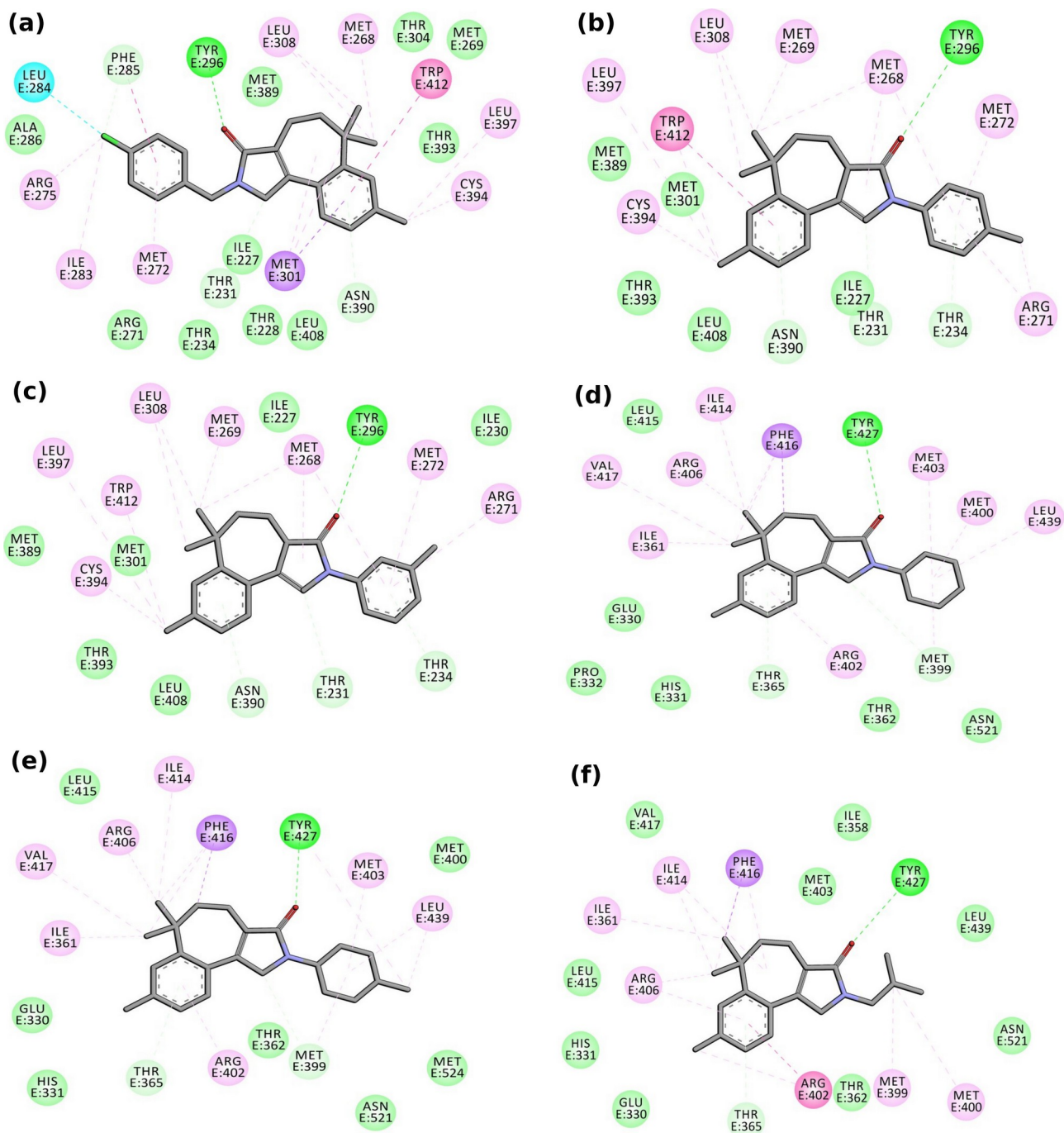
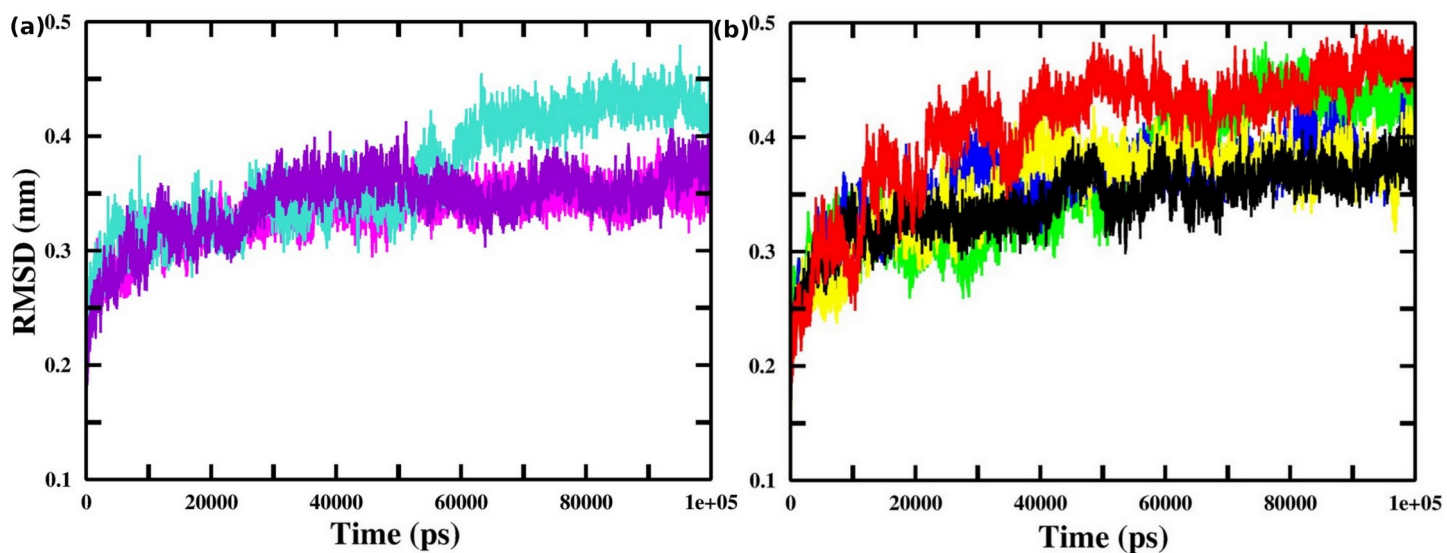


**Figure S1.** Superimposed protein 3-dimensional X-ray crystal structures (a) Hemiptera (b) Coleoptera. Color for experimental (blue) and docked (brown).









































**Figure S2.** 2D interactions of more relevant compounds from docking for Hemiptera (a) Com-5, (b) Com-8, and (c) Com-9. For Coleoptera (d) Com-10, (e) Com-11, and (f) Com-15.









































**Figure S3.** Backbone RMSDs are shown as a function of time at 300 K for (a) Hemiptera complex, ponasterone A (magenta), RH-5849 (violet), and Com-7 (turquoise). (b) Coleoptera complex, ponasterone A (black), RH-5849 (red), Com-3 (green), Com-8 (blue), and Com-12 (yellow).

**Table S1:** LE, Estimated Affinity, and Torsion values for Hemiptera.

<b>Molecules</b>	<b>LE</b>	<b>Estimated Affinity (Ki)</b>	<b>Torsion</b>
Com-1		5.15 $\mu$ M-52 nM	
Com-2		394.5 $\mu$ M-3971 nM	
Com-3		27.35 $\mu$ M-275 nM	
Com-4		4.06 $\mu$ M-41 nM	
Com-5		0.38 $\mu$ M-4 nM	
Com-6		10.96 $\mu$ M-110 nM	
Com-7		0.84 $\mu$ M-9 nM	
Com-8		0.703 $\mu$ M-7 nM	
Com-9		1.166 $\mu$ M-12 nM	
Com-10		123.11 $\mu$ M-1239 nM	
Com-11		9.65 $\mu$ M-97 nM	
Com-12		1.67 $\mu$ M-17 nM	
Com-13		26.94 $\mu$ M-271 nM	
Com-14		21.09 $\mu$ M-212 nM	
Com-15		9.96 $\mu$ M-100 nM	
Com-16		24.50 $\mu$ M-247 nM	
Com-17		6.53 $\mu$ M-66 nM	
Ponasterone A		0.164 nM	
RH-5849		33.73 $\mu$ M-340 nM	

**Table S2:** LE, Estimated Affinity, and Torsion values for Coleoptera.

<b>Molecules</b>	<b>LE</b>	<b>Estimated Affinity (Ki)</b>	<b>Torsion</b>
Com-1		542 nM-5 nM	
Com-2		1115.88 $\mu$ M-112.31 $\mu$ M	
Com-3		0.153 $\mu$ M-2 nM	
Com-4		169 nM-2 nM	
Com-5		622 nM-6 nM	
Com-6		1619 nM-16 nM	
Com-7		5248 nM-53 nM	
Com-8		0.199 $\mu$ M-2 nM	
Com-9		19.75 $\mu$ M-199 nM	
Com-10		835 nM-8 nM	
Com-11		293 nM-3 nM	
Com-12		58 nM-1 nM	
Com-13		2156 nM-22 nM	
Com-14		20.29 $\mu$ M-204 nM	
Com-15		3047 nM-31 nM	
Com-16		311 nM-3 nM	
Com-17		2228 nM-22 nM	
Ponasterone A		0.277 nM	
RH-5849		35.58 $\mu$ M-356 nM	

**Table S3.** Lennard-Jones (LJ) and Coulombic potential energies within R-coulomb (Coul) during MD simulations.

<b>Energy</b>	<b>Average</b>	<b>Error</b>	<b>Total (kJ/mol)</b>
<b>Hemiptera-Com-7</b>			
Coul-SR: Protein	-1.11834e+06	7.4	-9.59509
LJ-SR: Protein	145625	13	-72.1567
Coul-14:Protein	25707.4	7.1	-18.2572
LJ-14:Protein	861.694	16	-107.53
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14: Ligand	0	0	0
LJ-14: Ligand	199.28	0.48	-2.5251
<b>Total Energy</b>	<b>-784787</b>	<b>31</b>	<b>-203.227</b>
<b>Hemiptera-ponasterone A</b>			
Coul-SR: Protein	-1.12282e+06	240	-1329.26
LJ-SR: Protein	145530	5.6	-34.1932
Coul-14:Protein	25759	9.7	-2.32396
LJ-14:Protein	861.538	5.7	-41.1836
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14: Ligand	415.711	1.2	-2.53222
LJ-14: Ligand	152.862	1.4	-9.52315
<b>Total Energy</b>	<b>-784489</b>	<b>7.7</b>	<b>-45.1127</b>
<b>Hemiptera-RH-5849</b>			
Coul-SR: Protein	-1.12086e+06	120	692.856
LJ-SR: Protein	145586	8.8	-45.4901
Coul-14:Protein	25677.1	15	-36.266
LJ-14:Protein	855.08	12	-82.6284
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14: Ligand	113.874	2.8	-16.5788
LJ-14: Ligand	155.215	0.54	3.40295
<b>Total Energy</b>	<b>-784754</b>	<b>18</b>	<b>-105.501</b>
<b>Coleoptera-Com-3</b>			
Coul-SR: Protein	-910287	200	-1123.68
LJ-SR: Protein	114457	9.7	-68.83
Coul-14:Protein	25019.3	22	142.68
LJ-14:Protein	866.04	13	-88.36
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14:Ligand	0	0	0
LJ-14: Ligand	177.89	0.37	0.99
<b>Total Energy</b>	<b>-634613</b>	<b>14</b>	<b>-89.3596</b>

<b>Coleoptera-Com-8</b>			
Coul-SR: Protein	-907169	36	-242.71
LJ-SR: Protein	114528	8.5	-11.07
Coul-14: Protein	24965.1	9.6	-34.65
LJ-14:Protein	862.26	1.4	-0.28
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14:Ligand	0	0	0
LJ-14: Ligand	192.88	0.68	-1.99
<b>Total Energy</b>	<b>-634829</b>	<b>26</b>	<b>-161.377</b>
<b>Coleoptera-Com-12</b>			
Coul-SR: Protein	-906560	10	39.53
LJ-SR: Protein	114488	7.4	-53.81
Coul-14:Protein	24990.9	8.9	-48.72
LJ-14:Protein	839.89	13	-72.47
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14:Ligand	0	0	0
LJ-14: Ligand	139.67	1.8	11.65
<b>Total Energy</b>	<b>-634811</b>	<b>23</b>	<b>-98.1885</b>
<b>Coleoptera-ponasterone A</b>			
Coul-SR: Protein	-909110	100	-510.13
LJ-SR: Protein	114539	13	-92.6
Coul-14:Protein	25046.9	7	-4.1
LJ-14:Protein	854.66	3.7	-1.94
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14:Ligand	406.25	1.2	-6.74
LJ-14: Ligand	155.3	0.87	-5.17
<b>Total Energy</b>	<b>-634844</b>	<b>14</b>	<b>-6.22158</b>
<b>Coleoptera-RH-5849</b>			
Coul-SR: Protein	-909748	23	-140.06
LJ-SR: Protein	114503	7.8	-33.69
Coul-14:Protein	24985.7	14	2.9
LJ-14:Protein	860.73	4.6	-32.57
Coul-SR: Ligand	0	0	0
LJ-SR: Ligand	0	0	0
Coul-14:Ligand	120.01	1.4	6.45
LJ-14: Ligand	152.16	1.1	-5.54
<b>Total Energy</b>	<b>-634686</b>	<b>29</b>	<b>-194.186</b>