Chapter IV

Synthetic methodologies using ethylammonium nitrate (EAN) as an ionic liquid


Section-I

Solvent-free, highly efficient one-pot multi-component synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols catalyzed by ethylammonium nitrate as reusable ionic liquid under neat reaction condition at ambient temperature

4.1.1 Introduction

A variety of natural products containing 1,3-amino-oxygenated functional groups act as potential drugs, as antibiotic,\(^1\) antitumor,\(^2\) antimalarial,\(^3\) antianginal,\(^4\) antihypertensive,\(^5\) antirheumatics,\(^6\) and HIV protease inhibitors.\(^7a\) The bradycardiac effects of these motifs have also been reported.\(^7b\) Owing to the biological and/or medicinal as well pharmacological importance of 1-amidoalkyl-2-naphthols derivatives, efforts have been made by the various researchers in developing multi-component coupling reactions (MCRs) for the synthesis of 1-amidoalkyl-2-naphthols from aldehydes, beta-naphthols and amides/carbamates and/or urea under thermal and/or heating or sonication conditions using various catalysts such as montmorillonite K10,\(^8\) p-TSA,\(^9\) iodine,\(^10\) Fe(HSO\(_4\))\(_3\),\(^11\) K\(_5\)CoW\(_{12}\)O\(_{40}\)-3H\(_2\)O,\(^12\) HClO\(_4\)-SiO\(_2\),\(^13\) cationexchange resins,\(^14\) silica sulfuric acid,\(^15\) thiamine hydrochloride,\(^16\) zwitterionic salts\(^17\) and supported acid catalyst,\(^18\) and ionic liquids.\(^19\)

Recently, use of ionic liquids in organic synthesis has become the center of interest due to their dual role as catalyst and media along with their unique properties such as hydrophobicities/hydrophilicities, good solvating capability, easy recoverability, reusability, high thermal stability and non-flammability with almost no vapour pressure.\(^20\)
Due to novel properties of ionic liquids, their use in MCRs for name reactions such as Kabachnik-Field reaction,\textsuperscript{21} Biginelli reaction,\textsuperscript{22} Ugi reaction,\textsuperscript{23} and Mannich reaction\textsuperscript{24} have been well documented. However, the developed MCRs protocol for the synthesis \textsuperscript{1-amidoalkyl-2-naphthols} using ionic liquids\textsuperscript{19} reported at higher temperature is not compatible with sensitive functional groups and hence limits their application for the commercial exploitation as catalysts and/or reaction media to achieve high yield of the products. A cost effective construction of its structural unit (1-amidoalkyl-2-naphthols) using MCRs protocol under much milder, more efficient, environment friendly conditions using recyclable, ecofreindly ionic liquid as green catalyst is still a possibility to explore.

### 4.1.2 Review of literature

Literature survey revels that, there are several methods available for the synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols from the reaction of various substituted aldehydes, amides/ carbamates/ urea/ nitrile with 2-naphthols/phenols in the presence of the various catalysts and solvents at different reaction conditions, however, few of them are described below.

**Mishra’s approach\textsuperscript{18e}**

In this approach, Mishra \textit{et al.} have treated various aromatic aldehydes and 2-naphthol with benzamide or urea in the presence of MoZr catalyst at 80 °C under the neat reaction condition (Scheme 1).

\textbf{Scheme 1:} \textit{Reagents and reaction conditions:} (i) Aldehyde (1 mmol), 2-naphthol (1 mmol), amide/urea (1.1 mmol), MoZr (100 mg), 80 °C, 1-2 h.
**Tamaddon approach**\(^{18d}\)

In this approach, Tamaddon et al. have treated various aromatic aldehydes and 2-naphthol with amide or urea in the presence of \([\text{MeC(OH)}_2]^+\text{ClO}_4^-\) as a super acidic ionic liquid in ethyl acetate at room temperature or neat reaction condition at 80 °C (Scheme 2).

![Scheme 2: Reagents and reaction conditions: (i) Aldehyde (1 mmol), 2-naphthol (1 mmol), amide/urea (1 mmol), \([\text{MeC(OH)}_2]^+\text{ClO}_4^-\) (1 mol %), EtOAc/ neat, RT/ 80 °C, 8-35 min.](image)

**Kohansal approach**\(^{18f}\)

In this approach, Kohansal et al. have treated various aromatic aldehydes and 2-naphthols with acetamide in the presence of KAl(SO\(_4\))\(_2\).12H\(_2\)O as a heterogeneous catalyst at 85 °C under neat reaction condition (Scheme 3).

![Scheme 3: Reagents and reaction conditions: (i) Aldehyde (1 mmol), 2-naphthol (1 mmol), acetamide (1 mmol), and KAl(SO\(_4\))\(_2\).12H\(_2\)O (0.35 mmol), 85 °C, 10-25 min.](image)

**Perumal approach**\(^{18g}\)

In this approach, Perumal et al. have treated various aromatic aldehydes and 2-naphthol/phenols with various nitriles in the presence of I\(_2\) and acetyl chloride for 3-14 h at room temperature (Scheme 4).
Synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols

Chapter-IV

Scheme 4:  *Reagents and reaction conditions:* (i) Aldehyde (10 mmol), 2-naphthol/phenol (10 mmol), Iodine (0.4 mmol), acetyl chloride (2.8 mmol), and nitrile (10 mmol), RT, 3-14 h.

**Hajipour approach**

In this approach, Hajipour *et al.* have treated various aromatic aldehydes and 2-naphthol with amide or urea in the presence of ionic liquid [TEBSA] [HSO₄] at 120 °C for 10 min. (Scheme 5).

Scheme 5:  *Reagents and reaction conditions:* (i) Aldehyde (1 mmol), 2-naphthol (1 mmol), amide/urea (1.2 mmol), [TEBSA] [HSO₄] (5 mol %), 120 °C, 10 min.

**Lihong Hu approach**

In this approach, Lihong Hu *et al.* have treated various aromatic aldehydes and 2-naphthol with amide or urea in the presence of Thiamine hydrochloride (VB₁) at 80 °C for 4 h in alcohol (Scheme 6).

Scheme 6:  *Reagents and reaction conditions:* (i) Aldehyde (5 mmol), 2-naphthol (5 mmol), amide/urea (5.5 mmol), VB₁ (10 mol %), 80 °C, 4 h.

**Shaterian approach**

In this approach, Shaterian *et al.* have treated various aromatic aldehydes and 2-naphthol
with carbamates in the presence of SiO$_2$-NaHSO$_4$ at 100 °C under neat reaction condition (Scheme 7).

\[
\text{Scheme 7: Reagents and reaction conditions: (i) Aldehyde (1 mmol), 2-naphthol (1 mmol), carbamate (1.1 mmol), SiO$_2$-NaHSO$_4$ (50 mg), 100 °C, 3-30 min.}
\]

4.1.3 Present Work

4.1.3.1 Objectives

All these methods reported in the literature so far lack general applicability and suffer from one or other limitations such as high reaction temperature, longer reaction time, and lower yield of the desired product, tedious work-up and use of toxic reagents. Therefore, the development of more general and cost-effective MCRs protocol for the synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols is still challenging and an active research area. As compared to other ionic liquids, ethylammonium nitrate (EAN) with acidic properties (pH=5)$^{25}$ is cheap, easily recoverable and reusable at room temperature. Therefore, this section describes a highly efficient, cost-effective, general and much milder MCRs protocol for the synthesis of 1-amido- and 1-carbamato-alkyl-2-naphthols/phenols in good to excellent yields via one-pot three-component condensation of various aldehydes, amides/carbamates/urea and naphthols/phenols using ethylammonium nitrate as reusable ionic liquid catalyst under neat reaction conditions at ambient temperature (Scheme 8).
Scheme 8: Reagents and reaction conditions: (i) Aldehyde (6 mmol), beta-naphthol/phenol (1 mmol), amide/urea/carbamate (1.1 mmol) in EAN (0.8 mmol) RT 1 h.

4.1.4 Results and discussion

To investigate the optimal reaction conditions for the solvent-free MCRs protocol, the reaction was initially carried out by stirring the mixture of benzaldehyde (6 mmol), beta-naphthol (1 mmol) and acetamide (1.1 mmol) as model reaction in the presence of various loading of EAN (0.2-1 mmol) at room temperature for 1 h. The results obtained are shown in Table 1. Interestingly, increasing the molar concentration of EAN from 0.2 mmol to 0.8 mmol resulted in a dramatic improvement in the yield from 37 % to 93 % (Table 1, entries 2-5). However, further increase to 1 mmol concentration of EAN (Table 1, entry 6) did not improve the yield. In the absence of EAN (Table 1, entry 1), the desired product formation was not observed even after heating. These results clearly indicate that the EAN shows excellent performance under optimized reaction conditions (Table 1, entry 5).

The promising results on benzaldehyde, beta-naphthol and acetamide using 0.8 mmol EAN as catalyst at the optimized reaction conditions encouraged us to investigate the feasibility of solvent-free MCRs protocol to a wide range of substituted aldehydes, amides/ carbamates / urea and naphthols/phenols for the synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols. A variety of aromatic/heterocyclic aldehydes, amides/
Table 1: Influence of ethylammonium nitrate for the reaction of benzaldehyde, beta-naphthol and acetamide.¹

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ethylammonium nitrate (mmol)</th>
<th>Yield⁵ (%)</th>
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<td>0.0</td>
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<td>93</td>
</tr>
<tr>
<td>6</td>
<td>1.0</td>
<td>93</td>
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</table>

¹ Reaction conditions: Benzaldehyde (6 mmol), beta-naphthol (1 mmol), acetamide (1.1 mmol), RT, 1 h.
⁵ Isolated yields after column chromatography.

carbamates/urea possessing various electron donating and electron withdrawing functional groups reacted smoothly with naphthols/phenols under neat reaction conditions to give desired products in excellent yields over EAN at ambient temperature (Table 2, entries 1-24).

The results in Table 2 illustrate that the one-pot three component condensation reactions show excellent performance irrespective of the presence of electron withdrawing or electron donating groups on aromatic/heterocyclic aldehydes and hence solvent-free MCRs protocol is highly effective, promising and general for the synthesis of 1-amido- and 1-carbamato-alkyl-2-naphthols/phenols. The substituted aromatic aldehydes with electron withdrawing and electron donating groups reacted with beta-naphthol and acetamide/ benzamide/benzylamide provided desired products in excellent yields (Table 2, entries 2-4 and entries 7-12), whereas heterocyclic aldehydes such as furfural
**Table 2:** EAN mediated one-pot three-component reaction of aldehydes with beta-naphthol/phenol and amide/carbamate/urea giving the corresponding 1-amido- and 1-carbamato-alkyl naphthols/phenols.

<table>
<thead>
<tr>
<th>Entry</th>
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<th>Amide/Carbamate/Urea</th>
<th>Product</th>
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<tr>
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<td><img src="image15" alt="Structure 24" /></td>
<td><img src="image16" alt="Structure 2" /></td>
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</tbody>
</table>
and thiophene 2-carbaldehyde reacted with beta-naphthols and acetamide provided high yields (Table 2, entries 5-6). However, the condensation of aromatic aldehydes, carbamates /urea with beta-naphthol provided desired products in good to excellent yields (Table 2, entries 13-21). Interestingly, 3-formyl chromone reacted smoothly with beta-naphthols and acetamide/ ethylcarbamate to give expected product in excellent/good yield (Table 2, entries 7 and 17). To study the scope of this protocol with phenol, a reaction of benzaldehyde / 4-methylbenzaldehyde / 4-chlorobenzaldehyde and acetamide/ ethylcarbamate were carried out with 2, 5-dimethylphenol under optimized reaction conditions, which provided the corresponding 1-amido- and 1-carbamato-alkyl phenols in excellent yields (Table 2, entries 22-24). However, in all the cases 1-amido- and 1-carbamato-alkyl naphthols/phenols were the exclusive products. The results in Table 2 clearly indicate that solvent-free MCR protocol over EAN under neat reaction conditions at ambient temperature is applicable to large number of substrates having different functional groups; however, the yield obtained are dependent on the nature of substituents on aromatic/ heterocyclic aldehydes, amides/ carbamates as well on the phenols.

As per earlier reported literatures\(^9\),\(^{14}\) the probable mechanism proposed in scheme 9 for the synthesis of 1-amidoalkyl naphthol involves the activation of carbonyl group of aldehyde by EAN to form the activated intermediate I then subsequently nucleophilic addition of beta-naphthol to obtain complex II followed by removal of water from the
complex II produce intermediate III as a ortho-quinone methide then subsequently activation by EAN to generate intermediate IV as a Michael acceptor, which leads to in-situ Michael addition of amide or carbamate or urea to release instantly the corresponding products (Table 2, entries 1-24).

The recovery and recyclability of EAN was investigated for the synthesis of 1-amidoalkyl naphthols by one-pot three component condensations of benzaldehyde, beta-naphthol and acetamide as model substrates in the presence of EAN under neat reaction condition at ambient temperature for 1 h, and the results are summarized in Table 3. EAN was recovered quantitatively from the reaction mixture by extracting the organic compound by ethyl acetate and the insoluble EAN were reused for several times without loss of activity (Table 3, entries 1-5). The isolated yield obtained for the product even after the fourth recycle (Table 3, entries 2-5) is very much consistent with fresh EAN (Table 3, entry 1). The consistent activity of recovered and reused EAN indicates that the reused EAN also shows excellent performance for the synthesis of 1-amidoalkyl napthol.
Table 3: Recovery and recyclability of EAN.\(^a\)

<table>
<thead>
<tr>
<th>Cycles</th>
<th>Yield(^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<td>4</td>
<td>91</td>
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<tr>
<td>5</td>
<td>92</td>
</tr>
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</table>

\(^a\) Reaction conditions: Benzaldehyde (6 mmol), \(\text{beta}--\text{naphthol} (1 \text{ mmol}), \text{acetamide} \ (1.1 \text{ mmol})\) in EAN (0.8 mmol), RT, 1 h.  
\(^b\) Isolated yields after column chromatography.  
EAN recovery (%) = 98±2

4.1.5 Conclusion

In conclusion, a solvent-free, environmentally clean, much milder, inexpensive, general and simple one-pot multi-component protocol has been developed for efficient synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols in good to excellent yield via one-pot three component condensation of various aldehyde, amide/urea/carbamate and naphthols/phenols using ethylammonium nitrate (EAN) as reusable ionic liquid catalyst under neat reaction condition at ambient temperature. The present method is convenient and applicable to a wide variety of aldehydes, naphthols, phenols and amides or urea or carbamates for the synthesis of corresponding 1-amido- and 1-carbamato-alkyl naphthols /phenols. EAN was recovered and recycled several times without loss of catalytic activity.
4.1.6 Experimental Section

4.1.6.1 A typical procedure for the synthesis of Ethyl ammonium nitrate (EAN) ionic liquid

The ethyl ammonium nitrate used was synthesized according to the procedures reported in the literature.\textsuperscript{21} The aqueous solution of ethylamine (70 %, 100 mL) was taken in a 1 Lit. round bottom flask, which was maintained below 10 °C using an ice-water bath. To this cold solution, nitric acid (30 %, 330 mL) was added slowly drop-wise with vigorous stirring to attain a pH of the mixture of 7.3, the addition was stopped and the mixture was stirred further for 0.5 h. The water from the mixture was removed in a rotary evaporator in a boiling water bath at a pressure of 200 mmHg. The traces of water were removed at 100 °C and 1 mmHg pressure to afford the ethyl ammonium nitrate in quantitative yield (170 g).

4.1.6.2 A typical procedure for the synthesis of 1-amido- and 1-carbamato-alkyl naphthol/phenol using EAN

The reaction mixture of aldehyde (6 mmol), beta-naphthol/phenol (1 mmol) and amide/carbamate/urea (1.1 mmol) was stirred in presence of 0.8 mmol EAN at room temperature for 1 hour. The completion of reaction was monitored by TLC. On completion of reaction, the reaction mixture was extracted thrice with 10 mL ethyl acetate. The extract was dried over anhydrous sodium sulfate, evaporated under vacuum and the residue was purified by short column on silica gel (hexane/ethyl acetate, 70:30) to obtain pure 1-amido- and 1-carbamato-alkyl naphthols/phenols (Table 2). The recovered EAN was subjected to high vacuum at 80 °C to remove the water and then reused. All the isolated reaction products were characterized and confirmed by NMR.
4.1.6.3 Spectral data

N-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)acetamide

Yield: 93 %; white solid; mp: 240-242 °C $^1$H NMR (200 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$
1.92 (s, 3H), 7.17-6.97 (m, 7H), 7.28 (t, $J$=7.58 Hz, 1H), 7.63-7.52 (m, 2H), 7.84 (d, $J$=8.47 Hz, 1H), 7.96 (d, $J$=8.96 Hz, 1H). $^{13}$C NMR (50 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$
22.99, 48.50, 118.72, 122.44, 126.09, 128.28, 128.40, 128.92, 132.30, 135.34, 139.02, 152.98, 169.14.

N-((4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl)acetamide

Yield: 95 %; white solid; mp: 224-226 °C; $^1$H NMR (200 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$
2.00 (s, 3H), 7.05-7.35 (m, 7H), 7.59-7.70 (m, 2H), 7.90-8.05 (m, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$ 22.26, 47.35, 117.44, 117.84, 121.84, 126.96, 127.65, 128.53, 130.74, 152.30, 168.56.

N-((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)acetamide


Yield: 91 %; white solid; mp: 208-210 °C; \(^1\text{H NMR}\) (200 MHz, DMSO-d\(_6\)): \(\delta\) 2.04 (s, 3H), 3.74 (s, 3H), 6.87 (d, \(J=8.72\) Hz, 2H), 7.16 (d, \(J=8.21\) Hz, 3H), 7.32 (t, \(J=8.21\) Hz, 2H), 7.43 (t, \(J=7.84\) Hz, 1H), 7.80-7.95 (m, 3H), 8.52 (d, \(J=8.21\) Hz, 1H), 10.07 (s, 1H); \(^{13}\text{C NMR}\) (50 MHz, DMSO-d\(_6\)): \(\delta\) 22.91, 47.67, 55.19, 113.62, 118.72, 119.19, 122.57, 123.54, 126.45, 127.48, 128.68, 128.73, 129.31, 132.51, 134.61, 153.28, 157.89, 169.31.

N-((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl)acetamide

Yield: 95 %; white solid; mp: 222-224 °C; \(^1\text{H NMR}\) (200 MHz, CDCl\(_3\)+DMSO-d\(_6\)): \(\delta\) 2.04 (s, 3H), 2.25 (s, 3H), 6.98 (d, \(J=8.09\) Hz, 2H), 7.08-7.29 (m, 5H), 7.38 (t, \(J=8.21\) Hz, 1H), 7.63-7.74 (m, 2H), 7.98 (d, \(J=8.4\) Hz, 1H), 8.10 (d, \(J=9.22\) Hz, 1H); \(^{13}\text{C NMR}\) (50 MHz, CDCl\(_3\)+DMSO-d\(_6\)): \(\delta\) 19.92, 22.24, 47.75, 117.98, 121.70, 125.35, 127.65, 128.18, 131.62, 134.60, 138.27, 152.24, 168.39.

N-(furan-2-yl(2-hydroxynaphthalen-1-yl)methyl)acetamide

Yield: 87 %; Brown solid, mp: 226-228 °C; \(^1\text{H NMR}\) (200 MHz, DMSO-d\(_6\)): \(\delta\) 1.98 (s, 3H), 6.15 (d, \(J=3.03\) Hz, 1H), 6.40-6.42 (m, 1H), 7.13-7.54 (m, 5H), 7.84 (t, \(J=8.84\) Hz, 2H), 8.03 (d, \(J=8.46\) Hz, 1H), 8.66 (d, \(J=8.09\) Hz, 1H), 10.09 (s, 1H); \(^{13}\text{C NMR}\) (50 MHz, DMSO-d\(_6\)): \(\delta\) 22.91, 47.67, 55.19, 113.62, 118.72, 119.19, 122.57, 123.54, 126.45, 127.48, 128.68, 128.73, 129.31, 132.51, 134.61, 153.28, 157.89, 169.31.
Synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols

Chapter-IV

MHz, DMSO-d$_6$): $\delta$ 22.75, 43.66, 106.26, 110.56, 116.77, 118.60, 122.57, 126.45, 128.55, 128.69, 129.62, 132.61, 141.87, 153.51, 155.06, 169.11.

N-((2-hydroxynaphthalen-1-yl)(thiophen-2-yl)methyl)acetamide

Yield: 85 %; Brown solid, mp: 208-210 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): $\delta$ 1.98 (s, 3H), 6.14-6.42 (m, 2H), 7.14-7.54 (m, 5H), 7.79-8.06 (m, 4H), 8.66 (d, $J$=8.09 Hz, 1H), 10.10 (s, 1H); $^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta$ 22.31, 43.24, 105.81, 110.11, 116.35, 118.17, 122.13, 122.81 126.00, 128.12, 128.24, 129.17, 132.17, 141.42, 153.07, 154.63, 168.67.

N-((2-hydroxynaphthalen-1-yl)(4-oxo-4H-chromen-3-yl)methyl)acetamide

Yield: 91 %; Yellow solid, mp: 211-213 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): $\delta$ 1.96 (s, 3H), 7.08-7.25 (m, 3H), 7.46-7.58 (m, 2H), 7.72-7.92 (m, 6H), 8.33-8.48 (m, 2H), 10.04 (s, 1H); $^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta$ 22.47, 47.79, 111.72, 116.62, 118.43, 124.85, 125.17, 128.10, 129.04, 133.85, 136.95, 150.23, 153.48, 154.68, 168.49, 175.27, 188.53.

N-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)benzamide
Synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols

Chapter-IV

Yield: 94 %; White solid, mp: 230-232 °C; \(^1\text{H NMR}\) (200 MHz, CDCl\(_3\)+DMSO-d\(_6\)): \(\delta\) 7.13-7.51 (m, 14H), 7.66-7.84 (m, 4H), 8.02 (d, \(J=8.46\) Hz, 1H), 8.19 (d, \(J=8.59\) Hz, 1H), 8.80 (d, \(J=8.97\) Hz, 1H); \(^{13}\text{C NMR}\) (200 MHz, CDCl\(_3\)+DMSO-d\(_6\)): \(\delta\) 49.30, 118.61, 122.18, 122.65, 126.20, 126.74, 127.74, 128.09, 129.35, 130.92, 132.14, 141.99, 152.70, 165.92.

N-((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl)benzamide

Yield: 95 %; White solid, mp: 187-189 °C; \(^1\text{H NMR}\) (200 MHz, CDCl\(_3\)+DMSO-d\(_6\)): \(\delta\) 2.25 (s, 3H), 6.98 (d, \(J=8.09\) Hz, 2H), 7.17-7.44 (m, 10H), 7.64-7.86 (m, 4H), 8.15 (d, \(J=8.59\) Hz, 1H), 8.78 (d, \(J=8.97\) Hz, 1H); \(^{13}\text{C NMR}\) (50 MHz, CDCl\(_3\)+DMSO-d\(_6\)): \(\delta\) 20.71, 49.32, 118.71, 122.72, 126.33, 126.84, 128.53, 130.94, 152.73, 165.98.

N-((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)benzamide

Yield: 91 %; White solid, mp: 209-211 °C; \(^1\text{H NMR}\) (200 MHz, CDCl\(_3\)+DMSO-d\(_6\)): \(\delta\)
N-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)-2-phenylacetamide

Yield: 92 %; Brown solid, mp: 180-182 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): $\delta$ 3.70 (d, $J$=7.70 Hz, 2H), 7.14-7.50 (m, 13H), 7.82-7.94 (m, 3H), 8.68 (d, $J$=8.33 Hz, 1H), 10.13 (s, 1H); $^{13}$C NMR (200 MHz, DMSO-d$_6$): $\delta$ 48.14, 48.86, 118.77, 120.58, 122.60, 125.98, 126.62, 128.67, 128.82, 129.10, 132.50, 134.97, 141.50, 153.06, 158.85.

N-((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)-2-phenylacetamide

Yield: 90 %; Brown solid, mp: 192-194 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): $\delta$ 3.69-3.74 (m, 5H), 6.86 (d, $J$=8.72 Hz, 2H), 7.10 (d, $J$=8.59 Hz, 3H), 7.26-7.45 (m, 8H), 7.80-7.97 (m, 3H), 8.62 (d, $J$=8.46 Hz, 1H), 10.06 (s, 1H); $^{13}$C NMR (200 MHz, DMSO-d$_6$): $\delta$ 42.41, 47.83, 55.20, 113.63, 118.88, 122.60, 126.60, 127.43, 128.45, 129.40, 132.46, 134.43, 136.62, 153.29, 157.92, 170.06.
Synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols

Ethyl (2-hydroxynaphthalen-1-yl)(phenyl)methylcarbamate

Yield: 90 %; white solid, mp: 186-188 °C; $^{1}H$ NMR (200 MHz, DMSO-d$_6$): $\delta$ 1.22 (t, $J$=6.95 Hz, 3H), 4.08 (q, $J$=6.95 Hz, 2H), 6.90 (d, $J$=8.97 Hz, 1H), 7.21-7.48 (m, 8H), 7.65 (d, $J$=7.96 Hz, 1H), 7.85 (t, $J$=8.72 Hz, 2H), 7.96 (d, $J$=8.59 Hz, 1H), 10.18 (s, 1H); $^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta$ 15.16, 50.74, 60.63, 118.97, 123.06, 126.51, 126.87, 128.63, 129.08, 129.81, 132.56, 142.95, 153.38, 156.65.

Ethyl (4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate

Yield: 94 %; white solid, mp: 162-164 °C; $^{1}H$ NMR (200 MHz, DMSO-d$_6$): $\delta$ 1.23 (t, 3H), 4.08 (q, 2H), 6.90 (d, $J$=8.97 Hz, 1H), 7.24-7.50 (m, 7H), 7.69-7.97 (m, 4H), 10.21 (s, 1H); $^{13}$C NMR (200 MHz, DMSO-d$_6$): $\delta$ 14.97, 59.52, 60.54, 118.77, 122.95, 127.01, 128.25, 128.41, 128.54, 128.68, 129.87, 131.27, 132.29, 139.60, 141.88, 153.28, 157.16.

Ethyl ((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl)carbamate

Yield: 93 %; white solid, mp: 171-173 °C; $^{1}H$ NMR (200 MHz, Acetone-d$_6$): $\delta$ 1.19 (t,
Synthesis of 1-amido- and 1-carbamato-alkyl naphthols/phenols

\[ J=7.07 \text{ Hz, 3H}, \, 2.25 \text{ (s, 3H)}, \, 4.08 \text{ (q, 2H)}, \, 6.94-7.36 \text{ (m, 9H)}, \, 7.48 \text{ (t, } J=7.32 \text{ Hz, 1H)}, \]  
\[ 7.82 \text{ (t, } J=9.09 \text{ Hz, 2H)}, \, 8.10 \text{ (d, } J=8.59 \text{ Hz, 1H}); \]  
\[ ^{13}\text{C NMR (200 MHz, Acetone-d}_6\text{): } \delta 15.07, \, 21.02, \, 51.71, \, 54.69, \, 61.22, \, 98.51, \, 119.38, \, 120.65, \, 123.66, \, 123.87, \, 127.11, \, 127.77, \]  
\[ 129.63, \, 129.86, \, 130.07, \, 130.40, \, 133.54, \, 136.76, \, 140.74, \, 153.64, \, 157.26. \]  

Ethyl ((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)carbamate

\[
\begin{align*}
\text{Yield: 88 \%; white solid, mp: 169-171} \, ^{\circ}\text{C; } ^{1}\text{H NMR (200 MHz, DMSO-d}_6\text{): } \delta \, 1.22 \text{ (t, } J=6.95 \text{ Hz, 3H)}, \, 3.41 \text{ (s, 3H)}, \, 4.06 \text{ (q, } J=6.82 \text{ Hz, 2H)}, \, 6.90 \text{ (d, } J=8.97 \text{ Hz, 1H)}, \, 7.24-7.48 \text{ (m, 9H)}, \, 7.65 \text{ (d, } J=7.96 \text{ Hz, 1H)}, \, 7.85 \text{ (t, } J=8.72 \text{ Hz, 2H)}, \, 7.96 \text{ (d, } J=8.59 \text{ Hz, 1H)}, \, 10.18 \text{ (s, 1H)}; \, ^{13}\text{C NMR (200 MHz, Acetone-d}_6\text{): } \delta 14.95, \, 51.59, \, 54.57, \, 61.10, \, 119.26, \, 120.53, \]  
\[ 123.76, \, 126.99, \, 127.65, \, 129.74, \, 130.28, \, 133.43, \, 136.64, \, 140.62, \, 153.53, \, 157.15. \]

Ethyl(2-hydroxynaphthalen-1-yl)(4-oxo-4H-chromen-3-yl)methylcarbamate

\[
\begin{align*}
\text{Yield: 85 \%; Yellow solid, mp: 181-183} \, ^{\circ}\text{C; } ^{1}\text{H NMR (200 MHz, DMSO-d}_6\text{): } \delta \, 1.21 \text{ (t, } J=6.95 \text{ Hz, 3H)}, \, 4.03 \text{ (q, 2H)}, \, 7.01 \text{ (b, 1H)}, \, 7.43-7.17 \text{ (m, 2H)}, \, 7.69-7.50 \text{ (m, 4H)}, \, 7.82-7.71 \text{ (m, 3H)}, \]  
\[ 8.07-8.03 \text{ (d, } J=9 \text{ Hz, 1H)}, \, 8.43 \text{ (d, 2H)}, \, 8.54 \text{ (s, 1H)}, \, 10.18 \text{ (s, 1H)}; \, ^{13}\text{C NMR (50 MHz, DMSO-d}_6\text{): } \delta 19.92, \, 22.24, \, 47.75, \, 117.98, \, 121.70, \, 125.35, \, 127.53, \, 127.65, \, 128.18, \]
\]
131.62, 134.60, 138.27, 152.24, 168.39.

**Benzyl (2-hydroxynaphthalen-1-yl)(phenyl)methylcarbamate**

![Chemical Structure](image)

Yield: 91%; White solid, mp: 173-175 °C; **$^1$H NMR** (200 MHz, DMSO-d$_6$): $\delta$ 5.12 (d, J=4.04 Hz, 2H), 6.95 (d, J=8.84 Hz, 1H), 7.22-7.52 (m, 14H), 7.81-7.99 (m, 4H), 10.18 (s, 1H); **$^{13}$C NMR** (50 MHz, DMSO-d$_6$): $\delta$ 50.34, 65.67, 118.43, 118.80, 122.50, 126.36, 127.79, 128.11, 128.34, 128.55, 129.33, 132.04, 137.00, 142.31, 152.90, 156.04.

**Benzyl (4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate**

![Chemical Structure](image)

Yield: 90%; White solid, mp: 154-156 °C; **$^1$H NMR** (200 MHz, DMSO-d$_6$): $\delta$ 5.12 (d, J=3.54 Hz, 2H), 6.94 (d, J=8.72 Hz, 1H), 7.25-7.47 (m, 12H), 7.79-7.96 (m, 4H), 10.21 (s, 1H); **$^{13}$C NMR** (50 MHz, DMSO-d$_6$): $\delta$ 49.89, 65.75, 118.36, 122.57, 123.06, 126.59, 127.82, 127.91, 128.06, 128.35, 128.61, 129.56, 130.93, 131.93, 136.93, 141.43, 152.97, 156.07.

**1-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)urea**
1-amido- and 1-carbamato-alkyl naphthols/phenols

Yield: 96 %; White solid, mp: 173-175 °C; \( ^1H \text{NMR} \) (200 MHz, DMSO-\( \text{d}_6 \)): \( \delta \) 5.92 (s, 2H), 6.99-7.10 (m, 6H), 7.26-7.50 (m, 3H), 7.80-7.90 (m, 3H), 10.01 (s, 1H); \( ^{13}C \text{NMR} \) (50 MHz, DMSO-\( \text{d}_6 \)): \( \delta \) 55.19, 113.62, 118.72, 119.19, 122.57, 126.45, 127.48, 128.73, 129.31, 132.51, 134.61, 153.28, 157.89, 169.31.

1-((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl)urea

Yield: 93 %; White solid, mp: 118-120 °C; \( ^1H \text{NMR} \) (200 MHz, DMSO-\( \text{d}_6 \)): \( \delta \) 2.28 (s, 3H), 5.91 (s, 2H), 6.98-7.11 (m, 6H), 7.25-7.49 (m, 3H), 7.79-7.89 (m, 3H), 10.00 (s, 1H); \( ^{13}C \text{NMR} \) (50 MHz, DMSO-\( \text{d}_6 \)): \( \delta \) 20.77, 48.86, 118.77, 120.58, 122.60, 125.98, 128.67, 128.82, 129.10, 132.50, 134.97, 141.50, 153.06, 158.85.

N-((4-hydroxy-2,5-dimethylphenyl)(phenyl)methyl)acetamide

Yield: 93 %; White solid, mp: 178-180 °C; \( ^1H \text{NMR} \) (200 MHz, DMSO-\( \text{d}_6 \)): \( \delta \) 1.94 (s, 3H), 2.07 (s, 3H), 2.32 (s, 3H), 6.16 (d, \( J=8.46 \) Hz, 1H), 6.63 (s, 1H), 6.82 (s, 1H), 7.08-
7.19 (m, 5H), 8.56 (d, $J=8.58$ Hz, 1H), 9.18 (s, 1H); $^{13}$C NMR (50 MHz, DMSO-$d_6$): $\delta$

16.45, 19.35, 23.12, 52.33, 116.92, 121.37, 127.73, 129.36, 130.18, 131.58, 134.25, 136.21, 140.38, 154.62, 168.73.

**N-((4-hydroxy-2,5-dimethylphenyl)(p-tolyl)methyl)acetamide**

Yield: 94 %; White solid, mp: 184-186 °C; $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 1.89 (s, 3H), 2.02 (s, 3H), 2.12 (s, 3H), 2.27 (s, 3H), 6.10 (d, $J=8.46$ Hz, 1H), 6.58 (s, 1H), 6.77 (s, 1H), 7.10 (q, $J=8.22$ Hz, 4H), 8.50 (d, $J=8.58$ Hz, 1H), 9.12 (s, 1H); $^{13}$C NMR (50 MHz, DMSO-$d_6$): $\delta$ 15.19, 18.10, 19.98, 21.87, 51.08, 115.67, 120.12, 126.48, 128.11, 128.93, 130.33, 133.00, 134.96, 139.13, 153.37, 167.48.

**Ethyl (4-chlorophenyl)(4-hydroxy-2,5-dimethylphenyl)methylcarbamate**

Yield: 95 %; White solid, mp: 166-168 °C; $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 1.19 (t, $J=6.95$ Hz, 3H), 2.06 (s, 3H), 2.19 (s, 3H), 4.04 (q, $J=7.07$ Hz, 2H), 5.96 (d, $J=8.97$ Hz, 1H), 6.62 (s, 1H), 6.88 (s, 1H), 7.26 (d, $J=8.46$ Hz, 2H), 7.42 (d, $J=8.47$ Hz, 2H), 8.04 (d, $J=9.09$ Hz, 1H), 9.20 (s, 1H); $^{13}$C NMR (50 MHz, DMSO-$d_6$): $\delta$ 14.44, 15.60, 18.53, 53.34, 59.67, 116.04, 120.78, 127.94, 128.80, 129.34, 130.22, 131.02, 133.23, 141.60, 153.97, 155.50.
4.1.7 Spectra

Fig. 1: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)acetamide
Fig. 2: $^1$H and $^{13}$C NMR of N-((4-chlorophenyl)(2-hydoxy-naphthalen-1-yl)methyl) acetamide
Fig. 3: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl) acetamide
Fig. 4: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl)acetamide
Fig. 5: $^1$H and $^{13}$C NMR of N-(furan-2-yl(2-hydroxynaphthalen-1-yl)methyl)acetamide
Fig. 6: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(thiophen-2-yl)methyl) acetamide
Fig. 7: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(4-oxo-4H-chromen-3-yl)methyl) acetamide
Fig. 8: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)benzamide
Fig. 9: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl)benzamide
Fig. 10: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)benzamide
Fig. 11: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)-2-phenylacetamide
Fig. 12: $^1$H and $^{13}$C NMR of N-((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)-2-phenylacetamide
Fig. 13: $^1$H and $^{13}$C NMR of Ethyl (2-hydroxynaphthalen-1-yl)(phenyl)methylcarbamate
Fig. 14: $^1$H and $^{13}$C NMR of Ethyl (4-chlorophenyl)(2-hydroxynaphthalen-1-yl) methylcarbamate
Fig. 15: $^1$H and $^{13}$C NMR of Ethyl ((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl) carbamate
Fig. 16: $^1$H and $^{13}$C NMR of Ethyl ((2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl)carbamate
**Fig. 17:** $^1$H and $^{13}$C NMR of Ethyl(2-hydroxynaphthalen-1-yl)(4-oxo-4H-chromen-3-yl) methylcarbamate
Fig. 18: $^1$H and $^{13}$C NMR of Benzyl (2-hydroxynaphthalen-1-yl)(phenyl) methylcarbamate
Fig. 19: $^1$H and $^{13}$C NMR of Benzyl (4-chlorophenyl)(2-hydroxynaphthalen-1-yl) methylcarbamate
Fig. 20: $^1$H and $^{13}$C NMR of 1-((2-hydroxynaphthalen-1-yl)(phenyl)methyl)urea
Fig. 21: $^1$H and $^{13}$C NMR of 1-((2-hydroxynaphthalen-1-yl)(p-tolyl)methyl)urea


**Fig. 22:** $^1$H and $^{13}$C NMR of N-((4-hydroxy-2,5-dimethylphenyl)(phenyl)methyl) acetamide
Fig. 23: $^{1}$H and $^{13}$C NMR of N-((4-hydroxy-2,5-dimethylphenyl)(p-tolyl)methyl)acetamide
Fig. 24: $^1\text{H}$ and $^{13}\text{C}$ NMR of Ethyl (4-chlorophenyl)(4-hydroxy-2,5-dimethylphenyl) methylcarbamate
Section-II

Efficient, rapid synthesis of bis(indolyl)methane using ethyl ammonium nitrate as an ionic liquid

4.2.1 Introduction

Several bis(indolyl)alkanes and their derivatives have been isolated from plant and marine sources. Among the various derivatives of indoles, bis(indolyl)methanes have wide medicinal applications such as to induce apoptosis in human cancer cell and normalize abnormal cell growth associated with cervical dysplasia, to promote beneficial estrogen metabolism in both women and men, to prevent the breast cancer and also to increase the natural metabolism of body's hormones. Due to vast biological activity of bis(indolyl)methanes and their wide medicinal applications, various methods of their synthesis have been reported in the literature. However, almost all the methods have employed conventional Lewis acids as well as protic acids as catalysts to promote electrophilic substitution reaction of indoles with various aldehydes or carbonyl compounds. A variety of other catalysts such as H-Y zeolite, sulphamic acid, In(OTf)3, LiClO4, bis(cyclopentadienyl)ZrCl2, CuBr2, ZrCl4, Zn(HSO4)2, polyindole salt, CAN, N-tert-butanesulfinyl aldimines, ion exchange resin, acetic acid, InCl3, InF3, Dy(OTf)3, Ln(OTf)3, FeCl3.6H2O, V(HSO4)3, SBA-15/SO3H, oxalic acid, TBBDA, silica bonded S-sulfonic acid, Bi(NO3)3, Cu(BF4)2 SiO2, vanadomolybdophosphoric acid, Ph-PMO-SO3H, glycerin and CeCl3, B(C6F5)3, H2P2W18O62, phosphated zirconia, Ph3CCl, have been reported for synthesis of bis(indolyl)methanes. However, these methods suffer from drawbacks, such as toxic metal ions, expensive solvents, long reaction times, tedious work-up, low
product yields, higher catalyst loading and formation of large amounts of wastes.\textsuperscript{63-65}

Due to unique properties of ionic liquids as described in section I, their application for the synthesis of heterocyclic compounds.\textsuperscript{66} and the synthesis of bis(indolyl)methane using [bmim]BF\textsubscript{4},\textsuperscript{67} [bmim]PF\textsubscript{6},\textsuperscript{67} [acmim]Cl, [hmim]HSO\textsubscript{4}\textsuperscript{68} and TMGT,\textsuperscript{69} at room temperature have been reported in the literature.

4.2.2 Review of literature

Literature survey revels that, there are several methods available for the synthesis of bis(indolyl)methanes from the reaction of indoles with a variety of aldehydes in the presence of the various catalyst and solvent at different reaction conditions, however, few of them are described below.

**Dubey approach\textsuperscript{50}**

In this approach, Amit Dubey et al. have treated various aromatic aldehydes with indole in the presence of SBA-15/SO\textsubscript{3}H catalyst at 60 °C in a carbon tetrachloride solvent for 24 h (Scheme 10).

\[
\text{Scheme 10: Reagents and reaction conditions: (i) Aldehyde (1 mmol), indole (2 mmol), SBA-15/SO}_3\text{H (100 mg), CCl}_4, 60 ^\circ \text{C, 24 h.}
\]

**Niknam approach\textsuperscript{53}**

In this approach, Niknam et al. have treated various aromatic aldehydes with indole in the presence of silica bonded S-sulfonic acid (SBSSA) as a catalyst in an acetonitrile solvent at room temperature (Scheme 11).
Scheme 11: Reagents and reaction conditions: (i) Aldehyde (1 mmol), indole (2 mmol), SBSSA (100 mg), CH₃CN, RT.

Heravi approach

In this approach, Heravi et al. have treated various aromatic aldehydes with various indoles in the presence of diphosphooctadecatungstic acid (H₆P₂W₁₈O₆₂) as a catalyst at 110 °C under neat reaction conditions (Scheme 12).

Scheme 12: Reagents and reaction conditions: (i) Aldehyde (1 mmol), indole (2 mmol), H₆P₂W₁₈O₆₂ (0.7 mol %), 110 °C.

Hagiwara approach

In this approach, Hagiwara et al. have treated various aromatic aldehydes with various indoles in the presence of acidic ionic liquid immobilized on silica (ILIS) as a catalyst at room temperature in an acetonitrile solvent (Scheme 13).

Scheme 13: Reagents and reaction conditions: (i) Aldehyde (0.3 mmol), indole (0.5 mmol), ILIS (0.05 mmol), MeCN (3 mL), RT.
Yadav's approach⁶⁶

In this approach, Yadav et al. have treated various aromatic aldehydes/ketones with various indoles in the presence of 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF₄) or 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF₆) ionic liquid as a catalyst as well as reaction medium at room temperature for 3-5 h (Scheme 14).

Scheme 14:  
Reagents and reaction conditions: (i) Aldehyde (1 mmol), indole (2 mmol), [bmim]BF₄ or [bmim]PF₆ (3 mL), RT, 3-5 h.

Teck-Peng Loh approach⁴⁸

In this approach, Teck-Peng Loh et al. have treated various aromatic aldehydes with various indoles in the presence of FeCl₃·6H₂O as a catalyst at room temperature in a 1-methyl-3-octylimidazolium hexafluorophosphate ([omim]PF₆) ionic liquid as a solvent (Scheme 15).

Scheme 15:  
Reagents and reaction conditions: (i) Aldehyde (0.25 mmol), indole (0.5 mmol), FeCl₃·6H₂O (5 mol%), [omim]PF₆ (0.5 mL), RT.
4.2.3 Present Work

4.2.3.1 Objectives

All these methods reported in the literatures suffer certain disadvantages such as very long reaction times and lower product yields as well as use of toxic metal ions, expensive solvents, tedious work-up, higher catalyst loading and formation of large amounts of wastes. Due to wide medicinal application of bis(indolyl)methanes in life sciences, the development of more general and cost effective, an elegant, rapid and efficient protocol for the synthesis of bis(indolyl)methanes is still challenging and an active research area. As part of our continuous efforts to explore the possibility to develop green, and economical viable protocol for organic transformation, this section describes the use of ethyl ammonium nitrate \([\text{C}_2\text{H}_5\text{NH}_3\text{]}\text{NO}_3\) as a media as well as catalyst in the electrophilic substitution of indoles with a variety of aldehydes to provide bis(indolyl)methanes at ambient conditions (Scheme 16).

Scheme 16: Reagents and reaction conditions: (i) Indole (2 mmol), Aldehyde (1 mmol), Ethylammonium nitrate (EAN) (2 mmol) at 25 °C for 1-12 min.

4.2.4 Results and discussion

Using indole and benzaldehyde as test substrates, the reaction parameters were optimized to determine the optimal condition for the synthesis of bis(indolyl)methanes and results are shown in Table 4. When Indole (2 mmol) was treated with benzaldehyde (1 mmol)
for 5 h in ethylammonium nitrate (EAN) (0.2 mmol) as an ionic liquid without solvent at 25 °C, the corresponding bis(indolyl)methane (3a) was obtained in 30 % yield (Table 4, entry 2). When we carried out the same reaction in absence of EAN no reaction took place even at higher temperature (85 °C) (Table 4, entry 1); however the yield and reaction time could be significantly improved to 60 % yield in 1.5 h when 0.8 mmol of EAN was used (Table 4, entry 5). Interestingly, increasing the molar ratio of EAN (2 mmol) resulted in a dramatic improvement in the yield of 3a (95 %) in 3 min (Table 4, entry 7).

**Table 4:** Influence of ethyl ammonium nitrate for the reaction of benzaldehyde and indole

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ethyl ammonium Nitrate (mmol)</th>
<th>Reaction Time (min)</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>300</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0.2</td>
<td>300</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>0.4</td>
<td>300</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>0.6</td>
<td>210</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>0.8</td>
<td>90</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>1.0</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>2.0</td>
<td>03</td>
<td>95</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: Indole (2 mmol), Benzaldehyde (1 mmol), Ethylammonium nitrate at 25 °C.<br><br>\(^b\) Isolated yields after chromatographic purification.

In general, higher EAN concentration (2 mmol) gave better yields in shorter time. These results clearly indicate that the EAN acts as catalyst as well as a green reaction media. To
gauze the scope of this methodology, a variety of substituted aldehydes (2a-q) were reacted with indoles (1a-q) in the presence of 2 mmol of EAN at 25 °C to produce the corresponding bis(indolyl)methanes and results are shown in Table 5.

The nature of substitution on the aromatic ring showed some effect on product yields and reactions times. Aromatic aldehydes with electron-withdrawing groups at o- and p-positions, provided products in excellent yields with shorter reactions time (Table 5, entry d, g and i), the reaction is extremely fast often completing in < 3 min. However, in case of the 3-chlorobenzaldehyde, a low yield of the corresponding product was obtained in longer reaction time (Table 5, entry f). Substrates with electron-donating groups took longer time with moderate yields (Table 5, entry b, c and e). In the case of 3,4,5-trimethylbenzaldehyde, rate of reaction is found to be very slow, due to presence of three electron donating methyl groups (Table 5, entry e). Also, similar effect is observed in case of 5-methoxy indole with 4-methyl and 4-methoxy benzaldehyde (Table 5, entry p and q). This clearly indicates that the position and nature of the substitutions on aromatic ring play a key role on the rate of reaction. Heterocyclic aldehydes reacted smoothly with indole to give the corresponding product in excellent yield (Table 5, entry h and j). Furthermore aliphatic aldehydes also react smoothly with the indole to give the corresponding products in good yields (Table 5, entry k and l).

To further elaborate the scope of this protocol with substituted indole, a reaction of 5-nitro indole and 5-methoxy indole was carried out with different aromatics as well as aliphatic aldehyde, which provided the corresponding bis(indolyl)methanes in good to moderate yields (Table 5, entries m-q).
Table 5: EAN mediated synthesis of bis(indole) methane at 25 °C

<table>
<thead>
<tr>
<th>Entry</th>
<th>Indole (1)</th>
<th>Aldehyde (2)</th>
<th>Product (3)</th>
<th>Time (min)</th>
<th>Yield (%) b</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>03</td>
<td>95</td>
</tr>
<tr>
<td>b</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>05</td>
<td>92</td>
</tr>
<tr>
<td>c</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>08</td>
<td>91</td>
</tr>
<tr>
<td>d</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>03</td>
<td>92</td>
</tr>
<tr>
<td>e</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>f</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>10</td>
<td>88</td>
</tr>
<tr>
<td>g</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>01</td>
<td>95</td>
</tr>
<tr>
<td>h</td>
<td><img src="image1" alt="Indole" /></td>
<td><img src="image2" alt="Aldehyde" /></td>
<td><img src="image3" alt="Product" /></td>
<td>03</td>
<td>92</td>
</tr>
</tbody>
</table>
Table 5 (continued)

<table>
<thead>
<tr>
<th>i</th>
<th>CHO</th>
<th>NO2</th>
<th>01</th>
<th>95</th>
</tr>
</thead>
<tbody>
<tr>
<td>j</td>
<td>CHO</td>
<td>S</td>
<td>04</td>
<td>93</td>
</tr>
<tr>
<td>k</td>
<td>CHO</td>
<td></td>
<td>02</td>
<td>93</td>
</tr>
<tr>
<td>l</td>
<td>CHO</td>
<td></td>
<td>02</td>
<td>89</td>
</tr>
<tr>
<td>m</td>
<td>O2N</td>
<td>CHO</td>
<td>08</td>
<td>87</td>
</tr>
<tr>
<td>n</td>
<td>O2N</td>
<td>CHO</td>
<td>08</td>
<td>86</td>
</tr>
<tr>
<td>o</td>
<td>O2N</td>
<td>CHO</td>
<td>05</td>
<td>94</td>
</tr>
<tr>
<td>p</td>
<td>MeO</td>
<td>CHO</td>
<td>11</td>
<td>87</td>
</tr>
<tr>
<td>q</td>
<td>MeO</td>
<td>CHO</td>
<td>12</td>
<td>83</td>
</tr>
</tbody>
</table>

*a* Reaction conditions: Indole (2 mmol), Aldehyde (1 mmol), Ethylammonium nitrate (2 mmol) at 25 °C.

*b* Isolated yields after chromatographic purification.
A probable mechanism is shown in **Scheme 17** for synthesis of bis(indolyl) methanes. The mechanism involves activation of the carbonyl group by EAN followed by nucleophilic addition of indole to aldehyde proceeds to afford the intermediate \( A \). The subsequent dehydration of \( A \) gave \( B \) which on nucleophilic addition of another mole of indole gave \( C \), followed by aromatization to give the product 3a-q (**Scheme 17**).

**Scheme 17**: Plausible reaction mechanism for synthesis of bis(indolyl) methane over EAN

**Recyclability of Ethyl ammonium nitrate**

The EAN was recovered from aqueous layer by removal of water at 70 °C under reduced pressure and recycled several times with almost no loss of activity and results are shown in **Table 6**, Run1-4.

**Table 6**: Recoverability and reusability of ethyl ammonium nitrate\(^a\)

<table>
<thead>
<tr>
<th>No. of cycles</th>
<th>Fresh</th>
<th>Run 1</th>
<th>Run 2</th>
<th>Run 3</th>
<th>Run 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield (%)(^b)</td>
<td>95</td>
<td>95</td>
<td>94</td>
<td>94</td>
<td>93</td>
</tr>
<tr>
<td>EAN (%)Recovery</td>
<td>&gt;98</td>
<td>&gt;97</td>
<td>&gt;96</td>
<td>&gt;96</td>
<td>&gt;95</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: Indole (2 mmol), Benzaldehyde (1 mmol), Ethylammonium nitrate (2 mmol) at 25 °C.

\(^b\) Isolated yields after chromatographic purification.
The efficacy of EAN for the synthesis of bis(indolyl)methanes as compared to other acid catalysts and ionic liquids (ILs) reported in the literature can be understood from the results shown in Table 7.

The high rate can be rationalized due to high acidity associated with it (pH=5) coupled with its ability to absorb water formed during the reaction in the synthesis of bis(indolyl)methanes.

Table 7: Comparison between EAN and acid catalysts/ionic liquid used in synthesis of bis(indolyl)methanes.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Reaction Condition</th>
<th>Time</th>
<th>Catalyst</th>
<th>Yield (%)&lt;sup&gt;Ref.&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EAN, RT</td>
<td>03 min</td>
<td>EAN</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>Ionic liquid, 1 mL, RT</td>
<td>15 min</td>
<td>TMGT</td>
<td>93&lt;sup&gt;69&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td>Microwave oven, 450 W</td>
<td>05 min</td>
<td>[bmim] [HSO₄]</td>
<td>93&lt;sup&gt;68&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>Acetonitrile 3 mL, RT</td>
<td>5.5 h</td>
<td>Acidic Ionic Liquid Immobilized on Silica (ILIS)</td>
<td>97&lt;sup&gt;70&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>Ionic liquid 1 mL, RT</td>
<td>1.5 h</td>
<td>FeCl₃·6H₂O</td>
<td>98&lt;sup&gt;48&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>[bmim]BF₄ or [bmim]PF₆ 2 mL, RT</td>
<td>4.5 h</td>
<td></td>
<td>87&lt;sup&gt;67&lt;/sup&gt;</td>
</tr>
<tr>
<td>7</td>
<td>Ionic liquid 1 mL, RT</td>
<td>15 min</td>
<td>In(OTf)₃</td>
<td>90&lt;sup&gt;33&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
4.2.5 Conclusion

In conclusion, this section describes EAN mediated an efficient, rapid synthesis of bis(indolyl) methane from indoles and aldehydes in excellent yields at room temperature in shorter reaction time. Novel EAN acts as catalyst and green media for the reaction, making this method cheaper, simple, convenient, and environmentally friendly process for the synthesis of substituted bis(indolyl)methanes.

4.2.6 Experimental Section

4.2.6.1 A typical procedure for the synthesis of bis(indolyl)methane using EAN

A mixture of indole (2 mmol), benzaldehyde (1 mmol) and EAN (2 mmol) was stirred at room temperature. The completion of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was diluted by water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulphate and concentrated in vacuum to get crude product. The crude product was purified by column chromatography. All the isolated reaction products were characterized and confirmed by NMR.

4.2.6.2 Spectral data

3,3’-(phenylmethylene)bis(1H-indole)

Yield: 95 %; Red solid; mp: 124-126 °C (lit. 123-125 °C) $^1H$ NMR (200 MHz, CDCl$_3$): $\delta$ 5.60 (s, 1H), 6.67 (s, 2H), 7.04 (t, 2H), 7.18-7.27 (m, 3H), 7.29-7.32 (m, 2H), 7.35-7.46 (m, 6H); $^{13}$C NMR (50 MHz, CDCl$_3$): 8 41.1, 110.4, 119.8, 120.1, 121.5, 123.8, 126.5,
127.1, 128.6, 136.4, 144.4.

4-(di(1H-indol-3-yl)methyl)phenol

![Structure of 4-(di(1H-indol-3-yl)methyl)phenol]

Yield: 92 %; white solid; mp: 222-224 °C (lit. 124-125 °C); $^1$H NMR (200 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$ 4.67 (brs, 1H), 5.82 (s, 1H), 6.64 (s, 2H), 6.74-6.99 (m, 4H), 7.14-7.23 (m, 4H), 7.38 (t, $J$=9.2 Hz, 4H), 7.93 (s, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$ 59.9, 110.6, 114.2, 117.8, 118.9, 119.2, 120.8, 123.1, 126.6, 128.7, 134.5, 136.4, 154.4.

3, 3’-((p-tolylmethylene)bis(1H-indole)

![Structure of 3, 3’-((p-tolylmethylene)bis(1H-indole)]

Yield: 91 %; Yellow solid; mp: 98-100 °C (lit. 96-98 °C); $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 2.34 (s, 3H), 5.86 (s, 1H), 6.73 (d, $J$=2.5 Hz, 2H), 7.05 (t, $J$=8.1 Hz, 2H), 7.13 (d, $J$=8.0 Hz, 2H), 7.30-7.42 (m, 6H), 7.46 (d, $J$=8.1 Hz, 2H), 7.89 (s, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 22.91, 47.67, 55.19, 113.62, 118.72, 119.19, 122.57, 123.54, 126.45, 127.48, 128.68, 128.73, 129.31, 132.51, 134.61, 153.28.

3,3’-((2-chlorophenyl)methylene)bis(1H-indole)
Yield: 92%; Pinck solid; mp: 71-73 °C (lit. 72-74 °C); \(^1\text{H NMR}\) (200 MHz, CDCl\(_3\)): \(\delta\) 6.51 (s, 1H), 6.62 (s, 2H), 7.03 (t, 2H), 7.2-7.6 (m, 11H), 7.89 (s, 2H); \(^{13}\text{C NMR}\) (50 MHz, CDCl\(_3\)): \(\delta\) 39.4, 111.9, 120.5, 122.1, 123.8, 127.0, 128.3, 130.4, 131.5, 137.1, 142.5.

3,3’-((3,4,5-trimethylphenyl)methylene)bis(1H-indole)

Yield: 90 %; White solid, mp: 223-225 °C; \(^1\text{H NMR}\) (200 MHz, DMSO-d\(_6\)): \(\delta\) 2.32 (s, 3H), 2.46 (s, 6H), 5.81 (s, 1H), 6.73 (d, \(J=2.5\) Hz, 2H), 7.02-7.13 (m, 6H), 7.30-7.42 (m, 2H), 7.41 (d, \(J=8.1\) Hz, 2H), 7.89 (s, 2H); \(^{13}\text{C NMR}\) (50 MHz, DMSO-d\(_6\)): \(\delta\) 39.4, 43.66, 106.26, 110.56, 116.77, 118.60, 122.57, 126.45, 128.55, 128.69, 129.62, 132.61, 141.87.

3,3’-((3-chlorophenyl)methylene)bis(1H-indole)

Yield: 88 %; Brown solid, mp: 218-220 °C; \(^1\text{H NMR}\) (200 MHz, DMSO-d\(_6\)): \(\delta\) 5.87 (s, 1H), 6.49 (s, 2H), 6.88 (t, \(J=7.8\) Hz, 2H), 7.26 (t, \(J=7.8\) Hz, 2H), 7.30-7.41 (m, 8H), 8.13
(br, s, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 39.6, 111.6, 120.1, 122.4, 123.5, 127.2, 128.6, 130.1, 131.8, 136.9, 142.

**3,3'-((4-chlorophenyl)methylene)bis(1H-indole)**

![Image of 3,3'-((4-chlorophenyl)methylene)bis(1H-indole)](image)

Yield: 95%; Pink solid, mp: 78-80 °C (lit. 36 76-77 °C); $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 5.89 (s, 1H), 6.53 (s, 2H), 6.98 (t, $J$=7.8 Hz, 2H), 7.24 (t, $J$=7.8 Hz, 2H), 7.30-7.41 (m, 8H), 8.23 (br, s, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 39.6, 111.6, 120.1, 122.4, 123.5, 127.2, 128.6, 130.1, 131.8, 136.9, 142.

**3,3’-(furan-2-ylmethylene)bis(1H-indole)**

![Image of 3,3’-(furan-2-ylmethylene)bis(1H-indole)](image)

Yield: 92%; Black solid; mp: 321-322 °C (lit. 36 320-323 °C); $^1$H NMR (200 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$ 5.83 (s, 1H), 5.96 (d, $J$=3.4 Hz, 1H), 6.32 (d, $J$=2.2 Hz, 1H), 6.76 (d, $J$=2.4 Hz, 1H), 7.02 (t, 2H), 7.15 (t, 2H), 7.23-7.45 (m, 5H), 8.65 (s, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$ 35.1, 107.2, 109.5, 111.1, 117.6, 119.4, 122.1, 124.1, 126.5, 136.5, 141.0.

**3,3’-((4-nitrophenyl)methylene)bis(1H-indole)**
Synthesis of bis(indolyl)methane

Yield: 95 %; Brown solid; mp: 220-222 °C (lit. 36 221-223 °C); $^1$H NMR (200 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$ 5.96 (s, 1H), 6.78 (d, $J$=2.4 Hz, 2H), 6.9 (t, 2H), 7.1 (t, 2H), 7.31 (d, $J$=8.1 Hz, 2H), 7.38 (d, $J$=8.1 Hz, 2H), 7.56 (d, $J$=8.1 Hz, 2H), 8.10 (d, $J$=8.1 Hz, 2H), 10.41 (s, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$+DMSO-d$_6$): $\delta$ 49.32, 118.71, 122.72, 126.33, 126.84, 128.53, 130.94, 152.73.

3,3’-(thiophen-2-ylmethylene)bis(1H-indole)

Yield: 93 %; Red solid; mp: 189-191 °C (lit. 30 188-190 °C); $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 6.17 (s, 1H), 6.84 (s, 2H), 6.91-6.97 (m, 2H), 7.08 (t, $J$=7.5 Hz, 2H), 7.16 (d, $J$=5.1 Hz, 1H), 7.14 (t, $J$=7.5 Hz, 2H), 7.31 (t, $J$=8 Hz, 2H), 7.49 (d, $J$=8 Hz, 2H), 8.02 (s, 2H); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 35.8, 111.7, 119.4, 120.36, 122.1, 123.8, 124.1, 125.8, 126.4, 127.3, 136.5, 149.2.

3,3’-(propane-1, 1-diyl)bis(1H-indole)

Yield: 93 %; Brown gum; $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 1.08 (t, $J$=7.2 Hz, 3H), 2.26-2.31(m, 2H), 4.45 (t, $J$=7.2 Hz, 1H), 6.93 (s, 2H), 7.08 (t, $J$=7.3 Hz, 2H), 7.20-7.37 (m,
4H), 7.63 (d, J=7.8 Hz, 2H), 7.89 (s, 2H); \( ^{13}\text{C NMR} \) (200 MHz, CDCl\(_3\)): \( \delta \) 13.2, 28.7, 36.3, 111.1, 119.4, 119.8, 120.4, 121.6, 121.9, 127.5, 136.7.

**3,3’-(2-methylpropane-1, 1-diyl)bis(1H-indole)**

![Structure of 3,3’-(2-methylpropane-1, 1-diyl)bis(1H-indole)](image)

Yield: 89 %; White solid, mp: 66-68 °C; \(^1\text{H NMR} \) (200 MHz, CDCl\(_3\)): \( \delta \) 1.01 (d, \( J = 6.6 \) Hz, 6H.), 2.61-2.68 (m, 1H), 4.24 (d, \( J = 8.1 \) Hz, 1H.), 6.99-7.13 (m, 6H), 7.25-7.29 (m, 2H), 7.61 (d, \( J = 7.8 \) Hz, 2H.), 7.85 (s, 2H); \( ^{13}\text{C NMR} \) (200 MHz, CDCl\(_3\)): \( \delta \) 21.8, 32.9, 41.1, 111.1, 118.9, 119.3, 119.5, 121.4, 121.7, 127.4, 136.0.

**3,3’-(propane-1, 1-diyl)bis(5-nitro-1H-indole)**

Yield: 87 %; white gum; \(^1\text{H NMR} \) (200 MHz, CDCl\(_3\)): \( \delta \) 1.05 (t, \( J =6.95 \) Hz, 3H), 2.31-2.25 (m, 2H), 4.36-4.39 (m, 1H), 7.31-7.38 (m, 4H), 7.90 (d, 2H), 8.34 (s, 2H), 140.97 (br, s, 2H); \( ^{13}\text{C NMR} \) (50 MHz, CDCl\(_3\)): \( \delta \) 15.16, 50.74, 60.63, 118.97, 123.06, 126.51, 126.87, 128.63, 129.08, 129.81, 132.56, 142.95, 153.38, 156.65.

**3,3’-((4-chlorophenyl)methylene)bis(5-nitro-1H-indole)**

![Structure of 3,3’-((4-chlorophenyl)methylene)bis(5-nitro-1H-indole)](image)
Yield: 86%; Yellow solid, mp: 142-144 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): δ 5.96 (s, 1H), 6.78 (d, $J$=2.4 Hz, 2H), 6.9 (t, 2H), 7.1 (t, 2H), 7.31 (d, $J$=8.1 Hz, 2H), 7.38 (d, $J$=8.1 Hz, 2H), 8.10 (d, $J$=8.1 Hz, 2H), 10.41 (s, 2H); $^{13}$C NMR (50 MHz, DMSO-d$_6$): δ 49.32, 118.71, 122.72, 126.33, 126.84, 128.53, 130.94, 152.73.

3,3’-(p-tolylmethylene)bis(5-nitro-1H-indole)

Yield: 94%; Brown solid, mp: 215-216 °C; $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.27 (s, 3H), 5.7 (s, 1H), 6.64-6.77 (m, 6H), 7.03-7.09 (m, 2H), 7.19-7.25 (m, 4H), 10.6 (br, s, 2H); $^{13}$C NMR (200 MHz, DMSO-d$_6$): δ 15.33, 21.28, 51.97, 61.48, 119.64, 120.91, 123.92, 127.37, 128.03, 130.66, 133.80, 137.02, 141.03.

3,3’-(p-tolylmethylene)bis(5-methoxy-1H-indole)

Yield: 87%; Brown solid, mp: 215-216 °C; $^1$H NMR (400 MHz, DMSO-d$_6$): δ 2.27 (s, 3H), 3.60 (s, 6H), 5.64 (s, 1H), 6.64-6.77 (m, 6H), 7.03-7.07 (m, 2H), 7.19-7.25 (m, 4H), 10.59 (br, s, 2H); $^{13}$C NMR (200 MHz, DMSO-d$_6$): δ 20.58, 55.08, 101.25, 110.33, 111.75, 117.69, 124.08, 126.85, 128.07, 128.36, 131.71, 134.32, 141.72, 152.50.

3,3’-((4-methoxyphenyl)methylene)bis(5-methoxy-1H-indole)
Yield: 83 %; Brown solid, mp: 198-200 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): $\delta$ 3.62 (s, 6H), 3.73 (s, 3H), 5.81 (s, 1H), 6.63-6.76 (m, 8H), 7.15-7.21 (m, 4H), 10.03 (br, s, 2H);

$^{13}$C NMR (50 MHz, DMSO-d$_6$): $\delta$ 54.46, 54.99, 101.09, 110.33, 111.41, 112.79, 117.90, 124.00, 126.71, 128.91, 131.64, 152.47, 157.07.
4.2.7 Spectra for selected compounds

Fig. 25: $^1$H and $^{13}$C NMR 3,3'-(p-tolylmethylene)bis(5-methoxy-1H-indole)
Fig. 26: 3,3’-((4-methoxyphenyl)methylene)bis(5-methoxy-1H-indole)
4.2.8 References


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