Thiazepine derivatives like Diltiazem (215), clentiazem (216), have synthesized and reported for anticoagulant (217), antiarteriosclerotic (218), antihypertensive (221), antidepressant etc. activities were comparative study with diazepam (224), clobazam (223) etc. we have synthesized a series of new 1, 4-Thiazepines.

Thiazepine derivatives are a nondihydropyridine (non-DHP) one of the class of drugs, therapeutically applicable for hypertension, angina pectoris, and in the treatment of many types of arrhythmia.

Thiazepine is effective in preventive medication for migraine. They are of class III antianginal drug and class IV antiarrhythmic (227).

Thiazepine derivatives are rapidly metabolized and act as an inhibitor of the enzyme.

Thiazepine is effective in preventive medication for migraine. They are of class III antianginal drug and class IV antiarrhythmic (227). Thiazepine derivatives like Diltiazem (215), clentiazem (216), have synthesized and reported for anticoagulant (217), antiarteriosclerotic (218), antihypertensive (221), antidepressant etc. activities were comparative study with diazepam (224), clobazam (223) etc. we have synthesized a series of new 1, 4-Thiazepines.
REACTIONS:

Scheme – 4.1 Synthesis of 1,4-Thiazepine Derivatives

Where R as: (4a) -H (4b) 4-OCH₃ (4c) 2- OCH₃ (4d) 2-OH (4e) 2-Cl (4f) 4-Cl (4g) 2-NO₂ (4h) 3-Br (4i) 3,4-(OCH₃)₂ (4j) 3,4,5-(OCH₃)₃
EXPERIMENTAL

(4a) PREPARATION OF 2-METHYL-5-NITRO-N-(4-(3-(2-PHENYL-2,3-DIHYDRO BENZO[b][1,4]THIAZEPIN-1-YL)PHENOXY)PHENYL) BENZENE - SULFONAMIDE

A blend of (E)-N-(4-(3-cinnamoylphenoxy)phenyl)-2-methyl-5-nitro-benzene sulfonamide (4.2 g, 0.01 mol) with 2-aminobenzenethiol (1.1 g, 0.011 mol), dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70°C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4b) PREPARATION OF N-(4-(3-(2-(4-METHOXYPHENYL)-2,3-DIHYDRO - BENZO[b][1,4]THIAZEPIN-1-YL)PHENOXY)PHENYL)-2-METHYL-5-NITRO - BENZENE SULFONAMIDE.

A blend of (E)-N-(4-(3-(4-methoxyphenyl) acryloyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (4.5 g) with 2-aminobenzenethiol (1.4 g), dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70°C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4c) PREPARATION OF N-(4-(3-(2-(2-METHOXYPHENYL)-2,3-DIHYDRO - BENZO[b][1,4]THIAZEPIN-1-YL)PHENOXY)PHENYL)-2-METHYL-5 - NITROBENZENE SULFONAMIDE.

A blend of (E)-N-(4-(3-(3-(2-methoxyphenyl)acryloyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (4.5 g, 0.01 mol) with 2-aminobenzenethiol (1.4 g), dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70°C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4d) PREPARATION OF N-(4-(3-(2-(2-HYDROXYPHENYL)-2,3 - DIHYDROBENZO[b][1,4]THIAZEPIN-1-YL)PHENOXY)PHENYL)-2-METHYL-5-NITROBENZENE SULFONAMIDE.

A blend of (E)-N-(4-(3-(2-hydroxyphenyl)acryloyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (4.5 g, 0.01 mol) with 2-aminobenzenethiol (1.4 g) dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70°C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

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(4e) PREPARATION OF N-(4-(3-(2-CHLOROPHENYL)-2,3-DIHYDROBENZO[b][1,4]THIAZEPIN-1-YL)PHENOXY)PHENYL)-2-METHYL-5-NITROBENZENE SULFONAMIDE.

A blend of (E)-N-(4-(3-(2-chlorophenyl)acryloyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (4.6 g, 0.01 mol) with 2-aminobenzenethiol (1.4 g, dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70 °C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4f) PREPARATION OF N-(4-(3-(2-CHLOROPHENYL)-2,3-DIHYDROBENZO[b][1,4]THIAZEPIN-4-YL)PHENOXY)PHENYL)-2-METHYL-5-NITROBENZENE SULFONAMIDE.

A blend of (E)-N-(4-(3-(4-chlorophenyl)acryloyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (4.6 g, 0.01 mol) with 2-aminobenzenethiol (1.4 g, 0.011 mol), dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70 °C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4g) PREPARATION OF 2-METHYL-5-NITRO-N-(4-(3-(2-NITROPHENYL)-2,3-DIHYDROBENZO[b][1,4]THIAZEPIN-4-YL)PHENOXY)PHENYL) BENZENE SULFONAMIDE.

A blend of (E)-2-methyl-5-nitro-N-(4-(3-(2-nitrophenyl) acryloyl) phenoxy) phenyl) benzene sulfonamide (4.7 g, 0.01 mol) with 2-aminobenzenethiol dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70 °C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4h) PREPARATION OF N-(4-(3-(2-(3-BROMOPHENYL)-2,3-DIHYDROBENZO[b][1,4]THIAZEPIN-4-YL)PHENOXY)PHENYL)-2-METHYL-5-NITROBENZENE SULFONAMIDE.

A blend of (E)-N-(4-(3-(3-bromophenyl)acryloyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (5.1 g, 0.01 mol) with 2-aminobenzenethiol (1.4 g dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70 °C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4i) PREPARATION OF N-(4-(3-(2-(3,4-DIMETHOXYPHENYL)-2,3-DIHYDROBENZO[b][1,4]THIAZEPIN-1-YL)PHENOXY)PHENYL)-2-METHYL-5-NITROBENZENE SULFONAMIDE.

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A blend of (E)-N-(4-(3-(3,4-dimethoxyphenyl)acryloyl)phenoxy)phenyl)-2-methyl-5-nitrobenzenesulfonamide (5.1 g, 0.01 mol) with 2-aminobenzethiol (1.4 g, dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70°C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).

(4j) PREPARATION OF 2-METHYL-5-NITRO-N-(4-(3-(2,3,4,5-TRIMETHOXYPHENYL)-2,3-DIHYDROBENZO[b]1,4[1.4]THIAZEPIN-4-YL) PHENOXY) PHENYL) BENZENE SULFONAMIDE.

A blend of (E)-2-methyl-5-nitro-N-(4-(3-(3,4,5-trimethoxyphenyl) acryloyl) phenoxy) phenyl)benzene sulfonamide (5.2 g), 2-aminothiophenyl (1.4 g, dry alcohol and AcOH as a glacial form, this stuff are heated to refluxing temperature for two hours at 70°C. Now cool the reaction stuff with ice-bath and then filter it after separation and finally crystallized by using ethanol (90%).
### Table No – 4.1 Analytical Data of 1,4-Thiazepine Derivatives

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<th>R</th>
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<th>Molecular Weight (g/mol)</th>
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<th>M.P. °C</th>
<th>C %</th>
<th>H %</th>
<th>N %</th>
<th>Found C %</th>
<th>H %</th>
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