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4-Acetyl-N,N-dibenzylbenzenesulfonamide in Heterocyclic Synthesis: Synthesis and Biological Evaluation of Novel Sulfonamides Incorporating Thiazole, Pyrazolo[1,5-a]pyrimidine, 4-Oxothiazolidine and 1,3,4-Thiadiazole moieties

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This article describes the synthesis of some novel sulfonamide containing biologically active, pyridine **2, 4**; hydrazine carbothioamide **5**, **10**; thiazole **6-8, 12-14**; hydrazine carbodithioate **9**, **11a-c**; pyrazolo[1,5-a]pyrimidine **19**; 4-oxothiazolidine **22**, **24-26**, **36**, **37**, **39**, **40**, **43**, **44** and 1,3,4-thiadiazole **35** moieties starting with 4-acetyl-N,N-dibenzylbenzenesulfonamide **1**. The structure of the newly synthesized compounds was confirmed by elemental analysis, IR, ^{1}H NMR and mass spectral data. All the newly synthesized compounds were evaluated for their *in vitro* antimicrobial activities against gram positive bacteria (*B. subtilis*, *S. aureus*, *S. maxima*), gram negative bacteria (*K. pneumonia*, *Salmonella*, *P. aeruginosa*) and filamentous fungi (*Rhizopus*, *A. fumigatus*). Most of the screened compounds showed interesting highly active compared to ampicillin (AMD) and calforan.

Key Words: Sulphonamide, Thiazole, Pyrazolo[1,5-a]pyrimidine, 4-Oxothiazolidine, 1,3,4-Thiadiazole.

INTRODUCTION

Sulfonamides have been demonstrated to possess antibacterial[1-4], antifungal[5], insulin releasing[6-8], carbonic anhydrase inhibitory[9-12], hypoglycemic[13], anesthetic[14], antitumor[15,16], anticancer and antiinflammatory[17-19] activities. Some active sulfonamides as antibacterial are also known for their immune modifying effects[20].

The 4-oxothiazolidine derivatives, known as the "glitazones" (Fig. 1) are sometimes referred to as insulin enhancers[21].

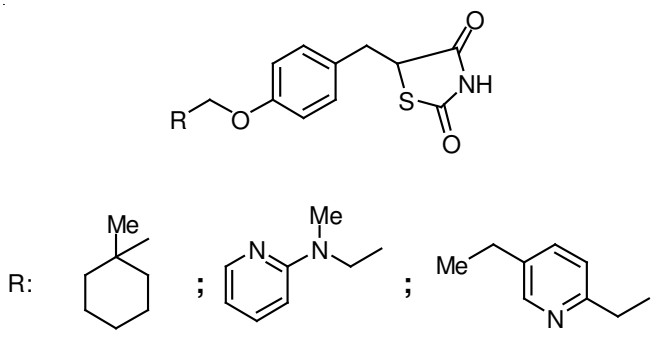


Fig. 1

Zaleplon (Sonata), (Fig. 2), a pyrazolo[1,5-a]pyrimidine derivative, is a sedative and hypnotic agent[21]. In view of these

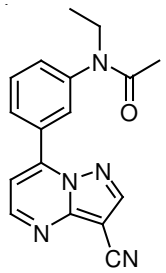


Fig. 2

reports and as a continuation of our previous work[22-25] directed towards the synthesis of substituted benzenesulfonamide conjugated with thiazole, pyrazolo[1,5-a]pyrimidine, 4-oxothiazolidine and 1,3,4-thiadiazole moieties. The author report a new and convenient method for the synthesis of such ring systems that are required to medicinal chemistry utilizing 4-acetyl-N,N-dibenzylbenzene sulfonamide (**1**) as reaction intermediate, since the carbonyl and the methyl functions of this compound are suitably situated to enable reaction with common bidentate reagents to form a variety of heterocyclic compounds having sulfonamide function.

EXPERIMENTAL

All melting points are uncorrected. IR spectra (KBr) were recorded on a FTIR 5300 spectrometer (ν, cm^{-1}). The ^{1}H NMR spectra were recorded at 300 MHz on a Varian Gemini NMR

spectrometer (δ, ppm) using TMS as an internal standard. Mass spectra were obtained on GC Ms-QP 1000 EX mass spectrometer at 70 eV. Elemental analyses were carried out by the Micro analytical Research Center, Faculty of Science, Cairo University.

N,N-Dibenzyl-4-(3-(pyridin-3-yl)acryloyl)benzenesulfonamide (2): A mixture of acetophenone derivative (**1**; 0.01 mol) and pyridine-3-carboxaldehyde (0.012 mol) in 50 mL ethanol with a few drops of piperidine was heated under reflux for 4 h, during the reflux period, a pale yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Yield 65 %; m.p. 138-140 ºC; IR (KBr, ν_{max}, cm^{-1}): 3034 (CH aromatic), 2918 (CH aliphatic), 1692 (CO), 1340, 1158 (SO_2). ^{1}H NMR $CDCl_3$: 4.37 (s, 4H, $(CH_2)_2N$), 7.06-7.57 (m, 14H, Ar-H and pyridine ring), 7.13-7.19 (dd, 2H, CH=CH), 7.89-8.06 (dd, 4H, AB-system). MS m/z (%): 368 [M^+] (3.8), 196 (100). Anal. calcd. (%) for $C_{28}H_{24}N_2O_3S$: C, 71.77; H, 5.16; N, 5.98; S, 6.84. Found (%): C, 71.64, H, 5.02; N, 5.84; S, 6.61.

Ethyl 4-(4-(N,N-dibenzylsulfamoyl)phenyl)-6-oxo-2-(pyridin-3-yl)cyclohexa-1,4-dienecarboxylate (4a) and ethyl 4'-(N,N-dibenzylsulfamoyl)-3-hydroxy-5-(pyridin-3-yl)biphenyl-4-carboxylate (4b): A mixture of chalcone derivative (**2**; 0.01 mol), ethyl acetoacetate (0.012 mol) and few drops of piperidine in ethanol 25 mL was heated under reflux for 8 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Yield 70 %; m.p. 204-206 ºC; IR (KBr, ν_{max}, cm^{-1}): 3030 (CH aromatic), 2915 (CH aliphatic), 1720 (CO ester), 1690 (CO cyclo), 1340, 1158 (SO_2). ^{1}H NMR $CDCl_3$: 1.67 (t, 3H, CH_3), 2.67 (s, 2H, CH_2), 3.88 (q, 2H, CH_2), 4.37 (s, 4H, $(CH_2)_2N$), 7.05-7.53 (m, 15H, Ar-H), 7.89-8.06 (dd, 4H, AB-system), 10.35 (br, 1H, OH exchangeable with D_2O). Anal. calcd. (%) for $C_{34}H_{30}N_2O_5S$: C, 70.57; H, 5.23; N, 4.84; S, 5.54. Found (%): C, 70.45, H, 5.10; N, 4.60; S, 5.31.

2-(1-(4-(N,N-Dibenzylsulfamoyl)phenyl)ethylidene) hydrazinecarbothioamide (5): A mixture of acetophenone derivative (**1**; 0.01 mol) and thiosemicarbazide (0.01 mol) in ethanol 50 mL was heated under reflux for 5 h during the reflux period, a pale yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from benzene.

Yield 64 %; m.p. 148-150 ºC; IR (KBr, ν_{max}, cm^{-1}): 3454, 3334 (NH_2), 3212 (NH), 3030 (CH aromatic), 2910 (CH aliphatic), 1342, 1160 (SO_2). ^{1}H NMR $CDCl_3$: 2.51 (s, 3H, CH_3), 4.37 (s, 4H, $2CH_2N$), 6.40 (br, 2H, NH_2), 7.05-7.53 (m, 10H, Ar-H), 7.86-8.06 (dd, 4H, AB-system), 8.71 (s, 1H, NH). Anal. calcd. (%) for $C_{23}H_{24}N_4O_2S_2$: C, 61.04; H, 5.34; N, 12.38; S, 14.17. Found (%): C, 61.20, H, 5.11; N, 12.15; S, 14.05.

N,N-Dibenzyl-4-(1-(2-(4-methylthiazol-2-yl) hydrazono)ethyl)benzenesulfonamide (6): A mixture of thiocarbamoyl derivative (**5**; 0.01 mol), chloro acetone (0.01 mol) and fused sodium acetate (0.08 mol) in ethanol 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Yield 66 %; m.p. 147-149 ºC; IR (KBr, ν_{max}, cm^{-1}): 3206 (NH), 3056 (CH aromatic), 2698 (CH aliphatic), 1340, 1158 (SO_2). ^{1}H NMR $CDCl_3$: 2.28 (s, 3H, CH_3 of 4-thiazole), 2.51 (s, 3H, CH_3), 4.37 (s, 4H, $(CH_2)_2N$), 7.06-7.25 (m, 10H, Ar-H), 7.73 (s, 1H, CH-thiazole), 7.88-8.01 (dd, 4H, AB-system), 9.02 (s, 1H, NH). Anal. calcd. (%) for $C_{26}H_{26}N_4O_2S_2$: C, 63.65; H, 5.34; N, 11.42; S, 13.07. Found (%): C, 63.42, H, 5.22; N, 11.20; S, 12.72.

N,N-Dibenzyl-4-(1-(2-(4-phenylthiazol-2-yl) hydrazono)ethyl)benzenesulfonamide (7): A mixture of thiocarbamoyl derivative (**5**; 0.01 mol), phenacyl bromide (0.01 mol) and fused sodium acetate (0.08 mol) in ethanol 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from dimethyl formamide.

Yield 72 %; m.p. 248-250 ºC; IR (KBr, ν_{max}, cm^{-1}): 3220 (NH), 3028 (CH aromatic), 2906 (CH aliphatic), 1340, 1154 (SO_2). ^{1}H NMR $CDCl_3$: 2.51 (s, 3H, CH_3), 4.36 (s, 4H, $(CH_2)_2N$), 7.00-7.30 (m, 15H, Ar-H), 7.73 (s, 1H, CH-thiazole), 7.89-8.00 (dd, 4H, AB-system), 9.10 (s, 1H, NH). MS m/z (%): 552 [M^+] (41.2), 77 (100). Anal. calcd. (%) for $C_{31}H_{28}N_4O_2S_2$: C, 67.36; H, 5.11; N, 10.14; S, 11.60. Found (%): C, 67.13, H, 5.08; N, 10.01; S, 11.38.

N,N-Dibenzyl-4-(1-(2-(4-phenyl-5-(phenyldiazenyl) thiazol-2-yl)hydrazono)ethyl)benzenesulfonamide (8): Procedure (A): A mixture of compound (**5**; 0.01 mol), 2-oxo-N',2-diphenylacetohydrazonoyl bromide (0.01 mol) and triethylamine 1 mL in ethanol 40 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from dioxane.

Procedure (B): Benzenediazonium chloride (prepared by adding sodium nitrite (0.01 mol) to aniline (0.01 mol) in conc. HCl 6 mL at (0-5 ºC) under stirring) was added drop wise with stirring to a cold solution of 4-phenylthiazole derivative (**7**; 0.01 mol) in ethanol 20 mL containing sodium acetate (0.08 mol), the obtained product was collected and recrystallized. m.p. and mixed m.p. determined with authentic sample gave no depression.

Yield 65 %; m.p. 237-239 ºC; IR (KBr, ν_{max}, cm^{-1}): 3218 (NH), 3022 (CH aromatic), 2912 (CH aliphatic), 1340, 1156 (SO_2). ^{1}H NMR (DMSO-d_6): 2.51 (s, 3H, CH_3), 4.37 (s, 4H, $(CH_2)_2N$), 7.06-7.51 (m, 20H, Ar-H), 7.89-8.07 (dd, 4H, AB-system), 10.01 (s, 1H, NH). Anal. calcd. (%) for $C_{37}H_{32}N_6O_2S_2$: C, 67.66; H, 4.91; N, 12.80; S, 9.76. Found (%): C, 67.44, H, 4.58; N, 12.57; S, 9.43.

Methyl 2-(1-(4-(N,N-dibenzylsulfamoyl)phenyl) ethylidene)hydrazinecarbodithioate (9): A mixture of 4-acetyl-N,N-dibenzylbenzenesulfonamide (**1**; 0.01 mol) and methyl hydrazinecarbodithioate (0.01 mol) in ethanol 50 mL was heated under reflux for 1 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from ethanol/benzene.

Yield 87 %; m.p. 170-172 ºC; IR (KBr, ν_{max}, cm^{-1}): 3172 (NH), 3022 (CH aromatic), 2916 (CH aliphatic), 1340, 1160 (SO_2). ^{1}H NMR $CDCl_3$: 2.36 (s, 3H, CH_3), 2.70 (s, 3H, SCH_3), 4.36 (s, 4H, $(CH_2)_2N$), 7.06-7.26 (m, 10H, Ar-H), 7.85-7.98

(dd, 4H, AB-system), 10.02 (s, 1H, NH). Anal. calcd. (%) for $C_{24}H_{25}N_3O_2S_3$: C, 59.60; H, 5.21; N, 8.69; S, 19.89. Found (%): C, 59.57, H, 5.19; N, 8.47; S, 19.67.

2-(1-(4-(N,N-Dibenzylsulfamoyl)phenyl)ethylidene)-N-phenylhydrazinecarbothioamide (10): Procedure (A): A mixture of acetophenone derivative (**1**; 0.01 mol) and 2-phenylhydrazinecarbothioamide (0.01 mol) in ethanol 40 mL was heated under reflux for 3 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from dimethyl formamide.

Procedure (B): A mixture of methyl hydrazine carbodithioate derivative (**9**; 0.01 mol) was treated with aniline (0.01 mol) in ethanol 50 mL the solution was heated under reflux until the evolution of methanethiol almost completely separated, the solvent was removed under reduced pressure the residue was collected and filtered off, m.p. and mixed m.p. determined with authentic sample gave no depression.

Yield 67%; m.p. 195-197 ºC; IR (KBr, ν_{max}, cm^{-1}): 3310, 3198 (2NH), 3020 (CH aromatic), 2914 (CH aliphatic), 1346, 1162 (SO_2). ^{1}H NMR (DMSO-d_6): 2.51 (s, 3H, CH_3), 4.37 (s, 4H, $(CH_2)_2N$), 7.01-7.29 (m, 15H, Ar-H), 7.89-8.06 (dd, 4H, AB-system), 10.26 and 10.88 (2s, 2H, 2NH exchangeable with D_2O). Anal. calcd. (%) for $C_{29}H_{28}N_4O_2S_2$: C, 65.88; H, 5.34; N, 10.60; S, 12.13. Found (%): C, 65.55, H, 5.12; N, 10.47; S, 12.01.

1-(4-(N,N-Dibenzylsulfamoyl)phenyl)ethylidenecarbonohydrazonodithioate derivatives (11a-c)

General procedure: A mixture of compound (**9**; 0.01 mol), phenacyl bromide, benzyl chloride and methyl iodide (0.01 mol) and triethylamine 1 mL in ethanol 40 mL was heated under reflux for 4 h during the reflux period, crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol, ethanol/benzene and ethanol to give (**11a-c**), respectively.

Methyl-2-oxo-2-phenylethyl-1-(4-(N,N-dibenzylsulfamoyl)- phenyl)ethylidenecarbonohydrazonodithioate (11a): Yield 75%; m.p. 150-152 ºC; IR (KBr, ν_{max}, cm^{-1}): 3028 (CH aromatic), 2916 (CH aliphatic), 1696 (CO), 1336, 1156 (SO_2). ^{1}H NMR $CDCl_3$: 2.16 (s, 3H, CH_3), 2.63 (s, 3H, SCH_3), 4.33 (s, 4H, $(CH_2)_2N$), 4.69 (s, 2H, SCH_2), 7.05-8.08 (m, 15H, Ar-H), 7.81-7.97 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{32}H_{31}N_3O_3S_3$: C, 63.87; H, 5.19; N, 6.98; S, 15.98. Found (%): C, 63.75, H, 5.07; N, 6.66; S, 15.84.

Benzyl methyl 1-(4-(N,N-dibenzylsulfamoyl)phenyl) ethylidenecarbonohydrazonodithioate (11b): Yield 68 %; m.p. 210-212 ºC; IR (KBr, ν_{max}, cm^{-1}): 3026 (CH aromatic), 2922 (CH aliphatic), 1338, 1158 (SO_2). ^{1}H NMR (DMSO-d_6): 2.23 (s, 3H, CH_3), 2.70 (s, 3H, SCH_3), 4.35 (s, 4H, $(CH_2)_2N$), 4.55 (s, 2H, SCH_2), 7.02-7.95 (m, 15H, Ar-H), 7.81-8.01 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{31}H_{31}N_3O_2S_3$: C, 64.89; H, 5.45; N, 7.32; S, 16.76. Found (%): C, 64.67, H, 5.22; N, 7.20; S, 16.54.

Dimethyl 1-(4-(N,N-dibenzylsulfamoyl)phenyl) ethylidenecarbonohydrazonodithioate (11c): Yield 62 %; m.p. 110-112 ºC; IR (KBr, ν_{max}, cm^{-1}): 3030 (CH aromatic), 2918 (CH aliphatic), 1336, 1156 (SO_2). ^{1}H NMR $CDCl_3$: 2.50 (s, 3H, CH_3), 2.72 (s, 6H, $2SCH_3$), 4.37 (s, 4H, $(CH_2)_2N$), 7.06-7.27 (m, 10H, Ar-H), 7.81-7.99 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{25}H_{27}N_3O_2S_3$: C, 60.33; H, 5.47; N, 8.44; S, 19.33. Found (%): C, 60.10, H, 5.23; N, 8.21; S, 19.10.

N,N-Dibenzyl-4-(1-((4-methyl-3-phenylthiazol-2(3*H*)-ylidene)hydrazono)ethyl)benzenesulfonamide (12): A mixture of phenylthiocarbamoyl derivative (**10**; 0.01 mol), 1-chloropropan-2-one (0.01 mol) and fused sodium acetate (0.08 mol) in ethanol 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Yield 70 %; m.p. 225-226 ºC; IR (KBr, ν_{max}, cm^{-1}): 3030 (CH aromatic), 2914 (CH aliphatic), 1338, 1156 (SO_2). ^{1}H NMR $CDCl_3$: 2.21 (s, 3H, CH_3 of 4-thiazole), 2.52 (s, 3H, CH_3), 4.37 (s, 4H, $(CH_2)_2N$), 7.02-7.72 (m, 15H, Ar-H), 7.73 (s, 1H, CH-thiazole), 7.78-8.01 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{32}H_{30}N_4O_2S_2$: C, 67.82; H, 5.34; N, 9.89; S, 11.32. Found (%): C, 67.60, H, 5.10; N, 9.56; S, 11.10.

N,N-Dibenzyl-4-(1-((3,4-diphenylthiazol-2(3*H*)-ylidene)hydrazono)ethyl)benzenesulfonamide (13): A mixture of phenylthiocarbamoyl derivative (**10**; 0.01 mol), phenacyl bromide (0.01 mol) and fused sodium acetate (0.08 mol) in ethanol 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Yield 69 %; m.p. 199-201 ºC; IR (KBr, ν_{max}, cm^{-1}): 3028 (CH aromatic), 2910 (CH aliphatic), 1336, 1158 (SO_2). ^{1}H NMR $CDCl_3$: 2.50 (s, 3H, CH_3), 4.35 (s, 4H, $(CH_2)_2N$), 7.03-7.71 (m, 20H, Ar-H), 7.72 (s, 1H, CH-thiazole), 7.81-7.97 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{37}H_{32}N_4O_2S_2$: C, 70.67; H, 5.13; N, 8.91; S, 10.20. Found (%): C, 70.33, H, 5.02; N, 8.78; S, 10.07.

N,N-Dibenzyl-4-(1-((3,4-diphenyl-5-(phenyldiazenyl) thiazol-2(3*H*)-ylidene)hydrazono)ethyl)benzenesulfonamide (14): Procedure (A): A mixture of compound (**10**; 0.01 mol), 2-oxo-N',2-diphenylacetohydrazonoyl bromide (0.01 mol) and triethylamine 1 mL in ethanol 40 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol, dried and recrystallized from ethanol.

Procedure (B): Benzenediazonium chloride (prepared by adding sod. nitrite (0.01 mol) to aniline (0.01 mol) in conc. HCl 6 mL at (0-5 ºC) under stirring) was added drop wise with stirring to a cold solution of (**13**; 0.01 mol) in ethanol 20 mL containing sodium acetate (0.08 mol), the obtained product was collected and recrystallized. m.p. and mixed m.p. determined with authentic sample gave no depression.

Yield 66 %; m.p. 230-232 ºC; IR (KBr, ν_{max}, cm^{-1}): 3030 (CH aromatic), 2912 (CH aliphatic), 1338, 1158 (SO_2). ^{1}H NMR $CDCl_3$: 2.23 (s, 3H, CH_3), 4.37 (s, 4H, $(CH_2)_2N$), 7.05-7.99 (m, 25H, Ar-H), 7.81-8.02 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{43}H_{36}N_6O_2S_2$: C, 70.47; H, 4.95; N, 11.47; S, 8.75. Found (%): C, 70.24, H, 4.71; N, 11.24; S, 8.51.

N,N-Dibenzyl-4-(3-cyano-2-(methylthio)-7-(pyridin-3-yl)pyrazolo[1,5-a]pyrimidin-5-yl)benzenesulfonamide (19): A mixture of chalcone derivative (**3**; 0.01 mol) and 5-amino-3-(methylthio)-1*H*-pyrazole-4-carbonitrile (0.01 mol) in acetic acid 30 mL was heated under reflux for 5 h during the reflux

period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from dioxane.

Yield 73 %; m.p. 260-262 ºC; IR (KBr, ν_{max}, cm^{-1}): 3036 (CH aromatic), 2920 (CH aliphatic), 2218 (CN), 1342, 1158 (SO_2). ^1H NMR (DMSO-d_6): 2.67 (s, 3H, SCH_3), 4.37 (s, 4H, $(CH_2)_2N$), 7.06-7.27 (m, 15H, Ar-H, pyridine and CH-pyrimidine), 7.89-8.07 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{33}H_{26}N_6O_2S_2$: C, 65.76; H, 4.35; N, 13.94; S, 10.64. Found (%): C, 65.53, H, 4.12; N, 13.81; S, 10.51.

N,N-Dibenzyl-4-(1-((4-oxothiazolidin-2-ylidene)-hydrazono)ethyl)benzenesulfonamide (22): A mixture of compound (**5**; 0.01 mol), ethyl chloroacetate (0.01 mol) and sodium acetate (0.08 mol) in dioxane 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with water and recrystallized from ethanol/benzene.

Yield 78 %; m.p. 222-223 ºC; IR (KBr, ν_{max}, cm^{-1}): 3212 (NH), 3030 (CH aromatic), 2910 (CH aliphatic), 1690 (CO), 1338, 1158 (SO_2). ^1H NMR $CDCl_3$: 2.40 (s, 3H, CH_3), 3.89 (s, 2H, CH_2-thiazolidinone), 4.35 (s, 4H, $(CH_2)_2N$), 7.05-7.24 (m, 10H, Ar-H), 7.88-8.06 (dd, 4H, AB-system), 11.78 (s, 1H, NH). Anal. calcd. (%) for $C_{25}H_{24}N_4O_3S_2$: C, 60.95; H, 4.91; N, 11.37; S, 13.02. Found (%): C, 60.82, H, 4.77; N, 11.25; S, 12.80.

Ethyl 2-(2-((1-(4-(N,N-dibenzylsulfamoyl)phenyl) ethylidene)hydrazono)-4-oxothiazolidin-3-yl)acetate (24): Procedure (A): A mixture of thiocarbamoyl derivative (**5**; 0.01 mol), ethyl chloroacetate (0.022 mol) and sodium acetate (0.08 mol) in dioxane 50 mL was heated under reflux for 6 h during the reflux period, a faint yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol.

Procedure (B): A mixture of 4-oxothiazolidine derivative (**22**; 0.01 mol), ethyl chloroacetate (0.012 mol) and fused sodium acetate (0.08 mol) in dioxane 50 mL was heated under reflux for 6 h during the reflux period, a faint yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized, m.p. and mixed m.p. determined with authentic sample gave no depression.

Yield 81 %; m.p. 113-115 ºC; IR (KBr, ν_{max}, cm^{-1}): 3030 (CH aromatic), 2910 (CH aliphatic), 1710 (CO ester), 1692 (CO), 1340, 1158 (SO_2). ^1H NMR $CDCl_3$: 1.31 (t, 3H, CH_2-$\underline{CH_3}$), 2.32 (s, 3H, CH_3), 3.87 (q, 2H, $\underline{CH_2}$-CH_3), 4.10 (s, 2H, CH_2-thiazolidinone), 4.35 (s, 4H, $(CH_2)_2N$), 4.52 (s, 2H, CH_2COO), 7.05-7.23 (m, 10H, Ar-H), 7.89-8.05 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{29}H_{30}N_4O_5S_2$: C, 60.19; H, 5.23; N, 9.68; S, 11.08. Found (%): C, 60.06, H, 5.10; N, 9.47; S, 10.83.

N,N-Dibenzyl-4-(1-((5-(4-methoxybenzylidene)-4-oxothiazolidin-2-ylidene)hydrazono)ethyl)-benzene-sulfonamide (25): Procedure (A): A mixture of 4-oxothiazolidine derivative (**22**; 0.01 mol), 2-(4-methoxybenzylidene)-malononitrile (0.01 mol) and 0.5 mL of piperidine in dioxane 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol.

Procedure (B): A mixture of compound (**22**; 0.01 mol), 4-methoxybenzaldehyde (0.012 mol) and 0.5 mL of piperidine in ethanol 40 mL was heated under reflux for 5 h to give (**25**), m.p. and mixed m.p. determined with authentic sample gave no depression.

Yield 73 %; m.p. 141-143 ºC; IR (KBr, ν_{max}, cm^{-1}): 3210 (NH), 3029 (CH aromatic), 2900 (CH aliphatic), 1692 (CO), 1338, 1158 (SO_2). ^1H NMR $CDCl_3$: 2.38 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 4.36 (s, 4H, $(CH_2)_2N$), 7.05-8.07 (m, 19 H, Ar-H and C=CH), 10.56 (s, 1H, NH). Anal. calcd. (%) for $C_{33}H_{30}N_4O_4S_2$: C, 64.90; H, 4.95; N, 9.17; S, 10.50. Found (%): C, 64.77, H, 4.81; N, 9.03; S, 11.32.

Ethyl 2-(2-((1-(4-(N,N-dibenzylsulfamoyl)phenyl) ethylidene)hydrazono)-5-(4-methoxybenzylidene)-4-oxothiazolidin-3-yl)acetate (26): Procedure (A): A mixture of 4-oxothiazolidine derivative (**24**; 0.01 mol), 2-(4-methoxybenzylidene)malononitrile (0.01 mol) and 0.5 mL of piperidine in dioxane 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol.

Procedure (B): A mixture of compound (**24**; 0.01 mol), 4-methoxybenzaldehyde (0.012 mol) and 0.5 mL of piperidine in ethanol 40 mL was heated under reflux for 5 h to give (**26**), m.p. and mixed m.p. determined with authentic sample gave no depression.

Procedure (C): A mixture of compound (**25**; 0.01 mol), ethyl chloroacetate (0.012 mol) and fused sodium acetate (0.08 mol) in dioxane 50 mL was heated under reflux for 6 h during the reflux period; a faint yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized; m.p. and mixed m.p. determined with authentic sample gave no depression.

Yield 62 %; m.p. 198-200 ºC; IR (KBr, ν_{max}, cm^{-1}): 3100 (CH aromatic), 2916 (CH aliphatic), 1720 (CO ester), 1690 (CO cyclo), 1340, 1158 (SO_2). ^1H NMR $CDCl_3$: 1.35 (t, 3H, CH_2-$\underline{CH_3}$), 2.30 (s, 3H, CH_3), 3.61 (s, 3H, OCH_3), 3.82 (q, 2H, $\underline{CH_2}$-CH_3), 4.37 (s, 4H, $(CH_2)_2N$), 4.51 (s, 2H, CH_2COO), 7.23-8.11 (m, 19H, Ar-H and C=CH). Anal. calcd. (%) for $C_{37}H_{36}N_4O_6S_2$: C, 63.77; H, 5.21; N, 8.04; S, 9.20. Found (%): C, 64.54, H, 5.07; N, 7.90; S, 9.09.

Ethyl 4-(4-chlorophenyl)-5-((1-(4-(N,N-dibenzyl sulfamoyl)phenyl)ethylidene)hydrazono)-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (35): A mixture of methyl hydrazinecarbodithioate derivative (**9**; 0.01 mol), ethyl 2-bromo-2-(2-(4-chlorophenyl)hydrazono)acetate (**31**; 0.01 mol) and triethylamine 1 mL in ethanol 40 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol.

Yield 70 %; m.p. 142-143 ºC; IR (KBr, ν_{max}, cm^{-1}): 3030 (CH aromatic), 2918 (CH aliphatic), 1718 (CO ester), 1338, 1158 (SO_2). ^1H NMR $CDCl_3$: 1.46 (t, 3H, CH_2-$\underline{CH_3}$), 2.51 (s, 3H, CH_3), 4.37 (s, 4H, $(CH_2)_2N$), 4.51 (q, 2H, $\underline{CH_2}$-CH_3), 7.07-8.10 (m, 18H, Ar-H). Anal. calcd. (%) for $C_{33}H_{30}N_5O_4S_2Cl$: C, 60.03; H, 4.58; N, 10.61; S, 9.71. Found (%): C, 59.73, H, 4.36; N, 10.40; S, 9.40.

N,N-Dibenzyl-4-(1-((4-oxo-3-phenylthiazolidin-2-ylidene)hydrazono)ethyl)benzenesulfonamide (36): A mixture of compound (**10**; 0.01 mol), ethyl chloroacetate (0.012 mol) and fused sodium acetate (0.08 mol) in ethanol

50 mL was heated under reflux for 6 h during the reflux period a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol.

Yield 68 %; m.p. 240-242 ºC; IR (KBr, ν_{max}, cm^{-1}): 3032 (CH aromatic), 2920 (CH aliphatic), 1718 (CO), 1342, 1158 (SO_2). ^1H NMR $CDCl_3$: 2.30 (s, 3H, CH_3), 3.87 (s, 2H, CH_2-thiazolidinone), 4.35 (s, 4H, $(CH_2)_2N$), 7.05-7.48 (m, 15H, Ar-H), 7.84-7.99 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{31}H_{28}N_4O_3S_2$: C, 65.47; H, 4.96; N, 9.85; S, 11.28. Found (%): C, 65.24, H, 4.73; N, 9.72; S, 11.15.

N,N-Dibenzyl-4-(1-((5-((dimethylamino)methylene)-4-oxo-3-phenylthiazolidin-2-ylidene)hydrazono)ethyl) benzenesulfonamide (37): A mixture of 4-oxo-3-phenylthiazolidine derivative (**36**; 0.01 mol) and dimethylformamide dimethylacetal (DMF-DMA) (0.012 mol) in DMF 50 mL was heated under reflux for 6 h during the reflux period a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol/benzene.

Yield 71 %; m.p. 275-276 ºC; IR (KBr, ν_{max}, cm^{-1}): 3030 (CH aromatic), 2910 (CH aliphatic), 1700 (CO), 1337, 1158 (SO_2). ^1H NMR $CDCl_3$: 2.31 (s, 3H, CH_3), 3.23 (s, 6H, $(CH_3)_2N$), 4.35 (s, 4H, $(CH_2)_2N$), 7.05-7.56 (m, 16H, Ar-H and C=CH), 7.84-8.00 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{34}H_{33}N_5O_3S_2$: C, 65.47; H, 5.33; N, 11.23; S, 10.28. Found (%): C, 65.24, H, 5.10; N, 11.10; S, 10.05.

2-((1-(4-(N,N-Dibenzylsulfamoyl)phenyl)ethylidene) hydrazono)-4-oxo-N,3-diphenylthiazolidine-5-carbothioamide (39): To a cooled suspension of finely grounded KOH (0.01 mol) in dry DMF 40 mL the 4-oxo-3-phenylthiazolidine derivative (**36**; 0.01 mol) and subsequently phenyl isothiocyanate (0.01 mol) were added the reaction mixture was stirred overnight at room temperature, then treated with cold H_2O 50 mL and neutralized with 1 N HCl the resulting precipitated solid was collected by filtration, washed with water, dried and recrystallized from dimethyl formamide.

Yield 74 %; m.p. 298-300 ºC; IR (KBr, ν_{max}, cm^{-1}): 3220 (NH), 3030 (CH aromatic), 2920 (CH aliphatic), 1710 (CO), 1338, 1158 (SO_2). MS m/z (%): 703 [M^+] (22.1), 196 (100). Anal. calcd. (%) for $C_{38}H_{33}N_5O_3S_3$: C, 64.84; H, 4.73; N, 9.95; S, 13.67. Found (%): C, 64.60, H, 4.50; N, 9.71; S, 13.43.

N,N-Dibenzyl-4-(1-((5-(4-methoxybenzylidene)-4-oxo-3-phenylthiazolidin-2-ylidene)hydrazono)ethyl) benzenesulfonamide (40): A mixture of compound (**36**; 0.01 mol), 2-(4-methoxybenzylidene)malononitrile or 4-methoxybenzaldehyde (0.01 mol) and 0.5 mL of piperidine in dioxane 50 mL was heated under reflux for 4 h during the reflux period, a yellow crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized from ethanol/benzene.

Yield 72 %; m.p. 221-222 ºC; IR (KBr, cm^{-1}): 3010 (CH aromatic), 2918 (CH aliphatic), 1699 (CO), 1338, 1156 (SO_2). ^1H NMR $CDCl_3$: 2.38 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 4.37 (s, 4H, $(CH_2)_2N$), 7.05-7.98 (m, 24H, Ar-H and C=CH). Anal. calcd. (%) for $C_{39}H_{34}N_4O_4S_2$: C, 68.20; H, 4.99; N, 8.16; S, 9.34. Found (%): C, 68.07, H, 4.76; N, 8.03; S, 9.11.

N,N-Dibenzyl-4-(1-((5-(*bis*(methylthio)methylene)-4-oxo-3-phenylthiazolidin-2-ylidene)hydrazono)ethyl) benzenesulfonamide (43): To a cooled suspension of finely grounded KOH (0.01 mol) in dry DMF 40 mL the 4-oxo-3-phenylthiazolidine derivative (**36**; 0.01 mol) and subsequently carbon disulfide (0.012 mol) were added the reaction mixture was stirred overnight at room temperature, then treated with the methyl iodide (0.021 mol) and left at room temperature for an additional 24 h the reaction mixture was then triturated with cold H_2O 50 mL and neutralized with 1 N HCl the resulting precipitated solid was collected by filtration, washed with water, dried and recrystallized from ethanol/benzene.

Yield 75 %; m.p. 140-142 ºC; IR (KBr, ν_{max}, cm^{-1}): 3010 (CH aromatic), 2915 (CH aliphatic), 1697 (CO), 1338, 1156 (SO_2). ^1H NMR (DMSO-d_6): 2.37 (s, 3H, CH_3), 2.80 (s, 6H, $2SCH_3$), 4.36 (s, 4H, $(CH_2)_2N$), 7.03-7.58 (m, 15H, Ar-H), 7.85-7.95 (dd, 4H, AB-system). Anal. calcd. (%) for $C_{34}H_{32}N_4O_3S_4$: C, 60.69; H, 4.79; N, 8.33; S, 19.06. Found (%): C, 60.46, H, 4.56; N, 8.10; S, 18.73.

N,N-Dibenzyl-4-(1-((5-((5-chloro-2-methoxyphenyl) diazenyl)-4-oxo-3-phenylthiazolidin-2-ylidene)hydrazono) ethyl)benzenesulfonamide (44): 5-Chloro-2-methoxybenzenediazonium chloride (prepared by adding sod. nitrite (0.01 mol) to 5-chloro-2-methoxyaniline (0.01 mol) in conc. HCl 6 mL at (0-5 ºC) under stirring) was added drop wise with stirring to a cold solution of (**36**; 0.01 mol) in pyridine, the obtained product was collected and recrystallized from ethanol.

Yield 73 %; m.p. 261-263 ºC; IR (KBr, ν_{max}, cm^{-1}): 3032 (CH aromatic), 2918 (CH aliphatic), 1702 (CO), 1338, 1158 (SO_2). MS m/z (%): 737 [M^+] (12.3), 196 (100). Anal. calcd. (%) for $C_{38}H_{33}ClN_6O_4S_2$: C, 61.90; H, 4.51; N, 11.40; S, 8.70. Found (%): C, 61.77, H, 4.40; N, 11.28; S, 8.57.

Antimicrobial and antifungal screening: The prepared compounds were evaluated for their antimicrobial activity using the agar diffusion technique[41,42]. A mg/mL solution in DMF was used. The test organisms were gram-positive *Bacillus subtilis* (NCTC-1040), *Staphylococcus aureus* (NCTC-7447), sarcina maxima (ATCC-33910); gram-negative *Klebsiella peneumonia* (NCIMB-9111), *Salmonella*, *Pseudomonas aeruginosa* (ATCC-10145) and antifungal activity, filamentous fungi *Rhizopus*, *Asperigillus fumigatus*. DMF showed no inhibition zones. The reference antibiotics were ampicillin (AMD) and calforan. The inhibition zones (IZ) of these compounds are listed in Table-1.

RESULTS AND DISCUSSION

Heating of 4-acetyl-N,N-dibenzylbenzenesulfonamide **1**[26] with pyridine-3-carboxaldehyde in the presence of a catalytic amount of piperidine in ethanol afforded the corresponding 4-[3-(pyridine-3-yl)acryloyl]benzenesulfonamide derivative **2**. The reactivity of compound **2** towards carbon nucleophile is studied. Thus compound **2** reacted with ethyl acetoacetate in the presence of a catalytic amount of piperidine in ethanol solution to afford a reaction product **4**, which exhibited singlet signal of two protons of cyclohexanone at δ = 2.67 ppm and D_2O exchangeable signal at δ = 10.35 ppm due to (OH) proton based on the data obtained the reaction product was formulated as mixture of ethyl-4-(4-(N,N-dibenzylsulfamoyl)phenyl)-6-oxo-2-(pyridine-3-yl)cyclohexa-1,4-dienecarboxylate **4a** and its enol form **4b**. The formation of **4** assumed to proceed *via*

TABLE-1
ANTIMICROBIAL AND ANTIFUNGAL ACTIVITIES; INHIBITION ZONE DIAMETER (mm)

Comp. No.	Gram-positive			Gram-negative			Filamentous fungi	
	B. subtilis (NCTC-1040)	*S. aureus* (NCTC-7447)	*S. maxima* (ATCC-33910)	*K. pneumonia* (NCIMB-9111)	*Salmonella*	*P. aeruginosa* (ATCC-10145)	*Rhizopus*	*A. fumigatus*
2	23	21	20	22	20	20	19	22
4	21	22	19	20	22	23	20	20
5	12	14	16	11	12	13	13	11
6	19	20	18	18	17	19	18	19
7	17	17	18	19	18	16	18	19
8	17	17	18	19	18	18	18	19
9	19	18	18	19	17	17	17	17
10	18	19	17	17	18	18	17	16
11a	17	15	14	13	15	14	11	10
11b	14	13	17	13	15	12	12	11
11c	14	15	15	18	13	12	13	15
12	17	18	18	19	16	17	18	19
13	19	18	18	16	17	18	17	17
14	19	19	18	17	17	18	19	18
19	23	21	22	20	24	23	20	19
22	17	17	19	18	18	20	18	19
24	20	18	19	19	18	17	18	19
25	21	22	20	20	19	20	20	19
26	22	20	21	23	22	22	21	19
35	23	21	21	20	19	18	19	18
36	18	19	19	20	21	18	19	18
37	23	22	21	20	20	22	20	19
39	20	20	21	22	21	20	19	20
40	13	12	11	15	12	15	14	16
43	20	20	22	21	19	20	20	20
44	22	23	21	20	20	19	19	20
Ampicillin (AMD) 25 mg	26	25	27	27	26	25	25	25
calforan 30 mg								

24-20 mm: high active, 19-18 mm: moderate active, 17-12 mm: weak active.

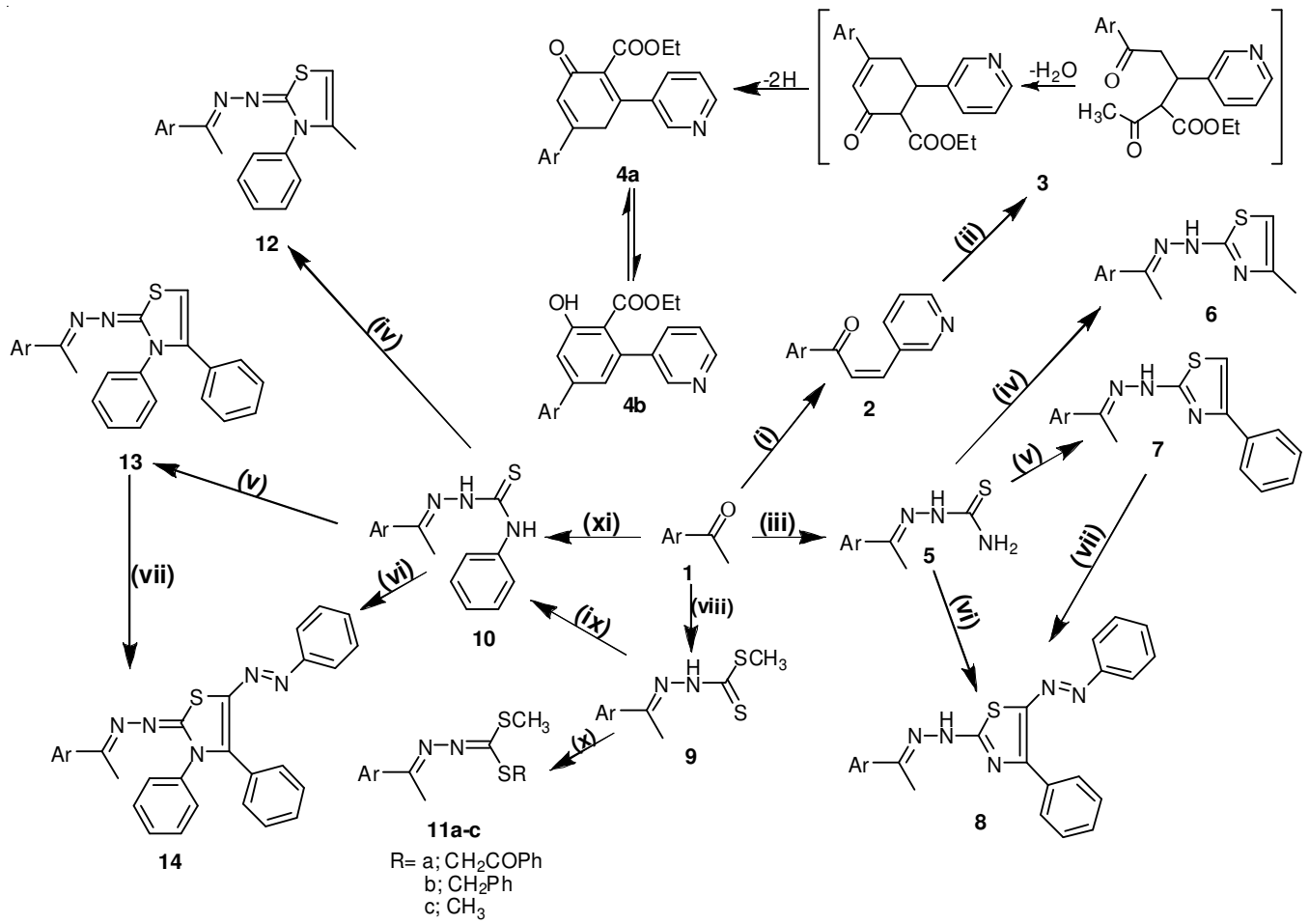
initial addition of active methylene to the activated double bond to give the non-isolable 1,5-dicarbonyl intermediate **3**, which underwent intramolecular cyclic condensation followed by oxidation to give 3-ketoester **4a** which tautomerise into aromatic phenolic ester **4b**, (*cf.* **Scheme-I** and experimental section).

Condensation of **1** with thiosemicarbazide and phenylthiosemicarbazide afforded the corresponding 2-ethylidenehydrazinecarbothioamide and phenylthioamide derivatives **5, 10**, respectively, these thiosemicarbazones where used for the synthesis of thiazole derivatives thus the reaction of compounds **5, 10** with double electrophilic reagents namely (chloro acetone, phenacyl bromide and 2-oxo-N',2-diphenylacetohydrazonoyl bromide) afforded the corresponding thiazoles **6-8** and 3-phenyl-3-hydrogenthiazole derivatives **12-14**, respectively, (*cf.* **Scheme-I** and experimental section).

An equivocal support for structures **8, 14** were achieved *via* its synthesis through coupling of benzenediazonium chloride with compounds **7, 13** in ethanol sodium acetate cold solution. Treatment of **1** with methylhydrazinecarbodithioate afforded ethylidenehydrazinecarbodithioate methyl ester derivative **9** which on reaction with phenacyl bromide, benzyl chloride and methyl iodide in ethanol triethylamine solution to produce the corresponding alkylthio derivatives **11a-c**, respectively. Treatment of compound **9** with aniline give a product which formulated as 2-ethylidenephenylhydrazine carbothioamide derivative, that is identical in all respects (m.p., mixed m.p. and spectral data) to compound **10**, (*cf.* **Scheme-I** and experimental section).

One of the most utilized synthesis approaches to the pyrazolo[1,5-a]pyrimidines is the reaction of α,β-unsaturated ketone with 3 or 5-aminopyrazoles[27-30]. Thus, chalcone **2** reacted with 5-amino-3-methylthio-1*H*-pyrazole-4-carbonitrile **15**[31] in acetic acid under reflux to yield a product which formulated as 7-(pyridine-3-yl)pyrazolo[1,5-a]pyrimidine derivative **19** or its 5-substituted isomer **20**. Structure **19** is considered most likely for the product based on similarity to the well established behaviour of α,β-unsaturated carbonyls towards aminopyrazole[32,33]. The formation of **19** was produced *via* initial alkylation at (N1) to give the non-isolable intermediate **16** and subsequent ring closed to **18** *via* water elimination followed by aromatization *via* elimination of hydrogen molecule. Alternatively condensations of carbonyl function in **2** with exocyclic amino group of **15** to give **17** and intramolecular cyclization to **18** followed by aromatization to **19**, (*cf.* **Scheme-II** and experimental section).

Cyclocondensation of compound **5** with an equimolar ratio of ethyl chloroacetate in ethanol sodium acetate under reflux afforded the corresponding 4-oxothiazolidine derivative **22**, but when compound **5** was treated with two moles of ethyl chloroacetate under the similar reaction conditions gave 4-



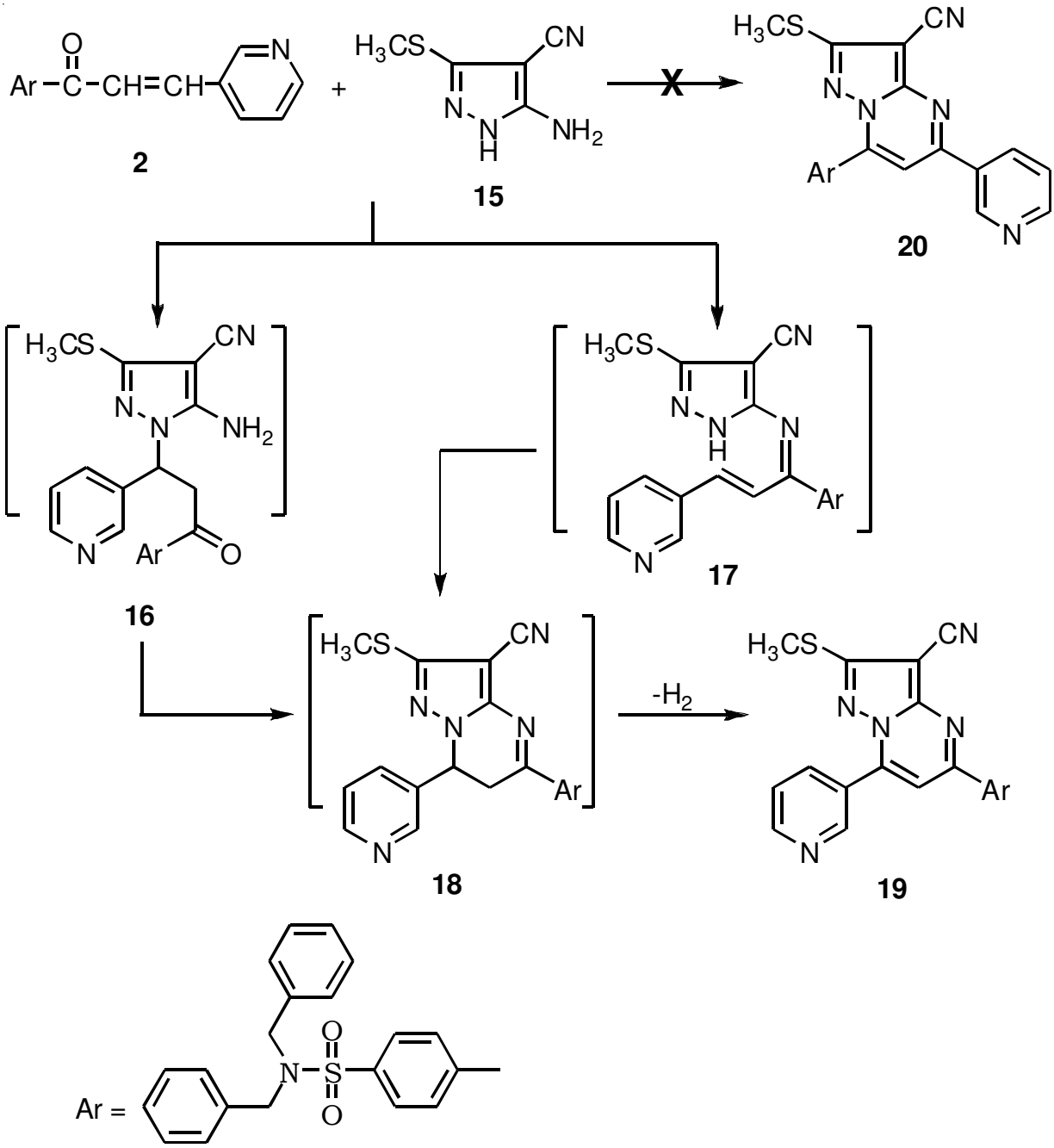
Scheme-I

oxo ethylidenehydrazonothiazolidin-3-yl acetic acid ethyl ester **24**. The formation of **22**, **24** were assumed to proceed *via* elimination of ethanol from intermediates ethoxycarbonylmethyl and *bis*(ethoxycarbonylmethyl) derivatives **21**, **23**, respectively. Structure **24** was further confirmed unequivocally by an independent synthesis from the reaction of **22** with ethyl chloroacetate in dioxane sodium acetate solution, (*cf.* **Scheme-III** and experimental section).

Efforts to cyclize **22**, **24** with 2-(4-methoxybenzylidene)malononitrile to afford enaminonitriles **29**, **30** were not successful. Instead the products were identified as N,N-dibenzyl-4-(-1-((-5-(4-methoxybenzylidene)-4-oxothiazolidin-2-ylidene)hydrazono)ethyl)benzenesulfon amide (**25**) and ethyl 2-(2-((1-(4-(N,N-dibenzylsulfamoyl) phenyl)ethylidene)-hydrazono)-5-(4-methoxybenzylidene)-4-oxothiazolidin-3-yl)acetate (**26**) were obtained, respectively. Structures **25**, **26** were further confirmed unequivocally by an independent synthesis from the reaction of **22**, **24** with 4-methoxybenzaldehyde in ethanolic piperidine solution, another evidence for the structure of **26** can be prepared from the reaction of **25** with ethyl chloroacetate in dioxane contains fused sodium acetate solution. The formation of **25** from 4-oxothiazolidine derivatives **22** and 2-(4-methoxybenzylidene)malononitrile can be explained by an addition of active methylene group of **22** at the olefinic bond of arylidene forming the intermediate **28**, which undergoes spontaneous elimination of malononitrile to give the final product **25**.

Also the formation of **26** from 4-oxothiazolidine (**24**) and 4-methoxybenzaldehyde two possible isomeric structure were proposed **26**, **27**, the absence of the signal for CH_2-thiazole around $\delta = 4.1$ ppm, together with the existence of the signal methylene of acetate moiety in its usual position at $\delta = 4.5$ ppm, in its ^{1}H NMR spectrum provided a firm support for the structure **26** and ruled out the other possible isomer **27**, (*cf.* **Scheme-III** and experimental section).

The reaction of methyldithioester **9** with hydrazonyl bromide derivative[34-40] (**31**) in ethanol in the presence of triethyl-amine afforded a product which analyzed correctly

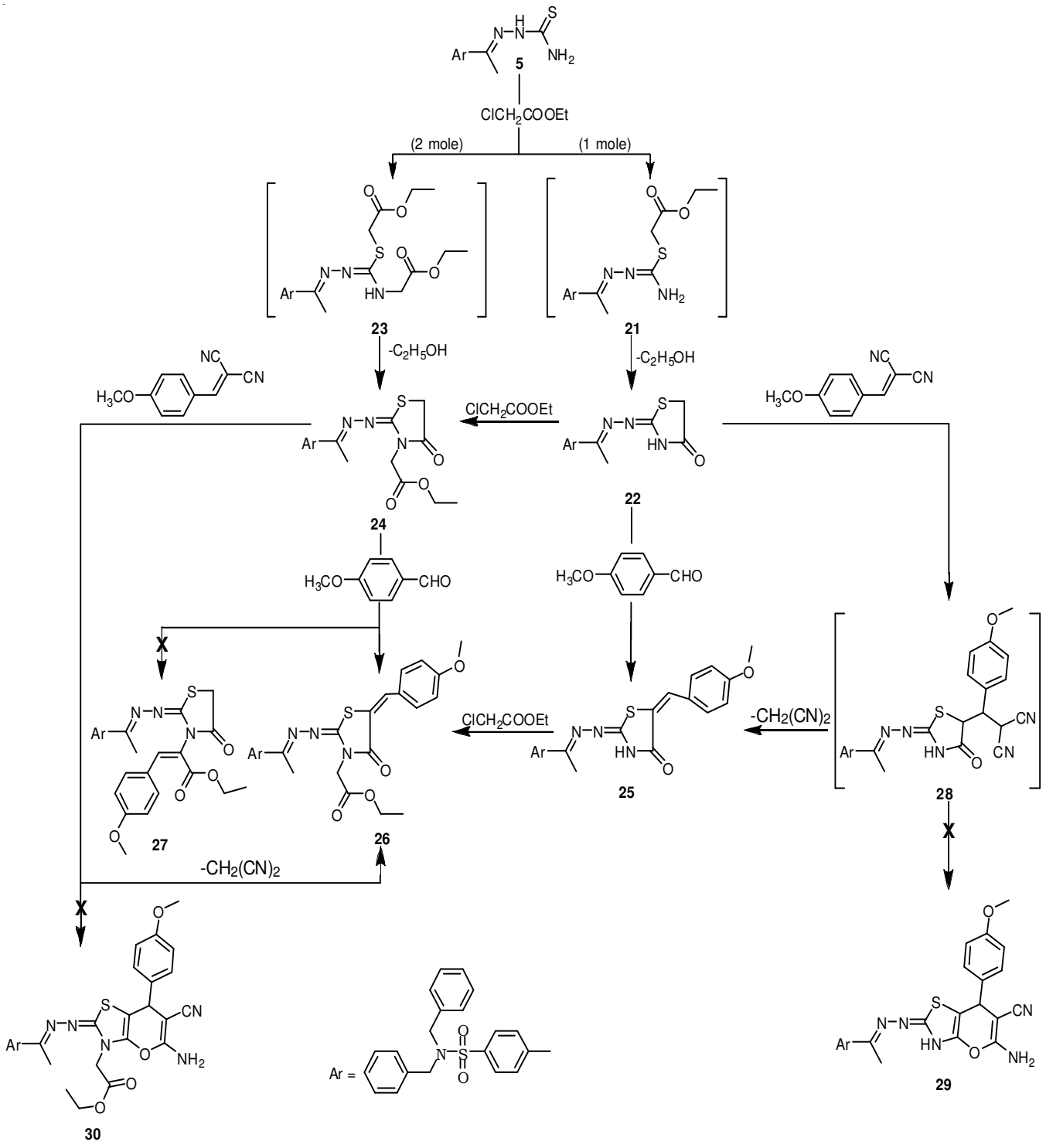


Scheme-II

for ($C_{33}H_{30}N_5O_4S_2Cl$). The structure of the latter product was identified as ethyl 4-(4-chlorophenyl)-5-((1-(4-(N,N-dibenzylsulfamoyl)phenyl)ethylidene)hydrazono)-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (**35**). The formation of compound **35** can be exhibited *via* elimination of methylthiol from the corresponding cyclo adduct **33**, which is assumed to be formed from the 1,3-dipolar cyclic addition of nitrile imine **32** (produced from **31** and triethylamine *in situ*) to the (C=S) double bond in **9**. Alternatively, the formation of **35** can also be explained by the stepwise path involving substitution to give the acyclic hydrazone **34**, which readily cyclized to give **33** which losses methylthiol to give the final product **35**, all attempts to isolate the cyclic adduct **33** or the open chain hydrazone **34** were unsuccessful. (*cf.* **Scheme-IV** and experimental section).

Cyclocondensation of phenyl thiosemicarbazone derivative **10** with ethyl chloroacetate in ethanol fused sodium acetate solution afforded 4-oxothiazolidine derivative **36**, which reacted with DMF-DMA in dry DMF to produce enaminone derivative **37**. The base promoted nucleophilic addition of the **36** to equimolar amount of phenyl isothiocyanate in dry DMF in the presence of KOH at room temperature afforded the non-isolable potassium salt **38**, which was acidified with 1 N HCl to give the compound **39**.

Efforts to cyclize **36** with 2-(4-methoxybenzylidine)-malononitrile to afford enaminonitrile **41** were not successful instead the product was identified as **40**, the latter structure was further confirmed by an independent synthesis from direct interaction of **36** with 4-methoxybenzaldehyde. Additionally

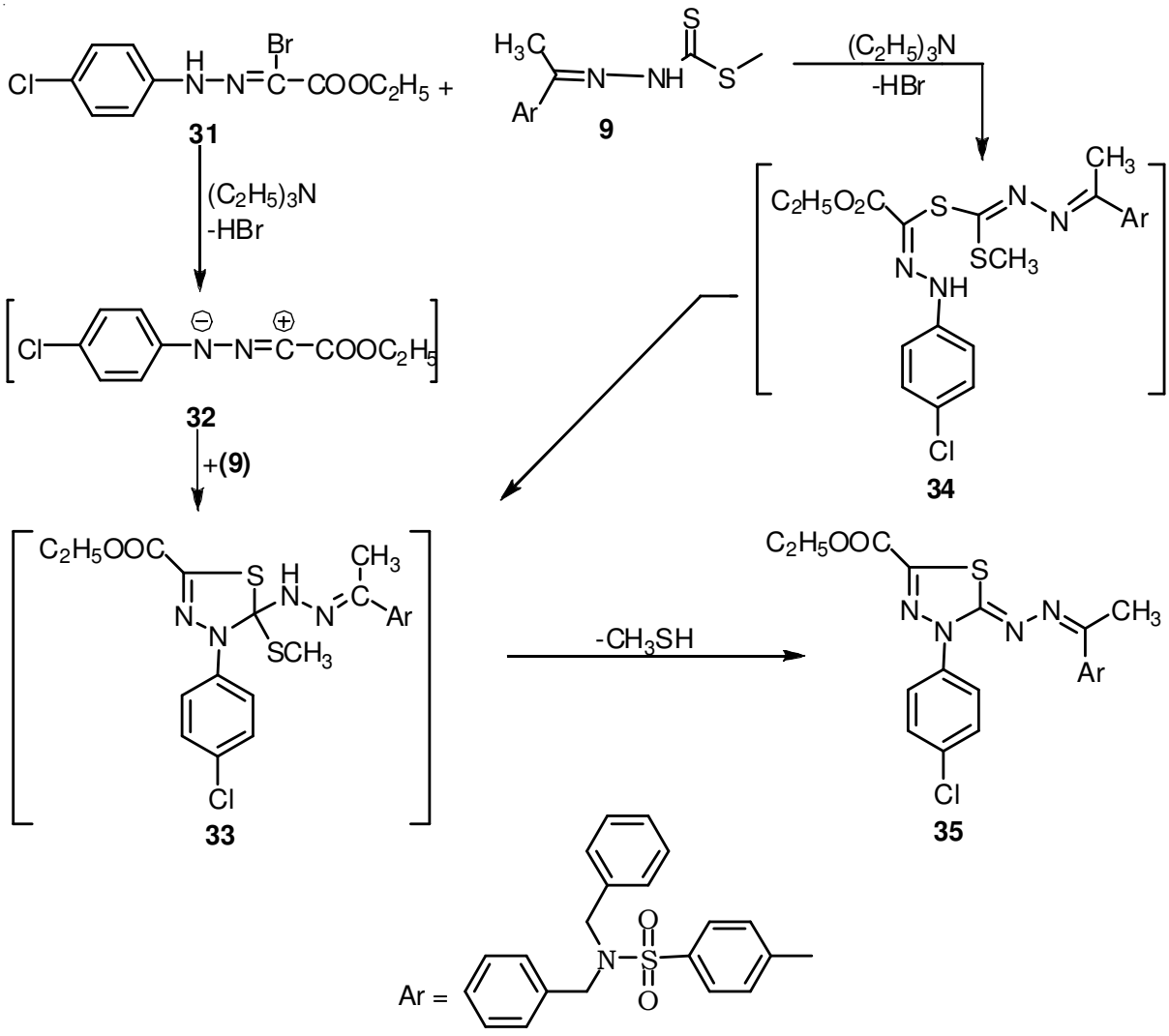


Scheme-III

when 4-oxothiazolidine derivative **36** was reacted with CS_2 in presence of KOH in DMF afforded **43** *via* the methylation of the non-isolated potassium dithioate **42** with two moles of CH_3I.

Finally, the methylene group in 4-oxothiazolidine derivative **36** proved to be highly reactivity, thus compound **36** underwent coupling with equimolar amount of 5-chloro-2-methoxybenzenediazonium chloride in pyridine solution at (0-5 ºC) to afford a coloured product **44**, (*cf.* **Scheme-V** and experimental section).

Antimicrobial and antifungal activities: The results of antimicrobial screening (Table-1) show that compounds (**2, 4, 19, 25, 26, 35, 37, 39, 43, 44**) are highly active against gram positive bacteria (*B. subtilis*, *S. aureus*, *S. maxima*), gram negative bacteria (*K. pneumonia*, *Salmonella*, *P. aeruginosa*) and filamentous fungi (*Rhizopus*, *A. fumigatus*). While the compounds (**6-8**, **10**, **12-14**, **22**, **24**, **36**) showed the moderate activity and the remaining compounds (**5**, **9**, **11a-c**, **40**) showed the weak activity (Table-1).



Scheme-IV

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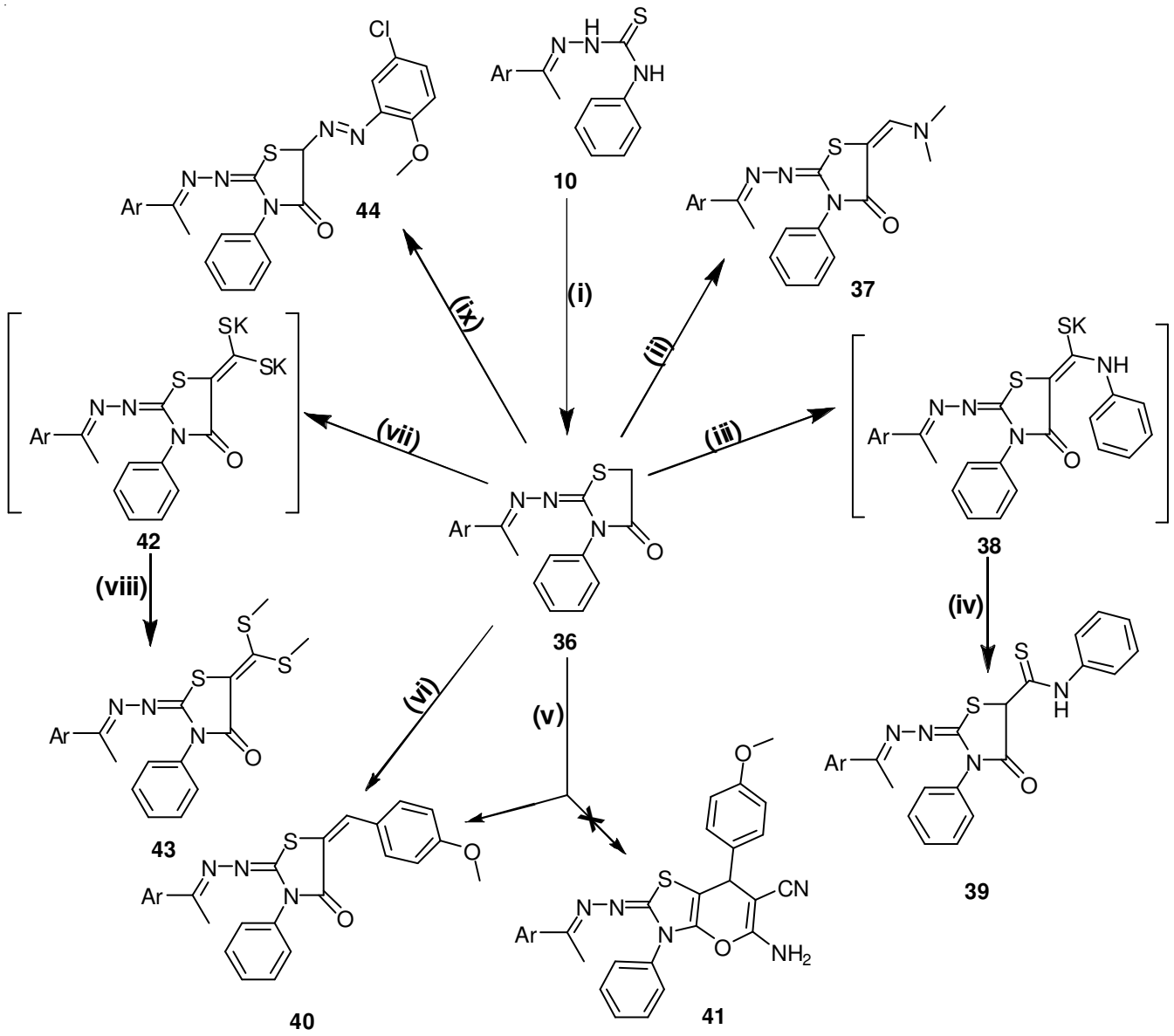

(i) $ClCH_2COOEt$ / CH_3COONa

(ii) $(H_3CO)_2CH\text{-}N(CH_3)_2$ / DMF

(iii) PhNCS / DMF-KOH

(iv) HCl / 1N

(v) H_3CO–C$_6$H$_4$–$CH{=}C(CN)_2$

(vi) H_3CO–C$_6$H$_4$–CHO

(vii) 2 CS_2 / DMF-KOH

(viii) 2 CH_3I

(ix) H_3CO–C$_6$H$_3$(N=N-Cl)–Cl

Ar =

Scheme-V

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