NOE STUDIES OF PYRIDO [1,2-a]PYRIMIDINE-2-ONE ACETIC ACIDS

BY

S.SASIDEVI

(REG.NO.11PCM08)

A dissertation submitted to

Avinashilingam institute for home science and higher education for women university

(Estd. u/s of UGC Act 1956)

Coimbatore-641043

In partial fulfilment of the requirement for the degree of

Master of science in chemistry

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Certified as Bonafide Research Work

R. Ruganda

Signature of
The Head of Department

Signature of The
Guide

ACKNOWLEDGEMENT

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S.SASIDEVI

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LIST OF ABBREVIVATION

NMR - Nuclear Magnetic Resonance

IR - Infrared

UV-VIS - Ultraviolet-Visible

CD - Circular Dichrosim

2D NMR - Two Dimensional Nuclear Magnetic Resonance

NOE - Nuclear Over Hauser Effect

NOESY - Nuclear Over Hauser Effect Spectroscopy

COSY - Correlational Spectroscopy

PPM - Parts Per Million

TOSY - Total correlational spectroscopy

HZ - Hertz

DHF - 2, 3 DiHydro furan

DHP - 3,4 DiHydro 2H Pyran

DEPT - Distrotionless Enhancement by Polarization Transfer

UV - Ultra Violet

HSQC - Heteronuclear Single Quantum Correlation

HMQC - Heteronuclear Multiple Quantum correlation

MS - Mass spectroscopy

3D - Three Dimensional

4D - Four Dimensional

1DNOESY – One Dimensional Nuclear Over Hauser Effect Spectroscopy

H^1 NMR - Proton Nuclear Magnetic Resonance

^{13}C - Isotope of Carbon

EtOH - Ethanol

HREIMS - High Resolution Electron Ionization Mass Spectroscopy

Pd - Lead

1. INTRODUCTION

Organic compounds constitute a variety of compounds that make up life. For examples DNA, protein, cell membrane nucleic acids etc. Structural elucidation of these compounds is important for the study of mechanism that occurs in nature. The structure of chemically uncharacterized substances are identified by spectroscopic methods.The various spectroscopic methods like NMR, IR, MASS, UV-VIS help in the determination of molecular constitution and structure of the compounds

1.1 VIBRATIONAL SPECTROSCOPY

Infra-red (IR) and Raman spectra result from vibrations that occur naturally but dictally within molecules. This spectrum provides a variety of information about the molecule's structure particularly its symmetry and functional group present in the molecule. Both IR and Raman are used for identification of functional group present in the molecules.

1.2 ELECTRONIC SPECTROSCOPY

Electronic absorption spectroscopy measures the energy and probability of promotion of molecule from its ground electronic state to an electronically excited state. Information about electronic transition can be obtained from the UV-VIS spectrum or circular dichroism (CD).

UV-VIS spectroscopy is used qualitatively to detect certain functional group, according to the position and intensity of the absorption band. From the UV-VISIBLE spectrum the number of conjugated double bonds and also aromatic conjugation within the various molecules, can be determined.

1.3 MASS SPECTROSCOPY

Mass spectroscopy accurately determines the molecular mass of the compounds and its elemental composition.

1.4 NUCLEAR MAGNETIC RESONANCE SPECRTOSCOPY

NMR spectroscopy is one of the best tool for the structural elucidation of organic compounds. It gives detail about the type, number, and connectivity of particular atoms. NMR spectroscopy is used to identify the structure of both pure compounds and mixtures. From the magnetic properties of the atomic nuclei and the surrounding electron, NMR provides the molecular structure of the compounds.

NMR always has been multidimensional methods. One dimensional (1D) NMR spectroscopy includes regular ^{1}H and ^{13}C carbon spectra of other nuclei.3D and 4D experiments can also be done sometimes by running the plus sequence from two or three 2D experiments in series.

2D NMR spectroscopy is a set of NMR spectroscopy methods which give data plotted in a space defined by two frequency axes rather than one. Types of 2D NMR include

1. Correlation spectroscopy (COSY)
2. J. spectroscopy
3. Exchange spectroscopy (EXSY)
4. Nuclear over Hauser effect spectroscopy(NOESY)

1.5 NUCLEAR OVER HAUSER SPECTROSCOPY

The nuclear over Hauser effect was first described by OVER HASUSER in 1953 as the technique by which the intensity of NMR signals can be enhanced significantly by saturation (irradiation) of some of the nearly nuclei within the molecule. The Nuclear over Hauser Effect, which can be used to determine intra- (and even inter-) molecular distances.

The nuclear Over Hauser effect (NOE) arises from dipole –dipole relaxation between two spin- ½ nuclei. It is therefore dependent on the distance between the nuclei and their motions. The NOE is widely used in molecular biology to measure distances, and thus to calculate structures; and also as one of a set of measurements to assess intermolecular motion.

1.6 CONDITIONS APPLICABLE TO NOE

1. It arises only during double irradiation of one nucleus and affects another nucleus which must be close but not necessarily coupling with the irradiated nucleus.

2. It is associated with dipolar relaxation mechanism and is caused, for example, by the decoupling of the hydrogen spins from carbon spins which leads to a transfer of spin polarization to the carbons and a consequent increase in the carbon intensities

Signal enhancement due to NOE is an example of cross-polarization: a through-space effect in which polarization of spin states of one type of nucleus (say ^{1}H) caused by irradiation (B_1) induces polarization of spin states of another nucleus (say, ^{13}C or ^{1}H).

In general, the *maximum* NOE enhancement is given by

$$NOE_{max} = \frac{1}{2}\left(\frac{\gamma_{irr}}{\gamma_{obs}}\right)$$

Here, γ_{irr} is the magnetogyric ratio of the nucleus being irradiated and γ_{obs} is that for the nucleus under observation. The total (maximum) line intensity is given by $1 + NOE_{max}$. Hence, in the case proton-decoupled ^{13}C NMR spectra, the ^{13}C signal can be enhanced up to 200% by the irradiation of protons. This value is a theoretical maximum: most actual ^{13}C lines exhibit less (sometimes much less) than maximum enhancement.

1.7 Application of NOE

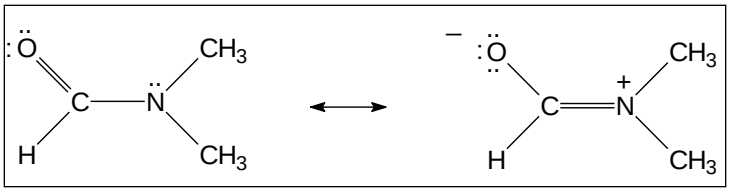
The two main areas in which the NOE is applied are for the generation of distance restraints in structure calculation, and as one of several measurements used to study macromolecular dynamics. Undoubtedly, the main role of the NOE is in providing distance restraints.

- **In Proton-Decoupled ^{13} C Spectra**

  In a proton-decoupled ^{13}C spectrum, the total NOE for a given ^{13}C nucleus increases as the number of nearby protons increases. Hence, the intensities of signals in a ^{13}C spectrum (assuming a single carbon of each type) are usually in the order $C < CH < CH_2 < CH_3$. This is often reliable for distinguishing unprotonated carbon atoms from protonated ones, but otherwise can be unreliable.

- ***Determination of Stereo chemical Relationship between Nuclei***

1. Dimethylformamide



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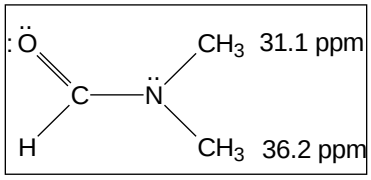
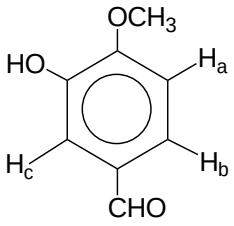
The methyl groups are non-equivalent, because of the considerable double bond character of the C-N bond: their ^{13}C nuclei resonate at 31.1 and 36.2 ppm. Irradiation at the ^{1}H frequency of the aldehyde group leads to a greater Nuclear over Hauser enhancement of the signal at 36.2 ppm. This must be the one spatially nearer the aldehyde proton, so the assignment is



2. Isovanillin



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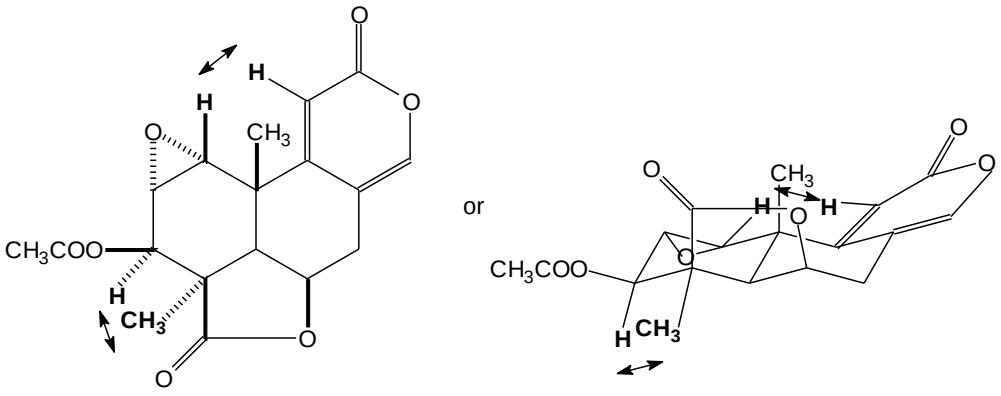
,

In the ^{1}H NMR spectrum of isovanillin, there are three aromatic ring protons and although it is possible to assign them according to chemical shift tables, observation of NOE can be of additional help. If the sample is irradiated at the proton frequency of the OCH_3 group, the intensity of the signal due to H_a is enhanced

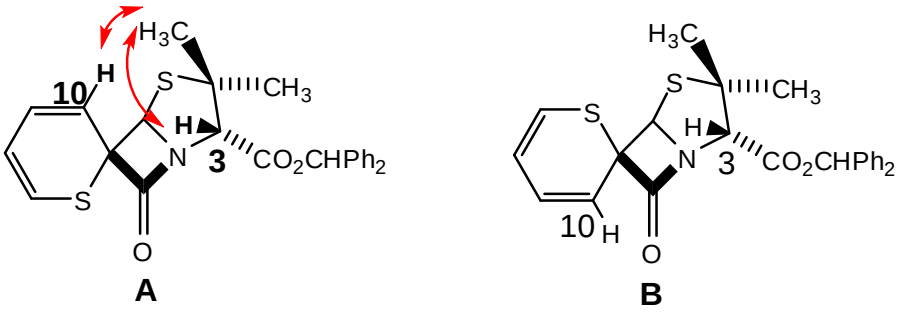
3.The proximities of the protons indicated by double-headed arrows were established by observation of NOE from double resonance experiments.



3 4

4.Confirguration of a synthetic penicillin Analog

Irradiation of the methyl protons shown causes enhancement of the signals due to H(10) and H(3), indicating that both of these are spatially close the methyl group: configuration A is the major one.



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5. The NOE in molecular biology

The NOE in molecular biology is to study the internal dynamicsin proteins. In most such applications,Not only the 1H-1H NOEs but{1H}-15N NOEs in the H-N bond are also studied.

1.8 Pyrido [1,2a] pyrimidine

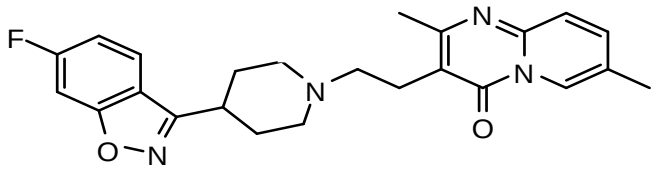
`Heterocyclic chemistry is of prime importance as a sub-discipline of Organic Chemistry, as millions of heterocyclic compounds are known, with more, being synthesized regularly. Hundreds and thousands of natural products and pharmaceutical active ingredients contain heterocyclic as central building blocks. They are present in many biologically important molecules such as amino acids, nucleic acids and hormones. They are also indispensable components of pharmaceuticals and therapeutic drugs; the most potent natural compounds, the alkaloids, are heterocyclic. The chemistry of heterocyclic compounds and methods for their synthesis form the back bone of modern medicinal chemical and pharmaceutical research.

Nitrogen hetero cycles of different ring sizes with different substitution patterns embedded in various molecular frame works constitute extremely important structural class in the search for bioactivity. Examples for such systems are quinolines, naphthyridines, pyrimidines, pyrido pyrimidines etc.

The bridgehead nitrogen hetero cycles are an important class of hetrocyclic compounds, because of their wide use in medicinal and agro

chemistry as scaffolds for active agents such as antiviral, antiulcer, anti-malarial, antifungal, and herbicidal, anti leprotic and immune suppressive agents. Saturated and partially saturated bicyclic 6-6 systems with one ring junction and one extra nitrogen atom viz pyrido[1,2-a] pyrimidines, pyrimido[1,2-a] pyrimidines and pyrazino[1,2-a] pyrimidines occur in many natural and biologically active compounds.

- Pyrido [1,2-a] pyrimidine represents a simple bicyclic ring system that contains a nitrogen-bridgehead condensed pyrimidine moiety. Pyrido[1,2-a] pyrimidine core had been a successful motif for the development of biologically interesting molecules including risperidone **7** and paliperidone **8** antipsychotic agents, metreperone **9** a selective $5HT_2$ receptor antagonist and lusaperidone **10** an antidepressant **(Alan R. Katritzky 2004 and Koilpillai Joseph et al, 2011).**



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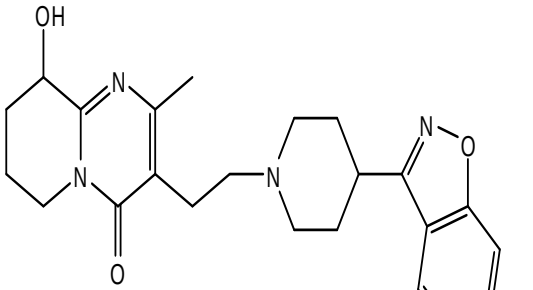

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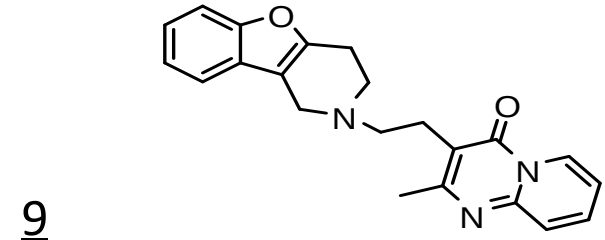

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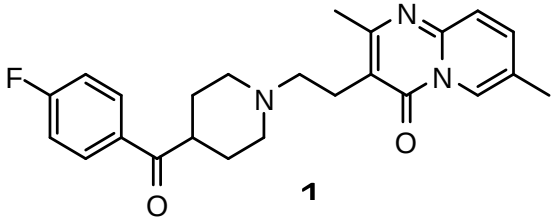

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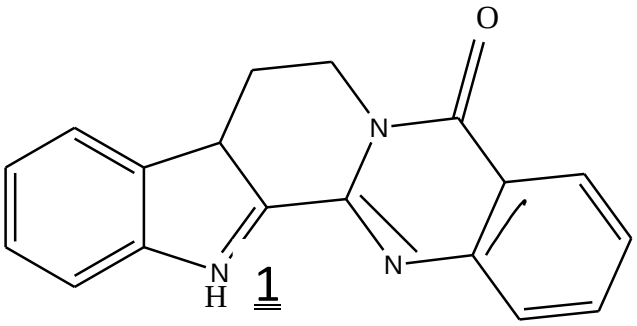
- Pyrido [1,2-a]pyrimidine core also form a part of several natural products. For e.g., Rutecarpine **11** contains the pyrido[1,2-a]pyrimidine moiety.



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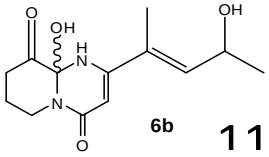
- Recently, three new naturally occurring bicyclic alkaloids, jenamidines **11a, 11b** and **11c**, were discovered and isolated from the culture broth of Streptomyces sp. (strain HKI0297) via the chemical screening approach by **Jin-Feng Hua et al, 2003.** The jenamidines have an unusual octahydro-pyrido[1,2-a]pyrimidine skeleton. Jenamidine **11a** showed antiproliferative effects against the chronic myeloid leukaemic cell line K-562.



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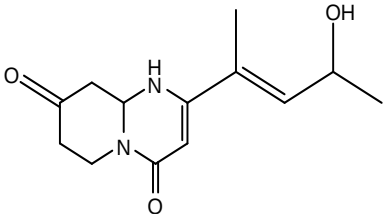

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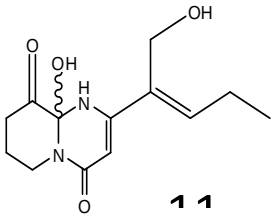
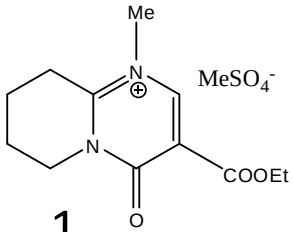


11

- The analgesic rimazolium methyl sulphate a quaternary ester of pyrido [1,2-a] pyrimidin4-one **12** was introduced into the drug market in second half of 1970's. It was successfully applied for the treatment of patients with postoperative pain, and rheumatic diseases **(Istvan Hermecz et al, 1988).**



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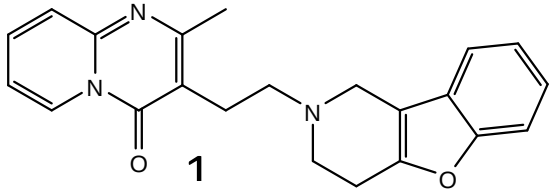
- The combination of rimazolium with either morphine or azidomorphine prevented the development of tolerance to the narcotic analgesics in cancer patients. The azidomorphine-rimazolium combination provided complete pain relief, without the development of addiction and or tolerance.Radiolabeled 2-methyl-3[2(1,2,3,4tetrahydrobenzo[4,5]furo[3,2-c]pyridin-2-yl)ethyl]-4H-pyrido[1,2-a]pyrimidin-4-one **13** was prepared and evaluated as a potential positron emission tomography (PET) ligand for studying central alpha(2)-adrenoceptor antagonist by **Van der Mey et al, 2006.**



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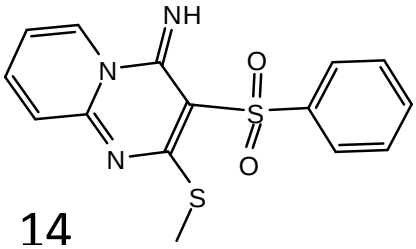
- (E)-3-(Benzenesulfonyl)-2-(methylsulfanyl)pyrido[1,2-a]pyrimidin-4 ylidenamine **14** was found to be a potent and selective 5-HT(6) antagonist **(Wu et al, 2003).**



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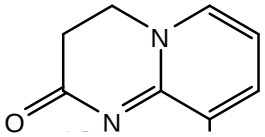

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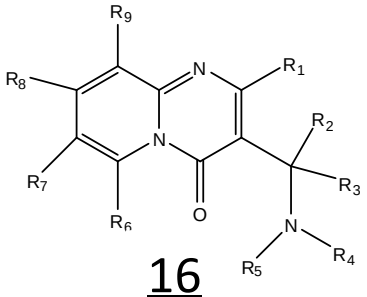
- (9-[4-acetyl-3-hydroxy-2-n-propylphenoxy) methyl]-3-(1H-tetrazol-5-yl)-4H-pyrido [1,2-a] pyrimidin-4-one) was found to contain anti-allergic property **(Hamasaki et al, 2000).** Pyridino[1,2-a]pyrimidinyl compounds of the structure **16** had been patented as anticancer agent **(Weibo Wang et al, 2011).** 2-(9-(2-Piperidinoethoxy)-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-2-yloxymethyl)-4-(1-methyl

ethyl)-6-methoxy-1,2-benzisothiazol-3(2*H*)-one-1,1-dioxide (SSR69071), **17** was found to be a novel, orally active elastase inhibitor **(Zolta'N Kapui et al, 2003).**



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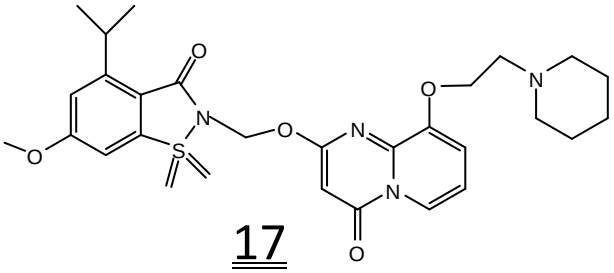

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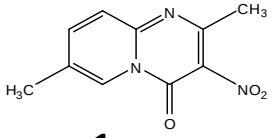
- Anti-histaminic, anti-inflammatory and bronchorelaxant activities of 2, 7-dimethyl-3-nitro-4H-pyrido [1,2-a] pyrimidine-4-one **19** were investigated by **Youssouf et al, 2008**. **Giorgio Roma et al, 2000** described, 2-2-piperazinyl04H-pyrido[1,2-a] pyrimidine-4-one **20** as invitro inhibitor of human platelet aggregation which specifically inhibited the activity of high affinity CAMP phosphodiesterase.



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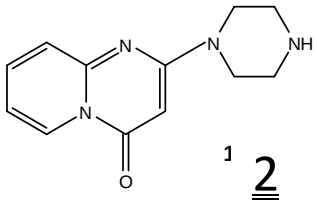

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OBJETIVES OF THE STUDY

Studies on pyrido [1,2a] pyrimidine derivatives are much valued due to their medicinal properties. The “structural elucidation” of these biologically active compounds, tends to paly vital role in organic synthesis and pharmacological studies, hence the present work has been undertaken with the following objectives,

- Preparation of pyrido [1,2-a] pyrimidines
- Characterization of the compound by 1D& 2D, spectral studies
- To study the stereochemistry of the synthesized compounds

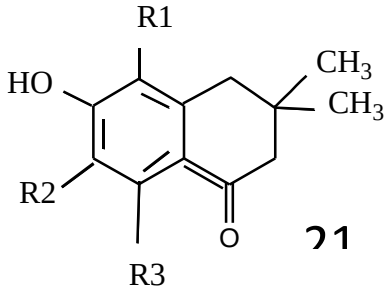
2. REVIEW OF LITERATURE

A research work is a gradual process and systematic unfoldment of important existing concepts, which have been dealt with the experiments by experts and science scholars. The literature of past finding and studies is essential and indispensable for further experimentation and research work where the discovery of new concepts is an extension of existing concepts. So the present work is reviewed under the following headings.

- NOESY studies of Heterocyclic compounds
- Synthesis of pyrido[1,2a] pyrimidine

NOESY studies of Heterocyclic compounds

- 8(3′-methyl-but-2′-ene-1′-oyl)-7-hydroxy-2,2,5-trimethyl-2H chromanone was obtanined as a byproduct in friedlcrafts acylation of active phenolic compound. Structural elucidation and conformational analysis of compound was reported using NMR methods. The homo nuclear proton 1D NOE difference spectrum of 8(3′-methyl-but-2′-ene-1′-oyl)-7-hydroxy-2,2,5-trimethyl-2H chromanone proton at 1.94 ppm. The ring peak (δ 6.39) at C-6 is seen to enhance (4.8%) its intensity. Irradiation of peak at 6.39 ppm produces an enhancement (5.0%) of the corresponding peak at 1.94 ppm**. Vijalakshmi C.S et,al 1991**



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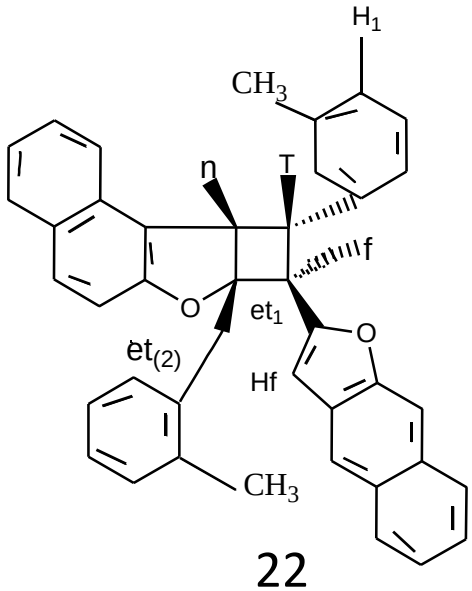
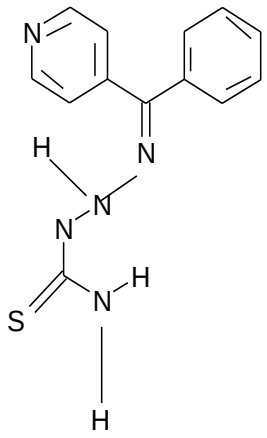
- **Irene Vujkovic Cvijim et,al 1998** prepared 6-(2 –methylphenyl)-1-[2-(2-methylphenyl)ethyl]-7-(2-naphtho-[2,1-b] furyl-3-[3.2.0]hept-3ene was prepared by photodimerization of 2-[2-(2-methyl-phenyl)ethyl)]naphtha[2.1-

b]furan. Structural elucidation of the compound were done by ^{1}H and ^{13}C NMR spectroscopy. A cross peak between one methyl group at 2.50ppm (CH_3) and the cyclobutane proton at 4.87ppm in NOESY experiment showed that tolyl group has to be on the same carbon as the middle hydrogen at the position 6 of the oxabicyclo[3.2.0] hept-3-ene ring.



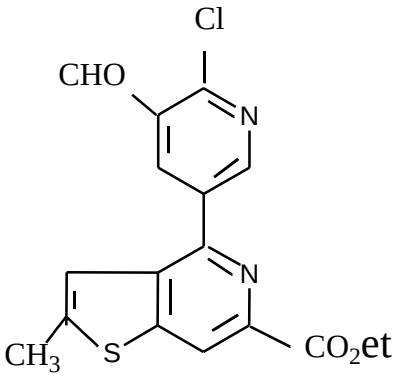
22

- E and Z -4 benzyl pyridine thio semi carbazone was prepared by the reaction of 4-benzoyl pyridine and thiosemicarbazide. Stutural determination of Z -4 benzyl pyridine thio semi carbazone was done by NOESY correlation spectroscopy. NOESY correlation were observed for H-2′(δ_H9.54) and H-3\5 (δ_H7.60), indicating the proximity of the pyridine and thiosemicarbazone hydrogen, characterstic of the Z-isomer **A.M. Barreto Bastos et,al. 2005.**



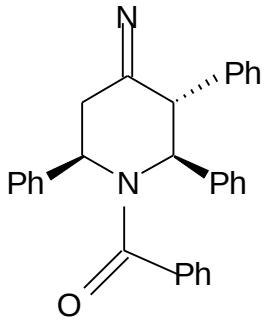
23

- Conformational studies of thieno pyridines and carboline biarylic compounds was done by 2D NMR spectroscopy and NOESY experiments. NOESY spectrum of 3-chloro-5-(2-methoxycarbonyl-thienol[2,3-b]pyridine-5-yl)-7-methoxycarbonyl-thienol[2,3-b:4,5-c]dipyridine was recorded in the diagonal crosspeak H-4 to both dipolar correlation between H-4 and H-3 it was possible to evaluate angle (50.0) between 4b-5 5′-6′.The interatomic distances between proton are H-4/H-6=2.58Å;H-3′/H-4′=2.71ÅH-4/H-6=2.58Å;H-4/H-4′=4.28;H-Å 3′/H-4′=2.71Å **D.Coronaa et,al 2009.**

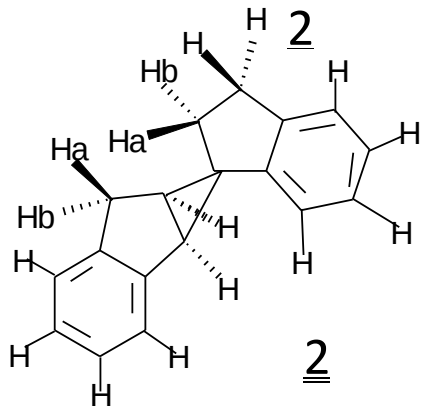


24

- **Chakkarvarthy et,al 2008** have done stereochemical study of some N-acyl-2r-6C diphenyl pipertidine-4-one oxime by using ^{1}H and ^{13}C and 2D NMR spectroscopy techniques. The NOESY spectrum of N-benzoyl-2r-6c diphenyl pipertidine-4-one oxime was NOE between H-2 and H-3′ and that between H-6 and H-5′ are strong.

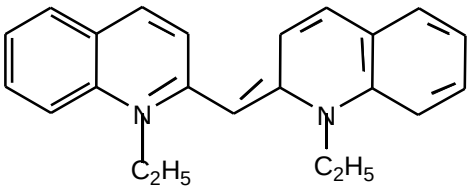


- The structure of the (1s,1aR,6aR)-2′,3′,6,6a-tetrahydro spiro[cyclo prop[a]indene -1-(1aH),1′[1H]indene] was confirmed by 1D and 2D analysis using COSY,NOESY,HSQC and HMBC measurements. **Peter spiteller et,al 2005**



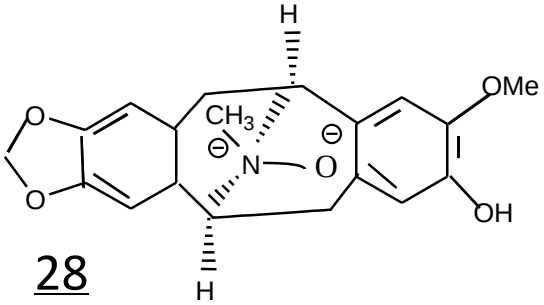
- Structural elucidation of 1,1′-diethyl 2,2′ cyanineiodide in water and methanol was suudied by 2D NMR techniques (COSY,NOESY, and TOCSY). The NOESY spectrum showed aromatic signal at 7.95 ppm and the signal from

CH_2 group at 4.65ppm and CH_3 group at 1.63ppm. Cross peak in NOESY spectrum are generated by cross relaxation. Therefore the protons close in space was confirmed by NOESY spectrum. **Irina Struganova et,al 2008**



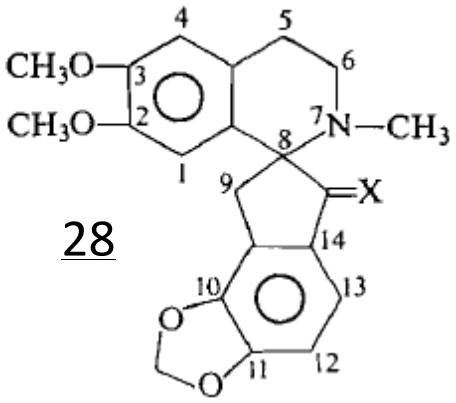
27

- **Fu-Wen Lin et,al 2002** isolated new pavine N-oxide alkaloids from the stem bark from crytocarya chinenesis. Structural elucidation of isolated compound was determined by spectral techniques. The relative stereochemistry of N-oxide was further determined by NOESY experiments. The presence of nuclear overhauser effect (NOE) correlation of H-7 with methoxy (δ 3.85) and H-6α(δ 4.63) indicated that the presence of methoxy group on C-8. The cross peak between NCH_3 (δ 3.35)H-5 α(δ 3.90) confirmed that NCH_3 is close to H-5. Based on the above spectral data, the structure was assigned for (-) isocaryachine-N-oxide B.



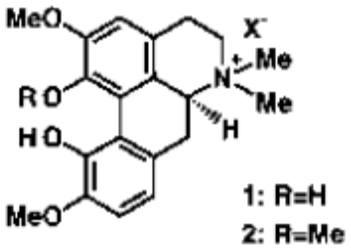
28

- **D.B.Maclean et,al 1969** have reported the structural elucidiation of fumaricine, fumartinie and fumariline, minor alkaloids from fumaria officialisL. by spectroscopic methods.Nuclear over hauser effect observed in these system aided in the confirmation of the structure.



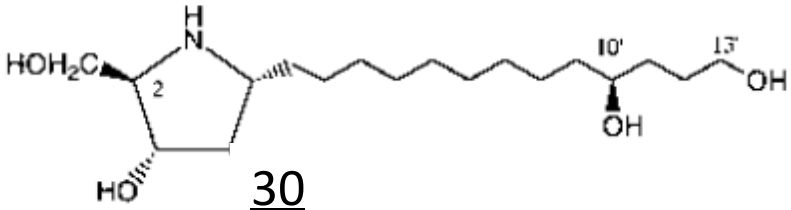
28

- Quaternary Isoquinoline alkaloids were isolated from sterphania cepharantha. Their structure was determined on the basis of spectroscopic evidences, stereochemistry of the compounds was confirmed by NOE experiments. **Takao Tanahashi et,al 2000.**



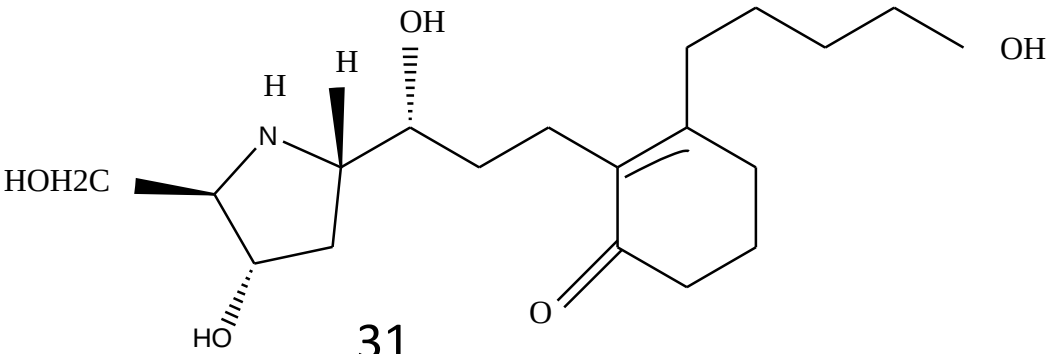
2

- **Makio shibano et,al 2000** isolated four new pyroline alkaloids, Broussonetines M, Broussonetines O, Broussonetines P, and Broussonetines Q.Structural elucidiation including absolute stereostructures and inhibitory activity of this pyroline alkaloids were deterimined by spectroscopic and chemical method.In NOESY spectrum NOEs were observed between H-2 and H-4 and H-3 and H-5 to establish the 2β hydroxyl methyl-3α,4β- dihydroxy methyl-3α,4β-dihydroxy -5α-alkyl pyrrolidine structure.



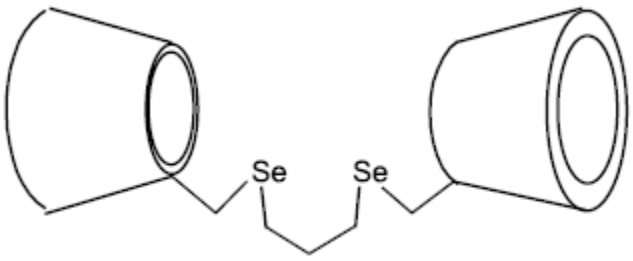
30

- Four new pyrrolidine alkaloids broussonetines R, Broussonetines S broussonetines T,broussonetines V and broussonetines U were isolated from the branches of Broussonetia Kazinoki SIEB in low yield.The structural elucidiation of this alkaloids were done by spectroscopic and chemical method.In NOESY spectrum NOEs were observed between H-2 and H-4 and H-3 and H-5 to establish the 2β hydroxyl methyl-3α,4β- dihydroxy methyl-3α,4β-dihydroxy -5α-alkyl pyrrolidine structure.**Daisuke Tsukamoto et,al 2001**



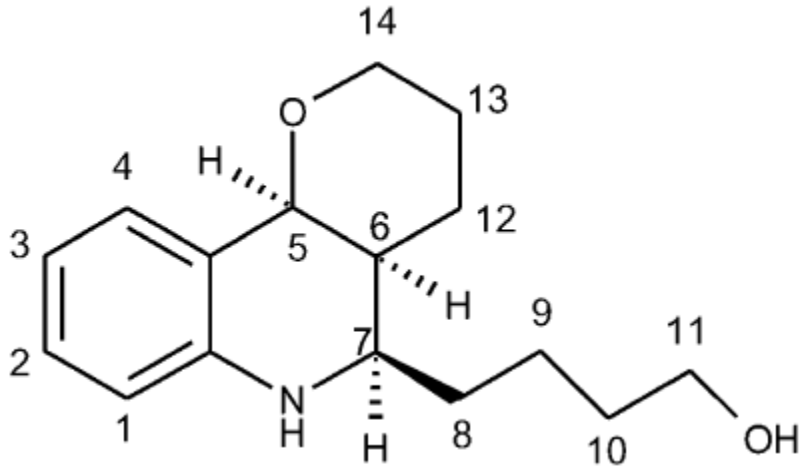
31

- **Yu lin et,al 2002** assessed the inclusion complexation behavior of chiral members of cinchona alkaloid with β and γ-cyclodextrins and 6,6′ trimethylenediseleno briged bis (β-cyclo dextrin) by fluorescence and 2D NMR spectroscopy.Stereo chemistry of complex was comfirmed by NOE experiments. NOESY spectra of complexes showed intermolecular cross peaks between the proton of the guest and the protons at C-3 and /or C-5 of the host cyclodextrin.



32

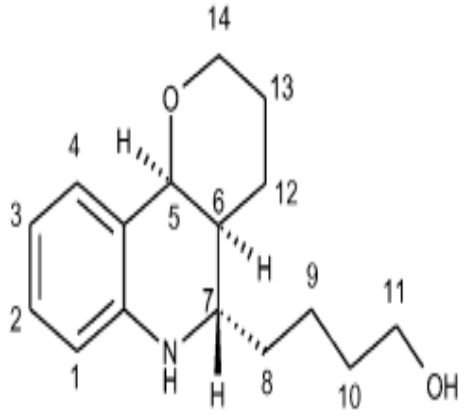
- Synthesis of pyrano and furano [3,2-c]-quinoline in aryl amines react with cyclic enol ethers such as 3,4-dihydro-2H-pyran (DHP) and 3,4 dihydro furan(DHF) on the surface of montmorillonite KSF under mild reaction condition were carried by **Yadav .J.S et,al 2002**. Stererochemistry of the compounds were dertermined by ^{1}H and NOESY experiments.The stereochemistry of the endo pyrano [3,2-c] quinoline derivatives was assigned on the basis of coupling constants and NOE studies . The two six membered quinoline and tertrahydropyran rings are cis –fused as indicated by the small coupling constant value JH-4-H-5=5.6HZ for H-5 proton as well as the observation of an NOE cross peak between them in the NOESY spectrum.



3

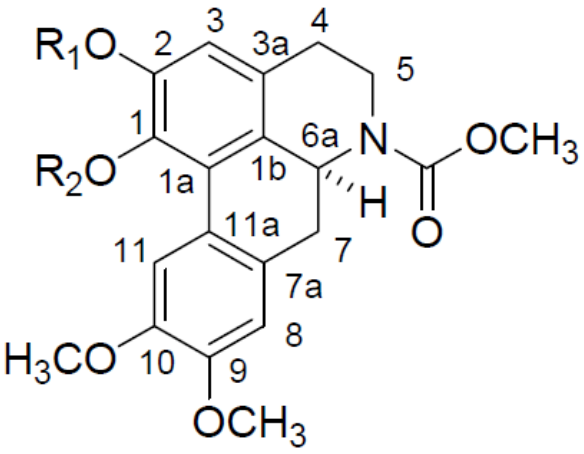
- Pyrano [3,2-c]-quinoline was synthesized by the cycloaddtion reaction of aryl amines with 3,4-dihydro-2H-pyran (DHP) under mild reaction condition in

presence of Indium trichloride catalyst. In exo isomer derivaties, the two six membered quinoline and tertrahydropyran rings are cis –fused as indicated by the small coupling constant value JH-5-H-6=3.2HZ for H-5 proton as well as the observation of an NOE cross peak between them and the absence of cross peak between H-6-H-7 in the NOESY spectrum **Yadav .J. S et,al 2002.**



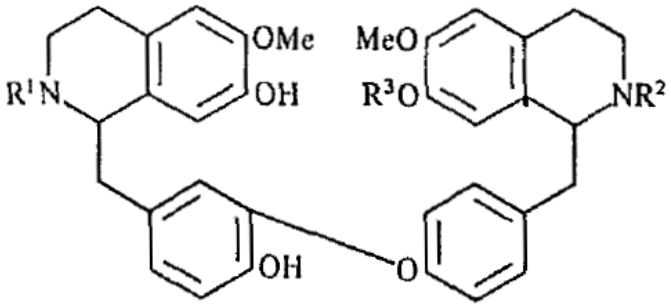
3

- **Wei Zhang et,al 2012** isolated five novel isoquinoline alkaloid (+)-(methyl carbonyl)-N- nordicetrin, (+)-(methyl carbonyl)-N- norpredicentrin, (+)-(methyl carbonyl)-N-norbulbodione , (+)-(methyl carbonyl)-N-norisocorydione and (+)-8-methoxisolaurenine-N-oxide from 70% EtOH extract of the barks of litsea cubeba . Structural elucidiation of all compound were done by spectroscopic methods such as IR, UV , HRESIMS, 1D and 2D NMR . The NOE correlations of H-8 and H-11 with the signals of two OCH_3(δ_{H3}.90and 3.93 respectively) positioned two methoxy at C-9 and C-10 which was with OCH_3 (H3.93) that the two OCH_3 respectively further supported by the HMBC of C-9(δ147.2) with OCH_3 (δ_{H3}.90) and C-10(δ_{H1}48.0)



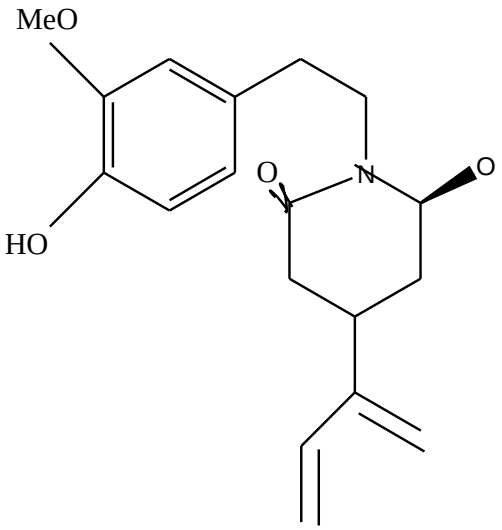
35

- **Pascale Dute et,al 1987** isolated eight isoquinoline alkaloids from the stems of Abuta Pahni. The structure of isoquinoline alkaloids were identified by spectroscopic methods and chemical correlations. The positions of amino groups in alkaloids are determined by NOE measurements.



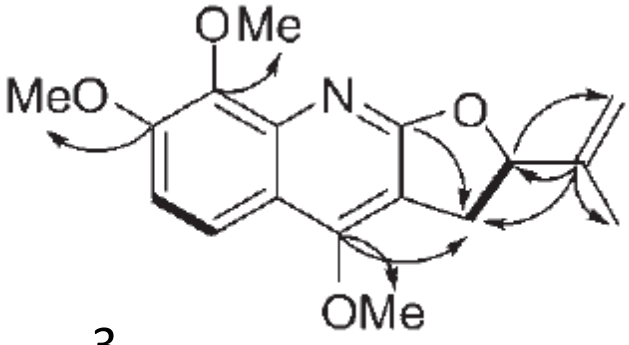
3

- A new type of monoterpenoid isoquinoline alkaloid(±)-Alangine was isolated from Alangium lammarckii. The stereochemistry was confirmed by total synthesis via N-acyliminium cyclization to construct the isoquinoline skeleton and reductive cleavage of vinyl epoxide with Pd(0) catalyst. Stereochemistry of alkaloid was confirmed by NOE measurements**. Hiromitsu Takayama et,al 2002**



37

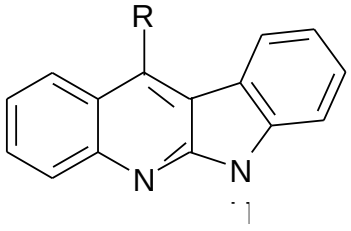
- **JU–Li Yang et,al 2010** isolated four new secondary metabolites from Dictamnus dasycar Pus Turcz. The structure of the compound was confirmed by spectroscopic analyses. The NOE difference spectrum of 1',1',-didehyro-7,8-dimethoxyplaty-desmine was showed that the characterstic C-4methoxy group at 4.20ppm did not correlate with the other methoxy groups, which also confirmed that the three methoxy groups should be at C-4,C-7 and C-8. The above observations indicated a structure close to that of 7,8-dimethoxyplatydesmine [38]



3

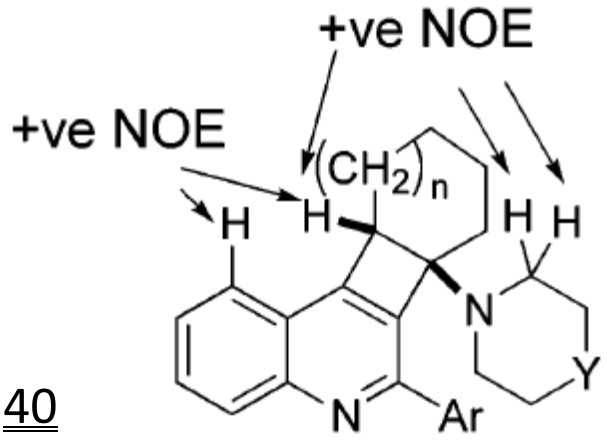
- 6H-indolo[2,3-b] quinoline derivatives were prepared from the commercially available 1,4 dihydroxyquinoline through alkylation,chlorination, nucleophilic reaction ,and ring cyclization . The

structre of quinoline derivaties was confirmed by ^{1}HNMR and NOESY spectrum. The position of methyl group in 11-methoxy-5-methyl-5H-indolo[2,3-b]quinoline , 11-methoxy -6-methyl-6H-indolo [2,3-b]quinoline, and 5,6 dimethyl-5,6 –dihydroindolo [2,3-b]quioline-11-one was confirmed by NOESY experiments. **Yeh-Longchen et,al 2004**



39

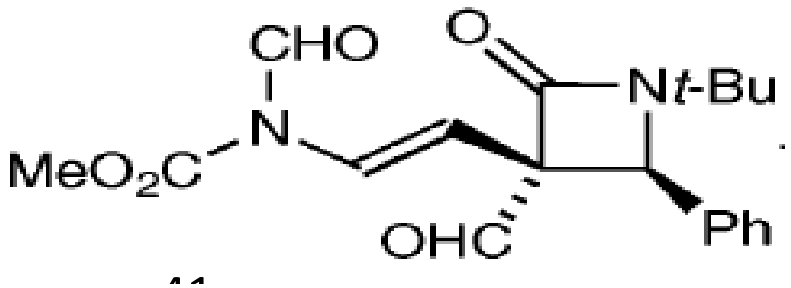
- **Elisabetta Rossi et,al 2001** synthesized bicyclo[4.2.0]-octane [7,8-c]-2-aryl quinoline or C-fused quinoline by β-(2-amiophenyl)-α,β-yones reacts with enamines of cyclic ketones by domino[2+2]cycloaddtion/annelation reaction. ^{1}H NMR and 2D COSY, HETOR,NOESY were used for structural determination of the quinoline NOESY experiments confirmed the assigned region- and stereochemistry showing diagnostic NOE effect between Csp^{3}-H and pyrrolidine nucleus and between Csp^{3}-H and the aromatic hydrogen at C-5 on the quinoline nucleus.



40

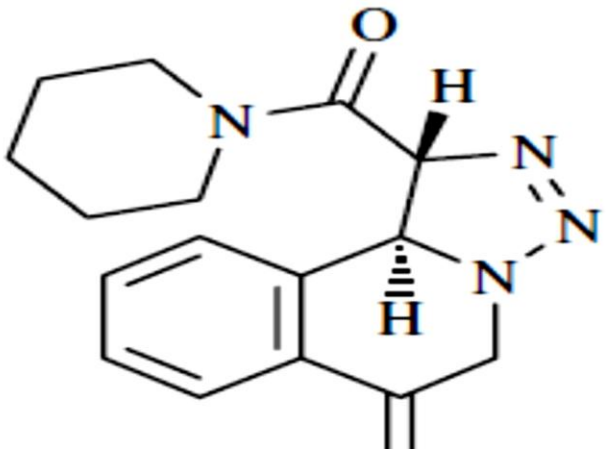
- **Jonathan claydon et,al 2005** done cyclization of Lithlated pyridine and quinoline carboxamides giving anions that undergo intermolecular attack on

the pyridine or quinoline ring to give pyrrolopyridines, pyrroloquinolines, benzonaphthyridines azapirocyclic β-lactams.The stereochemistry of monocyclic β-lactam was confirmed by NOE.



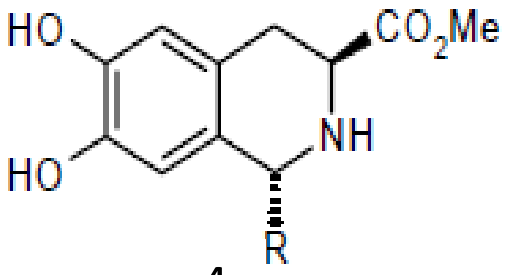
41

- Synthesis of triazolo and tetrazolo-tetrahydro isoquioline was carried by 1,3 dipolar cycloaddtion. The stereochemistry of cycloadducts was confirmed by NOE studies.**X.Gaiet,al 2005**



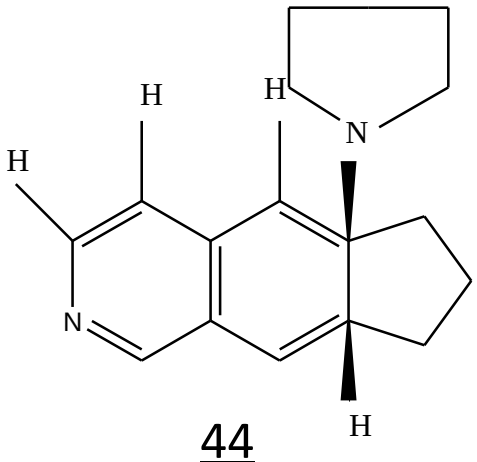
42

- **Ye WANG et,al 2004** synthesized cis -1-substituted-6,7-dihydroxy-1,2,3,4-tetrahydro isoquinoline -3- carboxylic acid ester by 1,3-induction pictet-spengler (p-s) cyclization of the L-DOPA (3,4-dihydroxy phenylalanine) methyl ester with aromatic or aliphatic aldehydes under acidic conditions.The stereochemistry cis -1-substituted-6,7-dihydroxy-1,2,3,4- tetrahydro isoquinoline -3- carboxylic acid ester was confirmed by NOE measurements.



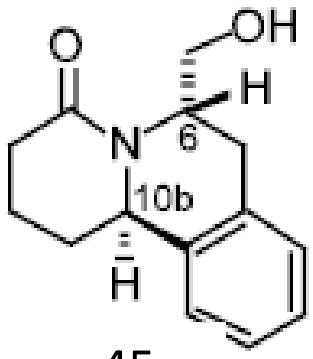
4

- Pyrido [3,4-d] pyridazine undergo thermally induced Diels –Alder reaction with enamines as electron rich dienophiles, yielding isoquinoline derivatives. Structure of 6,7,8,8a-tetrahydro-5a-pyrroline-5aH-cyclopenta[g] isoquinoline was confirmed by NOE difference spectroscopy. **Easm Abdel-Rehem et,al 2001**



44

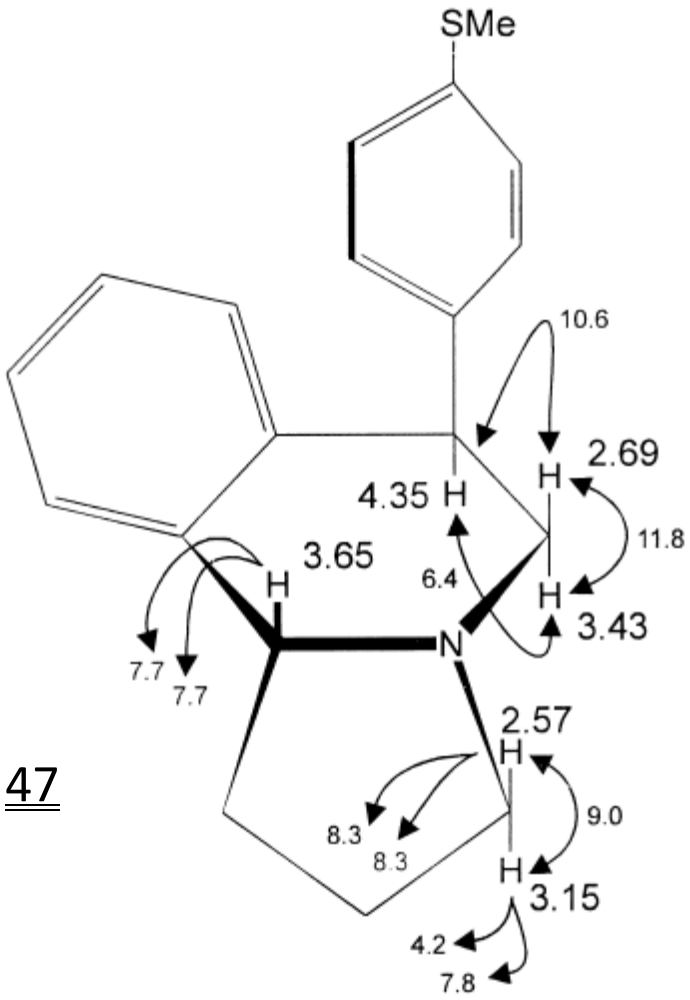
- Stereo selective synthesis of tricyclic tertrahydroisoquioline ring system from bicyclic lactam substrates.The Structure and stereo chemistry of isoquinoline was confirmed by NOE studies was carried out by **S.M.Allin et,al 2002**.



45

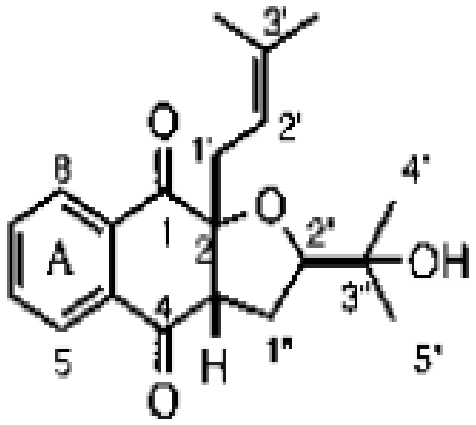
- Antdesmone alkaloid was isolated from antide membranaccum Mull.Aug. stereochemistry of alkaloid was confirmed by HREMIS and ^{1}H and ^{13}C ,1D and 2D experiments [HSQC,HMBC, COSY,NOESY] The NOE difference spectrum of 4-O-Methylantidesmone irradiation of 2-Me signal at 3.85 ppm ,which was therefore clearly proven to be 3-OMe **G.Bringmann et,al 2000**

- **O.Schulze et,al 2001** confirmed the configuration of the diasteroisomer of 6-(4-methylthiophenyl) -1,2,3,5,6,10b-hexa hydro pyrrolo [2,1-a] isoquinoline by NMR spectroscopy [NOE measuremen 4 X-ray structrural analysis. Stereochemistry of the compound was confirmed by NOE measurements.



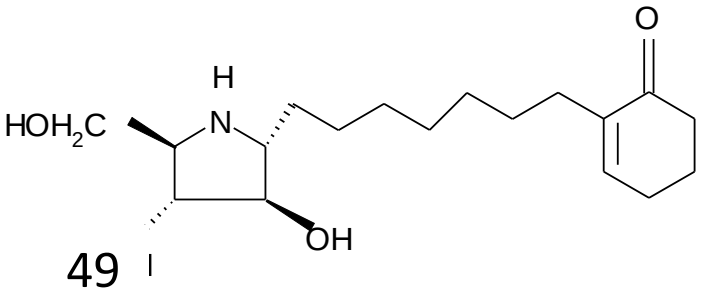
47

- **Chihiro Iro et,al 1999** isolated a novel naphhoquinone and new acridine alkaloid from chemical constituents of Methanol-CH_2Cl_2 extract of the stem of glycosmis penta phyla RETZ (rutaceae).Structural elucidation of the compounds was done by spectroscopic analysis. The relative stereochemistries of the three asymmetric centers in the molecule were proposed by observations of NOE enhancements between the methane proton signal at δ_H-3.41(H-3) and olefinic proton signal at δ_H5.03 (H-2′) and the phenyl moiety, and the methyl protons at δH 1.14 (H-3′) on the side chain and one of methylene proton at δ_H 2.46 (H-1″) which also have NOE with the methane proton at δ_H 3.41 (H-3)



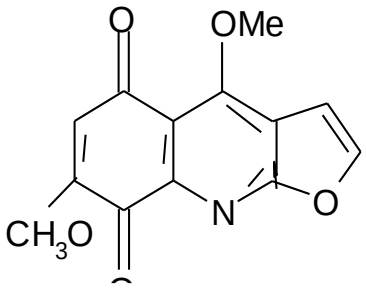
48

- **Daiuke Tsukamoto et,al 2001** isolated six new alkaloids Broussonetines W, Broussonetines X, Broussonetines M, BroussonetinesU, BroussonetinesJ1, BroussonetinesJ2 from the branches of Broussonetia Kazinoki SIBE (Moraceac). Stereostructure of 2β-hydroxy methyl- 3α,4β-dihydroxy-5α-alkyl pyrrolidine was confirmed by NOESY spectrum.



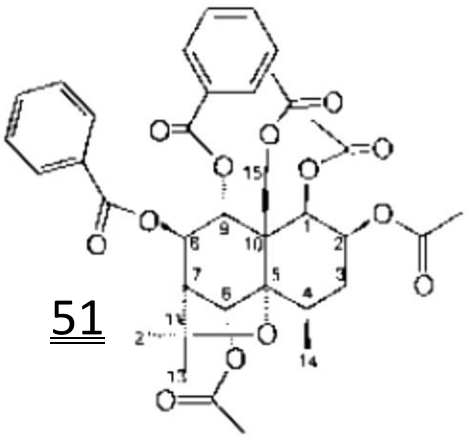
49

- Two alkaloids Megstioquinone I and Megstioquinone II were isolated from the bark of sarcomelicope megistophylla.Structral elucidation of the compound was confirmed by MS, NMRdata. Stereochemistry of the alkaloids were confirmed by NOE experiments **.Nikolas Fokialakis et,al 2002**



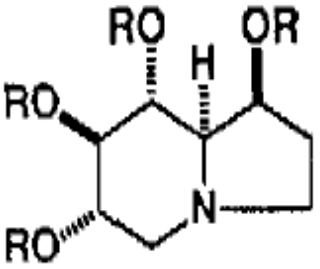
50

- A Novel agaro furan sesquiterpene polyol ester,1β,2β6α,15β-tetracetoxy-8β,9α-dibenzoyloxy-β- dihydro-agarofuran (celahinD) isolated from the stems of the celastrus hindsil BENTH. Structural elucidation of the celahin D was established by 2D NMR spectra. From the NOESY spectrum of celahin-D , the correlation between H-6 and H-15a and H-14 and between H-9 and H-15a indicated the presence of equatorial stereochemistry of H-9. **Hui-Chi Huang et,al 2000**



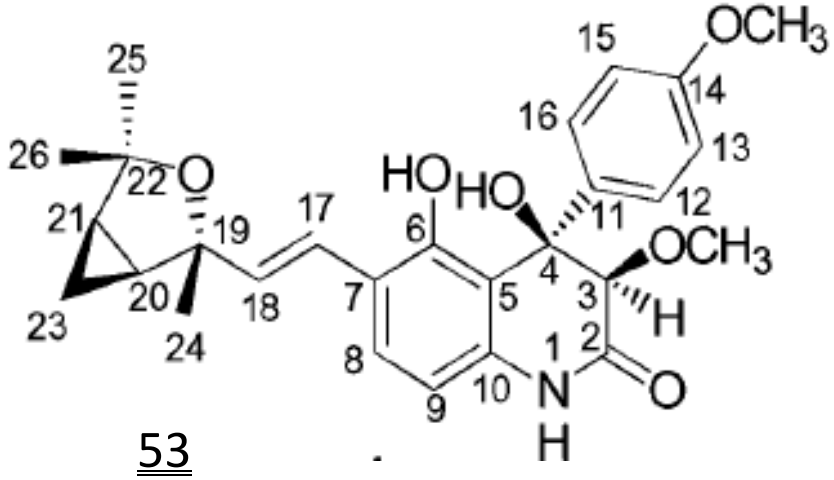
51

- **Constance M.Harris et,al 1989** isolated new pyrrolization alkaloid from the legume castanos permum astral A.cum (Leguminosae) and identified(1S,2R,3R,7S,7aR)-3-hydroxy methyl-1,2,7-trihydroxy pyrrolizidine on the basis of ^{1}H NMR NOE and spectroscopic analysis. Stereochemistry of alkaloids were confirmed by NOE.



52

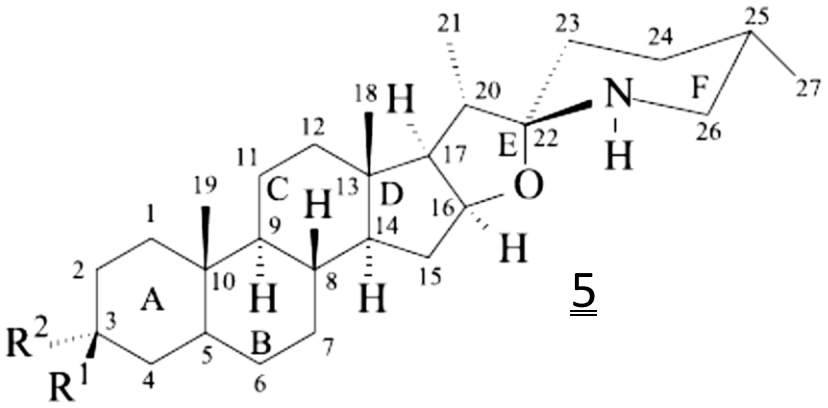
- **Kirstin Scherlach et,al 2006** discovered novel prenylated quinoline-2-one alkaloids from Asperillus nidulans, motivated by genome mining .The structure of the alkaloids was elucidated by extensive 1D and 2D NMR experiments. NOE interactions between H-3 and 3-OCH_3, H-3 and 4-OH and between H-3 and H-12 revealed the same relative stereochemistry of the 3-methoxy-4,6-dihydroxy-4-(4′-methoxyphenyl) quinoline uint.



53

- A novel steroidal alkaloid caavuranamide 4-tomatiden-3-one and 5α-tomatidan-3-one isolated by phytochemical investigation of the ripe fruits of soloanum cavvurana Vell.Their structure was elucidated by spectroscopic methods . The NOESY spectrum was used to confirm the proposed stereochemistry of caasvuranamide. A strong NOE was observed between the signal of CH_3-27 (δ_H 0.86) with the signal of H-26 (δ_H 2.74) and H-24_{ax}(δ_H

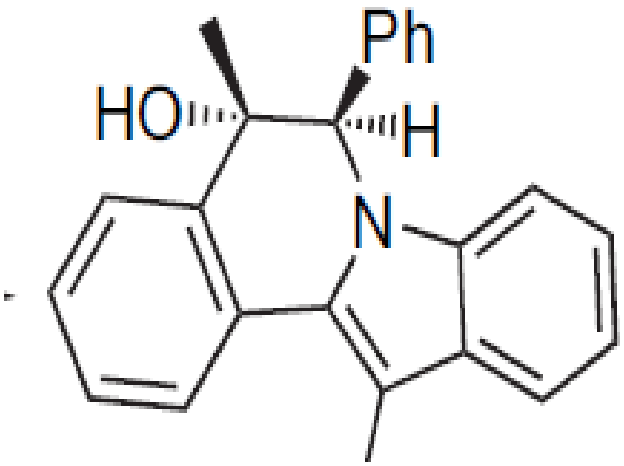
1.37), indicating that CH_3-27 is in equatorial position. **Nelissa Pachoo Vaz et,al 2012.**



5

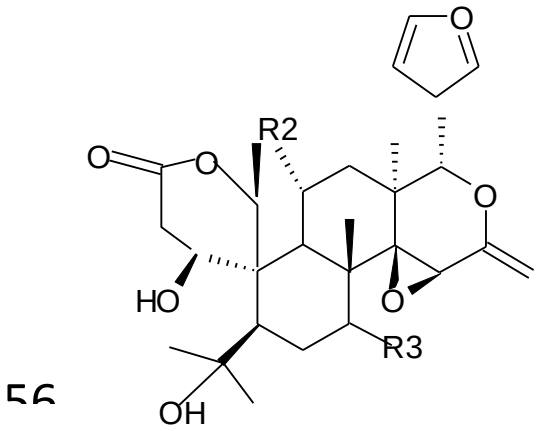
1 $R^1 = NHCHO$; $R^2 = H$
2 $R^1 = R^2 = O$; $\Delta^{4,5}$
3 $R^1 = R^2 = O$

- **Angelique N.C Lotter et,al 2006** synthesizded the indolo [2,1-a] isoquioline and pyrrolo[2,1-a] isoquioline nuclei from N-benzylindolo or ethyl 1H-indolo-1-yl acetate and N-benzyl pyrrolo precursors respectively. CH-correlated, NOE , NOESY and DEPT spectra were run on some sample for the complete assigniments of signals.



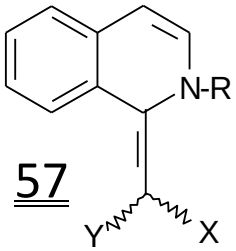
55

- A novel seco –limonoid rel (1S,5R,9S,7R,8S,9R,10S,11R13RS,14R,15R,17R)-11,19 dihydroxy -7-acetoxy-7-deoxichangin (rapatiolide) and two novel quioline alkaloids wereisolatedfromraputiahepetaphylla. Their structure were confirmed by spectroscopicanalysis.Seco limonoid rel(1S,5R,9S,7R,8S,9R,10S,11R,13R,14R15R, 17R)-11,19 dihydrooxy-7-acetoxy-7-de oxoichangin was confirmed by NOESY experiments. **Carlos Andres Coy barrera et,al 2011.**



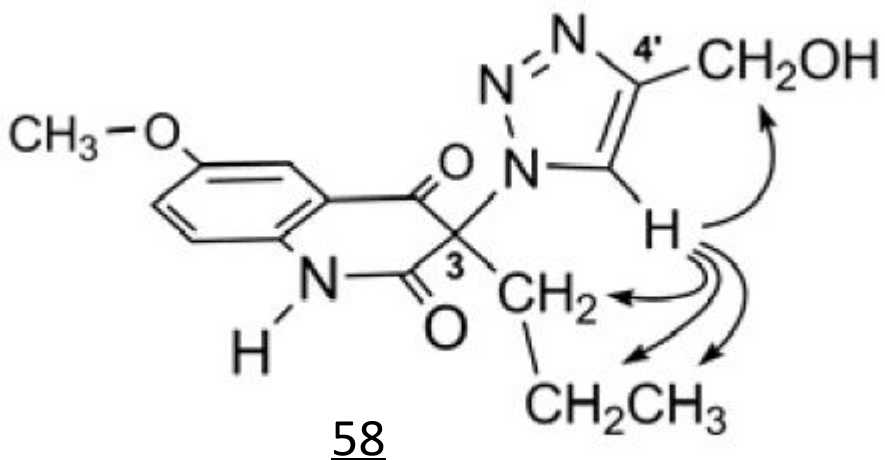
56

- 2-Alkyl-1-alkylthioquinoline salts were prepared from 2-alkyl-1-(2H)-isoquinoline via 2-alkyl-1-(2H)-thioisoqunoline.Spectroscopic studies of 2 benzyl-1-(substituted methylene)-isoquinoline showed NOESY spectroscopy. NOE correlation between the methyl of the ester and the 2-methylene groups and therefore their configuration was suggested to be the Z-from. **Reiko Fuijta et,al 2001**



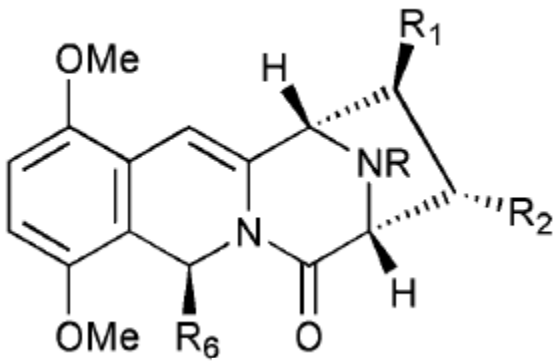
57

- 3-Azidoquinoline-2,4(1H,3H)-diones in copper (I)-catalyzed [3+2] cycloaddition reaction with teriminal acetylenes yielded 1,4 disubstitued 1,2,3 triazoles in moderate to excellent yields. The structure of compound was confirmed by ^{1}H and ^{13}C NMR spectroscopy,NOE combustion analysis and mass spectroscopy. **Stanis lav Kafka et,al 2011**



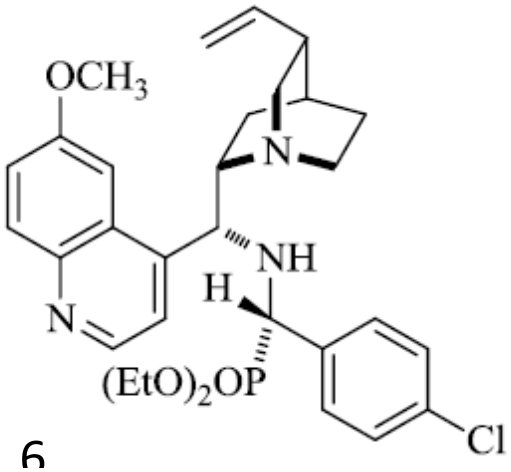
58

- The exo configuration for the R_1 group in compound (1S*,3R*,12S*,6S*)-13-Isopropoxy carbonyl-7,10-dimethoxy-6-methyl-1,2,3,4,6,12-hexahydro-3,12-iminoazepino[1,2,6]iso-quinoline-1-carbonitile was estbilished based on the NOE effect between H-1 and H-12 protons and H-11 and H-12. **Lena Huck et,al 2011**



59

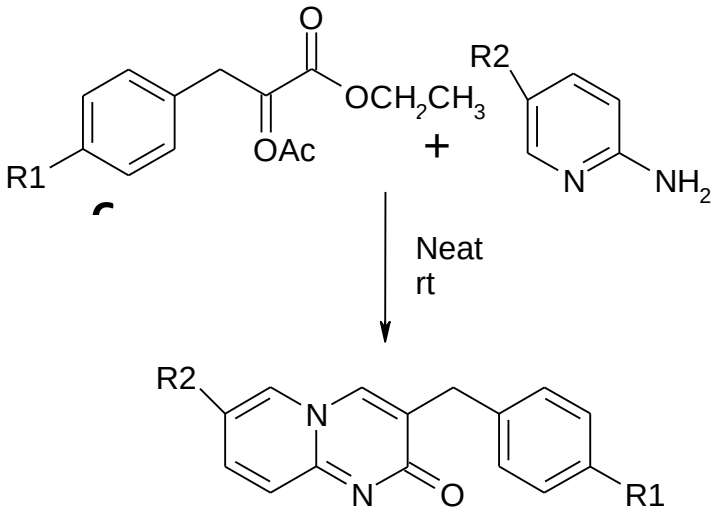
- NOESY experiments for Diethyl(R)-(4-chlorophenyl)((8S,9R)-6′methoxycinchonan-9-ylamino)methan phosphate showed only, interaction of quinoline structure with H-6X. **Prazmslaw J.Boratynski et,al 2012**



6

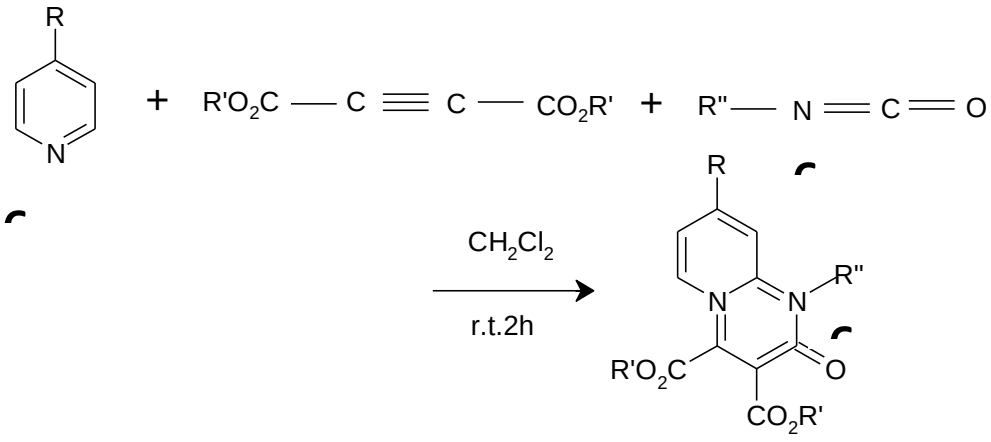
Synthesis of 2-oxo-2H-pyrido[1,2-a]pyrimidinone

- A facile one pot transformation of Baylis Hillman acetates 61 to pyrido[1,2-a]pyrimidin-2-ones 62 by reaction with 2-amino pyridine in a total solvent-free protocol was illustrated by **Sreevani et al, 2011.**

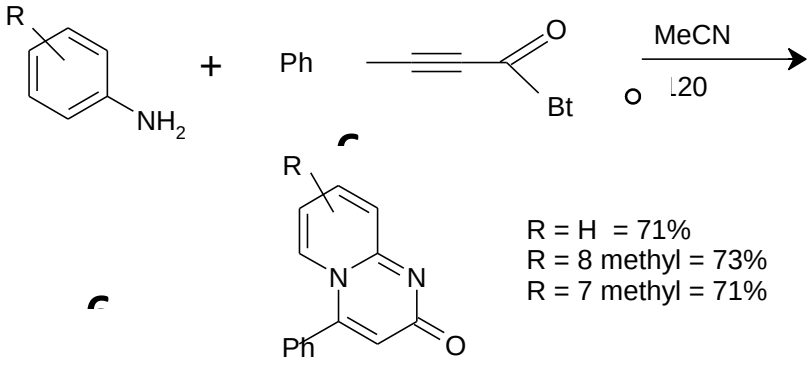


6

- **Mehdi Adib et al, (2004)** reported that pyridines **65** reacted. Smoothly with dialkyl acetylene dicarboxylates in the presence of isocyanates **66** in dry dichloro methane at ambient temperature to produce dialkyl 2-oxo 1,9a dihydro –2H-Pyrido [1,2-a] pyrimidine **67** in excellent yields.

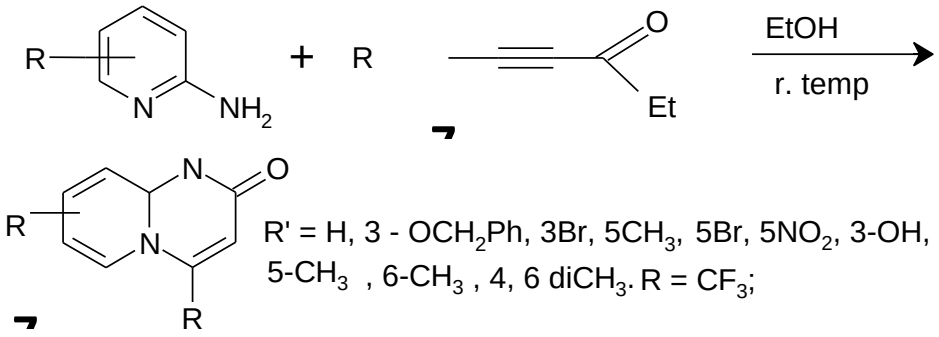


- **Alan Katritzky et al, (2004)** reported the synthesis of pyrido [1, 2-a] pyrimidin-2-ones **69** from a novel 1, 3 bis-electrophilic synthons (viz) 1-benzatriazol-1-yl-3-phenylpropynone **68** and 2-aminopyridines in good yields (71-73%).

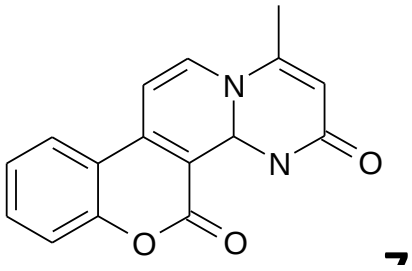


- **Geraldine Harriman et al, (2003)** prepared biologically relevant 4-tri fluoromethyl pyrido [1, 2-a] pyrimidine-2-one **71** in good yields by utilizing the reaction between electron rich amino pyridines and the highly electrophilic ethyl □-trifluoromethyl-alkynoate **70** in ethanol at room temperature. The 2-amino pyridine moiety with electron withdrawing group in the 5th position viz bromo and nitro reacted very slowly to afford the desired pyrido [1, 2-a]

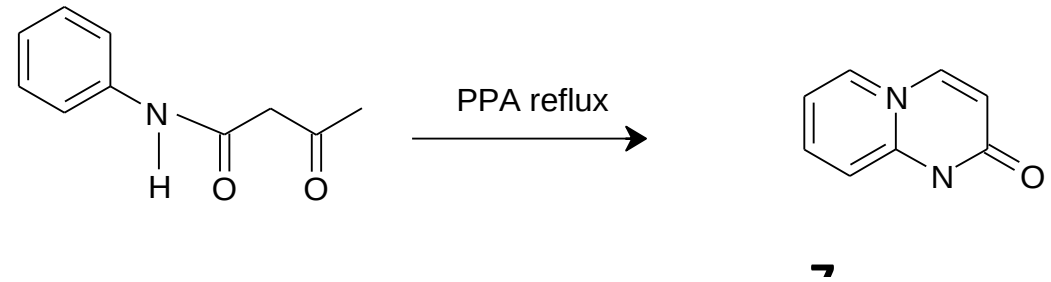
pyrimidin-2-ones in fair yields. The reaction was assumed to proceed via Michael addition at the pyridine nitrogen followed by lactam formation involving the 2-amino group to provide pyrido [1, 2-a] pyrimidinone.



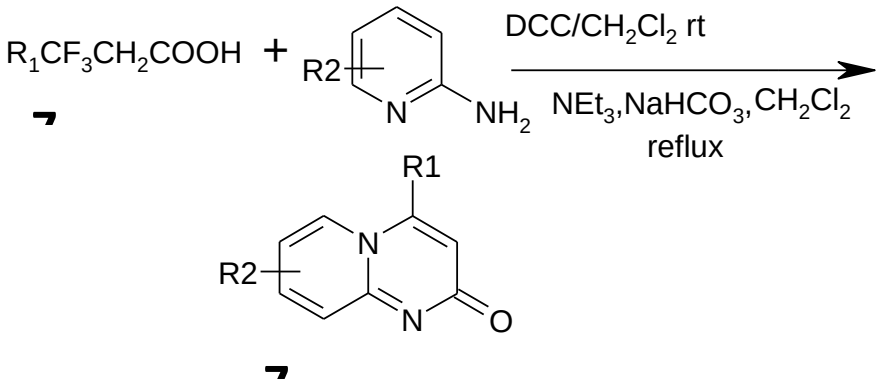
- **Fatima Al-Omran (2003)** reported new synthetic routes for triazolopyridine, Pyridopyrimidine **72**, Pyridazine derivatives, incorporating a coumarin moiety with biological activities.



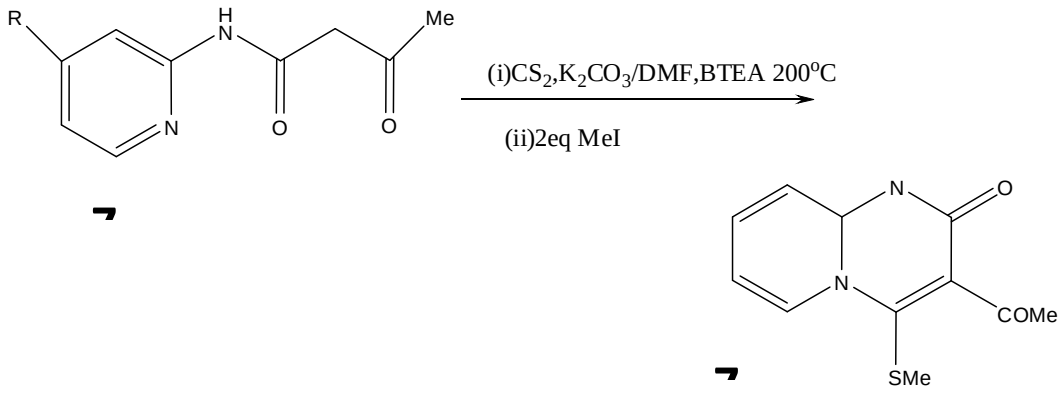
- **Suri et al, (2002)** reported an unequivocal high yielding synthesis of 4-methyl-2-oxo-2(H)-pyrido[1,2-a]pyrimidines **73** by the cyclisation of N-(1,3-dioxobutyl)–2 amino pyridines / picolines / quinolines with PPA. The examination of HOMOCOR and HETCOR Spectra of the compounds revealed that C_4-Methyl has an influence on the chemical shifts of C_6 and its proton. In all the end products, C_6-H possessed lower chemical shift in comparison to C_8. The abnormal shielding of C_6 in spite of being attached to nitrogen was attributed to peri-effect of C_4 methyl group.



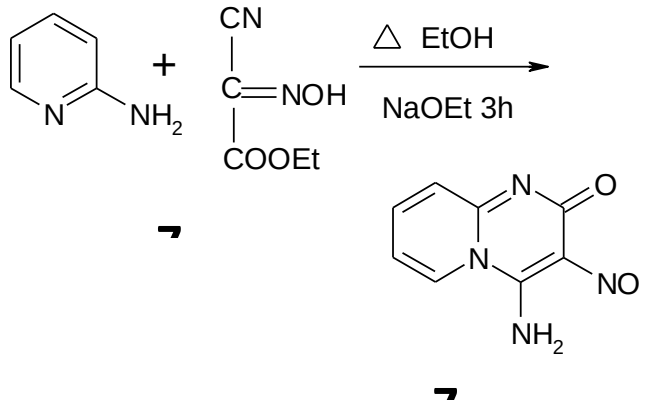
- The reaction of 2-amino pyridine with 2,2-dihydropolyfluoroalkonic acids **74** in presence of DCC gave the corresponding amides which subsequently cyclised by intramolecular Micheal addition-elimination reaction amides under basic condition to yield 4-fluoroalkyl-2H-pyrido[1,2-a]pyrimidin-2-ones **75 (LU et al, 2001).**



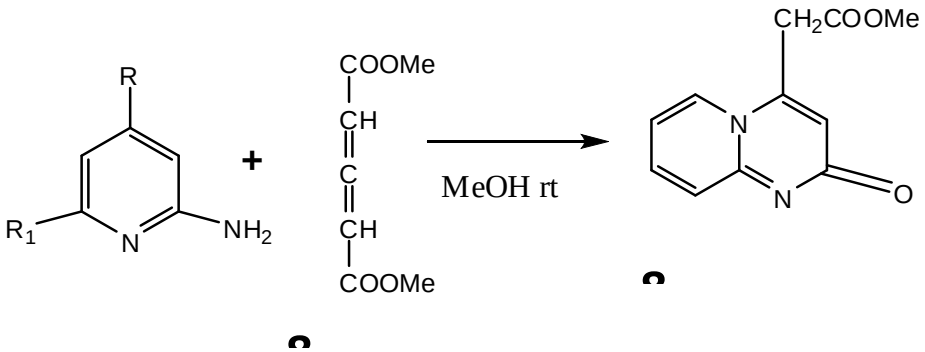
- 4-Methylthiopyrido[1,2-a]pyrimidin-2-one **77** was synthesized by the addition of *N*-(4-R-pyrid-2-yl)acetoacetamides **76** (R = H, Me) to CS_2 under phase-transfer conditions followed by the alkylation of the reaction products with Mel. The molecular structure of 3-acetyl-4-methylthiopyrido[1,2-α]pyrimidin-2-one is established by X-ray analysis **(Cherkasova et al, 1996).**



- Cyclocondensation of 2-aminopyridines and ethyl cyno(hydroxyimino) acetate **78** in presence of NaOEt gave 4-amino-3-nitroso-4H-pyrido[1,2-a]pyrimidin-2-ones **79 (Del Gandice et al, 1995).**

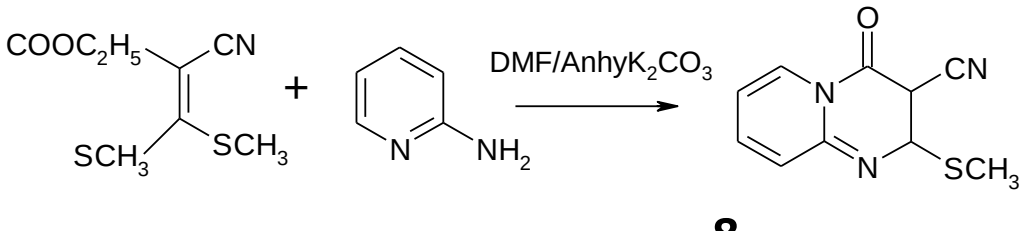


- Methyl 2-oxo-2H-pyrido[1,2-a]pyrimidine-4-acetate **81** was prepared in the reaction of 2-aminopyridine and dimethyl penta-2,3-diendioate **80** under argon **(Gurinder et al, 1988).**



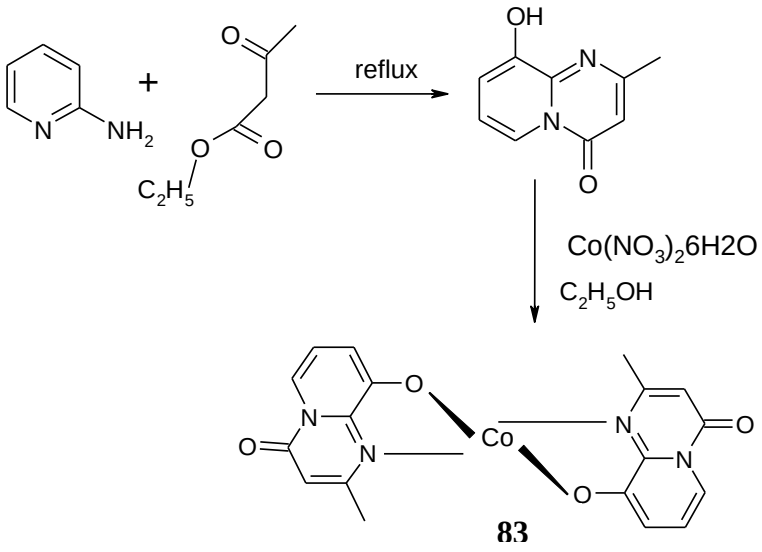
Synthesis of 4--oxo-4H-pyrido[1,2-a]pyrimidinone

- The synthesis and antimicrobial activity of 3-cyano-2-(methylthio)-4-oxo-4H-pyrido[1,2-a]pyrimidine **82** and their derivatives were reported by **Sambhaji Vartale et al, 2011.**



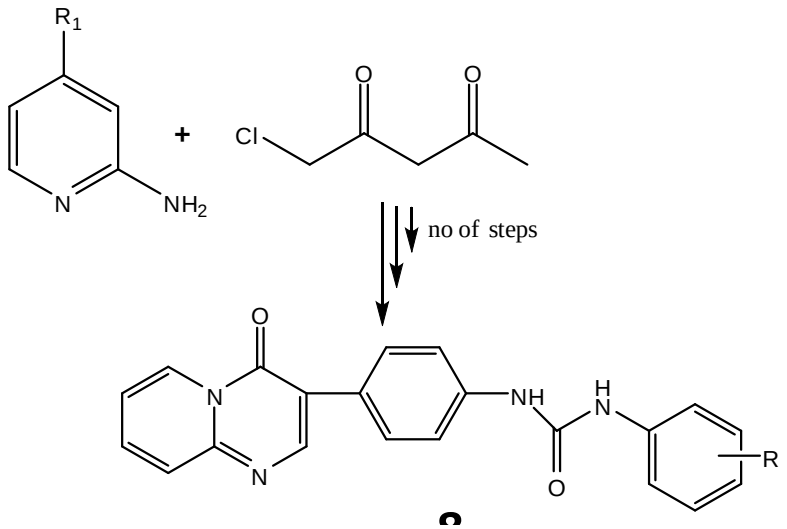
82

- Cobalt (II) complexes of 2-methyl-4-oxo-pyrido[1,2-a]pyrimidine **83** were prepared and their spectroscopic and crystal structure were studied by **Huaihong Zhang et al, 2011.** The complex existed as a mononuclear complex with distorted square-pyramidal geometry.



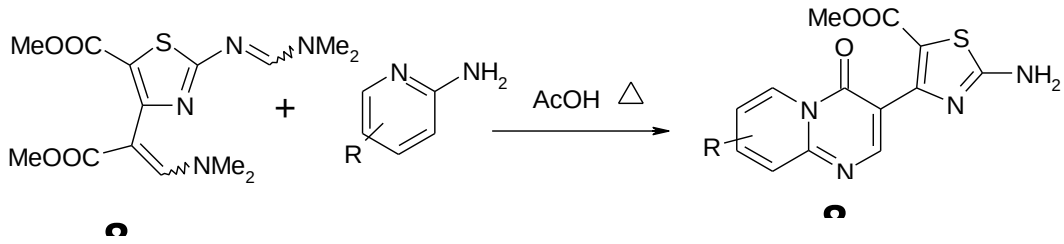
83

- Diaryl urea derivatives **84** possessing a 4H-pyrido[1,2-a] pyrimidine-4-one group were found to be potent anticancer compounds **(Peng YaO et al, 2010).**



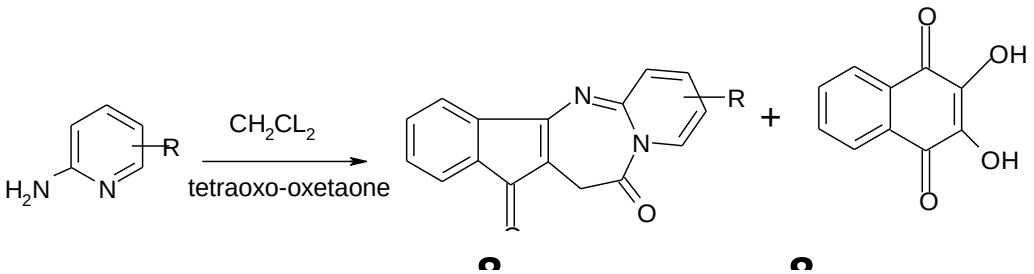
- A blue-emitting organic, 9-hydroxyl–3– hydroxylethyl– 2 –methyl – 4H– pyrido[1,2-a)pyrimidin–4– one was synthesized by **Huaihong Zhang (2010)** from 2-amino-3-hydroxylpyridine and 2-acetylbutyrolactone**.** At room temperature, the compound exhibited an intense blue emission at 432 nm upon 323 nm excitation in the solid state. The thermal stability of the compound was also investigated by thermogravimetric analysis.

- Methyl 2-amino-4-(2-methoxy-2-oxo-ethyl)thiazole-5-carboxylate prepared from dimethylacetone-1,3-dicarboxylate **85**, sulfuryl chloride and thiourea was transformed in two steps into (4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)thiazole-5-carboxylates **86 (Martina Žugelj et al, 2009).**



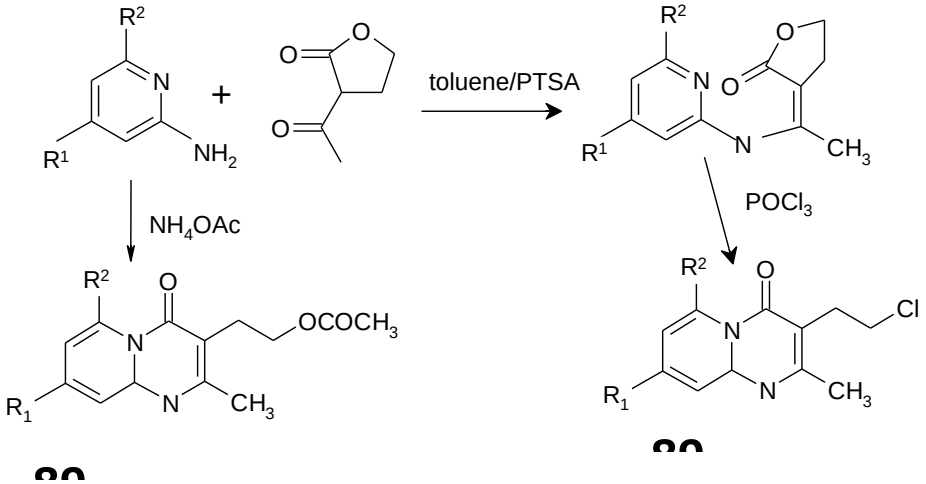
- The reaction of 2-aminopyridines with tetra oxo-oxetanone in dichloromethane afforded the indeno[1,2,d] pyrido[1,2-a]pyrimidines **87** and dihydroxy quinine **88** in good yields. The synthesized compounds were found to be inhibitors of epidermal growth factor receptor (EGFR), vascular

endothelial growth factor receptor 2 (VEGFR-2) and Flt-4-Kinases. Hence indeno pyrido pyrimidine diones were regarded as valuable agents in the discovery of drugs for cancer treatment **Maria Tsana Kopoulou et,al 2008**

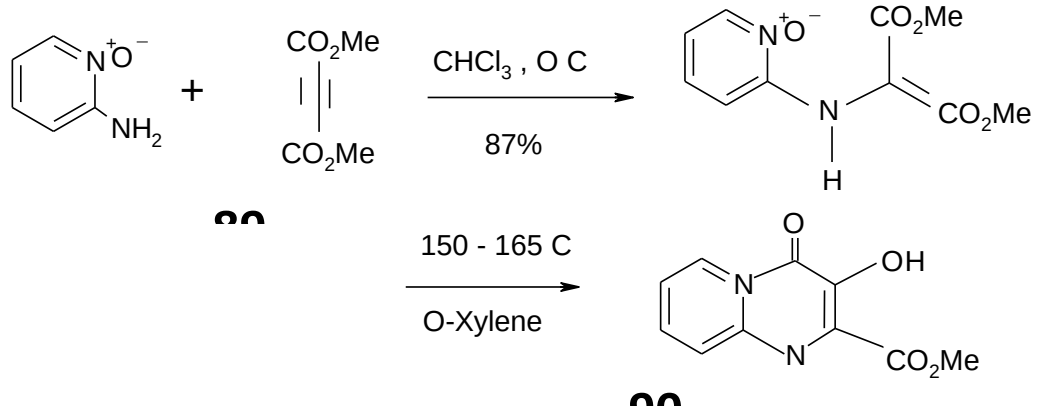


R = H; 8Methyl; 4Methyl; 6Methyl; 4, 6 dimethyl; 5Chloro; 3-hydroxy

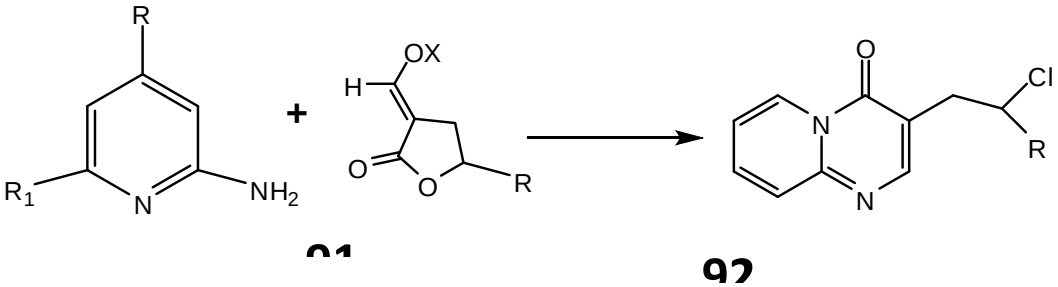
- A new method was developed by **Raghunath Toche et al, 2008** towards the synthesis of pyrido [1,2-a] pyrimidines with 3-hydroxy and 3-chloro ethyl side chain. The reaction involved the condensation of 2-amino pyridines with acetyl butyrolactone intermediates which on cyclisation with phosphorous oxy chloride or ethanol in sodium ethoxide yielded pyrido [1,2-a] pyrimidines **89a and 89b** in good yields.



- An efficient and reliable synthesis of the heterocyclic scaffold methyl–3–hydroxyl–4–oxo-4H-pyrido[1,2-a]pyrimidine–2–carboxylate **90** was described by **Olaf Kinzel et al, (2008),** from 2-aminopyridine N-oxide and dimethyl acetylene dicarboxylate **89** in chloroform at O°C.



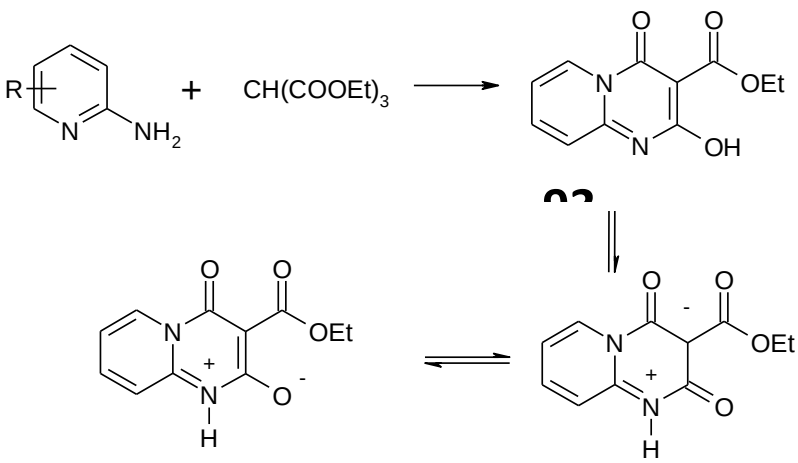
- A highly efficient method was successfully developed for the synthesis of fused pyrimidines **92** via aminoheterocyclic dihydrofurnone intermediates from 2-aminopyridine and cyclic □-formylesters **91** by three different methods **(Raghunath Toche et al, 2007).**



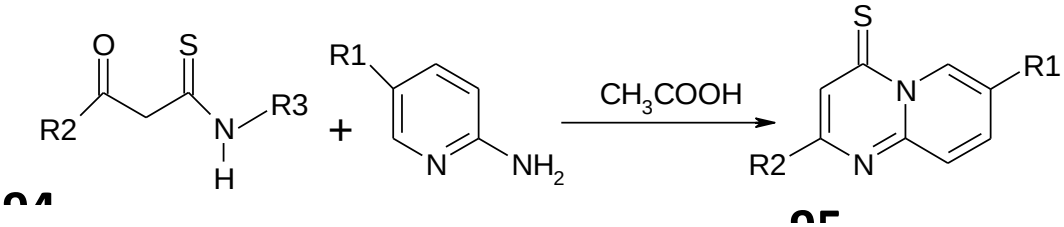
R=H, CH_3 X=Na^+

Method A= toluene/p-TsOH; Method B = $NH_4OAc/120^0C$; Method C= CH_2Cl_2/rt

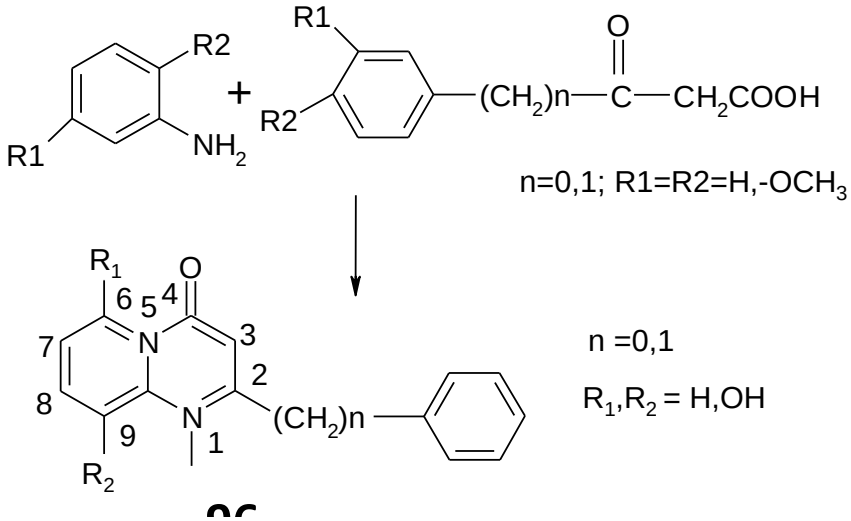
- An improved method for the preparation and purification of ethyl-2-hydroxyl-4-oxo-4H-pyrido[1,2-a]pyrimidine-3-carboxylates **93** was proposed by **Ukrianinets et al,2007l** ^1H and ^{13}C NMR and X- ray analysis of the compounds showed that in DMSO solution it existed as 2-hydroxy-4oxo form while in the crystalline form it occurred in the bipolar 2,4-dioxo form.



- **Britsun et al, 2007** reported the formation of 4H-pyrido[1,2-a]-pyrimidine-4-thiones **95** by the reaction between 3-oxo-propanethioamides with 2-amino -5-R-pyridines **94**.

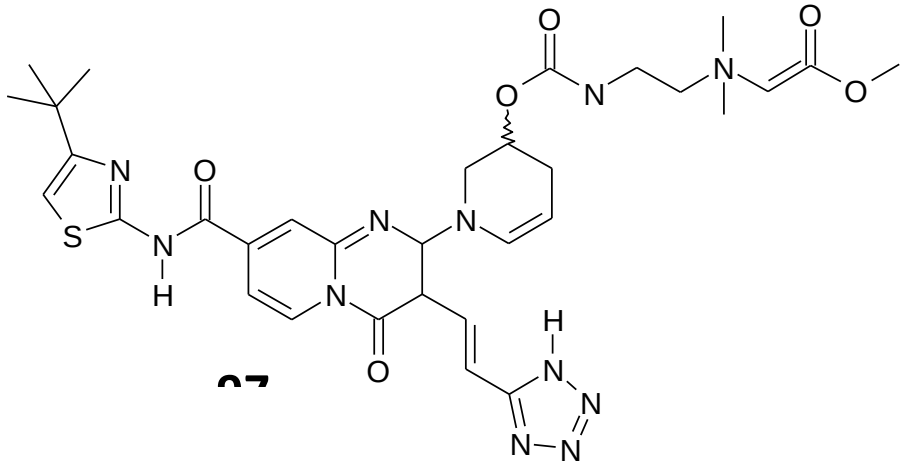


- 2-phenyl-pyrido[1,2-a] pyrimidin-4-one derivatives **96** bearing a phenol or a catechol moiety in position 2 were tested as aldose reductase (ALR2) inhibitors and exhibited activity levels in the micromolar / submicromolar range. Introduction of a hydroxyl group in position 9 gave an enhancement of the inhibitory potency. Lengthening of the side chain to benzyl determined a general reduction in activity. The lack or the methylation of the phenol or catechol hydroxyls gave inactive or scarcely active compounds, thus demonstrating that the phenol or catechol hydroxyls are involved in the enzyme pharmacophore recognition. All the pyrido pyrimidinones displayed significant antioxidant properties, with the best activity shown by catechol derivatives. The theoretical binding mode of the most active compounds obtained by docking simulations into the ALR2 crystal structure was fully consistent with the structure activity relationships in the pyrido [1,2-a] pyrimidin-4-one series **Concettina Motta et al, 2007.**



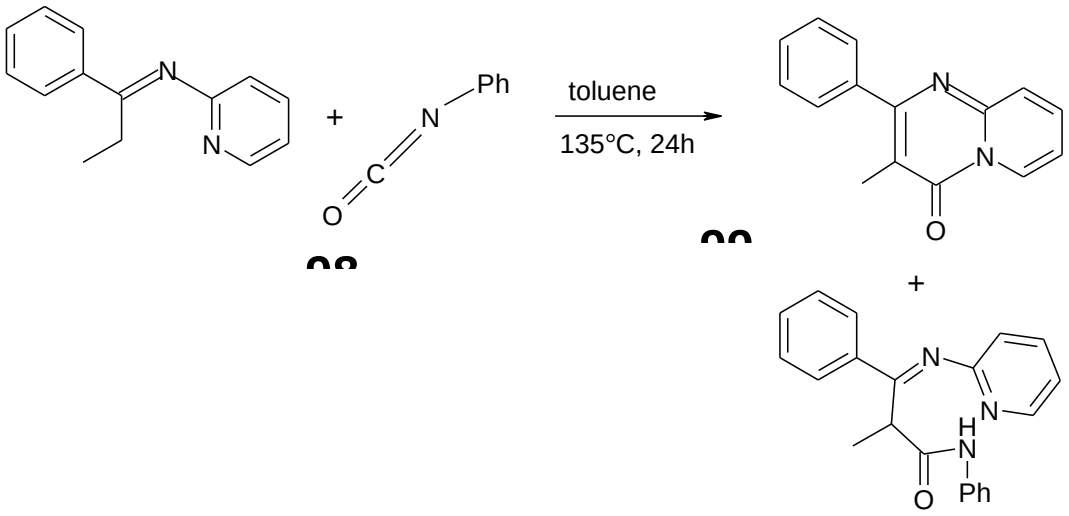
96

- A series of 4-oxo-4H-pyrido[1,2-a]pyrimidine derivatives **97** substituted at the 2-position with piperidines bearing quaternary ammonium salt side chains, were synthesized and evaluated, for their ability to potentiate the activity of the fluoxoquinolone levofloxacin (LVFX) and the β - lactam aztreonam (AZT) in pseudomonas aeruginosa, by **Ken-ichi Yoshi da et al, 2007.**

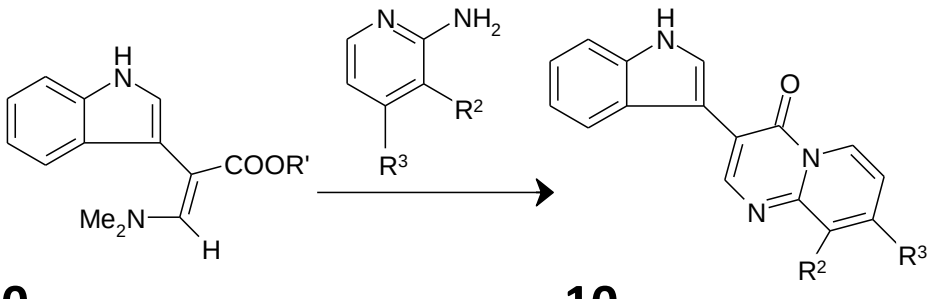


97

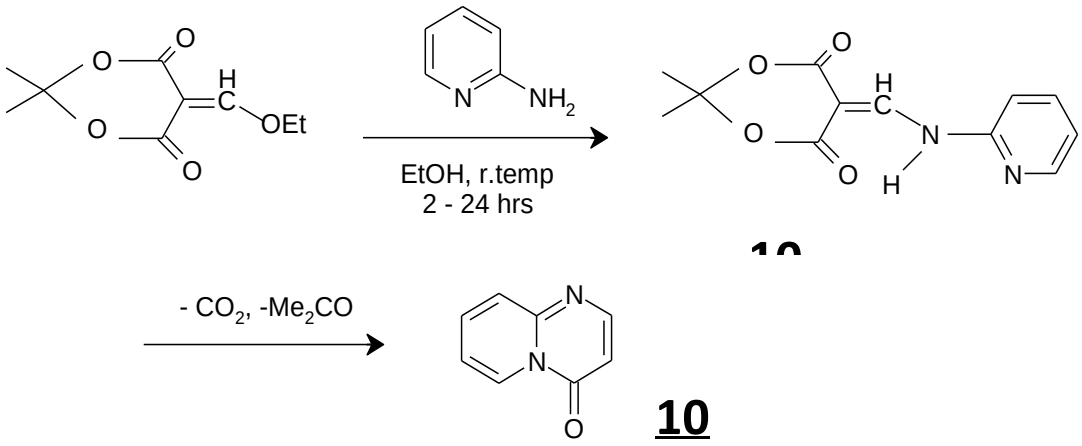
- **Yoichiro Kuniobu et al, (2006)** prepared 4H pyrido [1, 2-a] pyrimidin-4-ones **99**, by the reaction of ketimines **98** bearing a pyridyl or a picolyl group on a nitrogen atom of the imine moiety with tosyl isocyanate in toluene at 135°C for 24h, in quantitative yields. In these reactions tosyl isocyanate acts as a carbonyl precursor and the pyridyl or picolyl group is a key functional group.



- Methyl and ethyl 3-dimethyl amino-2 (indol-3-yl) propenoate were prepared from alkyl 3-indole acetates and ter butoxyl bisdimethyl amino) methane and treatment of thise N, N-dimethyl enaminone **100** with 2-aminopyridines as N, N, 1-2 dinucleophiles, yielded 3-(1H-indol-3yl) – 8 methyl–4H pyrido[1,2-a] pyrimidin–4 ones **101** in moderate yields. **RenataJakse et al, 2004**

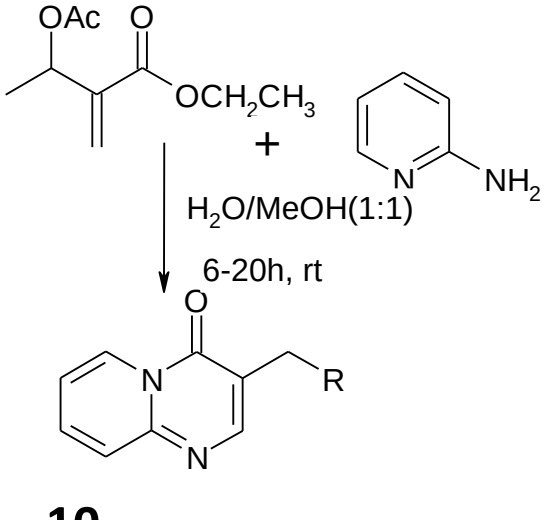


- **Ravina et al, (2002)** obtained 4-oxo-4H-pyrido[1,2-a]pyrimidines **103** by melting 2-pyridylamino methylene iso propylidene malonates **102**. 2-pyridylamino methylene iso propylidene malonates were prepared from ethoxymethylene isopropylidene malonates and 2-amino pyridines in ethanol at room temperature for 2-24h. When the pyridyl amino methylene malonates were heated to their melting points, the dioxane ring opened with evolution of acetone, which was followed by decarboxylation and cyclisation to afford the 4-oxo-4H-pyrido [1,-2-a] pyrimidines.



10

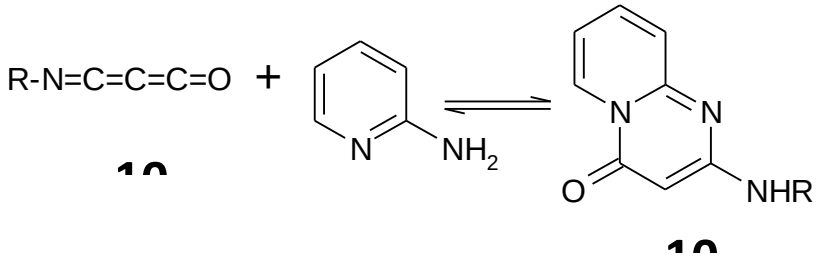
- A facile one-pot convenient transformation of the acetates of Baylis-Hillman adducts into fused pyrimidones i.e 3-substituted-1,5-diazabicyclo(4.4.0) deca-2,5,7,9-tetraen-4-ones **104** via reaction of 2-aminopyridine in environmentally friendly aqueous media was described by **Deevi Basavaiah et al, 2002**.



10

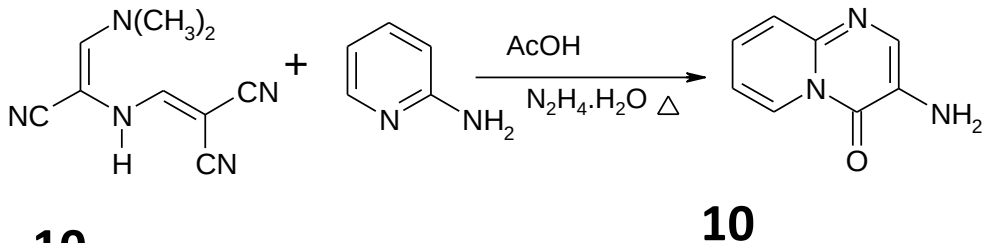
- The nucleophilic addition of primary 2-amino pyridines with stable (neopentylimino)-, (mesitylimino)- , and (o-tert-butylphenylimino) propadienones **105** were investigated by **Herve Bibas et al, (2002).** The reaction was initiated by the nucleophilic attack of the amine on the cumulenic carbonyl group to generate zwitterion intermediates which tautomerize to

mesoions Subsequent ring closure reaction produced pyridopyrimidinones **106** as major or exclusive product in methylene chloride at room temperature.



10

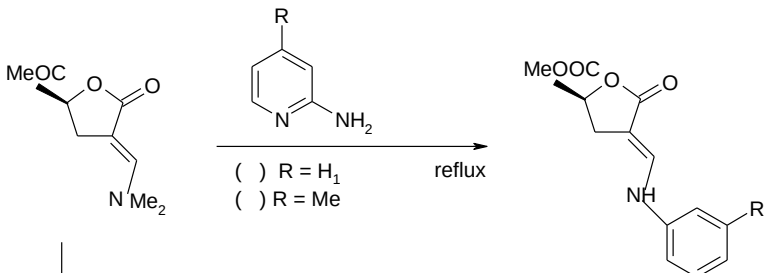
- The applicability and synthetic potency of the new reagent *N*-(2,2-dicyanoethenyl) aminoacetonitrile **107** to develop an expeditious convenient synthetic route to unique poly functionally substituted pyrroles, heterocyclo pyrimidines **108** and 2*H*-1-benzopyran-2-ones were reported with chemical and spectroscopic evidence for the structures of the newly synthesized compounds **(Ayman Erian et al, 2001).**



10

- A one step 'ring switching' transformation of (s)-3-[(dimethylamino)methylidene] -5-(methoxycarbonyl) tetra hydrofuran-12-one **109** with 2-amino pyridines afforded 3-(4-oxo-4H pyridine [1,2-a] pyrimidinyl-3) -2- hyroxy propanoates **110.** The reaction of **109** with 2-amino pyridine or 2-amino-4-methylpyridine in refluxing acetic acid gave only the substitution product **111**. The presence of sodium acetate was required to achieve the transformation of **111** into the corresponding methyl-3-(4-oxo-4H-pyrido[1,2-a]pyrimidinyl-3)-2-hydroxy propanoate **110 (Markoskof et al, 2000).**

R=neopentyl;mesity;o-tert-butylpenyl



10

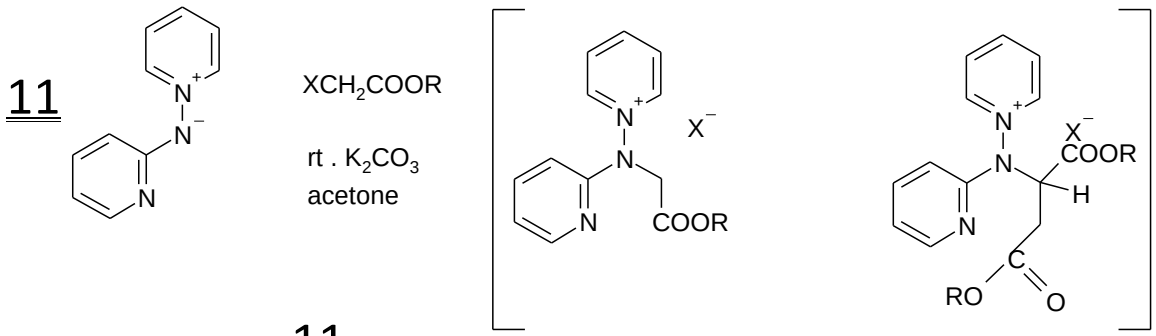
111

NH

111

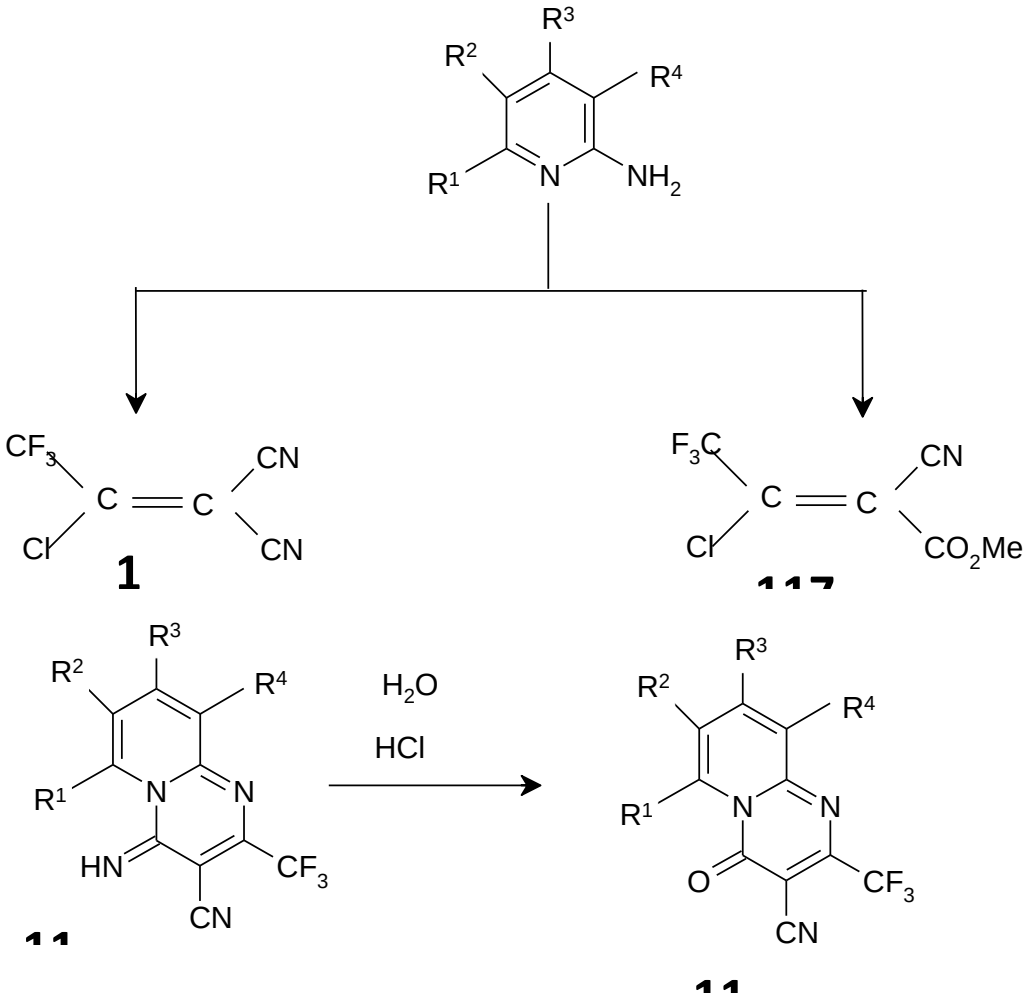
110

- Reaction of pyridinium-N-(2-pyridyl) amidine **112** and alkyl haloacetates in the presence of potassium carbonate afforded a mixture of 4-oxo-4H-pyrido[1,2-a] pyrimidine–2-carboxylates **114** and 2-aminopyridine derivatives through intermediates. Compound **113** could be cyclised by the action of heat or silica gel into **114.** The best yield was achieved in the case of ethyl bromoacetate **(Dela Rosa et al, 2000).**



11

- The reactions of 2-aminopyridine with 2-chloro–1,1 dicyano–2– trifluoro methylethylene **115** in chloroform at room temperature afforded, 3 cyano-4-imino-2– trifluoromethyl-4H-pyrido[1,-2-a]pyrimidines **116** in 51-84% yields. Under analogous conditions, 2-amino pyridine with 2-chloro-1-cyano-1-methoxycarbonyl-2-trifluoromethyl ethylene **117** afforded, 3-cyano-2-trifluoromethyl–4H–pyrido[1,2-a]pyrimidin–4–ones **118** in 23 – 53% yields. The NMR and X-ray diffraction analysis showed that the first stage of the reaction involved the alkenylation of the exocyclic nitrogen atom of 2-aminopyridine followed by the formation of pyrido[1, 2-a] pyrimidines **(Shidlovski et al, 2000).**


R3
R2
R4
R1
N
NH2
CF3
C
C
CN
Cl
CN
1
F3C
C
C
CN
Cl
CO2Me
R3
R2
R4
R1
N
N
HN
CF3
CN
H2O
HCl
R3
R2
R4
R1
N
N
O
CF3
CN

3. MATERIALS AND METHODS

3.1 PREPARATION OF ACONIC ACID [Campbell N.R and Hunt J.H 1947]

3.1.1Preparation of Sodium aconate

Itaconic acid (260g) was powdered and stirred to a paste with water (340ml) in 5-litre beaker. Bromine (320g) was slowly added, keeping the temperature below 50˚C. When all but trace of bromine had disappeared, the solution was neutralized with sodium bicarbonate (336g). The mixture was then heated to 50˚ C on a water bath and treated with a suspension of anhydrous sodium carbonate (106g) in water (158ml) at 50˚C, added in small portions until the solution remained neutral. The mixture was cooled and allowed to remain at 0˚C for an hour. The crystalline sodium salt was collected by filtration, washed with a small amount of ice water and then with 95% alcohol and dried under vacuum.

3.1.2 Preparation of Aconic acid

Dry sodium aconate 100g was suspended in dry ether (300ml). Dry hydrogen chloride gas was then passed with stirring, until a gain in weight (30g) was obtained. The mixture was left over night; the solid (115g) was filtered off and extracted with ether in a soxhlet. Evaporation of the solvent gave the white crystals of aconic acid.

3.2 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE ACETIC ACIDS

3.3 General Procedure

To a magnetically stirred solution of aconic acid (0.02mole) in alcohol, added drop wise the alcoholic solution of 2-amino pyridine (0.01mole) at room temperature. The precipitated solid was filtered, dried and was recrystallised from ethanol as colourless crystals.

2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene acetic acid

Aconic acid: 2.56g; 2-aminopyridine: 1.88g; Ethanol: 50ml

Melting point : 221˚C, Yield - 4g (91%)

IR (γ) $_{max:}$ 2954 cm^{-1} (-OH), 1741 cm^{-1} (-CO), 1670 cm^{-1} (-CO), 1637 cm^{-1}(-CN), 1271 cm^{-1},

985 cm^{-1}

2-oxo-7-methyl-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene acetic acid

Aconic acid: 2.56g; 5-methyl-2-aminopyridine: 2.38g; Ethanol: 50ml

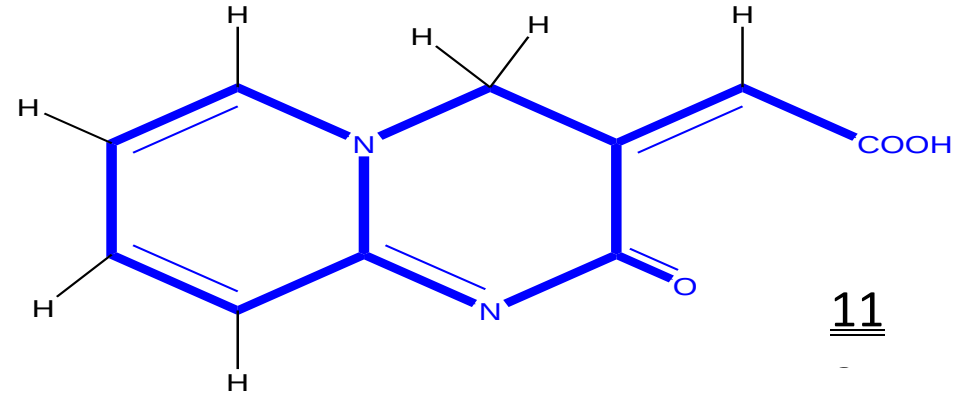
Melting point : 233˚C, Yield - 4.1g (88%)

IR (γ) $_{max:}$ 3012 cm^{-1} (-OH), 1752 cm^{-1} (-CO), 1671 cm^{-1} (-CO), 1642 cm^{-1}(-CN), 1271 cm^{-1},

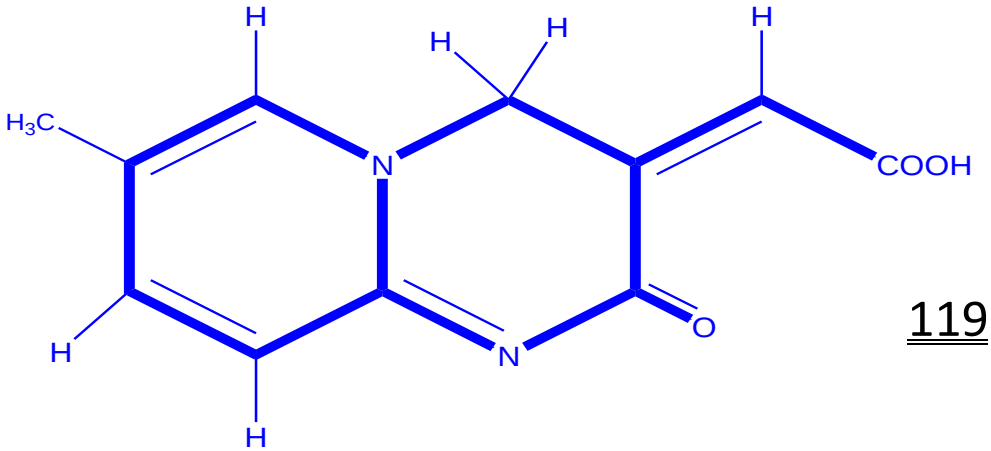
980 cm^{-1}

4. RESULTS AND DISCUSSION

The results pertaining to the stud y of " ***NOE STUDIES OF PYRIDO[1,2-a] pyrimidine-2-one aceticacids"*** are discussed below:



11



119

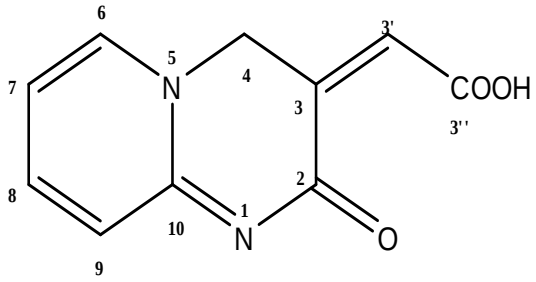
Analysis of the NMR spectrum of the compound **118** revealed six signals for protons at δ 5.00, 6.3, 6.8, 6.9, 7.7, 7.8 and ten signals for carbon at δ 73,112,113,122,134,144,153,164,167,177 **(Figures-1 and 2).** DEPT-135 (**Figure-3)** spectrum showed the presence of five methine carbons and one methylene carbon. Hence the remaining four carbons must be quaternary which was in accordance with the proposed structure **118.**

The complete structural analysis was made through ^{1}H, ^{13}C NMR spectrum, and 2D NMR - COSY, HETCOR and HMBC **(Figures-4, 5** and **6)** measurements. For the compound 2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene acetic acid **118** the signal at δ 7.8 was assigned to C_6-H, since it is deshielded by the neighboring nitrogen. C_7 proton and C_9 proton appeared at δ 6.8 and 6.9 as triplet and doublet respectively because they experience shielding effect by virtue of the position and nature of bonding **(Hikmat N. Al-Jallo et al, 1978).** The signal for proton at C_8 appeared as doublet at δ 7.7. The protons resonating at δ 6.3 and δ 5.0 were due to C_3-H and C_4-H.

The ^{13}C signals were assigned using HETCOR. The signals of carbon at δ 73,122,112,113,134 and144 correlated with the proton signals at δ5.00, 6.3, 6.8, 6.9,7.7 and7.8 respectively. The proton and carbon assignments are given in **Table-1**. The positions of the quaternary carbons were assigned using HMBC spectrum. The signals at δ 164 and 167 showed correlation with the exocyclic methine proton. Hence δ 167 was assigned to the carboxyl carbon and the signal at δ 164 to C_{10}. A long range ^{3}J coupling was observed between C_4-H and exocyclic methine (C_3') in the COSY spectrum. Other correlations observed in the COSY spectrum of 2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene acetic acid are given in the **Figure-7.** The HMBC correlations are given in **Table-2** and **Figure-8.**

TABLE -1

NMR DATA OF 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID



^{1}H Shift in ppm	Multip-licity/ no. of ^{1}H	Hydrogen	C^{13} shift in ppm	Carbon	Dept-135	C^{13} shift in ppm	Carbon	Dept-135
6.3	d/1	H_3'	177	C_2	-C	112	C_7	-CH
5.00	s/2	H_4	164	C_3	-C	134	C_8	-CH
7.8	t/1	H_6	122	C_3'	-CH	113	C_9	
6.8	t/1	H_7	167	C_3''	-C	153	C_{10}	
7.7	d/1	H_5	73	C_4	-CH_2			
6.9	d/1	H_9	144	C_6	-CH			

TABLE – 2

HMBC CORRELATIONS OBSERVED IN 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

^{1}H Shift in ppm	Hydrogen	Observed ^{13}C connectivities
6.3	H_3'	C_2, C_3, C_4, C_3''
5.00	H_4	C_2, C_3, C_3'

7.8	H_6	C_8, C_{10}
6.8	H_7	C_6, C_9
7.7	H_8	C_7, C_{10}
6.9	H_9	C_7, C_{10}

The formation of the 2-oxo isomer was confirmed by the C=O absorption at 1670 cm^{-1} in the IR spectrum which was the characteristic feature of 2-oxo isomer **(Liu et al, 1997).** Also, as expected, a strongly deshielded aromatic proton at the 6^{th} position (δ 8-9) due to the anisotropy of the carbonyl group at the 4^{th} position was not observed in the ^1H NMR spectrum **(Geraldine C 2008).** A long range $^3J_{CH}$ correlation between the H_6 and C_4 carbon was found to be absent in the HMBC spectrum again confirming the formation of 2-oxo isomer. The NMR data and the COSY and HMBC correlations for 7-methyl-2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene acetic acid **118** are given in **Tables 3, 4 and Figures – 9 -14.**

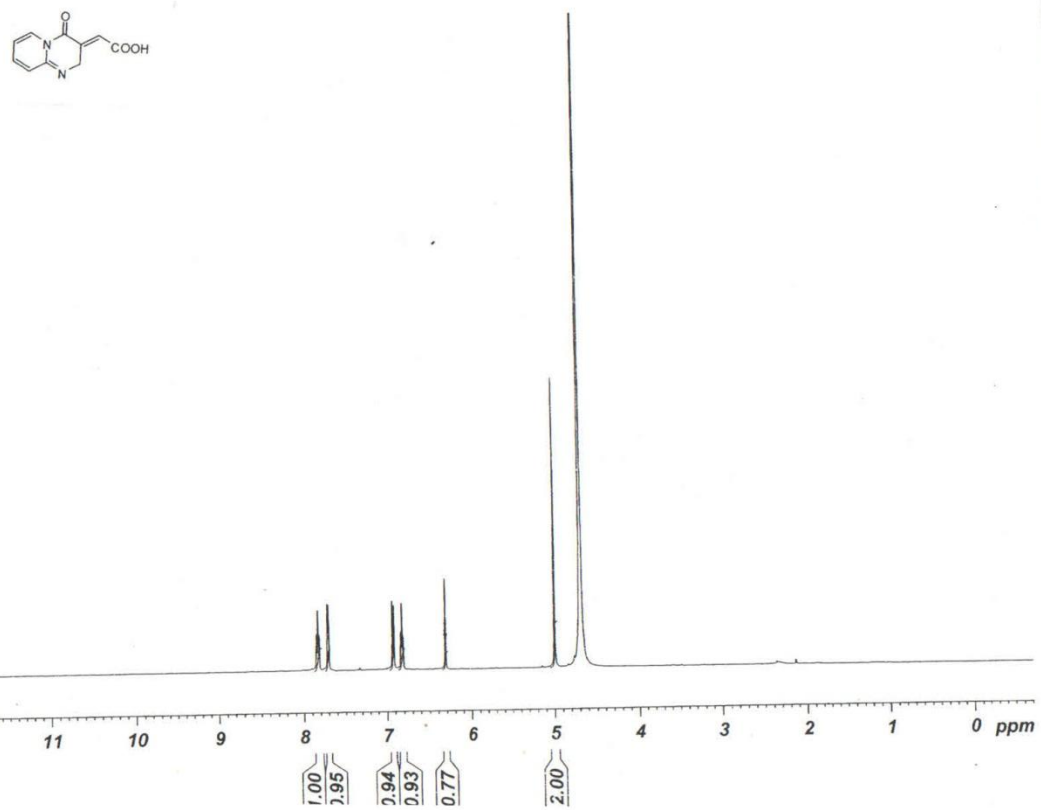
The structural elucidation and assigments of the compound were achieved by 1D and 2D NMR techniques (^1H,^{13}C,COSY,HMBC). Again correlations observed in the HMBC Spectrum, and the stereochemistry of the compound was confirmed by NOESY experiments. Based on the strong correlations observed between, H-4 and H-3 in the compound (118) proved the 'Z' Confirmation of the compound

The other significant correlations observed are between H-6 and H-7 with H-9, H-8 and H-9 with H6. These correlations were shown in figure from these datd the structre of the compound was confirmed to be 118- 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID.Similar observation were also seen in 119 7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID.

2AM-PY.....R

FIGURE -1

^{1}HNMR SPECTRUM OF 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

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PROCNO                         1

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PULPROG                     zg30
TD                         32768
SOLVENT                      D2O
NS                            16
DS                             2
SWH                  10330.578 Hz
FIDRES                0.315264 Hz
AQ                   1.5860212 sec
RG                           203
DW                    48.400 usec
DE                     6.00 usec
TE                        297.4 K
D1                   1.00000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                         1H
P1                    10.65 usec
PL1                    0.00 dB
SFO1          500.1330885 MHz

F2 - Processing parameters
SI                         32768
SF                500.1300000 MHz
WDW                           EM
SSB                            0
LB                     0.30 Hz
GB                             0
PC                          1.00
```

2AM-PY.....Reneela, Coimbatore

FIGURE -1a

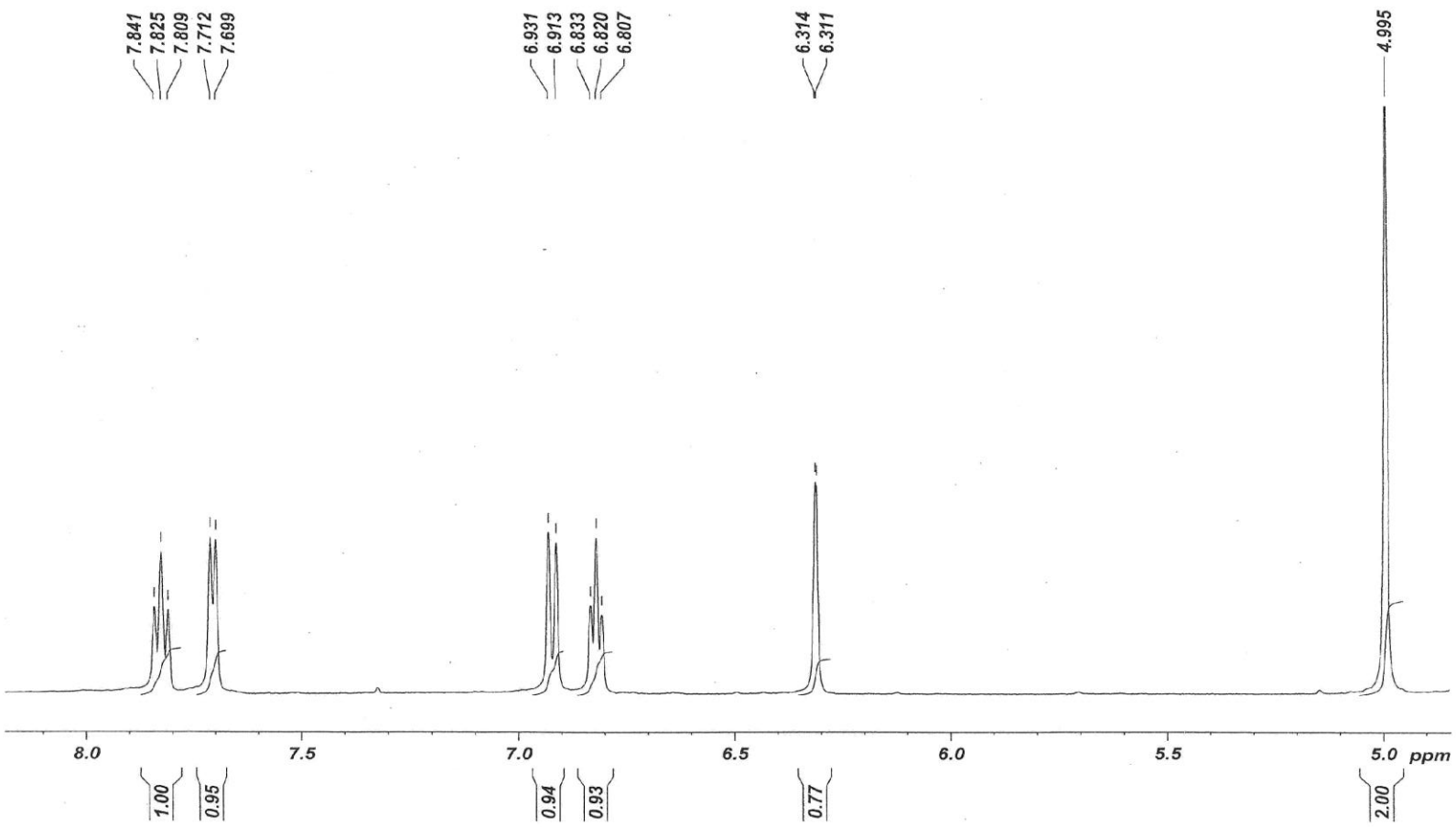
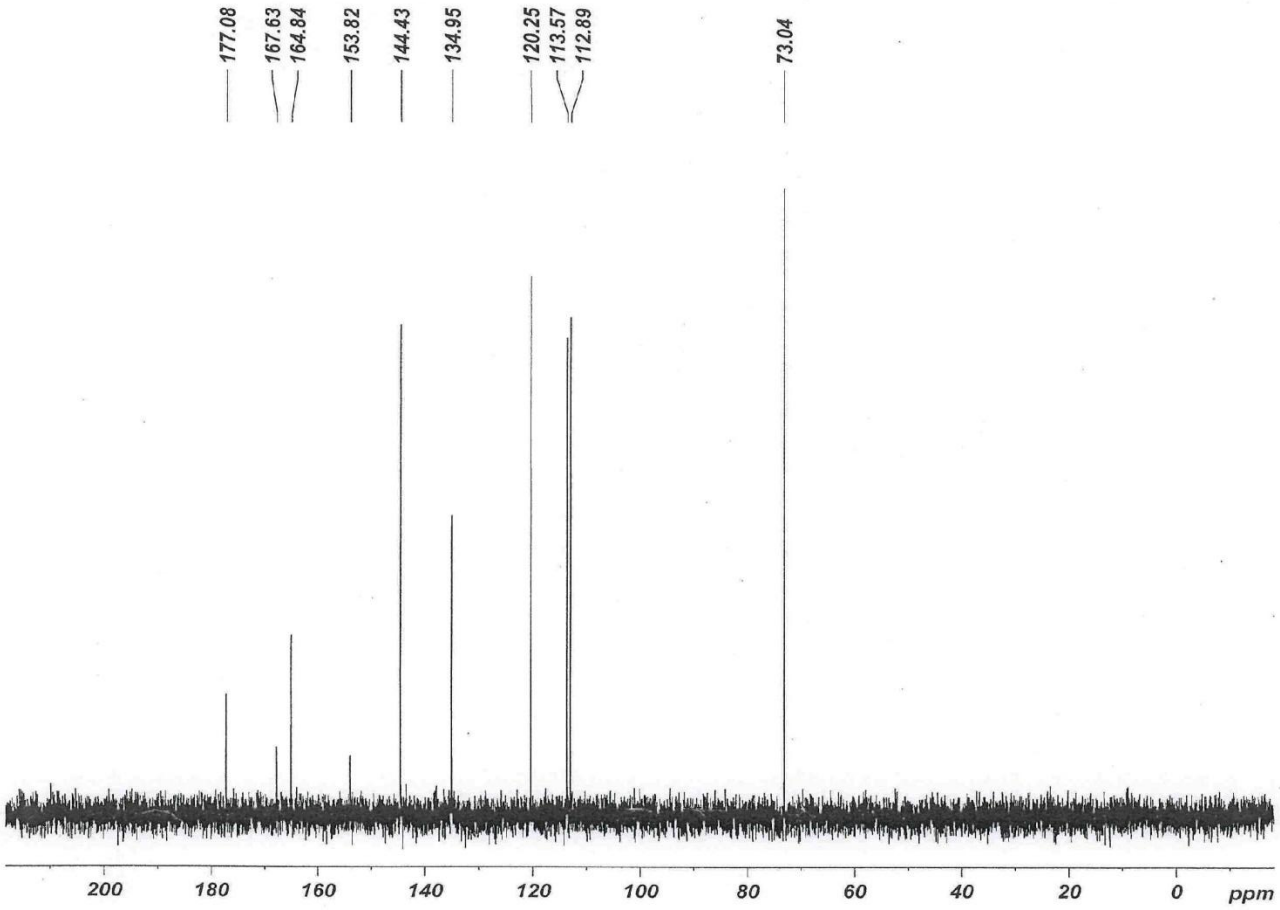


FIGURE -2

^{13}C NMR SPECTRUM OF 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

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PROCNO                       1

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PULPROG                zgpg30
TD                      32768
SOLVENT                   D2O
NS                       1024
DS                          4
SWH                 29761.904 Hz
FIDRES                0.908261 Hz
AQ                    0.5505524 sec
RG                          203
DW                       16.800 usec
DE                        6.00 usec
TE                       298.1 K
D1                  2.00000000 sec
d11                 0.03000000 sec
DELTA               1.89999998 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        13C
P1                         7.80 usec
PL1                        0.00 dB
SFO1                125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                     80.00 usec
PL12                      17.50 dB
PL13                      17.50 dB
PL2                        0.00 dB
SFO2                500.1320005 MHz

F2 - Processing parameters
SI                          32768
SF                  125.7577890 MHz
WDW                            EM
SSB                             0
LB                         1.00 Hz
GB                              0
PC                         1.40
```
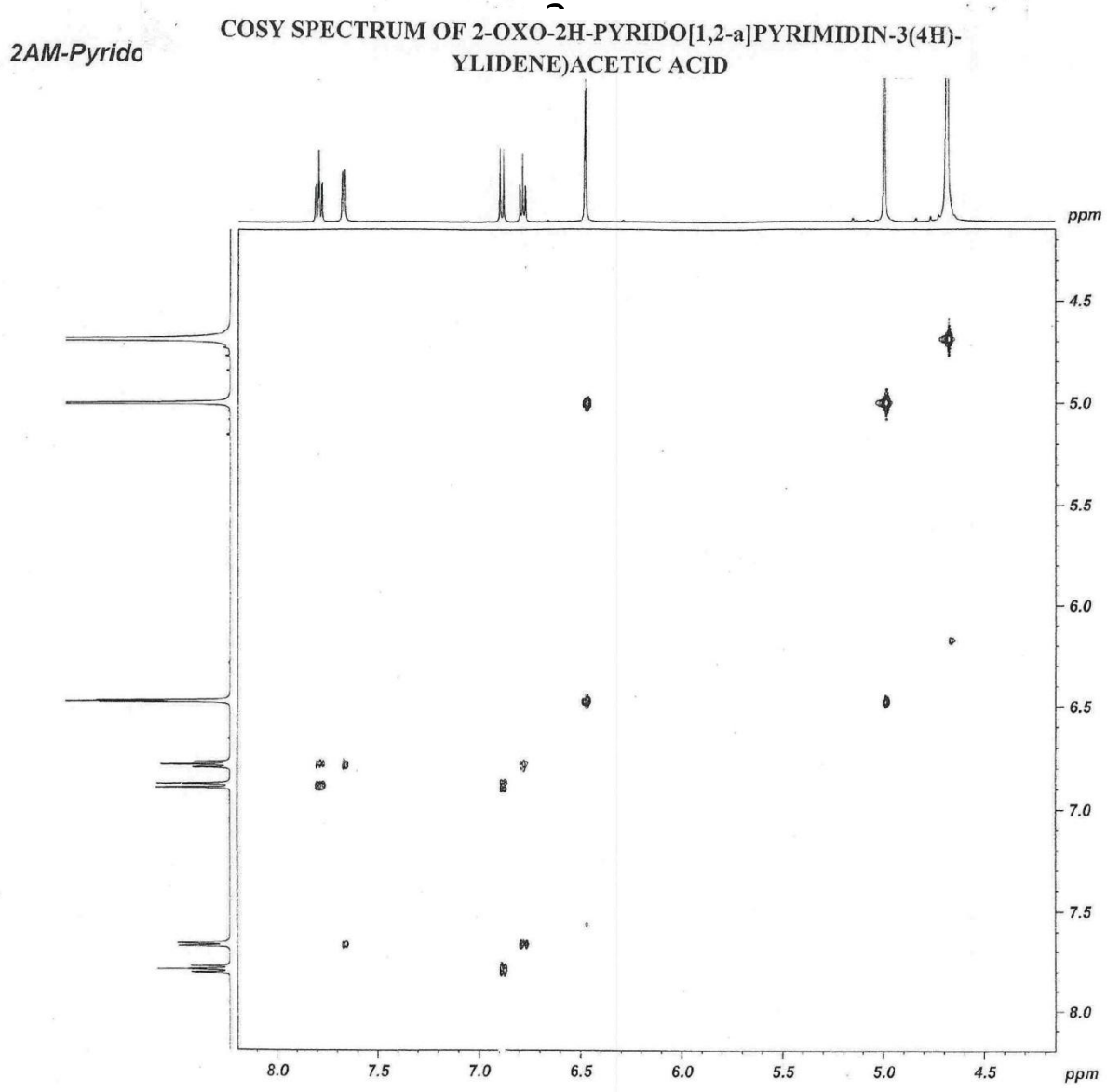

FIGURE-

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PROCNO                 1

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PULPROG         cosygpqf
TD                 2048
SOLVENT             D2O
NS                     1
DS                     8
SWH            2024.292 Hz
FIDRES         0.988424 Hz
AQ             0.5059060 sec
RG                    64
DW               247.000 usec
DE                 6.00 usec
TE                296.4 K
d0            0.00000300 sec
D1            1.13422596 sec
d13           0.00000400 sec
D16           0.00020000 sec
IN0           0.00049400 sec

======== CHANNEL f1 ========
NUC1                  1H
P0                10.65 usec
P1                10.65 usec
PL1                0.00 dB
SFO1        500.1330863 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPZ1               10.00 %
GPZ2               10.00 %
P16              1000.00 usec

F1 - Acquisition parameters
ND0                    1
TD                   128
SFO1          500.1331 MHz
FIDRES       15.814777 Hz
SW                4.048 ppm
FnMODE               QF

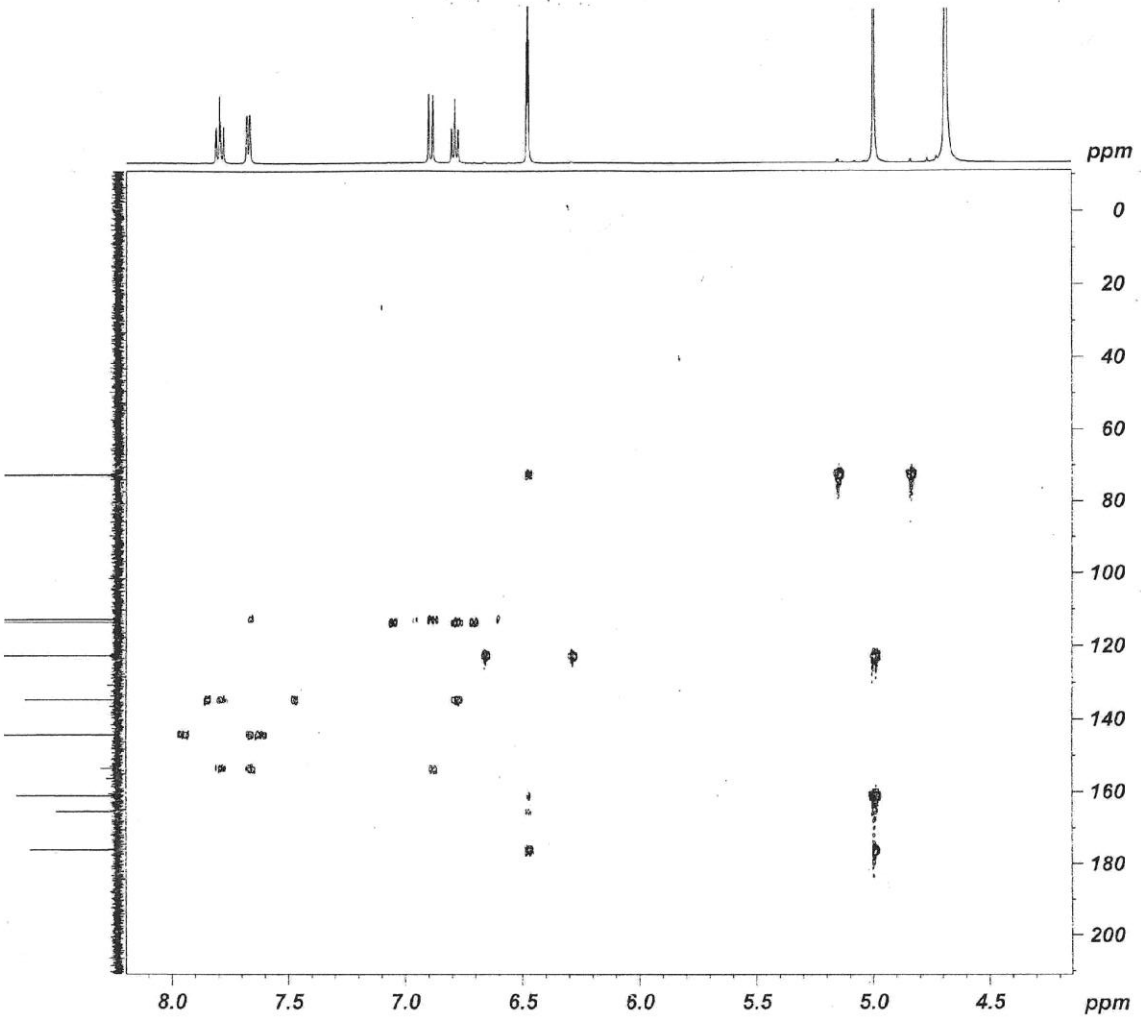
F2 - Processing parameters
SI                  1024
SF          500.1300000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.40

F1 - Processing parameters
SI                  1024
MC2                   QF
SF          500.1300000 MHz
WDW                SINE
SSB                   0
LB                 0.00 Hz
GB                    0
```

FIGURE-4

2AM-Pyrido.....

HMBC SPECTRUM OF 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

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PROCNO                       1

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INSTRUM                 spect
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PULPROG          hmbcgpndqf
TD                        4096
SOLVENT                   D2O
NS                           8
DS                          16
SWH                 2024.292 Hz
FIDRES              0.494212 Hz
AQ                  1.0117620 sec
RG                         203
DW                   247.000 usec
DE                     6.00 usec
TE                     297.1 K
CNST13              8.0000000
d0                  0.00000300 sec
D1                  0.79548788 sec
D16                 0.00020000 sec
d6                  0.06250000 sec
IN0                 0.00001790 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                      10.65 usec
p2                      21.30 usec
PL1                      0.00 dB
SFO1               500.1330363 MHz

======== CHANNEL f2 ========
NUC2                      13C
P3                       7.80 usec
PL2                      0.00 dB
SFO2               125.7703443 MHz

====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPNAM2                SINE.100
GPNAM3                SINE.100
GPZ1                     50.00 %
GPZ2                     30.00 %
GPZ3                     40.10 %
P16                    1000.00 usec

F1 - Acquisition parameters
ND0                          2
TD                         128
SFO1               125.7703 MHz
FIDRES             218.226257 Hz
SW                     222.095 ppm
FnMODE                      QF

F2 - Processing parameters
SI                        1024
SF                 500.1300000 MHz
WDW                       SINE
SSB                          2
LB                        0.00 Hz
GB                           0
PC                        1.40

F1 - Processing parameters
SI                        1024
MC2                         QF
SF                 125.7577890 MHz
WDW                       SINE
SSB                          0
LB                        0.00 Hz
GB                           0
```

FIGURE-5 NOE SPECTRUM OF 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

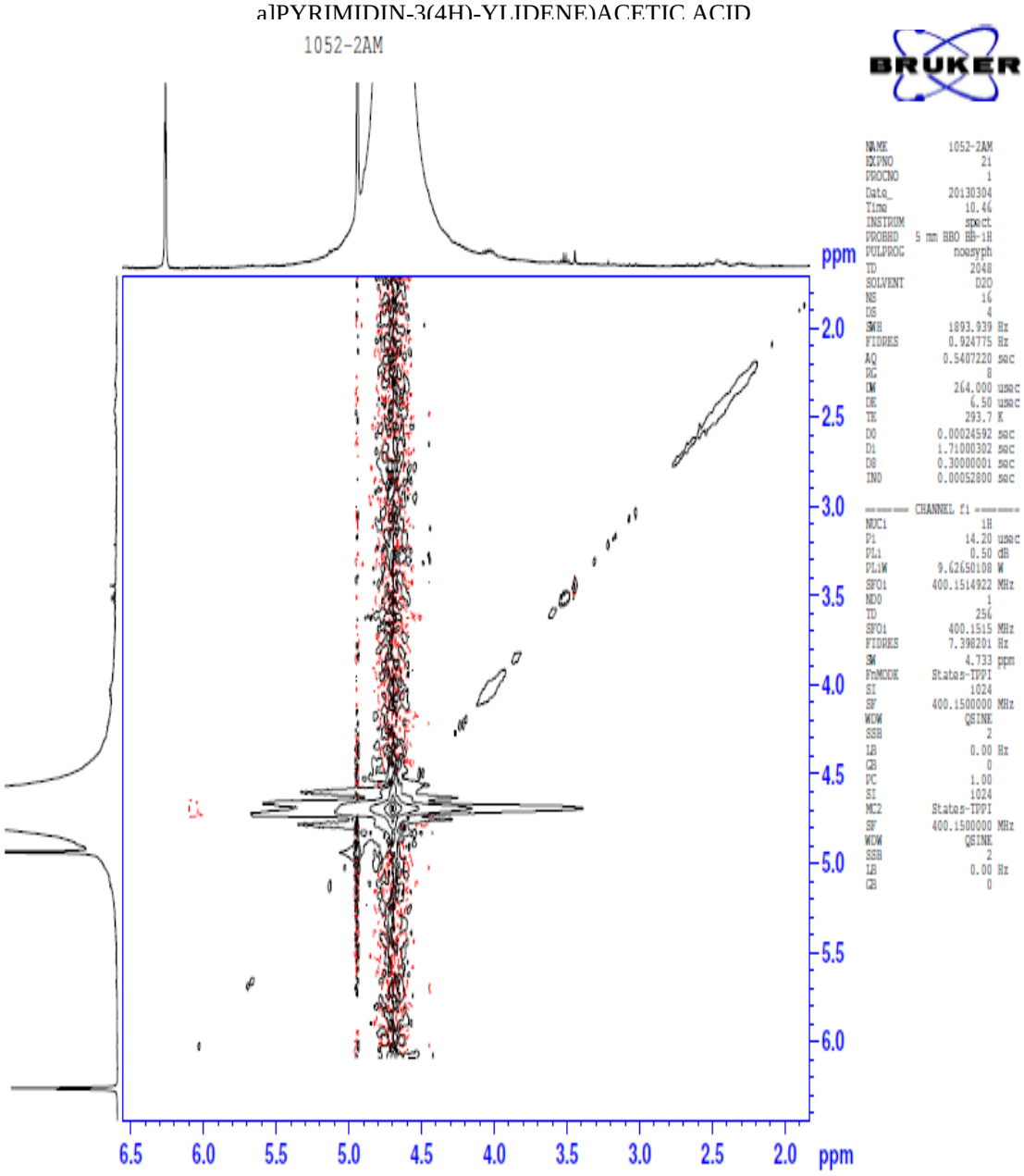


FIGURE-6

HMBC- ORRELATIONS OBSERVED IN 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

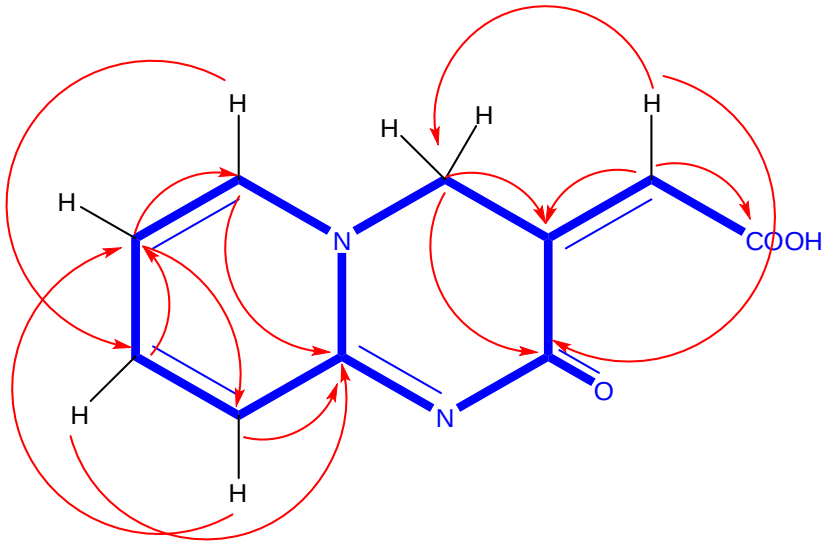


FIGURE-7

NOE-CORRELATIONS OBSERVED IN 2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

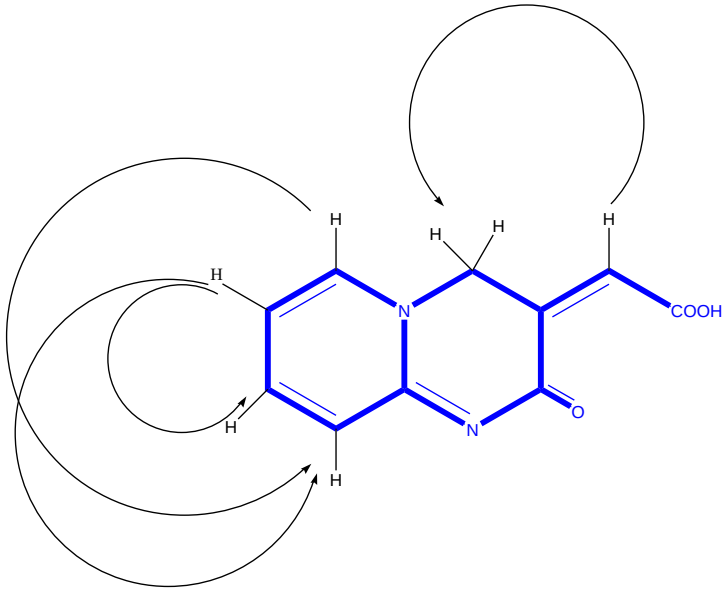


TABLE-3

NMR DATA OF 7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

^{1}H Shift in ppm	**Multip-licity/no. of ^{1}H**	**Hydrogen**	**C^{13} shift in ppm**	**Carbon**	**Dept-135**	**C^{13} shift in ppm**	**Carbon**	**Dept-135**
6.47	t/1	H_3'	176	C_2	-C	123	C_7	-C
5.00	d/2	H_4	161	C_3	-C	16	C_7-Me	$-CH_3$
7.6	d(d)/1	H_6	122	C_3'	-CH	132	C_s	CH
2.10	s/3	H_7- Me	165	C_3''	-C	113	C_9	CH
7.4	t/1	H_s	72	C_4	$-CH_2$	152	C_{10}	-C
6.8	d/1	H_9	146	C_6	-CH			

TABLE –4

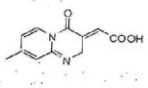
HMBC-CORRELATIONS OBSERVED IN 7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

^{1}H Shift in ppm	**Hydrogen**	**Observed ^{13}C connectivities**
6.47	H_{3}'	C_{2},C_{3},C_{4}, C_{3}''
5.00	H_{4}	C_{2},C_{3}, C_{3}'
7.6	H_{6}	C_{8},C_{10}
2.10	-	-
7.4	H_{s}	C_{7},C_{10}
6.8	H_{9}	C_{7},C_{10}

FIGURE-8

5ME-PY.....

^{1}HNMR SPECTRUM OF7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

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Current Data Parameters
NAME          Jun23-2009
EXPNO                  9
PROCNO                 1

F2 - Acquisition Parameters
Date_           20090623
Time              16.42
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG            zg30
TD                32768
SOLVENT             D2O
NS                   16
DS                    2
SWH           10330.578 Hz
FIDRES         0.315264 Hz
AQ            1.5860212 sec
RG                  203
DW               48.400 usec
DE                6.00 usec
TE               296.5 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                10.65 usec
PL1                0.00 dB
SFO1        500.1330885 MHz

F2 - Processing parameters
SI                32768
SF          500.1300000 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

FIGURE-9

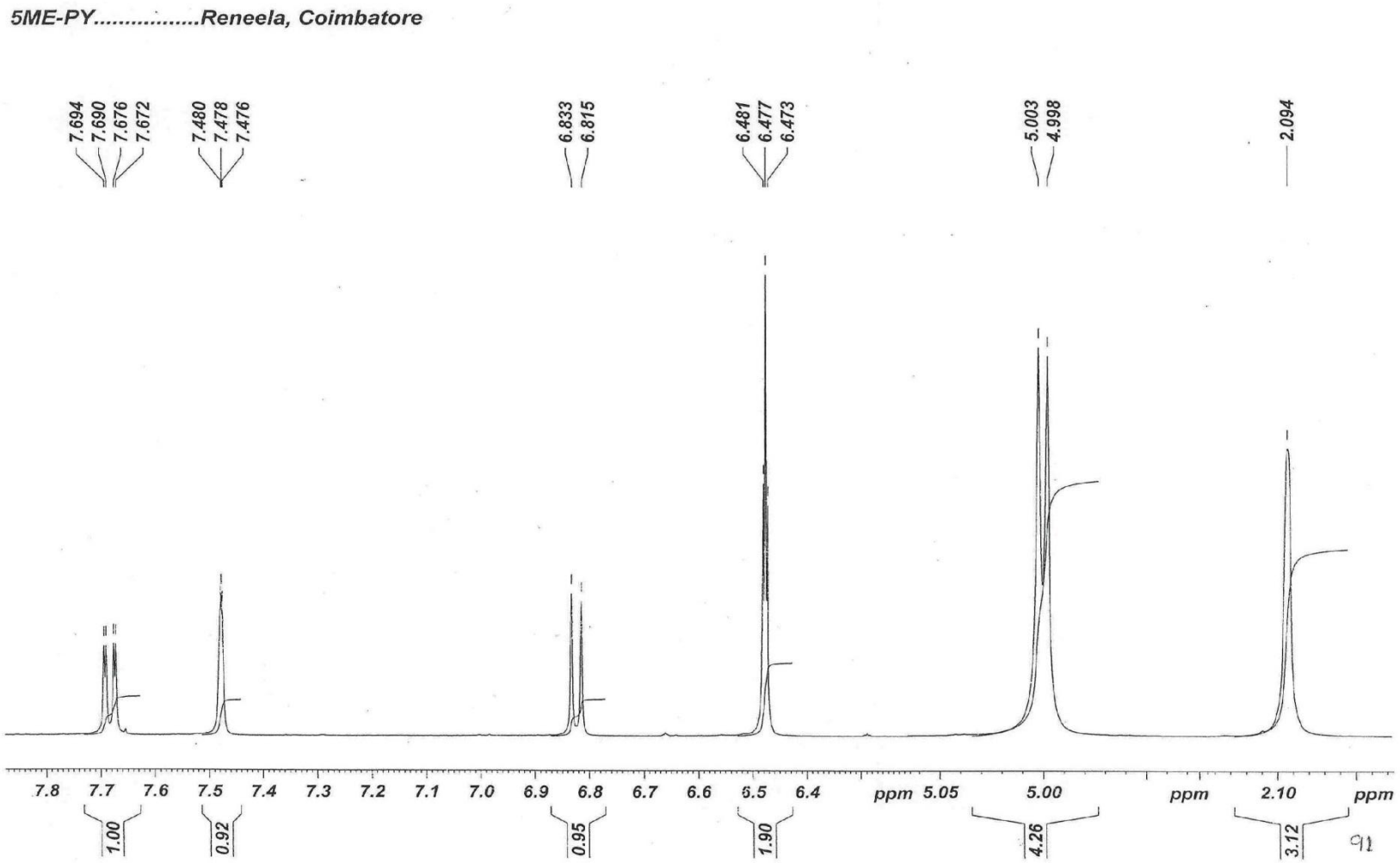
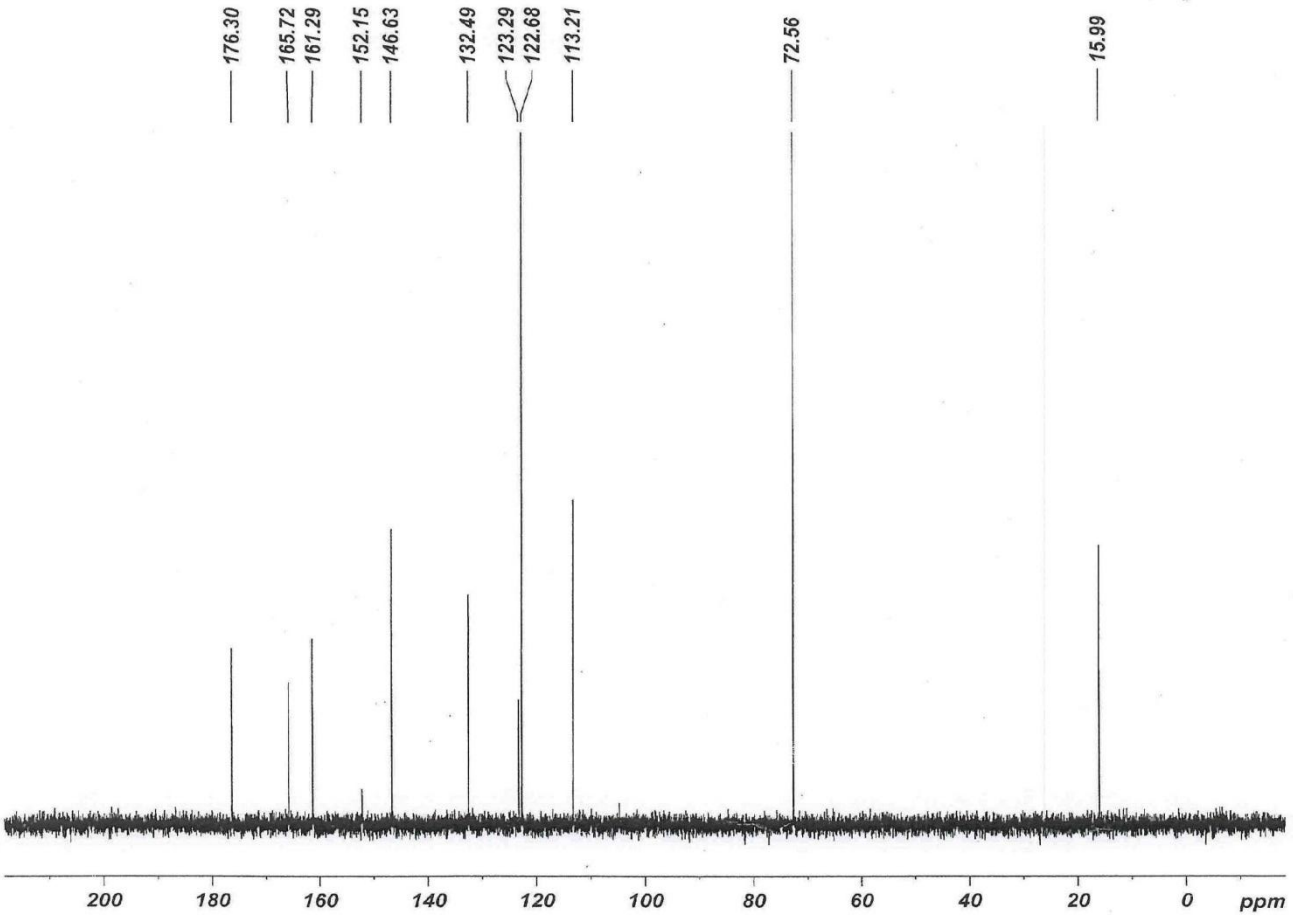

5ME-PY.....Reneela, Coimbatore
7.694
7.690
7.676
7.672
7.480
7.478
7.476
6.833
6.815
6.481
6.477
6.473
5.003
4.998
2.094
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
6.4
ppm
5.05
5.00
ppm
2.10
ppm
1.00
0.92
0.95
1.90
4.26
3.12

FIGURE - 10

^{13}CNMR SPECTRUM OF7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

5ME-PY.....

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Current Data Parameters
NAME                 Jun23-2009
EXPNO                         3
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20090623
Time                      15.46
INSTRUM                   spect
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                       32768
SOLVENT                    D2O
NS                        1024
DS                           4
SWH                  29761.904 Hz
FIDRES                0.908261 Hz
AQ                    0.5505524 sec
RG                         203
DW                      16.800 usec
DE                       6.00 usec
TE                      298.1 K
D1                 2.00000000 sec
d11                0.03000000 sec
DELTA              1.89999998 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                         7.80 usec
PL1                        0.00 dB
SFO1               125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                     80.00 usec
PL12                      17.50 dB
PL13                      17.50 dB
PL2                        0.00 dB
SFO2               500.1320005 MHz

F2 - Processing parameters
SI                        32768
SF                 125.7577890 MHz
WDW                          EM
SSB                           0
LB                         1.00 Hz
GB                            0
PC                         1.40
```
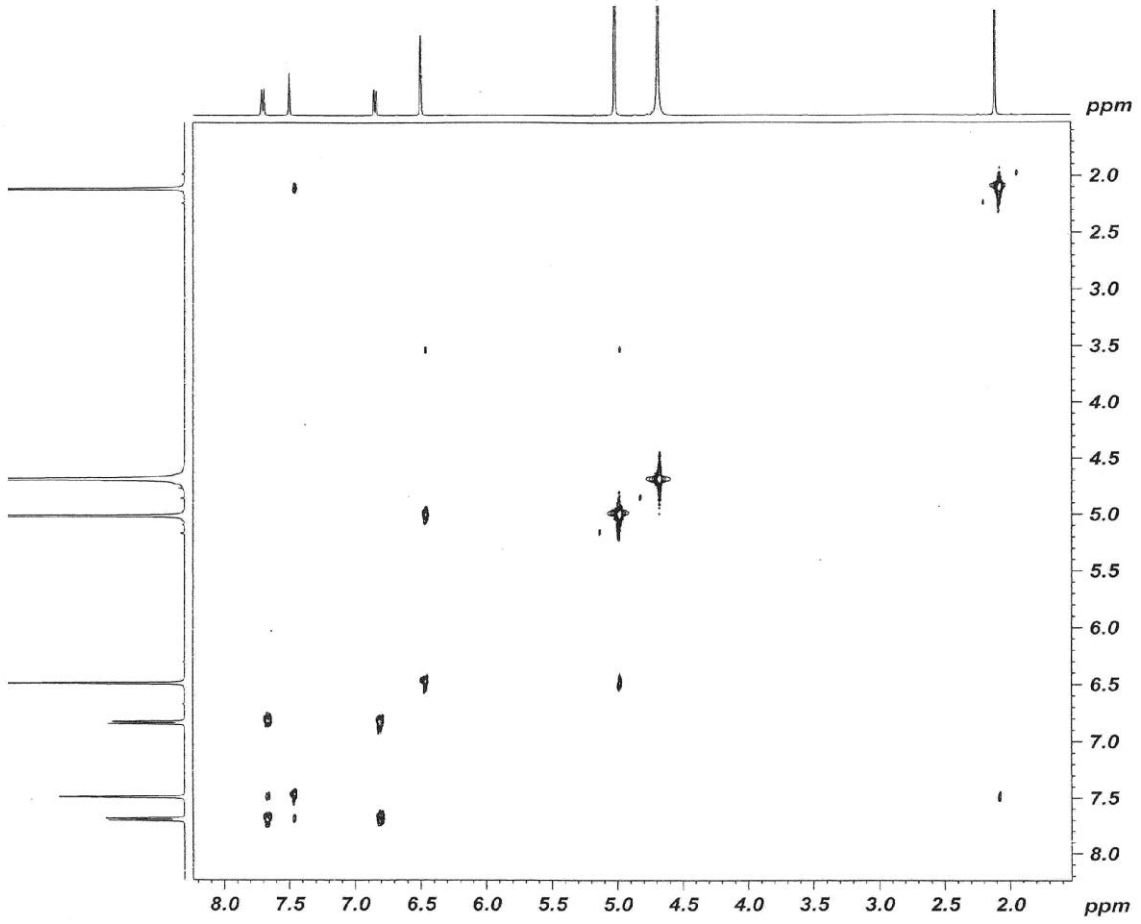

FIGURE-11

5Me-Pyrido.....

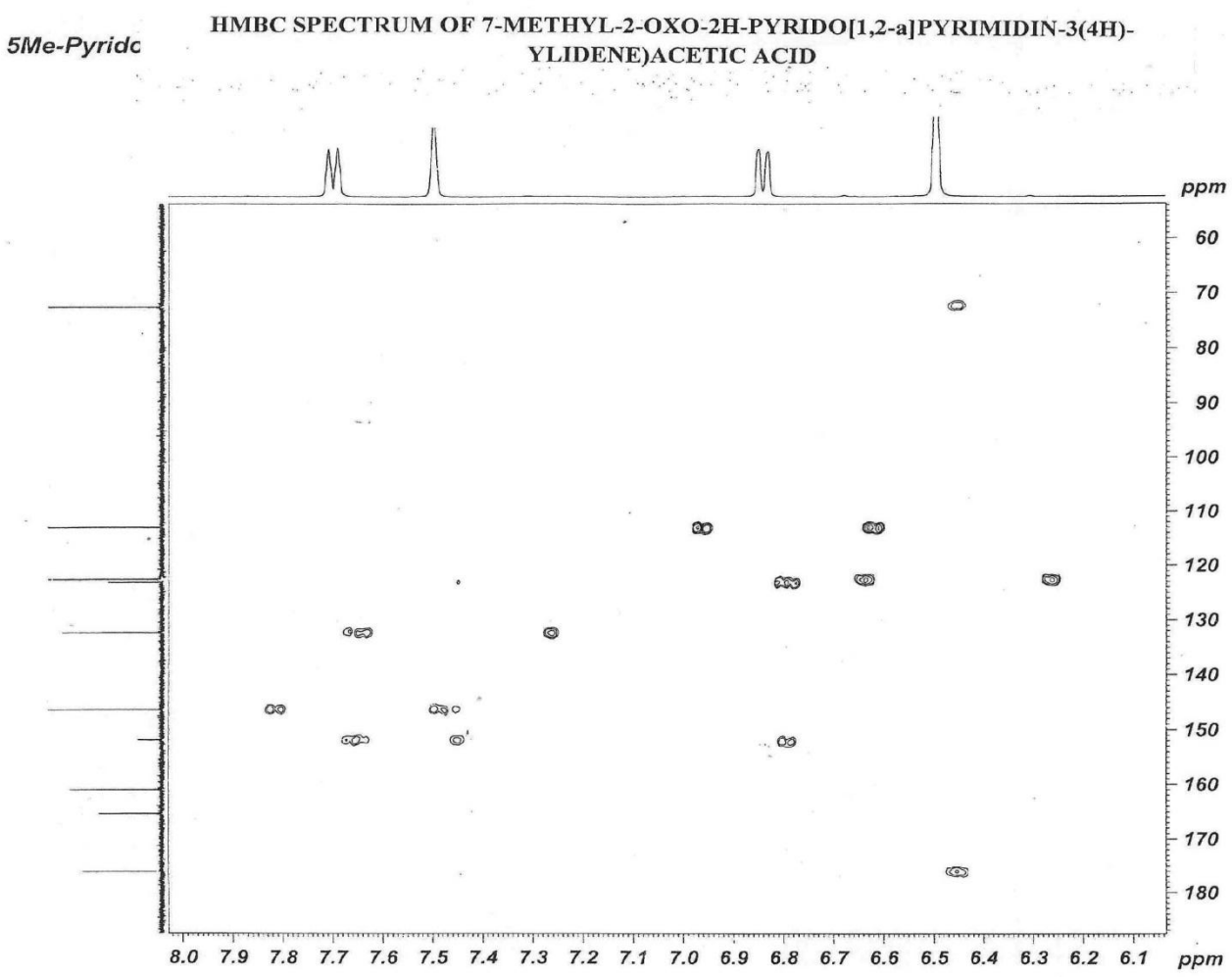
COSY SPECTRUM OF7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID




```
Current Data Parameters
NAME                  Jul21-2009
EXPNO                         32
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20090721
Time_                      19.47
INSTRUM                    spect
PROBHD     5 mm PABBO BB-
PULPROG                cosygpqf
TD                         2048
SOLVENT                     D2O
NS                             1
DS                             8
SWH                     3355.705 Hz
FIDRES                  1.638528 Hz
AQ                     0.3052020 sec
RG                            64
DW                       149.000 usec
DE                         6.00 usec
TE                        297.1 K
d0                    0.00000300 sec
D1                    1.33492994 sec
d13                   0.00000400 sec
D16                   0.00020000 sec
IN0                   0.00029800 sec

======== CHANNEL f1 ========
NUC1                          1H
P0                         10.65 usec
P1                         10.65 usec
PL1                         0.00 dB
SFO1                500.1324422 MHz

====== GRADIENT CHANNEL =====
GPNAM1                 SINE.100
GPNAM2                 SINE.100
GPZ1                      10.00 %
GPZ2                      10.00 %
P16                     1000.00 usec

F1 - Acquisition parameters
ND0                            1
TD                           128
SFO1                    500.1324 MHz
FIDRES                 26.216442 Hz
SW                         6.710 ppm
FnMODE                        QF

F2 - Processing parameters
SI                          1024
SF                  500.1300000 MHz
WDW                        SINE
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.40

F1 - Processing parameters
SI                          1024
MC2                           QF
SF                  500.1300000 MHz
WDW                        SINE
SSB                           0
LB                         0.00 Hz
GB                            0
```

94

FIGURE-




```
Current Data Parameters
NAME                  Jul21-2009
EXPNO                         34
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20090721
Time                       20.08
INSTRUM                    spect
PROBHD     5 mm PABBO BB-
PULPROG             hmbcgpndqf
TD                           4096
SOLVENT                     D2O
NS                             8
DS                            16
SWH                   3355.705 Hz
FIDRES                0.819264 Hz
AQ                    0.6103540 sec
RG                           203
DW                     149.000 usec
DE                       6.00 usec
TE                      298.7 K
CNST13                8.0000000
d0                    0.00000300 sec
D1                    1.19689596 sec
D16                   0.00020000 sec
d6                    0.06250000 sec
IN0                   0.00001790 sec

======== CHANNEL f1 ========
NUC1                         1H
P1                        10.65 usec
p2                        21.30 usec
PL1                        0.00 dB
SFO1                500.1324422 MHz

======== CHANNEL f2 ========
NUC2                        13C
P3                         7.80 usec
PL2                        0.00 dB
SFO2                125.7703443 MHz

====== GRADIENT CHANNEL =====
GPNAM1                 SINE.100
GPNAM2                 SINE.100
GPNAM3                 SINE.100
GPZ1                      50.00 %
GPZ2                      30.00 %
GPZ3                      40.10 %
P16                     1000.00 usec

F1 - Acquisition parameters
ND0                            2
TD                           128
SFO1                125.7703 MHz
FIDRES               218.226257 Hz
SW                      222.095 ppm
FnMODE                        QF

F2 - Processing parameters
SI                          1024
SF                  500.1300000 MHz
WDW                         SINE
SSB                            0
LB                          0.00 Hz
GB                             0
PC                          1.40

F1 - Processing parameters
SI                          1024
MC2                           QF
SF                  125.7577890 MHz
WDW                         SINE
SSB                            0
LB                          0.00 Hz
GB                             0
```

FIGURE-13-NOE SPECTRUM OF 7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

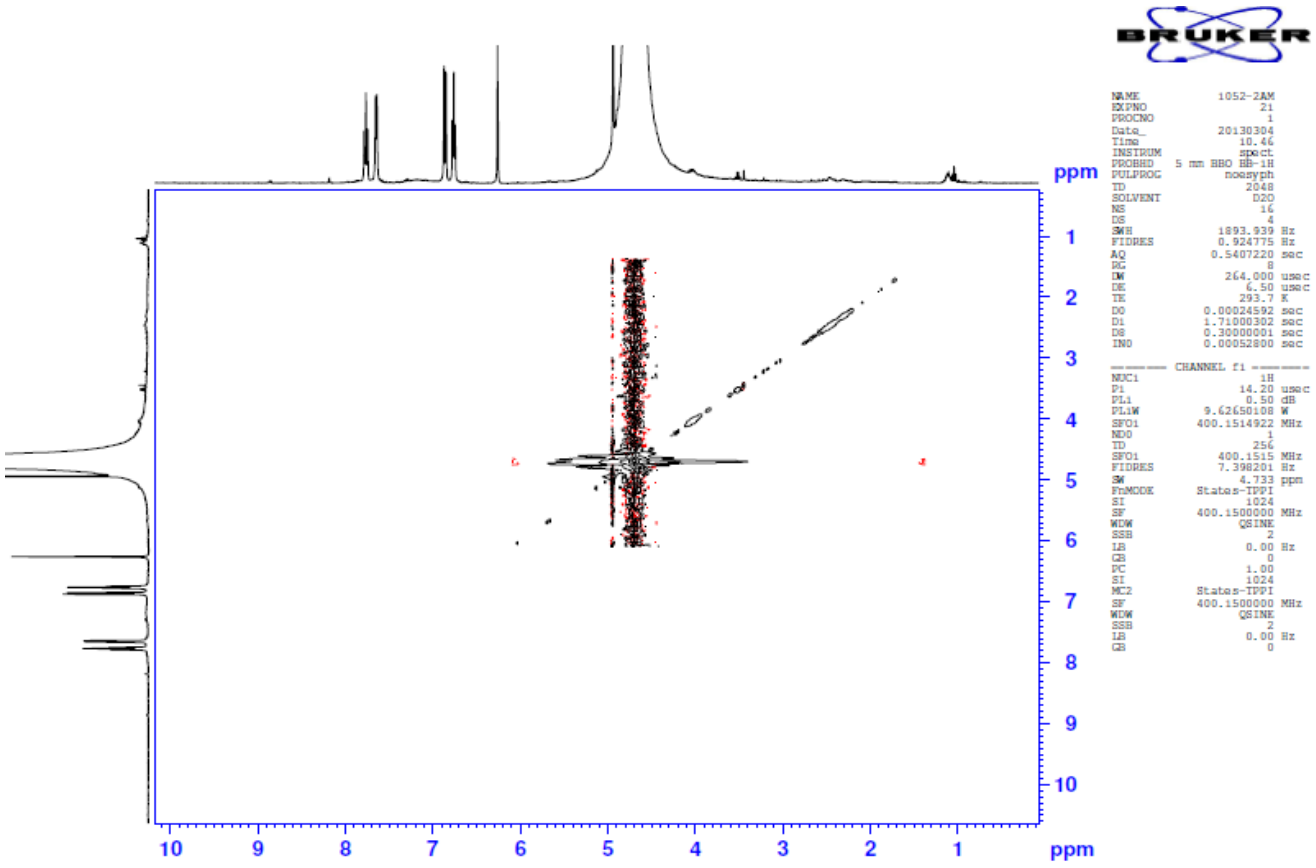


FIGURE – 14

HMBC CORRELATIONS OBSERVED IN 7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID

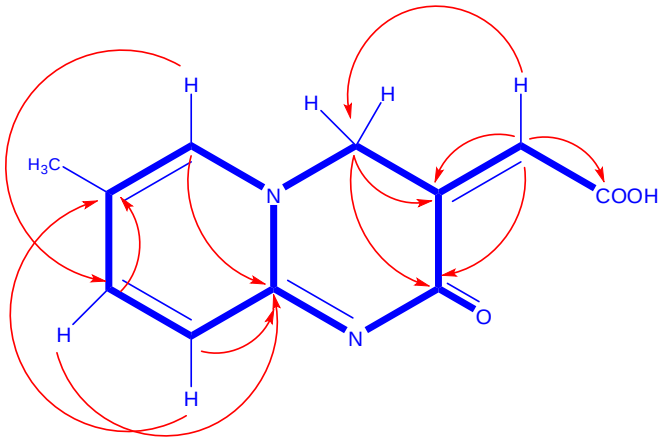
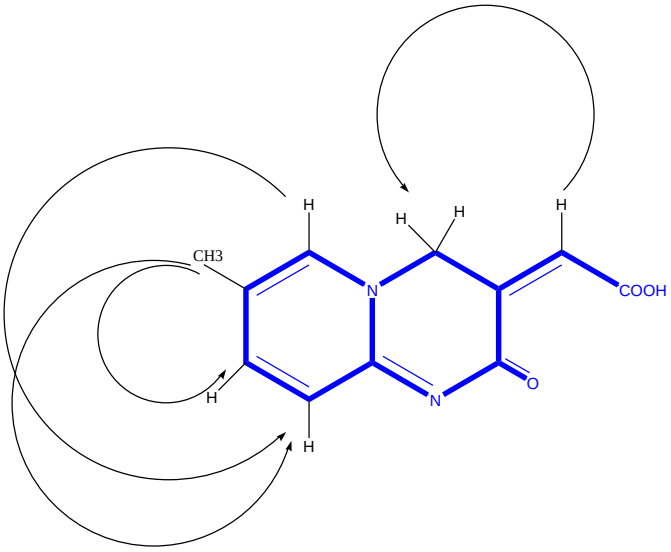


FIGURE – 15

NOE- CORRELATIONS OBSERVED IN 7-METHYL-2-OXO-2H-PYRIDO[1,2-a]PYRIMIDIN-3(4H)-YLIDENE)ACETIC ACID



5.SUMMARY AND CONCLUSION

- ✓ The following is the summary of the complete NMR analysis of the two compounds viz
    - **2-oxo-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene acetic acid**
    - **2-oxo-7-methoxy-2H-pyrido[1,2-a]pyrimidin-3(4H)-ylidene acetic acid**

- ✓ The NOE spectrum was obtained for both the compounds and wre compared with ^{1}H, ^{13}C,HMBC and COSY spectrum [sharulatha.v Thesis]
- ✓ The strong correlation observed between H4 and H3′ proved the "z" confirmation of the compound.
- ✓ The other correlation observed are H-6 and H-7 with H-9; H-8 and H-9 with H-6.

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