Supporting information

Conformational analysis of a model for the *trans*-fused FGH ether rings in brevetoxin A

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Force Field Analysis. The MacroModel package supports seven different force fields. To obtain the most accurate computational results possible, it is necessary to choose force fields well parameterized for the molecule under study, a model of the *trans*-fused FGH ether rings in brevetoxin A. To do so, the current energy of the *trans*-fused FGH ether rings model was calculated using MacroModel and the stretching, bending, and torsion interactions were evaluated according their quality in the calculation. The AMBER*, MM2*, OPLS2001, and OPLS2005 were all found to have no low quality parameters. Thus, the AMBER* and MM2* force fields were implemented in the conformational search of **3**. Since OPLS2001 and OPLS2005 are very similar force fields and both did not contain any low quality parameters, the newer OPLS2005 force field was also chosen.

Table 1S. Force field parameter analysis for a model of the *trans*-fused FGH ether rings in brevetoxin A. H = high quality parameter, M = medium quality parameter, L = low quality parameter.

Force Field	Interaction Type	Force field parameter analysis		
		H	M	L
AMBER* all-atom	stretch	30	0	0
	bend	82	8	0
	torsion	72	6	0
MMFF	stretch	52	0	0
	bend	100	0	0
	torsion	151	0	2
MM2*	stretch	54	0	0
	bend	109	3	0
	torsion	123	48	0
MM3*	stretch	24	8	8
	bend	79	0	0
	torsion	119	2	4
OPLS	stretch	30	0	0
	bend	87	0	3
	torsion	72	0	6
OPLS2001	stretch	52	0	0
	bend	100	0	0
	torsion	149	4	0
OPLS2005	stretch	52	0	0
	bend	100	0	0
	torsion	151	2	0

Table S2. LM:MC conformational search results on the OPLS2005 /GBSA(chloroform) surface for **3**.

Number of Steps	Number of Conformations Found*	Number of Conformations Minimized	Number of Global Minimum Visits	Minimum Energy (kJ/Mol)
5000	125	63	243	59.58
5000	144	71	655	59.58
5000	144	71	1000	59.58
5000	148	71	1165	59.58
5000	154	80	1667	59.58
5000	163	73	2259	59.58
5000	154	83	2880	59.57
5000	146	76	3264	59.57
5000	148	71	382	59.58
5000	150	79	4119	59.58
5000	167	81	4814	59.58
Mini-2500 steps	42	42	4867	59.59

* Within a 50 kJ/mol energetic window above the lowest energy structure.

Table S3. LM:MC conformational search results on the OPLS2005 /GBSA(water) surface for **3**.

Number of Steps	Number of Conformations Found*	Number of Conformations Minimized	Number of Global Minimum Visits	Minimum Energy (kJ/Mol)
5000	159	88	273	85.88
5000	164	94	621	85.88
5000	178	93	1078	85.88
5000	162	91	1424	85.88
5000	161	79	1858	85.88
5000	171	92	2191	85.88
5000	176	94	2702	85.89
5000	155	85	2995	85.89
5000	166	99	3369	85.88
5000	177	101	3799	85.89
5000	161	92	4190	85.89
Mini-2500 steps	48	48	4221	85.89

* Within a 50 kJ/mol energetic window above the lowest energy structure.

Table S4. LM:MC conformational search results on the AMBER /GBSA(chloroform) surface for **3**.

Number of Steps	Number of Conformations Found*	Number of Conformations Minimized	Number of Global Minimum Visits	Minimum Energy (kJ/Mol)
5000	176	60	211	45.65
5000	181	64	436	45.63
5000	190	67	683	45.64
5000	195	73	1010	45.64
5000	179	69	1304	45.64
5000	190	69	76	45.59
5000	189	68	204	45.58
5000	190	68	2122	45.56
5000	198	68	2315	45.56
5000	188	64	2552	45.56
5000	180	63	2768	45.56
Mini-2500 steps	31	31	2823	45.56

* Within a 50 kJ/mol energetic window above the lowest energy structure.

Table S5. LM:MC conformational search results on the AMBER /GBSA(water) surface for **3**.

Number of Steps	Number of Conformations Found*	Number of Conformations Minimized	Number of Global Minimum Visits	Minimum Energy (kJ/Mol)
5000	162	59	142	75.65
5000	170	63	343	75.65
5000	173	55	609	75.65
5000	171	65	793	75.65
5000	173	64	1039	75.65
5000	169	68	1300	75.65
5000	174	63	146	75.65
5000	163	63	1828	75.65
5000	174	65	2010	75.65
5000	169	61	2263	75.65
5000	162	66	2482	75.65
Mini-2500 steps	40	40	2499	75.65

* Within a 50 kJ/mol energetic window above the lowest energy structure.

Table S6. LM:MC conformational search results on the MM2 /GBSA(chloroform) surface for **3**.

Number of Steps	Number of Conformations Found*	Number of Conformations Minimized	Number of Global Minimum Visits	Minimum Energy (kJ/Mol)
5000	274	86	286	122.17
5000	285	96	171	122.15
5000	288	97	822	122.15
5000	286	109	135	122.15
5000	312	91	1501	122.14
5000	297	109	70	122.13
5000	268	107	2049	122.12
5000	277	92	2300	122.12
5000	278	104	2591	122.12
5000	279	95	2846	122.13
5000	280	90	3154	122.13
Mini-2500 steps	58	57	3183	122.14

* Within a 50 kJ/mol energetic window above the lowest energy structure.

Table S7. LM:MC conformational search results on the MM2 /GBSA(water) surface for **3**.

Number of Steps	Number of Conformations Found*	Number of Conformations Minimized	Number of Global Minimum Visits	Minimum Energy (kJ/Mol)
5000	280	109	136	181.98
5000	282	106	182	181.97
5000	288	109	715	181.97
5000	286	112	985	181.97
5000	282	113	1187	181.97
5000	285	123	1434	181.97
5000	282	116	1659	181.97
5000	284	112	1880	181.97
5000	277	113	2122	181.97
5000	289	114	2291	181.97
5000	296	121	2526	181.97
Mini-2500 steps	60	60	2554	181.97

* Within a 50 kJ/mol energetic window above the lowest energy structure.

Table S8. Superimposition of Low Energy Conformations with Their Quantum Mechanical Minimizations.

Low Energy Conformations Used in Superposition (FF/Solvent)	RMSD	
	All heavy ring atoms	All heavy atoms
OPLS2005/$CHCl_3$ – twist-crown	0.1195	0.1277
OPLS2005/$CHCl_3$ - crown	0.0591	0.0620
OPLS2005/$CHCl_3$ – boat-chair	0.0285	0.0746
OPLS2005/$CHCl_3$ - boat	0.0313	0.0900
OPLS2005/Water - twist-crown	0.2200	0.8564
OPLS2005/Water - crown	0.0407	0.0793
OPLS2005/Water – boat-chair	0.0725	0.1715
OPLS2005/Water - boat	0.1124	0.1497
AMBER/$CHCl_3$ - twist-crown	0.2995	0.7172
AMBER/$CHCl_3$ - crown	0.1021	0.1568
AMBER/$CHCl_3$ – boat-chair	0.0742	0.1401
AMBER/$CHCl_3$ - boat	0.2614	0.2763
AMBER/Water - twist-crown	0.0935	0.5343
AMBER/Water - crown	0.1380	0.2199
AMBER/Water – boat-chair	0.1217	0.2022
AMBER/Water - boat	0.3637	0.3784
MM2/$CHCl_3$ - twist-crown	0.2228	0.5208
MM2/$CHCl_3$ - crown	0.0779	0.1358
MM2/$CHCl_3$ – boat-chair	0.0651	0.1234
MM2/$CHCl_3$ - boat	0.2165	0.2289
MM2/Water - twist-crown	0.1872	0.6806
MM2/Water - crown	0.0949	0.1806
MM2/Water – boat-chair	0.1094	0.2051
MM2/Water - boat	0.3113	0.3347

Solvent Effects

In order to more quantitatively determine the effects of solvent on the low energy structure, the lowest energy conformations found using each force field were then superimposed (using all heavy ring atoms or all heavy atoms) against the lowest energy conformations calculated using the same force field but a different solvent model or without any solvent. A summary of the resulting RMSD comparisons is listed in Table 3. Through visualization of superimposed low energy conformations and RMSD analysis it is clear that each superimposed pair corresponds to the same low energy minima. An example of the molecular pair with the lowest RMSD and the highest RMSD are shown in Figure 5.

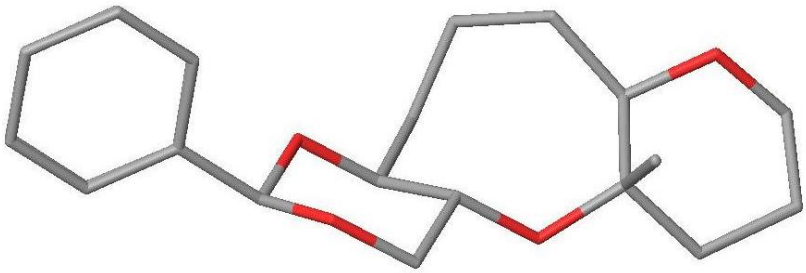


Figure 5a. Superimposition of the lowest energy conformation from AMBER/$CHCl_3$ and AMBER/Water. RMSD 0.0043 (All heavy ring atoms) 0.0244 (All heavy atoms)

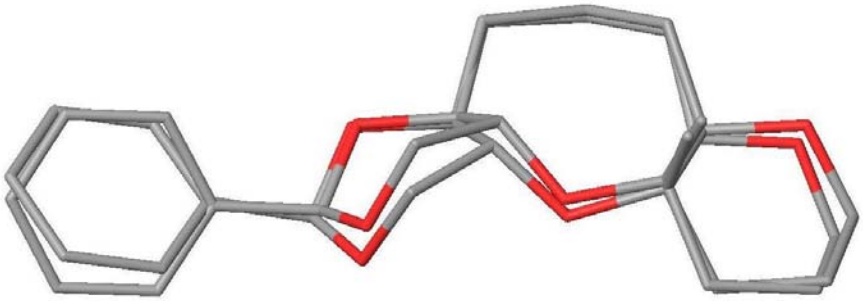


Figure 5b. Superimposition of the lowest energy conformation from OPLS2005/$CHCl_3$ and MM2/$CHCl_3$. RMSD 0.1334 (All heavy ring atoms) 0.5054 (All heavy atoms)

Table 3. Superimposition of Low Energy Conformations Using Various Force Field/Solvent Systems.

Low Energy Conformations Used in Superposition (FF/Solvent)	**RMSD**	
	All heavy ring atoms	**All heavy atoms**
OPLS2005/$CHCl_3$ and OPLS2005/Water	0.0365	0.4101
AMBER/$CHCl_3$ and AMBER/Water	0.0043	0.0244
MM2/$CHCl_3$ and MM2/Water	0.0126	0.0265
AMBER/$CHCl_3$ and AMBER/Vacuum	0.0043	0.0228
MM2/$CHCl_3$ and MM2/Vacuum	0.0104	0.0226

It is interesting to note that on changing solvents or removing the solvent, the global minima energy structure remains the same, indicating that solvent does not play a

major role in the conformational preferences. The reason why RMSD values increased when superimposing against all heavy atoms was that the side phenyl ring frequently differed slightly on changing solvents, which simply means that the torsion connecting the phenyl ring with the F′ ring is quite flexible.

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (twist-crown G-ring conformation) using as starting structure the lowest energy conformation found through the AMBER*/Water conformational search

Total energy: -1040.587450

Cartesian coordinates:

O	-3.70670	2.86950	2.32400
C	-2.37910	3.39610	2.32690
C	-2.02520	3.93330	0.90930
C	-1.02430	3.08390	0.13510
C	-1.60760	1.80330	-0.48550
C	-2.17720	0.72340	0.45910
C	-3.65740	0.87150	0.88190
H	-2.96480	4.02150	0.34470
H	-0.62350	3.70100	-0.67760
H	-0.17670	2.83470	0.78730
H	-2.37650	2.07740	-1.21940
H	-0.79870	1.34030	-1.06240
H	-1.52240	0.59390	1.32710
H	-2.13730	-0.22670	-0.08190
H	-4.17320	1.52240	0.15780
C	-2.34880	4.57850	3.29770
H	-2.88390	4.32850	4.21660
H	-1.31780	4.84950	3.55190
O	-3.05190	5.68310	2.71540
C	-2.42470	6.17160	1.52030
H	-3.24380	6.26030	0.78640
O	-1.46420	5.26220	1.04190
C	-5.50620	1.40670	2.49570
H	-5.74180	1.76050	3.50470
H	-5.94240	2.12800	1.79450
C	-5.65160	-0.47710	0.87310
H	-6.08340	0.14080	0.07010
H	-5.94700	-1.51540	0.69730
O	-4.22210	-0.45090	0.77670
H	-1.65020	2.64830	2.65320
C	-3.97280	1.45000	2.29560
C	-3.26050	0.70500	3.42860
H	-3.58300	1.10560	4.39490
H	-3.51080	-0.35810	3.39490
H	-2.17160	0.78110	3.37470
C	-0.82740	10.15200	2.00470
C	-0.22500	9.26880	1.10460
C	-0.71270	7.96890	0.96480
C	-1.80020	7.53770	1.73380
C	-2.39750	8.42510	2.63780
C	-1.91510	9.72590	2.77180

H	-0.45330	11.16620	2.10650
H	0.62370	9.59210	0.50680
H	-0.24690	7.28830	0.25940
H	-3.24300	8.09310	3.23260
H	-2.39050	10.40740	3.47180
C	-6.11240	0.02440	2.23480
H	-5.81110	-0.69020	3.00850
H	-7.20700	0.07870	2.26070

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (crown G-ring conformation) using as starting structure the lowest energy conformation found through the AMBER*/Water conformational search

Total energy: -1040.597027

Cartesian coordinates:

O	-4.00960	2.69500	1.95960
C	-3.02590	3.71030	2.10010
C	-2.67210	4.31470	0.73360
C	-1.84240	3.43630	-0.20130
C	-2.58470	2.30210	-0.93970
C	-2.68510	0.91700	-0.26640
C	-3.84810	0.65630	0.70080
H	-3.60900	4.60260	0.23000
H	-1.44010	4.11840	-0.96000
H	-0.97360	3.03890	0.34000
H	-3.58550	2.64510	-1.23360
H	-2.04360	2.14320	-1.87950
H	-1.72890	0.66160	0.20650
H	-2.82350	0.18110	-1.06680
H	-4.77470	1.04470	0.24770
C	-3.67290	4.78510	2.98070
H	-4.66430	5.03500	2.57550
H	-3.79660	4.42500	4.00520
O	-2.85710	5.95950	3.04160
C	-2.59420	6.47340	1.74300
H	-3.55480	6.70330	1.25010
O	-1.89620	5.51550	0.96750
C	-4.97640	0.78620	2.94490
H	-4.88560	1.15990	3.97060
H	-5.86840	1.25380	2.51150
C	-5.14330	-1.21660	1.47150
H	-6.02860	-0.84130	0.93430
H	-5.14270	-2.30840	1.40400
O	-3.95600	-0.77700	0.79790
H	-2.11170	3.35350	2.58150
C	-3.76090	1.27520	2.12300
C	-2.45250	0.94710	2.84030
H	-1.56920	1.31590	2.31350
H	-2.35190	-0.13830	2.92050
H	-2.45100	1.36270	3.85290
C	-0.20250	10.02530	2.20800
C	0.28890	8.78740	2.63480
C	-0.48100	7.63680	2.47520
C	-1.74970	7.71470	1.88770
C	-2.23620	8.95280	1.45980
C	-1.46460	10.10690	1.61940

H	0.39770	10.92210	2.33540
H	1.27150	8.72060	3.09310
H	-0.10170	6.67500	2.80590
H	-3.22130	9.01640	1.00460
H	-1.85010	11.06650	1.28630
C	-5.15550	-0.73630	2.91620
H	-4.35670	-1.23890	3.47360
H	-6.10250	-1.01710	3.39170

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (boat-chair G-ring conformation) using as starting structure the lowest energy conformation found through the OPLS2005/Water conformational search

Total energy: -1040.594830

Cartesian coordinates:

O	-1.20650	2.28700	0.56870
C	0.20350	2.12500	0.43910
C	0.71570	2.86270	-0.80590
C	0.15590	2.40210	-2.14960
C	0.08420	0.89520	-2.45660
C	-0.85860	0.00300	-1.60110
C	-2.13880	0.66570	-1.05530
H	0.46760	3.93070	-0.69140
H	-0.84110	2.84260	-2.24870
H	0.76470	2.88220	-2.92570
H	1.09070	0.46430	-2.41690
H	-0.23050	0.81700	-3.50390
H	-1.19000	-0.82540	-2.23600
H	-0.30000	-0.46720	-0.78780
H	-2.39520	1.54170	-1.67120
C	0.87070	2.74400	1.66970
H	0.52630	3.78150	1.79670
H	0.63200	2.18370	2.57720
O	2.29750	2.70350	1.52130
C	2.73290	3.35270	0.33220
H	2.41560	4.40910	0.36840
O	2.15630	2.74200	-0.81150
C	-3.47850	1.76300	0.75660
H	-3.49270	2.07310	1.80750
H	-3.58910	2.67160	0.15150
C	-4.50280	0.28160	-0.98070
H	-4.66760	1.09570	-1.70610
H	-5.22380	-0.51460	-1.19230
O	-3.20570	-0.29220	-1.19900
H	0.50260	1.07740	0.37870
C	-2.09870	1.15390	0.42790
C	-1.74650	0.04170	1.42260
H	-0.72220	-0.32080	1.30890
H	-1.86240	0.41130	2.44630
H	-2.41110	-0.81430	1.28680
C	7.02570	3.04080	0.16260
C	6.23670	1.88830	0.09940
C	4.84780	1.98900	0.14600
C	4.23520	3.24360	0.25640
C	5.02710	4.39320	0.31670
C	6.41980	4.29310	0.27000

H	8.10870	2.96070	0.12780
H	6.70580	0.91200	0.01440
H	4.23400	1.09560	0.09330
H	4.55510	5.36890	0.40190
H	7.02890	5.19130	0.31820
C	-4.63620	0.80610	0.44550
H	-4.64240	-0.03740	1.14670
H	-5.59600	1.32400	0.55950

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (boat G-ring conformation) using as starting structure the lowest energy conformation found through the AMBER*/Water conformational search

Total energy: -1040.587678

Cartesian coordinates:

O	-2.54820	2.02690	2.83000
C	-2.30650	3.40610	2.53370
C	-2.04060	3.81350	1.06690
C	-0.98900	3.00820	0.30650
C	-1.16250	1.47860	0.31350
C	-2.53890	0.92060	-0.09420
C	-3.76130	1.29210	0.76580
H	-2.97990	3.82870	0.50070
H	-0.97850	3.38120	-0.72480
H	-0.00870	3.24670	0.73630
H	-0.42450	1.06390	-0.38390
H	-0.89180	1.09480	1.29840
H	-2.76710	1.21670	-1.12600
H	-2.46820	-0.17350	-0.10250
H	-4.08140	2.31750	0.54100
C	-3.34250	4.38460	3.11050
H	-4.29640	4.33860	2.56790
H	-3.52710	4.18670	4.16940
O	-2.81570	5.71650	3.01660
C	-2.51970	6.07180	1.67190
H	-3.44770	6.01610	1.07650
O	-1.56410	5.18030	1.12120
C	-4.95630	1.50650	2.97200
H	-4.86780	1.36560	4.05460
H	-5.18890	2.56170	2.80360
C	-6.10440	0.78430	0.87270
H	-6.35500	1.81130	0.56350
H	-6.82740	0.10510	0.41190
O	-4.82370	0.42290	0.33500
H	-1.36920	3.60350	3.06810
C	-3.60010	1.17270	2.30690
C	-3.13820	-0.23340	2.71740
H	-3.81580	-0.99670	2.33070
H	-3.11440	-0.31290	3.80850
H	-2.13500	-0.44540	2.34040
C	-0.89640	10.06260	1.66610
C	-2.06370	9.78290	0.95270
C	-2.58870	8.48790	0.95170
C	-1.94900	7.46850	1.66210
C	-0.77620	7.75280	2.37530
C	-0.25280	9.04460	2.37750

H	-0.48800	11.06960	1.66940
H	-2.56610	10.57080	0.39820
H	-3.49900	8.26950	0.39750
H	-0.27690	6.96060	2.92450
H	0.65650	9.25900	2.93360
C	-6.10850	0.67060	2.39300
H	-6.01330	-0.38170	2.68130
H	-7.06880	1.02350	2.78550

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (twist-crown G-ring conformation) using as starting structure the lowest energy conformation found through the OPLS2005/Chloroform conformational search

Total energy: -1040.585686

Cartesian coordinates:

O	-0.84240	2.64210	-0.79130
C	0.33140	2.10850	-0.18100
C	0.64120	0.70200	-0.76040
C	0.22840	-0.47020	0.12320
C	-1.27730	-0.77110	0.20140
C	-2.20080	0.26200	0.88380
C	-2.80220	1.36230	-0.01450
H	0.15010	0.63510	-1.74290
H	0.73180	-1.36070	-0.27110
H	0.63150	-0.31120	1.13270
H	-1.65820	-0.98520	-0.80650
H	-1.37350	-1.71140	0.75680
H	-3.07170	-0.28070	1.26520
H	-1.70970	0.68710	1.76690
H	-2.83570	0.98840	-1.05230
C	1.51760	3.02710	-0.50980
H	1.19330	4.06940	-0.50530
H	2.31830	2.90120	0.22990
O	1.99290	2.75930	-1.83100
C	2.54640	1.44920	-1.95100
H	2.20150	1.09070	-2.93660
O	2.06870	0.59110	-0.94030
C	-2.92390	3.66240	-1.00270
H	-2.47270	4.66040	-1.01460
H	-2.82760	3.26010	-2.01850
C	-4.95640	2.31050	-0.45520
H	-4.99520	1.80500	-1.43520
H	-5.96820	2.31170	-0.03700
O	-4.15460	1.54560	0.44620
H	0.22800	2.05610	0.90740
C	-2.09070	2.74820	-0.07470
C	-1.93110	3.39490	1.30680
H	-1.31090	2.80930	1.98950
H	-1.48150	4.38770	1.20480
H	-2.90870	3.50170	1.78200
C	6.87080	1.45610	-1.97300
C	6.16190	2.59210	-2.36680
C	4.76640	2.59350	-2.33500
C	4.06720	1.45990	-1.90740
C	4.78110	0.32170	-1.51570
C	6.17670	0.32160	-1.54630

H	7.95740	1.45440	-1.99850
H	6.69510	3.47900	-2.69950
H	4.21050	3.47470	-2.63750
H	4.24120	-0.55830	-1.18170
H	6.72270	-0.56520	-1.23580
C	-4.40660	3.72510	-0.61530
H	-4.54200	4.27640	0.32280
H	-4.97670	4.26120	-1.38340

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (crown G-ring conformation) using as starting structure the lowest energy conformation found through the MM2*/Chloroform conformational search

Total energy: -1040.593804

Cartesian coordinates:

O	-3.55170	-0.31240	0.49170
C	-3.75660	0.07370	-0.85870
C	-2.50530	0.75700	-1.42730
C	-2.20260	2.16130	-0.90610
C	-1.61310	2.27980	0.51560
C	-2.58390	2.41680	1.70760
C	-3.10610	1.13470	2.36810
H	-1.63970	0.09990	-1.23510
H	-1.47300	2.57760	-1.61000
H	-3.10050	2.78600	-1.00190
H	-0.91540	1.45190	0.69810
H	-0.99550	3.18510	0.51860
H	-2.04860	2.93710	2.51010
H	-3.41890	3.07510	1.43840
H	-2.25530	0.44560	2.50880
C	-4.02440	-1.22010	-1.63940
H	-3.23070	-1.94750	-1.40750
H	-4.98440	-1.65640	-1.35220
O	-4.07770	-0.97180	-3.04510
C	-2.88440	-0.35470	-3.50160
H	-2.03090	-1.02040	-3.27720
O	-2.68300	0.88770	-2.85370
C	-4.61820	-0.86490	2.51820
H	-5.44210	-1.40460	2.03740
H	-3.76500	-1.55370	2.55140
C	-3.87570	0.43330	4.52270
H	-2.95990	-0.16350	4.67290
H	-4.15840	0.86390	5.48880
O	-3.59230	1.53700	3.66060
H	-4.60990	0.74490	-0.98590
C	-4.20270	0.32380	1.62030
C	-5.41820	1.17830	1.25590
H	-5.17520	2.00830	0.58860
H	-6.19720	0.57170	0.78310
H	-5.83110	1.61290	2.16900
C	-3.23150	0.35400	-7.73650
C	-2.21800	-0.47270	-7.25030
C	-2.10540	-0.70490	-5.87660
C	-3.00320	-0.11210	-4.98580
C	-4.01960	0.71650	-5.47780
C	-4.13300	0.94850	-6.84730

H	-3.32070	0.53640	-8.80440
H	-1.51540	-0.93670	-7.93750
H	-1.31530	-1.34920	-5.49740
H	-4.71410	1.17740	-4.78250
H	-4.92290	1.59310	-7.22390
C	-4.98440	-0.44370	3.94730
H	-5.93120	0.10950	3.96160
H	-5.12360	-1.32810	4.58050

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (boat-chair G-ring conformation) using as starting structure the lowest energy conformation found through the MM2*/Chloroform conformational search

Total energy: -1040.591647

Cartesian coordinates:

O	-3.75560	-0.68140	0.57190
C	-3.74380	-0.18460	-0.76180
C	-2.30360	-0.03670	-1.27000
C	-1.41100	0.90700	-0.47040
C	-1.94600	2.30790	-0.11760
C	-3.16500	2.42740	0.84050
C	-3.29800	1.35160	1.93510
H	-1.83450	-1.03520	-1.25310
H	-1.12840	0.37800	0.44520
H	-0.48370	1.02800	-1.04320
H	-1.10550	2.84760	0.33490
H	-2.18050	2.84660	-1.04250
H	-3.07780	3.38210	1.36910
H	-4.09520	2.50140	0.27040
H	-2.30720	0.91820	2.14700
C	-4.47560	-1.17100	-1.67640
H	-4.03440	-2.17430	-1.56920
H	-5.53840	-1.23380	-1.42920
O	-4.38910	-0.72350	-3.03420
C	-3.04450	-0.54580	-3.45680
H	-2.51750	-1.51420	-3.38100
O	-2.37340	0.40200	-2.64120
C	-4.21100	-0.78340	2.86770
H	-4.90390	-1.61670	2.71040
H	-3.20200	-1.21170	2.91300
C	-3.64490	1.20070	4.29240
H	-2.59110	0.91290	4.44450
H	-3.94750	1.82940	5.13520
O	-3.74960	2.02020	3.12490
H	-4.24050	0.78310	-0.85260
C	-4.26010	0.15300	1.64210
C	-5.70080	0.60560	1.36760
H	-6.35900	-0.26700	1.31270
H	-6.05250	1.26040	2.16770
H	-5.79940	1.16050	0.43140
C	-3.09010	0.88530	-7.51990
C	-2.47740	-0.33130	-7.21710
C	-2.46060	-0.79550	-5.89890
C	-3.05490	-0.04690	-4.88030
C	-3.66770	1.17430	-5.18830
C	-3.68540	1.63820	-6.50240

H	-3.10510	1.24770	-8.54460
H	-2.01350	-0.91940	-8.00440
H	-1.98390	-1.74410	-5.66280
H	-4.12720	1.75470	-4.39450
H	-4.16290	2.58630	-6.73590
C	-4.51690	-0.04790	4.17910
H	-5.57370	0.23950	4.22230
H	-4.33150	-0.70600	5.03620

Cartesian coordinates and energy for QM (B3LYP/6-31G**) minimized structure of **3** (boat G-ring conformation) using as starting structure the lowest energy conformation found through the AMBER*/Chloroform conformational search

Total energy: -1040.584319

Cartesian coordinates:

O	-1.15220	0.61670	0.78260
C	0.17920	1.12500	0.89160
C	1.04080	1.23180	-0.38620
C	1.19160	-0.04810	-1.21430
C	-0.08690	-0.85190	-1.51020
C	-1.21690	-0.12140	-2.25620
C	-1.79400	1.14270	-1.60520
H	0.67790	2.05740	-1.01380
H	1.69500	0.22050	-2.15150
H	1.88550	-0.69730	-0.66720
H	0.20710	-1.71200	-2.12420
H	-0.47380	-1.26380	-0.57560
H	-0.87700	0.16320	-3.26010
H	-2.04430	-0.82500	-2.40600
H	-1.07230	1.96620	-1.69810
C	0.27790	2.45680	1.65650
H	-0.24570	2.39270	2.61340
H	-0.15080	3.28760	1.07780
O	1.65110	2.74260	1.94310
C	2.42140	2.81230	0.75290
H	2.01080	3.61140	0.10960
O	2.37310	1.58390	0.04890
C	-2.78360	2.41830	0.31160
H	-3.12190	2.36690	1.35220
H	-1.98030	3.16200	0.27090
C	-3.44850	2.80210	-2.07540
H	-2.66760	3.55710	-2.26750
H	-4.27090	2.98550	-2.77310
O	-2.94370	1.50110	-2.38840
H	0.67680	0.37550	1.51910
C	-2.21640	1.04280	-0.10820
C	-3.26640	-0.06070	0.08950
H	-4.10320	0.06430	-0.59930
H	-2.82440	-1.04540	-0.08250
H	-3.64580	-0.03590	1.11590
C	6.52070	3.62130	1.79660
C	5.87110	2.49830	2.31940
C	4.54380	2.23850	1.98250
C	3.85510	3.10120	1.12020
C	4.50680	4.22220	0.60040
C	5.83760	4.48300	0.93660

H	7.55600	3.82240	2.05980
H	6.40100	1.82560	2.98920
H	4.03580	1.36720	2.38430
H	3.97400	4.89350	-0.06990
H	6.33840	5.35670	0.52740
C	-3.91240	2.88530	-0.62240
H	-4.80670	2.26730	-0.48770
H	-4.19990	3.91670	-0.38550

Cartesian coordinates and energy for QM (B3LYP/6-31G*) minimized structure of brevetoxin A using as starting structure the lowest energy conformation found through the OPLS2005/Water conformational search

Total energy: -2887.181654

Cartesian coordinates:

O	-0.24080	2.53920	0.15870
C	1.25930	1.95990	-1.71370
C	0.09930	1.27060	-2.44010
C	-0.30960	-0.16340	-2.05600
C	-0.86170	-0.41760	-0.63250
C	-1.78620	0.68410	-0.08680
H	-0.76700	1.93560	-2.35880
H	-1.08090	-0.46270	-2.77780
H	0.53530	-0.84150	-2.22570
H	-1.44350	-1.34620	-0.65730
H	-0.03980	-0.60930	0.06290
H	-2.15770	1.29600	-0.92080
C	-2.19880	2.65830	1.44440
H	-1.77110	3.28280	2.23730
H	-2.49740	3.32420	0.62500
C	-3.95370	1.02610	0.79820
H	-4.09990	1.65750	-0.09400
O	-2.94350	0.05800	0.50960
C	-1.12270	1.68120	0.91470
C	-0.43190	1.00630	2.11060
H	-1.15850	0.41620	2.67650
H	0.37780	0.32760	1.83300
H	-0.01840	1.77080	2.77760
C	-3.44050	1.92030	1.93460
H	-3.21220	1.27910	2.79970
O	-4.42150	2.88510	2.33650
C	-5.28630	0.36780	1.14030
H	-5.17570	-0.32160	1.98830
H	-5.67060	-0.20020	0.28520
C	-5.67310	2.28790	2.70270
C	-6.23780	1.50520	1.51090
H	-5.52980	1.59890	3.55040
H	-6.31300	2.19740	0.66090
O	-7.52540	0.98290	1.82510
C	-8.04600	2.89130	3.27010
C	-8.51140	2.00220	2.09770
H	-8.09330	2.29690	4.19170
H	-8.73280	3.73600	3.40250
H	-9.38590	1.43000	2.41810
C	-8.90440	2.80780	0.83010
H	-9.86280	3.29470	1.05690

H	-8.17930	3.60390	0.64870
C	-9.05180	1.97190	-0.41880
C	-10.13770	0.97900	-0.50020
C	1.09350	2.12970	-0.17280
H	1.33220	1.16050	0.27210
C	2.00370	3.20350	0.37730
C	3.32130	3.12280	0.58310
C	4.17570	1.92390	0.27830
H	5.03290	1.87940	0.96100
H	3.60350	1.00290	0.44320
C	4.71260	1.83640	-1.16710
H	5.16490	0.84480	-1.27020
C	3.64440	2.01360	-2.26120
H	3.36520	3.07310	-2.28630
O	2.47920	1.23640	-1.95750
H	3.82210	4.00370	0.97940
H	1.48520	4.13500	0.60010
H	1.34790	2.96050	-2.15800
O	5.70380	2.83350	-1.47970
C	4.19820	1.63500	-3.66630
H	3.33410	1.50800	-4.32930
C	7.03800	2.54710	-1.05780
C	7.97380	1.99950	-2.19050
H	8.66660	2.79900	-2.48450
C	5.06000	0.39730	-3.66690
C	6.39580	0.36890	-3.54080
H	6.88100	-0.60610	-3.49040
C	7.32370	1.55910	-3.51840
H	8.16300	1.34970	-4.19620
H	6.82220	2.44550	-3.91910
H	4.53060	-0.55590	-3.69460
C	7.63930	3.83340	-0.44870
H	7.55020	4.60870	-1.22280
O	8.74620	0.91750	-1.63990
C	9.14670	3.67430	-0.12150
C	9.88240	1.30480	-0.85700
H	10.61390	1.80990	-1.50930
C	9.58090	2.26810	0.31340
H	8.82310	1.81790	0.97010
H	9.76900	3.98200	-0.97080
H	9.39470	4.35900	0.69630
C	6.86220	4.31360	0.78370
H	6.92270	3.58920	1.60700
H	7.27220	5.26310	1.14650
H	5.80920	4.47220	0.54420
H	6.99350	1.76290	-0.29310

O	10.79910	2.46300	1.04360
C	11.40570	1.32080	1.71520
C	10.47610	0.01680	-0.29750
H	9.69960	-0.51060	0.27150
H	10.78250	-0.64610	-1.11440
C	11.68830	0.26860	0.60520
H	12.51700	0.64550	-0.00990
C	12.68280	1.98630	2.29950
H	13.37850	2.18960	1.47320
H	12.32910	2.96740	2.63640
C	13.46360	1.37520	3.48750
H	12.75250	0.96390	4.21560
C	14.47850	0.26780	3.13190
H	15.14700	0.61160	2.33000
H	15.10730	0.10130	4.01540
C	13.89300	-1.08750	2.76030
H	13.09410	-1.37110	3.45620
C	13.40500	-1.30740	1.31100
H	14.01540	-0.71370	0.61810
O	12.03540	-1.01280	1.13700
O	14.95540	-2.08780	2.91390
C	13.65830	-2.80120	1.09530
C	14.82240	-3.08790	2.01140
H	12.79210	-3.38240	1.44120
H	13.87860	-3.09000	0.06460
C	10.48470	0.79110	2.82090
H	10.94470	-0.05490	3.33610
H	10.29170	1.57790	3.55860
H	9.52300	0.44510	2.43140
C	-8.27050	2.09880	-1.50580
H	-8.42740	1.48000	-2.38660
H	-7.46040	2.82330	-1.55630
O	15.57490	-4.03800	2.01430
C	-6.61040	3.41960	3.13150
C	14.22370	2.51690	4.19420
H	14.94720	2.98800	3.51520
H	13.53220	3.29560	4.53670
H	14.77440	2.14480	5.06560
O	-10.96250	0.78010	0.38230
H	-6.27340	3.81030	4.10360
O	-6.57500	4.47470	2.16480
H	-5.63300	4.63730	1.97490
H	-10.18100	0.40340	-1.44470
H	4.76120	2.49500	-4.04070
H	0.36820	1.26120	-3.50430

Cartesian coordinates and energy for QM (B3LYP/6-31G*) minimized structure of brevetoxin A using as starting structure the lowest energy conformation found through the OPLS2005/Chloroform conformational search

Total energy: -2887.170185

Cartesian coordinates:

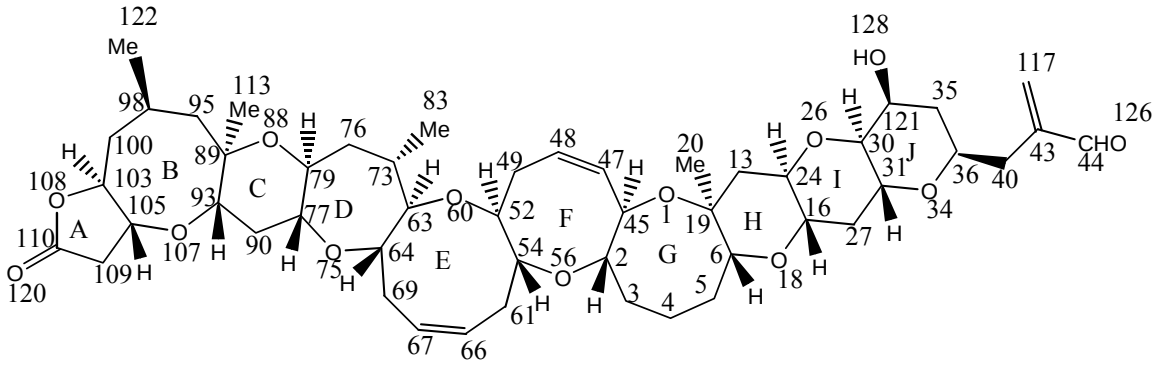
O	2.80020	2.74410	-10.80800
C	2.61530	0.29860	-10.55620
C	1.15430	0.39460	-11.00680
C	0.07950	0.76630	-9.96680
C	0.12980	2.16830	-9.30880
C	0.48520	3.32340	-10.26010
H	1.12080	1.09490	-11.84780
H	-0.88810	0.66820	-10.47740
H	0.07690	0.01130	-9.17230
H	-0.86590	2.38610	-8.90580
H	0.79770	2.15980	-8.44220
H	0.26700	3.01450	-11.29460
C	2.12690	4.94970	-11.26240
H	3.14580	5.35050	-11.21850
H	1.97450	4.55040	-12.27270
C	-0.31090	5.42780	-10.98680
H	-0.47380	4.93910	-11.96320
O	-0.37740	4.43950	-9.96190
C	1.97630	3.78920	-10.24910
C	2.45520	4.25340	-8.86390
H	1.80510	5.04810	-8.48900
H	2.44790	3.46200	-8.11090
H	3.47670	4.64240	-8.93380
C	1.09640	6.04570	-11.00980
H	1.27380	6.53080	-10.03770
O	1.20060	7.04530	-12.03280
C	-1.38310	6.49390	-10.79300
H	-2.38530	6.05510	-10.84920
H	-1.27600	6.96950	-9.80920
C	0.24300	8.09540	-11.85010
C	-1.18330	7.52960	-11.89800
H	0.39780	8.57760	-10.87100
H	-1.31390	7.03950	-12.87270
O	-2.13090	8.57900	-11.74740
C	-0.67460	10.16300	-12.92740
C	-2.08760	9.55320	-12.80800
H	-0.50820	10.81450	-12.06080
H	-0.60770	10.79650	-13.82010
H	-2.77620	10.32920	-12.46730
C	-2.62790	8.99750	-14.15300
H	-2.86550	9.86940	-14.77690

H	-1.84800	8.43720	-14.67260
C	-3.85870	8.13460	-14.00930
C	-5.10490	8.74110	-13.49750
C	3.20220	1.62870	-9.99690
H	2.80530	1.71850	-8.98420
C	4.71190	1.62090	-9.96110
C	5.47490	0.99830	-9.05600
C	4.94190	0.16960	-7.92000
H	5.62240	0.21150	-7.06170
H	3.98500	0.57850	-7.57570
C	4.67670	-1.31900	-8.24850
H	4.07580	-1.71750	-7.42530
C	3.89380	-1.54080	-9.55290
H	4.53390	-1.26010	-10.39780
O	2.72330	-0.71210	-9.54440
H	6.55660	1.06180	-9.16540
H	5.17800	2.16990	-10.77830
H	3.20570	-0.00300	-11.43360
O	5.87880	-2.10370	-8.36260
C	3.48430	-3.02740	-9.72870
H	2.76360	-3.06990	-10.55430
C	6.40450	-2.55350	-7.11170
C	6.04950	-4.03520	-6.73850
H	6.96220	-4.64150	-6.83000
C	2.89810	-3.63140	-8.47830
C	3.57150	-4.32160	-7.54650
H	3.03320	-4.63470	-6.65230
C	5.01200	-4.76230	-7.61570
H	5.05900	-5.81780	-7.31460
H	5.38670	-4.71530	-8.64310
H	1.84900	-3.40440	-8.28740
C	7.93650	-2.36230	-7.09960
H	8.33020	-2.94640	-7.94380
O	5.62220	-4.05780	-5.36990
C	8.56940	-2.92820	-5.79530
C	6.66370	-4.00990	-4.39350
H	7.24630	-4.94660	-4.43560
C	7.68180	-2.85260	-4.54330
H	7.14530	-1.89410	-4.52530
H	8.88940	-3.96840	-5.93240
H	9.47960	-2.36090	-5.57300
C	8.34370	-0.89960	-7.31900
H	8.01570	-0.26110	-6.48770
H	9.43410	-0.81180	-7.39100
H	7.90950	-0.50920	-8.24270
H	5.95930	-1.93820	-6.32180

O	8.57900	-2.91740	-3.42910
C	8.03430	-2.67560	-2.10100
C	5.96670	-3.87860	-3.04100
H	5.32480	-2.98920	-3.06470
H	5.30990	-4.73830	-2.87020
C	6.94940	-3.76670	-1.87010
H	7.46980	-4.72820	-1.74920
C	9.30970	-2.85200	-1.23040
H	9.57340	-3.91930	-1.21000
H	10.09140	-2.36800	-1.82730
C	9.41690	-2.27030	0.20220
H	8.92390	-1.28960	0.23300
C	8.82300	-3.13640	1.33550
H	9.20840	-4.16410	1.26620
H	9.18640	-2.73350	2.28930
C	7.30410	-3.17080	1.44100
H	6.88450	-2.16000	1.35250
C	6.52590	-4.11810	0.50070
H	7.12610	-5.01930	0.30960
O	6.14460	-3.51120	-0.71410
O	6.96470	-3.65840	2.77880
C	5.29810	-4.47400	1.34200
C	5.81670	-4.38150	2.76050
H	4.51910	-3.71250	1.20060
H	4.86220	-5.45450	1.13830
C	7.47310	-1.25180	-1.98890
H	7.09600	-1.06410	-0.98120
H	8.26010	-0.52230	-2.20970
H	6.64060	-1.07360	-2.67490
C	-3.91360	6.83530	-14.35490
H	-4.82890	6.25660	-14.23610
H	-3.05930	6.30890	-14.77560
O	5.34860	-4.84650	3.77410
C	0.46190	9.13030	-12.95650
C	10.90890	-2.03050	0.51270
H	11.47530	-2.97120	0.48480
H	11.35790	-1.35030	-0.22060
H	11.03990	-1.59070	1.50830
O	-5.23580	9.92480	-13.22190
H	1.41960	9.64380	-12.77800
O	0.50140	8.49080	-14.23510
H	1.10400	7.73150	-14.13610
H	-5.95810	8.04040	-13.38490
H	4.37290	-3.57950	-10.04870
H	0.88860	-0.58790	-11.41740

Details related to the conformational analysis of Brevetoxin A.

All rings were opened and all resulting torsions in all rings were varied with the LM:MC method using settings as described in the paper.



Conformational Analysis of the Full Brevetoxin A

In chloroform: (first 10 lowest E conformations of the G ring, starting with the lowest)
1. Boatchair
2. Boatchair
3. Boatchair
4. Boatchair
5. Boatchair
6. Boatchair
7. Boatchair
8. Crown-1
9. Boatchair
10. Boatchair

In water: (first 10 lowest E conformations of the G ring, starting with the lowest)
1. Boatchair
2. Boatchair
3. Boatchair
4. Boatchair
5. Boatchair
6. Boatchair
7. Boatchair
8. Boatchair
9. Boatchair
10. Crown-1