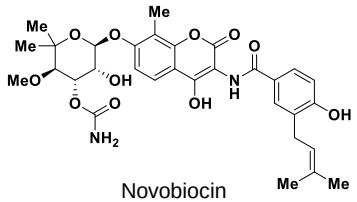
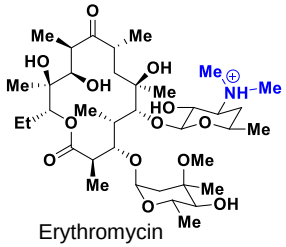
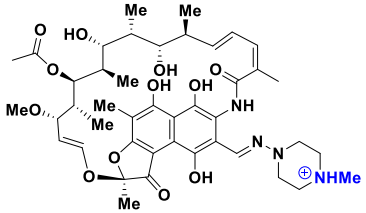
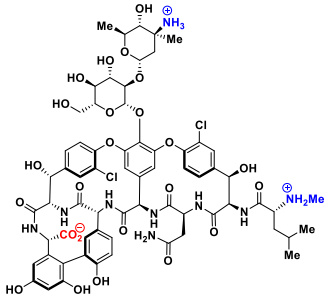
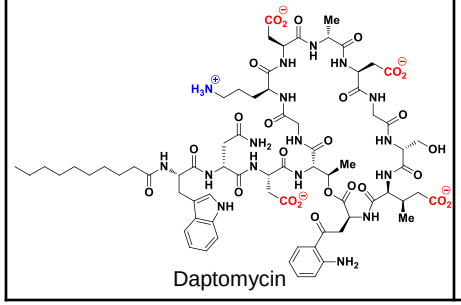
doi:10.1038/nature22308

Table S1

This table contains the structures of the antibiotics used to validate the accumulation assay in Figure 1.

Antibiotic structure/name	Gram-negative active?	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 Novobiocin	No	613	2.65	9	0.11	1.22	6.46	119	21
 Erythromycin	No	734	1.57	7	0.29	1.64	8.35	235	73
 Rifampicin	No	823	2.71	5	0.37	1.86	10.42	213	9
 Vancomycin	No	1449	-8.48	13	0.28	2.17	14.57	177	26
 Daptomycin	No	1621	-21.48	35	0.38	2.28	19.06	206	85

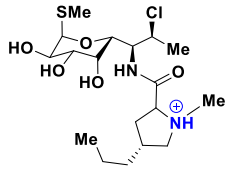
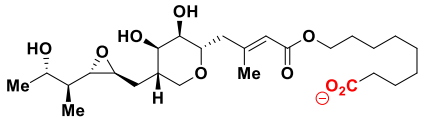
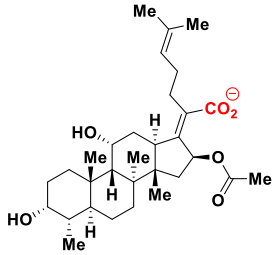
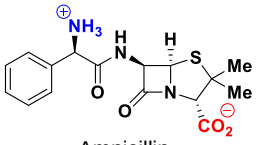
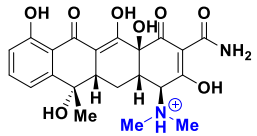
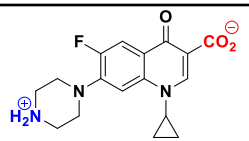
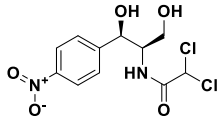
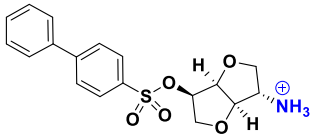
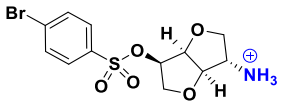
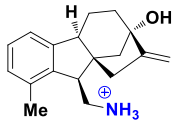
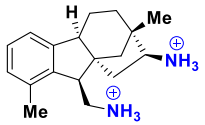
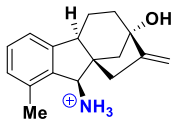
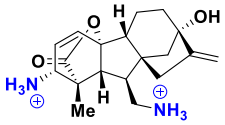
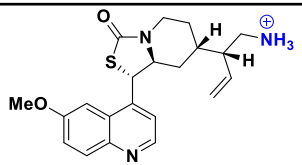
Antibiotic structure/name	Gram-negative active?	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 Clindamycin	No	425	0.65	7	0.16	1.13	5.19	221	19
 Mupirocin	No	501	-0.07	17	0.13	1.04	7.01	89	1
 Fusidic acid	No	517	1.75	6	0.10	1.05	3.17	52	5
 Ampicillin	Yes (but covalently modified)	349	-3.39	4	0.12	0.87	3.54	45	11
 Tetracycline	Yes	444	-2.84	2	0.20	1.11	4.11	1759	160
 Ciprofloxacin	Yes	331	-1.39	3	0.07	0.69	3.28	2263	286
 Chloramphenicol	Yes	323	0.66	6	0.15	0.88	3.47	709	45

Table S2

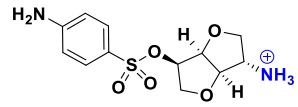
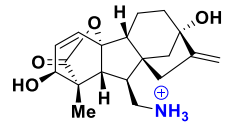
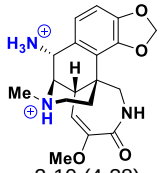
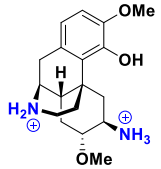
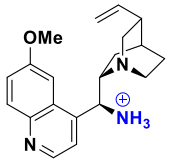
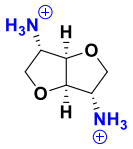
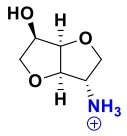
This table contains the structures of the 100 compounds analyzed for accumulation in *E. coli* MG1655, data presented in Figure 1C.

The compounds are listed as 2-1 through 2-100 in this table; compounds that also appear in figures from the main text or other supplementary tables are cross referenced with those names and table locations. Thus, 2-1 (16, 3-1, 4-1) means that this compound appears as 2-1 in Table S2, 3-1 in Table S3, 4-1 in Table S4, and 16 in the main text and figures.

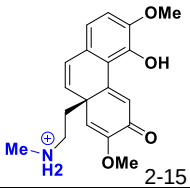
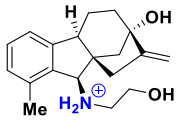
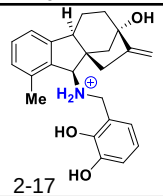
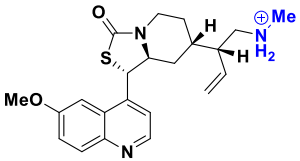
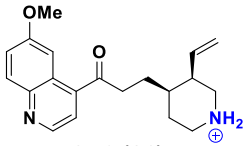
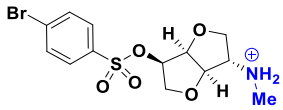
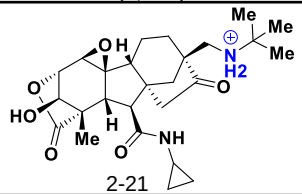
The synthesis of some of these compounds was described in *Nature Chemistry* **2013**, *5*, 195, and in those cases the compounds are also listed under the names given in that manuscript, for example 2-7 (Q1d, 3, 3-22, 4-26). Q1d is the compound name from the *Nature Chemistry* manuscript.

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-1 (16, 3-1, 4-1)	Primary amine	361	0.6	4	0.06	0.90	2.73	1965*	108
 2-2 (2, 3-3, 4-5)	Primary amine	364	-0.28	3	0.11	0.88	2.29	1647*	108
 2-3 (1, 3-8, 4-7)	Primary amine	269	-0.09	1	0.19	0.91	3.02	1335*	8
 2-4 (3-14, 4-8)	Primary amine (Di-amine)	270	-2.49	1	0.21	1.07	2.82	946*	138
 2-5 (30, 3-16, 4-13)	Primary amine	255	0.46	0	0.18	0.87	2.46	756*	94
 2-6 (3-20, 4-24)	Primary amine (Di-amine)	330	-4.37	1	0.21	1.07	3.47	504*	39
 2-7 (Q1d, 3, 3-22, 4-26)	Primary amine	384	0.14	5	0.33	1.31	6.41	458*	58

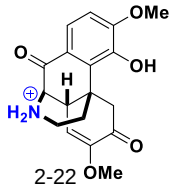
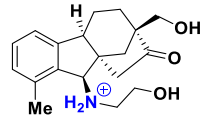
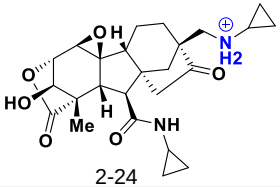
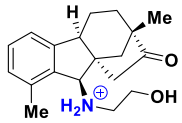
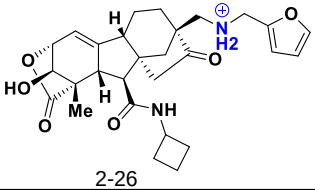
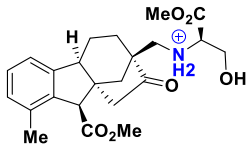
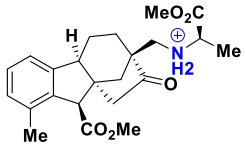
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-8 (21, 4-34)	Primary amine	300	-1.87	3	0.13	0.91	2.84	331	68
 2-9 (3-27, 4-32)	Primary amine	331	-2.64	1	0.22	1.08	3.39	309*	38
 2-10 (4-38)	Primary amine	357	-1.93	1	0.61	1.29	5.12	219	16
 2-11 (4-40)	Primary amine	318	-3.91	2	0.39	1.30	5.00	204	14
 2-12 (4-42)	Primary amine	323	0.33	4	0.24	1.13	4.59	167	12
 2-13 (4-56)	Primary amine (Di-amine)	144	-4.78	0	0.17	0.74	1.38	20	2
 2-14 (20, 4-61)	Primary amine	145	-2.81	0	0.24	0.74	1.61	0	0

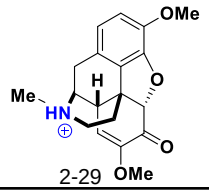
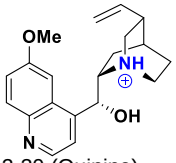
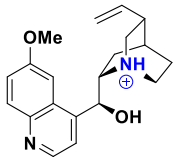
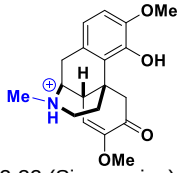
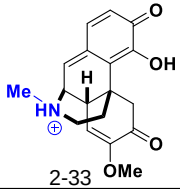
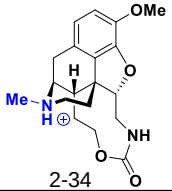
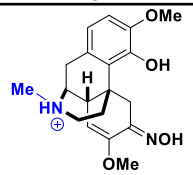
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-15 (3-32)	Secondary amine	327	-1.03	5	0.21	1.21	3.64	525*	22
 2-16	Secondary amine	299	0.11	3	0.20	0.93	4.37	497*	110
 2-17	Secondary amine	377	1.93	3	0.18	1.03	5.24	493	163
 2-18 (6, 3-23)	Secondary Amine	398	0.24	6	0.35	1.32	6.77	390*	24
 2-19 (Q8)	Secondary amine	324	0.04	6	0.15	0.97	4.29	201	6
 2-20 (5, 3-4)	Secondary amine	378	0.11	4	0.11	0.91	2.73	176	7
 2-21	Secondary amine	473	-2.25	5	0.12	1.07	5.69	175	65

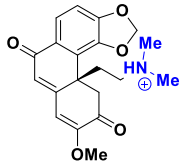
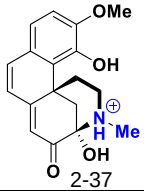
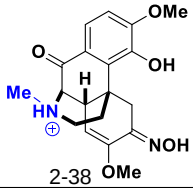
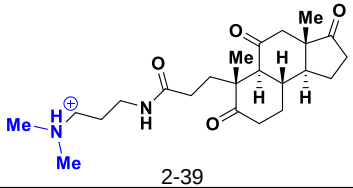
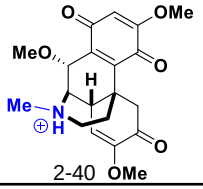
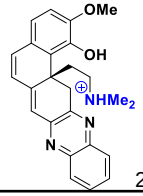
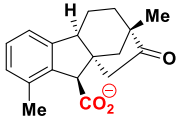
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-22	Secondary amine	329	0.01	2	0.37	1.23	5.24	154	89
 2-23	Secondary amine	315	-0.28	4	0.23	1.02	4.50	118	3
 2-24	Secondary amine	457	-2.47	5	0.14	1.04	5.79	113	0
 2-25	Secondary amine	299	1.01	3	0.22	1.00	4.51	98	30
 2-26	Secondary amine	495	0.15	6	0.12	1.04	6.29	67	3
 2-27	Secondary amine	415	1.79	8	0.26	1.29	5.33	54	24
 2-28	Secondary amine	399	2.8	7	0.23	1.24	5.04	16	4

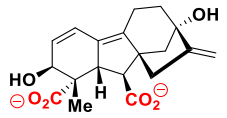
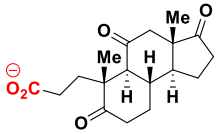
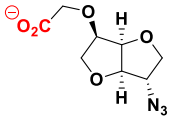
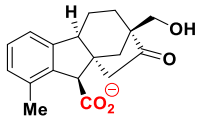
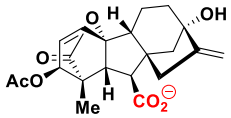
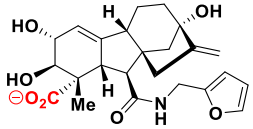
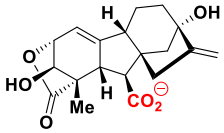
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-29	Tertiary amine	327	0.58	2	0.32	1.20	5.01	407*	6
 2-30 (Quinine)	Tertiary amine	324	0.86	4	0.20	1.06	4.38	261	16
 2-31 (Epi-quinine)	Tertiary amine	324	0.86	4	0.23	1.11	4.59	232	38
 2-32 (Sinomenine)	Tertiary amine	329	0.65	2	0.34	1.24	5.32	218	10
 2-33	Tertiary amine	313	0.84	1	0.44	1.27	5.06	213	38
 2-34	Tertiary amine	344	-0.55	1	0.31	1.19	4.63	209	24
 2-35	Tertiary amine	344	-0.09	2	0.38	1.33	5.66	204	26

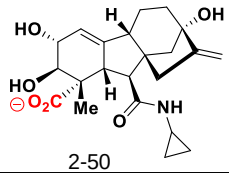
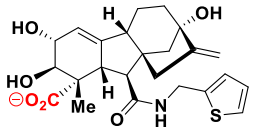
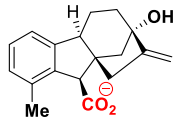
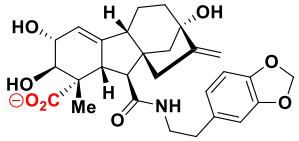
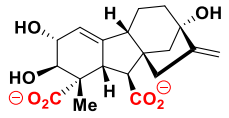
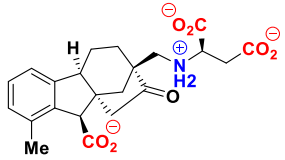
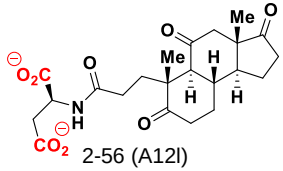
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-36	Tertiary amine	355	0.57	4	0.30	1.23	4.96	139	7
 2-37	Tertiary amine	313	1.85	1	0.11	0.74	3.12	134	65
 2-38	Tertiary amine	358	0.74	2	0.37	1.32	5.74	107	39
 2-39	Tertiary amine	405	0.69	7	0.14	1.11	4.50	72	5
 2-40	Tertiary amine	373	-0.03	3	0.50	1.48	5.92	3	0
 2-41	Tertiary amine	399	1.47	4	0.17	1.24	4.26	1	0
 2-42 (3-51)	Carboxylic acid	284	0.57	1	0.20	0.97	3.44	138	7

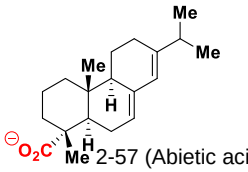
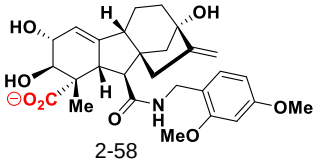
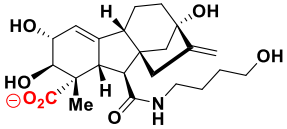
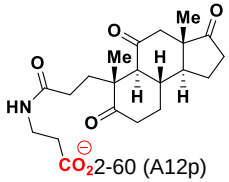
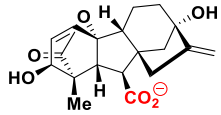
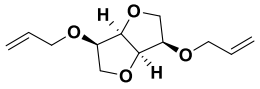
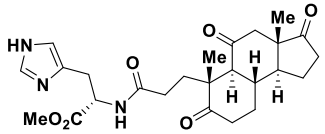
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-43 (G12)	Carboxylic acid	346	-5.79	2	0.21	1.08	3.82	104	20
 2-44 (A8)	Carboxylic acid	320	-0.5	3	0.28	1.10	3.87	103	27
 2-45	Carboxylic acid	229	-1.49	4	0.18	0.83	1.88	89	1
 2-46 (3-47)	Carboxylic acid	300	-0.79	2	0.21	0.99	3.55	84	13
 2-47	Carboxylic acid	388	-2.3	3	0.17	1.13	3.56	81	3
 2-48	Carboxylic acid	444	-3.05	4	0.17	1.03	5.89	72	3
 2-49 (G8)	Carboxylic acid	346	-2.82	1	0.22	0.97	3.97	70	4

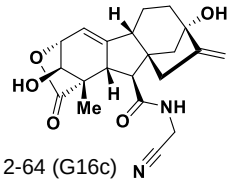
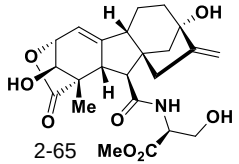
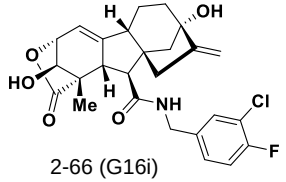
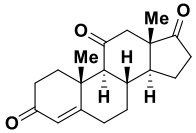
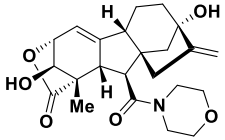
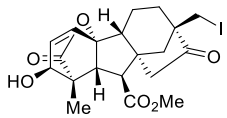
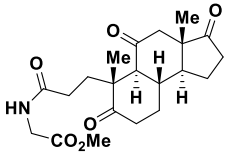
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-50	Carboxylic acid	403	-3.55	3	0.20	0.99	6.07	63	2
 2-51	Carboxylic acid	460	-2.09	4	0.17	1.03	5.74	61	13
 2-52 (3-18)	Carboxylic acid	284	-0.23	1	0.18	0.89	3.36	56	8
 2-53	Carboxylic acid	512	-2.44	5	0.19	1.18	5.96	56	2
 2-54 (G9)	Carboxylic acid (di-acid)	364	-6.53	2	0.24	1.07	4.34	55	3
 2-55	Tri-acid/secondary amine	415	-6.12	7	0.19	1.20	4.75	52	5
 2-56 (A12l)	Carboxylic acid (di-acid)	435	-4.28	7	0.31	1.25	6.02	45	1

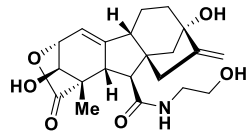
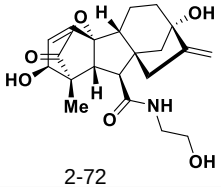
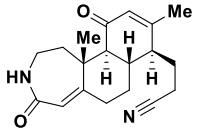
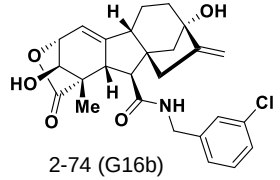
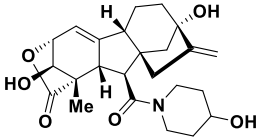
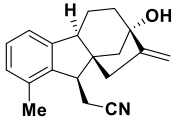
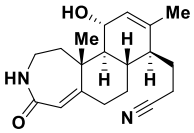
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-57 (Abietic acid)	Carboxylic acid	302	2.22	2	0.12	0.96	2.72	34	5
 2-58	Carboxylic acid	514	-2.79	6	0.17	1.22	5.84	17	0
 2-59	Carboxylic acid	436	-4.13	6	0.22	1.12	6.40	17	1
 2-60 (A12p)	Carboxylic acid	391	-1.54	6	0.34	1.22	5.39	17	1
 2-61 (Gibberellic acid, 3-28)	Carboxylic acid	346	-2.71	1	0.22	1.10	3.70	15	10
 2-62	Neutral	226	1.34	6	0.12	0.87	1.83	139	10
 2-63	Neutral	472	1.55	8	0.16	1.18	5.29	118	16

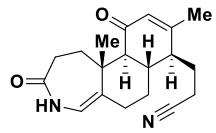
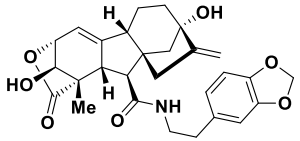
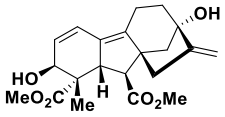
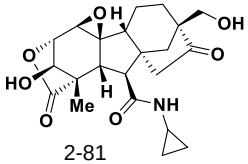
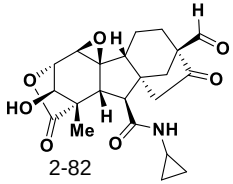
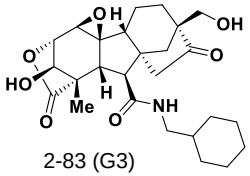
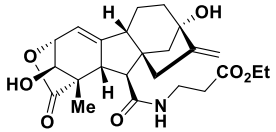
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-64 (G16c)	Neutral	384	-0.84	2	0.24	1.03	5.97	97	12
 2-65	Neutral	447	-1.2	5	0.20	1.09	6.22	96	8
 2-66 (G16i)	Neutral	488	2.12	3	0.19	1.10	5.35	93	26
 2-67 (Adrenosterone)	Neutral	300	3.01	0	0.18	0.98	2.68	92	37
 2-68 (G16n)	Neutral	415	-0.34	1	0.22	1.05	6.12	91	18
 2-69	Neutral	486	2.04	3	0.23	1.10	3.60	89	9
 2-70	Neutral	391	1.46	6	0.20	1.12	4.91	85	20

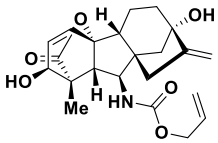
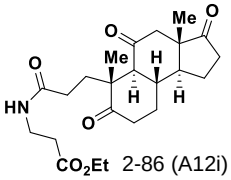
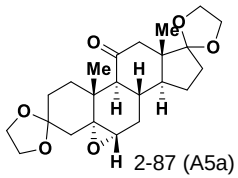
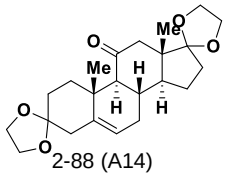
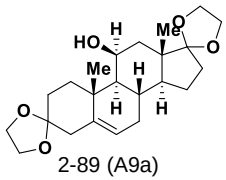
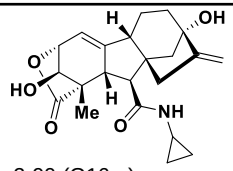
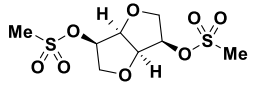
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-71	Neutral	389	-1.04	3	0.21	1.00	5.79	83	5
 2-72	Neutral	389	-2.21	3	0.22	1.08	5.68	80	3
 2-73 (A6)	Neutral	312	1.79	3	0.16	0.96	3.56	80	3
 2-74 (G16b)	Neutral	470	1.98	3	0.18	1.07	5.56	75	0
 2-75 (G16p)	Neutral	430	-0.81	1	0.19	1.05	6.11	69	3
 2-76 (3-13)	Neutral	279	2.87	1	0.19	0.91	3.48	65	13
 2-77 (A10)	Neutral	314	1.21	3	0.17	0.99	3.59	61	3

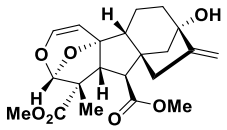
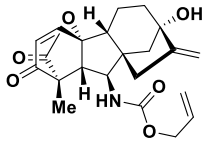
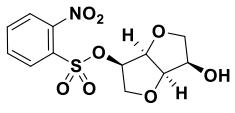
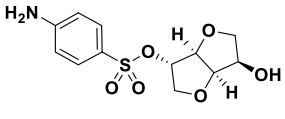
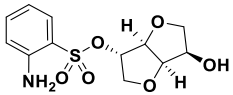
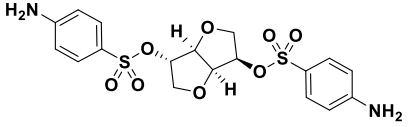
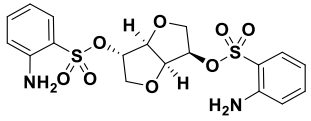
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF Score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-78 (A7)	Neutral	312	1.81	3	0.16	0.96	3.37	59	11
 2-79 (G16h)	Neutral	494	1.29	4	0.24	1.23	5.83	55	7
 2-80 (G13)	Neutral	374	-2.3	4	0.29	1.21	5.07	53	10
 2-81	Neutral	417	-0.87	3	0.23	1.05	6.13	53	5
 2-82	Neutral	415	-0.15	3	0.26	1.08	5.90	52	3
 2-83 (G3)	Neutral	474	0.83	4	0.17	1.10	6.42	50	26
 2-84	Neutral	446	-0.13	6	0.21	1.16	5.73	48	3

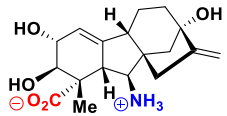
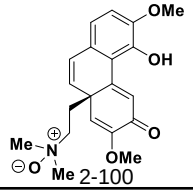
*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF Score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-85	Neutral	401	1	4	0.21	1.09	6.11	46	2
 2-86 (A12i)	Neutral	420	2.05	8	0.19	1.17	5.29	46	6
 2-87 (A5a)	Neutral	405	2.74	0	0.11	0.99	2.59	44	10
 2-88 (A14)	Neutral	389	3.04	0	0.12	1.05	2.63	40	4
 2-89 (A9a)	Neutral	391	2.65	0	0.14	1.12	2.79	40	6
 2-90 (G16m)	Neutral	385	0.12	2	0.22	0.99	6.20	33	2
 2-91	Neutral	302	-1.53	4	0.25	1.01	2.38	31	3

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF Score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-92 (G4)	Neutral	390	1.13	4	0.49	1.42	5.71	29	13
 2-93	Neutral	399	1.74	4	0.23	1.10	6.12	0	0
 2-94	Neutral (Nitro)	331	0.58	4	0.15	0.93	3.04	0	0
 2-95	Aniline	301	-0.18	3	0.12	0.91	2.93	193	15
 2-96	Aniline	301	-0.18	3	0.13	0.87	2.70	193	11
 2-97	Aniline	456	1.04	6	0.20	1.21	5.87	113	2
 2-98	Aniline	456	1.04	6	0.20	1.21	4.71	91	8

*Staistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF Score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 2-99	Zwitterionic	335	-3.41	1	0.19	0.99	3.53	91	3
 2-100	Zwitterionic	357	1.03	5	0.25	1.26	5.19	18	7

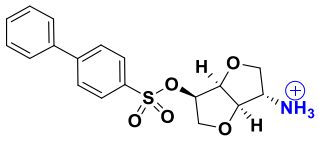
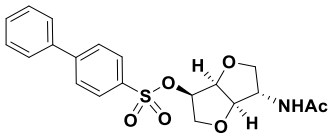
*Statistically significant level of accumulation

Table S3

This table contains the structures of the 54 compounds analyzed for accumulation in *E. coli* MG1655 to examine SAR, a portion of this data is also presented in Figure 2.

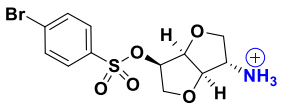
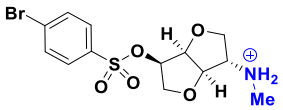
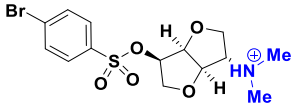
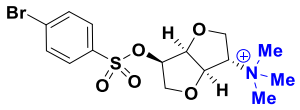
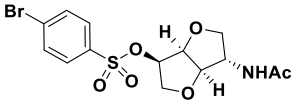
The compounds are listed as 3-1 through 3-54 in this table; compounds that also appear in figures from the main text or other supplementary tables are cross referenced with those names and table locations. Thus, 3-1 (16, 2-1, 4-1) means that this compound appears as 2-1 in Table S2, 3-1 in Table S3, 4-1 in Table S4, and 16 in the main text and figures.

The synthesis of some of these compounds was described in *Nature Chemistry* **2013**, *5*, 195, and in those cases the compounds are also listed under the names given in that manuscript, for example 3-22 (Q1d, 3, 2-7, 4-26). Q1d is the compound name from the *Nature Chemistry* manuscript.

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-1 (16, 2-1, 4-1)	Primary amine	361	0.6	4	0.06	0.90	2.73	1965*	108
 3-2	Amide	403	2.32	5	0.06	0.90	4.31	71	11

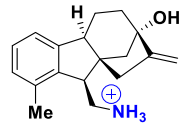
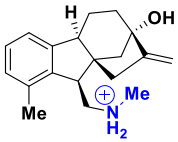
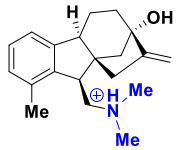
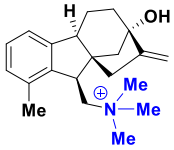
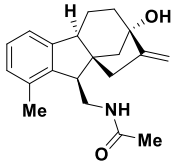
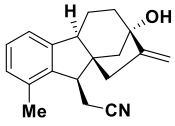
SAR of compound 16, from Figure 3A

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-3 (2, 2-2, 4-5)	Primary amine	364	-0.28	3	0.11	0.88	2.29	1647*	108
 3-4 (5, 2-20)	Secondary amine	378	0.11	4	0.11	0.91	2.73	176	7
 3-5 (8)	Tertiary amine	392	1.47	4	0.11	0.92	3.53	7	1
 3-6 (11)	Quaternary amine	407	-2.04	4	0.12	0.98	3.15	30	1
 3-7 (14)	Amide	406	1.12	4	0.10	0.89	3.63	8	1

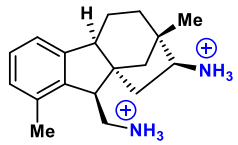
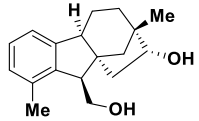
SAR of compound 2, from Figure 2

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-8 (1, 2-3, 4-7)	Primary amine	269	-0.09	1	0.19	0.91	3.02	1335*	8
 3-9 (4)	Secondary amine	283	-0.08	2	0.19	0.92	3.85	210	29
 3-10 (7)	Tertiary amine	297	0.95	2	0.21	0.98	4.14	100	27
 3-11 (10)	Quaternary amine	312	-1.13	2	0.21	0.94	4.99	30	1
 3-12 (13)	Amide	311	2.04	2	0.20	0.95	5.03	91	4
 3-13 (2-76)	Nitrile	279	2.87	1	0.19	0.91	3.48	65	13

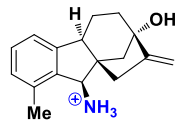
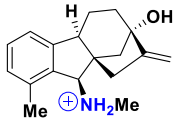
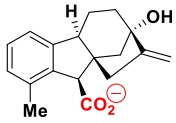
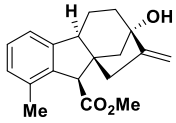
SAR of compound 1, from Figure 2

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-14 (2-4, 4-8)	Primary amine (Di-amine)	270	-2.49	1	0.21	1.07	2.82	946*	138
 3-15	Alcohol (Diol)	272	2.61	1	0.17	0.89	3.05	113	20

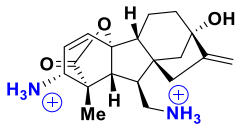
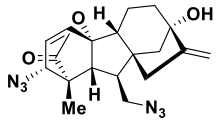
SAR of compound 2-4

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-16 (30, 2-5, 4-13)	Primary amine	255	0.46	0	0.18	0.87	2.46	756*	94
 3-17	Secondary amine	269	0.37	1	0.18	0.85	3.03	239	3
 3-18 (2-52)	Carboxylic acid	284	-0.23	1	0.18	0.89	3.36	56	8
 3-19	Methyl ester	298	2.77	2	0.19	0.91	4.10	49	1

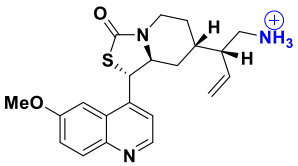
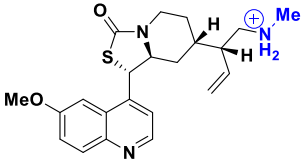
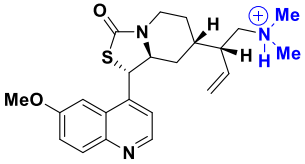
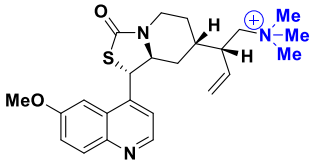
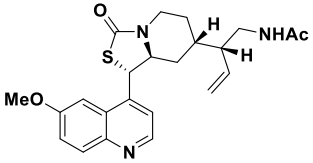
SAR of 30, from Figure 3E

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-20 (2-6,4-24)	Primary amine (Di-amine)	330	-4.37	1	0.21	1.07	3.47	504*	39
 3-21	Azide (Di-azide)	382	0.78	3	0.19	1.04	4.56	16	1

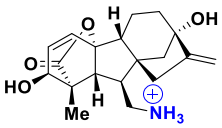
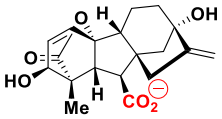
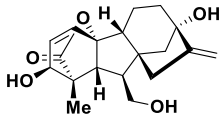
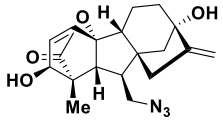
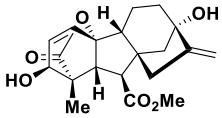
SAR of compound 2-6

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-22 (Q1d, 3, 2-7, 4-26)	Primary amine	384	0.14	5	0.33	1.31	6.41	458*	58
 3-23 (6, 2-18)	Secondary amine	398	0.24	6	0.35	1.32	6.77	390*	24
 3-24 (9)	Tertiary amine	412	1.04	6	0.40	1.34	6.84	48	3
 3-25 (12)	Quaternary amine	427	-0.63	6	0.43	1.38	7.09	44	7
 3-26 (Q1r, 15)	Amide	426	2.54	6	0.28	1.32	6.83	91	9

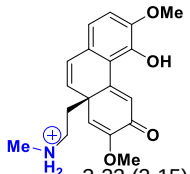
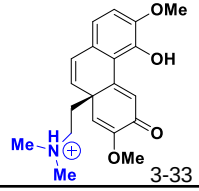
SAR of compound 3, from Figure 2

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-27 (2-9, 4-32)	Primary amine	331	-2.64	1	0.22	1.08	3.39	309*	38
 3-28 (Gibberellic acid, 2-61)	Carboxylic acid	346	-2.71	1	0.22	1.10	3.70	15	10
 3-29	Alcohol	332	0.06	1	0.22	1.09	3.35	21	1
 3-30	Azide	357	0.22	2	0.22	1.09	4.60	61	20
 3-31	Methyl ester	360	0.5	2	0.24	1.11	4.59	38	5

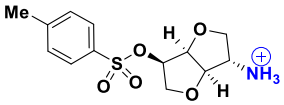
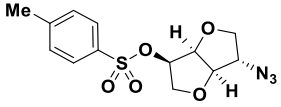
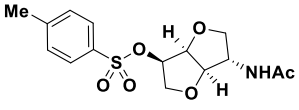
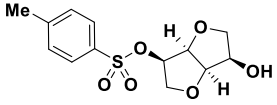
SAR of 2-9

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-32 (2-15)	Secondary amine	327	-1.03	5	0.21	1.21	3.64	525*	22
 3-33	Tertiary amine	341	0.4	5	0.24	1.26	4.29	126	17

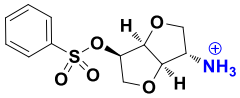
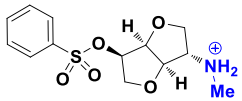
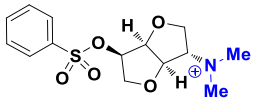
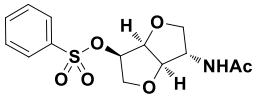
SAR of 2-15

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-34 (23, 4-10)	Primary amine	299	-0.53	3	0.10	0.89	2.68	877*	29
 3-35	Azide	325	1.46	4	0.10	0.89	3.26	25	0
 3-36	Amide	341	0.87	4	0.10	0.87	3.65	111	35
 3-37	Alcohol	300	1.16	3	0.11	0.90	2.91	152	29

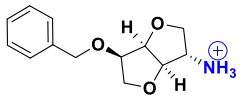
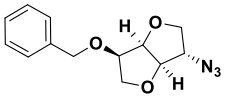
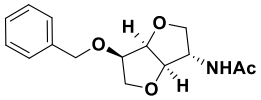
SAR of compound 23, from Figure 3C

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-38 (22, 4-19)	Primary amine	285	-1.05	3	0.13	0.90	2.49	616*	30
 3-39	Secondary amine	299	-0.66	4	0.12	0.90	2.70	339*	31
 3-40	Tertiary amine	313	0.7	4	0.11	0.92	2.93	116	7
 3-41	Amide	327	0.36	4	0.11	0.91	3.05	93	8

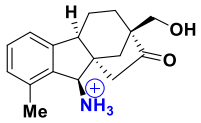
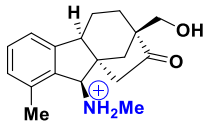
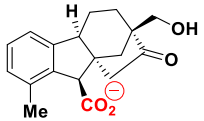
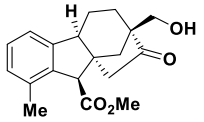
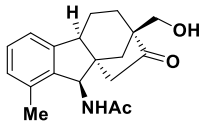
SAR of compound 22, from Figure 3C

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-42 (4-21)	Primary amine	235	-0.73	3	0.19	0.95	2.25	552*	12
 3-43	Azide	261	1.21	4	0.13	0.89	2.29	20	0
 3-44	Amide	277	0.67	4	0.11	0.89	2.49	103	3

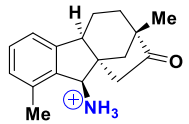
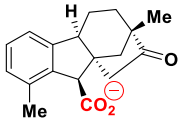
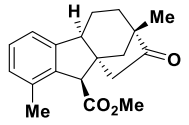
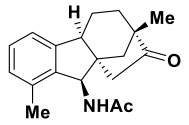
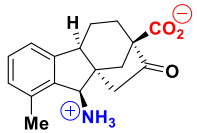
SAR of compound 3-42

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-45 (4-22)	Primary amine	271	0.16	1	0.20	0.95	2.80	542*	26
 3-46	Secondary amine	285	-0.02	2	0.19	0.93	3.24	179	8
 3-47 (2-46)	Carboxylic acid	300	-0.79	2	0.21	0.99	3.55	84	13
 3-48	Methyl ester	314	2.34	3	0.22	0.97	4.28	86	16
 3-49	Amide	313	1.61	2	0.21	0.95	4.54	69	5

SAR of compound 3-45

*Statistically significant level of accumulation

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 3-50 (4-23)	Primary amine	255	1.44	0	0.19	0.92	2.53	515*	50
 3-51 (2-42)	Carboxylic acid	284	0.57	1	0.20	0.97	3.44	138	7
 3-52	Methyl ester	298	3.62	2	0.22	0.98	4.17	28	12
 3-53	Amide	297	2.89	1	0.22	0.97	4.51	49	12
 3-54	Zwitterionic	285	-0.46	1	0.14	0.78	2.51	238	12

SAR of compound 3-50

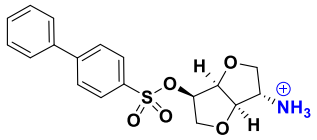
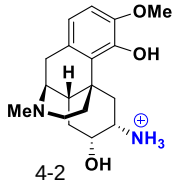
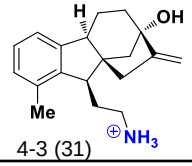
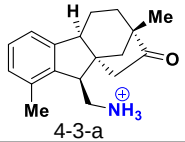
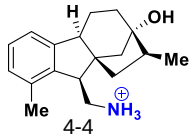
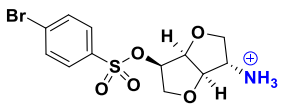
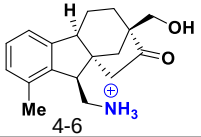
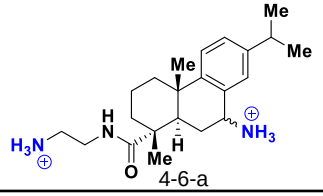
*Statistically significant level of accumulation

Table S4

This table contains the structures of the 68 primary amines analyzed for accumulation in *E. coli* MG1655, data presented in Extended Data Fig. 1.

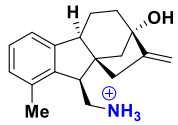
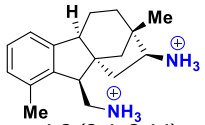
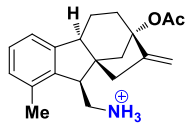
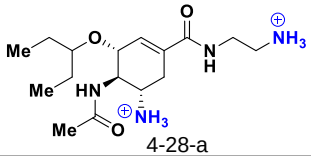
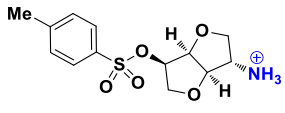
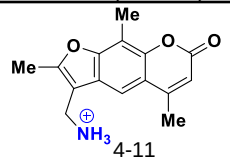
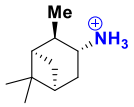
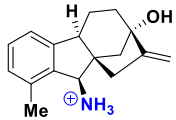
The compounds are listed as 4-1 through 4-63 in this table; compounds that also appear in figures from the main text or other supplementary tables are cross referenced with those names and table locations. Thus, 4-1 (16, 2-1, 3-1) means that this compound appears as 2-1 in Table S2, 3-1 in Table S3, 4-1 in Table S4, and 16 in the main text and figures.

The synthesis of some of these compounds was described in *Nature Chemistry* **2013**, *5*, 195, and in those cases the compounds are also listed under the names given in that manuscript, for example 4-26 (Q1d, 3, 2-7, 3-22). Q1d is the compound name from the *Nature Chemistry* manuscript.

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-1 (16, 2-1, 3-1)	Primary amine	361	0.6	4	0.06	0.90	2.73	1965*	108
 4-2	Primary amine	318	-3.23	1	0.30	1.14	4.69	1913*	156
 4-3 (31)	Primary amine	283	0.09	2	0.20	0.96	3.62	1887*	179
 4-3-a	Primary amine	270	0.95	1	0.20	0.95	3.01	1696*	203
 4-4	Primary amine	271	0	3	0.19	0.96	3.05	1650*	69
 4-5 (2, 2-2, 3-3)	Primary amine	364	-0.28	3	0.11	0.88	2.29	1647*	108
 4-6	Primary amine	285	-0.33	2	0.20	0.97	3.00	1487*	59
 4-6-a	Primary amine	360	-0.70	4	0.11	1.06	3.64	1344*	43

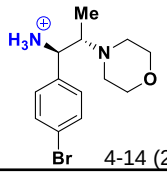
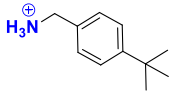
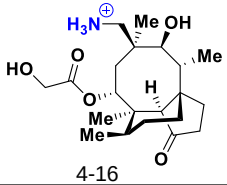
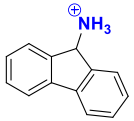
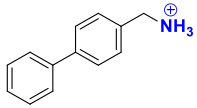
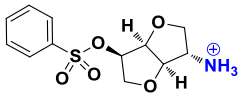
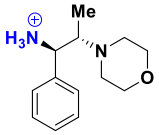
* Statistically significant level of accumulation

† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

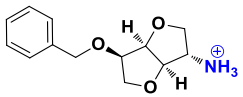
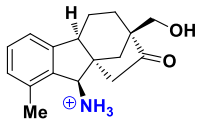
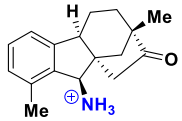
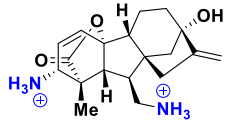
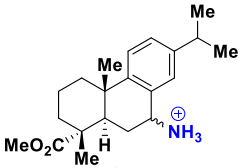
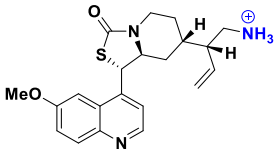
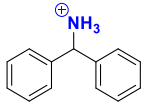
Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-7 (1, 2-3, 3-8)	Primary amine	269	-0.09	1	0.19	0.91	3.02	1335*	8
 4-8 (2-4, 3-14)	Primary amine (Di-amine)	270	-2.49	1	0.21	1.07	2.82	946*	138
 4-9 (18)	Primary amine	311	0.36	2	0.14	0.89	2.83	922*	46
 4-28-a	Primary amine	327	-3.91	8	0.15	0.99	4.73	895*	2
 4-10 (23, 3-34)	Primary amine	299	-0.53	3	0.10	0.89	2.68	877*	29
 4-11	Primary amine	257	0.24	1	0.05	0.47	2.73	817*	203
 4-12	Primary amine	153	-0.97	0	0.36	0.95	1.99	761*	65
 4-13 (30, 2-5, 3-16)	Primary amine	255	0.46	0	0.18	0.87	2.46	756*	94

* Statistically significant level of accumulation

† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

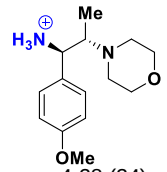
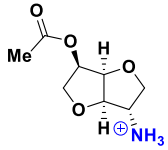
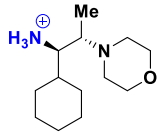
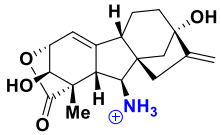
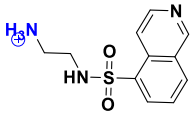
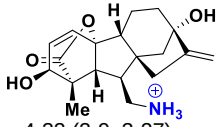
Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-14 (25)	Primary amine	299	0.59	3	0.18	0.93	1.76	739*	98
 4-15 (27)	Primary amine	163	0.56	2	0.12	0.80	1.37	726*	19
 4-16	Primary amine	382	-0.12	4	0.38	1.26	5.27	628*	86
 4-17	Primary amine	181	0.63	0	0.05	0.40	1.90	617*	10
 4-18	Primary amine	183	0.71	1	0.06	0.67	1.12	617*	1
 4-19 (22, 3-38)	Primary amine	285	-1.05	3	0.13	0.90	2.49	616*	30
 4-20	Primary amine	220	-0.22	3	0.19	0.93	1.95	613*	66

* Statistically significant level of accumulation
† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

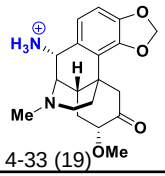
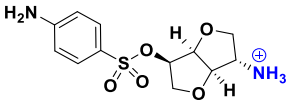
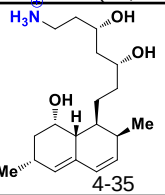
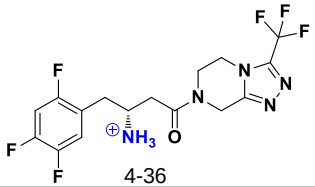
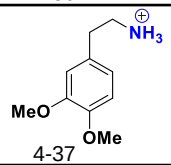
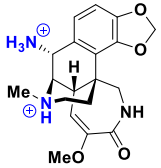
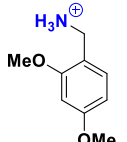
Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-21 (3-42)	Primary amine	235	-0.73	3	0.19	0.95	2.25	552*	12
 4-22 (3-45)	Primary amine	271	0.16	1	0.20	0.95	2.80	542*	26
 4-23 (3-50)	Primary amine	255	1.44	0	0.19	0.92	2.53	515*	50
 4-24 (2-6, 3-20)	Primary amine (Di-amine)	330	-4.37	1	0.21	1.07	3.47	504*	39
 4-25	Primary amine	329	2.31	3	0.17	1.16	3.48	477*	75
 4-26 (Q1d, 3, 2-7, 3-22)	Primary amine	384	0.14	5	0.33	1.31	6.41	458*	58
 4-27	Primary amine	183	1.24	2	0.17	0.86	1.81	415*	20

* Statistically significant level of accumulation

† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-28 (24)	Primary amine	250	-0.37	4	0.12	0.90	1.99	399*	30
 4-37-a	Primary amine	188	-2.66	2	0.16	0.79	1.79	372*	3
 4-29	Primary amine	226	-0.5	3	0.16	0.94	1.94	344*	19
 4-30	Primary amine	317	-2.32	0	0.19	0.93	3.04	330*	8
 4-31	Primary amine	251	-1.94	4	0.08	0.62	2.36	316*	12
 4-32 (2-9, 3-27)	Primary amine	331	-2.64	1	0.22	1.08	3.39	309*	38

* Statistically significant level of accumulation
† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-33 (19)	Primary amine	344	-0.51	1	0.49	1.34	5.18	335	78
 4-34 (21, 2-8)	Primary amine	300	-1.87	3	0.13	0.91	2.84	331†	68
 4-35	Primary amine	323	-1.68	7	0.21	1.07	4.56	323	60
 4-36	Primary amine	407	-0.14	5	0.16	1.02	4.10	275	9
 4-37	Primary amine	181	-1.24	4	0.12	0.73	2.21	255†	19
 4-38 (2-10)	Primary amine	357	-1.93	1	0.61	1.29	5.12	219	16
 4-39 (26)	Primary amine	167	-0.77	3	0.07	0.50	2.04	206†	22

* Statistically significant level of accumulation

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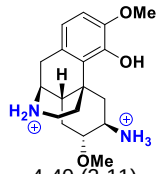
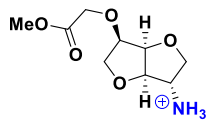
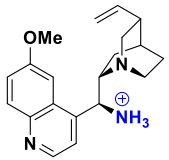
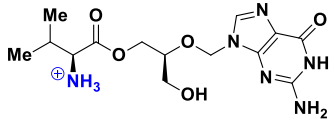
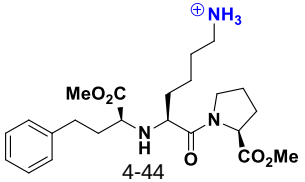
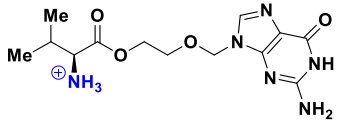
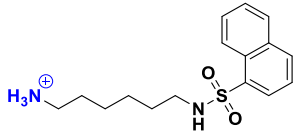
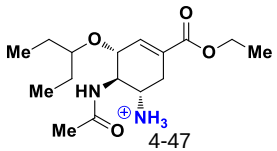
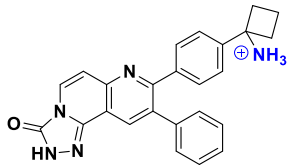
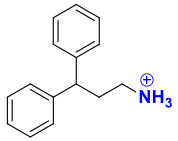
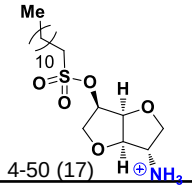
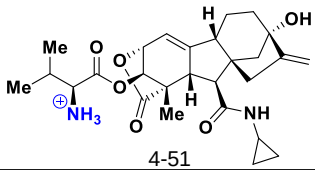
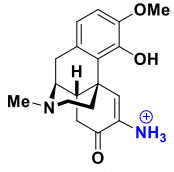
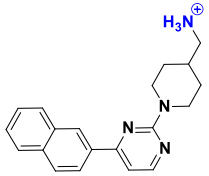
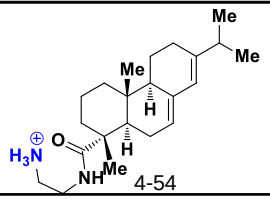
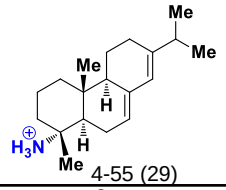
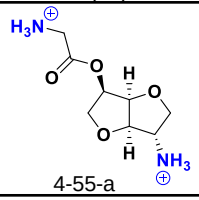
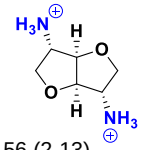
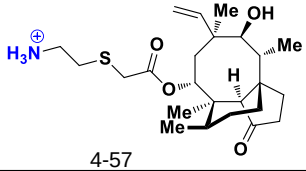
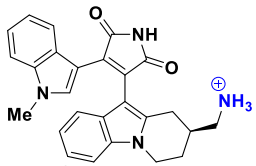
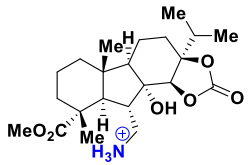
Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-40 (2-11)	Primary amine	318	-3.91	2	0.39	1.30	5.00	204	14
 4-41	Primary amine	217	-2.83	4	0.19	0.88	2.28	175†	14
 4-42 (2-12)	Primary amine	323	0.33	4	0.24	1.13	4.59	167	12
 4-43	Primary amine	354	-1.55	9	0.21	1.04	5.46	165	9
 4-44	Primary amine	434	-0.71	14	0.29	1.35	6.07	155	20
 4-45	Primary amine	324	-0.92	8	0.21	1.03	4.50	141	6
 4-46	Primary amine	306	-0.13	8	0.15	1.05	3.00	108	16

* Statistically significant level of accumulation
† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

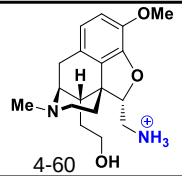
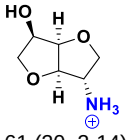
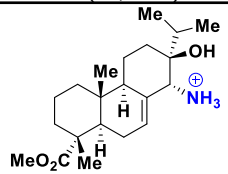
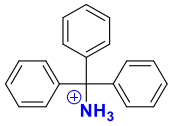
Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-47	Primary amine	312	-0.72	8	0.17	0.99	5.68	83	11
 4-48 (28)	Primary amine	407	2.18	3	0.06	0.74	4.27	81†	5
 4-49	Primary amine	211	0.77	4	0.20	0.90	2.91	61	3
 4-50 (17)	Primary amine	378	1.87	13	0.11	1.02	4.47	61	11
 4-51	Primary amine	485	0.75	6	0.24	1.33	6.60	47	1
 4-52	Primary amine	314	0.8	1	0.28	1.18	4.22	46	5
 4-53	Primary amine	318	0.92	3	0.08	0.89	3.20	40	3

* Statistically significant level of accumulation
† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-54	Primary amine	345	1.82	3	0.12	1.10	3.81	38	12
 4-55 (29)	Primary amine	273	1.19	1	0.12	0.96	2.29	28†	6
 4-55-a	Primary amine (Di-amine)	270	-3.75	3	0.16	0.95	2.02	23†	0
 4-56 (2-13)	Primary amine (Di-amine)	144	-4.78	0	0.17	0.74	1.38	20†	2
 4-57	Primary amine	438	0.74	7	0.36	1.39	5.58	20	5
 4-58	Primary amine	425	0.35	3	0.30	1.31	5.85	17	7
 4-59	Primary amine	410	0.34	4	0.16	1.07	3.87	16	6

* Statistically significant level of accumulation

† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

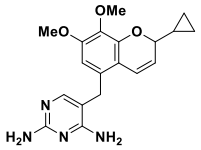
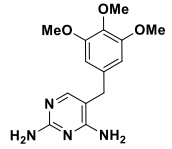
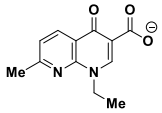
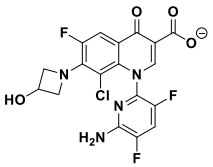
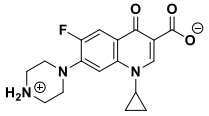
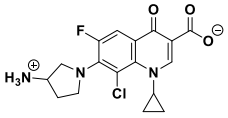
Structure/name	Functional group classification	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Accumulation (nmol/10^{12} CFUs)	Standard Error
 4-60	Primary amine	318	-3.13	4	0.32	1.23	4.07	5	0.1
 4-61 (20, 2-14)	Primary amine	145	-2.81	0	0.24	0.74	1.61	0†	0
 4-62	Primary amine	350	1.28	3	0.17	1.15	3.50	0	0
 4-63	Primary amine	259	3.31	3	0.27	1.04	5.22	0	0

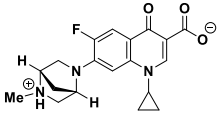
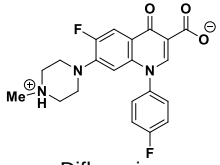
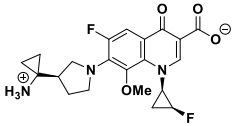
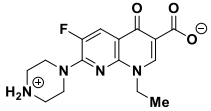
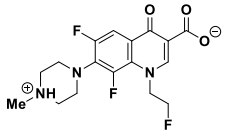
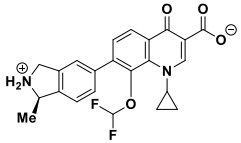
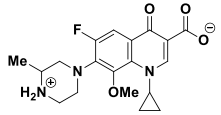
* Statistically significant level of accumulation

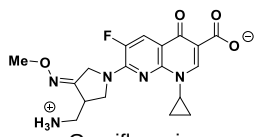
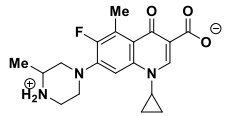
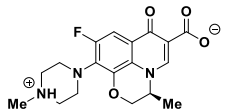
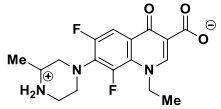
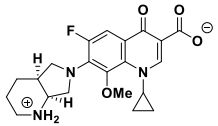
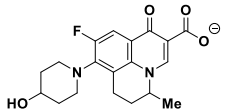
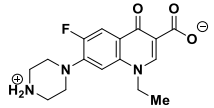
† Not included in flexibility vs. 3-dimensionality analysis in Figure 4A

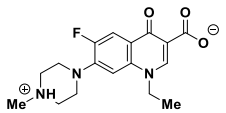
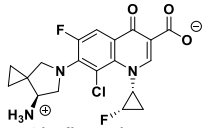
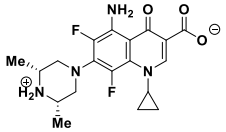
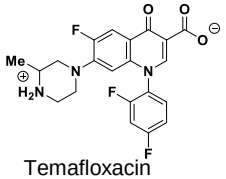
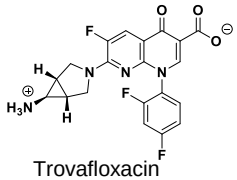
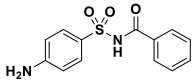
Table S6

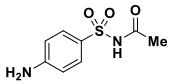
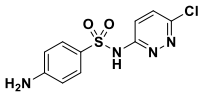
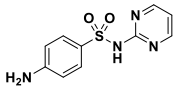
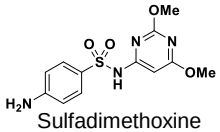
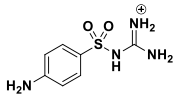
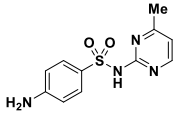
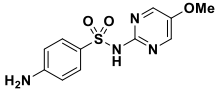
This table contains the structures of the antibiotics presented in Figures 4B and Extended Data Fig. 4c-e.

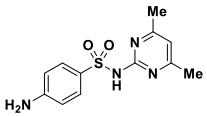
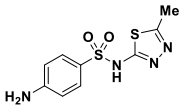
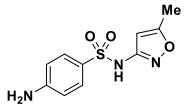
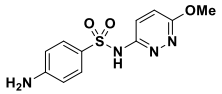
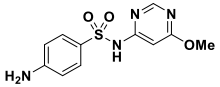
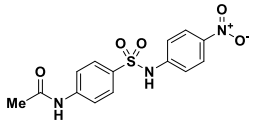
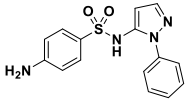
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of Activity
 Iclaprim	Dihydrofolate reductase inhibitor	354	2.3	5	0.16	1.05	5.06	Gram-negative
 Trimethoprim	Dihydrofolate reductase inhibitor	290	1.1	5	0.16	1.03	3.33	Gram-negative
 Nalidixic acid	Fluoroquinolone	232	-0.3	2	0.07	0.51	2.71	Gram-negative
 ABT-492	Fluoroquinolone	441	0.8	3	0.13	0.87	7.04	Gram-negative
 Ciprofloxacin	Fluoroquinolone	331	-1.4	3	0.07	0.69	3.28	Gram-negative
 Clinafloxacin	Fluoroquinolone	366	-2.1	3	0.18	0.99	4.44	Gram-negative

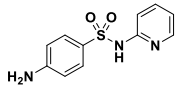
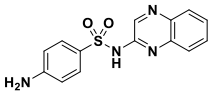
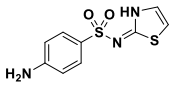
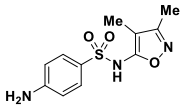
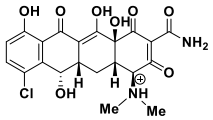
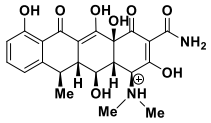
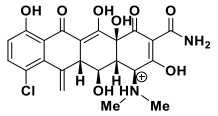
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Danofloxacin	Fluoroquinolone	357	0.2	3	0.08	0.77	3.34	Gram-negative
 Difloxacin	Fluoroquinolone	399	1.6	3	0.09	0.76	6.58	Gram-negative
 DX-619	Fluoroquinolone	419	-2.5	5	0.31	1.17	5.31	Gram-negative
 Enoxacin	Fluoroquinolone	320	-1.7	3	0.08	0.71	2.99	Gram-negative
 Fleroxacin	Fluoroquinolone	369	0.1	4	0.06	0.73	3.60	Gram-negative
 Garenoxacin	Fluoroquinolone	426	0.6	5	0.08	0.95	3.65	Gram-negative
 Gatifloxacin	Fluoroquinolone	375	-1.2	4	0.15	0.96	3.88	Gram-negative

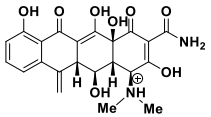
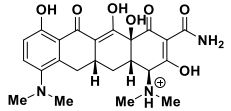
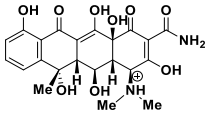
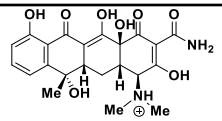
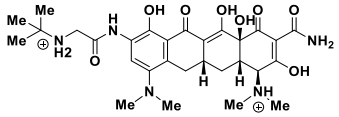
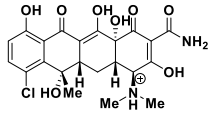
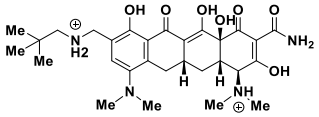
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Gemifloxacin	Fluoroquinolone	389	-2.6	5	0.48	1.40	5.88	Gram-negative
 Grepafloxacin	Fluoroquinolone	359	-0.4	3	0.11	0.83	3.87	Gram-negative
 Levofloxacin	Fluoroquinolone	361	-0.3	2	0.07	0.73	3.15	Gram-negative
 Lomefloxacin	Fluoroquinolone	351	-1.1	3	0.15	0.90	3.51	Gram-negative
 Moxifloxacin	Fluoroquinolone	401	-1.7	4	0.15	0.99	3.95	Gram-negative
 Nadifloxacin	Fluoroquinolone	360	0.6	2	0.09	0.76	3.15	Gram-negative
 Norfloxacin	Fluoroquinolone	319	-1.5	3	0.07	0.71	2.81	Gram-negative

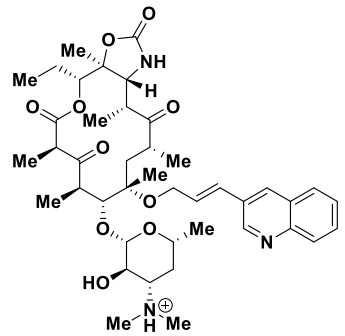
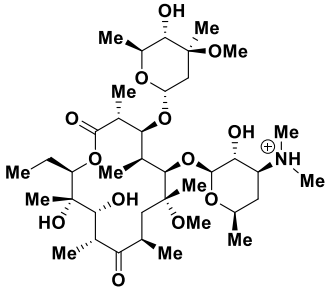
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Pefloxacin	Fluoroquinolone	333	0.2	3	0.06	0.72	2.75	Gram-negative
 Rufloxacin	Fluoroquinolone	363	-0.2	2	0.06	0.66	2.94	Gram-negative
 Sitafloxacin	Fluoroquinolone	410	-1.5	3	0.10	0.87	4.35	Gram-negative
 Sparfloxacin	Fluoroquinolone	392	-0.7	3	0.12	0.92	4.06	Gram-negative
 Temafloxacin	Fluoroquinolone	417	0.3	3	0.10	0.82	6.84	Gram-negative
 Trovafloxacin	Fluoroquinolone	416	-1.6	3	0.20	1.01	6.34	Gram-negative
 Sulfabenzamide	Sulfa	276	0.7	3	0.10	0.86	3.01	Gram-negative

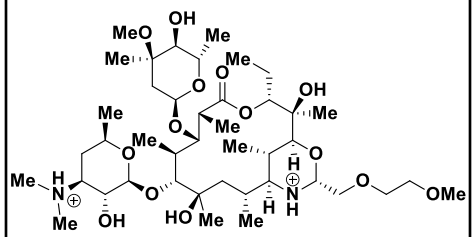
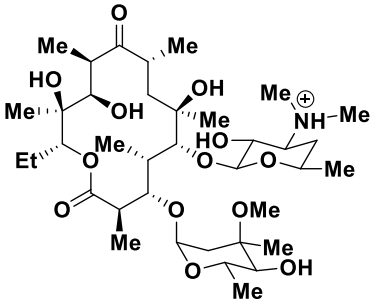
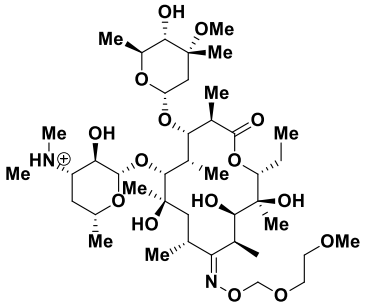
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Sulfacetamide	Sulfa	214	-1.2	2	0.16	0.88	2.01	Gram-negative
 Sulfachloropyridazine	Sulfa	285	0.2	3	0.14	0.89	2.92	Gram-negative
 Sulfadiazine	Sulfa	250	-0.1	3	0.15	0.86	2.70	Gram-negative
 Sulfadimethoxine	Sulfa	310	-0.1	3	0.16	0.99	3.83	Gram-negative
 Sulfaguanidine	Sulfa	214	-0.9	2	0.12	0.77	1.79	Gram-negative
 Sulfamerazine	Sulfa	264	0.1	3	0.14	0.90	2.98	Gram-negative
 Sulfameter	Sulfa	280	-0.2	4	0.09	0.72	2.92	Gram-negative

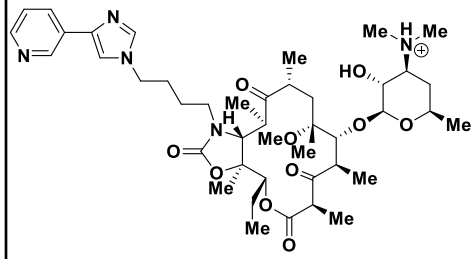
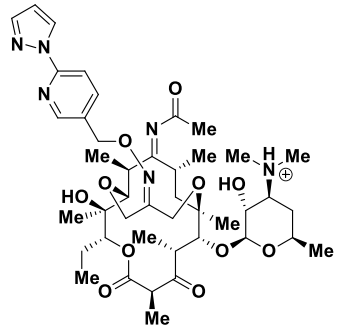
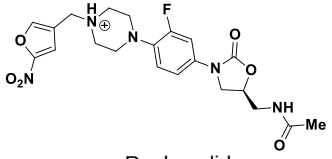
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Sulfmethazine	Sulfa	278	0.2	3	0.19	0.93	3.15	Gram-negative
 Sulfamethizole	Sulfa	270	-0.7	3	0.10	0.84	2.77	Gram-negative
 Sulfamethoxazole	Sulfa	253	0.0	3	0.13	0.83	2.84	Gram-negative
 Sulfamethoxypyridazine	Sulfa	280	-0.1	4	0.05	0.65	2.55	Gram-negative
 Sulfamonomethoxine	Sulfa	280	0.4	4	0.15	0.94	3.26	Gram-negative
 Sulfanitran	Sulfa	335	1.5	5	0.07	0.77	3.50	Gram-negative
 Sulfaphenazole	Sulfa	314	1.3	4	0.13	0.95	3.89	Gram-negative

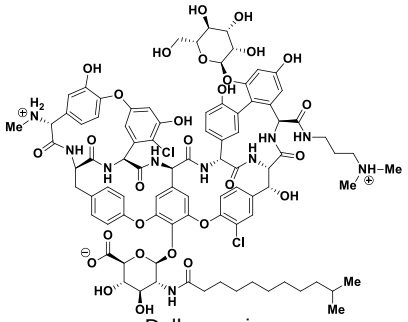
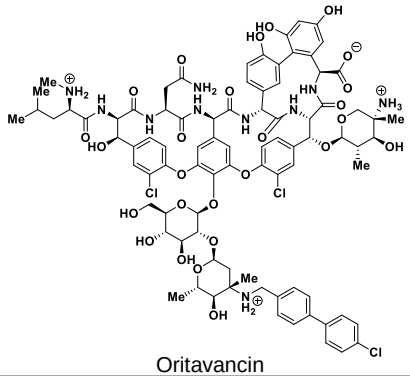
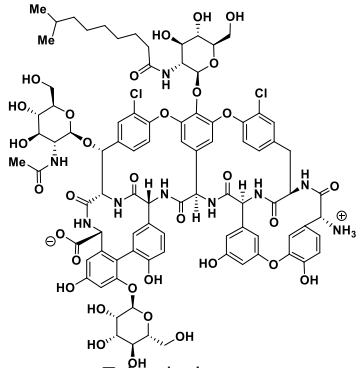
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Sulfapyridine	Sulfa	249	1.0	3	0.08	0.71	2.32	Gram-negative
 Sulfaquinoxaline	Sulfa	300	1.0	3	0.11	0.86	3.18	Gram-negative
 Sulfathiazole	Sulfa	255	0.1	3	0.14	0.83	2.61	Gram-negative
 Sulfisoxazole	Sulfa	267	-0.1	3	0.14	0.91	2.95	Gram-negative
 Demecycline	Tetracycline	465	-1.4	2	0.13	1.02	4.37	Gram-negative
 Doxycycline	Tetracycline	444	-2.7	2	0.18	0.99	4.22	Gram-negative
 Meclocycline	Tetracycline	477	-1.2	2	0.21	1.19	4.14	Gram-negative

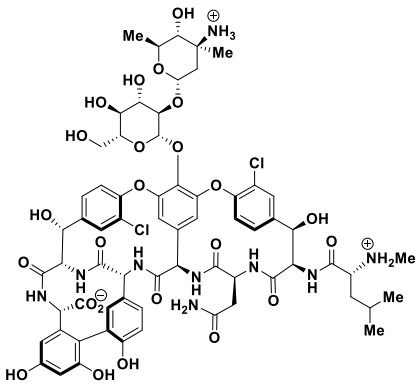
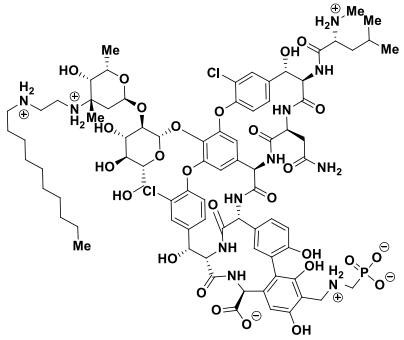
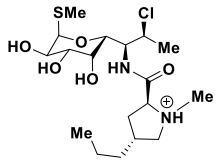
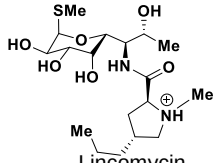
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Methacycline	Tetracycline	442	-1.8	2	0.19	1.11	4.13	Gram-negative
 Minocycline	Tetracycline	457	-0.7	3	0.15	1.02	3.96	Gram-negative
 Oxytetracycline	Tetracycline	460	-3.9	2	0.21	1.15	4.65	Gram-negative
 Tetracycline	Tetracycline	444	-2.8	2	0.20	1.11	4.11	Gram-negative
 Tigecycline	Tetracycline	586	-3.2	7	0.23	1.32	7.01	Gram-negative
 Chlortetracycline	Tetracycline	479	-2.3	2	0.14	1.02	4.54	Gram-negative
 PTK-0796	Tetracycline	557	-3.1	7	0.14	1.27	6.16	Gram-negative

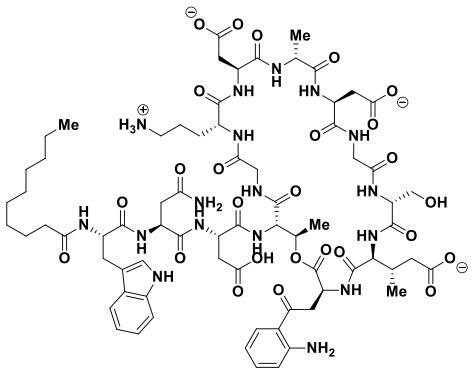
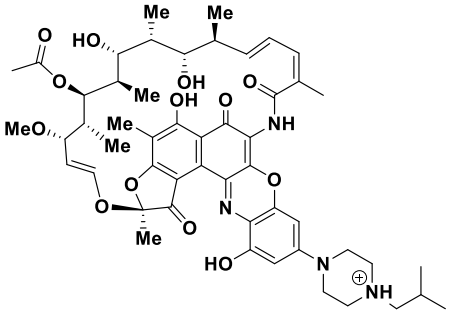
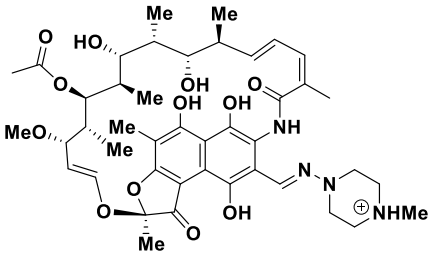
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Cethromycin	Macrolide	766	6.11	8	0.26	1.71	7.35	Gram-positive
 Clarithromycin	Macrolide	748	2.22	8	0.20	1.50	8.76	Gram-positive

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Dirithromycin	Macrolide	835	0.46	12	0.29	1.74	9.75	Gram-positive
 Erythromycin	Macrolide	734	1.57	7	0.29	1.64	8.35	Gram-positive
 Roxithromycin	Macrolide	837	1.32	13	0.28	1.77	9.99	Gram-positive

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Telithromycin	Macrolide	812	5.13	11	0.34	1.72	9.79	Gram-positive
 EP-13420	Macrolide	841	3.48	8	0.20	1.62	8.42	Gram-positive
 Ranbezolid	Oxazolidinone	461	1.58	7	0.12	1.08	4.36	Gram-positive

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Dalbavancin	Glycopeptide	1817		22	0.33	2.31	20.84	Gram-positive
 Oritavancin	Glycopeptide	1793		19	0.30	2.27	19.06	Gram-positive
 Telcoplanin	Glycopeptide	1880		19	0.29	2.31	19.82	Gram-positive

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Vancomycin	Glycopeptide	1449	-8.48	13	0.28	2.17	14.57	Gram-positive
 Telavancin	Glycopeptide	1756		30	0.30	2.46	17.19	Gram-positive
 Clindamycin	Lincosamide	425	0.65	7	0.16	1.13	5.19	Gram-positive
 Lincomycin	Lincosamide	407	-0.99	7	0.14	1.09	4.72	Gram-positive

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Daptomycin	Lipopeptide	1621	-21.48	35	0.38	2.28	19.06	Gram-positive
 Rifalazil	Ansamycin	941	3.73	6	0.34	1.79	13.10	Gram-positive
 Rifampicin	Ansamycin	823	2.71	5	0.37	1.86	10.42	Gram-positive

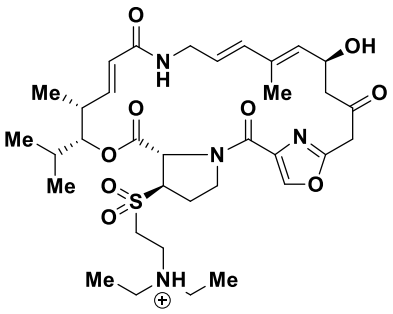
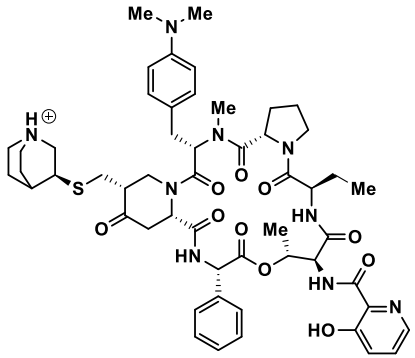
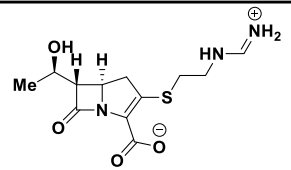
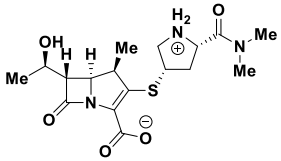
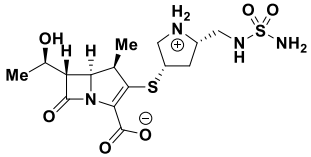
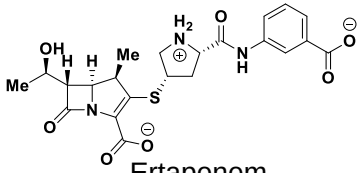
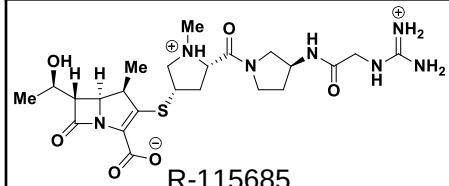
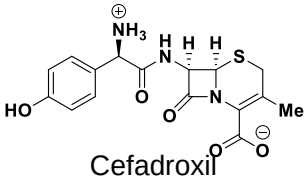
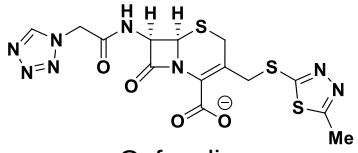
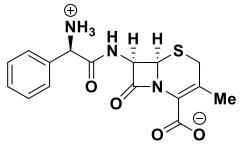
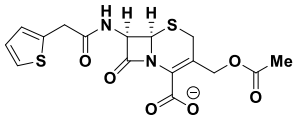
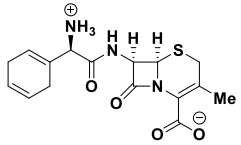
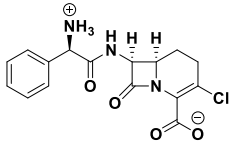
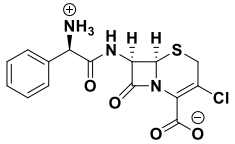
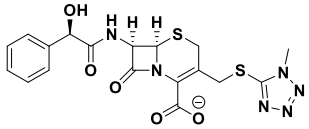
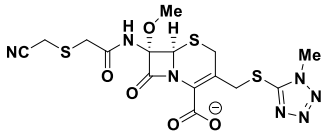
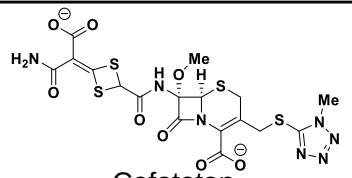
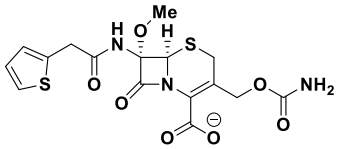
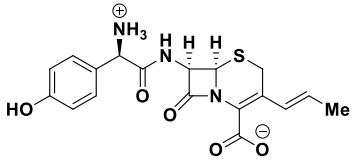
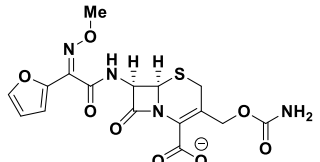
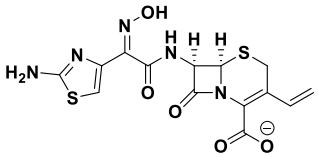
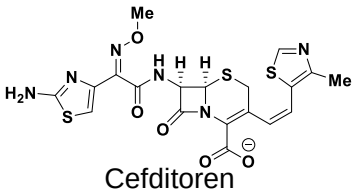
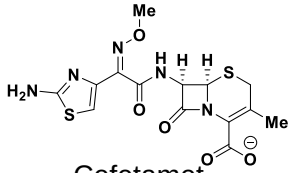
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF	PMI/MW	Spectrum of activity
 Dalfopristin	Steptogramin	691	1.41	7	0.38	1.72	9.81	Gram-positive
 Quinupristin	Steptogramin	1022	1.85	10	0.36	2.05	12.45	Gram-positive

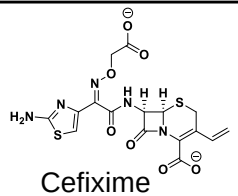
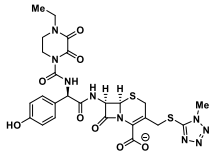
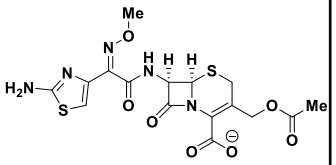
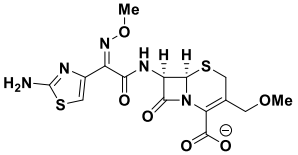
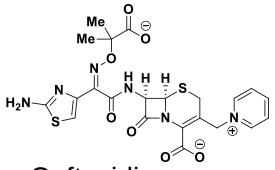
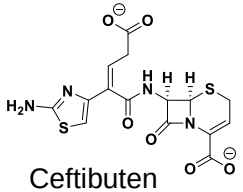
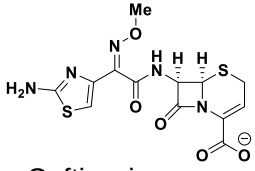
Table S7

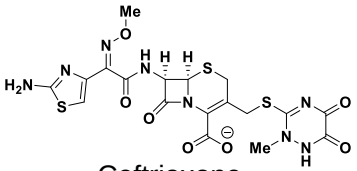
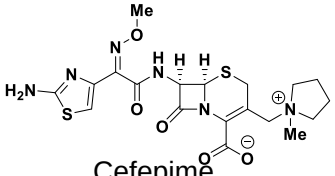
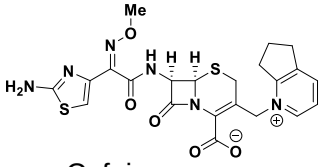
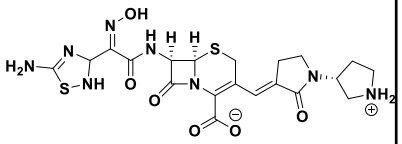
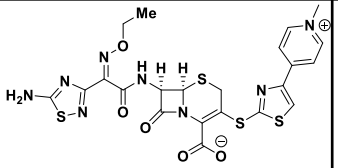
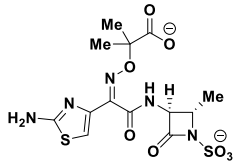
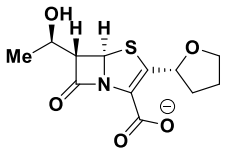
This table contains the structures and names of the Gram-negative β-lactams presented in Extended Data Fig. 4c-e.

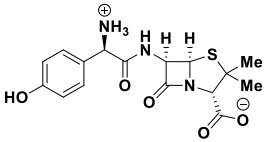
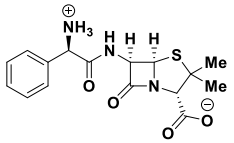
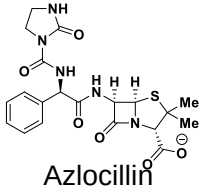
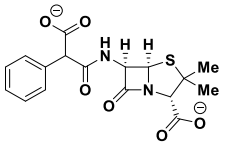
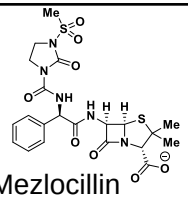
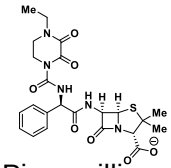
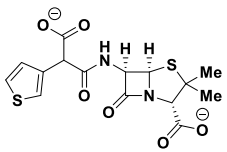
Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Spectrum of Activity	Generation
 Imipenem	Carbapenem	299	-5.5	7	0.09	0.80	2.65	Gram-negative	1
 Meropenem	Carbapenem	383	-4.5	5	0.13	1.04	3.57	Gram-negative	1
 Doripenem	Carbapenem	421	-6.3	7	0.08	0.98	2.75	Gram-negative	1
 Ertapenem	Carbapenem	476	-6.9	7	0.12	1.06	4.45	Gram-negative	1
 R-115685	Carbapenem	538	-9.64	9	0.18	1.16	7.59	Gram-negative	1
 Cefadroxil	Cephalosporin	363	-3.8	4	0.15	0.93	3.70	Gram-negative	1
 Cefazolin	Cephalosporin	455	-5.0	7	0.21	1.09	5.00	Gram-negative	1

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Spectrum of Activity	Generation
 Cephalexin	Cephalosporin	347	-3.5	4	0.17	0.95	3.74	Gram-negative	1
 Cephalothin	Cephalosporin	396	-3.3	7	0.16	1.02	4.70	Gram-negative	1
 Cefradine	Cephalosporin	349	-3.8	4	0.15	1.02	3.62	Gram-negative	1
 Loracarbef	Cephalosporin	350	-3.8	4	0.19	1.01	3.78	Gram-negative	2
 Cefaclor	Cephalosporin	368	-3.7	4	0.17	0.98	4.01	Gram-negative	2
 Cefamandole	Cephalosporin	463	-3.4	7	0.17	1.13	4.54	Gram-negative	2
 Cefmetazole	Cephalosporin	472	-4.1	9	0.22	1.18	5.06	Gram-negative	2

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Spectrum of Activity	Generation
 Cefotetan	Cephalosporin	576	-7.0	9	0.20	1.14	6.63	Gram-negative	2
 Cefoxitin	Cephalosporin	427	-3.1	8	0.16	1.06	4.50	Gram-negative	2
 Cefprozil	Cephalosporin	389	-3.3	5	0.14	0.93	4.76	Gram-negative	2
 Cefuroxime	Cephalosporin	424	-4.4	8	0.13	1.07	4.12	Gram-negative	2
 Cefdinir	Cephalosporin	395	-6.2	5	0.24	1.12	4.74	Gram-negative	3
 Cefditoren	Cephalosporin	507	-2.7	7	0.18	1.22	6.03	Gram-negative	3
 Cefetamet	Cephalosporin	397	-3.3	5	0.17	1.03	4.48	Gram-negative	3

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Spectrum of Activity	Generation
 Cefixime	Cephalosporin	453	-7.1	8	0.16	1.08	4.67	Gram-negative	3
 Cefoperazone	Cephalosporin	646	-4.3	9	0.18	1.23	7.52	Gram-negative	3
 Cefotaxime	Cephalosporin	455	-4.2	8	0.17	1.12	5.18	Gram-negative	3
 Cefpodoxime	Cephalosporin	427	-4.0	7	0.16	1.07	4.63	Gram-negative	3
 Ceftazidime	Cephalosporin	548	-7.4	9	0.29	1.37	6.55	Gram-negative	3
 Ceftibuten	Cephalosporin	410	-6.8	6	0.16	1.01	4.23	Gram-negative	3
 Ceftizoxime	Cephalosporin	383	-3.6	5	0.17	1.00	4.43	Gram-negative	3

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Spectrum of Activity	Generation
 Ceftriaxone	Cephalosporin	555	-5.0	8	0.17	1.16	7.29	Gram-negative	3
 Cefepime	Cephalosporin	482	-3.68	7	0.23	1.23	5.95	Gram-negative	4
 Cefpirome	Cephalosporin	516	-4.11	7	0.27	1.33	6.99	Gram-negative	4
 Ceftobiprole	Cephalosporin	535	-7.18	6	0.22	1.21	5.31	Gram-negative	5
 Ceftaroline	Cephalosporin	606	-5.96	8	0.26	1.44	6.43	Gram-negative	5
 Aztreonam	Monobactam	435	1	7	0.08	0.86	3.73	Gram-negative	1
 Faropenem	Penems	285	-3.81	3	0.08	0.77	2.97	Gram-negative	1

Antibiotic structure/name	Class	MW	ClogD$_{7.4}$	# RB	Glob	PBF score	PMI1/MW	Spectrum of Activity	Generation
 Amoxicillin	Penicillins	365	-3.7	4	0.12	0.86	3.60	Gram-negative	3
 Ampicillin	Penicillins	349	-3.39	4	0.12	0.87	3.54	Gram-negative	3
 Azlocillin	Penicillins	461	-3.72	5	0.16	1.14	4.96	Gram-negative	4
 Carbenicillin	Penicillins	378	-5.91	5	0.13	1.01	3.33	Gram-negative	4
 Mezlocillin	Penicillins	540	-4.22	6	0.19	1.19	7.54	Gram-negative	4
 Piperacillin	Penicillins	518	-3.64	6	0.16	1.14	7.45	Gram-negative	4
 Ticarcillin	Penicillins	384	-5.97	5	0.15	0.98	3.54	Gram-negative	4