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Tandem and transition metal-free synthesis of novel benzoimidazo-quinazoline as highly selective Hg^{2+} sensors

Morteza Shiri[1] · Majid M. Heravi[1] · Zeinab Faghihi[1] · Vahideh Zadsirjan[1] · Masoumeh Mohammadnejad[1] · Maryam Ranjbar[1]

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Abstract A one-pot procedure for the synthesis of novel planar aza-heterocycles possessing good fluorescence potencies was described. These benzoimidazopyrimido[4,5-*b*]quinolone derivatives came from the reaction of 2-chloroquinoline-3-carboxaldehydes and 2-aminobenzimidazole using K_2CO_3 in DMF. The fluorescence study of these conjugated systems was also considered, which revealed that they have highly selective sensing of mercury. Consequently, to investigate another aspect of the reaction, a three-component reaction was developed by adding malononitrile to the aforementioned starting materials in the presence of L-proline under reflux condition in H_2O/EtOH to provide amino-quinolin-3-yl-dihydrobenzoimidazo-pyrimidine-3-carbonitriles in good yields.

Keywords One-pot synthesis · Transition metal-free · Fluorescent · 2-Aminobenzimidazole · 2-Chloroquinoline-3-carboxaldehydes

Introduction

Quinolines are one of the most prevalent *N*-heteroaromatic molecules [1–4] incorporated into the buildings of various pharmaceuticals [5–11]. 2-Chloroquinoline-3-carbaldehydes are imperative quinolines employed for the formation of a number of heterocyclic compounds [12–14]. Benzimidazoles [15] are also found exclusively in many drugs [16–19]. For instance, 2-substituted-5-amino-benzimidazoles are known for cytotoxic activities [20]. According to the reports, the fused heterocycles [21, 22] are frequently of greater application than the monocyclic structures [23, 24]

✉ Morteza Shiri
mshiri@alzahra.ac.ir

[1] Department of Chemistry, Alzahra University, Vanak, Tehran 1993893973, Iran

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involving functional materials [25], molecular recognition [26], medicinal chemistry [27], and coordination chemistry [28]. A few fused-ring structures including the benzimidazole and quinazolinone structures have been explored to show a powerful immunosuppressive property [29] or antiproliferative activity in human tumor cell lines [30, 31].

Fluorescent probes for identifying heavy metal ions in biological and environmental systems have obtained significant attention [32]. One of the main and most hazardous impurity metal ions is mercury that can exert long-standing contaminative effects and create severe health difficulties because of its capability to pass via biological membranes [33]. Henceforth, there is a great need to plan, manufacture, and employ fluorescent sensors with extraordinary selectivity and sensitivity for Hg^{2+}.

Recently, benzo[4.5]imidazo[2,1-b]quinazolin-12-ones were synthesized from 2-aminobenzimidazole and 2-haloaroyl chlorides [34]. Also, Ma et al. [34] synthesized a range of benzo[4,5]imidazo[1,2-*a*]quinazoline and imidazo[1,2-*a*]quinazoline derivatives. To the best of our knowledge, there are only a few reports on the synthesis of such planar-fused heterocycles as mentioned above. The planarity of these fused systems allows them to easily interact with DNA for use in human tumor research [31, 35]. The assemblage of quinoline to pyrimidine and imidazole would lengthen the conjugated systems. A compound comprising more than four *N*-containing fused heterocycles seems plausible to acquire new thought-provoking potencies. Accordingly, in continuation of our research in developing heterocyclic compounds including 2-chloroquinoline-3-carbaldehydes [36–43], we employed a method to accumulate these various aromatic heterocycles via a one-pot tandem procedure. The two-component products, benzo-imidazopyrimido [4,5-*b*]quinolones, and the subsequent three-component derivatives, amino-quinolin-3-yl-dihydrobenzo-imidazo-pyrimidine-3-carbonitriles, were developed in easy mild conditions which are discussed here.

Experimental

General

Melting points were taken by using a 9200-Branread Electrothermal apparatus. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker 300 and 400 spectrometers. ^{1}H-NMR spectra were referenced to tetramethylsilane (0.00 ppm) using DMSO-d_6 or $CDCl_3$ as solvents. ^{13}C-NMR spectra were referenced to solvent carbons. IR spectra were recorded using a FT-IR Tensor 27. A Leco CHNS, model 932, was used for elemental analysis.

Synthesis of 3a–f: general procedure

A mixture of 1*H*-benzo[*d*]imidazole-2-amine **1** (1.0 mmol), 2-chloro-quinoline-3-carbaldehydes **2** (1.1 mmol) and K_2CO_3 (1 mmol) in DMF (5 mL) was stirred at

120 °C under reflux condition (or under MW conditions, 120 °C, 5 × 1 min) TLC was employed to monitor the end of the reaction. It was then poured onto water (20 mL) to precipitate a yellowish product. The pure product was collected after filtering and simply washing with water.

Synthesis of 4a–g: general procedure

A mixture of 1*H*-benzo[*d*]imidazole-2-amine 1 (1 mmol), 2-chloroquinoline-3-carbaldehydes 2 (1 mmol) and malononitrile (1.1 mmol) in the presence of L-proline (0.15 mmol) in EtOH/H_2O (1:1, 5 mL) was stirred under reflux condition for an appropriate reaction time. The progress of the reaction was monitored by TLC. Then, the mixture was cooled to room temperature, filtered off, and the obtained solid residue was washed with H_2O. The crude products were purified by recrystallization from EtOH and H_2O.

Experimental and physical data

*Benzo[4',5']imidazo[2',1':2,3]pyrimido[4,5-b]quinolone (**3a**)*

Yellow powder (95%), m.p. > 300 °C, Anal. calcd. for $C_{17}H_{10}N_4$: C, 75.54; H, 3.73; N, 20.73, Found: C, 75.62; H, 3.57; N, 20.51, FT-IR (KBr): ν_{max} = 3021, 1608, 1551, 1515, 1466, 1438, 1253, 1170, 730 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 7.64 (2H, m, CH-19, 20), 7.20 (1H, t, J = 14.8 Hz, J = 7.8 Hz, CH-1), 8.02 (1H, t, J = 15 Hz, J = 7.8 Hz, CH-2), 8.12 (2H, m, CH-18, 21), 8.33 (1H, d, J = 8.4 Hz, CH-6), 8.93 (1H, s, CH-10), 9.22 (1H, d, J = 8.4 Hz, CH-3), 9.35 (1H, s, CH-14) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 116.4, 119.9, 124.2, 124.9, 126.6, 128.0, 130.0, 133.9, 141.1 ppm.

*10-Methylbenzo[4',5']imidazo[2',1':2,3]-pyrimido[4,5-b]quinolone (**3b**)*

Yellow powder (90%), m.p. > 300 °C; Anal. calcd. for $C_{18}H_{12}N_{4-}$: C, 76.04; H, 4.25; N, 19.71, Found: C, 76.12; H, 4.17; N, 19.60, FT-IR (KBr): ν_{max} = 3012, 1603, 1550, 1509, 1444, 1222, 822, 758, 733 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.66 (3H, s, CH_3), 7.63 (2H, m, CH-19, 20), 7.86 (1H, d, J = 8.4 Hz, CH-21), 7.87 (1H, s, CH-6), 8.12 (1H, d, J = 7.2 Hz, CH-2), 8.24 (1H, d, J = 8.4 Hz, CH-18), 8.80 (1H, s, CH-10), 9.24 (1H, d, J = 7.2 Hz, CH-21), 9.30 (1H, s, CH-6) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 21.6, 116.6, 120.6, 124.6, 125.2, 125.6, 127.8, 128.4, 136.2, 136.8, 138.5, 145.6, 148.1, 158.3 ppm.

*12-Methylbenzo[4',5']imidazo[2',1':2,3]-pyrimido[4,5-b]quinoline (**3c**)*

Yellow powder (85%), m.p. > 300 °C; Anal. calcd. for $C_{18}H_{12}N_4$: C, 76.04; H, 4.25; N, 19.71, Found: C, 76.12; H, 4.12; N, 19.52; FT-IR (KBr): ν_{max} = 3012, 1603, 1550, 1509, 1444, 1222, 822, 758, 733 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 2.58 (3H, s, CH_3), 7.60 (2H, m, CH-19, 20), 7.94 (2H, m, CH-1, 2), 8.05 (1H, m,

CH-6), 8.22 (1H, d, J = 6.0 Hz, CH-21), 9.15 (1H, d, J = 6.0 Hz, CH-18), 9.24 (1H, s, CH-10), 9.48 (1H, s, CH-14) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 20.1, 116.3, 119.8, 124.1, 124.8, 136.2, 140.1, 144.0, 145.1, 160.1 ppm.

*10-Methoxybenzo[4',5']imidazo[2',1':2,3]-pyrimido[4,5-b]quinolone (**3d**)*

Yellow powder, m.p. > 300 °C; Anal. calcd. for $C_{18}H_{12}N_4O$: C, 71.99; H, 4.03; N, 18.66; Found: C, 71.74; H, 4.12; N, 18.54; FT-IR (KBr): ν_{max} = 3048, 1605, 1557, 1516, 1257, 1167, 1027 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 3.99 (3H, s, OCH_3), 7.27 (1H, m, CH-6), 7.50 (1H, m, CH-2), 7.59 (2H, m, CH-19, 20), 7.89 (1H, d, J = 9 Hz, CH-3), 8.01 (2H, m, CH-18, 19), 8.65 (1H, s, CH-10), 9.16 (1H, s, CH-14) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 53.5, 106.6, 111.2, 111.9, 117.2, 120.2, 121.9, 124.9, 128.1, 129.8, 130.5, 132.4, 134.1, 135.1, 140.0, 143.4, 147.0, 149.3, 154.3 ppm.

*11-Methoxybenzo[4',5']imidazo[2',1':2,3]-pyrimido[4,5-b]quinolone (**3e**)*

Yellow powder (83%), m.p. > 300 °C; Anal. calcd. for $C_{18}H_{12}N_4O$ (MW = 300.31), C, 71.99; H, 4.03; N, 18.66; Found: C, 71.73; H, 4.19; N, 18.52; FT-IR (KBr): ν_{max} = 3015, 1601, 1555, 1513, 1236, 1161, 754 cm^{-1}; ^{1}H-NMR (00 MHz, DMSO-d_6): δ = 4.07 (3H, s, OCH_3), 7.40 (H, m, CH-1) 7.55 (2H, m, CH-19, 20), 7.75 (1H, s, CH-3), 7.95 (1H, CH-6), 8.25 (1H, d, J = 6.0 Hz, CH-21), 9.15 (1H, d, J = 6.0 Hz, CH-18), 9.25 (1H, s, CH-10), 9.40 (1H, s, CH-14) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 56.1, 106.5, 106.7, 111.3, 116.5, 116.8, 119.7, 119.9, 123.8, 124.0, 124.9, 125.2. 131.3, 131.4, 140.2, 140.3, 142.7, 159.6 ppm.

*Benzo[h]benzo[4',5']imidazo[2',1':2,3]-pyrimido[4,5-b]quinoline (**3f**)*

Yellow powder (85%), m.p. > 300 °C; Anal. calcd. for $C_{21}H_{12}N_4$: C, 78.73; H, 3.78; N, 17.49; Found: C, 78.80; H, 3.70; N, 17.57; FT-IR (KBr): ν_{max} = 3026, 1598, 1553, 1508, 1454, 1390, 769, 739 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 7.62 (3H, m, CH-19, 20, 23), 7.80 (4H, m, CH-21, 22, 24), 8.16 (1H, d, J = 6.8 Hz, CH-3), 8.78 (1H, s, CH-10), 9.25 (2H, m, CH-6, 25), 9.39 (1H, s, CH-14) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 117.2, 119.4, 125.4, 125.9, 126.3, 126.4, 128.4, 128.6, 129.1, 129.3, 130.1, 131.3, 135.6, 140.1, 144.1 ppm.

*4-Amino-2-(2-chloroquinolin-3-yl)-1,2-dihydrobenzo[4,5]imidazo [1,2-a] pyrimidine-3-carbonitrile (**4a**)*

Yellow powder, m.p.: 260–263 °C; Anal. Calcd. for $C_{20}H_{13}ClN_6$: C, 64.43; H, 3.51; N, 22.54; Found: C, 64.28; H, 3.37; N, 22.39; FT-IR (KBr): ν_{max} = 3478, 3385, 3122, 3061, 3005, 2867, 2187, 1869, 1668, 1618, 1594, 1563, 1471, 1445 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): 5.83 (1H, s, CH-11), 7.02 (2H, s, NH_2), 7.17 (4H, m, CH-21-24), 7.87 (4H, m, CH-1-3, 6), 8.57 (2H, s, NH, CH-10) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 52.0, 60.6, 113.1, 119.1, 120.6, 123.9, 127.4,

128.0, 128.2, 128.8, 129.8, 131.8, 133.1, 138.8, 144.0, 147.0, 149.3, 150.2, 150.3, 152.2 ppm.

*4-Amino-2-(2-chloro-6-methoxyquinolin-3-yl)-1,2 dihydrobenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile (**4b**)*

Yellow powder, m.p.: 263–266 °C; Anal. calcd. for $C_{21}H_{15}ClN_6O$: C, 62.61; H, 3.75; N, 20.86; Found: C, 62.52; H, 3.85; N, 20.95; FT-IR (KBr): ν_{max} = 3477, 3377, 3121, 3003, 2874, 2177, 1666, 1620, 1591, 1473, 1447 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 3.89 (3H, s, OCH_3), 5.79 (1H, s, CH-11), 7.00 (1H, s, NH), 7.17 (4H, m, CH-21-24), 7.69 (5H, m, NH_2, CH-2, 3, 6), 8.41 (1H, s, CH-10) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): δ = 51.9, 56.2, 60.6, 106.5, 113.0, 116.7, 120.6, 123.9, 124.2, 128.8, 129.4, 129.8, 133.4, 137.4, 143.0, 146.4, 150.2, 158.5 ppm.

*4-Amino-2-(2-chloro-6-methylquinolin-3-yl)-1,2-dihydrobenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile (**4c**)*

Yellow powder, m.p.: 256–259 °C; Anal. calcd. for $C_{21}H_{15}ClN_6$: C, 65.20; H, 3.91; N, 21.72; Found: C, 65.11; H, 3.79; N, 21.58; FT-IR (KBr): ν_{max} = 3472, 3374, 3124, 2886, 2183, 1666, 1624, 1593, 1474, 1446 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 5.79 (1H, s, CH-11), 7.00 (1H, s, NH), 7.17 (4H, m, CH-21-24), 7.80 (5H, m, NH_2, CH-2, 3, 6), 8.40 (1H, s, CH-10) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): 21.5, 51.9, 60.6, 113.0, 116.7, 119.0, 120.6, 123.9, 127.4, 127.4, 127.7, 129.8, 133.1, 133.9, 137.9, 137.9, 145.6, 148.3, 150.2, 150.2, 152.1 ppm.

*4-Amino-2-(2-chloro-8-methylquinolin-3-yl)-1,2-dihydrobenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile (**4d**)*

Yellow powder, m.p.: 262–265 °C; Anal. calcd. for $C_{21}H_{15}ClN_6$: C, 65.20; H, 3.91; N, 21.72; Found: C, 65.28; H, 3.79; N, 21.57; FT-IR (KBr): ν_{max} = 3408, 3263, 3141, 2187, 1677, 1631, 1599, 1470, 1441, 1401 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 2.70 (3H, s, CH_3-26), 5.84 (1H, s, CH-11), 7.15 (4H, m, CH-21-24), 7.75 (5H, m, NH_2, CH-1, 2, 6), 8.52 (1H, s, CH-10), 8.57 (1H, s, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): 17.9, 51.9, 60.7, 112.9, 116.7, 119.0, 120.6, 123.9, 126.6, 127.5, 127.9, 129.8, 131.7, 132.8, 135.9, 139.1, 143.9, 146.1, 148.3, 150.2, 152.2 ppm.

*4-Amino-2-(2,6-dichloroquinolin-3-yl)-2,10-dihydrobenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile (**4e**)*

Yellow powder, m.p.: 220–225 °C; Anal. calcd. for $C_{20}H_{12}C_{l2}N_6$ C, 58.98; H, 2.97; N, 20.64; Found: C, 58.87; H, 2.76; N, 20.51; FT-IR (KBr): ν_{max} = 3391, 3321, 3319, 2857, 2177, 1672, 1645, 1595, 1473, 1449 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 5.83 (1H, s, CH-11), 7.03 (1H, s, NH), 7.16 (4H, m, CH-21-24), 7.89 (5H, m, NH_2, CH-1, 2, 6), 8.59 (1H, s, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): 51.9,

60.3, 113.1, 116.7, 119.0, 120.6, 123.9, 127.5, 128.3, 129.8, 130.1, 132.2, 132.5, 134.3, 138.1, 143.9, 145.5, 149.8, 150.4, 152.1 ppm.

*4-Amino-2-(2-chloropyridin-3-yl)-2,10-dihydrobenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile (**4f**)*

Yellow powder, m.p.: 234–238 °C; Anal. calcd. for $C_{16}H_{11}ClN_6$ C, 59.54; H, 3.44; N, 26.04; Found C, 59.43; H, 3.48; N, 26.11; FT-IR (KBr): ν_{max} = 3483, 3384, 3124, 2920, 2182, 1666, 1624, 1561, 1475, 1449 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 5.67 (1H, s, CH-9), 7.00 (1H, s, NH), 7.16 (4H, m, CH-17, 20), 7.89 (4H, m, NH_2, CH-1, 2, 6), 8.42 (1H, s, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): 51.4, 60.4, 113.0, 116.7, 118.9, 120.6, 123.9, 124.5, 129.8, 136.2, 138.5, 143.9, 149.0, 149.9, 150.3, 152.1 ppm.

*4-Amino-2-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)-2,10-dihydrobenzo-[4,5] imidazo-[1,2-a]pyrimidine-3-carbonitrile (**4g**)*

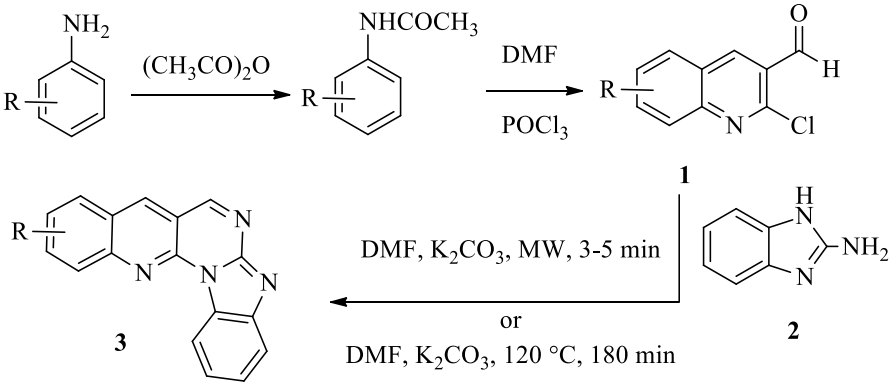
Yellow powder, m.p.: 242–246 °C; Anal. calcd. for $C_{21}H_{16}ClN_7$ C, 62.77; H, 4.01; N, 24.40; Found C, 62.66; H, 4.11; N, 24.23; FT-IR (KBr): ν_{max} = 3451, 3264, 3041, 2922, 2852, 2229, 1677, 1674, 1502, 1473, 1441 cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 2.19 (3H, s, Me), 4.41 (1H, s, NH), 5.42 (1H, s, CH-13), 7.15 (4H, m, CH-23-26), 7.89 (6H, m, NH_2, CH-7-11), 8.38 (1H, s, NH) ppm; ^{13}C-NMR (100 MHz, DMSO-d_6): 12.3, 43.3, 57.5, 109.5, 110.6, 117.3, 119.0, 119.4, 124.7, 126.3, 128.5, 129.2, 130.5, 137.1, 139.6, 147.0, 150.4, 157.8, 167.3 ppm.

Results and discussion

Initially, 2-chloroquinoline-3-carbaldehydes were synthesized according to the published procedure [44]. The reaction condition was optimized with 2-chloro-3-quinolinecarboxaldehyde **1a** and 1*H*-benzo[*d*]imidazole-2-amine **2** leading to **3a** (Scheme 1).

As shown in Table 1, Cs_2CO_3 was as equally efficient as K_2CO_3, and a strong inorganic base like NaOH and KOH did not favor the reaction (Table 1, entries 1–4). K_2CO_3 at 120 °C afforded the best yields (Table 1, entry 5). Moreover, among solvents such as EtOH, MeCN and DMF, the latter provided the best yields (Table 1). The reaction was also repeated under MW irradiation, which afforded the desired products in the shortest time.

A variety of 2-chloro-3-quinolinecarboxaldehydes containing electron-donating and electron-deficient substituents were then examined under both thermal and microwave conditions (Fig. 1). The best yield resulted from the reaction of 2-aminobenzimidazole with aldehydes containing electron-donating groups. The aldehydes containing electron-withdrawing groups such as Cl and Br were also examined. In the case of bromide, no product was almost formed even at lengthier time. Aldehydes containing chloride afforded the main products in very low yield, as did a mixture of side products.



R= H, 2-Me, 4-Me, 4-OMe, 3-OMe, 4,5-fused benzen

Scheme 1 Reaction of 2-aminobenzimidazole and 2-chloro-3-quinolinecarboxaldehyde

Table 1 Optimization of reaction conditions

Entry	Solvent	Catalyst	Temp (°C)	Time	Yield (%)[a]
1	DMF	Cs_2CO_3	100	3 h	71
2	DMF	K_2CO_3	100	3 h	70
3	DMF	NaOH	100	3 h	20
4	DMF	KOH	100	3 h	30
5	DMF	KtOBu	100	3 h	40
6	DMF	K_2CO_3	120	3 h	90
7	EtOH	HOAc	100	3 h	60
8	EtOH	L-proline	100	3 h	23
9	MeCN	L-proline	100	3 h	30
10	DMF	K_2CO_3	MW	5 min	91

Reaction conditions: 2-aminobenzimidazole (1 mmol), 2-chloro-3-quinolinecarboxaldehyde **2a** (1.1 mmol) and catalyst (1 equiv) in solvent (5 mL)

[a]Isolated yield

To extend the reaction scope, 2-aminobenzimidazole was replaced by more polar nitrogen containing the anlogue, 3-amino-1,2,4-triazole, and the reaction was repeated under the same conditions. The reaction with 2-chloroquinoline-3-carbaldehyde **2a** in the presence of K_2CO_3 in DMF under both reflux and MW conditions did not provide any of the desired product.

Next, we examined a three-component reaction adding malononitrile as a third fraction to investigate the cyclization pattern and the desired product. 2-Aminobenzimidazole **1**, 2-chloroquinoline-3-carbaldehyde **2a** and malononitrile were reacted under the same condition of K_2CO_3 in DMF/reflux. Interestingly, the characterization of the product demonstrated that the malononitrile had not participated in the

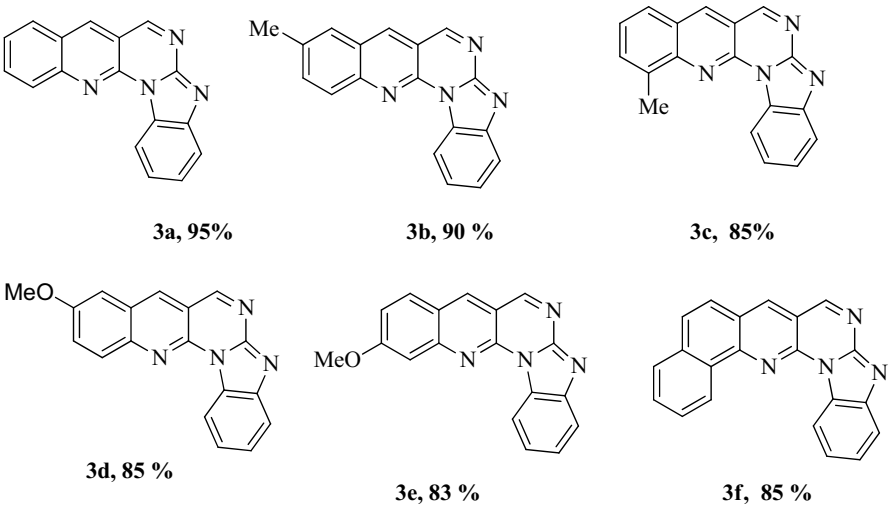
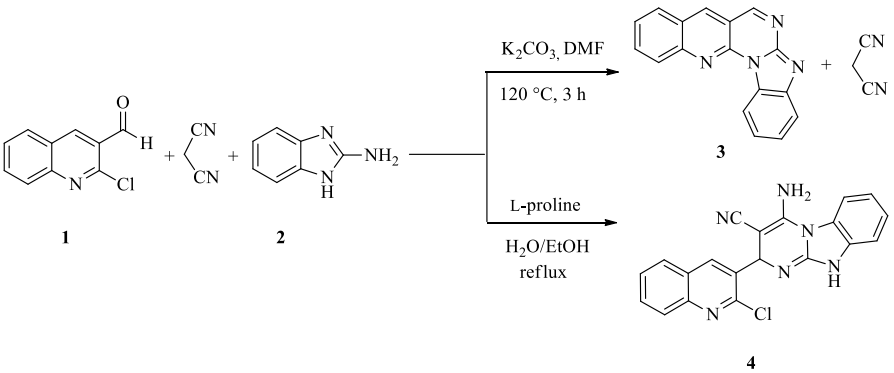


Fig. 1 Various benzo-imidazopyrimido-[4,5-*b*]quinolones **3a**–**f**

reaction and **3a** had been isolated again (Scheme 2). Changing the condition to EtOH/H_2O and L-proline as catalyst under the reflux condition provided a new product, characterized to be an imidazo-pyrimidine derivative **4a** (Scheme 2). ^{1}H-NMR spectrum of the purified product depicted the key signals including a down-fielded sharp singlet for benzylic hydrogen at 5.8 ppm, and three mobile hydrogens at 7.7 and 8.6 ppm for the NH and NH_2 groups, respectively. It also displayed 9 aromatic protons in predicted chemical shifts between 7.0 and 8.6 ppm.

To reach the best conditions for expanding the reaction, various solvents and quantities of the catalyst was tried. The best yield of the desired product was obtained in EtOH/H_2O as solvent and L-proline as catalyst. This optimal reaction



Scheme 2 Three-component reaction of 2-chloro-quinoline-3-carbaldehydes, 2-aminobenzimidazole and malononitrile

condition was then applied to the synthesis of different derivatives to establish the generality of the method (Fig. 2). As anticipated, the aldehydes containing electron-donating groups provided the corresponding products in higher yields than with electron-donating groups.

As a sample ligand, fluorescence spectra of benzo-imidazopyrimido [4,5-*b*]quinoline derivative **3a** were obtained at the excitation wavelength of 350 nm. The maximum fluorescence intensity was observed at 490 nm with a low concentration (1×10^{-5} mol L^{-1}) related to the extended π-electronic structure (Fig. 3).

To study the applicability of this important property, the affinity of this ligand to different metal ions was also investigated. The fluorescence intensity of the ligand **3a** was recorded in the presence of different metal ions, such as Zn^{2+}, Cu^{2+}, Ni^{2+}, Fe^{2+}, Cd^{2+}, Co^{2+}, Mn^{2+}, Mg^{2+}, K^{+}, Na^{+}, Al^{3+}, and Hg^{2+}. The effect of Hg^{2+} was dramatically different from the other metal ions and increased the fluorescence intensity of the ligand. Zn^{2+} showed a slight decrease in fluorescence intensity but Al^{3+} and Ni^{2+} showed a small enhancement. Moreover, the other metal ions did not display any change in this field. Therefore, the metal ions that might coexist in the diverse samples did not interfere in the fluorescence response to Hg^{2+}. In order to study the efficiency of the sensing effect of the ligand, titration with different concentrations of Hg^{2+} was performed. The fluorescence intensity of the ligand was gradually increased upon the concentration molar ratio addition of Hg^{2+} from 0.05 to 2.0 equivalents (Fig. 3). The efficient fluorescence response of the ligand toward Hg^{2+} demonstrated that the synthetic polycyclic ligand **3**, benzo-imidazopyrimido [4,5-*b*]quinoline, can be used as a novel sensor for the detection of this heavy toxic metal ion in real samples.

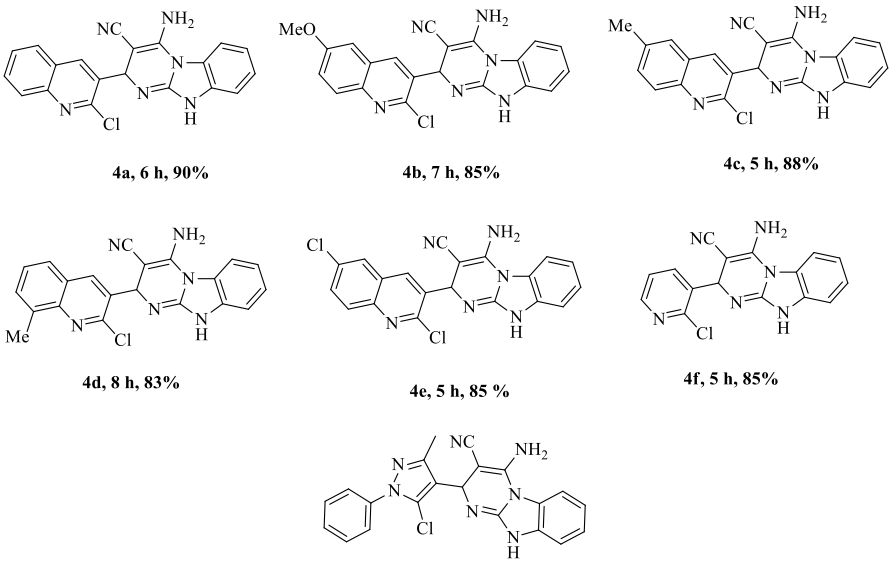


Fig. 2 Different amino-quinolin-3-yl-dihydrobenzo-imidazo-pyrimidine-3-carbonitriles **4**

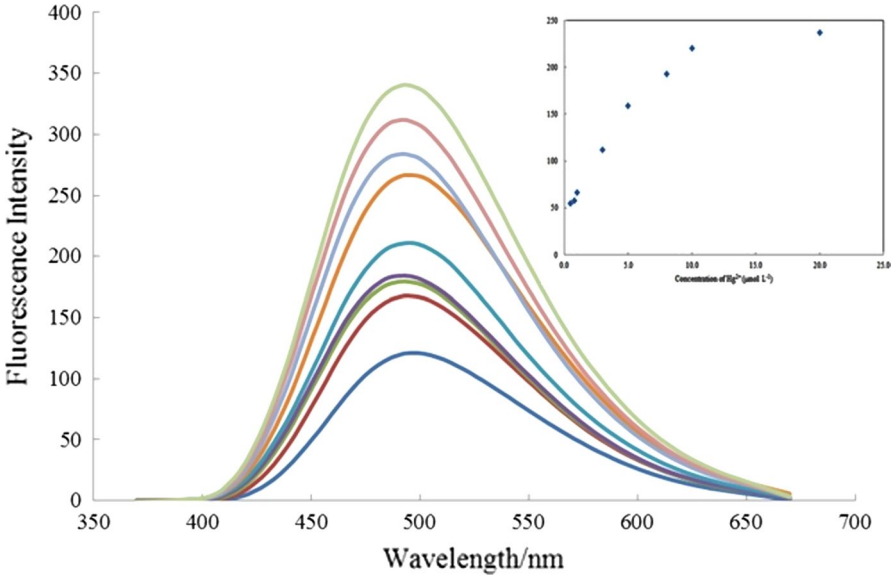


Fig. 3 Fluorescence spectra of polycyclic ligand **3a** (1×10^{-5} M) in DMSO with increasing amounts of Hg^{2+} (0, 0.05, 0.08, 0.1, 0.3, 0.5, 0.8, 1.0, 2.0 equiv.) ($\lambda_{ex} = 350$ nm). *Inset* the fluorescence intensity at 490 nm of ligand **3a** as a function of Hg^{2+} concentration

Conclusion

A series of *N*-containing planar aza-heterocycles were developed using K_2CO_3 in DMF via a one-pot transition metal-free cascade process. Since long conjugation was formed through the cyclization, these new benzo-imidazo-pyrimido-quinoline derivatives were demonstrated to be a potent sensor toward Hg^{2+} compared with a large number of different metal ions examined. Furthermore, the addition of a third reagent, malononitrile, to the previous starting materials, 2-chloro-quinoline-3-carbaldehyde and 2-aminobenzimidazole, did not achieve the expected product in the same reaction conditions. However, by changing the condition to L-proline/H_2O/EtOH/reflux, the novel amino-quinolin-3-yl-dihydrobenzo-imidazo-pyrimidine-3-carbonitrile derivatives were obtained in good yield.

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