7.1. Biological importance of fused-pyridine heterocycles

The fused-pyridine heterocyclic ring system is a widespread subunit in numerous natural products and synthetic pharmaceutical agents [1]. Among them, are the Sceletium alkaloids including (+)-sceletium A-4 1, (+)-tortuosamine 2 and (+)-N-formyltortuosamine 3 [2] are worth mentioning. Haplophyllidine 4 and its acetyl derivative 5 were isolated from aerial parts of the central Asian plant *Haplophyllum perforatum* [3], and the latter compound was also isolated from a Brazilian plant, *Almeida coerulia* [4]. Two more alkaloids of this family, megistosarcimine 6 and megistosarconine 7, (Figure 7.1) were isolated from the New Caledonian tree *Sarcomelicope megistophylla* [5].

![Structures of fused-pyridine heterocyclic natural products](image)

Figure 7.1. Structures of fused-pyridine heterocyclic natural products

Pyridine derivatives containing multi-functional groups can be used as drugs. For example, streptonigrin 10, streptonigrone and lavendamycin are reported to be anticancer drugs, and itavastatin, cerivastatin 11, is HMG-CoA enzyme inhibitors [6]. Moreover, substituted pyridines are reported as leukotriene B4 antagonists [7, 8]. Naturally occurring pyridine derivatives include nicotinamide 12, vitamin B₆ (pyridoxine) 13, nicotine 14, (Figure 7.2) and more complex systems such as nicotinamide adenine dinucleotide (NAD) [9]. Anabasine 15, nicotine and nornicotine 16 have been used as pesticides. Epibatidine 17, [10] a new class of alkaloid possessing a 7-azabicyclo(2.2.1)heptane ring system with 2-chloro-5-pyridyl substituent in an exo-orientation, isolated from the skin extract of Ecuadorian poison...
frog, *Epipedobates tricolour*, has been shown to exhibit non-opioid analgesic activity about 200-500 times than that of morphine.

![Figure 7.2. Structures of bioactive pyridine drugs](image)

**Figure 7.2.** Structures of bioactive pyridine drugs

### 7.2. Synthesis of fused-pyridine heterocycles

Polysubstituted or polycyclic pyridines have been synthesized by various methods, among which two procedures have distinct advantages over the other processes. One is the two-step Kröhnke synthesis [11] via the condensation of pyridinium salts with $\alpha, \beta$-unsaturated ketones in the presence of a mixture of ammonium acetate and acetic acid. The other is Hantzsch-type synthesis via the cyclocondensation of aromatic aldehyde, acetophenone and a nitrogen source such as ammonium acetate or urea [12]. The key step of this reaction is the Michael addition of second molecular acetophenone to $\alpha, \beta$-unsaturated ketones formed *in situ* from the aldol condensation of aromatic aldehyde with acetophenone to form 1,5-diketone. This 1,5-diketone undergoes enamine formation followed by cyclocondensation and air oxidation to furnish the pyridine derivatives. Some synthetic methods for the synthesis of polycyclic fused-pyridine derivatives are discussed below.

Cotterill *et al.* [13] reported the synthesis of highly functionalized pyridines 20-24 from ethyl acetoacetate, aldehydes and 1,3-dicarbonyl compounds 18 and 19 in the presence of ammonium nitrate and bentonite clay.
The monochlorine-substituted oxotetrahydroquinoline 26 is produced with an yield of 68% from the dichlorine-substituted oxo 1,5-diketone 25 and ammonium acetate in glacial acetic acid at 105 °C [14].

When heated with ammonium acetate in acetic acid the oxo 1,5-diketones 27, containing a pyrazolone ring, form the pyrazolo[4,5-b]-5,6,7,8-tetrahydroquinolines 28 [15].

During the action of ammonium acetate on the dibromo diketone 29 the initially formed product not only undergoes pyridinization, but one bromine atom is replaced by a hydroxyl group with the formation of the substituted dihydrobenzoquinone 30 [16].
Zhu et al. [17] reported the synthesis of a series of polysubstituted (3'-indolyl)pyrazolo[3,4-b]pyridine derivatives 33 from the one-pot multicomponent reactions of 3-cyanoacetylindoles 31 with aromatic aldehydes and 5-aminopyrazol 32 in ethylene glycol under microwave irradiation at 150 °C.

Quiroga et al. [18] reported the solvent-free synthesis of 6,8-dihydro-5H-benzo[f]pyrazolo[3,4-b]quinolines 36 from the three-component reaction of β-tetralone 35 with 5-aminopyrazoles 34 and aromatic aldehydes at 120 °C.

R = Me, (Me)₃C; Ar = C₆H₅, 4-ClC₆H₄; Ar' = C₆H₅, 4-ClC₆H₄, 4-FC₆H₄, 4-BrC₆H₄, 4-FC₅C₁H₄, 4-MeC₆H₄, 4-OMeC₆H₄, 4-pyridyl, 3-pyridyl

Powers et al. [19] described the synthesis of pyridine derivatives 41-43 from the enamines 38-40 respectively. These enamines 38-40 react with chalcones 37 in refluxing ethanol to give the pyridines 41-43 in moderate yields.
Patel et al. [20] described the synthesis of 3-(1-aryl-9,10-dihydro-4-azaphenanthren-9-yl)coumarins 46 from the reaction of 3-coumarinoyl methyl pyridinium bromides 44 with 2-arylidene-1-tetralone 45 in the presence of ammonium acetate and acetic acid under the Kröhnke’s reaction condition.

Rong et al. [21] reported the synthesis of 1-aryldiinden[1,2-b;2',1'-e]pyridine derivatives 49 from the four-component reaction of two moles of 2,3-dihydroinden-1-one 47 with different aromatic aldehydes 48 and ammonium acetate under solvent-free conditions.
Mukhopadhyay et al. [22] reported that L-proline is a very efficient catalyst for the one-pot synthesis of substituted 5H-indeno[1,2-b]pyridin-5-ones 53 at room temperature in ethanol.

Mei et al. [23] reported a one-pot multicomponent condensation reaction of three moles of aromatic aldehydes with two moles of cyclic ketones 54 having free \(\alpha,\alpha'\)-methylene positions such as cyclopentanone or cyclohexanone in the presence of ammonium acetate and acetic acid under microwave irradiation affording dicycloalkenopyridines 55 with two \(\alpha\)-arylidene groups in high yields.

Henry et al. [24] described the synthesis of tetrapyridine 59 from the reaction of 4-(5,6-dihydroquinolin-8-yl)morpholine 56 with pyridine aldehyde 57 in the presence of ammonium acetate under reflux condition [25].
Yan et al. [26] reported the synthesis of polycyclic pyridines 63 in high yields by four-component, one-pot cyclocondensation reactions of $N$-phenacylpyridinium bromide 60 aromatic aldehydes 62 cyclic ketones 61 in the presence of ammonium acetate and acetic acid under microwave irradiation.

$n = 0, 1, 2; \ R = H, Cl, CH_3, OCH_3$
7.3. Synthesis of fused-pyridine heterocycles 66-78 and 84 - The present work

The syntheses of fused-pyridine derivatives 66-78 have been achieved by reaction of different cyclic ketones 64 with various α, β-unsaturated compounds 65 in presence of ammonium acetate. The reaction was carried out in ionic liquid [Bmim][BF₄] under microwave irradiation conditions. The reaction proceeds without addition of any acid promoter. Even though the synthesis of pyridine and fused pyridine systems were reported earlier by other groups from similar reactions, many of which were discussed in the introductory part, the present investigation is benefited by high yield, less reaction time, use of ionic liquid medium for clean reaction, lack of byproducts and easy purification process. The generality of the reaction was also tested by screening a library of cyclic ketones with or without a heteroatom.

The reaction of cyclopentanone with 2-(4-chlorobenzylidene)-2,3-dihydro-1H-inden-1-one and ammonium acetate was initially investigated using various solvents, such as methanol, ethanol, ethylene glycol and acetic acid under conventional heating method for 7 h. In these cases, product 66 was formed in 51%, 55%, 47% and 44% respectively. When the reaction has also been conducted for 5 h under thermal condition, compound 66 was produced in 65% yield. Interestingly, the conventional thermal heating reaction of cyclopentanone with 2-(4-chlorobenzylidene)-2,3-dihydro-1H-inden-1-one and ammonium acetate in 0.5mL of [Bmim][BF₄] at 110 °C for 3 h, yielded 74% of 66. Considering the recent advances of microwave irradiation for rapid reactions, we carried out the same reaction in microwave at 120 °C. Surprisingly, the reaction was completed in 10 min with complete conversion of starting compounds and yield was improved to 87% of 66. This success encouraged us to extend this method to a wide range of cyclic ketones and α, β-unsaturated compounds (Table 7.1). The microwave reactions were performed in a CEM [27] discover model microwave synthesizer. After optimizing the conditions for the rapid
synthesis of these fused pyridine derivatives, various cyclic ketones and α, β-
unsaturated compounds were condensed with ammonium acetate to afford the
corresponding fused pyridine derivatives 66-78.

It is pertinent to note that, the ionic liquids have emerged as a set of green solvents
with unique properties such as tunable polarity, high thermal stability and
immiscibility with a number of organic solvents, negligible vapor pressure and
recyclability [28]. Among various ionic liquids, 1-butyl-3-
methylimidazoliumtetrafluoroborate ([Bmim][BF4]) has been used in the synthesis
of vicinal diamines [29], one-pot syntheses of 2H-indazolo[2,1-b]-phthalazine-triones
[30], and cyclisation of 1,6-diynes [31]. It has been proven recently that microwave
heating improves the preparative efficiency and reduces the reaction time for several
organic transformations [32].

In order to study the generality of the procedure, a number of cyclic ketones were
reacted with α, β-unsaturated compounds. The results and the yields of products
obtained are summarized in Table 7.1. After the completion of reaction (entry 1), the
reaction mixture was extracted with ethyl acetate (2 or 3 times) and the residual ionic
liquid was dried at 80 °C under vacuum and reused.

Table 7.1. Structure and yields of fused pyridines 66-78

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cyclic ketone</th>
<th>α, β-unsaturated compounds</th>
<th>Structure of the product</th>
<th>Yield (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td><img src="image" alt="Structure of the product" /></td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>Chemical Structure 1</td>
<td>Chemical Structure 2</td>
<td>Chemical Structure 3</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>----------------------</td>
<td>----------------------</td>
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<td></td>
</tr>
<tr>
<td>2</td>
<td><img src="image1.png" alt="Chemical Structure 1" /></td>
<td><img src="image2.png" alt="Chemical Structure 2" /></td>
<td><img src="image3.png" alt="Chemical Structure 3" /></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="image4.png" alt="Chemical Structure 1" /></td>
<td><img src="image5.png" alt="Chemical Structure 2" /></td>
<td><img src="image6.png" alt="Chemical Structure 3" /></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="Chemical Structure 1" /></td>
<td><img src="image8.png" alt="Chemical Structure 2" /></td>
<td><img src="image9.png" alt="Chemical Structure 3" /></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td><img src="image10.png" alt="Chemical Structure 1" /></td>
<td><img src="image11.png" alt="Chemical Structure 2" /></td>
<td><img src="image12.png" alt="Chemical Structure 3" /></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="image13.png" alt="Chemical Structure 1" /></td>
<td><img src="image14.png" alt="Chemical Structure 2" /></td>
<td><img src="image15.png" alt="Chemical Structure 3" /></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td><img src="image16.png" alt="Chemical Structure 1" /></td>
<td><img src="image17.png" alt="Chemical Structure 2" /></td>
<td><img src="image18.png" alt="Chemical Structure 3" /></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Structure 1</td>
<td>Structure 2</td>
<td>Structure 3</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>-------------</td>
<td>-------------</td>
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<td></td>
</tr>
<tr>
<td>8</td>
<td><img src="image" alt="Structure 8" /></td>
<td><img src="image" alt="Structure 9" /></td>
<td><img src="image" alt="Structure 10" /></td>
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<td>9</td>
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<tr>
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<td><img src="image" alt="Structure 18" /></td>
<td><img src="image" alt="Structure 19" /></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td><img src="image" alt="Structure 20" /></td>
<td><img src="image" alt="Structure 21" /></td>
<td><img src="image" alt="Structure 22" /></td>
<td></td>
</tr>
</tbody>
</table>
The exclusive formation of a single regio isomer while using $\beta$-tetralone or tetrahydro-3-thiophenone as the cyclic ketone can be explained from the additional stability of enamines 79 and 81 from extended conjugation compared to 80 and 82 (Figure 7.3).

![Figure 7.3. Structure of possible enamines](image-url)
The above reaction was also carried out using the cyclic ketone, 6,7-dihydro-1H-indol-4(5H)-one, 83 with simple chalcones 65 in presence of ammonium acetate under microwave irradiation in ionic liquid medium (Scheme 7.2). In this reaction in addition to the formation of pyridine ring 90, additional conversion happens. Thus the initially formed 90 reacts with another chalcone to give the final product 84. In order to check the possibility of exclusively synthesizing 90, the ketone to chalcone ratio is reduced upto 1:0.6 but resulted in 32% of 84b. The ratio of ketone to chalcone 65 was varied from 1:1, 1:1.5, 1:2, 1.2:3 and to 1:2.7 for 65b with yields 41, 63, 78, 77 and 78 respectively of 84b. It was observed that an increase in proportion of chalcone reflected in the yield of products up to 1:2 mole ratios and a further increase did not improve the yield. The scope of the reaction was tested by varying the chalcones and the yields for 1:2 mole ratio of cyclic ketone and chalcone are given in Table 7.2.

Scheme 7.2. Reaction of 6,7-dihydro-1H-indol-4(5H)-one with chalcone

Table 7.2. Yields and melting points of pyrroloquinolines 84

<table>
<thead>
<tr>
<th>Compd.</th>
<th>Ar</th>
<th>Ar'</th>
<th>Yield of 91 (%)^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>84a</td>
<td>C6H5</td>
<td>p-MeC6H4</td>
<td>74</td>
</tr>
<tr>
<td>84b</td>
<td>p-MeC6H4</td>
<td>p-ClC6H4</td>
<td>77</td>
</tr>
<tr>
<td>84c</td>
<td>p-ClC6H4</td>
<td>p-ClC6H4</td>
<td>80</td>
</tr>
<tr>
<td>84d</td>
<td>p-ClC6H4</td>
<td>p-MeOOC6H4</td>
<td>75</td>
</tr>
<tr>
<td>84e</td>
<td>p-MeOOC6H4</td>
<td>C6H5</td>
<td>78</td>
</tr>
<tr>
<td>84f</td>
<td>p-BrC6H4</td>
<td>C6H5</td>
<td>73</td>
</tr>
</tbody>
</table>

^aIsolated yield after purification by column

The structures of products are established from ^1^H, ^13^C and two dimensional NMR spectral data as illustrated for a representative example 67 (Figure 7.4). In the ^1^H NMR spectrum, the singlet at 3.56 ppm is assignable to H-11 which shows C,H-
COSY correlation with C-11 at 33.8 ppm, HMBC with C-10a at 133.0, C-11a at 141.1, C-4a at 143.7 and C-4b at 157.5 ppm respectively. The H-1 proton appears as a multiplet at 7.41-7.44 ppm along with H-3 proton. The H-1 is having HMBC with C-11 at 33.8 and C-11a at 141.1 ppm respectively. The H-2 proton appears at 7.35 ppm (td, $J = 7.5$, 1.2 Hz) which is having C,H-COSY with C-2 at 128.1 ppm and HMBC with C-4 at 120.7 ppm. The H-4 proton appears at 8.12 ppm ($J = 7.5$ Hz) and is having HMBC with C-4b at 157.5 ppm. The triplet at 3.12 ppm is assignable to H-6 which shows (i) H,H-COSY with the multiplet due to H-7 at 1.89-1.97 ppm (ii) C,H-COSY with C-6 at 33.3 ppm and (iii) HMBCs with C-8 at 23.0, C-9a at 127.3 and C-5a at 156.7 ppm respectively. The two multiplets due to H-7 and H-8 having their carbons merged together at 23.0 ppm. This type of accidental merging in the aliphatic region is quite rare. The H-8 protons at 1.75-1.80 ppm is giving (i) H,H-COSY with the triplet due to H-9 at 2.53 ppm and (ii) HMBC with C-9a at 127.3 ppm. The H-9 protons having corresponding carbon at 27.4 ppm and further giving HMBCs with C-9a at 127.3, C-10 at 145.1 and C-5a at 156.7 ppm respectively. The C-10 is having another HMBC from a doublet at aromatic region due to H'-2 ($J = 8.4$ Hz). From C,H-COSY the corresponding carbon is ascribable at 129.6 ppm. From H,H-COSY the doublet at 7.47 ppm is assignable to H'-3 with corresponding carbon at 128.9 ppm. The carbon signals due to C'-1 and C'-4 are assignable to 136.2 and 133.7 ppm from corresponding HMBCs with H'-3 and H'-2 respectively (Figure 7.5 to 7.14).

Figure 7.4. Selected HMBCs and chemical shifts for 67
Figure 7.5. $^1$H NMR Spectrum 67 (CDCl$_3$)

Figure 7.6. $^1$H NMR Spectrum 67 (expanded)
Figure 7.7. $^{13}$C NMR Spectrum of 67 (CDCl$_3$)

Figure 7.8. $^{13}$C NMR Spectrum of 67 (expanded)
Figure 7.9. DEPT-135 Spectrum of 67

Figure 7.10. H,H-COSY Spectrum of 67 (CDCl₃)
Figure 7.11. HMBC Spectrum of 67 (CDCl₃)

Figure 7.12. HMBC Spectrum of 67 (expanded)
Figure 7.13. C,H-COSY Spectrum of 67 (CDCl₃)

Figure 7.14. C,H-COSY Spectrum of 67 (expanded)
The structures of product were further confirmed from X-ray crystallographic studies of 68, 70 and 73 (Figure 7.15 to 7.17).

The structures of thienopyridines are established from ¹H, ¹³C and two dimensional NMR spectral data as illustrated for a representative example 78b (Figure 7.18). In the ¹H NMR spectrum, the triplet at 34.99 ppm is ascribable to H-2 \( (J = 8.4 \text{ Hz}) \) which shows (i) H,H-COSY with H-3 hydrogens (3.66 and 3.84 ppm, dd, \( J = 16.5, 8.4 \text{ Hz for each} \)) (ii) C,H-COSY relation with C-2 at 49.8 ppm and (iii) HMBC with C'-2 at 128.4, C'-1 at 139.5 and C-3a at 160.8 ppm respectively. The H-3 protons are having corresponding carbon at 45.1 ppm and HMBC relations with carbon signals at 132.8, 136.6 and 153.3 ppm respectively. The doublet at 7.35 ppm \( (J = 8.4 \text{ Hz}) \) is assignable to H'-2 and is giving (i) H,H-COSY with another doublet due to H'-3 at 7.27 ppm (ii) C,H-COSY with C'-2 at 128.4 ppm and (iii) HMBC with C-2 at 49.8 ppm. The H'-3 is having corresponding carbon at 128.9 ppm. The singlet at 7.48 ppm is ascribable to H-6 with C,H-COSY correlation at 118.3 ppm due to C-6, which is further giving HMBCs with signals at 132.8, 136.6 and 153.3 ppm.
ppm due to C-7a, C"-1 and C-5 respectively. The doublet at 7.91 ppm ($J = 8.4$ Hz) is due to H"-2 with corresponding carbon at 127.7 ppm and is further giving HMBC with C-5 at 153.3 ppm and H-H-COSY with another doublet at 7.40 ppm which is due to H"-3. The H"-3 proton is having an HMBC relation with C"-4 at 137.2 ppm (Figure 7.19 to 7.28).

Figure 7.18. Selected HMBCs and chemical shifts of thienopyridine 78b

Figure 7.19. $^1$H NMR Spectrum 78b (CDCl$_3$)
Figure 7.20. $^1$H NMR Spectrum of 78b (expanded)

Figure 7.21. $^{13}$C NMR Spectrum of 78b (CDCl$_3$)
Figure 7.22. $^{13}$C NMR Spectrum of 78b (expanded)

Figure 7.23. DEPT-135 Spectrum of 78b
Figure 7.24. H,H-COSY Spectrum of 78b (CDCl$_3$)

Figure 7.25. HMBC Spectrum of 78b
Figure 7.26. HMBC Spectrum of 78b (expanded)

Figure 7.27. C,H-COSY Spectrum of 78b
The structures of pyrroloquinolines were established from $^1$H, $^{13}$C and two dimensional NMR spectral data as illustrated for a representative example 84b (Figure 7.29). In the $^1$H NMR spectrum, the triplet at 4.14 ppm is ascribable to H'-1 which shows (i) C,H-COSY correlation with C'-1 at 34.1 ppm and (ii) HMBC with C-8 at 102.3, C"'-2 at 130.1 and C"'-1 at 137.1 ppm respectively. The doublet at 7.16 ppm ($J = 9.0$ Hz) is assignable to H"'-2 and is having (i) H,H-COSY with another doublet due to H"'-3 at 7.25 ppm (ii) C,H-COSY with C"'-2 at 130.1 ppm and (iii) HMBC with C'-1 at 34.1 and C"'-4 at 132.6 ppm respectively. The singlet at 7.27 ppm is ascribable to H-8, which is having C,H-COSY with C-8 at 102.3 ppm and HMBC with C-9a at 125.3 ppm. The doublet ($J = 9.0$ Hz) due to one hydrogen is assignable to H-6 and which shows (i) H,H-COSY with another doublet which is due to H-5 at 7.45 ppm (ii) C,H-COSY with C-6 at 112.7 ppm and (iii) HMBCs with carbon signals at 120.4 and 125.3 ppm due to C-4a and C-9a respectively. H-5 is having C,H-COSY with C-5 at 118.8 ppm and HMBCs with C-6a, C-4 and C-9b at 135.9, 144.1 and 147.9 ppm respectively. The singlet at 7.68 ppm is due to H-3 and corresponding carbon is assignable at 116.6 ppm, further giving HMBCs with C-4a at 120.4 ppm and C-2 at 155.3 ppm. The doublet at 8.17 ppm ($J = 8.1$ Hz) is ascribable to H"''-2 with corresponding carbon at 127.4 ppm and HMBC with C-2 at 155.3 ppm. H"''-2 is
having coupling partner at 7.31 ppm due to H''-3 with corresponding carbon at 129.4 ppm and HMBC with C''-1 at 137.2 ppm. The methyl signal is appearing at 2.42 ppm with corresponding carbon at 21.3 ppm. The methyl protons give HMBC with C''-3 at 129.4 and C''-4 at 139.0 ppm. The NH proton is appearing as a singlet at 8.26 ppm. (Figure 7.30 to 7.40).

**Figure 7.29.** Selected HMBCs and chemical shifts of 84b

**Figure 7.30.** $^1$H NMR Spectrum 84b (CDCl$_3$)
Figure 7.31. $^1$H NMR Spectrum of 84b (expanded)

Figure 7.32. $^{13}$C NMR Spectrum of 84b (CDCl$_3$)
Figure 7.33. $^{13}$C NMR Spectrum of 84b (expanded)

Figure 7.34. DEPT-135 Spectrum of 84b
Chapter 7

Results and discussion

Figure 7.35. H,H-COSY Spectrum of 84b (CDCl₃)

Figure 7.36. H,H-COSY Spectrum of 84b (expanded)
Figure 7.37. HMBC Spectrum of 84b (CDCl₃)

Figure 7.38. HMBC Spectrum of 84b (expanded)
A mechanism is proposed for the formation of 84 in (Scheme 7.3). This involves enamine formation-Michael addition-cyclocondensation-oxidation-Michael addition-elimination in a domino sequences. The reaction has initiated by the formation of enamine 85 which on Michael addition to chalcone results in intermediate 86. This on subsequent cyclization and aromatization results in pyridine ring system 90. The lone pair of electron on nitrogen in 90 facilitates the second Michael addition which
subsequently results in elimination of phenacyl group and aromatization to form product 84.

\[ \text{Scheme 7.3. Proposed mechanism for the formation of fused-pyridines 84} \]

### 7.4. Conclusion

A rapid, efficient and eco-friendly method for the synthesis of pyridine, thienopyridines and pyrroloquinolines from the reaction of cyclic ketones and cyclic/acyclic α, β-unsaturated compounds and ammonium acetate by using ionic liquid as reaction medium has been achieved. Operational simplicity, high yields, and reusability of ionic liquids are the notable features of the present protocol. When 6,7-dihydro-1H-indol-4(5H)-one is used as the cyclic ketone, an unusual product is formed by a second Michael addition-elimination pathway. A probable mechanism was proposed for the formation of products. The synthesized compounds were characterized using NMR and crystal analysis.
7.5. Experimental section

7.5.1. General method

Melting points were measured in open capillary tubes and are uncorrected. A CEM Discover microwave synthesizer (Model No: 908010) operating at 180/264 V and 50/60 Hz with microwave power maximum level of 300 W and microwave frequency of 2455 MHz was employed for the microwave-assisted experiments done in this work. The $^1$H NMR, $^{13}$C NMR and C,H-COSY were recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as internal standard and CDCl$_3$ as solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ-scale) and the coupling constants are given in Hertz. Silica gel-G plates (Merck) were used for TLC analysis with a mixture of petroleum ether (60–80 °C) and ethylacetate as eluant. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyzer.

7.5.2. General procedure for the synthesis of fused-pyridines 66-78: Cyclic ketones 64 (1 mmol), acyclic/cyclic $\alpha$, $\beta$-unsaturated compounds 65 (1 mmol), NH$_4$OAc (4 mmol) and 1-butyl-3-methylimidazolium tetrafluoroborate ([Bmim][BF$_4$]) (0.5 mL) were placed in a 10 mL sealed microwave vessel. The reaction tube was placed inside the cavity of a CEM Discover microwave oven, operated at 120 °C (temperature monitored by built-in infrared sensor), power 100 watt for 10 min. After completion of the reaction, the reaction mixture brought to room temperature and extracted with ethyl acetate (2x5 ml). The organic layer was washed with brine solution and dried over Na$_2$SO$_4$. The combined organic layers were evaporated and purified through column (10% ethyl acetate/petroleum ethers). The residual ionic liquid was dried under vacuum at 80 °C for 4 h and reused for subsequent cycles. The spectral data of all compounds are given below:

7.5.2.1. 10-(4-Chlorophenyl)-1,2,3,9-tetrahydrocyclopenta[b]indenol[2,1-e]pyridine (66). Isolated as colorless solid; m.p. 162-163 °C; $^1$H NMR (300 MHz, CDCl$_3$) δ: 2.12-2.24 (m, 2H, CH$_2$), 2.86 (t, 2H, J = 7.5 Hz, CH$_2$), 3.18 (t, 2H, J = 7.5 Hz, CH$_2$), 3.69 (s, 2H, CH$_2$), 7.35 (d, 2H, J = 8.1 Hz, Ar-H), 7.40-7.43 (m, 3H, Ar-H), 7.46 (d, 2H, J = 8.1 Hz, Ar-H), 8.12 (d, 1H, J = 7.8 Hz, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ: 23.6, 30.1, 33.7, 34.5, 120.6, 124.9, 127.1, 128.0, 128.8, 129.6, 132.7,
132.8, 134.0, 135.9, 141.1, 141.6, 143.7, 159.4, 165.4. Anal. Calcd for C_{21}H_{16}ClN: C, 79.36; H, 5.07; N, 4.41%. Found C, 79.33; H, 5.04; N, 4.43%.

7.5.2.2. 10-(4-Chlorophenyl)-7,8,9,11-tetrahydro-6H-indeno[1,2-b]quinoline (67).

Isolated as colorless solid; m.p. 209-210 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 1.75-1.80 (m, 2H, CH\(_2\)), 1.89-1.97 (m, 2H, CH\(_2\)), 2.53 (t, 2H, \(J = 6.3\) Hz, CH\(_2\)), 3.12 (t, 2H, \(J = 6.3\) Hz, CH\(_2\)), 3.56 (s, 2H, CH\(_2\)), 7.22 (d, 2H, J = 8.4 Hz, Ar-H), 7.35 (td, 1H, J = 7.5, 1.2 Hz, Ar-H), 7.41-7.44 (m, 2H, Ar-H), 7.47 (d, 2H, J = 8.4 Hz, Ar-H), 8.12 (d, 1H, J = 7.5 Hz, Ar-H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 23.0 (2C), 27.4, 33.3, 33.8, 120.7, 124.9, 127.1, 127.3, 128.1, 128.9, 129.6, 133.0, 133.7, 136.2, 141.1, 143.7, 145.1, 156.6, 157.5. Anal. Calcd for C\(_{22}\)H\(_{18}\)ClN: C, 79.63; H, 5.47; N, 4.22%. Found C, 79.59; H, 5.44; N, 4.25%.

7.5.2.3. 7-(4-Chlorophenyl)-6,8-dihydro-5H-benzo[h]indeno[1,2-b]quinoline (68).

Isolated as colorless solid; m.p. 228-229 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 2.71-2.81 (m, 4H, 2CH\(_2\)), 3.61 (s, 2H, CH\(_2\)), 7.20 (d, 1H, J = 7.5 Hz, Ar-H), 7.25 (d, 2H, J = 8.1 Hz, Ar-H), 7.29 (dd, 1H, J = 7.2, 1.2 Hz, Ar-H), 7.34 (dd, 1H, J = 7.5, 1.5 Hz, Ar-H), 7.37 (dd, 1H, J = 7.5, 2.1 Hz, Ar-H), 7.41-7.45 (m, 2H, Ar-H), 7.47 (d, 2H, J = 8.1 Hz, Ar-H), 8.21 (d, 1H, J = 8.1 Hz, Ar-H), 8.59 (d, 1H, J = 7.8 Hz, Ar-H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 25.6, 28.2, 34.3, 121.0, 124.9, 125.5, 127.1, 127.2, 127.3, 127.4, 128.2, 128.8, 129.9, 134.0, 134.3, 135.4, 136.0, 137.8, 141.5, 143.7, 144.0, 152.1, 158.3. Anal. Calcd for C\(_{26}\)H\(_{18}\)ClN: C, 82.20; H, 4.78; N, 3.69%. Found C, 82.16; H, 4.73; N, 3.73%.

7.5.2.4. 13-(4-Chlorophenyl)-6,12-dihydro-5H-benzo[f]indeno[1,2-b]quinoline (69).

Isolated as colorless solid; m.p. 213-214 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 2.96 (t, 2H, J = 7.2 Hz, CH\(_2\)), 3.18 (t, 2H, J = 7.2 Hz, CH\(_2\)), 3.63 (s, 2H, CH\(_2\)), 6.76 (d, 1H, J = 8.1 Hz, Ar-H), 6.84 (t, 1H, J = 8.1 Hz, Ar-H), 7.06 (td, 1H, J = 7.2, 1.2 Hz, Ar-H), 7.20-7.24 (m, 3H, Ar-H), 7.30-7.45 (m, 5H, Ar-H), 8.22 (d, 1H, J = 8.1 Hz, Ar-H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 29.4, 33.5, 34.6, 120.9, 124.9, 125.6, 125.8, 127.0, 127.2, 127.6, 128.4, 129.2, 129.3, 130.3, 132.8, 133.8, 135.1, 137.5, 139.1, 140.8, 142.1, 144.0, 158.1, 160.0. Anal. Calcd for C\(_{26}\)H\(_{18}\)ClN: C, 82.20; H, 4.78; N, 3.69%. Found C, 82.17; H, 4.74; N, 3.74%. 

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Chapter-7

Experimental section
7.5.2.5. 10-(4-Chlorophenyl)-3,9-dihydro-2H-indeno[1,2-b]thieno[2,3-e]pyridine (70). Isolated as colorless solid; m.p. 184-185 °C; 1H NMR (300 MHz, CDCl$_3$) δ$_H$: 3.33 (t, 2H, $J = 7.8$ Hz, CH$_2$), 3.52 (t, 2H, $J = 7.8$ Hz, CH$_2$), 3.16 (s, 2H, CH$_2$), 7.30 (d, 1H, $J = 7.2$ Hz, Ar-H), 7.37-7.54 (m, 6H, Ar-H), 8.00 (d, 1H, $J = 7.5$ Hz, Ar-H); 13C NMR (75 MHz, CDCl$_3$) δ$_C$: 30.2, 33.7, 37.1, 120.1, 124.8, 127.1, 127.8, 129.0, 129.3, 133.0, 133.5, 134.5, 135.8, 138.7, 140.7, 143.1, 157.4, 160.8. Anal. Calcd for C$_{20}$H$_{14}$ClNS: C, 71.52; H, 4.20; N, 4.17%. Found C, 71.50; H, 4.17; N, 4.20%.

7.5.2.6. 7-Phenyl-6,8,9,10-tetrahydro-5H-benzo[h]cyclopenta[b]quinoline (71). Isolated as colorless solid; m.p. 137-138 °C; 1H NMR (300 MHz, CDCl$_3$) δ$_H$: 2.09 (qnt, 2H, $J = 7.5$ Hz, CH$_2$), 2.71-2.78 (m, 6H, 3CH$_2$), 3.14 (t, 2H, $J = 7.5$ Hz, CH$_2$), 7.18-7.30 (m, 4H, Ar-H), 7.33-7.48 (m, 4H, Ar-H), 8.34 (d, 2H, $J = 7.8$ Hz, Ar-H); 13C NMR (75 MHz, CDCl$_3$) δ$_C$: 23.1, 25.5, 28.4, 30.5, 34.7, 125.1, 127.0, 127.1, 127.3, 127.6, 128.4 (2C), 128.5, 134.3, 135.4, 137.8, 137.9, 145.0, 151.2, 163.2. Anal. Calcd for C$_{22}$H$_{19}$N: C, 88.85; H, 6.44; N, 4.71%. Found C, 88.81; H, 6.41; N, 4.75%.

7.5.2.7. 7-Phenyl-5,6,8,9,10,11-hexahydrobenzo[c]acridine (72). Isolated as colorless solid; m.p. 185-186 °C; 1H NMR (300 MHz, CDCl$_3$) δ$_H$: 1.78-1.99 (m, 4H, 2CH$_2$), 2.61-2.74 (m, 4H, 2CH$_2$), 3.05-3.10 (m, 4H, CH$_2$), 7.29-7.46 (m, 6H, Ar-H), 7.53 (d, 2H, $J = 8.1$ Hz, Ar-H), 7.73 (dd, 1H, $J = 7.8$, 2.7 Hz, Ar-H); 13C NMR (75 MHz, CDCl$_3$) δ$_C$: 23.0, 23.6, 27.0, 29.8, 30.1, 32.9, 125.7, 127.5 (2C), 127.7, 128.1, 128.2, 128.8, 129.3 (2C), 132.9, 140.7 (2C), 142.4, 154.6, 155.7. Anal. Calcd for C$_{23}$H$_{21}$N: C, 88.71; H, 6.80; N, 4.50%. Found C, 88.68; H, 6.76; N, 4.54%.

7.5.2.8. 7-(4-Chlorophenyl)-6,8,9,10-tetrahydro-5H-benzo[h]cyclopenta[b]quinoline (73). Isolated as colorless solid; m.p. 140-141 °C; 1H NMR (300 MHz, CDCl$_3$) δ$_H$: 2.09 (qnt, 2H, $J = 7.5$ Hz, CH$_2$), 2.65-2.78 (m, 6H, 3CH$_2$), 3.13 (t, 2H, $J = 7.5$ Hz, CH$_2$), 7.16-7.19 (m, 3H, Ar-H), 7.28 (t, 1H, $J = 7.2$ Hz, Ar-H), 7.35 (t, 1H, $J = 7.5$ Hz, Ar-H), 7.43 (d, 2H, $J = 8.4$ Hz, Ar-H), 8.33 (d, 1H, $J = 7.5$ Hz, Ar-H); 13C NMR (75 MHz, CDCl$_3$) δ$_C$: 23.1, 25.5, 28.3, 30.4, 34.6, 125.1, 126.9, 127.0, 127.3, 128.5, 128.7, 129.9, 133.7, 134.2, 135.3, 136.2, 137.7, 143.7, 151.3, 163.3. Anal. Calcd for C$_{22}$H$_{18}$ClN: C, 79.63; H, 5.47; N, 4.22%. Found C, 79.60; H, 5.43; N, 4.26%.
7.5.2.9. **7-(4-Chlorophenyl)-5,6,8,9,10,11-hexahydrobenzo[c]acridine** (74). Isolated as colorless solid; m.p. 177-178 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 1.73-1.81 (m, 2H, CH$_2$), 1.94-2.02 (m, 2H, CH$_2$), 2.63 (dd, 2H, $J = 8.7, 4.2$ Hz, CH$_2$), 2.71 (dd, 2H $J = 8.7, 4.2$ Hz, CH$_2$), 3.07 (t, 4H, $J = 6.6$ Hz, 2CH$_2$), $7.31-7.38$ (m, 3H, Ar-H), $7.41$ (d, 2H, $J = 8.7$ Hz, Ar-H), $7.49$ (d, 2H, $J = 8.7$ Hz, Ar-H), $7.72$ (dd, 1H, $J = 8.4, 3.3$ Hz, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$: 22.9, 23.5, 26.9, 29.6, 30.0, 32.9, 125.7, 127.4, 127.7, 128.2, 128.6, 128.7 (2C), 130.6, 132.6, 133.7, 139.1, 140.5, 142.5, 153.2, 155.8. Anal. Calcd for C$_{23}$H$_{20}$ClN: C, 79.87; H, 5.83; N, 4.05%. Found C, 79.83; H, 5.79; N, 4.10%.

7.5.2.10. **7-(4-Chlorophenyl)-6,8,9,10,11,12-hexahydro-5H-benzo[h]cyclohepta[b]quinoline** (75). Isolated as colorless solid; m.p. 137-138 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 1.82-1.97 (m, 6H, 3CH$_2$), 2.62-2.72 (m, 4H, 2CH$_2$), 3.10-3.19 (m, 4H, 2CH$_2$), 7.28-7.41 (m, 6H, Ar-H), $7.49$ (d, 2H, $J = 8.4$ Hz, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$: 26.8, 27.2, 27.9, 29.7, 30.5, 32.2, 39.4, 126.0, 127.5, 128.1, 128.2, 128.8, 129.2, 130.8, 132.8, 133.1, 133.7, 139.1, 140.4, 142.4, 151.9, 162.7. Anal. Calcd for C$_{24}$H$_{22}$ClN: C, 80.10; H, 6.16; N, 3.89%. Found C, 80.06; H, 6.13; N, 3.93%.

7.5.2.11. **14-(4-Chlorophenyl)-5,6,12,13-tetrahydrodibenzo[a,h]acridine** (76). Isolated as colorless solid; m.p. 181-182 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 2.63-2.68 (m, 2H, CH$_2$), 2.78-2.83 (m, 2H, CH$_2$), 2.92-2.96 (m, 2H, CH$_2$), 3.09-3.14 (m, 2H, CH$_2$), 6.64 (d, 1H, $J = 8.1$ Hz, Ar-H), 6.82 (td, 1H, $J = 8.7, 1.2$ Hz, Ar-H), 7.07 (td, 1H, $J = 7.5, 1.2$ Hz, Ar-H), 7.13 (d, 2H, $J = 8.4$ Hz, Ar-H), 7.19-7.24 (m, 2H, Ar-H), 7.29 (td, 1H, $J = 7.5, 1.2$ Hz, Ar-H), 7.34-7.41 (m, 3H, Ar-H), 8.36 (dd, 1H, $J = 7.8, 1.2$ Hz, Ar-H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$: 25.6, 28.2, 29.5, 33.3, 125.3, 125.6, 127.0 (2C), 127.1, 127.4, 127.6, 128.6, 128.9, 129.1, 129.2 (2C), 131.0, 133.0, 135.0, 137.7, 137.9, 139.4, 144.0, 150.4, 158.1. Anal. Calcd for C$_{27}$H$_{20}$ClN: C, 82.33; H, 5.12; N, 3.56%. Found C, 82.29; H, 5.07; N, 3.60%.

7.5.2.12. **7-(4-Chlorophenyl)-5,6,9,10-tetrahydrobenzo[h][thieno]3,2-bquinoline** (77). Isolated as colorless solid; m.p. 154-155 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 2.65-2.77 (m, 4H, 2CH$_2$), 3.32 (t, 2H, $J = 7.8$ Hz, CH$_2$), 3.50 (t, 2H, $J = 8.1$ Hz, CH$_2$), 7.17 (d, 1H, $J = 7.2$ Hz, Ar-H), 7.23-7.29 (m, 2H, Ar-H), 7.34 (t, 2H, $J = 7.2$ Hz, Ar-H), 7.44 (d, 2H, $J = 8.4$ Hz, Ar-H), 8.26 (d, 1H, $J = 7.8$ Hz, Ar-H); $^{13}$C NMR (75
MHZ, CDCl 3) δ: 25.4, 28.1, 29.9, 37.2, 124.6, 127.0, 127.4, 127.7, 128.4, 129.0, 129.8, 134.3, 134.8, 134.9, 136.3, 137.2, 140.6, 149.1, 158.8. Anal. Calcd for C 21H 16ClN S: C, 72.09; H, 4.61; N, 4.00%. Found C, 72.07; H, 4.58; N, 4.03%.

7.5.2.13. 2,5,7-Triphenyl-2,3-dihydrothieno[3,2-b]pyridine (78a). Isolated as colorless solid; m.p. 94-95 °C; 1H NMR (300 MHz, CDCl 3) δ: 3.76 (dd, 1H, J = 16.5, 8.7 Hz, CH), 3.88 (dd, 1H, J = 16.5, 8.7 Hz, CH), 5.06 (t, 1H, J = 8.7 Hz, CH), 7.28-7.35 (m, 5H, Ar-H), 7.38-7.48 (m, 6H, Ar-H), 7.58 (s, 1H, Ar-H), 7.64 (d, 2H, J = 8.4 Hz, Ar-H), 8.00 (d, 2H, J = 8.4 Hz, Ar-H); 13C NMR (75 MHz, CDCl 3) δ: 45.3, 50.6, 118.8, 126.6, 127.2, 127.3, 127.6, 127.8, 127.9, 128.5, 128.7 (2C), 132.9, 138.6, 139.2, 141.1, 142.9, 154.4, 160.9. Anal. Calcd for C 25H 19NS: C, 82.15; H, 5.24; N, 3.83%. Found C, 82.11; H, 5.21; N, 3.87%.

7.5.2.14. 2,5,7-tri(4-Chlorophenyl)-2,3-dihydrothieno[3,2-b]pyridine (78b). Isolated as colorless solid; m.p. 91-92 °C; 1H NMR (300 MHz, CDCl 3) δ: 3.66 (dd, 1H, J = 16.5, 8.4 Hz, CH), 3.84 (dd, 1H, J = 16.5, 8.4 Hz, CH), 4.99 (t, 1H, J = 8.4 Hz, CH), 7.27 (d, 2H, J = 8.7 Hz, Ar-H), 7.35 (d, 2H, J = 8.4 Hz, Ar-H), 7.41 (d, 2H, J = 8.4 Hz, Ar-H), 7.43 (d, 2H, J = 8.4 Hz, Ar-H), 7.48 (s, 1H, Ar-H), 7.53 (d, 2H, J = 8.7 Hz, Ar-H), 7.91 (d, 2H, J = 8.4 Hz, Ar-H); 13C NMR (75 MHz, CDCl 3) δ: 45.1, 49.8, 118.3, 127.7, 128.4, 128.8, 128.9 (2C) 129.0, 132.8, 133.7, 134.7, 135.0, 136.7, 137.2, 139.5, 141.8, 153.3, 160.8. Anal. Calcd for C 25H 19Cl 3NS: C, 64.05; H, 3.44; N, 2.99%. Found C, 64.01; H, 3.41; N, 3.03%.

7.5.2.15. 7-(4-Bromophenyl)-5-(4-chlorophenyl)-2-phenyl-2,3-dihydrothieno[3,2-b]pyridine (78c). Isolated as colorless solid; m.p. 112-113 °C; 1H NMR (300 MHz, CDCl 3) δ: 3.74 (dd, 1H, J = 16.5, 8.4 Hz, CH), 3.87 (dd, 1H, J = 16.5, 8.4 Hz, CH), 5.07 (t, 1H, J = 8.4 Hz, CH), 7.28-7.62 (m, 11H, Ar-H), 7.75 (s, 1H, Ar-H), 7.93 (d, 2H, J = 8.4 Hz, Ar-H); 13C NMR (75 MHz, CDCl 3) δ: 45.1, 50.7, 118.3, 122.9, 126.2, 127.1, 127.8, 128.8, 128.9, 130.3, 130.6, 131.8, 134.7, 137.3, 140.4, 140.8, 141.4, 153.1, 161.3. Anal. Calcd for C 25H 17BrClNS: C, 62.71; H, 3.58; N, 2.93%. Found C, 62.68; H, 3.56; N, 2.97%.

7.5.2.16. 7-(4-Chlorophenyl)-5-(4-methoxyphenyl)-2-phenyl-2,3-dihydrothieno[3,2-b]pyridine (78d). Isolated as colorless solid; m.p. 89-90 °C; 1H NMR (300 MHz, CDCl 3) δ: 3.71-3.91 (m, 5H, OCH 3, CH 2), 5.03 (t, 1H, J = 8.7 Hz,
7.5.3. General procedure for the synthesis of pyrroloquinolines 84: 6,7-Dihydro-1H-indol-4(5H)-one 83, chalcones 65 (2 mmol), NH₄OAc (4 mmol) and 1-butyl-3-methylimidazolium tetrafluoroborate ([Bmim][BF₄]) (0.5 mL) were placed in a 10 mL sealed microwave vessel. The reaction tube was placed inside the cavity of a CEM Discover microwave oven, operated at 120 °C (temperature monitored by built-in infrared sensor), power 100 watt for 15 min. After completion of the reaction, the reaction mixture brought to room temperature and extracted with ethylacetate (2x5 ml). The organic layer was washed with brine solution and dried over Na₂SO₄. The combined organic layers were evaporated and purified through column (10% ethylacetate/petroleum ethers). The residual ionic liquid was dried under vacuum at 80 °C for 4 h and reused for subsequent cycles. The spectral data of all compounds are given below:

7.5.3.1. 9-(4-Methylbenzyl)-4-(4-methylphenyl)-2-phenyl-7H-pyrrolo[2,3-h]quinoline (84a). Isolated as colorless solid; m.p. 137-138 °C; ¹H NMR (300 MHz, CDCl₃) δH: 2.32 (s, 3H, CH₃), 2.46 (s, 3H, CH₃), 4.12 (s, 2H, CH₂), 7.10-7.17 (m, 4H, Ar-H), 7.28-7.34 (m, 4H, Ar-H), 7.39-7.55 (m, 6H, Ar-H), 7.73 (s, 1H, Ar-H), 8.18 (bvs, 1H, NH), 8.29 (d, 2H, J = 8.4 Hz, Ar-H); ¹³C NMR (75 MHz, CDCl₃) δC: 21.0, 21.2, 34.4, 102.0, 112.6, 116.8, 119.0, 120.9, 125.5, 127.5, 128.6, 128.7, 129.1 (2C), 129.4, 129.6, 135.1, 135.6, 136.3, 136.7, 136.9, 137.8, 140.3, 144.2, 149.3, 155.1. Anal. Calcd for C₃₂H₂₆N₂: C, 87.84; H, 5.98; N, 6.39%. Found C, 87.80; H, 5.95; N, 6.42%.

7.5.3.2. 9-(4-Chlorobenzyl)-4-(4-chlorophenyl)-2-(4-methylphenyl)-7H-pyrrolo[2,3-h] quinoline (84b). Isolated as colorless solid; m.p. 209-210 °C; ¹H NMR (300 MHz, CDCl₃) δH: 2.42 (s, 3H, CH₃), 4.14 (s, 2H, CH₂), 7.16 (d, 2H, J = 9.0 Hz, Ar-H), 7.25 (d, 2H, J = 9.0 Hz, Ar-H), 7.27 (s, 1H, Ar-H), 7.31 (d, 2H, J = 8.1 Hz, Ar-H), 7.34 (d, 2H, J = 9.0 Hz, Ar-H), 7.45 (d, 2H, J = 9.0 Hz, Ar-H), 7.47-7.49
 Experimental section

7.5.3.3. 9-(4-Chlorobenzyl)-2,4-di(4-chlorophenyl)-7H-pyrrolo[2,3-h]quinoline (84c). Isolated as colorless solid; m.p. 125–126 °C; \( ^1H \) NMR (300 MHz, CDCl\(_3\)) \( \delta \): 4.17 (s, 2H, CH\(_2\)), 7.17-7.29 (m, 5H, Ar-H), 7.36-7.49 (m, 8H, Ar-H), 7.66 (s, 1H, Ar-H), 8.22 (d, 2H, \( J = 8.4 \) Hz, Ar-H), 8.33 (brs, 1H, NH); \( ^{13}C \) NMR (75 MHz, CDCl\(_3\)) \( \delta \): 34.7, 102.3, 113.2, 116.5, 119.7, 120.8, 123.5, 125.7, 126.5, 128.3, 128.6, 128.9, 129.0, 129.1, 129.5, 131.5, 135.3, 136.5, 138.8, 139.4, 139.7, 144.3, 149.5, 153.7. Anal. Calcd for C\(_{30}H_{19}Cl_3N_2\): C, 70.12; H, 3.73; N, 5.45%. Found C, 70.09; H, 3.70; N, 5.49%.

7.5.3.4. 2-(4-Chlorophenyl)-9-(4-methoxybenzyl)-4-(4-methoxyphenyl)-7H-pyrrolo [2,3-h]quinoline (84d). Isolated as colorless solid; m.p. 158-159 °C; \( ^1H \) NMR (300 MHz, CDCl\(_3\)) \( \delta \): 3.79 (s, 3H, OCH\(_3\)), 3.90 (s, 3H, OCH\(_3\)), 4.17 (s, 2H, CH\(_2\)), 6.86 (d, 2H, \( J = 8.4 \) Hz, Ar-H), 7.06 (d, 2H, \( J = 8.7 \) Hz, Ar-H), 7.20 (d, 2H, \( J = 8.4 \) Hz, Ar-H), 7.28 (brs, 1H, Ar-H), 7.35 (d, 1H, \( J = 9.0 \) Hz, Ar-H), 7.46-7.51 (m, 4H, Ar-H), 7.56 (d, 1H, \( J = 9.0 \) Hz, Ar-H), 7.68 (s, 1H, Ar-H), 8.21 (brs, 1H, NH), 8.24 (d, 2H, \( J = 8.4 \) Hz, Ar-H); \( ^{13}C \) NMR (75 MHz, CDCl\(_3\)) \( \delta \): 34.0, 55.3, 55.4, 101.9, 112.9, 114.0, 114.3, 116.5, 119.0, 121.1, 125.4, 128.7, 128.8, 129.9, 130.7, 130.8, 132.0, 135.0, 135.2, 137.1, 138.8, 144.2, 149.2, 153.8, 158.6, 159.7. Anal. Calcd for C\(_{32}H_{25}ClN_2O_2\): C, 76.11; H, 4.99; N, 5.55%. Found C, 76.07; H, 4.96; N, 5.60%.

7.5.3.5. 9-Benzyl-2-(4-methoxyphenyl)-4-phenyl-7H-pyrrolo[2,3-h]quinoline (84e). Isolated as colorless solid; m.p. 157-158 °C; \( ^1H \) NMR (300 MHz, CDCl\(_3\)) \( \delta \): 3.89 (s, 3H, OCH\(_3\)), 4.27 (s, 2H, CH\(_2\)), 7.05 (d, 2H, \( J = 8.7 \) Hz, Ar-H), 7.30-7.36 (m, 7H, Ar-H), 7.43-7.59 (m, 6H, Ar-H), 7.70 (s, 1H, Ar-H), 8.20 (brs, 1H, NH), 8.27 (d, 2H, \( J = 9.0 \) Hz, Ar-H); \( ^{13}C \) NMR (75 MHz, CDCl\(_3\)) \( \delta \): 34.9, 55.4, 102.2, 112.3, 114.2, 116.4, 119.1, 120.3, 126.7, 127.9, 128.4, 128.8 (3C), 128.9, 129.7, 133.0,
7.5.3.6. 9-Benzyl-2-(4-bromophenyl)-4-phenyl-7H-pyrrolo[2,3-h]quinoline (84f).

Isolated as colorless solid; m.p. 113-114 °C; $^1$H NMR (300 MHz, CDCl$_3$) $\delta_H$: 4.26 (s, 2H, CH$_2$), 7.27-7.36 (m, 5H, Ar-H), 7.39 (s, 1H, Ar-H), 7.48-7.57 (m, 6H, Ar-H), 7.64 (d, 2H, $J = 8.4$ Hz, Ar-H), 7.71 (s, 1H, Ar-H), 8.19 (d, 2H, $J = 8.4$ Hz, Ar-H), 8.22 (brs, 1H, NH); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta_C$: 34.9, 102.2, 113.0, 116.4, 119.1, 121.0, 123.4, 125.4, 126.8, 128.1, 128.4, 128.8, 128.9, 129.1, 129.6, 131.8, 135.2, 136.6, 138.7, 139.1, 139.7, 144.2, 149.6, 153.8. Anal. Calcd for C$_{30}$H$_{21}$BrN$_2$: C, 73.62; H, 4.32; N, 5.72%. Found C, 73.57; H, 4.28; N, 5.76%.


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27. CEM Corporation, PO Box 200, Matthews, NC 28106.


