Synthesis and Conformational Studies of $\alpha/\beta^{2,3}$-Peptides Derived from Alternating $\beta^{2,3}$-Amino Acids and L-Ala Repeats

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Contents

Conformational studies of peptides 4 and 5:

Like other peptides, the NMR studies of peptides **4** and **5** were undertaken in ~ 5mM $CDCl_3$ solution. The $^3J_{NH\text{-}C\beta H}$ > 9.0 Hz, imply *anti*-periplanar disposition of the NH and CβH protons, which is consistent with the dihedral angle C(O)-N-Cβ-Cα (ϕ_β) ~ 120°. Additionally small values of $^3J_{C\alpha H\text{-}C\beta H}$ < 3.5 Hz, correspond to N-Cβ-Cα-C(O) (θ_β) ~ ± 60°. The side chain conformations are is discussed in the following section along with other peptide.

Side chain conformations for the peptides:

a) $\beta^{2,3}$-Caa-allyl group:

For monomer (**1** and **2**) and dimer (**4** and **5**), the two $^3J_{C\alpha H\text{-}C3'H}$ are ~ 8.5 Hz and ~ 6.5 Hz, which along with one strong and other weak CβH/C3'H nOe correlation, support predominance of dihedral angle Cβ-Cα-C3'-Cγ (χ1') ~ 180° and allows prochiral assignment of C3'H protons. Thus, the C3'proton with $^3J_{C\alpha H\text{-}C3'H}$ ~ 8.5Hz and weak nOe correlation (W) with CβH proton was assigned as a C3'H(*pro-S*), and the second C3'proton with $^3J_{C\alpha H\text{-}C3'H}$ ~ 6.5Hz and strong intra-residue nOe correlation (S) with CβH was then assigned as a C3'H(*pro-R*). The $^3J_{C\beta H\text{-}C4H}$ ~ 7.8 Hz are not very distinctive and arise probably due to conformational averaging about Cβ-C4 bond.

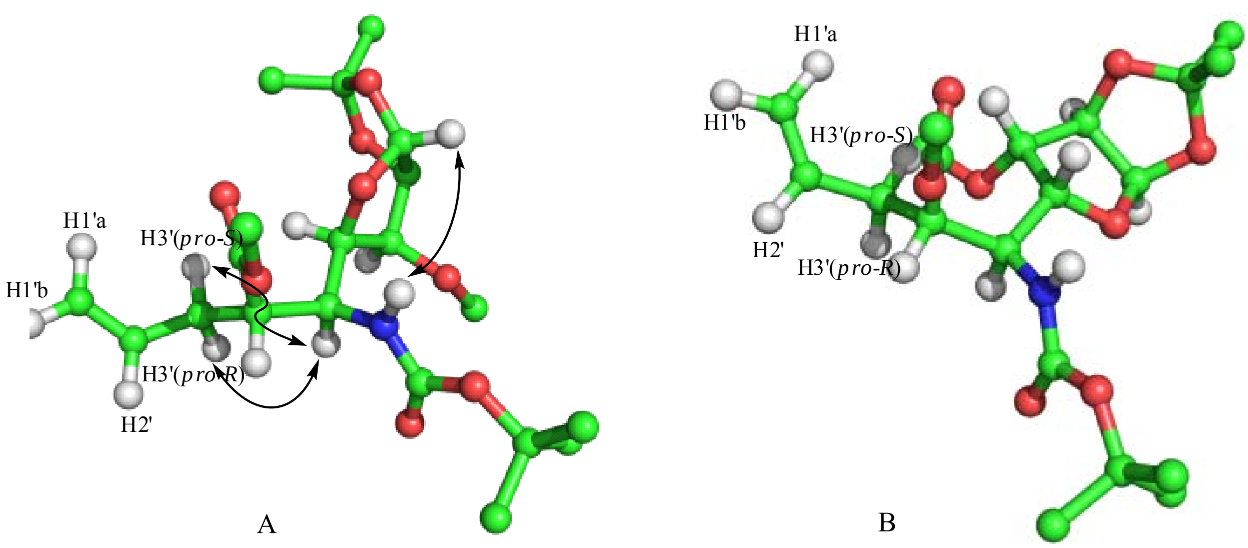


Figure *S1*. Side chain conformation of C-allyl substituted $\beta^{2,3}$-Caa. (A) with χ1 ~ 60° and (B) with χ1 ~ 180°.

Though we have reported the side chain assignments and conformations for some of the peptides in the main text, the details for all of them are not discussed. In this section the results for all the peptides have been analyzed. For all the larger peptides, the first residue is L-Ala, thus the β-residues occupy the positions as residue 2, 4 or 6. An interesting observation emerged from the studies that the stereospecific assignments of the C3' protons in the allyl groups in $\beta^{2,3}$-Caa(2) residues (peptides **6**, **8**, **11**, **13a, 14**, and **16**) could not be achieved. However in these residues with ${}^{3}J_{C\beta H\text{-}C4H}$ > 9 Hz, predominance of N-Cβ-C4-C3 (χ1) ~ 180° is implied (Figure ***S1***B). On the other hand for the allyl groups in $\beta^{2,3}$-Caa(4) and $\beta^{2,3}$-Caa(6) (peptides **8**, **13a**, **14** , and **16)**, it was possible to make stereospecific assignments of C3' protons in addition with ${}^{3}J_{C\beta H\text{-}C4H}$ < 6.5 Hz (for the terminal $\beta^{2,3}$-Caa residues), the χ1 appears to differ from a value of ~ 180° with a propensity for ~ 60° (Figure ***S1***A). Like **1** and **4,** the C3' proton in $\beta^{2,3}$-Caa(4) and $\beta^{2,3}$-Caa(6) residues of peptides **8**, **10**, and **16** having ${}^{3}J_{C\alpha H\text{-}C3'H}$ < 7 Hz and showing strong nOe correlation with CβH, were assigned as C3'H(*pro-R*). Similarly, the protons with ${}^{3}J_{C\alpha H\text{-}C3'H}$ > 9 Hz and showing weak nOe correlation with CβH, were assigned as C3'H(*pro-S*) (like in Figure ***S1***A).

$\beta^{2,3}$-Caa-propargyl group

For **2** and **5**, C3' protons display ${}^{3}J_{C\alpha H\text{-}C3'H}$ ~ 6.2 Hz and ~ 9.2 Hz, along with one strong(S) and other weak(W) nOe correlation involving C3' protons (CβH/C3'H, C3'H/C3H) not only enable us to make prochiral-assignments but also fix the dihedral angle with χ1' ~ 180°. Thus, the C3' protons with ${}^{3}J_{C\alpha H\text{-}C3'H}$ ~ 9.2 Hz and showing weak nOe correlation C3'H/CβH, were assigned as C3'H(*pro-S*). Similarly, the protons with ${}^{3}J_{C\alpha H\text{-}C3'H}$ ~ 6.2 Hz and strong nOe correlation C3'H/CβH were assigned as C3'H(*pro-R*). In addition ${}^{3}J_{C\beta H\text{-}C4H}$ < 6.8 Hz, along with medium intensity (M) NH(*i*)/C1H(*i*) nOe correlations suggest structures with predominance of χ1 ~ 60° (Figure ***S2*A**).

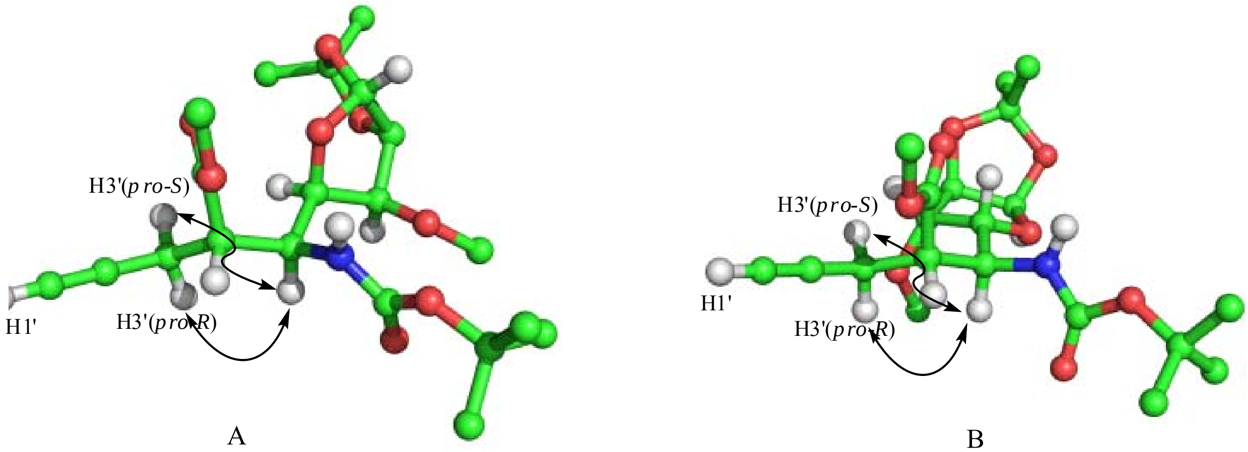


Figure *S2*. Side chain conformation of C-propargyl substituted $\beta^{2,3}$-Caa. (A) with $\chi1 \sim 60°$ and (B) with $\chi1 \sim 180°$.

The propargyl group appears in peptides **7**, **9**, **12**, **15** and **17**. For these peptides, the $^3J_{C\alpha H\text{-}C3'H}$ are either in the range of 9.6-11.0 Hz or 4.8-7.6 Hz, implying constrained values of the dihedral angle $\chi1'$. As discussed above, even for propargyl group, the C3' protons with $^3J_{C\alpha H\text{-}C3'H}$ > 9.6 Hz and weak nOe correlation with CβH and strong nOe with C3H, were assigned as C3'H(*pro-S*). Similarly the C3' proton with C3H/C3'H (W) and CβH/C3'H (S) nOe correlations and $^3J_{C\alpha H\text{-}C3'H} \leq 7.8$ Hz were assigned C3'H(*pro-R*). The small values of $^3J_{C\beta H\text{-}C4H} < 6.4$ Hz in $\beta^{2,3}$-Caa(4) and $\beta^{2,3}$-Caa(6) residues in peptides **9** and **17**, along with medium intensity intra-residue NH/C1H support $\chi1 \sim 60°$ (Figure ***S2***A). However, the $\beta^{2,3}$-Caa(2) residue in peptides **7**, **9**, **12** and **15** and $\beta^{2,3}$-Caa(4) residues in **12**, **15** and **17**show large $^3J_{C\beta H\text{-}C4H} > 9.0$ Hz value**,** which is distinctive and imply preponderance of $\chi1 \sim 180°$ (Figure ***S2***B).

Solvent Titration Studies:

***Table S1*: Variation of δNH (in ppm) on addition of DMSO-d_6 to 600µL solution of 6 in $CDCl_3$**

Vol. of DMSO-d_6 added (µL)	NH(1)	NH(2)	NH(3)
0	5.01	7.51	7.46
50	5.65	7.48	7.71
100	6.05	7.46	7.87
150	6.36	7.47	8.00
200	6.56	7.48	8.10
250	6.70	7.49	8.17
300	6.80	7.50	8.24
ΔδNH	1.79	- 0.01	0.78

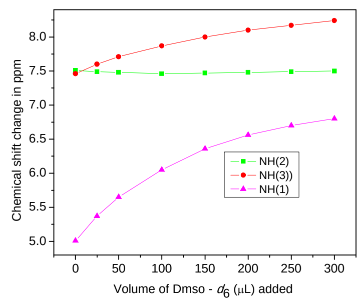


***Table S2*: Variation of δNH on addition of DMSO-d_6 to 600µL solution of 7 in $CDCl_3$**

Vol. of DMSO-d_6 added (µL)	NH-1	NH-2	NH-3
0	5.00	7.40	7.46
50	5.57	7.37	7.72
100	6.01	7.37	7.93
150	6.30	7.37	8.07
200	6.49	7.39	8.17
300	6.70	7.42	8.31
ΔδNH	1.70	0.02	0.85

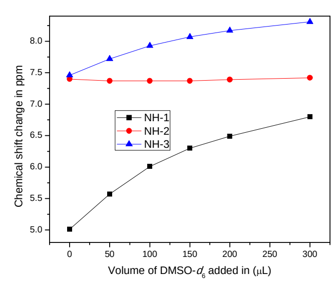


Table S3: Variation of δNH on addition of DMSO-d_6 to 600μL solution of 8 in $CDCl_3$

Vol. of DMSO-d_6 added (μL)	NH(1)	NH(2)	NH(3)	NH(4)
0	5.02	7.96	7.32	6.40
50	5.64	7.91	7.72	6.76
100	6.04	7.89	7.91	6.97
150	6.33	7.89	8.01	7.14
200	6.54	7.89	8.07	7.27
250	6.68	7.89	8.11	7.36
300	6.76	7.89	8.14	7.41
ΔδNH	1.76	0.07	0.82	1.01

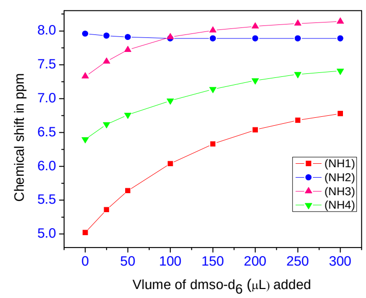


Table S4: Variation of δNH on addition of DMSO-d_6 to 600μL solution of 9 in $CDCl_3$

Vol. of DMSO-d_6 added (μL)	NH-1	NH-2	NH-3	NH-4
0	5.04	7.83	7.37	6.37
50	5.57	7.77	7.76	6.75
100	5.95	7.76	7.96	6.99
150	6.23	7.78	8.05	7.17
200	6.45	7.80	8.11	7.32
250	6.61	7.81	8.15	7.43
300	6.73	7.81	8.18	7.52
ΔδNH	1.69	0.02	0.81	1.15

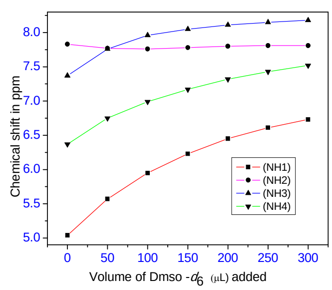


***Table S5*: Variation of δNH on addition of DMSO-d_6 to 600μL solution of 10 in $CDCl_3$**

Vol. of DMSO-d_6 added (μL)	NH(1)	NH(2)	NH(3)	NH(4)
0	5.05	7.58	7.46	6.50
50	5.64	7.62	7.65	6.71
100	6.00	7.65	7.74	6.96
150	6.21	7.68	7.80	7.07
200	6.36	7.70	7.83	7.21
250	6.44	7.70	7.84	7.32
300	6.52	7.71	7.86	7.42
ΔδNH	1.47	0.13	0.40	0.92

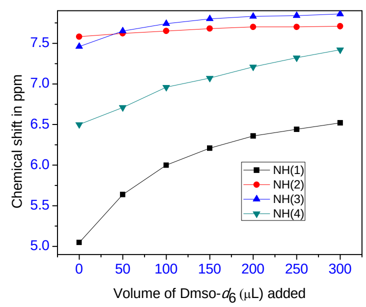


***Table S6*: Variation of δNH on addition of DMSO-d_6 to 600μL solution of 11 in $CDCl_3$**

Vol. of DMSO-d_6 added (μL)	NH(1)	NH(2)	NH(3)	NH(4)
0	4.99	7.90	7.38	6.48
50	5.49	7.90	7.61	6.98
100	5.89	7.94	7.75	7.31
150	6.19	7.97	7.83	7.52
200	6.44	7.99	7.90	7.67
250	6.60	7.99	7.94	7.75
300	6.72	7.99	7.98	7.82
ΔδNH	1.73	0.09	0.60	1.34

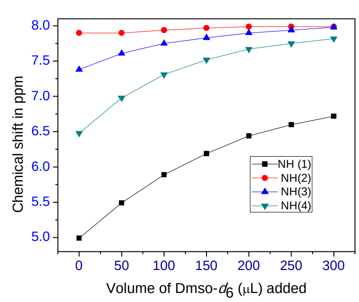


***Table S7*: Variation of δNH on addition of DMSO-d_6 to 600μL solution of **12** in $CDCl_3$**

Vol of DMSO-d_6 added(μL)	NH-1	NH-2	NH-3	NH-4	NH-5
0	4.94	7.99	7.71	7.23	7.93
50	5.61	7.99	7.79	7.41	8.04
100	6.05	7.94	7.85	7.48	8.08
150	6.35	7.91	7.91	7.53	8.11
200	6.54	7.90	7.95	7.56	8.13
250	6.67	7.90	7.99	7.59	8.15
300	6.76	7.89	8.02	7.61	8.16
ΔδNH	1.82	-0.10	0.31	0.38	0.23

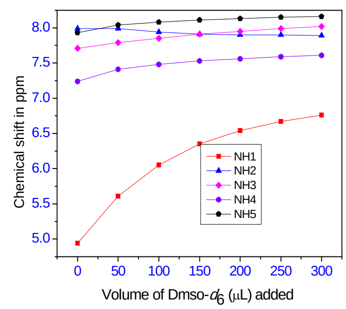


***Table S8*: Variation of δNH on addition of DMSO-d_6 to 600μL solution of **13** in $CDCl_3$**

Vol. of DMSO-d_6 added (μL)	NH(1)	NH(2)	NH(3)	NH(4)	NH(5)
0	5.11	7.87	7.56	7.40	7.60
50	5.61	7.69	7.89	7.33	8.10
100	5.99	7.73	8.02	7.32	8.43
150	6.30	7.77	8.11	7.31	8.63
200	6.53	7.79	8.17	7.32	8.74
250	6.67	7.80	8.22	7.33	8.80
300	6.78	7.80	8.25	7.34	8.85
ΔδNH	1.67	0.07	0.69	0.16	1.25

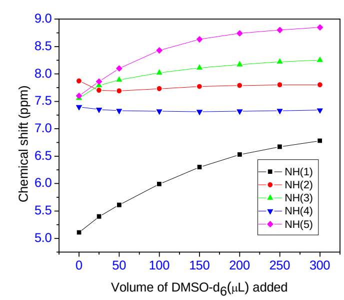


***Table S9*:** Variation of δNH on addition of DMSO-d_6 to 600µL solution of **14** in $CDCl_3$

Vol. of DMSO-d_6 added (µL)	NH(1)	NH(2)	NH(3)	NH(4)	NH(5)	NH(6)
0	4.98	7.74	7.28	7.67	7.10	6.45
50	5.43	7.70	7.63	7.58	7.70	7.15
100	5.82	7.71	7.82	7.58	7.95	7.25
150	6.15	7.74	8.00	7.62	8.14	7.43
200	6.38	7.75	8.11	7.63	8.24	7.54
250	6.56	7.76	8.20	7.64	8.32	7.64
300	6.70	7.78	8.28	7.67	8.40	7.67
ΔδNH	1.72	0.04	1.00	0.00	1.30	1.22

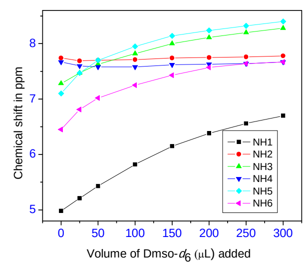


***Table S10*:** Variation of δNH on addition of DMSO-d_6 to 600µL solution of **15** in $CDCl_3$

Vol. of DMSO-d_6 added	NH-1	NH-2	NH-3	NH-4	NH-5	NH-6
0µL	5.10	7.73	7.42	7.63	7.24	6.53
50µL	5.54	7.90	7.98	7.63	7.78	7.13
100µL	5.87	7.86	8.19	7.58	7.96	7.31
150µL	6.13	7.84	8.31	7.57	8.06	7.41
200µL	6.31	7.83	8.38	7.56	8.14	7.48
250µL	6.45	7.82	8.43	7.56	8.19	7.53
300µL	6.56	7.81	8.47	7.56	8.23	7.57
ΔδNH	1.46	0.08	1.05	-0.07	0.99	1.05

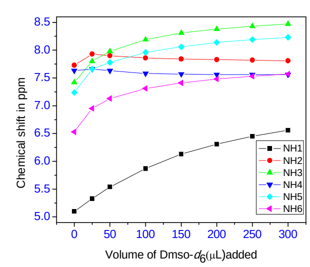


***Table S11*: Variation of δNH on addition of DMSO-d_6 to 600μL solution of 16 in $CDCl_3$**

Vol. of DMSO-d_6 added	NH-1	NH-2	NH-3	NH-4	NH-5	NH-6
0 μL	5.01	8.12	7.65	7.89	7.85	6.56
50 μL	5.51	8.01	7.74	7.92	7.82	6.72
100 μL	5.99	7.96	7.82	7.95	7.82	6.92
150 μL	6.31	7.93	7.89	7.97	7.82	7.10
200 μL	6.53	7.93	7.93	7.98	7.86	7.26
250 μL	6.69	7.90	7.97	7.97	7.86	7.39
300 μL	6.78	7.88	7.97	7.97	7.86	7.46
ΔδNH	1.77	-0.24	0.32	0.08	0.01	0.90

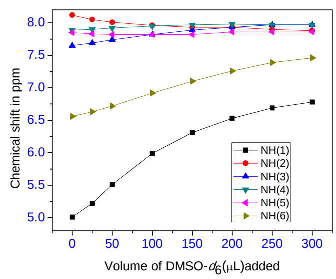


***Table S12*: Variation of δNH on addition of DMSO-d_6 to 600μL solution of 17 in $CDCl_3$**

Vol. of DMSO-d_6 added(μL)	NH-1	NH-2	NH-3	NH-4	NH-5	NH-6
0	5.36	7.59	7.37	7.76	7.42	6.42
50	5.72	7.66	770	7.68	7.99	6.87
100	6.00	7.70	7.80	7.64	8.19	7.07
150	6.19	7.71	7.88	7.65	8.31	7.21
200	6.34	7.72	7.92	7.65	8.38	7.33
250	6.44	7.72	7.95	7.66	8.42	7.43
300	6.52	7.72	7.97	7.67	8.46	7.50
ΔδNH	1.21	0.13	0.6	-0.09	1.04	1.08

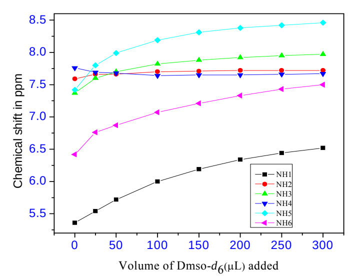


***Table S13*: Side chain $^3J_{C\alpha H\text{-}C3'H}$ and $^3J_{C\beta H\text{-}C4H}$ values in Hz for β^{2,3}-Caa and β^3-Caa residues in peptides 6-12, 13a and 14-17**

Peptides	Residue-2	Residue-4	Residue-6
Peptide **6(A)**	* $^3J_{C\beta H\text{-}C4H}$ = 10.5		
Peptide **7(P)**	* $^3J_{C\beta H\text{-}C4H}$ = 9.8		
peptide **8(A)**	* $^3J_{C\beta H\text{-}C4H}$ = 9.6	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 9.4 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.2 $^3J_{C\beta H\text{-}C4H}$ = 6.2	-
Peptide **9(P)**	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 10.1 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 6.2 $^3J_{C\beta H\text{-}C4H}$ = 9.8	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 9.9 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.1 $^3J_{C\beta H\text{-}C4H}$ = 6.2	-
Peptide **10(A)**	$^3J_{C\beta H\text{-}C4H}$ = 9.4 (**β^3-Caa**)	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 9.4 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.7 $^3J_{C\beta H\text{-}C4H}$ = 6.2	-
Peptide **11(A)**	* $^3J_{C\beta H\text{-}C4H}$ = 9.8	$^3J_{C\beta H\text{-}C4H}$ = 6.2 (**β^3-Caa**)	-
Peptide **12(P)**	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 10.1 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.9 $^3J_{C\beta H\text{-}C4H}$ = 9.3	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 10.8 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 4.8 $^3J_{C\beta H\text{-}C4H}$ = 9.8	
Peptide **13a(A)**	* $^3J_{C\beta H\text{-}C4H}$ = 10.2	$^3J_{C\beta H\text{-}C4H}$ = 9.6 (**β^3-Caa**)	-
Peptide **14(A)**	* $^3J_{C\beta H\text{-}C4H}$ = 9.4	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 9.4 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.7 $^3J_{C\beta H\text{-}C4H}$ = 9.5	$^3J_{C\beta H\text{-}C4H}$ = 6.5 (**β^3-Caa**)
Peptide **15(P)**	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 9.6 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.5 $^3J_{C\beta H\text{-}C4H}$ = 8.8	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 11.0 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 4.9 $^3J_{C\beta H\text{-}C4H}$ = 8.8	$^3J_{C\beta H\text{-}C4H}$ = 6.1 (**β^3-Caa**)
Peptide **16(A)**	* $^3J_{C\beta H\text{-}C4H}$ = 9.9	$^3J_{C\beta H\text{-}C4H}$ = 10.1 (**β^3-Caa**)	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ =9.4 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.2 $^3J_{C\beta H\text{-}C4H}$ = 6.4
Peptide **17(P)**	$^3J_{C\beta H\text{-}C4H}$ = 9.2 (**β^3-Caa**)	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ = 11.0 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 4.9 $^3J_{C\beta H\text{-}C4H}$ = 9.8	$^3J_{C\alpha H\text{-}C3'H(pro\text{-}S)}$ =9.6 $^3J_{C\alpha H\text{-}C3'H(pro\text{-}R)}$ = 5.5 $^3J_{C\beta H\text{-}C4H}$ = 6.4

* Since the stereospecific assignment of C3'H could not be made, no $^3J_{C\alpha H\text{-}C3'H}$ values are reported; (A) and (P) are indicative of the β2-allyl or propargyl substitution in β^{2,3}-Caas, in the corresponding peptides.

Expansions of ROESY spectra

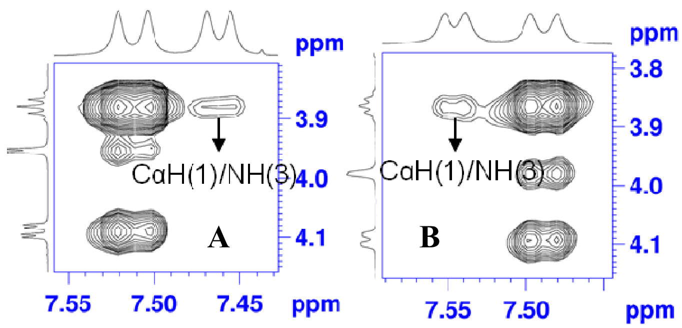


Figure S3: Expansion of ROESY spectrum representing characteristic nOes: (A) Peptide **6** and (B) peptide **7**

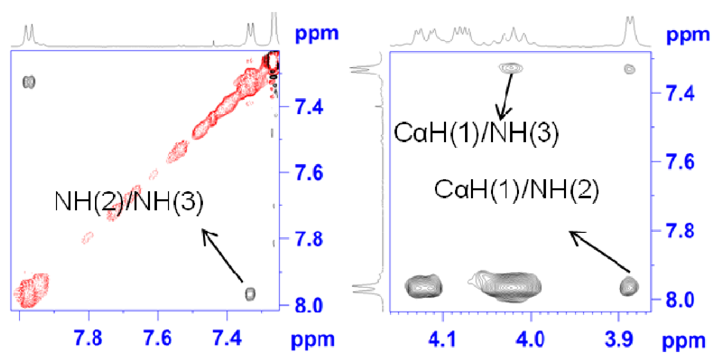


Figure S4: Expansion of ROESY spectrum representing characteristic nOes of **8**

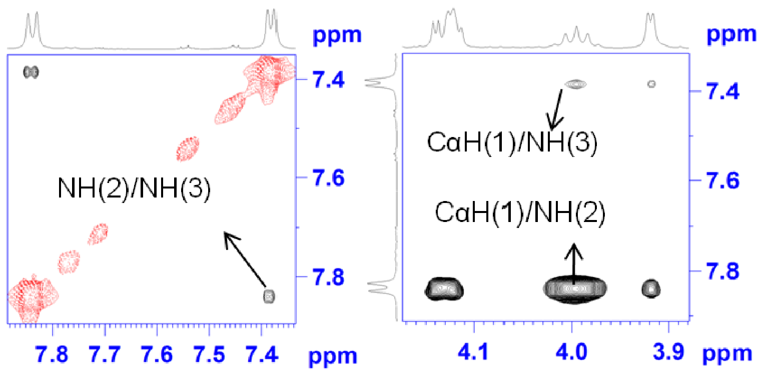


Figure S5: Expansion of ROESY spectrum representing characteristic nOes of **9**

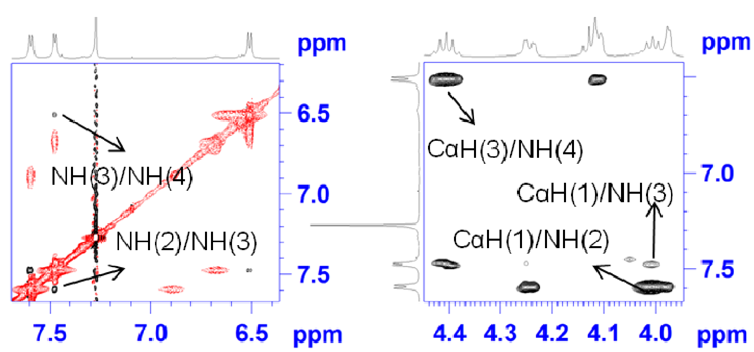


Figure S6: Expansion of ROESY spectrum representing characteristic nOes of **10**

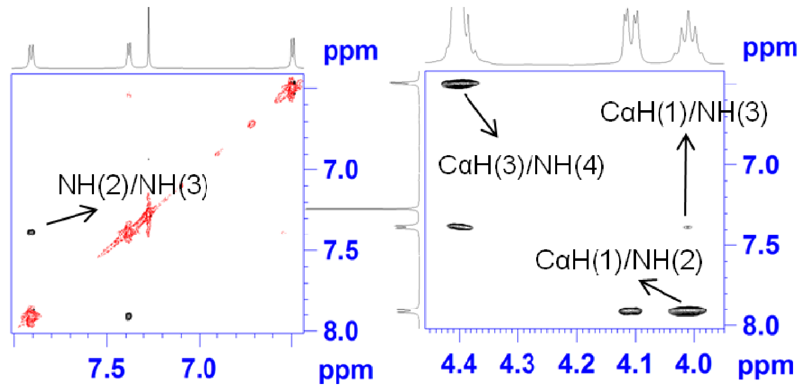


Figure S7: Expansion of ROESY spectrum representing characteristic nOes of **11**

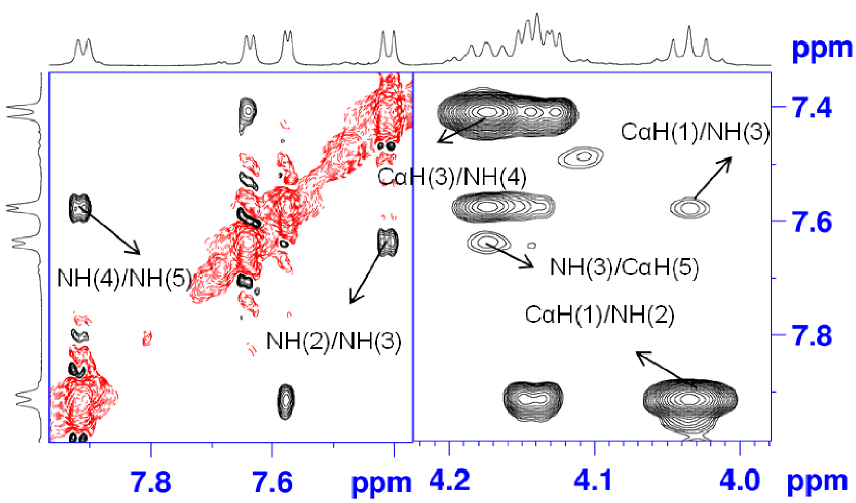


Figure S8: Expansion of ROESY spectrum representing characteristic nOes of **12**

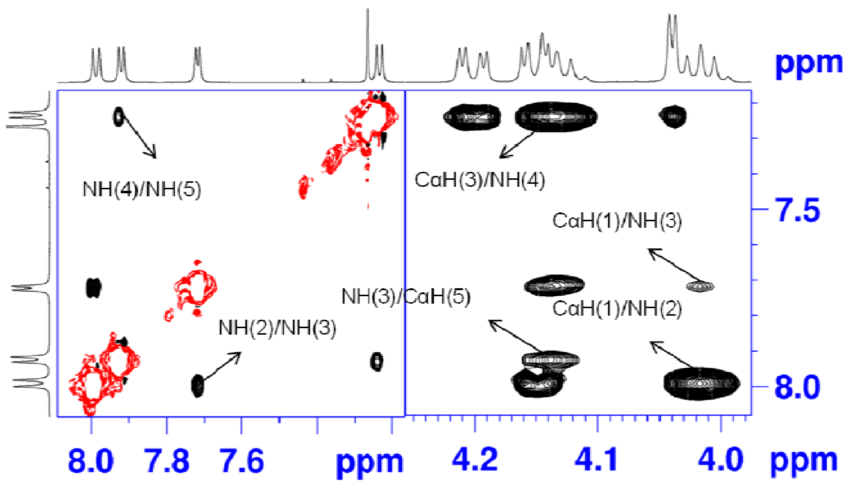


Figure S9: Expansion of ROESY spectrum representing characteristic nOes of **13a**

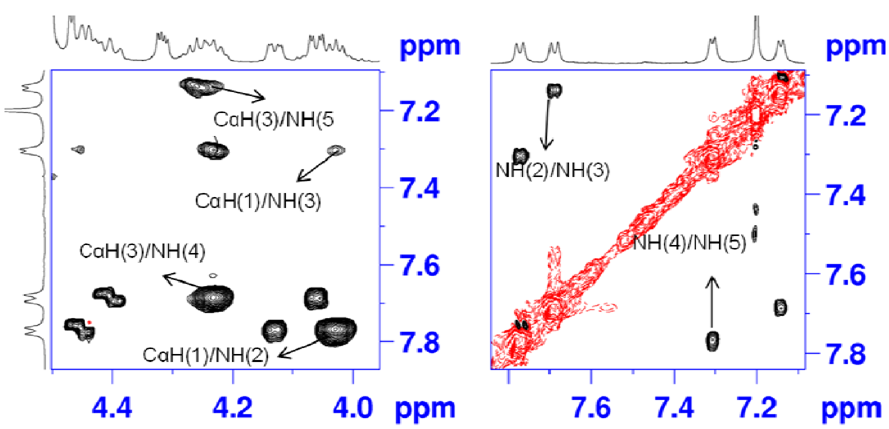


Figure S10: Expansion of ROESY spectrum representing characteristic nOes of **14**

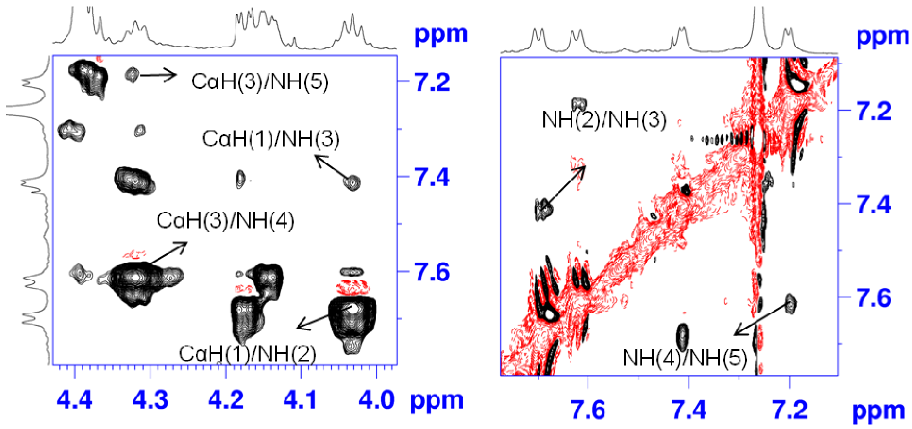


Figure S11: Expansion of ROESY spectrum representing characteristic nOes of **15**

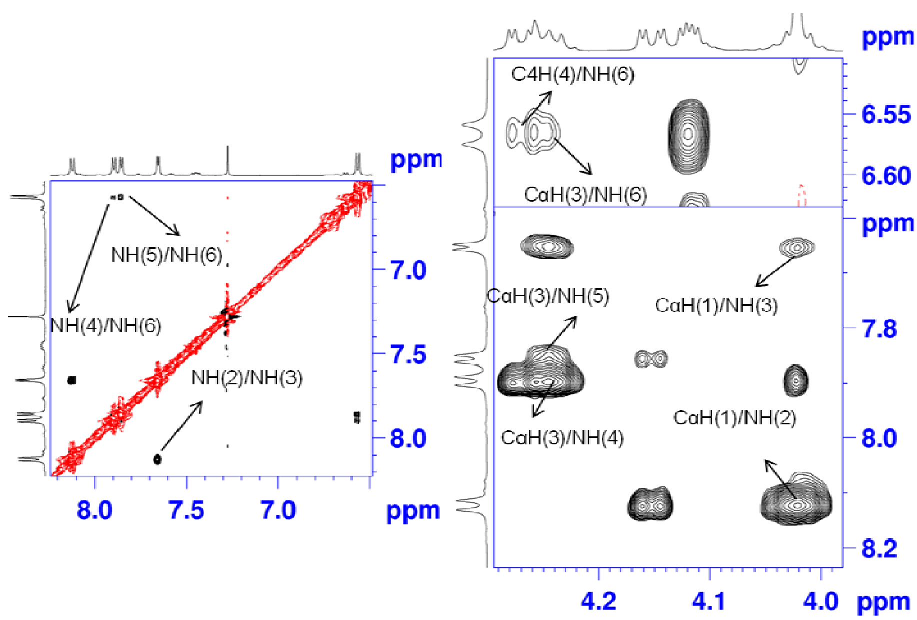


Figure S12: Expansion of ROESY spectrum representing characteristic nOes of **16**

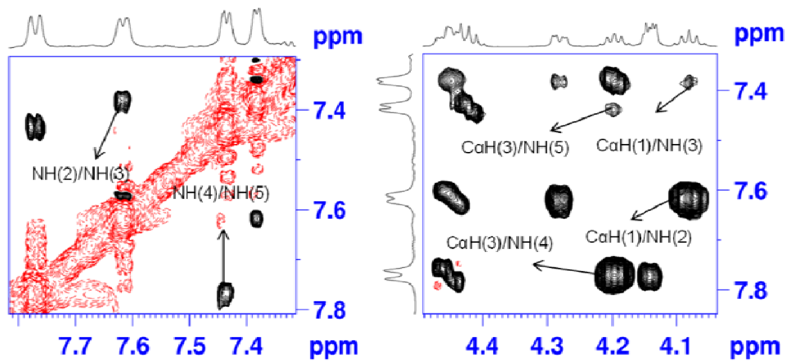


Figure S13: Expansion of ROESY spectrum representing characteristic nOes of **17**

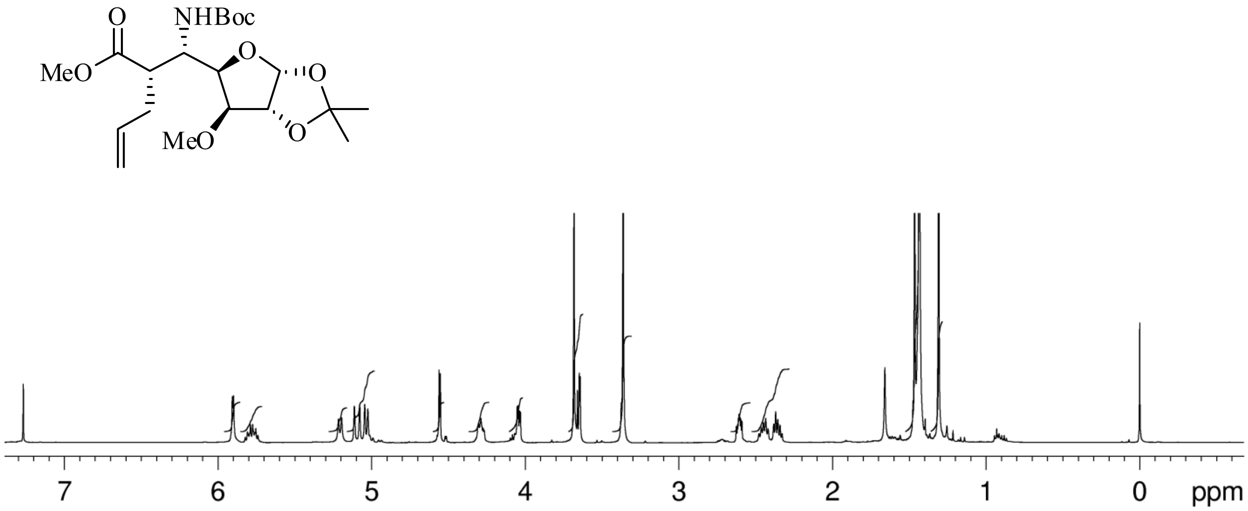


Figure S14: **^{1}H-**NMR Spectrum of **1** (500 MHz, $CDCl_3$, 298 K).

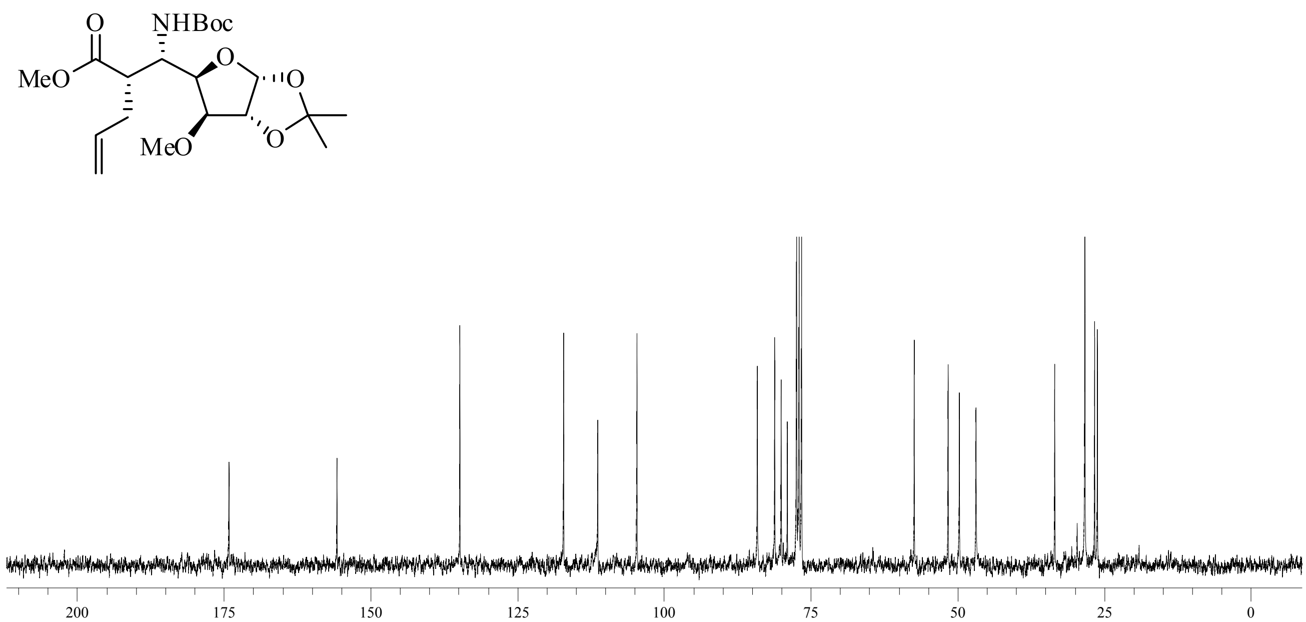


Figure S15: ^{13}C-NMR Spectrum of **1** ($CDCl_3$, 125 MHz, 298 K)

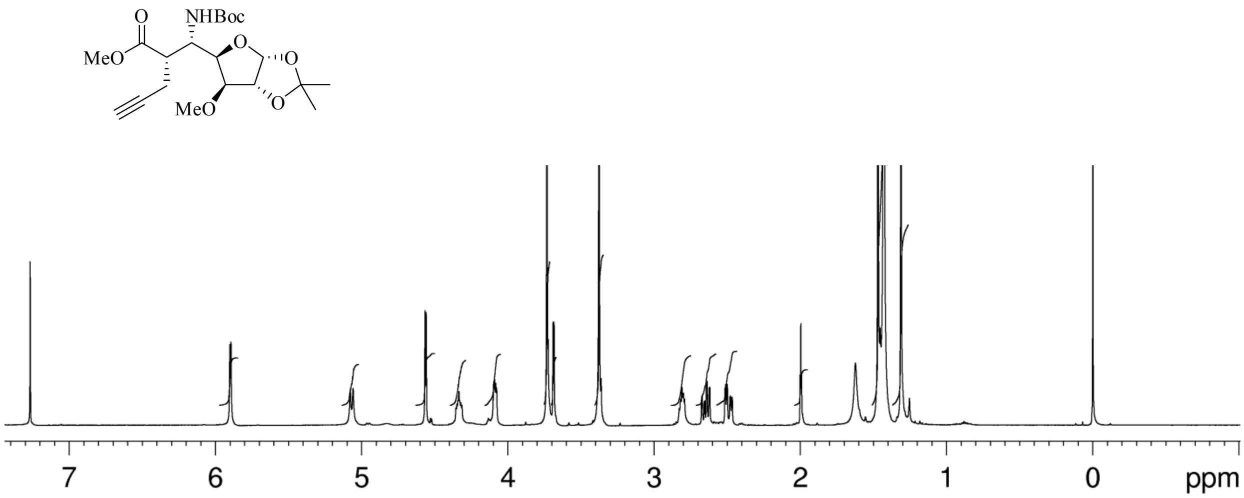


Figure S16: ^{1}H-NMR Spectrum of **2** (500 MHz, $CDCl_3$, 298 K).

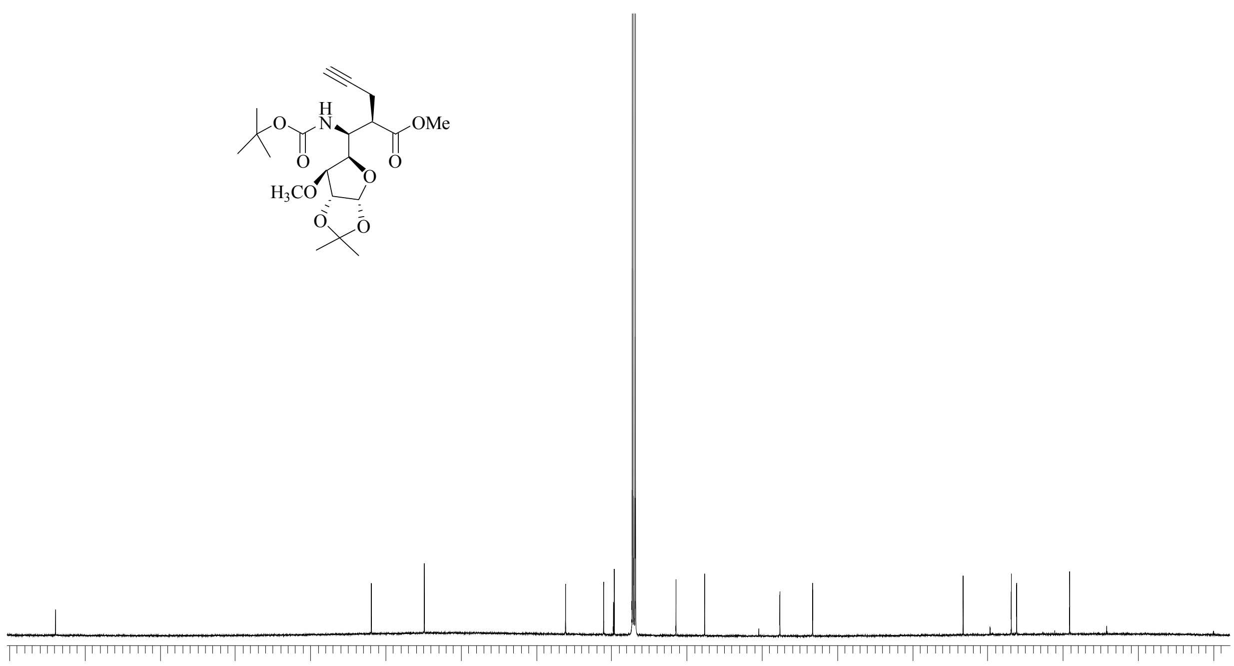
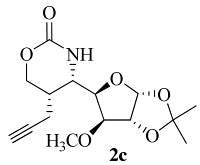


Figure S17: ^{13}C-NMR Spectrum of **2** (125 MHz, $CDCl_3$, 298 K)



2c

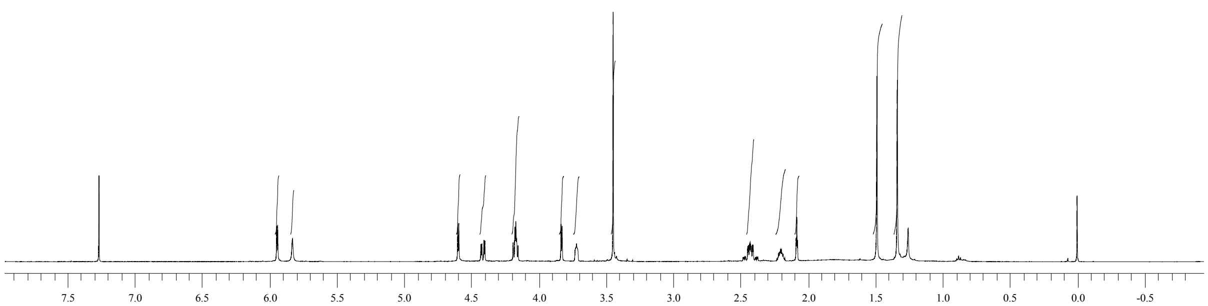
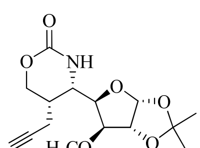


Figure S18: [1]H NMR Spectrum of **2c** ($CDCl_3$, 300 MHz, 298 K)



2c

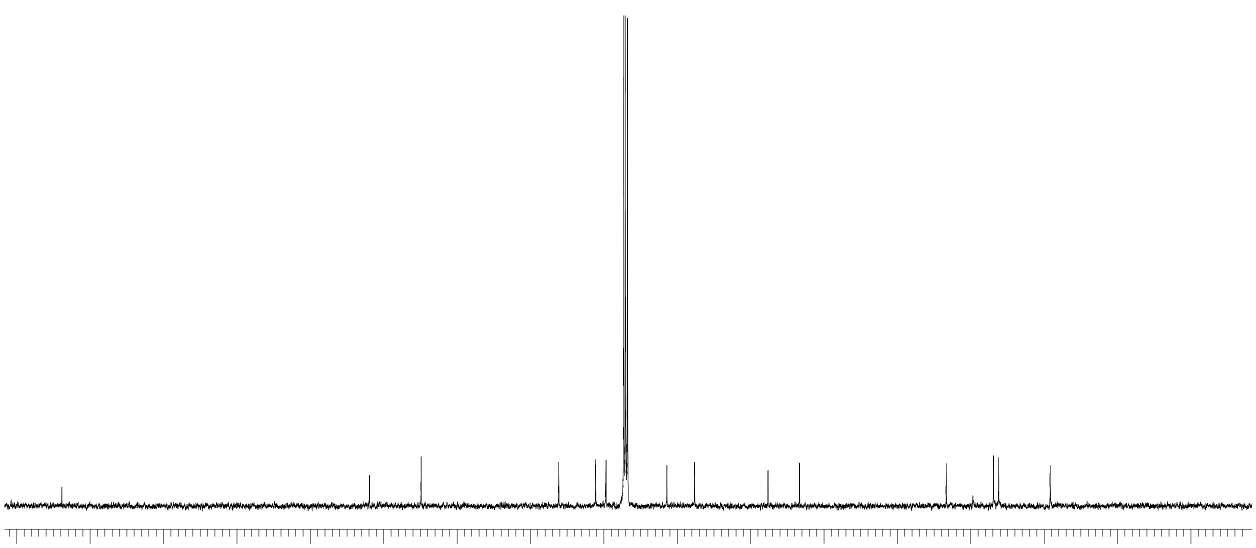
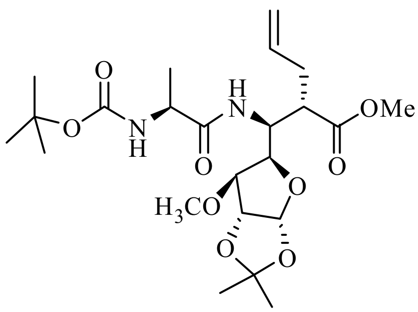


Figure S19: [13]C-NMR Spectrum of **2c** ($CDCl_3$, 75 MHz, 298 K)



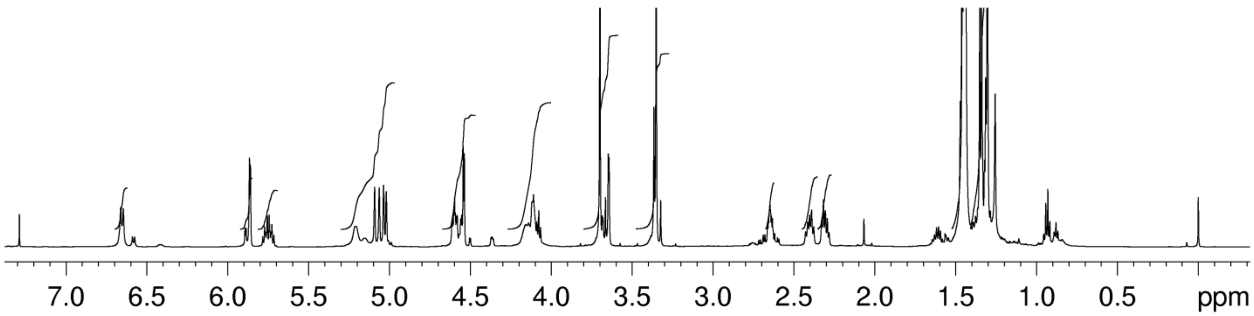
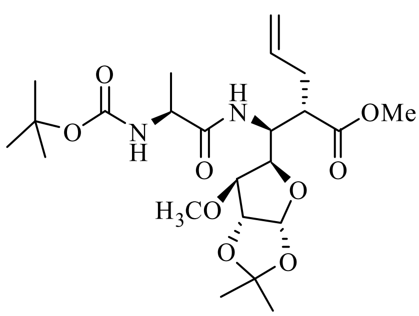


Figure S20: ^{1}H-NMR Spectrum of **4** (500 MHz, $CDCl_3$, 298 K).



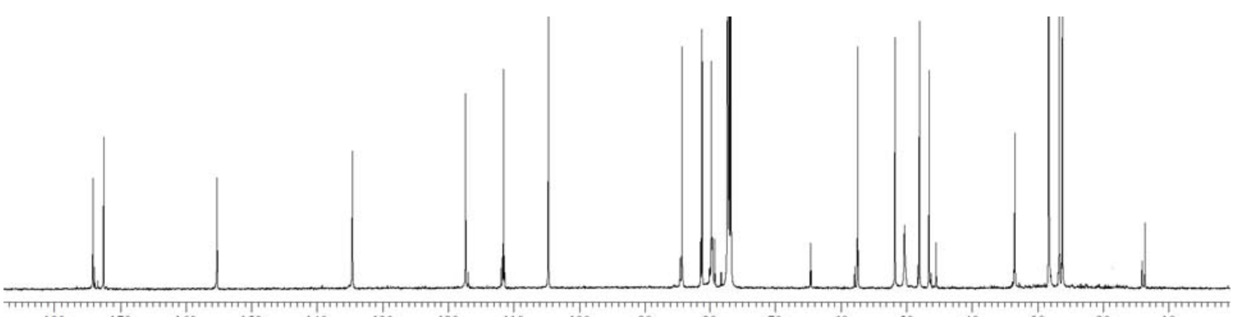


Figure S21: ^{13}C-NMR Spectrum of **4** (125 MHz, $CDCl_3$, 298 K).

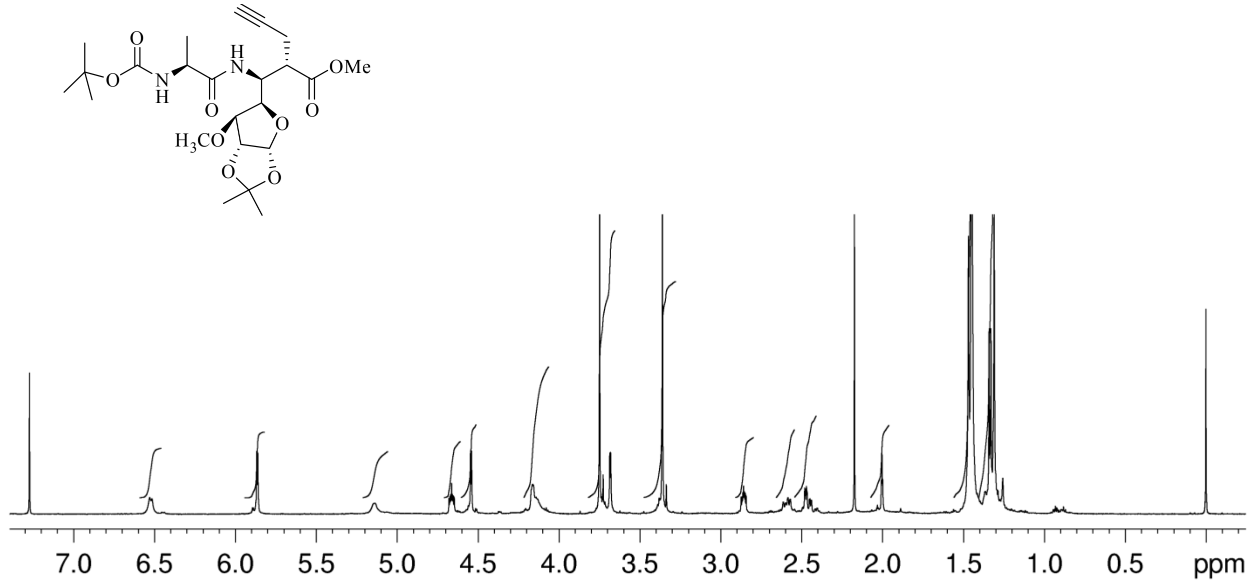


Figure S22: ^{1}H-NMR Spectrum of **5** (500 MHz, $CDCl_3$, 298 K).

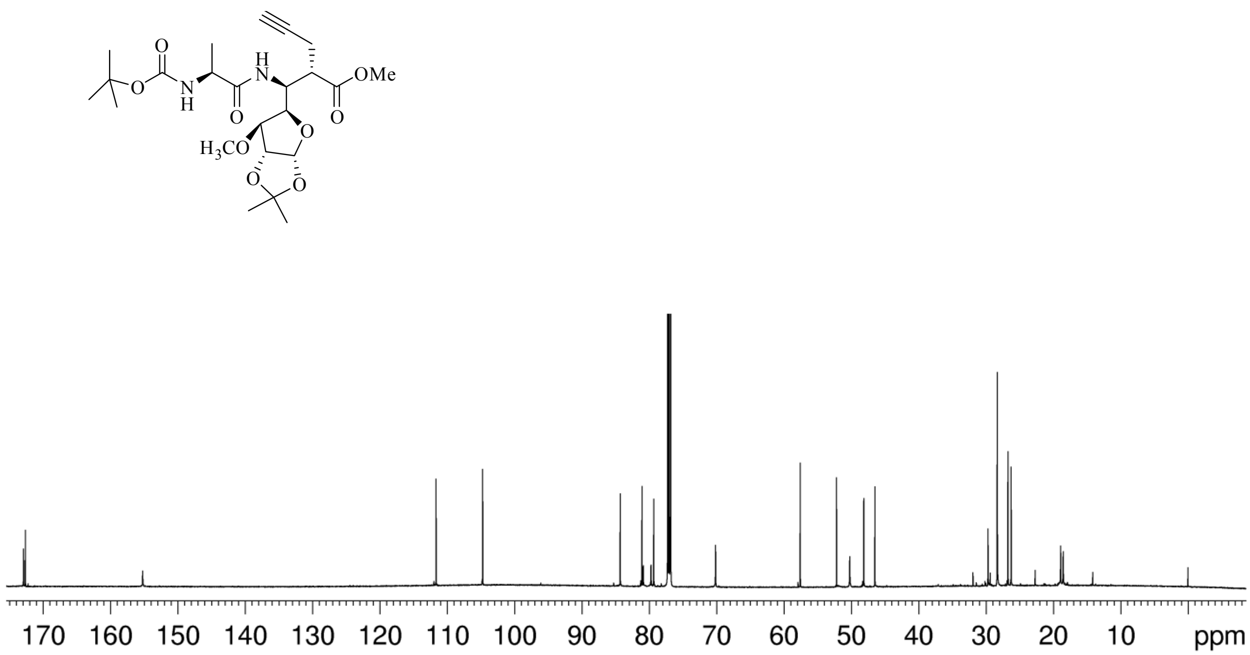


Figure S23: ^{13}C-NMR Spectrum of **5** (125 MHz, $CDCl_3$, 298 K).

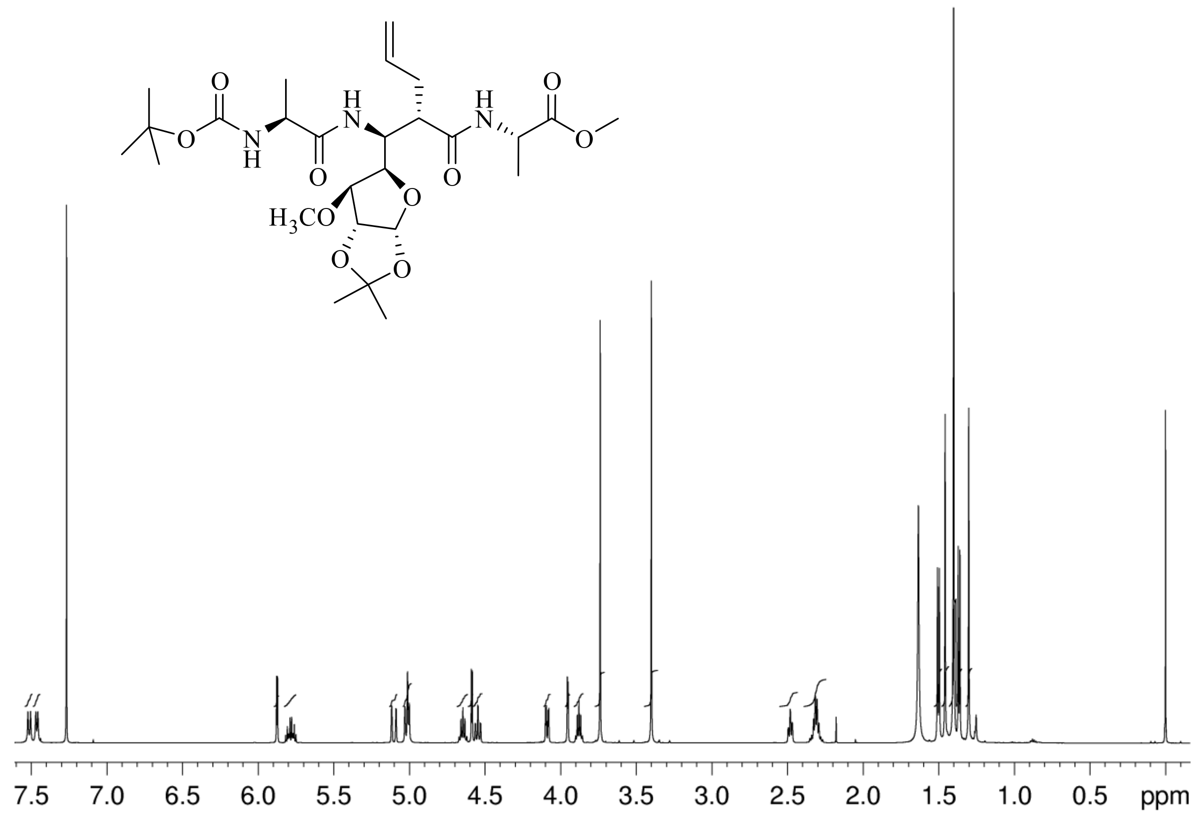


Figure S24: ^{1}H-NMR Spectrum of **6** (600 MHz, $CDCl_3$, 298 K).

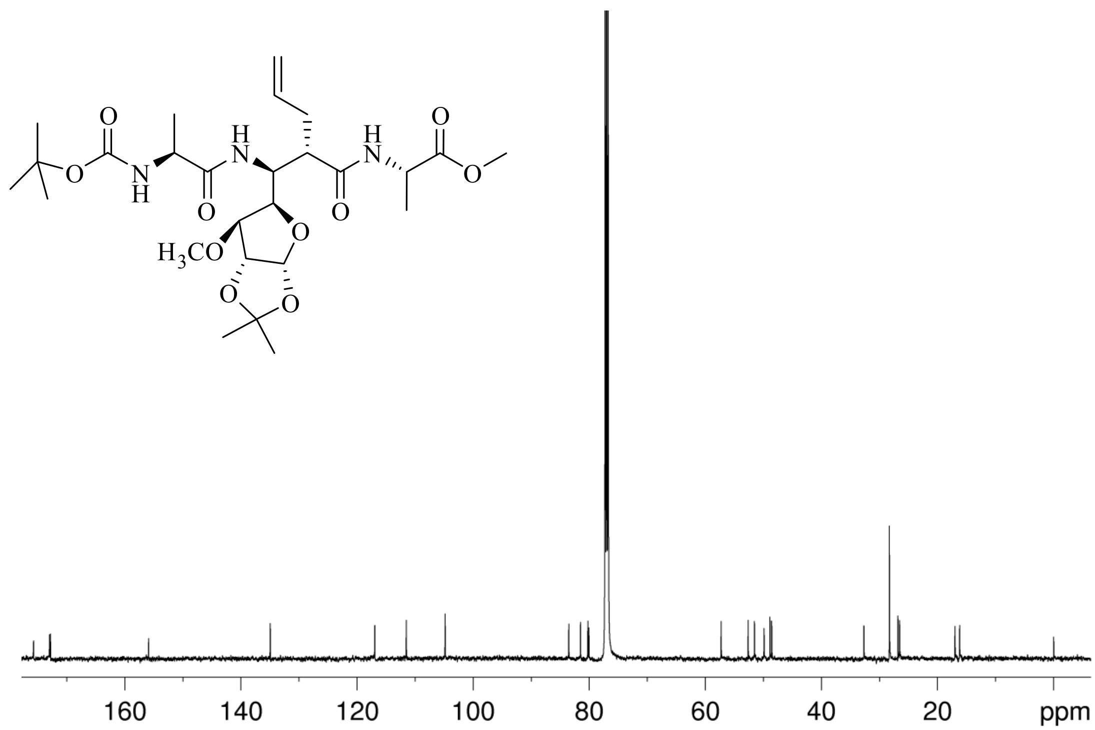


Figure S25: ^{13}C-NMR Spectrum of **6** (125 MHz, $CDCl_3$, 298 K).

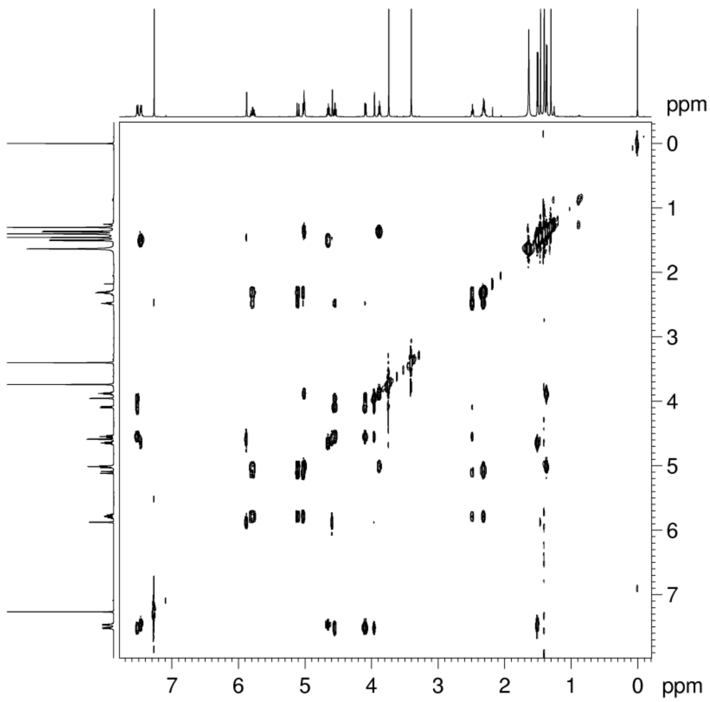


Figure S26: TOCSY Spectrum of **6** (600 MHz, $CDCl_3$, 298 K).

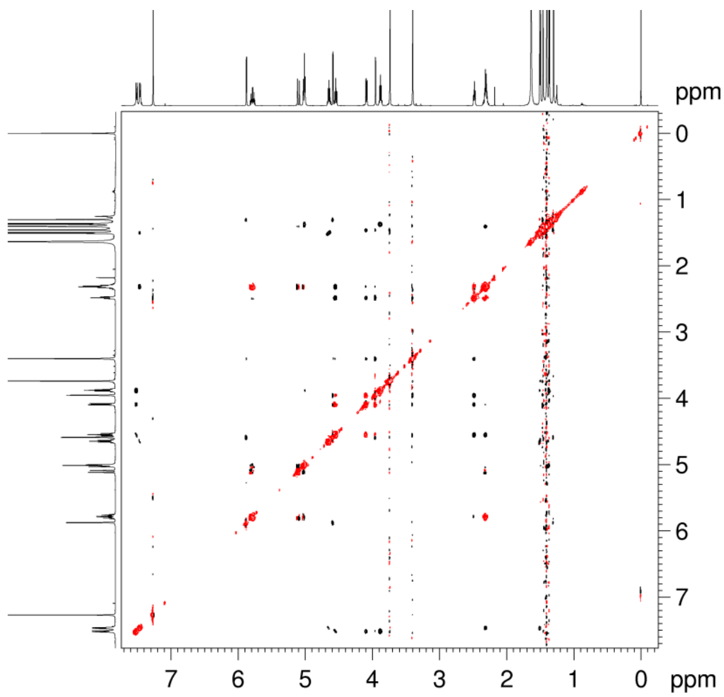


Figure S27: ROESY Spectrum of **6** (600 MHz, $CDCl_3$, 298 K).

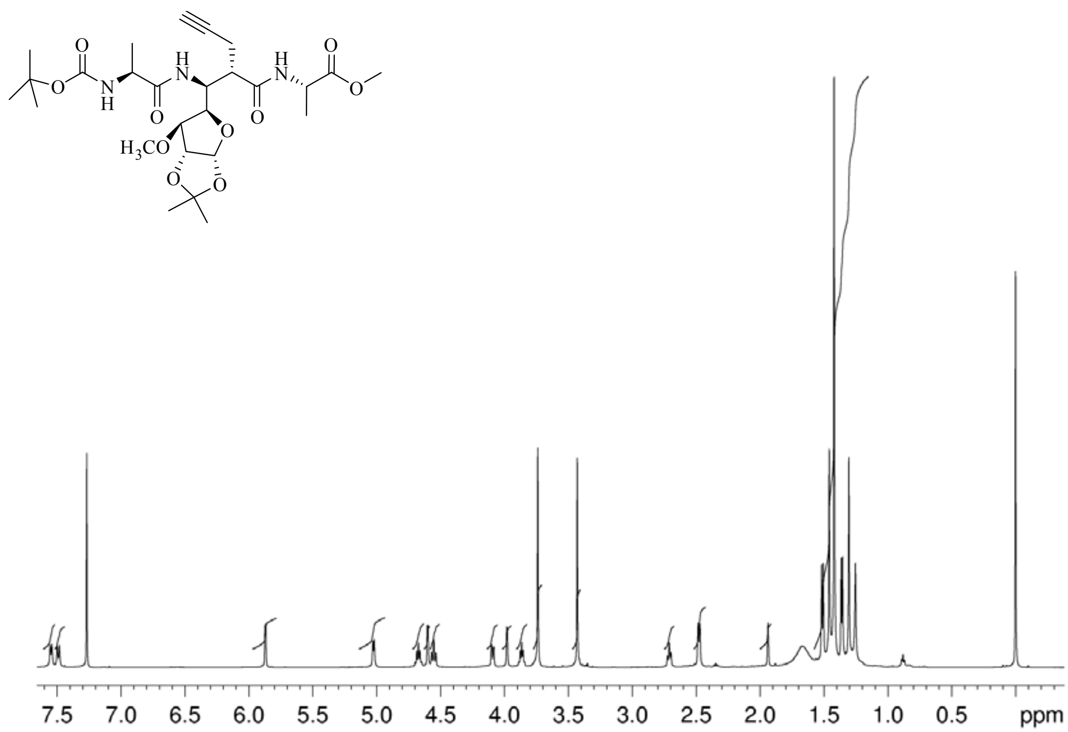


Figure S28: ^{1}H-NMR Spectrum of **7** (600 MHz, $CDCl_3$, 298 K).

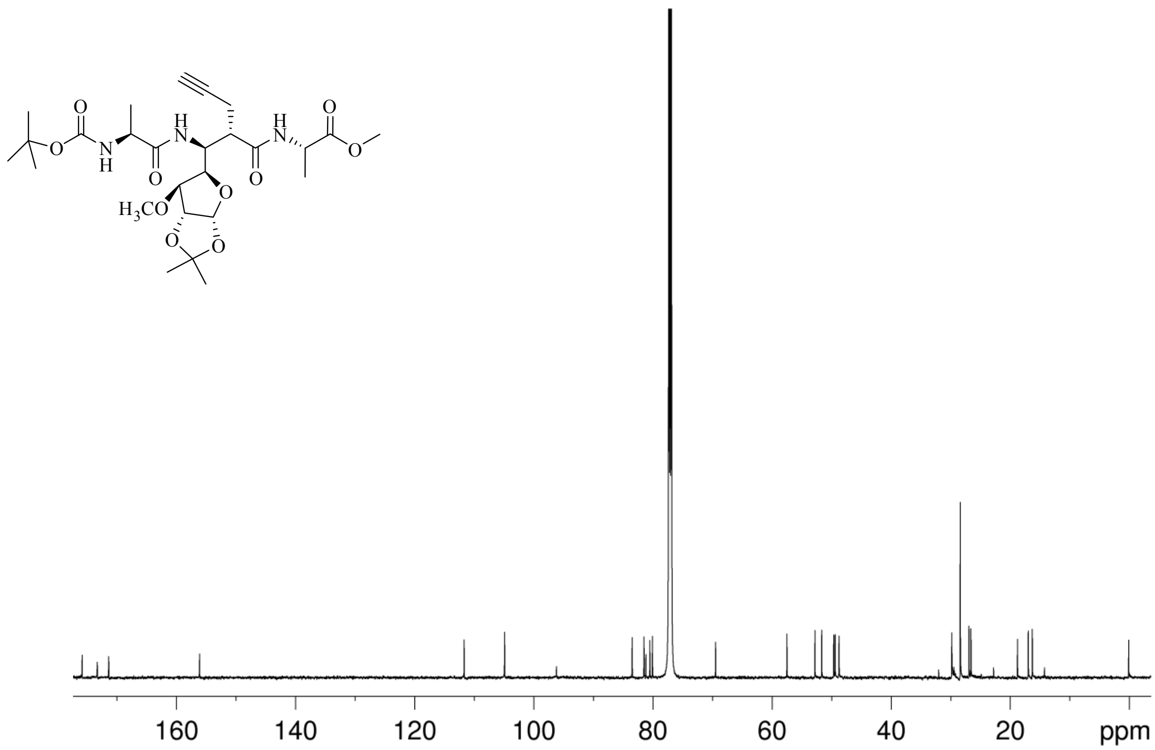


Figure S29: ^{13}C-NMR Spectrum of **7** (150 MHz, $CDCl_3$, 298 K).

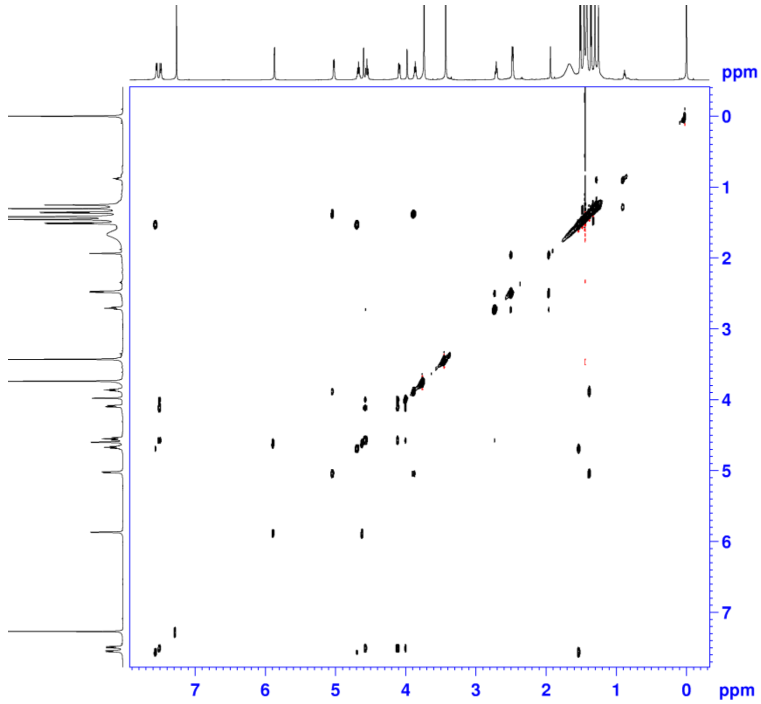


Figure S30: TOCSY Spectrum of **7** (600 MHz, $CDCl_3$, 298 K).

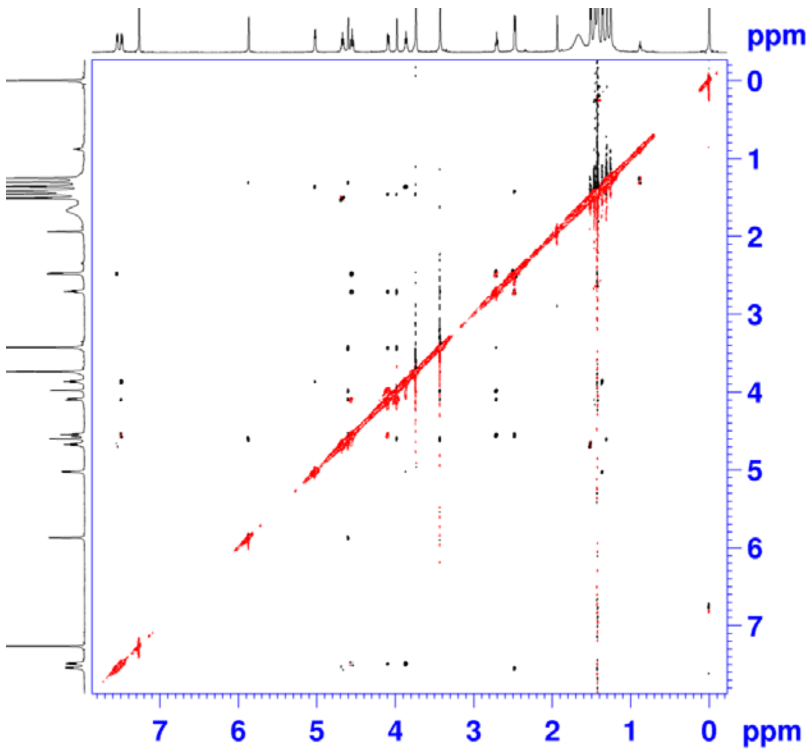


Figure S31: ROESY Spectrum of **7** (600 MHz, $CDCl_3$, 303 K).

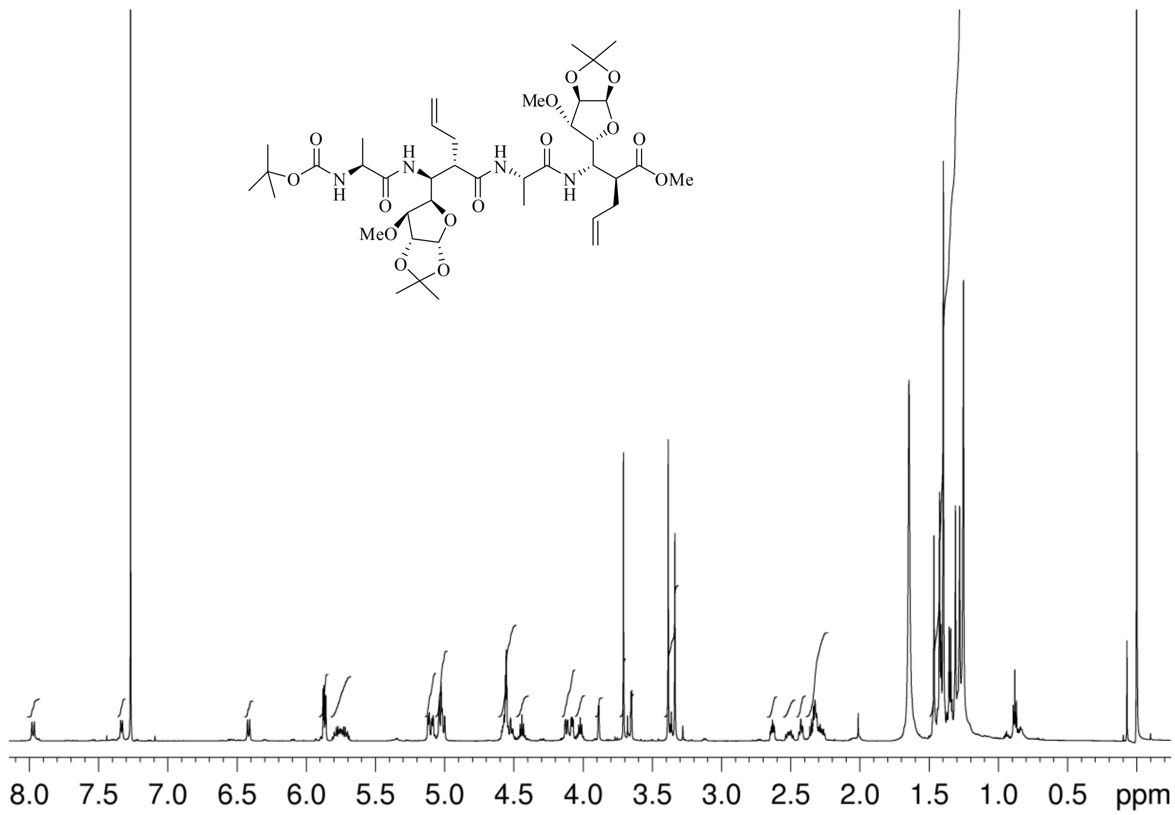


Figure S32: ^{1}H-NMR Spectrum of **8** (600 MHz, $CDCl_3$, 288 K).

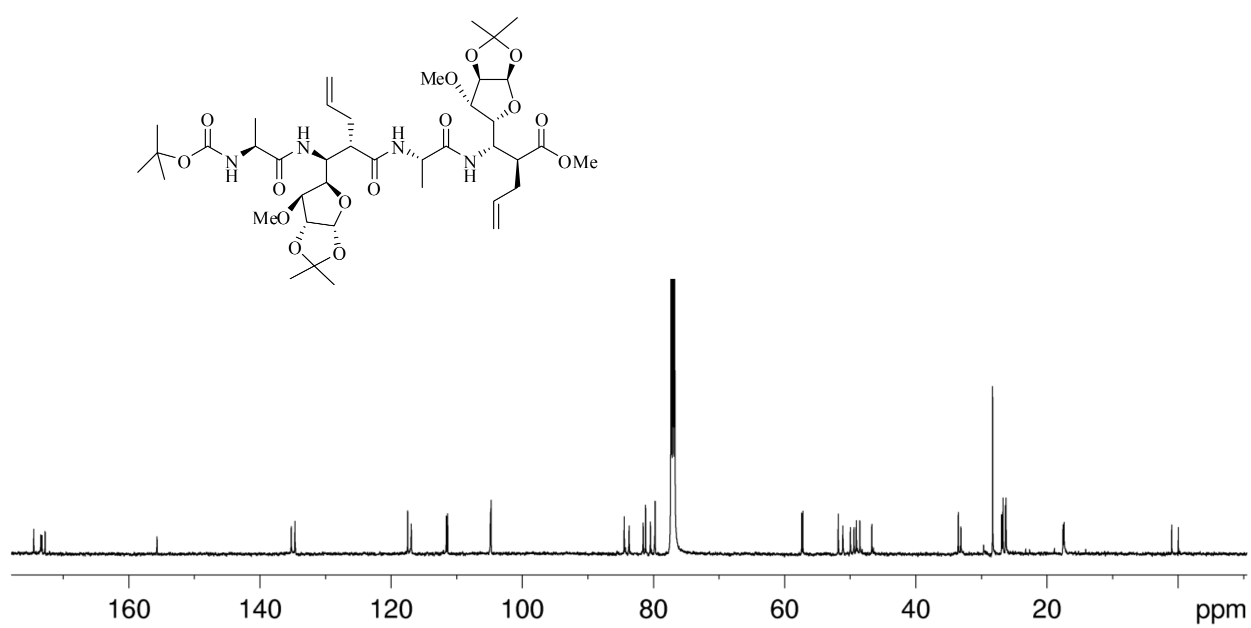


Figure S33: ^{13}C-NMR Spectrum of **8** (125 MHz, $CDCl_3$, 298 K).

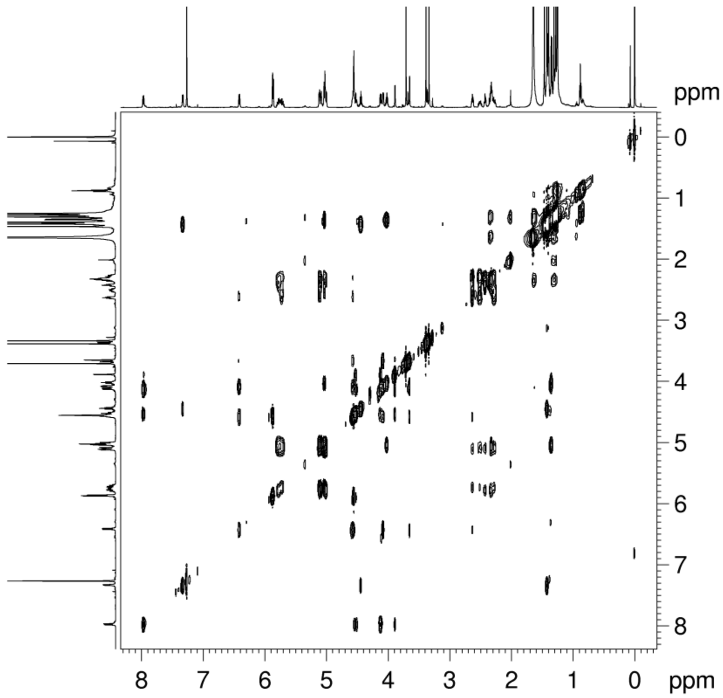


Figure S34: TOCSY Spectrum of **8** (600 MHz, $CDCl_3$, 288 K).

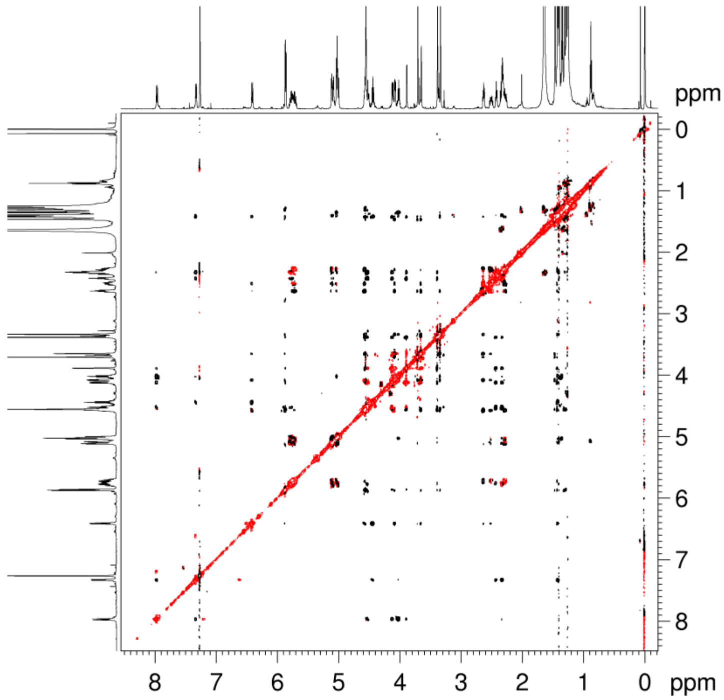


Figure S35: ROESY Spectrum of **8** (600 MHz, $CDCl_3$, 288 K).

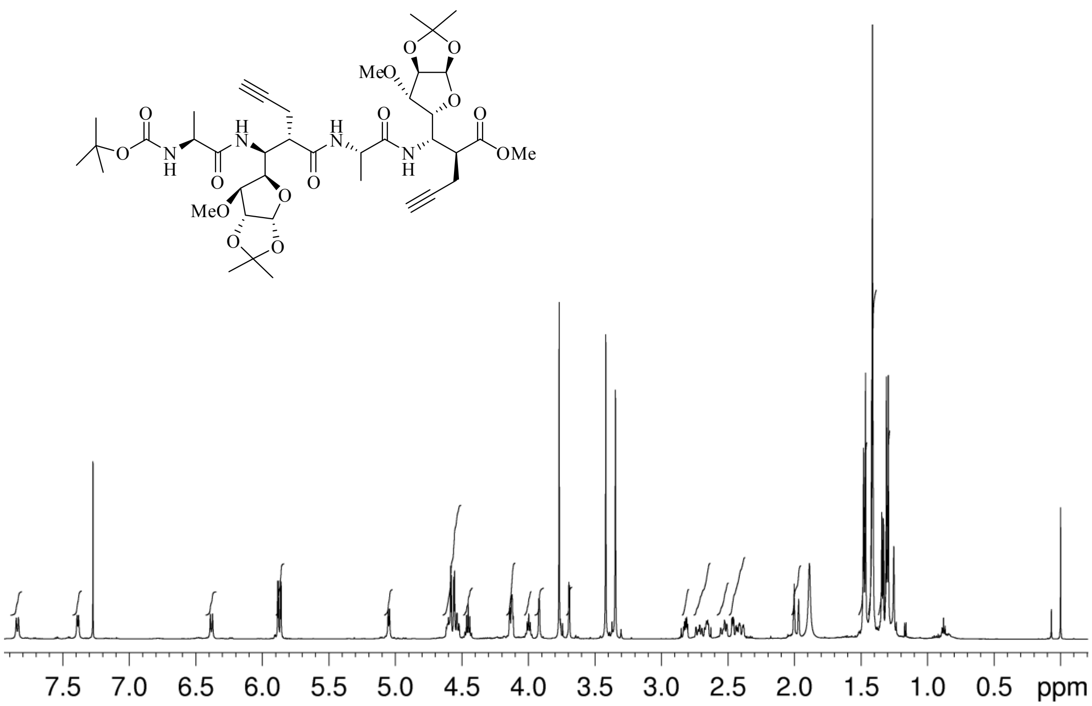


Figure S36: ^{1}H-NMR Spectrum of **9** (600 MHz, $CDCl_3$, 298 K).

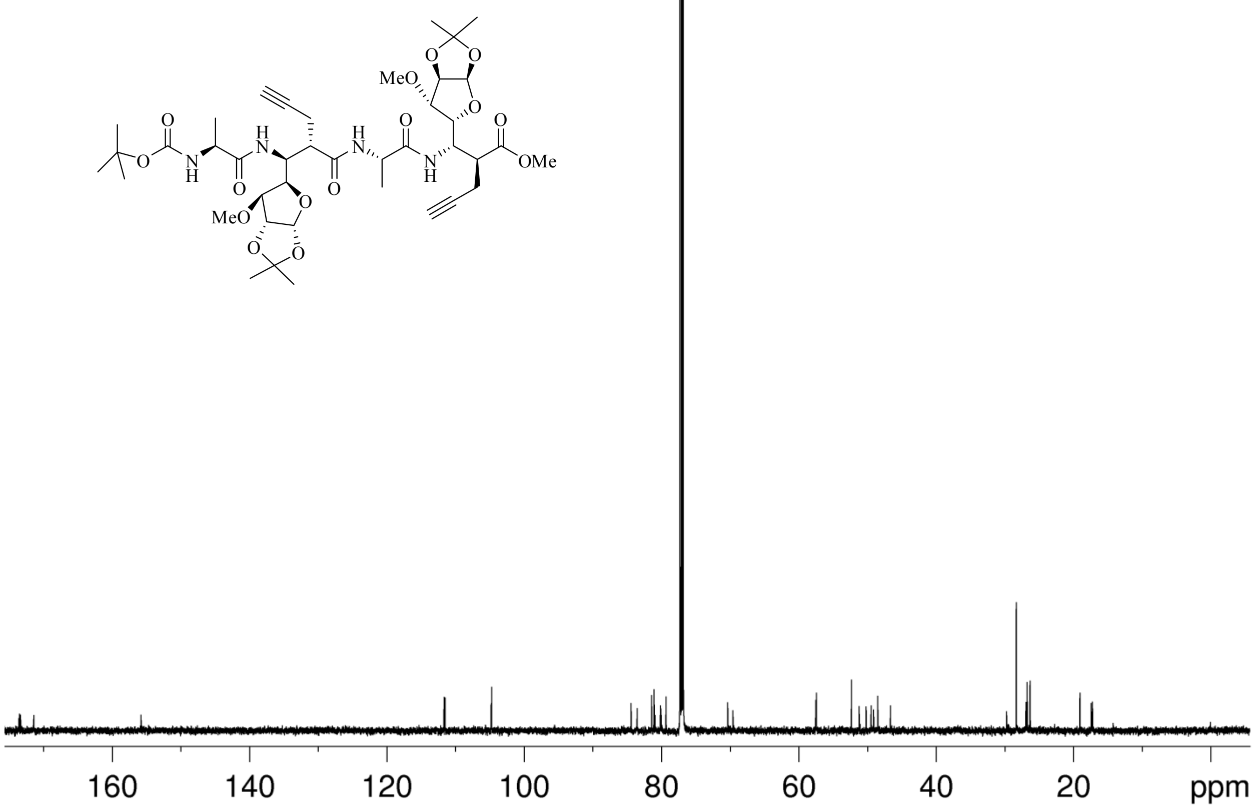


Figure S37: ^{13}C-NMR Spectrum of **9** (150 MHz, $CDCl_3$, 298 K).

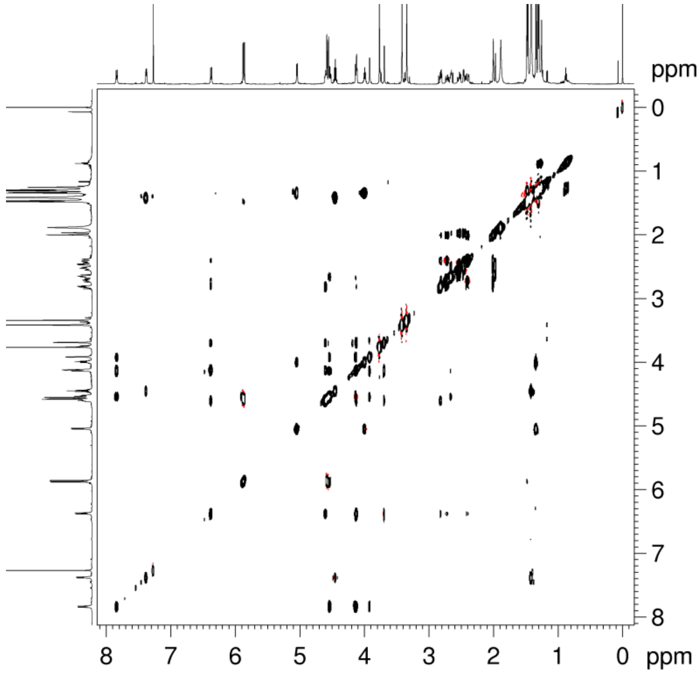


Figure S38: TOCSY Spectrum of **9** (600 MHz, $CDCl_3$, 298 K).

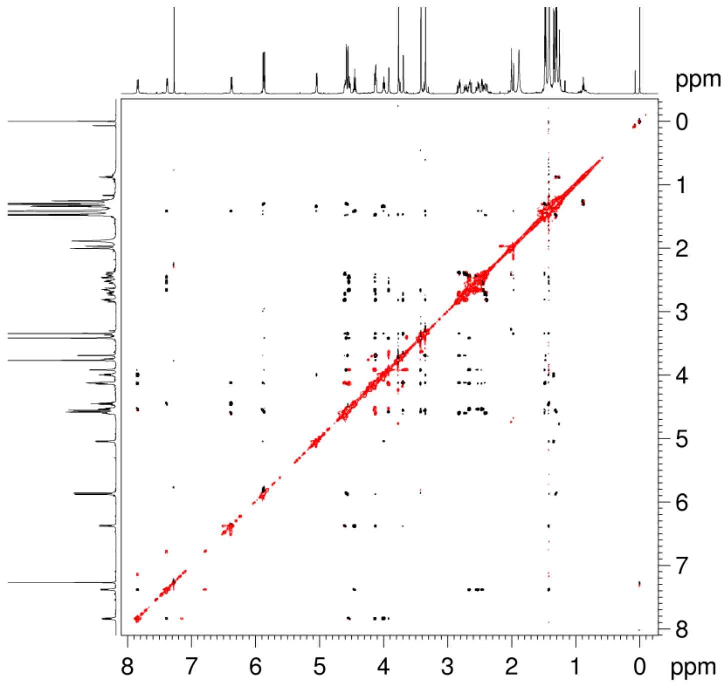


Figure S39: ROESY Spectrum of **9** (600 MHz, $CDCl_3$, 298 K).

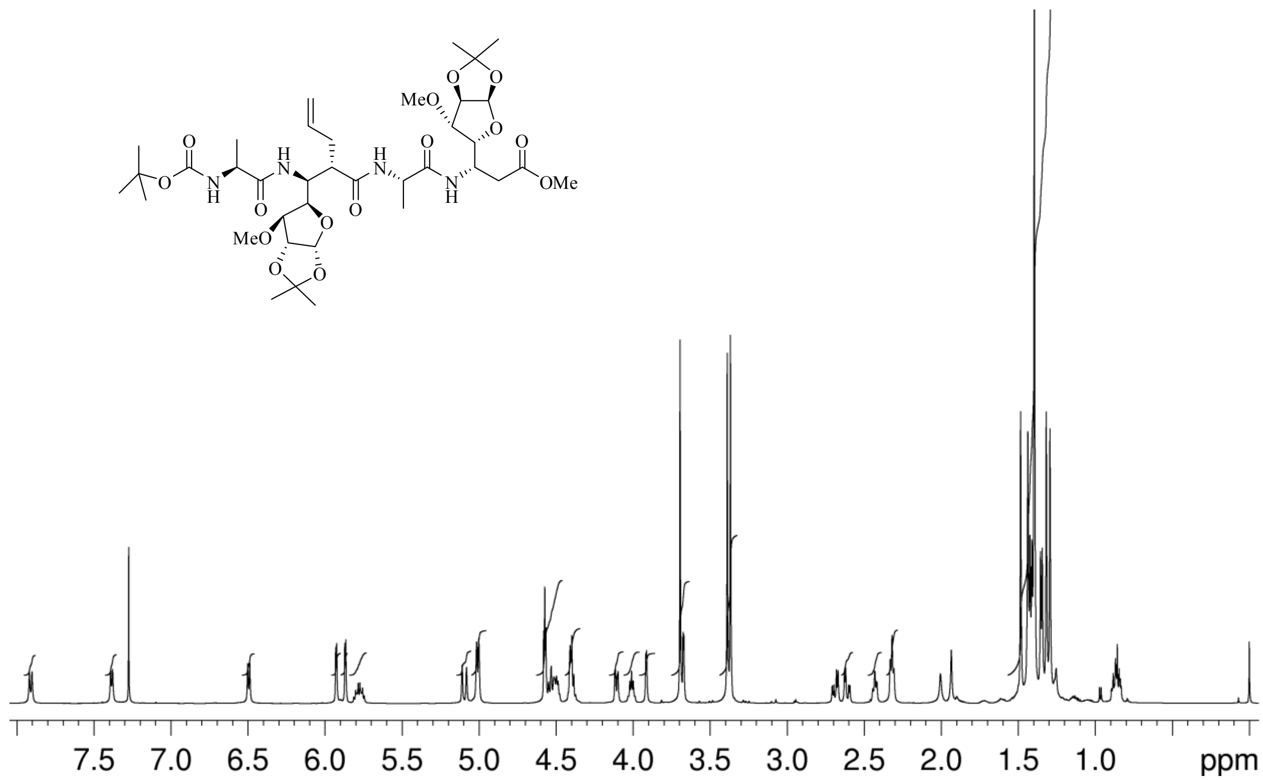


Figure S40: ^{1}H-NMR Spectrum of **10** (600 MHz, $CDCl_3$, 298 K)

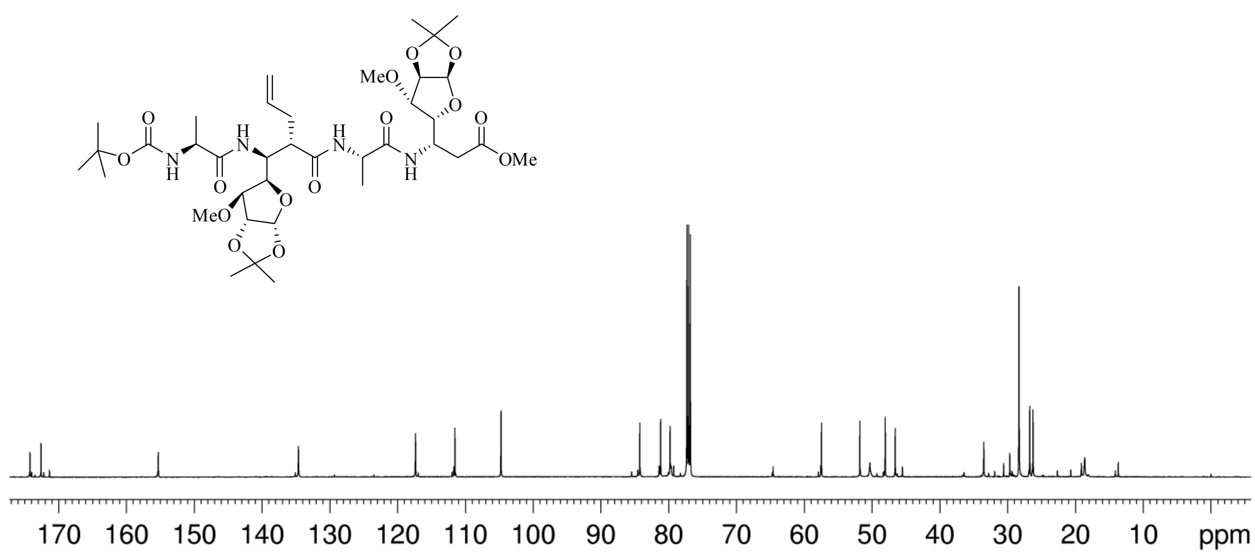


Figure S41: ^{13}C-NMR Spectrum of **10** (150 MHz, $CDCl_3$, 298 K).

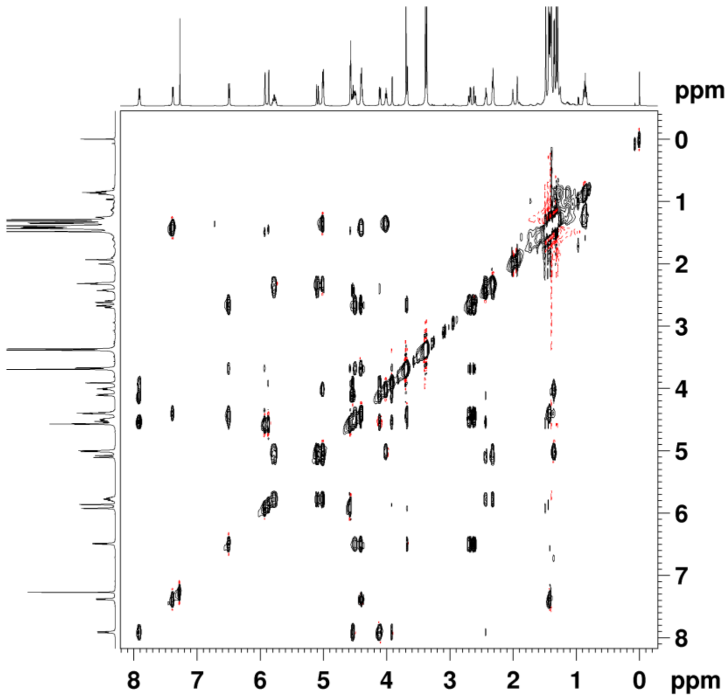


Figure S42: TOCSY Spectrum of **10** (600 MHz, $CDCl_3$, 298 K).

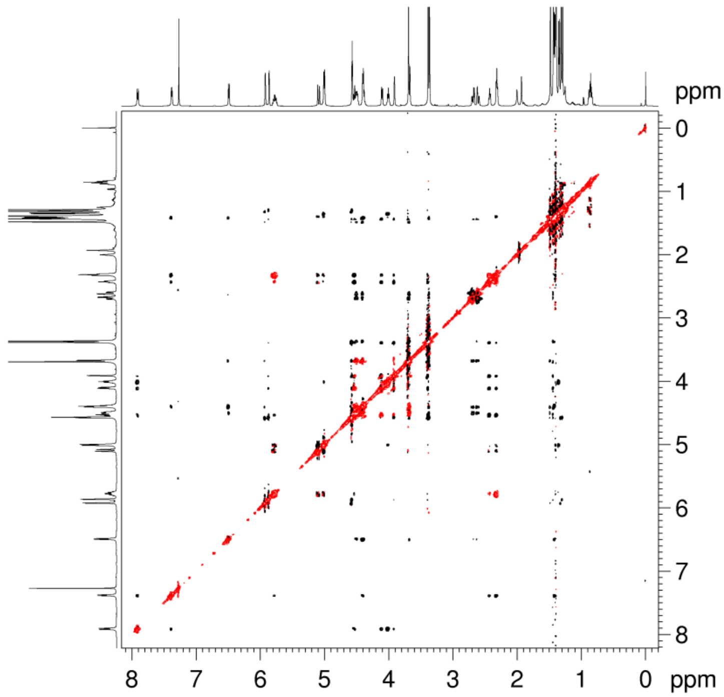


Figure S43: ROESY Spectrum of **10** (600 MHz, $CDCl_3$, 298 K).

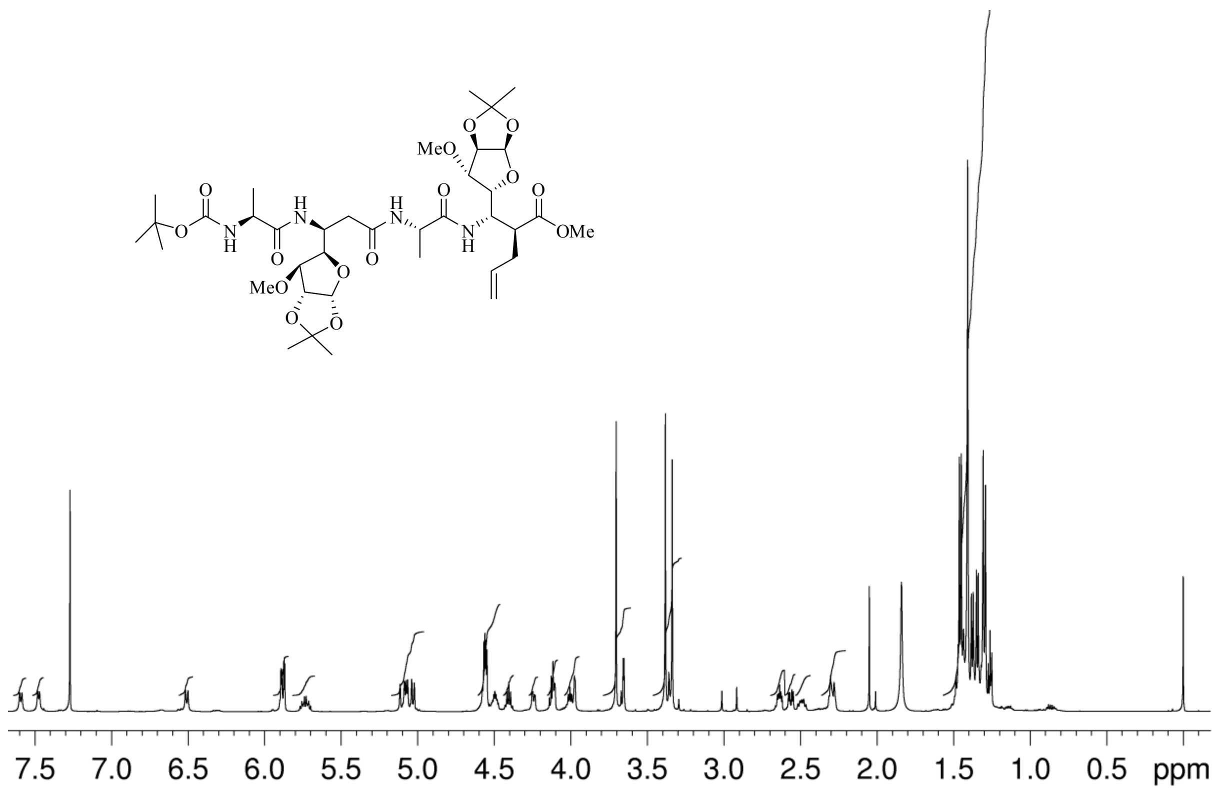


Figure S44: ^{1}H-NMR Spectrum of **11** (600 MHz, $CDCl_3$, 298 K).

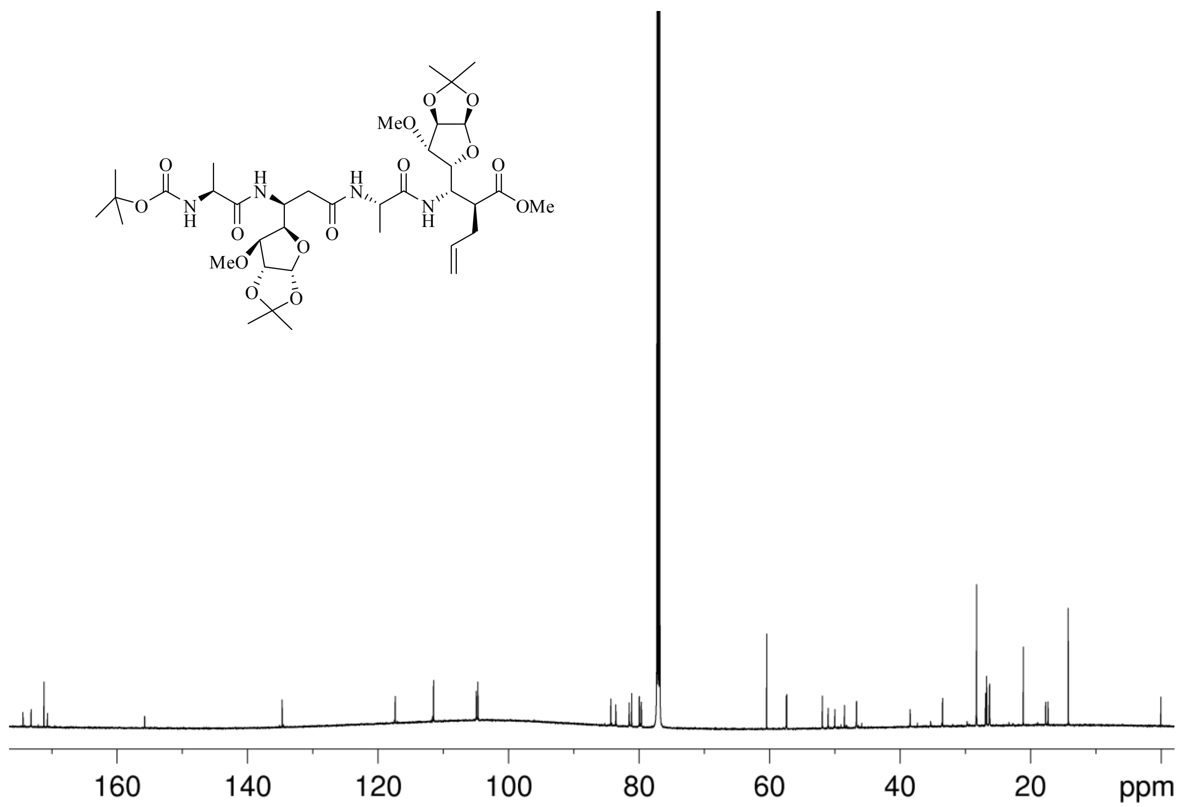


Figure S45: ^{13}C-NMR Spectrum of **11** (150 MHz, $CDCl_3$, 298 K).

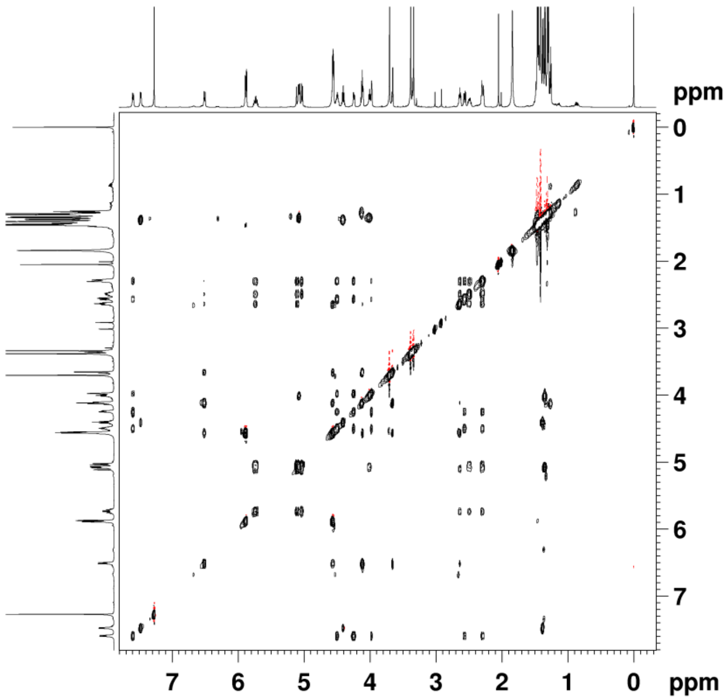


Figure S46: TOCSY Spectrum of **11** (600 MHz, $CDCl_3$, 298 K).

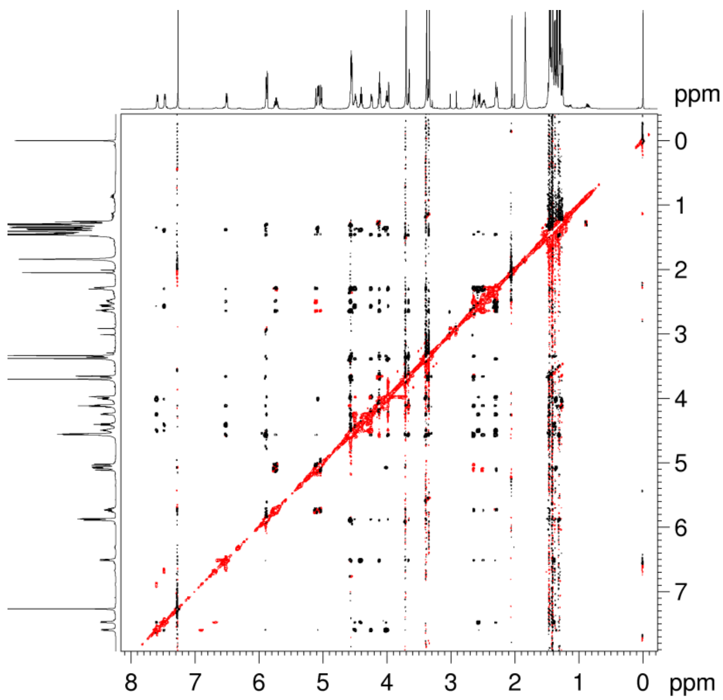


Figure S47: ROESY Spectrum of **11** (600 MHz, $CDCl_3$, 298 K).

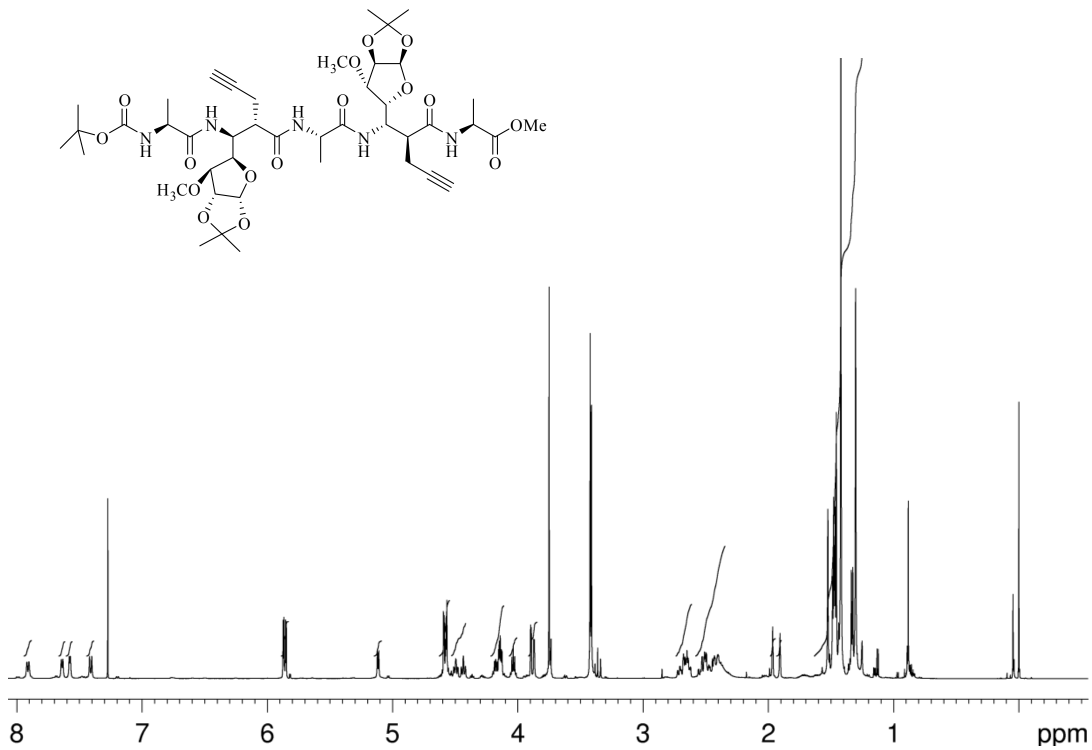


Figure S48: ^{1}H-NMR Spectrum of **12** (600 MHz, $CDCl_3$, 298 K).

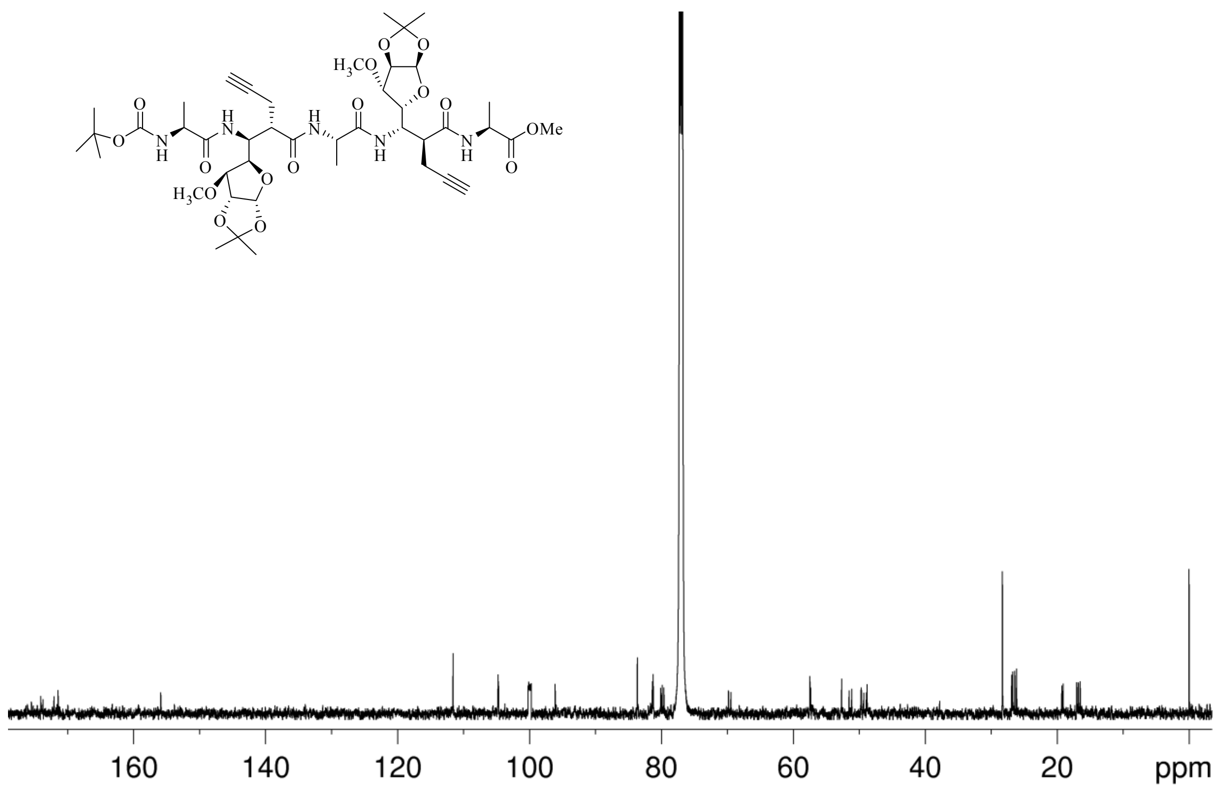


Figure S49: ^{13}C-NMR Spectrum of **12** (150 MHz, $CDCl_3$, 298 K).

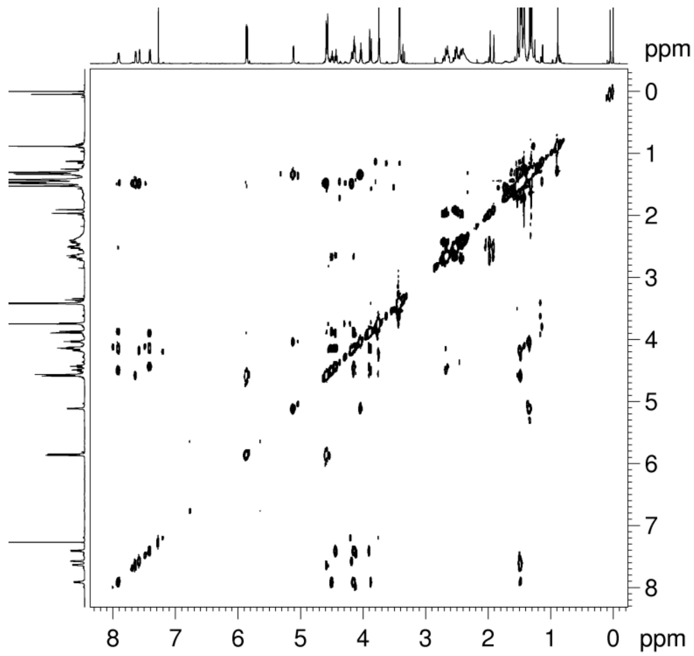


Figure S50: TOCSY Spectrum of **12** (600 MHz, $CDCl_3$, 298 K).

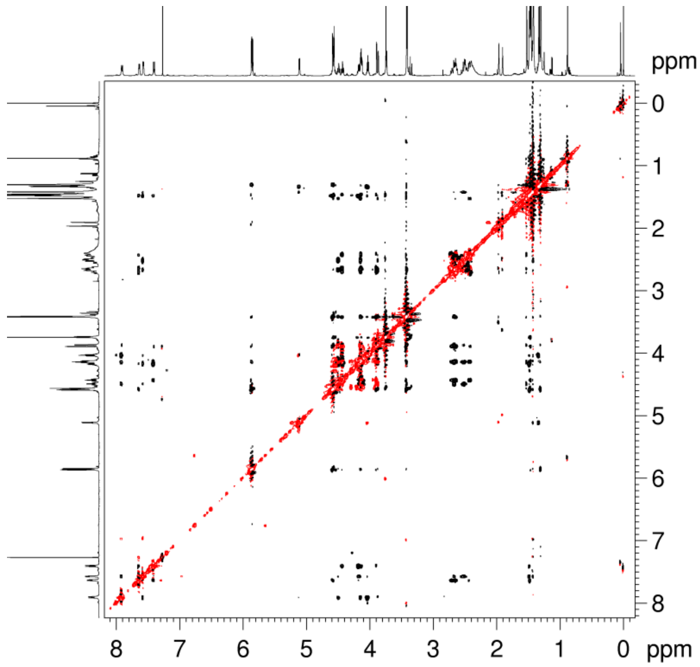


Figure S51: ROESY Spectrum of **12** (600 MHz, $CDCl_3$, 298 K).

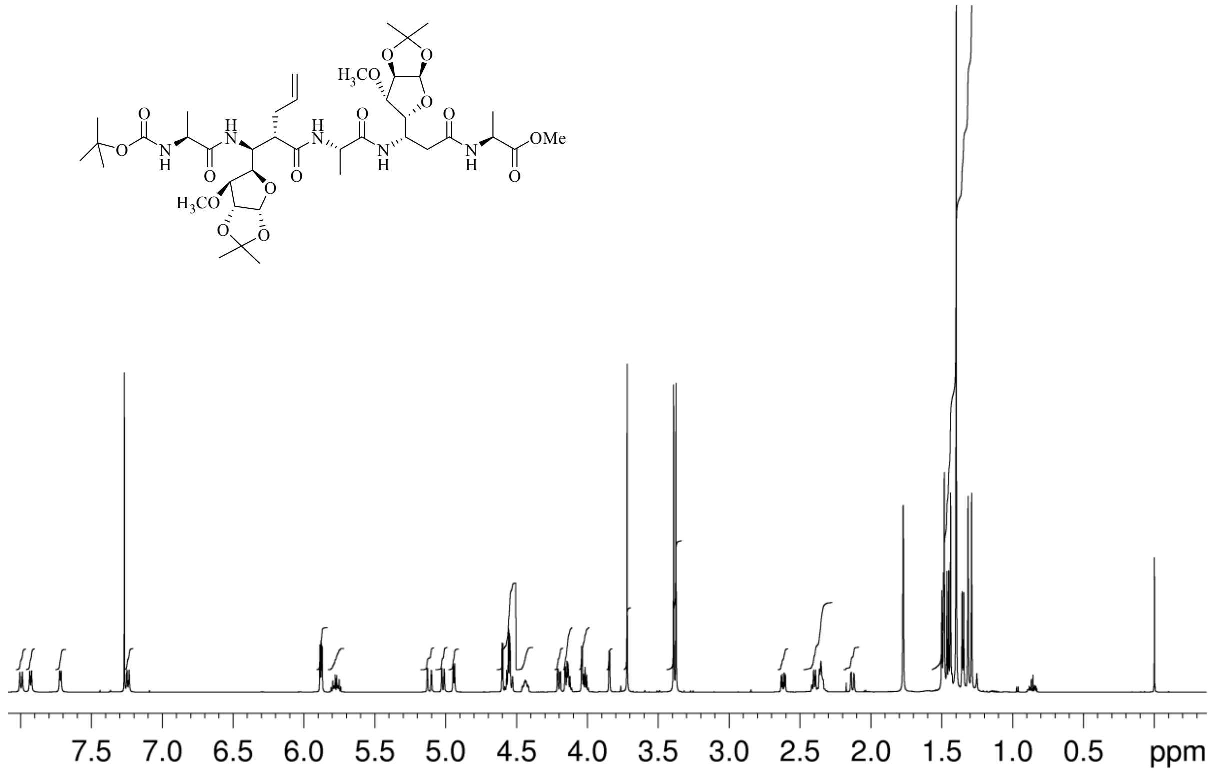


Figure S52: ^{1}H-NMR Spectrum of **13a** (600 MHz, $CDCl_3$, 303 K).

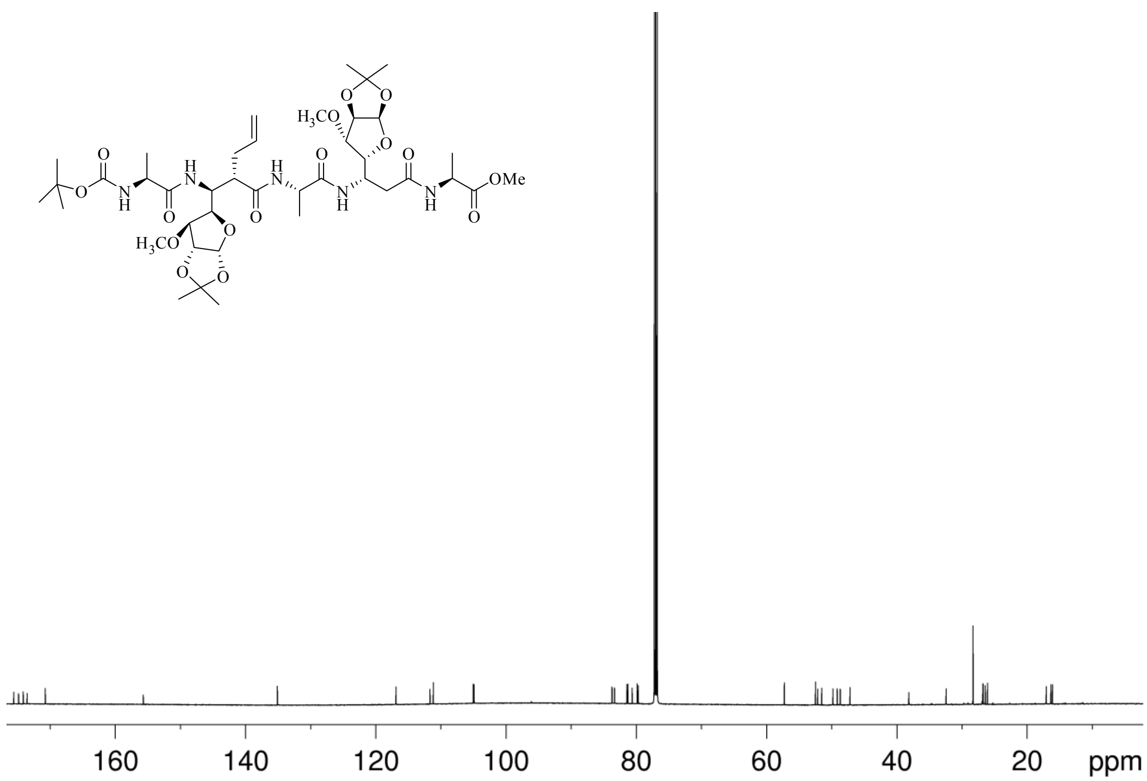


Figure S53: ^{13}C-NMR Spectrum of **13a** (150 MHz, $CDCl_3$, 303 K).

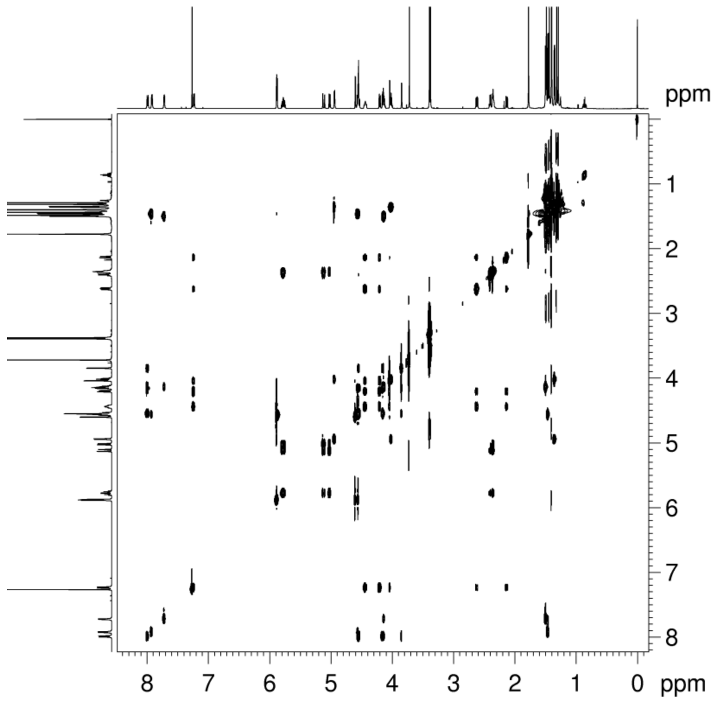


Figure S54: TOCSY Spectrum of **13a** (600 MHz, $CDCl_3$, 303 K).

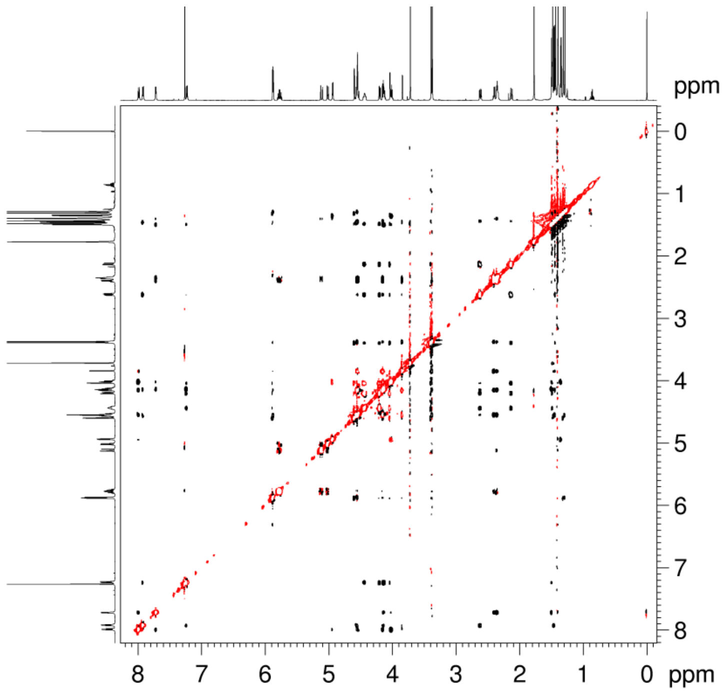


Figure S55: ROESY Spectrum of **13a** (600 MHz, $CDCl_3$, 303 K).

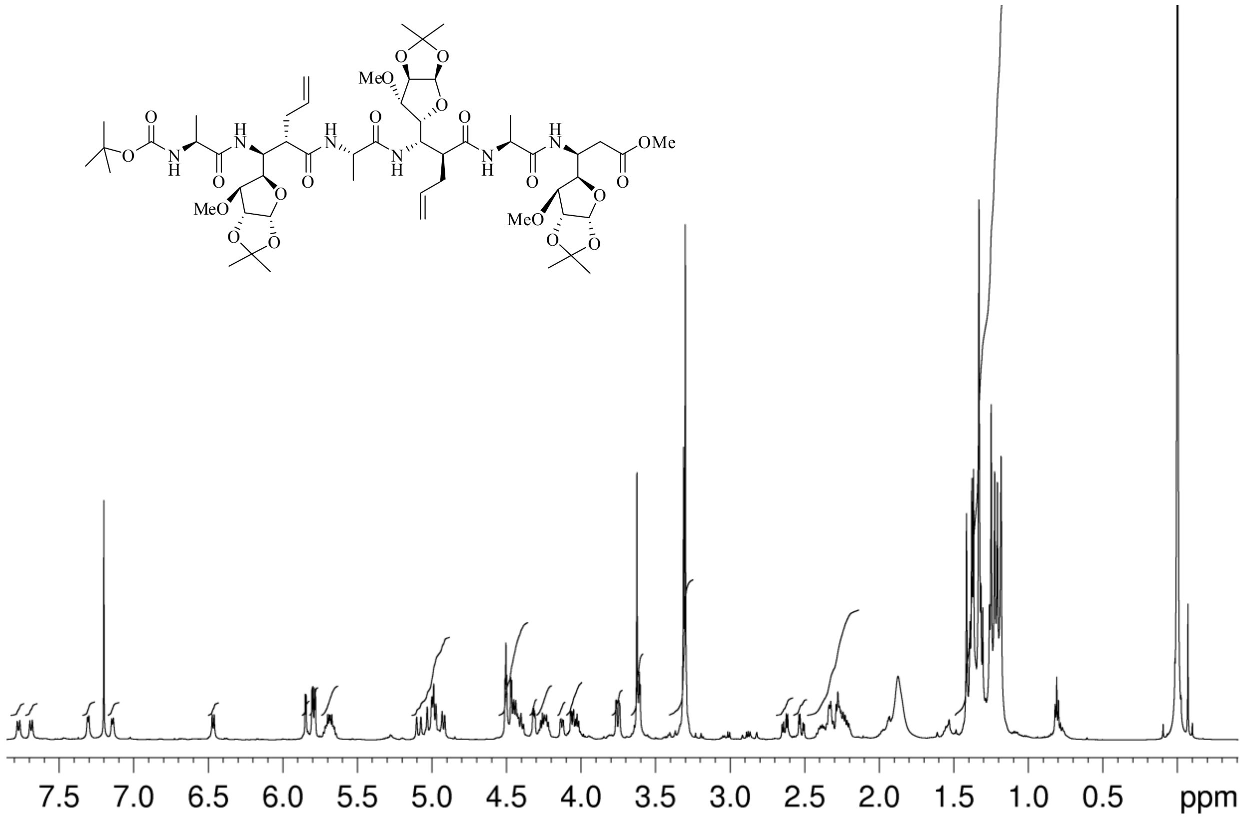


Figure S56: ^{1}H-NMR Spectrum of **14** (600 MHz, $CDCl_3$, 298 K).

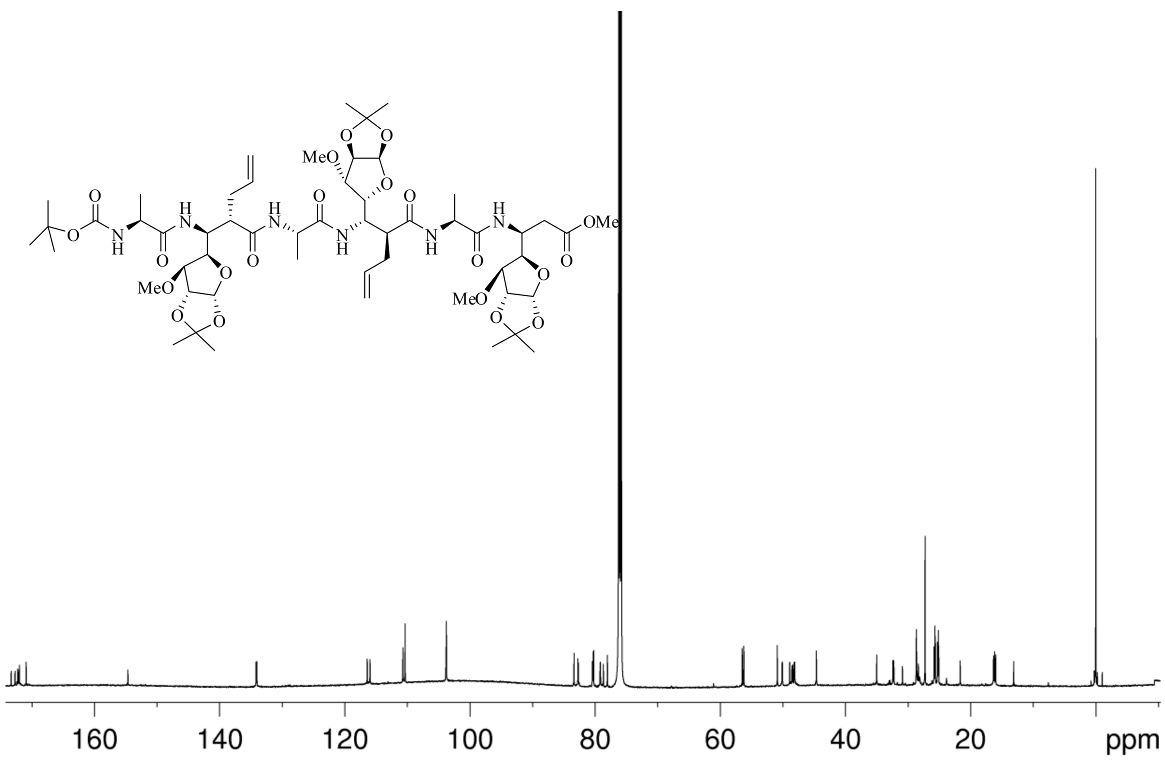


Figure S57: ^{13}C-NMR Spectrum of **14** (600 MHz, $CDCl_3$, 298 K).

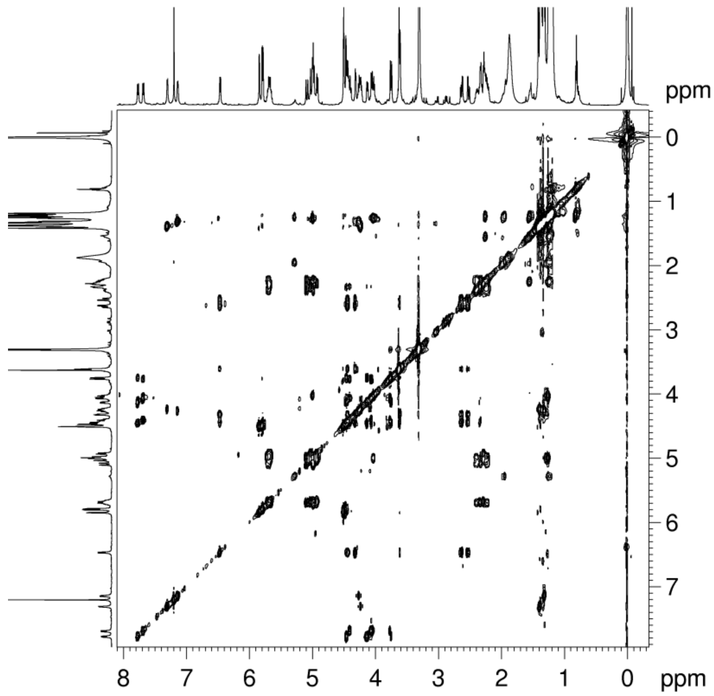


Figure S58: TOCSY Spectrum of **14** (600 MHz, $CDCl_3$, 298 K).

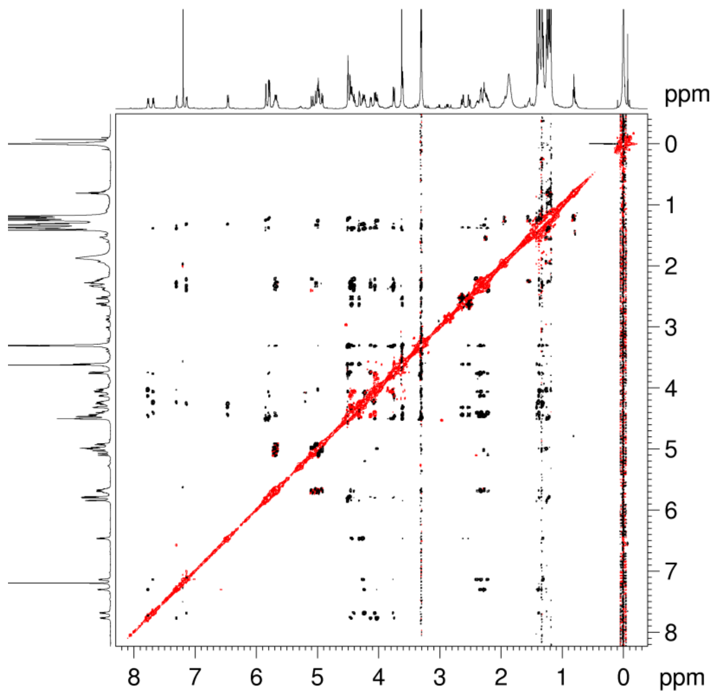


Figure S59: ROESY Spectrum of **14** (600 MHz, $CDCl_3$, 298 K).

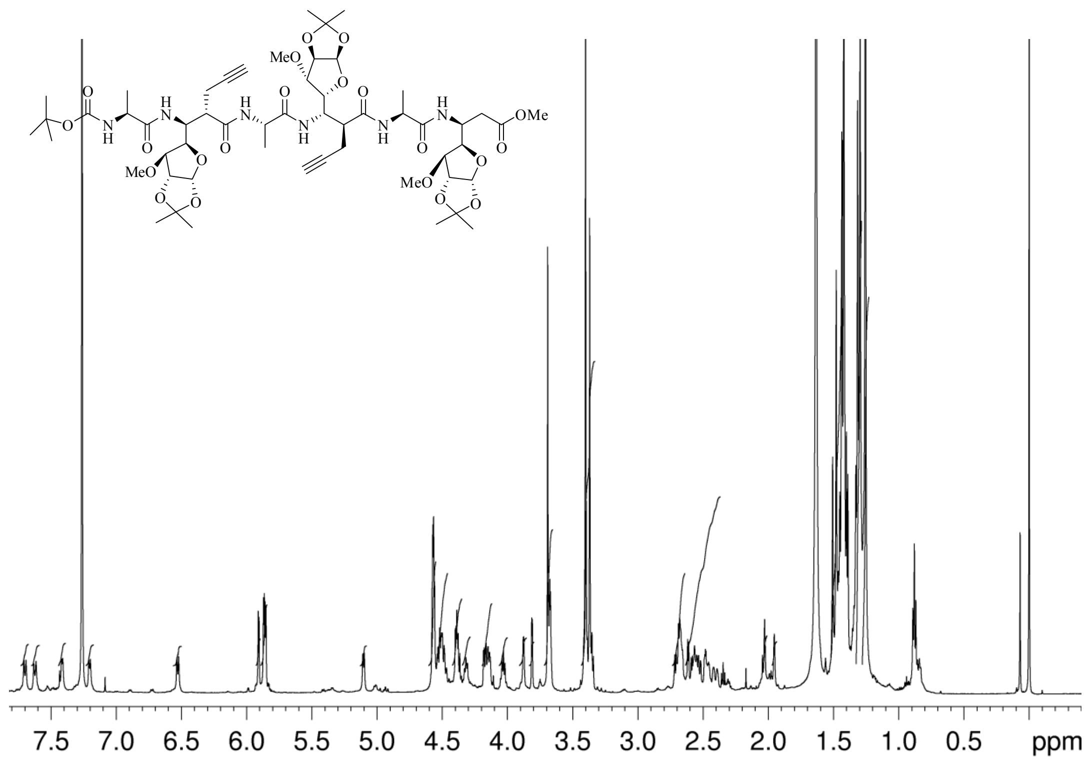


Figure S60: ^{1}H-NMR Spectrum of **15** (600 MHz, $CDCl_3$, 298 K).

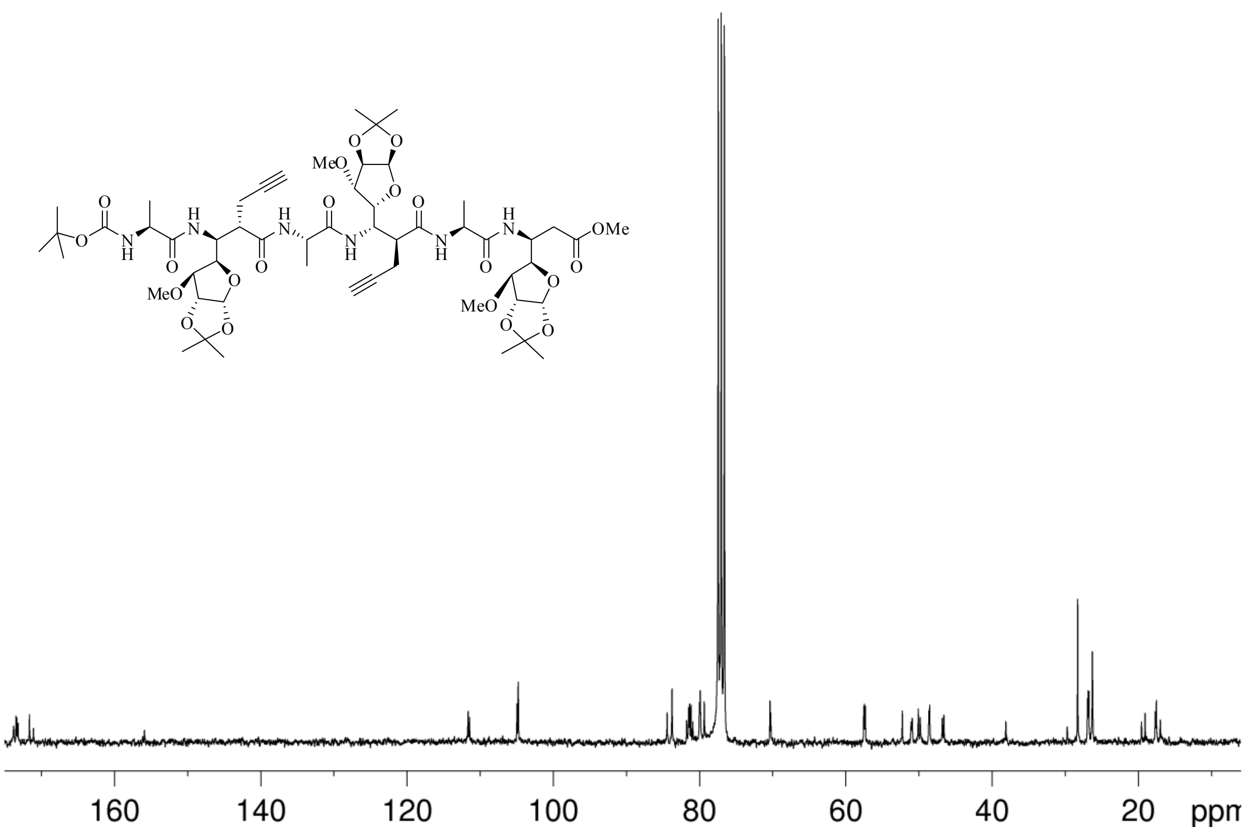


Figure S61: ^{13}C-NMR Spectrum of **15** (600 MHz, $CDCl_3$, 298 K).

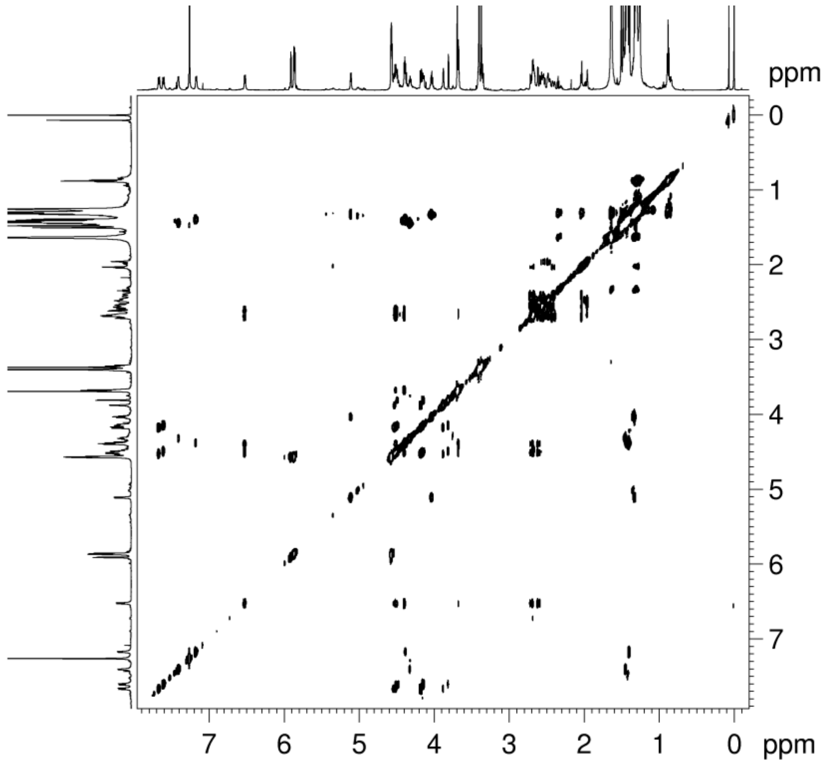


Figure S62: TOCSY Spectrum of **15** (600 MHz, $CDCl_3$, 298 K)

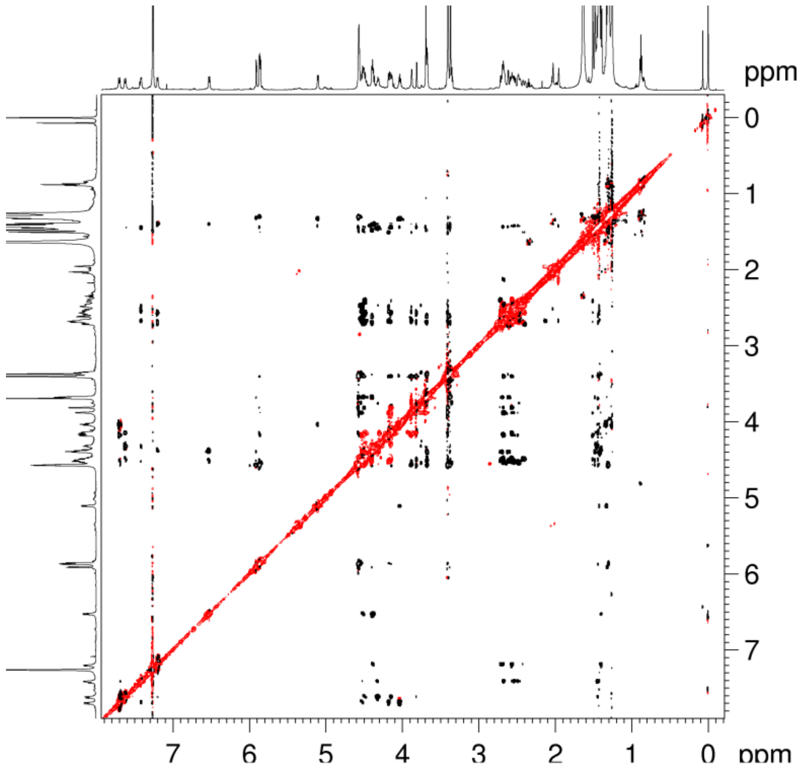


Figure S63: ROESY Spectrum of **15** (600 MHz, $CDCl_3$, 298 K).

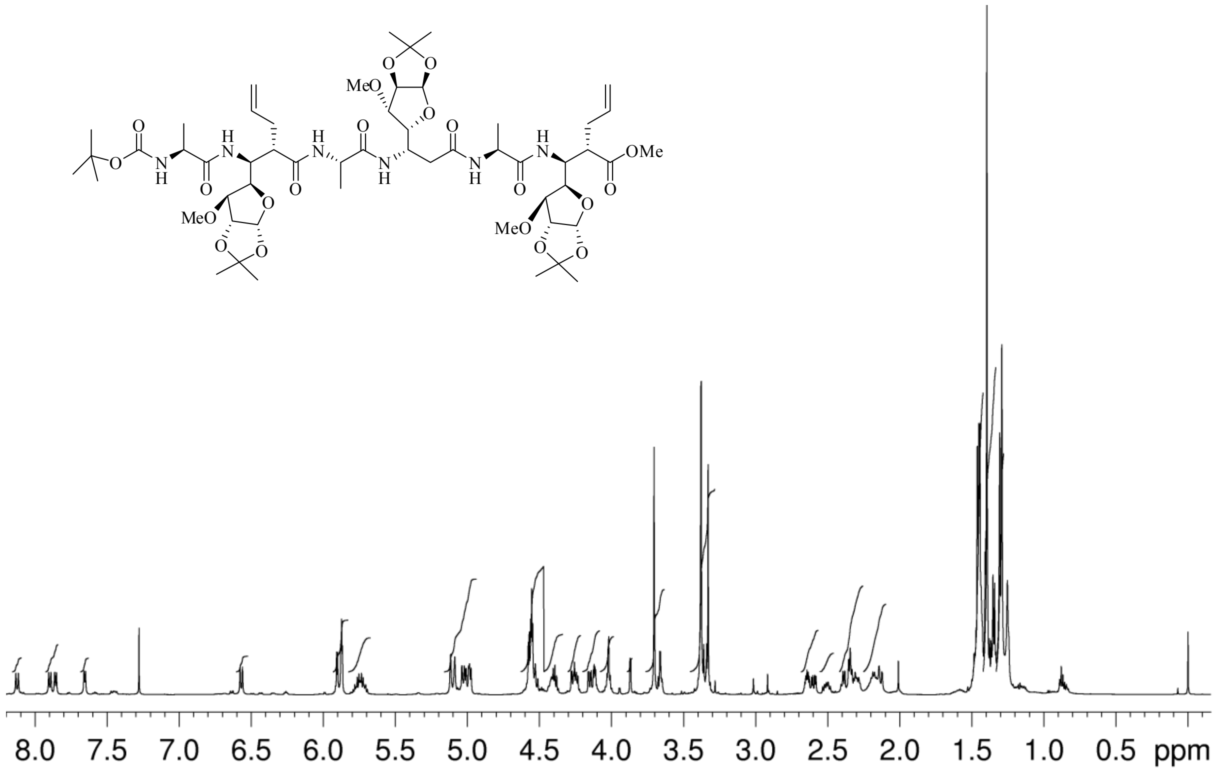


Figure S64: ^{1}H-NMR Spectrum of **16** (600 MHz, $CDCl_3$, 298 K).

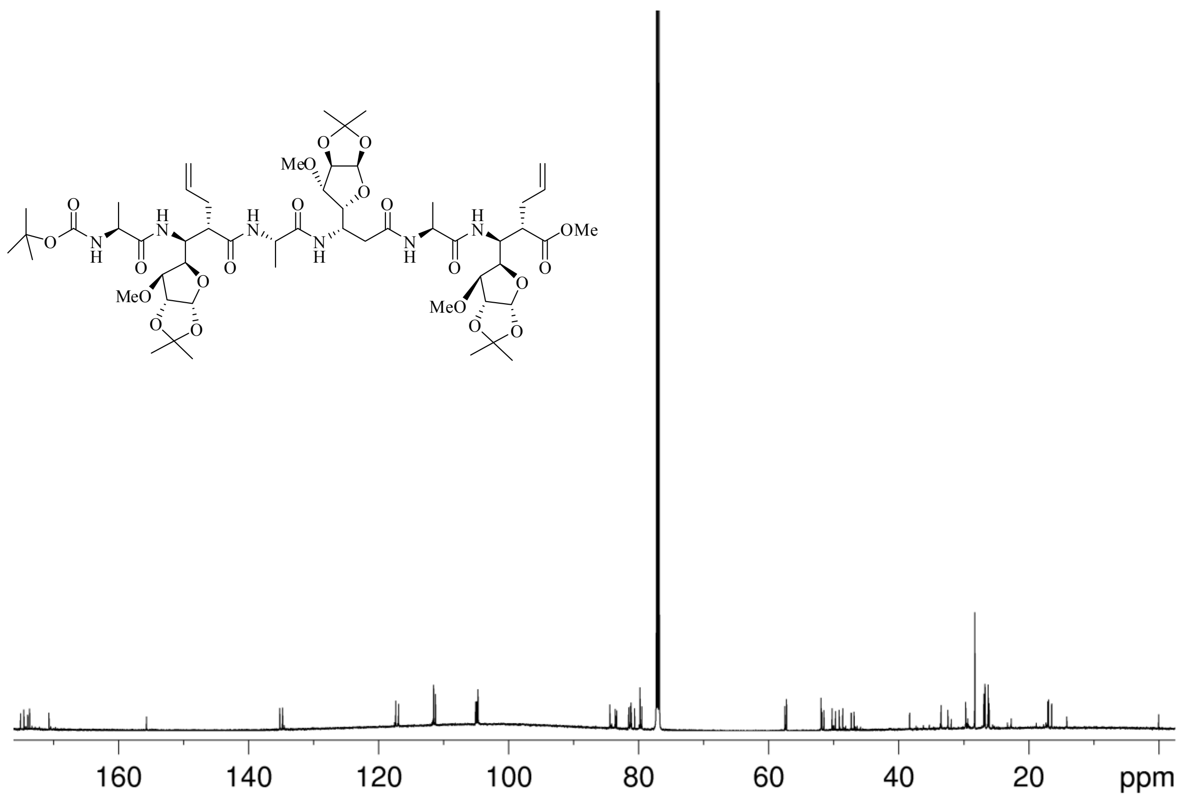


Figure S65: ^{13}C-NMR Spectrum of **16** (150 MHz, $CDCl_3$, 298 K).

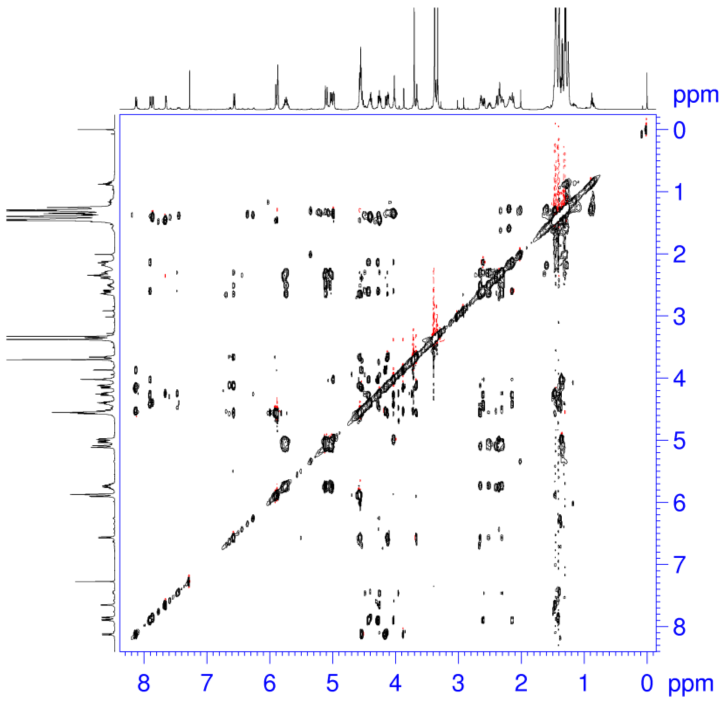


Figure S66: TOCSY Spectrum of **16** (600 MHz, $CDCl_3$, 298 K).

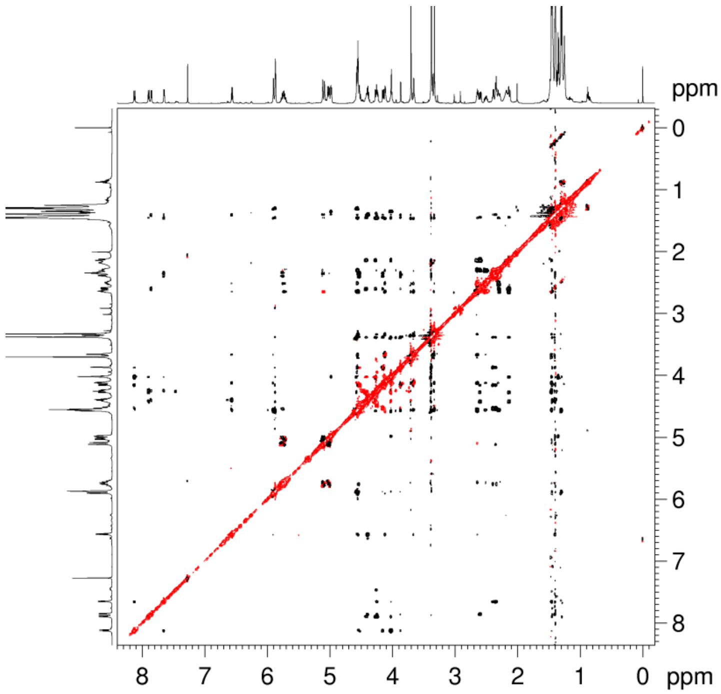


Figure S67: ROESY Spectrum of **16** (600 MHz, $CDCl_3$, 298 K).

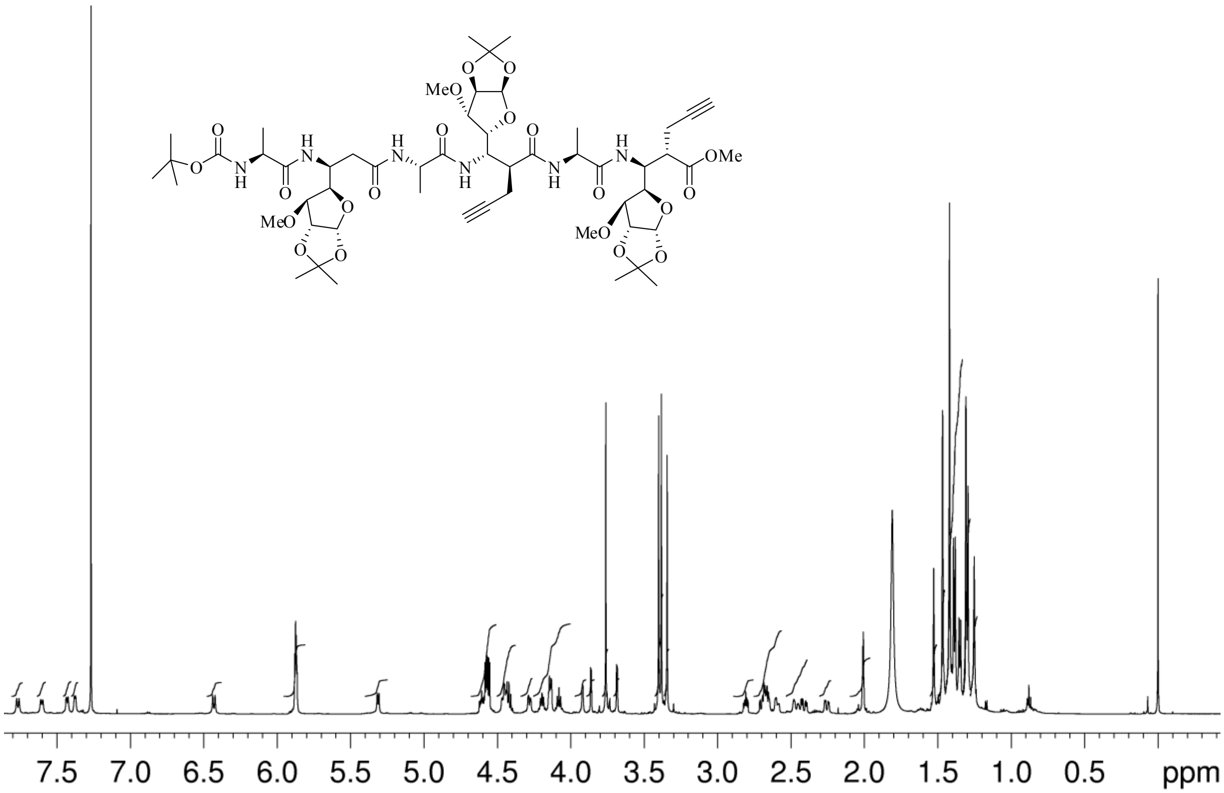


Figure S68: ^{1}H-NMR Spectrum of **17** (600 MHz, $CDCl_3$, 298 K).

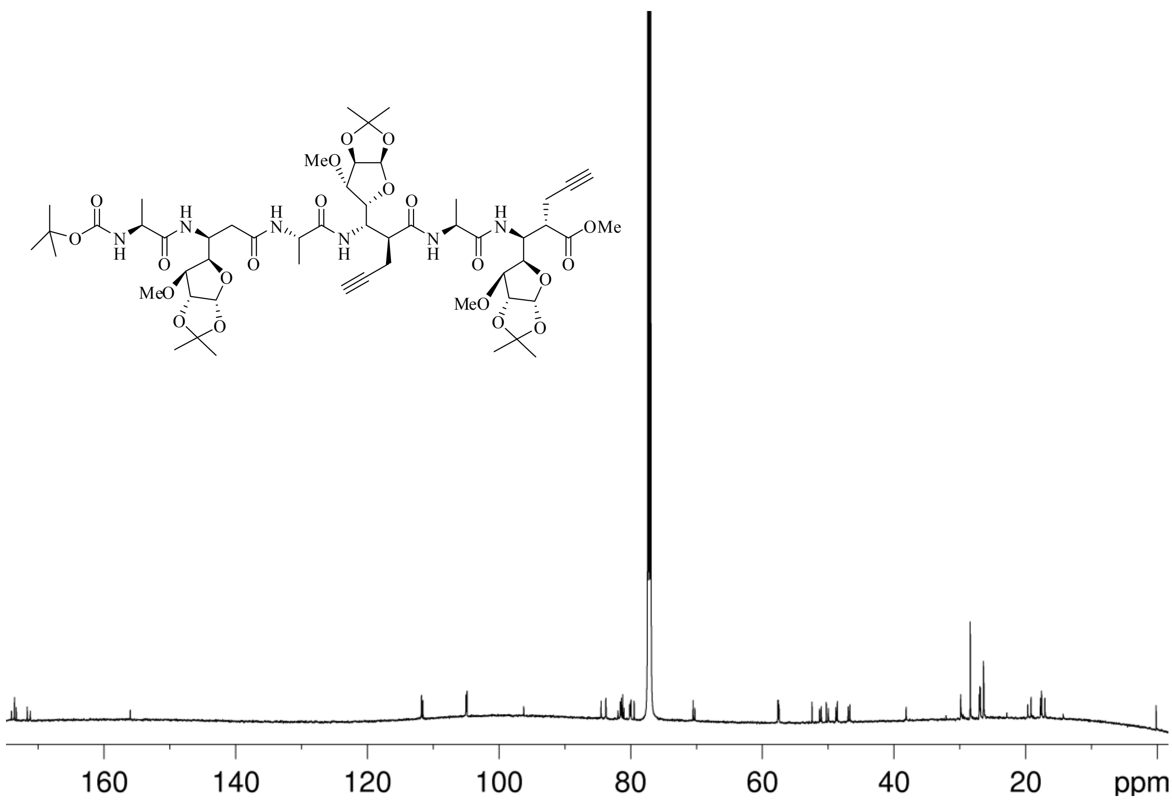


Figure S69: ^{13}C-NMR Spectrum of **17** (600 MHz, $CDCl_3$, 298 K).

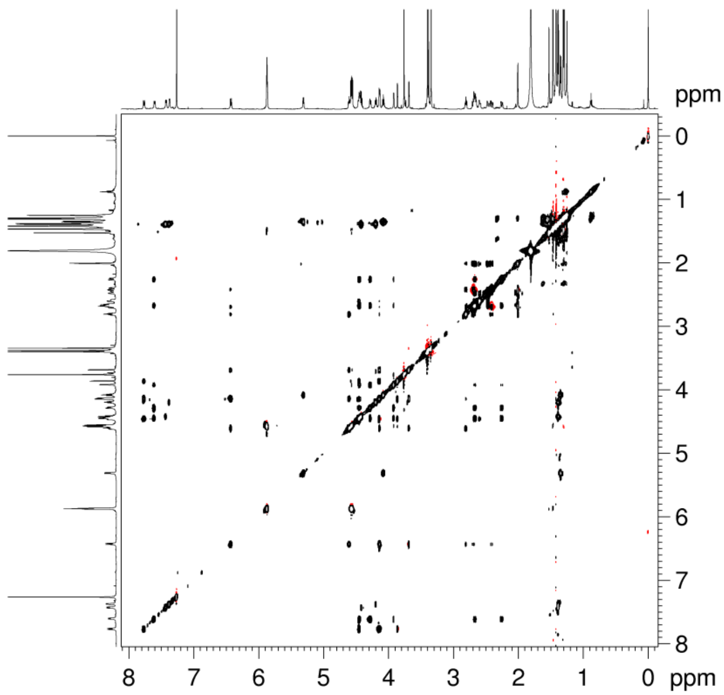


Figure S70: TOCSY Spectrum of **17** (600 MHz, $CDCl_3$, 298 K).

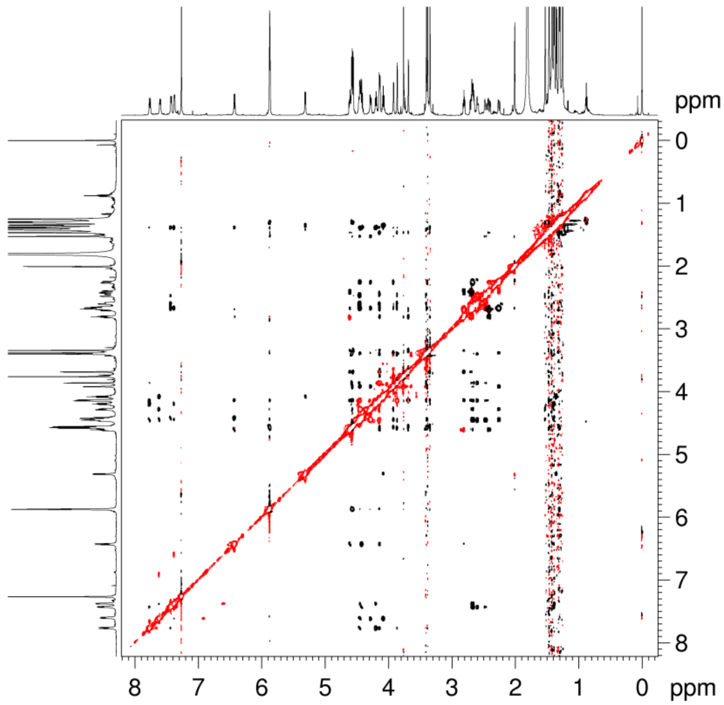


Figure S71: ROESY Spectrum of **17** (600 MHz, $CDCl_3$, 298 K).

Molecular Dynamics Studies

Table S14: List of constraints used in MD study for peptide **12**									
1	CαH	2	NH	1.80-2.50	3	CH_3	4	NH	1.80-3.50
1	CH_3	2	NH	1.80-3.50	3	CαH	4	NH	1.80-2.50
2	CβH	2	C3'H(*pro-R*)	1.80-2.50	3	CαH	5	NH	1.80-5.00
2	C3H	2	C3'H(*pro-S*)	1.80-3.50	4	C3H	4	C3'H(*pro-S*)	1.80-3.50
1	CαH	3	NH	1.80-5.00	4	CβH	4	C3'H(*pro-R*)	1.80-5.00
2	NH	2	C_4H	1.80-3.50	4	C_4H	4	NH	1.80-3.50
2	NH	3	NH	1.80-3.50	4	NH	5	NH	1.80-3.50
2	CβH	3	NH	1.80-5.00	4	CβH	5	NH	1.80-5.00
2	NH	3	CH_3	1.80-5.00	4	CαH	5	NH	1.80-2.50
2	CαH	3	NH	1.80-2.50	4	NH	5	CH_3	1.80-5.00
2	NH	4	CβH	1.80-5.00					

Table S14A: Dihedral angle constraints used in MD calculation for peptide **12**.					
Dihedral angles / Residues	ϕ_β	θ_β	ψ_α or ψ_β	$\chi 1$	$\chi 1'$
L-Ala[1]					
β-Caa[2]	120±30°	60±30°	-120±30°	180±30°	180±30°
L-Ala[3]			120±30°		
β-Caa[4]	120±30°	60±30°	-120±30°	180±30°	180±30°
L-Ala[5]					

***Table S15*: List of constraints used in MD study for peptide 13a**									
Res	Proton	Res	Proton	Distance	Res	proton	Res	Proton	Distance
1	CαH	2	NH	1.80-2.50	2	NH	3	CH_3	1.80-5.00
1	CH_3	2	NH	1.80-3.50	3	CαH	4	NH	1.80-2.50
1	CαH	3	NH	1.80-3.50	3	CH_3	4	NH	1.80-3.50
2	NH	2	C_4H	1.80-2.50	3	CαH	5	NH	1.80-3.50
2	NH	4	CαH	1.80-5.00	4	C_3H	4	CαH	1.80-2.50
2	C4H	4	CαH	1.80-5.00	4	NH	4	C_4H	1.80-2.50
2	NH	3	NH	1.80-3.50	4	NH	5	NH	1.80-3.50
2	CαH	3	NH	1.80-2.50	4	CαH	5	NH	1.80-2.50
2	CβH	3	NH	1.80-5.00	4	CβH	5	NH	1.80-5.00

Table S15A: Dihedral angle constraints used in MD calculation for peptide **13a**.					
Dihedral angles / Residues	ϕ_β	θ_β	ψ_α or ψ_β	χ1	χ1'
L-Ala[1]					
β-Caa[2]	120±30°	60±30°	-120±30°	180±30°	
L-Ala[3]			120±30°		
β-Caa[4]	120±30°	60±30°	-120±30°	180±30°	
L-Ala[5]					

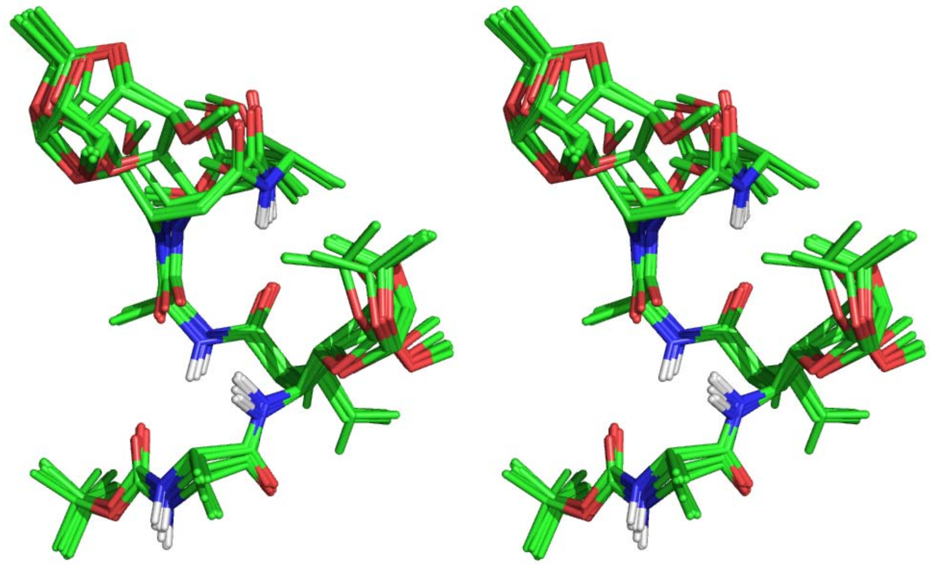


Figure *S72*: Stereoview of the superposition of 10 best structures for peptide **13a** from MD calculations (for the clarity, the protons are removed)

Table S16: List of constraints used in MD study for peptide **14**									
1	CαH	2	NH	1.80-2.50	4	NH	5	NH	1.80-3.50
1	CH_3	2	NH	1.80-3.50	3	CH_3	4	NH	1.80-3.50
1	CαH	3	CH_3	1.80-5.00	3	NH	5	CH_3	1.80-5.00
1	CαH	2	NH	1.80-2.50	3	CαH	5	NH	1.80-3.50
2	NH	2	C_4H	1.80-2.50	3	CαH	5	CH_3	1.80-5.00
2	NH	3	NH	1.80-3.50	4	NH	4	C_4H	1.80-2.50
2	CαH	3	NH	1.80-2.50	4	CαH	5	NH	1.80-2.50
2	CβH	3	NH	1.80-5.00	4	CβH	5	NH	1.80-5.00
2	NH	3	CH_3	1.80-5.00	4	NH	6	CβH	1.80-5.00
2	NH	4	CβH	1.80-5.00	4	C3H	6	CαH	1.80-5.00
2	C4H	4	C3'aH	1.80-5.00	4	C4H	6	CαH	1.80-5.00
2	C4H	4	C3'bH	1.80-5.00	5	CαH	6	NH	1.80-2.50
2	C_3H	5	NH	1.80-5.00	5	CH_3	6	NH	1.80-3.50
2	C_4H	5	NH	1.80-5.00	6	C3H	6	CαH	1.80-2.50
3	CαH	4	NH	1.80-2.50	6	C4H	6	CαH	1.80-2.50

Table S16A: Dihedral angle constraints used in MD calculation for peptide **14**.					
Dihedral angles / Residues	ϕ_β	θ_β	ψ_α or ψ_β	$\chi 1$	$\chi 1'$
L-Ala[1]					
β-Caa[2]	120±30°	60±30°	-120±30°	180±30°	
L-Ala[3]			120±30°		
β-Caa[4]	120±30°	60±30°	-120±30°	180±30°	
L-Ala[5]			120±30°		
β-Caa[6]					

Table S17**:** List of constraints used in MD study for peptide **15**									
1	CαH	2	NH	1.80-2.50	3	CH_3	4	NH	1.80-3.50
1	CH_3	2	NH	1.80-3.50	3	NH	5	CH_3	1.80-5.00
1	CαH	3	NH	1.80-5.00	3	CαH	5	NH	1.80-5.00
2	NH	2	C_4H	1.80-2.50	3	CαH	5	CH_3	1.80-5.00
2	CβH	2	C3'$H_{(pro\text{-}R)}$	1.80-3.50	4	NH	4	C_4H	1.80-2.50
2	C3H	2	C3'$H_{(pro\text{-}S)}$	1.80-3.50	4	CβH	4	C3'$H_{(pro\text{-}R)}$	1.80-3.50
2	NH	3	NH	1.80-3.50	4	C3H	4	C3'$H_{(pro\text{-}S)}$	1.80-3.50
2	CαH	3	NH	1.80-2.50	4	NH	5	NH	1.80-5.00
2	CβH	3	NH	1.80-5.00	4	CαH	5	NH	1.80-2.50
2	NH	3	CH_3	1.80-5.00	4	CβH	5	NH	1.80-5.00
2	NH	4	CβH	1.80-5.00	4	NH	6	CβH	1.80-5.00
2	NH	4	CαH	1.80-5.00	4	C_4H	6	CαH	1.80-5.00
2	C_4H	5	NH	1.80-5.00	5	CαH	6	NH	1.80-2.50
3	CαH	4	NH	1.80-2.50	5	CH_3	6	NH	1.80-3.50

Table S17A: Dihedral angle constraints used in MD calculation for peptide **15**.					
Dihedral angles / Residues	ϕ_β	θ_β	ψ_α or ψ_β	χ1	χ1'
L-Ala[1]					
β-Caa[2]	120±30°	60±30°	-120±30°	180±30°	180±30°
L-Ala[3]			120±30°		
β-Caa[4]	120±30°	60±30°	-120±30°	180±30°	180±30°
L-Ala[5]			120±30°		
β-Caa[6]					

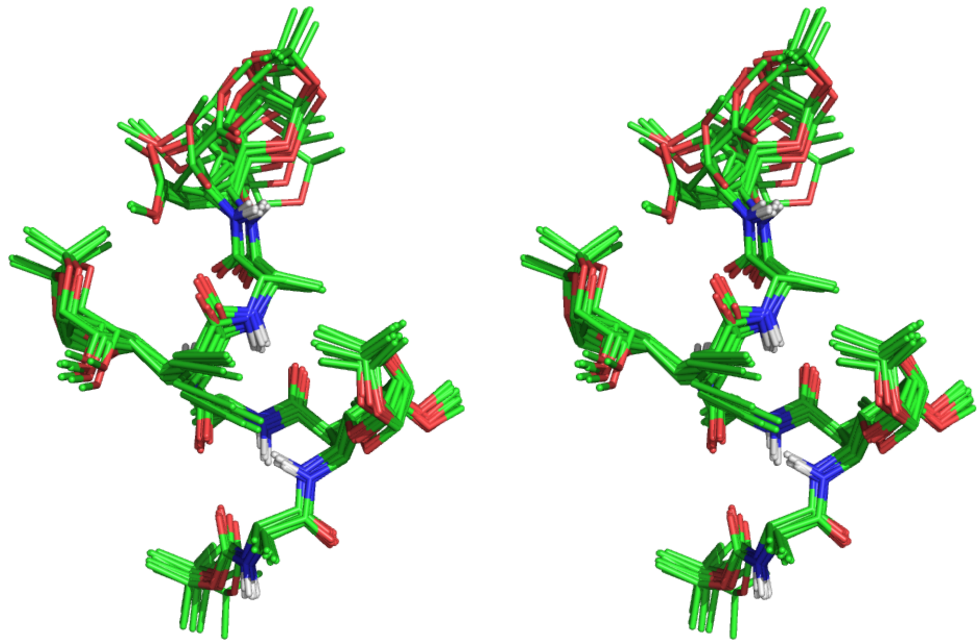


Figure *S73*: Stereoview of the superposition of 10 best structures for peptide **15** from MD calculations (for the clarity, the protons are removed)

***Table S18*: List of constraints used in MD study for peptide 16**									
1	CαH	2	NH	1.80-2.50	3	CαH	5	NH	1.80-3.50
1	CH_3	2	NH	1.80-3.50	3	CαH	5	CH_3	1.80-5.00
1	CαH	3	NH	1.80-3.50	3	CαH	6	NH	1.80-5.00
2	NH	2	C_4H	1.80-2.50	4	NH	4	C_4H	1.80-2.50
2	NH	3	NH	1.80-3.50	4	C3H	4	CαH *(pro-R)*	1.80-3.50
2	CαH	3	NH	1.80-2.50	4	C4H	4	CαH *(pro-R)*	1.80-3.50
2	CβH	3	NH	1.80-5.00	4	CαH	5	NH	1.80-2.50
2	NH	3	CH_3	1.80-5.00	4	CβH	5	NH	1.80-5.00
2	NH	4	CβH	1.80-5.00	4	NH	6	CβH	1.80-5.00
2	NH	4	CαH*(pro-S)*	1.80-5.00	4	C_4H	6	NH	1.80-5.00
2	C4H	4	CαH*(pro-S)*	1.80-3.50	5	CαH	6	NH	1.80-2.50
2	C_4H	5	NH	1.80-3.50	5	CH_3	6	NH	1.80-3.50
3	CαH	4	NH	1.80-2.50	4	NH	6	NH	1.80-5.00
4	NH	5	NH	1.80-3.50	5	NH	6	NH	1.80-5.00
3	CH_3	4	NH	1.80-3.50	6	CβH	6	C3'H*(pro-R)*	1.80-3.50
3	NH	5	CH_3	1.80-5.00	6	C3H	6	C3'H*(pro-S)*	1.80-3.50

***Table S18A*: Dihedral angle constraints used in MD calculation for peptide 16.**					
Dihedral angles / Residues	ϕ_β	θ_β	ψ_α or ψ_β	χ1	χ1'
L-Ala[1]					
β-Caa[2]	120±30°	60±30°	-120±30°	180±30°	
L-Ala[3]			120±30°		
β-Caa[4]	120±30°	60±30°	-120±30°	180±30°	
L-Ala[5]			120±30°		
β-Caa[6]					180±30°

***Table S19*: List of constraints used in MD study for peptide 17**									
1	CαH	2	NH	1.80-2.50	3	CH_3	4	NH	1.80-3.50
1	CH_3	2	NH	1.80-3.50	3	NH	5	CH_3	1.80-5.00
1	CαH	3	NH	1.80-5.00	3	CαH	5	NH	1.80-5.00
1	CαH	3	CH_3	1.80-5.00	3	CαH	5	CH_3	1.80-5.00
2	NH	2	C_4H	1.80-2.50	4	NH	4	C_4H	1.80-2.50
2	C3H	2	CαH*(pro-R)*	1.80-3.50	4	CβH	4	C3'H*(pro-R)*	1.80-3.50
2	C4H	2	CαH*(pro-R)*	1.80-3.50	4	C3H	4	C3'H*(pro-S)*	1.80-3.50
2	C_3H	2	CαH	1.80-3.50	4	NH	5	NH	1.80-3.50
2	NH	3	NH	1.80-3.50	4	CαH	5	NH	1.80-2.50
2	CαH	3	NH	1.80-2.50	4	CβH	5	NH	1.80-5.00
2	CβH	3	NH	1.80-5.00	4	NH	6	CβH	1.80-5.00
2	NH	3	CH_3	1.80-5.00	4	C_3H	6	CαH	1.80-5.00
2	NH	4	CβH	1.80-5.00	5	CαH	6	NH	1.80-2.50
2	NH	4	CαH	1.80-5.00	5	CH_3	6	NH	1.80-3.50
2	C_4H	5	NH	1.80-5.00	6	CβH	6	C3'H*(pro-R)*	1.80-3.50
2	C_3H	5	NH	1.80-5.00	6	C3H	6	C3'H*(pro-S)*	1.80-3.50
3	CαH	4	NH	1.80-2.50					

***Table S19A*: Dihedral angle constraints used in MD calculation for peptide 17.**					
Dihedral angles / Residues	ϕ_β	θ_β	ψ_α or ψ_β	χ1	χ1'
L-Ala[1]					
β-Caa[2]	120±30°	60±30°	-120±30°		
L-Ala[3]			120±30°		
β-Caa[4]	120±30°	60±30°	-120±30°		180±30°
L-Ala[5]			120±30°		
β-Caa[6]					180±30°

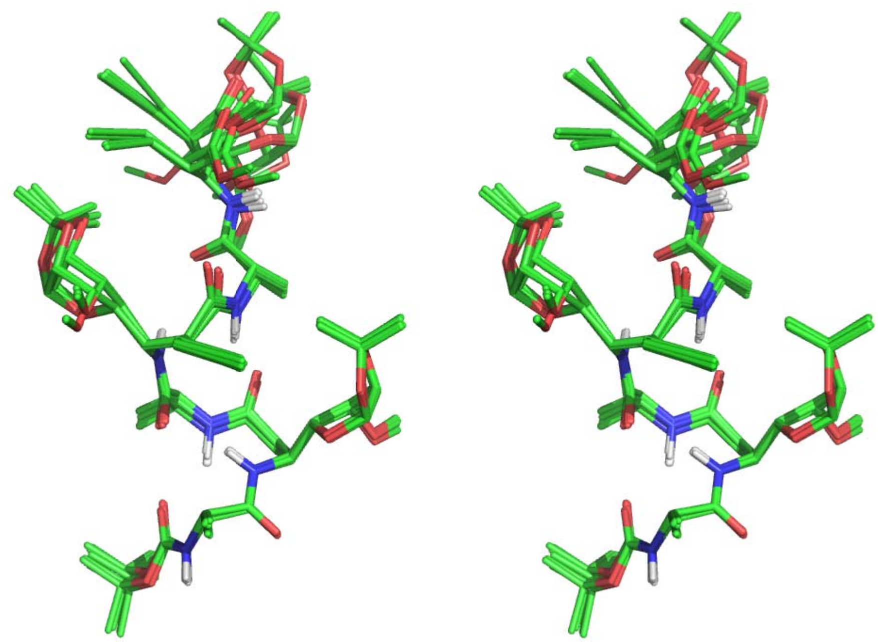


Figure *S74*: Stereoview of the superposition of 10 best structures for peptide **17** from MD calculations (for the clarity, the protons are removed)