Identification of Bis Cyclic Guanidines as Antiplasmodial Compounds from Positional Scanning Mixture Based Libraries

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Supporting Information

Pages 2-4: Building blocks used for the synthesis of library TPI-1955

Pages 5-7: Structures of all compounds derived from the deconvolution of library TPI-1955

Pages 8-14: LCMS of reported active compounds

Pages 15-28: $^1$H NMR and $^{13}$C of reported active compounds

Page 29: Stability in mouse plasma of compound TPI 2359-47
|   | R1                | R2               | R3               | R4               |
|---|------------------|-----------------|-----------------|------------------|
| TPI-1955-1 | Boc-Ala-OH       | X               | X               | X                |
| TPI-1955-2 | Boc-Phe-OH       | X               | X               | X                |
| TPI-1955-3 | Boc-Gly-OH       | X               | X               | X                |
| TPI-1955-4 | Boc-Ile-OH·½H₂O  | X               | X               | X                |
| TPI-1955-5 | Boc-Leu-OH·H₂O   | X               | X               | X                |
| TPI-1955-6 | Boc-Ser(Bzl)-oh  | X               | X               | X                |
| TPI-1955-7 | Boc-Thr(Bzl)-OH  | X               | X               | X                |
| TPI-1955-8 | Boc-Val-OH       | X               | X               | X                |
| TPI-1955-9 | Boc-Tyr(2-Br-Z)-OH | X   | X               | X                |
| TPI-1955-10 | Boc-D-Ala-OH     | X               | X               | X                |
| TPI-1955-11 | Boc-D-Phe-OH     | X               | X               | X                |
| TPI-1955-12 | Boc-D-Ile-OH     | X               | X               | X                |
| TPI-1955-13 | Boc-D-Leu-OH·H₂O | X               | X               | X                |
| TPI-1955-14 | Boc-D-Ser(Bzl)-oh | X  | X               | X                |
| TPI-1955-15 | Boc-D-Thr(Bzl)-OH | X  | X               | X                |
| TPI-1955-16 | Boc-D-Val-OH     | X               | X               | X                |
| TPI-1955-17 | Boc-D-Tyr(2-Br-Z)-OH | X | X               | X                |
| TPI-1955-18 | Boc-Phg-OH       | X               | X               | X                |
| TPI-1955-19 | Boc-Nva-OH       | X               | X               | X                |
| TPI-1955-20 | Boc-D-Nva-OH     | X               | X               | X                |
| TPI-1955-21 | Boc-Nle-OH       | X               | X               | X                |
| TPI-1955-22 | Boc-D-Nle-OH     | X               | X               | X                |
| TPI-1955-23 | Boc-Ala(2-naphthyl)-OH | X | X               | X                |
| TPI-1955-24 | Boc-D-Ala(2-naphthyl)-OH | X | X               | X                |
| TPI-1955-25 | Boc-Cha-OH       | X               | X               | X                |
| TPI-1955-26 | Boc-D-Cha-OH     | X               | X               | X                |
| TPI-1955-27 | X                | Boc-Ala-OH      | X               | X                |
| TPI-1955-28 | X                | Boc-Phe-OH      | X               | X                |
| TPI-1955-29 | X                | Boc-Gly-OH      | X               | X                |
| TPI-1955-30 | X                | Boc-Ile-OH·½H₂O | X               | X                |
| TPI-1955-31 | X                | Boc-Leu-OH·H₂O  | X               | X                |
| TPI-1955-32 | X                | Boc-Ser(Bzl)-oh | X               | X                |
| TPI-1955-33 | X                | Boc-Thr(Bzl)-OH | X               | X                |
| TPI-1955-34 | X                | Boc-Val-OH      | X               | X                |
| TPI-1955-35 | X                | Boc-Tyr(2-Br-Z)-OH | X | X               |
| TPI-1955-36 | X                | Boc-D-Ala-OH    | X               | X                |
| TPI-1955-37 | X                | Boc-D-Phe-OH    | X               | X                |
| TPI-1955-38 | X                | Boc-D-Ile-OH    | X               | X                |
| TPI-1955-39 | X                | Boc-D-Leu-OH·H₂O | X  | X               |
| TPI-1955-40 | X                | Boc-D-Ser(Bzl)-oh | X | X                |
| TPI-1955-41 | X | Boc-D-Thr(Bzl)-OH | X | X |
| TPI-1955-42 | X | Boc-D-Val-OH | X | X |
| TPI-1955-43 | X | Boc-D-Tyr(2-Br-Z)-OH | X | X |
| TPI-1955-44 | X | Boc-Phg-OH | X | X |
| TPI-1955-45 | X | Boc-Nva-OH | X | X |
| TPI-1955-46 | X | Boc-D-Nva-OH | X | X |
| TPI-1955-47 | X | Boc-Nle-OH | X | X |
| TPI-1955-48 | X | Boc-D-Nle-OH | X | X |
| TPI-1955-49 | X | Boc-Ala(2-naphthyl)-OH | X | X |
| TPI-1955-50 | X | Boc-D-Ala(2-naphthyl)-OH | X | X |
| TPI-1955-51 | X | Boc-Cha-OH | X | X |
| TPI-1955-52 | X | Boc-D-Cha-OH | X | X |
| TPI-1955-53 | X | X | Boc-Ala-OH | X |
| TPI-1955-54 | X | X | Boc-Phe-OH | X |
| TPI-1955-55 | X | X | Boc-Gly-OH | X |
| TPI-1955-56 | X | X | Boc-Ile-OH·½H₂O | X |
| TPI-1955-57 | X | X | Boc-Leu-OH·H₂O | X |
| TPI-1955-58 | X | X | Boc-Ser(Bzl)-OH | X |
| TPI-1955-59 | X | X | Boc-Thr(Bzl)-OH | X |
| TPI-1955-60 | X | X | Boc-Val-OH | X |
| TPI-1955-61 | X | X | Boc-Tyr(2-Br-Z)-OH | X |
| TPI-1955-62 | X | X | Boc-D-Ala-OH | X |
| TPI-1955-63 | X | X | Boc-D-Phe-OH | X |
| TPI-1955-64 | X | X | Boc-D-Ile-OH | X |
| TPI-1955-65 | X | X | Boc-D-Leu-OH·H₂O | X |
| TPI-1955-66 | X | X | Boc-D-Ser(Bzl)-OH | X |
| TPI-1955-67 | X | X | Boc-D-Thr(Bzl)-OH | X |
| TPI-1955-68 | X | X | Boc-D-Val-OH | X |
| TPI-1955-69 | X | X | Boc-D-Tyr(2-Br-Z)-OH | X |
| TPI-1955-70 | X | X | Boc-Phg-OH | X |
| TPI-1955-71 | X | X | Boc-Nva-OH | X |
| TPI-1955-72 | X | X | Boc-D-Nva-OH | X |
| TPI-1955-73 | X | X | Boc-Nle-OH | X |
| TPI-1955-74 | X | X | Boc-D-Nle-OH | X |
| TPI-1955-75 | X | X | Boc-Ala(2-naphthyl)-OH | X |
| TPI-1955-76 | X | X | Boc-D-Ala(2-naphthyl)-OH | X |
| TPI-1955-77 | X | X | Boc-Cha-OH | X |
| TPI-1955-78 | X | X | Boc-D-Cha-OH | X |
| TPI-1955-79 | X | X | 1-phenyl-1-cyclopropanecarboxylic acid | X |
| TPI-1955-80 | X | X | 2-Phenylbutyric Acid | X |
| TPI-1955-81 | X | X | 3-Phenylbutyric Acid | X |
| TPI-1955-82 | X | X | m-Tolylacetic acid | X |
| Code     | Code | Code | Code | 3-Fluorophenylacetic Acid |
|----------|------|------|------|---------------------------|
| TPI-1955-83 | X   | X    | X    |                           |
| TPI-1955-84 | X   | X    | X    | 3-Bromophenylacetic Acid  |
| TPI-1955-85 | X   | X    | X    | (α, α, α Trifluoro-m-Toly) acetic acid |
| TPI-1955-86 | X   | X    | X    | p-Tolylacetic acid        |
| TPI-1955-87 | X   | X    | X    | 4-Fluorophenylacetic acid |
| TPI-1955-88 | X   | X    | X    | 3-Methoxyphenylacetic acid |
| TPI-1955-89 | X   | X    | X    | 4-Bromophenylacetic acid  |
| TPI-1955-90 | X   | X    | X    | 4-Methoxyphenylacetic acid |
| TPI-1955-91 | X   | X    | X    | 4-ethoxyphenylacetic acid |
| TPI-1955-92 | X   | X    | X    | 4-isobutyl-alpha-Methylphenylacetic Acid |
| TPI-1955-93 | X   | X    | X    | 3,4-Dichlorophenylacetic acid |
| TPI-1955-94 | X   | X    | X    | 3,5-Bis(Trifluoromethyl)-Phenylacetic acid |
| TPI-1955-95 | X   | X    | X    | 3-(3,4-Dimethoxyphenyl)-propionic Acid |
| TPI-1955-96 | X   | X    | X    | Phenylacetic acid         |
| TPI-1955-97 | X   | X    | X    | 3,4,5-Trimethoxycbenzoic acid |
| TPI-1955-98 | X   | X    | X    | Butyric Acid              |
| TPI-1955-99 | X   | X    | X    | Heptanoic Acid            |
| TPI-1955-100 | X  | X    | X    | Isobutyric Acid           |
| TPI-1955-101 | X  | X    | X    | 2-Methylbutiric Acid      |
| TPI-1955-102 | X  | X    | X    | Isovaleric acid           |
| TPI-1955-103 | X  | X    | X    | 3-Methylvaleric acid      |
| TPI-1955-104 | X  | X    | X    | 4-Methylvaleric acid      |
| TPI-1955-105 | X  | X    | X    | p-Toluic Acid             |
| TPI-1955-106 | X  | X    | X    | cyclopentanecarboxylic acid |
| TPI-1955-107 | X  | X    | X    | cyclohexanecarboxilic acid |
| TPI-1955-108 | X  | X    | X    | cyclohexylacetic acid     |
| TPI-1955-109 | X  | X    | X    | cyclohexanebutyric acid   |
| TPI-1955-110 | X  | X    | X    | cycloheptanecarboxylic acid |
| TPI-1955-111 | X  | X    | X    | 2-Methylcyclopropanecarboxylic acid |
| TPI-1955-112 | X  | X    | X    | cyclobutanecarboxylic acid |
| TPI-1955-113 | X  | X    | X    | 3-cyclopentylpropionic acid |
| TPI-1955-114 | X  | X    | X    | cyclohexanepropionic acid  |
| TPI-1955-115 | X  | X    | X    | 4-methyl-1-cyclohexancarboxylic acid |
| TPI-1955-116 | X  | X    | X    | 4-tert-butyl-cyclohexancarboxylic acid |
| TPI-1955-117 | X  | X    | X    | 4-biphenylacetic acid     |
| TPI-1955-118 | X  | X    | X    | 1-Adamantanececarboxylic acid |
| TPI-1955-119 | X  | X    | X    | 1-adamantaneacetic acid   |
| TPI-1955-120 | X  | X    | X    | 2-norbornaneacetic acid   |
2359-48
Molecular Weight: 503.810

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Graphs and data analysis for molecular weight and mass spectrometry results.
The percentage of analyte detected compared to time point zero.