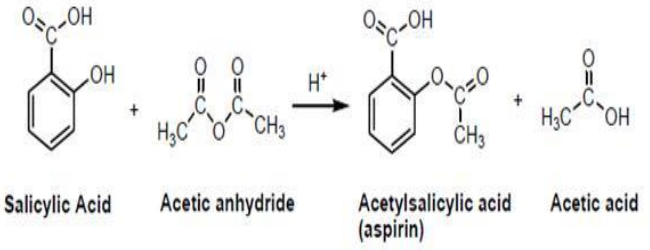
Pharmaceutical Chemistry

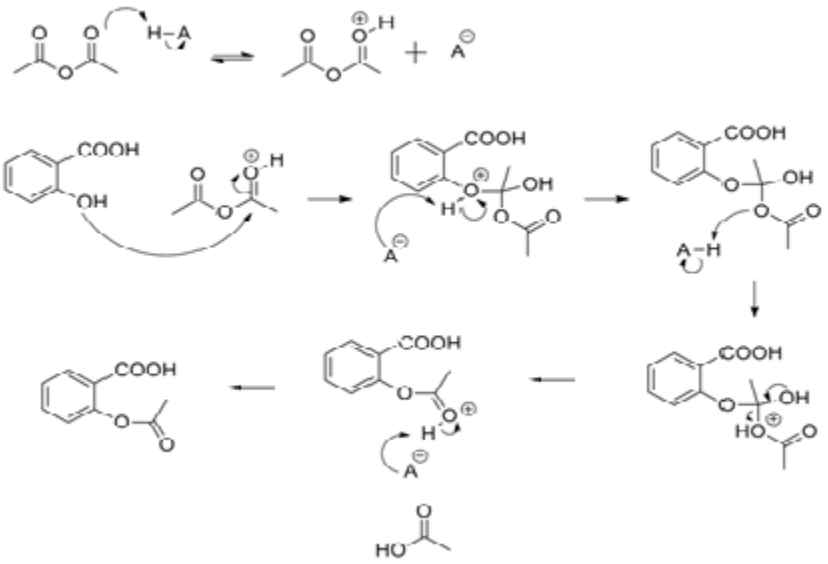
Synthesis of Aspirin

Principle : Synthesis of Aspirin from salicylic acid occurs by acetylating process in acidic medium. Salicylic acid interacts with acetic anhydrides in presence of few drops of conc. sulphuric acid to produce aspirin and a molecule of acetic acid. The purpose of adding sulphuric acid (catalyst) is to aid and augent the process of detaching the acetate ion from acetic anhydride which ultimately get associate with H+ ion from phenolic hydroxyl group in salicylic acid to be eliminated as a mole of acetic acid.

Chemical Reaction :



Mechanism :

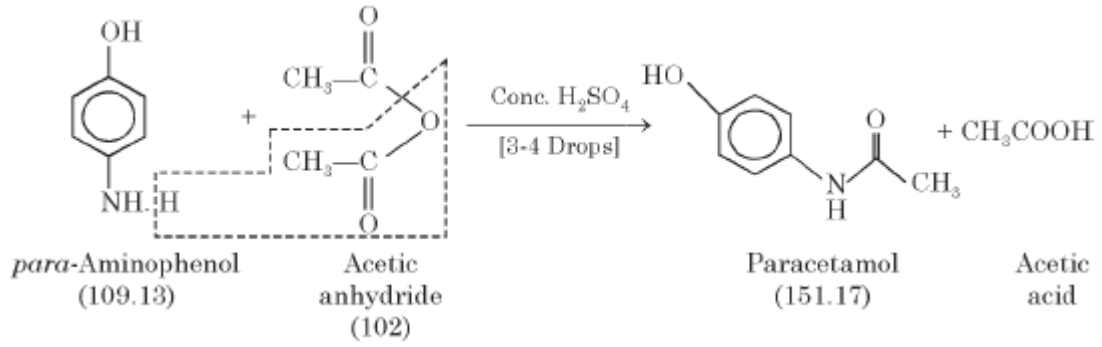


Uses : Use for the relief for minor pains/ aches and also mild to moderate pain. It is recommended for arthritis and related arthritic conditions, myocardial infarction prophylaxis. It reduces the risk of transient ischemic attacks in men.

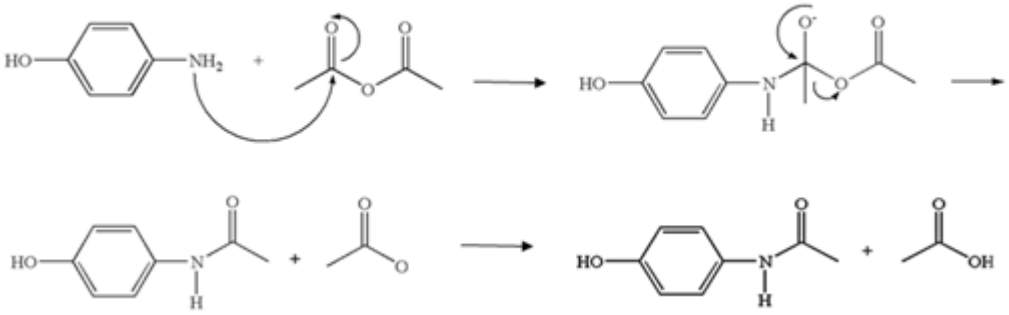
Synthesis of Paracetamol :

Principle: The synthesis of amide essentially just requires running the reaction under certain temperature conditions with an appropriate catalyst . Pracetamol prepare from para-amino phenol by acetylating it with acetic anhydride in the presence of 3 to 4 drops of concentrated sulphuric acid as catalyst.

Chemical Reaction



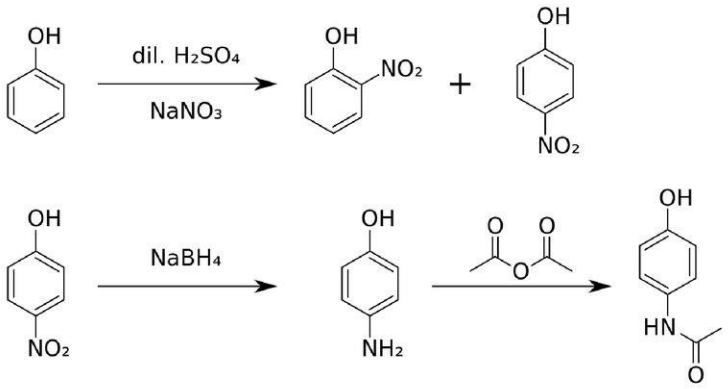
Mechanism :



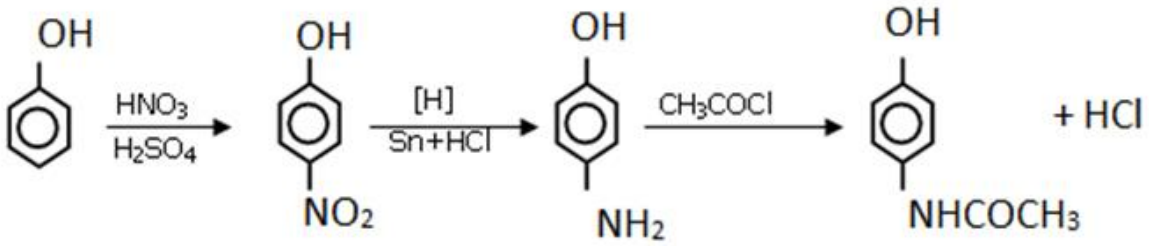
From Phenol

Synthesis of Paracetamol

In the laboratory, **paracetamol** is easily prepared by **nitrating** phenol with **sodium nitrate**, separating the desired ***p*-nitro phenol** from the *ortho*- byproduct, and **reducing** the **nitro group** with **sodium boro hydride**. The resultant *p*-aminophenol is then **acetylated** with **acetic anhydride.** In this reaction, phenol is strongly activating, thus the reaction requires only mild conditions nitration The industrial process is analogous, but **hydrogenation** is used instead of the sodium boro hydride reduction



Alternative method:

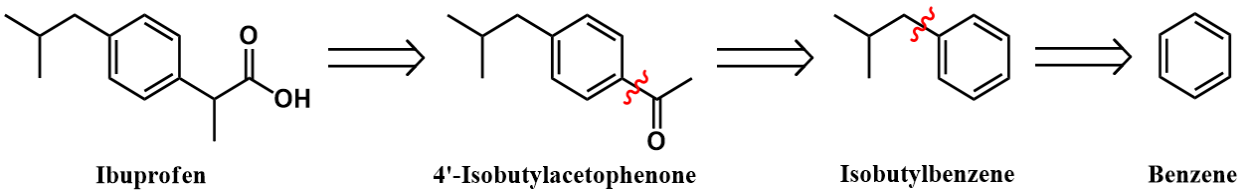


Uses : It is an effective antipyretics and analgesic. Activity of the drug on the hypothalamic heat – regulating centre is the mechanism behind the antipyretic effect, whereas analgesia is shown due to elevation of the pain threshold. It is also found to be useful in diseases accompanied by pain , discomfort, and fever , for instant common cold and other viral infections. It is also active against arthritic and rheumatic disorders involving musculoskeletal pain as well as the pain occurred due to headache, myalgia, dismenorrhea and neuralgia.

Synthesis of Ibuprofen

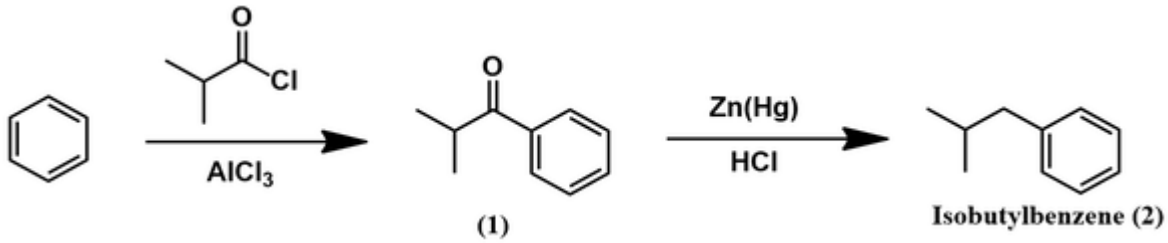
To appraise the synthetic challenges of preparing ibuprofen, we begin with a retro synthetic analysis.

Retro synthetic analysis :



Synthesis of isobutylbenzene from benzene

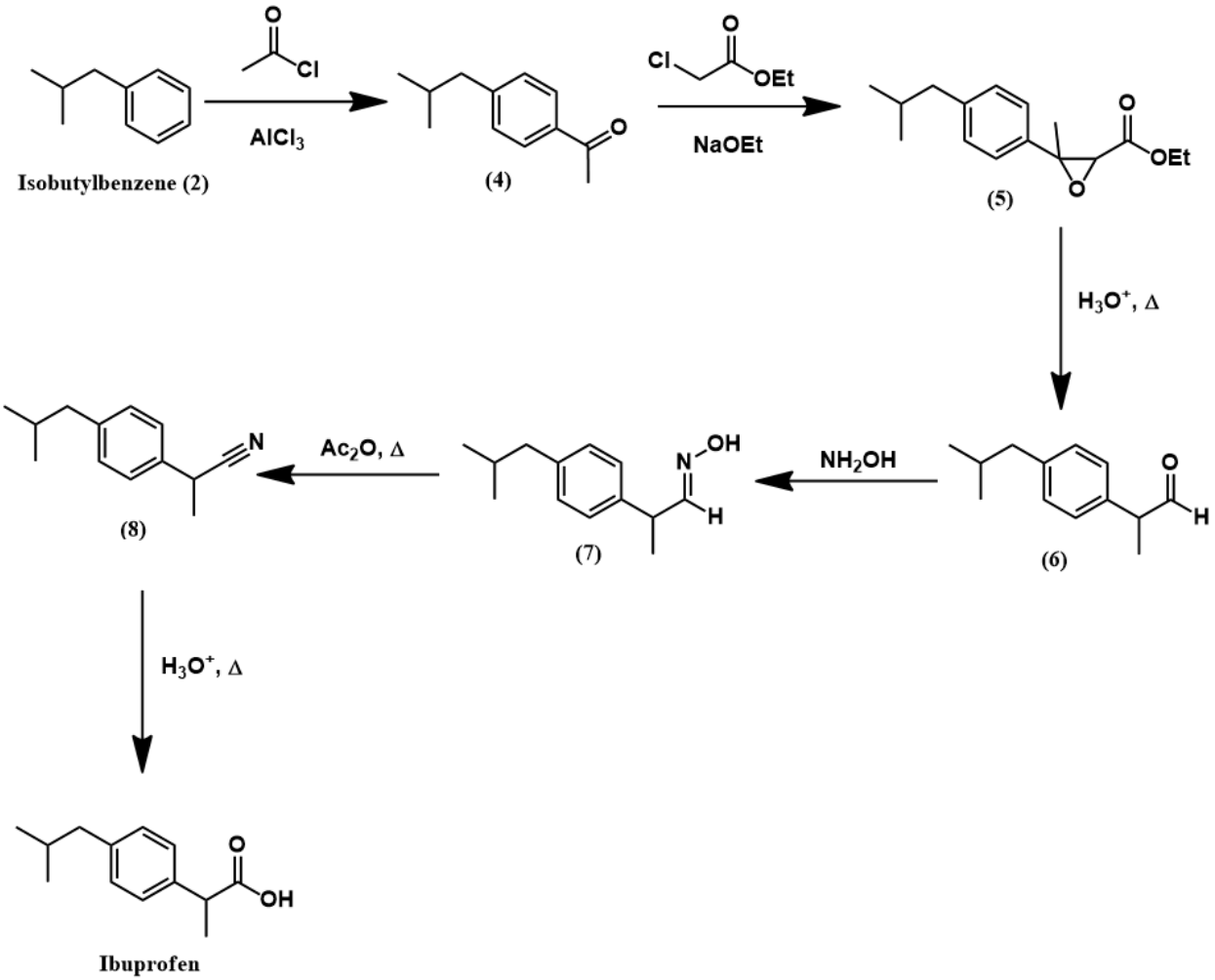
First, a Friedel-Crafts acylation functionalizes benzene with an isobutyryl moiety **(1)**. This substituent is reduced to an isobutyl group through a Clemmensen reduction, yielding **isobutylbenzene (2)**.



Synthesis of ibuprofen by the Boots process

Having prepared isobutylbenzene, we now review the historic synthesis of ibuprofen developed the Boots company. This is the company which originally discovered the analgesic activity of this compound. A full synthetic scheme is presented below. The synthesis begins with another Friedel-Crafts acylation on isobutylbenzene with acetyl chloride to give **(4)**. The next synthetic steps work to convert this compound's *para*-acetyl group to ibuprofen's propionic acid substituent. First, The acetyl group is converted to an α,β-epoxy ester **(5)** via a Darzens reaction with ethyl chloroacetate. Next, hydrolysis and decarboxylation give the aldehyde **(6)**. Condensation with hydroxylamine affords an aldoxime **(7)** which is then dehydrated to the nitrile

(**8**) using acetic anhydride. Lastly, acid-catalyzed hydrolysis of the nitrile to a carboxylic acid yields **ibuprofen**.



Uses

Ibuprofen (brand name Advil or Motrin) is one of the most widely used nonsteroidal anti-inflammatory drugs (NSAIDs). It is useful for reducing pain, inflammation, and fever.

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