Supporting Information of "New Oxazole-Based Peptidomimetics: Useful Building-Blocks for the Synthesis of Orthogonally Protected Macrocyclic Scaffolds" by E. Mann et al.

Abbreviations.

DIPEA = diisopropylethylamine; DPPA = diphenylphosphoryl azide; HATU = *N*-[(dimethylamino)-1*H*-1,2,3-triazolo[4,5-*b*]pyridino-1-ylmethylene]-*N*-methylmethanaminium hexafluorophosphate *N*-oxide; HFIP = hexafluoro-2-propanol; HOAt = 1-hydroxy-7-azabenzotriazole; HOBt = 1-hydroxybenzotriazol; TFA = trifluoroacetic acid; TBTU = 1-[bis(dimethylamino)methylene]-1-*H*-benzotriazolium tetrafluoroborate 3-oxide; Z = benzyloxycarbonyl

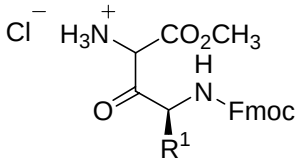
General

Materials obtained commercially were reagent grade unless otherwise stated. For solid phase synthesis, CTC resin was bought from PepChem Goldammer & Clausen, TBTU from MultiSynTech GmbH, HOBt from Quantum Appligene and HATU and HOAt from Perspective Biosystems. ^{1}H, ^{13}C and 2D NMR spectra were recorded on a Bruker DMX 500 spectrometer. Assignment of proton and carbon signals was achieved by HMQC, COSY, TOCSY, ROESY and HMBC experiments. Analytical reverse phase HPLC separations were performed on an Amersham Pharmacia Biotech (Äkta Basic 10/100, autosampler A-900) using a ODS-A YMC C18 column; preparative scale reverse phase HPLC separations were carried out on a Beckman System Gold (high pressure pump module 126, UV detector 166) employing a ODS-A YMC C18 column. As solvents for analytical and preparative HPLC, H_2O + 0.1 % CF_3CO_2H (solvent A) and CH_3CN + 0.1 % CF_3CO_2H (solvent B) were used. HPLC-ESI mass espectra were recorded on a Finnigan NCQ-ESI with HPLC conjuntion LCQ (HPLC-system Hewlett-Packard HP 1100, Nucleosil 100 $5C_{18}$).

General procedure 1. Synthesis of compounds 2a-e

A solution of ^{t}BuOK (20 mmol) in anhydrous THF (50 ml) was cooled under argon to -

78°C, and a solution of N-(diphenylmethylene)glycine methyl ester (20 mmol), prepared as described by O'Donnell et al.,[1] in THF (50 ml) was added while maintaining the reaction temp. at -78°C. After 30 min. this orange solution was added via cannula to a vigorously stirred solution of the corresponding amino acid chloride (20 mmol) in anhydrous THF (50 ml) at -78°C. Half an hour after completion of addition, the reaction mixture was quenched with 3N HCl solution (50 ml) and allowed to stir at room temperature for 1h. THF was evaporated and the resultant aqueous phase extracted with ether (2 x 50 ml). The aqueous solution was concentrated *in vacuo* (<40°C) and lyophilised. Methanol was added to the residue and the insoluble white solid (KCl) removed by filtration. The filtrate was concentrated *in vacuo* to give compounds **2a-e** as yellowish solids which were used without further purification.



2a-e

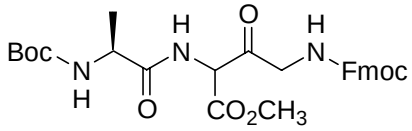
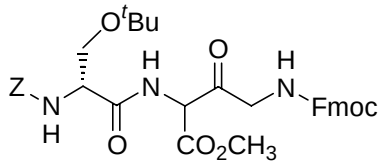
Compound	*R^1*	*Yield (%)*	*HPLC Rt (min)[a]*	*ESI-MS*
2a	H	82	15.84	369.2 $[M-Cl]^+$
2b	Me	71	17.68	383.2 $[M-Cl]^+$
2c	Bn	80	20.41	459.3 $[M-Cl]^+$ 497.2 $[M-HCl+K]^+$
2d	$(CH_2)_2CO_2Bn$	68	20.72	531.5 $[M-Cl]^+$
2e	$(CH_2)_4NHCbz$	77	24.88	574.3 $[M-Cl]^+$ 596.2 $[M-HCl+Na]^+$

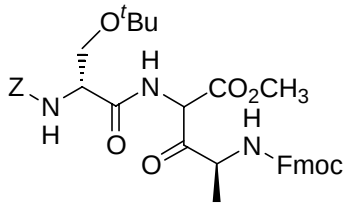
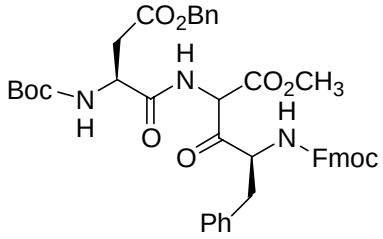
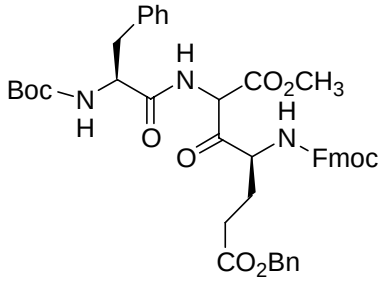
a): 5 μm ODS-A YMC 4.6 x 250 mm HPLC-column 10 – 90 % B in 30 min.

[1] O'Donnell, M. J.; Polt, R. L. *J. Org. Chem*. **1982**, **47**, 2663-2666.

General procedure 2. Synthesis of compounds 3a-f

A solution of the N-protected amino acid (10 mmol) in THF (60 ml) was cooled to -20°C under Ar atmosphere. N-Methylmorpholine (10 mmol) was added, followed by the dropwise addition of isobutylchloroformate (10 mmol). After the addition was complete, the reaction mixture was stirred for 30 min at -20°C. The cooling bath was removed, and the corresponding compound **2** (10 mmol) dissolved in DMF (30 ml) was added. N-Methylmorpholine (10 mmol) was added dropwise to the mixture for 30 min. Once the addition was complete, the reaction was allowed to stir at room temperature overnight. The solvents were removed in vacuo, and the residue was taken up in EtOAc. The organic layer was washed sequentially with saturated $NaHCO_3$ solution, 1 N HCl, and brine, dried over $MgSO_4$, and evaporated under reduced pressure. Purification by flash column chromatography (EtOAc/hexane mixtures) of the resulting oil afforded compounds **3a-f** as a 1:1 diastereomeric mixture

Compound	***Yield***	***HPLC Rt (min)***	***ESI-MS***
 **3a**	70 %	24.40 [a]	440.3 $[M\text{-Boc}]^+$ 562.3 $[M+Na]^+$
 **3b**	68 %	27.88 [a]	646.3 $[M+H]^+$ 668.4 $[M+Na]^+$ 1313.2 $[2M+Na]^+$

Compound	*Yield*	*HPLC Rt (min)*	*ESI-MS*
 **3c**	57 %	28.68 / 28.97 [a]	682.4 $[M + Na]^+$ 698.3 $[M + K]^+$
 **3d**	66 %	23.71 / 23.84 [b]	786.3 $[M+Na]^+$
 **3e**	73 %	27.25 [a]	778.3 $[M + H]^+$ 800.2 $[M + Na]^+$

a): 5 μm ODS-A YMC 4.6 x 250 mm HPLC-column 10 – 90 % B in 30 min.

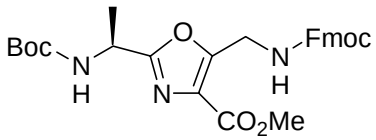
b): 5 μm ODS-A YMC 4.6 x 250 mm HPLC-column 50 – 100 % B in 30 min

General procedure 3. Synthesis of oxazoles 4a-f

To a stirred solution of compound **3** (10 mmol) in CH_2Cl_2 (150 ml), triphenylphosphine (20 mmol), iodine (20 mmol) and triethylamine (40 mmol) were added at 0°C. The cooling bath was removed after 30 min. and stirring was continued at rt for 2 h. Water (100 ml) was added and stirring was continued for 1 h. The phases were separated and the organic layer was dried over $MgSO_4$ and concentrated in vacuo. Pure oxazole **4** was

obtained after flash column chromatography with EtOAc/hexane mixtures.

Methyl 2-{(1*S*)-1-[(*tert*-butoxycarbonyl)amino]ethyl}-5-{(1*S*)-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}methyl}-1,3-oxazole-4-carboxylate (4a)



Yield : 67 %

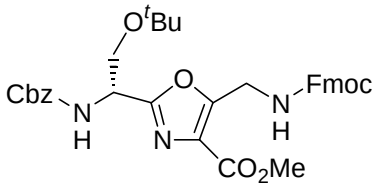
Analytical HPLC Rt = 25.56 min (10 – 90 % B, 30 min).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.75 (m, 2H, H^{Fmoc}), 7.56 (m, 2H, H^{Fmoc}), 7.39 (m, 2H, H^{Fmoc}), 7.29 (m, 2H, H^{Fmoc}), 5.69 (br t, 1H, NHFmoc), 5.26 (br s, 1H, NHBoc), 4.99 (m, 1H, CHα ^{Ala}), 4.73 (d, *J* = 6.0 Hz, 2H, C$\underline{H}_2$NHFmoc), 4.49 (m, 2H, CH_2^{Fmoc}), 4.24 (m, 1H, CH^{Fmoc}), 3.93 (s, 3H, $CO_2C\underline{H}_3$), 1.53 (d, *J* = 6.9 Hz, 3H, C$\underline{H}_3$CH), 1.44 (s, 9H, $C(C\underline{H}_3)_3$).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 164.0 ($\underline{C}O_2Me$), 162.3 (Ox-C2), 156.4 (Ox-C^5), 156.1 (CO^{Fmoc}), 155.4 (CO^{Boc}), 143.7 (2C, C^{Fmoc}), 141.2 (2C,C^{Fmoc}), 127.7 (2C, CH^{Fmoc}), 127.0 (2C, CH^{Fmoc}), 124.9 (2C, CH^{Fmoc}), 119.9 (2C, CH^{Fmoc}), 80.1 ($\underline{C}(CH_3)_3$), 67.7 (CH_2^{Fmoc}), 52.7 (CO_2CH_3), 47.4 (CH^{Fmoc}), 44.9 (CHα ^{Ala}), 36.5 ($\underline{C}H_2$NHFmoc), 28.7 (3C, ^{t}Bu), 20.5 (CH_3^{Ala}).

ESI-MS: 522.3 $[M + H]^+$; 544.2 $[M + Na]^+$; 1065.3 $[2M + Na]^+$;

Methyl 2-{(1*S*)-2-*tert*-butoxy-1-[(benzyloxycarbonyl)amino]ethyl}-5-{(1*S*)-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}methyl}-1,3-oxazole-4- carboxylate (4b)



Yield : 68 %

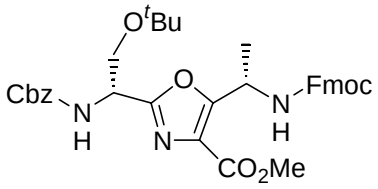
Analytical HPLC Rt =28.48 min (10 – 90 % B, 30 min).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.77 (m, 2H, H^{Fmoc}), 7.58 (m, 2H, H^{Fmoc}), 7.39 (m, 2H, H^{Fmoc}), 7.33 (m, 5H, H^{Cbz}), 7.29 (m, 2H, H^{Fmoc}), 5.77 (br s, 1H, NHCbz), 5.55 (br s, 1H, NHFmoc), 5.14 (m, 2H, CH_2^{Cbz}), 5.09 (m, 1H, $CH\alpha^{Ser}$), 4.74 (m, 2H, CH_2NHFmoc), 4.43 (m, 2H, CH_2^{Fmoc}), 4.24 (m, 1H, CH^{Fmoc}), 3.95 (s, 3H, CO_2CH_3), 3.81 (m, 1H, CHHO^{t}Bu), 3.68 (m, 1H, CHHO^{t}Bu), 1.06 (s, 9H, $C(CH_3)_3$).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 162.2 (CO_2CH_3), 161.6 (Ox-C^2), 155.9 (COFmoc), 155.6 (COCbz), 155.4 (Ox-C^5), 144.2 (2C, C^{Fmoc}), 141.7 (2C, C^{Fmoc}), 136.5 (C^{Ph}), 128.8 (2C, CH^{Ph}), 128.5 (2C, CH^{Ph}), 128.2 (CH^{Ph}), 128.1 (2C, CH^{Fmoc}), 127.4 (2C, CH^{Fmoc}), 126.8 (Ox-C^4), 125.4 (2C, CH^{Fmoc}), 120.3 (2C, CH^{Fmoc}), 74.2 ($C(CH_3)_3$), 67.6 (CH_2^{Fmoc}), 67.5 (CH_2Ph^{Cbz}), 63.1 (CH_2O^tBu), 52.8 (CO_2CH_3), 51.1 ($CHCH_2O^t$Bu), 47.6 (CH^{Fmoc}), 37.1 (CH_2NHFmoc), 27.4 (3C, $C(CH_3)_3$).

ESI-MS: 628.3 $[M + H]^+$; 650.4 $[M + Na]^+$; 1277.1 $[2M + Na]^+$.

Methyl 2-{(1*S*)-2-*tert*-butoxy-1-[(benzyloxycarbonyl)amino]ethyl}-5-{(1*S*)-1-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}ethyl}-1,3-oxazole-4- carboxylate (4c)



Yield : 63 %

Analytical HPLC Rt = 29.15 min (10 – 90 % B, 30 min).

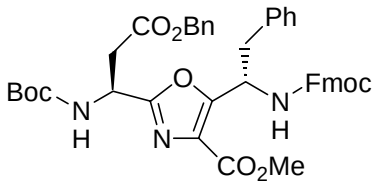
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.77 (m, 2H, H^{Fmoc}), 7.58 (m, 2H, H^{Fmoc}), 7.41 (m, 2H, H^{Fmoc}), 7.39 (m, 5H, Ph), 7.29 (m, 2H, H^{Fmoc}), 6.00 (br s, 1H, NH^{Fmoc}), 5.77 (br s, 1H, NH^{Cbz}), 5.47 (m, 1H, $CH\alpha^{Ala}$), 5.13 (m, 2H, CH_2^{Cbz}), 5.08 (m, 1H, $CH\alpha^{Ser}$), 4.39 (m, 2H, CH_2^{Fmoc}), 4.20 (m, 1H, CH^{Fmoc}), 3.93 (s, 3H, CO_2CH_3), 3.81 (m, 1H, CHHO^{t}Bu), 3.67 (m, 1H, CHHO^{t}Bu), 1.52 (d, *J* = 6.9 Hz, 3H, CH_3^{Ala}), 1.06 (s, 9H, ^{t}Bu).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 162.9 (CO_2CH_3), 161.3 (Ox-C^2), 159.9 (Ox-

C^5), 156.2 (COFmoc), 155.7 (COCbz), 144.2 (2C, C^{Fmoc}), 141.6 (2C, C^{Fmoc}), 136.6 (C^{Ph}), 128.7 (2C, CH^{Ph}), 128.4 (2C, CH^{Ph}), 128.1 (CH^{Ph}), 128.0 (2C, CH^{Fmoc}), 127.3 (2C, CH^{Fmoc}), 127.2 (Ox-C^4), 125.4 (2C, CH^{Fmoc}), 120.3 (2C, CH^{Fmoc}), 74.2 ($\underline{C}(CH_3)_3$), 67.5 ($\underline{C}H_2Ph^{Cbz}$), 67.4 ($\underline{C}H_2{}^{Fmoc}$), 63.2 ($\underline{C}H_2O^tBu$), 52.8 ($CO_2\underline{C}H_3$), 51.1 ($\underline{C}HCH_2O^tBu$), 50.67 ($CH\alpha^{Ala}$), 47.4 ($CH^{Fmoc}$), 27.4 (3C, $C(\underline{C}H_3)_3$), 20.8 ($CH_3{}^{Ala}$).

ESI-MS: 642.3 $[M + H]^+$; 664.4 $[M + Na]^+$.

Methyl 2-{(1*S*)-2-(benzyloxycarbonyl)-1-[(*tert*-butoxycarbonyl)amino]ethyl}-5-{(1*S*)-1-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-2-phenylethyl}-1,3-oxazole-4-carboxylate (4d)



Yield : 85 %

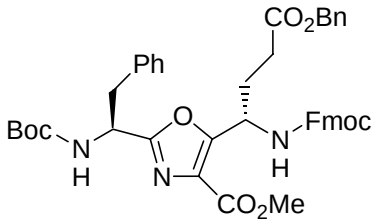
Analytical HPLC Rt = 24.54 min (50 – 100 % B, 30 min).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.78 (m, 2H, H^{Fmoc}), 7.57 (m, 2H, H^{Fmoc}), 7.42 (m, 2H, H^{Fmoc}), 7.33 (m, 5H, $CO_2\underline{Ph}$), 7.32 (m, 2H, H^{Fmoc}), 7.25 (m, 3H, H^{Ph}), 7.07 (m, 2H, H^{Ph}), 6.11 (br d, *J* = 8.8 Hz, 1H, NH^{Fmoc}), 5.63 (m, 1H, $CH\alpha^{Phe}$), 5.53 (br s, 1H, NH^{Boc}), 5.23 (m, 1H, $CH\alpha^{Asp}$), 5.12 (s, 2H, $CH_2{}^{Cbz}$), 4.44 (m, 2H, $CH_2{}^{Fmoc}$), 4.24 (m, 1H, CH^{Fmoc}), 3.91 (s, 3H, $CO_2C\underline{H}_3$), 3.12 (m, 2H, $CH_2\beta^{Phe}$), 2.99 (m, 2H, $C\underline{H}_2\beta^{Asp}$), 1.44 (s, 9H, $C(C\underline{H}_3)_3$).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 169.8 (CO_2Bn), 162.1 (CO_2Me), 161.0(Ox-C^2), 157.9 (Ox-C5), 155.3 (CO^{Fmoc}), 154.7 (CO^{Boc}), 143.6 (2C, C^{Fmoc}), 141.1 (2C, C^{Fmoc}), 135.5 (C^{Bn}), 135.2 (C^{Ph}), 129.1 (2C, CH^{Ph}), 129.0 (2C, CH^{Bn}), 128.4 (3C, CH^{Bn}), 128.2 (CH^{Ph}), 128.1 (2C, CH^{Bn}), 127.7 (Ox-C^4), 127.5 (2C, CH^{Fmoc}), 126.8 (4C, CH^{Ph}, CH^{Fmoc}), 124.8 (2C, CH^{Fmoc}), 119.8 (2C, CH^{Fmoc}), 80.3 ($\underline{C}(CH_3)_3$), 66.9 ($CH_2{}^{Fmoc}$), 66.6 ($CO_2\underline{C}H_2$), 52.3 ($CO_2\underline{C}H_3$), 48.9 ($CH\alpha^{Phe}$), 47.0 (CH^{Fmoc}), 45.4 ($CH\alpha^{Asp}$), 40.7 ($CH_2\beta^{Phe}$), 37.7 ($C\underline{H}_2\beta^{Asp}$), 28.1 (3C, $C(\underline{C}H_3)_3$).

ESI-MS: 768.4 $[M + Na]^+$; 1513.2 $[2M + Na]^+$.

Methyl 2-{(1*S*)-2-phenyl-1-[(*tert*-butoxycarbonyl)amino]ethyl}-5-{(1*S*)-1-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-3-(benzyloxycarbonyl)propyl}-1,3-oxazole-4-carboxylate (4e)



Yield : 71 %

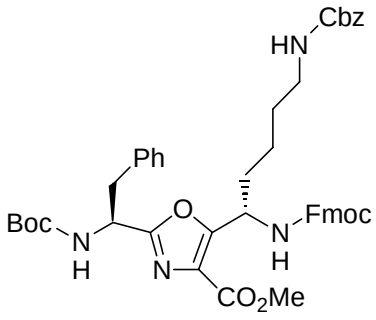
Analytical HPLC Rt = 28.69 min (10 – 90 % B, 30 min).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.76 (m, 2H, H^{Fmoc}), 7.57 (m, 2H, H^{Fmoc}), 7.39 (m, 2H, H^{Fmoc}), 7.36 (m, 5H, Ph), 7.30 (m, 2H, H^{Fmoc}), 7.20 (m, 2H, Ph), 7.14 (m, 1H, Ph), 7.02 (m, 2H, Ph), 5.87 (br s, 1H, NH^{Fmoc}), 5.37 (m, 1H, $CH\alpha^{Glu}$), 5.23 (br s, 1H, NH^{Boc}), 5.17 (m, $CH\alpha^{Phe}$), 5.12 (s, 2H, CH_2^{Cbz}), 4.40 (m, 2H, CH_2^{Fmoc}), 4.24 (m, 1H, CH^{Fmoc}), 3.94 (s, 3H, $CO_2C\underline{H}_3$), 3.16 (m, 2H, $CH_2\beta^{Phe}$), 2.33 (m, 2H, $CH_2\gamma^{Glu}$), 2.09 (m, 1H,$C\underline{H}HCH_2CO_2Bn$), 1.99 (m, 1H, $CH\underline{H}CH_2CO_2Bn$), 1.41 (s, 9H, $C(C\underline{H}_3)_3$).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 172.1 (CO_2Bn) , 162.2 ($Ox\text{-}C^2$), 162.1 ($\underline{C}O_2Me$), 157.4 (Ox-C5), 155.4 (CO^{Fmoc}), 154.5 (CO^{Boc}), 143.5 (2C, C^{Fmoc}), 141.1 (2C, C^{Fmoc}), 135.5 (C^{Bn}), 135.3 (C^{Ph}), 129.0 (2C, CH^{Ph}), 128.5 (3C, CH^{Bn}), 128.4 (CH^{Ph}), 128.2 (2C, CH^{Bn}), 127.5 (2C, CH^{Fmoc}), 127.4 ($Ox\text{-}C^4$), 126.9 (2C, CH^{Fmoc}), 126.8 (2C, CH^{Ph}), 124.8 (2C, CH^{Fmoc}), 119.8 (2C, CH^{Fmoc}), 80.1 ($\underline{C}(CH_3)_3$), 66.8 (CH_2^{Fmoc}), 66.4 ($CO_2\underline{C}H_2Ph$), 52.3 ($CO_2\underline{C}H_3$), 50.0 ($CH\alpha^{Phe}$), 47.0 (2C, CH^{Fmoc}, $CH\alpha^{Glu}$), 40.5 ($CH_2\beta^{Phe}$), 30.3 ($CH_2\gamma^{Glu}$), 29.8 ($CH_2\beta^{Glu}$), 28.1 (3C, $C(\underline{C}H_3)_3$).

ESI-MS: 760.1 $[M + H]^+$; 782.2 $[M + Na]^+$; 1541.1 $[2M + Na]^+$.

Methyl 5-{(1*S*)-5-[(benzyloxycarbonyl)amino]-1-{[(9*H*-fluoren-9-ylmethoxy) carbonyl]amino}pentyl}-2-{(1*S*)-1-[(*tert*-butoxycarbonyl)amino]-2-phenylethyl}-1,3-oxazole-4- carboxylate (4f)



Yield : 84 %

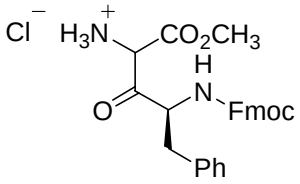
Analytical HPLC Rt = 23.30 min min (50 – 100 % B, 30 min).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.76 (m, 2H, H^{Fmoc}), 7.57 (m, 2H, H^{Fmoc}), 7.39 (m, 2H, H^{Fmoc}), 7.34 (m, 5H, Ph), 7.30 (m, 2H, H^{Fmoc}), 7.21 (m, 3H, Ph), 7.03 (m, 2H, Ph), 5.83 (br s, 1H, NH^{Fmoc}), 5.29 (m, 2H, C<u>H</u>NHFmoc, NH^{Boc}), 5.15 (m, 1H, $CH\alpha^{Lys}$), 5.08 (s, 2H, $CO_2C\underline{H}_2Ph$), 4.85 (br s, 1H, NH^{Cbz}), 4.40 (m, 2H, CH_2^{Fmoc}), 4.20 (m, 1H, CH^{Fmoc}), 3.95 (s, 3H, $CO_2C\underline{H}_3$), 3.18 (m, 4H, $CH_2\beta^{Phe}$, $CH_2\varepsilon^{Lys}$), 1.73 (m, 1H, C<u>H</u>HCHNHFmoc), 1.67 (m, 1H, CH<u>H</u>CHNHFmoc), 1.53 (m, 2H, $CH_2\delta^{Lys}$), 1.40 (s, 9H, $C(C\underline{H}_3)_3$), 1.32 (m, 2H, $CH_2\gamma^{Lys}$).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 162.3 ($\underline{C}O_2Me$), 162.0 (Ox-C^2), 158.3 (Ox-C^5), 156.3 (CO^{Cbz}), 155.5 (CO^{Fmoc}), 154.7 (CO^{Boc}), 143.6 (2C, C^{Fmoc}), 141.1 (2C, C^{Fmoc}), 136.4 (C^{Ph}), 135.4 (C^{Ph}), 129.0 (2C, CH^{Ph}), 128.5 (CH^{Ph}), 128.4 (2C, CH^{Ph}), 128.3 (C, CH^{Ph}), 127.9 (2C, CH^{Ph}), 127.1 (Ox-C^4), 127.0 (2C, CH^{Fmoc}), 126.9 (2C, CH^{Ph}), 126.3 (2C, CH^{Fmoc}), 124.3 (2C, CH^{Fmoc}), 119.8 (2C, CH^{Fmoc}), 80.1 ($\underline{C}(CH_3)_3$), 66.7 (CH_2^{Fmoc}), 66.4 (CH_2^{Cbz}) 52.3 ($CO_2\underline{C}H_3$), 50.8 ($CH\alpha^{Phe}$), 47.1 ($CH\alpha^{Lys}$), 47.0 (CH^{Fmoc}), 40.6 ($CH_2\beta^{Phe}$), 40.5 ($CH_2\varepsilon^{Lys}$), 34.0 ($CH_2\beta^{Lys}$), 29.1 ($CH_2\delta^{Lys}$), 28.0 (3C, $C(\underline{C}H_3)_3$), 22.5 ($CH_2\gamma^{Lys}$).

ESI-MS: 703.4 $[M – Boc + 2H]^+$; 803.2 $[M + H]^+$; 825.3 $[M + Na]^+$; 1605.0 $[2M + H]^+$.

β–Keto ester 6



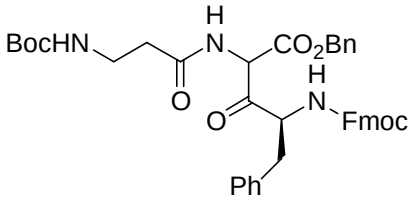
Following the general procedure 1, hydrochloride salt **6** was prepared employing N-(diphenylmethylene)glycine benzyl ester[2] and Fmoc-Phe-Cl. It was used without further purification.

Yield : 80 %

Analytical HPLC Rt = 23.11 min (10 – 90 % B, 30 min).

ESI-MS: 532.2 $[M - Cl + H]^+$;

Benzyl (4*S*)-4-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-2-{{3-[(*tert*-butoxycarbonyl)amino]propanoyl}amino}-3-oxo-5-phenylpentanoate (7)



Following general procedure 2, compound **7** was obtained after column chromatography (EtOAc/hexane 2:8), employing Boc-β-alanine and hydrochloride salt **6**.

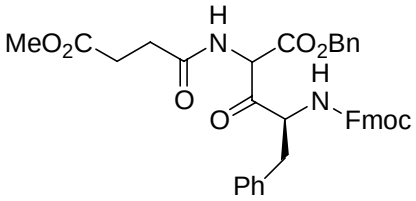
Yield : 75%

Analytical HPLC Rt = 29.96 and 29.99 min (10 – 90 % B, 30 min).

ESI-MS: 606.4 $[M - Boc + H]^+$; 706.1 $[M + H]^+$; 728.3 $[M + Na]^+$.

[2] Grabowska, U.; Rizzo, A.; Quibell, M. *J. Comb. Chem*. **2000**, *2*, 475-490.

Benzyl (4*S*)-4-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-2-{[3-(methoxycarbonyl)propanoyl]amino}-3-oxo-5-phenylpentanoate (8)



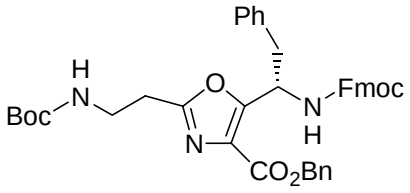
Following general procedure 2, compound **8** was obtained after column chromatography (EtOAc/hexane 3:7), employing mono methyl succinate and hydrochloride salt **6**.

Yield : 78%

Analytical HPLC Rt = 28.75 min (10 – 90 % B, 30 min).

ESI-MS: 649.3 $[M + H]^+$; 671.3 $[M + Na]^+$.

Benzyl 2-{2-[(*tert*-butoxycarbonyl)amino]ethyl}-5-{(1*S*)-1-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-2-phenylethyl}-1,3-oxazole-4-carboxilate (9)



Following general procedure 3, compound **9** was obtained pure after column chromatography (EtOAc/hexane 3:7).

Yield : 81 %

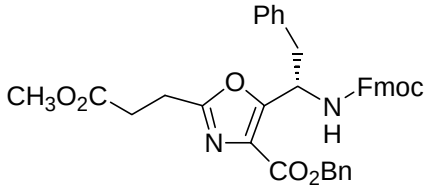
Analytical HPLC Rt = 23.12 min (50 – 90 % B, 30 min).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.77 (m, 2H, H^{Fmoc}), 7.58 (m, 2H, H^{Fmoc}), 7.40 (m, 2H, H^{Fmoc}), 7.31 (m, 2H, H^{Fmoc}), 7.30 (m, 5H, H^{Ph}), 7.24 (m, 5H, H^{Ph}), 5.69 (br s, 1H, NHFmoc), 5.56 (m, 1H, $H\alpha^{Phe}$), 5.37 (s, 2H, CH_2^{OBn}), 4.84 (b s, 1H, NH^{Boc}), 4.39 (m, 2H, CH_2^{Fmoc}), 4,18 (m, 1H, CH^{Fmoc}), 3.47 (m, 2H, $C\underline{H}_2NHBoc$), 3.09 (m, 2H, $CH_2\beta^{Phe}$), 2.91 (m, 2H, $C\underline{H}_2CH_2NHBoc$), 1.43 (s, 9H, ^{t}Bu).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 169.8 ($\underline{C}O_2Bn$), 161.9 (Ox-C2), 158.6 (Ox-C5), 155.9 (CO^{Boc}), 155.5 (CO^{Fmoc}), 143.8 (2C, C^{Fmoc}), 140.7 (2C,C^{Fmoc}), 136.4 (C^{Ph}), 133.2 (C^{Ph}), 129.5 (4C, CH^{Ph}), 129.2 (CH^{Ph}), 129.1 (CH^{Ph}), 129.0 (2C, CH^{Ph}), 128.9 (2C,CH^{Ph}), 128.1 (2C, CH^{Fmoc}), 127.4 (2C, CH^{Fmoc}), 127.3 (Ox-C4), 125.5 (2C, CH^{Fmoc}), 120.4 (2C, CH^{Fmoc}), 80.2 ($(CH_3)_3\underline{C}$), 67.7 (CH_2OBn), 67.4 (CH_2^{Fmoc}), 49.6 ($C\alpha^{Phe}$), 47.6 (CH^{Fmoc}), 40.8 ($\underline{C}H_2\beta^{Phe}$), 37.8 ($\underline{C}H_2NH$), 29.13 ($\underline{C}H_2CH_2NH$), 28.6 (3C, ^{t}Bu).

ESI-MS: 588.3 $[M - Boc + 2H]^+$; 688.3 $[M + H]^+$; 710.2 $[M + Na]^+$; 1397.4 $[2M + Na]^+$.

Benzyl 2-[2-(methoxycarbonyl)ethyl]-5-{(1*S*)-1-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-2-phenylethyl}-1,3-oxazole-4-carboxilate (10)



Following general procedure 3, compound **10** was obtained pure after column chromatography (EtOAc/hexane 3:7).

Yield : 83 %

Analytical HPLC Rt = 29.70 min (10 – 90 % B, 30 min).

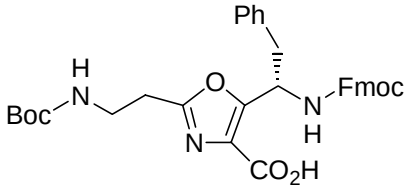
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 7.78 (m, 2H, H^{Fmoc}), 7.55 (m, 2H, H^{Fmoc}), 7.44 (m, 2H, H^{Ph}), 7.40 (m, 2H, H^{Fmoc}), 7.35 (m, 3H, H^{Ph}), 7.31 (m, 2H, H^{Fmoc}), 7.21 (m, 3H, H^{Ph}), 6.98 (m, 2H, H^{Ph}), 6.00 (b s, 1H, NH^{Fmoc}), 5.57 (m, 1H, $CH\alpha^{Phe}$), 5.38 (s, 2H, CH_2^{OBn}), 4.38 (m, 2H, CH_2^{Fmoc}), 4.19 (m, 1H, CH^{Fmoc}), 3.72 (s, 3H, CO_2CH_3), 3.08 (m,

2H $CH_2\beta^{Phe}$), 3.03 (m, 2H, $C\underline{H}_2CO_2Me$), 2.75 (m, 2H, $C\underline{H}_2CH_2CO_2Me$).

^{13}C NMR (500 MHz, $CDCl_3$, 300 K): δ = 172.3 ($\underline{C}O_2Me$), 169.6 ($\underline{C}O_2Bn$), 161.6 (Ox-C^2), 158.2 (Ox-C^5), 155.3 (CO^{Fmoc}), 143.7 (2C, C^{Fmoc}), 140.8 (2C,C^{Fmoc}), 136.2 (C^{Ph}), 135.6 (C^{Ph}), 129.5 (2C, CH^{Ph}), 129.0 (2C, CH^{Ph}), 128.9 (4C,CH^{Ph}), 128.1 (2C, CH^{Fmoc}), 127.4 (4C, CH^{Ph}, CH^{Fmoc}), 127.4 (Ox-C^4), 125.5 (2C, CH^{Fmoc}), 120.4 (2C, CH^{Fmoc}), 67.4 (CH_2^{OBn}), 67.0 (CH_2^{Fmoc}), 52.2 ($CO_2\underline{C}H_3$), 49.6 ($CH\alpha^{Phe}$), 47.6 (CH^{Fmoc}), 41.1 ($CH_2\beta^{Phe}$), 31.0 ($\underline{C}H_2CH_2CO_2Me$), 23.65 ($\underline{C}H_2CO_2Me$).

ESI-MS: 631.2 $[M + H]^+$; 653.3 $[M + Na]^+$.

2-{2-[(*tert*-butoxycarbonyl)amino]ethyl}-5-{(1*S*)-1-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-2-phenylethyl}-1,3-oxazole-4-carboxilic acid (11)



Benzyl protected oxazole **9** was dissolved in methanol and 20% palladium on carbon was added; the system was then evacuated and hydrogen was introduced. After 1.5 h. deprotection was complete by HPLC analysis. The reaction mixture was filtered over celite and the catalyst washed with methanol several times. The combined washings were concentrated in vacuo to afford compound **11** which was used without further purification.

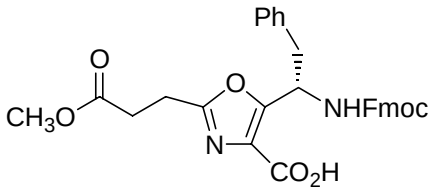
Analytical HPLC Rt = 26.04 min (10 – 90 % B, 30 min).

^1H NMR (500 MHz, DMSO-d_6, 300 K): δ = 8.08 (br s, 1H, NHFmoc), 7.88 (m, 2H, H^{Fmoc}), 7.63 (m, 2H, H^{Fmoc}), 7.40 (m, 2H, H^{Fmoc}), 7.31 (m, 2H, H^{Fmoc}), 7.20 (m, 3H, H^{Ph}), 7.18 (m, 2H, H^{Ph}), 6.97 (NHBoc), 5.53 (m, 1H, $CH\alpha^{Phe}$), 4.18 (m, 2H, CH_2^{Fmoc}), 4.15 (m, 1H, CH^{Fmoc}), 3.33 (m, 2H, $C\underline{H}_2NHBoc$), 3.02 (m, 2H, $CH_2\beta^{Phe}$), 2.87 (m, 2H,

CH_2CH_2NHBoc), 1.36 (s, 9H, ^tBu).

ESI-MS: 498.3 $[M - Boc]^+$; 542.2 $[M - {}^tBu + 2H]^+$ 598.1 $[M + H]^+$; 620.3 $[M + Na]^+$; 1217.2 $[2M + Na]^+$.

2-[2-(methoxycarbonyl)ethyl]-5-{(1*S*)-1-{[(9*H*-fluoren-9-ylmethoxy)carbonyl]amino}-2-phenylethyl}-1,3-oxazole-4-carboxilic acid (12)



The title compound was prepared in a similar fashion as **11** from benzyl ester **10**.

Analytical HPLC Rt = 24.37 min (10 – 90 % B, 30 min).

^1H NMR (500 MHz, DMSO-d_6, 300 K): δ = 8.22 (br s, 1H, NH), 7.87 (m, 2H, H^{Fmoc}), 7.61 (m, 2H, H^{Fmoc}), 7.39 (m, 2H, H^{Fmoc}), 7.28 (m, 2H, H^{Fmoc}), 7.22 (m, 3H, H^{Ph}), 7.18 (m, 2H, H^{Ph}), 5,48 (m, 1H, C<u>H</u>NHFmoc), 4.19 (m, 2H, $CH_2{}^{Fmoc}$), 4.15 (m, 1H, CH^{Fmoc}), 3.60 (s, 3H, $CO_2C\underline{H}_3$), 3.04 (m, 2H, $CH_2\beta^{Phe}$), 3.00 (m, 2H, $C\underline{H}_2CO_2CH_3$), 2.78 (m, 2H, $C\underline{H}_2CH_2CO_2CH_3$).

ESI-MS: 541.3 $[M + H]^+$; 563.2 $[M + Na]^+$; 1103.3 $[2M + Na]^+$;

Synthesis of compound 13

Procedure for resin loading:

In a syringe (10 ml), equipped with a frit, CTC resin (1.0 g, 0.9 mmol/g) was swelled in NMP (1 h). After filtering off the resin, a solution of Fmoc-Ala-OH (1.08 mmol) and DIPEA (2.7 mmol) in dry CH_2Cl_2 (8 ml) was added. After 1 h a mixture of DIPEA (0.2

ml) in MeOH (1 ml) was added. After 15 min. the resin was filtered off, washed with CH_2Cl_2 (2 x), DMF (3x), DMF/MeOH 2:1, DMF/MeOH 1:2 and MeOH before being dried under reduced pressure overnight. The resin loading was 0.58 mmol/g according to gravimetric measurements.

Procedure for 1st (Fmoc-Ile-OH) and 3rd (Ac-Val-OH) couplings:

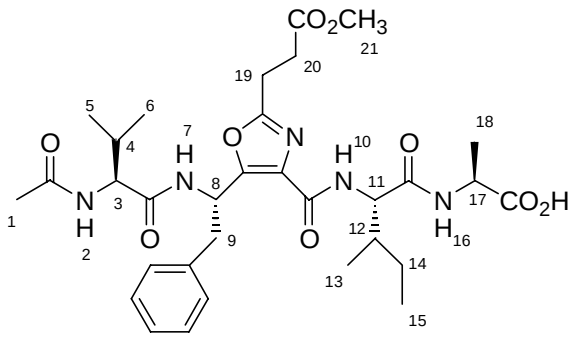
The Fmoc-protecting group was removed by treating with a 20% piperidine solution in DMF (2 x 10 min.). The resin was filtered off and washed with NMP (5 x 2min) before a solution of Fmoc-Ile-OH (1st coupling, 3eq.) or Ac-Val-OH (3rd coupling, 3 equiv.), TBTU (3 equiv.), HOBt (3 equiv.) and DIPEA (8.7 equiv.) in DMF (5 ml) was added. After 2 h reaction is complete (monitoring by analytical HPLC of a cleaved sample) and the resin is filtered off and washed with NMP (5 x 2 min).

Procedure for 2nd coupling:

After Fmoc deprotection of the prior amino group with 20% piperidine in DMF (2 x 10 min) the resin was filtered off and washed with NMP (5 x 2 min). A solution of compound **12** (1.3 equiv.), HATU (1.3 equiv.), HOAt (1.3 equiv.) and DIPEA (3.4 equiv.) in dry DMF (4 ml) was added. After 12 h reaction is complete (monitoring by analytical HPLC of a cleaved sample) and the resin was filtered off and washed with NMP (5 x 2 min).

Cleavage from the resin:

After the 3rd coupling, resin was washed with NMP (5 x 2 min), CH_2Cl_2 (3 x 2 min) and dried under vacuo. Then, the resin was treated with 20 % hexafluoroisopropanol in CH_2Cl_2 (2 x 45 min). Afterwards, the resin was washed with CH_2Cl_2 (3 x). All solutions were combined and evaporated to get the crude peptide. Purification by HPLC (40 – 80 % B in 25 min) afforded **13** as a white solid. Yield : 71 %.



Analytical HPLC Rt = 18.33 min (10 – 90 % B, 30 min).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = 8.98 (d, *J* = 7.9 Hz, 1H, PheNH), 7.66 (d, *J* = 8.0 Hz, 1H, IleNH), 7.37 (d, *J* = 4.0 Hz, 1H, AlaNH), 7.21 (m, 3H, H^{arom}), 7.03 (m, 2H, H^{arom}), 6.28 (d, *J* = 8.0 Hz, 1H, ValNH), 5.55 (m, 1H, CH^{α}Phe), 4.72 (m, 1H, CH^{α}Ala), 4.43 (m, 1H, CH^{α}Ile), 4.30 (m, 1H, CH^{α}Val), 3.74 (s, 3H, $CO_2C\underline{H}_3$), 3.10 (m, 2H, $C\underline{H}_2Ph$), 2.97 (m, 2H, $C\underline{H}_2CO_2$), 2.71 (m, 2H, $C\underline{H}_2CH_2CO_2$), 2.11 (s, 3H, $COC\underline{H}_3$), 2.04 (m, 1H, CH^{β}Ile), 2.02 (m, 1H, CH^{β}Val), 1.59 (3H, $C\underline{H}_3CH_2CH^{\beta}$Ile), 1.54 (3H, $C\underline{H}_3$Ala), 1.19 (m, 1H, $C\underline{H}HCH^{\beta}$Ile), 1.00 (3H, $C\underline{H}_3$Val), 0.94(m, 1H, $CH\underline{H}CH^{\beta}$Ile), 0.85 (3H, $C\underline{H}_3CH^{\beta}$Ile), 0.84 (3H, $C\underline{H}_3$Val).

^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 175.01 (CO_2H), 172.34 ($\underline{C}O_2CH_3$), 171.89 ($CH_3\underline{C}O$), 171.20 (CO^{Val}), 171.07 (CO^{Ile}), 161.29 (Ox-C^2), 155.32 (Ox-C^5), 136.02 (C^{Ph}), 129.6 (2C, CH^{Ph}), 128.7 (CH^{Ph}), 127.2 (2C, CH^{Ph}), 127.1 (Ox-C^4), 80.1 ($C(CH_3)_3$), 59.2 ($CH\alpha^{Val}$), 58.5 ($CH\alpha^{Ile}$), 52.6 ($CO_2\underline{C}H_3$), 48.6 ($CH\alpha^{Ala}$), 48.2 ($CH\alpha^{Phe}$), 41.7 ($\underline{C}H_2Ph$), 37.8 ($CH\beta^{Ile}$), 31.4 ($CH\beta^{Val}$), 30.6 ($\underline{C}H_2CH_2CO_2Me$), 25.34 ($CH_3\delta^{Ile}$), 25.28 ($CH_2\gamma^{Ile}$), 23.5 ($\underline{C}H_3CO$), 23.4 ($\underline{C}H_2CO_2Me$), 19.3 ($\underline{C}H_3^{Val}$), 18.5 ($CH_3^{Ala}$), 17.9 ($CH_3\gamma^{Ile}$), 15.6 ($\underline{C}H_3^{Val}$).

ESI-MS: 644.3 $[M + H]^+$; 666.4 $[M + Na]^+$; 682 $[M + K]^+$; 1325 $[2M + K]^+$.

Synthesis of cyclic peptides 14, 15 and 17

Resin loading:

In a syringe (10 ml), equipped with a frit, CTC resin (1g, 0.9 mmol/g) was swelled in NMP (1 h). After filtering off the resin, a solution of Fmoc-aa-OH (1.8 equiv.) and DIPEA (4.5 equiv.) in dry CH_2Cl_2 (8 ml) was added. After 2 h the resin was filtered off, washed with CH_2Cl_2 (2 x), DMF (3 x), DMF/MeOH 2:1, DMF/MeOH 1:2 and MeOH before being dried under reduced pressure overnight.

Procedure for 1st and 3rd couplings:

In a syringe (10 ml) the resin was swelled for 1 h in NMP. The Fmoc-protecting group of the prior amino acid was removed by treating with a 20% piperidine solution in DMF (2 x 10 min.). The resin was filtered off and washed with NMP (5 x 2min) before a solution of the corresponding oxazole amino acid (**11** or **12**, 1.5 equiv.) HATU (1.5 equiv.), HOAt (1.5 equiv.) and DIPEA (3.9 equiv.) in dry DMF (3 ml) was added. After 12-15 h reaction was complete (monitoring by analytical HPLC) and the resin was filtered off and washed with NMP (5 x 2 min).

Procedure for 2nd coupling:

After Fmoc deprotection of the prior amino group with 20% piperidine in DMF (2 x 10 min) the resin was filtered off and washed with NMP (5 x 2 min). A solution of Fmoc-aa-OH (2 equiv.), HATU (2 equiv), HOAt (2 equiv) and DIPEA (5.2 equiv), in dry DMF (4 ml) was added. After 12 h reaction is complete (monitoring by analytical HPLC) and the resin was filtered off and washed with NMP (5 x 2 min).

Cleavage from the resin:

After Fmoc deprotection with 20% piperidine in DMF (2 x 10 min) the resin was washed with NMP (5 x 2 min), CH_2Cl_2 (3 x 2 min) and dried under vacuo. Then, the resin was treated with 20 % hexafluoroisopropanol in CH_2Cl_2 (2 x 45 min) and washed with CH_2Cl_2 (3 x). All solutions were combined and evaporated to get the crude linear oligomers which were characterized with ESI-MS and HPLC.

General procedure for cyclization of linear oligomers:

A highly diluted solution (1mM) of corresponding linear oligomer in DMF is prepared. $NaHCO_3$ (5 equiv.) and DPPA (3 equiv) are added with stirring. After 12 hours the solvent is evaporated and the product is purified by HPLC to afford the corresponding cyclopeptide.

Cyclo 14

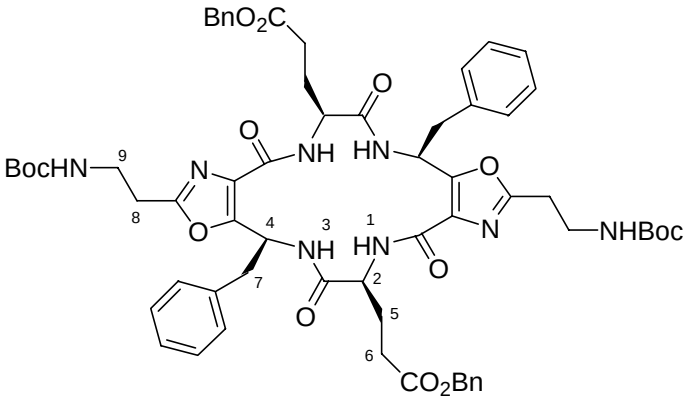
Purification by RP-HPLC (50 – 95 % B in 30 min) afforded compound **14** as a white solid.

Yield : 57 %

Analytical HPLC Rt = 24.31 min (50 – 100 % B, 30 min).

ESI-MS: 953.6 $[M - 2Boc + 3H]^+$; 1053.4 5 $[M - Boc + 2H]^+$; 1175.5 $[M + Na]^+$.

^1H and ^{13}C data ($CDCl_3$, 300K).



Position	*^1H / ^{13}C*	*Position*	*^1H / ^{13}C*
1	7.63 (2H)	**8**	2.86 (4H) / 29.2 (2C)
2	3.99 (2H) / 55.4 (2C)	**9**	3.51 (4H) / 37.6 (2C)
3	7.83 (2H)	**CH_2^{Bn}**	5.17 (4H) / 67.1 (2C)
4	5.32 (2H) / 48.3 (2C)	**NHBoc**	5.17 (2H)
5	2.41 - 2.26 (4H) / 25.4 (2C)	**^{t}Bu**	1.47 (18H) / 28.7 (6C)
6	2.44 – 2.36 (4H) / 31.2 (2C)	**Ph–C^7**	7.24 (4H) / 128.8 (4C)
			7.19 (2H) / 127.1 (2C)
			7.15 (4H) / 129.4 (4C)
7	3.42 –3.26 (4H) /37.5 (2C)	**Ph^{Bn}**	7.35 (10H) / 128.7-128.6 (10C)

Cyclo 15

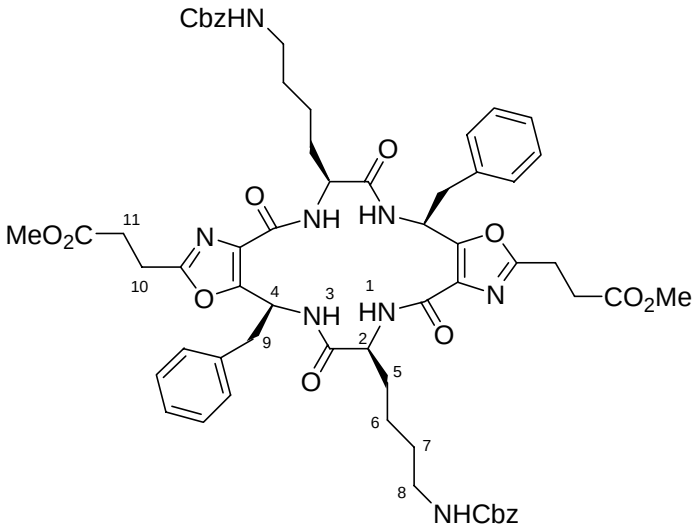
Purification by RP-HPLC (40 – 90 % B in 30 min) afforded compound **15** as a white solid.

Yield : 68 %

Analytical HPLC Rt = 26.82 min (10 – 90 % B, 30 min).

ESI-MS: 1147.6 $[M + Na]^+$.

^1H and ^{13}C data ($CDCl_3$, 300K).



Position	***^1H / ^{13}C***	***Position***	***^1H / ^{13}C***
1	7.23 (2H)	**9**	3.41-3.28 (4H) / 37.9 (2C)
2	3.85 (2H) / 56.3 (2C)	**10**	2.76 (4H) / 23.6 (2C)
3	8.14 (2H)	**11**	3.02 (4H) / 67.1 (2C)
4	5.38 (2H) / 48.3 (2C)	**OMe**	3.72 (6H) / 52.5 (2C)
5	1.91 (4H) / 29.8 (2C)	**NH^{Cbz}**	4.87 (2H)
6	1.28 (4H) / 23.6 (2C)	**CH_2^{Cbz}**	5.12 (4H) / 67.9 (2C)
7	1.53 (4H) / 30.0 (2C)	**Ph-C^9**	7.26 (4H) / 128.8 (4C)
			7.20 (2H) / 127.1 (2C)
			7.16 (4H) / 129.5 (4C)
8	3.18 (4H) / 37.5 (2C)	**Ph^{Cbz}**	7.35 (10H) / 128.7-128.6 (10C)

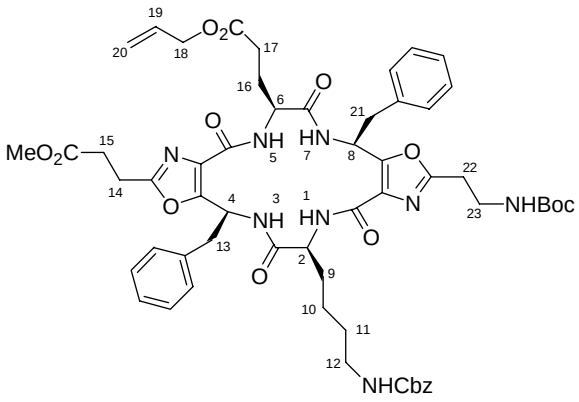
Cyclo 17

Purification by RP-HPLC (40 – 90 % B in 30 min) afforded **17** as a white solid.

Yield : 61 %

Analytical HPLC Rt = 27.49 min (10 – 90 % B, 30 min).

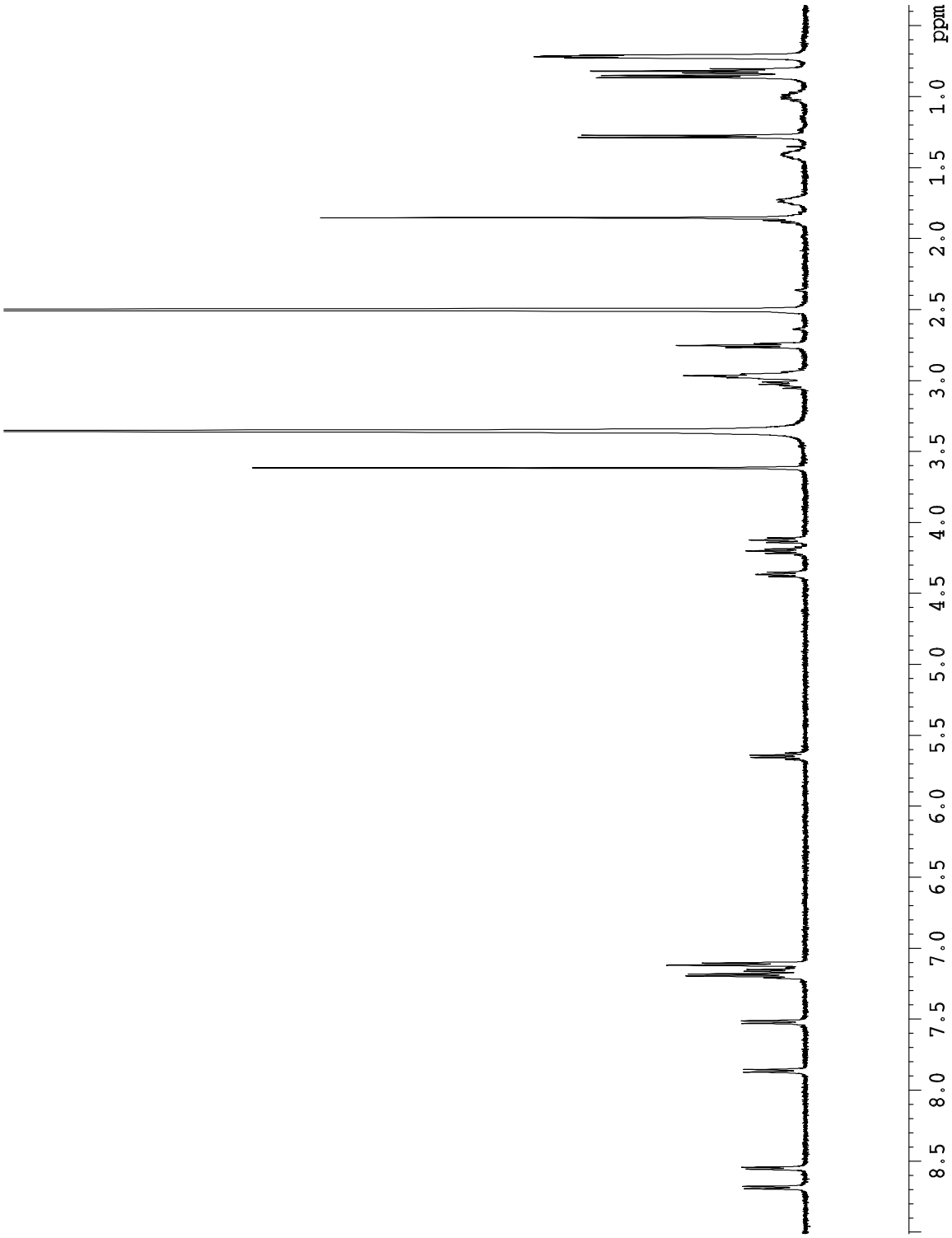
ESI-MS: 989.6 $[M - Boc]^+$; 1111.5 $[M + Na]^+$.



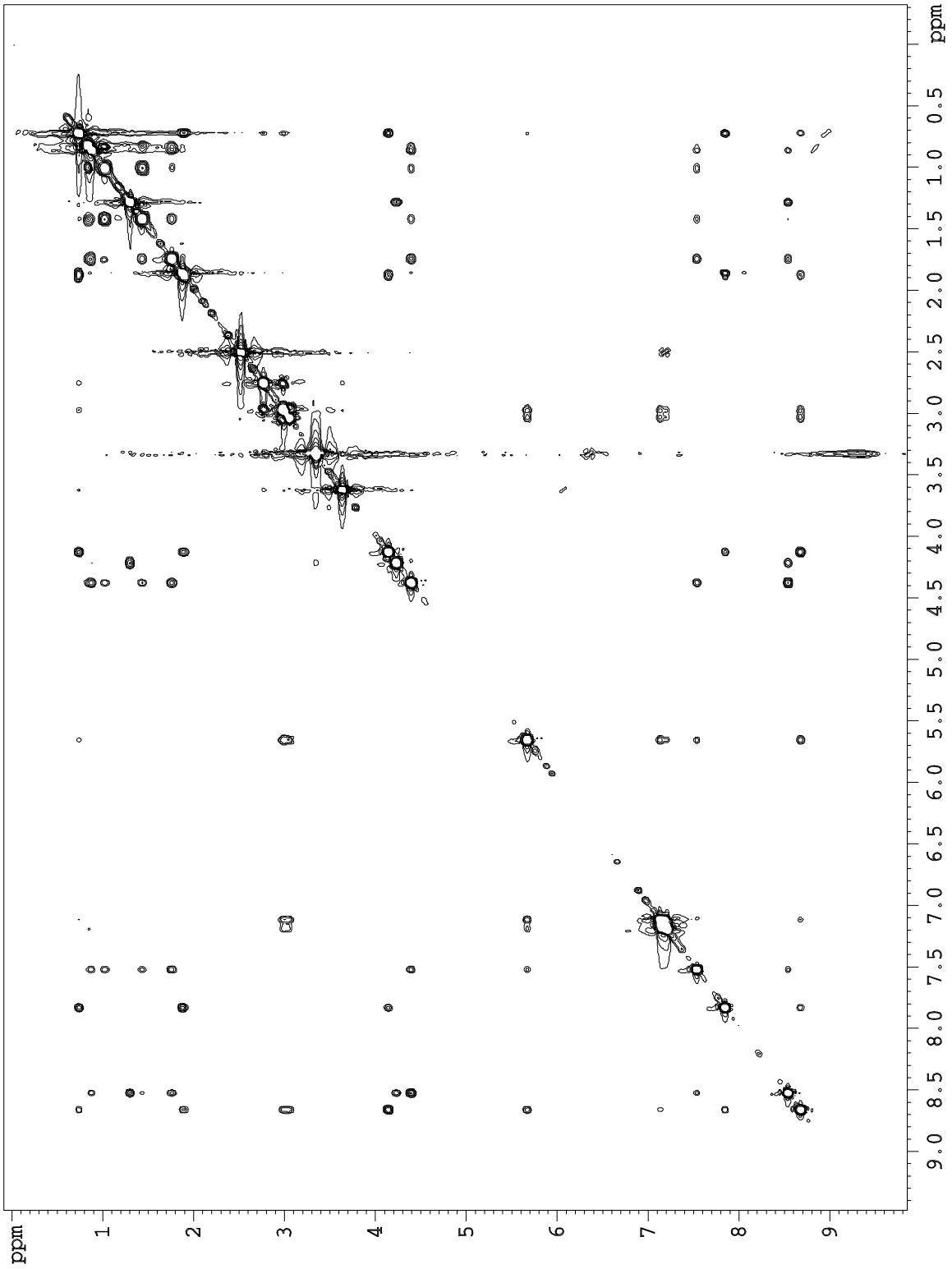
Position	*^1H / ^{13}C* [a]	*Position*	*^1H / ^{13}C* [a]
1	8.44 (J = 7.5 Hz)	**16**	2.11-2.02 / 25.4
2	3.80 / 54.9	**17**	2.27 / 31.3
3	8.36	**18**	4.50 / 65.3
4	5.17 / 48.3	**19**	5.91 /133.7
5	8.48 (J = 7.5 Hz)	**20**	5.26-5.18 / 118.7
6	3.80 / 54.9	**21**	3.16 / 38.6
7	8.33	**22**	2.85 / 29.1
8	5.24 / 47.9	**23**	3.30 / 38.3
9	1.74 / 30.1	**NH^{Cbz}**	7.18
10	1.21 / 29.9	**CH_2^{Cbz}**	4.98 / 66.2
11	1.35 / 29.1	**OMe**	3.62 / 52.4
12	2.95 / 41.0	**NH^{Boc}**	6.92 (J = 6.0 Hz)
13	3.24 / 37.7	**^{t}Bu**	1.37 / 29.0
14	2.72 / 30.8	**Ph-C^{13} and Ph-C^{21}**	7.11 (2H) / 129.8 (2C)
			7.16 (2H) / 129.9 (2C)
			7.17 (2H) / 127.2 (2C)
			7.23 (2H) / 129.1 (2C)
			7.24 (2H) / 129.9 (2C)
15	2.93 / 23.4	**Ph^{Cbz}**	7.31-7.36 (5H) /128.8-128.4 (5C)

a) DMSO-d_6, 300K

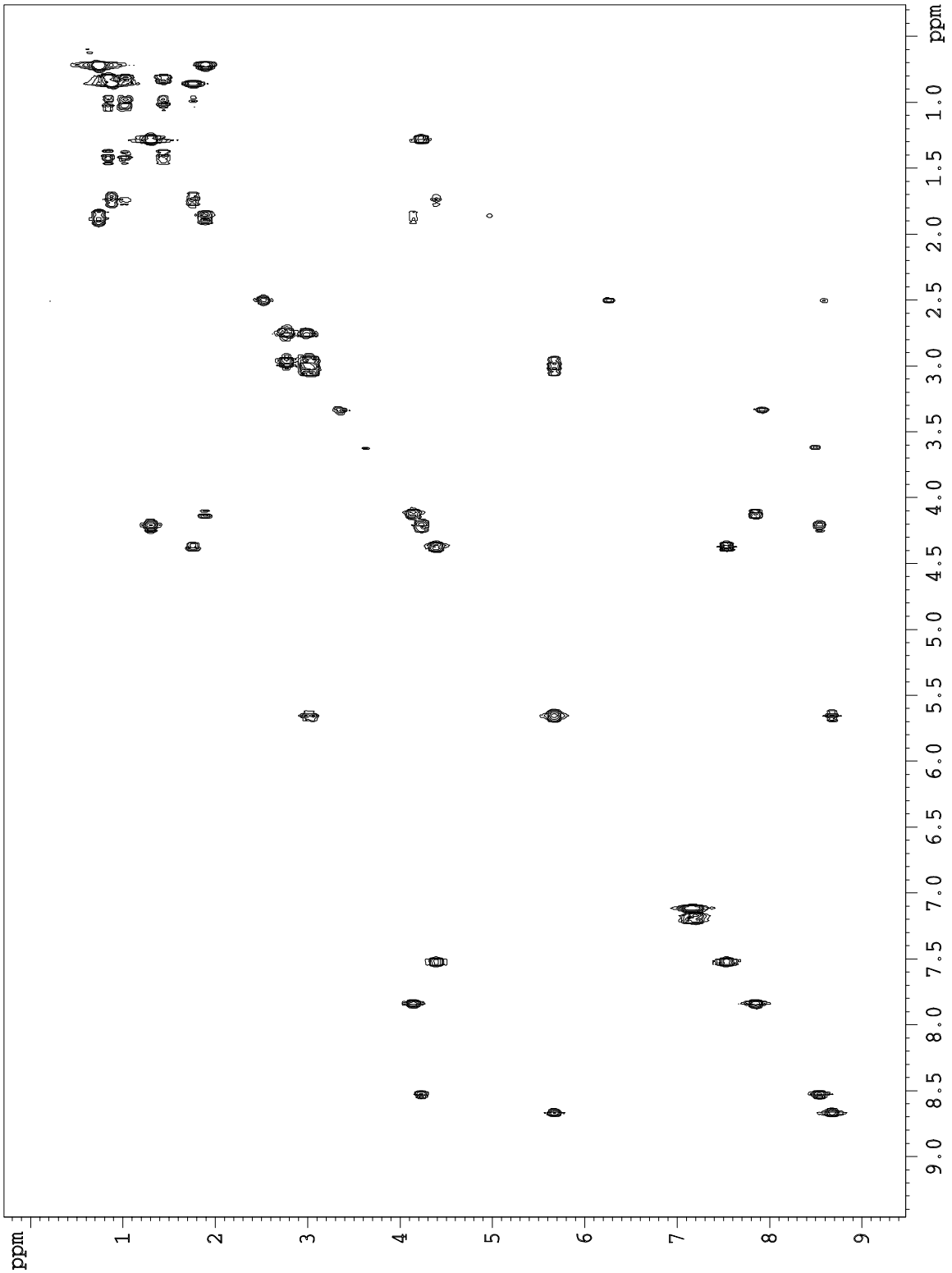
^{1}H spectrum of compound 13 (500 MHz, DMSO-d_6, 300K, 1 mM).



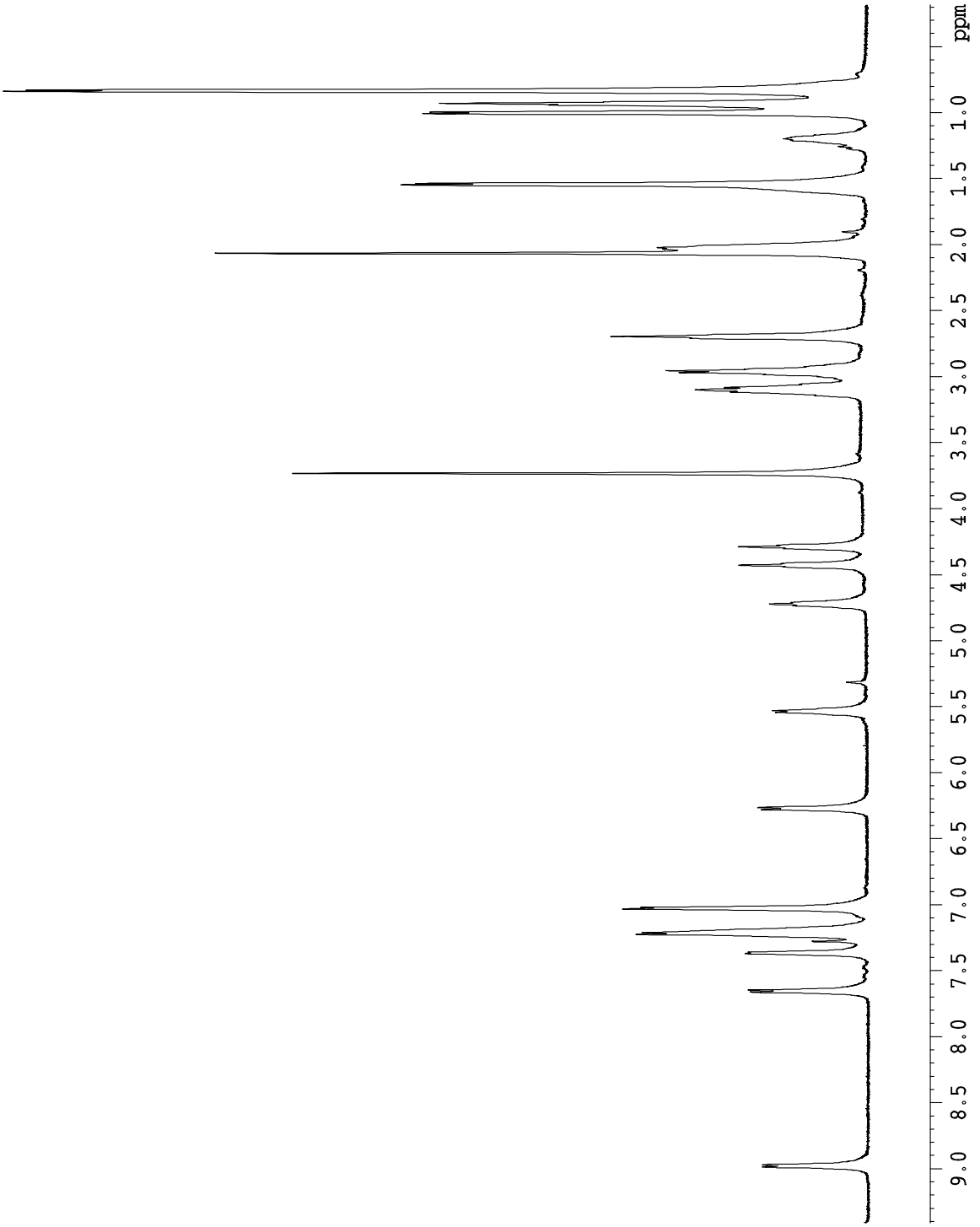
ROESY spectrum of compound 13 (500 MHz, DMSO-d_6, 300K, 1 mM).



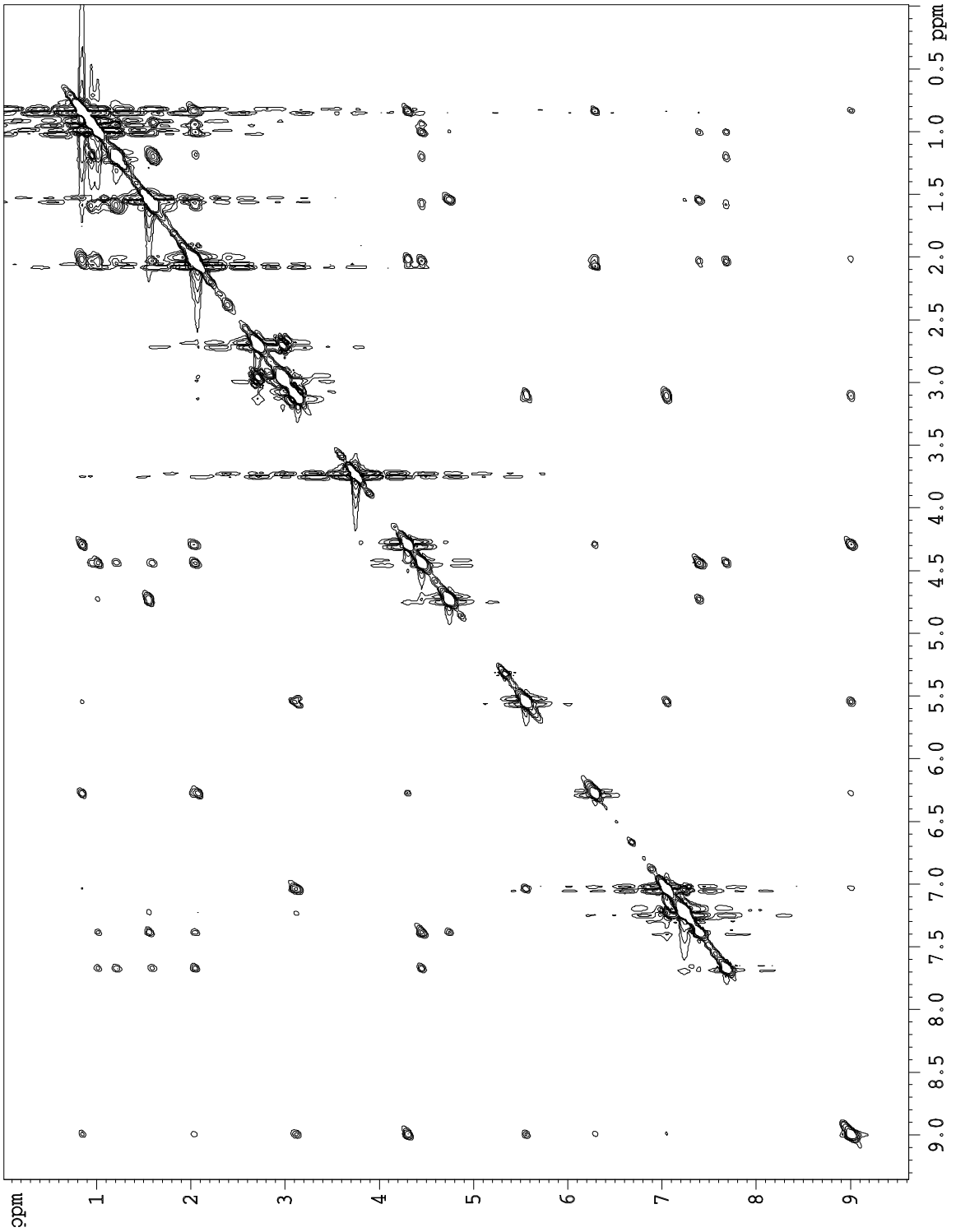
COSY spectrum of compound 13 (500 MHz, DMSO-d_6, 300K, 1 mM).



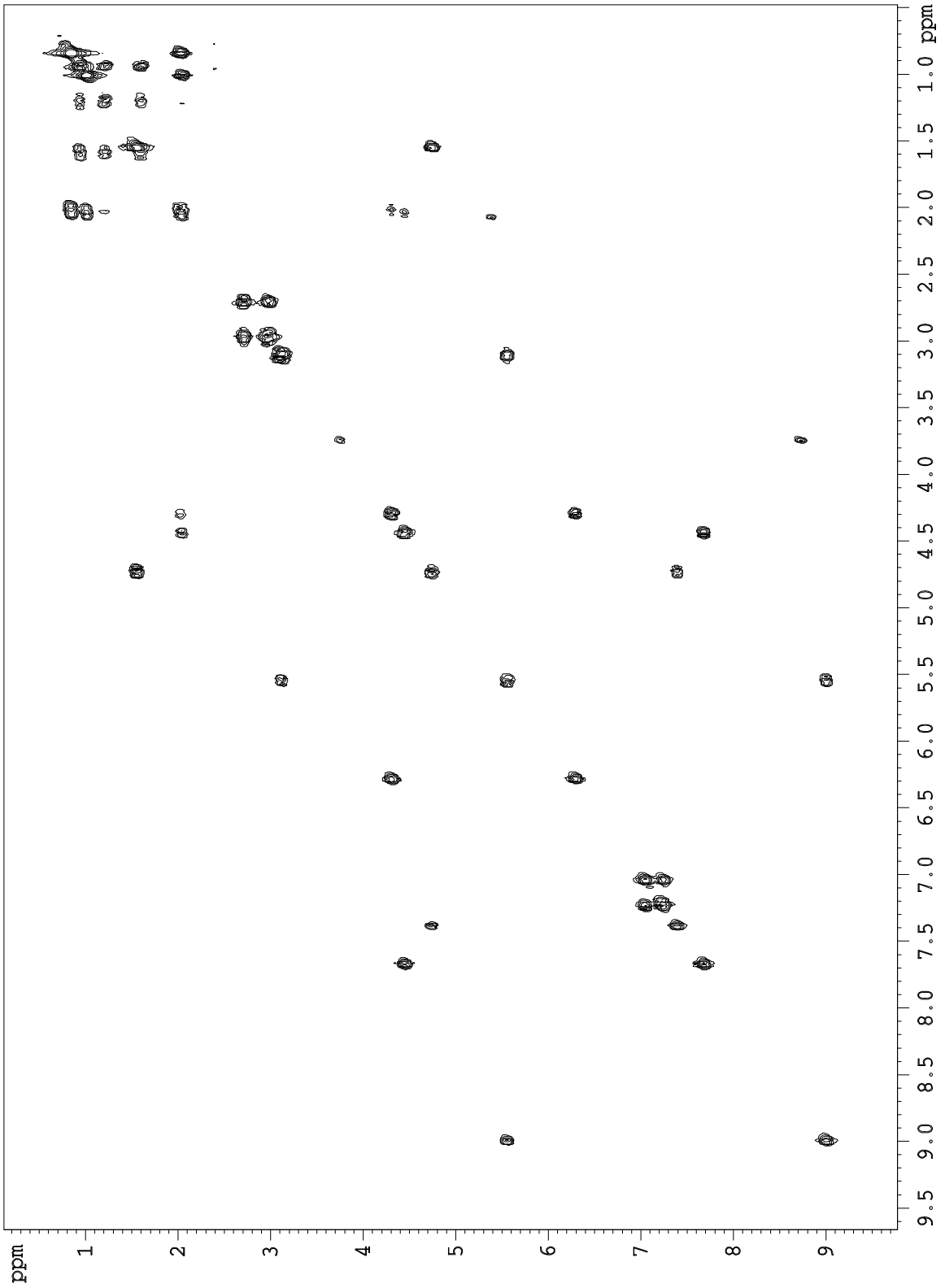
^{1}H spectrum of compound 13 (500 MHz, $CDCl_3$, 300K, 1 mM).



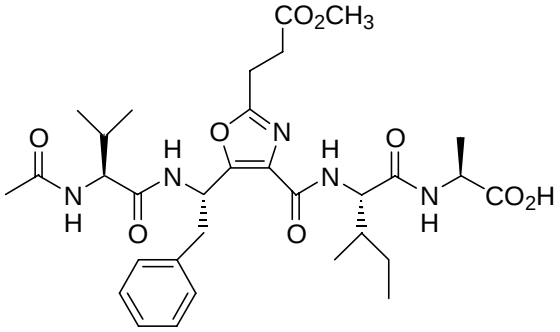
ROESY spectrum of compound 13 (500 MHz, $CDCl_3$, 300K, 1 mM).

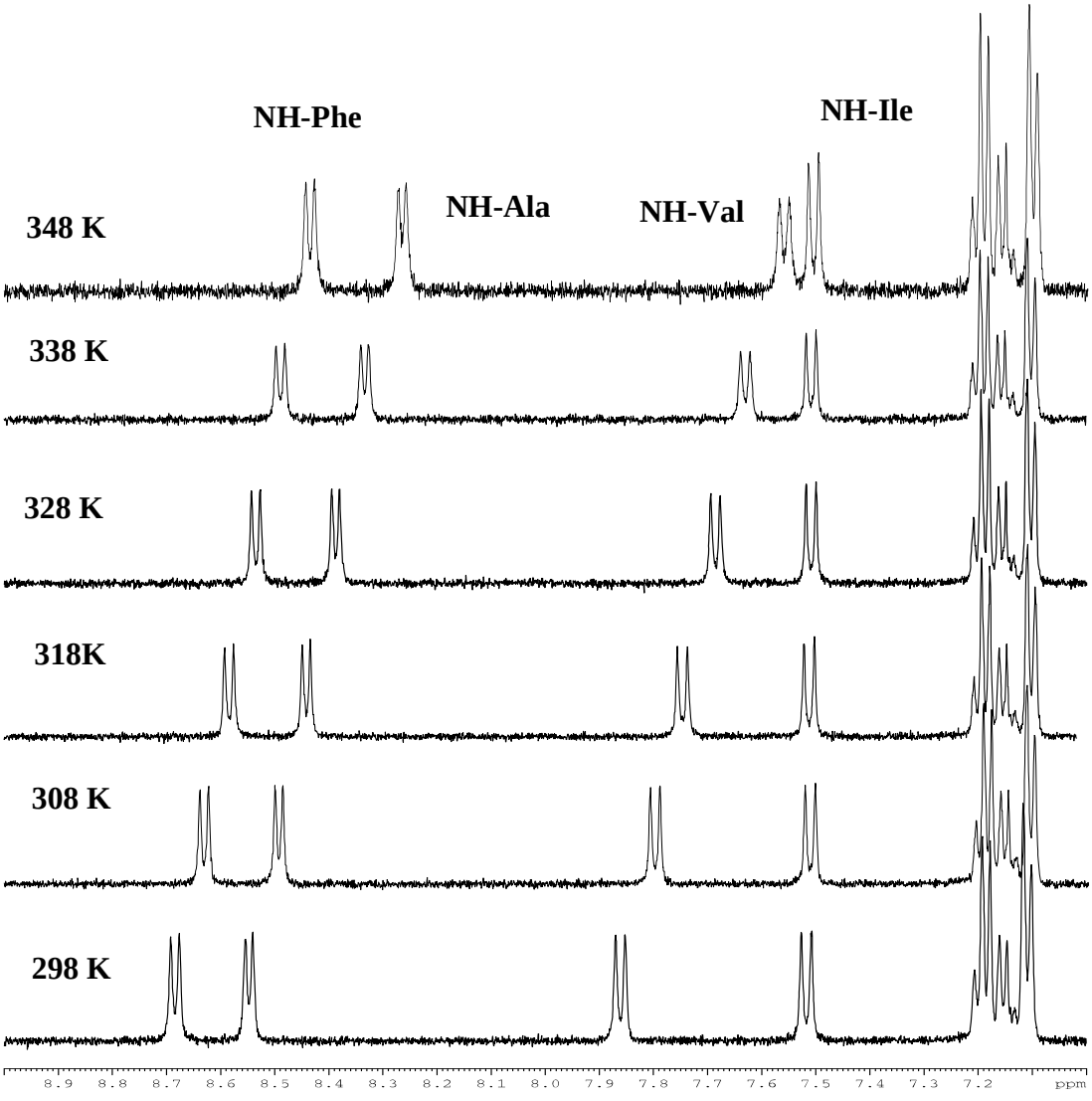


COSY spectrum of compound 13 (500 MHz, $CDCl_3$, 300K, 1 mM).

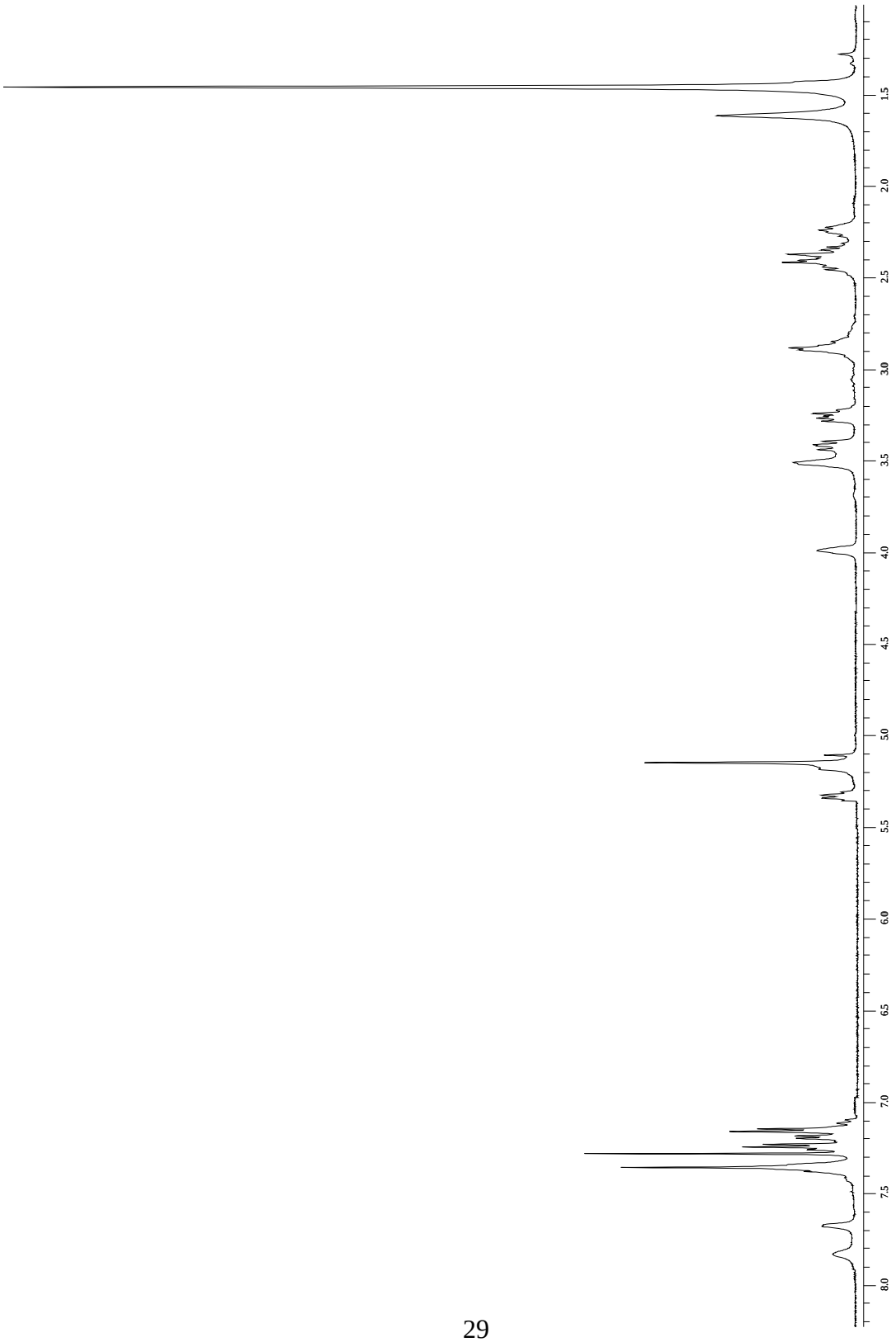


Variable Temperature NMR data for compound 13 (DMSO-d_6, 1mM).

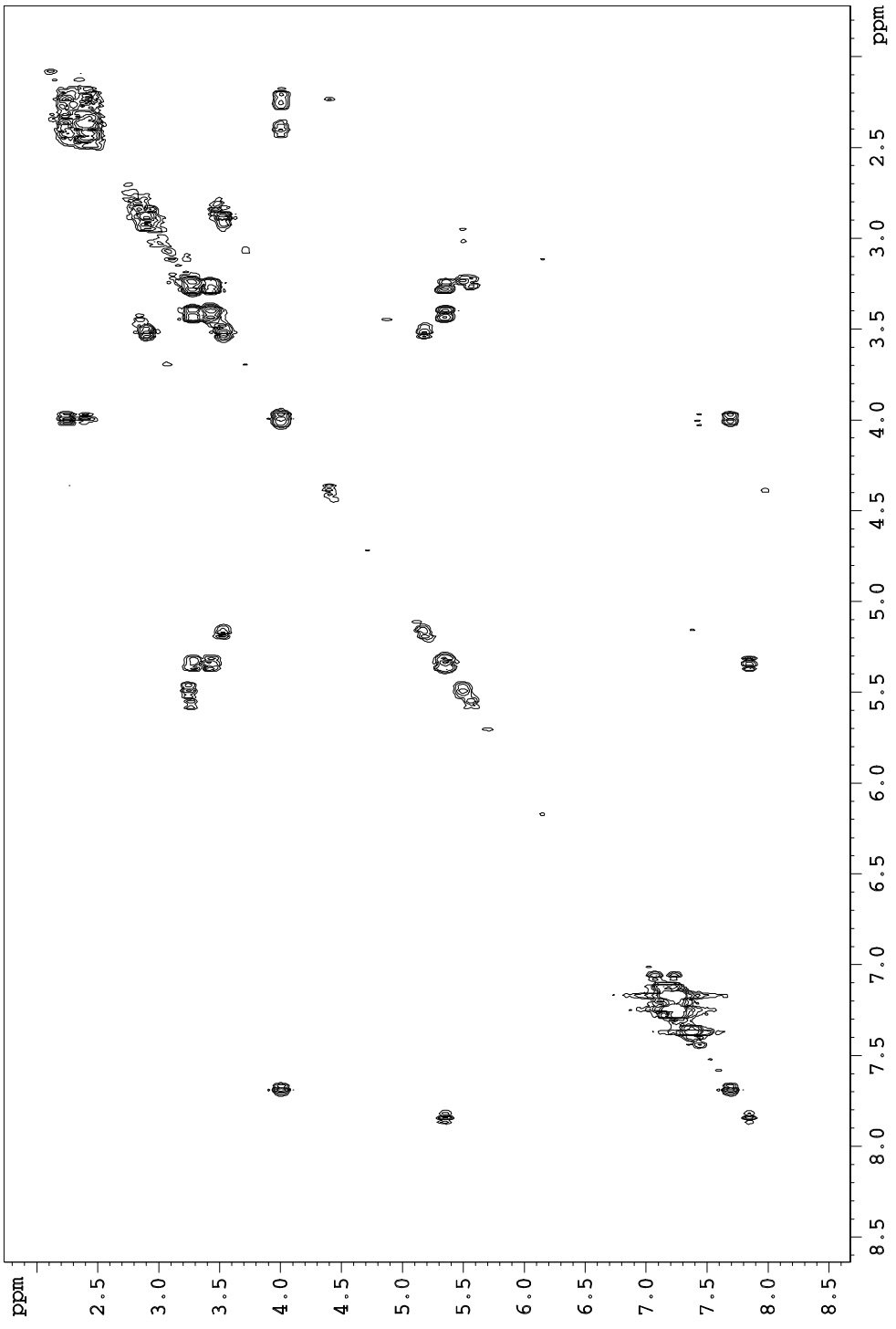




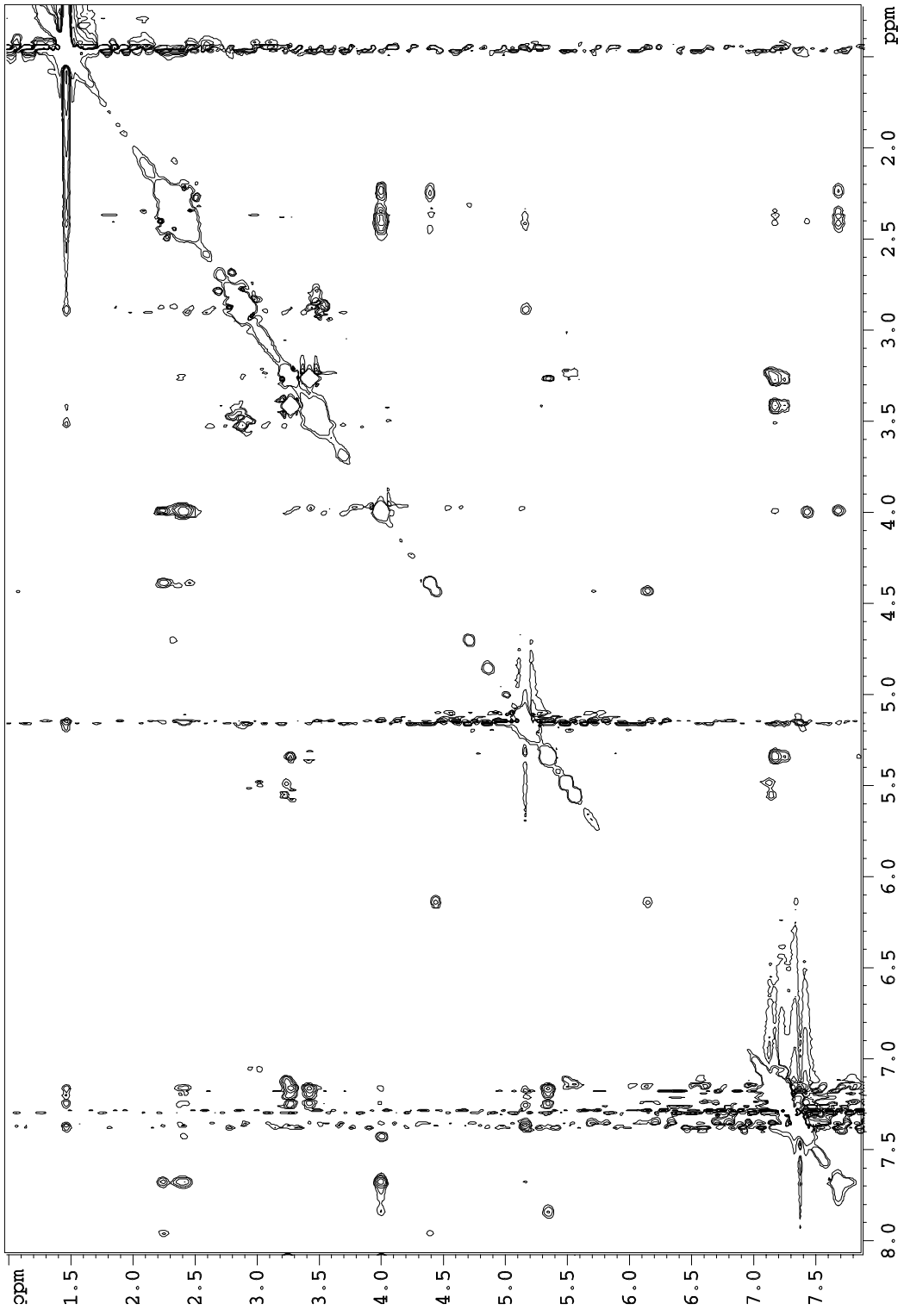
^{1}H spectrum of compound 14 (500 MHz, $CDCl_3$, 300K, 1 mM).



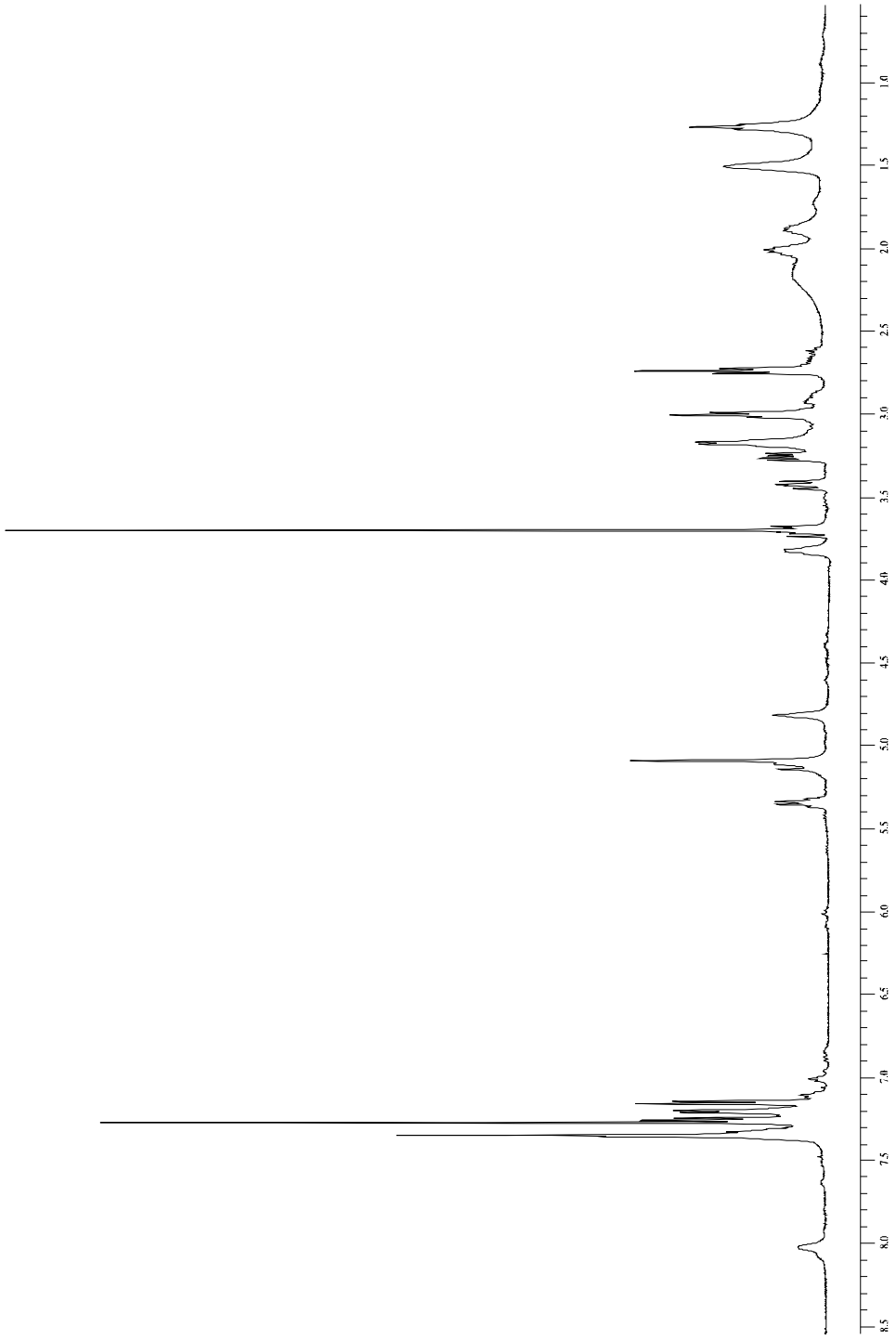
COSY spectrum of compound 14 (500 MHz, $CDCl_3$, 300K, 1 mM).



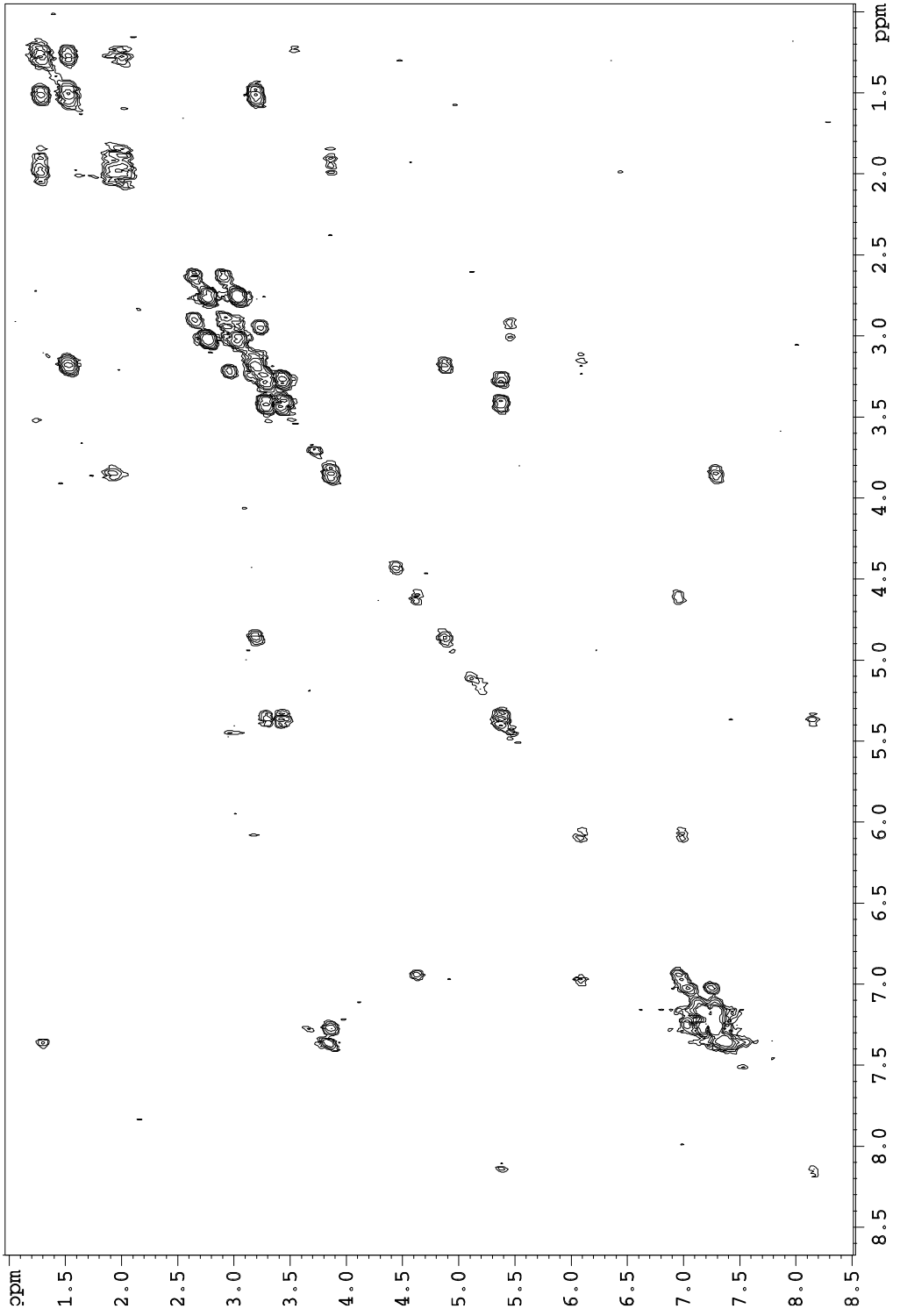
ROESY spectrum of compound 14 (500 MHz, $CDCl_3$, 300K, 1 mM).



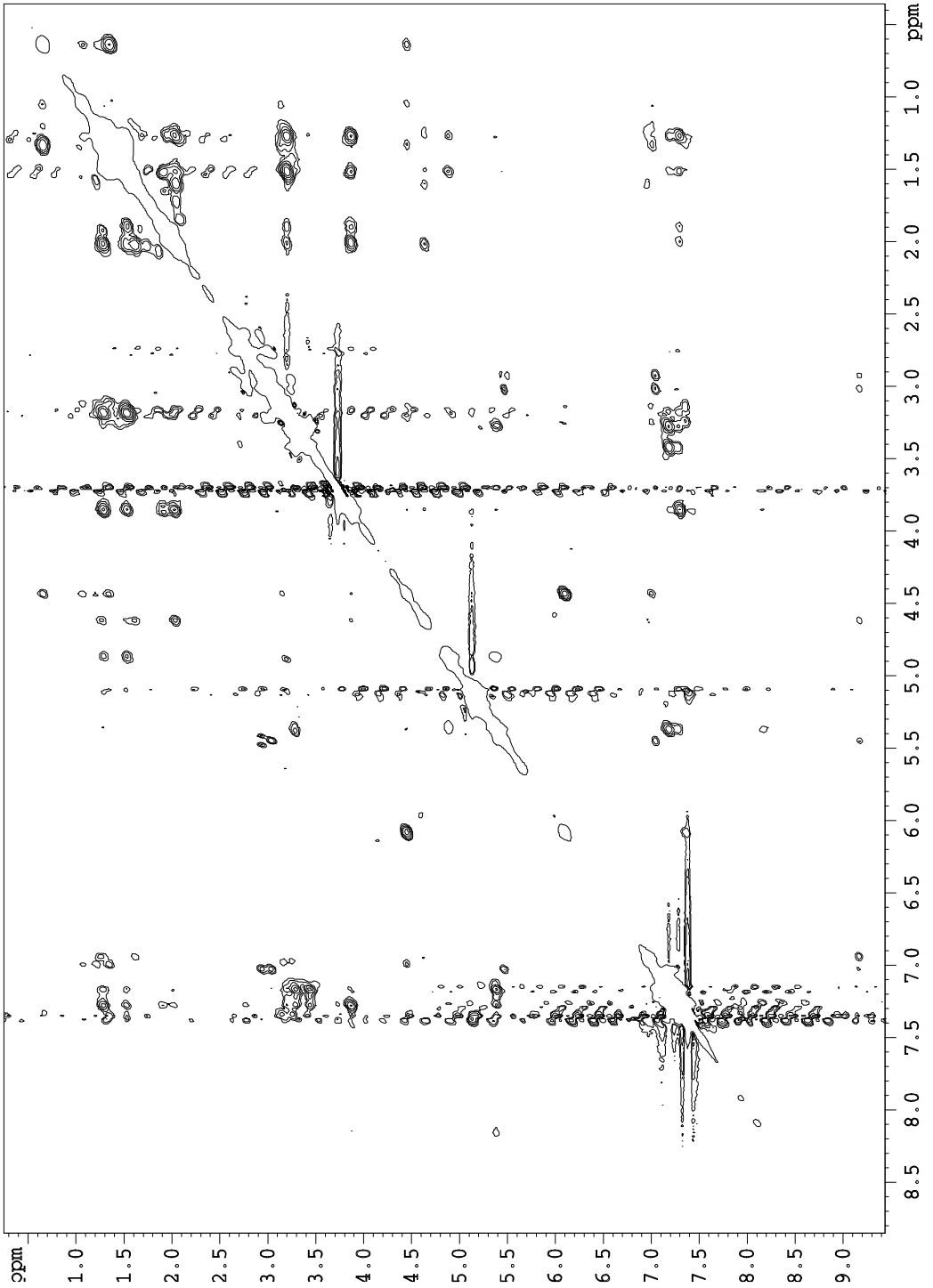
^{1}H spectrum of compound 15 (500 MHz, $CDCl_3$, 300K, 1 mM).



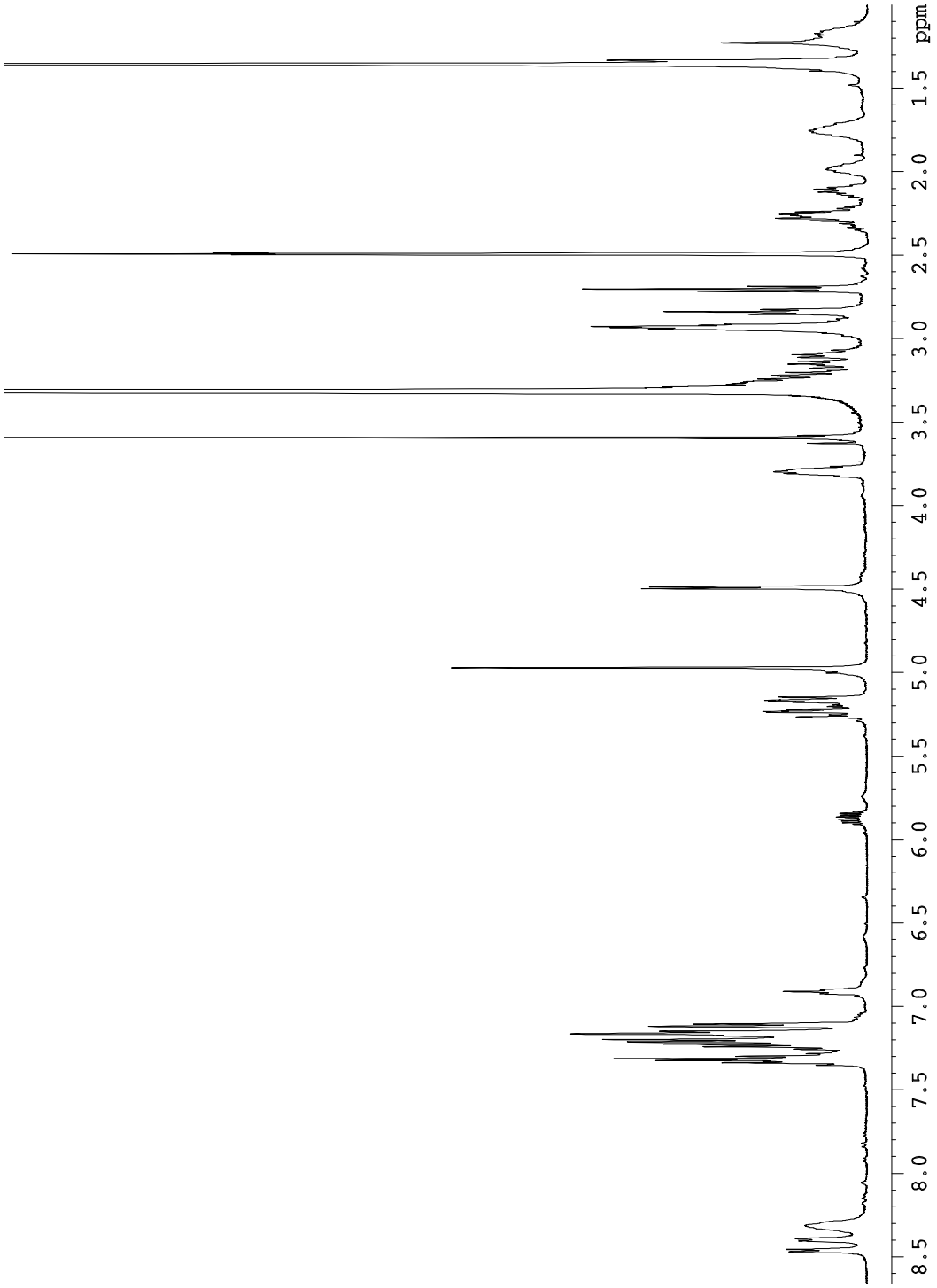
COSY spectrum of compound 15 (500 MHz, $CDCl_3$, 300K, 1 mM).



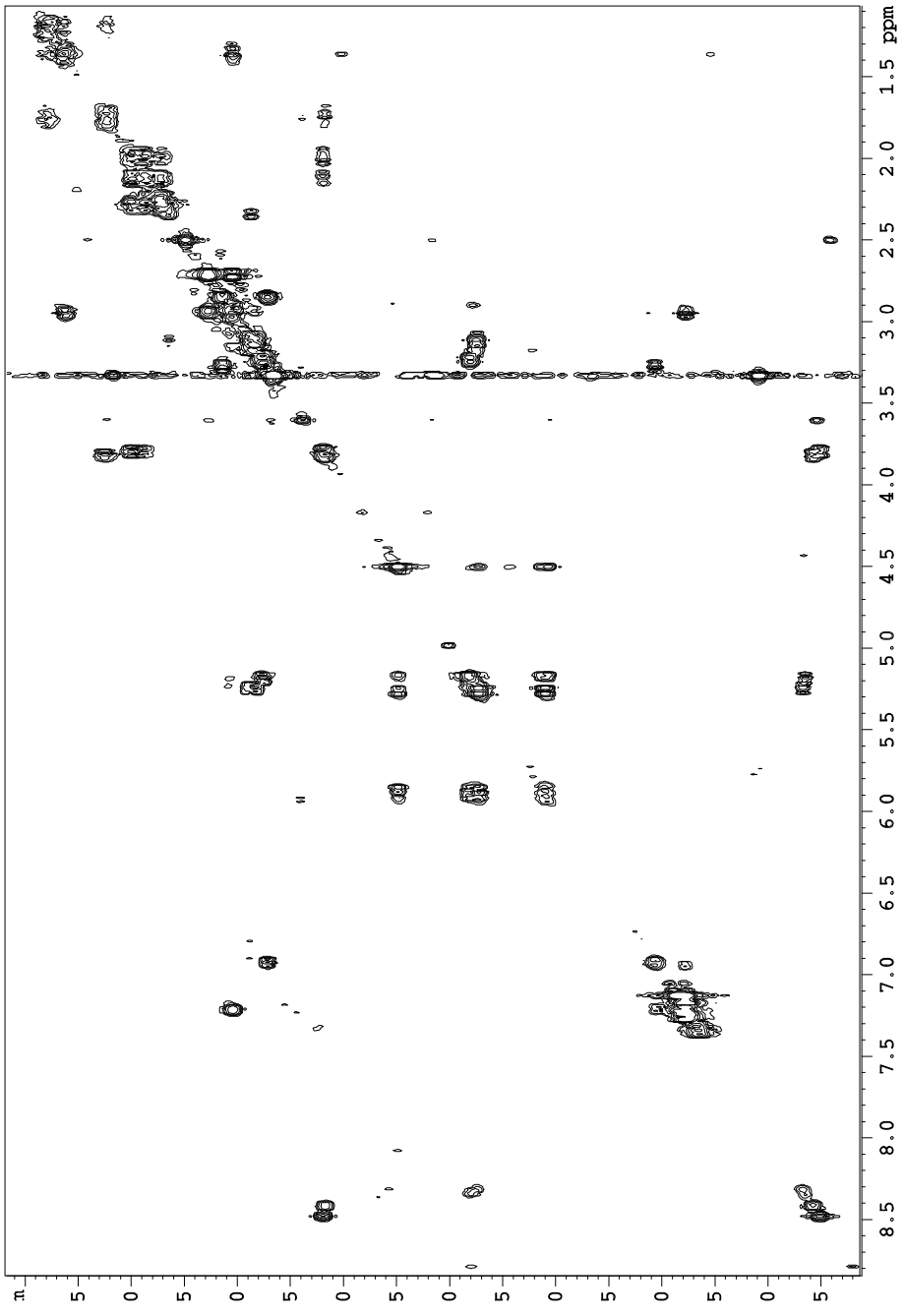
ROESY spectrum of compound 15 (500 MHz, $CDCl_3$, 300K, 1 mM).



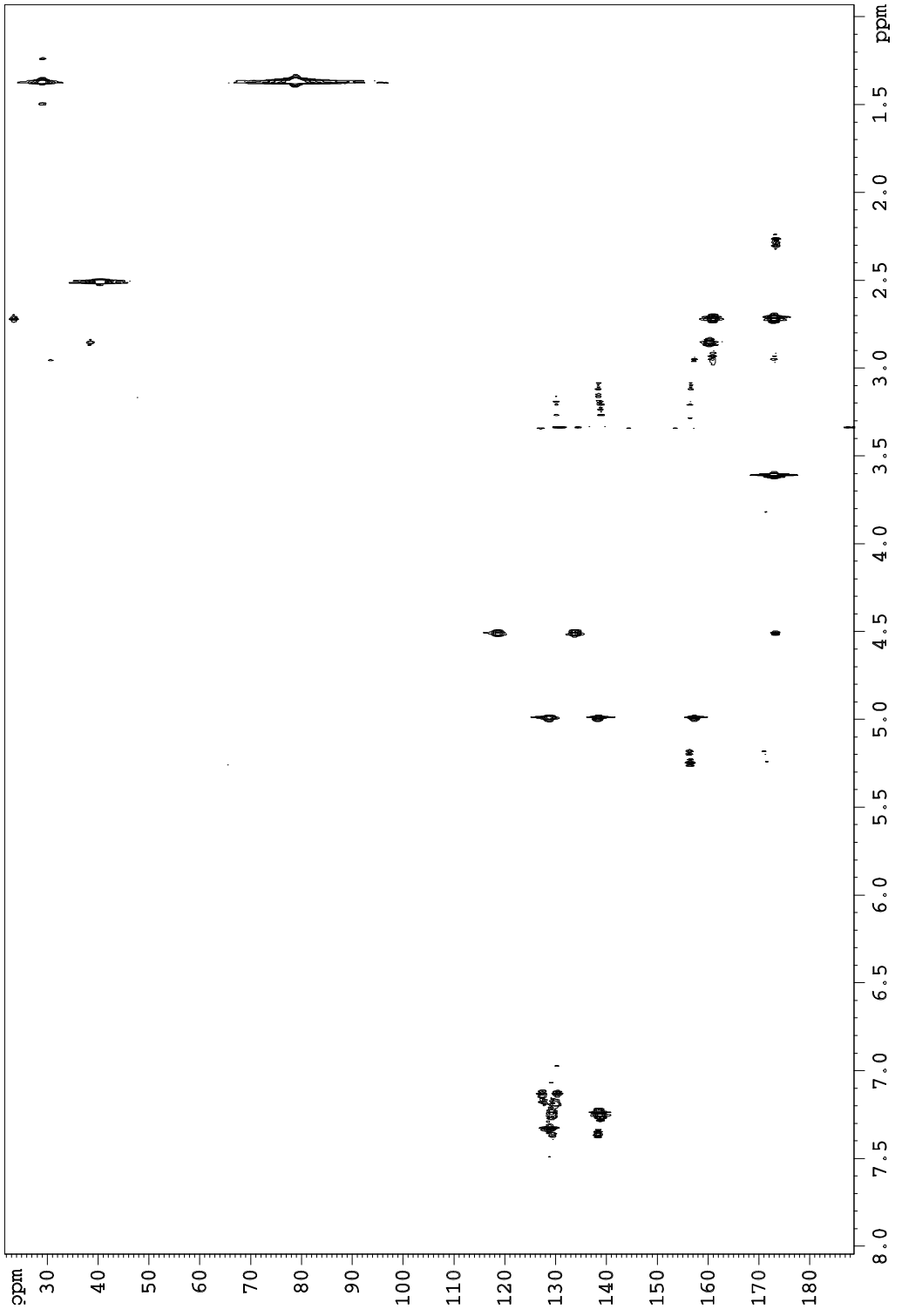
^{1}H spectrum of compound 17 (500 MHz, DMSO-d$_{6}$, 300K, 1 mM)



COSY spectrum of compound 17 (500 MHz, DMSO-d_6, 300K, 1 mM).



HMBC spectrum of compound 17 (500 MHz, DMSO-d_6, 300K, 1 mM).



ROESY spectrum of compound 17 (500 MHz, DMSO-d_6, 300K, 1 mM).