

Interlocking the Catalyst: Thread versus Rotaxane-Mediated Enantiodivergent Michael Addition of Ketones to β -Nitrostyrene

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1. General Experimental Section

Unless stated otherwise, all reagents were purchased from Aldrich Chemicals and used without further purification. HPLC grade solvents (Scharlab) were nitrogen saturated and were dried and deoxygenated using an Innovative Technology Inc. Pure-Solv 400 Solvent Purification System. Column chromatography was carried out using silica gel (60 Å, 70-200 µm, SDS) as stationary phase, and TLC was performed on precoated silica gel on aluminum cards (0.25 mm thick, with fluorescent indicator 254 nm, Fluka) and observed under UV light. All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. ¹H- and ¹³C-NMR spectra were recorded at 298 K on a Bruker Avance 300 and 400 MHz instruments. ¹H NMR chemical shifts are reported relative to Me₄Si and were referenced via residual proton resonances of the corresponding deuterated solvent whereas ¹³C NMR spectra are reported relative to Me₄Si using the carbon signals of the deuterated solvent. Signals in the ¹H and ¹³C NMR spectra of the synthesized compounds were assigned with the aid of DEPT, APT, or two-dimensional NMR experiments (COSY, HMQC and HMBC). Abbreviations of coupling patterns are as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet. Coupling constants (*J*) are expressed in Hz. High-resolution mass spectra (HRMS) were obtained using a time-of-flight (TOF) instrument equipped with electrospray ionization (ESI). Optical rotation ($[\alpha]_D^{25}$) was measured with a JASCO P-1020 polarimeter (concentration: g/mL in chloroform as solvent). The enantiomeric ratios were determined by HPLC analysis employing a chiral stationary phase column specified in the individual experiment, by comparing the samples with the appropriate racemic mixtures.

Abbreviation list:

DIPEA: *N,N*-Diisopropylethylamine

DMAP: dimethylaminopyridine

EDCI: *N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride

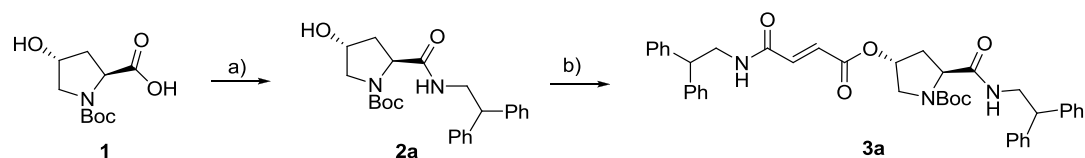
DMF: *N,N*-dimethylformamide

p-NO₂-BA: *p*-nitrobenzoic acid

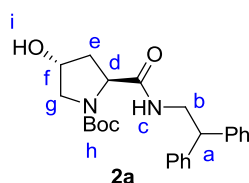
TFA: trifluoroacetic acid

HOBt: Hydroxybenzotriazole

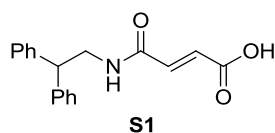
2. Synthesis of thread 3a



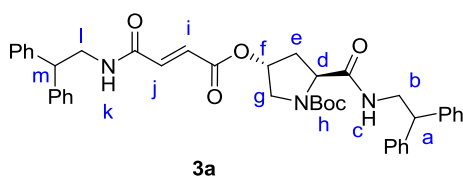
Scheme S1. a) 2,2-diphenylethylamine, EDCI, DIPEA, HOBt, CH₂Cl₂, 0°C to r.t., overnight; b) **S1**, EDCI, DMAP, CH₂Cl₂, 0°C to r.t., overnight.



To a suspension of compound **1** (2.15 g, 10 mmol) in dry dichloromethane (50 mL) under N₂ atmosphere was added 3,3-diphenylethylamine (2.36 g, 12 mmol), HOBt (1.62 g, 12 mmol) and DIPEA (4 mL, 24 mmol) at 0°C. The mixture was stirred for 10 min and EDCI (2.35 g, 12 mmol) was added. The reaction mixture was stirred at room temperature overnight. After this time the reaction mixture was washed with water (2 x 100 mL), HCl 1N (2 x 100 mL), NaHCO₃ (2 x 100 mL) and brine (2 x 100 mL). The organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The solid crude was subjected to column chromatography on silica gel using CHCl₃/MeOH (20/1) mixture as eluent to give the title product as a white solid (**2a**, 2.06 g, 50%); mp 126-128 °C; [α]_D²⁵ -58.2° (*c* 0.015, CHCl₃); ¹H NMR (300 MHz, CDCl₃, 298 K) δ 7.32-7.15 (m, 10H, Ph), 6.41 (s, 1H, NH_c), 4.33-4.21 (m, 2H, H_{d+f}), 4.17 (t, *J* = 7.9 Hz, 1H, H_a), 4.00-3.90 (m, 1H, H_b), 3.87-3.76 (m, 1H, H_b), 3.45-3.35 (m, 1H, H_g), 3.27 (dd, *J* = 11.5, 5.0 Hz, 1H, H_g), 2.35-1.90 (m, 3H, H_e + OH_i), 1.37 (s, 9H, H_h); ¹³C NMR (100 MHz, CDCl₃, 298 K) δ 172.1 (CO), 155.5 (CO), 142.0 (C), 128.8 (CH), 128.2 (CH), 127.0 (CH), 80.8 (C), 69.9 (CH), 59.5 (CH), 54.7 (CH₂), 50.9 (CH), 43.9 (CH₂), 28.5 (CH₃); HRMS (ESI) calcd for C₂₄H₃₁N₂O₄ [M + H]⁺ 411.2278, found 411.2291.

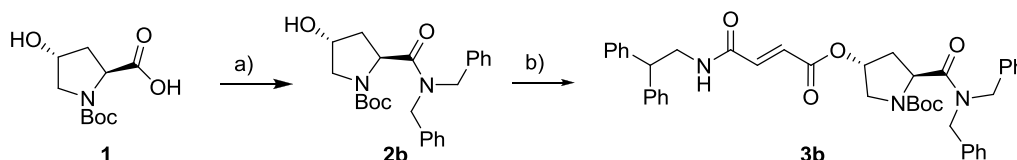


Fragment **S1** was synthesized following the described procedure reported in A. Martinez-Cuezva, S. Valero-Moya, M. Alajarin and J. Berna, *Chem. Commun.* **2015**, 51, 14501-14504 and showed identical spectroscopic data as those reported therein.

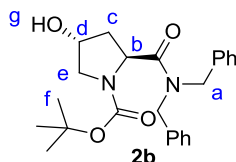


To a solution of compound **2a** (2.23 g, 5.44 mmol) in dry dichloromethane (100 mL) under N₂ atmosphere was added fragment **S1** (1.92 g, 6.53 mmol) and DMAP (132 mg, 1.09 mmol) at 0°C. The mixture was stirred for 10 min and EDCI (1.25 g, 6.53 mmol) was added. The reaction mixture was stirred at room temperature overnight. After this time the reaction mixture was washed with water (2 x 100 mL), HCl 1N (2 x 100 mL), NaHCO₃ (2 x 100 mL) and brine (2 x 100 mL). The organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure. The solid crude was subjected to column chromatography on silica gel using hexane/AcOEt (1/1) mixture as eluent to give the title product as a white solid (**3a**, 1.50 g, 40%); mp 81-83 °C; [α]_D²⁵ -22.5° (*c* 0.0043, CHCl₃); ¹H NMR (300 MHz, CDCl₃, 298 K) δ 7.36-7.18 (m, 20H, Ph), 6.70 (s, 2H, H_{i+j}), 6.00-5.80 (m, 2H, NH_{c+k}), 5.18 (s, 1H, H_f), 4.30-4.10 (m, 3H, H_{a+m+d}), 4.04-3.80 (m, 4H, H_{b+l}), 3.79-3.03 (m, 2H, H_g), 2.55-2.00 (m, 2H, H_e), 1.36 (s, 9H, H_h); ¹³C NMR (75 MHz, CDCl₃, 298 K) δ 171.7 (CO), 171.0 (CO), 164.9 (CO), 163.3 (CO), 155.5 (CO), 141.8 (C), 141.5 (CH), 136.9 (CH), 129.9 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 127.2 (CH), 127.0 (CH), 81.2 (C), 73.6 (CH), 58.5 (CH), 52.2 (CH₂), 50.8 (CH), 50.5 (CH), 44.2 (CH), 43.8 (CH), 36.7 (CH₂), 33.8 (CH₂), 29.8 (CH₂), 28.4 (CH₃); HRMS (ESI) calcd for C₄₂H₄₆N₃O₆ [M + H]⁺ 688.3381, found 688.3383.

3. Synthesis of thread **3b**

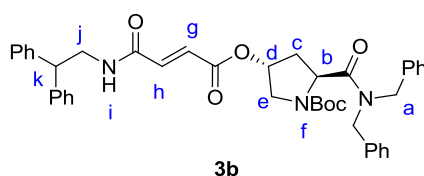


Scheme S2. a) dibenzylamine, EDCI, DIPEA, HOBT, CH₂Cl₂, 0°C to r.t., overnight; c) **S1**, EDCI, DMAP, Et₃N, CH₂Cl₂, 0°C to r.t., overnight.



To a suspension of compound **1** (6.00 g, 26.0 mmol) in dry dichloromethane (100 mL) under N₂ atmosphere was added dibenzylamine (4.90 mL, 39.0 mmol), HOBT (4.46 g, 29.0 mmol) and DIPEA (12.00 mL, 69.0 mmol) at 0°C. The mixture was stirred for 10 min and EDCI (6.55 g, 34.00 mmol) was added. The reaction mixture was stirred at room temperature overnight. After this time the reaction mixture was washed with water (2 x 100 mL), HCl 1N (2 x 100 mL), NaOH 1N (2 x 100 mL) and brine

(2 x 100 mL). The organic phase was dried over anhydrous MgSO_4 and concentrated under reduced pressure. The solid crude was subjected to column chromatography on silica gel using $\text{CHCl}_3/\text{AcOEt}$ (4:1 to 1:1) mixture as eluent to give the title product as a white solid (**2b**, 3.61 g, 34 %); $[\alpha]_D^{25} + 43.5^\circ$ (c 0.01, CHCl_3); mp 190-192 $^\circ\text{C}$; *mixture of rotamers* (1:1); ^1H NMR (400 MHz, CDCl_3 , 298 K) δ 7.40-7.16 (m, 10H, Ph), 5.40-4.96 (m, 1H, H_a), 4.84-4.73 (m, 2H, H_{a+b}), 4.63-4.24 (m, 3H, H_{a+b+d}), 3.76-3.70 (m, 1H, H_e), 3.64-3.44 (m, 1H, H_e), 2.20-1.84 (m, 3H, H_{c+g}), 1.49 (s, 9H, H_f), 1.34 (s, 9H, H_f); ^{13}C NMR (100 MHz, CDCl_3 , 298 K) δ 174.2 (CO), 173.7 (CO), 154.8 (CO), 154.2 (CO), 137.2 (C), 137.1 (C), 137.0 (C), 136.5 (C), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 127.3 (CH), 126.8 (CH), 126.6 (CH), 80.5 (C), 80.0 (C), 70.8 (CH), 69.7 (CH), 55.5 (CH_2), 55.4 (CH_2), 55.2 (CH), 54.8 (CH), 50.5 (CH_2), 49.9 (CH_2), 49.6 (CH_2), 49.3 (CH_2), 40.2 (CH_2), 39.2 (CH_2), 28.6 (CH_3), 28.5 (CH_3); HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_4$ $[\text{M} + \text{H}]^+$ 411.2278, found 411.2291.

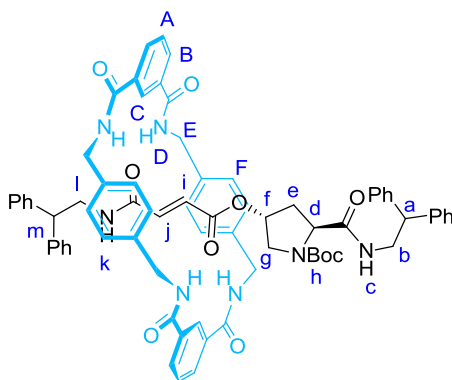


To a solution of compound **2b** (1.00 g, 2.30 mmol) in dry dichloromethane (40 mL) under N_2 atmosphere was added fragment **S1** (1.30 g, 4.60 mmol), DMAP (56 mg, 0.46 mmol) and Et_3N (640 μL , 4.60 mmol) at 0°C . The mixture was stirred for 10 min and EDCI (878 mg, 4.60 mmol) was added. The reaction mixture was stirred at room temperature overnight. After this time the reaction mixture was washed with water (2 x 100 mL), HCl 1N (2 x 100 mL), NaOH 1N (2 x 100 mL) and brine (2 x 100 mL). The organic phase was dried over anhydrous MgSO_4 and concentrated under reduced pressure. The solid crude was subjected to column chromatography on silica gel using hexane/ AcOEt (1:1) mixture as eluent to give the title product as a white solid (**3b**, 817 mg, 70%); $[\alpha]_D^{25} + 32.0^\circ$ (c 0.0099, CHCl_3); mp 73-75 $^\circ\text{C}$; *mixture of rotamers* (1.4:1); ^1H NMR (400 MHz, CDCl_3 , 298 K) δ 7.40-7.13 (m, 20H, Ph), 6.74-6.63 (m, 2H, H_{g+h}), 5.70-5.62 (m, 1H, NH_i), 5.45-5.32 (m, 1H, H_d), 5.08-4.97 (m, 1H, H_a), 4.87-4.59 (m, 2H, H_{a+b}), 4.45-4.20 (m, 3H, H_{a+k}), 4.02-3.96 (m, 2H, H_j), 3.86 (td, $J = 12.5, 4.7$ Hz, 1H, H_e), 3.75 (d, $J = 12.5$ Hz, 1H, H_e), 3.57 (d, $J = 12.5$ Hz, 1H, H_e), 2.35-2.32 (m, 1H, H_c), 2.05-1.90 (m, 1H, H_c), 1.48 (s, 4H, H_f), 1.36 (s, 4H, H_f); ^{13}C NMR (100 MHz, CDCl_3 , 298 K) δ 173.7 (CO), 173.2 (CO), 165.0 (CO), 164.9 (CO), 163.7 (CO), 154.4 (CO), 153.7 (CO), 141.6 (C), 137.1 (C), 137.0 (C), 136.9 (CH), 136.9 (CH), 136.4 (C), 129.9 (CH), 129.8 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.6 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.3 (CH), 127.0 (CH), 126.7 (CH), 126.5 (CH), 80.8 (C), 80.3 (C), 74.3 (CH), 73.2 (CH), 55.1 (CH), 54.8 (CH), 52.7 (CH_2), 52.6 (CH_2), 50.6 (CH_2), 50.4 (CH), 50.1 (CH_2), 49.8 (CH_2), 49.6 (CH_2), 44.2 (CH_2), 37.6 (CH_2), 36.1 (CH_2), 28.5 (CH_3), 28.4 (CH_3); HRMS (ESI) calcd for $\text{C}_{42}\text{H}_{46}\text{N}_3\text{O}_6$ $[\text{M} + \text{H}]^+$ 688.3381, found 688.3390.

4. General procedure for the preparation of the [2]rotaxanes **5a,b**

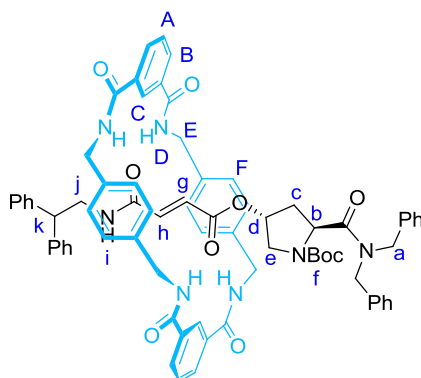
The thread (1 equiv.) and Et₃N (24 equiv.) in anhydrous CHCl₃ (250 mL) were stirred vigorously whilst solutions of *p*-xylylenediamine (8 equiv.) in anhydrous CHCl₃ (20 mL) and isophthaloyl chloride (8 equiv.) in anhydrous CHCl₃ (20 mL) were simultaneously added over a period of 4 h using motor-driven syringe pumps. After a further 4 h the resulting suspension was filtered through a Celite[®] pad, washed with water (2 x 50 mL), an aqueous solution of HCl 1N (2 x 50 mL), a saturated solution of NaHCO₃ (2 x 50 mL) and brine (2 x 50 mL). The organic phase was dried over MgSO₄ and the solvent removed under reduced pressure. The resulting solid was subjected to column chromatography (silica gel) to yield unconsumed thread and [2]rotaxane.

Rotaxane **5a**



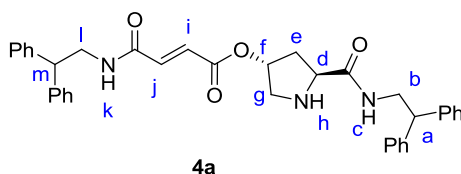
Rotaxane **5a** was obtained following the described method from thread **3a** (1.00 g, 1.46 mmol). The solid crude was subjected to column chromatography on silica gel using CHCl₃/AcOEt (3:1) mixture to pure AcOEt as eluent to give the title product as a white solid (**5a**, 526 mg, 28%); mp 140-142 °C; [α]_D²⁵ – 10.8° (*c* 0.056, CHCl₃); mixture of rotamers: 2:1; ¹H NMR (300 MHz, CDCl₃, 298 K) δ 8.20-7.84 (m, 7H, H_{B+C} + NH_k), 7.75-7.50 (m, 4H, H_A + NH_D), 7.40-7.05 (m, 22H, Ph + NH_D), 6.98-6.88 (m, 8H, H_F), 6.80 (s, 1H, NH_c), 6.41 (s, 1H, NH_c), 5.75-5.50 (m, 2H, H_{i+j}), 4.95-4.60 (m, 1H, H_f), 4.55-4.30 (m, 8H, H_E), 4.25-3.80 (m, 3H, H_{a+d+m}), 3.65-3.40 (m, 2H, H_b), 3.35-3.10 (m, 2H, H_l), 2.30-2.10 (m, 3H, H_{e+g}), 1.80-1.50 (m, 1H, H_e), 1.33 (s, 9H, H_h); ¹³C NMR (75 MHz, CDCl₃, 298 K) δ 166.9 (CO), 164.6 (CO), 141.9 (CO), 141.8 (CO), 137.6 (C), 137.5 (C), 137.3 (C), 136.3 (CH), 134.1 (C), 131.4 (CH), 131.3 (CH), 129.4 (CH), 128.9 (CH), 128.1 (CH), 127.1 (CH), 124.8 (CH), 81.6 (C), 73.7 (CH), 59.2 (CH), 51.9 (CH), 50.8 (CH₂), 49.8 (CH), 45.1 (CH), 44.4 (CH₂), 44.3 (CH₂), 43.8 (CH₂), 28.4 (CH₃); HRMS (ESI) calcd for C₇₄H₇₄N₇O₁₀ [M + H]⁺ 1220.5492, found 1220.5504.

Rotaxane 5b



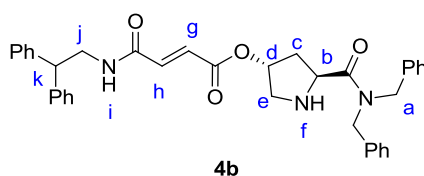
Rotaxane **5b** was obtained following the described method from thread **3b** (750 mg, 1.10 mmol). The solid crude was subjected to column chromatography on silica gel using CHCl₃/AcOEt (1:1) mixture to pure AcOEt as eluent to give the title product as a white solid (**5b**, 307 mg, 24%); mp 116-118 °C; $[\alpha]_D^{25} + 3.4^\circ$ (*c* 0.011, CHCl₃); mixture of rotamers: 1.6:1; ¹H NMR (300 MHz, CDCl₃, 298 K) δ 8.51 (t, *J* = 4.3 Hz, 1H, NH_i), 8.35 (t, *J* = 4.6 Hz, 1H, NH_i), 8.20-8.03 (m, 6H, H_{B+C}), 7.73 (t, *J* = 4.9 Hz, 2H, NH_D), 7.57-7.50 (m, 2H, H_A), 7.48-7.08 (m, 22H, Ph+NH_D), 6.96-6.90 (m, 8H, H_F), 5.87 (d, *J* = 15.3 Hz, 1H, H_h), 5.74 (d, *J* = 15.4 Hz, 1H, H_h), 5.56 (d, *J* = 15.3 Hz, 1H, H_g), 5.54 (d, *J* = 15.4 Hz, 1H, H_g), 5.31-4.10 (m, 15H, H_{E+d+a+k+b}), 3.92-3.48 (m, 3H, H_{j+e}), 3.42-3.14 (m, 1H, H_e), 2.22-1.78 (m, 2H, H_c), 1.34 (s, 9H, H_f), 1.48 (s, 9H, H_f); ¹³C NMR (75 MHz, CDCl₃, 298 K) δ 173.7 (CO), 172.8 (CO), 167.0 (CO), 166.7 (CO), 166.5 (CO), 166.2 (CO), 164.6 (CO), 164.5 (CO), 154.0 (CO), 153.8 (CO), 141.7 (C), 141.6 (C), 141.5 (C), 137.4 (C), 137.2 (C), 137.0 (C), 136.9 (C), 136.7 (C), 136.5 (C), 136.1 (C), 135.8 (CH), 135.5 (CH), 134.1 (C), 133.9 (C), 133.8 (C), 131.4 (CH), 131.2 (CH), 131.0 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.6 (CH), 128.1 (CH), 127.9 (CH), 127.6 (CH), 127.3 (CH), 127.0 (CH), 126.5 (CH), 126.3 (CH), 126.1 (CH), 124.5 (CH), 81.2 (C), 80.8 (C), 74.7 (CH), 73.9 (CH), 54.9 (CH), 54.8 (CH), 52.3 (CH₂), 52.0 (CH₂), 50.7 (CH₂), 50.0 (CH₂), 49.9 (CH₂), 49.5 (CH₂), 45.1 (CH₂), 44.2 (CH₂), 36.8 (CH₂), 35.3 (CH₂), 28.4 (CH₃), 28.3 (CH₃); HRMS (ESI) calcd for C₇₄H₇₄N₇O₁₀ [M + H]⁺ 1220.5492, found 1220.5513.

5. Boc-deprotection of threads 3a,b and rotaxanes 5a,b

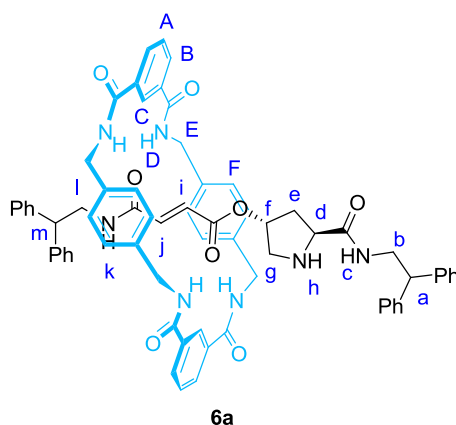


To a solution of Boc-protected thread **3a** (50 mg, 0.07 mmol) in chloroform (2 mL) was added TFA (55 μ L, 0.72 mmol). The reaction was stirred at room temperature overnight. After this time the reaction

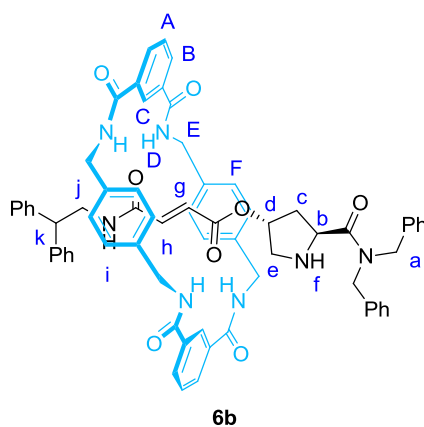
mixture was diluted chloroform (20 mL) and washed NaHCO₃ (2 x 20 mL) and brine (2 x 20 mL). The organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure, to give the title product as a white solid (**4a**, 40 mg, 94%); mp 81-83 °C; $[\alpha]_D^{25} +16.2^\circ$ (*c* 0.027, CHCl₃); ¹H NMR (400 MHz, CDCl₃, 298 K) δ 7.62 (t, *J* = 5.9 Hz, 1H, NH_c), 7.35-7.15 (m, 20H, Ph), 6.75 (d, *J* = 15.4 Hz, 1H, H_j), 6.68 (d, *J* = 15.4 Hz, 1H, H_i), 6.14 (t, *J* = 5.6 Hz, 1H, NH_k), 5.13 (t, *J* = 3.9 Hz, 1H, H_f), 4.26-4.18 (m, 2H, H_{a+m}), 4.02-3.94 (m, 3H, H_{b+l}), 3.87-3.72 (m, 2H, H_{b+d}), 2.98 (d, *J* = 13.4 Hz, 1H, H_g), 2.65-2.45 (m, 2H, H_g+NH_h), 2.26 (dd, *J* = 8.5, 14.6 Hz, 1H, H_e), 1.87 (ddd, *J* = 5.1, 7.9, 14.6 Hz, 1H, H_e); ¹³C NMR (100 MHz, CDCl₃, 298 K) δ 173.6 (CO), 164.9 (CO), 163.4 (CO), 142.0 (C), 141.9 (C), 141.5 (C), 136.7 (CH), 130.2 (CH), 129.0 (CH), 128.8 (CH), 128.8 (CH), 128.2 (CH), 128.1 (CH), 127.2 (CH), 126.9 (CH), 77.3 (CH), 59.8 (CH), 52.7 (CH₂), 50.8 (CH), 50.5 (CH), 44.2 (CH₂), 43.3 (CH₂), 36.8 (CH₂); HRMS (ESI) calcd for C₃₇H₃₈N₃O₄ [M + H]⁺ 588.2857, found 588.2864.



To a solution of Boc-protected thread **3b** (90 mg, 0.13 mmol) in chloroform (2 mL) was added TFA (100 μ L, 1.3 mmol). The reaction was stirred at room temperature overnight. After this time the reaction mixture was diluted chloroform (20 mL) and washed NaHCO₃ (2 x 20 mL) and brine (2 x 20 mL). The organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure, to give the title product as a white solid (**4b**, 76 mg, 99%); mp 58-60 °C; $[\alpha]_D^{25} -3.3^\circ$ (*c* 0.0063, CHCl₃); ¹H NMR (400 MHz, CDCl₃, 298 K) δ 7.10-7.10 (m, 20H, Ph), 6.75-6.65 (m, 2H, H_{g+h}), 5.96 (t, *J* = 5.1 Hz, 1H, H_i), 5.38-5.31 (m, 1H, H_d), 4.78 (d, *J* = 14.8 Hz, 1H, H_a), 4.55-4.39 (m, 3H, H_a), 4.26-4.14 (m, 2H, H_{k+b}), 4.00-3.94 (m, 2H, H_j), 3.52 (dd, *J* = 5.4, 12.7 Hz, 1H, H_e), 2.95 (dd, *J* = 2.4, 12.7 Hz, 1H, H_e), 2.81 (s, 1H, NH_f), 2.17-2.01 (m, 2H, H_c); ¹³C NMR (100 MHz, CDCl₃, 298 K) δ 173.5 (CO), 165.1 (CO), 163.5 (CO), 141.6 (C), 136.9 (C), 136.7 (CH), 136.0 (C), 130.2 (CH), 129.2 (CH), 128.9 (CH), 128.8 (CH), 128.2 (CH), 128.1 (CH), 127.7 (CH), 127.1 (CH), 126.7 (CH), 77.4 (CH), 57.4 (CH), 53.1 (CH₂), 50.5 (CH), 49.6 (CH₂), 48.6 (CH₂), 44.2 (CH₂), 38.1 (CH₂); HRMS (ESI) calcd for C₃₇H₃₈N₃O₄ [M + H]⁺ 588.2857, found 588.2846.



To a solution of Boc-protected rotaxane **5a** (460 mg, 0.38 mmol) in chloroform (4 mL) was added TFA (370 μ L, 3.8 mmol). The reaction was stirred at room temperature overnight. After this time the reaction mixture was diluted chloroform (20 mL) and washed NaHCO₃ (2 x 20 mL) and brine (2 x 20 mL). The organic phase was dried over anhydrous MgSO₄ and concentrated under reduced pressure, to give the title product as a white solid (**6a**, 423 mg, 99%); mp 123-125 °C; $[\alpha]_D^{25} +10.1^\circ$ (*c* 0.0032, CHCl₃); ¹H NMR (400 MHz, CDCl₃, 298 K) δ 8.13-8.03 (m, 7H, NH_k + H_{B+C}), 7.77-7.53 (m, 5H, NH_{D+C}), 7.49 (m, *J* = 7.9 Hz, 2H, H_A), 7.31-7.13 (m, 20H, Ph), 6.95-6.88 (m, 8H, H_F), 5.76 (d, *J* = 15.5 Hz, 1H, H_j), 5.70 (d, *J* = 15.5 Hz, 1H, H_i), 4.75-4.70 (m, 1H, H_F), 4.49-4.35 (m, 8H, H_E), 4.24-4.15 (m, 2H, H_{a+m}), 3.93-3.75 (m, 2H, H_b), 3.73-3.59 (m, 2H, H_l), 3.14 (t, *J* = 8.2 Hz, 1H, H_d), 2.99 (s, 1H, NH_h), 2.56 (dt, *J* = 8.4, 13.2 Hz, 2H, H_g), 1.60 (dd, *J* = 7.4, 12.2 Hz, 1H, H_e), 1.50-1.41 (m, 1H, H_e); ¹³C NMR (100 MHz, CDCl₃, 298 K) δ 173.1 (CO), 167.1 (CO), 166.9 (CO), 165.1 (CO), 164.6 (CO), 141.9 (C), 141.8 (C), 137.4 (C), 136.0 (CH), 134.4 (C), 134.2 (C), 131.2 (CH), 131.2 (CH), 129.3 (CH), 128.8 (CH), 128.2 (CH), 128.1 (CH), 127.5 (CH), 127.0 (CH), 124.8 (CH), 76.8 (CH), 59.4 (CH), 51.9 (CH₂), 50.6 (CH), 49.9 (CH), 45.0 (CH₂), 44.4 (CH₂), 44.2 (CH₂), 43.6 (CH₂), 36.7 (CH₂); HRMS (ESI) calcd for C₆₉H₆₆N₇O₈ [M + H]⁺ 1120.4967, found 1120.4938.



To a solution of Boc-protected rotaxane **5b** (235 mg, 0.19 mmol) in chloroform (2 mL) was added TFA (145 μ L, 1.9 mmol). The reaction was stirred at room temperature overnight. After this time the reaction mixture was diluted chloroform (20 mL) and washed NaHCO₃ (2 x 20 mL) and brine (2 x 20 mL). The

organic phase was dried over anhydrous MgSO_4 and concentrated under reduced pressure, to give the title product as a white solid (**6b**, 209 mg, 99%); mp 117-119 °C; $[\alpha]_{\text{D}}^{25} - 12.6^\circ$ (c 0.01, CHCl_3); ^1H NMR (300 MHz, CDCl_3 , 298 K) δ 8.12-8.00 (m, 7H, $\text{NH}_i + \text{H}_{\text{B+C}}$), 7.59 (t, $J = 4.5$ Hz, 2H, NH_D), 7.50-7.38 (m, 4H, $\text{H}_\text{A} + \text{NH}_\text{D}$), 7.36-7.08 (m, 20H, Ph), 6.87 (s, 8H, H_F), 5.80 (d, $J = 15.4$ Hz, 1H, H_h), 5.66 (d, $J = 15.4$ Hz, 1H, H_g), 4.99-4.92 (m, 1H, H_d), 4.70 (d, $J = 14.7$ Hz, 1H, H_a), 4.49-4.29 (m, 9H, $\text{H}_{\text{a+E}}$), 4.14 (t, $J = 7.8$ Hz, 1H, H_k), 4.01 (t, $J = 7.6$ Hz, 1H, H_b), 3.71-3.53 (m, 2H, H_j), 3.28-3.16 (m, 2H, $\text{NH}_\text{f} + \text{H}_\text{e}$), 2.47 (dd, $J = 1.4, 12.4$ Hz, 1H, H_e), 2.06-1.78 (m, 2H, H_c); ^{13}C NMR (75 MHz, CDCl_3 , 298 K) δ 172.9 (CO), 167.1 (CO), 166.9 (CO), 166.1 (CO), 164.6 (CO), 141.9 (C), 141.8 (C), 137.2 (C), 136.5 (C), 136.0 (CH), 135.7 (C), 134.3 (C), 134.2 (C), 131.3 (CH), 131.2 (CH), 129.7 (CH), 128.8 (CH), 128.2 (CH), 128.0 (CH), 127.8 (CH), 127.1 (CH), 127.0 (CH), 126.5 (CH), 124.6 (CH), 76.7 (CH), 57.2 (CH), 52.4 (CH_2), 50.0 (CH), 49.5 (CH_2), 48.7 (CH_2), 45.0 (CH_2), 44.3 (CH_2), 44.2 (CH_2), 36.9 (CH_2); HRMS (ESI) calcd for $\text{C}_{69}\text{H}_{66}\text{N}_7\text{O}_8$ $[\text{M} + \text{H}]^+$ 1120.4967, found 1120.4956.

6. Stacked ^1H NMR spectra of thread **4a** and rotaxane **6a**

Figure S1 displays the stacked ^1H NMR spectra of the unprotected thread **4a** and its corresponding rotaxane **6a**. The comparison of these spectra allows determining the location of the macrocycle on the thread in the interlocked systems. The signals referred to the double bond (H_i and H_j , green) in thread **4a** appear at higher chemical shift if compared with those signals in rotaxane **6a** ($\Delta\delta = -0.99$ ppm). This variation is similar to the previously described for a closely related system, with a monoamide-monoester one-station template with a level of occupancy of the binding site of 100% (Gatti, F. G.; Leigh, D. A.; Nepogodiev, S. A.; Slawin, A. M. Z.; Teat, S. J.; Wong, J. K. Y. *J. Am. Chem. Soc.* **2001**, *123*, 5983–5989). In a similar way signals referred to the stopper close to the binding site (H_m and H_l) are shifted -0.13 ppm and -0.38 ppm upfield, respectively. Remarkably the signal of the amide hydrogen NH_k is shifted to higher ppm ($\Delta\delta = +1.28$ ppm), as a consequence of the interaction with the macrocycle. Regarding the signals relative to the pyrrolidine moiety, all appear at lower chemical shifts (H_f , $\Delta\delta = -0.35$ ppm; H_j , $\Delta\delta = -0.91$ ppm; H_e , $\Delta\delta = -0.76$ ppm; H_g , $\Delta\delta = -0.40$ ppm). These shifts could be a consequence of the establishment of $\text{CH}\cdots\pi$ interactions between the aliphatic pyrrolidine core and the aromatic rings of the macrocycle. Conversely the signals referred to the amide moiety of the stopper (NH_c , H_a and H_b) did not experience any displacement when the macrocycle is assembled. All these data suggest that the macrocycle spends most of the time on the fumaramide binding site in **6a**. In this scenario the active site of the pyrrolidine core is potentially not covered and possible catalysis pathways are totally feasible.

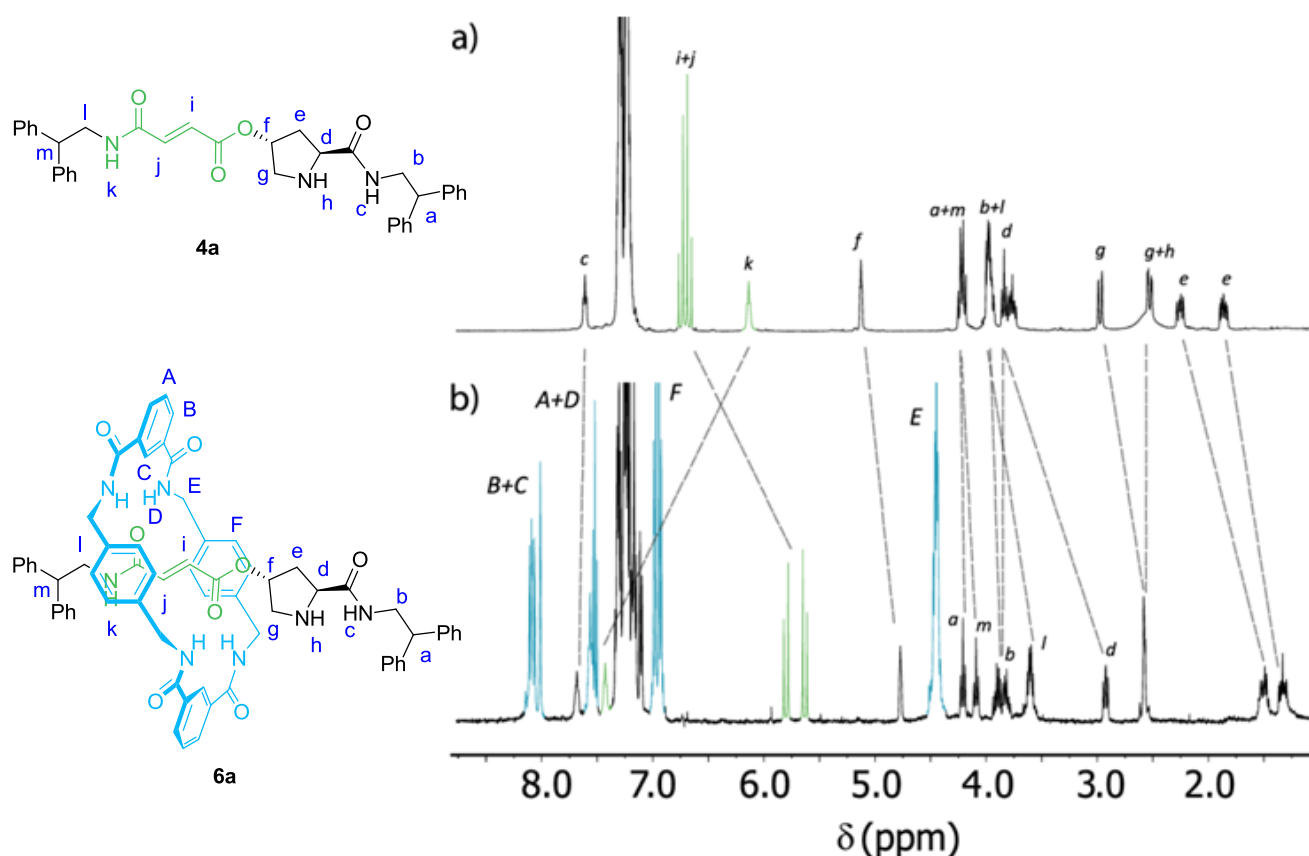
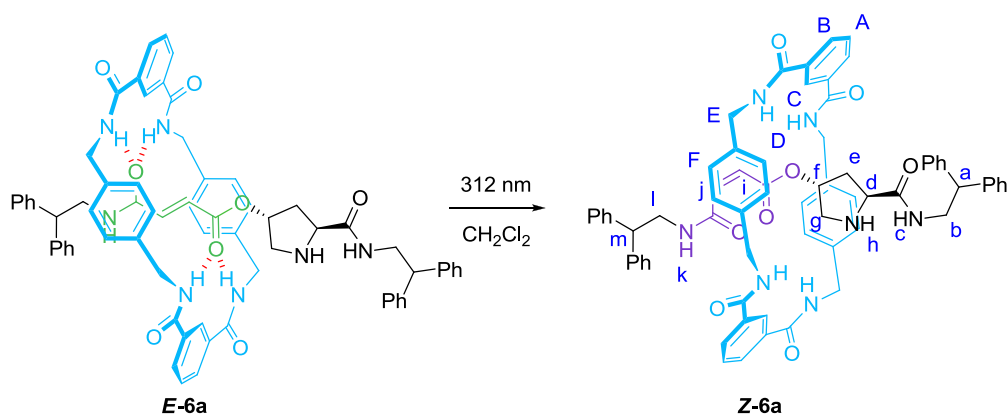


Figure S1. Partial ^1H NMR spectra (400 MHz, CDCl_3 , 298 K) of: a) thread **4a**; b) [2]rotaxane **6a**.

7. Photoisomerization of rotaxane **6a**



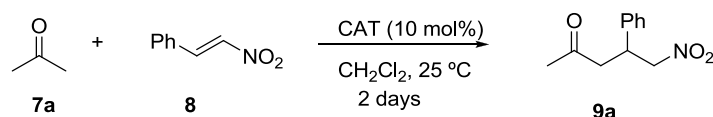
A solution of rotaxane **E-6a** (20 mg, 0.02 mmol) in anhydrous CH_2Cl_2 (30 mL) was irradiated at 312 nm for 30 minutes under N_2 atmosphere. The reaction mixture was purified by using column chromatography on silica gel employing a $\text{CHCl}_3/\text{MeOH}$ (20/1) mixture as eluent to give the title product as a white solid (**Z-6a**, 9 mg, 45%); mp 119-121 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3 , 298 K) δ 8.13-8.06 (m, 6H, $\text{H}_{\text{B+C}}$), 7.78 (t, $J = 5.1$ Hz, 2H, NH_{D}), 7.63 (t, $J = 4.8$ Hz, 2H, NH_{D}), 7.51 (t, $J = 8.0$ Hz, 2H, H_{A}), 7.34-7.14 (m, 17H, $\text{Ph} + \text{NH}_{\text{C}}$), 7.06-7.00 (m, 4H, Ph), 6.99 (s, 8H, H_{F}), 6.90-6.86 (m, 1H, NH_{K}), 5.40 (d, $J = 12.1$ Hz, 1H, H_{J}), 5.31 (d, $J = 12.1$ Hz, 1H, H_{I}), 4.64-4.58 (m, 1H, H_{F}), 4.52-4.39 (m, 8H, H_{E}), 4.15 (t, $J = 8.1$ Hz, 1H, H_{A}), 3.89 (t, $J = 8.2$ Hz, 1H, H_{M}), 3.75-3.55 (m, 3H, $\text{H}_{\text{B}} + \text{NH}_{\text{H}}$), 3.50-3.45 (m, 2H, H_{I}), 2.84 (t, $J = 8.0$ Hz, 1H,

H_d), 2.50-2.35 (m, 2H, H_g), 1.62 (dd, *J* = 7.7, 14.2 Hz, 1H, H_e), 1.35-1.30 (m, 1H, H_e); ¹³C NMR (101 MHz, CDCl₃, 298 K) δ 172.9 (CO), 167.0 (CO), 166.8 (CO), 165.3 (CO), 164.5 (CO), 142.1 (C), 141.9 (C), 141.8 (C), 141.7 (C), 137.6 (C), 137.4 (C), 134.5 (C), 134.3 (C), 132.5 (CH), 131.4 (CH), 131.2 (CH), 129.3 (CH), 129.1 (CH), 128.9 (CH), 128.9 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.2 (CH), 127.0 (CH), 127.0 (CH), 125.1 (CH), 76.8 (CH), 59.2 (CH), 52.0 (CH₂), 50.2 (CH), 50.2 (CH), 44.6 (CH₂), 44.5 (CH₂), 44.3 (CH₂), 44.1 (CH₂), 36.4 (CH₂); HRMS (ESI) calcd for C₆₉H₆₆N₇O₈ [M + H]⁺ 1120.4967, found 1120.4951.

8. Michael reaction between ketones **7** and β-nitrostyrene **8**.

The asymmetric Michael reaction between different ketones and β-nitrostyrene in the presence of catalytic amounts of the suitable prolinamide (10 mol%). Different additives and temperatures were screened.

Table S1. Catalyst screening.^a

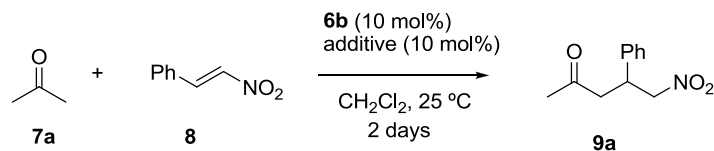


entry	CAT	Conv. (%) ^b	e.r. ^c	Configuration
1	6a	57	26.5: 73.5	<i>R</i>
2	4a	59	68.5 :31.5	<i>S</i>
3	Z-6a	-	-	-
4	6b	100	29.5: 70.5	<i>R</i>
5	4b	100	74.5 :25.5	<i>S</i>
^a Reaction conditions: 8 (0.025 mmol), acetone 7a (18 μL), catalyst (10 mol%), CH ₂ Cl ₂ (100 μL), 25 °C, 2 days; ^b Calculated by ¹ H NMR; ^c Determined by HPLC with chiral stationary phase.				

NOTE:

- **Z-6a** was tested as catalyst, showing to be unstable under the reaction conditions, founding the formation of an important amount of the *E*-isomer. Thus the obtained results are not reliable, since both isomers (*E* and *Z* isomers) are present as catalysts in the reaction media.

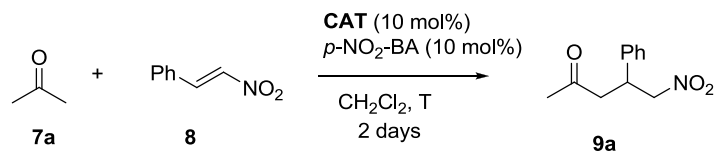
Table S2. Additive screening.^a



entry	Additive	Conv. (%) ^b	e.r. ^c	Configuration
1	-	100	29.5:70.5	<i>R</i>
2	acetic acid	90	27.5:72.5	<i>R</i>
3	benzoic acid	82	28.5:71.5	<i>R</i>
4	<i>p</i> -nitrobenzoic acid (<i>p</i> -NO ₂ -BA)	100	27:73	<i>R</i>
5	TFA	75	37.5:62.5	<i>R</i>

^aReaction conditions: **8** (0.025 mmol), acetone **7a** (18 μL), 10 equiv.), CH_2Cl_2 (100 μL), **6b** (10 mol%), additive (10 mol%), 25 °C, 2 days; ^bCalculated by ¹H NMR; ^cDetermined by HPLC with a chiral stationary phase.


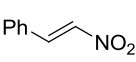
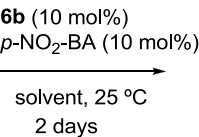
Table S3. Temperature screening.^a



entry	CAT	T (°C)	Conv. (%) ^b	e.r. ^c	Configuration
1	6b	25	100	27:73	<i>R</i>
2	4b	25	100	76:24	<i>S</i>
3	6b	0	54	31.5:68.5	<i>R</i>
4	4b	0	50	75:25	<i>S</i>

^aReaction conditions: **8** (0.025 mmol), acetone **7a** (18 μL), catalyst (10 mol%), *p*-nitrobenzoic acid (10 mol%), CH_2Cl_2 (100 μL), 2 days; ^bCalculated by ¹H NMR; ^cDetermined by HPLC with chiral stationary phase.

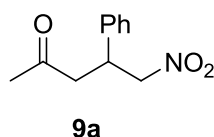
Table S4. Solvent screening.^a

<div><div><div><div><div></div><div>7a</div></div><div>+</div><div><div><div><div></div><div>8</div></div><div><div><div><div></div><div>9a</div></div></div></div></div></div></div></div></div>				
entry	Solvent	Conv. (%) ^b	e.r. ^c	Configuration
1	CH ₂ Cl ₂	100	27:73	<i>R</i>
2	CHCl ₃	72	27:73	<i>R</i>
3	DMF	100	33.5:66.5	<i>R</i>
4	brine	75	50:50	-
5	acetone	100	32:68	<i>R</i>
^a Reaction conditions: 8 (0.025 mmol), acetone 7a (18 μL), 6b (10 mol%), <i>p</i> -nitrobenzoic acid (10 mol%), CH ₂ Cl ₂ (100 μL), 2 days; ^b Calculated by ¹ H NMR; ^c Determined by HPLC with chiral stationary phase.				

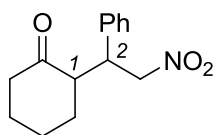
General procedure: A solution of the β-nitrostyrene **8** (0.025 mmol), ketone **7** (0.25 mmol), *p*-nitrobenzoic acid (0.0025 mmol) and the corresponding prolinamide (**4b** or **6b**, 0.1 equiv.) in dry CH₂Cl₂ (100 μL) at room temperature were stirred for a period of 2 days. After this time pentane was added and the suspension was filtered through a pad of Celite[®] to remove the catalyst. The filtrate was concentrated under vacuum and analyzed by ¹H NMR spectroscopy. The desired Michael adduct **9** was purified by preparative TLC and the enantiomeric excess analyzed by chiral HPLC.

NOTE:

- Racemates were synthesized following the described procedure, employing pyrrolidine (30 mol%) as catalyst.

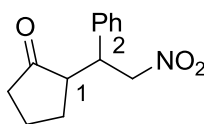


Compound **9a** was described in H. Huang, E. N. Jacobsen, *J. Am. Chem. Soc.* **2006**, *128*, 7170; and showed identical spectroscopic data as those reported therein. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak AS-H; hexane:iPrOH = 75:25, 1 mL/min, λ = 254 nm: t_r = 10.5 min (*S* enantiomer), t_r = 12.6 min (*R* enantiomer). The HPLC protocol was described in the same reference, where the two enantiomers are identified.



9b

Compound **9b** was described in C.-L. Cao, M.-C. Ye, X.-L. Sun, Y. Tang, *Org. Lett.* **2006**, 8, 2901, and showed identical spectroscopic data as those reported therein. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralpak® AS-H column; hexane:iPrOH = 95:5, flow rate 1 mL/min, λ = 210 nm; *syn* enantiomers: t_r = 13.9 min (*1R,2S* enantiomer), t_r = 18.9 min (*1S,2R* enantiomer). The HPLC protocol is described in: N. Mase, K. Watanabe, H. Yoda, K. Takabe, F. Tanaka, C. F. Barbas III, *J. Am. Chem. Soc.* **2006**, 128, 4966; where the two *syn* enantiomers are identified.



9c

Compound **9b** was described in T. C. Nugent, A. Bibi, A. Sadiq, M. Shoaib, M. N. Umar, F. N. Tehrani, *Org. Biomol. Chem.* **2012**, 10, 9287, and showed identical spectroscopic data as those reported therein. The enantiomeric ratio was determined by HPLC analysis using Daicel Chiralcel OD-H column; hexane:iPrOH = 90:10, flow rate 1 mL/min, λ = 210 nm; *syn* enantiomers: t_r = 17.3 min (*1S,2R* enantiomer), t_r = 20.4 min (*1R,2S* enantiomer). The HPLC protocol was described in the same reference, where the 4 different enantiomers were identified.

9. Computational Studies

COMPUTATIONAL METHODS

Geometries of the molecules were optimized by using the wB97XD functional¹ and the cc-pVDZ² basis set. This method was used previously in related structures.³ Solvent effects were calculated with the PCM continuum solvation model⁴ for dichloromethane. The nature of transition structures of all stationary points was confirmed by frequency analysis at the same level of theory. The wave function stability was

¹ Chai, J.-D.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2008**, 10, 6615.

² Dunning, T.H. *J. Chem. Phys.* **1989**, 90, 1007.

³ Martins, M. A. P.; Rodrigues, L. V.; Meyer, A. R.; Frizzo, C. P.; Hörner, M.; Zanatta, N.; Bonacorso, H. G.; Berná, J.; Alajarin, M. *Cryst. Growth Des.* **2017**, 17, 5845.

⁴ Tomasi, J.; Persico, M. *Chem. Rev.* **1994**, 94, 2027.

confirmed in all stationary points.⁵ All calculations were performed using the ultrafine grid implemented in Gaussian 09 E.01.⁶

COMPUTATIONAL RESULTS

A set of conformers of the transition structure for the *Si*- and *Re*-attack of both simplified enamine-thread **4c'** and enamine-rotaxane **6c'** over both faces of (*E*)- β -nitrostyrene **8** were computed at PCM(dichloromethane)/wB97XD/cc-pVDZ theoretical level. For that pathway involving the enamine-thread **4c'** the transition structure TS_{4c'-Si8} leading to the (*S*)-**9a** Michael adduct was computed to be 7.0 kJ/mol lower in energy than that TS_{4c'-Re8} furnishing the enantiomer (*R*)-**9a** (Figure S2a). Front and side view of corresponding transition structures to that attack are shown in Figure S3 and a topological analysis in Figure S4. In both cases a NH \cdots ONO hydrogen bond between the NH of the amide group and the nitro group is observed (1.99 Å in both cases). So, the Michael addition orientation seems to be driven by a hydrogen bond. The length for the C-C making bond is of 2.00 Å for the *Re*-attack while for the *Si*-attack the related distance is longer, 2.20 Å. This indicates a less steric hindrance around the reactive site in the transition structure of the *Si*-attack than that of the *Re*-attack.

In contrast, if the rotaxane **6c** acts as catalyst the Michael addition over the *Re*-face of the nitrostyrene is preferred in 7.3 kJ/mol respect to the *Si*-attack (Figure S2b). As shown in Figure S5 and S6, this preference could be justified by attending to the NH \cdots ONO hydrogen bond between one NH group of the ring with the nitro group (2.50 Å). A similar hydrogen bond is missed in the transition structure for the *Si*-attack. This absence could be related to the less available space to accommodate the styrene molecule due to the bulky macrocycle.

⁵ Bauernschmitt, R.; Ahlrichs, R. *J. Chem. Phys.* **1996**, *104*, 9047.

⁶ Gaussian 09, Revision E.01, Frisch M. J., Trucks G. W., Schlegel H. B., Scuseria G. E. et al, Gaussian, Inc., Wallingford CT, 2013.

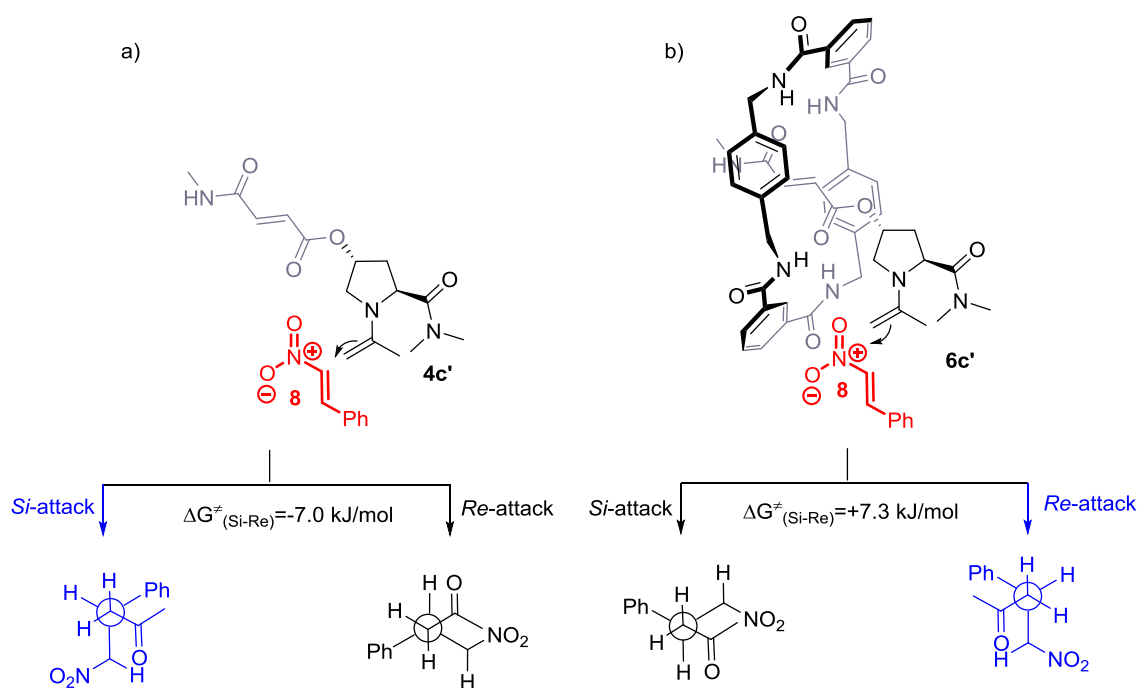


Figure S2. General scheme for the nucleophilic attack of the enamine of: a) simplified enamine-thread **4c'** plus **8**; b) simplified enamine-rotaxane **6c'** plus **8**. Energy differences, $\Delta G^{\ddagger}_{(\text{Si-Re})}$, between the two possible transition structures are shown in kJ/mol.

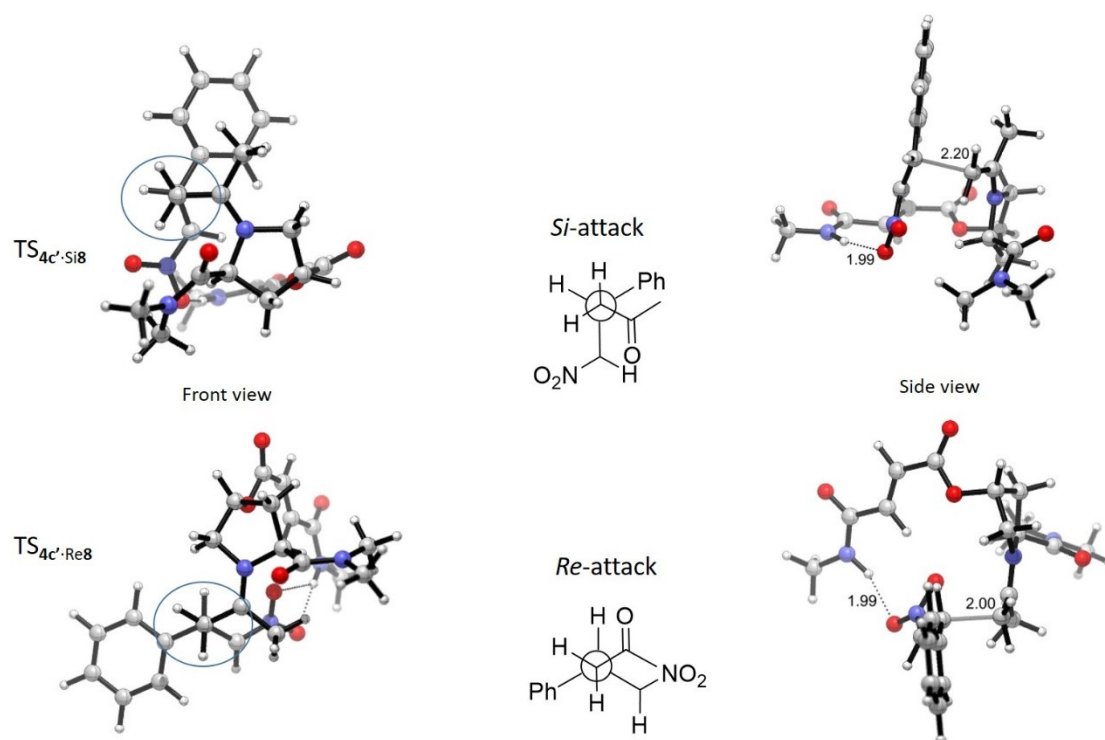


Figure S3. Computed transition structures for the both *Si*- and *Re*-attack TS_{4c'-Si8} and TS_{4c'-Re8}.

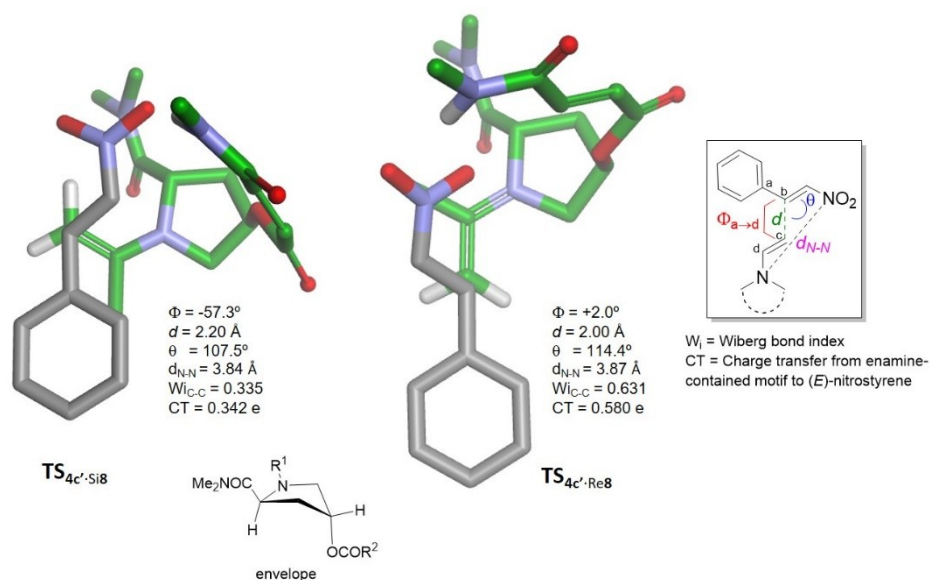


Figure S4. Topological analysis of computed transition structures for the both *Si*- and *Re*-attack TS_{4c'-Si8} and TS_{4c'-Re8}. Hydrogen atoms have been removed for clarity.

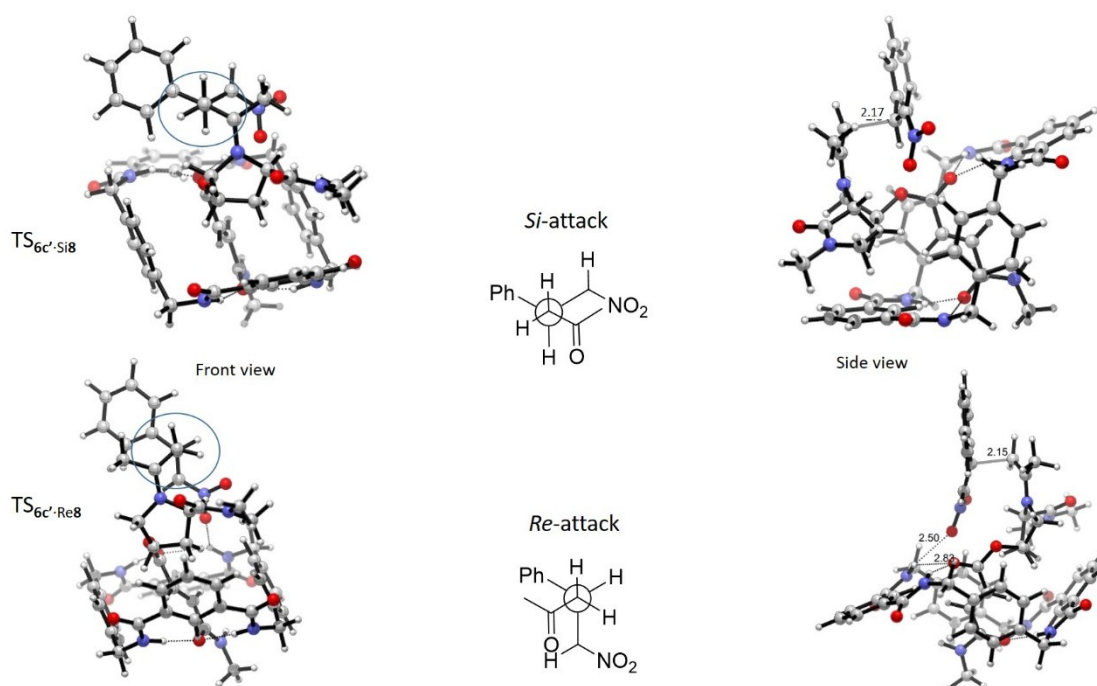


Figure S5. Computed transition structures for the both *Si*- and *Re*-attack TS_{6c'-Si8} and TS_{6c'-Re8}.

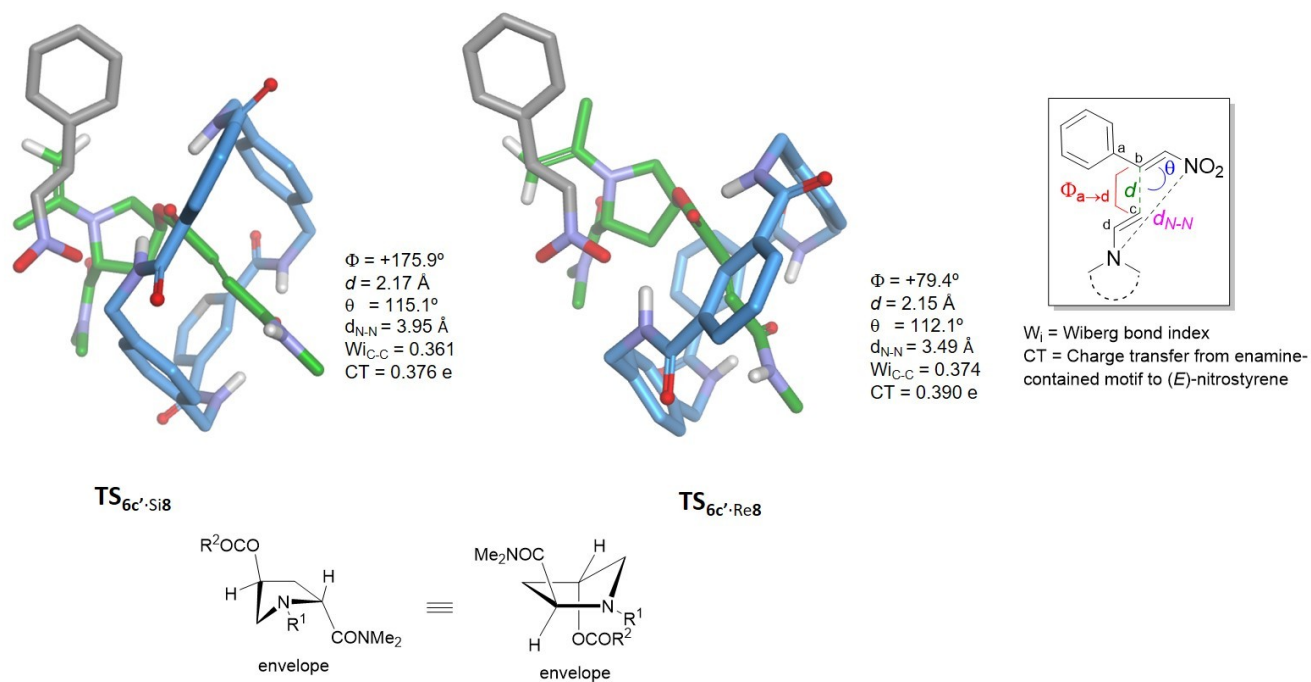


Figure S6. Topological analysis of computed transition structures for the both *Si*- and *Re*-attack TS_{6c'.Si8} and TS_{6c'.Re8}. Hydrogen atoms have been removed for clarity.

Table S5. Value of imaginary frequencies, electronic, free and enthalpy energies (in Hartrees) of all computed conformers for systems shown in **Figures S3-S6**. Free energies and enthalpy energies in solution at 298.15 K ($G_{298,\text{sol}}$ and $H_{298,\text{sol}}$) were calculated at the PCM(dichloromethane)/wB97XD/cc-pVDZ level. Note that the filenames are used in our calculations and do not follow any guide.

Filename	Imag. Freq	$E_{\text{SCF}, 298, \text{sol}}$ PCM/wB97XD/cc- pVDZ	$G_{298, \text{sol}}$ PCM/wB97XD/cc- pVDZ	$H_{298, \text{sol}}$ PCM/wB97XD/cc- pVDZ
TS_{4c}·Si8 and TS_{4c}·Re8.				
ts_threadsmall_si_16	-374.9	-1564.392385	-1563.937956	-1563.838331
ts_threadsmall_re_01	-432.6	-1564.38835	-1563.935283	-1563.834586
ts_threadsmall_si_20	-393.9	-1564.387181	-1563.933033	-1563.832841
ts_threadsmall_si_21	-389.3	-1564.387134	-1563.932865	-1563.832588
ts_threadsmall_si_05	-441.3	-1564.379058	-1563.928409	-1563.825675
ts_threadsmall_re_04	-484.8	-1564.375361	-1563.925231	-1563.821667
ts_threadsmall_re_03	-448.7	-1564.375607	-1563.923173	-1563.821137
TS_{6c}·Si8 and TS_{6c}·Re8				
ts_rtxsmall_re_05	-416.8	-3320.307782	-3319.335104	-3319.163182
ts_rtxsmall_si_10	-406.1	-3320.301879	-3319.332321	-3319.157869
ts_rtxsmall_si_04	-467.6	-3320.296511	-3319.326016	-3319.151932
ts_rtxsmall_si_07	-467.7	-3320.296511	-3319.326001	-3319.151925
ts_rtxsmall_re_06	-441.2	-3320.294241	-3319.323289	-3319.149714
ts_rtxsmall_re_04	-446.0	-3320.296909	-3319.323166	-3319.152293

Cartesian Coordinates of the best conformer

Enamine-thread 4c' plus nitrostyrene (Si-attack) : TS_{4c'Si8}

C	-2.137839	-0.681901	0.583697
C	-1.189097	0.516705	2.462638
C	-1.026797	-0.976411	2.698339
C	-2.135577	-1.567646	1.846739
H	-1.505628	-1.130004	-0.190717
H	-0.268194	1.072919	2.670772
H	-1.992228	0.911179	3.107584
H	-1.067033	-1.249765	3.758937
H	-1.968288	-2.627290	1.622037
H	-3.088301	-1.461255	2.383814
N	-1.555007	0.583087	1.048416
C	-3.582889	-0.472319	0.103288
O	-4.276082	0.392252	0.630207
N	-4.023432	-1.308161	-0.866015
C	-5.386832	-1.173061	-1.351354
H	-5.841587	-0.296068	-0.880515
H	-5.386562	-1.043888	-2.444336
C	-3.216858	-2.383469	-1.436926
H	-2.776646	-3.019680	-0.656076
H	-3.878492	-3.019185	-2.037338
O	0.199126	-1.441865	2.116211
C	1.346361	-1.189323	2.768320
O	1.397959	-0.665736	3.858971
C	2.530512	-1.593683	1.973743
H	3.505141	-1.419547	2.432158
C	2.413457	-2.087997	0.738673
H	1.424793	-2.242305	0.300432
C	3.600733	-2.380235	-0.123845
O	4.749403	-2.397306	0.310585
N	3.257437	-2.590687	-1.414319
H	2.271237	-2.504318	-1.665594
C	4.229717	-2.827871	-2.457097
H	4.227766	-2.007903	-3.191512
H	4.014202	-3.770114	-2.982227
C	-1.574603	1.727674	0.340394
C	-1.740155	1.744592	-1.035462
C	-1.308983	2.997757	1.089426

H	-1.928257	2.708566	-1.507384
H	-2.091261	0.865288	-1.577405
H	-0.308032	2.989162	1.547640
H	-1.364224	3.859699	0.415876
H	-2.047005	3.123114	1.896151
C	0.345344	1.456299	-1.681514
C	0.685114	0.134321	-1.416733
C	1.085640	2.571942	-1.056920
C	0.975594	3.854851	-1.610927
C	1.888252	2.396247	0.080260
C	1.645758	4.935388	-1.044872
H	0.351314	4.004622	-2.494811
C	2.561239	3.476728	0.645202
H	1.988602	1.412082	0.541008
C	2.440381	4.749432	0.087076
H	1.548708	5.927144	-1.489571
H	3.181951	3.322553	1.529238
H	2.966284	5.595294	0.532900
H	-0.077989	1.655982	-2.665502
N	0.068784	-0.881186	-2.110124
O	0.334525	-2.071924	-1.804861
O	-0.775563	-0.625947	-2.983810
H	1.322653	-0.198585	-0.606812
H	5.221825	-2.891752	-1.995238
H	-2.415850	-2.003441	-2.088771
H	-5.979151	-2.067775	-1.101758

Enamine-thread 4c' plus nitrostyrene (Re-attack) : TS_{4c'Re8}

C	1.900341	-1.626124	0.271986
C	0.131789	-1.562183	1.931291
C	1.344003	-0.814067	2.456736
C	2.491456	-1.445871	1.679429
H	2.013547	-0.710033	-0.325351
H	-0.781253	-0.966856	2.027953
H	0.004252	-2.518282	2.460662
H	1.457737	-0.876538	3.544781
H	3.399775	-0.832838	1.689935
H	2.727984	-2.425934	2.118673
N	0.464585	-1.803947	0.521217
C	2.497782	-2.862884	-0.411490
O	1.980324	-3.960551	-0.234805

N	3.610922	-2.662105	-1.155217
C	4.201535	-3.786434	-1.863210
H	3.642774	-4.692680	-1.610787
H	4.154737	-3.618879	-2.950919
C	4.190205	-1.351716	-1.417046
H	4.200478	-0.721368	-0.519934
H	5.234108	-1.492850	-1.723580
O	1.179190	0.550023	2.049834
C	2.052276	1.452605	2.543317
O	2.810920	1.210823	3.456033
C	1.998949	2.741572	1.817045
H	2.547808	3.571579	2.265299
C	1.392323	2.854429	0.631841
H	0.869241	1.999522	0.191686
C	1.419040	4.125589	-0.156013
O	1.922640	5.165849	0.268167
N	0.839322	4.017680	-1.369722
H	0.453623	3.126301	-1.696525
C	0.763233	5.146466	-2.269370
H	1.729987	5.345302	-2.761228
H	0.472269	6.052495	-1.719002
C	-0.428915	-1.951893	-0.435006
C	-1.835926	-2.004961	-0.157319
C	-0.017159	-2.092171	-1.863314
H	-2.138399	-2.298722	0.850426
H	-2.419841	-2.489456	-0.943410
H	-0.018317	-3.161425	-2.124259
H	-0.770481	-1.590994	-2.489031
H	0.967461	-1.671487	-2.087594
C	-6.224367	-0.959382	-0.536815
C	-4.888388	-0.767093	-0.880143
C	-6.653851	-0.728609	0.771185
H	-6.934940	-1.294029	-1.294737
C	-3.961290	-0.337445	0.078581
H	-4.560947	-0.961856	-1.903953
C	-5.737176	-0.307661	1.733881
H	-7.701019	-0.879516	1.039115
C	-2.523329	-0.130004	-0.260935
C	-4.399782	-0.117456	1.389311
H	-6.063739	-0.125363	2.759298
C	-2.229874	0.542642	-1.497578
H	-1.926208	0.253141	0.572907

H	-3.685017	0.212620	2.146901
H	-2.966067	0.802523	-2.252281
N	-0.988367	1.026728	-1.689123
O	-0.728251	1.822559	-2.631610
O	-0.067549	0.662718	-0.897235
H	0.012239	4.932908	-3.039805
H	3.662465	-0.821253	-2.226688
H	5.255067	-3.909998	-1.569890

Enamine-rotaxane 6c' plus nitrostyrene
(Si-attack) : TS_{6c'Si8}

O	-0.206446	1.257481	0.858207
C	-0.645565	0.052249	0.510690
O	-1.761923	-0.024923	0.026695
C	0.215118	-1.127528	0.764055
H	1.054258	-1.041504	1.454116
C	-0.054914	-2.296824	0.182064
H	-0.892846	-2.385553	-0.514908
C	0.777367	-3.500499	0.471306
O	1.821564	-3.448248	1.141085
N	0.303804	-4.649320	-0.025202
H	-0.502648	-4.614784	-0.636518
C	1.005304	-5.907447	0.126127
H	1.476541	-5.942001	1.115586
H	1.789569	-6.019622	-0.639579
N	2.444401	-1.748549	3.591851
H	2.418429	-2.382407	2.796513
N	-4.210566	-0.250982	1.893293
H	-3.617428	-0.045215	1.096123
N	4.119257	-2.989366	-1.027177
H	3.578962	-3.211380	-0.196725
N	-2.504890	-1.438456	-2.735411
H	-2.503010	-0.791412	-1.954489
O	3.223112	0.174063	4.507470
O	-5.935265	-1.488291	2.706773
O	5.542451	-1.535816	-2.033202
O	-3.549154	-3.142574	-3.809367
C	4.204795	-0.506153	2.449152
C	5.142671	0.528882	2.506314
H	5.160671	1.170077	3.387480
C	6.022298	0.734650	1.445585
H	6.750039	1.545826	1.491358

C	5.966643	-0.087240	0.322548
H	6.641465	0.060965	-0.520949
C	5.023458	-1.115543	0.248346
C	4.147145	-1.315488	1.314335
H	3.367882	-2.069489	1.233000
C	3.252618	-0.660754	3.604196
C	1.458425	-1.975129	4.636961
H	1.839140	-1.507227	5.553713
H	1.385206	-3.057637	4.806792
C	0.101557	-1.409148	4.280906
C	-0.112437	-0.026897	4.298075
H	0.702220	0.633477	4.603828
C	-1.347892	0.502500	3.928329
H	-1.497830	1.585088	3.941448
C	-2.399318	-0.336280	3.551126
C	-2.181768	-1.717344	3.528539
H	-2.991749	-2.387313	3.230984
C	-0.945446	-2.246565	3.887222
H	-0.792310	-3.328232	3.861867
C	-3.754852	0.227449	3.181854
H	-4.513503	-0.077702	3.915274
H	-3.714153	1.326621	3.185886
C	-5.208131	-1.165683	1.771707
C	-5.386070	-1.766896	0.404536
C	-6.612356	-2.361612	0.095340
H	-7.402695	-2.356228	0.846486
C	-6.808160	-2.951442	-1.151118
H	-7.767464	-3.412550	-1.390624
C	-5.781870	-2.953509	-2.093421
H	-5.917514	-3.412147	-3.073203
C	-4.552706	-2.359043	-1.795158
C	-4.356188	-1.786166	-0.537763
H	-3.379423	-1.380160	-0.277509
C	-3.490944	-2.361288	-2.862000
C	-1.499550	-1.244223	-3.769502
H	-1.379954	-0.165992	-3.946139
H	-1.896788	-1.703173	-4.684362
C	-0.164651	-1.859985	-3.415418
C	0.925074	-1.044419	-3.099916
H	0.798936	0.040902	-3.116299
C	2.145310	-1.608706	-2.742163
H	2.988234	-0.958167	-2.502846

C	2.310453	-2.996499	-2.688612
C	1.223101	-3.809126	-3.018888
H	1.331858	-4.896543	-2.990427
C	-0.002884	-3.248253	-3.378591
H	-0.849994	-3.891922	-3.629153
C	3.644716	-3.582576	-2.265819
H	3.564004	-4.670592	-2.137182
H	4.409453	-3.389229	-3.029635
C	4.929799	-1.901692	-1.030466
C	1.153190	1.536233	1.257344
C	1.185794	3.041744	1.445329
C	2.168832	1.300317	0.134738
H	1.377579	0.993647	2.185241
H	2.062281	3.323670	2.047579
H	0.279501	3.418420	1.925561
C	2.273576	2.647938	-0.626129
H	1.867434	0.484985	-0.535983
H	3.133477	1.027442	0.579776
H	1.889794	2.526798	-1.642785
N	1.366897	3.539723	0.088727
C	3.710348	3.184996	-0.590940
N	4.590577	2.659214	-1.479417
C	5.967552	3.118865	-1.467200
H	6.118144	3.768681	-0.599920
H	6.193684	3.679396	-2.389040
C	4.280715	1.677403	-2.504532
H	3.218917	1.413510	-2.507912
H	4.529336	2.082874	-3.498235
O	4.022808	4.027245	0.245724
C	0.576894	4.430230	-0.539568
C	-0.656319	4.855927	-0.055637
C	0.984320	4.931861	-1.891824
H	-1.090291	5.742926	-0.518098
H	-0.957099	4.672415	0.974450
H	1.966029	4.581383	-2.225681
H	0.221349	4.640276	-2.634728
H	0.999624	6.030322	-1.872455
O	-0.974677	2.235590	-4.154848
N	-0.934260	2.432789	-2.930809
C	-1.863277	3.280121	-2.351673
O	-0.077389	1.875213	-2.210036
C	-1.943785	3.364713	-0.963624

H	-2.531126	3.758979	-3.061576
C	-3.196486	3.826111	-0.320136
H	-1.410639	2.581599	-0.427144
C	-3.620669	3.164907	0.838918
C	-3.984360	4.861202	-0.838689
C	-4.820787	3.510537	1.455551
H	-2.996190	2.365251	1.243566
C	-5.177890	5.215849	-0.215087
H	-3.659434	5.399557	-1.731520
C	-5.602546	4.538910	0.929966
H	-5.151347	2.974680	2.347394
H	-5.783239	6.025469	-0.626410
H	-6.541607	4.814674	1.412573
H	6.651399	2.258502	-1.410219
H	0.290370	-6.732163	0.029409
H	4.865832	0.756828	-2.346460

Enamine-rotaxane 6c' plus nitrostyrene

(Re-attack) : TS_{6c'Re8}

O	0.597388	1.130608	1.153766
C	-0.641786	0.798345	0.780076
O	-1.402008	1.684797	0.449588
C	-1.026378	-0.633897	0.823001
H	-0.513819	-1.302128	1.514078
C	-1.990036	-1.124013	0.044401
H	-2.505471	-0.493483	-0.683729
C	-2.373771	-2.560723	0.152351
O	-1.743781	-3.370025	0.853423
N	-3.468812	-2.908016	-0.533103
H	-3.878204	-2.232388	-1.166930
C	-3.985012	-4.260431	-0.531328
H	-3.884452	-4.685679	0.474762
H	-3.432956	-4.899636	-1.237972
N	-0.402082	-3.029175	3.532798
H	-0.803208	-3.235441	2.617901
N	-3.546532	2.959458	1.863180
H	-2.894071	2.707585	1.127666
N	0.171173	-5.050802	-1.035888
H	-0.389971	-4.586916	-0.324757
N	-2.803105	0.907446	-2.903407
H	-2.332006	1.491833	-2.220221
O	1.460904	-2.503481	4.720795

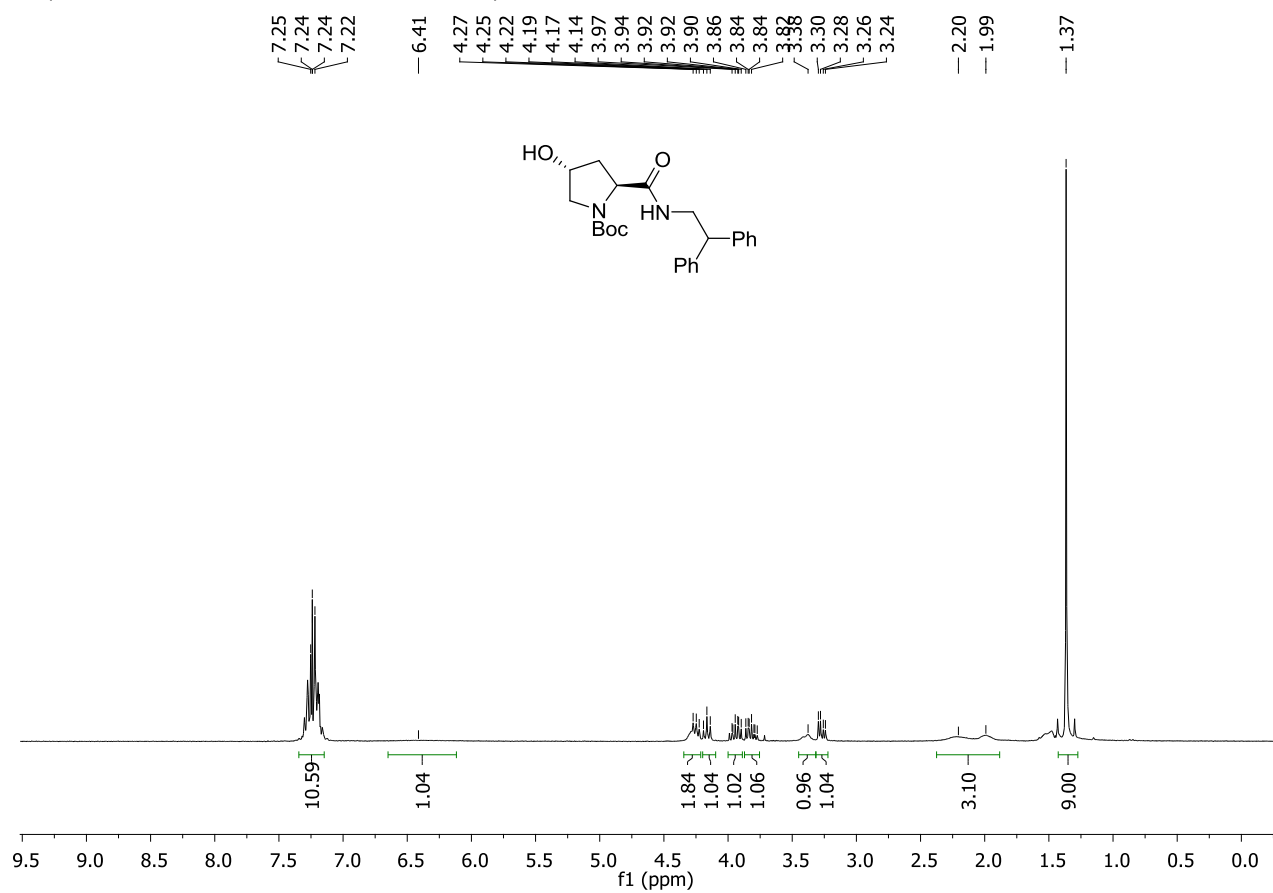
O	-5.723164	3.150770	2.485064
O	2.283687	-5.330302	-1.829912
O	-4.731047	0.305161	-3.922069
C	1.790021	-3.431109	2.553789
C	3.160531	-3.154847	2.596035
H	3.560929	-2.634041	3.466132
C	3.984731	-3.534984	1.539882
H	5.049931	-3.304966	1.569340
C	3.439250	-4.173685	0.428963
H	4.058770	-4.462133	-0.419498
C	2.069201	-4.441091	0.367217
C	1.257374	-4.094336	1.447915
H	0.199066	-4.341121	1.431352
C	0.940986	-2.954600	3.701469
C	-1.321634	-2.523730	4.539830
H	-0.802118	-2.567409	5.505302
H	-2.189500	-3.195798	4.584059
C	-1.771354	-1.110423	4.240971
C	-0.870175	-0.044939	4.343966
H	0.150621	-0.240616	4.681112
C	-1.265702	1.251016	4.016070
H	-0.546421	2.070292	4.089926
C	-2.569661	1.513623	3.588012
C	-3.469770	0.448211	3.491230
H	-4.494176	0.635686	3.161386
C	-3.073996	-0.847771	3.810724
H	-3.789457	-1.668920	3.721467
C	-3.009227	2.914391	3.209636
H	-3.801000	3.266726	3.884215
H	-2.161647	3.609730	3.287280
C	-4.877598	2.945439	1.616477
C	-5.290811	2.663081	0.195003
C	-6.581667	3.039875	-0.184637
H	-7.209973	3.552133	0.544370
C	-7.051811	2.749084	-1.462122
H	-8.058717	3.049616	-1.755406
C	-6.242731	2.058121	-2.358944
H	-6.602648	1.795816	-3.353866
C	-4.947172	1.676950	-1.994296
C	-4.474722	1.981126	-0.714671
H	-3.482274	1.647173	-0.407090
C	-4.155174	0.904161	-3.015210

C	-1.973510	0.291364	-3.934673
H	-1.072935	0.906761	-4.036902
H	-2.542171	0.318396	-4.873267
C	-1.579114	-1.130539	-3.599700
C	-0.326319	-1.387864	-3.035937
H	0.358235	-0.552461	-2.879771
C	0.020707	-2.674654	-2.647360
H	0.991452	-2.843905	-2.181189
C	-0.858489	-3.746606	-2.828449
C	-2.093084	-3.496571	-3.431244
H	-2.794402	-4.319284	-3.593503
C	-2.454662	-2.200600	-3.805947
H	-3.435876	-2.008454	-4.245421
C	-0.461335	-5.128413	-2.342030
H	-1.339246	-5.787759	-2.290094
H	0.264963	-5.590073	-3.024348
C	1.525234	-5.000051	-0.921060
C	1.600631	0.124181	1.403381
C	2.854244	0.887460	1.783977
C	1.993686	-0.626895	0.123673
H	1.270161	-0.529420	2.220888
H	3.549464	0.228744	2.328861
H	2.622763	1.765822	2.393934
C	3.213681	0.138343	-0.443756
H	1.168356	-0.643709	-0.598663
H	2.250656	-1.665685	0.365171
H	3.007841	0.526719	-1.446981
N	3.406787	1.244084	0.485336
C	4.491666	-0.726785	-0.464959
N	4.620780	-1.615785	-1.479949
C	5.829831	-2.414768	-1.574121
H	6.441481	-2.244613	-0.683206
H	6.402906	-2.131721	-2.471845

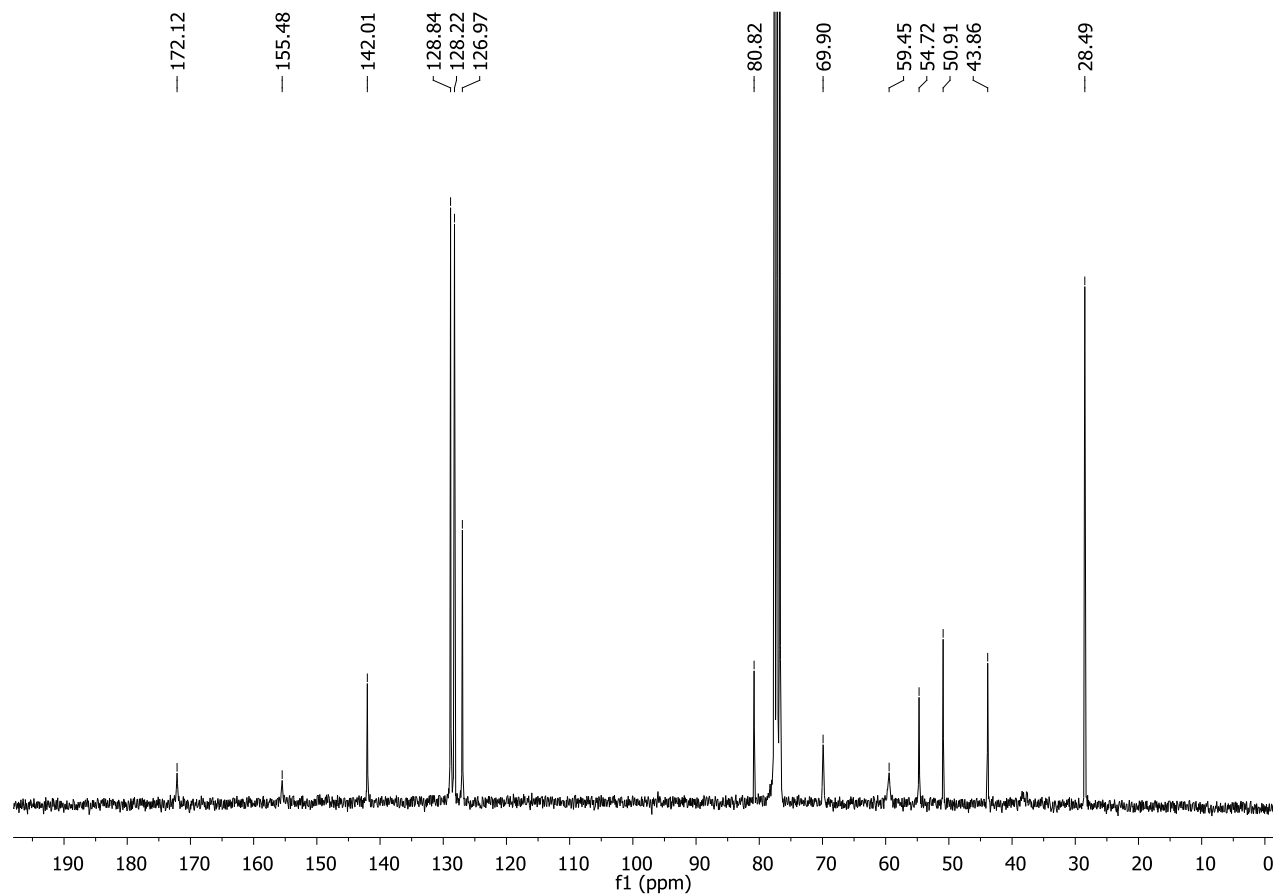
C	3.639605	-1.863774	-2.521247
H	2.795365	-1.169506	-2.465914
H	4.106241	-1.742215	-3.510980
O	5.332800	-0.591446	0.418752
C	4.214295	2.284269	0.242197
C	4.583718	2.620283	-1.055862
C	4.566384	3.176537	1.391322
H	4.513553	1.888808	-1.859960
H	5.349017	3.385818	-1.175901
H	5.077561	2.600882	2.177331
H	5.220783	3.989811	1.059273
H	3.664100	3.626931	1.834039
O	0.157383	1.506811	-1.972747
N	1.275621	2.026314	-2.166933
C	1.662282	3.073187	-1.365275
O	2.044679	1.583311	-3.048061
C	2.850399	3.759652	-1.624607
H	0.972821	3.266797	-0.550606
C	3.118515	5.069052	-0.980615
H	3.237955	3.649821	-2.638116
C	2.446504	5.491840	0.174806
C	4.078151	5.921027	-1.546077
C	2.734927	6.726664	0.751931
H	1.690095	4.856273	0.637782
C	4.365793	7.155498	-0.971434
H	4.607119	5.607035	-2.449046
C	3.696331	7.561747	0.183789
H	2.202537	7.038068	1.652217
H	5.114861	7.804604	-1.428122
H	3.920899	8.528494	0.637516
H	5.575818	-3.482811	-1.653478
H	-5.042017	-4.240784	-0.819539
H	3.259035	-2.896158	-2.443291

10. ¹H and ¹³C NMR Spectra of synthesized compounds

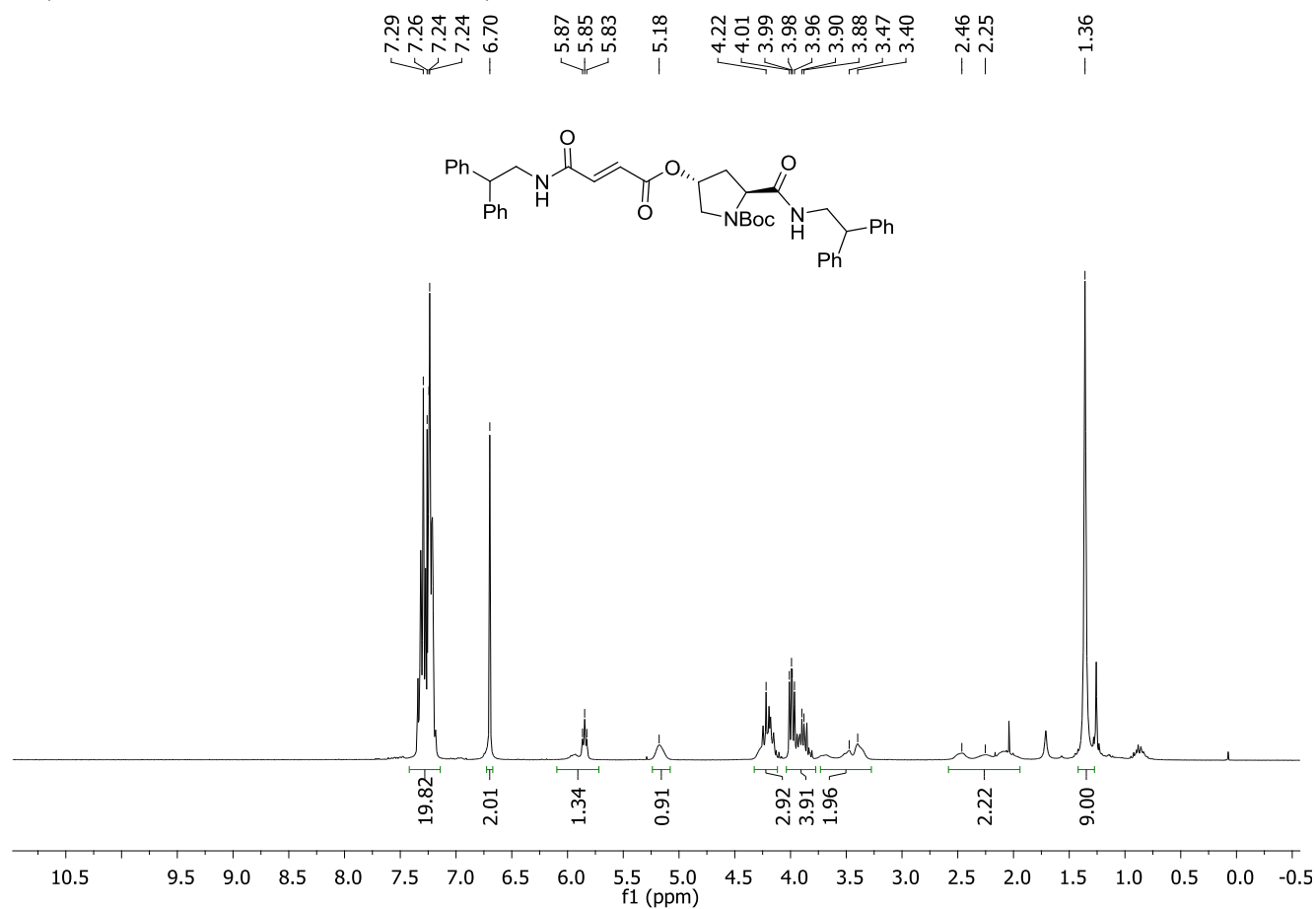
2a (¹H NMR, 300 MHz, CDCl₃, 298K)



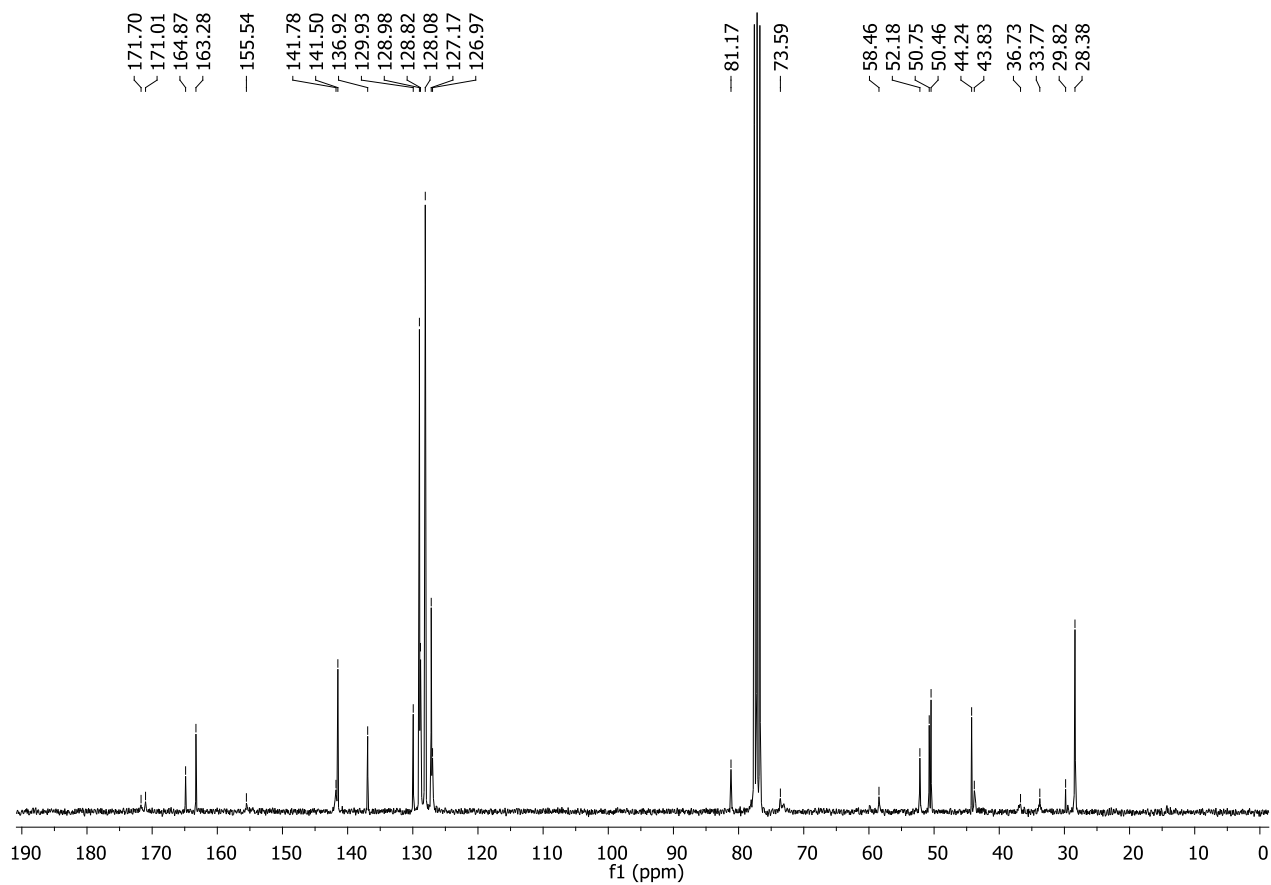
2a (¹³C NMR, 75 MHz, CDCl₃, 298K)



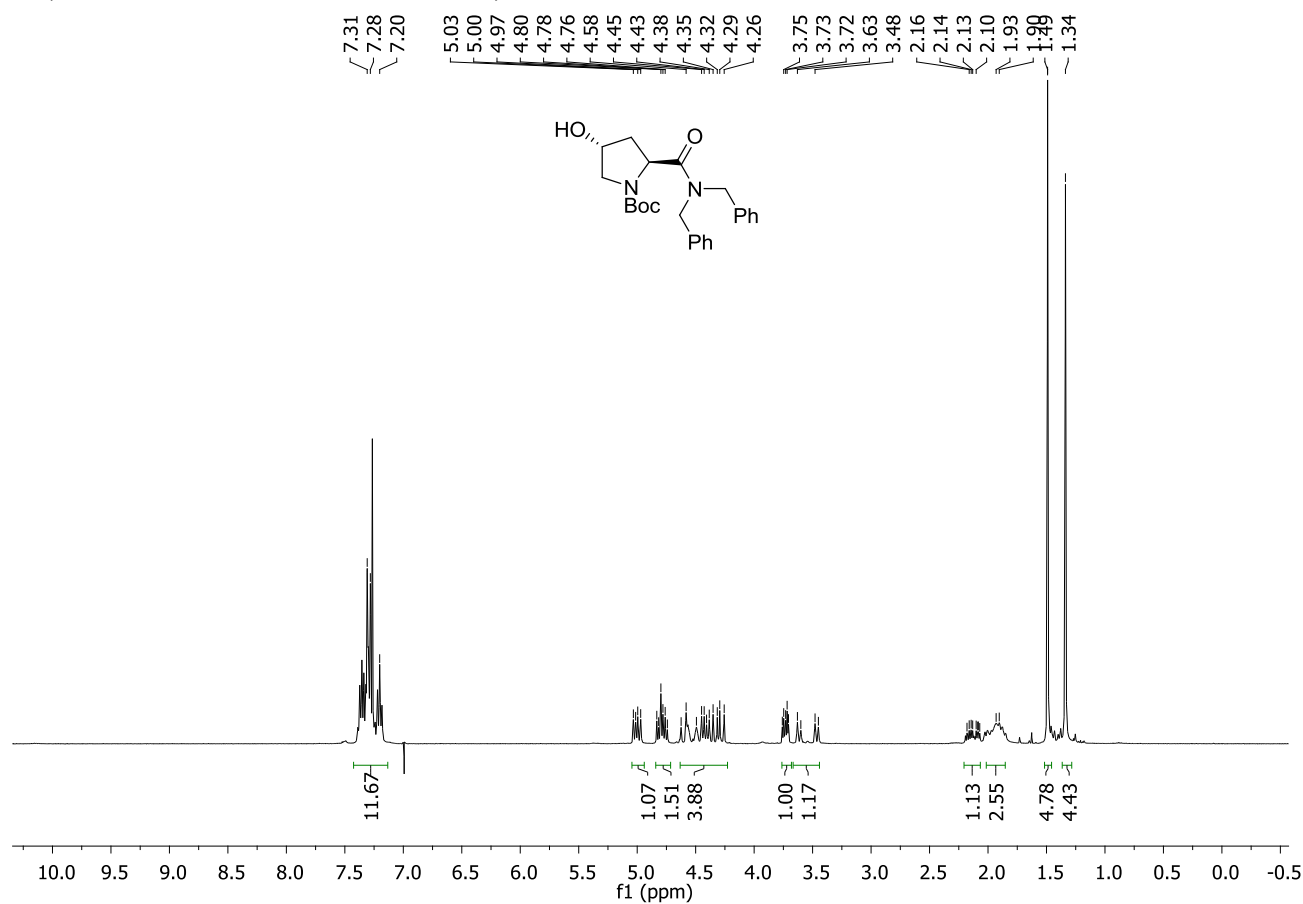
3a (^1H NMR, 300 MHz, CDCl_3 , 298K)



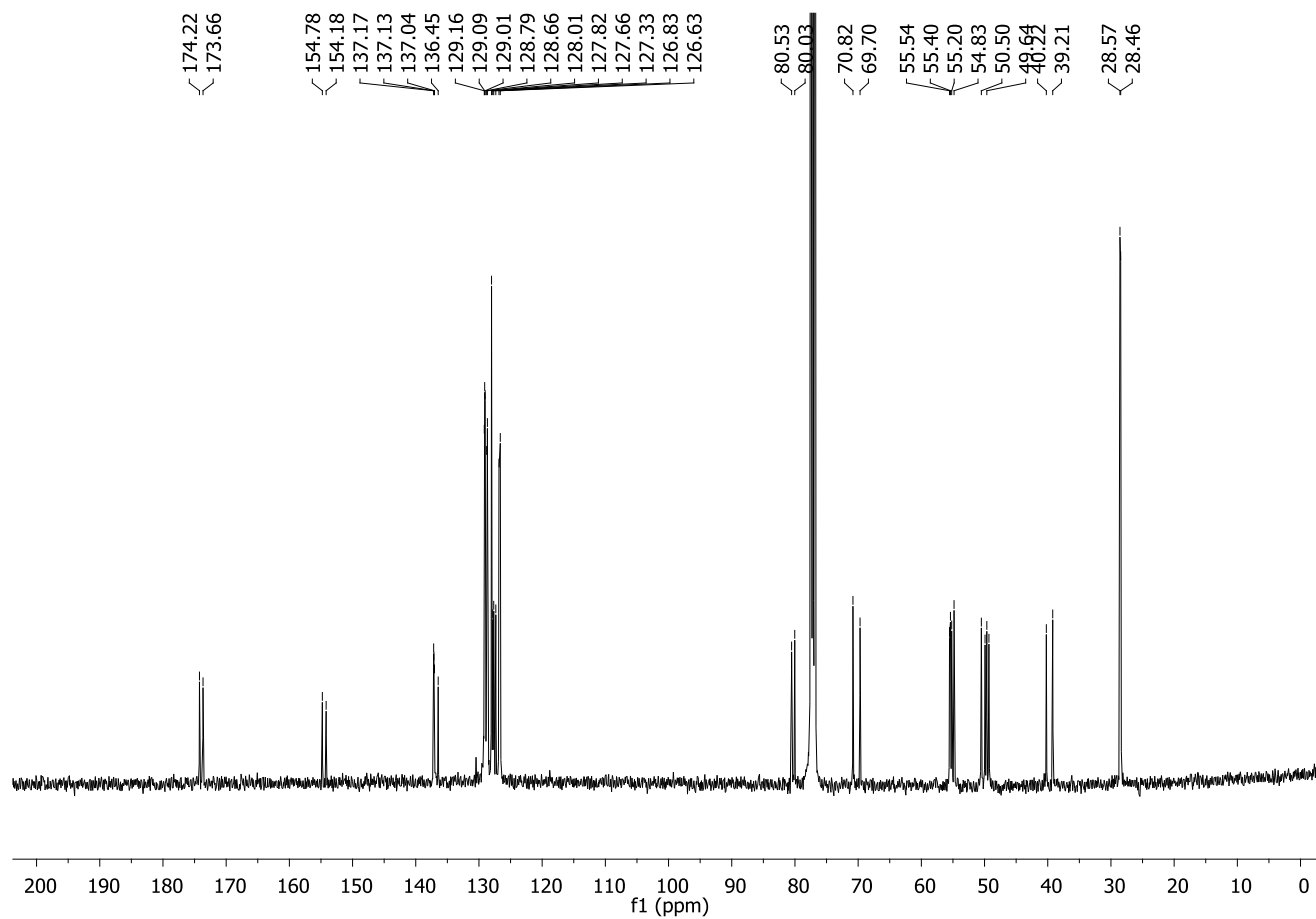
3a (^{13}C NMR, 75 MHz, CDCl_3 , 298K)



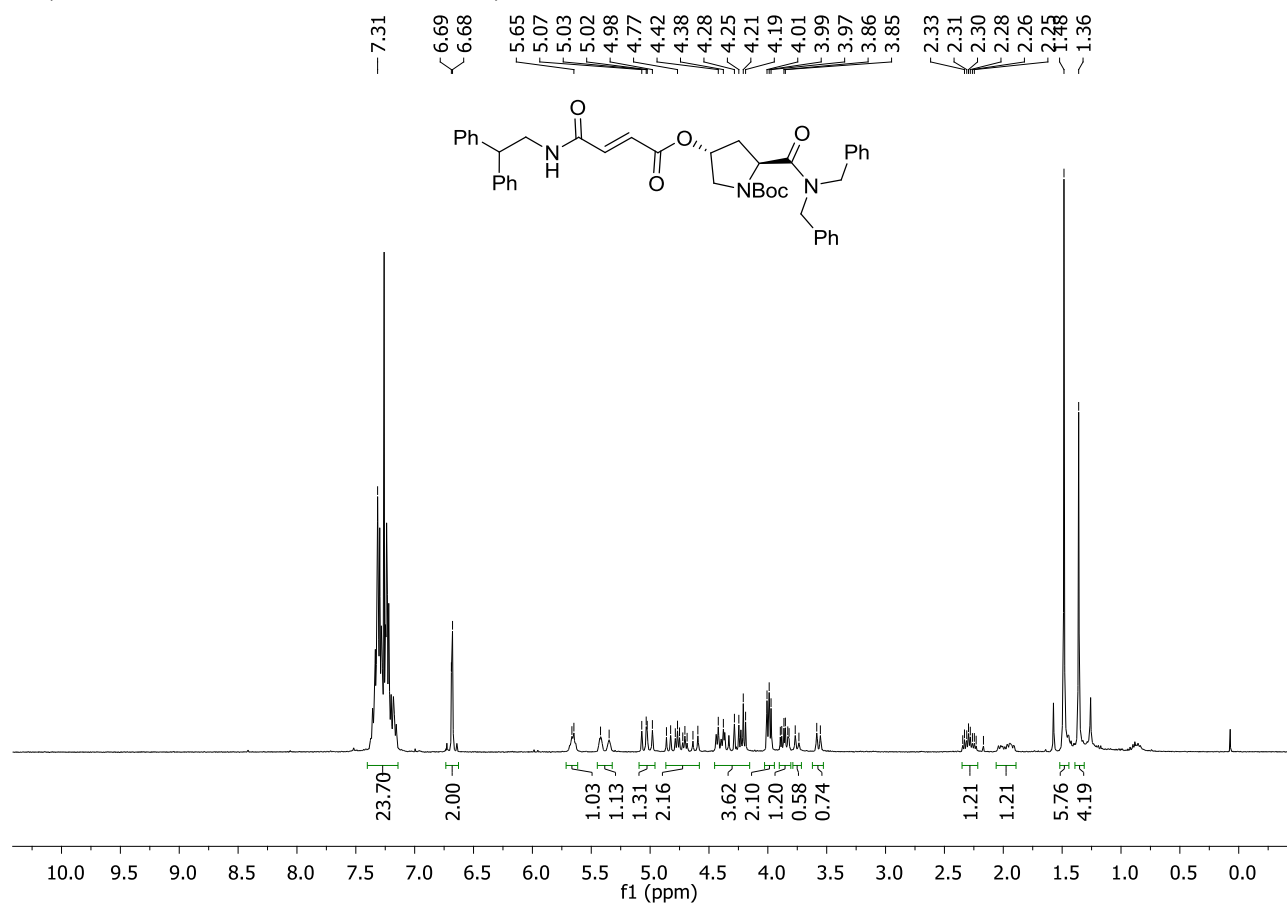
2b (^1H NMR, 400 MHz, CDCl_3 , 298K)



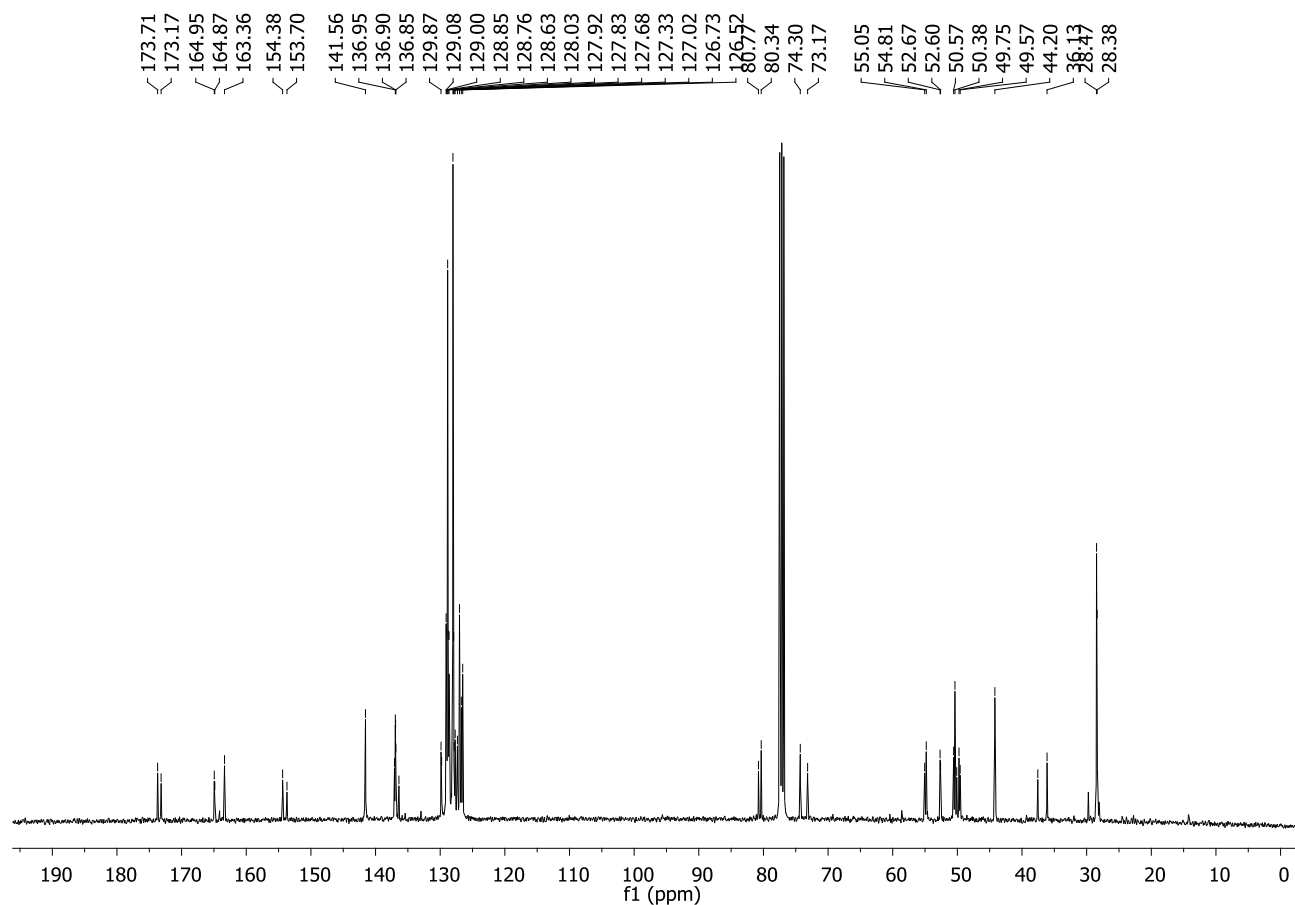
2b (^{13}C NMR, 100 MHz, CDCl_3 , 298K)



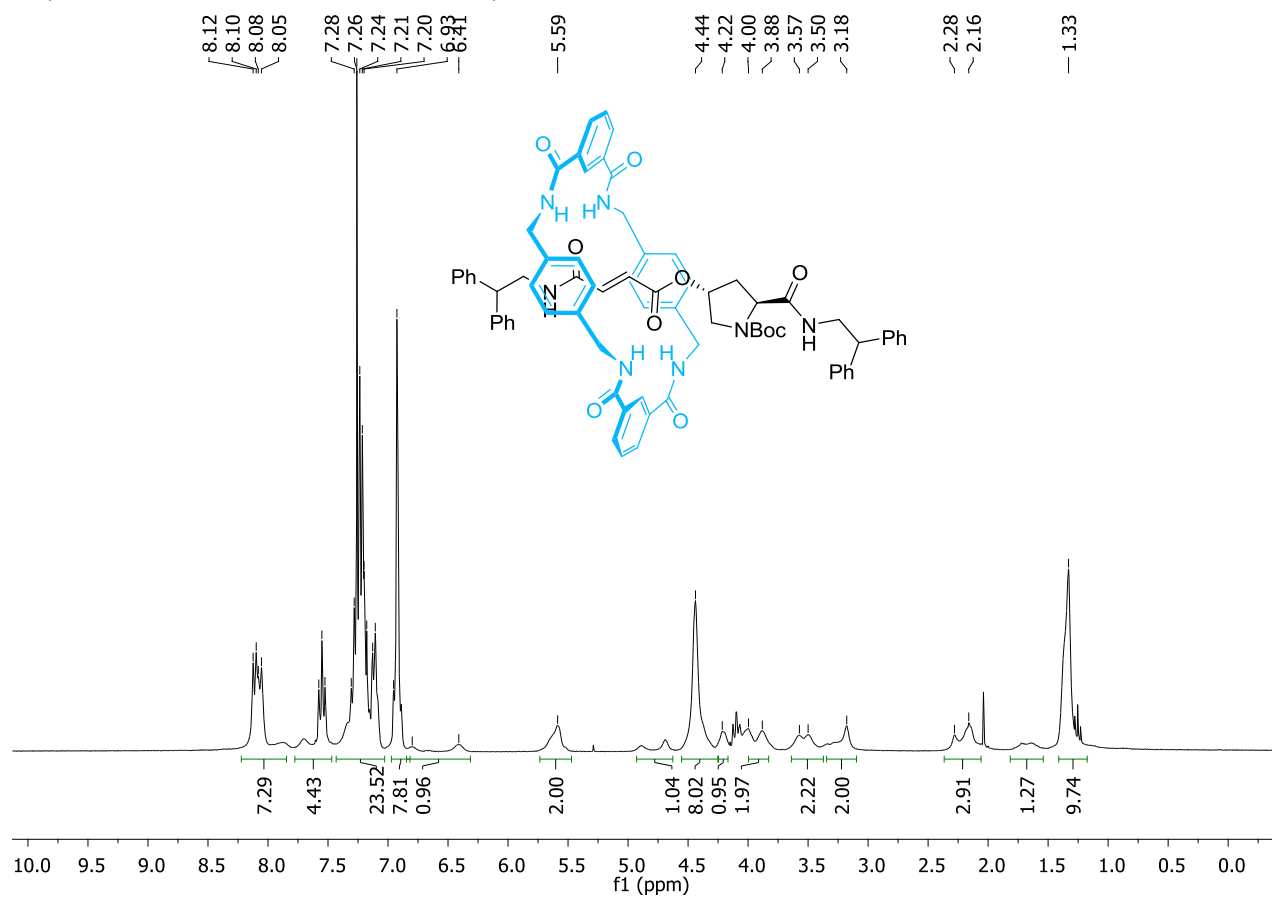
3b (^1H NMR, 400 MHz, CDCl_3 , 298K)



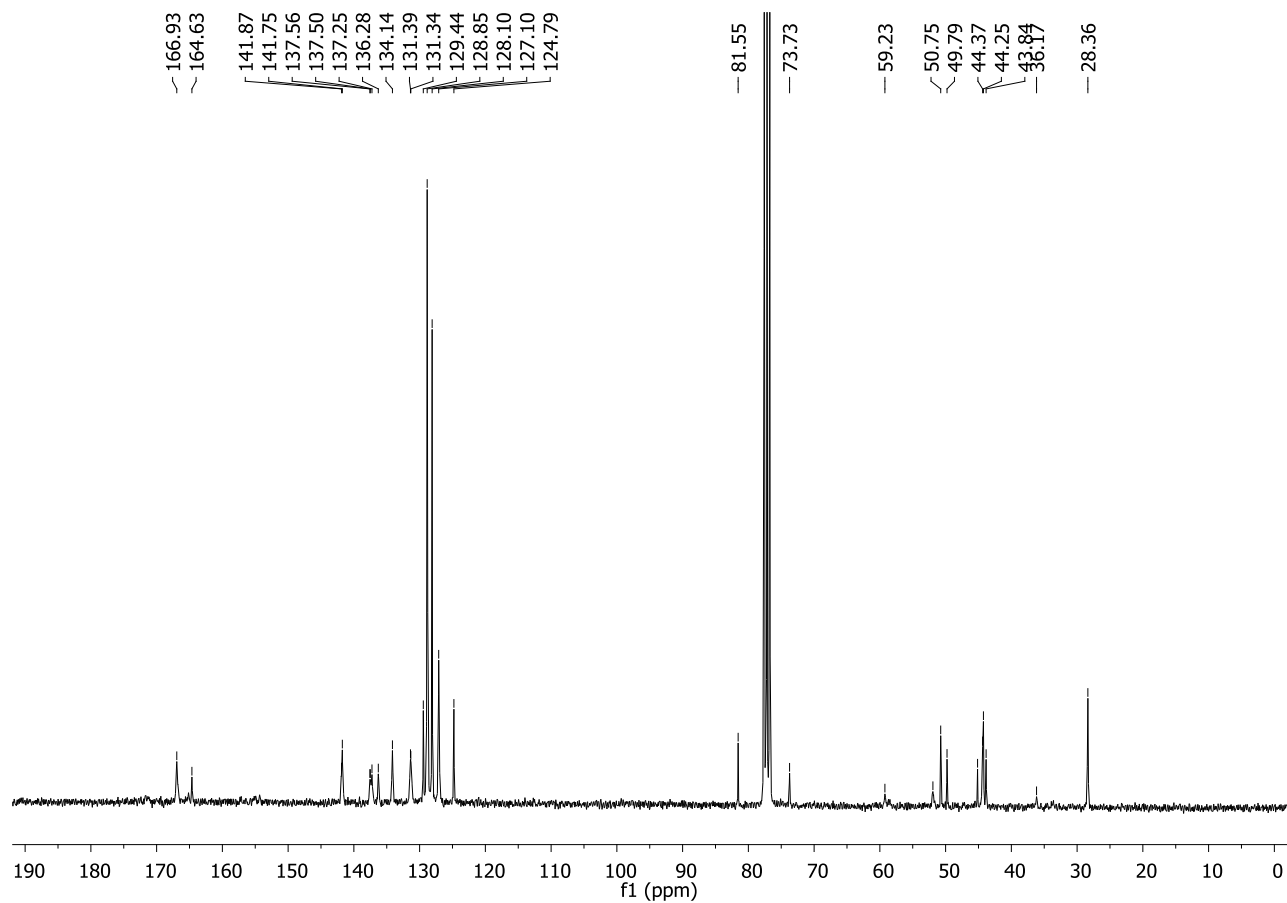
3b (^{13}C NMR, 100 MHz, CDCl_3 , 298K)



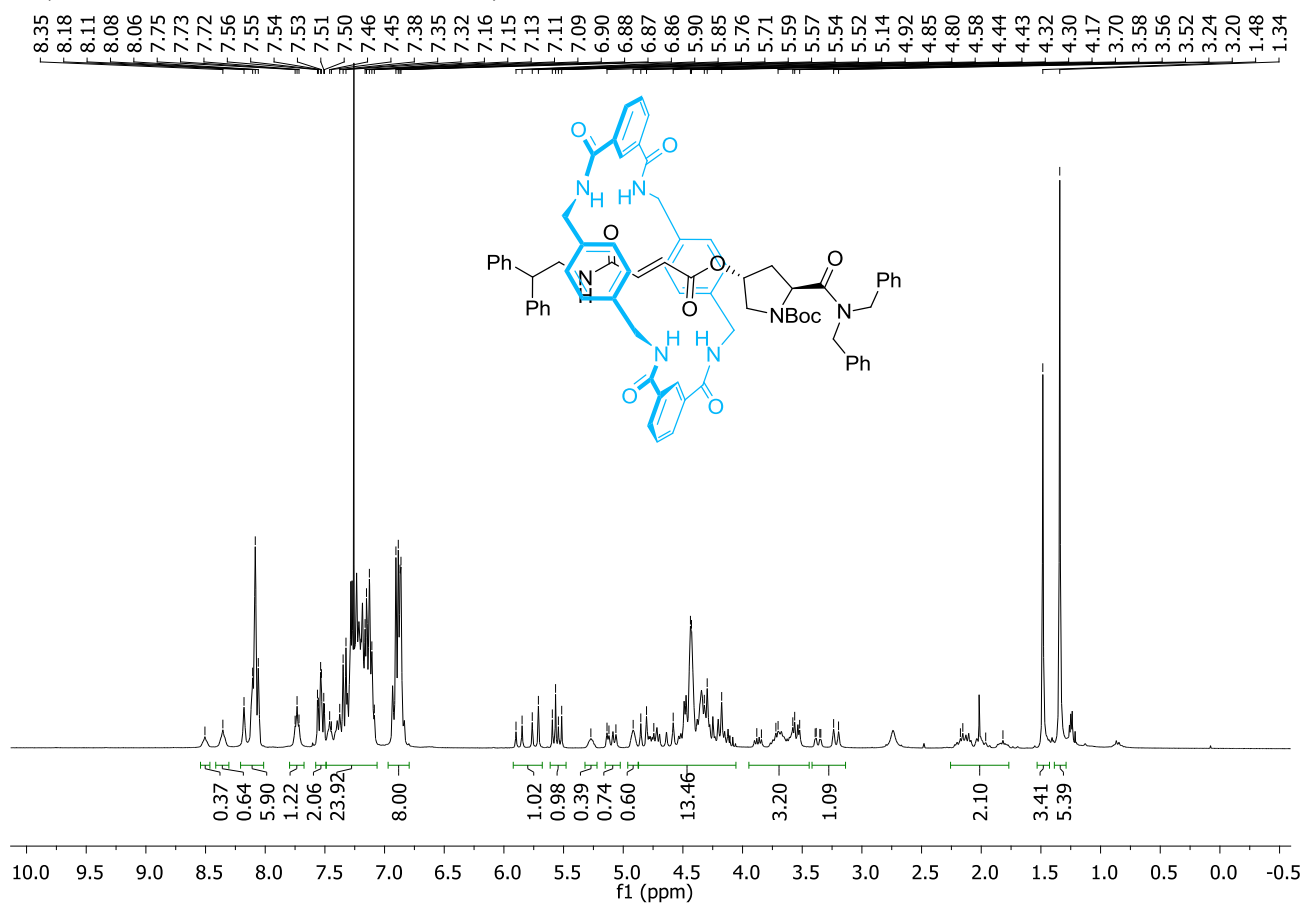
5a (^1H NMR, 300 MHz, CDCl_3 , 298K)



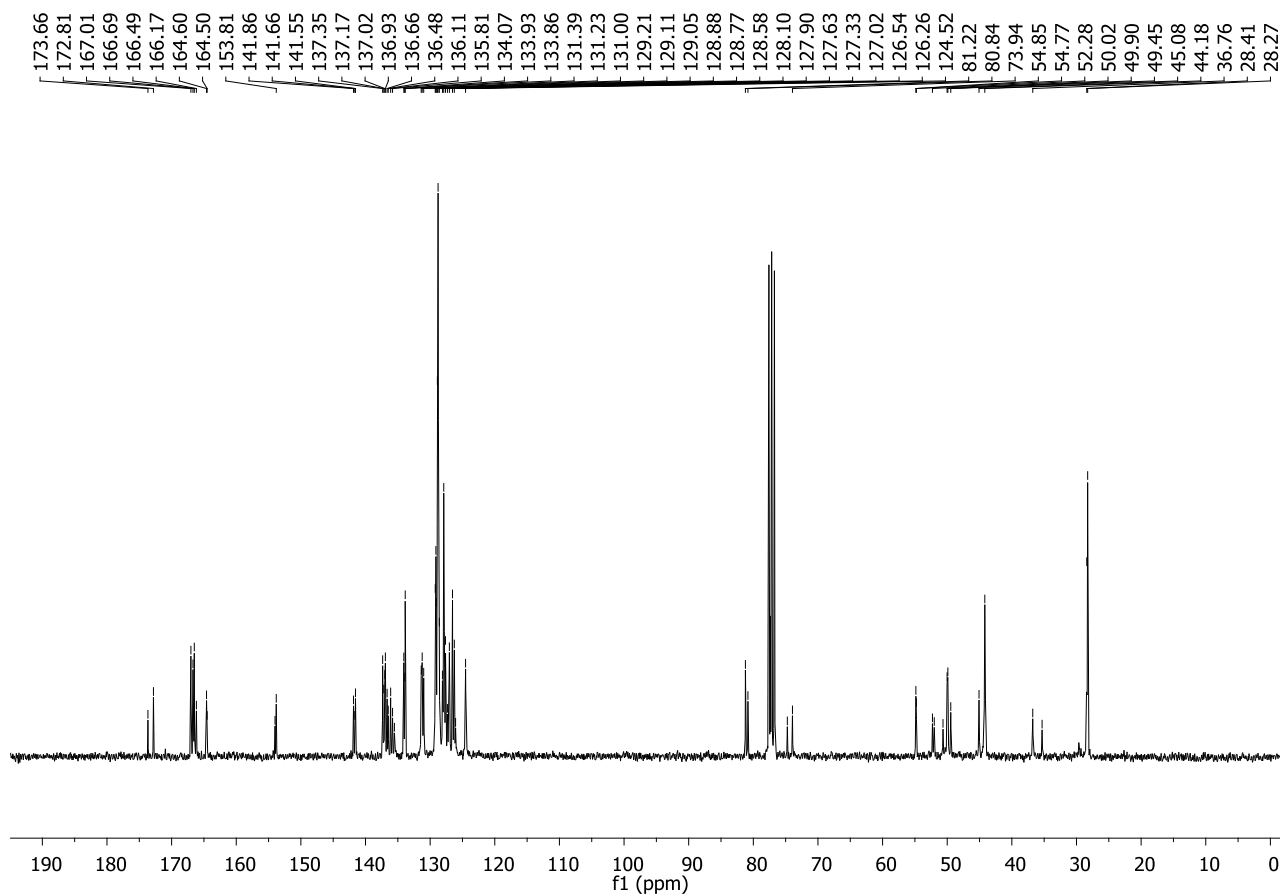
5a (^{13}C NMR, 75 MHz, CDCl_3 , 298K)



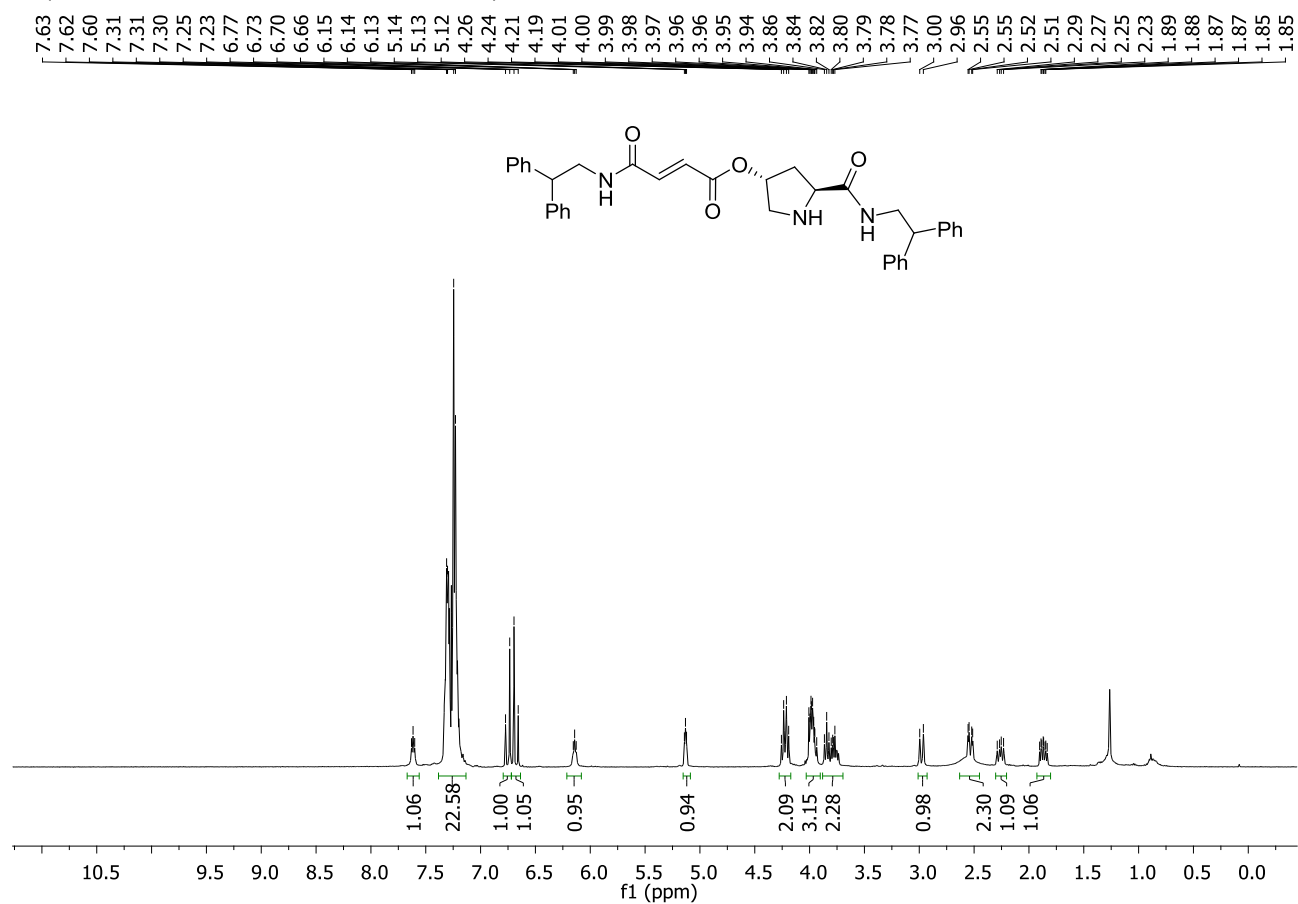
5b (^1H NMR, 300 MHz, CDCl_3 , 298K)



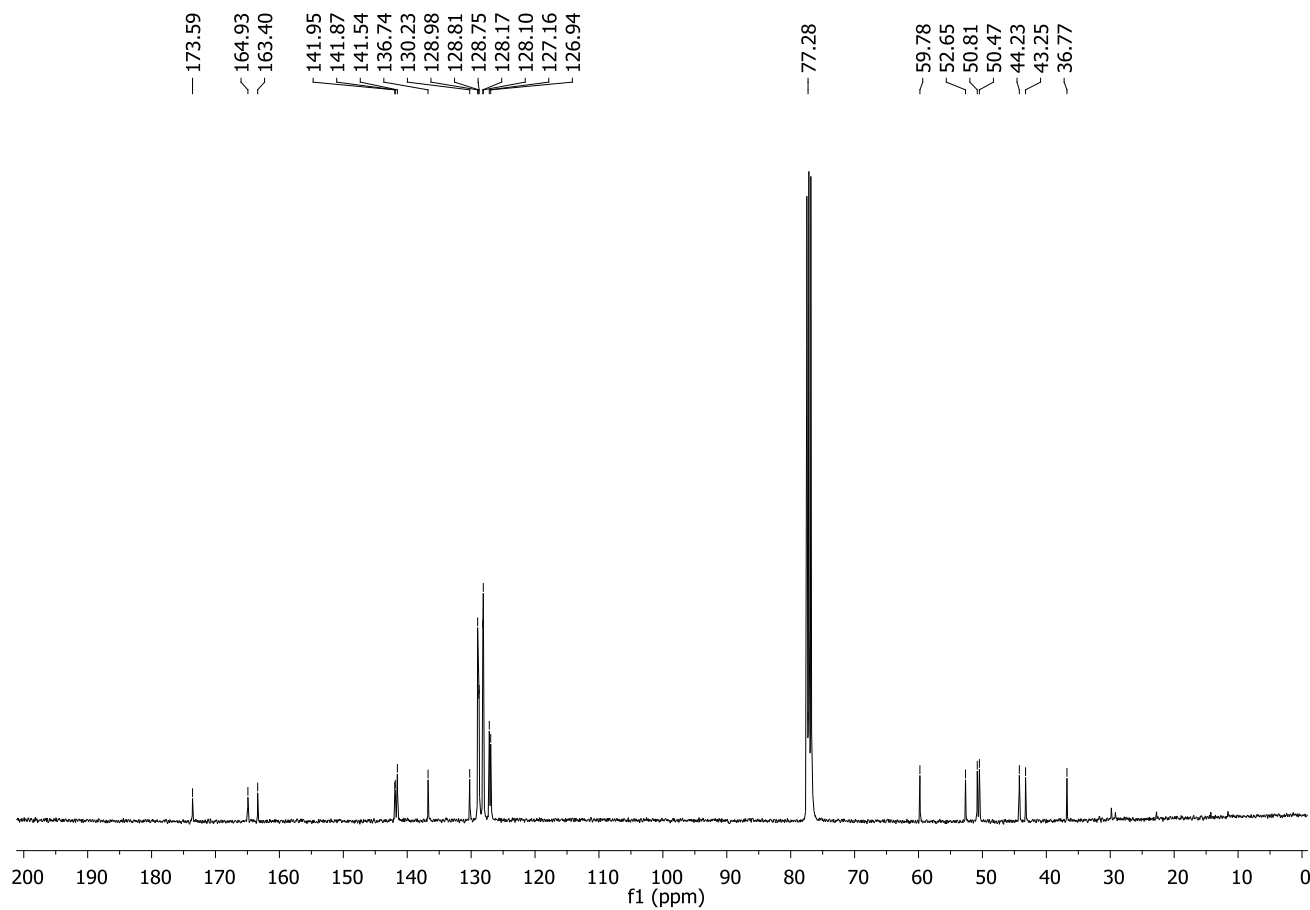
5b (^{13}C NMR, 75 MHz, CDCl_3 , 298K)



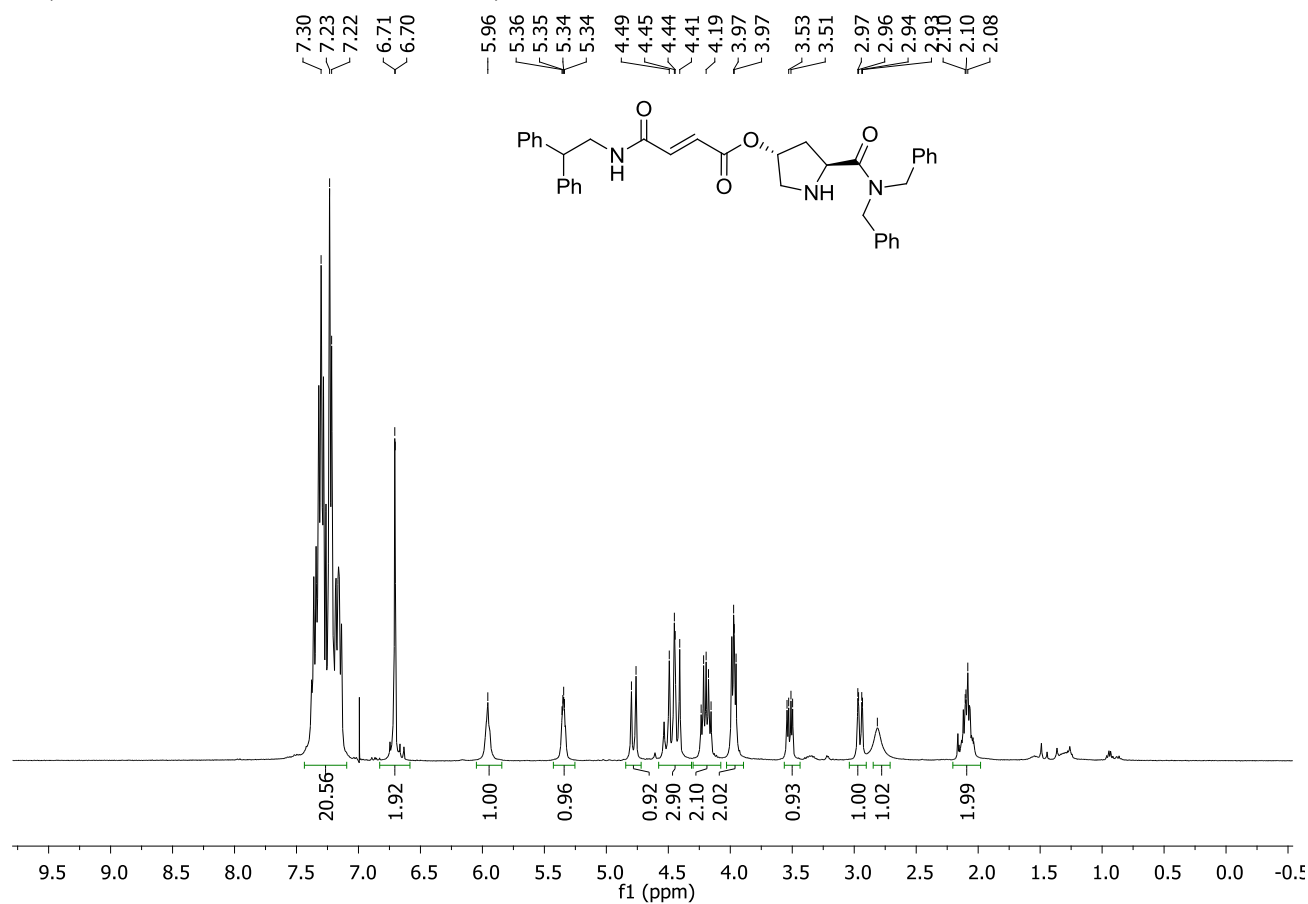
4a (^1H NMR, 400 MHz, CDCl_3 , 298K)



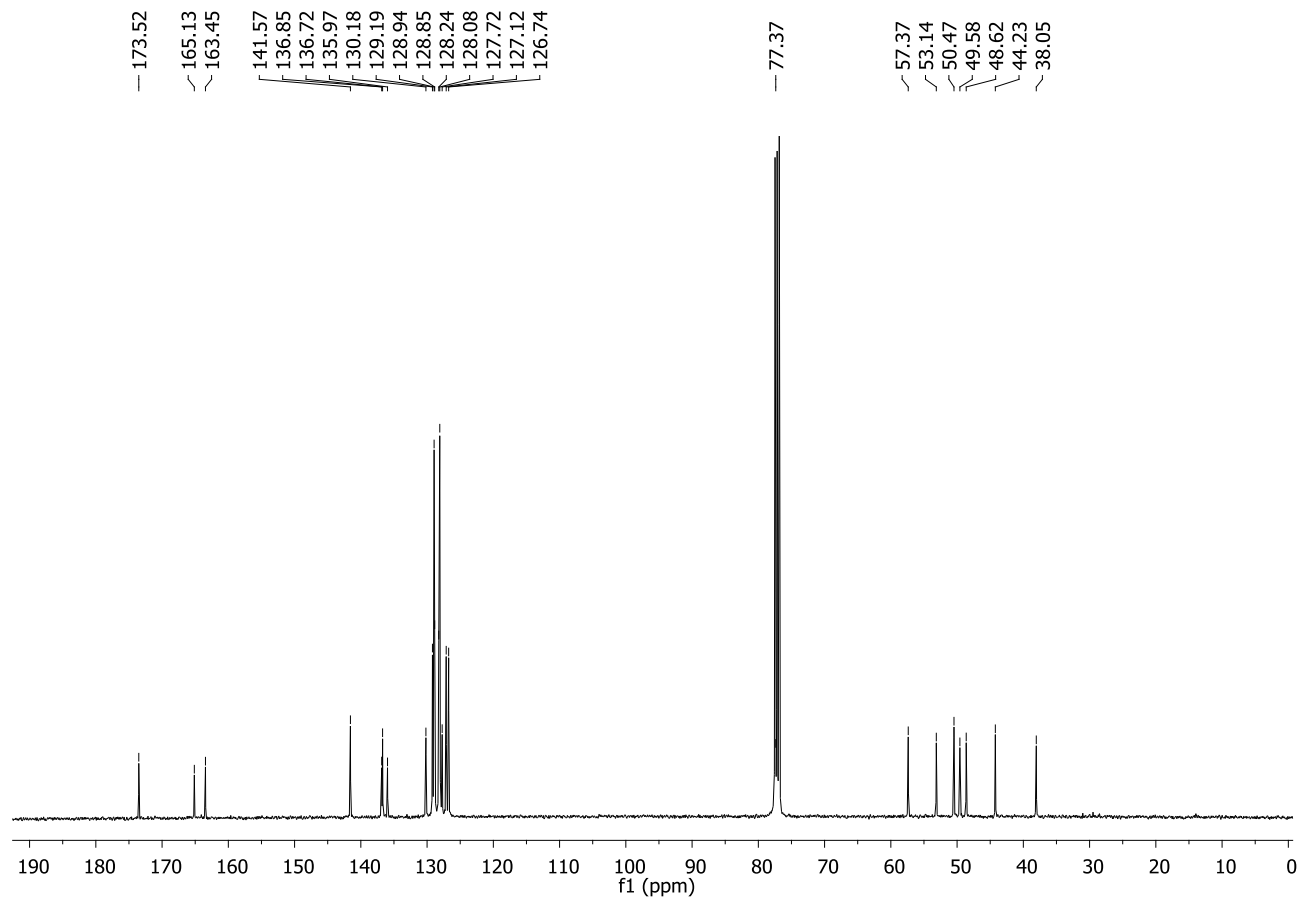
4a (^{13}C NMR, 100 MHz, CDCl_3 , 298K)



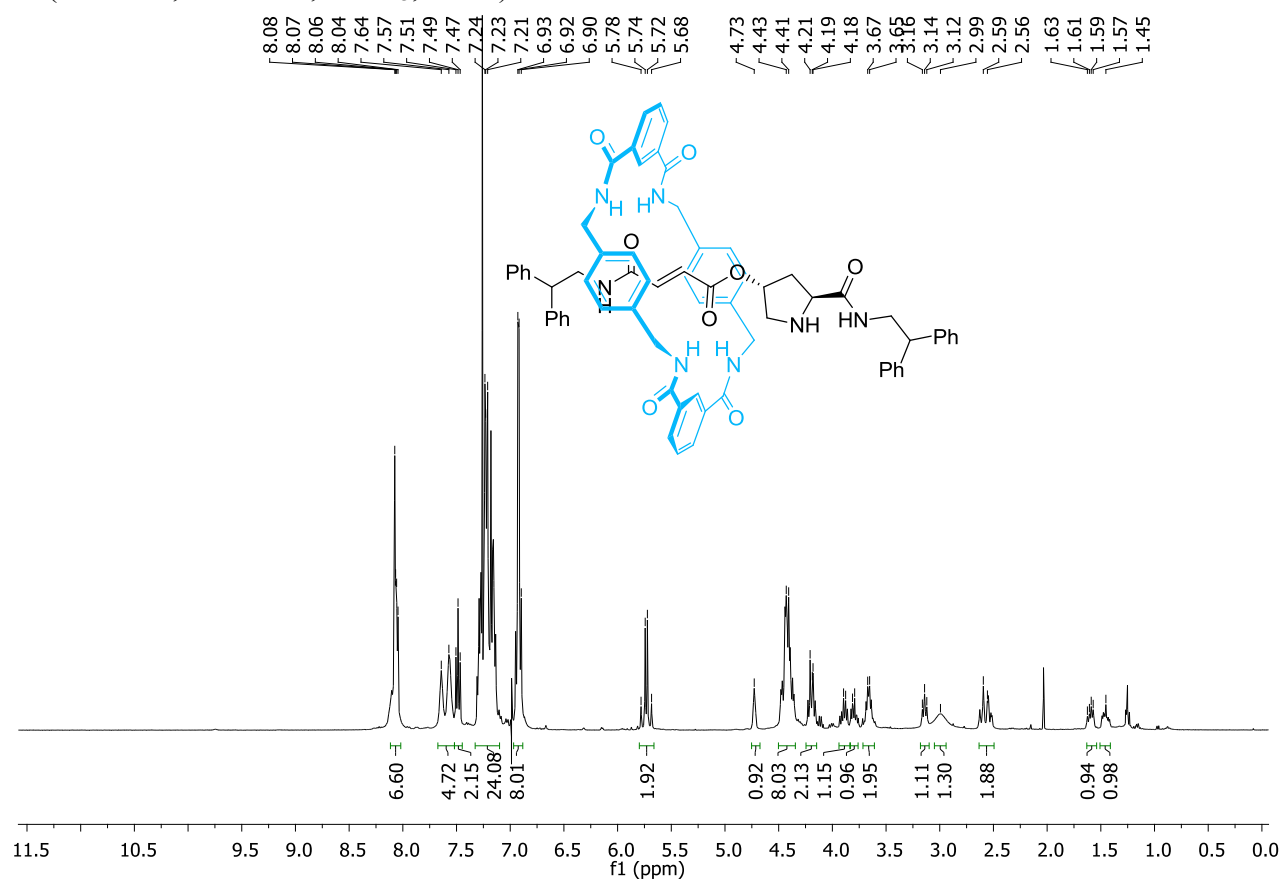
4b (^1H NMR, 400 MHz, CDCl_3 , 298K)



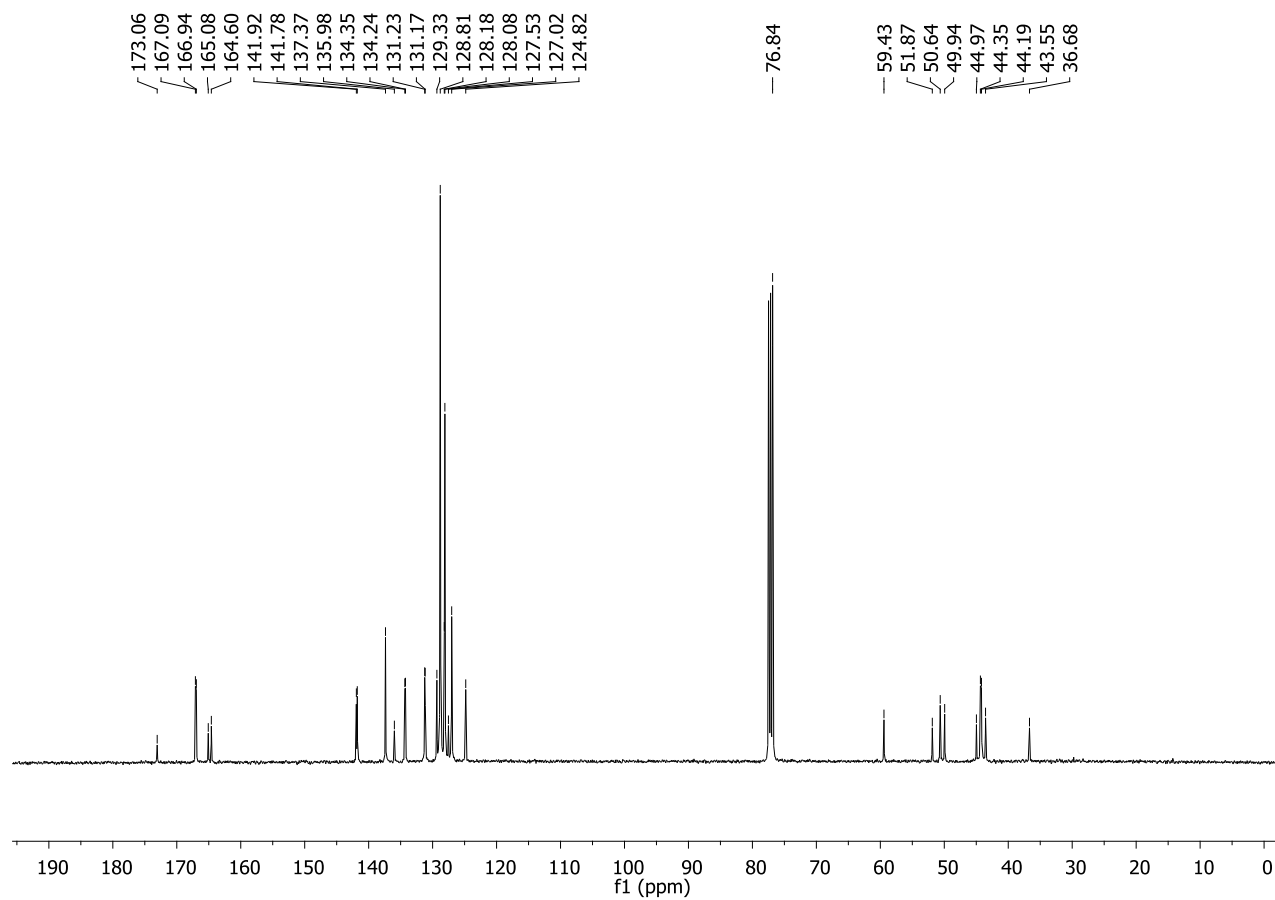
4b (^{13}C NMR, 100 MHz, CDCl_3 , 298K)



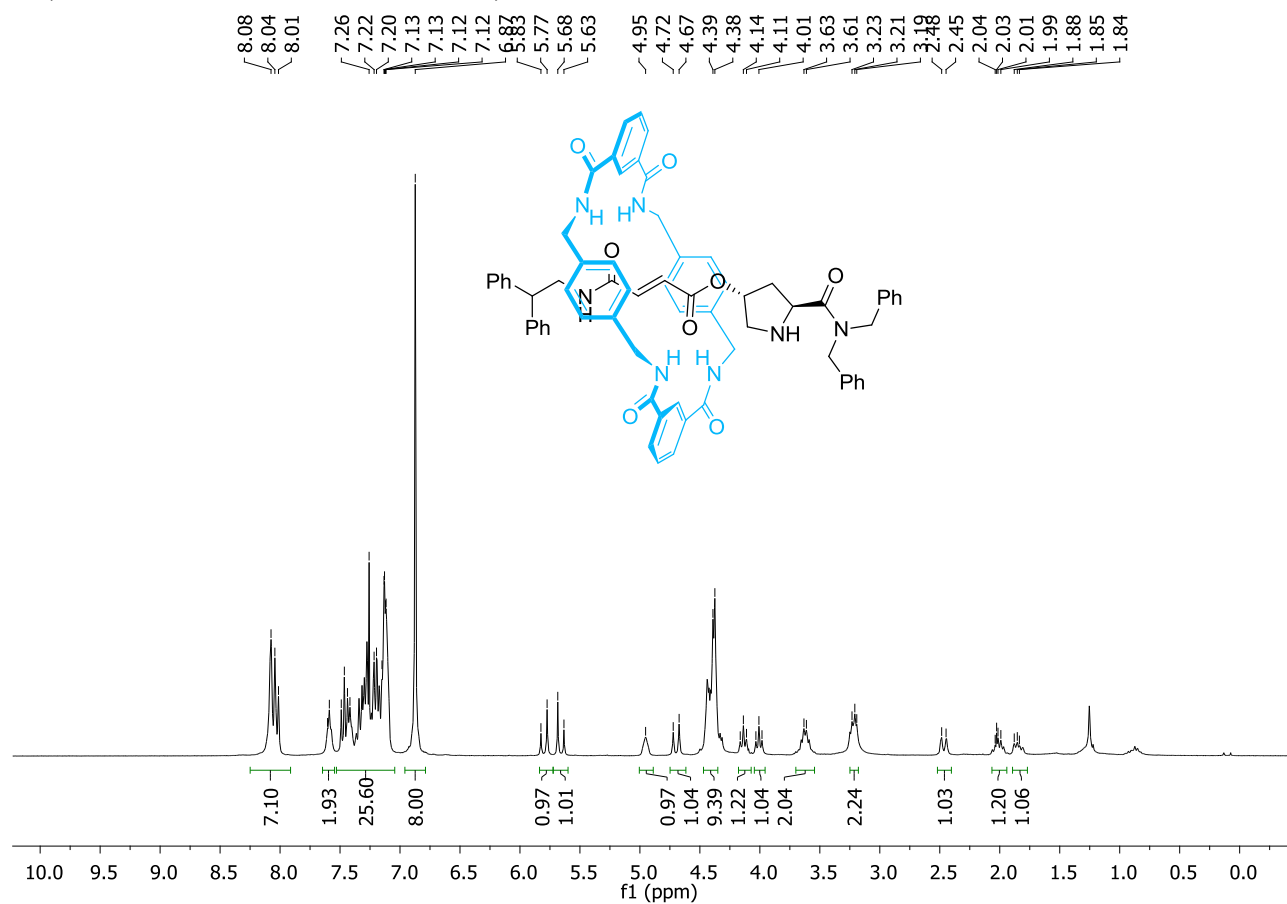
6a (^1H NMR, 400 MHz, CDCl_3 , 298K)



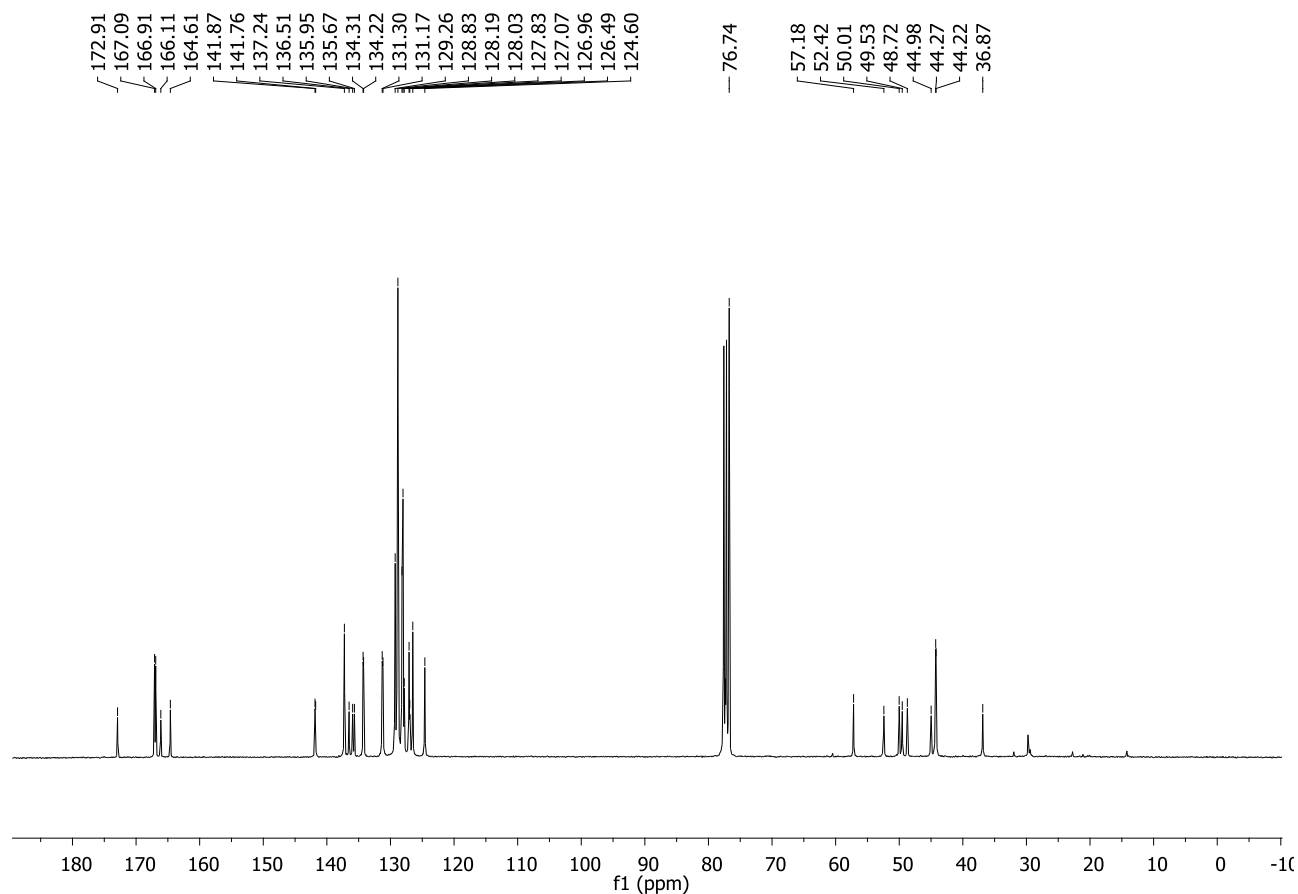
6a (^{13}C NMR, 100 MHz, CDCl_3 , 298K)



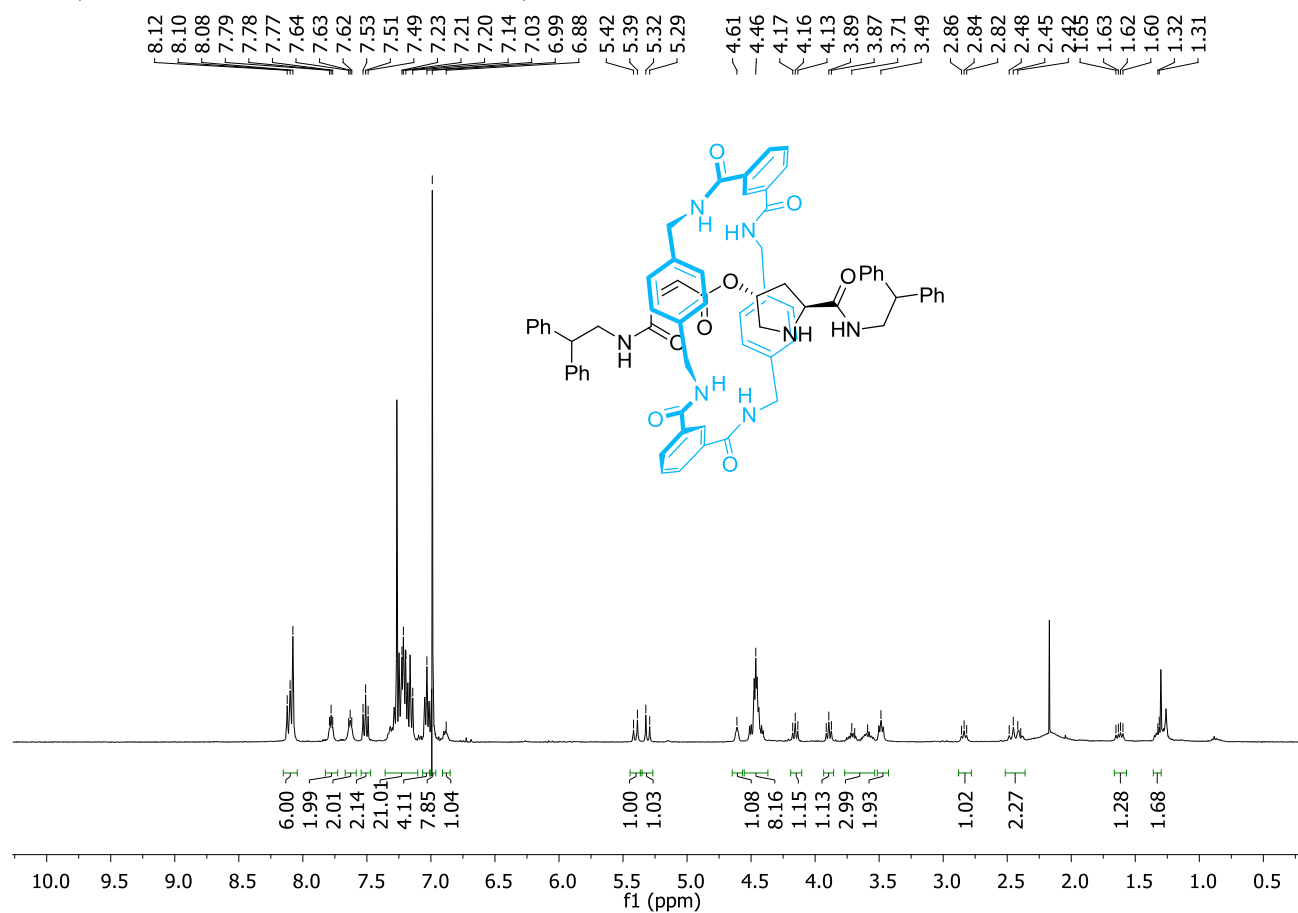
6b (^1H NMR, 300 MHz, CDCl_3 , 298K)



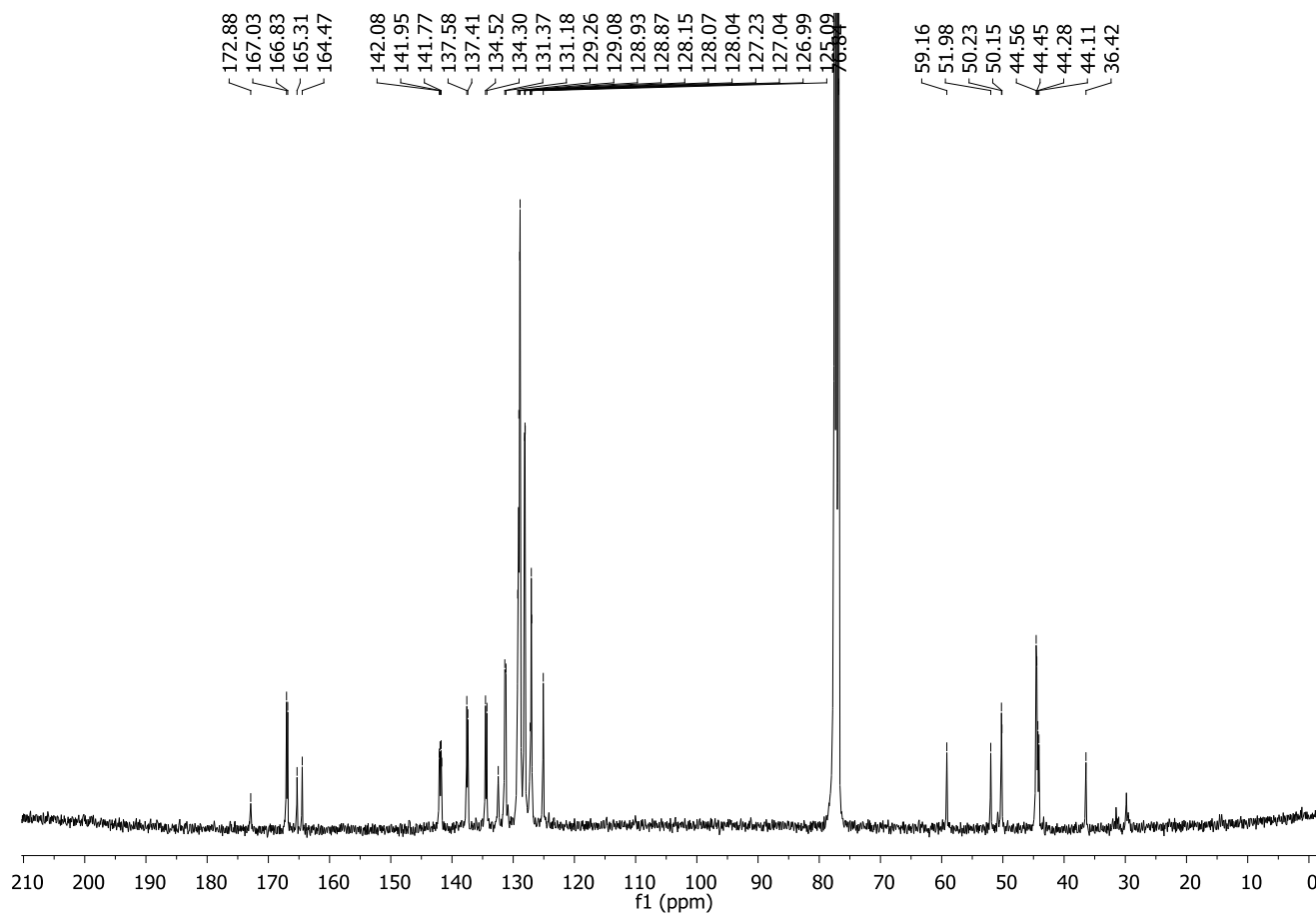
6b (^{13}C NMR, 75 MHz, CDCl_3 , 298K)



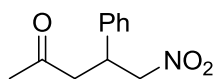
Z-6a (^1H NMR, 400 MHz, CDCl_3 , 298K)



Z-6a (^{13}C NMR, 101 MHz, CDCl_3 , 298K)

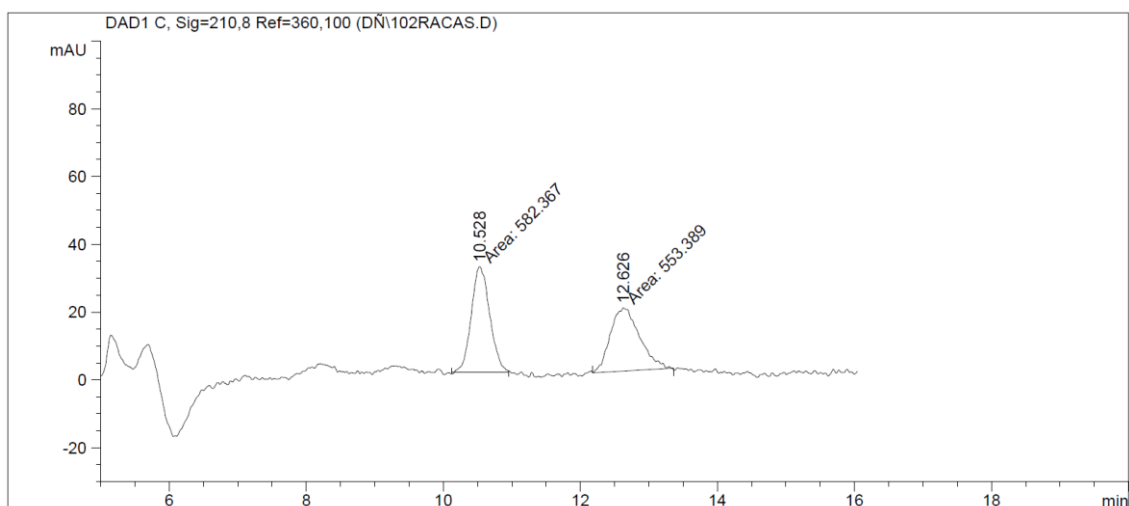


11. Copies of HPLC Traces of Synthesized Compounds



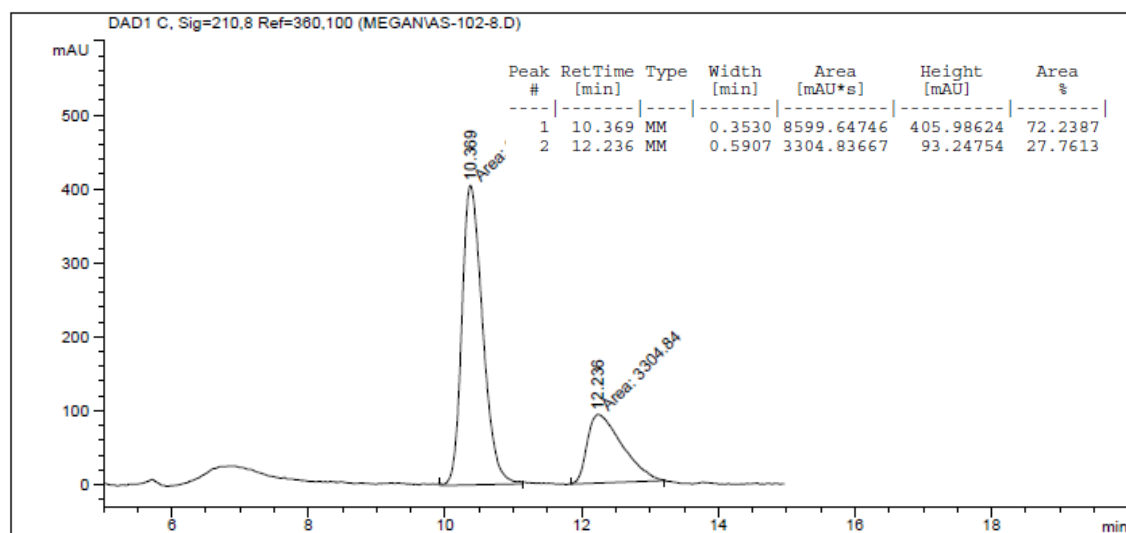
9a

Racemate



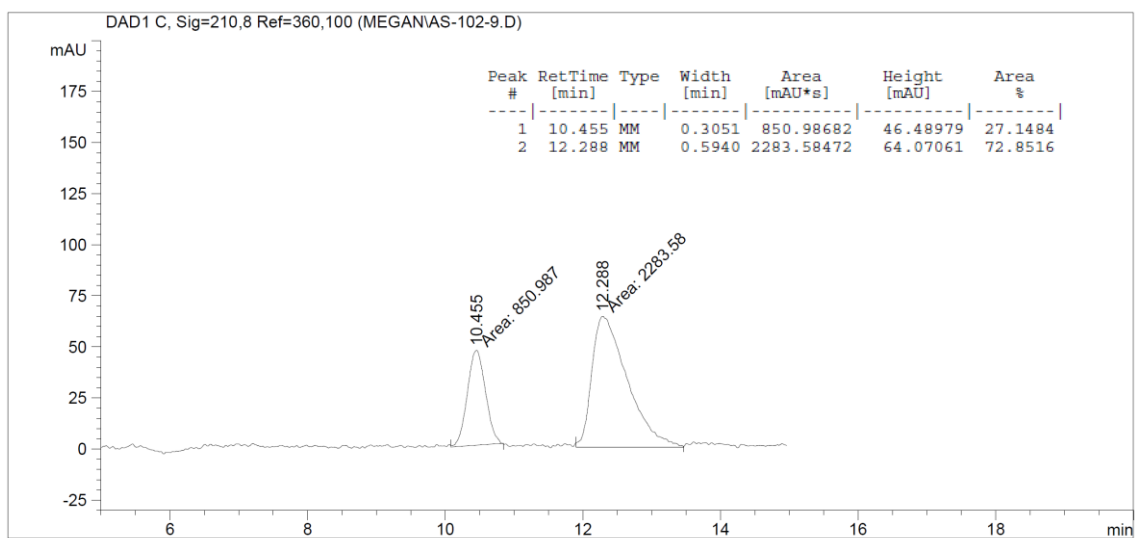
Employing thread 4b as catalyst

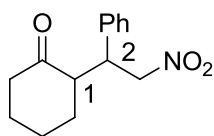
(S)-9a



Employing rotaxane 6b as catalyst

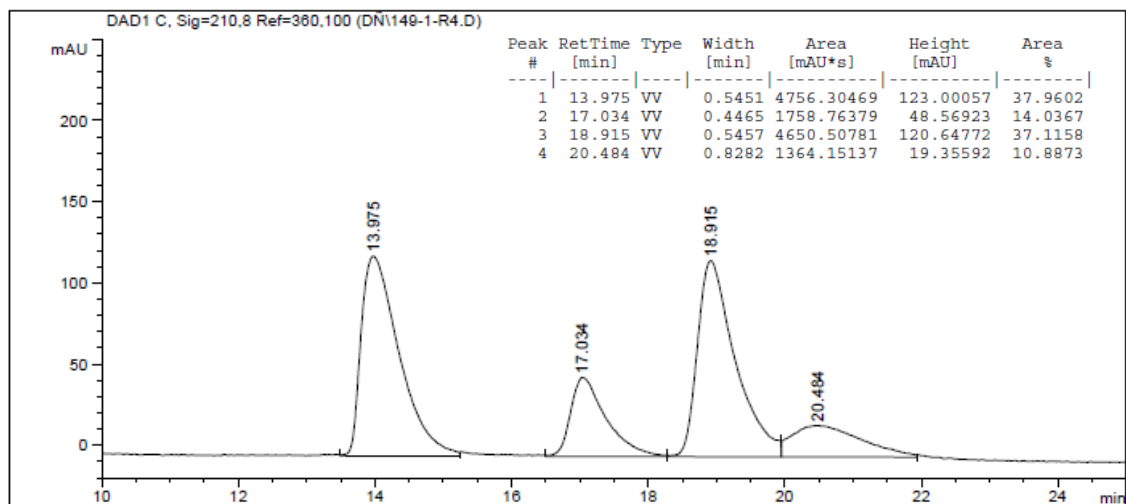
(*R*)-9a





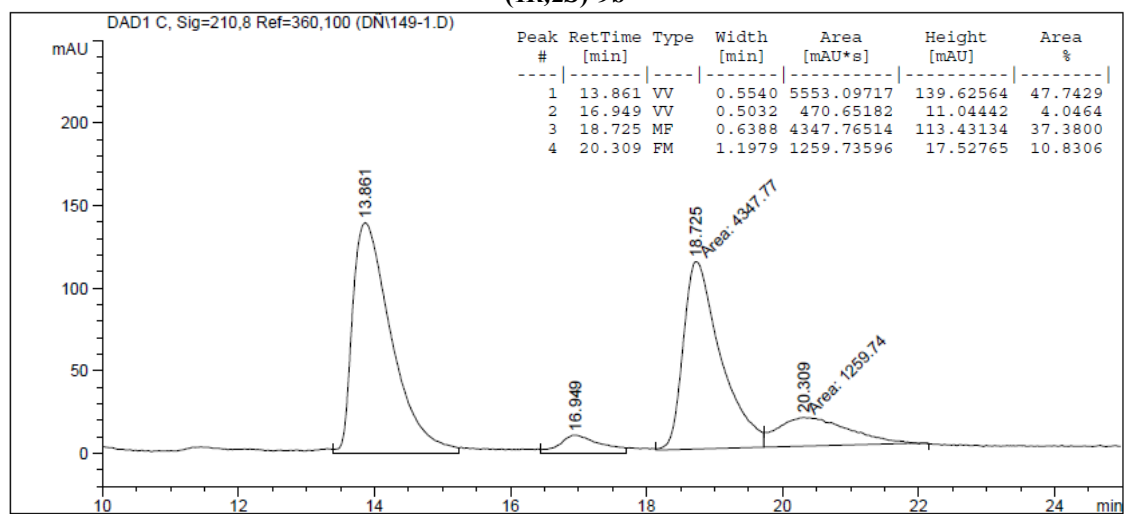
9b

Racemate



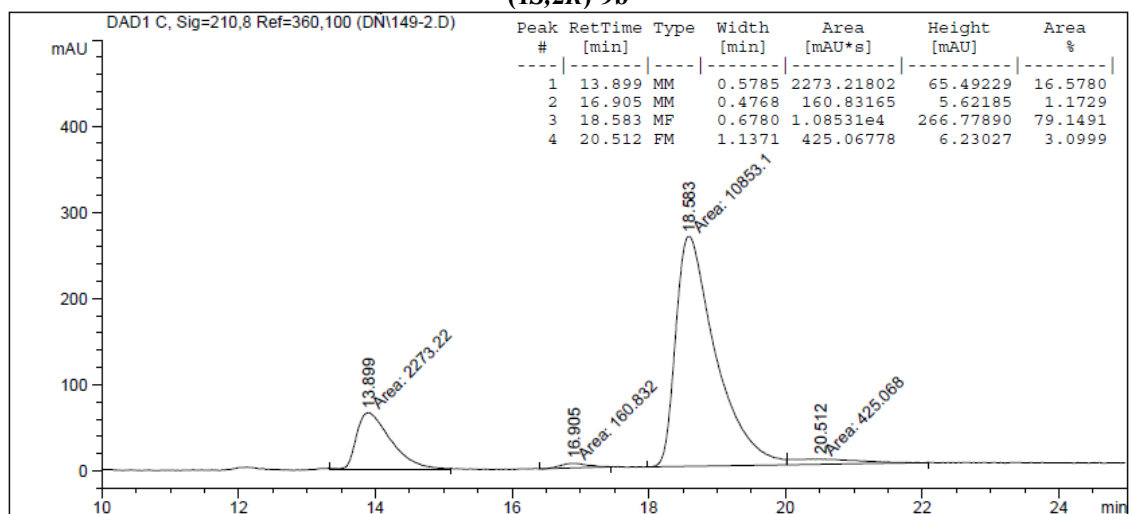
Employing thread 4b as catalyst

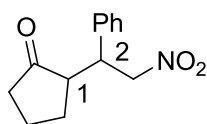
(1*R*,2*S*)-9b



Employing rotaxane 6b as catalyst

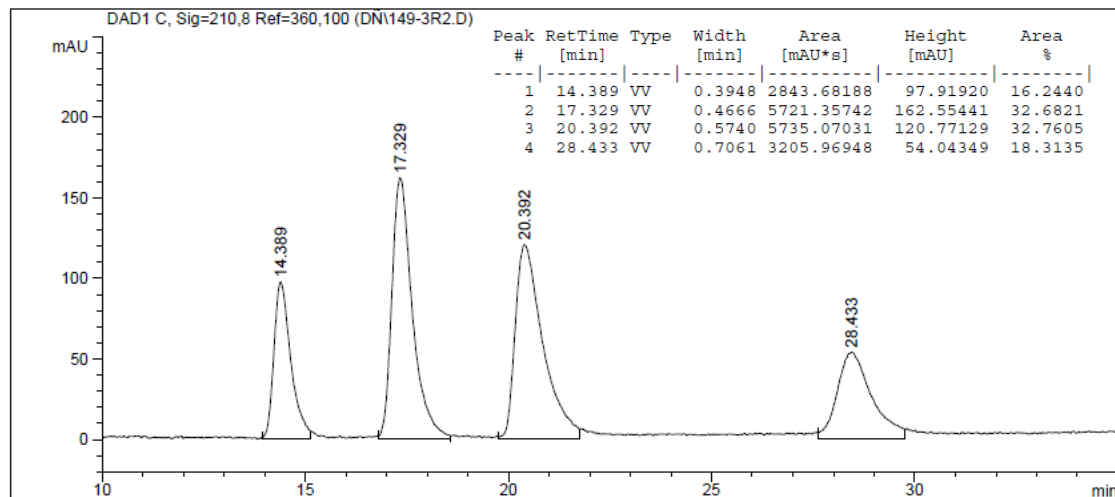
(1*S*,2*R*)-9b





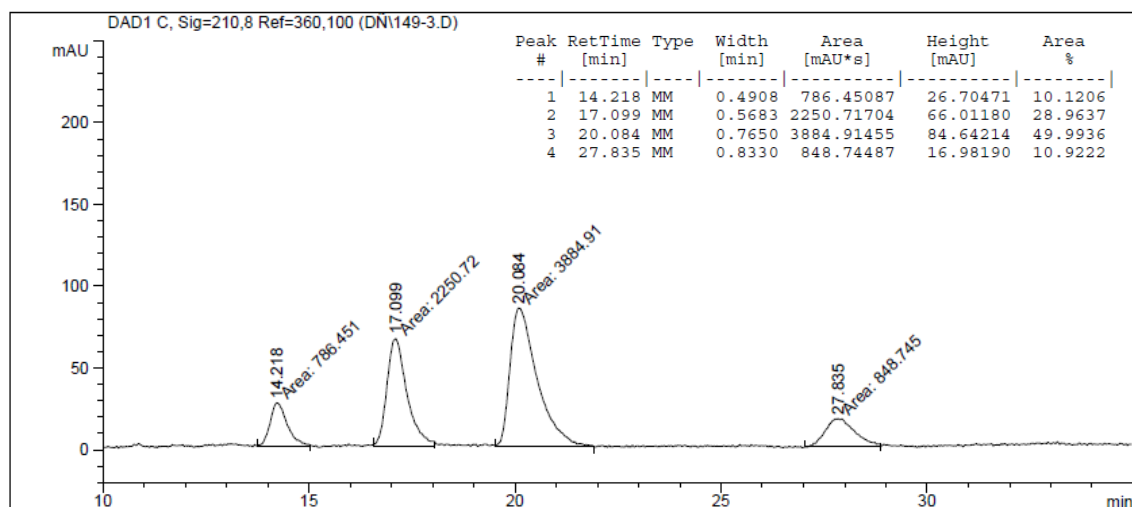
9c

Racemate



Employing thread 4b as catalyst

(1*R*,2*S*)-9c



Employing rotaxane 6b as catalyst

(1*S*,2*R*)-9c

