Electronic Supplementary Material (ESI) for Chemical Science.

Effect of the Enamine Pyramidalization Direction on the Reactivity of Secondary Amine Organocatalysts

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Supporting Information

1. General Aspects and Materials

Reagents and materials were of the highest commercially available grade and used without further purification. Reactions were monitored by thin layer chromatography using Merck silica gel 60 F254 aluminium sheets. Visualization of the compounds was achieved by UV-Vis or $KMnO_4$. Flash chromatography and plug filtrations were performed using silica gel 60 (particle size 0.040 – 0.063 mm, 200 – 400 mesh) manufactured by Fluka. Solvents for extraction and chromatography were of technical quality and distilled before use. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 400, a Bruker AV III 400 (400 MHz/100 MHz) or a Bruker AV III 600 (600 MHz/150 MHz). All spectra were recorded at 25 °C, unless stated otherwise. Chemical shifts (δ) are reported in parts per million (ppm) relative to the signal of tetramethylsilane (TMS) using the residual solvent signals. SFC analyses were performed on an analytical SFC with a diode array detector ACQUITY-UPLC-PDA from Waters using chiral stationary phase columns (Trefoil, AS, AD, IA, Whelk, IC, OD, OJ) (150 mm x 30 mm) from Daicel or Waters under the reported conditions. HPLC analyses were performed on an analytical Ultimate 3000 HPLC system from Dionex with a diode array detector and chiral stationary phase columns (Daicel AD-H, Daicel AS-H, AY-H, OD-H or Daicel OJ-H). High-resolution electron ionization (HR-EI) mass spectra were measured on a Waters Micromass AutoSpec Ultima spectrometer. High-resolution MALDI spectra were acquired on a Bruker solariX 94 (ESI/MALDI-FT-ICR) and a Bruker Ultra-Flex II (MALDI-TOF) spectrometer. In-situ FT-IR spectroscopy was carried out on a ReactIR R4000 (SiComb probe) with a spectral range of 4000–650 cm^{-1}.

2. Synthesis and Analytical Data of the Peptides

2.1. General Protocols for Solid Phase Peptide Synthesis

Peptides were prepared on solid phase using Rink Amide resin. The general protocol for Fmoc/*t*Bu peptide synthesis was followed according to the general procedures below.

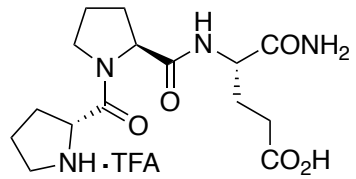
General procedure for peptide couplings: *i*Pr_2NEt (6 equiv.) was added to a solution of Fmoc-Xaa-OH (3 equiv.) and HATU (3 equiv.) in DMF. The solution of the activated amino acid (≈ 100 mM) was added to the amino-functionalized resin (preswollen in CH_2Cl_2) and the mixture was agitated for 1 h before washing with DMF (3 ×) and CH_2Cl_2 (3 ×).

General procedure for Fmoc-deprotections: A solution of 20% piperidine in DMF was added to the resin (preswollen in CH_2Cl_2) and the reaction mixture was agitated for 10 min, drained and the piperidine treatment was repeated for 10 min. Finally, the resin was washed with DMF (3 ×) and CH_2Cl_2 (3 ×). The couplings as well as the Fmoc-deprotections were monitored by qualitative Kaiser (primary amines),[1] and chloranil tests (secondary amines).[2]

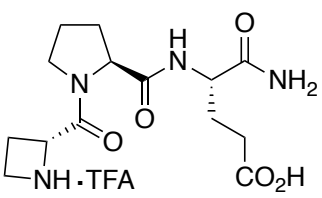
General procedure for side chain deprotection and cleavage of the peptides from the solid support: The peptides were side-chain deprotected and cleaved from the resin by shaking in a mixture of TFA/TIS/H_2O (95:2.5:2.5) for 1 h and a second time for 30 min. Pooling of the filtrates and removal of all volatiles under reduced pressure followed by precipitation and thorough washing with Et_2O afforded the peptides as their TFA-salts. The peptides were redissolved in MeCN/H_2O 1:1, dried by lyophilisation and used without further purification.

2.2. Analytical Data of Peptides

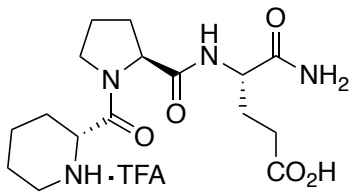
TFA·H-DPro-Pro-Glu-NH₂ (1): The peptide was synthesized according to the general procedures for solid phase peptide synthesis. The analytical data is in agreement with the previously published data.[3,4]



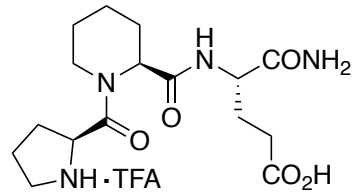
TFA·H-DAze-Pro-Glu-NH₂ (1a): The peptide was synthesized according to the general procedures for solid phase peptide synthesis. Only the signals of the *trans* isomer are reported (*trans*/*cis* amide bond ratio: 18:1). ^{1}H NMR (600 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 8.76 (d, J = 7.2 Hz, 1H), 7.08 (s, 1H), 6.34 (s, 1H), 5.50 – 5.38 (m, 1H), 4.48 (dd, J = 8.8, 4.0 Hz, 1H), 4.38 (td, J = 7.5, 3.1 Hz, 1H), 4.29 (ddd, J = 10.4, 9.4, 7.8 Hz, 1H), 3.97 (td, J = 10.2, 6.2 Hz, 1H), 3.73 (dt, J = 9.8, 6.1 Hz, 1H), 3.34 (dt, J = 9.8, 7.5 Hz, 1H), 2.97 – 2.88 (m, 1H), 2.64 – 2.40 (m, 3H), 2.32 – 2.23 (m, 1H), 2.22 – 2.09 (m, 2H), 2.09 – 2.02 (m, 2H), 1.98 (ddt, J = 14.4, 10.5, 3.6 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 178.4, 174.5, 171.1, 167.5, 61.7, 58.1, 53.3, 46.9, 43.4, 30.4, 29.4, 25.4, 24.7, 22.5. **HRMS** (MALDI): *m/z* calcd. for $[M + Na]^+$ $C_{14}H_{22}N_4NaO_5^+$: 349.1482; found: 349.1482.



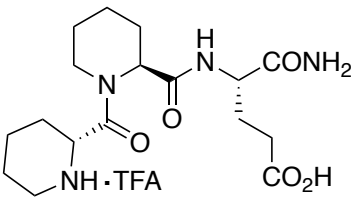
TFA·H-DPip-Pro-Glu-NH₂ (1b): The peptide was synthesized according to the general procedures for solid phase peptide synthesis. Only the signals of the *trans* isomer are reported (*trans*/*cis* amide bond ratio: 25:1). ^{1}H NMR (600 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 8.43 (d, J = 7.4 Hz, 1H), 7.08 (s, 1H), 6.34 (s, 1H), 4.37 (dq, J = 7.9, 3.7 Hz, 2H), 4.14 (dd, J = 11.7, 3.1 Hz, 1H), 3.91 (ddd, J = 9.8, 7.5, 4.4 Hz, 1H), 3.49 – 3.40 (m, 2H), 3.10 (td, J = 12.9, 3.3 Hz, 1H), 2.49 – 2.33 (m, 2H), 2.31 – 1.97 (m, 8H), 1.95 – 1.86 (m, 1H), 1.82 – 1.58 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 178.0, 175.0, 171.7, 169.1, 62.1, 57.1, 53.6, 47.5, 43.9, 31.4, 29.5, 25.9, 25.6, 24.7, 21.9, 21.9. **HRMS** (MALDI): *m/z* calcd. for $[M + Na]^+$ $C_{16}H_{26}N_4NaO_5^+$: 377.1795; found: 377.1798.



TFA·H-DPro-Pip-Glu-NH₂ (2): The peptide was synthesized according to the general procedures for solid phase peptide synthesis. The analytical data is in agreement with the previously published data.[4]

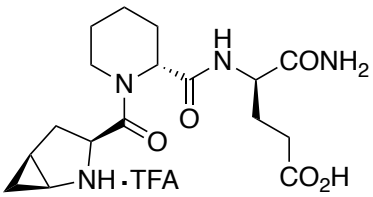


TFA·H-DAze-Pip-Glu-NH₂ (2a): The peptide was synthesized according to the general procedures for solid phase peptide synthesis. Only the signals of the *trans* isomer are reported (*trans*/*cis* amide bond ratio: 20:1). **^{1}H NMR** (600 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 8.41 (d, *J* = 6.5 Hz, 1H), 7.03 (s, 1H), 6.16 (s, 1H), 5.72 – 5.56 (m, 1H), 5.23 – 5.12 (m, 1H), 4.34 (ddd, *J* = 7.8, 6.5, 3.3 Hz, 1H), 4.29 (ddd, *J* = 10.4, 9.5, 7.6 Hz, 1H), 4.02 – 3.95 (m, 1H), 3.41 – 3.37 (m, 1H), 3.08 (ddd, *J* = 13.7, 12.5, 2.9 Hz, 1H), 2.94 (dtd, *J* = 11.9, 9.6, 6.3 Hz, 1H), 2.62 – 2.46 (m, 4H), 2.14 (dtd, *J* = 15.2, 7.6, 2.9 Hz, 1H), 1.97 (ddt, *J* = 15.1, 9.8, 3.0 Hz, 1H), 1.82 – 1.67 (m, 2H), 1.60 – 1.33 (m, 3H).**^{13}C NMR** (151 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 178.6, 174.2, 169.8, 168.2, 57.6, 54.1, 54.0, 43.7, 43.1, 30.3, 25.3, 25.2, 24.9, 23.0, 20.4. **HRMS** (MALDI): *m/z* calcd. for $[M + Na]^+$ $C_{15}H_{24}N_4NaO_5^+$: 363.1639; found: 363.1642.



TFA·H-DPip-Pip-Glu-NH₂ (2b): The peptide was synthesized according to the general procedures for solid phase peptide synthesis. Only the signals of the *trans* isomer are reported (*trans*/*cis* amide bond ratio: 30:1). **^{1}H NMR** (600 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 8.03 (d, *J* = 6.8 Hz, 1H), 7.15 (s, 1H), 6.14 (s, 1H), 5.21 – 5.04 (m, 1H), 4.42 (dd, *J* = 11.5, 3.3 Hz, 1H), 4.33 (ddd, *J* = 8.1, 6.7, 3.8 Hz, 1H), 3.69 (d, *J* = 13.7 Hz, 1H), 3.54 (d, *J* = 12.9 Hz, 1H), 3.12 (tt, *J* = 12.5, 3.4 Hz, 2H), 2.61 – 2.36 (m, 3H), 2.16 – 1.35 (m, 13H).**^{13}C NMR** (151 MHz, $CDCl_3/CD_3OH$ 9:1) δ = 178.8, 174.6, 170.2, 169.6, 55.9, 54.3, 53.8, 44.0, 43.9, 31.2, 26.9, 25.5, 25.3, 25.0, 22.0, 21.8, 20.3. **HRMS** (MALDI): *m/z* calcd. for $[M + H]^+$ $C_{17}H_{29}N_4O_5^+$: 369.2132; found: 369.2130.

TFA·H-MetPro-DPip-DGlu-NH₂ (2c): The peptide was synthesized according to the general procedures for solid phase peptide synthesis. Only the signals of the *trans* isomer are reported**.** **^{1}H NMR** (600 MHz, $CDCl_3/CD_3OH$ 9:1) 8.35 (d, *J* = 6.6 Hz, 1H), 6.95 (s, 1H), 6.13 (s, 1H), 5.15 (dd, *J* = 11.6, 4.1 Hz, 1H), 5.04 – 4.89 (m, 1H), 4.24 (ddd, *J* = 8.0, 6.6,



3.3 Hz, 1H, e-a), 3.53 – 3.47 (m, 1H, solvent suppr.) 3.42 (ddd, *J* = 6.8, 5.8, 2.7 Hz, 1H, solvent suppr.), 3.02 – 2.91 (m, 1H), 2.86 – 2.80 (m, 1H), 2.54 – 2.34 (m, 3H), 2.06 – 1.99 (m, 1H), 1.96 – 1.91 (m, 1H), 1.90 – 1.83 (m, 1H), 1.82 – 1.78 (m, 1H), 1.73 – 1.66 (m, 2H), 1.47 – 1.33 (m, 3H), 0.92 (ddd, *J* = 8.7, 7.1, 1.3 Hz, 1H), 0.86 (ddd, *J* = 7.5, 5.3, 2.7 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$/CD_3OH 9:1) δ = 178.7, 174.3, 170.6, 169.7, 60.9, 54.2, 53.9, 43.8, 37.7, 32.0, 30.5, 25.3, 24.8, 24.7, 20.2, 18.2, 11.2. **HRMS** (ESI): *m/z* calcd. for $[M + H]^+$ $C_{17}H_{27}N_4O_5^+$: 367.1976; found: 367.1974.

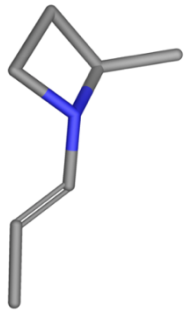
3. Computational Analysis of the Enamines

General Procedure: Conformational searches (10,000 steps) were performed using MacroModel 11.0 with the OPLS3e force field[5] in $CHCl_3$ or DMSO and a cutoff of 21 kJ/mol. Jaguar[6] was used to perform geometry optimizations of all obtained conformers at the M06-2X-D3/6-31+G** level of theory.[7] Solvation corrections were performed on gas-phase geometries using a PBF implicit solvent model for $CHCl_3$ or DMSO. Frequency calculations on the optimized structures yielded no imaginary frequencies, indicating stationary points on the potential energy surface. All energies are listed in kcal/mol relative to the conformation with the lowest total free energy for each derivative. The population of the structures was calculated according to the Boltzmann distribution (only structures with a population of >3% are listed). Positive pyramidalization Δ refers to an *endo*, negative to an *exo* pyramidalized enamine nitrogen. To determine the degree of N pyramidalization (Δ), the Boltzmann weighted average over the absolute values of all obtained structures was calculated.

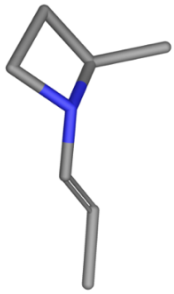
Conformational Analysis of 3a, 3 and 3b in $CHCl_3$:

	Total Free Energy (au)	Relative Energy (kcal/mol)	Population (%)	Pyramidalization Δ (Å)
3a I	-328.981568	0.00	68.5	0.415
3a II	-328.980833	0.46	31.5	0.423
3 I	-368.277321	0.00	35.8	0.212
3 II	-368.277222	0.06	32.3	0.230
3 III	-368.276650	0.42	17.6	-0.270
3 IV	-368.276169	0.72	10.6	0.247
3 V	-368.275100	1.35	3.4	0.259
3b I	-407.548874	0.00	55.0	-0.322
3b II	-407.547919	0.60	20.0	0.358
3b III	-407.547680	0.75	15.5	-0.268
3b IV	-407.546587	1.44	4.9	-0.324
3c I	-406.333674	0.00	71.3	0.241
3c II	-406.332816	0.54	28.7	0.294

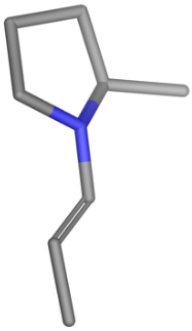
3a I:



3a II:



3 I:



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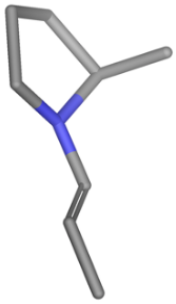
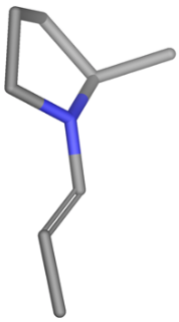
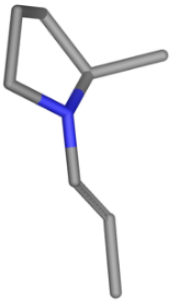


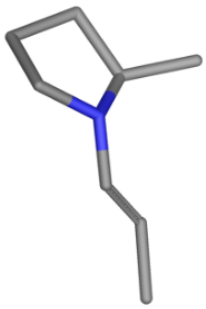
3 III:



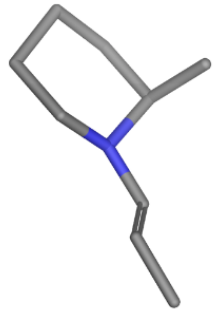
3 IV:



3 V:



3b I:



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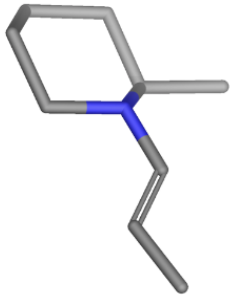
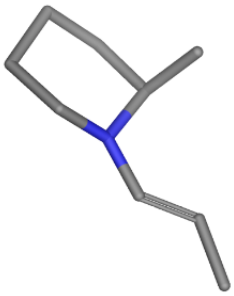
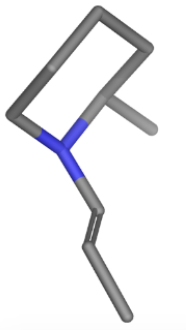


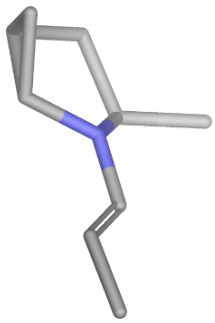
3b III:



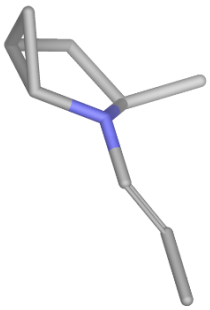
3b IV:



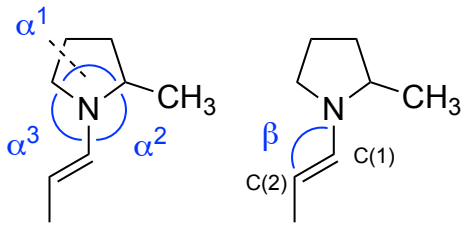
3c I:



3c II:



Distances and angles found in the lowest energy structures of **3a**, **3** and **3b**:



$CHCl_3$:

	d(N–C(1))	d(C(1)–C(2))	α^1	α^2	α^3	β
3a I	1.39	1.34	91.4	121.4	122.2	125.7
3a II	1.40	1.34	91.4	122.2	120.6	126.2
3 I	1.38	1.35	112.4	120.6	120.5	126.7
3 II	1.38	1.35	111.5	121.1	119.7	126.7
3 III	1.38	1.35	109.9	119.7	119.9	126.7
3 IV	1.38	1.35	111.3	120.8	119.1	127.6
3 V	1.38	1.35	111.1	119.9	119.4	127.7
3b I	1.40	1.34	115.4	113.8	116.3	128.2
3b II	1.40	1.34	113.0	114.8	114.5	127.8
3b III	1.39	1.35	115.4	118.4	116.0	128.7
3b IV	1.40	1.34	111.0	117.2	117.2	128.5

Coordinates of the Calculated Lowest Energy Structures:

3a I:

N	-0.13380	-0.08030	0.28430
C	-0.42090	1.21730	-0.37440
C	-1.70970	0.58500	-0.94580
C	-1.08110	-0.78040	-0.59820
C	-0.52640	2.41310	0.54870
C	1.17290	-0.52570	0.47140
C	1.60690	-1.78130	0.28410
C	3.01210	-2.22700	0.57930
H	0.30450	1.41220	-1.18060
H	-1.93170	0.77790	-1.99570
H	-2.58370	0.81350	-0.32960
H	-0.57180	-1.24080	-1.45900
H	-1.70630	-1.53100	-0.10590
H	-0.83310	3.30170	-0.01330
H	-1.26400	2.21830	1.33370
H	0.43650	2.62940	1.02400
H	1.85220	0.24810	0.83590
H	0.90570	-2.53710	-0.07020
H	3.03820	-2.98910	1.36740
H	3.48830	-2.66740	-0.30400
H	3.62940	-1.38520	0.90900

3a II:

N	-0.12000	-0.05340	0.27640
C	-0.42240	1.20520	-0.43690
C	-1.69700	0.53590	-0.99650
C	-1.06030	-0.80790	-0.58200
C	-0.56790	2.44340	0.42730
C	1.18650	-0.50520	0.46580
C	2.29960	0.24230	0.40610
C	3.67520	-0.29170	0.69800
H	0.31530	1.37680	-1.23950
H	-1.90820	0.67850	-2.05660
H	-2.58130	0.78240	-0.40230
H	-0.55260	-1.30320	-1.42180
H	-1.68580	-1.53300	-0.05390
H	-1.30210	2.26130	1.21870
H	0.38250	2.71850	0.89600
H	-0.90760	3.28980	-0.17910
H	1.24770	-1.56720	0.71420
H	2.22010	1.30140	0.16150
H	3.64390	-1.36640	0.90270
H	4.35520	-0.12950	-0.14580
H	4.12460	0.20120	1.56820

3 I:

N	-0.17810	2.37860	-0.76940
C	-1.62590	2.13850	-0.64810
C	-1.86390	0.94000	-1.58590
C	0.47590	1.40210	-1.62650
C	-2.02520	1.85730	0.79960

C	0.33480	3.65190	-0.63930
C	1.53110	4.08690	-1.08280
C	2.02930	5.48820	-0.85170
C	-0.50460	0.22960	-1.62920
H	-2.17930	3.01720	-1.00660
H	-2.12290	1.29860	-2.58820
H	-2.67810	0.29940	-1.23570
H	0.62150	1.80600	-2.64450
H	1.46380	1.13570	-1.23270
H	-1.54700	0.93760	1.15530
H	-1.70860	2.67700	1.45310
H	-3.11140	1.74640	0.88660
H	-0.32170	4.33870	-0.10060
H	2.19000	3.40460	-1.61700
H	1.28440	6.08510	-0.31540
H	2.95260	5.50280	-0.26020
H	2.24950	6.00220	-1.79460
H	-0.35860	-0.38040	-0.73130
H	-0.38500	-0.41690	-2.50140

3 II:

N	-0.17880	2.37850	-0.75370
C	-1.62330	2.13430	-0.65510
C	-1.69670	0.62490	-0.88580
C	0.47060	1.40520	-1.62940
C	-2.21010	2.57410	0.67920
C	0.33810	3.65320	-0.64520
C	1.55300	4.06690	-1.05560
C	2.05100	5.47050	-0.84240
C	-0.63040	0.38030	-1.95840
H	-2.15780	2.64980	-1.47420
H	-1.43210	0.10950	0.04620
H	-2.69630	0.30100	-1.18710
H	0.85100	1.89450	-2.53860
H	1.33080	0.95150	-1.12030
H	-1.66130	2.10230	1.50150
H	-2.17270	3.65940	0.81270
H	-3.26070	2.27050	0.73620
H	-0.32270	4.36230	-0.14530
H	2.23090	3.36580	-1.53870
H	1.28670	6.08870	-0.36020
H	2.94530	5.49520	-0.20800
H	2.32110	5.95480	-1.78800
H	-1.04710	0.58990	-2.94890
H	-0.25650	-0.64600	-1.96580

3 III:

N	-0.27820	2.52020	-1.08650
C	-1.57660	2.08920	-0.55490
C	-1.91810	0.93960	-1.50710
C	0.49150	1.35890	-1.52200
C	-1.50600	1.64300	0.90860
C	0.37010	3.60290	-0.51990
C	1.69770	3.82150	-0.49280
C	2.30780	5.07790	0.06640

C	-0.56000	0.24760	-1.73790
H	-2.28760	2.91860	-0.64970
H	-2.30160	1.35000	-2.44650
H	-2.67300	0.26500	-1.09380
H	1.05090	1.60320	-2.43260
H	1.22970	1.06630	-0.75790
H	-0.82080	0.79610	1.03070
H	-2.49490	1.33580	1.26280
H	-1.15070	2.45790	1.54740
H	-0.30910	4.34940	-0.10250
H	2.37600	3.08110	-0.91210
H	2.85180	5.64550	-0.69820
H	1.53750	5.73580	0.48100
H	3.02440	4.85870	0.86640
H	-0.41050	-0.55760	-1.01350
H	-0.48990	-0.19740	-2.73270

3 IV:

N	-0.17690	2.37310	-0.74250
C	-1.62370	2.13640	-0.65830
C	-1.83720	0.86150	-1.50010
C	0.47030	1.40770	-1.63270
C	-2.07750	1.97740	0.79240
C	0.33700	3.65390	-0.64980
C	-0.31050	4.77480	-0.27980
C	0.37400	6.10950	-0.16220
C	-0.45390	0.19890	-1.53380
H	-2.15890	2.98390	-1.11330
H	-2.14070	1.13050	-2.51760
H	-2.61530	0.21960	-1.07740
H	0.51160	1.77590	-2.67190
H	1.49400	1.20560	-1.30110
H	-1.63880	1.07150	1.22550
H	-3.16850	1.89640	0.84610
H	-1.76240	2.83190	1.39860
H	1.40150	3.70840	-0.88780
H	-1.36790	4.73800	-0.02450
H	0.34700	6.49440	0.86450
H	1.42450	6.04020	-0.46260
H	-0.10350	6.86630	-0.79530
H	-0.26110	-0.34060	-0.60010
H	-0.33040	-0.49820	-2.36570

3 V:

N	-0.17220	2.37000	-0.73550
C	-1.62120	2.14220	-0.66000
C	-1.82560	0.82700	-1.42620
C	0.47070	1.40180	-1.63820
C	-2.13860	2.08640	0.77440
C	0.32940	3.65710	-0.64960
C	-0.33090	4.77700	-0.29660
C	0.34130	6.12050	-0.20580
C	-0.69220	0.83080	-2.45320
H	-2.13300	2.95820	-1.19940
H	-2.82280	0.76760	-1.86950

H	-1.70850	-0.02120	-0.73940
H	1.22800	1.89180	-2.25670
H	0.96390	0.60590	-1.06430
H	-1.65150	1.26580	1.31180
H	-1.93900	3.01600	1.31470
H	-3.22030	1.91160	0.77750
H	1.39380	3.72390	-0.88210
H	-1.38890	4.73710	-0.04660
H	1.39370	6.05330	-0.50060
H	-0.13960	6.85930	-0.85770
H	0.30810	6.52920	0.81160
H	-0.47530	-0.15750	-2.86590
H	-0.93510	1.50560	-3.28180

3b I:

N	1.29540	-1.57240	-1.98100
C	1.94660	-2.77700	-1.42640
C	2.85610	-3.40600	-2.48630
C	2.20010	-0.57220	-2.53860
C	2.68890	-2.49560	-0.11290
C	0.24420	-1.08860	-1.19930
C	-0.09920	0.19000	-0.96790
C	-1.32340	0.57190	-0.18070
C	3.12280	-1.18330	-3.59020
C	3.86590	-2.40040	-3.04240
H	1.13640	-3.48510	-1.21090
H	2.22920	-3.77340	-3.30850
H	3.36510	-4.27240	-2.04980
H	2.79380	-0.08470	-1.74350
H	1.59070	0.20980	-3.00190
H	3.52290	-1.80030	-0.25020
H	3.09240	-3.42590	0.29960
H	2.00920	-2.05940	0.62580
H	-0.36230	-1.88740	-0.76510
H	0.50500	1.00360	-1.36280
H	-1.06880	1.21520	0.66910
H	-2.04630	1.12460	-0.79260
H	-1.83000	-0.31580	0.21050
H	3.82440	-0.41660	-3.93490
H	2.51760	-1.48620	-4.45410
H	4.56280	-2.08550	-2.25520
H	4.47110	-2.86650	-3.82690

3b II:

N	1.52100	-1.39590	-1.55980
C	1.88920	-2.83120	-1.56970
C	3.41310	-2.97790	-1.56370
C	2.12000	-0.64430	-2.66080
C	1.29100	-3.59610	-0.39060
C	0.15610	-1.13880	-1.35500
C	-0.63600	-0.29780	-2.04080
C	-2.06610	-0.03800	-1.65290
C	3.63980	-0.76020	-2.66940
C	4.06830	-2.22280	-2.71580
H	1.50860	-3.28030	-2.50880

H	3.65640	-4.04510	-1.61490
H	3.79390	-2.59950	-0.60420
H	1.83310	0.40500	-2.54730
H	1.71270	-0.99190	-3.63020
H	1.51850	-3.08500	0.55220
H	1.73690	-4.59470	-0.35340
H	0.20890	-3.72430	-0.46920
H	-0.26840	-1.66640	-0.50340
H	-0.25940	0.24220	-2.90590
H	-2.74890	-0.25300	-2.48270
H	-2.36330	-0.66020	-0.80300
H	-2.22760	1.00940	-1.37220
H	4.03840	-0.28700	-1.76310
H	4.03180	-0.20570	-3.52870
H	5.15840	-2.31400	-2.66820
H	3.75030	-2.66720	-3.66930

3b III:

N	1.30520	-1.57230	-1.93730
C	1.96310	-2.79010	-1.44800
C	2.78080	-3.41900	-2.58510
C	2.19200	-0.57900	-2.54320
C	2.80740	-2.54850	-0.18810
C	0.22600	-1.06880	-1.21690
C	-0.43290	-1.62850	-0.18550
C	-1.66300	-1.00830	0.42140
C	2.98080	-1.18630	-3.69900
C	3.74690	-2.42390	-3.23160
H	1.16140	-3.49290	-1.19480
H	2.08340	-3.78380	-3.34930
H	3.32150	-4.28820	-2.19380
H	2.89300	-0.16270	-1.79780
H	1.57500	0.25220	-2.89860
H	3.67640	-1.91620	-0.39600
H	3.17480	-3.50070	0.20760
H	2.21350	-2.05950	0.58890
H	-0.12650	-0.11010	-1.60290
H	-0.09790	-2.57140	0.24220
H	-1.53210	-0.81600	1.49270
H	-1.90200	-0.05540	-0.06190
H	-2.54000	-1.65900	0.32110
H	3.66440	-0.43350	-4.10540
H	2.28140	-1.46640	-4.49710
H	4.52120	-2.12460	-2.51340
H	4.26680	-2.89640	-4.07150

3b IV:

N	1.27160	-1.57350	-1.96900
C	1.98120	-2.76270	-1.45070
C	2.99220	-2.35890	-0.36690
C	2.21380	-0.60430	-2.52790
C	1.04020	-3.86170	-0.97030
C	0.21970	-1.06960	-1.19780
C	-0.14530	0.21090	-1.01400
C	-1.39190	0.59500	-0.26400

C	3.22710	-0.11350	-1.48780
C	3.97630	-1.30800	-0.88950
H	2.54390	-3.15630	-2.31020
H	3.52920	-3.24870	-0.01700
H	2.43600	-1.95570	0.49220
H	1.65180	0.22190	-2.97220
H	2.75020	-1.10490	-3.34510
H	0.24610	-4.05040	-1.69990
H	1.61110	-4.78540	-0.83740
H	0.58150	-3.61720	-0.00680
H	-0.40180	-1.84630	-0.75500
H	0.44970	1.02520	-1.42220
H	-2.11280	1.11360	-0.90750
H	-1.89110	-0.28860	0.14640
H	-1.16760	1.27060	0.56960
H	2.70010	0.42630	-0.69170
H	3.92610	0.59010	-1.95320
H	4.64810	-0.97990	-0.08900
H	4.60650	-1.76370	-1.66630

3c I:

C	-1.93520	1.09550	-3.05590
C	-2.61110	-0.28820	-3.09570
C	-1.47900	-1.26310	-3.41630
C	-0.19820	-0.53490	-3.13690
N	-0.56380	0.76450	-2.63220
C	-0.58220	-1.71630	-2.28780
C	-2.62820	2.07760	-2.12410
C	0.39840	1.74280	-2.46560
C	1.73040	1.55980	-2.39960
C	2.69750	2.68800	-2.16510
H	-1.91670	1.51360	-4.07860
H	-3.40240	-0.31820	-3.85000
H	-3.06540	-0.51050	-2.12140
H	-1.56010	-1.89840	-4.29160
H	0.65620	-0.58080	-3.80960
H	-0.03560	-2.64500	-2.42580
H	-0.89760	-1.49910	-1.27070
H	-2.16490	3.06820	-2.14460
H	-2.60180	1.70000	-1.09600
H	-3.67350	2.19600	-2.42800
H	-0.00670	2.74900	-2.35410
H	2.14220	0.55550	-2.48460
H	3.26580	2.55290	-1.23690
H	3.43140	2.77110	-2.97520
H	2.17200	3.64600	-2.09490

3c II:

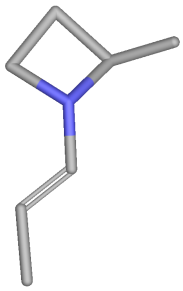
C	-1.92710	1.10380	-3.05450
C	-2.51420	-0.19760	-3.65290
C	-1.32680	-1.11760	-3.90610
C	-0.13130	-0.48200	-3.26470
N	-0.56320	0.75040	-2.63050
C	-0.68410	-1.75910	-2.69810
C	-2.77080	1.64380	-1.90450
C	0.38970	1.74860	-2.46870
C	0.20250	3.08000	-2.51140

C	1.31470	4.06310	-2.26610
H	-1.85900	1.86930	-3.84760
H	-3.05340	0.01830	-4.57920
H	-3.22910	-0.65090	-2.95530
H	-1.23540	-1.61460	-4.86600
H	0.84250	-0.46710	-3.74580
H	-1.20830	-1.68340	-1.74800
H	-0.11980	-2.67410	-2.85240
H	-2.86620	0.87790	-1.12740
H	-3.77290	1.89880	-2.26510
H	-2.33020	2.53650	-1.45410
H	1.38840	1.35880	-2.26370
H	-0.78360	3.49320	-2.71120
H	1.12220	4.68680	-1.38480
H	2.26710	3.54740	-2.10580
H	1.44290	4.74550	-3.11430

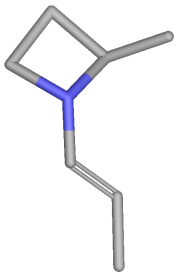
Conformational Analysis of 3a, 3 and 3b in DMSO:

	Total Free Energy (au)	Relative Energy (kcal/mol)	Population (%)	Pyramidalization Δ (Å)
3a I	-328.983517	0.00	67.7	0.425
3a II	-328.98282	0.44	32.3	0.433
3 I	-368.278907	0.00	35.7	0.217
3 II	-368.278887	0.01	34.9	0.242
3 III	-368.278129	0.49	15.6	-0.292
3 IV	-368.277689	0.76	9.8	0.268
3 V	-368.276681	1.40	3.4	0.280
3b I	-407.55068	0.00	54.7	-0.335
3b II	-407.549798	0.55	21.5	0.370
3b III	-407.549297	0.87	12.6	-0.280
3b IV	-407.548407	1.43	4.9	-0.334

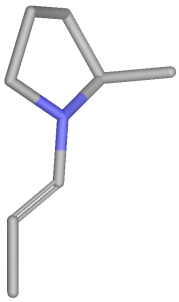
3a I:



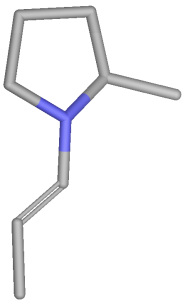
3a II:



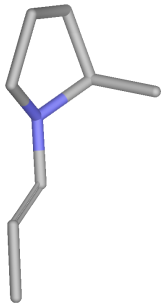
3 I:



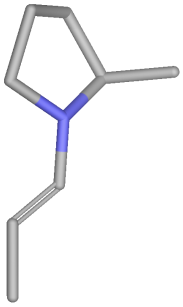
3 II:



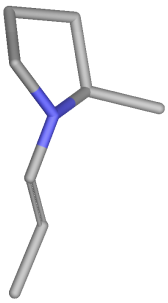
3 III:



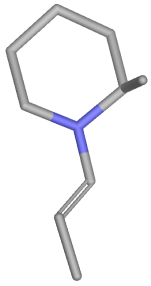
3 IV:



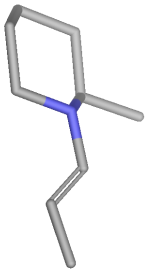
3 V:



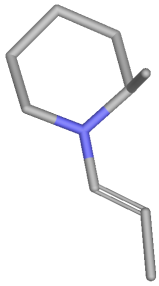
3b I:



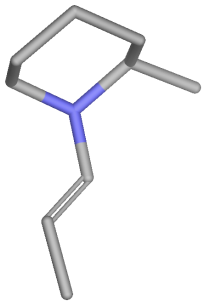
3b II:



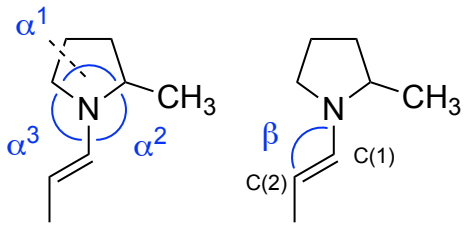
3b III:



3b IV:



Distances and angles found in the lowest energy structures of **3a**, **3** and **3b**:



DMSO:

	d(N–C(1))	d(C(1)–C(2))	α^1	α^2	α^3	β
3a I	1.40	1.34	91.2	120.9	121.8	125.6
3a II	1.40	1.34	91.1	121.8	120.1	126.1
3 I	1.38	1.35	112.2	120.5	120.5	126.5
3 II	1.38	1.35	111.2	120.7	119.6	126.6
3 III	1.39	1.35	109.4	119.1	119.4	126.6
3 IV	1.39	1.35	110.9	120.3	118.5	127.5
3 V	1.39	1.35	110.7	119.5	118.8	127.6
3b I	1.40	1.34	115.0	113.3	116.1	128.1
3b II	1.41	1.34	112.7	114.3	114.2	127.0
3b III	1.39	1.35	115.1	118.2	115.6	128.6
3b IV	1.40	1.34	110.8	116.8	116.9	128.5

Coordinates of the Calculated Lowest Energy Structures:

3a I:

N	-0.13900	-0.08220	0.29790
C	-0.42020	1.21570	-0.37050
C	-1.70540	0.58430	-0.95000
C	-1.08210	-0.78170	-0.59590
C	-0.52790	2.41750	0.54380
C	1.17240	-0.52630	0.47730
C	1.60660	-1.78110	0.28180
C	3.01460	-2.22590	0.56860
H	0.31230	1.40300	-1.17110
H	-1.91840	0.77640	-2.00200
H	-2.58440	0.81520	-0.34110
H	-0.56450	-1.24080	-1.45160
H	-1.71250	-1.53380	-0.11280
H	-0.82680	3.30210	-0.02840
H	-1.27440	2.23330	1.32330
H	0.43260	2.63390	1.02470
H	1.85330	0.24750	0.84080
H	0.90550	-2.53740	-0.07370
H	3.04520	-2.99090	1.35390
H	3.48570	-2.66480	-0.31830
H	3.63310	-1.38440	0.89710

3a II:

N	-0.12440	-0.05510	0.28750
C	-0.42220	1.20490	-0.43210
C	-1.69290	0.53650	-0.99770
C	-1.05740	-0.80750	-0.58640
C	-0.56890	2.44740	0.42430
C	1.18590	-0.50800	0.47040
C	2.29720	0.24160	0.40610
C	3.67480	-0.29230	0.68970
H	0.32050	1.37110	-1.23040
H	-1.89870	0.68380	-2.05840
H	-2.58040	0.77950	-0.40620
H	-0.53750	-1.29410	-1.42300
H	-1.68360	-1.54010	-0.06980
H	-1.31020	2.27540	1.21200
H	0.38040	2.72470	0.89440
H	-0.90260	3.28970	-0.19150
H	1.24860	-1.57130	0.71520
H	2.21740	1.30110	0.16180
H	3.64500	-1.36650	0.89760
H	4.34930	-0.13190	-0.15920
H	4.13140	0.20410	1.55450

3 I:

N	-0.20250	2.43350	-0.73080
C	-1.66890	2.28020	-0.69090
C	-1.91990	1.06350	-1.60030
C	0.43960	1.38670	-1.51380
C	-2.16800	2.07660	0.73810
C	0.37280	3.68190	-0.62440
C	1.61800	4.02650	-1.01100
C	2.18320	5.40690	-0.80940
C	-0.60660	0.27420	-1.53140
H	-2.14580	3.17560	-1.11140
H	-2.09430	1.39840	-2.62880
H	-2.79190	0.48570	-1.28100
H	0.66530	1.74200	-2.53510
H	1.38740	1.08020	-1.05570
H	-1.76690	1.14530	1.15470
H	-1.84580	2.90350	1.38010
H	-3.26230	2.03000	0.75930
H	-0.27380	4.42930	-0.15810
H	2.26630	3.28340	-1.47290
H	1.44230	6.07000	-0.35060
H	3.06710	5.39820	-0.15990
H	2.49470	5.86250	-1.75690
H	-0.55130	-0.30600	-0.60390
H	-0.47300	-0.41330	-2.36950

3 II:

N	-0.17190	2.37300	-0.74200
C	-1.62090	2.13470	-0.65310
C	-1.69970	0.62670	-0.88920
C	0.47120	1.40440	-1.63130
C	-2.21410	2.57480	0.67810
C	0.34080	3.65110	-0.63940
C	1.55360	4.06740	-1.05700
C	2.04760	5.47420	-0.84920
C	-0.63150	0.38040	-1.95990
H	-2.14560	2.65510	-1.47500
H	-1.44140	0.10560	0.04170
H	-2.69980	0.30980	-1.19570
H	0.84330	1.90000	-2.54030
H	1.33650	0.94730	-1.13510
H	-1.67750	2.09340	1.50380
H	-2.16880	3.65970	0.81630
H	-3.26750	2.27870	0.72450
H	-0.32130	4.36060	-0.14030
H	2.23180	3.36720	-1.54180
H	1.28130	6.09170	-0.36930
H	2.94280	5.50530	-0.21590
H	2.31700	5.95620	-1.79640
H	-1.04610	0.58900	-2.95140
H	-0.25820	-0.64620	-1.96500

3 III:

N	-0.34450	2.55680	-1.30280
C	-1.69060	2.25020	-0.79500
C	-1.92100	0.86010	-1.39250
C	0.47490	1.34580	-1.26990
C	-1.76800	2.25300	0.73470
C	0.23200	3.77820	-0.98820
C	1.54700	4.03600	-0.86250
C	2.08890	5.41620	-0.60740
C	-0.54070	0.18180	-1.27520
H	-2.39490	2.98770	-1.19800
H	-2.21030	0.96100	-2.44330
H	-2.71000	0.30950	-0.87290
H	1.15280	1.32790	-2.13120
H	1.10340	1.32230	-0.36500
H	-1.08950	1.50790	1.16700
H	-2.78530	2.01890	1.06450
H	-1.49470	3.23370	1.13710
H	-0.49230	4.58950	-0.88230
H	2.26980	3.22910	-0.97080
H	2.72590	5.76450	-1.43000
H	1.27650	6.14040	-0.48710
H	2.70240	5.44760	0.30090
H	-0.46630	-0.38500	-0.34310
H	-0.35670	-0.51870	-2.09280

3 IV:

N	0.09270	2.15090	-0.70380
C	-1.33240	2.39940	-0.97350
C	-1.82510	1.08480	-1.61340
C	0.50820	0.84930	-1.23910
C	-2.08620	2.76090	0.30540
C	1.00140	3.19650	-0.72710
C	0.73230	4.51640	-0.74530
C	1.80970	5.56700	-0.71050
C	-0.78480	0.04340	-1.18190
H	-1.42660	3.22750	-1.69220
H	-2.84310	0.83660	-1.29970
H	-1.82390	1.17560	-2.70500
H	0.86320	0.93220	-2.28020
H	1.31730	0.42620	-0.63490
H	-2.09900	1.90430	0.98940
H	-1.61060	3.60270	0.81840
H	-3.12070	3.03630	0.07270
H	2.04220	2.86500	-0.69060
H	-0.29850	4.86730	-0.76330
H	1.74250	6.19390	0.18730
H	2.80440	5.10960	-0.72220
H	1.74380	6.24340	-1.57100
H	-0.76380	-0.83640	-1.82930
H	-0.97190	-0.28910	-0.15470

3 V:

N	0.10560	2.11060	-0.61030
C	-1.34060	2.34410	-0.75160
C	-1.88670	0.99470	-1.23840
C	0.47800	0.79440	-1.16530
C	-1.99540	2.82710	0.53860
C	0.98570	3.17140	-0.76030
C	0.69110	4.48560	-0.79900
C	1.74930	5.54820	-0.93030
C	-0.72050	0.40590	-2.03280
H	-1.49600	3.09910	-1.54100
H	-2.80190	1.11980	-1.82270
H	-2.11780	0.35530	-0.37650
H	1.41420	0.86280	-1.72630
H	0.61680	0.06400	-0.35770
H	-1.86430	2.07720	1.32630
H	-1.56710	3.77240	0.88390
H	-3.06900	2.97640	0.37720
H	2.03080	2.86240	-0.82940
H	-0.34000	4.82370	-0.72020
H	2.74460	5.10160	-1.02310
H	1.58490	6.17930	-1.81200
H	1.76750	6.22120	-0.06400
H	-0.79730	-0.67350	-2.18620
H	-0.64760	0.89020	-3.01360

3b I:

N	1.42330	-1.14490	-1.65820
C	1.76130	-2.58460	-1.57430
C	3.22740	-2.79430	-1.96420
C	2.29290	-0.25980	-0.88440
C	1.43040	-3.19080	-0.20350
C	0.04930	-0.89300	-1.56790
C	-0.56800	0.12550	-0.94680
C	-2.05760	0.32880	-1.00840
C	3.76180	-0.46500	-1.24730
C	4.17060	-1.93160	-1.12470
H	1.13450	-3.08460	-2.32350
H	3.34860	-2.53000	-3.02250
H	3.47180	-3.85760	-1.86310
H	2.14160	-0.40630	0.20040
H	2.00640	0.77300	-1.10520
H	2.01870	-2.74110	0.60280
H	1.63720	-4.26600	-0.20950
H	0.37140	-3.04770	0.03400
H	-0.55240	-1.62960	-2.10660
H	0.00380	0.85470	-0.37740
H	-2.49860	0.36190	-0.00570
H	-2.32130	1.27250	-1.50090
H	-2.54140	-0.48170	-1.56170
H	4.37630	0.16960	-0.60020
H	3.92110	-0.12900	-2.28030
H	4.13370	-2.24030	-0.07220
H	5.20540	-2.07040	-1.45410

3b II:

N	1.47860	-1.18570	-0.89080
C	1.83380	-2.55040	-1.35730
C	3.32400	-2.81060	-1.12240
C	2.29480	-0.14460	-1.51860
C	1.00380	-3.63590	-0.67480
C	0.09800	-0.91500	-0.89070
C	-0.52850	0.17050	-1.37550
C	-2.01170	0.37950	-1.22830
C	3.78480	-0.37040	-1.28880
C	4.20320	-1.75190	-1.78030
H	1.64900	-2.60120	-2.44880
H	3.56360	-3.80630	-1.51220
H	3.50820	-2.82970	-0.03820
H	1.99980	0.82010	-1.09510
H	2.08750	-0.09960	-2.60500
H	1.03530	-3.51650	0.41500
H	1.42970	-4.61320	-0.92290
H	-0.04040	-3.64250	-0.99660
H	-0.50040	-1.67550	-0.39240
H	0.02530	0.95280	-1.88910
H	-2.49100	0.52760	-2.20270
H	-2.48530	-0.48170	-0.74720
H	-2.24040	1.26700	-0.62640
H	4.00080	-0.27820	-0.21640
H	4.34340	0.41860	-1.80320
H	5.26070	-1.94030	-1.56820
H	4.08050	-1.80470	-2.87110

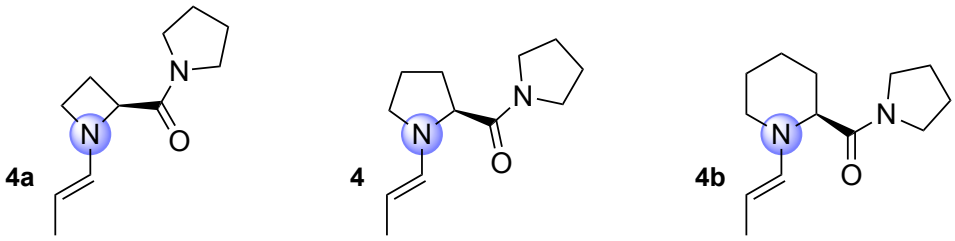
3b III:

N	1.56410	-0.80830	-1.29180
C	1.61220	-2.22210	-1.69320
C	2.96640	-2.51690	-2.35300
C	2.66350	-0.36930	-0.42740
C	1.31060	-3.18480	-0.53520
C	0.32000	-0.24270	-1.01960
C	-0.90310	-0.75820	-1.24140
C	-2.16570	0.02360	-0.99320
C	4.01350	-0.62860	-1.08780
C	4.14770	-2.10160	-1.47390
H	0.83890	-2.35240	-2.45880
H	3.01670	-1.96620	-3.30080
H	3.01490	-3.58480	-2.59390
H	2.62860	-0.88170	0.55020
H	2.53200	0.69930	-0.23120
H	2.09300	-3.16080	0.23000
H	1.24280	-4.21050	-0.91200
H	0.36060	-2.93310	-0.05600
H	0.39610	0.76790	-0.61140
H	-1.02120	-1.77060	-1.62380
H	-2.82220	-0.48590	-0.27760
H	-1.94070	1.01720	-0.59160
H	-2.74880	0.16100	-1.91210
H	4.81250	-0.32910	-0.40140
H	4.09760	-0.00330	-1.98640
H	4.17870	-2.71600	-0.56480
H	5.09070	-2.27820	-2.00180

3b IV:

N	1.34890	-1.46540	-2.03610
C	1.99330	-2.72880	-1.60550
C	2.89230	-2.48910	-0.38340
C	2.35730	-0.45370	-2.36500
C	0.99750	-3.85810	-1.36450
C	0.23870	-1.03780	-1.29640
C	-0.12410	0.21770	-0.98110
C	-1.42500	0.53170	-0.29170
C	3.26520	-0.12590	-1.17450
C	3.93630	-1.40460	-0.66460
H	2.63680	-3.02270	-2.44770
H	3.38080	-3.42920	-0.10070
H	2.25640	-2.18660	0.46190
H	1.85440	0.43830	-2.74960
H	2.96880	-0.85740	-3.18290
H	0.27530	-3.93420	-2.18430
H	1.54410	-4.80370	-1.29960
H	0.44920	-3.72950	-0.42540
H	-0.42960	-1.84960	-1.01150
H	0.51320	1.06420	-1.23000
H	-2.08490	1.14210	-0.92020
H	-1.96580	-0.38520	-0.03640
H	-1.26290	1.09490	0.63470
H	2.66820	0.32250	-0.37130
H	4.01540	0.61350	-1.47520
H	4.52630	-1.19740	0.23480
H	4.63720	-1.77240	-1.42700

Conformational Analysis of Pyrrolidinylamides 4a, 4, and 4b in $CHCl_3$

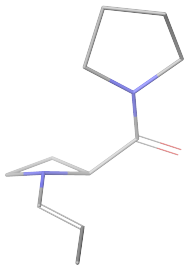


Δ = 0.40 Å	Δ = 0.13 Å	Δ = 0.31 Å
>100 : 1	71 : 29	52: 48
endo : exo	***endo : exo***	***endo : exo***

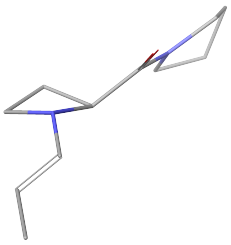
Note, the N-pyramidalization and *endo*/*exo* ratio of pyrrolidinylamides **4a**, **4** and **4b** were averaged over all conformations in energy minima. Several of them differ in the Ψ dihedral angle (N^1–C^2–C^{Amide}–N^{Amide}) and are likely not relevant for the conformational space of the peptidic catalysts **2a**, **2**, and **2b** since NMR spectroscopic analyses of peptide **2** had revealed a defined conformation around the DPro-Pro moiety.

	Total Free Energy (au)	Relative Energy (kcal/mol)	Population (%)	Pyramidalization Δ (Å)
4a I	-614.229328	0.00	21.9	0.366
4a II	-614.229324	0.00	21.8	0.411
4a III	-614.229031	0.19	16.0	0.408
4a IV	-614.228726	0.38	11.6	0.427
4a V	-614.228580	0.47	9.9	0.347
4a VI	-614.228554	0.49	9.6	0.420
4a VII	-614.228517	0.51	9.3	0.404
4 I	-653.527484	0.00	21.9	0.153
4 II	-653.526790	0.44	13.2	0.037
4 III	-653.526519	0.61	9.9	0.133
4 IV	-653.526396	0.68	8.7	-0.120
4 V	-653.526354	0.71	8.3	0.079
4 VI	-653.526071	0.89	6.2	0.318
4 VII	-653.526057	0.90	6.1	-0.020
4 VIII	-653.526005	0.93	5.7	0.151
4 IX	-653.525894	1.00	5.1	-0.191
4 X	-653.525874	1.01	5.0	-0.132
4 XI	-653.525756	1.08	4.4	-0.189
4b I	-692.798007	0.00	19.4	-0.259
4b II	-692.797860	0.09	16.6	0.357
4b III	-692.797786	0.14	15.4	-0.262
4b IV	-692.797603	0.25	12.7	0.285
4b V	-692.797294	0.45	9.1	0.343
4b VI	-692.797250	0.48	8.7	-0.323
4b VII	-692.796766	0.78	5.2	0.344
4b VIII	-692.796651	0.85	4.6	0.381
4b IX	-692.796579	0.90	4.3	-0.329
4b X	-692.79647	0.96	3.8	0.363

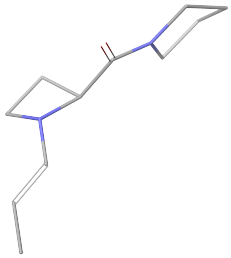
4a I:



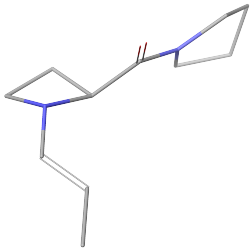
4a II:



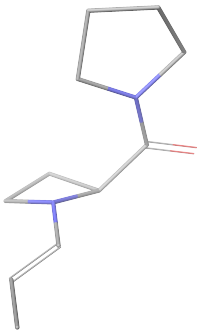
4a III:



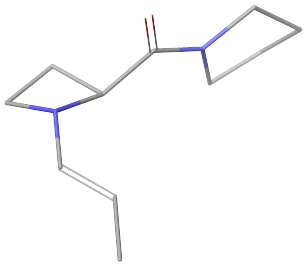
4a IV:



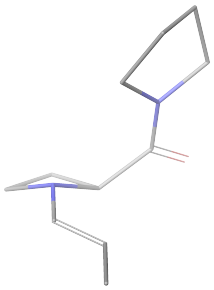
4a V:



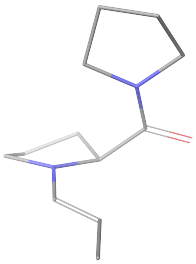
4a VI:



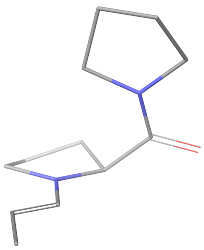
4a VII:



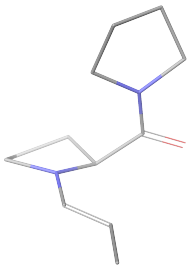
4 I:



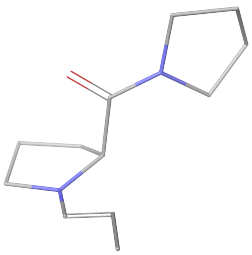
4 II:



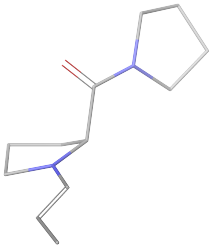
4 III:



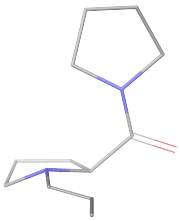
4 IV:



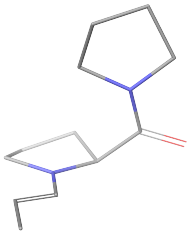
4 V:



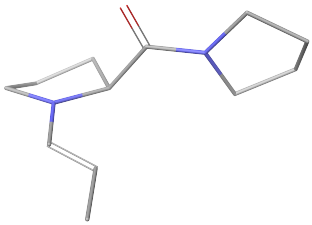
4 VI:



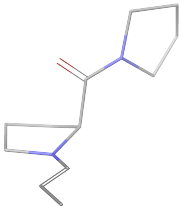
4 VII:



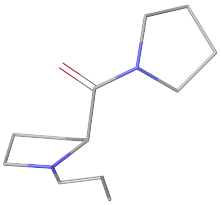
4 VIII:



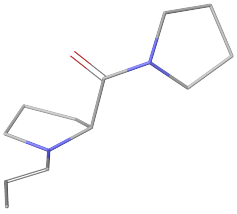
4 IX:



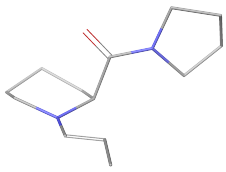
4 X:



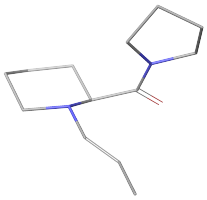
4 XI:



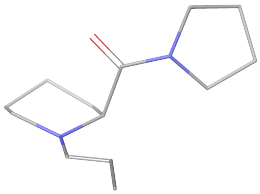
4b I:



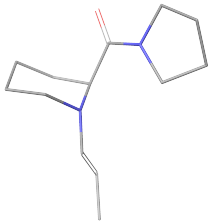
4b II:



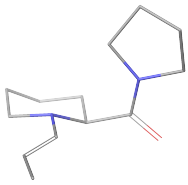
4b III:



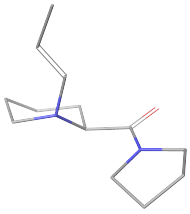
4b IV:



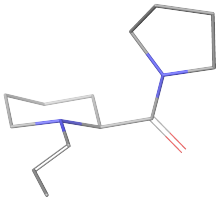
4b V:



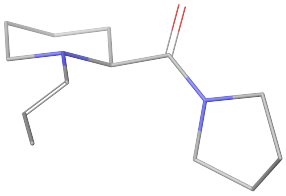
4b VI:



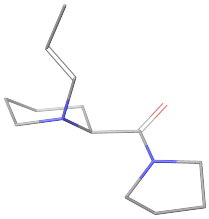
4b VII:



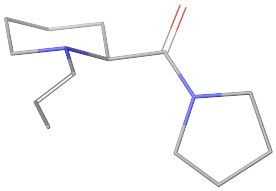
4b VIII:



4b IX:



4b X:



Coordinates of the Calculated Lowest Energy Structures:

4a I:

C	1.26290	-0.73900	-0.62710
N	1.45060	-1.57760	0.56870
C	0.31360	-0.96550	1.24850
C	2.67310	-1.80550	1.18710
C	2.86020	-1.90820	2.51190
C	4.18180	-2.25310	3.13970
C	-0.65250	-1.81630	2.06350
N	-0.80080	-3.12410	1.79680
O	-1.31620	-1.25640	2.95290
C	-1.73300	-3.92010	2.61290
C	-1.43140	-5.35910	2.19280
C	-1.01990	-5.20710	0.72600
C	-0.16780	-3.93560	0.73680
C	-0.16580	-0.42880	-0.12560
H	1.36460	-1.27020	-1.57860
H	1.90930	0.14960	-0.63080
H	0.62360	-0.14640	1.91630
H	3.49850	-1.95390	0.48810
H	2.01330	-1.75730	3.18270
H	4.12840	-3.19450	3.69940
H	4.96230	-2.36040	2.37970
H	4.50440	-1.48080	3.84700
H	-2.76590	-3.63130	2.37910
H	-1.56120	-3.72360	3.67410
H	-0.59330	-5.75270	2.77940
H	-2.28890	-6.02010	2.33650
H	-0.46720	-6.06490	0.33510
H	-1.90690	-5.05750	0.09930
H	0.87380	-4.15210	0.99920
H	-0.17450	-3.41260	-0.22030
H	-0.92430	-1.06900	-0.58300
H	-0.49070	0.61040	-0.14930

4a II:

C	1.44730	-0.43890	0.35110
N	2.05830	-1.65770	0.90250
C	0.75280	-2.16550	1.33330
C	3.14560	-1.62030	1.77580
C	4.00020	-0.59500	1.90260
C	5.20680	-0.62780	2.79850
C	0.54040	-3.66040	1.14110
N	-0.72950	-4.09090	1.25130
O	1.48400	-4.42800	0.92160
C	-1.90820	-3.26480	1.55710
C	-2.94590	-4.30410	1.98730
C	-2.59380	-5.51540	1.11630
C	-1.06320	-5.51620	1.12050
C	0.08300	-1.15720	0.36440
H	1.85100	-0.11530	-0.61240
H	1.48210	0.39950	1.06380
H	0.53310	-1.91120	2.38510
H	3.28000	-2.54310	2.34170
H	3.84280	0.30510	1.30780
H	6.13750	-0.53540	2.22610
H	5.19330	0.19850	3.51850
H	5.25240	-1.56500	3.36220
H	-2.24100	-2.72520	0.66100
H	-1.68650	-2.53570	2.34160
H	-3.96870	-3.94830	1.84520
H	-2.81030	-4.54710	3.04710
H	-2.96450	-5.36270	0.09660
H	-3.00950	-6.45240	1.49260
H	-0.65440	-6.07030	1.97490
H	-0.62030	-5.92580	0.20910
H	-0.16770	-1.61170	-0.59740
H	-0.76700	-0.59520	0.75140

4a III:

C	1.34880	-0.18060	0.53080
N	1.97450	-1.46980	0.85800
C	0.67950	-2.07250	1.17500
C	3.05130	-1.58510	1.73520
C	3.89450	-0.59680	2.06710
C	5.08600	-0.79050	2.96200
C	0.46610	-3.49390	0.66820
N	-0.68770	-4.07370	1.04960
O	1.28720	-4.06730	-0.05400
C	-1.72170	-3.47240	1.90700
C	-2.90850	-4.42210	1.72630
C	-2.23080	-5.78050	1.52120
C	-1.03090	-5.43990	0.63280
C	-0.00470	-0.91040	0.40340
H	1.75130	0.31580	-0.35660
H	1.36760	0.51720	1.38210
H	0.45050	-2.02300	2.25210
H	3.18870	-2.59580	2.12290
H	3.73700	0.39860	1.65170
H	6.02510	-0.58090	2.43690
H	5.04940	-0.12000	3.82800
H	5.13320	-1.81840	3.33440
H	-1.94890	-2.45120	1.59470
H	-1.38900	-3.45260	2.95220
H	-3.47290	-4.14300	0.83060
H	-3.58850	-4.39890	2.58050
H	-2.88680	-6.52430	1.06530
H	-1.88350	-6.17430	2.48300
H	-0.17350	-6.10330	0.77490
H	-1.29390	-5.44800	-0.43310
H	-0.24510	-1.18460	-0.62650
H	-0.86460	-0.44150	0.88290

4a IV:

C	0.84310	0.24860	0.57380
N	1.76040	-0.90370	0.71170
C	0.67830	-1.75810	1.19180
C	2.95570	-0.79000	1.42490
C	3.44020	-1.70120	2.27980
C	4.76000	-1.56150	2.98460
C	0.64700	-3.18010	0.64600
N	-0.42320	-3.91240	1.01520
O	1.53490	-3.62910	-0.08510
C	-1.53700	-3.46600	1.86610
C	-2.23410	-4.77970	2.22620
C	-2.03300	-5.62730	0.96500
C	-0.60000	-5.29240	0.54050
C	-0.34580	-0.73320	0.64130
H	0.97290	0.82780	-0.34410
H	0.87580	0.91860	1.44410
H	0.65770	-1.79290	2.29560
H	3.50850	0.12560	1.20750
H	2.87770	-2.61820	2.45440
H	5.45750	-2.35690	2.69690
H	4.64170	-1.62050	4.07250
H	5.22980	-0.60180	2.74970
H	-2.20960	-2.80620	1.30290
H	-1.17540	-2.92480	2.74500
H	-1.72880	-5.24480	3.08000
H	-3.28390	-4.63060	2.48880
H	-2.17520	-6.69620	1.13700
H	-2.73650	-5.31120	0.18690
H	0.13670	-5.94680	1.02300
H	-0.43980	-5.34340	-0.53960
H	-0.72530	-1.01350	-0.34460
H	-1.17020	-0.46200	1.30090

4a V:

C	1.41490	-0.96180	-0.13680
N	1.35780	-1.62440	1.16820
C	0.07660	-1.01110	1.51440
C	2.42870	-1.73810	2.04100
C	3.72200	-1.66280	1.68980
C	4.85800	-1.87290	2.65130
C	-1.01650	-1.88430	2.11940
N	-1.07970	-3.19190	1.81460
O	-1.85110	-1.35350	2.87070
C	-0.26700	-3.96540	0.85290
C	-1.11600	-5.21720	0.62050
C	-1.78770	-5.43330	1.97910
C	-2.14920	-4.01180	2.40890
C	-0.07820	-0.59440	0.02430
H	1.68890	-1.61760	-0.97080
H	2.08090	-0.08630	-0.13400
H	0.17330	-0.14040	2.17700
H	2.13680	-1.94510	3.07290
H	3.97560	-1.46150	0.64870
H	5.52130	-1.00160	2.68790
H	4.48660	-2.05400	3.66470
H	5.47760	-2.73070	2.36480
H	0.70430	-4.21670	1.29090
H	-0.08720	-3.40140	-0.06360
H	-0.51020	-6.06490	0.29280
H	-1.87270	-5.01960	-0.14710
H	-1.07300	-5.86930	2.68590
H	-2.66170	-6.08610	1.93220
H	-3.12030	-3.69600	2.00780
H	-2.17140	-3.86970	3.49210
H	-0.75180	-1.24660	-0.53670
H	-0.34950	0.44680	-0.14510

4a VI:

C	0.96780	0.38560	0.48500
N	1.76310	-0.85220	0.62840
C	0.58020	-1.61970	1.00250
C	2.91920	-0.89730	1.40820
C	3.24750	-1.88580	2.25310
C	4.53690	-1.92900	3.02490
C	0.43670	-3.00080	0.37290
N	-0.45330	-3.82030	0.96760
O	1.05970	-3.32720	-0.64160
C	-1.27790	-3.51030	2.14860
C	-2.32030	-4.63220	2.14260
C	-1.55180	-5.81500	1.54300
C	-0.72330	-5.16240	0.43400
C	-0.30240	-0.48870	0.41340
H	1.21780	0.99370	-0.38840
H	0.99240	1.00740	1.39070
H	0.48020	-1.68090	2.09810
H	3.58670	-0.04790	1.25250
H	2.56860	-2.73040	2.37530
H	5.13370	-1.03090	2.84170
H	4.35660	-1.99850	4.10370
H	5.14460	-2.79720	2.74780
H	-1.73100	-2.51860	2.06700
H	-0.66890	-3.54270	3.06170
H	-2.71510	-4.83040	3.14160
H	-3.15760	-4.35680	1.49190
H	-0.88830	-6.25300	2.29710
H	-2.20480	-6.60390	1.16410
H	0.21650	-5.67800	0.22090
H	-1.28710	-5.08270	-0.50460
H	-0.60640	-0.70450	-0.61350
H	-1.16010	-0.17310	1.00840

4a VII:

C	1.24640	-0.55560	-0.56670
N	1.41620	-1.53770	0.52250
C	0.29870	-0.96770	1.27930
C	2.65420	-1.78710	1.10790
C	2.86000	-2.02770	2.41170
C	4.20330	-2.36850	2.99360
C	-0.77440	-1.81760	1.94550
N	-0.85850	-3.14200	1.74560
O	-1.62030	-1.20900	2.62420
C	0.07880	-4.04310	1.04370
C	-0.38870	-5.43130	1.48700
C	-1.89940	-5.25370	1.65530
C	-2.00840	-3.87480	2.30500
C	-0.16090	-0.24710	-0.01510
H	1.31670	-0.97770	-1.57310
H	1.93130	0.29800	-0.47470
H	0.64460	-0.25270	2.04220
H	3.47860	-1.82300	0.39360
H	2.01330	-1.98900	3.09910
H	4.49520	-1.65380	3.77110
H	4.20200	-3.36130	3.45820
H	4.97890	-2.36120	2.22140
H	1.10920	-3.83660	1.33080
H	-0.01300	-3.91730	-0.04090
H	0.06890	-5.68750	2.44930
H	-0.11610	-6.20350	0.76420
H	-2.38850	-5.24550	0.67470
H	-2.36360	-6.03430	2.26170
H	-2.93590	-3.34760	2.07100
H	-1.91680	-3.92780	3.39700
H	-0.94850	-0.79920	-0.53430
H	-0.44310	0.79950	0.08760

4 I:

C	-1.78870	-0.37300	6.40280
N	-3.17070	0.09630	6.32740
C	-3.27450	1.53920	6.38820
C	-4.24270	-0.71810	6.62380
C	-5.51790	-0.33010	6.81160
C	-6.62630	-1.30190	7.11000
C	-4.18890	2.20380	5.35290
N	-4.28380	1.69450	4.11350
O	-4.79810	3.23570	5.67780
C	-1.01840	0.86490	6.86930
C	-1.81530	2.01530	6.24480
C	-5.17520	2.33890	3.13540
C	-5.20840	1.34210	1.97600
C	-3.82020	0.69890	2.03740
C	-3.59020	0.52770	3.54080
H	-1.43230	-0.71010	5.41640
H	-1.70150	-1.21440	7.09730
H	-3.68980	1.85500	7.35880
H	-3.98380	-1.77660	6.68080
H	-5.78410	0.72430	6.75510
H	-7.11000	-1.08370	8.06900
H	-7.41080	-1.27090	6.34520
H	-6.24650	-2.32760	7.15520
H	0.02900	0.85280	6.55880
H	-1.05510	0.93480	7.96160
H	-1.65750	2.97920	6.73180
H	-1.55760	2.12430	5.18400
H	-6.15290	2.52360	3.58730
H	-4.75460	3.30640	2.83360
H	-5.41990	1.82510	1.01970
H	-5.98040	0.58540	2.15550
H	-3.06970	1.37920	1.61900
H	-3.75510	-0.25220	1.50360
H	-2.53040	0.52550	3.80410
H	-4.04170	-0.39970	3.91050

4 II:

C	-2.21710	-0.41220	6.51010
N	-3.39600	0.43260	6.50620
C	-3.10210	1.84640	6.36030
C	-4.66480	-0.04720	6.73060
C	-5.02060	-1.34420	6.80710
C	-6.43110	-1.79410	7.06870
C	-3.91740	2.57780	5.28840
N	-4.20450	1.95640	4.13040
O	-4.28280	3.74330	5.50710
C	-1.06960	0.58420	6.70660
C	-1.58970	1.87170	6.05370
C	-3.75270	0.63340	3.65720
C	-4.04940	0.68690	2.15600
C	-5.30040	1.56690	2.08480
C	-5.00690	2.65740	3.11510
H	-2.12280	-0.97510	5.56580
H	-2.27840	-1.14590	7.32350
H	-3.31200	2.39490	7.29000
H	-5.42300	0.73210	6.83410
H	-4.26380	-2.11680	6.68140
H	-6.51040	-2.37210	7.99710
H	-7.10630	-0.93670	7.15290
H	-6.80700	-2.43580	6.26330
H	-0.13040	0.23850	6.26810
H	-0.90700	0.74730	7.77690
H	-1.11900	2.77700	6.44140
H	-1.42120	1.84570	4.97140
H	-2.69130	0.47650	3.86280
H	-4.32190	-0.16380	4.14850
H	-4.19180	-0.31050	1.73360
H	-3.21980	1.16840	1.62600
H	-6.18210	0.99180	2.38930
H	-5.48680	1.97570	1.08950
H	-5.90120	3.08340	3.57590
H	-4.42250	3.48090	2.68540

4 III:

C	-1.82990	-0.41880	6.36460
N	-3.21040	0.05640	6.36760
C	-3.30820	1.49940	6.38580
C	-4.27510	-0.74660	6.71290
C	-5.54580	-0.34740	6.91030
C	-6.65090	-1.29930	7.27660
C	-4.23530	2.16130	5.35610
N	-4.31600	1.67820	4.10390
O	-4.83920	3.19200	5.69370
C	-1.03420	0.81710	6.78920
C	-1.85050	1.96420	6.18440
C	-3.68840	0.46570	3.54400
C	-4.25800	0.39680	2.12140
C	-4.54130	1.85980	1.77270
C	-5.07860	2.42110	3.08770
H	-1.52880	-0.75350	5.35910
H	-1.70980	-1.26240	7.05150
H	-3.69680	1.84260	7.35770
H	-4.01590	-1.80240	6.80550
H	-5.80850	0.70510	6.81520
H	-7.10300	-1.04360	8.24180
H	-7.45840	-1.28710	6.53570
H	-6.27820	-2.32620	7.34580
H	-0.00030	0.79720	6.43660
H	-1.02810	0.89650	7.88150
H	-1.66940	2.93360	6.65240
H	-1.63400	2.05730	5.11310
H	-2.59550	0.57030	3.53140
H	-3.94750	-0.41440	4.13290
H	-5.19330	-0.17390	2.12720
H	-3.56800	-0.09210	1.42980
H	-5.24900	1.97830	0.94910
H	-3.61110	2.37260	1.50230
H	-6.15210	2.22380	3.20720
H	-4.91410	3.49310	3.21250

4 IV:

C	-1.95220	0.17670	7.67670
N	-3.31190	0.34750	7.16370
C	-3.37100	1.17180	5.98560
C	-4.35770	-0.46550	7.53760
C	-5.55850	-0.56200	6.93530
C	-6.67210	-1.42600	7.46130
C	-3.33190	0.35230	4.68150
N	-3.88900	0.92930	3.59780
O	-2.77230	-0.74710	4.62820
C	-1.09480	1.03840	6.73550
C	-2.09350	2.02430	6.11140
C	-4.52540	2.25590	3.53670
C	-4.60870	2.52580	2.03160
C	-4.80340	1.12510	1.44060
C	-3.86910	0.26000	2.28950
H	-1.64450	-0.87500	7.64850
H	-1.89230	0.52400	8.71670
H	-4.27980	1.78580	6.00850
H	-4.15600	-1.04890	8.43740
H	-5.75410	-0.00060	6.02210
H	-7.56130	-0.83810	7.71960
H	-6.98940	-2.17360	6.72450
H	-6.35880	-1.96090	8.36380
H	-0.66220	0.40970	5.95330
H	-0.27950	1.54250	7.25950
H	-2.29380	2.86340	6.78540
H	-1.75150	2.42520	5.15260
H	-5.52580	2.22460	3.98870
H	-3.93070	3.00730	4.06360
H	-3.66410	2.95550	1.67920
H	-5.41420	3.22020	1.78290
H	-4.56780	1.07060	0.37560
H	-5.84110	0.80110	1.57790
H	-2.84600	0.25160	1.89230
H	-4.19950	-0.77640	2.39390

4 V:

C	-2.45530	0.12990	7.55370
N	-3.68850	0.14170	6.78880
C	-3.67160	1.06160	5.67690
C	-4.83270	-0.48210	7.21850
C	-4.96850	-1.21610	8.34080
C	-6.26130	-1.87880	8.72970
C	-3.52740	0.35020	4.31930
N	-3.87020	1.07500	3.23370
O	-3.07330	-0.79390	4.22630
C	-1.49210	0.94680	6.68840
C	-2.42090	1.92500	5.95790
C	-4.44710	2.43070	3.22140
C	-4.81810	2.63520	1.74910
C	-3.76720	1.80570	1.00460
C	-3.63320	0.55800	1.87880
H	-2.10660	-0.89740	7.71590
H	-2.61140	0.59120	8.54330
H	-4.58090	1.67360	5.67370
H	-5.68830	-0.34540	6.55360
H	-4.11190	-1.35920	8.99840
H	-6.60490	-1.55520	9.71900
H	-7.05300	-1.64250	8.01200
H	-6.16800	-2.97020	8.76930
H	-0.99520	0.29130	5.96720
H	-0.72590	1.45440	7.27800
H	-2.70090	2.75380	6.61750
H	-1.97680	2.34330	5.04940
H	-3.70730	3.17170	3.55220
H	-5.31930	2.49870	3.87650
H	-4.82030	3.69080	1.46960
H	-5.81820	2.22970	1.56170
H	-4.05540	1.56680	-0.02100
H	-2.81370	2.34510	0.97600
H	-2.65060	0.08390	1.82820
H	-4.38770	-0.19880	1.63010

4 VI:

C	-1.86600	-0.29360	6.85880
N	-3.18360	0.05180	6.32590
C	-3.33220	1.49460	6.39500
C	-4.25830	-0.76590	6.66240
C	-5.52790	-0.38330	6.87730
C	-6.63880	-1.36050	7.14470
C	-4.29400	2.11190	5.37680
N	-4.32970	1.64320	4.11940
O	-4.99380	3.07610	5.72690
C	-0.97010	0.79930	6.27970
C	-1.88410	2.04320	6.23870
C	-3.50070	0.59010	3.50700
C	-3.67010	0.85370	2.00940
C	-5.11170	1.36200	1.91510
C	-5.23650	2.26700	3.14190
H	-1.58420	-1.30420	6.54740
H	-1.86250	-0.25950	7.96170
H	-3.74340	1.79630	7.37250
H	-3.99410	-1.82440	6.70390
H	-5.79580	0.67160	6.84850
H	-7.13690	-1.14880	8.09720
H	-7.41010	-1.31680	6.36720
H	-6.26030	-2.38650	7.18300
H	-0.65150	0.52100	5.27110
H	-0.07260	0.96110	6.88020
H	-1.66530	2.73300	7.05560
H	-1.76430	2.59980	5.30480
H	-2.46410	0.66200	3.83940
H	-3.87960	-0.39950	3.78610
H	-3.48210	-0.04180	1.41250
H	-2.97270	1.63480	1.68570
H	-5.81060	0.52200	1.99620
H	-5.32470	1.89330	0.98510
H	-6.24890	2.32070	3.54990
H	-4.90270	3.29110	2.93200

4 VII:

C	-2.24570	-0.45350	6.51960
N	-3.39730	0.42440	6.59930
C	-3.07960	1.82460	6.38040
C	-4.67850	-0.03070	6.80290
C	-5.06400	-1.32100	6.83310
C	-6.48360	-1.74620	7.08560
C	-3.92180	2.54970	5.32210
N	-4.19470	1.95320	4.14590
O	-4.30650	3.70430	5.56430
C	-1.06580	0.51200	6.65660
C	-1.58360	1.79830	6.00030
C	-4.91990	2.71070	3.11060
C	-4.69040	1.89020	1.84130
C	-4.59180	0.45800	2.37130
C	-3.79040	0.61710	3.66630
H	-2.21930	-1.00230	5.56160
H	-2.28050	-1.19810	7.32410
H	-3.23340	2.40960	7.29790
H	-5.41710	0.76280	6.93460
H	-4.32460	-2.10650	6.68390
H	-6.87350	-2.35860	6.26440
H	-6.57490	-2.34550	7.99930
H	-7.13950	-0.87640	7.19250
H	-0.15450	0.13510	6.18590
H	-0.85690	0.68720	7.71710
H	-1.06850	2.69950	6.33810
H	-1.47390	1.73650	4.91200
H	-5.98330	2.76940	3.37470
H	-4.52960	3.72900	3.05350
H	-3.74400	2.18380	1.37340
H	-5.48940	2.02760	1.10950
H	-4.11060	-0.23490	1.67720
H	-5.59090	0.07140	2.60250
H	-2.71150	0.58970	3.46200
H	-4.03430	-0.15540	4.39500

4 VIII:

C	-1.87240	0.14470	7.75850
N	-3.07350	-0.00720	6.94140
C	-3.10200	0.90460	5.82260
C	-4.22930	-0.59380	7.39850
C	-5.43030	-0.58520	6.78670
C	-6.65290	-1.23360	7.37470
C	-3.25360	0.18480	4.47330
N	-3.91940	0.85060	3.50720
O	-2.74770	-0.92300	4.27580
C	-1.37200	1.53960	7.37850
C	-1.73710	1.62560	5.89230
C	-4.08200	0.26030	2.17110
C	-5.06630	1.21170	1.48700
C	-4.74230	2.56480	2.12830
C	-4.50410	2.20110	3.59530
H	-1.12430	-0.62020	7.50620
H	-2.11650	0.05090	8.82160
H	-3.93370	1.61500	5.95630
H	-4.11810	-1.09670	8.35920
H	-5.54300	-0.10590	5.81570
H	-7.46450	-0.51220	7.52710
H	-7.05000	-2.02330	6.72760
H	-6.42630	-1.68450	8.34530
H	-0.30330	1.67300	7.56090
H	-1.91910	2.29920	7.94790
H	-1.79210	2.64900	5.51240
H	-1.00430	1.07250	5.29320
H	-3.11240	0.23230	1.65790
H	-4.44650	-0.76620	2.25610
H	-6.09540	0.92140	1.72680
H	-4.95700	1.21120	0.40060
H	-5.53530	3.30690	2.01110
H	-3.82310	2.97410	1.69590
H	-5.44900	2.17590	4.15410
H	-3.82490	2.89720	4.09190

4 IX:

C	-2.40840	0.06620	7.49850
N	-3.70170	0.50040	6.98380
C	-3.56800	1.31220	5.79530
C	-4.85320	-0.21710	7.23340
C	-4.99100	-1.22500	8.11330
C	-6.30570	-1.90620	8.37570
C	-3.51740	0.48000	4.50250
N	-3.88330	1.11360	3.37120
O	-3.13010	-0.69390	4.50700
C	-1.38260	0.89140	6.69920
C	-2.21160	2.00160	6.03240
C	-4.32910	2.51220	3.25520
C	-4.27230	2.76520	1.74620
C	-4.60360	1.39100	1.15380
C	-3.84870	0.42800	2.07250
H	-2.26940	-1.01210	7.33810
H	-2.35570	0.25570	8.57920
H	-4.39370	2.03030	5.74360
H	-5.71910	0.13060	6.66660
H	-4.12570	-1.57180	8.67510
H	-7.09550	-1.48930	7.74200
H	-6.25230	-2.98300	8.17600
H	-6.62290	-1.79210	9.41950
H	-0.92250	0.26250	5.93310
H	-0.58650	1.29250	7.33050
H	-2.36060	2.84390	6.71480
H	-1.75420	2.37770	5.11290
H	-5.35300	2.62270	3.63580
H	-3.67680	3.18670	3.81650
H	-3.25890	3.06620	1.45820
H	-4.96390	3.55190	1.43700
H	-4.30460	1.28930	0.10870
H	-5.68090	1.20330	1.22130
H	-2.80850	0.28740	1.75240
H	-4.31260	-0.55760	2.15750

4 X:

C	-1.95770	0.20790	7.67030
N	-3.32710	0.35810	7.17460
C	-3.41070	1.17440	5.99380
C	-4.34720	-0.48730	7.54680
C	-5.54930	-0.60660	6.95250
C	-6.63650	-1.50620	7.47200
C	-3.36070	0.35130	4.69260
N	-3.93210	0.90960	3.60600
O	-2.76020	-0.72640	4.64140
C	-1.12480	1.08880	6.72490
C	-2.14770	2.05070	6.10330
C	-3.77570	0.30730	2.27470
C	-4.11250	1.46330	1.33170
C	-5.17430	2.24360	2.11230
C	-4.66390	2.18790	3.55660
H	-1.63380	-0.83890	7.63240
H	-1.89280	0.55060	8.71200
H	-4.32480	1.77740	6.02410
H	-4.12320	-1.07470	8.43880
H	-5.76560	-0.03680	6.04910
H	-7.54070	-0.94540	7.73820
H	-6.93480	-2.25450	6.72850
H	-6.30570	-2.04130	8.36790
H	-0.67790	0.47010	5.94270
H	-0.32130	1.61420	7.24620
H	-1.82400	2.45490	5.13970
H	-2.35820	2.88850	6.77570
H	-2.75980	-0.07710	2.16050
H	-4.47270	-0.53220	2.15740
H	-4.46290	1.11880	0.35640
H	-3.22530	2.08710	1.17500
H	-5.30450	3.27070	1.76400
H	-6.14140	1.73360	2.04220
H	-3.99040	3.02680	3.77430
H	-5.48340	2.20640	4.28040

4 XI:

C	-2.42900	0.10360	7.48100
N	-3.74890	0.48240	6.99240
C	-3.67330	1.29820	5.80200
C	-4.86370	-0.28200	7.27020
C	-4.93800	-1.29120	8.15520
C	-6.21600	-2.02680	8.45010
C	-3.61700	0.46930	4.50750
N	-3.95040	1.11160	3.36800
O	-3.24030	-0.70760	4.51570
C	-1.45410	0.96240	6.65460
C	-2.33920	2.04010	6.00730
C	-4.39960	2.50970	3.24360
C	-4.79350	2.61590	1.76730
C	-3.84080	1.63190	1.07980
C	-3.78960	0.45920	2.06060
H	-2.25130	-0.96950	7.32500
H	-2.36000	0.30360	8.55900
H	-4.52390	1.98750	5.77090
H	-5.75690	0.02750	6.72470
H	-4.04590	-1.59820	8.69630
H	-6.50880	-1.93360	9.50200
H	-7.03860	-1.63890	7.84240
H	-6.12600	-3.09820	8.24070
H	-0.99060	0.34770	5.87850
H	-0.65650	1.39260	7.26460
H	-2.50510	2.87640	6.69350
H	-1.91810	2.43390	5.07780
H	-5.24090	2.71870	3.90990
H	-3.58320	3.20260	3.48810
H	-4.70900	3.63910	1.39370
H	-5.83140	2.28850	1.63760
H	-2.84490	2.07910	0.98080
H	-4.17880	1.32880	0.08670
H	-2.85040	-0.09900	2.03770
H	-4.61020	-0.25040	1.89360

4b I:

C	1.73420	1.00180	-1.61250
N	1.40130	-0.35720	-1.16470
C	0.87500	-1.28620	-2.14860
C	2.22850	-0.88360	-0.17410
C	2.55210	-2.17050	0.04050
C	3.37860	-2.61580	1.21610
C	1.95680	-1.84000	-3.09850
N	1.75630	-3.08750	-3.57220
O	2.93180	-1.16240	-3.44330
C	0.57690	1.63040	-2.37690
C	-0.25670	-0.64020	-2.97100
C	0.65120	-3.99940	-3.23480
C	0.76930	-5.08980	-4.30330
C	2.27790	-5.15940	-4.55760
C	2.70240	-3.69030	-4.52260
C	0.14670	0.72360	-3.52770
H	2.63210	0.98910	-2.24490
H	1.95970	1.59010	-0.71730
H	0.45050	-2.12440	-1.58560
H	2.60810	-0.12150	0.50910
H	2.22080	-2.94750	-0.64580
H	3.69130	-1.75990	1.82270
H	2.82350	-3.29930	1.86960
H	4.28170	-3.14630	0.89320
H	0.88740	2.61280	-2.74630
H	-0.27050	1.78500	-1.69660
H	-1.12540	-0.52270	-2.31170
H	-0.54990	-1.31840	-3.77940
H	-0.31530	-3.49190	-3.26590
H	0.78880	-4.41760	-2.22820
H	0.24760	-4.77360	-5.21350
H	0.33830	-6.03650	-3.97300
H	2.53350	-5.64470	-5.50190
H	2.76920	-5.70950	-3.74780
H	3.72720	-3.53570	-4.17840
H	2.59800	-3.21100	-5.50400
H	0.97670	0.60900	-4.23620
H	-0.69220	1.16290	-4.07670

4b II:

C	1.65460	1.13890	-0.31970
N	1.51710	-0.15720	-1.00090
C	0.13880	-0.60540	-1.16030
C	2.43250	-1.09820	-0.50230
C	2.21370	-2.37680	-0.16070
C	3.31960	-3.29510	0.27980
C	-0.03740	-1.84290	-2.04960
N	0.69110	-1.98610	-3.16890
O	-0.92930	-2.65480	-1.75370
C	0.83420	2.23340	-0.98540
C	-0.75490	0.49240	-1.77170
C	0.45510	-3.15750	-4.02960
C	1.58500	-3.08010	-5.05790
C	1.85130	-1.57590	-5.16570
C	1.74320	-1.11020	-3.71340
C	-0.63320	1.81880	-1.02920
H	2.71840	1.39740	-0.31930
H	1.34140	1.04450	0.73680
H	-0.28650	-0.90150	-0.18420
H	3.44240	-0.69090	-0.41790
H	1.21340	-2.80280	-0.20030
H	3.44260	-4.13660	-0.41150
H	4.27540	-2.76470	0.33670
H	3.10980	-3.72260	1.26630
H	1.20560	2.40130	-2.00470
H	0.96650	3.16640	-0.42790
H	-1.78550	0.12430	-1.76320
H	-0.47140	0.64210	-2.82180
H	-0.53370	-3.07370	-4.49720
H	0.46570	-4.07160	-3.43060
H	1.31090	-3.54310	-6.00830
H	2.47600	-3.58960	-4.67450
H	1.07430	-1.09620	-5.77190
H	2.82330	-1.33420	-5.60200
H	2.68350	-1.27310	-3.17290
H	1.47520	-0.05860	-3.61150
H	-1.24590	2.58130	-1.52050
H	-1.01340	1.70710	-0.00480

4b III:

C	1.71520	1.00150	-1.61890
N	1.41250	-0.35500	-1.14300
C	0.89030	-1.30950	-2.10310
C	2.26840	-0.85280	-0.16250
C	2.61660	-2.13130	0.06280
C	3.47630	-2.54860	1.22450
C	1.96840	-1.86300	-3.05680
N	1.75780	-3.10270	-3.55080
O	2.94340	-1.18540	-3.39990
C	0.53820	1.59420	-2.38270
C	-0.26090	-0.69940	-2.92560
C	0.68150	-4.03900	-3.18460
C	1.09760	-5.33950	-3.88090
C	1.85330	-4.84840	-5.11890
C	2.64570	-3.65520	-4.58350
C	0.11290	0.65960	-3.51300
H	2.60660	0.99320	-2.26010
H	1.93830	1.61010	-0.73640
H	0.47970	-2.13990	-1.52060
H	2.64950	-0.07490	0.50140
H	2.28430	-2.92260	-0.60690
H	3.78770	-1.68020	1.81360
H	2.94810	-3.23390	1.89820
H	4.38090	-3.06700	0.88690
H	0.82670	2.57550	-2.77280
H	-0.30530	1.74540	-1.69630
H	-1.12390	-0.58230	-2.25900
H	-0.55150	-1.40250	-3.71350
H	-0.28820	-3.68450	-3.55640
H	0.60910	-4.16180	-2.10010
H	0.23800	-5.97070	-4.11610
H	1.77160	-5.90790	-3.23090
H	1.14480	-4.51240	-5.88430
H	2.49590	-5.61210	-5.56150
H	3.59750	-3.96380	-4.13270
H	2.85940	-2.89280	-5.33580
H	0.93700	0.54710	-4.22890
H	-0.73970	1.07400	-4.06040

4b IV:

C	1.70290	0.94200	-1.58220
N	1.62370	-0.49590	-1.32440
C	0.26140	-1.01400	-1.40340
C	2.48650	-0.99820	-0.35390
C	2.32090	-2.05040	0.46610
C	3.40640	-2.53200	1.39070
C	-0.24680	-0.96340	-2.85770
N	0.57370	-1.44820	-3.80900
O	-1.36960	-0.52340	-3.13740
C	0.85410	1.73480	-0.58660
C	-0.67430	-0.27420	-0.43890
C	0.12970	-1.47380	-5.21050
C	1.32400	-2.08290	-5.94930
C	1.94850	-3.00400	-4.89570
C	1.84480	-2.16730	-3.61980
C	-0.59680	1.24580	-0.63250
H	1.34980	1.12700	-2.60710
H	2.75510	1.24050	-1.54190
H	0.28860	-2.08010	-1.14550
H	3.43460	-0.45690	-0.32470
H	1.37940	-2.59550	0.49320
H	3.07400	-2.53120	2.43530
H	3.71750	-3.55740	1.15790
H	4.29300	-1.89360	1.32180
H	0.91050	2.80450	-0.81550
H	1.26780	1.59200	0.42120
H	-0.35800	-0.53050	0.57990
H	-1.69930	-0.62910	-0.57200
H	-0.12780	-0.46530	-5.54540
H	-0.76970	-2.09560	-5.29850
H	2.03530	-1.29660	-6.22570
H	1.02370	-2.60410	-6.86070
H	2.97990	-3.28590	-5.11940
H	1.35480	-3.91960	-4.79370
H	1.82720	-2.76500	-2.70470
H	2.67470	-1.45680	-3.54030
H	-1.03760	1.50580	-1.60180
H	-1.19280	1.74660	0.13750

4b V:

C	1.55400	0.73250	-0.17190
N	1.32150	-0.46180	-0.97940
C	-0.08000	-0.69850	-1.34430
C	1.99320	-1.61050	-0.54010
C	2.90740	-1.71180	0.43810
C	3.62220	-2.99820	0.74830
C	-0.26890	-1.84030	-2.34940
N	0.56930	-1.96390	-3.39520
O	-1.23720	-2.60260	-2.20800
C	0.92020	1.97750	-0.77870
C	-0.75760	0.55330	-1.92700
C	1.71410	-1.11530	-3.77930
C	1.91000	-1.46170	-5.25550
C	1.54320	-2.94760	-5.30510
C	0.32800	-3.03290	-4.38020
C	-0.57050	1.76040	-1.01400
H	2.63650	0.87110	-0.09260
H	1.16800	0.58020	0.85390
H	-0.65550	-1.01220	-0.45660
H	1.73750	-2.50740	-1.10570
H	3.17360	-0.84830	1.04240
H	3.26110	-3.81450	0.11510
H	4.70370	-2.90700	0.59290
H	3.47520	-3.29240	1.79360
H	1.41400	2.20880	-1.73140
H	1.09640	2.82300	-0.10600
H	-1.81770	0.32040	-2.06970
H	-0.33760	0.77890	-2.91540
H	2.59960	-1.38210	-3.18990
H	1.50490	-0.06010	-3.60430
H	2.92760	-1.25170	-5.59260
H	1.21600	-0.87960	-5.87240
H	1.32140	-3.30790	-6.31170
H	2.36600	-3.54850	-4.90140
H	-0.61000	-2.83310	-4.91280
H	0.22570	-3.99600	-3.87370
H	-1.03180	2.64690	-1.46020
H	-1.07380	1.58090	-0.05440

4b VI:

C	-0.09240	-0.51630	-1.24010
N	0.96870	-1.32180	-1.84060
C	1.16510	-0.96490	-3.25180
C	2.12510	-1.54520	-1.08740
C	2.33070	-1.31200	0.21880
C	3.59460	-1.72260	0.92450
C	2.14360	-1.92340	-3.94180
N	1.84760	-3.23450	-3.88930
O	3.15100	-1.50720	-4.52940
C	0.23450	0.97920	-1.30170
C	1.56720	0.50220	-3.40440
C	0.66240	-3.86600	-3.28530
C	0.64380	-5.24400	-3.94860
C	2.13510	-5.56250	-4.10000
C	2.73730	-4.21930	-4.52200
C	0.50590	1.39660	-2.75200
H	-0.26340	-0.85930	-0.21610
H	-1.01390	-0.71640	-1.80400
H	0.19050	-1.10920	-3.74590
H	2.92490	-2.01970	-1.65820
H	1.57270	-0.81650	0.82190
H	3.39850	-2.45460	1.71700
H	4.30730	-2.17210	0.22570
H	4.08590	-0.86540	1.39890
H	1.12150	1.17890	-0.68830
H	-0.59250	1.56040	-0.87970
H	1.68710	0.74630	-4.46420
H	2.54340	0.65050	-2.92540
H	-0.23790	-3.27820	-3.48190
H	0.78560	-3.94570	-2.19970
H	0.16780	-5.17970	-4.93360
H	0.10090	-5.98010	-3.35160
H	2.33880	-6.35310	-4.82490
H	2.54920	-5.87200	-3.13380
H	3.76610	-4.07220	-4.18210
H	2.72070	-4.08340	-5.61050
H	0.81780	2.44500	-2.79500
H	-0.42770	1.31990	-3.32730

4b VII:

C	1.54390	0.66820	-0.05840
N	1.32970	-0.46530	-0.95320
C	-0.06970	-0.63940	-1.37210
C	1.97090	-1.65440	-0.57690
C	2.83780	-1.84390	0.43030
C	3.52760	-3.15910	0.66650
C	-0.26130	-1.79490	-2.36410
N	0.45710	-1.83090	-3.50100
O	-1.10230	-2.67090	-2.11140
C	0.98580	1.96590	-0.63090
C	-0.65410	0.65210	-1.95980
C	1.48500	-0.89490	-3.98730
C	2.35050	-1.79220	-4.86960
C	1.30880	-2.70050	-5.53280
C	0.30800	-2.98430	-4.40590
C	-0.49020	1.81430	-0.98460
H	2.62230	0.76910	0.09540
H	1.08800	0.46540	0.92900
H	-0.68370	-0.92880	-0.50230
H	1.73970	-2.49860	-1.22750
H	3.07760	-1.03620	1.11720
H	3.18720	-3.91750	-0.04520
H	4.61540	-3.06910	0.56560
H	3.33190	-3.53370	1.67730
H	1.55400	2.23490	-1.53050
H	1.13630	2.76560	0.10150
H	-1.70940	0.47420	-2.19280
H	-0.14450	0.89440	-2.89960
H	2.01580	-0.43680	-3.15370
H	1.01690	-0.10650	-4.59250
H	3.03120	-2.38030	-4.24300
H	2.94690	-1.22020	-5.58370
H	0.81440	-2.16120	-6.34820
H	1.73270	-3.61910	-5.94420
H	-0.72540	-3.06840	-4.75340
H	0.54890	-3.90150	-3.85540
H	-0.88340	2.73630	-1.42400
H	-1.07070	1.61640	-0.07350

4b VIII:

C	0.75100	0.23580	0.53100
N	1.45930	0.07570	-0.73670
C	0.53670	-0.11020	-1.86940
C	2.50100	-0.87040	-0.71890
C	2.92930	-1.60320	0.32030
C	4.11630	-2.52150	0.23030
C	1.32330	-0.19900	-3.18240
N	1.20630	-1.32920	-3.90450
O	2.02240	0.74870	-3.55950
C	-0.24270	1.39090	0.48290
C	-0.45760	1.04930	-1.97430
C	1.97510	-1.50020	-5.14600
C	1.94140	-3.01200	-5.36680
C	0.56710	-3.40660	-4.81690
C	0.42130	-2.53320	-3.56710
C	-1.22930	1.21580	-0.66840
H	1.49660	0.41920	1.31000
H	0.22240	-0.70100	0.79600
H	-0.03150	-1.04040	-1.70560
H	3.02200	-0.95890	-1.67290
H	2.43110	-1.54090	1.28500
H	4.92150	-2.20840	0.90500
H	3.84660	-3.54630	0.51020
H	4.52110	-2.54380	-0.78610
H	0.30850	2.33030	0.35500
H	-0.76570	1.44470	1.44340
H	-1.13720	0.85410	-2.81250
H	0.10500	1.96050	-2.20650
H	2.97940	-1.09060	-5.01720
H	1.48860	-0.95570	-5.96560
H	2.73340	-3.49150	-4.78110
H	2.08040	-3.28320	-6.41510
H	-0.21450	-3.15040	-5.54020
H	0.47880	-4.46960	-4.58220
H	-0.62260	-2.28310	-3.36240
H	0.84310	-3.02580	-2.68210
H	-1.90830	2.07170	-0.73340
H	-1.84990	0.32640	-0.49010

4b IX:

C	-0.03100	-0.57390	-1.11810
N	1.03770	-1.35370	-1.74150
C	1.15450	-1.02750	-3.17330
C	2.23820	-1.49400	-1.03520
C	2.48460	-1.20870	0.25300
C	3.79760	-1.52860	0.91390
C	2.15580	-1.96440	-3.86150
N	1.79010	-3.25320	-3.96470
O	3.24620	-1.55640	-4.28270
C	0.22470	0.93150	-1.23840
C	1.48430	0.45000	-3.38230
C	2.69440	-4.24830	-4.55840
C	1.81990	-5.50170	-4.66540
C	0.82580	-5.33920	-3.51010
C	0.50920	-3.84350	-3.54280
C	0.41230	1.31670	-2.71050
H	-0.14110	-0.89140	-0.07770
H	-0.96640	-0.83240	-1.63310
H	0.16630	-1.23050	-3.61320
H	3.03710	-1.93920	-1.62860
H	1.72620	-0.73700	0.87440
H	4.50420	-1.95930	0.19730
H	4.25940	-0.63180	1.34230
H	3.67550	-2.24590	1.73420
H	1.12760	1.18940	-0.67200
H	-0.60910	1.48720	-0.79580
H	1.54900	0.66800	-4.45340
H	2.47180	0.65290	-2.95030
H	3.55450	-4.40120	-3.89490
H	3.07140	-3.89340	-5.52110
H	2.40630	-6.42090	-4.60590
H	1.28330	-5.50210	-5.62060
H	-0.07090	-5.95300	-3.61800
H	1.30400	-5.59390	-2.55780
H	-0.26930	-3.62420	-4.28600
H	0.20620	-3.44250	-2.57430
H	0.67450	2.37600	-2.79660
H	-0.54120	1.18170	-3.24080

4b X:

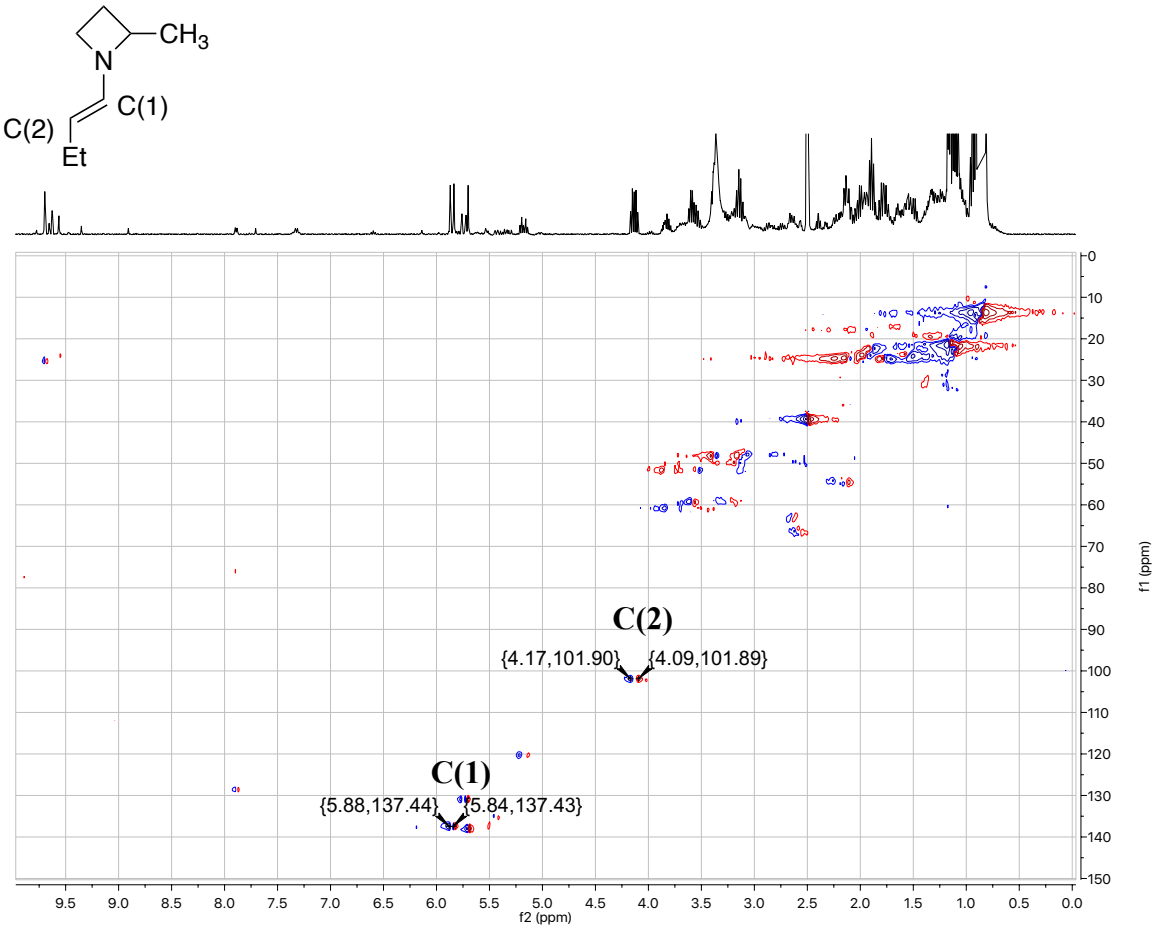
C	0.70500	0.08250	0.53640
N	1.36550	0.02210	-0.76490
C	0.39990	-0.05300	-1.87710
C	2.42660	-0.89530	-0.85750
C	2.91080	-1.69540	0.10450
C	4.12160	-2.56300	-0.10210
C	1.13490	-0.09060	-3.22300
N	1.15150	-1.26030	-3.88890
O	1.66830	0.92710	-3.68040
C	-0.26240	1.25840	0.62130
C	-0.54970	1.14580	-1.85330
C	1.81680	-1.35600	-5.19680
C	1.48810	-2.77810	-5.65300
C	1.41180	-3.55270	-4.33350
C	0.69410	-2.57550	-3.39990
C	-1.28100	1.21610	-0.51500
H	1.48020	0.18620	1.30100
H	0.16710	-0.86480	0.73840
H	-0.20900	-0.96710	-1.76370
H	2.91920	-0.89250	-1.83110
H	2.44360	-1.73030	1.08560
H	3.89370	-3.61640	0.09630
H	4.49120	-2.48450	-1.12940
H	4.94110	-2.28190	0.56960
H	0.31010	2.19220	0.56670
H	-0.76030	1.23470	1.59630
H	-1.25770	1.04970	-2.68430
H	0.03870	2.05400	-2.02110
H	2.89650	-1.20400	-5.07160
H	1.44360	-0.57700	-5.86560
H	2.23560	-3.17420	-6.34350
H	0.51460	-2.79600	-6.15530
H	0.88420	-4.50540	-4.41460
H	2.42090	-3.75080	-3.95490
H	-0.39530	-2.66140	-3.49600
H	0.96890	-2.71980	-2.35210
H	-1.93510	2.09300	-0.48240
H	-1.92390	0.33220	-0.39980

4. Preparation and NMR Spectroscopic Analysis of the Enamines

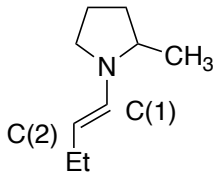
General Procedure: The secondary amine (1 equiv., 100 μmol) and butanal (1.5 equiv., 150 μmol) was stirred over pre-activated molecular sieve (3 Å) in d^6-DMSO (1.0 mL) for 30 min. The NMR spectra of the crude mixture were recorded after filtration.

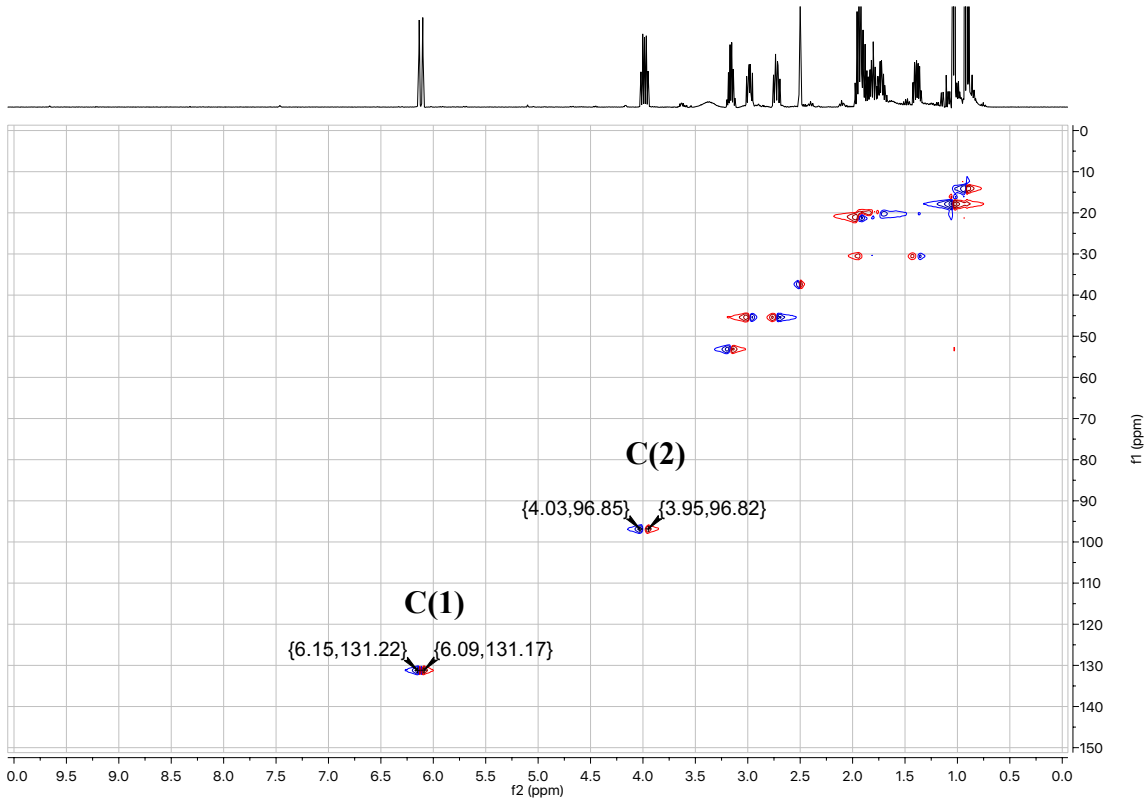
4.1. Enamines 3a`, 3` and 3b`

3a`:

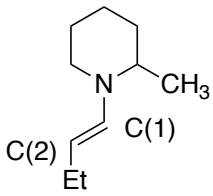


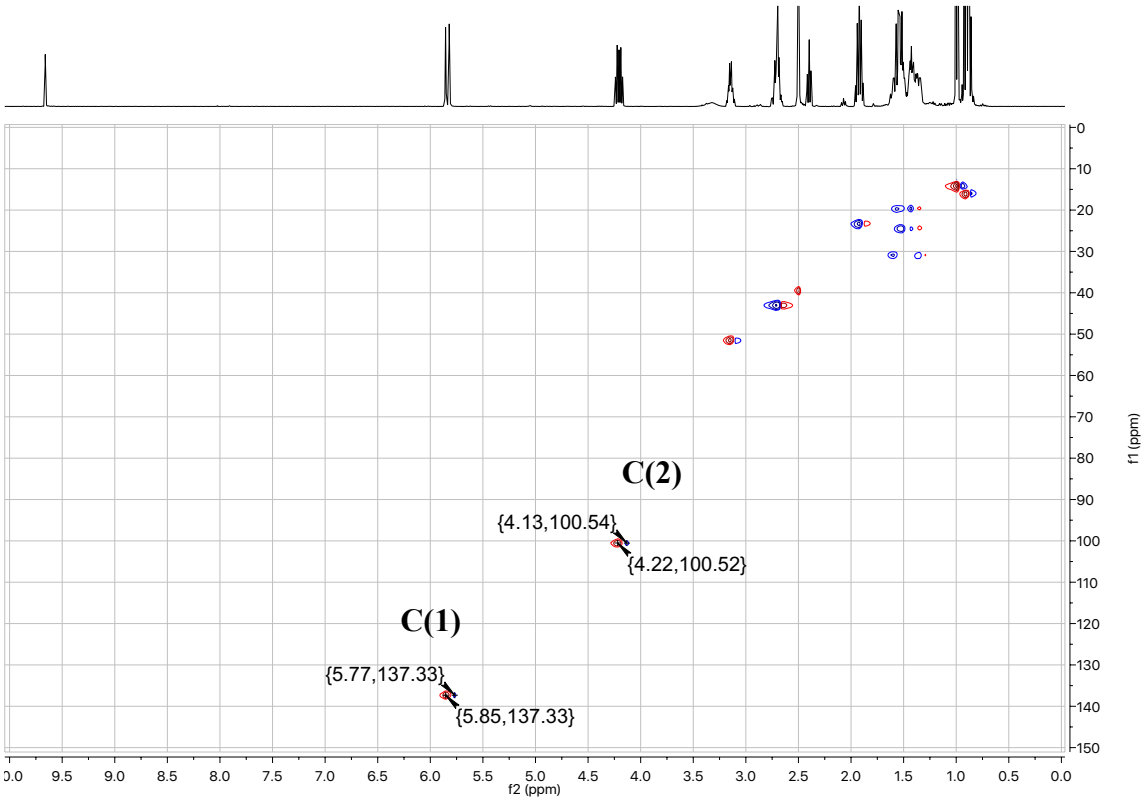
3`:


N
CH3
C(1)
C(2)
Et


C(2)
{4.03,96.85}
{3.95,96.82}
C(1)
{6.15,131.22}
{6.09,131.17}
f2 (ppm)
f1 (ppm)

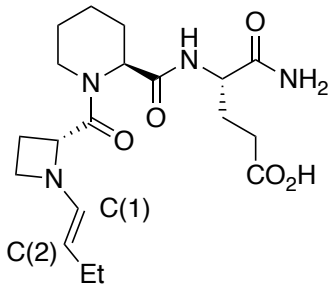
3b`:

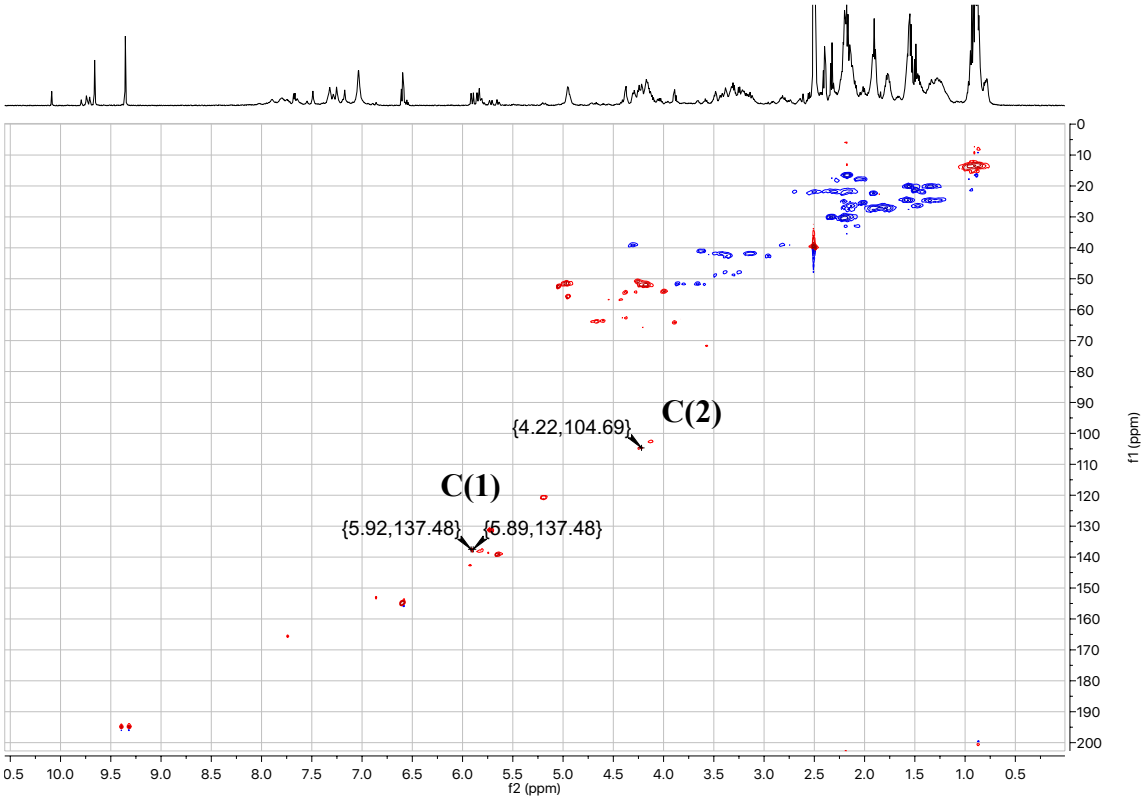

N
CH3
C(1)
C(2)
Et


C(2)
{4.13,100.54}
{4.22,100.52}
C(1)
{5.77,137.33}
{5.85,137.33}
f2 (ppm)
f1 (ppm)

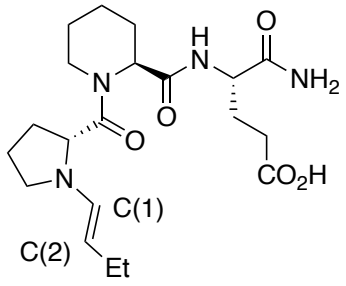
4.2. Enamines 2a-En, 2-En and 2b-En

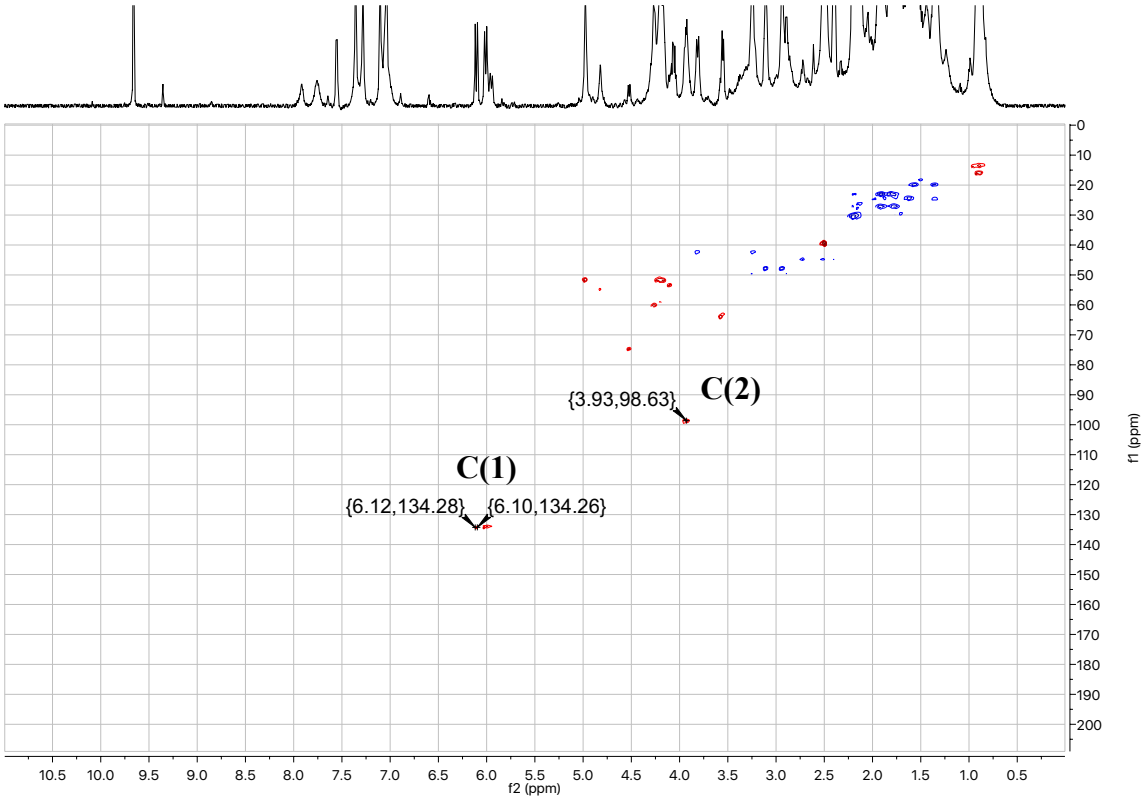
2a-En:



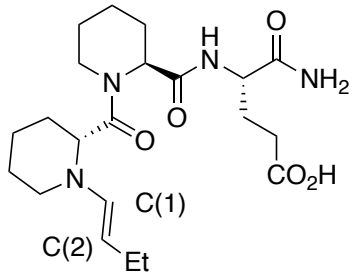


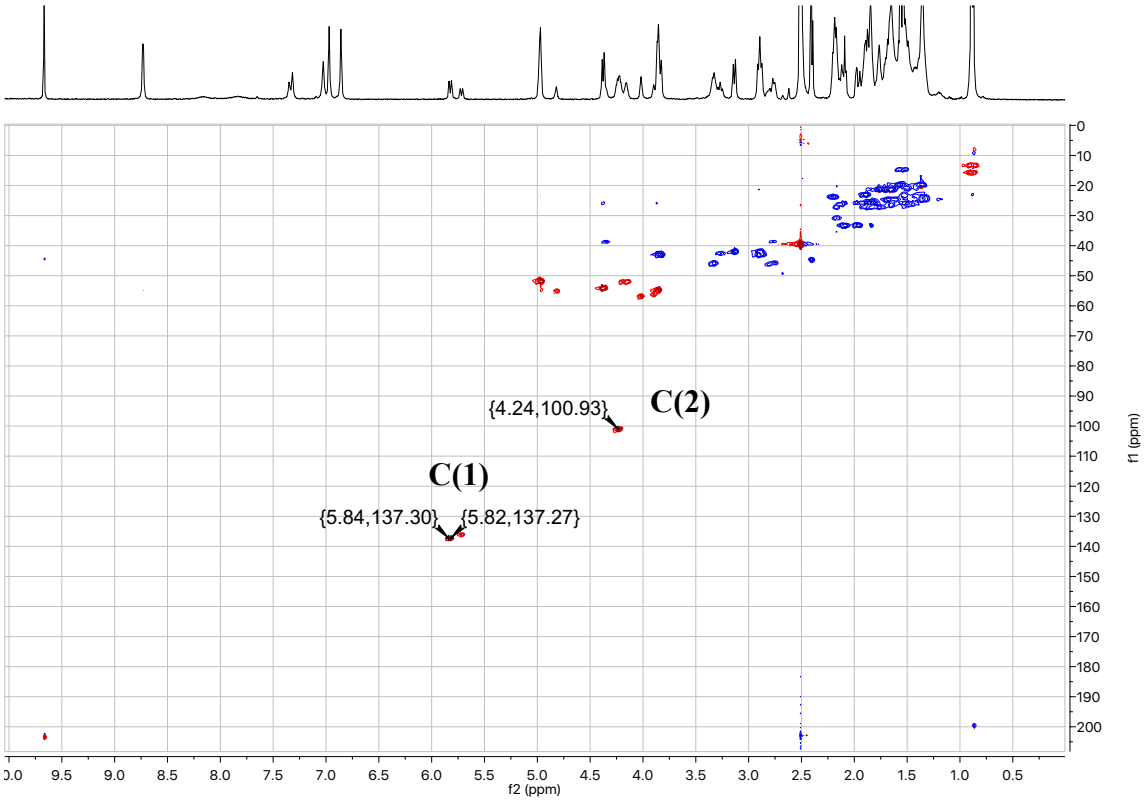
2-En:


O
H
N
NH2
N
O
O
N
CO2H
C(1)
C(2)
Et


{3.93,98.63}
C(2)
C(1)
{6.12,134.28}
{6.10,134.26}
f2 (ppm)
f1 (ppm)

2b-En:


H
N
O
NH2
N
O
O
N
CO2H
C(1)
C(2)
Et


{4.24,100.93}
C(2)
C(1)
{5.84,137.30}
{5.82,137.27}
f2 (ppm)
f1 (ppm)

5. *In Situ* IR Monitoring – Kinetic Experiments

All experiments were carried out at room temperature using butanal and (*E*)-nitrostyrene. Chloroform was filtered through a plug of basic alumina prior to use. Reaction progress was monitored by following the N-O-stretching mode of the γ-nitroaldehyde product at 1554 cm^{-1}.

General Procedure to determine the rate-order of butanal: A volumetric flask (1 mL) was charged with the peptide TFA salt (3 mol%, 15 μmol) and (*E*)-nitrostyrene (74.6 mg, 0.5 mmol). The mixture was dissolved in $CHCl_3$/^{i}PrOH 9:1 (0.2 mL). Subsequently, the specified amount of butanal and N-methylmorpholine (3 mol%, 15 μmol, 1.65 μL) and additional $CHCl_3$/^{i}PrOH 9:1 were added to a total volume of 1 mL. The resulting mixture was sonicated until a homogeneous solution was obtained and transferred into a 5 mL round bottom flask that was equipped with the IR probe. A water bath with circulator was used to keep the temperature of the reaction mixture constant at 20 °C during the measurement (± 0.1 °C).

General Procedure to determine the rate-order of nitrostyrene: A volumetric flask (1 mL) was charged with the peptide TFA salt (3 mol%, 15 μmol) and the specified amount of (*E*)-nitrostyrene. The mixture was dissolved in $CHCl_3$/^{i}PrOH 9:1 (0.2 mL). Subsequently, butanal (135.2 μL, 1.5 mmol) and N-methylmorpholine (3 mol%, 15 μmol, 1.65 μL) and additional $CHCl_3$/^{i}PrOH 9:1 were added to a total volume of 1 mL. The resulting mixture was sonicated until a homogeneous solution was obtained and transferred into a 5 mL round bottom flask that was equipped with the IR probe. A water bath with circulator was used to keep the temperature of the reaction mixture constant at 20 °C during the measurements (± 0.1 °C).

General Procedure to determine the activation energy: A volumetric flask (1 mL) was charged with the peptide TFA salt (3 mol%, 15 μmol) and (*E*)-nitrostyrene (74.6 mg, 0.5 mmol, 1 equiv.). The mixture was dissolved in $CHCl_3$/^{i}PrOH 9:1 (0.2 mL). Subsequently, butanal (135.2 μL, 1.5 mmol, 3 equiv.) and N-methylmorpholine (3 mol%, 15 μmol, 1.65 μL) and additional $CHCl_3$/^{i}PrOH 9:1 were added to a total volume of 1 mL. The resulting mixture was sonicated until a homogeneous solution was obtained and transferred into a 5 mL round bottom flask that was equipped with the IR probe. A water bath with circulator was used to keep the specified temperature of the reaction mixture constant during the measurements (± 0.1 °C).

Data Treatment: Initial rates k_{obs} and corresponding standard errors (SE) were determined by fitting a linear regression model ($f(x) = intercept + k_{obs} \cdot x$) to the ReactIR data using the function fitlm in Matlab (The MathWorks, Inc).

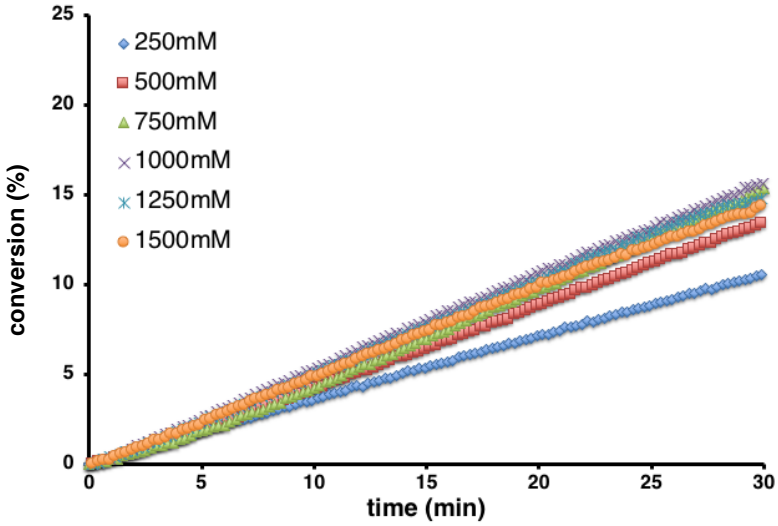
In order to determine the activation energy, the natural logarithm of all corresponding initial rates were plotted against 1/T ('Arrhenius plot') and fitted to a linear regression model ($f(x) = intercept + slope \cdot x$) using the function fitlm in Matlab. In order to account for the error of the initial rates, the observations were weighted according to the normalized standard error: ($weight = \frac{1}{SE/k_{obs}}$) resulting in lower weights for initial rates with high relative error and vice versa. The activation energy was calculated according to the following formula: $E_A = slope * -R$. Here, R refers to the ideal gas constant. The error of the activation energy was calculated according to the following formula: $Error\_E_A = SE_{slope} * -R$.

In order to determine the rate order, the logarithm of all corresponding initial rates were plotted against the logarithm of the concentration of the respective component (butanal or nitrostyrene) and fitted to the linear regression model ($f(x) = intercept + rate\_order \cdot x$) using the function fitlm in Matlab. In order to account for the error of the initial rates, the observations were weighted according to the normalized standard error: ($weight = \frac{1}{SE/k_{obs}}$) resulting in lower weights for initial rates with high relative error and vice versa. The slope of the linear fit represents the rate order.

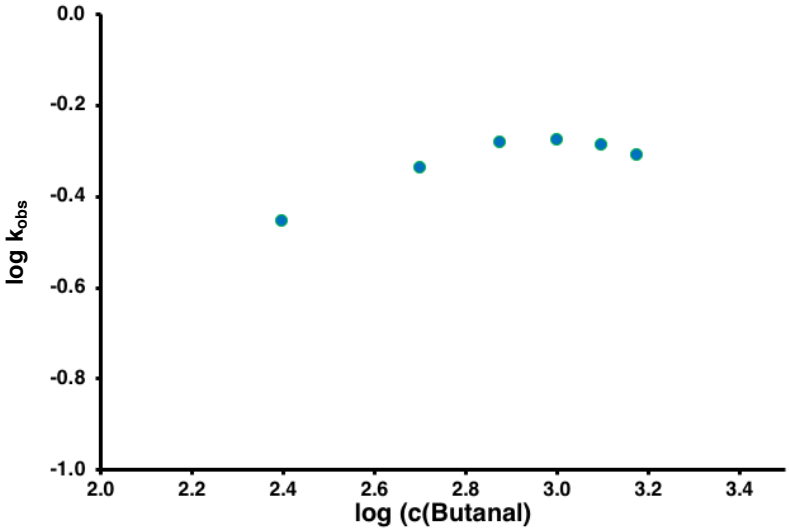
5.1 Determination of Rate Orders and Activation Energies Using 3 mol% of Catalysts 2a, 2, 2b and 2c

Rate Order of Butanal for 2a (3 mol%):

Variation of the butanal concentration (c(nitrostyrene) = 0.5 M):



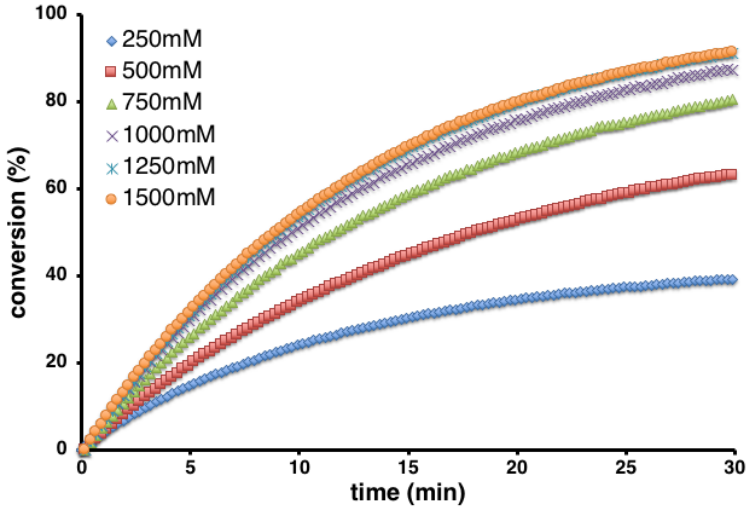
Zero order in butanal at a concentration of ≥ 750 mM:



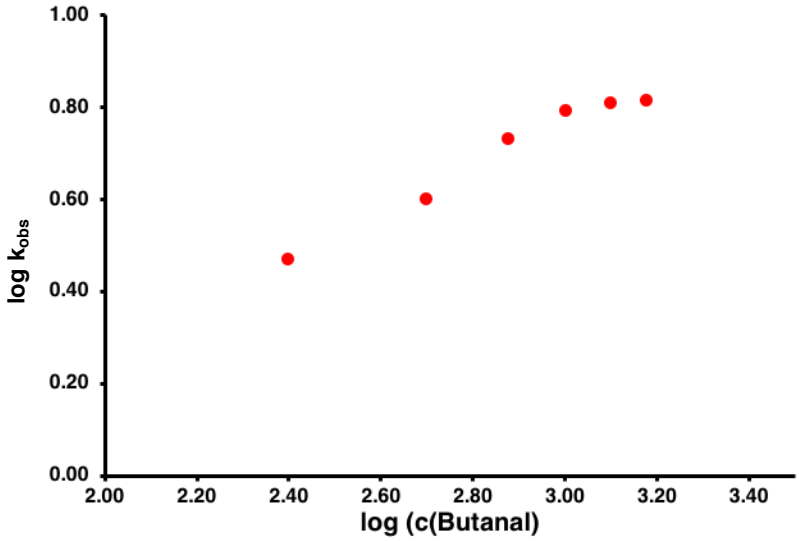
c(Butanal) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
250	2.40	0.352	0.001	-0.453	0.002	586.8
500	2.70	0.462	0.001	-0.336	0.002	512.8
750	2.88	0.524	0.003	-0.280	0.005	209.7
1000	3.00	0.533	0.001	-0.274	0.002	591.7
1250	3.10	0.516	0.001	-0.287	0.003	397.2
1500	3.18	0.491	0.001	-0.309	0.003	377.6

Rate Order of Butanal for 2 (3 mol%):

Variation of the butanal concentration (c(nitrostyrene) = 0.5 M):



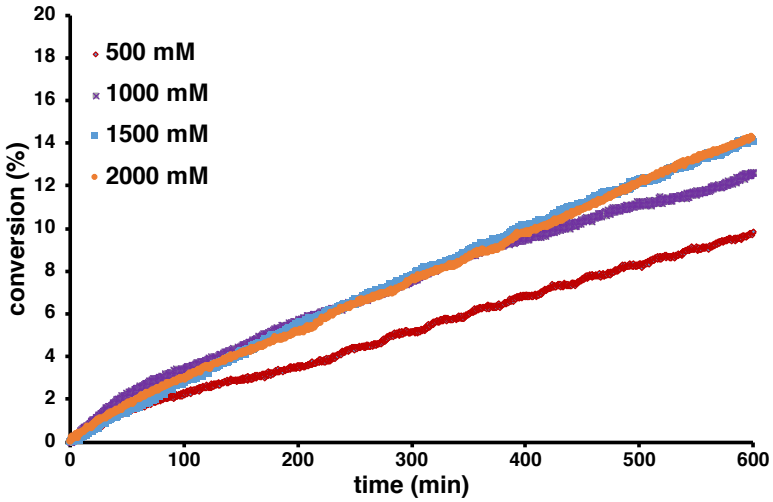
Zero order in butanal at a concentration of ≥ 1250 mM:



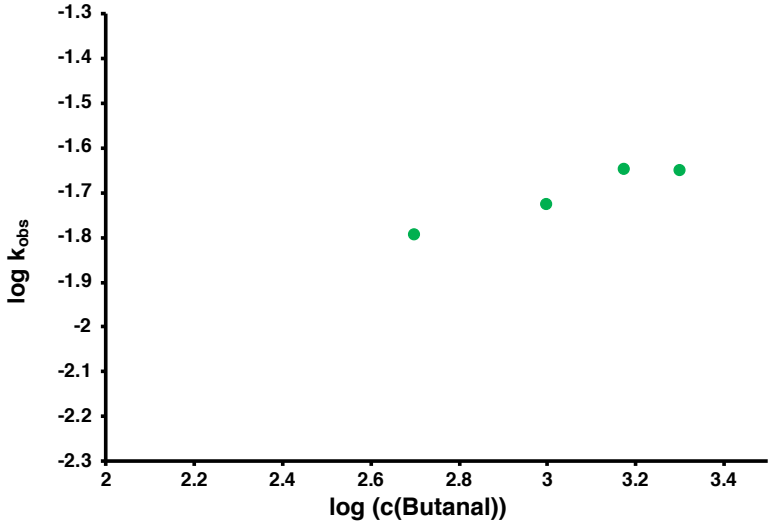
c(Butanal) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
250	2.40	2.93	0.04	0.466	0.014	71.8
500	2.70	4.00	0.05	0.602	0.012	86.5
750	2.88	5.34	0.07	0.728	0.013	79.2
1000	3.00	6.15	0.08	0.789	0.013	79.3
1250	3.10	6.42	0.07	0.807	0.011	93.4
1500	3.18	6.49	0.08	0.812	0.013	76.7

Rate Order of Butanal for 2b (3 mol%):

Variation of the butanal concentration (c(nitrostyrene) = 0.5 M):



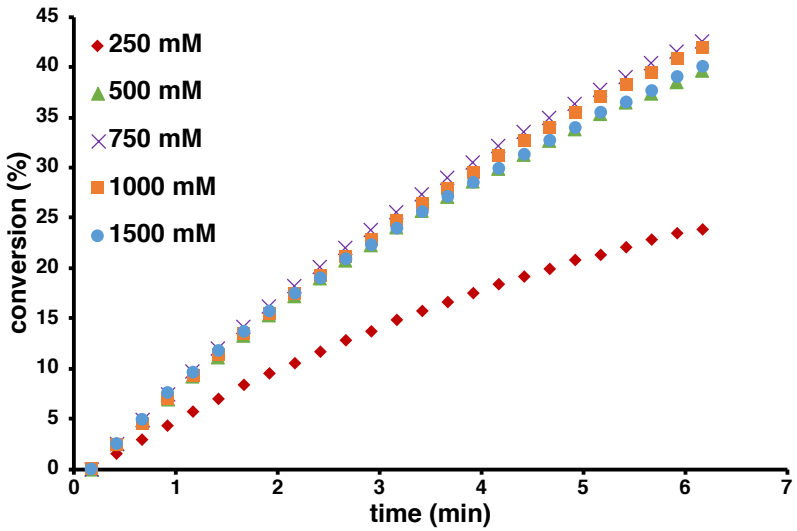
Zero order in butanal at a concentration of ≥ 1500 mM:



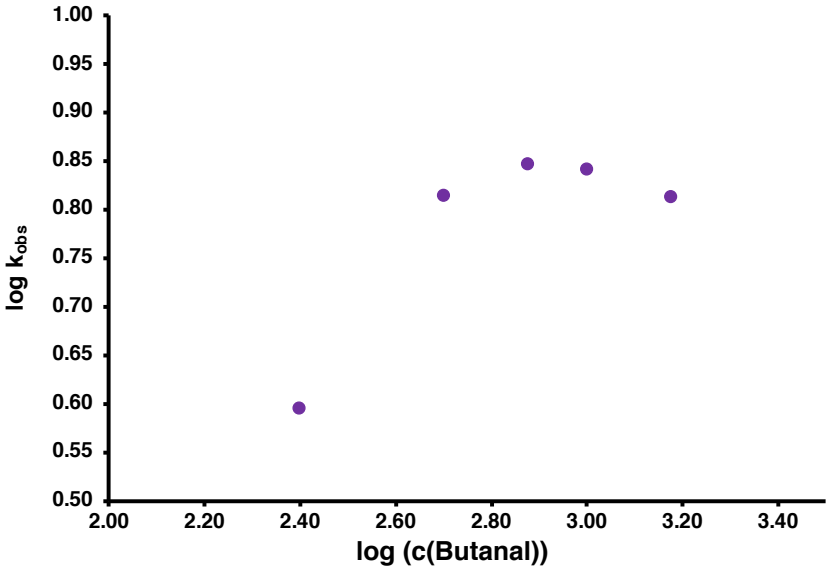
c(Butanal) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
500	2.70	0.01596	0.00002	-1.797	0.001	798.0
1000	3.00	0.01867	0.00003	-1.729	0.002	622.3
1500	3.18	0.02235	0.00002	-1.651	0.001	1117.5
2000	3.30	0.02225	0.00002	-1.653	0.001	1112.5

Rate Order of Butanal for 2c (3 mol%):

Variation of the butanal concentration (c(nitrostyrene) = 0.5 M):



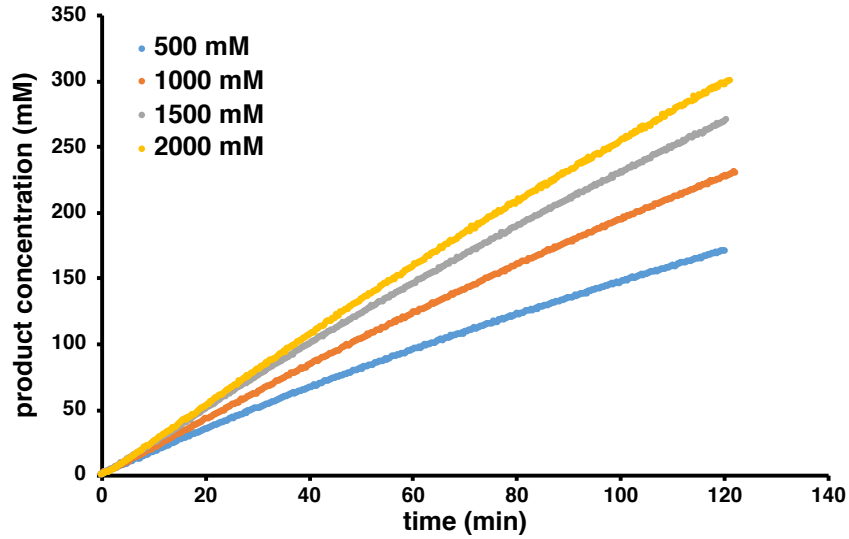
Zero order in butanal at a concentration of ≥ 500 mM:

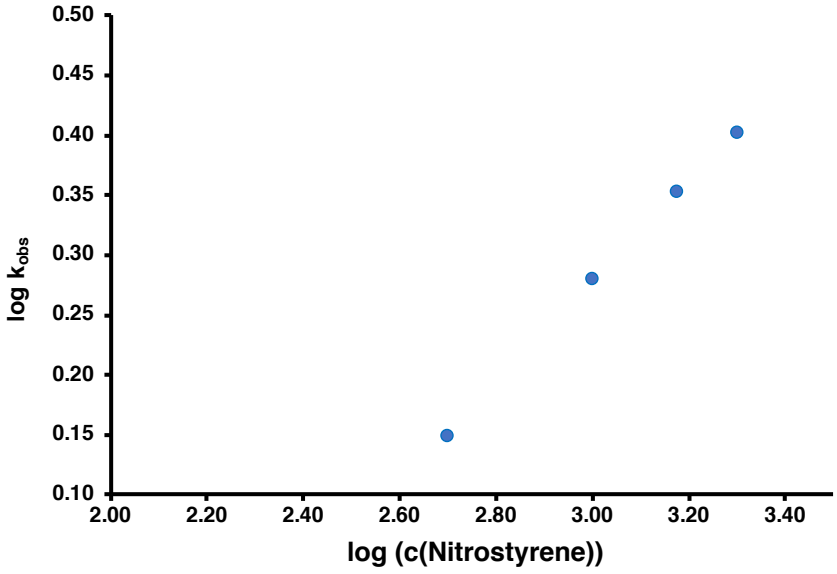


c(Butanal) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
250	2.40	3.95	0.11	0.596	0.027	37.6
500	2.70	6.53	0.16	0.815	0.024	41.3
750	2.88	7.05	0.16	0.848	0.023	44.3
1000	3.00	6.95	0.14	0.842	0.020	50.0
1500	3.18	6.51	0.15	0.814	0.023	42.8

Rate Order of Nitrostyrene for 2a (3 mol%):

Variation of the nitrostyrene concentration (c(butanal) = 1.5 M):



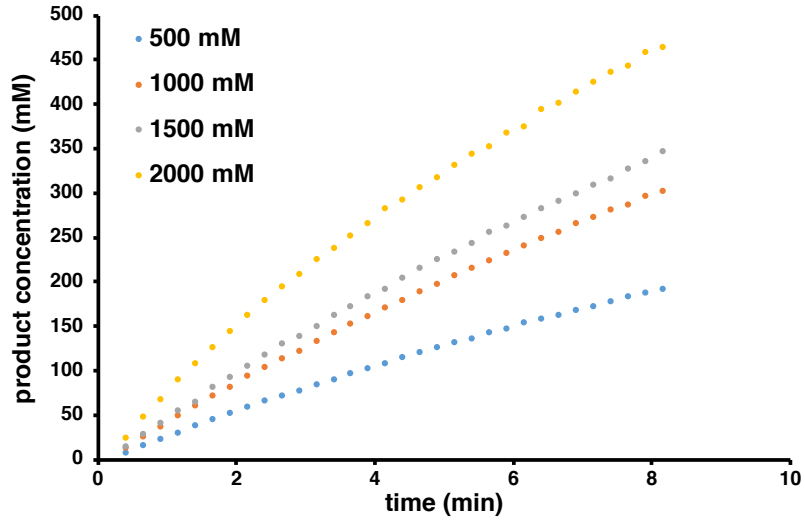


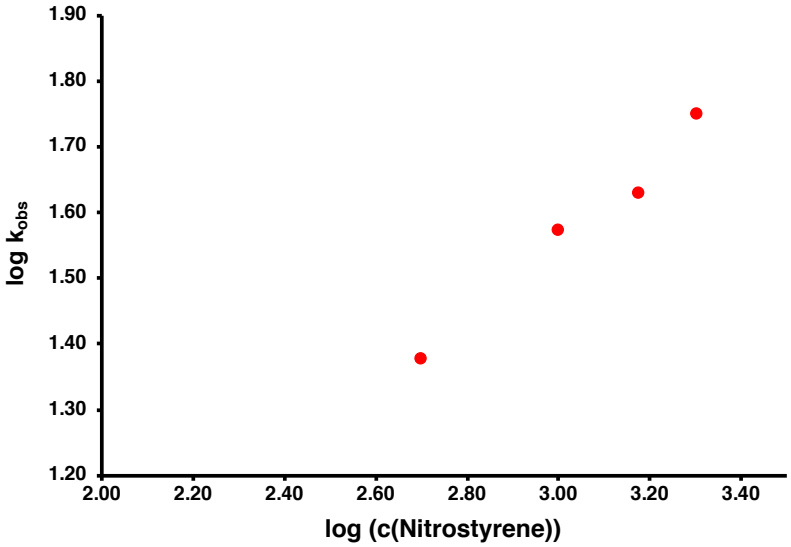
c(Nitrostyrene) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
500	2.70	1.409	0.004	0.149	0.003	352.3
1000	3.00	1.904	0.004	0.280	0.002	476.0
1500	3.18	2.253	0.005	0.353	0.002	450.6
2000	3.30	2.520	0.004	0.401	0.002	630.0

rate order of nitrostyrene: 0.42±0.01.

Rate Order of Nitrostyrene for 2 (3 mol%):

Variation of the nitrostyrene concentration (c(butanal) = 1.5 M):



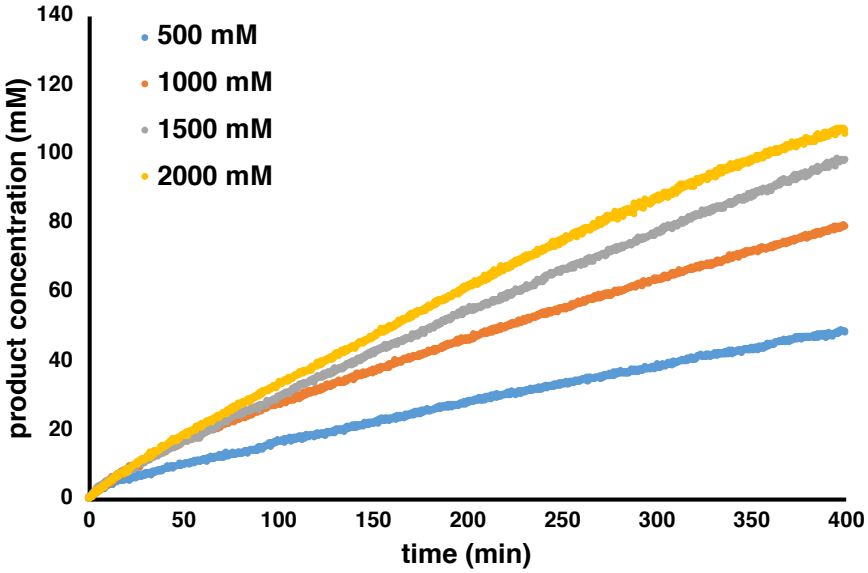


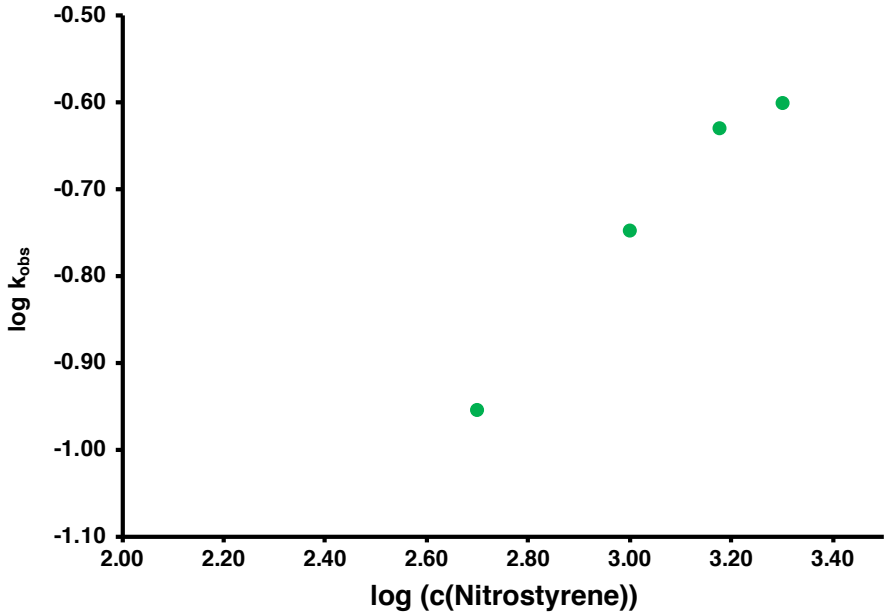
c(Nitrostyrene) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
500	2.70	23.76	0.30	1.376	0.012	80.3
1000	3.00	37.41	0.46	1.573	0.012	81.5
1500	3.18	42.45	0.52	1.628	0.012	81.2
2000	3.30	56.19	1.13	1.750	0.020	49.8

rate order of nitrostyrene: 0.58±0.07.

Rate Order of Nitrostyrene for 2b (3 mol%):

Variation of the nitrostyrene concentration (c(butanal) = 1.5 M):



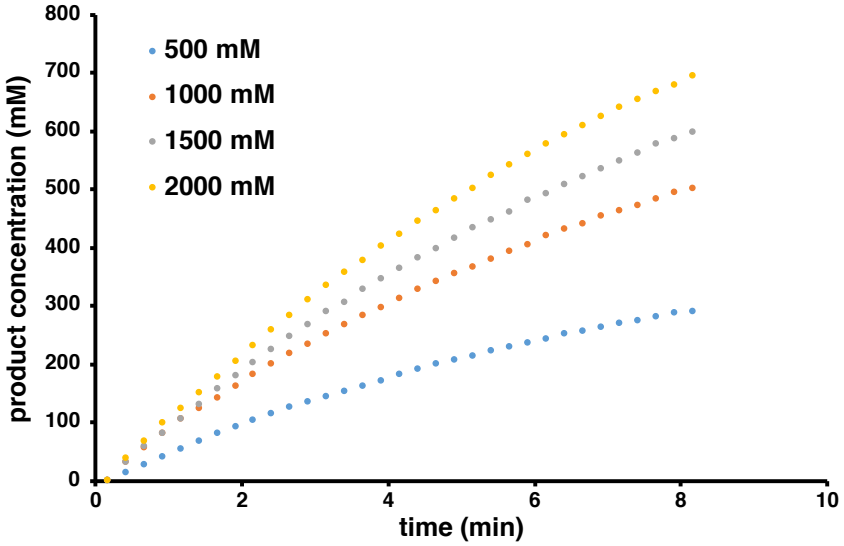


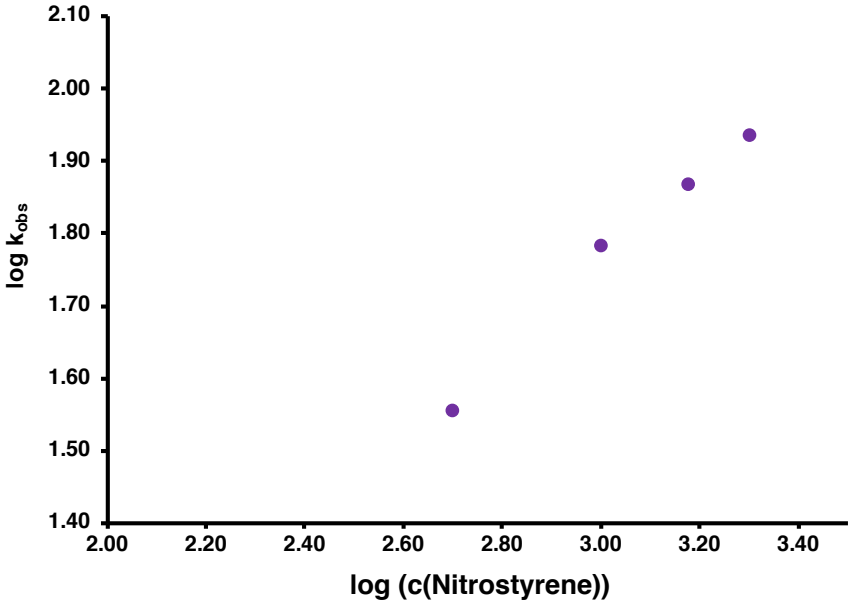
c(Nitrostyrene) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
500	2.70	0.1111	0.0001	-0.954	0.001	1111.0
1000	3.00	0.1787	0.0003	-0.748	0.002	595.7
1500	3.18	0.2342	0.0002	-0.630	0.001	1171.0
2000	3.30	0.2502	0.0005	-0.602	0.002	500.4

rate order of nitrostyrene: 0.63±0.05.

Rate Order of Nitrostyrene for 2c (3 mol%):

Variation of the nitrostyrene concentration (c(butanal) = 1.5 M):



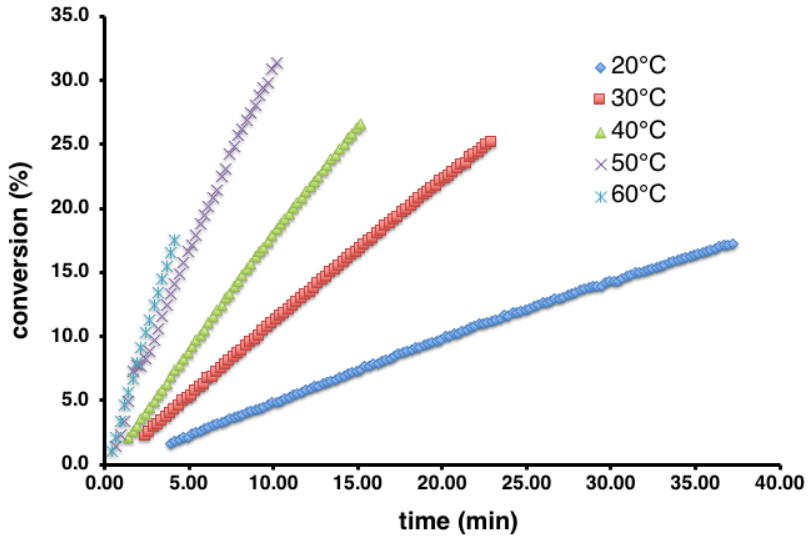


c(Nitrostyrene) (mM)	log (conc)	k_{obs}	SE of k_{obs}	log(k_{obs})	SE in perc	1/(SE in perc)
500	2.70	35.78	0.85	1.554	0.024	41.9
1000	3.00	60.63	1.40	1.783	0.023	43.4
1500	3.18	73.69	1.51	1.867	0.021	48.7
2000	3.30	86.02	1.76	1.935	0.020	48.9

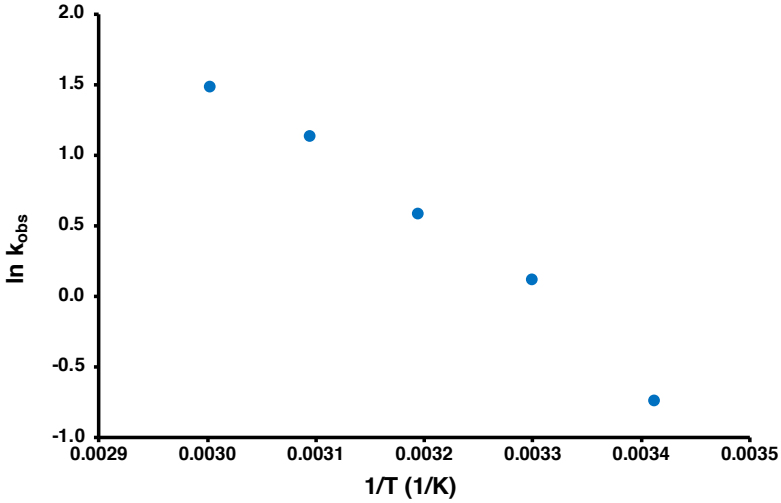
rate order of nitrostyrene: 0.63±0.05.

Activation Energy of 2a:

Variation of the temperature (c(nitrostyrene)= 0.5 M, c(butanal)= 1.5 M):



Arrhenius Plot:

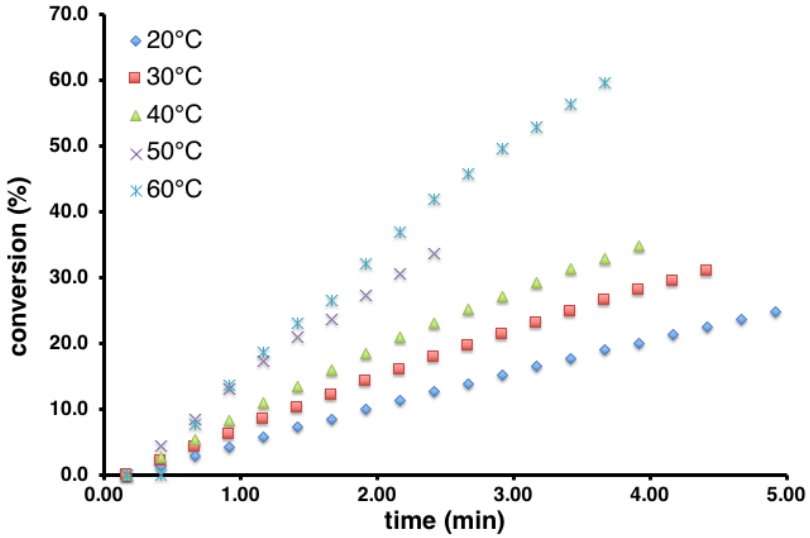


T (°C)	T (K)	1/T	k_{obs}	SE of k_{obs}	ln(k_{obs})	SE in perc	1/(SE in perc)
20	293.15	0.0034	0.476	0.002	-0.7423	0.0042	238.0
30	303.15	0.0033	1.126	0.002	0.1187	0.0018	563.0
40	313.15	0.0032	1.799	0.006	0.5872	0.0033	299.8
50	323.15	0.0031	3.121	0.024	1.1382	0.0077	130.0
60	333.15	0.0030	4.427	0.031	1.4877	0.0070	142.8

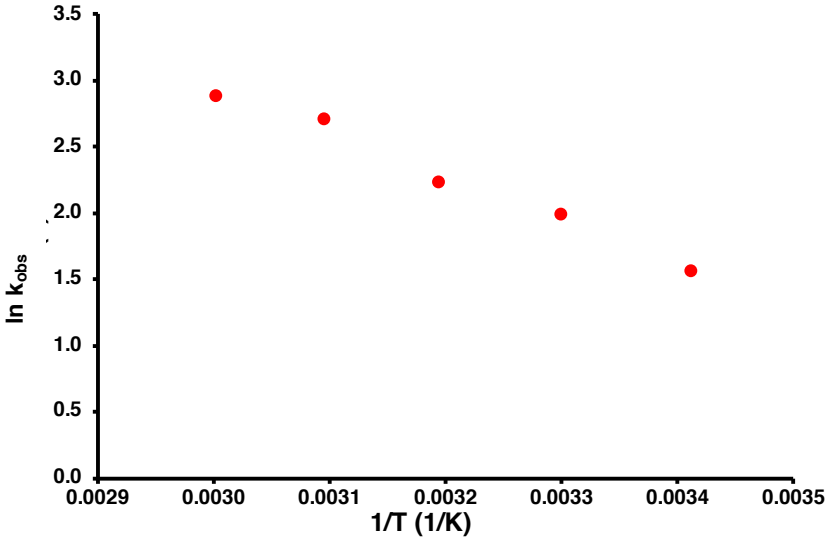
Slope of the Arrhenius plot: -5446.7±600.3 K, activation energy: 10.8±1.2 kcal/mol.

Activation Energy of 2:

Variation of the temperature (c(nitrostyrene) = 0.5 M, c(butanal) = 1.5 M):



Arrhenius Plot:

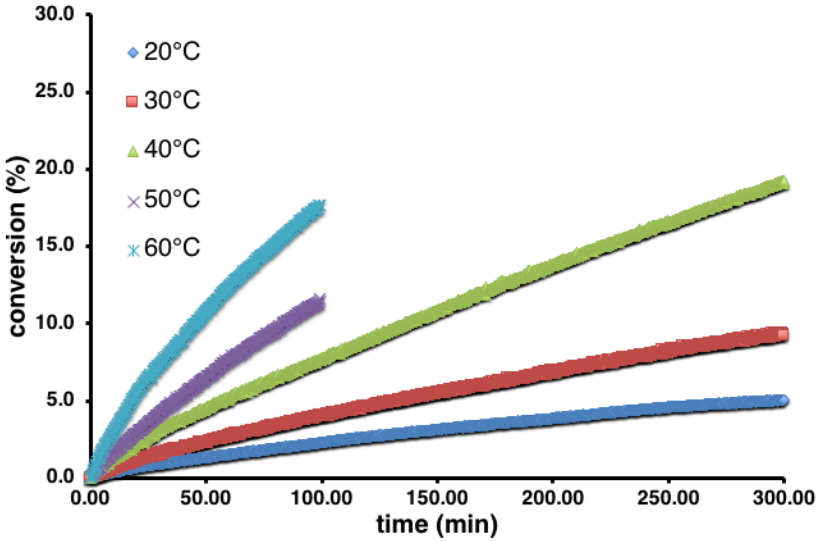


T (°C)	T (K)	1/T	k_{obs}	SE of k_{obs}	ln(k_{obs})	SE in perc	1/(SE in perc)
20	293.15	0.0034	4.77	0.06	1.5621	0.0128	78.2
30	303.15	0.0033	7.32	0.10	1.9901	0.0134	74.7
40	313.15	0.0032	9.33	0.18	2.2330	0.0197	50.7
50	323.15	0.0031	14.98	0.40	2.7065	0.0268	37.3
60	333.15	0.0030	17.93	0.42	2.8865	0.0236	42.3

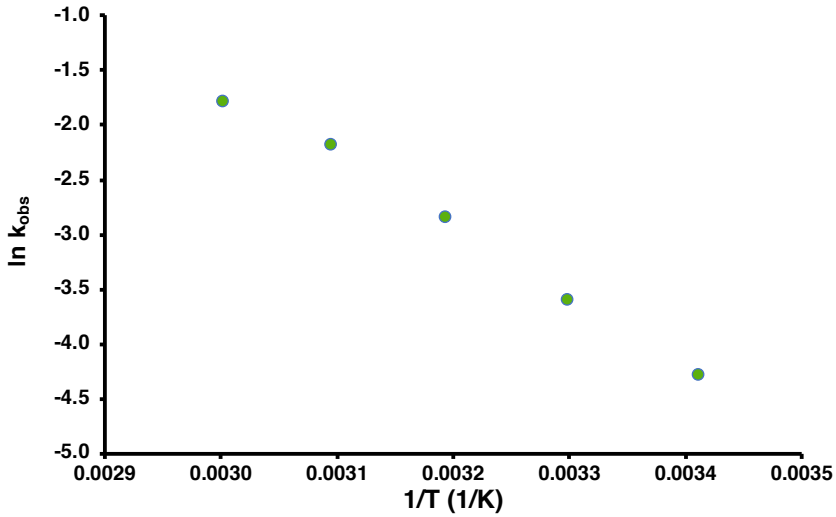
Slope of the Arrhenius plot: -3375.2±234.2 K, activation energy: 6.7±0.5 kcal/mol.

Activation Energy of 2b:

Variation of the temperature (c(nitrostyrene) = 0.5 M, c(butanal) = 1.5 M):



Arrhenius Plot:

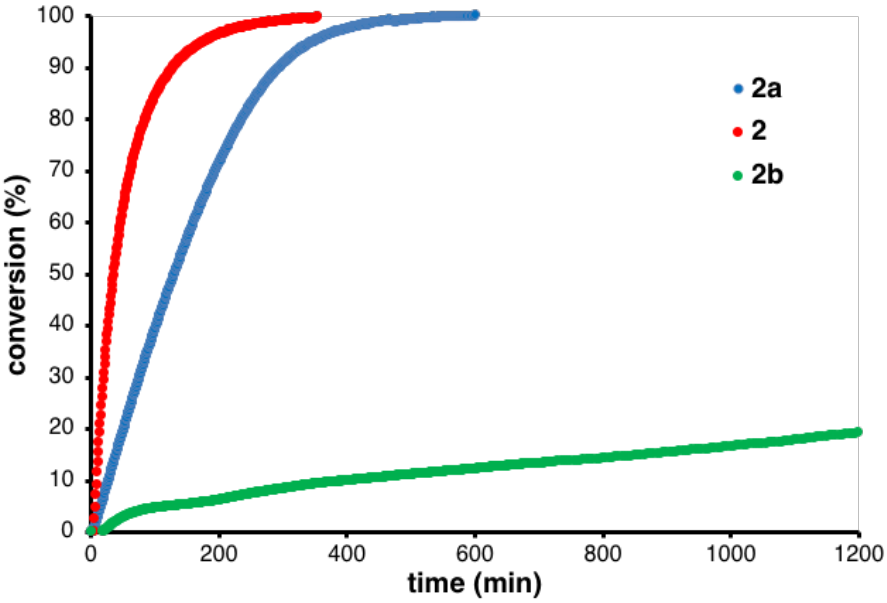


T (°C)	T (K)	1/T	k_{obs}	SE of k_{obs}	ln(k_{obs})	SE in perc	1/(SE in perc)
20	293.15	0.0034	0.0138	0.0001	-4.2831	0.0044	226.2
30	303.15	0.0033	0.0273	0.0001	-3.6009	0.0026	390.0
40	313.15	0.0032	0.0584	0.0001	-2.8404	0.0015	687.1
50	323.15	0.0031	0.1129	0.0004	-2.1813	0.0034	297.9
60	333.15	0.0030	0.1687	0.0010	-1.7796	0.0057	176.1

Slope of the Arrhenius plot: -6560.1±418.7 K, activation energy: 13.0±0.8 kcal/mol.

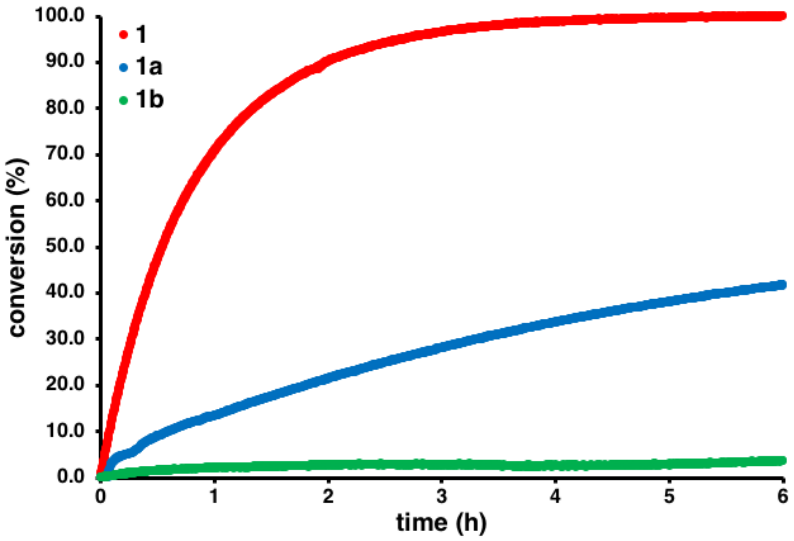
5.2 Kinetic Profiles Using 1 mol% of Catalysts 2a, 2 and 2b

The *in situ* IR experiments were also performed using previously established standard reaction conditions for the tripeptide catalyzed conjugate addition reaction (1 mol% peptide TFA salt, 1 mol% NMM, 1 equiv. nitrostyrene (0.5 M), 1.5 equiv. butanal (0.75 M)).[3,4]



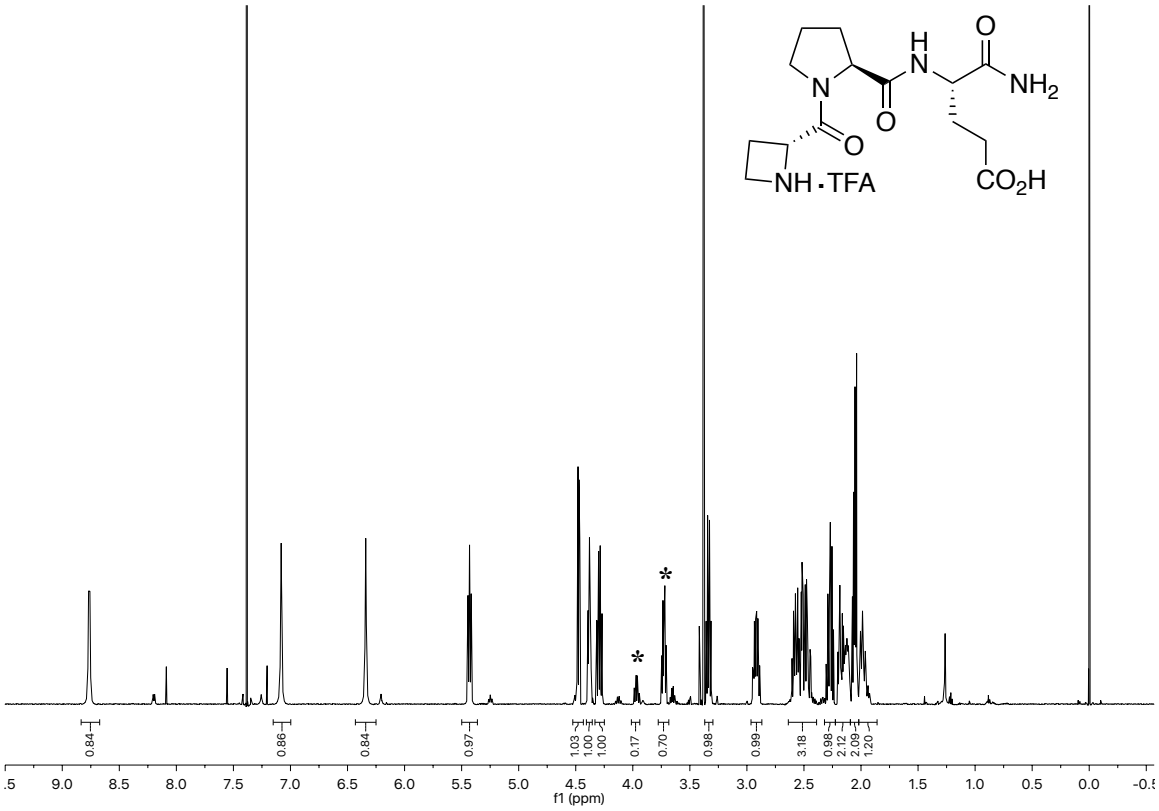
5.3 Kinetic Profiles Using 3 mol% of Catalysts 1a, 1 and 1b

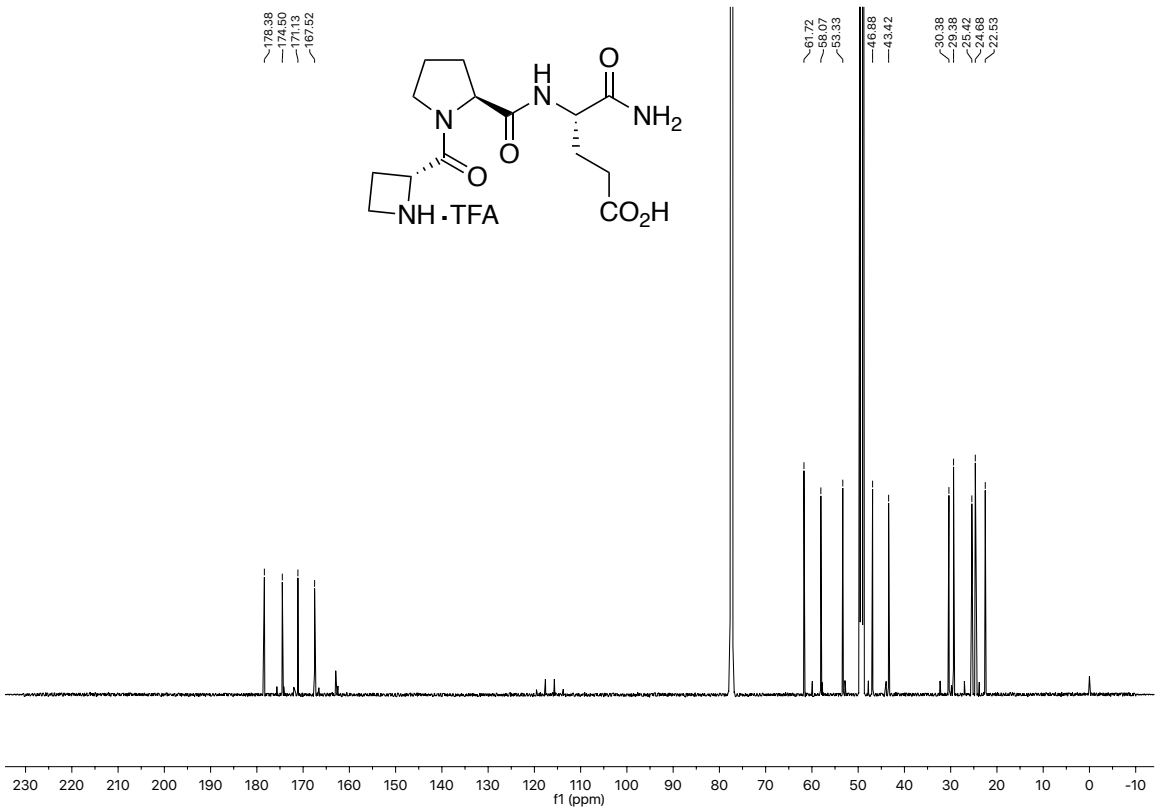
The *in situ* IR experiments were also performed with the catalysts H-DAze-Pro-Glu-NH_2 **1a**, H-DPro-Pro-Glu-NH_2 **1** and H-DPip-Pro-Glu-NH_2 **1b** using the same reaction conditions as for **2a**, **2** and **2b** (3 mol% peptide TFA salt, 3 mol% NMM, 1 equiv. nitrostyrene (0.5 M), 3 equiv. butanal (1.5 M)).



6. NMR Spectra of the Peptides in $CDCl_3/CD_3OH$ 9:1

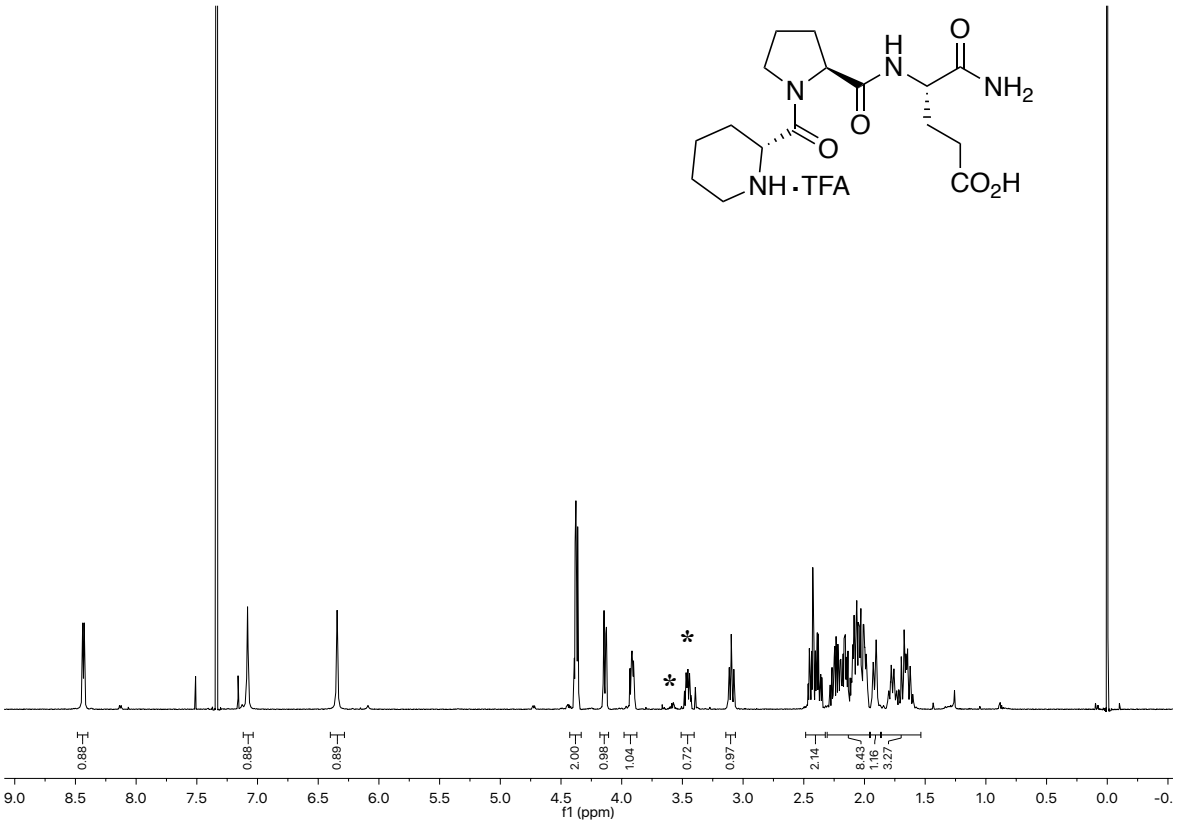
TFA-salt of H-DAze-Pro-Glu-NH_2 **1a**

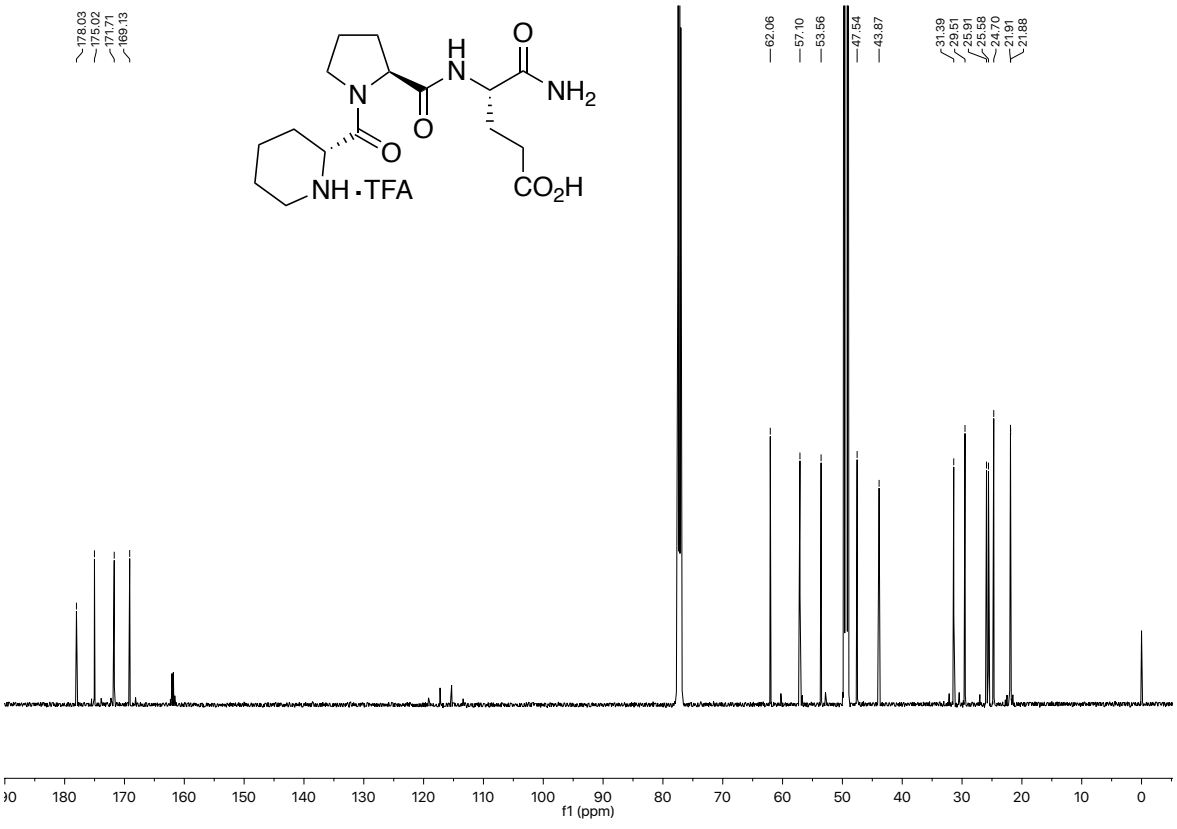




***** Reduced signal intensity due to solvent (CD_3OH) suppression.

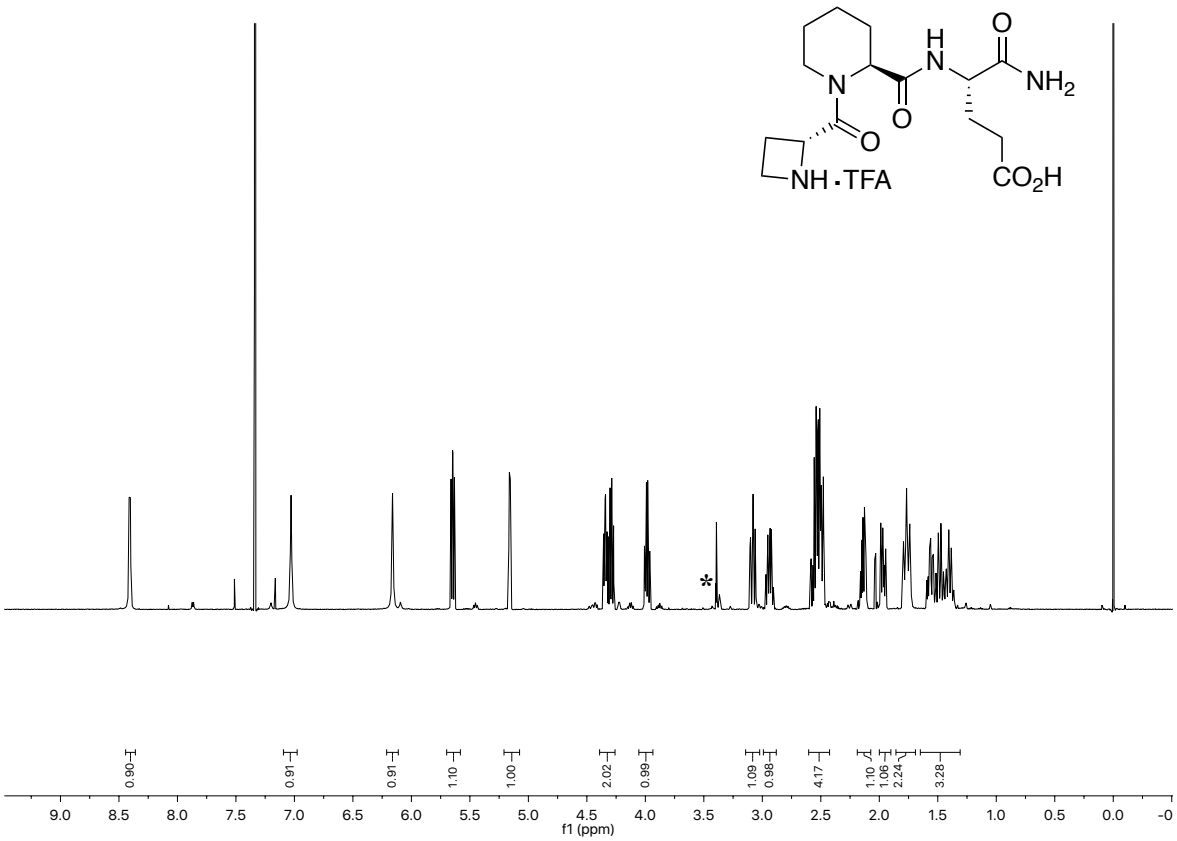
TFA-salt of H-DPip-Pro-Glu-NH_2 **1b**

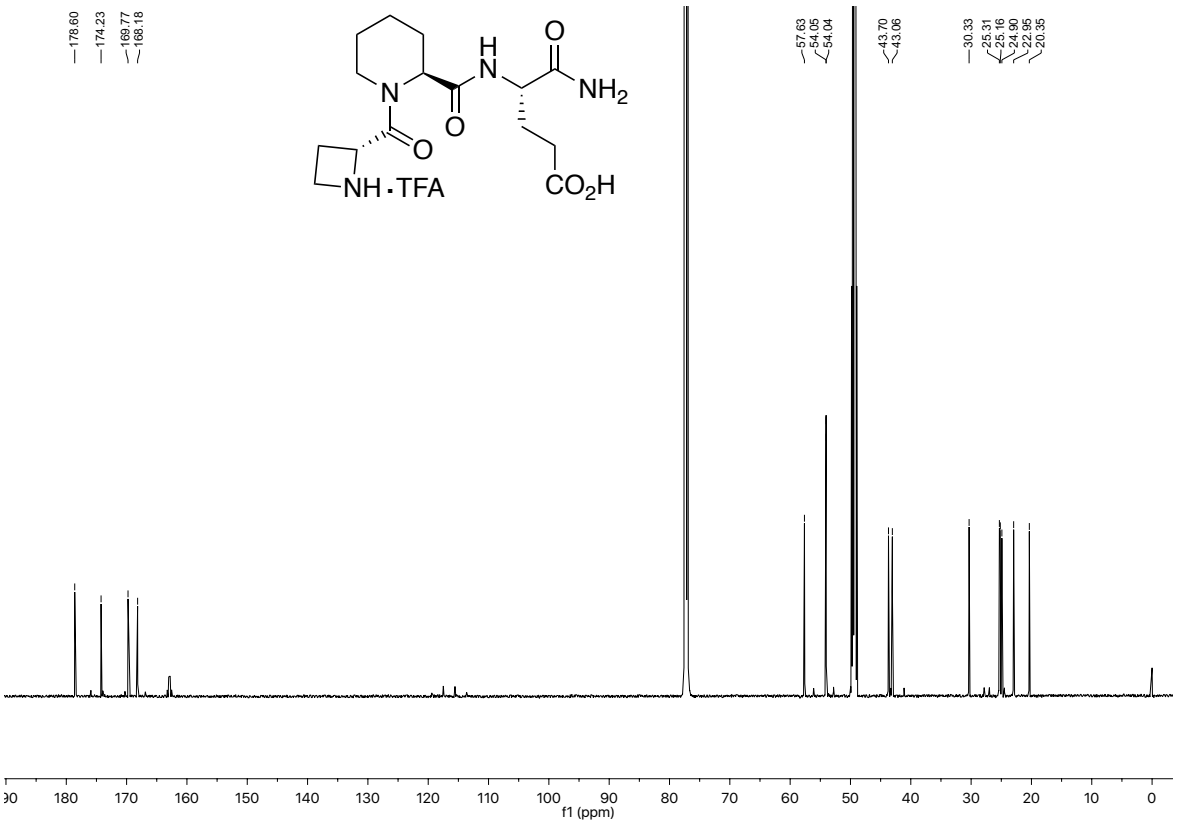




***** Reduced signal intensity due to solvent (CD_3OH) suppression.

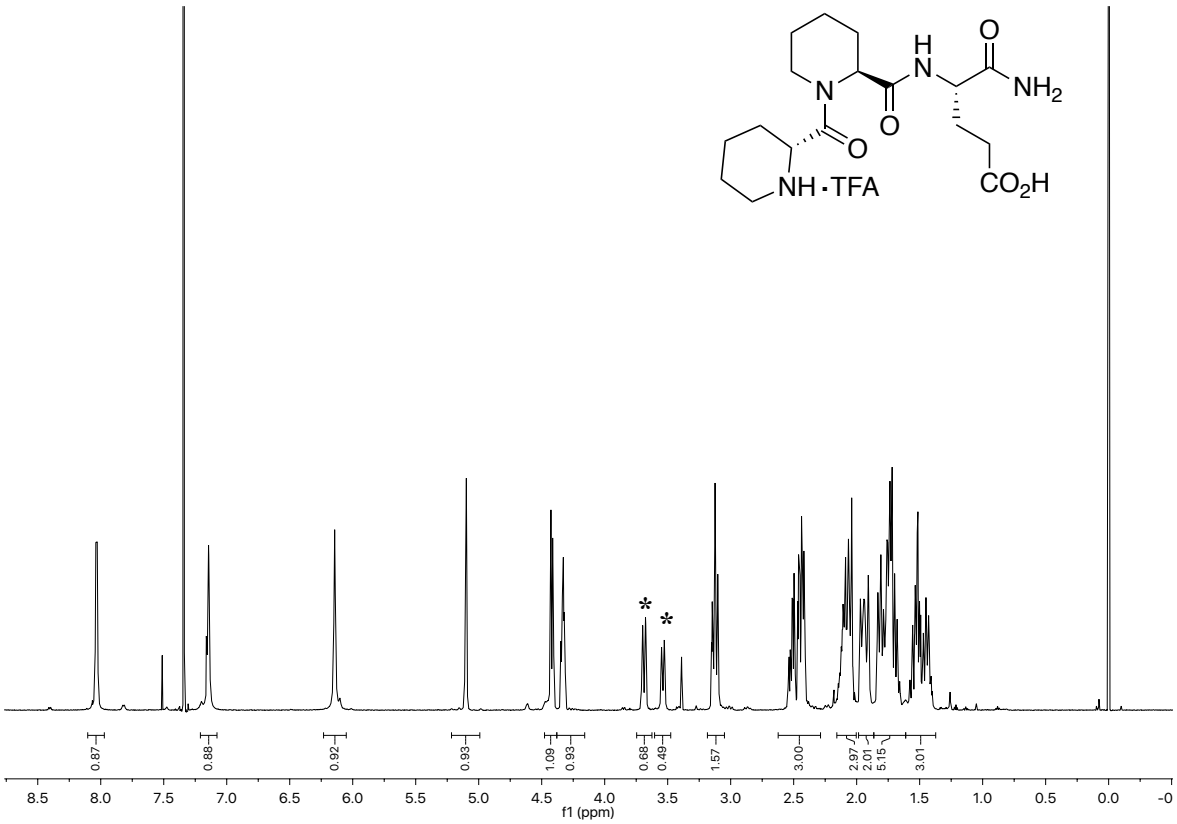
TFA-salt of H-DAze-Pip-Glu-NH_2 **2a**

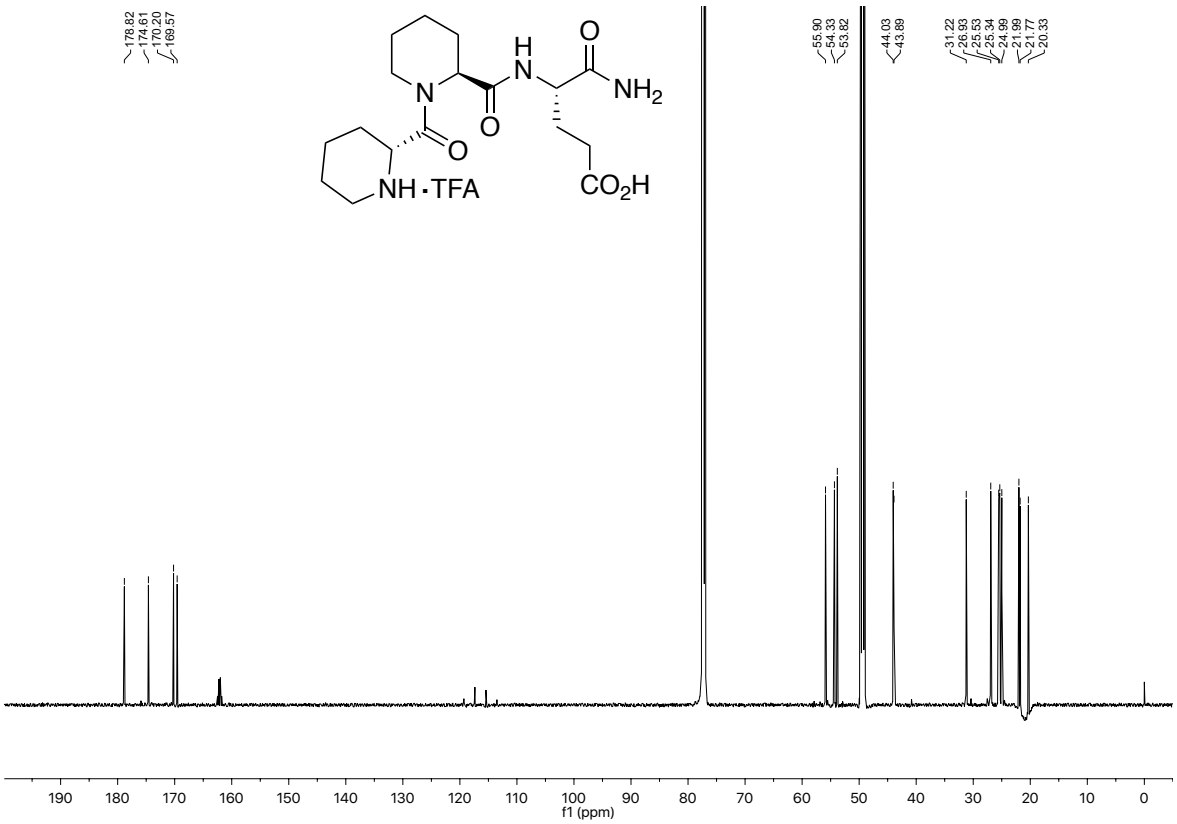




***** Reduced signal intensity due to solvent (CD_3OH) suppression.

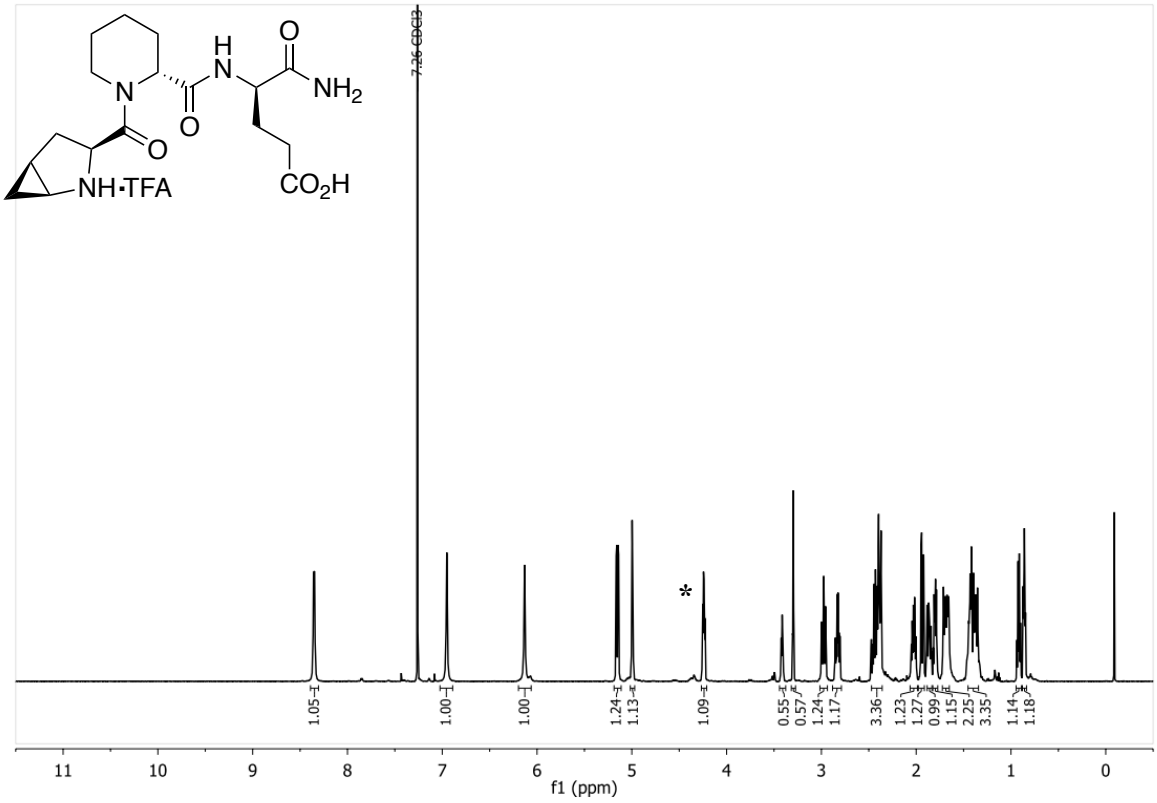
TFA-salt of H-DPip-Pip-Glu-NH_2 **2b**

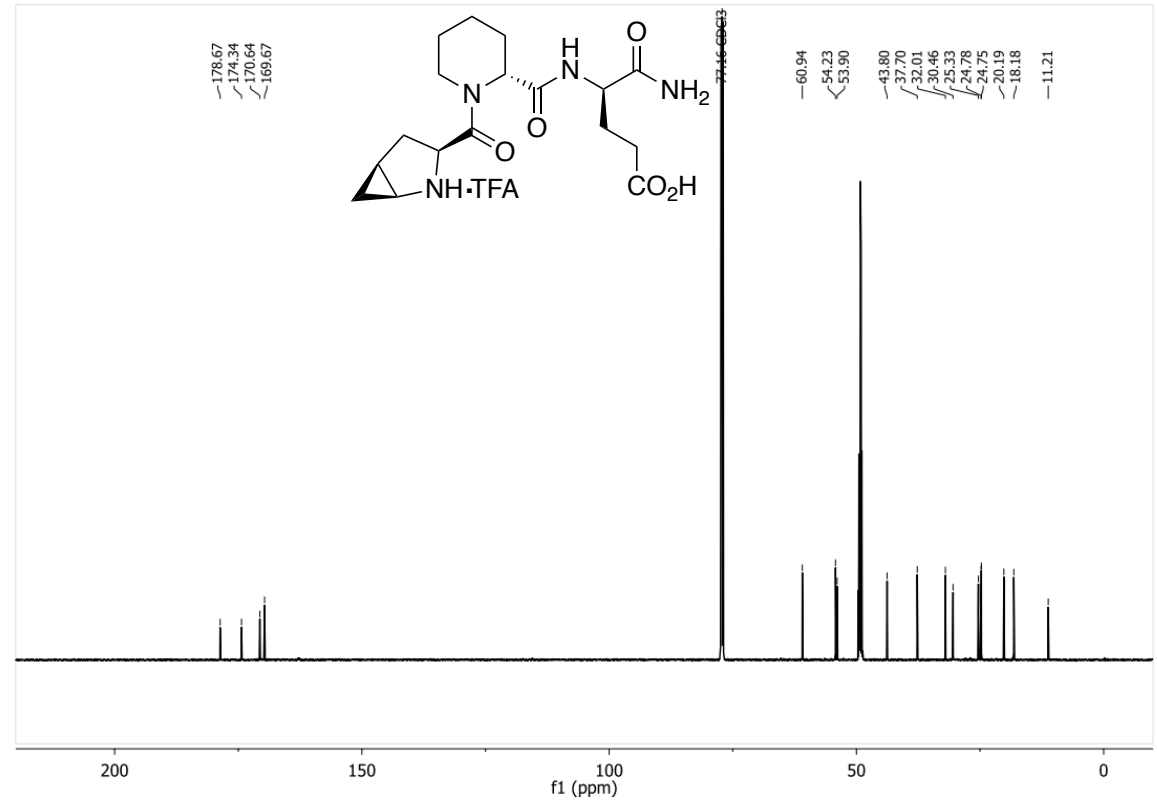




***** Reduced signal intensity due to solvent (CD_3OH) suppression.

TFA-salt of H-MetPro-DPip-DGlu-NH_2 **2c**



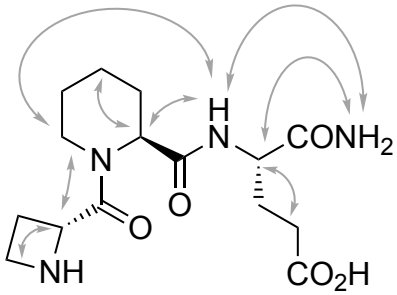


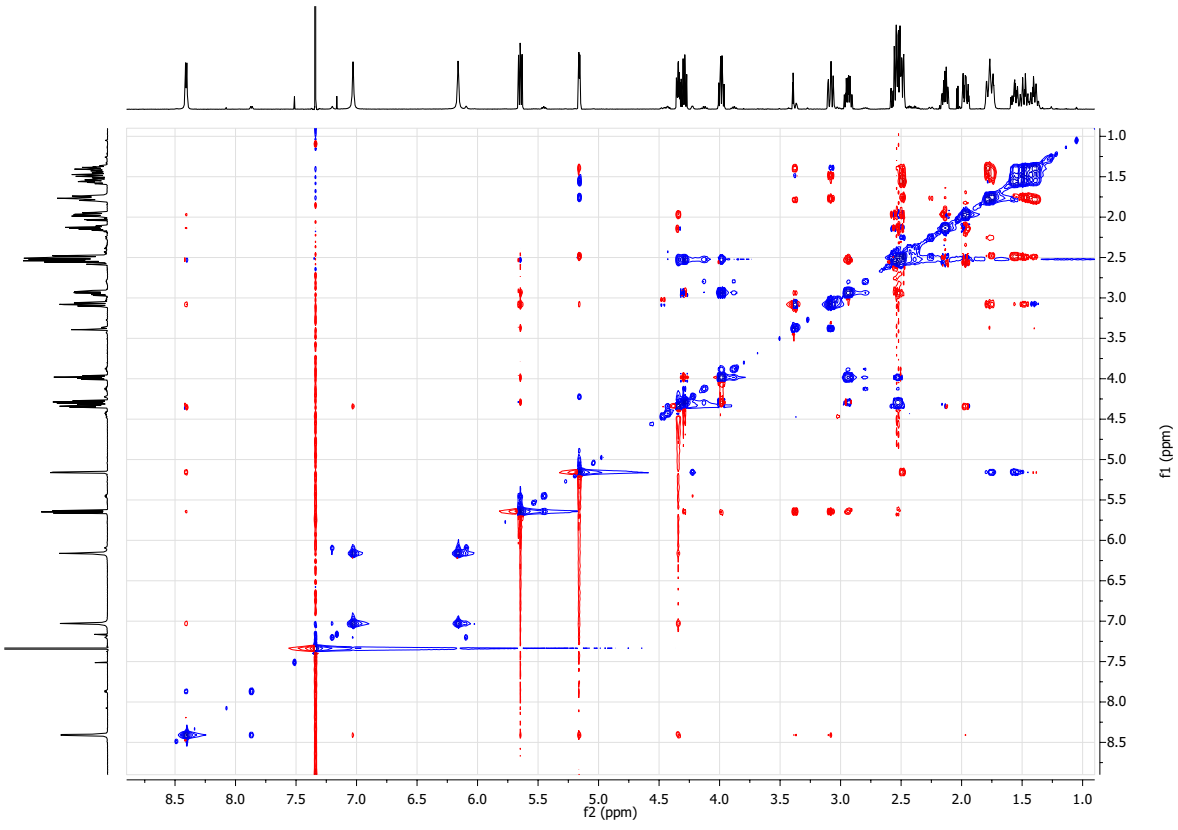
***** Reduced signal intensity due to solvent (CD_3OH) suppression.

7. ROESY Spectra of the TFA-salts of 2a, 2, and 2b in $CDCl_3/CD_3OH$ 9:1

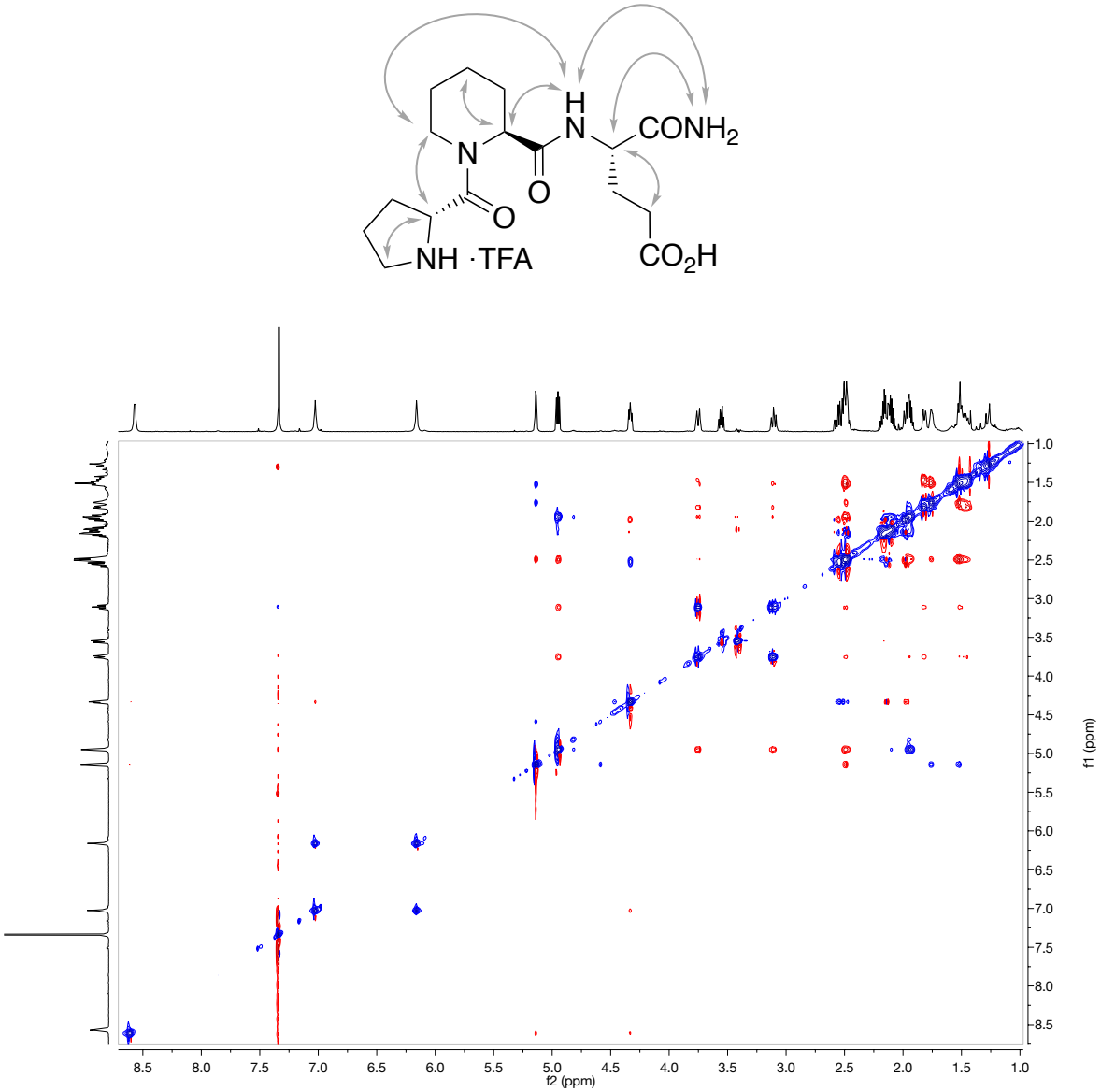
Only non-vicinal NOEs are indicated with arrows.

H-DAze-Pip-Glu-NH_2 **2a**



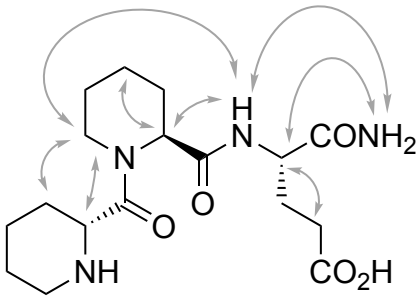


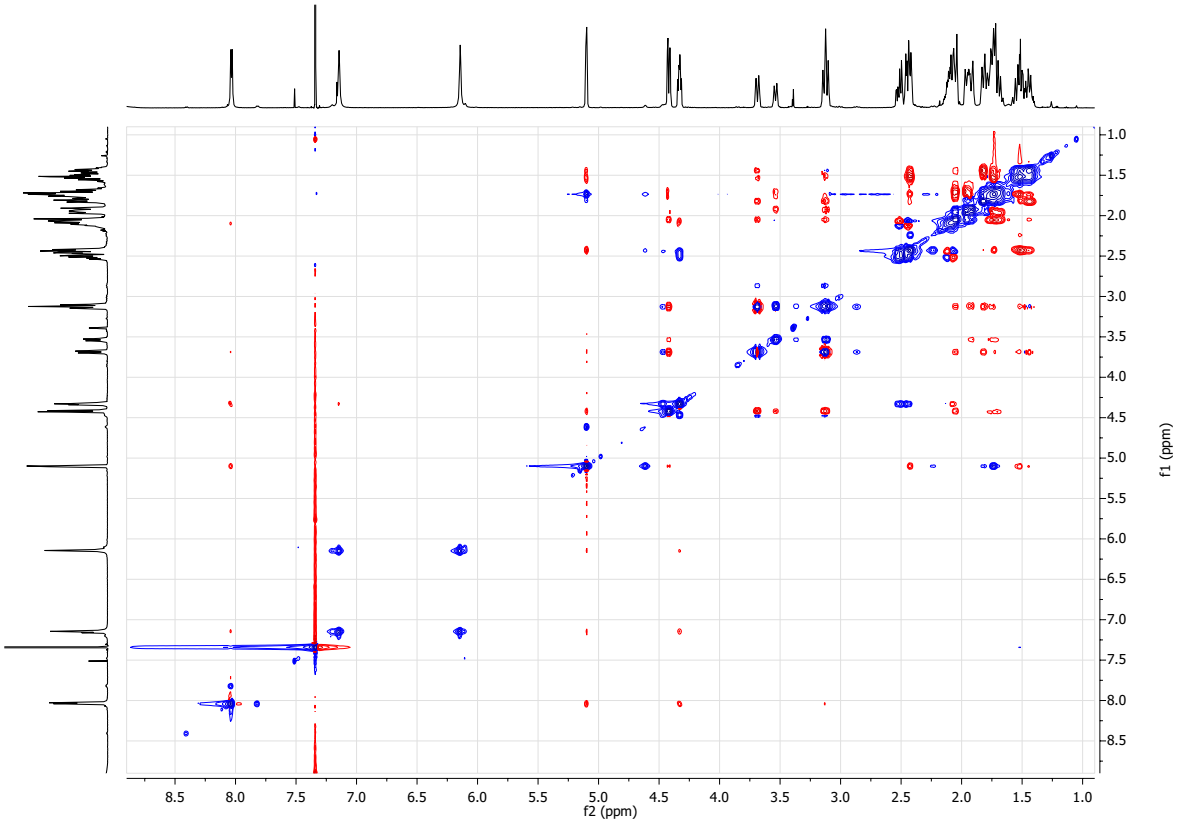
H-DPro-Pip-Glu-NH_2 **2**



Spectrum taken from ref. 4

H-DAze-Pip-Glu-NH_2 **2b**





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