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Article

Pyrimidine

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Abstract

Purines and pyrimidines are two of the building blocks of nucleic acids. Only two purines andthree pyrimidines occur widely in nucleic acids.

Key words: Purines, pyrimidines, nucleic acids, 2, 4, 6-trichloropyrimidine, 2-aminopyrimidines.

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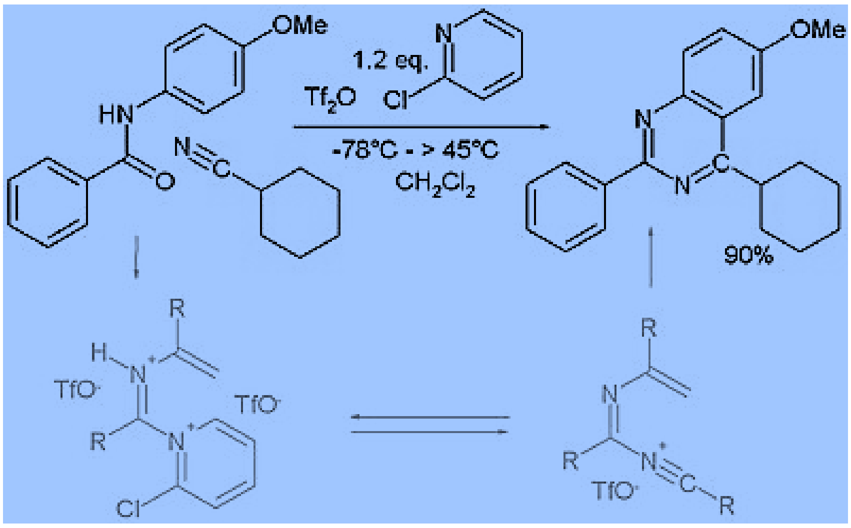
Pyrimidine is an aromatic heterocyclic organic compound similar to pyridine. [1][2] One of the three diazines (six-membered heterocyclics with two nitrogen atoms in the ring), it has the nitrogens at posi- tions 1 and 3 in the ring.[3] The other diazines are pyrazine (nitrogens 1 and 4) and pyridazine (nitrogens 1 and 2). In nucleic acids, three types of nucleobases are pyrimidine derivatives: cytosine (C), thymine (T), and uracil (U).

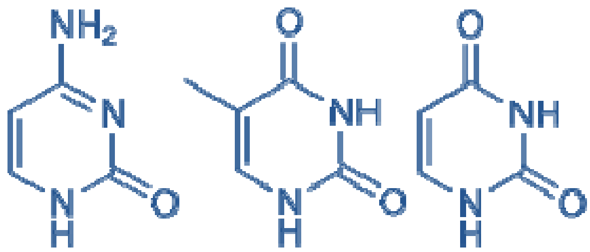
The pyrimidine ring system has wide occurrence in nature[4] as substituted and ring fused com- pounds and derivatives, including the nucleotides, thiamine (vitaminB1) and alloxan. It is also found in many synthetic compounds such as barbiturates and the HIV drug, zidovudine. Although pyrimidine de- rivatives such as uric acid and alloxan were known in the early 19th century, a laboratory synthesis of a pyrimidine was not carried out until 1879,[4]when Grimaux reported the preparation of barbituric ac- idfrom Ivy ure and malonic acid in the presence ofphosphorus oxychloride.[5] The systematic study of pyrimidines began[6] in 1884 with Pinner,[7] who synthesized derivatives by condensing ethyl acetoace- tate with amidines. Pinner first proposed the name “pyrimidin” in 1885.[8] The parent compound was firstprepared by Gabriel & Colman in 1900,[9] [10] by conversion of barbituric acid to 2,4,6- trichloropyrimidine followed by reduction using zinc dust in hot water.

As is often the case with parent heterocyclic ring systems, the synthesis of pyrimidine is not that common and is usually performed by removing functional groups from derivatives. Primary syntheses in quantity involving formamide have been reported.[11]

Reaction of the former with amidines to give 2-substituted pyrimidines, with urea to give 2- pyrimidiones, and guanidines to give 2-aminopyrimidines are typical.[12] Pyrimidines can be prepared via the Biginelli reaction. Many other methods rely on condensation of carbonyls with diamines for instance the synthesis of 2-Thio-6-methyluracil from thiourea and ethyl acetoacetate [13] or the synthesis of 4-methylpyrimidine with 4,4-dimethoxy-2-butanone and formamide.[14] A novel method is by reaction of certain amides with carbonitriles under electrophilic activation of the amide with 2-chloro-pyridine and trifluoromethanesulfonic anhydride:[15]



Three nucleobases found in nucleic acids, cytosine (C), thymine (T), and uracil(U), are pyrimidine derivatives:



Cytosine (C) Thymine (T) Uracil (U)

In DNA and RNA, these bases form hydrogen bonds with their complementarypurines. Thus, in DNA, the purines adenine (A) and guanine (G) pair up with the pyrimidines thymine (T) and cytosine(C), respectively. In RNA, the complement of adenine (A) is uracil (U) instead of thymine (T), so the pairs that form are adenine:uracil and guanine:cytosine. Very rarely, thymine can appear in RNA, or ura- cil in DNA. Other than the three major pyrimidine bases presented, some minor pyrimidine bases can also occur in nucleic acids. These minor pyrimidines are usually methylatedversions of major ones and are postulated to have regulatory functions.[21]

These hydrogen bonding modes are for classical Watson-Crick base pairing. Other hydrogen bond-ing modes ("wobble pairings") are available in both DNA and RNA, although the additional 2'-hydroxyl group of RNA expands the configurations, through which RNA can form hydrogen bonds.

In March 2015, NASA Ames scientists reported that, for the first time, complex DNA and RNA organic compounds of life, including uracil, cytosine and thymine, have been formed in the laboratory under outer space conditions, using starting chemicals, such as pyrimidine, found in meteorites. Pyrimidine, like polycyclic aromatic hydrocarbons (PAHs), the most carbon-rich chemical found in the Universe, may have been formed in red giants or in interstellar dust and gasclouds, according to the scientists.[22][23][24]

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