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Pyridine based Drugs and its Importance for the Health of the Society

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Abstract:

Chemistry plays important role for the betterment of the society. It helps in the better knowledge for selection of substance which is used by the society for its day by day activity. Chemical nature of the food material, agriculture and its related material, medicine, building construction material, cloths forming materials help in effectiveness of these materials toward better health of the society. The research in the field of medicine helps in development of many drugs and medicine for helping the society to be healthy and disease free. The chemistry of pyridine, as we understand it today, could be attributed in part to a number of discoveries made in the latter half of the 19th century. Pyridine derivatives are very important chemicals with tremendous biological application therefore they are very helpful in maintain the good health of society by fighting against a no of disease. In medicinal applications these compounds share an important part they are the part of many drugs.

Key words: *Pyridine, Drugs, Health, Society, Chemicals, Biological implication, Compounds.*

Introduction:

Pyridine derivatives are very important chemicals with tremendous biological application therefore they are very helpful in maintain the good health of society by fighting against a no of disease. The chemistry of pyridine, as we understand it today, could be attributed in part to a number of discoveries made in the latter half of the 19th century. Now days there are many methods for synthesis of pyridine and derivatives. As pyridine and there derivatives shows good biological activity they may be used as drugs. They helps the society in fighting against a no of disease therefore are very helpful for the betterment of the society in terms of health and related issues.

DISCUSSION:

1.1. Pyridines and their biological activity.

The chemistry of pyridine, as we understand it today, could be attributed in part to a number of discoveries made in the latter half of the 19th century. Thomas Anderson isolated the first pyridine base, picoline, in 1846 from bone oil [1]. In 1869 the chemistry of pyridine started to be rationalized when Wilhelm Körner and James Dewar (1871) independently formulated a mono-aza-analogue of benzene [2].Following structural understanding a number of synthetic processes were developed, starting with Baeyer who reported the synthesis of 2-picoline (**2**), albeit in low yield [3,4] from the reaction of acrolein (**1**) with aqueous ammonia (**Scheme 1**).

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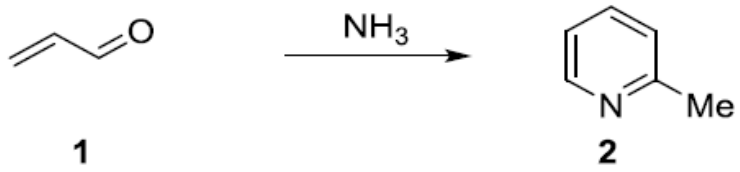
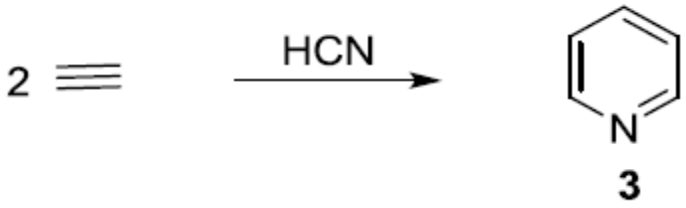


1 **2**

Scheme 1: Synthesis of 2-picoline (**2**) from acrolein (**1**) and ammonia.

In 1876 Ramsey discovered the original laboratory synthesis of pyridine (3) [5]. Reacting a mixture of acetylene and hydrogen cyanide in a red-hot tube gave the parent heterocycle (3) **(Scheme 2)** [5], although large quantities of pyridine were more reliably obtained from natural sources *via* coal tar distillation.



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Scheme 2: Synthesis of pyridine (**3**) from acetylene and HCN.

Koehn and Elvehjem were able to isolate nicotinamide (**4**) and nicotinic acid (**5**) from vitamin B2 in the 1930s (**Figure 1**) [6] Their discovery provided a new treatment for human pellagra, a vitamin deficiency causing dermatitis and dementia. From that date, researchers started to pay closer attention to the synthesis and properties of pyridine derivatives.

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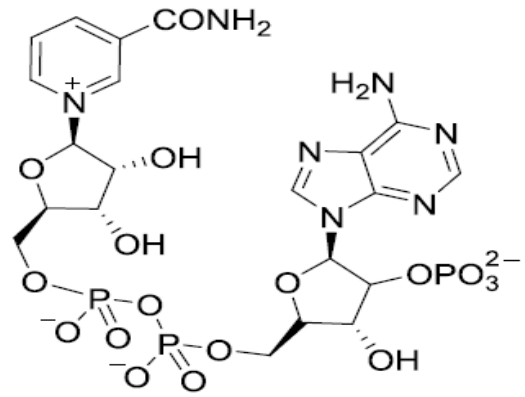
Figure 1: Structures of nicotinamide (**4**) and nicotinic acid (**5**).

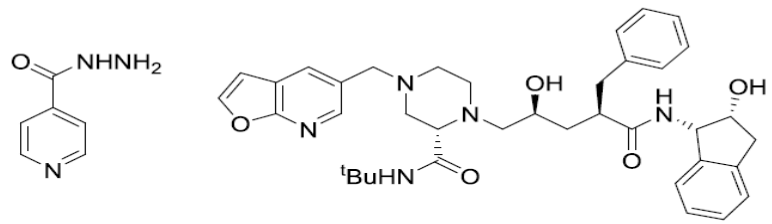
The chemistry of pyridine provided fundamental understanding of the chemistry and properties of biological systems, since this heterocycle plays an important role in both biological and chemical coordination. The pyridine ring system is one of the most common heterocyclic motifs that is found to modulate the enzymes of living organisms. For example, nicotinamide adenine dinucleotide phosphate, NADP+ (**6**) (**Figure 2**), is intimately involved in various oxidation–reduction processes in biology [7].



NADP+ (**6**)

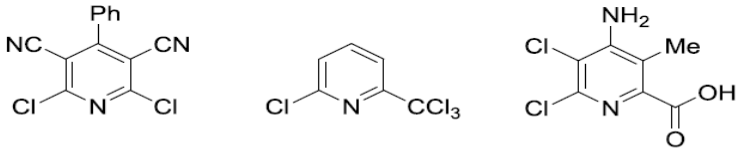
Figure 2: Structure of nicotinamide adenine dinucleotide phosphate, NADP+ (**6**).

The pyridine moiety can be found in over 7000 pharmaceutical drugs such as the anti-tuberculosis drug (7), the HIV inhibitor L-754,394 (8), agrochemicals **(9-11)** (Figure 3) [8] and a large number of natural products [9-11].



Isoniazid (**7**) (antituberculosis)

L-754,394 (**8**) (potent HIV protease inhibitor)



Pyridinenitrile (**9**) (Fungicide)

Nitrapyrin (**10**) (Bactericide)

Picloram (**11**) (Herbicide)

Figure 3: Structures of some pyridine containing pharmaceutical drugs and agrochemicals.

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The presence of the pyridine motif in a wide range of molecules makes it a very important heterocyclic class in chemistry. In modern pharmaceuticals the motif is very common, with over one hundred currently marketed drugs containing this vital unit [12]. Thepyridine motif is common in nature and is present in a number of biologically active natural products. In biological systems the potency of pyridines is well demonstrated by the essential vitamins niacin (**5**) (vitamin B3) and pyridoxine (**12**) (vitamin B6) as well as the toxic alkaloid nicotine (**13**) (**Figure 4**) [13].

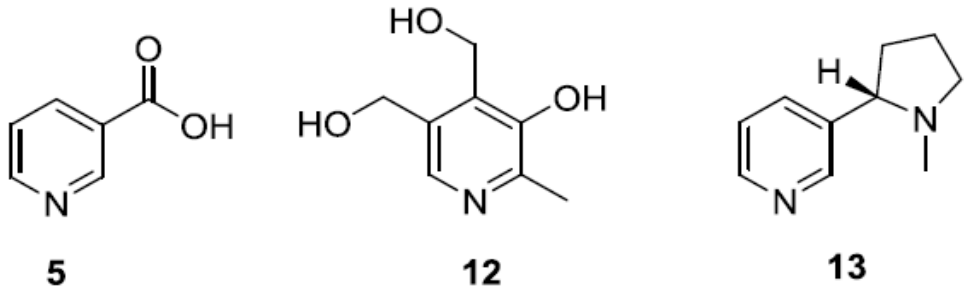

Figure 4: The pyridine motif is present in a number of biologically active molecules.

As well as natural products, the pyridine structure is commonly found in pharmaceutical agents. Sulfapyridine (**14**) was one of the first antibiotics, used to treat Winston Churchill's bacterial pneumonia in 1942. Currently marketed drugs containing the pyridine unit include the blockbuster drugs Omeprazole (**15**) (Nexium)® and loratadine (**16**) (Claritin)® (**Figure 5**) [12].

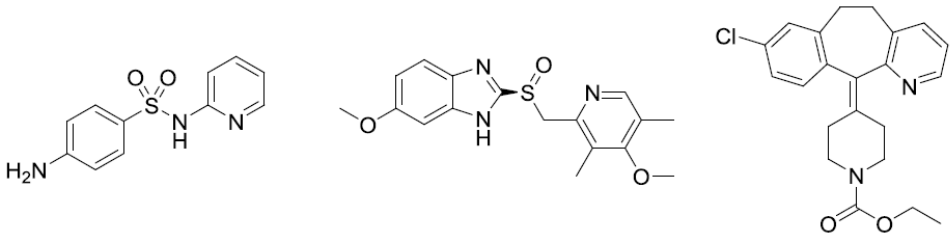

Figure 5: The pyridine structure is found in pharmaceutical agents.

Pyridines have also found applications as ligands in organic and inorganic chemistry. 2,2'-Bipyridine (bipy) is a bidentate chelating ligand that is used in the rhenium catalyzed reduction of carbon dioxide [14]. Additionally, bipy has been incorporated into metal organic frameworks as a heterogenous catalyst for the epoxidation of alkenes [15]. In synthetic organic chemistry, with potential for biological applications, pyridines have found use as nucleophilic catalysts in organic transformations. For example, 4-dimethylaminopyridine (DMAP) (**17**) has been widely used in a range of transformations including acylation and esterification reactions [16,17]. With this wide range of applications, methods for pyridine synthesis are an ever-present focus of new

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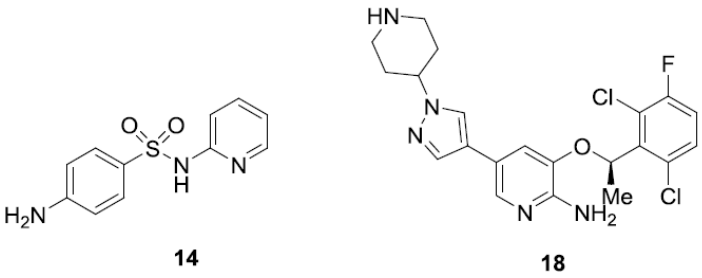
research, with reviews even focusing on the most recent advances in the synthesis of pyridine derivatives [18].

1.2. Aminopyridines and their biological activity.

There is a wide array of different substituents and possible substitution patterns of pyridine derivatives and of these, 2-aminopyridines have featured prominently in recent times as they have been incorporated into new cancer treatments[19]. Amongst many other applications, 2-aminopyridines are important as nitric oxide synthase inhibitors[20] intermediates in the industrial synthesis of zolpidem (Ambien)[21] and also as ligands in organic and inorganic chemistry [22].Aminopyridines are important compounds biologically, able to elicit a wide range of biological responses in a number of different organisms. Sulfapyridine (**14**) was one of the first effective antibiotics but their therapeutic application is just as relevant today[23]. 4-Aminopyridine (Fampridine) has been used for the symptomatic treatment of multiple sclerosis [24]. Furthermore, a 2-aminopyridine has recently been approved as a new anaplastic lymphoma kinase (ALK) inhibitor (**18**) for treatment of non-small cell lung cancer (**Figure 6**) [19].



14 18

Figure 6: 2-Aminopyridines are important in the pharmaceutical industry**.**

Pyridine Based DurgsAnd Their Utility

1. **Niacin (nicotinic acid):**itis prepared by the following methods

(a) The molecule 2-methyl-5-ethylpyridine (1.11) can be prepared directly by the condensation between acetaldehyde molecule and ammonia. In this reaction nitric acid mediated oxidation then converts this to nicotinic acid (1.12). Although the initial pyridine formation is high yielding but the process is not without environmental issues as it produced the large excess of nitric acid and high temperatures combined with the liberation of large amounts of gases such as nitric oxides and carbon dioxide which must be scrubbed from the system (Scheme 1).this will help in protection of environment and this will help in maintain the good health of society. Interestingly, despite these considerations this method of synthesis is currently still run by the specialty chemicals company Lonza but now as a continuous flow process at their main plant in Visp, Switzerland.

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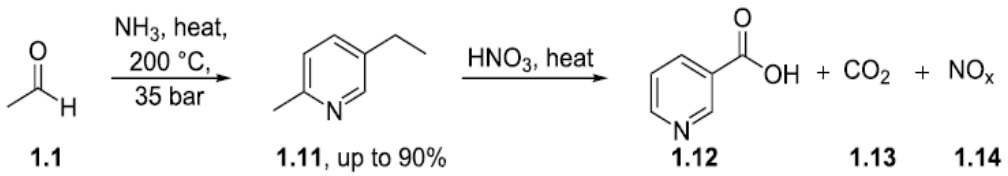
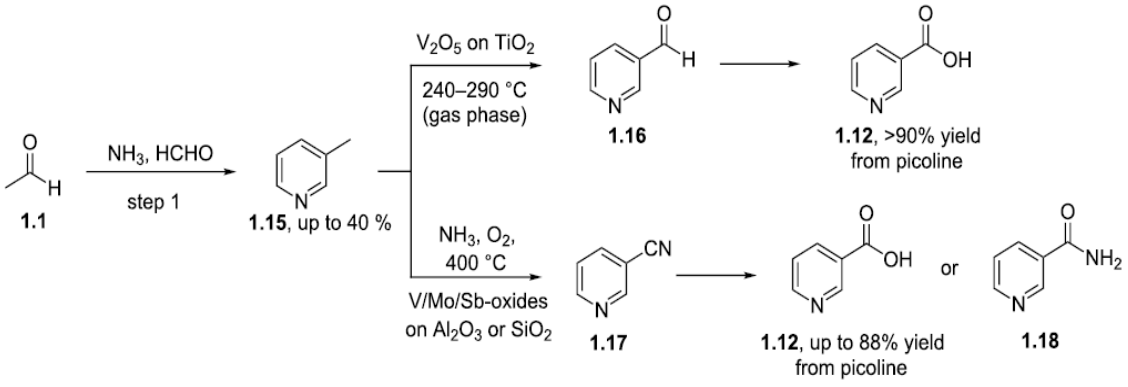


Scheme-1

(b) There is another alternative process is based on the availability of 3-picoline (**1.15**) which is generated as a major side product in the synthesis of pyridine, prepared from the reaction between formaldehyde, acetaldehyde and ammonia in a gas phase. (Scheme 3) [25]. The 3-picoline can be readily oxidised via another gas-phase protocol route using a fixed-bed reactor charged with vanadium pentoxide on high surface titanium dioxide (5–50 wt % vanadium). A modification of the sequence utilizes a dehydrativeamminolys to furnish the corresponding 3-cyanopyridine, which can then be subsequently hydrolyses to nicotinic acid. The catalyst systems most commonly used in this high temperature ammoxidation are based on vanadium, molybdenum or antimony oxides supported on silica or alumina in solid phase.



Use:

Niacin is used to prevent and treat niacin deficiency known as pellagra. Niacin deficienc results from certain medical conditions like alcohol abuse, malabsorption syndrome, Hartnup disease etc.), poor diet, or long-term use of certain medications like isoniazid .Therefore niacin is a good chemical to protect the health of the society.

2. **Clarinex (Desloratadine):** It is synthesized by following method.

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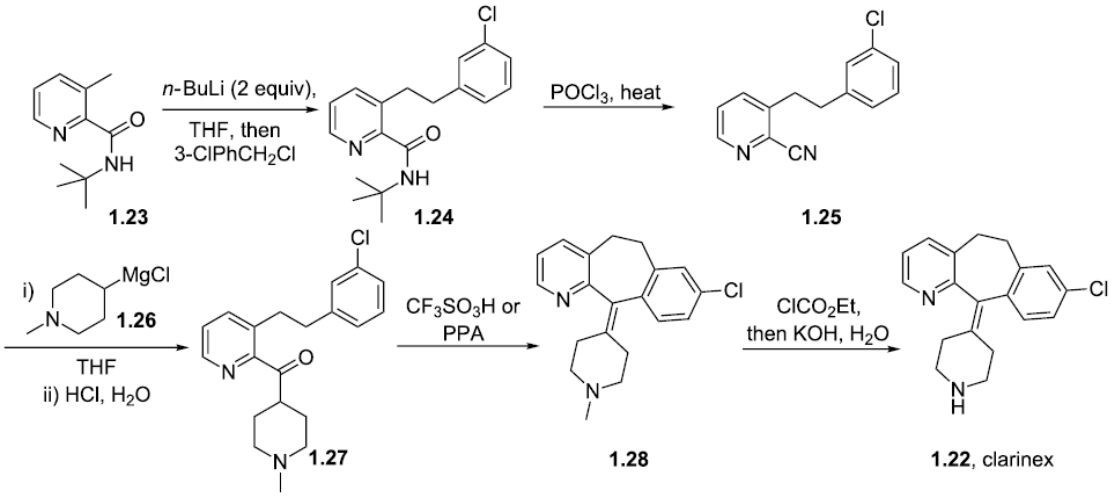
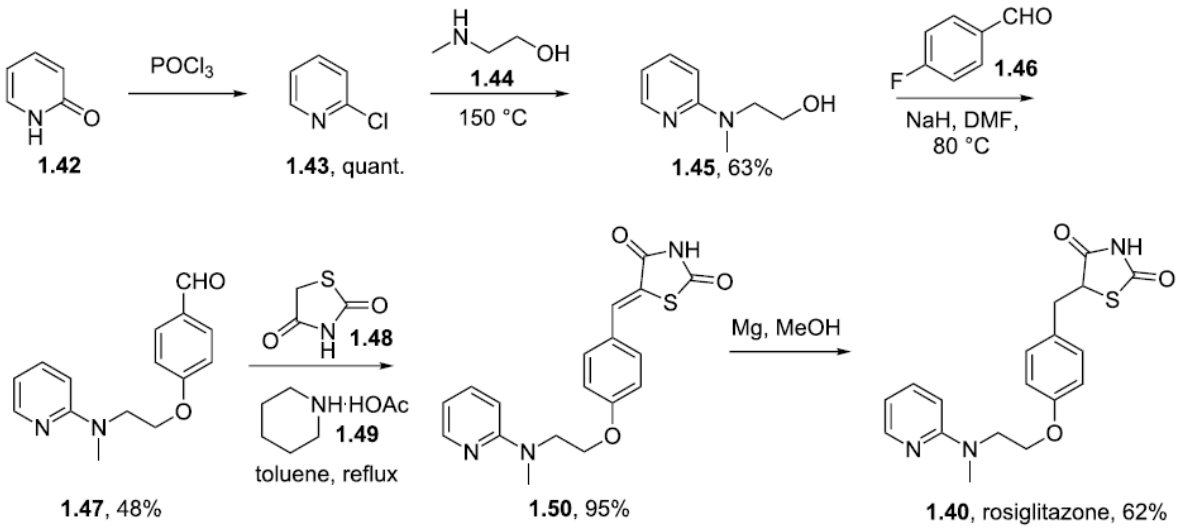


Uses:

Desloratadine is a medicinal molecule which act as an antihistamine used to relieve allergy symptoms such as watery eyes, runny nose, itching eyes,eatcing nose, sneezing, hives, and itching in whole body. It works by blocking a certain natural substance (histamine) that the human body makes during an allergic reaction.

3. **Rosiglitazone.**It is synthesized by the following methods



Used:

Rosiglitazone is a very sensitive drug and is used with a proper diet and exercise program to control high blood sugar in people suffering from type 2 diabetes. Controlling the high blood sugar level in blood helps prevent kidney damage, blindness, nerve problems, loss of limbs, and sexual problems in humans. Proper controls

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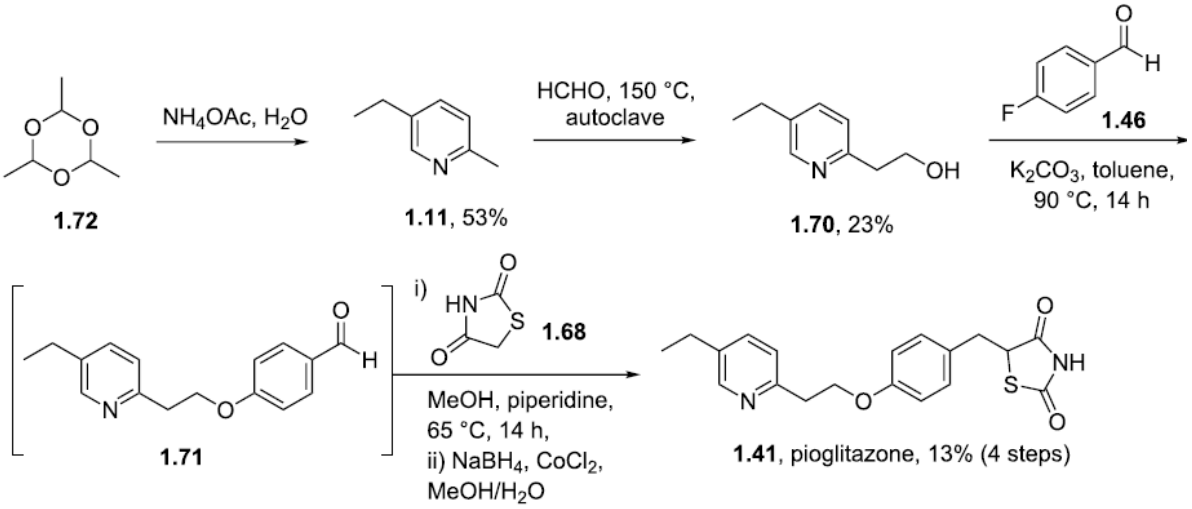
of diabetes also lessen your risk of a heart attack or stroke. Rosiglitazone belongs to the class of drugs known as glitziness. It also help in lowering blood sugar to restore your body's proper response to insulin. Thus this medicine is very helpful for maintain the good health of diabetic person.

4. **Pioglitazone :** It is synthesized by the following methods



Uses

Pioglitazone is also a diabetes drug .it is a thiazolidinedione-type drug. This is also used along with a proper diet and exercise program to control high blood sugar level in blood in patients with type 2 diabetes. It works by helping to restore the body's proper response to insulin conc., thereby lowering blood sugar level in blood .Controlling high blood sugar in the blood helps prevent kidney damage, blindness, nerve problems, loss of limbs, and sexual function problems in peoples. Proper control of diabetes with the help of this medivine may also lessen your risk of a heart attack or stroke. Pioglitazone is used either alone or in combination with other diabetes medications like metformin or a sulfonylurea such as glyburide.

5. Etoricoxib: It is prepared by the following method

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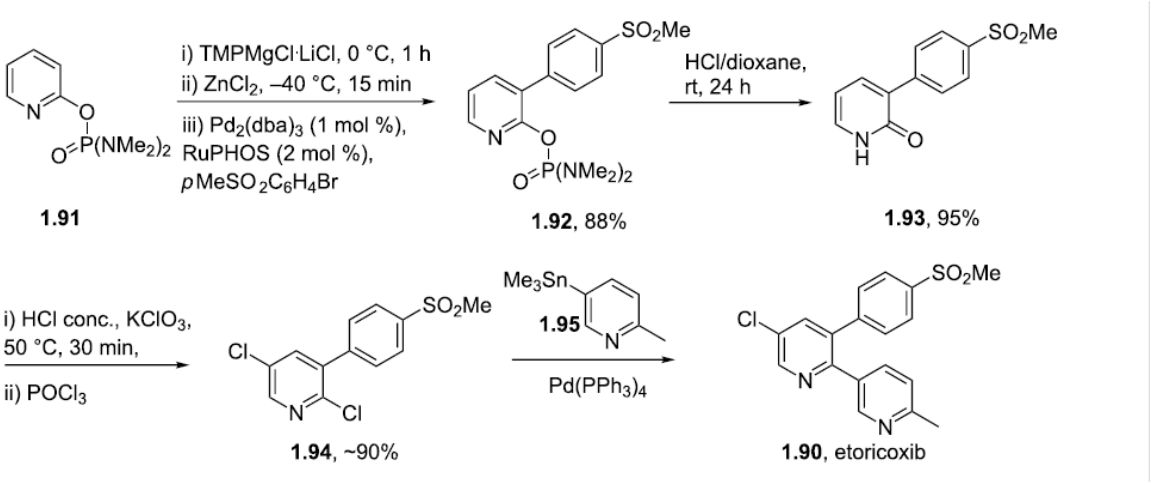
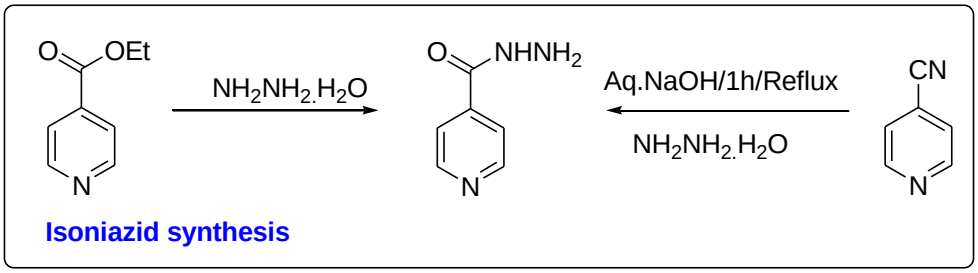


Used:

Etoricoxib is a medicine comes under the non-steroidal anti-inflammatory drug. It is also known as an 'NSAID. Etoricoxib helps in easing pain and swelling (inflammation) in conditions like osteoarthritis, rheumatoid arthritis and ankylosing, spondylitis and related.

6. **Isoniazid:** It is prepared by the following method



Uses:

Isoniazid is a complimentary medicine used with other medications to treat active tuberculosis (TB) infections in peoples suffering from it. Sometimes It is also used alone to prevent active TB infections in people who may be infected with the bacteria. Isoniazid also work is an antibiotic. It works by stopping the growth of bacteria.This antibiotic treats only bacterial infections and it will not work for viral infections like common cold, flu.

Conclusion:

Pyridine derivatives are very important chemicals with tremendous biological application therefore they are very helpful in maintain the good health of society by fighting against a no of disease. In medicinal applications these compounds share an important part they

are the part of many drugs. With changing substituents on the pyridine ring, the biological targets vary from microbial diseased to viral diseases and variety of cancerous cells and much other disease.

Works cited and consulted:

[1]. Anderson, T. *Trans. R. Soc. Edinb. I* 1849, *16*, 123.
[2]. Dobbin, L. *J. Chem. Ed*. 1934, *11*, 596.
[3]. Baeyer, A. *Ber*. 1869, *2*, 398.
[4]. Baeyer, A. *Ann*. 1870, *155*, 281.
[5]. Ramsey, W. *Philos. Mag*. 1876, *2*, 269.
[6]. Koehn C. J.; Elvehjem C. A. *J. Biol. Chem*. 1937, *118*, 693.
[7].Farhanullah; Agarwal, N.; Goel, A.; Ram, V. J. *J. Org. Chem*. 2003, *68*, 2983.
[8].Matolcsy, Gy.;Nádasy, M.; Andriska, V. In *Pesticide Chemistry*; AkadémiaiKiadó: Budapest, 1988, 427–430.
[9]. Henkel, T.; Brunne, R. M.; Müller, H.; Reichel, F. *Angew. Chem., Int. Ed.Engl.* 1999, *38*, 643.
[10]. Santos, V. A. F. F. M.; Regasini, L. O.; Nogueira, C. R.; Passerini, G. D.; Martinez, I.; Bolzani, V. S.; Graminha, M. A. S.; Cicarelli, R. M. B.; Furlan M. *J. Nat. Prod*. 2012, *75*, 991.
[11]. Bull, J. A.; Mousseau, J. J.; Pelletier, G.; Charette, A. B. *Chem. Rev*. 2012, *112*, 2642.
[12]. Goetz, A. E.; Garg, N. K. *Nature Chem*. 2013, *5*, 54.
[13]. Henry, G. D. *Tetrahedron* 2004, *60*, 6043.
[14].Smieja, J. M.; Kubiak, C. P. *Inorg. Chem*. 2010, *49*, 9283.
[15]. Brown, K.; Zolezzi, S.; Aguirre, P.; Venegas-Yazigi, D.; Paredes-Garcia V.; Baggio, R.; Novak, M. A.; Spodine, E. *Dalton Trans*. 2009, 1422.
[16]. Berry, D. J.; Digiovanna, C. V.; Metrick, S. S.; Murugan, R. *Arkivoc*2001, *2*, 944.
[17].Brotzel, F.; Kempf, B.; Singer, T.; Zipse, H.; Mayr, H. *Chem. Eur. J*. 2007, *13*, 336.
[18]. Hill, M. D. *Chem. Eur. J*. 2010, *16*, 12052.
[19].Gerber, D. E.; Minna, J. D. *Cancer Cell* 2010, *18*, 548.
[20].Hagmann, W. H.; Caldwell, C. G.; Chen, P.; Durette, P. L.; Esser, C. K.; Lanza, T. J.; Kopka, I. E.; Guthikonda, R.; Shah, S. K.; MacCoss, M.; Chabin, R. M.; Fletcher, D.; Grant, S. K.; Green, B. G.; Humes, J. L.; Kelly, T. M.; Luell, S.; Meurer, R.; Moore, V.; Pacholok, S. G.; Pavia, T.; Williams, H. R.; Wong, K. K. *Bioorg. Med. Chem. Lett*. 2000, *10*, 1975. 139
[21].Guzzo, P. R. In *The Art of Drug Synthesis,* ed. Johnson, D. S.; Li, J. J.; John Wiley& Sons, Inc.: Hoboken, New Jersey, 2007, 215–223.
[22]. Ma, H. R.; Wang, Y. Y.; Liu, P.; Li, D. S.; Shi, Q. Z.; Lee, G. H.; Peng, S. M. *Polyhedron*, 2005, *24*, 215.
[23].Clayden, J.; Greeves, N.; Warren, S. In *Organic Chemistry*, 2nd edn.; Oxford University Press: New York, 2012, 565–765.
[24].Solari, A.; Uitdehaag, B. M. J.; Giuliani, G.; Pucci, E.; Taus, C. *Cochrane Database Syst. Rev*. 2002, (4).