# On-the-fly Integration of Data from a Spin-Diffusion-Based NMR Experiment into Protein-Ligand Docking

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## Supporting Information

### Supplementary Tables

**Table S1:** ChemPLP-only results for the re-docking and cross-docking experiments of the 5 PKA ligands used. RMSD values below 2 Å are shown in green.

| protein | LL1 | | LL2 | | M77 | |
|---|---|---|---|---|---|---|
| | RMSD | ChemPLP score | RMSD | ChemPLP score | RMSD | ChemPLP score |
| 3DNE | 0.22 | -84.65 | 5.36 | -74.34 | 7.91 | -64.52 |
| 3DNE | 0.22 | -84.62 | 5.36 | -74.17 | 0.82 | -65.97 |
| 3DNE | 0.24 | -84.47 | 5.37 | -74.10 | 0.87 | -65.93 |
| 3DNE | 0.22 | -84.67 | 5.38 | -74.08 | 0.88 | -65.93 |
| 3DNE | 0.23 | -84.48 | 5.36 | -74.03 | 0.92 | -65.86 |
| 3DNE | 0.23 | -84.55 | 5.37 | -74.17 | 0.83 | -65.82 |
| 3DNE | 0.22 | -84.55 | 5.37 | -74.07 | 0.83 | -65.95 |
| 3DNE | 0.23 | -84.54 | 5.35 | -74.07 | 0.91 | -65.84 |
| 3DNE | 0.24 | -84.54 | 5.36 | -74.10 | 0.88 | -65.95 |
| 3DNE | 0.21 | -84.57 | 5.37 | -74.15 | 0.87 | -65.84 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3DND | 0.37 | -71.63 | 1.36 | -69.76 | 0.64 | -70.56 |
| 3DND | 0.47 | -71.95 | 1.41 | -69.77 | 0.76 | -71.68 |
| 3DND | 0.48 | -71.79 | 1.43 | -69.75 | 0.74 | -71.19 |
| 3DND | 0.47 | -71.85 | 1.40 | -69.85 | 0.83 | -70.73 |
| 3DND | 0.47 | -71.68 | 1.41 | -69.86 | 0.86 | -70.84 |
| 3DND | 0.40 | -71.68 | 1.40 | -69.78 | 0.85 | -70.91 |
| 3DND | 0.52 | -71.81 | 1.45 | -69.75 | 0.75 | -71.46 |
| 3DND | 0.46 | -71.83 | 1.34 | -69.65 | 0.75 | -71.75 |
| 3DND | 0.39 | -71.76 | 1.39 | -69.80 | 0.77 | -71.03 |
| 3DND | 0.46 | -71.81 | 1.42 | -69.69 | 0.76 | -70.88 |
| 1Q8W | 0.53 | -68.78 | 5.45 | -68.52 | 0.71 | -75.49 |
| 1Q8W | 0.71 | -68.67 | 5.44 | -68.44 | 0.66 | -75.25 |
| 1Q8W | 0.67 | -68.75 | 5.44 | -68.45 | 0.74 | -75.55 |
| 1Q8W | 0.60 | -68.88 | 5.43 | -67.31 | 0.74 | -75.68 |
| 1Q8W | 0.59 | -69.01 | 5.45 | -68.32 | 0.71 | -75.63 |
| 1Q8W | 0.67 | -68.99 | 5.35 | -67.85 | 0.77 | -75.31 |
| 1Q8W | 0.64 | -68.83 | 5.46 | -68.39 | 0.75 | -75.53 |
| 1Q8W | 0.59 | -68.97 | 5.45 | -68.48 | 0.76 | -75.53 |
| 1Q8W | 0.55 | -69.01 | 5.45 | -68.33 | 0.74 | -75.51 |
| 1Q8W | 0.68 | -68.82 | 5.47 | -68.30 | 0.72 | -75.47 |
| 4IJ9 | 0.49 | -79.95 | 5.27 | -71.42 | 0.65 | -70.55 |
| 4IJ9 | 0.51 | -80.01 | 5.25 | -71.31 | 0.62 | -70.54 |
| 4IJ9 | 0.55 | -79.96 | 5.25 | -71.62 | 0.61 | -70.54 |
| 4IJ9 | 0.52 | -79.93 | 5.24 | -71.55 | 0.64 | -70.38 |
| 4IJ9 | 0.47 | -79.87 | 5.27 | -71.29 | 0.61 | -70.47 |
| 4IJ9 | 0.55 | -79.69 | 5.25 | -71.88 | 0.62 | -70.57 |
| 4IJ9 | 0.55 | -79.80 | 5.35 | -71.82 | 0.64 | -70.45 |
| 4IJ9 | 0.55 | -79.86 | 5.39 | -71.57 | 0.64 | -70.58 |
| 4IJ9 | 0.53 | -79.88 | 5.25 | -71.36 | 0.65 | -70.56 |
| 4IJ9 | 0.49 | -79.90 | 5.25 | -71.49 | 0.61 | -70.46 |
| 4IE9 | 0.34 | -73.68 | 1.35 | -70.79 | 0.70 | -75.71 |
| 4IE9 | 0.32 | -73.76 | 1.38 | -70.80 | 0.72 | -75.42 |
| 4IE9 | 0.36 | -73.87 | 1.38 | -70.63 | 0.65 | -74.84 |
| 4IE9 | 0.29 | -73.62 | 1.40 | -70.70 | 0.69 | -75.47 |
| 4IE9 | 0.31 | -73.69 | 1.41 | -70.74 | 0.69 | -75.15 |
| 4IE9 | 0.32 | -73.68 | 1.37 | -70.69 | 0.70 | -75.69 |
| 4IE9 | 0.35 | -73.73 | 1.36 | -70.71 | 0.73 | -75.50 |
| 4IE9 | 0.32 | -73.76 | 1.43 | -70.73 | 0.61 | -74.89 |
| 4IE9 | 0.38 | -73.69 | 1.35 | -70.66 | 0.63 | -74.86 |
| 4IE9 | 0.36 | -73.67 | 1.34 | -70.68 | 0.72 | -75.45 |

| protein | PTV RMSD | PTV ChemPLP score | PZX RMSD | PZX ChemPLP score |
|---|---|---|---|---|
| 3DNE | 1.63 | -80.64 | 5.90 | -68.16 |
| 3DNE | 1.26 | -84.07 | 4.50 | -66.51 |
| 3DNE | 1.29 | -84.27 | 3.31 | -68.60 |
| 3DNE | 1.27 | -83.82 | 5.01 | -67.86 |
| 3DNE | 1.28 | -84.18 | 3.36 | -68.55 |
| 3DNE | 1.27 | -84.16 | 3.36 | -68.69 |
| 3DNE | 1.27 | -81.35 | 5.78 | -68.00 |
| 3DNE | 1.27 | -83.92 | 3.35 | -68.78 |
| 3DNE | 1.28 | -84.29 | 5.78 | -67.89 |
| 3DNE | 1.28 | -84.22 | 3.35 | -68.83 |
| 3DND | 1.73 | -82.21 | 3.33 | -69.96 |
| 3DND | 1.65 | -86.18 | 3.74 | -67.83 |
| 3DND | 1.68 | -85.52 | 3.33 | -69.70 |
| 3DND | 1.64 | -85.60 | 3.29 | -69.80 |
| 3DND | 1.63 | -83.16 | 3.33 | -69.47 |
| 3DND | 1.67 | -83.37 | 3.29 | -69.98 |
| 3DND | 1.63 | -85.96 | 3.38 | -69.87 |
| 3DND | 1.65 | -83.25 | 3.27 | -69.41 |
| 3DND | 1.63 | -83.26 | 3.74 | -67.63 |
| 3DND | 2.22 | -77.78 | 3.33 | -69.58 |
| 1Q8W | 1.56 | -81.86 | 3.92 | -66.82 |
| 1Q8W | 1.76 | -81.42 | 3.91 | -66.76 |
| 1Q8W | 1.77 | -81.92 | 3.92 | -66.92 |
| 1Q8W | 1.77 | -81.89 | 3.89 | -66.83 |
| 1Q8W | 1.56 | -81.39 | 3.19 | -66.84 |
| 1Q8W | 1.77 | -81.99 | 1.14 | -66.93 |
| 1Q8W | 1.56 | -81.23 | 3.91 | -66.89 |
| 1Q8W | 1.83 | -81.16 | 3.93 | -66.81 |
| 1Q8W | 1.76 | -82.06 | 3.91 | -66.95 |
| 1Q8W | 1.54 | -81.45 | 3.91 | -66.75 |
| 4IJ9 | 1.27 | -89.14 | 4.95 | -77.07 |
| 4IJ9 | 1.27 | -88.42 | 4.94 | -76.87 |
| 4IJ9 | 1.03 | -93.07 | 3.12 | -73.60 |
| 4IJ9 | 1.05 | -92.29 | 4.91 | -76.98 |
| 4IJ9 | 1.28 | -89.17 | 4.88 | -76.57 |
| 4IJ9 | 1.25 | -88.68 | 4.90 | -77.08 |
| 4IJ9 | 1.02 | -92.22 | 4.87 | -76.66 |
| 4IJ9 | 1.27 | -88.58 | 4.97 | -76.92 |
| 4IJ9 | 1.01 | -92.42 | 4.82 | -76.97 |
| 4IJ9 | 1.02 | -92.91 | 5.01 | -77.10 |

| | | | | |
|---|---|---|---|---|
| 4IE9 | 1.64 | -83.55 | 3.45 | -71.85 |
| 4IE9 | 1.68 | -83.42 | 3.46 | -71.79 |
| 4IE9 | 1.38 | -81.95 | 3.48 | -71.55 |
| 4IE9 | 1.65 | -83.29 | 3.46 | -71.60 |
| 4IE9 | 1.64 | -83.48 | 3.45 | -71.58 |
| 4IE9 | 1.59 | -81.02 | 3.48 | -71.79 |
| 4IE9 | 1.61 | -83.19 | 3.45 | -71.75 |
| 4IE9 | 1.68 | -83.35 | 3.48 | -71.49 |
| 4IE9 | 1.43 | -82.66 | 3.45 | -71.82 |
| 4IE9 | 1.68 | -83.34 | 3.44 | -71.72 |

**Table S2:** ChemPLP-INPHARMA docking results for the standard setup (scoring function $S_1$). A weight of 250 was used for the INPHARMA score. RMSD values below 2 Å are shown in green.

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | LL1 | LL2 | score | weighted | real | score |
| 3DNE | 0.28 | 5.25 | -129.52 | 14.61 | 0.058 | -114.91 |
| 3DNE | 0.32 | 5.27 | -127.88 | 13.21 | 0.053 | -114.67 |
| 3DNE | 0.24 | 2.06 | -124.40 | 11.81 | 0.047 | -112.59 |
| 3DNE | 0.34 | 5.27 | -127.27 | 12.61 | 0.050 | -114.67 |
| 3DNE | 0.26 | 5.25 | -132.80 | 22.18 | 0.089 | -110.62 |
| 3DNE | 0.34 | 5.25 | -127.86 | 13.33 | 0.053 | -114.53 |
| 3DNE | 0.23 | 5.28 | -124.31 | 13.40 | 0.054 | -110.91 |
| 3DNE | 0.30 | 5.26 | -125.61 | 14.37 | 0.057 | -111.24 |
| 3DNE | 0.35 | 5.25 | -125.99 | 14.54 | 0.058 | -111.45 |
| 3DNE | 0.34 | 5.26 | -126.76 | 15.59 | 0.062 | -111.17 |
| 3DNE | 0.32 | 5.25 | -127.23 | 15.55 | 0.062 | -111.68 |
| 3DNE | 0.30 | 5.25 | -125.50 | 14.32 | 0.057 | -111.19 |
| 3DNE | 0.30 | 5.25 | -124.65 | 13.77 | 0.055 | -110.88 |
| 3DNE | 0.32 | 5.25 | -125.98 | 14.36 | 0.057 | -111.62 |
| 3DNE | 0.35 | 5.25 | -124.49 | 13.48 | 0.054 | -111.01 |
| 3DNE | 0.29 | 5.25 | -125.92 | 14.29 | 0.057 | -111.63 |
| 3DND | 0.37 | 4.60 | -115.57 | 10.19 | 0.041 | -105.38 |
| 3DND | 0.34 | 4.60 | -115.90 | 10.38 | 0.042 | -105.52 |
| 3DND | 0.39 | 2.73 | -111.58 | 8.65 | 0.035 | -102.94 |
| 3DND | 0.37 | 2.57 | -111.09 | 8.30 | 0.033 | -102.80 |
| 3DND | 0.36 | 2.68 | -111.29 | 8.33 | 0.033 | -102.96 |
| 3DND | 0.39 | 2.69 | -111.24 | 8.34 | 0.033 | -102.89 |
| 3DND | 0.31 | 4.67 | -113.80 | 9.94 | 0.040 | -103.87 |
| 3DND | 0.26 | 4.88 | -109.28 | 8.89 | 0.036 | -100.39 |
| 3DND | 0.53 | 4.75 | -108.30 | 9.10 | 0.036 | -99.20 |
| 3DND | 0.34 | 4.66 | -113.98 | 10.28 | 0.041 | -103.69 |
| 3DND | 0.32 | 4.59 | -114.19 | 10.69 | 0.043 | -103.50 |
| 3DND | 0.60 | 5.16 | -111.64 | 13.32 | 0.053 | -98.32 |
| 3DND | 0.30 | 4.76 | -112.21 | 8.75 | 0.035 | -103.46 |
| 3DND | 0.35 | 4.63 | -113.97 | 10.40 | 0.042 | -103.57 |
| 3DND | 0.31 | 4.64 | -114.30 | 10.26 | 0.041 | -104.04 |
| 3DND | 0.34 | 4.61 | -113.91 | 10.01 | 0.040 | -103.90 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | LL1 | M77 | score | weighted | real | score |
| 3DNE | 0.47 | 7.78 | -111.19 | 25.12 | 0.100 | -86.06 |
| 3DNE | 5.11 | 4.90 | -107.36 | 22.91 | 0.092 | -84.45 |
| 3DNE | 0.27 | 6.01 | -117.84 | 30.29 | 0.121 | -87.55 |
| 3DNE | 0.46 | 7.85 | -119.14 | 32.20 | 0.129 | -86.94 |
| 3DNE | 0.50 | 7.81 | -110.64 | 24.85 | 0.099 | -85.78 |
| 3DNE | 0.43 | 6.70 | -116.94 | 27.47 | 0.110 | -89.47 |
| 3DNE | 0.25 | 3.54 | -106.15 | 25.72 | 0.103 | -80.43 |
| 3DNE | 0.23 | 6.02 | -110.66 | 28.23 | 0.113 | -82.43 |
| 3DNE | 0.34 | 0.45 | -120.76 | 28.04 | 0.112 | -92.72 |
| 3DNE | 0.51 | 7.75 | -104.20 | 24.13 | 0.097 | -80.07 |
| 3DNE | 0.26 | 5.97 | -110.87 | 28.47 | 0.114 | -82.40 |
| 3DNE | 0.33 | 0.49 | -120.32 | 27.53 | 0.110 | -92.78 |
| 3DNE | 0.29 | 0.49 | -120.66 | 27.88 | 0.112 | -92.77 |
| 3DNE | 0.49 | 8.11 | -115.27 | 30.86 | 0.123 | -84.41 |
| 3DNE | 0.30 | 0.48 | -120.24 | 27.53 | 0.110 | -92.70 |
| 3DNE | 0.32 | 0.52 | -120.89 | 28.36 | 0.113 | -92.53 |
| 1Q8W | 0.68 | 2.69 | -111.09 | 23.82 | 0.095 | -87.27 |
| 1Q8W | 0.93 | 0.78 | -123.85 | 22.00 | 0.088 | -101.84 |
| 1Q8W | 5.08 | 0.58 | -119.48 | 21.55 | 0.086 | -97.93 |
| 1Q8W | 5.09 | 1.37 | -113.23 | 18.34 | 0.073 | -94.89 |
| 1Q8W | 0.95 | 0.76 | -123.67 | 21.82 | 0.087 | -101.85 |
| 1Q8W | 6.45 | 0.81 | -110.50 | 24.68 | 0.099 | -85.81 |
| 1Q8W | 0.93 | 0.80 | -117.38 | 21.65 | 0.087 | -95.73 |
| 1Q8W | 0.93 | 0.79 | -117.83 | 21.94 | 0.088 | -95.89 |
| 1Q8W | 0.97 | 0.79 | -117.00 | 21.10 | 0.084 | -95.90 |
| 1Q8W | 0.94 | 0.78 | -117.58 | 21.71 | 0.087 | -95.86 |
| 1Q8W | 0.88 | 0.79 | -117.40 | 21.68 | 0.087 | -95.72 |
| 1Q8W | 0.90 | 0.77 | -117.60 | 21.75 | 0.087 | -95.85 |
| 1Q8W | 0.91 | 0.76 | -117.66 | 21.81 | 0.087 | -95.85 |
| 1Q8W | 0.93 | 0.81 | -118.03 | 22.21 | 0.089 | -95.82 |
| 1Q8W | 0.96 | 0.77 | -118.11 | 22.34 | 0.089 | -95.77 |
| 1Q8W | 0.91 | 0.75 | -117.52 | 21.77 | 0.087 | -95.75 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | LL1 | PTV | score | weighted | real | score |
| 3DNE | 0.53 | 8.01 | -127.24 | 31.33 | 0.125 | -95.90 |
| 3DNE | 0.29 | 4.81 | -126.10 | 24.98 | 0.100 | -101.13 |
| 3DNE | 5.10 | 7.84 | -125.31 | 29.84 | 0.119 | -95.47 |
| 3DNE | 0.35 | 8.58 | -125.53 | 25.37 | 0.101 | -100.16 |
| 3DNE | 0.55 | 7.58 | -125.83 | 30.12 | 0.120 | -95.71 |
| 3DNE | 3.71 | 7.56 | -106.72 | 24.04 | 0.096 | -82.67 |
| 3DNE | 0.31 | 1.51 | -139.54 | 36.18 | 0.145 | -103.36 |
| 3DNE | 0.33 | 10.03 | -120.73 | 30.68 | 0.123 | -90.05 |
| 3DNE | 0.26 | 1.03 | -143.37 | 36.41 | 0.146 | -106.96 |
| 3DNE | 0.28 | 1.48 | -141.01 | 36.84 | 0.147 | -104.17 |
| 3DNE | 0.26 | 1.48 | -141.46 | 36.31 | 0.145 | -105.16 |
| 3DNE | 0.26 | 1.32 | -145.09 | 39.06 | 0.156 | -106.03 |
| 3DNE | 0.26 | 1.53 | -138.57 | 38.80 | 0.155 | -99.77 |
| 3DNE | 0.60 | 7.82 | -121.89 | 30.86 | 0.123 | -91.03 |
| 3DNE | 0.27 | 10.09 | -120.74 | 28.83 | 0.115 | -91.92 |
| 3DNE | 0.55 | 7.97 | -116.07 | 26.07 | 0.104 | -90.00 |
| 4IJ9 | 5.15 | 8.50 | -126.26 | 28.87 | 0.115 | -97.39 |
| 4IJ9 | 0.82 | 5.57 | -133.37 | 23.93 | 0.096 | -109.44 |
| 4IJ9 | 5.15 | 8.47 | -124.93 | 26.37 | 0.105 | -98.56 |
| 4IJ9 | 0.84 | 5.56 | -123.57 | 26.10 | 0.104 | -97.47 |
| 4IJ9 | 10.86 | 8.14 | -114.78 | 30.55 | 0.122 | -84.24 |
| 4IJ9 | 0.54 | 4.07 | -127.40 | 42.08 | 0.168 | -85.32 |
| 4IJ9 | 0.60 | 1.30 | -146.02 | 40.77 | 0.163 | -105.25 |
| 4IJ9 | 10.66 | 8.70 | -106.08 | 32.15 | 0.129 | -73.93 |
| 4IJ9 | 0.67 | 1.31 | -143.61 | 39.52 | 0.158 | -104.10 |
| 4IJ9 | 10.74 | 8.44 | -116.45 | 29.40 | 0.118 | -87.06 |
| 4IJ9 | 5.10 | 5.39 | -119.93 | 27.87 | 0.111 | -92.06 |
| 4IJ9 | 0.54 | 1.72 | -134.00 | 41.96 | 0.168 | -92.04 |
| 4IJ9 | 5.13 | 6.13 | -117.13 | 23.57 | 0.094 | -93.57 |
| 4IJ9 | 0.66 | 1.29 | -144.01 | 38.80 | 0.155 | -105.21 |
| 4IJ9 | 10.96 | 8.44 | -107.79 | 27.22 | 0.109 | -80.57 |
| 4IJ9 | 0.52 | 1.75 | -133.80 | 42.29 | 0.169 | -91.51 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | LL1 | PZX | score | weighted | real | score |
| 3DNE | 0.39 | 4.70 | -120.49 | 17.41 | 0.070 | -103.08 |
| 3DNE | 5.10 | 3.44 | -120.02 | 19.25 | 0.077 | -100.77 |
| 3DNE | 0.34 | 3.32 | -126.20 | 19.86 | 0.079 | -106.34 |
| 3DNE | 0.29 | 3.35 | -126.27 | 14.09 | 0.056 | -112.18 |
| 3DNE | 0.35 | 2.99 | -120.58 | 13.71 | 0.055 | -106.87 |
| 3DNE | 0.30 | 3.25 | -126.47 | 13.85 | 0.055 | -112.62 |
| 3DNE | 5.11 | 4.43 | -112.57 | 20.74 | 0.083 | -91.83 |
| 3DNE | 0.41 | 4.09 | -114.19 | 15.83 | 0.063 | -98.36 |
| 3DNE | 5.11 | 6.93 | -109.78 | 19.00 | 0.076 | -90.78 |
| 3DNE | 5.12 | 7.24 | -107.90 | 17.47 | 0.070 | -90.43 |
| 3DNE | 0.44 | 4.26 | -113.82 | 16.56 | 0.066 | -97.26 |
| 3DNE | 0.38 | 4.10 | -114.79 | 16.77 | 0.067 | -98.02 |
| 3DNE | 0.34 | 3.99 | -114.65 | 16.26 | 0.065 | -98.39 |
| 3DNE | 0.49 | 3.03 | -118.65 | 24.05 | 0.096 | -94.61 |
| 3DNE | 0.36 | 4.08 | -114.27 | 15.79 | 0.063 | -98.48 |
| 3DNE | 0.42 | 4.01 | -114.05 | 17.48 | 0.070 | -96.57 |
| 4IE9 | 5.08 | 2.77 | -110.28 | 17.38 | 0.070 | -92.90 |
| 4IE9 | 2.60 | 2.66 | -119.89 | 19.78 | 0.079 | -100.12 |
| 4IE9 | 2.54 | 3.23 | -118.99 | 25.40 | 0.102 | -93.59 |
| 4IE9 | 2.64 | 5.25 | -109.03 | 13.65 | 0.055 | -95.38 |
| 4IE9 | 2.59 | 4.13 | -113.17 | 13.65 | 0.055 | -99.52 |
| 4IE9 | 5.13 | 5.20 | -112.18 | 20.79 | 0.083 | -91.39 |
| 4IE9 | 2.51 | 3.30 | -112.95 | 28.89 | 0.116 | -84.06 |
| 4IE9 | 2.59 | 2.27 | -106.97 | 21.05 | 0.084 | -85.92 |
| 4IE9 | 2.47 | 3.21 | -112.27 | 28.91 | 0.116 | -83.36 |
| 4IE9 | 5.12 | 4.82 | -107.36 | 19.60 | 0.078 | -87.76 |
| 4IE9 | 5.12 | 4.71 | -103.95 | 16.65 | 0.067 | -87.30 |
| 4IE9 | 0.41 | 1.04 | -112.80 | 21.33 | 0.085 | -91.47 |
| 4IE9 | 5.10 | 3.39 | -110.79 | 26.43 | 0.106 | -84.36 |
| 4IE9 | 2.37 | 3.16 | -103.90 | 22.80 | 0.091 | -81.10 |
| 4IE9 | 0.39 | 1.43 | -114.32 | 22.56 | 0.090 | -91.75 |
| 4IE9 | 0.54 | 3.66 | -104.78 | 20.98 | 0.084 | -83.81 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | LL2 | M77 | score | weighted | real | score |
| 3DND | 6.12 | 0.55 | -103.64 | 45.85 | 0.183 | -57.79 |
| 3DND | 2.23 | 2.95 | -80.14 | 29.89 | 0.120 | -50.25 |
| 3DND | 5.25 | 3.35 | -87.03 | 29.81 | 0.119 | -57.22 |
| 3DND | 6.38 | 6.22 | -83.54 | 26.12 | 0.104 | -57.42 |
| 3DND | 5.46 | 0.69 | -100.96 | 44.71 | 0.179 | -56.24 |
| 3DND | 5.33 | 5.55 | -107.84 | 33.68 | 0.135 | -74.15 |
| 3DND | 0.81 | 2.53 | -99.52 | 32.94 | 0.132 | -66.58 |
| 3DND | 6.23 | 0.81 | -92.83 | 39.27 | 0.157 | -53.56 |
| 3DND | 6.89 | 4.87 | -77.84 | 36.84 | 0.147 | -41.00 |
| 3DND | 0.94 | 2.81 | -98.92 | 31.21 | 0.125 | -67.70 |
| 3DND | 6.16 | 3.28 | -82.96 | 27.24 | 0.109 | -55.72 |
| 3DND | 5.76 | 3.41 | -82.78 | 34.12 | 0.136 | -48.66 |
| 3DND | 6.22 | 0.75 | -92.74 | 39.15 | 0.157 | -53.60 |
| 3DND | 5.78 | 5.32 | -81.42 | 42.30 | 0.169 | -39.12 |
| 3DND | 0.76 | 2.56 | -100.55 | 33.32 | 0.133 | -67.22 |
| 3DND | 0.92 | 2.79 | -98.56 | 30.60 | 0.122 | -67.97 |
| 1Q8W | 5.20 | 1.75 | -113.65 | 50.81 | 0.203 | -62.84 |
| 1Q8W | 5.34 | 1.78 | -112.20 | 50.01 | 0.200 | -62.19 |
| 1Q8W | 5.50 | 1.70 | -107.61 | 39.40 | 0.158 | -68.21 |
| 1Q8W | 7.18 | 3.50 | -92.00 | 35.00 | 0.140 | -57.00 |
| 1Q8W | 5.45 | 2.67 | -102.29 | 48.02 | 0.192 | -54.27 |
| 1Q8W | 8.82 | 2.31 | -90.05 | 28.59 | 0.114 | -61.46 |
| 1Q8W | 5.42 | 2.04 | -98.81 | 36.83 | 0.147 | -61.97 |
| 1Q8W | 5.45 | 2.04 | -98.87 | 37.10 | 0.148 | -61.77 |
| 1Q8W | 5.39 | 2.05 | -98.98 | 37.20 | 0.149 | -61.79 |
| 1Q8W | 5.42 | 2.06 | -99.35 | 38.70 | 0.155 | -60.65 |
| 1Q8W | 5.21 | 2.58 | -96.36 | 41.62 | 0.166 | -54.74 |
| 1Q8W | 5.43 | 2.04 | -98.04 | 36.27 | 0.145 | -61.77 |
| 1Q8W | 5.40 | 2.07 | -98.59 | 37.12 | 0.148 | -61.47 |
| 1Q8W | 5.39 | 2.07 | -98.60 | 36.93 | 0.148 | -61.67 |
| 1Q8W | 5.37 | 2.11 | -94.15 | 35.68 | 0.143 | -58.46 |
| 1Q8W | 5.42 | 5.38 | -89.81 | 37.88 | 0.152 | -51.93 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | LL2 | PTV | score | weighted | real | score |
| 3DND | 1.93 | 7.12 | -112.24 | 6.90 | 0.028 | -105.35 |
| 3DND | 3.09 | 7.08 | -114.02 | 8.29 | 0.033 | -105.73 |
| 3DND | 6.14 | 4.30 | -108.57 | 9.69 | 0.039 | -98.88 |
| 3DND | 5.29 | 4.26 | -124.50 | 6.80 | 0.027 | -117.70 |
| 3DND | 10.90 | 6.62 | -116.41 | 10.71 | 0.043 | -105.70 |
| 3DND | 5.40 | 6.67 | -125.06 | 11.05 | 0.044 | -114.01 |
| 3DND | 5.28 | 2.21 | -112.92 | 7.11 | 0.028 | -105.81 |
| 3DND | 5.24 | 4.34 | -118.48 | 8.22 | 0.033 | -110.26 |
| 3DND | 5.81 | 1.37 | -113.54 | 7.08 | 0.028 | -106.47 |
| 3DND | 5.22 | 1.82 | -123.59 | 8.68 | 0.035 | -114.91 |
| 3DND | 5.90 | 1.57 | -110.77 | 9.80 | 0.039 | -100.97 |
| 3DND | 5.22 | 1.74 | -120.41 | 6.89 | 0.028 | -113.52 |
| 3DND | 5.22 | 4.27 | -115.06 | 6.81 | 0.027 | -108.26 |
| 3DND | 5.77 | 1.88 | -105.74 | 7.10 | 0.028 | -98.63 |
| 3DND | 5.21 | 1.73 | -120.74 | 7.15 | 0.029 | -113.59 |
| 3DND | 1.50 | 3.69 | -106.93 | 12.49 | 0.050 | -94.43 |
| 4IJ9 | 6.37 | 6.74 | -108.05 | 11.87 | 0.047 | -96.18 |
| 4IJ9 | 5.88 | 8.27 | -116.43 | 11.47 | 0.046 | -104.96 |
| 4IJ9 | 5.46 | 1.80 | -124.37 | 9.23 | 0.037 | -115.13 |
| 4IJ9 | 6.97 | 8.72 | -121.10 | 14.57 | 0.058 | -106.53 |
| 4IJ9 | 10.66 | 5.90 | -106.30 | 13.58 | 0.054 | -92.72 |
| 4IJ9 | 10.92 | 4.42 | -122.71 | 10.78 | 0.043 | -111.92 |
| 4IJ9 | 5.23 | 7.97 | -127.99 | 13.73 | 0.055 | -114.26 |
| 4IJ9 | 5.28 | 4.13 | -114.54 | 8.22 | 0.033 | -106.31 |
| 4IJ9 | 5.29 | 1.83 | -115.62 | 11.22 | 0.045 | -104.40 |
| 4IJ9 | 5.18 | 1.32 | -126.86 | 14.86 | 0.059 | -112.00 |
| 4IJ9 | 10.40 | 8.20 | -115.64 | 9.99 | 0.040 | -105.65 |
| 4IJ9 | 0.94 | 8.04 | -124.42 | 13.10 | 0.052 | -111.31 |
| 4IJ9 | 0.96 | 8.04 | -125.01 | 13.60 | 0.054 | -111.42 |
| 4IJ9 | 5.41 | 1.21 | -120.03 | 12.64 | 0.051 | -107.39 |
| 4IJ9 | 5.58 | 4.13 | -106.15 | 8.18 | 0.033 | -97.96 |
| 4IJ9 | 5.42 | 1.37 | -122.32 | 14.26 | 0.057 | -108.06 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | LL2 | PZX | score | weighted | real | score |
| 3DND | 1.43 | 2.80 | -104.38 | 12.01 | 0.048 | -92.37 |
| 3DND | 1.39 | 2.54 | -110.66 | 15.66 | 0.063 | -94.99 |
| 3DND | 0.56 | 1.88 | -117.02 | 17.42 | 0.070 | -99.60 |
| 3DND | 1.44 | 2.68 | -105.14 | 12.72 | 0.051 | -92.42 |
| 3DND | 1.56 | 2.17 | -115.03 | 17.55 | 0.070 | -97.48 |
| 3DND | 1.18 | 3.49 | -110.45 | 17.57 | 0.070 | -92.88 |
| 3DND | 2.56 | 3.31 | -96.27 | 12.49 | 0.050 | -83.77 |
| 3DND | 4.72 | 1.94 | -96.77 | 12.62 | 0.050 | -84.14 |
| 3DND | 0.81 | 2.25 | -104.55 | 13.31 | 0.053 | -91.24 |
| 3DND | 1.33 | 0.55 | -108.34 | 15.20 | 0.061 | -93.13 |
| 3DND | 0.89 | 2.28 | -104.80 | 13.54 | 0.054 | -91.26 |
| 3DND | 0.90 | 2.30 | -104.52 | 13.32 | 0.053 | -91.20 |
| 3DND | 4.70 | 1.90 | -97.53 | 13.09 | 0.052 | -84.45 |
| 3DND | 0.88 | 2.27 | -105.24 | 13.53 | 0.054 | -91.71 |
| 3DND | 2.57 | 3.30 | -97.36 | 13.73 | 0.055 | -83.63 |
| 3DND | 0.89 | 2.21 | -104.50 | 13.51 | 0.054 | -91.00 |
| 4IE9 | 2.34 | 2.14 | -110.49 | 18.75 | 0.075 | -91.75 |
| 4IE9 | 2.74 | 3.72 | -104.05 | 19.13 | 0.077 | -84.92 |
| 4IE9 | 1.45 | 2.03 | -113.96 | 13.91 | 0.056 | -100.05 |
| 4IE9 | 1.35 | 3.22 | -116.47 | 13.24 | 0.053 | -103.23 |
| 4IE9 | 3.01 | 3.31 | -110.42 | 16.65 | 0.067 | -93.77 |
| 4IE9 | 2.59 | 3.49 | -98.68 | 10.47 | 0.042 | -88.21 |
| 4IE9 | 2.36 | 3.27 | -98.23 | 11.26 | 0.045 | -86.97 |
| 4IE9 | 1.42 | 2.48 | -91.89 | 16.06 | 0.064 | -75.83 |
| 4IE9 | 3.17 | 3.49 | -103.04 | 13.17 | 0.053 | -89.87 |
| 4IE9 | 2.35 | 3.26 | -98.96 | 11.85 | 0.047 | -87.11 |
| 4IE9 | 4.34 | 1.82 | -103.78 | 11.40 | 0.046 | -92.39 |
| 4IE9 | 5.23 | 3.95 | -102.21 | 21.45 | 0.086 | -80.77 |
| 4IE9 | 5.18 | 3.27 | -90.90 | 13.44 | 0.054 | -77.45 |
| 4IE9 | 5.84 | 5.14 | -92.78 | 13.02 | 0.052 | -79.76 |
| 4IE9 | 1.42 | 2.13 | -108.01 | 12.77 | 0.051 | -95.25 |
| 4IE9 | 5.22 | 3.90 | -101.49 | 20.75 | 0.083 | -80.75 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | M77 | PTV | score | weighted | real | score |
| 1Q8W | 0.64 | 1.54 | -134.02 | 19.62 | 0.078 | -114.41 |
| 1Q8W | 0.52 | 4.54 | -130.49 | 20.70 | 0.083 | -109.79 |
| 1Q8W | 2.85 | 7.48 | -110.99 | 11.13 | 0.045 | -99.85 |
| 1Q8W | 3.30 | 7.53 | -102.65 | 12.76 | 0.051 | -89.89 |
| 1Q8W | 7.89 | 3.18 | -109.14 | 16.56 | 0.066 | -92.57 |
| 1Q8W | 2.81 | 7.55 | -112.24 | 12.13 | 0.049 | -100.11 |
| 1Q8W | 0.72 | 1.22 | -125.29 | 24.25 | 0.097 | -101.04 |
| 1Q8W | 2.97 | 9.07 | -103.63 | 9.04 | 0.036 | -94.59 |
| 1Q8W | 0.73 | 1.51 | -120.52 | 22.95 | 0.092 | -97.58 |
| 1Q8W | 0.76 | 0.91 | -120.63 | 21.10 | 0.084 | -99.53 |
| 1Q8W | 0.95 | 1.50 | -121.32 | 15.58 | 0.062 | -105.74 |
| 1Q8W | 0.98 | 1.58 | -119.76 | 15.18 | 0.061 | -104.58 |
| 1Q8W | 2.86 | 2.60 | -103.62 | 18.98 | 0.076 | -84.63 |
| 1Q8W | 0.71 | 1.86 | -120.22 | 22.47 | 0.090 | -97.75 |
| 1Q8W | 1.86 | 8.09 | -106.57 | 17.77 | 0.071 | -88.80 |
| 1Q8W | 1.89 | 8.07 | -110.60 | 17.42 | 0.070 | -93.18 |
| 4IJ9 | 7.51 | 8.82 | -107.51 | 16.00 | 0.064 | -91.51 |
| 4IJ9 | 10.38 | 9.13 | -110.91 | 23.09 | 0.092 | -87.81 |
| 4IJ9 | 8.20 | 9.17 | -110.54 | 17.15 | 0.069 | -93.40 |
| 4IJ9 | 10.33 | 9.35 | -109.66 | 17.51 | 0.070 | -92.15 |
| 4IJ9 | 8.81 | 8.82 | -103.82 | 14.51 | 0.058 | -89.31 |
| 4IJ9 | 8.84 | 9.72 | -101.97 | 19.84 | 0.079 | -82.13 |
| 4IJ9 | 8.80 | 8.35 | -98.76 | 16.67 | 0.067 | -82.09 |
| 4IJ9 | 10.24 | 7.69 | -100.18 | 20.74 | 0.083 | -79.44 |
| 4IJ9 | 8.91 | 8.91 | -90.58 | 14.18 | 0.057 | -76.40 |
| 4IJ9 | 8.76 | 8.99 | -96.97 | 17.05 | 0.068 | -79.92 |
| 4IJ9 | 10.14 | 7.94 | -116.71 | 25.55 | 0.102 | -91.15 |
| 4IJ9 | 10.41 | 8.96 | -106.13 | 21.24 | 0.085 | -84.88 |
| 4IJ9 | 8.87 | 8.64 | -107.10 | 26.37 | 0.105 | -80.73 |
| 4IJ9 | 10.31 | 8.11 | -98.57 | 21.87 | 0.087 | -76.71 |
| 4IJ9 | 10.22 | 7.90 | -99.50 | 20.55 | 0.082 | -78.95 |
| 4IJ9 | 0.85 | 3.88 | -117.68 | 21.15 | 0.085 | -96.53 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | M77 | PZX | score | weighted | real | score |
| 1Q8W | 3.92 | 3.44 | -106.02 | 17.67 | 0.071 | -88.35 |
| 1Q8W | 7.94 | 4.68 | -101.63 | 23.90 | 0.096 | -77.73 |
| 1Q8W | 0.62 | 2.67 | -118.81 | 27.98 | 0.112 | -90.82 |
| 1Q8W | 1.84 | 2.85 | -111.31 | 16.89 | 0.068 | -94.42 |
| 1Q8W | 2.98 | 3.21 | -105.15 | 18.83 | 0.075 | -86.32 |
| 1Q8W | 1.72 | 2.51 | -117.28 | 24.60 | 0.098 | -92.68 |
| 1Q8W | 0.81 | 3.59 | -106.97 | 29.31 | 0.117 | -77.66 |
| 1Q8W | 1.72 | 2.98 | -113.69 | 25.42 | 0.102 | -88.28 |
| 1Q8W | 3.63 | 3.61 | -102.76 | 20.85 | 0.083 | -81.91 |
| 1Q8W | 1.72 | 2.98 | -114.26 | 25.75 | 0.103 | -88.50 |
| 1Q8W | 2.97 | 1.65 | -106.85 | 16.22 | 0.065 | -90.63 |
| 1Q8W | 4.11 | 3.78 | -106.26 | 23.33 | 0.093 | -82.93 |
| 1Q8W | 3.47 | 2.24 | -100.49 | 17.36 | 0.069 | -83.13 |
| 1Q8W | 1.74 | 2.93 | -112.62 | 24.04 | 0.096 | -88.58 |
| 1Q8W | 3.63 | 3.01 | -105.11 | 18.97 | 0.076 | -86.14 |
| 1Q8W | 3.63 | 3.03 | -105.87 | 19.33 | 0.077 | -86.54 |
| 4IE9 | 5.23 | 3.05 | -121.09 | 22.88 | 0.092 | -98.21 |
| 4IE9 | 0.72 | 2.97 | -127.15 | 34.51 | 0.138 | -92.64 |
| 4IE9 | 5.00 | 4.52 | -102.76 | 15.93 | 0.064 | -86.83 |
| 4IE9 | 4.79 | 3.20 | -107.53 | 19.57 | 0.078 | -87.96 |
| 4IE9 | 7.46 | 9.11 | -96.43 | 22.31 | 0.089 | -74.13 |
| 4IE9 | 4.44 | 5.26 | -105.24 | 14.74 | 0.059 | -90.50 |
| 4IE9 | 4.53 | 0.39 | -108.76 | 23.12 | 0.092 | -85.65 |
| 4IE9 | 4.12 | 3.39 | -99.65 | 21.89 | 0.088 | -77.77 |
| 4IE9 | 4.76 | 3.61 | -104.05 | 24.04 | 0.096 | -80.01 |
| 4IE9 | 3.99 | 3.26 | -101.52 | 21.19 | 0.085 | -80.33 |
| 4IE9 | 3.96 | 3.26 | -101.13 | 20.85 | 0.083 | -80.28 |
| 4IE9 | 4.80 | 2.90 | -102.28 | 21.87 | 0.087 | -80.40 |
| 4IE9 | 3.76 | 3.19 | -103.78 | 23.14 | 0.093 | -80.64 |
| 4IE9 | 3.96 | 3.22 | -102.81 | 16.82 | 0.067 | -85.99 |
| 4IE9 | 5.06 | 3.24 | -97.58 | 20.60 | 0.082 | -76.98 |
| 4IE9 | 3.34 | 3.28 | -101.36 | 17.68 | 0.071 | -83.68 |

| protein | RMSD | | ChemPLP | INPHARMA score | | Total |
|---|---|---|---|---|---|---|
| | PTV | PZX | score | weighted | real | score |
| 4IJ9 | 8.67 | 5.57 | -117.14 | 12.09 | 0.048 | -105.05 |
| 4IJ9 | 9.56 | 6.83 | -115.87 | 11.21 | 0.045 | -104.65 |
| 4IJ9 | 7.99 | 8.36 | -136.44 | 20.40 | 0.082 | -116.04 |
| 4IJ9 | 9.42 | 8.24 | -130.45 | 16.06 | 0.064 | -114.40 |
| 4IJ9 | 8.23 | 10.10 | -101.93 | 14.63 | 0.059 | -87.31 |
| 4IJ9 | 8.62 | 9.68 | -111.77 | 19.38 | 0.078 | -92.39 |
| 4IJ9 | 8.45 | 7.80 | -105.91 | 9.89 | 0.040 | -96.02 |
| 4IJ9 | 8.26 | 9.95 | -121.17 | 17.48 | 0.070 | -103.69 |
| 4IJ9 | 7.91 | 10.01 | -112.62 | 16.52 | 0.066 | -96.11 |
| 4IJ9 | 7.73 | 7.64 | -104.52 | 17.98 | 0.072 | -86.54 |
| 4IJ9 | 7.96 | 8.60 | -110.04 | 16.08 | 0.064 | -93.96 |
| 4IJ9 | 7.98 | 9.87 | -114.38 | 16.37 | 0.065 | -98.01 |
| 4IJ9 | 5.54 | 5.36 | -98.26 | 18.11 | 0.072 | -80.15 |
| 4IJ9 | 7.83 | 3.27 | -101.13 | 14.37 | 0.057 | -86.76 |
| 4IJ9 | 8.37 | 9.01 | -111.29 | 15.09 | 0.060 | -96.20 |
| 4IJ9 | 5.21 | 3.21 | -106.47 | 18.51 | 0.074 | -87.97 |
| 4IE9 | 9.11 | 7.80 | -112.36 | 16.18 | 0.065 | -96.17 |
| 4IE9 | 6.46 | 7.95 | -122.72 | 18.51 | 0.074 | -104.22 |
| 4IE9 | 5.98 | 3.64 | -105.88 | 11.37 | 0.045 | -94.50 |
| 4IE9 | 8.29 | 2.04 | -105.74 | 12.28 | 0.049 | -93.46 |
| 4IE9 | 8.12 | 9.09 | -119.65 | 15.24 | 0.061 | -104.41 |
| 4IE9 | 7.08 | 5.88 | -125.86 | 14.99 | 0.060 | -110.87 |
| 4IE9 | 8.00 | 9.13 | -115.75 | 14.75 | 0.059 | -101.01 |
| 4IE9 | 8.72 | 8.27 | -98.41 | 12.61 | 0.050 | -85.81 |
| 4IE9 | 2.09 | 3.58 | -115.97 | 19.37 | 0.077 | -96.60 |
| 4IE9 | 8.58 | 3.27 | -108.40 | 13.41 | 0.054 | -95.00 |
| 4IE9 | 8.58 | 3.09 | -103.22 | 13.54 | 0.054 | -89.68 |
| 4IE9 | 2.06 | 3.52 | -123.87 | 17.55 | 0.070 | -106.32 |
| 4IE9 | 7.10 | 9.14 | -104.71 | 10.11 | 0.040 | -94.60 |
| 4IE9 | 2.04 | 4.23 | -108.45 | 15.63 | 0.063 | -92.82 |
| 4IE9 | 8.08 | 9.12 | -110.11 | 15.86 | 0.063 | -94.25 |
| 4IE9 | 6.76 | 7.01 | -106.52 | 11.99 | 0.048 | -94.53 |

**Table S3:** ChemPLP-INPHARMA docking results for the optimized setup (scoring function $S_2$). Weights of 250 and 50 were used for the INPHARMA and trNOE score, respectively. RMSD values below 2 Å are shown in green.

| protein | RMSD LL1 | RMSD LL2 | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| 3DNE | 0.25 | 1.99 | -119.71 | 14.18 | -105.53 |
| 3DNE | 0.27 | 2.03 | -120.14 | 14.40 | -105.74 |
| 3DNE | 0.26 | 1.99 | -120.28 | 14.33 | -105.95 |
| 3DNE | 0.30 | 2.00 | -119.67 | 13.88 | -105.79 |
| 3DNE | 0.31 | 1.97 | -120.43 | 14.57 | -105.87 |
| 3DNE | 0.32 | 1.95 | -120.02 | 14.25 | -105.77 |
| 3DNE | 0.27 | 2.02 | -120.56 | 14.84 | -105.72 |
| 3DNE | 0.27 | 1.98 | -119.61 | 13.95 | -105.66 |
| 3DNE | 0.32 | 2.00 | -119.63 | 13.95 | -105.67 |
| 3DNE | 0.32 | 2.00 | -119.30 | 13.73 | -105.58 |
| 3DND | 0.33 | 4.86 | -112.30 | 13.80 | -98.50 |
| 3DND | 0.37 | 4.68 | -113.40 | 15.19 | -98.21 |
| 3DND | 0.34 | 4.67 | -113.56 | 15.19 | -98.36 |
| 3DND | 0.43 | 4.69 | -113.42 | 15.68 | -97.74 |
| 3DND | 0.34 | 4.64 | -113.19 | 15.04 | -98.15 |
| 3DND | 0.30 | 4.65 | -113.73 | 15.05 | -98.68 |
| 3DND | 0.34 | 4.63 | -114.05 | 15.33 | -98.71 |
| 3DND | 0.38 | 4.66 | -113.85 | 15.26 | -98.60 |
| 3DND | 0.35 | 4.67 | -114.01 | 15.33 | -98.68 |
| 3DND | 0.36 | 4.61 | -113.55 | 15.46 | -98.09 |

| protein | RMSD LL1 | RMSD M77 | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| 3DNE | 0.46 | 8.10 | -115.33 | 32.61 | -82.72 |
| 3DNE | 0.33 | 0.51 | -120.46 | 29.13 | -91.32 |
| 3DNE | 0.22 | 5.96 | -110.96 | 31.22 | -79.74 |
| 3DNE | 0.32 | 0.48 | -120.77 | 29.52 | -91.24 |
| 3DNE | 0.46 | 7.83 | -112.93 | 33.27 | -79.66 |
| 3DNE | 0.32 | 0.47 | -121.12 | 29.65 | -91.47 |
| 3DNE | 0.46 | 7.83 | -113.55 | 33.92 | -79.63 |
| 3DNE | 0.49 | 8.09 | -115.25 | 32.66 | -82.58 |
| 3DNE | 0.51 | 8.12 | -114.43 | 31.86 | -82.57 |
| 3DNE | 0.47 | 7.82 | -113.14 | 33.54 | -79.60 |
| 1Q8W | 0.93 | 0.77 | -117.96 | 23.82 | -94.15 |
| 1Q8W | 0.90 | 0.77 | -117.84 | 23.82 | -94.02 |
| 1Q8W | 0.95 | 0.79 | -117.67 | 23.63 | -94.04 |
| 1Q8W | 0.95 | 0.80 | -117.55 | 23.49 | -94.06 |
| 1Q8W | 0.97 | 0.76 | -117.74 | 23.73 | -94.01 |
| 1Q8W | 0.89 | 0.79 | -118.01 | 23.99 | -94.02 |
| 1Q8W | 0.93 | 0.79 | -117.39 | 23.31 | -94.09 |
| 1Q8W | 0.96 | 0.75 | -117.47 | 23.45 | -94.01 |
| 1Q8W | 0.91 | 0.78 | -117.52 | 23.44 | -94.08 |
| 1Q8W | 0.93 | 0.79 | -117.52 | 23.48 | -94.05 |

| protein | RMSD LL1 | RMSD PTV | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| 3DNE | 0.30 | 1.47 | -147.87 | 39.07 | -108.81 |
| 3DNE | 0.24 | 1.57 | -144.69 | 40.91 | -103.78 |
| 3DNE | 0.26 | 1.32 | -149.59 | 40.07 | -109.52 |
| 3DNE | 5.10 | 7.73 | -113.80 | 28.88 | -84.93 |
| 3DNE | 0.25 | 1.46 | -148.55 | 40.99 | -107.56 |
| 3DNE | 0.28 | 1.30 | -149.28 | 41.10 | -108.18 |
| 3DNE | 0.26 | 1.33 | -150.08 | 41.62 | -108.46 |
| 3DNE | 0.29 | 1.27 | -143.24 | 38.66 | -104.58 |
| 3DNE | 0.55 | 7.88 | -116.34 | 27.88 | -88.45 |
| 3DNE | 0.53 | 7.89 | -121.46 | 33.08 | -88.38 |
| 4IJ9 | 0.62 | 1.33 | -146.77 | 43.07 | -103.70 |
| 4IJ9 | 0.76 | 1.07 | -147.54 | 42.26 | -105.27 |
| 4IJ9 | 0.67 | 3.87 | -127.57 | 38.91 | -88.66 |
| 4IJ9 | 0.72 | 3.91 | -131.00 | 34.26 | -96.74 |
| 4IJ9 | 0.54 | 8.62 | -120.39 | 28.85 | -91.54 |
| 4IJ9 | 0.68 | 1.02 | -148.90 | 40.97 | -107.92 |
| 4IJ9 | 0.66 | 1.01 | -145.10 | 47.48 | -97.62 |
| 4IJ9 | 5.11 | 6.88 | -99.85 | 29.25 | -70.60 |
| 4IJ9 | 0.66 | 1.48 | -138.20 | 45.68 | -92.52 |
| 4IJ9 | 10.99 | 8.75 | -107.92 | 28.77 | -79.15 |

| protein | RMSD LL1 | RMSD PZX | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| 3DNE | 5.11 | 4.62 | -112.31 | 23.88 | -88.43 |
| 3DNE | 0.42 | 4.08 | -114.10 | 21.56 | -92.53 |
| 3DNE | 5.11 | 7.28 | -106.72 | 20.58 | -86.14 |
| 3DNE | 0.38 | 4.12 | -113.66 | 21.17 | -92.50 |
| 3DNE | 9.33 | 3.24 | -108.63 | 26.31 | -82.32 |
| 3DNE | 5.11 | 7.02 | -108.51 | 21.22 | -87.30 |
| 3DNE | 5.11 | 7.31 | -108.46 | 21.11 | -87.35 |
| 3DNE | 0.27 | 3.02 | -114.63 | 24.55 | -90.08 |
| 3DNE | 0.40 | 4.07 | -114.18 | 21.88 | -92.30 |
| 3DNE | 5.12 | 4.61 | -111.81 | 23.35 | -88.46 |
| 4IE9 | 5.12 | 4.81 | -105.68 | 21.38 | -84.30 |
| 4IE9 | 0.42 | 1.02 | -112.86 | 26.09 | -86.78 |
| 4IE9 | 0.44 | 1.02 | -112.91 | 26.57 | -86.34 |
| 4IE9 | 5.12 | 4.75 | -104.97 | 21.25 | -83.71 |
| 4IE9 | 2.52 | 5.50 | -99.59 | 20.50 | -79.08 |
| 4IE9 | 5.29 | 2.02 | -102.78 | 19.75 | -83.03 |
| 4IE9 | 5.12 | 5.21 | -108.14 | 25.17 | -82.97 |
| 4IE9 | 0.38 | 1.03 | -112.41 | 25.65 | -86.76 |
| 4IE9 | 5.12 | 4.67 | -108.15 | 25.16 | -82.99 |
| 4IE9 | 0.40 | 1.00 | -113.71 | 26.77 | -86.94 |

| protein | RMSD | | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| | LL2 | M77 | | | |
| 3DND | 9.57 | 5.78 | -69.57 | 26.24 | -43.33 |
| 3DND | 5.35 | 3.10 | -97.97 | 46.27 | -51.70 |
| 3DND | 5.35 | 3.04 | -98.78 | 47.39 | -51.39 |
| 3DND | 5.20 | 3.36 | -96.36 | 44.42 | -51.94 |
| 3DND | 0.73 | 2.86 | -92.04 | 37.10 | -54.94 |
| 3DND | 7.72 | 3.24 | -78.75 | 27.53 | -51.22 |
| 3DND | 5.34 | 4.95 | -98.90 | 38.45 | -60.45 |
| 3DND | 5.52 | 3.37 | -84.93 | 33.83 | -51.10 |
| 3DND | 0.78 | 2.54 | -100.93 | 34.99 | -65.94 |
| 3DND | 6.26 | 4.07 | -85.42 | 35.85 | -49.57 |
| 1Q8W | 5.40 | 2.07 | -99.08 | 39.61 | -59.47 |
| 1Q8W | 4.87 | 6.34 | -71.18 | 32.45 | -38.74 |
| 1Q8W | 5.17 | 1.70 | -105.44 | 46.41 | -59.03 |
| 1Q8W | 5.20 | 0.57 | -106.86 | 47.04 | -59.81 |
| 1Q8W | 5.21 | 0.63 | -107.03 | 47.72 | -59.32 |
| 1Q8W | 5.55 | 0.79 | -104.02 | 50.91 | -53.10 |
| 1Q8W | 5.11 | 0.48 | -106.20 | 47.30 | -58.91 |
| 1Q8W | 5.19 | 0.59 | -108.15 | 48.02 | -60.13 |
| 1Q8W | 7.78 | 2.07 | -86.38 | 37.39 | -48.99 |
| 1Q8W | 5.10 | 0.72 | -106.92 | 47.45 | -59.48 |

| protein | RMSD | | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| | LL2 | PTV | | | |
| 3DND | 5.86 | 1.52 | -111.89 | 8.70 | -103.20 |
| 3DND | 5.39 | 2.14 | -108.60 | 11.30 | -97.30 |
| 3DND | 5.31 | 2.09 | -110.38 | 10.73 | -99.65 |
| 3DND | 5.18 | 2.06 | -116.67 | 13.60 | -103.08 |
| 3DND | 6.05 | 4.37 | -105.39 | 11.15 | -94.25 |
| 3DND | 5.22 | 1.73 | -123.20 | 10.17 | -113.04 |
| 3DND | 5.11 | 1.64 | -115.84 | 8.91 | -106.93 |
| 3DND | 5.22 | 1.83 | -122.72 | 10.42 | -112.31 |
| 3DND | 1.56 | 1.45 | -124.47 | 15.87 | -108.60 |
| 3DND | 5.28 | 2.08 | -114.20 | 9.51 | -104.69 |
| 4IJ9 | 5.37 | 2.20 | -122.30 | 15.53 | -106.76 |
| 4IJ9 | 5.47 | 1.95 | -118.34 | 15.10 | -103.24 |
| 4IJ9 | 5.20 | 1.91 | -120.38 | 10.64 | -109.75 |
| 4IJ9 | 5.43 | 2.00 | -121.03 | 12.59 | -108.44 |
| 4IJ9 | 5.48 | 1.86 | -122.62 | 14.07 | -108.55 |
| 4IJ9 | 5.59 | 1.88 | -117.47 | 11.72 | -105.75 |
| 4IJ9 | 11.35 | 1.09 | -126.72 | 28.77 | -97.95 |
| 4IJ9 | 5.29 | 1.47 | -117.46 | 11.09 | -106.37 |
| 4IJ9 | 5.29 | 1.55 | -116.93 | 11.56 | -105.37 |
| 4IJ9 | 1.59 | 7.84 | -117.45 | 9.26 | -108.19 |

| protein | RMSD LL2 | RMSD PZX | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| 3DND | 2.71 | 3.76 | -100.45 | 16.82 | -83.63 |
| 3DND | 1.41 | 1.52 | -103.98 | 16.96 | -87.02 |
| 3DND | 1.37 | 1.47 | -103.49 | 16.55 | -86.93 |
| 3DND | 5.21 | 3.87 | -95.29 | 20.77 | -74.51 |
| 3DND | 0.86 | 2.21 | -104.74 | 17.75 | -86.99 |
| 3DND | 1.31 | 2.26 | -103.56 | 16.94 | -86.61 |
| 3DND | 0.87 | 2.32 | -104.78 | 17.79 | -86.98 |
| 3DND | 0.87 | 2.25 | -105.11 | 18.02 | -87.10 |
| 3DND | 0.86 | 2.30 | -105.43 | 18.28 | -87.15 |
| 3DND | 2.73 | 3.79 | -100.91 | 16.81 | -84.10 |
| 4IE9 | 2.38 | 3.25 | -99.25 | 16.81 | -82.43 |
| 4IE9 | 5.19 | 4.96 | -97.34 | 23.55 | -73.79 |
| 4IE9 | 2.09 | 2.18 | -94.42 | 17.22 | -77.20 |
| 4IE9 | 1.42 | 2.14 | -107.91 | 16.72 | -91.19 |
| 4IE9 | 1.41 | 0.33 | -114.05 | 22.93 | -91.12 |
| 4IE9 | 5.81 | 4.68 | -88.63 | 15.30 | -73.33 |
| 4IE9 | 1.44 | 2.15 | -109.47 | 18.10 | -91.37 |
| 4IE9 | 1.38 | 2.15 | -109.32 | 17.96 | -91.36 |
| 4IE9 | 2.35 | 3.24 | -98.58 | 16.51 | -82.07 |
| 4IE9 | 3.19 | 3.35 | -103.31 | 18.06 | -85.25 |

| protein | RMSD M77 | RMSD PTV | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| 1Q8W | 1.82 | 1.21 | -122.94 | 23.37 | -99.57 |
| 1Q8W | 0.97 | 1.85 | -116.22 | 16.32 | -99.89 |
| 1Q8W | 1.01 | 1.83 | -116.01 | 16.25 | -99.76 |
| 1Q8W | 1.80 | 8.19 | -110.42 | 17.84 | -92.57 |
| 1Q8W | 2.89 | 7.78 | -102.51 | 13.62 | -88.89 |
| 1Q8W | 0.77 | 0.97 | -125.16 | 24.51 | -100.65 |
| 1Q8W | 2.68 | 2.17 | -109.29 | 27.15 | -82.14 |
| 1Q8W | 0.42 | 4.24 | -115.23 | 24.19 | -91.04 |
| 1Q8W | 0.79 | 7.81 | -108.08 | 24.05 | -84.03 |
| 1Q8W | 1.85 | 1.05 | -117.19 | 19.06 | -98.13 |
| 4IJ9 | 10.25 | 9.24 | -89.28 | 22.34 | -66.94 |
| 4IJ9 | 9.78 | 8.58 | -93.58 | 24.03 | -69.56 |
| 4IJ9 | 0.65 | 1.74 | -124.77 | 25.40 | -99.37 |
| 4IJ9 | 8.61 | 8.79 | -87.99 | 17.46 | -70.53 |
| 4IJ9 | 10.31 | 10.22 | -92.39 | 24.69 | -67.69 |
| 4IJ9 | 0.62 | 0.75 | -122.63 | 26.09 | -96.55 |
| 4IJ9 | 0.81 | 3.82 | -121.86 | 23.45 | -98.41 |
| 4IJ9 | 0.91 | 3.88 | -121.87 | 22.95 | -98.92 |
| 4IJ9 | 10.57 | 6.77 | -86.77 | 19.84 | -66.93 |
| 4IJ9 | 7.83 | 8.85 | -91.32 | 16.44 | -74.88 |

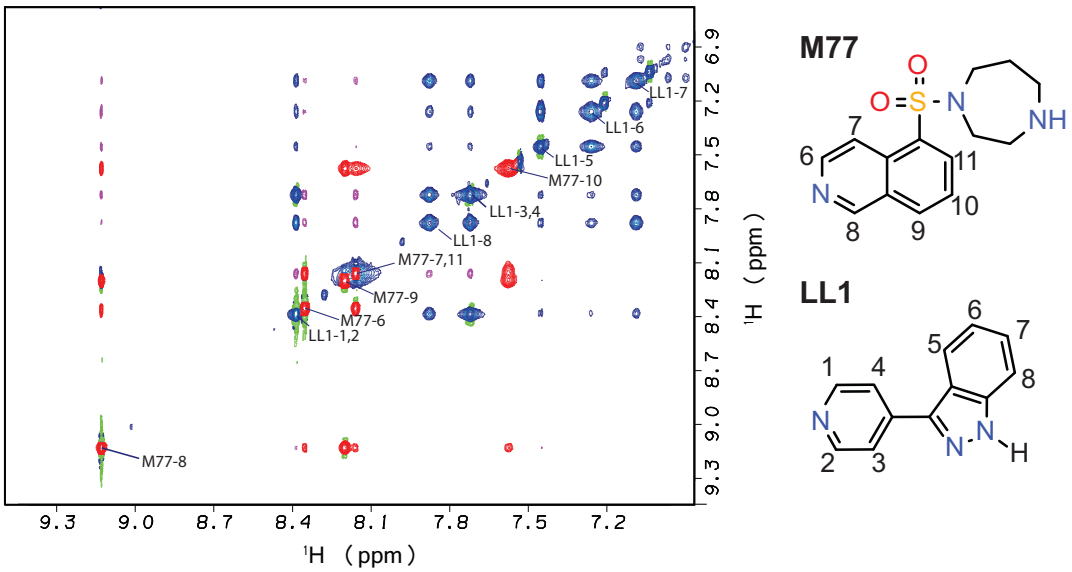
| protein | RMSD | | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| | M77 | PZX | | | |
| 1Q8W | 2.62 | 3.65 | -103.20 | 26.84 | -76.36 |
| 1Q8W | 3.93 | 3.04 | -100.53 | 24.82 | -75.71 |
| 1Q8W | 2.99 | 4.02 | -101.74 | 23.80 | -77.94 |
| 1Q8W | 2.99 | 1.66 | -106.49 | 18.94 | -87.56 |
| 1Q8W | 1.79 | 2.90 | -115.72 | 24.78 | -90.94 |
| 1Q8W | 1.74 | 2.90 | -117.64 | 27.09 | -90.54 |
| 1Q8W | 3.65 | 2.99 | -110.11 | 23.24 | -86.87 |
| 1Q8W | 0.74 | 3.78 | -114.09 | 33.06 | -81.04 |
| 1Q8W | 1.80 | 2.97 | -109.17 | 28.69 | -80.48 |
| 1Q8W | 2.87 | 2.45 | -96.25 | 22.34 | -73.91 |
| 4IE9 | 4.79 | 5.04 | -96.04 | 20.31 | -75.73 |
| 4IE9 | 4.94 | 5.19 | -96.47 | 18.46 | -78.01 |
| 4IE9 | 4.81 | 5.21 | -98.47 | 21.48 | -77.00 |
| 4IE9 | 4.47 | 0.39 | -107.19 | 25.61 | -81.58 |
| 4IE9 | 5.43 | 2.98 | -107.86 | 31.44 | -76.42 |
| 4IE9 | 4.74 | 5.09 | -93.14 | 29.01 | -64.13 |
| 4IE9 | 4.82 | 5.10 | -95.50 | 19.73 | -75.77 |
| 4IE9 | 4.51 | 4.90 | -89.51 | 22.85 | -66.66 |
| 4IE9 | 4.21 | 3.29 | -105.05 | 25.33 | -79.73 |
| 4IE9 | 5.47 | 2.93 | -106.78 | 29.92 | -76.85 |

| protein | RMSD | | ChemPLP score | INPHARMA + trNOE | Total score |
|---|---|---|---|---|---|
| | PTV | PZX | | | |
| 4IJ9 | 8.04 | 10.40 | -116.13 | 21.77 | -94.37 |
| 4IJ9 | 9.48 | 5.87 | -100.90 | 15.18 | -85.71 |
| 4IJ9 | 5.19 | 3.28 | -124.70 | 25.24 | -99.46 |
| 4IJ9 | 5.12 | 8.49 | -101.19 | 19.63 | -81.57 |
| 4IJ9 | 8.00 | 8.36 | -122.83 | 20.47 | -102.36 |
| 4IJ9 | 10.50 | 9.95 | -95.54 | 18.42 | -77.12 |
| 4IJ9 | 8.74 | 7.85 | -102.56 | 23.14 | -79.42 |
| 4IJ9 | 6.63 | 3.57 | -96.35 | 20.97 | -75.38 |
| 4IJ9 | 8.16 | 10.04 | -113.11 | 21.97 | -91.14 |
| 4IJ9 | 7.94 | 9.53 | -115.87 | 19.67 | -96.20 |
| 4IE9 | 3.45 | 1.72 | -111.13 | 17.97 | -93.16 |
| 4IE9 | 1.94 | 0.40 | -120.90 | 22.28 | -98.63 |
| 4IE9 | 6.44 | 7.38 | -101.41 | 14.87 | -86.55 |
| 4IE9 | 2.41 | 3.37 | -121.74 | 20.82 | -100.92 |
| 4IE9 | 7.84 | 7.15 | -84.96 | 12.18 | -72.78 |
| 4IE9 | 7.50 | 9.79 | -108.13 | 20.40 | -87.73 |
| 4IE9 | 8.25 | 9.11 | -103.20 | 17.41 | -85.79 |
| 4IE9 | 2.64 | 3.38 | -110.27 | 23.93 | -86.34 |
| 4IE9 | 8.13 | 8.28 | -110.81 | 17.37 | -93.44 |
| 4IE9 | 8.10 | 9.51 | -97.28 | 22.11 | -75.16 |

## Supplementary Figures

**Figure S1:** Spectral excerpt from two 700 ms INPHARMA NOESY for the ligand pairs LL1-M77 a) and LL1-PTV b) showing the aromatic region. Red and blue areas evidence respectively intra-ligand signals from M77 or PTV and LL1; purple areas evidence INPHARMA signals whereas gray areas indicate non interacting impurities present in the sample.

a)




b)

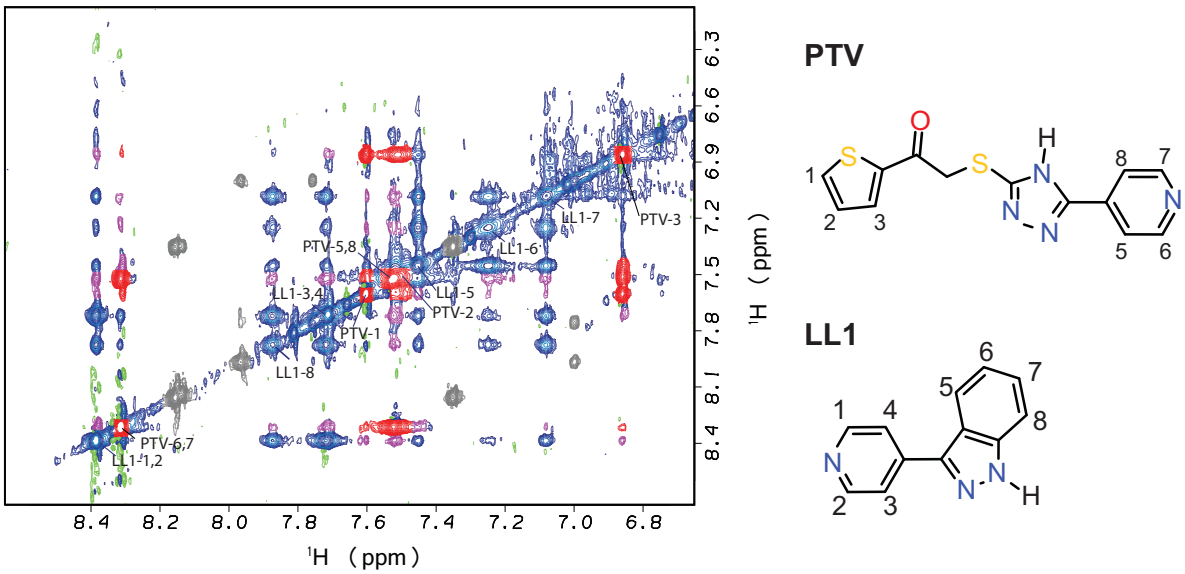


**Figure S2:** Poses of the pair LL1 (left) and LL2 (right) ranked highest by scoring function $S_1$ in the protein structures 3DNE (up) and 3DND (bottom).

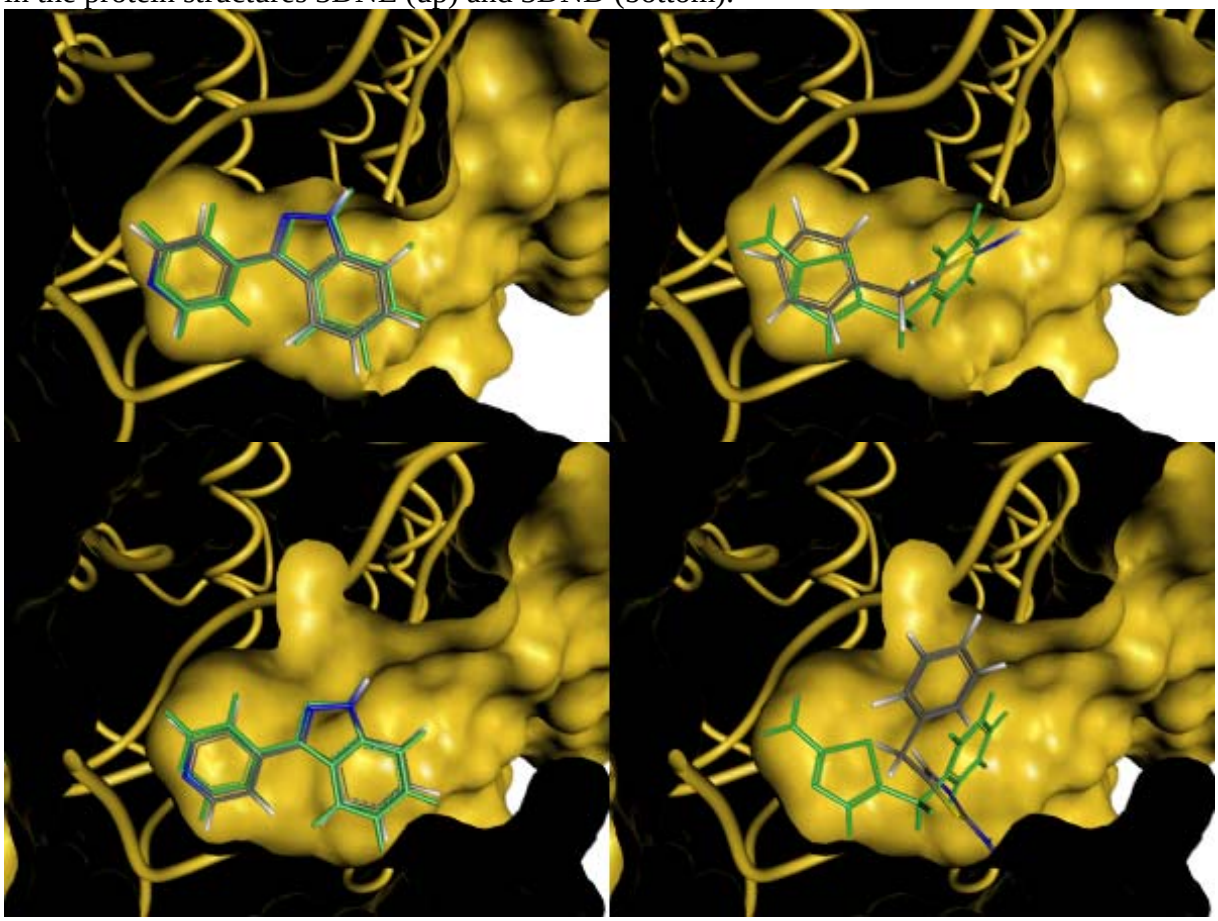


**Figure S3:** Poses of the pair LL1 (left) and M77 (right) ranked highest by scoring function $S_1$ in the protein structures 3DNE (up) and 1Q8W (bottom).

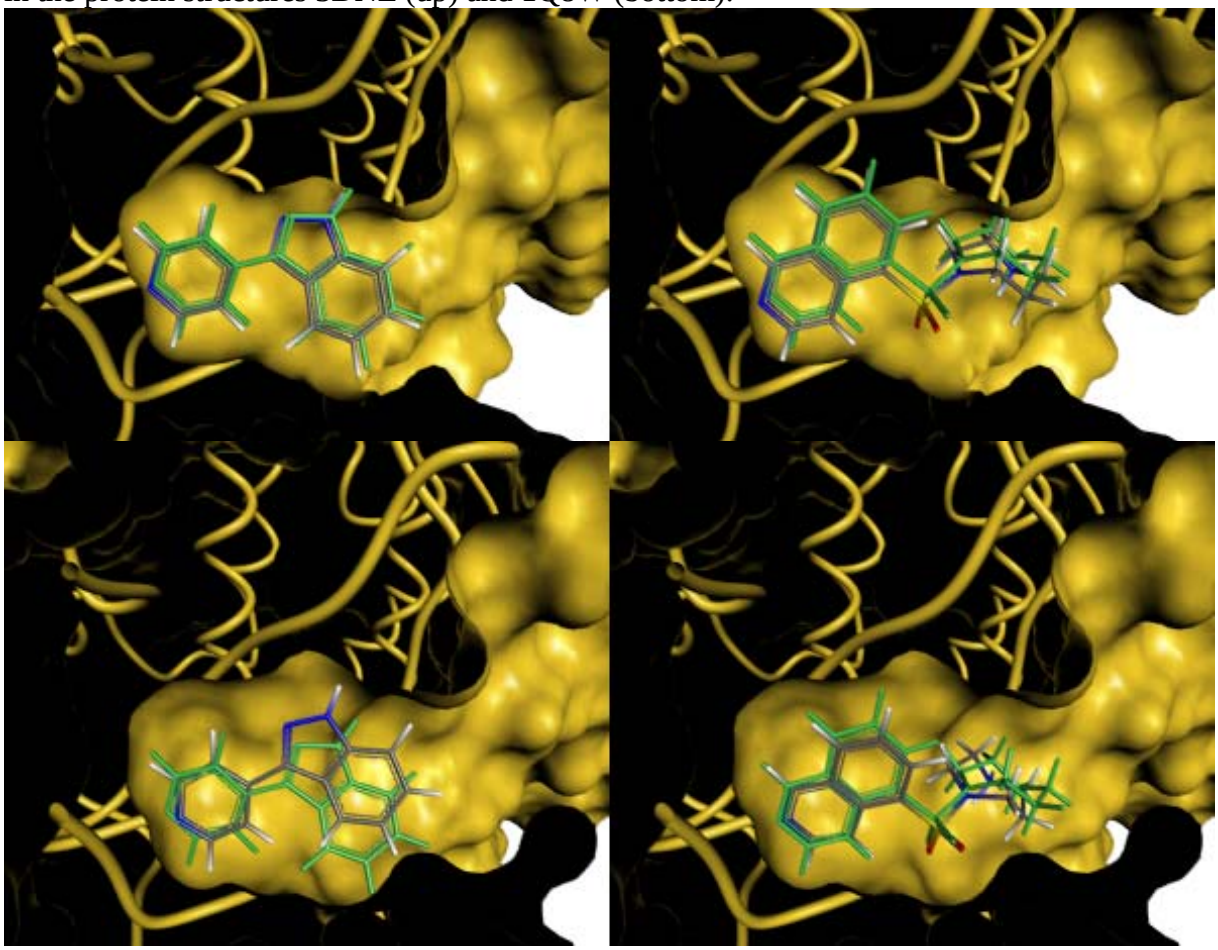


**Figure S4:** Poses of the pair LL1 (left) and PTV (right) ranked highest by scoring function $S_1$ in the protein structures 3DNE (up) and 4IJ9 (bottom).

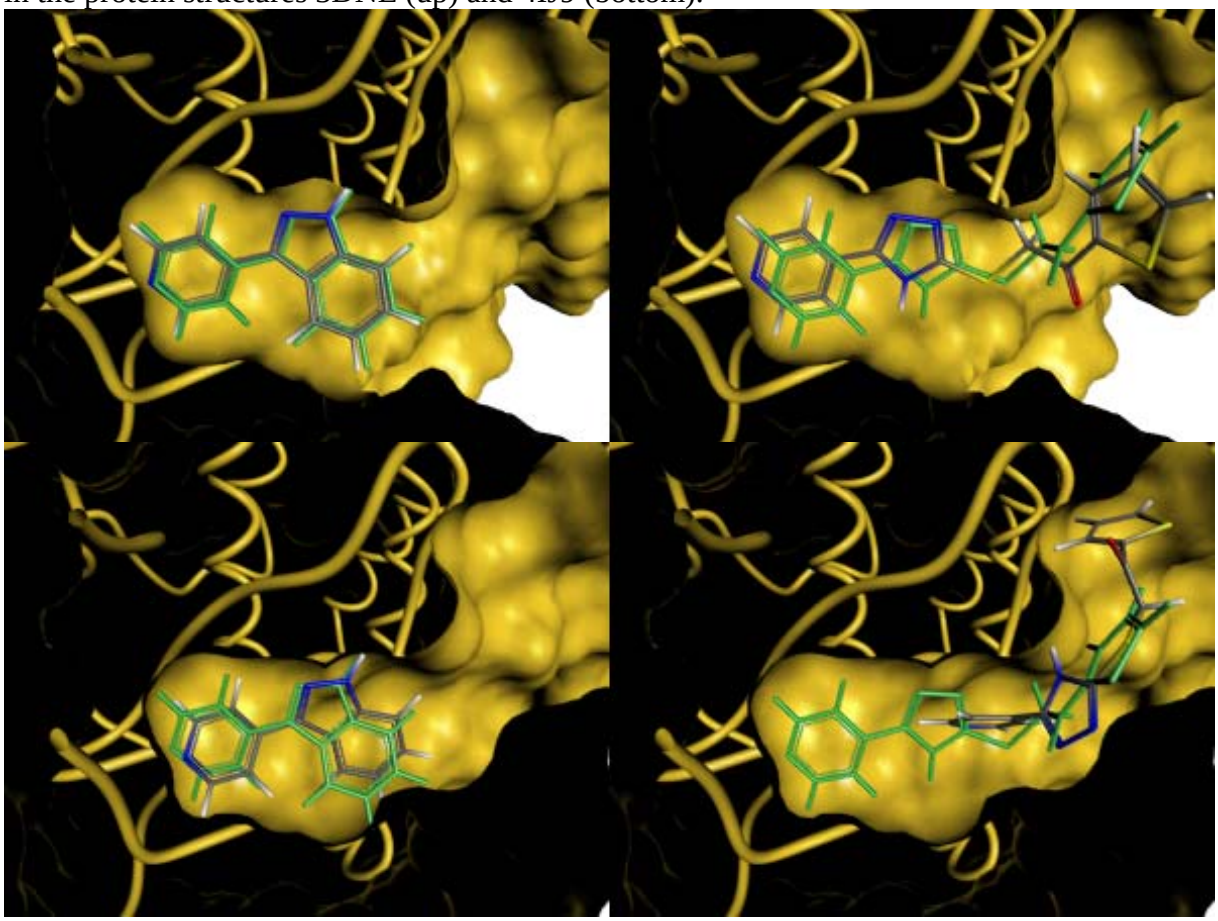


**Figure S5:** Poses of the pair LL1 (left) and PZX (right) ranked highest by scoring function $S_1$ in the protein structures 3DNE (up) and 4IE9 (bottom).

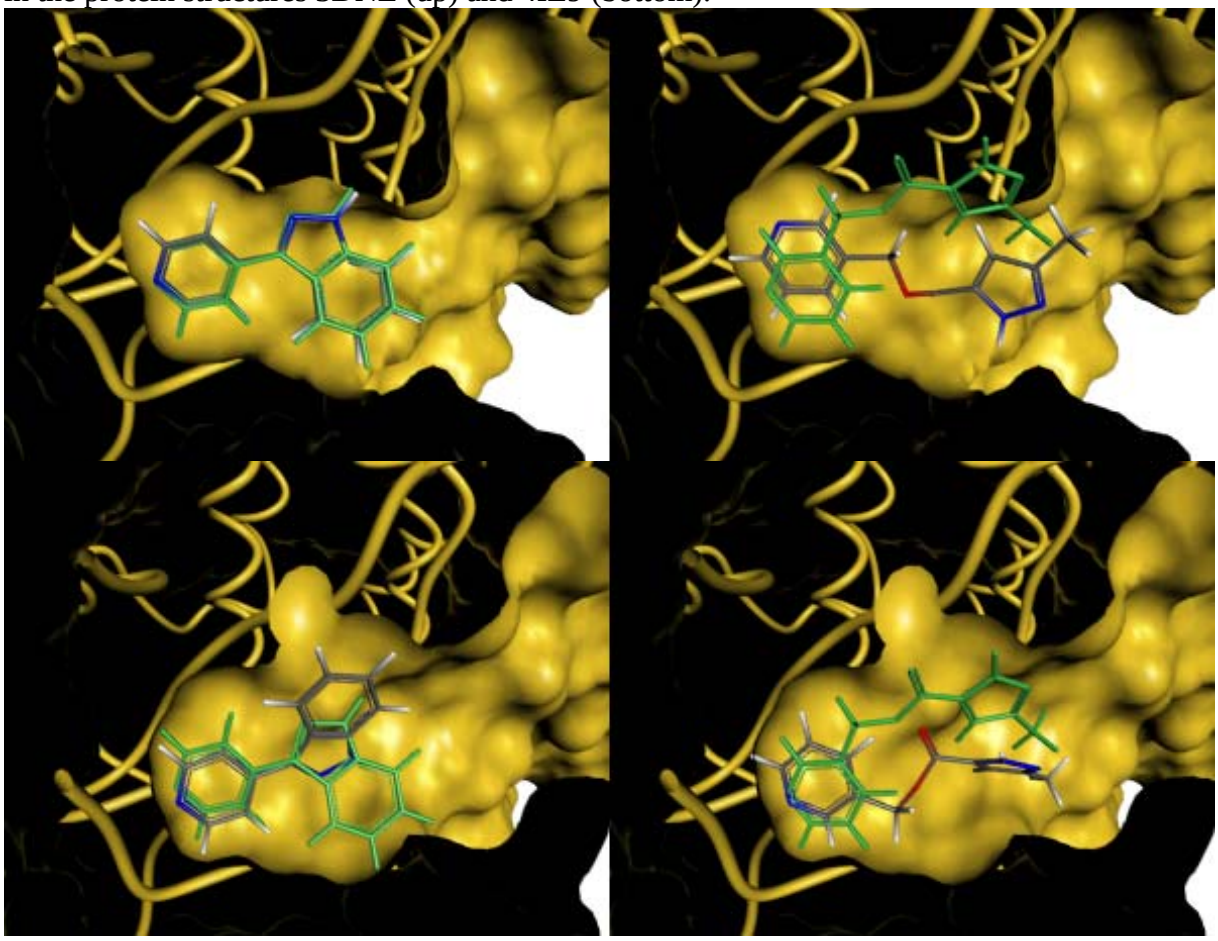


**Figure S6:** Poses of the pair LL2 (left) and M77 (right) ranked highest by scoring function $S_1$ in the protein structures 3DND (up) and 1Q8W (bottom).

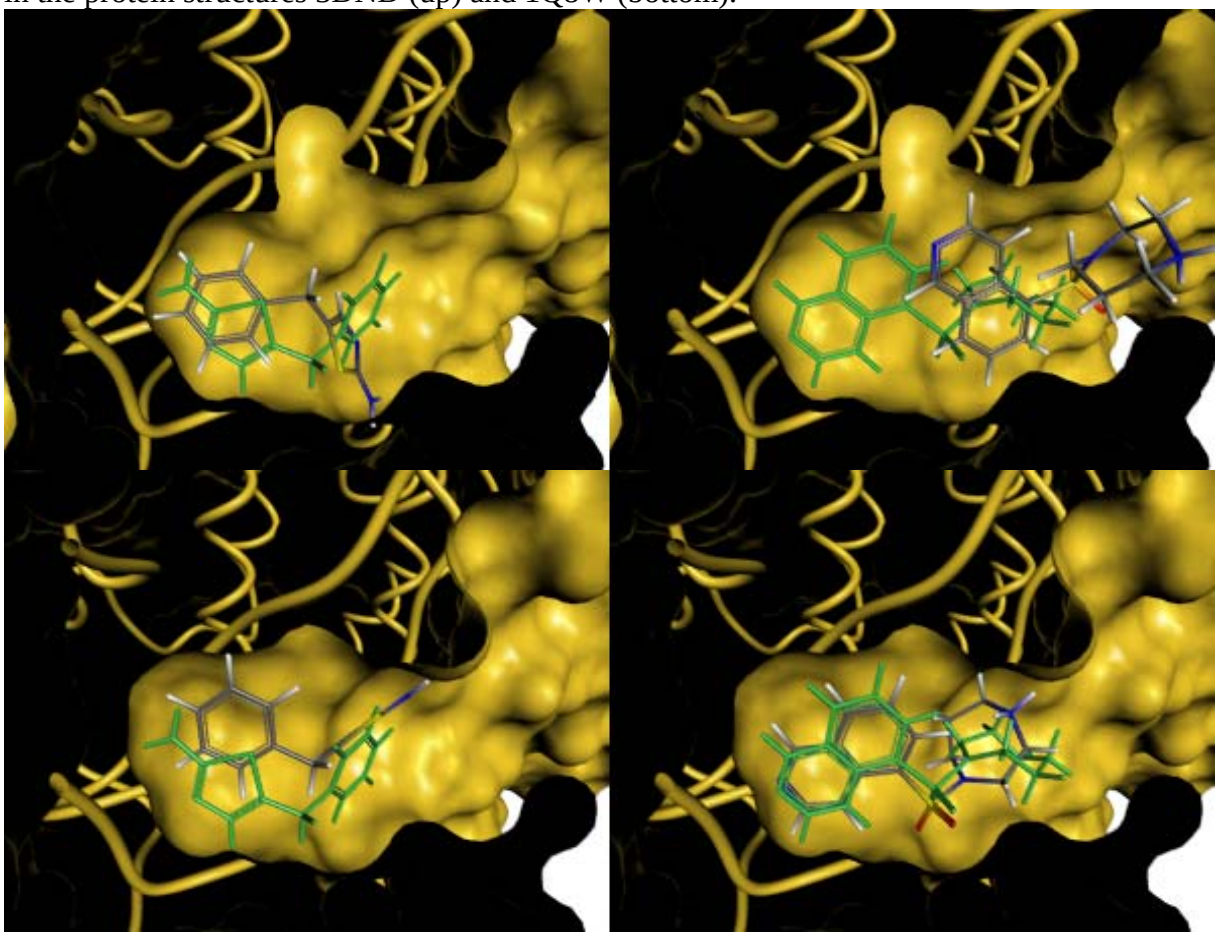


**Figure S7:** Poses of the pair LL2 (left) and PTV (right) ranked highest by scoring function $S_1$ in the protein structures 3DND (up) and 4IJ9 (bottom).

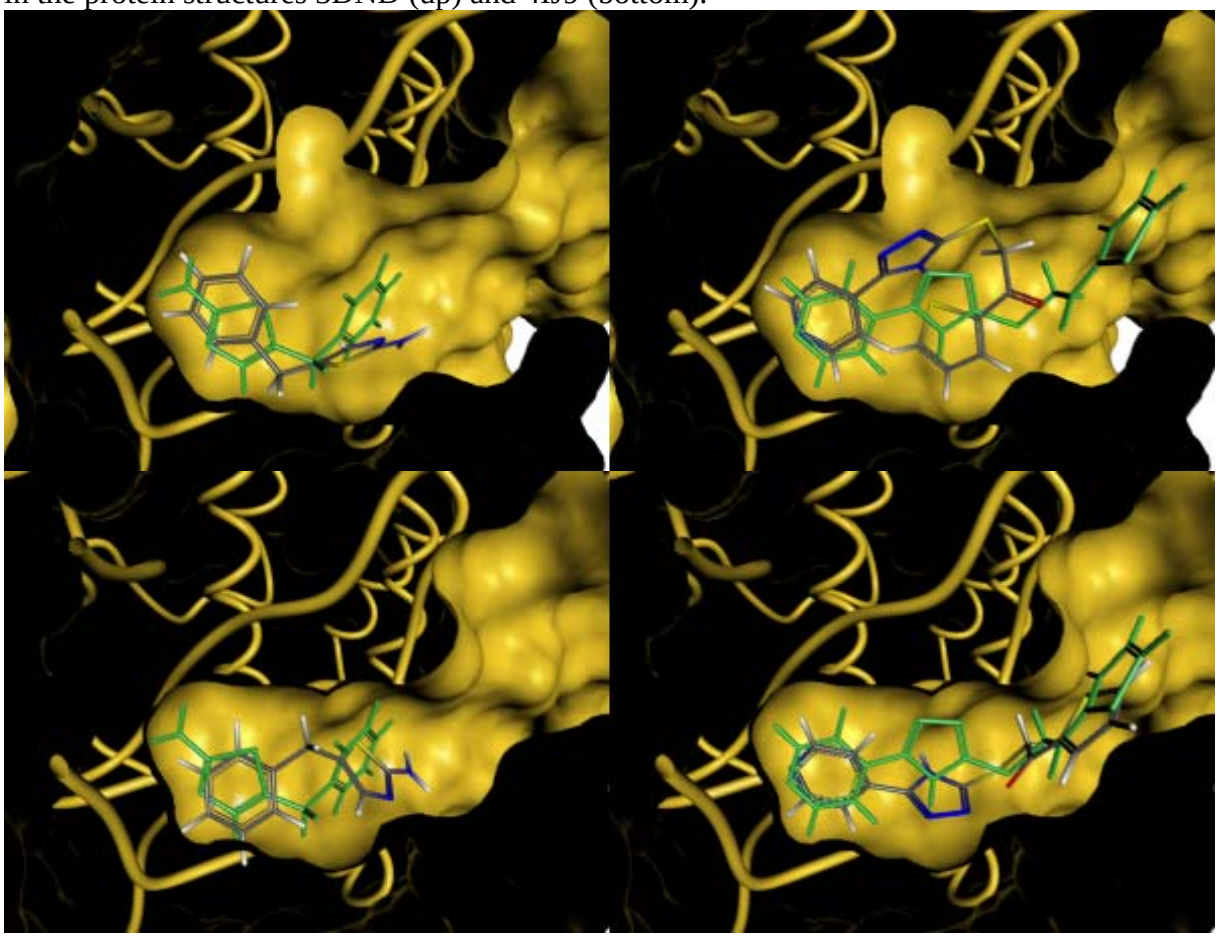


**Figure S8:** Poses of the pair LL2 (left) and PZX (right) ranked highest by scoring function $S_1$ in the protein structures 3DND (up) and 4IE9 (bottom).

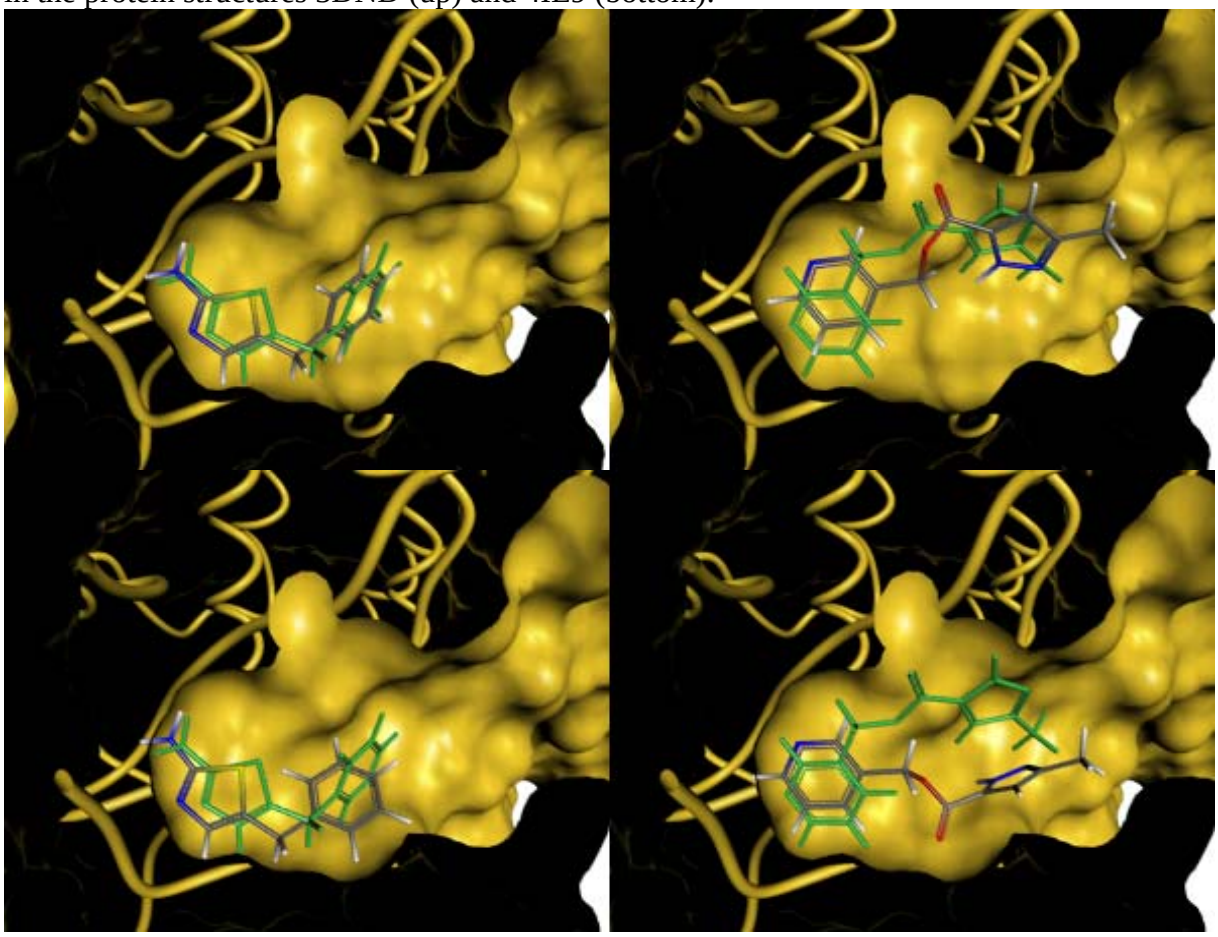


**Figure S9:** Poses of the pair M77 (left) and PTV (right) ranked highest by scoring function $S_1$ in the protein structures 1Q8W (up) and 4IJ9 (bottom).

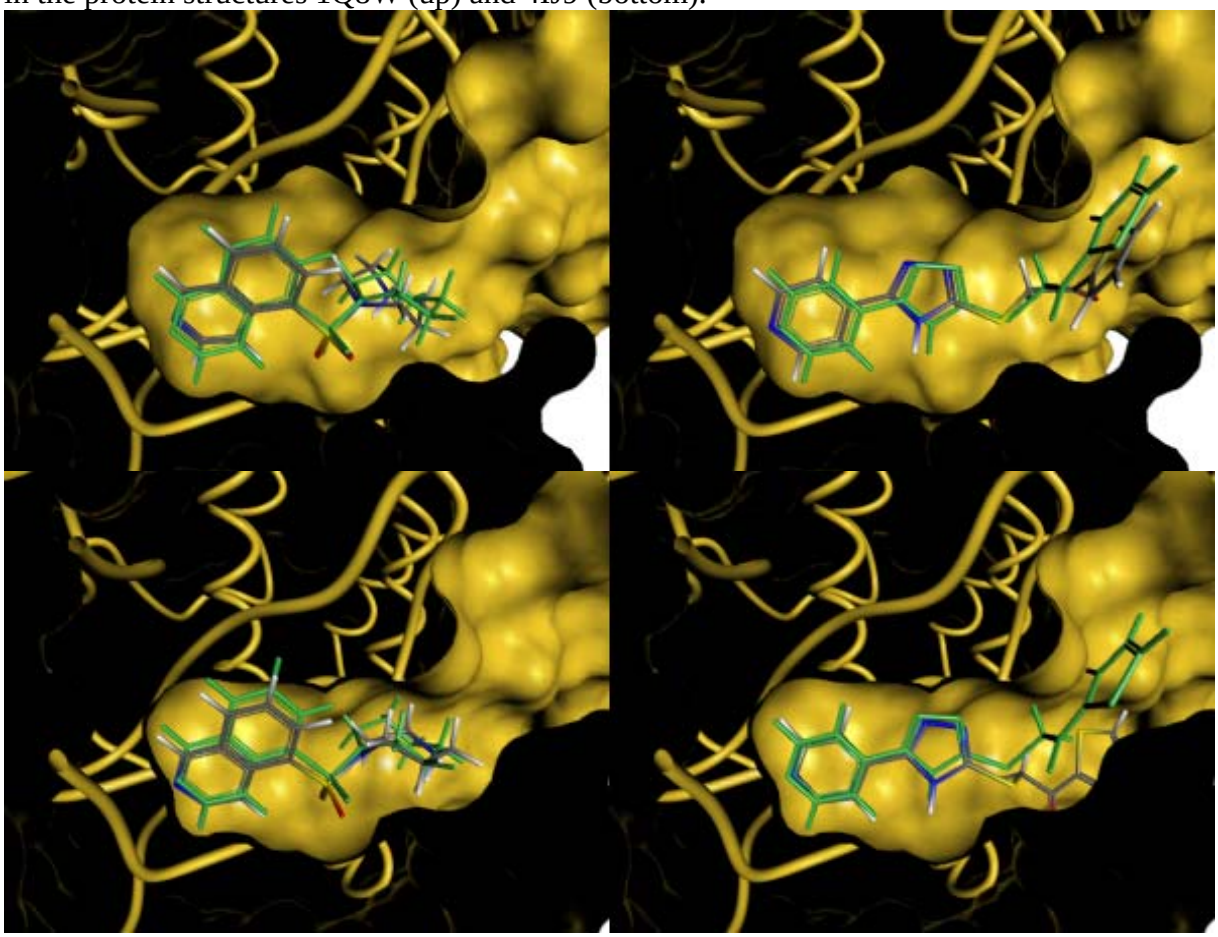


**Figure S10:** Poses of the pair M77 (left) and PZX (right) ranked highest by scoring function $S_1$ in the protein structures 1Q8W (up) and 4IE9 (bottom).

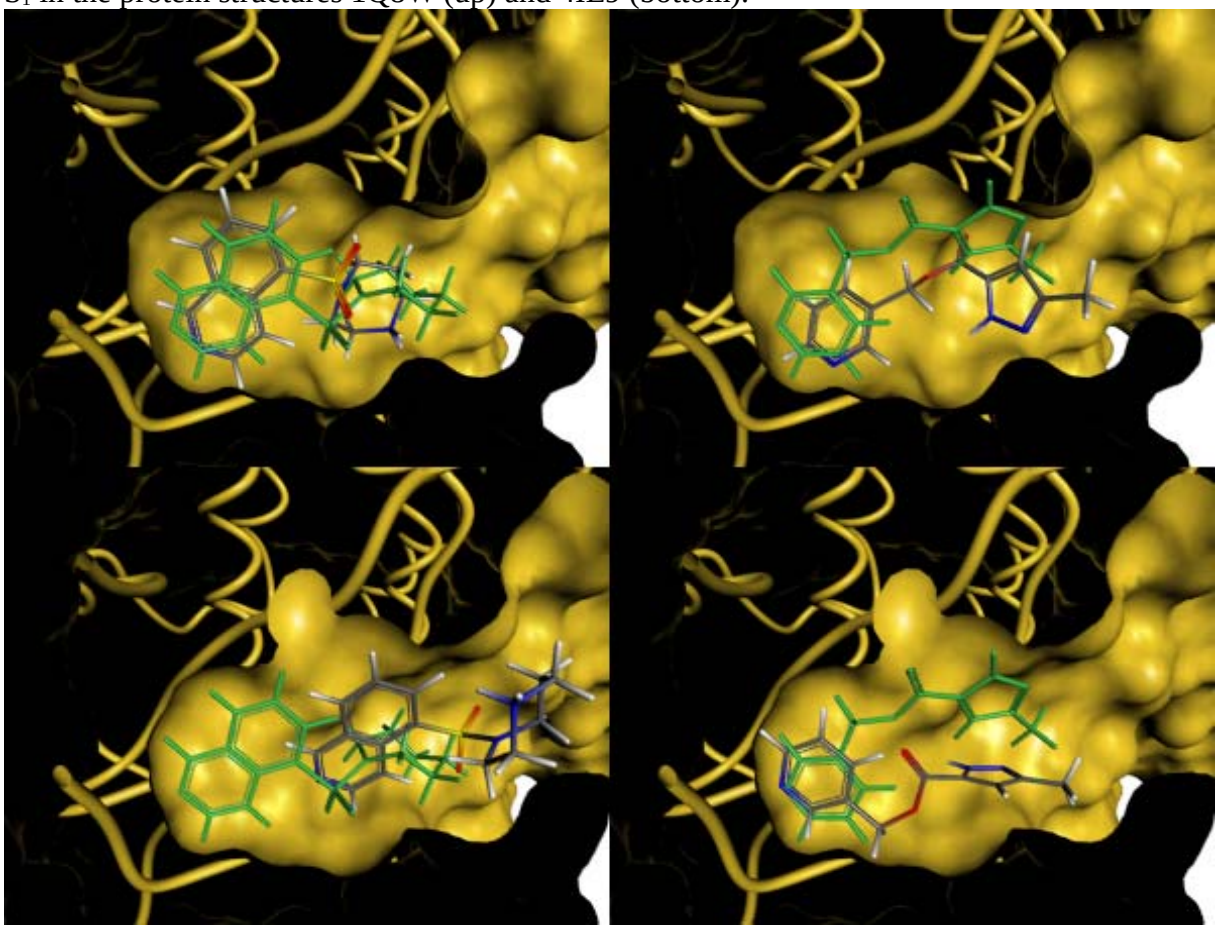


**Figure S11:** Poses of the pair PTV (left) and PZX (right) ranked highest by scoring function $S_1$ in the protein structures 4IJ9 (up) and 4IE9 (bottom).

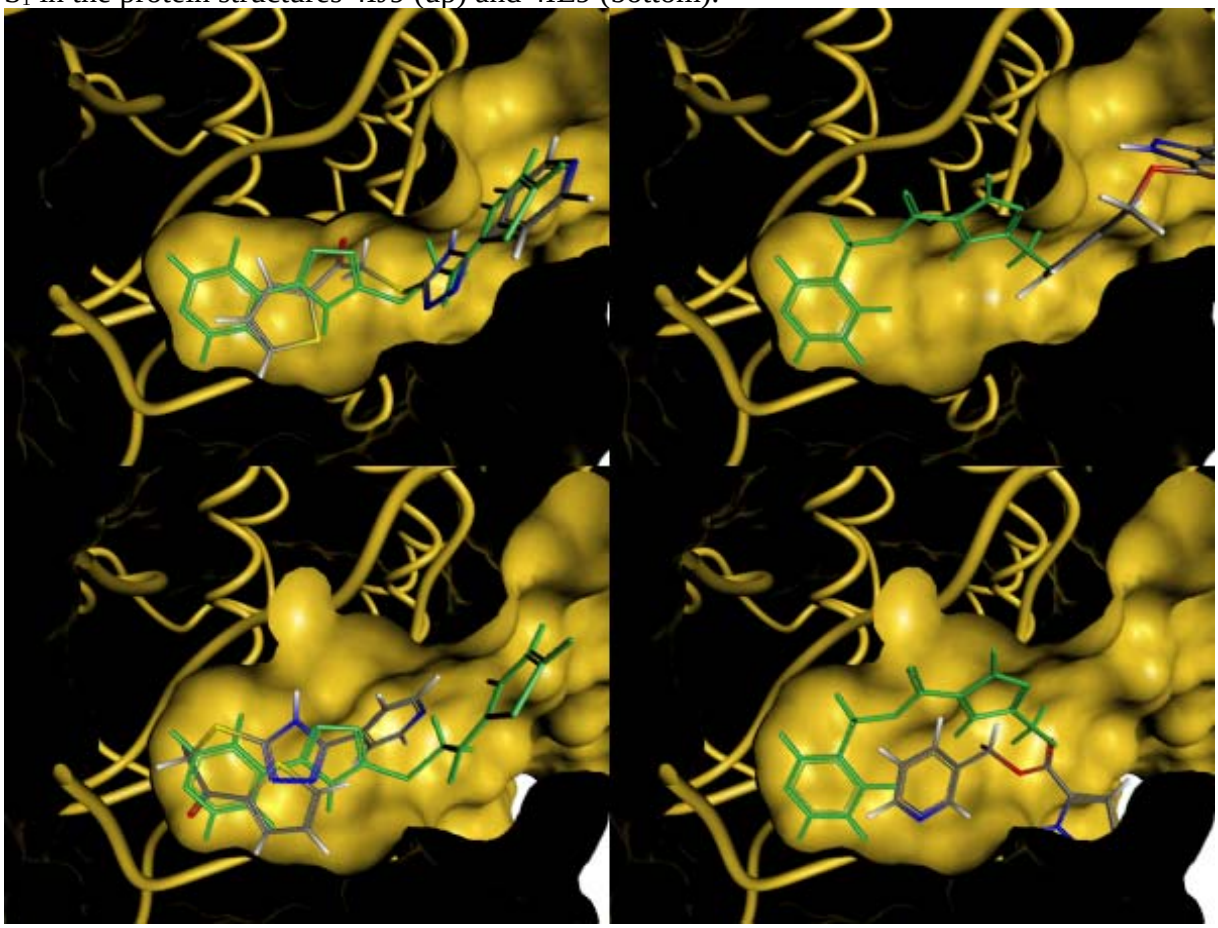


**Figure S12:** Poses of the pair LL1 (left) and LL2 (right) ranked highest by scoring function $S_2$ in the protein structures 3DNE (up) and 3DND (bottom).

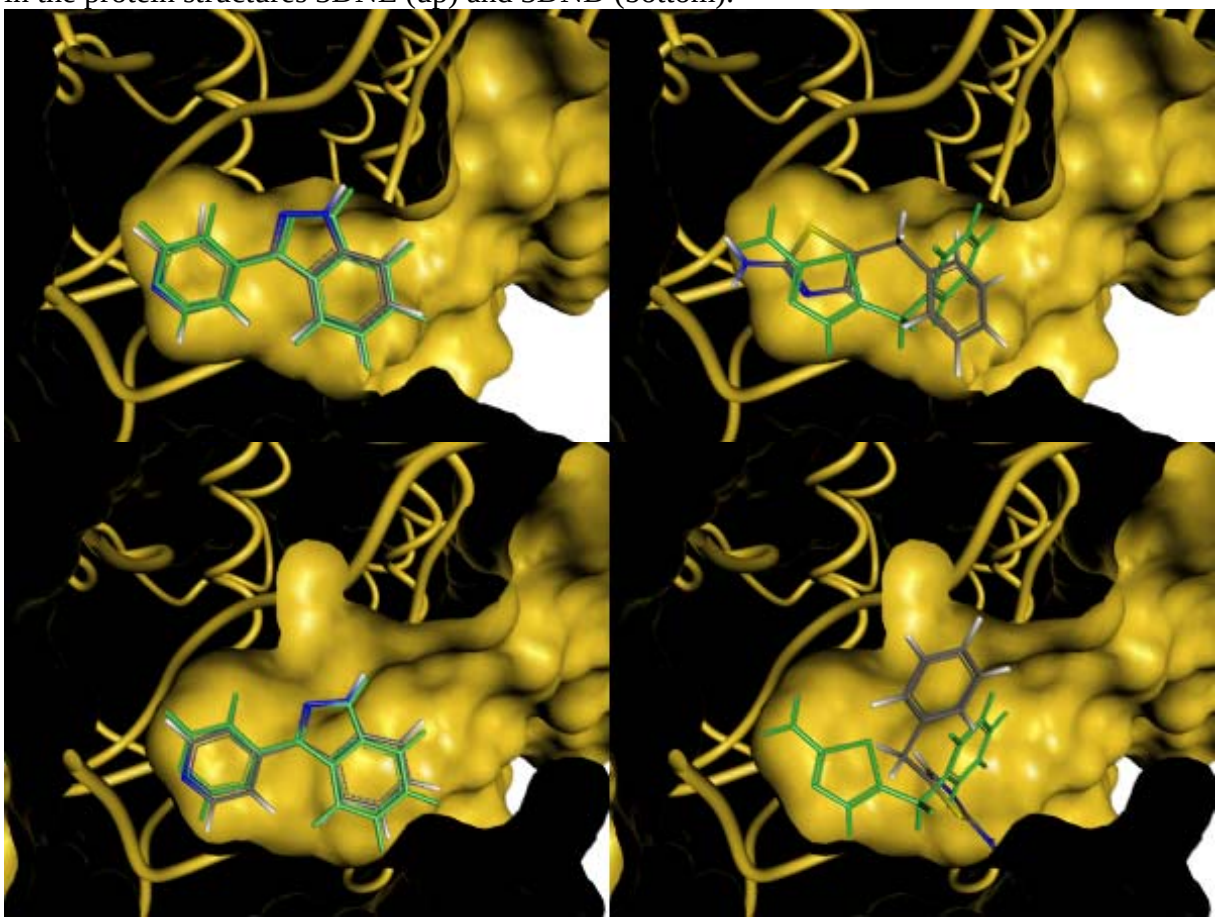


**Figure S13:** Poses of the pair LL1 (left) and M77 (right) ranked highest by scoring function $S_2$ in the protein structures 3DNE (up) and 1Q8W (bottom).

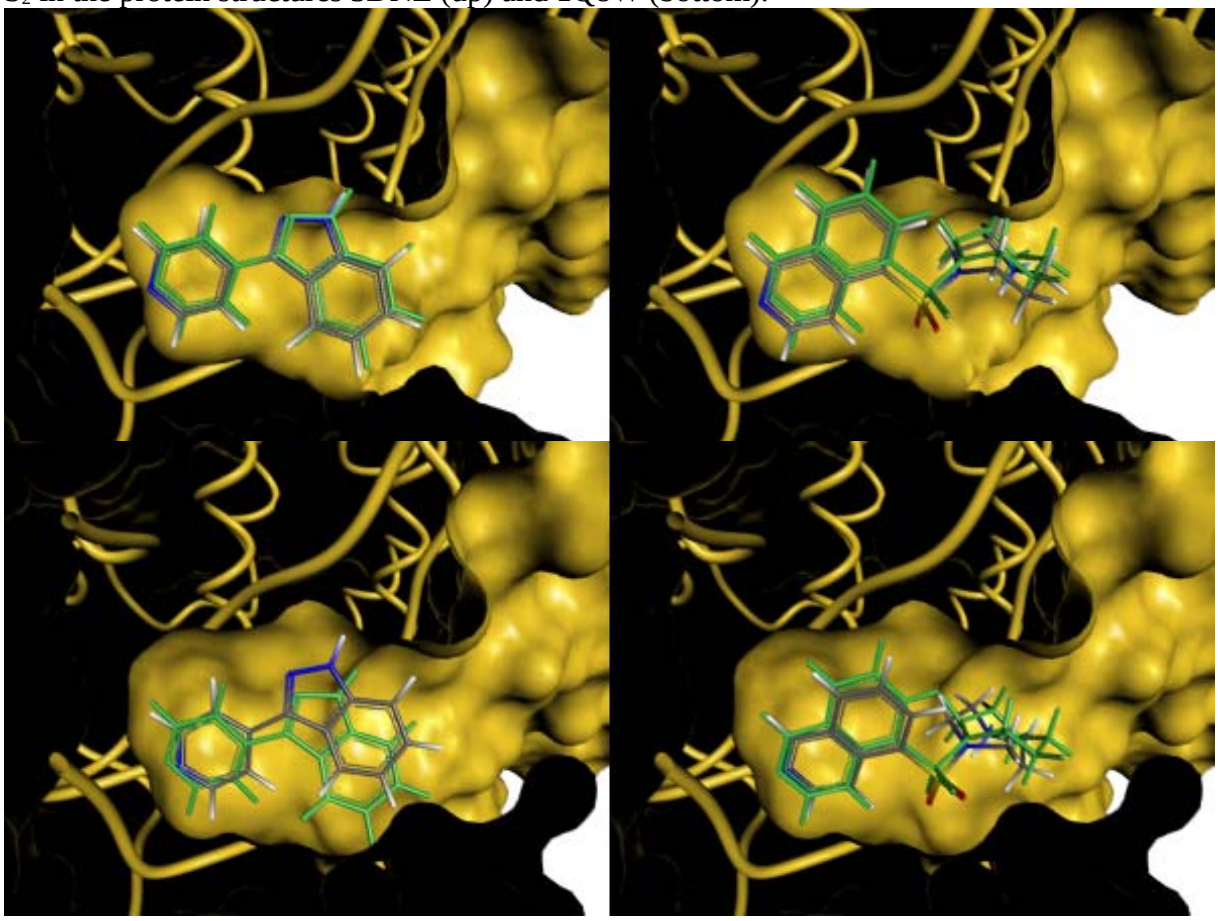


**Figure S14:** Poses of the pair LL1 (left) and PTV (right) ranked highest by scoring function $S_2$ in the protein structures 3DNE (up) and 4IJ9 (bottom).

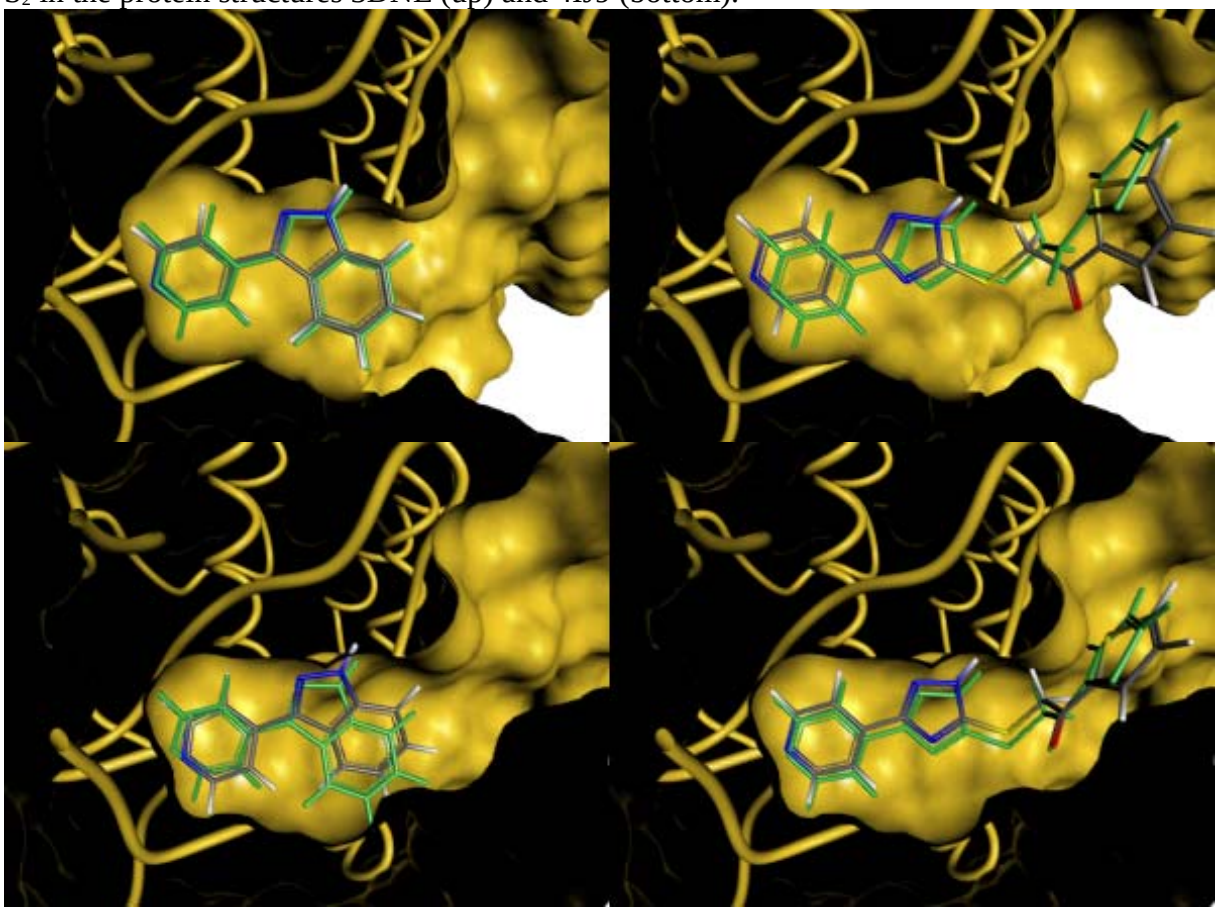


**Figure S15:** Poses of the pair LL1 (left) and PZX (right) ranked highest by scoring function $S_2$ in the protein structures 3DNE (up) and 4IE9 (bottom).

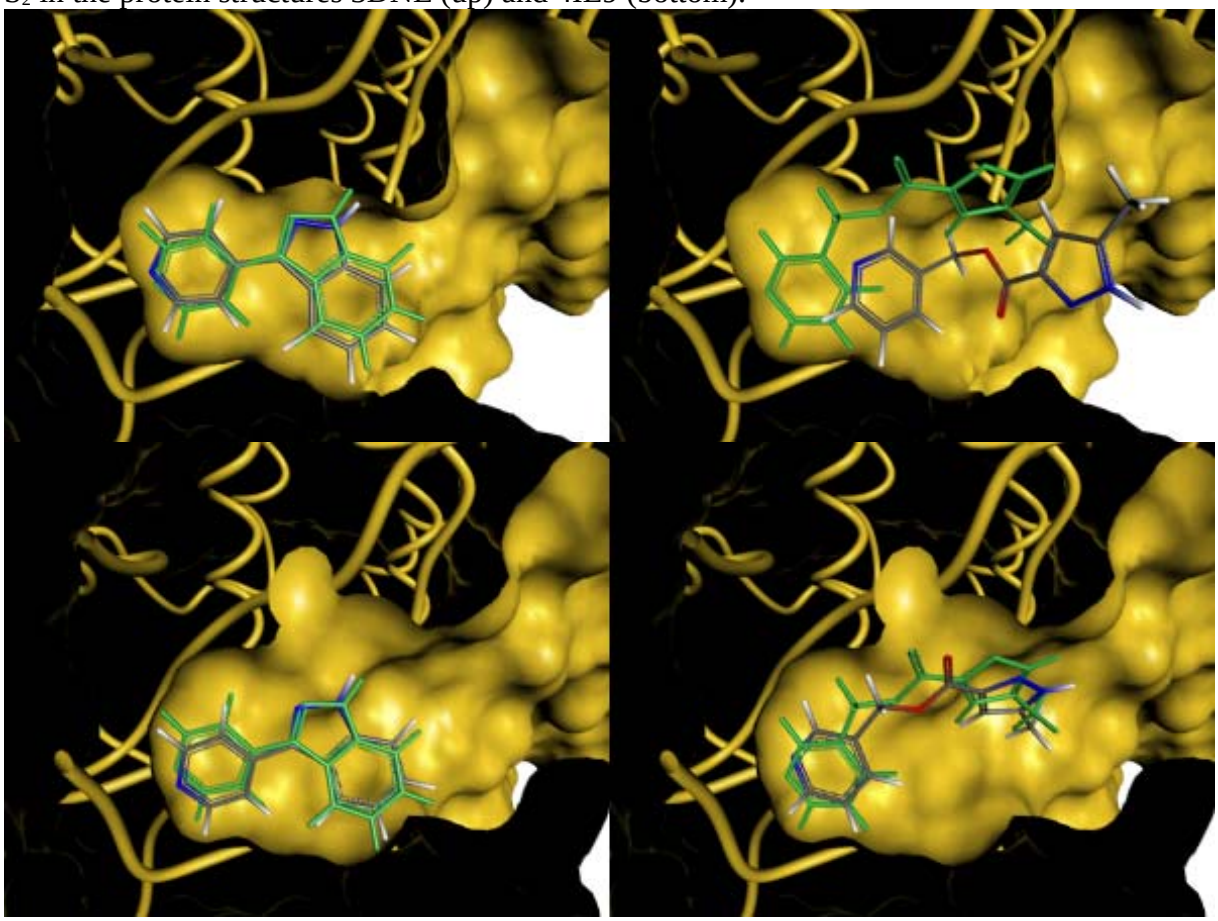


**Figure S16:** Poses of the pair LL2 (left) and M77 (right) ranked highest by scoring function $S_2$ in the protein structures 3DND (up) and 1Q8W (bottom).

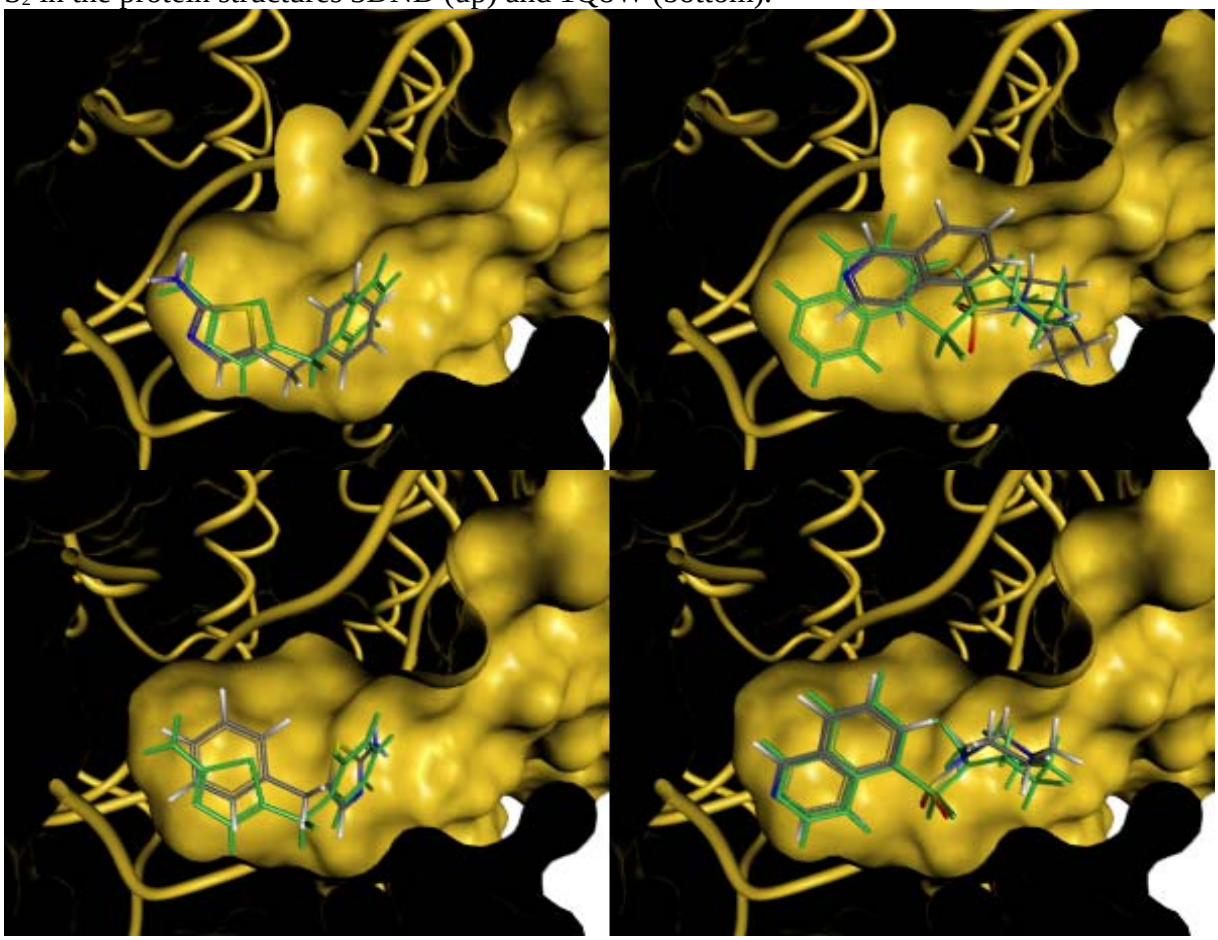


**Figure S17:** Poses of the pair LL2 (left) and PTV (right) ranked highest by scoring function $S_2$ in the protein structures 3DND (up) and 4IJ9 (bottom).

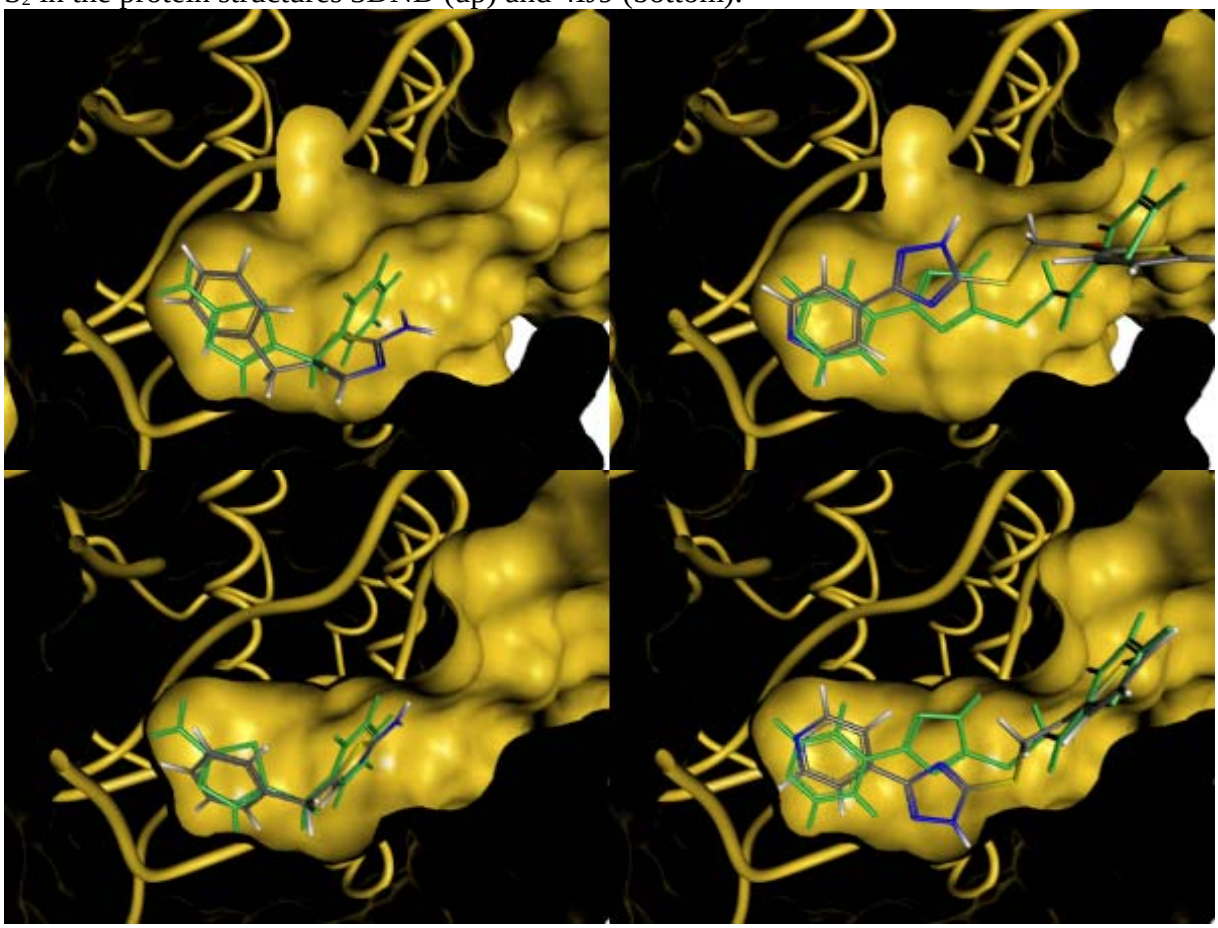


**Figure S18:** Poses of the pair LL2 (left) and PZX (right) ranked highest by scoring function $S_2$ in the protein structures 3DND (up) and 4IE9 (bottom).

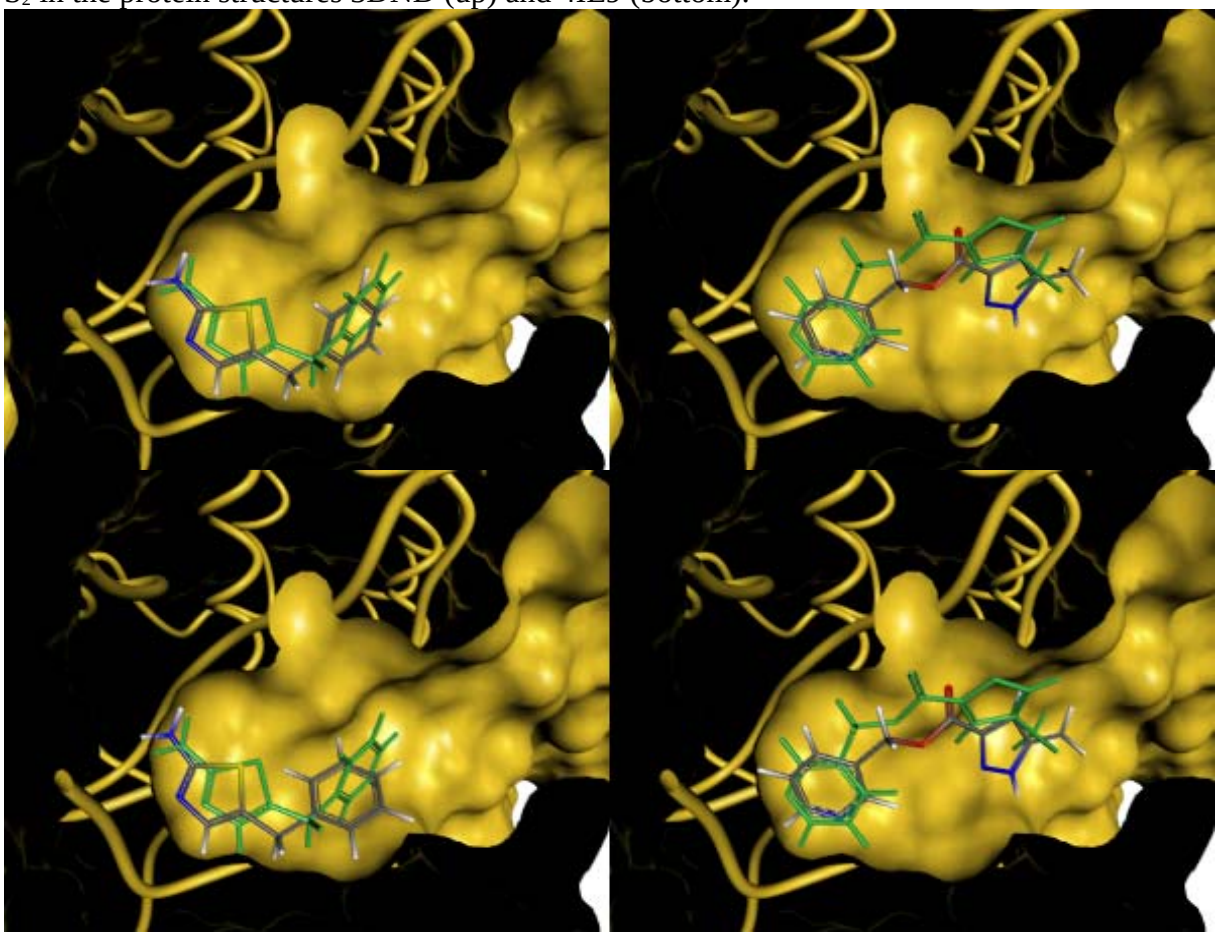


**Figure S19:** Poses of the pair M77 (left) and PTV (right) ranked highest by scoring function $S_2$ in the protein structures 1Q8W (up) and 4IJ9 (bottom).

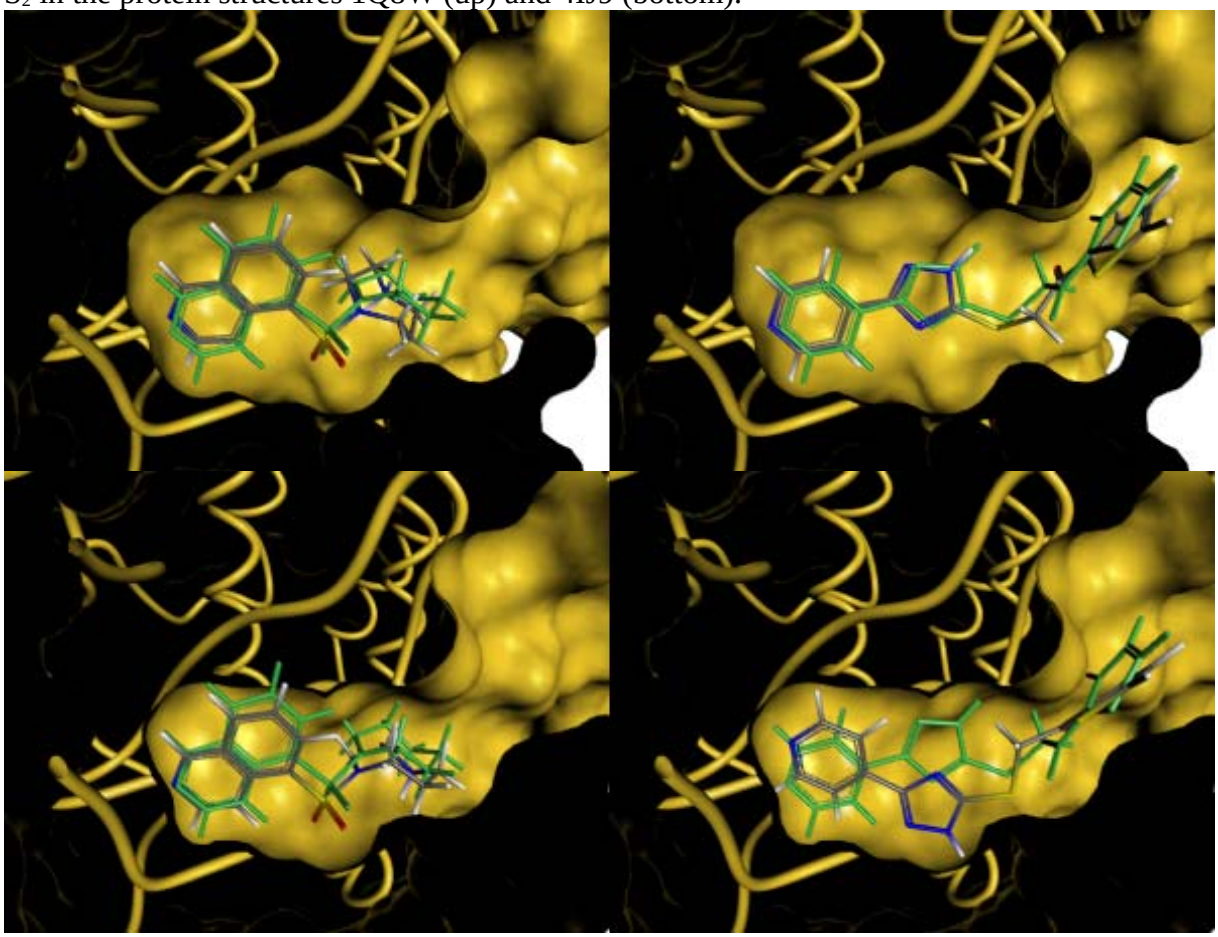


**Figure S20:** Poses of the pair M77 (left) and PZX (right) ranked highest by scoring function $S_2$ in the protein structures 1Q8W (up) and 4IE9 (bottom).

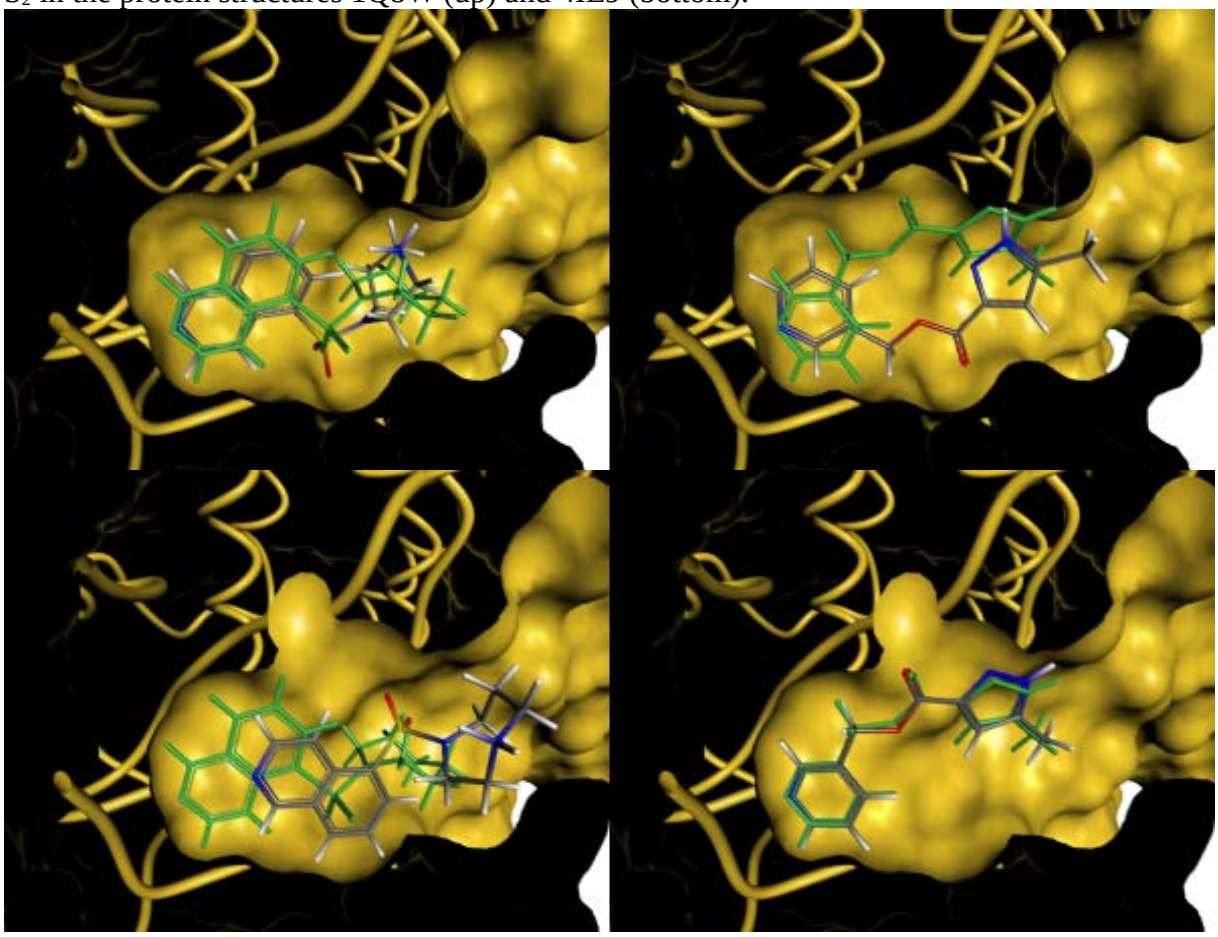
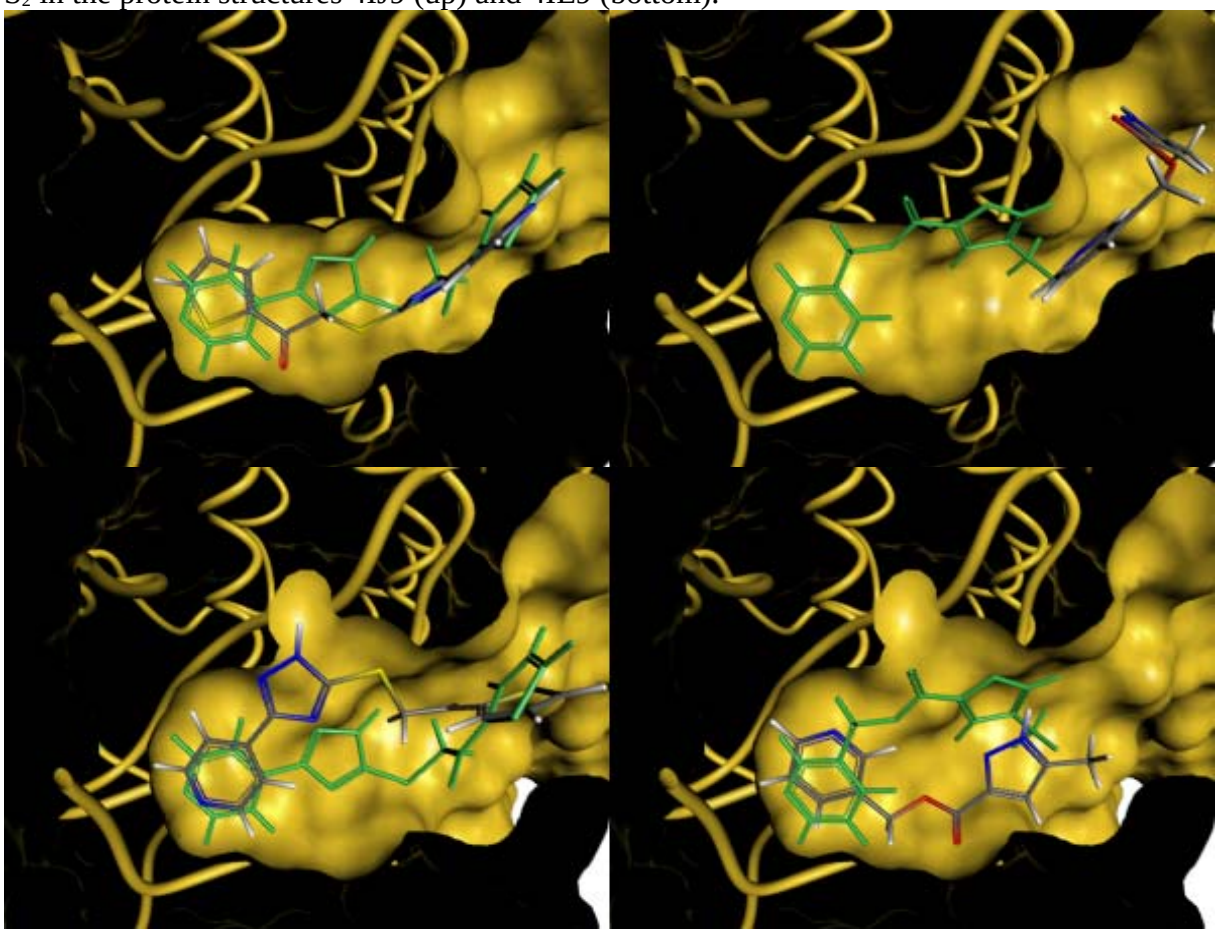



**Figure S21:** Poses of the pair PTV (left) and PZX (right) ranked highest by scoring function $S_2$ in the protein structures 4IJ9 (up) and 4IE9 (bottom).