

Electronic Supplementary Material

Performance evaluation of molecular docking and free energy calculations protocols using the D3R Grand Challenge 4 dataset

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Table S1. Templates used for manually building the three-dimensional BACE structures

| Ligand | Template macrocycle | Template lateral chains | Type of macrocycle and number of atoms |
|---------|---------------------|-------------------------|--|
| BACE_1 | 0N1 | AR9 | B15 |
| BACE_2 | BAV | 1R6/8 | A16 |
| BACE_3 | BAV | BAV | A16 |
| BACE_4 | BAV | 0BI | A16 |
| BACE_5 | BAV | 0XA | A16 |
| BACE_6 | 0N1 | BAV | B15 |
| BACE_7 | 0N1 | BAV | B15 |
| BACE_8 | 0BI | BAV | B16 |
| BACE_9 | 0BI | BAV | B16 |
| BACE_10 | 0BI | BAV | B16 |
| BACE_11 | BAV | BAV | B16 |
| BACE_12 | 0BI | BAV | C15 |
| BACE_13 | 0BI | - | C16 |
| BACE_14 | 0BI | 0BI | C16 |
| BACE_15 | 0BI | BAV | C16 |
| BACE_16 | 0BI | BAV | C16 |
| BACE_17 | 0BI | - | C16 |
| BACE_18 | 0BI | BAV | B16 |
| BACE_19 | 1QT | AR9 | B14 |
| BACE_20 | - | AR9 | - |
| BACE_21 | BAV | BAV | A16 |
| BACE_22 | BAV | BAV | A16 |
| BACE_23 | BAV | 0BI | A16 |
| BACE_24 | BAV | BAV | A16 |
| BACE_25 | BAV | BAV | A16 |
| BACE_26 | BAV | BAV | A16 |

| | | | |
|---------|-----|-----|-----|
| BACE_27 | BAV | 0XA | A16 |
| BACE_28 | BAV | BAV | A16 |
| BACE_29 | BAV | 0XA | A16 |
| BACE_30 | BAV | 0XA | A16 |
| BACE_31 | BAV | 0XA | A16 |
| BACE_32 | BAV | BAV | A16 |
| BACE_33 | BAV | BAV | A16 |
| BACE_34 | AR9 | BAV | A15 |
| BACE_35 | BAV | BAV | A16 |
| BACE_36 | BAV | BAV | A16 |
| BACE_37 | AR9 | BAV | A15 |
| BACE_38 | BAV | 0BI | A16 |
| BACE_39 | BAV | 0XA | A16 |
| BACE_40 | 0N1 | BAV | B15 |
| BACE_41 | 0BI | BAV | B16 |
| BACE_42 | 0BI | BAV | B16 |
| BACE_43 | 0BI | BAV | B16 |
| BACE_44 | 0N1 | BAV | B15 |
| BACE_45 | 0BI | BAV | B16 |
| BACE_46 | 0BI | BAV | B16 |
| BACE_47 | 0BI | BAV | B16 |
| BACE_48 | 0BI | 0XA | B16 |
| BACE_49 | 0BI | BAV | B16 |
| BACE_50 | 0BI | BAV | B16 |
| BACE_51 | 0BI | BAV | B16 |
| BACE_52 | 0BI | 0BI | B16 |
| BACE_53 | 0BI | BAV | B16 |
| BACE_54 | 0N1 | BAV | B15 |
| BACE_55 | 0BI | BAV | B16 |

| | | | |
|---------|-----|-------|-----|
| BACE_56 | 0BI | BAV | B16 |
| BACE_57 | 0BI | 0XA | B16 |
| BACE_58 | 0BI | 0XA | B16 |
| BACE_59 | 0BI | 0BI | B16 |
| BACE_60 | 0BI | BAV | B16 |
| BACE_61 | 0BI | BAV | B16 |
| BACE_62 | 0BI | BAV | B16 |
| BACE_63 | 0BI | 1R6/8 | B16 |
| BACE_64 | 0BI | 0XA | B16 |
| BACE_65 | 0BI | BAV | B16 |
| BACE_66 | 0BI | BAV | B16 |
| BACE_67 | 0BI | 0XA | B16 |
| BACE_68 | 0BI | 0BI | B16 |
| BACE_69 | 0BI | BAV | B16 |
| BACE_70 | 0BI | BAV | B16 |
| BACE_71 | 0BI | BAV | B16 |
| BACE_72 | 0BI | BAV | B16 |
| BACE_73 | 0BI | BAV | B16 |
| BACE_74 | 0BI | BAV | B16 |
| BACE_75 | 0BI | 0BI | B16 |
| BACE_76 | 0BI | BAV | B16 |
| BACE_77 | 0BI | 0BI | B16 |
| BACE_78 | 0BI | BAV | B16 |
| BACE_79 | 0BI | 0XA | B16 |
| BACE_80 | 0BI | BAV | B16 |
| BACE_81 | 0BI | 0BI | B16 |
| BACE_82 | 0BI | BAV | B16 |
| BACE_83 | 0BI | 0BI | B16 |
| BACE_84 | 0BI | 0XA | B16 |

| | | | |
|----------|-----|-------|-----|
| BACE_85 | BAV | BAV | A16 |
| BACE_86 | BAV | BAV | A16 |
| BACE_87 | BAV | BAV | B16 |
| BACE_88 | BAV | BAV | C15 |
| BACE_89 | 0BI | BAV | B17 |
| BACE_90 | BAV | 0BI | B16 |
| BACE_91 | BAV | 1R6/8 | B16 |
| BACE_92 | BAV | BAV | B16 |
| BACE_93 | BAV | BAV | B16 |
| BACE_94 | 0BI | BAV | B15 |
| BACE_95 | 0BI | 0BI | B15 |
| BACE_96 | 0BI | 0XA | C16 |
| BACE_97 | 0BI | BAV | C15 |
| BACE_98 | 0BI | 0BI | C15 |
| BACE_99 | 0BI | BAV | C15 |
| BACE_100 | 0BI | BAV | C16 |
| BACE_101 | 0BI | BAV | C16 |
| BACE_102 | 0BI | 0BI | C16 |
| BACE_103 | 0BI | BAV | C16 |
| BACE_104 | 0BI | - | C16 |
| BACE_105 | 0BI | BAV | C16 |
| BACE_106 | 0BI | BAV | C15 |
| BACE_107 | 0BI | BAV | C15 |
| BACE_108 | 0BI | 0XA | C15 |
| BACE_109 | 0BI | 0XA | C16 |
| BACE_110 | 0BI | 0XA | C16 |
| BACE_111 | 0BI | 1R6/8 | C16 |
| BACE_112 | 0BI | 0BI | C16 |
| BACE_113 | 0BI | BAV | C15 |

| | | | |
|----------|-----|-------|-----|
| BACE_114 | 0BI | BAV | C16 |
| BACE_115 | 0BI | BAV | C15 |
| BACE_116 | 0BI | BAV | C15 |
| BACE_117 | 0BI | 0XA | C16 |
| BACE_118 | 0BI | BAV | C15 |
| BACE_119 | 0BI | 0BI | C15 |
| BACE_120 | 0BI | BAV | C15 |
| BACE_121 | 0BI | BAV | C15 |
| BACE_122 | 0BI | BAV | C16 |
| BACE_123 | 0BI | BAV | C16 |
| BACE_124 | 0BI | BAV | C16 |
| BACE_125 | 0BI | 0XA | C16 |
| BACE_126 | 0BI | - | C16 |
| BACE_127 | 0BI | 0XA | C16 |
| BACE_128 | 0BI | 1R6/8 | C16 |
| BACE_129 | 0BI | 0XA | C16 |
| BACE_130 | 0BI | BAV | C16 |
| BACE_131 | 0BI | 0BI | C16 |
| BACE_132 | 0BI | BAV | C15 |
| BACE_133 | 0BI | 0BI | C15 |
| BACE_134 | 0BI | BAV | C15 |
| BACE_135 | 0BI | BAV | C15 |
| BACE_136 | 0BI | BAV | C15 |
| BACE_137 | 0BI | BAV | C15 |
| BACE_138 | 0BI | BAV | C16 |
| BACE_139 | 0BI | BAV | C16 |
| BACE_140 | 0BI | 0BI | C15 |
| BACE_141 | 0BI | BAV | C16 |
| BACE_142 | 0BI | - | B16 |

| | | | |
|----------|-----|-----|-----|
| BACE_143 | BAV | BAV | A16 |
| BACE_144 | 0BI | 0BI | C17 |
| BACE_145 | - | 0BI | - |
| BACE_146 | - | BAV | - |
| BACE_147 | AR9 | AR9 | A15 |
| BACE_148 | BAV | AR9 | A16 |
| BACE_149 | BAV | AR9 | A16 |
| BACE_150 | BAV | AR9 | A16 |
| BACE_151 | BAV | AR9 | A16 |
| BACE_152 | 0N1 | AR9 | B15 |
| BACE_153 | BAV | AR9 | B16 |
| BACE_154 | 0BI | AR9 | C16 |
| BACE_155 | 0BI | AR9 | C15 |
| BACE_156 | 0BI | AR9 | B15 |
| BACE_157 | BAV | AR9 | C15 |
| BACE_158 | BAV | AR9 | C15 |

Table S2. Ligands composing the BACE training dataset

| PDB structure | Ligand | IC50 (μM) | pIC50 |
|---------------|--------|------------------------|-------|
| 3K5C | 0BI | 17 | 4.77 |
| 4DPF | 0LG | 400 | 3.40 |
| 4DPI | 0N1 | 78 | 4.11 |
| 4GMI | 0XA | – | – |
| 4K8S | 1QT | 36 | 4.44 |
| 4KE1 | 1R6 | 2.5 | 5.60 |
| 4KE0 | 1R8 | 17 | 4.77 |
| 2PH8 | 35A | 1800 | 2.74 |
| 3DV1 | AR9 | 590 | 3.23 |
| 2F3F | AXF | 190 | 3.72 |
| 2F3E | AXQ | 156 | 3.81 |
| 3DV5 | BAV | 27 | 4.57 |
| 2QZK | I21 | 27 | 4.57 |
| 1XS7 | MMI | – | – |

Table S3. Absolute alchemical free energies for the Cathepsin S ligand set after applying cycle closure correction (kcal/mol). The GAFF and CGenFF values were obtained by averaging results from 3 independent repeats.

| Ligand | Experiment | GAFF | CGenFF | Consensus |
|-----------------|------------|-------------------|-------------------|-------------------|
| CatS_4 | -8.93 | -9.24 \pm 0.40 | -10.03 \pm 0.07 | -9.65 \pm 0.21 |
| CatS_9 | -9.41 | -9.01 \pm 0.63 | -10.09 \pm 0.46 | -9.57 \pm 0.39 |
| CatS_29 | -9.70 | -10.06 \pm 0.10 | -9.90 \pm 0.07 | -9.98 \pm 0.06 |
| CatS_30 | -9.37 | -9.57 \pm 0.27 | -10.01 \pm 0.89 | -9.79 \pm 0.47 |
| CatS_52 | -8.88 | -10.07 \pm 0.39 | -10.32 \pm 0.20 | -10.21 \pm 0.22 |
| CatS_76 | -9.17 | -9.03 \pm 0.28 | -9.57 \pm 0.10 | -9.31 \pm 0.15 |
| CatS_79 | -9.61 | -9.54 \pm 0.26 | -9.54 \pm 0.26 | -9.54 \pm 0.19 |
| CatS_84 | -8.90 | -8.73 \pm 0.26 | -9.24 \pm 0.11 | -9.01 \pm 0.14 |
| CatS_122 | -10.57 | -11.10 \pm 0.52 | -10.58 \pm 0.84 | -10.85 \pm 0.49 |
| CatS_127 | -9.78 | -10.19 \pm 0.26 | -9.58 \pm 0.26 | -9.88 \pm 0.19 |

| | | | | |
|-----------------|--------|-------------|-------------|-------------|
| CatS_130 | -8.25 | -8.83±1.13 | -8.73±0.26 | -8.77±0.58 |
| CatS_131 | -9.02 | -9.78±0.36 | -9.72±0.82 | -9.76±0.45 |
| CatS_132 | -9.11 | -9.53±0.61 | -9.48±0.37 | -9.50±0.36 |
| CatS_139 | -9.29 | -8.81±0.35 | -9.42±0.09 | -9.12±0.18 |
| CatS_141 | -8.53 | -8.83±0.44 | -9.31±0.32 | -9.08±0.27 |
| CatS_142 | -8.55 | -8.90±0.18 | -9.27±0.14 | -9.08±0.11 |
| CatS_144 | -9.06 | -8.70±0.37 | -9.84±0.67 | -9.26±0.38 |
| CatS_153 | -8.97 | -9.37±0.36 | -9.52±0.09 | -9.44±0.18 |
| CatS_155 | -10.02 | -9.67±0.62 | -10.05±0.20 | -9.86±0.33 |
| CatS_157 | -9.41 | -9.20±0.37 | -9.74±0.24 | -9.46±0.22 |
| CatS_160 | -9.82 | -9.64±0.25 | -10.18±0.13 | -9.91±0.14 |
| CatS_162 | -8.50 | -9.07±0.14 | -8.56±0.54 | -8.82±0.28 |
| CatS_165 | -8.28 | -7.82±0.54 | -8.98±0.24 | -8.39±0.30 |
| CatS_167 | -9.45 | -9.10±0.35 | -9.05±0.41 | -9.07±0.27 |
| CatS_172 | -9.33 | -9.26±0.40 | -9.44±0.10 | -9.35±0.21 |
| CatS_174 | -9.71 | -9.19±0.27 | -9.62±0.12 | -9.41±0.15 |
| CatS_176 | -10.09 | -9.60±0.19 | -9.54±0.15 | -9.57±0.12 |
| CatS_177 | -9.45 | -9.19±0.51 | -9.41±0.16 | -9.30±0.27 |
| CatS_178 | -10.09 | -9.87±0.10 | -9.58±0.18 | -9.72±0.10 |
| CatS_180 | -10.33 | -9.73±0.34 | -9.85±0.21 | -9.79±0.20 |
| CatS_181 | -10.57 | -10.71±0.16 | -10.42±0.43 | -10.56±0.23 |
| CatS_184 | -9.26 | -9.36±0.10 | -9.69±0.19 | -9.51±0.11 |
| CatS_185 | -9.91 | -9.68±0.71 | -10.03±0.50 | -9.86±0.43 |
| CatS_186 | -8.57 | -9.16±0.26 | -9.46±0.06 | -9.31±0.13 |
| CatS_191 | -9.87 | -9.94±0.21 | -9.78±0.85 | -9.85±0.44 |
| CatS_195 | -9.55 | -9.27±0.22 | -9.58±0.09 | -9.43±0.12 |
| CatS_252 | -8.36 | -9.22±0.20 | -9.52±0.07 | -9.38±0.11 |
| CatS_253 | -8.63 | -9.60±0.06 | -9.86±0.13 | -9.74±0.07 |
| CatS_255 | -8.30 | -8.84±0.12 | -9.58±0.22 | -9.21±0.13 |

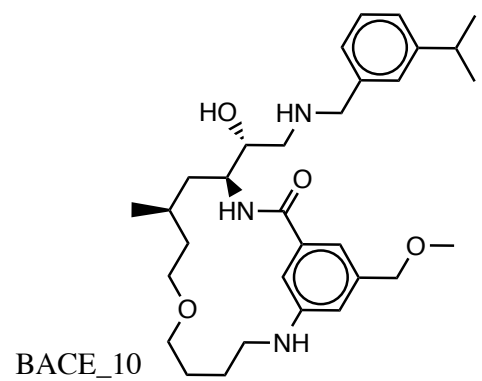
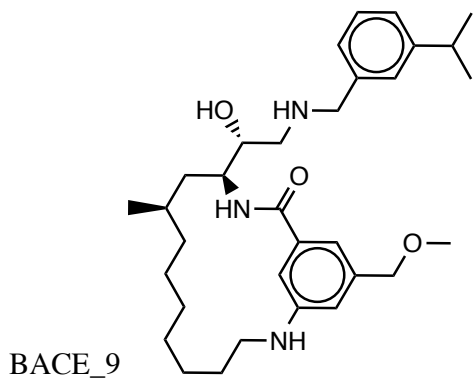
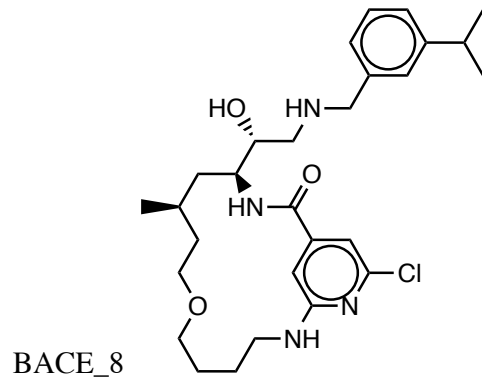
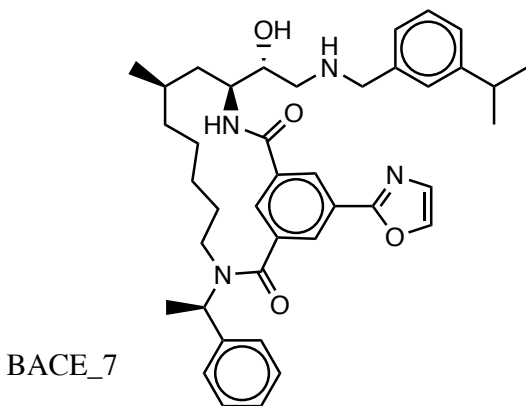
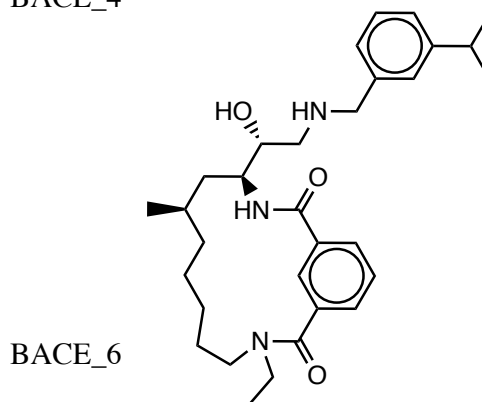
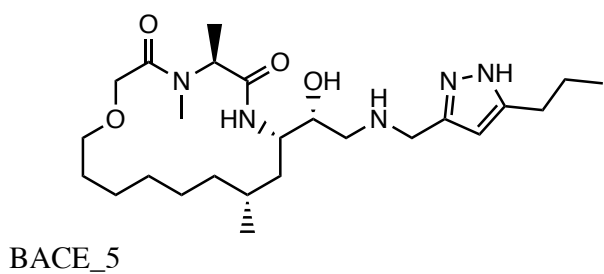
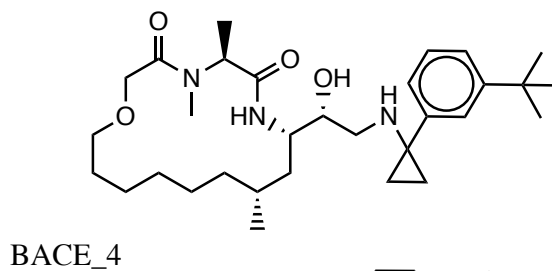
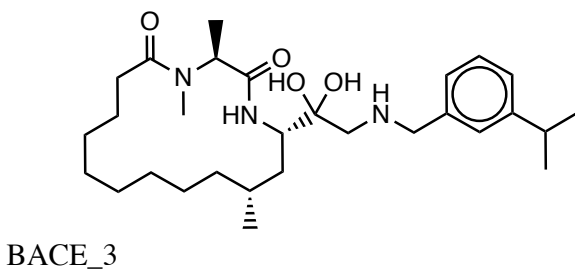
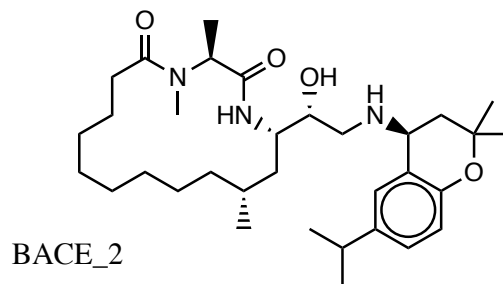
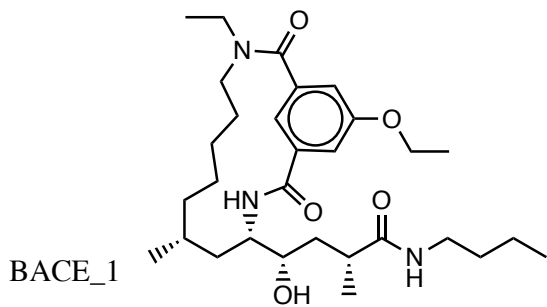
Table S4. Relative alchemical free energies for the Cathepsin S ligand set prior to applying cycle closure correction (kcal/mol). The GAFF and CGenFF values were obtained by averaging results from 3 independent repeats.

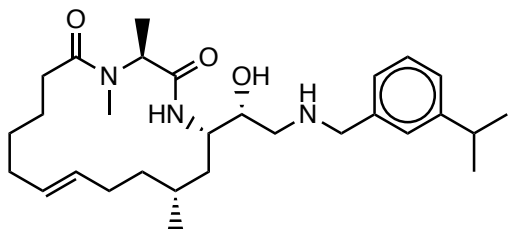
| Edge | GAFF | CGenFF | Consensus |
|-------------------------|------------|------------|------------|
| CatS_79-CatS_127 | -0.43±0.37 | 0.05±0.37 | -0.19±0.26 |
| CatS_79-CatS_130 | 0.90±1.11 | 1.35±0.21 | 1.12±0.57 |
| CatS_79-CatS_131 | -0.08±0.36 | -0.35±0.82 | -0.22±0.45 |
| CatS_79-CatS_132 | -0.25±0.61 | 0.28±0.37 | 0.01±0.36 |
| CatS_79-CatS_139 | 0.43±0.08 | 0.45±0.16 | 0.44±0.09 |
| CatS_79-CatS_141 | 0.64±0.36 | 0.00±0.30 | 0.32±0.23 |
| CatS_79-CatS_142 | 0.72±0.13 | 0.11±0.41 | 0.41±0.22 |
| CatS_79-CatS_144 | 0.43±0.37 | -0.20±0.67 | 0.12±0.38 |
| CatS_79-CatS_153 | -0.15±0.34 | 0.13±0.18 | -0.01±0.19 |
| CatS_79-CatS_155 | 0.24±0.51 | -0.67±0.17 | -0.21±0.27 |
| CatS_79-CatS_4 | 0.22±0.43 | -0.48±0.69 | -0.13±0.41 |
| CatS_79-CatS_157 | 0.14±0.35 | -0.31±0.14 | -0.09±0.19 |
| CatS_79-CatS_160 | 0.02±0.34 | -0.94±0.27 | -0.46±0.22 |
| CatS_79-CatS_162 | 0.47±0.14 | 1.78±0.54 | 1.13±0.28 |
| CatS_79-CatS_165 | 1.70±0.54 | -0.35±0.24 | 0.67±0.30 |
| CatS_79-CatS_167 | 0.38±0.35 | 0.14±0.41 | 0.26±0.27 |
| CatS_79-CatS_172 | 0.55±0.43 | -0.08±0.08 | 0.24±0.22 |
| CatS_79-CatS_174 | 0.10±0.27 | 0.12±0.12 | 0.11±0.15 |
| CatS_79-CatS_176 | -0.18±0.19 | 0.15±0.15 | -0.02±0.12 |
| CatS_79-CatS_177 | 0.44±0.17 | -0.06±0.11 | 0.19±0.10 |
| CatS_79-CatS_178 | -0.17±0.54 | -0.40±0.22 | -0.28±0.29 |
| CatS_79-CatS_9 | 0.61±0.30 | -0.72±0.41 | -0.05±0.25 |
| CatS_79-CatS_180 | -0.25±0.24 | -0.47±0.17 | -0.36±0.15 |
| CatS_79-CatS_181 | -1.29±0.16 | -0.89±0.43 | -1.09±0.23 |

| | | | |
|--------------------------|------------|------------|------------|
| CatS_79-CatS_184 | 0.39±0.12 | -0.25±0.18 | 0.07±0.11 |
| CatS_79-CatS_185 | 0.52±0.62 | -0.44±0.49 | 0.04±0.39 |
| CatS_79-CatS_186 | 0.37±0.10 | 0.04±0.33 | 0.21±0.17 |
| CatS_79-CatS_191 | -0.59±0.18 | 0.63±0.83 | 0.02±0.43 |
| CatS_79-CatS_195 | 0.36±0.34 | 0.06±0.06 | 0.21±0.17 |
| CatS_79-CatS_252 | 0.17±0.20 | 0.10±0.07 | 0.13±0.11 |
| CatS_79-CatS_253 | -0.26±0.62 | -0.27±0.25 | -0.26±0.33 |
| CatS_79-CatS_255 | 1.13±0.11 | -0.15±0.19 | 0.49±0.11 |
| CatS_79-CatS_29 | -0.12±0.43 | -0.75±0.69 | -0.43±0.41 |
| CatS_79-CatS_30 | -0.52±0.25 | -0.52±0.89 | -0.52±0.46 |
| CatS_79-CatS_52 | -0.56±0.50 | -0.11±0.31 | -0.34±0.30 |
| CatS_79-CatS_76 | 0.02±0.18 | -0.17±0.04 | -0.07±0.09 |
| CatS_79-CatS_84 | 1.18±0.18 | 0.08±0.27 | 0.63±0.16 |
| CatS_79-CatS_122 | -1.45±0.52 | -0.85±0.84 | -1.15±0.49 |
| CatS_127-CatS_142 | 1.60±0.29 | 0.36±0.22 | 0.98±0.18 |
| CatS_130-CatS_142 | -0.12±0.25 | -0.33±0.20 | -0.23±0.16 |
| CatS_131-CatS_252 | 0.65±0.77 | 0.36±0.22 | 0.50±0.40 |
| CatS_132-CatS_142 | 0.32±0.30 | 0.42±0.27 | 0.37±0.20 |
| CatS_139-CatS_76 | -0.11±0.12 | -0.28±0.08 | -0.20±0.07 |
| CatS_141-CatS_252 | -0.84±0.23 | -0.38±0.48 | -0.61±0.27 |
| CatS_142-CatS_139 | 0.16±0.34 | -0.40±0.32 | -0.12±0.24 |
| CatS_144-CatS_142 | -0.19±0.30 | 0.58±0.50 | 0.20±0.29 |
| CatS_155-CatS_30 | 0.40±0.27 | -0.19±0.69 | 0.11±0.37 |
| CatS_4-CatS_9 | 0.45±0.57 | 0.13±0.10 | 0.29±0.29 |
| CatS_157-CatS_153 | -0.04±0.25 | 0.22±0.10 | 0.09±0.14 |
| CatS_160-CatS_180 | -0.23±0.35 | 0.30±0.19 | 0.03±0.20 |
| CatS_162-CatS_167 | -0.29±0.56 | -0.29±0.28 | -0.29±0.32 |
| CatS_165-CatS_142 | -1.10±0.22 | -1.16±0.19 | -1.13±0.15 |
| CatS_167-CatS_252 | -0.44±0.28 | -0.24±0.09 | -0.34±0.15 |

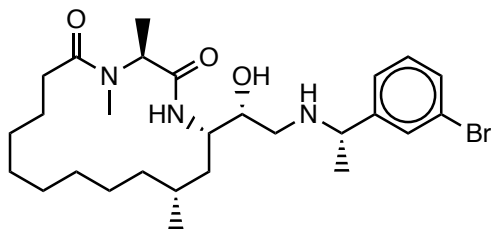
| | | | |
|--------------------------|------------|------------|------------|
| CatS_174-CatS_177 | -0.26±0.26 | 0.16±0.20 | -0.05±0.16 |
| CatS_176-CatS_180 | -0.23±0.09 | -0.15±0.17 | -0.19±0.09 |
| CatS_177-CatS_172 | 0.13±0.57 | -0.09±0.14 | 0.02±0.29 |
| CatS_178-CatS_191 | 0.04±0.15 | -0.04±0.25 | 0.00±0.15 |
| CatS_9-CatS_52 | -0.89±0.55 | -0.68±0.29 | -0.78±0.31 |
| CatS_180-CatS_172 | 0.16±0.31 | 0.42±0.16 | 0.29±0.18 |
| CatS_181-CatS_167 | 1.84±0.33 | 1.25±0.26 | 1.55±0.21 |
| CatS_184-CatS_186 | 0.19±0.33 | 0.21±0.34 | 0.20±0.24 |
| CatS_185-CatS_139 | 1.68±0.50 | 0.58±0.13 | 1.13±0.26 |
| CatS_191-CatS_30 | 0.20±0.31 | 0.44±0.58 | 0.32±0.33 |
| CatS_195-CatS_76 | 0.49±0.31 | 0.28±0.12 | 0.39±0.17 |
| CatS_252-CatS_177 | 0.70±0.30 | -0.04±0.14 | 0.33±0.17 |
| CatS_253-CatS_255 | 0.52±0.08 | 0.37±0.18 | 0.45±0.10 |
| CatS_255-CatS_252 | -0.55±0.47 | 0.03±0.14 | -0.26±0.24 |
| CatS_29-CatS_30 | 0.63±0.15 | 0.22±0.09 | 0.43±0.09 |
| CatS_30-CatS_178 | -0.65±0.17 | 1.26±0.31 | 0.31±0.18 |
| CatS_52-CatS_4 | 0.73±0.07 | 0.59±0.28 | 0.66±0.14 |
| CatS_84-CatS_139 | -0.14±0.25 | -0.38±0.20 | -0.26±0.16 |
| CatS_122-CatS_139 | 2.49±0.57 | 1.27±0.67 | 1.88±0.44 |
| CatS_127-CatS_139 | 1.28±0.13 | 0.21±0.47 | 0.74±0.24 |
| CatS_130-CatS_139 | 0.24±0.77 | -0.43±0.51 | -0.09±0.46 |
| CatS_131-CatS_139 | 1.02±0.41 | -0.02±0.30 | 0.50±0.25 |
| CatS_132-CatS_139 | 0.75±0.39 | 0.05±0.38 | 0.40±0.27 |
| CatS_139-CatS_186 | -0.23±0.63 | 0.03±0.17 | -0.10±0.33 |
| CatS_141-CatS_84 | 0.46±0.37 | 0.01±0.16 | 0.24±0.20 |
| CatS_142-CatS_84 | 0.13±0.05 | -0.27±0.29 | -0.07±0.15 |
| CatS_144-CatS_139 | -0.53±0.07 | 0.50±0.26 | -0.02±0.13 |
| CatS_153-CatS_76 | -0.24±0.13 | -0.12±0.39 | -0.18±0.21 |
| CatS_155-CatS_153 | 0.36±0.50 | 0.53±0.13 | 0.45±0.26 |

| | | | |
|--------------------------|------------|------------|------------|
| CatS_4-CatS_255 | -0.00±0.40 | 0.57±0.85 | 0.28±0.47 |
| CatS_157-CatS_184 | -0.11±0.14 | 0.15±0.27 | 0.02±0.15 |
| CatS_160-CatS_157 | 0.69±0.34 | 0.17±0.19 | 0.43±0.19 |
| CatS_162-CatS_252 | -0.43±0.33 | 0.17±0.81 | -0.13±0.44 |
| CatS_165-CatS_130 | -1.03±0.77 | 0.20±0.23 | -0.42±0.40 |
| CatS_167-CatS_177 | -0.15±0.40 | -0.37±0.15 | -0.26±0.22 |
| CatS_172-CatS_186 | 0.27±0.14 | 0.03±0.10 | 0.15±0.09 |
| CatS_174-CatS_172 | -0.08±0.20 | 0.44±0.14 | 0.18±0.12 |
| CatS_176-CatS_177 | 0.39±0.20 | 0.12±0.20 | 0.25±0.14 |
| CatS_177-CatS_184 | -0.37±0.17 | -0.17±0.10 | -0.27±0.10 |
| CatS_178-CatS_155 | -0.13±0.23 | -0.13±0.12 | -0.13±0.13 |
| CatS_9-CatS_157 | -0.05±0.28 | 0.85±0.55 | 0.40±0.31 |
| CatS_180-CatS_177 | 0.55±0.17 | 0.40±0.13 | 0.47±0.11 |
| CatS_181-CatS_252 | 0.59±0.31 | 1.54±0.73 | 1.06±0.40 |
| CatS_185-CatS_252 | 0.30±0.14 | 0.59±0.22 | 0.44±0.13 |
| CatS_186-CatS_177 | 0.12±0.37 | 0.08±0.08 | 0.10±0.19 |
| CatS_191-CatS_155 | 0.33±0.19 | 0.08±0.13 | 0.21±0.12 |
| CatS_195-CatS_184 | -0.15±0.27 | -0.22±0.23 | -0.18±0.18 |
| CatS_252-CatS_139 | 0.09±0.09 | -0.04±0.26 | 0.02±0.14 |
| CatS_253-CatS_252 | 0.43±0.15 | 0.30±0.43 | 0.36±0.23 |
| CatS_255-CatS_139 | -0.05±0.60 | 0.27±0.23 | 0.11±0.32 |
| CatS_29-CatS_155 | 0.62±0.22 | -0.89±0.89 | -0.13±0.46 |
| CatS_30-CatS_76 | 0.28±0.52 | 0.18±0.55 | 0.23±0.38 |
| CatS_52-CatS_167 | 1.26±0.95 | 1.21±0.48 | 1.24±0.53 |
| CatS_76-CatS_84 | 0.17±0.13 | 0.35±0.22 | 0.26±0.13 |
| CatS_84-CatS_252 | 0.07±0.23 | -0.63±0.16 | -0.28±0.14 |
| CatS_122-CatS_252 | 1.78±0.58 | 1.15±0.62 | 1.47±0.42 |

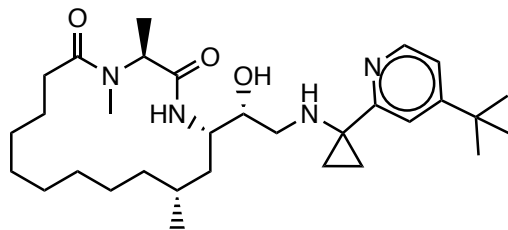




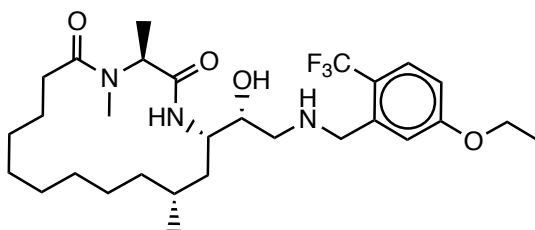
BACE_21



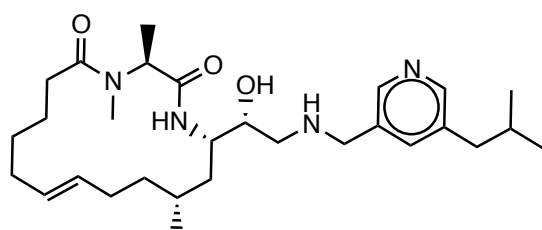
BACE_22



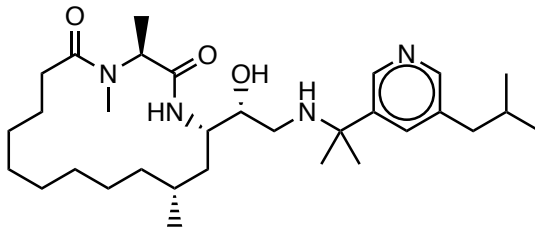
BACE_23



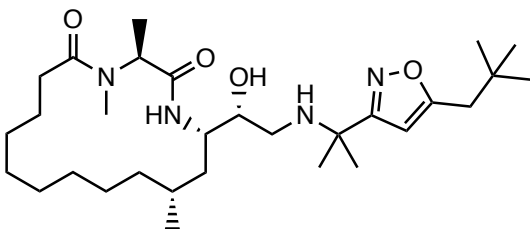
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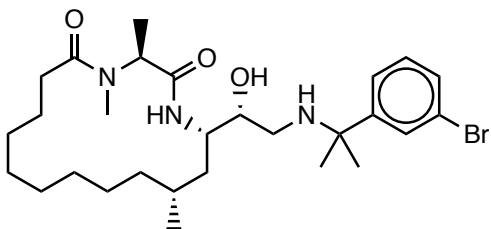
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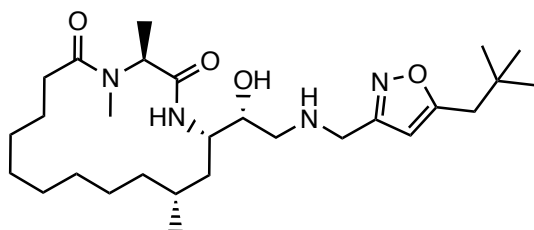
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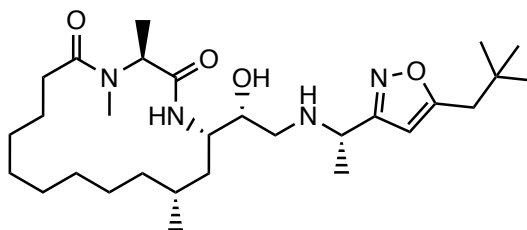
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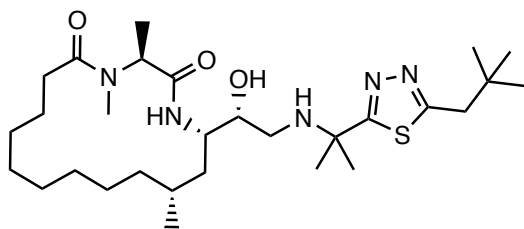
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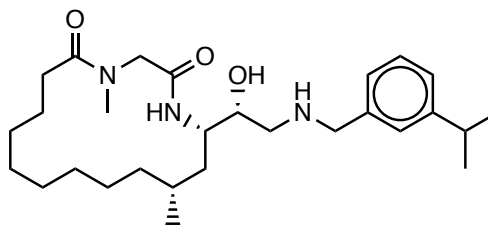
BACE_29



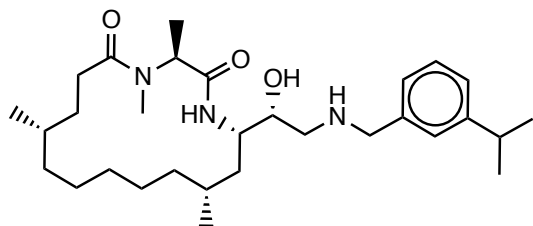
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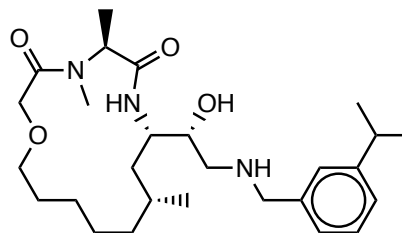
BACE_31



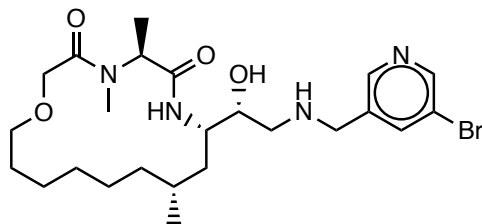
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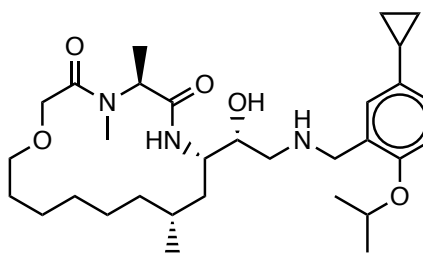
BACE_33



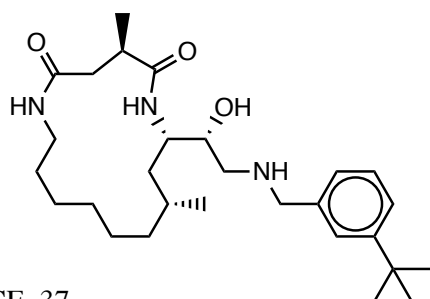
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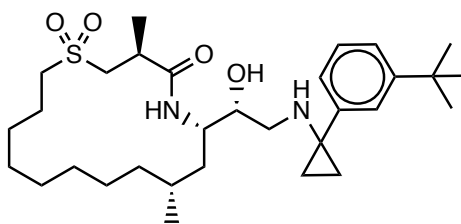
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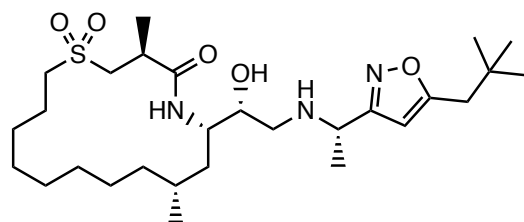
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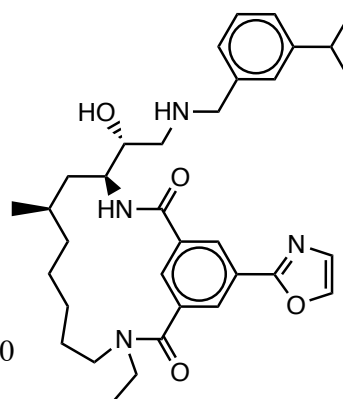
BACE_37



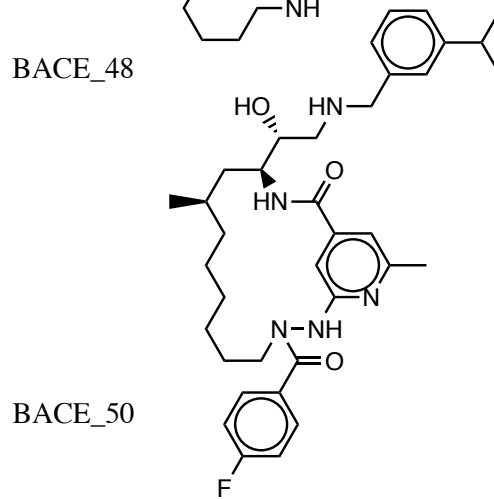
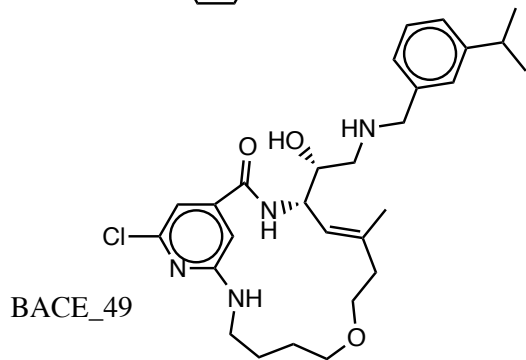
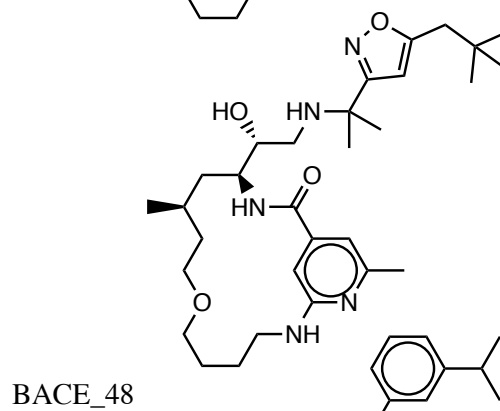
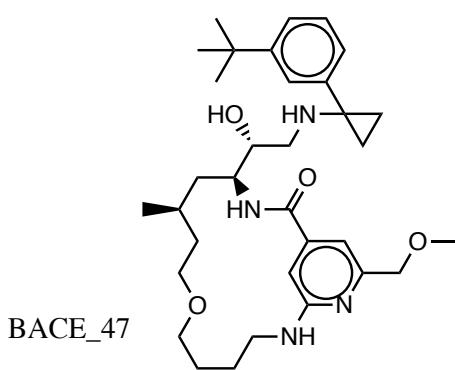
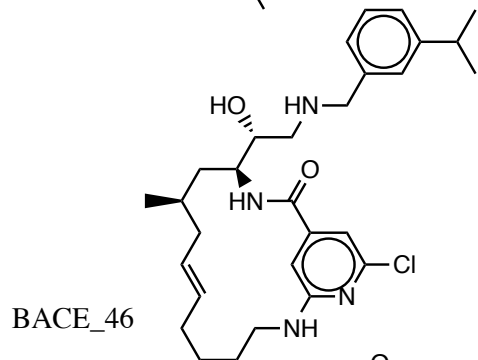
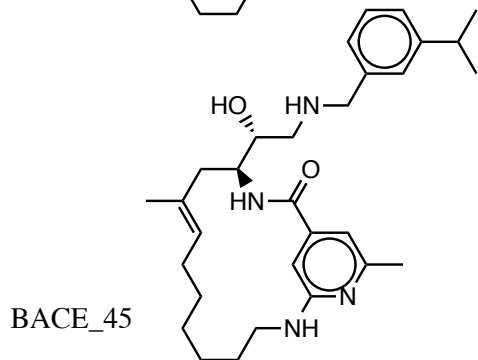
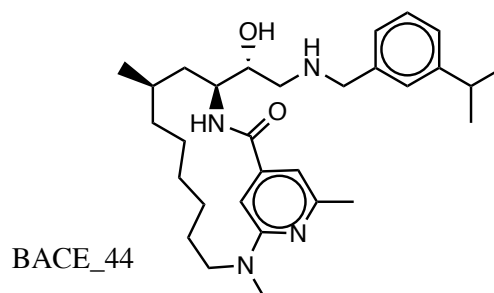
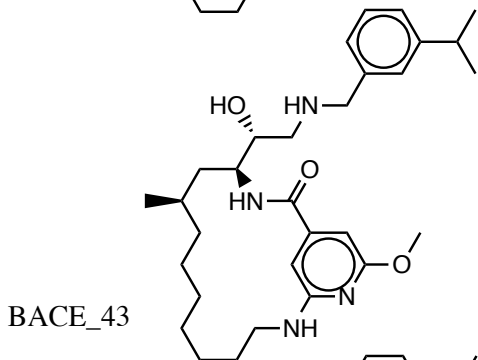
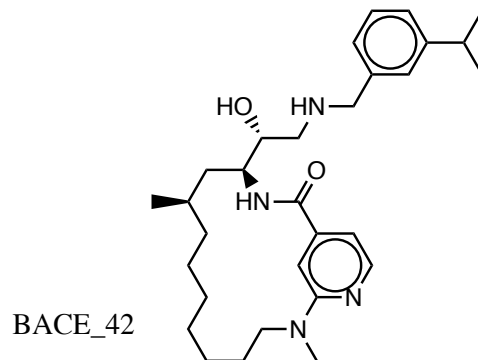
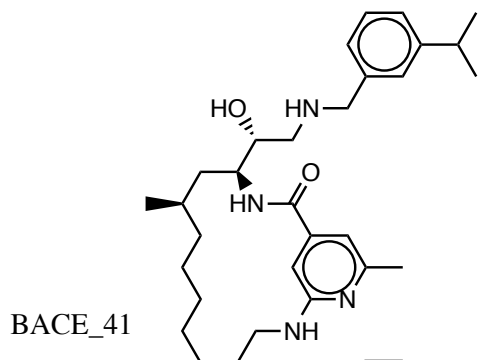
BACE_38



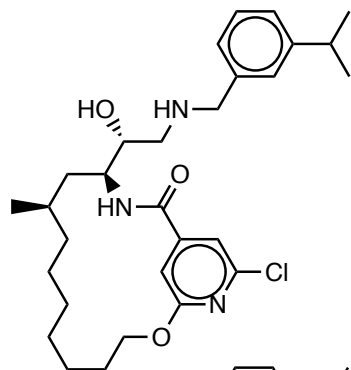
BACE_39



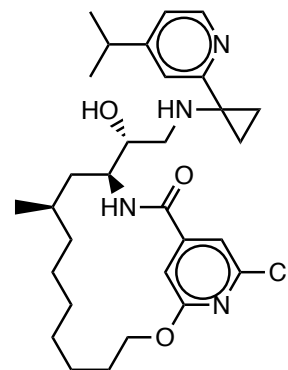
BACE_40



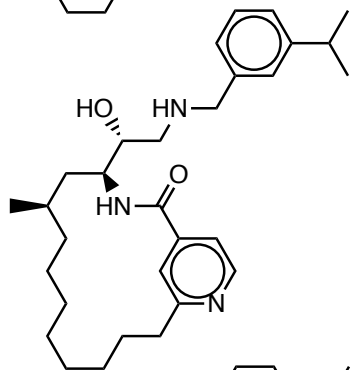
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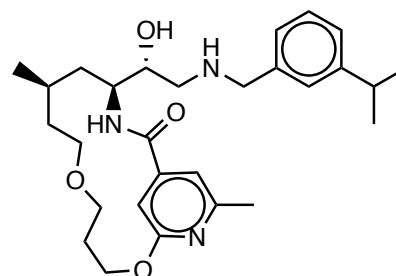
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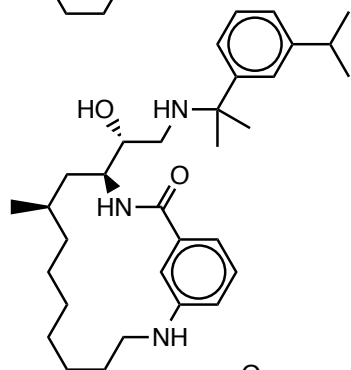
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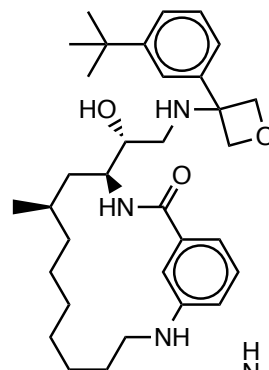
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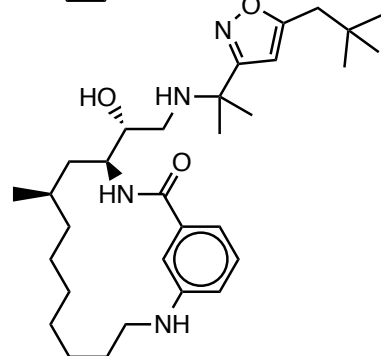
BACE_55



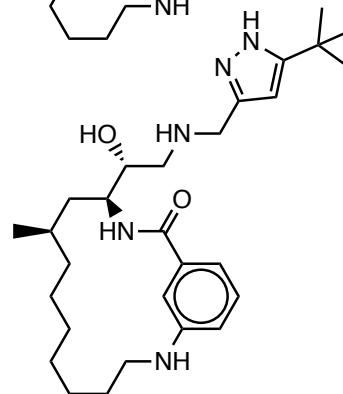
BACE_56



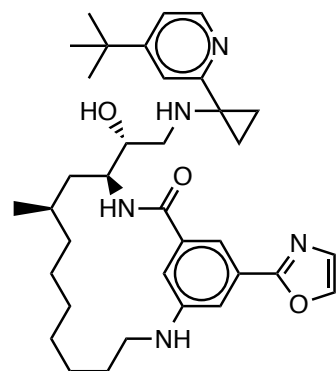
BACE_57



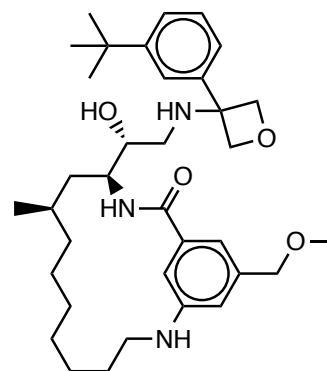
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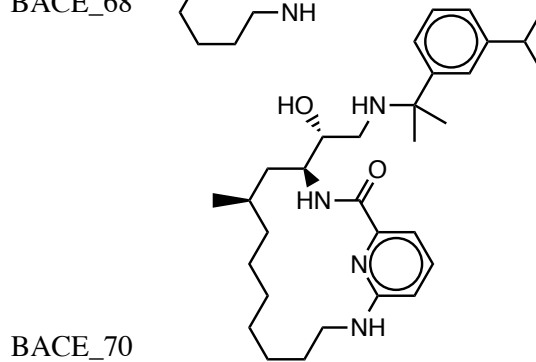
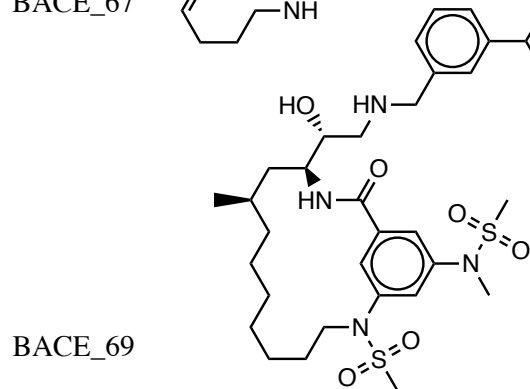
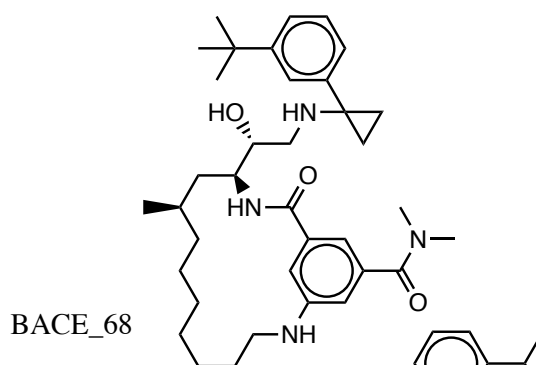
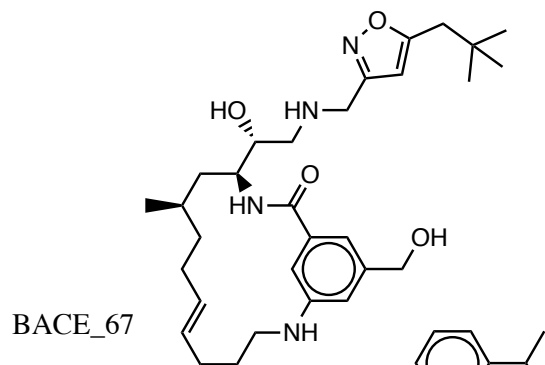
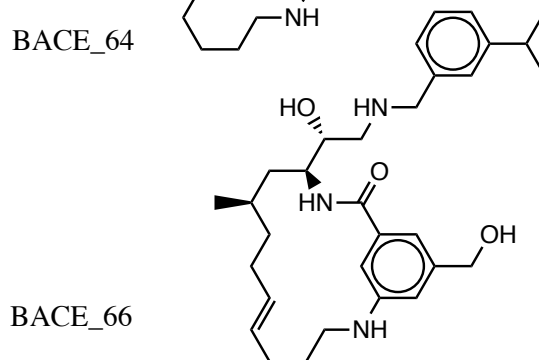
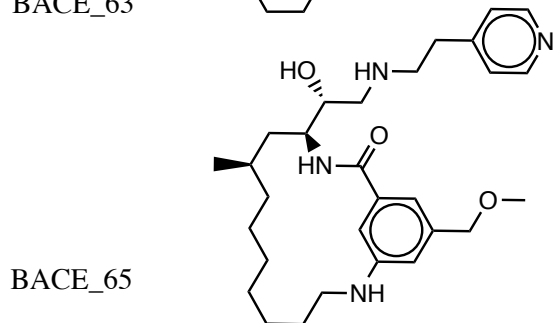
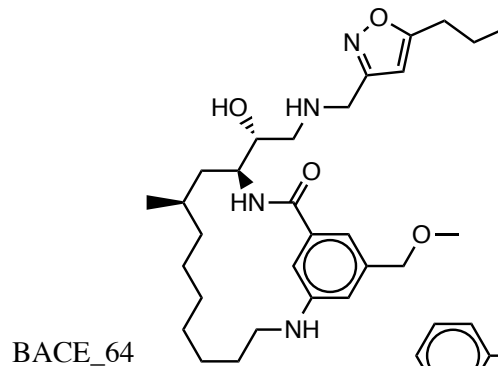
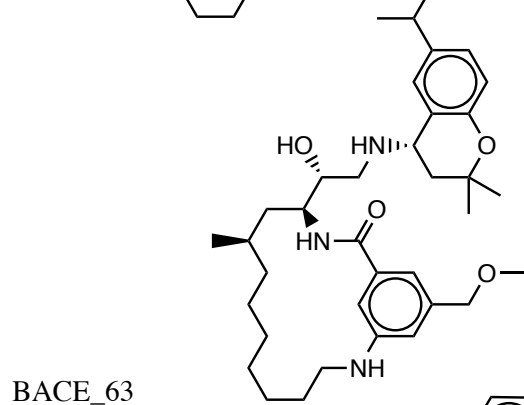
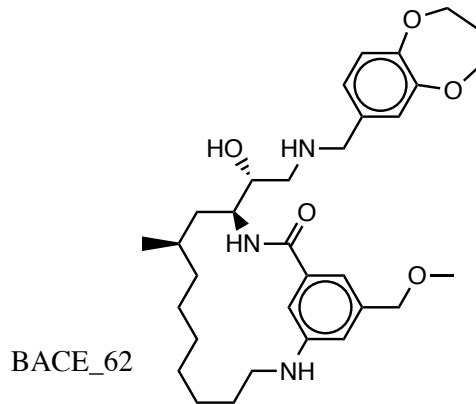
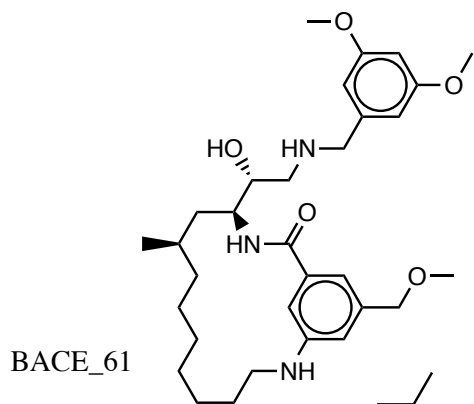


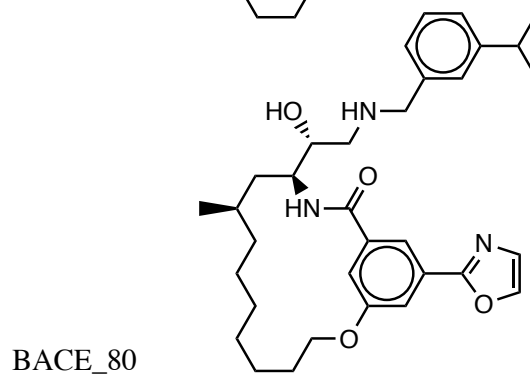
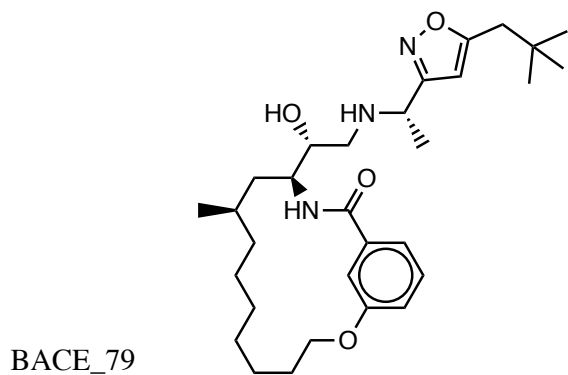
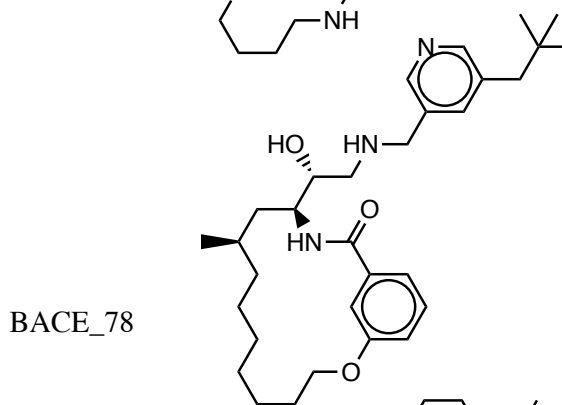
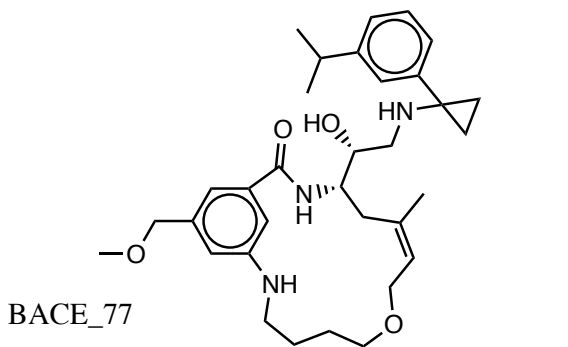
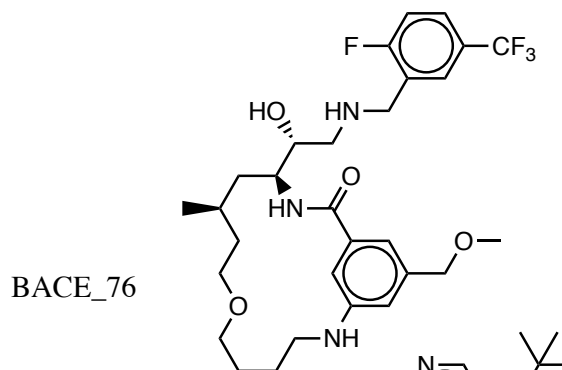
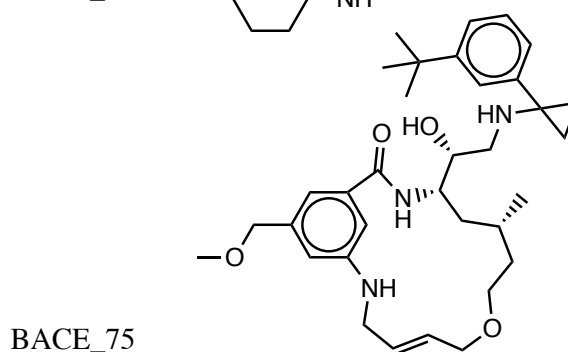
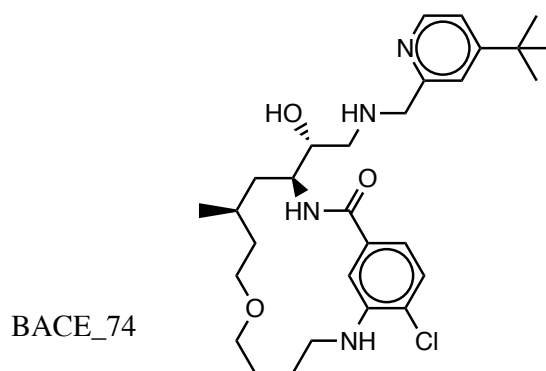
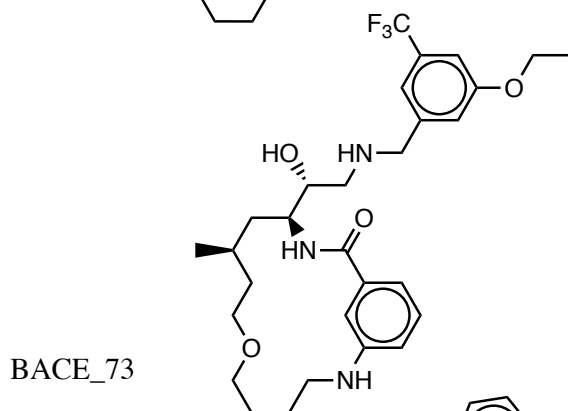
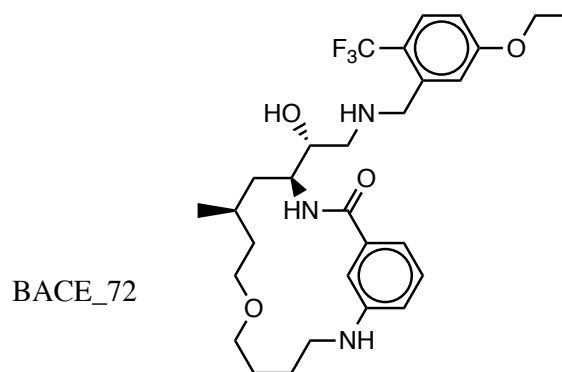
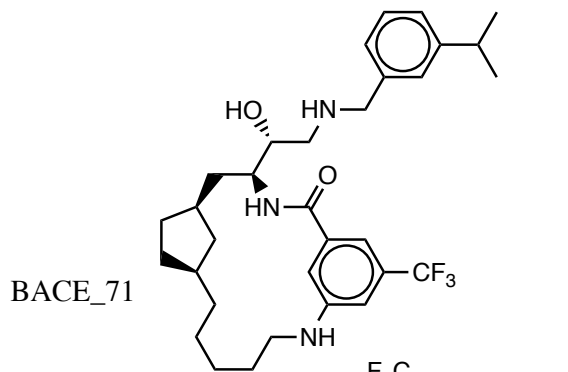
BACE_59

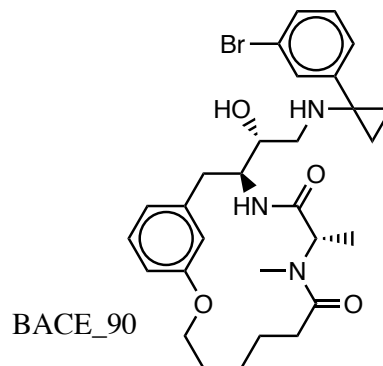
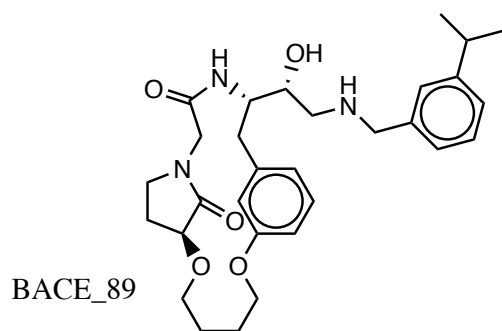
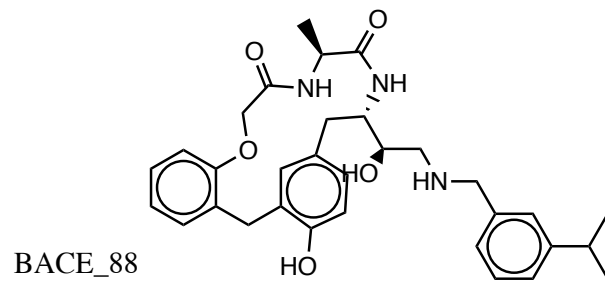
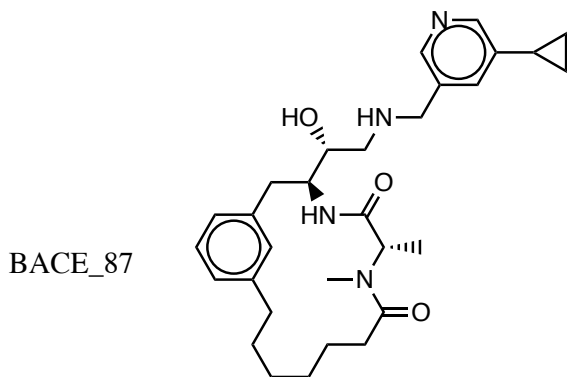
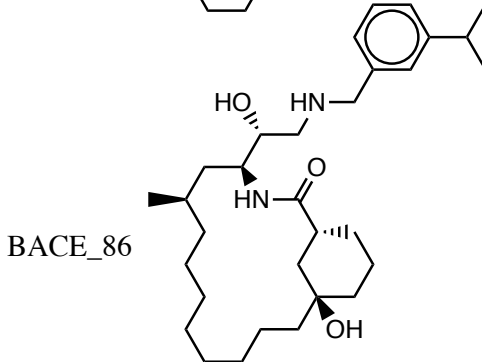
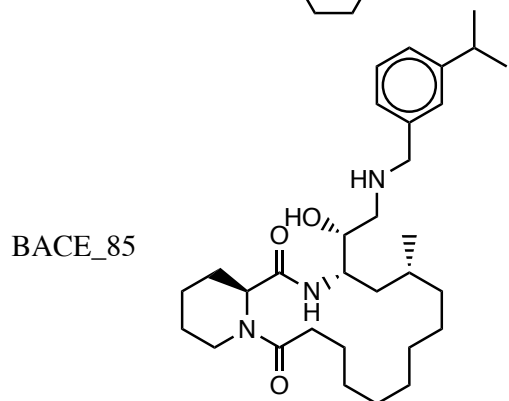
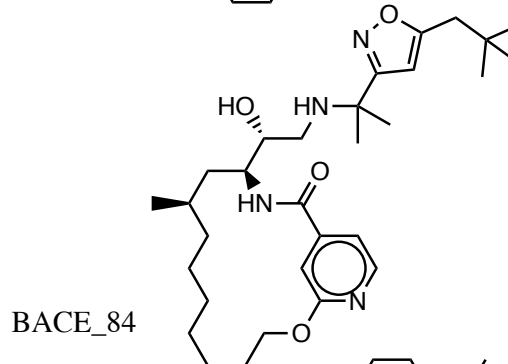
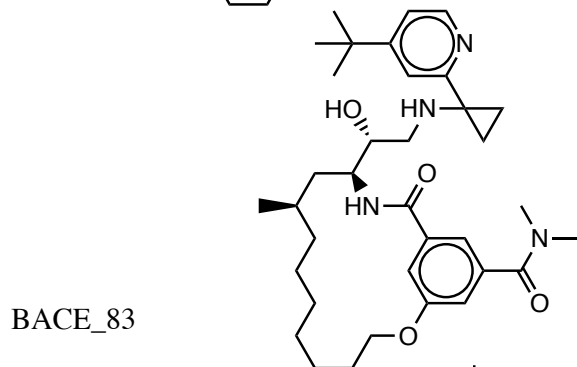
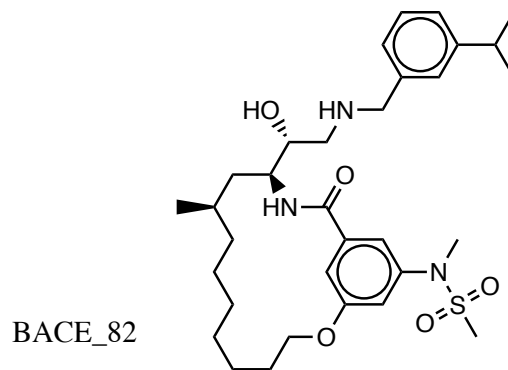
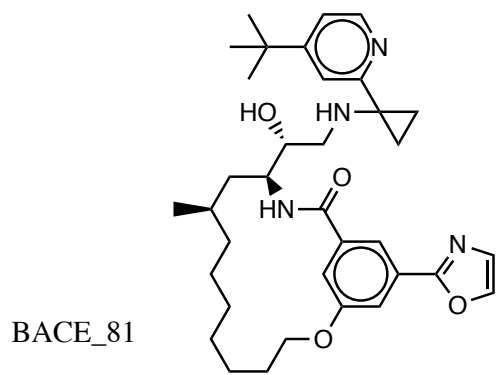


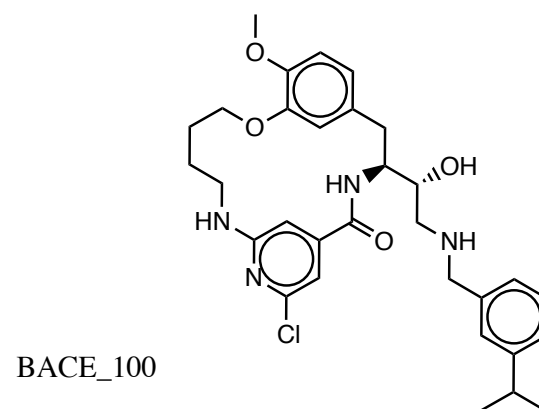
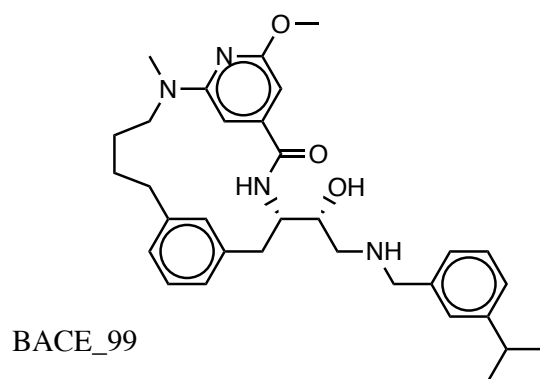
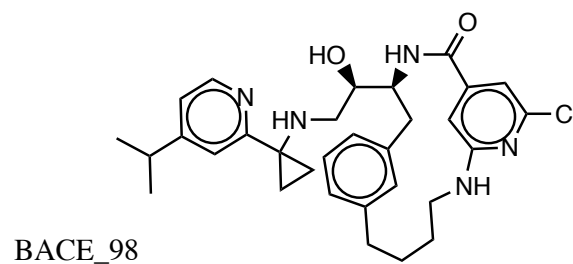
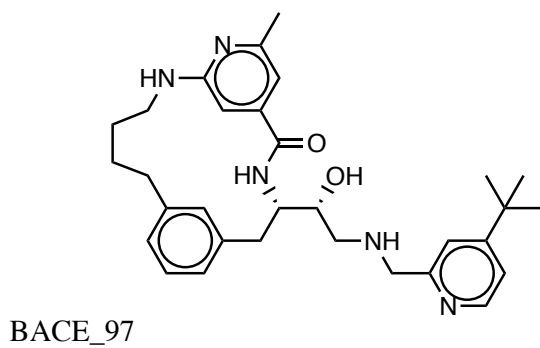
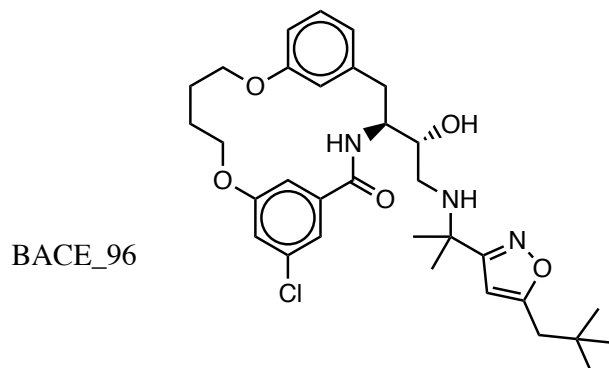
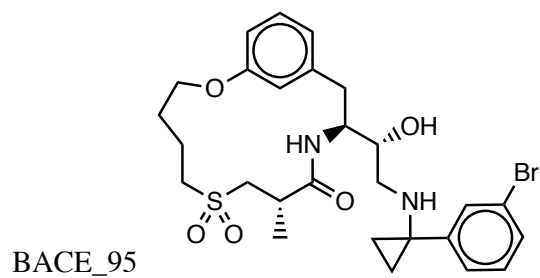
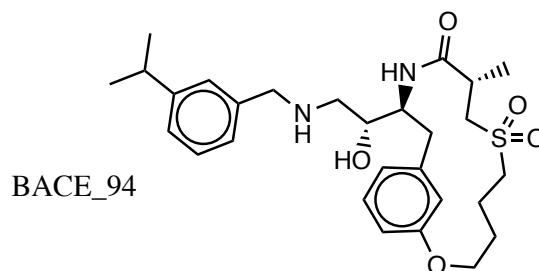
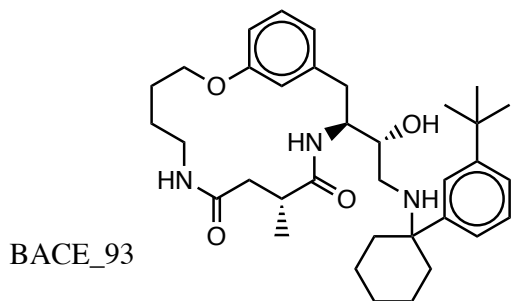
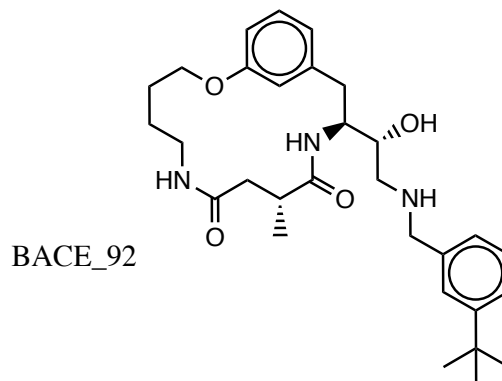
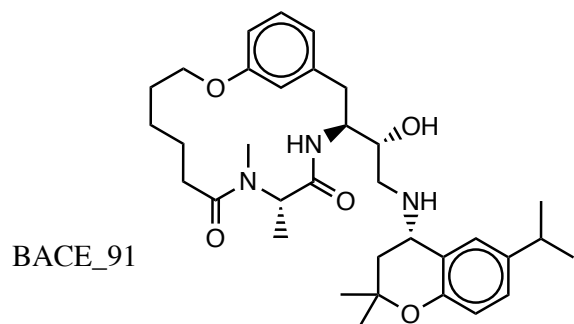
BACE_60

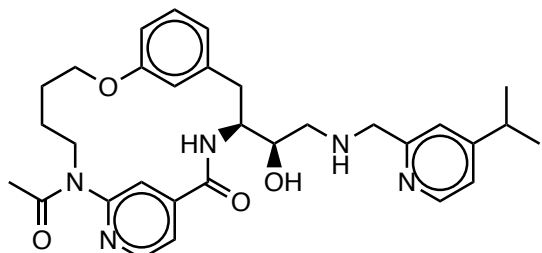




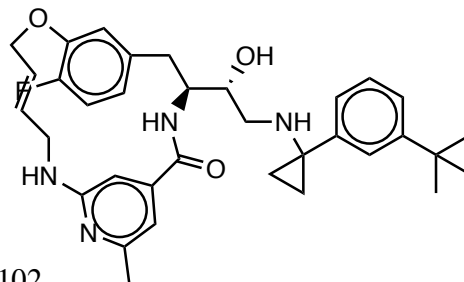




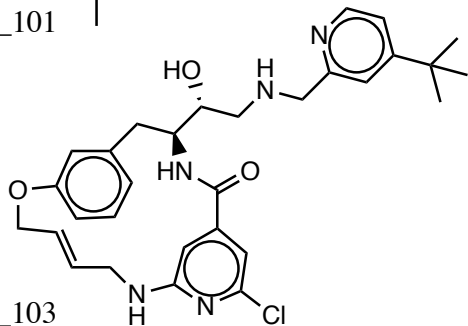




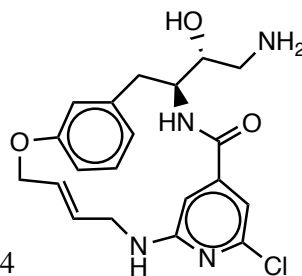
BACE_101



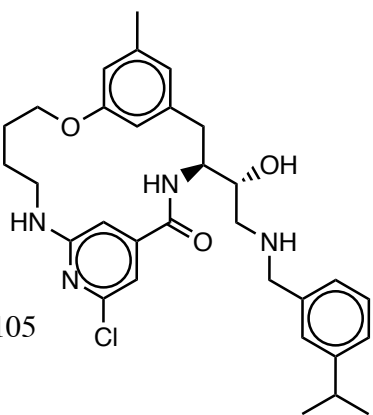
BACE_102



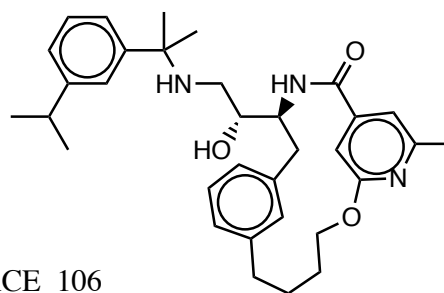
BACE_103



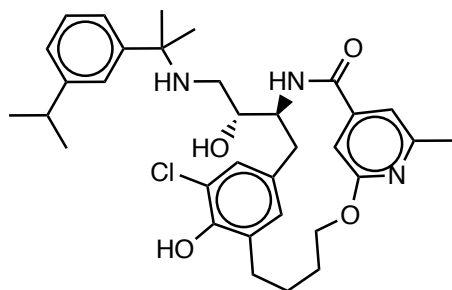
BACE_104



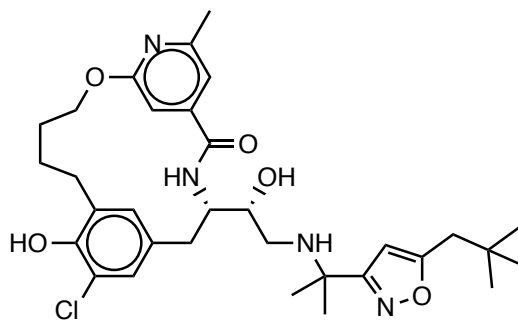
BACE_105



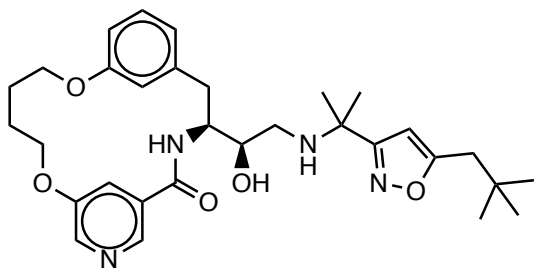
BACE_106



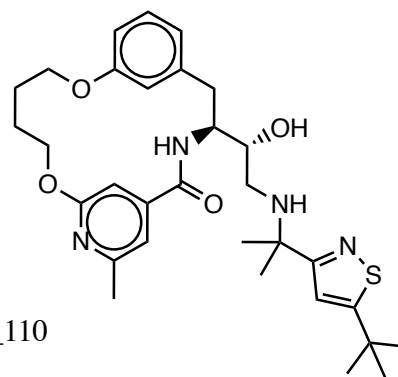
BACE_107



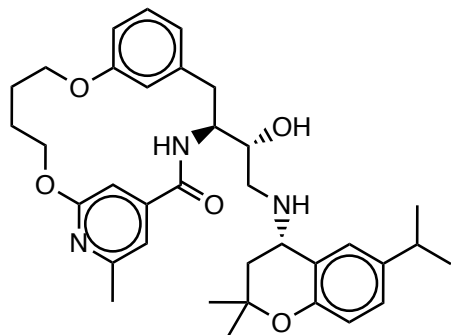
BACE_108



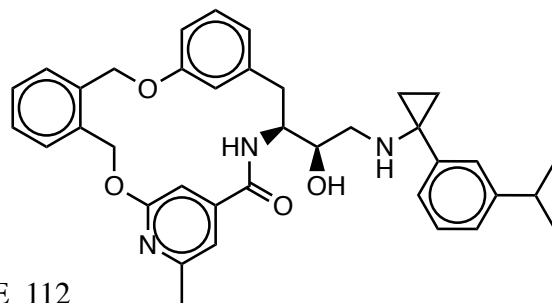
BACE_109



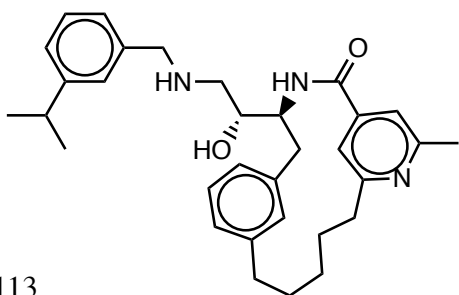
BACE_110



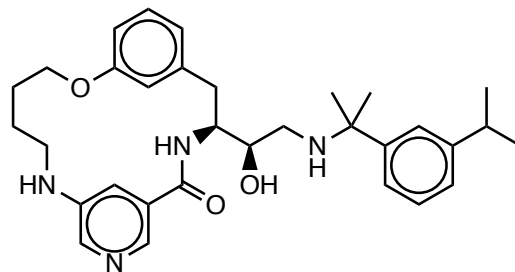
BACE_111



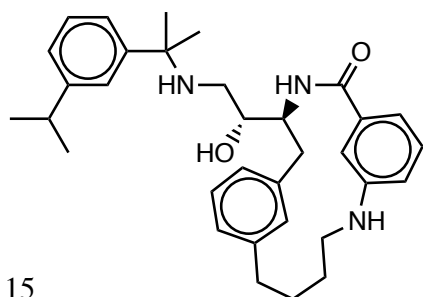
BACE_112



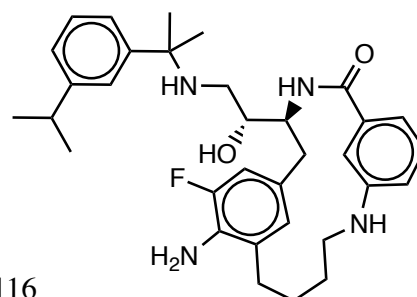
BACE_113



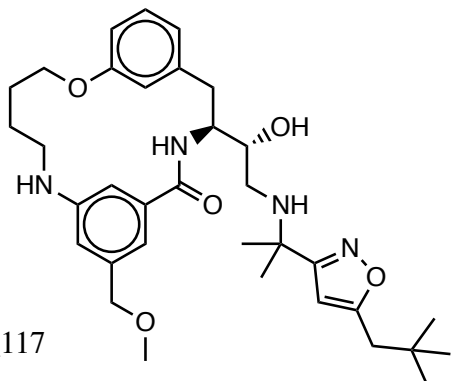
BACE_114



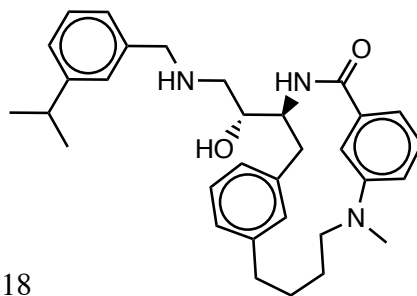
BACE_115



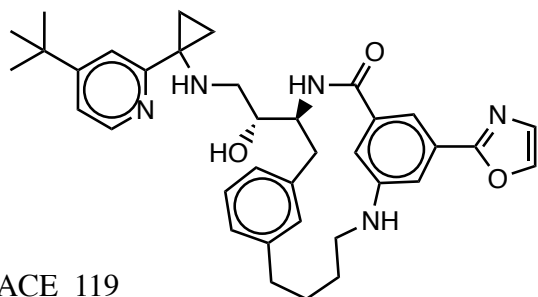
BACE_116



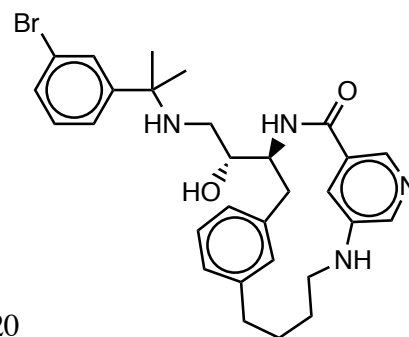
BACE_117



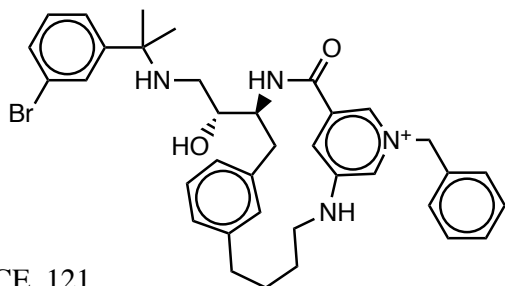
BACE_118



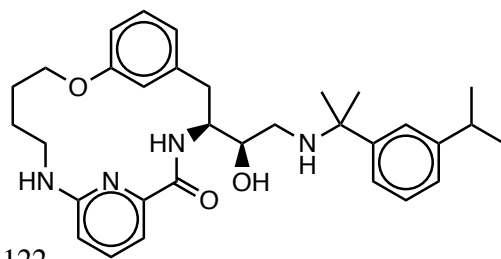
BACE_119



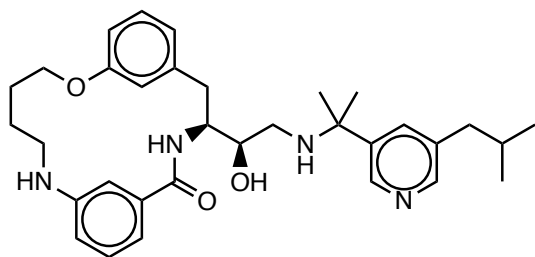
BACE_120



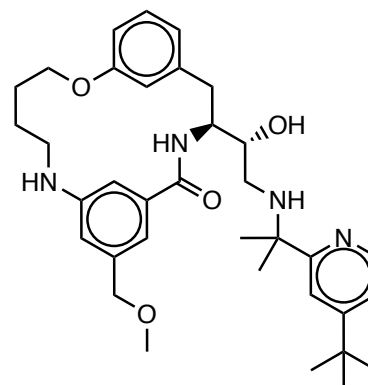
BACE_121



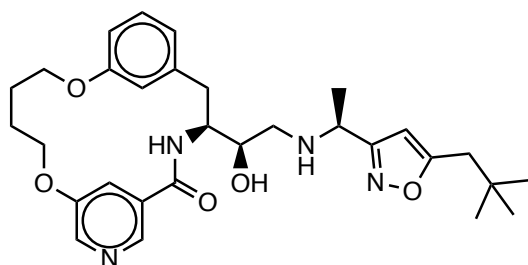
BACE_122



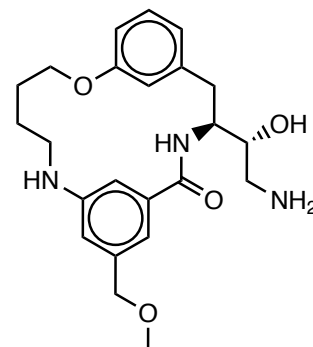
BACE_123



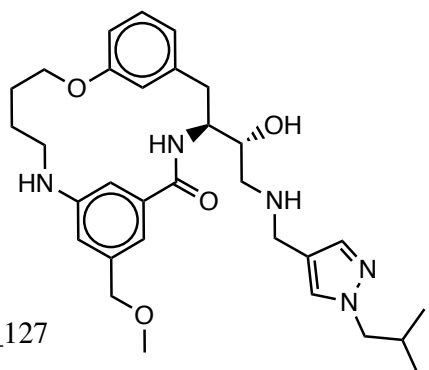
BACE_124



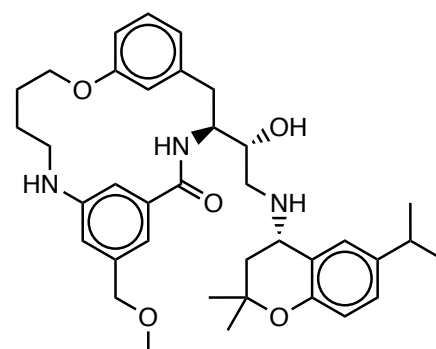
BACE_125



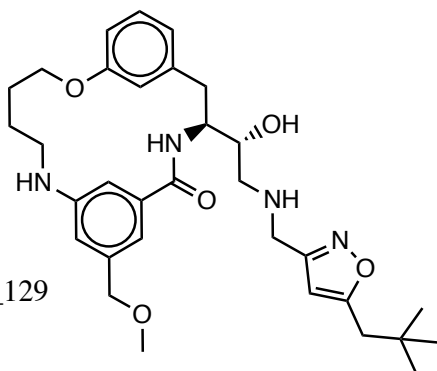
BACE_126



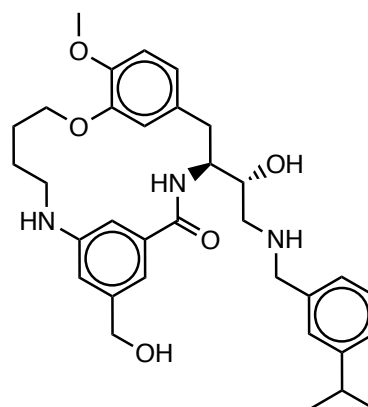
BACE_127



BACE_128

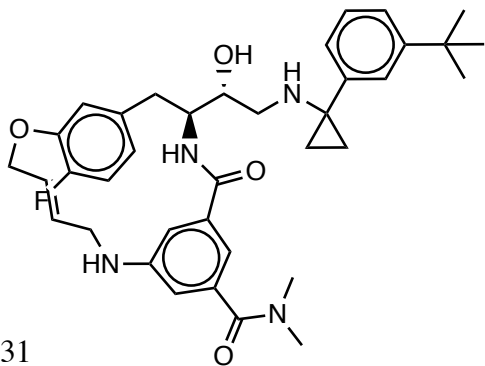


BACE_129

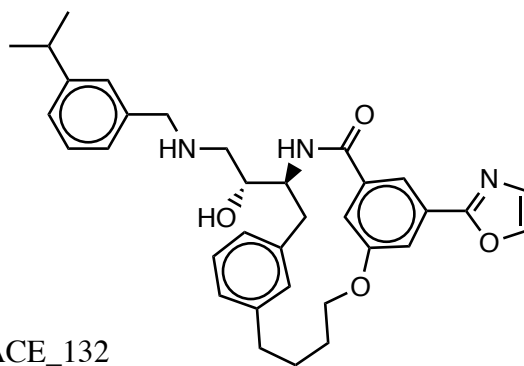


BACE_130

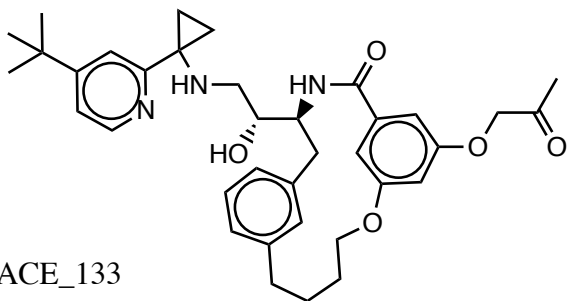
BACE_131



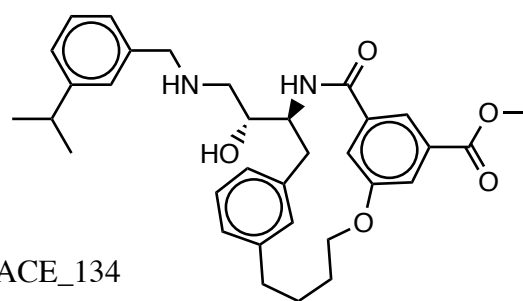
BACE_132



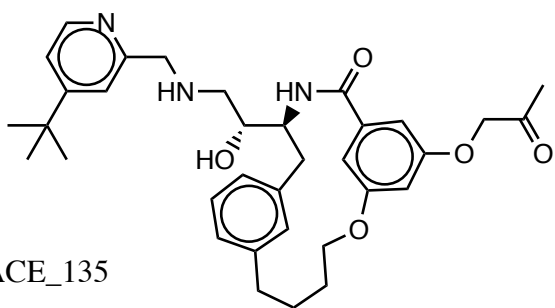
BACE_133



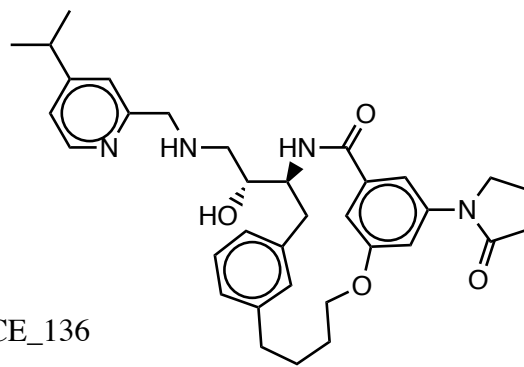
BACE_134



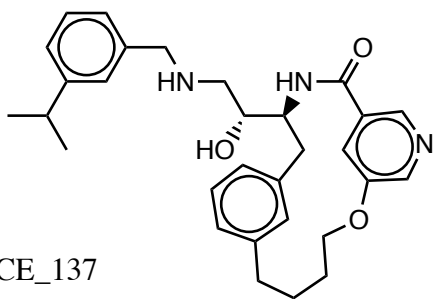
BACE_135



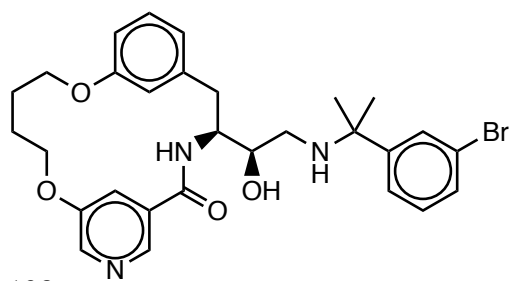
BACE_136



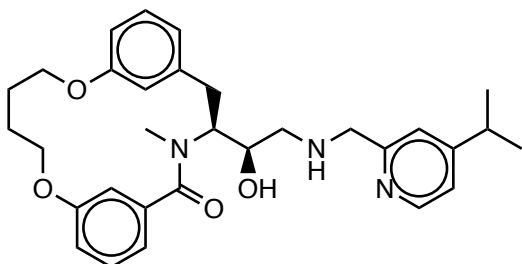
BACE_137



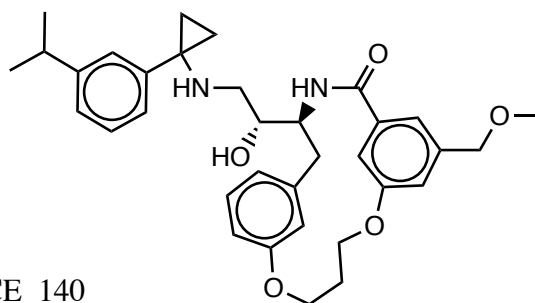
BACE_138

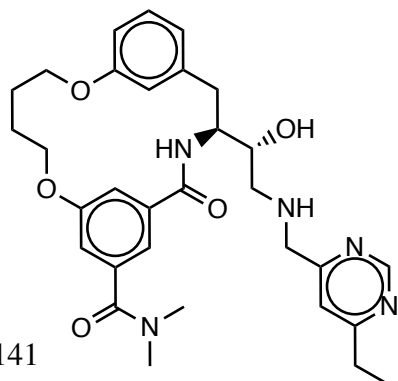


BACE_139

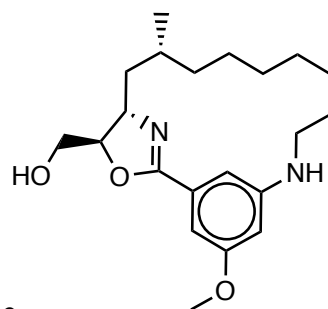


BACE_140

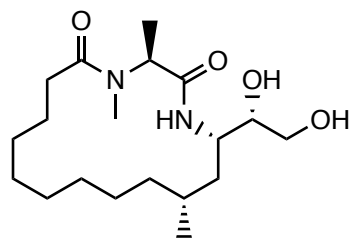




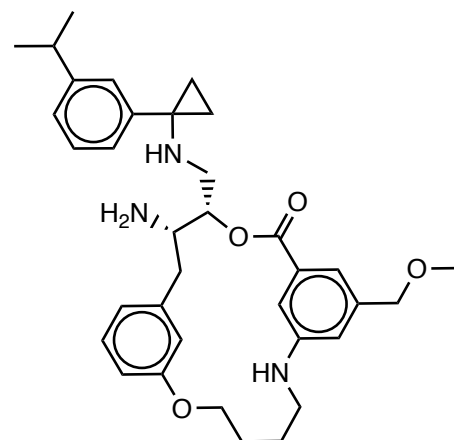
BACE_141



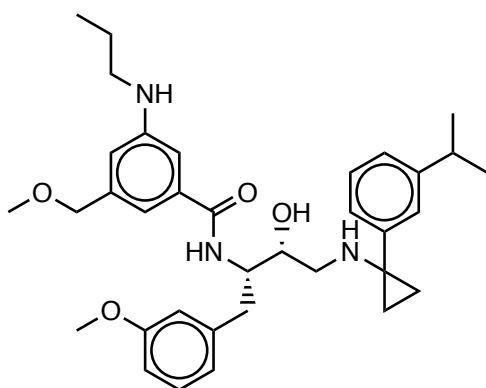
BACE_142



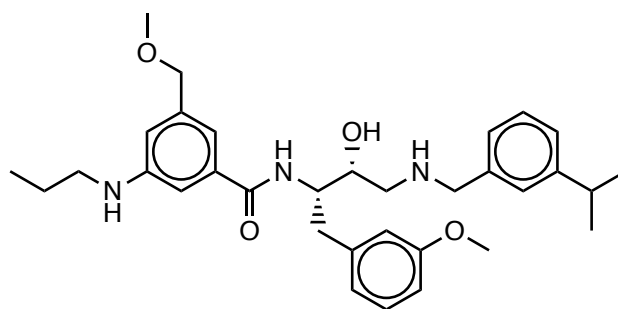
BACE_143



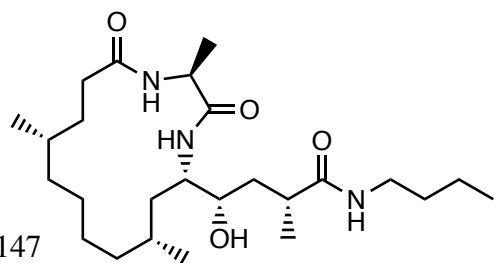
BACE_144



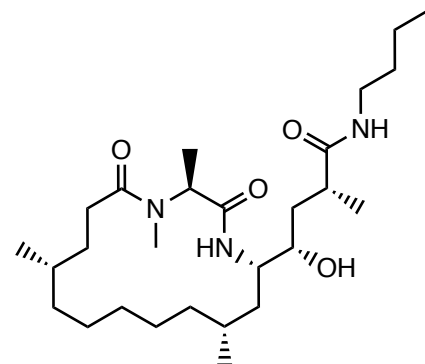
BACE_145



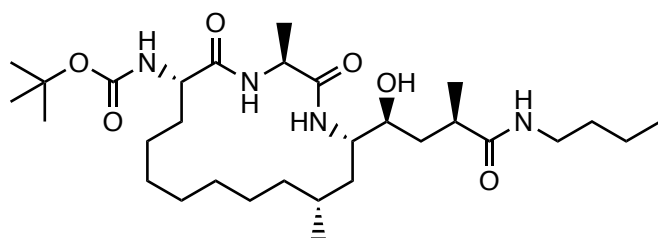
BACE_146



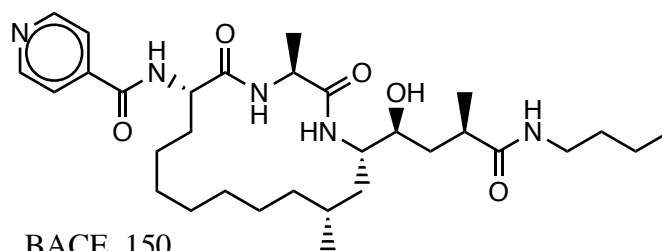
BACE_147



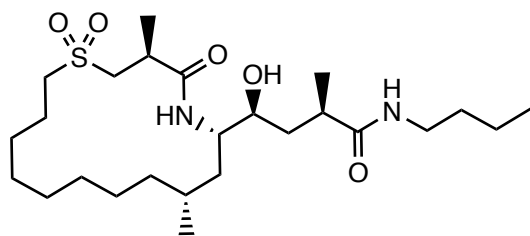
BACE_148



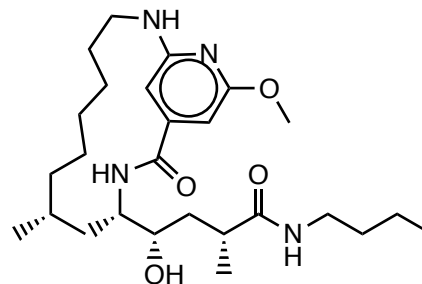
BACE_149



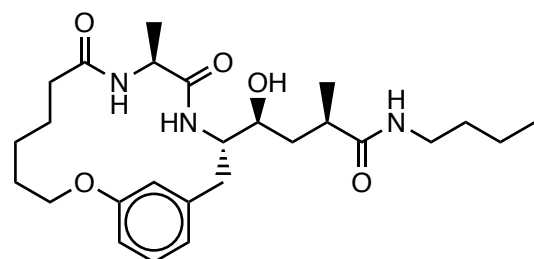
BACE_150



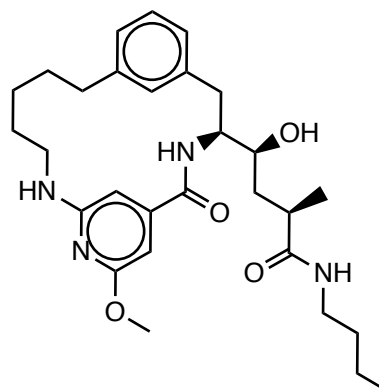
BACE_151



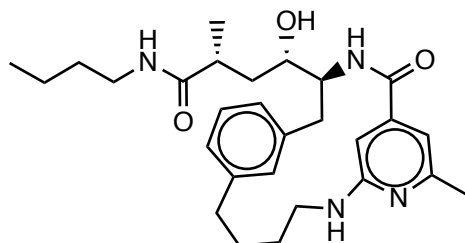
BACE_152



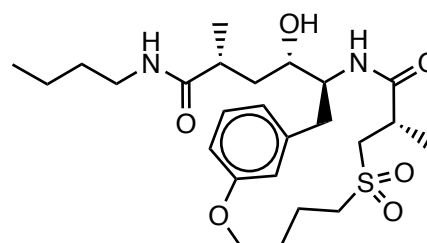
BACE_153



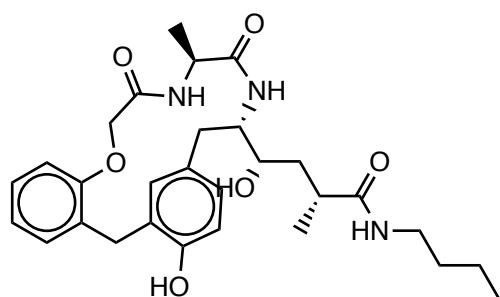
BACE_154



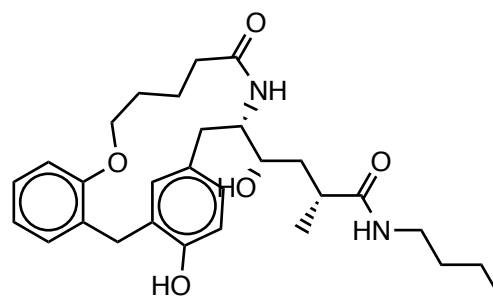
BACE_155



BACE_156



BACE_157



BACE_158

Figure S1. Chemical structures of the 158 ligands composing the BACE dataset. The pose prediction subset is composed of 20 compounds, **BACE_1** to **BACE_20**. The ranking subset is composed of 154 compounds, i.e. all with the exception of **BACE_2**, **BACE_3**, **BACE_17** and **BACE_18**.