SUPPORTING INFORMATION

Vancomycin-iridium (III) interaction: an unexplored route for enantioselective imine reduction.

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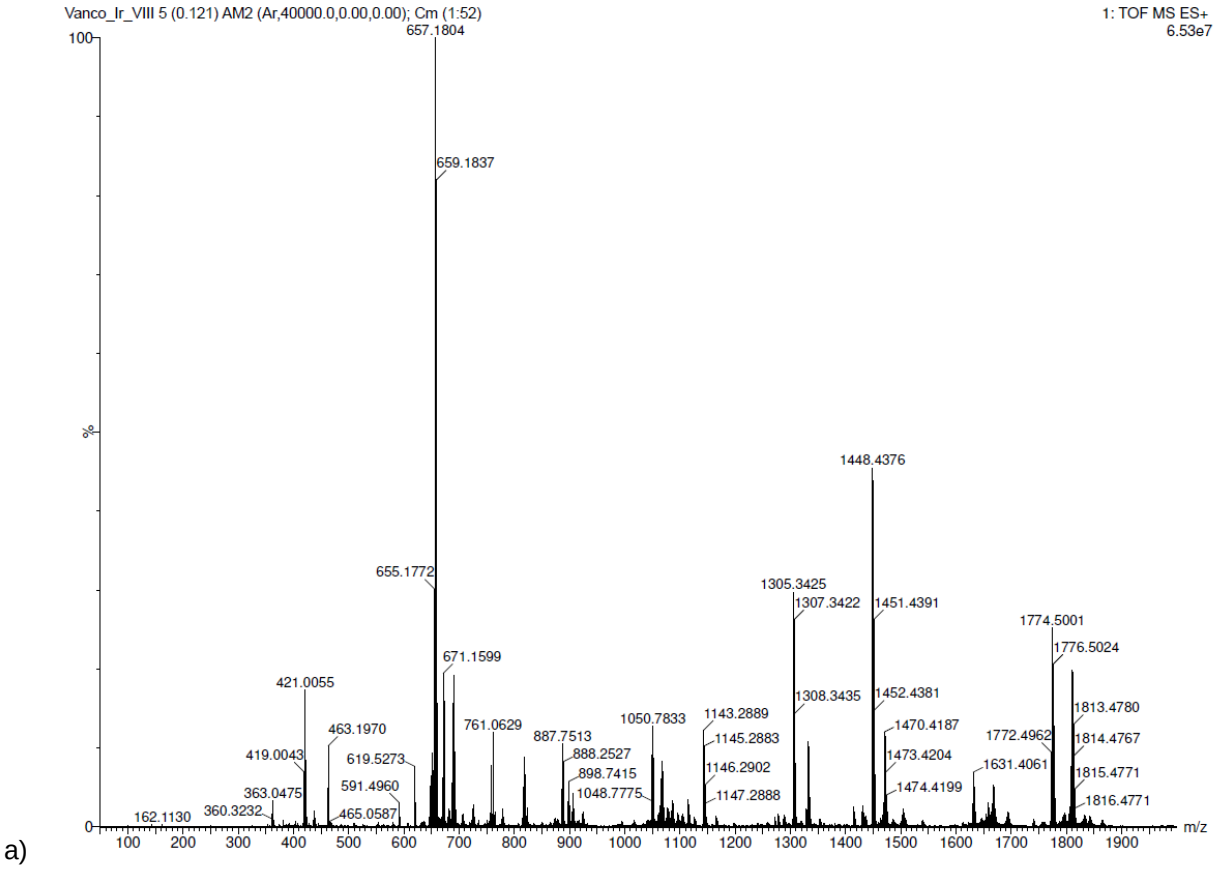
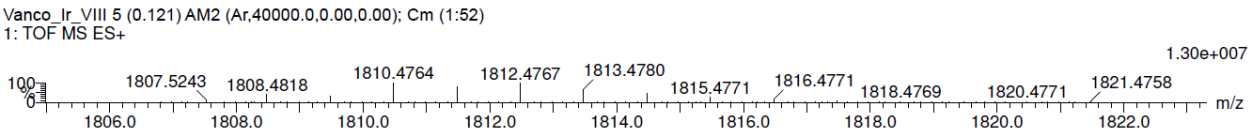
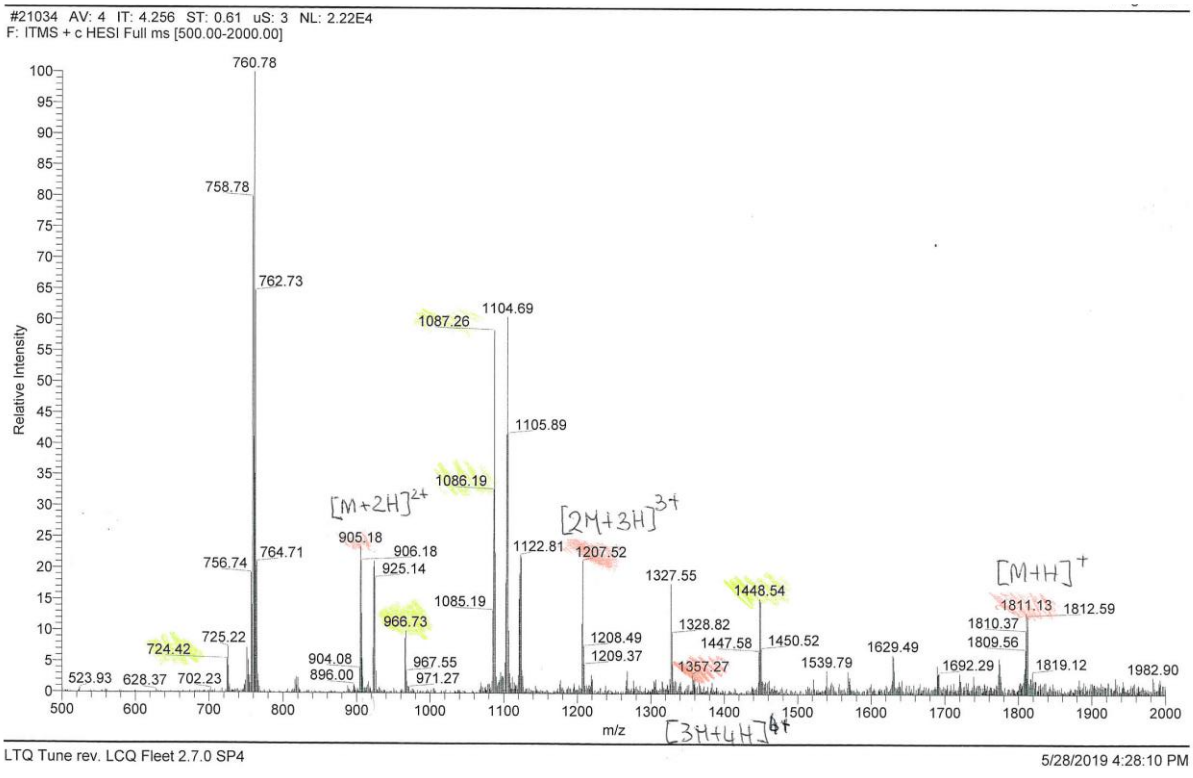
Van/[IrCp*Cl_2]$_2$ complex characterization

1.1. MS of $C_{76}H_{90}Cl_2IrN_9O_{24}$



a)



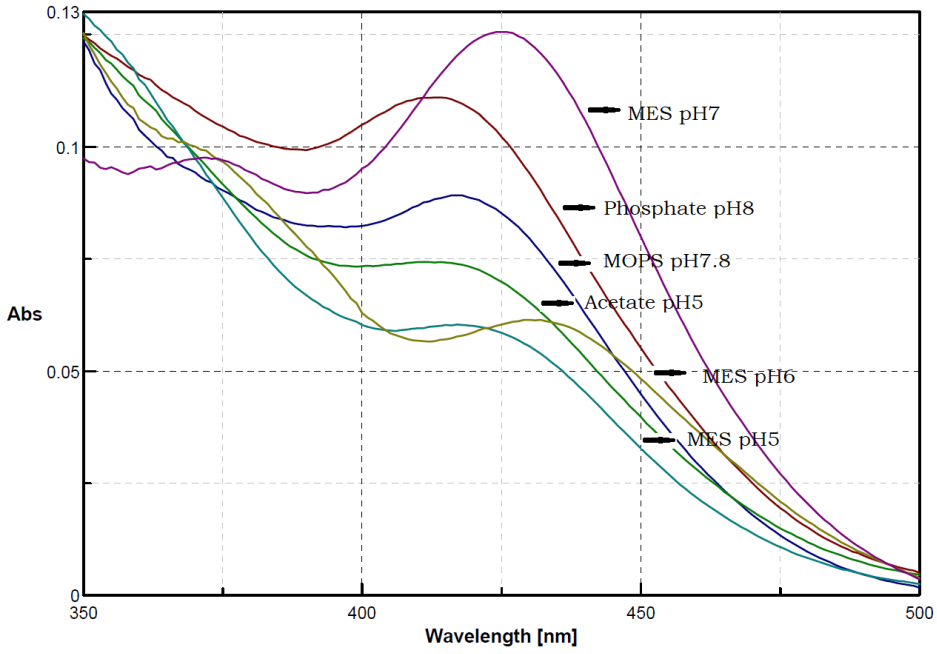


b)

Figure S1. a) MALDI-TOF and b) ESI spectra of [Ir(Cp*)(Van)Cl] complex (25 mM, 1:1 ratio Van/Ir) (red highlight for complex referred to free Van in green highlight).

1.2. **UV spectroscopy**

Stock solutions of [Ir(Cp*)(Van)Cl] complex (25 mM water with 1% DMSO) were diluted to a final concentration of 250 µM in the appropriate buffer and sonicated for complete dissolution.



a)

b)

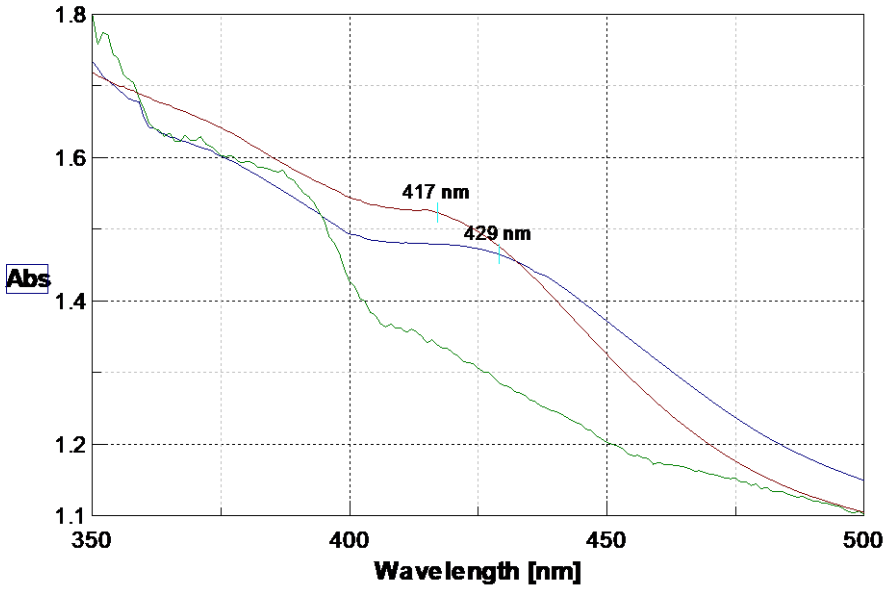


Figure S2. a) UV spectra of Van/[IrCp*Cl_2]$_2$ complex (250 µM, 1:0.5 ratio) at different pH values; b) UV spectra of Van alone (green line), [IrCp*Cl_2]$_2$ alone (red line) and Van/[IrCp*Cl_2]$_2$ (blue line) in MES buffer pH 5.

1.3. **NMR spectroscopy**

Van was characterized by ^{1}H, ^{13}C, HSQC NMR experiments and [Ir(Cp*)(Van)Cl] complex by ^{1}H, ^{13}C, HSQC, TOCSY, ROESY, NOESY and COSY NMR experiments on 600 MHZ (^{1}H) and 150 MHZ (^{13}C) instruments. The spectra were recorded in D_2O with 1% [d_6]DMSO (25 mM, 298K). The proton naming convention is the one from Świątek et al. [1]

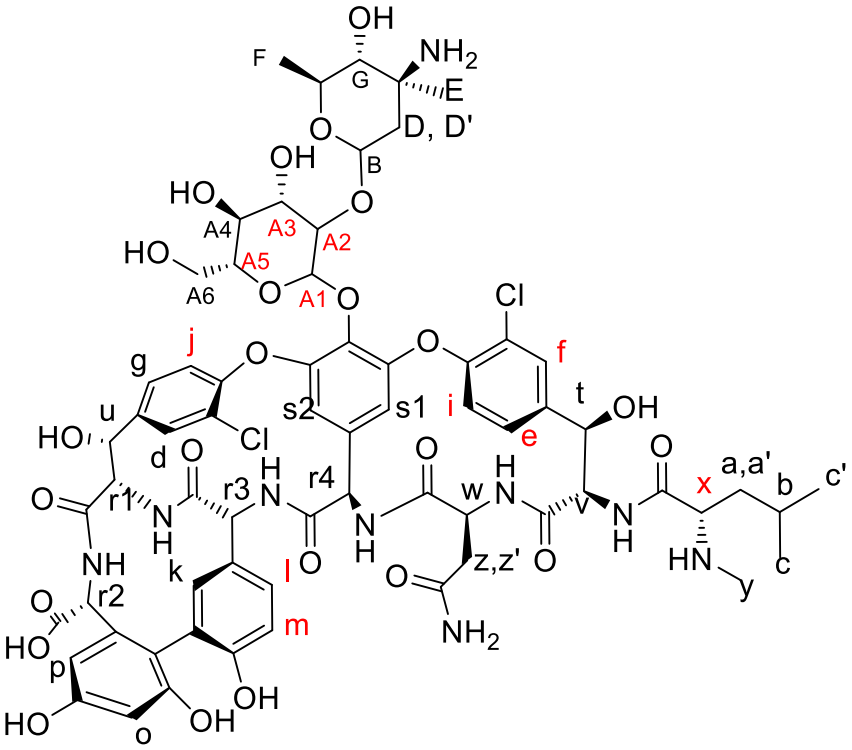


Table T1a: Vancomycin

Signal	^{1}H	^{13}C	Signal	^{1}H	^{13}C
d	7.67	128.3	r3	4.55	59.0
f	7.58	129.5[a]	r2	4.21	63.1
e	7.52[b]	126.4[b]	w	4.08[b]	60.6[b]
g	7.52[b]	126.4[b]	r1	3.82	60.6[b]
j	7.24[b]	124.6[b]	x	4.74[b]	60.6[b]
i	7.24[b]	124.6[b]	A2	3.74[b]	60.6[b]
k	7.11	135.6	A5	3.61[b]	69.1[b]
m	6.88	118.1[b]	A6	3.73-4.04	60.7
l	6.87	118.1[b]	A3	3.61[b]	69.1[b]
o	6.50	103.0	A4	3.61[b]	69.1[b]
p	6.44	107.8	G	3.41	70.7
r4	6.11	54.9	zz’	2.74-2.70	35.7
s1	5.74	-	y	2.72	31.8
u	5.53	71.4[b]	DD’	2.03	33.0
A1	5.49	71.4[b]	aa’	1.76-1.65	38.8
t	5.39	71.8	b	1.52	23.9
s2	5.38	105.4	E	1.40	22.3
B	5.31	97.8	F	1.12	16.2[a]
v	4.84[b]	64.0[b]	cc’	0.81-0.78	21.8-21.6
c	4.84[b]	64.0[b]			

[a]from HSQC analysis; [b]overlapped signals

Table T1b: [Ir(Cp*)(Van)Cl] complex

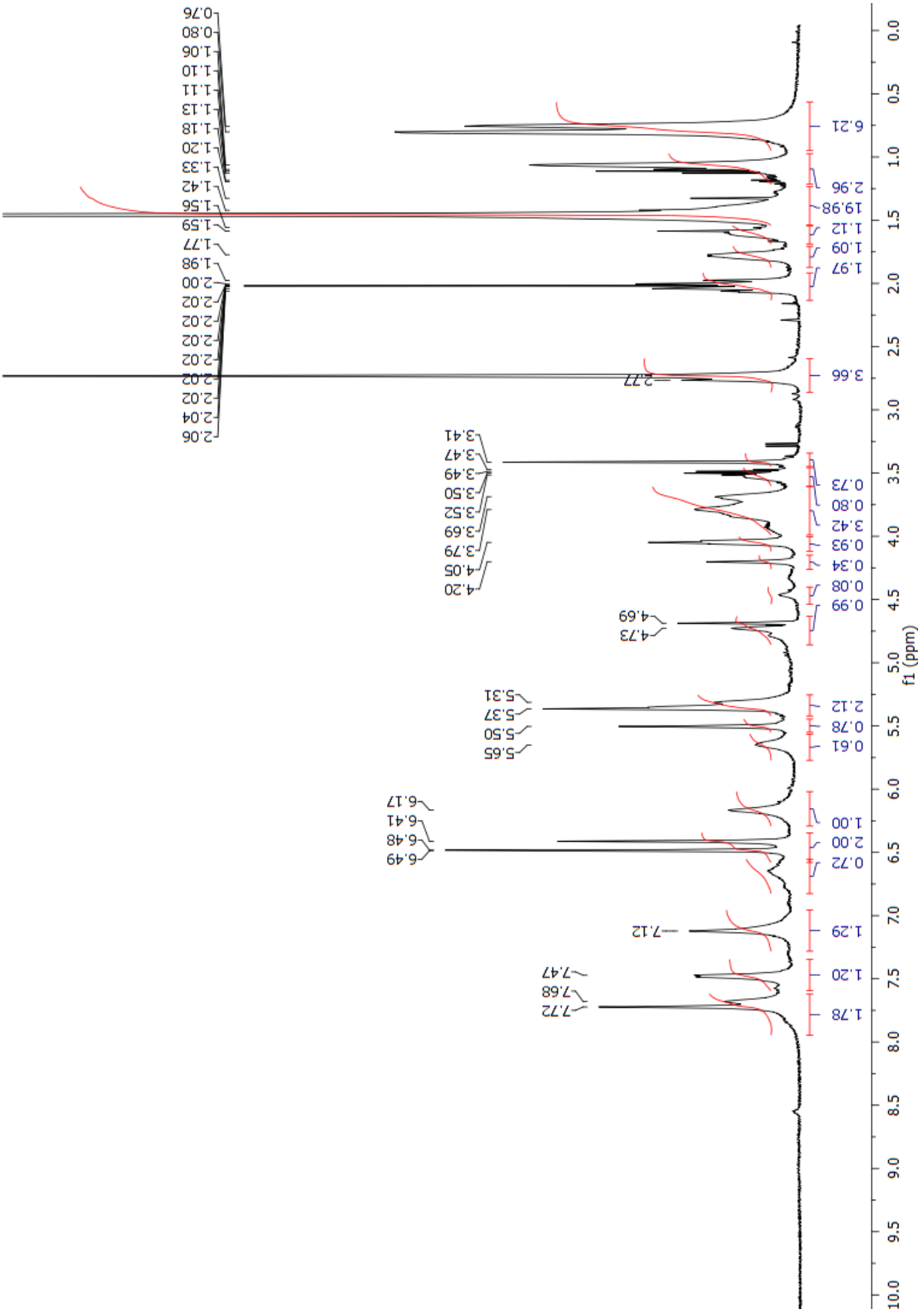
Signal	^{1}H	^{13}C	Signal	^{1}H	^{13}C
d	7.72	127.7[a,b]	r3	4.47	59.1
f	7.70	127.7[a,b]	r2	4.21	62.7[a]
e	7.67	127.7[a,b]	w	4.05[b]	60.8[a,b]
g	7.49[b]	126.2[b]	r1	3.84[b]	60.8[a,b]
j	7.48[b]	126.2[b]	x	3.85	60.8[a,b]
i	7.11[b]	135.3[b]	A2	3.68	69.1
k	7.11[b]	135.3[b]	A5	3.77	79.1
m	6.67	118.1	A3	3.50	76.2
l	6.49[b]	103.0[b]	A6	3.84-4.04	60.6[a]
o	6.49[b]	103.0b	A4	3.69	69.1
p	6.41	107.8	G	3.41	70.7
r4	6.17	55.2	zz’	2.77-2.73	35.7
s1	5.66	101.0[a]	y	2.73	32.0
u	5.52	72.1	DD’	2.01	33.0
A1	5.32	71.6[b]	aa’	1.78-1.61	38.7
t	5.29	71.6[b]	b	1.46	24.0
s2	5.37	107.5[a]	E	1.44	22.2
B	5.35	97.6	F	1.06	13.1
v	4.80	64.0[b]	cc’	0.80-0.75	21.7
c	4.76	64.0[b]			

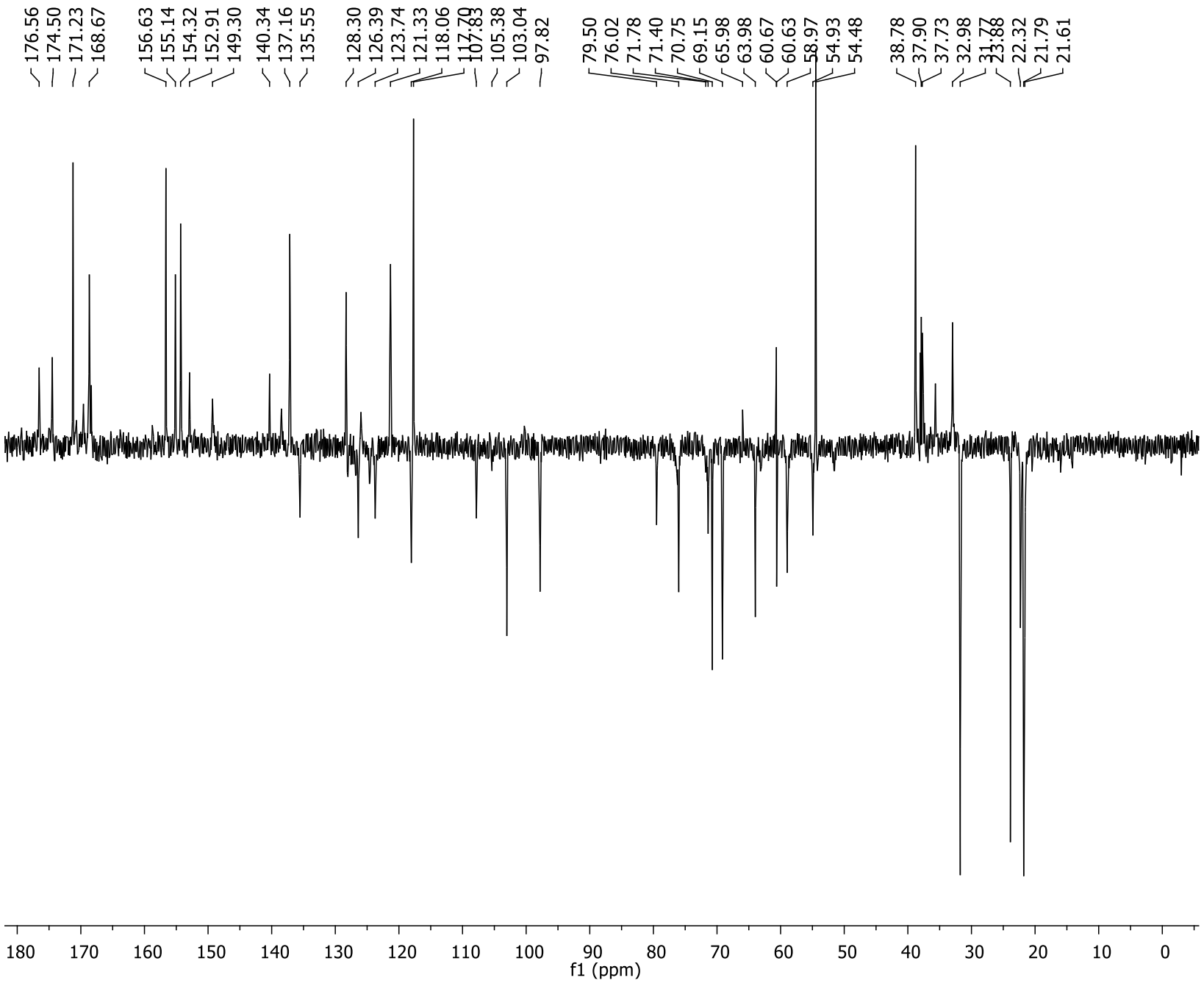
[a]from HSQC analysis; [b]overlapped signals

Table T1c: Shift difference analysis between Van and [Ir(Cp*)(Van)Cl] complex.

Signal	^{1}H	^{13}C	Signal	^{1}H	^{13}C
d	+0.05	-0.6	r3	-0.08	+0.1
f	+0.12	-1.8	r2	-	-0.05
e	+0.15	+1.3	w	-0.03	+0.2
g	-0.03	-0.2	r1	+0.02	+0.2
j	+0.24	+1.6	x	-0.89	+0.2
i	-0.13	+10.7	A2	-0.08	+8.5
k	-	-0.3	A5	+0.15	-10
m	-0.21	-	A6	-	-0.1
l	-0.38	-15.1	A3	-0.11	+6
o	-0.01	-	A4	+0.08	-
p	-0.03	-	G	-	-
r4	+0.06	+0.3	zz’	-	-
s1	-0.08	-	y	+0.01	+0.2
u	-0.01	+0.7	DD’	-0.02	-
A1	-0.17	+0.2	aa’	0.02-0.04	-0.1
t	-0.1	-0.2	b	-0.06	+0.1
s2	-0.01	+2.1	E	+0.04	-0.1
B	+0.04	-0.2	F	-0.06	-2.9
v	-0.04	-	cc’	0.01-0.03	-
c	-0.08	-			

Figure S3. ^{1}H, ^{13}C-NMR and HSQC of Van.

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156.63
155.14
154.32
152.91
149.30
140.34
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135.55
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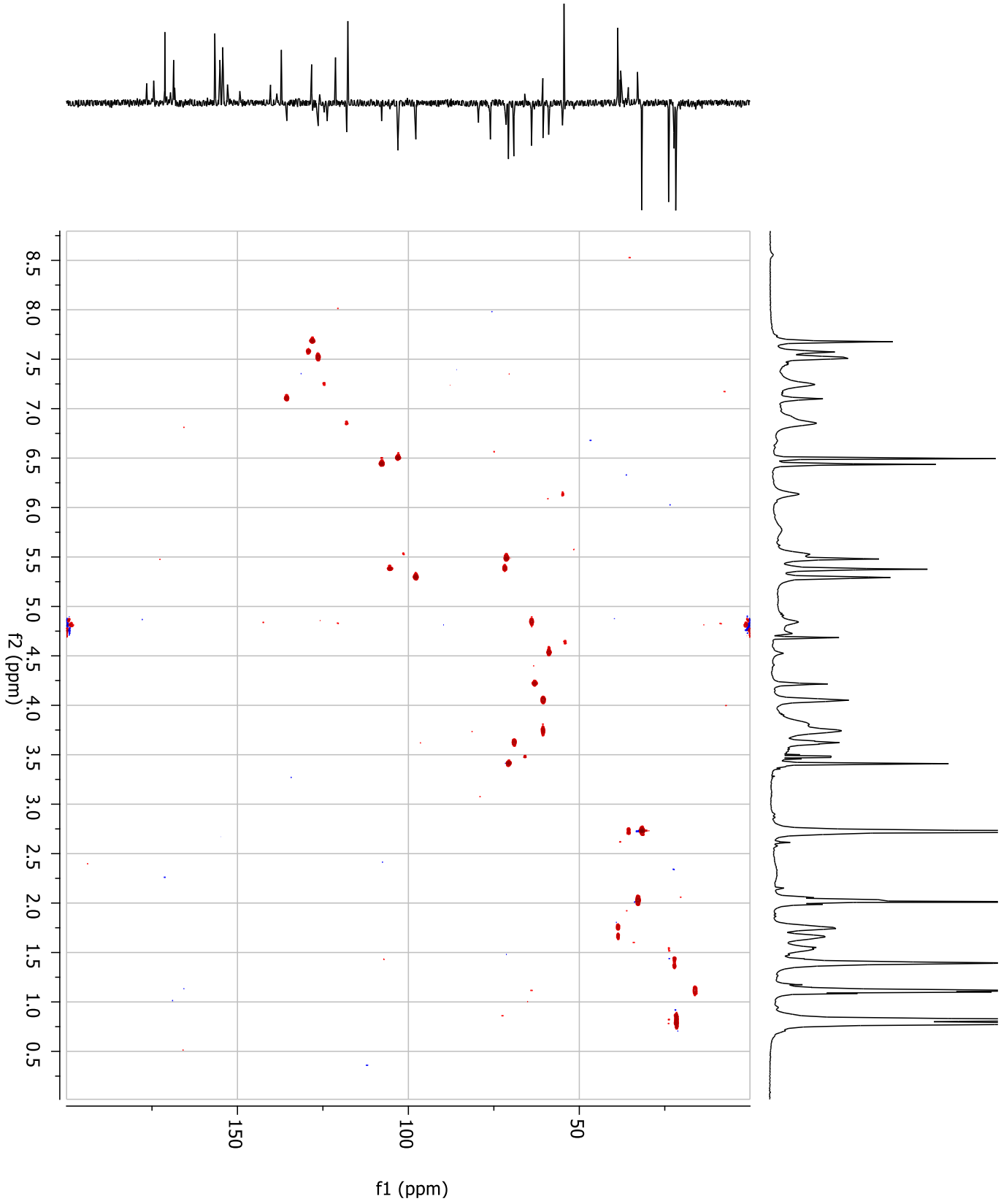
126.39
123.74
121.33
118.06
117.70
107.83
105.38
103.04
97.82
79.50
76.02
71.78
71.40
70.75
69.15
65.98
63.98
60.67
60.63
58.97
54.93
54.48
38.78
37.90
37.73
32.98
31.77
23.88
22.32
21.79
21.61
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


f2 (ppm)
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7.0
6.5
6.0
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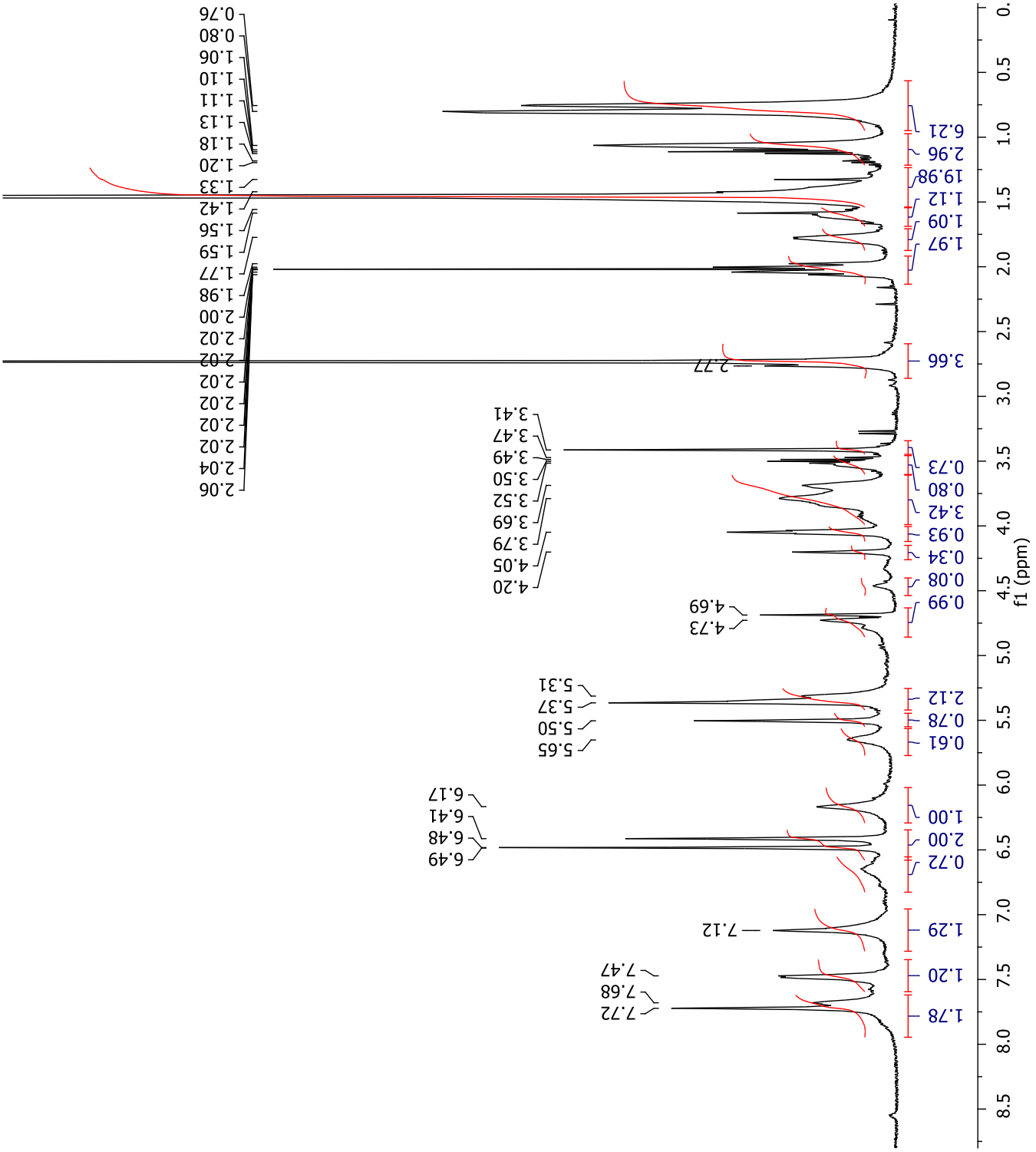
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
150
100
50
f1 (ppm)

Figure S4. ^{1}H, ^{13}C-NMR, HSQC, TOCSY, ROESY, NOESY and COSY of [Ir(Cp*)(Van)Cl] complex.



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24.00
31.96
32.97
35.69
38.70
54.46
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65.99
69.06
70.71
71.62
76.16
93.87
97.60
103.03
117.91
118.07
121.86
123.99
126.20
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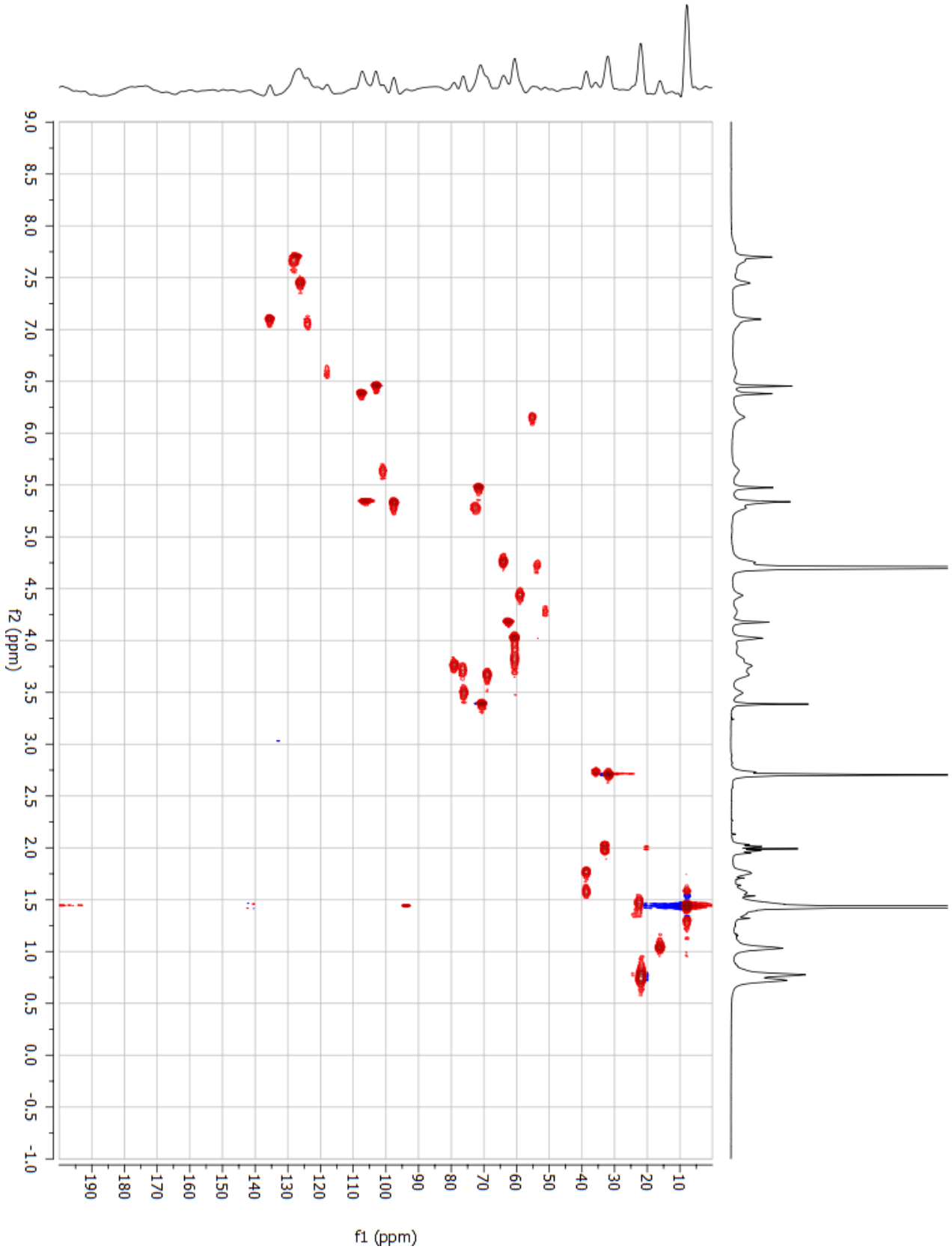
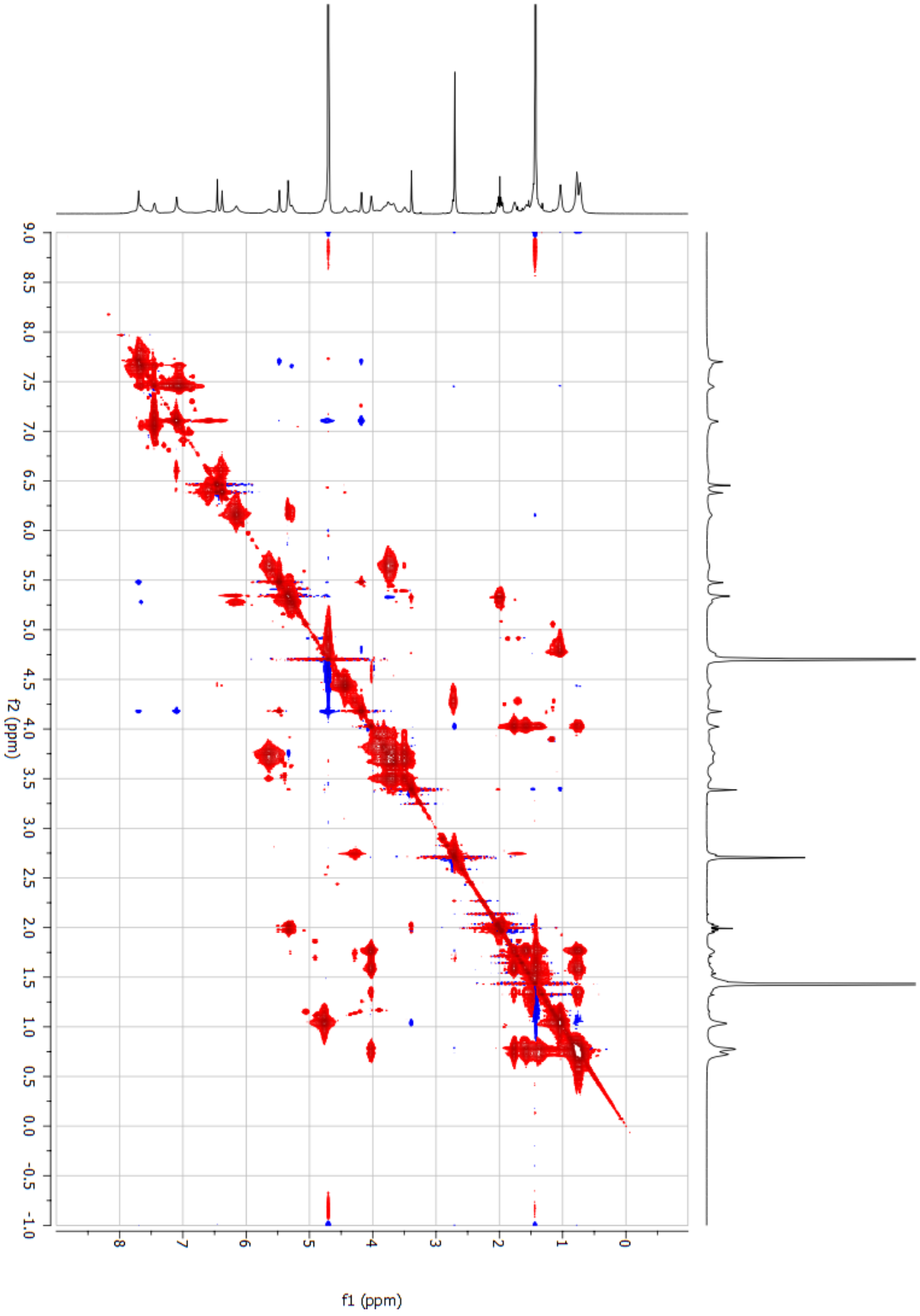
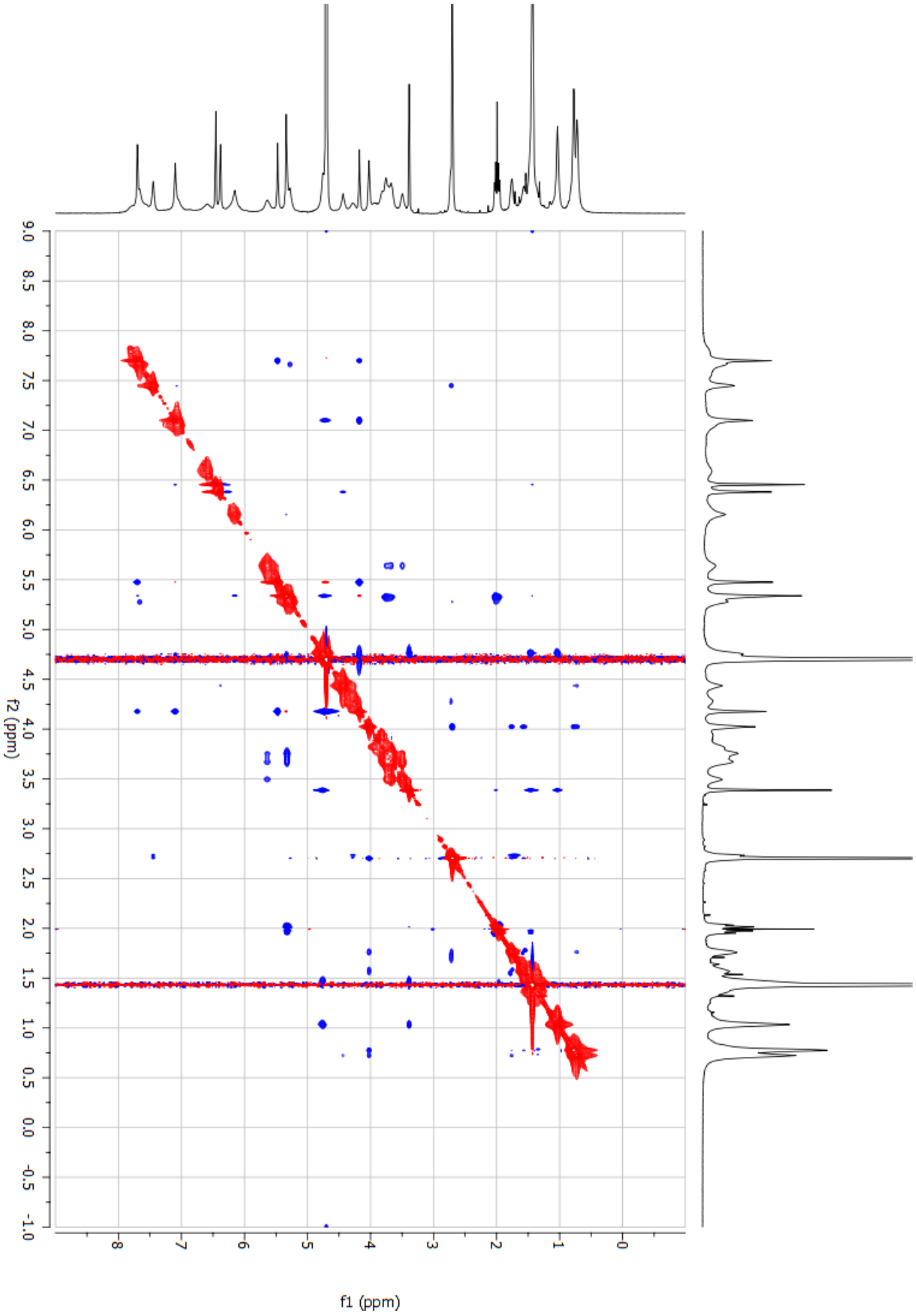
f1 (ppm)



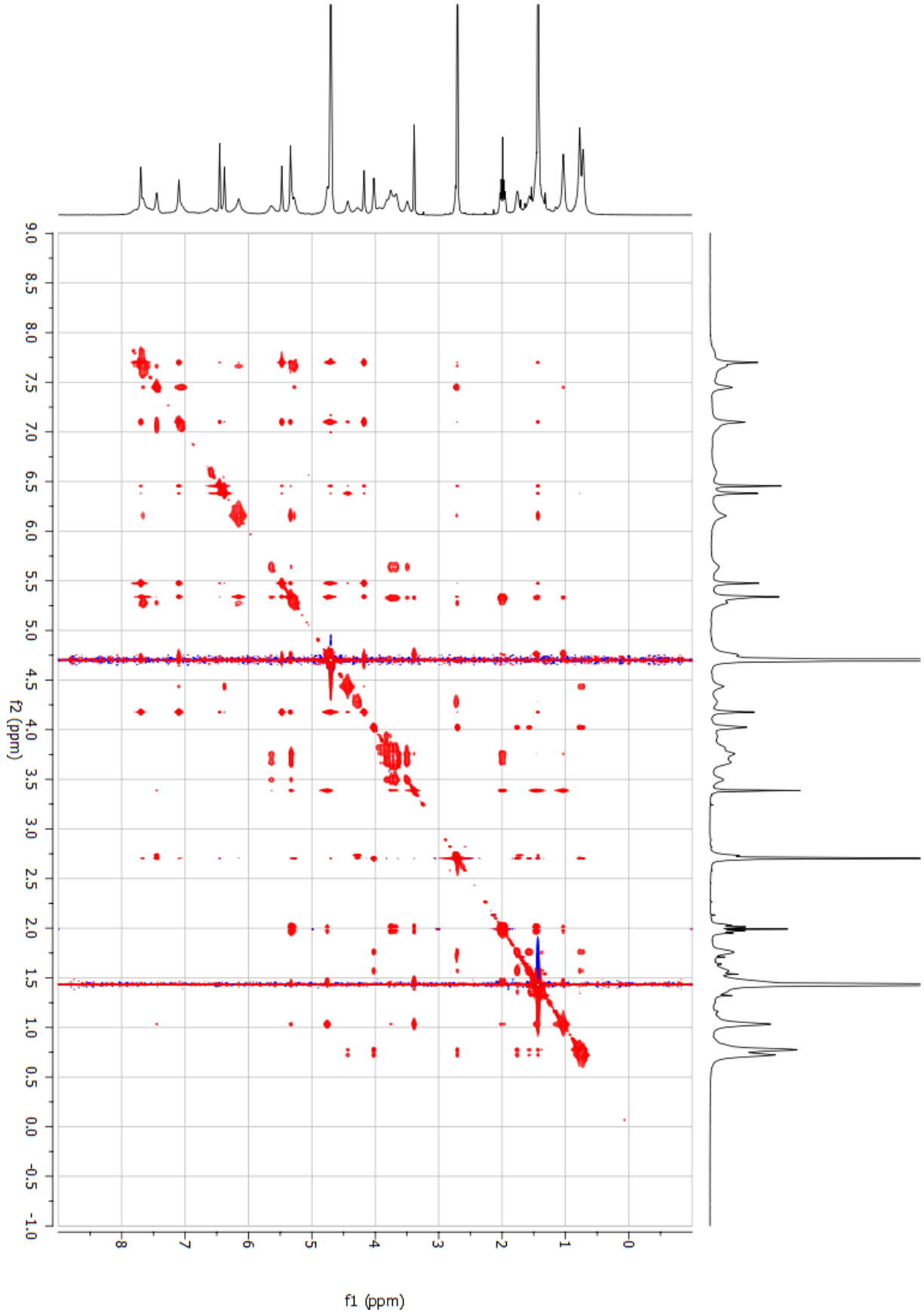
HSQC of [Ir(Cp*)(Van)Cl] complex



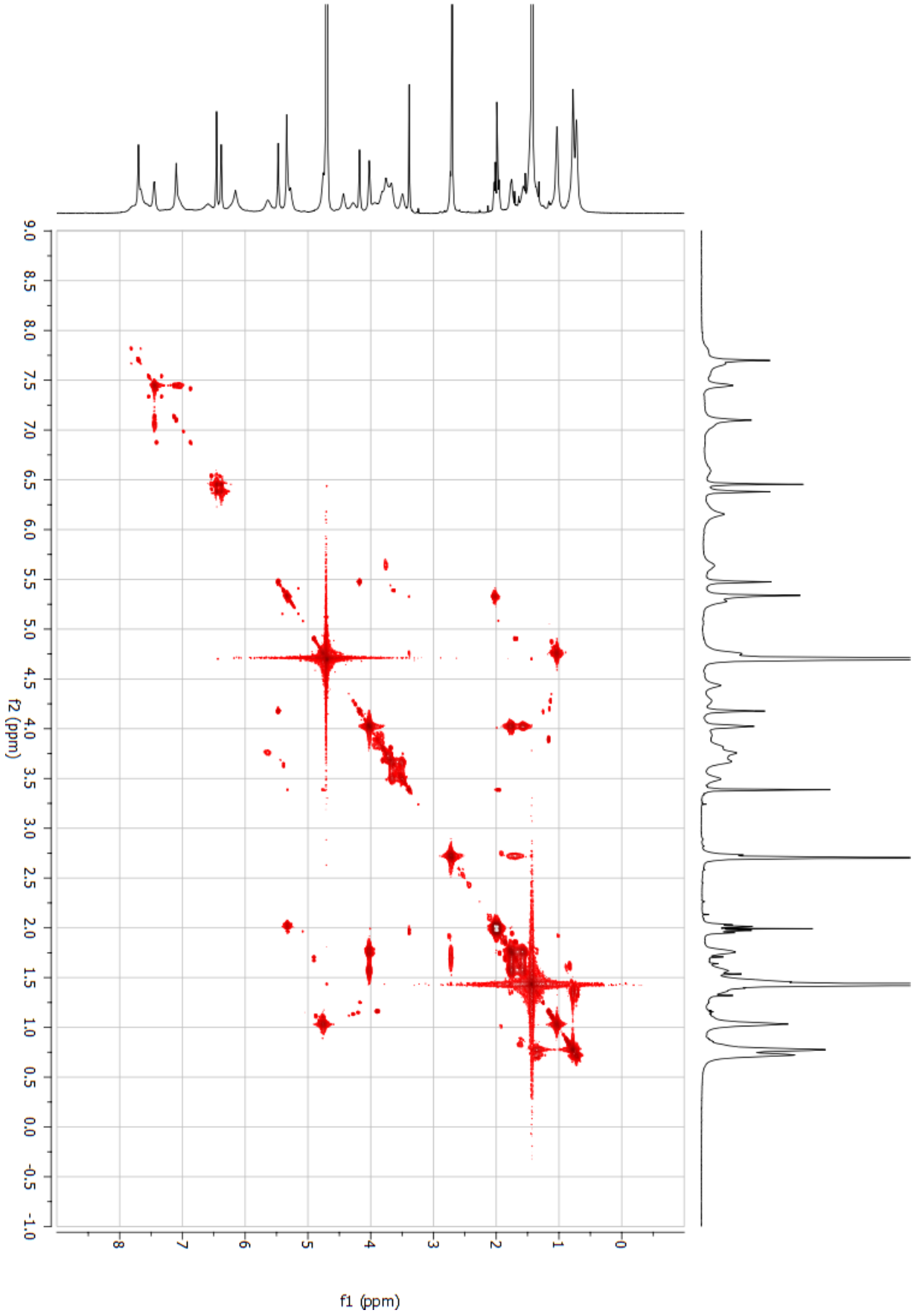
TOCSY of [Ir(Cp*)(Van)Cl] complex



ROESY of [Ir(Cp*)(Van)Cl] complex



NOESY of [Ir(Cp*)(Van)Cl] complex



COSY of [Ir(Cp*)(Van)Cl] complex

1.4. **Raman Spectroscopy**

The Raman spectra were obtained using a diode laser with a 1064 nm excitation wavelength and an 80-mW output power directed towards a sample holder with the cuvette for sample irradiation.

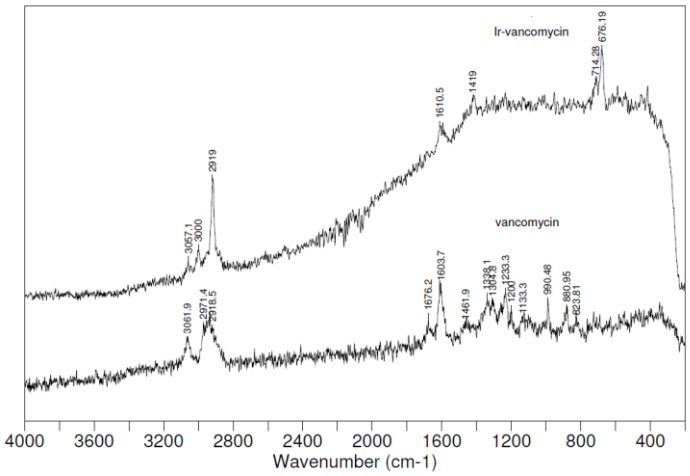


Figure S5. Raman spectra for overlay of 25 mM vancomycin alone (the band at 1603 cm^{-1}, attributed to carbonyl group; the band at 1338 cm^{-1} attributed to CH_3 bending, the band at 990 cm^{-1} represents breathing of the aromatic ring and the band at 880 cm^{-1} represents the stretching of the C-C bond) and of 25 mM [Ir(Cp*)(Van)Cl] complex.[2]

1.5. **Kinetic experiments**

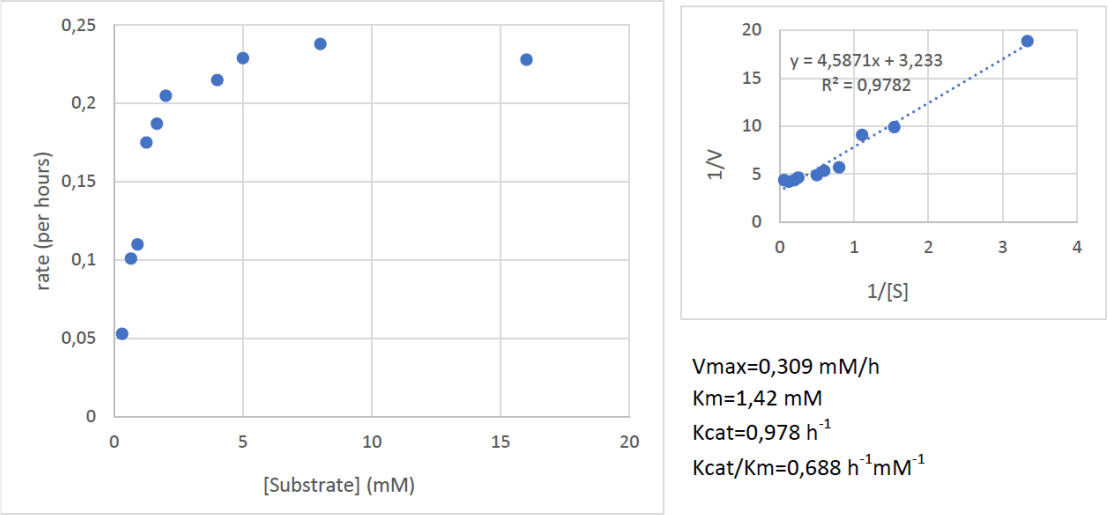


Figure S6: Kinetic parameter describing the reduction of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline **1** by [Ir(Cp*)(Van)Cl] complex in ATH reaction conditions.

2. Additional catalysis data

Table T2. Evaluation of different reaction conditions for ATH of cyclic imines

Entry	Buffer	Van/Ir ratio	$[sub]_{final}$ mM	Temp	**1** conv.%(e.e.%)	**2** conv.%(e.e.%)	**3** conv.%(e.e.%)
1	Phosphate 0.1 M pH 8	0:1	16	25°C	32	-	63
2	MOPS 1.2 M pH 7.8	0:1	16	25°C	38	-	61
3	MES 1.2 M pH 7	0:1	16	25°C	85	4	44
4	MES 1.2 M pH 6	0:1	16	25°C	99	8	35
5	Acetate 0.1 M pH 5	0:1	16	25°C	99	10	18
6	MES 1.2 M pH 5	0:1	16	25°C	99	12	13
7	Phosphate 0.1 M pH 8	1:0	16	25°C	-	-	-
8	MOPS 1.2 M pH 7.8	1:0	16	25°C	-	-	-
9	MES 1.2 M pH 7	1:0	16	25°C	-	-	-
10	MES 1.2 M pH 6	1:0	16	25°C	-	-	-
11	Acetate 0.1 M pH 5	1:0	16	25°C	-	-	-
12	Phosphate 0.1 M pH 8	2:1	16	25°C	42 (8 *S*)	30 (36 *R*)	92 (42 *R*)
13	MOPS 1.2 M pH 7.8	2:1	16	25°C	34 (*rac*)	40 (46 *R*)	64 (*rac*)
14	MES 1.2 M pH 7	2:1	16	25°C	82 (4 *S*)	30 (9 *R*)	60 (4 *R*)
15	MES 1.2 M pH 6	2:1	16	25°C	40 (4 *S*)	67 (12 *R*)	25 (*rac*)
16	Acetate 0.1 M pH 5	2:1	16	25°C	34 (*rac*)	20 (21 *R*)	30 (*rac*)
17	MES 1.2 M pH 5	2:1	16	25°C	75 (*rac*)	35 (61 *R*)	20 (30 *S*)
18	MES 1.2 M pH 5	1:1	16	25°C	63 (*rac*)	31 (22 *R*)	21 (28 *S*)
19	MES 1.2 M pH 5	2:1	32	25°C	25 (*rac*)	15 (23 *R*)	8 (4 *R*)
20	MES 1.2 M pH 5	2:1	16	25°C	60 (*rac*)	40 (29 *R*)	39 (23 *S*)
21	MES 1.2 M pH 5	2:1	32	25°C	31 (*rac*)	18 (22 *R*)	15 (29 *S*)
22	MES 1.2 M pH 5	2:1	16	25°C	-	8 (15 *R*)	16 (30 *S*)
23	MES 1.2 M pH 5	2:1	16	10°C	-	13 (43 *R*)	n.d.
24	MES 1.2 M pH 5	2:1	16	40°C	95 (*rac*)	50 (26 *R*)	36 (16 *S*)
25	Phosphate 0.1 M pH 8	4:1	16	25°C	56 (20 *S*)	20 (10 *R*)	70 (35 *R*)
26	MOPS 1.2 M pH 7.8	4:1	16	25°C	49 (*rac*)	20 (*rac*)	70 (11 *R*)
27	MES 1.2 M pH 7	4:1	16	25°C	87 (5 *S*)	19 (50 *R*)	62 (5 *R*)
28	MES 1.2 M pH 6	4:1	16	25°C	55 (*rac*)	30 (17 *R*)	22 (*rac*)
29	Acetate 0.1 M pH 5	4:1	16	25°C	38 (4 *S*)	20 (37 *R*)	21 (*rac*)
30	MES 1.2 M pH 5	4:1	16	25°C	4 (*rac*)	23 (48 *R*)	18 (38 *S*)

31	MES 1.2 M pH 5	4:1	16	10°C	-	35 (47 *R*)	n.d.

Reaction conditions: HCOONa 3 M, 18 h, activation time 60 min.

3. HPLC analysis

Substrate **1**: eluent hexane/ethanol/DEA=95/5/0.1; λ=283 nm; flow=1.0 mL/min; retention time for **1** 10.9 min; enantiomers of **4**: t_S=15.2 min; t_R=18.7 min.

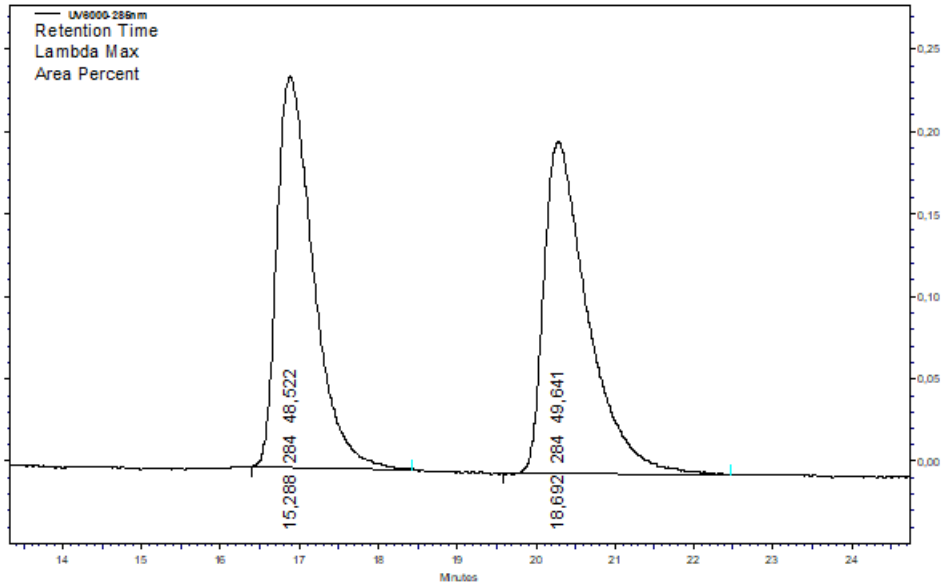


Figure S7. HPLC of standard for (*R*) and (*S*)- 6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline.

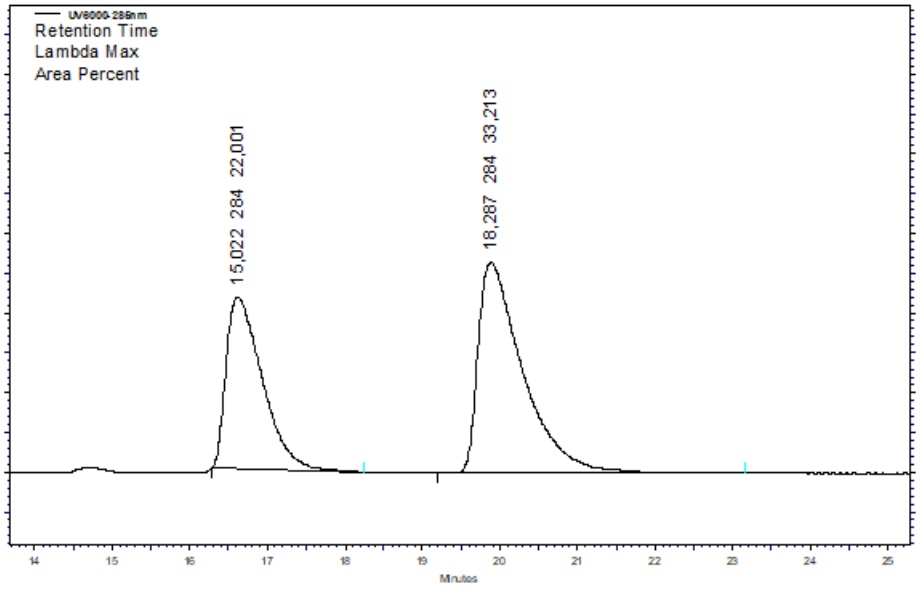


Figure S8. ATH of **1** in optimized reaction conditions (see manuscript, Table 1, entry 1-sub **1**).

Substrate **2**: eluent hexane/*iso*-propanol=90/10; λ=254 nm; flow=0.8 mL/min; retention time for **2** 14.8 min; enantiomers of **5**: t_S=6.6 min; t_R=7.4 min.

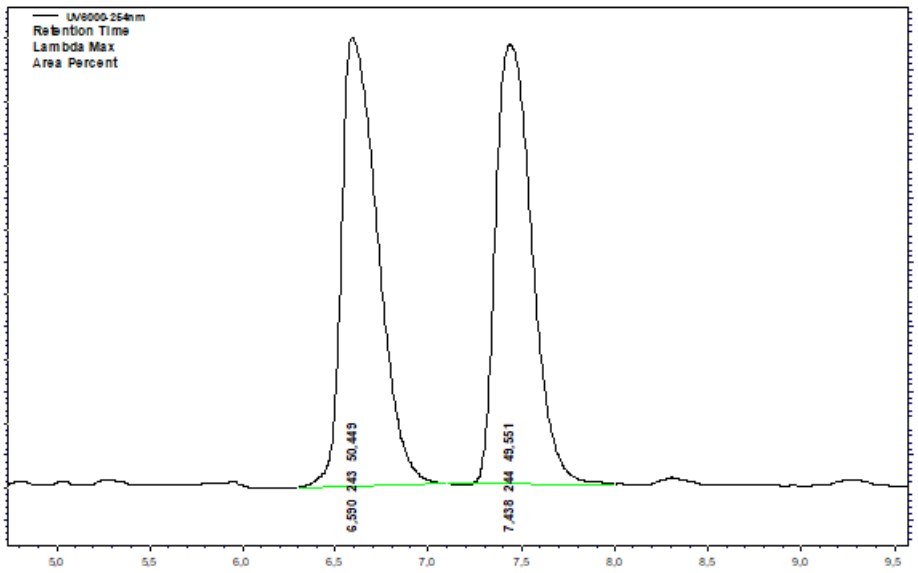


Figure S9. HPLC of standard for (*R*) and (*S*)- 2-methyl-1,2,3,4-tetrahydroquinoline.

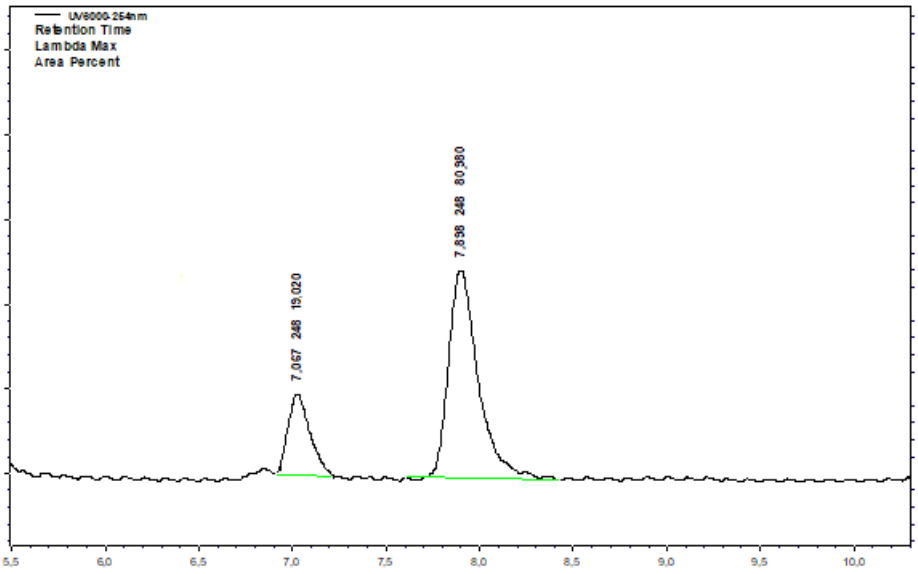


Figure S10. ATH of **2** in optimized reaction conditions (see manuscript, Table 1, entry 6-sub **2**).

Substrate **3**: eluent hexane/*iso*-propanol=80/20; λ=220 nm; flow=0.7 mL/min; retention time for **3** 28.6 min; enantiomers of **6**: $t_{(S)}$=19.5 min; $t_{(R)}$=24.6 min.[3]

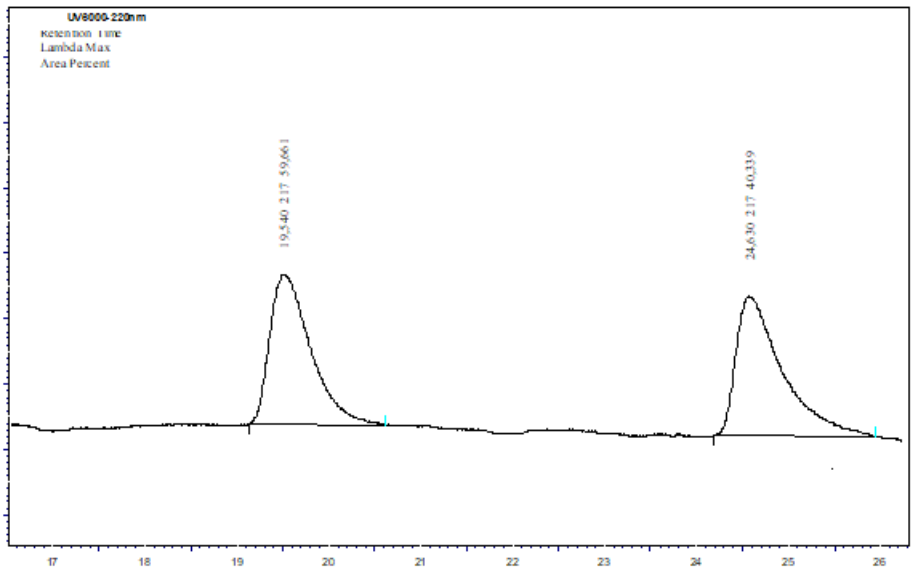


Figure S11. HPLC of standard for (*R*) and (*S*)- 3-methyl-2,3-dihydrobenzo[d]isothiazole 1,1-dioxide.

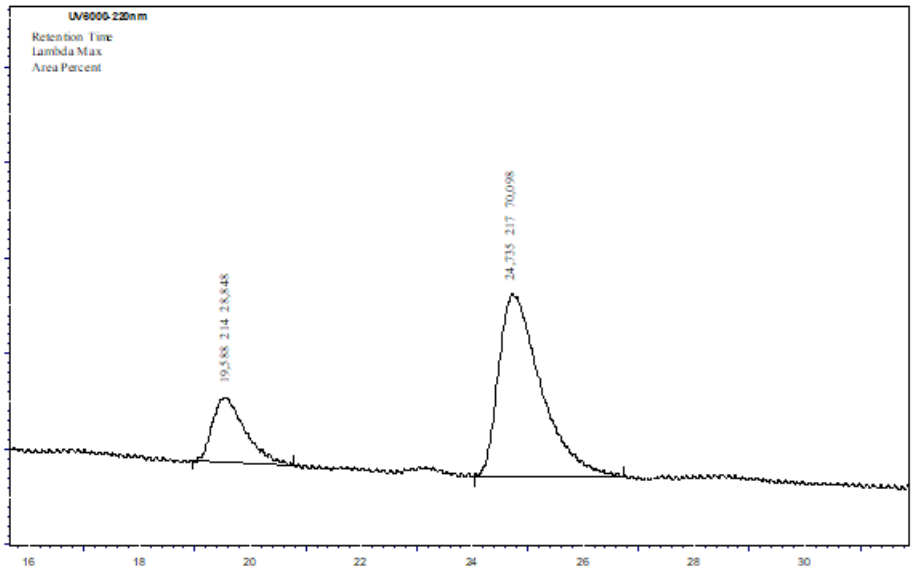


Figure S12. ATH of **3** under optimized reaction conditions (see manuscript, Table 1, entry 1-sub **3**).

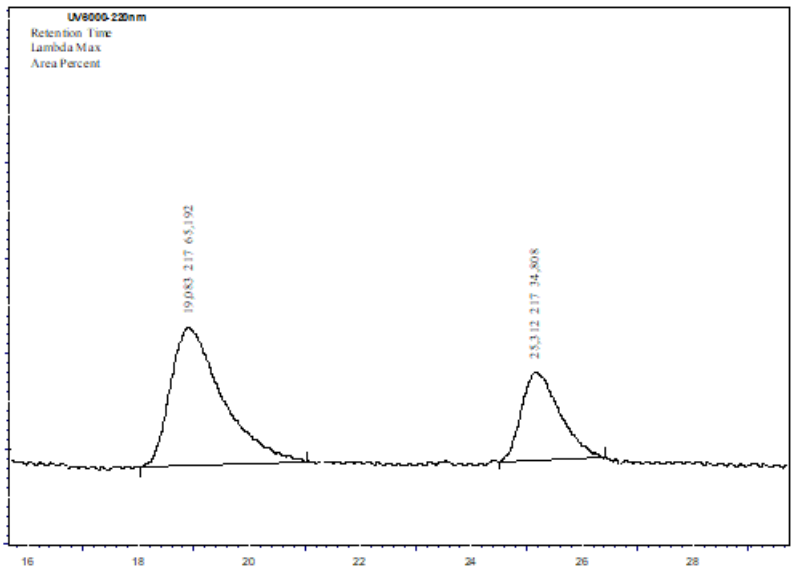


Figure S13. ATH of **C** under optimized reaction conditions (see manuscript, Table 1, entry 6-sub **3**).

REFERENCES

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