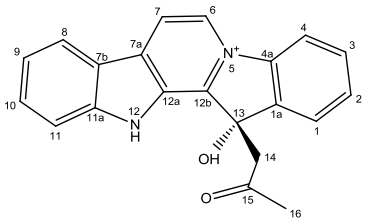
3-Bromohomofascaplysin A, a fascaplysin analogue from a Fijian *Didemnum* sp. ascidian–Supporting Information

Zhenyu Lu,[a] Yuanqing Ding,[b] Xing-Cong Li,[b] Daignon R. Djigbenou,[c,d] Brian T. Grimberg,[d] Daneel Ferreira,[b] Chris M. Ireland,[a] and Ryan M. Van Wagoner[a,*]

[a]*Department of Medicinal Chemistry, University of Utah, Salt Lake City, UT 84112, USA*

[b]*Department of Pharmacognosy and National Center for Natural Products Research, School of Pharmacy, University of Mississippi, University, MS 38677, USA*

[c]*Division of Infectious Disease and* [d]*Center for Global Health & Diseases, Case Western Reserve University, Cleveland, OH 44106, USA*



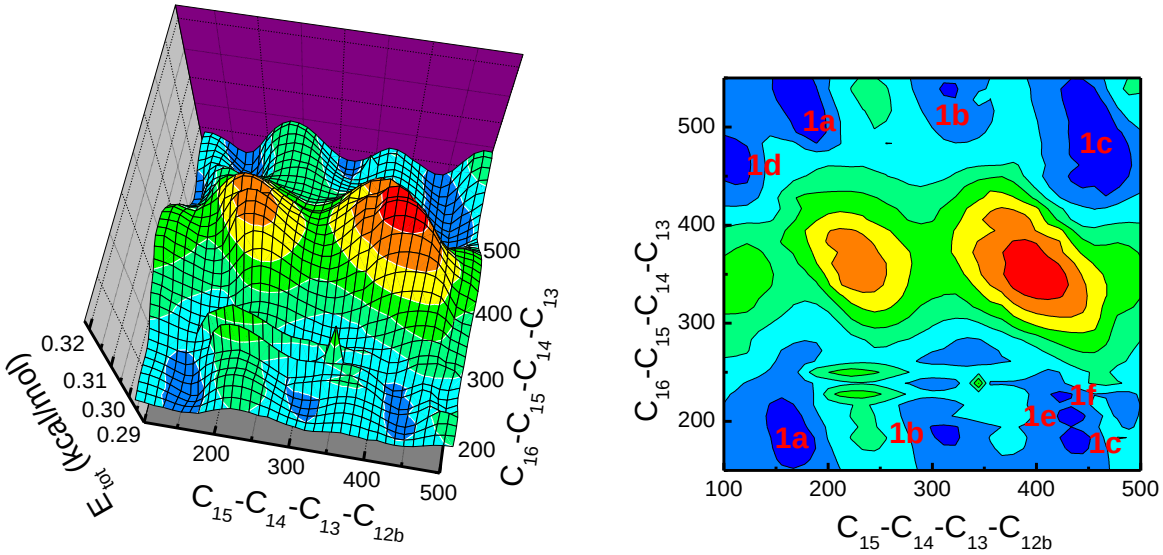


Figure S-1. Potential energy surface of compound **2** at the AM1 level in the gas phase.

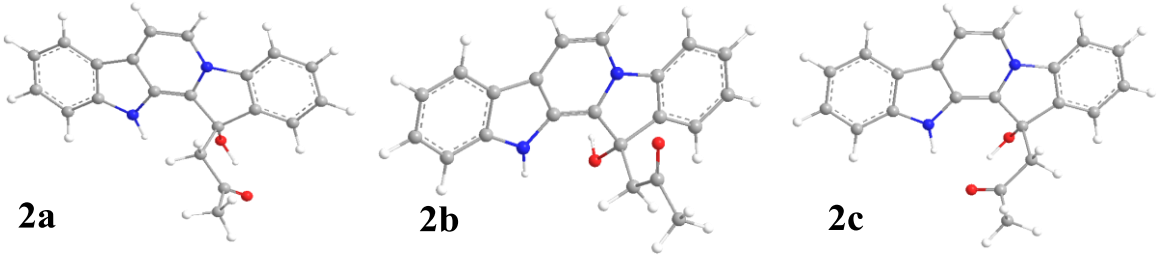


Figure S-2. Optimized geometries of individual conformers of compound **2** at the B3LYP/6-31G** level in the gas phase.

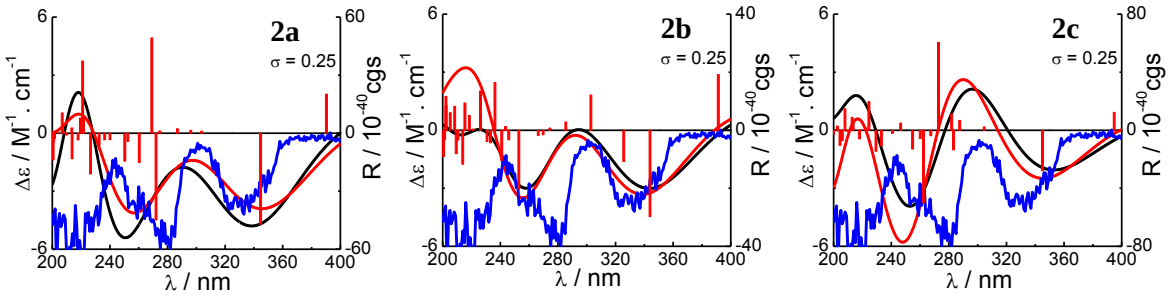


Figure S-3. Experimental and calculated ECD spectra of compound **2** (blue- experimental ECD in MeOH; black- calculated at the B3LYP/6-31G** level in the gas phase; red- calculated at the B3LYP-SCRF/6-31G**//B3LYP/6-31G** level with COSMO in MeOH).

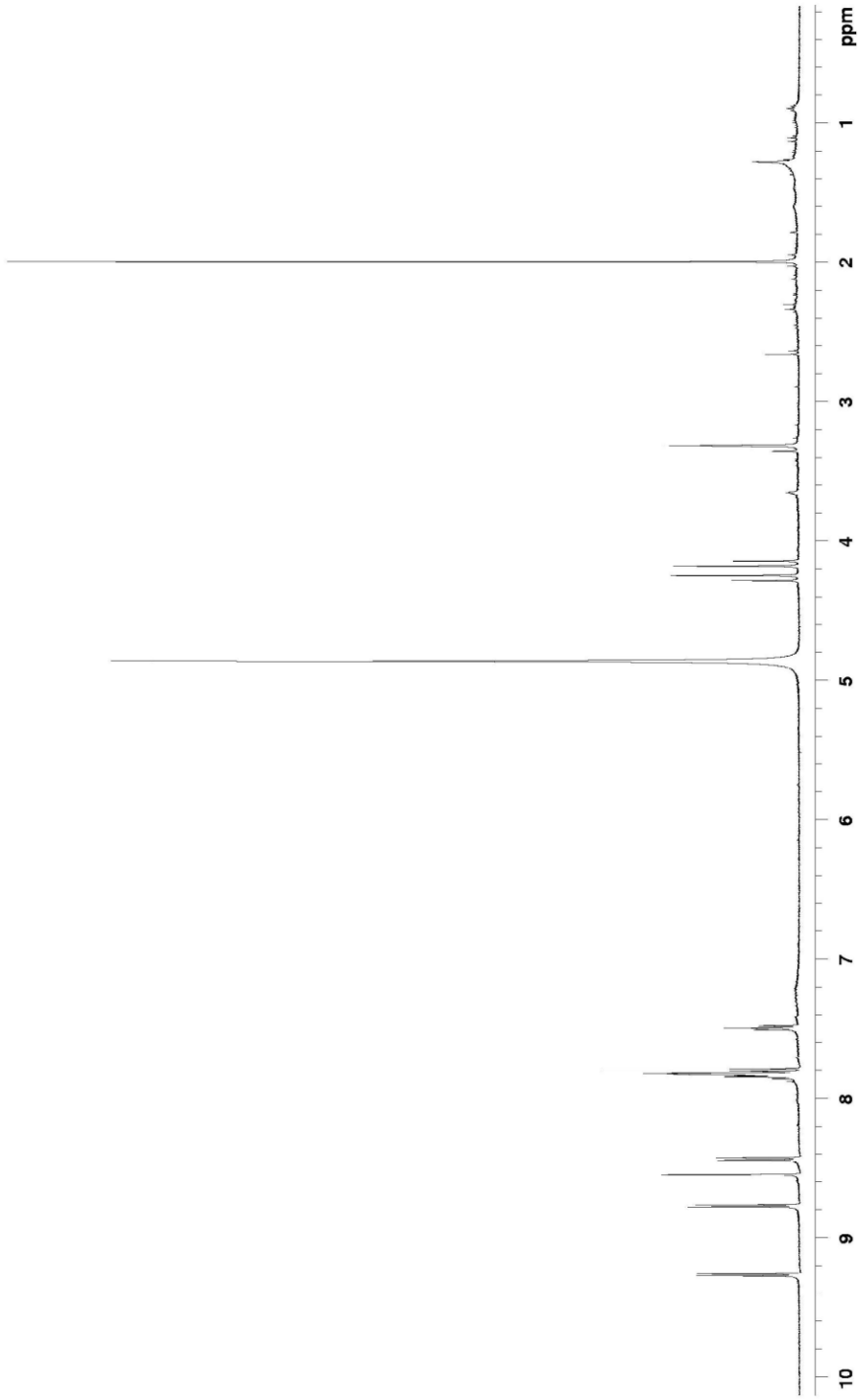


Figure S-4. ^{1}H NMR spectrum of 3-bromohomofascaplysin (**1**) in methanol-d_4 at 500 MHz.

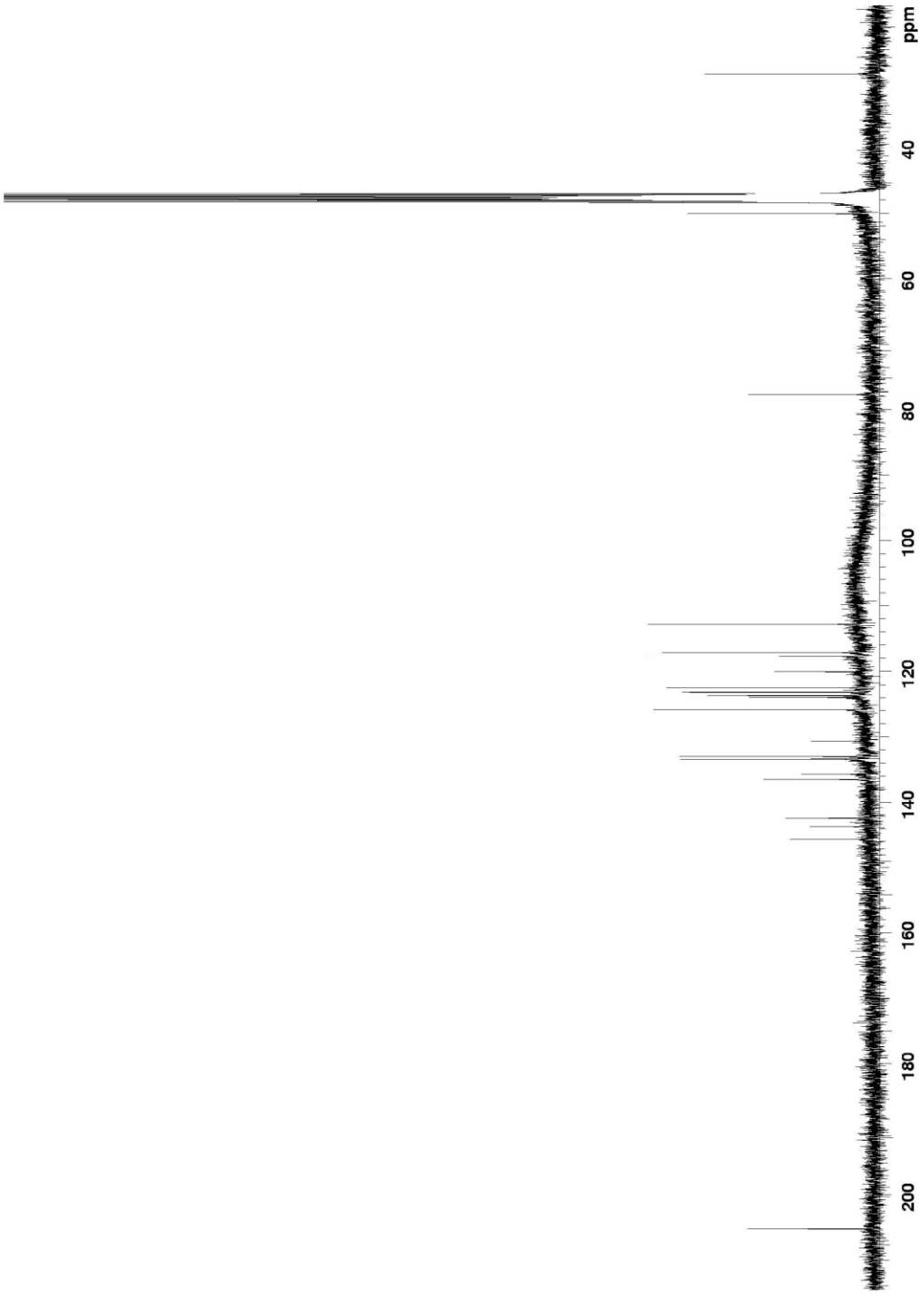


Figure S-5. ^{13}C NMR spectrum of 3-bromohomofascaplysin (**1**) in methanol-d_4 at 100 MHz.

Table S-1. Important Thermodynamic Parameters of Conformers of Compound **2** (au).

Species	In Gas Phase				In Methanol
	E	*E´=E+ZPE*	*H*	*G*	E_s
2a	-1070.2779145	-1069.941808	-1069.921432	-1069.989415	-1070.3489139
2b	-1070.2731356	-1069.937993	-1069.917127	-1069.986347	-1070.3461257
2c	-1070.278921	-1069.943082	-1069.922628	-1069.990854	-1070.3491905

E, E′, H, G: total energy, total energy with zero point energy (*ZPE*), enthalpy and Gibbs free energy, respectively, in the gas phase at B3LYP/6-31G** level; E_s: single point energy in MeOH at the B3LYP-SCRF/6-31G**//B3LYP/6-31G** level with COSMO model.

Table S-2. Conformational Analysis of Conformers of Compound **2**

Species	In Gas Phase				In Methanol	
	ΔE^a	$P_E\%^b$	$\Delta E'^c$	$P_{E'}\%^d$	ΔEs^e	$P_{Es}\%^f$
2a	0.63	25.6	0.80	20.5	0.17	41.8
2b	3.63	0.2	3.19	0.4	1.92	2.2
2c	0.00	74.3	0.00	79.1	0.00	56.0

[a,c] Relative energy and relative energy with *ZPE* at the B3LYP/6-31G** level in the gas phase, respectively (kcal/mol).

[b,d] Conformational distribution calculated by using the respective parameters above at the B3LYP/6-31G** level in the gas phase.

[e,f] Relative energy (kcal/mol) and conformational distribution in MeOH at the B3LYP-SCRF/6-31G**//B3LYP/6-31G** level with the COSMO model, respectively.

Table S-3. Important Dihedral Angles (degrees) and Hydrogen Bond Lengths (Å) in Conformers of Compound **2**.

	C-15-C-14-C-13-C-12b	C-16-C-15-C-14-C-13	(C-15)O···H-O(C-13)	(C15)O···H-N-12
2a	175°	160°	1.88 Å	4.56 Å
2b	-55°	-168°	4.83 Å	4.54 Å
2c	79°	-174°	1.96 Å	1.93 Å

Tabel S-4. Optimized Z-Matrix of Conformers of Compound **2** at the B3LYP/6-31G** Level in the Gas Phase.

2a				**2b**			
C	-0.014915	-0.142792	-0.278294	C	-3.946783	0.257541	-0.954956
C	-0.091836	-0.160798	1.120009	C	-4.930376	-0.686959	-0.633422
C	1.056296	-0.036141	1.907293	C	-4.589038	-1.896568	-0.019747
C	2.319873	0.093341	1.321798	C	-3.257818	-2.204971	0.285989
C	2.367993	0.096476	-0.064215	C	-2.306463	-1.252886	-0.046699
N	3.535135	0.154515	-0.907630	N	-0.882137	-1.320039	0.133666
C	4.838430	0.205921	-0.516556	C	-0.182900	-2.349002	0.681729
C	5.848042	0.143533	-1.457777	C	1.193326	-2.278030	0.768317
C	5.515411	-0.010055	-2.812175	C	1.848242	-1.146556	0.265319
C	6.252591	-0.173775	-4.032289	C	3.221419	-0.740651	0.153658
C	7.624802	-0.220801	-4.338269	C	4.441155	-1.334299	0.523770
C	8.000989	-0.433518	-5.653998	C	5.617776	-0.654659	0.246599
C	7.031678	-0.600703	-6.666834	C	5.593531	0.604237	-0.394056
C	5.669023	-0.554444	-6.395973	C	4.402531	1.215135	-0.770127
C	5.291445	-0.335414	-5.070255	C	3.217422	0.529750	-0.486590
N	4.014017	-0.232681	-4.526544	N	1.907179	0.905700	-0.740782
C	4.129353	-0.059570	-3.172364	C	1.068804	-0.089162	-0.306942
C	3.151203	0.069218	-2.213671	C	-0.307452	-0.174158	-0.332411
C	1.641008	0.094640	-2.348085	C	-1.364219	0.787771	-0.868467
C	1.233588	-0.009154	-0.873940	C	-2.624767	-0.037087	-0.651024
C	1.188487	1.456387	-2.957658	C	-1.390824	2.147380	-0.142275
C	-0.312700	1.521643	-3.247511	C	-1.548494	2.107341	1.369112
C	-0.917759	2.888527	-3.426169	C	-1.846883	3.427037	2.036787
O	1.279790	-0.978809	-3.191719	O	-1.105901	1.123594	-2.229030
O	-0.979132	0.499739	-3.341185	O	-1.433620	1.067047	1.999837
H	-0.909769	-0.241917	-0.882312	H	-4.213659	1.194124	-1.434378
H	-1.058142	-0.276039	1.599516	H	-5.969856	-0.477703	-0.863825
H	0.972857	-0.048787	2.988675	H	-5.365129	-2.614516	0.223936
H	3.208148	0.175744	1.938222	H	-3.002409	-3.146129	0.759301

H	5.024789	0.285057	0.545220	H	-0.752910	-3.198554	1.030165
H	6.878501	0.188768	-1.125872	H	1.735497	-3.104439	1.211901
H	8.371744	-0.096230	-3.560912	H	4.459389	-2.302391	1.014222
H	9.052764	-0.474737	-5.914995	H	6.571653	-1.091657	0.522992
H	7.359827	-0.768785	-7.687536	H	6.531959	1.110528	-0.598333
H	4.933481	-0.682310	-7.182861	H	4.391862	2.182297	-1.260896
H	3.153399	-0.523837	-4.969779	H	1.628802	1.703727	-1.293980
H	0.323260	-0.864070	-3.362906	H	-1.176832	0.319032	-2.767360
H	1.704061	1.613171	-3.915343	H	-2.192698	2.750229	-0.583274
H	1.478443	2.291309	-2.310886	H	-0.464722	2.693062	-0.365440
H	-0.298997	3.511303	-4.080948	H	-2.873433	3.727975	1.794998
H	-1.926694	2.800422	-3.829620	H	-1.745702	3.330889	3.118508
H	-0.960771	3.394839	-2.453740	H	-1.186225	4.215123	1.661835
2c							
C	-4.133109	0.147498	-0.626938				
C	-5.097898	-0.848604	-0.439782				
C	-4.736725	-2.117317	0.024999				
C	-3.402574	-2.433406	0.300013				
C	-2.467763	-1.427447	0.097325				
N	-1.039331	-1.495374	0.244472				
C	-0.333169	-2.608880	0.579338				
C	1.044700	-2.577207	0.594517				
C	1.697269	-1.388227	0.250110				
C	3.071344	-1.003574	0.132146				
C	4.290700	-1.679532	0.324999				
C	5.469116	-0.985173	0.111922				
C	5.450373	0.369131	-0.290561				
C	4.262482	1.061523	-0.489164				
C	3.074370	0.358997	-0.272165				
N	1.764719	0.797865	-0.394358				
C	0.911465	-0.229134	-0.089137				
C	-0.472413	-0.286863	-0.072639				

C	-1.576991	0.734327	-0.439419				
C	-2.808441	-0.153657	-0.342713				
C	-1.706973	1.895719	0.587965				
C	-0.691184	3.024178	0.485897				
C	-0.721803	4.074064	1.563331				
O	-1.451360	1.210550	-1.759097				
O	0.106744	3.087271	-0.446364				
H	-4.412213	1.125909	-1.004153				
H	-6.138207	-0.636704	-0.662375				
H	-5.499324	-2.875371	0.167666				
H	-3.132968	-3.424489	0.646870				
H	-0.906954	-3.494523	0.811824				
H	1.592990	-3.473114	0.860163				
H	4.307559	-2.720212	0.632474				
H	6.422393	-1.482686	0.252697				
H	6.392540	0.883469	-0.450669				
H	4.259489	2.100235	-0.801511				
H	1.466270	1.734105	-0.642937				
H	-0.802614	1.935578	-1.743474				
H	-1.722652	1.511882	1.614990				
H	-2.691037	2.360072	0.438148				
H	-0.356677	3.641833	2.503346				
H	-0.087397	4.915234	1.283554				
H	-1.744636	4.417058	1.750267				

Table S-5. Frequencies of Conformers of Compound **2** at the B3LYP/6-31G** Level in the Gas Phase.

Species	**Frequencies** (cm^{-1})
2a	37 49 58 76 104 117 124 126 138 173 220 237 258 283 300 311 331 338 364 408 447 474 480 488 507 532 539 551 567 576 589 603 636 645 659 689 701 733 748 757 767 772 777 777 788 823 831 864 874 878 889 941 947 955 963 968 991 1003 1007 1013 1041 1053 1061 1097 1109 1136 1148 1157 1185 1188 1196 1200 1223 1241 1250 1258 1285 1317 1337 1353 1357 1370 1373 1392 1406 1416 1436 1457 1469 1476 1485 1491 1506 1513 1537 1563 1603 1627 1644 1667 1670 1701 1781 3040 3049 3099 3112 3176 3202 3207 3207 3215 3217 3224 3226 3230 3233 3267 3610 3642
2b	33 47 56 61 99 108 112 114 148 187 189 218 241 279 295 301 324 334 364 384 412 447 467 477 486 491 509 535 559 564 575 580 607 629 646 656 686 714 748 755 766 767 775 785 791 824 835 854 874 884 886 938 947 952 960 962 971 1006 1008 1039 1042 1050 1061 1071 1111 1125 1147 1157 1185 1186 1193 1201 1226 1248 1249 1256 1266 1320 1340 1343 1352 1371 1374 1379 1394 1406 1422 1459 1472 1476 1487 1491 1506 1514 1537 1563 1605 1627 1650 1668 1671 1696 1809 3046 3052 3099 3112 3174 3202 3203 3207 3211 3216 3219 3226 3228 3234 3267 3659 3788
2c	34 40 68 82 89 113 118 141 156 162 205 236 246 282 300 302 329 334 361 402 448 461 482 490 510 535 553 557 568 576 595 603 632 648 654 673 702 713 752 756 758 769 773 786 810 821 826 852 876 882 887 932 947 950 961 963 984 997 1006 1008 1040 1051 1060 1099 1111 1140 1151 1155 1185 1191 1197 1200 1213 1246 1258 1270 1275 1318 1339 1356 1364 1373 1376 1392 1406 1414 1427 1440 1467 1471 1483 1492 1507 1521 1537 1567 1606 1626 1651 1664 1672 1681 1762 3044 3052 3089 3114 3177 3201 3205 3206 3212 3217 3220 3225 3228 3234 3269 3571 3700