Electronic Supplementary Material (ESI) for Metallomics.

Structure-Function Studies of Acinetobactin Analogs

Supporting Information

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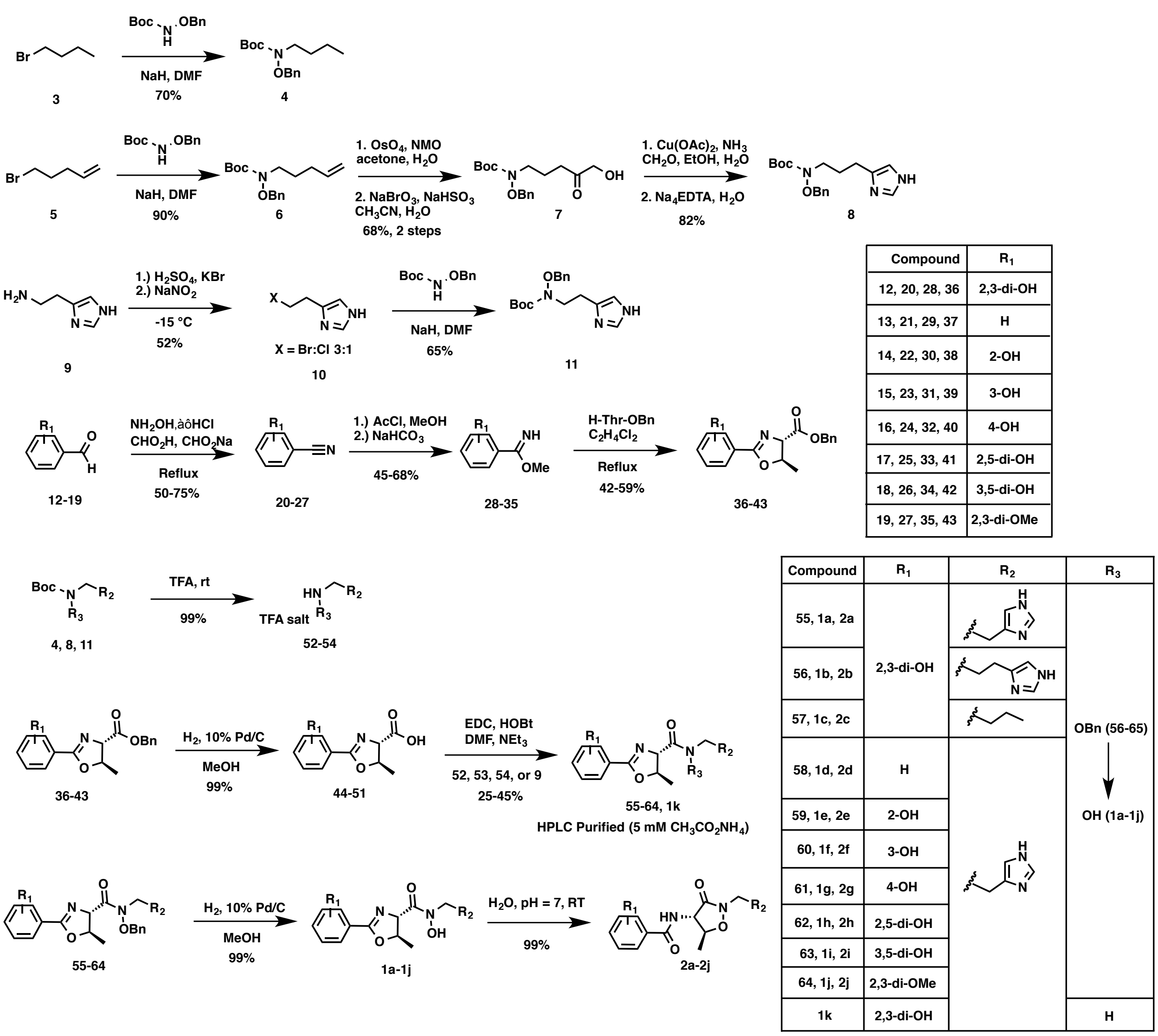
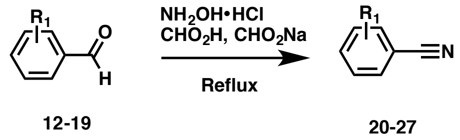
I. Procedures for Compound Synthesis



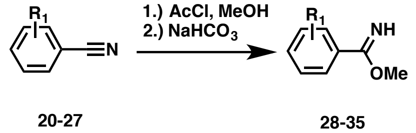
Compound	R_1
12, 20, 28, 36	2,3-di-OH
13, 21, 29, 37	H
14, 22, 30, 38	2-OH
15, 23, 31, 39	3-OH
16, 24, 32, 40	4-OH
17, 25, 33, 41	2,5-di-OH
18, 26, 34, 42	3,5-di-OH
19, 27, 35, 43	2,3-di-OMe

Compound	R_1	R_2	R_3
55, 1a, 2a	2,3-di-OH		OBn (56-65) ↓ OH (1a-1j)
56, 1b, 2b			
57, 1c, 2c			
58, 1d, 2d	H		
59, 1e, 2e	2-OH		
60, 1f, 2f	3-OH		
61, 1g, 2g	4-OH		
62, 1h, 2h	2,5-di-OH		
63, 1i, 2i	3,5-di-OH		
64, 1j, 2j	2,3-di-OMe		
1k	2,3-di-OH		H

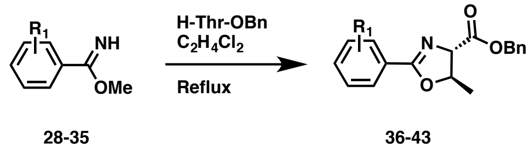
Scheme 1. Synthesis of pre-acinetobactin analogs **1a** – **1k** and acinetobactin analogs **2a** – **2j**.



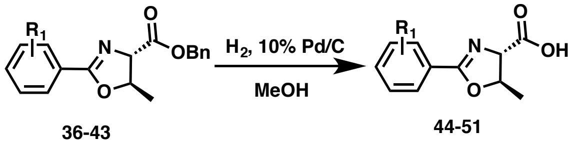
General Procedure A. Nitriles **20** – **27** were synthesized by following a literature protocol.[1] Briefly, benzaldehydes **12** – **19** were refluxed and stirred for 5 hrs in formic acid with 1.3 equivalents of hydroxylamine hydrochloride and 1.3 equivalents of sodium formate. The reaction mixture was diluted with ice water, neutralized with a saturated aqueous solution of sodium bicarbonate, extracted with Et_2O, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation under reduced pressure. Nitriles **20** – **27** were obtained in 50 – 75% yield and used without purification or characterization.



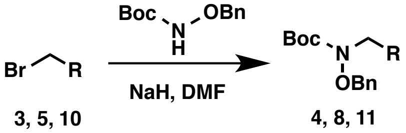
General Procedure B. Imidatess **28** – **35** were synthesized following a literature protocol.[1] Briefly, nitriles **20** – **27** were dissolved in approximately 48 equivalents of freshly distilled MeOH in a round bottom flask fit with a rubber septum under positive pressure from a balloon of dry argon. Acetyl chloride (32 equivalents) was added dropwise via syringe causing heat and the evolution of gas into the balloon. After stirring for 48 hrs the reaction mixture was cooled in an ice bath and quenched by addition of a saturated aqueous solution of sodium bicarbonate. The aqueous mixture was extracted with Et_2O and the organic layer was washed with water and brine, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation under reduced pressure. Imidates **28** – **35** were obtained in 45 – 68% yield and used without purification or characterization.



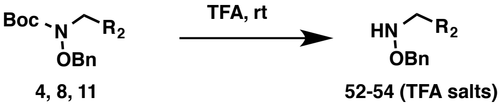
General Procedure C. Oxazoline benzyl esters **36** – **43** were synthesized following a literature protocol.[1] Briefly, imidates **28** – **35** were refluxed overnight with 1 equivalent of *O*-benzyl-L-threonine oxalate salt in 1,2-dichloroethane. The reaction mixture was allowed to cool and was concentrated by rotary evaporation under reduced pressure. The concentrated mixture was dissolved into 5% aqueous citric acid and extracted with EtOAc. The organic layer was washed with water and brine and then concentrated by rotary evaporation under reduced pressure. Oxazoline benzyl esters **36** – **43** were obtained in 42 – 59% yield, characterized by confirmed by 1H NMR, and used without purification.



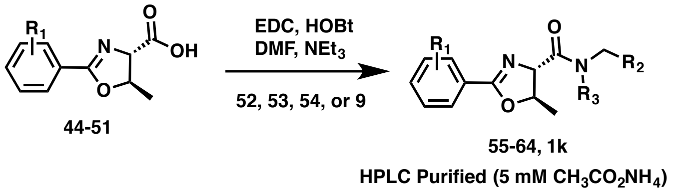
General Procedure D. Oxazoline carboxylic acids **44** – **51** were synthesized using a literature protocol.[1] Briefly, oxazoline benzyl esters **36** – **43** were dissolved in MeOH and approximately 10 wt. % of 10% palladium/carbon was added under argon. The reaction flask was flushed with hydrogen gas and left to stir for 2 hrs under positive pressure from a hydrogen balloon. The flask was flushed with argon and the reaction mixture was filtered and concentrated by rotary evaporation under reduced pressure. Oxazoline carboxylic acids **44** – **51** were obtained in quantitative mass yield and used without purification or characterization.



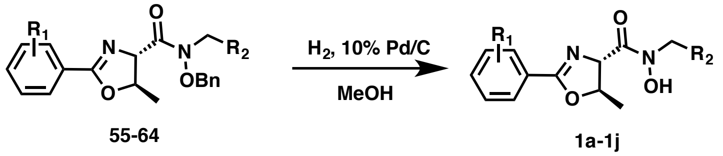
General Procedure E. *N*-Boc-*O*-Benzylhydroxylamines **4**, **8**, and **11** were prepared via S_N2 reaction of *N*-Boc-*O*-benzylhydroxylamin with alkyl halides **3**, **5**, and **10**, respectively, following a literature protocol.[1] Briefly, *N*-Boc-*O*-Benzylhydroxylamine was stirred in anhydrous DMF at 0 °C and 3 equivalents of sodium hydride (60% in oil) was added as a solid. The reaction was warmed to room temperature and stirred for 30 min under dry argon. After 30 min, 1 equivalent of alkyl bromide **3**, **5**, or **10** was added dropwise, causing bubbling and the evolution of heat. The mixture was stirred for 2 hours under dry argon and then quenched by slow addition of ddH$_2$O. The mixture was extracted with 3 portions of EtOAc and the organic layer was washed with brine, dried over anhydrous MgSO$_4$, filtered and concentrated by rotary evaporation under reduced pressure. *N*-Boc-*O*-Benzylhydroxylamines **4**, **8**, and **11** were used without purification or characterization.



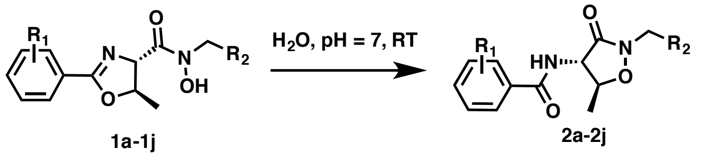
General Procedure F. The *N*-Boc was removed from *N*-Boc-*O*-benzylhydroxylamines **4**, **8**, and **11** following a literature protocol.[1] Briefly, *N*-Boc-*O*-benzylhydroxylamines **4**, **8**, and **11** were dissolved in neat TFA and allowed to react for 1 hr. TFA was removed via rotary evaporation under reduced pressure to give the TFA salts of *O*-benzylhydroxylamines **52** – **54** as confirmed by LC-MS in quantitative yield. Compounds **52** – **54** were used without purification.



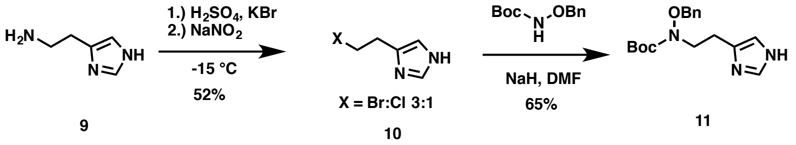
General Procedure G. Oxazoline carboxylic acids **44** – **51** were coupled via amide bond formation with amines **52**, **53**, **54**, or **9** following a literature protocol.[1,2] Briefly, one equivalent of the oxazoline carboxylic acid **44** – **51** was added to one equivalent of amine **52**, **53**, **54**, or **9** dissolved in anhydrous DMF. Four equivalents of EDC•HCl and four equivalents of HOBt•H_2O were added and the reaction mixture was brought to pH = 9 by the dropwise addition of Et_3N. The mixture was sealed under argon and stirred overnight at room temperature. The reaction mixture was then extracted with 2 x 25 mL portions of EtOAc and the organic layer was concentrated by rotary evaporation under reduced pressure. The crude residue was purified by preparatory HPLC with a gradient of MeCN/H_2O buffered to pH 4.8 with 5 mM ammonium acetate to give oxazoline amides **55** – **64** in 25 – 45% yield. Compounds **55** – **64** were analyzed by LC-MS and taken onto the final benzyl deprotection step. Compound **1k** was analyzed by LC-MS and characterized by 2D-NMR (**Supplementary Table 20**; **Supplementary Fig. 76 – 79**).



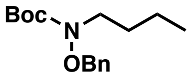
General Procedure H. Pre-acinetobactin analogs **1a** – **1j** were obtained via hydrogenation of oxazoline amides **55** – **64** following a literature protocol.[2] Briefly, oxazoline amides **55** – **64** were dissolved in MeOH and approximately 10 wt. % of 10% palladium/carbon was added under argon. The reaction flask was purged with hydrogen gas and the mixture was left stirring under positive pressure from a hydrogen balloon for 2 hours. The mixture was filtered and concentrated under reduced pressure using rotary evaporation. Analogs **1a** – **1j** were obtained in quantitative yield were characterized by 2D-NMR (**Supplementary Table 2,4,6,8,10,12,14,16,18**; **Supplementary Fig. 4–7,12–15,20–23,28–31,36–39,44–47,52–55,60–63,68–71**).



General Procedure I. Acinetobactin analogs **2a** – **2j** were synthesized following a literature protocol.[2] Pre-acinetobactin analogs **1a** – **1j** were dissolved in phosphate buffered 10% D_2O/H_2O at pH 7 for 1H NMR kinetic studies. Pre-acinetobactin analogs **1a** – **1j** were stirred overnight in pH 7 phosphate buffered ddH_2O to give quantitative conversion to the corresponding acinetobactin analogs **2a** – **2j** for evaluation in CAS assays and *A. baumannii* growth assays. Solutions of acinetobactin analogs **2a** – **2j** were concentrated by rotary evaporation prior to characterization by 2D-NMR (**Supplementary Table 3,5,7,9,11,13,15,17,19**; **Supplementary Fig. 8–11,16–19,24–27,32–35,40–43,48–51,56–59,64–67,72–75**).

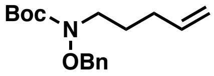


Compound 11 was synthesized and characterized as described previously by our group.[2]



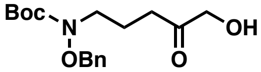
4

Compound 4 was synthesized from starting material **3** using general procedure **E**. The product was obtained in 70% yield with no need for purification. 1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.35 (m, 5 H), 4.81 (s, 2 H), 3.40 (t, *J* = 7.1 Hz, 2 H), 1.59 (m, 2 H), 1.50 (s, 9 H), 1.35 (m, 2 H), 0.89 (t, *J* = 7.5 Hz, 3 H).



6

Compound 6 was synthesized from starting material **5** by general procedure **E**. Compound was purified by silica gel column using 10% EtoAc in hexanes. Product was obtained in 90% yield. 1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.40 – 7.33 (m, 5 H), 4.80 (s, 2 H), 4.16 (s, 1 H), 3.49 - 3.40 (m, 2 H), 2.40 (t, *J* = 7.3 Hz, 2 H), 1.90 (dd, *J* = 5.9, 7.6 Hz, 2 H), 1.52 – 1.47 (m, 9 H).

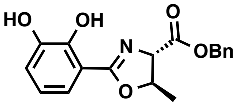


7

Compound 7 was synthesized following a literature protocol.[3] Briefly, one equivalent of compound **6** and one equivalent of *N*-methyl morpholine-*N*-oxide were dissolved in 1:1 acetone:H_2O mixture. A catalytic amount of OsO_4 was added at room temperature. The reaction mixture was stirred for 6 hrs and quenched with an aqueous solution of 0.2 M $NaHSO_3$. The mixture was extracted with 3 portions of EtOAc. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation under reduced pressure. The resulting oil was immediately dissolved in acetonitrile and treated with an aqueous solution of $NaBrO_3$ and stirred at room temperature. An aqueous solution of $NaHSO_3$ was added dropwise via syringe. After 5 hrs the reaction was quenched with an aqueous 0.2 M $NaHSO_3$ solution and the mixture was extracted with 3 portions of Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation under reduced pressure. Product **7** was afforded in 68% yield over 2 steps. 1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.40 – 7.33 (m, 5 H), 4.80 (s, 2 H), 4.16 (s, 1 H), 3.49 – 3.40 (m, 2 H), 2.40 (t, *J* = 7.3 Hz, 2 H), 1.90 (dd, *J* = 5.9, 7.6 Hz, 2 H), 1.52 – 1.47 (m, 9 H).

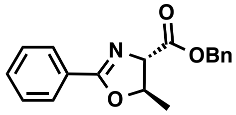
8

Compound 8 was synthesized following a literature protocol.[3] Briefly, one equivalent of compound **7** was dissolved in EtOH and diluted with half a volume of warm water. To this solution was added 2 equivalents of cupric acetate monohydrate, 1.2 volumes 28% ammonia water, and 0.2 volumes 37% formalin. The mixture was allowed stirred for 3 hrs at 75 °C and then concentrated by rotary evaporation under reduced pressure. The residue was dissolved/partitioned between EtOAc and an aqueous solution of tetrasodium EDTA. The bilayer was stirred vigorously overnight and the layers were separated. The organic layer was washed with 2 portions of aqueous tetrasodium EDTA solution and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation under reduced pressure. The product was obtained in 82% yield. 1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.53 (s, 1 H), 7.43 – 7.33 (m, 5 H), 6.78 (s, 1 H), 4.84 (s, 2 H), 3.52 (t, J = 6.4 Hz, 2 H), 2.60 (t, *J* = 6.7 Hz, 2 H), 1.93 – 1.80 (m, 2 H), 1.53 (s, 9 H).



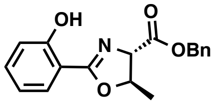
36

Compound 36 was synthesized and characterized as described previously by our group.[2]



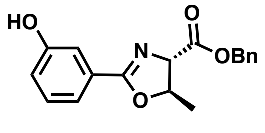
37

Compound 37 was synthesized by transforming compound **13** into compound **21** by general procedure **A**, subsequently transforming compound **21** into compound **29** by general procedure **B**, and finally transforming compound **29** into compound **37** by general procedure **C**. 1H NMR (300 MHz, DMSO-*d6*) δ (ppm) 7.80 (d, *J* = 7.9 Hz, 2 H), 7.58 – 7.54 (m, 1 H), 7.50 – 7.46 (m, 2 H), 7.40 – 7.32 (m, 5 H), 5.20 (s, 2 H), 4.95 – 4.90 (m, 1 H), 4.78 (d, *J* = 5.5 Hz, 1 H), 1.43 (d, *J* = 6.3 Hz, 3 H).



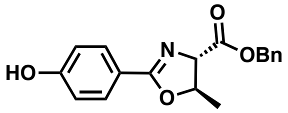
38

Compound 38 was synthesized by transforming compound **14** into compound **22** by general procedure **A**, subsequently transforming compound **22** into compound **30** by general procedure **B**, and finally transforming compound **30** into compound **38** by general procedure **C**. 1H NMR (300 MHz, DMSO-*d6*) δ (ppm) 7.63 (dd, *J* = 1.6, 7.9 Hz, 1 H), 7.48 (t, *J* = 8.3 Hz, 1 H), 7.42 – 7.33 (m, 5 H) 7.01 (d, *J* = 7.9 Hz, 1 H), 6.98 – 6.92 (m, 1 H), 5.20 (s, 2 H), 4.98 – 4.90 (m, 1 H), 4.73 (d, *J* = 5.5 Hz, 1 H), 1.45 (d, *J* = 6.3 Hz, 3 H).



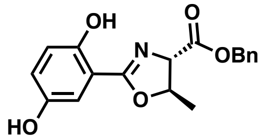
39

Compound 39 was synthesized by transforming compound **15** into compound **23** by general procedure **A**, subsequently transforming compound **23** into compound **31** by general procedure **B**, and finally transforming compound **31** into compound **39** by general procedure **C**. 1H NMR (300 MHz, DMSO-*d*6) δ (ppm) 7.41 – 7.33 (m, 5 H), 7.29 – 7.25 (m, 2 H), 7.22 (s, 1 H), 6.88 – 6.82 (m, 1 H), 5.20 (s, 1 H), 4.92 – 4.84 (m, 1 H), 4.75 (d, *J* = 6.3 Hz, 1 H), 1.40 (d, *J* = 6.3 Hz, 3 H).



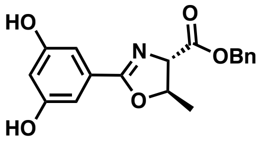
40

Compound 40 was synthesized by transforming compound **16** into compound **24** by general procedure **A**, subsequently transforming compound **24** into compound **32** by general procedure **B**, and finally transforming compound **32** into compound **40** by general procedure **C**. 1H NMR (300 MHz, DMSO-*d*6) δ (ppm) 7.72 (d, *J* = 8.7 Hz, 2 H), 7.37 – 7.29 (m, 5 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 5.20 (s, 1 H), 4.82 (m, 1 H), 4.65 (d, *J* = 6.3 Hz, 1 H), 1.34 (d, *J* = 6.3 Hz, 3 H).



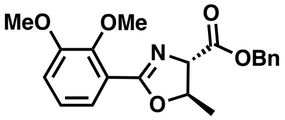
41

Compound 41 was synthesized by transforming compound **17** into compound **25** by general procedure **A**, subsequently transforming compound **25** into compound **33** by general procedure **B**, and finally transforming compound **33** into compound **41** by general procedure **C**. 1H NMR (300 MHz, DMSO-*d*6) δ (ppm) 7.40 – 7.32 (m, 5 H), 7.01 (d, *J* = 3.1 Hz, 1 H), 6.82 (d, *J* = 3.1 Hz, 1 H), 6.84 - 6.82 (s, 1 H), 5.20 (s, 1 H), 4.92 (m, 1 H), 4.74 (d, *J* = 5.5 Hz, 1 H), 1.46 (d, *J* = 6.3 Hz, 3 H).



42

Compound 42 was synthesized by transforming compound **18** into compound **26** by general procedure **A**, subsequently transforming compound **26** into compound **34** by general procedure **B**, and finally transforming compound **34** into compound **42** by general procedure **C**. 1H NMR (300 MHz, DMSO-*d*6) δ (ppm) 7.38 – 7.29 (m, 5 H), 6.73 (d, *J* = 1.6 Hz, 2 H), 6.38 - 6.30 (m, 1 H), 5.18 (s, 1 H), 4.92 – 4.88 (m, 1 H), 4.79 – 4.68 (m, 1 H), 1.41 (d, *J* = 6.3 Hz, 3 H).

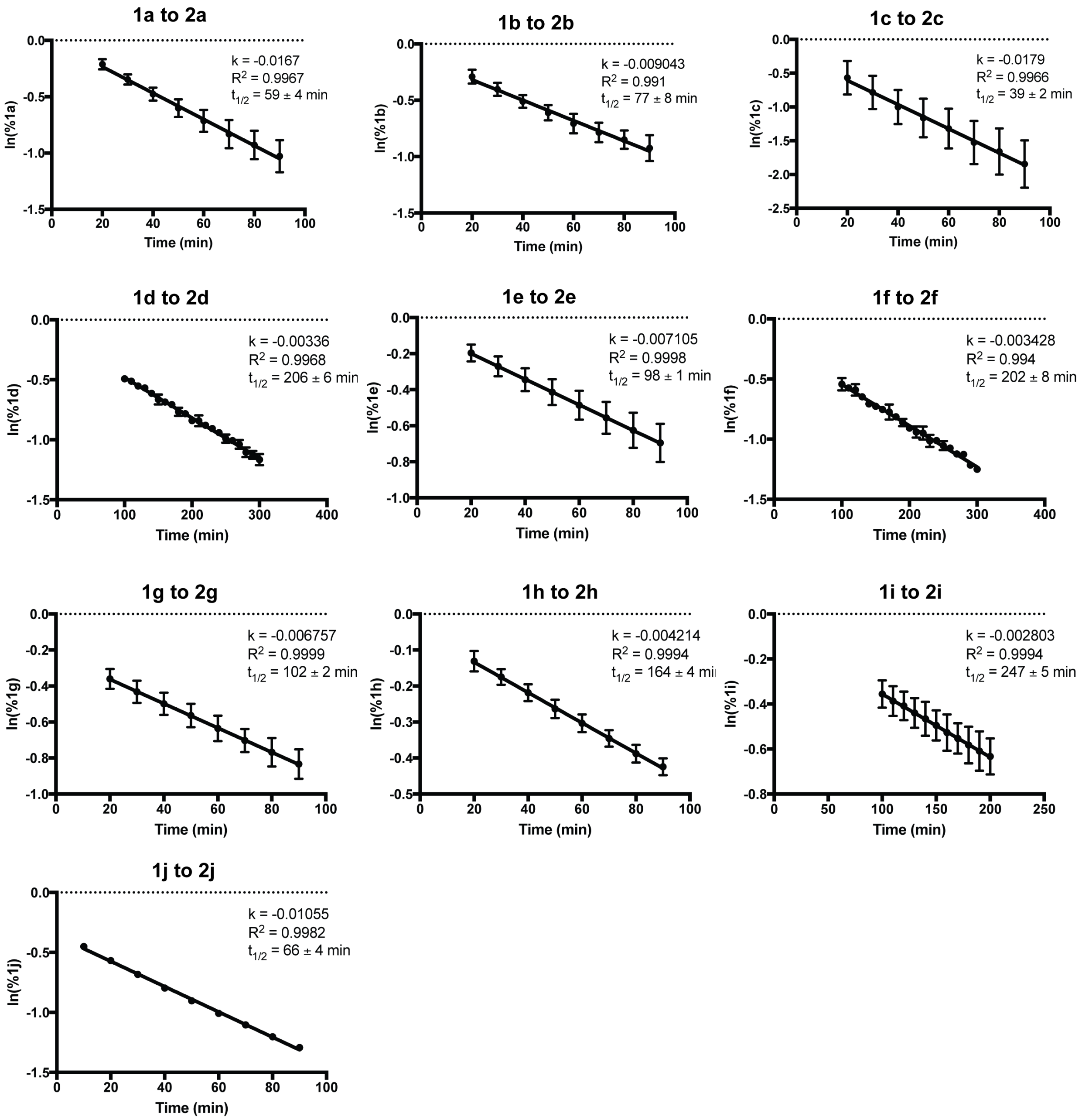


43

Compound 43 was synthesized by transforming compound **19** into compound **27** by general procedure **A**, subsequently transforming compound **27** into compound **35** by general procedure **B**, and finally transforming compound **35** into compound **43** by general procedure **C**. 1H NMR (300 MHz, DMSO-*d*6) δ (ppm) 7.21 – 7.19 (m, 1 H), 7.18 (br. s., 1 H), 7.13 (d, *J* = 7.9 Hz, 1 H), 5.20 (s, 1 H), 4.82 (m, 1 H), 4.74 (d, *J* = 5.5 Hz, 1 H), 3.84 (s, 3 H), 3.75 (s, 3 H), 1.38 (d, *J* = 5.5 Hz, 3 H).

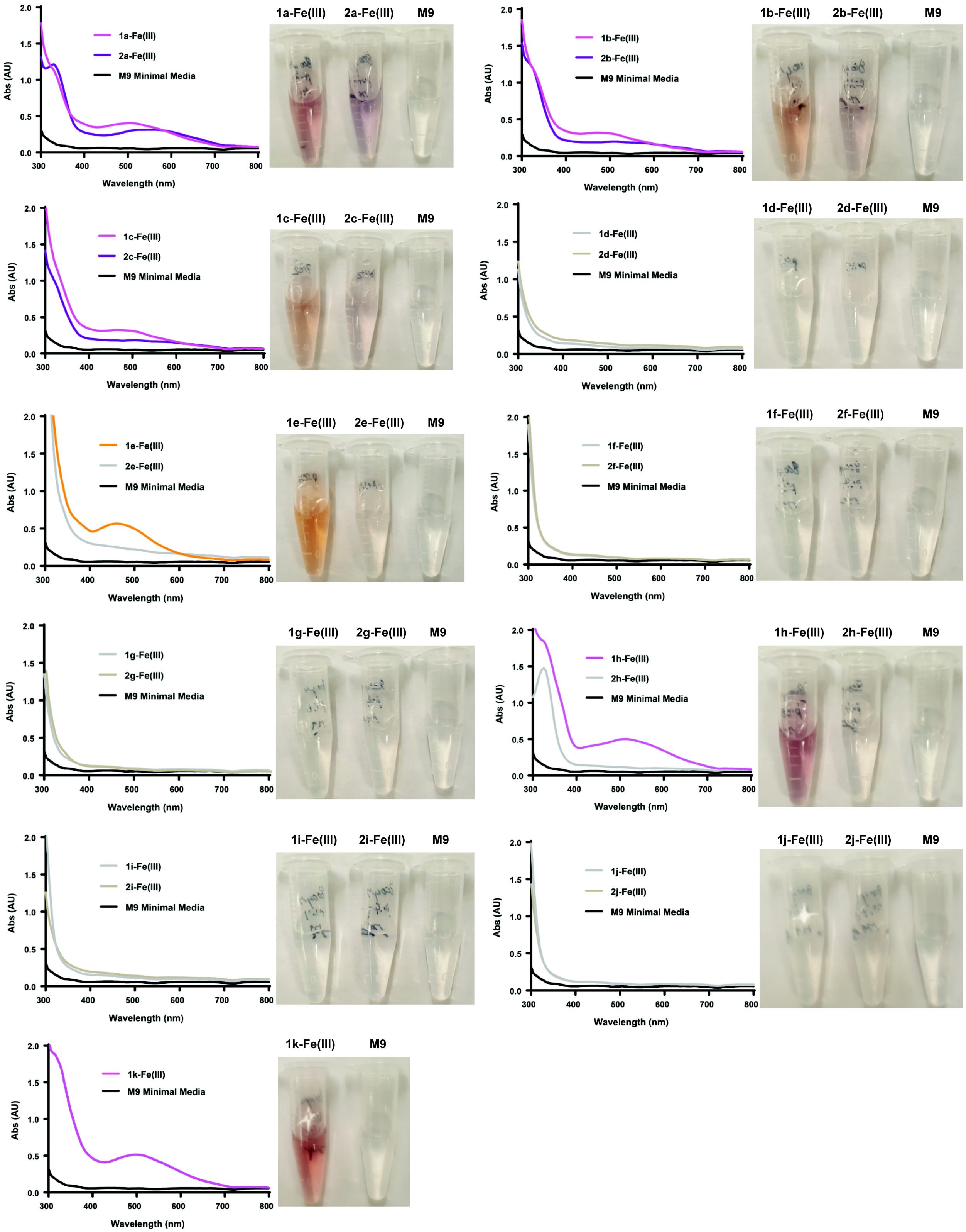
II. First-Order Rate Plots

Isomerization half-lives ($t_{1/2}$) were determined for compounds **1a – 1j** using kinetic ^{1}H NMR. One milligram of pre-acinetobactin analogs **1a** – **1j** was isolated and dissolved in 0.6 mL of 0.1 M phosphate buffered 10% D_2O/H_2O (pH = 7). The solution was immediately transferred into an NMR tube and spectra (average of 32 scans) were taken once every 10 min on a 500 MHz NMR at 27 °C. Integration values for the resonance signal corresponding to the methyl group of the pre-acinetobactin compounds **1a** – **1j** and corresponding acinetobaction products **2a** – **2j** were recorded. The ratio of integration values for the pre-acinetobactin methyl peak over the combined integration values of the pre-acinetobactin and acinetobactin peaks was calculated. The natural log of this ratio was also plotted against time to give a straight line. The slope of this line was taken as the first-order isomerization rate constant, which was used to calculate a $t_{1/2}$ values as an average of 3 independent trials. Time windows for data collection used to calculate $t_{1/2}$ values were chosen to minimize baseline noise. Error bars represent standard deviation. For data points where error bars would be smaller than the symbol, error bars were omitted.



Supplementary Figure 1. First-order rate plots for the isomerization of pre-acinetobactin analogs **1a** – **1j** to acinetobactin analogs **2a** – **2j**.

III. Optical Absorbance Spectra of Analog-Fe Complexes in M9 Media at pH 7



Supplementary Figure 2. Optical absorbance spectra for 2:1 mixtures of pre-acinetobactin analogs **1a** – **1k** and acinetobactin analogs **2a** – **2j** with Fe(acac)$_3$ in M9 media at pH 7.

IV. P-Values for Growth Promotion Assay

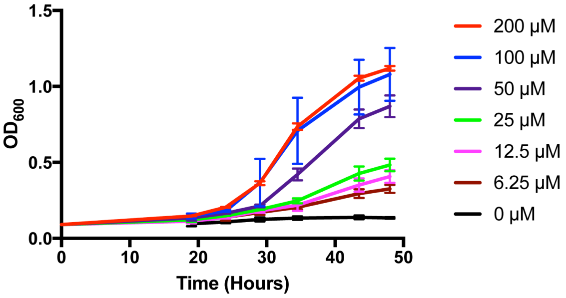
Each acinetobactin analog was dissolved in DMSO to 0.016 M, diluted in M9 minimal media to 800 µM (50 µL DMSO stock into 950 µL media) and treated with 1 µL Fe(acac)$_3$ stock solution (0.1 M in methanol). This analog-Fe solution was then serially diluted in a growth promotion assay with *A. baumnnii* ATCC 19606 s1 mutant. To determine whether an analog was truly acting as a siderophore or if *A. baumannii* s1 was growing simply due to higher concentration of iron in solution, an Fe(acac)$_3$ control for each concentration of analog was run by diluting pure DMSO into media and adding 1 µL of Fe(acac)$_3$ stock. This control was serially diluted in the same manner as the analog solutions. *A. baumannii* s1 growth is depicted in **Figure 5** as a percentage of the basal growth at the corresponding concentration of Fe(acac)$_3$ after 43.5 hrs at 37 °C. All data collected for 200 µM siderophore analog is compared to a 200 µM Fe(acac)$_3$ control, all data collected for 100 µM siderophore analog is compared to a 100 µM Fe(acac)$_3$ control, etc. P-values of analogs at each concentration as compared to their corresponding controls are listed below in **Supplementary Table 1**. P-values indicating that the difference between analog and control was not statistically significant are marked with an asterisk (*).

Supplementary Table 1: P-values for *A. baumannii* growth promotion bar graph in **Figure 5**.

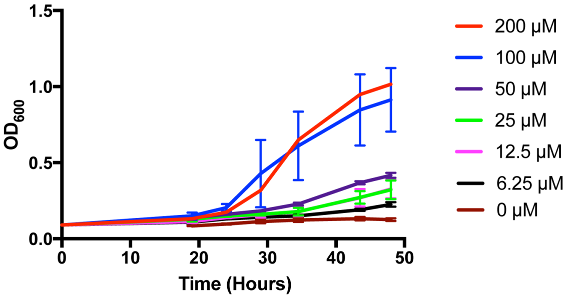
	200 µM	**100 µM**	**50 µM**	**25 µM**		**200 µM**	**100 µM**	**50 µM**	**25 µM**
1a	0.0002	0.0037	0.0006	0.0203	**1f**	0.0002	<0.0001	0.0529*	0.0238
2a	0.0007	0.0211	0.1199*	0.9525*	**2f**	0.0007	0.0003	0.0447	0.0424
1b	0.0002	<0.0001	0.0014	0.1432*	**1g**	<0.0001	<0.0001	0.0299	0.0320
2b	0.0032	0.0418	0.3534*	0.5951*	**2g**	0.0001	<0.0001	0.0122	0.0434
1c	0.001	<0.0001	0.0811*	0.8905*	**1h**	0.0005	0.0072	0.0007	0.0391
2c	0.0077	0.0159	0.8942*	0.4231*	**2h**	<0.0001	0.0003	0.0181	0.0227
1d	0.0001	<0.0001	0.0158	0.0279	**1i**	0.0004	0.0008	0.0334	0.0533*
2d	0.0002	0.0018	0.0205	0.0215	**2i**	0.0004	0.0037	0.0453	0.0843*
1e	0.0004	<0.0001	0.0005	0.0075	**1j**	0.0001	<0.0001	0.0213	0.0241
2e	0.0027	0.1696*	0.9956*	0.6180*	**2j**	0.0003	<0.0001	0.0186	0.0782*
					1k	0.0007	0.0015	0.0221	0.1402*

V. Growth Curves for *A. baumannii* ATCC 19606-s1 Supplemented with Analogs

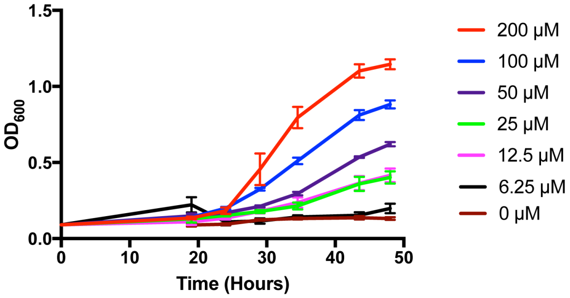
1a



2a



1b



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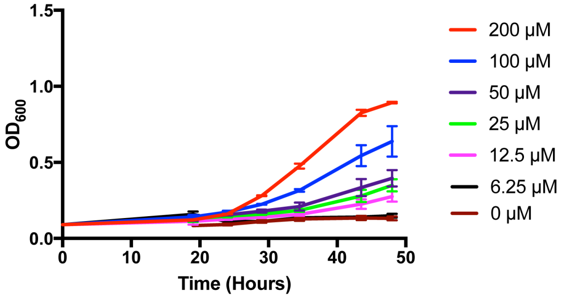
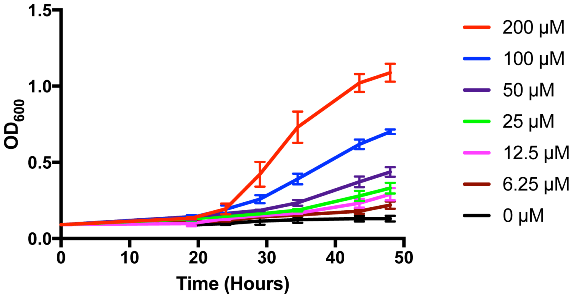
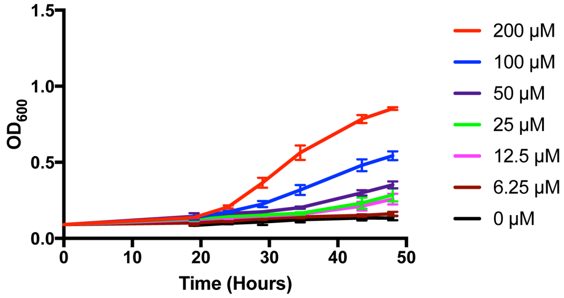


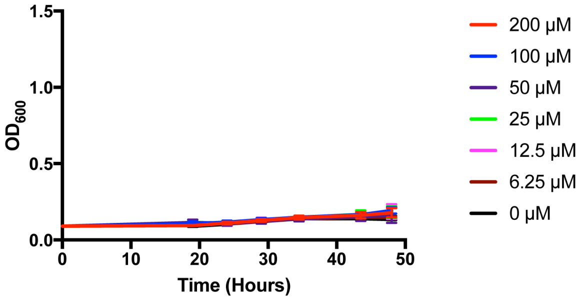
1c



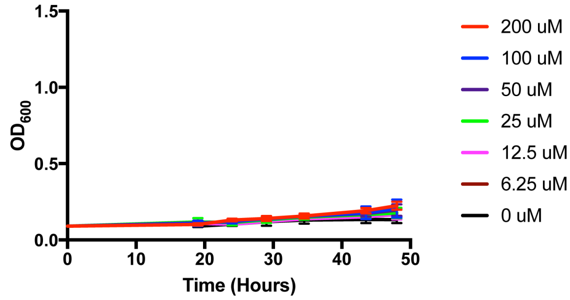
2c



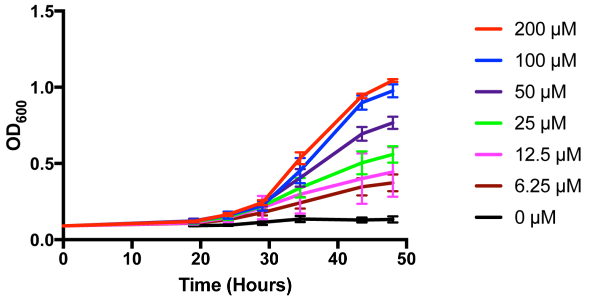
1d



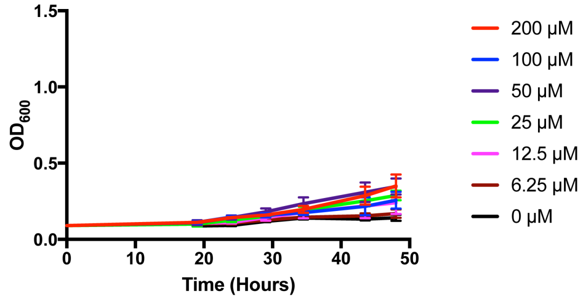
2d



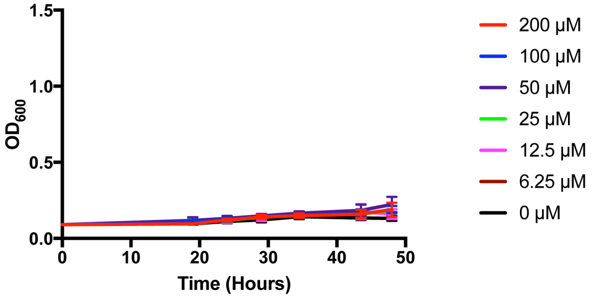
1e



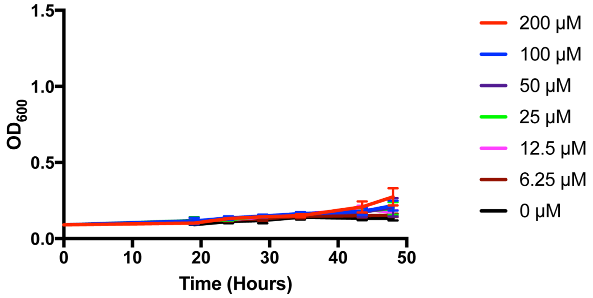
2e



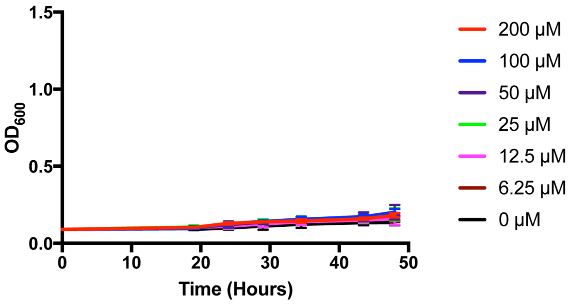
1f



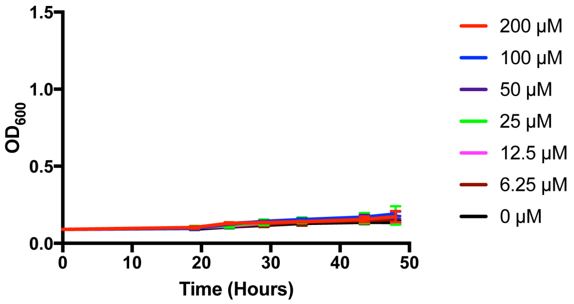
2f



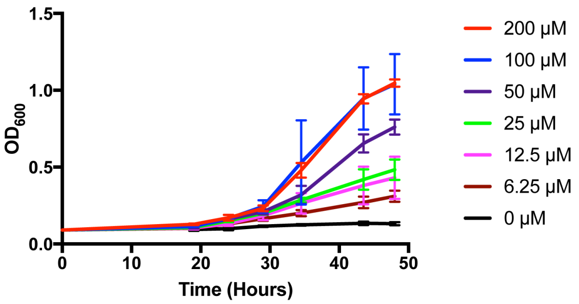
1g



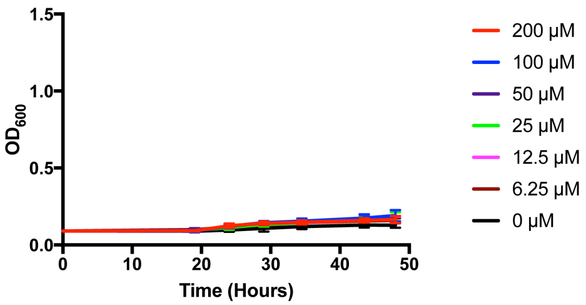
2g

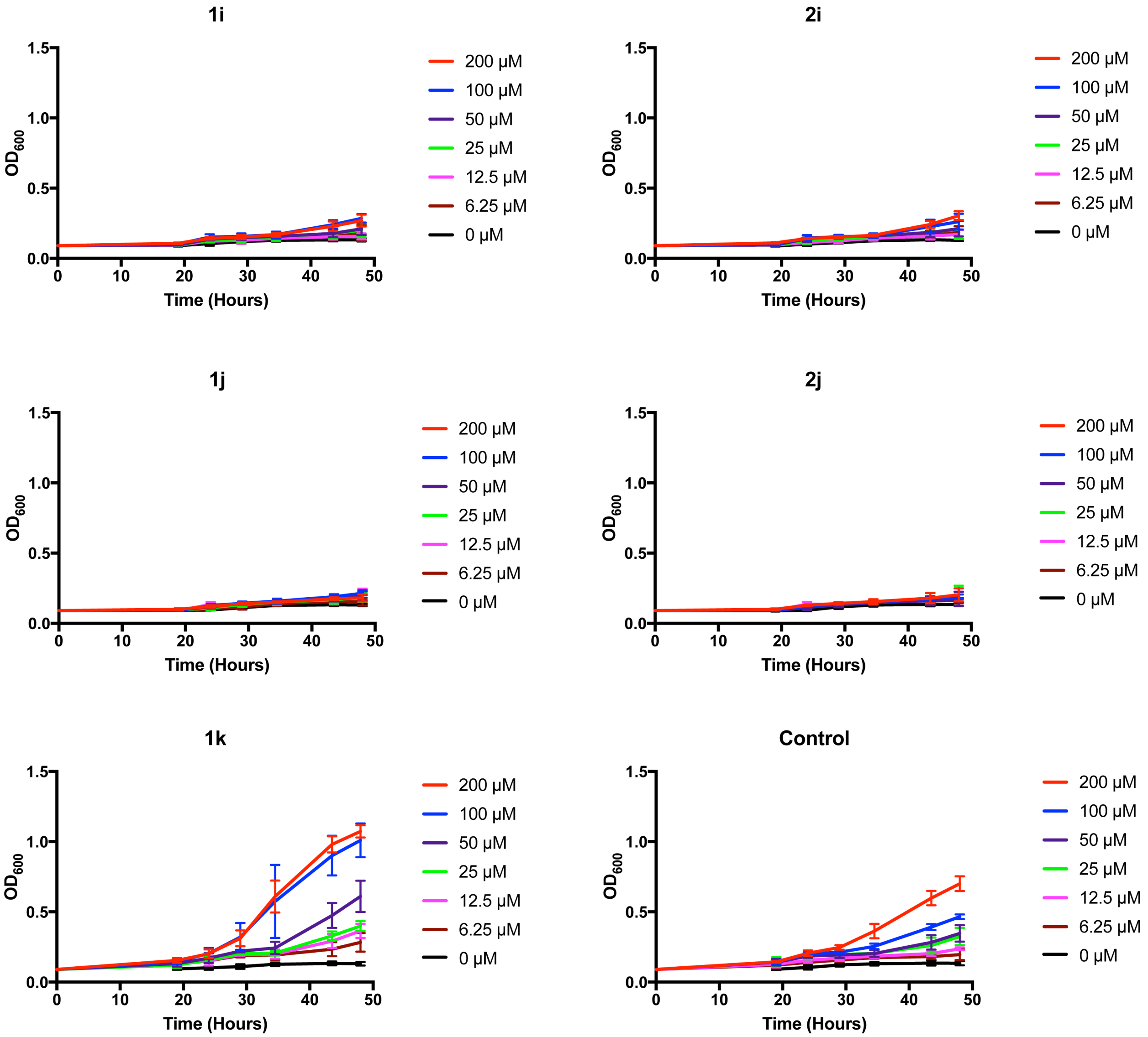


1h



2h

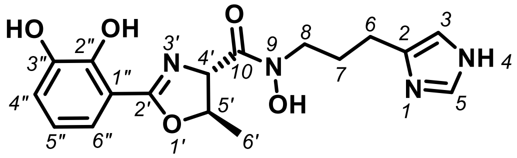




Supplementary Figure 3. Growth of *A. baumannii* ATCC 19606 s1 in pH 7 M9 minimal media supplemented with 150 µM 2,2'-dipyridyl as measured by OD$_{600}$ from 0 to 48 hours at 37 °C. Each analog was dissolved to 0.016 M in DMSO, diluted to 800 µM in M9 media (50 µL DMSO stock into 950 µL media), and treated with 1 µL of 0.1 M Fe(acac)$_3$ in MeOH. The M9 media stock solution of Fe(acac)$_3$/analog was serially diluted in 96-well plates and inoculated with bacteria. The control M9 solution was prepared as above using pure DMSO.

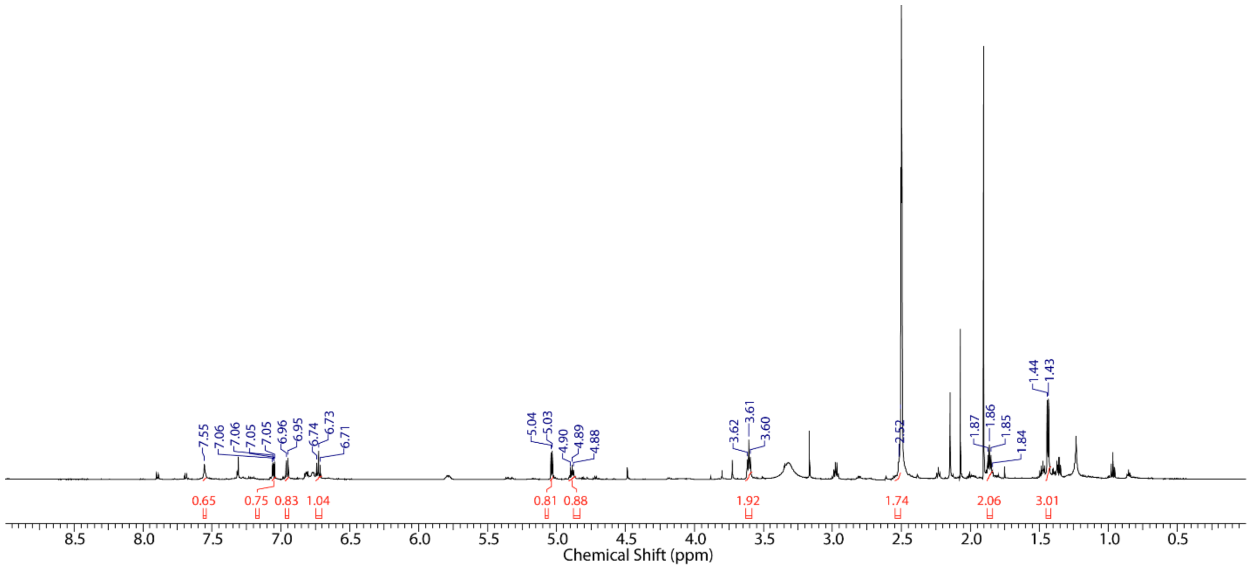
VI. NMR and HRMS Data for Pure Compounds

Supplementary Table 2. NMR characterization data of compound **1b** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{17}H_{21}N_5O_4]^+$ ($[M+H]^+$) calculated: 361.1506, found: 361.1498.

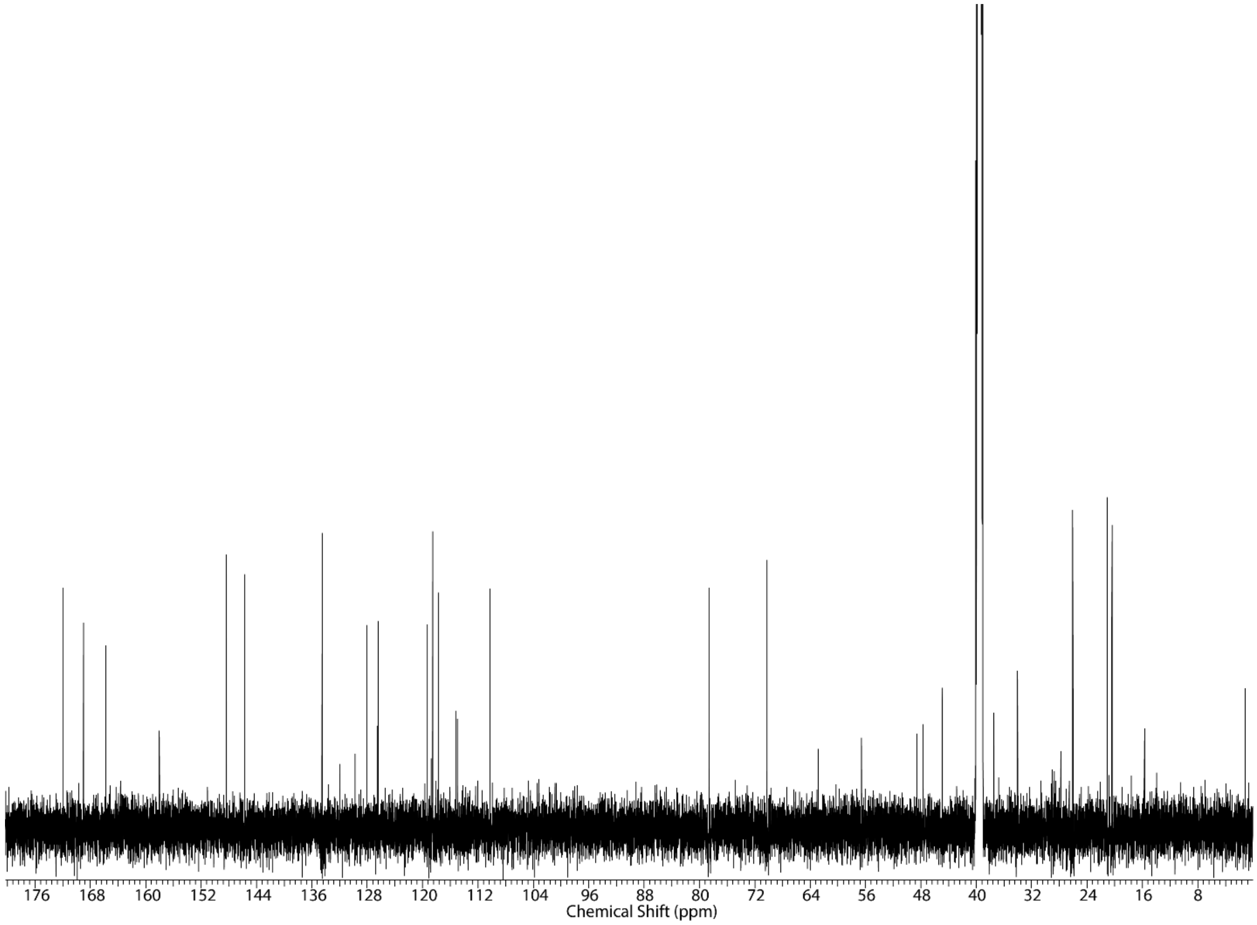


Compound **1b**

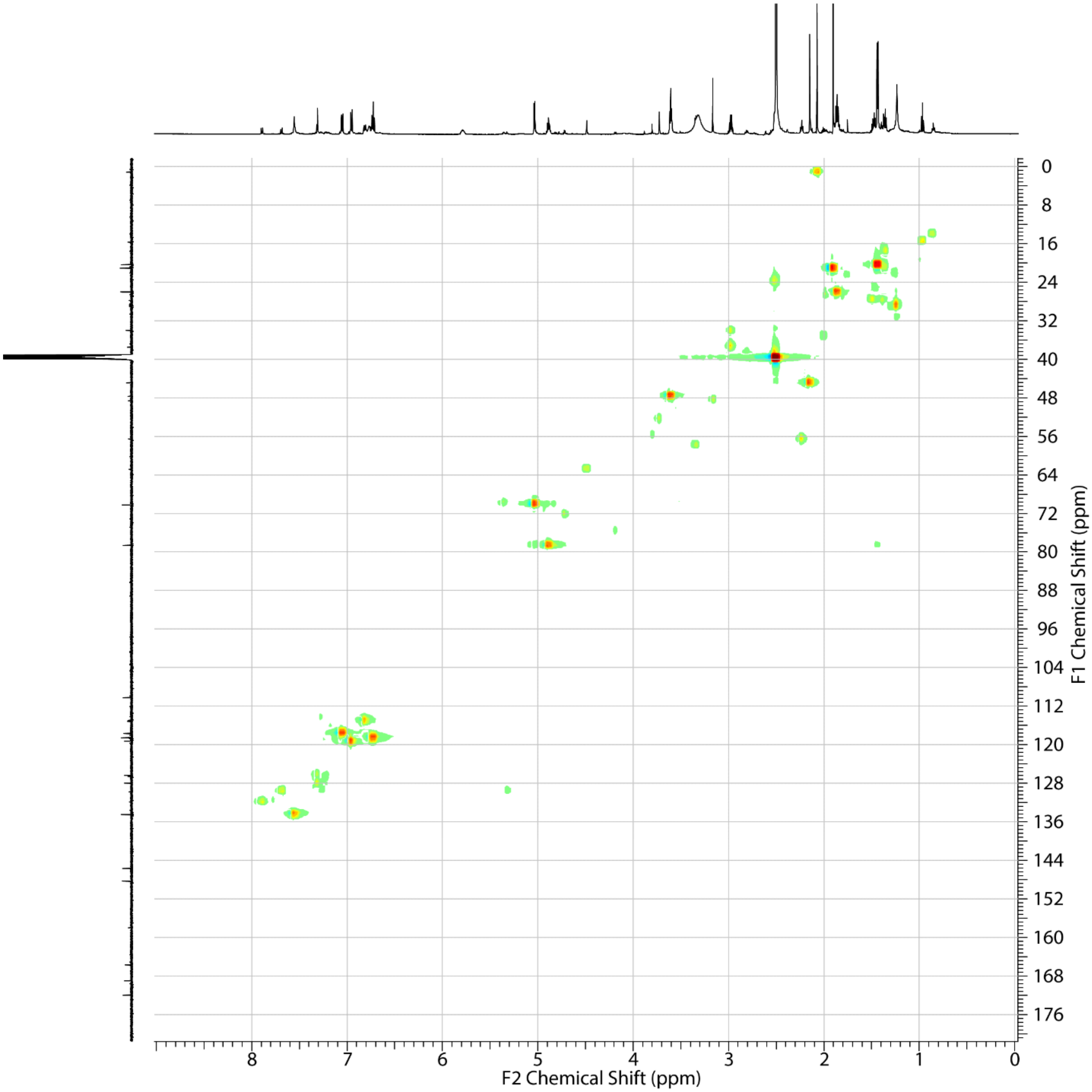
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H–^{13}C 2–3 bond
3 or 5	134.5	7.55 (br. s., 1 H)	
6	23.3	2.52 (m, 2 H)	7, 8
7	26.0	1.88 – 1.84 (m, 2 H)	6, 8
8	47.6	3.61 (t, *J* = 6.7 Hz, 2 H)	6, 7
2’	165.6		4’, 6”
4’	70.2	5.04 (d, *J* = 5.5 Hz, 1 H)	2’, 5’, 6’
5’	78.6	4.89 (t, *J* = 6.3 Hz, 1 H)	4’, 6’
6’	20.4	1.44 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	148.3		4”, 6”
4”	119.2	6.95 (dd, *J* = 1.6, 7.9 Hz, 1 H)	2”, 6”
5”	118.5	6.73 (t, *J* = 7.9 Hz, 1 H)	
6”	117.6	7.05 (dd, *J* = 1.6, 7.9 Hz, 1 H)	2’, 2”, 4”



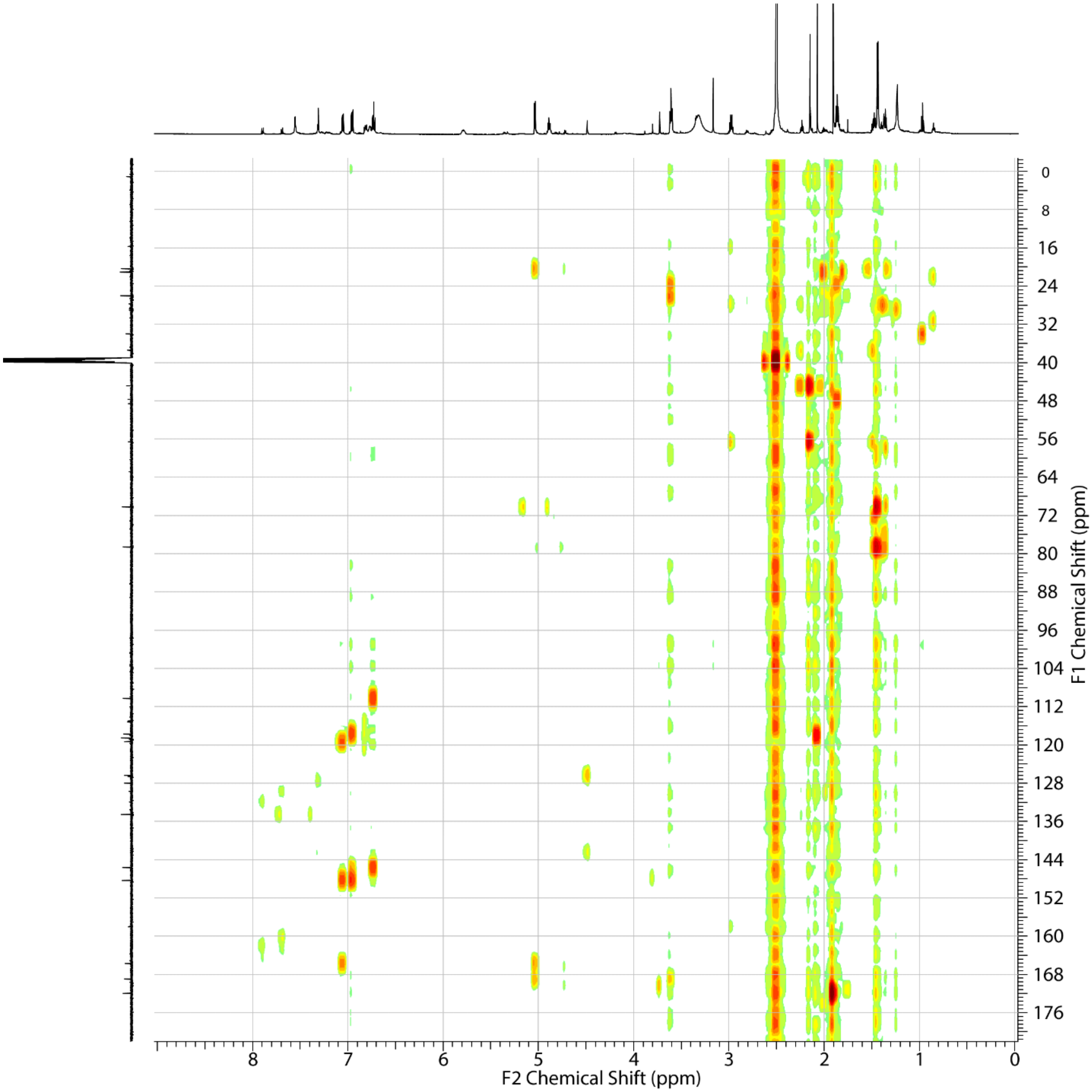
Supplementary Figure 4. ^{1}H-NMR spectrum (600 MHz) of compound **1b** in DMSO-*d*6.



Supplementary Figure 5. ^{13}C NMR spectrum (600 MHz) of compound **1b** in DMSO-*d*6.

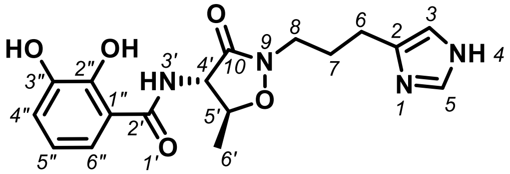


Supplementary Figure 6. gHSQC spectrum (600 MHz) of compound **1b** in DMSO-*d*6.



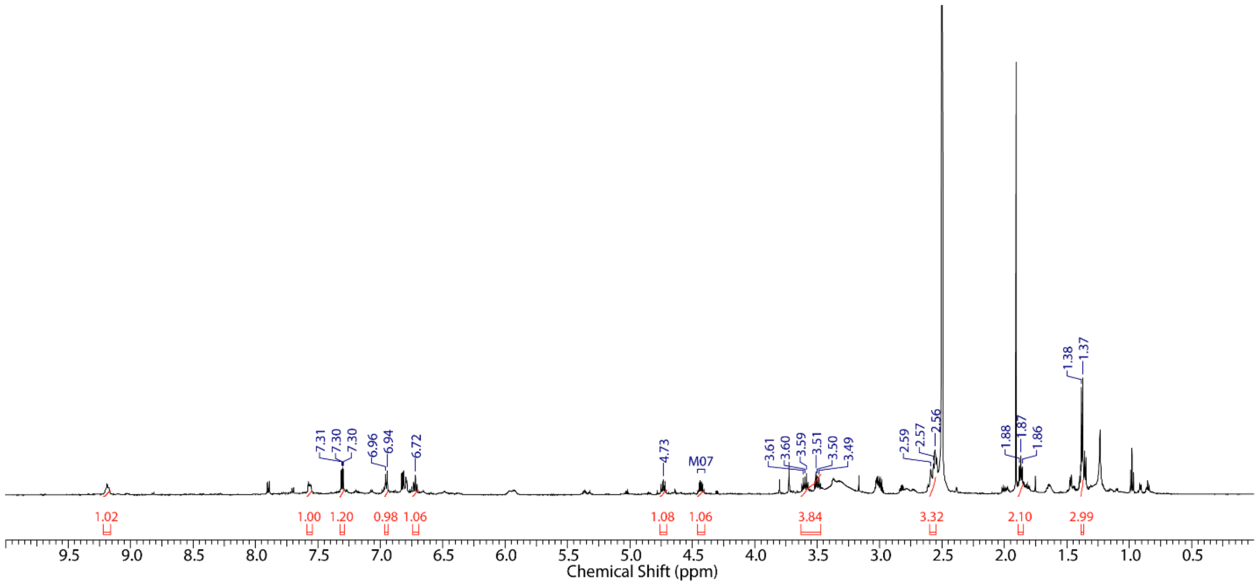
Supplementary Figure 7. HMBC spectrum (600 MHz) of compound **1b** in DMSO-*d*6.

Supplementary Table 3. NMR characterization data of compound **2b** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{17}H_{21}N_5O_4]^+$ ($[M+H]^+$) calculated: 361.1506, found: 361.1499.

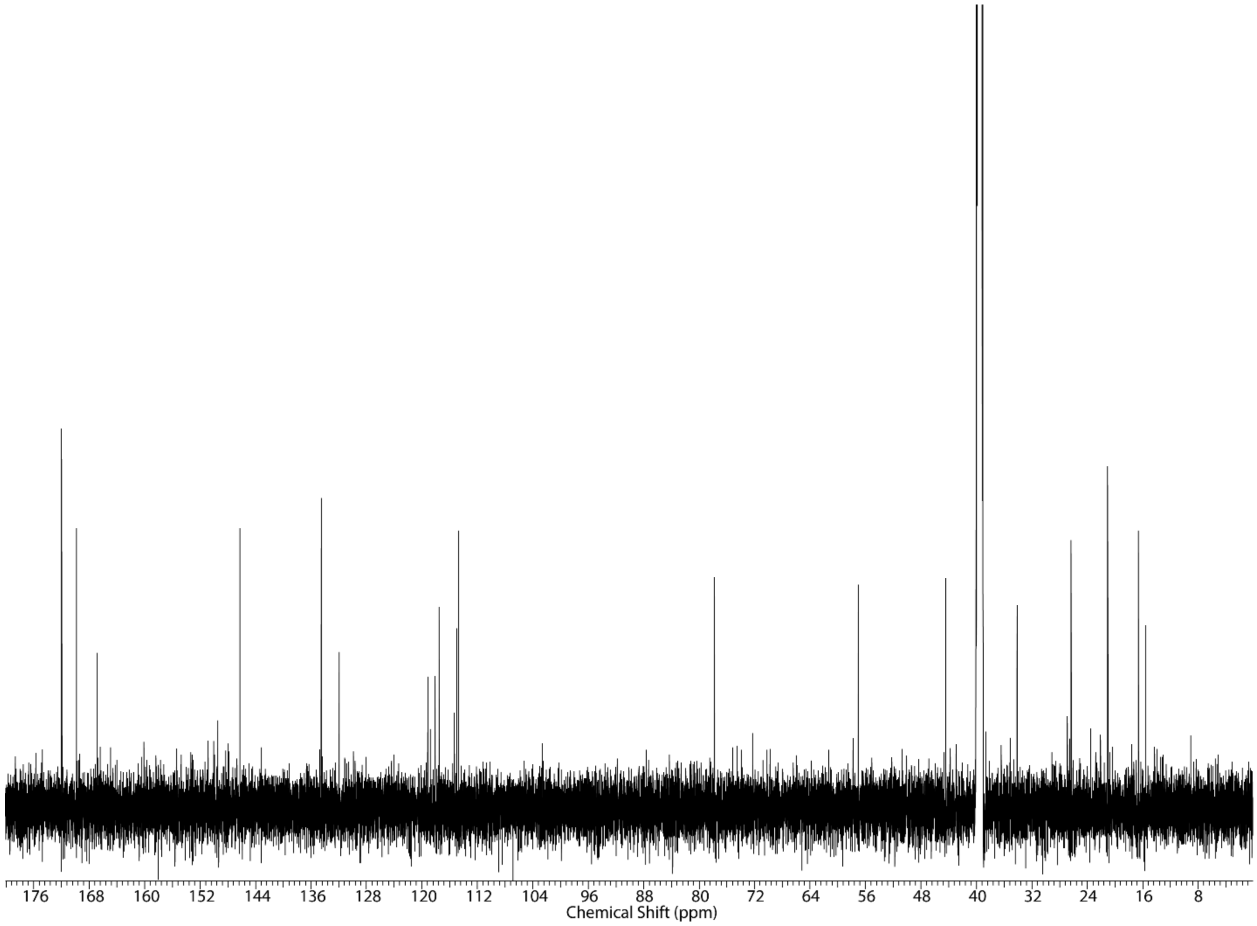


Compound **2b**

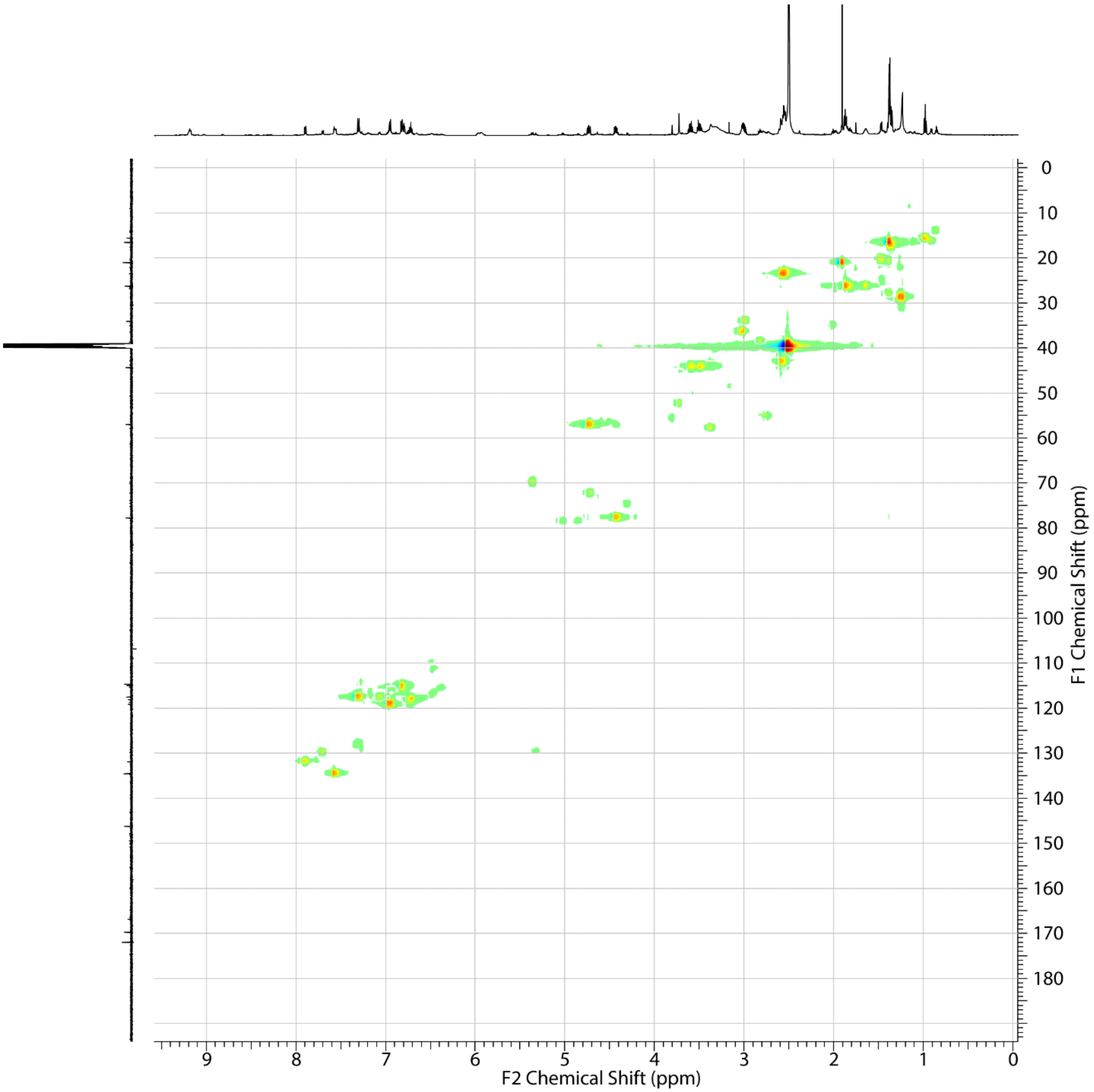
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.4	7.59 – 7.54 (m, 1 H)	
6	23.5	2.60 – 2.55 (m, 2 H	7, 8
7	26.1	1.89 – 1.85 (m, 2 H)	6, 8
8	44.4	3.63 – 3.47 (m, 2 H)	6, 7
10	166.9		8, 4’
2’	169.8		4’, 6”
3’		9.22 – 9.16 (m, 1 H)	2’
4’	57.0	4.73 (s, 1 H)	10, 2’, 5’, 6’
5’	77.7	4.46 – 4.40 (m, 1 H)	4’, 6’
6’	16.6	1.38 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	149.4		4”, 6”
4”	119.1	6.95 (d, *J* = 7.9 Hz, 1 H)	2”, 6”
5”	118.0	6.72 (t, *J* = 7.9 Hz, 1 H)	
6”	117.5	7.32 – 7.29 (m, 1 H)	2’, 2”, 4”



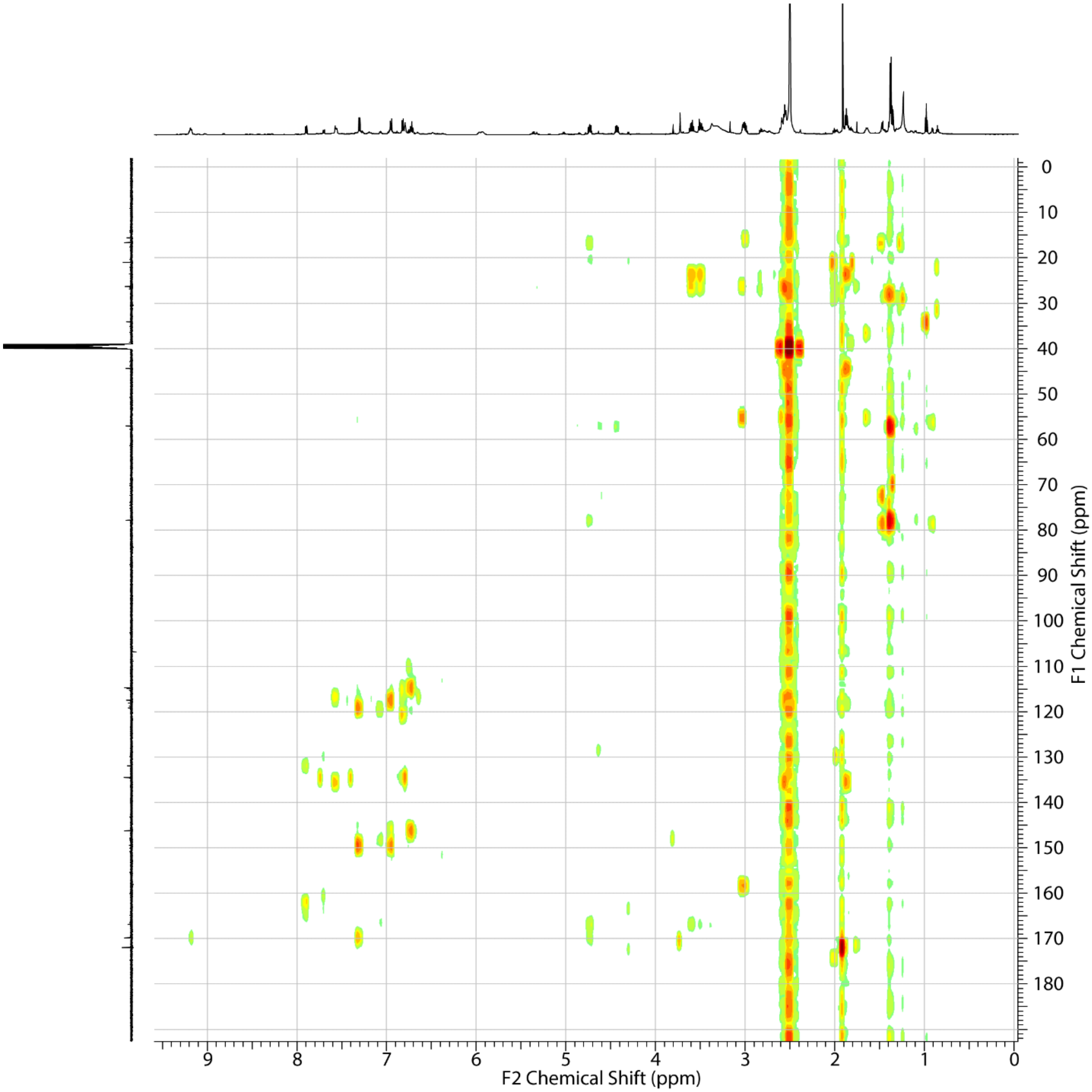
Supplementary Figure 8. ^{1}H-NMR spectrum (600 MHz) of compound **2b** in DMSO-*d*6.



Supplementary Figure 9. ^{13}C-NMR spectrum (600 MHz) of compound **2b** in DMSO-*d*6.

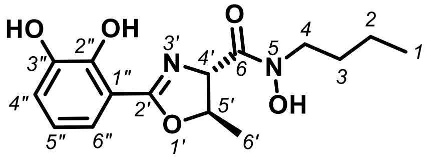


Supplementary Figure 10. gHSQC spectrum (600 MHz) of compound **2b** in DMSO-*d*6.



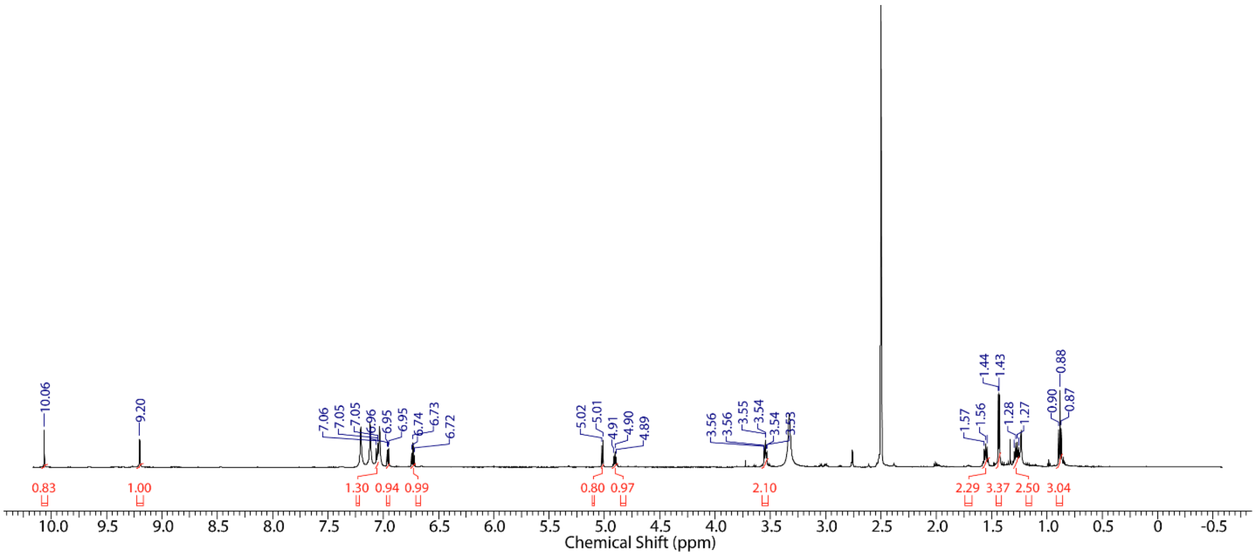
Supplementary Figure 11. HMBC spectrum (600 MHz) of compound **2b** in DMSO-*d*6.

Supplementary Table 4. NMR characterization data of compound **1c** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{15}H_{21}N_2O_5]^+$ ($[M+H]^+$) calculated: 309.1445, found: 309.1438.

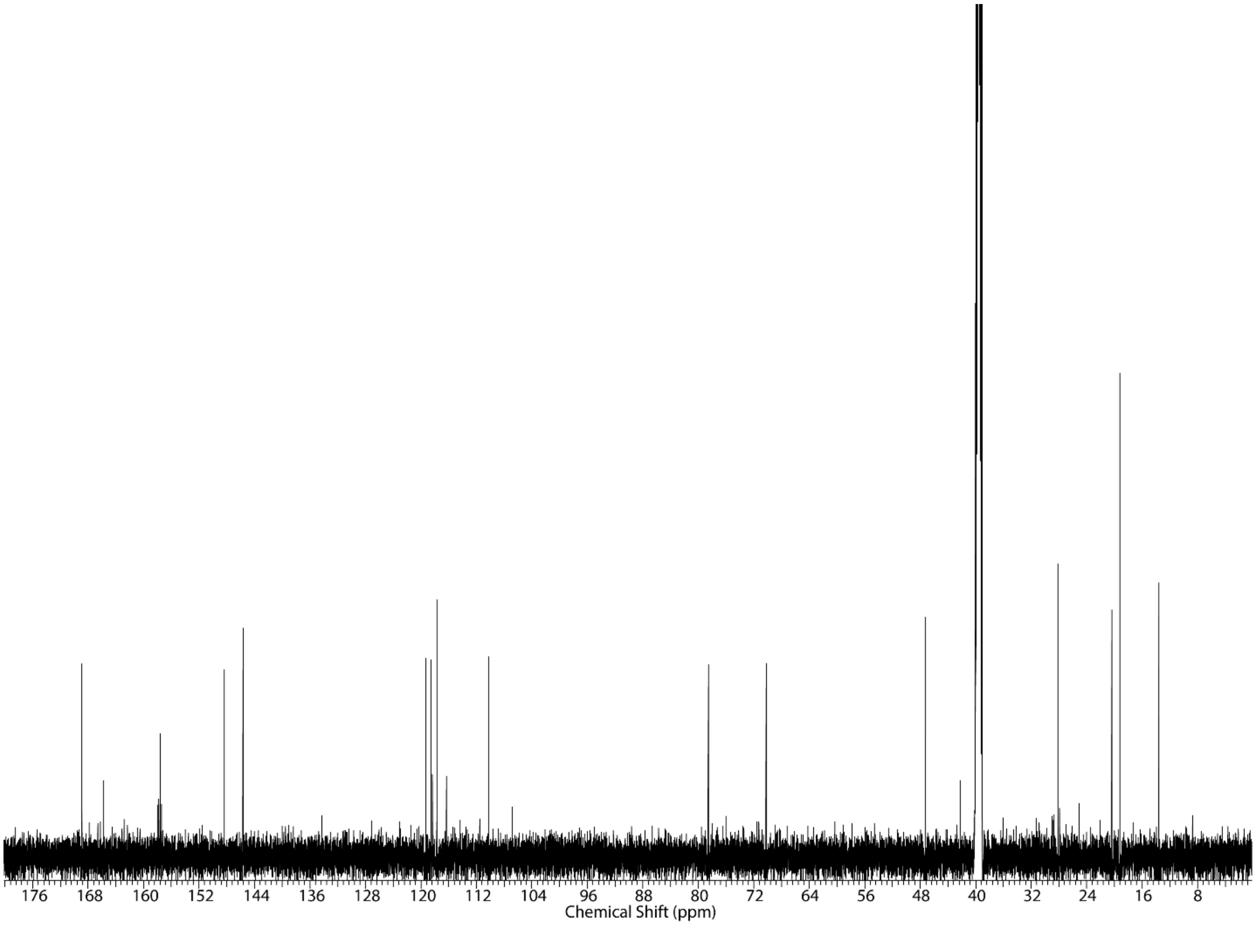


Compound **1c**

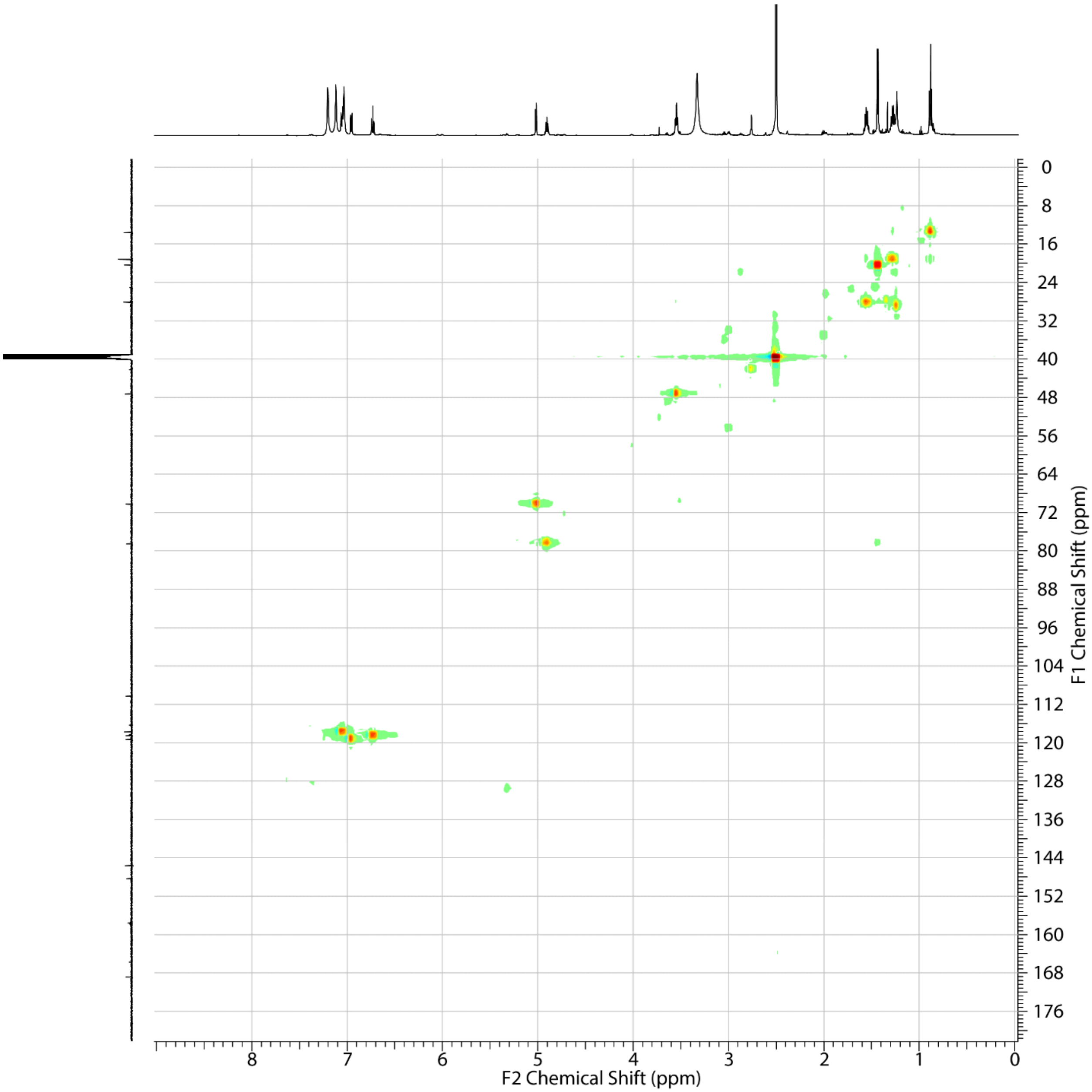
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
1	13.6	0.88 (t, *J* = 7.5 Hz, 3 H)	2, 3
2	19.2	1.28 (dd, *J* = 7.9, 14.9 Hz, 2 H)	1, 3, 4
3	28.1	1.58 – 1.52 (m, 2 H)	1, 2, 4
4	47.2	3.55 (dt, *J* = 2.4, 7.1 Hz, 2 H)	2, 3
2’	165.6		4’, 6”
4’	70.2	5.02 (d, *J* = 5.5 Hz, 1 H)	2’, 5’, 6’
5’	78.5	4.90 (t, *J* = 6.3 Hz, 1 H)	4’, 6’
6’	20.3	1.44 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	148.3		4”, 6”
4”	119.2	6.96 (dd, *J* = 1.6, 7.9 Hz, 1 H)	2”, 6”
5”	118.3	6.73 (t, *J* = 7.9 Hz, 1 H)	
6”	117.7	7.06 (dd, *J* = 1.6, 7.9 Hz, 1 H)	2’, 2”, 4”



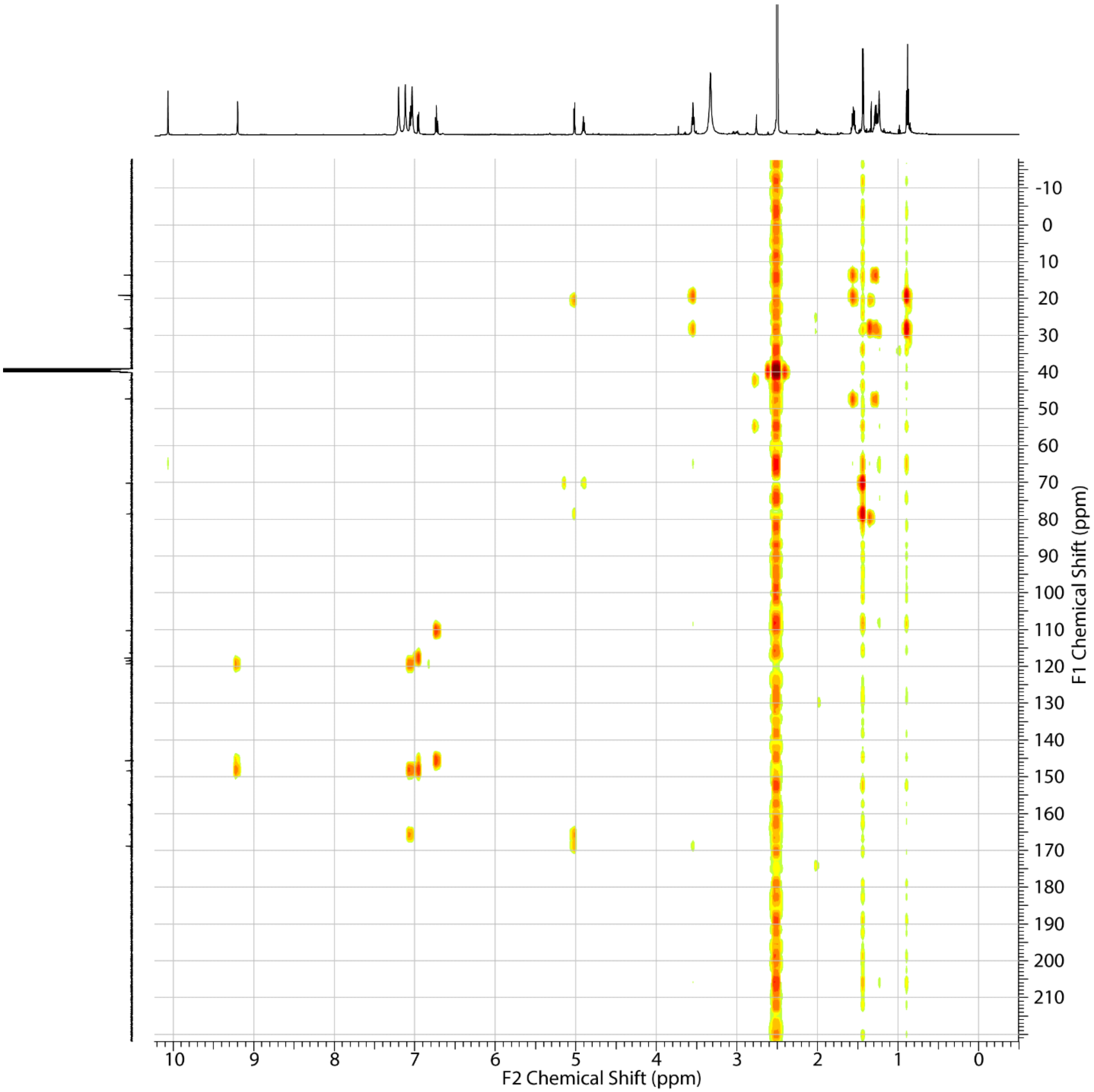
Supplementary Figure 12. ^{1}H-NMR spectrum (600 MHz) of compound **1c** in DMSO-*d*6.



Supplementary Figure 13. ^{13}C-NMR spectrum (600 MHz) of compound **1c** in DMSO-*d*6.

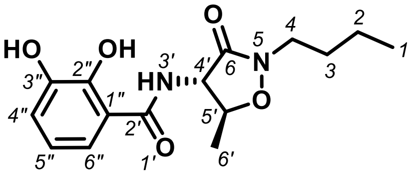


Supplementary Figure 14. gHSQC spectrum (600 MHz) of compound **1c** in DMSO-*d*6.



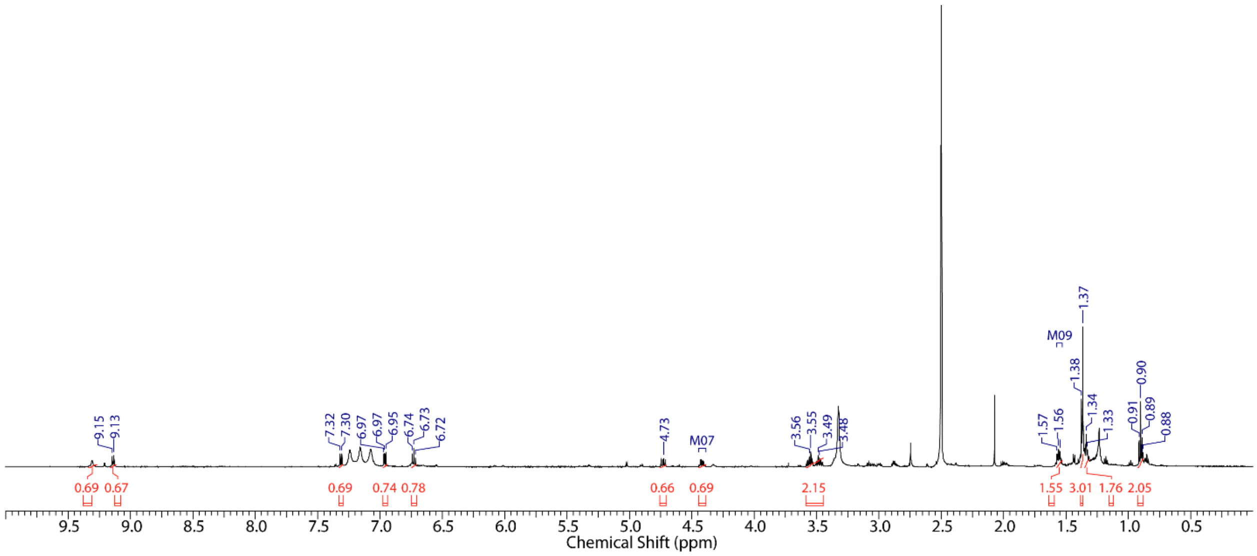
Supplementary Figure 15. HMBC spectrum (600 MHz) of compound **1c** in DMSO-*d*6.

Supplementary Table 5. NMR characterization data of compound **2c** in DMSO-d6. HR-MS (ESI+) m/z for $[C_{15}H_{21}N_2O_5]^+$ ($[M+H]^+$) calculated: 309.1445, found: 309.1439.

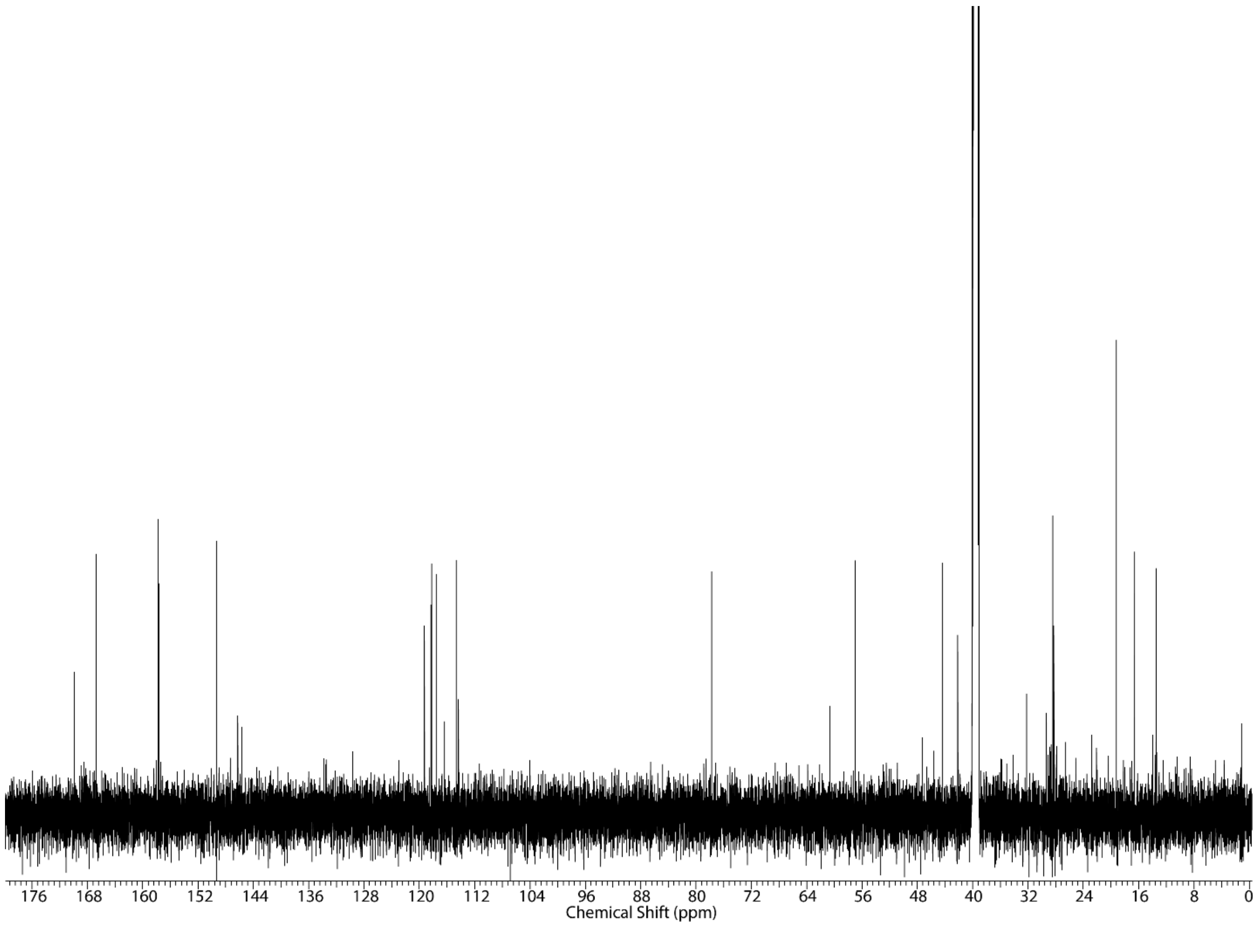


Compound **2c**

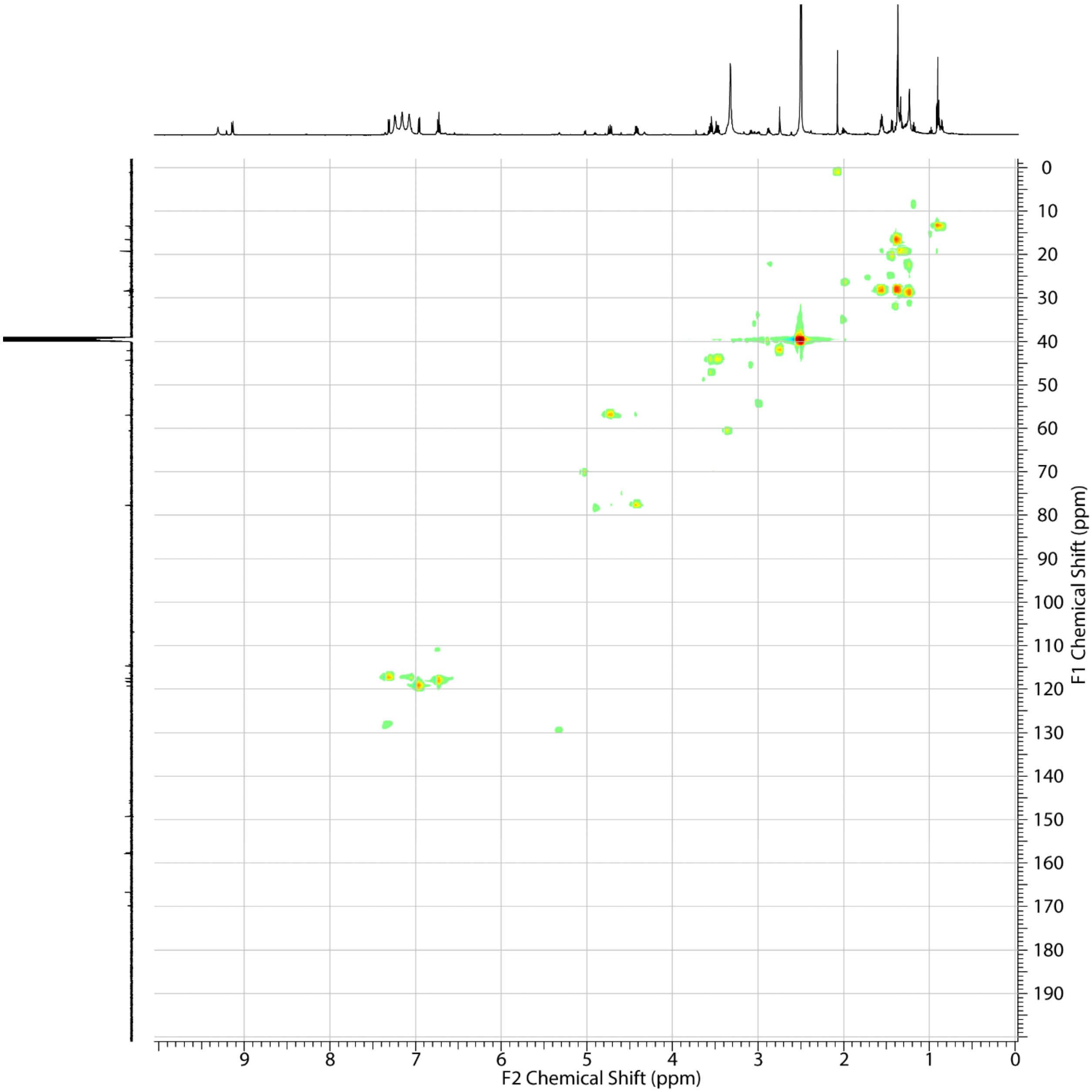
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
1	13.4	0.92 – 0.89 (m, 3 H)	2, 3
2	19.2	1.35 – 1.32 (m, 2 H)	1, 3, 4
3	28.2	1.58 – 1.53 (m, 2 H)	1, 2, 4
4	44.3	3.58 – 3.45 (m, 2 H)	2, 3
2'	169.8		3', 6"
3'		9.34 – 9.27 (m, 1 H)	2'
4'	57.0	4.73 (s, 1 H)	2', 5', 6'
5'	118.2	4.45 – 4.39 (m, 1 H)	4', 6'
6'	16.5	1.38 – 1.36 (m, 3 H)	4', 5'
2"			4", 6"
4"	119.2	6.96 (dd, *J* =1.6, 7.9 Hz, 1 H)	2", 6"
5"	118.2	6.75 – 6.71 (m, 1 H)	
6"	117.4	7.33 – 7.30 (m, 1 H)	2', 2", 4"



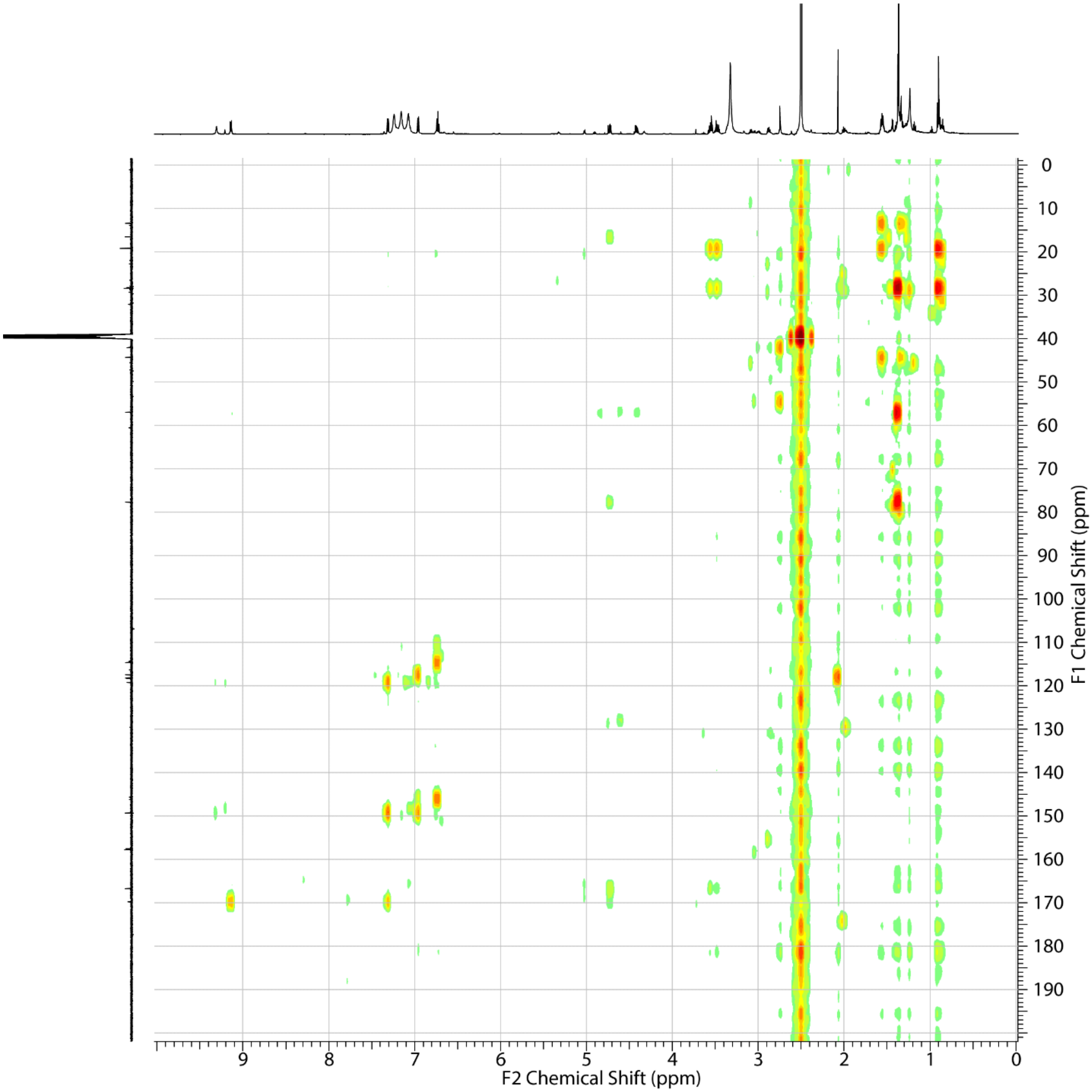
Supplementary Figure 16. ^{1}H-NMR spectrum (600 MHz) of compound **2c** in DMSO-*d*6.



Supplmentary Figure 17. ^{13}C-NMR spectrum (600 MHz) of compound **2c** in DMSO-*d*6.

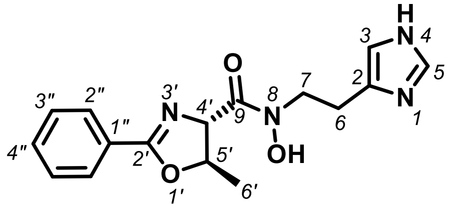


Supplmentary Figure 18. gHSQC spectrum (600 MHz) of compound **2c** in DMSO-*d*6.



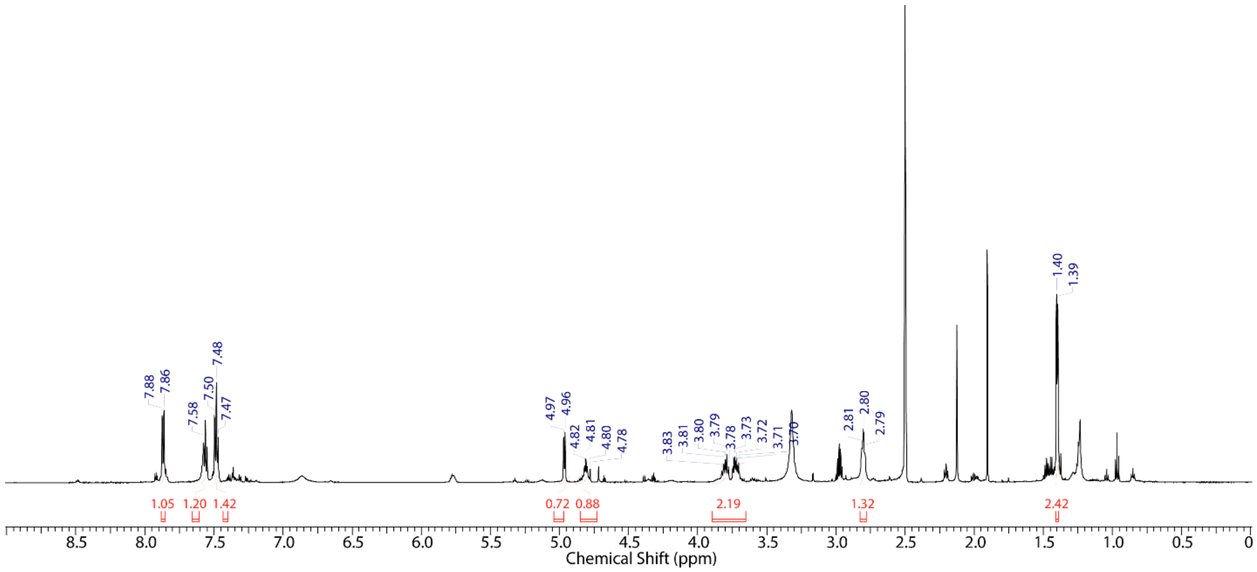
Supplementary Figure 19. HMBC spectrum (600 MHz) of compound **2c** in DMSO-*d*6.

Supplementary Table 6. NMR characterization data of compound **1d** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_3]^+$ ($[M+H]^+$) calculated: 315.1452, found: 315.1444.

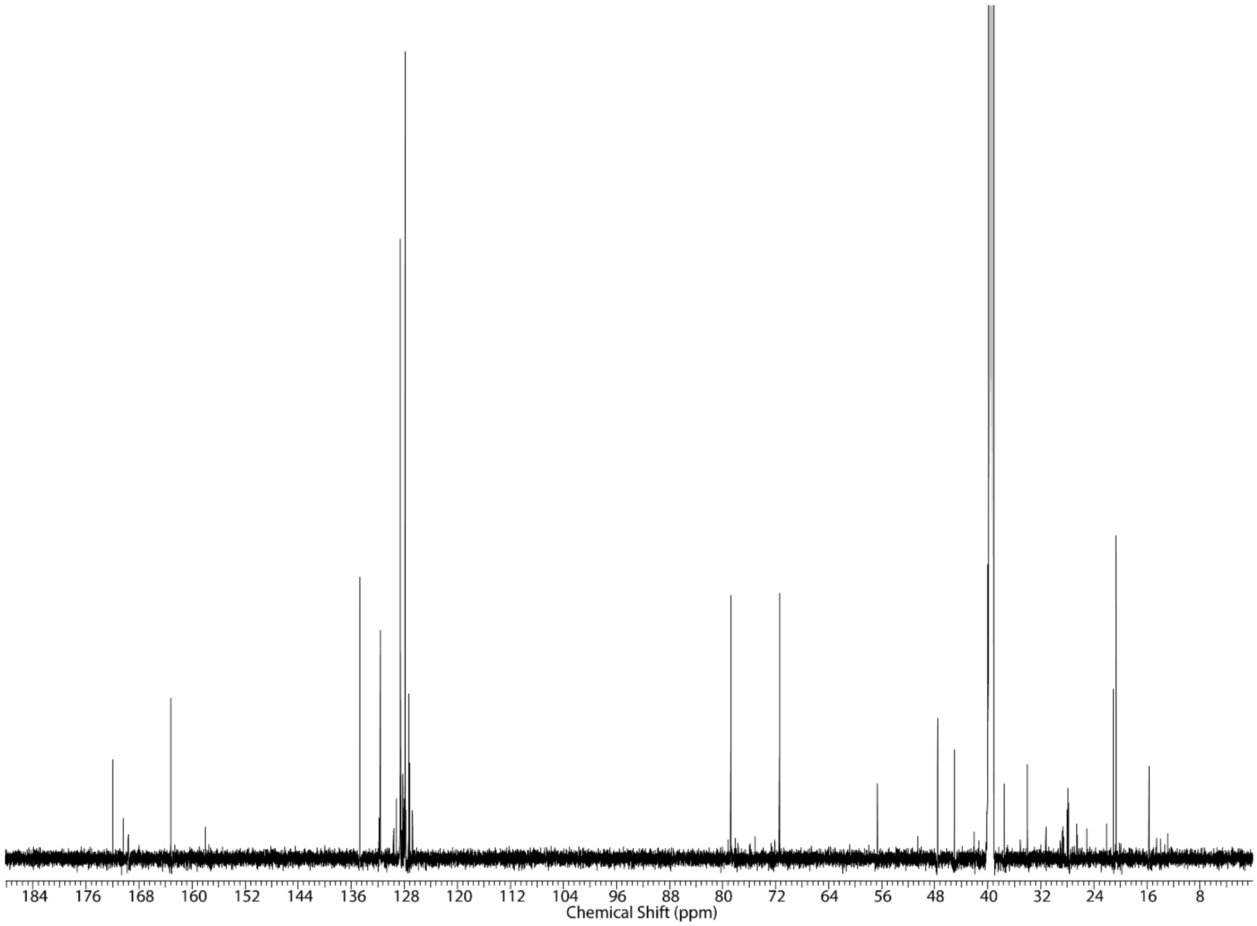


Compound **1d**

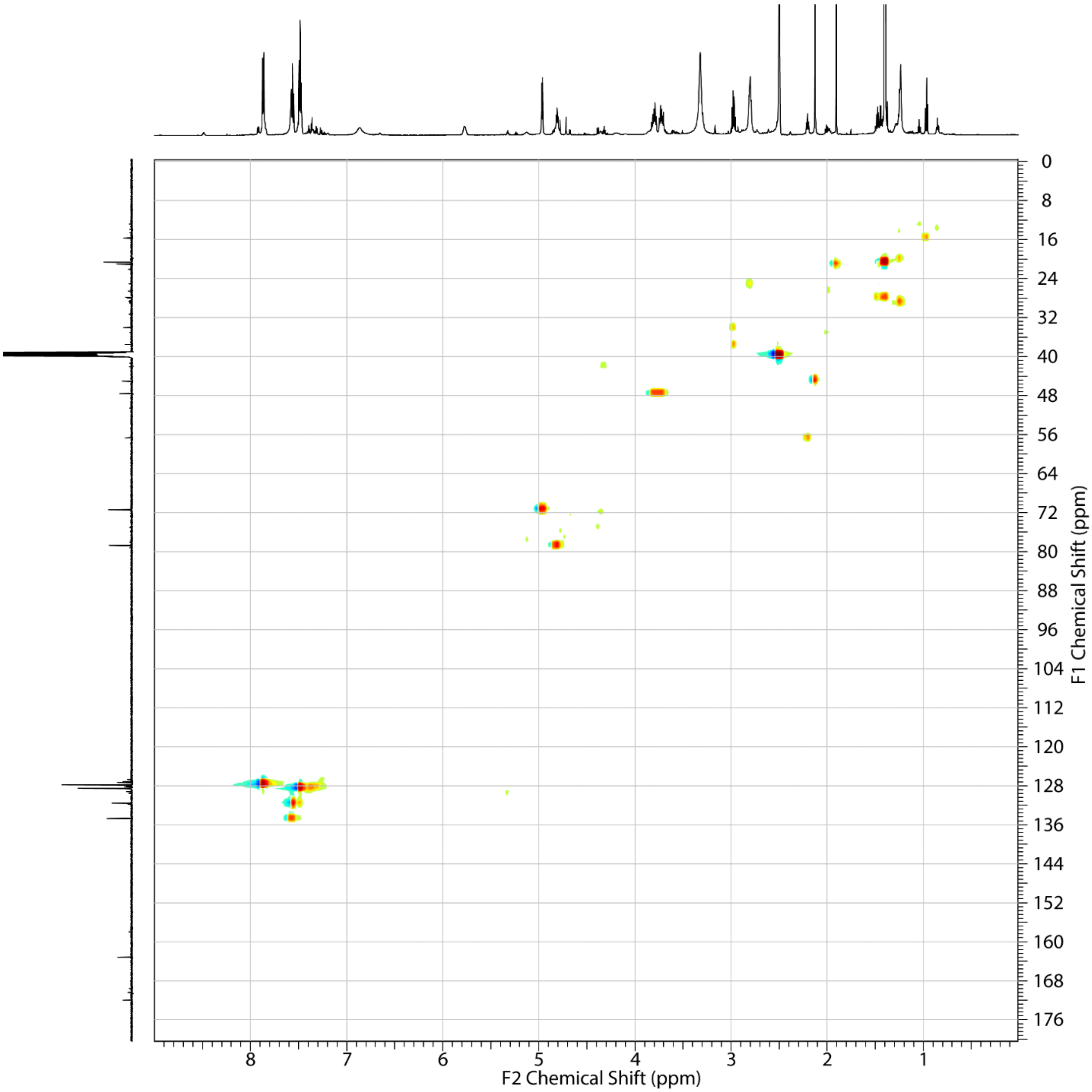
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.7	7.58 (br. s., 1 H)	
6	25.0	2.80 (t, *J* = 6.7 Hz, 2 H)	7
7	47.5	3.90 – 3.65 (m, 2 H)	6
9	169.6		4’
2’	163.2		2”
4’	71.4	4.97 (d, *J* = 5.5 Hz, 1 H)	2’, 6’, 9
5’	78.7	4.89 – 4.77 (m, 1 H)	4’, 6’
6’	20.6	1.40 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	127.9	7.87 (d, *J* = 7.9 Hz, 2 H)	2’, 4”
3”	128.6	7.50 – 7.46 (m, 2 H)	2”
4”	131.59	7.58 – 7.54 (m, 1 H)	3”



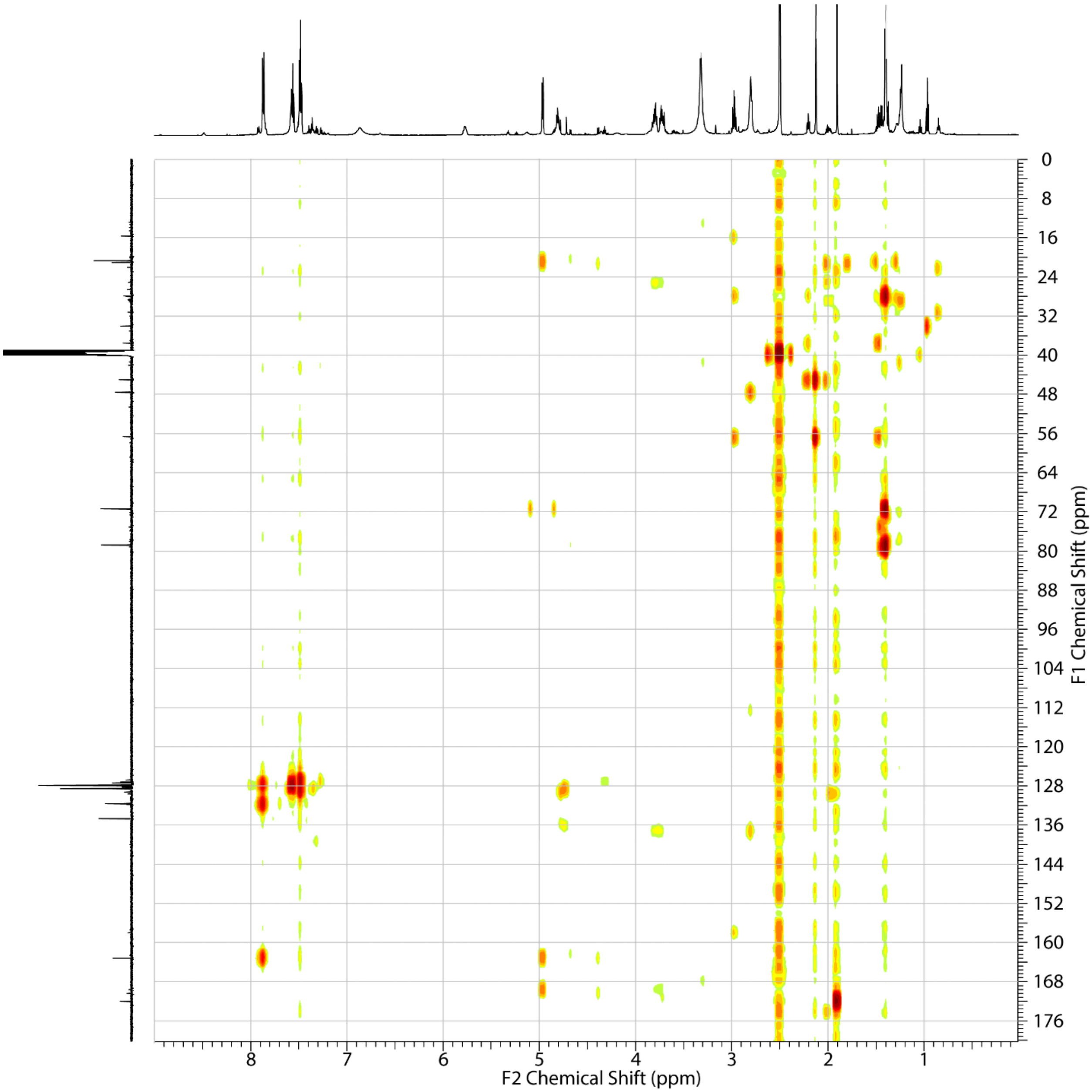
Supplementary Figure 20. ^{1}H-NMR spectrum (600 MHz) of compound **1d** in DMSO-*d*6.



Supplementary Figure 21. ^{13}C-NMR spectrum (600 MHz) of compound **1d** in DMSO-*d*6.

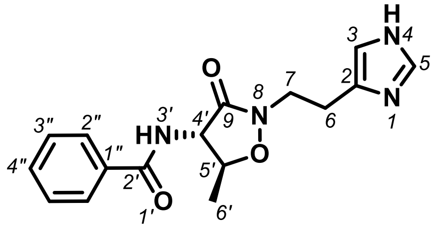


SupplementaryFigure 22. gHSQC spectrum (600 MHz) of compound **1d** in DMSO-*d*6.



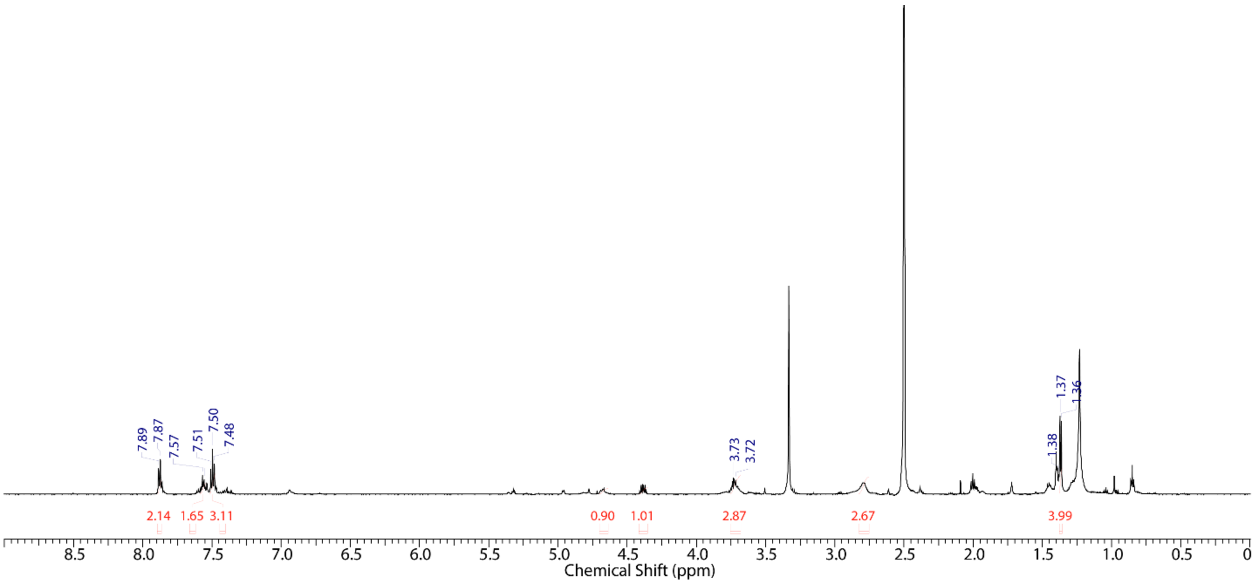
Supplementary Figure 23. HMBC spectrum (600 MHz) of compound **1d** in DMSO-*d*6.

Supplementary Table 7. NMR characterization data of compound **2d** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_3]^+$ ($[M+H]^+$) calculated: 315.1452, found: 315.1447.

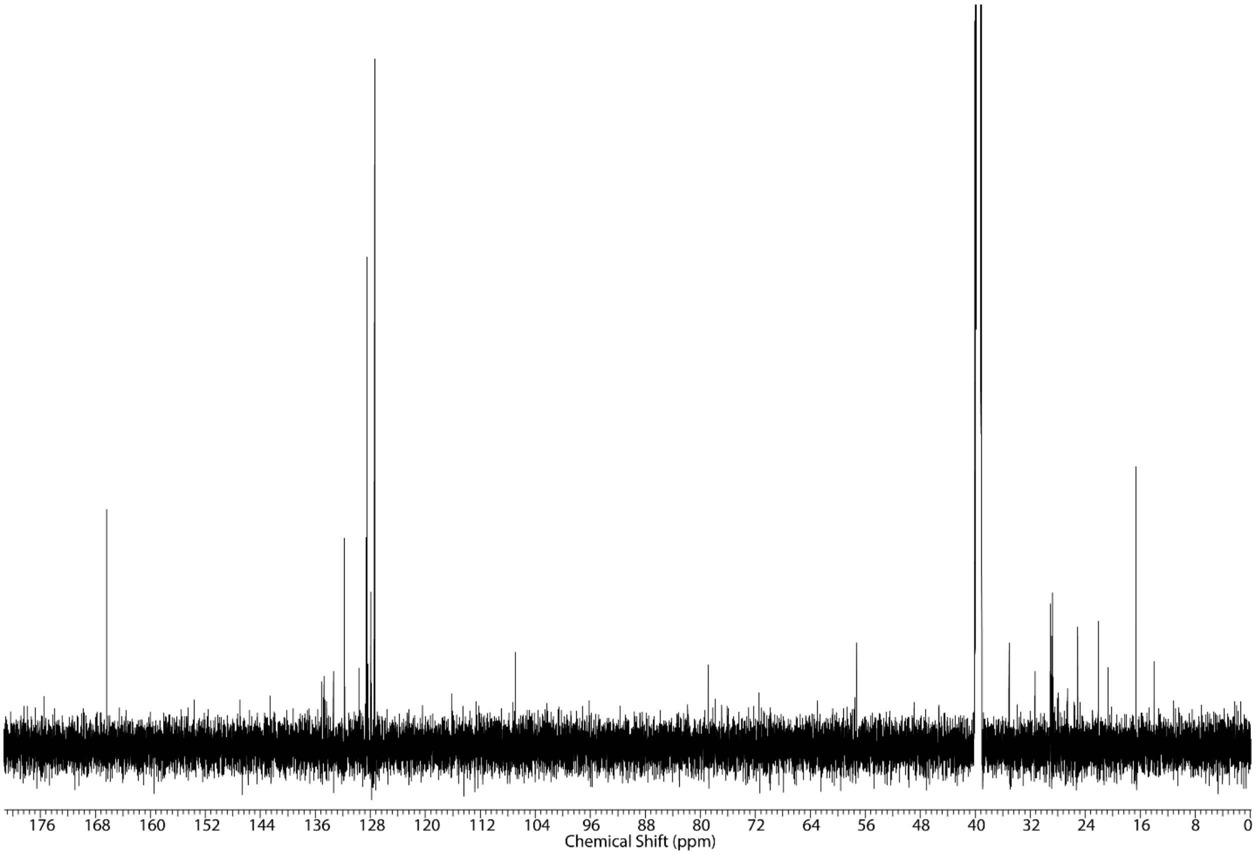


Compound **2d**

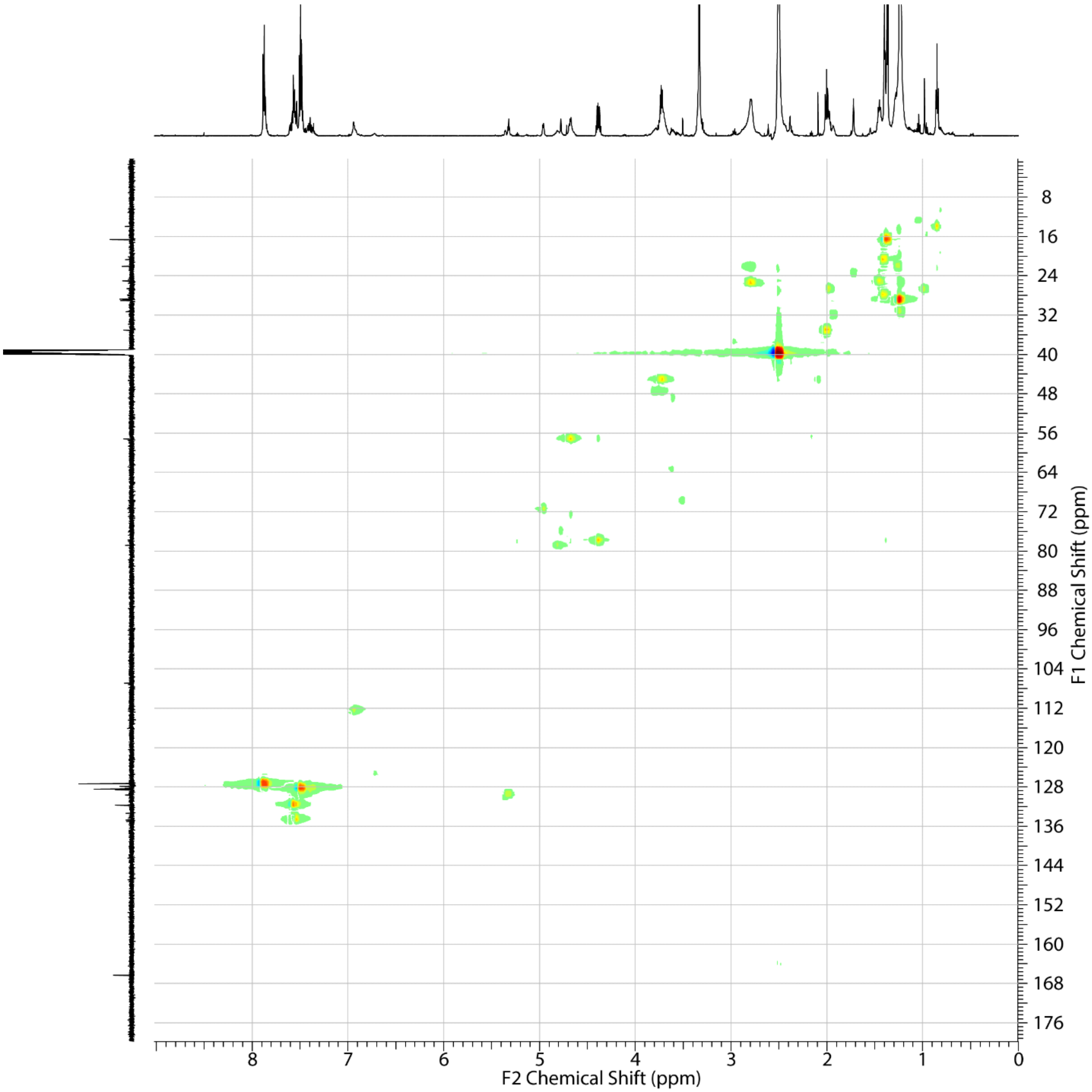
Atom	^{13}C (ppm)	^1H (ppm), multiplets in Hz	HMBC ^1H-^{13}C 2-3 bond
6	16.5	2.86 – 2.75 (m, 2 H)	7
7		3.72 (d, *J* = 8.7 Hz, 2 H)	6
9	168.3		
2’	166.3		2”
4’	57.2	4.70 – 4.63 (m, 1 H)	5’, 6’, 9
5’	78.8	4.42 – 4.35 (m, 1 H)	4’, 6’
6’	20.6	1.40 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	127.4	7.88 (d, *J* = 7.1 Hz, 2 H)	2’, 4”
3”	128.4	7.50 (t, *J* = 7.9 Hz, 2 H)	
4”	131.7	7.59 – 7.55 (m, 1 H)	2”



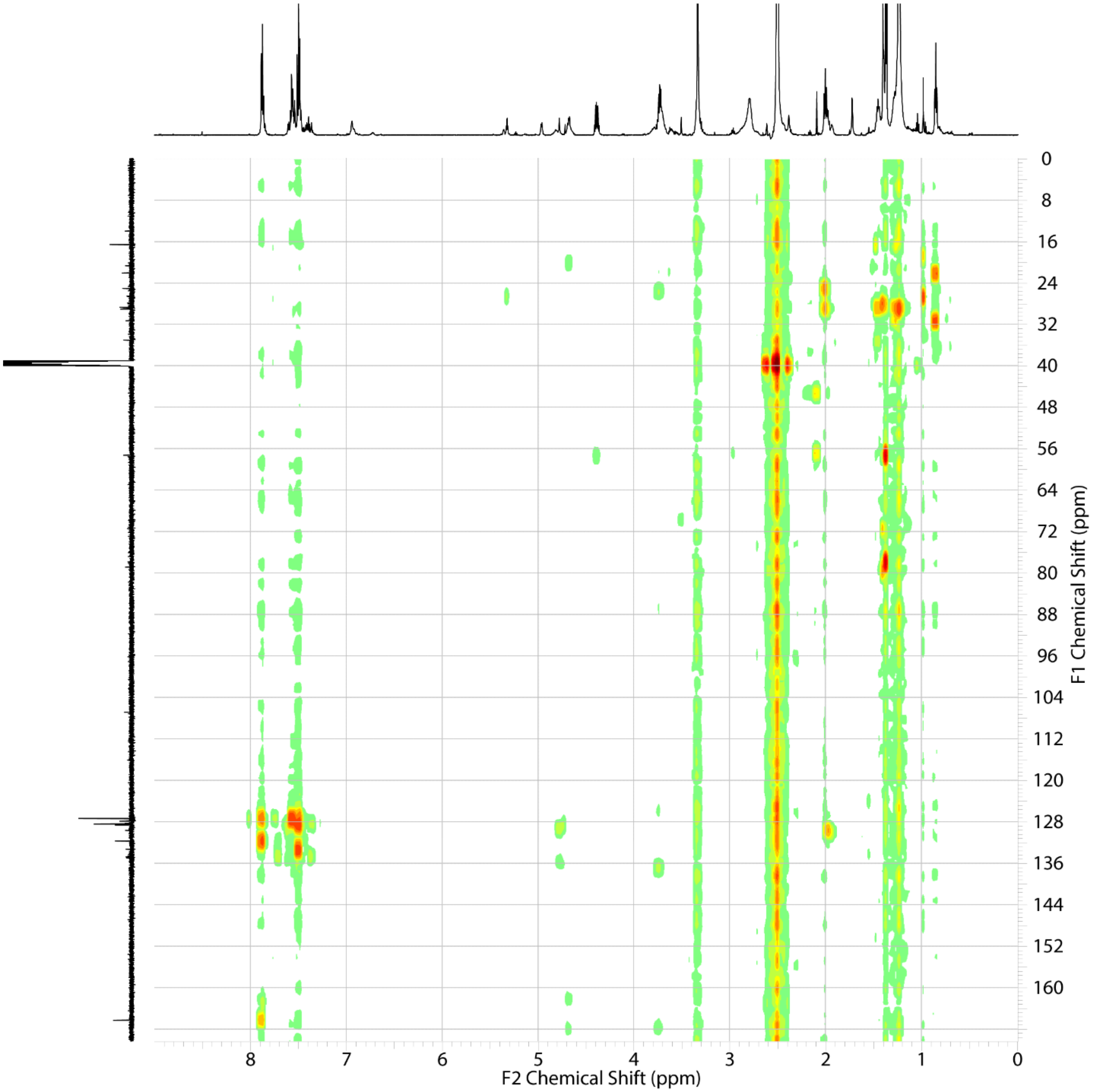
Supplementary Figure 24. ^{1}H-NMR spectrum (600 MHz) of compound **2d** in DMSO-*d*6.



Supplementary Figure 25. ^{13}C-NMR spectrum (600 MHz) of compound **2d** in DMSO-*d*6.

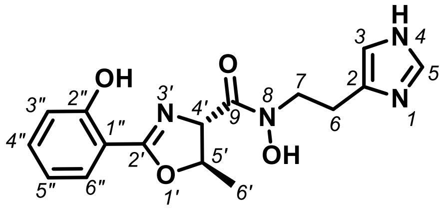


Supplementary Figure 26. gHSQC spectrum (600 MHz) of compound **2d** in DMSO-*d*6.



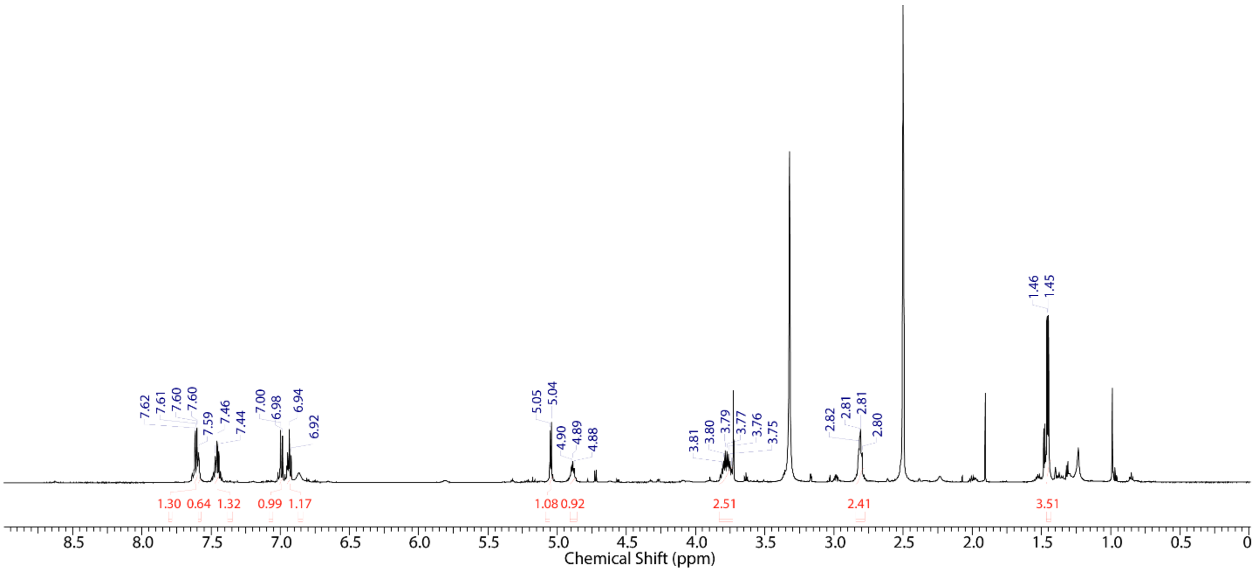
Supplementary Figure 27. HMBC spectrum (600 MHz) of compound **2d** in DMSO-*d*6.

Supplementary Table 8. NMR characterization data of compound **1e** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_4]^+$ ($[M+H]^+$) calculated: 331.1401, found: 331.1390.

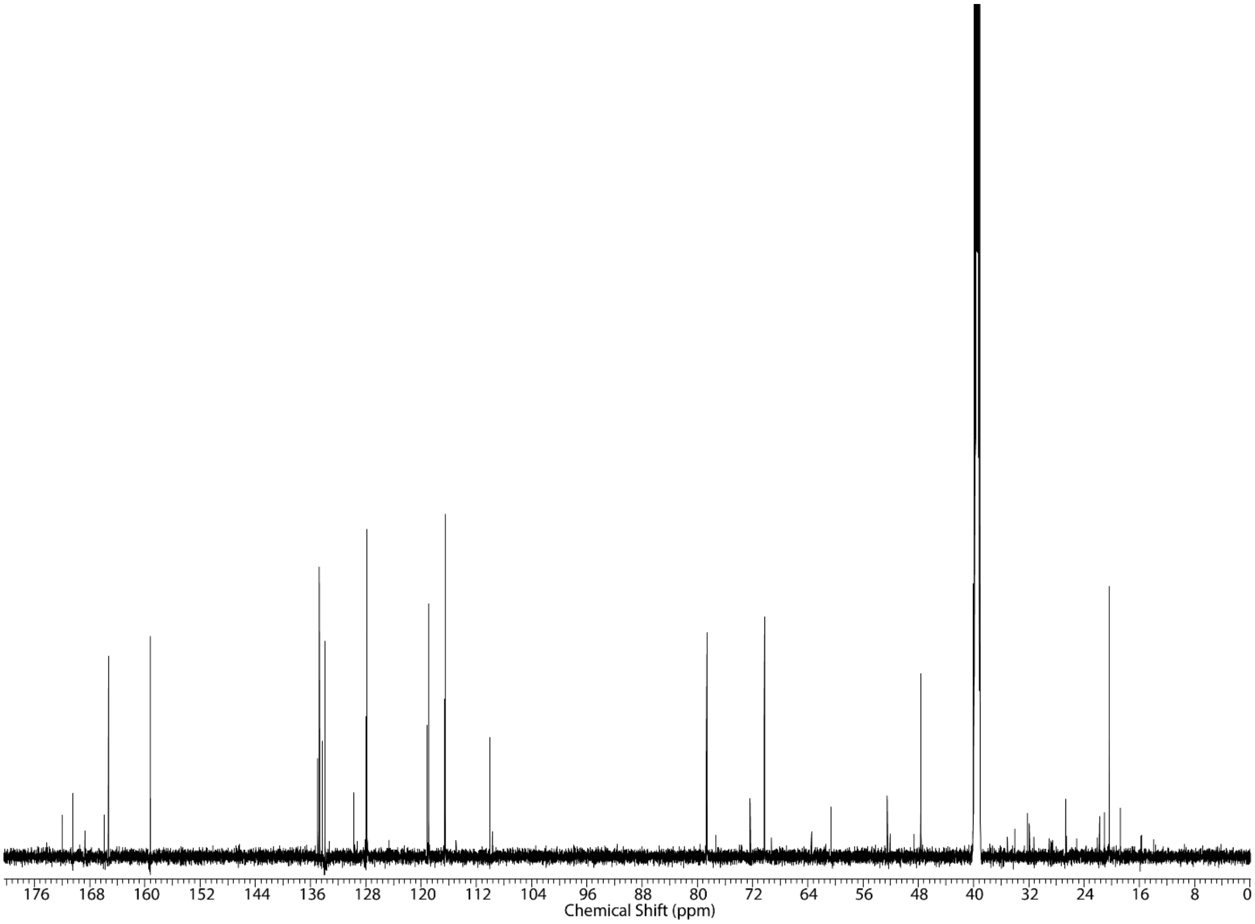


Compound **1e**

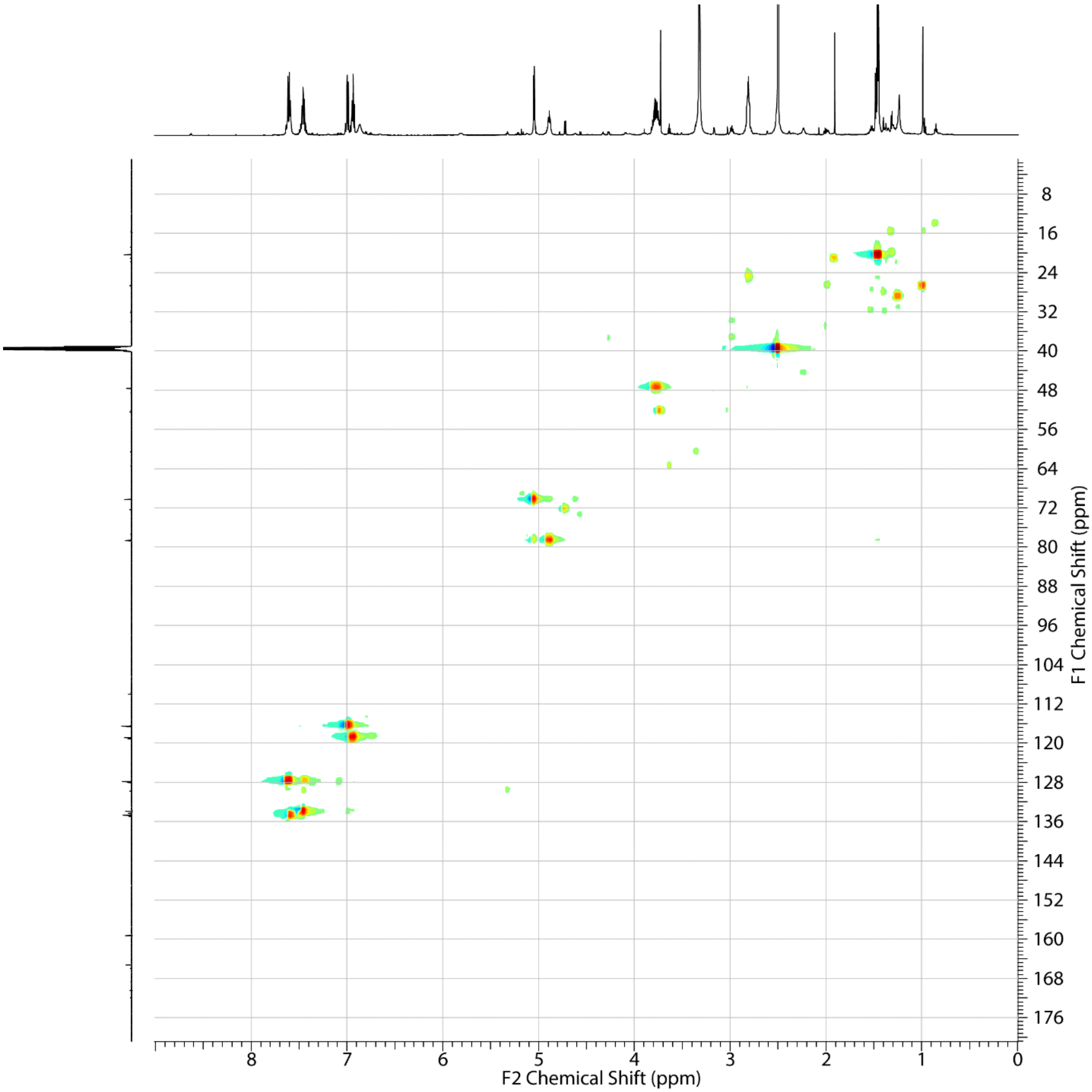
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.7	7.59 (br. s., 1 H)	
6	24.5	2.84 – 2.79 (m, 2 H)	7
7	47.6	3.77 (tt, *J* = 6.8,14.1 Hz, 2 H)	6
9	165.2		4’
2’	159.1		5”, 6”
4’	70.3	5.05 (d, *J* = 5.5 Hz, 1 H)	6’, 9
5’	78.7	4.90 – 4.87 (m, 1 H)	4’, 6’
6’	20.6	1.45 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	109.9		3”, 4”
3”	116.5	6.99 (d, *J* = 7.9 Hz, 1 H)	2”, 4”
4”	118.8	6.95 – 6.92 (m, 1 H)	2”, 3”
5”	133.8	7.46 (t, *J* = 8.3 Hz, 2 H)	2’, 6”
6”	127.8	7.61 (dd, *J* =1.6, 7.9 Hz, 1 H)	2’, 5”



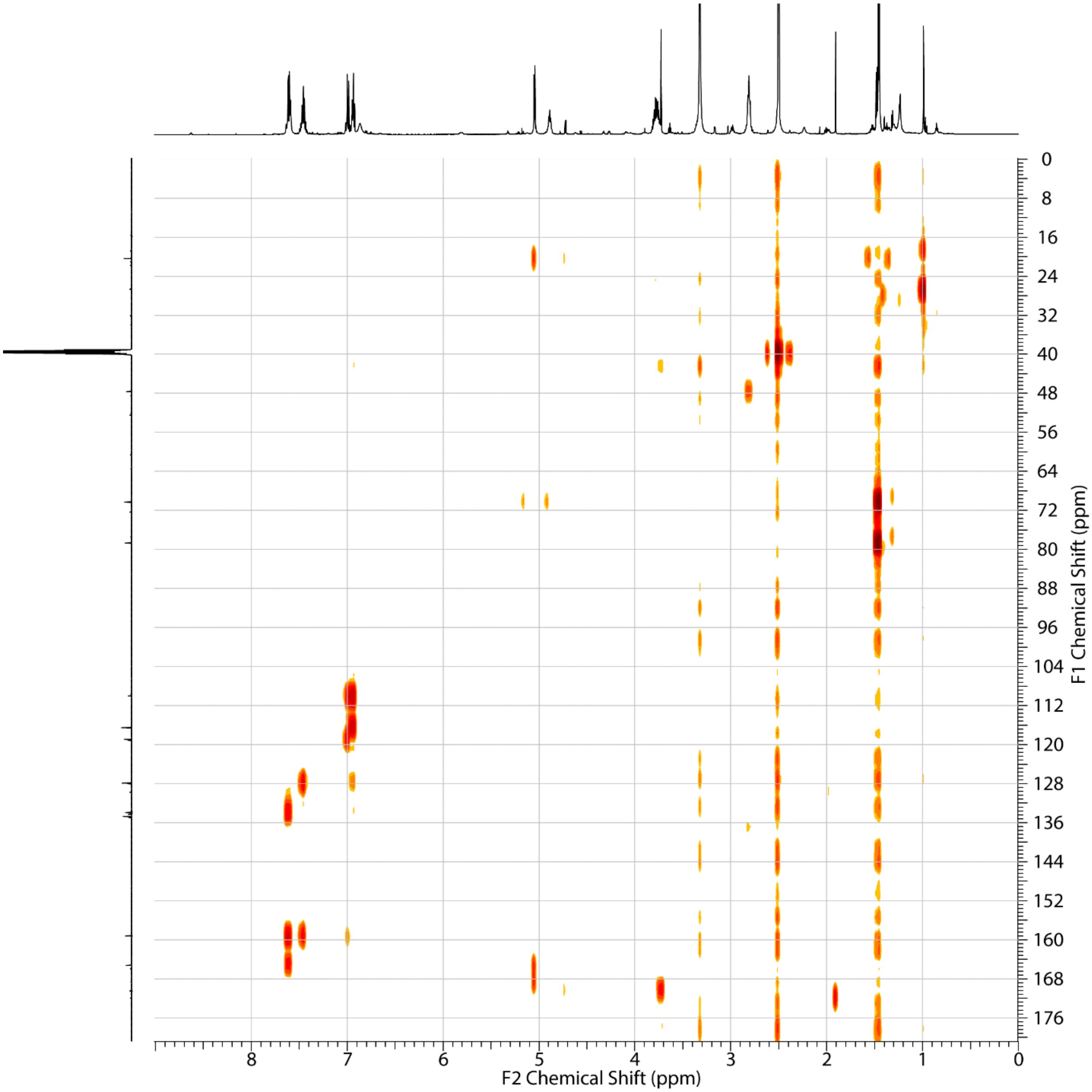
Supplementary Figure 28. ^{1}H-NMR spectrum (600 MHz) of compound **1e** in DMSO-*d*6.



Supplementary Figure 29. ^{13}C-NMR spectrum (600 MHz) of compound **1e** in DMSO-*d*6.

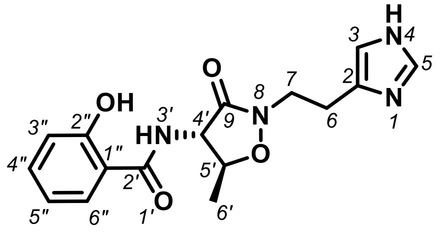


Supplementary Figure 30. gHSQC spectrum (600 MHz) of compound **1e** in DMSO-*d*6.



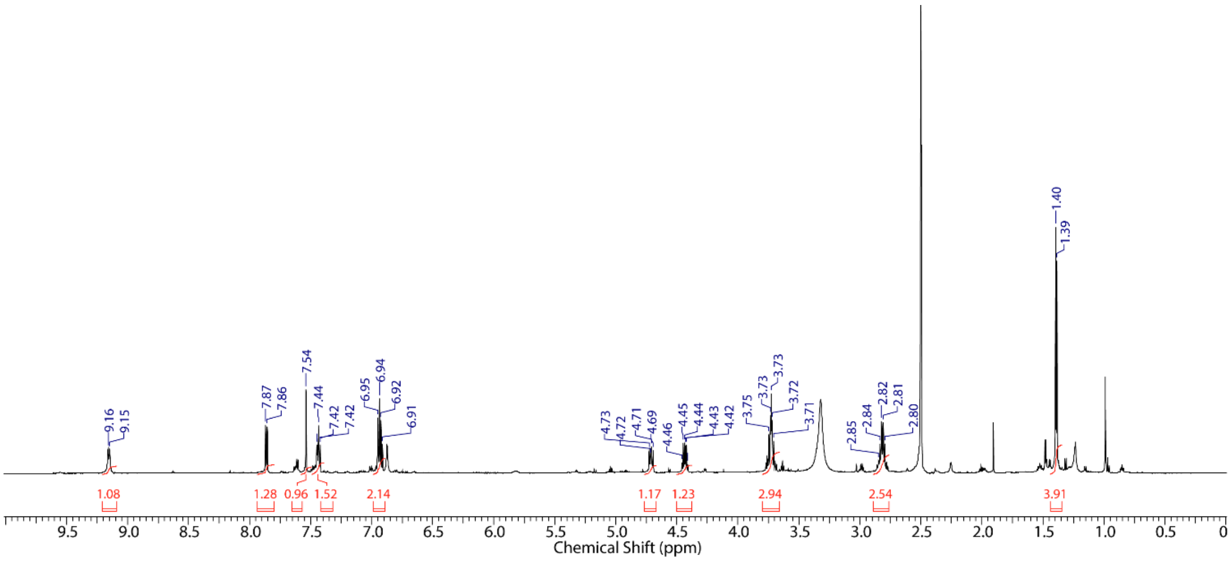
Supplementary Figure 31. HMBC spectrum (600 MHz) of compound **1e** in DMSO-*d*6.

Supplementary Table 9. NMR characterization data of compound **2e** in DMSO-*d*6. HR-MS (ESI+) m/z for $[C_{16}H_{19}N_4O_4]^+$ ($[M+H]^+$) calculated: 331.1401, found: 331.1396.

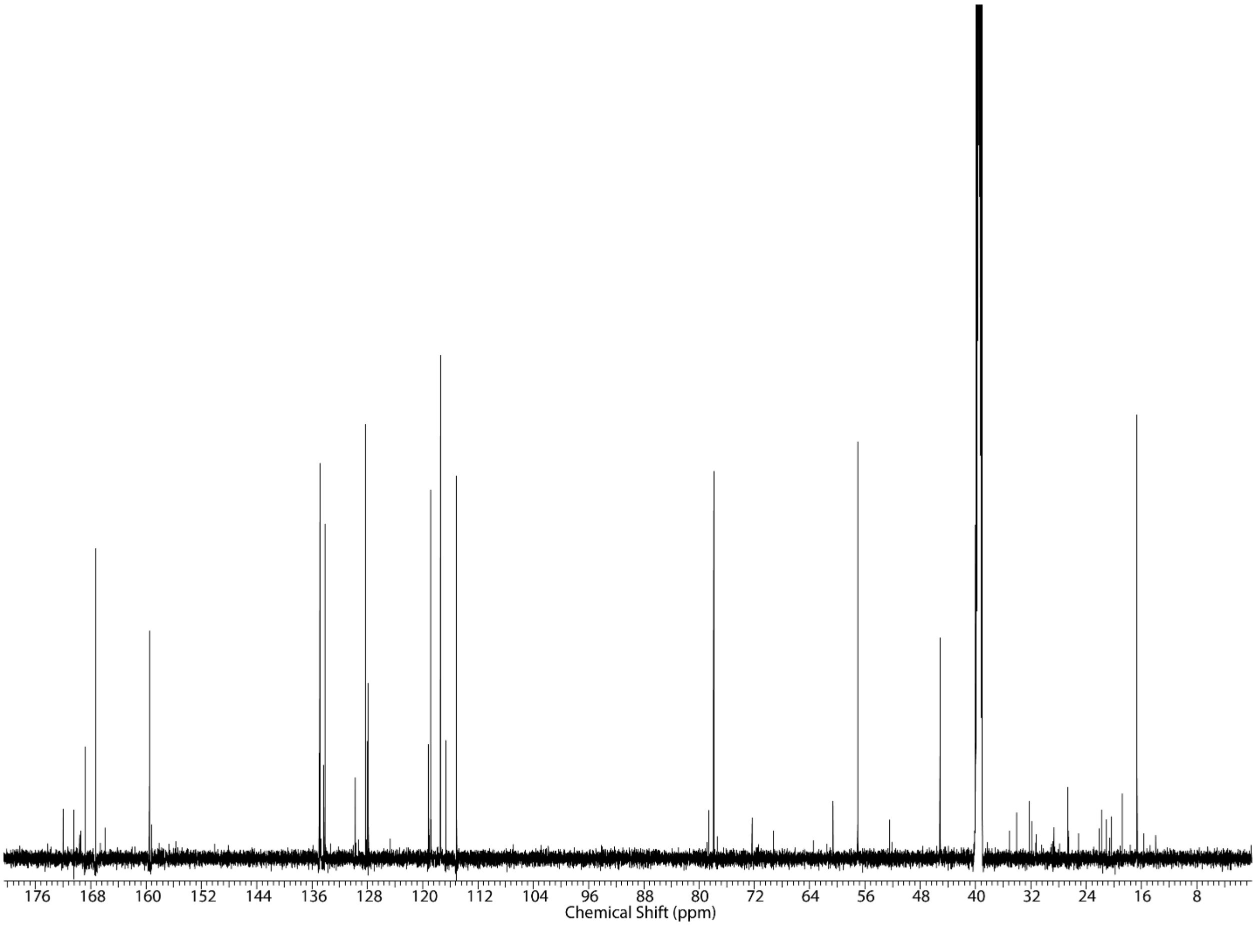


Compound **2e**

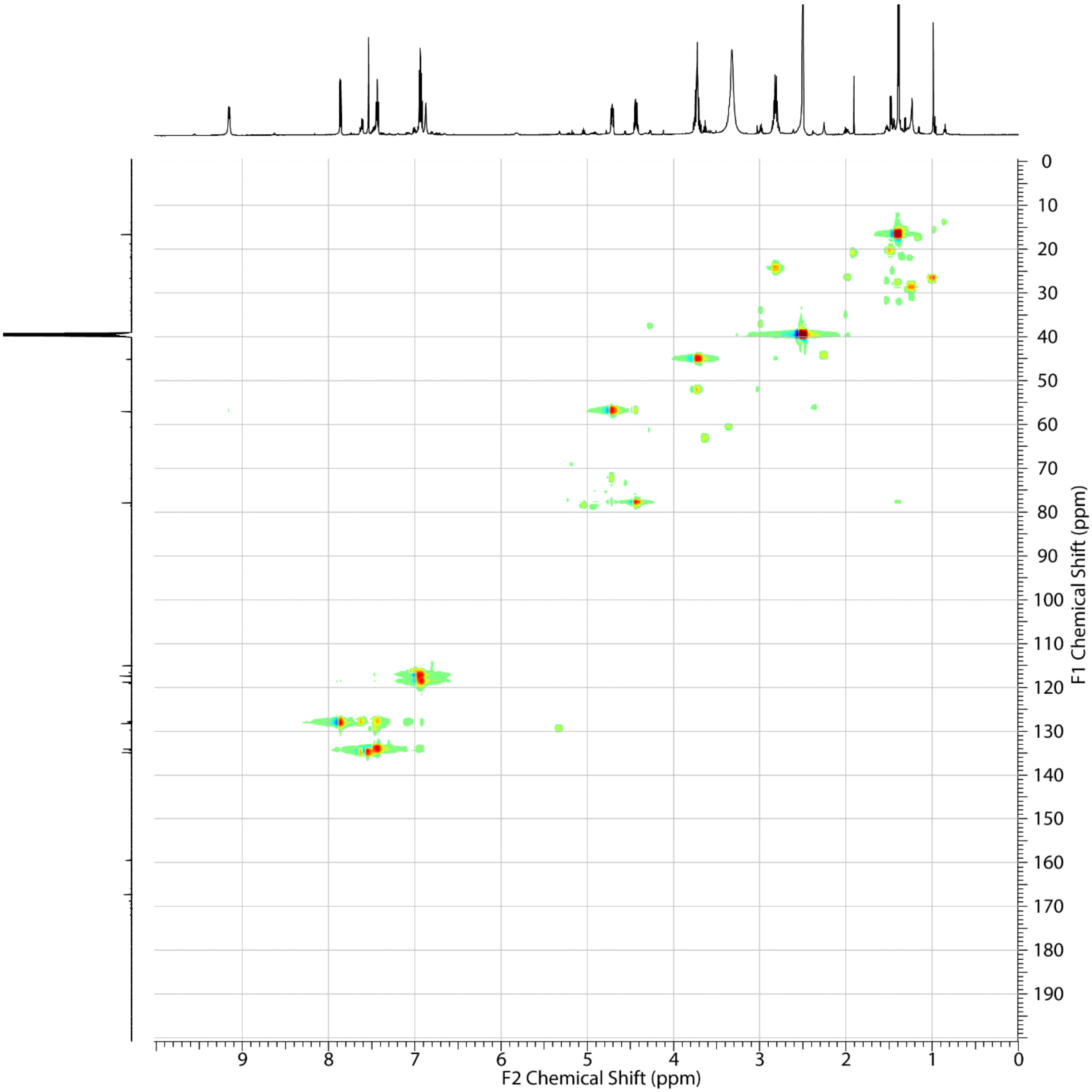
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.8	7.54 (s, 1 H)	
6	24.1	2.85 – 2.79 (m, 2 H)	7
7	45.0	3.76 – 3.70 (m, 2 H)	6
9	167.3		4’
2’	168.6		3’, 6”
3’		9.15 (d, *J* = 7.9 Hz, 1 H)	2’
4’	57.0	4.74 – 4.68 (m, 1 H)	5’, 6’, 9
5’	77.8	4.47 – 4.40 (m, 1 H)	4’, 6’
6’	16.6	1.39 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
1”	159.5		5”, 6”
3”	118.7	6.93 – 6.91 (m, 1 H)	4”
4”	117.4	6.94 (d, *J* = 7.9 Hz, 1 H)	3”
5”	134.0	7.46 – 7.41 (m, 1 H)	1”, 6”
6”	128.2	7.88 – 7.85 (m, 1 H)	1”, 5”



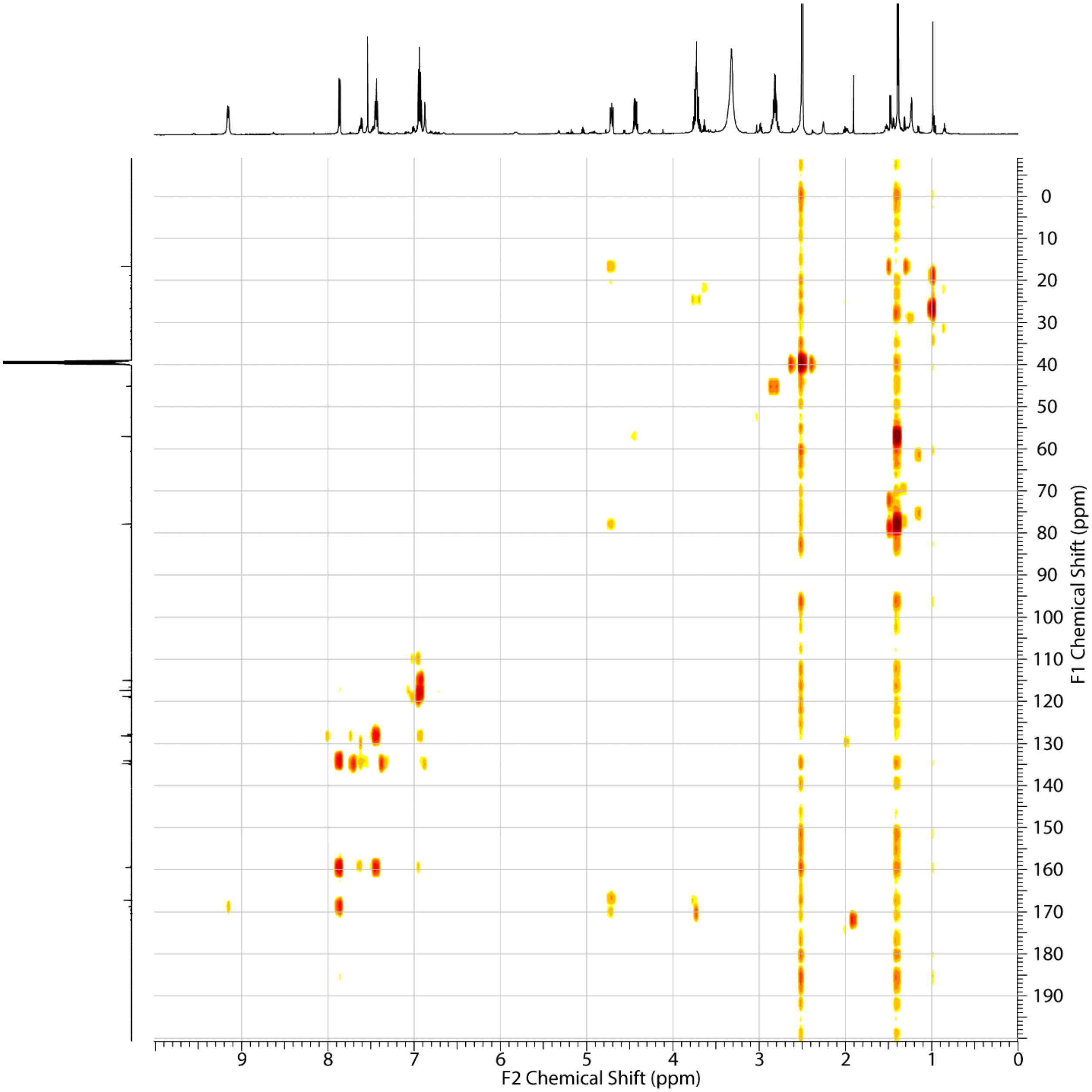
Supplementary Figure 32. ^{1}H-NMR spectrum (600 MHz) of compound **2e** in DMSO-*d*6.



Supplementary Figure 33. ^{13}C-NMR spectrum (600 MHz) of compound **2e** in DMSO-*d*6.

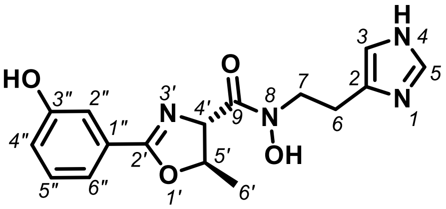


Supplementary Figure 34. gHSQC spectrum (600 MHz) of compound **2e** in DMSO-*d*6.



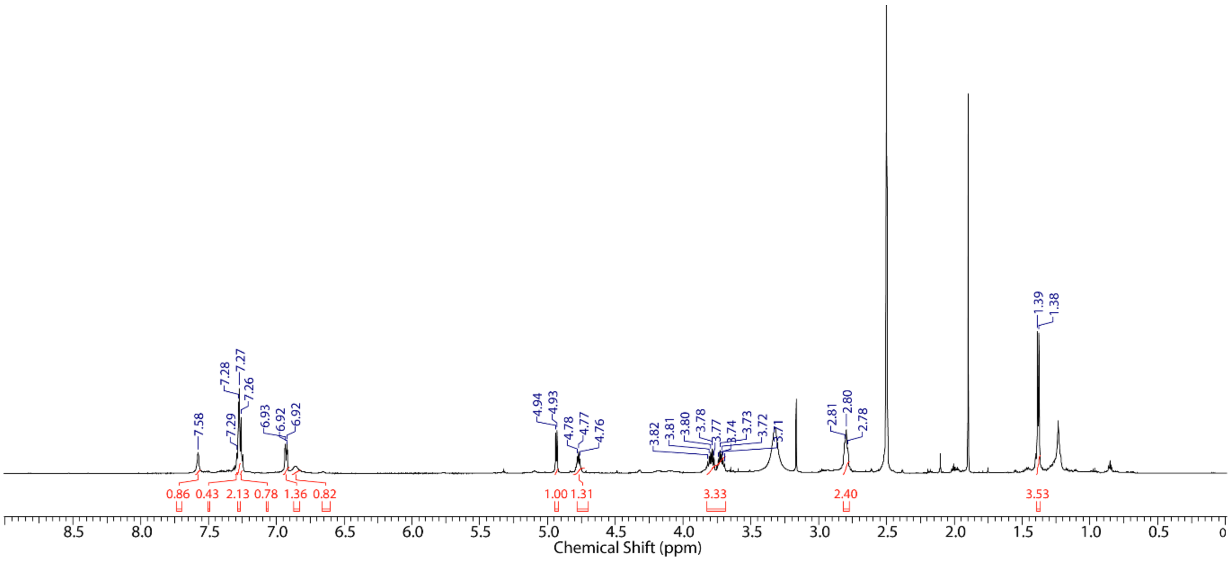
Supplementary Figure 35. HMBC spectrum (600 MHz) of compound **2e** in DMSO-*d*6.

Supplementary Table 10. NMR characterization data of compound **1f** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_4]^+$ ($[M+H]^+$) calculated: 331.1401, found: 331.1390.

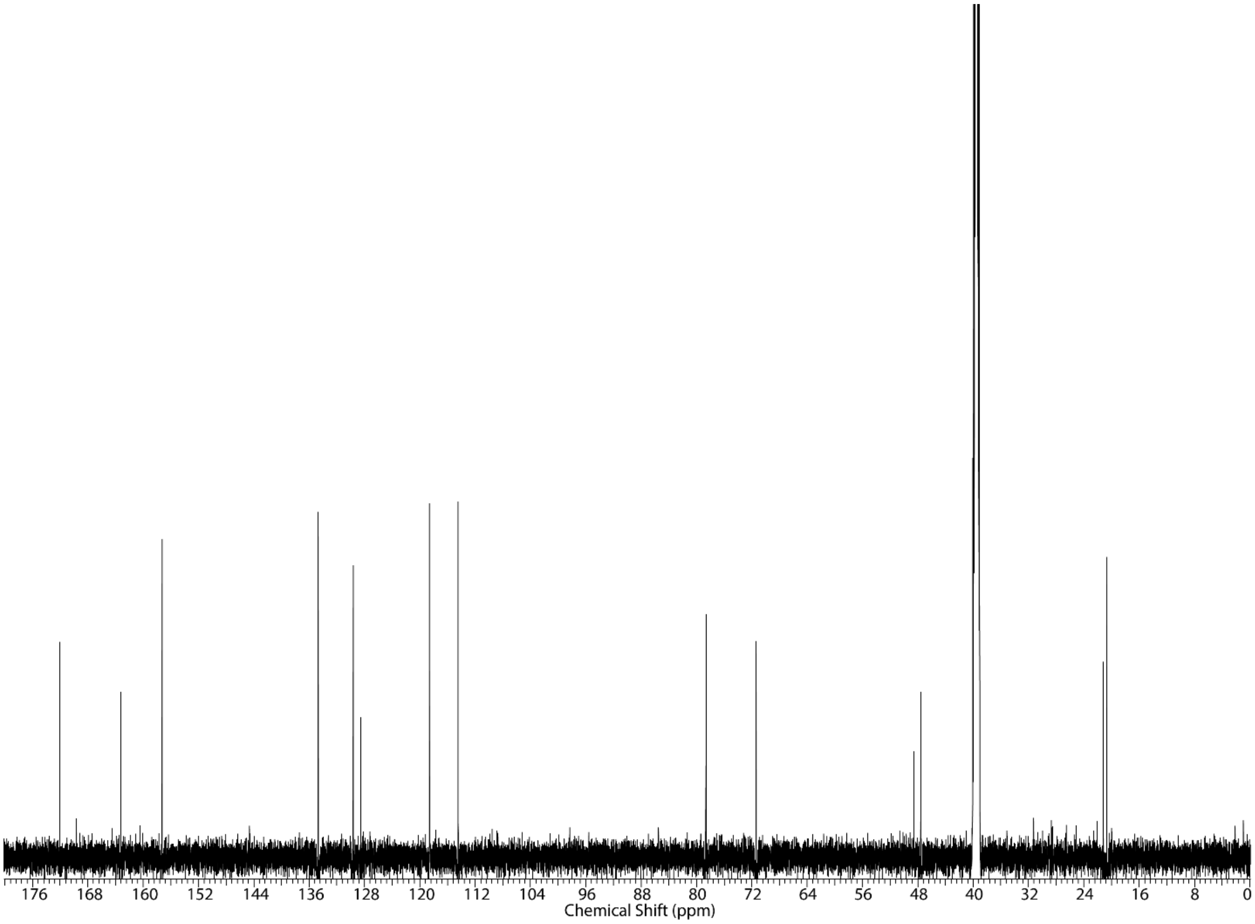


Compound **1f**

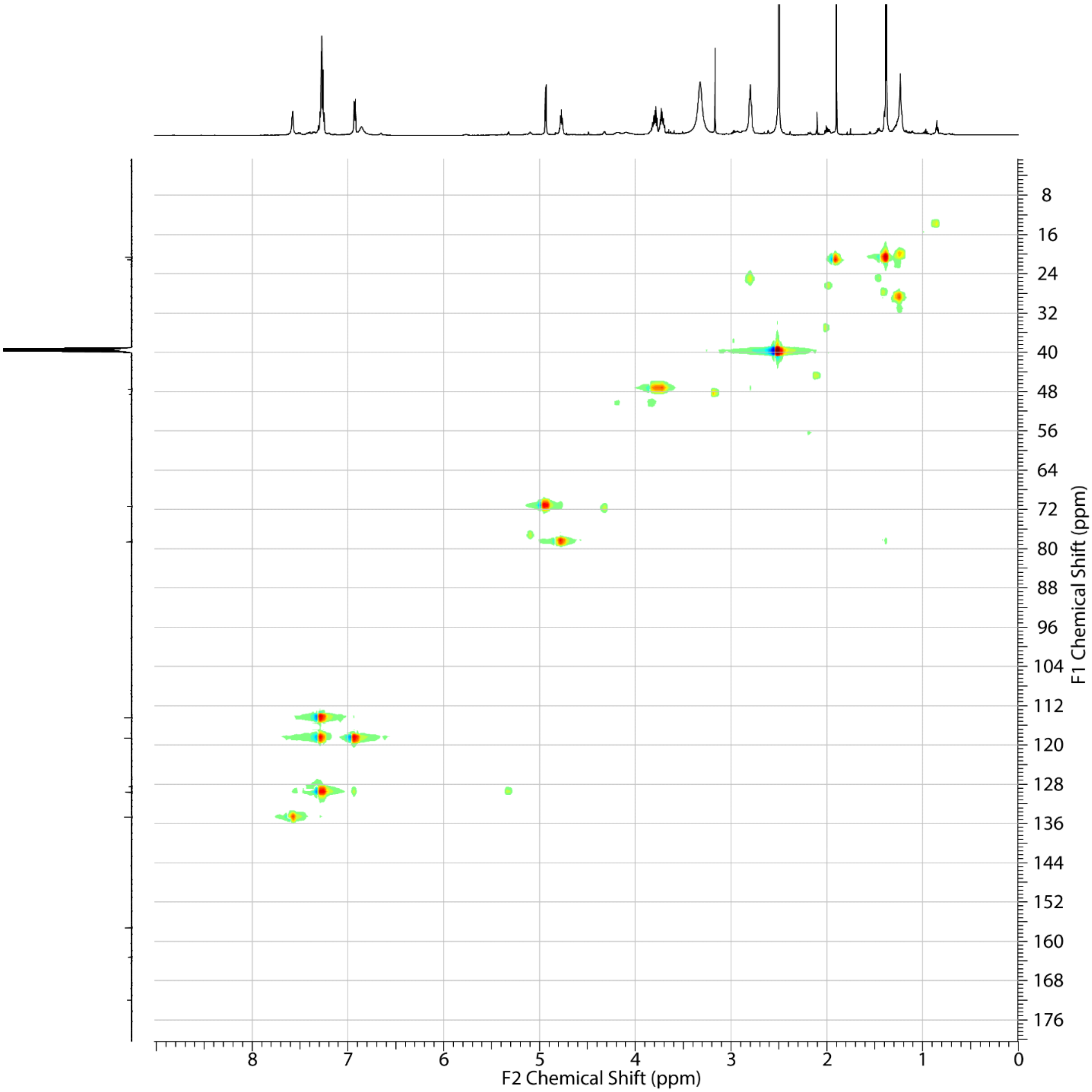
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
2	136.1		6, 7
3 or 5	134.6	7.58 (br. s., 1 H)	
6	24.8	2.80 (t, *J* = 7.1 Hz, 2 H)	2, 7
7	47.5	3.84 – 3.68 (m, 2 H)	2, 6, 9
9	169.6		4’, 7
2’	163.2		4’
4’	71.3	4.93 (d, *J* = 6.3 Hz, 1 H)	2’, 6’, 9
5’	78.6	4.80 – 4.74 (m, 1 H)	4’, 6’
6’	20.6	1.38 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
1”	157.1		2”
2”	129.5	7.26 (s, 1 H)	1”, 3”
3”	128.5		2”
4” + 5”	114.4 and 118.61	7.30 – 7.27 (m, 2 H)	6”
6”	118.63	6.95 – 6.91 (m, 1 H),	4” + 5”



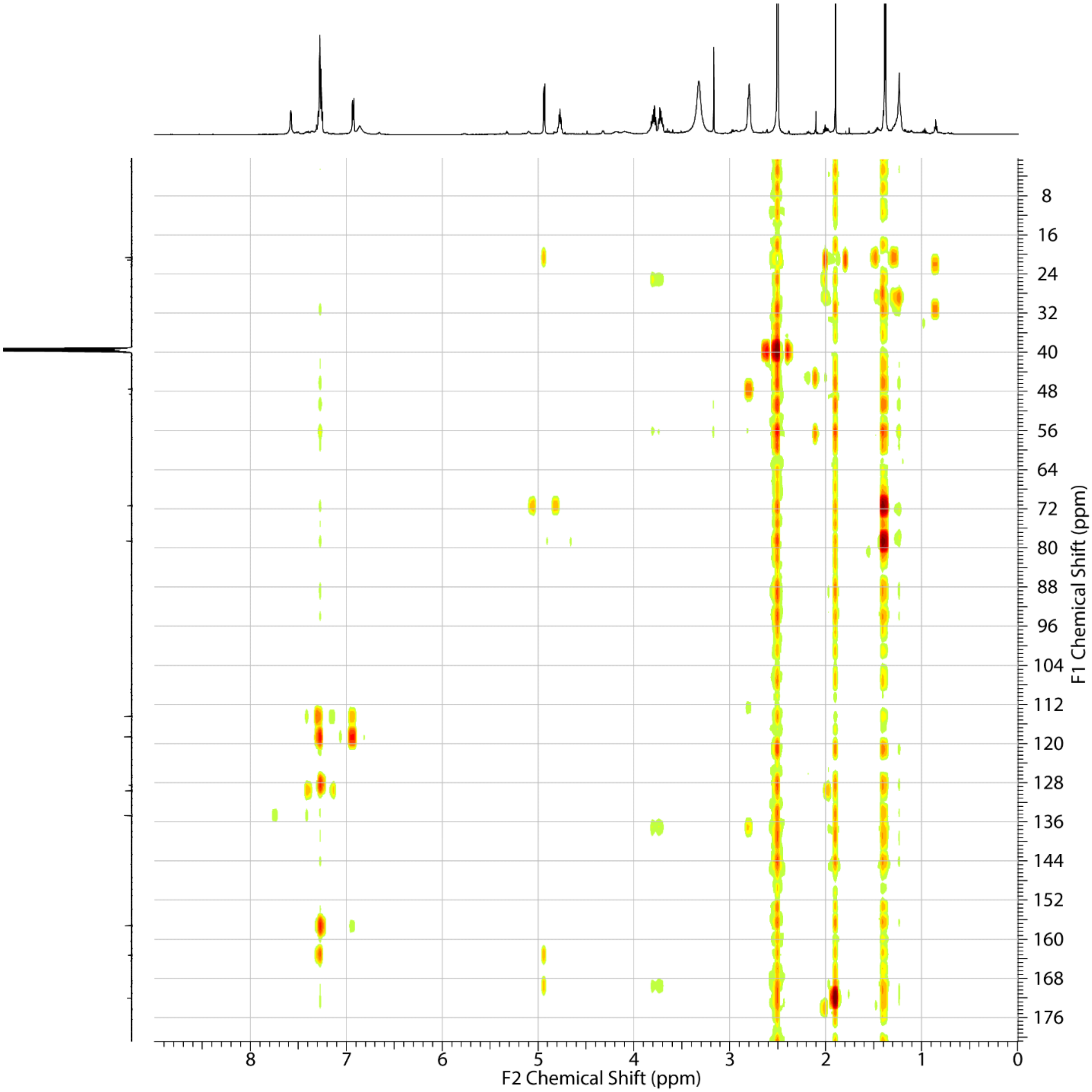
Supplementary Figure 36. ^{1}H-NMR spectrum (600 MHz) of compound **1f** in DMSO-*d*6.



Supplementary Figure 37. ^{13}C-NMR spectrum (600 MHz) of compound **1f** in DMSO-*d*6.

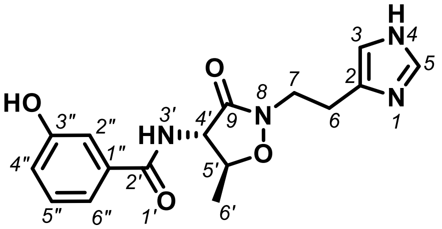


Supplementary Figure 38. gHSQC spectrum (600 MHz) of compound **1f** in DMSO-*d*6.



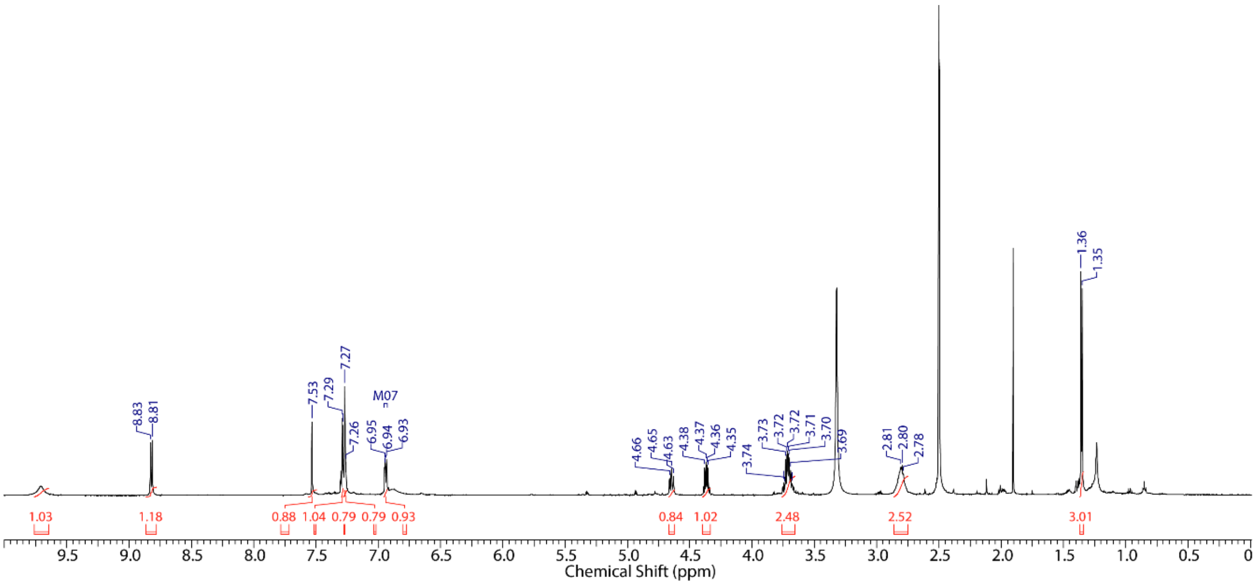
Supplementary Figure 39. HMBC spectrum (600 MHz) of compound **1f** in DMSO-*d*6.

Supplementary Table 11. NMR characterization data of compound **2f** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_4]^+$ ($[M+H]^+$) calculated: 331.1401, found: 331.1396.

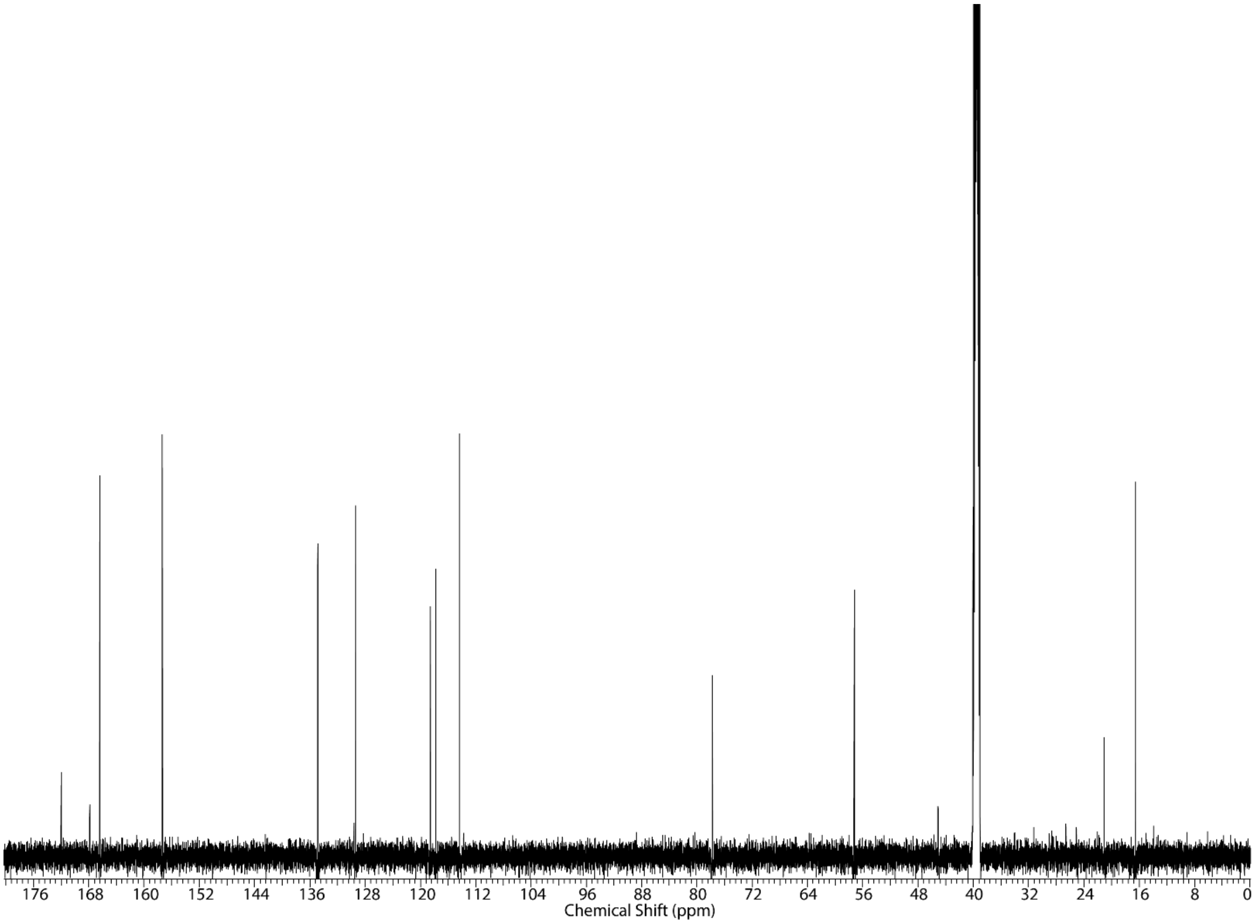


Compound **2f**

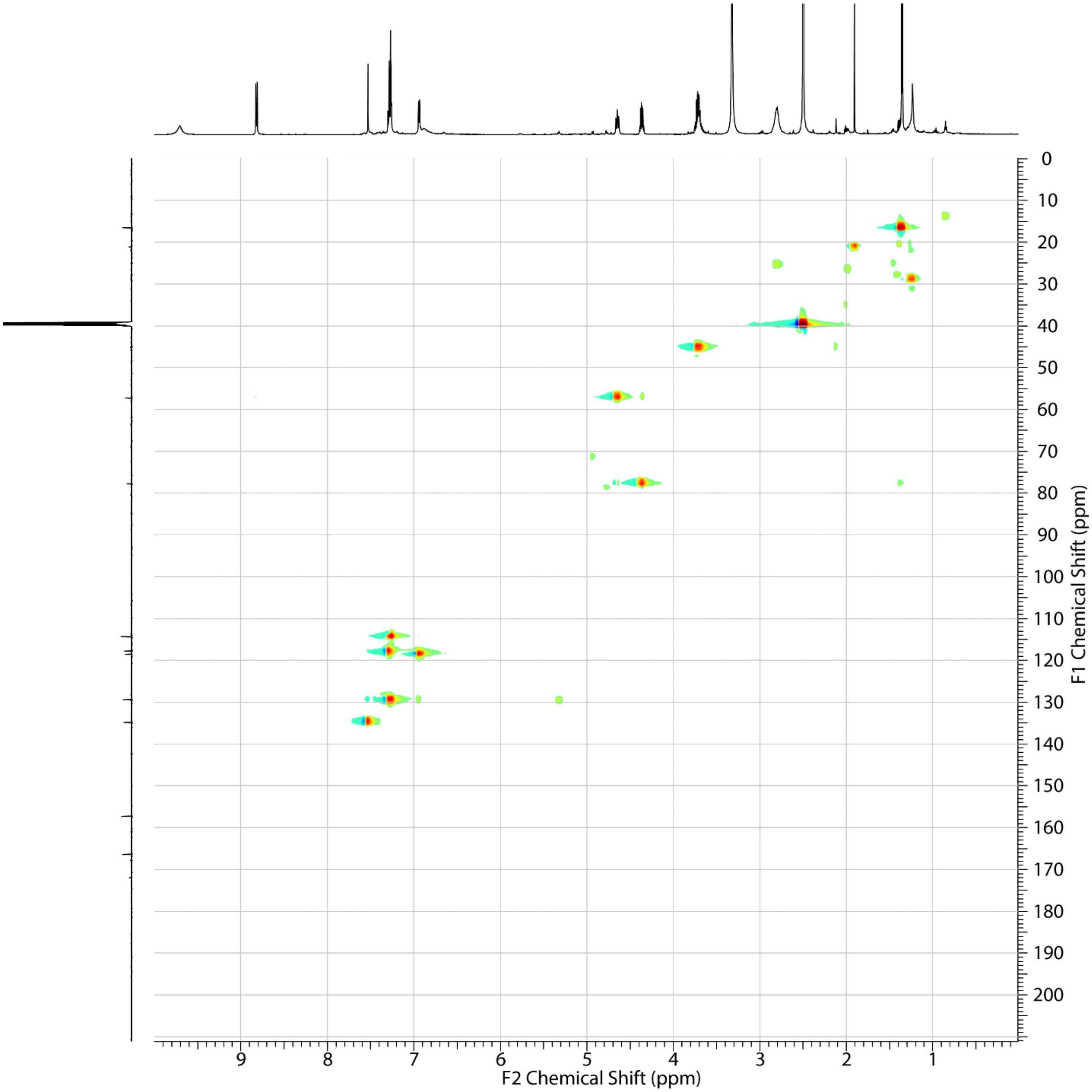
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
2	166.3		3, 5
3	129.3	7.27 (s, 1 H)	2
5		8.82 (d, *J* = 8.7 Hz, 2 H)	2
6	25.0	2.86 – 2.75 (m, 2 H)	7
7	44.8	3.76 – 3.66 (m, 2 H)	2, 6, 9
9	167.8		4’, 7
2’	157.2		6”
4’	57.2	4.67 – 4.62 (m, 1 H)	5’, 6’, 9
5’	77.7	4.37 (dd, *J* = 6.3, 11.0 Hz, 1 H)	4’, 6’
6’	16.5	1.36 (d, *J* = 5.5 Hz, 3 H)	4’, 5’
2”	134.8	7.53 (s, 1 H)	6”
4”	117.7	7.26 (m, 1 H)	5”, 6”
5”	118.5	6.95 – 6.93 (m, 1 H)	4”, 6”
6”	114.3	7.29 (d, *J* = 3.1 Hz, 1 H)	2’, 2”, 4”



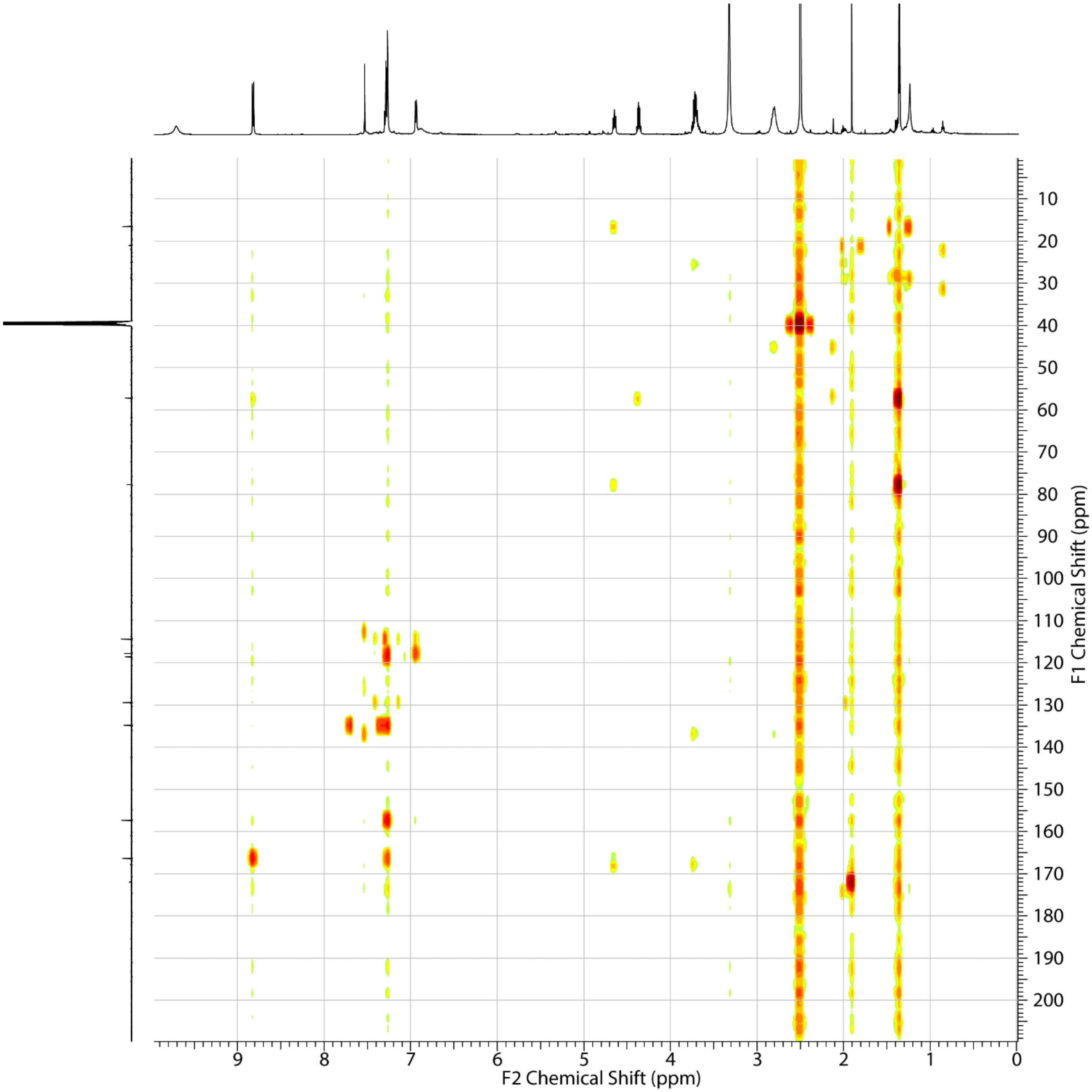
Supplementary Figure 40. ^{1}H-NMR spectrum (600 MHz) of compound **2f** in DMSO-*d*6.



Supplementary Figure 41. ^{13}C-NMR spectrum (600 MHz) of compound **2f** in DMSO-*d*6.

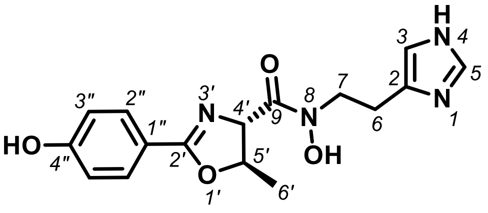


Supplementary Figure 42. gHSQC spectrum (600 MHz) of compound **2f** in DMSO-*d*6.



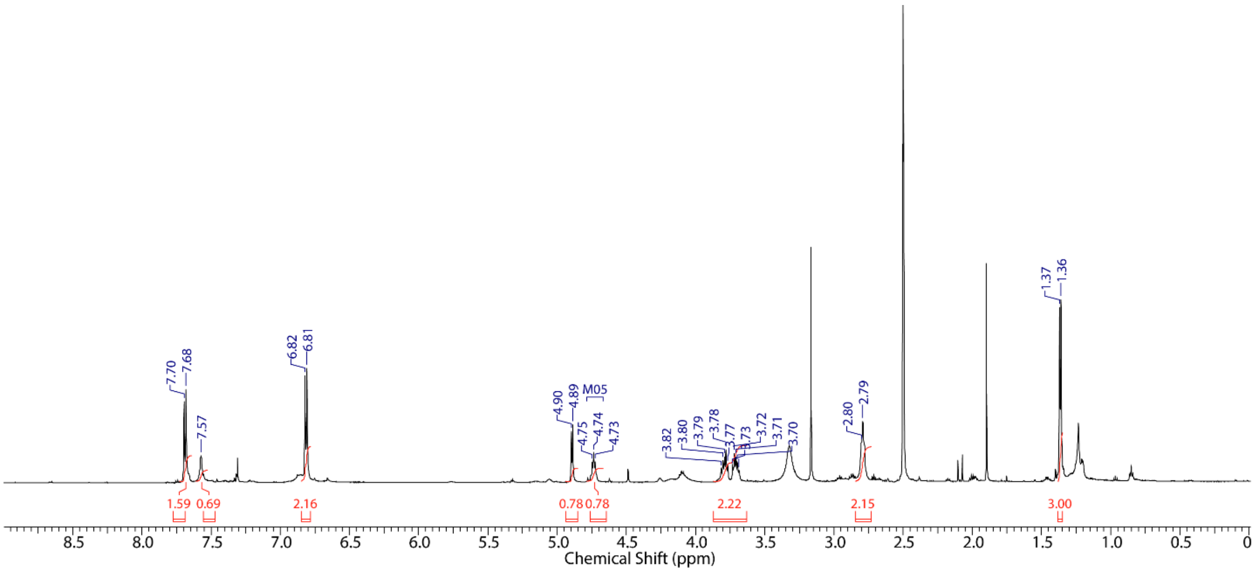
Supplementary Figure 43. HMBC spectrum (600 MHz) of compound **2f** in DMSO-*d*6.

Supplementary Table 12. NMR characterization data of compound **1g** in DMSO-*d*6. HRMS (ESI+) m/z for [$C_{16}H_{19}N_4O_4$]$^+$ ([M+H]$^+$) calculated: 331.1401, found: 331.1390.

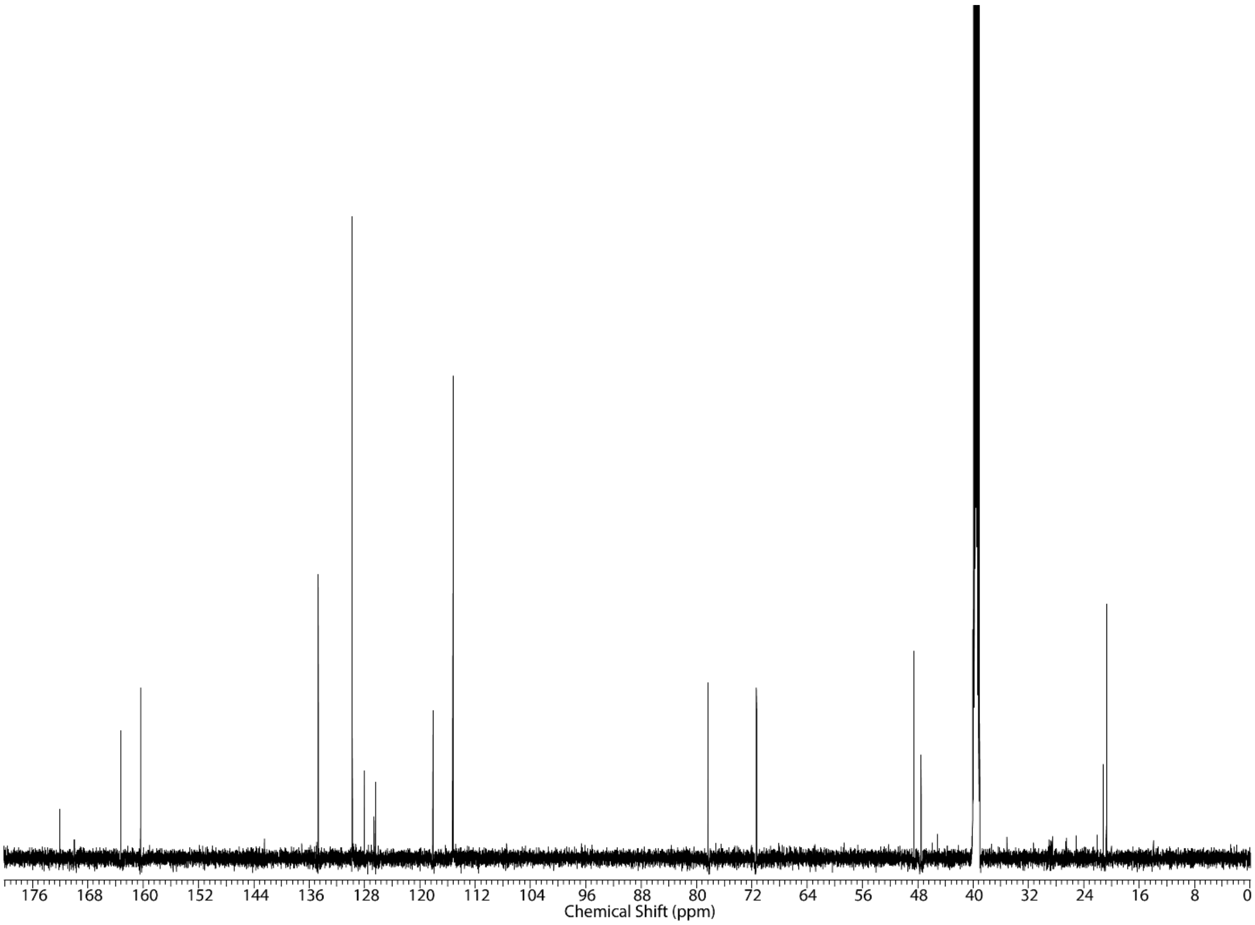


Compound **1g**

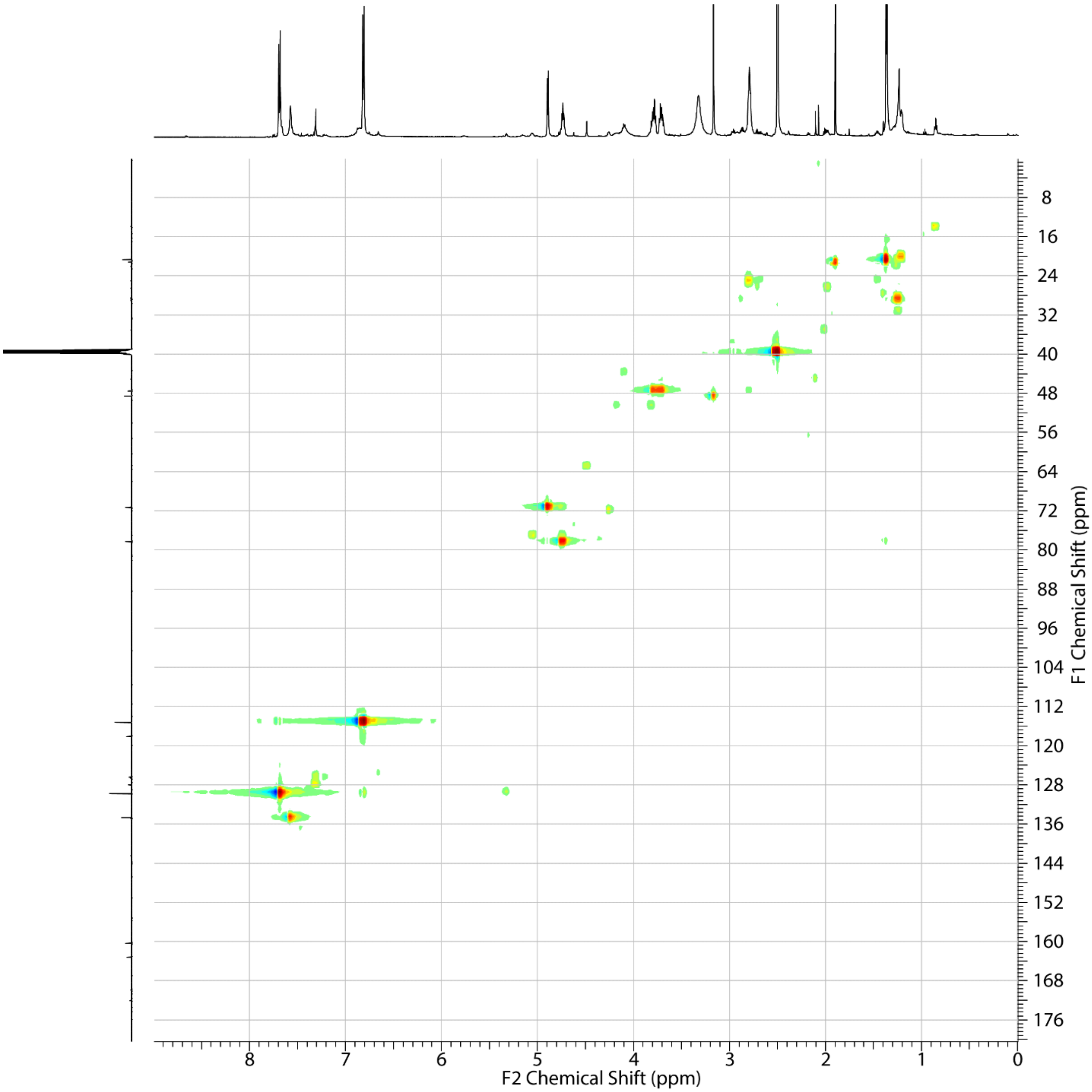
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.7	7.57 (br. s., 1 H)	
6	25.0	2.84 – 2.73 (m, 2 H)	7, 2
7	47.5	3.87 – 3.63 (m, 2 H)	6, 2
9	169.6		4’, 5’
2’	160.2		2”, 3”
4’	71.2	4.89 (d, *J* = 6.3 Hz, 1 H)	6’, 9
5’	78.2	4.74 (t, *J* = 5.9 Hz, 1 H)	4’, 6’, 9
6’	20.6	1.37 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	129.7	7.69 (d, *J* = 8.7 Hz, 2 H)	2’
3”	115.2	6.81 (d, *J* = 8.7 Hz, 2 H)	2’, 4”
4”	118.0		3”



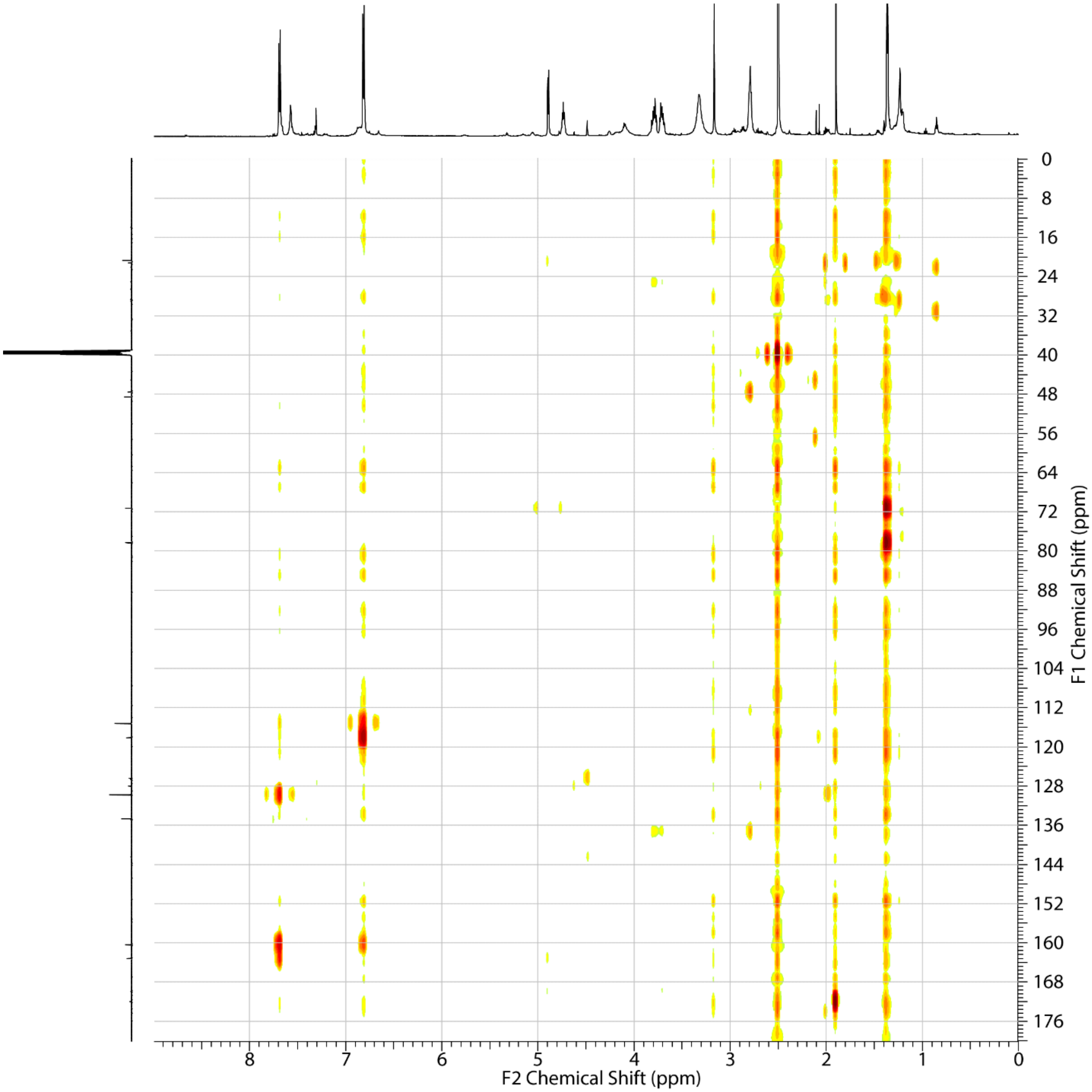
Supplementary Figure 44. ^{1}H-NMR spectrum (600 MHz) of compound **1g** in DMSO-*d*6.



Supplementary Figure 45. ^{13}C-NMR spectrum (600 MHz) of compound **1g** in DMSO-*d*6.

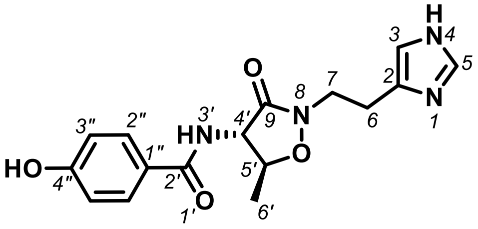


Supplementary Figure 46. gHSQC spectrum (600 MHz) of compound **1g** in DMSO-*d*6.



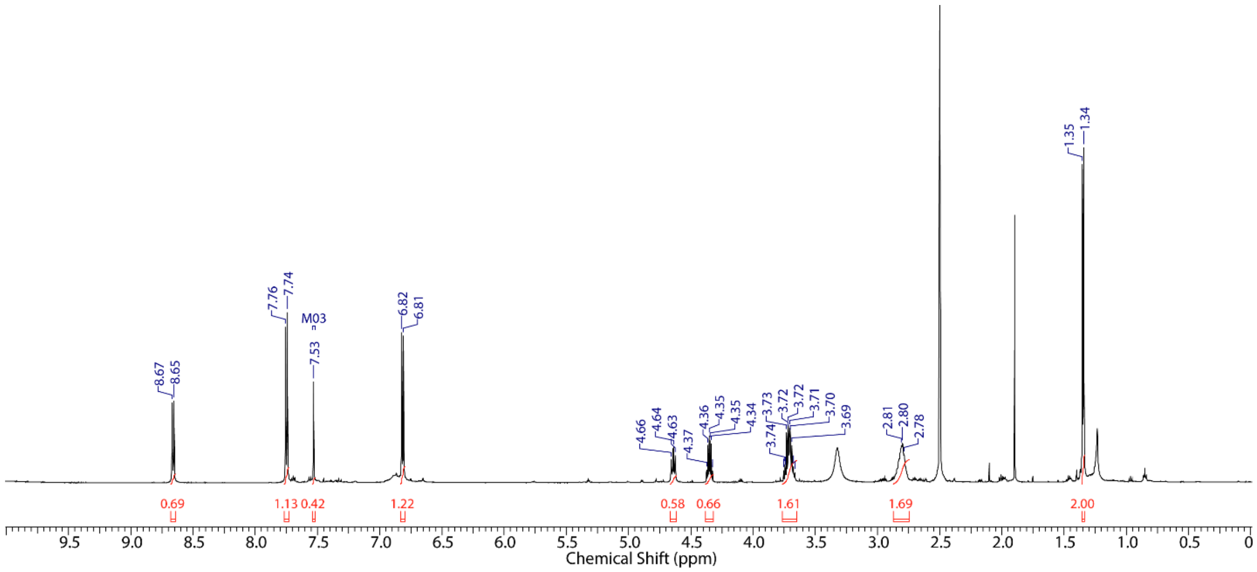
Supplementary Figure 47. HMBC spectrum (600 MHz) of compound **1g** in DMSO-*d*6.

Supplementary Table 13. NMR characterization data of compound **2g** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_4]^+$ ($[M+H]^+$) calculated: 331.1401, found: 331.1396.

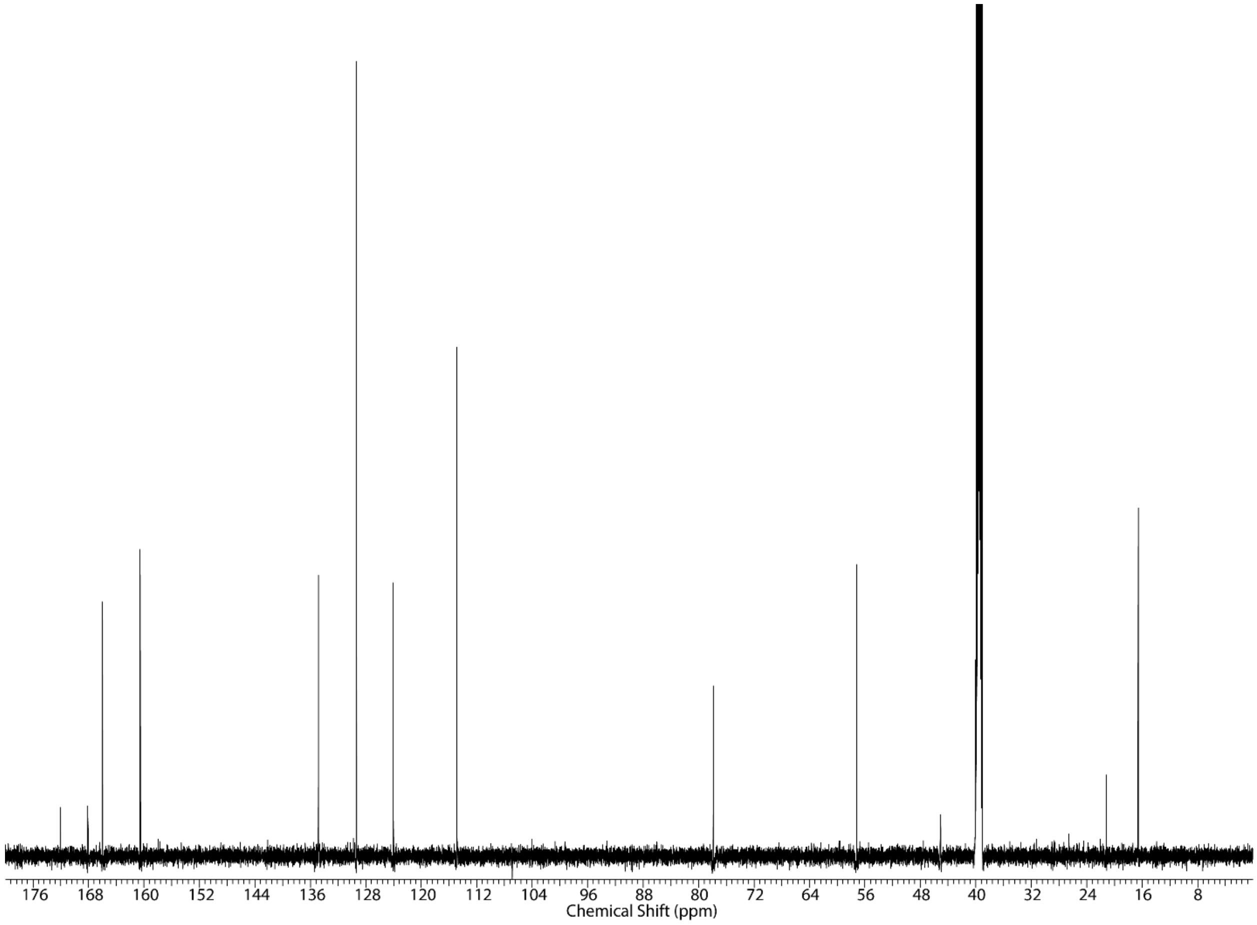


Compound **2g**

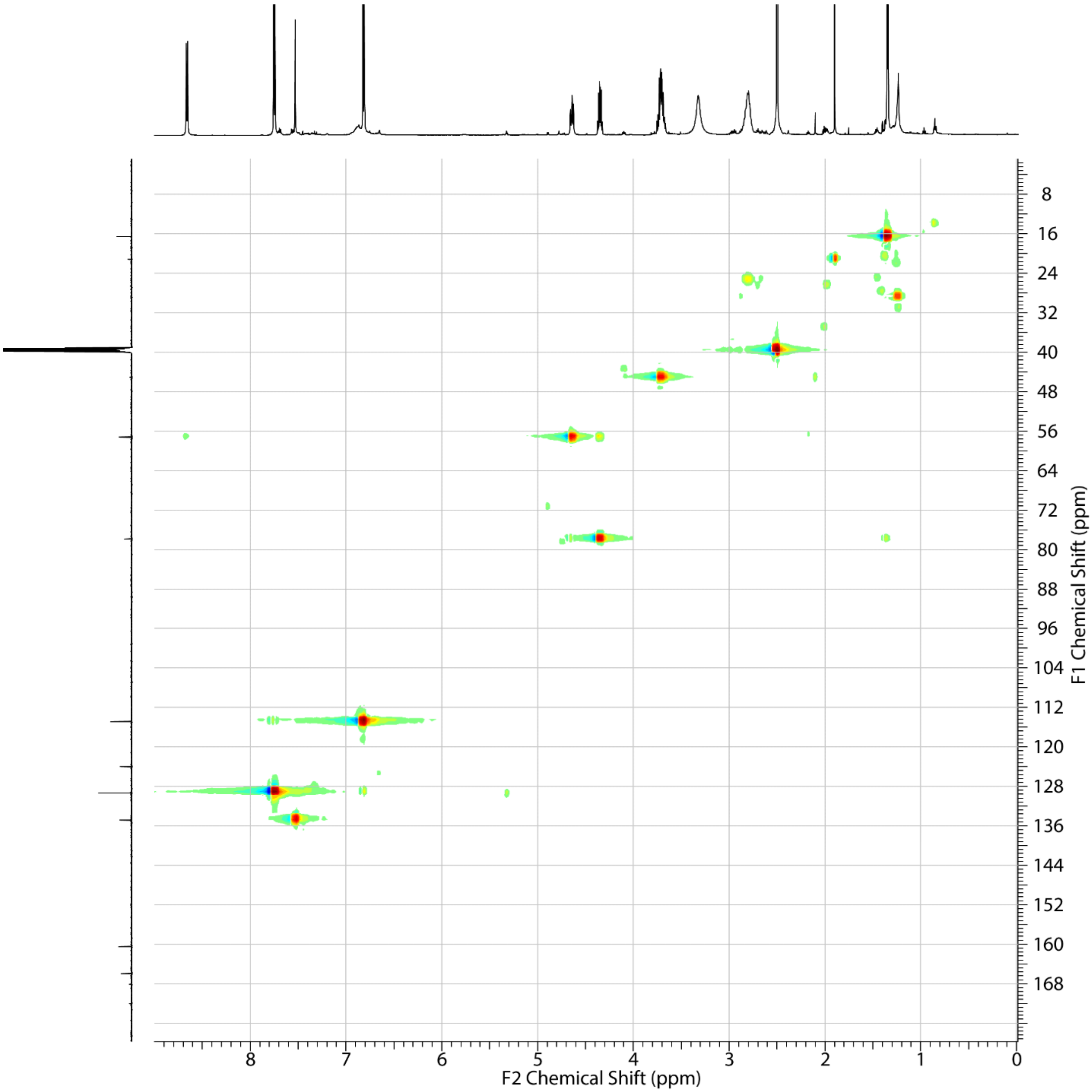
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3	134.9	7.53 (s, 1 H)	
5		8.66 (d, *J* = 8.7 Hz, 1 H)	
6	25.1	2.87 – 2.74 (m, 2 H)	7
7	44.9	3.77 – 3.65 (m, 2 H)	2, 6, 9
9	167.8		7, 4’
2’	160.5		2”, 3”
4’	57.1	4.66 – 4.62 (m, 1 H)	5’, 6’, 9
5’	77.8	4.38 – 4.32 (m, 1 H)	4’, 6’
6’	16.5	1.35 (d, *J* = 6.3 Hz, 2 H)	4’, 5’
2”	129.2	7.75 (d, *J* = 8.7 Hz, 2 H)	2’
3”	114.8	6.82 (d, *J* = 8.7 Hz, 2 H)	2’, 4”
4”	124.0		3”



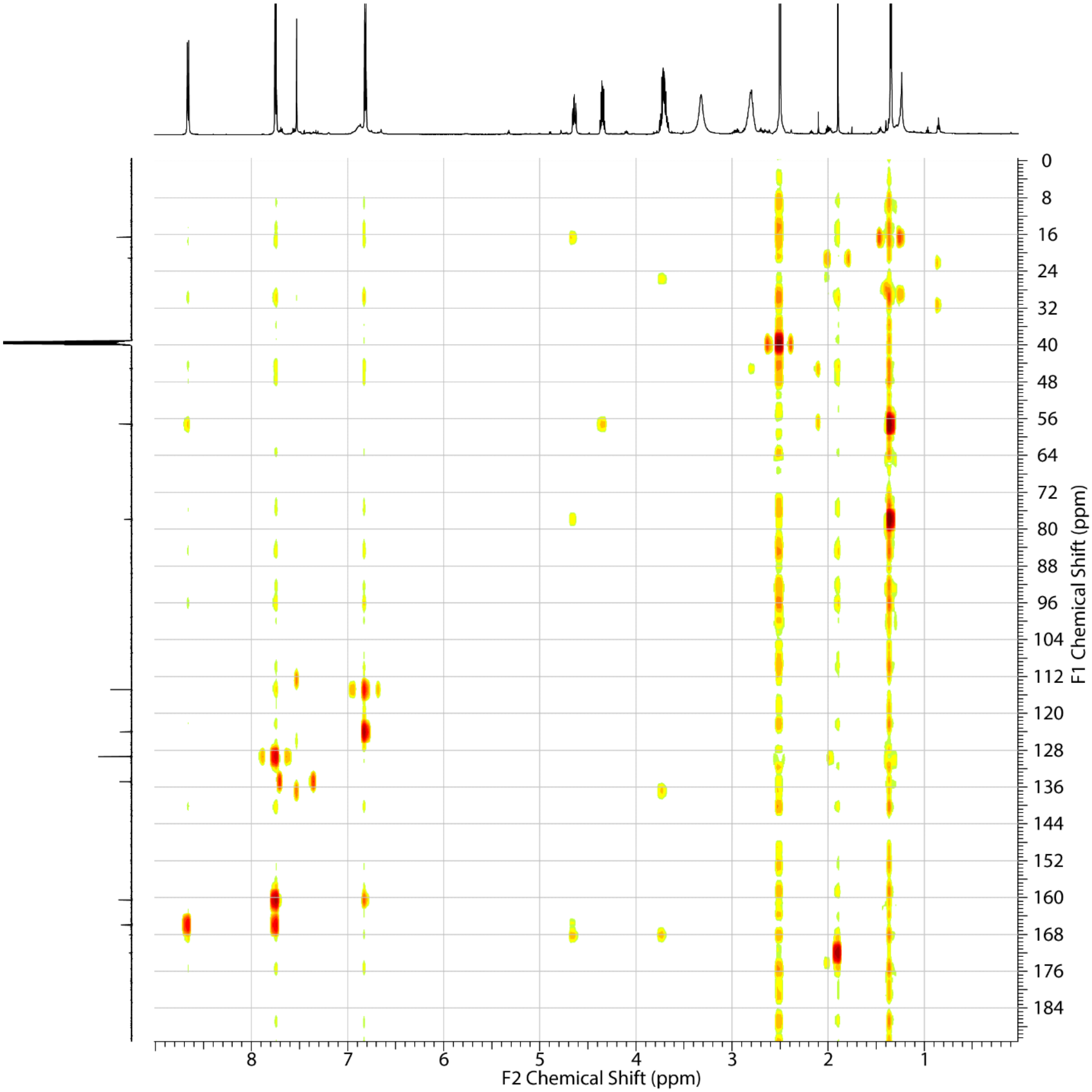
Supplementary Figure 48. ^{1}H-NMR spectrum (600 MHz) of compound **2g** in DMSO-*d*6.



Supplementary Figure 49. ^{13}C-NMR spectrum (600 MHz) of compound **2g** in DMSO-*d*6.

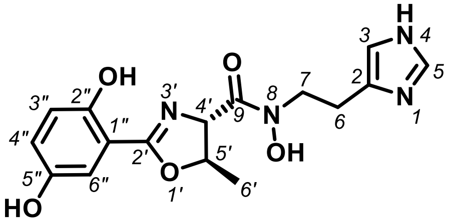


Supplementary Figure 50. gHSQC spectrum (600 MHz) of compound **2g** in DMSO-*d*6.



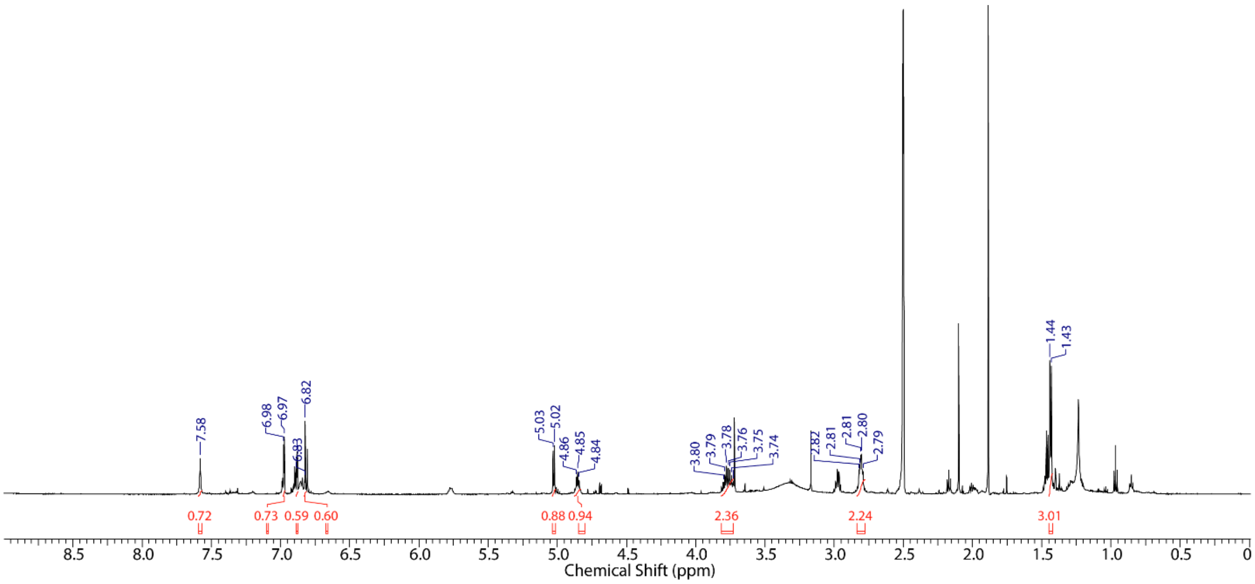
Supplementary Figure 51. HMBC spectrum (600 MHz) of compound **2g** in DMSO-*d*6.

Supplementary Table 14. NMR characterization data of compound **1h** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_5]^+$ ($[M+H]^+$) calculated: 347.1350, found: 347.1338.

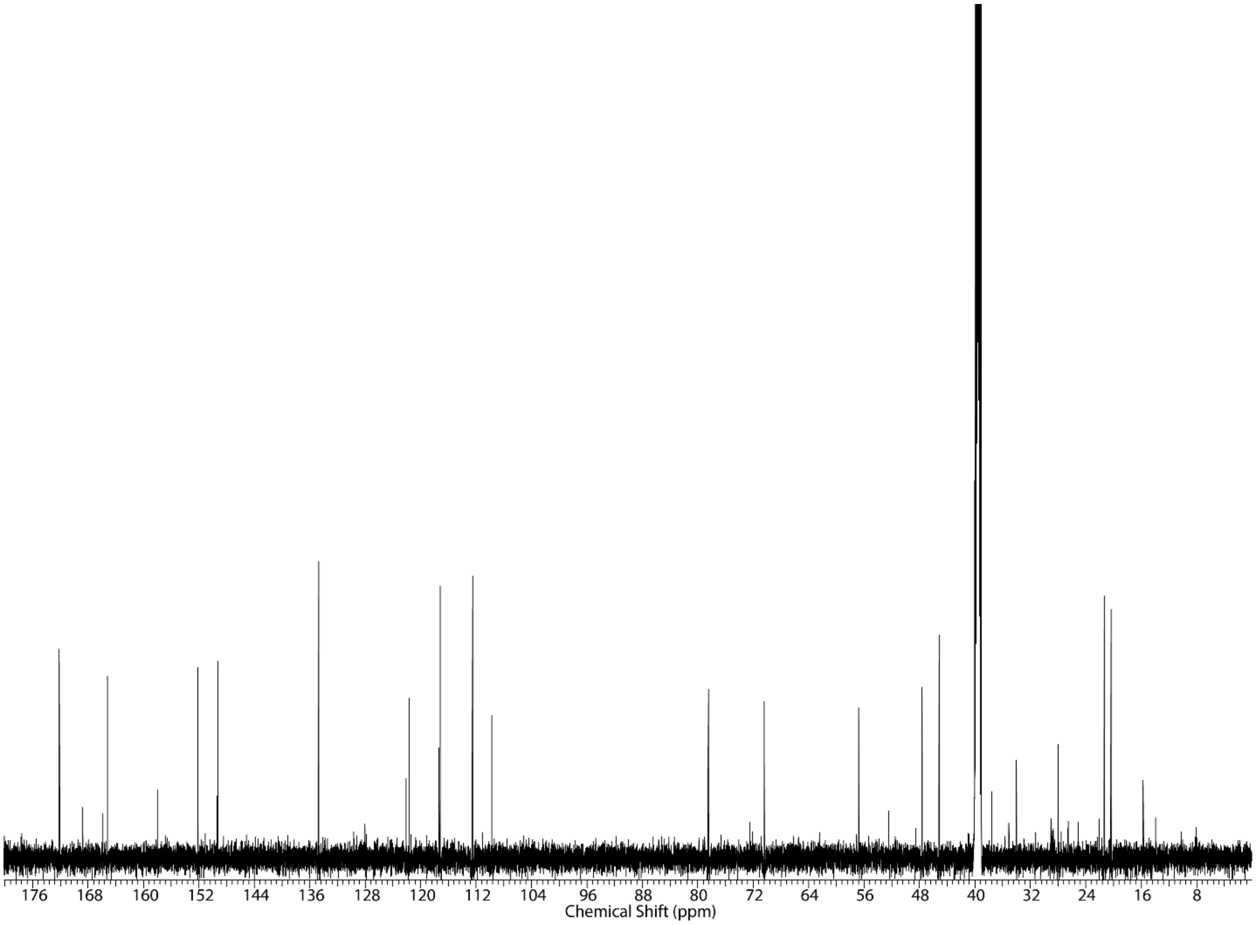


Compound **1h**

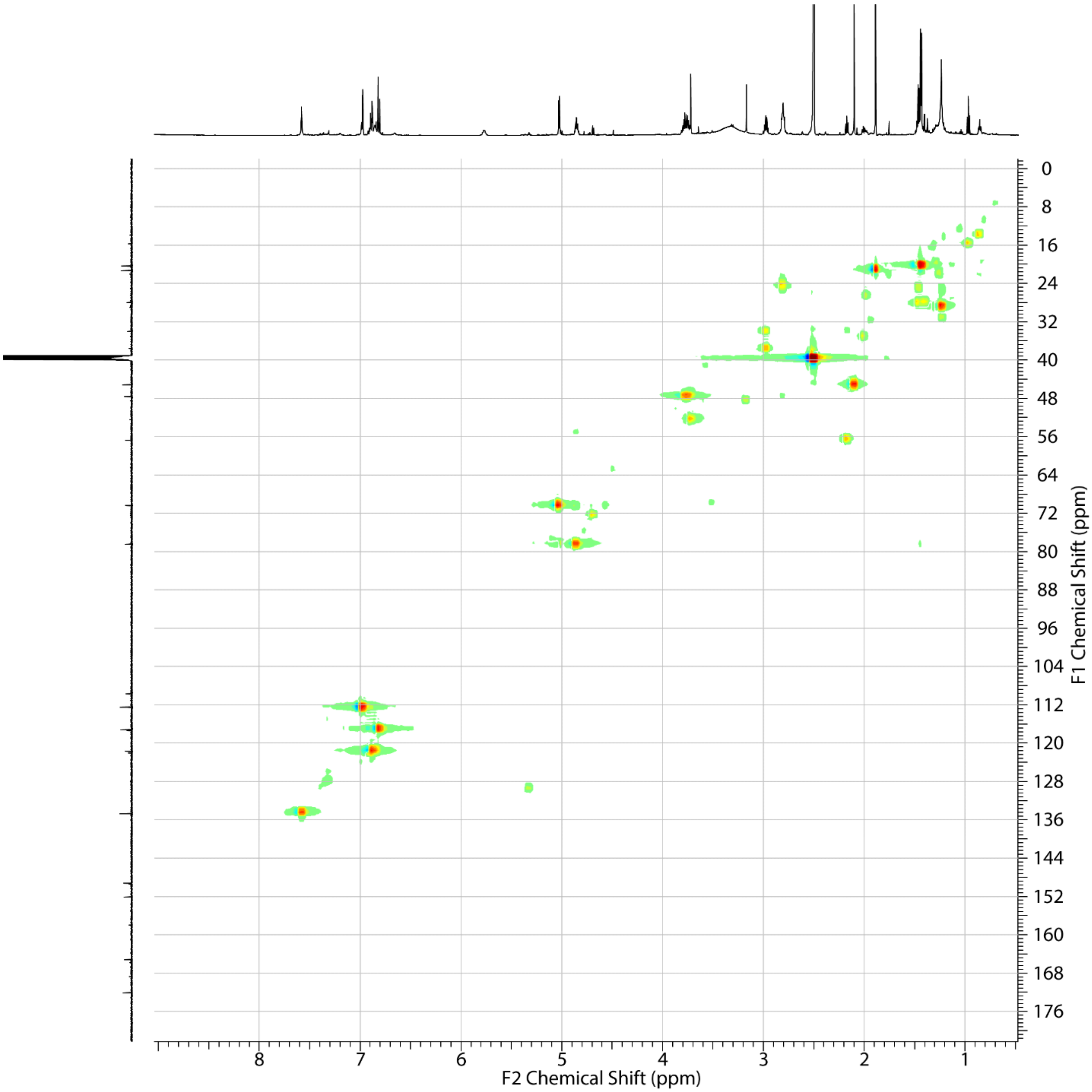
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.6	7.58 (s, 1 H)	
6	24.1	2.84 – 2.78 (m, 2 H)	7
7	47.6	3.82 – 3.73 (m, 2 H)	6, 9
9	168.7		7, 4’
2’	165.1		4’
4’	70.3	5.03 (d, *J* = 5.5 Hz, 1 H)	6’, 9
5’	78.4	4.85 (t, *J* = 5.9 Hz, 1 H)	6’
6’	20.4	1.44 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
3”	112.5	6.97 (d, *J* = 3.1 Hz, 1 H)	4”, 5”
4”	121.6	6.88 (d, *J* = 3.1 Hz, 1 H)	3”, 5”
5”	152.1		3”, 4”, 6”
6”	117.1	6.83 – 6.81 (m, 1 H)	5”



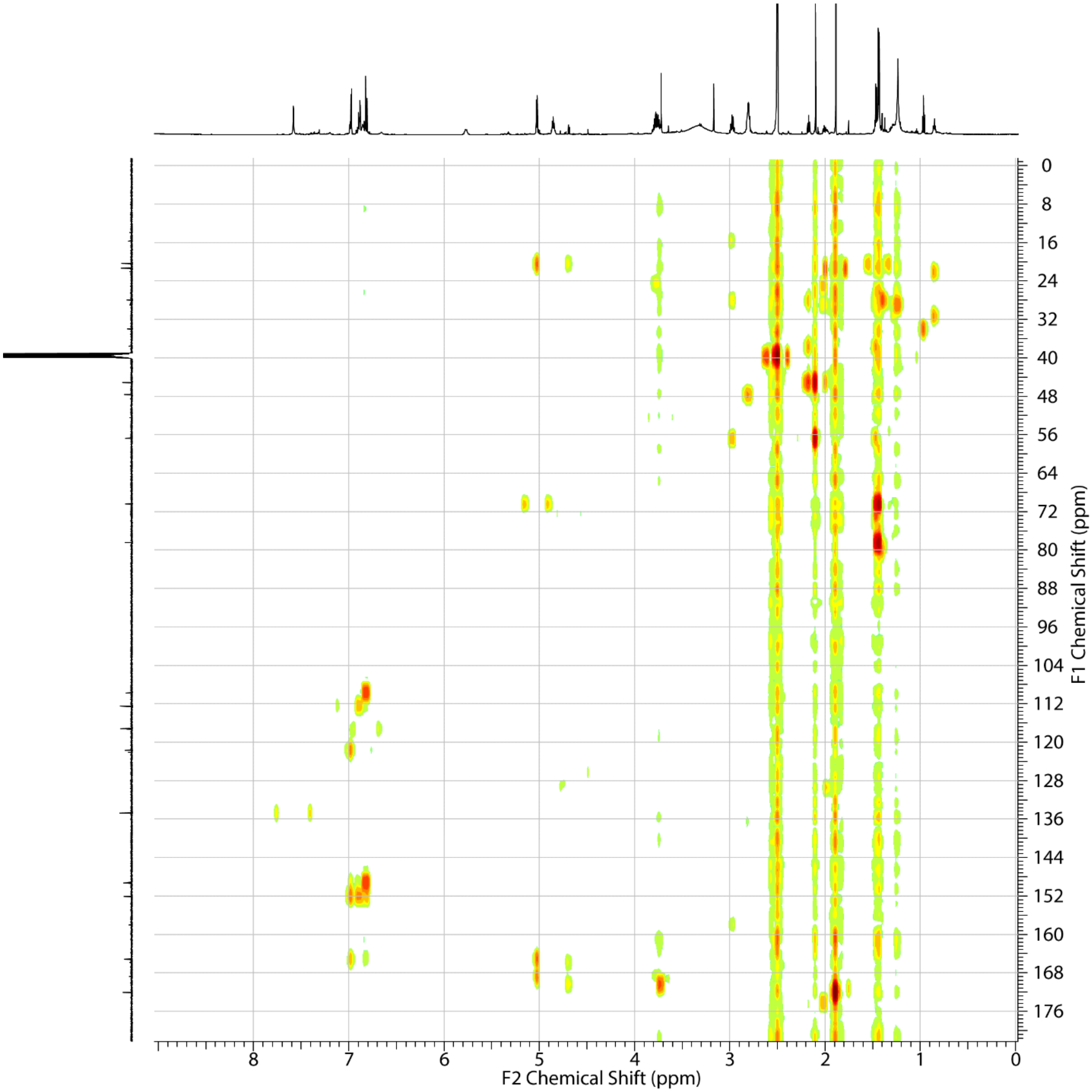
Supplementary Figure 52. ^{1}H-NMR spectrum (600 MHz) of compound **1h** in DMSO-*d*6.



Supplementary Figure 53. ^{13}C-NMR spectrum (600 MHz) of compound **1h** in DMSO-*d*6.

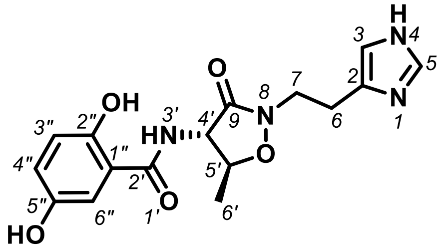


Supplementary Figure 54. gHSQC spectrum (600 MHz) of compound **1h** in DMSO-*d*6.



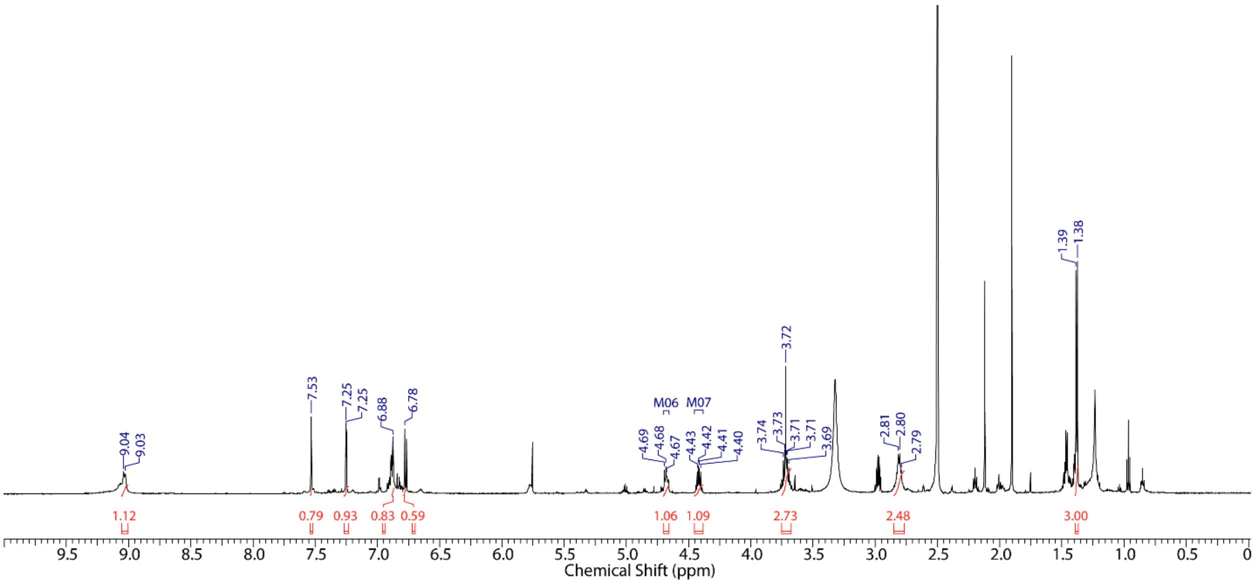
Supplementary Figure 55. HMBC spectrum (600 MHz) of compound **1h** in DMSO-*d*6.

Supplementary Table 15. NMR characterization data of compound **2h** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_5]^+$ ($[M+H]^+$) calculated: 347.1350, found: 347.1345.

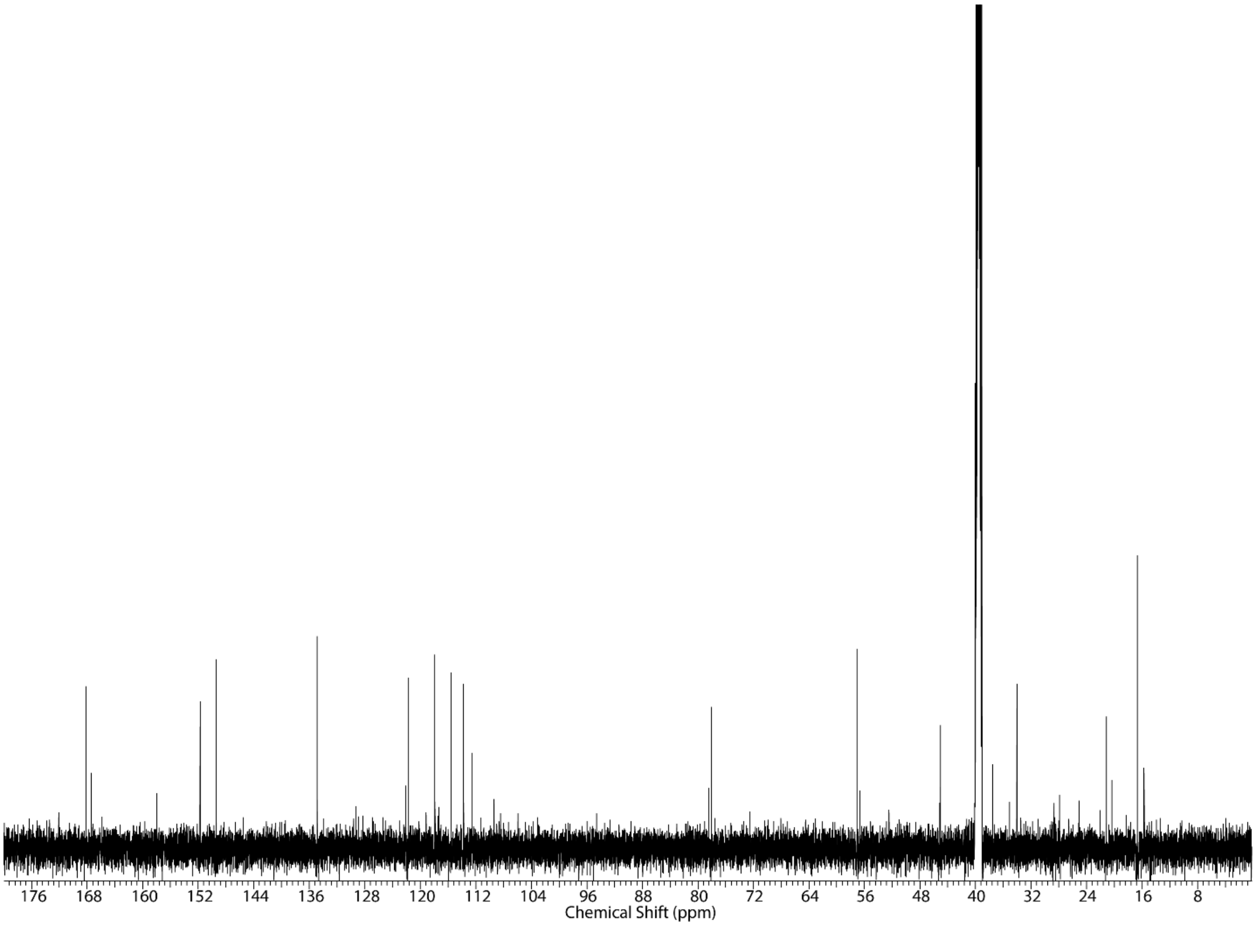


Compound **2h**

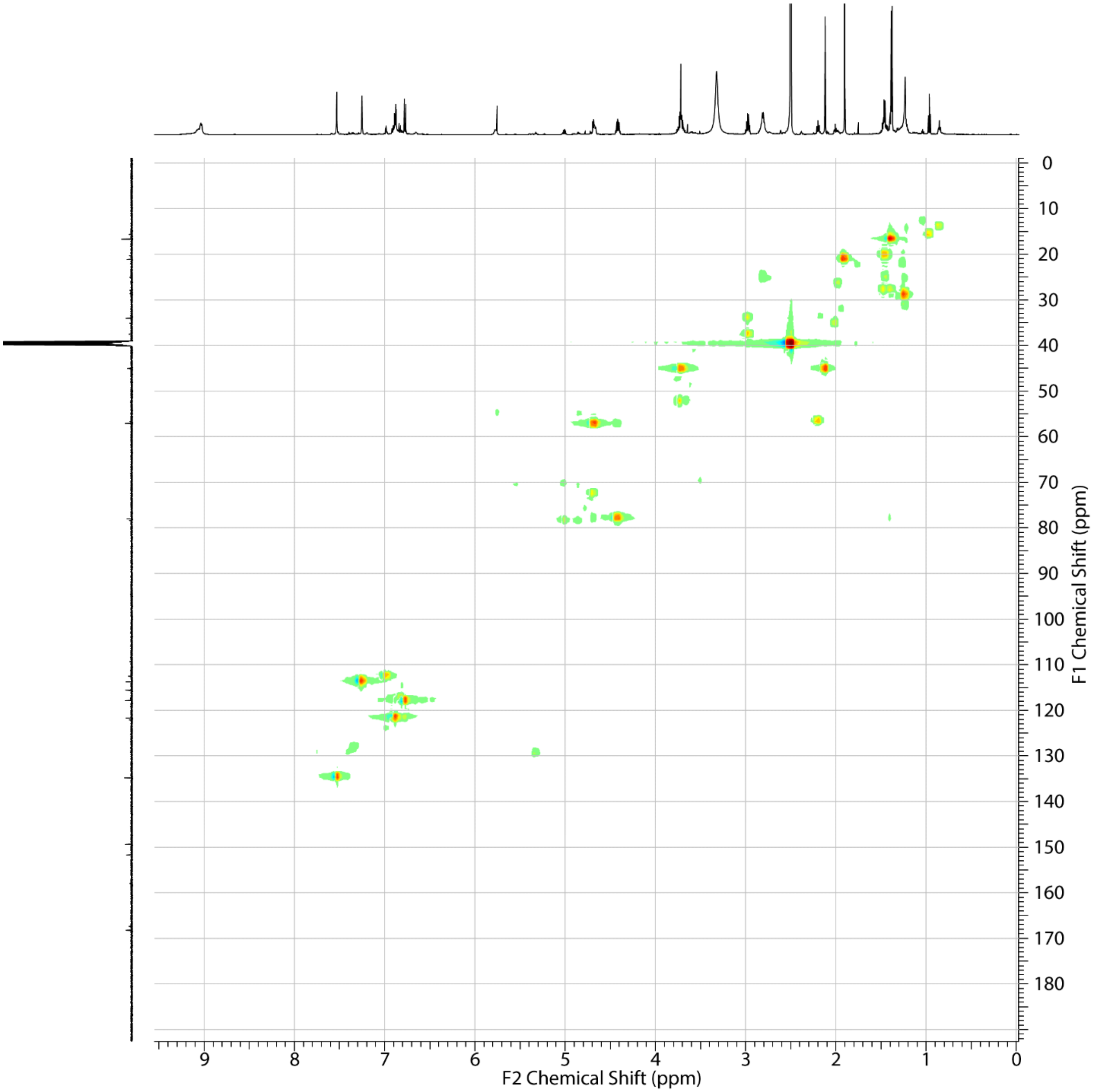
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.7	7.53 (s, 1 H)	
6	24.8	2.85 – 2.77 (m, 2 H)	7
7	44.6	3.75 – 3.68 (m, 2 H)	6
2'	168.2		3', 3"
3'		9.03 (d, *J* = 7.1 Hz, 1 H)	2'
4'	57.0	4.70 – 4.66 (m, 1 H)	5', 6'
5'	77.9	4.42 (dd, *J* = 6.3, 11.0 Hz, 1 H)	4', 6'
6'	16.6	1.38 (d, *J* = 6.3 Hz, 3 H)	4', 5'
3"	113.7	7.25 (d, *J* = 2.4 Hz, 1 H)	4", 5"
4"	121.6	6.87 (d, *J* = 3.1 Hz, 1 H)	3", 5"
5"	151.6		3", 4", 6"
6"	117.6	6.78 (s, 1 H)	5"



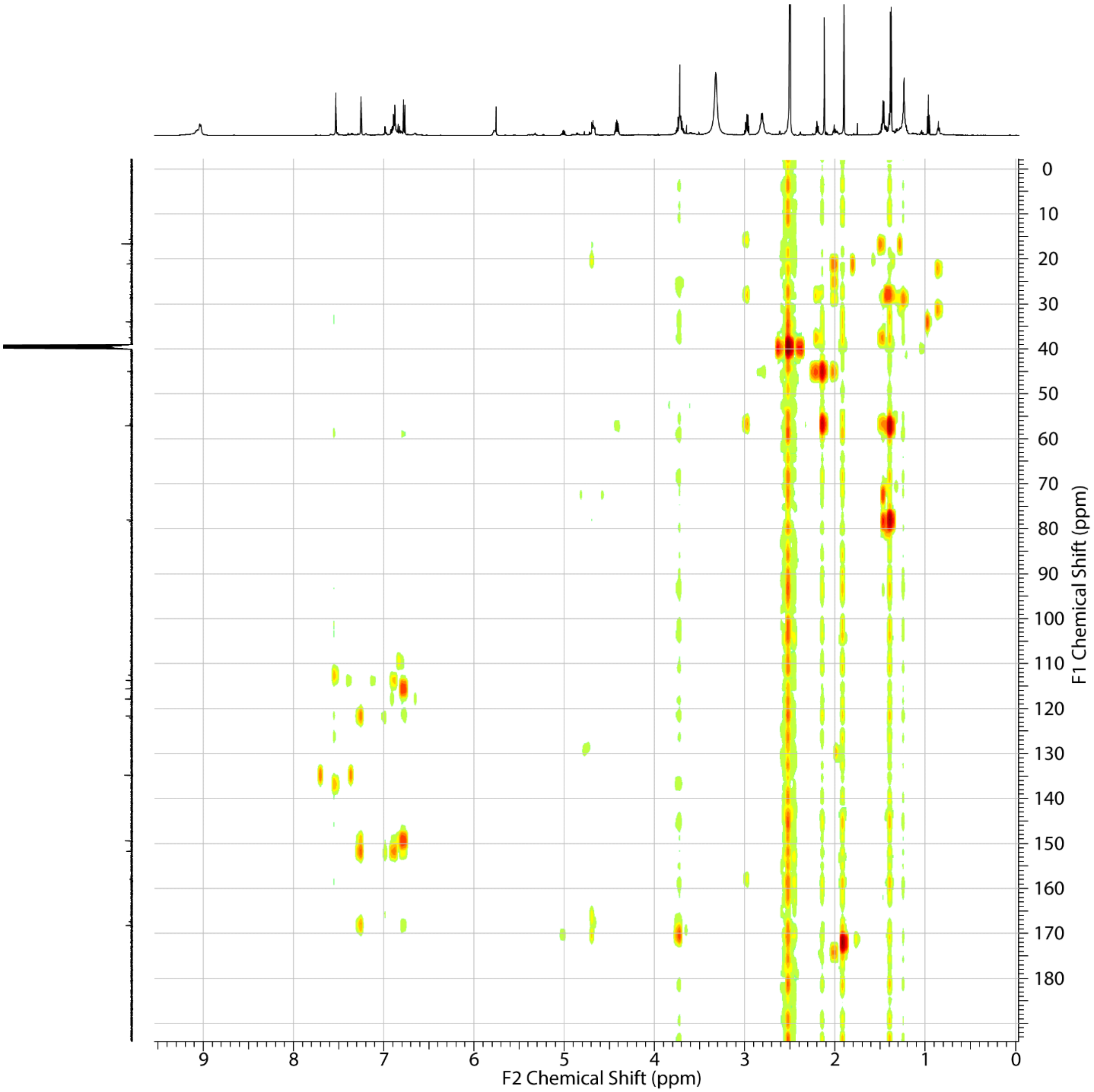
Supplementary Figure 56. ^{1}H-NMR spectrum (600 MHz) of compound **2h** in DMSO-*d*6.



Supplementary Figure 57. ^{13}C-NMR spectrum (600 MHz) of compound **2h** in DMSO-*d*6.

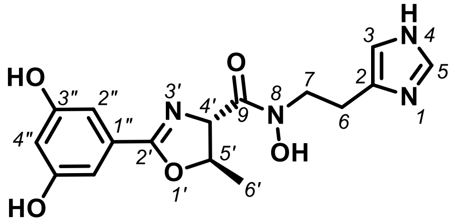


Supplementary Figure 58. gHSQC spectrum (600 MHz) of compound **2h** in DMSO-*d*6.



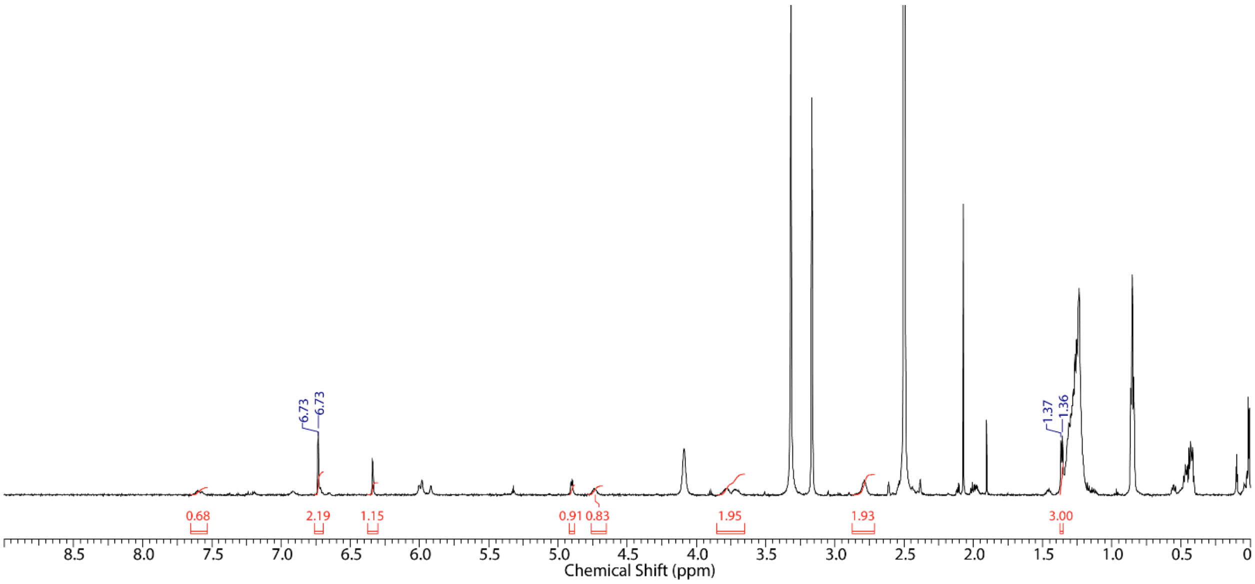
Suppplementary Figure 59. HMBC spectrum (600 MHz) of compound **2h** in DMSO-*d*6.

Supplementary Table 16. NMR characterization data of compound **1i** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_5]^+$ ($[M+H]^+$) calculated: 347.1350, found: 347.1142.

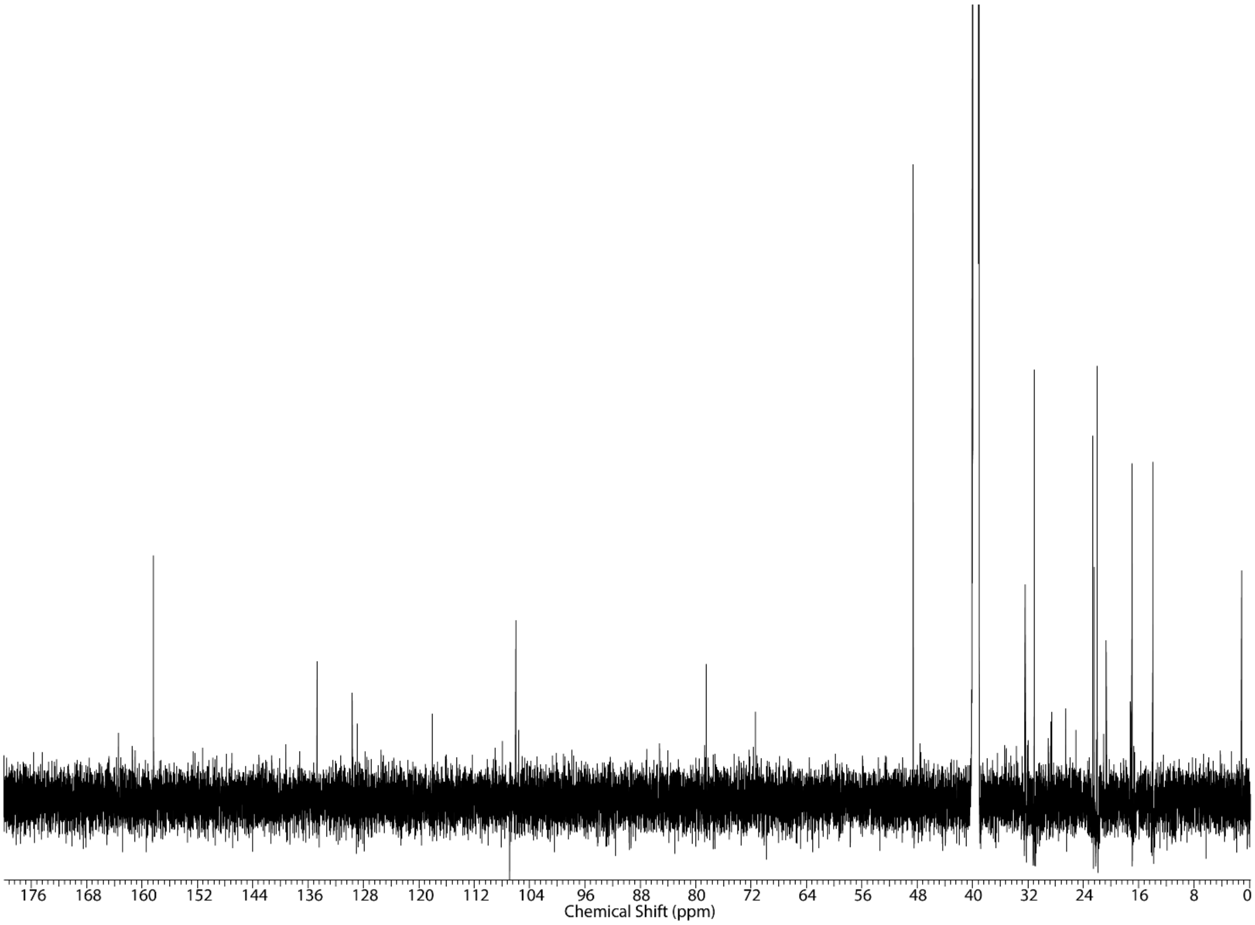


Compound **1i**

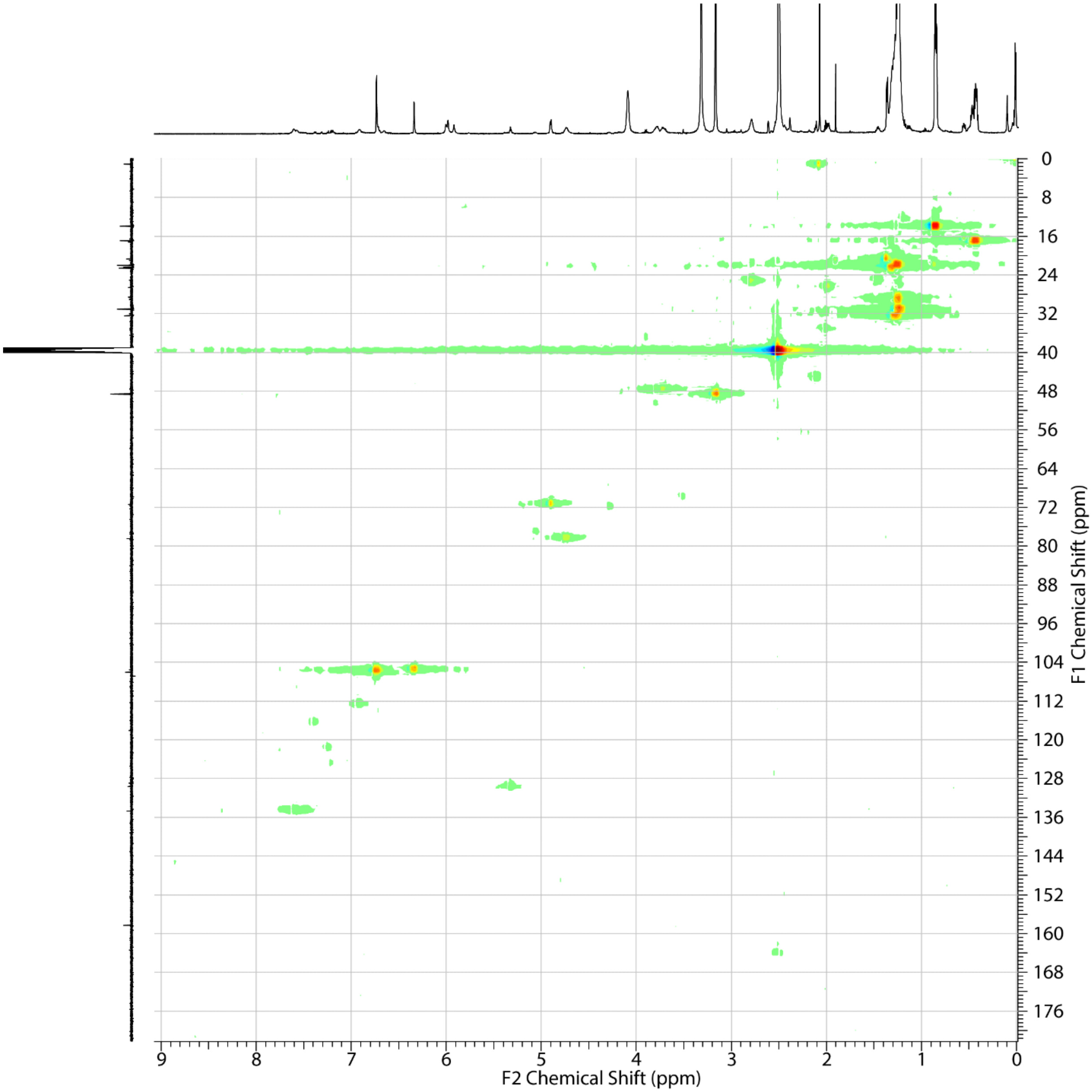
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5		7.66 – 7.53 (m, 1 H)	
6	25.0	2.87 – 2.71 (m, 2 H)	
7	47.2	3.85 – 3.65 (m, 2 H)	
2’	163.3		2”
4’	71.3	4.92 – 4.88 (m, 1 H)	6’
5’	78.4	4.79 – 4.68 (m, 1 H)	6’
6’	20.6	1.36 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	106.4	6.73 (d, *J* = 1.6 Hz, 2 H)	2’, 3”, 4”
3”	158.2		2”, 4”
4”	105.5	6.38 – 6.30 (m, 1 H)	2”, 3”



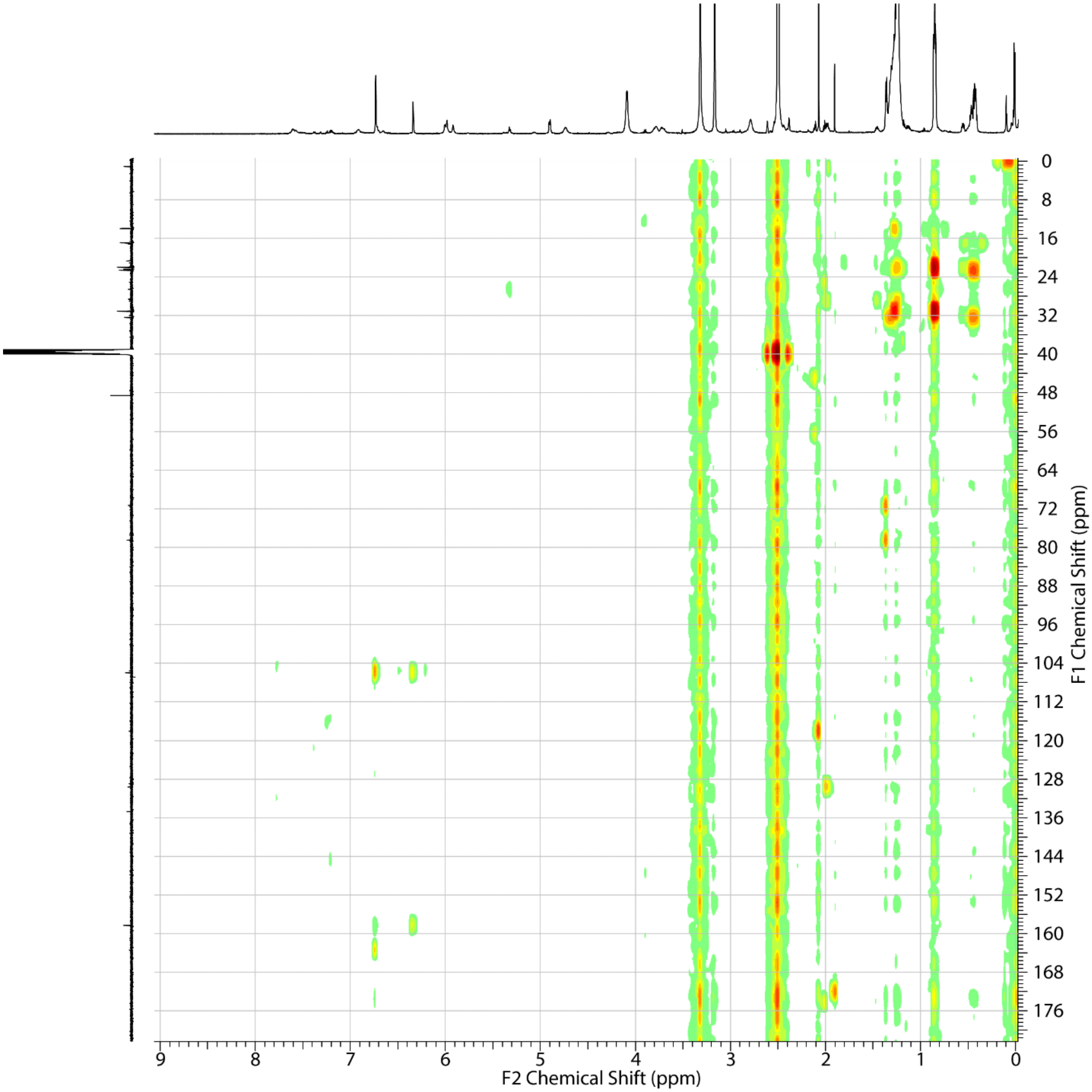
Supplementary Figure 60. ^{1}H-NMR spectrum (600 MHz) of compound **1i** in DMSO-*d*6.



Supplementary Figure 61. ^{13}C-NMR spectrum (600 MHz) of compound **1i** in DMSO-*d*6.

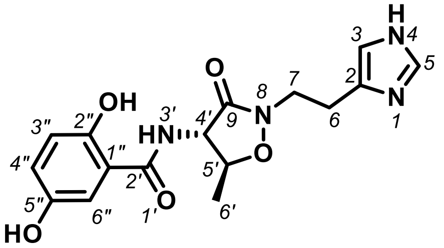


Supplementary Figure 62. gHSQC spectrum (600 MHz) of compound **1i** in DMSO-*d*6.



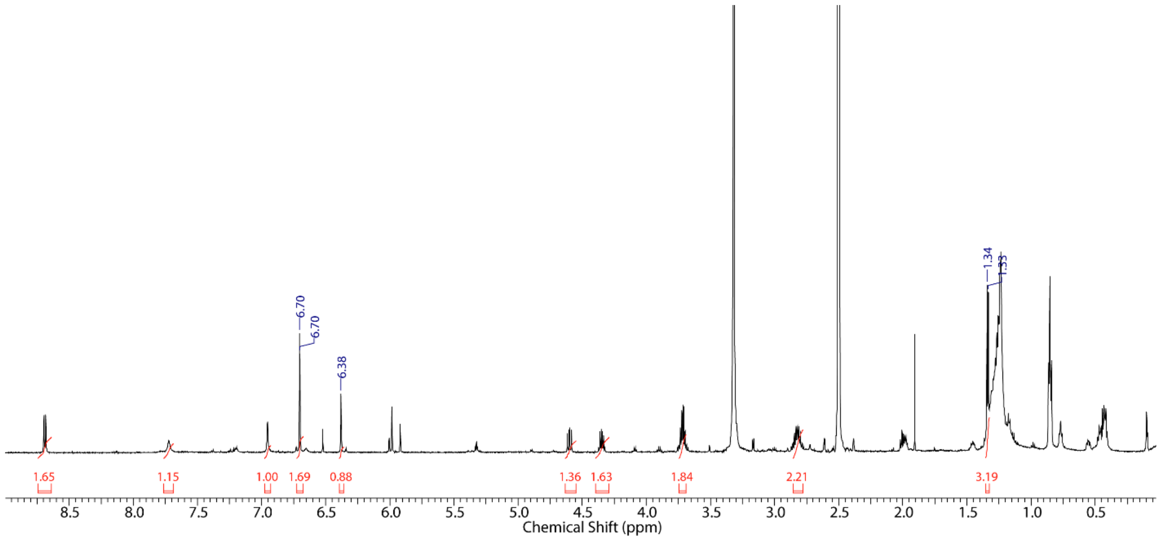
Supplementary Figure 63. HMBC spectrum (600 MHz) of compound **1i** in DMSO-*d*6.

Supplementary Table 17. NMR characterization data of compound **2i** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{16}H_{19}N_4O_5]^+$ ($[M+H]^+$) calculated: 347.1350, found: 347.1345.

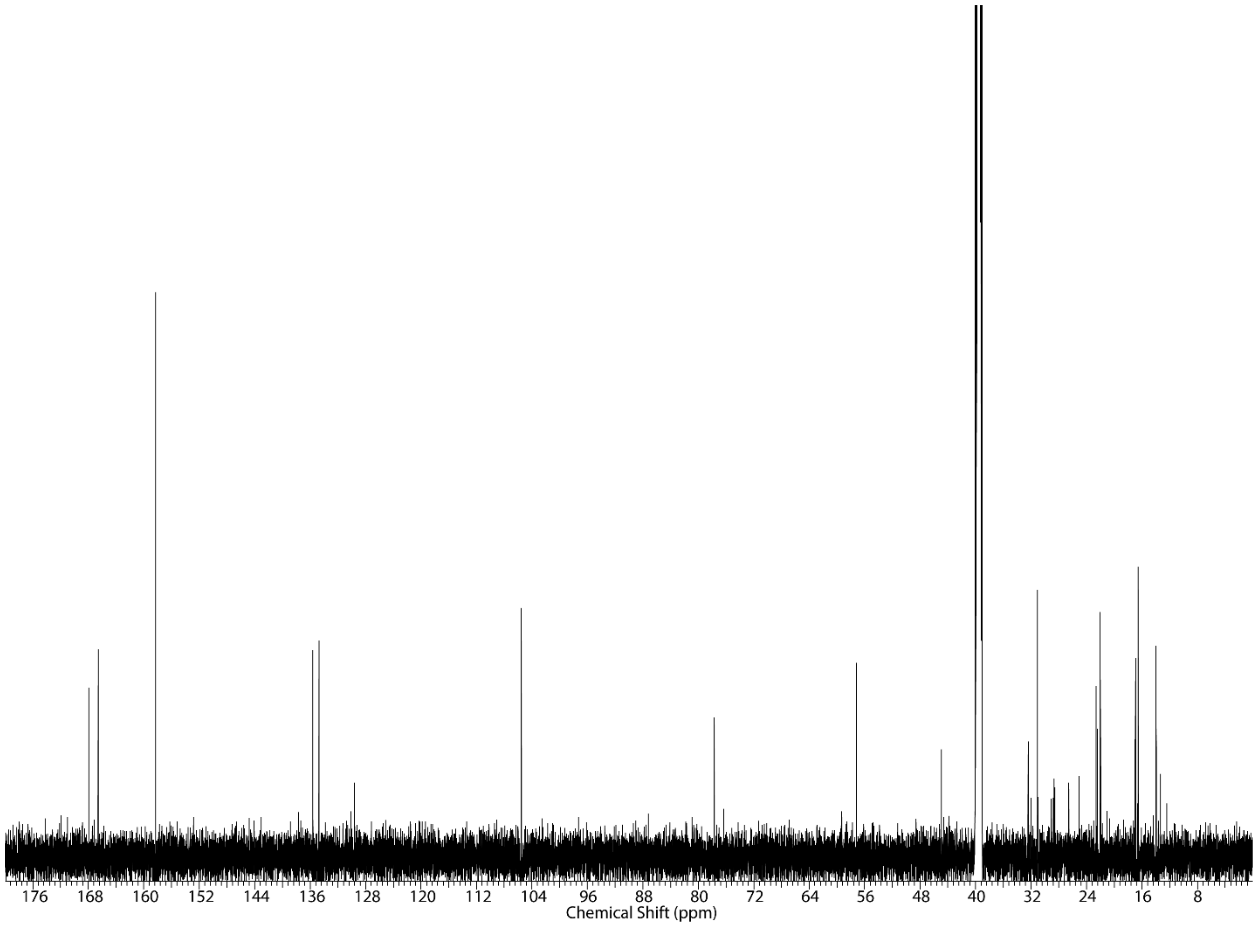


Compound **2i**

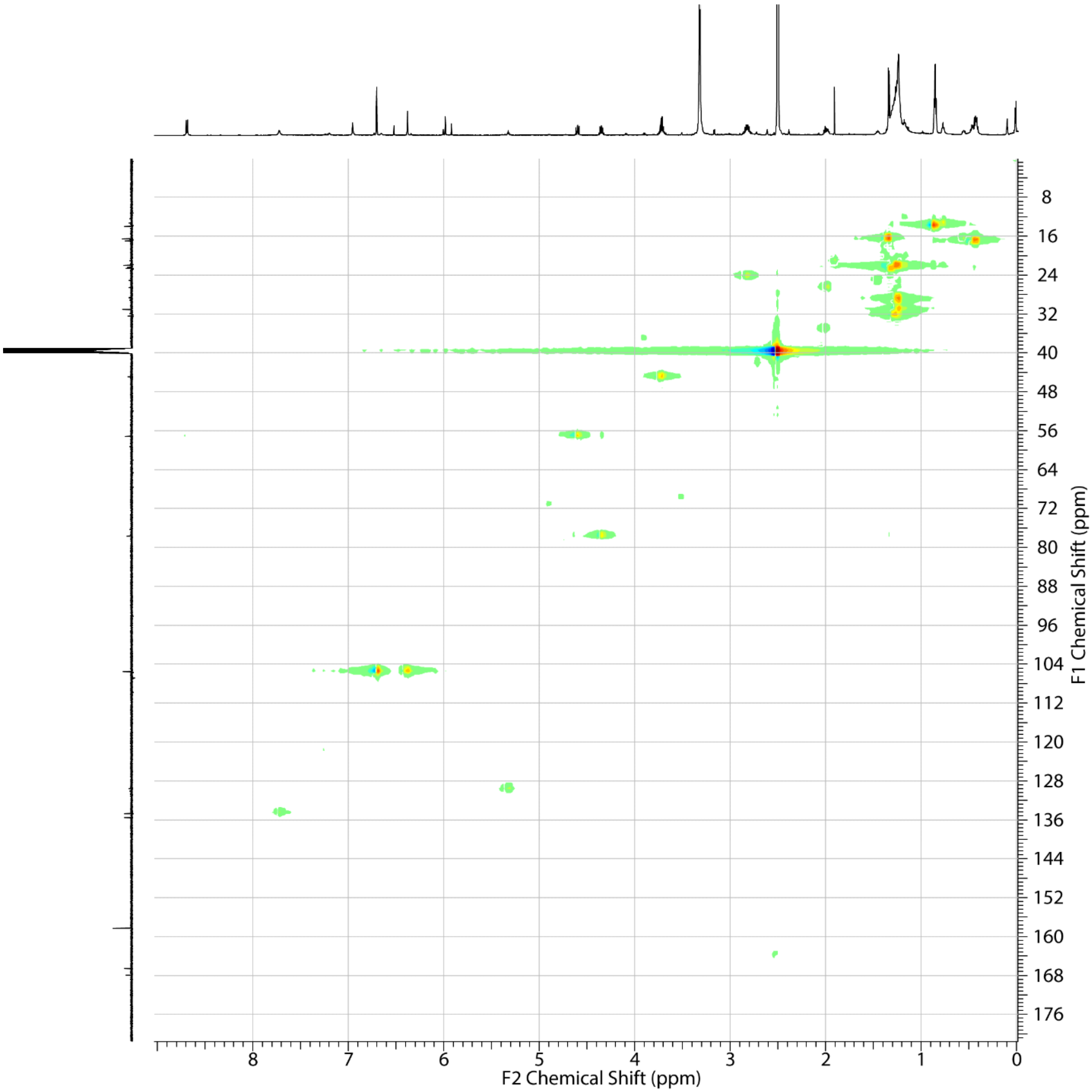
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3	134.7	7.76 – 7.69 (m, 1 H)	5
5		6.98 – 6.93 (m, 1 H)	3
6	23.9	2.85 – 2.78 (m, 2 H)	7
7	44.9	3.74 – 3.69 (m, 2 H)	6, 9
9	167.9		7, 4’
2’	166.5		3’, 2”
3’		8.74 – 8.64 (m, 1 H)	2’, 4’
4’	57.2	4.63 – 4.55 (m, 1 H)	9, 3’, 5’, 6’
5’	77.6	4.40 – 4.29 (m, 1 H)	4’
6’	16.5	1.34 (d, *J* = 5.5 Hz, 3 H)	4’, 5’
2”	105.55	6.70 (d, *J* = 2.4 Hz, 2 H)	2’, 3”, 4”
3”	158.0		2”, 4”
4”	105.50	6.38 (s, 1 H)	2”, 3”



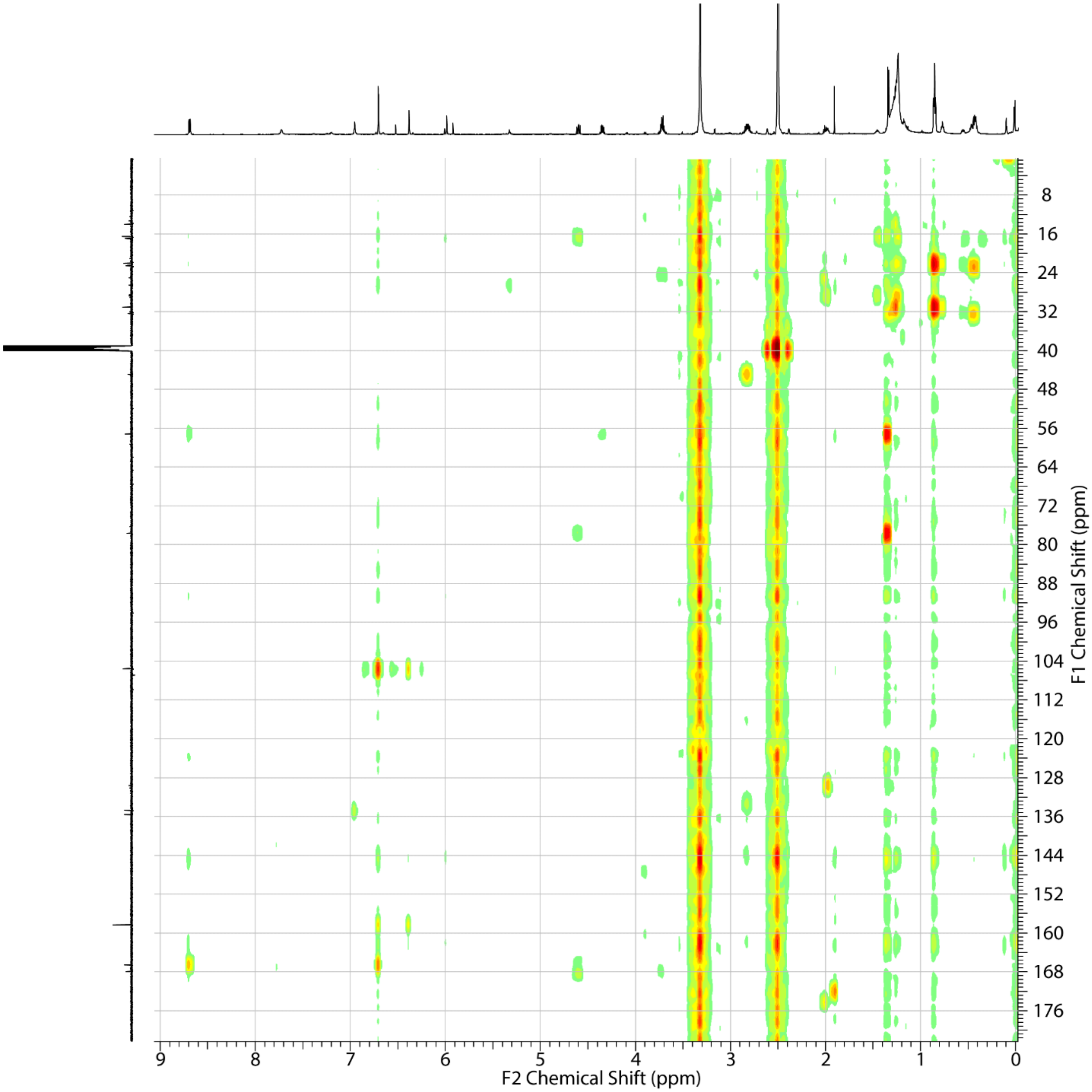
Supplementary Figure 64. ^{1}H-NMR spectrum (600 MHz) of compound **2i** in DMSO-*d*6.



Supplementary Figure 65. ^{13}C-NMR spectrum (600 MHz) of compound **2i** in DMSO-*d*6.

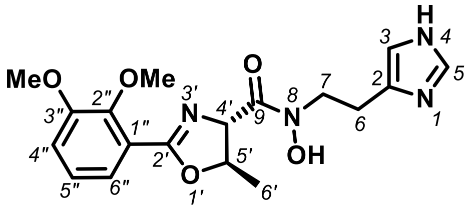


Supplementary Figure 66. gHSQC spectrum (600 MHz) of compound **2i** in DMSO-*d*6.



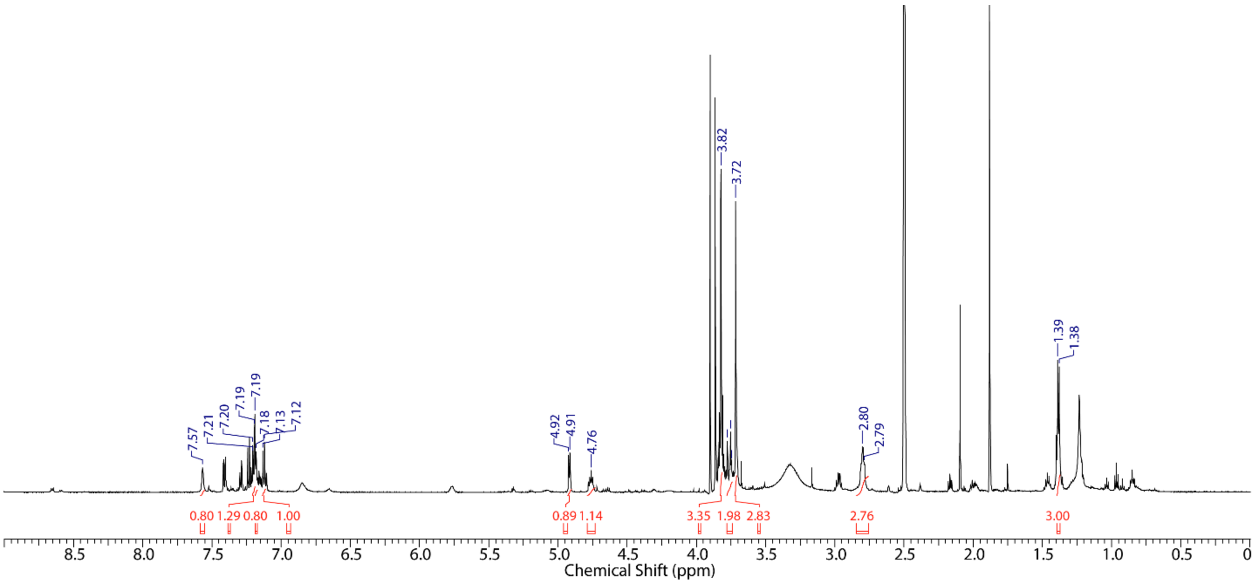
Supplementary Figure 67. HMBC spectrum (600 MHz) of compound **2i** in DMSO-*d*6.

Supplementary Table 18. NMR characterization data of compound **1j** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{18}H_{23}N_4O_5]^+$ ($[M+H]^+$) calculated: 375.1663, found: 375.1650.

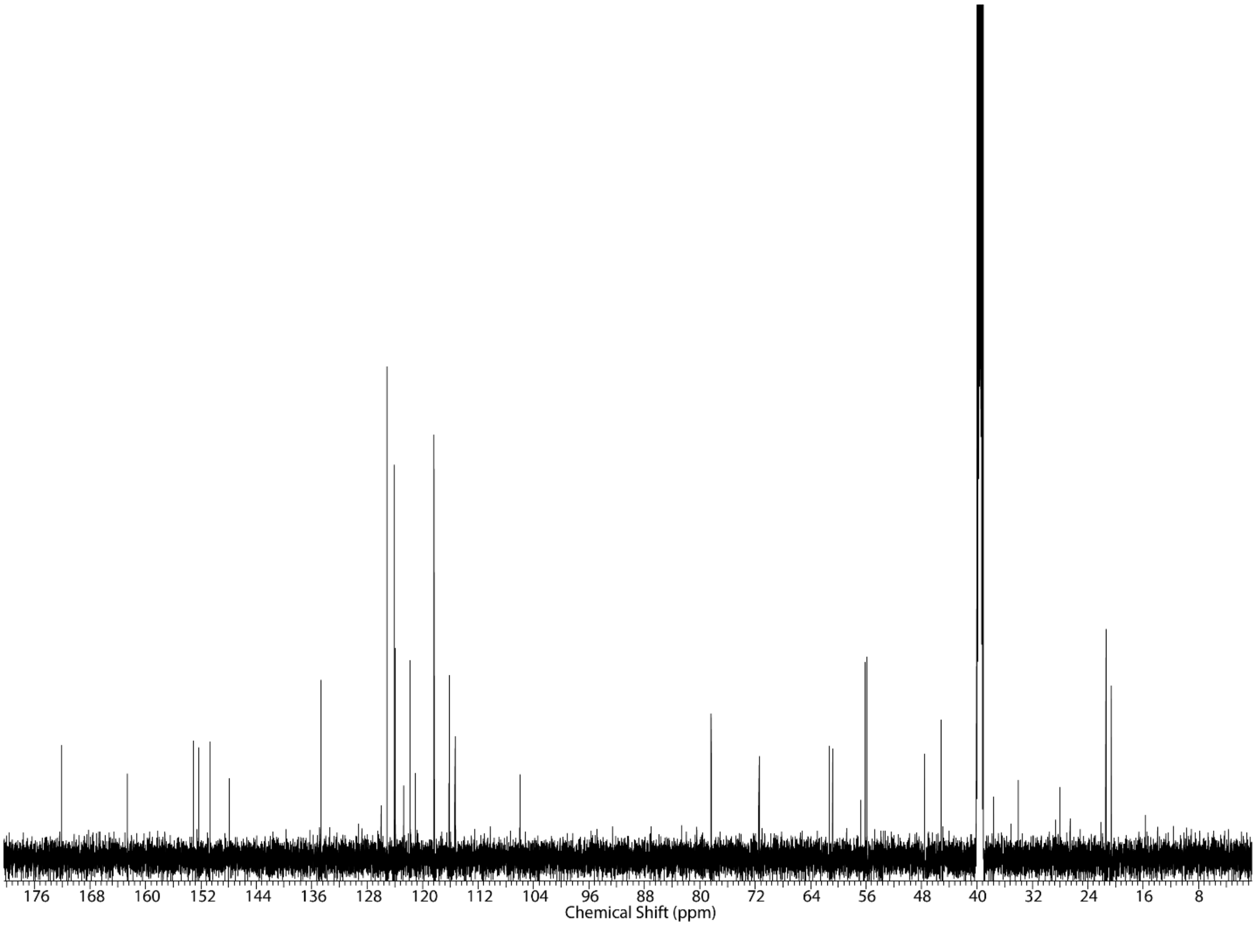


Compound **1j**

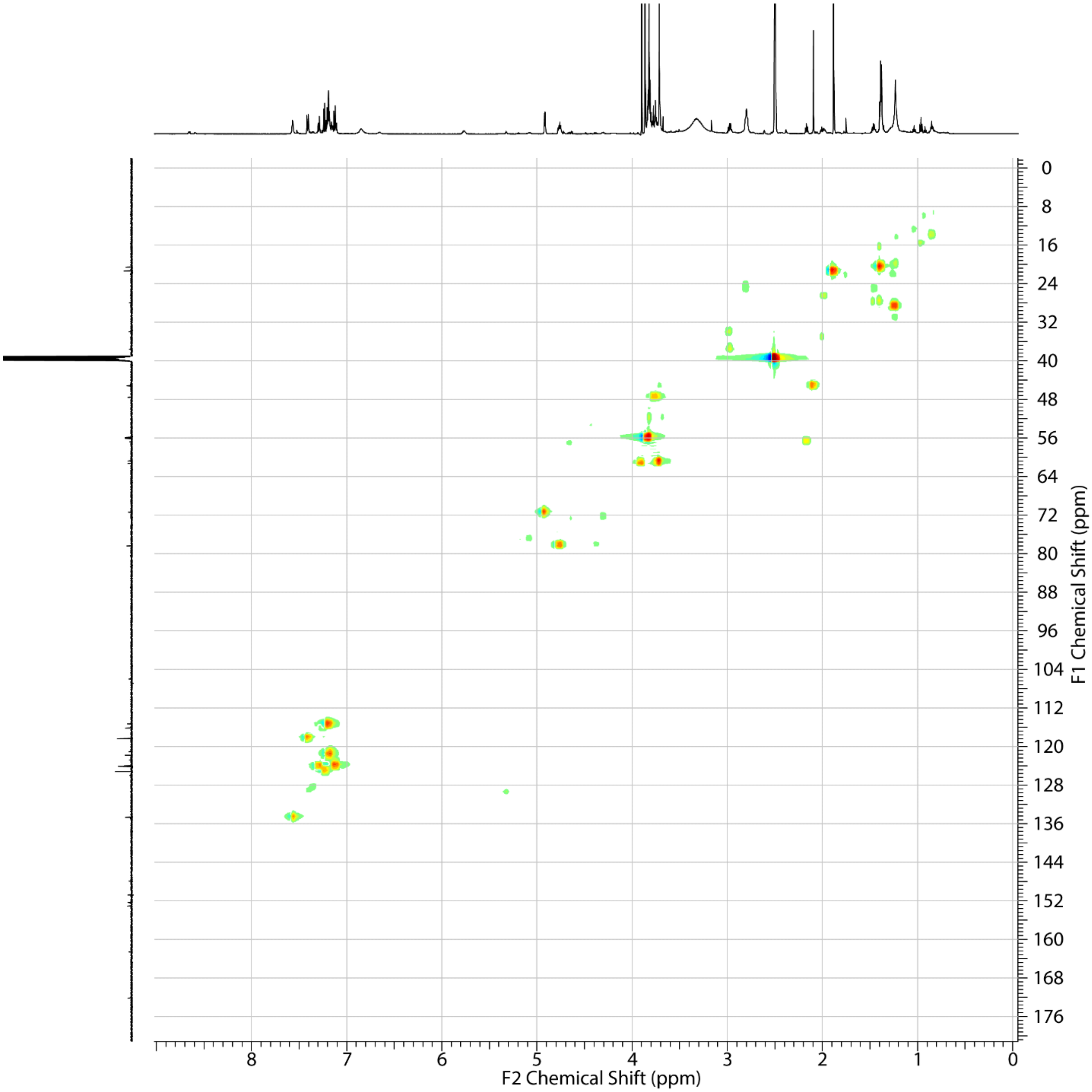
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.6	7.57 (br. s., 1 H)	
6	24.5	2.84 – 2.76 (m, 2 H)	7
7	47.6	3.78 – 3.74 (m, 2 H)	6
4’	71.4	4.92 (d, *J* = 5.5 Hz, 1 H)	5’, 6’
5’	78.3	4.76 (m, 1 H)	4’, 6’
6’	20.6	1.38 (d, *J* = 5.5 Hz, 3 H)	4’, 5’
2”	152.9		6”, 7”
3”	147.8		4”, 8”
4”	115.3	7.21 – 7.19 (m, 1 H),	3”, 5”
5”	121.7	7.18 (br. s., 1 H)	4”
6”	123.9	7.13 (d, *J* = 7.9 Hz, 1 H)	2”
7”	55.8	3.82 (s, 3 H)	2”
8”	60.8	3.72 (s, 3 H)	3”



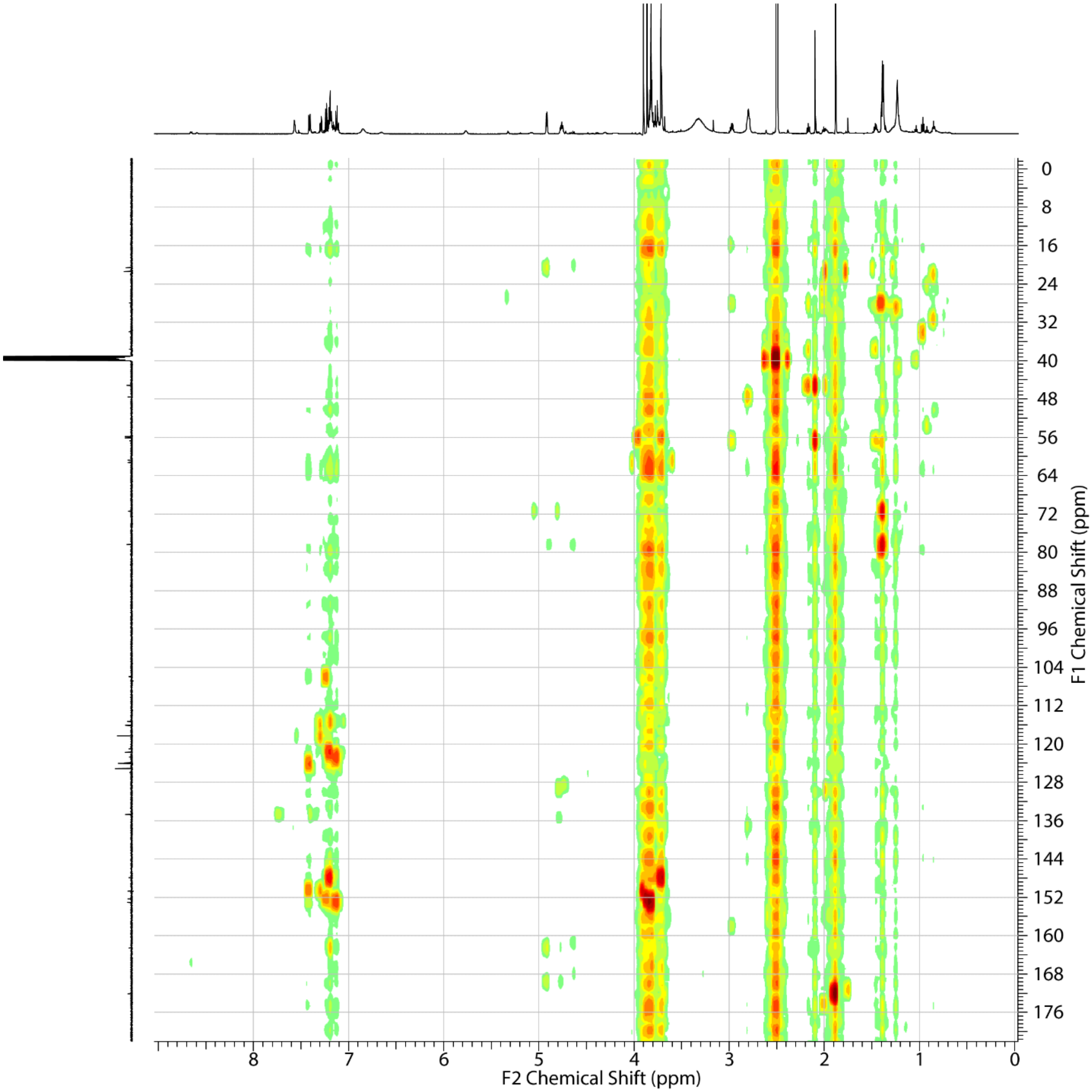
Supplementary Figure 68. ^{1}H-NMR spectrum (600 MHz) of compound **1j** in DMSO-*d*6.



Supplementary Figure 69. ^{13}C-NMR spectrum (600 MHz) of compound **1j** in DMSO-*d*6.

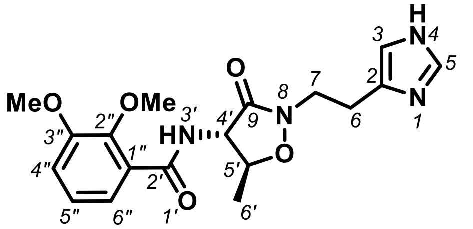


Supplementary Figure 70. gHSQC spectrum (600 MHz) of compound **1j** in DMSO-*d6*.



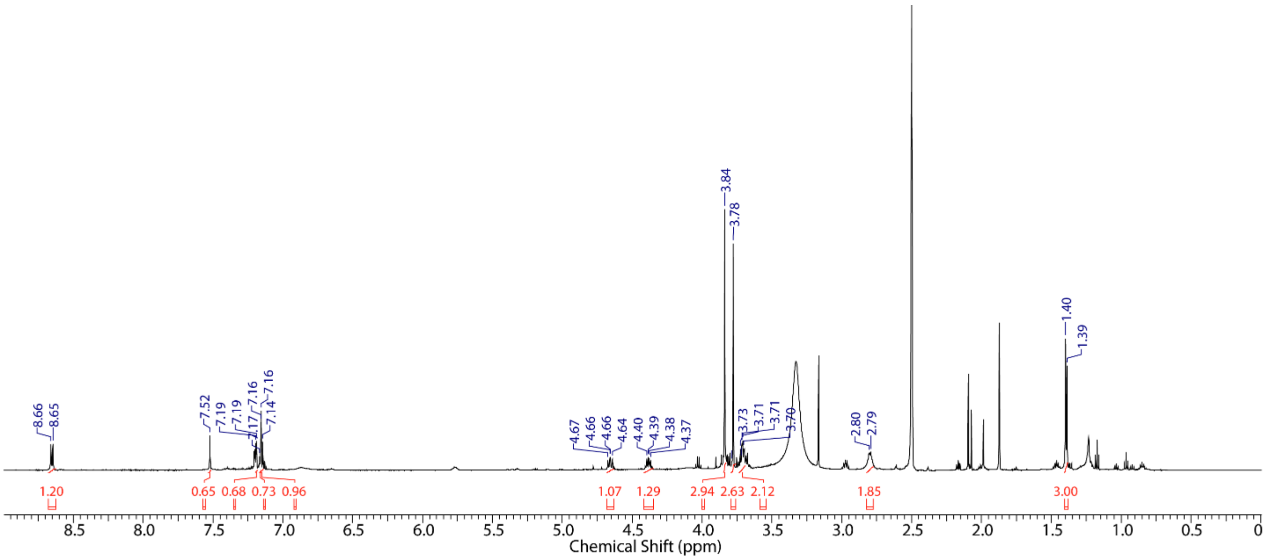
Supplementary Figure 71. HMBC spectrum (600 MHz) of compound **1j** in DMSO-*d*6.

Supplementary Table 19. NMR characterization data of compound **2j** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{18}H_{23}N_4O_5]^+$ ($[M+H]^+$) calculated: 375.1663, found: 375.1658.

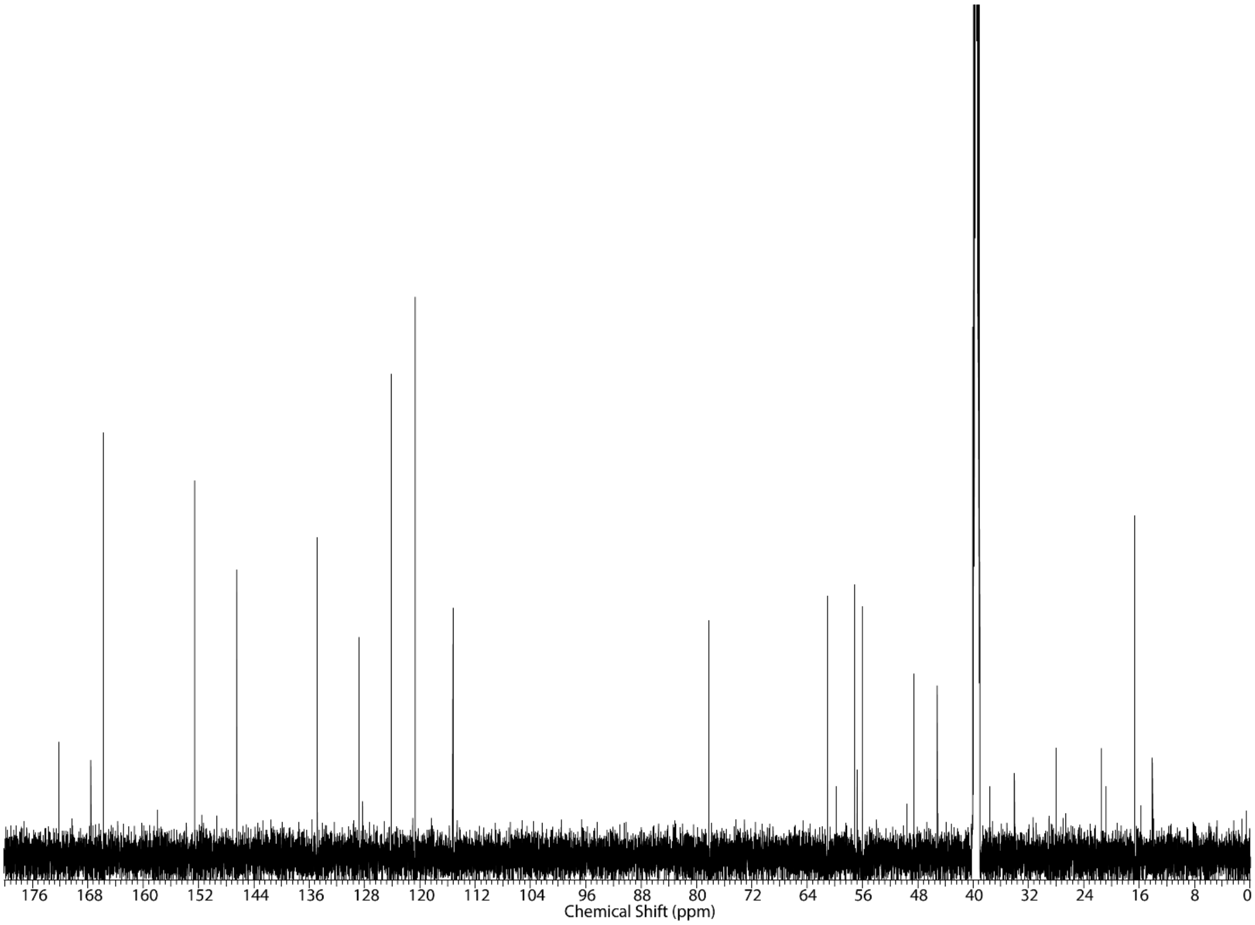


Compound **2j**

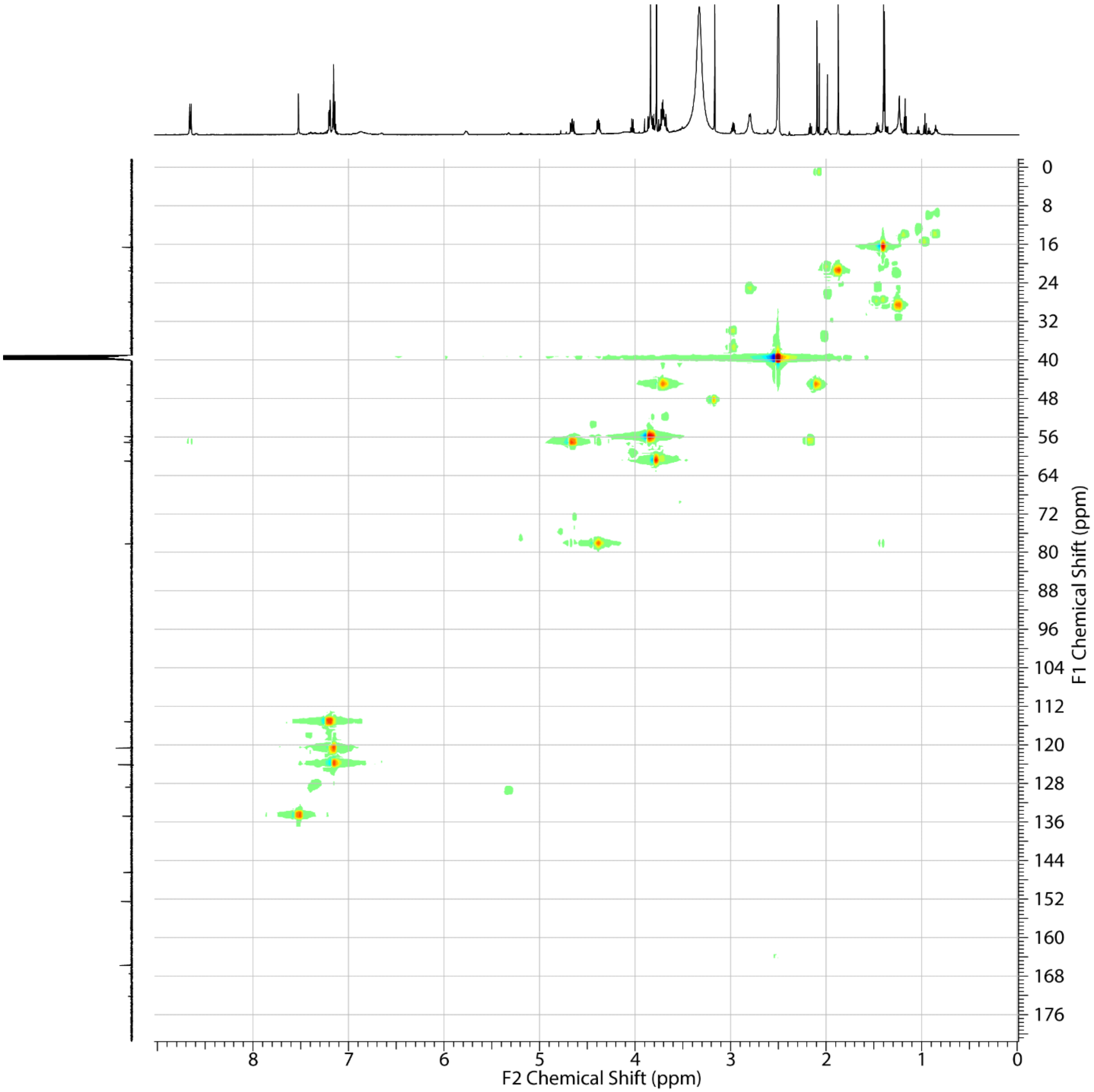
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3 or 5	134.7	7.52 (s, 1 H)	
6	25.1	2.80 (d, *J* = 6.3 Hz, 2 H)	7
7	45.1	3.73 – 3.69 (m, 2 H)	6
4’	56.8	4.66 (dd, *J* = 8.7, 11.0 Hz, 1 H)	5’, 6’
5’	78.1	4.38 (dd, *J* = 6.3, 11.0 Hz, 1 H)	4’, 6’
6’	16.6	1.39 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	152.5		6”, 7”
3”	146.4		8”
4”	115.2	7.19 (d, *J* = 2.4 Hz, 1 H)	5”
5”	120.6	7.17 – 7.16 (m, 1 H)	4”
6”	123.7	7.16 – 7.14 (m, 1 H)	2”
7”	55.9	3.84 (s, 3 H)	2”
8”	61.0	3.79 – 3.76 (s, 3 H)	3”



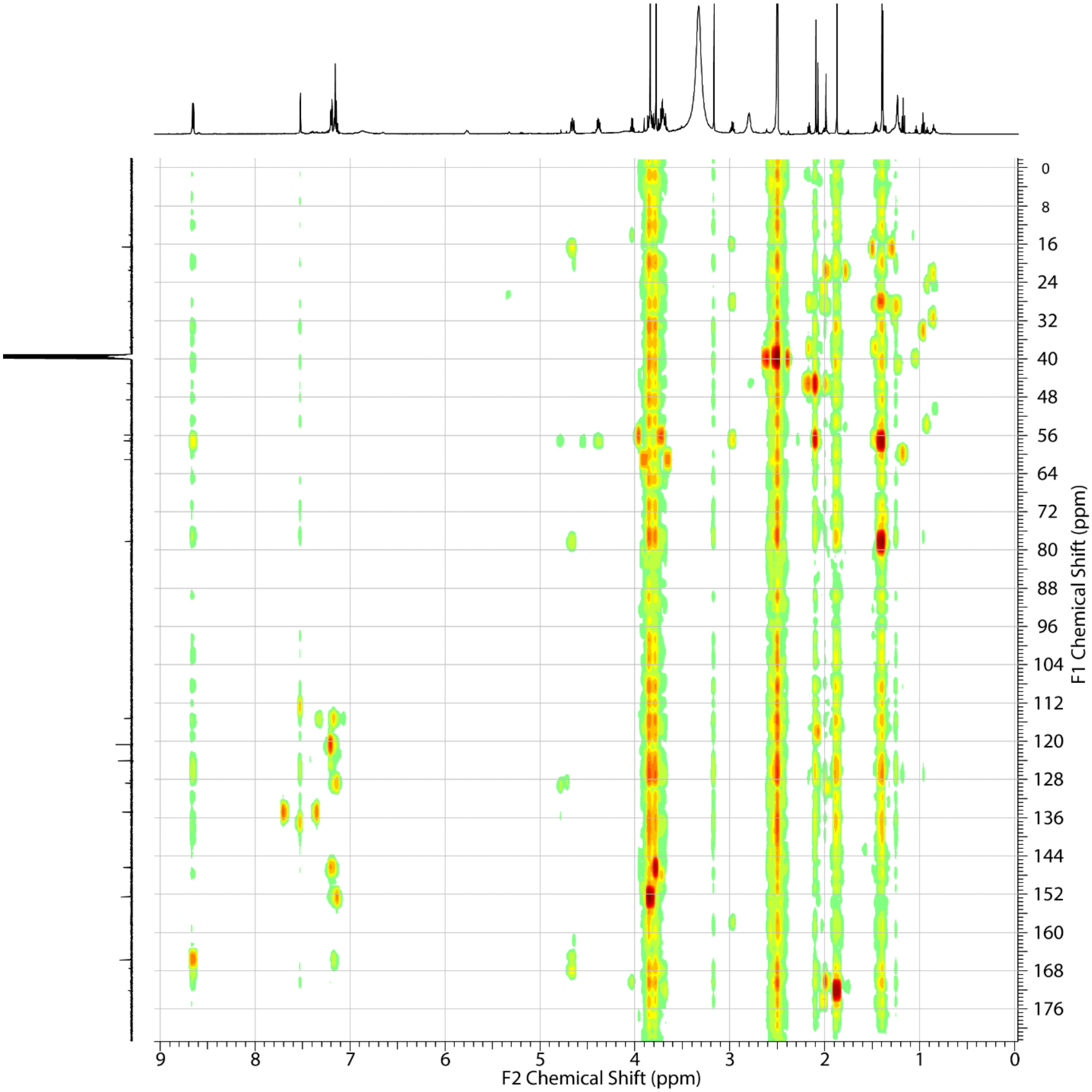
Supplementary Figure 72. ^{1}H-NMR spectrum (600 MHz) of compound **2j** in DMSO-*d*6.



Supplementary Figure 73. ^{13}C-NMR spectrum (600 MHz) of compound **2j** in DMSO-*d*6.

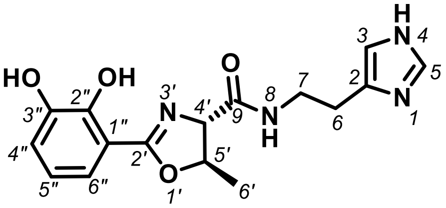


Supplementary Figure 74. gHSQC spectrum (600 MHz) of compound **2j** in DMSO-*d*6.



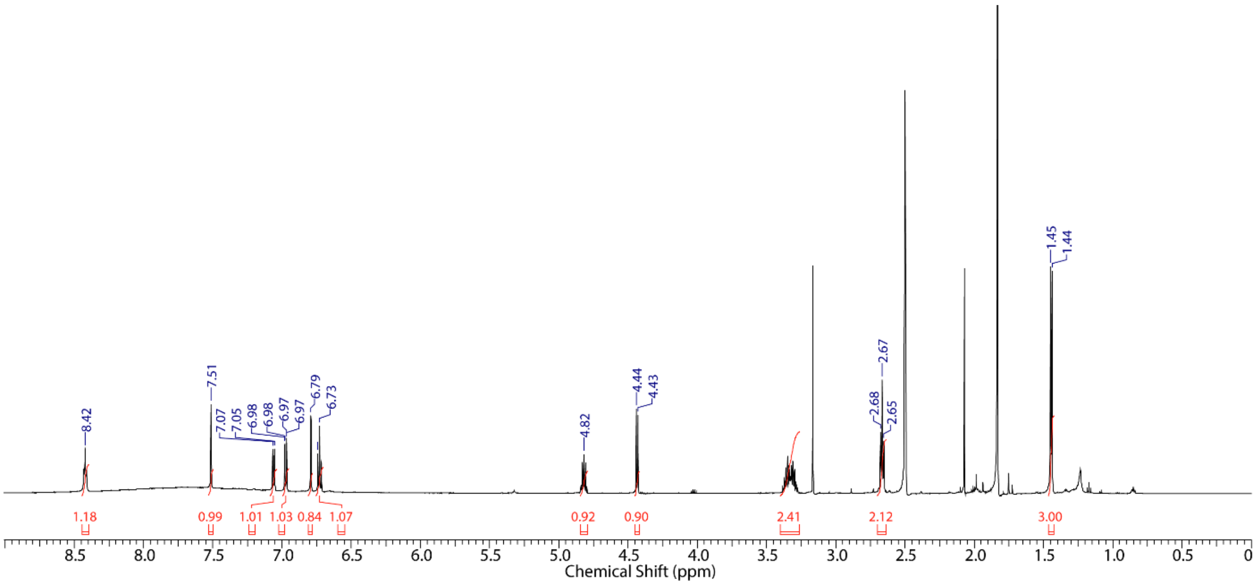
Supplementary Figure 75. HMBC spectrum (600 MHz) of compound **2j** in DMSO-*d*6.

Supplementary Table 20. NMR characterization data of compound **1k** in DMSO-*d*6. HRMS (ESI+) m/z for $[C_{18}H_{23}N_4O_5]^+$ ($[M+H]^+$) calculated: 331.1401, found: 331.1388.

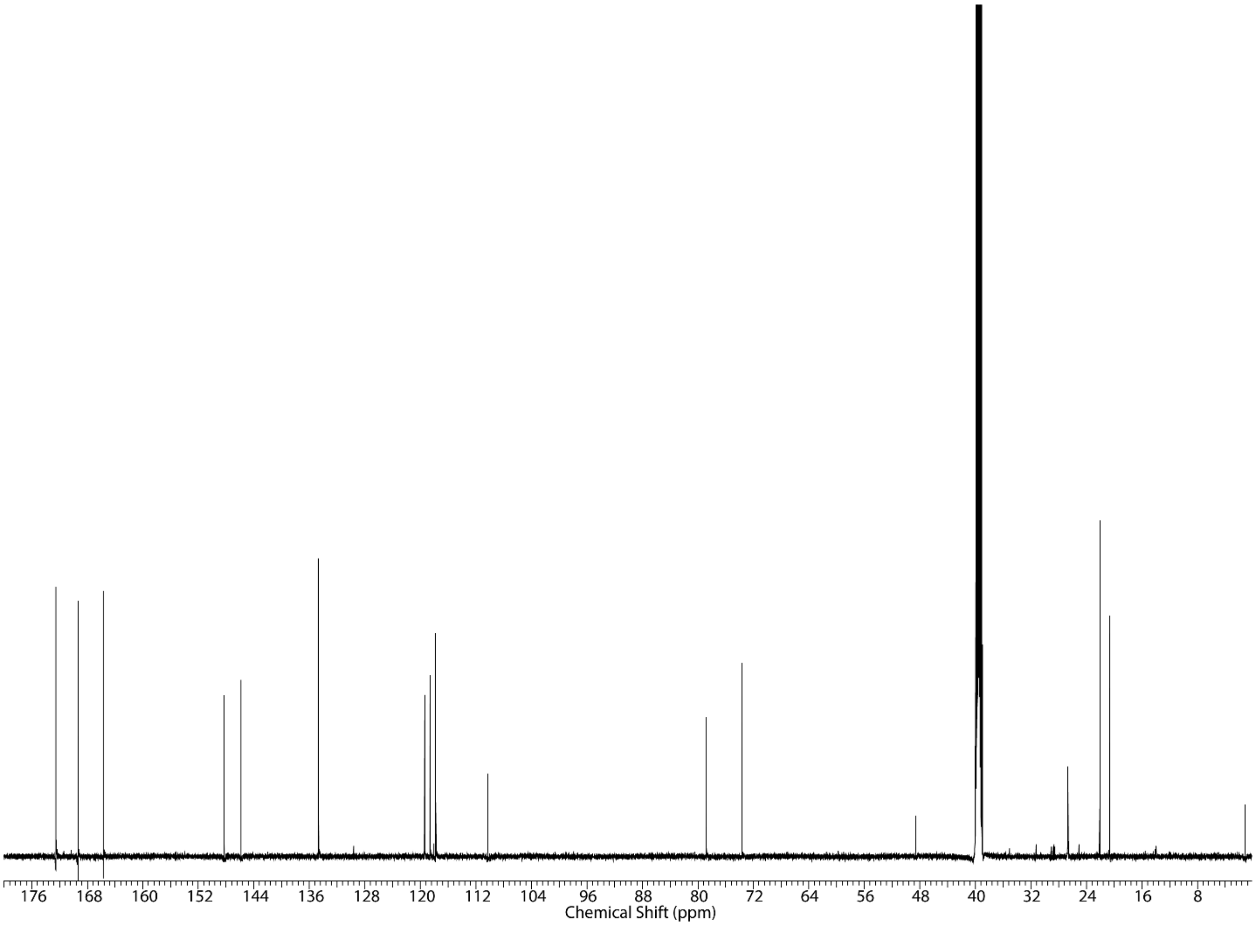


Compound **1k**

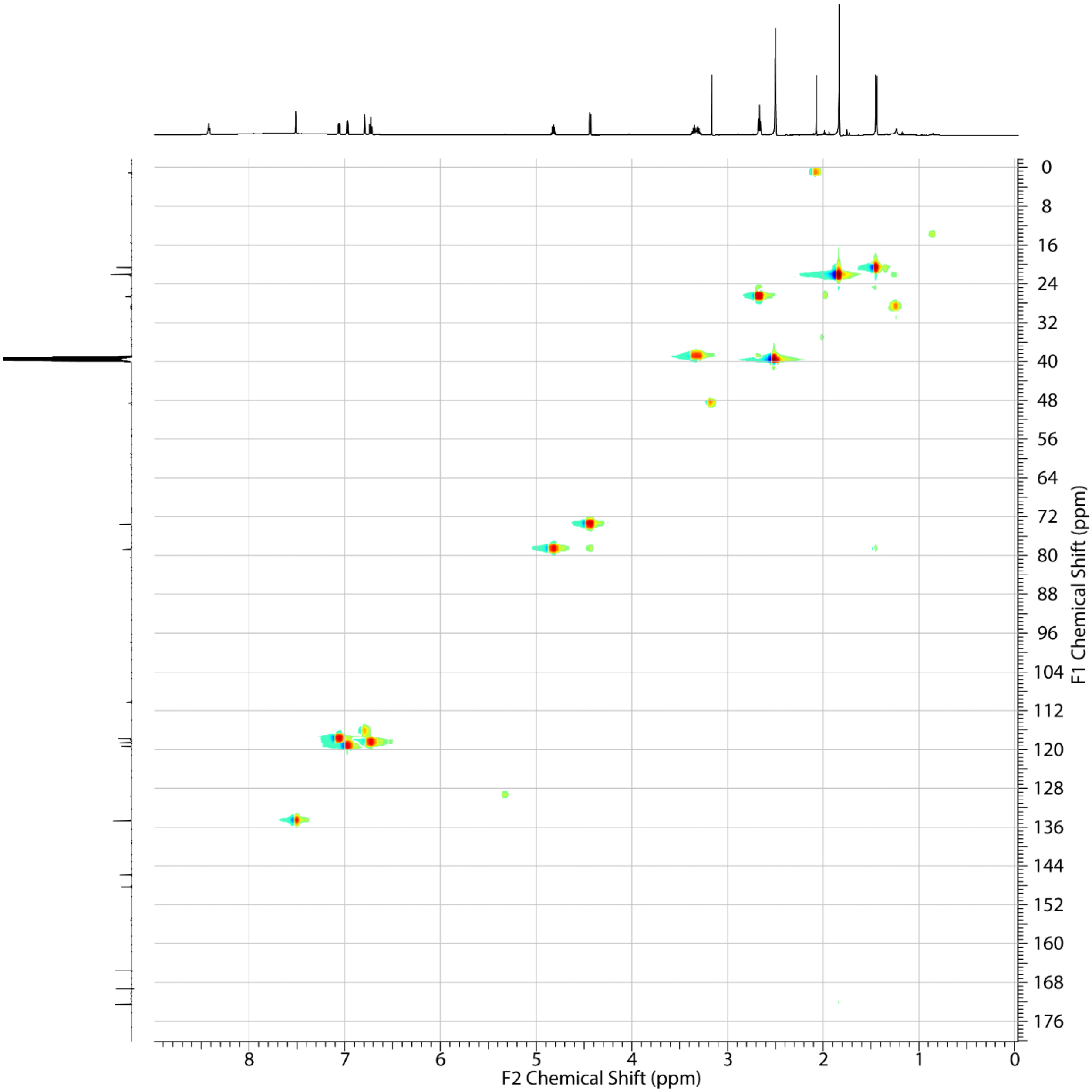
Atom	^{13}C (ppm)	^{1}H (ppm), multiplets in Hz	HMBC ^{1}H-^{13}C 2-3 bond
3	134.6	7.51 (s, 1 H)	5
5	116.3	6.79 (s, 1 H)	3
6	26.6	2.67 (t, *J* = 7.1 Hz, 2 H)	3, 5, 7
7	38.55	3.40 – 3.26 (m, 2 H)	3, 6, 9
8		8.42 (s, 1 H)	
9	169.3		7, 4’
2’	165.5		2”
4’	73.6	4.44 (d, *J* = 7.1 Hz, 1 H)	2’, 6’, 9
5’	78.7	4.82 (m, 1 H)	9, 4’, 6’
6’	20.6	1.40 (d, *J* = 6.3 Hz, 3 H)	4’, 5’
2”	148.2		4”, 6”
4”	119.3	6.97 (dd, *J* = 1.6, 7.9 Hz, 1 H)	2”, 6”
5”	118.5	6.75 – 6.70 (m, 1 H)	
6”	117.7	7.06 (d, *J* = 7.9 Hz, 1 H)	2’, 2”, 4”



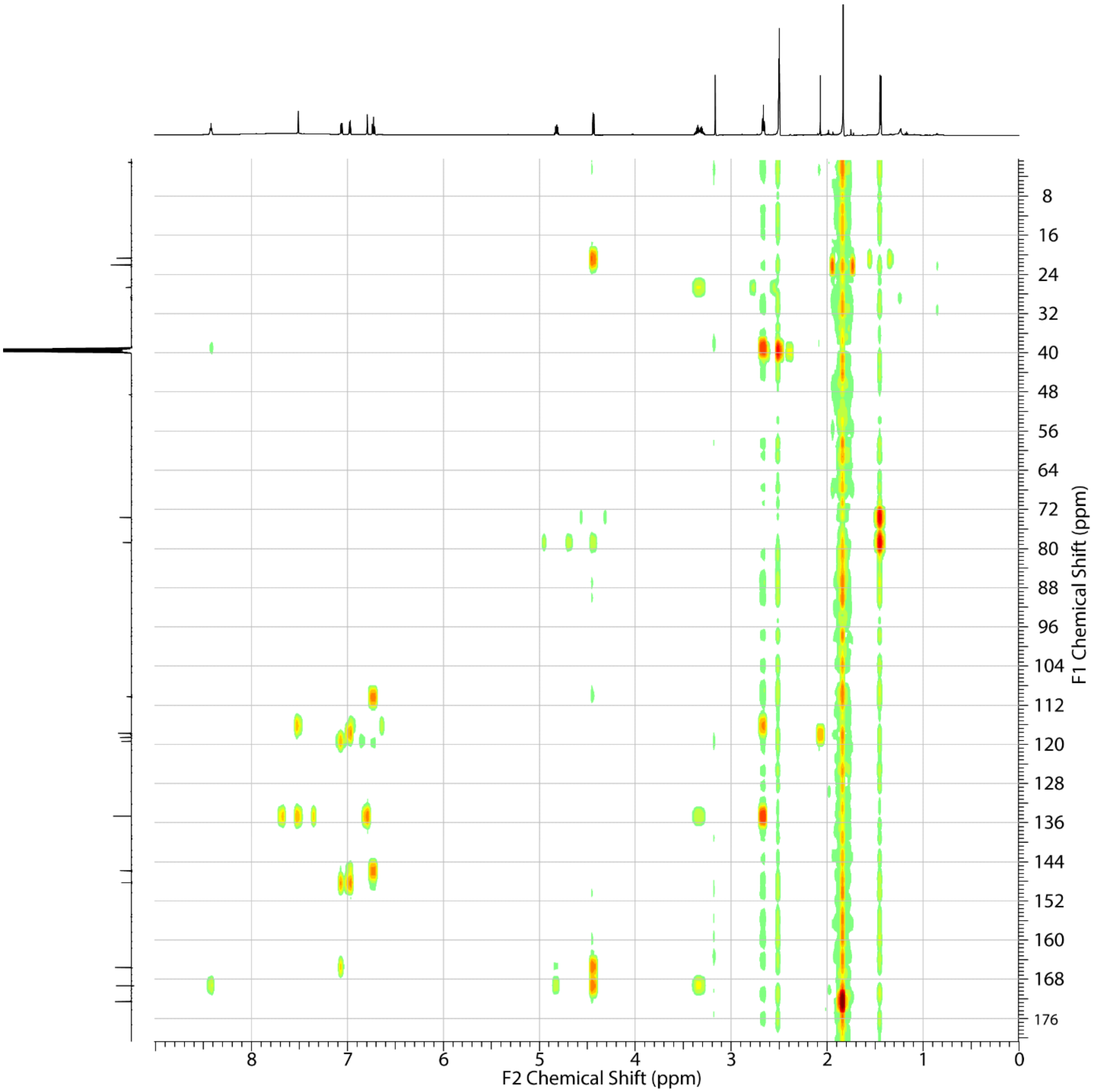
Supplementary Figure 76. ^{1}H-NMR spectrum (600 MHz) of compound **1K** in DMSO-*d*6.



Supplementary Figure 77. ^{13}C-NMR spectrum (600 MHz) of compound **1k** in DMSO-*d*6.



Supplementary Figure 78. gHSQC spectrum (600 MHz) of compound **1k** in DMSO-*d*6.



Supplementary Figure 79. HMBC spectrum (600 MHz) of compound **1k** in DMSO-*d*6.

VII. Acknowledgements

We thank J. Kao (WUSTL, Dept. of Chemistry) for assistance in the acquisition of 2D NMR spectra. We thank B. Evans at the Proteomics & Mass Spectrometry Facility at the Donald Danforth Plant Science Center, St. Louis, MO for assistance with the acquisition of high-resolution MS-MS spectra (Grant No. DBI-0922879). A special thanks to Dr. Luis Actis (Miami University, Dept. of Microbiology) for providing *A. baumannii* ATCC 19606 s1 mutant.

VIII. References

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2. Shapiro, J.; Wencewicz, T. A. *ACS Infectious Diseases* **2016**, *2*, 157.
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