

B.Sc Sem – IV
Chemistry Honours
Paper : SEC – 2
Pharmaceutical Chemistry
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Zidovudine (AZT)

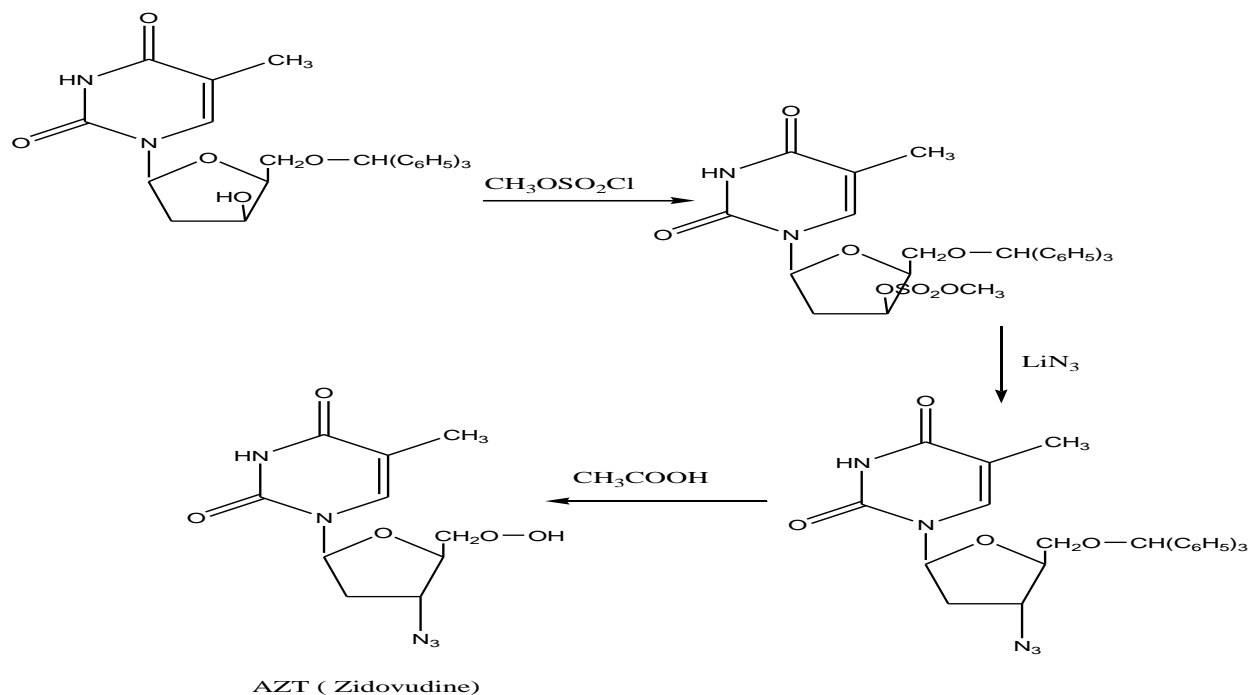
Zidovudine (ZDV), also known as **azidothymidine (AZT)**, is an antiretroviral medication used to prevent and treat HIV/AIDS. It is generally recommended for use with other antiretrovirals. It may be used to prevent mother-to-child spread during birth or after a needlestick injury or other potential exposure. It is sold both by itself and together as lamivudine/zidovudine and abacavir/lamivudine/zidovudine. It can be used by mouth or by slow injection into a vein.

AZT crystallizes into an asymmetric nucleated monoclinic salt structure, forming an equalized hydrogen-nitrogen-oxygen bonded network of base-paired dimers; its multiscaled crystallized lattice superstructure and surfactant headgroup electrostatic bond polarity was reported in 1988 and 1987

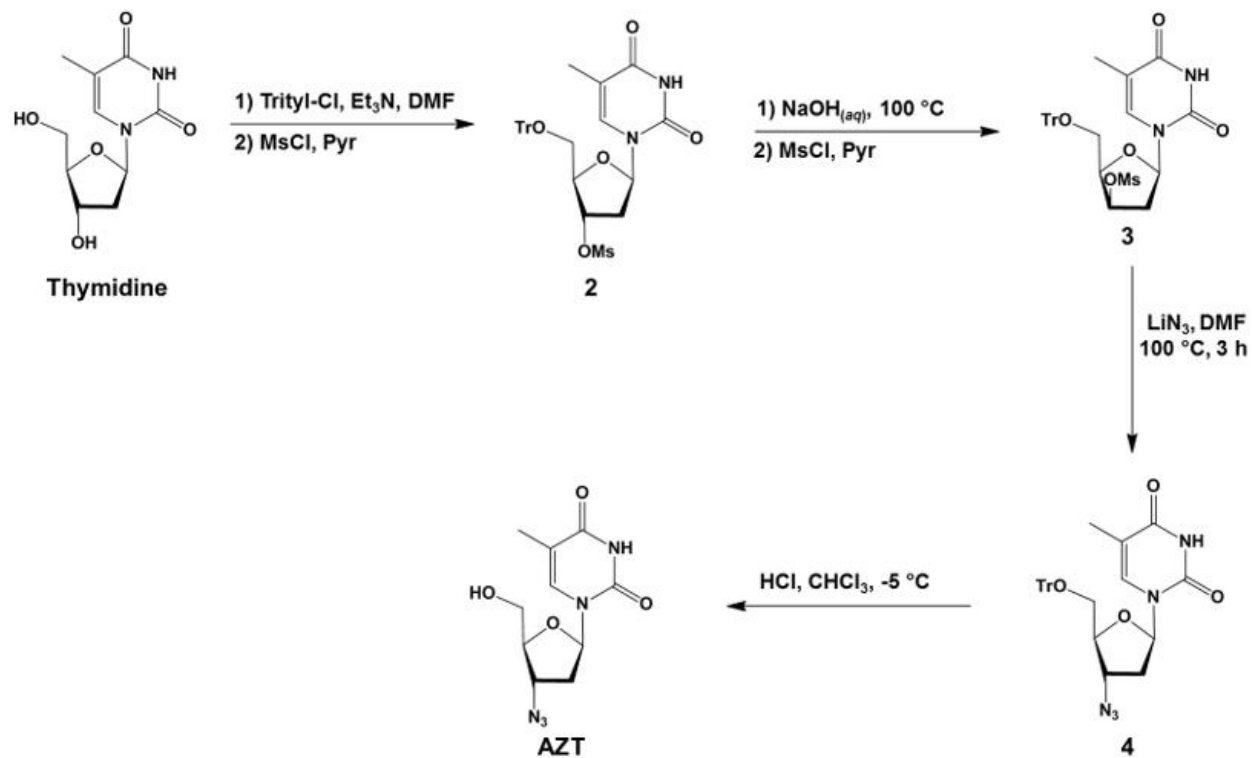
Synthesis

Zidovudine is 3'-azido-3'-deoxythymidine, is **synthesized** from 1-(2'-deoxy-5'-O-trityl-β-d-lyxosyl)thymine, which is treated with methanesulfonyl chloride in pyridine to make the corresponding mesylate. Heating this in 80% acetic acid removes the trityl protection, giving **zidovudine**.

Method - 1



Method – 2



Medical uses

HIV treatment

AZT is usually dosed twice a day in combination with other antiretroviral therapies. This approach is referred to as Highly Active Antiretroviral Therapy (HAART) and is used to prevent the likelihood of HIV resistance.

HIV prevention

AZT has been used for post-exposure prophylaxis (PEP) in combination with another antiretroviral drug called lamivudine. Together they work to substantially reduce the risk of HIV infection following the first single exposure to the virus. More recently, AZT has been replaced by other antiretrovirals such as tenofovir to provide PEP.

Side effects

Most common side-effects include nausea, vomiting, acid reflux (heartburn), headache, cosmetic reduction in abdominal body fat, light sleeping, and loss of appetite. Less common side effects include faint discoloration of fingernails and toenails, mood elevation, occasional tingling or transient numbness of the hands or feet, and minor skin discoloration. Allergic reactions are rare.

Mechanism of action

AZT in oral, injectable, and suppository form

AZT is a thymidine analogue. AZT works by selectively inhibiting HIV's reverse transcriptase, the enzyme that the virus uses to make a DNA copy of its RNA. Reverse transcription is necessary for production of HIV's double-stranded DNA, which would be subsequently integrated into the genetic material of the infected cell (where it is called a provirus).

Cellular enzymes convert AZT into the effective 5'-triphosphate form. Studies have shown that the termination of HIV's forming DNA chains is the specific factor in the inhibitory effect.

At very high doses, AZT's triphosphate form may also inhibit DNA polymerase used by human cells to undergo cell division, but regardless of dosage AZT has an approximately 100-fold greater affinity for HIV's reverse transcriptase. The selectivity has been suggested to be due to the cell's ability to quickly repair its own DNA chain if it is disrupted by AZT during its formation, whereas the HIV virus lacks that ability.¹ Thus AZT inhibits HIV replication without affecting the function of uninfected cells. At sufficiently high dosages, AZT begins to inhibit the cellular DNA polymerase used by mitochondria to replicate, accounting for its potentially toxic but reversible effects on cardiac and skeletal muscles, causing myositis.

Mechanism of action

AZT works by selectively inhibiting HIV's reverse transcriptase, the enzyme that the virus uses to make a DNA copy of its RNA.

What is AZT used for?

AZT, in full azidothymidine, also called zidovudine, drug **used to** delay development of AIDS (acquired immunodeficiency syndrome) in patients infected with HIV (human immunodeficiency virus). **AZT** belongs to a group of drugs known as nucleoside reverse transcriptase inhibitors (NRTIs).

What class of drug is zidovudine?

Zidovudine belongs to a class of drugs known as nucleoside **reverse transcriptase inhibitors-NRTIs**.