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Synthesis of 3-substituted imidazo[1,5-*a*]pyridines having 1-(*N*-picolinamidin-2-yl) group

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ABSTRACT

The 3-substituted imidazo[1,5-*a*]pyridine compounds having 1-(*N*-picolinamidin-2-yl) group (**1a**–**h**) were synthesized by heating 1 equiv of an aldehyde (eight examples), 2 equiv of 2-cyanopyridine and ammonium acetate in PEG-400. By heating 2 equiv of the aldehyde and 1 equiv of 2-cyanopyridine under the same experimental conditions, 2,4,5-trisubstituted imidazoles (**2a**–**c**) were isolated. All the reported compounds were thoroughly characterized and the molecular structures of **1a** and **2b** were established by single crystal X-ray diffraction studies.

1. Introduction

Imidazo[1,5-*a*]pyridine is a class of fused bicyclic 5:6 system having two nitrogen atoms.[1] Some of its derivatives are shown to be active as thromboxane A_2 synthetase inhibitors[2] and positive ionotropic agents.[3] The de novo synthesis of imidazo[1,5-*a*]pyridine nucleus having different substituents at pyridine[2–5] and at 3- and/or 1-positions of the imidazole[6–25] rings have been reported. This nucleus is generally generated from imines or methylamines derived from di-2-pyridyl ketone and 2-aminomethylpyridine or 2-cyanopyridine.

We recently reported[26] the synthesis of some 2,4,5-trisubstituted imidazoles and formation of imidazo[1,5-*a*]pyridine nucleus from a reaction between 2-cyanopyridine and picolylamines. This reaction is limited to *N*-(3-(2-pyridyl)imidazo[1,5-*a*]pyridine)picolinamidines and they were obtained in low yields as minor product along with 2,4,6-tris(2-pyridyl)1,3,5-triazine, hence required further chromatographic separation. As its continuation, we examined the reaction of 2-cyanopyridine with some aldehydes in presence of ammonium acetate. This reaction afforded 3-substituted imidazo[1,5-*a*]pyridine compounds having 1-(*N*-picolinamidin-2-yl) group, as clean unique product in good yields and the results are described here.

2. Results and discussion

Heating a mixture of 1 equiv of an aldehyde and 2 equiv of 2-cyanopyridine along with ammonium acetate (as a source of free ammonia) in PEG-400 at 100 °C, yielded a viscous liquid, which on pouring into water precipitated the product (Scheme 1) as solid. Thorough characterization of the solid confirmed the presence of 1,3-disubstitued imidazo[1,5-*a*]pyridine nucleus in which the 3-substituent arise from the aldehyde and 1-substituent arise from the 2-cyanopyridine (Scheme 1). It is important to note that 1 equiv of 2-cyanopyridine is required to form the imidazo[1,5-*a*]pyridine nucleus while the second equivalent becomes part of amidine group. Our attempts to isolate the 1-amino substituted imidazo[1,5-*a*]pyridine by using a 1:1 equiv of the reactants (attempted only in the case of salicylaldehyde with 2-cyanopyridine) could not succeed and led to 2,4,5-trisubstituted imidazole compound (vide infra).

However, under the same experimental conditions performing the reaction with 2 equiv of an aldehyde and 1 equiv of 2-cyanopyridine yielded 2,4,5-trisubstitued imidazole compounds. In this case, the 4- and 5-substituents arise from the aldehyde group while that at 2-position arise from the nitrile reactant (Scheme 2). It is pertinent to note that the synthesis of 2,4,5-trisubstitued imidazole from 2:1 mixture of an aldehyde and 2-cyanopyridine has been reported by heating in microwave[27] and as well as by using various ratios[28] in hot acetic acid. We have provided the synthetic details of **2a**–**c** and their spectroscopic data were not provided here as they were identical.

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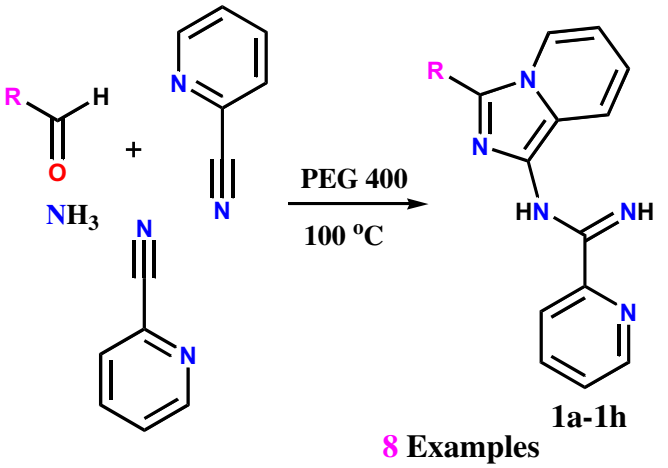
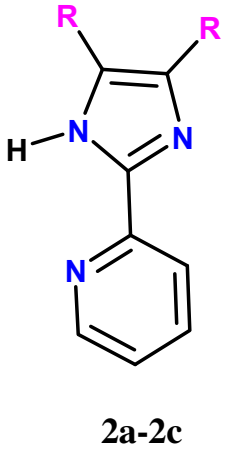


Scheme 1. Synthesis of 3-substituted imidazo[1,5-*a*]pyridine compounds having 1-(*N*-picolinamidin-2-yl) group.



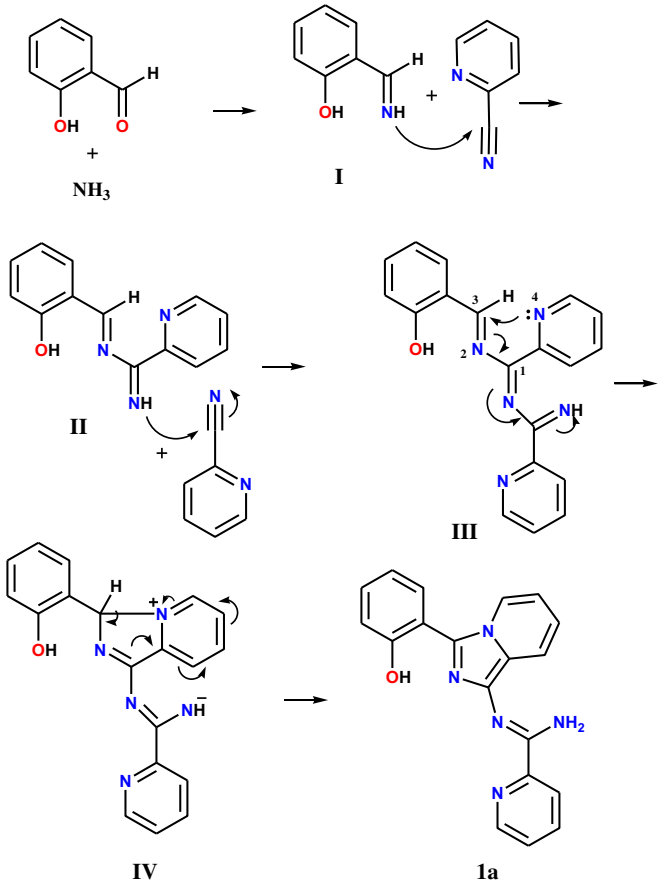
Scheme 2. General structure of compound **2**.

Hence by having control over stoichiometric ratio of aldehyde and 2-cyanopyridine, imidazo[1,5-*a*]pyridine or imidazole nuclei can be generated in PEG-400. To explore the scope of this reaction, we have used eight aldehydes for the synthesis of imidazo [1,5-*a*]pyridine compounds. With aldehydes having heterocyclic or aromatic rings, the reaction afforded the expected products in very good yields. But only to test the use of PEG-400 for synthesis of imidazoles, three aldehydes were employed, in which their yields were good (Table 1) and we have not examined any further.

Table 1
Synthesis of 3-substituted imidazo[1,5-*a*]pyridine compounds having 1-(*N*-picolinamidin-2-yl) group and 2,4,5-trisubstitued imidazole compounds

Entry	R group	Product	Yield (%)
1	2-Hydroxyphenyl	**1a**	83
2	Phenyl	**1b**	80
3	2-Thienyl	**1c**	65
4	4-Methoxyphenyl	**1d**	75
5	2-Pyrenyl	**1e**	82
6	9-Anthracenyl	**1f**	70
7	4-Methylphenyl	**1g**	78
8	2-Bromophenyl	**1h**	60
9	2-Hydroxyphenyl	**2a**	65
10	Phenyl	**2b**	70
11	2-Thienyl	**2c**	60

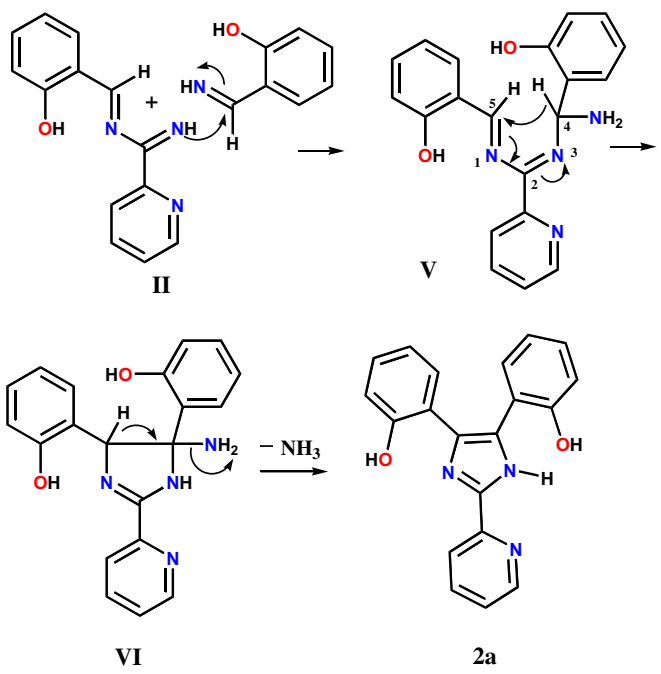
A plausible mechanism for the formation of **1a** is shown in Scheme 3. Salicylaldehyde is known to form an imine (**I**) with ammonia, which can react further with 2-cyanopyridine to form an amidine (**II**). The amidine nitrogen of intermediate **II** can attack the carbon atom of another molecule of 2-cyanopyridine to form the diamidine intermediate **III**. The lone pair of electron on nitrogen atom-4 can attack carbon-3 of the diamidine group resulting in the formation of the fused five-membered rings in **IV**. Subsequent proton removal and delocalization of the negative charge will lead to the final product **1a**.



Scheme 3. Plausible mechanism for the formation of **1a**.

A plausible mechanism for the formation of **2a** is shown in Scheme 4. The amidine nitrogen in **II** can attack the carbon atom of another molecule of imine (**I**) to generate the intermediate **V**. Attack by C(4)–H bond pair of electron on carbon-5 lead to formation of the sigma bond between them. This results in the generation of five-membered ring as in **VI**. Elimination of one molecule of ammonia will yield the final product **2a** that contain the imidazole ring.

All the compounds have been thoroughly characterized using various techniques. ^{1}H and ^{13}C NMR spectra of **1a**–**h** are consistent with the expected structures. Characteristically, compounds **1a**, **1b**, **1d**-**h** exhibit two distinct triplet at δ=6.5–7.0 ppm in their ^{1}H NMR spectra for the fused pyridine ring of imidazo[1,5-*a*]pyridine nucleus, but **1c** exhibit a multiplet at δ=6.7 ppm. The molecular ion M^{+}+H peak in the HRMS/ESI-MS of **1a**–**h**, were found at respective *m*/*z* values with good agreement. The molecular structure of **1a** has been determined by single crystal X-ray diffraction method,[29] which reveals the presence of 3-(2-hydroxyphenyl) substituted imidazo[1,5-*a*]pyridine compound having 1-(*N*-picolinamidin-2-yl) group. The molecular structure **2b** has also been determined[30] and perspective views of **1a** and **2b** are shown in Figs. 1 and 2, respectively.



Scheme 4. A plausible mechanism for the formation of **2a**.

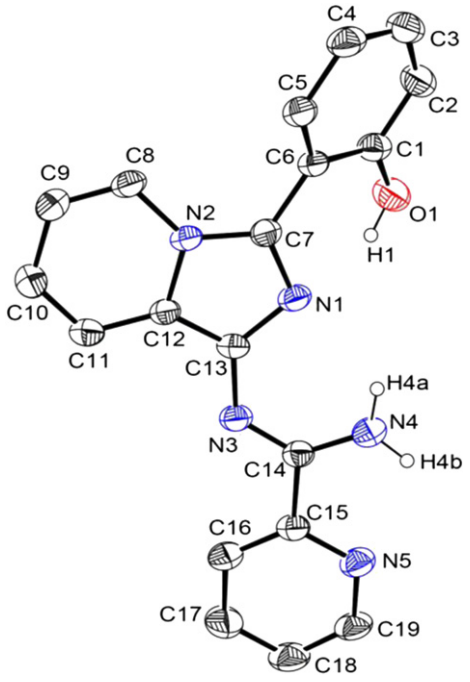


Fig. 1. ORTEP (30% probability ellipsoids) plot of **1a**. Hydrogen atoms in the aromatic rings are omitted for clarity. Selected distances (Å): N2–C7 1.369(3), N2–C8 1.390(3), C8–C9 1.338(3), C10–C9 1.421(3), C11–C10 1.348(3), C12–C11 1.397(3), N2–C12 1.405(3), C12–C13 1.380(3), N1–C13 1.378(3), N1–C7 1.344(3), N3–C13 1.391(3), N3–C14 1.291(3), N4–C14 1.344(3).

3. Conclusion

In conclusion, we have described a simple and efficient method for the synthesis of 3-substituted 1-(*N*-2-picolinamidinyl)imidazo [1,5-*a*]pyridine by reacting an aldehyde and 2-cyanopyridine in 1:2 ratio with ammonium acetate in PEG-400 at 100 °C. On the other hand, 2,4,5-trisubstituted imidazoles were obtained by reacting an aldehyde and 2-cyanopyridine in 2:1 ratio under the same

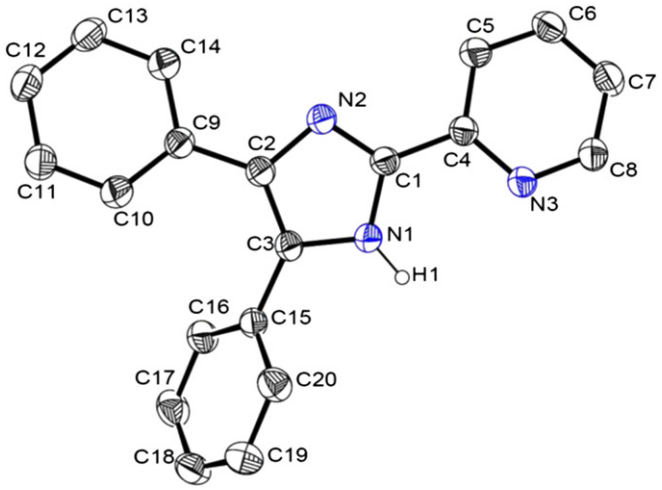


Fig. 2. ORTEP (30% probability ellipsoids) plot of **2b**. Hydrogen atoms in the aromatic rings are omitted for clarity. Selected distances (Å): N1–C1 1.3620(18), N2–C1 1.3180(19), N2–C2 1.384(2), C2–C3 1.387(2), N1–C3 1.374(2).

experimental conditions. We believe that this method can be useful for the synthesis of different imidazo[1,5-*a*]pyridines and 2,4,5-trisubstituted imidazoles using PEG as solvent.

4. Experimental section

4.1. General methods

2-Cyanopyridine, all the aldehydes (Aldrich, USA); PEG-400 NH_4OAc (Merck India Ltd) and solvents were used as received without further purification.

X-ray crystallographic data were collected using a Bruker SMART APEX-CCD diffractometer with Mo Kα radiation (λ=0.71073 Å). The intensity data were corrected for Lorentz and polarization effects and empirical absorption corrections were applied using the SAINT program.[31,32] All the structures were solved by direct methods using SHELXS-97.[32] Non-hydrogen atoms located from the difference Fourier maps were refined anisotropically by full-matrix least-squares on F^2, using SHELXL-97.[33] All hydrogen atoms were included in the calculated positions and refined isotropically using a riding model.

4.2. Syntheses

*4.2.1. N-(3-(2-Hydroxyphenyl)H-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1a**).* A mixture of salicylaldehyde (0.500 g, 4.13 mmol), 2-cyanopyridine (0.860 g, 8.26 mmol) and ammonium acetate (0.636 g, 8.26 mmol) in PEG-400 (2.0 g) was heated at 100 °C in an oil-bath for 12 h. The mixture was cooled and then added to water (50 mL) with stirring. After stirring for 1 h, the greenish-yellow precipitate was filtered washed with water and dried in vacuum over P_4O_{10} and recrystallized from dichloromethane. Crystals suitable for X-ray studies were obtained by slow evaporation of dichloromethane solution of **1a**. Yield: 1.13 g (83%). Mp 198 °C; HRMS-Mass: calcd for $C_{19}H_{15}N_5O^+$ 329.1277 found (M^++H) 330.1288. 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 10.10 (1H, s), 8.60 (2H, d, 7.2), 8.35 (1H, d, 7.2), 8.13 (1H, s), 7.93 (1H, d, 8.8), 7.82 (1H, t, 8.8), 7.71 (1H, d, 7.6), 7.50 (1H, s), 7.34 (2H, m), 7.16 (1H, d, 9.2), 7.04 (1H, t, 8.8), 6.75 (1H, t, 6.4), 6.68(1H, t, 6.0). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 155.5, 152.5, 150.7, 148.2, 138.7, 136.6, 130.2, 130.0, 125.4, 125.0, 125.0, 121.7, 121.0, 120.0, 120.0, 118.0, 117.5, 115.5, 115.0. FTIR (KBr, cm^{-1}): 3080, 3046, 1625, 1580, 1563, 1533, 1508, 1467, 1436, 1396, 1369, 1314, 1283, 1249, 1230, 1158, 1140, 1089, 1039, 994, 957, 870, 826, 796, 770, 747, 731, 703, 689, 656, 488, 470. Anal. Calcd for

$C_{19}H_{15}N_5O$: C, 69.29; H, 4.59; N, 21.26. Found: C, 69.20; H, 4.54; N, 21.19.

Compounds **1b**–**h** were synthesized by adopting the same procedure described for **1a**, using 8.26 mmol of 2-cyanopyridine.

*4.2.2. N-(3-PhenylH-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1b**).* Yield: 1.03 g (80%). Mp 188 °C; HRMS-Mass: calcd for $C_{19}H_{15}N_5$ $^+$ 313.1327 found (M^++H) 314.1328. 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 9.30 (1H, s), 8.60 (2H, t, 8), 8.22 (1H, d, 7.2), 7.85 (4H, m), 7.53 (2H, t, 8.0), 7.42 (2H, t, 7.2), 7.33 (1H, t, 7.6), 6.78 (1H, t, 6.4), 6.60 (1H, t, 7.2). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 153.0, 151.0, 148.1, 141.0, 136.4, 133.0, 131.0, 129.1, 128.3, 127.8, 125.5, 124.3, 122.0, 120.5, 120.0, 117.0, 115.0. FTIR (KBr, cm^{-1}): 3048, 1620, 1584, 1563, 1531, 1515, 1506, 1468, 1415, 1380, 1324, 1307, 1252, 1235, 1177, 1156, 1137, 1077, 1044, 996, 954, 816, 795, 761, 775, 736, 707, 660, 623, 599, 571, 493, 475. Anal. Calcd for $C_{19}H_{15}N_5$: C, 72.83; H, 4.82; N, 22.35. Found: C, 72.75; H, 4.80; N, 22.32.

*4.2.3. N-(3-(Thiophen-2-yl)H-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1c**).* Yield: 0.86 g (65%). Mp 170 °C; HRMS-Mass: calcd for $C_{17}H_{13}N_5S^+$ 319.0892 found (M^++H) 320.0893. 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 9.23 (1H, s), 8.60 (2H, m), 8.26 (1H, d, 8.4), 7.92 (1H, t, 8.0), 7.80 (1H, t, 7.6), 7.50 (1H, d, 4.4), 7.50 (1H, s), 7.40 (1H, d, 6), 7.34 (1H, t, 6.4), 7.20 (1H, t, 3.2), 6.70 (2H, m). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 153.0, 151.0, 148.2, 148.1, 140.6, 136.4, 133.0, 128.0, 126.0, 125.2, 124.4, 124.0, 121.6, 121.0, 120.0, 117.0, 115.2. FTIR (KBr, cm^{-1}): 1635, 1619, 1591, 1562, 1530, 1497, 1472, 1447, 1410, 1391, 1320, 1300, 1245, 1146, 1097, 1048, 1030, 997, 908, 843, 797, 742, 729, 714, 684, 648, 625, 572, 523, 489. Anal. Calcd for $C_{17}H_{13}N_5S$: C, 63.93; H, 4.10; N, 21.93. Found: C, 63.88; H, 4.08; N, 21.85.

*4.2.4. N-(3-(4-Methoxyphenyl)H-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1d**).* Yield: 1.06 g (75%). Mp 165 °C; HRMS-Mass: calcd for $C_{20}H_{17}N_5O$ 343.1433, found 344.1576 (M^++H). 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 9.30 (1H, s), 8.60(2H, d, 8.8), 8.13 (1H, d, 7.2), 7.90 (1H, d, 9.2), 7.80 (3H, m), 7.38 (1H, s), 7.32 (1H, t, 7.2), 7.06 (2H, d, 8.4), 6.63 (1H, t, 9.2), 6.65 (1H, t, 11.2), 3.09 (3H, s). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 159.8, 153.0, 150.70, 150.64, 148.1, 136.5, 133.0, 129.3, 125.2, 124.3, 123.2, 121.6, 120.4, 119.7, 116.5, 114.5, 114.4, 55.6. FTIR (KBr, cm^{-1}): 1636, 1625, 1584, 1562, 1523, 1470, 1382, 1312, 1284, 1247, 1235, 1186, 1176, 1135, 1111, 1049, 1036, 1017, 994, 954, 838, 802, 749, 723, 707, 681, 616, 579, 501, 486, 446, 429. Anal. Calcd for $C_{20}H_{17}N_5O$: C, 69.96; H, 4.99; N, 20.40. Found: C, 69.82; H, 4.93; N, 20.33.

*4.2.5. N-(3-(Pyren-2-yl)H-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1e**).* Yield: 1.48 g (82%). Mp 214 °C; HRMS-Mass: calcd for $C_{29}H_{19}N_5$ $^+$ 437.1640, found (M^++H) 438.1929. 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 9.35 (1H, s), 8.70(1H, d, 8.0), 8.60 (1H, d, 4.8), 8.20 (10H, m), 7.85 (1H, t, 7.6), 7.70 (1H, d, 7.6), 7.42 (1H, s), 7.40 (1H, t, 5.6), 6.76 (1H, t, 6.4), 6.55 (1H, t, 7.2). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 153.0, 151.0, 148.1, 141.0, 136.5, 132.2, 132.0, 131.4, 131.0, 131.0, 129.0, 128.4, 128.0, 127.4, 126.4, 126.0, 125.6, 125.4, 125.1, 125.0, 124.7, 124.5, 124.3, 122.0, 121.0, 119.5, 117.2, 114.4. FTIR (KBr, cm^{-1}): 1619, 1586, 1563, 1532, 1500, 1467, 1443, 1385, 1316, 1253, 1179, 1141, 1096, 1064, 994, 950, 847, 832, 801, 746, 729, 715, 682, 642. Anal. Calcd for $C_{29}H_{19}N_5$: C, 79.60; H, 4.38; N, 16.01. Found: C, 79.42; H, 4.28; N, 15.94.

*4.2.6. N-(3-(Anthracen-9-yl)H-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1f**).* Yield: 1.19 g (70%). Mp 240 °C; HRMS-Mass: calcd for $C_{27}H_{19}N_5$ 413.1640 found (M^++H) 414.1781. 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 10.70 (1H, s), 9.10 (2H, d, 8.8), 8.70 (1H, s), 8.52 (1H, s), 8.13 (3H, m), 8.05 (2H, d, 8.0), 7.70 (2H, d, 8.4), 7.54 (4H, m), 7.15 (1H, d, 6.8), 7.00 (1H, t, 6.4), 6.50 (1H, t, 6.8). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 153.1, 140.0, 134.0, 132.0, 132.0, 132.0, 131.0, 130.0, 130.0, 129.0, 129.0, 127.3, 127.0, 127.0, 126.0, 126.0, 126.0, 125.4, 123.0, 122.0, 120.4, 118.6, 114.0. FTIR (KBr, cm^{-1}): 3048, 1621, 1550, 1505, 1441, 1365, 1314, 1294, 1230, 1134, 1096, 1051, 1014, 990, 955, 914, 888, 849, 787, 760, 728, 707, 590, 571, 538, 512. Anal. Calcd for $C_{27}H_{19}N_5$: C, 78.43; H, 4.63; N, 16.94. Found: C, 78.30; H, 4.57; N, 16.91.

*4.2.7. N-(3-p-TolylH-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1g**).* Yield: 1.05 g (78%). Mp 164 °C; HRMS-Mass: calcd for $C_{20}H_{17}N_5$ 327.1484 found (M^++H) 328.1643. 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 9.30 (1H, s), 8.60 (2H, m), 8.16 (1H, d, 10.8), 7.90 (1H, d, 8.4), 7.79 (1H, t, 12.0), 7.73 (2H, d, 8.0), 7.33 (4H, m), 6.64 (1H, t, 6.4), 6.55 (1H, t, 6.8), 2.43 (3H, s). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 153.0, 150.6, 148.0, 140.4, 138.2, 136.4, 133.0, 130.0, 128.0, 128.0, 125.3, 124.2, 121.5, 120.4, 119.6, 116.5, 114.4, 21.5. FTIR (KBr, cm^{-1}): 3423, 3278, 3054, 2994, 2912, 2851, 1633, 1621, 1587, 1559, 1523, 1504, 1469, 1446, 1388, 1311, 1297, 1251, 1185, 1135, 1108, 1033, 995, 954, 824, 801, 748, 727, 714, 626, 577, 503. Anal. Calcd for $C_{20}H_{17}N_5$: C, 73.37; H, 5.23; N, 21.39. Found: C, 73.25; H, 5.20; N, 21.32.

*4.2.8. N-(3-(2-Bromophenyl)H-imidazo[1,5-a]pyridin-1-yl)picolinamidine (**1h**).* Yield: 0.97 g (60%). Mp 174 °C; HRMS-Mass: calcd for $C_{19}H_{14}BrN_5$ 391.0433 found (M^++^{23}Na) 414.0693. 400 MHz ^{1}H NMR (δ (*J*, Hz), $CDCl_3$): 9.20 (1H, s), 8.60 (2H, m), 7.94 (1H, d, 8.8), 7.81 (1H, t, 7.6), 7.76 (1H, d, 8.4), 7.64 (1H, d, 7.6), 7.57 (1H, d, 7.2), 7.48 (1H, t, 7.6), 7.36 (3H, m), 6.73 (1H, t, 6.4), 6.61 (1H, t, 7.2). 100 MHz ^{13}C NMR (δ, $CDCl_3$): 153.0, 151.0, 148.0, 140.0, 136.5, 133.5, 133.1, 131.6, 131.5, 131.0, 128.0, 125.0, 124.3, 124.2, 121.5, 121.2, 119.3, 117.0, 114.0. FTIR (KBr, cm^{-1}): 3459, 3324, 3192, 2976, 2919, 1618, 1587, 1562, 1504, 1428, 1370, 1295, 1266, 1248, 1204, 1180, 1135, 1059, 992, 891, 812, 796, 752, 732, 694, 640, 570, 524, 456. Anal. Calcd for $C_{19}H_{14}BrN_5$: C, 58.18; H, 3.60; N, 17.85. Found: C, 58.05; H, 3.52; N, 17.76.

*4.2.9. 2-(2-Pyridyl)-4,5-bis(2-hydroxyphenyl)imidazole (**2a**).* A mixture of salicylaldehyde (1.0 g, 8.26 mmol), 2-cyanopyridine (0.430 g, 4.13 mmol) and ammonium acetate (1.27 g, 16.52 mmol) in PEG-400 (2.0 g) was heated at 100 °C in an oil-bath for 12 h. The mixture was cooled and then added to water (50 mL) with stirring. After stirring for 1 h, the yellow precipitate was filtered washed with water, dried in vacuum over P_4O_{10} and recrystallized from dichloromethane. Yield of **2a**: 0.89 g (65%).

Compounds 2-(2-pyridyl)-4,5-bis(phenyl)imidazole (**2b**) and 2-(2-pyridyl)-4,5-bis(2-thienyl)imidazole (**2c**) were synthesized by adopting the same procedure described for **2a**.

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Supplementary data

CIF for **1a**, **2b** and ^{1}H NMR, ^{13}C NMR and HRMS of **1a**–**h** and **2a**–**c**. Crystallographic data (excluding structure factors) for the structure **1a** and **2b** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC # 848475 and 848476. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2012.03.095.

References and notes

1. Couty, F.; Evano, G. In; Katritzky, A. R., Ramsden, C. A., Eric, F. V. A. A. A., Taylor, R. J. K., Eds. *Comprehensive Heterocyclic Chemistry III*; Elsevier Ltd.: 2008; Vol. 11, pp 435–443.
2. Ford, N. F.; Browne, L. J.; Campbell, T.; Gemenden, C.; Goldstein, R.; Gude, C.; Wasley, J. W. F. *J. Med. Chem.* **1985**, *28*, 164–170.
3. Davey, D.; Erhardt, P. W.; Lumma, W. C., Jr.; Wiggins, J.; Sullivan, M.; Pang, D.; Cantor, E. *J. Med. Chem.* **1987**, *30*, 1337–1342.
4. Browne, L. J.; Gude, C.; Rodriguez, H.; Steele, R. E. *J. Med. Chem.* **1991**, *34*, 725–736.
5. Davey, D. D. *J. Org. Chem.* **1987**, *52*, 1863–1867.
6. Bower, J. D.; Ramage, G. R. *J. Chem. Soc.* **1955**, 2834–2837.
7. Palacios, F.; Alonso, C.; Rubiales, G. *Tetrahedron* **1995**, *51*, 3683–3690.
8. Krapcho, A. P.; Powell, J. R. *Tetrahedron Lett.* **1986**, *27*, 3713–3714.
9. Sasaki, K.; Tsurumori, A.; Hirota, T. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3851–3856.
10. Katritzky, A. R.; Qiu, G. *J. Org. Chem.* **2001**, *66*, 2862–2864.
11. Bluhm, M. E.; Ciesielski, M.; Görls, H.; Döring, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 2962–2965.
12. Wang, J.; Mason, R.; VanDerveer, D.; Feng, K.; Bu, X. R. *J. Org. Chem.* **2003**, *68*, 5415–5418.
13. Wang, J.; Dyers, L., Jr.; Mason, R., Jr.; Amoyaw, P.; Bu, X. R. *J. Org. Chem.* **2005**, *70*, 2353–2356.
14. Kim, D.; Wang, L.; Hale, J. J.; Lynch, C. L.; Budhu, R. J.; MacCoss, M.; Mills, S. G.; Malkowitz, L.; Gould, S. L.; DeMartino, J. A.; Springer, M. S.; Hazuda, D.; Miller, M.; Kessler, J.; Hrin, R. C.; Carver, G.; Carella, A.; Henry, K.; Lineberger, J.; Schleif, W. A.; Emini, E. A. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2129–2134.
15. Shibahara, F.; Kitagawa, A.; Yamaguchi, E.; Murai, T. *Org. Lett.* **2006**, *8*, 5621–5624.
16. Shibahara, F.; Sugiura, R.; Yamaguchi, E.; Kitagawa, A.; Murai, T. *J. Org. Chem.* **2009**, *74*, 3566–3568.
17. Crawforth, J. M.; Paoletti, M. *Tetrahedron Lett.* **2009**, *50*, 4916–4918.
18. Shibahara, F.; Yamaguchi, E.; Kitagawa, A.; Imai, A.; Murai, T. *Tetrahedron* **2009**, *65*, 5062–5073.
19. Tahara, S.; Shibahara, F.; Maruyama, T.; Murai, T. *Chem. Commun.* **2009**, 7009–7011.
20. Arvapalli, V. S.; Chen, G.; Kosarev, S.; Tan, M. E.; Xie, D.; Yet, L. *Tetrahedron Lett.* **2010**, *51*, 284–286.
21. Zhang, A.; Zheng, X.; Fan, J.; Shen, W. *Tetrahedron Lett.* **2010**, *51*, 828–831.
22. Niyomura, O.; Yamaguchi, Y.; Tamura, S.; Minoura, M.; Okamoto, Y. *Chem. Lett.* **2011**, *40*, 449–451.
23. Huang, C.; Giokaris, A.; Gevorgyan, V. *Chem. Lett.* **2011**, *40*, 1053–1054.
24. Yamaguchi, E.; Shibahara, F.; Murai, T. *Chem. Lett.* **2011**, *40*, 939–940.
25. Fulwa, V. K.; Manivannan, V. *Tetrahedron Lett.* **2012**, *53*, 2420–2423.
26. Fulwa, V. K.; Sahu, R.; Jena, H. S.; Manivannan, V. *Tetrahedron Lett.* **2009**, *50*, 6264–6267.
27. Jiang, B.; Wang, X.; Shi, F.; Tu, S. J.; Ai, T.; Ballew, A.; Li, G. *J. Org. Chem.* **2009**, *74*, 9486–9489.
28. Wu, X.; Jiang, R.; Xu, X.; Su, X.; Lu, W.; Ji, S. *J. Comb. Chem.* **2010**, *12*, 829–835.
29. X-ray diffraction data: **1a**: (296(2) K, Mo Kα): $C_{19}H_{15}N_5O$, 329.34, $P2_1/n$, a=8.9812(7), b=12.1712(11), c=15.0575(13) Å, β=100.863(6)°, V=1616.5(2) Å^3, Z=4, D_{calcd}=1.345 g cm^{-3}, μ=0.88 mm^{-1}, F(000)=688, R_{int}=0.0487, R_1 ($I > 2\sigma$)=0.0399, wR_2 ($I > 2\sigma$)=0.1030 (227 param., 1213 obsd refl., 1473 unique).
30. X-ray diffraction data: **2b**: (296(2) K, Mo Kα): $C_{20}H_{14}N_3$, 296.34, $C2/c$, a=23.5453(12), b=11.1287(7), c=13.0794(7) Å, β=116.320(5)°, V=3071.9 (3) Å^3, Z=8, D_{calcd}=1.282 g cm^{-3}, μ=0.77 mm^{-1}, F(000)=1248, R_{int}=0.0598, R_1 ($I > 2\sigma$)=0.0423, wR_2 ($I > 2\sigma$)=0.1150 (212 param., 2049 obsd refl., 2684 unique).
31. Sheldrick, G. M. *SADABS*; University of Göttingen: Göttingen, Germany, 1996.
32. SMART and SAINT; Siemens Analytical X-ray Instruments: Madison, WI, 1996.
33. Sheldrick, G. M. *SHELXS-97 and SHELXL-97*; University of Göttingen: Göttingen, Germany, 1997.