Supporting Information

8-Azatetracyclines: Synthesis and Evaluation of a Novel Class of Tetracycline Antibacterial Agents

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A) Full panel MIC data for all compounds.

Table 9. Gram-positive MIC data for all compounds.

Cmpd	MIC (μg/mL)							
	SA101[a]	SA100[a] Smith	SA161[a] *tet*(M)	SA158[a] *tet*(K)	EF103[b]	EF159[b] *tet*(M)	SP106[c]	SP160[c] *tet*(M)
20a	0.5	1	32	16	16	>32	0.25	32
20b	1	1	32	32	32	>32	1	32
20d	0.5	1	32	0.5	>32	>32	0.25	>32
20e	0.063	0.063	32	1	4	>32	0.031	4
20f	0.031	0.25	32	1	1	32	0.063	8
20g	0.125	0.125	8	4	8	>32	0.063	16
20i	0.031	0.063	8	8	4	32	0.016	8
20j	0.063	0.016	4	8	1	32	0.016	4
20k	0.063	0.063	2	8	0.5	16	0.063	2
21a	2	2	32	32	8	>32	1	16
21b	4	4	16	16	8	32	2	8
21c	16	16	32	8	8	16	4	4
24a	0.031	0.031	1	0.5	0.063	4	0.031	4
24b	0.016	0.016	1	2	0.125	8	0.016	4
24c	0.031	0.063	1	0.5	0.5	2	0.25	8
24d	1	1	4	2	2	2	2	16
24e	0.25	0.5	1	0.5	0.5	1	1	8
24f	0.5	0.25	2	0.25	2	2	8	32
24g	0.016	0.031	4	1	0.25	8	0.063	4
24h	0.25	0.5	2	0.25	2	4	0.031	4
24i	2	2	8	2	4	32	1	4
24j	1	1	2	0.5	0.5	2	0.5	1
24k	1	2	4	1	2	8	0.5	2
24l	0.25	0.5	2	0.125	0.25	2	0.016	0.125
24m	0.25	0.5	2	0.125	0.5	2	0.031	0.25
24n	0.25	0.25	2	0.25	0.5	4	4	4
24o	>32	>32	>32	>32	>32	>32	8	>32
26a	0.5	1	2	1	1	2	1	2
26b	1	1	4	4	4	4	1	4
26c	2	2	8	16	8	16	0.5	8
26d	4	4	32	32	16	>32	1	16
26e	1	1	2	1	1	1	8	8
26f	4	4	8	16	4	4	2	8
2	0.5	1	>32	32	16	>32	0.25	32
4	0.063	0.125	16	0.25	1	16	<0.016	8
5	0.063	0.063	0.125	0.063	0.031	0.063	0.016	0.016
6	0.5	0.5	2	0.25	0.25	0.5	0.031	0.125

[a] *S. aureus.* [b] *E. faecalis.* [c] *S. pneumoniae.*

Table 10. Gram-negative MIC data for all compounds.

Cmpd	Organism, MIC (μg/mL)						
	EC107[a]	EC155[a] *tet*(A)	AB110[b]	PA111[c]	EC108[d]	KP109[e]	KP153[e] *tet*(A)
20a	0.5	>32	2	8	1	1	>32
20b	2	>32	32	>32	8	4	>32
20d	1	>32	1	16	1	1	>32
20e	0.5	>32	0.125	>32	2	2	>32
20f	0.125	>32	0.5	8	0.5	0.25	>32
20g	0.25	>32	0.5	>32	1	1	>32
20i	0.25	>32	0.25	8	0.5	0.5	>32
20j	0.25	>32	0.5	8	1	0.5	>32
20k	0.25	>32	0.5	4	0.5	1	>32
21a	4	>32	8	>32	8	8	>32
21b	8	>32	16	>32	16	16	>32
21c	32	>32	>32	>32	32	>32	>32
24a	0.5	16	0.031	16	4	2	32
24b	0.125	32	0.031	8	0.5	0.5	32
24c	4	16	N/A	32	16	8	32
24d	32	>32	1	>32	32	32	>32
24e	16	>32	2	>32	>32	>32	>32
24f	>32	>32	4	>32	>32	>32	>32
24g	1	32	0.063	32	4	4	>32
24h	8	>32	0.25	>32	32	16	>32
24i	8	>32	>32	>32	16	16	>32
24j	1	8	4	32	2	2	8
24k	4	32	32	32	8	8	32
24l	0.5	8	2	32	2	2	8
24m	2	8	2	32	4	4	8
24n	2	16	0.125	16	8	8	32
24o	>32	>32	>32	>32	>32	>32	>32
26a	16	>32	2	>32	>32	16	>32
26b	16	32	4	>32	32	32	>32
26c	8	>32	4	>32	32	8	>32
26d	8	>32	4	32	8	8	>32
26e	>32	>32	16	>32	>32	>32	>32
26f	16	>32	8	>32	>32	32	>32
2	2	>32	1	16	2	4	>32
4	0.5	8	0.063	16	2	1	8
5	0.125	0.5	0.25	8	0.25	0.125	1
6	2	16	1	>32	4	2	16

[a] *E. coli.* [b] *A. baumannii.* [c] *P. aeruginosa.* [d] *E. cloacae.* [e] *K. pneumoniae.*

B) MIC Data for *S. aureus* MIC_{90} calculations.

Table 11. Individual MIC data for *S. aureus* MIC_{90} calculations.[a]

S. aureus strain	Compound, MIC (μg/mL)			
	2	**5**	**20f**	**24l**
102	32	0.25	4	1
113	0.063	0.031	≤0.016	0.125
114	0.063	0.031	≤0.016	0.125
115	0.125	0.031	≤0.016	0.125
116	0.125	0.031	≤0.016	0.125
117	0.063	≤0.016	≤0.016	0.125
118	0.125	0.063	≤0.016	0.125
119	0.25	0.063	≤0.016	0.125
120	0.125	0.063	≤0.016	0.125
121	0.125	0.031	≤0.016	0.125
122	0.25	0.063	≤0.016	0.25
123	0.125	0.063	≤0.016	0.125
124	0.125	0.063	≤0.016	0.125
125	0.125	0.063	≤0.016	0.125
126	0.125	0.031	≤0.016	0.125
127	0.125	0.031	≤0.016	0.25
128	0.125	0.063	≤0.016	0.25
129	0.125	0.031	≤0.016	0.063
130	0.125	0.063	≤0.016	0.25
131	32	0.125	1	0.5
132	0.125	0.063	≤0.016	0.125
158	32	0.063	2	0.125
160	>32	0.125	16	2
176	>64	1	8	2
177	>64	0.25	32	1
178	>64	0.25	32	1
179	>64	0.25	32	1
180	64	0.25	2	0.25
181	>64	1	8	2
183	64	1	8	2
184	>64	1	16	4

[a] *S. aureus* strains were collected from various geographical sources.

C) MIC Data for *S. pneumoniae* MIC_{90} calculations.

Table 12. Individual MIC data for *S. pneumoniae* MIC_{90} calculations.[a]

S. pneumoniae strain	Compound, MIC (μg/mL)			
	2	**5**	**20f**	**24l**
106	0.125	≤0.016	≤0.016	≤0.016
160	32	≤0.016	8	0.063
287	>32	≤0.016	4	0.063
289	>32	≤0.016	1	0.063
290	32	≤0.016	4	0.031
291	>32	≤0.016	4	0.063
292	>32	≤0.016	4	0.063
294	0.063	≤0.016	≤0.016	≤0.016
295	16	≤0.016	2	≤0.016
296	>32	≤0.016	8	0.063
297	32	≤0.016	4	0.031
298	0.063	≤0.016	≤0.016	≤0.016
299	0.125	≤0.016	≤0.016	≤0.016
300	0.125	≤0.016	≤0.016	≤0.016
301	0.125	≤0.016	≤0.016	≤0.016
302	0.125	≤0.016	≤0.016	≤0.016
305	16	≤0.016	2	≤0.016
307	32	≤0.016	2	≤0.016
465	32	≤0.016	4	0.031

[a] *S. pneumoniae* isolates were obtained from Eurofins-Medinet and are recent clinical isolates.

D) MIC Data for *H. influenzae* MIC_{90} calculations.

Table 13. Individual MIC data for *H. influenzae* MIC_{90} calculations.[a]

H. influenzae strain	Compound, MIC (μg/mL)			
	2	**5**	**20f**	**24l**
175	8	0.25	0.25	0.25
262	8	0.5	1	0.5
275	4	0.5	1	1
276	4	0.5	0.5	0.5
278	0.5	0.5	0.125	1
280	16	1	2	1
281	0.25	0.5	0.125	1
282	0.5	0.5	0.125	1
283	0.5	0.5	0.063	0.25
284	32	0.5	4	2
286	4	0.5	0.5	1

[a] *H. influenzae* isolates were obtained from Eurofins-Medinet and are recent clinical isolates.

E) MIC Data for *E. coli* MIC_{90} calculations.

Table 14. Individual MIC data for *E. coli* MIC_{90} calculations.[a]

E. coli strain	Compound, MIC (μg/mL)			
	2	**5**	**20f**	**24l**
133	>64	0.25	>32	1
134	1	0.25	0.125	1
135	>64	0.5	>32	4
136	2	0.25	0.25	2
137	>64	0.25	>32	2
138	2	0.5	0.25	4
139	>64	0.5	32	4
140	0.5	0.125	0.063	0.5
141	4	2	1	8
142	1	0.25	0.063	0.5
143	0.5	0.5	0.5	0.5
144	1	0.25	0.25	1
145	0.25	0.25	0.031	0.5
146	0.5	0.125	≤0.016	0.5
147	2	0.25	0.125	1
148	>64	0.5	32	2
149	>64	0.5	32	2
150	1	0.25	0.25	2
151	2	0.25	0.125	1
152	1	0.125	0.125	0.5

[a] *E. coli* isolates were obtained from Eurofins-Medinet and are recent clinical isolates.