Supporting Information

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

Kornelia Czaja 1, Jacek Kujawski 1*, Paweł Śliwa 2, Rafał Kurczab 3, Radosław Kujawski 4, Anna Stodolna 1, Agnieszka Myślińska 1 and Marek K. Bernard 1*

1Chair and Department of Organic Chemistry, Faculty of Pharmacy, Poznan University of Medical Sciences, ul. Grunwaldzka 6, 60-780 Poznań, Poland
2Cracow University of Technology, Faculty of Chemical Engineering and Technology, ul. Warszawska 24, 31-155 Kraków, Poland
3Maj Institute of Pharmacology, Polish Academy of Sciences, ul. Smętna 12, 31-343 Kraków, Poland
4Chair and Department of Pharmacology, Faculty of Pharmacy, Poznan University of Medical Sciences, ul. Rokietnicka 5a, 60-806 Poznań, Poland
* Correspondence: mbernard@ump.edu.pl (M.K.B.), jacekkuj@ump.edu.pl (J.K.), phone 48618546670, fax 48618546680

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. ......................................................................................................................................... 4

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. ......................................................................................................................................... 4

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): ................................................................. 5

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). ................................................................. 13

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). ................................................................. 13

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). ................................................................. 14

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). ................................................................. 14

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). ................................................................. 15
Fig. S9 Calculated interaction energies (E_{tot}; kcal/mol) and the contributions to the total energy (E_{es}, E_{ex}, E_{et} + mix, E_{dis}, G_{sol}; kcal/mol) between docked azole 7 and selected residues of 3ewh.pdb kinase (GAMESS program). ................................................................. 15

Fig. S10 Calculated interaction energies (E_{tot}; kcal/mol) and the contributions to the total energy (E_{es}, E_{ex}, E_{et} + mix, E_{dis}, G_{sol}; kcal/mol) between docked azole 8 and selected residues of 3ewh.pdb kinase (GAMESS program). ................................................................. 16

Fig. S11 Calculated interaction energies (E_{tot}; kcal/mol) and the contributions to the total energy (E_{es}, E_{ex}, E_{et} + mix, E_{dis}, G_{sol}; kcal/mol) between docked azole 9 and selected residues of 3ewh.pdb kinase (GAMESS program). ................................................................. 16

Fig. S12 Example of input file for SAPt calculations regarding the 1–Glu917 complex:............. 17

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. .................................................................................................................. 19

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. .................................................................................................................. 20

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. .................................................................................................................. 21

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. .................................................................................................................. 22

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. .................................................................................................................. 23

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. .................................................................................................................. 24

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. .................................................................................................................. 25

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. .................................................................................................................. 26

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. .................................................................................................................. 27

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). .................................................................................................................. 28
Fig. S23 Hydrogen contacts with Thr916 during the MD productive phase calculated complex of kinase with derivative 3; red – angles [°], blue – distances [Å]. .............................................. 28

Fig. S24 Hydrogen contacts with Glu917 during the MD productive phase calculated complex of kinase with derivative 3; red – angles [°], blue – distances [Å]. .............................................. 29

Fig. S25 Hydrogen contacts with Thr916 during the MD productive phase calculated complex of kinase with derivative 6; red – angles [°], blue – distances [Å]. .............................................. 29

Fig. S26 Hydrogen contacts with Glu917 during the MD productive phase calculated complex of kinase with derivative 6; red – angles [°], blue – distances [Å]. .............................................. 30
**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 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:

| Atom | X      | Y      | Z     |
|------|--------|--------|-------|
| C    | 16.0510| -6.9860| 7.7230|
| C    | 16.2670| -7.4220| 6.3760|
| C    | 15.4640| -8.5850| 6.2730|
| N    | 14.8610| -8.7350| 7.4960|
| N    | 15.2170| -7.7770| 8.3740|
| C    | 15.3870| -9.3380| 5.0920|
| C    | 16.1370| -8.8980| 4.0150|
| C    | 16.9400| -7.7370| 4.1160|
| C    | 17.0280| -6.9870| 5.2750|
| H    | 14.2270| -9.4570| 7.7970|
| Cl   | 17.8510| -7.2510| 2.7180|
| S    | 16.7820| -5.5790| 8.5570|
| O    | 15.7730| -4.5110| 8.4580|
| O    | 18.1450| -5.3940| 8.0450|
| C    | 16.8960| -6.0800| 10.2750|
| C    | 16.0530| -5.4900| 11.2160|
| C    | 16.1540| -5.8780| 12.5510|
| C    | 17.0840| -6.8450| 12.9560|
| C    | 17.2090| -7.2370| 14.4070|
| C    | 17.9190| -7.4200| 11.9850|
| C    | 17.8360| -7.0440| 10.6480|
| H    | 14.7700| -10.2220| 5.0260|
| H    | 16.1090| -9.4480| 3.0860|
| H    | 17.6520| -6.1080| 5.3320|
| H    | 15.3330| -4.7440| 10.9150|
| H    | 15.5040| -5.4260| 13.2860|
| H    | 18.6390| -8.1680| 12.2810|
| H    | 18.4870| -7.4900| 9.9110|
| H    | 16.4780| -6.6840| 14.9970|
| H    | 18.2130| -7.0040| 14.7610|
| H    | 17.0260| -8.3060| 14.5110|

### Azole 2
Cartesian coordinates:

| Atom | X      | Y      | Z     |
|------|--------|--------|-------|
| C    | 17.0350| -7.0480| 5.3230|
| C    | 16.9240| -7.7510| 4.1500|
| C    | 16.0610| -8.8830| 4.0560|
| C    | 15.3260| -9.3180| 5.1190|
| C    | 15.4390| -8.5880| 6.3190|
| N    | 14.8480| -8.7540| 7.5700|
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
Azole 4

Cartesian coordinates:
C  17.04700  -7.07600  5.28200  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
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
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
Azole 7
Cartesian coordinates:

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

Fig. S5 Calculated interaction energies ($E_{\text{tot}}$; kcal/mol) and the contributions to the total energy ($E_{\text{es}}, E_{\text{ex}}, E_{\text{ct} + \text{mix}}, E_{\text{dis}}, G_{\text{sol}}$; 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 (\(E_{\text{tot}}\); kcal/mol) and the contributions to the total energy (\(E_{\text{es}}, E_{\text{ex}}, E_{\text{ct} + \text{mix}}, E_{\text{dis}}, G_{\text{sol}}\); kcal/mol) between docked azole 5 and selected residues of 3ewh.pdb kinase (GAMESS program).

**Fig. S9** Calculated interaction energies (\(E_{\text{tot}}\); kcal/mol) and the contributions to the total energy (\(E_{\text{es}}, E_{\text{ex}}, E_{\text{ct} + \text{mix}}, E_{\text{dis}}, G_{\text{sol}}\); kcal/mol) between docked azole 7 and selected residues of 3ewh.pdb kinase (GAMESS program).
Fig. S10 Calculated interaction energies ($E_{\text{tot}}$; kcal/mol) and the contributions to the total energy ($E_{\text{es}}, E_{\text{ex}}, E_{\text{et + mix}}, E_{\text{dis}}, G_{\text{sol}}$; kcal/mol) between docked azole 8 and selected residues of 3ewh.pdb kinase (GAMESS program).

Fig. S11 Calculated interaction energies ($E_{\text{tot}}$; kcal/mol) and the contributions to the total energy ($E_{\text{es}}, E_{\text{ex}}, E_{\text{et + mix}}, E_{\text{dis}}, G_{\text{sol}}$; 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
```
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, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (b) for chlorine derivative 1.
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.
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.
**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.
**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.
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.
**Fig. S19** The protein–ligand interactions (a; hydrogen bonds – green, hydrophobic – white, ionic – pink, water bridges – blue) and schematic of detailed ligand atom interactions (b) for carbazole derivative 8.
**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].