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# Synthesis and Antibacterial Activity of 2-Amino-4-(2′,4′-Dichloro-5′-Fluorophen-1′-yl)-6-Aryl Pyrimidine Derivatives and Related Compounds

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2′,4′-Dichloro-5′-fluorochalcones (1a–j) react with an alcoholic solution of guanidine nitrate containing aqueous sodium hydroxide solution to give the corresponding 2-amino-4-(2′,4′-dichloro-5′-flurophen-1′-yl)-6-aryl pyrimidines (2a–j). Compounds (2a–j) were converted to diacetyl (3a-j); sulphonamide (4a–j); and N-acetyl sulphonamide (5a–j) pyrimidine derivitives. These varied products have been characterised by spectral studies and screened for antibacterial activity.

Previous workers[1, 2] have reported the synthesis of various pyrimidine derivatives. The present investigation describes a new route to the synthesis of pyrimidine derivatives of potential biological activity. Thus the different chalcones were prepared and reacted with guanidine nitrate to produce the corresponding substituted pyrimidines (2a–j)[3].

In the present work, 2′,4′-dichloro-5′-fluorochalcones (1a–j) were reacted with an alcoholic solution of guanidine nitrate containing aqueous sodium hydroxide solution when 2-amino-4-(2′,4′-dichloro-5′-fluorophen-1′-yl)-6-aryl pyrimidines were obtained. With acetic anhydride they (2a–j) gave the diacetyl pyrimidine derivatives (3a–j). Further the reaction of (2a–j) with *para*-acetyl amino-benzene sulphonyl chloride in pyridine gave the sulphapyrimidine derivatives (4a–j) which on treatment with acetic anhydride gave the N-acetyl sulphapyrimidine derivatives (5a–j).

The products were screened for antibacterial activity at a concentration of 50 μg by cup-plate method[4] aganinst gram-positive bacteria *Staphylococcus aureus* and gram-negative bacteria *Escherichia coli*. The results were compared against ampicillin and gentamycin. All compounds showed mild activity.

All melting points were taken in open capillary tubes and are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer-377 spectrophotometer. All compounds gave satisfactory elemental analysis.

**General method for preparation of 2-amino-4-(2′,4′-dichloro-5′-fluorophen-1′-yl)-6-aryl pyrimidine derivatives (2a–j).**

2′,4′-Dichloro-5′-fluorochalcone (0.01 mole) (1a–j) was treated with guanidine nitrate (0.01 mole) in ethanol. The reaction mixture was refluxed and aqueous solution of sodium hydroxide (40%, 5 mL) added to it portionwise during 3 h.

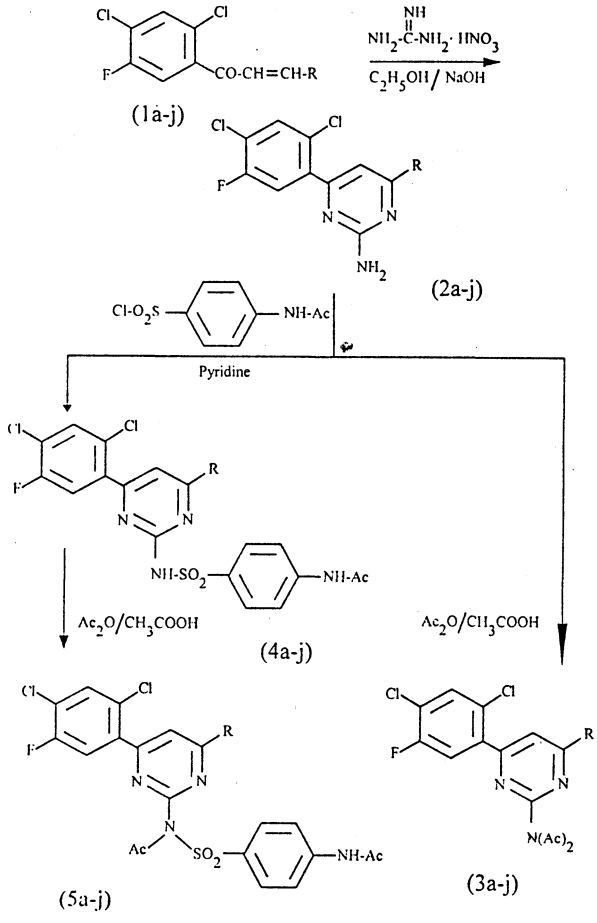
The reflux was continued further for 6 h. The reaction mixture was cooled, poured into ice-water. The product obtained was filtered, washed with water, dried and crystallized from DMF to give (2a–j).

m.p. (°C): 2a: 121; 2b: 177; 2c: 124; 2d: 173; 2e: 116; 2f: 134; 2g: 147; 2h: 141; 2i: 186; 2j: 158.

IR ($cm^{-1}$) (KBr): 3460–3330 ν(N—H); 1660–1640 ν(C=N); 1650–1590 δ(N—H); 1340–1310 ν(C—N); 740–725 ν(C—Cl); 1250–1100 ν(C—F).

**General method for preparation of 2-[N,N-diacetyl-amino]-4-(2′,4 -dichloro-5′-fluorophen-1′-yl)-6-aryl pyrimidine derivatives (3a–j).**

A mixture of (2a-j) (0.01 mole) and acetic anhydride (10 mL) in glacial acetic acid (10 mL) was heated under reflux for 2 h. The reaction mixture was cooled,




R = a: phenyl; b: 2-chlorophenyl; c: 4-chlorophenyl; d: 4-methylphenyl; e: 4-methoxyphenyl; f: 3,4,5-trimethoxyphenyl; g: 4-N,N-dimethylamino- phenyl; h: 2-nitrophenyl; i: 2-furfuryl; j: thiophene.

poured into ice-water. The solid obtained was filtered, washed with water and crystallized from ethanol to give (3a–j).

m.p. (°C): 3a: 93; 3b: 128; 3c: 117; 3d: 130; 3e: 107; 3f: 121; 3g: 113; 3h: 129; 3i: 174; 3j: 134.

IR ($cm^{-1}$) (KBr): 1610–1590 ν(C=N); 1670–1630 ν(C=O); 1360–1340 ν(C—N); 740–710 ν(C—Cl); 1250–1100 ν(C—F).

**General method for the preparation of 2-(*p*-acetyl amino benzene sulphonamide)-4-(2′,4′-dichloro-5′-fluorophen-1′-yl)-6-aryl pyrimidine derivatives (4a–j).**

A mixture of (2a–j) (0.01 mole) and *p*-acetyl amino benzene sulphonyl chloride (0.012 mole) in dry pyridine (20 mL) were heated under reflux on a water-bath at 70–75°C for 4 h. It was then treated with cold dil. hydrochloric acid (2N). The solid obtained was filtered, washed with hot water, dried and crystallized from glacial acetic acid to give (4a–j).

m.p. (°C): 4a: 214; 4b: 197; 4c: 148; 4d: 238; 4e: 216; 4f: 230; 4g: 191; 4h: 210; 4i: 258; 4j: 226.

IR ($cm^{-1}$) (KBr): 3350–3310 ν(N—H); 1610–1595 ν(C=N); 1340–1280 ν(C—N); 1350–1330 ν(S=O); 1560–1530 ν(N—H); 1680–1630 ν(C=O); 1260–1100 ν(C—F); 740–725 ν(C—Cl).

**General method for preparation of 2-[N-acetyl-N-(p-acetyl amino benzene) sulphonamido]-4-(2′,4′-dichloro-5′-fluorophen-1′-yl)-6-aryl pyrimidine derivatives (5a–j).**

A mixture of (4a–j) (0.01 mole) and acetic anhydride (10 mL) in glacial acetic acid (5 mL) was heated under reflux for 2 h. The reaction mixture was cooled, poured into ice-water. The solid was separated and filtered, washed with water and crystallized from benzene to give (5a–j).

m.p. (°C): 5a: 171; 5b: 159; 5c: 132; 5d: 195; 5e: 184; 5f: 179; 5g: 170; 5h: 117; 5i: 155; 5j: 112.

IR ($cm^{-1}$) (KBr): 3380–3340 ν(N—H); 1570–1530 δ(N—H); 1680–1630 ν(C=O); 1620–1590 ν(C=N); 1350–1330 ν(S=O); 1320–1280 ν(C—N); 1250–1100 ν(C—F); 740–720 ν(C—Cl).

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