Supporting information for

An improved synthesis of telmisartan via the copper-catalyzed

cyclization of o-haloarylamidines

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I) General procedures

¹H NMR and ¹³C NMR spectra were recorded on a Brucker 500 Hz instrument. Data for ¹H NMR were presented as the chemical shift in ppm, and multiplicities were denoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Data for ¹³C NMR were reported as chemical shift. The ESI mass spectra were determined on a Thermo Fisher FINNIGAN LTQ instrument. All high-resolution mass spectra (HRMS) results were obtained on an Agilent 1290-6545 UHPLC-QTOF LC/MS spectrometer. Thin-layer chromatography (TLC) inspections were performed on silica gel plates (GF-254). All commercially available chemicals and solvents were directly used without further purification unless otherwise noted.

II) Experimental details for the reactions

1-Methyl-2-(3-methyl-4-nitrophenyl)-1H-benzoimidazole (8). Oxalyl chloride (15.4 g, 121.4 mmol) was added dropwise to a flask containing 3-methyl-4-nitrobenzoic acid **7** (20.0 g, 110.4 mmol), catalytic amount of DMF (804.0 mg, 11.0 mmol), and 100 ml of CH_2Cl_2 under ice bath, then the mixture was stirred for 3 h at room temperature. Meanwhile, *N*-methyl-1,2-benzenediamine dihydrochloride (22.6 g, 115.9 mmol), DIPEA (57.1 g, 441.6 mmol), and CH_2Cl_2 (100 ml) were added to another flask and stirred. Afterwards, the former solution was added dropwise to the latter one under ice bath, and the mixture was stirred for 30 min at room temperature. The solution was successively washed with saturated ammonium chloride solution (200 ml) and brine (200 ml), and the organic layer was dried with Na₂SO₄. After that, the solvent was removed under reduced pressure. Subsequently, 200 ml of toluene, and catalytic amount of TsOH·H₂O (6.3 g, 33.0 mmol) were added to the residue, and the mixture was heated to reflux for 4 h in an azeotropic distillation instrument to separate out water. Then the pH was adjusted to 9-10 using saturated sodium carbonate solution, and the organic layer was washed with brine, and dried with Na₂SO₄. Removed the solvent by a rotary evaporator, then the resulting crude was purified by silica gel column chromatography, afforded **8** (25.2 g, 85%) as a lightyellow solid.

¹H NMR (500 MHz, CDCl₃): δ 8.11 (d, *J* = 8.5 Hz, 1H), 7.82 – 7.86 (m, 2H), 7.70 – 7.73 (m, 1H), 7.40 – 7.43 (m, 1H), 7.32 – 7.39 (m, 2H), 3.90 (s, 3H), 2.69 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 151.31, 149.63, 142.88, 136.80, 134.80, 134.55, 134.03, 127.56, 125.15, 123.81, 123.18, 120.28, 110.00, 32.01, 20.66. HRMS (ESI-QTOF): m/z Calcd for C₁₅H₁₄N₃O₂ [M + H]⁺: 268.1081; found: 268.1080.

2-Methyl-4-(1-methyl-1*H***-benzoimidazol-2-yl)aniline (9). 8** (20.0 g, 74.8 mmol) was reduced with 5% Pd/C (1 g) and hydrogen (5 bar) in a mixture of MeOH (250 ml) and THF (50 ml) at 50 °C for 12 h. The insoluble substances were filtered away, then the solvent was removed by a rotary evaporator, MTBE (40 ml) was added to the residue and stirred for 2h, the precipitated solid was filtered and dried in vacuum at 50 °C, gave 9 (17.1 g, 96%) as a light-yellow solid.

¹H NMR (500 MHz, DMSO-*d*6): δ 7.59 (d, J = 7.2 Hz, 1H), 7.49 – 7.55 (m, 1H), 7.46 (d, J = 2.1 Hz, 1H), 7.39 – 7.44 (m, 1H), 7.15 – 7.26 (m, 2H), 6.75 (d, J = 8.2 Hz, 1H), 5.37 (s, 2H), 3.83 (s, 3H), 2.15 (s, 3H). ¹³C NMR (125 MHz, DMSO-*d*6): δ 154.24, 148.32, 142.54, 136.61, 131.13, 127.84, 121.51, 121.48, 120.77, 118.25, 116.98, 113.34, 110.04, 31.75, 17.44. HRMS (ESI-QTOF): m/z Calcd for C₁₅H₁₆N₃ [M + H]⁺: 238.1339; found: 238.1336.

2-Bromo-6-methyl-4-(1-methyl-1H-benzoimidazol-2-yl)aniline (10b). N-bromosuccinimide

(9.9 g, 55.7 mmol) was added to the solution of **9** (12.0 g, 50.6 mmol) in 40 ml of MeCN, and heated to reflux for 1.5 h, then the solvent was removed under reduced pressure. To the remaining oily matter, saturated sodium carbonate solution was added to adjust the PH to 9-10, then 60 ml of CH_2Cl_2 was added. The organic layer was washed with 30 ml of brine, and dried with Na₂SO₄. Removed the solvent by a rotary evaporator, and the resulting crude was purified by silica gel column chromatography, provided the title compound **10b** (13.7 g, 86%) as a light-yellow solid.

¹H NMR (500 MHz, CDCl₃): δ 7.76 – 7.82 (m, 1H), 7.73 (d, J = 2.0 Hz, 1H) , 7.47 – 7.49 (m, 1H), 7.33 – 7.38 (m, 1H), 7.27 – 7.32 (m, 2H), 4.34 (s, 2H), 3.86 (s, 3H), 2.29 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 153.13, 143.93, 142.87, 136.69, 131.25, 130.73, 123.38, 122.67, 122.53, 120.43, 119.62, 109.61, 108.90, 31.93, 18.48. HRMS (ESI-QTOF): m/z Calcd for C₁₅H₁₅BrN₃ [M + H]⁺: 316.0444; found: 316.0437.

2-Chloro-6-methyl-4-(1-methyl-1*H*-benzoimidazol-2-yl)aniline (10a). The title compound 10a was obtained from 9 in 70% yield using *N*-chlorosuccinimide by the same method as described for the preparation of 10b.

¹H NMR (500 MHz, CDCl₃): δ 7.76 – 7.81 (m, 1H), 7.56 (s, 1H), 7.44 (s, 1H), 7.32 – 7.38(m, 1H), 7.27 – 7.31 (m, 2H), 4.29 (s, 2H), 3.84 (s, 3H), 2.26 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 153.29, 142.91, 142.80, 136.69, 130.02, 128.01, 123.51, 122.60, 122.46, 119.89, 119.59, 118.82, 109.59, 31.89, 18.09. HRMS (ESI-QTOF): m/z Calcd for C₁₅H₁₅ClN₃ [M + H]⁺: 272.0949; found: 272.0946.

2-Iodo-6-methyl-4-(1-methyl-1*H***-benzoimidazol-2-yl)aniline (10c).** *N*-iodosuccinimide (2.47 g, 11 mmol) was added to the solution of **9** (2.37 g, 10 mmol) in 10 ml of AcOH and stirred for 2 h at 25 °C, then the solvent was removed under reduced pressure. To the remaining oily matter, saturated sodium carbonate solution was added to adjust the PH to 9-10, and the mixture was extracted with 20 ml of CH₂Cl₂. The organic layer was washed with 20 ml of brine, and dried with Na₂SO₄. Removed the solvent by a rotary evaporator, and the resulting crude was purified by silica gel column chromatography, provided the title compound **10c** (3.24 g, 89%) as a light-yellow solid.

¹H NMR (500 MHz, CDCl₃): δ 7.94 (d, J = 2.0 Hz, 1H), 7.76 – 7.82(m, 1H), 7.46 – 7.48 (m, 1H), 7.31 – 7.38(m, 1H), 7.26 – 7.31 (m, 2H), 4.36 (s, 2H), 3.83 (s, 3H), 2.29 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 152.88, 146.44, 142.88, 137.71, 136.67, 131.65, 122.61, 122.47, 122.21, 121.24, 119.58, 109.59, 83.73, 31.89, 19.01. HRMS (ESI-QTOF): m/z Calcd for C₁₅H₁₅IN₃ [M + H]⁺: 364.0305; found: 364.0310.

N-(2-bromo-6-methyl-4-(1-methyl-1H-benzoimidazol-2-yl)phenyl)butyramide

monohydrochloride (11b). Butyryl chloride (3.7 g, 34.8 mmol) was added dropwise to the suspension of **10b** (10.0 g, 31.6 mmol) in 50 ml of acetonitrile under ice-bath. Then the mixture was heated to reflux for 3 h, produced a large amount of light-yellow solid. The precipitate was filtered, then to the filter cake, 15 ml of 5M aqueous sodium hydroxide solution was added, and the mixture was extracted with 60 ml of CH_2Cl_2 , then the organic layer was washed water. Removed the solvent under reduced pressure, and the residue was dissolved in 40 ml of methanol. Concentrated hydrochloric acid (2.8 ml, 33.2 mmol) was added, and the solvent was removed by a rotary evaporator. 50 ml of acetonitrile was added to the residue and stirred for 0.5 h, the precipitated solid was filtered and dried in vacuum at 50 °C, afforded **11b** (12.6 g, 94%) as an off-white solid.

¹H NMR (500 MHz, DMSO-*d*6): δ 10.05 (s, 1H), 8.16 (d, J = 1.9 Hz, 1H), 8.04 – 8.08 (m, 1H), 7.93 (d, J = 2.0 Hz, 1H), 7.86 – 7.90 (m, 1H), 7.60 – 7.68 (m, 2H), 4.07 (s, 3H), 2.39 (t, J = 7.2 Hz, 2H), 2.33 (s, 3H), 1.63 – 1.73 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H). ¹³C NMR (125 MHz, DMSO-*d*6): δ 171.01, 148.26, 139.80, 139.18, 133.40, 131.74, 131.28, 131.18, 126.40, 125.90, 123.46, 122.46, 114.56,

113.20, 37.27, 32.79, 18.96, 18.77, 13.81. HRMS (ESI-QTOF): m/z Calcd for C₁₉H₂₁BrN₃O [M + H]⁺: 386.0863; found: 386.0862.

N-(2-chloro-6-methyl-4-(1-methyl-1*H*-benzoimidazol-2-yl)phenyl)butyramide monohydrochloride (11a). The title compound 11a was obtained from 10a in 89% yield by the same

monohydrochloride (11a). The title compound 11a was obtained from 10a in 89% yield by the same method as described for the preparation of 11b.

¹H NMR (500 MHz, DMSO-*d*6): δ 10.08 (s, 1H), 8.05 – 8.09 (m, 1H), 8.02 (d, J = 2.0 Hz, 1H), 7.87 – 7.91 (m, 2H), 7.61 – 7.68 (m, 2H), 4.07 (s, 3H), 2.40 (t, J = 7.2 Hz, 2H), 2.33 (s, 3H), 1.62 – 1.72 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H). ¹³C NMR (125 MHz, DMSO-*d*6) δ 171.12, 148.40, 139.12, 138.26, 133.42, 132.50, 131.20, 130.72, 128.68, 126.41, 125.91, 122.02, 114.58, 113.21, 37.23, 32.80, 18.81, 18.73, 13.74. HRMS (ESI-QTOF): m/z Calcd for C₁₉H₂₁ClN₃O [M + H]⁺: 342.1368; found: 342.1368.

N-(2-iodo-6-methyl-4-(1-methyl-1*H*-benzoimidazol-2-yl)phenyl)butyramide monohydrochloride (11c). The title compound 11c was obtained from 10c in 93% yield by the same method as described for the preparation of 11b.

¹H NMR (500 MHz, DMSO-*d*6): δ 9.96 (s, 1H), 8.31 (d, J = 2.2 Hz, 1H), 8.01 – 8.09 (m, 1H), 7.91 (d, J = 2.0 Hz, 1H), 7.85 – 7.90 (m, 1H), 7.58 – 7.68 (m, 2H), 4.05 (s, 3H), 2.37 (t, J = 7.3 Hz, 2H), 2.32 (s, 3H), 1.64 – 1.75 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H). ¹³C NMR (125 MHz, DMSO-*d*6): δ 170.85, 148.23, 143.14, 138.13, 137.76, 133.44, 131.83, 131.33, 126.31, 125.83, 122.93, 114.61, 113.15, 101.94, 37.41, 32.75, 19.29, 18.71, 13.94. HRMS (ESI-QTOF): m/z Calcd for C₁₉H₂₁IN₃O [M + H]⁺: 434.0724; found: 434.0729.

N-(2-bromo-6-methyl-4-(1-methyl-1*H*-benzoimidazol-2-yl)phenyl)butyrimidamide (12b). To the suspension of 11b (8.0 g, 18.9 mmol) in 40 ml of dry acetonitrile was added DMF (138.9 mg, 1.9 mmol), and triphosgene (2.26 g, 7.6 mmol), purged the heterogeneous mixture with nitrogen, and the solution was heated to reflux for 30 min. Then the mixture was added dropwise to 27 ml of ammonia solution (7.0 M solution in MeOH) under ice bath. The solvent was concentrated, and 30 ml of 5M aqueous sodium hydroxide solution was used to adjust the PH to 10, then the mixture was extracted with 60 ml of CH_2Cl_2 . The organic layer was washed with brine, and dried with Na_2SO_4 . Removed the solvent under reduced pressure, and 30 ml of MTBE was added to the residue and stirred for 1 h, the precipitated solid was filtered and dried in vacuum at 50 °C, gave 12b (6.7 g, 92%) as an off-white solid.

¹H NMR (500 MHz, CDCl₃): δ 7.77 (d, J = 5.4 Hz, 2H), 7.54 (s, 1H), 7.34 – 7.40 (m, 1H), 7.26 – 7.34 (m, 2H), 4.51 (br, 2H), 3.86 (s, 3H), 2.38 (t, J = 7.6 Hz, 2H), 2.23 (s, 3H), 1.76 – 1.91 (m, 2H), 1.09 (t, J = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 158.20, 152.90, 148.16, 142.90, 136.63, 132.31, 131.44, 130.77, 125.68, 122.90, 122.60, 119.73, 116.64, 109.74, 37.86, 31.85, 20.77, 18.68, 14.10. HRMS (ESI-QTOF): m/z Calcd for C₁₉H₂₂BrN₄ [M + H]⁺: 385.1022; found: 385.1025.

N-(2-chloro-6-methyl-4-(1-methyl-1*H*-benzoimidazol-2-yl)phenyl)butyrimidamide (12a). The title compound 12a was obtained from 11a in 93% yield by the same method as described for the preparation of 12b.

¹H NMR (500 MHz, CDCl₃): δ 7.75 – 7.80 (m, 1H), 7.58 – 7. 62 (m, 1H), 7.48 – 7.52 (m, 1H), 7.34 – 7.39 (m, 1H), 7.27 – 7.33 (m, 2H), 4.54 (br, 2H), 3.85 (s, 3H), 2.38 (t, *J* = 7.6 Hz, 2H), 2.22 (s, 3H), 1.71 – 1.90 (m, 2H), 1.08 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 158.40, 153.05, 146.71, 142.88, 136.63, 132.56, 130.06, 128.31, 126.44, 125.22, 122.89, 122.60, 119.71, 109.74, 37.87, 31.84, 20.82, 18.39, 13.98. HRMS (ESI-QTOF): m/z Calcd for C₁₉H₂₂ClN₄ [M + H]⁺: 341.1528; found: 341.1519.

N-(2-iodo-6-methyl-4-(1-methyl-1*H*-benzoimidazol-2-yl)phenyl)butyrimidamide (12c). The title compound 12c was obtained from 11c in 95% yield by the same method as described for the preparation of 12b.

¹H NMR (500 MHz, CDCl₃): δ 8.04 (d, *J* = 1.9 Hz, 1H), 7.76 – 7.80 (m, 1H), 7.58 (d, *J* = 1.9 Hz, 1H), 7.36 – 7.40 (m, 1H), 7.28–7.34 (m, 2H), 4.40 (br, 2H), 3.87 (s, 3H), 2.39 (t, *J* = 7.6 Hz, 2H), 2.24 (s, 3H), 1.80 – 1.92 (m, 2H), 1.11 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 157.78, 152.76, 151.34, 143.03, 137.65, 136.70, 131.84, 130.84, 126.29, 122.86, 122.58, 119.82, 109.73, 92.58, 37.94, 31.87, 20.66, 19.12, 14.29. HRMS (ESI-QTOF): m/z Calcd for C₁₉H₂₂IN₄ [M + H]⁺: 433.0884; found: 433.0882.

(Z)-N'-(2-bromo-6-methyl-4-(1-methyl-1*H*-benzoimidazol-2-yl)phenyl)-N-((2'-cyano-[1,1'biphenyl]-4-yl)methyl)butyrimidamide (14). To the suspension of 11b (1.0 g, 2.4 mmol) in 15 ml of dry acetonitrile was added DMF (14.6 mg, 0.2 mmol), and triphosgene (284.9 mg, 0.96 mmol), purged the heterogeneous mixture with nitrogen, and the solution was heated to reflux for 30 min. To another flask were charged with 4'-(aminomethyl)-[1,1'-biphenyl]-2-carbonitrile 13 (1.5 g, 7.2 mmol), triethylamine (728.6 mg, 7.2 mmol), and CH_2Cl_2 (20 ml), and the former solution was added dropwise to the latter one under ice bath. The solvent was concentrated, then the residue was dissolved in 30 ml of CH_2Cl_2 , the organic phase was washed with 20 ml of saturated ammonium chloride solution, then 20 ml of 5M aqueous sodium hydroxide solution was used to adjust the PH to 10. The organic layer was washed with brine, and dried with Na₂SO₄. Removed the solvent under reduced pressure, then the residue was purified by silica gel column chromatography, afforded an off-white wax. Then 10 ml of MTBE was added, the precipitated solid was filtered and dried in vacuum, provided 14 (1.3 g, 94%) as an off-white solid.

¹H NMR (500 MHz, DMSO-*d*6): δ 7.94 (dd, J = 7.8, 1.3 Hz, 1H), 7.85 (d, J = 2.1 Hz, 1H), 7.78 (td, J = 7.7, 1.4 Hz, 1H), 7.59 – 7.69 (m, 4H), 7.54 – 7.58 (m, 6H), 7.19 – 7.29 (m, 2H), 4.60 (d, J = 6.2 Hz, 2H), 3.87 (s, 3H), 1.94 – 2.10 (m, 5H), 1.41 – 1.59 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H). ¹³C NMR (125 MHz, DMSO-*d*6): δ 158.55, 152.23, 150.03, 144.58, 142.46, 141.07, 136.64, 136.07, 133.91, 133.56, 131.40, 130.53, 130.11, 129.94, 128.50, 128.08, 127.65, 123.64, 122.17, 121.88, 118.77, 118.68, 116.60, 110.45, 110.19, 43.68, 33.67, 31.75, 19.78, 18.88, 14.00. HRMS (ESI-QTOF): m/z Calcd for C₃₃H₃₁BrN₅ [M + H]⁺: 576.1757; found: 576.1751.

1,7'-Dimethyl-2'-propyl-1H,3'H-2,5'-bibenzoimidazole (5). To a 100 ml flask were charged with **12b** (2.0 g, 5.2 mmol), CuI (95.2 mg, 0.5 mmol), Cs_2CO_3 (5.1 g, 15.6 mmol), and DMSO (30 ml), then purged the mixture with nitrogen. The solution was heated to 130 °C for 8 h. The insoluble substances were filtered away, and CH_2Cl_2 (100 ml), methanol (10 ml), and water (120 ml) were then added to the filtrate. The organic layer was washed with 100 ml of brine, then removed the solvent by a rotary evaporator, the resulting crude was purified by silica gel column chromatography, provided **5** (1.45 g, 92%) as a white solid.

¹H NMR (500 MHz, CDCl₃): δ 7.74 – 7.77 (m, 1H), 7.73 (s, 1H), 7.41 – 7.45 (m, 1H), 7.29 – 7.37 (m, 2H), 7.28 (s, 1H), 3.88 (s, 3H), 2.74 (t, *J* = 7.7 Hz, 2H), 2.51 (s, 3H), 1.67 – 1.76 (m, 2H), 0.82 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 157.41, 155.37, 142.20, 136.50, 123.45, 122.93, 122.81, 122.64, 118.85, 110.06, 31.98, 31.25, 21.93, 17.29, 13.90. HRMS (ESI-QTOF): m/z Calcd for C₁₉H₂₁N₄ [M + H]⁺: 305.1761; found: 305.1756..

4'-((1,7'-Dimethyl-2'-propyl-1*H***,3'***H***-[2**,**5'-bibenzoimidazol**]-**3'-yl)methyl)-[1,1'-biphenyl**]-**2carbonitrile (15).** To a 25 ml flask were charged with **14** (288.3 mg, 0.5 mmol), CuI (9.5 mg, 0.05 mmol), Cs₂CO₃ (488.7 mg, 1.5 mmol), and DMSO (6 ml), purged the mixture with nitrogen, then the solution was heated to 110 °C for 8 h. The insoluble substances were filtered away, then CH_2Cl_2 (20 ml), methanol (2 ml), and water (20 ml) were added to the filtrate. The organic layer was washed with 20 ml of brine, and dried with Na₂SO₄. Removed the solvent, and the residue was purified by silica gel column chromatography, afforded **15** (221.5 mg, 89%) as a white solid.

¹H NMR (500 MHz, DMSO-*d*6): δ 7.92 (dd, J = 7.8, 1.2 Hz, 1H), 7.77 (d, J = 1.5 Hz, 1H), 7.75 (td, J = 7.7, 1.4 Hz, 1H), 7.62 – 7.67 (m, 1H), 7.53 – 7.59 (m, 5H), 7.49 (t, J = 1.2 Hz, 1H), 7.28 (dd, J = 8.6, 1.9 Hz, 2H), 7.19 – 7.27 (m, 2H), 5.69 (s, 2H), 3.82 (s, 3H), 2.92 (t, J = 7.6 Hz, 2H), 2.64 (s, 3H), 1.76 – 1.87 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H). ¹³C NMR (125 MHz, DMSO-*d*6): δ 156.18, 154.01, 143.99, 142.67, 142.50, 137.79, 137.00, 136.65, 134.74, 133.81, 133.49, 130.05, 129.13, 128.28, 128.23, 126.85, 123.38, 123.27, 122.01, 121.76, 118.69, 118.45, 110.34, 110.13, 109.19, 45.94, 31.71, 28.71, 20.72, 16.46, 13.81. HRMS (ESI-QTOF): m/z Calcd for C₃₃H₃₀N₅ [M + H]⁺: 496.2496; found: 496.2504.

Telmisartan (1). Potassium hydroxide (112.2 mg, 2.0 mmol) was added to a mixture of **14** (198.3 mg, 0.4 mmol), ethylene glycol (4 ml) and water (0.2 ml). Stirred the reaction mixture and heated to 150 °C for 10 h, then cooled the solution to room temperature. 20 ml of water was added to the mixture, then acetic acid was utilized to adjust the pH to 4-5, the precipitate was filtered and dried, provided **1** (200 mg, 97%) as a white solid.

¹H NMR (500 MHz, CDCl₃): δ 8.37 (dt, J = 7.8, 1.1 Hz, 1H), 8.02 (dd, J = 7.6, 1.4 Hz, 1H), 7.50 (td, J = 7.4, 1.5 Hz, 1H), 7.44 (td, J = 7.5, 1.4 Hz, 1H), 7.39 (dd, J = 7.5, 1.4 Hz, 1H), 7.29 – 7.37 (m, 5H), 7.14 – 7.19 (m, 2H), 7.05 (s, 1H), 6.99 (s, 1H), 5.39 (s, 2H), 3.73 (s, 3H), 3.09 – 3.15 (m, 2H), 2.69 (s, 3H), 1.92 – 2.03 (m, 2H), 1.14 (t, J = 7.4 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 171.30, 156.62, 154.00, 143.42, 142.82, 141.79, 141.03, 135.62, 134.57, 134.02, 133.79, 130.55, 130.30, 129.45, 129.01, 128.94, 127.53, 127.20, 123.74, 123.31, 123.29, 121.91, 119.77, 111.37, 109.55, 48.83, 31.92, 30.06, 22.53, 17.11, 14.26. HRMS (ESI-QTOF): m/z Calcd for C₃₃H₃₁N₄O₂ [M + H]⁺: 515.2442; found: 515.2448.

III) Copies of NMR Spectra

1. ¹H NMR (500 MHz) and $^{13}C\{1H\}$ NMR (125 MHz) of Compound 8 in CDCl₃



2. ¹H NMR (500 MHz) and ¹³C{1H} NMR (125 MHz) of Compound **9** in DMSO ¹H NMR δ 3.07, 1.10 (solvent peak of MTBE)



3. ¹H NMR (500 MHz) and ¹³C{1H} NMR (125 MHz) of Compound 10a in CDCl₃







4. ¹H NMR (500 MHz) and $^{13}C\{1H\}$ NMR (125 MHz) of Compound 10b in CDCl₃

f1 (ppm)

5. ¹H NMR (500 MHz) and ¹³C {1H} NMR (125 MHz) of Compound 10c in CDCl₃





6. ¹H NMR (500 MHz) and ¹³C{1H} NMR (125 MHz) of Compound 11a in DMSO

7. ¹H NMR (500 MHz) and ¹³C{1H} NMR (125 MHz) of Compound **11b** in DMSO ¹H NMR δ 2.08 solvent peak (acetonitrile)













9. ¹H NMR (500 MHz) and ¹³C{1H} NMR (125 MHz) of Compound 12a in CDCl₃

10. ¹H NMR (500 MHz) and ¹³C{1H} NMR (125 MHz) of Compound **12b** in CDCl₃ ¹H NMR δ 2.12 solvent peak (H₂O) drift





11. ¹H NMR (500 MHz) and ¹³C {1H} NMR (125 MHz) of Compound 12c in CDCl₃







13. ¹H NMR (500 MHz) and $^{13}C\{1H\}$ NMR (125 MHz) of Compound 5 in CDCl₃



14. ¹H NMR (500 MHz) and $^{13}C{1H}$ NMR (125 MHz) of Compound 15 in DMSO



15. ¹H NMR (500 MHz) and ¹³C{1H} NMR (125 MHz) of Telmisartan (1) in CDCl₃