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Antimycobacterial *N*-pyridinylsalicylamides, isosters of salicylamides

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Abstract

The series of derivatives of substituted *N*-pyridinylsalicylamides were synthesized. The compounds were evaluated for in vitro antimycobacterial activity against *Mycobacterium avium* and two strains of *Mycobacterium kansasii*. In the quantitative structure activity relationships analysis (QSAR), the Free–Wilson and Hansch approaches were used but the analysis was not significant. (The standard deviations of regression coefficients were greater than the values of the coefficients). The molecules were separated the heterocyclic and salicyl moiety in the molecules, and the study of influences of substituents on salicyl moiety was used, as well. 5-Chloro-pyridin-2-yl, and the substitution of the salicyl moiety by chlorine in position 4 or 5 had the strongest influence on the increase in antimycobacterial activity.

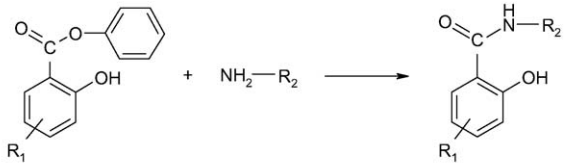
Keywords: *N*-pyridinylsalicylamide; Tuberculostatics; Antimycobacterial activity; Mycobacterium

1. Introduction

Search for new antimycobacterial compounds is one of the most challenging tasks of current medicinal chemistry. In particular, the study of antimycobacterial properties of salicylanilides [1,2] is of great interest, as salicylanilides can inhibit the bacterial two-component systems [3,4], which can also be important in mycobacteria. In our previous papers, we systematically studied isosters of salicylanilides, i.e. 3-hydroxypicolinanilides [5], 2-sulfanylbenzanilides [5] and *N*-benzylsalicylamides [6]. The goal of this paper was to study the antimycobacterial activity of *N*-pyridinylsalicylamides. In the 20th century, the development of antimycobacterial agents was directed towards antituberculotics and antileprotics. However, while the diseases caused by potentially pathogenic mycobacterial strains are rare in the human population, they usually end up in a fatal way. Our attention is thus concentrated on the potentially pathogenic mycobacterial strains as well [7].

2. Chemistry

The synthetic pathway leading to *N*-pyridinylsalicylanilides is depicted in Fig. 1. *N*-pyridinylsalicylanilides were prepared by the treatment of phenyl salicylates with substituted amino pyridines. The structural assignment is based on ^{1}H NMR, ^{13}C NMR and IR spectra. An overview of the compounds under study is in Fig. 2.



R_1	R_1	R_2	R_2	R_2
1 H	**5** 5-F	**a** 2-pyridyl	**e** 4-methyl-2-pyridyl	**i** 5-nitro-2-pyridyl
2 4-CH_3	**6** 5-Br	**b** 3-pyridyl	**f** 5-methyl-2-pyridyl	**j** 5-brom-2-pyridyl
3 4-OCH_3	**7** 5-Cl	**c** 4-pyridyl	**g** 6-methyl-2-pyridyl	
4 4-Cl		**d** 5-chlor-2-pyridyl	**h** 3-hydroxy-2-pyridyl	

Fig. 1. Synthesis of *N*-pyridinyl-2-hydroxy-benzamides (i.e. *N*-pyridinylsalicylanilides).

3. Results and discussion

For the purpose of an initial investigation of structure–activity relationships, we used the Free–Wilson and Hansch approaches. We separated the molecules on heterocyclic and

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salicyl moiety. We studied the influence of the substituents on the heterocyclic and salicyl moieties. 5-Chloro-pyridin-2-yl, and the substitution of the salicyl moiety by chlorine in position 4 or 5 have the strongest influence on the increase in antimycobacterial activity. The quantitative structure–antimycobacterial activity was not statistically significant. (The standard deviations of regression coefficients were greater than the values of the coefficients.)

N-Pyridinylsalicylamides constitute a new group of potential antituberculotics. Some compounds under study are more active than INH against potentially pathogenic strains (e.g. **4f, 5i, 6i, 7e, 7i, 7j**).

4. Experimental

4.1. Chemistry

The melting points (m.p.) were determined on a Kofler apparatus. The samples for analysis and antimycobacterial tests were dried over phosphorous pentoxide at 61 °C and at pressure 66 Pa for 24 h. Elemental analyses (C, H, N) were performed on a CHNS–O CE elemental analyzer (Fisons EA 1110, Milano) and were within ±0.4% of the theoretical values. The IR spectra were measured in KBr pellets on a Nicolet Impact 400 apparatus; the wave numbers are given in cm^{-1}. The bonding vibrations of the C=O group [*ν* (C=O)] were found in the region 1641–1691 cm^{-1}.

TLC was performed on silica gel plates precoated with a fluorescent indicator Silufol UV 254 + 366 (Kavalier, Votice Czech Republic), with petrolether/acetone (3:1) as the mobile phase. The ^{1}H NMR and ^{13}C NMR spectra of new compounds were recorded in DMSO-d_6 solution at ambient temperature on a Varian Mercury-Vx BB 300 spectrometer operating at 300 MHz. Chemical shifts were recorded as *δ* values in parts per millions (ppm) and were indirectly referenced to tetramethylsilane via the solvent signal (2.49 for ^{1}H or 39.7 for ^{13}C).

4.1.1. Synthesis of N*-pyridinylsalicylamides: general procedure*

A mixture of an amine (1 g) and phenyl salicylate (1.2 equivalents) was melted at 190–210 °C for 90 min under an air condenser. The reaction mixture was then heated at reflux with ethanol for 10 min, filtered off and the product was crystallized from the same solvent (yields 55–89%).

4.1.1.1. N*-(Pyridin-2-yl)-2-hydroxy-benzamide (***1a***).* White crystals. Yield 65%, m.p. 212–213 °C [8] 210–212°C. IR (KBr): *ν* (C=O) 1674 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.72 (bs, 1H, NH), 10.91 (bs, 1H, OH), 8.34 (ddd, 1H, *J* = 4.95 Hz, *J* = 1.92 Hz, *J* = 0.97 Hz, H6′), 8.26 (d, 1H, *J* = 7.97 Hz, H3′), 8.04 (dd, 1H, *J* = 8.11 Hz, *J* = 1.37 Hz, H6), 7.87–7.79 (m, 1H, H4′), 7.48–7.40 (m, 1H, H4), 7.14 (ddd, 1H, *J* = 7.97 Hz, *J* = 4.95 Hz, *J* = 0.97 Hz, H5′), 7.04 (dd, 1H, *J* = 8.11 Hz, *J* = 1.37 Hz, H3), 7.02–6.95 (m, 1H, H5). ^{13}C NMR (75 MHz): *δ* 164.3, 156.8, 151.8, 148.4, 138.6, 134.1, 131.0, 120.1, 120.0, 118.4, 117.3, 114.2.

4.1.1.2. N*-(Pyridin-3-yl)-2-hydroxy-benzamide (***1b***).* Pink crystals. Yield 67%, m.p. 227–228 °C [8] 224–228°C. IR (KBr): *ν* (C=O) 1667 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 10.53 (bs, 1H, OH), 8.86 (d, 1H, *J* = 2.33 Hz, H2′), 8.33 (dd, 1H, *J* = 4.67 Hz, *J* = 1.51 Hz, H6′), 8.15 (ddd, 1H, *J* = 8.24 Hz, *J* = 2.33 Hz, *J* = 1.51 Hz, H4′), 7.93 (dd, 1H, *J* = 7.97 Hz, *J* = 1.65 Hz, H6), 7.48–7.36 (m, 2H, H4, H5′), 7.03–6.92 (m, 2H, H3, H5). ^{13}C NMR (75 MHz): *δ* 167.1, 158.5, 145.2, 142.6, 135.2, 134.1, 129.5, 128.2, 123.9, 119.4, 117.8, 117.5.

4.1.1.3. N*-(Pyridin-4-yl)-2-hydroxy-benzamide (***1c***).* Yellow crystals. Yield 72%, m.p. 234–236 °C, IR (KBr): *ν* (C=O) 1676 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 10.65 (bs, 1H, NH), 8.52–8.42 (m, H2′, H6′), 7.86 (dd, 1H, *J* = 7.70 Hz, *J* = 1.65 Hz, H6), 7.75–7.70 (m, 2H, H3′, H5′), 7.47–7.39 (m, 1H, H4), 7.03–6.92 (m, 2H, H3, H5). ^{13}C NMR (75 MHz): *δ* 167.0, 157.8, 150.6, 145.5, 134.0, 129.9, 119.4, 118.8, 117.3, 114.4.

4.1.1.4. N*-(5-Chloro-pyridin-2-yl)-2-hydroxy-benzamide (***1d***).* Yellow crystals. Yield 61%, m.p. 209–211 °C [8] 209–211°C. IR (KBr): *ν* (C=O) 1656 cm^{-1}. ^{1}H NMR (300 MHz,): *δ* 11.74 (bs, 1H, NH), 11.00 (bs, 1H, OH), 8.38 (d, 1H, *J* = 2.61 Hz, H6′), 8.29 (d, 1H, *J* = 8.93 Hz, H3′), 8.01 (dd, 1H, *J* = 7.97 Hz, *J* = 1.92 Hz, H6), 7.95 (dd, 1H, *J* = 8.93 Hz, *J* = 2.61 Hz, H4′), 7.49–7.41 (m, 1H, H4), 7.06–6.95 (m, 2H, H3, H5). ^{13}C NMR (75 MHz, DMSO): *δ* 164.3, 156.8, 150.4, 146.8, 138.4, 134.3, 131.0, 125.7, 120.1, 118.2, 117.3, 115.2.

4.1.1.5. N*-(4-Methyl-pyridin-2-yl)-2-hydroxy-benzamide (***1e***).* White crystals. Yield 58%, m.p. 202–204 °C, IR (KBr): *ν* (C=O) 1684 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.71 (bs, 1H, NH), 10.85 (bs, 1H, OH), 8.18 (d, 1H, *J* = 5.22 Hz, H6′), 8.12 (s, 1H, H3′), 8.03 (dd, 1H, *J* = 8.10 Hz, *J* = 1.38 Hz, H6), 7.49–7.39 (m, 1H, H4), 7.04 (dd, 1H, *J* = 8.10 Hz, *J* = 1.38 Hz, H3), 7.01–6.95 (m, 2H, H5, H5′), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 164.2, 156.8, 151.9, 149.4, 148.0, 134.1, 130.9, 121.0, 120.0, 118.4, 117.3, 114.7, 21.2.

4.1.1.6. N*-(5-Methyl-pyridin-2yl)-2-hydroxy-benzamide (***1f***).* White crystals. Yield 55%, m.p. 218–220 °C, IR (KBr): *ν* (C=O) 1670 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.72 (bs, 1H, NH), 10.84 (bs, 1H, OH), 8.18–8.13 (m, 2H, H3′, H6′), 8.04 (dd, 1H, *J* = 8.10 Hz, *J* = 1.38 Hz, H6), 7.64 (ddd, 1H, *J* = 8.52 Hz, *J* = 2.47 Hz, *J* = 0.55 Hz, H4′), 7.47–7.39 (m, 1H, H4), 7.03 (dd, 1H, *J* = 8.10 Hz, *J* = 1.37 Hz, H3), 7.01–6.94 (m, 1H, H5), 2.25 (s, 3H, CH_3).

4.1.1.7. N*-(6-Methyl-pyridin-2yl)-2-hydroxy-benzamide (***1g***).* White crystals. Yield 66%, m.p. 188–190 °C, IR (KBr): *ν* (C=O) 1679 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.68 (bs, 1H,

NH), 10.82 (bs, 1H, OH), 8.08–8.01 (m, 3H, Ar), 7.71 (t, 1H, *J* = 7.97 Hz, Ar), 7.47–7.40 (m, 1H, Ar), 7.06–6.95 (m, 3H, Ar), 2.41 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 164.3, 157.0, 156.8, 151.1, 138.9, 134.1, 131.0, 120.0, 119.3, 118.4, 117.3, 111.2, 23.9.

4.1.1.8. N-*(3-Hydroxy-pyridin-2-yl)-2-hydroxy-benzamide (***1h***).* Brown crystals. Yield 71%, m.p. 256–259 °C, IR (KBr): *v* (C=O) 1670 cm^{-1}. ^{1}H NMR (300 MHz): δ 12.02 (bs, 1H, NH), 8.05–7.98 (m, 2H, H4′, H6′), 7.93 (dd, 1H, *J* = 8.24 Hz, *J* = 1.10 Hz, H6), 7.57–7.50 (m, 1H, H4), 7.46 (dd, 1H, *J* = 7.96 Hz, *J* = 6.04 Hz, H5′), 7.21 (dd, 1H, *J* = 8.24 Hz, *J* = 1.10 Hz, H3), 7.04 (dt, 1H, *J* = 8.24 Hz, *J* = 1.10 Hz, H5). ^{13}C NMR (75 MHz): δ 165.6, 157.5, 144.9, 139.1, 135.9, 131.1, 128.1, 127.4, 120.8, 120.5, 117.7, 116.4.

4.1.1.9. N-*(5-Nitro-pyridin-2-yl)-2-hydroxy-benzamide (***1i***).* White crystals. Yield 89%, m.p. 281–282 °C, IR (KBr): *v* (C=O) 1667 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.38 (bs, 1H, NH), 9.14 (dd,1H, *J* = 2.75 Hz, *J* = 0.52, H6′), 8.61 (dd, 1H, *J* = 9.34 Hz, *J* = 2.74 Hz, H4′), 8.44 (dd, 1H, *J* = 9.34 Hz, *J* = 0.53 Hz, H3′), 7.98 (dd, 1H, *J* = 8.10 Hz, *J* = 1.38 Hz, H6), 7.50–7.42 (m, 1H, H4), 7.04 (dd, *J* = 8.11 Hz, *J* = 1.37 Hz, H3), 7.02–6.95 (m, 1H, H5). ^{13}C NMR (75 MHz): δ 164.5, 156.8, 155.8, 145.1, 140.3, 134.8, 134.7, 131.3, 120.2, 118.0, 117.4, 113.2.

4.1.1.10. N-*(5-Bromo-pyridin-2-yl)-2-hydroxy-benzamide (***1j***).* Beige crystals. Yield 59%, m.p. 211–213 °C, IR (KBr): *v* (C=O) 1658 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.75 (bs, 1H, NH), 11.01 (bs, 1H, OH), 8.46 (dd, 1H, *J* = 2.48 Hz, *J* = 0.69 Hz, H6′), 8.25 (dd, 1H, *J* = 9.07 Hz, *J* = 0.69 Hz, H3′), 8.07 (dd, 1H, *J* = 9.07 Hz, *J* = 2.48 Hz, H4′), 8.01 (dd, 1H, *J* = 8.10 Hz, *J* = 1.38 Hz, H6), 7.49–7.41 (m, 1H, H4), 7.04 (dd, 1H, *J* = 8.11 Hz, *J* = 1.37 Hz, H3), 7.02–6.95 (m, 1H, H5). ^{13}C NMR (75 MHz): δ 164.3, 156.8, 150.7, 149.0, 141.1, 134.3, 131.0, 120.0, 118.2, 117.3, 115.8, 114.1.

4.1.1.11. N-*(Pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2a***).* Beige crystals. Yield 65%, m.p. 175–177 °C, IR (KBr): *v* (C=O) 1673 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.66 (bs, 1H, NH), 10.86 (bs, 1H, OH), 8.33 (ddd, 1H, *J* = 4.81 Hz, *J* = 1.93 Hz, *J* = 0.96 Hz, H6′), 8.27–8.22 (m, 1H, H3′), 7.93 (d, 1H, *J* = 7.97 Hz, H6), 7.86–7.79 (m, 1H, H4′), 7.14 (ddd, 1H, *J* = 7.41 Hz, *J* = 4.81 Hz, *J* = 0.96 Hz, H5′), 6.85–6.78 (m, 2H, H3, H5), 2.29 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO): δ 164.4, 156.9, 151.9, 148.4, 144.7, 138.6, 130.9, 121.1, 120.0, 117.5, 115.6, 114.2, 21.3.

4.1.1.12. N-*(Pyridin-3-yl)-2-hydroxy-4-methyl-benzamide (***2b***).* Beige crystals. Yield 59%, m.p. 194–177 °C, IR (KBr): *v* (C=O) 1664 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.77 (bs, 1H, NH), 10.45 (bs, 1H, OH), 8.85 (s, 1H, H2′), 8.38–8.28 (m, 1H, H6′), 8.16–8.11 (m, 1H, H4′), 8.87 (d, 1H, *J* = 8.52 Hz, H6), 7.40 (dd, 1H, *J* = 8.24 Hz, *J* = 4.67 Hz, H5′), 6.82–6.77 (m, 2H, H3, H5), 2.30 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 167.4, 159.0, 145.2, 144.9, 142.7, 135.1, 129.2, 128.3, 123.8, 120.4, 117.7, 114.3, 21.3.

4.1.1.13. N-*(Pyridin-4-yl)-2-hydroxy-4-methyl-benzamide (***2c***).* Beige crystals. Yield 61%, m.p. 264–266 °C, IR (KBr): *v* (C=O) 1677 cm^{-1}. ^{1}H NMR (300 MHz): δ 10.58 (bs, 1H, OH), 8.49–8.44 (m, 2H, H2′, H6′), 7.83 (d, 1H, *J* = 7.69 Hz, H6), 7.74–7.70 (m, 2H, H3′, H5′), 6.83–6.76 (m, 2H, H3, H5), 2.29 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 167.3, 158.4, 150.5, 145.5, 144.9, 129.7, 120.5, 117.6, 115.1, 114.5, 21.3.

4.1.1.14. N-*(5-Chloro-pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2d***).* Beige crystals. Yield 60%, m.p. 158–160 °C, IR (KBr): *v* (C=O) 1677 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.71 (bs, 1H, NH), 10.98 (bs, 1H, OH), 8.39–8.37 (m, 1H, H6′), 8.30–8.26 (m, 1H, H3′), 7.94 (dd overlapped, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H4′), 7.91 (d overlapped, 1H, *J* = 7.97 Hz, H6), 6.85–6.77 (m, 2H, H3, H5), 2.29 (s, 3H, CH_3).

4.1.1.15. N-*(4-Methyl-pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2e***).* Beige crystals. Yield 78%, m.p. 206–207 °C, IR (KBr): *v* (C=O) 1682 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.64 (bs, 1H, NH), 10.79 (bs, 1H, OH), 8.17 (d, 1H, *J* = 5.22 Hz, H6′), 8.10 (s, 1H, H3′), 7.92 (d, 1H, *J* = 7.97 Hz, H6), 6.99–6.95 (m, 1H, H5′), 6.84–6.77 (m, 2H, H3, H5). ^{13}C NMR (75 MHz): δ 164.4, 156.9, 151.9, 149.3, 148.0, 144.6, 130.8, 121.0, 120.9, 117.5, 115.6, 114.7, 21.3, 21.2.

4.1.1.16. N-*(5-Methyl-pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2f***).* Beige crystals. Yield 79%, m.p. 235–237 °C, IR (KBr): *v* (C=O) 1675 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.67 (bs, 1H, NH), 10.79 (bs, 1H, OH), 8.17–8.15 (m, 1H, H6′), 8.13 (d, 1H, *J* = 8.52 Hz, H3′), 7.93 (d, 1H, *J* = 7.96 Hz, H6), 7.67–7.61 (m, 1H, H4′), 6.84–6.76 (m, 2H, H3, H5), 2.28 (s, 3H, CH_3), 2.25 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 164.4, 157.0, 149.7, 148.1, 144.5, 138.9, 130.7, 128.9, 121.0, 117.5, 115.5, 113.8, 21.3, 17.5.

4.1.1.17. N-*(6-Methyl-pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2g***).* Beige crystals. Yield 68%, m.p. 205–207 °C, IR (KBr): *v* (C=O) 1671 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.63 (bs, 1H, NH), 10.77 (bs, 1H, OH), 8.04 (d, 1H, *J* = 7.87 Hz, H3′), 7.93 (d, 1H, *J* = 7.96 Hz, H6), 7.70 (t, 1H, *J* = 7.87 Hz, H4′), 6.99 (d, 1H, *J* = 7.87 Hz, H5′), 6.84–6.77 (m, 2H, H3, H5), 2.40 (s, 3H, CH_3), 2.29 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 164.4, 157.0, 156.9, 151.2, 144.6, 138.8, 130.8, 121.0, 119.2, 117.5, 115.6, 111.2, 23.9, 21.3.

4.1.1.18. N-*(3-Hydroxy-pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2h***).* Beige crystals. Yield 60%, m.p. 268–270 °C, IR (KBr): *v* (C=O) 1642 cm^{-1}. ^{1}H NMR (300 MHz): δ 7.95–7.88 (m, 2H, H6, H6′), 7.32 (dd, 1H, *J* = 8.11 Hz, *J* = 1.65 Hz, H4′), 7.15 (dd, 1H, *J* = 8.11 Hz, *J* = 4.67 Hz, H5′), 6.84–6.76 (m, 2H, H3, H5), 2.29 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 166.7, 158.6, 146.1, 145.2, 140.4, 138.2, 130.3, 125.1, 122.5, 120.7, 117.6, 114.1, 21.4.

4.1.1.19. N-*(5-Nitro-pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2i***).* Beige crystals. Yield 69%, m.p. 301–304 °C, IR (KBr): *ν* (C=O) 1669 cm^{-1}. ^1H NMR (300 MHz) *δ* 11.32 (bs, 1H, NH), 9.14–9.12 (m, 1H, H6′), 8.60 (dd, 1H, *J* = 9.34 Hz, *J* = 2.74 Hz, H4′), 8.46–8.41 (m, 1H, H3′), 7.88 (d, 1H, *J* = 7.97 Hz, H6), 6.84–6.78 (m, 2H, H3, H5), 2.28 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 164.4, 156.8, 155.9, 145.4, 145.1, 140.2, 134.6, 131.2, 121.3, 117.5, 115.2, 113.1, 21.3.

4.1.1.20. N-*(5-Bromo-pyridin-2-yl)-2-hydroxy-4-methyl-benzamide (***2j***).* Beige crystals. Yield 61%, m.p. 263–265 °C, IR (KBr): *ν* (C=O) 1671 cm^{-1}. ^1H NMR (300 MHz): *δ* 11.69 (bs, 1H, NH), 10.94 (bs, 1H, OH), 8.45–8.43 (m, 1H, H6′), 8.23 (dd, 1H, *J* = 8.79 Hz, *J* = 0.82 Hz, H3′), 8.04 (dd, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H4′), 7.91 (d, 1H, *J* = 7.97 Hz, H6), 6.85–6.77 (m, 2H, H3, H5), 2.28 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 164.4, 156.8, 150.8, 148.9, 144.9, 141.0, 130.9, 121.1, 117.5, 115.8, 115.4, 114.0, 21.3.

4.1.1.21. N-*(Pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3a***).* White crystals. Yield 67%, m.p. 188–190 °C, IR (KBr): *ν* (C=O) 1681 cm^{-1}. ^1H NMR (300 MHz): *δ* 11.94 (bs, 1H, NH), 10.76 (bs, 1H, OH), 8.36–8.31 (m, 1H, H6′), 8.22 (d, 1H, *J* = 8.52 Hz, H3′), 8.01 (d, 1H, *J* = 8.79 Hz, H6), 7.86–7.77 (m, 1H, H4′), 7.17–7.09 (m, 1H, H5′), 6.62–6.52 (m, 2H, H3, H5), 3.78 (s, 3H, OCH_3). ^{13}C NMR (75 MHz): *δ* 164.6, 163.9, 159.1, 151.9, 148.4, 138.5, 132.3, 119.9, 114.3, 110.9, 106.9, 101.6, 55.6.

4.1.1.22. N-*(5-Chloro-pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3d***).* Beige crystals. Yield 55%, m.p. 225–228 °C, IR (KBr): *ν* (C=O) 1647 cm^{-1}. ^1H NMR (300 MHz) *δ* 11.97 (bs, 1H, NH), 10.87 (bs, 1H, OH), 8.38–8.36 (m, 1H, H6′), 8.28–8.24 (m, 1H, H3′), 7.98 (d, 1H, *J* = 8.93 Hz, H6), 7.93 (dd, 1H, *J* = 9.06 Hz, *J* = 2.75 Hz, H4′), 6.58 (dd, 1H, *J* = 8.93 Hz, *J* = 2.34 Hz, H5), 6.53 (d, 1H, *J* = 2.34 Hz, H3), 3.78 (s, 3H, OCH_3). ^{13}C NMR (75 MHz): *δ* 164.5, 164.0, 159.0, 150.6, 146.7, 138.3, 132.4, 125.5, 115.3, 110.7, 107.0, 101.6, 55.6.

4.1.1.23. N-*(4-Methyl-pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3e***).* White crystals. Yield 64%, m.p. 222–224 °C, IR (KBr): *ν* (C=O) 1680 cm^{-1}. ^1H NMR (300 MHz): *δ* 11.92 (bs, 1H, NH), 10.69 (bs, 1H, OH), 8.17 (d, 1H, *J* = 5.22 Hz, H6′), 8.07 (bs, 1H, H3′), 8.00 (d, 1H, *J* = 8.79 Hz, H6), 6.98–6.94 (m, 1H, H5′), 6.57 (dd, 1H, *J* = 8.79 Hz, *J* = 2.48 Hz, H5), 6.53 (d, 1H, *J* = 2.47 Hz, H3), 3.78 (s, 3H, OCH_3), 2.33 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 164.6, 163.9, 159.1, 152.00, 149.3, 147.9, 132.3, 120.9, 114.8, 110.9, 106.9, 101.6, 55.6, 21.2.

4.1.1.24. N-*(5-Methyl-pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3f***).* Beige crystals. Yield 72%, m.p. 203–204 °C, IR (KBr): *ν* (C=O) 1678 cm^{-1}. ^1H NMR (300 MHz): *δ* 11.95 (bs, 1H, NH), 10.67 (bs, 1H, OH), 8.17–8.14 (m, 1H, H6′), 810 (d, 1H, *J* = 8.51 Hz, H3′), 8.01 (d, 1H, *J* = 8.79 Hz, H6), 7.62 (ddd, 1H, *J* = 8.52 Hz, *J* = 2.47 Hz, *J* = 0.54 Hz, H4′), 6.56 (dd, 1H, *J* = 8.79 Hz, *J* = 2.33 Hz, H5), 6.52 (d, 1H, *J* = 2.33 Hz, H3), 3.78 (s, 3H, OCH_3), 2.24 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 164.7, 163.8, 159.2, 149.7, 148.1, 138.8, 132.2, 128.8, 114.0, 110.8, 106.8, 101.6, 55.6, 17.5.

4.1.1.25. N-*(6-Methyl-pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3g***).* Beige crystals. Yield 59%, m.p. 145–148 °C, IR (KBr): *ν* (C=O) 1671 cm^{-1}. ^1H NMR (300 MHz): *δ* 11.92 (bs, 1H, NH), 10.67 (bs, 1H, OH), 8.02 (d, 1H, *J* = 7.78 Hz, H3′), 8.00 (d, 1H, *J* = 8.79 Hz, H6), 7.69 (t, 1H, *J* = 7.78 Hz, H4′), 6.99 (d, 1H, *J* = 7.78 Hz, H5′), 6.57 (dd, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H5), 6.52 (d, 1H, *J* = 2.47 Hz, H3), 3.78 (s, 3H, OCH_3), 2.41 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 164.6, 163.8, 159.1, 156.9, 151.2, 138.8, 132.3, 119.1, 111.3, 110.9, 106.9, 101.5, 55.6, 23.9.

4.1.1.26. N-*(3-Hydroxy-pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3h***).* Brown crystals. Yield 74%, m.p. 248–251 °C, IR (KBr): *ν* (C=O) 1684 cm^{-1}. ^1H NMR (300 MHz) *δ* 10.85 (bs, 1H, NH), 7.98 (d, 1H, *J* = 8.79 Hz, H6), 7.90 (dd, 1H, *J* = 4.67 Hz, *J* = 1.65 Hz, H6′), 7.32 (dd, 1H, *J* = 7.97 Hz, *J* = 1.65 Hz, H4′), 7.16 (dd, 1H, *J* = 7.97 Hz, *J* = 4.67 Hz, H5′), 6.56 (dd, 1H, *J* = 8.79 Hz, *J* = 2.48 Hz, H5), 6.51 (d, 1H, *J* = 2.47 Hz, H3), 3.79 (s, 3H, OCH_3). ^{13}C NMR (75 MHz): *δ* 166.9, 164.3, 160.9, 146.2, 140.4, 138.2, 131.7 125.2, 122.5, 109.3, 106.8, 101.5, 55.6.

4.1.1.27. N-*(5-Nitro-pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3i***).* Beige crystals. Yield 60%, m.p. 251–252 °C, IR (KBr): *ν* (C=O) 1656 cm^{-1}. ^1H NMR (300 MHz): *δ* 11.97 (bs, 1H, NH), 11.20 (bs, 1H, OH), 9.12–9.10 (m, 1H, H6′), 8.58 (dd, 1H, *J* = 9.34 Hz, *J* = 2.75 Hz, H4′), 8.41 (d, 1H, *J* = 9.34 Hz, H3′), 7.94 (d, 1H, *J* = 8.79 Hz, H6), 6.58 (dd, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H5), 6.51 (d, 1H, *J* = 2.47 Hz, H3), 3.78 (s, 3H, OCH_3). ^{13}C NMR (75 MHz): *δ* 164.4, 164.3, 158.8, 156.0, 145.0, 140.9, 134.5, 132.8, 113.1, 110.6, 107.3, 101.5, 55.7.

4.1.1.28. N-*(5-Bromo-pyridin-2-yl)-2-hydroxy-4-methoxy-benzamide (***3j***).* Beige crystals. Yield 62%, m.p. 216–218 °C, IR (KBr): *ν* (C=O) 1654 cm^{-1}. ^1H NMR (300 MHz): *δ* 11.93 (bs, 1H, NH), 10.83 (bs, 1H, OH), 8.45–8.43 (m, 1H, H6′), 8.21 (d, 1H, *J* = 8.93 Hz, H3′), 8.04 (dd, 1H, *J* = 8.93 Hz, *J* = 2.47 Hz, H4′), 7.98 (d, 1H, *J* = 8.79 Hz, H6), 6.58 (dd, 1H, *J* = 8.79 Hz, *J* = 2.48 Hz, H5), 6.53 (d, 1H, *J* = 2.47 Hz, H3), 3.78 (s, 3H, OCH_3). ^{13}C NMR (75 MHz): *δ* 164.5, 164.0, 159.0, 150.9, 148.9, 141.0, 132.4, 115.8, 113.9, 110.7, 107.0, 101.6, 55.6.

4.1.1.29. N-*(Pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4a***).* White crystals. Yield 67%, m.p. 222–223 °C, IR (KBr): *ν* (C=O) 1686 cm^{-1}. ^1H NMR (300 MHz): *δ* 12.18 (bs, 1H, OH), 10.79 (bs, 1H, NH), 8.34 (ddd, 1H, *J* = 4.95 Hz, *J* = 1.93 Hz, *J* = 0.82 Hz, H6′), 8.25–8.21 (m, 1H, H4′), 8.01

(d, 1H, *J* = 8.52 Hz, H6), 7.87–7.79 (m, 1H, H5′), 7.14 (ddd, 1H, *J* = 7.42 Hz, *J* = 4.94 Hz, *J* = 0.83 Hz, H3′), 7.06 (d, 1H, *J* = 1.93 Hz, H3), 7.03 (dd, 1H, *J* = 8.51 Hz, *J* = 1.93 Hz, H5). ^{13}C NMR (75 MHz): *δ* 163.5, 157.5, 151.6, 148.4, 138.7, 137.9, 132.6, 120.2, 120.1, 117.8, 116.9, 114.3.

4.1.1.30. N-*(Pyridin-3-yl)-4-chloro-2-hydroxy-benzamide (***4b***).* Beige crystals. Yield 60%, m.p. 237–238 °C, IR (KBr): *ν* (C=O) 1665 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 10.50 (bs, 1H, OH), 8.85 (d, 1H, *J* = 2.34 Hz, H2′), 8.33 (dd, 1H, *J* = 4.62 Hz, *J* = 1.10 Hz, H6′), 8.14 (ddd, *J* = 8.24 Hz, *J* = 2.34 Hz, *J* = 1.10 Hz, H4′), 7.94–7.88 (m, 1H, H6), 7.40 (ddd, 1H, *J* = 8.24 Hz, *J* = 4.62 Hz, *J* = 1.10 Hz, H5′), 7.07–7.01 (m, 2H, H3, H5). ^{13}C NMR (75 MHz): *δ* 165.9, 158.9, 145.2, 142.5, 137.7, 135.1, 131.2, 128.0, 123.8, 119.5, 117.5, 117.0.

4.1.1.31. N-*(Pyridin-4-yl)-4-chloro-2-hydroxy-benzamide (***4c***).* Yellow crystals. Yield 63%, m.p. 268–270 °C, IR (KBr): *ν* (C=O) 1679 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 10.92 (bs, 1H, OH), 8.50–8.46 (m, 2H, H2′, H6′), 7.83 (d, 1H, *J* = 8.51 Hz, H6), 7.75–7.70 (m, 2H, H3′, H5′), 7.04–7.01 (m, 1H, H3), 7.01–6.96 (m, 1H, H5). ^{13}C NMR (75 MHz): *δ* 166.0, 158.9, 150.1, 145.9, 137.7, 131.6, 119.3, 118.5, 117.1, 114.4.

4.1.1.32. N-*(5-Chloro-pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4d***).* Brown crystals. Yield 61%, m.p. 263–265 °C, IR (KBr): *ν* (C=O) 1683 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.19 (bs, 1H, NH), 10.87 (bs, 1H, OH), 8.37 (d, 1H, *J* = 2.47 Hz, H6′), 8.25 (d, 1H, *J* = 9.06 Hz, H3′), 7.98 (d, 1H, *J* = 8.24 Hz, H6), 7.93 (dd, 1H, *J* = 9.06 Hz, *J* = 2.47 Hz, H4′), 7.06–7.00 (m, 2H, H3, H5). ^{13}C NMR (75 MHz): *δ* 163.4, 157.5, 150.3, 146.8, 138.3, 138.0, 132.6, 125.8, 120.1, 117.6, 116.9, 115.3.

4.1.1.33. N-*(4-Methyl-pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4e***).* White crystals. Yield 72%, m.p. 257–259 °C, IR (KBr): *ν* (C=O) 1682 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.16 (bs, 1H, NH), 10.75 (bs, 1H, OH), 8.18 (d, 1H, *J* = 5.22 Hz, H6′), 8.03 (bs, 1H, H3′), 8.01 (d, 1H, *J* = 8.24 Hz, H6), 7.07–7.01 (m, 2H, H3, H5′), 7.00–6.96 (m, 1H, H5), 2.33 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 163.4, 157.6, 151.7, 149.5, 147.9, 137.8, 132.6, 121.1, 120.1, 117.8, 116.9, 114.7, 21.2.

4.1.1.34. N-*(5-Methyl-pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4f***).* White crystals. Yield 73%, m.p. 228–230 °C, IR (KBr): *ν* (C=O) 1683 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.12 (bs, 1H, NH), 10.73 (bs, 1H, OH), 8.18–8.15 (m, 1H, H6′), 8.12 (d, 1H, *J* = 8.52 Hz, H3′), 8.01 (d, 1H, *J* = 8.52 Hz, H6), 7.64 (dd, 1H, *J* = 8.52 Hz, *J* = 2.47 Hz, H4′), 7.06 (d, 1H, *J* = 1.92 Hz, H3), 7.03 (dd, 1H, *J* = 8.52 Hz, *J* = 1.92 Hz, H5), 2.25 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 163.6, 157.6, 149.5, 148.1, 139.0, 137.8, 132.5, 129.2, 120.1, 117.7, 116.9, 113.9, 17.5.

4.1.1.35. N-*(6-Methyl-pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4g***).* White crystals. Yield 68%, m.p. 222–223 °C, IR (KBr): *ν* (C=O) 1679 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.16 (bs, 1H, NH), 10.71 (bs, 1H, OH), 8.03 (d, 1H, *J* = 8.10 Hz, H3′), 8.01 (d, 1H, *J* = 8.24 Hz, H6), 7.71 (t, 1H, *J* = 8.10, H4′), 7.07–6.98 (m, 3H, H3, H5, H5′), 2.41 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO): *δ* 163.4, 157.6, 157.0, 150.9, 138.9, 137.8, 132.6, 120.1, 119.5, 117.8, 116.9, 111.2, 23.9.

4.1.1.36. N-*(3-Hydroxy-pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4h***).* Yellow crystals. Yield 57%, m.p. 275–277 °C, IR (KBr): *ν* (C=O) 1637 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.37 (bs, 1H, NH), 8.00 (d, 1H, *J* = 8.38 Hz, H6), 7.88 (dd, 1H, *J* = 4.94 Hz, *J* = 1.38 Hz, H6′), 7.34 (dd, 1H, *J* = 7.96 Hz, *J* = 1.37 Hz, H4′), 7.15 (dd, 1H, *J* = 7.96 Hz, *J* = 4.95 Hz, H5′), 7.02 (d, 1H, *J* = 1.92 Hz, H3), 6.99 (dd, 1H, *J* = 8.38 Hz, *J* = 1.92 Hz, H5). ^{13}C NMR (75 MHz): *δ* 166.4, 160.0, 146.2, 141.0, 138.2, 136.7, 131.8, 124.7, 121.8, 119.3, 117.2, 116.5.

4.1.1.37. N-*(5-Nitro-pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4i***).* Brown crystals. Yield 63%, m.p. 296–297 °C, IR (KBr): *ν* (C=O) 1686 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.28 (bs, 1H, NH), 11.22 (bs, 1H, OH), 9.14 (d, 1H, *J* = 2.75 Hz, H6′), 8.63 (dd, 1H, *J* = 9.34 Hz, *J* = 2.75 Hz, H4′), 8.41 (d, 1H, *J* = 9.34 Hz, H3′), 7.95 (d, 1H, *J* = 9.07 Hz, H6), 7.07–7.01 (m, 2H, H3, H5). ^{13}C NMR (75 MHz): *δ* 163.7, 157.4, 155.6, 145.1, 140.4, 138.5, 134.7, 132.8, 120.3, 117.5, 116.9, 113.2.

4.1.1.38. N-*(5-Bromo-pyridin-2-yl)-4-chloro-2-hydroxy-benzamide (***4j***).* White crystals. Yield 68%, m.p. 266–268 °C, IR (KBr): *ν* (C=O) 1684 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.18 (bs, 1H, NH), 10.04 (bs, 1H, OH), 8.43 (dd, 1H, *J* = 2.47 Hz, *J* = 0.82 Hz, H6′), 8.20 (dd, 1H, *J* = 8.93 Hz, *J* = 0.83 Hz, H3′), 8.03 (dd, 1H, *J* = 8.93 Hz, *J* = 2.47 Hz, H4′), 7.97 (d, 1H, *J* = 8.24 Hz, H6), 7.05–6.99 (m, 2H, H3, H5). ^{13}C NMR (75 MHz): *δ* 163.4, 157.4, 150.5, 149.0, 141.1, 138.0, 132.6, 120.1, 117.6, 116.9, 115.8, 114.2.

4.1.1.39. N-*(Pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5a***).* Green crystals. Yield 70%, m.p. 228–230 °C, IR (KBr): *ν* (C=O) 1685 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.76 (bs, 1H, NH), 10.95 (bs, 1H, OH), 8.37–8.32 (m, 1H, H6′), 8.24 (d, 1H, *J* = 7.97 Hz, H3′), 7.88–7.80 (m, 1H, H4′), 7.74 (dd, 1H, *J* = 9.35 Hz, *J* = 3.30 Hz, H6), 7.36–7.27 (m, 1H, H4), 7.16 (ddd, 1H, *J* = 7.97 Hz, *J* = 4.95 Hz, *J* = 0.82 Hz, H5′), 7.05 (dd, 1H, *J* = 9.35 Hz, *J* = 4.67 Hz, H3). ^{13}C NMR (75 MHz): *δ* 163.1, 157.2 and 154.0 (*J* = 235.6 Hz); 153.1, 151.6, 148.5, 138.7, 121.2 and 120.9 (*J* = 23.5 Hz); 120.3, 119.4 and 119.3 (*J* = 6.9 Hz); 118.9 and 118.8 (*J* = 7.5 Hz); 116.3 and 116.0 (*J* = 24.6 Hz), 114.2.

4.1.1.40. N-*(Pyridin-3-yl)-5-fluoro-2-hydroxy-benzamide (***5b***).* Brown crystals. Yield 73%, m.p. 255–258 °C, IR (KBr): *ν* (C=O) 1672 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.49 (bs, 1H, NH), 10.53 (bs, 1H, OH), 8.85 (d, 1H, *J* = 2.47 Hz, H2′),

8.35–8.32 (m, 1H, H6′), 8.17–8.12 (m, 1H, H4′), 7.71 (dd, 1H, *J* = 9.34 Hz, *J* = 3.30 Hz, H6), 7.43–7.37 (m, 1H, H5′), 7.35–7.27 (m, 1H, H4), 7.01 (dd, 1H, *J* = 9.34 Hz, *J* = 4.67 Hz, H3). ^{13}C NMR (75 MHz): δ 165.6 and 165.6 (*J* = 2.0 Hz); 156.7 and 153.5 (*J* = 235.4 Hz); 154.4, 145.3, 142.5, 135.1, 128.0, 123.9, 121.0 and 120.7 (*J* = 23.2 Hz); 118.8 and 118.7 (*J* = 7.5 Hz); 115.3 and 114.9 (*J* = 24.6 Hz).

4.1.1.41. N-*(Pyridin-4-yl)-5-fluoro-2-hydroxy-benzamide (***5c***).* Yellow crystals. Yield 82%, m.p. 321–322 °C, IR (KBr): *ν* (C=O) 1683 cm^{-1}. ^{1}H NMR (300 MHz): δ 10.72 (bs, 1H, OH), 8.52–8.44 (m, 2H, H2′, H6′), 7.73–7.68 (m, 2H, H3′, H5′), 7.63 (dd, 1H, *J* = 9.35 Hz, *J* = 3.30 Hz, H6), 7.34–7.26 (m, 1H, H4), 7.01 (dd, 1H, *J* = 9.35 Hz, *J* = 4.67 Hz, H3). ^{13}C NMR (75 MHz): δ 165.6 and 165.6 (*J* = 2.3 Hz); 156.7 and 153.6 (*J* = 235.3 Hz); 153.9 and 153.9 (*J* = 1.4 Hz); 150.5, 145.4, 120.9 and 120.6 (*J* = 23.2 Hz); 119.8 and 119.7 (*J* = 6.9 Hz); 118.8 and 118.7 (*J* = 7.5 Hz); 115.6 and 115.2 (*J* = 24.3 Hz); 114.4.

4.1.1.42. N-*(5-Chloro-pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5d***).* White crystals. Yield 69%, m.p. 240–242 °C, IR (KBr): *ν* (C=O) 1666 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.77 (bs, 1H, NH), 11.02 (bs, 1H, OH), 8.38 (d, 1H, *J* = 2.75 Hz, H6′), 8.26 (d, 1H, *J* = 9.07 Hz, H3′), 7.95 (dd, 1H, *J* = 9.06 Hz, *J* = 2.74 Hz, H4′), 7.70 (dd, 1H, *J* = 9.48 Hz, *J* = 3.29 Hz, H6), 7.36–7.27 (m, 1H, H4), 7.05 (dd, 1H, *J* = 9.48 Hz, *J* = 4.67 Hz, H3). ^{13}C NMR (75 MHz): δ 163.1 and 163.0 (*J* = 2.3 Hz); 157.2 and 154.0 (*J* = 235.7 Hz); 153.1 and 153.0 (*J* = 1.7 Hz); 150.2, 146.8, 138.4, 125.9, 121.3 and 121.0 (*J* = 23.2 Hz); 119.2 and 119.1 (*J* = 6.9 Hz); 118.9 and 118.8 (*J* = 7.5 Hz); 116.3 and 116.0 (*J* = 24.6 Hz); 115.2.

4.1.1.43. N-*(4-Methyl-pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5e***).* White crystals. Yield 62%, m.p. 225–226 °C, IR (KBr): *ν* (C=O) 1680 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.72 (bs, 1H, NH), 10.86 (bs, 1H, OH), 8.04 (d, 1H, *J* = 7.97 Hz, H3′), 7.74 (dd, 1H, *J* = 7.42 Hz, *J* = 3.29 Hz, H6), 7.72–7.68 (m, 1H, H4′), 7.35–7.26 (m, 1H, H4), 7.08–6.98 (m, 2H, H3, H5′), 2.41 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 163.0, 157.2 and 154.0 (*J* = 235.4 Hz); 157.1, 153.1, 150.9, 138.9, 121.1 and 120.8 (*J* = 23.5 Hz); 119.5, 119.4 and 119.4 (*J* = 6.9 Hz); 118.9 and 118.8 (*J* = 7.5 Hz); 116.3 and 116.0 (*J* = 24.3 Hz); 111.2, 23.9.

4.1.1.44. N-*(5-Methyl-pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5f***).* White crystals. Yield 71%, m.p. 265–269 °C, IR (KBr): *ν* (C=O) 1679 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.71 (bs, 1H, NH), 10.87 (bs, 1H, OH), 8.18–8.15 (m, 1H, H6′), 8.13 (d, 1H, *J* = 8.24 Hz, H4′), 7.74 (dd, 1H, *J* = 9.48 Hz, *J* = 3.30 Hz, H6), 7.67–7.60 (m, 1H, H3′), 7.34–7.25 (m, 1H, H4), 7.04 (dd, 1H, *J* = 9.48 Hz, *J* = 4.67 Hz, H3), 2.24 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 163.0, 157.2 and 154.0 (*J* = 235.4 Hz); 153.2, 149.4, 148.2, 139.0, 129.2, 121.0 and 120.7 (*J* = 23.5 Hz); 119.4 and 119.3 (*J* = 6.6 Hz); 118.9 and 118.8 (*J* = 7.4 Hz); 116.2 and 115.9 (*J* = 24.4 Hz); 113.8, 17.5.

4.1.1.45. N-*(6-Methyl-pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5g***).* White crystals. Yield 60%, m.p. 228–229 °C, IR (KBr): *ν* (C=O) 1679 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.72 (bs, 1H, NH), 10.86 (bs, 1H, OH), 8.04 (d, 1H, *J* = 7.97 Hz, H3′), 7.74 (dd, 1H, *J* = 7.42 Hz, *J* = 3.29 Hz, H6), 7.72–7.68 (m, 1H, H4′), 7.35–7.26 (m, 1H, H4), 7.08–6.98 (m, 2H, H3, H5′), 2.41 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 163.0, 157.2 and 154.0 (*J* = 235.4 Hz); 157.1, 153.1, 150.9, 138.9, 121.1 and 120.8 (*J* = 23.5 Hz); 119.5, 119.4 and 119.4 (*J* = 6.9 Hz); 118.9 and 118.8 (*J* = 7.5 Hz); 116.3 and 116.0 (*J* = 24.3 Hz); 111.2, 23.9.

4.1.1.46. N-*(3-Hydroxy-pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5h***).* Yellow crystals. Yield 57%, m.p. 285–286 °C, IR (KBr): *ν* (C=O) 1670 cm^{-1}. ^{1}H NMR (300 MHz): δ 7.89 (dd, 1H, *J* = 4.95 Hz, *J* = 1.37 Hz, H6′), 7.76 (dd, 1H, *J* = 9.35 Hz, *J* = 3.29 Hz, H6), 7.38–7.29 (m, 2H, H4, H4′), 7.15 (dd, 7.96 Hz, *J* = 4.95 Hz, H5′), 7.01 (dd, 1H, *J* = 9.35 Hz, *J* = 4.67 Hz, H3). ^{13}C NMR (75 MHz): δ 165.5, 156.7 and 153.6 (*J* = 235.1 Hz); 155.0, 146.2, 140.6, 137.7, 124.6, 122.2, 121.5 and 121.2 (*J* = 23.5 Hz); 119.0 and 118.9 (*J* = 7.5 Hz); 118.0 and 117.9 (*J* = 6.9 Hz); 115.6 and 115.3 (*J* = 24.6 Hz).

4.1.1.47. N-*(5-Nitro-pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5i***).* Brown crystals. Yield 56%, m.p. 264–267 °C, IR (KBr): *ν* (C=O) 1668 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.38 (bs, 1H, NH), 9.12 (dd, 1H, *J* = 2.75 Hz, *J* = 0.55 Hz, H6′), 8.60 (dd, 1H, *J* = 9.34 Hz, *J* = 2.75 Hz, H4′), 8.40 (dd, 1H, *J* = 9.34 Hz, *J* = 0.55 Hz, H3′), 7.64 (dd, 1H, *J* = 9.34 Hz, *J* = 3.30 Hz, H6), 7.36–7.27 (m, 1H, H4), 7.03 (dd, 1H, *J* = 9.34 Hz, *J* = 4.40 Hz, H3). ^{13}C NMR (75 MHz): δ 163.4 and 163.3 (*J* = 2.3 Hz); 157.2 and 154.1 (*J* = 235.9 Hz); 155.6, 153.2, 145.1, 140.5, 134.8, 121.9 and 121.6 (*J* = 23.5 Hz); 119.1 and 119.0 (*J* = 7.7 Hz); 119.0 and 118.9 (*J* = 6.9 Hz); 116.4 and 116.1 (*J* = 24.6 Hz); 113.3.

4.1.1.48. N-*(5-Bromo-pyridin-2-yl)-5-fluoro-2-hydroxy-benzamide (***5j***).* White crystals. Yield 65%, m.p. 252–254 °C, IR (KBr): *ν* (C=O) 1664 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.78 (bs, 1H, NH), 11.02 (bs, 1H, OH), 8.46 (dd, 1H, *J* = 2.48 Hz, *J* = 0.69 Hz, H6′), 8.22 (dd, 1H, *J* = 8.93 Hz, *J* = 0.69 Hz, H3′), 8.07 (dd, 1H, *J* = 8.93 Hz, *J* = 2.47 Hz, H4′), 7.70 (dd, 1H, *J* = 9.34 Hz, *J* = 3.29 Hz, H6), 7.37–7.28 (m, 1H, H4), 7.05 (dd, 1H, *J* = 9.34 Hz, *J* = 4.67 Hz, H3). ^{13}C NMR (75 MHz): δ 163.1 and 163.1 (*J* = 2.0 Hz); 157.2 and 154.0 (*J* = 235.7 Hz); 153.1 and 153.0 (*J* = 1.7 Hz); 150.5, 149.0, 141.2, 121.4 and 121.0 (*J* = 23.8 Hz); 119.3 and 119.2 (*J* = 6.9 Hz); 119.0 and 118.9 (*J* = 7.5 Hz); 116.3 and 116.0 (*J* = 24.6 Hz); 115.8, 114.3.

4.1.1.49. N-*(Pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6a***).* White crystals. Yield 66%, m.p. 244–246 °C, IR (KBr): *ν* (C=O) 1691 cm^{-1}. ^{1}H NMR (300 MHz): δ 12.00 (bs, 1H, NH), 10.88 (bs, 1H OH), 8.34 (ddd, 1H, *J* = 4.94 Hz, *J* = 1.93 Hz, *J* = 0.83 Hz, H6′), 8.23 (d, 1H, *J* = 8.52 Hz, H3′),

8.09 (d, 1H, *J* = 2.75 Hz, H6), 7.88–7.80 (m, 1H, H4′), 7.58 (dd, 1H, *J* = 8.79 Hz, *J* = 2.75 Hz, H4), 7.16 (ddd, 1H, *J* = 7.42 Hz, *J* = 4.94 Hz, *J* = 1.10 Hz, H5′), 7.01 (d, 1H, *J* = 8.79 Hz, H3). ^{13}C NMR (75 MHz): *δ* 162.9, 156.1, 151.5, 148.5, 138.7, 136.4, 132.9, 120.6 120.3, 119.7, 114.3, 111.1.

4.1.1.50. N-*(Pyridin-3-yl)-5-bromo-2-hydroxy-benzamide (***6b***).* Beige crystals. Yield 58%, m.p. 289–291 °C, IR (KBr): *ν* (C=O) 1671 cm^{-1}. ^{1}H NMR (300 MHz) *δ* 11.73 (bs, 1H, NH), 10.54 (bs, 1H, OH), 8.85 (d, 1H, *J* = 2.20 Hz, H2′), 8.37–8.30 (m, 1H, H6′), 8.18–8.10 (m, 1H, H4′), 8.03 (d, 1H, *J* = 2.47 Hz, H6), 7.57 (dd, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H4), 7.40 (dd, 1H, *J* = 8.24 Hz, *J* = 4.67 Hz, H5′), 6.96 (d, 1H, *J* = 8.79 Hz, H3). ^{13}C NMR (75 MHz): *δ* 165.5, 157.3, 145.3, 142.5, 136.2, 135.1, 131.6, 128.0, 123.9, 120.4, 119.7, 110.4.

4.1.1.51. N-*(Pyridin-4-yl)-5-bromo-2-hydroxy-benzamide (***6c***).* Yellow crystals. Yield 86%, m.p. 304–305 °C, IR (KBr): *ν* (C=O) 1677 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 10.84 (bs, 1H, OH), 8.51–8.45 (m, 2H, H2′, H6′), 7.93 (d, 1H, *J* = 2.74 Hz, H6), 7.73–7.69 (m, 2H, H3′, H5′), 7.55 (dd, 1H, *J* = 8.79 Hz, *J* = 2.48 Hz, H4), 6.96 (d, 1H, *J* = 8.79 Hz, H3). ^{13}C NMR (75 MHz): *δ* 165.5, 157.1, 150.4, 145.6, 136.1, 131.9, 121.4, 119.7, 114.4, 110.1.

4.1.1.52. N-*(5-Chloro-pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6d***).* White crystals. Yield 56%, m.p. 271–273 °C, IR (KBr): *ν* (C=O) 1658 cm^{-1}. ^{1}H NMR (300 MHz, DMSO): *δ* 12.01 (bs, 1H, NH), 10.91 (bs, 1H, OH), 8.35 (d, 1H, *J* = 2.47 Hz, H6′), 8.24 (d, 1H, *J* = 9.06 Hz, H3′), 8.04 (d, 1H, *J* = 2.48 Hz, H6), 7.91 (dd, 1H, *J* = 9.06 Hz, *J* = 2.47 Hz, H4′), 7.56 (dd, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H4), 6.98 (d, 1H, *J* = 8.79 Hz, H3). ^{13}C NMR (75 MHz): *δ* 162.9, 156.0, 150.1, 146.8, 138.3, 136.5, 132.9, 125.9, 120.4, 119.7, 115.3, 111.1.

4.1.1.53. N-*(4-Methyl-pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6e***).* White crystals. Yield 60%, m.p. 245–247 °C, IR (KBr): *ν* (C=O) 1677 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 10.89 (bs, 1H, NH), 8.18 (d, 1H, *J* = 4.94 Hz, H6′), 8.09–8.07 (m, 2H, H6, H3′), 7.57 (dd, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H4), 7.00 (d overlapped 1H, *J* = 8.79 Hz, H3), 7.01–6.97 (m, 1H, H5′), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 162.9, 156.2, 151.6, 149.5, 148.0, 136.3, 132.9, 121.2, 120.6, 119.8, 114.7, 110.9, 21.2.

4.1.1.54. N-*(5-Methyl-pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6f***).* White crystals. Yield 72%, m.p. 293–294 °C, IR (KBr): *ν* (C=O) 1678 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 11.99 (bs, 1H, NH), 10.81 (bs, 1H, OH), 8.19–8.15 (m, 1H, H6′), 8.12 (d, 1H, *J* = 8.38 Hz, H3′), 8.09 (d, 1H, *J* = 2.75 Hz, H6), 7.64 (dd, 1H, *J* = 8.38 Hz, *J* = 2.20 Hz, H4′), 7.57 (dd, 1H, *J* = 8.79 Hz, *J* = 2.74 Hz, H4), 7.00 (d, 1H, *J* = 8.79 Hz, H3), 2.25 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 162.8, 156.1, 149.4, 148.2, 139.0, 136.3, 132.8, 129.3, 120.5, 119.7, 113.9, 111.0, 17.5.

4.1.1.55. N-*(6-Methyl-pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6g***).* White crystals. Yield 61%, m.p. 223–224 °C, IR (KBr): *ν* (C=O) 1679 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.00 (bs, 1H, NH), 10.79 (bs, 1H, OH), 8.09 (d, 1H, *J* = 2.61 Hz, H6), 8.05–8.01 (m, 1H, H3′), 7.71 (t, 1H, *J* = 7.56 Hz, H4′), 7.57 (dd, 1H, *J* = 8.79 Hz, *J* = 2.61 Hz, H4), 7.00 (d overlapped, 1H, *J* = 7.56 Hz, H5′), 6.99 (d overlapped, 1H, *J* = 8.79 Hz, H3), 2.40 (s, 3H, CH_3). ^{13}C NMR (75 MHz): *δ* 162.9, 157.1, 156.1, 150.9, 138.9, 136.3, 132.9, 120.6, 119.7, 119.5, 111.2, 111.1, 23.9.

4.1.1.56. N-*(3-Hydroxy-pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6h***).* Yellow crystals. Yield 73%, m.p. 288–291 °C, IR (KBr): *ν* (C=O) 1641 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 8.12 (d, 1H, *J* = 2.74 Hz, H6), 7.88 (dd, 1H, *J* = 4.94 Hz, *J* = 1.37 Hz, H6′), 7.58 (dd, 1H, *J* = 8.79 Hz, *J* = 2.47 Hz, H4), 7.33 (dd, 1H, *J* = 7.96 Hz, *J* = 1.65 Hz, H4′), 7.14 (dd, 1H, *J* = 7.97 Hz, *J* = 4.95 Hz, H5′), 6.95 (d, 1H, *J* = 8.79 Hz, H3). ^{13}C NMR (75 MHz): *δ* 165.7, 158.2, 146.3, 140.8, 136.9, 136.6, 132.2, 124.5, 123.9, 120.0, 119.4, 110.2.

4.1.1.57. N-*(5-Nitro-pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6i***).* White crystals. Yield 62%, m.p. 301–303 °C, IR (KBr): *ν* (C=O) 1663 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.11 (bs, 1H, NH), 11.30 (bs, 1H, OH), 9.14–9.12 (m, 1H, H6′), 8.62 (dd, 1H, *J* = 9.34 Hz, *J* = 2.75 Hz, H4′), 8.40 (d, 1H, *J* = 9.34 Hz, H3′), 7.99 (d, 1H, *J* = 2.61 Hz, H6), 7.58 (dd, 1H, *J* = 8.79 Hz, *J* = 2.61 Hz, H4), 6.99 (d, 1H, *J* = 8.79 Hz, H3). ^{13}C NMR (75 MHz): *δ* 163.2, 156.1, 155.5, 145.0, 140.4, 136.9, 134.7, 133.0, 120.2, 119.8, 113.3, 111.2.

4.1.1.58. N-*(5-Bromo-pyridin-2-yl)-5-bromo-2-hydroxy-benzamide (***6j***).* White crystals. Yield 57%, m.p. 279–281 °C, IR (KBr): *ν* (C=O) 1658 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.03 (bs, 1H, NH), 10.92 (bs, 1H, OH), 8.47–8.44 (m, 1H, H6′), 8.21 (dd, 1H, 8.79 Hz, *J* = 0.55 Hz, H3′), 8.06 (dd overlapped, 1H, *J* = 8.79 Hz, *J* = 2.75 Hz, H4′), 8.05 (d overlapped 1H, *J* = 2.75 Hz, H6), 7.58 (dd, 1H, *J* = 8.79 Hz, *J* = 2.74 Hz, H4), 7.00 (d, 1H, *J* = 8.79 Hz, H3). ^{13}C NMR (75 MHz): *δ* 162.9, 156.0, 150.4, 149.0, 141.1, 136.5, 132.9, 120.4, 119.7, 115.8, 114.3, 111.1.

4.1.1.59. N-*(Pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7a***).* White crystals. Yield 72%, m.p. 243–245 °C, IR (KBr): *ν* (C=O) 1690 cm^{-1}. ^{1}H NMR (300 MHz): *δ* 12.00 (bs, 1H, NH), 10.87 (bs, 1H OH), 8.34 (ddd, 1H, *J* = 4.94 Hz, *J* = 1.92 Hz, *J* = 0.82 Hz, H6′), 8.23 (d, 1H, *J* = 7.83 Hz, H3′), 7.96 (d, 1H, *J* = 2.89 Hz, H6), 7.87–7.80 (m, 1H, H4′), 7.47 (dd, 1H, *J* = 8.79 Hz, *J* = 2.89 Hz, H4), 7.16 (ddd, 1H, *J* = 7.83 Hz, *J* = 4.95 Hz, *J* = 1.10 Hz, H5′), 7.06 (d, 1H, *J* = 8.80 Hz, H3). ^{13}C NMR (75 MHz): *δ* 163.0, 155.6, 151.6, 148.5, 138.7, 133.6, 130.0, 123.7, 120.3, 120.1, 119.2, 114.3.

4.1.1.60. N-*(Pyridin-4-yl)-5-chloro-2-hydroxy-benzamide (***7c***).* Yellow crystals. Yield 79%, m.p. 314–316 °C, IR

(KBr): ν (C=O) 1678 cm^{-1}. ^{1}H NMR (300 MHz): δ 10.83 (bs, 1H, OH), 8.52–8.44 (m, 2H, H2′, H6′), 7.82 (d, 1H, J = 2.61 Hz, H6), 7.74–7.68 (m, 2H, H3′, H5′), 7.44 (dd, 1H, J = 7.89 Hz, J = 2.61 Hz, H4), 7.01 (d, 1H, J = 7.89 Hz, H3). ^{13}C NMR (75 MHz): δ 165.6, 156.7, 150.5, 145.6, 133.3, 129.0, 122.7, 120.9, 119.3, 114.4.

4.1.1.61. N-*(5-Chloro-pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7d***).* White crystals. Yield 59%, m.p. 266–268 °C, IR (KBr): ν (C=O) 1660 cm^{-1}. ^{1}H NMR (300 MHz): δ 12.00 (bs, 1H, NH), 10.93 (bs, 1H, OH), 8.36 (d, 1H, J = 2.75 Hz, H6′), 8.25 (d, 1H, J = 8.93 Hz, H3′), 7.93 (dd, overlapped, 1H, J = 8.93 Hz, J = 2.75 Hz, H4′), 7.91 (d overlapped, 1H, J = 2.75 Hz, H6), 7.46 (dd, 1H, J = 8.79 Hz, J = 2.75 Hz, H4), 7.04 (d, 1H, J = 8.79 Hz, H3). ^{13}C NMR (75 MHz): δ 163.0, 155.5, 150.2, 146.8, 138.4, 133.7, 130.0, 125.9, 123.7, 119.9, 119.3, 115.3.

4.1.1.62. N-*(4-Methyl-pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7e***).* White crystals. Yield 63%, m.p. 255–257 °C, IR (KBr): ν (C=O) 1682 cm^{-1}. ^{1}H NMR (300 MHz): δ 12.00 (bs, 1H, NH), 10.83 (bs, 1H, OH), 8.19 (d, 1H, J = 5.23 Hz, H6′), 8.08 (bs, 1H, H3′), 7.95 (d, 1H, J = 2.75 Hz, H6), 7.47 (dd, 1H, J = 8.79 Hz, J = 2.75 Hz, H4), 7.05 (d, 1H, J = 8.79 Hz, H3), 6.99 (ddd, J = 5.22 Hz, J = 1.37 Hz, J = 0.55 Hz, H5′), 2.34 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 162.9, 155.6, 151.6, 149.5, 148.0, 133.5, 129.9, 123.6, 121.2, 120.1, 119.3, 114.7, 21.2.

4.1.1.63. N-*(5-Methyl-pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7f***).* White crystals. Yield 60%, m.p. 280–282 °C, IR (KBr): ν (C=O) 1680 cm^{-1}. ^{1}H NMR (300 MHz): δ 12.12 (bs, 1H, NH), 10.73 (bs, 1H, OH), 8.18–8.15 (m, 1H, H6′), 8.12 (d, 1H, J = 8.52 Hz, H3′), 8.01 (d, 1H, J = 8.52 Hz, H6), 7.64 (dd, 1H, J = 8.52 Hz, J = 2.47 Hz, H4′), 7.06 (d, 1H, J = 1.92 Hz, H3), 7.03 (dd, 1H, J = 8.52 Hz, J = 1.92 Hz, H5), 2.25 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 163.6, 157.6, 149.5, 148.1, 139.0, 137.8, 132.5, 129.2, 120.1, 117.7, 116.9, 113.9, 17.5.

4.1.1.64. N-*(6-Methyl-pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7g***).* White crystals. Yield 71%, m.p. 231–232 °C, IR (KBr): ν (C=O) 1680 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.96 (bs, 1H, NH), 10.78 (bs, 1H, OH), 8.03 (d, 1H, J = 7.83 Hz, H3′), 7.96 (d, 1H, J = 2.89 Hz, H6), 7.71 (t, 1H, J = 7.83 Hz, H4′), 7.47 (dd, 1H, J = 8.79 Hz, J = 2.89 Hz, H4), 7.05 (d, 1H, J = 8.79 Hz, H3), 7.01 (d, 1H, J = 7.83 Hz, H5′), 2.40 (s, 3H, CH_3). ^{13}C NMR (75 MHz): δ 162.9, 157.1, 155.6, 150.8, 139.0, 133.5, 130.0, 123.7 120.1, 119.6, 119.3, 111.2, 23.9.

4.1.1.65. N-*(3-Hydroxy-pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7h***).* Yellow crystals. Yield 82%, m.p. 284–286 °C, IR (KBr): ν (C=O) 1641 cm^{-1}. ^{1}H NMR (300 MHz): δ 11.24 (bs, 1H, NH), 7.99 (d, 1H, J = 2.75 Hz, H6), 7.88 (dd, 1H, J = 4.81 Hz, J = 1.37 Hz, H6′), 7.47 (dd, 1H, J = 8.79 Hz, J = 2.74 Hz, H4), 7.33 (dd, 1H, J = 7.97 Hz, J = 1.38 Hz, H4′), 7.15 (dd, 1H, J = 7.97 Hz, J = 4.81 Hz, H5′), 7.01 (d, 1H, J = 8.79 Hz, H3). ^{13}C NMR (75 MHz): δ 165.7, 157.8, 146.2, 140.9, 136.9, 133.8, 129.3, 124.6, 122.9, 121.9, 119.5, 118.9.

4.1.1.66. N-*(5-Nitro-pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7i***).* Beige crystals. Yield 72%, m.p. 293–295 °C, IR (KBr): ν (C=O) 1664 cm^{-1}. ^{1}H NMR (300 MHz): δ 12.10 (bs, 1H, NH), 11.79 (bs, 1H, OH), 9.14–9.11 (m, 1H, H6′), 8.64–8.58 (m, 1H, H4′), 8.39 (d, 1H, J = 9.07 Hz, H3′), 7.88–7.84 (m, 1H, H6), 7.47 (dd, 1H, J = 8.79 Hz, J = 2.75 Hz, H4), 7.04 (d, 1H, J = 8.80 Hz, H3). ^{13}C NMR (75 MHz): δ 163.3, 155.6, 155.5, 145.0, 140.4, 134.7, 134.1, 130.0, 123.8, 119.7, 119.6, 113.3.

4.1.1.67. N-*(5-Bromo-pyridin-2-yl)-5-chloro-2-hydroxy-benzamide (***7j***).* Yellow crystals. Yield 59%, m.p. 272–274 °C, IR (KBr): ν (C=O) 1661 cm^{-1}. ^{1}H NMR (300 MHz): δ 12.00 (bs, 1H, NH), 10.94 (bs, 1H, OH), 8.46 (dd, 1H, J = 2.47 Hz, J = 0.55 Hz, H6′), 8.23–8.19 (m, 1H, H3′), 8.06 (dd, 1H, J = 8.79 Hz, J = 2.47 Hz, H4′), 7.92 (d, 1H, J = 2.83 Hz, H6), 7.48 (dd, 1H, J = 8.79 Hz, J = 2.83 Hz, H4), 7.06 (d, 1H, J = 8.79 Hz, H3). ^{13}C NMR (75 MHz): δ 163.0, 155.5, 150.4, 149.0, 141.1, 133.7, 129.9, 123.7, 120.0, 119.3, 115.8, 114.3.

4.2. Microbiology

The following strains, obtained from the Czech National Collection of Type Cultures (CNCTC), National Institute of Public Health, Prague, were used for the evaluation of in vitro antimycobacterial activity: *M. kansasii* CNCTC My 235/80, *M. avium* CNCTC My 330/88 and a clinical isolate of *M. kansasii* 6509/96. Antimycobacterial activity of the compounds against these strains was determined in the Šula semisynthetic medium (SEVAC, Prague). The Šula liquid medium (with bovine serum) is routinely used in the Czech Republic. Each strain was simultaneously inoculated into a Petri dish containing the Löwenstein–Jensen medium for the control of the sterility of the inoculum and its growth. The compounds were added to the medium in DMSO solutions. The final concentrations were 1000, 500, 250, 125, 62.5, 32, 16, 8, 4, 2 and 1 μmol/l. The minimum inhibitory concentrations (MICs) were determined after incubation at 37 °C for 14 days (see Table 1). MIC was the lowest concentration of an antimycobacterially effective substance (on the above-stated concentration scale), at which inhibition of the growth of the mycobacteria occurred.

4.3. Calculations

The logarithms of the partition coefficients were calculated using ChemOffice 5 software (Table 2). All regression calculations were set up using the Multireg H programme (Klemera) for Microsoft Excel.

Table 1
In vitro antimycobacterial activity of *N*-pyridinylsalicylamides

Compounds			MICs (μmol l^{-1})			
	R_1	R_2	*Mycobacterium tuberculosis* My 331/88 14 days	*M. avium* My 330/88 14 days	*M. kansasii* My 235/80 14 days	*M. kansasii* My 6509/96 14 days
1a	H	2-pyridyl	n	n	n	n
1b	H	3-pyridyl	125	n	n	n
1c	H	4-pyridyl	62.5	500	1000	1000
1d	H	5-chloro-2-pyridyl	62.5	n	n	n
1e	H	4-methyl-2-pyridyl	125	n	n	n
1f	H	5-methyl-2-pyridyl	n	n	n	n
1g	H	6-methyl-2-pyridyl	n	n	n	n
1h	H	3-hydroxy-2-pyridyl	250	500	500	500
1i	H	5-nitro-2-pyridyl	32	n	n	n
1j	H	5-bromo-2-pyridyl	n	n	n	n
2a	4-CH_3	2-pyridyl	32	125	n	125
2b	4-CH_3	3-pyridyl	16	125	62.5	32
2c	4-CH_3	4-pyridyl	16	n	n	250
2d	4-CH_3	5-chloro-2-pyridyl	n	n	n	n
2e	4-CH_3	4-methyl-2-pyridyl	16	n	n	n
2f	4-CH_3	5-methyl-2-pyridyl	16	n	n	n
2g	4-CH_3	6-methyl-2-pyridyl	32	n	n	n
2h	4-CH_3	3-hydroxy-2-pyridyl	250	1000	250	250
2i	4-CH_3	5-nitro-2-pyridyl	n	n	n	n
2j	4-CH_3	5-bromo-2-pyridyl	n	n	n	n
3a	4-OCH_3	2-pyridyl	8	n	n	n
3d	4-OCH_3	5-chloro-2-pyridyl	8	32	62.5	32
3e	4-OCH_3	4-methyl-2-pyridyl	8	n	n	n
3f	4-OCH_3	5-methyl-2-pyridyl	8	125	n	n
3g	4-OCH_3	6-methyl-2-pyridyl	n	125	250	250
3h	4-OCH_3	3-hydroxy-2-pyridyl	125	500	250	250
3i	4-OCH_3	5-nitro-2-pyridyl	8	32	16	32
3j	4-OCH_3	5-bromo-2-pyridyl	8	n	n	n
4a	4-Cl	2-pyridyl	8	32	62.5	62.5
4b	4-Cl	3-pyridyl	16	125	250	125
4c	4-Cl	4-pyridyl	32	n	n	n
4d	4-Cl	5-chloro-2-pyridyl	8	32	16	16
4e	4-Cl	4-methyl-2-pyridyl	8	32	32	32
4f	4-Cl	5-methyl-2-pyridyl	4	8	8	4
4g	4-Cl	6-methyl-2-pyridyl	4	62.5	8	8
4h	4-Cl	3-hydroxy-2-pyridyl	250	500	500	500
4i	4-Cl	5-nitro-2-pyridyl	8	32	8	16
4j	4-Cl	5-bromo-2-pyridyl	4	16	2	2
5a	5-F	2-pyridyl	62.5	62.5	n	62.5
5b	5-F	3-pyridyl	250	n	n	250
5c	5-F	4-pyridyl	n	n	n	n
5d	5-F	5-chloro-2-pyridyl	4	32	16	16
5e	5-F	4-methyl-2-pyridyl	32	32	32	32
5f	5-F	5-methyl-2-pyridyl	n	n	n	n
5g	5-F	6-methyl-2-pyridyl	n	n	n	n
5h	5-F	3-hydroxy-2-pyridyl	250	500	250	250
5i	5-F	5-nitro-2-pyridyl	4	32	8	16
5j	5-F	5-bromo-2-pyridyl	16	32	32	32
6a	5-Br	2-pyridyl	n	n	n	n
6b	5-Br	3-pyridyl	n	n	n	n
6c	5-Br	4-pyridyl	n	n	nn	

(continued on next page)

Table 1
(continued)

Compounds	R_1	R_2	MICs (μmol l^{-1}) *Mycobacterium tuberculosis* My 331/88 14 days	*M. avium* My 330/88 14 days	*M. kansasii* My 235/80 14 days	*M. kansasii* My 6509/96 14 days
6d	5-Br	5-chloro-2-pyridyl	8	32	8	16
6e	5-Br	4-methyl-2-pyridyl	62.5	125	62.5	32
6f	5-Br	5-methyl-2-pyridyl	n	n	n	n
6g	5-Br	6-methyl-2-pyridyl	62.5	125	125	62.5
6h	5-Br	3-hydroxy-2-pyridyl	250	500	500	500
6i	5-Br	5-nitro-2-pyridyl	8	32	8	8
6j	5-Br	5-bromo-2-pyridyl	8	62.5	16	16
7a	5-Cl	2-pyridyl	62.5	62.5	62.5	62.5
7c	5-Cl	4-pyridyl	n	n	n	n
7d	5-Cl	5-chloro-2-pyridyl	8	62.5	16	16
7e	5-Cl	4-methyl-2-pyridyl	8	32	8	8
7f	5-Cl	5-methyl-2-pyridyl	n	n	n	n
7g	5-Cl	6-methyl-2-pyridyl	16	62.5	32	n
7h	5-Cl	3-hydroxy-2-pyridyl	125	500	250	250
7i	5-Cl	5-nitro-2-pyridyl	2	16	4	8
7j	5-Cl	5-bromo-2-pyridyl	4	n	8	16
INH			1	250	250	4

n: MIC values could not be determined due to the low solubility.

Table 2
Lipophilicity (log *P*) of compounds **1a–7j**

Compounds	log *P*	Compounds	log *P*	Compounds	log *P*	Compounds	log *P*
1a	1.30	**3a**	1.70	**5a**	1.99	**7a**	1.92
1b	1.07			**5b**	1.27		
1c	1.07			**5c**	1.27	**7c**	1.69
1d	1.92	**3d**	2.26	**5d**	2.55	**7d**	2.95
1e	1.72	**3e**	2.19	**5e**	2.47	**7e**	2.87
1f	1.72	**3f**	2.19	**5f**	2.47	**7f**	2.87
1g	1.77	**3g**	2.41	**5g**	2.69	**7g**	3.09
1h	0.92	**3h**	1.31	**5h**	1.60	**7h**	2.00
1i	1.12	**3i**	1.00	**5i**	1.28	**7i**	1.68
1j	3.07	**3j**	2.53	**5j**	2.82	**7j**	3.22
2a	1.72	**4a**	1.92	**6a**	2.66	**INH**	
2b	1.49	**4b**	1.69	**6b**	1.94		
2c	1.49	**4c**	1.69	**6c**	1.94		
2d	2.87	**4d**	2.95	**6d**	3.22		
2e	2.13	**4e**	2.87	**6e**	3.14		
2f	2.13	**4f**	2.87	**6f**	3.14		
2g	3.02	**4g**	3.09	**6g**	3.36		
2h	1.93	**4h**	2.00	**6h**	2.27		
2i	1.61	**4i**	1.68	**6i**	1.95		
2j	3.14	**4j**	3.62	**6j**	3.49		

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