Supporting Information
Experimental

Highly Enantioselective Borane Reduction of Heteroaryl and Heterocyclic Ketoxime Ethers Catalyzed by Novel Spiroborate Ester derived from Diphenyl Valinol· Application to the Synthesis of Nicotine Analogues

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I. General Procedures

Air- and moisture sensitive reactions were carried out in dried glassware under N_2 atmosphere. Common solvents were dried and distilled by standard procedures. All reagents were obtained commercially unless otherwise noted. Chromatographic purification of products was accomplished using flash chromatography on a silica gel Si 60 Å (200-400 mesh).

GC-MS analysis was processed on a GC/ Mass detector using a Restek RTX- 5MS column. Chiral gas chromatography analysis was processed on a GC equipped with a CP-Chirasil-DexCB column (30 m × 0.25 mm ×0.25μm). Chiral HPLC analysis was processed with a Chiralcel-IB or OD-H column.

II Experimental procedures and characterizations

1. General Procedure for Oximes Synthesis: Method A: To a suspension of $NH_2OH{\cdot}HCl$ (20 mmol) in EtOH (50 mL) was added the corresponding ketone (10 mmol) in 10 mL ethanol. Then, a solution of Na_2CO_3 (10 mmol) in water (10 mL) was added dropwise. The resulting solution was heated at 60-65 ^{o}C overnight. Most of the ethanol was evaporated and then 60 mL water was added. The aqueous phase was extracted with ether (3×50 mL) and the combined organic phases were dried over Na_2SO_4. The solvents were removed under vacuum and the residue was recrystallized. **Method B:** A 100 mL round bottom flask was charged with magnetic stirrer, corresponding ketone (10 mmol), $NH_2OH{\cdot}HCl$ (30 mmol), pyridine (3 mL) and EtOH (40 mL). The mixture was stirred and monitored by TLC until the ketone was consumed (around 3 h). The solvents were evaporated under reduced pressure and the residue treated with 5% aqueous $NaHCO_3$ solution (40 mL). The aqueous phase was extracted with ether (3×50 mL) and the combined organic phases were dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the residue was recrystallized or purified by flash column chromatography.

2. Experimental Data of new and known oximes

(*E*)-1-(Thiophen-3yl)ethanone oxime[1](13a). Method A, Purified by recrystallization in hexane; yield 98% (20.6 g); mp 117-118 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H, CH_3), 7.3-7.5 (m, 3H, Het), 9.45 (br, 1H, OH) ppm; ^{13}CNMR (100 MHz, $CDCl_3$): δ 12.6, 123.9, 125.0, 126.3, 138.6, 152.3 ppm; IR ν (cm^{-1}) 2921, 1639, 1467, 1584, 1364; GC-MS *m/z* 141.0 (M^{+}).

(*E*)-1-(2,5-Dimethylthiophen-3-yl)ethanone oxime[2] (13b). Method B, Purified by recry-stallization in hexane; yield 75 % (1.9 g); mp 80-81 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.54 (s, 3H, CH_3), 6.7 (d, 1H, J = 0.8 Hz, Het), 9.01 (br, 1H, OH)

ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.7, 14.9, 15.1, 125.5, 133.4, 135.6, 135.7, 153.8 ppm; GC-MS *m/z* 169.0 (M^+)

(*E*)-Chroman-4-one oxime[3] (13c) (Method A). Purified by recrystallization in hexane; yield 91% (3.0 g); mp 132-133 ºC (lit.[3c] mp 139-141 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.05 (t, 2H *J* = 6.4 Hz, CH_2), 4.31 (t, *J* = 6.4 Hz, 2H, CH_2), 6.98 (m, 2H, Ar), 7.32 (m, 1H, Ar), 7.86 (m, 1H, Ar), 8.15 (s, 1H, OH) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 23.4, 65.0, 117.8, 118.3, 121.5, 124.1, 131.2, 150.0, 156.7 ppm; GC-MS *m/z* 163.1 (M^+).

(*E*)-6-Chlorochroman-4-one oxime[4] (13d) (Method A). Purified by recrystallization in hexane; yield 73% (2.2 g): mp 128 ºC, yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.02 (t, 2H, *J* = 6.4 Hz, CH_2), 4.28 (t, 2H, *J* = 6.4 Hz, CH_2), 6.91 (m, 1H, Ar), 7.26 (m, 1H, Ar), 7.80 (s, 1H, OH), 7.85 (m, 1H, Ar) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 65.1, 119.2, 119.5, 123.7, 126.7, 131.0, 149.1, 155.2 ppm; GC-MS *m/z* 197.1 (M^+).

(*E*)-Thiochroman-4-one oxime[3] (13e) (Method A). Purified by recrystallization in hexane; yield 78% (2.5 g): mp 89-91 ºC; ^{1}H NMR (400 Hz, $CDCl_3$) δ 3.03 (t, 2H, *J* = 6 Hz, CH_2), 3.23 (t, 2H, *J* = 6 Hz, CH_2), 7.2 (m, 1H, Ar), 7.3 (m, 2H, Ar), 7.96 (m, 1H, Ar), 8.27 (s,1H, OH) ppm ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 26.1, 125.5, 125.9, 128.4, 129.3, 129.6, 136.2, 153.6 ppm; GC-MS *m/z* 179.1 (M^+).

(*E*)-6-Chlorothiochroman-4-one oxime[5](13f) (Method B). Purified by crystallization using Hex/AcOEt (8:2); yield 74% (1.48 g); mp 78-80 ^{o}C; ^{1}HNMR (400 MHz, $CDCl_3$): δ 2.27(t, 2H, *J* = 6.0 Hz, CH_2), 2.83(t, 2H, *J* = 6.0 Hz, CH_2), 6.9 (m, 2H, Ar), 7.72 (s, 1H, Ar), 8.33 (s, 1H, Ar) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ 25.2, 25.3, 125.8, 128.9, 129.4, 131.0, 131.4, 135.0, 152.0 ppm; IR ν (cm^{-1}) 3738, 3166, 2939, 2369, 2182, 1900, 1546, 1458, 1391, 1294, 1238, 1090, 1052, 967; GC-MS *m/z* 213.1 (M^+), 196.1 (M^+-OH).

(*E*)-1-(Pyridine-2-yl)ethanone oxime (14) (Method B). Purified by recrystallization in hexane:AcOEt (1:1); yield 88 % (6.5 g): mp 108-109 ºC (lit.[6a] mp 124-125 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 3H, CH_3), 7.32 (m, 1H, Py), 7.7 (m, 1H, Py), 7.9 (m, 1H, Py), 8.7 (m, 1H, Py), 9.02 (br, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.7, 120.6, 123.7, 136.4, 149.0, 154.4, 157.1; GC-MS *m/z* 136.1 (M^+).

(*E*)-1-(Pyridine-3-yl)ethanone oxime (14a) (Method B). Purified by recrystallization in hexane:AcOEt (1:1); yield 70% (5.2 g): mp 117-118 ºC (lit. [6d] mp 118 ^{0}C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H, CH_3), 7.36 (m, 1H, Py), 8.0 (m, 1H, Py), 8.65 (m, 1H, Py), 9.00 (m, 1H, Py), 9.9 (br, 1H, OH); ^{13}CNMR (100 MHz, $CDCl_3$): δ 11.7, 123.4, 132.8, 133.6, 147.3, 149.6, 153.1; GC-MS *m/z* 136.2 (M^+).

(*E*)-1-(Pyridine-3-yl)propan-1-one oxime[7] (14b) (Method B). Purified by recrystallization in EtOH; yield 59 % (0.89 g): mp 107-108 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, 3H, *J* = 7.6, CH_3), 2.90 (q, 2H, *J* = 7.6, CH_2), 7.4 (m, 1H, Py), 8.0 (m, 1H, Py), 8.7 (m, 1H, Py), 8.97 (m, 1H, Py), 9.41 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): 10.8, 19.2, 123.4, 131.7, 133.7, 147.5, 149.7, 158.2; GC-MS *m/z* 150.1 (M^+).

(*E*)-1-(6-Methoxypyridin-3-yl)ethanone oxime (14c) (Method B). Purified by recrystallization in hexane:AcOEt (1:1); yield 84 % (0.69 g): mp 101-102 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27 (s, 3H, CH_3), 3.97 (s, 3H, CH_3), 6.76 (m, 1H, Py), 7.9 (m, 1H, Py), 8.40 (m, 1H, Py), 8.73 (s, 1H, OH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.7, 53.7, 110.9, 125.8, 136.2, 144.9, 153.5, 164.7 ppm; IR ν (cm^{-1}) 3198, 3059, 2915, 1607, 1568, 1501, 1360, 1294, 1254, 1175, 1128, 1085, 1021, 999, 920, 824, 731; GC-MS *m/z* 166.1 (M^+); Anal. Calcd for $C_8H_{10}N_2O_2$; C, 57.82; H, 6.07; N, 16.86; Found: C, 57.77; H, 6.01; N, 16.69.

(*E*)-Cyclopropyl(pyridine-3-yl)methanone oxime (14d) (Method B). Purified by column chromatography on silica gel/hex: AcOEt (1:2-1:1); yield 58 % (1.89 g): mp 126-127 ºC; ^{1}HNMR (400 MHz, $CDCl_3$): δ 0.71 (m, 2H, CH_2), 1.1 (m, 2H, CH_2), 2.3 (m, 1H, CH), 7.3 (m, 1H, Py), 7.8 (m, 1H, Py), 8.6 (m, 1H, Py), 8.7 (m, 1H, Py), 10.1 (s, 1H, OH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.6, 8.9, 123.0, 130.8, 135.8, 149.0, 149.4, 158.3 ppm; IR ν (cm^{-1}) 3135, 3020, 2842, 2754, 1624, 1593, 1574, 1480, 1463, 1412, 1352, 1309, 1191, 1104, 1029, 994, 939, 907, 882, 809, 711; GC-MS *m/z* 162.1 (M^+); Anal. Calcd for $C_9H_{10}N_2O$; C, 66.65; H, 6.21; N, 17.27; Found: C, 66.77; H, 6.21; N, 17.23.

(*E*)-Phenyl(pyridine-3-yl)methanone oxime[8] (14e) (Method B). Purified by recrystallization in EtOH; yield 62 % (1.22 g): mp 167-168 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.53 (m, 6H, Ph, Py), 7.84 (m, 1H, Py), 8.73 (d, 1H, *J* = 2.0 Hz, Py), 9.49 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 123.2, 127.7, 128.6, 129.0, 129.8, 135.7, 137.3, 149.7, 150.1, 155.0; GC-MS *m/z* 197.1 (M^+).

(*E*)-1-(Pyridine-4-yl)ethanone oxime[6b,c] (14f) (Method B). Purified by recrystallization in hexane:AcOEt (1:1); yield 82 % (6.1 g): mp 153-155 ºC (lit.[6c] mp 156-157 ^{0}C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (s, 3H, CH_3), 7.6 (m, 2H, Py), 8.6 (m, 2H, Py), 10.54 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.3, 120.4, 144.7, 149.7, 153.2; GC-MS m/z 136.1 (M^+).

(*E*)-1-(Pyridine-4-yl)propan-1-one oxime[9] (14g) (Method B). Purified by recrystallization in EtOH; yield 66 % (0.99 g): mp 144-145 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23 (t, 3H, *J* = 7.6, CH3), 2.9 (q, 2H, *J* = 7.6, CH_2), 7.6 (dd, 2H, J_1 = 2, J_2 = 6.4, Py), 8.7 (dd, 2H, J_1 =2, J_2 = 6.4,

Py), 9.17 (s, 1H, OH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.8, 18.7, 120.5, 143.4, 150.0, 158.5 ppm; GC-MS *m/z* 150.1 (M^+).

(*E*)-Cyclopropyl(pyridine-4-yl)methanone oxime (14h$_E$) (Method B). Purified by column chromatography on silica gel/hexane: AcOEt (1:1); yield 57% (1.81 g): mp 90-91 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.73 (m, 2H, CH_2), 1.1 (m, 2H, CH_2), 2.2 (m, 1H, CH), 7.45 (dd, 2H, *J* = 1.6, 6.4 Hz, Py), 8.7 (dd, 2H, *J* = 1.6, 6.4 Hz, Py), 9.38 (s, 1H, OH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.9, 8.5, 122.6, 143.0, 149.6, 158.7 ppm; IR ν (cm^{-1}) 3071, 2902, 2793, 1642, 1606, 1545, 1486, 1408, 1314, 1346, 1262, 1067, 1033, 1001, 950, 905, 816, 754; GC-MS *m/z* 162.1 (M^+); Anal. Calcd for $C_9H_{10}N_2O$; C, 66.65; H, 6.21; N, 17.27; Found: C, 66.69; H, 6.23; N, 17.30.

(*Z*)-Cyclopropyl(pyridine-4-yl)methanone oxime (14h$_Z$) (Method B). Yield 9.5% (0.325g): mp 87-88 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (m, 4H, $2CH_2$), 1.8 (m, 1H, CH), 7.4 (dd, 2H, *J* = 1.6, 6.4 Hz Py), 8.46 (br, 1H, OH), 8.7 (dd, 2H, *J* = 1.6, 6.4 Hz, Py) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.9, 14.9, 122.7, 141.5, 149.8, 157.2 ppm ; GC-MS *m/z* 162.2 (M^+).

(*E*)-1-(Pyridine-3-yl)-4-(triisopropylsilyloxy)-butan-1-one oxime (14i) (Method B). Purified by recrystallization in hexane; yield 74% (2.5 g): mp 68-69 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09-1.18 (m, 21H, TIPS), 1.9 (m, 2H, CH_2), 2.98 (m, 2H, CH_2), 3.83 (t, 2H, *J* = 6.0 Hz, OCH_2), 7.33-7.37 (m, 1H, Py), 8.0 (m, 1H, Py), 8.7 (m, 1H, Py), 8.75 (br, 1H, OH), 9.00 (s, 1H, Py) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 18.0, 22.4, 29.5, 62.8, 123.3, 131.8, 133.7, 147.7, 149.9, 157.4 ppm; IR ν (cm^{-1}) 3142, 3047, 1941, 2921, 1625, 1494, 1458, 1406, 1383, 1329, 1240, 1178, 1094, 1064, 1.039, 995, 974, 947, 881, 808, 725, 708; GC-MS *m/z* 336.3 (M^+); Anal. Calcd for $C_{18}H_{32}N_2O_2Si$; C, 64.24; H, 9.58; N, 8.32; Found: C, 64.09; H, 9.30; N, 8.26.

3. Experimental Data of Known Benzyloximes:

(*E*)-Chroman-4-one *O*-benzyl-oxime[10] (15c) Purified by column chromatography on silica gel/hex: AcOEt (9:1) as an colorless oil; yield 88% (2.1 g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.03 (t, *J* = 6.0 Hz, 2H, CH_2), 4.26 (t, *J* = 6.0 Hz, 2H, CH_2), 5.31 (s, 2H, CH_2), 7.02 (m, 2H, Ar), 7.31 (m, 1H, Ar), 7.37 (m, 1H, Ar), 7.40 (m, 2H, Ar), 7.46 (m, 1H, Ar), 7.50 (m, 1H, Ar), 8.01 (m,1H, Ar) ppm; ^{13}C NMR (100MHz, $CDCl_3$) δ 24.3, 65.0, 76.5, 117.7, 118.6, 121.4, 124.4, 127.9, 128.2 3, 128.4, 130.9, 137.9, 148.8, 156.7 ppm; GC/MS *m/z* 253.1 (M^+), 91.1 ($PhCH_2^+$).

(*E*)-1-(Pyridine-3-yl)ethanone *O*-benzyl oxime[11] (16a). Purified by column chromatography on silica gel/hex: AcOEt (2:1) as a colorless oil; yield 92% (6.21 g); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H, CH_3), 5.31 (s, 2H, OCH_2Ph), 7.30-7.49 (m, 6H, Ph, Py), 7.99 (m, 1H, Py),

8.63 (m, 1H, Py), 8.92 (m, 1H, Py) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.5, 76.5, 123.2, 127.9, 128.3, 128.4, 132.3, 133.3, 137.8, 147.5, 150.0, 152.5 ppm; GC-MS *m/z* 226.2 (M^+).

(*E*)-Phenyl(pyridine-3-yl)methanone *O*-benzyl oxime[12] (17). Purified by column chromatography on silica gel/hex: AcOEt (2:1) as a colorless oil; yield 87 % (0.625 g); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.30 (s, 2H, OCH_2Ph), 7.3-7.5 (m, 11H, Ph, Py), 7.73 (m, 1H, Py), 8.68 (d, 1H, *J* = 1.2, Py) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 76.7, 123.1, 127.8, 127.9, 128.2, 128.4, 128.5, 129.3, 129.7, 135.7, 136.9, 137.7, 149.8, 150.2, 154.3 ppm; GC-MS *m/z* 288.2 (M^+).

(*E*)-1-(Pyridine-4-yl)ethanone O-benzyl oxime[13] (18a). Purified by column chromatography on silicon gel/hex: AcOEt (2:1) as a white solid; yield 89% (5.75 g): mp 41-42 ºC ^{1}HNMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3H, CH_3), 5.32 (s, 2H, OCH_2Ph), 7.4-7.5 (m, 5H, Ph), 7.7 (m, 2H, Ar), 8.66 (m, 2H, Ar) ppm; ^{13}CNMR (100 MHz, $CDCl_3$): δ 12.1, 76.7, 120.2, 128.0, 128.3, 128.5, 137.6, 143.8, 150.1, 152.7 ppm; GC-MS *m/z* 226.2 (M^+).

(*E*)-1-(Pyridine-2-yl)ethanone *O*-benzyl oxime[13] (25). Purified by column chromatography on silica gel/hex: AcOEt (2:1) as a colorless oil; yield 89% (5.78 g); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 3H, CH_3), 5.33 (s, 2H, OCH_2Ph), 7.3-7.5 (m, 6H, Ar), 7.7 (m, 1H, Py), 7.9 (m, 1H, Py), 8.6 (m, 1H, Py) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.4, 76.4, 120.7, 123.5, 127.8, 128.1, 128.4, 136.1, 138.0, 148.8, 154.4, 156.2 ppm; GC-MS *m/z* 226.2 (M^+).

4. Experimental Data of Known Acetamides

(*S*)-*N*-(Chroman-4-yl)acetamide (20c). Purified by column chromatography on silica gel /hex: AcOEt (1:1) as a white solid; yield: 76 % (0.145 g), mp 186-187 ^{0}C (lit[14] mp 189 − 190 ^{o}C); 94% *ee*, $[\alpha]^{20}_D$ = -83.2(*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08 (s, 3H, CH_3), 2.3 (m, 2H, CH_2), 4.21 (m, 2H, CH_2), 5.18 (m, 2H, CH), 5.60 (s, 1H, NH), 6.87 (m, 1H, Ar), 6.96 (m, 1H, Ar), 7.23 (m, 1H, Ar) ppm; ^{13}C NMR (100MHz, $CDCl_3$) δ 23.5, 29.0, 43.7, 63.2, 117.2, 120.8, 121.9, 129.3, 129.4, 155.2, 169.4 ppm; GC/MS *m/z* 191.1 (M^+), 132.0 (M^+-NHAc).

(*S*)-*N*-(1-(Pyridine-2-yl) ethyl)acetamide[15] (27). Purified by column chromatography on silicon gel/CH_2Cl_2: CH_3OH (10:1) as a colorless oil; yield 75% (123 mg); 73% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$): 1.39 (t, 3H, *J* = 6.8 Hz, CH_3), 1.96 (s, 3H, CH_3), 5.1 (m, 1H, *J* = 6.8 Hz, CH), 6.85 (s, 1H, NH), 7.2 (m, 2H, Py), 7.6 (m, 1H, Py), 8.5 (m, 1H, Py) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.7, 23.5, 49.7, 121.8, 122.5, 137.2, 148.8, 161.0, 169.4 ppm; GC-MS *m/z* 164.2 (M^+).

(*S*)-*N*-(1-(Pyridine-3-yl) ethyl)acetamide[15] (22a). Purified by column chromatography on silicon gel/CH_2Cl_2: CH_3OH (10:1) as a colorless oil; yield 75% (61 mg); 98% *ee*; $[\alpha]^{20}_D$ = -28.3

(*c* 1.30, $CHCl_3$); ^{1}HNMR (400 MHz, $CDCl_3$): 1.38 (t, 3H, *J* = 7.2 Hz, CH_3), 1.88 (s, 3H, CH_3), 5.0 (m, 1H, *J* = 7.2 Hz, CH), 7.2 (m, 1H, Py), 7.6 (m, 1H, Py), 7.9 (m, 1H, Py), 8.4 (m, 1H, Py), 8.48 (s, 1H, NH); ^{13}CNMR (100 MHz, $CDCl_3$): δ 21.6, 22.8, 46.5, 123.3, 133.9, 139.5, 147.8, 147.9, 169.7; GC-MS *m/z* 164.1 (M^+).

(*S*)-*N*-(1-(Pyridine-4-yl) ethyl)acetamide[15] (24a). Purified by column chromatography on silicon gel/CH_2Cl_2: CH_3OH (10:1) as a colorless oil; yield 84% (69 mg); 99% *ee*; $[\alpha]^{20}_D$ = -74.0 (*c* 1.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (d, 3H, *J* = 7.2 Hz, CH_3), 1.92 (s, 3H, CH_3), 4.98 (m, 1H, *J* = 7.2 Hz, CH), 6.7 (s, 1H, NH), 7.15 (d, 2H, *J* = 6.0 Hz, Ar), 8.43 (d, 2H, *J* = 4.4 Hz, Ar) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 23.1, 47.9, 121.3, 149.8, 152.7, 169.7 ppm; GC-MS *m/z* 164.2 (M^+).

(*S*)-*N*-(phenyl(pyridine-3-yl)methyl)acetamine[16] (31). Purified by column chromatography on silicon gel/CH_2Cl_2: CH_3OH (10:1) as a colorless oil; yield 82% (151 mg); 95% *ee*; $[\alpha]^{20}_D$ = -3.0 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.90 (s, 2H, NH_2), 5.35 (s, 1H, CH), 7.3-7.4 (m, 6H, Ph, Py), 7.8 (m, 1H, Py), 8.53 (d, 1H, *J* = 4.4 Hz, Py), 8.70 (s, 1H, Py) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 57.7, 123.5, 126.8, 127.4, 128.8, 134.5, 140.8, 144.6, 148.5, 148.9 ppm.

References:

(1) Tomcufcik, A. S.; Meyer, W. E.; Marsico, J. W. Eur. Pat. Appl. 1991. 48 pp. CODEN: EPXXDW EP 446604.

(2) Goldfarb, Y. L.; Gorushkina, G. I.; Fedorov, B. P.; *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya* **1956**, 340.

(3) (a) Sebok, P.; Levai, A.; Timar, T.; *Heterocyclic Commun*. **1998**, *4*, 547. (b) Pratap, R.; Gupta, R. C.; Anand, N. *Indian J. Chem. Sect. B* **1981**, *20*, 1063-1067. (c) Clive, D. L. J.; Pham, M. P.; Subedi, R. *J. Am. Chem. Soc*. **2007;** *129*, 2713.

(4) Wright, G C.; Schwan, T. J.; Goldenberg, M. M.; White, Ronald. E. *J. Pharmaceutical Sciences* **1983**, *72*, 1361.

(5) Hoerlein, G.; Salbeck, G.; Emmel, L. Ger. Offen. **1973**, 23 pp, CODEN: GWXXBX DE 2214297 19731011.

(6) (a) Tagawa, Y. Chem. Pharmaceutical Bull. **1986**, *34*, 4984. (b)Lamattina, J. L.; Suleske, R. T. *Org. Syntheses*. **1986**, *64*, 19. (c) Biniecki, S. *Acta Poloniae Pharmaceutica* **1983**, *40*, 533. (d) Am Ende, David J.; Brown Ripin, D. H.; Weston, N. P. *Thermochim. Acta* **2004**, *419*, 83.

(7) Barlaam, B.; Pape, A.; Thomas, A. PCT Int. Appl. 2003, 78 pp. CODEN: PIXXD2 WO 2003048133.

(8) Niemers, E.; Hiltmann, R. *Synthesis* **1976**, *9*, 593.

(9) Stout, D. M.; Yamamoto, D. M. PCT Int. Appl. 1985, 16 pp. CODEN: PIXXD2 WO 8502402.

(10) Zagorevskii, V. A.; Dudykina, N. V.; Meshcheryakova, L. M. *Khimiya Geterotsiklicheskikh Soedinenni* **1970**, *3*, 302-308.

(11) Jung, M. H.; Park, J. G.; Oh, J. S.; Cheon, H. G. *Korean. J. Med. Chem*. **1998**, *8*, 38.

(12) Otsuka, K.; Ishiyama, N.; Watanabe, M.; Seri, K.; Sanai, K.; Muraoka, K. Eur. Pat. Appl. 1990, 19 pp. CODEN: EPXXDW EP 366006 A1 19900502.

(13) Abele, E.; Abele, R.; Propelis, J.; Lukevics, E. *Latvijas Kimijas Zurnals* **1998**, *2*, 61.

(14) (a) Kim, M.-J.; Kim,W.-H.; Han, K., Choi, Y. K.; Park, J. *Org. Lett.* **2007**, *9*, 1157. (b) Tang, W. J.; Chi, Y. X.; Zhang, X. M. *Org Lett*. **2002**, *4*, 1695.

(15) Gervinka, O.; Belovsky, O.; Rejmanova, P. *Collection of Czechoslovak Chem Commun*. **1973**, *38*, 1358.

(16) Hirata, Y.; Tamura, J.; Yanagisawa, I.; Takeda, M. Jan. Kokai tokkyo Koho. 1978, 10pp. CODEN: JKXXAF JP 0141271.