SYNTHESIS AND CHARACTERISATION OF AROYL HYDRAZONES AND ITS ANTI EPILEPTIC PROPERTY

A.Arunkumar[1], G.Vanaja[2], .Vivekanandan[3], V.Gokila[4]

Assistant professor

[1] Department of chemistry,Dhanalakshmi Srinivasan College of arts and science for women, Perambalur, Tamil Nadu

Abstract:

A probe into the literature survey clearly reveals no work has been carried out for the synthesis of (E)-N'-(2,4-dichlorobenzylidene) nicotinohydrazide) using 2,4-dichlorobenzaldehyde and nicotine hydrazide. Aim and scope of the work is highly effective medicinal hydrazide derivatives have been synthesized from Schiff base route. The structure of the ligand (E)-N'-(2,4-dichlorobenzylidene) nicotinohydrazide) and its complexes were carried various spectral studies. From these studies, I know about the knowledge of organic chemistry and spectroscopy.In my present work, we have to synthesis (E)-N'-(2,4-dichlorobenzylidene) nicotinohydrazide) and establish the structure through the analytical (elemental and TLC) and spectral (IR, H^1 NMR and C^{13} NMR) methods of characterization.

Key Words: Aroyl Hydrazones, IR spectroscopy ,H^1 NMR and C^{13} NMR spectroscopy

INTRODUCTION

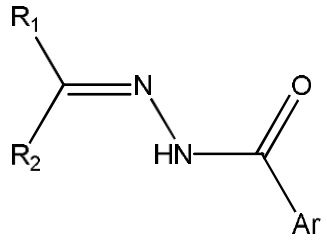
The coordination chemistry of aroyl hydrazones are quite interesting as it presents a combination of donor sites such as protonated / deprotonated amide oxygen, an imine nitrogen of hydrazone moiety and additional donor site (usually N or O) provided from the aldehyde or ketone forming the Schiff base.Due to biological activities, the coordination chemistry of tridentate aroylhydrazones derived from orthohydroxy aromatic aldehydes(**1,2,3**) and 2-N-heterocyclic aldehydes (**4**) have been extensively studied (**5**).

Alfred Werner received the Nobel Prize in Chemistry in 1913 for recognition of his work on the linkage of atoms in compounds by which he has thrown new insights on earlier investigations and opened up new fields of research especially in coordination chemistry.

The chemistry of coordination compounds is an important and challenging area of modern inorganic chemistry. During the last fifty years, advances in this area have provided development of new concepts and models of bonding and molecular structure, novel breakthroughs in chemical industry and new insights into the functioning of critical components of biological systems. The living system is partially supported by coordination compounds. Chlorophyll, the pigment responsible for photosynthesis is a coordination compound of magnesium. Hemoglobin, the red pigment of blood which acts as oxygen carrier is a coordination compound of iron. Coordination compounds also find extensive applications in metallurgical process, analytical and medicinal chemistry.

Schiff bases containing poly donor atoms have not only produced stable metal complexes of transition metal ions, but these ligands and their metal complexes have also played a significant role in the domain of stereochemistry, structure, magnetism, spectroscopy and model compounds of biochemical interest. In addition Schiff bases and their metal complexes have a variety of application in industry, agriculture and medicine.

CHARACTERISATION OF HYDRAZINES:



Aroyl hydrazones are a class of azomethines having the group –C=N-N- and are widely employed as ligands in coordination chemistry. These ligands are readily available, versatile and can exhibit various denticities and functionalities depending on the nature of the starting materials employed for their preparation.General formula for a substituted aroylhydrazone is shown in Fig. 1

Hydrazones are a class of organic compounds which possess the structure R1R2C=NNH2. They are related to ketone and aldehyde in which oxygen has been replaced with NNH2 group. These azometine -NHN=CH- proton constitute an important class of compounds for new drug development. Hydrazones are formed by the reaction of hydrazine

or hydrazide with aldehydes and ketones. The structure of a hydrazone reveals that (i) nucleophilic imine and amino-type nitrogens, (ii) an imine carbon that has both electrophilic and nucleophilic character, (iii) configurational isomerism stemming from the intrinsic nature of the C=N bond and (iv) inmost cases an acidic N–H proton(**6**).

CLASSIFICATION, TYPES AND FUNCTIONAL GROUP OF HYDRAZONE DERIVATIVES:

Hydrazones are mainly classified into five types. They are amine hydrazones, phenyl hydrazones, acyl hydrazones, benzoyl hydrazones, heteroaryl hydrazones.From this the benzoyl hydrazones further divided into two types. They are aliphatic carbonyl derivative and aromatic carbonyl derivative. Then aromatic carbonyl derivative classified as heterocyclic and non- heterocyclic. Thus, it shows the classification of hydrazones.

These hydrazones are classified into two classes.

A. Aroylhydrazones synthesized using aliphatic carbonylcompounds.
B. Aroylhydrazones prepared usingaromatic carbonyl compounds.

This class is further divided into two types (a) Aroylhydrazones prepared using non- heterocyclic aromatic carbonyl compounds (b) Aroylhydrazones prepared using heterocyclic aromatic carbonyl compounds and (c) Heterocyclic hydrazones derived form heterocyclic aromatic carbonyl compounds.

Benzoyl and salicyloylhydrazones of β-diketones were synthesized and characterized by analytical data, thermal analysis, conductivity and infrared spectral studies. These hydrazones behave (**7**)either as mono basic bidentate or dibasic tridentate ligands towards the metal ions. Cobalt (II) complexes are tetrahedral while the copper (II) complexes have either tetragonally distorted octahedral or square planar geometry. Later the same workers have reported the synthesis, spectral and magnetic studies of manganese (II) and iron (II) complexes with benzoyl and salicyloyl- hydrazone ligands (I, II) derived from p-diketones.

APPLICATIONS OF HYDRAZONES:

Hydrazone and its derivatives with azomethine -NHN=CH- group represents an important class of compounds with broad spectrum of pharmacological activities (**8**). A variety of hydrazone derivatives have been synthesized with the potential pharmacological activities like antiinflammatory, antibacterial, analgesic, antifungal, antihypertensive, antiplatelet, anticancer, antimalarial, antidepressant, anticonvulsant and antiviral etc (**9**). In addition to their extended biological properties they also combine with other functional groups to provide pharmacologically active molecules. The main theme of this study is to explore the biological and pharmacological importance of hydarzone derivatives for future development of new drug entities. There has been considerable interest in the development of novel compounds with anticonvulsant activities. Thus the introduction concludes with further studies based on the anticonvulsant activity.

Tuberculosis is a chronic, infectious and most prevalent disease all over the world. It is caused by different strains of the Mycobacterium tuberculosis. Lungs, liver and bones are most susceptible to infection. The activity of the newer agents is mostly tested against virulent H37Rv strain. (**10**) synthesized nitroheterocyclic based 1,2,4-benzothiadizines , which exhibited MIC of 1 μg/mL. (**11**) synthesized hydrazone derivatives and reported to have MIC of 6.25 μg/mL. benzofuran-3-carbohydrazide derivatives reported as with good anti-tubercular activity. Hydrazone derivativessynthesized by (**12**) exhibited MIC of 6.25 μg/mL with significant antitubercular activity.(**13**) reported the antibacterial activity of hydrazine derivatives against various bacterial strains. Hydrazine derivatives synthesized byjubie et al., (2006) are promising antibacterial agents.(**14**) synthesized vanillin based hydrazine derivatives and reported their antibacterial activity specifically against *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

EXPERIMENTAL METHOD

Chemicals used :

All the chemicals used were of Merck and Sigma Aldrich products, available commercially in AR grade. The purchased chemicals were used without any further purification. The physicochemical techniques employed for the present study is discussed below.

Spectral methods:

Infrared spectroscopy:

Most of the spectra give sufficient information about the structure of the compound. The Infra Red spectrum is one of the spectra. Unlike UV spectrum which comprises of relatively few peaks, IR technique provides a spectrum containing a large number of absorption bands from which a wealth of information can be derived about the structure of an organic compound. The absorption of Infra-Red radiations causes the various bands in a molecule to stretch and bend with respect to one another.

The IR spectroscopy is widely used as a characterization technique for metal complexes. The basic theory involved is that the stretching modes of the ligands changes upon complexation due to weakening or strengthening of the bonds involved in the bond formation resulting in subsequent change in the position of the bands appearing in the IR Spectrum. The changes in the structural features of the ligands are observed as changes in bands observed, mainly in the fingerprint region (4000-400 cm^{-1}). The bands due to the metal ligand bonds are mainly observed in the far IR region (600-100 cm^{-1}).

In the present study, IR spectra of the compounds were recorded using Perkin Elmer spectrum RXI using KBr pellets at frequency range 4000-400 cm^{-1}at ACIC, St. Joseph′s College (Autonomous), Trichirapalli and Shimadzu FT IR 400 Spectrophotometer, frequency range 4000-400 cm^{-1} using KBr disc at St Joseph's College, Trichy.

Nuclear Magnetic Resonance spectroscopy:

^{1}H NMR:

NMR is a study of transitions between the magnetically inducted spin states. It is concerned with the magnetic properties of atomic nuclei with an integral value I. This technique consists of exposing the protons in an organic molecule to a powerful field. The protons will process at different frequencies. Now, these processing protons are irradiating with steady changing frequencies and observe the frequencies at which absorptions occur. The signals obtained corresponding to the absorption is known as NMR Spectrum.

Studying a molecule by NMR spectroscopy enables us to record differences in the magnetic properties of various magnetic nuclei present and to deduce the positions of this nucleus within the molecule. One can deduce how many different kinds of environments there are in the molecule and also which atoms are present in neighboring groups. Usually, the number of atoms present in each of these environments is measured. Therefore, the diagnostic features of the NMR Spectra are the number of signals, position of signals, splitting pattern of signals and area of signals. ^{1}H NMR of the ligands were recorded using Bruker 300 MHz Avance –II FT- NMR Spectrometer with DMSO-d6 as the solvent and TMS as internal standard at SASTRA University, Tanjore.

^{13}C NMR:

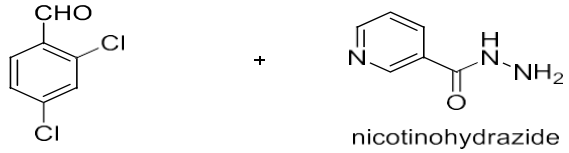
There are many differences between ^{1}H NMR and ^{13}C NMR spectra both in the mode of recording as well as appearance. The spin quantum number, I for ^{12}C is equal to zero since ^{12}C isotope has an even number of protons and even number of neutrons and hence no magnetic spin. It is, therefore, non-magnetic and does not give any NMR signal. The natural abundance of ^{13}C is only about 1.1% and has an odd number of neutrons. So, ^{13}C has a spin quantum number equal to ½ and its nuclear magnetic resonance can be observed in a magnetic field of 23,500 gauss at 25.2 mega cycles per second. ^{1}H spectrum is normally obtained by sweeping either the excitation frequency or the held through the region of precession frequencies. The inefficiency of this method is clear from the fact that only one line can be observed at a given point in time. The problem arises when ^{13}C with intrinsically narrow lines covering a wide absorption range are studied. It is, therefore, advantageous to excite the whole band of frequencies simultaneously. It is done by strong pulse of radio-frequency covering a large band of frequencies which is capable of exciting all resonance of interest at once. At the end of the pulse period, the nuclei will process freely with their characteristic frequencies reflecting with the chemical environment (Ele. Org. spec-231 &) and exhibit chemical shifts. ^{13}C NMR of the synthesized compounds were recorded on 75 MHz Bruker Spectrometer at 298.6 K using DMSO-d6 as solvent at SASTRA University Tanjore.

SYNTHESISOF (DICHOLOROBENZYLIDENE) NICOTINOHYDRAZIDE,

REQUIREMENTS:

2,4 dicholorobenzaldehyde	=0.875g
Nicotinic acid hydrazide	=0.685g
Methanol	=10mL
Water	=20mL

PROCEDURE: 0.875g of 2,4 dichloro benzaldehyde is taken in a clean conical flask. Then it is dissolved in 10ml of methanol. 0.685g of Nicotinic acid hydrazide is dissolved in 20ml of water. Then these two mixture are mixed using magnetic stirrer. After 10 minutes in stirring the white precipitate crude is yielded. The crude sample was recrystallised from ethanol. The purity of the compound was checked by Thin Layer Chromatography(TLC)



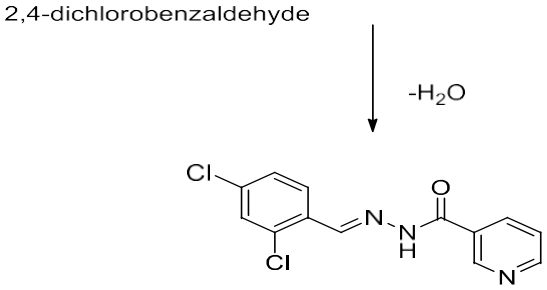


Fig 2: Structure of(E)-N'-(2,4-dichlorobenzylidene) nicotinohydrazide.

SOLUBILITY TEST:

(E)-N'-(2,4-dichlorobenzylidene)nicotinohydrazide

Solubility of compound was tested using water, methanol, ethanol, hexane, dichloromethane, benzene, ethyl acetate, chloroform and DMSO. 1mg of compound was added to 10ml of solvent and solubility was tested under two different conditions such as cold condition and hot condition corresponding to the boiling point of the solvent.

CRYSTALLIZATION:

Half portion of the sample is dissolved in ethanol while heating. Then this solution is allowed to slow evaporation. After 2-3 days crystals are formed.

TLC:

Thin Layer Chromatography has been used as an analytical tool, especially in organic chemistry because of its high speed of separation and its applicability in a large number of chemical compounds. The high sensitivity of TLC is used to check the purity of the samples. With the help of TLC, it is possible to know whether a reaction is complete and had followed the expected course.

Thin Layer Chromotography was made by dipping a glass plate in slurry of silica gel G, prepared by shaking silica gel G with chloroform-methanol (2:1) mixture at room temperature. The homogeneity of the compounds was monitored by this TLC plates and visualized by iodine vapour.

Characterization:

Some physical methods were used to elucidate the bonding and structure of the synthesized ligands and complexes and to confirm the expected properties. While the ligands were characterized by usual methods such as analytical technique such as TLC, molar conductance, magnetic susceptibility and spectral techniques such as IR, UV- Visible, NMR and mass spectral techniques, it differs for complexes depending on the nature of the ligands and the metal ions involved. The presence of paired or unpaired electrons of the metal ions imparts the magnetic behavior of the complexes.

UV analysis:

The synthesized compound is subjected to UV-visible analysis. DMSO used as blank. The OD is recorded between 200-700nm.

FTIR:

Infrared spectra were obtained on a Bomen FT IR MB-102 spectrometer in KBr pellets.

NMR:

^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recored on BrukerAvance DRX200 spectrometer at the SASTRA university, thanjavur

Analytical techniques

Elemental Analysis:

Our objective is to detect the presence of nitrogen, sulphur, chlorine, bromine and iodine in synthesized ligands by Lassaigne's test. A small piece of dry sodium was melted in a fusion tube. Then 0.1g of solid substance was added to the molten sodium. It was heated gently at first, then to red hotness. Quickly plunged red hot end of tube into 10mL distilled water in a china dish. It is stirred well with broken end of tube, boiled and filtered.

Test for nitrogen:

Few crystals of ferrous sulphatewas added with 1ml of fusion extract. It was boiled, cooled and then added two-ml of diluted sulfuric acid. Sodium cyanide is converted to sodium ferrocyanide on treating with ferrous sulphate. The green colour solution developed, it indicates the presence of nitrogen.

$$Na + \underset{\text{(From organic compound)}}{C + N} \xrightarrow{\text{Fuse}} NaCN$$

$$FeSO_4 + 2NaOH \rightarrow \underset{\text{(Green ppt.)}}{Fe(OH)_2} + Na_2SO_4$$

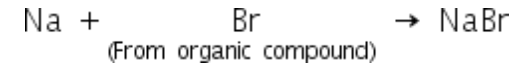
$$Fe(OH)_2 + \underset{\text{(From Sodium extract)}}{2NaCN} \rightarrow Fe(CN)_2 + 2NaOH$$

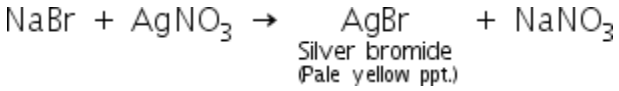
$$Fe(CN)_2 + 4NaCN \rightarrow \underset{\text{Sod. ferrocyanide}}{Na_4[Fe(CN)_6]}$$

$$3Na_4[Fe(CN)_6] + 4FeCl_3 \rightarrow \underset{Ferric\ ferrocyanide}{Fe_4[Fe(CN)_6]_3} + 12NaCl$$

Test for halogen :

One-ml of dilute nitric acid is mixed with one-ml of fusion extract. It is boiled, cooled and then added 1ml of silver nitrate solution. The halide ions chloride, bromide and iodide ions are giving white, pale yellow and yellow precipitate respectively but the compound does not form pale yellow precipitate . Hence we have conclude the ligand has bromine is absent.





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BIOLOGICAL ACTIVITY:

ANTICONVULSANTACTIVITY

Zebrafish maintenance

Zebrafish were maintained in a light- and temperature controlled aquaculture facility under a standard 14:10 h light/ dark photoperiod. Adult zebrafish were housed in 1.5 l tanks at a density of 25 fish per tank and fed twice per day (dry flake and/or flake supplemented with live brine shrimp). Water quality was continuously monitored: temperature, 28–30C; pH 7.4 were maintained.

Drugs used

Pentylenetetrazole (PTZ) was used to induce zebrafish epileptic seizure. phenytoin (PHT) as negative control were selected for the development and validation of zebrafishepileptic seizure model. 100 mg/ml Stock solutions were prepared in 100% dimethyl sulfoxide (DMSO) andstored at -20 °C,

Treatment group

Three months old fish were selected with a weight range of 0.5–0.6 g. Animal were divided into following groups,

Group I: Vehicle control (10% DMSO);

Group II: Pentylenetetrazole (PTZ-Negative control group) 100 mg/Kg; Group

III: Phenytoin 20 mg/kg (PHY) + PTZ (100 mg/kg);

Group IV: compound 20 mg/kg + PTZ (100 mg/kg).

In the experiment every group tested with 5 fishes Drug Treatment

Fish was captured individually by fish holding net, then transfer into ice water to give anesthesia. Fish was taken out once anaesthesized and weighed to calculate the dose and the

injection volume. A soft sponge of approximately 20 mm in height was saturated with water and set into 60 mm Petri dish. A cut of 10–15 mm deep was made on the sponge to restrain and hold the fish for injection. Intra peritoneal injection was made using a dissecting microscope by inserting the needle into the midline between the pelvic fins. Precautions include using a small injection volume of 10 µl per gram body weight. After injection, fish was immediately transferred to the tank and subjected for behavior recording

T-maze Test

The T-maze is composed of one long (18′) and two short (12′) arms. One of the short arms is connected to a deeper square chamber (9 × 9′) which serve as a favorable environment for the fish . Favorable environment is the chamber which is deeper and wider compare to other arms in T-maze and once fish finds it, they spend the majority of

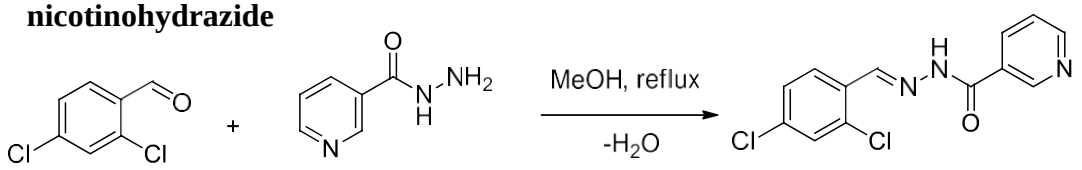
their time in it. The T-maze behavior test was performed in the behavior room of constant room temperature of 25°C – 26°C

SCORE	Behavior phenotype
0	Short swim mainly in the bottom of the tank.
1	Increased swimming activity and high frequency of opercular movement.
2	Burst swimming, left and right movements, and erratic movements.
3	Circular movements.
4	Clonic seizure-like behavior (abnormal whole-body rhythmic muscular contraction).
5	Fall to the bottom of the tank, tonic seizure-like behavior (sinking to the bottom of the tank, loss of body posture, and principally by rigid extension of the body).
6	Death.

Table 1: scoring standard for induced T-maze Seizure

RESULT AND DISCUSSION

Synthesis of (*E*)-*N*'-(2,4-dichlorobenzylidene) nicotinohydrazide



2,4-dichlorobenzaldehyde nicotinohydrazide (E)-N'-(2,4-dichlorobenzylidene) nicotinohydrazide

(*E*)-*N*'-(2,4-dichlorobenzylidene) nicotinohydrazide was synthesized by Schiff base as given in above. The crystallized powder (plate 1) tested for solubility and the data given in table 1. Analytical TLC was performed on pre-coated aluminum sheets of silica (60F254) and visualized by short-wave UV light at λ 254 nm. The compounds are crystallized and tested for solubility among different solvent (plate 2).The data given in table 1 reveals that the synthesized compound was insoluble among hexane and water under RT and cold condition. Solubility is higher in methanol, ethanol, ethylacetate, benzene, chloroform, DMSO and dichloromethane TLC(plate 3) reveals that the compound is pure and having higher Rf value ranges from higher value of ethyl acetate (0.95) and lower value of DCM (0.44). The TLC plate for (E)-N'-(2,4- dichlorobenzylidene)nicotinohydrazide in above solvent act as eluent.

Table 2. Solubility test for MBSPDO

S.no.	Solvents	Room temperature	Hot condition	Rf value
1	Water	Insoluble	Insoluble	-
2	Methanol	Soluble	Soluble	0.90 cm-1
3	Ethanol	Soluble	Soluble	0.73 cm-1
4	Hexane	Insoluble	Insoluble	-
5	Benzene	Soluble	Soluble	0.9 cm-1
6	Ethyl acetate	Soluble	Soluble	0.95 cm-1
7	Chloroform	Soluble	Soluble	0.45cm-1
8	Dimethylsulphoxide	Soluble	Soluble	0.93cm-1
9	Dichloromethane	Soluble	Soluble	0.44 cm-1

Spectral Characterization:

FT-IR Spectral studies:

In order to study of functional group of the synthesized Schiff base, the IR spectrum was compared with the general functional ranges. The IR spectrum of Schiff base showed characteristic broad band at 3248 cm^{-1} can be attributed to ν(N-H) and aromatic ν(ArC-H) stretching vibrations appeared at 3051 cm^{-1}. It is indicated, the Schiff base also having intermolecular O…H hydrogen bonding. The weak interaction was depends on the concentration of the solution. In this spectrum was recorded with very dilute sample. Another distinctive vibration expected for N-N observed at 1918 cm^{-1}. Generally carbonyl group stretching vibrations appears at 1680-1700 cm^{-1} but in this case appeared at 1629 cm^{-1}; this is due to amide group present in the compound which decreases the carbonyl functional group. The newly generated C=N stretching vibration appeared at 1491 cm^{-1} along with other finger print region signal and all other peaks are good agreement with the proposed structure. The FT-IR spectral data are given in table 3 and figure 1.

Table 3 Important IR bands of Schiff base with their assignments.

Vibrations	**ν(N-H)**	**ν(ArC-H)**	**ν(N-N)**	**ν(C=O)**	**ν(C=N)**
Peak (cm^{-1})	**3248**	**3051**	**1918**	**1629**	**1491**

NMR spectra analysis:

In ^{1}H NMR spectrum, the proton attached to C7 & C3 carbon showed as a singlet at δ = 8.99 and 7.78 ppm. It was the unique proton appeared as a sharp singlet without multiplicity and used to calibrate other peaks. The characteristic amine N-H was appeared as broad singlet at δ = 7.65 ppm. The three protons attached on the phenyl ring were appeared as two doublets at δ = 7.40 and 8.05 ppm and one singlet as discussed early. On the other hand, the four protons associated with pyridine ring were identified as two doublets at δ = 8.20 & 8.85 ppm, one multiplet at δ = 7.63 ppm and one sharp singlet at δ = 9.27 ppm. The detailed assignments of protons were given in table 4 and figure 2a.

Table 4 NMR Spectroscopic Data (δ) of (*E*)-*N*'-(2,4-dichlorobenzylidene)nicotinohydrazide

S. No	Position Assignment	^{1}H (δ, ppm)	^{13}C(δ, ppm)
1	1	--	132.8
2	2	--	131.0
3	3	7.78, s	129.1
4	4	--	128.4
5	5	7.40, d	127.5
6	6	8.05, d	129.2
7	7	8.99, s	138.7
8	8	--	--
9	9	7.65, br	--
10	10	--	163.2
11	1’	--	--
12	2’	9.27, s	148.9
13	3’	--	130.7
14	4’	8.20, d	135.6
15	5’	7.63, m	125.5
16	6’	8.85, d	148.6

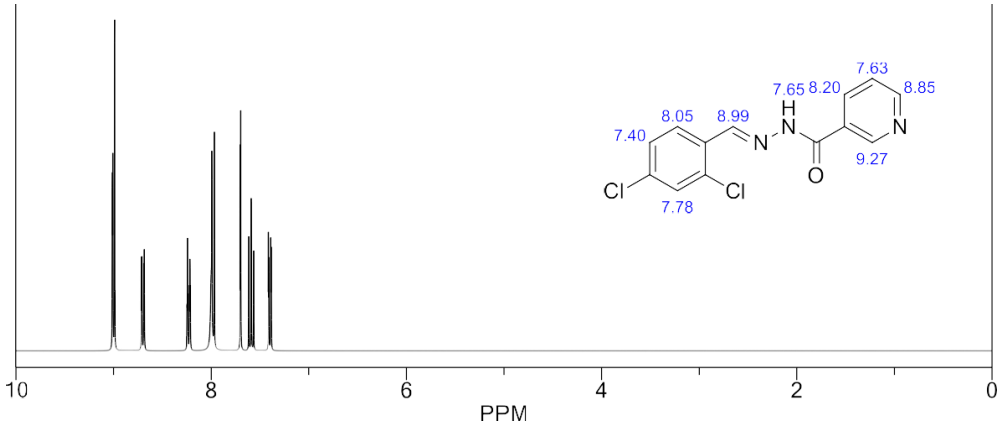


Figure 2. ^{1}H NMR spectrum of (*E*)-*N*'-(2,4-dichlorobenzylidene)nicotinohydrazide

In ^{13}C NMR spectrum, the discernible amide carbonyl appeared at δ = 163.2 ppm and it clearly indicates that molecule having amide group on its skeleton. Next, the carbon attached to the adjacent to the nitrogen atom on pyridine ring was appeared at δ = 148.9 and 148.6 ppm. The newly formed imine carbon peak appeared around at δ = 138.7 ppm. The chlorine attached quaternary carbon appeared at δ = 131.0 and 128.4 ppm. The remaining six C-H carbons are showed six signals in the range of δ = 125.5 to 135.6 ppm. Peak assigning of other carbons was showed in table 2 and figure 3.

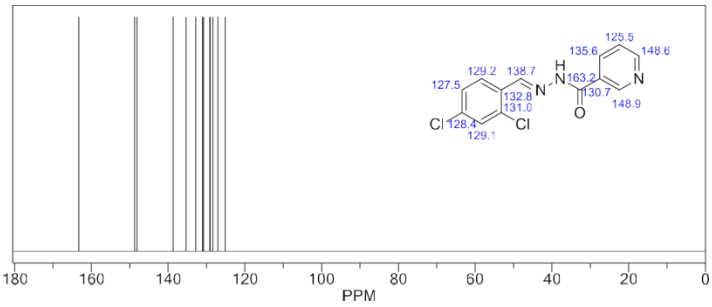


Figure 3. ^{13}C NMR spectrum of (*E*)-*N*'-(2,4-dichlorobenzylidene)nicotinohydrazide

ANTICONVULSANT ACTIVITY:

The behavioral analysis shown in table 5 reveals that movement of adult zebrafish in T maze (plate 4) towards unfavourable and favourable(table 5). In control 100% are under favourable environment and scoring 2 with Short bottom swimming. Group II treatment of PTZ induced seizure shows changes in behavior with scoring of 6 due to death of zebrafish. Nearly 80% were survived under unfavourable condition (plate 4c). there was a rapid score progression in the first 1h and reached maximum at 3h min period for PTZ**.**Where as in control group the score ranges 0-1 an ideal experimental condition exhibited spontaneous usual swimming movements consisted by repeated constant short swims. The induced seizure is reverted by Phenytoin within 2h and only 20% moved unfavorable compartment. Similar to positive control nicotinohydrazide maintained Short swim and 80% are maintained favourable condition. On the other hand, animals immersed into PTZ solution presented behavioral epileptic seizures, classified in different scores as shown in Table 6. Pentylenetetrazole (PTZ) induced seizure in adult zebrafish clonus-like behavior and have had maximum unfavourable score. The PTZ concentrations induced seizures with score 3≥4≥6 with in 3h(table 6). Group 4 PTZ seizure is inverted by Phenytoin with in 3 h and the score is 2≥2≥1 between 0-3 h. Similarly the synthesized tested

compound nicotinohydrazide has score 2≥0≥0 between 0-3h and completely reduced the Seizure score 2 to 0 and confirms the antiepileptic drug activity. Hydrazide/hydrazone derivatives that possess a -CO-NHN=CH- group constitute an important class of compounds for drug development. This review highlights the specific characteristics of various hydrazide/hydrazone derivatives and structurally related semicarbazones tested as as Anticonvulsant Agents in animals(44)

Table 5. T-maze behavior analysis among control and treatment

Groups	**Number of Zebra fishes**	**Favourable Environment**	**Unfavourable Environment**
Group I – Control (untreated)	5	5	0
Group II – PTZ (Negative control)	5	0	5
Group III – Phenytoin + PTZ	5	4	1
Group IV – compound + PTZ	5	5	0

Table 6. T-maze Seizure score analysis among control and treatment

Group	**Event of Behaviour**	**Scores**		
		1h	**2h**	**3h**
Group I - Control (untreated)	Short bottom swimming Increased swimming	0	1	1
Group II - PTZ (Negative control)	Circular erratic, clonic movements Fall to the bottom of the tank and Dead	3	4	6
Group III - Phenytoin + PTZ	Burst swimming, increaesed swimming and opercula activity	2	2	1
Group IV - MU compound + PTZ	Burst swimming, Increased swimming and Short swim	2	0	0

CONCLUSION

In the conclusion of the literature survey clearly reveals no work has been carried out for the synthesis of (E)-N'-(2,4-dichlorobenzylidene) nicotinohydrazide) using 2,4- dichlorobenzaldehyde and nicotine hydrazide. Aim and scope of the work is highly effective medicinal hydrazide derivatives have been synthesized from Schiff base route. The structure of the ligand (E)-N'-(2,4-dichlorobenzylidene) nicotinohydrazide) and its complexes were carried various spectral studies. From these studies, I know about the knowledge of organic chemistry and spectroscopy.In my present work, we have to synthesis (E)-N'-(2,4- dichlorobenzylidene) nicotinohydrazide) and establish the structure through the analytical (elemental and TLC) and spectral (IR, H^1 NMR and C^{13} NMR) methods of characterization.

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