CHAPTER-5
CHAPTER – 5

REACTION OF QUINAZOLINONE ACIDHYDRAZIDES WITH VARIOUS CARBONYL FUNCTIONAL GROUPS

5.1 INTRODUCTION:

2-Mercapto-3-phenyl-3H-quinazolin-4-one derivatives have diverse types of biological activities associated with them [66]. The types of biological activity sometimes depend on the group(s) present in the molecule, particularly at C-2 and N-3 positions. They are important as antiparkinson [67], antitubercular [68] and antibacterial [69]. The heteroalkyl derivatives are known to exhibit increased pharmacological activities [70]. The heteroalkyl derivatives are known to exhibit increased pharmacological activities compared to the corresponding individual heterocycle or 2-heterylquinazolinones.

5.2 Literature Survey:

Gursoy et. al. reported [71] the synthesis of (3-ethyl-4-oxo-3,4-dihydroquinazolin-2-ylsulfanyl)acetic acid (3,5-dimethyl-4-oxothiazolidin-2-ylidene)hydrazide (102) and 2-(3-ethyl-4-oxo-3,4-dihydroquinazolin-2-ylsulfanyl)-N-(3-methyl-5-methyllimino-2-oxopyrrolidin-1-yl)acetamide (103) by the cyclization of (3-ethyl-4-oxo-3,4-dihydroquinazolin-2-ylsulfanyl)acetic acid N’-[mercapto-methylamino)methyl]hydrazide (101) with ethyl 2–bromo propionate in the presence of anhydrous sodium acetate in ethanol …(Scheme – 5.1).
El-Feky et.al. reported \[72\] the synthesis of 2-[4-(benzylideneamino)-5-mercapto-4H-[1,2,4]triazol-3-ylmethylsulfanyl]-3-phenyl-3H-quinazolin-4-one \([106]\). In this method, the hydrazide \([104]\) was reacted with hydrazine hydrate and carbon disulphide to obtain 2-(4-amino-5-mercapto-4H-[1,2,4]triazol-3-ylmethylsulfanyl)-3-phenyl-3H-quinazolin-4-one \([105]\), which were then reacted with benzaldehydes to convert them into the Schiff’s base \([106]\) \((\text{Scheme – 5.2})\).
Alagarsamy et al. reported [73] the synthesis of 1-methyl-4-phenyl-4H-[1,2,4]triazolo[4,3-a]quinazolin-5-one (109). These researchers reacted 26 with dimethyl sulphate in alkaline medium to obtain 2-methylsulfanyl-3-phenyl-3H-quinazolin-4-one (107). The latter was treated with hydrazine hydrate yielding 2-hydrazinyl-3-phenylquinazolin-4(3H)-one (108) which on heating acetic acid gave 109. (Scheme – 5.3).

Muthuswamy et al. reported [74] the condensation of anthranilic acid (4) with aryl isothiocyanates yielding 2-mercapto-3-arylinzolinone-4-one (26) which on stirring with iodine in aq. NaOH containing KI resulted in the formation of 2, 2-dithiois[3-aryl-4(3H)quinazolinones (110). (Scheme – 5.4).
5.3 Present Work:

It is obvious from the brief literature survey given above that not much systematic work seems to have been done on the reactions of (4-oxo-3-phenyl-3,4-dihydroquinazolin-2-ylsulfanyl)-acetic acid hydrazide. Condensation of the latter with carbonyl derivatives will yield a variety of products which may be new chemical entities having useful biological properties.

5.4 Results and Discussions:

(4-Oxo-3-phenyl-3,4-dihydroquinazolin-2-ylsulfanyl)acetic acid hydrazide (104) was on treatment with benzaldehyde (111) (i.e. 18, R=H) in ethanol under refluxing conditions for 1 h resulted in the formation of (4-oxo-3-phenyl-3,4-dihydroquinazolin-2-ylsulfanyl)acetic acid benzylidenehydrazide (112). The structure of the product was assigned based on spectral and analytical data. Thus, its IR (KBr) showed a very strong, sharp peak at 1660 cm\(^{-1}\) assignable to the carbonyl groups. Its \(^1\)H NMR (DMSO-\(d_6\)) showed signals at \(\delta\) 4.00 (s, 2H, \(-\text{CH}_2\)), 7.14-8.07 (m, 14H, aryl protons), 9.72 (br, s, 1H, D\(_2\)O exchangeable protons –NH). Its LCMS spectrum showed the molecular ion peak at 416 corresponding to a
molecular mass of 414 when recorded in the Q+2 mode. **(Scheme – 5.5).**

![Scheme 5.5](image)

The above reaction of **104** with **111** was found to be a general one and extended to other benzaldehydes such as **111b** (i.e. **111**, R=-NO$_2$) & **111c** (i.e. **111**, R=-OCH$_3$).

**112** (i.e. **112**, R=H) on treatment with iodobenzene diaacetate (IBD) in chloroform under refluxing conditions for 2 h yielded 3-phenyl-2-(5-phenyl-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-3H-quinazolin-4-one (**113**) (i.e. **113**, R=H). The structure of the product was assigned on the basis of its spectral and analytical data. Thus, its IR (KBr) (**Fig-5.1**) showed a very strong, sharp peak at 1660 cm$^{-1}$ assignable to the two carbonyl groups. Its $^1$H NMR (DMSO-$d_6$) (**Fig-5.2**) showed signals at $\delta$ 4.00 (s, 2H, -CH$_2$), 7.14-8.07 (m, 14H, aryl protons). The $^{13}$C-NMR (**Fig-5.4**) spectrum (DMSO-$d_6$/TMS) $\delta$ 34.84, 119.47, 125.11, 126.03, 126.19, 126.46, 128.02, 129.39, 129.51, 129.97, 134.78, 135.80, 133.00, 134.40, 135.69, 138.90, 147.05, 156.70, 160.60, 166.66, 180.78. Its LCMS (**Fig-5.3**) spectrum showed the molecular ion peak at 413 corresponding to a molecular mass of 412 when recorded in the Q+1 mode. **(Scheme – 5.6).**
104 on treatment with benzoic acid (114, R=H). in POCl₃ under refluxing conditions at 120 °C for 2 h gave 113 (113, i.e. 113, R=H). The product obtained has been compared in its identity (i.e. m.p., m.m.p., and Co-TLC) with that of the same product obtained in the earlier route (112 → 113). Scheme – 5.7

The above reaction of 104 with 114 was found to be a general one and was extended to other benzaldehydes such as 114b (i.e. 114, R=NO₂) & 114c (i.e. 114, R=OCH₃).

104 on treatment with acetylacetone in ethanol under refluxing conditions for 2 h yielded 2-[2-(3,5-dimethyl pyrazol-1-yl)-2-oxo-ethylsulfany]-3-phenyl-3H-quinazolin-4-one (115). The structure of the product was assigned on the basis of its spectral and analytical data. Thus,
its IR (KBr) (Fig. 5.5) showed a very broad band in the region 3200 cm\(^{-1}\) (due to the two \(-\text{NH}\)- stretching vibrations and a sharp, strong peak at 1670 cm\(^{-1}\) due to the two \(-\text{CO}\)- stretchings due to the two carbonyl groups. Its \(^1\)H NMR (DMSO-\(d_6\)) (Fig. 5.6) showed signals at \(\delta\) 2.24 (s, 3H, \(-\text{CH}_3\)), 2.68 (s, 3H, \(-\text{CH}_3\)), 4.00 (s, 2H, \(-\text{CH}_2\)), 6.27 (s, 1H, \(=\text{CH}\)), 7.14-8.11 (m, 9H, aryl protons). Its LCMS spectrum (Fig. 5.7) showed the molecular ion peak at 392 corresponding to a molecular mass of 390 when recorded in the Q+2 mode.

\(\text{104}\) on treatment with isatin (116) in ethanol under refluxing conditions for 2 h gave (4-oxo-3-phenyl-3,4-dihydroquinoxalin-2-ylsulfanyl)acetic acid (2-oxo-1,2-dihydro indol-3-ylidene)hydrazide (117). The structure of the product was assigned based on its spectral and analytical data. Thus, its IR (KBr) (Fig. 5.8) showed a very broad band in the region 3200-3100 cm\(^{-1}\) (due to the two \(-\text{NH}\)- stretching vibrations and a sharp, strong peak at 1680 cm\(^{-1}\) (strong due to \(-\text{CO}\)- stretching) due to the two carbonyl groups. Its \(^1\)H NMR (DMSO-\(d_6\)) (Fig. 5.9) showed signals at \(\delta\) 4.00 (s, 2H, \(-\text{CH}_2\)), 6.5-8.26 (m, 15H, aryl protons) 10.42 (br, s, 1H, D\(_2\)O exchangeable protons \(-\text{NH}\)), 11.60 (br, s, 2H, D\(_2\)O exchangeable protons \(-\text{NH}\)), The \(^{13}\)C-NMR (Fig. 5.10) spectrum (DMSO-\(d_6\)/TMS) \(\delta\) 34.84, 109.46, 115.33, 116.81, 117.51, 120.89, 123.10, 127.08, 127.23, 128.02, 128.82,
129.18, 129.42, 129.54, 130.75, 135.27, 136.74, 139.25, 142.51, 144.46, 146.95, 155.09, 160.42, 165.67. Its LCMS (Fig-5.11) spectrum showed the molecular ion peak at 357 corresponding to a molecular mass of 355 when recorded in the Q+2 mode. (Scheme-5.9).

\[\text{Scheme - 5.9}\]

\textbf{104} on treatment with acetophenone (118) in ethanol under refluxing conditions for 3 h gave (4-oxo-3-phenyl-3,4-dihydroquinazolin-2-ylsulfanyl)acetic acid (1-phenyl ethylidene)hydrazide (119). The structure of the product was assigned based on its spectral and analytical data. Thus, its IR (KBr) showed a very broad band in the region 3200-3100 cm\(^{-1}\) (due to the \(-\text{NH-}\) stretching vibrations and a sharp, strong peak at 1670 cm\(^{-1}\) due to the two \(-\text{CO-}\) stretchings. Its \(^{1}\text{H NMR}\) (DMSO-\(d_6\)) showed signals at \(\delta\) 2.28 (s, 3H, -CH\(_3\)), 4.00 (s, 2H, -CH\(_2\)-), 4.46 (s, 1H, D\(_2\)O exchangeable protons \(-\text{NH-}\)) 7.2-8.00 (m, 14H, \textbf{aryl protons}) and at 12.85 (br, s, 2H, D\(_2\)O exchangeable protons \(-\text{NH-}\)). Its LCMS spectrum showed the molecular ion peak at 429 corresponding to a molecular mass of 428 when recorded in the Q+1 mode. (Scheme-5.10).
104 on treatment with pthalic anhydride (120) in ethanol under refluxing conditions for 3 h gave 2-[2-(4-oxo-3-phenyl-3,4-dihydro quinazolin-2-ylsulfanyl)acetyl]-2,3-dihydro phthalazine-1,4-dione (121). The structure of the product was assigned based on its spectral and analytical data. Thus, its IR (KBr) showed a very broad band in the region 3200-3100 cm\(^{-1}\) (due to -NH- stretching vibrations a sharp, strong peak at 1670 cm\(^{-1}\) (strong due to –CO- stretching) due to the carbonyl group as diagnostic absorptions. Its \(^1\)H NMR (DMSO-\(d_6\)) showed signals at \(\delta\) 4.00 (s, 2H, -CH\(_2\)-), 7.15-8.11 (m, 13H, aryl protons) and at 11.85 (br, s, 1H, D\(_2\)O exchangeable protons –NH-) Its LCMS spectrum showed the molecular ion peak at 473 corresponding to a molecular mass of 472 when recorded in the Q+1 mode. (Scheme–5.11).
Reaction of 104 with phenylisothiocyanate (25) in ethanol under refluxing conditions for 1 h resulted in the formation of N-(2-(4-oxo-3-phenyl-3,4-dihydroquinazolin-2-ylthiol0acetyl)-N-phenylcarbamohydrasonothioic acid (122). The structure of the product was assigned on the basis of its spectral and analytical data. Thus, its IR (KBr) showed a broad medium peak at ≈1670 cm\(^{-1}\) due to the carbonyl group as diagnostic absorption. Thus, its IR (KBr) showed a very strong, sharp peak at 1660 cm\(^{-1}\) assignable to the two carbonyl groups put together. Its \(^1\)H NMR (DMSO-\(d_6\)) showed signals at δ 4.00 (s, 2H, \(\text{-CH}_2\)), 7.14-8.07 (m, 14H, aryl protons), 9.51 (br, 1H, D\(_2\)O exchangeable proton –\(\text{SH}\)) 9.72 (br, s, 1H, D\(_2\)O exchangeable protons –\(\text{NH}\)), 10.32 (br, s, 1H, D\(_2\)O exchangeable protons –\(\text{NH-N=}\)), Its LCMS spectrum showed the molecular ion peak at 461 corresponding to a molecular mass of 460 when recorded in the Q+1 mode. (Scheme–5.12).

Cyclization of 122 in acidic medium yielded 3-phenyl-2-(5-phenylamino-[1,3,4]thiadiazol-2-ylmethysulfanyl)-3H-quinazolin-4-one (123). The structure of the product was assigned on the basis of its spectral and analytical data. Thus, its IR in KBr showed absorptions at 3200-3100 cm\(^{-1}\) (broad, strong, NH-stretching) and strong, sharp peak at 1660 cm\(^{-1}\)
due to the carbonyl group (Fig. 5.11). Its $^1$H NMR (DMSO-$d_6$) showed signals at $\delta$ 4.00 (s, 2H, -CH$_2$-), 7.14-8.07 (m, 14H, aryl protons), 9.72 (br, s, 1H, D$_2$O exchangeable protons -NH). Its LCMS spectrum showed the molecular ion peak at 444 corresponding to a molecular mass of 443 when recorded in the Q+1 mode. ...(Scheme–5.13).

![Scheme – 5.13](image)

The reaction involves cyclization of 122 in 2 N NaOH yielded 2-(5-mercapto-4-phenyl-4H-[1,2,4]triazol-3-ylmethylsulfanyl)-3-phenyl-3H-quinazolin-4-one (124). The structure of the product was assigned on the basis of its spectral and analytical data. Thus, its IR in KBr (Fig. 5.12) showed absorptions at 3200 cm$^{-1}$ (broad, strong, NH-stretching) and strong, sharp peak at 1660 cm$^{-1}$ due to the carbonyl group. Its $^1$H NMR (DMSO-$d_6$) (Fig. 5.13) showed signals at $\delta$ 4.00 (s, 2H, -CH$_2$-), 7.14-8.07 (m, 14H, aryl protons), 9.51 (br, s, 1H, D$_2$O exchangeable protons -SH). The $^{13}$C-NMR (Fig. 5.15) spectrum (DMSO-$d_6$/TMS) $\delta$ 34.84, 119.47, 125.11, 126.03, 126.19, 126.46, 128.02, 129.39, 129.51, 129.97, 134.78, 135.80, 133.00, 134.40, 135.69, 138.90, 147.05, 156.70, 160.60, 166.66, 180.78. Its LCMS (Fig. 5.14) spectrum showed the molecular ion peak at 444 corresponding to a molecular mass of 443 when recorded in the Q+1 mode ...(Scheme–5.14).
The mechanism probably involves formation of the intermediate tautomer anion 122a in basic medium from the condensation product 122 which cyclizes to the anion 122B that is converted into the sodium salt 122C with the loss of a molecule of water followed by protonation yielding 124..(Scheme–5.15).
Treatment of 104 with CS₂ in ethanol in the presence of KOH gave 2-(5-mercapto-[1,3,4]oxadiazol-2-ylmethylsulfanyl)-3-phenyl-3H-quinazolin-4-one (125). The structure of the product was assigned on the basis of its spectral and analytical data. Thus, its IR in KBr showed absorptions at 3200-3100 cm⁻¹ (broad, strong, NH-stretching) and strong, sharp peak at 1660 cm⁻¹ due to the carbonyl group. Its ¹H NMR (DMSO-ｄ₆) showed signals at δ 4.00 (s, 2H, -CH₂⁻), 7.14-8.07 (m, 9H, aryI protons), 11.64 (br, s, 1H, D₂O exchangeable protons -SH). Its LCMS spectrum showed the molecular ion peak at 369 corresponding to a molecular mass of 368 when recorded in the Q+1 mode ...(Scheme–5.16).

![Scheme 5.16](image-url)

124 could also be prepared alternatively by reaction of 125 with aniline (126) in xylene under refluxing conditions for 3 h. The structure of the product was assigned based on its identity (i.e. m.p., m.m.p, Co-TLC) with that of the same compound obtained earlier in the route 122 → 124..(Scheme–5.17).

![Scheme 5.17](image-url)
The conversion of 125 to 124 seems to follow the mechanism given in Scheme -5.17.

The mechanism probably involves the nucleophilic attack of aniline (126) on the carbon atom α to the thiol group of the oxadiazole ring (125) resulting in the formation of the intermediate 125A which cyclises intramolecularly to form the intermediates 125B and 125C, that lose a water molecule to form 124. (Scheme–5.18).
Scheme 5.19

Scheme 5.20
Scheme 5.21

PTSA/DMF/\(\Delta\)
1-2 h

Ethanol / \(\Delta\)
2 h

\(\text{Scheme 5.21}\)
Experimental Section

Preparation of 112a-112c from 104 and 111a-111c: A mixture of 104 (3.26 gms, 10 mM), 111 (3.56 gms, 20 mM), and ethanol (40 mL) was refluxed for 2 h. At the end of this period, the reaction mixture was poured into ice-cold water (50 mL). The separated solid was filtered, washed with water (2×10 mL) and dried to obtain 112a. (i.e. 112, X=H) : Yield : 2.95 gms (75%) ; M.P. 180-183 °C ; For spectral data, please see the section on result and Discussion.

112b: Yield : 2.90 gms (70%); M.P. 170-172 °C; IR (KBr): 3400 cm⁻¹ (broad, medium –NH-), 1667 cm⁻¹ (strong, sharp, -CO-). ¹H-NMR (400 MHz, DMSO d₆/TMS): δ 4.00 (s, 2H, -CH₂-), 7.14-8.07 (m, 13H, aryl protons), 9.72 (br, s, 1H, D₂O exchangeable protons –NH) ; MS : m/z 460 (M+H)+.

112c: Yield : 3.10 gms (80%); M.P. 168-170 °C; IR (KBr): 3400 cm⁻¹ (broad, medium, –NH-), 1667 cm⁻¹ (strong, sharp, -CO-). ¹H-NMR (400 MHz, DMSO d₆/TMS): δ 3.80 (s, 3H, OCH₃), 4.00 (s, 2H, -CH₂-), 7.14-8.07 (m, 13H, aryl protons), 9.72 (br, s, 1H, D₂O exchangeable protons –NH) ; MS : m/z 445 (M+H)+.

Preparation of 113a-113c from 112a-112c: A mixture of 112a-112c (10 mM), iodobenzene diacetate (2 mM) and chloroform (40 mL) was refluxed for 4 h on a water bath. At the end of this period, the reaction mixture was cooled to room temperature. Excess of solvent was distilled off and separated solid was filtered, washed with chloroform (10 mL) and dried to obtain 113a-113c.
113a. (i.e. 113, X=H) : Yield : 3.15 gms (73%) ; M.P. 165-168 °C ; For spectral data, please see Results and Discussion Section.

113b: Yield : 2.90 gms (70%); M.P. 155-158 °C; IR (KBr): 3400 cm⁻¹ (broad, medium −NH−), 1667 cm⁻¹ (strong, sharp, -CO-). ¹H-NMR (400 MHz, DMSO d₆/TMS): δ 4.00 (s, 2H, -CH₂-), 7.14-8.07 (m, 13H, aryl protons) ; MS : m/z 457 (M+H)⁺.

113c: Yield : 3.20 gms (80%); M.P. 161-163 °C; IR (KBr): 3400 cm⁻¹ (broad, medium −NH−), 1667 cm⁻¹ (strong, sharp, -CO-). ¹H-NMR (400 MHz, DMSO d₆/TMS): δ 3.80 (s, 3H, -OC₃H₃), 4.00 (s, 2H, -CH₂-), 7.14-8.07 (m, 13H, aryl protons) ; m/z 443 (M+H)⁺.

Preparation of 113 from 104 and 114: A mixture of 104 (1.52 gms, 10 mM), 114 (10 mM) and POCl₃ (10 mL) was refluxed at 120 °C for 2 h. At the end of this period, the excess POCl₃ was distilled off and the residue diluted with ice-cold water (50 mL). The mixture was neutralized with sodium bicarbonate solution. The separated solid was filtered, washed with water (20 ml) and dried to obtain 113a-113c.

113a. (i.e. 113, X=H) Yield = 1.13 gms (88%)
113b. (i.e. 113, X=-NO₂) Yield = 0.90 gms (72%)
113c. (i.e. 113, X=-OCH₃) Yield = 1.01 gms (76%)

Preparation of 115 from 104: A mixture of 104 (1.52 gms, 10 mM), acetylacetone (10 mM) and ethanol (25 mL) was refluxed for 2h. At the end of the period, the reaction mixture was poured into ice-cold water (25 mL).
The separated solid was filtered, washed with water (25 mL) and dried. To obtained **115**.

**115**: Yield : 3.20 gms (77%); M.P. 193-195 °C; IR (KBr): 3200-3100 cm⁻¹ (broad, medium -NH-), 1667 cm⁻¹ (strong, sharp, -CO-). ¹H-NMR (400 MHz, DMSO d₆/TMS): δ 2.24 (s, 3H, -CH₃), 2.68 (s, 3H, -CH₃), 6.27 (s, 1H, =CH⁻), 7.14-8.11 (m, 9H, **aryl protons**); MS : m/z 391 (M+H)⁺.

**Preparation of 117 from 104 and 116**: A mixture of **104** (3.42 gms, 10 Mm), **116** (1.47 gms, 10 mM) and ethanol (20 mL) was refluxed for 2 h. At the end of this period, the reaction mixture was poured into ice cold water (25 mL). The separated solid was filtered, washed with water (25 mL) and dried to obtain **117**.

**117**: Yield : 3.10 gms (74%); M.P. 212-215 °C; IR (KBr): 3200-3100 cm⁻¹ (broad, medium -NH-), 1670 cm⁻¹ (strong, sharp, -CO-). ¹H-NMR (400 MHz, DMSO d₆/TMS): δ 4.00 (s, 2H, -CH₂⁻), 7.2-8.10 (m, 13H, **aryl protons**), 9.72 (br, s, 2H, D₂O exchangeable proton -NH⁻) ; The **¹³C-NMR (Fig-5.11)** spectrum (DMSO-d₆/TMS) δ 34.84, 109.46, 115.33, 116.81, 117.51, 120.89, 123.10, 127.08, 127.23, 128.02, 128.82, 129.18, 129.42, 129.54, 130.75, 135.27, 136.74, 139.25, 142.51, 144.46, 146.95, 155.09, 160.42, 165.67. MS : m/z 457 (M+2)⁺.

**Preparation of 119 from 104 and 118**: A mixture of **104** (3.42 gms, 10 mM), **118** (10 mM) and ethanol (20 mL) was refluxed for 3 h. At the end of the period, the reaction mixture was poured into ice cold water (25 mL). The
separated solid was filtered, washed with water (25 mL) and dried. The crude product was recrystallized from hot ethanol (20 mL) to get pure 119.

**119:** Yield : 3.20 gms (77%); M.P. 231-233 °C; IR (KBr): 3200-3100 cm\(^{-1}\) (broad, medium –NH-), 1670 cm\(^{-1}\) (strong, sharp, -CO-). \(^1\)H-NMR (400 MHz, DMSO \(d_6/TMS\)): \(\delta\) 2.28 (s, 3H, -CH\(_3\)), 4.00 (s, 2H, -CH\(_2\)-) 4.46 (s, 1H, D\(_2\)O exchangeable proton –NH-), 7.2-8.00 (m, 14H, **aryl protons**) and 12.85 (br, s, 2H, D\(_2\)O exchangeable proton –N\(\text{H}\)-); MS : m/z 429 (M+H)^+.

**Preparation of 121 from 104 and 120:** A mixture of 104 (10 mM), 120 (10 mM) and xylene (20 mL) was refluxed for 1 h at 150 °C. At the end of this period, the reaction mixture was concentrated to volume on the rotavapour. The separated solid was filtered, washed and dried to obtain 121.

**121:** Yield : 3.10 gms (73%); M.P. 194-197 °C; IR (KBr): 3200-3100 cm\(^{-1}\) (broad, medium –NH-), 1670 cm\(^{-1}\) (strong, sharp, -CO-). \(^1\)H-NMR (400 MHz, DMSO \(d_6/TMS\)): \(\delta\) 4.00 (s, 2H, -CH\(_2\)-) 7.15-8.11 (m, 13H, **aryl protons**) and 11.85 (br, s, 1H, D\(_2\)O exchangeable proton –N\(\text{H}\)-); MS : m/z 473 (M+H)^+.

**Preparation of 122 from 104 and 25:** A mixture of 104 (10 mM), 25 (10 mM) and ethanol (25 mL) was refluxed for 1 h. At the end of this period, the reaction mixture was poured into ice-cold water (25 mL) and stirred for 10 mins. The separated solid was filtered, washed with water (25 mL) and dried to obtain 122.

**122:** Yield : 3.18 gms (76%); M.P. 228-234 °C; IR (KBr): 3200-3100 cm\(^{-1}\) (broad, medium –NH-), 1670 cm\(^{-1}\) (strong, sharp, -CO-). \(^1\)H-NMR (400 MHz, DMSO \(d_6/TMS\)): \(\delta\) 4.00 (s, 2H, -CH\(_2\)-), 7.14-8.07 (m, 14H, **arylprotons**),
Preparation of 124 from 122: A solution of 122 (10 mM) in 2N NaOH (25 mL) was refluxed at 100 °C for 1h. At the end of this period, the reaction mixture was cooled to RT and neutralized with conc. HCl (5 mL). The separated solid was filtered, washed with water (20 mL) and dried to obtain 124.

Preparation of 124 from 125 and 126: A mixture of 125 (10 mM), 126 (10 mM) and xylene (25 mL) was refluxed for 3h. At the end of this period, the excess of xylene was distilled off under reduced pressure. The separated solid was filtered, washed with hexane and dried to obtain 124.

Preparation of 125 from 104: A mixture of 104 (10 Mm, 3.26 gms) CS₂ (20 mL), (KOH 3 gms) and ethanol (50 mL) was refluxed for 3 h. At the end of this period the reaction mixture cooled to RT and neutralized with acetic acid (3 mL). The separated solid was filtered, washed with water and dried to obtain 125.

125: Yield : 2.96 gms (78%); M.P. 154-157 °C; IR (KBr): 3200-3100 cm⁻¹ (broad, medium –NH-), 1660 cm⁻¹ (strong, sharp, -CO-). ¹H-NMR (400 MHz, DMSO d₆/TMS): δ 4.00 (s, 2H, -CH₂-), 7.14-8.07 (m, 9H, arylprotons), 11.64 (br, s, 1H, D₂O exchangeable protons -SH); MS : m/z 369 (M+1)⁺.

Alternate preparation of 124 from 125 and 126: A mixture of 125 (10 mM, 3.68), 126 (10 mM) and xylene (30 mL) was refluxed for 3 h. At the end of this period. The excess of xylene was distilled off under reduced pressure.
pressure. The separated solid was filtered, washed with hexane and dried to obtain 124.

124: Yield : 3.40 gms (80%); M.P. 161-163 °C; IR (KBr): 3200-3100 cm⁻¹ (broad, medium -NH-), 1667 cm⁻¹ (strong, sharp, -CO-). 1H-NMR (400 MHz, DMSO d₆/TMS): δ 4.00 (s, 2H, -CH₂-), 7.14-8.07 (m, 14H, arylprotons), 11.64 (br, s, 1H, D₂O exchangeable protons -SH); MS : m/z 445 (M+2)⁺.