106.3(2)
N9	C8	C7	117.6(2)	N43	C44	C47	110.1(2)
N9	C10	C11	114.0(2)	C45	C44	C46	109.0(3)
N9	C10	C18	109.6(2)	C45	C44	C47	111.3(3)
C18	C10	C11	111.4(2)	C46	C44	C47	109.8(3)
O17	C11	N12	123.7(3)	N49	C48	C36	110.7(2)
O17	C11	C10	118.7(2)	N49	C48	C62	107.7(2)
N12	C11	C10	117.6(2)	N49	C48	C63	110.2(2)
N12	C13	C14	110.2(2)	C62	C48	C36	107.7(2)
N12	C13	C15	109.6(3)	C63	C48	C36	109.6(2)
N12	C13	C16	106.7(2)	C63	C48	C62	110.9(3)
C15	C13	C14	110.5(3)	O61	C50	N49	122.1(3)
C15	C13	C16	110.4(3)	O61	C50	C51	121.4(2)
C16	C13	C14	109.3(3)	N49	C50	C51	116.5(2)
N23	C22	C2	110.3(2)	N52	C51	C50	109.7(2)
N23	C22	C30	109.8(3)	N52	C51	C59	110.0(3)
N23	C22	C31	107.7(2)	N52	C51	C60	108.8(2)
C30	C22	C2	110.2(2)	C59	C51	C50	110.0(2)
C30	C22	C31	111.0(2)	C60	C51	C50	107.4(2)
C31	C22	C2	107.8(2)	C60	C51	C59	111.0(2)

Table S6 Bond Angles for s6125r.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
O29	C24	N23	122.0(3)	O58	C53	N52	121.2(3)
O29	C24	C25	120.3(3)	O58	C53	C54	120.6(2)
N23	C24	C25	117.7(2)	N52	C53	C54	118.2(2)
N27	C25	C24	113.2(2)	N1	C54	C53	111.6(2)
N27	C25	C26	108.6(3)	N1	C54	C55	111.6(3)
N27	C25	C28	109.9(3)	N1	C54	C57	108.9(3)
C26	C25	C24	107.3(3)	C53	C54	C55	107.4(2)
C26	C25	C28	110.6(3)	C57	C54	C53	107.9(3)
C28	C25	C24	107.2(3)	C57	C54	C55	109.4(3)

Table S7: Torsion Angles for s6125r.

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
O1	C2	C22	N23	143.1(3)	O35	C36	C48	N49	-142.4(3)
O1	C2	C22	C30	21.7(4)	O35	C36	C48	C62	100.1(3)
O1	C2	C22	C31	-99.5(3)	O35	C36	C48	C63	-20.6(4)
O29	C24	C25	N27	177.3(3)	O58	C53	C54	N1	179.9(3)
O29	C24	C25	C26	-62.9(4)	O58	C53	C54	C55	-57.6(4)
O29	C24	C25	C28	55.9(4)	O58	C53	C54	C57	60.3(4)
N3	C2	C22	N23	-39.5(3)	O61	C50	C51	N52	-140.9(3)
N3	C2	C22	C30	-160.9(2)	O61	C50	C51	C59	-19.9(4)
N3	C2	C22	C31	77.9(3)	O61	C50	C51	C60	101.0(3)
N3	C4	C5	O32	146.4(2)	N37	C36	C48	N49	41.1(3)
N3	C4	C5	N6	-36.7(3)	N37	C36	C48	C62	-76.4(3)
N6	C7	C8	O19	164.9(2)	N37	C36	C48	C63	162.9(3)
N6	C7	C8	N9	-19.8(3)	N37	C38	C39	O66	-154.0(3)
N9	C10	C11	O17	-171.4(2)	N37	C38	C39	N40	29.3(3)
N9	C10	C11	N12	10.6(3)	N40	C41	C42	O64	-158.1(2)
N23	C24	C25	N27	-2.6(4)	N40	C41	C42	N43	26.1(3)
N23	C24	C25	C26	117.2(3)	N49	C50	C51	N52	41.2(3)
N23	C24	C25	C28	-124.0(3)	N49	C50	C51	C59	162.3(3)
C2	N3	C4	C5	-52.8(3)	N49	C50	C51	C60	-76.8(3)
C2	N3	C4	C33	69.7(3)	N52	C53	C54	N1	-1.5(4)
C2	N3	C4	C34	-170.0(2)	N52	C53	C54	C55	121.1(3)
C4	N3	C2	O1	2.7(4)	N52	C53	C54	C57	-121.1(3)
C4	N3	C2	C22	-174.6(2)	C36	N37	C38	C39	57.6(3)
C5	N6	C7	C8	-60.1(3)	C36	N37	C38	C67	-65.7(3)
C5	N6	C7	C20	-176.5(2)	C36	N37	C38	C68	174.6(2)
C5	N6	C7	C21	63.2(3)	C38	N37	C36	O35	1.7(4)
C7	N6	C5	O32	0.4(4)	C38	N37	C36	C48	178.2(2)
C7	N6	C5	C4	-176.4(2)	C39	N40	C41	C42	68.0(3)
C8	N9	C10	C11	-107.6(3)	C39	N40	C41	C65	-61.1(4)
C8	N9	C10	C18	126.7(3)	C41	N40	C39	O66	1.0(5)
C10	N9	C8	O19	1.2(4)	C41	N40	C39	C38	177.7(2)
C10	N9	C8	C7	-174.0(2)	C42	N43	C44	C45	-59.9(4)
C11	N12	C13	C14	-61.0(4)	C42	N43	C44	C46	-177.9(3)
C11	N12	C13	C15	60.8(3)	C42	N43	C44	C47	63.3(4)
C11	N12	C13	C16	-179.6(3)	C44	N43	C42	O64	-5.4(4)
C13	N12	C11	O17	1.7(4)	C44	N43	C42	C41	170.2(2)
C13	N12	C11	C10	179.6(2)	C48	N49	C50	O61	-1.5(4)
C18	C10	C11	O17	-46.7(3)	C48	N49	C50	C51	176.3(2)
C18	C10	C11	N12	135.3(2)	C50	N49	C48	C36	53.0(3)
C20	C7	C8	O19	-78.3(3)	C50	N49	C48	C62	170.6(2)
C20	C7	C8	N9	97.0(3)	C50	N49	C48	C63	-68.4(3)
C21	C7	C8	O19	41.0(4)	C51	N52	C53	O58	4.6(4)
C21	C7	C8	N9	-143.7(2)	C51	N52	C53	C54	-174.0(3)
C22	N23	C24	O29	1.8(4)	C53	N52	C51	C50	47.4(4)

Table S7: Torsion Angles for s6125r.

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
C22	N23	C24	C25	-178.3(3)	C53	N52	C51	C59	-73.6(3)
C24	N23	C22	C2	-50.3(4)	C53	N52	C51	C60	164.6(3)
C24	N23	C22	C30	71.3(3)	C65	C41	C42	O64	-28.0(3)
C24	N23	C22	C31	-167.7(3)	C65	C41	C42	N43	156.2(2)
C33	C4	C5	O32	23.5(4)	C67	C38	C39	O66	-31.0(4)
C33	C4	C5	N6	-159.6(2)	C67	C38	C39	N40	152.2(3)
C34	C4	C5	O32	-96.1(3)	C68	C38	C39	O66	88.9(3)
C34	C4	C5	N6	80.8(3)	C68	C38	C39	N40	-87.8(3)

Table S8: Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for s6125r.

Atom	*x*	*y*	*z*	U(eq)
H3	4748.6	4640.46	2931.75	31
H6	4173.49	5359.25	4434.6	27
H9	1792.17	5235.49	4061.52	28
H12	916.56	3989.9	4499.21	34
H23	4790.29	5923.38	1699.52	37
H27A	6588.32	6145	2171.87	56
H27B	6037.92	6877.5	1759.47	56
H10	-135.6	5669.68	4731.37	30
H14A	-1498.51	2366.89	4576.73	72
H14B	-1874.89	3306.1	4447.65	72
H14C	-883.45	3029.97	5303.64	72
H15A	-173.12	3051.15	2795.51	75
H15B	-1470.04	3241.96	2921.41	75
H15C	-967.21	2330.5	3046.63	75
H16A	510.24	1948.33	4420.97	73
H16B	1078.97	2637.95	5130.93	73
H16C	1375.16	2614.31	4154.64	73
H18A	117.92	5800.97	2920.75	47
H18B	71.71	6542.38	3596.42	47
H18C	-1078.66	6005.11	3220.01	47
H20A	3362.22	6635.75	4883.91	48
H20B	4588.67	6423.35	5557.64	48
H20C	3484.52	6689.01	5951.15	48
H21A	3625.26	5417.52	6864.87	46
H21B	4758.89	5158.99	6504.98	46
H21C	3665.67	4548.77	6392.25	46
H26A	6404.87	7992.61	3202.63	84
H26B	5278.52	7773.45	3590.97	84
H26C	5147.98	7882.78	2527.93	84
H28A	6873.09	5886.5	3797.38	78
H28B	6291.95	6521.16	4367.41	78
H28C	7429.58	6776.84	4011.26	78
H30A	1467.1	5820.97	1550.24	55
H30B	2292.6	6463.3	1196.97	55
H30C	2250.18	6447.82	2240.57	55
H31A	3879.12	4595.08	1185.14	56
H31B	3225.46	5306.52	542.39	56
H31C	2474.16	4636.87	932.03	56
H33A	3412.57	2769.35	3879.22	52
H33B	3777.72	2931.44	2942.17	52
H33C	2588.14	3313.21	3117.39	52
H34A	5774.77	4210.15	4464.4	46
H34B	5713.97	3467.35	3772.55	46

Table S8: Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for s6125r.

Atom	*x*	*y*	*z*	U(eq)
H34C	5364.94	3326.25	4719.28	46
H1A	11824.34	2814.68	7436.03	57
H1B	11648.54	3679.08	7497.33	57
H37	9132.8	4700.74	9468.69	31
H40	6823.16	4659.45	8877.37	30
H43	5896.88	6108.57	9130.08	35
H49	9791.05	5293.27	7917.7	33
H52	9785.01	3882.25	6822.56	38
H41	5036.44	4633.44	8139.92	33
H45A	3617.77	7750.65	8052.2	78
H45B	3167.32	6825.63	7996.39	78
H45C	4284.84	7066.62	7607.01	78
H46A	6171.83	7457.61	8675.57	60
H46B	6227.62	7482.99	9735.64	60
H46C	5456.92	8140.61	9080.01	60
H47A	3773.66	7699.8	9765.21	67
H47B	4552.41	6994.87	10337	67
H47C	3332.33	6772.81	9660.22	67
H55A	11537.3	4163.38	9044.55	56
H55B	12096.1	3305.48	9420.94	56
H55C	10870.18	3592.23	9620.78	56
H57A	9937.69	2288.16	8937.99	72
H57B	11195.03	2024.32	8780.42	72
H57C	10071.47	2026.32	7953.06	72
H59A	6464.76	4243.4	6393.54	61
H59B	7069.84	3618.08	7167.72	61
H59C	7253.93	3510.29	6163.6	61
H60A	8432.28	4556.9	5538.59	59
H60B	9130.65	5250.67	6184.32	59
H60C	7733.24	5307.54	5840.89	59
H62A	10404.63	6669.65	9644.36	56
H62B	10820.67	6439.24	8743.15	56
H62C	10744.97	5747.14	9469.85	56
H63A	7715.71	6717.21	7926.97	60
H63B	8965.31	7050.2	7821	60
H63C	8503.01	7262.71	8707.22	60
H65A	4338.53	4033.21	9681.77	52
H65B	4830.08	3467.67	8992.48	52
H65C	3622.45	3954.19	8656.49	52
H67A	8276.52	5639.6	11270.02	48
H67B	9438.18	5089.81	11441.6	48
H67C	8311.53	4783.9	11782.41	48
H68A	8058.6	3490.75	10931.77	49
H68B	9302.94	3695.18	10709.94	49
H68C	8197.76	3482.6	9909.53	49

Table S8: Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for s6125r.

Atom	*x*	*y*	*z*	U(eq)
H69A	1973.64	5357.29	7970.52	66
H69B	1388.84	5352.59	7077.92	66
H70A	6379.71	4548.16	1952.89	74
H70B	6975.71	4489.66	2840.29	74

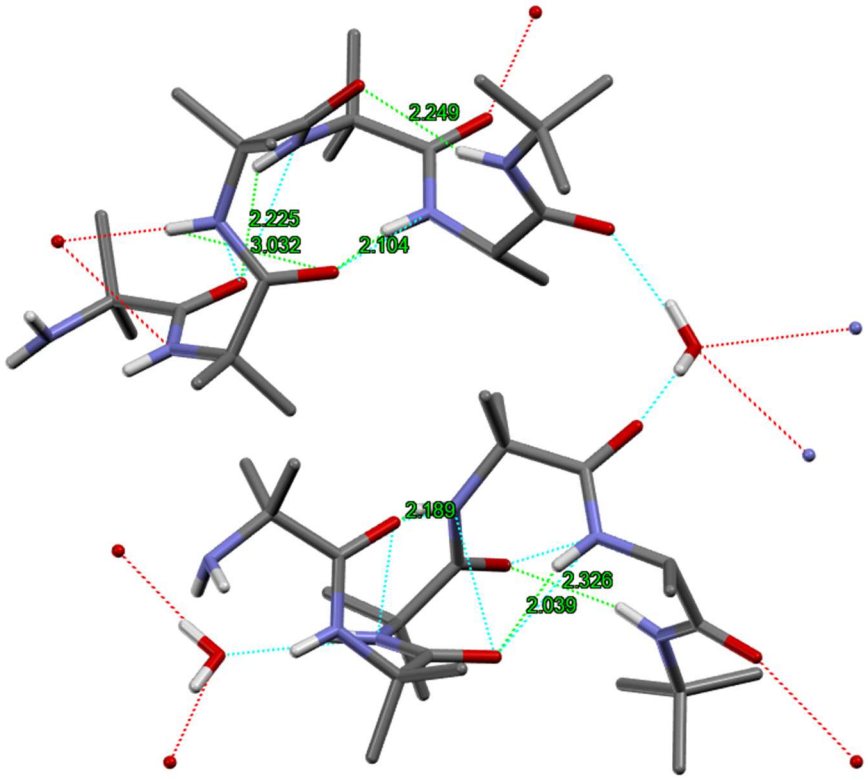


Figure S105. Crystal structure of Aib$_4$(L-Ala)NH^{t}Bu **1**. Intramolecular hydrogen bonds shown. C atoms are shown in grey, N in light blue, O in red. Some H atoms have been removed for clarity.

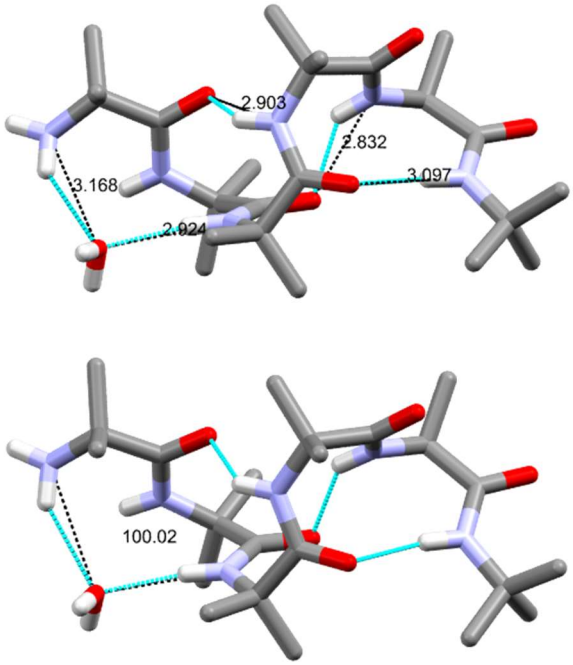


Figure S106. Crystallographic structures showing the *M* helical diastereomer of peptide **1** in longitudinal view, showing the hydrogen bonded water. Heavy atom (N···O) lengths in ångströms (a) and angles in degrees shown for proposed hydrogen bonds. Dashed cyan lines show hydrogen-bonds. Water molecules of solvation are shown. C atoms are shown in grey, N in light blue, O in red. The H atoms of the CH_3 groups have been removed for clarity.

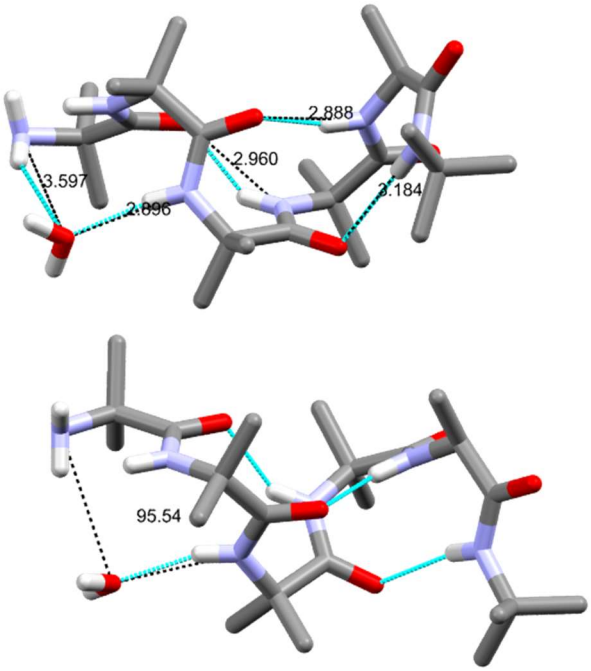


Figure S107. Crystallographic structures showing the *P* helical diastereomer of peptide **1** in longitudinal view, showing the hydrogen bonded water. Heavy atom (N···O) lengths in ångströms (a) and angles in degrees shown for proposed hydrogen bonds. Dashed cyan lines show hydrogen-bonds. Water molecules of solvation are shown. C atoms are shown in grey, N in light blue, O in red. The H atoms of the CH_3 groups have been removed for clarity.

12. FTIR spectra of peptides 1 and 3

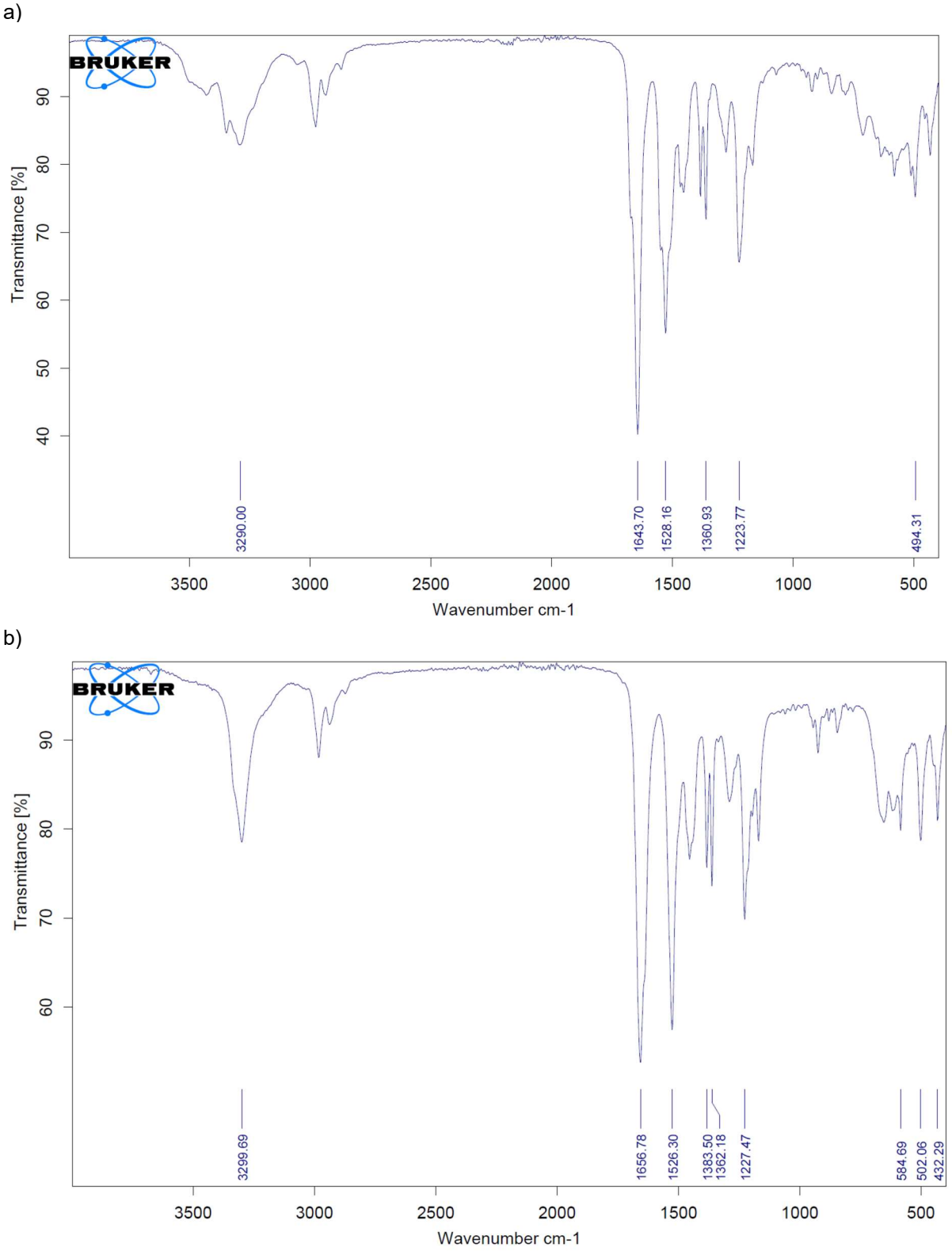


Figure S108. (a) Solid-state Fourier-transform infrared spectroscopy (FTIR) spectra of (a) peptide **1** and (b) peptide **3**.

13. References

[1] D. P. Tilly, W. Cullen, H. Zhong, R. Jamagne, I. Vitórica-Yrezábal and S. Webb, *Chem. Eur. J.*, 2022, **28**, e202104293.

[2] A. D. Peters, S. Borsley, F. della Sala, D. F. Cairns-Gibson, M. Leonidou, J. Clayden, G. F. S. Whitehead, I. J. Vitorica-Yrezabal, E. Takano, J. Burthem, S. L. Cockroft and S. J. Webb, *Chem. Sci*., 2020, **11**, 7023–7030.

[3] L. Fabris, S. Antonello, L. Armelao, R. L. Donkers, F. Polo, C. Toniolo and F. Maran, *J. Am. Chem. Soc*., 2006, **128***,* 326–336.

[4] (a) B. A. F. Le Bailly and J. Clayden, *Chem. Commun*., 2014, **50**, 7949–7952.

[5] V. Diemer, J. Maury, B. A. F. Le Bailly, S. J. Webb and J. Clayden, *Chemical Commun.*, 2017, **53**, 10768–10771.

[6] D. F. Chen, P. Y. Wu and L. -Z. Gong, O*rg. Lett.*, 2013, **15**, 3958–3961.

[7] (a) T. Okino, Y. Hoashi, T. Furukawa, X. Xu and Y. Takemoto, *J. Am. Chem. Soc*., 2005, **127**, 119–125; (b) J. P. Malerich, K. Hagihara and V. H. Rawal, *J. Am. Chem. Soc*., 2008, **130**, 14416–14417.

[8] (a) J. Deutsch, H. J. Niclas and M. J. Ramm, *J. Prakt. Chem.-Chem. Ztg.*, 1995, **337**, 23–28; (b) A. M. Flock, A. Krebs and C. Bolm, *Synlett*., 2010, **8**, 1219–1222.

[9] Z. Yu, X. Liu, L. Zhou, L. Lin and X. Feng, *Angew. Chem. Int. Ed*., 2009, **48**, 5195–5198.

[10] A. Shirakawa and S. Kobayashi, *Synlett*., 2006, **9**, 1410–1412.

[11] K. S. Rao, R. Trivedi and M. L. Kantam, *Synlett.* 2015, **26**, 221–227.

[12] C. Q. Kabes, R. F. Lucas, J. H. Gunn and J. A. Gladysz, *ACS Catal*., 2021, **11**, 7762–7771.

[13] A. Buzas and J. Y. Merour, *Synthesis*, 1989, **6**, 458–461.

[14] H. Y. Bae, S. Some, J. S. Oh, Y. S. Lee and C. E. Song, *Chem. Commun*., 2011, **47**, 9621–9623.

[15] S. Ričko, J. Svete, B. Štefane, A. Perdih, A. Golobič, A. Meden and U. Grošelj, *Adv. Synth. Catal.*, 2016, **358**, 3786–3796.

[16] M. Vakili, A. R. Nekoei, S. F. Tayyari, A. Kanaani and N. Sanati., *J. Mol. Struct.* 2012, **1021**, 102–111.

[17] (a) J. H. Shim, M. J. Lee, M. H. Lee, B. -S. Kim and D. -C. Ha, *RSC Advances*, 2020, **10**, 31808–31814; (b) Z.-H. Zhang, X. -Q. Dong, D. Chen and C. -J. Wang, *Chem. Eur. J.*, 2008, **14**, 8780–8783.

[18] M. K. Chahal, D. T. Payne, Y. Matsushita, J. Labuta, K. Ariga and J. P. Hill, *Eur. J. Org. Chem*., 2020, **1**, 82–90.

[19] Thordarson, P., *Chem. Soc. Rev*., 2011, **40**, 1305–1323.