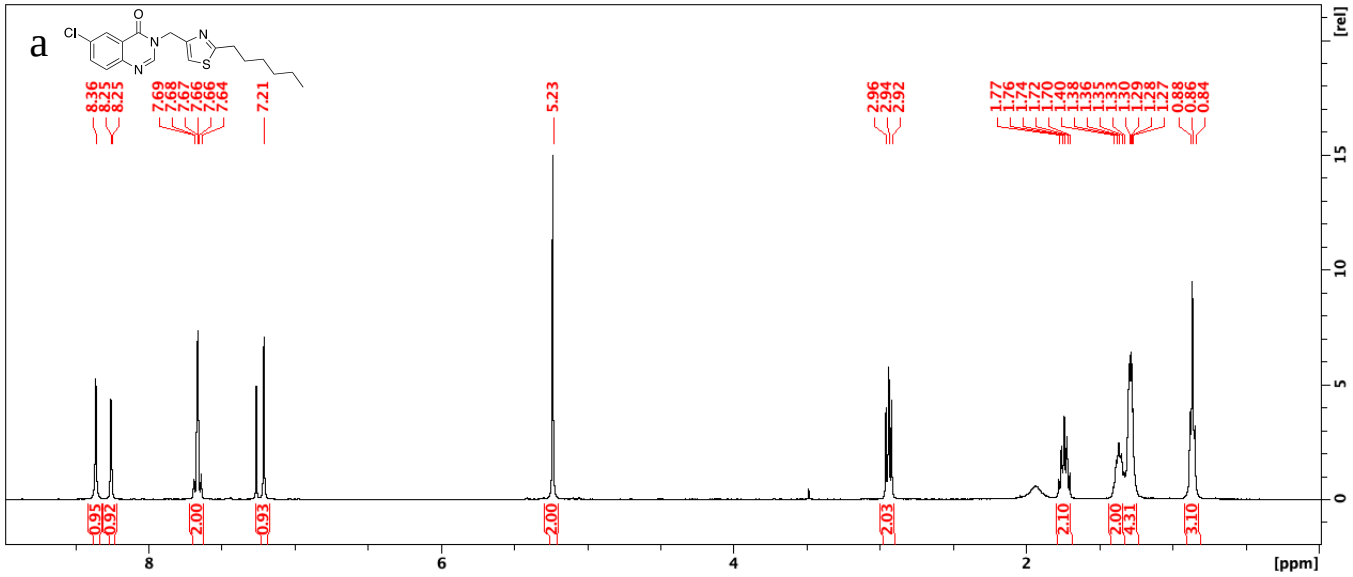
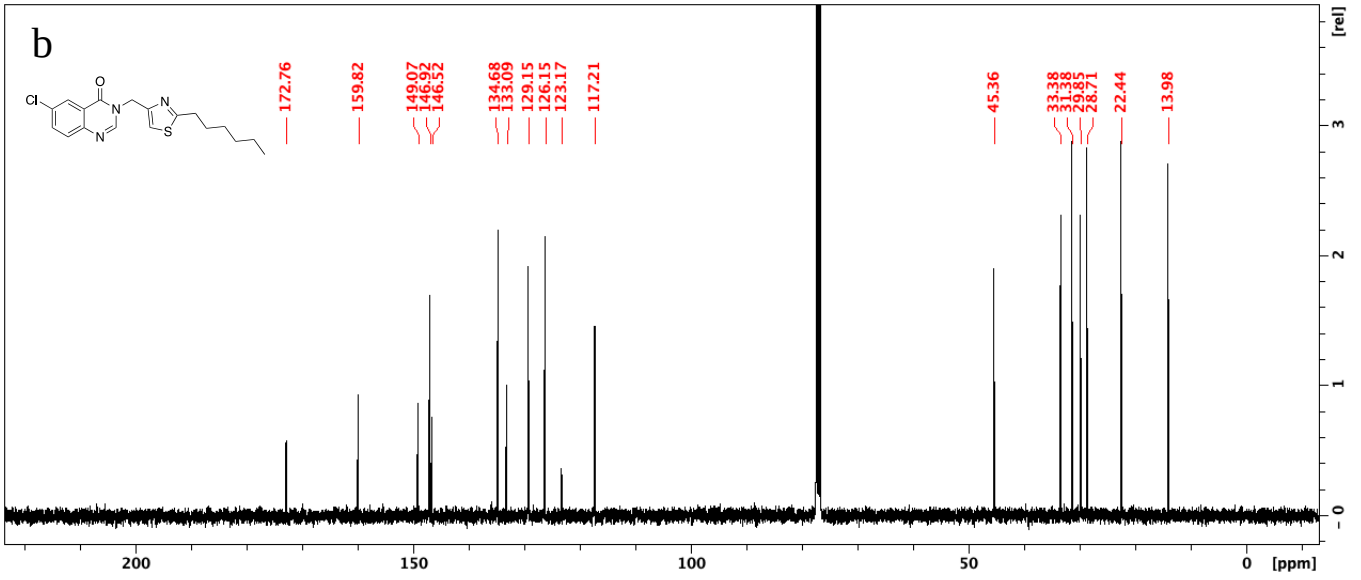
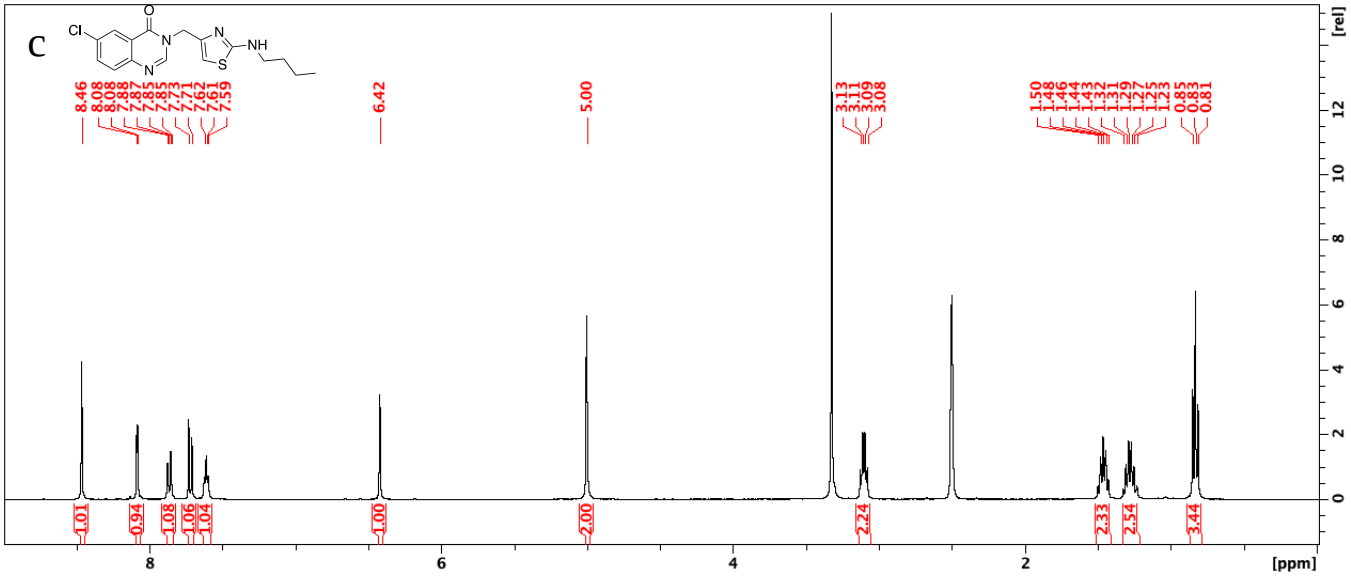
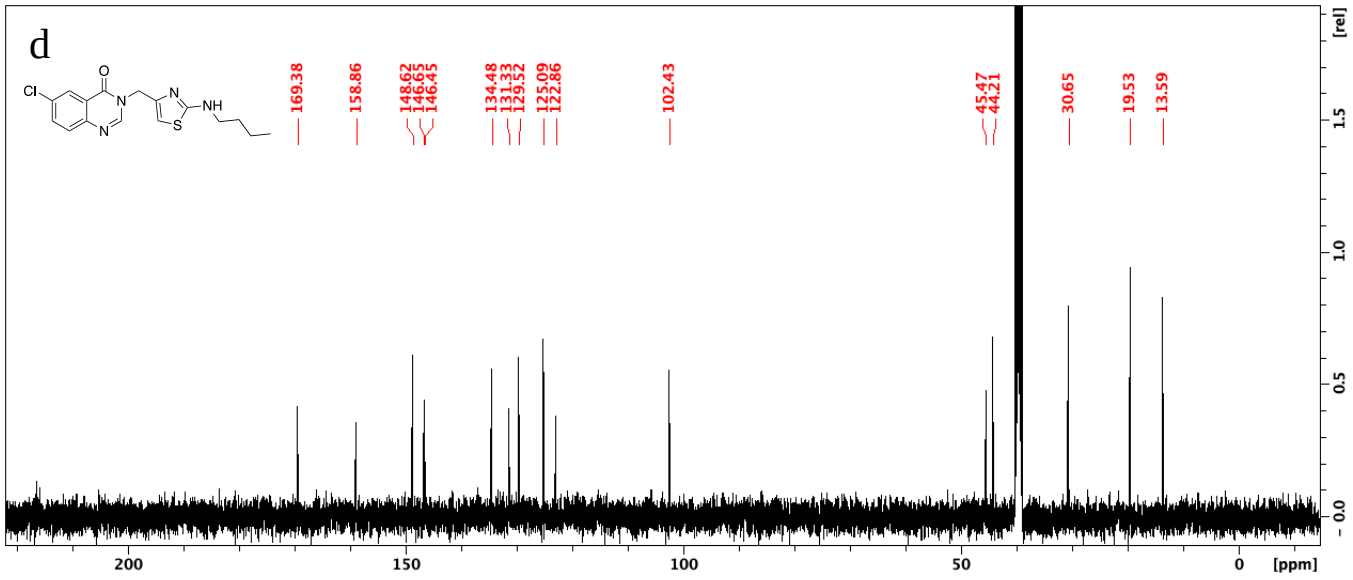
Supplementary Information:

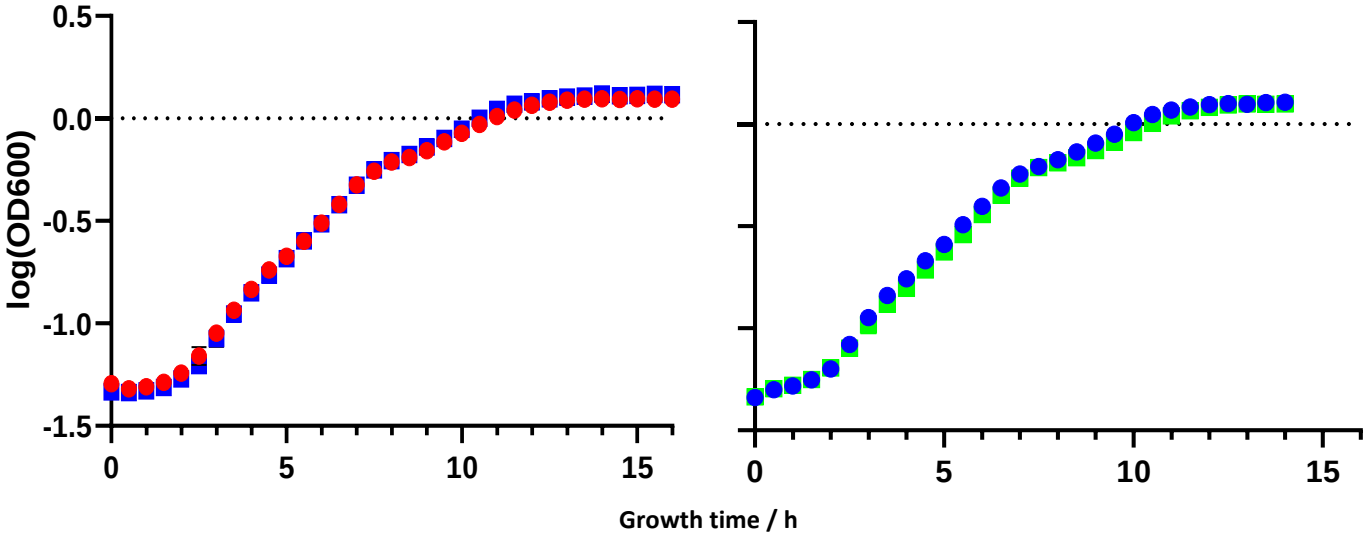
S1: Representative NMR spectra of compounds **18** (a, 1H; b, 13C) and **25** (c, 1H; d, 13C)



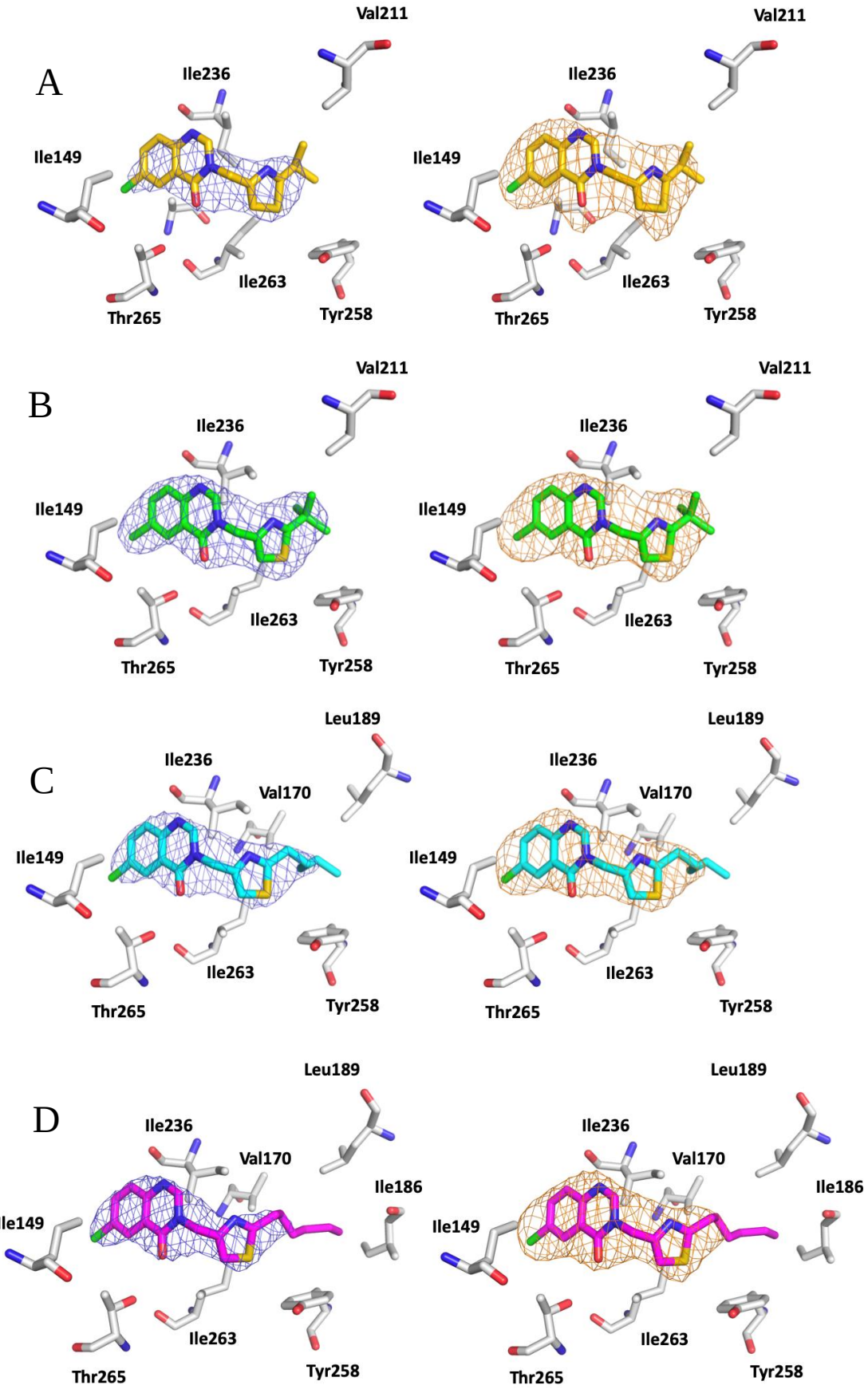



c
8.46
8.08
8.08
7.88
7.87
7.85
7.85
7.73
7.71
7.62
7.61
7.59
6.42
5.00
3.13
3.11
3.09
3.08
1.50
1.48
1.46
1.44
1.43
1.32
1.31
1.29
1.27
1.25
1.23
0.85
0.83
0.81
1.01
0.94
1.08
1.06
1.04
1.00
2.00
2.24
2.33
2.54
3.44
[ppm]
[rel]

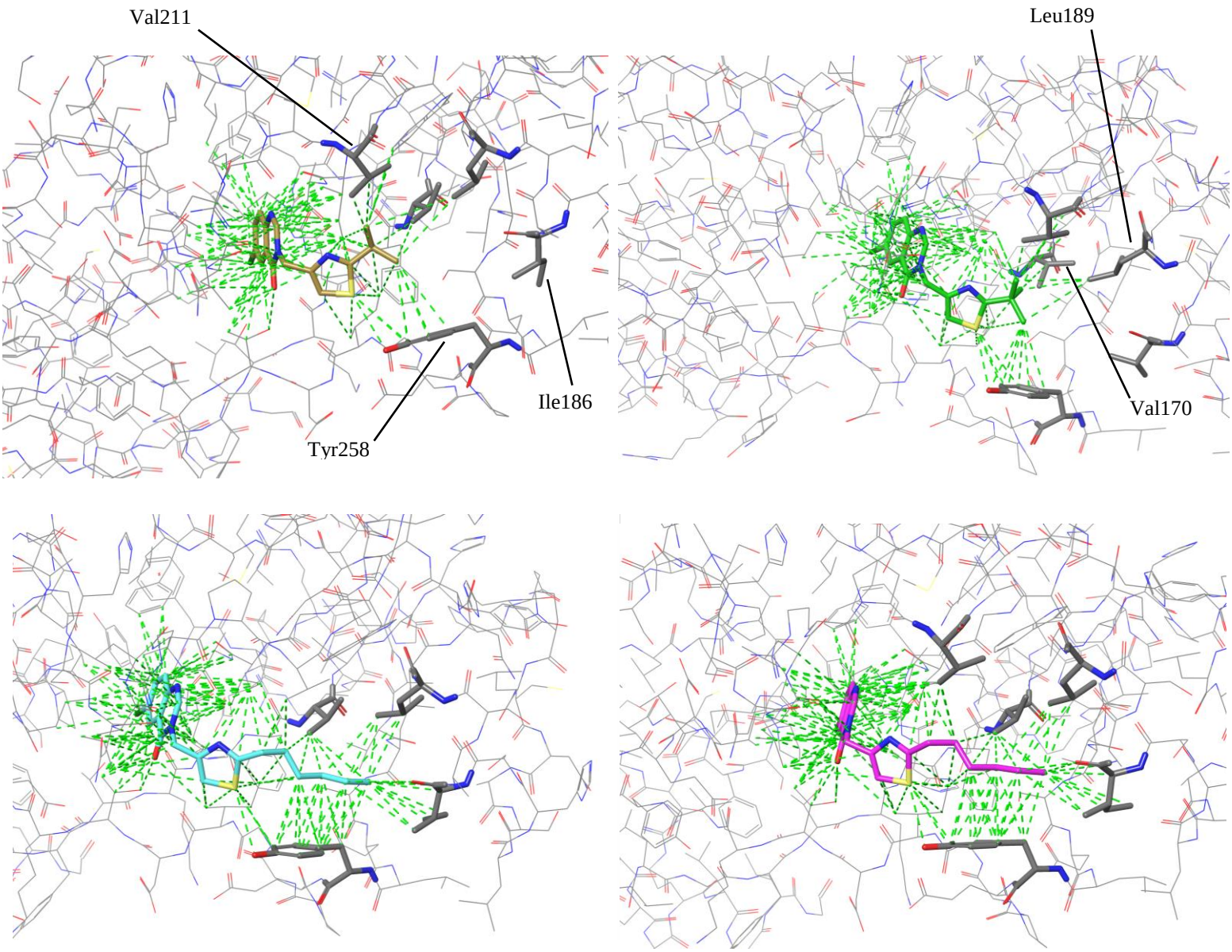

d
169.38
158.86
148.62
146.65
146.45
134.48
131.33
129.52
125.09
122.86
102.43
45.47
44.21
30.65
19.53
13.59
[ppm]
[rel]



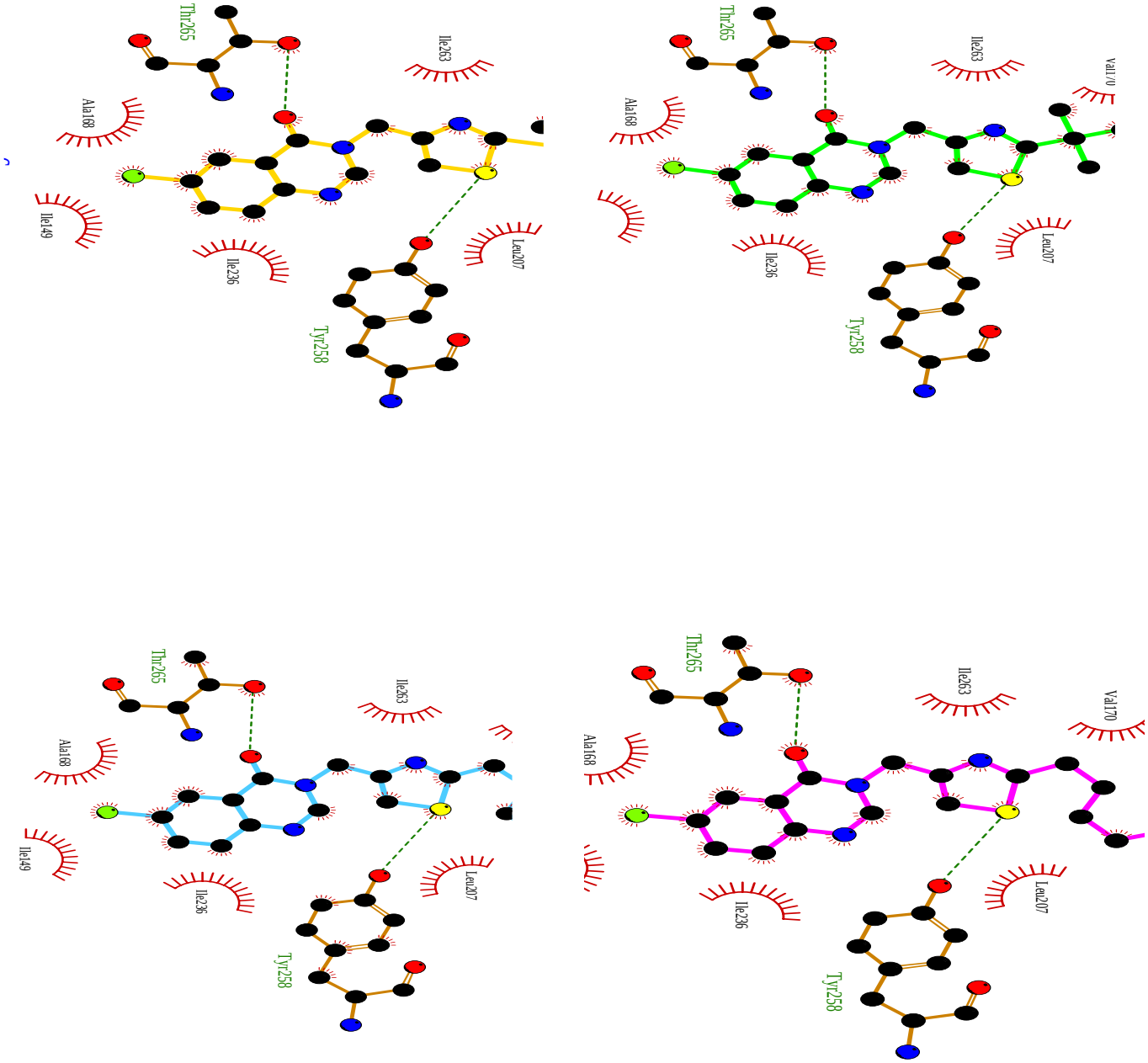
S2: Growth curves of *Pseudomonas aeruginosa* strain PA01-L containing (left, red) **18** or (right, green) **19** compared to a control of 0.1% DMSO (left and right, blue). No difference in growth over a 15 h incubation was observed, confirming a lack of bactericidal activity



S3: Electron density maps for **6**, **12**, **18** and **19** (A – gold, B – green, C – cyan, and D – magenta, respectively) in complex with $PqsR^{LBD}$: left 2mFoDFc map (σ = 1) generated by REFMAC, and right OMIT map mFo-DFc (σ = 3) generated by PHENIX.polder



S4: Predicted hydrophobic interactions between LBD and (top left) **6**, (top right) **12**, (bottom left) **18** and (bottom right) **19**, as calculated by Schrodinger's Meastro software. The longer alkyl chains of **18** and **19** are capable of forming a dense network of interactions, in particular with Ile186 and Leu189, compared with **6** and **12** which formed fewer interactions with Leu189 and none with Ile186



S5: LigPlot schematics depicting the polar (green dashed lines) and hydrophobic (red dashed semicircles) between all four crystallised ligands and the PqsR LBD

S6: Crystallographic table of data collection and refinement:

Data collection	**6**	**12**	**18**	**19**
Beamline	I04	I04	I04	I04
Wavelength (Å)	0.9795	0.9795	0.9795	0.9795
Space group	$P6_522$	$P6_522$	$P6_522$	$P6_522$
a ,b, c (Å)	120.27, 120.27 115.04	120.79, 120.79, 114.39	118.91, 118.91, 115.46	119.32, 119.32, 114.76
α, β, γ (°)	90. 90. 120	90, 90, 120	90, 90, 120	90, 90, 120
Resolution	60.13 – 3.15	60.39 - 2.95	115.46 – 3.2	59.66 – 3.00
No. of unique reflections	8476 (1514)	10879 (1704)	7628 (1370)	10169 (1599)
R_{merge} (%)	8.1 (80.3)	8.5 (107)	6.1 (39.8)	9.7 (170)
Mean I/Sig(I)	13.9 (2.9)	12.6 (1.7)	16.6 (3.1)	17.1 (1.7)
Completeness	95.7 (96.6)	100 (100)	92.4 (93.7)	100 (100)
Redundancy	10.1 (10.4)	9.6 (10.2)	9 (9)	19.2 (20.2)
CC½	0.970 (0.966)	0.998 (0.917)	0.997 (0.972)	0.999 (0.932)
Refinement				
Resolution range (Å)	60.20-3.15	60.47 - 2.95	76.97 – 3.2	59.73 – 3.00
R/Rfree	0.195 / 0.241	0.20/0.257	0.204/0.261	0.193/0.255
Mean B-Factor (Å)	143.6	131.6	146.2	139
r.m.s.d bond lengths (Å)	0.0077	0.0081	0.0025	0.0076
r.m.s.d bond angles (°)	1.653	1.671	1.236	1.364
Ramachandran plot statistics (%)				
Preferred regions	97.51	95.52	96.52	94.53
Outliers	0	0	0	0
PDB ID	6Z17	6Z07	6Z5K	6YZ3

Values in parentheses are for highest-resolution shell.