Supporting Information

Indolylarylsulfones as HIV-1 Non-Nucleoside Reverse Transcriptase Inhibitors: New Cyclic Substituents at the Indole-2-carboxamide

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TOC Graphic

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1) Preparative and spectroscopic data of derivatives 14, 16, 18, 20 and 22.

3-[(3,5-Dimethylphenyl)sulfonyl]-5-nitro-*N*-(pyrrolidin-1-ylmethyl)-1*H*-indole-2-carboxamide (14). Was synthesized as **12** using **49**. Yield 27%, yellow solid, mp 256-259 °C. ¹H NMR (DMSO-*d*₆): δ 1.71-1.75 (m, 4H), 2.29 (s, 6H), 2.73-2.78 (m, 4H), 4.37 (d, *J* = 6.2 Hz, 2H), 7.24 (s, 1H), 7.62 (s, 2H), 7.67 (d, *J* = 9.0 Hz, 1H), 8.11 (dd, *J* = 2.2 and 9.0 Hz, 1H), 8.84 (d, *J* = 2.3 Hz, 1H), 9.27 (br s, 1H, disappeared on treatment with D₂O), 13.46 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1642, 3175, 3231 cm⁻¹. Anal. (C₂₂H₂₄N₄O₅S (456.51)) C, H, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(piperidin-1-ylmethyl)-1*H*-indole-2-carboxamide (16). Was synthesized as **12** using piperidine. Yield 50%, white solid, mp 172-174 °C. ¹H NMR (DMSO-*d*₆): δ 1.35-1.37 (m, 2H), 1.50-1.51 (m, 4H), 2.31 (s, 6H), 2.54-2.57 (m, 4H), 4.21 (d, *J* = 5.9 Hz, 2H), 7.26 (s, 1H), 7.34 (dd, *J* = 1.9 and 8.8 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.62 (s, 2H), 7.93 (d, *J* = 2.0 Hz, 1H), 9.19 (br s, 1H, disappeared on treatment with D₂O), 13.47 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1634, 3189 cm⁻¹. Anal. (C₂₃H₂₆ClN₃O₃S (459.99)) C, H, Cl, N, S.

3-[(3,5-Dimethylphenyl)sulfonyl]-5-nitro-*N*-(piperidin-1-ylmethyl)-1*H*-indole-2-carboxamide (18). Was synthesized as **12** using **49** and piperidine. Yield 41%, white solid, mp 188-191 °C. ¹H NMR (DMSO-*d*₆): δ 1.37 (s, 2H), 1.48-1.51 (m, 4H), 2.30 (s, 6H), 2.56-2.60 (m, 4H), 4.22 (d, *J* = 6.0 Hz, 2H), 7.26 (s, 1H), 7.63 (s, 2H), 7.69 (d, *J* = 9.1 Hz, 1H), 8.15 (dd, *J* = 2.1 and 9.2 Hz, 1H), 8.83 (d, *J* = 2.2 Hz, 1H), 9.19 (br s, 1H, disappeared on treatment with D₂O), 13.42 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1638, 3161, 3280 cm⁻¹. Anal. (C₂₃H₂₆N₄O₅S (470.54)) C, H, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(morpholinomethyl)-1*H*-indole-2-carboxamide (20). Was synthesized as **12** using morpholine. Yield 57%, white solid, mp 209-211 °C. ¹H NMR (DMSO-*d*₆): δ 2.31 (s, 6H), 2.61 (t, *J* = 4.6 Hz, 4H), 3.60 (t, *J* = 4.4 Hz, 4H), 4.22 (d, *J* = 6.1 Hz, 2H), 7.26 (s, 1H), 7.34 (dd, *J* = 2.0 and 8.8 Hz, 1H), 7.54 (d, *J* = 8.7 Hz, 1H), 7.65 (s, 2H), 7.92 (d, *J* = 2.1 Hz, 1H), 9.25 (br s, 1H, disappeared on treatment with D₂O), 13.03 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1650, 3201 cm⁻¹. Anal. (C₂₂H₂₄ClN₃O₄S (461.96)) C, H, Cl, N, S.

3-[(3,5-Dimethylphenyl)sulfonyl]-*N*-(morpholinomethyl)-5-nitro-1*H*-indole-2-carboxamide (22). Was synthesized as **12** using **49** and morpholine. Yield 41%, yellow solid, mp 183-185 °C. ¹H NMR (DMSO-*d*₆): δ 2.30 (s, 6H), 2.58-2.62 (m, 4H), 3.57-3.62 (m, 4H), 4.21 (d, *J* = 6.0 Hz, 2H), 7.27 (s, 1H), 7.65 (s, 2H), 7.70 (d, *J* = 9.0 Hz, 1H), 8.17 (dd, *J* = 2.3 and 9.1 Hz, 1H), 8.82 (d, *J* = 2.7 Hz, 1H), 9.26 (br s, 1H, disappeared on treatment with D₂O), 13.48 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1642, 3180, 3213 cm⁻¹. Anal. (C₂₂H₂₄N₄O₆S (472.51)) C, H, N, S.

2) Preparative and spectroscopic data of derivatives 15, 17, 19, 21 and 23.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-4-fluoro-*N*-(pyrrolidin-1-ylmethyl)-1*H*-indole-2-carboxamide (15). Was synthesized as **13** using **6**. Yield 58%, white solid, mp 119-124 °C. ¹H NMR (DMSO-*d*₆): δ 1.57-1.61 (m, 4H), 2.31 (s, 6H), 2.64-2.68 (m, 4H), 4.29 (d, *J* = 5.2 Hz, 2H), 7.24 (s, 1H), 7.27-7.40 (m, 2H), 7.64 (s, 2H), 9.23 (br s, 1H, disappeared on treatment with D₂O), 13.01 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1671, 3319 cm⁻¹. Anal. (C₂₂H₂₃ClFN₃O₃S (463.95)) C, H, Cl, F, N, S.

5-Bromo-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(piperidin-1-ylmethyl)-1*H*-indole-2-carboxamide (17). Was synthesized as **13** using piperidine. Yield 46%, white solid, mp 177-180 °C. ¹H NMR (DMSO-*d*₆): δ 1.34-1.37 (m, 2H), 1.48-1.52 (m, 4H), 2.31 (s, 6H), 2.54-2.58 (m, 4H), 4.20 (d, *J* = 5.9 Hz, 2H), 7.27 (s, 1H), 7.43-7.50 (m, 2H), 7.61 (s, 2H), 8.06 (s, 1H), 9.18 (br s, 1H, disappeared on treatment with D₂O), 12.95 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1649, 3194, 3274 cm⁻¹. Anal. (C₂₃H₂₆BrN₃O₃S (504.44)) C, H, Br, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-4-fluoro-*N*-(piperidin-1-ylmethyl)-1*H*-indole-2-carboxamide (19). Was synthesized as **13** using **6** and piperidine. Yield 69%, white solid, mp 175-177 °C. ¹H NMR (DMSO-*d*₆): δ 1.35-1.38 (m, 2H), 1.46-1.51 (m, 4H), 2.32 (s, 6H), 2.63-2.66 (m, 4H), 4.15 (d, *J* = 5.9 Hz, 2H), 7.26 (s, 1H), 7.36-7.43 (m, 2H), 7.63 (s, 2H), 9.24 (br s, 1H, disappeared on treatment with D₂O), 13.01 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1682, 3353 cm⁻¹. Anal. (C₂₃H₂₅ClFN₃O₃S (477.98)) C, H, Cl, F, N, S.

5-Bromo-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(morpholinomethyl)-1*H*-indole-2-carboxamide (21). Was synthesized as **13** using morpholine. Yield 24%, white solid, mp 267-271 °C. ¹H NMR (DMSO-*d*₆): δ 2.30 (s, 6H), 2.56-2.58 (m, 4H), 3.57-3.61 (m, 4H), 4.21 (d, *J* = 5.8 Hz, 2H), 7.25 (s, 1H), 7.43-7.49 (m, 2H), 7.63 (s, 2H), 8.05 (s, 1H), 9.24 (br s, 1H, disappeared on treatment with D₂O), 13.02 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1654, 3210 cm⁻¹. Anal. (C₂₂H₂₄BrN₃O₄S (506.41)) C, H, Br, N, S.

5-Chloro-3-(3,5-dimethylphenylsulfonyl)-4-fluoro-*N*-(morpholinomethyl)-1*H*-indole-2-carboxamide (23). Was synthesized as **13** using **6** and morpholine. Yield 69%, white solid, mp 197-199 °C. ¹H NMR (DMSO-*d*₆): δ 2.32 (s, 6H), 2.62-2.64 (m, 4H), 3.58-3.61 (m, 4H), 4.17 (d, *J* = 6.0 Hz, 2H), 7.26 (s, 1H), 7.32-7.38 (m, 2H), 7.66 (s, 2H), 9.31 (br s, 1H, disappeared on treatment with D₂O), 13.18 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1649, 3238 cm⁻¹. Anal. (C₂₂H₂₃ClFN₃O₄S (479.95)) C, H, Cl, F, N, S.

3) Preparative and spectroscopic data of derivatives 25, 26, 29, 30, 32-34, 36-38, 40-42 and 44-46.

***N*-Benzyl-5-bromo-3-[(3,5-dimethylphenyl)sulfonyl]-1*H*-indole-2-carboxamide (25).** Was synthesized as **24** using **51** and benzylamine. Yield 50%, white solid, mp 266-269 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.26 (s, 6H), 4.58 (d, *J* = 5.6 Hz, 2H), 7.24 (s, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.1 Hz, 2H), 7.43-7.50 (m, 4H), 7.58 (s, 2H), 8.08 (s, 1H), 9.42 (br s, 1H, disappeared on treatment with D₂O), 13.03 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1645, 3214 cm⁻¹. Anal. (C₂₄H₂₁BrN₂O₃S (497.40)) C, H, Br, N, S.

***N*-Benzyl-3-[(3,5-dimethylphenyl)sulfonyl]-5-nitro-1*H*-indole-2-carboxamide (26).** Was synthesized as **24** from **52** using benzylamine. Yield 55%, white solid, mp 246-248 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.26 (s, 6H), 4.58 (d, *J* = 5.7 Hz, 2H), 7.25 (s, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.45 (d, *J* = 7.3 Hz, 2H), 7.61 (s, 2H), 7.70 (d, *J* = 9.1 Hz, 1H), 8.17 (dd, *J* = 2.3 and 9.0 Hz, 1H), 8.83 (d, *J* = 2.3 Hz, 1H) 9.47 (br s, 1H, disappeared on treatment with D₂O), 13.50 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1637, 3190, 3281 cm⁻¹. Anal. (C₂₄H₂₁N₃O₅S (463.51)) C, H, N, S.

5-Bromo-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(2-(pyrrolidin-1-yl)ethyl)-1*H*-indole-2-carboxamide (29). Was synthesized as **24** using **51** and 2-(pyrrolidin-1-yl)ethanamine. Yield 70%, white solid, mp 207-210 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 1.67-1.71 (m, 4H), 2.30 (s, 6H), 2.52-2.56 (m, 4H), 2.66 (t, *J* = 6.8 Hz, 2H), 3.47 (q, *J* = 6.9 Hz, 2H), 7.25 (s, 1H), 7.38-7.48 (m, 2H), 7.61 (s, 2H), 8.1 (s, 1H), 9.00 (br s, 1H, disappeared on treatment with D₂O), 13.05 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1648, 3204 cm⁻¹. Anal. (C₂₃H₂₆BrN₃O₃S (504.44)) C, H, Br, N, S.

3-[(3,5-Dimethylphenyl)sulfonyl]-5-nitro-*N*-(2-(pyrrolidin-1-yl)ethyl)-1*H*-indole-2-carboxamide (30). Was synthesized as **24** using **52** and 2-(pyrrolidin-1-yl)ethanamine. Yield 46%, white solid, mp 216-218 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 1.74-1.78 (m, 4H), 2.28 (s, 6H), 2.81-2.85 (m, 4H), 2.90 (t, *J* = 6.3 Hz, 2H), 3.50 (q, *J* = 6.2 Hz, 2H), 7.20 (s, 1H), 7.57-7.62 (m, 3H), 8.02 (dd, *J* = 2.1 and 9.0 Hz, 1H), 8.84-8.89 (m, 2H), 13.46 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1643, 3181 cm⁻¹. Anal. (C₂₃H₂₆N₄O₅S (470.54)) C, H, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(2-morpholinoethyl)-1*H*-indole-2-carboxamide (32). Was synthesized as **24** using 2-morpholin-4-ylethanamine. Yield 25%, white solid, mp 208-210 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.31 (s, 6H), 2.48-2.53 (m, 4H), 3.50-3.59 (m, 8H), 7.28 (s, 1H), 7.34 (d, *J* = 9.0 Hz, 1H), 7.54 (d, *J* = 8.12 Hz, 1H), 7.63 (s, 2H), 7.97 (s, 1H), 9.09 (br s, 1H, disappeared on treatment with D₂O), 13.04 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1646, 3213 cm⁻¹. Anal. (C₂₃H₂₆ClN₃O₄S (475.99)) C, H, Cl, N, S.

5-Bromo-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(2-morpholinoethyl)-1*H*-indole-2-carboxamide (33). Was synthesized as **24** using **51** and 2-morpholin-4-yl-ethanamine. Yield 53%, white solid, mp 218-223 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.30 (s, 6H), 2.43-2.47 (m, 4H), 2.53 (t, *J* = 6.4 Hz, 2H), 3.49 (q, *J* = 6.0 Hz, 2H), 3.56-3.59 (m, 4H), 7.26 (s, 1H), 7.43-7.49 (m, 2H), 7.60 (s, 2H), 8.10 (s, 1H), 9.06 (br s, 1H, disappeared on treatment with D₂O), 13.01 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1640, 3196 cm⁻¹. Anal. (C₂₃H₂₆BrN₃O₄S (520.44)) C, H, Br, N, S.

3-(3,5-Dimethylphenylsulfonyl)-*N*-(2-morpholinoethyl)-5-nitro-1*H*-indole-2-carboxamide (34). Was synthesized as **24** using **52** and 2-morpholin-4-yl-ethanamine. Yield 63%, yellow solid, mp 243-246 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.30 (s, 6H), 2.46-2.49 (m, 4H), 2.55 (t, *J* = 6.4 Hz, 2H), 3.50 (q, *J* = 6.0 Hz, 2H), 3.58-3.60 (m, 4H), 7.27 (s, 1H), 7.63 (s, 2H), 7.69 (d, *J* = 9.1 Hz, 1H), 8.17 (dd, *J* = 1.8 and 8.9 Hz, 1H), 8.86 (d, *J* = 2.1 Hz, 1H), 9.05 (br s, 1H, disappeared on treatment with D₂O), 13.46 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1648, 3163 cm⁻¹. Anal. (C₂₃H₂₆N₄O₆S (486.54)) C, H, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-phenethyl-1*H*-indole-2-carboxamide (36). Was synthesized as **24** using 2-phenylethanamine. Yield 60%, white solid, mp 227-228 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.32 (s, 6H), 2.91 (t, *J* = 7.4 Hz, 2H), 3.58-3.63 (m, 2H), 7.23-7.37 (m, 7H), 7.47 (d, *J* = 7.1 Hz, 1H), 7.52 (s, 2H), 7.94 (d, *J* = 2.0 Hz, 1H), 9.10 (br s, 1H, disappeared on treatment with D₂O), 13.05 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1643, 3195, 3287 cm⁻¹. Anal. (C₂₅H₂₃ClN₂O₃S (466.98)) C, H, Cl, N, S.

5-Bromo-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-phenethyl-1*H*-indole-2-carboxamide (37). Was synthesized as **24** using **51** and 2-phenylethanamine. Yield 30%, white solid, mp 231-236 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.29 (s, 6H), 2.90 (t, *J* = 7.4 Hz, 2H), 3.58 (q, *J* = 6.7 Hz, 2H), 7.22-7.31 (m, 6H), 7.43-7.49 (m, 2H), 7.59 (s, 2H), 8.07 (s, 1H), 9.08 (br s, 1H, disappeared on treatment with D₂O), 13.00 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1640, 3191, 3290 cm⁻¹. Anal. (C₂₅H₂₃BrN₂O₃S (511.43)) C, H, Br, N, S.

3-[(3,5-Dimethylphenyl)sulfonyl]-5-nitro-*N*-phenethyl-1*H*-indole-2-carboxamide (38). Was synthesized as **24** using **52** and 2-phenylethanamine. Yield 74%, white solid, mp 261-262 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.29 (s, 6H), 2.89 (t, *J* = 7.4 Hz, 2H), 3.56 (q, *J* = 6.7 Hz, 2H), 7.20-7.24 (m, 3H), 7.28-7.31 (m, 4H), 7.63-7.67 (m, 2H), 8.11 (dd, *J* = 1.9 and 8.9 Hz, 1H), 8.85 (d, *J* = 1.9 Hz, 1H), 8.98 (br s, 1H, disappeared on treatment with D₂O), 13.47 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1641, 3176, 3284 cm⁻¹. Anal. (C₂₅H₂₃N₃O₅S (477.53)) C, H, N, S.

***N*-[2-(1*H*-Pyrrol-1-yl)ethyl]-5-chloro-3-[(3,5-dimethylphenyl)sulfonyl]-1*H*-indole-2-carboxamide (40).** Was synthesized as **24** using 2-(1*H*-pyrrol-1-yl)ethylamine. Yield 38%, white solid, mp 200-203 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.31 (s, 6H), 3.66 (q, *J* = 6.1 Hz, 2H), 4.14 (t, *J* = 6.2 Hz, 2H), 6.01 (t, *J* = 2.1 Hz, 2H), 6.87 (t, *J* = 2.1 Hz, 2H), 7.26 (s, 1H), 7.34 (dd, *J* = 2.0 and 8.8 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 1H), 7.65 (s, 2H), 7.91 (d, *J* = 1.9 Hz, 1H), 9.18 (br s, 1H, disappeared on treatment with D₂O), 13.08 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1638, 3215 cm⁻¹. Anal. (C₂₃H₂₂ClN₃O₃S (455.96)) C, H, Cl, N, S.

***N*-[2-(1*H*-Pyrrol-1-yl)ethyl]-5-bromo-3-[(3,5-dimethylphenyl)sulfonyl]-1*H*-indole-2-carboxamide (41).** Was synthesized as **24** using **51** and 2-(1*H*-pyrrol-1-yl)ethylamine. Yield 29%, white solid, mp 213-216 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.30 (s, 6H), 3.65 (q, *J* = 5.2 Hz, 2H), 4.12 (t, *J* = 6.4 Hz, 2H), 5.99 (s, 2H), 6.84 (s, 2H), 7.25 (s, 1H), 7.43-7.49 (m, 2H), 7.16 (s, 2H), 8.04 (s, 1H), 9.14 (br s, 1H, disappeared on treatment with D₂O), 13.00 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1655, 3195 cm⁻¹. Anal. (C₂₃H₂₂BrN₃O₃S (500.41)) C, H, Br, N, S.

***N*-[2-(1*H*-Pyrrol-1-yl)ethyl]-3-[(3,5-dimethylphenyl)sulfonyl]-5-nitro-1*H*-indole-2-carboxamide (42).** Was synthesized as **24** using **52** and 2-(1*H*-pyrrol-1-yl)ethylamine. Yield 76%, yellow solid, mp 234-237 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.30 (s, 6H), 3.65 (q, *J* = 5.9 Hz, 2H), 4.12 (t, *J* = 6.1 Hz, 2H), 5.99 (s, 2H), 6.85 (s, 2H), 7.27 (s, 1H), 7.65 (s, 2H), 7.69 (d, *J* = 9.1 Hz, 1H), 8.16 (dd, *J* = 1.7 and 9.2 Hz, 1H), 8.80 (d, *J* = 1.9 Hz, 1H), 9.18 (br s, 1H, disappeared on treatment with D₂O), 13.44 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1648, 3228 cm⁻¹. Anal. (C₂₃H₂₂N₄O₅S (466.51)) C, H, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(2-phenoxyethyl)-1*H*-indole-2-carboxamide (44). Was synthesized as **24** using 2-phenoxyethanamine. Yield 83%, white solid, mp 227-228 °C (from ethanol). ¹H NMR (CDCl₃): δ 2.17 (s, 6H), 3.97 (q, *J* = 6.3 Hz, 2H), 4.23 (t, *J* = 5.2 Hz, 2H), 6.95-7.00 (m, 3H), 7.09 (s, 1H), 7.26-7.34 (m, 3H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.51 (s, 2H), 8.28 (d, *J* = 1.8 Hz, 1H), 10.05 (br s, 1H, disappeared with D₂O), 10.31 ppm (br s, 1H, disappeared with D₂O). IR: ν 1650, 3209 cm⁻¹. Anal. (C₂₅H₂₃ClN₂O₄S (482.98)) C, H, Cl, N, S.

5-Bromo-3-[(3,5-dimethylphenyl)sulfonyl]-*N*-(2-phenoxyethyl)-1*H*-indole-2-carboxamide (45). Was synthesized as **24** using **51** and 2-phenoxyethanamine. Yield 52%, white solid, mp 214-219 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.18 (s, 6H), 4.62 (q, *J* = 6.2 Hz, 2H), 4.07 (t, *J* = 6.4 Hz,

2H), 6.88-6.97 (m, 3H), 7.04-7.08 (m, 2H), 7.26-7.37 (m, 3H), 7.55 (s, 2H), 8.09 (s, 1H), 8.50 (br s, 1H, disappeared on treatment with D₂O), 13.05 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1644, 3206 cm⁻¹. Anal. (C₂₅H₂₃BrN₂O₄S (527.43)) C, H, Br, N, S.

3-[(3,5-Dimethylphenyl)sulfonyl]-5-nitro-*N*-(2-phenoxyethyl)-1*H*-indole-2-carboxamide (46). Was synthesized as **24** using **52** and 2-phenoxyethanamine. Yield 93%, white solid, mp 278-280 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.23 (s, 6H), 3.77 (q, *J* = 5.4 Hz, 2H), 4.18 (t, *J* = 5.2 Hz, 2H), 6.93-7.00 (m, 3H), 7.24 (s, 1H), 7.30 (t, *J* = 7.3 Hz, 2H), 7.62 (s, 2H), 7.70 (d, *J* = 9.1 Hz, 1H), 8.18 (dd, *J* = 1.8 and 8.8 Hz, 1H), 8.88 (d, *J* = 2.2 Hz, 1H), 9.33 (br s, 1H, disappeared on treatment with D₂O), 13.48 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1642, 3188, 3279 cm⁻¹. Anal. (C₂₅H₂₃N₃O₆S (493.53)) C, H, N, S.

4) Preparative and spectroscopic data of derivatives **28**, **31**, **35**, **39**, **43** and **47**.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-N-[2-(pyrrolidin-1-yl)ethyl]-1H-indole-2-carboxamide (28). Was synthesized as **27** using **54** and 2-(pyrrolidin-1-yl)ethanamine. Yield 82%, white solid, mp 200-203 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.29 (s, 6H), 2.54 (m, 8H), 2.66 (t, *J* = 6.6 Hz, 2H), 3.40 (q, *J* = 6.1 Hz, 2H), 7.25 (s, 1H), 7.31 (dd, *J* = 1.9 and 8.8 Hz, 1H), 7.51 (d, *J* = 8.7 Hz, 1H), 7.61 (s, 2H), 7.94 (d, *J* = 1.7 Hz, 1H), 9.00 (br s, 1H, disappeared on treatment with D₂O), 13.02 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1648, 3204 cm⁻¹. Anal. (C₂₃H₂₆ClN₃O₃S (459.99)) C, H, Cl, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-4-fluoro-N-[2-(pyrrolidin-1-yl)ethyl]-1H-indole-2-carboxamide (31). Was synthesized as **27** using 2-(pyrrolidin-1-yl)ethanamine. Yield 59%, white solid, mp 194-195 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 1.69-1.71 (m, 4H), 2.32 (s, 6H), 2.55-2.58 (m, 4H), 2.68 (t, *J* = 7.0 Hz, 2H), 3.43 (q, *J* = 6.5 Hz, 2H), 7.24 (s, 1H), 7.29-7.32 (m, 2H), 7.67 (s, 2H), 8.92 (br s, 1H, disappeared on treatment with D₂O), 13.21 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1655, 3344 cm⁻¹. Anal. (C₂₃H₂₅ClFN₃O₃S (477.98)) C, H, Cl, F, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-4-fluoro-N-[2-(morpholin-4-yl)ethyl]-1H-indole-2-carboxamide (35). Was synthesized as **27** using 2-(morpholin-4-yl)ethanamine. Yield 93%, white solid, mp 216-217 °C (from ethanol). ¹H NMR (CDCl₃): δ 2.37 (s, 6H), 2.54-2.56 (m, 4H), 2.68 (t, *J* = 6.1 Hz, 2H), 3.69-3.71 (m, 6H), 7.20 (s, 1H), 7.22 (s, 1H), 7.33 (dd, *J* = 6.4 and 8.8 Hz, 1H), 7.59 (s, 2H), 10.14 (br s, 1H, disappeared on treatment with D₂O), 10.38 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1646, 3181, 3266 cm⁻¹. Anal. (C₂₃H₂₅ClFN₃O₄S (493.98)) C, H, Cl, F, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-4-fluoro-N-phenethyl-1H-indole-2-carboxamide (39). Was synthesized as **27** using 2-phenylethanamine. Yield 88%, white solid, mp 184-185 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.32 (s, 6H), 2.90 (t, *J* = 7.5 Hz, 2H), 3.54 (q, *J* = 5.5 Hz, 2H), 7.22-7.42 (m, 8H), 7.66 (s, 2H), 9.16 (br s, 1H, disappeared on treatment with D₂O), 13.24 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1649, 3197 cm⁻¹. Anal. (C₂₅H₂₂ClFN₂O₃S (484.97)) C, H, Cl, F, N, S.

N-[2-(1H-Pyrrol-1-yl)ethyl]-5-chloro-3-[(3,5-dimethylphenyl)sulfonyl]-4-fluoro-1H-indole-2-carboxamide (43). Was synthesized as **27** using 2-(1H-pyrrol-1-yl)ethanamine. Yield 88%, white solid, mp 234-236 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.31 (s, 6H), 3.59 (q, *J* = 5.9 Hz, 2H), 4.10 (t, *J* = 6.2 Hz, 2H), 5.98-5.99 (m, 2H), 6.86-6.87 (m, 2H), 7.26 (s, 1H), 7.31-7.39 (m, 2H), 7.66 (s, 2H), 9.25 (br s, 1H, disappeared on treatment with D₂O), 13.21 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1643, 3261 cm⁻¹. Anal. (C₂₃H₂₁ClFN₃O₃S (473.95)) C, H, Cl, F, N, S.

5-Chloro-3-[(3,5-dimethylphenyl)sulfonyl]-4-fluoro-N-(2-phenoxyethyl)-1H-indole-2-carboxamide (47). Was synthesized as **27** using 2-phenoxyethylamine. Yield 76%, white solid, mp 198-201 °C (from ethanol). ¹H NMR (DMSO-*d*₆): δ 2.29 (s, 6H), 3.71 (q, *J* = 5.2 Hz, 2H), 5.15 (t, *J* = 5.1 Hz, 2H), 6.93-6.98 (m, 3H), 7.34-7.37 (m, 5H), 7.65 (s, 2H), 9.33 (br s, 1H, disappeared on treatment with D₂O), 13.22 ppm (br s, 1H, disappeared on treatment with D₂O). IR: ν 1643, 3204 cm⁻¹. Anal. (C₂₅H₂₂ClFN₂O₄S (500.97)) C, H, Cl, F, N, S.

Figure 1S. Binding conformation of derivative **12** (cyan) into the NNBS of the HIV-1 L100I mutated RT. Mutated residues are highlighted as yellow stick. Hydrogen atoms are not shown for clarity. H-bonds are reported as dotted yellow lines.

Figure 2S. Binding conformation of derivative **12** (cyan) into the NNBS of the HIV-1 K103N mutated RT. Mutated residues are highlighted as yellow stick. Hydrogen atoms are not shown for clarity. H-bonds are reported as dotted yellow lines.

Figure 3S. Binding conformation of derivative **12** (cyan) into the NNBS of the HIV-1 Y181C mutated RT. Mutated residues are highlighted as yellow stick. Hydrogen atoms are not shown for clarity. H-bonds are reported as dotted yellow lines.

Table 1S. Anti-HIV-1 Activity, Cytotoxicity, Selectivity Index and Relative Factor of Compounds **20**, **24-26**, **28**, **36**, **40** and **44** against Mutant HIV-1 Strains in MT-4 Cells.

Compd	HIV-1 Strain	IC ₅₀ (nM)	CC ₅₀ (nM)	SI	RF
20	III _B	3.2 ± 0.8	>1000	>312	1.0
	L100I	8.0 ± 5.6	>1000	>125	2.5
	K103N	11 ± 3	>1000	>90	3.5
	Y181C	23 ± 6	>1000	>43	7.1
	Y188L	440 ± 60	>1000	>2	137.5
	E138K	14 ± 0	>1000	>71	4.2
24	III _B	11 ± 7	>1000	>90	1.0
	L100I	6.1 ± 2.4	>1000	>164	0.5
	K103N	11 ± 0	>1000	>93	1.0
	Y181C	46 ± 11	>1000	>21	4.0
	Y188L	480 ± 90	>1000	>2	43.6
	E138K	18 ± 5	>1000	>55	1.6
25	III _B	16 ± 3	>1000	>62	1.0
	L100I	11 ± 8	>1000	>90	0.7
	K103N	15 ± 3	>1000	>66	0.9
	Y181C	59 ± 37	>1000	>17	3.7
	Y188L	≥450	>1000	-	-
	E138K	51 ± 41	>1000	>19	3.2
26	III _B	10 ± 7	>1000	>100	1.0
	L100I	7 ± 5.1	>1000	>142	0.7
	K103N	11 ± 5	>1000	>90	1.1
	Y181C	54 ± 30	>1000	>18	5.4
	Y188L	470 ± 200	>1000	>2	47.0
	E138K	16 ± 0	>1000	>62	1.6
28	III _B	19 ± 1	>1000	>52	1.0
	L100I	84 ± 8	>1000	>11	4.4
	K103N	80 ± 5	>1000	>12	4.2
	Y181C	380 ± 20	>1000	>2.6	20.0
	Y188L	>1000	>1000	-	-
	E138K	260 ± 100	>1000	>3.8	13.7
36	III _B	21 ± 3	>1000	>47	1.0
	L100I	19 ± 1	>1000	>52	0.9
	K103N	52 ± 6	>1000	>19	2.5
	Y181C	100 ± 10	>1000	>10	4.8
	Y188L	>1000	>1000	-	-
	E138K	65 ± 3	>1000	>15	3.1
40	III _B	15 ± 1	>1000	>66	1.0
	L100I	11 ± 1	>1000	>90	0.7
	K103N	15 ± 0	>1000	>66	1.0
	Y181C	67 ± 22	>1000	>15	4.4
	Y188L	>1000	>1000	-	-
	E138K	18 ± 1	>1000	>55	1.2
44	III _B	300 ± 140	>1000	>3.3	1.0
	L100I	440 ± 200	>1000	>2.3	1.5
	K103N	>1000	>1000	-	-
	Y181C	>1000	>1000	-	-
	Y188L	>1000	>1000	-	-
	E138K	380 ± 20	>1000	>2.6	1.3

Table 2S. Inhibitory Effects of New IASs **12-47** and Reference Compound **4** on the Proliferation of Murine Leukemia Cells (L1210) and Human T-Lymphocyte Cells (Molt4/C8).

Compd	CC ₅₀ (μM)	
	L1210	Molt4/C8
12	18 ± 14	4.9 ± 3.6
13	11 ± 2	2.5 ± 0.1
14	23 ± 1	8.6 ± 2.8
15	9.0 ± 1.3	6.5 ± 3.2
16	13 ± 2	6.4 ± 1.2
17	11 ± 0	7.2 ± 1.2
18	35 ± 5	10 ± 1
19	43 ± 11	26 ± 3
20	18 ± 7	6.3 ± 3.6
21	43 ± 1	18 v 12
22	49 ± 1	42 ± 8
23	59 ± 10	45 ± 5
24	≥500	306 ± 12
25	104 ± 70	158 ± 2
26	12 ± 6	3.7 ± 2.2
27	139 ± 31	15 ± 5
28	5.3 ± 2.6	6.4 ± 4.0
29	3.2 ± 2.1	4.5 ± 3.5
30	14 ± 0	9.5 ± 1.9
31	4.8 ± 0.1	3.9 ± 2.7
32	181 ± 62	4.4 ± 2.9
33	>500	238 ± 49
34	59 ± 20	12 ± 3
35	13 ± 2	8.4 ± 0.6
36	215 ± 63	243 ± 81
37	>500	238 ± 49
38	>500	≥500
39	42 ± 9	11 ± 3
40	93 ± 33	66 ± 17
41	114 ± 45	150 ± 11
42	192 ± 13	194 ± 52
43	8.9 ± 1.5	8.5 ± 0.8
44	200 ± 77	231 ± 96
45	>500	≥500
46	>500	>500
47	18 ± 9	9.0 ± 1.1
4	12 ± 1	3.8 ± 1.3

Table 3S. Elemental Analyses of Derivatives **12-47** and **49**.

Compd	Calculated	Found
12	C, 59.25; H, 5.42; Cl, 7.95; N, 9.42; S, 7.19	C, 59.17; H, 5.38; Cl, 7.80; N, 9.35; S, 7.12
13	C, 53.88; H, 4.93; Br, 16.29; N, 8.57; S, 6.54	C, 53.66; H, 4.90; Br, 16.11; N, 8.30; S, 6.22
14	C, 57.88; H, 5.30; N, 12.27; S, 7.02	C, 57.59; H, 5.27; N, 12.09; S, 6.89
15	C, 56.95; H, 5.00; Cl, 7.64; F, 4.09; N, 9.06; S, 6.91	C, 56.76; H, 4.97; Cl, 7.49; F, 3.93; N, 9.88; S, 6.76
16	C, 60.05; H, 5.70; Cl, 7.71; N, 9.14; S, 6.97	C, 59.88; H, 5.67; Cl, 7.56; N, 9.01; S, 6.84
17	C, 54.76; H, 5.20; Br, 15.84; N, 8.33; S, 6.36	C, 54.59; H, 5.18; Br, 15.69; N, 8.19; S, 6.21
18	C, 58.71; H, 5.57; N, 11.91; S, 6.81	C, 58.44; H, 5.53; N, 11.74; S, 6.74
19	C, 57.79; H, 5.27; Cl, 7.42; F, 3.97; N, 8.79; S, 6.71	C, 57.66; H, 5.22; Cl, 7.27; F, 3.84; N, 8.52; S, 6.48
20	C, 57.20; H, 5.24; Cl, 7.67; N, 9.10; S, 6.94	C, 56.97; H, 5.22; Cl, 7.52; N, 9.04; S, 6.88
21	C, 52.18; H, 4.78; Br, 15.78; N, 8.30; S, 6.33	C, 51.89; H, 4.72; Br, 15.59; N, 8.14; S, 6.19
22	C, 63.64; H, 4.67; Cl, 7.83; N, 6.18; S, 7.08	C, 63.48; H, 4.63; Cl, 7.68; N, 6.03; S, 6.92
23	C, 57.95; H, 4.26; Br, 16.06; N, 5.63; S, 6.45	C, 57.78; H, 4.21; Br, 15.88; N, 5.50; S, 6.30
24	C, 62.19; H, 4.57; N, 9.07; S, 6.92	C, 61.89; H, 4.52; N, 8.93; S, 6.79
25	C, 61.21; H, 4.28; Cl, 7.53; F, 4.03; N, 5.95; S, 6.81	C, 60.98; H, 4.23; Cl, 7.09; F, 3.81; N, 5.71; S, 6.66
26	C, 55.92; H, 5.12; N, 11.86; S, 6.79	C, 55.66; H, 5.07; N, 11.77; S, 6.58
27	C, 55.05; H, 4.83; Cl, 7.39; F, 3.96; N, 8.76; S, 6.68	C, 54.76; H, 4.80; Cl, 7.26; F, 3.90; N, 8.62; S, 6.45
28	C, 60.05; H, 5.70; Cl, 7.71; N, 9.14; S, 6.97	C, 59.68; H, 5.68; Cl, 7.57; N, 9.02; S, 6.62
29	C, 54.76; H, 5.20; Br, 15.84; N, 8.33; S, 6.36	C, 54.58; H, 5.18; Br, 15.60; N, 8.19; S, 6.01
30	C, 58.71; H, 5.57; N, 11.91; S, 6.81	C, 58.47; H, 5.52; N, 11.84; S, 6.67
31	C, 57.79; H, 5.27; Cl, 7.42; F, 3.97; N, 8.79; S, 6.71	C, 57.41; H, 5.21; Cl, 7.28; F, 3.84; N, 8.82; S, 6.56
32	C, 58.04; H, 5.51; Cl, 7.45; N, 8.83; S, 6.74	C, 57.89; H, 5.48; Cl, 7.32; N, 8.68; S, 6.59
33	C, 53.08; H, 5.04; Br, 15.35; N, 8.07; S, 6.16	C, 52.87; H, 4.95; Br, 15.17; N, 7.92; S, 6.04
34	C, 56.78; H, 5.39; N, 11.52; S, 6.59	C, 56.49; H, 5.31; N, 11.07; S, 6.01
35	C, 55.92; H, 5.10; Cl, 7.18; F, 3.85; N, 8.51; S, 6.49	C, 55.77; H, 5.03; Cl, 7.05; F, 3.74; N, 8.38; S, 6.26
36	C, 64.30; H, 4.96; Cl, 7.59; N, 6.00; S, 6.87	C, 64.18; H, 4.93; Cl, 7.43; N, 5.89; S, 6.63
37	C, 58.71; H, 4.53; Br, 15.62; N, 5.48; S, 6.27	C, 58.58; H, 4.51; Br, 15.47; N, 5.40; S, 6.14
38	C, 62.88; H, 4.85; N, 8.80; S, 6.71	C, 62.65; H, 4.80; N, 8.65; S, 6.59
39	C, 61.91; H, 4.57; Cl, 7.31; F, 3.92; N, 5.78; S, 6.61	C, 61.79; H, 4.51; Cl, 7.18; F, 3.78; N, 5.56; S, 6.35
40	C, 60.59; H, 4.86; Cl, 7.78; N, 9.22; S, 7.03	C, 60.36; H, 4.81; Cl, 7.62; N, 9.05; S, 6.88
41	C, 55.20; H, 4.43; Br, 15.97; N, 8.40; S, 6.41	C, 55.01; H, 4.39; Br, 15.82; N, 8.33; S, 6.27
42	C, 59.22; H, 4.75; N, 12.01; S, 6.87	C, 58.98; H, 4.70; N, 11.86; S, 6.64
43	C, 58.29; H, 4.47; Cl, 7.48; F, 4.01; N, 8.87; S, 6.77	C, 58.02; H, 4.20; Cl, 7.22; F, 3.79; N, 8.23; S, 6.53
44	C, 62.17; H, 4.80; Cl, 7.34; N, 5.80; S, 6.64	C, 61.88; H, 4.74; Cl, 7.21; N, 5.57; S, 6.42
45	C, 56.93; H, 4.40; Br, 15.15; N, 5.31; S, 6.08	C, 56.62; H, 4.32; Br, 15.01; N, 5.18; S, 5.85
46	C, 60.84; H, 4.70; N, 8.51; S, 6.50	C, 60.57; H, 4.68; N, 8.37; S, 6.38
47	C, 59.94; H, 4.43; Cl, 7.08; F, 3.79; N, 5.59; S, 6.40	C, 59.65; H, 4.42; Cl, 6.82; F, 3.58; N, 5.35; S, 6.27
49	C, 54.39; H, 4.56; N, 11.19; S, 8.54	C, 54.11; H, 4.48; N, 10.95; S, 8.28