CHAPTER-5

SYNTHESIS AND CHARACTERIZATION OF N\(^1\)-SUBSTITUTED-3-AMINOALKOXYINDOLES AND THEIR TETRACYCLIC DERIVATIVES

AS 5-HT\(_6\) RECEPTOR LIGANDS
CHAPTER 5

SYNTHESIS AND CHARACTERIZATION OF N\textsuperscript{1}-SUBSTITUTED-3-AMINO ALKOOXYINDOLES AND THEIR TETRACYCLIC DERIVATIVES AS 5-HT\textsubscript{6} RECEPTOR LIGANDS.

5.1 Introduction:

This chapter deals with the preparation of N\textsuperscript{1}-substituted-3-aminoalkoxyindoles and their tetracyclic derivatives. The synthesis was carried out by using O-alkylation, N\textsuperscript{1}-sulfonylation, N\textsuperscript{1}-benzoylation, N\textsuperscript{1}-benzylolation and intramolecular Heck reaction. All the compounds were characterized with their spectral & analytical data.

5.2 Literature Background:

Since, the work described in this chapter is related to 3-aminoalkoxyindoles and their tetracyclic derivatives as 5-HT\textsubscript{6} receptor ligands, a brief literature survey about the molecules bearing these features is discussed. All these molecules are known to be 5-HT\textsubscript{6} receptor ligands.

Karolin et al. reported [88] the reaction of N-methyl-N-phenyl-hydrazine (91) with tert-butyldimethyl(prop-2-yn-1-yloxy)silane (92) in the presence of tetrakis(diethylamino)titanium and followed by treatment with zinc chloride resulting in 3-(tert-butyldimethylsilyloxy)-1,2-dimethyl-1\textit{H}-indole (93). Compound 93 was reacted with 2-chloro-N,N-
diethylethanamine (94) in the presence of tetra-n-butylammonium fluoride (TBAF) giving \([2-(1,2\text{-dimethyl}-1H\text{-indol-3-yloxy})\text{ethyl}]\text{diethylamine}\) (95). The latter was reacted with 6-chloroimidazo[2,1-b]thiazole-5-sulfonyl chloride (96) in the presence of sodium hydride resulting in the formation of \([2-[2-(6\text{-Chloro-imidazo[2,1-b]thiazole-5-sulfonyl methyl})-1\text{-methyl}-1H\text{-indol-3-yloxy}]\text{ethyl}]\text{diethylamine}\) (97) (Scheme-5.1). Compound 97 was reported to be active towards 5-HT\textsubscript{6} receptor.

![Chemical structures and reactions](image)

Choy et al. reported [89] the reaction of 5-methoxy-1-methyl-1H-indole (98) with iodosobenzenediacetate (99) in the presence of palladium di-acetate catalyst giving 3-acetyloxy-5-methoxy-1-methyl-1H-indole (100). The latter was reacted with 2-chloro-N,N-
dimethylethanamine resulting in the formation of \([2-(5\text{-methoxy-1-methyl-1H-indol-3-yloxy})\text{ethyl}]\text{dimethyl amine} \) (102) (Scheme-5.2).

\[
\begin{align*}
\text{MeO}& + \text{Pd(OAc)}_2 \\
\text{(98)} & \xrightarrow{2 \text{ mof\% Pd(OAc)}_2} \text{MeO} \\
\text{(99)} & \xrightarrow{\text{KOH/THF}} \text{MeO} \\
\text{(100)} & \xrightarrow{60 \text{ C}/12 \text{ h}} \text{Cl} \xrightarrow{\text{N,N-dimethylamine}} \text{MeO} \\
\text{(101)} & \xrightarrow{\text{N,N-dimethylamine}} \text{MeO} \\
\text{(102)}
\end{align*}
\]

Jasti et al. reported [71] the reaction of 5-methoxyindole with oxalyl chloride, yielding \(2-(5\text{-methoxy-1H-indol-3-yl})-2\text{-oxoacetyl chloride} \) (104). The latter was reacted with N,N-dimethylamine resulting in \(2-(5\text{-methoxy-1H-indol-3-yl})\text{-N,N-dimethyl-2-oxoacetamide} \) (105). 105 was reduced with lithium aluminumhydride, giving \(2-(5\text{-methoxy-1H-indol-3-yl})\text{-N,N-dimethylethanamine} \) (106). The latter was reacted with 2-bromobenzenesulfonyl chloride (90) which yielded \(2-[1-(2\text{-Bromobenzenesulfonyl})\text{-5-methoxy-1H-indol-3-yl}]\text{ethyl}]\text{dimethylamine} \) (107). 107 was intramolecularly cyclized in the presence of potassium acetate and tetrakis triphenylphosphine palladium (0) catalyst, resulting in the formation of 11-(2-(dimethylamino)ethyl)-9-methoxybenzo[4,5]-
isothiazolo[2,3-a]indole-5,5-dioxide (108) (Scheme-5.3). Compound 108 was reported to be 5-HT$_6$ receptor ligand.

Jasti et al. reported [73] the reaction of maleic anhydride (109) with methylamine giving 1-methylpyrrole-2,5-dione (110). The latter was reacted with 5-methoxyindole under Grignard conditions yielding 3-(5-methoxy-1H-indol-3-yl)-1-methylpyrrolidine-2,5-dione (111). Compound 111 was reduced with lithium aluminumhydride, which yielded 5-methoxy-3-(1-methylpyrrolidin-3-yl)-1H-indole (112).
The latter was reacted with 2-bromobenzenesulfonyl chloride yielding 1-(2-bromobenzenesulfonyl)-5-methoxy-3-(1-methyl-pyrrolidin-3-yl)-1H-indole (113). 113 was intramolecularly cyclized in presence of potassium acetate and tetrakis triphenylphosphine palladium (0) catalyst, which resulted in the formation of 2-methoxy-10-(1-methylpyrrolidin-3-yl)-5-thia-4b-aza-indeno[2,1-a]indene-5,5-dioxide (114) (Scheme-5.4). This compound was reported to be a 5-HT₆ receptor ligand.

Ramakrishna et al. reported [72] the reaction of 7-bromoindole (115) with oxalyl chloride, yielding (7-bromo-1H-indol-3-yl)oxoacetyl chloride (116). The latter was reacted with N,N-dimethylamine resulting in the
formation of 2-(7-bromo-1H-indol-3-yl)-N,N-dimethyl-2-oxoacetamide (117). 117 was reduced with lithium aluminiumhydride, leading to the formation of [2-(7-bromo-1H-indol-3-yl)ethyl]dimethyl-amine (118). The latter was reacted with benzenesulfonyl chloride (90) forming [2-(1-benzene sulfonyl-7-bromo-1H-indol-3-yl)ethyl]dimethyl-amine (119). 119 was intramolecularly cyclized in the presence of potassium acetate and tetrakis triphenylphosphine palladium (0) catalyst, giving [2-(6,6-dioxo-6H-thia-5a-aza-acephenanthrylen-4-yl)ethyl]dimethylamine (120) (Scheme-5.5). Compound 120 was reported to be a potent 5-HT₆ receptor ligand.
5.3 Present work:

A brief literature survey given above revealed about some of the indolyl ethers and tertracyclic indole derivatives useful as 5-HT$_6$ receptor ligands. However, not much work seems to have been reported around N$^1$-substituted-3-aminoalkoxyindoles and their tetracyclic derivatives. Hence, it was thought worthwhile to prepare these derivatives and test their affinities towards 5-HT$_6$ receptor. This chapter deals with the synthesis and characterization of these compounds.

5.4. Results and Discussion:

The preparation of substituted-3-aminoalkoxyindoles were carried out by using Method-A & Method-B. Method-A was used in most of the cases since it gave the product in single step with good yields. Method-B was also used to prepare the targeted series, but it was found not much useful when we require substitutions on side chain (i.e. compounds bearing R$^2$=H, R$^3$=Me & R$^2$=Me, R$^3$=H). The details of these methods are given in the following sections:

5.4.1 METHOD-A: Preparation of substituted-3-aminoalkoxyindoles (123):

83a (i.e. 83, R$^1$=6-Cl, please see chapter-4) was reacted with 2-chloro-N,N-dimethylethanamine hydrochloride (121) in presence of potassium carbonate as a base and THF as solvent. The mixture was processed and the isolated product was identified as 6-chloro-1-acetyl-3-
(2-dimethylaminoethoxy)-1H-indole (122a) (i.e. 122, R¹=6-Cl, R²=R³=H) (Scheme-5.6) based on its spectral and analytical data. Thus, its IR (KBr) (Fig: 5.1) showed the peak at 1693 cm⁻¹ (sharp, strong, due to –CO-stretching) with disappearance of peaks near 1730 cm⁻¹ region, which was origionally present in the IR of 83a. Its ¹H-NMR (CDCl₃/TMS) (Fig: 5.2) showed peaks at δ 2.38 (s, 6H; N(CH₃)₂), 2.66 (s, 3H; COCH₃), 2.77 – 2.82 (t, 2H; Me₂NCH₂), 4.43 – 4.46 (t, 2H; OCH₂), 7.20 – 7.22 (d, J = 8.24 Hz, 1H; Ar-H), 7.36 – 7.39 (dd, J = 1.54, 8.79 Hz, 1H; Ar-H), 7.93 (s, 1H; Ar-H) and 8.73 (d, 1H; Ar-H). Its ESI-MS (Fig: 5.3) showed molecular ion peaks at 283 [M⁺+3] & 281 [M⁺+1] corresponding to the molecular masses of 282 [M⁺+2] & 280 [M⁺] when recorded in the Q+1 mode.

![Reaction Scheme](image)

The above reaction of 83a with 121 was found to be a general one and has been extended to prepare different derivatives of 122 (where, R¹=H, 5-OMe, 5-Cl, 4-F, 5-OEt, 5-OiPr, 5,6-Difluoro, 6-F, 5-Br; R²=H or Me & R³=Me or H). The products were assigned their structures by analogy and on the basis of their ESI-MS data. The crude products were
used in the next step without any purification. For details, please see the Experimental Section of this chapter.

However, when 83 was reacted with 121 there was chance for the formation of C-C product through C-2 position of 83, but it was found that only 122 was formed as a major product. The reason could be the hindrance of N\(^1\)-acetyl functionality and the use of mild base like K\(_2\)CO\(_3\).

122a (i.e. 122, R\(^1\)=6-Cl, R\(^2\)=R\(^3\)=H) was reacted with sodium hydroxide in methanol : water (1:1) mixture under reflux conditions. The reaction mixture was processed and the isolated product was identified as 6-chloro-3-(2-dimethylaminoethoxy)-1H-indole (123a) (i.e. 123, R\(^1\)=6-Cl, R\(^2\)=R\(^3\)=H) (Scheme-5.7), based on its spectral and analytical data. Thus, its IR (KBr) (Fig: 5.4) showed diagnostic peak at \(~3430\) cm\(^{-1}\) (broad, medium, due to –NH stretching) \& 1618 cm\(^{-1}\) (strong, sharp, due to –NH bending) with disappearance of peaks in the region 1750 – 1680 cm\(^{-1}\), indicating the absence of –CO- group which was originally present in the IR of 122. Its \(^1\)H-NMR (Fig: 5.5) showed signals at \(\delta 2.34\) (s, 6H; N(CH\(_3\)\(_3\)))\), 2.76 – 2.78 (t, 2H; Me\(_2\)NCH\(_2\)\)), 4.07 – 4.10 (t, 2H; OCH\(_2\)\)), 6.70 – 6.71 (d, J = 2.32 Hz, 1H; Ar-H), 6.94 – 6.96 (dd, J = 1.68, 8.48 Hz, 1H; Ar-H), 7.28 (d, 1H; Ar-H), 7.43 – 7.52 (d, J = 8.45 Hz, 1H; Ar-H) and 9.48 (s, 1H; NH). Its ESI-MS (Fig: 5.6) showed the molecular ion peaks at 241 [M\(^{+3}\)] \& 239 [M\(^{+1}\)] corresponding to the molecular masses of 240 [M\(^{+2}\)] \& 238 [M\(^{+}\)] when recorded in the Q+1 mode.
The above deacetylation of 122a using NaOH was found to be a general one and has been extended to prepare different derivatives of 123 (where, R1=H, 5-OMe, 5-Cl, 4-F, 5-OEt, 5-OiPr, 5,6-Difluoro, 6-F, 5-Br; R2=H or Me & R3=Me or H). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section of this chapter.

5.4.2 METHOD-B: Preparation of substituted 3-aminoalkoxyindoles (123):

83a (i.e. 83, R1=6-Cl, R2=R3=H) was reacted with 1-bromo-2-chloroethane 124 (R2=R3=H) using potassium carbonate as a base and acetonitrile as a reaction medium. The mixture was processed and the isolated product was identified as 1-acetyl-6-chloro-3-(2-chloroethoxy)-1H-indole 125a (i.e. 125, R1=6-Cl, R2=R3=H) (Scheme-5.8) based on its spectral and analytical data. Thus, its IR (KBr) (Fig: 5.7) showed single peak at 1694 cm⁻¹ (strong, sharp, due to –CO- stretching) with disappearance of peak near region 1730 cm⁻¹, which was originally
present in the IR of 83a. Its ¹H-NMR (Fig: 5.8) showed signals at δ 2.57 (s, 3H; COCH₃), 4.00 – 4.03 (t, 2H; CH₂Cl), 4.33 – 4.36 (t, 2H; CH₂O), 7.49 – 7.52 (dd, J = 2.1, 8.8 Hz, 1H; Ar-H), 7.55 (s, 1H; Ar-H), 7.64 – 7.65 (m, J = 1.99 Hz, 1H; Ar-H), 8.25 – 8.27 (d, J = 8.8 Hz, 1H; Ar-H). Its ESI-MS showed (Fig: 5.9) the molecular ion peaks at 274 [M⁺+3] & 272 [M⁺+1] corresponding to the molecular masses of 273 [M⁺+2] & 271 [M⁺] when recorded in the Q+1 mode.

![Scheme-5.8](image)

The above reaction of 83a with 124 was found to be a general one and has been extended to prepare different derivatives of 125 (where, R¹=5-OMe, 5-Cl & R²=R³=H). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section of this chapter.

125a (i.e. 125, R¹=6-Cl, R²=R³=H) was reacted with sodium hydroxide in water : MeOH (1:1) mixture under reflux conditions. The mixture was processed and the isolated product was identified as 6-chloro-3-(2-chloroethoxy)-1H-indole (126a) (i.e. 126, R¹=6-Cl, R²=R³=H)
(Scheme-5.9) based on its spectral and analytical data. Thus, its IR (KBr) (Fig: 5.10) showed a diagnostic peak at ~3440 cm\(^{-1}\) (broad, medium, due to \(-\text{NH}\)) with absence of \(-\text{CO-}\) absorption peak in the region 1720 – 1680 cm\(^{-1}\), which was originally present in the IR of 125a. Its \(^1\text{H}-\text{NMR}\) (CDCl\(_3\)/TMS) (Fig: 5.11) showed signals at \(\delta 3.92 – 3.95\) (t, 2H; CH\(_2\)Cl), 4.20 – 4.23 (t, 2H; CH\(_2\)O), 7.04 – 7.10 (m, 2H; Ar-H), 7.29 – 7.31 (d, \(J = 8.3\) Hz, 1H; Ar-H), 7.44 (d, \(J = 2.0\) Hz, 1H; Ar-H), 10.74 (bs, 1H; -NH). Its ESI-MS (Fig: 5.12) showed the presence of molecular ion peaks at 228 [M\(^+\)-3] \& 230 [M\(^+\)-1] corresponding to the molecular masses of 229 [M\(^+\)-2] \& 231 [M\(^+\)] when recorded in the Q-1 mode.

![Scheme-5.9](image)

The above reaction of 125a with NaOH was found to be a general one and has been extended to prepare different derivatives of 126 (where, R\(^1\)=5-OMe, 5-Cl \& R\(^2\)=R\(^3\)=H). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section.
The above reaction of 125a with NaOH was found to give 126a as a major product. However the byproduct 6-chloro-3-(2-hydroxyethoxy)-1H-indole was found to be very minor and got washed away during workup.

126a (i.e. 126, R₁=6-Cl, R²=R³=H) was reacted with dimethylammonium chloride using potassium carbonate as a base and DMF as solvent (Scheme-5.10). The mixture was processed and the isolated product was found to be identical with (123a) (i.e. 123, R₁=6-Cl, R²=R³=H), which was prepared using Method-A.

The above reaction of 126a with dimethylammonium chloride was found to be a general one and has been extended to prepare different derivatives of 123 (where, R₁=OMe, 5-Cl & R²=R³=H). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section.
5.5 Preparation of substituted-N\textsuperscript{1}-sulfonyl-3-aminoalkoxyindoles (127):

123a (i.e. 123, R\textsubscript{1}=6-Cl, R\textsubscript{2}=R\textsubscript{3}=H) was reacted with 2-bromobenzenesulfonyl chloride (90) (please, see chapter-4) using powdered potassium hydroxide as a base and THF as solvent. The mixture was processed and the isolated product was assigned as 6-chloro-1-(2-bromobenzenesulfonyl)-3-(2-dimethylaminoethoxy)-1H-indole (127a) (i.e. 127, R\textsubscript{1}=6-Cl, R\textsubscript{2}=R\textsubscript{3}=H) (Scheme-5.11) based on its spectral and analytical data. Thus, its IR (CCl\textsubscript{4}) (Fig: 5.13) showed unequal doublets at 1369 and 1178 cm\textsuperscript{-1} (strong, sharp, due to asymmetric and symmetric stretching of -SO\textsubscript{2} group). There was absence of any absorption peak in the region 3400 – 3300 cm\textsuperscript{-1}, which was originally present in the IR of 123a. Its \textsuperscript{1}H-NMR (CDCl\textsubscript{3}/TMS) (Fig: 5.14) showed signals at δ 2.36 (s, 6H; N(CH\textsubscript{3})\textsubscript{2}), 2.77 – 2.80 (t, 2H; Me\textsubscript{2}NCH\textsubscript{2}), 4.09 – 4.13 (t, 2H; OCH\textsubscript{2}), 7.10 (s, 1H; Ar-H), 7.19 – 7.21 (dd, J = 1.72, 8.36 Hz, 1H; Ar-H), 7.39 – 7.43 (m, 2H; Ar-H), 7.52 – 7.54 (d, J = 8.40 Hz, 1H; Ar-H), 7.68 – 7.69 (m, 1H; Ar-H), 7.76 (d, J = 1.64 Hz, 1H; Ar-H) and 7.83 – 7.84 (m, 1H; Ar-H). Its ESI-MS showed (Fig: 5.15) molecular ion peaks at 461 [M\textsuperscript{+}+5], 459 [M\textsuperscript{+}+3] & 457 [M\textsuperscript{+}+1] corresponding to the molecular masses of 460 [M\textsuperscript{+}+4], 458 [M\textsuperscript{+}+2] & 456 [M\textsuperscript{+}] when recorded in the Q+1 mode.
The above reaction of 123a with 90 was found to be a general one and has been extended to prepare different derivatives of 127a-p (where, R^1=H, 5-OMe, 5-Cl, 4-F, 5-OEt, 5-OiPr, 5,6-Difluoro, 6-F, 5-Br; R^2=H or Me & R^3=Me or H). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section of this chapter.

5.6 Preparation of substituted-N^1-benzoyl-3-aminoalkoxyindoles (129):

123a (i.e. 123, R^1=6-Cl, R^2=R^3=H) was reacted with commercially available 2-bromobenzoyl chloride (128, R^4=Br) using strong base like sodium hydride in DMF solvent. The mixture was processed and the isolated product was identified as 6-chloro-1-(2-bromobenzoyl)-3-(2-dimethylaminoethoxy)-1H-indole (129a) (i.e. 129, R^1=6-Cl, R^2=R^3=H, R^4=Br) (Scheme-5.12) based on its spectral & analytical data. Thus, its IR (CCl₄) (Fig: 5.16) showed peak at 1678 cm⁻¹ (sharp, strong, due to -CO-
stretching) with absence of -NH absorption peak around 3200 – 3500 cm\(^{-1}\), which was originally present in the IR of 123a. Its \(^1\)H-NMR (CDCl\(_3\)/TMS) (Fig: 5.17) showed signals at \(\delta\) 2.36 (s, 6H; N(CH\(_3\))\(_2\)), 2.77 – 2.80 (t, 2H; NCH\(_2\)), 4.00 (t, 2H; OCH\(_2\)), 6.20 (s, 1H; Ar-H), 7.28 – 7.31 (m, 1H; Ar-H), 7.43 – 7.55 (m, 4H; Ar-H), 7.69 – 7.71 (d, J = 7.88 Hz, 1H; Ar-H), 8.52 (s, 1H; Ar-H). Its ESI-MS showed (Fig: 5.18) the presence of molecular ion peaks at 425 [\(M^+\) +5], 423 [\(M^+\) +3] & 421 [\(M^+\) +1] corresponding to the molecular masses of 424 [\(M^+\) +4], 422 [\(M^+\) +2] & 420 [\(M^+\)] when recorded in the Q+1 mode.

\[\text{(123)} \quad \text{(128)} \quad \text{NaH} / \text{DMF} \quad \text{RT} \quad \text{60-70\%} \quad \text{(129)}\]

\(R^1=5\text{-OMe, 5-Cl, 5-H, 5-OEt, 5-Br;}\)
\(R^2=\text{H or Me} \& R^3=\text{Me or H}; R^4=\text{Br or H}.

......Scheme-5.12

The above reaction of 123a with 128 was found to be a general one and has been extended to prepare different derivatives of 129 (where, \(R^1=5\text{-OMe, 5-Cl, 5-H, 5-OEt, 5-Br;}\) \(R^2=\text{H or Me} \& R^3=\text{Me or H}; R^4=\text{Br or H}.

The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section of this chapter.
5.7 Preparation of substituted-$N^1$-benzyl-3-aminoalkoxyindoles (131):

123a (i.e. 123, $R^1=6$-Cl, $R^2=R^3=H$) was reacted with commercially available 2-bromobenzyl bromide (130) using strong base like sodium hydride in DMF solvent. The mixture was processed and the isolated product was identified as 6-chloro-1-(2-bromobenzyl)-3-(2-dimethylaminoethoxy)-$1H$-indole (131a) (i.e. 131, $R^1=6$-Cl, $R^2=R^3=H$) (Scheme-5.13) based on its spectral and analytical data. Thus, its IR (CCl₄) (Fig: 5.19) showed absence of strong peak in the region 3500 – 3100 cm⁻¹ indicating the absence of -NH group. Its $^1$H-NMR (CDCl₃/TMS) (Fig: 5.20) showed signals at $\delta$ 2.36 (s, 6H; N(CH₃)₂), 2.74 – 2.80 (t, 2H; CH₂N), 4.02 – 4.08 (t, 2H; OCH₂), 5.22 (s, 2H; CH₂-benzyl), 6.49 – 7.61 (m, 8H; Ar-H). Its ESI-MS showed (Fig: 5.21) the presence of molecular ion peaks at 411 [M⁺+5], 409 [M⁺+3] & 407 [M⁺+1] corresponding to the molecular masses of 410 [M⁺+4], 408 [M⁺+2] & 406 [M⁺] when recorded in the Q+1 mode.

\[
\begin{align*}
(123) + (130) & \xrightarrow{NaH / DMF} (131) \\
& \text{RT} 60-80\% \\
R^1 &= 5$-OMe, 5-Cl, 5-H, 5-Br; \\
R^2 &= H \text{ or } Me & R^3 &= Me \text{ or } H
\end{align*}
\]

.....Scheme-5.13
The above reaction of 123a with 130 was found to be a general one and has been extended to prepare different derivatives of 131 (where, R¹=5-OMe, 5-Cl, 5-H, 5-Br; R²=H or Me & R³=Me or H; N¹ was 2-bromobenzyl). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section of this chapter.

5.8. Preparation of Tetracyclic derivatives:

The compounds 127a-p, 129a & 131a-b were intramolecularly cyclized under Heck reaction conditions. The compounds were divided into three different series (Series-I to Series-III). The spectral detail of these series is discussed under following section:-

5.8.1 SERIES-I: N¹-Sulfonyl tetracyclic compounds.

127a (i.e. 127, R¹=6-Cl, R²=R³=H) was cyclized in presence of commercially procured tetrakis triphenylphosphine palladium (0) using dry potassium acetate as a base in N, N-dimethylacetamide (DMA) medium. The mixture was processed and the isolated product was identified as 3-chloro-10-(2-N,N-dimethylaminoethoxy)-5-thia-4b-azaindeno[2,1-alindene-5,5-Dioxide (132a) (i.e. 132, R¹=3-Cl, R²=R³=H) (Scheme-5.14) based on its spectral & analytical data. Thus, its IR (KBr) (Fig: 5.22) showed doublets at 1310 and 1175 cm⁻¹ (very strong, sharp, due to asymmetric and symmetric stretching of -SO₂ group). Its ¹H-NMR (CDCl₃/TMS) (Fig: 5.23) showed signals at δ 2.36 (s, 6H; N-(CH₃)₂), 2.74 –
2.77 (t, 2H; Me₂NCH₂), 4.35 – 4.38 (t, 2H; OCH₂), 7.20 – 7.23 (dd, J = 1.77, 8.50 Hz, 1H; Ar-H), 7.46 – 7.48 m, 1H; Ar-H), 7.57 – 7.60 (d, J = 8.47 Hz, 1H; Ar-H), 7.67 – 7.69 (m, 2H; Ar-H), 7.79 – 7.81 (m, 1H; Ar-H) & 7.92 – 7.94 (m, 1H; Ar-H). Its ¹³C-NMR (CDCl₃/TMS) (Fig: 5.24) showed characteristic peaks at δ 45.83 (N-(CH₃)₂), 58.85 (NCH₂), 72.13 (OCH₂) & 117 – 137 (Ar-C). Its ESI-MS showed (Fig: 5.25) the molecular ion peaks at 379 [M⁺+3] & 377 [M⁺+1] corresponding to the molecular masses of 378 [M⁺+2] & 376 [M⁺] when recorded in the Q+1 mode.

![Scheme-5.14](image)

The above Heck cyclization reaction of 127 was found to be a general one and has been extended to prepare different derivatives of 132 (where, R¹=1-F, 2-Cl, 2-OMe, 2-OEt, 2-OiPr, 2,3-difluoro, 3-F, H; R²=H or Me & R³=Me or H). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section.
Mechanistic cycle in intramolecular Heck reactions:

Following is the generalized and simplified mechanism of intramolecular Heck reaction [90, 91] (Scheme-5.15). The first step is oxidative addition of Pd catalyst to form intermediate I. This process is concerted, where the C-X bond breaks synchronously with the formation of Pd-C and Pd-X bonds. The second step is migratory insertion of Pd, where the ligand deligation followed by coordination bond formation occurs between the olefin and and Pd (II). This step has been recognized as the step that governs stereo and regiochemistry of the olefinated aryl product. The next step in the catalytic cycle is elimination of the alkene. It is generally accepted that this occurs via β-hydride elimination (III). In the last step, regeneration of the Pd (0) species occurs by deprotonation of the palladium. In presence of bases (like triethylamine), the reductive elimination of Pd-H occurs with the regeneration of Pd(0) catalyst.
Scheme 5.15

Pd(PPh₃)₄ \rightleftharpoons -2PPh₃ \rightarrow Pd(PPh₃)₂

\[
Pd(PPh₃)₂ \rightarrow \text{II}
\]

\[
PdL₂X \rightarrow \text{II}
\]

\[
Pd⁻ \rightarrow \text{III}
\]

\[
\text{HPdL₂X} \rightarrow \text{IV}
\]

\[
\text{HPdL₂X} \quad \tilde{B} \quad \text{HB⁻X}⁻ \quad \text{Pd(PPh₃)₂}
\]

\[
\text{I}
\]

\[
\text{II}
\]

\[
\text{III}
\]

\[
\text{IV}
\]
5.8.2 SERIES-II: N\textsuperscript{1}-Benzoyl tetracyclics:

129\textsuperscript{a} (i.e. 129, R\textsuperscript{1}=6-Cl, R\textsuperscript{2}=R\textsuperscript{3}=H; N\textsuperscript{1}-2-bromobenzoyl) was cyclized in presence of commercially procured tetrakis triphenylphosphine palladium (0) using dry potassium acetate as a base in N, N-dimethylacetamide (DMA) as a reaction medium. The mixture was processed and the isolated product was identified as 3-chloro-10-(2-N,N-dimethylaminoethoxy)-4b-azaindeno [2,1-a]indene-5-one (133a) (i.e. 133, R\textsuperscript{1}=3-Cl, R\textsuperscript{2}=R\textsuperscript{3}=H) (Scheme-5.16) based on its spectral & analytical data. Thus, its IR (KBr) (Fig: 5.26) showed the peaks at 1676 cm\textsuperscript{-1} (medium, sharp, due to -CO- stretching). Its \textsuperscript{1}H-NMR (DMSO-\textit{d}\textsubscript{6}/TMS) (Fig: 5.27) showed signals at δ 2.24 (s, 6H; N-(CH\textsubscript{3})\textsubscript{2}), 2.66 – 2.69 (t, 2H; Me\textsubscript{2}NCH\textsubscript{2}), 4.40 – 4.43 (t, 2H; OCH\textsubscript{2}), 7.36 – 7.38 (dd, J = 1.58, 8.56 Hz, 1H; Ar-H), 7.61 – 7.69 (m, 2H; Ar-H), 7.85 – 7.89 (m, 2H; Ar-H), 8.02 – 8.04 (d, J = 7.77 Hz, 1H; Ar-H), 8.16 – 8.18 (d, J = 7.87 Hz, 1H; Ar-H). Its ESI-MS showed (Fig: 5.28) the molecular ion peaks at 343 [M\textsuperscript{+}+3] \& 341 [M\textsuperscript{+}+1] corresponding to molecular masses of 342 [M\textsuperscript{+}+2] \& 340 [M\textsuperscript{+}] when recorded in the Q+1 mode.
5.8.3 Series-III: N^1-Benzyl tetracyclics (134):

131a (i.e. 131, R^1=6-Cl, R^2=R^3=H; N^1-2-bromobenzyl) was cyclized in presence of commercially procured tetrakis triphenylphosphine palladium (0) using dry potassium acetate as a base and DMA as a solvent. The mixture was processed and the isolated product was identified as 2-((2-methoxy-6H-isoindolo[2,1-a]indol-11-yl)oxy)-N,N-dimethylethanamine (134a) (i.e. 134, R^1=3-Cl, R^2=R^3=H) (Scheme-5.17).

Thus, its ^1^H-NMR (DMSO-d_6/TMS) (Fig: 5.30) showed signals at δ 2.22 (s, 6H; N-(CH_3)_2), 2.64 – 2.67 (t, 2H; Me_2NCH_2), 4.00 – 4.03 (t, 2H; OCH_2), 5.36 (s, 2H; CH_2Ar), 6.86 – 6.96 (m, 1H; Ar-H), 6.97 – 7.06 (m, 1H; Ar-H), 7.22 – 7.25 (m, 2H; Ar-H), 7.47 – 7.50 (m, J = 1.8, 8.12 Hz, 2H; Ar-H), 7.65 – 7.67 (m, 1H; Ar-H). Its ESI-MS showed (Fig: 5.31) the molecular ion peaks at 329 [M^+3] & 327 [M^+1] corresponding to the molecular masses of 328 [M^+2] & 326 [M^+1] when recorded in the Q+1 mode.

where, R^1=3-Cl, 2-OMe & R^2=R^3=H

......Scheme-5.17
The above Heck cyclization reaction of 131 was found to be a general one and has been extended to prepare different derivatives of 134 (where, R1=2-OMe & R2=R3=H). The products were assigned their structures by analogy and on the basis of their spectral and analytical data. For details, please see the Experimental Section.
All the above reactions were summarized and presented in Scheme-5.18 & Scheme-5.19.

![Diagram of chemical reactions]

...Scheme-5.18
5.9 Conclusion:

Synthesis of N$_1$-substituted-3-aminoalkoxyindoles and their tetracyclic derivatives were achieved using above reaction sequences. All the compounds were fully characterized before testing for their in-vitro binding affinities towards 5-HT$_6$ receptor. The detail of these results will be discussed in subsequent Chapter-6.
5.10 Experimental Section:

Preparation of 122 (METHOD-A) (General procedure):

A mixture of potassium carbonate (6.6g, 47.6 mmol), 83 (23.8 mmol) and tetrahydrofuran (50 mL) was stirred at RT for 90 min. A previously liberated free base of 121 (10.3g, 71.4 mmol) was added to the reaction mixture and the resulting mixture was refluxed for 4 hr. After completion of the reaction (TLC), the mixture was cooled to RT and filtered under suction to remove the inorganic matter. The solid cake was washed with ethyl acetate (100 mL x 3). The filtrate was concentrated under reduced pressure to obtain residue, which was purified by flash column chromatography over silica gel with 1% triethylamine (TEA) in ethyl acetate : n-Hexane (1:1) to obtain 122a.

122a (i.e. 122, R¹=6-Cl; R²=R³=H):
Yield = 4.00g (60%); syrupy mass. For details, please see under Results & Discussion section.

The other substituted products 122b-s were isolated as crude and were confirmed on the basis of their ESI-MS. They were used in the next step without any purification.

122b (i.e. 122, R¹=R²=R³=H):
Yield = 5.60g (95%); syrupy mass (crude); ESI-MS (m/z): 247 [M⁺+1].
122c (i.e. 122, R¹=5-Cl, R²=R³=H):

Yield = 6.70g (100%); syrupy mass (crude); ESI-MS (m/z): 283 [M⁺+3],
281 [M⁺+1].

122d (i.e. 122, R¹=5-OMe, R²=R³=H):

Yield = 6.50g (100%); syrupy mass (crude); ESI-MS (m/z): 277 [M⁺+1].

122e (i.e. 122, R¹=5-OiPr, R²=R³=H):

Yield = 6.50g (90%); syrupy mass (crude); ESI-MS (m/z): 305 [M⁺+1].

122f (i.e. 122, R¹=5-OMe, R²=Me, R³=H):

Yield = 6.90g (100%); syrupy mass (crude); ESI-MS (m/z): 291 [M⁺+1].

122g (i.e. 122, R¹=6-F, R²=H, R³=Me):

Yield = 6.00g (90%); syrupy mass (crude); ESI-MS (m/z): 279 [M⁺+1].

122h (i.e. 122, R¹=5-Cl, R²=Me, R³=H):

Yield = 6.30g (90%); syrupy mass (crude); ESI-MS (m/z): 297 [M⁺+3], 295
[M⁺+1].

122i (i.e. 122, R¹=5-Cl, R²=H, R³=Me):

Yield = 6.60g (95%); syrupy mass (crude); ESI-MS (m/z): 297 [M⁺+3], 295
[M⁺+1].

122j (i.e. 122, R¹=H; R²=Me, R³=H):

Yield = 5.90g (95%); syrupy mass (crude); ESI-MS (m/z): 261 [M⁺+1].

122k (i.e. 122, R¹=OEt, R²=R³=H):

Yield = 6.60g (95%); syrupy mass (crude); ESI-MS (m/z): 291 [M⁺+1].
1221 (i.e. 122, R₁=R₂=H, R₃=Me):

Yield = 6.20g (100%); syrupy mass (crude); ESI-MS (m/z): 261 [M⁺+1].

122m (i.e. 122, R₁=6-F, R₂=Me, R₃=H):

Yield = 6.60g (100%); syrupy mass (crude); ESI-MS (m/z): 279 [M⁺+1].

122n (i.e. 122, R₁=5-OMe, R₂=H, R₃=Me):

Yield = 6.90g (90%); syrupy mass (crude); ESI-MS (m/z): 291 [M⁺+1].

122o (i.e. 122, R₁=4-F, R₂=R₃=H):

Yield = 5.70g (90%); syrupy mass (crude); ESI-MS (m/z): 265 [M⁺+1].

122p (i.e. 122, R₁=5,6-Di-F, R₂=R₃=H):

Yield = 6.40g (90%); syrupy mass (crude); ESI-MS (m/z): 283 [M⁺+1].

122q (i.e. 122, R₁=5-Br, R₂=R₃=H):

Yield = 7.00g (90%); syrupy mass (crude); ESI-MS (m/z): 328 [M⁺+3], 326 [M⁺+1].

122r (i.e. 122, R₁=5-Br, R₂=Me, R₃=H):

Yield = 7.00g (90%); syrupy mass (crude); ESI-MS (m/z): 342 [M⁺+3], 340 [M⁺+1].

122s (i.e. 122, R₁=5-Br, R₂=H, R₃=Me):

Yield = 7.05g (90%); syrupy mass (crude); ESI-MS (m/z): 342 [M⁺+3], 340 [M⁺+1].
**Preparation of 123 (General procedure):**

A mixture of crude 122 (15 mmol), methanol (20 mL), sodium hydroxide (1.2g, 30 mmol) and water (20 mL) was refluxed for 2 hr. After completion of the reaction (TLC), the mixture was cooled to RT and distilled off solvent under reduced pressure. The residue was poured into water (100 mL) and the mixture was extracted with ethyl acetate (3 x 50 mL). The combined ethyl acetate layer was washed with brine solution (75 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure. The products 123a-s were purified by flash column chromatography over silica gel using 1% triethylamine (TEA) in ethyl acetate.

**123a** (i.e. 123, R^1=6-Cl; R^2=R^3=H):

Yield = 1.85g (52%); Syrupy mass; HPLC purity = 97.44%. For details, please see the Results & Discussion section.

**123b** (i.e. 123, R^1=H; R^2=R^3=H):

Yield = 1.70g (55%); Syrupy mass; IR (KBr): 3401 cm^{-1} (due to -NH-); ^1H-NMR (CDCl_3/TMS): δ 2.36 (s, 6H; N(CH_3)_2), 2.75 – 2.78 (t, 2H; NCH_2), 4.09 – 4.12 (t, 2H; OCH_2), 6.79 (d, J = 2.5 Hz, 1H; Ar-H), 7.06 – 7.08 (m, 1H; Ar-H), 7.14 – 7.18 (m, 1H; Ar-H), 7.26 – 7.28 (d, 1H; Ar-H), 7.50 (bs, 1H; NH), 7.63 – 7.64 (dd, 1H; Ar-H); ESI-MS (m/z): 205 [M^+1]; Purity by HPLC = 96%.

**123c** (i.e. 123, R^1=5-Cl, R^2=R^3=H):

Yield = 2.10g (60%); M.R (°C) = 103 – 108; IR (KBr): ~3150 cm^{-1} (due to -
NH-); ¹H-NMR (CDCl₃/TMS): δ 2.36 (s, 6H; N(CH₃)₂), 2.75 – 2.78 (t, 2H; NCH₂), 4.09 – 4.10 (t, 2H; OCH₂), 6.71 – 7.63 (m, 5H; Ar-H & NH); ESI-MS (m/z): 241 [M⁺+3], 239 [M⁺+1]; Purity by HPLC = 93%.

123d (i.e. 123, R¹=5-OMe, R²=R³=H):

Yield = 2.10g (60%); Syrupy mass; IR (KBr): 3119 cm⁻¹ (due to -NH-), 1239; ¹H-NMR (CDCl₃/TMS): δ 2.38 (s, 6H; N(CH₃)₂), 2.79 – 2.82 (t, 2H; NCH₂), 3.86 (s, 3H; OCH₃), 4.08 – 4.13 (t, 2H; OCH₂), 6.67 – 7.15 (m, 4H; Ar-H), 7.48 (s, 1H; NH); ESI-MS (m/z): 235 [M⁺+1]; HPLC = 95%.

123e (i.e. 123, R¹=5-OiPr, R²=R³=H):

Yield = 2.00g (50%); Syrupy mass; IR (KBr): 3153 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 1.32 – 1.37 (d, 6H; CH(CH₃)₂), 2.38 (s, 6H; N(CH₃)₂), 2.78 – 2.81 (t, 2H; NCH₂), 4.09 – 4.12 (t, 2H; OCH₂), 4.48 – 4.55 (m, 1H; CH(CH₃)₂), 6.69 – 7.16 (m, 4H; Ar-H), 7.42 (s, 1H; NH); ESI-MS (m/z): 263 [M⁺+1]; HPLC purity: 94.93%.

123f (i.e. 123, R¹=5-OMe, R²=Me, R³=H):

Yield = 2.00g (55%); Syrupy mass; IR (CCl₄): 3410 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 1.34 – 1.35 (d, 3H; CH₃CH), 2.34 (s, 6H; N(CH₃)₂), 2.45 – 2.50 (m, 1H; CH₂NMe), 2.69 – 2.74 (m, 1H; CH₂NMe), 3.84 (s, 3H; OCH₃), 4.26 – 4.30 (m, 1H; OCH(CH₃)), 6.76 – 7.17 (m, 4H; Ar-H), 7.48 (s, 1H; NH); ESI-MS (m/z): 249 [M⁺+1]; HPLC purity: 94.52%.

123g (i.e. 123, R¹=6-F, R²=H; R³=Me):

Yield = 2.30g (65%); Syrupy mass; IR (KBr): 3146 cm⁻¹ (-NH-); ¹H-NMR
(CDCl₃/TMS): δ 1.17 – 1.18 (d, 3H; CHCH₃), 2.38 (s, 6H; N(CH₃)₂), 3.04 – 3.09 (m, 1H; CHCH₃), 3.89 – 3.93 (m, 1H; CH₂O), 4.09 – 4.13 (m, 1H; CH₂O), 7.13 – 7.66 (s, 5H; Ar-H & NH); ESI-MS (m/z): 237 [M⁺+1]; HPLC purity: 97.69%.

123h (i.e. 123, R¹=5-Cl, R²=Me, R³=H):

Yield = 1.90g (50%); Syrupy mass; IR (KBr): 3130 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 1.32 – 1.34 (d, 3H; C(CH₃)₂), 2.33 (s, 6H; N(CH₃)₂), 2.43 – 2.50 (m, 1H; CH₂N), 2.66 – 2.71 (m, 1H; CH₂N), 4.23 – 4.31 (m, 1H; CHO), 6.79 – 7.61 (m, 5H; Ar-H & NH); ESI-MS (m/z): 255 [M⁺+3], 253 [M⁺+1]; HPLC purity: 96%.

123i (i.e. 123, R¹=5-Cl, R²=H; R³=Me):

Yield = 1.90g (50%); Syrupy mass; IR (CCl₄): 3133 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 1.16 – 1.18 (d, 3H; CH₃CH), 2.35 (s, 6H; N(CH₃)₂), 2.98 – 3.03 (m, 1H; CHN), 3.80 – 3.84 (m, 1H; CH₂O), 4.01 – 4.08 (m, 1H; CH₂O), 6.71 – 7.54 (m, 5H; Ar-H & NH); ESI-MS (m/z): 255 [M⁺+3], 253 [M⁺+1]; HPLC purity: 92.74%.

123j (i.e. 123, R¹= H; R²= Me, R³= H):

Yield = 2.00g (60%); Syrupy mass; IR (KBr): 3141 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 1.31 – 1.33 (d, 3H; CH₃CH), 2.36 (s, 6H; N(CH₃)₂), 3.01 – 3.05 (m, 1H; CHN), 3.88 – 3.91 (m, 1H; CH₂O), 4.08 – 4.12 (m, 1H; CH₂O), 6.71 – 7.68 (m, 6H; Ar-H & NH); ESI-MS (m/z): 219 [M⁺+1]; HPLC purity: 94%.
**123k** (i.e. **123**, R¹=5-OEt, R²=R³=H):

Yield = 1.85g (50%); Syrupy mass; IR (KBr): ~3200 cm⁻¹ (due to -NH-); ¹H-NMR (CDCl₃/TMS): δ 1.41 – 1.44 (t, 3H; CH₃CH₂O), 2.37 (s, 6H; N(CH₃)₂), 2.77 – 2.78 (t, 2H; CH₂N), 4.01 – 4.06 (q, 2H; CH₃CH₂O), 4.09 – 4.10 (t, 2H; CH₂O), 6.69 – 7.26 (m, 4H; Ar-H), 7.52 (s, 1H; NH); ESI-MS (m/z): 249 [M⁺+1]; HPLC = 95%.

**123l** (i.e. **123**, R¹=H; R²=H; R³=Me):

Yield = 1.80g (55%); Syrupy mass; IR (CCl₄): 3130 cm⁻¹ (due to -NH-); ¹H-NMR (CDCl₃/TMS): δ 1.33 – 1.36 (d, 3H; CH₃CH), 2.35 (s, 6H; N(CH₃)₂), 2.48 – 2.54 (m, 1H; CH₂N), 2.68 – 2.73 (m, 1H; CH₂N), 4.29 – 4.35 (m, 1H; OCH), 6.77 – 7.66 (m, 6H; Ar-H & NH); ESI-MS (m/z): 219 [M⁺+1]; Purity by HPLC = 95%.

**123m** (i.e. **123**, R¹=6-F, R²=Me, R³=H):

Yield = 2.10g (60%); Syrupy mass; IR (KBr): 3100 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 1.33 – 1.35 (d, 3H; CH₃CH), 2.33 (s, 6H; N(CH₃)₂), 2.49 (m, 1H; CH₂N), 2.67 – 2.72 (m, 1H; CH₂N), 4.24 – 4.32 (m, 1H; CHO), 6.71 – 7.56 (m, 5H; Ar-H & NH); ESI-MS (m/z): 237 [M⁺+1]; HPLC purity: 97.35%.

**123n** (i.e. **123**, R¹=5-OMe, R²=H; R³=Me):

Yield = 2.40g (65%); Syrupy mass; IR (KBr): 3138 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 1.17 – 1.18 (d, 3H; CH₃), 2.39 (s, 6H; N(CH₃)₂), 3.01 – 3.06 (m, 1H; CHN), 3.84 (s, 3H; OCH₃), 3.86 – 3.88 (m, 1H; CH₂O), 4.07 –
4.11 (m, 1H; CH₂O), 6.69 – 7.17 (m, 4H; Ar-H), 7.43 (s, 1H; NH); ESI-MS (m/z): 249 [M⁺+1]; HPLC purity: 98.25%.

123o (i.e. 123, R¹=4-F, R²=R³=H):

Yield = 2.00g (60%); Syrupy mass; IR (KBr): 3128 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 2.35 (s, 6H; N(CH₃)₂), 2.77 – 2.80 (t, 2H; CH₂N), 4.10 – 4.13 (t, 2H; CH₂O), 6.68 – 7.08 (m, 4H; Ar-H), 7.80 (s, 1H; NH); ESI-MS (m/z): 223 [M⁺+1]; HPLC purity: 95.63%.

123p (i.e. 123, R¹=5,6-DiF, R²=R³=H):

Yield = 2.10g (60%); Syrupy mass; IR (KBr): 3200 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 2.37 (s, 6H; N(CH₃)₂), 2.74 – 2.79 (t, 2H; CH₂N), 4.06 – 4.09 (t, 2H; CH₂O), 6.69 – 7.38 (m, 3H; Ar-H), 7.67 (s, 1H; NH); ESI-MS (m/z): 241 [M⁺+1]; HPLC purity: 95.85%.

123q (i.e. 123, R¹= 5-Br, R²= H, R³= H):

Yield = 2.10g (60%); Syrupy mass; IR (KBr): 3100 cm⁻¹ (-NH-); ¹H-NMR (CDCl₃/TMS): δ 2.35 (s, 6H; N(CH₃)₂), 2.74 – 2.79 (t, 2H; NCH₂), 4.08 – 4.12 (t, 2H; OCH₂), 6.61 – 7.76 (m, 5H; Ar-H & NH); ESI-MS (m/z): 285 [M⁺+3], 283 [M⁺+1]; HPLC = 98%.

123r (i.e. 123, R¹=5-Br, R²=Me, R³=H):

Yield = 1.80g (40%); Syrupy mass; IR (KBr): 3100 cm⁻¹ (due to -NH-); ¹H-NMR (CDCl₃/TMS): δ 1.31 – 1.35 (d, 3H; CH₃CH), 2.35 (s, 6H; N(CH₃)₂), 2.41 – 2.51 (m, 1H; CH₂N), 2.69 – 2.72 (m, 1H; CH₂N), 4.20 – 4.29 (m, 1H; CHO), 6.62 – 7.78 (m, 5H; Ar-H & NH); ESI-MS (m/z): 300 [M⁺+3],
298 [M^+1]; HPLC purity: 97%.

123s (i.e. 123, R^1=5-Br, R^2=H; R^3=Me):
Yield = 2.00g (45%); Syrupy mass; IR (KBr): 3133 cm\(^{-1}\) (-NH-); \(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 1.15 – 1.18 (d, 3H; C\(\text{H}_3\)CH), 2.37 (s, 6H; N(C\(\text{H}_3\)_2)), 2.99 – 3.04 (m, 1H; C\(\text{H}\)N), 3.82 – 3.86 (m, 1H; C\(\text{H}_2\)O), 4.01 – 4.08 (m, 1H; C\(\text{H}_2\)O), 6.77 – 7.59 (m, 5H; Ar-H & NH); ESI-MS (m/z): 300 [M^+3], 298 [M^+1]; HPLC purity: 95%.

**Preparation of 125 METHOD-B (General procedure):**

A mixture of 83 (25 mmol), potassium carbonate (6.9g, 50 mmol), acetonitrile (50 mL) and 124 (8.9g, 62.5 mmol) was heated to reflux for 5 hr. After completion of the reaction (TLC), the mixture was cooled to RT, slowly poured into ice water (100 mL) and extracted into ethyl acetate (100 mL x 2). The combined organic layers were washed with brine solution (75 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure to obtain technical product, which was purified by flash column chromatography using ethyl acetate and n-Hexane (1:1) as an eluent.

125a (i.e. 125, R^1=6-Cl, R^2=R^3=H):
Yield = 4.40g (65%); Syrupy mass. For details, please see the Results & Discussion section.

125b (i.e. 125, R^1=5-Cl, R^2=R^3=H):
Yield = 4.10g (60%); M.R (\(^0\)C) = 124.3 – 126.5; IR (KBr): 1694 cm\(^{-1}\)
(-CO-); $^1$H-NMR (DMSO-$d_6$/TMS): 2.57 (s, 3H; CH$_3$CO), 4.01 – 4.03 (t, 2H; ClCH$_2$), 4.34 – 4.36 (t, 2H; CH$_2$O), 7.37 – 7.51 (m, 2H; Ar-H), 7.56 (s, 1H; Ar-H), 8.30 – 8.32 (d, 1H; Ar-H); ESI-MS (m/z): 275 [M$^+$+3], 273 [M$^+$+1].

**125c** (i.e. **125**, R$^1$=5-OMe, R$^2$=R$^3$=H):

Yield = 4.00g (60%); Syrupy mass; IR (CHCl$_3$, cm$^{-1}$): 1704 cm$^{-1}$ (-CO-); $^1$H-NMR (DMSO-$d_6$/TMS): 2.57 (s, 3H; CH$_3$CO), 3.83 (s, 3H; OC$_2$H$_3$), 3.99 – 4.02 (t, 2H; ClCH$_2$), 4.31 – 4.33 (t, 2H; CH$_2$O), 7.02 – 7.35 (m, 2H; Ar-H), 7.46 (s, 1H; Ar-H), 8.15 – 8.17 (d, 1H; Ar-H); ESI-MS (m/z): 268 [M$^+$+1].

**Preparation of 126 (General procedure):**

A mixture of **125** (20 mmol), methanol (25 mL), sodium hydroxide (0.8g, 40 mmol) & water (25 mL) was stirred & heated to reflux for 2 hr. After completion of the reaction (TLC), the mixture was cooled to RT and distilled off solvent under reduced pressure. The reaction mixture was poured into water (200 mL) and extracted the product into ethyl acetate (100 mL x 2). The combined ethyl acetate layers were washed with brine solution (75 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure to obtain product as residual mass. The crude products were purified by flash column chromatography over silica gel using ethyl acetate and n-Hexane (1:1).

**126a** (i.e. **126**, R$^1$=6-Cl, R$^2$=R$^3$=H):

Yield = 3.20g (70%); Syrupy mass. For details, please see the Results & Discussion section.
**126b** (i.e. **126**, $R^1=5$-Cl, $R^2=R^3=H$):

Yield = 2.80g (60%); Syrupy mass; IR (KBr): 3451 cm$^{-1}$ (-NH-); $^1$H-NMR (DMSO-$d_6$/TMS): 3.92 – 3.95 (t, 2H; ClC$_2$H$_2$), 4.20 – 4.23 (t, 2H; OCH$_2$), 7.04 – 7.10 (m, 2H; Ar-$\mathbf{H}$), 7.29 – 7.39 (d, $J = 7.9$ Hz, 1H; Ar-$\mathbf{H}$), 7.44 (d, $J = 2.1$ Hz, 1H; Ar-$\mathbf{H}$), 10.8 (s, 1H; -NH); ESI-MS (m/z): 229 [M$^+$-1], 227 [M$^+$-3].

**126c** (i.e. **126**, $R^1=5$-OMe, $R^2=R^3=H$):

Yield = 3.40g (75%); Syrupy mass; IR (CHCl$_3$): 3440 cm$^{-1}$ (-NH-); $^1$H-NMR (DMSO-$d_6$/TMS): 3.81 (s, 3H; C$_3$H$_3$O), 3.98 – 4.01 (t, 2H; ClC$_2$H$_2$), 4.22 – 4.25 (t, 2H; OCH$_2$), 7.11 – 7.36 (m, 2H; Ar-$\mathbf{H}$), 7.41 – 7.59 (m, 3H; Ar-$\mathbf{H}$), 10.80 (s, 1H; NH); ESI-MS (m/z): 224 [M$^+$-1].

**Preparation of 123 (General procedure):**

A mixture of **126** (15 mmol), N,N-dimethyl formamide (15 mL), potassium carbonate (8.3g, 60 mmoles) and N,N-dimethylamine hydrochloride (3g, 37.5 mmoles) was heated to 100 - 110 °C and stirred for 6 hr. After completion of the reaction (TLC), the mixture was cooled to RT and poured into water (100 mL). The mixture was extracted into ethyl acetate (75 mL x 2). The ethyl acetate layer was washed with brine solution (25 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure to obtain residual mass. The products, thus obtained, were purified by flash column chromatography over silica gel using 1% triethylamine in ethyl acetate : Hexane (1:1).
123a (i.e. 123, R¹=6-Cl, R²=R³=H):

Yield = 1.95g (55%); Syrupy mass; For details, please see the Results & Discussion section.

123c (i.e. 123, R¹=5-Cl, R²=R³=H):

Yield = 1.80g (50%); M.R (⁰C) = 103 – 109; For details, please see the Experimental section under METHOD-A.

123d (i.e. 123, R¹=5-OMe, R²=R³=H):

Yield = 2.30g (65%); Syrupy mass; For details, please see the Experimental section under METHOD-A.

**Preparation of 127 (General procedure):**

A mixture of KOH powder (0.7g, 12.54 mmol), 123 (6.27 mmol), tetrahydrofuran (25 mL) and 90 (2.3g, 9.4 mmol) was stirred at RT for 1 hr, under nitrogen blanket. After completion of the reaction (TLC), the solvent was distilled off completely under reduced pressure. The mixture was added to water (100 mL) & extracted the product into dichloromethane (2 x 50 mL). Combined the organic layers, washed with brine solution (50 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure. The product was purified using flash column chromatography over silica gel with 1% triethylamine (TEA) & ethyl acetate.

127a (i.e. 127, R¹=6-Cl; R²=R³=H):

Yield = 2.15g (75%); Syrupy mass; HPLC purity: 97.80%. (For other
spectral details, please see the Results & Discussion section).

**127b** (i.e. **127**, R\(^1\)=H; R\(^2\)=R\(^3\)=H):

Yield = 1.85g (70%); Syrupy mass; IR (KBr): 1363 & 1173 cm\(^{-1}\) (-SO\(_2\));

\(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 2.36 (s, 6H; N(CH\(_3\)_3)_2), 2.77 – 2.83 (t, 2H; CH\(_2\)N),
4.11 – 4.16 (t, 2H; CH\(_2\)O), 7.13 (s, 1H; Ar-H), 7.13 – 7.42 (m, 4H; Ar-H),
7.59 – 7.84 (m, 4H; Ar-H); ESI-MS (m/z): 425 [M\(^+\)+3], 423 [M\(^+\)+1].

**127c** (i.e. **127**, R\(^1\)=5-Cl, R\(^2\)=R\(^3\)=H):

Yield = 1.70g (60%); Syrupy mass; IR (KBr): 1366 & 1180 cm\(^{-1}\) (-SO\(_2\));

\(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 2.35 (s, 6H; N(CH\(_3\)_3)_2), 2.75 – 2.78 (t, 2H; CH\(_2\)N),
4.06 – 4.09 (t, 2H; CH\(_2\)O), 6.87 (s, 1H; Ar-H), 7.28 – 7.31 (dd, J = 2.12,
8.80 Hz, 1H; Ar-H), 7.52 – 7.55 (m, 3H; Ar-H), 7.61 – 7.63 (m, 2H; Ar-H),
7.88 – 7.90 (d, J = 10.28 Hz, 1H; Ar-H); ESI-MS (m/z): 459 [M\(^+\)+3], 457 [M\(^+\)+1].

**127d** (i.e. **127**, R\(^1\)=5-OMe, R\(^2\)=R\(^3\)=H):

Yield = 1.70g (60%); Syrupy mass; IR (KBr): 1370 & 1176 cm\(^{-1}\) (-SO\(_2\));

\(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 2.37 (s, 6H; N(CH\(_3\)_3)_2), 2.81 – 2.83 (t, 2H; CH\(_2\)N),
3.82 (s, 3H; CH\(_3\)O), 4.09 – 4.15 (t, 2H; OCH\(_2\)H), 6.86 – 6.89 (dd, J = 2.6,
9.08 Hz, 1H; Ar-H), 7.02 7.03 (d, J = 2.52 Hz, 1H; Ar-H), 7.10 (s, 1H; Ar-H),
7.33 – 7.36 (m, 2H; Ar-H), 7.63 – 7.74 (m, 3H; Ar-H); ESI-MS (m/z): 455 [M\(^+\)+3], 453 [M\(^+\)+1].

**127e** (i.e. **127**, R\(^1\)=5-OiPr, R\(^2\)=R\(^3\)=H):

Yield = 1.65g (55%); Syrupy mass; IR (KBr): 1371 & 1176 cm\(^{-1}\) (-SO\(_2\));
\textbf{1H-NMR (CDCl}_3/TMS): \( \delta \) 1.31 - 1.32 (d, 6H; CH(CH}_3)_2), 2.39 (s, 6H; N(CH}_3)_2), 2.82 - 2.85 (t, 2H; CH}_2N), 4.11 - 4.15 (t, 2H; CH}_2O), 4.50 - 4.55 (m, 1H; CH(CH}_3)_2), 6.84 - 6.86 (dd, \( J = 2.49, 8.99 \) Hz, 1H; Ar-\textbf{H}), 7.02 - 7.03 (d, \( J = 2.43 \) Hz, 1H; Ar-\textbf{H}), 7.09 (s, 1H; Ar-\textbf{H}), 7.33 - 7.36 (m, 2H; Ar-\textbf{H}), 7.61 - 7.63 (d, \( J = 9.01 \) Hz, 1H; Ar-\textbf{H}), 7.65 - 7.75 (m, 2H; Ar-\textbf{H});

ESI-MS (m/z): 483 [M\(^+\)+3], 481 [M\(^+\)+1].

\textbf{127f} (i.e. \textbf{127}, \( R^1=5\)-OMe, \( R^2=\text{Me}, R^3=\text{H})): 

Yield = 1.45g (50%); Syrupy mass; IR (KBr): 1372 & 1177 cm\(^{-1}\) (-SO\(_2\)-);

\textbf{1H-NMR (CDCl}_3/TMS): \( \delta \) 1.37 - 1.39 (d, 3H; C\text{H}_3CH), 2.32 (s, 6H; N(CH}_3)_2), 2.47 - 2.51 (m, 1H; CH}_2N), 2.69 - 2.74 (m, 1H; CH}_2N), 3.82 (s, 3H; OCH}_3), 4.35 - 4.39 (m, 1H; CH}_2O), 6.87 - 6.88 (dd, \( J = 2.56 \) Hz, 1H; Ar-\textbf{H}), 7.00 - 7.01 (d, \( J = 2.52 \) Hz, 1H; Ar-\textbf{H}), 7.13 (s, 1H; Ar-\textbf{H}), 7.33 - 7.36 (m, 2H; Ar-\textbf{H}), 7.62 - 7.36 (m, 2H; Ar-\textbf{H}), 7.77 - 7.79 (m, 1H; Ar-\textbf{H});

ESI-MS (m/z): 469 [M\(^+\)+3], 467 [M\(^+\)+1].

\textbf{127g} (i.e. \textbf{127}, \( R^1=6\)-F, \( R^2=\text{H}; R^3=\text{Me})): 

Yield = 1.90g (65%); Syrupy mass; IR (KBr): 1363 & 1176 cm\(^{-1}\) (-SO\(_2\)-);

\textbf{1H-NMR (CDCl}_3/TMS): \( \delta \) 1.16 - 1.17 (d, 3H; CH}_3CH), 2.37 (s, 6H; N(CH}_3)_2), 3.02 - 3.08 (m, 1H; CH}_2N), 3.87 - 3.91 (m, 1H; CH}_2O), 4.06 - 4.10 (m, 1H; CH}_2O), 7.12 - 7.88 (m, 8H; Ar-\textbf{H}); ESI-MS (m/z): 457 [M\(^+\)+3], 455 [M\(^+\)+1].

\textbf{127h} (i.e. \textbf{127}, \( R^1=5\)-Cl, \( R^2=\text{Me}, R^3=\text{H})): 

Yield = 1.60g (55%); Syrupy mass; IR (KBr): 1374, 1178 cm\(^{-1}\) (-SO\(_2\)-); \textbf{1H-}
NMR (CDCl$_3$/TMS): $\delta$ 1.36 – 1.38 (d, 3H; CH$_3$CH), 2.31 (s, 6H; N(CH$_3$)$_2$), 2.45 – 2.49 (m, 1H; CH$_2$N), 2.67 – 2.72 (m, 1H; CH$_2$N), 4.33 – 4.37 (m, 1H; CHO), 7.17 – 7.21 (m, 2H; Ar-H), 7.37 – 7.42 (m, 2H; Ar-H), 7.56 – 7.567 (d, J = 2.04 Hz, 1H; Ar-H), 7.64 – 7.67 (m, 2H; Ar-H), 7.88 – 7.90 (dd, J = 7.60 Hz, 1H; Ar-H); ESI-MS (m/z): 473 [M$^+$+3], 471 [M$^+$+1].

127i (i.e. 127, R$^1$=5-Cl, R$^2$=H; R$^3$=Me):

Yield = 1.45g (50%); Syrupy mass; IR (KBr): 1370 & 1177 cm$^{-1}$ (-SO$_2$-);
$^1$H-NMR (CDCl$_3$/TMS): $\delta$ 1.16 – 1.18 (d, 3H; CH$_3$CH), 2.37 (s, 6H; N(CH$_3$)$_2$), 3.03 – 3.07 (m, 1H; CHN), 3.87 – 3.91 (m, 1H; CH$_2$O), 4.08 – 4.11 (m, 1H; CH$_2$O), 6.87 – 7.76 (m, 8H; Ar-H); ESI-MS (m/z): 473 [M$^+$+3], 471 [M$^+$+1].

127j (i.e. 127, R$^1$=H; R$^2$=Me, R$^3$=H):

Yield = 1.65g (60%); Syrupy mass; IR (KBr): 1367 & 1178 cm$^{-1}$ (-SO$_2$-);
$^1$H-NMR (CDCl$_3$/TMS): $\delta$ 1.38 – 1.39 (d, 3H; CH$_3$CH), 2.32 (s, 6H; N(CH$_3$)$_2$), 2.49 – 2.53 (m, 1H; CH$_2$N), 2.69 – 2.84 (m, 1H; CH$_2$N), 4.35 – 4.41 (m, 1H; CHO), 7.18 (s, 1H; Ar-H), 7.21 – 7.26 (m, 2H; Ar-H), 7.35 – 7.39 (m, 2H; Ar-H), 7.58 – 7.65 (m, 2H; Ar-H), 7.71 – 7.73 (m, 1H; Ar-H), 7.86 – 7.88 (m, 1H; Ar-H); ESI-MS (m/z): 439 [M$^+$+3], 437 [M$^+$+1].

127k (i.e. 127, R$^1$=5-OEt, R$^2$=R$^3$=H):

Yield = 1.90g (65%); Syrupy mass; IR (KBr): 1369 & 1176 cm$^{-1}$ (-SO$_2$-);
$^1$H-NMR (CDCl$_3$/TMS): $\delta$ 1.38 – 1.42 (t, 3H; CH$_3$CH$_2$O), 2.38 (s, 6H; N(CH$_3$)$_2$), 2.82 – 2.85 (t, 2H; CH$_2$N), 4.00 – 4.06 (q, 2H; CH$_3$CH$_2$O), 4.11 –
4.13 (t, 2H; CH_2O), 6.85 – 6.88 (dd, J = 2.52, 9.0 Hz, 1H; Ar-H), 7.01 – 7.019 (d, J = 2.44 Hz, 1H; Ar-H), 7.09 (s, 1H; Ar-H), 7.33 – 7.35 (m, 2H; Ar-H), 7.62 – 7.65 (d, J = 9.28 Hz, 1H; Ar-H), 7.65 – 7.74 (m, 2H; Ar-H); ESI-MS (m/z): 469 [M^+3], 467 [M^+1].

**127i** (i.e. **127i**, R^1=R^2=H; R^3=Me):

Yield = 1.5g (60%); Syrupy mass; IR (KBr): 1359 & 1174 cm\(^{-1}\) (-SO_2-);

\(^1\)H-NMR (CDCl_3/TMS): δ 1.17 – 1.18 (d, 3H; CH_3CH), 2.38 (s, 6H; N(CH_3)_2), 3.04 – 3.09 (m, 1H; CHN), 3.89 – 3.93 (m, 1H; CH_2O), 4.09 – 4.13 (m, 1H; CH_2O), 7.13 (s, 1H; Ar-H), 7.22 – 7.27 (m, 2H; Ar-H), 7.34 – 7.39 (m, 2H; Ar-H), 7.66 – 7.83 (m, 4H; Ar-H); ESI-MS (m/z): 439 [M^+3], 437 [M^+1].

**127m** (i.e. **127m**, R^1=6-F, R^2=Me, R^3=H):

Yield = 1.85g (65%); Syrupy mass; IR (KBr): 1370 & 1174 cm\(^{-1}\) (-SO_2-);

\(^1\)H-NMR (CDCl_3/TMS): δ 1.36 – 1.38 (d, 3H; CH_3CH), 2.31 (s, 6H; N(CH_3)_2), 2.45 – 2.50 (m, 1H; CH_2N), 2.67 – 2.72 (m, 1H; CH_2N), 4.3 – 4.37 (m, 1H; CH_2O), 6.97 – 6.977 (m, 1H; Ar-H), 7.13 (s, 1H; Ar-H), 7.38 – 7.45 (m, 4H; Ar-H), 7.68 – 7.70 (dd, J = 1.44, 7.68 Hz, 1H; Ar-H), 7.87 – 7.90 (dd, J = 1.96, 7.72 Hz, 1H; Ar-H); ESI-MS (m/z): 457 [M^+3], 455 [M^+1].

**127n** (i.e. **127n**, R^1=5-OMe, R^2=H; R^3=Me):

Yield = 1.90g (65%); Syrupy mass; IR (KBr): 1370 & 1177 cm\(^{-1}\) (-SO_2-);

\(^1\)H-NMR (CDCl_3/TMS): δ 1.16 – 1.18 (d, 3H; CH_3CH), 2.37 (s, 6H; N(CH_3)_2), 3.03 – 3.07 (m, 1H; CHN), 3.82 (s, 3H; OCH_3), 3.87 – 3.91 (m, 1H; CH_2O), 4.08 – 4.11 (m, 1H; CH_2O), 6.87 – 7.76 (m, 8H; Ar-H); ESI-MS
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(m/z): 469 [M⁺+3], 467 [M⁺+1].

127o (i.e. 127, R¹=4-F, R²=R³=H):

Yield = 1.65g (60%); Syrupy mass; IR (KBr): 1362 & 1182 cm⁻¹ (-SO₂-);

¹H-NMR (CDCl₃/TMS): δ 2.43 (s, 6H; N(CH₃)₂), 2.89 – 2.92 (t, 2H; NCH₂),
4.15 – 4.18 (t, 2H; CH₂O), 6.85 – 6.87 (m, 1H; Ar-H), 7.12 (s, 1H; Ar-H),
7.17 -7.18 (m, 1H; Ar-H), 7.39 – 7.50 (m, 3H; Ar-H), 7.68 – 7.686 (dd, J =
1.56 Hz, 1H; Ar-H), 7.91 – 7.93 (dd, J = 1.96, 9.64 Hz, 1H; Ar-H); ¹³C-
NMR (CDCl₃/TMS): δ 22.07, 45.28, 57.18, 69.11, 106.7, 108.95, 109.14,
109.42, 109.46, 112.76, 112.94, 120.42, 126.11, 126.18, 127.74,
130.93, 134.56, 135.35, 135.44, 136, 137.85, 141.91, 154.41, 156.92,
175.77; ESI-MS (m/z): 443 [M⁺+3], 441 [M⁺+1].

127p (i.e. 127, R¹=5,6-DiF, R²=R³=H):

Yield = 1.85g (65%); Syrupy mass; IR (KBr): 1370 & 1178 cm⁻¹ (-SO₂-);

¹H-NMR (CDCl₃/TMS): δ 2.35 (s, 6H; N(CH₃)₂), 2.76 – 2.78 (t, 2H; CH₂N),
4.08 – 4.11 (t, 2H; CH₂O), 7.10 (s, 1H; Ar-H), 7.36 – 7.44 (m, 3H; Ar-H),
7.63 – 7.71 (m, 1H; Ar-H), 7.84 – 7.845 (m, 1H; Ar-H), 7.85 – 7.86 (m,
1H; Ar-H); ¹³C-NMR (CDCl₃/TMS): δ 45.91, 57.94, 69.19, 102.79,
103.03, 106.15, 106.36, 106.97, 107.01, 119.72, 119.79, 120.33,
127.87, 128.67, 128.77, 130.65, 134.61, 136.07, 137.83, 143.4, 146.74,
146.89, 148.01, 148.17, 149.17, 149.32, 150.46, 150.62; ESI-MS (m/z):
461 [M⁺+3], 459 [M⁺+1].
**Preparation of 129 (General procedure):**

A mixture of sodium hydride (50% on mineral oil) (0.06g, 1.25 mmol), 123 (0.836 mmol), N,N-dimethyl formamide (4 mL) and 2-bromobenzoyl chloride (0.219g, 1.0 mmol) was stirred at RT for 1 hr, under nitrogen blanket. After completion (TLC), the reaction mixture was poured into ice water (25 mL) and extracted into ethyl acetate (2 x 20 mL). The organic layer was washed with brine solution (20 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure. The residual mass, thus obtained, was purified with flash column chromatography over silica gel using 1% triethylamine (TEA) in ethyl acetate.

**129a** (i.e. 129, R\(^1\)=6-Cl, R\(^2\)=R\(^3\)=H, R\(^4\)=Br):

Yield = 0.24g (70%); Syrupy mass; HPLC purity: 97.76%. (For other spectral details, please see the Results & Discussion section).

**129b** (i.e. 129, R\(^1\)=5-Cl, R\(^2\)=H, R\(^3\)=H, R\(^4\)=H):

Yield = 0.18g (65%); Syrupy mass; IR (KBr): ~1680 cm\(^{-1}\) (due to -CO-);

\(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 2.34 (s, 6H; N(C\(_3\)H\(_2\))\(_2\)), 2.74 – 2.78 (t, 2H; CH\(_2\)N), 4.02 – 4.05 (t, 2H; CH\(_2\)N), 6.75 (s, 1H; Ar-H), 7.33 – 7.35 (dd, J = 2.04, 8.80 Hz, 1H; Ar-H), 7.52 – 7.55 (m, 2H; Ar-H), 7.58 – 7.62 (m, 2H; Ar-H), 7.68 – 7.71 (m, 2H; Ar-H), 8.19 - 8.21 (d, J = 8.72 Hz, 1H; Ar-H); \(^{13}\)C-NMR (CDCl\(_3\)/TMS): 45.83, 57.87, 68.93, 106.30, 116.84, 117.90, 121.06, 126.08, 128.63, 128.77, 131.73, 133.12, 134.53, 143.46, 167.98; ESI-MS (m/z): 345 [M\(^+\)+3], 343 [M\(^+\)+1]; HPLC = 99%. 
129c (i.e. 129, R₁=H; R²= R³=H, R⁴=H):

Yield = 0.18g (70%); Syrupy mass; IR (KBr): 1678 cm⁻¹ (due to -CO-); ¹H-NMR (CDCl₃/TMS): δ 2.34 (s, 6H; N(CH₃)₂), 2.74 – 2.80 (t, 2H; NCH₂), 4.01 – 4.07 (t, 2H; OCH₂), 6.72 – 8.27 (m, 10H; Ar-H); ESI-MS (m/z): 309 [M⁺+1]; HPLC purity: 99.47%.

129d (i.e. 129, R₁=OC₂H₅, R²= R³=H, R⁴=H):

Yield = 0.19g (65%); Syrupy mass; IR (KBr): 1671 cm⁻¹ (-CO-); ¹H-NMR (CDCl₃/TMS): δ 1.4 – 1.27 (t, 3H; OCH₂CH₃), 2.34 (s, 6H; N(CH₃)₂), 2.75 – 2.78 (t, 2H; CH₂N), 4.01 – 4.03 (t, 2H; CH₂O), 4.07 – 4.12 (q, 2H; OCH₂CH₃), 6.68 – 8.18 (m, 9H; Ar-H); ESI-MS (m/z): 353 [M⁺+1]; HPLC purity: 92.47%.

129e (i.e. 129, R₁=6-Cl, R²= R³=H, R⁴=H):

Yield = 0.17g (60%); Syrupy mass; IR (KBr): 1681 cm⁻¹ (-CO-); ¹H-NMR (CDCl₃/TMS): δ 2.34 (s, 6H; N(CH₃)₂), 2.73 – 2.79 (t, 2H; CH₂N), 3.99 – 4.04 (t, 2H; CH₂O), 6.69 – 8.37 (m, 9H; Ar-H); ESI-MS (m/z): 345 [M⁺+3], 343 [M⁺+1]; HPLC purity: 98.91%.

129f (i.e. 129, R₁=5-OMe, R²= R³=H, R⁴=Br):

Yield = 0.22g (65%); Syrupy mass; IR (KBr): 1678 cm⁻¹ (-CO-); ¹H-NMR (CDCl₃/TMS): δ 2.33 (s, 6H; N(CH₃)₂), 2.73 – 2.79 (bs, 2H; CH₂N), 3.87 (s, 3H; OCH₃), 4.09 – 4.13 (bs, 2H; CH₂O), 6.17 – 8.50 (m, 8H; Ar-H); HPLC purity: 95.38%.

129g (i.e. 129, R₁=H, R²= R³=H, R⁴= Br):
Yield = 0.21g (65%); Syrupy mass; IR (KBr): 1680 cm\(^{-1}\) (due to -CO-); \(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 2.36 (s, 6H; N(CH\(_3\)_2), 2.76 – 2.82 (t, 2H; CH\(_2\)N), 4.10 – 4.17 (t, 2H; CH\(_2\)O), 7.15 (s, 1H; Ar-H), 7.12 – 7.44 (m, 4H; Ar-H), 7.57 – 7.82 (m; 4H; Ar-H); ESI-MS (m/z): 389 [M\(^{+}\)+3], 387 [M\(^{+}\)+1].

129h (i.e. 129, R\(^1\)=H, R\(^2\)=Me, R\(^3\)=H, R\(^4\)=Br):

Yield = 0.23g (70%); Syrupy mass; IR (KBr): 1680 cm\(^{-1}\) (-CO-); \(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 1.15 – 1.18 (d, 3H; CH\(_3\)CH), 2.36 (s, 6H; N(CH\(_3\)_2), 3.10 – 3.12 (m, 1H; CH\(_2\)N), 3.86 – 3.88 (m, 1H; CH\(_2\)N), 4.12 – 4.16 (m, 1H; OCH), 7.14 (s, 1H; Ar-H), 7.25 – 7.28 (m, 2H; Ar-H), 7.36 – 7.42 (m, 2H; Ar-H), 7.68 – 7.79 (m, 4H; Ar-H); ESI-MS (m/z): 403 [M\(^{+}\)+5], 401 [M\(^{+}\)+3], 465 [M\(^{+}\)+1].

129i (i.e. 129, R\(^1\)=5-Br, R\(^2\)=R\(^3\)=H, R\(^4\)=Br):

Yield = 0.23g (60%); Syrupy mass; IR (KBr): 1680 cm\(^{-1}\) (-CO-); \(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 2.35 (s, 6H; N(CH\(_3\)_2), 2.75 – 2.78 (t, 2H; CH\(_2\)N), 4.00 – 4.02 (t, 2H; CH\(_2\)O), 6.15 (bs, 1H; Ar-H), 7.20 – 7.80 (m, 6H; Ar-H), 8.45 (bs, 1H; Ar-H); ESI-MS (m/z): 467 [M\(^{+}\)+5], 465 [M\(^{+}\)+3], 463 [M\(^{+}\)+1].

129j (i.e. 129, R\(^1\)=5-Br, R\(^2\)=H; R\(^3\)=Me, R\(^4\)=Br):

Yield = 0.24g (60%); Syrupy mass; IR (KBr): 1680 cm\(^{-1}\) (-CO-); \(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 1.36 –1.38 (d, 3H; CH\(_3\)CH), 2.31 (s, 6H; N(CH\(_3\)_2), 2.45 – 2.49 (m, 1H; Me\(_2\)NCH), 4.33 – 4.37 (m, 1H; CH\(_2\)O), 7.17 – 7.21 (m, 2H; CH\(_2\)O), 7.37 – 7.42 (m, 2H; Ar-H), 7.56 – 7.567 (d, J = 2.04 Hz, 1H; Ar-H), 7.64 – 7.67 (m, 2H; Ar-H), 7.88 – 7.90 (dd, J = 7.60 Hz, 1H; Ar-H); ESI-MS (m/z): 475 [M\(^{+}\)+5], 473 [M\(^{+}\)+3], 471 [M\(^{+}\)+1].
**129k** (i.e. **129**, R$_1$=5-Br, R$_2$=R$_3$=H, R$_4$=H):

Yield = 0.21g (65%); Syrupy mass; IR (KBr): 1685 cm$^{-1}$ (-CO-); $^1$H-NMR (CDCl$_3$/TMS): $\delta$ 2.36 (s, 6H; N(CH$_3$)$_2$), 2.77 – 2.80 (t, 2H; NCH$_2$), 4.02 – 4.05 (t, 2H; OCH$_2$), 6.72 (s, 1H; Ar-H), 7.45 – 7.47 (dd, J = 8.8 Hz, 1H; Ar-H), 7.50 – 7.71 (m, 5H; Ar-H), 7.78 (d, J = 1.90 Hz, 1H; Ar-H), 8.15 – 8.17 (d, J = 8.76 Hz, 1H; Ar-H); ESI-MS (m/z): 389 [M$^+$+3], 387 [M$^+$+1]; HPLC purity: 95.20%.

**Preparation of 131 (General procedure):**

A mixture of sodium hydride (50% on mineral oil) (0.092 g, 1.92 mmol), **123** (0.3 g, 1.28 mmol), N,N-dimethylformamide (8 mL) and 2-bromobenzyl chloride (0.31 g, 1.53 mmol) was stirred at RT for 2 hr, under nitrogen blanket. After completion of the reaction (TLC) the mixture poured in water (50 mL) and extracted the product with ethyl acetate (2 x 25 mL). The ethyl acetate layer was washed with brine solution (20 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure. The crude products were purified by flash column chromatography over silica gel using 0.5% TEA in ethyl acetate.

**131a** (i.e. **131**, R$_1$=6-Cl, R$_2$=R$_3$=H):

Yield = 0.42g (80%); Syrupy mass; HPLC purity: 98.20%; (For other spectral details, please see the Results & Discussion section).
131b (i.e. 131, R¹=5-OCH₃, R²=R³=H):

Yield = 0.39g (75%); Syrupy mass; ¹H-NMR (CDCl₃/TMS): δ 2.37 (s, 6H; N(CH₃)₂), 2.77 – 2.80 (t, 2H; CH₂N), 3.86 (s, 3H; OCH₃), 4.07 – 4.12 (t, 2H; OCH₂), 5.25 (s, 2H; N¹-CH₂Ar), 6.49 – 7.59 (m, 8H; Ar-H); MS: 405 [M⁺+3], 403 [M⁺+1]; HPLC purity: 96%.

131c (i.e. 131, R¹=R²=H; R³=Me):

Yield = 0.33g (70%); Syrupy mass; IR (KBr): 745, 1329, 1470 cm⁻¹; ¹H-NMR (CDCl₃/TMS): δ 1.18 – 1.19 (d, 3H; CH₃CH), 2.39 (s, 6H; N(CH₃)₂), 3.02 – 3.07 (m, 1H; CH₃CH₂), 3.86 – 3.89 (m, 1H; CH₂O), 4.07 – 4.11 (m, 1H; CH₂O), 5.28 (s, 2H; N¹-CH₂Ar), 6.53 – 6.55 (d, J = 9.44 Hz, 1H; Ar-H), 6.62 (s, 1H; Ar-H), 7.07 – 7.12 (m, 3H; Ar-H), 7.16 – 7.25 (m, 2H; Ar-H), 7.57 – 7.59 (m, 1H; Ar-H), 7.68 – 7.70 (m, 1H; Ar-H); ESI-MS (m/z): 389 [M⁺+3], 387 [M⁺+1]; HPLC purity: 97.05%.

131d (i.e. 131, R¹=H; R²=Me, R³=H):

Yield = 0.41g (80%); Syrupy mass; IR (KBr): 745, 1330, 1565 cm⁻¹; ¹H-NMR (CDCl₃/TMS): δ 1.15 – 1.16 (d, 3H; CH₃CH), 2.38 (s, 6H; N(CH₃)₂), 2.56 – 2.59 (m, 1H; Me₂NCH₂), 3.05 – 3.08 (m, 1H; Me₂NCH₂), 4.09 – 4.13 (m, 1H; CH₂O), 5.30 (s, 2H; CH₂Ar), 7.10 (s, 1H; Ar-H), 7.25 – 7.31 (m, 2H; Ar-H), 7.34 – 7.39 (m, 2H; Ar-H), 7.66 – 7.83 (m, 4H; Ar-H); ESI-MS (m/z): 389 [M⁺+3], 387 [M⁺+1].

131e (i.e. 131, R¹=5-Cl, R²=H, R³=Me):

Yield = 0.37g (75%); Syrupy mass; IR (KBr): 745, 1329, 1563 cm⁻¹; ¹H-NMR (CDCl₃/TMS): δ 1.19 (d, 3H; CH₃CH), 2.39 (s, 6H; N(CH₃)₂), 3.02 –
3.07 (m, 1H; CHNMe₂), 3.86 – 3.89 (m, 1H; CH₂O), 4.07 – 4.11 (m, 1H; CH₂O), 5.28 (s, 2H; CH₂Ar), 6.51 – 6.62 (m, 3H; Ar-H), 7.07 – 7.12 (m, 3H; Ar-H), 7.16 – 7.25 (m, 2H; Ar-H), 7.57 – 7.59 (m, 1H; Ar-H), 7.68 – 7.70 (d, 1H; Ar-H); ESI-MS (m/z): 425 [M⁺+5], 423 [M⁺+3], 421 [M⁺+1]; HPLC purity: 97.05%.

131f (i.e. 131, R¹=5-Br, R²=R³=H):

Yield = 0.40g (70%); Syrupy mass; IR (KBr): 1285, 1468, 1559, 1571, 2941 cm⁻¹; ¹H-NMR (CDCl₃/TMS): δ 2.36 (s, 6H; N(CH₃)₂), 2.69 – 2.79 (t, 2H; NCH₂), 4.05 – 4.13 (t, 2H; OCH₂), 5.24 (s, 2H; CH₂Ar), 6.47 – 6.62 (m, 2H; Ar-H), 7.00 – 7.26 (m, 4H; Ar-H), 7.54 – 7.62 (m, 1H; Ar-H), 7.81 – 7.82 (d, 1H; Ar-H); ESI-MS (m/z): 455 [M⁺+5], 453 [M⁺+3], 451 [M⁺+1].

131g (i.e. 131, R¹=5-Br, R²=Me, R³=H):

Yield = 0.36g (60%); Syrupy mass; IR (KBr): 1026, 1262, 1466, 1569, 2963 cm⁻¹; ¹H-NMR (CDCl₃/TMS): δ 1.32 – 1.34 (d, 3H; CH₃CH), 2.36 (s, 6H; N(CH₃)₂), 2.51 – 2.55 (m, 1H; CH₂N), 2.70 – 2.75 (m, 1H; CH₂N), 4.31 – 4.33 (m, 1H; OCHMe), 5.26 (s, 2H; CH₂Ar), 6.48 – 6.51 (m, 1H; Ar-H), 6.71 (s, 1H; Ar-H), 7.02 – 7.04 (d, J = 8.72 Hz, 1H; Ar-H), 7.11 – 7.14 (dd, J = 2.72 Hz, 2H; Ar-H), 7.21 – 7.24 (dd, J = 1.84, 8.76 Hz, 1H; Ar-H), 7.57 – 7.59 (m, 1H; Ar-H), 7.79 – 7.80 (d, J = 1.76 Hz, 1H; Ar-H); ESI-MS (m/z): 470 [M⁺+5], 468 [M⁺+3], 466 [M⁺+1].
Preparation of 132 (General procedure):

A mixture of potassium acetate (0.196 g, 2.006 mmol), tetrakis triphenyl phosphine palladium (0.07 g, 0.059 mmol), 127 (1.18 mmol) & N,N-dimethylacetamide (DMA) was heated to 120 – 125 °C and stirred for 1 hr. After completion (TLC), the reaction mixture was cooled to RT & poured into water (50 mL). The mixture was extracted in ethyl acetate (20 mL x 2). The combined ethyl acetate layer was washed with brine solution (25 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure. The products were purified by flash column chromatography over silica gel using 0.5% methanol in chloroform.

132a (i.e. 132, R1=3-Cl; R2=R3=H):
Yield = 0.15 g (35%); M.R (0°C): 104 – 110; HPLC Purity: 94.48%. For details, please see under Results & Discussion section.

132b (i.e. 132, R1=H; R2=R3=H):
Yield = 0.12 g (30%); M.R (0°C): 72 – 74; IR (KBr): 1334 & 1179 cm⁻¹ (-SO₂-);
¹H-NMR (ppm): 2.37 (s, 6H; N(CH₃)₂), 2.75 – 2.78 (t, 2H; CH₂-N(CH₃)₂), 4.38 – 4.41 (t, 2H; CH₂O), 7.24 – 7.26 (m, 1H; Ar-H), 7.38 – 7.46 (m, 2H; Ar-H), 7.66 – 7.69 (m, 3H; Ar-H), 7.79 – 7.81 (d, J = 7.84 Hz, 1H; Ar-H), 7.93 – 7.94 (d, J = 7.84 Hz, 1H; Ar-H); ¹³C-NMR (CDCl₃) δ: 45.82, 58.87, 72.14, 112.32, 120.19, 120.44, 122.29, 123, 123.12, 126.30, 126.92, 127.08, 128.10, 131.36, 133.92, 137.24, 137.59; ESI-MS (m/z): 343 [M⁺]
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+1]; HPLC Purity: 97.01%.

132c (i.e. 132, R₁=2-Cl, R²=R³=H):

Yield = 0.18 (40%); Syrupy mass; IR (KBr): 1317 & 1174 cm⁻¹ (-SO₂-); ¹H-NMR (CDCl₃/TMS): δ 2.38 (s, 6H; N(CH₃)₂), 2.75 – 2.78 (t, 2H; CH₂N(CH₃)₂), 4.34 – 4.37 (t, 2H; CH₂O); 7.32 – 7.35 (dd, J = 1.86, 8.56 Hz, 1H; Ar-H), 7.48 – 7.50 (m, 1H; Ar-H), 7.58 – 7.60 (d, J = 8.77 Hz, 1H; Ar-H), 7.65 – 7.68 (m, 2H; Ar-H), 7.94 – 7.96 (d, J = 7.84 Hz, 1H; Ar-H); ESI-MS (m/z): 379 [M⁺+3], 377 [M⁺+1]; HPLC Purity: 98.37%.

132d (i.e. 132, R₁=2-OMe, R²=R³=H):

Yield = 0.18g (40%); Syrupy mass; IR (KBr): 1324 & 1170 cm⁻¹ (-SO₂-); ¹H-NMR (CDCl₃/TMS): δ 2.37 (s, 6H; N(CH₃)₂), 2.74 – 2.77 (t, 2H; CH₂N(CH₃)₂), 3.87 (s, 3H; OCH₃), 4.33 – 4.36 (t, 2H; CH₂O); 6.98 – 7.01 (dd, J = 2.0, 8.8 Hz, 1H; Ar-H), 7.10 – 7.11 (d, J = 2.36 Hz, 1H; Ar-H), 7.44 – 7.45 (m, 1H; Ar-H), 7.55 – 7.57 (d, J = 8.88 Hz, 1H; Ar-H), 7.63 – 7.67 (m, 1H; Ar-H), 7.78 – 7.80 (d, J = 7.8 Hz, 1H; Ar-H), 7.90 – 7.92 (d, J = 7.8 Hz, 1H; Ar-H); ¹³C-NMR (CDCl₃/TMS): δ 45.83, 55.72, 58.85, 72.13, 102.55, 113.12, 115.48, 121.59, 122.30, 123.01, 126.23, 126.97, 128.08, 133.90, 137.30, 137.53, 156.16; ESI-MS (m/z): 373 [M⁺+1]; HPLC Purity: 96.15%.

132e (i.e. 132, R₁=2-OiPr, R²=R³=H):

Yield = 0.21g (45%); M.R (⁰C): 70.4 – 74.1; IR (KBr): 1333 & 1177 cm⁻¹ (-SO₂-); ¹H-NMR (CDCl₃/TMS): δ 1.35 – 1.37 (d, 6H; (CH₃)₂CH), 2.37 (s, 6H;
N(CH$_3$)$_2$), 2.74 – 2.77 (t, 2H; CH$_2$-N(CH$_3$)$_2$), 4.33 – 4.36 (t, 2H; CH$_2$O), 4.53 – 4.59 (sep, 1H; CH(CH$_3$)$_2$), 6.97 – 7.00 (dd, J = 2.42, 8.87 Hz, 1H; Ar-H), 7.12 (d, J = 2.29 Hz, 1H; Ar-H), 7.43 – 7.45 (m, 1H; Ar-H), 7.54 – 7.56 (d, J = 8.82 Hz, 1H; Ar-H), 7.64 (m, 1H; Ar-H), 7.77 – 7.79 (d, 1H; Ar-H), 7.90 – 7.92 (d, 1H; Ar-H); $^{13}$C-NMR (CDCl$_3$/TMS): δ 21.95, 45.82, 58.87, 71.08, 72.11, 106.07, 113.07, 117.24, 121.48, 122.27, 123.01, 126.35, 127, 128.02, 128.15, 133.85, 137.35, 137.52, 154.26; ESI-MS (m/z): 401 [M$^+1$]; HPLC Purity: 97.66%.

132f (i.e. 132, R$^1$=2-OCH$_3$, R$^2$=H, R$^3$=Me):

Yield = 0.16g (35%); M.R (°C): 77.6 – 80.1; IR (KBr): 1324 & 1175 cm$^{-1}$ (-SO$_2$-); $^1$H-NMR (CDCl$_3$/TMS): δ 1.15 – 1.17 (d, 3H; CH$_3$CH), 2.37 (s, 6H; N(CH$_3$)$_2$), 3.01 – 3.09 (m, 1H; CH$_3$CH), 3.87 (s, 3H; OCH$_3$), 4.09 – 4.11 (dd, 1H; CH$_2$O), 4.30 – 4.34 (dd, 1H; OCH$_2$), 6.98 – 7.01 (dd; J = 2.36, 8.8 Hz, 1H; Ar-H), 7.09 – 7.10 (d, J = 2.36 Hz, 1H; Ar-H), 7.43 – 7.45 (m, 1H; Ar-H), 7.55 – 7.58 (d, J = 8.80 Hz, 1H; Ar-H), 7.63 – 7.65 (m, 1H; Ar-H), 7.78 – 7.80 (d, J = 7.8 Hz, 1H; Ar-H), 7.88 – 7.90 (d, J = 7.76 Hz, 1H; Ar-H); $^{13}$C-NMR (CDCl$_3$/TMS): δ 19.19, 46.39, 65.39, 79.27, 113.2, 119.94, 122.39, 123.21, 126.45, 126.71, 128.49, 128.89, 129.55, 134.02, 137.23; ESI-MS (m/z): 387 [M$^+1$]; HPLC Purity: 97.4%.

132g (i.e. 132, R$^1$=3-F, R$^2$= Me; R$^3$=H):

Yield = 0.15g (35%); M.R (°C): 82.6 – 85.5; IR (KBr): 1337 & 1184 cm$^{-1}$ (-SO$_2$-); $^1$H-NMR (CDCl$_3$/TMS): δ 1.33 – 1.35 (d, J = 5.4 Hz, 3H; CH$_3$CH), 2.37 (s, 6H; N(CH$_3$)$_2$), 2.49 – 2.54 (m, 1H; CH$_2$N(CH$_3$)$_2$), 2.75 – 2.80 (m,
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\begin{align*}
&1H; CH_2N(CH_3)_2, 4.55 - 4.60 (m, J = 5.4 Hz, 1H; CHCH_3), 6.99 - 7.0 (m, J = 2.2 Hz, 1H; Ar-H), 7.39 - 7.40 (dd, 1H; Ar-H), 7.44 - 7.46 (m, 1H; Ar-H), 7.61 - 7.66 (m, 2H; Ar-H), 7.79 - 7.81 (d, J = 7.8 Hz, 1H; Ar-H), 7.93 - 7.95 (d, J = 7.8 Hz, 1H; Ar-H); \ ^13C-NMR (CDCl_3/TMS): \delta 19.14, 46.38, 65.33, 79.09, 99.74, 111.74, 121.43, 122.82, 124.15, 126.92, 128.07, 131.48, 134.02, 136.20, 136.88, 160.54, 162.98; ESI-MS (m/z): 375 [M^+ +1]; HPLC Purity: 94.43%. \\
&132h (i.e. 132, R^1=2-Cl, R^2=H, R^3=Me): Yield = 0.27g (60%); Syrupy mass; IR (KBr): 1331 & 1172 cm\(^{-1}\) (-SO_2-); \ ^1H-NMR (CDCl_3/TMS): \delta 1.15 - 1.16 (d, J = 5.4 Hz, 3H; CH_3CH), 2.37 (s, 6H; N(CH_3)_2), 3.01 - 3.11 (m, 1H; CHN(CH_3)_2), 4.10 - 4.11 (m, 1H; OCH_2), 4.29 - 4.34 (m, 1H; OCH_2), 7.32 - 7.35 (dd, J = 1.88, 8.60 Hz, 1H; Ar-H), 7.48 - 7.49 (m, 1H; Ar-H), 7.58 - 7.60 (d, J = 8.70 Hz, 1H; Ar-H), 7.64 - 7.65 (d, J = 1.68 Hz, 1H; Ar-H), 7.66 - 7.68 (m, 1H; Ar-H), 7.80 - 7.82 (d, J = 7.80 Hz, 1H; Ar-H); ESI-MS (m/z): 393 [M^+ +3], 391 [M^+ +1]; HPLC Purity: 91.09%. \\
&132i (i.e. 132, R^1=2-Cl, R^2=Me; R^3=H): Yield = 0.23g (50%); M.R (0\(^0\)C): 88.6 - 92.0; IR (KBr): 1346 & 1177 cm\(^{-1}\) (-SO_2-); \ ^1H-NMR (CDCl_3/TMS): \delta 1.34 - 1.35 (d, J = 6.24 Hz, 3H; CH_3CH), 2.37 (s, 6H; N(CH_3)_2), 2.49 - 2.53 (m, 1H; CH_2N(CH_3)_2), 2.76 - 2.81 (m, 1H; CH_2N(CH_3)_2), 4.52 - 4.57 (m, J = 6.24 Hz, 1H; CHCH_3), 7.32 - 7.34 (dd, J = 1.92, 8.56 Hz, 1H; Ar-H), 7.47 - 7.49 (m, 1H; Ar-H), 7.58 - 7.60 (d, J = 8.64 Hz, 1H; Ar-H), 7.67 - 7.68 (m, 2H; Ar-H), 7.80 - 7.82 (d, J =
7.88 Hz, 1H; Ar-H), 7.98 – 7.99 (d, J = 7.84 Hz, 1H; Ar-H); ESI-MS (m/z): 393 [M+3], 391 [M+1]; HPLC Purity: 94.11%.

132j (i.e. 132, R¹=H; R²=H, R³=Me):
Yield = 0.19g (45%); M.R (⁰C): 60.1 – 63.3; IR (KBr): 1335 & 1180 cm⁻¹ (-SO₂-); ¹H-NMR (CDCl₃/TMS): δ 1.15 – 1.17 (d, 3H; CH₃CH), 2.37 (s, 6H; N(CH₃)₂), 3.01 – 3.09 (m, 1H; CH₃CH), 4.09 – 4.11 (dd, 1H; OCH₂), 4.30 – 4.34 (dd, 1H; OCH₂), 7.32 – 7.34 (dd, J = 1.9, 8.56 Hz, 1H; Ar-H), 7.24 – 7.26 (m, 1H; Ar-H), 7.38 – 7.46 (m, 2H; Ar-H), 7.66 – 7.69 (m, 3H; Ar-H), 7.79 – 7.81 (d, J = 7.84 Hz, 1H; Ar-H); ¹³C-NMR (CDCl₃/TMS): δ 10.95, 41.20, 58.79, 112.38, 120.17, 122.38, 123.09, 126.36, 127.04, 128.11, 131.40, 133.98, 137.21, 137.85; ESI-MS (m/z): 357 [M⁺+1]; HPLC Purity: 96.41%.

132k (i.e. 132, R¹=2-OEt, R²=R³=H):
Yield = 0.25g (55%); M.R (⁰C): 101.2 – 103.8; IR (KBr): 1315 & 1175 cm⁻¹ (-SO₂-); ¹H-NMR (CDCl₃/TMS): δ 1.40 – 1.46 (t, 3H; CH₃CH₂O), 2.37 (s, 6H; N(CH₃)₂), 2.74 – 2.77 (t, 2H; CH₂N(CH₃)₂), 4.05 – 4.10 (q, 2H; CH₃CH₂O), 4.33 – 4.36 (t, 2H; CH₂O), 6.98 – 7.01 (dd, J = 2.44, 8.92 Hz, 1H; Ar-H), 7.09 – 7.10 (d, J = 2.32 Hz, 1H; Ar-H), 7.43 – 7.45 (m, 1H; Ar-H), 7.54 – 7.57 (d, J = 8.80 Hz, 1H; Ar-H), 7.62 – 7.64 (m, 1H; Ar-H), 7.77 – 7.79 (d, J = 7.88 Hz, 1H; Ar-H), 7.90 – 7.92 (d, J = 7.84 Hz, 1H; Ar-H); ¹³C-NMR (CDCl₃/TMS): δ 14.76, 45.82, 58.87, 64.11, 72.09, 103.58, 113.10, 115.91, 121.51, 122.30, 122.99, 126.26, 127.03, 128.08, 128.07, 133.84, 137.38, 137.55, 155.48; ESI-MS (m/z): 387 [M⁺+1];
HPLC Purity: 94.56%.

**132i** (i.e. **132**, R\(^1\)=H; R\(^2\)=Me; R\(^3\)=H):

Yield = 0.21g (50%); Syrupy mass; IR (KBr): 1335 & 1180 cm\(^{-1}\) (-SO\(_2\)-);

\(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 1.34 – 1.36 (d, J = 6.20 Hz, 3H; CH\(_3\)CH), 2.37 (s, 6H; N(CH\(_3\))\(_2\)), 2.51 – 2.55 (m, 1H; CH\(_2\)N(CH\(_3\))\(_2\)), 2.76 – 2.81 (m, 1H; CH\(_2\)N(CH\(_3\))\(_2\)), 4.61 – 4.65 (m, J = 6.20 Hz, 1H; CHCH\(_3\)), 7.24 – 7.26 (m, 1H; Ar-H), 7.35 – 7.46 (m, 2H; Ar-H), 7.63 – 7.69 (m, 3H; Ar-H), 7.79 – 7.81 (d, J = 7.84 Hz, 1H; Ar-H), 7.95 – 7.97 (d, J = 7.84 Hz, 1H; Ar-H);

\(^{13}\)C-NMR (CDCl\(_3\)/TMS): \(\delta\) 19.17, 46.36, 65.37, 78.68, 112.29, 120.29, 121.37, 122.32, 122.97, 126.25, 127.09, 127.63, 128.03, 131.42, 133.86, 136.43, 137.27; ESI-MS (m/z): 357 [M\(^{+}\)+1]; HPLC Purity: 98%.

**132m** (i.e. **132**, R\(^1\)=3-F, R\(^2\)=H, R\(^3\)=Me):

Yield = 0.20g (45%); M.R (\(^{0}\)C): 108.9 – 111.9; IR (KBr): 1336 & 1184 cm\(^{-1}\) (-SO\(_2\)-); \(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 1.15 – 1.17 (d, 3H; CH\(_3\)CH), 2.37 (s, 6H; N(CH\(_3\))\(_2\)), 3.04 – 3.09 (m, 1H; CHCH\(_3\)), 4.12 – 4.16 (dd, 1H; CH\(_2\)O), 4.32 – 4.36 (dd, 1H; CH\(_2\)O), 6.99 – 7.0 (m, J = 2.2 Hz, 1H; Ar-H), 7.39 – 7.40 (dd, 1H; Ar-H), 7.44 – 7.46 (m, 1H; Ar-H), 7.59 – 7.68 (m, 2H; Ar-H), 7.79 – 7.81 (d, J = 7.8 Hz, 1H; Ar-H), 7.87 – 7.89 (d, J = 7.8 Hz, 1H; Ar-H);

\(^{13}\)C-NMR (CDCl\(_3\)/TMS): \(\delta\) 10.77, 41.13, 58.72, 99.52, 111.72, 120.38, 121.30, 122.36, 122.88, 123.49, 126.81, 128.03, 131.33, 134.04, 136.82, 137.57, 160.54, 162.99; ESI-MS (m/z): 375 [M\(^{+}\)+1]; HPLC Purity: 96.72%.
132n (i.e. 132, R¹=2-OMe, R²=Me; R³=H):

Yield = 0.23g (50%); Syrupy mass; IR (KBr): 1335 & 1180 cm⁻¹ (-SO₂-);

\(^1\)H-NMR (CDCl₃/TMS): δ 1.34 – 1.36 (d, J = 6.20 Hz, 3H; CH₃CH), 2.37 (s, 6H; N(CH₃)₂), 2.51 – 2.55 (m, 1H; CH₂N(CH₃)₂), 2.76 – 2.81 (m, 1H; CH₂N(CH₃)₂), 3.85 (s, 3H; OCH₃), 4.61 – 4.65 (m, J = 6.20 Hz, 1H; CHCH₃), 6.98 – 7.01 (dd, J = 2.0, 8.8 Hz, 1H; Ar-H), 7.10 – 7.11 (d, J = 2.36 Hz, 1H; Ar-H), 7.44 – 7.45 (m, 1H ; Ar-H), 7.55 – 7.57 (d, J = 8.88 Hz, 1H; Ar-H), 7.63 – 7.67 (m, 1H; Ar-H), 7.78 – 7.80 (d, J = 7.8 Hz, 1H; Ar-H), 7.90 – 7.92 (d, J = 7.8 Hz, 1H; Ar-H); \(^1^3\)C-NMR (CDCl₃/TMS): δ 19.21, 46.44, 55.68, 65.43, 78.93, 102.86, 113.07, 115.35, 122.31, 122.39, 122.86, 126.33, 127.18, 128, 128.67, 133.80, 136.44, 137.39, 156.17; ESI-MS (m/z): 387 [M⁺+1]; HPLC Purity: 97.51%.

132o (i.e. 132, R¹=1-F, R²=R³=H):

Yield = 0.19g (45%); Syrupy mass; IR (KBr): 1334 & 1179 cm⁻¹ (-SO₂-);

\(^1\)H-NMR (CDCl₃/TMS): δ 2.37 (s, 6H; N(CH₃)₂), 2.75 – 2.78 (t, 2H; CH₂N(CH₃)₂), 4.38 – 4.41 (t, 2H; CH₂O), 6.72 – 6.73 (m, 1H; Ar-H), 7.1 – 7.21 (m, 2H; Ar-H), 7.31 – 7.33 (m, 1H; Ar-H), 7.55 – 7.57 (d, J = 8.88 Hz, 1H; Ar-H), 7.78 – 7.80 (d, J = 7.8 Hz, 1H; Ar-H), 7.90 – 7.92 (d, J = 7.8 Hz, 1H; Ar-H); \(^1^3\)C-NMR (CDCl₃/TMS): δ 45.55, 58.66, 73.16, 108.37, 109.10, 116.12, 121.15, 122.27, 123.44, 126.46, 127.27, 128.33, 132.03, 133.09, 134.11, 135.43, 137.22, 154.42, 156.92; ESI-MS (m/z): 361 [M⁺+1]; HPLC Purity: 92.42%.
**132p** (i.e. 132, R\(^1\)=2,3-Difluoro, R\(^2\)=R\(^3\)=H):

Yield = 0.18g (40%); Syrupy mass; IR (KBr): 1327 & 1176 cm\(^{-1}\) (-SO\(_2\)-);

\(^1\)H-NMR (CDCl\(_3\)/TMS): \(\delta\) 2.36 (s, 6H; N(CH\(_3\))\(_2\)), 2.73 – 2.76 (t, 2H; CH\(_2\)N(CH\(_3\))\(_2\)), 4.30 – 4.33 (t, 2H; CH\(_2\)O), 7.44 – 7.50 (m, 3H; Ar-H), 7.66 – 7.70 (m, 1H; Ar-H), 7.71 (m, 1H; Ar-H), 7.91 – 7.93 (m, 1H; Ar-H); ESI-MS (m/z): 379 [M\(^{+1}\)]; HPLC Purity: 90.27%.

**Preparation of 133 (General procedure):**

A mixture of potassium acetate (0.079g, 0.807 mmol), tetrakis triphenyl phosphine palladium (0.026g, 0.023 mmol), 129 (0.475 mmol) and DMA (10 mL) was heated to 120 – 125 °C for 4 hr, under nitrogen blanket. After completion (TLC), the reaction mixture was cooled to RT and poured into water (50 mL). The mixture was extracted into ethyl acetate (25 mL x 2), washed with brine solution (25 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure. The technical product was purified by flash column chromatography over silica gel using 1% methanol in chloroform.

**133a** (i.e. 133, R\(^1\)=3-Cl, R\(^2\)=R\(^3\)=H):

Yield = 0.07g (45%); Syrupy mass; For details, please see under Results & Discussion section.
Preparation of 134 (General procedure):

A mixture of potassium acetate (0.165g, 1.68 mmol), tetrakis triphenyl phosphine palladium (0.057g, 0.049 mmol), 131 (0.992 mmol) and DMA (5 mL) was heated to 120 – 125 °C & stirred for 3 hr under nitrogen blanket. After completion of the reaction (TLC), the mixture was cooled to RT and poured into water (50 mL). The mixture was extracted in ethyl acetate (25 mL x 2). The combined ethyl acetate layer was washed with brine solution (25 mL), dried over anhyd. sodium sulfate, filtered and concentrated under reduced pressure. The technical products were purified by flash column chromatography over silica gel using 0.5% methanol in chloroform.

134a (i.e. 134, R1=3-Cl, R2=R3=H):
Yield = 0.16g (50%); Syrupy mass; HPLC purity: 94.86%. (For details of spectral data, please see the Results & Discussion section).

134b (i.e. 134, R1=2-OMe, R2=R3=H):
Yield = 0.11g (35%); Syrupy mass; IR (KBr): 1494, 1235 cm⁻¹; ¹H-NMR (δ, ppm): 2.37 (s, 6H; N-(C₃H₃)₂), 2.77 – 2.80 (t, 2H; Me₂NCH₂), 3.85 (s, 3H; OCH₃), 4.08 – 4.13 (t, 2H; OCH₂), 5.24 (s, 2H; CH₂-N₁), 6.49 – 6.52 (m, 2H; Ar-H), 6.81 – 6.84 (dd, J = 2.48, 8.88 Hz, 1H; Ar-H), 7.04 – 7.06 (d, J = 8.96 Hz, 1H; Ar-H), 7.10 – 7.12 (m, 2H; Ar-H), 7.56 – 7.58 (m, 1H; Ar-H); ESI-MS (m/z): 323 [M⁺].