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Mesoionic Compounds

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History of Mesoionic Compounds

The history of Mesoionic compounds is quite extensive going back over a hundred years ago. Mesoionic compounds began to be developed beginning in the late 1800th century. Although the term mesoionic had yet to be used, a mesoionic compound, benzothazole, had been described in 1879. [2] Other mesoionic compounds were created between 1879 and when the term mesoionic was first used. The compounds produced during this time puzzled the chemist who produced them. Some of the compounds produced before were: 1,3,4-thiadiazolium-2-thiolate prepared by Busch in 1895 and 1,2,3,4-tetrazolium-5-thiolate, or dehydrodithizone, prepared by the chemists Fischer and Besthorn in 1882.[2][6] Around sixty years later the compound which would eventually lead to the modern day group of mesoionic compounds was created. A fused ring structure was suggest for a compound prepared in 1935 by two chemists Earl and Mackney which they called a "Sydnone." [2] The newly created Sydnone was considered to be a type of Lactone, however, in 1949 two other chemists, Baker and Ollis disagreed because the properties of the Sydnone did not match that of a lactone.[2][6][4] A definition for the type of compounds like Sydnones was first presented by Baker and Ollis the same year. The term mesoionic though was not introduced right away and is debated as to who was the first to coin the term. It, Mesoionic, has been attributed to multiple chemists: Baker, Ollis, Poole, and Simpson. [1][4][6][2]

1. The University of Sydney where the first Sydnone was produced

Uses of Mesoionic Compounds

Mesoionic compounds can be used for a variety of purposes even being used in areas outside the medical environment. Still, the overwhelming area that mesoionic compounds have been beneficial to has been the medical field. In the medicinal field, mesoionic compounds are used as drugs as antibacterial, antimalarial, anti-inflammatory, antitumor, antifungal, analgesic, and many more.[2] Most of the biological activity of mesoionic compounds are found in type A compounds while none have been found in type B compounds.[6][1] In many cases mesoionic compounds not only contain one medicinal, biological property, but also include another as well.[1] Another important aspect to the medical field is using mesoionic compounds as dyes. The sydnone ring specifically is very good at absorbing invisible spectra of ultraviolet and infrared light. [5][2] Mesoionic compounds are really useful not only for medicinal value, but because they are natural occurring being found in many other products. Some other products include vitamins such as vitamin B_1 contain a mesoionic group. [2] A couple other products which contain mesoionic compounds are insecticides, herbicides, and even some teas.[2] Mesoionic compounds have also been used to make elastomeric polymers, in the paper industry, and tire industry.[2]

Pictures of some uses of mesoionic compounds (2-3)

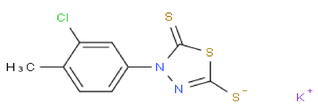
MESOIONIC COMPOUNDS

By Mark Gordon

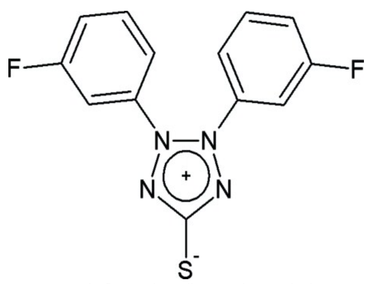
Mentor: Dr. Douglas Armstrong

What is a Mesoionic Compound?

A mesoionic compound is a type of organic heterocyclic compound. Heterocyclic compounds are ring organic molecules containing other elements in ring structure besides just carbon. Some of the elements found in heterocyclic compounds include sulfur, oxygen, or nitrogen, and sometimes some heavier elements such as selenium and tellurium. [2][5][6] Besides being a heterocyclic compound, mesoionic compounds are also a subclass of the type of compounds called betaines.[2] Currently there are two popular proposed definitions of mesoionic compounds. In one definition, mesoionic compounds are classified as five-membered heterocycles that cannot be structurally represented any opne covalent or polar structure and have a sextet of electrons with the five atoms comprising the ring.[3] The other definition is less restrictive and includes heterocyclic compounds comprising of six atoms. Six member rings are sometimes excluded because they can easily be associated with mesoionic betaines which are slightly different than true mesoionic compounds. [6] Mesoionic compounds are also commonly held to be aromatic upholding Hückel's Rule. The sextet of pi elections found in mesionic compounds, the ability to undergo electrophilic substitution, and the delocalization of the positive charge in the sydnone ring are used as evidence for aromaticity. [4] In fact in all examples of mesoionic compounds, the sydnone ring structure is the most important part of the compound. [1] The delocalized positive charge is located on the members of ring, while the negative charge is likewise delocalized.[2] The negative charge in mesoionic is typically located on an exocyclic atom, therefore balancing the positive charge on the ring.[4] The last major aspect to mesoionic compounds is the division of sydnones into two classes. The two classes of sydnones are split up based on the location of electrons respectively called type A and type B. [6] [3]



10. 1,3,4-thiadiazole-2-thiolate
Type A

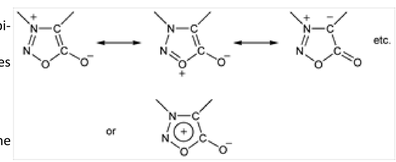


11. 2,3-Bis(3-fluoro-phen-yl)tetra-zolium-5-thiol-ate
Type B

Common Mesoionic Compounds

Sydnones:

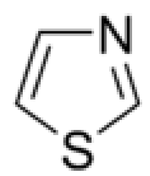
Sydnones are considered the building block for all other mesoionic compounds. Besides being the building block for all other mesoionic compounds, the physical characteristics of sydnones make them advantageous to the medicinal world. Sydnones are small, planar, and overall neutral. Such characteristics are a couple of the reasons why sydnones show promise in a variety of types of drugs. A specific reason is the overall neutrality of the molecule to pass through certain membranes other drugs cannot pass through. There are various methods to produce sydnones, but the most common method requires two steps: N-nitrosation followed by cyclohydration. The process uses the cyclodehydration of N-substituted-N-nitroso-amino acids with an anhydride like acetic anhydride. The product of the mesoionic compound is typically a crystalline solid at room temperature , but some alkylated sydnones sometimes can be a liquid .[1][7][2]



5. General structure of a Sydnone

Thiazoles:

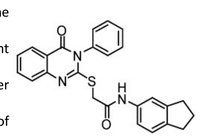
Thiazoles are mesoionic compounds that contain a sulfur atom in the sydnone ring. Many of the thiazoles are naturally occurring and constitute one of the most studied groups of mesoionic compounds after sydnones. In the medical field, thiazoles are the bases for sulfa drugs which have been widely used worldwide. Along with being used in sulfa drugs, thiazololium salts have been used as dyes, fungicides, discovered to have antioxidant characteristics, and used in the production of rubber products. A majority of the Thiazoles have been used to develop drugs and will continue to be one of the key building blocks for future drugs. [2]



7. Basic Thiazole ring

Quinazolines:

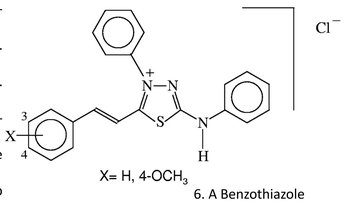
Quinazolines, until the 1960s, had not been studied much and the biological benefits were unknown. After the 1960s, the importance of quinazoline was discovered with the extraction of one of its derivatives from the Chinese plant "chan-shan." The derivative proved to be a good antimalarial agent, but was too toxic for human consumption. Further investigation brought about the discovery of the desired antimalrial compound. The structure of quinazolines consists of two fused six member simple aromatic rings. Relative ease of synthesis, availability of its derivatives, and multiple biological characteristics will continue to attract future chemists. [2]



8. Quinazolines

Benzothiazoles:

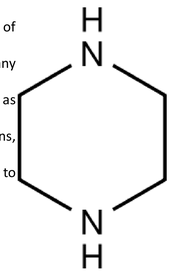
When thiazoles are fused with a benzene derivative, the compound is called a Benzothiazole. Such compounds are specialized products and most commonly are synthetic compounds. The combination of a thiazole with a benzene derivative results in a quite stable compound. Many such fused mesoionic compounds have been used in a variety of areas including herbicides, the paper industry as slimicides, and in special types of photography. The ability to be used not only as a medicinal agent but also in many other industrial areas will work to keep chemist looking to discover new ways to use Benzothiazoles.[2]



6. A Benzothiazole

Piperazine:

Piperazine is a mesoionic compound consisting of a six member ring with two opposite nitrogen atoms. The development of piperazine was originally intended only for the treatment of gout. It was not effective as a drug against gout because of many adverse side-effects. Later derivatives of piperazine resulted in many of the already mentioned medicinal characteristics such as anticancer and antidepressants. Like benzothiazoles, piperazines are widely used in other industries to make plastics, resins, brake fluid, and other materials. Another negative to this mesoionic compound is that its popularity is due also to the ability to abuse its effects which are not quite as potent as other illicit drugs. [2]



9. Basic Piperazine Ring Structure

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Picture Citations

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