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NOTE

Synthesis of 2-Amino-4-(2′-hydroxy-4′-isopropoxy-5′-bromophen-1′-yl)-6-substituted aryl Pyrimidine Derivatives and Related Compounds

J.A. DESAI and K.K. DESAI*
Department of Chemistry, South Gujarat University, Surat-395 007, India

2′-Hydroxy-4′-isopropoxy-5′-bromochalcones react with an alcoholic solution of guanidine nitrate in alkaline solution to give the corresponding 2-amino-4-(2′-hydroxy-4′-isopropoxy-5′-bromophen-1′-yl)-6-substituted aryl pyrimidines (**2a–j**). Compounds (**2a–j**) were converted to 2-phthalimido-4-(2′-hydroxy-4′-isopropoxy-5′-bromophen-1′-yl)-6-substituted aryl pyrimidines (**3a–j**) and 1-phenyl-3-[4′-(2″-hydroxy-4″-isopropoxy-5″-bromophen-1′-yl-6′-substituted aryl pyrimidine-2′-yl]-thiocarbamide derivatives (**4a–j**). All the synthesized compounds have been characterized by elemental analysis and spectral data.

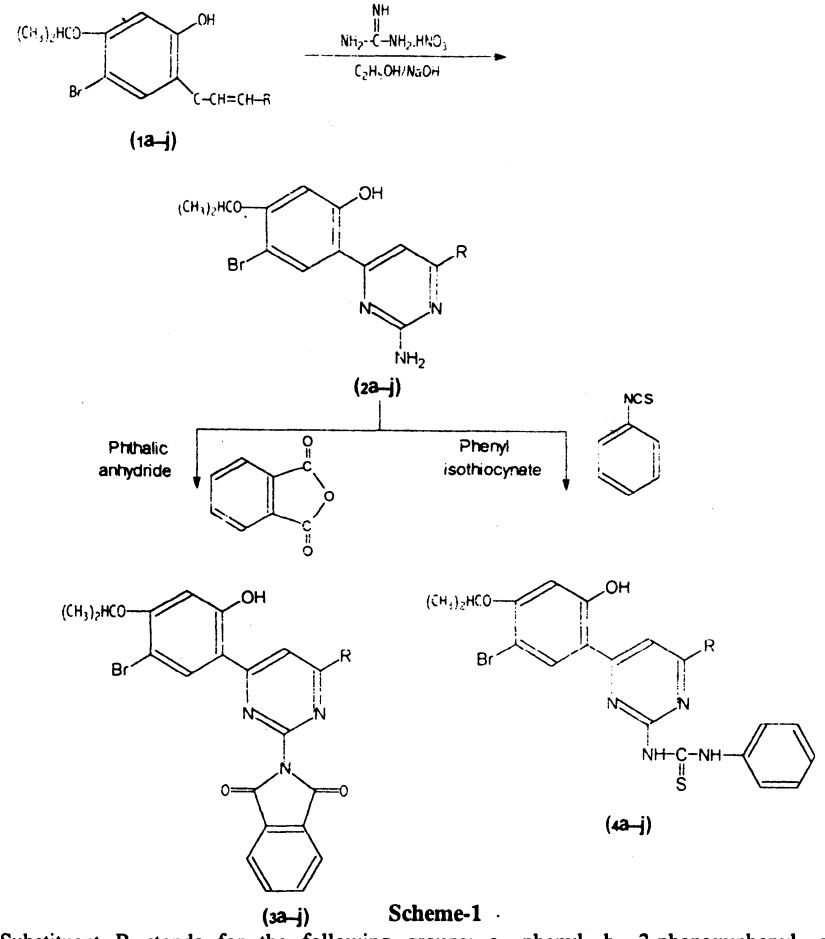
Key Words: Synthesis, 2-Amino-4-(2′-hydroxy-4′-isopropoxy-5′-bromophen-1′-yl)-6-substituted aryl pyrimidines, Derivatives.

In the present age of pharmacogenetics too, the pyrimidines have been given considerable importance due to their wide spectrum biological properties. Extensive work on the synthesis of these heterocyclics was done by various routes, owing to their antifungal[1], antihistaminic[2], antimalarial[3], antidiabetic[4], antitumour[5], anti-coagulant[6] and anticancer[7] properties. The present investigation describes the synthesis of some new pyrimidine derivatives and heterocyclics derived from these and their characterization[8, 9].

Preparation of 2-amino-4-(2′-hydroxy-4′-isopropoxy-5′-bromophen-1′-yl)-6-substituted aryl pyrimidine derivatives (2a–j)

2′-Hydroxy-4′-isopropoxy-5′-bromochalcones (**1a–j**), prepared by condensing ketone with ten different aldehydes, were treated with guanidine nitrate (0.01 mol) in ethanol. The reaction mixture was refluxed and aqueous solution of sodium hydroxide (40%, 5 mL) added to it portionwise during 3 h. The heating was continued further for 6 h. The reaction mixture was cooled and poured into ice. The product obtained was filtered, washed with water, dried and crystallized from ethanol to give (**2a–j**). m.p. (°C): **2a**, 165; **2b**, 187; **2c**, 193; **2d**, 198; **2e**, 218; **2f**, 204; **2g**, 209; **2h**, 233; **2i**, 221; **2j**, 238. IR absorption bands observed in **2c** (cm^{-1}): 3235–3200 ν(O—H), 3420–3300 ν(N—H), 1680–1530 ν(N—H), 1500–1350

ν(C—N), 1272–1200 ν(C—O—C). NMR signals observed in **2i** (in ppm): δ = 2.86: six protons of $—CH_3$ in isopropyl group. δ = 3.33: one proton of—CH in isopropyl group, δ = 6.0–8.0: protons of aromatic, heterocyclic ring and $—NH_2$ group, δ = 8.0: proton of —OH group.



Scheme-1

Substituent R stands for the following groups: a = phenyl, b = 3-phenoxyphenyl, c = 2-chlorophenyl, d = 4-chlorophenyl, e = 2,4-dichlorophenyl, f = 2-methoxyphenyl, g = 4-methoxyphenyl, h = 3,4,5-trimethoxyphenyl, i = N,N-dimethylaminophenyl, j = 2-hydroxyphenyl

Preparation of 2-phthalimido-4-(2′-hydroxy-4′-isopropoxy-5-bromophen-1′-yl)-6-substituted aryl pyrimidines (3a–j)

A mixture of **(2a–j)** (0.01 mol) and phthalic anhydride (0.01 mol) was refluxed at 180–200°C for 4 h in an oil-bath. The reaction mixture after cooling was triturated with glacial acetic acid and poured into cold water. The solid that separated out was filtered, washed, dried and crystallized from dioxane to give 2-phthalimide-4-(2′-hydroxy-4′-isopropoxy-5′-bromophen-1′-yl)-6-substituted aryl pyrimidines **(3a–j)**. m.p. (°C): **3a**, 185; **3b**, 205; **3c**, 178; **3d**, 196; **3e**,

213; **3f**, 200; **3g**, 218; **3h**, 220; **3k**, 225; **3j**, 207. IR spectra of **3f** (cm^{-1}): 3420–3300 ν(O—H), 1620–1530 ν(C—N), 1700–1640 ν(C=O), 1220–1200 ν(C—O—C). NMR spectra of **3e** (ppm): δ = 2.50: six protons of —CH_3 in isopropyl group. δ = 3.16: one proton of —CH in isopropyl group, δ = 8.0: proton of —OH, δ = 6.0–8.0: protons of aromatic and heterocyclic ring.

Preparation of 1-phenyl-3-[4′-(2″-hydroxy-4″-isopropoxy-5″-bromophen-1″-yl)-6-substituted aryl pyrimidine-2′-yl]-thiocarbamide (4a–g)

A mixture of (**2a–j**) (0.01 mol) and phenylisothiocyanate in benzene was refluxed on a water-bath for 1 h. The reaction mixture was cooled; when a crystalline solid separated out, it was filtered, washed with benzene and dried to get (**4a–j**). m.p. (°C): **4a**, 140, **4b**, 162, **4c**, 170, **4d**, 185, **4e**, 198, **4f**, 176, **4g**, 184, **4h**, 202, **4i**, 208, **4j**, 195. IR spectra of **4i** (cm^{-1}): 3450–3320 ν(N—H), 3200–3150 ν(O—H), 1650–1530 ν(N—H), 1375–1260 ν(C—N), 1250–1020 ν(C=S). NMR spectra of **4a** (ppm): δ = 2.50, six protons of —CH_3 in isopropyl group, δ = 3.55: one proton of —CH in isopropyl group, δ = 6.0–8.0: protons of aromatic, heterocyclic ring and —NH group, δ = 8.0: proton of —OH group.

For other compounds of the series spectral data obtained were almost similar.

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