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KF-AL_2O_3 MEDIATED MICROWAVE ASSISTED ONE POT SYNTHESIS OF BENZOPYRANYLPYRIMIDINES

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ABSTRACT

One pot three component condensation reaction between flavanone, aromatic aldehydes and guanidine hydrochloride in presence of KF-Al_2O_3 under microwave irradiation affords benzopyranylpyrimidine in good yield. The synthesized benzopyranylpyrimidine derivatives were characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR spectroscopic techniques and elemental analysis.

KEYWORDS: Benzopyranylpyrimidine, KF-Al_2O_3, Microwave irradiation, three component condensation.

1. INTRODUCTION

Pyrimidine is an important class of heterocycle in the field of medicinal chemistry. Pyrimidine exhibits potential biological activities,[1] Pyrimidine derivatives are known to exhibit anti-HIV,[2] antiplasmodial,[3] anticancer,[4] activities. Benzopyranylpyrimidine derivatives are reported to exhibit antimicrobial,[5] antiproliferative,[5] and antiplatelet activity,[6] The reported methods,[7-9] for synthesis of pyrimidines have certain limitations like poor yield, multi-step reaction, longer reaction time, use of solvents etc. Therefore there is need to develop simple and rapid method for synthesis of benzopyranylpyrimidines.

The use of solid supported reagents,[10] in organic synthesis has received considerable attention due to their eco-friendly nature, reaction rate enhancement, selectivity and avoidance of aqueous workup. Due to surface properties of KF-Al_2O_3, variety of reactions occur easily,[11] KF-Al_2O_3 is an inexpensive and commercially available reagent which has

been used in several organic transformations, such as acetylation of amines, alcohols and phenol, preparation of amides from nitriles and N-arylation of amines.[12-15]

We report for the first time one pot three component condensation reaction between flavanone, aromatic aldehyde and guanidine hydrochloride under microwave irradiation in presence of KF-Al_2O_3.

2. EXPERIMENTAL SECTION

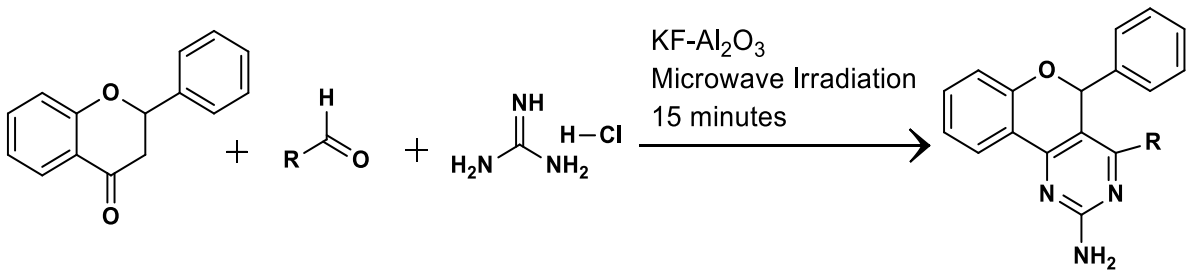
Unless otherwise stated, all reagents were purchased from Sigma-Aldrich (India) and used without purification. The melting points were determined using capillary tube and are uncorrected. IR spectra were recorded on Frontier Perkin Elmer IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker AVANCE 300 MHz instrument in $CDCl_3$ using TMS as internal standard. Chemical shifts (δ) are expressed in ppm and coupling constants *J* are given in Hz. Elemental analyses were carried out in EA 3000, Euro Vector, Italy. The reactions were carried out in Samsung Grill microwave model GW732KD-B.

3. RESULTS AND DISCUSSION

We have carried out solvent free one pot three component condensation reaction between flavanone, aldehyde and guanidine hydrochloride for the synthesis of novel benzopyranylpyrimidine derivatives in presence of KF-Al_2O_3 under microwave irradiation for 15 minutes (**Scheme-1**).

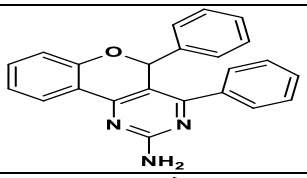
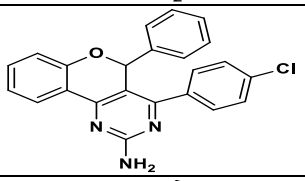
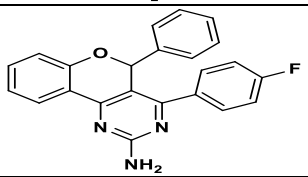
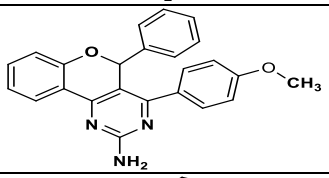
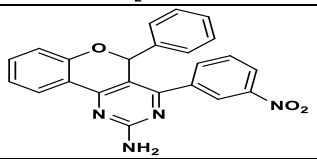
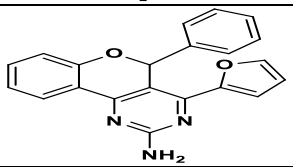
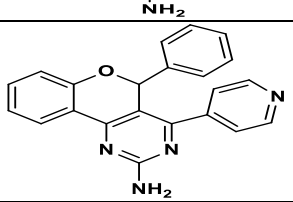
3.1 General Procedure

In a round bottom flask, mix dry KF (0.5g) and Al_2O_3 (1g). Add flavanone **1** (0.001M), aromatic aldehyde **2** (0.001M) and guanidine hydrochloride (0.0015M) into it and subject the reaction mixture to microwave irradiation for 15 minutes (**Scheme-1**). After completion of reaction (TLC), it was extracted with chloroform and filtered. The chloroform extract was distilled and residue was purified by column chromatography to afford benzopyranylpyrimidine **3** as yellow solid.



Flavanone **1** | Aromatic aldehyde **2a-g** | Guanidine Hydrochloride | Substituted Benzopyranylpyrimidine **3a-g**

Scheme-1

Entry	R	Product	Yield %
3a	Phenyl		81
3b	4-Chlorophenyl		80
3c	4-Fluorophenyl		82
3d	4-Methoxyphenyl		85
3e	3-Nitrophenyl		78
3f	2-Furyl		82
3g	4-Pyridyl		78

4, 5-diphenyl-5H-chromeno [4, 3-d] pyrimidin-2-amine (3a)

M.P. 184^0C

IR (cm^{-1}): 3505.14, 3351.89, 1624.07, 1568.57, 1225.19, 755.92, 697.03.

^{1}H NMR ($CDCl_3$): 5.36(s, 2H, NH_2), 6.91-7.03(m, 5H, aromatic and H-5), 7.35-7.56(m, 4H aromatic), 7.85-7.86(m, 5H aromatic).

^{13}C NMR ($CDCl_3$): 102.12, 117.51, 118.77, 119.09, 127.13, 127.24, 128.91, 130.99, 133.17, 137.01, 160.44, 160.87, 166.17.

Elemental analysis: $C_{23}H_{17}N_3O$

Calculated: C (78.61%), H (4.81%), N (11.96%).

Observed: C (78.69%), H (4.79%), N (11.88%).

4-(4-chlorophenyl)-5-phenyl-5H-chromeno [4, 3-d] pyrimidin-2-amine (3b)

M.P. 186^0C

IR (cm^{-1}): 3505.76, 3352.87, 1624.63, 1569.87, 1225.47, 755.68, 696.76.

^{1}H NMR ($CDCl_3$): 5.40(s, 2H, NH_2), 6.90-7.02(m, 5H, aromatic and H-5), 7.34-7.54(m, 4H aromatic), 7.84-7.88(m, 4H aromatic.)

^{13}C NMR ($CDCl_3$): 102.08, 117.53, 118.75, 119.08, 127.12, 127.23, 128.51, 128.89, 129.08, 130.96, 133.14, 137.05, 160.46, 160.85, 166.12, 166.20.

Elemental analysis: $C_{23}H_{16}N_3ClO$

Calculated: C (71.59%), H (4.18%), N (10.89%), Cl (9.19%).

Observed: C (71.87%), H (4.12%), N (10.67%), Cl (9.15%).

4-(4-fluorophenyl)-5-phenyl-5H-chromeno [4, 3-d] pyrimidin-2-amine (3c)

M.P. 187^0C

IR (cm^{-1}): 3506.80, 3352.73, 1624.63, 1568.27, 1226.26, 756.77, 698.34.

^{1}H NMR ($CDCl_3$): 5.36(s, 2H, NH_2), 6.90-7.02(m, 5H, aromatic and H-5), 7.34-7.55(m, 4H aromatic), 7.85-8.07(m, 4H aromatic.)

^{13}C NMR ($CDCl_3$): 102.09, 117.58, 118.76, 119.07, 127.10, 127.23, 128.88, 130.93, 133.10, 137.14, 160.53, 160.87, 166.08, 166.30.

Elemental analysis: $C_{23}H_{16}N_3OF$

Calculated: C (74.78%), H (4.37%), N (11.38%).

Observed: C (74.68%), H (4.41%), N (11.29%).

4-(4-methoxyphenyl)-5-phenyl-5H-chromeno [4, 3-d] pyrimidin-2-amine (3d)

M.P. 184^{0}C

IR (cm^{-1}): 3506.63, 3352.65, 1624.62, 1568.06, 1539.11, 1226.23, 756.75, 698.39.

^{1}H NMR ($CDCl_3$): 2.16(s, 3H –OCH_3), 5.46(s, 2H, NH_2), 6.91-7.03(m, 5H, aromatic and H-5), 7.35-7.55(m, 4H aromatic), 7.85-8.06(m, 4H aromatic).

^{13}C NMR ($CDCl_3$): 30.92, 102.10, 117.47, 118.80, 119.12, 127.17, 127.27 128.94, 131.08, 133.29, 136.76, 160.29, 160.91, 165.86, 166.33.

Elemental analysis: $C_{24}H_{19}N_3O_2$

Calculated: C (75.57%), H (5.02%), N (11.02%).

Observed: C (75.89%), H (5.04%), N (10.92%).

4-(3-nitrophenyl)-5-phenyl-5H-chromeno [4, 3-d] pyrimidin-2-amine (3e)

M.P. 187^{0}C

IR (cm^{-1}): 3507.21, 3352.70, 1624.51, 1567.91, 1538.85, 1380.88, 1358.32, 1226.26 756.01, 698.53.

^{1}H NMR ($CDCl_3$): 5.51(s, 2H, NH_2), 6.91-7.03(m, 5H, aromatic and H-5), 7.35-7.54(m, 4H aromatic), 7.85-8.04 (m, 4H aromatic).

^{13}C NMR ($CDCl_3$): 102.10, 117.44, 118.80, 119.14, 127.19, 127.28, 128.95, 131.10, 133.31, 136.72, 160.26, 160.92, 165.83, 166.34.

Elemental analysis: $C_{23}H_{16}N_4O_3$

Calculated: C (69.69%), H (4.07%), N (14.23%).

Observed: C (69.76%), H (4.02%), N (14.18%).

4-(furan-2-yl)-5-phenyl-5H-chromeno [4, 3-d] pyrimidin-2-amine (3f)

M.P. 184^{0}C

IR (cm^{-1}): 3507.21, 3352.70, 1624.51, 1567.91, 1538.85, 1226.22, 756.01, 635.07.

^{1} H NMR ($CDCl_3$): 5.34(s, 2H, NH_2), 6.45-7.03(m, 5H, aromatic and H-5), 7.23-7.39(m, 4H aromatic), 7.85-8.13 (m, 3H aromatic).

^{13}C NMR ($CDCl_3$): 102.08, 110.71, 112.02, 114.63, 117.58, 118.70, 121.60, 121.91, 125.17, 127.06, 127.69, 128.21, 128.34, 130.82, 132.99, 133.149, 139.25, 144.94, 151.34, 152.49, 155.49, 157.94, 160.69, 160.80, 162.31, 165.93.

Elemental analysis: $C_{21}H_{15}N_3O_2$

Calculated: C (73.89%), H (4.43%), N (12.31%).

Observed: C (74.21%), H (4.27%), N (12.24%).

5-phenyl-4-(pyridin-4-yl)-5H-chromeno [4, 3 -d] pyrimidin-2-amine (3g)

M.P. 185^0C

IR (cm^{-1}): 3505.63, 3351.98, 1624.39, 1567.88, 1538.80, 1296.63, 755.79, 698.38

^{1} H NMR ($CDCl_3$): 5.28(s, 2H, NH_2), 6.90-7.03(m, 5H, aromatic and H-5), 7.34-7.55(m, 4H aromatic), 7.85-8.07 (m, 4H aromatic).

^{13}C NMR ($CDCl_3$): 102.10, 110.71, 112.02, 117.58, 118.73, 119.04, 127.08, 127.21, 128.86, 130.87, 133.03, 137.30, 160.63, 160.82, 165.99, 166.51.

Elemental analysis: $C_{22}H_{16}N_4O$

Calculated: C (74.98%), H (4.58%), N (15.90%).

Observed: C (74.87%), H (4.71%), N (15.84%).

4. CONCLUSION

In summary, we have described an efficient and one pot three component condensation reaction for the synthesis of benzopyranylpyrimidine derivatives under microwave irradiation in presence of KF-Al_2O_3. The method is short, eco-friendly, inexpensive, shortens the reaction time and gives good yield.

5. ACKNOWLEDGEMENT

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