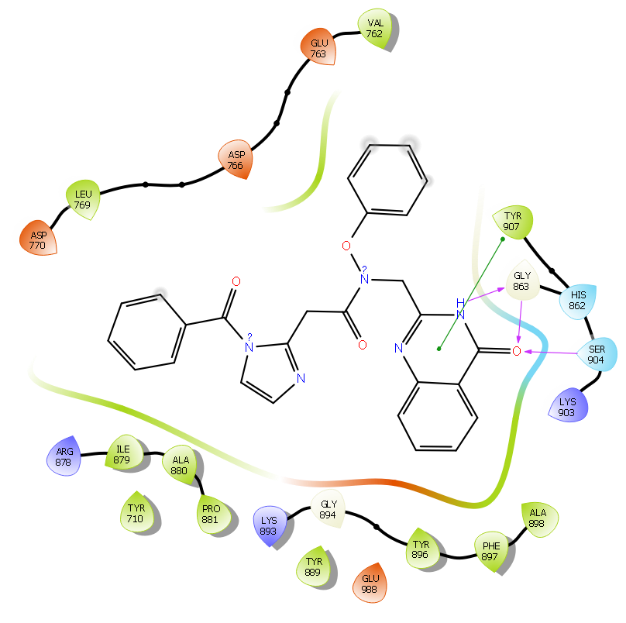
**Supplementary file**



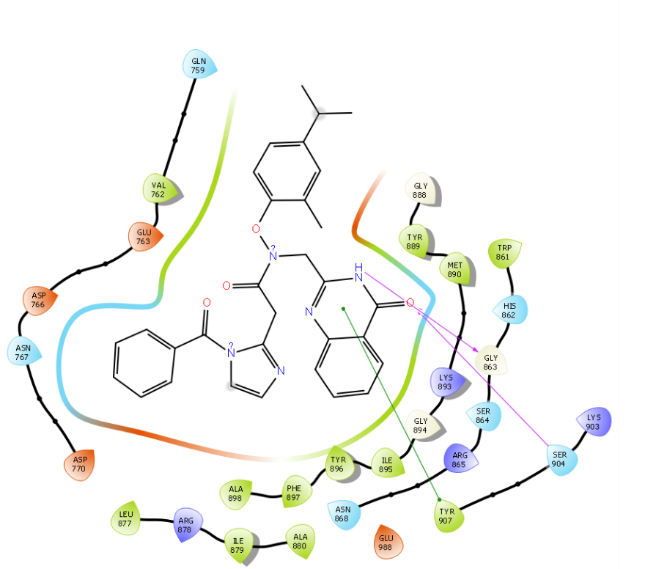




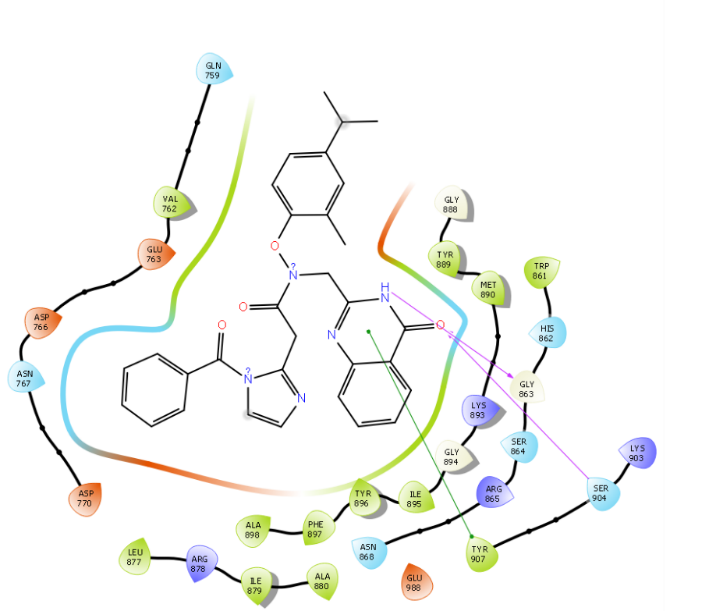
**Figure 1.** Newly designed Dual inhibitors.



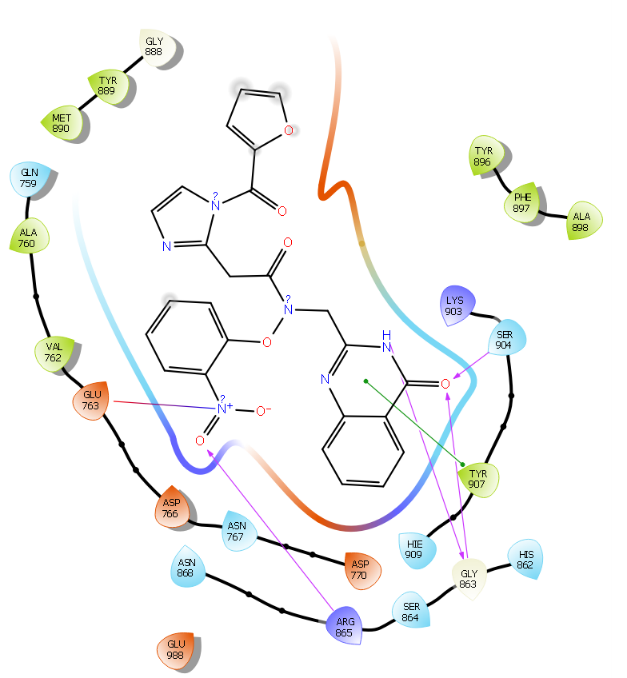
**Figure 2.** Fitting pose interactions of compound 1d in the pocket of **4ZZZ** in 2D view.



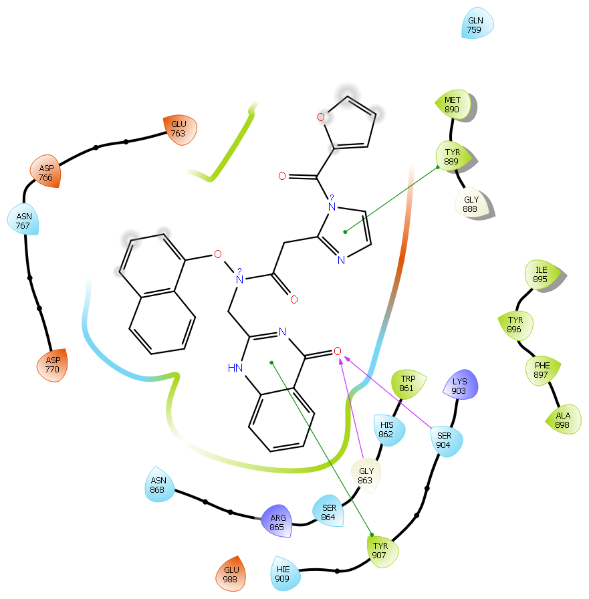
**Figure 3.** Fitting pose interactions of compound 1m in the pocket of **4ZZZ** in 2D view.



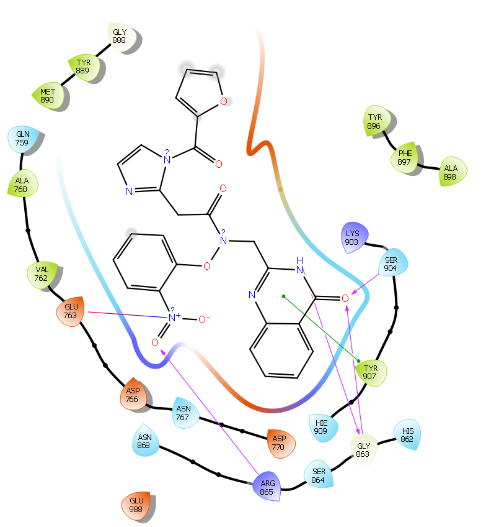
**Figure 4.** Fitting pose interactions of compound 2k in the pocket of **4ZZZ** in 2D view.



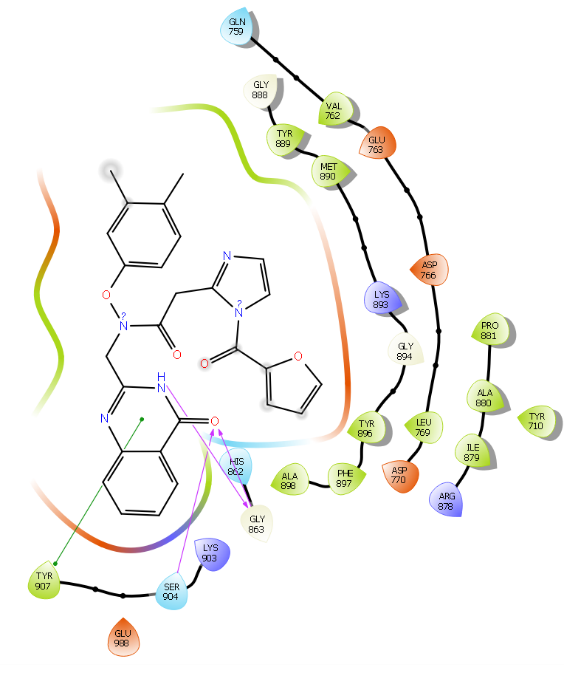
**Figure 5.** Fitting pose interactions of compound 2l in the pocket of **4ZZZ** in 2D view.



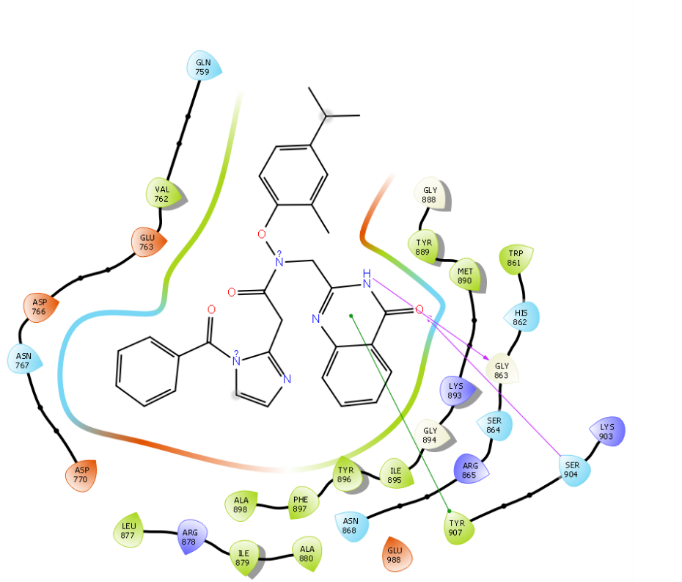
**Figure 6.** Fitting pose interactions of compound 2m in the pocket of **4ZZZ** in 2D view.



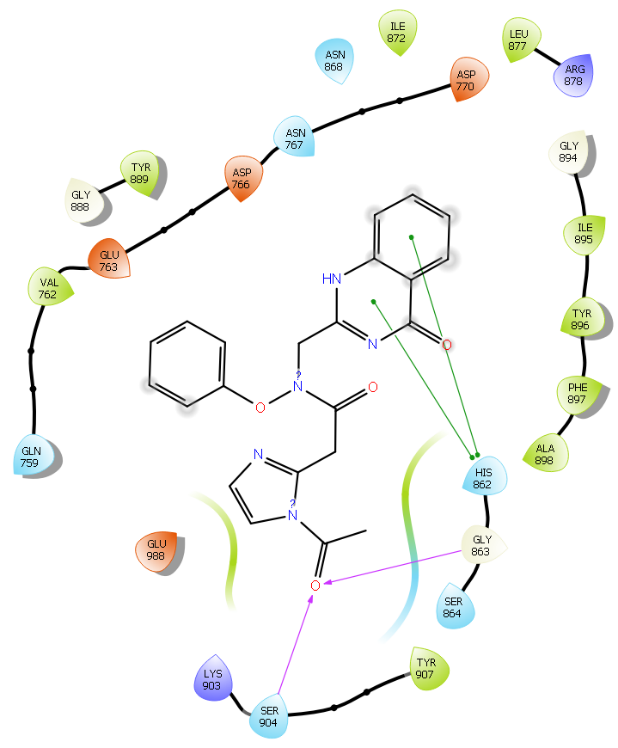
**Figure 7.** Fitting pose interactions of compound 3g in the pocket of **4ZZZ** in 2D view.



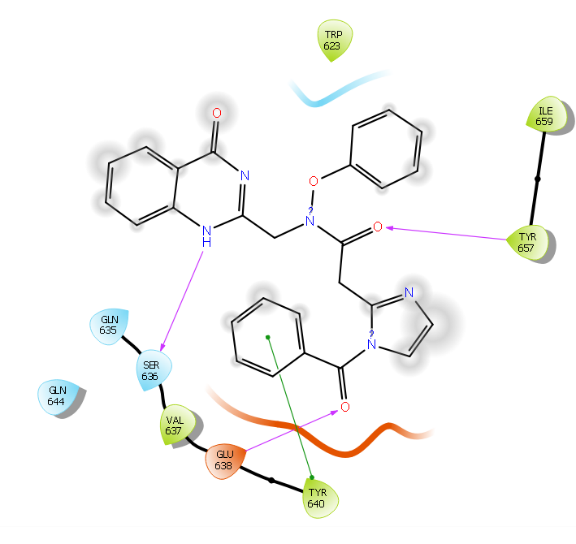
**Figure 8.** Fitting pose interactions of compound 3h in the pocket of **4ZZZ** in 2D view.



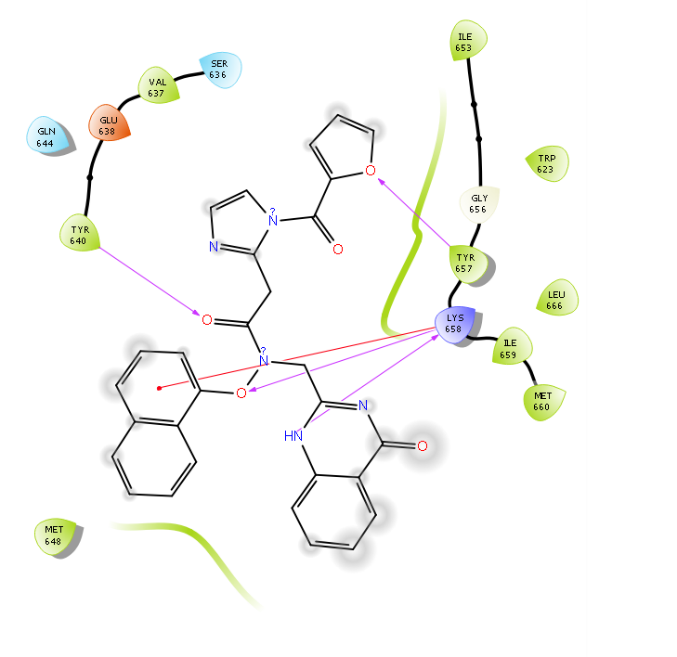
**Figure 9.** Fitting pose interactions of compound 3j in the pocket of **4ZZZ** in 2D view.



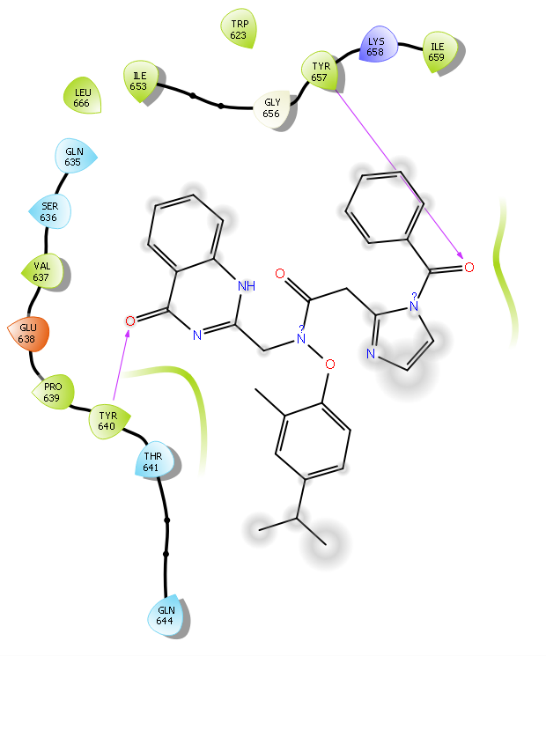
**Figure 10.** Fitting pose interactions of compound 3k in the pocket of **4ZZZ** in 2D view.



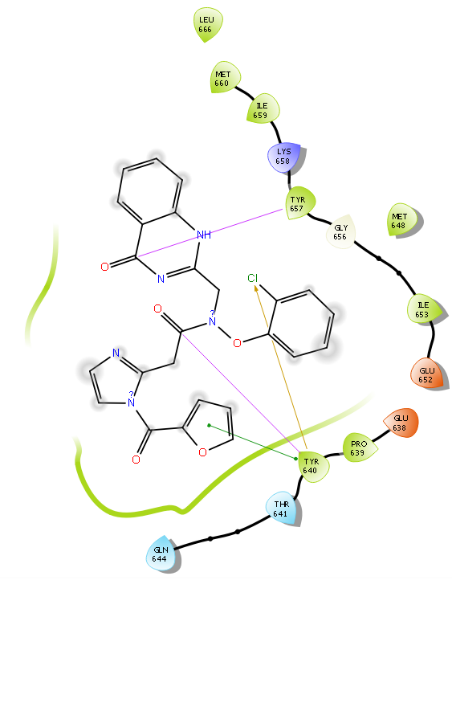
**Figure 11.** Fitting pose interactions of compound 1d in the pocket of **6NJS** in 2D view.



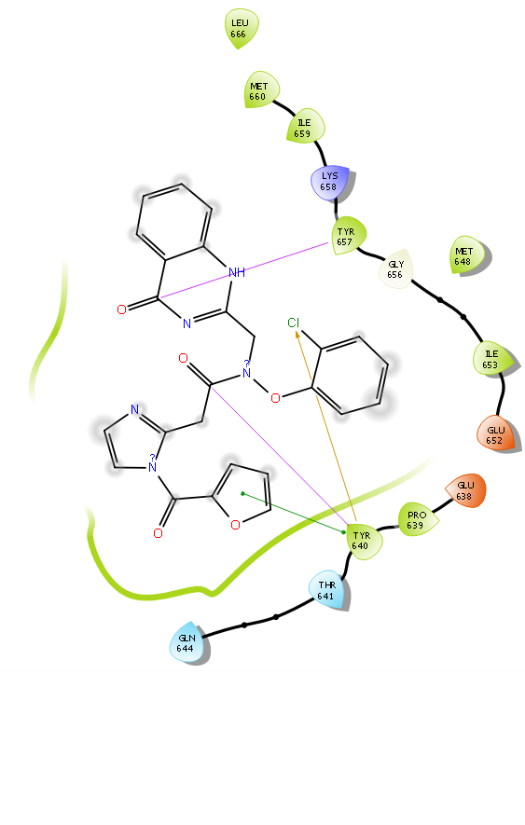
**Figure 12.** Fitting pose interactions of compound 1m in the pocket of **6NJS** in 2D view.



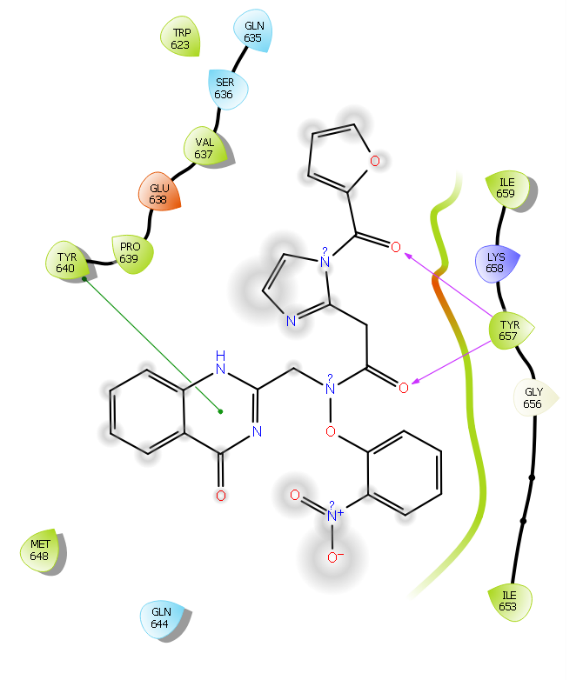
**Figure 13.** Fitting pose interactions of compound 2k in the pocket of **6NJS** in 2D view.



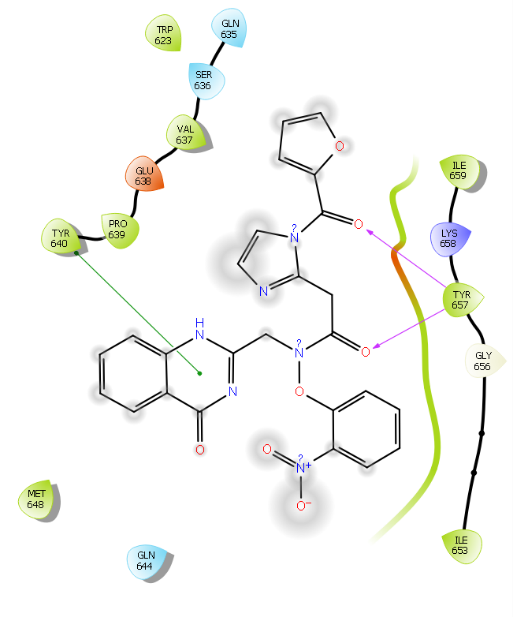
**Figure 14.** Fitting pose interactions of compound 2l in the pocket of **6NJS** in 2D view.



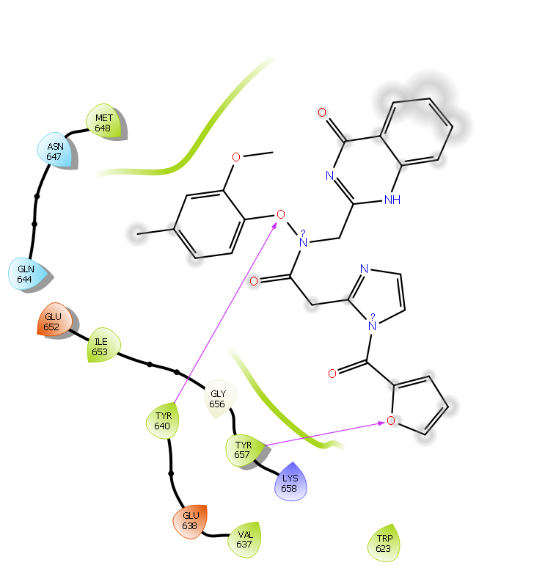
**Figure 15.** Fitting pose interactions of compound 2m in the pocket of **6NJS** in 2D view.



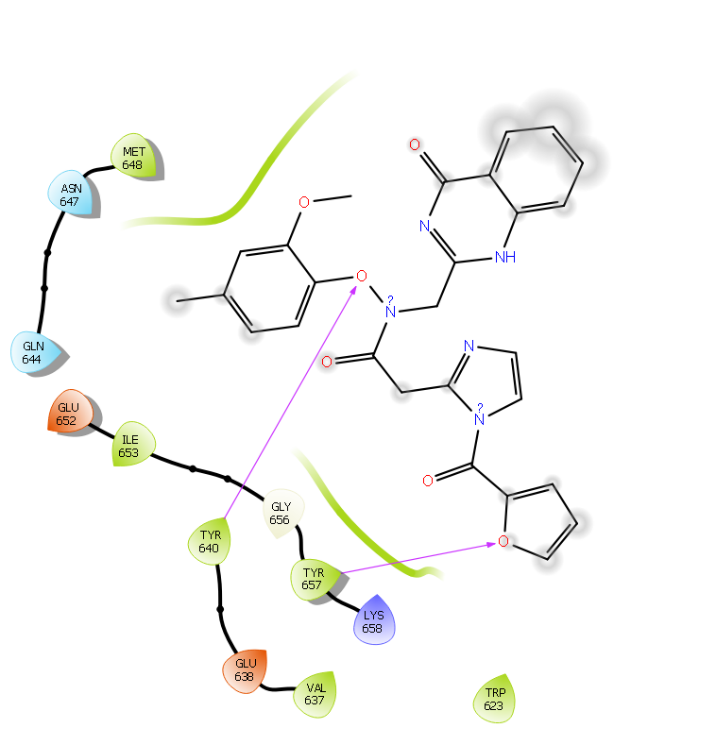
**Figure 16.** Fitting pose interactions of compound 3g in the pocket of **6NJS** in 2D view.



**Figure 17.** Fitting pose interactions of compound 3h in the pocket of **6NJS** in 2D view.



**Figure 18.** Fitting pose interactions of compound 3j in the pocket of **6NJS** in 2D view.



**Figure 19.** Fitting pose interactions of compound 3k in the pocket of **6NJS** in 2D view.

**Table 1.** Compounds with PARP1 (PDB ID: 4ZZZ) (kcal/mol) have Gibbs (G) free energy of binding MM-GBSA.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Title** | **MMGBSA dG Bind** | **MMGBSA dG Bind Coulomb** | **MMGBSA dG Bind Covalent** | **MMGBSA dG Bind Hbond** | **MMGBSA dG Bind Lipo** | **MMGBSA dG Bin d Solv GB** | **MMGBSA dG Bind vdW** |
| 1d | -107. 03 | -41.60 | -3.51 | -0.44 | -24.24 | 23.39 | -71.58 |
| 1e | -108.21 | -51.65 | -0.59 | -1.93 | -24.01 | 32.10 | -57.11 |
| 1f | -115.89 | -34.53 | 2.29 | -1.85 | -18.18 | -3.40 | -63.08 |
| 1g | -101.34 | -46.86 | -19.30 | 0.99 | -15.01 | 8.68 | -40.85 |
| 1h | -101.67 | -40.41 | -10.14 | -1.25 | -11.71 | 25.72 | -44.96 |
| 1i | -114.31 | -39.14 | 5.76 | -1.35 | -22.54 | 58.18 | -62.94 |
| 1j | -100.91 | -42.97 | -7.63 | 0.36 | -15.88 | 6.00 | -48.25 |
| 1k | -107.94 | -49.04 | -13.92 | -1.48 | -13.37 | 6.71 | -52.76 |
| 1l | -103.77 | -44.25 | -1.23 | -0.61 | -18.97 | 39.32 | -69.00 |
| 1m | -104.10 | -47.08 | 4.55 | -3.09 | -22.05 | 53.05 | -66.94 |
| 2d | -94.86 | -36.54 | -2.28 | -2.04 | -18.54 | 38.22 | -59.98 |
| 2e | -98.52 | -47.61 | -0.86 | -0.86 | -15.67 | 26.41 | -44.54 |
| 2f | -107.77 | -44.15 | -1.90 | 0.57 | -13.85 | 35.88 | -53.74 |
| 2g | -105.79 | -41.71 | 3.92 | -2.26 | -21.13 | 27.54 | -72.54 |
| 2h | -103.77 | -44.25 | -1.23 | -0.61 | -18.97 | 39.32 | -69.00 |
| 2i | -112.31 | -45.18 | -6.74 | 0.55 | -21.79 | 2.69 | -58.76 |
| 2j | -79.33 | -33.84 | -2.79 | 0.61 | -18.90 | 28.70 | -50.74 |
| 2k | -119.11 | -46.37 | 1.22 | -0.36 | -19.63 | 34.62 | -60.61 |
| 2l | -100.19 | -32.80 | -5.62 | 1.07 | -12.58 | 26.15 | -53.94 |
| 2m | -104.10 | -47.08 | 4.55 | -3.09 | -22.05 | 53.05 | -66.94 |
| 3d | -99.64 | -36.50 | 3.02 | -0.54 | -10.91 | 15.38 | -46.41 |
| 3e | -106.93 | -50.71 | -2.32 | -2.29 | -11.16 | 18.35 | -42.40 |
| 3f | -103.96 | -37.78 | -5.48 | 0.68 | -17.69 | 32.55 | -58.19 |
| 3g | -107.90 | -32.73 | 1.56 | -2.20 | -17.92 | 32.82 | -58.12 |
| 3h | -115.23 | -43.54 | -8.18 | 0.30 | -25.11 | 29.42 | -73.29 |
| 3i | -99.15 | -42.43 | -13.67 | 1.02 | -10.23 | 5.05 | -48.84 |
| 3j | -111.61 | -53.95 | 1.63 | -2.36 | -20.87 | 12.66 | -58.93 |
| 3k | -102.49 | -36.97 | -5.57 | -2.48 | -19.88 | 18.00 | -57.36 |
| 3l | -107.94 | -49.04 | -13.92 | -1.48 | -13.37 | 6.71 | -52.76 |
| 3m | -103.77 | -44.25 | -1.23 | -0.61 | -18.97 | 39.32 | -69.00 |

**Table 2.** Compounds with STAT3 (PDB ID: 6NJS) (kcal/mol) have Gibbs (G) free energy of binding MM-GBSA.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Title** | **MMGBSA dG Bind** | **MMGBSA dG Bind Coulomb** | **MMGBSA dG Bind Covalent** | **MMGBSA dG Bind Hbond** | **MMGBSA dG Bind Lipo** | **MMGBSA dG Bind Solv GB** | **MMGBSA dG Bind vdW** |
| 1d | -79.90 | 6.64 | -3.51 | -0.44 | -24.24 | 23.39 | -71.58 |
| 1e | -66.13 | -4.38 | -0.59 | -1.93 | -24.01 | 32.10 | -57.11 |
| 1f | -89.38 | 5.34 | 2.29 | -1.85 | -18.18 | -3.40 | -63.08 |
| 1g | -69.64 | 6.42 | -19.30 | 0.99 | -15.01 | 8.68 | -40.85 |
| 1h | -79.81 | -28.21 | -10.14 | -1.25 | -11.71 | 25.72 | -44.96 |
| 1i | -73.74 | -42.55 | 5.76 | -1.35 | -22.54 | 58.18 | -62.94 |
| 1j | -67.42 | 3.96 | -7.63 | 0.36 | -15.88 | 6.00 | -48.25 |
| 1k | -82.92 | 0.63 | -13.92 | -1.48 | -13.37 | 6.71 | -52.76 |
| 1l | -71.93 | -14.30 | -1.23 | -0.61 | -18.97 | 39.32 | -69.00 |
| 1m | -81.86 | -35.43 | 4.55 | -3.09 | -22.05 | 53.05 | -66.94 |
| 2d | -79.60 | -22.70 | -2.28 | -2.04 | -18.54 | 38.22 | -59.98 |
| 2e | -67.24 | -23.16 | -0.86 | -0.86 | -15.67 | 26.41 | -44.54 |
| 2f | -75.71 | 7.89 | 2.37 | -2.05 | -19.98 | 4.11 | -60.29 |
| 2g | -78.46 | -1.60 | 3.92 | -2.26 | -21.13 | 27.54 | -72.54 |
| 2h | -71.93 | -14.30 | -1.23 | -0.61 | -18.97 | 39.32 | -69.00 |
| 2i | -72.50 | 20.56 | -6.74 | 0.55 | -21.79 | 2.69 | -58.76 |
| 2j | -46.31 | 19.18 | -4.10 | 1.76 | -19.09 | 7.32 | -43.19 |
| 2k | -83.45 | -30.57 | 1.22 | -0.36 | -19.63 | 34.62 | -60.61 |
| 2l | -69.34 | -15.57 | -5.62 | 1.07 | -12.58 | 26.15 | -53.94 |
| 2m | -81.86 | -35.43 | 4.55 | -3.09 | -22.05 | 53.05 | -66.94 |
| 3d | -76.55 | -28.16 | 3.02 | -0.54 | -10.91 | 15.38 | -46.41 |
| 3e | -87.42 | -39.78 | -2.32 | -2.29 | -11.16 | 18.35 | -42.40 |
| 3f | -71.36 | -14.85 | -2.29 | -0.71 | -21.23 | 33.27 | -56.05 |
| 3g | -65.26 | -10.19 | 1.56 | -2.20 | -17.92 | 32.82 | -58.12 |
| 3h | -85.46 | 0.90 | -8.18 | 0.30 | -25.11 | 29.42 | -73.29 |
| 3i | -69.56 | -13.18 | 7.98 | -0.51 | -16.15 | 23.39 | -62.16 |
| 3j | -76.90 | 1.64 | 1.63 | -2.36 | -20.87 | 12.66 | -58.93 |
| 3k | -81.33 | -2.76 | -5.57 | -2.48 | -19.88 | 18.00 | -57.36 |
| 3l | -82.92 | 0.63 | -13.92 | -1.48 | -13.37 | 6.71 | -52.76 |
| 3m | -71.93 | -14.30 | -1.23 | -0.61 | -18.97 | 39.32 | -69.00 |

**Table 3.** The details of the *in-silico* ADMET properties for the quinazolinone based derivatives

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Title** | **MW** | **Donor HB** | **Acpt HB** | **Log P o/w** | **metab** | **% Human oral absorption** | **Rule of Five** |
| 1d | 479.49 | 1 | 11 | 2.689 | 3 | 83.987 | 0 |
| 1e | 513.93 | 1 | 11 | 2.813 | 3 | 76.706 | 1 |
| 1f | 524.49 | 1 | 12 | 1.900 | 4 | 84.996 | 2 |
| 1g | 493.52 | 1 | 11 | 3.050 | 4 | 96.355 | 0 |
| 1h | 431.450 | 1 | 11 | 1.902 | 4 | 87.074 | 0 |
| 1i | 523.54 | 1 | 11 | 2.672 | 5 | 78.751 | 1 |
| 1j | 461.47 | 1 | 11 | 2.045 | 5 | 84.874 | 0 |
| 1k | 433.42 | 2 | 11 | 0.815 | 4 | 66.535 | 0 |
| 1l | 467.48 | 1 | 11 | 2.518 | 3 | 88.358 | 0 |
| 1m | 519.51 | 1 | 11 | 3.128 | 4 | 76.688 | 1 |
| 2d | 469.45 | 1 | 11 | 2.353 | 4 | 91.978 | 0 |
| 2e | 499.48 | 1 | 12 | 2.207 | 5 | 77.298 | 1 |
| 2f | 462.42 | 1 | 12 | 0.842 | 4 | 83.667 | 1 |
| 2g | 483.48 | 1 | 11 | 2.457 | 5 | 86.277 | 0 |
| 2h | 467.48 | 1 | 11 | 2.518 | 3 | 88.358 | 0 |
| 2i | 445.47 | 1 | 11 | 1.617 | 5 | 83.150 | 0 |
| 2j | 473.53 | 1 | 11 | 2.607 | 5 | 87.581 | 0 |
| 2k | 535.60 | 1 | 11 | 4.189 | 5 | 90.287 | 1 |
| 2l | 485.45 | 2 | 12 | 1.587 | 5 | 60.700 | 1 |
| 2m | 519.51 | 1 | 11 | 3.128 | 4 | 76.688 | 1 |
| 3d | 417.42 | 1 | 11 | 1.498 | 3 | 82.949 | 0 |
| 3e | 447.44 | 1 | 11 | 1.756 | 4 | 83.277 | 0 |
| 3f | 503.90 | 1 | 11 | 1.944 | 4 | 70.653 | 1 |
| 3g | 514.45 | 1 | 12 | 1.442 | 5 | 80.390 | 2 |
| 3h | 497.50 | 1 | 11 | 2.263 | 6 | 88.192 | 0 |
| 3i | 445.47 | 1 | 11 | 1.617 | 5 | 83.150 | 0 |
| 3j | 513.50 | 1 | 12 | 2.504 | 6 | 66.092 | 2 |
| 3k | 525.56 | 1 | 11 | 2.686 | 6 | 74.197 | 1 |