Drug Synthesis الاصطناع (التخليق) الدوائي

13. Diphenylmethanes Derivatives

Synthesis of anti-histamininic aminoalkyl ethers: diphenhydramine and Clemastine

• They are prepared by wiliamson synthesis

$$CH - O - CH_2CH_2N(CH_3)_2$$

$$CI - CH_2CH_2 - CH_2CH_2$$

$$CH_3 - CH_3$$

Clemastine

Diphenhydramine

Synthesis of anti-histamininic diphenhydramine

Diphenhydramine

2- diphenylmethoxy-*N,N*-dimethylethylamine

Synthesis of anti-histamininic Clemastine

$$CI$$
 CH_3
 CH_3
 CH_3
 CH_3
 CH_3
 CH_3
 CH_3
 CH_3
 CH_3

Clemastine

(RR) 2-[2-[1-(4- chlorophenyl)-1- phenylethoxy]ethyl]-1-methylpyrrolidine

Synthesis of muscle relaxant Orphenadrine



Drug Synthesis الاصطناع (التخليق) الدوائي

14. Phenol and Benzoic acid derivatives

Phenol derivatives

Anti-Fever Analgesic paracetamol

P-Aminophenol

Paracetamol

Synthesis of Paracetamol from p-aminophenol

$$\begin{array}{c|c} & & & & & & & \\ & NH - C - CH_3 \\ \hline \\ OH \\ \hline \\ p-aminophenol \\ \end{array}$$

Synthesis of Intermediate, p-aminophenol from chlorobenzene

Action and use of Paracetamol

- Analgesic ,fever reducing
- · Devoid of anti-inflammatory and anti-rheumatic properties

Benzoic acid derivatives

- Orthohydroxybenzoic acid (salicylic acid) derivatives: Aspirin, Diflunisal
- p-aminobenzoic acid derivatives: Procaine...
- o-aminobenzoic acid (anthranilic acid) derivatives:mefenamic acid.....

Salicylic acid

Benzoic acid

Salicylic acid (o-hydroxybenzoic acid)

Salicylic acid derivatives

Acetylsalicylic acid (Aspirin)

Diflunisal

Synthesis of Aspirin

Synthesis of Diflunisal

$$F \longrightarrow F \longrightarrow F \longrightarrow F$$

$$CO_2/HO \longrightarrow F \longrightarrow F$$

$$COOH$$

Diflunisal

2',4'-difluoro-4-hydroxy-3-biphenylcarboxylic acid

Action and use of Diflunisal

- Analgesic, fever reducing and has anti-inflammatory action
- It is used in rhematoid arthritis, osteoarthritis...
- Synonym for this drug: dolobid

Synthesis of p-aminobenzoic acid derivatives

- Local anesthetic Procaine
- Topical anesthetic Benzocaine
- Antiarrythmic Procainamide
- Anti-emetic Metoclopramide

p-Aminobenzoic acid derivatives

p-aminobenzoic acid

Pracainamide

Metoclopramide

Synthesis of procaine starting from p-nitrobenzoic acid

COOCH₂CH₂N(C₂H₅)₂

$$\begin{array}{c}
COOCH_2CH_2N(C_2H_5)_2\\
\hline
NO_2\\
\hline
NO_2\\
\hline
H_2/Ni\\
\hline
NH_2
\end{array}$$
COOCH₂CH₂N(C₂H₅)₂

Synthesis of topical anesthetic Benzocaine

1- From p-aminobenzoic acid