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Synthesis of Tetra- and Pentaaza Heterocyclic Systems and Benzimidazo[1,2-*c*]quinazoline Derivatives

A. A. Harutyunyan

Mndzhoyan Institute of Fine Organic Chemistry, Research Technological Center of Organic and Pharmaceutical Chemistry, National Academy of Sciences of Armenia, pr. Azatutyan 26, Yerevan, 0014 Armenia
e-mail: harutyunyan.arthur@yahoo.com

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Abstract—5,6-Dihydropyrimido[5′,4′:5,6]pyrido[1,2-*a*]benzimidazole and pyrimido[4′,5′:4,5]pyrimido[1,6-*a*]-benzimidazole derivatives were synthesized starting from 3-[4-hydroxy-6-methyl(hydroxy)-2-phenylpyrimidin-5-yl]propanoic and 4-hydroxy-2-phenylpyrimidine-5-carboxylic acids. New 6-sulfanyl-substituted benzimidazo-[1,2-*c*]quinazolines were also prepared.

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Heteroannulated benzimidazoles constitute an extensively explored class of polyazaheterocyclic compounds many of which are increasingly used in biology and medicine [1, 2]. Ninety five years after the first synthesis of the benzimidazo[1,2-*c*]quinazoline system [3], some compounds of this series were found to exhibit high cytotoxicity against tumor cells *in vitro* [4, 5]. Their activity is determined by the ability of fused benzimidazoles having a planar structure to intercalate DNA between neighboring nucleobases and thus interfere replication and transcription [2, 4].

Taking into account the above stated, in continuation of studies directed toward search for new biologically active derivatives of pyrimidines and other aza heterocycles [6, 7], the present article reports on the synthesis of new 2-(pyrimidin-5-yl)benzimidazoles and tetracyclic compounds that are derivatives of tetra- and pentaaza heterocyclic systems, pyrimido[5′,4′:5,6]-pyrido[1,2-*a*]benzimidazole and pyrimido[4′,5′:4,5]-pyrimido[1,6-*a*]benzimidazole (pyrimidine isostere of benzimidazo[1,2-*c*]quinazoline). Also, new 6-benzylsulfanyl derivatives of benzimidazo[1,2-*c*]quinazoline and dimeric structures were synthesized.

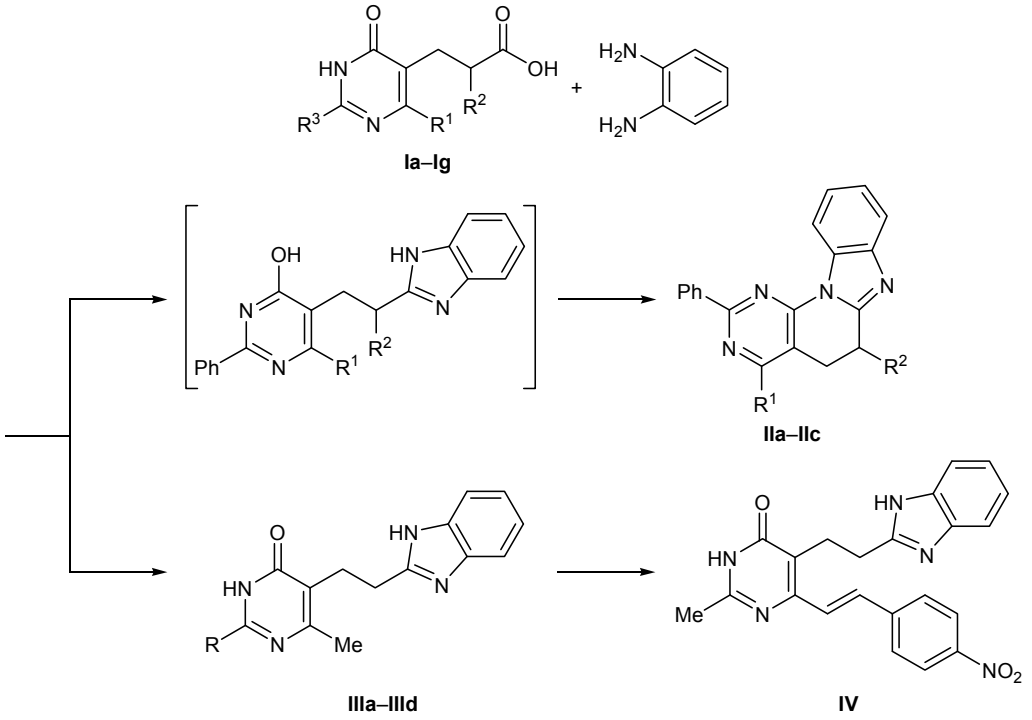
Pyrimidinylbenzimidazoles and 5,6-dihydropyrimido[5′,4′:5,6]pyrido[1,2-*a*]benzimidazole derivatives were prepared starting from 2-substituted 3-(pyrimidin-5-yl)propanoic acids **Ia**–**Ig** which were obtained in turn by reaction of the corresponding amidines, guanidine, or thiourea with adducts derived from ethyl acetoacetate or diethyl malonate and ethyl acrylate or methyl methacrylate in anhydrous ethanol in the presence of sodium ethoxide (Scheme 1). Acids **Ia**–**Ig** reacted with *o*-phenylenediamine in polyphosphoric acid (PPA) along different pathways, depending on the substituent in position *2* of the pyrimidine ring. The condensation with 2-phenyl-substituted pyrimidinylpropanoic acids **Ia**, **Ib** [8], and **Ic** [6] afforded 4-hydroxy-6-methyl-2-phenyl-, 4-methyl-2-phenyl-, and 4,6-dimethyl-2-phenyl-5,6-dihydropyrimido-[5′,4′:5,6]pyrido[1,2-*a*]benzimidazoles **IIa**–**IIc** [6].

However, the reactions with 2-methyl, 2-amino, 2-hydroxy, and 2-sulfanyl derivatives **Id**–**Ig** lead to the formation of benzimidazole derivatives **IIIa**–**IIId** which did not undergo further cyclization to tetracyclic structure **II**. Compound **IIIa** readily reacted with 4-nitrobenzaldehyde in the presence of $ZnCl_2$ according to Claisen to give styrylpyrimidine **IV** as the only product.

The reactions with 2-phenylpyrimidinyl derivatives **Ia**–**Ic** are likely to include two steps with initial formation of benzimidazole derivatives which then undergo cyclization to compounds **IIa**–**IIc**. Replacement of the methyl group in position *6* of the pyrimidine ring by hydroxy (acid **Ia**) does not prevent this reaction pathway. If the 2-position in the pyrimidine ring is replaced by Me, NH_2, OH, or SH group, the second step is not accomplished.

Derivative of a new heterocyclic system, 3-phenylpyrimido[4′,5′:4,5]pyrimido[1,6-*a*]benzimidazole-6(5*H*)-thione (**IX**), was synthesized according to the classical approach developed for the synthesis of benzimidazo[1,2-*c*]quinazolines from anthranilic acid and

Scheme 1.

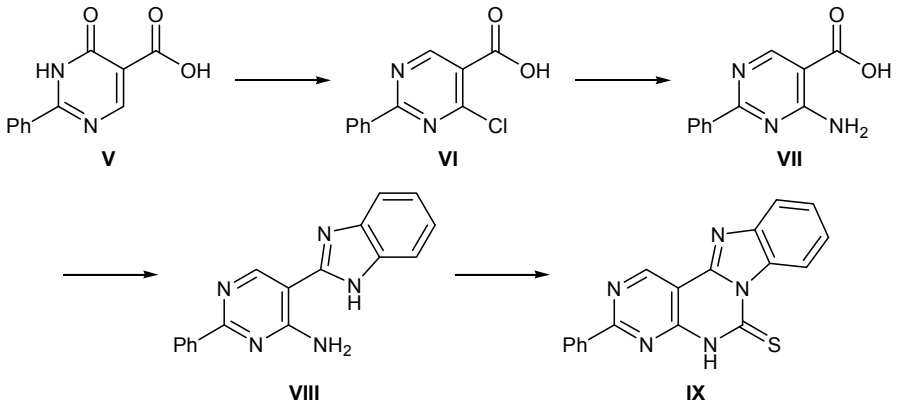


I, R^3 = Ph: R^1 = OH, R^2= Me (**a**); R^1 = Me, R^2 = H (**b**); R^1 = R^2 = Me (**c**); R^1 = Me, R^2 = H, R^3 = Me (**d**), NH_2 (**e**), OH (**f**), SH (**g**); **II**, R^1 = OH, R^2 = Me (**a**); R^1 = Me, R^2 = H (**b**); R^1 = R^2 = Me (**c**); **III**, R = Me (**a**), NH_2 (**b**), OH (**c**), SH (**d**).

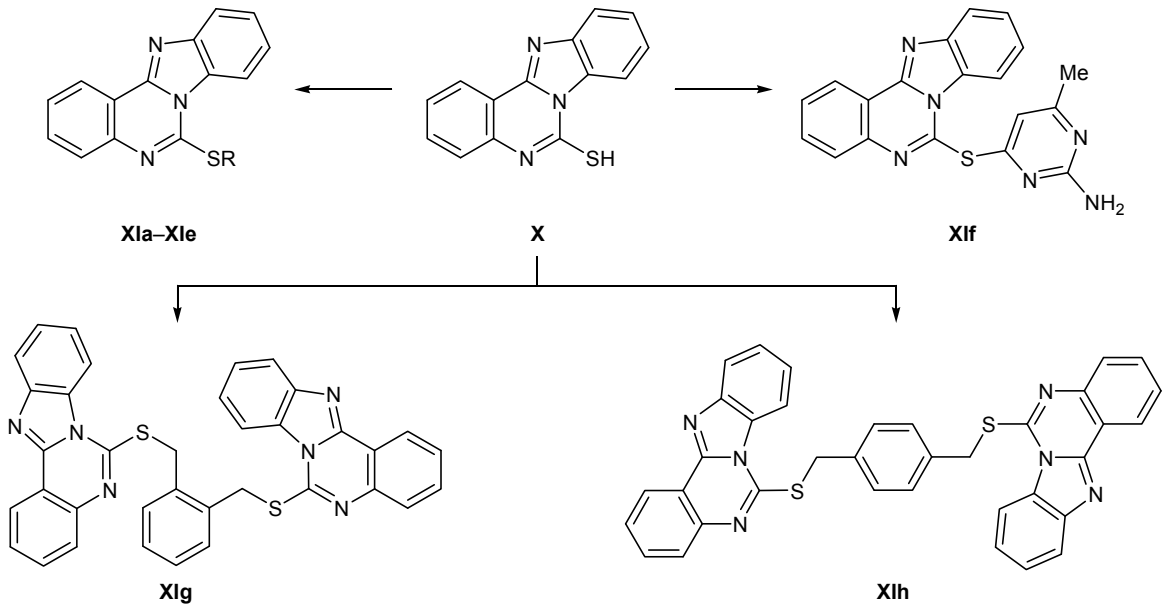
o-phenylenediamine [3]. Following this approach, initial 2-phenyl-4-oxo-3,4-dihydropyrimidine-5-carboxylic acid (**V**) [9] was treated with $POCl_3$, and the resulting 4-chloro derivative **VI** was brought into reaction with alcoholic ammonia. Heating of 4-aminopyrimidine **VII** with *o*-phenylenediamine in polyphosphoric acid afforded key benzimidazole **VIII**, and the latter reacted with carbon disulfide in the presence of potassium hydroxide, yielding target product **IX** (Scheme 2). The average yield of **IX** was 34%; neither variation of the reaction conditions and solvent nor the use of tetrabutylammonium bromide improved the yield of **IX**. Identification of other possible reaction products was not performed.

Taking into account intercalating and antitumor activity of substituted benzimidazo[1,2-*c*]quinazolines, benzimidazo[1,2-*c*]quinazoline-2-thiol (**X**) [3] was alkylated with benzyl chlorides, 4-methyl-6-chloropyrimidin-2-amine, and *o*- and *p*-xylylene dichlorides in the presence of sodium hydroxide to obtain new sulfanyl derivatives **XIa**–**XIf** and dimeric structures **XIg** and **XIh** (Scheme 3).

Scheme 2.



Scheme 3.



XI, R = 2-$ClC_6H_4CH_2$ (**a**), 4-MeO-3-$O_2NC_6H_3CH_2$ (**b**), 2,4-$Me_2C_6H_3CH_2$ (**c**), 2,4,6-$Me_3C_6H_2CH_2$ (**d**), 4-$FC_6H_4CH_2$ (**e**).

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Avatar 330 spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Varian Mercury-300 spectrometer at 300 MHz using tetramethylsilane as internal reference. Thin-layer chromatography was performed on Silufol UV-254 plates; spots were visualized by treatment with iodine vapor. The elemental compositions of the isolated compounds were consistent with the calculated values.

3-(4-Hydroxy-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl)-2-methylpropanoic acid (Ia). Metallic sodium, 2.3 g (0.1 mol), was dissolved in 640 g (4 mol) of diethyl malonate, 100 g (1 mol) of methyl methacrylate was added, and the solution was heated for 24 h at 70–80°C. The mixture was neutralized with 10% aqueous HCl, and the oily material was separated, washed with water, dried over Na_2SO_4, and distilled under reduced pressure to collect a fraction boiling at 200–210°C (110 mm). The product, 26.0 g (0.1 mol), was added to a suspension of 15.7 g (0.1 mol) of benzamidine hydrochloride in a solution of 4.6 g (0.2 mol) of sodium in 250 mL of anhydrous ethanol. The mixture was heated for 5 h under reflux and evaporated to dryness, a solution of 4 g (0.1 mol) of sodium hydroxide in 100 mL of water was added, and the mixture was heated for 4 h under reflux and acidified to pH 3 with aqueous HCl. The precipitate was filtered off and dried. Yield 70%, mp >320°C (decomp.; from DMF), R_f 0.55 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 1706, 1660 (C=O), 1618 (C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.09 d (3H, CH_3, J = 6.8 Hz), 2.65–2.78 m (3H, $CHCH_2$), 7.37–7.51 m (3H) and 8.12–8.16 m (2H) (C_6H_5), 11.58 br (3H, NH, OH, COOH). Found, %: N 10.52. $C_{14}H_{14}N_2O_4$. Calculated, %: N 10.21.

Condensation of 3-(pyrimidin-5-yl)propanoic acids with *o*-phenylenediamine (*general procedure*). A mixture of 1.08 *g* (0.01 mol) of *o*-phenylenediamine and 0.01 mol of acid **Ia**–**Ig** in 10.0 g of polyphosphoric acid was heated for 3 h at 210–220°C. The mixture was cooled and treated with excess aqueous ammonia, and the precipitate was filtered off and dried.

(*RS*)-6-Methyl-2-phenyl-5,6-dihydropyrimido-[5′,4′:5,6]pyrido[1,2-*a*]benzimidazole-4-ol (IIa). Yield 72%, yellow powder, mp >340°C (from DMF), R_f 0.64 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 1643 (C=O), 1611 (C=N). ^{1}H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 1.57 d (3H, CH_3, J = 6.8 Hz), 2.52 d.d (1H, CH_2, J = 16.4, 11.2 Hz), 3.16 d.d (1H, CH_2, J = 16.4, 6.6 Hz), 3.32 m (1H, CH); 7.25 m, 7.30 m, 7.62 m, 8.45 m (1H each, C_6H_4); 7.53–7.65 m (3H) and 8.28 m (2H) (C_6H_5), 12.95 br (1H, OH). Found, %: N 17.25. $C_{20}H_{16}N_4O$. Calculated, %: N 17.06.

4-Methyl-2-phenyl-5,6-dihydropyrimido-[5′,4′:5,6]pyrido[1,2-*a*]benzimidazole (IIb) and (*RS*)-4,6-dimethyl-2-phenyl-5,6-dihydropyrimido-

[5′,4′:5,6]pyrido[1,2-*a*]benzimidazole (IIc) were synthesized from acids **Ib** [8] and **Ic** [6], respectively, and *o*-phenylenediamine according to the procedure described in [6].

5-[2-(1*H*-Benzimidazol-2-yl)ethyl]-2,6-dimethylpyrimidin-4(3*H*)-one (IIIa) was synthesized from acid **Id** [8] and *o*-phenylenediamine. Yield 75%, mp 306–307°C (from DMF), R_f 0.67 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3350 (NH), 1652 (C=O), 1610 (C=N). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 2.07 s and 2.30 s (3H each, CH_3), 2.82–2.96 m (4H, CH_2CH_2), 7.07–7.13 m and 7.42–7.48 m (2H each, C_6H_4), 12.20 br.s and 12.24 br.s (1H each, OH, NH). Found, %: N 20.62. $C_{15}H_{16}N_4O$. Calculated, %: N 20.88.

2-Amino-5-[2-(1*H*-benzimidazol-2-yl)ethyl]-6-methylpyrimidin-4(3*H*)-one (IIIb) was synthesized from acid **Ie** [10] and *o*-phenylenediamine. Yield 68%, mp 223–225°C (from EtOH), R_f 0.69 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3340, 3180 (NH_2, NH), 1656 (C=O), 1608 (C=N). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 2.04 s (3H, CH_3), 2.76–2.83 m (2H, CH_2), 2.88–2.95 m (2H, CH_2), 6.24 br.s (2H, NH_2), 7.00–7.05 m and 7.36–7.42 m (2H each, C_6H_4), 11.07 br.s and 11.86 br.s (1H each, NH). Found, %: N 26.30. $C_{14}H_{15}N_5O$. Calculated, %: N 26.01.

5-[2-(1*H*-Benzimidazol-2-yl)ethyl]-6-methyl-1,2,3,4-tetrahydropyrimidine-2,4-dione (IIIc) was synthesized from acid **If** [11] and *o*-phenylenediamine. Yield 63%, mp 200–202°C, R_f 0.49 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3400 (NH), 1651 (C=O), 1572 (C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.87 s (3H, CH_3), 2.69 m (2H, CH_2), 2.87 m (2H, CH_2), 7.07–7.13 m and 7.35–7.53 m (2H each, C_6H_4), 10.54 s and 10.94 s (1H each, CONH), 12.17 br.s (1H, NH). Found, %: N 20.47. $C_{14}H_{14}N_4O_2$. Calculated, %: N 20.73.

5-[2-(1*H*-Benzimidazol-2-yl)ethyl]-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-4-one (IIId) was synthesized from acid **Ig** [10] and *o*-phenylenediamine. Yield 82%, mp 325–327°C (from EtOH), R_f 0.78 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3440 (NH), 1660–1575 (C=O, C=N, NH–C=S). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 1.96 s (3H, CH_3), 2.73–2.82 m (2H, CH_2), 2.89–2.97 m (2H, CH_2), 7.01–7.07 m and 7.36–7.43 m (2H each, C_6H_4); 11.84 br.s, 11.92 br.s, and 12.03 br.s (1H each, NH). Found, %: N 19.30. $C_{14}H_{14}N_4OS$. Calculated, %: N 19.57.

5-[2-(1*H*-Benzimidazol-2-yl)ethyl]-2-methyl-6-[(*E*)-2-(4-nitrophenyl)-1-ethenyl]pyrimidin-4(3*H*)-one (IV). A mixture of 2.68 g (0.01 mol) of pyrimidine **IIIa**, 1.51 g (0.01 mol) of 4-nitrobenzaldehyde, and 1.36 g (0.01 mol) of $ZnCl_2$ was fused for 2 h at 150–160°C on a Wood bath. The mixture was cooled and treated with water, and the product was recrystallized from DMF. Yield 65%, mp 297–298°C, R_f 0.54 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3623 (OH), 3364 (NH), 1648 (C=O), 1600 (C=N). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 2.13 s (3H, CH_3), 2.93 t and 3.09 t (2H each, CH_2CH_2, J = 7.5 Hz), 7.06 d (1H, =CH, J = 16.1 Hz), 7.13–7.19 m and 7.48–7.64 m (2H each, C_6H_4), 7.87 m and 8.27 m (2H each, $C_6H_4NO_2$), 7.89 d (1H, =CH, J = 16.1 Hz), 12.52 br.s (2H, NH, OH). Found, %: N 17.34. $C_{22}H_{19}N_5O_3$. Calculated, %: N 17.45.

4-Chloro-2-phenylpyrimidine-5-carboxylic acid (VI). A mixture of 2.16 g (0.01 mol) of acid **V** and 5.0 mL of $POCl_3$ was heated for 2 h under reflux, excess $POCl_3$ was distilled off, and the oily residue was poured onto 50 g of ice. After 1 h, the precipitate was filtered off, washed with cold water, and dried. Yield 87%, mp 114–115°C (from dioxane), R_f 0.80 (ethyl acetate–octane, 1:2). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 7.49–7.56 m (2H, 3′-H, 5′-H, C_6H_5), 7.58–7.64 m (1H, 4′-H, C_6H_5), 8.24–8.29 m (2H, 2′-H, 6′-H, C_6H_5), 8.78 s (1H, N=CH), 13.73 br.s (1H, OH). Found, %: N 11.70. $C_{11}H_7ClN_2O_2$. Calculated, %: N 11.94.

4-Amino-2-phenylpyrimidine-5-carboxylic acid (VII). A solution of 2.35 g (0.01 mol) of 4-chloropyrimidine **VI** in 50 mL of a saturated alcoholic solution of ammonia was heated for 4 h at 120–130°C in a high pressure reactor. The solvent was distilled off, the residue was treated with 30 mL of water, and the precipitate was filtered off and dried. Yield 82%, mp 273–274°C (from 1,2-dimethoxyethane), R_f 0.59 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3484, 3309, 3170 (NH_2), 1683 (C=O), 1620 (C=N). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 7.07 br.s, 7.68 br.s, and 7.91 br.s (1H each, NH_2, COOH), 7.36–7.43 m (3H, 3′-H, 4′-H, 5′-H, C_6H_5), 8.33–8.40 m (2H, 2′-H, 6′-H, C_6H_5), 8.78 s (1H, N=CH). Found, %: N 19.81. $C_{11}H_9N_3O_2$. Calculated, %: N 19.53.

5-(1*H*-Benzimidazol-2-yl)-2-phenylpyrimidin-4-amine (VIII). A mixture of 2.15 g (0.01 mol) of acid **VII**, 1.19 g (0.011 mol) of *o*-phenylenediamine, and 10.0 g of polyphosphoric acid was heated for 2 h at

220–230°C on a Wood bath. The mixture was cooled to room temperature and neutralized with aqueous ammonia, and the precipitate was filtered off and dried. Yield 85%, mp >330°C (from dioxane), R_f 0.68 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3379, 3268 (NH_2, NH), 1625 (C=N). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 7.12–7.22 m (2H), 7.39–7.55 m (4H), 7.59–7.66 m (1H), 8.40–8.46 m (2H) (H_{arom}); 9.05 s (1H, N=CH), 9.28 br.s (2H, NH_2), 12.76 br.s (1H, NH). Found, %: N 24.58. $C_{17}H_{13}N_5$. Calculated, %: N 24.37.

3-Phenylpyrimido[4′,5′:4,5]pyrimido[1,6-*a*]-benzimidazole-6(5*H*)-thione (IX). A mixture of 1.44 g (5 mmol) of amine **VIII**, 1.4 g (25 mmol) of potassium hydroxide, 0.76 g (0.6 mL, 10 mmol) of carbon disulfide, 5 mL of water, and 35 mL of dioxane was heated for 24 h under reflux. The mixture was evaporated to dryness, 50 mL of water was added to the residue, and the mixture was heated to the boiling point, filtered, and acidified to pH 5 with aqueous HCl. The mixture was kept in the cold, and the precipitate was filtered off and dried. Yield 0.56 g (34%), mp >340°C (from 1,2-dimethoxyethane), R_f 0.61 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1596 cm^{-1} (NHC=S). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 7.11–7.18 m and 7.58–7.65 m (2H each, C_6H_4), 7.47–7.56 m (3H) and 8.28–8.34 m (2H) (C_6H_5), 9.14 br.s (1H, =CH), 12.54 br.s (1H, NH). Found, %: N 21.40. $C_{18}H_{11}N_5S$. Calculated, %: N 21.26.

Benzimidazo[1,2-*c*]quinazolines XIa–XIi (*general procedure*). Compound **X**, 2.51 g (0.01 mol), was dissolved in 50 mL of 0.2 N aqueous sodium hydroxide, 0.011 mol of substituted benzyl chloride or 2-amino-4-chloro-6-methylpyrimidine or 0.005 mol of *o*- or *p*-xylylene dihalide was added, and the resulting suspension was heated for 24 h on a water bath. The precipitate was filtered off, washed with water, and dried.

6-(2-Chlorobenzylsulfanyl)benzimidazo[1,2-*c*]-quinazoline (XIa) was synthesized from compound **X** and 2-chlorobenzyl chloride. Yield 79%, mp 205–207°C (from dioxane), R_f 0.59 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1615 cm^{-1} (C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 4.94 s (2H, CH_2), 7.23–7.32 m (2H), 7.38–7.63 m (4H), 7.73–7.81 m (2H), 7.86–7.90 m (2H), 8.39 br.d (1H, J = 8.2 Hz), 8.56 d.d (1H, J = 8.0, 1.4 Hz). Found, %: N 11.42. $C_{21}H_{14}ClN_3S$. Calculated, %: N 11.18.

6-(4-Methoxy-3-nitrobenzylsulfanyl)benzimidazo[1,2-*c*]quinazoline (XIb) was synthesized from compound **X** and 4-methoxy-3-nitrobenzyl chloride. Yield 82%, mp 253–255°C (from DMF), R_f 0.54 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1621 cm^{-1} (C=N). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 3.93 s (3H, OCH_3), 4.82 s (2H, CH_2), 7.21 d (1H, 6′-H, J = 8.7 Hz), 7.42 d.d.d (1H, C_6H_4, J = 8.2, 7.2, 1.5 Hz), 7.51 d.d.d (1H, C_6H_4, J = 8.0, 7.2, 1.2 Hz), 7.60 d.d.d (1H, C_6H_4, J = 7.9, 7.2, 1.2 Hz), 7.77 d.d.d (1H, C_6H_4, J = 8.7, 7.2, 1.7 Hz), 7.83–7.90 m (2H, H_{arom}), 7.85 d.d (1H, 5′-H, J = 8.7, 2.3 Hz), 8.15 d (1H, 3′-H, J = 2.3 Hz), 8.40 br.d (1H, C_6H_4, J = 8.2 Hz), 8.56 d.d (1H, C_6H_4, J = 8.0, 1.7 Hz).

6-(2,4-Dimethylbenzylsulfanyl)benzimidazo-[1,2-*c*]quinazoline (XIc) was synthesized from compound **X** and 2,4-dimethylbenzyl chloride. Yield 74%, mp 155–156°C (from EtOH), R_f 0.61 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1620 cm^{-1} (C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.31 s (3H, CH_3), 2.48 s (3H, CH_3), 4.80 s (2H, CH_2), 6.96 d.d (1H, 5′-H, J = 7.9, 1.9 Hz), 7.01 d (1H, 3′-H, J = 1.9 Hz), 7.35–7.41 m (2H, C_6H_4), 7.50 d.d.d (1H, C_6H_4, J = 8.1, 7.3, 1.0 Hz), 7.60 d.d.d (1H, C_6H_4, J = 7.9, 7.1, 1.3 Hz), 7.76 d.d.d (1H, C_6H_4, J = 8.2, 7.1, 1.5 Hz), 7.83–7.90 m (2H, C_6H_4), 8.38 br.d (1H, C_6H_4, J = 8.3 Hz), 8.57 d.d (1H, C_6H_4, J = 7.9, 1.5 Hz). Found, %: N 11.08. $C_{23}H_{19}N_3S$. Calculated, %: N 11.37.

6-(2,4,6-Trimethylbenzylsulfanyl)benzimidazo-[1,2-*c*]quinazoline (XId) was synthesized from compound **X** and 2,4,6-trimethylbenzyl chloride. Yield 67%, mp 186–187°C (from EtOH), R_f 0.76 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1621 cm^{-1} (C=N). ^1H NMR spectrum (DMSO-d_6–CCl_4, 1:3), δ, ppm: 2.29 s (3H, CH_3), 2.46 s (6H, CH_3), 4.81 s (2H, CH_2), 6.87 s (2H, 3′-H, 5′-H), 7.35 d.d.d (1H, C_6H_4, J = 8.3, 7.3, 1.2 Hz), 7.49 d.d.d (1H, C_6H_4, J = 8.0, 7.1, 1.0 Hz), 7.60 d.d.d (1H, C_6H_4, J = 8.0, 7.0, 1.2 Hz), 7.75 d.d.d (1H, C_6H_4, J = 8.1, 7.1, 1.5 Hz), 7.84 d.d (1H, C_6H_4, J = 8.1, 1.0 Hz), 7.89 br.d (1H, C_6H_4, J = 8.1 Hz), 8.35 br.d (1H, C_6H_4, J = 8.3 Hz), 8.59 d.d (1H, C_6H_4, J = 8.0, 1.4 Hz). Found, %: N 11.17. $C_{24}H_{21}N_3S$. Calculated, %: N 10.96.

6-(4-Fluorobenzylsulfanyl)benzimidazo[1,2-*c*]-quinazoline (XIe) was synthesized from compound **X** and 4-fluorobenzyl chloride. Yield 80%, mp 160–161°C (from EtOH), R_f 0.50 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1618 cm^{-1} (C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 4.82 s (2H, CH_2), 7.04 m (2H, 3′-H, 5′-H), 7.41 d.d.d (1H, C_6H_4, J = 8.3, 7.2, 1.4 Hz), 7.51 d.d.d (1H, C_6H_4, J = 8.0, 7.3, 1.2 Hz), 7.57–7.63 m (3H, 2′-H, 6′-H, C_6H_4),

7.76 d.d.d (1H, C_6H_4, J = 8.2, 7.1, 1.6 Hz), 7.83–7.90 m (2H, C_6H_4), 8.40 br.d (1H, C_6H_4, J = 8.3 Hz), 8.57 d.d (1H, C_6H_4, J = 8.0, 1.2 Hz). Found, %: N 11.52. $C_{21}H_{14}FN_3S$. Calculated, %: N 11.69.

4-(Benzimidazo[1,2-*c*]quinazolin-6-ylsulfanyl)-6-methylpyrimidin-2-amine (XIf) was synthesized from compound **X** and 4-chloro-6-methylpyrimidin-2-amine. Yield 85%, mp 305–307°C (from H_2O), R_f 0.74 (ethanol–dichloroethane, 1:10). IR spectrum, ν, cm^{-1}: 3416, 3309 (NH_2), 1628 (C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.24 s (3H, CH_3), 6.38 s (1H, 5′-H), 6.54 br.s (2H, NH_2); 7.34–7.40 m (2H), 7.47 d.d.d (1H, J = 8.0, 7.3, 1.2 Hz), 7.56–7.64 m (2H), 7.80 br.d (1H, J = 7.9 Hz), 8.41 br.d (1H, J = 8.0 Hz), and 9.49 br.d (1H, J = 8.2 Hz) (C_6H_4). Found, %: N 23.63. $C_{19}H_{14}N_6S$. Calculated, %: N 23.45.

6-[2-(Benzimidazo[1,2-*c*]quinazolin-6-ylsulfanylmethyl)benzylsulfanyl]benzimidazo[1,2-*c*]quinazoline (XIg) was synthesized from compound **X** and 1,2-bis(bromomethyl)benzene. Yield 52%, mp 288–290°C (from DMF), R_f 0.60 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1620 cm^{-1} (C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 5.18 s (4H, CH_2), 7.21 d.d.d (2H, H_{arom}, J = 8.4, 7.2, 1.2 Hz), 7.36–7.58 m (10H, H_{arom}), 7.69–7.74 m (2H, H_{arom}), 7.84 br.d (2H, H_{arom}, J = 8.1 Hz), 8.23 br.d (2H, H_{arom}, J = 8.4 Hz), 8.27 d.d (2H, H_{arom}, J = 7.5, 1.8 Hz). Found, %: N 13.72. $C_{36}H_{24}N_6S_2$. Calculated, %: N 13.90.

6-[4-(Benzimidazo[1,2-*c*]quinazolin-6-ylsulfanylmethyl)benzylsulfanyl]benzimidazo[1,2-*c*]quinazoline (XIh) was synthesized from compound **X** and 1,4-bis(chloromethyl)benzene. Yield 52%, mp 290–292°C (from DMF), R_f 0.62 (ethanol–dichloroethane, 1:10). IR spectrum: ν 1620 cm^{-1} (C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 4.84 s (4H, CH_2), 7.37–7.67 m (6H, H_{arom}), 7.62 s (4H, C_6H_4), 7.79–7.96 m (6H, H_{arom}), 8.41 br.d (2H, H_{arom}, J = 8.2 Hz), 8.51 br.d (2H, H_{arom}, J = 7.7 Hz). Found, %: N 13.65. $C_{36}H_{24}N_6S_2$. Calculated, %: N 13.90.

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