**Table S1.** EC50 values of compounds determined using the SYBR Green I assay following treatment of parasite cultures with serial dilutions of the compounds for 48 h or 96 h, and stage of action determined by microscopy for a subset of compounds. Values are from a single experiment with duplicate samples for each compound, unless indicated by the presence of the standard deviation of the mean in parentheses after the EC50 value. Where this is present, the EC50 given is the mean of triplicate independent experiments.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Compound** | **Structure** | **Aromatic linker** | **EC50 (µM)** | | **ratio EC5048:EC5096** | **aStage of action (before or after DNA synthesis)** |
| **48 hours** | **96 hours** |
| 1 |  | pyridine | 0.29 | 0.29 | 1.0 |  |
| 2 |  | difluorophenyl | 1.28 | 1.04 | 1.2 |  |
| 3 |  | phenyl | 0.76 | 0.61 | 1.3 |  |
| 4 |  | pyridine | 0.30 | 0.22 | 1.4 |  |
| 5 |  | pyridine | 0.54 | 0.39 | 1.4 |  |
| 6 |  | pyridine | 0.59 | 0.42 | 1.4 |  |
| 7  **Cpd D** |  | pyridine | 0.36(0.08) | 0.31(0.10) | 1.1 | trophozoite  (before) |
| 8 |  | difluorophenyl | 0.99 | 0.66 | 1.5 |  |
| 9 |  | phenyl | 0.62 | 0.40 | 1.6 |  |
| 10 |  | pyrazole | 0.72 | 0.46 | 1.6 |  |
| 11 |  | pyridine | 0.96 | 0.60 | 1.6 |  |
| 12 |  | pyridine | 0.41 | 0.25 | 1.6 |  |
| 13 |  | phenyl | 1.25 | 0.76 | 1.7 |  |
| 14 |  | pyridine | 2.10 | 1.18 | 1.8 |  |
| 15 |  | fluoropyridine | 1.74 | 0.96 | 1.9 |  |
| 16 |  | fluorophenyl | 0.80 | 0.40 | 2.0 |  |
| 17 |  | pyridine | 1.15 | 0.58 | 2.0 |  |
| 18 |  | phenyl | 1.22 | 0.60 | 2.0 |  |
| 19 |  | pyridine | 0.57 | 0.26 | 2.2 |  |
| 20  **Cpd. E** |  | fluoropyridine | 0.30(0.07) | 0.14(0.02) | 2.1 | trophozoite (before) |
| 21 |  | fluorophenyl | 1.63 | 0.69 | 2.4 |  |
| 22 |  | pyridine | 0.55(0.08) | 0.30(0.14) | 1.8 | trophozoite  (before) |
| 23 |  | pyrimidine | 2.49 | 0.99 | 2.5 |  |
| 24 |  | pyridine | 2.45 | 0.71 | 3.4 |  |
| 25 |  | fluoropyridine | 1.96 | 0.54 | 3.6 |  |
| 26 |  | pyrimidine | 0.83 | 0.20 | 4.2 |  |
| 27 |  | fluoropyridine | 4.30 | 0.84 | 5.1 |  |
| 28 |  | pyrimidine | 0.17(0.01) | 0.04(0.01) | 4.4 | late schizont  (after) |
| 29 |  | pyrimidine | 3.46 | 0.64 | 5.4 |  |
| 30 |  | pyrimidine | 0.31 | 0.05 | 6.0 |  |
| 31 |  | pyrimidine | 1.66(0.65) | 0.24(0.05) | 7.0 | late schizont (after) |
| 32 |  | pyrimidine | 1.79 | 0.11 | 16.6 |  |
| 33 |  | pyrimidine | 100 | 0.03 | >1000 |  |
| 34 |  | pyrimidine | > 1000 | 1.18 | > 847 |  |
| 35 |  | pyrimidine | > 1000 | 0.81(0.45) | > 1000 | late schizont  (after) |
| 36  **Cpd A** |  | pyrimidine | > 1000 | 0.02(0.01) | > 1000 | late schizont  (after) |
| 37 |  | pyrimidine | > 1000 | 0.65 | > 1000 |  |
| 38 |  | pyrimidine | > 1000 | 0.05(0.02) | > 1000 | late schizont  (after) |
| 39  **Cpd. B** |  | pyrimidine | > 1000 | 0.02(0.01) | > 1000 | late schizont  (after) |
| 40 |  | pyrimidine | > 1000 | 1.23 | > 813 |  |
| 41  **Cpd. C** |  | pyrimidine | > 1000 | 0.04(0.01) | > 1000 | late schizont  (after) |

aring-stage parasites treated with 10x EC50 concentration of compound for 48h followed by microscopic examination of Giemsa-stained parasite smears.