**Supporting Information**

# Theoretical investigations on interactions of arylsulphonyl indazole derivatives as potential ligands of VEGFR2 kinase

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Table of Contents:

**Fig. S1** Electrostatic potential (ESP) map of docked azole **5** (1st pose) calculated at the B3LYP/6-311++G(2d,3p)//B3LYP-631G(d,p) level of theory (gaseous phase); isovalue = 0.002 a.u.

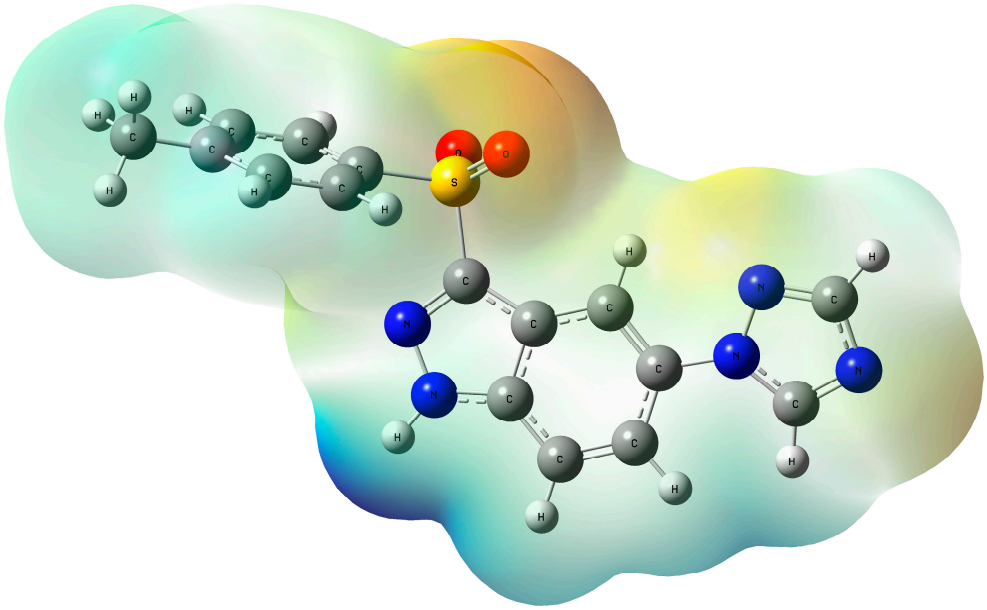
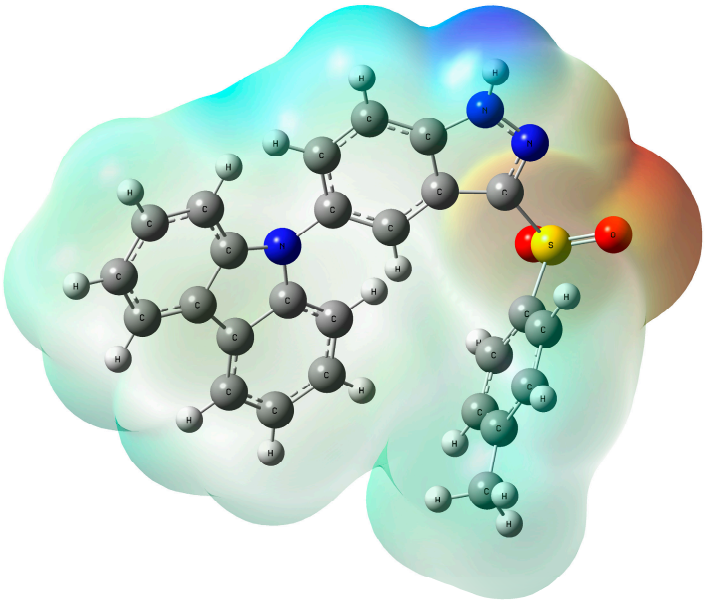


**Fig. S2** Electrostatic potential (ESP) map of docked azole **7** (1st pose) calculated at the B3LYP/6-311++G(2d,3p)//B3LYP-631G(d,p) level of theory (gaseous phase); isovalue = 0.002 a.u.



Electrostatic potential (ESP) map of ligands **1**–**4**, **6**, **8**–**9** are given in the our previous reports:

Czaja K., Kujawski J., Kamel K., Bernard M.K. Selected arylsulphonyl pyrazole derivatives as potential Chk1 kinase ligands – computational investigations. *J. Mol. Model.* **2020**, *accepted*. doi: 10.1007/s00894-020-04407-3.

**Fig. S3**: Geometry of the first poses of azoles **1**–**9** after docking procedure to 3ewh.pdb protein and their Cartesian coordinates (charge=0, multiplicity=1):

**Azole 1**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 16.051000000 | -6.986000000 | 7.723000000 |
| C | 16.267000000 | -7.422000000 | 6.376000000 |
| C | 15.464000000 | -8.585000000 | 6.273000000 |
| N | 14.861000000 | -8.735000000 | 7.496000000 |
| N | 15.217000000 | -7.777000000 | 8.374000000 |
| C | 15.387000000 | -9.338000000 | 5.092000000 |
| C | 16.137000000 | -8.898000000 | 4.015000000 |
| C | 16.940000000 | -7.737000000 | 4.116000000 |
| C | 17.028000000 | -6.987000000 | 5.275000000 |
| H | 14.227000000 | -9.457000000 | 7.797000000 |
| Cl | 17.851000000 | -7.251000000 | 2.718000000 |
| S | 16.782000000 | -5.579000000 | 8.557000000 |
| O | 15.773000000 | -4.511000000 | 8.458000000 |
| O | 18.145000000 | -5.394000000 | 8.045000000 |
| C | 16.896000000 | -6.080000000 | 10.275000000 |
| C | 16.053000000 | -5.490000000 | 11.216000000 |
| C | 16.154000000 | -5.878000000 | 12.551000000 |
| C | 17.084000000 | -6.845000000 | 12.956000000 |
| C | 17.209000000 | -7.237000000 | 14.407000000 |
| C | 17.919000000 | -7.420000000 | 11.985000000 |
| C | 17.836000000 | -7.044000000 | 10.648000000 |
| H | 14.770000000 | -10.222000000 | 5.026000000 |
| H | 16.109000000 | -9.448000000 | 3.086000000 |
| H | 17.652000000 | -6.108000000 | 5.332000000 |
| H | 15.333000000 | -4.744000000 | 10.915000000 |
| H | 15.504000000 | -5.426000000 | 13.286000000 |
| H | 18.639000000 | -8.168000000 | 12.281000000 |
| H | 18.487000000 | -7.490000000 | 9.911000000 |
| H | 16.478000000 | -6.684000000 | 14.997000000 |
| H | 18.213000000 | -7.004000000 | 14.761000000 |
| H | 17.026000000 | -8.306000000 | 14.511000000 |

**Azole 2**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 17.03500 | -7.04800 | 5.32300 |
| C | 16.92400 | -7.75100 | 4.15000 |
| C | 16.06100 | -8.88300 | 4.05600 |
| C | 15.32600 | -9.31800 | 5.11900 |
| C | 15.43900 | -8.58800 | 6.31900 |
| N | 14.84800 | -8.75400 | 7.57000 |

| | | | |
|---|---|---|---|
| H | 14.15800 | -9.45200 | 7.85900 |
| N | 15.25100 | -7.77200 | 8.46700 |
| C | 16.09700 | -7.02300 | 7.78600 |
| C | 16.26600 | -7.47400 | 6.42300 |
| N | 17.67800 | -7.35300 | 2.98300 |
| C | 18.67200 | -6.37000 | 2.93200 |
| C | 19.11800 | -6.27900 | 1.66300 |
| C | 18.39200 | -7.23000 | 0.87500 |
| C | 17.52500 | -7.86400 | 1.69000 |
| S | 16.86700 | -5.57500 | 8.51400 |
| O | 18.59400 | -5.55200 | 7.84300 |
| O | 15.60300 | -4.20700 | 8.45400 |
| C | 16.99200 | -6.07100 | 10.24500 |
| C | 16.17100 | -5.47100 | 11.18800 |
| C | 16.25600 | -5.87100 | 12.51100 |
| C | 17.14900 | -6.86700 | 12.90000 |
| C | 17.95600 | -7.46300 | 11.93400 |
| C | 17.25200 | -7.28700 | 14.36400 |
| C | 17.88000 | -7.07200 | 10.60600 |
| H | 17.69200 | -6.19400 | 5.40000 |
| H | 15.98800 | -9.41000 | 3.11600 |
| H | 14.68500 | -10.18400 | 5.04400 |
| H | 19.02300 | -5.78300 | 3.76800 |
| H | 19.88500 | -5.60900 | 1.30500 |
| H | 18.51700 | -7.40700 | -0.18300 |
| H | 16.83000 | -8.63600 | 1.39400 |
| H | 15.47300 | -4.70100 | 10.89400 |
| H | 15.62200 | -5.40500 | 13.25100 |
| H | 18.64900 | -8.23900 | 12.22300 |
| H | 18.50500 | -7.54200 | 9.86200 |
| H | 18.00000 | -8.07300 | 14.46500 |
| H | 17.54400 | -6.42800 | 14.96800 |
| H | 16.28600 | -7.65900 | 14.70400 |

**Azole 3**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 16.03800 | -7.00000 | 7.70700 |
| C | 16.24500 | -7.42800 | 6.35600 |
| C | 15.44900 | -8.59400 | 6.25700 |
| N | 14.86300 | -8.75700 | 7.48600 |
| N | 15.21900 | -7.80000 | 8.36600 |
| C | 15.36700 | -9.33300 | 5.06600 |
| C | 16.10500 | -8.88500 | 3.98900 |
| C | 16.90700 | -7.71600 | 4.08000 |
| C | 16.97800 | -6.97300 | 5.24700 |
| H | 14.23600 | -9.48600 | 7.78900 |
| S | 16.77700 | -5.59700 | 8.53800 |
| O | 18.14100 | -5.41500 | 8.02800 |
| O | 15.77400 | -4.52100 | 8.43800 |
| C | 16.88800 | -6.09400 | 10.25900 |

| | | | |
|---|---|---|---|
| C | 16.02000 | -5.52800 | 11.19100 |
| C | 16.11800 | -5.91400 | 12.52700 |
| C | 17.07200 | -6.85300 | 12.94100 |
| C | 17.93200 | -7.40300 | 11.97900 |
| C | 17.19400 | -7.24200 | 14.39400 |
| C | 17.85200 | -7.02900 | 10.64000 |
| N | 17.64900 | -7.32400 | 2.93500 |
| C | 18.62700 | -6.37300 | 2.84800 |
| C | 19.04600 | -6.34700 | 1.53600 |
| C | 18.26000 | -7.33200 | 0.89400 |
| N | 17.41700 | -7.92300 | 1.73500 |
| H | 14.75100 | -10.21700 | 4.99500 |
| H | 16.07200 | -9.43400 | 3.05900 |
| H | 17.57600 | -6.07500 | 5.30200 |
| H | 15.28300 | -4.80100 | 10.88300 |
| H | 15.44700 | -5.48200 | 13.25500 |
| H | 18.67000 | -8.13000 | 12.28300 |
| H | 18.52400 | -7.45500 | 9.90900 |
| H | 19.00000 | -5.75900 | 3.65400 |
| H | 19.80400 | -5.71600 | 1.09600 |
| H | 18.33600 | -7.57500 | -0.15600 |
| H | 16.44200 | -6.71100 | 14.97700 |
| H | 18.18800 | -6.98000 | 14.75800 |
| H | 17.04100 | -8.31600 | 14.49700 |

**Azole 4**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 17.04700 | -7.07600 | 5.28200 |
| C | 16.26900 | -7.48200 | 6.38100 |
| C | 16.94000 | -7.80700 | 4.10800 |
| C | 15.43500 | -8.62100 | 6.28400 |
| C | 16.10000 | -8.95200 | 4.02600 |
| C | 15.34900 | -9.37700 | 5.10300 |
| C | 16.06300 | -7.03300 | 7.72400 |
| N | 15.20700 | -7.79600 | 8.38100 |
| N | 14.83500 | -8.75500 | 7.51000 |
| H | 14.17000 | -9.45000 | 7.80800 |
| S | 16.78000 | -5.60400 | 8.52700 |
| O | 18.14400 | -5.49500 | 7.97300 |
| O | 15.83200 | -4.48800 | 8.43600 |
| C | 16.91800 | -6.07500 | 10.25200 |
| C | 16.08900 | -5.46800 | 11.19600 |
| C | 16.19300 | -5.85100 | 12.53200 |
| C | 17.11600 | -6.82500 | 12.93700 |
| C | 17.24400 | -7.21200 | 14.39000 |
| C | 17.93100 | -7.42200 | 11.96300 |
| C | 17.84000 | -7.05600 | 10.62400 |
| N | 17.67700 | -7.44800 | 2.95000 |
| N | 17.44100 | -8.13700 | 1.79200 |
| C | 18.22900 | -7.57400 | 0.88200 |

| | | | |
|---|---|---|---|
| C | 18.24800 | -8.08700 | -0.52500 |
| C | 18.97400 | -6.50700 | 1.44500 |
| C | 18.60000 | -6.44000 | 2.77200 |
| C | 19.02600 | -5.46600 | 3.82600 |
| H | 17.70600 | -6.22300 | 5.35000 |
| H | 16.04900 | -9.50200 | 3.09800 |
| H | 14.72200 | -10.25400 | 5.04100 |
| H | 15.37800 | -4.71300 | 10.89600 |
| H | 15.55100 | -5.38900 | 13.26800 |
| H | 18.64200 | -8.17900 | 12.25800 |
| H | 18.47200 | -7.52300 | 9.88400 |
| H | 19.68900 | -5.87500 | 0.93900 |
| H | 18.95100 | -7.50100 | -1.11700 |
| H | 18.55600 | -9.13300 | -0.52600 |
| H | 17.25100 | -8.00200 | -0.95600 |
| H | 19.79000 | -4.80300 | 3.42100 |
| H | 18.16600 | -4.87700 | 4.14500 |
| H | 19.43200 | -6.00900 | 4.68000 |
| H | 16.53000 | -6.64100 | 14.98300 |
| H | 18.25500 | -6.99800 | 14.73500 |
| H | 17.04000 | -8.27700 | 14.50200 |

**Azole 5**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 16.98300 | -6.97900 | 5.25600 |
| C | 16.90800 | -7.72700 | 4.09200 |
| C | 16.10300 | -8.89100 | 3.99600 |
| C | 15.36000 | -9.33500 | 5.07300 |
| C | 15.44500 | -8.59400 | 6.26200 |
| N | 14.85500 | -8.75000 | 7.49000 |
| H | 14.22300 | -9.47500 | 7.79300 |
| N | 15.21300 | -7.79400 | 8.36900 |
| C | 16.03900 | -6.99800 | 7.71300 |
| C | 16.24600 | -7.43000 | 6.36300 |
| N | 17.65800 | -7.33800 | 2.94900 |
| N | 18.63000 | -6.38300 | 3.02900 |
| C | 19.06400 | -6.31700 | 1.78100 |
| N | 18.44400 | -7.15300 | 0.89900 |
| C | 17.56800 | -7.77600 | 1.66300 |
| S | 16.78700 | -5.59700 | 8.54200 |
| O | 18.15000 | -5.42500 | 8.02600 |
| O | 15.78700 | -4.51900 | 8.44000 |
| C | 16.89900 | -6.09300 | 10.26200 |
| C | 17.84700 | -7.04600 | 10.64000 |
| C | 17.92900 | -7.41700 | 11.97800 |
| C | 17.08400 | -6.84900 | 12.94400 |
| C | 16.14500 | -5.89300 | 12.53400 |
| C | 17.20700 | -7.23800 | 14.39700 |
| C | 16.04600 | -5.50800 | 11.19800 |
| H | 17.58500 | -6.08400 | 5.31000 |

| | | | |
|---|---|---|---|
| H | 16.07000 | -9.43900 | 3.06600 |
| H | 14.73900 | -10.21600 | 5.00300 |
| H | 19.85600 | -5.64700 | 1.48100 |
| H | 16.87600 | -8.52900 | 1.31700 |
| H | 18.50500 | -7.48700 | 9.90600 |
| H | 18.65700 | -8.15600 | 12.27900 |
| H | 15.48700 | -5.44700 | 13.26500 |
| H | 15.32100 | -4.76900 | 10.89200 |
| H | 16.46800 | -6.69200 | 14.98400 |
| H | 18.20700 | -6.99400 | 14.75500 |
| H | 17.03500 | -8.30900 | 14.50200 |

**Azole 6**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 16.06000 | -6.99700 | 7.72800 |
| C | 16.28200 | -7.40700 | 6.37400 |
| C | 15.46900 | -8.56100 | 6.24400 |
| N | 14.86800 | -8.73800 | 7.46400 |
| N | 15.21800 | -7.79500 | 8.36100 |
| C | 15.39200 | -9.28300 | 5.04400 |
| C | 16.15700 | -8.82700 | 3.98600 |
| C | 16.96600 | -7.66200 | 4.09300 |
| C | 17.02900 | -6.94000 | 5.27900 |
| H | 14.22200 | -9.45800 | 7.74500 |
| S | 16.73900 | -5.57000 | 8.57100 |
| O | 18.10500 | -5.42500 | 8.03700 |
| O | 15.76600 | -4.47400 | 8.48600 |
| C | 16.86400 | -6.07100 | 10.28900 |
| C | 17.82100 | -7.01800 | 10.65500 |
| C | 17.91900 | -7.39400 | 11.99300 |
| C | 17.07700 | -6.84000 | 12.96600 |
| C | 17.21000 | -7.23000 | 14.41800 |
| C | 16.12500 | -5.88900 | 12.56500 |
| C | 16.01300 | -5.49800 | 11.23500 |
| N | 17.70100 | -7.24800 | 2.95400 |
| C | 18.72700 | -6.30500 | 2.97500 |
| C | 19.22100 | -6.11500 | 1.71700 |
| C | 18.47600 | -6.97100 | 0.83600 |
| C | 18.50700 | -7.20300 | -0.55000 |
| C | 17.53100 | -7.67100 | 1.63500 |
| C | 17.60500 | -8.10200 | -1.10300 |
| C | 16.66500 | -8.77200 | -0.29700 |
| C | 16.61100 | -8.56700 | 1.07700 |
| H | 14.76300 | -10.15600 | 4.95000 |
| H | 16.14000 | -9.37000 | 3.05300 |
| H | 17.63300 | -6.04800 | 5.35700 |
| H | 18.47500 | -7.45200 | 9.91300 |
| H | 18.65700 | -8.12600 | 12.28500 |
| H | 15.46800 | -5.45300 | 13.30300 |
| H | 15.27900 | -4.76300 | 10.93900 |

| | | | |
|---|---|---|---|
| H | 19.08100 | -5.79700 | 3.86000 |
| H | 20.02200 | -5.44700 | 1.43600 |
| H | 19.22200 | -6.68900 | -1.17600 |
| H | 17.62500 | -8.29000 | -2.16600 |
| H | 15.97100 | -9.46000 | -0.75600 |
| H | 15.88600 | -9.08000 | 1.69100 |
| H | 17.99800 | -7.97600 | 14.52400 |
| H | 17.46200 | -6.34900 | 15.00900 |
| H | 16.26600 | -7.64600 | 14.77000 |

**Azole 7**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 17.39000 | -7.13500 | 1.97600 |
| N | 16.52300 | -7.95000 | 1.35600 |
| N | 15.78900 | -8.59300 | 2.29400 |
| H | 15.08800 | -9.24400 | 2.01200 |
| C | 16.17200 | -8.20300 | 3.57800 |
| C | 15.72000 | -8.59900 | 4.84600 |
| C | 16.32100 | -8.02300 | 5.94500 |
| C | 17.35600 | -7.06400 | 5.78100 |
| C | 17.80400 | -6.66400 | 4.53100 |
| C | 17.21800 | -7.23700 | 3.40300 |
| N | 17.93300 | -6.48800 | 6.94200 |
| C | 17.22000 | -6.29700 | 8.14700 |
| C | 16.09800 | -6.97300 | 8.62200 |
| C | 15.62500 | -6.62100 | 9.88100 |
| C | 16.25600 | -5.63200 | 10.64900 |
| C | 17.38400 | -4.96500 | 10.18100 |
| C | 17.87300 | -5.28700 | 8.92200 |
| C | 18.98100 | -4.80100 | 8.13100 |
| C | 19.94900 | -3.83000 | 8.34800 |
| C | 20.88100 | -3.58200 | 7.34400 |
| C | 20.85100 | -4.29100 | 6.13500 |
| C | 19.89700 | -5.27400 | 5.89100 |
| C | 18.96900 | -5.52800 | 6.89900 |
| S | 18.53100 | -6.15400 | 1.03400 |
| O | 18.05900 | -6.13400 | -0.33300 |
| O | 19.86300 | -6.60000 | 1.36600 |
| C | 18.29900 | -4.54700 | 1.71400 |
| C | 19.30200 | -3.96800 | 2.49100 |
| C | 19.17300 | -2.65100 | 2.92200 |
| C | 18.03200 | -1.91000 | 2.58800 |
| C | 17.00500 | -2.51600 | 1.86100 |
| C | 17.93400 | -0.48100 | 2.99000 |
| C | 17.13300 | -3.83500 | 1.43500 |
| H | 14.93100 | -9.32800 | 4.95700 |
| H | 16.00200 | -8.30300 | 6.93800 |
| H | 18.58700 | -5.92700 | 4.43400 |
| H | 15.61500 | -7.74000 | 8.03500 |
| H | 14.75300 | -7.12000 | 10.27600 |

| | | | |
|---|---|---|---|
| H | 15.85900 | -5.38300 | 11.62200 |
| H | 17.86900 | -4.21200 | 10.78500 |
| H | 19.97800 | -3.27900 | 9.27600 |
| H | 21.64100 | -2.83000 | 7.49900 |
| H | 21.58600 | -4.06900 | 5.37500 |
| H | 19.87700 | -5.81800 | 4.95800 |
| H | 20.17800 | -4.54100 | 2.75800 |
| H | 19.95400 | -2.19900 | 3.51500 |
| H | 16.10900 | -1.96000 | 1.62900 |
| H | 16.33000 | -4.30700 | 0.88900 |
| H | 16.98400 | -0.07100 | 2.64700 |
| H | 18.75500 | 0.07900 | 2.54200 |
| H | 17.99200 | -0.40400 | 4.07600 |

**Azole 8**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| O | 14.76600 | -6.12700 | 8.96700 |
| S | 16.22000 | -6.00400 | 8.74400 |
| O | 16.89000 | -4.70000 | 8.82700 |
| C | 16.59500 | -6.72200 | 7.14300 |
| C | 17.79200 | -6.38800 | 6.50800 |
| C | 18.06800 | -6.93900 | 5.26000 |
| C | 17.16500 | -7.81600 | 4.63700 |
| C | 17.48800 | -8.42600 | 3.29500 |
| C | 15.96700 | -8.12100 | 5.29600 |
| C | 15.67400 | -7.58200 | 6.54800 |
| C | 16.97000 | -7.10900 | 9.93000 |
| N | 17.63600 | -8.17700 | 9.49200 |
| N | 18.11700 | -8.80300 | 10.58400 |
| H | 18.66100 | -9.64000 | 10.45900 |
| C | 17.77600 | -8.15000 | 11.73800 |
| C | 17.02100 | -7.03700 | 11.35100 |
| C | 17.85700 | -8.09700 | 13.14800 |
| N | 16.69400 | -6.37500 | 12.49900 |
| N | 17.19500 | -7.02500 | 13.58100 |
| C | 15.87000 | -5.19200 | 12.69800 |
| H | 18.49300 | -5.71300 | 6.97700 |
| H | 18.99300 | -6.68800 | 4.76200 |
| H | 15.25800 | -8.78600 | 4.82600 |
| H | 14.74900 | -7.82700 | 7.04800 |
| H | 18.37300 | -8.81100 | 13.77400 |
| H | 16.66800 | -9.07300 | 2.98300 |
| H | 18.40300 | -9.01200 | 3.37400 |
| H | 17.62600 | -7.63400 | 2.55900 |
| H | 15.55600 | -4.80100 | 11.73000 |
| H | 14.99100 | -5.45600 | 13.28600 |
| H | 16.44600 | -4.43300 | 13.22700 |

**Azole 9**

Cartesian coordinates:

| | | | |
|---|---|---|---|
| C | 17.09300 | -7.24300 | 5.16600 |
| C | 16.85800 | -8.01100 | 3.98100 |
| C | 18.06800 | -6.22400 | 5.09800 |
| N | 17.52000 | -7.78500 | 2.81500 |
| C | 18.72800 | -6.00900 | 3.90500 |
| C | 18.41600 | -6.81300 | 2.79000 |
| C | 16.31400 | -7.57800 | 6.32700 |
| C | 15.38900 | -8.63800 | 6.25100 |
| C | 15.89800 | -9.08000 | 3.97300 |
| C | 15.16800 | -9.40700 | 5.07900 |
| C | 16.16600 | -7.12000 | 7.67700 |
| N | 15.25600 | -7.81100 | 8.34800 |
| N | 14.79800 | -8.72900 | 7.47700 |
| H | 14.09400 | -9.38300 | 7.78500 |
| S | 16.91800 | -5.71300 | 8.50600 |
| O | 18.30500 | -5.61200 | 8.01400 |
| O | 16.00600 | -4.56700 | 8.36700 |
| C | 16.97800 | -6.18700 | 10.23100 |
| C | 17.89900 | -7.15300 | 10.63900 |
| C | 17.97100 | -7.48700 | 11.98900 |
| C | 17.13900 | -6.86900 | 12.93400 |
| C | 17.20500 | -7.25800 | 14.39100 |
| C | 16.23200 | -5.89200 | 12.49400 |
| C | 16.14500 | -5.54600 | 11.14800 |
| H | 18.29400 | -5.62200 | 5.96600 |
| H | 19.47500 | -5.23300 | 3.82700 |
| H | 18.93800 | -6.62500 | 1.86400 |
| H | 15.74900 | -9.64300 | 3.06300 |
| H | 14.45300 | -10.21600 | 5.06300 |
| H | 18.54500 | -7.63400 | 9.91900 |
| H | 18.68000 | -8.23500 | 12.31400 |
| H | 15.59100 | -5.40100 | 13.21100 |
| H | 15.44400 | -4.79300 | 10.81900 |
| H | 17.96600 | -8.02600 | 14.52800 |
| H | 16.23700 | -7.64600 | 14.70800 |
| H | 17.45900 | -6.38300 | 14.98900 |

**Fig. S4** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **1** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

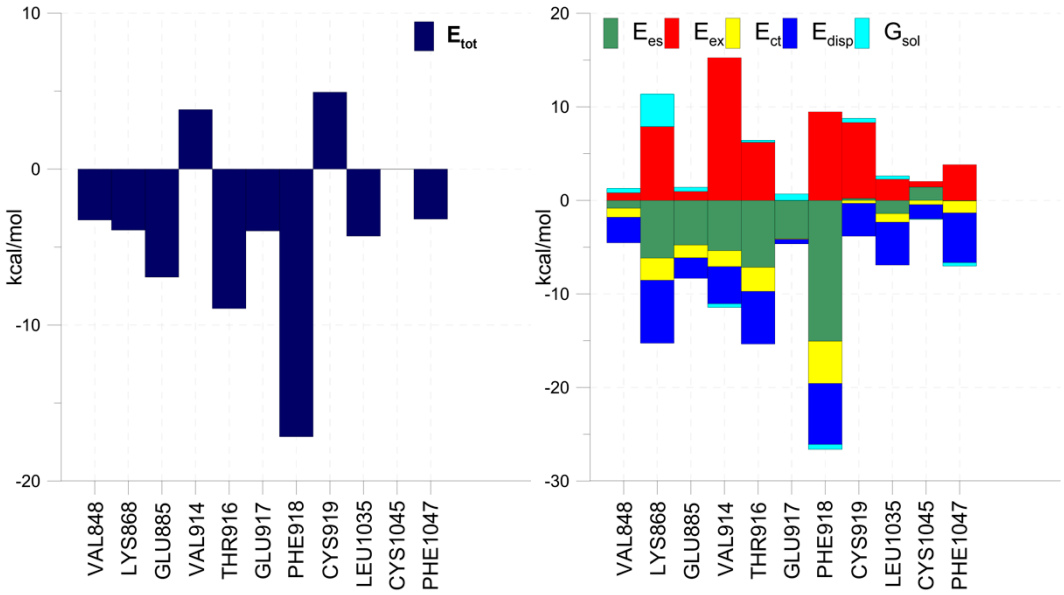



**Fig. S5** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **2** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

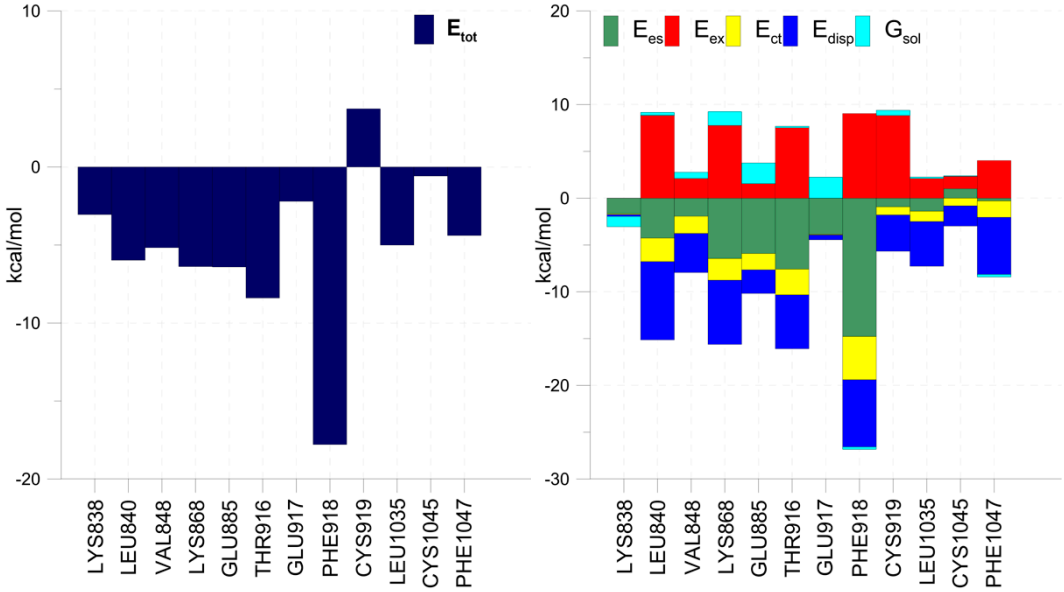


**Fig. S6** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **3** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

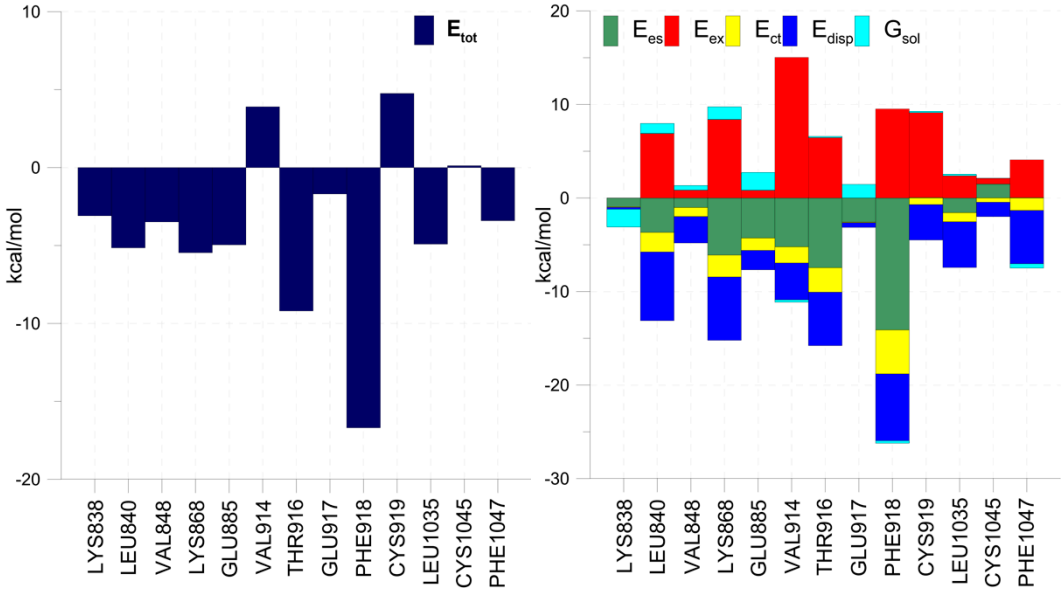



**Fig. S7** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **4** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

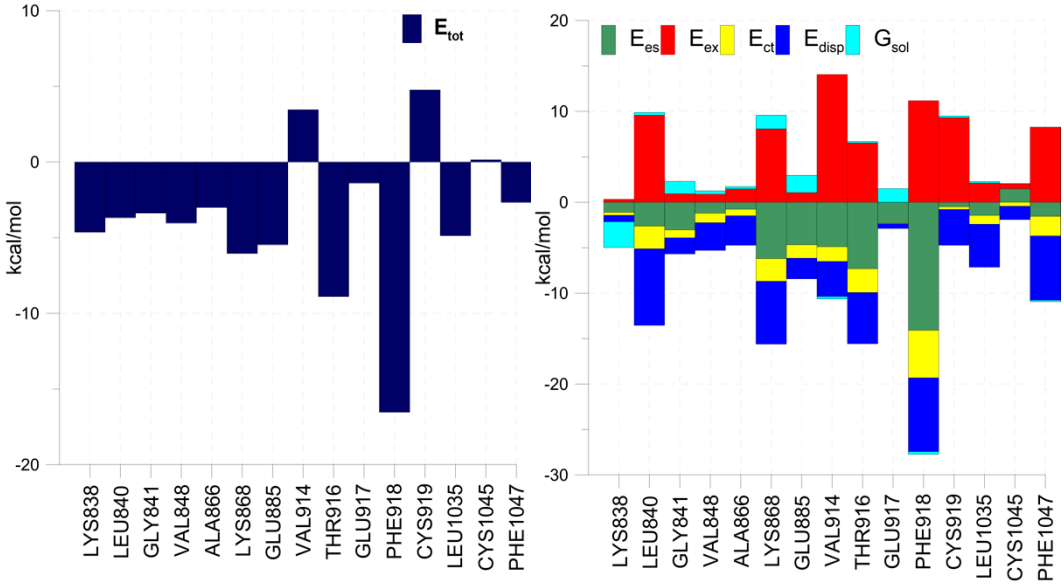


**Fig. S8** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **5** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

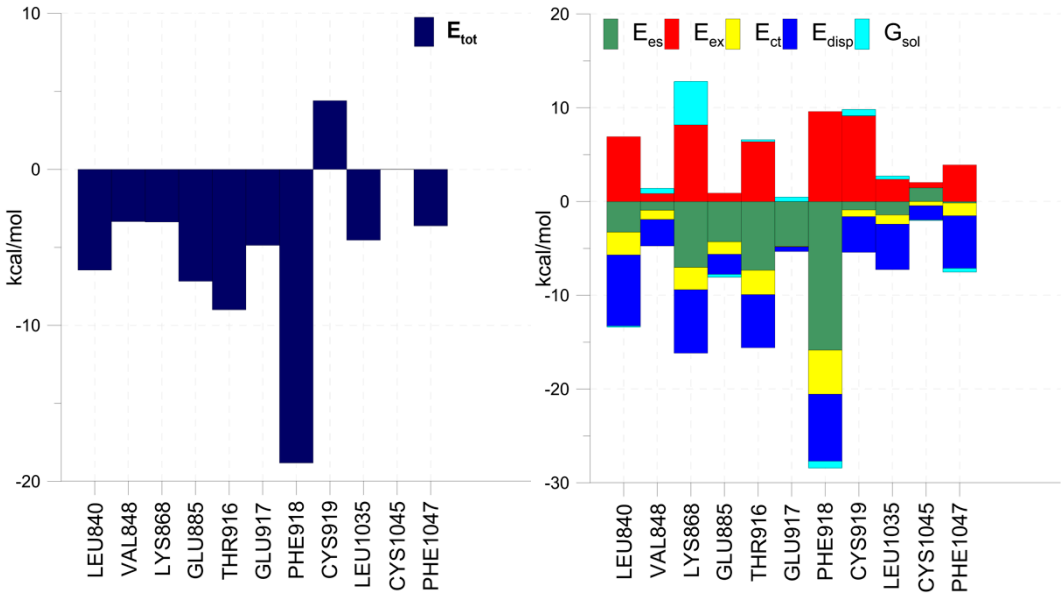



**Fig. S9** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **7** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

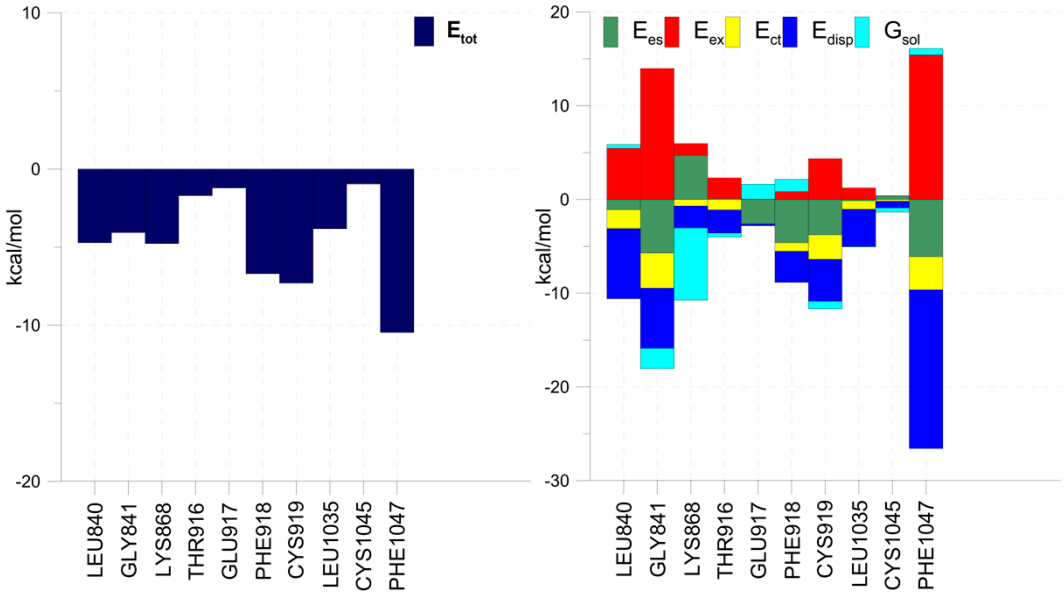


**Fig. S10** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **8** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

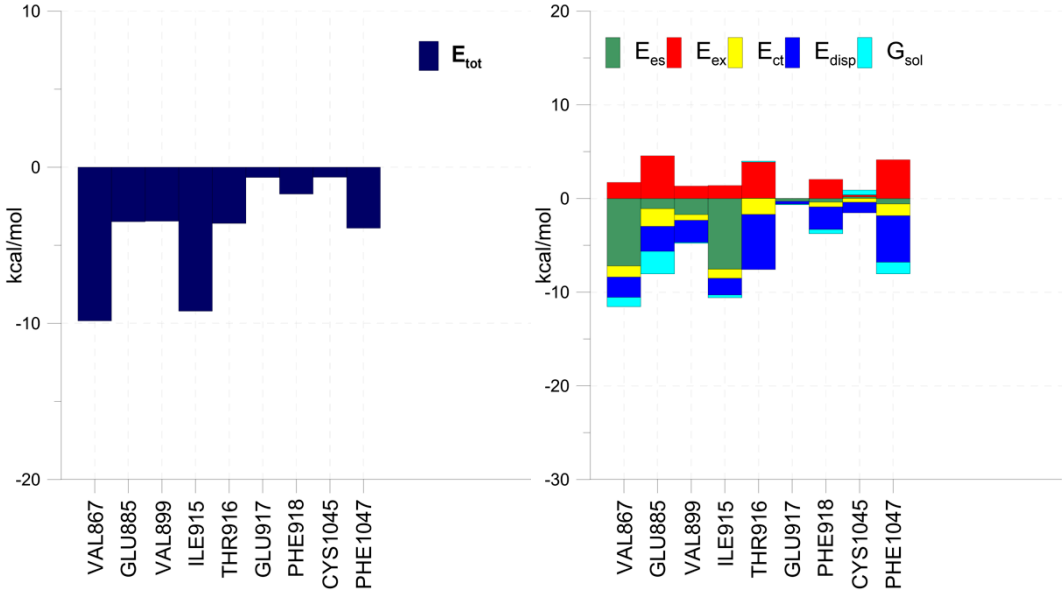



**Fig. S11** Calculated interaction energies ($E_{tot}$; kcal/mol) and the contributions to the total energy ($E_{es}$, $E_{ex}$, $E_{ct}$ + mix, $E_{dis}$, $G_{sol}$; kcal/mol) between docked azole **9** and selected residues of 3ewh.pdb kinase(*GAMESS* program).

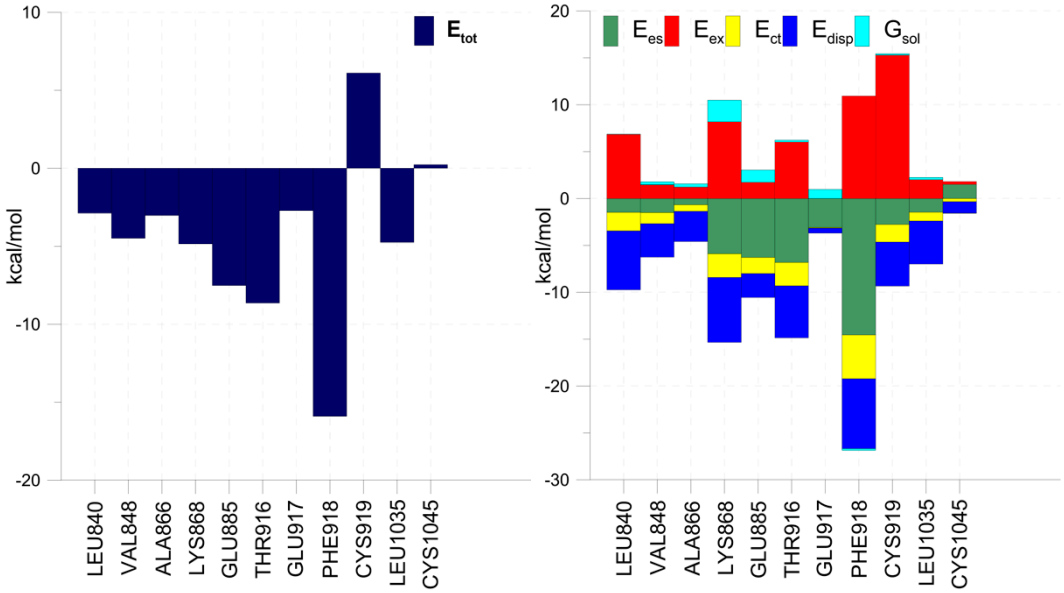
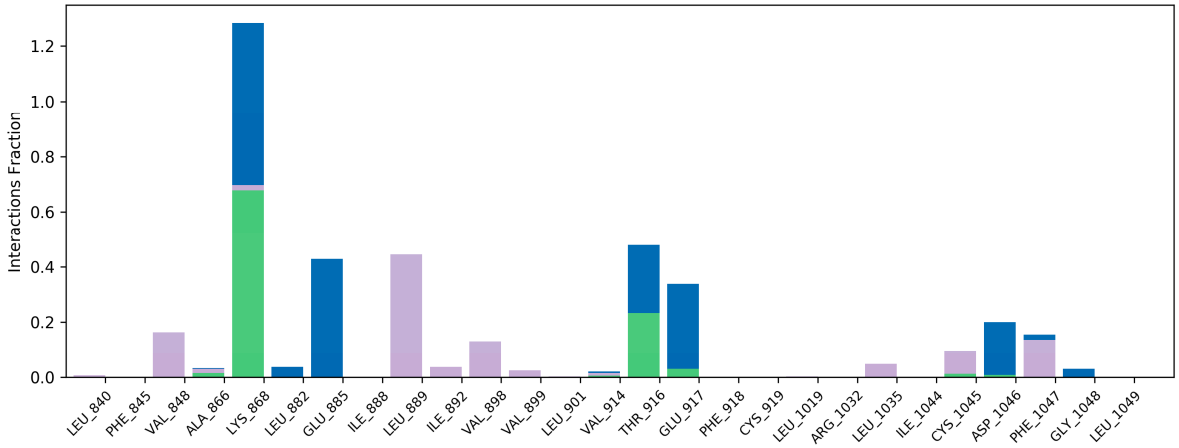


**Fig. S12** Example of input file for SAPt calculations regarding the **1**–Glu917 complex: memory 12 Gb

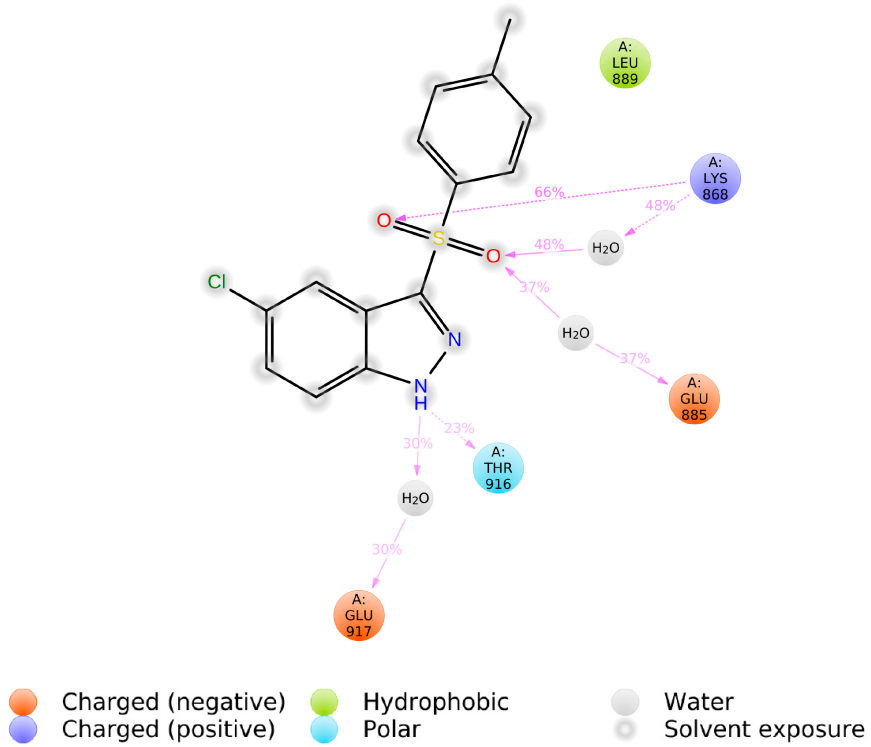
```
molecule {
0 1
N       13.09300    -12.93400     9.83300
H       12.37400    -12.58900    10.46800
C       12.68400    -13.52800     8.56300
H       13.03400    -14.58600     8.53500
C       13.30300    -12.77600     7.38300
O       13.43000    -11.55100     7.41100
C       11.16200    -13.51300     8.43700
H       10.83100    -14.12700     7.56700
H       10.69100    -14.09500     9.26300
C       10.57300    -12.10200     8.36200
H       11.10600    -11.49200     7.59600
H       10.83000    -11.51800     9.27600
C        9.07900    -12.08400     8.11700
O        8.59300    -12.87700     7.28200
O        8.37100    -11.22400     8.77700
H       14.07100    -12.86600    10.07800
H        7.84600    -10.58600     9.26700
O       13.69900    -13.43600     6.34100
H       13.99200    -13.92500     5.56900
--
C       16.05100     -6.98600     7.72300
C       16.26700     -7.42200     6.37600
C       15.46400     -8.58500     6.27300
N       14.86100     -8.73500     7.49600
N       15.21700     -7.77700     8.37400
C       15.38700     -9.33800     5.09200
C       16.13700     -8.89800     4.01500
C       16.94000     -7.73700     4.11600
C       17.02800     -6.98700     5.27500
H       14.22700     -9.45700     7.79700
Cl      17.85100     -7.25100     2.71800
S       16.78200     -5.57900     8.55700
O       15.77300     -4.51100     8.45800
O       18.14500     -5.39400     8.04500
C       16.89600     -6.08000    10.27500
C       16.05300     -5.49000    11.21600
C       16.15400     -5.87800    12.55100
C       17.08400     -6.84500    12.95600
C       17.20900     -7.23700    14.40700
C       17.91900     -7.42000    11.98500
C       17.83600     -7.04400    10.64800
H       14.77000    -10.22200     5.02600
H       16.10900     -9.44800     3.08600
H       17.65200     -6.10800     5.33200
```

```
H        15.33300      -4.74400      10.91500
H        15.50400      -5.42600      13.28600
H        18.63900      -8.16800      12.28100
H        18.48700      -7.49000       9.91100
H        16.47800      -6.68400      14.99700
H        18.21300      -7.00400      14.76100
H        17.02600      -8.30600      14.51100

units angstrom
}

set globals {
   basis         jun-cc-pvdz
   df_basis_scf  jun-cc-pvdz-jkfit
   df_basis_mp2  jun-cc-pvdz-ri
   guess         sad
   scf_type      df
}

set sapt { print 1 }

energy('sapt0')
```

**Fig. S13** The protein–ligand interactions (**a;** hydrogen bonds – green, hydrophobic – white purple, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (**b**) for chlorine derivative **1**.

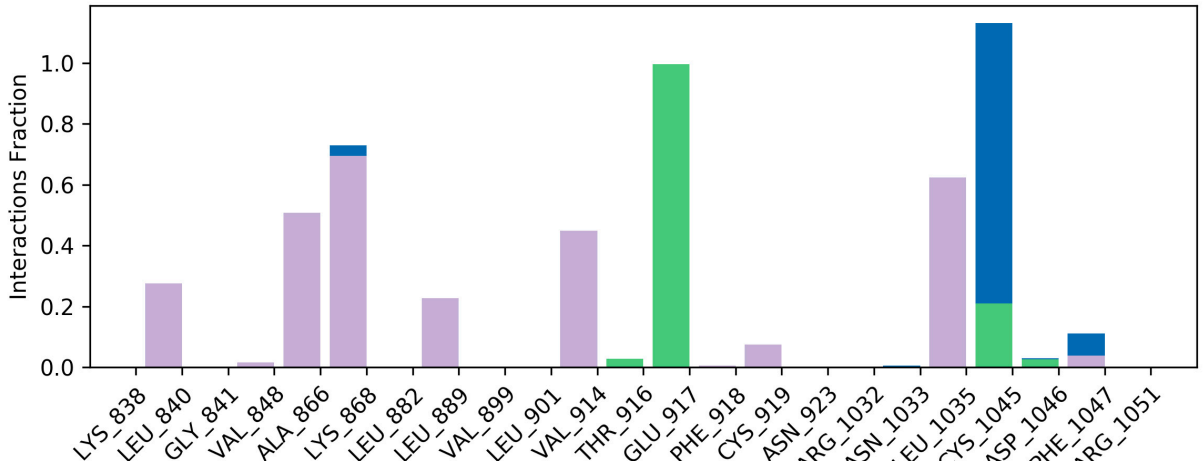



**a**

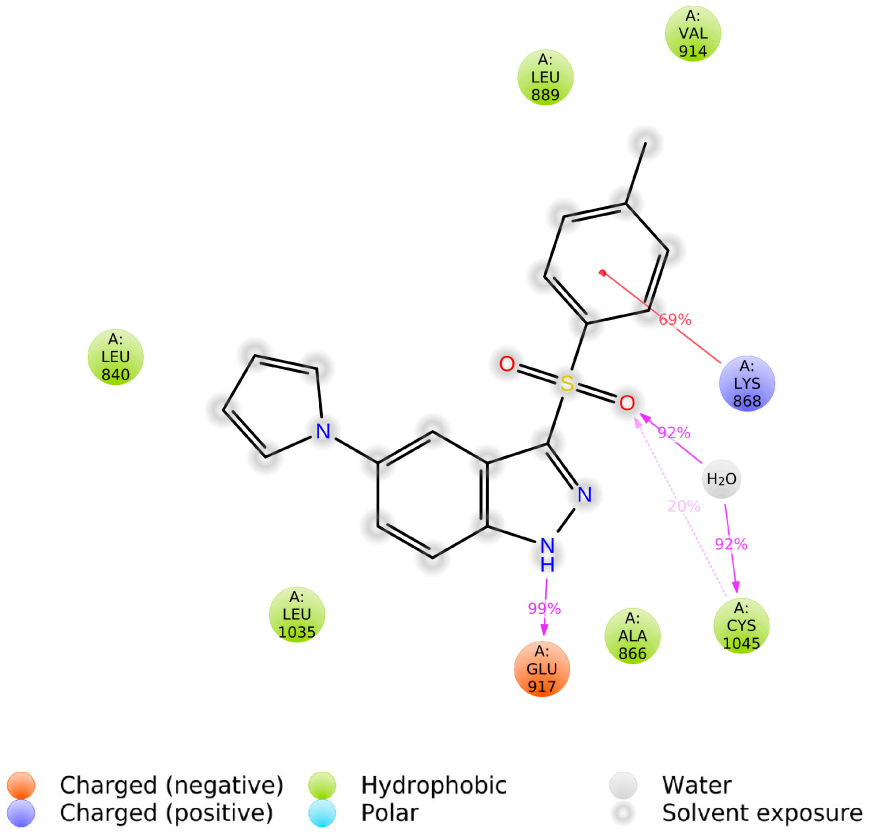



**b**

**Fig. S14** The protein–ligand interactions (**a;** hydrogen bonds – green, hydrophobic – white purple, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (**b**) for pyrrole derivative **2**.

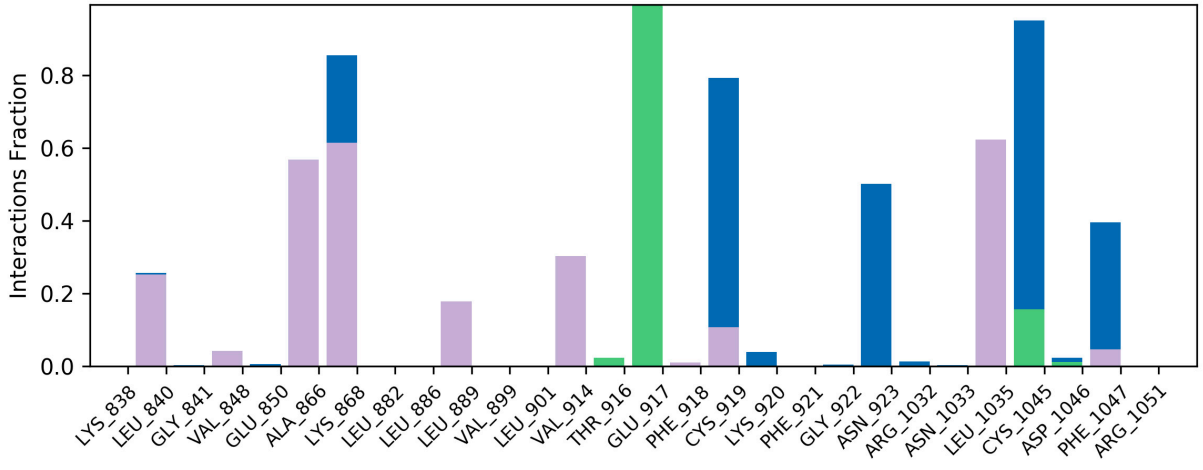



**a**

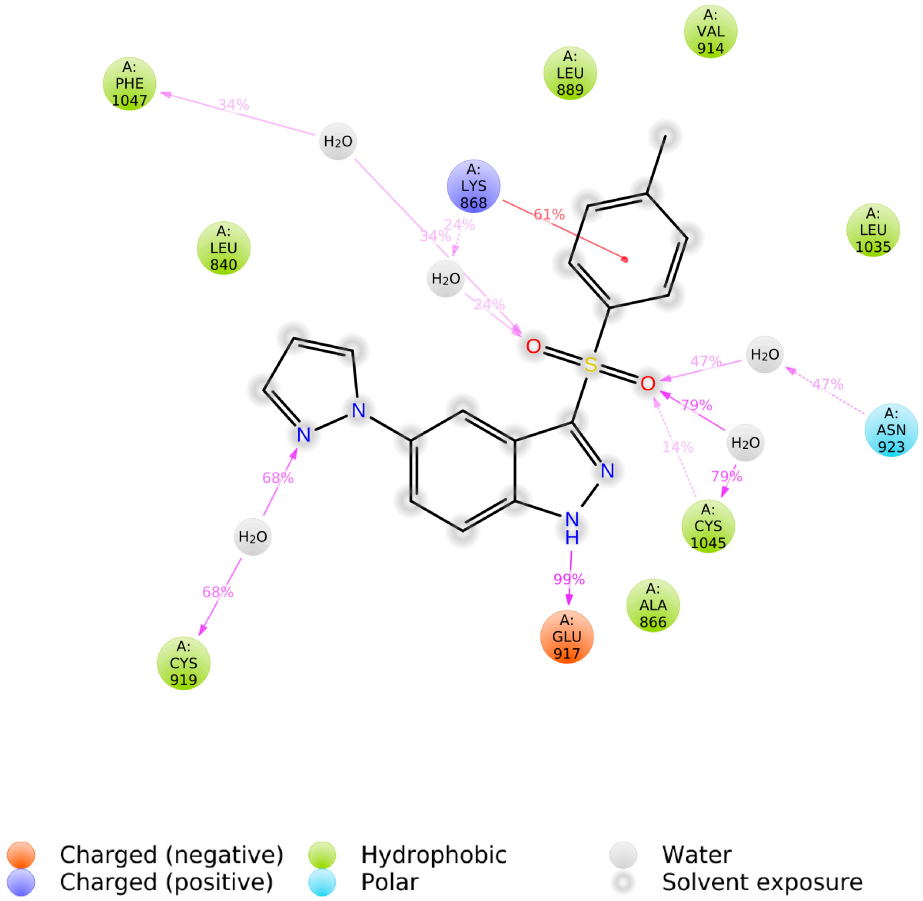



**b**

**Fig. S15** The protein–ligand interactions (**a;** hydrogen bonds – green, hydrophobic – white purple, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (**b**) for pyrazole derivative **3**.

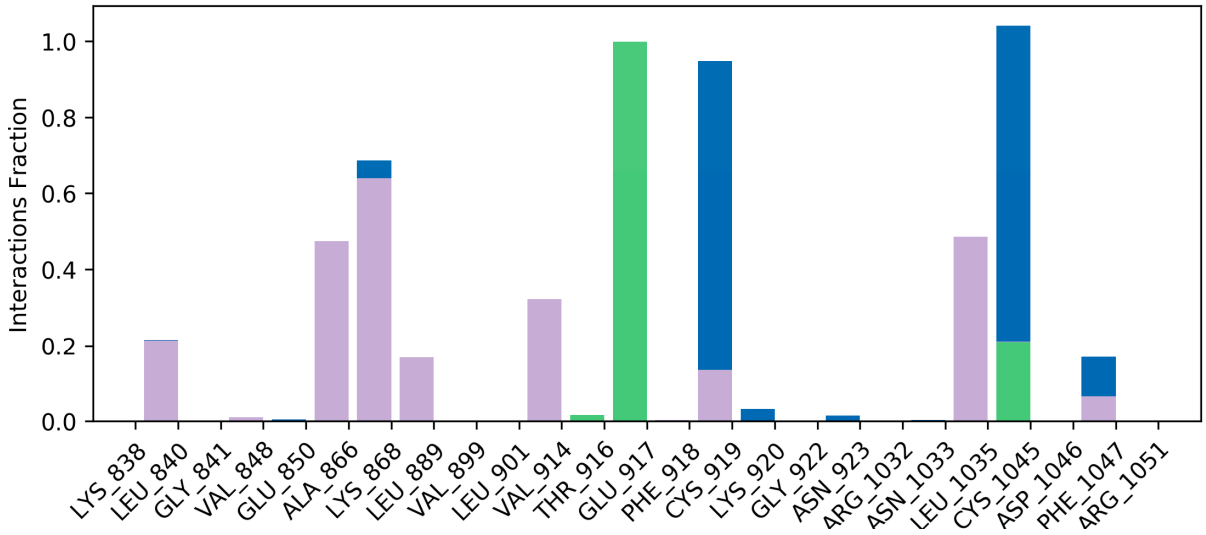



**a**

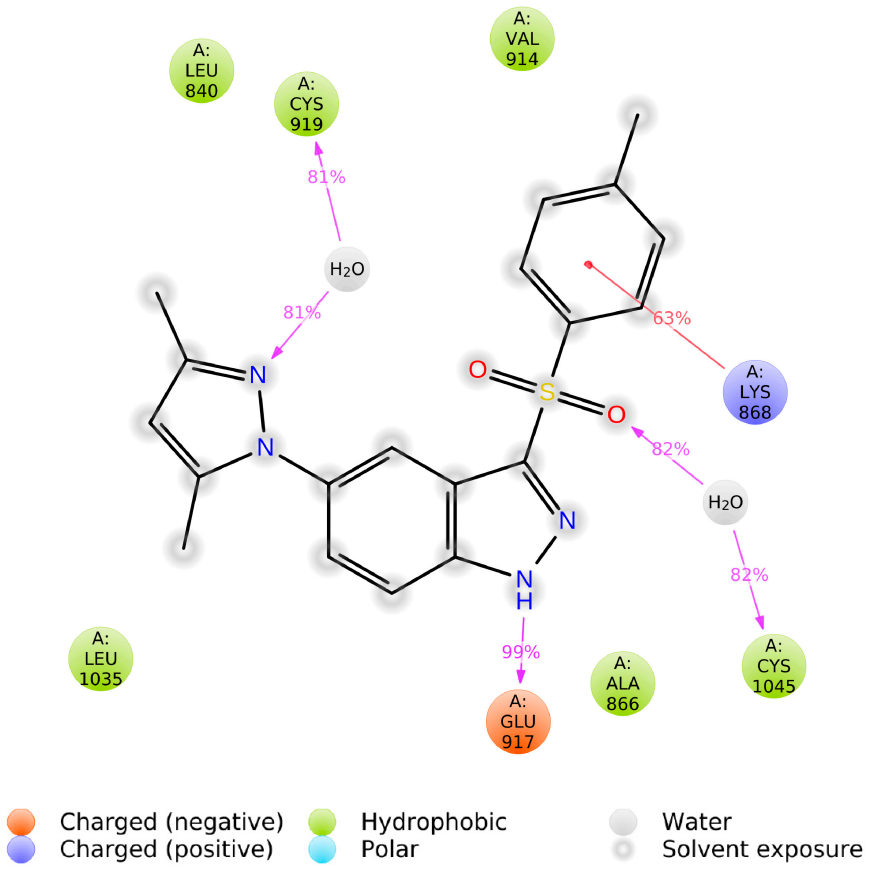



**b**

**Fig. S16** The protein–ligand interactions (**a;** hydrogen bonds – green, hydrophobic – white purple, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (**b**) for dimethyl pyrazole derivative **4**.

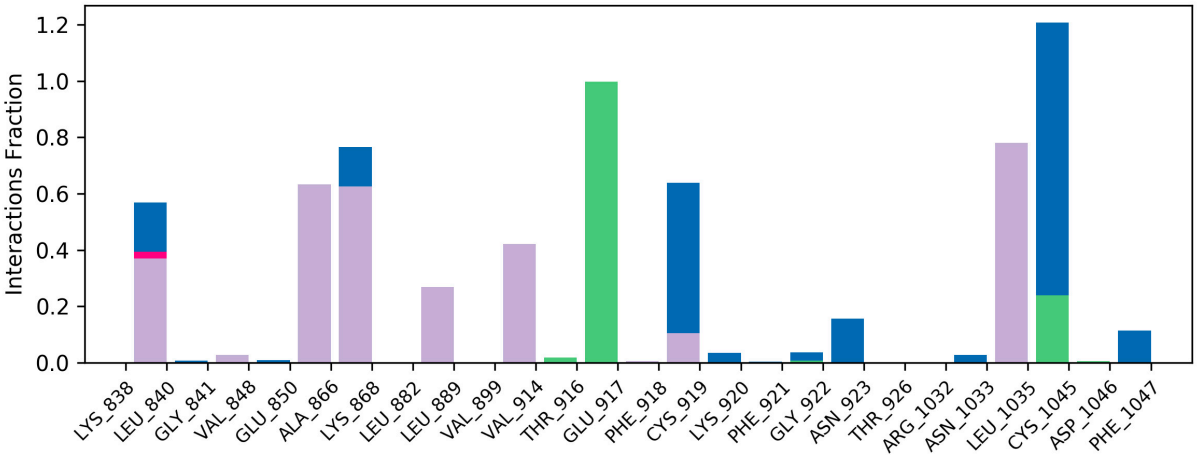



**a**

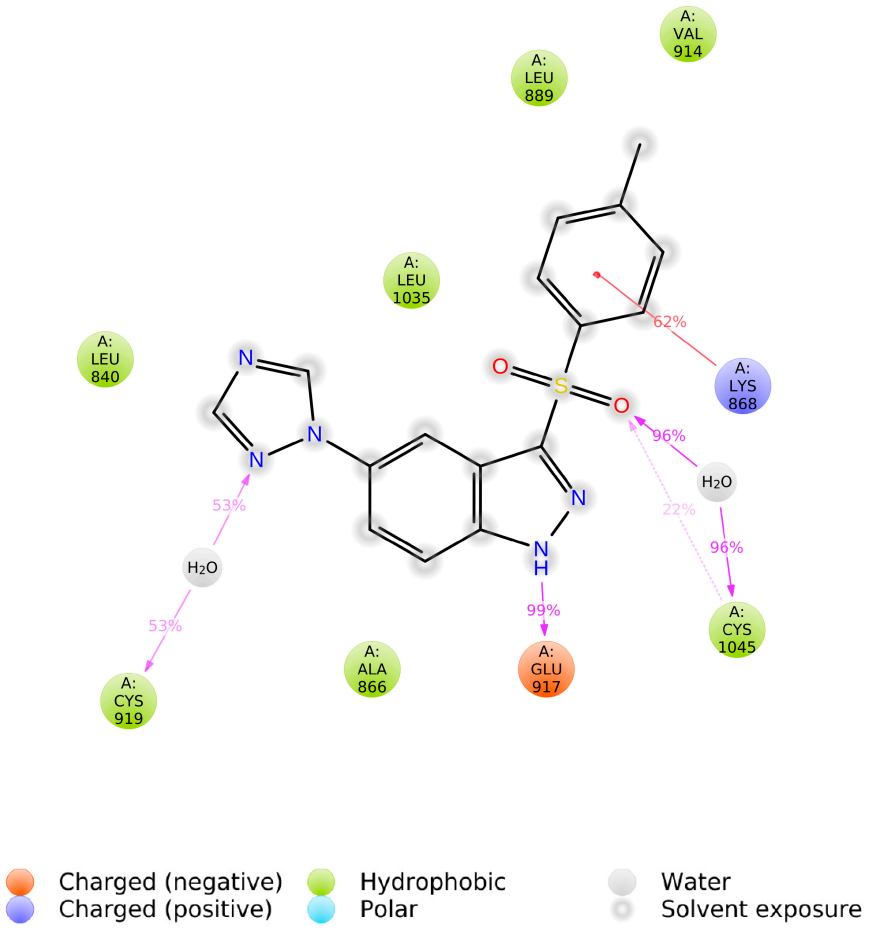



**b**

**Fig. S17** The protein–ligand interactions (**a;** hydrogen bonds – green, hydrophobic – white purple, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (**b**) for triazole derivative **5**.

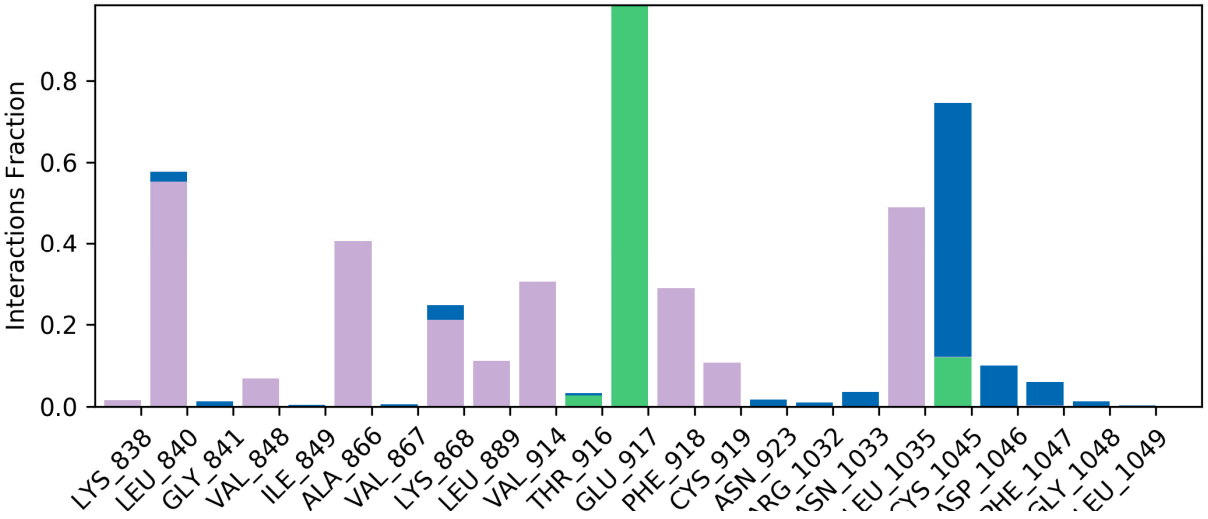



**a**

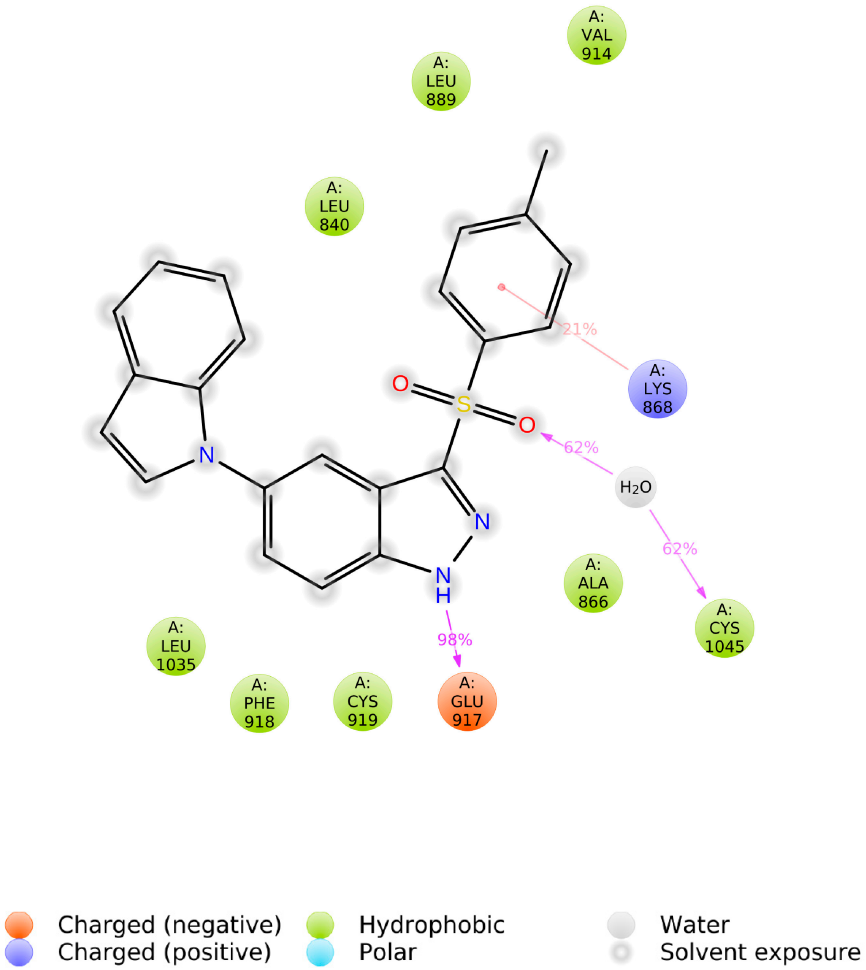



**b**

**Fig. S18** The protein–ligand interactions (**a;** hydrogen bonds – green, hydrophobic – white purple, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (**b**) for indole derivative **6**.

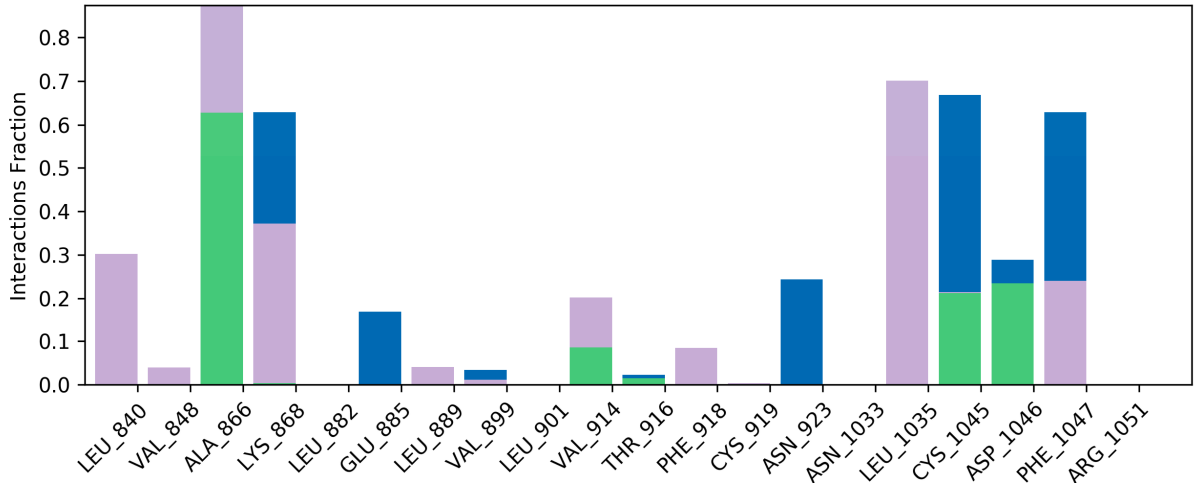



**a**

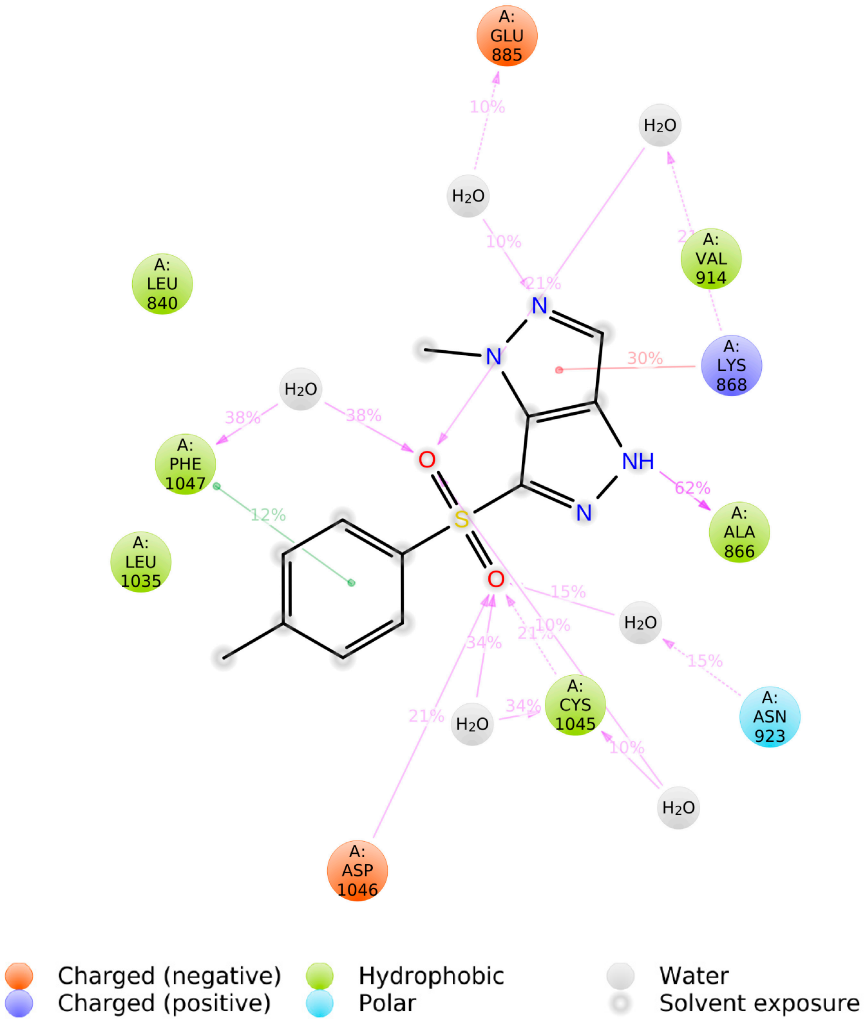



**b**

**Fig. S19** The protein–ligand interactions (**a;** hydrogen bonds – green, hydrophobic – white purple, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (**b**) for carbazole derivative **8**.




**a**




**b**

**Fig. S20** Atoms numbering for RMSF calculations of the ligand **1** and the RMSF plot for **1** within ligand–protein complex during the MD productive phase calculated complex of kinase with **1**.

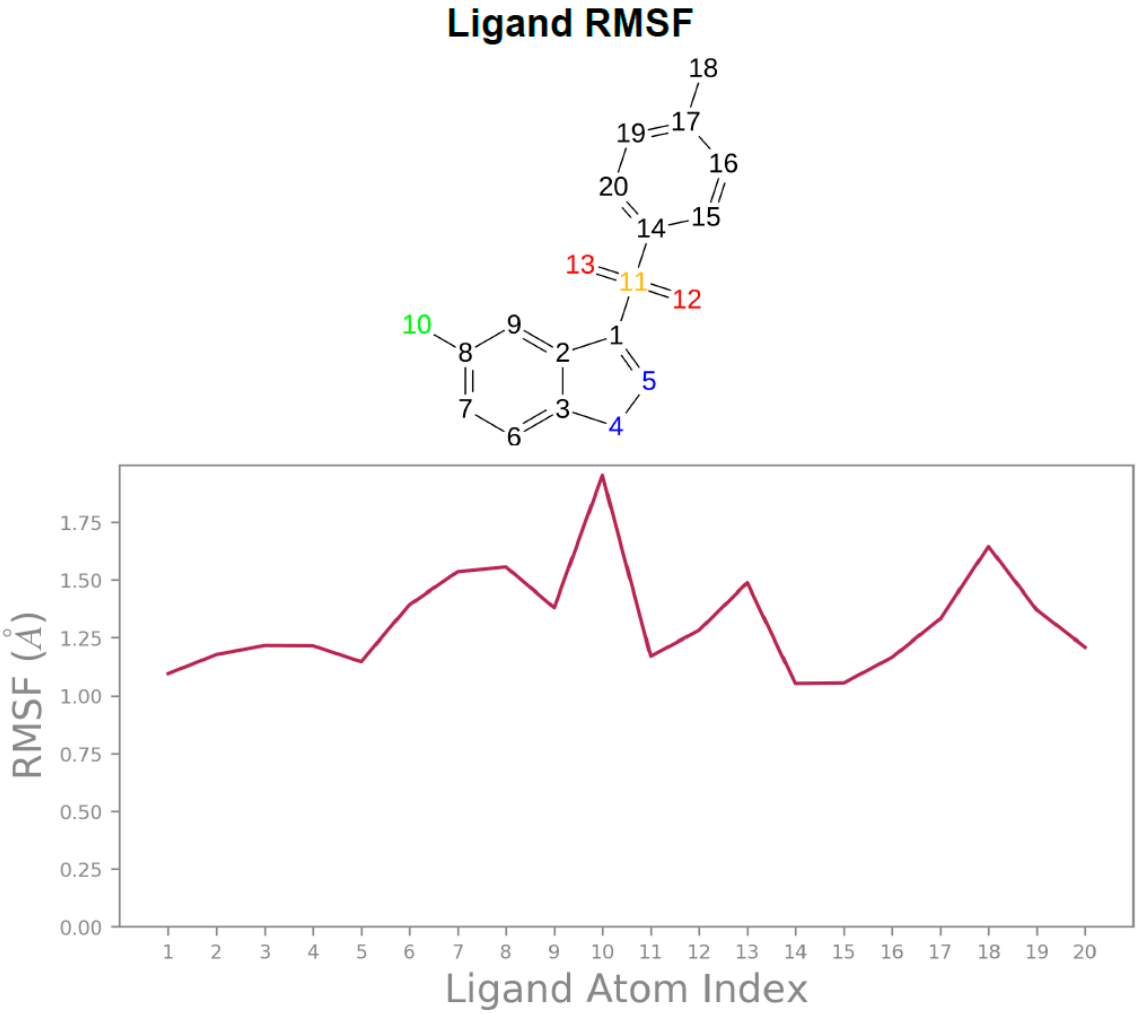


**Fig. S21** The RMSD plot for the backbone within ligand-protein complex during the MD productive phase calculated complex of kinase with: **1**–**9** (*Y*-axis in Å); colors related with **Fig. 4** given in the manuscript.

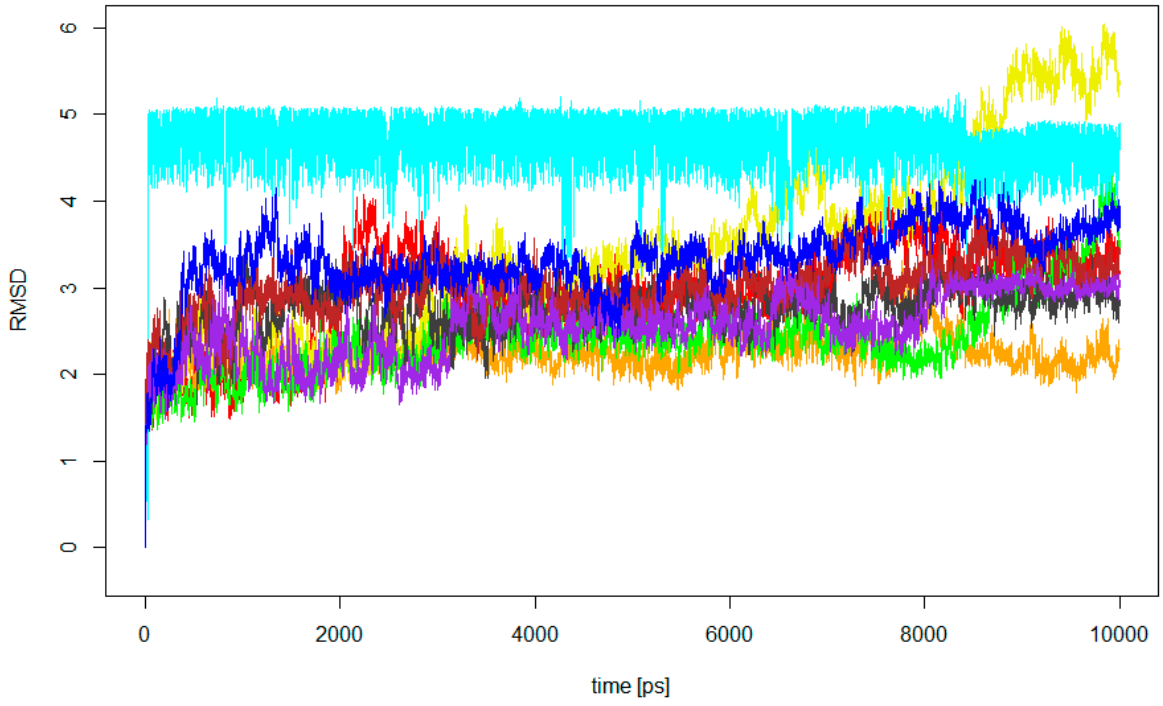


**Fig. S22** Representative MD cluster for binding mode of **1** within the **1**–3ewh complex (**A**) and its comparison with results using docking protocol (**B**).

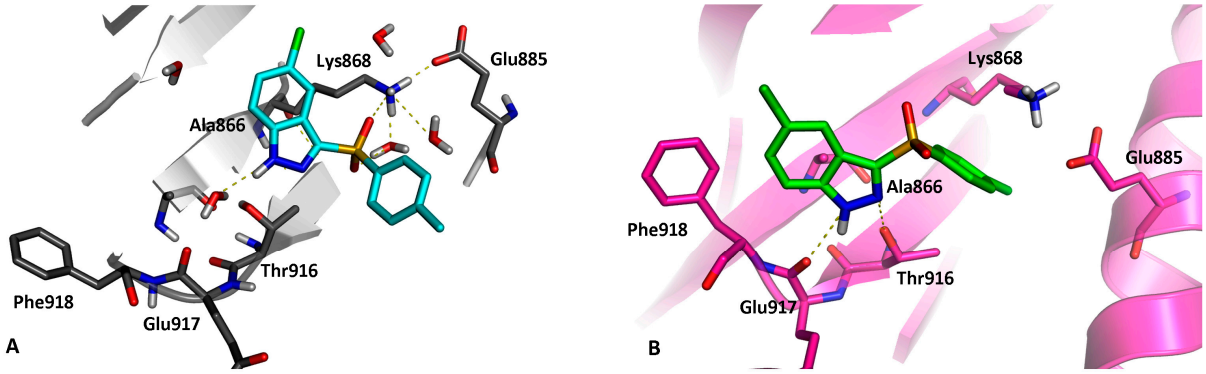



**Fig. S23** Hydrogen contacts with Thr916 during the MD productive phase calculated complex of kinase with derivative **3**; red – angles [°], blue – distances [Å].

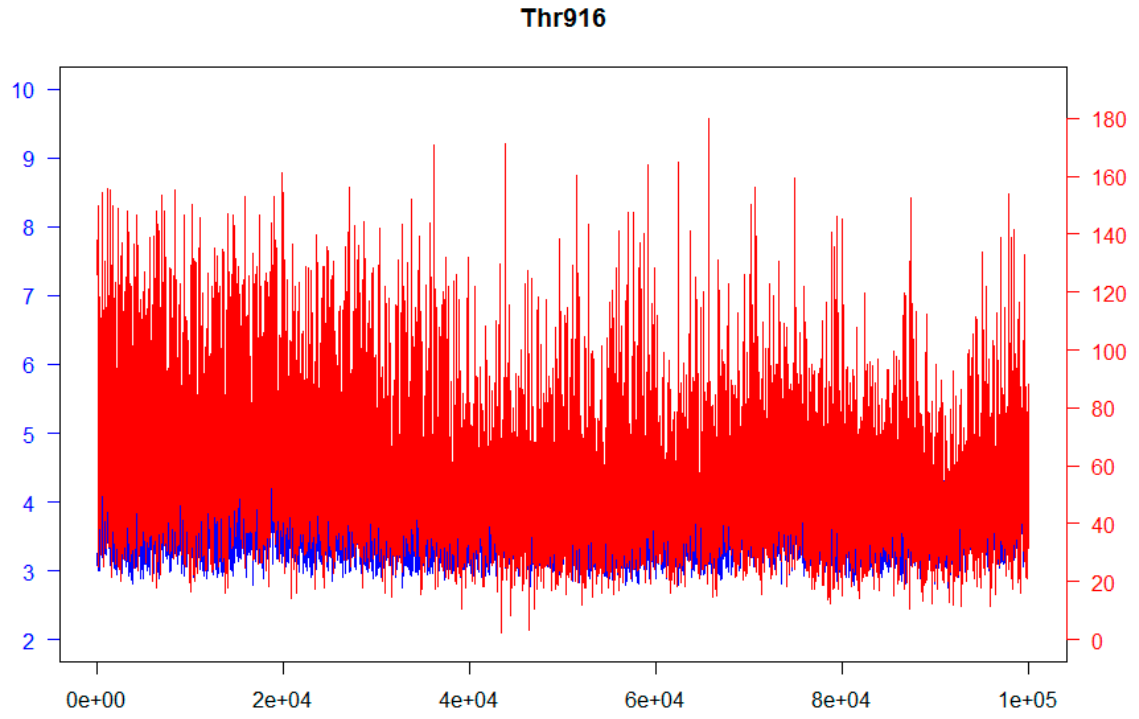


**Fig. S24** Hydrogen contacts with Glu917 during the MD productive phase calculated complex of kinase with derivative **3**; red – angles [°], blue – distances [Å].

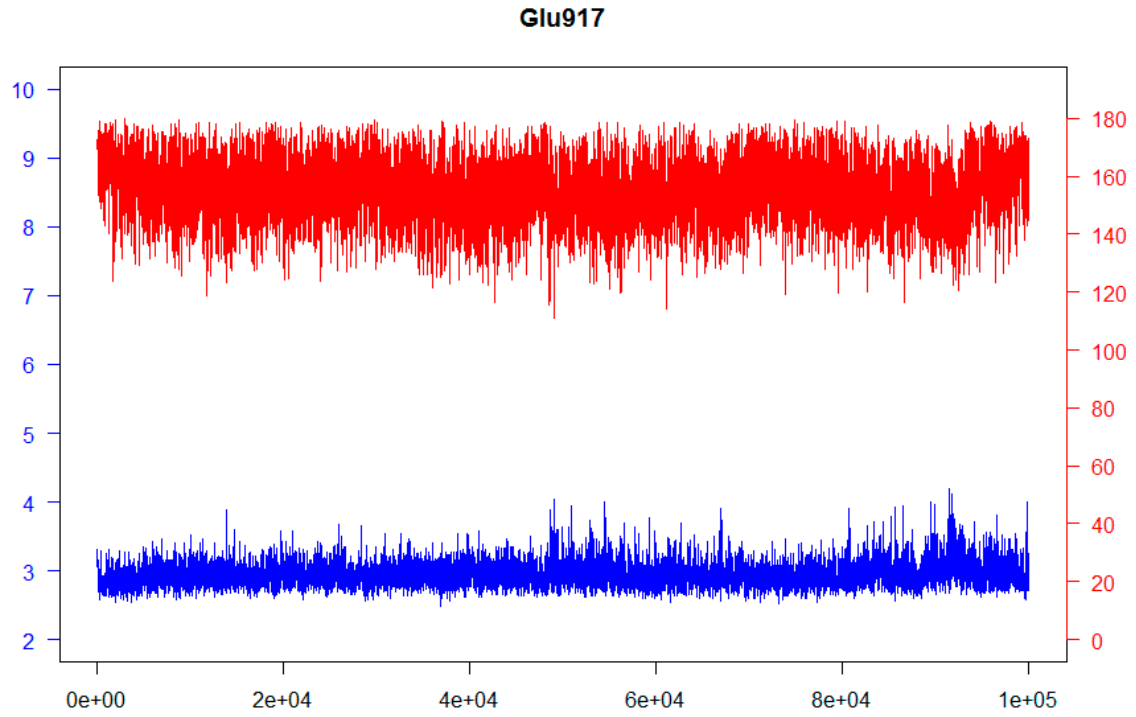



**Fig. S25** Hydrogen contacts with Thr916 during the MD productive phase calculated complex of kinase with derivative **6**; red – angles [°], blue – distances [Å].

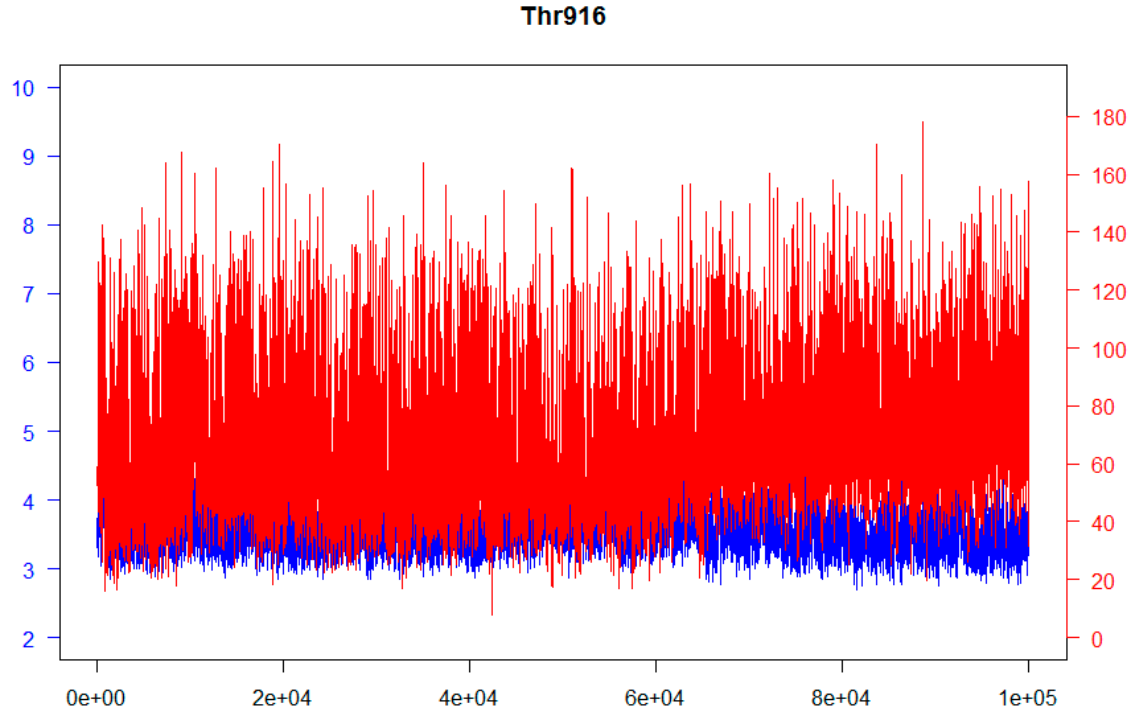


**Fig. S26** Hydrogen contacts with Glu917 during the MD productive phase calculated complex of kinase with derivative **6**; red – angles [°], blue – distances [Å].