KF-AL₂O₃ MEDIATED MICROWAVE ASSISTED ONE POT SYNTHESIS OF BENZOPYRANYLPYRIMIDINES


Department of Chemistry, University of Mumbai, Vidyanagari, Santacruz (East), Mumbai-400098.

ABSTRACT

One pot three component condensation reaction between flavanone, aromatic aldehydes and guanidine hydrochloride in presence of KF-Al₂O₃ under microwave irradiation affords benzopyranylpyrimidine in good yield. The synthesized benzopyranylpyrimidine derivatives were characterized by FT-IR, ¹H-NMR, ¹³C-NMR spectroscopic techniques and elemental analysis.

KEYWORDS: Benzopyranylpyrimidine, KF-Al₂O₃, 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-Al₂O₃, variety of reactions occur easily,[¹¹] KF-Al₂O₃ 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.\textsuperscript{[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\textsubscript{2}O\textsubscript{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. \textsuperscript{1}H NMR and \textsuperscript{13}C NMR spectra were obtained on a Bruker AVANCE 300 MHz instrument in CDCl\textsubscript{3} using TMS as internal standard. Chemical shifts (\(\delta\)) 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 benzopyranlypyrimidine derivatives in presence of KF-Al\textsubscript{2}O\textsubscript{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\textsubscript{2}O\textsubscript{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 benzopyranlypyrimidine 3 as yellow solid.
\[
\text{Flavanone } \quad 1 \\
\text{Aromatic aldehyde } \quad 2a-g \\
\text{Guanidine Hydrochloride} \\
\text{Substituted Benzopyranopyrimidine } \quad 3a-g
\]

Scheme-1

<table>
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<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield %</th>
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<td>3a</td>
<td>Phenyl</td>
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<td>4-Chlorophenyl</td>
<td><img src="image2.png" alt="Product Image" /></td>
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<tr>
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<td>4-Fluorophenyl</td>
<td><img src="image3.png" alt="Product Image" /></td>
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<tr>
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<tr>
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<td>4-Pyridyl</td>
<td><img src="image7.png" alt="Product Image" /></td>
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</table>
4, 5-diphenyl-5H-chromeno [4, 3-d] pyrimidin-2-amine (3a)
M.P. 184°C
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\(_3\)O
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°C
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\(_3\)ClO
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°C
IR (cm\(^{-1}\)): 3506.80, 3352.73, 1624.63, 1568.28, 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\(_3\)OF
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°C
IR (cm⁻¹): 3506.63, 3352.65, 1624.62, 1568.06, 1539.11, 1226.23, 756.75, 698.39.
¹H NMR (CDCl₃): 2.16(s, 3H –OCH₃), 5.46(s, 2H, NH₂), 6.91-7.03(m, 5H, aromatic and H-5), 7.35-7.55(m, 4H aromatic), 7.85-8.06(m, 4H aromatic).
¹³C NMR (CDCl₃): 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: C₂₄H₁₉N₃O₂
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°C
IR (cm⁻¹): 3507.21, 3352.70, 1624.51, 1567.91, 1538.85, 1380.88, 1358.32, 1226.26 756.01, 698.39.
¹H NMR (CDCl₃): 5.51(s, 2H, NH₂), 6.91-7.03(m, 5H, aromatic and H-5), 7.35-7.54(m, 4H aromatic), 7.85-8.04 (m, 4H aromatic).
¹³C NMR (CDCl₃): 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: C₂₃H₁₆N₄O₃
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°C
IR (cm⁻¹): 3507.21, 3352.70, 1624.51, 1567.91, 1538.85, 1226.22 756.01, 635.07.
¹H NMR (CDCl₃): 5.34(s, 2H, NH₂), 6.45-7.03(m, 5H, aromatic and H-5), 7.23-7.39(m, 4H aromatic), 7.85-8.13 (m, 3H aromatic).
¹³C NMR (CDCl₃): 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: C₂₁H₁₃N₃O₂
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\(^0\)C
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\(_4\)O
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\(_2\)O\(_3\). The method is short, eco-friendly, inexpensive, shortens the reaction time and gives good yield.

5. ACKNOWLEDGEMENT
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6. REFERENCES
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