Urinary Tract Anti Infective Agent

Presented By:-

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Specialization - Pharmaceutical Chemistry

Urinary Tract Anti Infective Agent

- A **Urinary Tract Anti-Infective Agent** is any **drug or substance specifically used to treat infections of the urinary tract** (bladder, urethra, ureters, and kidneys).
- These agents help kill or inhibit the growth of bacteria that cause **urinary tract infections (UTIs)**.

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Classification;-Urinary Tract Anti Infective Agent

1. **Sulfonamides**
   - **Mechanism:-**These are synthetic bacteriostatic agents that inhibit bacterial growth by interfering with folate synthesis, a crucial process for bacterial cell division.
   - **Examples include** sulfadiazine, sulfathiazole, and sulfacetamide.
2. **Quinolones**
   - **Mechanism:-** These are bactericidal agents that disrupt bacterial DNA replication by inhibiting DNA gyrase and topoisomerase IV.
   - **First-generation quinolones:** Nalidixic acid, Cinoxacin.
   - **Second-generation quinolones:** Norfloxacin, Ciprofloxacin, Ofloxacin, Levofloxacin, Lomefloxacin, Gatifloxacin, Sparfloxacin, Balofloxacin, Enoxacin.
3. **Nitrofurans**
   - **Mechanism:-** These agents are converted into active metabolites within bacteria, which then interfere with several metabolic processes, including DNA replication and protein synthesis.
   - **Examples include** Nitrofurazone, Furazolidone, and Nitrofurantoin.

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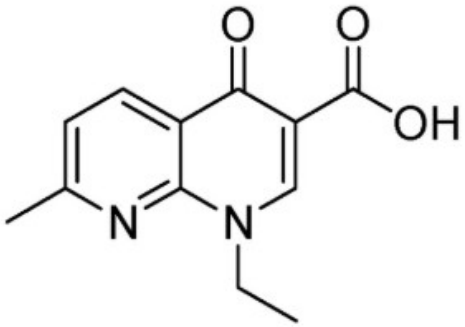
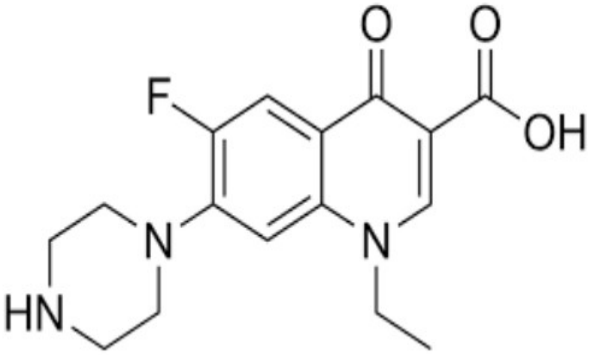
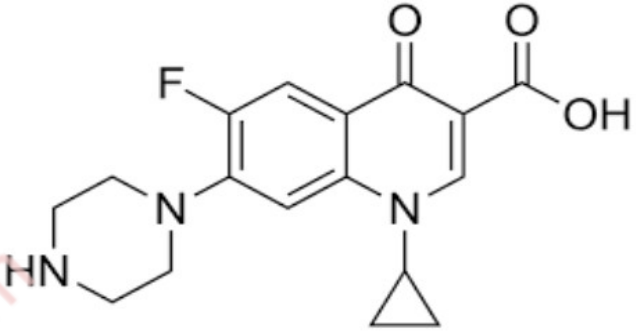


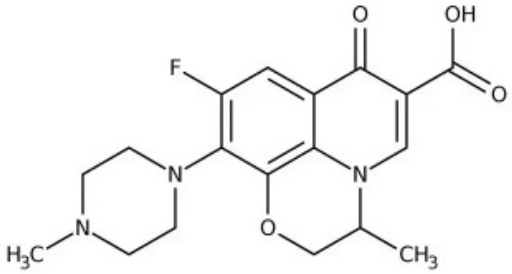
Nalidixic acid



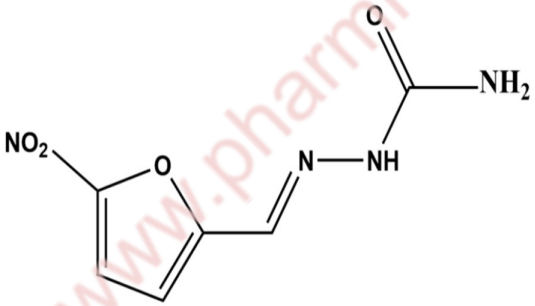
Norfloxacin



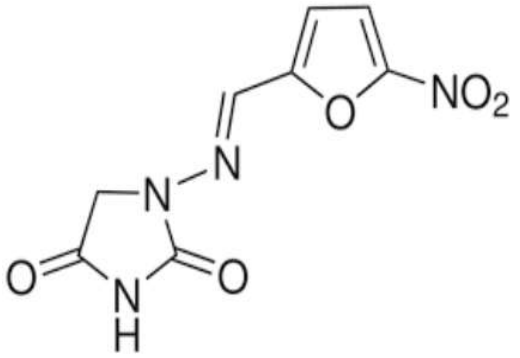
Ciprofloxacin



Ofloxacin



Nitrofurazone



Nitrofurantoin

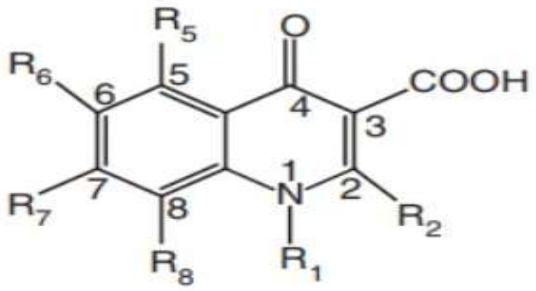
Quinolones

- **Quinolones** are a class of **synthetic antibacterial drugs** that are widely used to treat a variety of infections caused by bacteria.
- They are especially effective against **Gram-negative bacteria**, and some newer versions (like fluoroquinolones) also have strong activity against **Gram-positive bacteria**.

MOA:-

Quinolones specifically target and inhibit bacterial DNA gyrase and topoisomerase IV, which are crucial for DNA replication and supercoiling.

SAR of Quinolones



1. **N-1 substituent:** Substitutions at the N-1 position can impact the stability, solubility, and absorption of the quinolone.
2. **Carboxyl group at position 3:** This group is essential for the antibacterial activity of quinolones.
3. **Keto group at position 4:** This group is also crucial for the antibacterial activity of quinolones.
4. **Fluorine at position 6:** Adding a fluorine atom at the 6-position (creating a fluoroquinolone) significantly enhances antimicrobial activity and potency.
5. **Substituent at C-7:** Modifications at this position can influence the spectrum of activity and pharmacokinetic properties.

Nalidixic Acid, Norfloxacin, Enoxacin, Ciprofloxacin*, Ofloxacin, Lomefloxacin, Sparfloxacin, Gatifloxacin, Moxifloxacin

Note:- All drugs MOA and uses are mostly common.

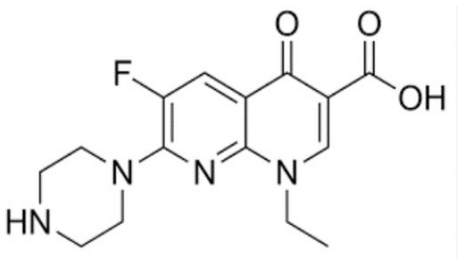
MOA:-

Inhibits **bacterial DNA gyrase** → prevents DNA supercoiling → halts DNA replication and transcription → **bacterial death**.

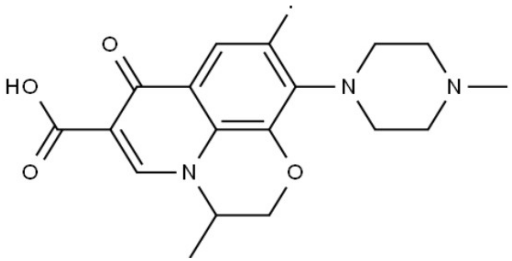
Uses:-

1. **It** used primarily to treat **urinary tract infections (UTIs)**, **prostatitis**, and **gastrointestinal infections** caused by susceptible bacteria.
2. It used to treat a wide range of **bacterial infections**, especially those involving the **respiratory tract**, **skin**, **eyes**, and **abdomen**.

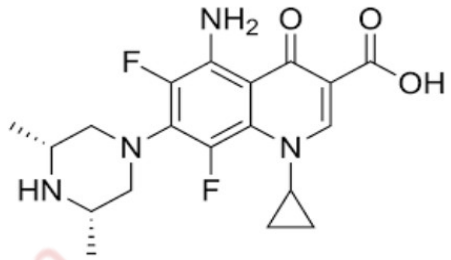
Structure:- On next page.



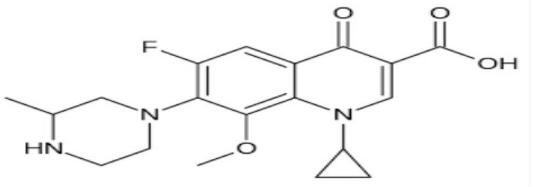
Enoxacin



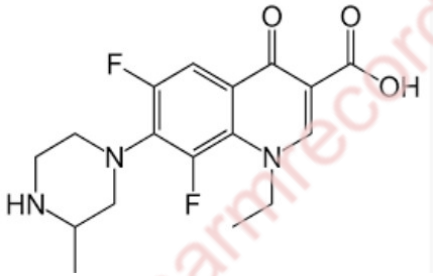
Ofloxacin



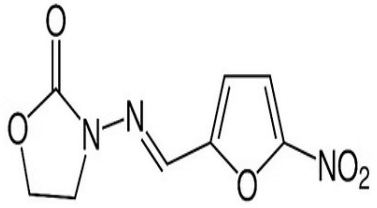
Sparfloxacin



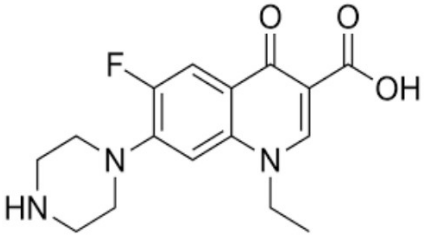
Gatifloxacin



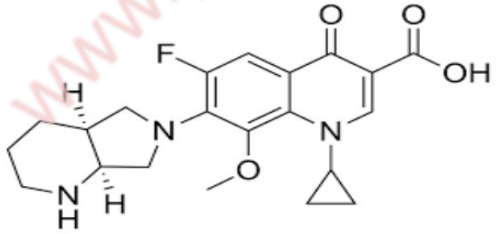
Lomefloxacin



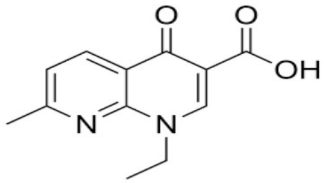
Furazolidine



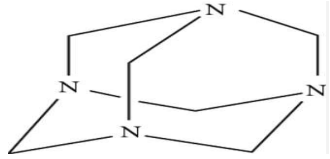
Norfloxacin



Moxifloxacin



Nalidixic Acid



Methylamine

Ciprofloxacin

Ciprofloxacin is a **second-generation** antibiotic.

It's used to treat **urinary tract infections (UTIs)** and chest infections (including pneumonia) skin and bone infections.

MOA:- Inhibits **bacterial DNA gyrase** → prevents DNA supercoiling → halts DNA replication and transcription → **bacterial death**.

Synthesis of Ciprofloxacin

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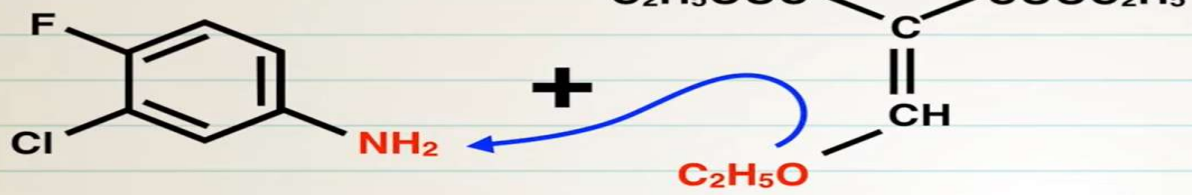
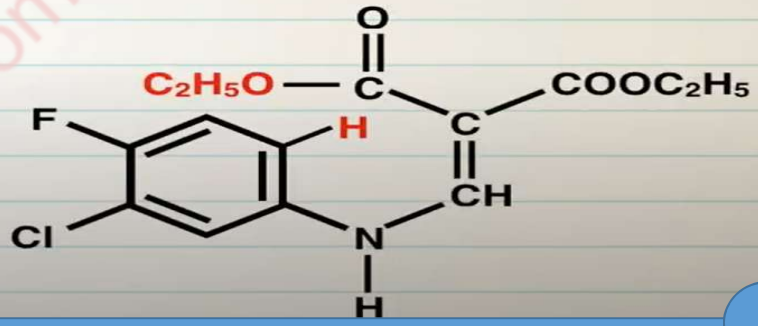
Step-I



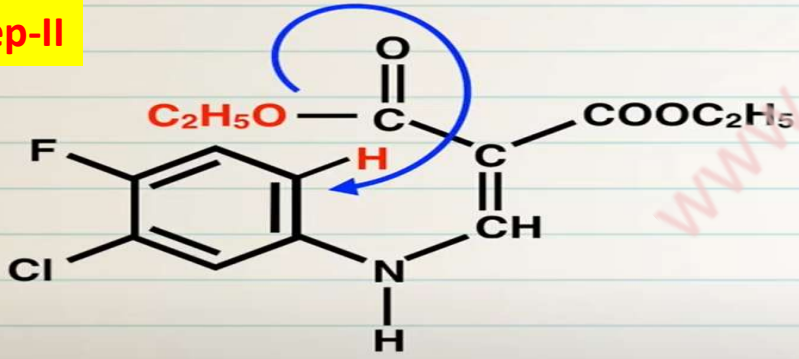
— C_2H_5OH

3 - chloro 4 - Fluoro aniline

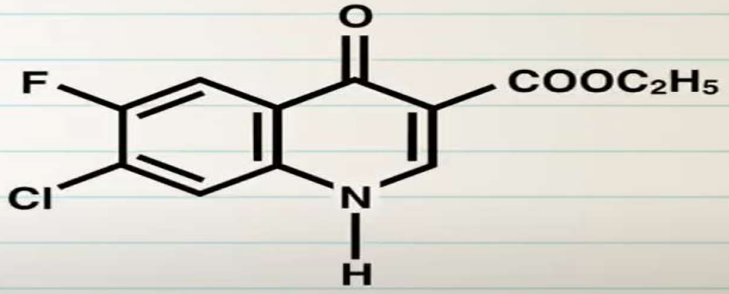
Diethyl ethoxymethylene malonate



Step-II

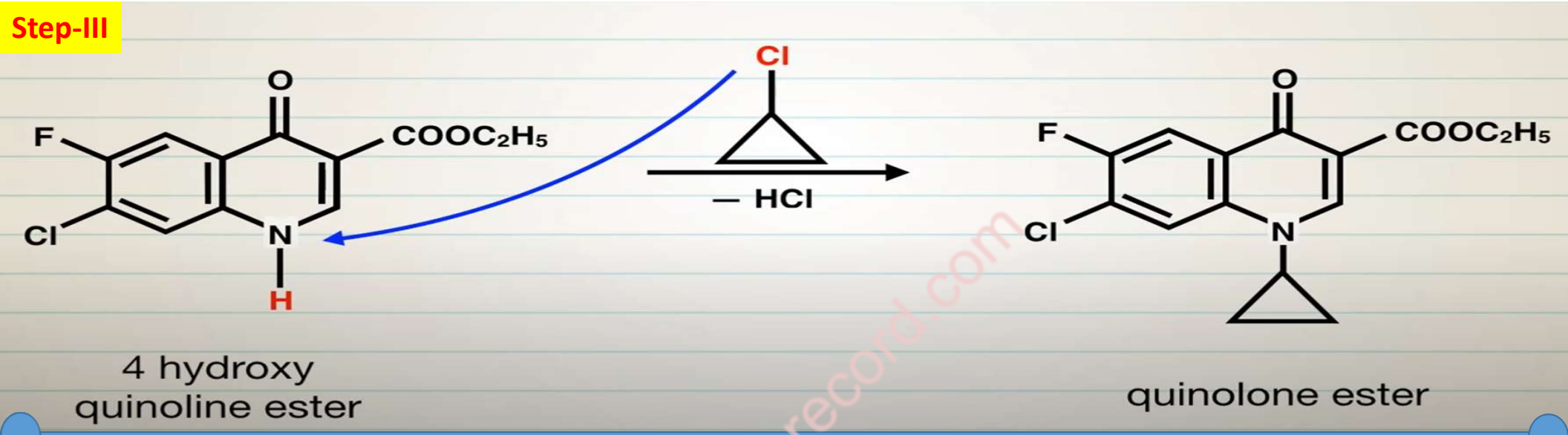


$\xrightarrow[-\ C_2H_5OH]{\triangle}$



4 hydroxy quinoline ester

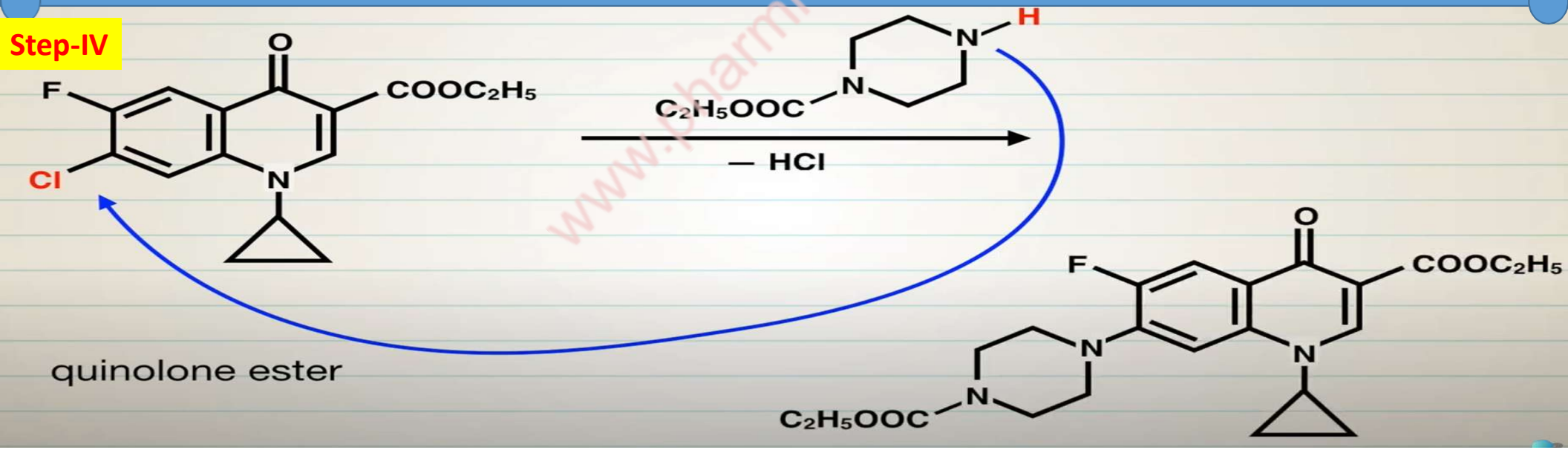
Step-III



4 hydroxy quinoline ester

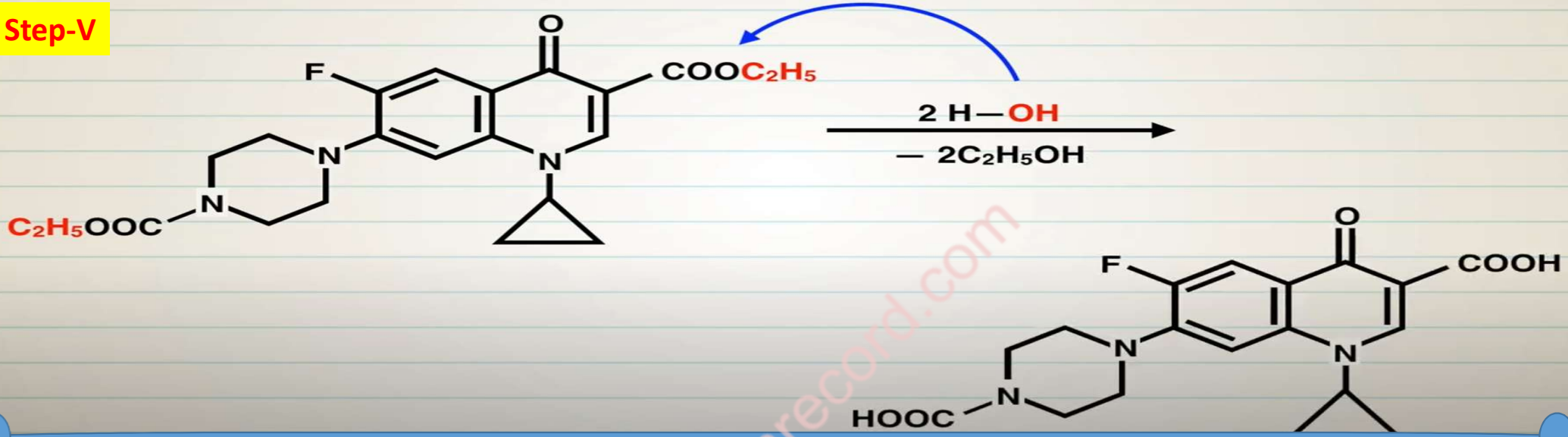
quinolone ester

Step-IV

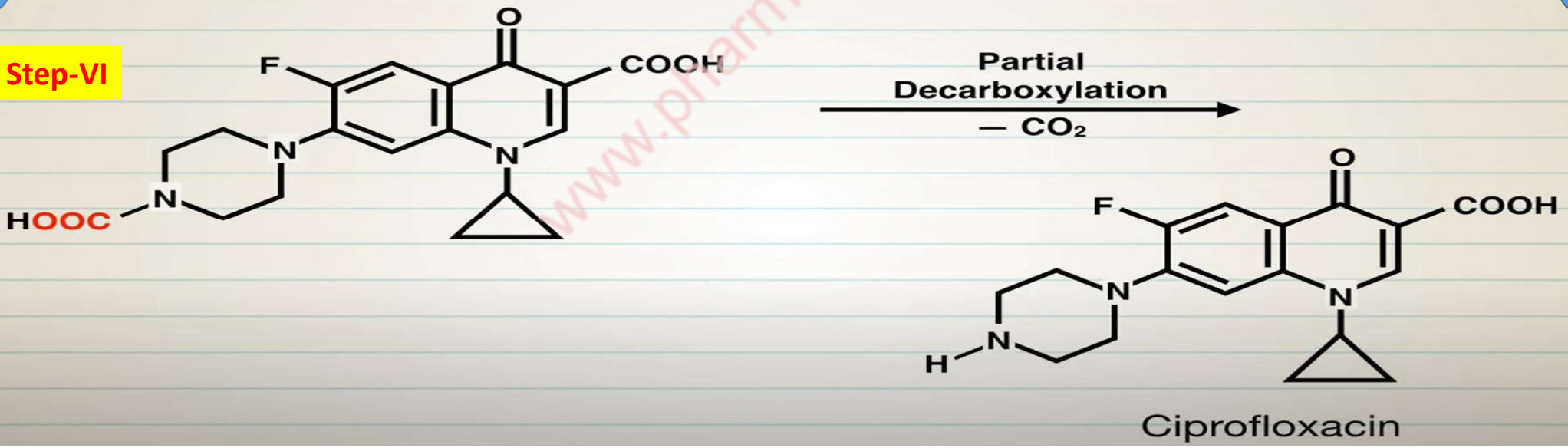


quinolone ester

Step-V



Step-VI



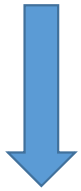
Ciprofloxacin

Nitrofurantoin

Nitrofurantoin is an **antibiotic** that is mainly used to treat **urinary tract infections (UTIs)**.

MOA:-Nitrofurantoin is converted by bacterial nitroreductases to electrophilic intermediates which inhibit the citric acid cycle as well as synthesis of DNA, RNA, and protein.

Synthesis of Nitrofurantoin



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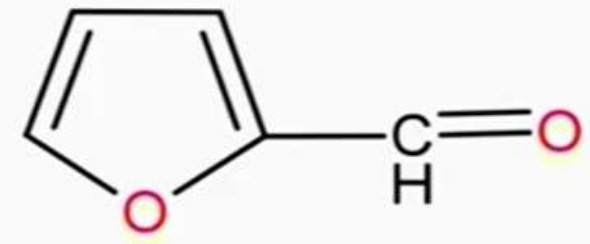
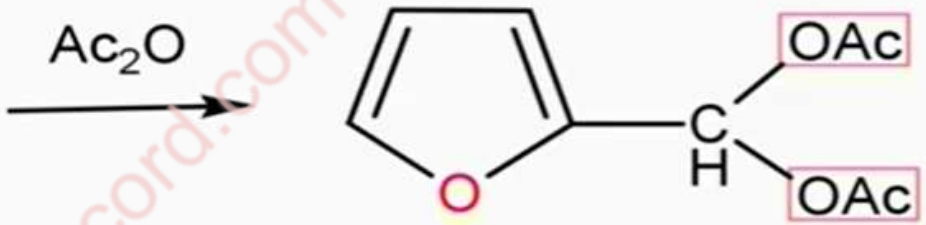
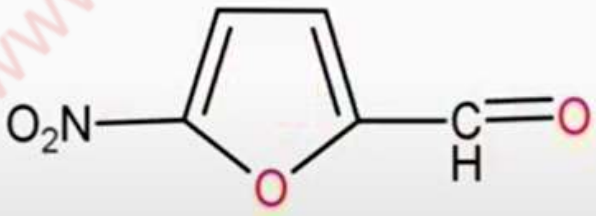
Step:-I Synthesis of nitro furfuraldehyde



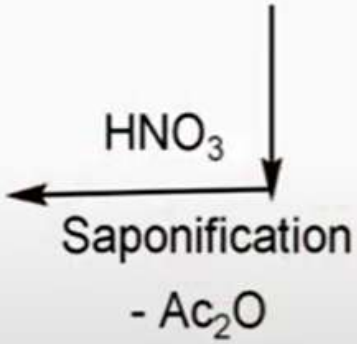
Furan-2-carbaldehyde

(2-Furfuraldehyde)

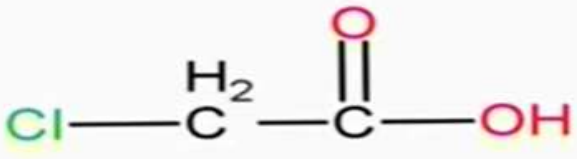




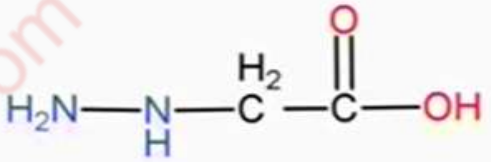
5-nitrofuran-2-carbaldehyde



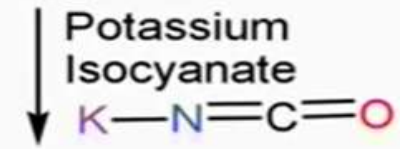
Step:-II Synthesis of Hydantoin Derv.

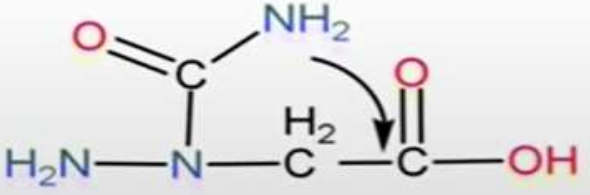


2-chloroacetic acid

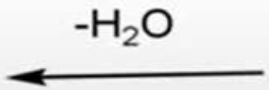


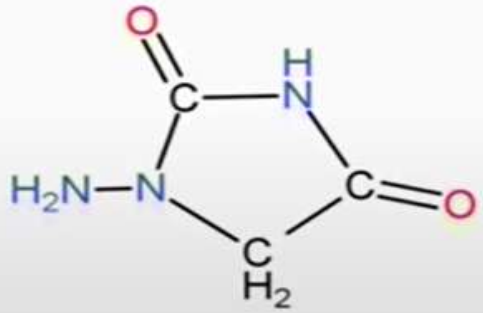
2-hydrazinylacetic acid





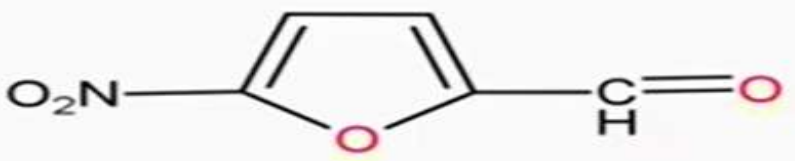
2-(1-carbamoylhydrazin-1-yl)
acetic acid





1-aminoimidazolidine-2,4-dione

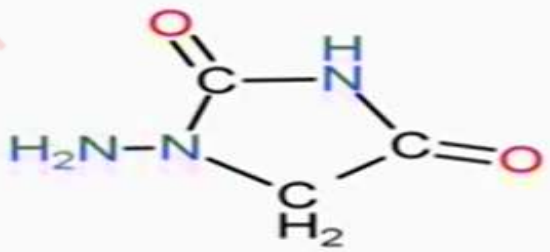
Step:-III Synthesis of nitrofurantoin



5-nitrofuran-2-carbaldehyde

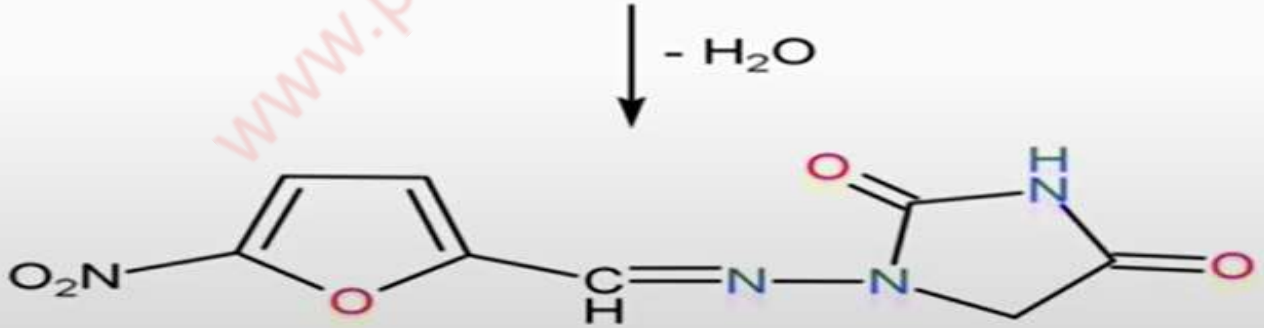
Step-I Product

+



1-aminoimidazolidine-2,4-dione

Step-II Product



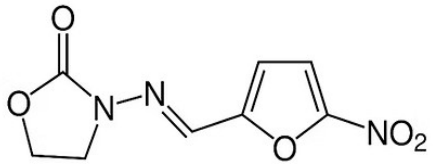
NITROFURANTOIN

Furazolidine

Methanamine

MOA:-

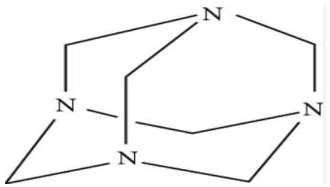
Nitrofurantoin is converted by bacterial nitroreductases to electrophilic intermediates which inhibit the citric acid cycle as well as synthesis of DNA, RNA, and protein.



Furazolidine

Furazolidine is used to treat bacterial and protozoal infections.

It was used primarily to treat gastrointestinal infections such as:-Bacterial dysentery, Traveler's diarrhea, Giardiasis, Urinary tract infections.



Methylamine

It's a simple organic compound.

Methenamine used for the prevention of urinary tract infections (UTIs)

Thank You