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# FACILE SYNTHESIS OF SOME NOVEL TRIAZOLE AND TRIAZINE DERIVATIVES

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## ABSTRACT
A new approach towards the synthesis of substituted triazolo-triazoles and triazin-6-ones derivatives is described. The starting substituted semicarbazones were synthesized from semicarbazide hydrochloride and appropriate aldehyde, which on oxidative cyclization afforded 2-amino-5-(substituted phenyl)-1,3,4-oxadiazole derivatives. These oxadiazoles were then converted into corresponding 5-(substituted phenyl)-[1,2,4]triazol-3,4-diamine derivatives. The triazol-3,4-diamines on reaction with phenoxy/phenylthioacetic acid and chlorophenylthioacetic acid afforded desired substituted triazolo-triazoles and triazolo-triazines derivatives respectively. All the synthesized compounds were characterized by FT-IR, NMR spectroscopy ($^{1}$H and $^{13}$C) and elemental analysis (CHN).

## KEYWORDS
Semicarbazones, oxadiazole, triazoles, triazolo-triazoles, triazole-triazin-6-ones

## INTRODUCTION
Heterocycles are harmoniously woven into day to day life processes and their importance in drug discovery makes them much more valuable for mankind. A vast number of pharmacologically active heterocyclic compounds are being used clinically. The triazole scaffold has received significant recognition as one of the most important heterocycle owing to its many synthetic and medicinal application.[i]Two possible isomers of five membered triazole are 1,2,3-triazole **I** and 1,2,4-triazole **II** (Figure 1), however, 1,2,4-triazole have drawn major attention of medicinal chemists owing to its wide range of activity,good pharmacodynamic and pharmacokinetic profile and low toxicity.[ii]1,2,4-Triazole derivatives have been shown to act as a antifungal, anti-inflammatory, anticonvulsant, antimalarial, analgesic, antimigraine, antitubercular, antibacterial, antiviral, antioxidant, anticancer agents and as activator of potassium channel.[iii,iv]Figure 1 shows some of the commericiallyavailable

drugs containing 1,2,4-triazole moiety such as Fluconazole **III**, Triadimefon, **IV** and Anastrozole**V**.

Triazine, another important heterocycle exhibits different types of isomers depending upon the position of nitrogen atoms (Figure 1), namely 1,2,3-triazine **VI**, 1,2,4-triazine **VII** and1,3,5-triazine (s-triazine) **VIII**. Triazine derivatives possess various biological activities such as antitubercular, fungicidal, antibacterial, hypothermic, hypotensive,[v]antiviral,[vi,vii]antiparkinson,[viii] potent neuroprotective[ix] and anticonvulsant activities[x] such as Lamotrigine**IX**(Figure 1).

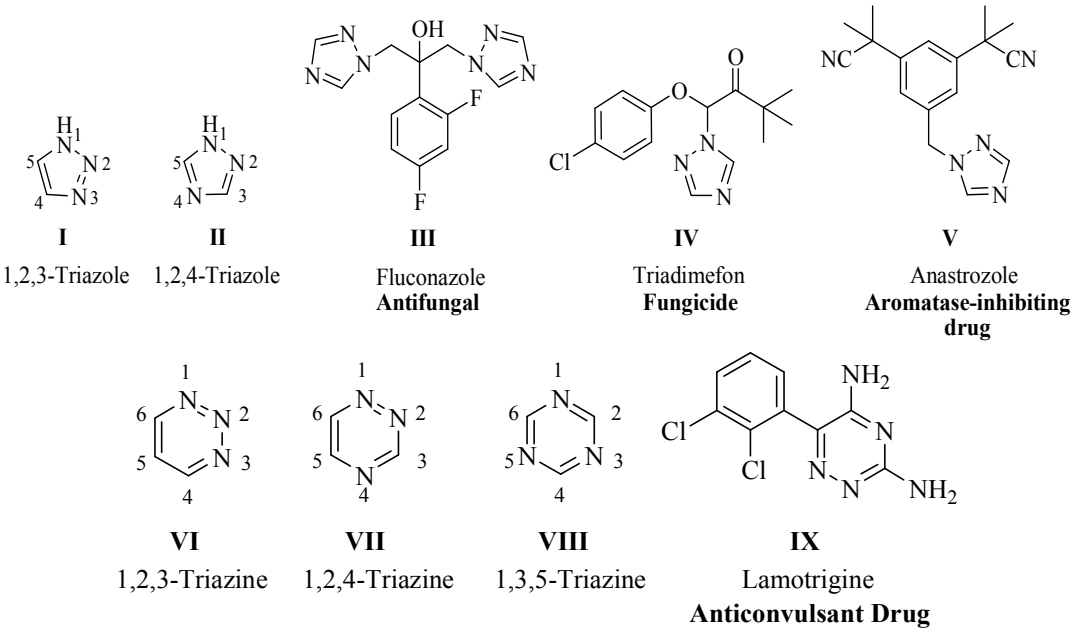



**Fig. 1** Triazole/triazineisomers andclinically relevant 1,2,4-triazole/triazinesubstituted drugs.

We are actively engaged in the β-lactam and the heterocyclic chemistry[xi,xii] and in connection to above reports, we envisaged the facile synthesis of some new 3-(substituted phenyl)-s-triazolo[4,3-*b*]-1,2,4-triazoles and 1,2,4-triazin-6-one derivatives containing 1,3,4-oxadiazole/1,2,4-triazole moieties.

## EXPERIMENTAL

### General

$^1$H NMR (300 MHz) was recorded using JEOL 300 MHz NMR spectrometer. The chemical shifts are expressed in δ values (ppm) using tetramethylsilane as an internal standard. Infrared spectra were recorded using Perkin-Elmer Model 1430 spectrophotometer with potassium bromide (KBr) plates or Nujol with NaCl optic plates and are reported in $cm^{-1}$. The elemental analysis (C, H, N) was carried out using a PERKIN–ELMER 2400 elemental analyzer. Thin-layer chromatography (TLC) was performed using Merck Silica Gel G. For visualization, TLC plates were stained with iodine vapours. All the melting points are uncorrected and are expressed in degree centigrade ($^oC$). Melting points were determined with a Thomas-Hoover capillary melting point apparatus. The synthesis of fused triazoles derivatives were carried out under dry and deoxygenated nitrogen atmosphere. Phosphorus oxychloride (Merck), ethanol (Merck) and all other commercially available compounds/reagents/solvents were of reagent grade quality and used without any further purification.

Compounds **3a-d**,[xiii] **4a-d**[xiii]and **5a-d**[xiv] were prepared by the procedures described in the cited references. The spectroscopic data of compounds **3a-d, 4a-d** and **5a-c** were also reported in the cited references.[xiii,xiv]

**5-Phenyl-[1,2,4]-triazol-3,4-diamine [(5d)** 70%**]** was obtained as a yellow solid, m.p. 232-234 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 1.21 (s, 6H, 2x$CH_3$), 2.89(s, 4H, 2x$NH_2$), 7.21-7.95 (m, 4H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 13.5, 28.02, 109.10, 110.99, 111.48, 113.24, 136.09, 149.93, 163.09;IR : 3320, 1659 cm$^{-1}$; (Found : C 54.91; H 6.35; N 38.48; $C_{10}H_{14}N_6$ requires 55.03; H 6.47; N 38.50%).

**General procedure for the synthesis of 3-(substituted phenyl)-s-triazolo[4,3-b]-1,2,4-triazoles 6a-b/7a-d.**

To a solution of triazol-3,4-diamines **5a-d** (1 mmol) and 2-phenyloxo/thioethanoic acid (1 mmol) in phosphorus oxychloride ($POCl_3$) was refluxed and the progress of the reaction was monitored by TLC. After completion of the reaction, excess of $POCl_3$ was removed under reduced pressure and the content after cooling was poured into crushed ice. The pH of the mixture was brought to 7 by adding liquid ammonia. The precipitates thus obtained were filtered, washed with water, dried and recrystallized from methanol to furnish desired triazolo-triazoles**6a-b/7a-d**.

**3-(4-Methoxyphenyl)-6-phenoxymethyl-7*H*-[1,2,4]triazolo[4,3-b][1,2,4]triazole [(6a)** 64%**]** was obtained as a yellow solid, m.p. 221-223 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 3.26(s, 2H, $CH_2$), 3.86 (s, 3H, $OCH_3$), 6.90 (bs, 1H, NH), 6.91-7.74 (m, 9H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 36.4, 55.4, 111.0, 113.7, 121.5, 127.1, 129.1, 129.4, 130.0, 131.3, 132.4, 135.5, 175.0;IR : 3392, 1653 cm$^{-1}$; (Found : C 63.49; H 4.73; N 21.65; $C_{17}H_{15}N_5O_2$ requires C 63.54; H 4.71; N 21.79 %).

**3-(4-Chlorophenyl)-6-phenoxymethyl-7*H*-[1,2,4]triazolo[4,3-b][1,2,4]triazole [(6b)**77%**]** was obtainedasa yellow solid, m.p. 202-204 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 3.36(s, 2H, $CH_2$), 6.01 (bs, 1H, NH), 7.15-7.47 (m, 9H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 36.4, 55.4, 111.0, 113.7, 121.5, 127.1, 127.1, 129.1, 129.4, 130.0, 131.3, 132.4, 135.5, 175.0; IR : 3400, 1657 cm$^{-1}$;(Found : C 58.94; H 3.63; N 21.43; $C_{16}H_{12}N_5OCl$ requires C 58.99; H 3.71; N 21.50 %).

**3-(4-Methoxyphenyl)-6-phenylsulfanylmethyl-7*H*-[1,2,4]triazolo[4,3 b][1,2,4]triazole[(7a)**56%**]**was obtained as a yellow solid, m.p. 220-223 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 3.67(s, 3H, $OCH_3$), 3.84 (s, 2H, $CH_2$), 6.00 (bs, 1H, NH), 6.90-8.26 (m, 9H, ArH); IR 3330, 1604 cm$^{-1}$; $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 36.6, 55.4, 111.0, 113.7, 121.3, 127.1, 127.6, 129.1, 130.0, 131.3, 132.3, 134.5, 135.4, 164.1, 170.7, 175.0;IR : 3418, 1584 cm$^{-1}$; (Found : C 60.40; H 4.39; N 20.72; $C_{17}H_{15}N_5OS$ requires C 60.52; H 4.48; N 20.76%).

**3-(4-Chlorophenyl)-6-phenylsulfanylmethyl-7*H*-[1,2,4]triazolo[4,3-*b*][1,2,4]triazole [(7b)**72%**]** was obtained as ayellow solid, m.p. 218-220 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 3.67 (s, 2H, $CH_2$), 5.42 (bs, 1H, NH), 7.15-7.72 (m, 9H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 35.5, 126.8, 127.0, 127.5, 128.7, 129.0, 129.8, 129.8, 130.1, 131.6, 135.3, 163.1, 173.7;IR: 3418, 1584 cm$^{-1}$; (Found : C 56.08; H 3.45; N 20.42; $C_{16}H_{12}N_5SCl$ requires C 56.22; H 3.54; N 20.49 %).

**3-phenyl-6-phenylsulfanylmethyl-7*H*-[1,2,4]triazolo[4,3-b][1,2,4]triazole [(7c)**57%**]**was obtained as a yellow solid, m.p. 220-222 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 3.29 (s, 2H, $CH_2$), 6.02 (bs, 1H, NH), 7.11-7.74 (m, 10H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 34.9, 111.7, 126.8, 128.3, 128.6, 128.9, 129.0, 129.2, 129.3, 130.2, 133.4, 134.9, 168.3, 173.0; IR : 3387, 1654 cm$^{-1}$;(Found : C 62.61; H 4.20; N 22.80; $C_{16}H_{13}N_5S$ requires C 62.52; H 4.26; N 22.78%).

**3-(*N*,*N*-Dimethylphenyl-6-phenylsulfanylmethyl-7*H*-[1,2,4]triazolo[4,3b][1,2,4]triazole [(7d)** 64%**]** was obtained as a yellow solid, m.p. 230-232 ºC; $^1$H NMR (300 MHz, $CDCl_3$ +

DMSO) δ 1.27 (s, 6H, 2x$CH_3$), 3.67 (s, 2H, $CH_2$), 6.01 (bs, 1H, NH), 6.59-7.09 (m, 9H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 34.9, 111.7, 126.8, 128.3, 128.6, 128.9, 129.0, 129.2, 129.3, 130.2, 133.4, 134.9, 168.3, 173.0; IR : 3401, 1659 cm$^{-1}$;(Found C 61.57; H 5.10; N 23.93 5; $C_{18}H_{18}N_6S$ requires C 61.69; H 5.18; N 23.98%).

**General procedure for the synthesis of 3-(substituted phenyl)-7-phenylsufanyl-7,8-dihydro-[1,2,4]triazolo[4,3-b][1,2,4]triazin-6-ones** (±)**-8a-d**.

A mixture of triazol-3,4-diamines **5a-d** (1 mmol), 2-chlorophenylthioacetic acid (2 mmol) and fused sodium acetate (2 mmol) in anhydrous ethanol (30 mL) was refluxed and the progress of the reaction was monitored by TLC. After completion of the reaction, the content was cooled to room temperature. The product thus separated was filtered, washed with water, dried and recrystallized from ethanol to yield desired triazolo-triazin-6-ones (±)**-8a-d**.

**3-(4-Methoxyphenyl)-7-phenylsufanyl-7,8-dihydro-[1,2,4]triazolo[4,3-b][1,2,4]triazin-6-ones [(**(±)**-8a)**64%**]** was obtained as a yellow solid,m.p. 235-237 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 3.84 (s, 3H, $OCH_3$), 4.62 (s, 1H, CH),4.99 (bs, 2H, 2xNH), 7.18-7.52 (m, 9H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 55.3, 71.5, 111.9, 127.1, 127.4, 127.6, 128.0, 128.9, 133.3, 135.1, 136.9, 156.8, 164.8, 174.2; IR: 3032, 1660, 1602 cm$^{-1}$;(Found C 57.82; H 4.18; N 19.85; $C_{17}H_{15}N_5O_2S$ requires C 57.78; H 4.28; N 19.82%).

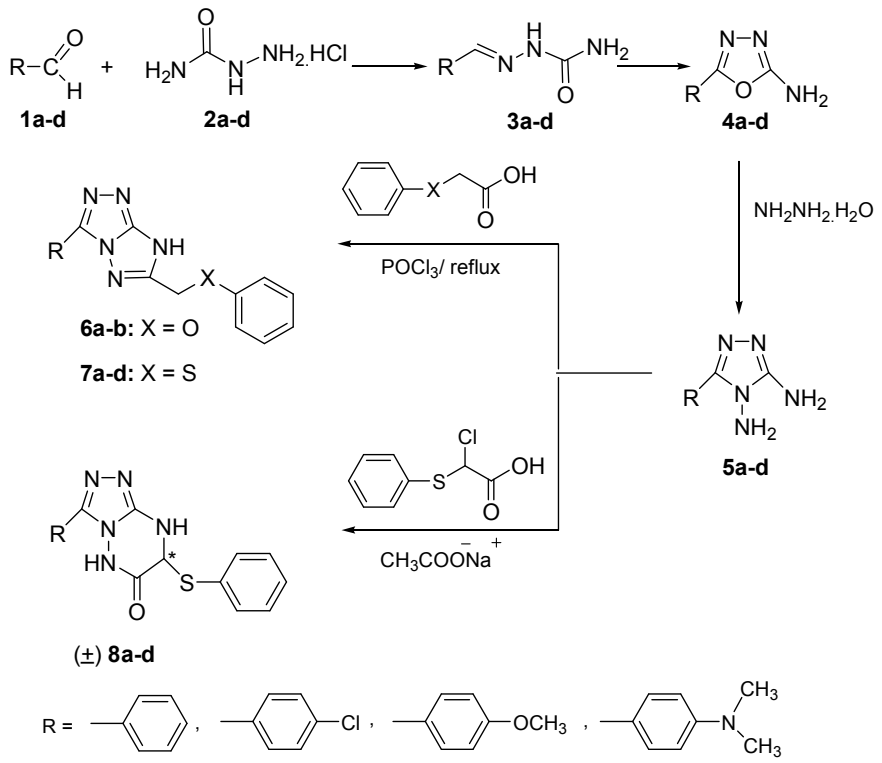
**3-(4-Chlorophenyl)-7-phenylsufanyl-7,8-dihydro-[1,2,4]triazolo[4,3-b][1,2,4]triazin-6-ones [(**(±)**-8b)** 57%**]**was obtained as a yellow solid, m.p. 185-187 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 4.49 (s, 1H, CH),6.00 (bs, 2H, 2xNH), 6.94-7.43 (m, 9H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 71.2, 123.0, 125.6, 126.6, 126.3, 128.8, 129.6, 130.1, 135.1, 156.6, 163.8, 173.8;IR: 3173, 1701, 1584 cm$^{-1}$; (Found C 53.72; H 3.02; N 19.56; $C_{16}H_{12}N_5OSCl$ requires C 53.71; H 3.38; N 19.57 %).

**3-phenyl-7-phenylsufanyl-7,8-dihydro-[1,2,4]triazolo[4,3-b][1,2,4]triazin-6-ones [(**(±)**-8c)** 65%**]** was obtained as a yellow solid, m.p. 219-222 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 4.72 (s, 1H, CH), 5.72 (bs, 2H, 2xNH), 6.21-6.73 (m, 10H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 70.9, 123.1, 123.8, 123.9, 124.0, 126.9, 127.4, 128.3, 128.5, 128.8, 129.9, 156.2, 162.4, 173.7;IR : 3266, 1653, 1597 cm-1; (Found C 59.49; H 3.95; N 21.70; $C_{16}H_{13}N_5OS$ requires C 59.43; H 4.05; N 21.66 %).

**3-(*N*,*N*-DiMethylphenyl)-7-phenylsufanyl-7,8-dihydro-[1,2,4]triazolo[4,3-b][1,2,4]triazin-6-ones [**(±)**-(8d)** 50%**]** was obtained asayellow solid, m.p. 231-233 ºC; $^1$H NMR (300 MHz, $CDCl_3$ + DMSO) δ 1.27 (s, 6H, 2x$CH_3$), 4.58 (s, 1H, CH), 5.99 (bs, 2H, 2xNH), 7.02-7.69 (m, 9H, ArH); $^{13}$C NMR (75 MHz, $CDCl_3$ + DMSO): δ 70.9, 123.1, 123.8, 123.9, 124.0, 126.9, 127.4, 128.3, 128.5, 128.8, 129.9, 156.2, 162.4, 173.7; IR 3401, 1609, 1595 cm$^{-1}$; (Found C 59.03; H 4.88; N 22.98; $C_{18}H_{18}N_6OS$ requires C 59.00; H 4.95; N 22.93 %).

## RESULTS AND DISCUSSION

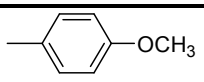
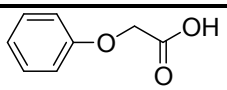
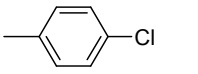
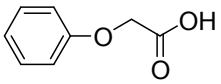
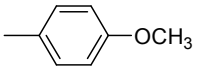
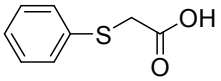
Starting substrates, substituted benzalsemicarbazones**3**, were obtained by refluxing a mixture of semicarbazide hydrochloride with appropriate aldehydes using reported procedure.[xv] Further, compounds**3** on oxidative cyclization afforded 2-amino-5-(substituted phenyl)-1,3,4-oxadiazole derivatives **4** which on reaction with hydrazine hydrate yielded 5-(substituted phenyl)-[1,2,4]triazol-3,4-diamines**5**.[xiii,xiv] Triazol-3,4-diamine derivatives **5** were then subjected to reaction with 2-phenyloxo/thioethanoic acids and 2-chlorophenylthioethanoic acid to afford novel triazolo-triazoles**6/7** and triazolo-triazines(±)**-8** (Scheme 1).

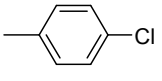
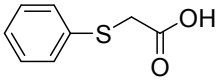
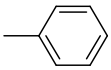
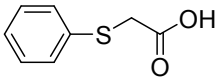
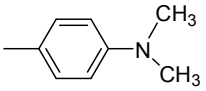
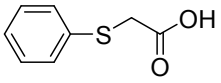



**Scheme 1.** Synthesis of triazolo-triazole**6/7** and triazolo-triazines(±)**-8**

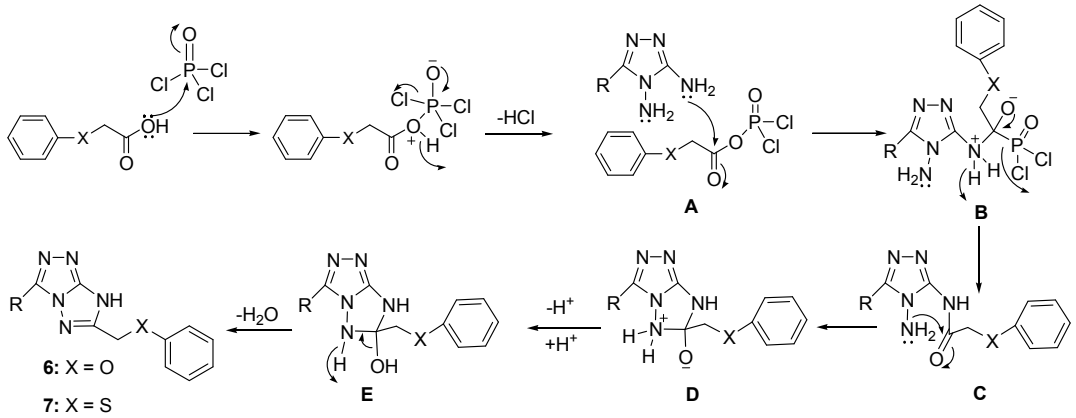
Initially, 5-(substituted phenyl)-[1,2,4]triazol-3,4-diamines **5a** was subjected to cyclocondensationreaction with 2-phenyloxoethanoic acid in the presence of phosphorus oxychloride ($POCl_3$), acting as both condensing agent and medium for the reaction, under refluxing conditions. The progress of the reaction was monitored by thin layer chromatography (TLC). The excess of $POCl_3$ was removed in vacuo. The desired triazolo-triazole**6a** was obtained as a solid by pouring the reaction mixture into ice cold water followed by the addition of liq. ammonia to attain a pH of 7. Compound **6a** was then purified through recrystallization from methanol (entry 1, Table 1). Further, cyclocondensationreaction of **5a-d** was performed with 2-phenyloxo/thioethanoic acid under similar conditions to furnish triazolo-triazoles**6b/7a-d** derivatives in good yields (Table 1). All the synthesized **6/7**compounds were characterized using various spectroscopic techniques (IR, $^{1}H$ and $^{13}C$ NMR) and elemental analysis (CHN).

**Table 1:** Synthesis of triazolo-triazoles**6a-b/7a-d**

| Entry | **55(a-d)** | R | | Product **6a-b/7a-d** | Yield[a] % |
|---|---|---|---|---|---|
| 1 | **55a** |  |  | **6a** | 64 |
| 2 | **55b** |  |  | **6b** | 77 |
| 3 | **55a** |  |  | **7a** | 56 |

| | | | | | |
|---|---|---|---|---|---|
| 4 | **55b** |  |  | **7b** | 72 |
| 5 | **55c** |  |  | **7c** | 57 |
| 6 | **55d** |  |  | **7d** | 65 |

[a]Yield of pure, isolated product after recrystallization with correct analytical and spectral data.

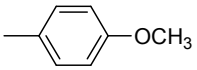
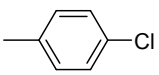
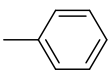


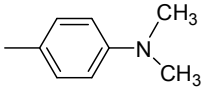
**Scheme 2.**Proposed mechanism for synthesis of triazolo-triazoles**6/7**

A plausible mechanism for the synthesis of triazolo-triazoles is depicted in Scheme2. Initially, 2-phenyloxo/thioethanoic acidreacts with phosphorus oxychlorideto generate an ester **A**.Further, nucleophilic attack of amino group at C-5 position of triazole on the carbonyl carbon of **A** generates an intermediate **B** which undergo elimination reaction to yield intermediate **C**. Subsequent intramoleculernucleophilic attack of the amino group at *N*-1 to the the carbonyl group gives intermediate **D** which on elimination and addition of $H^+$generates intermediate **E**.Finally, elimination of water molecule from intermediate **E** furnishes the desired triazolo-triazoles**6/7**.

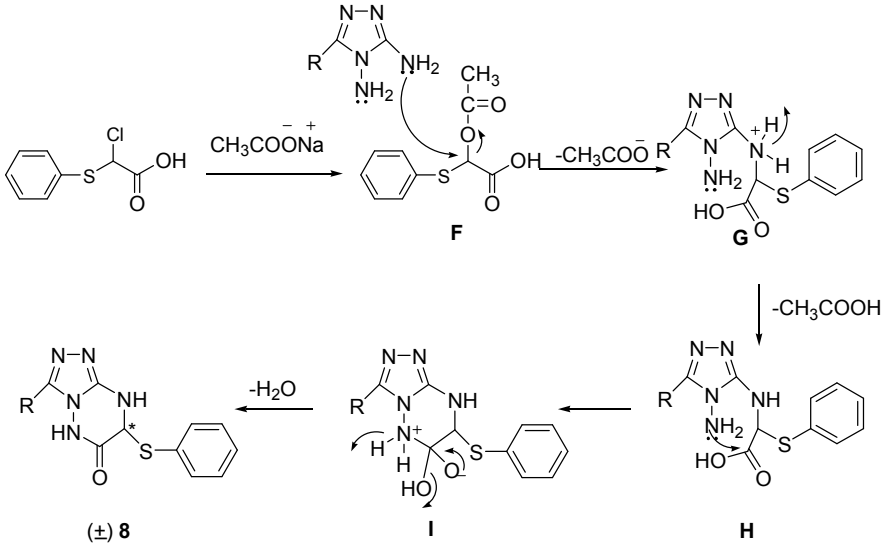
The 5-(substituted phenyl)-[1,2,4]triazol-3,4-diamine **5a** was further reacted with 2-chlorophenylthioethanoic acid in the presence of fused sodium acetate in refluxing ethanol to achieve triazolo-triazines derivatives i.e 3-(substituted phenyl)-7-phenylsulfanyl-7,8-dihydro-[1,2,4]triazolo[4,3-*b*][1,2,4]-triazin-6-ones (±)**-8a** (Scheme 1, entry 1, Table 2). Compounds**5b-d** were condensed with 2-chlorophenylthioacetic acid under similar conditions to furnish a series of triazolo-triazines**8b-d**, which were purified through recrystallization from methanol and characterized using various spectroscopic techniques (IR, $^1$H and $^{13}$C NMR) and elemental analysis (CHN) (Table 2).

**Table 2:** Synthesis of triazolo-triazines(±)**-8a-d**

| Entry | **55a-d** | **R** | Products (±)**-8a-d** | Yield[a] % |
|---|---|---|---|---|
| 1 | **55a** |  | (±)**-8a** | 64 |
| 2 | **55b** |  | (±)**-8b** | 57 |
| 3 | **55c** |  | (±)**-8c** | 65 |

| | | | | |
|---|---|---|---|---|
| 4 | **55d** |  | (±)**-8d** | 50 |

[a]Yield of pure, isolated product after recrystallization with correct analytical and spectral data.




**Scheme 3.**Proposed mechanism for synthesis of triazolo-triazines(±)**-8**

A persuasive mechanism for synthesis of triazol-triazines derivatives (±)**-8** is illustrated in Scheme 3. The 2-chlorophenylthioethanoic acid reacts with sodium acetate to form **F**. The initially formed 2-acetoxy-2-phenythioacetic acid **F**undergoesnucleophilic attack at the methyl carbon by the amino group at C-5 position of triazole.This is followed by elimination of acetic acid molecule to generate an intermediate **H** via an intermediate **G**. Further, intranucleophilic attack of amino group at *N*-1 position on the carbonyl carbon gives intermediate **I** which undergoes simultaneous rearrangement and dehydration to yield the required triazolo-triazoles(±)**-8**.

All the synthesized triazolo-triazoles**6a-b/7a-d** and triazolo-triazines(±)**-8a-d** were air and moisture stable, sparingly soluble in solvents like dichloromethane, chloroform, ethyl acetate and freely soluble in more polar solvents such as ethanol and methanol.

## CONCLUSION

In conclusion, successful attempts have been made towards the synthesis of newand structurally uniquetriazolo-triazoles and triazolo-triazines derivatives **6**/**7** and (±)**-8** from triazol-3,4-diamine derivatives **5** using a simple and efficient strategy. Substrate scope was also investigated by varying R group of triazol-3,4-diamine **4**. A careful mechanistic route is also proposed to explain the formation of products. The representative triazolo-triazoles and triazolo-triazines will be submitted for their molecular docking, *in vitro* as well as *in silico* studies. Further functionalization and their use as synthons to other complex heterocycles is underway in our laboratory.

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**REFERENCES**

i. P. Rifat, C. Amitand B. Nusrat, Asian J. Biomed. Pharm. Sci. 4, 44 (2014).
ii. U. Upmanyu, Pharmainfo.net4, 3 (2006).
iii. S.B. Holla,B. Veerendra and M.K. Shivananda, Eur. J. Med. Chem. 38, 759(2003) and references cited therein.
iv. V. Calderone, I. Giorgi, O. Livi, O. Martinotti, E. Mantuano, A. Martelli and A. Nardi, Eur. J. Med. Chem. 40, 521(2005) and references cited therein.
v. H. Schroeder and C. Grundmann, J. Am. Chem. Soc. 78, 2447(1956).
vi. Z.H. Chohan, H. Pervez, A. Rauf, K.M. Khan, G.M.Maharvi andC.T. Supuran, J. Enzyme Inhib. Med. Chem. 19, 161(2004).
vii. M. Mashaly, H.A. Bayoumi and A. Taha, Chem. Papers Chem. Zvesti.53, 299 (1999).
viii. M. Congreve, S.P. Andrews, A.S. Dore, K. Hollenstein, E. Hurrel, C.J. Langmead, J.S. Mason, I.W. Ng, B. Tehan, A. Zhukov, M. Weir and F.H. Marshal, J. Med. Chem.55, 1898 (2012).
ix. H. Irannejad, M. Amini, F. Khodaghi, N. Ansari, T.S. Khoramian, M. Sharifzadeh and A. Shafiee, Bioorg. Med. Chem.18, 4224 (2010).
x. H. Irannejad, N. Naderi, S. Emami, A.Foroumadi, R. QobadiGhadikolaei, T. Zafari, A. Mazar-Atabaki and S. Dadashpour, Med. Chem. Res. 23, 2503 (2014).
xi. A. Bhalla, G. Modi, S.S. Bari, A. Kumari, D. Narula and S. Berry, Tetrahedron: Asymmetry 28, 307 (2017).
xii. A. Bhalla, G. Modi, S.S. Bari, A. Kumari, S. Berry and G. Hundal, Tetrahedron Lett. 58, 1160 (2017) and references cited therein.
xiii. V. Gupta, S.K. Kashaw, V. Jatav and P. Mishra, Med. Chem. Res. 17, 205 (2008).
xiv. M. Gupta, Bioorg. Med. Chem. Lett. 21, 4919 (2011).
xv. M.N. Ibrahim and H.A. Al-Difar, Der Chemica Sinica 2, 171 (2011).

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