**Supplementary Materials**

**QSAR modeling on a series of arylsulphonamide-based hydroxamates as potent MMP-2 inhibitors**

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**Table S1.** Various metrics used as validation parameters

|  |  |
| --- | --- |
| Name of the metric | Working formula |
| *R2* | $$R^{2}= 1-\frac{\sum\_{}^{}(Y\_{obs}-Y\_{calc})^{2}}{\sum\_{}^{}(Y\_{obs}-Y̅\_{train})^{2}}$$ |
| *Q2* | $$Q^{2}= 1-\frac{\sum\_{}^{}(Y\_{obs(training)}-Y\_{pred(training)})^{2}}{\sum\_{}^{}(Y\_{obs(training)}-Y̅\_{train})^{2}}$$ |
| *Q2(F1)* | $$Q^{2}\_{(F1)}= 1-\frac{\sum\_{}^{}(Y\_{obs(test)}-Y\_{pred(training)})^{2}}{\sum\_{}^{}(Y\_{obs(training)}-Y̅\_{training})^{2}}$$ |
| *r2m(test)* | $$r\_{m(test)}^{2}=r^{2}(1-\sqrt{r^{2}-r\_{0}^{2})}$$ |
| *Variable Inflation Factor (VIF)* | $$VIF= \frac{1}{1-r^{2}}$$ |
| *Standard error of estimation (SEE)* | $$SEE= \sqrt{\frac{\sum\_{}^{}(Y\_{Obs}-Y\_{Calc})^{2}}{n-p-1}}$$ |
| *Euclidean distance* | $$d\_{ij}= \sqrt{\sum\_{k=1}^{m}(x\_{ik}-x\_{jk})^{2}}$$ |
| *Mean distance of the equation* | $$d̅\_{i}= \sum\_{j=1}^{m}\frac{d\_{ij}}{n}-1$$ |
| *A squared mean correlation of the randomised model* | $$\sqrt{R^{2}-R\_{r}^{2}}$$ |

**Table S2.** List of variables and their corresponding values for arylsulphonamide-based hydroxamates having MMP-2 inhibitory activities.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Noa** | ***SpMax1\_Bhv*** | ***MATS3m*** | ***SsssCH*** | ***AATS4m*** | ***VE3\_Dze*** | ***VE3\_DzZ*** | ***GATS4p*** | ***SpMax4\_Bhv*** | **BAc** |
| **1b** | 3.945 | -0.127 | 0.069 | 64.987 | -5.352 | -4.207 | 0.935 | 3.224 | 8.161 |
| **2** | 3.937 | -0.104 | -0.431 | 84.126 | -7.329 | -5.122 | 1.128 | 3.223 | 5.444 |
| **3** | 3.936 | -0.065 | 0.000 | 90.519 | -5.807 | -4.598 | 1.378 | 3.108 | 5.018 |
| **4** | 3.937 | -0.120 | 0.000 | 71.770 | -4.171 | -2.710 | 1.222 | 3.507 | 5.678 |
| **5b** | 4.015 | -0.100 | 0.069 | 63.994 | -6.792 | -8.363 | 0.905 | 3.328 | 7.886 |
| **6** | 4.012 | -0.070 | -0.431 | 79.592 | -9.998 | -5.916 | 1.057 | 3.279 | 7.921 |
| **7b** | 4.012 | -0.050 | 0.000 | 81.623 | -8.405 | -6.535 | 1.188 | 3.312 | 7.481 |
| **8** | 4.012 | -0.091 | 0.000 | 70.120 | -4.695 | -3.022 | 1.176 | 3.757 | 7.387 |
| **9** | 3.954 | -0.059 | -1.393 | 74.536 | -9.092 | -5.174 | 1.027 | 3.377 | 7.699 |
| **10** | 3.958 | -0.296 | -0.836 | 85.587 | -5.397 | -3.536 | 0.996 | 3.376 | 10.081 |
| **11b** | 3.937 | -0.118 | 0.000 | 79.327 | -6.100 | -3.394 | 1.283 | 3.227 | 5.975 |
| **12** | 3.937 | -0.185 | 0.000 | 84.307 | -5.527 | -3.502 | 1.265 | 3.227 | 5.824 |
| **13** | 3.936 | 0.113 | 0.000 | 50.084 | -1.106 | -0.627 | 1.122 | 3.465 | 4.523 |
| **14** | 3.943 | -0.106 | 1.726 | 56.210 | -10.529 | -4.343 | 0.913 | 3.227 | 5.703 |
| **15b** | 3.942 | 0.041 | -2.027 | 81.319 | -7.324 | -6.776 | 1.100 | 3.282 | 6.180 |
| **16** | 3.941 | 0.060 | -1.497 | 71.820 | -11.169 | -5.676 | 1.049 | 3.369 | 6.137 |
| **17** | 4.014 | 0.047 | -1.949 | 77.713 | -4.711 | -2.843 | 1.129 | 3.524 | 8.824 |
| **18b** | 4.014 | -0.065 | -2.030 | 80.340 | -7.719 | -9.363 | 1.082 | 3.506 | 9.000 |
| **19** | 4.014 | 0.001 | -1.878 | 78.490 | -7.239 | -4.938 | 1.162 | 3.372 | 9.481 |
| **20** | 4.014 | 0.003 | -1.936 | 74.189 | -3.630 | -2.160 | 1.140 | 3.529 | 8.854 |
| **21** | 4.015 | -0.017 | -1.908 | 77.253 | -16.752 | -15.618 | 1.201 | 3.380 | 9.886 |
| **22b** | 4.015 | -0.013 | -1.966 | 73.381 | -4.646 | -2.939 | 1.173 | 3.536 | 9.432 |
| **23** | 3.936 | 0.010 | -1.816 | 83.353 | -2.469 | -1.200 | 1.189 | 3.278 | 6.229 |
| **24** | 4.015 | 0.035 | -2.185 | 81.040 | -14.774 | -7.378 | 1.165 | 3.530 | 9.174 |
| **25** | 4.014 | 0.046 | -2.025 | 78.375 | -7.339 | -5.525 | 1.044 | 3.357 | 9.092 |
| **26** | 3.951 | -0.003 | -1.180 | 67.121 | -10.085 | -6.105 | 0.980 | 3.334 | 7.538 |
| **27** | 4.017 | 0.004 | -1.178 | 66.130 | -9.287 | -6.516 | 0.945 | 3.396 | 8.523 |
| **28b** | 4.011 | -0.087 | 0.000 | 64.612 | -2.689 | -3.176 | 1.116 | 3.316 | 5.620 |
| **29** | 4.033 | -0.072 | 0.000 | 80.466 | -6.455 | -3.274 | 1.381 | 3.247 | 6.638 |
| **30b** | 3.901 | 0.050 | -1.179 | 68.195 | -9.409 | -9.392 | 0.961 | 3.511 | 5.046 |
| **31** | 3.951 | -0.081 | -0.344 | 145.541 | -3.439 | -1.050 | 0.734 | 3.203 | 5.959 |
| **32b** | 3.783 | 0.053 | -0.529 | 44.160 | -4.663 | -4.661 | 0.919 | 2.965 | 4.469 |
| **33b** | 3.934 | -0.150 | 0.000 | 68.069 | -10.604 | -3.728 | 1.050 | 3.226 | 8.420 |
| **34** | 3.934 | -0.128 | 0.000 | 81.089 | -9.868 | -4.303 | 1.005 | 3.227 | 8.921 |
| **35** | 3.934 | -0.200 | 0.000 | 71.038 | -11.437 | -3.952 | 1.044 | 3.226 | 8.523 |
| **36** | 3.934 | -0.172 | 0.000 | 80.821 | -19.692 | -4.955 | 1.103 | 3.228 | 8.125 |
| **37** | 3.970 | -0.133 | 0.000 | 65.701 | -8.131 | -6.521 | 1.062 | 3.490 | 7.319 |
| **38** | 3.934 | -0.128 | 0.000 | 91.302 | -11.474 | -4.669 | 0.933 | 3.226 | 7.824 |
| **39** | 3.934 | -0.200 | 0.000 | 73.367 | -9.983 | -4.298 | 1.049 | 3.226 | 8.108 |
| **40** | 3.934 | -0.172 | 0.000 | 82.558 | -7.810 | -6.153 | 1.098 | 3.227 | 7.699 |
| **41b** | 3.972 | -0.133 | 0.000 | 66.773 | -6.071 | -8.875 | 1.031 | 3.490 | 7.387 |
| **42** | 3.972 | -0.134 | 0.000 | 73.000 | -5.004 | -11.429 | 1.037 | 3.320 | 6.174 |
| **43** | 3.934 | -0.257 | 0.000 | 82.472 | -7.357 | -5.205 | 1.047 | 3.226 | 7.745 |
| **44b** | 3.934 | -0.152 | 0.000 | 187.765 | -8.058 | -6.247 | 0.728 | 3.227 | 5.757 |
| **45b** | 3.933 | -0.200 | 0.000 | 78.669 | -6.820 | -2.970 | 1.155 | 3.218 | 6.959 |
| **46** | 3.943 | -0.179 | 0.000 | 162.427 | -9.460 | -4.981 | 0.671 | 3.229 | 5.728 |
| **47** | 3.934 | -0.163 | 0.000 | 196.766 | -9.926 | -5.215 | 0.748 | 3.182 | 3.903 |
| **48** | 3.986 | -0.126 | 0.000 | 89.300 | -5.631 | -14.046 | 0.916 | 3.493 | 5.420 |
| **49** | 3.969 | -0.126 | 0.000 | 94.663 | -5.103 | -10.596 | 0.879 | 3.490 | 5.981 |
| **50b** | 4.016 | -0.112 | -0.428 | 79.812 | -7.285 | -5.625 | 1.045 | 3.285 | 8.824 |
| **51** | 4.014 | -0.093 | -0.445 | 77.835 | -8.796 | -4.330 | 1.109 | 3.282 | 8.377 |
| **52** | 4.014 | 0.009 | -0.446 | 71.120 | -4.119 | -2.258 | 1.042 | 3.368 | 8.260 |
| **53** | 4.014 | -0.124 | -0.454 | 75.795 | -5.393 | -3.322 | 1.048 | 3.472 | 7.398 |
| **54** | 3.982 | -0.077 | -0.447 | 71.203 | -7.233 | -4.306 | 1.063 | 3.534 | 7.131 |
| **55** | 3.940 | -0.089 | -0.452 | 83.410 | -6.600 | -3.832 | 1.003 | 3.280 | 7.585 |
| **56** | 3.970 | 0.059 | -0.411 | 79.915 | -3.480 | -1.592 | 0.896 | 3.368 | 6.444 |
| **57b** | 4.033 | -0.059 | -0.432 | 103.375 | -7.650 | -6.320 | 1.036 | 3.271 | 6.509 |
| **58** | 4.036 | 0.029 | -0.391 | 89.293 | -7.643 | -4.362 | 1.077 | 3.279 | 7.252 |
| **59** | 4.033 | -0.035 | -0.405 | 96.471 | -13.191 | -6.070 | 1.083 | 3.272 | 7.770 |
| **60** | 3.932 | -0.202 | 0.000 | 76.795 | -3.001 | -3.069 | 1.159 | 2.793 | 7.495 |
| **61** | 3.938 | -0.162 | 0.000 | 102.896 | -2.543 | -1.699 | 1.036 | 2.646 | 7.398 |
| **62** | 4.012 | -0.058 | -1.170 | 70.497 | -4.352 | -3.781 | 1.199 | 3.362 | 9.155 |
| **63** | 4.025 | 0.035 | -1.518 | 87.012 | -8.278 | -6.504 | 1.175 | 3.520 | 6.409 |
| **64** | 3.942 | -0.085 | -1.125 | 86.885 | -3.005 | -1.450 | 1.114 | 3.249 | 6.721 |
| **65** | 3.942 | -0.060 | -1.312 | 90.720 | -11.674 | -4.516 | 1.091 | 3.368 | 8.824 |
| **66** | 3.937 | -0.035 | -1.280 | 72.444 | -4.746 | -3.116 | 1.091 | 3.399 | 7.770 |
| **67** | 3.938 | -0.006 | -1.382 | 82.511 | -11.455 | -7.038 | 1.133 | 3.393 | 8.377 |
| **68b** | 3.951 | 0.011 | -1.477 | 75.145 | -10.552 | -5.348 | 1.016 | 3.395 | 7.678 |
| **69b** | 3.936 | -0.045 | -1.277 | 70.532 | -5.834 | -3.859 | 1.174 | 3.439 | 7.770 |
| **70** | 3.938 | -0.082 | -1.077 | 134.705 | -7.748 | -7.796 | 0.815 | 3.417 | 6.620 |
| **71** | 3.938 | -0.083 | -1.277 | 143.282 | -9.845 | -7.093 | 0.856 | 3.558 | 5.387 |
| **72** | 3.938 | -0.069 | -1.189 | 135.774 | -7.218 | -5.295 | 0.847 | 3.567 | 5.842 |

**a Compound number; b Test set compounds; c MMP-2 inhibitory activity.**

**Table S3.**  Observed (Obs), calculated (Calc), LOO-predicted (Pred) activities of training set compounds (arylsulphonamide-based hydroxamates having MMP-2 inhibitory activities) for MLR and PLS models.

|  |  |  |  |
| --- | --- | --- | --- |
| **CpdNo** | **Obs** | **MLR model** | **PLS model** |
| **Calc** | **Pred** | **Pred** | **Pred** |
| **2** | 5.444 | 6.714 | 6.781 | 6.762 | 6.844 |
| **3** | 5.018 | 4.734 | 4.603 | 5.109 | 5.433 |
| **4** | 5.678 | 5.817 | 5.846 | 5.826 | 5.939 |
| **6** | 7.921 | 8.251 | 8.278 | 8.215 | 8.238 |
| **8** | 7.387 | 6.650 | 6.372 | 6.570 | 6.330 |
| **9** | 7.699 | 8.554 | 8.619 | 8.477 | 8.523 |
| **10** | 10.081 | 9.719 | 9.550 | 9.509 | 8.776 |
| **12** | 5.824 | 6.478 | 6.584 | 6.621 | 6.810 |
| **13** | 4.523 | 4.412 | 4.352 | 4.316 | 4.367 |
| **14** | 5.703 | 6.002 | 6.151 | 5.645 | 5.869 |
| **16** | 6.137 | 7.482 | 7.725 | 7.511 | 7.837 |
| **17** | 8.824 | 8.314 | 8.251 | 8.404 | 8.342 |
| **19** | 9.481 | 8.895 | 8.838 | 9.001 | 8.942 |
| **20** | 8.854 | 8.780 | 8.768 | 8.826 | 8.793 |
| **21** | 9.886 | 8.970 | 8.425 | 8.979 | 8.572 |
| **23** | 6.229 | 7.079 | 7.259 | 7.300 | 7.486 |
| **24** | 9.174 | 9.314 | 9.342 | 9.507 | 9.552 |
| **25** | 9.092 | 8.984 | 8.968 | 8.988 | 8.926 |
| **26** | 7.538 | 8.113 | 8.185 | 7.963 | 7.999 |
| **27** | 8.523 | 9.111 | 9.208 | 8.877 | 8.869 |
| **29** | 6.638 | 6.881 | 6.972 | 7.189 | 7.580 |
| **31** | 5.959 | 5.667 | 5.590 | 5.813 | 5.712 |
| **34** | 8.921 | 7.235 | 7.128 | 7.170 | 7.043 |
| **35** | 8.523 | 8.477 | 8.471 | 8.366 | 8.321 |
| **36** | 8.125 | 8.608 | 8.831 | 8.753 | 9.004 |
| **37** | 7.319 | 7.343 | 7.345 | 7.095 | 7.092 |
| **38** | 7.824 | 7.262 | 7.213 | 7.213 | 7.150 |
| **39** | 8.108 | 8.144 | 8.148 | 8.023 | 8.010 |
| **40** | 7.699 | 6.842 | 6.785 | 6.777 | 6.719 |
| **42** | 6.174 | 6.460 | 6.541 | 6.088 | 6.226 |
| **43** | 7.745 | 7.952 | 7.979 | 7.795 | 7.806 |
| **46** | 5.728 | 5.893 | 5.938 | 6.023 | 6.103 |
| **47** | 3.903 | 4.182 | 4.353 | 4.666 | 5.041 |
| **48** | 5.420 | 5.862 | 6.085 | 5.409 | 5.686 |
| **49** | 5.981 | 5.851 | 5.819 | 5.480 | 5.407 |
| **51** | 8.377 | 8.477 | 8.485 | 8.487 | 8.483 |
| **52** | 8.260 | 7.374 | 7.267 | 7.296 | 7.143 |
| **53** | 7.398 | 8.438 | 8.584 | 8.296 | 8.376 |
| **54** | 7.131 | 7.486 | 7.510 | 7.358 | 7.373 |
| **55** | 7.585 | 7.041 | 7.020 | 6.977 | 6.950 |
| **56** | 6.444 | 6.173 | 6.116 | 6.055 | 5.965 |
| **58** | 7.252 | 7.057 | 7.020 | 7.173 | 7.219 |
| **59** | 7.770 | 7.944 | 7.982 | 8.125 | 8.246 |
| **60** | 7.495 | 7.669 | 7.728 | 7.663 | 7.804 |
| **61** | 7.398 | 7.168 | 7.040 | 7.299 | 7.069 |
| **62** | 9.155 | 8.425 | 8.358 | 8.444 | 8.363 |
| **63** | 6.409 | 7.563 | 7.691 | 7.716 | 7.872 |
| **64** | 6.721 | 7.388 | 7.456 | 7.488 | 7.546 |
| **65** | 8.824 | 7.885 | 7.795 | 8.052 | 7.954 |
| **66** | 7.770 | 7.357 | 7.317 | 7.327 | 7.258 |
| **67** | 8.377 | 7.107 | 6.935 | 7.225 | 7.094 |
| **70** | 6.620 | 5.961 | 5.864 | 5.998 | 5.858 |
| **71** | 5.387 | 5.928 | 6.044 | 6.106 | 6.126 |
| **72** | 5.842 | 5.821 | 5.817 | 5.944 | 5.868 |

**Table S4.**  Observed (Obs), predicted (Pred) activities of test set compounds (arylsulphonamide-based hydroxamates having MMP-2 inhibitory activities) for MLR and PLS models.

|  |  |  |  |
| --- | --- | --- | --- |
| **CpdNo** | **Obs** | **MLR model** | **PLS model** |
| **Pred** | **Pred** |
| **1** | 8.161 | 7.566 | 7.237 |
| **5** | 7.886 | 8.146 | 7.687 |
| **7** | 7.481 | 6.587 | 6.662 |
| **11** | 5.975 | 5.984 | 6.164 |
| **15** | 6.180 | 7.444 | 7.516 |
| **18** | 9.000 | 9.257 | 9.133 |
| **22** | 9.432 | 8.971 | 9.031 |
| **28** | 5.620 | 7.467 | 7.310 |
| **30** | 5.046 | 5.878 | 5.642 |
| **32** | 4.469 | 4.774 | 4.444 |
| **33** | 8.420 | 7.966 | 7.864 |
| **41** | 7.387 | 6.870 | 6.506 |
| **44** | 5.757 | 4.008 | 4.350 |
| **45** | 6.959 | 7.361 | 7.374 |
| **50** | 8.824 | 8.441 | 8.329 |
| **57** | 6.509 | 7.370 | 7.444 |
| **68** | 7.678 | 8.045 | 8.024 |
| **69** | 7.770 | 7.232 | 7.262 |