ELECTRONIC SUPPORTING INFORMATION

Folding and self-assembling with β-oligomers based on (1*R*,2*S*)-2-aminocyclobutane-1-carboxylic acid

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SUMMARY

STRUCTURAL STUDY BY MEANS OF THEORETICAL CALCULATIONS

The molecules under study were built taking profit of the modular philosophy of Amber 7 and the parm99 Force Field was employed in all cases. The fragments of the molecules are split up into are shown in Fig. S1.

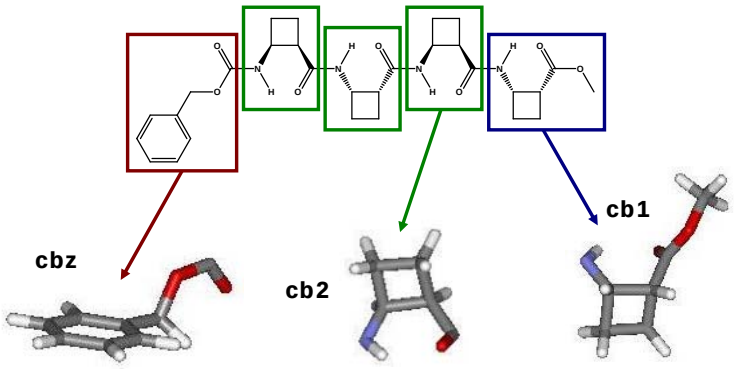


Fig. S1 Schematic depiction of the tetramer **8a**. Three units are necessary for creating these molecules.

CONFORMATIONAL SEARCH

```
int i = 1;
while (i <= numberSteps)
{
        C(i+1) = simulatedAnnealing[C(i)];
        conformationPool = store[(i+1)];
        i = i + 1;
}
```

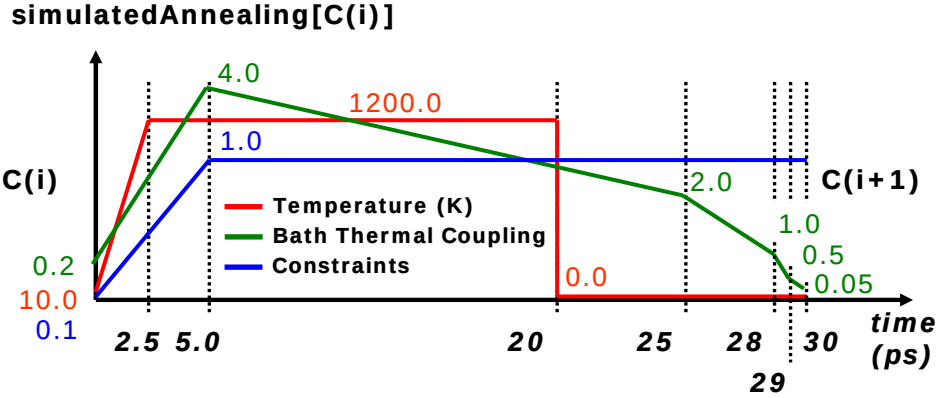


Fig. S2 Simulated Annealing algorithm used in this work: The iterative process concatenates a series of individual steps where a thermal shock is applied to the molecules under study. The output from step "n-1 "is the input of step "n".

SA.in

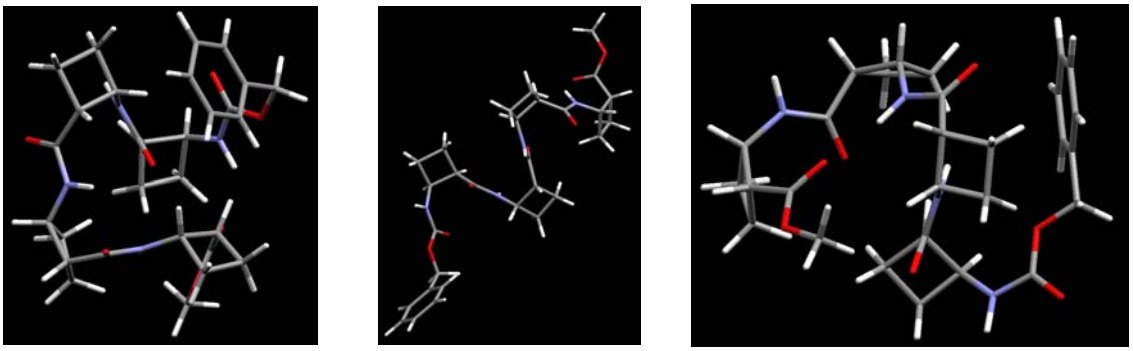
Simulated Annealing input file for AMBER 7.

```
Simulated Annealing calculation for SA - Fast Calculation
 &cntrl
imin=0, nmropt=1,
ntx=1, irest=0, ntrx=1,
ntxo=1, ntpr=1000, ntwr=1000,
iwrap=0, ntwx=1000, ntwv=0, ntwe=1000,
lastrst=3000000,
ioutfm=0, ntwprt=0, idecomp=0,
ntf=2, ntb=0, igb=0, nsnb=25,
ipol=0, gbsa=0,
dielc=1.0, cut=12.0, intdiel=1.0,
scnb=2.0, scee=1.2,
nstlim=30000, nscm=1000, nrespa=1,
t=0.0, dt=0.001, vlimit=10.0,
ig=71277, ntt=1, vrand=0,
temp0= 1000.0, tempi=0.0, heat=0.0,
dtemp=5.0, tautp=0.5,
ntc=2,
tol=0.00001
 &end
 &wt type='TEMP0', istep1=1,     istep2=2500,  value1=10.0,   value2=1200.0, &end
 &wt type='TEMP0', istep1=2501,  istep2=20000, value1=1200.0, value2=1200.0, &end
 &wt type='TEMP0', istep1=20001, istep2=30000, value1=0.0,    value2=0.0,    &end
 &wt type='TAUTP', istep1=1,     istep2=5000,  value1=0.2,    value2=4.0,    &end
 &wt type='TAUTP', istep1=5001,  istep2=25000, value1=4.0,    value2=2.0,    &end
 &wt type='TAUTP', istep1=25001, istep2=28000, value1=2.0,    value2=1.0,    &end
 &wt type='TAUTP', istep1=28001, istep2=29000, value1=1.0,    value2=0.5,    &end
 &wt type='TAUTP', istep1=29001, istep2=30000, value1=0.5,    value2=0.05,   &end
 &wt type='REST',  istep1=1,     istep2=5000,  value1=0.1,    value2=1.0,    &end
 &wt type='REST',  istep1=5001,  istep2=30000, value1=1.0,    value2=1.0,    &end
 &wt type='END'
 &end
DISANG=tetraSA_rst.f
```

Conformations obtained from Conformational Search

The wide conformational freedom within these molecules does not allow selecting a single major representative conformation for any of the polypeptides. Nevertheless, 3 structures have been selected in each case on the basis of the analysis of the two-dimensional plots of principal components (Fig. S3).

Tetrapeptide 8a



Octapeptide 10a

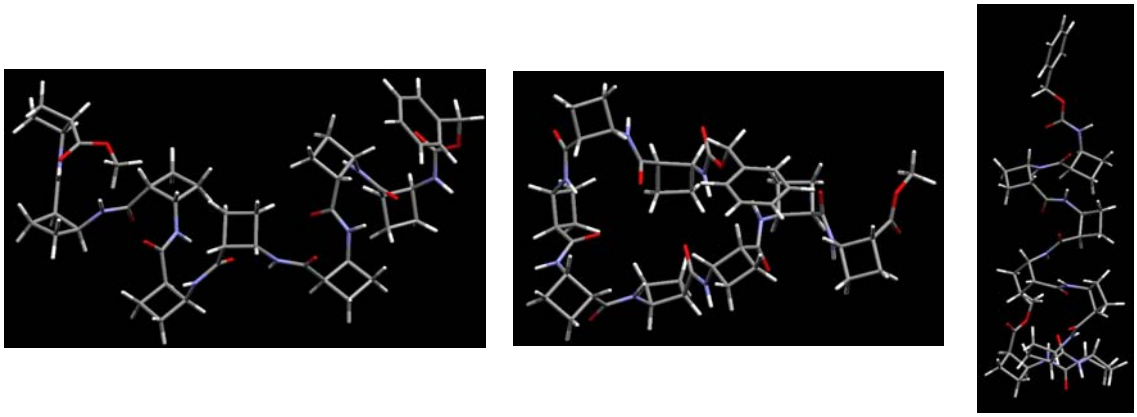


Fig. S3 Selected conformers for the tetramer **8a** and the octamer **10a**.

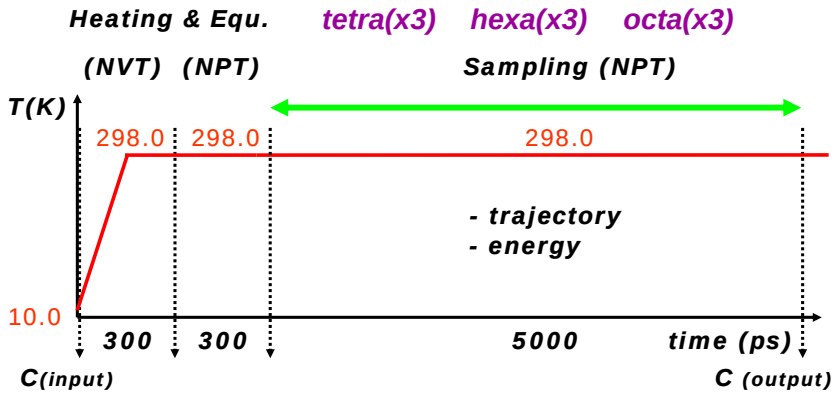


Fig. S4 Schematic depiction of the 3-step Molecular Dynamics process in $CHCl_3$.

Step 0: Geometrical Optimization.

```
stp0. Energy Minimization – Geometrical Optimization (Restricted)
 &cntrl
   imin=1,     nmropt=1,
   ntx=1,      irest=0,     ntrx=1,
   ntb=1,      igb=0,       nsnb=25,
   ipol=0,     gbsa=0,
   dielc=1.0,  cut=12.0,    intdiel=1.0,
   scnb=2.0,   scee=1.2,
   ibelly=0,   ntr=0,
   maxcyc=50000,
 &end
1.0
 &wt type='END' &end
DISANG=hexaSA_rst.f
```

Step 1: Heating and Equilibration (NVT).

```
stp1. Heating and Equilibration (Restricted) V cte. (NVT).
 &cntrl
   imin=0,         nmropt=1,
   ntx=1,          irest=0,     ntrx=1,
   ntxo=1,         ntpr=1000,   ntwr=1000,
   iwrap=1,
   ntwx=1000,      ntwv=0,      ntwe=1000,
   lastrst=50000000,
   ntf=2,          ntb=1,
   igb=0,          nsnb=25,
   ntc=2,          cut=12.0,
   nstlim=300000,  nscm=1000,   nrespa=1,
   t=0.0,          dt=0.001,    vlimit=20.0,
   ig=71277,       ntt=1,       vrand=0,
   temp0=298.0,    tempi=0.0,   heat=0.0,
   dtemp=5.0,      tautp=0.5,
   tol=0.00001,
 &end
 &wt type='TEMP0', istep1=0,      istep2=100000, value1=0.0,   value2=298.0, &end
 &wt type='TEMP0', istep1=100001, istep2=300000, value1=298.0, value2=298.0, &end
 &wt type='TAUTP', istep1=1,      istep2=50000,  value1=0.2,   value2=4.0,   &end
 &wt type='TAUTP', istep1=50001,  istep2=250000, value1=4.0,   value2=2.0,   &end
 &wt type='TAUTP', istep1=250001, istep2=280000, value1=2.0,   value2=1.0,   &end
 &wt type='TAUTP', istep1=280001, istep2=290000, value1=1.0,   value2=0.5,   &end
 &wt type='TAUTP', istep1=290001, istep2=300000, value1=0.5,   value2=0.05,  &end
 &wt type='REST',  istep1=1,      istep2=100000, value1=0.1,   value2=1.0,   &end
 &wt type='REST',  istep1=100001, istep2=300000, value1=1.0,   value2=1.0,   &end
 &wt type='END'
 &end
DISANG=hexaSA_rst.f
```

Step 2: Equilibration (NPT).

```
stp2. Equilibration (Restricted) P cte. (NPT).
 &cntrl
   imin=0,         nmropt=1,
   ntx=1,          irest=0,     ntrx=1,
   ntxo=1,         ntpr=1000,   ntwr=1000,
   iwrap=1,
   ntwx=1000,      ntwv=0,      ntwe=1000,
   lastrst=50000000,
   ntf=2,          ntb=2,       ntp=1,
   igb=0,          nsnb=25,
   ntc=2,          cut=12.0,
   nstlim=300000,  nscm=1000,   nrespa=1,
   t=0.0,          dt=0.001,    vlimit=20.0,
   ig=71277,       ntt=1,       vrand=0,
   temp0=298.0,    tempi=298.0, heat=0.0,
   dtemp=5.0,      tautp=0.5,   comp=97.4,
   tol=0.00001,
 &end
 &wt type='TEMP0', istep1=0, istep2=300000, value1=298.0, value2=298.0, &end
 &wt type='END'
 &end
DISANG=hexaSA_rst.f
```

Step 3: Sampling (NPT).

```
stp3. Sampling (Restricted) a P cte. (NPT).
 &cntrl
   imin=0,         nmropt=1,
   ntx=1,          irest=0,      ntrx=1,
   ntxo=1,         ntpr=1000,    ntwr=1000,
   iwrap=0,
   ntwx=1000,      ntwv=0,       ntwe=1000,
   lastrst=50000000,
   ntf=2,          ntb=2,        ntp=1,
   igb=0,          nsnb=25,
   ntc=2,          cut=12.0,
   nstlim=5000000, nscm=1000,    nrespa=1,
   t=0.0,          dt=0.001,     vlimit=20.0,
   ig=71277,       ntt=1,        vrand=0,
   temp0=298.0,    tempi=298.0,  heat=0.0,
```

```
   dtemp=5.0,       tautp=0.5,     comp=97.4,
   tol=0.00001,
 &end
 &wt type='TEMP0', istep1=0, istep2=5000000, value1=298.0, value2=298.0, &end
 &wt type='END'
 &end
DISANG=hexaSA_rst.f
```

The results point that the hexapeptide **9a**, likewise the tetrapeptide **8a** and octapeptide **10a**, adopts in chloroform extended conformations, as show the average structures from the MD trajectories and also informations in Table 1.

	tetra conf.	distances (Å) NH···HC (No Rstr) d1	d2	d3
Average	1	2.36	2.35	2.35
	2	2.43	2.39	2.35
	3	2.54	2.25	2.32
Std.Dev.	1	0.33	0.31	0.33
	2	0.36	0.35	0.32
	3	0.40	0.22	0.30

	octa conf.	distances (Å) NH···HC (No Rstr) d1	d2	d3	d4	d5	d6	d7
Average	1	2.37	2.27	2.47	2.28	2.42	2.40	2.40
	2	2.38	2.32	2.35	2.36	2.29	2.29	2.29
	3	2.37	2.35	2.38	2.21	2.31	2.29	2.29
Std.Dev.	1	0.33	0.25	0.39	0.27	0.37	0.36	0.36
	2	0.35	0.30	0.34	0.34	0.27	0.27	0.27
	3	0.34	0.32	0.34	0.16	0.29	0.26	0.26

Tabla 1

AGGREGATION STUDIES: HYDROGEN-BONDING INTERACTIONS.

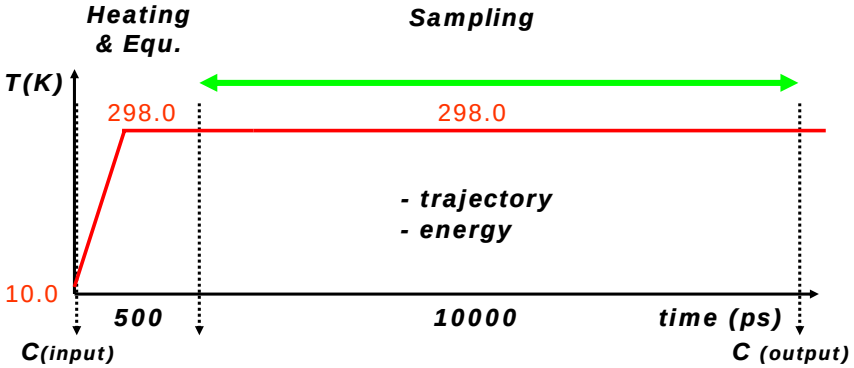


Fig. S5 Schematic depiction of the 2-step Molecular Dynamics process in vacuo.

Step 0: Geometrical Optimization.

```
stp0. Energetical Minimization – Geometrical Optimization (Restricted - Vacuum no Box).
 &cntrl
```

```
  imin=1,    nmropt=1,
  ntx=1,     irest=0,  ntrx=1,
  ntb=0,     igb=0,    nsnb=25,
  ipol=0,    gbsa=0,
  dielc=1.0, cut=12.0, intdiel=1.0,
  scnb=2.0,  scee=1.2,
  ibelly=0,  ntr=0,
  lastrst=5000000,
  maxcyc=50000,
 &end
 &wt type='END' &end
DISANG=tetra9A_rst.f
```

Step 1: Heating and Equilibration.

```
stp1. Heating and equilibration. Vacuum. Bath Thermal Coupling. (Restricted).
 &cntrl
  imin=0,         nmropt=1,
  ntx=1,          irest=0,    ntrx=1,
  ntxo=1,         ntpr=1000,  ntwr=1000,
  iwrap=0,        ntwx=1000,  ntwv=0, ntwe=1000,
  lastrst=5000000,
  ioutfm=0,       ntwprt=0,   idecomp=0,
  ntf=2,          ntb=0,      igb=0, nsnb=25,
  ipol=0,         gbsa=0,
  dielc=1.0,      cut=12.0,   intdiel=1.0,
  scnb=2.0,       scee=1.2,
  nstlim=500000,  nscm=1000,  nrespa=1,
  t=0.0,          dt=0.001,   vlimit=10.0,
  ig=71277,       ntt=1,      vrand=0,
  temp0=298.0,    tempi=0.0,  heat=0.0,
  dtemp=5.0,      tautp=0.5,
  ntc=2,          tol=0.00001
 &end
 &wt type='TEMP0', istep1=1,      istep2=100000, value1=10.0,   value2=298.0, &end
 &wt type='TEMP0', istep1=100001, istep2=500000, value1=298.0,  value2=298.0, &end
 &wt type='TAUTP', istep1=1,      istep2=50000,  value1=0.2,    value2=4.0,   &end
 &wt type='TAUTP', istep1=50001,  istep2=150000, value1=4.0,    value2=2.0,   &end
 &wt type='TAUTP', istep1=150001, istep2=200000, value1=2.0,    value2=0.5,   &end
 &wt type='TAUTP', istep1=200001, istep2=500000, value1=0.5,    value2=0.5,   &end
 &wt type='REST',  istep1=1,      istep2=50000,  value1=0.1,    value2=1.0,   &end
 &wt type='REST',  istep1=50001,  istep2=250000, value1=1.0,    value2=1.0,   &end
 &wt type='REST',  istep1=250001, istep2=500000, value1=1.0,    value2=0.1,   &end
 &wt type='END' &end
DISANG=tetra9A_rst.f
```

Step 2. Sampling.

```
stp2. Sampling in Equilibrium. Vacuum. Bath Thermal Coupling. (Restricted).
 &cntrl
  imin=0,      nmropt=1,
  ntx=5,       irest=1,     ntrx=1,
  ntxo=1,      ntpr=10000,  ntwr=10000,
  iwrap=0,     ntwx=10000,  ntwv=0,      ntwe=10000,
  lastrst=5000000,
  ioutfm=0,    ntwprt=0,    idecomp=0,
  ntf=2,       ntb=0,       igb=0,       nsnb=25,
  ipol=0,      gbsa=0,
  dielc=1.0,   cut=12.0,    intdiel=1.0,
  scnb=2.0,    scee=1.2,
  nstlim=10000000,          nscm=1000,   nrespa=1,
  t=0.0,       dt=0.001,    vlimit=10.0,
  ig=71277,    ntt=1,       vrand=0,
  temp0=298.0, tempi=298.0, heat=0.0,
  dtemp=5.0,   tautp=0.5,
  ntc=2,       tol=0.00001,
 &end
 &wt type='END' &end
DISANG=tetra9A_rst.f
```

The tables next comprise detailed information about parallel and alternate Hydrogen bonding calculations. All the particular inter and intramolecular Hydrogen bonding are included in percentage ratio.

Parallel Arrangement:

By Atom Number			By Residues			INTERmolecular Hbond [Parallel]				
Donor [O]	Acceptor [N-H]		Donor [O]	Acceptor [N-H]		Freq. [%]	Dist. O···H [Ang.]		Angle O-H-N [Deg.]	
O	H	N	O	H	N		Average	Std.Dev.	Average	Std.Dev.
78	135	134	:5@O2	:9@H1	:9@N1	91.3	3.08	0.17	25.25	11.08
593	341	340	:38@O1	:22@H1	:22@N1	84.3	3.12	0.17	28.18	13.26
373	589	588	:24@O1	:38@H1	:38@N1	78.5	3.21	0.16	29.56	12.39
33	244	243	:2@O1	:16@H1	:16@N1	72.6	3.15	0.16	27.27	13.78
217	355	354	:14@O1	:23@H1	:23@N1	26.0	3.17	0.17	19.55	11.30
281	29	28	:18@O1	:2@H1	:2@N1	14.4	3.32	0.12	36.58	13.71
312	57	56	:20@O2	:4@H1	:4@N1	12.4	3.12	0.19	50.54	8.84

By Atom Number			By Residues			INTRAmolecular Hbond [Parallel]				
Donor [O]	Acceptor [N-H]		Donor [O]	Acceptor [N-H]		Freq. [%]	Dist. O···H [Ang.]		Angle O-H-N [Deg.]	
O	H	N	O	H	N		Average	Std.Dev.	Average	Std.Dev.
281	277	276	:18@O1	:18@H1	:18@N1	87.1	2.941	0.15	50.54	5.12
638	634	633	:41@O1	:41@H1	:41@N1	87.0	2.878	0.11	49.61	5.63
170	166	165	:11@O1	:11@H1	:11@N1	85.3	2.896	0.12	49.87	5.36
61	57	56	:4@O1	:4@H1	:4@N1	85.2	2.907	0.12	51.42	5.08
515	511	510	:33@O1	:33@H1	:33@N1	84.0	2.831	0.10	49.04	6.16
579	575	574	:37@O1	:37@H1	:37@N1	81.6	3.016	0.15	51.54	5.00
482	478	477	:31@O1	:31@H1	:31@N1	79.7	2.890	0.11	50.56	5.59
47	43	42	:3@O1	:3@H1	:3@N1	76.8	2.991	0.14	51.15	5.08
501	497	496	:32@O1	:32@H1	:32@N1	73.0	2.959	0.13	52.21	4.88
295	291	290	:19@O1	:19@H1	:19@N1	72.8	2.925	0.13	51.98	4.94
451	447	446	:29@O1	:29@H1	:29@N1	68.4	2.878	0.11	51.88	5.04
560	556	555	:36@O1	:36@H1	:36@N1	65.5	3.065	0.18	51.75	5.21
203	199	198	:13@O1	:13@H1	:13@N1	63.6	2.896	0.15	49.13	5.97
404	400	399	:26@O1	:26@H1	:26@N1	54.9	2.852	0.10	50.15	5.79
671	667	666	:43@O1	:43@H1	:43@N1	54.5	2.904	0.11	51.14	5.74
217	213	212	:14@O1	:14@H1	:14@N1	37.7	2.875	0.11	52.48	5.02
125	121	120	:8@O1	:8@H1	:8@N1	36.0	3.046	0.17	52.00	5.03
685	681	680	:44@O1	:44@H1	:44@N1	34.5	2.878	0.10	53.59	4.71
267	263	262	:17@O1	:17@H1	:17@N1	28.9	3.141	0.19	51.18	5.68
437	433	432	:28@O1	:28@H1	:28@N1	27.5	2.925	0.13	50.31	5.37
189	185	184	:12@O1	:12@H1	:12@N1	25.9	2.814	0.09	51.62	5.65
529	525	524	:34@O1	:34@H1	:34@N1	23.2	2.886	0.13	52.98	4.94
14	10	9	:1@O1	:1@H1	:1@N1	20.5	2.920	0.11	51.84	5.59
33	29	28	:2@O1	:2@H1	:2@N1	19.5	2.987	0.18	49.39	6.52
111	107	106	:7@O1	:7@H1	:7@N1	17.5	2.866	0.12	49.46	5.57
326	322	321	:21@O1	:21@H1	:21@N1	12.5	2.911	0.16	51.87	5.00
373	369	368	:24@O1	:24@H1	:24@N1	12.4	2.910	0.13	52.80	5.07
345	341	340	:22@O1	:22@H1	:22@N1	10.2	2.902	0.10	53.22	4.94

Alternate Arrangement:

By Atom Number			By Residues			INTERmolecular Hbond [Alternate]				
Donor [O]	Acceptor [N-H]		Donor [O]	Acceptor [N-H]		Freq. [%]	Dist. O···H [Ang.]		Angle O-H-N [Deg.]	
O	H	N	O	H	N		Average	Std.Dev.	Average	Std.Dev.
685	341	340	:44@O1	:22@H1	:22@N1	39.8	3.227	0.16	26.68	12.08
345	653	652	:22@O1	:42@H1	:42@N1	28.8	3.127	0.18	35.69	15.42
92	213	212	:6@O1	:14@H1	:14@N1	25.7	3.199	0.17	30.96	13.60
92	355	354	:6@O1	:23@H1	:23@N1	23.0	3.195	0.17	45.91	10.74
93	213	212	:6@O2	:14@H1	:14@N1	19.0	3.151	0.18	29.43	12.93
111	29	28	:7@O1	:2@H1	:2@N1	12.6	3.329	0.13	44.29	11.66
14	135	134	:1@O1	:9@H1	:9@N1	10.2	3.192	0.20	32.54	15.92

By Atom Number			By Residues			INTRAmolecular Hbond [Alternate]				
Donor [O]	Acceptor [N-H]		Donor [O]	Acceptor [N-H]		Freq. [%]	Dist. O···H [Ang.]		Angle O-H-N [Deg.]	
O	H	N	O	H	N		Average	Std.Dev.	Average	Std.Dev.
482	478	477	:31@O1	:31@H1	:31@N1	84.4	2.927	0.12	50.36	5.65
685	681	680	:44@O1	:44@H1	:44@N1	82.8	2.864	0.11	51.30	5.25
33	29	28	:2@O1	:2@H1	:2@N1	81.2	2.911	0.13	49.93	5.61
638	634	633	:41@O1	:41@H1	:41@N1	79.5	2.910	0.10	51.62	5.06
560	556	555	:36@O1	:36@H1	:36@N1	77.9	2.905	0.12	51.61	4.87
281	277	276	:18@O1	:18@H1	:18@N1	77.5	2.907	0.13	50.32	5.61
203	199	198	:13@O1	:13@H1	:13@N1	77.4	2.862	0.10	50.07	5.75
501	497	496	:32@O1	:32@H1	:32@N1	76.6	2.909	0.12	51.45	5.23
170	166	165	:11@O1	:11@H1	:11@N1	71.7	2.892	0.11	51.54	5.18
14	10	9	:1@O1	:1@H1	:1@N1	71.1	2.948	0.15	50.87	5.50
111	107	106	:7@O1	:7@H1	:7@N1	70.1	2.942	0.15	51.13	5.23
607	603	602	:39@O1	:39@H1	:39@N1	62.0	2.853	0.11	51.86	5.33
451	447	446	:29@O1	:29@H1	:29@N1	58.0	2.991	0.15	52.48	5.15
61	57	56	:4@O1	:4@H1	:4@N1	57.8	2.894	0.12	51.42	5.26
92	88	87	:6@O1	:6@H1	:6@N1	55.2	2.936	0.14	52.73	4.98
373	369	368	:24@O1	:24@H1	:24@N1	54.0	3.003	0.16	51.48	5.06
593	589	588	:38@O1	:38@H1	:38@N1	53.8	2.910	0.11	49.89	5.31
404	400	399	:26@O1	:26@H1	:26@N1	46.9	2.953	0.15	51.86	5.27
423	419	418	:27@O1	:27@H1	:27@N1	46.3	2.853	0.12	49.86	5.53
579	575	574	:37@O1	:37@H1	:37@N1	45.0	2.797	0.10	51.69	5.67
189	185	184	:12@O1	:12@H1	:12@N1	41.4	2.807	0.09	50.14	6.15
326	322	321	:21@O1	:21@H1	:21@N1	35.1	3.040	0.16	51.06	5.41
139	135	134	:9@O1	:9@H1	:9@N1	33.0	2.911	0.13	51.16	5.60
657	653	652	:42@O1	:42@H1	:42@N1	31.2	2.799	0.10	51.63	5.89
47	43	42	:3@O1	:3@H1	:3@N1	28.3	2.916	0.13	50.71	5.65
248	244	243	:16@O1	:16@H1	:16@N1	28.1	2.993	0.14	51.53	5.33
529	525	524	:34@O1	:34@H1	:34@N1	24.7	2.964	0.13	55.17	3.62
437	433	432	:28@O1	:28@H1	:28@N1	24.7	2.893	0.13	51.25	5.51
295	291	290	:19@O1	:19@H1	:19@N1	24.6	2.930	0.12	53.01	5.43
515	511	510	:33@O1	:33@H1	:33@N1	20.8	2.903	0.13	54.18	4.46
217	213	212	:14@O1	:14@H1	:14@N1	16.4	2.829	0.10	53.72	4.68
267	263	262	:17@O1	:17@H1	:17@N1	15.8	2.914	0.17	49.50	6.07

NMR STUDIES

^{1}H-NMR spectrum for tetrapeptide 8b

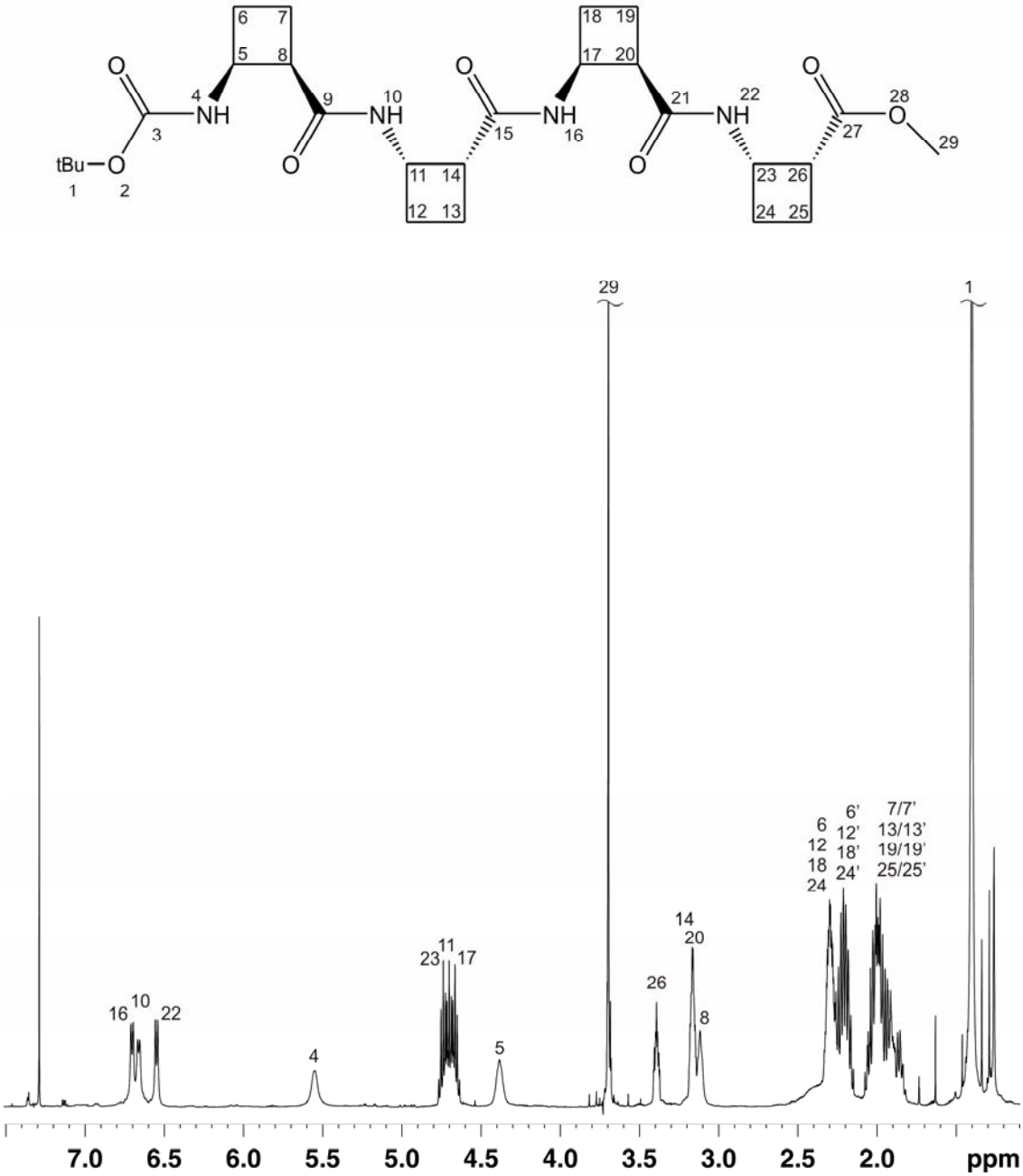


Fig. S6 ^{1}H NMR spectrum of tetrapeptide **8b** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 600.13 MHz for ^{1}H.

^{13}C-NMR spectrum for tetrapeptide 8b

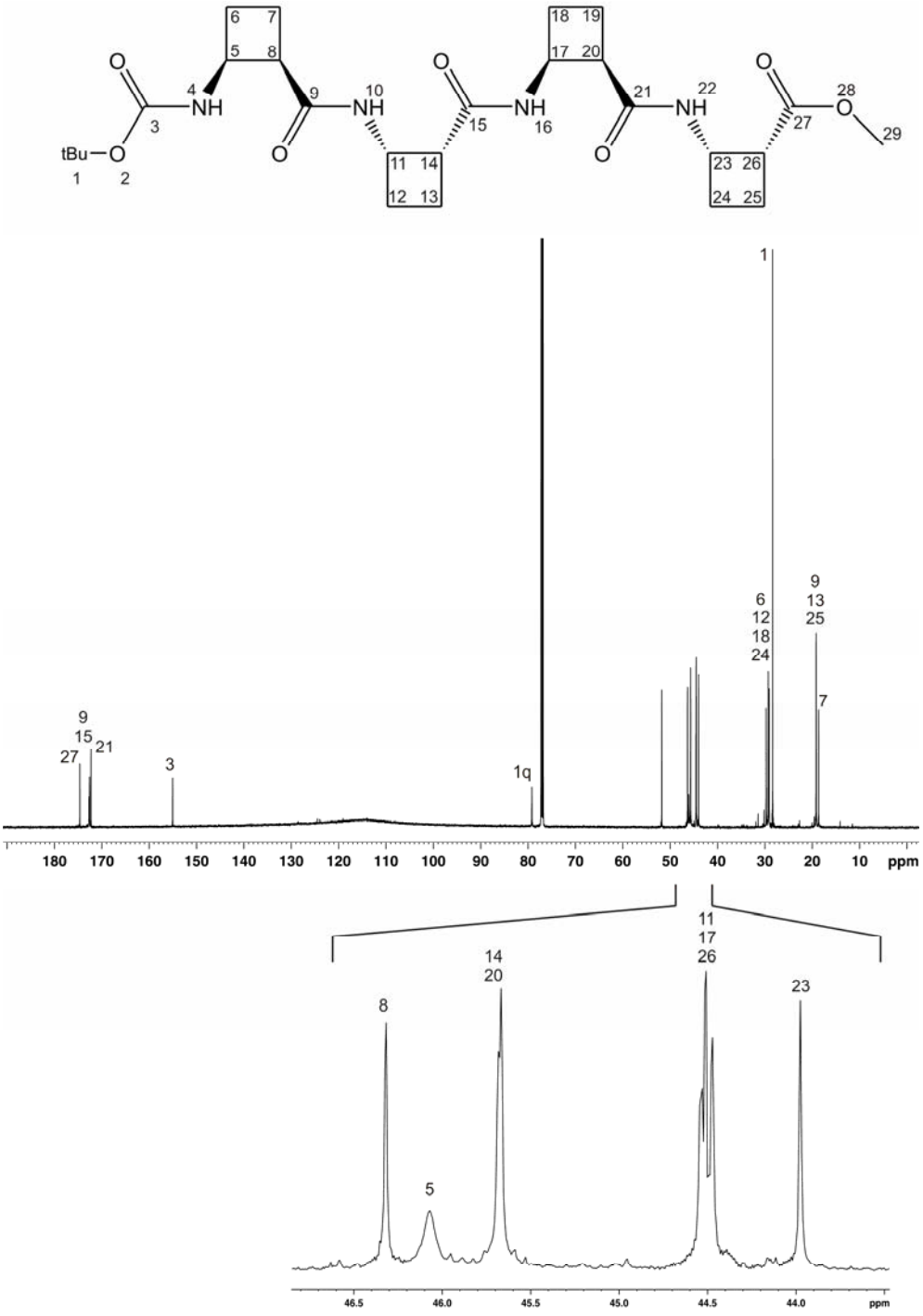


Fig. S7 ^{13}C NMR spectrum of tetrapeptide **8b** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 150.03 MHz for ^{13}C.

Variable temperature ^{1}H-NMR spectra for tetrapeptide 8b

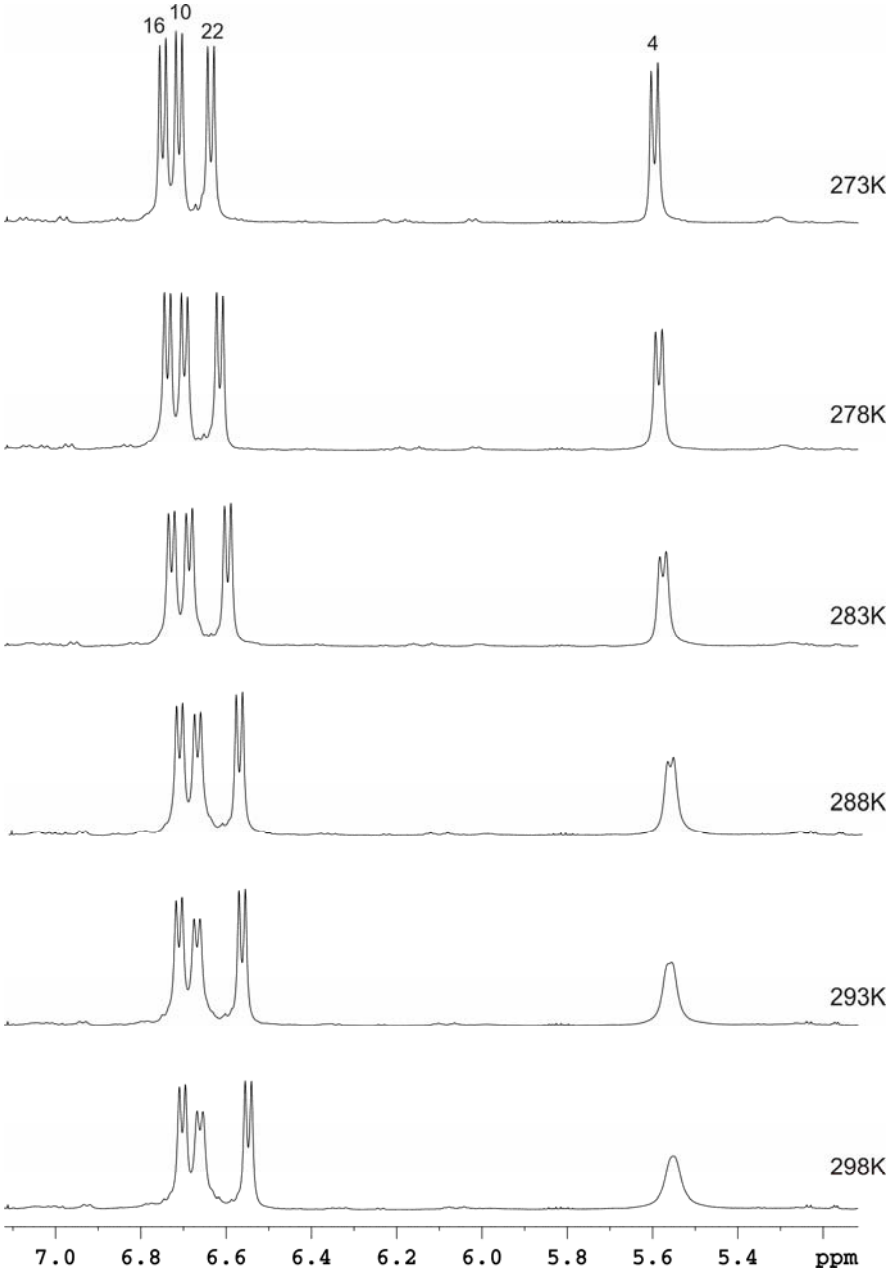


Fig. S8 ^{1}H NMR spectra of NH region at different temperatures of tetrapeptide **8b** in $CDCl_3$ recorded in a Bruker Avance spectrometer operating at 600.13 MHz for ^{1}H. It is observed that hydrogen bond involving NH_4 is starting to be fixed at 288K.

COSY spectrum for tetrapeptide 8b

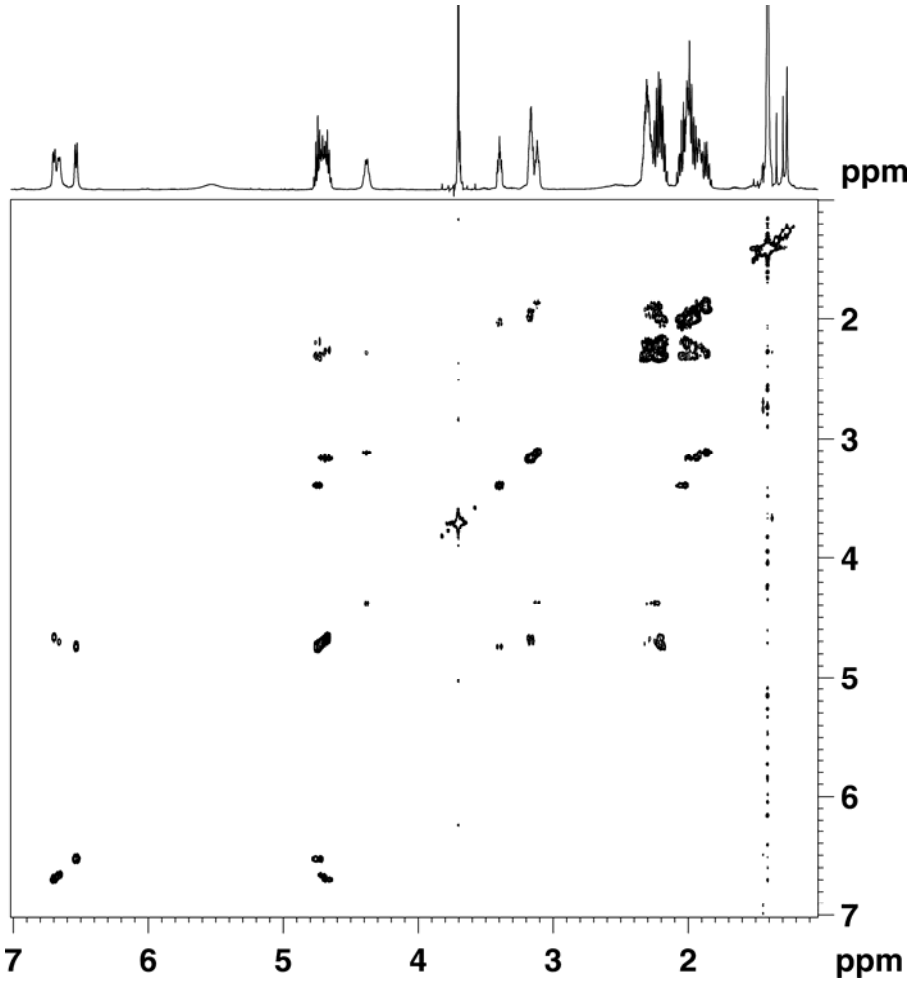


Fig. S9 Two dimensional ^{1}H-^{1}H COSY spectrum of tetrapeptide **8b** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 600.13 MHz for ^{1}H.

HSQC spectrum for tetrapeptide 8b

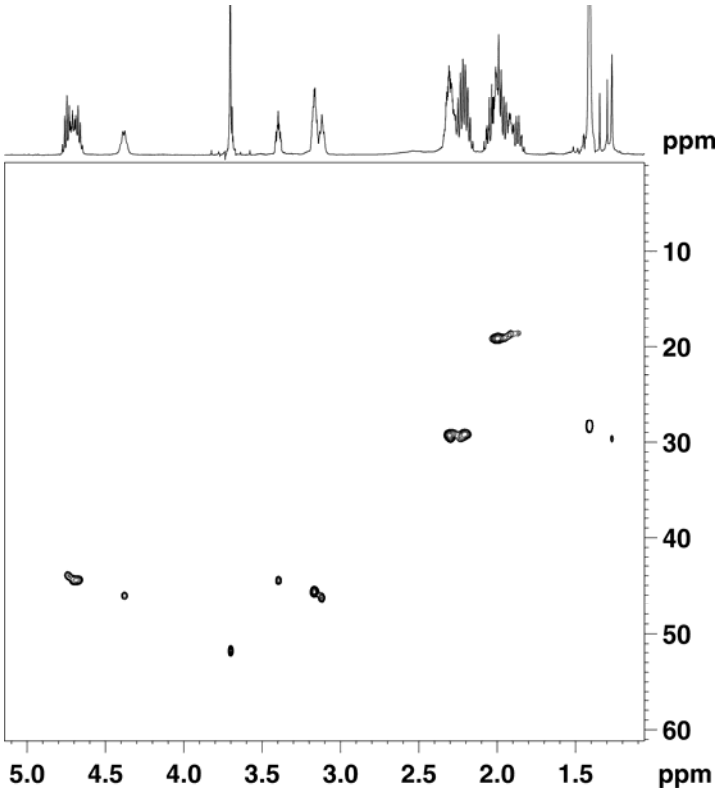


Fig. S10 Expansion plot of the two-dimensional ^{1}H-^{13}C HSQC spectrum of tetrapeptide **8b** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 600.13 MHz for ^{1}H and 150.03 MHz for ^{13}C.

HMBC spectrum for tetrapeptide 8b

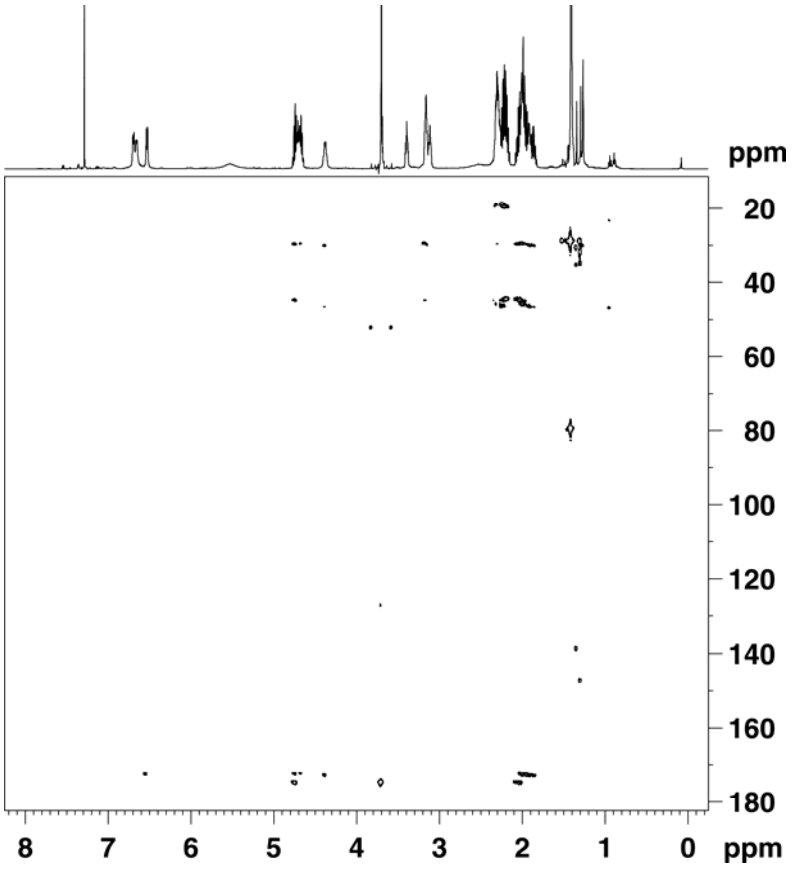


Fig. S11 Expansion plot of the two-dimensional ^{1}H-^{13}C HMBC spectrum of tetrapeptide **8b** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 600.13 MHz for ^{1}H and 150.03 MHz for ^{13}C.

NOESY spectrum for tetrapeptide 8b

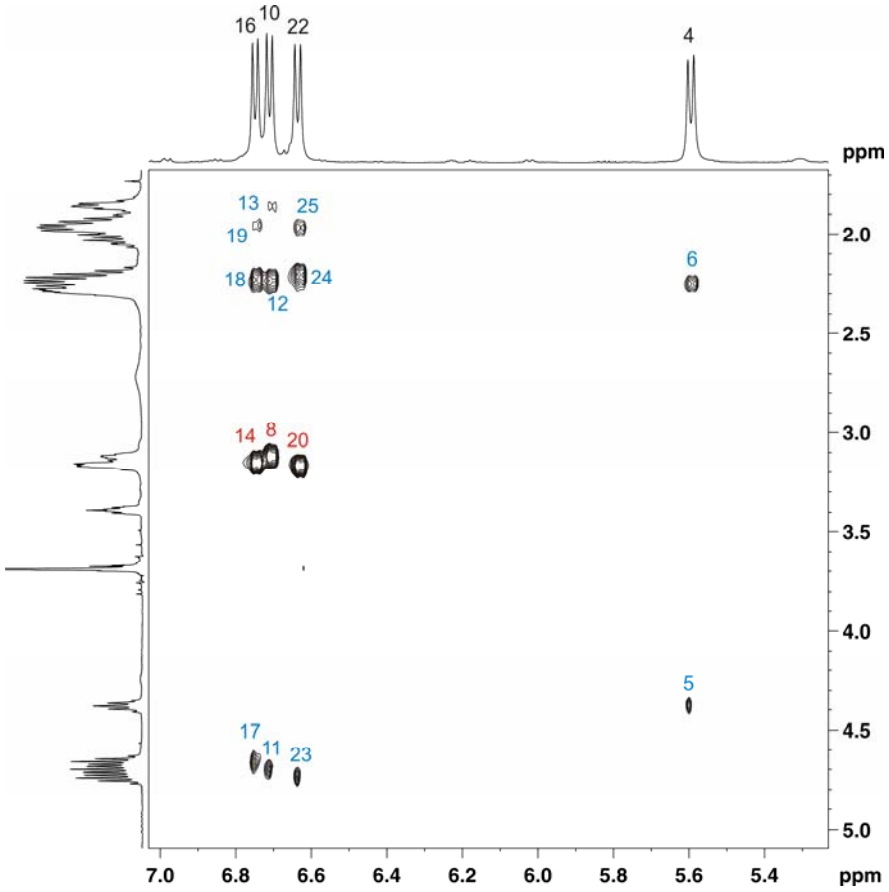


Fig. S12 Expansion plot of the two-dimensional ^{1}H-^{1}H NOESY spectrum (mixing time of 500 ms) of tetrapeptide **8b** in $CDCl_3$ recorded at 278 K in a Bruker Avance spectrometer operating at 600.13 MHz for ^{1}H. In blue and red are marked the intra- and inter-resiude NOE contacts, respectively.

Selective TOCSY-NMR spectra for tetrapetide 8b

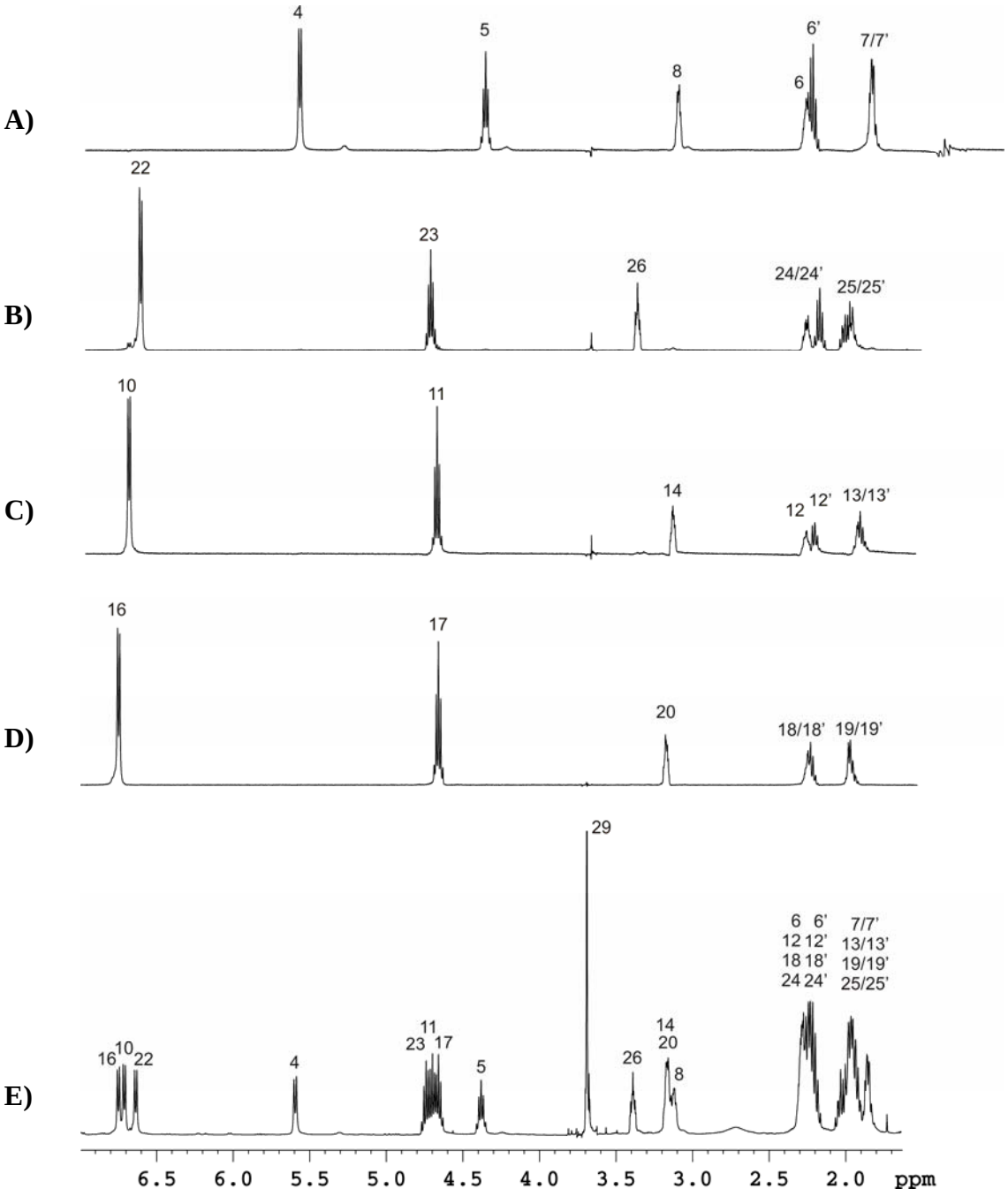


Fig. S13 Selective 1D TOCSY experiments irradiating at NH protons of tetrapeptide **8b** in $CDCl_3$. Magnetization is transferred to the whole residue spin system by using a 60 ms TOCSY mixing time. A) Selective irradiation at H_4. B) Selective irradiation at H_{22}. C) Selective irradiation at H_{10}. D) Selective irradiation at H_{16}. E) ^{1}H-NMR for comparison. Experiments are recorded at 278 K in a Bruker Avance spectrometer operating at 600.13 MHz for ^{1}H.

^{1}H-NMR spectrum for hexapeptide 9a

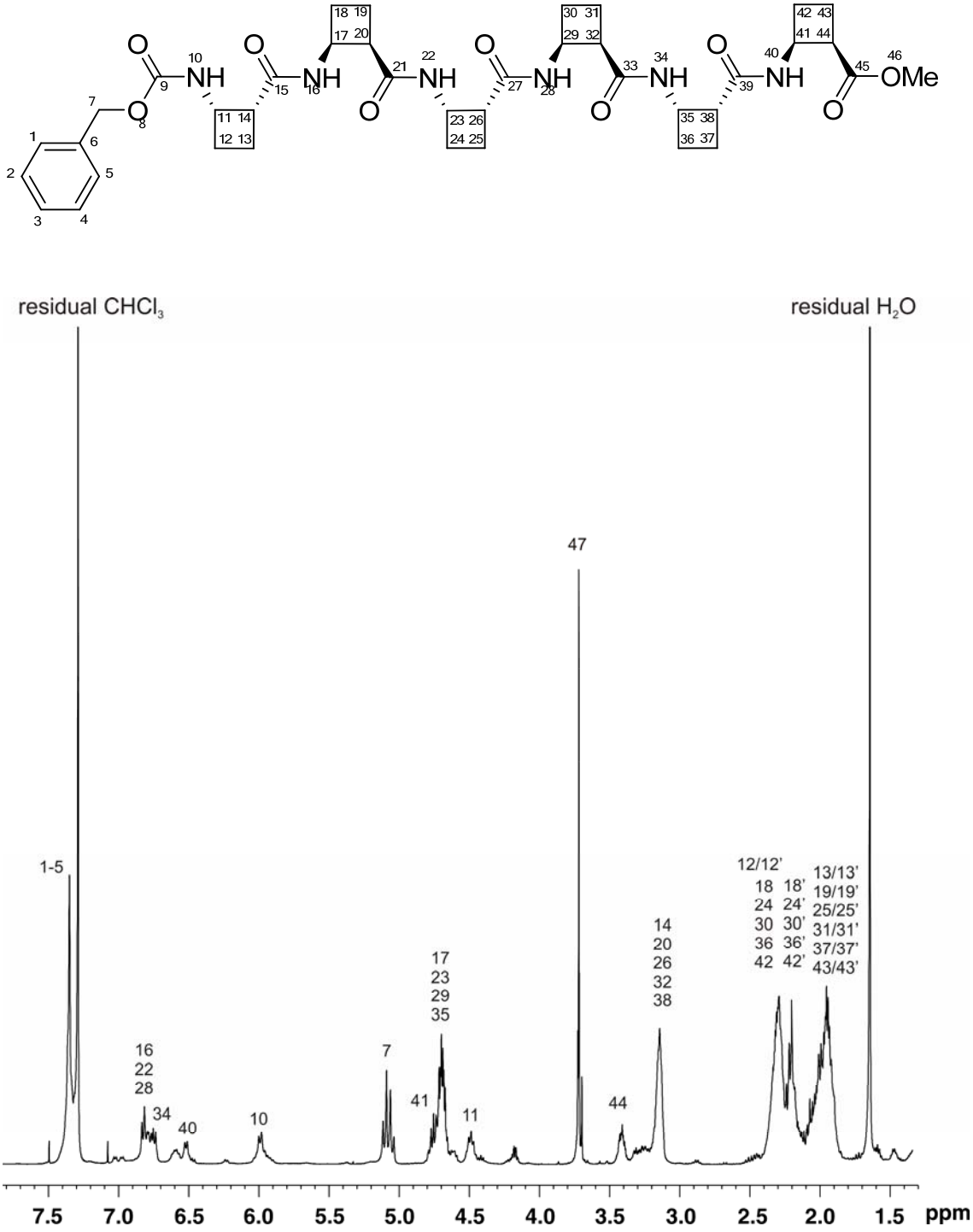


Figure S14: ^{1}H NMR spectrum of hexapeptide **9a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13 MHz for ^{1}H.

^{13}C-NMR spectrum for hexapeptide 9a

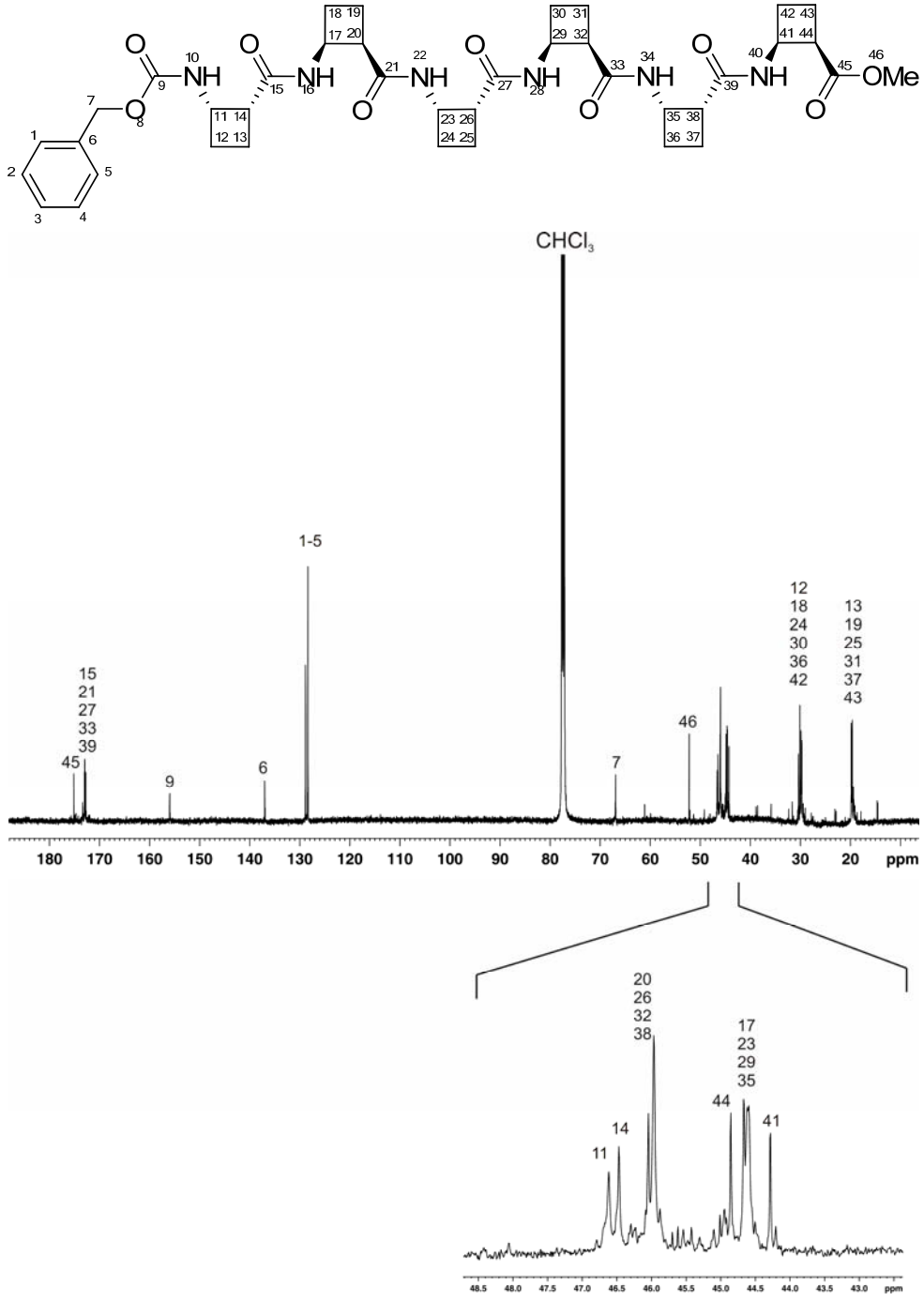


Fig. S15 ^{13}C NMR spectrum of hexapeptide **9a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 125.03 MHz for ^{13}C.

COSY-NMR spectrum for hexapeptide 9a

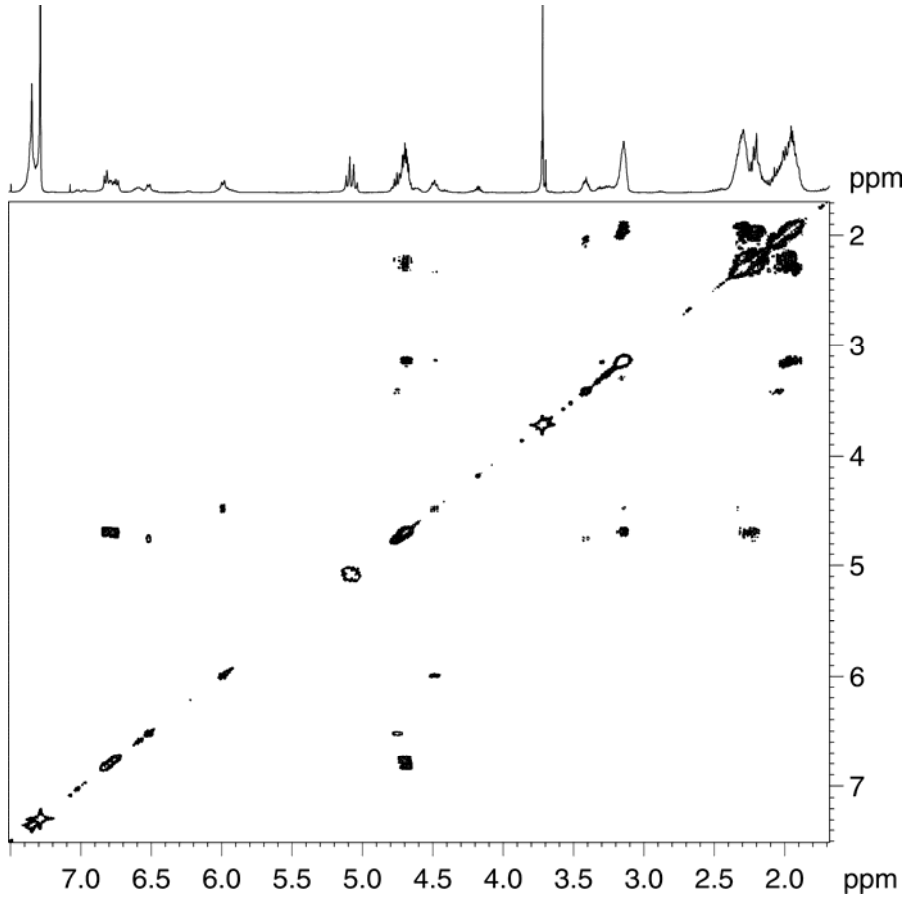


Fig. S16 Two dimensional ^{1}H-^{1}H COSY spectrum of hexapeptide **9a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13 MHz for ^{1}H.

^{1}H-^{13}C HSQC-NMR spectrum for hexapeptide 9a

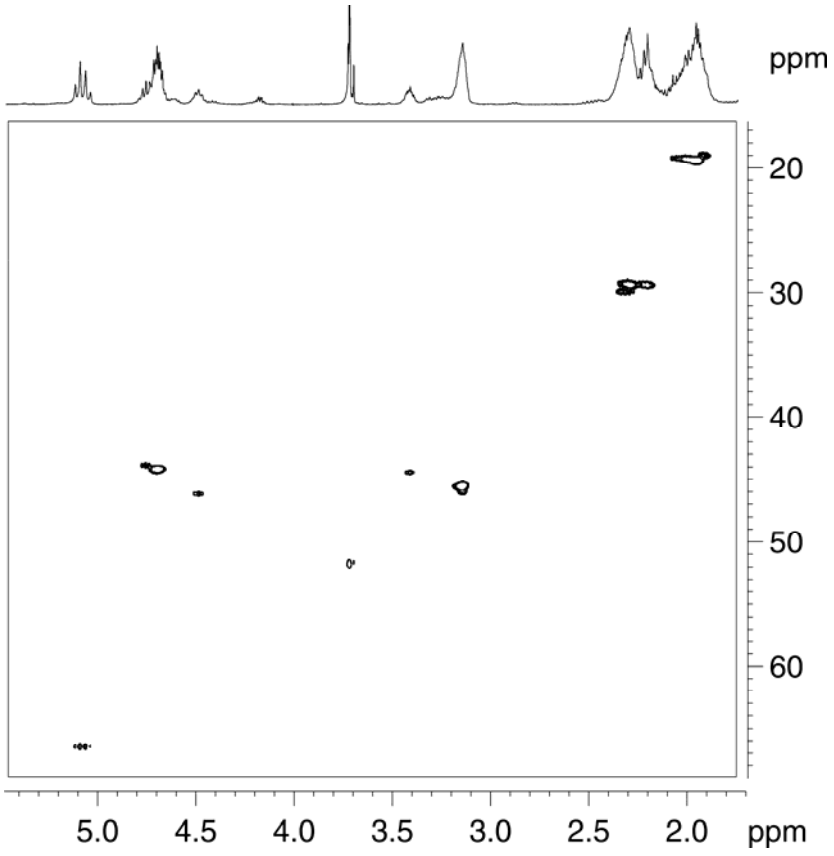


Fig. S17 Expansion plot of the two-dimensional ^{1}H-^{13}C HSQC spectrum of hexapeptide **9a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13MHz for ^{1}H and 125.03 MHz for ^{13}C.

^{1}H-^{15}N HSQC-NMR spectrum for hexapeptide 9a

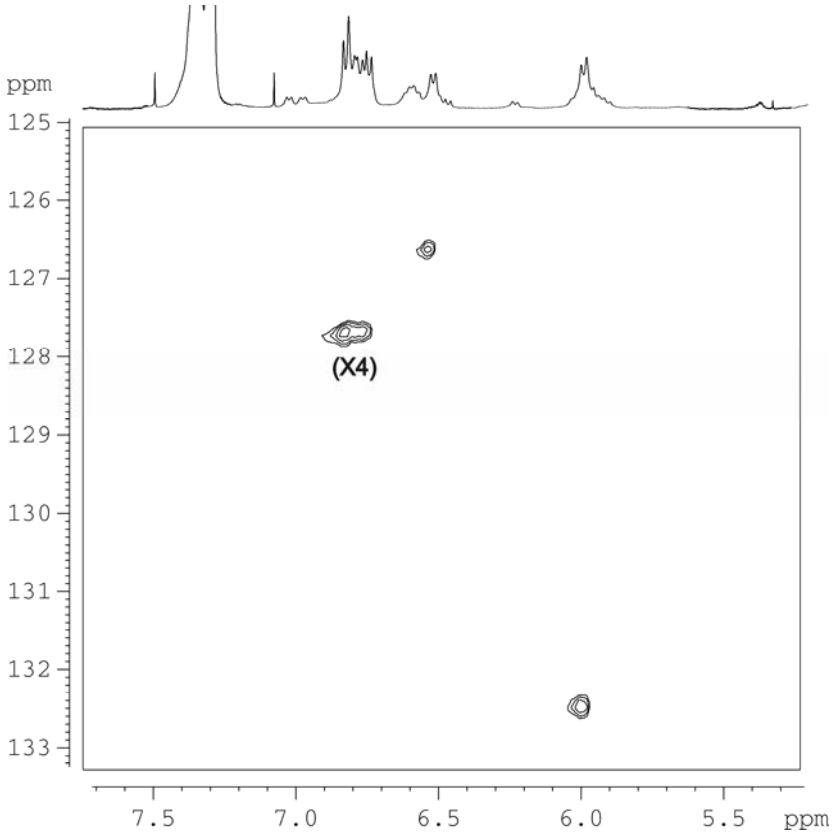


Fig. S18 Expansion plot of the two-dimensional ^{1}H-^{15}N HSQC spectrum of hexapeptide **9a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13 MHz for ^{1}H and 50.01 MHz for ^{15}N.

^{1}H-^{13}C HMBC-NMR spectrum for hexapeptide 9a

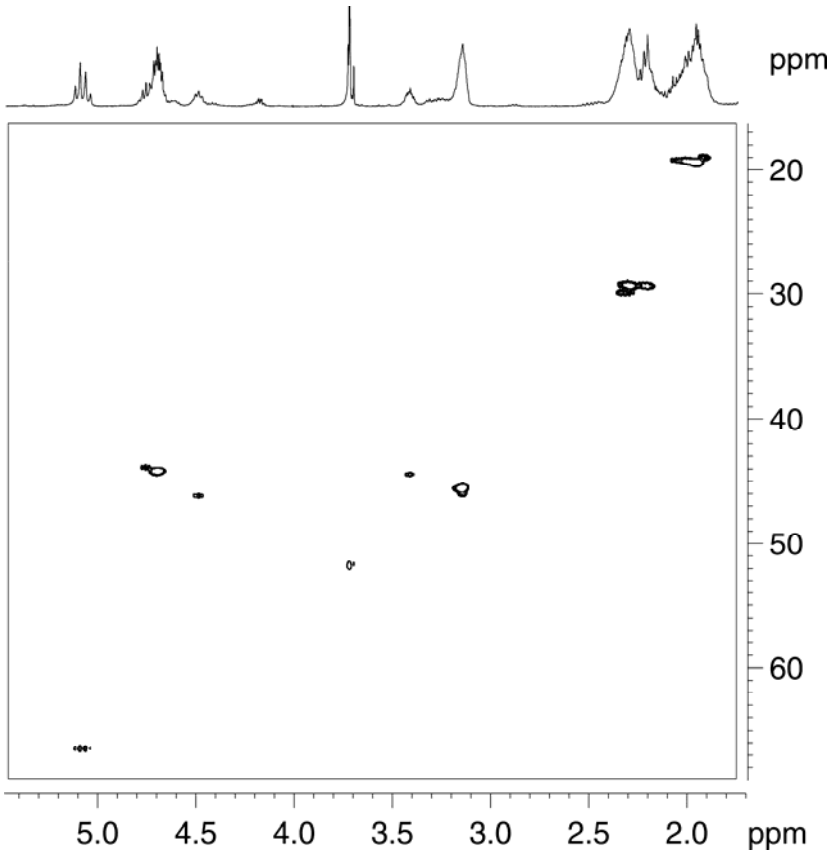


Fig. S19 Expansion plot of the two-dimensional ^{1}H-^{13}C HMBC spectrum of hexapeptide **9a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13 MHz for ^{1}H 125.03 MHz for ^{13}C.

2D NOESY-NMR spectrum for hexapeptide 9a

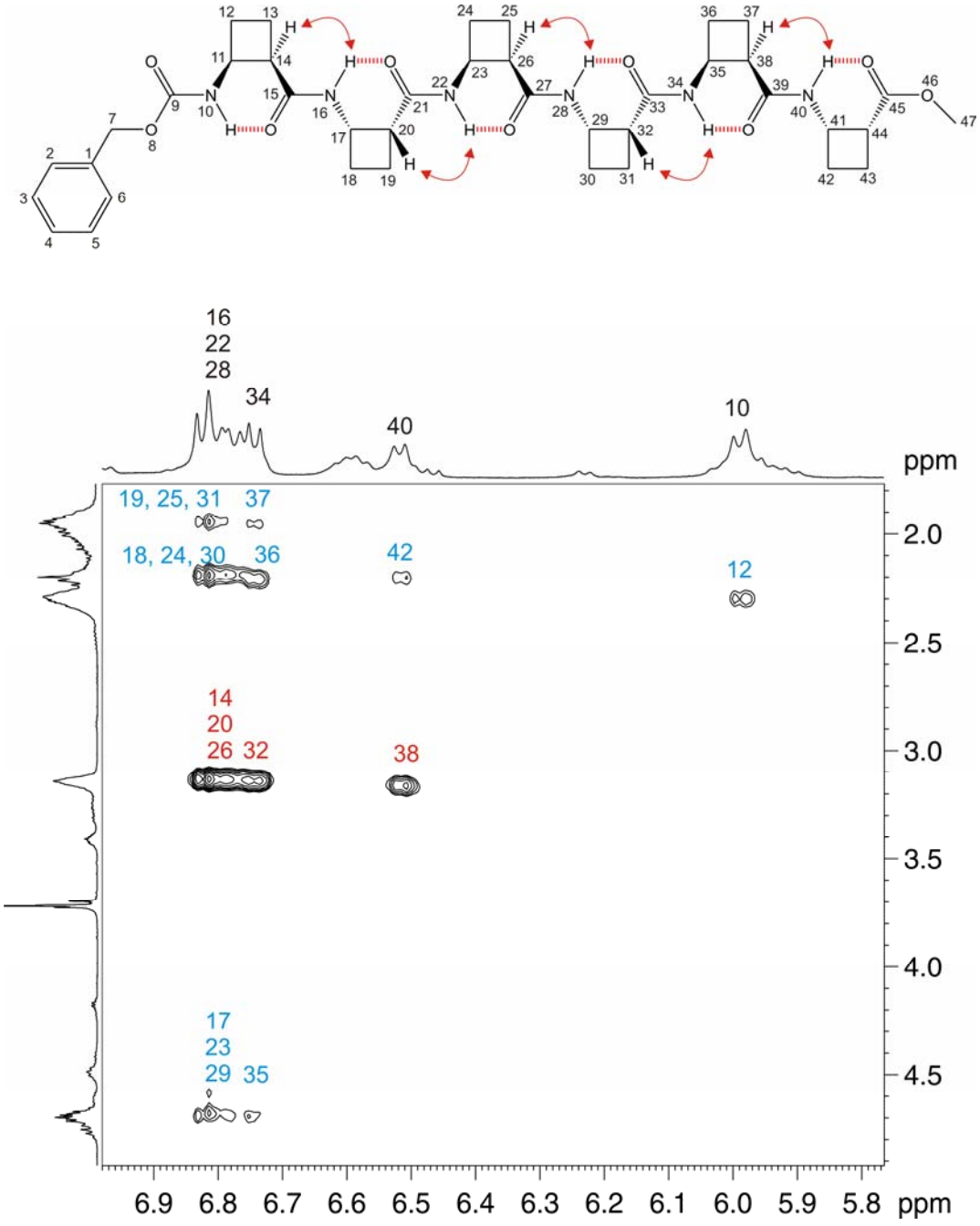


Fig. S20 Expansion plot of the two-dimensional ^{1}H-^{1}H NOESY spectrum (mixing time of 500 ms) of hexapeptide **9a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13 MHz for ^{1}H. In blue and red are marked the intra- and inter-residue NOE contacts, respectively.

Selective TOCSY-NMR spectra for hexapeptide 9a

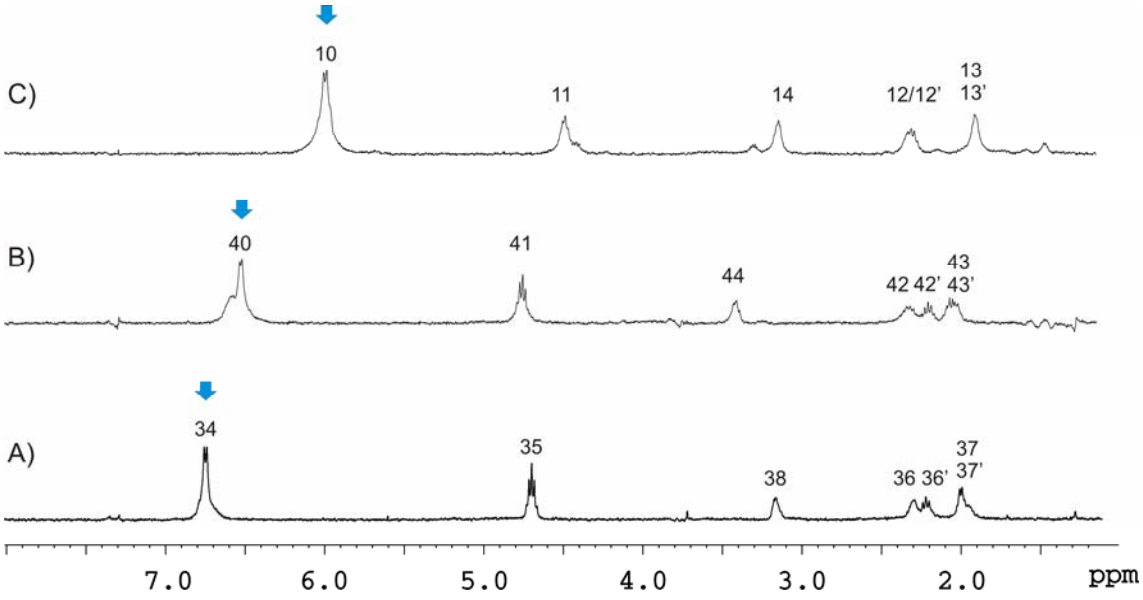


Fig. S21 Selective 1D TOCSY experiments irradiating at NH protons. Magnetization is transferred to the whole residue spin system by using a 60 ms TOCSY mixing time. A) Selective irradiation at H_{34}. B) Selective irradiation at H_{40}. C) Selective irradiation at H_{10}.

^{1}H and ^{13}C NMR spectra for trimer, 7a

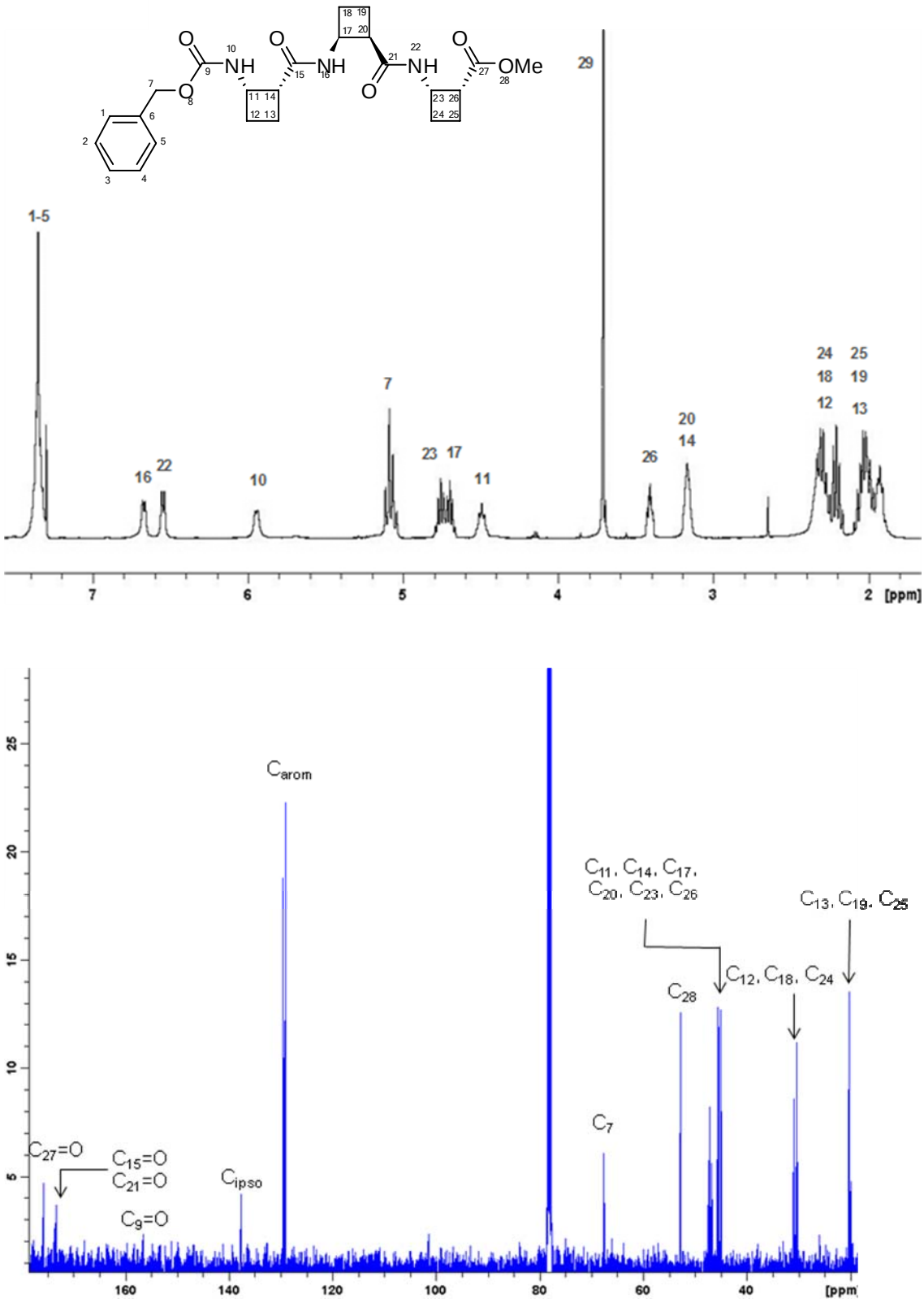


Fig. S22 ^{1}H (top) and ^{13}C (down) NMRspectra of tripeptide **7a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13 MHz for ^{1}H and 125.03 for ^{13}C.

^{1}H and ^{13}C NMR spectra for octamer, 10a

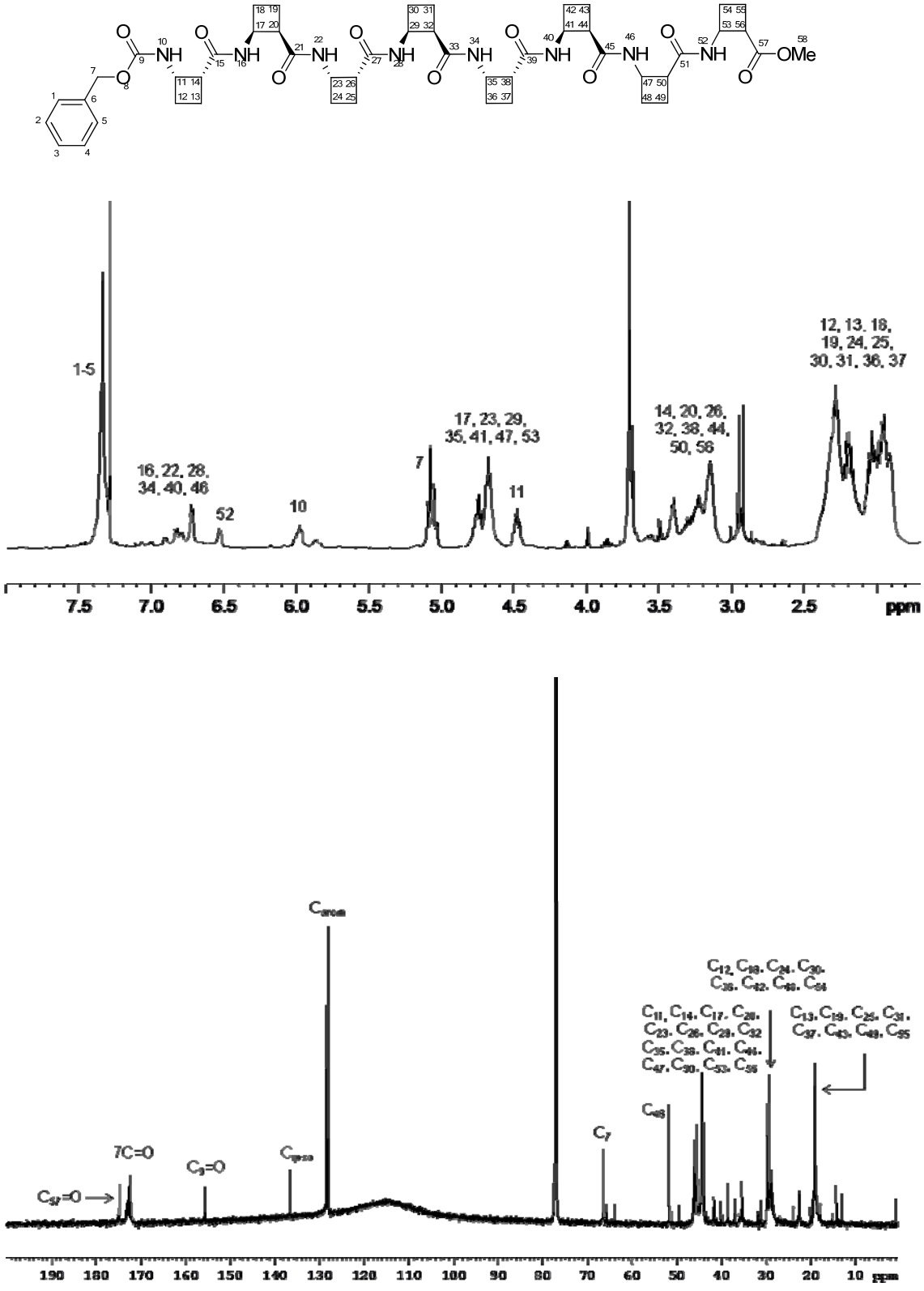


Fig. S23 ^{1}H (top) and ^{13}C (down) NMR spectra of octapeptide **10a** in $CDCl_3$ recorded at 298 K in a Bruker Avance spectrometer operating at 500.13 MHz for ^{1}H and 125.03 for ^{13}C.

^{1}H NMR spectrum for methyl 3,4-dichlorocyclobutane-1,2-dicarboxylate, 12 (mixture of diastereomers).

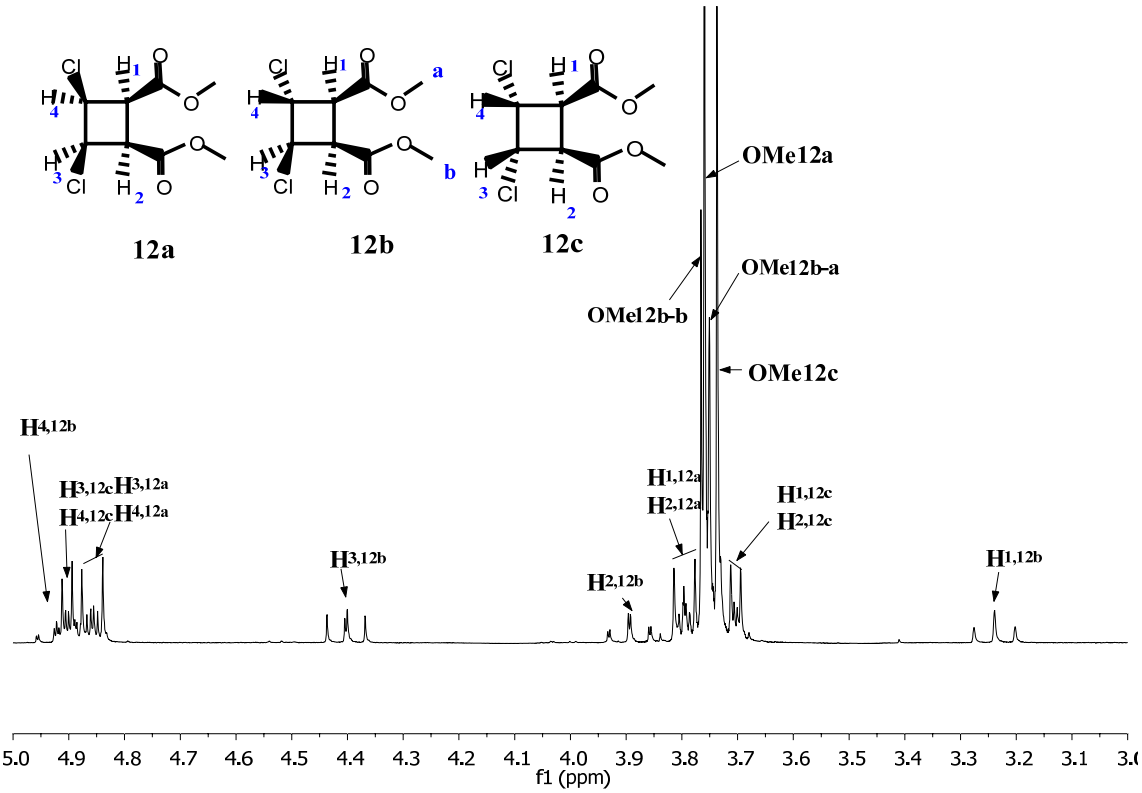
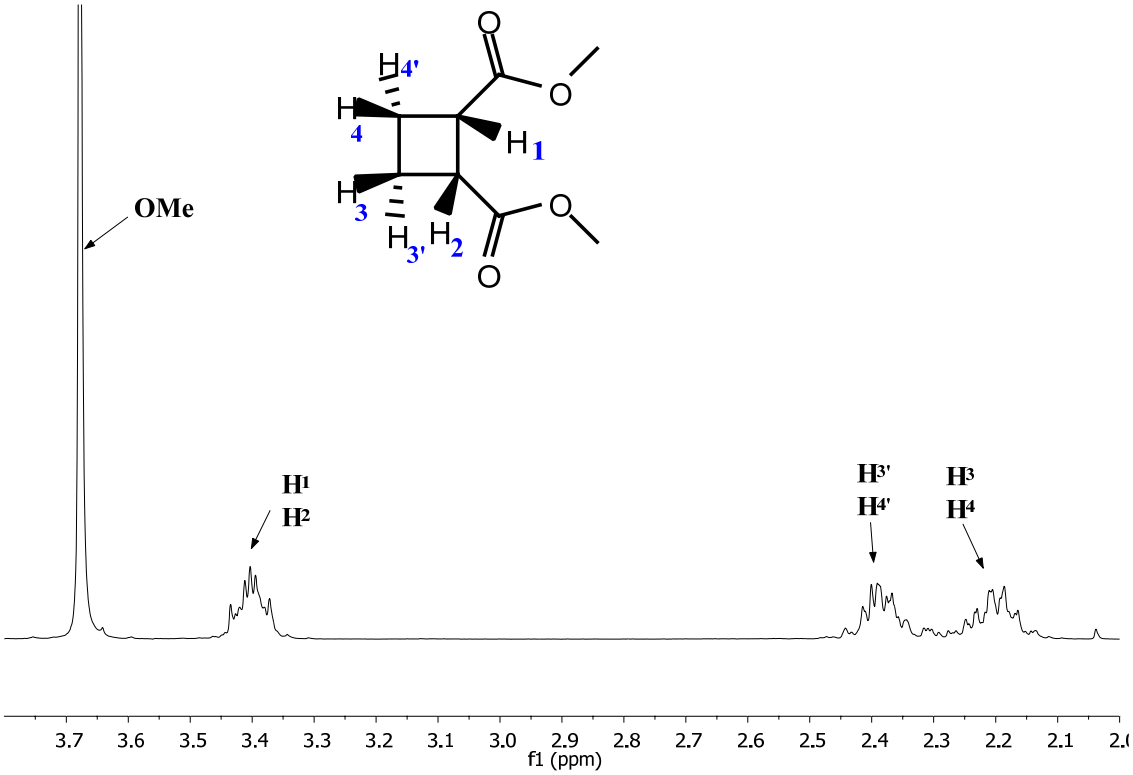


Fig. S24 ^{1}H NMR spectrum ($CDCl_3$, 250 MHz) of the diastereomeric mixture **12**.

^{1}H and ^{13}C NMR spectra for dimethyl cyclobutane-1,2-dicarboxylate, 13.



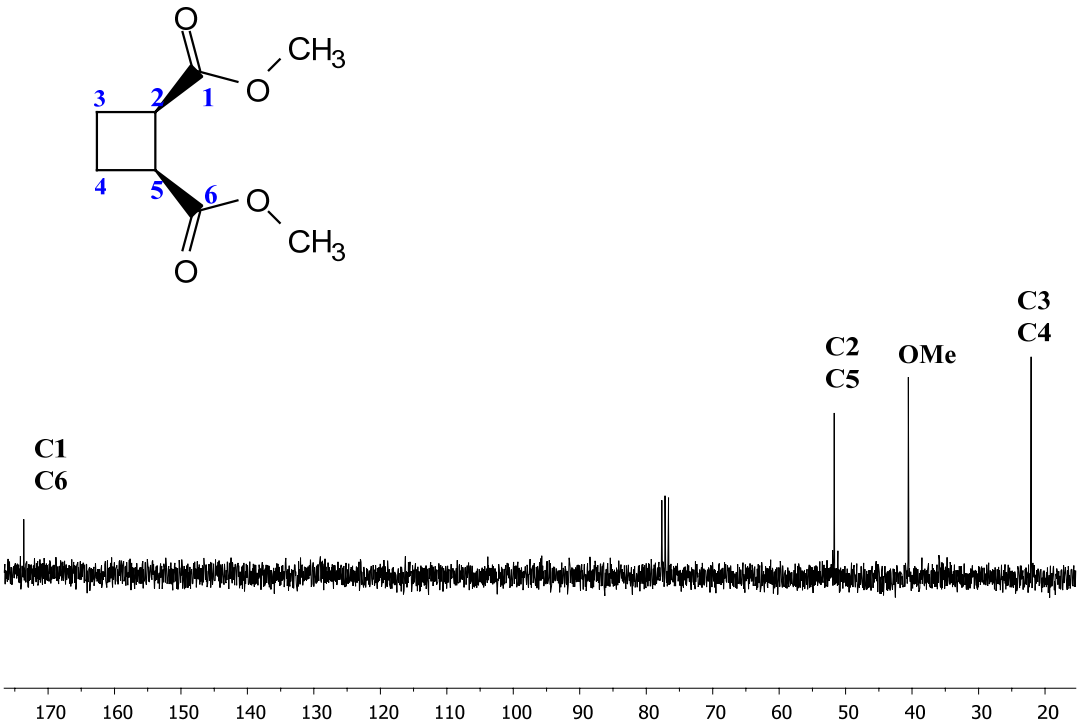


Fig. S25 250 MHz-^{1}H (top) and 62.5 MHz-^{13}C (down) NMR spectra ($CDCl_3$) of compound **13**.

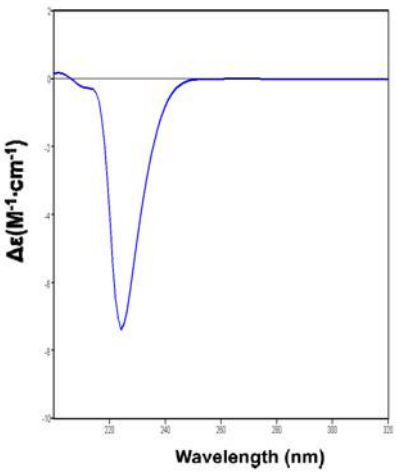


Fig. S26 CD spectra of a 0.5 mM methanol solution of **8b.**

Fig. S27 Gel formed from a 1:3 dichloromethane-pentane 5.8 mM solution of **8b**

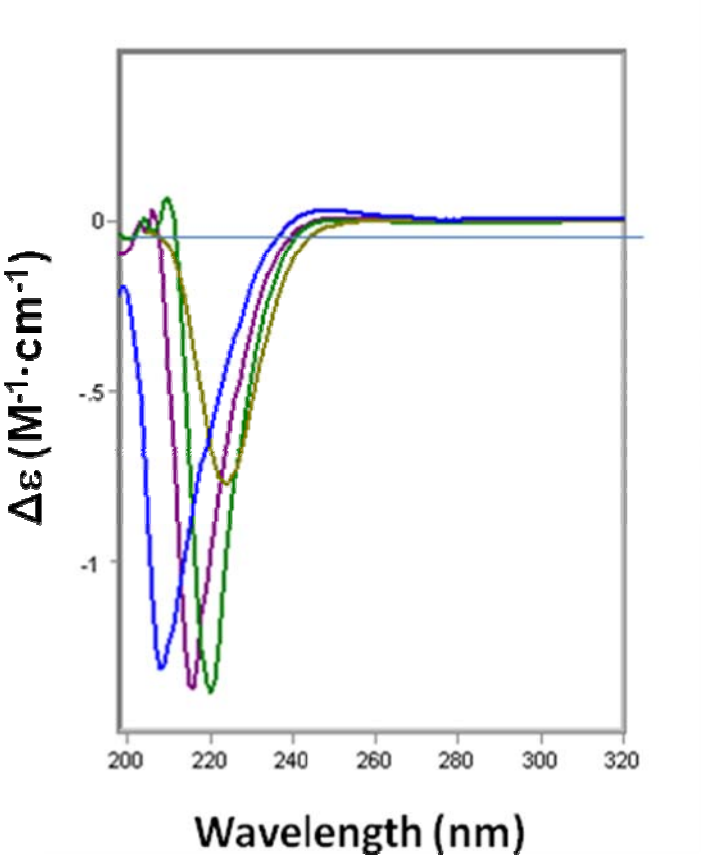


Fig. S28. CD spectra of 0.5 mM methanol solutions of **2a** (blue), **8a** (violet), **9a** (green), and **10a** (grey). Molar ellipticity is normalized per residue.