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Microwave-assisted synthesis of oxadiazole and thiazolidine derivatives

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ABSTRACT

1,3,4-oxadiazole derivatives constitute a group of biologically important compounds that have been used as analgesic, anti-inflammatory, antibacterial, antifungal, antispasmodic, or psychotropic drugs in addition to their role in plant growth regulation and monoamine oxidase inhibition. This study focused on the use of microwaves in the synthesis of oxadiazole derivatives containing thiazolidinediones, which are promising for use as new drugs. For the first time, thiazolidinediones were synthesized by reacting benzaldehyde with cysteine with very good yield using microwave radiation at 340 watt. Subsequently, thiazolidine hydrazide (L3) was synthesized, which was reacted with carboxylic acid or carbon disulfide to be obtained in the presence of a base oxadiazole derivatives L4, L5, L6, L7, L8. The subjectivity of the synthetic compounds was verified by melting point measurement, E. Analy, and analysis using thin layer chromatography (TLC), FT-IR, mass spectrometry (EI-MS), and NMR spectroscopy.

Key words: oxadiazole, thiazolidinedione, microwave radiation, thiazolidine hydrazide, cysteine.

INTRODUCTION

Malignant growth is one of the destructive sicknesses that causes the demise of millions of individuals consistently [1-12]. There are different sorts of disease like leukemia, melanoma, non-Hodgkin's lymphoma, bosom malignant growth, thyroid disease, lung, bronchial, kidney, renal pelvis disease, and so forth, all of which can ultimately prompt passing. Boundless chemotherapy and radiotherapy are not just compelling in cutting edge stages, they likewise produce extra side results for patients that might prompt passing. This requires extraordinary work to foster elective helpful systems that can successfully treat the sickness without aftereffects or with insignificant incidental effects [2-18]. Most drug arrangements and naturally dynamic mixtures are heterocyclic mixtures. There are significant underlying elements accessible in heterocyclic rings that keep on being utilized to incredible benefit by the drug business. What recognizes these rings is that they show various exercises by changing the replacements on these rings [3-22].

1,3,4-oxadiazole, heterocyclic rings bearing one oxygen and two nitrogen iotas in a pentagonal ring. They are found as restricted metabolites. 1,3,4-oxadiazole is useful in therapeutic science because

of its low lipid solvency, and this ring is likewise referred to act as a frail base. The presence of two kinds of nitrogen molecules, pyridine, lessens the fragrance of the ring so much that it acts as a formed diene [4-,23-2-30]. Due to the somewhat low electron thickness on the carbon particle, electrophilic replacement responses are undeniably challenging at the carbon molecule. This low electron thickness on the carbon iota is because of the idea of the electron mists applied from nitrogen iotas of the pyridine type [8-10,20-39].

Because of its wide applications, specialists overall are associated with the plan and advancement of oxadiazole-inferred drugs [2-10,35-44]. The most well-known strategy for its amalgamation includes the response between corrosive hydrazides and corrosive chlorides/carboxylic acids or direct cyclization of diacyl hydrazines within the sight of different hydrophobic specialists, for example, phosphorous oxychloride, thionyl chloride, phosphorous pentaoxide and phosphorous corrosive. For this large number of reasons, the significance of amalgamation and advancement of this kind of compound in the field of pharmacological science is featured [8-12, 42-55].

Microwave-helped natural combination is a promising new procedure in natural union. This innovation gives a perfect, basic, proficient, fast and prudent strategy for the union of various new natural atoms [5-15, 54-66]. It was incorporated utilizing microwave radiation for a huge scope to acquire unadulterated response items. This innovation is a significant methodology towards green science since this innovation is all the more harmless to the ecosystem and utilizations this innovation in the research center and can possibly essentially impact the fields of combinatorial science, therapeutic science and medication advancement processes [6-18,66-80]. The customary strategy for natural union as a rule requires a more extended warming time, hardware arrangement which brings about greater expense for amalgamation and extreme utilization of solvents or reagents prompts ecological contamination. The development of green science holds the vital potential to diminish side-effect, decrease squander creation and lower energy costs.[13-28,77-81].

MATERIAL AND METHODS

The importance and objectives of the research:

One of the issues of natural combination is the yield, immaculateness, the utilization of stores, as well as the gear for every response. The utilization of microwave innovation is viewed as a significant leap forward in natural amalgamation, as the utilization of microwaves scattered the greater part of the past issues or diminished them to an astounding degree. It helped increment the yield in the responses in which it was utilized, improved the selectivity of the items and incredibly diminished the optional items, notwithstanding Limit extreme utilization of natural stores. What is significant or considered progressive is to diminish the synthetic response time from hours to minutes, and lessen the expense of energy, and the expense of glass gadgets for every response.

The exploration focuses on the natural amalgamation of oxadiazoles and thiazolidine subordinates from the response of benzaldehyde with cysteine in the conventional manner and contrasting it and blend involving microwave radiation as far as response time, yield, virtue and selectivity.

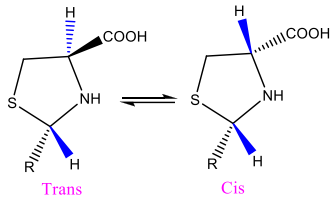
Research method and materials:

Different methods were utilized in this review: recrystallization, liquefying point meter, TLC meager layer chromatography, FT-IR spectroscopy, 1H-and 13C NMR, mass spectrometry (EI-MS), microwave at 340watt. The examination was led from 2018 to 2021 at the Faculty of Pharmacy at Al-Rasheed University,

• Combination of 2-phenylthiazolidine-4-carboxylic corrosive

Blend 0.01mM benzaldehyde with 0.01mM cysteine in a combination of 10ml of water and 50ml of ethanol. Mix well and afterward set back refining at a temperature of 95 ° C for 19 hours. The outcome is a white encourage that is sifted and washed well with diethyl ether and afterward recrystallized from water and ethanol in the proportion.

of one volume of water to three volumes of ethyl joule



• Union of 3-acetyl, 2-phenylthiazolidine-4-carboxylic corrosive 3-Acetyl-2-Phenyl thiazolidine-4-carboxylic corrosive (L1)

0.01 mol (2.09 g) of (L) is disintegrated in (40 mL) of (6%) cold Na2CO3 in an ice shower, trailed by the expansion of 0.04 mol (3.77 mL) of acidic anhydride in drops. The combination was blended for 1 hour and fermented with hydrochloric corrosive, extricated with ethyl acetic acid derivation, dissipated and left a white strong, then, at that point, washed with water, dried and recrystallized with ethyl liquor [29] to give the base material for the amalgamation (L2). Amalgamation of Ethyl 3-Acetyl-2-Phenyl thiazolidine-4-carboxylate (L2)

A combination of 0.01 mol (L1) and 30 mL ethanol and drops of concentrated H2SO4 was put under reflux for 6 hours. The item was separated and vanished to get a yellow oil [16]. Utilizing a microwave, it is under 340 watt radiation for a time of just 4 minutes.

• Synthesis of 3-Acetyl,2-phenylthiazolidine-4-carbohydrazide 3-Acetyl-2-Phenyl thiazolidine-4-carbohydrazide (L3)

L2 arrangement in (30 ml) of ethanol was added to (5 ml) of (80%) hydrazine hydrate. The combination was set under reflux for 26 hours, and the arrangement was dissipated to give a white encourage that recrystallized a blend with water: ethanol (2: 8) [31], to give (L3). While utilizing the microwave, it is under 340watt radiation for a time of just 15 minutes.

L2 solution in (30 ml) of ethanol was added to (5 ml) of (80%) hydrazine hydrate. The mixture was placed under reflux for 26 hours, and the solution was evaporated to give a white precipitate that recrystallized a mixture with water: ethanol (2: 8) [31], to give (L3). While using the microwave, it is under 340watt radiation for a period of only 15 minutes.

General technique for planning 2-(2-phenylthiazolidine-4yl)- 5-aryl-1,3,4-oxadiazole

2-(2-Phenyl thiazolidine-4-yl)- 5-(aryl)- 1,3, 4-Oxadiazole (L4-7)

The mixtures are fabricated totally by a similar strategy [32]. An answer of 0.01 mole of compound (L3) and 0.01 mole of fragrant carboxylic corrosive in (5mL POCl3) was refluxed (90°C) for 10 hours in a water shower. The response is proceeded and checked utilizing TLC (ethyl ethanol: acetic acid derivation 2: 8), when the response is done, the combination is dense and filled squashed ice, killed with (NaHCO3% 10%) and left to shape a hasten, and afterward the item is separated, and washed a few times utilizing water. In the wake of washing, dry the strong well and recrystallize utilizing a combination of chloroform: hexane or ethanol: water [33]. With respect to the response utilizing the microwave, it requires just 9 minutes, utilizing a power of radiation of 340 watts.

Preparation of 2-(3-acetyl-2-phenylthiazolidine)-5-mercapto1,3,4-oxadiazole

2-(3-Acetyl-2-Phenyl thiazolidine)-5-mercapto-1,3,4-oxadiazole (L8)

A mixture of 0.01 mol of (L3) in ethanol, 0.015 mol of KOH and (5 mL) CS2 added at 0 °C, the mixture was refluxed for 8 h while the reaction continued to be monitored with TLC (ethanol:ethyl acetate 2:8). The mixture was concentrated and poured into (100 ml) ice water, and the mixture was acidified with dilute 10% hydrochloric acid. The product was filtered, washed, dried [34], and recrystallized from ethyl alcohol to give (L8).

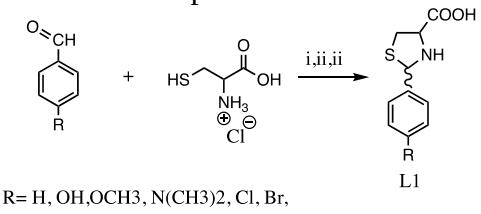
RESULT AND DISCUSSION

In this review, a gathering of thiazolidinediones was incorporated. These mixtures are characterized into gatherings (L1-L8) where the L shows a ligand being a possible ligand for a particular protein. L alludes to a gathering of mixtures orchestrated in a similar general manner, the distinction being just the kind of substituent on the fragrant ring.

The actual constants (liquefying point, yield, atomic recipe, sub-atomic weight, essential) not entirely set in stone for the pre-arranged compounds. The response items were concentrated by the strategies utilized in the natural amalgamation, which are proton NMR1-NMR1 and carbon-13C-NMR spectroscopy, notwithstanding infrared spectroscopy, FT-IR and mass spectrometry (MS).

Blend of 2-phenylthiazolidine-4-carboxylic corrosive (L1)

The response happens between the amino corrosive L-cysteine, which is monetarily accessible as L-Cysteine hydrochloride. The amino corrosive goes after the carbonyl gathering in benzaldehyde through the two amine bunches NH2 (subsequent to eliminating the hydrochloric corrosive atom from the amino corrosive) and SH to deliver thiazolidine-4-carboxylic corrosive (L1). We get the result of thiazolidines by return refining for over 18 hours with a yield of 80-75%, however the item is made out of a combination of diastereomers (4R) - Cis-(2R) and Trans-(2S-4R), which can't be separated.When utilizing the microwave the yield improves to 90-95% with The response time doesn't surpass 15 minutes, as displayed in Figure 1.



R= H, OH,OCH3, N(CH3)2, Cl, Br,

i): $NaHCO_3$ / EtOH, -H_2O, r.t; ii): $NaHCO_3$ / EtOH, r.t;iii):$NaHCO_3$ / EtOH, reflux 19h, or reflux with MW at 340Watt for 12min.

Figure 1: General diagram showing the synthesis of thiazolidine (thiazolidine-4-carboxylic acid) and its derivatives..

We note that there is an equilibrium between the two trans/paired isomers due to the deselectivity of the C(2) carbon atom. This balance strongly depends on the type and nature of the shop used. In chloroform, the equilibrium is shifted to give the isomers two pairs. While the equilibrium shifts towards the formation of trans isomers when using DMSO, D6 dimethyl sulfoxide.

Synthesis Amalgamation of 3-acetyl-2-phenylthiazolidine-4-carboxylic corrosive 3-Acetyl-2-Phenyl thiazolidine-4-carboxylic corrosive (L2) and 3-acetyl-2-phenylthiazolidine-4-carbohydrazide 3-Acetyl-2 - Phenyl thiazolidine-4-carbohydrazide(L3)

The amine bunch is safeguarded by the response of the item L1 with anhydrous acidic corrosive to frame 3-acetyl-2-phenylthiazolidine-4-carboxylic corrosive (L2). The item is dense with hydrazine (80%) utilizing an ethanol arrangement. The subsequent combination was treated with H2SO4 sulfuric corrosive to give 3-acetyl-2-phenylthiazolidine-4-carbohydrazide (L3) as displayed in Figure 2.In the conventional strategy for union, the principal stage is completed at room temperature, and afterward the response is set by reflux refining for a time of 7-8 hours. While utilizing the microwave, the response requires just 6 minutes. In the subsequent stage, the response is made with hydrazine, and this requires setting the combination in a back refining for 26 hours, with a yield of 73%, while this stage needs just 15 minutes utilizing the microwave, and the yield ascends to 95%

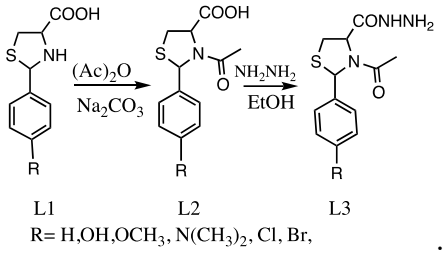


Figure 2: L2 and L3 synthesis diagram.

Synthesis of compounds L4-L7

L3 is reacted with aromatic carboxylic acid derivatives or a heterocyclic ring in the presence of phosphoryl chloride (POCl3) to obtain 1,3,4-oxadiazole (L4-L7) derivatives as shown in Figure 3.

These compounds are prepared for reactions in the traditional way by back-distillation for a period of time ranging between 8-9 hours, while the reaction is carried out using the microwave with a period of time that does not exceed 9 minutes only. The yield by the traditional method did not exceed 25%, while it increased to more than 50% when using the microwave. The yield was indicated for each synthesis when the identification of each compound was mentioned.

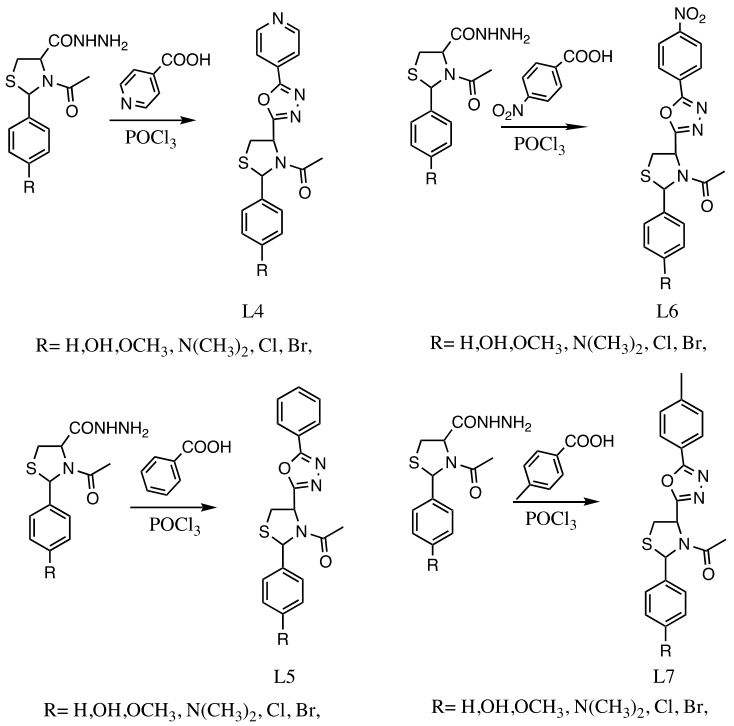
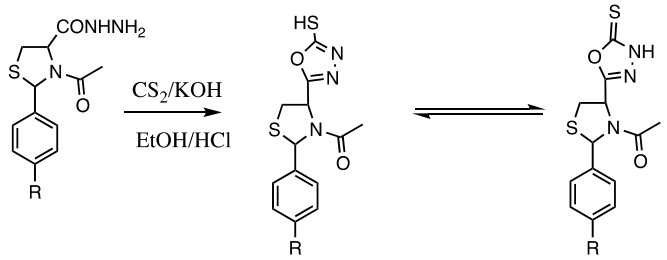


Figure 3: Synthesis diagram of L4-L7 compounds

Synthesis of 2-(3-Acetyl-2-phenylthiazolidine)-5-mercapto-1,3,4-oxadiazole2-(3-Acetyl-2-phenylthiazolidine)-5-mercapto-1,3,4-oxadiazole (L8)

L3 can be condensed with carbon disulfide and potassium hydroxide KOH to produce 2-(3-acetyl-2-phenylthiazolidine)-5-mercapto-1,3,4-oxadiazole as shown in Figure 4. The reaction starts in the conventional way at a temperature of 0°C, then we move to a temperature of 90°C by back-distillation for a period of up to 10 hours, while the reaction using the microwave at the same temperatures for a period of no more than 12 minutes



R= H,OH,OCH3, N(CH3)2, Cl, Br,

Figure 4: L8 . synthesis diagram

Results of tests for identification of synthetic compounds:

(2R, 4R) 2-Phenyl thiazolidine-4-carboxylic acid 73%Cis Isomer (Trans27%)

$C_{10}H_{11}NO_2S$, M.W= 209.26, E. Analy.: Calculated C, 57.40; H, 5.30; N, 6.69. E. Analy: founded: C, 57.42; H, 5.33; N, 6.71. R= H, mp:159-161°C. FT-IR(KBr): 3100- 2700(ZwitterionNH_2^+), 1573s

(COO^-). ^1H NMR(400 MHz, $CDCl_3$): δ2.9 dd, 1H, J=10.28, 8.7 Hz (2.99dd, J=10.51, 5.58Hz) (**H5a**), δ3.24dd, 1H, J=10.33, 7.25Hz (3.14 dd, J=10.51, 7.51Hz) (**H5b**), δ3.77 dd, 1H, J=8.36,7.32Hz (3.96t, J=5.91) (**H4**), δ5.29 s, 1H (5.56s) (**H2**), 7.00-7.27(5H) (**Har**).

(2*R*,4*R*)-2-(4-chlorophenyl)thiazolidine-4-carboxylic acid

$C_{10}H_{10}ClNO_2S$, MW=243.71, E. Analy: Calculated C, 49.28; H, 4.14; N, 5.75. E. Analy: founded: C, 49.24; H, 4.10; N, 5.71. R= Cl, mp:164°C. FT-IR(KBr): 3100- 2700(ZwitterionNH_2^+), 1573s (COO^-). ^1H NMR(400 MHz, $CDCl_3$): δ2.9 dd, 1H, J=10.28, 8.7 Hz (2.99dd, J=10.51, 5.58Hz) (**H4a**), δ3.24dd, 1H, J=10.33, 7.25Hz (3.14 dd, J=10.51, 7.51Hz) (**H5b**), δ3.77 dd, 1H, J=8.36,7.32Hz (3.96t, J=5.91) (**H4**), δ5.29 s, 1H (5.56s) (**H2**), 7.27(2H),7.38-7.38 (2H) .

(2*R*,4*R*)-2-(4-bromophenyl)thiazolidine-4-carboxylic acid

$C_{10}H_{10}BrNO_2S$ M.W=288.16, E. Analy: Calculated C, 41.68; H, 3.50; N, 4.84. E. Analy: founded: C, 41.64; H, 3.46; N, 4.82, R= Br, mp:169°C. FT-IR(KBr): 3100- 2700(ZwitterionNH_2^+), 1573s (COO^-). ^1H NMR(400 MHz, $CDCl_3$): δ2.9 dd, 1H, J=10.28, 8.7 Hz (2.99dd, J=10.51, 5.58Hz) (**H4a**), δ3.24dd, 1H, J=10.33, 7.25Hz (3.14 dd, J=10.51, 7.51Hz) (H5b), δ3.77 dd, 1H, J=8.36,7.32Hz (3.96t, J=5.91) (**H4**), δ5.29 s, 1H (5.56s) (**H2**), 7.27(**2H**), 7.34-7.34 (**2H**).

(2*R*,4*R*)-2-(4-hydroxyphenyl)thiazolidine-4-carboxylic acid

$C_{10}H_{11}NO_3S$, M.W= 225.26, E. Analy: thioritcalC, 53.32; H, 4.92; N, 6.22; E. Analy: founded: C, 53.30; H, 4.91; N, 6.20, R=OH, mp:166°C. FT-IR(KBr): 3100- 2700(ZwitterionNH_2^+), 1573s (COO^-). ^1H NMR(400 MHz, $CDCl_3$): δ2.9 dd, 1H, J=10.28, 8.7 Hz (2.99dd, J=10.51, 5.58Hz) (**H4a**), δ3.24dd, 1H, J=10.33, 7.25Hz (3.14 dd, J=10.51, 7.51Hz) (**H5b**), δ3.77 dd, 1H, J=8.36,7.32Hz (3.96t, J=5.91) (**H4**), δ5.29 s, 1H (5.56s) (**H2**), 7.25(2H)7.28(2H) .

(2*R*,4*R*)-2-(4-methoxyphenyl)thiazolidine-4-carboxylic acid

$C_{11}H_{13}NO_3S$, M.W= 239.29, E. Analy: thioritcalC, 55.21; H, 5.48; N, 5.85 E. Analy: founded: C, 55.19; H, 5.46; N, 5.82, R= OCH_3, mp:162°C. FT-IR(KBr): 3100- 2700(ZwitterionNH_2^+), 1573s (COO^-). ^1H NMR(400 MHz, $CDCl_3$): δ2.9 dd, 1H, J=10.28, 8.7 Hz (2.99dd, J=10.51, 5.58Hz) (**H4a**), δ3.24dd, 1H, J=10.33, δ 3.3s(3H), 7.25Hz (3.14 dd, J=10.51, 7.51Hz) (**H5b**), δ3.77 dd, 1H, J=8.36,7.32Hz (3.96t, J=5.91) (**H4**), δ5.29 s, 1H (5.56s) (**H2**), 7.00-7.27(4H) (**Har**).

(2*R*,4*R*)-2-(4-(dimethylamino)phenyl)thiazolidine-4-carboxylic acid

C12H16N2O2S, M.W= 252.33, E. Analy: thioritcalC, 57.12; H, 6.39; N, 11.10. E. Analy: founded: C, 57.15; H, 6.41; N, 11.13., R=$N(CH_3)_2$, mp:163°C. FT-IR(KBr): 3100- 2700(ZwitterionNH_2^+), 1573s (COO^-). ^1H NMR(400 MHz, $CDCl_3$): δ2.9 dd, 1H, J=10.28, 8.7 Hz (2.99dd, J=10.51, 5.58Hz) (**H5a**), δ3.24dd, 1H, J=10.33, δ 3.2 (6H) 7.25Hz (3.14 dd, J=10.51, 7.51Hz) (**H5b**), δ3.77 dd, 1H, J=8.36,7.32Hz (3.96t, J=5.91) (H4), δ5.29 s, 1H (5.56s) (H2), 7.00-7.27(**4H**) (Har).

(2R, 4R)-N-Acetyl-2-Phenyl thiazolidine-4-carboxylic acid 93%Cis Isomer (Trans7%)

C12H13NO3S, M.W= 251.30, E. Analy: thioritcalC, 57.35; H, 5.21; N, 5.57; E. Analy: founded: C, 57.37; H, 5.23; N, 5.58 mp:147-149°C. FT-IR(KBr): 3327s (OH), 1743s (C=O amide) 1650s (C=O acid). ^1H NMR (400 MHz, $CDCl_3$): δ1.98s, 3H (2.19s) (**H7**), 3.32dd, 1H, J=12.12, 6.66Hz (3.42d, J=6.4Hz) (**H5a**), δ3.36dd, 1H, J=12.07, 6.98Hz (3.42, d, J=6.4Hz) (**H5b**), δ5.06t, 1H, J=6.8Hz (4.8s) (**H4**), δ6.05s, 1H (6.39s) (**H2**), 7.27-7.35(5H) (**Har**), δ11.13s, 1H (11.13s) (**H6**)(**OH**).

(2*R*,4*R*)-3-acetyl-2-(4-chlorophenyl)thiazolidine-4-carboxylic acid

$C_{12}H_{12}ClNO_3S$, M.W= 285.74, E. Analy: thioritcalC, 50.44; H, 4.23; N, 4.90; E. Analy: founded: C, 50.40; H, 4.18; N, 4.86; mp:143-145°C. FT-IR(KBr): 3327s (OH), 1743s (C=O amide) 1650s (C=O acid). ^{1}H NMR (400 MHz, $CDCl_3$): δ1.98s, 3H (2.19s) (H7), 3.32dd, 1H, J=12.12, 6.66Hz (3.42d, J=6.4Hz) (H5a), δ3.36dd, 1H, J=12.07, 6.98Hz (3.42, d, J=6.4Hz) (H5b), δ5.06t, 1H, J=6.8Hz (4.8s) (H4), δ6.05s, 1H (6.39s) (H2), 7.26-7.38(4H) (Har), δ11.13s, 1H (11.13s) (H6)(OH).

(2*R*,4*R*)-3-acetyl-2-(4-bromophenyl)thiazolidine-4-carboxylic acid

$C_{12}H_{12}BrNO_3S$, M.W=330.20 E. Analy: thioritcalC, 43.65; H, 3.66; N, 4.24; E. Analy: founded: C, 43.60; H, 3.61; N, 4.18, mp:148-150°C. FT-IR(KBr): 3327s (OH), 1743s (C=O amide) 1650s (C=O acid). ^{1}H NMR (400 MHz, $CDCl_3$): δ1.98s, 3H (2.19s) (H7), 3.32dd, 1H, J=12.12, 6.66Hz (3.42d, J=6.4Hz) (H5a), δ3.36dd, 1H, J=12.07, 6.98Hz (3.42, d, J=6.4Hz) (H5b), δ5.06t, 1H, J=6.8Hz (4.8s) (H4), δ6.05s, 1H (6.39s) (H2), 7.27-7.37(4H) (Har), δ11.13s, 1H (11.13s) (H6)(OH).

(2*R*,4*R*)-3-acetyl-2-(4-hydroxyphenyl)thiazolidine-4-carboxylic acid

$C_{12}H_{13}NO_4S$, M.W= 267.30, E. Analy: thioritcalC, 53.92; H, 4.90; N, 5.24; E. Analy: founded: C, 53.90; H, 4.87; N, 5.20 mp:140-142°C. FT-IR(KBr): 3327s (OH), 1743s (C=O amide) 1650s (C=O acid). ^{1}H NMR (400 MHz, $CDCl_3$): δ1.98s, 3H (2.19s) (H7), 3.32dd, 1H, J=12.12, 6.66Hz (3.42d, J=6.4Hz) (H5a), δ3.36dd, 1H, J=12.07, 6.98Hz (3.42, d, J=6.4Hz) (H5b), δ5.06t, 1H, J=6.8Hz (4.8s) (H4), δ6.05s, 1H (6.39s) (H2), 7.23-7.32(4H) (Har), δ11.13s, 1H (11.13s) (H6)(OH).

(2*R*,4*R*)-3-acetyl-2-(4-methoxyphenyl)thiazolidine-4-carboxylic acid

$C_{13}H_{15}NO_4S$, M.W=281.33, E. Analy: thioritcalC, 55.50; H, 5.37; N, 4.98, E. Analy: founded: C, 55.49; H, 5.35; N, 4.97. mp:138-140°C. FT-IR(KBr): 3327s (OH), 1743s (C=O amide) 1650s (C=O acid). ^{1}H NMR (400 MHz, $CDCl_3$): δ1.98s, 3H (2.19s) (H7), 3.32dd, 1H, J=12.12, 6.66Hz (3.42d, J=6.4Hz) (H5a), δ3.36dd, 1H, J=12.07, 6.98Hz (3.42, d, J=6.4Hz) (H5b), δ5.06t, 1H, J=6.8Hz (4.8s) (H4), δ6.05s, 1H (6.39s) (H2), 7.23-7.32(4H) (Har), δ11.13s, 1H (11.13s) (H6)(OH).

(2*R*,4*R*)-3-acetyl-2-(4-(dimethylamino)phenyl)thiazolidine-4-carboxylic acid

$C_{14}H_{18}N_2O_3S$, M.W= 294.37,E. Analy: thioritcalC, 57.12; H, 6.16; N, 9.52; E. Analy: founded: C, 57.09; H, 6.13; N, 9.49, mp:134-136°C. FT-IR(KBr): 3327s (OH), 1743s (C=O amide) 1650s (C=O acid). ^{1}H NMR (400 MHz, $CDCl_3$): δ1.98s, 3H (2.19s) (**H7**), 3.09 s (6H)3.32dd, 1H, J=12.12, 6.66Hz (3.42d, J=6.4Hz) (**H5a**), δ3.36dd, 1H, J=12.07, 6.98Hz (3.42, d, J=6.4Hz) (**H5b**), δ5.06t, 1H, J=6.8Hz (4.8s) (**H4**), δ6.05s, 1H (6.39s) (**H2**), 7.27-7.35(4H) (**Har**), δ11.13s, 1H (11.13s) (**H6**)(**OH**).

3-Acetyl-2-Phenyl thiazolidine-4-carbohydrazide (L_3) 75%Trans Isomer (Cis25%)

(2R,4S)-3-acetyl-2-phenylthiazolidine-4-carbohydrazide

C12H15N3O2S, M.W=265.33,E. Analy: thioritcalC, 54.32; H, 5.70; N, 15.84, E. Analy: founded: C, 54.34; H, 5.71; N, 15.86, mp:122-125C° FT-IR(KBr): 3317, 3182s (NH_2), 3226w(NH), 1700, 1662 (C=O). ^{1}HNMR (400MHz, DMSO-d_6): δ1.86s, 3H (2.08s) (**H7**), 3.1 dd, 1H, J=10,4Hz (3.3m,) (**H5a**), δ3.46 m, 1H, J=4 Hz (3.37m) (H5b), δ4.21 m, 1H, J=8, 4Hz (4.21s) (**H4**), δ4.78 d, 2H, J=4 (4.79s) (**H5**), δ5.3 d, 1H, J=4 (5.3) (**H6**) δ6.43 s,1H (6.22s) (**H2**) 7.22-7.71(5H) (**Har**). Mass(EI):265.1 M.Wt, 185.1 peas beak.

(2R,4S)-3-acetyl-2-(4-chlorophenyl)thiazolidine-4-carbohydrazide

C12H14ClN3O2S, M.W=299.77, E. Analy: thioritcalC, 48.08; H, 4.71;N, 14.02; E. Analy: founded: C, 48.04; H, 4.68;N, 13.99 mp:124-127Cº FT-IR(KBr): 3317, 3182s (NH_2), 3226w(NH), 1700, 1662 (C=O). ^{1}HNMR (400MHz, DMSO-d_6): δ1.86s, 3H (2.08s) (**H7**), 3.1 dd, 1H, J=10,4Hz (3.3m,) (**H5a**), δ3.46 m, 1H, J=4 Hz (3.37m) (**H5b**), δ4.21 m, 1H, J=8, 4Hz (4.21s) (**H4**), δ4.78 d, 2H, J=4 (4.79s) (**H5**), δ5.3 d, 1H, J=4 (5.3) (**H6**) δ6.43 s,1H (6.22s) (**H2**) 7.28-7.75(4H) (**Har**). Mass(EI):299.5 M.Wt, 185.1 peas beak.

(2R,4S)-3-acetyl-2-(4-bromophenyl)thiazolidine-4-carbohydrazide

C12H14BrN3O2S, M.W=344.23, E. Analy: thioritcalC, 41.87; H, 4.10;N, 12.21; E. Analy: founded: C, 41.82; H, 4.05;N, 12.16; mp:130-134Cº FT-IR(KBr): 3317, 3182s (NH_2), 3226w(NH), 1700, 1662 (C=O). ^{1}HNMR (400MHz, DMSO-d_6): δ1.86s, 3H (2.08s) (**H7**), 3.1 dd, 1H, J=10,4Hz (3.3m,) (**H5a**), δ3.46 m, 1H, J=4 Hz (3.37m) (**H5b**), δ4.21 m, 1H, J=8, 4Hz (4.21s) (**H4**), δ4.78 d, 2H, J=4 (4.79s) (**H5**), δ5.3 d, 1H, J=4 (5.3) (**H6**) δ6.43 s,1H (6.22s) (**H2**) 7.27-7.74(4H) (**Har**). Mass(EI):344.2 M.Wt, 185.1 peas beak.

(2R,4S)-3-acetyl-2-(4-hydroxyphenyl)thiazolidine-4-carbohydrazide

C12H15N3O3S, M.W=281.33, E. Analy: thioritcalC, 51.23; H, 5.37; N, 14.94; E. Analy: founded: C, 51.21; H, 5.35; N, 14.91; mp:136-138Cº FT-IR(KBr): 3317, 3182s (NH_2), 3226w(NH), 1700, 1662 (C=O). ^{1}HNMR (400MHz, DMSO-d_6): δ1.86s, 3H (2.08s) (**H7**), 3.1 dd, 1H, J=10,4Hz (3.3m,) (**H5a**), δ3.46 m, 1H, J=4 Hz (3.37m) (**H5b**), δ4.21 m, 1H, J=8, 4Hz (4.21s) (**H4**), δ4.78 d, 2H, J=4 (4.79s) (**H5**), δ5.3 d, 1H, J=4 (5.3) (**H6**) δ6.43 s,1H (6.22s) (**H2**) 7.26-7.78(4H) (**Har**). Mass(EI):281.2 M.Wt, 185.1 peas beak.

(2R,4S)-3-acetyl-2-(4-methoxyphenyl)thiazolidine-4-carbohydrazide

C13H17N3O3S, M.W=295.36, E. Analy: thioritcalC, 52.87; H, 5.80; N, 14.23; E. Analy: founded: C, 52.88; H, 5.82; N, 14.25, mp:125-127Cº FT-IR(KBr): 3317, 3182s (NH_2), 3226w(NH), 1700, 1662 (C=O). ^{1}HNMR (400MHz, DMSO-d_6): δ1.86s, 3H (2.08s) (**H7**), 3.1 dd, 1H, J=10,4Hz 3,10 s (3H), (3.3m,) (**H5a**), δ3.46 m, 1H, J=4 Hz (3.37m) (**H5b**), δ4.21 m, 1H, J=8, 4Hz (4.21s) (**H4**), δ4.78 d, 2H, J=4 (4.79s) (**H5**), δ5.3 d, 1H, J=4 (5.3) (**H6**) δ6.43 s,1H (6.22s) (**H2**) 7.22-7.71(4H) (**Har**). Mass(EI):295.2 M.Wt, 185.1 peas beak.

(2R,4S)-3-acetyl-2-(4-(dimethylamino)phenyl)thiazolidine-4-carbohydrazide

C14H20N4O2S, M.W= 308.40, E. Analy: thioritcalC, 54.52; H, 6.54; N, 18.17; E. Analy: founded: C, 54.54; H, 6.55; N, 18.19; mp:127-129Cº FT-IR(KBr): 3317, 3182s (NH_2), 3226w(NH), 1700, 1662 (C=O). ^{1}HNMR (400MHz, DMSO-d_6): δ1.86s, 3H (2.08s) (**H7**), 3.1 dd, 1H, J=10,4Hz 3.15 s (6H), (3.3m,) (**H5a**), δ3.46 m, 1H, J=4 Hz (3.37m) (**H5b**), δ4.21 m, 1H, J=8, 4Hz (4.21s) (**H4**), δ4.78 d, 2H, J=4 (4.79s) (**H5**), δ5.3 d, 1H, J=4 (5.3) (**H6**) δ6.43 s,1H (6.22s) (**H2**) 7.22-7.71(5H) (**Har**). Mass(EI):308.4 M.Wt, 185.1 peas beak.

2-((2R,4S)-N-Acetyl-2-phenyl 1,3,hiazolidine-4-yl)-5-(thiazoli-4-yl)-1,3,4-oxadiazole (L_4) 90%Trans Isomer (Cis10%)

$C_{18}H_{16}N_4O_2S$, M.W= 352.41 E. Analy: thioritcalC, 61.35; H, 4.58; N, 15.90; E. Analy: founded: C, 61.36; H, 4.60; N, 15.93; Yield:20%, in classical way, Yield:55% by Microwave way, mp:187-189°C, FT-IR(KBr disk): 1701s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (2.08s) (**H7**), 3.13t, 1H, J=8Hz (3.32m, J=4Hz) (**H5a**), δ3.46m, 1H, J=8 Hz (3.40m, J=4Hz) (**H5b**), δ4.46t, 1H, J=8Hz (4.45s) (**H4**), δ6.36 s, 1H (6.16s) (**H2**), 7.30-8.24(9H) (**Har**). ^{13}CNMR: δ 22.42(**CH_3**), 30.44(CH_2)C_5, 64.9(CH)C_4, 73.3(CH) C_2, 121-150 **(CAr)**, 159, 163 **(2C=N)**, 170.55

(C=O) Mass(EI): 352.2 M.Wt, 180.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-chlorophenyl) 1,3,hiazolidine-4-yl)-5-(thiazoli-4-yl)-1,3,4-oxadiazole

$C_{18}H_{15}ClN_4O_2S$, M.W= 386.85, E. Analy: thioritcalC, 55.89; H, 3.91; N, 14.48;E. Analy: founded: C, 55.85; H, 3.87; N, 14.45; Yield:19%, in classical way, Yield:52% by Microwave way,mp:195-197°C, FT-IR(KBr disk): 1701s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (2.08s) (**H7**), 3.13t, 1H, J=8Hz (3.32m, J=4Hz) (**H5a**), δ3.46m, 1H, J=8 Hz (3.40m, J=4Hz) (**H5b**), δ4.46t, 1H, J=8Hz (4.45s) (**H4**), δ6.36 s, 1H (6.16s) (**H2**), 7.30-8.24(8H) (**Har**). ^{13}CNMR: δ 22.42(**CH_3**), 30.44(CH_2)**C_5**, 64.9(CH)**C_4**, 73.3(CH) **C_2**, 121-150 (**CAr**),133 (C-Cl) 159, 163 **(2C=N),** 170.55 **(C=O)** Mass(EI): 386.5 M.Wt, 180.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-bromophenyl) 1,3,hiazolidine-4-yl)-5-(thiazoli-4-yl)-1,3,4-oxadiazole

$C_{18}H_{15}BrN_4O_2S$, M.W=431.31 E. Analy: thioritcalC, 50.13; H, 3.51; N, 12.99; E. Analy: founded: C, 50.09; H, 3.48; N, 12.96; Yield:21%, in classical way, Yield:49% by Microwave way,mp:mp:198-201°C, FT-IR(KBr disk): 1701s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (2.08s) (**H7**), 3.13t, 1H, J=8Hz (3.32m, J=4Hz) (**H5a**), δ3.46m, 1H, J=8 Hz (3.40m, J=4Hz) (**H5b**), δ4.46t, 1H, J=8Hz (4.45s) (**H4**), δ6.36 s, 1H (6.16s) (**H2**), 7.30-8.24(8H) (**Har**). ^{13}CNMR: δ 22.42(**CH_3**), 30.44(CH_2)**C_5**, 64.9(CH)**C_4**, 73.3(CH) **C_2**, 121-150 (**CAr**), 134 (C-Br) 159, 163 **(2C=N),** 170.55 **(C=O)** Mass(EI): 431.1 M.Wt, 180.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-hydroxyphenyl)1,3,hiazolidine-4-yl)-5-(thiazoli-4-yl)-1,3,4-oxadiazole.

$C_{18}H_{16}N_4O_3S$, M.W= 368.41,E. Analy: thioritcalC, 58.68; H, 4.38; N, 15.21; E. Analy: founded: C, 58.70; H, 4.41; N, 15.22, Yield:22%, in classical way, Yield:51% by Microwave way,mp:203-205°C, FT-IR(KBr disk): 1701s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (2.08s) (H7), 3.13t, 1H, J=8Hz (3.32m, J=4Hz) (H5a), δ3.46m, 1H, J=8 Hz (3.40m, J=4Hz) (**H5b**), δ4.46t, 1H, J=8Hz (4.45s) (**H4**), δ6.36 s, 1H (6.16s) (**H2**), 7.30-8.24(8H) (**Har**). ^{13}CNMR: δ 22.42(**CH_3**), 30.44(CH_2)**C_5**, 64.9(CH)**C_4**, 73.3(CH) **C_2**, 121-150 (**CAr**),156 (C-OH), 159, 163 **(2C=N),** 170.55 **(C=O)** Mass(EI): 368.1M.Wt, 180.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-methoxyphenyl)1,3,hiazolidine-4-yl)-5-(thiazoli-4-yl)-1,3,4-oxadiazole.

$C_{19}H_{18}N_4O_3S$, M.W=382.44, E. Analy: thioritcalC, 59.67; H, 4.74; N, 14.65; E. Analy: founded: C, 59.69; H, 4.76; N, 14.66; Yield:22%, in classical way, Yield:51% by Microwave way,mp:191-193°C, FT-IR(KBr disk): 1701s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (2.08s) (**H7**), 3.13t, 1H, J=8Hz (3.32m, J=4Hz) (**H5a**), δ3.46m, 1H, J=8 Hz (3.40m, J=4Hz) (**H5b**), 3,8s (3H), δ4.46t, 1H, J=8Hz (4.45s) (**H4**), δ6.36 s, 1H (6.16s) (**H2**), 7.30-8.24(8H) (**Har**). ^{13}CNMR: δ 22.42(**CH_3**), 30.44(CH_2)**C_5**,55,2 (CH3-O), 64.9(CH)**C_4**, 73.3(CH) **C_2**, 121-150 (**CAr**), 158 (C-O-C), 159, 163 **(2C=N),** 170.55 **(C=O)** Mass(EI): 382.1M.Wt, 180.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-(dimethylamino)phenyl))1,3,hiazolidine-4-yl)-5-(thiazoli-4-yl)-1,3,4-oxadiazole.

$C_{20}H_{21}N_5O_2S$, M.W= 395.48, E. Analy: thioritcalC, 60.74; H, 5.35; N, 17.71;;E. Analy: founded: C, 60.72; H, 5.33; N, 17.69, Yield:23%, in classical way, Yield:56% by Microwave way, mp:185-187°C, FT-IR(KBr disk): 1701s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (2.08s) (**H7**),2.80s (6H), 3.13t, 1H, J=8Hz (3.32m, J=4Hz) (**H5a**), δ3.46m, 1H, J=8 Hz (3.40m,

J=4Hz) (**H5b**), δ4.46t, 1H, J=8Hz (4.45s) (**H4**), δ6.36 s, 1H (6.16s) (**H2**), 7.30-8.24(8H) (**Har**). ^{13}CNMR: δ 22.42(**CH_3**), 30.44(CH_2)**C_5**, 42.3, (N-(CH_3)$_2$), 64.9(CH)**C_4**, 73.3(CH) **C_2**, 121-150 (**CAr**), 148.1 (C-N), 159, 163 **(2C=N),** 170.55 **(C=O)** Mass(EI): 395.1M.Wt, 180.2 peas beak.

2-((2R,4S)N-Acetyl-2-phenylthiazolidin-4-yl)-5-Phenyl-1,3,4-oxadiazole(L_5)73%Trans Isomer (Cis27%)

$C_{19}H_{17}N_3O_2S$, M.W= 351.42, E. Analy: thioritcalC, 64.94; H, 4.88; N, 11.96;E. Analy: founded: C, 64.95; H, 4.90; N, 11.97; Yield:24%, in classical way, Yield:60% by Microwave way, mp:164-167°C. FT-IR(KBr): 3390s (OH), 3300w (NH). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.83s, 3H (2.06s) (**H6**), δ3.1dd, 1H, J=10,4Hz (3.3m) (H5a), δ3.47 m, 1H, J=4Hz (3.41d) (**H5b**), δ4.21 m, 1H, J=4Hz (4.21m) (**H4**), δ6.42 s, 1H (6.2s) (**H2**), 7.23-7.81(10H) (**Har**). ^{13}CNMR: δ 23.37(**CH_3**), 34.13(CH_2)**C_5**, 67.7(CH)**C_4**, 74.15(CH)**C_2**, 120-140 (**CAr**), 159, 162**(2C=N),** 170 **(C=O)**. Mass(EI): 351.2 M.Wt, 180.2 peas beak.

2-((2R,4S)N-Acetyl-2-(4-chlorophenyl)thiazolidin-4-yl)-5-Phenyl-1,3,4- oxadiazole

$C_{19}H_{16}ClN_3O_2S$, M.W= 385.87, E. Analy: thioritcalC, 59.14; H, 4.18; N, 10.89;E. Analy: founded: C, 59.10; H, 4.14; N, 10.84; Yield:23%, in classical way, Yield:58% by Microwave way mp:170-172°C. FT-IR(KBr): 3390s (OH), 3300w (NH). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.83s, 3H (2.06s) (**H6**), δ3.1dd, 1H, J=10,4Hz (3.3m) (**H5a**), δ3.47 m, 1H, J=4Hz (3.41d) (**H5b**), δ4.21 m, 1H, J=4Hz (4.21m) (**H4**), δ6.42 s, 1H (6.2s) (**H2**), 7.23-7.81(9H) (**Har**). ^{13}CNMR: δ 23.37(**CH_3**), 34.13(CH_2)**C_5**, 67.7(CH)**C_4**, 74.15(CH)**C_2**, 120-140 (**CAr**), 133(C-Cl), 159-162**(2C=N),** 170 **(C=O)**. Mass(EI): 385.07M.Wt, 180.2 peas beak.

2-((2R,4S)N-Acetyl-2-(4-Bromophenyl)thiazolidin-4-yl)-5-Phenyl-1,3,4- oxadiazole

$C_{19}H_{16}BrN_3O_2S$, M.W= 430.32, E. Analy: thioritcalC, 53.03; H, 3.75; N, 9.77; E. Analy: founded: C, 53.00; H, 3.72; N, 9.74; Yield:24%, in classical way, Yield:59% by Microwave way, mp:167-170°C. FT-IR(KBr): 3390s (OH), 3300w (NH). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.83s, 3H (2.06s) (**H6**), δ3.1dd, 1H, J=10,4Hz (3.3m) (**H5a**), δ3.47 m, 1H, J=4Hz (3.41d) (**H5b**), δ4.21 m, 1H, J=4Hz (4.21m) (**H4**), δ6.42 s, 1H (6.2s) (**H2**), 7.23-7.81(9H) (**Har**). ^{13}CNMR: δ 23.37(**CH_3**), 34.13(CH_2)**C_5**, 67.7(CH)**C_4**, 74.15(CH)**C_2**, 120-140 (**CAr**), 132(C-Br), 159-162**(2C=N),** 170 **(C=O)**. Mass(EI): 430.01M.Wt, 180.2 peas beak.

2-((2R,4S)N-Acetyl-2-(4- hydroxyphenyl)thiazolidin-4-yl)-5-Phenyl-1,3,4- oxadiazole

$C_{19}H_{17}N_3O_3S$, M.W=367.42, E. Analy: thioritcalC, 62.11; H, 4.66; N, 11.44; E. Analy: founded: C, 62.14; H, 4.68; N, 11.46; Yield:28%, in classical way, Yield:66% by Microwave way,mp:160-162°C). FT-IR(KBr): 3390s (OH), 3300w (NH). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.83s, 3H (2.06s) (**H6**), δ3.1dd, 1H, J=10,4Hz (3.3m) (**H5a**), δ3.47 m, 1H, J=4Hz (3.41d) (**H5b**), δ4.21 m, 1H, J=4Hz (4.21m) (**H4**), δ6.42 s, 1H (6.2s) (**H2**), 7.23-7.81(9H) (**Har**). ^{13}CNMR: δ 23.37(**CH_3**), 34.13(CH_2)**C_5**, 67.7(CH)**C_4**, 74.15(CH)**C_2**, 120-140 (**CAr**), 156 (C-OH), 159, 162**(2C=N),** 170 **(C=O)**. Mass(EI): 367.10M.Wt, 180.2 peas beak.

2-((2R,4S)N-Acetyl-2-(4-methoxyphenyl)thiazolidin-4-yl)-5-Phenyl-1,3,4- oxadiazole

$C_{20}H_{19}N_3O_3S$, M.W= 381.45, E. Analy: thioritcalC, 62.98; H, 5.02; N, 11.02;E. Analy: founded: C, 62.97; H, 5.05; N, 11.04; Yield:28%, in classical way, Yield:65% by Microwave way,mp:164-167°C). FT-IR(KBr): 3390s (OH), 3300w (NH). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.83s, 3H (2.06s) (**H6**), δ3.1dd, 1H, J=10,4Hz (3.3m) (**H5a**), δ3.47 m, 1H, J=4Hz (3.41d) (**H5b**), 3.8s (3H), δ4.21

m, 1H, J=4Hz (4.21m) (**H4**), δ6.42 s, 1H (6.2s) (**H2**), 7.23-7.81(10H) (**Har**). ^{13}CNMR: δ 23.37(**C**H_3), 34.13(CH_2)**C**$_5$, 55,2 (CH3-O), 67.7(CH)**C**$_4$, 74.15(CH)**C**$_2$, 120-140 (**CAr**), 158 (C-O-C), 159, 162**(2C=N),** 170 **(C=O)**. Mass(EI): 381.11,M.Wt, 180.2 peas beak.

2-((2R,4S)N-Acetyl-2-(4-(dimethylamino)phenyl))thiazolidin-4-yl)-5-Phenyl-1,3,4- oxadiazole

$C_{21}H_{22}N_4O_2S$, M.W=394.49 E. Analy: thioritcalC, 63.94; H, 5.62; N, 14.20; E. Analy: founded: C, 63.95; H, 5.63; N, 14.22; Yield:28%, in classical way, Yield:65% by Microwave way,mp:160-162°C. FT-IR(KBr): 3390s (OH), 3300w (NH). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.83s, 3H (2.06s) (**H6**), 2.80s (6H), δ3.1dd, 1H, J=10,4Hz (3.3m) (**H5a**), δ3.47 m, 1H, J=4Hz (3.41d) (**H5b**), δ4.21 m, 1H, J=4Hz (4.21m) (**H4**), δ6.42 s, 1H (6.2s) (**H2**), 7.23-7.81(10H) (**Har**). ^{13}CNMR: δ 23.37(**C**H_3), 34.13(CH_2)**C**$_5$, 42.3, (N-(CH_3)$_2$), 67.7(CH)**C**$_4$, 74.15(CH)**C**$_2$, 120-140 (**CAr**), 148.1 (C-N), 159, 162**(2C=N),** 170 **(C=O)**. Mass(EI): 394.15M.Wt 180.2 peas beak.

2-((2R,4S)-N-Acetyl-2-phenylthiazolidin-4-yl)-5-(4-nitrophenyl)-1,3,4-oxadiazole (L_6) 92% Trans Isomer (Cis 8%)

$C_{19}H_{16}N_4O_4S$, M.W=396.42, E. Analy: thioritcalC, 57.57; H, 4.07; N, 14.13; E. Analy: founded: C, 57.58; H, 4.09; N, 14.12;Yield:25%, in classical way, Yield:66% by Microwave way, mp:191-194°C, FT-IR(KBr disk): 1689s (C=O), 1635m (C=N), 1346, 1540 (NO_2). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (1.78s) (**H7**), 3.1m, 1H, J=4Hz (3.3m) (**H5a**), δ3.37m, 1H, J=8 Hz (3.7m) (**H5b**), δ4.27m, 1H, J=8Hz (4.27m) (**H4**), δ6.38 s, 1H (6.34s) (**H2**), 7.2-8.1(9H) (**Har**). Mass(EI): 396 M.Wt, 43.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-chlorophenyl)thiazolidin-4-yl)-5-(4-nitrophenyl)-1,3,4-oxadiazole

$C_{19}H_{15}ClN_4O_4S$, M.W=430.86, E. Analy: thioritcalC, 52.97; H, 3.51; N, 13.00;E. Analy: founded: C, 52.93; H, 3.46; N, 12.93;Yield:22%, in classical way, Yield:60% by Microwave way mp:193-195°C, FT-IR(KBr disk): 1689s (C=O), 1635m (C=N), 1346, 1540 (NO_2). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (1.78s) (**H7**), 3.1m, 1H, J=4Hz (3.3m) (**H5a**), δ3.37m, 1H, J=8 Hz (3.7m) (**H5b**), δ4.27m, 1H, J=8Hz (4.27m) (**H4**), δ6.38 s, 1H (6.34s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 430 M.Wt, 43.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-Bromophenyl)thiazolidin-4-yl)-5-(4-nitrophenyl)-1,3,4-oxadiazole

$C_{19}H_{15}BrN_4O_4S$, M.W=475.32, E. Analy: thioritcalC, 48.01; H, 3.18; N, 11.79; E. Analy: founded: C, 47.96; H, 3.14; N, 11.74; Yield:24%, in classical way, Yield:59% by Microwave way, mp:195-198°C, FT-IR(KBr disk): 1689s (C=O), 1635m (C=N), 1346, 1540 (NO_2). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (1.78s) (**H7**), 3.1m, 1H, J=4Hz (3.3m) (**H5a**), δ3.37m, 1H, J=8 Hz (3.7m) (**H5b**), δ4.27m, 1H, J=8Hz (4.27m) (**H4**), δ6.38 s, 1H (6.34s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 475 M.Wt, 43.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-hydroxyphenyl)thiazolidin-4-yl)-5-(4-nitrophenyl)-1,3,4-oxadiazole

$C_{19}H_{16}N_4O_5S$, M.W= 412.42, E. Analy: thioritcalC, 55.33; H, 3.91; N, 13.59; O, 19.40; S, 7.77 E. Analy: founded: C, 55.35; H, 3.93; N, 13.60; Yield:20%, in classical way, Yield:57% by Microwave way ,mp:180-183°C, FT-IR(KBr disk): 1689s (C=O), 1635m (C=N), 1346, 1540 (NO_2). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (1.78s) (**H7**), 3.1m, 1H, J=4Hz (3.3m) (**H5a**), δ3.37m, 1H, J=8 Hz (3.7m) (**H5b**), δ4.27m, 1H, J=8Hz (4.27m) (**H4**), δ6.38 s, 1H (6.34s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 412 M.Wt, 43.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-methoxyphenyl)thiazolidin-4-yl)-5-(4-nitrophenyl)-1,3,4-oxadiazole

$C_{20}H_{18}N_4O_5S$, M.W=426.45, E. Analy: thioritcalC, 56.33; H, 4.25; N, 13.14; E. Analy: founded: C, 56.35; H, 4.27; N, 13.16; Yield:22%, in classical way, Yield:63% by Microwave way ,mp:174-176°C, FT-IR(KBr disk): 1689s (C=O), 1635m (C=N), 1346, 1540 (NO_2). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (1.78s) (**H7**), 3.1m, 1H, J=4Hz (3.3m) (**H5a**), δ3.37m, 1H, J=8 Hz (3.7m) (**H5b**), 3.81s (3H),δ4.27m, 1H, J=8Hz (4.27m) (**H4**), δ6.38 s, 1H (6.34s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 426 M.Wt, 43.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-(dimethylamino)phenyl)thiazolidin-4-yl)-5-(4-nitrophenyl)-1,3,4-oxadiazole

$C_{21}H_{21}N_5O_4S$, M.W=439.49, E. Analy: thioritcalC, 57.39; H, 4.82; N, 15.94; E. Analy: founded: C, 57.40; H, 4.83; N, 15.93;Yield:20%, in classical way, Yield:60% by Microwave way ,mp:167-169°C, FT-IR(KBr disk): 1689s (C=O), 1635m (C=N), 1346, 1540 (NO_2). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.81s, 3H (1.78s) (**H7**), 3s (6H), 3.1m, 1H, J=4Hz (3.3m) (**H5a**), δ3.37m, 1H, J=8 Hz (3.7m) (**H5b**), δ4.27m, 1H, J=8Hz (4.27m) (**H4**), δ6.38 s, 1H (6.34s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 439, M.Wt, 43.2 peas beak.

2-((2R,4S)-N-Acetyl-2-phenylthiazolidine-4-yl)-5-(4-tollyl)-1,3,4-oxadiazole (L_7) 78%Trans Isomer (Cis22%)

$C_{20}H_{19}N_3O_2S$, M.W=365.45, E. Analy: thioritcalC, 65.73; H, 5.24; N, 11.50; E. Analy: founded: C, 65.75; H, 5.26; N, 11.53;Yield:16% in classical way, Yield:45% by Microwave way, mp:177-179°C, FT-IR(KBr disk): 1741s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.85s, 3H (2.05s) (**H7**), 3.13dd, 1H, J=8,4Hz (3.3m) (**H5a**), δ3.45m, 1H, J=8 Hz (3.38m) (**H5b**), δ4.28m, 1H, J=8Hz (4.4m) (**H4**), δ6.34 s, 1H (6.14s) (**H2**), 7.2-8.1(9H) (**Har**). Mass(EI): 362.2 M.Wt, 65.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-chloro phenyl)thiazolidine-4-yl)-5-(4-tollyl)-1,3,4-oxadiazole

$C_{20}H_{18}ClN_3O_2S$, M.W= 399.89, E. Analy: thioritcalC, 60.07; H, 4.54; N, 10.51; E. Analy: founded: C, 60.00; H, 4.47; N, 10.47; Yield:18% in classical way, Yield:43% by Microwave way, mp:181-183°C, FT-IR(KBr disk): 1741s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.85s, 3H (2.05s) (**H7**), 3.13dd, 1H, J=8,4Hz (3.3m) (**H5a**), δ3.45m, 1H, J=8 Hz (3.38m) (**H5b**), δ4.28m, 1H, J=8Hz (4.4m) (**H4**), δ6.34 s, 1H (6.14s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 399M.Wt, 65.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-bromo phenyl)thiazolidine-4-yl)-5-(4-tollyl)-1,3,4-oxadiazole

$C_{20}H_{18}BrN_3O_2S$, M.W= 444.35, E. Analy: thioritcalC, 54.06; H, 4.08;N, 9.46;E. Analy: founded: C, 54.00; H, 4.02; N, 9.43;Yield:18% in classical way, Yield:44% by Microwave way mp:186-188°C, FT-IR(KBr disk): 1741s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.85s, 3H (2.05s) (**H7**), 3.13dd, 1H, J=8,4Hz (3.3m) (**H5a**), δ3.45m, 1H, J=8 Hz (3.38m) (H5b), δ4.28m, 1H, J=8Hz (4.4m) (**H4**), δ6.34 s, 1H (6.14s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 444, M.Wt, 65.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-hydoxy phenyl)thiazolidine-4-yl)-5-(4-tollyl)-1,3,4-oxadiazole

$C_{20}H_{19}N_3O_3S$, M.W=381.45, E. Analy: thioritcalC, 62.98; H, 5.02; N, 11.02; E. Analy: founded: C, 62.97; H, 5.05; N, 11.03; Yield:16% in classical way, Yield:41% by Microwave way mp:169-

171°C, FT-IR(KBr disk): 1741s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.85s, 3H (2.05s) (**H7**), 3.13dd, 1H, J=8,4Hz (3.3m) (**H5a**), δ3.45m, 1H, J=8 Hz (3.38m) (**H5b**), δ4.28m, 1H, J=8Hz (4.4m) (**H4**), δ6.34 s, 1H (6.14s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 381, M.Wt, 65.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-methoxy phenyl)thiazolidine-4-yl)-5-(4-tollyl)-1,3,4-oxadiazole

$C_{21}H_{21}N_3O_3S$, M.W= 395.48, E. Analy: thioritcalC, 63.78; H, 5.35; N, 10.63; E. Analy: founded: C, 63.76; H, 5.33; N, 10.61;Yield:16% in classical way, Yield:41% by Microwave way, mp:171-172°C, FT-IR(KBr disk): 1741s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.85s, 3H (2.05s) (**H7**), 3.13dd, 1H, J=8,4Hz (3.3m) (**H5a**), δ3.45m, 1H, J=8 Hz (3.38m) (**H5b**), 3.8s (3H), δ4.28m, 1H, J=8Hz (4.4m) (**H4**), δ6.34 s, 1H (6.14s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 395, M.Wt, 65.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-(dimethylamino)phenyl)thiazolidine-4-yl)-5-(4-tollyl)-1,3,4-oxadiazole

$C_{22}H_{24}N_4O_2S$, M.W= 408.52, E. Analy: thioritcalC, 64.68; H, 5.92; N, 13.71;E. Analy: founded: C, 64.70; H, 5.93; N, 13.74; Yield:17% in classical way, Yield:43% by Microwave way, mp:174-176°C, FT-IR(KBr disk): 1741s (C=O), 1627m (C=N). ^{1}HNMR(400 MHz, DMSO-d_6): δ1.85s, 3H (2.05s) (**H7**), 3,04s (6H), 3.13dd, 1H, J=8,4Hz (3.3m) (**H5a**), δ3.45m, 1H, J=8 Hz (3.38m) (**H5b**), δ4.28m, 1H, J=8Hz (4.4m) (**H4**), δ6.34 s, 1H (6.14s) (**H2**), 7.2-8.1(8H) (**Har**). Mass(EI): 408,M.Wt, 65.2 peas beak.

2-((2R,4S)-N-Acetyl-2-phenyl,39hiazolidine-4-yl)-5-mercapto-1,3,4-oxadiazole (L_8) 55%Trans Isomer (Trans45%)

$C_{13}H_{13}N_3O_2S_2$, M.W= 307.39, E. Analy: thioritcalC, 50.80; H, 4.26; N, 13.67;E. Analy: founded: C, 50.81; H, 4.26; N, 13.65;Yield:37%, mp:200-202°C. FT-IR(KBr): 3122 w(NH), 2626w(SH), 1720 (C=O), 1612s(C=N). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.78s, 3H (1.96s) (**H7**), δ2.89t, 1H, J=12Hz (3.1m, J=4) (**H5a**), δ3.4m,1H, J=4 Hz (3.34) (**H5b**), δ4.24t, 1H, J=4Hz (4.55t) (**H4**), δ6.42s, 1H (6.54s) (**H2**), δ6.2s, 1H (**SH**) 7.34-7.84(5H) (**Har**). Mass(EI):307.1M.Wt, 237.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-chlorophenyl),thiazolidine-4-yl)-5-mercapto-1,3,4-oxadiazole

$C_{13}H_{12}ClN_3O_2S_2$, M. W= 341.83, E. Analy: thioritcalC, 45.68; H, 3.54; N, 12.29; E. Analy: founded: C, 45.68; H, 3.54; N, 12.29; Yield:33%, mp:203-205°C. FT-IR(KBr): 3122 w(NH), 2626w(SH), 1720 (C=O), 1612s(C=N). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.78s, 3H (1.96s) (**H7**), δ2.89t, 1H, J=12Hz (3.1m, J=4) (**H5a**), δ3.4m,1H, J=4 Hz (3.34) (**H5b**), δ4.24t, 1H, J=4Hz (4.55t) (**H4**), δ6.42s, 1H (6.54s) (**H2**), δ6.2s, 1H (**SH**) 7.34-7.84(4H) (**Har**). Mass(EI): 341M.Wt, 237.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-Bromophenyl)thiazolidine-4-yl)-5-mercapto-1,3,4-oxadiazole

$C_{13}H_{12}BrN_3O_2S2$, M.W= 386.28, E. Analy: thioritcalC, 40.42; H, 3.13; N, 10.88; E. Analy: founded: C, 40.36; H, 3.09; N, 10.84; Yield:35%, mp:206-208°C. FT-IR(KBr): 3122 w(NH), 2626w(SH), 1720 (C=O), 1612s(C=N). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.78s, 3H (1.96s) (**H7**), δ2.89t, 1H, J=12Hz (3.1m, J=4) (**H5a**), δ3.4m,1H, J=4 Hz (3.34) (**H5b**), δ4.24t, 1H, J=4Hz (4.55t) (**H4**), δ6.42s, 1H (6.54s) (**H2**), δ6.2s, 1H (**SH**) 7.34-7.84(4H) (**Har**). Mass(EI): 386.28M.Wt, 237.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-hydroxyphenyl)thiazolidine-4-yl)-5-mercapto-1,3,4-oxadiazole

C13H13N3O3S2, M.W=323.39, E. Analy: thioritcalC, 48.28; H, 4.05; N, 12.99; E. Analy: founded: C, 48.30; H, 4.07; N, 13.01; Yield:31%, mp:201-203°C. FT-IR(KBr): 3122 w(NH), 2626w(SH), 1720 (C=O), 1612s(C=N). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.78s, 3H (1.96s) (**H7**), δ2.89t, 1H, J=12Hz (3.1m, J=4) (**H5a**), δ3.4m,1H, J=4 Hz (3.34) (**H5b**), δ4.24t, 1H, J=4Hz (4.55t) (**H4**), δ6.42s, 1H (6.54s) (**H2**), δ6.2s, 1H (**SH**) 7.34-7.84(4H) (**Har**). Mass(EI): 323M.Wt, 237.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-methoxyphenyl)thiazolidine-4-yl)-5-mercapto-1,3,4-oxadiazole

$C_{14}H_{15}N_3O_3S_2$, M.W=337.41, E. Analy: thioritcalC, 49.84; H, 4.48; N, 12.45; E. Analy: founded: C, 49.85; H, 4.50; N, 12.47; Yield:33%, mp:191-193°C. FT-IR(KBr): 3122 w(NH), 2626w(SH), 1720 (C=O), 1612s(C=N). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.78s, 3H (1.96s) (**H7**), δ2.89t, 1H, J=12Hz (3.1m, J=4) (**H5a**), δ3.4m,1H, J=4 Hz (3.34) (**H5b**), 3.81s (3H), δ4.24t, 1H, J=4Hz (4.55t) (**H4**), δ6.42s, 1H (6.54s) (**H2**), δ6.2s, 1H (**SH**) 7.34-7.84(4H) (**Har**). Mass(EI): 337M.Wt, 237.2 peas beak.

2-((2R,4S)-N-Acetyl-2-(4-(dimethylamino)phenyl)thiazolidine-4-yl)-5-mercapto-1,3,4-oxadiazole

C15H18N4O2S2, M.W=350.46, E. Analy: thioritcalC, 51.41; H, 5.18; N, 15.99; E. Analy: founded: C, 51.38; H, 5.16; N, 15.97; Yield:29%, mp:200-202°C. FT-IR(KBr): 3122 w(NH), 2626w(SH), 1720 (C=O), 1612s(C=N). ^{1}H NMR(400 MHz, DMSO-d_6): δ1.78s, 3H (1.96s) (**H7**), δ2.89t, 1H, J=12Hz (3.1m, J=4) (**H5a**),3.2s (6H), δ3.4m,1H, J=4 Hz (3.34) (**H5b**), δ4.24t, 1H, J=4Hz (4.55t) (**H4**), δ6.42s, 1H (6.54s) (**H2**), δ6.2s, 1H (**SH**) 7.34-7.84(4H) (**Har**). Mass(EI): 350 M.Wt, 237.2 peas beak.

CONCLUSION

Since the primary distributions on the utilization of microwaves in natural union, it has been certain that this procedure will fundamentally affect all region of this discipline. The utilization of a microwave enjoys a few upper hands over regular convection warming of the reactants. Customary convection warming as a rule includes the utilization of a heater or an oil shower that warms the reactor dividers by convection or conduction. Arriving at the ideal temperature takes more time and doesn't warm the example equitably likewise with microwave warming. Energy is likewise squandered while warming a heater or an oil shower. Bringing microwave energy into a compound response can bring about a lot higher warming rates contrasted with traditional warming. Shortening response times, further developing yield, altering selectivity, expanding item immaculateness, and working on successive strategies have been accounted for, and as a rule these circumstances and results can't be accomplished by traditional warming. This technique can be joined into the green science idea, since the solid ingestion of microwave radiation by one of the response parts prompts more limited response times and further developed energy proficiency. - oxadiazole. The cyclocondensation responses of different analogs of 1,3,4 occurred. We incorporated a progression of thiazolidine subordinates with an assortment of fragrant and heterotropic thiazolidines in exceptional returns by the old style technique utilizing microwaves. The physical constants((melting point, yield, sub-atomic recipe, sub-atomic weight, E. Analy) of the pre-arranged compounds and the response items were analyzed by the strategies utilized in natural union, in particular atomic attractive reverberation spectroscopy of proton and carbon notwithstanding 1H spectrometry, NMR, 13C-NMR , FT-IR red and mass spectrometry.L1, L2, L3, L4, L5, L6, L7, L8. We combined a

gathering of mixtures ordered into gatherings, the gathering, where every image had a gathering of mixtures with a similar engineered methodology, yet the outcomes are different relying upon the substituents on the sweet-smelling ring, and the outcomes have been worked on in a bright unmistakable manner, particularly when the yield in the response as per the old style techniques is low, however the prominent variable that should be halted , the decrease accordingly time is shockingly encouraging for a more extensive scope of purposes z in the production of meds.

This combination can likewise be arranged from the green science way to deal with natural blend, where the reactants are microwaved within the sight of very little and once in a while no solvents. A new and straightforward methodology has been created for the combination of some heteroaromatic and fragrant thiazolidine subsidiaries. Furthermore, these mixtures were likewise integrated by making an examination between customary blend and microwave-helped combination by looking at the all-out response time and level of item. These outcomes show that the microwave-helped combination prompts better returns in extremely short response times. These mixtures can be exposed to nitty gritty examinations utilizing the PC and an equal examination of the viability of these mixtures on living cells in glass after they have been displayed. to affirm the similarity of the displaying with concentrates in glass, notwithstanding future examination and speculation of this review to a few mutagenic illnesses in live creature models.

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