CHAPTER - 2

SYNTHESIS OF SUBSTITUTED-2,4-DIHYDRO [1,2,4]TRIAZOL-3-ONE.

2.1 INTRODUCTION:

1,2,4-Triazol-3-ones and their derivatives show a broad spectrum of biological activities [78] such as antivirals [79], antihypertensives [80], antifungals [81], antidepressants [82], fungicides [83] and herbicides [84]. Various pharmacological activities associated with 1,2,4-triazole-3-ones led to the discovery of several drugs such as nefazadone [85], IDPH-85184 [86] posaconazole [87] and apritipent [88]. The potential pharmacological importance of these compounds prompted us to synthesize some new 1,2,4-triazole-3-one derivatives bearing benzene methane sulfonamides.

2.2 LITERATURE SURVEY

Several synthetic methods have been reported in the literature for [1, 2, 4-triazol]-3-one and a few of them are discussed below:

Curtius and Heidenrich [89] reported the formation of 4-amino-1, 2, 4-triazole-3-one (2) on heating carboydrazide (1) with triethylorthioformate (Scheme-2.1).

\[
\begin{align*}
\text{H}_2\text{NHN}_2 \quad & \xrightarrow{\text{HC(OE)}_3} \quad \text{N}_2\text{NH} \text{N}\text{N} \\
\text{HN} \quad & \quad \text{NH}_2 \\
\text{NH}_2 \quad & \quad \text{NH}_2
\end{align*}
\]

..... Scheme - 2.1
Madding et. al. [90] reported that the reaction of substituted amide (3) with oxalyl chloride, followed by treatment with methyl carbazate, afforded the amidrazone 4, which on cyclization in the presence of sodium methoxide, gave substituted 1, 2, 4-triazole-3-one (5) (Scheme-2.2).

\[
\begin{align*}
R^1 \text{NH} & \quad \text{COCl}_2 \quad \begin{array}{c} \text{Cl} \end{array} \quad R^1 \text{N} \quad \text{Cl} \quad \text{N} \quad \text{H} \\
& \quad \text{O} \quad \text{O} \quad \text{O} \\
(3) & \quad \text{H}_2 \text{N} \quad \text{N} \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O} \\
(4) & \quad \text{R}^1 \text{N} \quad \text{N} \quad \text{H} \\
& \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O} \\
(5) & \quad \text{R}^1 \text{N} \quad \text{N} \quad \text{H} \\
& \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O}
\end{align*}
\]

...... Scheme - 2.2

Madding et. al. [90] described yet another method, i.e. condensation of substituted hydrazine derivative (6) with N-ethoxycarboxythiopropionamide (7) by heating which resulted in the formation of substituted-1, 2, 4-triazole-3-one (8) (Scheme-2.3).

\[
\begin{align*}
R^1 \text{H} \quad \text{N} \quad \text{NH}_2 & \quad + \quad \text{R}^2 \left[\begin{array}{c} \text{S} \end{array}\right] \text{O} \quad \text{CH}_3 \quad \text{CH}_3 \\
& \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O} \\
(6) & \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O} \\
(7) & \quad \text{R}^2 \text{N} \quad \text{N} \quad \text{H} \\
& \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O} \\
(8) & \quad \text{R}^1 \text{N} \quad \text{N} \quad \text{H} \\
& \quad \text{O} \quad \text{O} \\
& \quad \text{O} \quad \text{O}
\end{align*}
\]

...... Scheme - 2.3

Heerres et. al. [91] reported a new method by reacting substituted amine (9) with phenyl chloroformate followed by treatment with hydrazine hydrate to afford the hydrazine carboxamide 11 which on cyclisation with formamidine hydrochloride gave 1, 2, 4-triazole-3-one (12) (Scheme-2.4).
Lipken et al. [92] described a single step method for condensation of substituted acid hydrazides (13) with urea (14) in the presence of aq. KOH to yield 1, 2, 4-triazole-3-one (15) (Scheme-2.5) in low yields.

Kubota and Uda [93] reported that the reaction of substituted acid hydrazides (13) with substituted isocyanates to give substituted-semi carbazides 16, which on cyclisation in aq. NaOH gave 1, 2, 4-triazole-3-one (17) (Scheme-2.6).

In another method, triazole-3-one was prepared from triazole-3-thione (18). Thus, S-methylation of triazole-3-thione resulted in a thioether derivative (19), which on oxidation with m-chloroperbenzoic
acid afforded sulphone (20) [93&94]. The methyl triazole derivative on hydrolysis yielded 1, 2, 4-triazole-3-one (21) (Scheme-2.7).

![Reaction Scheme](image)

#### 2.3 PRESENT WORK

In the present work we have synthesized new substituted 1,2,4-triazole-3-one compounds bearing cyclicbenzenemethane sulfonamide functionality as potentially biologically active compounds.

#### 2.4 RESULTS AND DISCUSSIONS

4-(Cyclic-1-sulfonylmethyl)phenyl amine [95] (26a-c) (cyclic = pyrrolidine, morpholine and piperidine) is the starting material in the present work. It was prepared in the present work using a reported procedure [96]. Thus, commercially available 4-nitrobenzyl bromide/chloride (22) was reacted with sodium sulfite to obtain sodium 4-nitrobenzyl sulfonate (23) (Scheme-2.8).

![Reaction Scheme](image)

23, on treatment with thionylchloride yielded the corresponding 4-nitrobenzylsulfonyl chloride (24) (Scheme-2.9).
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24, on treatment with excess cyclic amine, gave corresponding 1-(4-nitrobenzylsulfonyl) pyrrolidine (25a) (i.e. 25, Cyclic amine = pyrrolidine) (Scheme-2.10).

25a (i.e. 25, Cyclic amine = pyrrolidine) was hydrogenated using palladium on carbon as a catalyst in methanol to yield the corresponding amino derivative, the known 4-((pyrrolidin-1-ylsulfonyl)methyl)aniline (26a) (i.e. 26, Cyclic amine = pyrrolidine) [95] (Scheme-2.11).

Treatment of 26a with 2-chloroacetyl chloride in dichloromethane containing triethylamine, followed by simple processing gave 2-chloro-N-[4-(pyrrolidine-1-sulfonylmethyl)-phenyl]-acetamide as nice crystals (27a) (i.e. 27, Cyclic amine = pyrrolidine) (Scheme-2.12). The structures of all the products were confirmed by
their spectral and analytical data. *(for spectral and analytical data, see the Experimental section).*

![Chemical Reaction Diagram]

**Scheme - 2.12**

The above reaction of the amine **26a** *(i.e. 26, Cyclic amine = pyrrolidine)* with chloroacetyl chloride was found to be a general one and has been extended to substituted amines **26b** and **26c**.

The chloroacetamide derivative **27a** *(i.e. 27, Cyclic amine = pyrrolidine)*, on reaction with substituted phenol in the presence of potassium carbonate in acetone, gave 2-phenoxy-N-[4-(pyrrolidine-1-sulfonylmethyl)-phenyl]-acetamide **(28a)** *(i.e. 28, Cyclic amine = pyrrolidine, R = H)* *(Scheme-2.13)* in 40% yield. The product was characterized by spectral methods. Thus, its IR spectrum *(Fig. 2.1)* in KBr showed a peak at 1709 cm$^{-1}$ (very strong, very sharp) as diagnostic absorption assignable to -C=O of –CONH group and broad peak at 3347 cm$^{-1}$ absorption assignable to –NH of –CONH group. Peaks at 1306 cm$^{-1}$ and 1143 cm$^{-1}$ absorptions assignable to asymmetric and symmetric stretching of –SO$_2$ group. Its $^1$H-NMR spectrum *(DMSO-d$_6$/TMS) (Fig.2.2)* showed signals at δ 1.70 -1.80 (m, 4H, pyrrolidine), 3.1-3.2 (m, 4H, pyrrolidine), 4.2 (s, 2H, -SO$_2$CH$_2$), 4.6 (s, 2H, -OCH$_2$), 6.90-7.1 (m, 3H, Ar-H), 7.2-7.4 (m, 4H, Ar-H), 7.6 (m, 2H Ar-H), 9.5 (br, s, 1H, -NH D$_2$O exchangeable). Its
mass spectrum (Fig. 2.3) showed its molecular ion peak at \( m/z \) 375 corresponding to molecular mass of 374 when recorded in the Q+1 mode.

\[ \text{Scheme - 2.13} \]

The above reaction of (27a) (i.e. 27, Cyclic amine = pyrrolidine) with phenol has been found to be a general one and has been extended to substituted phenols. The products obtained have been assigned structures 28b-i on the basis of their spectral data.

To avoid the two step procedure and low yield in phenol coupling reaction, alternatively phenoxyacetyl chloride [97] was prepared and reacted with the amine compound 26a. Thus, 26a was treated with phenoxyacetyl chloride in dichloromethane containing triethylamine giving 28a (i.e. 28, Cyclic amine = pyrrolidine, \( R = H \)) (Scheme-2.14) in 90-95 \% yield and identical, in all respects with the product obtained earlier. The phenoxyacetyl chloride was prepared by reacting phenol with chloroacetic acid in aq.NaOH solution to obtain phenoxyacetic acid, which was converted to the phenoxyacetyl chloride by treating with thionyl chloride in dichloromethane and catalytic amount of DMF.
Thiation of 28 was tried with various reagents like Lawesson’s reagent, H₂S, H₂S/HCl, Na₂S/H₂SO₄, P₂S₅, P₂S₅/pyridine etc. However, finally we succeeded with P₂S₅/K₂CO₃/EDC in the presence of a phase transfer catalyst tetrabutylammonium bromide (TBAB) [98] in dichloroethane solvent. Treatment of 28a (i.e. 28, Cyclic amine = pyrrolidine, R = H) in boiling dichloroethane containing P₂S₅/K₂CO₃ in the presence of a phase transfer catalyst (PTC) like TBAB (5 mol %) gave a crystalline product 2-phenoxy-N-(4-((pyrrolidin-1-ylsulfonyl)methyl)phenyl)ethanethioamide (30a) (i.e. 30, Cyclic amine = pyrrolidine, R = H) (Scheme - 2.15) different from the starting material. The structure of the compounds was established by IR, ¹H NMR and Mass. Thus, its IR (KBr) spectrum (Fig. 2.4) does not display absorption peak in the region 1780-1650 cm⁻¹ due to -C=O of -CONH group indicating absence of ketone group. The peaks at 1326 cm⁻¹ and 1137 cm⁻¹ characteristic absorptions assignable to asymmetric and symmetric stretching of –SO₂ group. Its ¹H-NMR spectrum (DMSO-d₆/TMS) (Fig. 2.5) showed signals at δ 1.70-1.80 (m, 4H, pyrrolidine), 2.90-3.10 (m, 4H, pyrrolidine), 4.2 (s, 2H, -SO₂CH₂), 4.6 (s, 2H, -OCH₂), 6.80-7.00 (m, 3H, Ar-H), 7.2-7.3 (m, 4H, Ar-H), 7.5-7.7 (m, 2H, Ar-H), 9.5 (br, s, 1H, -NH, D₂O exchangeable). Its mass spectrum (Fig. 2.6) showed its molecular ion peak at m/z
391.5 corresponding to molecular mass of 390 when recorded in the Q+1 mode.

\[ \text{Scheme - 2.15} \]

The above reaction of 28a has been found to be a general one and has been extended to substituted ketones. The products 30b-i obtained were assigned on the basis of their spectral data.

Compound 30a (i.e. 30, Cyclic amine = pyrrolidine, R = H) was converted to 2-phenoxy-N-[4-(pyrrolidine-1-sulfonylmethyl)-phenyl]-thioacetimidic acid methyl ester (31a) (i.e. 31, Cyclic amine = pyrrolidine, R = H) \textbf{(Scheme-2.16)} by reacting with methyl iodide in the presence of potassium carbonate in acetone at reflux and subsequent processing to give a white crystalline compound. The structure of 31a (i.e. 31, Cyclic amine = pyrrolidine, R = H) was assigned on the basis of its spectral data. Thus, its IR (KBr) spectrum \textbf{(Fig. 2.7)} showed the presence of an absorption peak at 1611 cm\(^{-1}\) due to the \(-\text{C}=\text{N}\) group. The peaks at 1324 cm\(^{-1}\) and 1146 cm\(^{-1}\) absorptions assignable due to asymmetric and symmetric stretching of \(-\text{SO}_2\) group. Its \(^1\)H-NMR spectrum (DMSO-d\(_6\)/TMS) \textbf{(Fig. 2.8)} showed signals at \(\delta\) 1.80 (m, 4H, \text{pyrrolidine}), 2.5 (s, 3H, -SCH\(_3\)), 3.0-3.2 (m, 4H, \text{pyrrolidine}), 4.20 (s, 2H, -SO\(_2\)CH\(_2\)), 4.67 (s, 2H, -OCH\(_2\)), 6.8-7.3 (m, 9H, Ar-H). Its mass spectrum \textbf{(Fig. 2.9)} showed its
molecular ion peak at m/z 405 corresponding to molecular mass of 404 when recorded in the Q+1 mode.

![Diagram](image)

**Scheme - 2.16**

The above methylation reaction of 30a has been found to be a general one and has been extended to substituted thio ketones. The products 31b-i obtained have been assigned on the basis of their spectral data.

Methyl carbazate (MCZ) is an important intermediate in organic synthesis and is widely used in synthesis of [1,2,4] triazolones. This was prepared from dimethyl carbonate and hydrazine hydrate by following the reported procedure of Rodefeld *et al.* [99].

Thus, 31a (**i.e.** 31, Cyclic amine = pyrrolidine, R = H) was reacted with methyl carbazate in DMF at 140 °C to obtain 32a (**i.e.** 32, Cyclic amine = pyrrolidine, R = H) (**Scheme-2.17**) in very good yield. The structure of 32a was established analytical and spectral data. The IR spectrum (KBr) (**Fig. 2.10**) showed a peak at 1693 cm⁻¹ (very strong, very sharp) as diagnostic absorption assignable to >C=O group of triazolone ring. The peaks at 1322 cm⁻¹ and 1126 cm⁻¹ absorptions assignable to asymmetric and symmetric stretching of –SO₂ group. Its ¹H-NMR spectrum (DMSO-d₆/TMS) (**Fig. 2.11**) showed signals at δ 1.70 (m, 4H, pyrrolidine), 2.9-3.0 (m, 4H, pyrrolidine),
4.30 (s, 2H, -SO₂CH₂), 4.67 (s, 2H, -OCH₂), 6.8-7.7 (m, 9H, four aryl protons of the sulfonamide phenyl ring and five aryl protons of the phenyl ring), 12.0 (bs, 1H, -NH, D₂O exchangeable). Its mass spectrum (Fig. 2.12) showed its molecular ion peak at m/z 415.3 corresponding to molecular mass of 414 when recorded in the Q+1 mode. Its ¹³C NMR (Fig. 2.13) spectrum showed peaks at δ 25.63, 47.97, 53.27, 61.38, 115.18, 121.89, 127.10, 129.84, 130.90, 132.30, 132.85, 143.16, 154.44, 157.54; Anal. Calcd for (C₂₀H₂₂N₄O₄S) requires: C, 57.96; H, 5.35; N, 13.52. Found: C, 56.96; H, 5.31; N, 13.42. Based on the above data, the compound was assigned structure 32a.

.. Scheme - 2.17

The above reaction of 31a has been found to be a general one and has been extended to other substituted derivatives. The products 32b-i obtained have been assigned structures on the basis of their spectral data.
There are two possible mechanistic pathways path-A and path-B for the conversion of 31a to 32a is depicted in the Scheme-2.18 and Scheme-2.19.

**PATH-A**

![Chemical reaction diagram for PATH-A](attachment:image.png)
PATH-B: The other plausible way of the reaction mechanism is given below in the Scheme-2.19

In order to avoid the hazardous thiation procedure and reduce the number of steps in the above synthesis, it was planned to treat 28a \((\text{i.e. } 28, \text{ Cyclic amine } = \text{ pyrrolidine, } R = \text{ H})\), with phosphorus oxychloride to get the corresponding 2-phenoxy-N-(4-((pyrrolidin-1-ylsulfonyl)methyl)phenyl)acetimidoyl chloride (29a) \((\text{i.e. } 29, \text{ Cyclic amine } = \text{ pyrrolidine, } R = \text{ H})\) which on heating with methyl carbazate, would yield 5-phenoxyethyl-4-[4-(pyrrolidine-1-sulfonylmethyl)-phenyl]-2,4-dihydro-[1,2,4]triazole-3-one (32a) \((\text{i.e. } 32, \text{ Cyclic amine } = \text{ pyrrolidine, } R = \text{ H})\). However, we were not successful in preparing the
imidoyl chloro derivative 29a (i.e. 29, Cyclic amine = pyrrolidine, R = H) and so this sequence of reactions could not be completed (Scheme 2.20).

All the above sequences of reactions are summarised in Scheme-2.21 and Scheme-2.22 respectively.
Scheme - 2.22
2.5. EXPERIMENTAL SECTION:

PREPARATION OF 32:

2.5.1. GENERAL PROCEDURE FOR THE PREPARATION OF 27(a-c):

Chloroacetyl chloride (0.012 mol) was added to a mixture of 26(a-c) (0.01 mol) and triethylamine (0.025 mol) in dichloromethane (100 mL) at 25-30 °C in about 30 min. The reaction mass was maintained at the same temperature 25-30 °C for 3 hours. The reaction mass was then quenched into water (100 mL) and organic phase was separated. The aqueous phase was extracted with dichloromethane (25 mL). The combined organic layer was dried over anh.Na₂SO₄ and the solvent was distilled off under reduced pressure. The crude product was recrystallized from suitable solvent to give pure 27(a-c).

27a: Cyclic amine = pyrrolidine, Yield: 2.8 gm (90 %), M.R: 132-131°C; IR (KBr, cm⁻¹) 3434, 3365, 1696, 1318, 1138; ¹H NMR (DMSO-d₆/TMS) δ 1.82 (m, 4H, pyrrolidine), 3.3 (m, 4H, pyrrolidine), 4.2 (s, 2H, -CH₂Cl), 4.4 (s, 2H, -SO₂CH₂), 7.2 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H), 9.6 (br, s, -NH, D₂O exchangeable); M⁺+1: 317; Anal.Calcd for (C₁₃H₁₇ClN₂O₃S) requires: C, 49.29; H, 5.41; N, 8.84; Found: C, 49.23; H, 5.39; N, 8.80.

27b: Cyclic amine = morpholine, Yield: 2.6 gm (79 %), M.R: 142-145 °C; IR (KBr, cm⁻¹) 3439, 3340, 1698, 1329, 1145; ¹H NMR (DMSO-d₆/TMS) δ 2.9 (m, 4H, morpholine), 3.6 (m, 4H, morpholine), 4.2 (s, 2H, -CH₂Cl), 4.4 (s, 2H, -SO₂CH₂), 7.2 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H),
9.6 (br, s, -NH, D$_2$O exchangeable); M$^+$+1: 333; Anal. Calcd for (C$_{13}$H$_{17}$ClN$_2$O$_4$S) requires: C, 46.92; H, 5.15; N, 8.42; Found: C, 46.90; H, 5.11; N, 8.39.

27c: Cyclic amine = piperidine, Yield: 3.1 gm (94 %), M.R: 128-130 ºC; IR (KBr, cm$^{-1}$) 3442, 1701, 1314, 1123; $^1$H NMR (DMSO-d$_6$/TMS) δ 1.45-1.57 (m, 6H, piperidine), 3.0 (m, 4H, piperidine), 4.1 (s, 2H, -CH$_2$Cl), 4.3 (s, 2H, -SO$_2$CH$_2$), 7.2 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H), 9.6 (br, s, -NH, D$_2$O exchangeable); M$^+$+1: 331; Anal. Calcd for (C$_{14}$H$_{19}$ClN$_2$O$_3$S) requires: C, 50.83; H, 5.79; N, 8.47; Found: C, 50.80; H, 5.74; N, 8.43.

2.5.2. GENERAL PROCEDURE FOR THE PREPARATION OF 28(a-i):

METHOD-A:

A mixture of 27(a-c) (0.01 mol), phenol (0.011 mol), K$_2$CO$_3$ (0.015 mol) and acetone (50 mL) was refluxed for 10 hours. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure, added water (25 mL), extracted with dichloromethane (50 mL). The organic layer was dried over anh.Na$_2$SO$_4$ and concentrated under reduced pressure. The crude compound was recrystallized from a suitable solvent to obtain pure 28(a-i).

METHOD-B:

Substituted phenoxyacetyl chloride (0.062 mol) was added to a mixture of 26(a-c) (0.05 mol), triethylamine (0.125 mol) in dichloroethane (250 mL) at 25-30 ºC in about 30 min. The reaction mixture was stirred at 25-30 ºC for 3 hours. The reaction mass was
then quenched into water (250 mL) and organic phase was separated. The aqueous phase was extracted with dichloroethane (125 mL). The combined organic layer was dried over anh.Na₂SO₄ and concentrated under reduced pressure. The residual crude product was recrystallized from methanol to yield pure 28(a-i).

**28a:** Cyclic amine = pyrrolidine, and R=H, Yield: 18.0 gm (97 %), M.R: 184-186 °C; IR (KBr,cm⁻¹) 3347, 1709, 1306, 1143; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.80 (m, 4H, pyrrolidine), 3.0-3.2 (m, 4H, pyrrolidine), 4.2 (s, 2H, -SO₂CH₂), 4.6 (s, 2H, -OCH₂), 6.9-7.1 (m, 3H, Ar-H), 7.2-7.4 (m, 2H, Ar-H), 7.6-7.8 (m, 4H, Ar-H), 9.5 (s, 1H, -NH, D₂O exchangable); M⁺+1: 375; Anal.Calcd for (C₁₉H₂₂N₂O₄S) requires: C, 60.94; H, 5.92; N, 7.48. Found: C, 60.84; H, 5.72; N, 7.40.

**28b:** Cyclic amine = pyrrolidine, and R=CH₃, Yield: 18.5 gm (96 %), M.R: 180-184 °C; IR (KBr,cm⁻¹) 3344, 1710, 1324, 1144; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.80 (m, 4H, pyrrolidine), 2.20 (s, 3H, -CH₃), 3.0-3.1 (m, 4H, pyrrolidine), 4.24 (s, 2H, -SO₂CH₂), 4.68 (s, 2H, -OCH₂), 6.8-7.0 (d, 2H, Ar-H), 7.2-7.4 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (s, 1H, -NH, D₂O exchangable); M⁺+1: 389; Anal.Calcd for (C₂₀H₂₄N₂O₄S) requires: C, 61.83; H, 6.23; N, 7.21. Found: C, 61.43; H, 6.13; N, 7.21.

**28c:** Cyclic amine = pyrrolidine, and R=Cl, Yield: 18.3 gm (90 %), M.R: 158-162 °C; IR (KBr, cm⁻¹) 3437, 1705, 1314, 1134; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.80 (m, 4H, pyrrolidine), 3.0-3.2 (m, 4H, pyrrolidine), 4.2 (s, 2H, -SO₂CH₂), 4.6 (s, 2H, -OCH₂), 6.90-7.00 (d, 2H, Ar-H), 7.0-7.3 (d, 2H, Ar-H), 7.6-7.8 (m, 4H, Ar-H), 9.5 (br, s, -NH,
D₂O exchangable); M⁺+1: 409; Anal.Calcd for (C₁₉H₂₁ClN₂O₄S) requires:
C, 55.81; H, 5.18; N, 6.85. Found: C, 55.71; H, 5.08; N, 6.82.

28d: Cyclic amine = morpholine and R=H, Yield: 18.0 gm (93 %), M.R:
190-192 °C; IR (KBr, cm⁻¹) 3440, 1710, 1337, 1114; ¹H NMR (DMSO-
d₆/TMS) δ 3.0-3.1 (m, 4H, morpholine), 3.4-3.6 (m, 4H, morpholine),
4.3 (s, 2H, -CH₂SO₂), 4.7 (s, 2H, -OCH₂), 6.90-7.00 (m, 3H, Ar-H),
7.0-7.2 (m, 2H, Ar-H), 7.6-7.8 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O
exchangable); M⁺+1: 391; Anal.Calcd for (C₁₉H₂₂N₂O₅S) requires: C,
58.45; H, 5.68; N, 7.17. Found: C, 58.35; H, 5.58; N, 7.15.

28e: Cyclic amine = morpholine and R=CH₃, Yield: 18.3 (91 %), M.R:
195-196 °C; IR (KBr, cm⁻¹) 3447, 1710, 1327, 1124; ¹H NMR (DMSO-
d₆/TMS) δ 2.3 (s, 3H, -CH₃), 3.0-3.1 (m, 4H, morpholine), 3.4-3.6 (m,
4H, morpholine), 4.4 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.8-6.9 (d,
2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 2H, Ar-H), 9.5 (br, s, -NH,
D₂O exchangable); M⁺+1: 405; Anal.Calcd for (C₂₀H₂₄N₂O₅S) requires:

28f: Cyclic amine = morpholine and R=Cl, Yield: 19.3 gm (91 %), M.R:
189-194 °C; IR (KBr, cm⁻¹) 3347, 1710, 1284, 1154; ¹H NMR (DMSO-
d₆/TMS) δ 3.05-3.15 (m, 4H, morpholine), 3.4-3.6 (m, 4H,
morpholine), 4.35 (s, 2H, -SO₂CH₂), 4.75 (s, 2H, -OCH₂), 6.9-7.0 (d,
2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH,
D₂O exchangable); M⁺+1: 425; Anal.Calcd for (C₁₉H₂₁ClN₂O₅S)
requires: C, 53.71; H, 4.98; N, 6.59. Found: C, 53.61; H, 4.88; N,
6.56.
28g: Cyclic amine = piperidine and R=H, Yield: 18.2 gm (94 %), M.R: 182-193 °C; IR (KBr, cm⁻¹) 3347, 1710, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.40-1.60 (m, 6H, piperidine), 3.0-3.2 (m, 4H, piperidine), 4.25 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.8-6.9 (m, 3H, Ar-H), 7.1-7.2 (m, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangable); M⁺+1: 389; Anal.Calcd for (C₂₀H₂₄N₂O₄S) requires: C, 61.83; H, 6.23; N, 7.21. Found: C, 61.71; H, 6.12; N, 7.11.

28h: Cyclic amine = piperidine and R=CH₃, Yield: 19.2 gm (96 %), M.R: 200-202 °C; IR (KBr, cm⁻¹) 3440, 1710, 1337, 1126; ¹H NMR (DMSO-d₆/TMS) δ 1.40-1.60 (m, 6H, piperidine), 2.3 (s, 3H, -CH₃), 3.0-3.2 (m, 4H, piperidine), 4.3 (s, 2H, -SO₂CH₂), 4.7 (s, 2H, -OCH₂), 6.8-6.9 (d, 2H, Ar-H), 7.0-7.2 (m, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangable); M⁺+1: 403; Anal.Calcd for (C₂₁H₂₆N₂O₄S) requires: C, 62.66; H, 6.51; N, 6.96. Found: C, 62.54; H, 6.42; N, 6.89.

28i: Cyclic amine = piperidine and R=Cl, Yield: 18.8 gm (89 %), M.R: 195-197 °C; IR (KBr, cm⁻¹) 3437,1710, 1317, 1126; ¹H NMR (DMSO-d₆/TMS) δ 1.40-1.60 (m, 6H, piperidine), 3.05-3.21 (m, 4H, piperidine), 4.3 (s, 2H, -SO₂CH₂), 4.2 (s, 2H, -OCH₂), 6.8-6.9 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (d, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangable); M⁺+1: 423; Anal.Calcd for (C₂₀H₂₃ClN₂O₄S) (422.93): C, 56.80; H, 5.48; N, 6.62. Found: C, 56.75; H, 5.43; N, 6.59.

2.5.3. GENERAL PROCEDURE FOR THE PREPARATION OF 30(a-i):

K₂CO₃ (0.019 mol), P₂S₅ (0.014 mol), TBAB (0.05 g) and dichloroethane (50 mL) were heated to 80-85 °C and maintained for 45
min. The reaction mixture was cooled to 40 °C and 28(a-i) (0.013 mol) was added. The reaction mixture was again heated to reflux temperature for 45 min and filtered at 80-85 °C. The filtrate was concentrated under reduced pressure. The crude product was recrystallized from ethanol to get 30(a-i).

30a: Cyclic amine = pyrrolidine and R=H, Yield: 3.6 gm (72 %), M.R: 110-115 °C; IR (KBr, cm⁻¹) 3318, 1326, 1137; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.80 (m, 4H, pyrrolidine), 3.0-3.2 (m, 4H, pyrrolidine), 4.2 (s, 2H, -SO₂CH₂), 4.6 (s, 2H, -OCH₂), 6.8-6.9 (m, 3H, Ar-H), 7.0-7.2 (m, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangeable); M⁺+1: 391; Anal.Calcd for (C₁₉H₂₂N₂O₃S₂) requires: C, 58.44; H, 5.68; N, 7.17. Found: C, 58.42; H, 5.56; N, 7.10.

30b: Cyclic amine = pyrrolidine and R=CH₃, Yield: 3.7 gm (73 %), M.R: 174-178 °C; IR (KBr, cm⁻¹) 3318, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.80 (m, 4H, pyrrolidine), 2.3 (s, 3H, -CH₃), 3.0-3.1 (m, 4H, pyrrolidine), 4.24 (s, 2H, -SO₂CH₂), 4.68 (s, 2H, -OCH₂), 6.80-6.9 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangeable); M⁺+1: 405; Anal.Calcd for (C₂₀H₂₄N₂O₃S₂) requires: C, 59.38; H, 5.98; N, 6.92. Found: C, 59.28; H, 5.86; N, 6.90.

30c: Cyclic amine = pyrrolidine and R=Cl, Yield: 4.0 gm (73 %), M.R: 164-168 °C; IR (KBr, cm⁻¹) 3318, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.80 (m, 4H, pyrrolidine), 3.0-3.2 (m, 4H, pyrrolidine), 4.25 (s, 2H, -SO₂CH₂), 4.63 (s, 2H, -OCH₂), 6.8-6.9 (d,
2H, **Ar-H**), 7.0-7.2 (d, 2H, **Ar-H**), 7.4-7.8 (m, 4H, **Ar-H**), 9.5 (br, s, -NH D$_2$O exchangable); M$^+$+1: 425; Anal. Calcd for (C$_{19}$H$_{21}$ClN$_2$O$_3$S$_2$) requires: C, 53.70; H, 4.98; N, 6.59. Found: C, 53.68; H, 4.93; N, 6.61.

**30d:** Cyclic amine = morpholine and R=H, Yield: 3.4 gm (65 %), M.R: 190-193 °C; IR (KBr, cm$^{-1}$) 3318, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) δ 3.0-3.1 (m, 4H, morpholine), 3.4-3.6 (m, 4H, morpholine), 4.30 (s, 2H, -SO$_2$CH$_2$), 4.68 (s, 2H, -OCH$_2$), 6.9-7.0 (m, 3H, **Ar-H**), 7.2-7.4 (m, 2H, **Ar-H**), 7.4-7.8 (m, 4H, **Ar-H**), 9.5 (br, s, -NH, D$_2$O exchangable); M$^+$+1: 407; Anal. Calcd for (C$_{19}$H$_{22}$N$_2$O$_4$S$_2$) requires: C, 56.14; H, 5.45; N, 6.89. Found: C, 56.12; H, 5.49; N, 6.71.

**30e:** Cyclic amine = morpholine and R=CH$_3$, Yield: 3.8 gm (68 %), M.R: 175-179 °C; IR (KBr, cm$^{-1}$) 3318, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) δ 2.2 (s, 3H, -CH$_3$), 3.0-3.1 (m, 4H, morpholine), 3.4-3.6 (m, 4H, morpholine), 4.4 (s, 2H, -SO$_2$CH$_2$), 4.8 (s, 2H, -OCH$_2$), 6.8 (d, 2H, **Ar-H**), 7.2-7.4 (d, 2H, **Ar-H**), 7.4-7.6 (m, 4H, **Ar-H**), 9.5 (br, s, -NH, D$_2$O exchangable); M$^+$+1: 421; Anal. Calcd for (C$_{20}$H$_{24}$N$_2$O$_4$S$_2$) requires: C, 57.12; H, 5.75; N, 6.66. Found: C, 57.10; H, 5.65; N, 6.60.

**30f:** Cyclic amine = morpholine and R=Cl, Yield: 4.0 gm (68 %), M.R: 175-179 °C; IR (KBr, cm$^{-1}$) 3318, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) δ 3.05-3.15 (m, 4H, morpholine), 3.0-3.2 (m, 4H, morpholine), 4.35 (s, 2H, -SO$_2$CH$_2$), 4.75 (s, 2H, -OCH$_2$), 6.8-6.9 (d, 2H, **Ar-H**), 7.0-7.2 (d, 4H, **Ar-H**), 7.4-7.6 (m, 4H, **Ar-H**), 9.5 (br, s, -NH, D$_2$O exchangable); M$^+$+1: 442; Anal. Calcd for (C$_{19}$H$_{21}$ClN$_2$O$_3$S$_2$)
requires: C, 51.75; H, 4.80; N, 6.35. Found: C, 51.65; H, 4.78; N, 6.33.

**30g:** Cyclic amine = piperidine and R=H, Yield: 3.2 gm (60 %), M.R: 178-170 °C; IR (KBr, cm⁻¹) 3318, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.4-1.6 (m, 6H, piperidine), 3.0-3.2 (m, 4H, piperidine), 4.25 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.8-7.0 (m, 3H, Ar-H), 7.0-7.2 (m, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangable); M⁺+1: 405. Anal.Calcd for (C₂₀H₂₄N₂O₃S₂) requires: C, 59.38; H, 5.98; N, 6.92. Found: C, 59.48; H, 5.88; N, 6.97.

**30h:** Cyclic amine = piperidine and R=CH₃, Yield: 3.4 gm (62 %), M.R: 179-184 °C; IR (KBr, cm⁻¹) 3318, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.4-1.6 (m, 6H, piperidine), 2.3 (s, 3H, -CH₃) 3.0-3.1 (m, 4H, piperidine), 4.3 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.8-6.9 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangable); M⁺+1: 419; Anal.Calcd for (C₂₁H₂₆N₂O₃S₂) requires: C, 60.26; H, 6.26; N, 6.69. Found: C, 60.26; H, 6.26; N, 6.69.

**30i:** Cyclic amine = piperidine and R=Cl, Yield: 3.8 gm (65 %), M.R: 174-178 °C; IR (KBr, cm⁻¹) 3318, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.4-1.6 (m, 6H, piperidine), 3.0-3.1 (m, 4H, piperidine), 4.30 (s, 2H, -SO₂CH₂), 4.80 (s, 2H, -OCH₂), 6.8 (d, 2H, Ar-H), 7.0-7.2 (m, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 9.5 (br, s, -NH, D₂O exchangable); M⁺+1: 439; Anal.Calcd for (C₂₀H₂₃ClN₂O₃S₂) requires: C, 54.72; H, 5.28; N, 6.38. Found: C, 54.69; H, 5.30; N, 6.41.
2.5.4. GENERAL PROCEDURE FOR THE PREPARATION OF 31(a-i):

K$_2$CO$_3$ (0.015 mol), 30(a-i) (0.01 mol) methyl iodide (0.012 mol) and acetone (50 mL) were heated to reflux and maintained for 6 hours. The reaction mixture was cooled to 25-30 °C and filtered. The filtrate was distilled under reduced pressure and added water (25 mL) then extracted with ethyl acetate (50 mL). The organic layer dried over anh.Na$_2$SO$_4$ and concentrated completely under vaccum. To the crude residue was added diisopropylether (20 mL) and cooled to 25-30 °C. The precipitated solid was filtered to get pure 31(a-i).

31a: Cyclic amine = pyrrolidine and R=H, Yield: 3.2 gm (80 %), M.R: 92-95 °C; IR (KBr, cm$^{-1}$) 3433, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) $\delta$ 1.60-1.70 (m, 4H, pyrrolidine), 2.50 (s, 3H, -SCH$_3$), 3.0-3.1 (m, 4H, pyrrolidine), 4.3 (s, 2H, -SO$_2$CH$_2$), 4.6 (s, 2H, -OCH$_2$), 6.8-6.9 (m, 3H, Ar-H), 7.0-7.2 (m, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M$^+$+1: 405; Anal.Calcd for (C$_{20}$H$_{24}$N$_2$O$_3$S$_2$) requires: C, 59.38; H, 5.98; N, 6.92. Found: C, 59.48; H, 5.50; N, 6.82.

31b: Cyclic amine = pyrrolidine and R=CH$_3$, Yield: 3.4 gm (82 %), M.R: 116-118 °C; IR (KBr, cm$^{-1}$) 3433, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) $\delta$ 1.60-1.70 (m, 4H, pyrrolidine), 2.23 (s, 3H, CH$_3$), 2.5 (s, 3H, -SCH$_3$), 3.0-3.1 (m, 4H, pyrrolidine), 4.3 (s, 2H, -SO$_2$CH$_2$), 4.6 (s, 2H, -OCH$_2$), 6.8-6.9 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M$^+$+1: 419; Anal.Calcd for (C$_{21}$H$_{26}$N$_2$O$_3$S$_2$) requires: C, 60.26; H, 6.26; N, 6.69. Found: C, 60.16; H, 6.28; N, 6.70.

31c: Cyclic amine = pyrrolidine and R=Cl, Yield: 3.3 gm (79 %), m.p: 97-99 °C; IR (KBr, cm$^{-1}$) 3433, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) $\delta$
1.60-1.70 (m, 4H, pyrrolidine), 2.50 (s, 3H, -SCH₃), 3.0-3.1 (m, 4H, pyrrolidine), 4.4 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.8-6.9 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M⁺+1: 439; Anal.Calcd for (C₂₀H₂₃ClN₂O₃S₂) requires: C, 54.72; H, 5.28; N, 6.38. Found: C, 54.69; H, 5.30; N, 6.48.

31d: Cyclic amine = morpholine and R=H, Yield: 2.7 gm (65 %), M.R: 124-126 °C; IR (KBr, cm⁻¹) 3433, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 2.55 (s, 3H, -SCH₃) 3.0-3.1 (m, 4H, morpholine), 3.4-3.6 (m, 4H, morpholine), 4.30 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.8-6.9 (m, 3H, Ar-H), 7.0-7.2 (m, 2H, Ar-H) 7.4-7.6 (m, 4H, Ar-H); M⁺+1: 421; Anal.Calcd for (C₂₀H₂₄N₂O₄S₂) requires: C, 57.12; H, 5.75; N, 6.66. Found: C, 57.11; H, 5.65; N, 6.60.

31e. Cyclic amine = morpholine and R=CH₃, Yield: 3.4 gm (81 %), m.p: 140-143 °C; IR (KBr, cm⁻¹) 3433, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 2.24 (s, 3H, -CH₃), 2.55 (s, 3H, -SCH₃), 3.0-3.1 (m, 4H, morpholine), 3.41-3.65 (m, 4H, morpholine), 4.30 (s, 2H, -SO₂CH₂), 4.73 (s, 2H, -OCH₂), 6.8-6.9 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M⁺+1: 435; Anal.Calcd for (C₂₁H₂₆N₂O₄S₂) requires: C, 58.04; H, 6.03; N, 6.45. Found: C, 58.00; H, 6.00; N, 6.45.

31f: Cyclic amine = morpholine and R=Cl, Yield: 3.5 gm (78 %), M.R: 132-135 °C; IR (KBr, cm⁻¹) 3433, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 2.55 (s, 3H, -SCH₃), 3.0-3.1 (m, 4H, morpholine), 3.4-3.6 (m, 4H, morpholine), 4.30 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M⁺+1:
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456; Anal.Calcd for (C_{20}H_{23}ClN_{2}O_{4}S_{2}) requires: C, 52.80; H, 5.10; N, 6.16. Found: C, 52.78; H, 5.12; N, 6.10.

31g: Cyclic amine = piperidine and R=H, Yield: 3.4 gm (84 %), M.R: 141-143 °C; IR (KBr, cm^{-1}) 3433, 1284, 1154; ^1H NMR (DMSO-d_{6}/TMS) δ 1.4-1.6 (m, 6H, piperidine), 2.56 (s, 3H, -SCH_{3}), 3.0-3.1 (m, 4H, piperidine), 4.20 (s, 2H, -SO_{2}CH_{2}), 4.8 (s, 2H, -OCH_{2}), 6.7-6.8 (m, 3H, Ar-H), 7.0-7.2 (m, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M^+1: 419; Anal.Calcd for (C_{21}H_{26}N_{2}O_{3}S_{2}) requires: C, 60.26; H, 6.26; N, 6.69. Found: C, 60.23; H, 6.16; N, 6.65.

31h: Cyclic amine = piperidine and R=CH_{3}, Yield: 3.1 gm (73 %), M.R: 120-126 °C; IR (KBr, cm^{-1}) 3433, 1284, 1154; ^1H NMR (DMSO-d_{6}/TMS) δ 1.4-1.6 (m, 6H, piperidine), 2.26 (s, 3H, -CH_{3}), 2.56 (s, 3H, -SCH_{3}), 3.0-3.1 (m, 4H, piperidine), 4.25 (s, 2H, -SO_{2}CH_{2}), 4.80 (s, 2H, -OCH_{2}), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M^+1: 433; Anal.Calcd for (C_{22}H_{28}N_{2}O_{3}S_{2}) requires: C, 61.08; H, 6.52; N, 6.48. Found: C, 61.08; H, 6.57; N, 6.45.

31i: Cyclic amine = piperidine and R=Cl, Yield: 3.7 gm (83 %), M.R: 103-106 °C; IR (KBr, cm^{-1}) 3433, 1284, 1154; ^1H NMR (DMSO-d_{6}/TMS) δ 1.4-1.6 (m, 6H, piperidine), 2.56 (s, 3H, -SCH_{3}), 3.0-3.2 (m, 4H, piperidine), 4.30 (s, 2H, -SO_{2}CH_{2}), 4.80 (s, 2H, -OCH_{2}), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.1 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H); M^+1: 454; Anal.Calcd for (C_{21}H_{25}ClN_{2}O_{3}S_{2}) requires: C, 55.68; H, 5.56; N, 6.18. Found: C, 55.58; H, 5.59; N, 6.23.
2.5.5. GENERAL PROCEDURE FOR THE PREPARATION OF 32(a-i):

31(a-i) (0.01 mol) methyl carbazate (0.012 mol) and dimethylformamide (35 mL) were heated to reflux and maintained for 6 hours. The reaction mixture was cooled to 25-30 °C and quenched into ice cold water (100 mL). Separated crystals were filtered and recrystallized from acetonitrile to get pure 32(a-i).

32a: Cyclic amine = pyrrolidine and R=H, Yield: 2.5 gm (61 %); M.R: 245-250 °C; IR (KBr, cm⁻¹) 3427, 3179, 1693, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.70 (m, 4H, pyrrolidine), 3.0-3.1 (m, 4H, pyrrolidine), 4.4 (s, 2H, -SO₂CH₂), 4.9 (s, 2H, -OCH₂), 6.8-7.0 (m, 3H, Ar-H), 7.20 -7.30 (m, 2H, Ar-H), 7.4 -7.6 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D₂O exchangeable); M⁺+1: 414; ¹³C NMR δ 25.63, 47.97, 53.27, 61.38, 115.18, 121.89, 127.10, 129.84, 130.9, 132.3, 132.85, 143.16, 154.44, 157.54; Anal.Calcd for (C₂₀H₂₂N₄O₄S) requires: C, 57.96; H, 5.35; N, 13.52. Found: C, 56.96; H, 5.31; N, 13.42.

32b: Cyclic amine = pyrrolidine and R=CH₃, Yield: 2.9 gm (70 %), M.R: 238-240 °C; IR (KBr, cm⁻¹) 3427, 3179, 1693, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 1.60-1.70 (m, 4H, pyrrolidine), 2.2 (s, 3H, -CH₃), 3.1-3.2 (m, 4H, pyrrolidine), 4.4 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.2 (d, 2H, Ar-H), 7.4-7.5 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D₂O exchangeable); M⁺+1: 429; ¹³C NMR δ 20.41, 25.62, 47.98, 53.24, 61.54, 115.15, 127.05, 130.15, 130.7, 130.86, 132.01, 132.87, 143.25, 154.43, 155.45; Anal.Calcd for (C₂₁H₂₄N₄O₄S)
requires: C, 58.86; H, 5.65; N, 13.07. Found: C, 58.66; H, 5.61; N, 13.00.

32c: Cyclic amine = pyrrolidine and R=Cl, Yield: 3.1 gm (72%), M.R: 246-248 °C; IR (KBr, cm\(^{-1}\)) 3427, 3179, 1693, 1284, 1154; \(^1\)H NMR (DMSO-d\(_6\)/TMS) \(\delta\) 1.6-1.7 (m, 4H, pyrrolidine), 3.0-3.1 (m, 4H, pyrrolidine), 4.47 (s, 2H, -SO\(_2\)CH\(_2\)), 4.89 (s, 2H, -OCH\(_2\)), 6.8-6.9 (d, 2H, Ar-H), 7.25-7.41 (d, 2H, Ar-H), 7.5-7.6 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D\(_2\)O exchangable); M\(^+\)+1: 449; \(^{13}\)C NMR \(\delta\) 25.63, 47, 97, 53.21, 61.82, 117.09, 125.69, 127.11, 129.60, 130.94, 132.05, 132.79, 142.91, 154.42, 156.40; Anal.Calcd for (C\(_{20}\)H\(_{21}\)ClN\(_4\)O\(_4\)S) requires: C, 53.51; H, 4.72; N, 12.48. Found: C, 53.56; H, 4.62; N, 12.40.

32d: Cyclic amine = morpholine, and R=H, Yield: 2.8 gm (66%), M.R: 235-240 °C; IR (KBr, cm\(^{-1}\)) 3427, 3179, 1693, 1284, 1154; \(^1\)H NMR (DMSO-d\(_6\)/TMS) \(\delta\) 3.0-3.1 (m, 4H, morpholine), 3.40-3.65 (m, 4H, morpholine), 4.3 (s, 2H, -SO\(_2\)CH\(_2\)), 4.9 (s, 2H, -OCH\(_2\)), 6.8-6.9 (m, 3H, Ar-H), 7.20-7.30 (m, 2H, Ar-H), 7.5-7.6 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D\(_2\)O exchangable); M\(^+\)+1: 431; \(^{13}\)C NMR \(\delta\) 45.21, 53.27, 61.38, 65.41, 115.18, 121.89, 127.10, 129.84, 130.90, 132.03, 132.85, 143.16, 154.44, 157.54; Anal.Calcd for (C\(_{20}\)H\(_{22}\)N\(_4\)O\(_5\)S) requires: C, 55.80; H, 5.15; N, 13.02. Found: C, 55.62; H, 5.10; N, 13.12.

32e: Cyclic amine = morpholine, and R=CH\(_3\), Yield: 2.5 gm (59%), M.R: 225-230 °C; IR (KBr, cm\(^{-1}\)) 3427, 3179, 1693, 1284, 1154; \(^1\)H NMR (DMSO-d\(_6\)/TMS) \(\delta\) 2.2 (s, 3H, -CH\(_3\)), 3.0-3.1 (m, 4H, morpholine), 3.5-3.6 (m, 4H, morpholine), 4.3 (s, 2H, -SO\(_2\)CH\(_2\)), 4.8
(s, 2H, -OCH₂), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.1 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D₂O exchangeable); M⁺+1: 445; ¹³C NMR δ 20.71, 45.61, 53.72, 61.54, 65.42, 115.11, 127.05, 130.15, 130.70, 130.86, 132.01, 132.87, 143.25, 154.43, 155.45; Anal. Calcd for (C₂₁H₂₄N₄O₅S) requires: C, 56.74; H, 5.44; N, 12.60. Found: C, 56.64; H, 5.34; N, 12.50.

32f: Cyclic amine = morpholine, and R=Cl, Yield: 3.0 gm (67 %), M.R: 239-241 °C; IR (KBr, cm⁻¹) 3427, 3179, 1693, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) δ 3.0-3.1 (m, 4H, morpholine), 3.5-3.6 (m, 4H, morpholine), 4.3 (s, 2H, -SO₂CH₂), 4.8 (s, 2H, -OCH₂), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.1 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D₂O exchangeable); M⁺+1: 465; ¹³C NMR δ 45.21, 53.27, 61.38, 65.41, 115.18, 121.89, 127.10, 129.84, 130.90, 132.03, 132.85, 143.16, 154.44, 157.54; Anal. Calcd for (C₂₀H₂₁ClN₄O₅S) requires: C, 51.67; H, 4.55; N, 12.05. Found: C, 51.65; H, 4.52; N, 12.03.

32g: Cyclic amine = piperidine and R=H, Yield: 2.6 gm (63 %), M.R: 250-260 °C; IR (KBr, cm⁻¹) 3427, 3179, 1693, 1284, 1154; ¹H NMR (DMSO-d₆/TMS) 1.40-1.60 (m, 6H, piperidine), 3.00-3.10 (m, 4H, piperidine), 4.40 (s, 2H, -SO₂CH₂), 4.80 (s, 2H, -OCH₂), 6.72-6.84 (m, 3H, Ar-H), 7.0-7.2 (m, 2H, Ar-H), 7.4 -7.6 (m, 4H, Ar-H), 12.0 (s, 1H, -NH, D₂O exchangeable); M⁺+1: 429; ¹³C NMR δ 24.21, 24.52, 47.00, 53.28, 61.40, 115.21, 121.89, 127.10, 129.84, 130.90, 132.03, 132.85, 143.16, 154.44, 157.54; Anal. Calcd for (C₂₁H₂₄N₄O₄S) requires: C, 58.86; H, 5.65; N, 13.07. Found: C, 58.76; H, 5.75; N, 13.00.
**32h:** Cyclic amine = piperidine and R=CH$_3$, Yield: 2.8 gm (64 %), M.R: 226-230 °C; IR (KBr, cm$^{-1}$) 3427, 3179, 1693, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) 1.40-1.60 (m, 6H, piperidine), 3.00-3.20 (m, 4H, piperidine), 4.30 (s, 2H, -SO$_2$CH$_2$), 4.80 (s, 2H, -OCH$_2$), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.1 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D$_2$O exchangable); M$^+$+1: 443; $^{13}$C NMR δ 24.21, 24.52, 47.05, 53.24, 61.54, 115.15, 127.05, 130.15, 130.70, 130.86, 132.01, 132.87, 143.25, 154.43, 155.45; Anal.Calcd for (C$_{22}$H$_{26}$N$_4$O$_4$S) requires: C, 59.71; H, 5.92; N, 12.66. Found: C, 59.61; H, 5.82; N, 12.60.

**32i:** Cyclic amine = piperidine and R=Cl, Yield: 3.3 gm (72 %), M.R: 262-266 °C; IR (KBr, cm$^{-1}$) 3427, 3179, 1693, 1284, 1154; $^1$H NMR (DMSO-d$_6$/TMS) 1.40-1.60 (m, 6H, piperidine), 3.00-3.20 (m, 4H, piperidine), 4.20 (s, 2H, -SO$_2$CH$_2$), 4.80 (s, 2H, -OCH$_2$), 6.7-6.8 (d, 2H, Ar-H), 7.0-7.1 (d, 2H, Ar-H), 7.4-7.6 (m, 4H, Ar-H), 12.0 (br, s, 1H, -NH, D$_2$O exchangable); M$^+$+1: 463; $^{13}$C NMR δ 24.21, 24.52, 47.05, 53.21, 61.84, 117.05, 125.67, 127.11, 129.60 130.95, 132.79, 142.91, 154.42, 156.40; Anal.Calcd for (C$_{21}$H$_{23}$ClN$_4$O$_4$S) requires: C, 54.48; H, 5.01; N, 12.10. Found: C, 54.40; H, 5.00; N, 12.10.