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SYNTHESIS AND CHARACRTERIZATION OF 4 THIAZOLIDINEONE DERIVATIVES

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Abstract: **The thiazolidin-4-one core is unusually most valuable and has foreground in various clinically used medications. Most of the researchers are synthesized Thiazolidin-4-ones by using lot of conventional synthetic methods. These methods are more time consuming as well as worthful for the synthesis of compounds. Objective: Synthesis of novel substituted Thiazolidin-4-one analogues, Characterization of substituted thiazolidin-4-one analogues with chemico-spectral analysis by FT-IR, NMR and Mass spectroscopy. Method: DCC method (dicyclohexyl carbodimide). Result: Synthesized of novel substituted Thiazolidin-4-one analogues and characterized the substituted thiazolidin-4-one analogues by FT-IR, NMR and Mass spectroscopy. Conclusion: We synthesized novel thiazolidin-4-one by using conventional method like DCC method. Then the synthesized compounds were characterized by FT- IR, MASS, 1H NMR and ^{13}C NMR. All the data of substituted Thiazolidin-4-one analogues were interpreted and tabulated.**

Keywords: **Thiazolidin-4-one; Dicyclohexyl Carbodimide; Mass spectroscopy; NMR spectroscopy; Furan; Fourier transform Infrared spectroscopy.**

1. INTRODUCTION

1.1 Thiazolidin-4-ones:

Thiazolidin-4-one substituted moieties have broad spectrum of activities like anti-fungal, anti –viral, anti- histaminic, anti-microbial, anti-bacterial, anti-inflammatory ,analgesic, anti-tubercular, yellow fever virus ,anti-oxidant, cytotoxic etc. The presence of anti-bacterial activity is based on the substitution at positions. It was interest that thiazole, thiazolidin-4-one and pyrazole inone frame produce new compounds to enhance the biological activities.

Currently many of drugs have been developed with thiazolidinone which includes anti-hypoglycemics, analgesics and anti-diuretics. Using modern technologies like high throughput screening, computer modeling and combinatorial chemistry it was established that are selective inhibitors of UDP-MurNAc/L-Ala ligase.

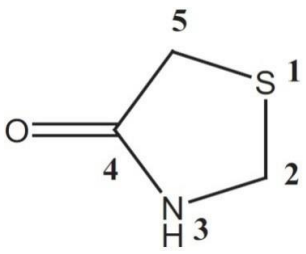

Figure 1: Thiazolidine-4-one ring

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Characterization:

Infrared spectra of substituted 4- thiazolidinones was reported by Taylor et al. The 13C NMR spectra of a series of substituted 4-thiazolidinones in CDCl3 was studied by Nagase et al. Mass spectra of different 4- thiazolidinones were also studied and reported. Based on the above factors, synthesis of novel C-2, N-3 substituted Thiazolidin-4-one analogues compounds by using DCC method (dicyclohexyl carbodimide) and Characterization of substituted thiazolidine-4-one analogues with chemico-spectralasis

2. MATERIALS AND METHODS

2.1 Materials :

The materials used in this process are of the analytical grade .Melting point was determined by one end capillary tube method by using DIGIMELT apparatus and IR spectra of the synthesized compounds were determined by CARY 6O manufactured by AGILENT SOLUTIONS, NMR spectra of the synthesized compounds were determined by DRX-300 manufactured by BRUCKER and mass spectra of the synthesized compounds were determined by AGILENT 6520(Q-TOF).

2.1.1 Experimental synthtic procedure for the preparation of compound TZ-1to5 by using DCCmethod (dicyclohexyl carbodimide):

The aromatic primary amine (1M mol), aromatic aldehyde (1.4M mol) were dissolved in tetrahydro furan (20ml) then add thioglycolic acid and N,N'-Dicyclohexylcarbodimide (DCC) at 0°C. The reaction was carried out at 0-50°C for 1 hr using magnetic stirrer, the stirring was continued for 2hrs at room temperature. THF was evaporated under reduced pressure, and excessethyl acetate was added.

The organic layer washed with citric acid, sodium bicarbonate, water and brine, and then dried. Then the final product was purified by column chromatography.

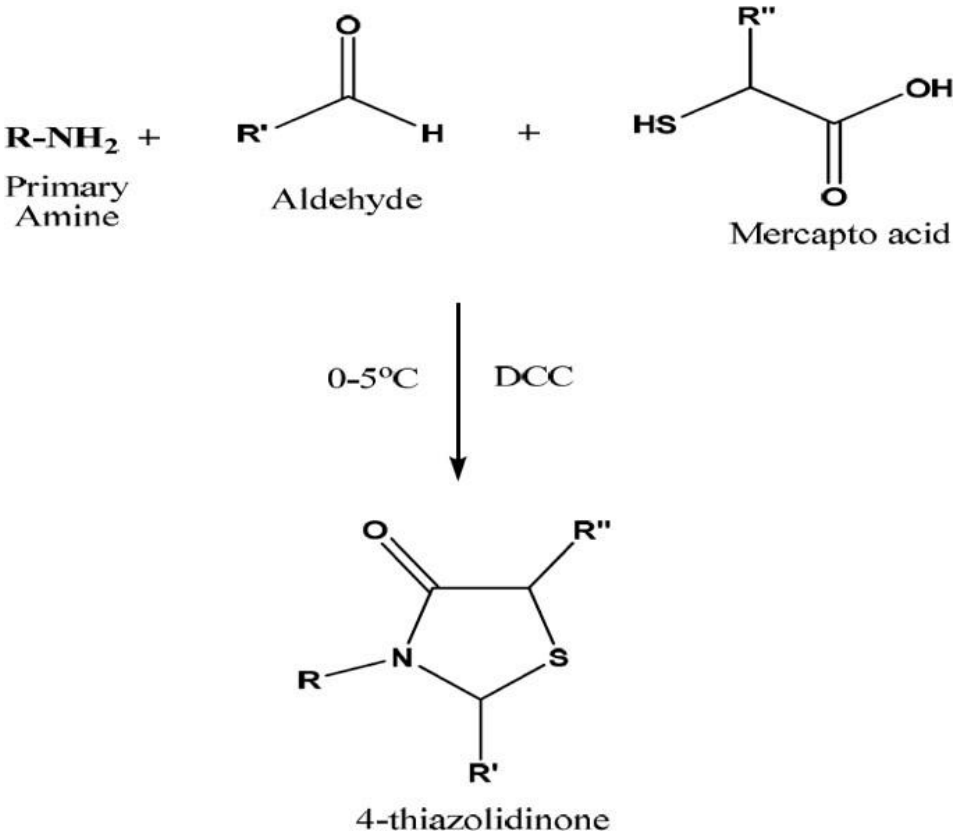

Figure 2

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2.2 Characterization of synthesized compounds :

The Thiazolidine-4-one compounds were characterized by Physical characterization Spectral characterization by FT-IR, NMR, and Mass spectroscopy.

2.3 Physical Characterization

Physical characterization was carried out through melting point and TLC analysis and its optimized chromatographic conditions shown in table no 1.

Table 1: Optimized chromatographic conditions for Thiazolidin-4-one.

Parameters	Data
Solvent	Ethyl acetate
Mobile phase	Hexane:ethyl acetate (6:4) Hexane :ethyl acetate (8:2) Hexane :ethyl acetate (2:8)
Stationary phase	Silica gel 60F254

2.4 Melting point

Small amount of synthesized compound was loaded into the capillary tube (one side closed) by gently tapping the capillary tube. The capillary tube was placed in melting point apparatus (Digimelt) and the melting point of the compound was observed.

Spectral characterization

2.5 Fourier Transform Infrared (FT-IR) Spectroscopy

The Fourier transform infrared (FTIR) spectra of samples were obtained using FTIR spectrophotometer (Agilent Cary 630). Pure drug Thiazolidin-4-one compounds were subjected to FTIR study. 10mg of the sample was directly placed in sample holder in Cary 630 FTIR. Data were collected over a spectral region from 4000 to 800 cm-1.

2.6 Nuclear Magnetic Resonance Spectroscopy (1HNMR and 13C NMR)

1H NMR and 13C NMR of Thiazolidin-4-one compounds were recorded on Bruker (DRX300MHz) Advance NMR spectrophotometer using CDCl3 as solvent and chemical shiftswere recorded in ppm relative to tetra methyl silane (TMS).

2.7 Mass Spectroscopy

Solid samples of Thiazolidin-4-one compounds were recorded in Agilent 6520 (Q-TOF) High resolution mass spectrometer instrument in positive mode using CDCl3 as solvent and ion peakswere given in m/z ratio.

3. RESULTS AND DISCUSSIONS

3.1 CHEMICAL PREPARATIONS

Thiazolidine-4-one derivatives play a vital role in the field of medicinal science and lot of well applied medicinal values. Scientists have been screened them for huge pharmacological practices to acquire an atom which shows eminent pharmacological action with modest antagonistic impacts. Sometimes this thiazolidine-4-one can subordinates to preferred movement over standard medications and then could turn into another medicinal value for the market in upcoming generations. The thiazolidin-4-one core is unusually most valuable and has foreground in various clinically used medications.

Most of the researchers are synthesized Thiazolidine-4-ones by using lot of conventional synthetic methods. These methods are more time consuming as well as worthful for the synthesis of compounds. But this is the most important compound in the medications due to the presence c-s which acts as a core. The IUPAC name and structures of the compound is shown in table no 2. The physic-chemical properties of synthesized thiazolidin-4-one derivatives is shown in table no 3 and characterized by using thin layer chromatography, melting point and the spectral analysis was done by using UV, IR, and NMR. Due to the availability of Literature reviews, we are aware of various methods for synthesis of the thiazolidin-4-ones As per commercial availability and laboratory conditions, one method was chosen solvent free method,

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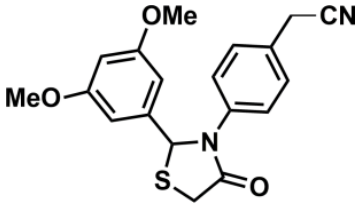
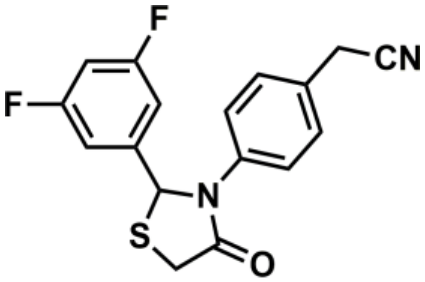
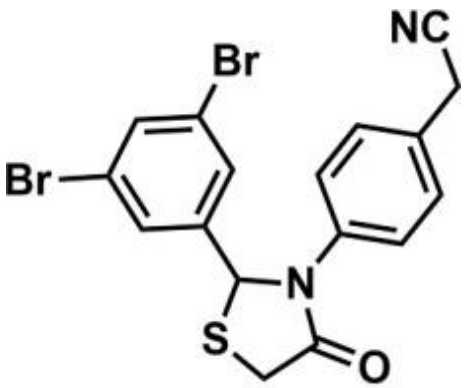
i.e…., The aromatic primary amine (1M mol), aromatic aldehyde (1.4M mol) are dissolved in tetrahydro furan (20ml) then add thioglycolic acid and N,N'-Dicyclohexylcarbodimide (DCC) at 0°C. The reaction was carried out at 0-50°C for 1 hr using magnetic stirrer, the stirring was continued for 2hrs at room temperature. THF was evaporated under reduced pressure, and excess ethyl acetate was added. The organic layer washed with citric acid, sodium bicarbonate, water and brine, and then dried. Then the final product was purified by column chromatography. FT-IR ranges for the synthesized compounds were 1682-1828 cm^{-1}, and the aromatic CH range 2924 to 3438. The aromatic primary amine and aldehyde substitution is shown in the table no 4. This indicates the formation of substituted thiazolidine-4-one analogues were shown in table no 5.

The synthesized compounds showed 1 proton at C2 position of thiazolidine-4-one ring between the range 6.07 to 5.834 ppm and 2 proton peaks at C5 position of thiazolidine-4-one ring between the range 4.83 to 4.00 ppm in 1H NMR which indicates the formation of Thiazolidine-4-one analogues were shown in table no 6 . The synthesized compound showed carbon peaks in Carbon 2, Carbon 4 & Carbon 5 positions of thiazolidin-4-one ring between the range of 61.35 to 64.892, 170 to 177& 48.3 to 55.67 ppm respectively in 13C NMR which indicates formation of Thiazolidin-4-one compounds were shown in table no 7.The synthesized compound showed exact mass of the compounds as parent peak in ESI-MS which indicates formation of Thiazolidin-4-one compounds were shown in table no 8.

Table 2: The IUPAC name and structure of the compounds

01	**2-(4-(2-(3,5-dimethoxyphenyl)-4-oxothiazolidin-3-l)phenyl)acetonitrile**  **TZ-01**
02	**2-(4-(2-(3,5-difluorophenyl)-4-oxothiazolidin-3-yl)phenyl)acetonitrile**  **TZ-02**
03	**2-(4-(2-(3,5-dibromophenyl)-4-oxothiazolidin-3-yl)phenyl)acetonitrile**  **TZ-03**

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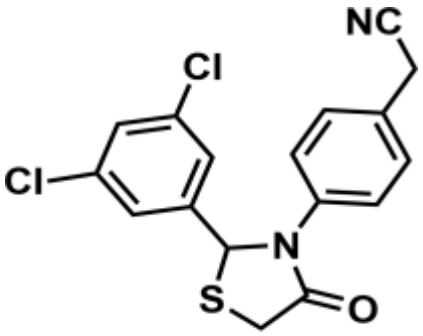
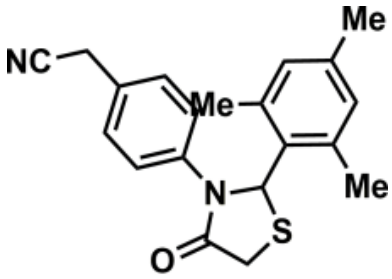
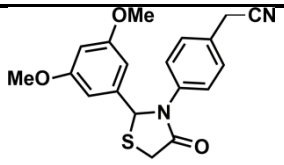
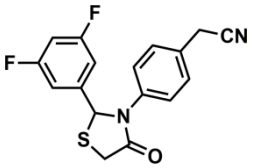
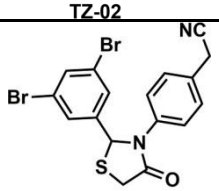
04	2-(4-(2-(3,5-dichlorophenyl)-4-oxothiazolidin-3-yl)phenyl)acetonitrile  TZ-04
05	**2-(3,12b-dihydro-10,12-dimethyl-3-oxo-2H-thiazolo[3,2-flphenanthridin-7-yl)acetonitrile**  TZ-05

Table 3: Physico-chemical properties of compound TZ01 to TZ05.

S.No	Compound code	Chemical Structure	Method of synthesis	Percentage yield	Melting point	Thin Layer Chromatography – RF value (Hexane: Ethylacetate)
1.	TZ01	 TZ-01	DCC	45.74%	145-150^{0}C	0.283 (6:4)
2.	TZ02	 TZ-02	DCC	56 %	184-188^{0}C	0.515 (6:4)
3.	TZ03	 TZ-03	DCC	57.78%	211-215^{0}C	0.515 (6:4)

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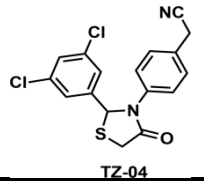
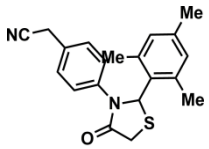
4.	TZ04	 TZ-04	DCC	48 %	206-211^{0}C	0.545 (6:4)
5.	TZ05	 TZ-05	DCC	43.1%	162-167^{0}C	0.454 (6:4)

Table 4: The aromatic primary amine and aromatic aldehyde substitution

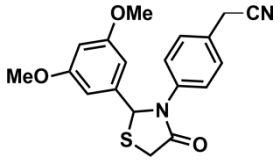
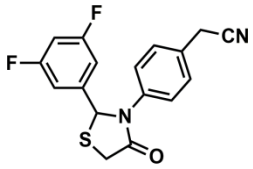
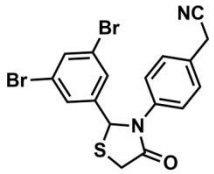
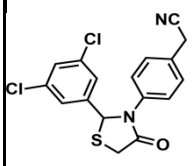
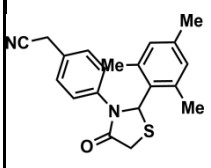
AROMATIC PRIMARY AMINE	AROMATICALDEHYDE	PRODUCT
4-amino benzyl nitrile	3,5- dimethoxy benzaldehyde	 TZ-01
4-amino benzyl nitrile	3,5- difluoro benzaldehyde	 TZ-02
4-amino benzyl nitrile	3,5- dibromo benzaldehyde	 TZ-03
4-amino benzyl nitrile	3,5- dichloro benzaldehyde	 TZ-04
4-amino benzyl nitrile	2,4,6- trimethyl benzaldehyde	 TZ-05

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Table 5: Interpretation of FT-IR data of the compound TZ01 to TZ05

Assignment	IR datas(1/cm)				
	TZ01	TZ02	TZ03	TZ04	TZ05
C=O	1697	1619	1674	1674	1659
Aromatic C-H	3400	3321	3065	3118	3321
C-Cl	-----	-----	------	796	-----
C-F	-----	1376	------	-----	-----
C-Br	-----	-----	826	-----	-----
CN	2243	2845	2249	2156	2243

FT-IR range for the synthesized compounds are 1697-1697 cm^{-1}, and the aromatic CH range 3065 to 3400.This indicate the formation of substituted thiazolidin-4-one analogues

Table 6: Interpretation of ^{1}H NMR of the compounds TZ01 to TZ05

Assignment	Chemical shifts (ppm)				
	TZ01	TZ02	TZ03	TZ04	TZ05
Aromatic C-H	7.2582-7.265	6.060-7.310	7.202-7.574	6.017-7.323	7.217-7.261
CH	7.258	6.060	7.202	6.017	6.724
CH2	3.856-4.003	3.887-4.008	4.020-5.989	3.892-4.020	3.642-3.920

The synthesized compounds showed 1 proton at C2 position of thiazolidin-4-one ring between the range 6.06 to 5.989 ppm and 2 proton peaks at C5 position of thiazolidin-4-one ring between the range 4.020 to 4.003 ppm in 1H NMR which indicates the formation of Thiazolidin-4-one analogues.

Table 7: Interpretation of ^{13}C NMR of the compound TZ01 to TZ05

Assignment	**Chemical shift(ppm)**				
	TZ01	TZ02	TZ03	TZ04	TZ05
C=O	171.35	170.99	170.98	169.70	170.87
CH	65.42	64.41	64.12	62.97	60.47
CH2	55.57	49.37	33.41	48.12	49.90

The synthesized compound showed carbon peaks in C2, C4 & C5 positions of thiazolidin-4-one ring between the range of 60.47 to 64.892, 169 to 171& 33.41 to 55.57 ppm respectively in 13C NMR which indicates formation of Thiazolidin-4-one compounds.

Table 8: Interpretation of mass spectra compound TZ01 to TZ05

Assignment	**Characteristic m/z ratio**				
	TZ01	TZ02	TZ03	TZ04	TZ05
ParentPeak	356	332	453	364	338
Base peak	355	331	452	363	337

4. CONCLUSION

As the heterocyclic compounds have most of the biological compounds, among these thiazolidin-4-one compounds were more potent because of the presence of nitrogen and sulphur in a five member ring. We synthesized novel thiazolidine-4-one derivatives by using conventional method like DCC method and characterized by FT- IR, MASS, 1H NMR and ^{13}C NMR.

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