Microwave assisted synthesis and antimicrobial screening of fused triazoles

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Abstract

In the present study, a series of *N*-{4-[(4-amino-5-sulfanyl-4*H*-1,2,4-triazol-3-yl)methyl]-1,3-thiazol-2-yl}-2-substituted amide derivatives (**1a-d**) were synthesized in good yields and characterized. The compounds were evaluated for their preliminary *in vitro* antibacterial activity against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* and *Salmonella typhosa* and then were screened for antitubercular activity against *Mycobacterium tuberculosis* H37 Rv strain by the MABA assay method. The antibacterial data of the tested compounds indicated that compounds **6b**, **6c**, **8a**, **8b** and **8c** showed better activity against bacteria compared to reference drugs. The *in vitro* antitubercular activity reports of compounds tested against *M. tuberculosis* strain H37 Rv showed better activity by **8a**, **8b** and **8c**.

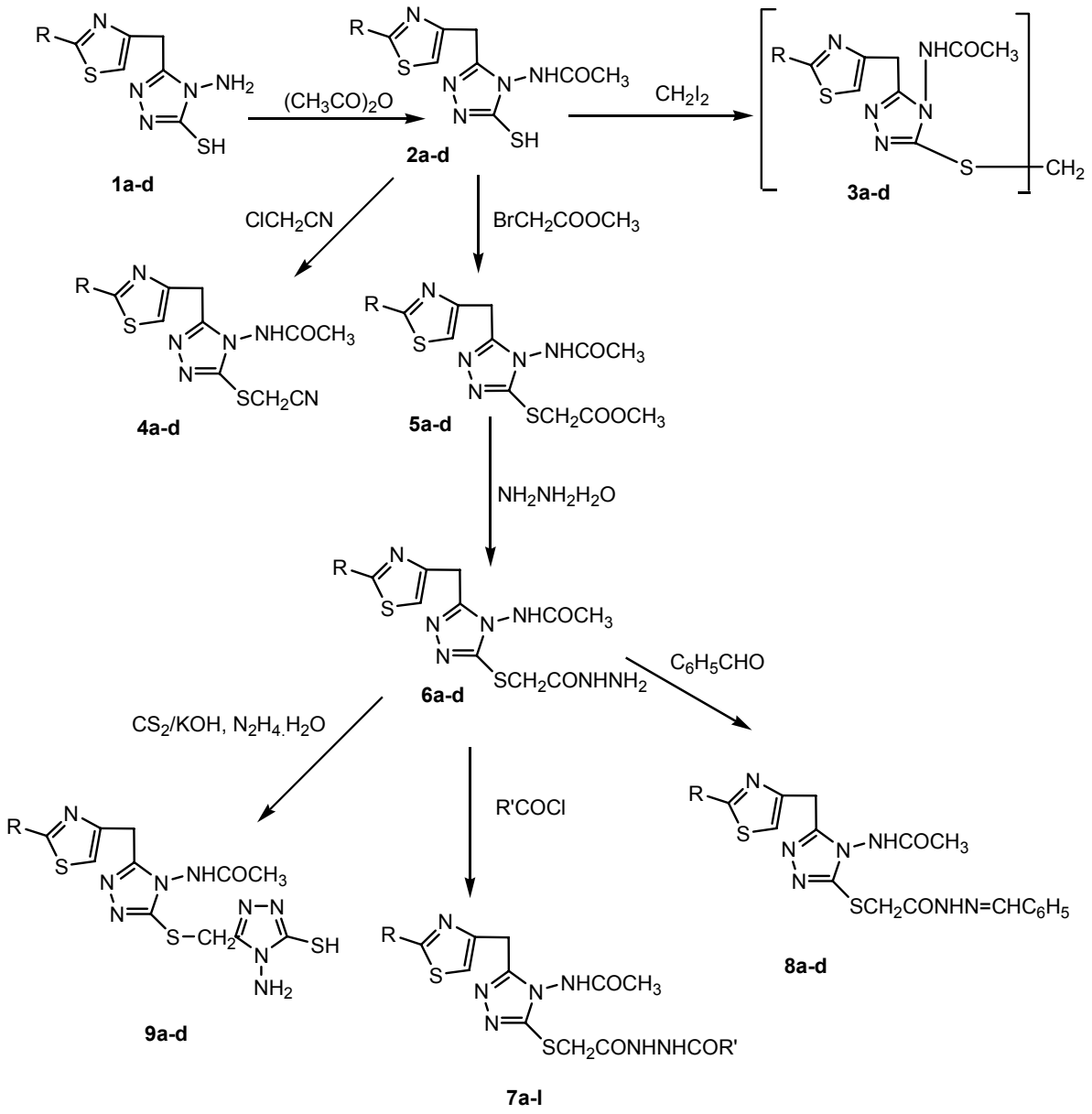
Keywords: Thiazole, triazole, antimicrobial, antimycobacterial

Introduction

Tuberculosis remains the major cause of death over the world and the emergence of multi-drug resistant tuberculosis has made the condition most alarming. Up to 4% of all tuberculosis cases worldwide are resistant to more than one antitubercular drug because of incomplete or partial therapy.[1] Therefore, there is an urgent demand for a new class of antitubercular agent with a different mode of action and it has led medicinal chemists to explore a wide variety of chemical structures. While reports[2-4] are available stating the emergence of thiazoles and/or triazoles as potent antitubercular agents, appreciation of these findings, coupled with our observation that, today, the trend in antimycobacterial drug design[5-7] is to join together two or three molecules having different sites or mechanisms of action, initiated our construction of compounds

containing both the thiazole and triazole ring systems in the same matrix to serve as a new scaffold towards the development of novel antimycobacterial agents.

Microwave assisted reactions[8] using dry media[9] have attracted much interest because of the simplicity in operation, greater selectivity and rapid synthesis of a variety of heterocyclic compounds.[10] Thus, it was thought worthwhile to synthesize the title compounds using a Green Route, the MORE (Microwave Organic Reaction Enhancement) method.



Scheme 1

Compounds **1a-d** were synthesized according to the literature.[11] Compounds **1a-d**, adsorbed on acidic alumina[12], were treated with acetic anhydride at 0 °C to yield **2a-d**. The transformed

compounds **2a-d** on treatment with diiodomethane in the presence of strong alkali, *i.e*. sodium hydroxide, gave **3a-d**.

The title compounds **2a-d** were treated with chloroacetonitrile, which on neutralization with sodium carbonate gave precipitates of compounds **4a-d**.

Further, compounds **2a-d**, when treated with methyl bromoacetate under basic conditions produced **5a-d**. Chemical transformation of **5a-d** to **6a-d** was achieved by treating the former with hydrazine hydrate, while compounds **6a-d**, on treatment with appropriate acid chlorides, furnished **7a-l**.

Schiff bases, the condensation products of **8a-d**, were synthesized by treating **6a-d** with benzaldehyde and confirmed by the absence of the hydrazide NH triplet.

Compounds **6a-d** were converted to thiocarbazate salts by treatment with carbon di sulphide and potassium hydroxide, which on treatment with hydrazine hydrate gave **9a-d**. The NMR spectra confirmed formation of triazole derivatives from the hydrazides by the presence of the sulfhydryl proton at 12.5 δ.

Table 1. Substituents for compounds **1a-d, 2a-d, 3a-d, 4a-d, 5a-d, 6a-d, 7a-l, 8a-d** and **9a-d**

COMP	R	R”	COMP	R	R”
1a	$NHCOCH_2Cl$		**6c**	$NHCOC_6H_5$	
1b	$NHCOCH_3$		**6d**	$NHCH_2CH_2COOH$	
1c	$NHCOC_6H_5$		**7a**	$NHCOCH_2Cl$	CH_3
1d	$NHCH_2CH_2COOH$		**7b**	$NHCOCH_3$	CH_3
2a	$NHCOCH_2Cl$		**7c**	$NHCOC_6H_5$	CH_3
2b	$NHCOCH_3$		**7d**	$NHCH_2CH_2COOH$	CH_3
2c	$NHCOC_6H_5$		**7e**	$NHCOCH_2Cl$	C_6H_5
2d	$NHCH_2CH_2COOH$		**7f**	$NHCOCH_3$	C_6H_5
3a	$NHCOCH_2Cl$		**7g**	$NHCOC_6H_5$	C_6H_5
3b	$NHCOCH_3$		**7h**	$NHCH_2CH_2COOH$	C_6H_5
3c	$NHCOC_6H_5$		**7i**	$NHCOCH_2Cl$	CH_2Cl
3d	$NHCH_2CH_2COOH$		**7j**	$NHCOCH_3$	CH_2Cl
4a	$NHCOCH_2Cl$		**7k**	$NHCOC_6H_5$	CH_2Cl
4b	$NHCOCH_3$		**7l**	$NHCH_2CH_2COOH$	CH_2Cl
4c	$NHCOC_6H_5$		**8a**	$NHCOCH_2Cl$	
4d	$NHCH_2CH_2COOH$		**8b**	$NHCOCH_3$	
5a	$NHCOCH_2Cl$		**8c**	$NHCOC_6H_5$	
5b	$NHCOCH_3$		**8d**	$NHCH_2CH_2COOH$	
5c	$NHCOC_6H_5$		**9a**	$NHCOCH_2Cl$	
5d	$NHCH_2CH_2COOH$		**9b**	$NHCOCH_3$	
6a	$NHCOCH_2Cl$		**9c**	$NHCOC_6H_5$	
6b	$NHCOCH_3$		**9d**	$NHCH_2CH_2COOH$	

Results and Discussion

Antitubercular activity

The above-synthesized products were screened against *M. tuberculosis* using the Microplate Alamar Blue Assay (MABA)[13] on a High Throughput Screening (HTS) machine at 25 μg/mL and lower concentrations using *M. tuberculosis* H37Ra as a surrogate for the virulent H37Rv strain. The results are shown in Table 2. The results of MABA have been found comparable to the standard BACTEC 460 system based assay. The standard antitubercular drugs *Rifamycin*, *Isoniazid*, *p-aminosalicylic acid*, *Ethambutol* and *Ethionamide* (MIC range 0.3-3 μg/mL) were taken as positive controls. We have also performed a cytotoxicity analysis of the above-synthesized compounds, using neutral red uptake by using the Vero-C-1008 cell line at various concentrations (6.25 μg/mL to 50 μg/mL), none of them were found toxic. Hence the activities of the above-synthesized compounds were not due to cytotoxicity of the compounds.

Table 2. Percent inhibition at 25μg/mL concentration

Compd	Activity in %	Compd	Activity in %	Compd	Activity in %
1a	8	**4a**	7	**7a**	5
1b	96	**4b**	97	**7b**	8
1c	87	**4c**	97	**7f**	6
1d	5	**4d**	8	**7j**	8
2a	2	**5a**	96	**8a***	96
2b	5	**5b**	6	**8b***	96
2c	81	**5c**	6	**8c***	96
2d	64	**5d**	3	**8d**	2
3a	3	**6a**	92	**9a**	4
3b	7	**6b**	95	**9b**	8
3c	8	**6c**	97	**9c**	8
3d	68	**6d**	92	**9d**	7

*Compounds showed 94, 96 and 94% inhibition at 12.5 μg/mL concentration.

During the preliminary screening, four compounds **1a**–**d** were tested (Table 2) at 25 μg/mL concentration for their antimycobacterial activity. One of the compounds, *viz*. **1b** exhibited 96% inhibition at this concentration while other compounds exhibited less than 90% inhibition at the same concentration.

Thus, we have considered **1b** as a lead molecule and subsequent structural modifications were carried out. As a first step towards lead optimization, the amino group was protected to the corresponding acetamide **2a-d**, however, all of these modifications resulted in a substantial decrease in activity. The next structural modification made was a dimeric product of **2a-d** but this change also resulted in a substantial loss of biological activity.

Compounds **4b** and **4c** showed 97% inhibition at 25 μg/mL (Table 2), which was obtained by S-alkylation with acetonitrile. Thus, looking at the activity, it was decided to modify the structure at the SH group. In order to optimize the sulfhydryl component, four compounds **5a-d** were synthesized and investigated, which revealed loss of activity. A further modification of compounds **5a-d** produced compounds **6a-d**. The results of the antimycobacterial activity are quite interesting because all of these compounds have shown inhibition above 90% at 25 μg/mL (Table 2).

On the other hand, in secondary screening at 12.5 μg/mL concentration these compounds were found to have decreased antimycobacterial activity. Compounds **6a-d** were selected for further studies as they had a protected and free amino group, which opened an area for further modification at this point. Compounds **7a-l** were obtained by treatment with acid chlorides, which ultimately showed decreased antimycobacterial activity. Furthermore, compounds **6a–d** were investigated after conversion to Schiff bases with benzaldehyde, all of the compounds **8a–d** showed more than 95% inhibition at 25 μg/mL concentration and, more interestingly, compounds **8a**, **8b** and **8c** showed more than 94% inhibition at 12.5 μg/mL concentration. Although we have not been able to substantially enhance the activity of these compounds in the present study, the data presented here are encouraging and deserve further investigation.

Antimicrobial activity

The compounds listed in Table 1 were screened for antimicrobial activity against different microorganisms under the following conditions.

Method: Well diffusion method,[14] **Medium**: The nutrient agar medium,

Solvent: Chloroform. **Concentrations**: 50μM and 100 μM.

Condition: 24 hours at 24-28 °C, **Standard**: The antibiotic *Gentamycin*

The nutrient agar medium, 20 mL was poured into the sterile petri dishes. To the solidified plates, wells were made using a sterile cork borer 10 mm in diameter. The 24 hour subcultured bacteria was inoculated in the petri-plates, with a sterile cotton swab dipped in the nutrient broth medium. After inoculating, the compounds were dissolved separately with the chloroform solvent and poured into the wells with varying concentrations ranging from 50 and 100 μM using a micropipette. The plates were left over 24 hours at 24-28 °C. The antibiotic *Gentamycin* was used as a standard for comparative study.

The percentage of inhibition was calculated by the formula

% Inhibition = Diameter of the inhibition zone x 100

From these data, it has been found that all the compounds tested showed a broad spectrum of inhibitory properties. From the antibacterial screening it was observed that all the compounds exhibited activity against all the organisms employed. Looking at the structure activity relationship, marked inhibition in bacteria was observed with compounds **6b**, **6c**, **8a**, **8b** and **8c**, whereas **1d**, **3a**, **4b**, **4c**, and **4d** have shown moderate activity and others showed the least activity.

Table 3. Antibacterial activity of the synthesized compounds

Comp.	Organisms				Comp.	Organisms			
	Sa	Pa	Ec	St		Sa	Pa	Ec	St
1a	18	17	14	12	**5c**	22	22	20	20
1b	18	16	15	14	**5d**	16	18	12	12
1c	22	20	18	14	**6a**	16	16	12	14
1d	25	22	20	16	**6b**	32	32	26	24
2a	20	20	18	14	**6c**	33	34	30	29
2b	16	16	20	16	**6d**	20	18	14	12
2c	16	10	10	18	**7a**	24	10	14	14
2d	11	17	15	22	**7b**	21	18	10	18
3a	22	22	20	16	**7f**	22	12	16	14
3b	16	16	12	12	**7j**	18	14	11	14
3c	11	24	16	12	**8a**	32	31	31	29
3d	18	16	10	12	**8b**	30	29	30	26
4a	20	16	10	10	**8c**	32	30	30	27
4b	22	22	20	16	**8d**	18	12	14	12
4c	26	24	22	18	**9a**	12	10	10	14
4d	26	24	20	20	**9b**	14	16	12	18
5a	24	22	20	18	**9c**	12	18	18	14
5b	22	11	24	24	**9d**	14	11	18	12
Gentamycin	34	35	31	30	*Gentamycin*	34	35	31	30

Sa- S*taphylococcus aureus,* Ec- *Escherichia coli,* Pa-*Pseudomonas aeruginosa,*
St- *Salmonella typhosa*

Experimental Section

General Procedures. The melting points were recorded on an Electrothermal apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Avance 300 MHz instrument using $CDCl_3$ as solvent (chemical shifts in δ' ppm) using TMS as internal standard; mass spectra on a Finning LCQ mass spectrometer. Microwave irradiation was carried out in a Raga Scientific Microwave System, Model RG31L at 2450 MHz. Elemental analyses were performed on a Heracus CHN-Rapid Analyser. The purity of the compounds was checked on silica gel coated Al plates (Merck).

Preparation of *N*-{4-[(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))methyl](1,3-thiazol-2-yl)}-acetamide (1b), *N*-{4-[(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))methyl](1,3-thiazol-2-yl)}-2-chloroacetamide (1a), *N*-{4-[(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))methyl](1,3-thiazol-2-

yl)}-benzamide (1c), 3-({4-[(4-amino-5-sulfanyl-1,2,4-triazol-3-yl)methyl]-1,3-thiazol-2-yl}amino)propionic acid (1d). The above titled compounds were prepared according the literature.[15]

Preparation of *N*-(5-{[2-(acetylamino)(1,3-thiazol-4-yl)]methyl}-3-sulfanyl-(1,2,4-triazol-4-yl))-acetamide (2b). The triazole **1b** (0.01 mole) in 20 mL of DMF was treated dropwise with an equimolar amount of acetic anhydride in 15 mL DMF at 0 °C, which was stirred for 30-45 min. At the end of stirring a buff colored precipitate was observed. The precipitate was then filtered, washed thoroughly with water and crystallized from ethanol. Yield 77 %; buff white; mp 250-252 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.12 (s, 6H, CH_3), 4.27 (s, 2H, CH_2), 6.11 (s, 1H, Thiazole CH), 8.07 (s, 2H, NH), 12.53 (s, 1H, SH); MS (%) 312 (M+, 100), 268 (29.6), 251 (9.8), 223 (15.1), 211 (10.8), 107 (14.7), 087 (10.1), 82 (7.6); $C_{10}H_{12}N_6O_2S_2$ requires: C, 38.45; H, 3.87; N, 26.90; found: C, 38.22; H, 3.68; N, 26.76. Other compounds in this series were prepared in a similar way.

***N*-(4-{[4-(2-chloroacetylamino)-5-sulfanyl(1,2,4-triazol-3-yl)]methyl}(1,3-thiazol-2-yl))acetamide (2a).** Yield 71 %; brown; mp 241-243 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.21 (s, 3H, CH_3), 4.13 (s, 4H, CH_2), 6.21 (s, 1H, Thiazole CH), 8.06 (s, 2H, NH), 12.31 (s, 1H, SH); MS (%)346 (M+, 100), 323 (33.8), 309 (17.4), 248 (14.7), 247 (29.8), 233 (9.8), 220 (10.8), 180 (10.1), 095 (15.1), 86 (9.3); $C_{10}H_{11}N_6O_2S_2Cl$ requires: C, 34.63; H, 3.20; N, 24.23; found: C, 34.67; H, 3.41; N, 24.54.

***N*-(5-{[2-(phenylamino)(1,3-thiazol-4-yl)]methyl}-3-sulfanyl-(1,2,4-triazol-4-yl))-acetamide (2c).** Yield 76 %; brown; mp 280-282 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H, CH_3), 4.18 (s, 2H, CH_2), 6.17 (s, 1H, Thiazole CH), 7.42-7.86 (m, 5H, ArH), 8.13 (s, 2H, NH), 12.13 (s, 1H, SH); MS (%) 374 (M+, 80), 306 (28), 292 (8.4), 251 (20), 214 (100), 195 (15), 154 (7), 106 (65); $C_{15}H_{14}N_6O_2S_2$ requires: C, 48.11; H, 3.77; N, 22.44; found: C, 48.34; H, 3.58; N, 22.28.

3-[(4-{[4-acetylamino-5-sulfanyl-1,2,4-triazol-3-yl]methyl}-1,3-thiazol-2-yl)amino] propionic acid (2d). Yield 69 %; brown; mp 271-273 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H, CH_3), 2.46-2.51 (t, 2H, CH_2, J = 4.3 Hz), 3.33-3.39 (q, 2H, CH_2, J = 7.6 Hz), 4.01-4.11 (t, 1H, NH, J = 8.1 Hz), 4.32 (s, 2H, CH_2), 6.27 (s, 1H, Thiazole CH), 8.16 (s, 1H, NH), 10.43 (bs, 1H, OH), 12.43 (s, 1H, SH); MS (%) 342 (M+, 100), 323 (14), 309 (17.1), 280 (6), 134 (35.9); $C_{11}H_{14}N_6O_3S_2$ requires: C, 38.59; H, 4.12; N, 24.54; found: C, 38.74; H, 4.03; N, 24.29.

Preparation of *N*-[3-(4-acetylamino-5-{[2-(acetylcarbonylamino)(1,3-thiazol-4-yl)] methyl}(1,2,4-triazol-3-ylthio))-5-{[2-(acetylcarbonylamino)(1,3-thiazol-4-yl)]methyl} (1,2,4-triazol-4-yl)]acetamide (3b). The triazole 2b (0.01 mol), diiodomethane (0.01 mol) and 5.6 g (0.01 mol) potassium hydroxide were dissolved in 20 mL of dichloromethane. To the said mixture acidic alumina (20 g) was added. Dichloromethane was evaporated invacuo, and mixture was kept inside the alumina bath and irradiated for 5-6 min at the power level of 300W. The mixture was cooled. The solid thus separated was dissolved in hot ethanol, filtered. After cooling, the filtrate gave white crystals of product 3b. Other compounds in this series were prepared in similar way. Yield 77 %; brown; mp 262-264° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.71-2.32 (s, 12H, CH_3), 4.34 (s, 4H, CH_2), 4.64 (s, 2H, CH_2), 5.93 (s, 2H, thiazole CH), 8.15 (s,

4H, NH); MS (%) 637 (14.1), 624 (15.7), 616 (14.3), 601 (100), 542 (23.5), 465 (3.9) 421 (13.2), 312 (5.8), 279 (7.2), 263 (11.0), 257 (11.7), 256(35.8), 216 (32.8), 91 (22), 83 (27.1), 69 (29.6); $C_{21}H_{24}N_{12}O_4S_4$ requires: C, 39.61; H, 3.80; N, 26.40; found: C, 39.48; H, 3.71; N, 26.38.

***N*-(4-{[4-acetylamino-5-[4-(2-chloroacetylamino)-5-{[2-(2-chloroacetylamino)(1,3-thiazol-4-yl)]methyl}(1,2,4-triazol-3-ylthio))(1,2,4-triazol-3-yl)]-methyl}(1,3-thiazol-2-yl))acetamide (3a).** Yield 84 %; brown; mp 278-280° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74-2.30 (s, 6H, CH_3), 3.67 (s, 4H, CH_2), 4.19 (s, 4H, CH_2), 4.58 (s, 2H, CH_2), 6.27 (s, 2H, Thiazole CH), 7.84 (s, 4H, NH); MS (%) 706 (7.1), 679 (27.5), 622 (5.5), 607 (100), 516 (3.4), 484 (4.7) 453 (8.2), 347(9.6), 234 (10.3), 185(13.8), 146(8.7), 123 (13.2), 104 (10.5), 87 (26.8), 78 (40); $C_{21}H_{22}N_{12}O_4S_4Cl_2$ requires: C, 35.74; H, 3.14; N, 23.82; found: C, 35.58; H, 3.11; N, 23.64.

***N*-[3-(4-acetylamino-5-{[2-(phenylcarbonylamino)(1,3-thiazol-4-yl)]methyl}(1,2,4-triazol-3-ylthio))-5-{[2-(phenylcarbonylamino)(1,3-thiazol-4-yl)]methyl}(1,2,4-triazol-4-yl)]acetamide (3c).** Yield 79 %; brown; mp 274-276° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.69-2.29 (s, 6H, CH_3), 3.73 (s, 4H, CH_2), 4.43 (s, 2H, CH_2), 6.27 (s, 2H, thiazole CH), 7.44-7.80 (m, 10H, ArH), 8.16 (s, 4H, NH); MS (%) 761 (35.9), 709 (11.1), 659 (13.2), 667 (23.6), 619 (100), 541 (3.6), 454 (3.7) 419 (9.8), 307 (8.2), 277 (8.1), 254 (11.9), 241 (15.4), 223(35.8), 216 (24.9), 91 (23.8), 83 (54.2), 69 (25.7); $C_{31}H_{28}N_{12}O_4S_4$ requires: C, 48.93; H, 3.71; N, 22.09; found: C, 48.74; H, 3.67; N, 22.24.

3-{[4-({5-[5-({2-[(2-carboxyethyl)amino](1,3-thiazol-4-yl)}methyl)-4-(acetylamino) (1,2,4-triazol-3-ylthio)]-4-(acetylamino)-1,2,4-triazol-3-yl}methyl)-1,3-thiazol-2-yl]amino} propionic acid (3d). Yield 89 %; yellow; mp 255-257° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.65-2.24 (bs, 6H, CH_3), 2.21-2.30 (t, 4H, CH_2, J = 4.5 Hz), 3.28-3.35 (q, 4H, CH_2, J = 7.4 Hz), 3.76 (s, 4H, CH_2), 4.01-4.12 (t, 2H, NH, J = 7.9 Hz), 4.63 (s, 2H, CH_2), 6.26 (s, 2H, thiazole CH), 8.21 (s, 4H, NH), 10.65 (bs, 2H, OH); MS (%) 697 (M+,13.6), 691 (100), 625 (40.9), 593 (6), 578 (7.3), 512 (4.1), 472 (13.6), 371 (5), 356 (3.4), 283 (13.7), 269 (6.4), 155 (14.4); $C_{23}H_{28}N_{12}O_6S_4$ requires: C, 39.64; H, 4.05; N, 24.12; found: C, 39.56; H, 4.18; N, 24.07.

Preparation of *N*-(3-{[2-(acetylamino)(1,3-thiazol-4-yl)]methyl}-5-(cyanomethylthio) (1, 2, 4-triazol-4-yl))-acetamide (4b). The triazole **2b** (0.01 mol) was mixed with 1.2 mL (0.02 mol) of chloroacetonitrile and dissolved in 25 mL of water. Neutralization with sodium carbonate gave a precipitate, which was filtered, washed with cold water (2 X 20 mL), and crystallized from ethanol. Yield 82 %; yellow; mp 264-266° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.05 (s, 6H, CH_3), 3.62 (s, 2H, CH_2), 4.04 (s, 2H, CH_2), 6.18 (s, 1H, Thiazole CH), 7.91 (s, 2H, NH); MS (%) 351 (M+, 93.3), 330 (10.9), 319 (4.1), 273 (46), 272 (100), 271 (14.3), 256 (9.3), 228 (4.4), 217 (3.2), 189 (3.6), 124 (8.9), 109 (5.8), 81 (4.5), 53 (3); $C_{12}H_{13}N_7O_2S_2$ requires: C, 41.01; H, 3.73; N, 27.90; found: C, 41.17; H, 3.57; N, 27.73.

***N*-(4-{[4-(2-chloroacetylamino)-5-(cyanomethylthio)(1,2,4-triazol-3-yl)]methyl}(1,3-thiazol-2-yl))acetamide (4a).** Yield 86 %; yellow; mp 241-243° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 3H, CH_3), 3.74 (s, 2H, CH_2), 4.17 (s, 2H, CH_2), 4.32 (s, 2H, CH_2), 6.26 (s, 1H, thiazole CH), 8.24 (s, 2H, NH); MS (%) 386 (M+, 100), 384 (21.9), 369 (20.6), 272 (34.2), 270 (40.8), 256

(17.9), 83 (28.9), 69 (16.1), 55 (11.3); $C_{12}H_{12}N_7O_2S_2Cl$ requires: C, 37.35; H, 3.13; N, 25.41; found: C, 37.41; H, 3.27; N, 25.28.

***N*-(3-{[2-(phenylamino)(1,3-thiazol-4-yl)]methyl}-5-(cyanomethylthio)(1, 2, 4-triazol-4-yl))-acetamide (4c).** Yield 81 %; yellow; mp 267-269° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.18 (s, 3H, CH_3), 3.73 (s, 2H, CH_2), 4.14 (s, 2H, CH_2), 6.24 (s, 1H, Thiazole CH), 7.41-7.83 (m, 5H, ArH), 8.24 (s, 2H, NH); MS (%) 413 (M+, 100), 384 (21.9), 369 (20.6), 272 (34.2), 270 (40.8), 256 (17.9), 83 (28.9), 69 (16.1), 55 (11.3); $C_{17}H_{15}N_7O_2S_2$ requires: C, 49.38; H, 3.66; N, 23.71; found: C, 49.22; H, 3.54; N, 23.68.

3-[(4-{[4-(acetylamino)-5-(cyanomethylthio)-1,2,4-triazol-3-yl]methyl}-1,3-thiazol-2-yl)amino]propionic acid (4d). Yield 78 %; yellow; mp 275-277° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11 (s, 3H, CH_3), 2.43-2.48 (t, 2H, CH_2, J = 4.1 Hz), 3.31-3.37 (q, 2H, CH_2, J = 7.3 Hz), 3.84 (s, 2H, CH_2), 4.11-4.18 (t, 1H, NH, J = 7.8 Hz), 4.34 (s, 2H, CH_2), 6.26 (s, 1H, Thiazole CH), 8.25 (s, 2H, NH), 10.84 (bs, 1H, OH); MS (%) 381 (M+, 56.8), 362 (100) 351 (6.9), 349 (16), 348 (12.8), 347 (26.8), 337 (9.7), 331 (12.4), 323 (9.7), 256 (8.8); $C_{13}H_{15}N_7O_3S_2$ requires: C, 40.93; H, 3.96; N, 25.70; found: C, 40.87; H, 3.73; N, 25.58.

Preparation of methyl-2-(5-{(2-(acetylamino)(1,3-thiazol-4-yl)]methyl}-4-(acetyl amino)-1,2,4-triazol-3-ylthio)acetate (5b). A solution of triazole **2b** (0.01 mol), 0.4 g (0.01 mol) of sodium hydroxide and methyl bromoacetate 1.53 g (0.01 mol) was prepared and to this, acidic alumina was added. The reaction mixture was mixed, and mixture was kept inside the alumina bath and irradiated for 4-5 min at the power level of 300W. The mixture was cooled and poured on ice. The solid thus separated was extracted with hot ethanol, filtered. After cooling, filtrate gave pure product **5b**. Other compounds in this series were prepared in similar way. Yield 78 %; yellow; mp 261-263° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 6H, CH_3), 3.52 (s, 3H, OCH_3), 3.74 (s, 2H, CH_2), 3.92 (s, 2H, SCH_2), 6.46 (s, 1H, CH of thiazole), 8.13 (broad, 2H, NH); MS (%) 384 (69.9, M+), 356 (5.4), 354 (4.3), 248 (100), 233 (3.9), 232 (13.5); $C_{13}H_{16}N_6O_4S_2$ requires: C, 40.62; H, 4.20; N, 21.86; found: C, 40.51; H, 4.38; N, 21.74.

Methyl-2-(4-acetylamino-5-{[2-(2-chloroacetylamino)(1,3-thiazol-4-yl)]methyl}-1,2,4-triazol-3-ylthio)acetate (5a). Yield 82 %; yellow; mp 259-251° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.81 (s, 2H, CH_2), 3.89 (s, 2H, SCH_2), 4.28 (s, 2H, CH_2Cl), 6.32 (s, 1H, CH of thiazole), 8.32 (broad, 2H, NH); MS (%) 419 (M+, 100), 400 (14), 386 (12.3), 385 (11.3), 373 (7.2), 316 (7.7), 279 (79), 278 (10), 363 (8.2), 262 (19.5), 248 (7.7), 234 (7.9), 222 (10.5), 220 (5.7), 250 (31.6); $C_{13}H_{15}N_6O_4S_2Cl$ requires: C, 37.28; H, 3.61; N, 20.06; found: C, 37.42; H, 3.53; N, 20.18.

Methyl-2-(5-{(2-(phenylamino)(1,3-thiazol-4-yl)]methyl}-4-acetylamino-1,2,4-triazol-3-ylthio)acetate (5c). Yield 75 %; brown; mp 226-228° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.27 (s, 3H, CH_3), 3.32 (s, 3H, OCH_3), 3.62 (s, 2H, CH_2), 3.83 (s, 2H, SCH_2), 6.25 (s, 1H, CH of thiazole), 6.93-7.51 (m, 5H, ArH), 8.22 (broad, 2H, NH); MS (%) 447 (M+, 9), 387 (31), 337 (1), 323 (2), 309 (1), 273 (100), 272 (8); $C_{18}H_{18}N_6O_4S_2$ requires: C, 48.42; H, 4.06; N, 18.82; found: C, 48.28; H, 4.17; N, 18.75.

3-{[4-({4-acetylamino)-5-[(methoxycarbonyl)methylthio]1,2,4-triazol-3-yl} methyl)-1,3-thiazol-2-yl]amino}propionic acid (5d). Yield 79 %; pale green; mp above 300° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.19 (s, 3H, CH_3), 2.30-2.41 (q, 2H, CH_2, *J* = 4.0 Hz), 3.18-3.23 (t, 2H, CH_2, *J* = 7.3 Hz), 3.46 (s, 3H, OCH_3), 3.61 (s, 2H, CH_2), 3.93 (s, 2H, SCH_2), 6.26 (s, 1H, CH of thiazole), 8.29 (broad, 2H, NH, , *J* = 7.9 Hz), 11.13 (broad, 1H, OH); MS (%) 414 (M+, 100), 309 (41), 272 (58),131 (16), 120 (60), 117 (44), 94 (27), 91(48), 84 (81); $C_{14}H_{18}N_6O_5S_2$ requires: C, 40.57; H, 4.38; N, 20.28; found: C, 40.34; H, 4.26; N, 20.41.

Preparation of *N*-(5-[(*N*-aminocarbamoyl)methylthio]-3-{[-acetylcarbonylamino)(1,3-thiazol-4-yl)]methyl(1,2,4-triazol-4-yl))-acetamide (VIb)

A solution of **5b** (0.01 mol) with 5 mL (0.01 mol) hydrazine hydrate was prepared in 10 mL ethanol. To this acidic alumina was added. Ethanol then was evaporated invacuo, and mixture was kept inside the alumina bath and irradiated for 5-6 min at the power level of 300W. The mixture was cooled and the product was extracted with ether. Ether was distilled off and product thus obtained was crystallized from *n*-hexane-carbon tetrachloride mixture. Other compounds in this series were prepared in similar way. Yield 82%; brown; mp 250-252° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84 (d, 2H, NH_2, , *J* = 6.5 Hz), 2.16 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.67 (s, 2H, CH_2), 3.81 (s, 2H, SCH_2), 6.69 (s, 1H, CH of thiazole), 8.12 (broad, 3H, NH); MS (%) 384 (89, M+), 378 (14.3), 352 (45.2), 305 (24.3), 241 (7.3), 208 (5.6), 174 (66), 146 (100), 109 (17.8), 88 (10.5); $C_{12}H_{16}N_8O_3S_2$ requires: C, 37.49; H, 4.19; N, 29.15; found: C, 37.67; H, 4.26; N, 29.31.

***N*-[4-({5-[(N-aminocarbamoyl)methylthio]-4-acetylamino-(1,2,4-triazol-3-yl)}methyl) (1,3-thiazol-2-yl)]- 2-chloroacetamide (6a).** Yield 83 %; brown; mp 245-247° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93 (s, 3H, CH_3), 2.13 (d, 2H, NH_2, *J* = 6.4 Hz), 3.64 (s, 2H, CH_2), 3.94 (s, 2H, SCH_2), 4.47 (s, 2H, CH_2Cl), 6.65 (s, 1H, CH of thiazole), 8.21 (broad, 3H, NH); MS (%) 452 (65, M+), 419 (6.9), 386 (14.5), 356 (6.1), 328 (7.8), 311 (8.4), 269 (24), 235 (100), 201 (11.3), 184 (10.8), 156 (5.3), 124 (23.5), 89 (4.9); $C_{12}H_{15}N_8O_3S_2Cl$ requires: C, 34.41; H, 3.61; N, 26.75; found: C, 34.54; H, 3.42; N, 26.89.

***N*-(5-[(*N*-aminocarbamoyl)methylthio]-3-{[-phenylcarbonylamino)(1,3-thiazol-4-yl)] methyl(1,2,4-triazol-4-yl))-acetamide (6c).** Yield 71 %; brown; mp 222-224° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93 (s, 3H, CH_3), 2.11 (d, 2H, NH_2, *J* = 6.6 Hz), 3.38 (s, 2H, CH_2), 3.76 (s, 2H, SCH_2), 6.11 (s, 1H, CH of thiazole), 7.13-7.68 (m, 5H, ArH), 8.10 (broad, 3H, NH); MS (%) 447 (78, M+), 390 (72), 321 (26.3), 247 (6.3), 215 (18.3), 174 (65.3), 136 (25), 88 (100), 69 (14.3); $C_{17}H_{18}N_8O_3S_2$ requires: C, 45.73; H, 4.06; N, 25.10; found: C, 45.62; H, 4.24; N, 25.19.

3-{[4-({5-[(*N*-aminocarbamoyl)methylthio]-4-acetylamino-1,2,4-triazol-3-yl}methyl]-1,3-thiazol-2-yl]amino}propionic acid (6d). Yield 84 %; brown; mp 243-245°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.91 (d, 2H, NH_2, *J* = 6.1 Hz), 2.13 (s, 3H, CH_3), 2.27-2.31 (q, 2H, CH_2, *J* = 4.2 Hz), 3.16-3.27 (t, 2H, CH_2, *J* = 7.1 Hz), 3.46 (s, 2H, CH_2), 3.84 (s, 2H, SCH_2), 6.14 (s, 1H, CH of thiazole), 8.03 (broad, 3H, NH, *J* = 4.1 Hz, *J* = 8.1 Hz), 11.09 (broad, 1H, OH); MS (%) 414 (93.3, M+), 334 (56.4), 306 (28), 247 (64), 217 (100), 147 (83), 108 (71), 79 (10.2); $C_{13}H_{18}N_8O_4S_2$ requires: C, 37.67; H, 4.38; N, 27.04; found: C, 37.54; H, 4.22; N, 27.17.

Preparation of *N*-[3-{[2-(acetylamino)(1,3-thiazol-4-yl)]methyl}-5-{[*N'*-acetylamino) carbamoyl]methylthio}(1, 2, 4-triazol-4-yl))-acetamide (7b). A solution of 6b (0.01 mol) with appropriate acid chloride (0.01 mol) was prepared in 10 mL ethanol. To this acidic alumina was added. Ethanol then was evaporated invacuo, and mixture was kept inside the alumina bath and irradiated for 5-6 min at the power level of 300W. The mixture was cooled and the product was extracted with ether. Ether was distilled off and product thus obtained was crystallized from n-hexane-carbon tetrachloride mixture. Other compounds in this series were prepared in similar way. Yield 71 %; yellow; mp 227-229°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.98 (s, 9H, CH_3), 2.75 (s, 1H, NH), 3.74 (s, 2H, CH_2), 3.91 (s, 2H, SCH_2), 6.27 (s, 1H, Thiazole CH), 8.18 (s, 3H, NH, *J* = 4.1 Hz, *J* = 8.1 Hz); MS (%) 426 (97, M+), 408 (62), 398 (17.2), 359 (9.1), 327 (74), 297 (54), 241 (8.3), 223 (100), 174 (24), 146 (27); $C_{14}H_{18}N_8O_4S_2$ requires: C, 39.43; H, 4.25; N, 26.27; found: C, 39.26; H, 4.47; N, 26.09.

***N*- [3-{[2-(acetylamino)(1, 3-thiazol-4-yl)] methyl} – 5 - {[*N'*-phenyl carbonyl amino) carbamoyl]methylthio}(1, 2, 4-triazol-4-yl))-acetamide (7f).** Yield 74 %; yellow; mp 286-288 ^{0}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.94 (s, 6H, CH_3), 2.46 (s, 1H, NH), 3.74 (s, 2H, CH_2), 4.11 (s, 2H, SCH_2), 6.26 (s, 1H, Thiazole CH), 7.45-7.80 (m, 5H, ArH), 8.32 (s, 3H, NH, *J* = 4.5 Hz, *J* = 4.9 Hz); MS (%) 489 (86, M+), 431 (11.4), 357 (78), 329 (32.8), 305 (41), 287 (13.7), 241 (35), 167 (100), 109 (32.7), 98 (19.3); $C_{19}H_{20}N_8O_4S_2$ requires: C, 46.71; H, 4.13; N, 22.94; found: C, 46.57; H, 4.23; N, 22.71.

***N*- [2-(5-{[2-(acetyl amino)(1, 3-thiazol-4-yl)] methyl} -4- acetylamino-(1, 2, 4-triazol-4-ylthio)) acetyl amino]- 2-chloroacetamide (7j).** Yield 57 %; dark brown; mp 166-168°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93 (s, 6H, CH_3), 2.64 (s, 1H, NH), 3.69 (s, 2H, CH_2), 4.05 (s, 2H, SCH_2), 4.32 (s, 2H, CH_2), 6.28 (s, 1H, Thiazole CH), 8.23 (s, 3H, NH, *J* = 4.3 Hz, *J* = 4.7 Hz); MS (%) 461 (54, M+), 437 (84), 369 (54.2), 284 (9.3), 238 (100), 158 (11.2), 128 (37), 77 (36.2); $C_{14}H_{17}N_8O_4S_2Cl$ requires: C, 36.48; H, 3.72; N, 24.31; found: C, 36.23; H, 3.59; N, 24.24.

Preparation of *N*- (5-{[*N*-((1E)-1-aza-2-phenylvinyl) carbamoyl] methylthio} -3- {[2-(acetylamino)(1,3-thiazol-4-yl])methyl}(1,2,4-triazol-4-yl))-acetamide (8b). A solution of **6b** (0.01 mol) with appropriate aromatic aldehyde (0.01 mol) was prepared in 10 mL ethanol. To this acidic alumina was added. Ethanol then was evaporated invacuo, and mixture was kept inside the alumina bath and irradiated for 5-6 min at the power level of 300W. The mixture was cooled and poured on ice. The solid thus separated was filtered, extracted with ether. Ether was distilled off and product thus obtained was crystallized from hot ethanol. Other compounds in this series were prepared in similar way. Yield 83%; pale brown; mp 178-180 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 6H, CH_3), 3.97 (s, 2H, CH_2), 4.14 (s, 2H, SCH_2), 6.25 (s, 1H, Thiazole CH), 7.31-7.65 (m, 5H, ArH), 8.26 (s, 3H, NH), 8.36 (s, 1H, N=CH); MS (%) 473 (79, M+), 455 (52), 413 (63), 368 (9.2), 308 (41), 284 (31), 242 (37), 178 (100), 128 (15.2), 97 (28), 87 (7.4); $C_{19}H_{20}N_8O_3S_2$ requires: C, 48.29; H, 4.27; N, 23.71; found: C, 48.14; H, 4.42; N, 23.63.

***N*-{4-[(5-{[*N*-((1E)-1-aza-2-phenylvinyl)carbamoyl]methylthio}-4-acetylamino(1, 2, 4-triazol-3-yl))methyl](1,3-thiazol-2-yl)}- 2-chloroacetamide (8a).** Yield 81 %; brown; mp 222-

224 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.27 (s, 3H, CH_3), 3.77 (s, 2H, CH_2), 4.16 (s, 2H, CH_2), 4.28 (s, 2H, SCH_2), 6.22 (s, 1H, Thiazole CH), 7.30-7.62 (m, 5H, ArH), 8.16 (S, 3H, NH), 8.27 (S, 1H, N=CH); MS (%) 507 (69, M+), 502 (16.9), 457 (32.7), 379 (26.1), 315 (5.8), 246 (21.4), 195 (31.5), 134 (100), 107 (11.4), 88 (12.3), $C_{19}H_{19}N_8O_3S_2Cl$ requires: C, 45.01; H, 3.78; N, 22.10; found: C, 45.17; H, 3.81; N, 22.18.

***N*-(5-{[*N*-((1E)-1-aza-2-phenylvinyl)carbamoyl]methylthio}-3-{[2-(phenylamino)(1,3-thiazol-4-yl])methyl}(1, 2, 4-triazol-4-yl))-acetamide (8c).** Yield 81%; pale brown; mp 217-219 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 3H, CH_3), 3.63 (s, 2H, CH_2), 4.33 (s, 2H, SCH_2), 6.23 (s, 1H, Thiazole CH), 7.21-7.64 (m, 10H, ArH), 8.16 (s, 3H, NH), 8.41 (s, 1H, N=CH); MS (%) 535 (94, M+), 519 (41), 487 (9.6), 431 (26), 413 (8.4), 389 (100), 365 (20); $C_{24}H_{22}N_8O_3S_2$ requires: C, 53.92; H, 4.15; N, 20.96; found: C, 53.79; H, 4.26; N, 20.77.

3-({4-[(5-{[*N*-((1E)-1-aza-2-phenylvinyl)carbamoyl]methylthio}-4-acetylamino-1,2,4-triazol-3-yl)methyl]-1,3-thiazol-2-yl}amino)propionic acid (8d). Yield 78 %; brown; mp 120-122 ° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.21 (s, 3H, CH_3), 2.65-2.71 (t, 2H, CH_2, J = 4.7 Hz), 3.23-3.31 (q, 2H, CH_2, J = 7.5 Hz), 3.92 (s, 2H, CH_2), 4.10 (s, 2H, SCH_2), 4.32 (t, 1H, NH, J = 8.3 Hz), 6.23 (s, 1H, Thiazole CH), 7.17-7.63 (m, 5H, ArH), 8.15 (s, 2H, NH), 8.32 (s, 1H, N=CH), 10.87 (bs, 1H, OH); MS (%) 503 (74, M+), 497 (45), 426 (11.3), 364 (62.3), 326 (3.2), 248 (6.5), 185 (12), 146 (100), 109 (32.7), 87 (4.2); $C_{20}H_{22}N_8O_4S_2$ requires: C, 47.80; H, 4.41; N, 22.30; found: C, 47.68; H, 4.34; N, 22.21.

Preparation of *N*-(5-[(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))methylthio]-3-{[2-(acetyl carbonylamino)(1,3-thiazol-4-yl)]methyl}(1,2,4-triazol-4-yl))-acetamide (9b). The 6b (0.01 mol) was dissolved in alcoholic potassium hydroxide (0.01 mol) and kept for stirring. Carbon disulphide (0.015 mol) was added drop wise to the solution with stirring. Thick solid mass was obtained, to which 50 mL of absolute alcohol was added. Stirring was continued for 16 h. At the end of 16th h dry ether was added to the mixture. The precipitate (thiocarbazate) obtained was taken immediately for the next step.

A solution of thiocarbazate (0.01 mol) with hydrazine hydrate (0.01 mol) was prepared in 10 mL ethanol. To this acidic alumina was added. Ethanol then was evaporated invacuo, and mixture was kept inside the alumina bath and irradiated for 5-6 min at the power level of 300W. The mixture was cooled and poured on ice. The solid thus separated was filtered, extracted with ether. Ether was distilled off and product thus obtained was crystallized from hot ethanol. Other compounds in this series were prepared in similar way. Yield 71 %; brown; mp 252-254 ° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 2H, NH_2), 2.35 (s, 6H, CH_3), 3.79 (s, 2H, CH_2), 4.14 (s, 2H, CH_2), 6.19 (s, 1H, Thiazole CH), 8.08 (s, 2H, NH), 12.43 (s, 1H, SH); MS (%) 441 (93.3, M+), 432 (14.6), 421 (11.2), 323 (65), 308 (41), 289 (2.7), 230 (38), 207 (100), 142 (35.7), 109 (23); $C_{13}H_{16}N_{10}O_2S_3$ requires: C, 35.44; H, 3.66; N, 31.80; found: C, 35.27; H, 3.45; N, 31.71.

***N*-[4-({5-[(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))methylthio]-4-acetylamino(1,2,4-triazol-4-yl)} methyl)(1,3-thiazol-4-yl)] -2-chloroacetamide (9a).** Yield 72 %; brown; mp 228-230 ° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.16 (s, 2H, NH_2), 2.65 (s, 3H, CH_3), 3.76 (s, 2H, CH_2), 4.25 (s, 2H, CH_2), 6.20 (s, 1H, Thiazole CH), 8.11 (s, 2H, NH), 12.49 (s, 1H, SH); MS (%) 475 (82,

M+), 467 (31), 431 (26), 384 (31), 326 (13.2), 247 (15), 226 (17), 125 (100); $C_{13}H_{15}N_{10}O_2S_3Cl$ requires: C, 32.87; H, 3.18; N, 29.49; found: C, 32.64; H, 3.26; N, 29.67.

***N*-(5-[(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))methylthio]-3-{[2-(phenylcarbonylamino) (1,3-thiazol-4-yl)]methyl}(1,2,4-triazol-4-yl))-acetamide (9c).** Yield 80 %; brown; mp 264-266 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.04 (s, 2H, NH_2), 2.63 (s, 3H, CH_3), 3.75 (s, 2H, CH_2), 4.34 (s, 2H, CH_2), 6.23 (s, 1H, Thiazole CH), 7.14-7.74 (m, 5H, ArH), 8.17 (s, 2H, NH), 12.63 (s, 1H, SH); MS (%) 503 (76, M+), 454 (32), 350 (30), 335 (100), 323 (2.93), 222 (12.26), 220 (3.73), 207 (5.86), 192 (7.07); $C_{18}H_{18}N_{10}O_2S_3$ requires: C, 43.02; H, 3.61; N, 27.87; found: C, 43.17; H, 3.48; N, 27.76.

3-{[4-({5-[(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))methylthio]-4-acetylamino-1,2,4-triazol-3-yl}methyl)-1,3-thiazol-2-yl]amino}propionic acid (9d). Yield 77 %; brown; mp 237-239 ° C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 2H, NH_2), 2.22 (s, 3H, CH_3), 2.46-2.49 (t, 2H, CH_2, J = 4.3 Hz), 3.14-3.20 (q, 2H, CH_2, J = 6.7 Hz), 3.98 (s, 2H, CH_2), 4.23-4.29 (t, 1H, NH, J = 7.3 Hz), 4.36 (s, 2H, CH_2), 6.26 (s, 1H, Thiazole CH), 8.17 (s, 2H, NH), 10.64 (bs, 1H, OH), 12.35 (s, 1H, SH); MS (%) 471 (84, M+), 450 (14.74), 438 (3.78), 371 (2.95), 370 (7.95), 354 (14.10), 235 (100), 220 (2.12), 207 (6.38), 192 (7.40); $C_{14}H_{18}N_{10}O_3S_3$ requires: C, 35.73; H, 3.86; N, 29.77; found: C, 35.62; H, 3.74; N, 29.89.

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