**Supplementary Materials**

**Supplementary Table ST1.** Chemical structure and biological activitiy of a series of HRV 3Cpro inhibitors.



|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cpda** | **X** | **Y** | **X** | **Y** | **Z** | **n** | **R** | **EC50(µM)** | ***pEC50*** |
| **1** | COOMe | H | -- | -- | -- | -- | -- | 1.3 | 5.886 |
| **2** | H | COOMe | -- | -- | -- | -- | -- | 3.2 | 5.495 |
| **3** | COOEt | Me | -- | -- | -- | -- | -- | 3 | 5.523 |
| **4** | COO-c-Pent | H | -- | -- | -- | -- | -- | 0.56 | 6.252 |
| **5** | COO-c-Hex | H | -- | -- | -- | -- | -- | 3.6 | 5.444 |
| **6** | COOBnz | H | -- | -- | -- | -- | -- | 3.2 | 5.495 |
| **7** | COOCH2-t-But | H | -- | -- | -- | -- | -- | 0.5 | 6.301 |
| **8** | CONME2 | H | -- | -- | -- | -- | -- | 56 | 4.252 |
| **9** | COPyrrolidine | H | -- | -- | -- | -- | -- | 22 | 4.658 |
| **10** | CON(Me)Ph | H | -- | -- | -- | -- | -- | 158 | 3.801 |
| **11** | COTetrahydroquinoline | H | -- | -- | -- | -- | -- | 126 | 3.900 |
| **12** | COIndoline | H | -- | -- | -- | -- | -- | 16 | 4.796 |
| **13** | CON(Me)OMe | H | -- | -- | -- | -- | -- | 4 | 5.398 |
| **14** | CON(Me)OH | H | -- | -- | -- | -- | -- | 42 | 4.377 |
| **15** | COIsoxazolidine | H | -- | -- | -- | -- | -- | 45 | 4.347 |
| **16** | CO[1,2]Oxazinan | H | -- | -- | -- | -- | -- | 16 | 4.796 |
| **17** | COPyrrole | H | -- | -- | -- | -- | -- | 1.4 | 5.854 |
| **18** | COIndole | H | -- | -- | -- | -- | -- | 1.8 | 5.745 |
| **19** | COMe | H | -- | -- | -- | -- | -- | 2 | 5.699 |
| **20** | CO-t-Butyl | H | -- | -- | -- | -- | -- | 1.7 | 5.770 |
| **21** | COPh | H | -- | -- | -- | -- | -- | 4 | 5.398 |
| **22** | 4-OMeCOPh | H | -- | -- | -- | -- | -- | 22 | 4.658 |
| **23** | 4-NO2COPh | H | -- | -- | -- | -- | -- | 32 | 4.495 |
| **24** | 4-CNCOPh | H | -- | -- | -- | -- | -- | 50 | 4.301 |
| **25** | CO-2-(1,3-Benzodioxole) | H | -- | -- | -- | -- | -- | 3.2 | 5.495 |
| **26** | CO-2-furyl | H | -- | -- | -- | -- | -- | 2.4 | 5.620 |
| **27** | SO2Ph | H | -- | -- | -- | -- | -- | 200 | 3.699 |
| **28** | CN | H | -- | -- | -- | -- | -- | 18 | 4.745 |
| **29** | C=NOMe | H | -- | -- | -- | -- | -- | 100 | 4.000 |
| **30** | 2-Oxopyrrolidine | H | -- | -- | -- | -- | -- | 0.89 | 6.051 |
| **31** | 2-Oxooxazolidine | H | -- | -- | -- | -- | -- | 1.6 | 5.796 |
| **32** | 3-Me-2-oxo-imidazolidine | H | -- | -- | -- | -- | -- | 5 | 5.301 |
| **33** | -- | -- | H | NO2 | -- | -- | -- | 17 | 4.770 |
| **34** | -- | -- | H | F | -- | -- | -- | 11 | 4.959 |
| **35** | -- | -- | Cl | H | -- | -- | -- | 56 | 4.252 |
| **36** | -- | -- | H | Cl | -- | -- | -- | 5.6 | 5.252 |
| **37** | -- | -- | H | Br | -- | -- | -- | 47 | 4.328 |
| **38** | -- | -- | -- | -- | O | 1 | -- | 5.2 | 5.284 |
| **39** | -- | -- | -- | -- | O | 2 | -- | 16 | 4.796 |
| **40** | -- | -- | -- | -- | N | 1 | COMe | 0.71 | 6.149 |
| **41** | -- | -- | -- | -- | N | 1 | COOMe | 28 | 4.553 |
| **42** | -- | -- | -- | -- | N | 1 | OMe | 18 | 4.745 |

aCompound number



|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Cpda** | **R1** | **R2** | **R3** | **R4** | **EC50(µM)** | ***pEC50*** |
| **43** | (CH2)2CONHTr | Bnz | i-But | Cbz | 100 | 4.000 |
| **44** | (CH2)2CONHMe | Bnz | i-But | Cbz | 5.6 | 5.252 |
| **45** | (CH2)2CONMe2 | Bnz | i-But | Cbz | 4 | 5.398 |
| **46** | (CH2)2COOH | Bnz | i-But | Cbz | 14 | 4.854 |
| **47** | (CH2)2COMe | Bnz | i-But | Cbz | 1.6 | 5.796 |
| **48** | (CH2)2SOMe | Bnz | i-But | Cbz | 1.6 | 5.796 |
| **49** | CH2NHCOMe | Bnz | i-But | Cbz | 2.2 | 5.658 |
| **50** | CH2NHCONH2 | Bnz | i-But | Cbz | 32 | 4.495 |
| **51** | CH2OCONH2 | Bnz | i-But | Cbz | 1.6 | 5.796 |
| **52** | (CH2)2CONH2 | H | i-But | Cbz | 141 | 3.851 |
| **53** | (CH2)2CONH2 | Me | i-But | Cbz | 20 | 4.699 |
| **54** | (CH2)2CONH2 | Et | i-But | Cbz | 6 | 5.222 |
| **55** | (CH2)2CONH2 | n-Pr | i-But | Cbz | 5 | 5.301 |
| **56** | (CH2)2CONH2 | i-But | i-But | Cbz | 5.4 | 5.268 |
| **57** | (CH2)2CONH2 | CH2SMe | i-But | Cbz | 8.9 | 5.051 |
| **58** | (CH2)2CONH2 | CH2SEt | i-But | Cbz | 10 | 5.000 |
| **59** | (CH2)2CONH2 | CH2C-Hex | i-But | Cbz | 1.9 | 5.721 |
| **60** | (CH2)2CONH2 | 4-FBnz | i-But | Cbz | 1.8 | 5.745 |
| **61** | (CH2)2CONH2 | 4-MeBnz | i-But | Cbz | 0.18 | 6.745 |
| **62** | (CH2)2CONH2 | 4-OHBnz | i-But | Cbz | 5.3 | 5.276 |
| **63** | (CH2)2CONH2 | 4-OAcBnz | i-But | Cbz | 11 | 4.959 |
| **64** | (CH2)2CONH2 | 4-OMeBnz | i-But | Cbz | 1.7 | 5.770 |
| **65** | (CH2)2CONH2 | 4-OPO3H2Bnz | i-But | Cbz | 14 | 4.854 |
| **66** | (CH2)2CONH2 | 4-CH2OHBnz | i-But | Cbz | 0.55 | 6.260 |
| **67** | (CH2)2CONH2 | 4-CH2OMeBnz | i-But | Cbz | 39 | 4.409 |
| **68** | (CH2)2CONH2 | 4-(CH2)2OHBnz | i-But | Cbz | 3.5 | 5.456 |
| **69** | (CH2)2CONH2 | 4-CNBnz | i-But | Cbz | 5.6 | 5.252 |
| **70** | (CH2)2CONH2 | CH2-2-Imidazol | i-But | Cbz | 27 | 4.569 |
| **71** | (CH2)2CONH2 | CH2-2-(N-MeImid) | i-But | Cbz | 10 | 5.000 |
| **72** | (CH2)2CONH2 | CH2-2-Thienyl | i-But | Cbz | 0.56 | 6.252 |
| **73** | (CH2)2CONH2 | CH(*R*-OH)Me | i-But | Cbz | 56 | 4.252 |
| **74** | (CH2)2CONH2 | Bnz | H | Cbz | 5.6 | 5.252 |
| **75** | (CH2)2CONH2 | Bnz | Me | Cbz | 2 | 5.699 |
| **76** | (CH2)2CONH2 | Bnz | i-Pr | Cbz | 0.38 | 6.420 |
| **77** | (CH2)2CONH2 | Bnz | CH(*S*-Me)Et | Cbz | 0.79 | 6.102 |
| **78** | (CH2)2CONH2 | Bnz | t-But | Cbz | 0.32 | 6.495 |
| **79** | (CH2)2CONH2 | Bnz | (CH2)2SMe | Cbz | 1.4 | 5.854 |
| **80** | (CH2)2CONH2 | Bnz | CH2SMe | Cbz | 0.18 | 6.745 |
| **81** | (CH2)2CONH2 | Bnz | CH(*R*-Me)S-i-Pr | Cbz | 10 | 5.000 |
| **82** | (CH2)2CONH2 | Bnz | c-Hex | Cbz | 1 | 6.000 |
| **83** | (CH2)2CONH2 | Bnz | CH2c-Hex | Cbz | 1.2 | 5.921 |
| **84** | (CH2)2CONH2 | Bnz | Bnz | Cbz | 0.56 | 6.252 |
| **85** | (CH2)2CONH2 | Bnz | CH2SPh | Cbz | 0.12 | 6.921 |
| **86** | (CH2)2CONH2 | Bnz | CH2SBnz | Cbz | 0.2 | 6.699 |
| **87** | (CH2)2CONH2 | Bnz | Phenethyl | Cbz | 0.25 | 6.602 |
| **88** | (CH2)2CONH2 | Bnz | CH2OH | Cbz | 1.8 | 5.745 |
| **89** | (CH2)2CONH2 | Bnz | CH(*R*-OH)Me | Cbz | 1.8 | 5.745 |
| **90** | (CH2)2CONH2 | Bnz | CMe2OH | Cbz | 0.66 | 6.180 |
| **91** | (CH2)2CONH2 | Bnz | CMe2CH2OH | Cbz | 1.3 | 5.886 |
| **92** | (CH2)2CONH2 | Bnz | (CH2)4NH2 | Cbz | 205 | 3.688 |
| **93** | (CH2)2CONH2 | Bnz | (CH2)2Morphol | Cbz | 5.1 | 5.292 |
| **94** | (CH2)2CONH2 | Bnz | (CH2)3Morphol | Cbz | 7.1 | 5.149 |
| **95** | (CH2)2CONH2 | Bnz | CH2COOH | Cbz | 2.4 | 5.620 |
| **96** | (CH2)2CONH2 | Bnz | (CH2)2COOH | Cbz | 5.5 | 5.260 |
| **97** | (CH2)2CONH2 | Bnz | CH2CONMe2 | Cbz | 5.9 | 5.229 |
| **98** | (CH2)2CONH2 | Bnz | i-But | 2-MeCbz | 1 | 6.000 |
| **99** | (CH2)2CONH2 | Bnz | i-But | 2-ClCbz | 0.63 | 6.201 |
| **100** | (CH2)2CONH2 | Bnz | i-But | COOCH2(4-Pyr) | 56 | 4.252 |
| **101** | (CH2)2CONH2 | Bnz | i-But | COOMe | 1.3 | 5.886 |
| **102** | (CH2)2CONH2 | Bnz | i-But | COO-c-Hex | 7.6 | 5.119 |
| **103** | (CH2)2CONH2 | Bnz | i-But | COO-t-But | 4.5 | 5.347 |
| **104** | (CH2)2CONH2 | Bnz | i-But | COSMe | 1.1 | 5.959 |
| **105** | (CH2)2CONH2 | Bnz | i-But | COSEt | 0.46 | 6.337 |
| **106** | (CH2)2CONH2 | Bnz | i-But | COS-c-Pent | 0.18 | 6.745 |
| **107** | (CH2)2CONH2 | Bnz | i-But | COSBnz | 0.27 | 6.569 |
| **108** | (CH2)2CONH2 | Bnz | i-But | CO-2-Napthyl | 1 | 6.000 |
| **109** | (CH2)2CONH2 | Bnz | i-But | COPh | 5.2 | 5.284 |
| **110** | (CH2)2CONH2 | Bnz | i-But | COPhOPh | 5.2 | 5.284 |
| **111** | (CH2)2CONH2 | Bnz | i-But | COMe | 14 | 4.854 |
| **112** | (CH2)2CONH2 | Bnz | i-But | CO-i-Pr | 1 | 6.000 |
| **113** | (CH2)2CONH2 | Bnz | i-But | CO-t-But | 1.8 | 5.745 |
| **114** | (CH2)2CONH2 | Bnz | i-But | CO-c-Pent | 0.6 | 6.222 |
| **115** | (CH2)2CONH2 | Bnz | i-But | COCH2OH | 30 | 4.523 |
| **116** | (CH2)2CONH2 | Bnz | i-But | CO(CH2)2OH | 19 | 4.721 |
| **117** | (CH2)2CONH2 | Bnz | i-But | CON(Me)Bnz | 5.6 | 5.252 |
| **118** | (CH2)2CONH2 | Bnz | i-But | Ac-L-Val | 63 | 4.201 |
| **119** | (CH2)2CONH2 | Bnz | i-But | Ac-L-Ala | 20 | 4.699 |

aCompound number



|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Cpda** | **Ar** | **Y** | **X** | **R1** | **R2** | **EC50(µM)** | ***pEC50*** |
| **120** | Bnz | O | CH2 | Bnz | i-But | 0.36 | 6.444 |
| **121** | Bnz | S | CH2 | Bnz | i-But | 0.68 | 6.167 |
| **122** | Bnz | S | CH2 | Bnz | i-Pr | 0.19 | 6.721 |
| **123** | *c*-pent | S | CH2 | Bnz | i-But | 0.19 | 6.721 |
| **124** | *c*-pent | S | CH2 | 4F-Bnz | i-But | 0.28 | 6.553 |
| **125** | *c*-pent | S | CH2 | 4-MeBnz | i-But | 0.16 | 6.796 |
| **126** | *c*-pent | S | CH2 | Bnz | i-Pr | 0.02 | 7.699 |
| **127** | *c*-pent | S | CH2 | 4F-Bnz | i-Pr | 0.02 | 7.699 |
| **128** | *c*-pent | S | CH2 | 4-MeBnz | i-Pr | 0.006 | 8.222 |
| **129** | *c*-pent | S | CH2 | 4-CF3Bnz | i-Pr | 0.05 | 7.301 |
| **130** | *c*-pent | S | CH2 | 4F-Bnz | Bnz | 0.48 | 6.319 |
| **131** | *c*-pent | S | CH2 | 4-MeBnz | Bnz | 0.14 | 6.854 |
| **132** | *c*-pent | S | CH2 | Bnz | t-But | 0.05 | 7.301 |

aCompound number



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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Cpda** | **Ar** | **Ar1** | **R** | **R1** | **R2** | **n** | **X** | **Y** | **EC50(µM)** | ***pEC50*** |
| **133** | Cbz | Bnz | i-But | -- | -- | 1 | (*S*)-CH | NH | 0.1 | 7.000 |
| **134** | Cbz | Bnz | i-But | -- | -- | 2 | (*S*)-CH | NH | 0.03 | 7.523 |
| **135** | Cbz | Bnz | i-But | -- | -- | 1 | (*R*)-CH | NH | 1.6 | 5.796 |
| **136** | Cbz | Bnz | i-But | -- | -- | 1 | N | NH | 0.6 | 6.222 |
| **137** | Cbz | Bnz | i-Pr | -- | -- | 1 | (*S*)-CH | NH | 0.03 | 7.523 |
| **138** | 5-Me-isoxazole-3-CO | 4F-Bnz | i-Pr | -- | -- | 2 | (*S*)-CH | NH | 0.02 | 7.699 |
| **139** | 5-Me-isoxazole-3-CO | 4F-Bnz | i-Pr | -- | -- | 2 | (*S*)-CH | CH2 | 0.001 | 9.000 |
| **140** | 5-Me-isoxazole-3-CO | 4F-Bnz | t-But | -- | -- | 1 | (*S*)-CH | NH | 0.01 | 8.000 |
| **141** | 5-Me-isoxazole-3-CO | 4F-Bnz | i-Pr | -- | -- | -- | -- | CH2 | 0.32 | 6.495 |

aCompound number



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| **Cpda** | **R** | **EC50 (μM)** | ***pEC50*** |
| **142** | 2-(1,2,3,4-tetrahydronaphthalene) | 1.40 | 5.854 |
| **143** | CH(Cl)CH2CH(CH3)2 | 2.00 | 5.699 |
| **144** | CH=CH-thiophen-2-yl | 0.55 | 6.260 |
| **145** | 2-(2,5-dihydro-1H-pyrrole) | 25.00 | 4.602 |
| **146** | 5-methyl-isoxazole-3-yl | 0.25 | 6.602 |
| **147** | Phenethyl | 2.80 | 5.553 |
| **148** | Isoxazole-5-yl | 1.60 | 5.796 |

aCompound number



|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Cpda** | **R** | **R1** | **R2** | **Ar** | **EC50(µM)** | ***pEC50*** |
| **149** | NHCbz | Me | i-But | Bnz | 1 | 6.000 |
| **150** | CO-S-c-Pent | Me | i-But | Bnz | 0.32 | 6.495 |
| **151** | CO-S-c-Pent | Me | i-Pr | Bnz | 0.19 | 6.721 |
| **152** | CO-S-c-Pent | Me | CH2SPh | Bnz | 0.54 | 6.268 |
| **153** | 5-methyl-isoxazole-3-carbonyl | Me | i-But | Bnz | 0.14 | 6.854 |
| **154** | 5-methyl-isoxazole-3-carbonyl | Me | i-But | 4-FBnz | 0.4 | 6.398 |
| **155** | 5-methyl-isoxazole-3-carbonyl | Me | CH2(1-Napthyl) | 4-FBnz | 0.2 | 6.699 |
| **156** | 5-methyl-isoxazole-3-carbonyl | Me | CH2(2-Napthyl) | 4-FBnz | 0.16 | 6.796 |
| **157** | 5-methyl-isoxazole-3-carbonyl | Me | CH2(4-Imidazole) | 4-FBnz | 1.8 | 5.745 |
| **158** | 5-methyl-isoxazole-3-carbonyl | Me | i-But | 4-FBnz | 0.03 | 7.523 |

aCompound number



|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Cpda** | **R** | **R1** | **R2** | **R3** | **EC50(µM)** | ***pEC50*** |
| **159** | Benzothiazol-2-yl | CH2CONH2 | =O | | 17 | 4.770 |
| **160** | Benzothiazol-2-yl | CH2CONH2 | OH | H | 4.495 | 5.456 |
| **161** | Benzothiazol-2-yl | 2-oxo-pyrrolidin-3-yl | =O | | 3.2 | 5.495 |
| **162** | Benzothiazol-2-yl | 2-oxo-pyrrolidin-3-yl | OH | H | 5.102 | 4.469 |
| **163** | Thiazol-2-yl | 2-oxo-pyrrolidin-3-yl | =O  =O  =O | | 7.9 | 5.102 |
| **164** | 2-Pyridyl | 2-oxo-pyrrolidin-3-yl | 4 | 5.398 |
| **165** | Benzothiazol-2-yl | 2-oxo-pyrrolidin-3-yl | 0.01 | 8.000 |

aCompound number



|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cpda** | **R** | **R1** | **X** | **EC50 (μM)** | **Obs** |
| **166** | S-c-pent | (CH2)2CONH2 | O | 1 | 6.000 |
| **167** | S-c-pent | (CH2)2CONH2 | NH | 0.19 | 6.721 |
| **168** | 5-Methyl-isoxazole | (CH2)2CONH2 | O | 0.1 | 7.000 |
| **169** | 5-Methyl-isoxazole | (CH2)2CONH2 | NH | 0.42 | 6.377 |
| **170** | 5-Methyl-isoxazole | 5-(2-oxo-pyrrolidin-3-yl) | O | 0.007 | 8.155 |
| **171** | 5-Methyl-isoxazole | 5-(2-oxo-pyrrolidin-3-yl) | NH | 0.01 | 8.000 |
| **172** | 5-Methyl-isoxazole | 5-(2-oxo-pyrrolidin-3-yl) | CH2 | 0.005 | 8.301 |

aCompound number



|  |  |  |  |
| --- | --- | --- | --- |
| **Cpda** | **R** | **EC50 (μM)** | ***pEC50*** |
| **173** | Cbz | 9 | 5.046 |
| **174** | CO-(5-Methyl-isoxazole) | 0.162 | 6.790 |

aCompound number



|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Cpda** | **R1** | **R2** | **R3** | **EC50 (μM)** | ***pEC50*** |
| **175** | (CH2)2CONH2 | Bnz | OBnz | 0.033 | 7.481 |
| **176** | (CH2)2CONH2 | 4-FBnz | OBnz | 0.014 | 7.854 |
| **177** | (CH2)2CONH2 | 3,4-diFBnz | OBnz | 0.003 | 8.523 |
| **178** | (CH2)2CONH2 | CH2-c-Hex | OBnz | 0.178 | 6.750 |
| **179** | (CH2)2CONH2 | Bnz | Me | 0.888 | 6.052 |
| **180** | (CH2)2CONH2 | Bnz | c-Pent | 0.034 | 7.469 |
| **181** | (CH2)2CONH2 | Bnz | [1,3]Dithiolane-2-yl | 0.104 | 6.983 |
| **182** | (CH2)2CONH2 | Bnz | Tetrahydrofuran-2-yl | 1.78 | 5.750 |
| **183** | (CH2)2CONH2 | Bnz | *t*-Butyl | 0.518 | 6.286 |
| **184** | (CH2)2CONH2 | Bnz | 5-Me-isoxazol-3-yl | 0.016 | 7.796 |
| **185** | (CH2)2CONH2 | Bnz | 5-Cl-isoxazol-3-yl | 0.024 | 7.620 |
| **186** | (*R*)-2-Oxopyrrodine-3-yl | Bnz | OBnz | 0.003 | 8.523 |
| **187** | (*S*)-2-Oxopyrrodine-3-yl | Bnz | OBnz | 0.469 | 6.329 |
| **188** | (*R*)-2-Oxopyrrodine-3-yl | 4-FBnz | 5-Me-isoxazol-3-yl | 0.002 | 8.699 |
| **189** | (*R*)-2-Oxopyrrodine-3-yl | 3,4-diFBnz | 5-Me-isoxazol-3-yl | 0.001 | 9.000 |
| **190** | (*R*)-2-Oxopyrrodine-3-yl | 3,4-diFBnz | 5-Me-isoxazol-3-yl | 0.003 | 8.523 |

aCompound number



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| --- | --- | --- | --- |
| **Cpda** | **R** | **EC50 (μM)** | ***pEC50*** |
| **191** | 3-BrPhCH=CH | 1.4 | 5.854 |
| **192** | 3-Br,4-MePhCH=CH | 1.29 | 5.889 |
| **193** | 3-Br,4-FPhCH=CH | 0.63 | 6.201 |
| **194** | Benzo[1,3]dioxole | 1.81 | 5.742 |
| **195** | 5-Bromo-benzo[1,3]dioxole | 0.49 | 6.310 |
| **196** | 2-Methyl-5-phenyl-furan | 1.94 | 5.712 |
| **197** | 2H-Chromene-3-yl | 1.19 | 5.924 |
| **198** | 6-Chloro-2H-chromene-3-yl | 0.16 | 6.796 |
| **199** | 6-Bromo-2H-chromene-3-yl | 0.18 | 6.745 |
| **200** | Napthaleny-2-yl | 0.15 | 6.824 |
| **201** | 6-Methyl-Napthaleny-2-yl | 0.88 | 6.056 |
| **202** | 7-Bromo-Napthaleny-2-yl | 0.18 | 6.745 |

aCompound number



|  |  |  |
| --- | --- | --- |
| **Cpda** | **EC50 (μM)** | ***pEC50*** |
| **203** | 1.46 | 5.835 |

aCompound number

**Supplementary Table ST2. The observed and predicted responses of training and test set human rhinovirus 3C protease (HRV 3Cpro) inhibitors as per Bayesian classification modelling**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cpda** | ***pEC50*** | **Observed responseb** | **Predicted response** |
| **1** | 5.886 | *Inactive* | *Inactive* |
| **2** | 5.495 | *Inactive* | *Inactive* |
| **3** | 5.523 | *Inactive* | *Inactive* |
| **4** | 6.252 | *Inactive* | *Inactive* |
| **5** | 5.444 | *Inactive* | *Inactive* |
| **6** | 5.495 | *Inactive* | *Inactive* |
| **7** | 6.301 | *Inactive* | *Inactive* |
| **8** | 4.252 | *Inactive* | *Inactive* |
| **9** | 4.658 | *Inactive* | *Inactive* |
| **10** | 3.801 | *Inactive* | *Inactive* |
| **11** | 3.9 | *Inactive* | *Inactive* |
| **12** | 4.796 | *Inactive* | *Inactive* |
| **13** | 5.398 | *Inactive* | *Inactive* |
| **14** | 4.377 | *Inactive* | *Inactive* |
| **15** | 4.347 | *Inactive* | *Inactive* |
| **16** | 4.796 | *Inactive* | *Inactive* |
| **17** | 5.854 | *Inactive* | *Inactive* |
| **18** | 5.745 | *Inactive* | *Inactive* |
| **19** | 5.699 | *Inactive* | *Inactive* |
| **20** | 5.77 | *Inactive* | *Inactive* |
| **21** | 5.398 | *Inactive* | *Inactive* |
| **22** | 4.658 | *Inactive* | *Inactive* |
| **23** | 4.495 | *Inactive* | *Inactive* |
| **24** | 4.301 | *Inactive* | *Inactive* |
| **25** | 5.495 | *Inactive* | *Inactive* |
| **26** | 5.62 | *Inactive* | *Inactive* |
| **27** | 3.699 | *Inactive* | *Inactive* |
| **28** | 4.745 | *Inactive* | *Inactive* |
| **29** | 4 | *Inactive* | *Inactive* |
| **30** | 6.051 | *Inactive* | *Inactive* |
| **31** | 5.796 | *Inactive* | *Inactive* |
| **32** | 5.301 | *Inactive* | *Inactive* |
| **33** | 4.77 | *Inactive* | *Inactive* |
| **34** | 4.959 | *Inactive* | *Inactive* |
| **35** | 4.252 | *Inactive* | *Inactive* |
| **36** | 5.252 | *Inactive* | *Inactive* |
| **37** | 4.328 | *Inactive* | *Inactive* |
| **38** | 5.284 | *Inactive* | *Inactive* |
| **39** | 4.796 | *Inactive* | *Inactive* |
| **40** | 6.149 | *Inactive* | *Inactive* |
| **41** | 4.553 | *Inactive* | *Inactive* |
| **42** | 4.745 | *Inactive* | *Inactive* |
| **43** | 4 | *Inactive* | *Inactive* |
| **44** | 5.252 | *Inactive* | *Inactive* |
| **45** | 5.398 | *Inactive* | *Inactive* |
| **46** | 4.854 | *Inactive* | *Inactive* |
| **47** | 5.796 | *Inactive* | *Inactive* |
| **48** | 5.796 | *Inactive* | *Inactive* |
| **49** | 5.658 | *Inactive* | *Inactive* |
| **50** | 4.495 | *Inactive* | *Inactive* |
| **51** | 5.796 | *Inactive* | *Inactive* |
| **52** | 3.851 | *Inactive* | *Inactive* |
| **53** | 4.699 | *Inactive* | *Inactive* |
| **54** | 5.222 | *Inactive* | *Inactive* |
| **55** | 5.301 | *Inactive* | *Inactive* |
| **56** | 5.268 | *Inactive* | *Inactive* |
| **57** | 5.051 | *Inactive* | *Inactive* |
| **58** | 5 | *Inactive* | *Inactive* |
| **59** | 5.721 | *Inactive* | *Inactive* |
| **60** | 5.745 | *Inactive* | *Inactive* |
| **61** | 6.745 | *Active* | *Inactive* |
| **62** | 5.276 | *Inactive* | *Inactive* |
| **63** | 4.959 | *Inactive* | *Inactive* |
| **64** | 5.77 | *Inactive* | *Inactive* |
| **65** | 4.854 | *Inactive* | *Inactive* |
| **66** | 6.26 | *Inactive* | *Inactive* |
| **67** | 4.409 | *Inactive* | *Inactive* |
| **68** | 5.456 | *Inactive* | *Inactive* |
| **69** | 5.252 | *Inactive* | *Inactive* |
| **70** | 4.569 | *Inactive* | *Inactive* |
| **71** | 5 | *Inactive* | *Inactive* |
| **72** | 6.252 | *Inactive* | *Inactive* |
| **73** | 4.252 | *Inactive* | *Inactive* |
| **74** | 5.252 | *Inactive* | *Inactive* |
| **75** | 5.699 | *Inactive* | *Inactive* |
| **76** | 6.42 | *Inactive* | *Inactive* |
| **77** | 6.102 | *Inactive* | *Inactive* |
| **78** | 6.495 | *Inactive* | *Inactive* |
| **79** | 5.854 | *Inactive* | *Inactive* |
| **80** | 6.745 | *Active* | *Active* |
| **81** | 5 | *Inactive* | *Inactive* |
| **82** | 6 | *Inactive* | *Inactive* |
| **83** | 5.921 | *Inactive* | *Inactive* |
| **84** | 6.252 | *Inactive* | *Inactive* |
| **85** | 6.921 | *Active* | *Active* |
| **86** | 6.699 | *Active* | *Active* |
| **87** | 6.602 | *Active* | *Inactive* |
| **88** | 5.745 | *Inactive* | *Inactive* |
| **89** | 5.745 | *Inactive* | *Inactive* |
| **90** | 6.18 | *Inactive* | *Inactive* |
| **91** | 5.886 | *Inactive* | *Inactive* |
| **92** | 3.688 | *Inactive* | *Inactive* |
| **93** | 5.292 | *Inactive* | *Inactive* |
| **94** | 5.149 | *Inactive* | *Inactive* |
| **95** | 5.62 | *Inactive* | *Inactive* |
| **96** | 5.26 | *Inactive* | *Inactive* |
| **97** | 5.229 | *Inactive* | *Inactive* |
| **98** | 6 | *Inactive* | *Inactive* |
| **99** | 6.201 | *Inactive* | *Inactive* |
| **100** | 4.252 | *Inactive* | *Inactive* |
| **101** | 5.886 | *Inactive* | *Inactive* |
| **102** | 5.119 | *Inactive* | *Inactive* |
| **103** | 5.347 | *Inactive* | *Inactive* |
| **104** | 5.959 | *Inactive* | *Inactive* |
| **105** | 6.337 | *Inactive* | *Inactive* |
| **106** | 6.745 | *Active* | *Active* |
| **107** | 6.569 | *Active* | *Active* |
| **108** | 6 | *Inactive* | *Active* |
| **109** | 5.284 | *Inactive* | *Inactive* |
| **110** | 5.284 | *Inactive* | *Inactive* |
| **111** | 4.854 | *Inactive* | *Inactive* |
| **112** | 6 | *Inactive* | *Inactive* |
| **113** | 5.745 | *Inactive* | *Inactive* |
| **114** | 6.222 | *Inactive* | *Inactive* |
| **115** | 4.523 | *Inactive* | *Inactive* |
| **116** | 4.721 | *Inactive* | *Inactive* |
| **117** | 5.252 | *Inactive* | *Inactive* |
| **118** | 4.201 | *Inactive* | *Inactive* |
| **119** | 4.699 | *Inactive* | *Inactive* |
| **120** | 6.444 | *Inactive* | *Active* |
| **121** | 6.167 | *Inactive* | *Active* |
| **122** | 6.721 | *Active* | *Active* |
| **123** | 6.721 | *Active* | *Active* |
| **124** | 6.553 | *Active* | *Active* |
| **125** | 6.796 | *Active* | *Active* |
| **126** | 7.699 | *Active* | *Active* |
| **127** | 7.699 | *Active* | *Active* |
| **128** | 8.222 | *Active* | *Active* |
| **129** | 7.301 | *Active* | *Active* |
| **130** | 6.319 | *Inactive* | *Active* |
| **131** | 6.854 | *Active* | *Active* |
| **132** | 7.301 | *Active* | *Active* |
| **133** | 7 | *Active* | *Active* |
| **134** | 7.523 | *Active* | *Active* |
| **135** | 5.796 | *Inactive* | *Active* |
| **136** | 6.222 | *Inactive* | *Inactive* |
| **137** | 7.523 | *Active* | *Active* |
| **138** | 7.699 | *Active* | *Active* |
| **139** | 9 | *Active* | *Active* |
| **140** | 8 | *Active* | *Active* |
| **141** | 6.495 | *Inactive* | *Active* |
| **142** | 5.854 | *Inactive* | *Inactive* |
| **143** | 5.699 | *Inactive* | *Inactive* |
| **144** | 6.26 | *Inactive* | *Inactive* |
| **145** | 4.602 | *Inactive* | *Inactive* |
| **146** | 6.602 | *Active* | *Active* |
| **147** | 5.553 | *Inactive* | *Inactive* |
| **148** | 5.796 | *Inactive* | *Inactive* |
| **149** | 6 | *Inactive* | *Active* |
| **150** | 6.495 | *Inactive* | *Active* |
| **151** | 6.721 | *Active* | *Active* |
| **152** | 6.268 | *Inactive* | *Active* |
| **153** | 6.854 | *Active* | *Active* |
| **154** | 6.398 | *Inactive* | *Active* |
| **155** | 6.699 | *Active* | *Active* |
| **156** | 6.796 | *Active* | *Active* |
| **157** | 5.745 | *Inactive* | *Active* |
| **158** | 7.523 | *Active* | *Active* |
| **159** | 4.77 | *Inactive* | *Inactive* |
| **160** | 4.495 | *Inactive* | *Inactive* |
| **161** | 5.495 | *Inactive* | *Inactive* |
| **162** | 5.102 | *Inactive* | *Inactive* |
| **163** | 5.102 | *Inactive* | *Inactive* |
| **164** | 5.398 | *Inactive* | *Inactive* |
| **165** | 6.469 | *Inactive* | *Active* |
| **166** | 6 | *Inactive* | *Active* |
| **167** | 6.721 | *Active* | *Active* |
| **168** | 7 | *Active* | *Active* |
| **169** | 6.377 | *Inactive* | *Active* |
| **170** | 8.155 | *Active* | *Active* |
| **171** | 8 | *Active* | *Active* |
| **172** | 8.301 | *Active* | *Active* |
| **173** | 5.046 | *Inactive* | *Active* |
| **174** | 6.79 | *Active* | *Active* |
| **175** | 7.481 | *Active* | *Active* |
| **176** | 7.854 | *Active* | *Active* |
| **177** | 8.523 | *Active* | *Active* |
| **178** | 6.75 | *Active* | *Active* |
| **179** | 6.052 | *Inactive* | *Active* |
| **180** | 7.469 | *Active* | *Active* |
| **181** | 6.983 | *Active* | *Active* |
| **182** | 5.75 | *Inactive* | *Active* |
| **183** | 6.286 | *Inactive* | *Active* |
| **184** | 7.796 | *Active* | *Active* |
| **185** | 7.62 | *Active* | *Active* |
| **186** | 8.523 | *Active* | *Active* |
| **187** | 6.329 | *Inactive* | *Active* |
| **188** | 8.699 | *Active* | *Active* |
| **189** | 9 | *Active* | *Active* |
| **190** | 8.523 | *Active* | *Active* |
| **191** | 5.854 | *Inactive* | *Active* |
| **192** | 5.889 | *Inactive* | *Active* |
| **193** | 6.201 | *Inactive* | *Active* |
| **194** | 5.742 | *Inactive* | *Active* |
| **195** | 6.31 | *Inactive* | *Active* |
| **196** | 5.712 | *Inactive* | *Active* |
| **197** | 5.924 | *Inactive* | *Active* |
| **198** | 6.796 | *Active* | *Active* |
| **199** | 6.745 | *Active* | *Active* |
| **200** | 6.824 | *Active* | *Active* |
| **201** | 6.056 | *Inactive* | *Active* |
| **202** | 6.745 | *Active* | *Active* |
| **203** | 5.836 | *Inactive* | *Active* |

aCompound number; bDepending on the activity threshold value (6.50): *Active* (> 6.50), *Inactive* (< 6.50).

**Supplementary Figure SF1.** Twenty good (G1-G20) Bayesian fingerprints for the HRV 3Cpro inhibitors.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10180.png | | G1: 1205303806 6 out of 6 good Bayesian Score: 0.943 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10181.png | | G2: -707682703 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10182.png | | G3: -1154461392 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10183.png | | G4: -858278988 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10184.png | | G5: -2143073750 11 out of 13 good Bayesian Score: 0.928 | |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10185.png | | G6: -2141022431 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10186.png | | G7: 997428483 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10187.png | | G8: 668694624 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10188.png | | G9: -216124697 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10189.png | | G10: 1645627429 11 out of 13 good Bayesian Score: 0.928 | |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10190.png | | G11: 1334045270 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10191.png | | G12: -1708879314 11 out of 13 good Bayesian Score: 0.928 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10192.png | | G13: -2147193863 16 out of 20 good Bayesian Score: 0.923 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10193.png | | G14: 1279696542 16 out of 20 good Bayesian Score: 0.923 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10194.png | | G15: 835229868 16 out of 20 good Bayesian Score: 0.923 | |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10195.png | | G16: 101091333 16 out of 20 good Bayesian Score: 0.923 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10196.png | | G17: 1139861560 16 out of 20 good Bayesian Score: 0.923 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10197.png | | G18: 813085235 16 out of 20 good Bayesian Score: 0.923 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10198.png | | G19: -1357068470 16 out of 20 good Bayesian Score: 0.923 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10199.png | | G20: 197319323 16 out of 20 good Bayesian Score: 0.923 | |

**Supplementary Figure SF2.** Twenty bad (B1-B20) Bayesian fingerprints for the HRV 3Cpro inhibitors.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10200.png | | B1: 771857573 0 out of 36 good Bayesian Score: -2.430 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10201.png | | B2: 1732465867 0 out of 36 good Bayesian Score: -2.430 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10202.png | | B3: -1331010955 0 out of 34 good Bayesian Score: -2.378 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10203.png | | B4: 1737023319 0 out of 34 good Bayesian Score: -2.378 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10204.png | | B5: 1095548801 0 out of 33 good Bayesian Score: -2.351 | |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10205.png | | B6: -376760891 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10206.png | | B7: -546103044 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10207.png | | B8: 1506472846 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10208.png | | B9: -1562315313 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10209.png | | B10: 1481812153 0 out of 33 good Bayesian Score: -2.351 | |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10210.png | | B11: -763715471 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10211.png | | B12: 831034507 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10212.png | | B13: 60328660 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10213.png | | B14: -1708493639 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10214.png | | B15: 370838010 0 out of 33 good Bayesian Score: -2.351 | |
| |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10215.png | | B16: -1575106178 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10216.png | | B17: 923916355 0 out of 33 good Bayesian Score: -2.351 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10217.png | | B18: -757679000 0 out of 13 good Bayesian Score: -1.556 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10218.png | | B19: 1219149254 0 out of 11 good Bayesian Score: -1.427 | | |  | | --- | | C:\Users\Tarun Jha\Documents\Discovery Studio Client\Results\CreateBayesianModel_2017_05_17_164657_155\Output\GoodAndBadFingerprints\images\image10219.png | | B20: 953718348 0 out of 11 good Bayesian Score: -1.427 | |