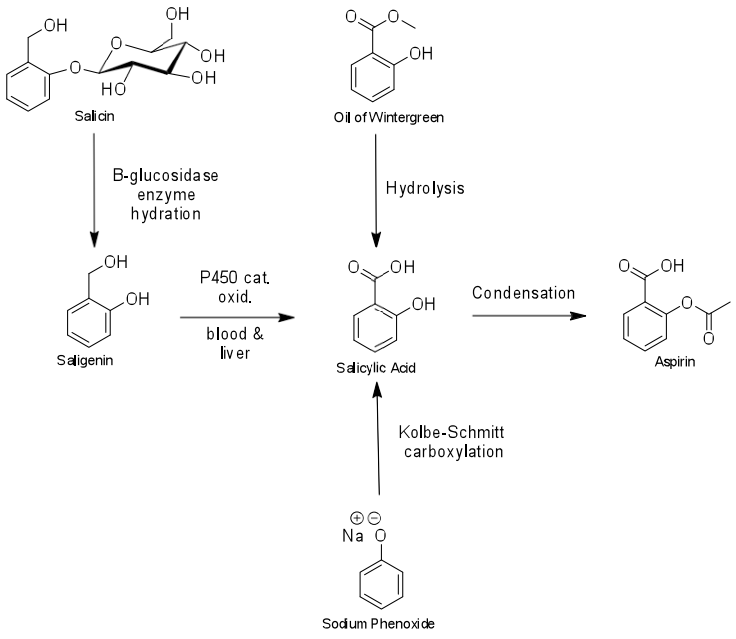
Aspirin Analogs of Medicine

Introduction

A. General History of Painkillers

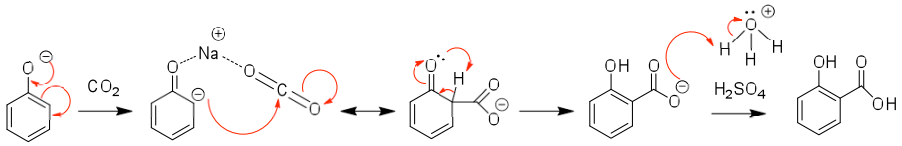
B. General History of Aspirin

Aspirin, also known as acetylsalicylic acid, is a member of a group of drugs known as non-steroidal anti-inflammatory drugs or NSAIDs.[1] The pain-killing characteristics of salicylic acid, the naturally occurring form of the drug, were first observed in willow bark.[2] The first company to synthesize acetylsalicylic acid was Bayer in 1897 and the term "aspirin" was not coined until 1899.[2] The mechanism by which aspirin reduces pain is the disruption of the enzyme known as cyclooxygenase or COX.[1] COX is responsible for synthesizing prostaglandins in response to pain signals which will cause the affected area of the body to become inflamed.[3] Although very effective at stopping pain via blocked prostaglandin synthesis, aspirin can also have a negative side effect of stomach toxicity which may lead to gastritis, peptic ulcers, and gastrointestinal hemorrhages.[1] One way aspirin can be synthesized easily is by taking oil of wintergreen and performing a two step synthesis including a hydrolysis and a condensation reaction (Scheme 1).[4]



Scheme 1. Various methods of synthesizing aspirin.

The overall Kolbe-Schmitt carboxylation combines a phenoxide ion with a carbon dioxide under high temperature and pressure to form ortho-substitued aromatic ring. In the particular case of aspirin, sodium phenoxide is reacted under these conditions to form salicylic acid (Scheme 2), the precursor to aspirin. In the first part of the Kolbe-Schmitt carboxylation, the phenoxide ion acts as a nucleophile and attacks the electrophilic carbon of carbon dioxide. The two compounds are brought into close proximity by aggregation with sodium ion and the aggregate's geometry leads to regiospecific attack in the ortho-position of the arene. The intermediate this formed lacks aromaticity and tautomerization restores aromaticity. Protonation afford the free acid.



Scheme 2. Kolbe-Schmitt carboxylation mechanism.
This reaction is performed at 125°C and 100 atm.

C. General History of Aspirin Analogs

Materials and Methods

Results

Discussion

Conclusion

References

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