Pharmaceutical Chemistry

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Synthesis of Essential Drugs

By *R.S. Vardanyan* and *V.J. Hruby*, Elsevier, 2006

3. Analgesics

Analgesics are drugs that **eliminate** or **alleviate** the **feeling of pain** that accompanies many pathologic conditions, and situations including muscle aches and headaches (for which aspirin-like analgesics are usually used), and where there is no possibility of becoming addicted.

More **intense pain** originating during and after surgical intervention is relieved by utilizing **opioid analgesics**, such as morphine and meperidine. Unfortunately, even extremely short use of these analgesics can lead to habitual use, development of drug dependence, and tolerance.

For **chronic pain** associated with chronic inflammatory reactions (rheumatoid arthritis, etc.), patients can use nonsteroidal, **anti-inflammatory** analgesics for years, though their pain modulatory effects vary greatly.

Pain is a very important protective phenomenon that accompanies many pathological conditions. Its function of signaling, it can aggravate the course of the primary disease, and in some cases such as severe trauma can facilitate the development of shock.

Analgesics are divided into two groups:

1. opioids (morphine-like substances), which predominantly influence the **central nervous system** (**CNS**)

2. nonopioids (nonsteroidal anti-inflammatory or fever-reducing drugs—**NSAID**), which act predominantly on the **peripheral nervous system**

Opioid and nonopioid analgesics differ in many ways, making it useful to distinguish them by the following: opioids are the strongest analgesics; they do not possess anti-inflammatory capabilities.

Opioids can cause **dependence and tolerance**, and therefore their use should be short term.

In addition, **nonopioid** analgesics are **rarely used in the form of injections**.

Despite the fact that drugs of both groups relieve pain, **their pharmacological actions are different**, which is why they are examined separately.

3.1 Opioid Analgesics

Opioids are subdivided into three large subgroups according to their action on opioid receptors: **agonists**, **mixed agonists–antagonists**, and **antagonists**.

Opioid agonists have an affinity for opioid receptors, imitating the activity of endogenous opioid analgesics.

Mixed agonists–antagonists can be semisynthetic derivatives of morphine or peptide analogs of endogenous opioids that display agonistic activity at some opioid receptors and antagonistic activity in others.

Opioid antagonists bind to opioid receptors but do not activate them. These compounds are not used for analgesia. Their therapeutic value is in **relieving side effects** that result from either absolute of relative **overdoses** or **intolerance** of drugs by patients, and also in treating cases of opioid dependency.

Agonists: include natural alkaloids of opium (morphine, codeine, and a large blend of natural alkaloids, pantopon, and omnopon), their analogs (hydrocodon and hydromorphone, oxycodone, and oxymorphone), derivatives of morphinane (levorphanol), and a number of synthetic compounds: derivatives of phenylpiperidine (meperidine, promedol), 4-anilidopiperidines (fentanyl, sufentanyl, alfentanil), and derivatives of diphenylheptane (methadone, propoxyphene).

Mixture of agonists–antagonists: includes derivatives of morphinane (nalorphine, butorphanol), phenanthrene (nalbuphine), derivatives of benzomorphane (pentazocine, dezocine), and derivatives of opipravin (buprenorphine).

Antagonists: naloxone and naltrexone

It is universally accepted that the action of opioids is mediated by specific receptors. Several types of opioid receptors exist: μ, κ, δ, and σ. A few of these are in turn subdivided into subtypes.

It has been found that opioid receptors are **seven** transmembrane G-protein-coupled receptors that are localized in the membranous part of the synaptosomal head; they are glycoproteins. They are prone to conformational changes in certain situations, which is essential for their selective binding with agonists or antagonists.

Opioids have various chemical structures, and their relative **analgesic** potential **depends on** several different factors, including their affinity to specific binding sites on receptors, activity on the receptors themselves, and distinctive pharmacokinetic properties.

Various types of opioid receptors have been postulated solely for explaining the different actions of opioids.

Receptors that cause reactions in the organism that are analogous to the reactions upon introduction of morphine (**suppression of respiration**, **myosis**, **disorders of the gastrointestinal tract**, **euphoria**) have been named μ-receptors.

Receptors that cause effects analogous to those caused by ketazocine (**analgesia**, **sedative effects**, **myosis**) have been named κ-receptors.

Analgesic receptors that also cause psychotomimetic reactions (**hallucination dysphoria**, **stimulation of respiratory and cardiovascular system**, **mydriasis**) are characteristic of those included in the class of the agonist–antagonists of the type of *N*-allylnormethazocine named σ-receptors.

Receptors that react to the action of enkephalins and that cause analgesia and release of growth hormone have been named δ-receptors.

The **physiological** role of the endogenous opioid system is not limited to pain and analgesia. It plays a role in the regulation of the endocrine, behavioral, thermoregulating, immunological, and gastrointestinal systems.

The distribution frequency of opioid-binding sites varies significantly in different regions of the CNS; it is especially high in brain structures.

Opiate receptors are found outside the CNS, in particular in the vagus and the gastrointestinal tract.

The reaction of agonists with opioid *μ*-receptors leads to an increase in the flow of potassium ions from the cell, simultaneously making it difficult for calcium ions to flow into the cell, which makes neurons less excitable.

κ-Receptor agonists directly inhibit entrance of calcium ions into neurons by simply reducing their flow through voltage-gated calcium channels.

Opioids cause side effects that limits their use, including **respiratory depression**, **nausea**, **vomiting**, **constipation**, a **heightened level of blood pressure**, **urine retention**, **perspiration**, and **itching**. Opioids cause dependency and addiction.

3.1.1 Agonists

The most widely used agonists in medical practice are the opium alkaloids morphine and codeine.

Semisynthetic derivatives (hydromorphone, oxymorphone, hydrycodon, oxycodone) and synthetic compounds (methadone, meperidin, fentanyl, sufentanyl, and others) have found wide use.

Opioid agonists act first and foremost on *μ*-receptors.

The **use** of compounds of this class **should be avoided** in the event of cranial trauma, bronchial asthma and other hypoxic conditions, severe alcohol intoxication, convulsive conditions, and severe pain of organs in the abdominal cavity.

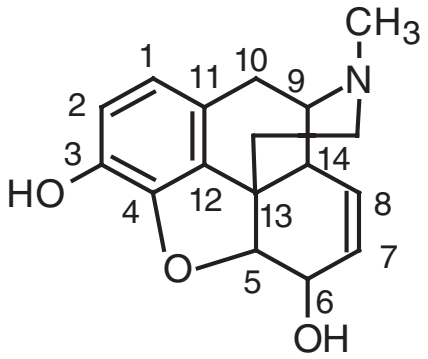
Morphine:

Morphine, 4,5-epoxy-17-methymorphin-7-ene-3,6-diol, is the oldest and most well-known analgesic.

It is made from opium—the dried, milky sap of unripe opium poppy bulbs, whose analgesic properties have been known for over 3000 years.

This plant also contains a large number of other alkaloids that are subdivided into groups of phenanthrenes and benzylisoquinoline.

The synthesis of morphine is not economically practical, since it is much cheaper to obtain from natural resources.



Morphine is the primary representative and primary prototype of the group of strong opioid analgesics. The most important use of morphine is its ability to eliminate pain.

It is used in surgery and as a preanesthetic medication for surgical interventions before the general anesthesia procedure begins.

It is widely used in myocardial infarction not only to relieve pain, but also for calming the patient and even for reducing the need of oxygen. It is used in pulmonary edema and in a few forms of diarrhea.

Morphine is prescribed in all cases when NSAID action is not sufficient and requires the use of strong opioid analgesics.

Relatively simple modifications of morphine molecules lead to the formation of a number of compounds that differ in their analgesic activity.

Codeine:

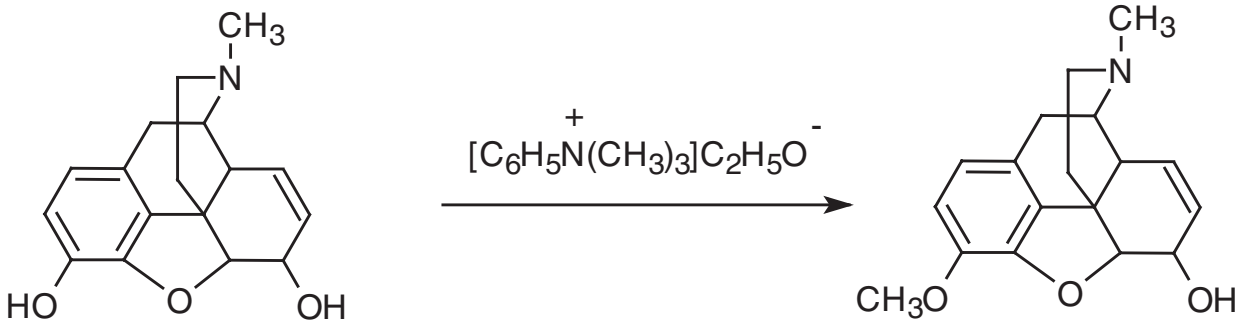
Codeine is an elemental part of opium poppy alkaloids. Codeine differs from morphine in that hydroxyl group on C_3 of the aromatic ring is methylated.

The content of codeine in opium does not satisfy medicinal requirements and therefore codeine is made in a semisynthetic manner from morphine by selective methylation of the aromatic hydroxyl group on C_3.

Codeine is similar to morphine in terms of properties, but its pain-relieving ability is significantly less and it causes addiction to some degree.

This drug is very effective in oral use and is used for average to moderate pain. It is often used as an antitussive drug.

Synonym: codyl and acutus



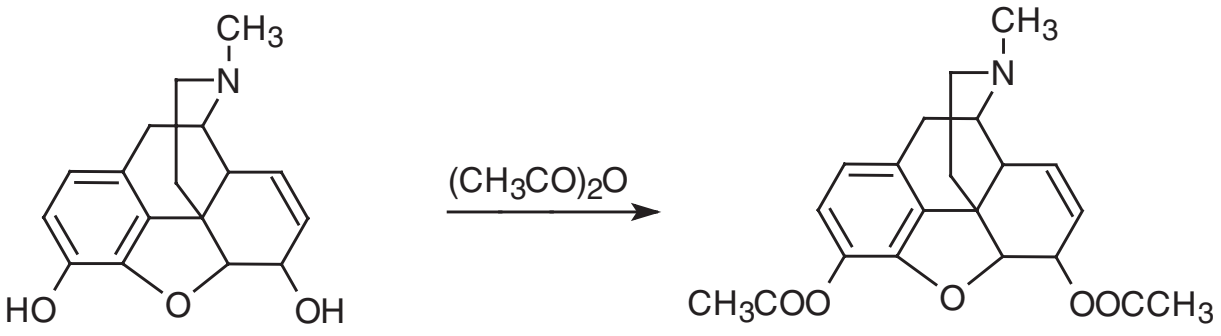
Heroin:

Heroin is synthesized by the simultaneous acetylation of the two hydroxyl groups of morphine with acetic anhydride or acetyl chloride.

Owing to its high solubility in lipids (compared to morphine), heroin quickly passes through the blood–brain barrier (acts like morphine) and transform in the brain.

Narcotic effects, respiratory depression, toxicity, narrow range of therapeutic action, and high danger of addiction make it less advantageous than morphine.

Heroin use is prohibited in medicine, since it does not have any therapeutic value which cannot be found in other drugs.



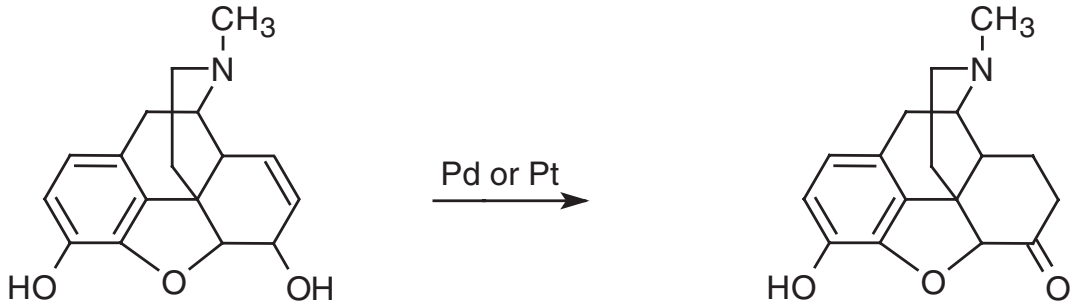
Hydromorphone:

Hydromorphone is more soluble than morphine and approximately eight times more active upon parenteral administration.

High solubility permits a lower volume of injected fluid, which is important if multiple injections are needed. It begins to work faster than morphine, but lasts for a shorter amount of time.

It has a high sedative effect and a lessened capability of causing euphoria. Hydromorphone is used the same way as morphine.

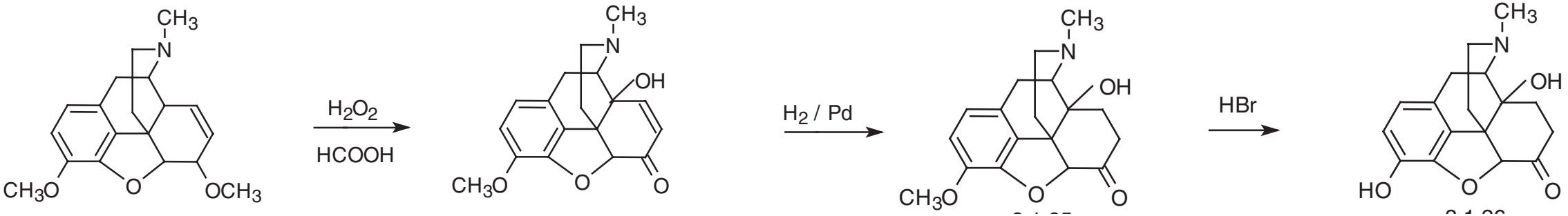
Synonym: dilaudid



Oxymorphone:

Oxymorphone is approximately 10 times more active than morphine. Euphoric effects as well as vomiting are expressed significantly stronger than in morphine. Oxymorphone also displays poor antitussive activity.

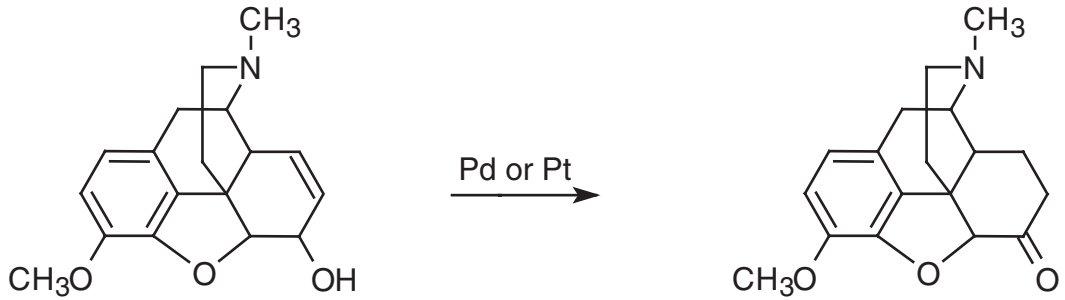
Side effects are analogous to those of morphine. It is intended for relieving moderate to severe pain in surgical and gynecological interventions and for post-operational pain.



Hydrocodone:

Hydrocodone exhibits expressed analgesic and antitussive properties, which make up its primary clinical use. It may cause dependence and addiction.

Synonyms: dicodid, detussin, and vicodin

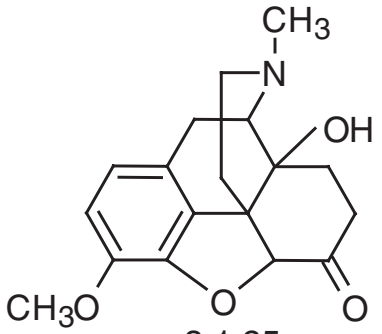


Oxycodone:

Unlike hydrocodone, it is used as an analgesic in combination with other drugs, such as aspirin or acetaminophen.

Oxycodone is similar to morphine in terms of durational efficacy and is intended for oral use.

Synonym: roxicodone, proladone, perketan, eutagen, and oxycon



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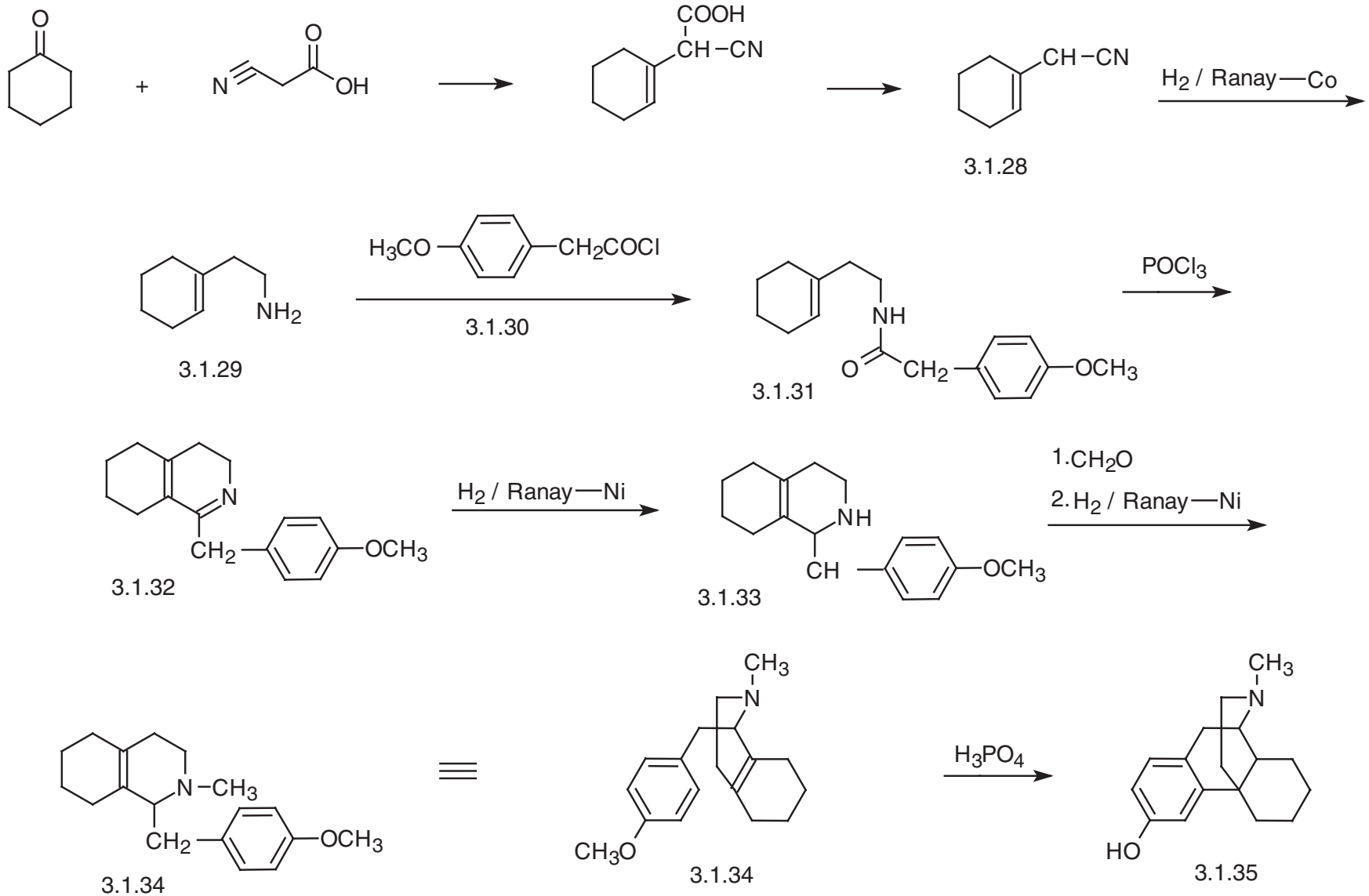
Levorphanol:

The dextrorotatory isomer is not an analgesic, it has antitussive properties.

The levorotatory isomer exhibits activity similar to that of morphine; however, a number of side effects including nausea, vomiting, and the potential of causing constipation are less prevalent.

It is 4–8 times more effective than morphine when injected. It also lasts longer than morphine.

This drug is recommended for relieving moderate to high pain in biliary and renal colic, myocardial infarction, in serious trauma, and for relieving cancer pain and post-operative pain.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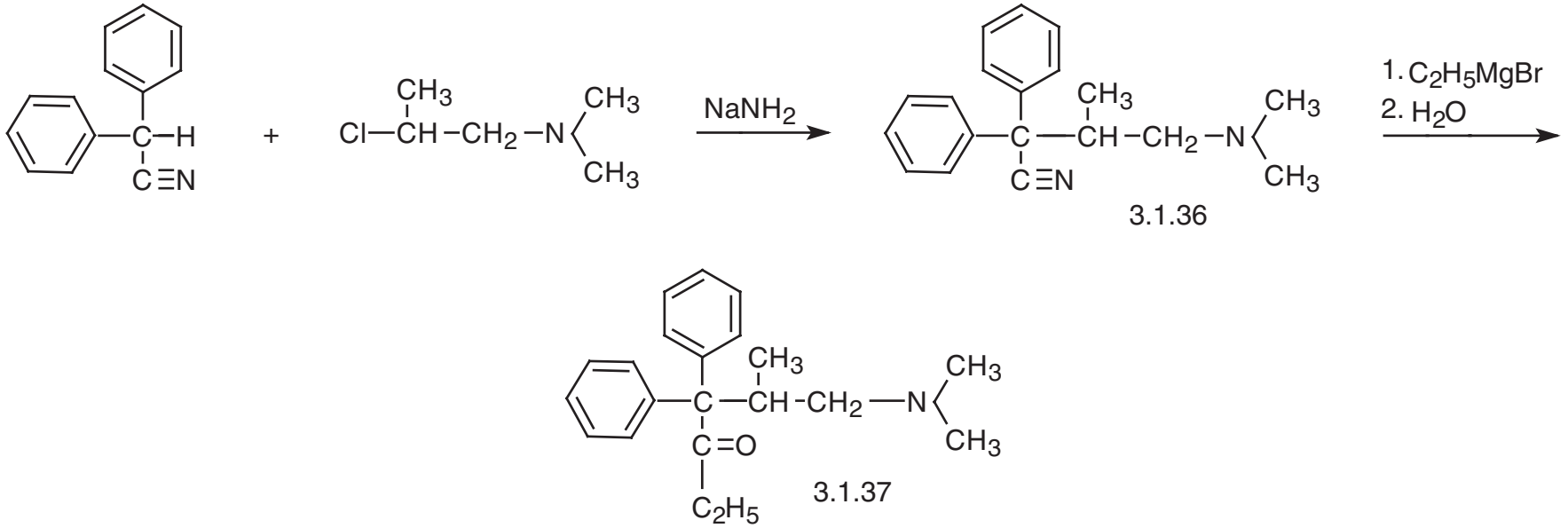
Methadone:

Methadone is a **synthetic opioid** that acts on the *μ*-receptors and is both qualitatively and quantitatively analogous to morphine. The principal difference lies in its higher efficacy when taken orally, and its long-lasting effect.

As a strong analgesic, it is used in treating drug addiction, since it replaces other agonists on the receptor.

Synonym: fizepton, methenone, and dolofin



Meperidine:

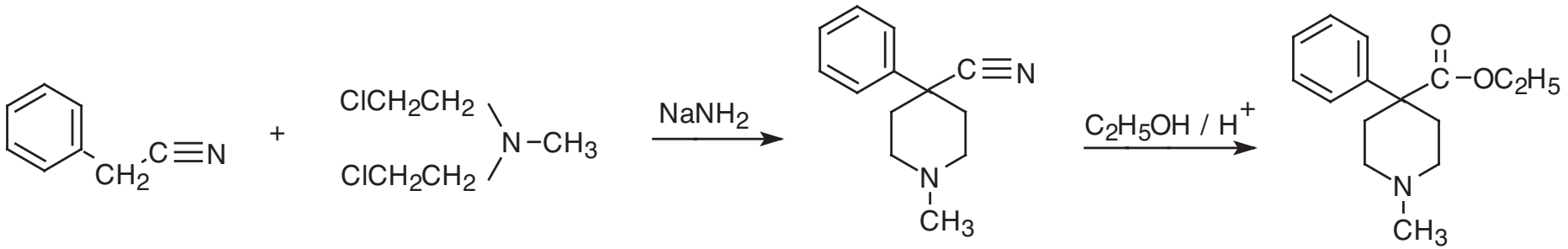
Meperidine is related to analgesics of the phenylpiperidine series.

This drug also exhibits anticholinergic activity. Like morphine, it causes histamine release and spasm of the smooth muscles. It is **practically inactive upon oral administration**.

Most of the pharmacological properties and administration indications are similar to those of morphine; however, this drug lacks antitussive properties. During parenteral administration, activity is basically one-eighth that of morphine.

Meperidine is widely used in premedical and stabilizing anesthesia. It is preferred for use in obstetrical practice due to the quick onset of analgesia and its short-lasting action.

Synonym: pethidine, dolantin, and demerol

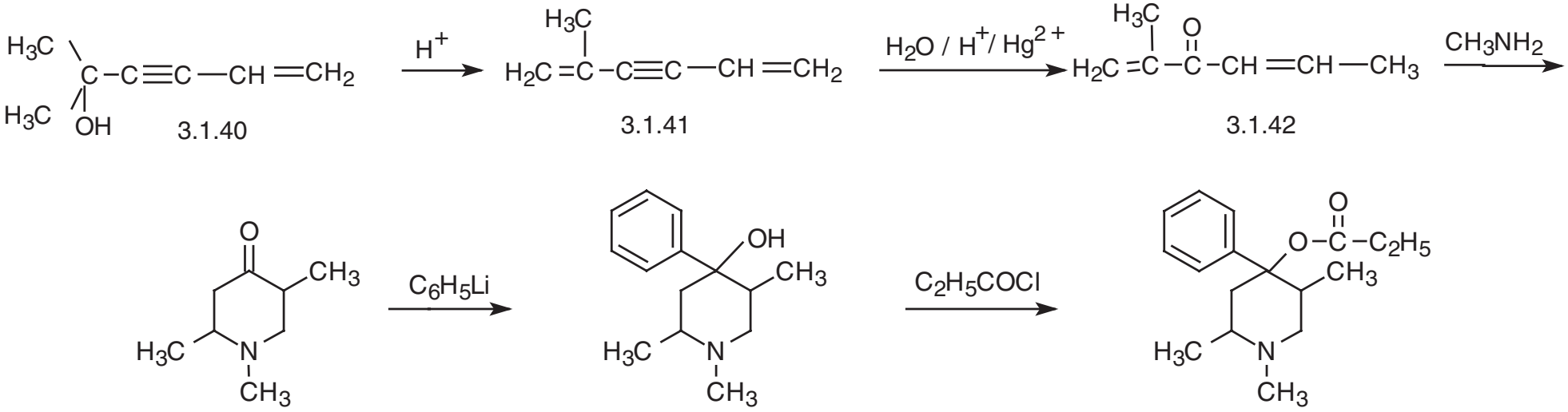


Promedol:

Promedol is quickly absorbed and displays strong analgesic action during both parenteral and oral administration.

It gives less respiratory suppression than morphine. It also displays anti-spasmodic effects on smooth muscle. It is used as a pain-relieving agent during surgical intervention, trauma, and diseases that are accompanied by painful sensations.

Synonym: trimeperidine

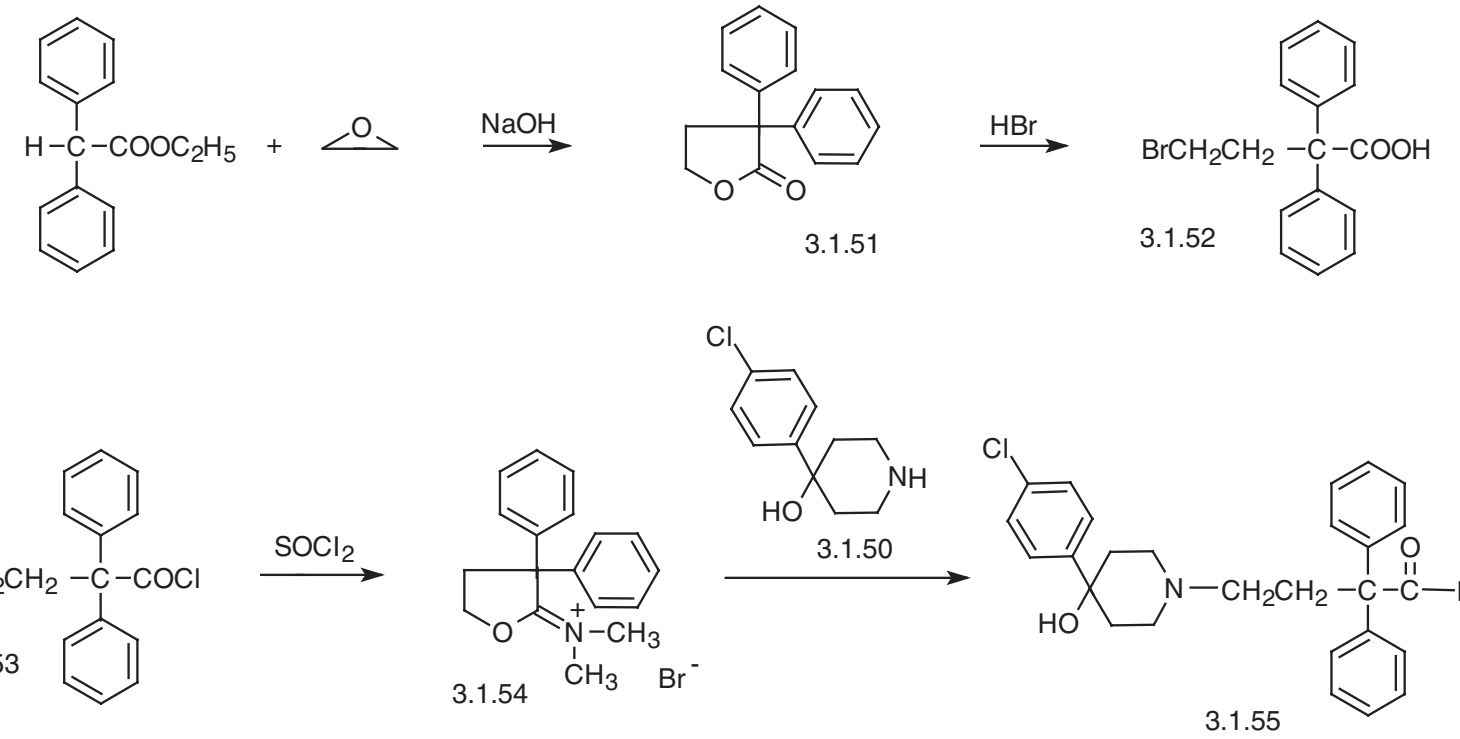


Loperamide:

Loperamide is presently used more often as an anti-diarrheal drug than as an analgesic, and it is also included in the list of **over-the-counter drugs** because of its insignificant action on the CNS.

It reduces intestinal smooth muscle tone and motility as a result of binding to intestinal opiate receptors. It is used for symptomatic treatment of severe and chronic diarrhea of various origins.

Synonym: imodium



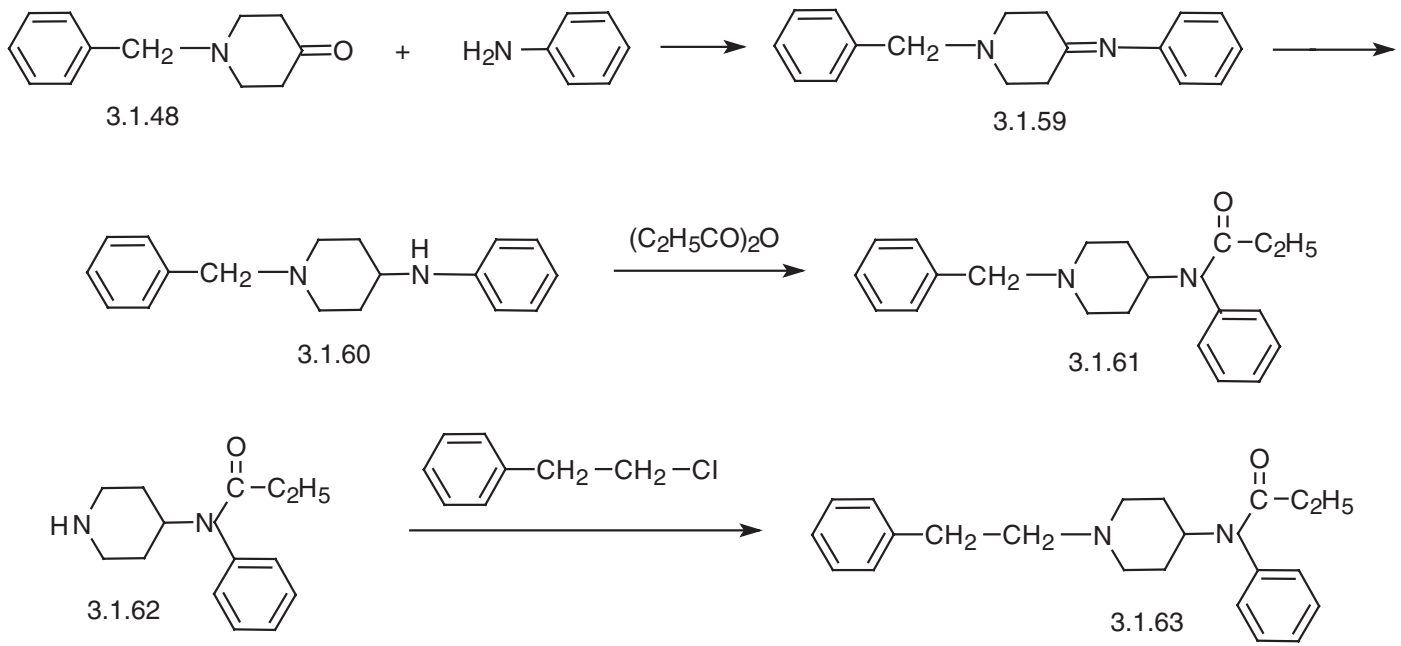
Fentanyl:

The analgesic action of fentanyl surpasses that of morphine by approximately 100-fold. It has a suppressive action on the respiratory center and slows heart rate.

Fentanyl is used in anesthesiology both independently and in combination with droperidol for neurolepthanalgesia, and in preanesthetic medication, in different forms of narcosis, and in post-operational anesthesia.

Unlike morphine, it does not cause a release of histamines. It is used only in specialized hospital conditions.

Synonym: fentanest and leprofen



3.1.2 Mixed agonists/antagonists

The agonist activity is exhibited as a result of the interaction with *μ*-receptors, while its antagonistic activity on *κ*- and *σ*-receptors.

Interestingly, tolerance to the agonistic properties of these drugs may result, but not to the antagonistic properties.

Dependence can also originate from their long-term use.

This group of compounds is used for analgesia in cases of moderate to severe pain.

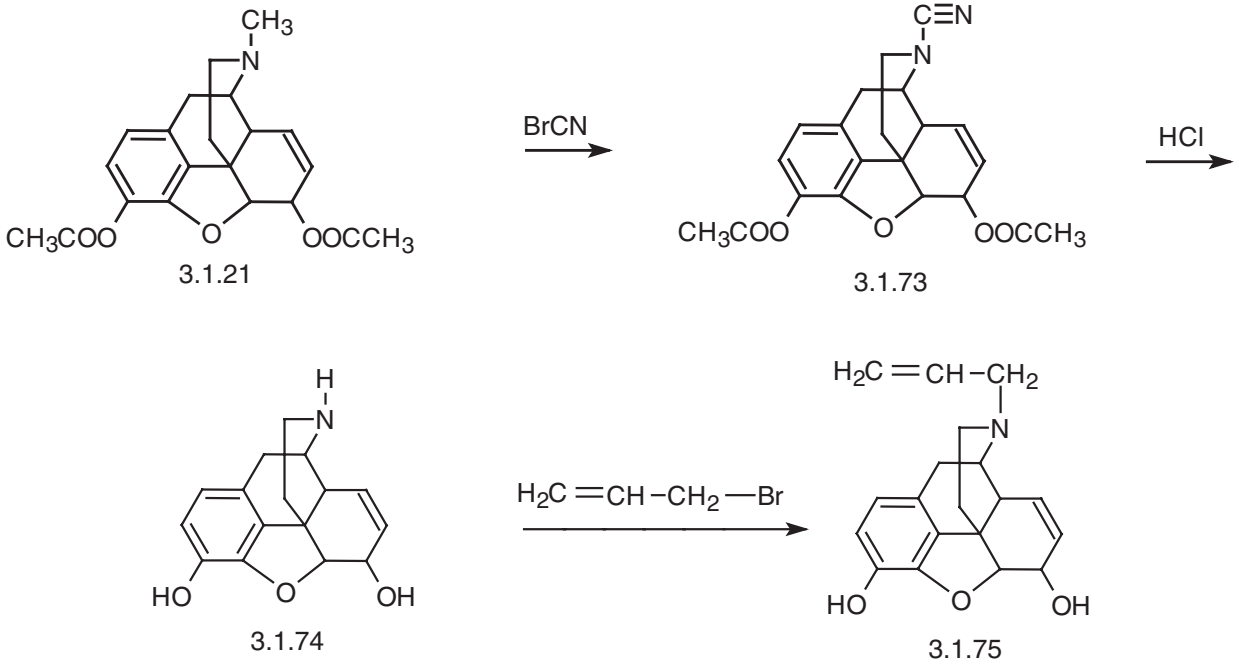
They are less effective than morphine; however, they do not cause severe respiratory depression upon overdose.

Nalorphine:

Nalorphine has less of an analgesic effect than morphine; however, it does not have much value as an independent analgesic. It is used as an antagonist to narcotic analgesics. It eliminates suppression of the respiratory center, bradycardia, and vomiting caused by opiate receptor agonists.

Nalorphine was the first compound used for narcotic (in particular for heroin) **overdose treatment**; however, it exhibits a number of side effects such as visual hallucinations, and therefore its use is prohibited in some countries.

Synonym: narkan

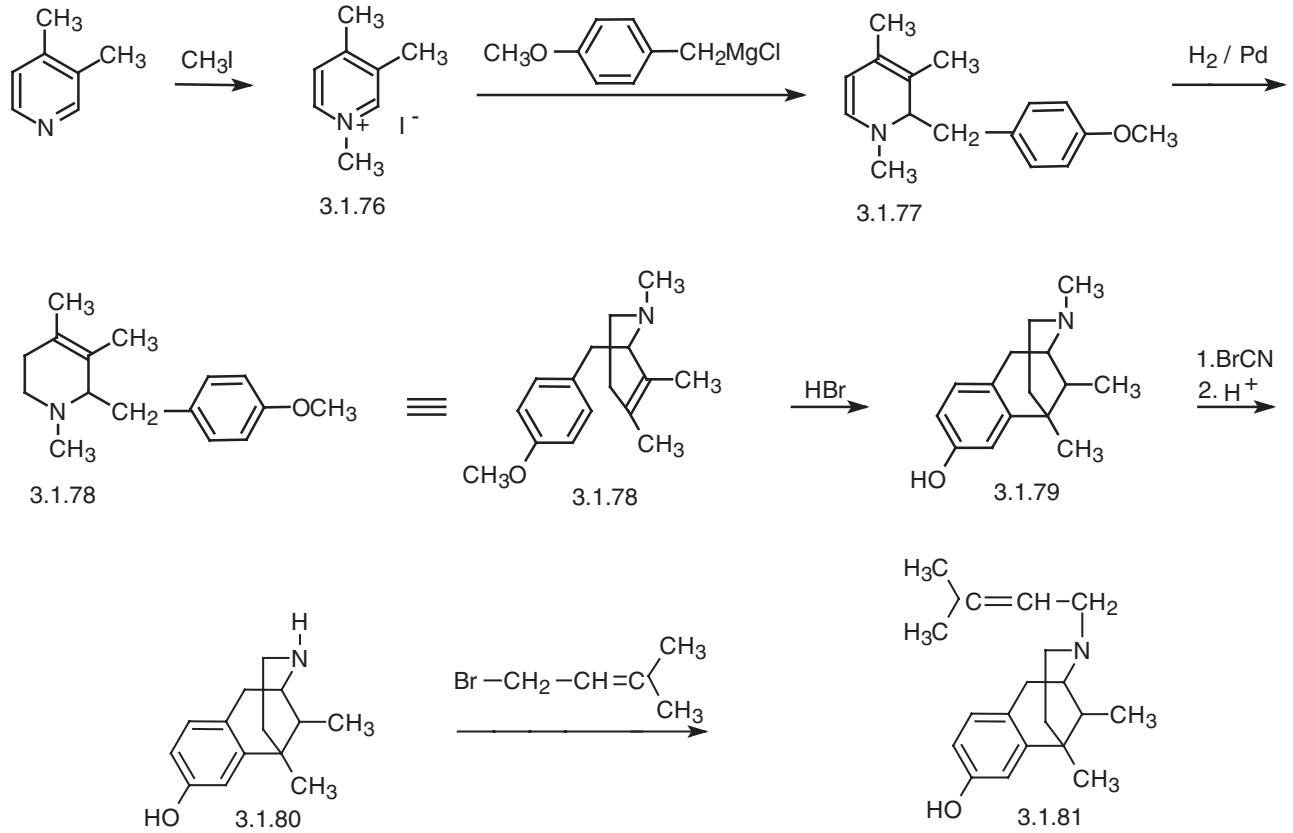


Pentazocine:

It is substantially weaker than nalorphine. It was the first agonist–antagonist analgesic to appear on the pharmaceutical market.

When taken orally, its activity is comparable to that of codeine. It is used for various degrees of pain and for pre-anesthesia medication prior to surgical intervention.

Synonym: fortral

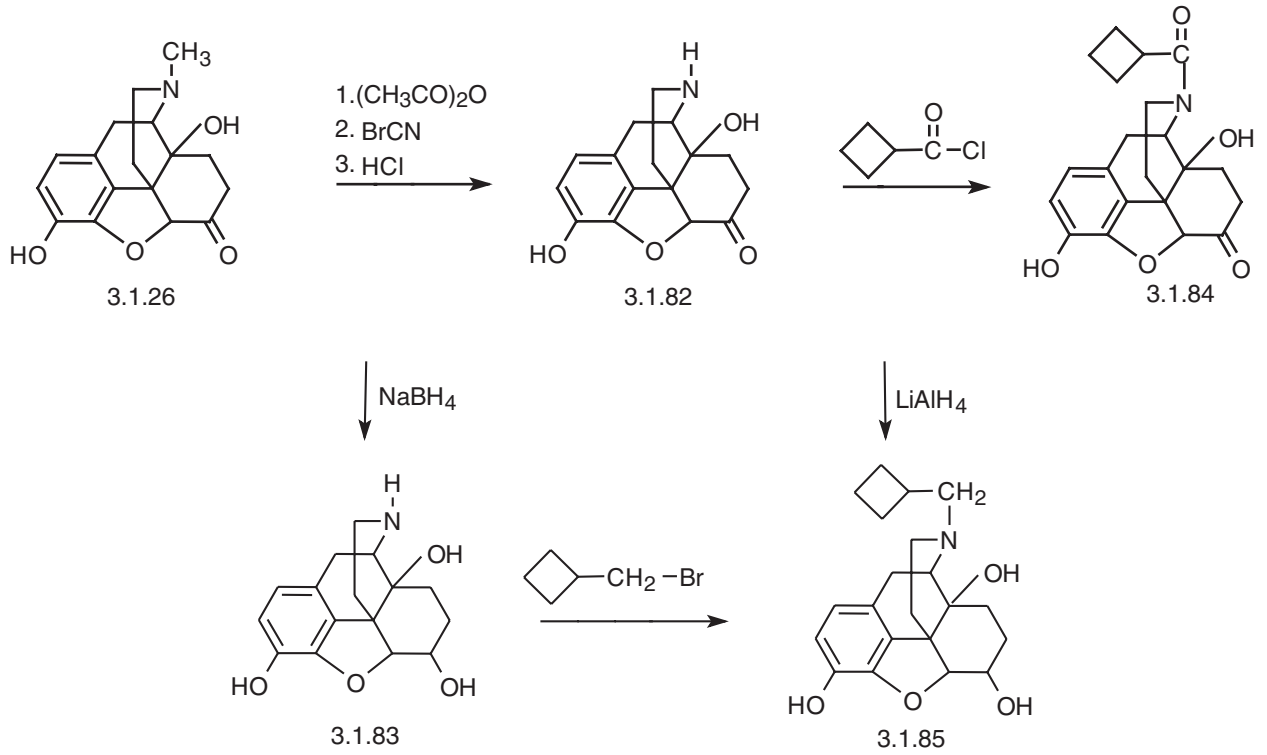


Nalbuphine:

Nalbuphine is a strong analgesic with activity equal to that of morphine. It is structurally similar to oxymorphone and the opioid antagonist naloxone. It exhibits fewer side effects than nalorphine.

Nalbuphine is prescribed as a drug for alleviating moderate to severe pain. It is used as a supplementary drug for balanced anesthesia, for pre- and post-operational analgesia, and in gynecological interventions.

Synonym: nubaine



3.1.3 Opioid antagonists

The efficacy and strength of opioid antagonists varies depending on the type of opioid receptors (μ-, κ-, δ-, and σ-), which they interact.

The mechanism of their action has been suggested that they antagonize the action of endogenous opioid peptides.

They do not result in dependence or tolerance.

They are used upon overdose of opioid analgesics or in the event of patient intolerance to them, and also in treating drug addiction.

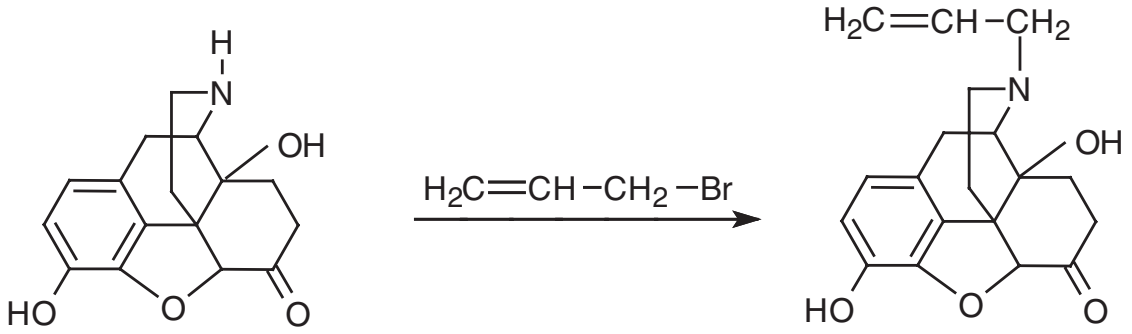
Naloxone:

N-allylic substitution in a number of morphine derivatives leads to antagonistic properties.

Naloxone is a few times stronger than nalorphine as an antagonist. It blocks opiate receptors.

It eliminates central and peripheral action of opioids, including respiratory depression. Naloxone is used upon overdose of narcotic analgesics.

Synonyms: narkan, and talwin



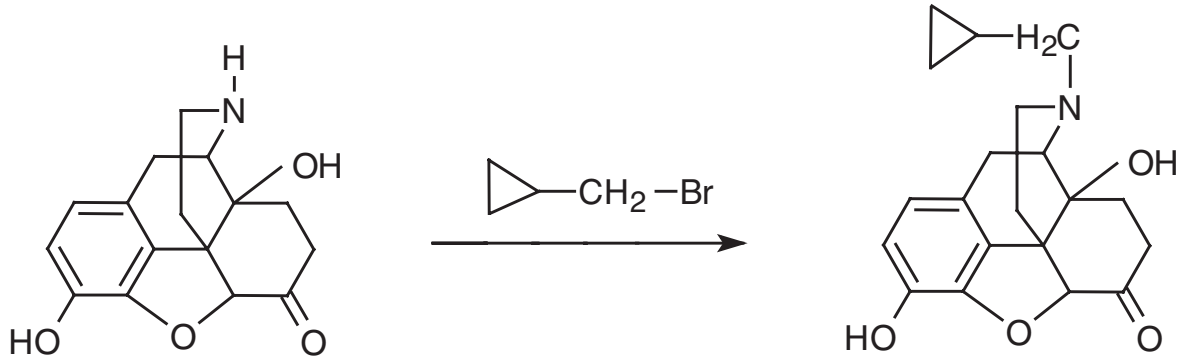
3.1.82 3.1.92

Naltrexone:

It is similar to naloxone in terms of pharmacological characteristics; however, it differs in two important ways: long-lasting action and its metabolite 6-*β*-naltrexol.

Naltrexone is potentially hepatotoxic. Naltrexone is used for blocking pharmacological effects of opioids upon their overdose.

Synonym: nalorex, and trexan



3.1.82 3.1.93

3.2 Nonsteroid Anti-inflammatory Drugs and Anti-fever Analgesics

They are devoid of many undesirable effects that accompany opioid analgesics (respiratory depression, addiction, etc.). They are called nonnarcotic analgesics, aspirin-like substances, anti-fever analgesics.

The mechanism of its action is supposed to its ability to inhibit synthesis of prostaglandins, which reduces their sensitizing influence on nerve endings, which in turn reduces the effect of neurotransmitter action.

Experiments in animals show that the analgesic action of this series of drugs is peripheral.

In general, nonopioid analgesics are characterized by three fundamental types of action: **analgesic**, **anti-inflammatory**, and **fever-reducing action**, which are used for alleviation of headaches, myalgia, arthralgia, and that do not have sedative or soporific effects.

Euphoria, **addiction**, and drug dependence **do not result from their use**.

Nonsteroidal anti-inflammatory and fever-reducing analgesics are **classified as**:

- salicylic acid derivatives (aspirin, diflusinal, etc.),
- pyrazolones (phenylbutazone, metamizol, etc.),
- acetominophen,
- anthranylic acid derivatives (flufenamic acid, mephenamic acid, and meclophenamic acid),
- arylacetic acid derivatives (diclofenak, phenclofenak),
- arylpropionic acid derivatives (ibuprofen, ketoprofen, naproxene, fenprofen, etc.),
- indolyl/indeneacetic acid derivatives (indomethacin, sulindac, etc.), and
- oxicames (pyroxicam, isoxycam).

3.2.1 Salicylic acid derivatives

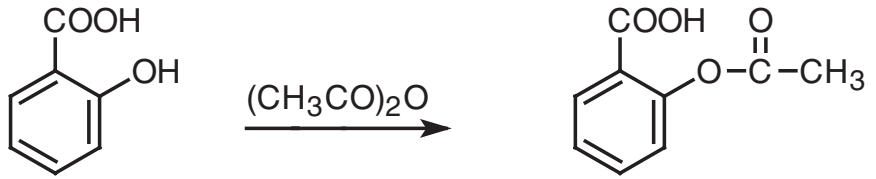
Aspirin:

Aspirin or acetylsalicylic acid (3.2.2), is synthesized by the acetylation of salicylic acid (3.2.1) using acetic anhydride or acetyl chloride.

Aspirin exhibits analgesic, fever-reducing, and anti-inflammatory action, and it also reduces aggregation of thrombocytes. The primary mechanism of action is the irreversible acetylation of cyclooxygenase, which results in the inability to synthesize prostaglandins, prostacyclins, and thromboxane.

Aspirin is widely used for head and neuralgic pains, rheumatic conditions, painful symptoms of various etiologies, and eliminating painful feelings during menstruation. It is used in conditions such as fevers, prevention and treatment of thrombosis and embolism, and for prevention of ischemic abnormalities and cerebral blood circulation.

Synonym: acetosal, acetylsalicylic acid, and cetosal



3.2.1 3.2.2

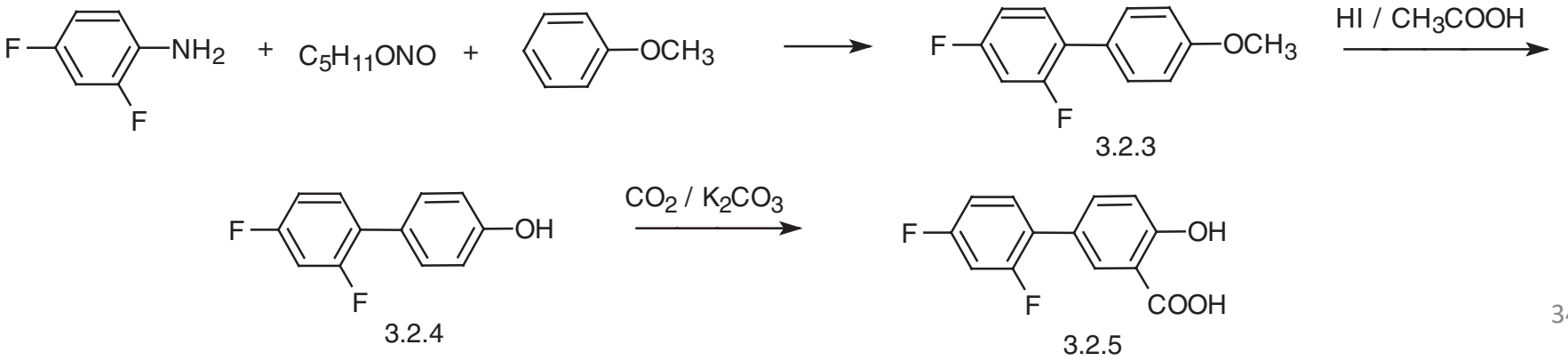
Diflunisal:

It is used for long- and short-lasting symptomatic relief of low to moderate pain in osteoarthritis and rheumatoid arthritis.

Synonym: dolobid, adomal, and noladol

In medical practice, other salicylic acid derivatives are used in the form of salts. Magnesium and sodium salicylates are less effective than respective doses of aspirin; they are easier on patients that are sensitive to aspirin.

Choline magnesium trisalicylate represents a mixture of choline salicylate and magnesium salicylate, which has the same effect as aspirin; however, it is easier on patients in which gastrointestinal effects are observed upon taking aspirin.



3.2.2 Pyrazolones

In medicine, pyrazolone derivatives play a significant role as analgesics, anti-inflammatory, and fever-reducing agents.

Among these are antipyrin, butadion, amidopyrin, phenylpyrazon, sulfinpyrazone, sodium methamizol sodium (analgin), and a few others.

In terms of analgesic and anti-inflammatory action, they are similar to salicylic acid derivatives.

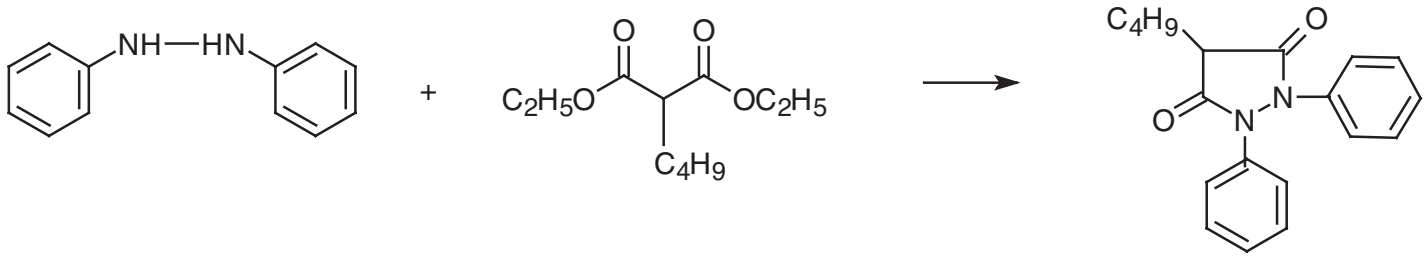
Although the mechanism of their action is not completely known, it is supposed that pyrazolone derivatives, like aspirin, inhibit biosynthesis of prostaglandins and reduce permeability of capillaries, thus preventing the development of inflammatory reactions.

A serious limitation to the wide use of pyrazolone in medicine is the cases of onset of agranulocytosis upon use of methamizol sodium (although it is prohibited in some countries). It can be used by combining with other drugs.

Phenylbutazone:

Phenylbutazone is used for relieving low to moderate pain in headaches, rheumatoid arthritis, and osteoarthritis.

Synonym: algoverin, azolid, and butazolidin

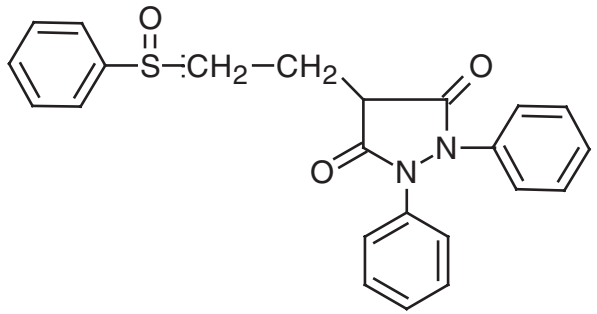


3.2.6

Sulfinpyrazone:

Sulfinpyrazone is used upon exactly the same indications as phenylbutazone.

Synonym: anturane and enturen



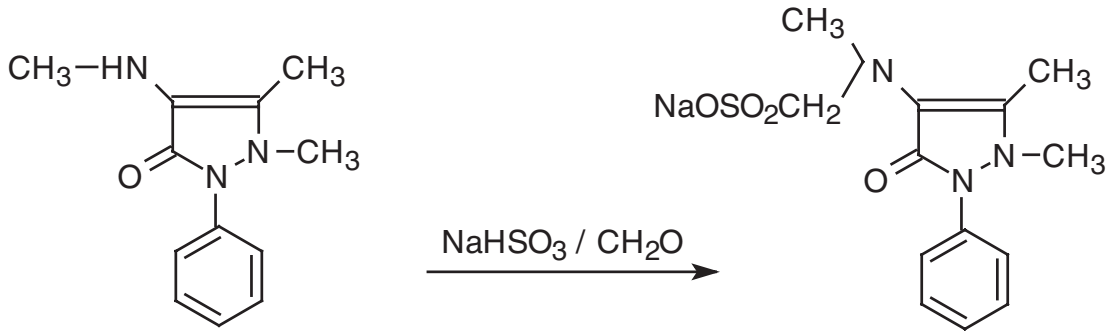
Metamizole sodium:

Methamizole sodium has expressed analgesic and fever-reducing properties and poorly expressed anti-inflammatory action, and is very convenient in cases where high concentrations of drug need to be quickly reached.

Methamizole sodium is used for relieving pain of various origins (renal and biliary colic, neuralgia, myalgia, trauma, burns, headaches, and toothaches).

Use of this drug may cause allergic reactions, and long-term use may cause granulocytopenia.

Synonym: dipyrone, and analgin



3.2.3 *p*-Aminophenol derivatives

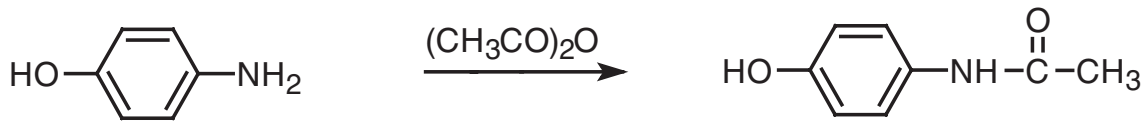
Acetaminophen:

Acetaminophen is widely used as an analgesic and fever-reducing agent, without anti-inflammatory and antirheumatic properties.

Acetaminophen is designed for moderate analgesia. It is also effective like aspirin and used for headaches (from weak to moderate pain), myalgia, arthralgia, chronic pain, for oncological and post-operational pain, etc.

It was recently shown that acetaminophen, like aspirin, inhibits cyclooxygenase action in the brain and is even stronger than aspirin.

Synonym: paracetamol and tylenol



3.2.4 Anthranylic acid derivatives

Anthranylic acid derivatives are direct structural analogs of salicylic acid derivatives. They possess analgesic, anti-inflammatory, and fever-reducing activity.

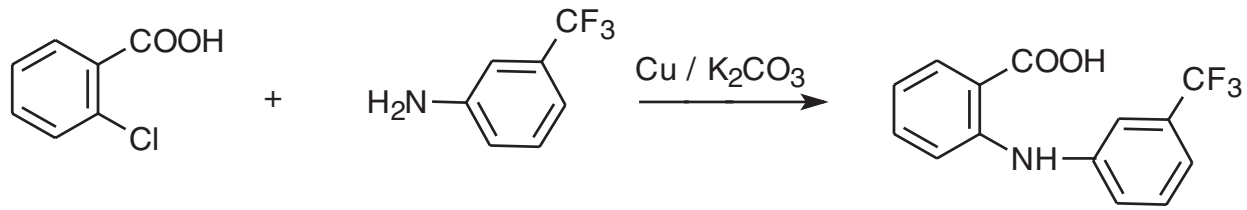
They are similar to pyrazolones in terms of analgesic and fever-reducing activity, yet they exceed the anti-inflammatory activity of salicylates.

Flufenamic acid:

It is used for moderate pain and dysmenorrhea, but it should not be used for more than 1 week due to the possibility of nephrotoxicity, gastrointestinal toxicity, and anemia.

It is frequently used in combination with the anticoagulant warfarin, the effect of which is strengthened when combined with flufenamic acid.

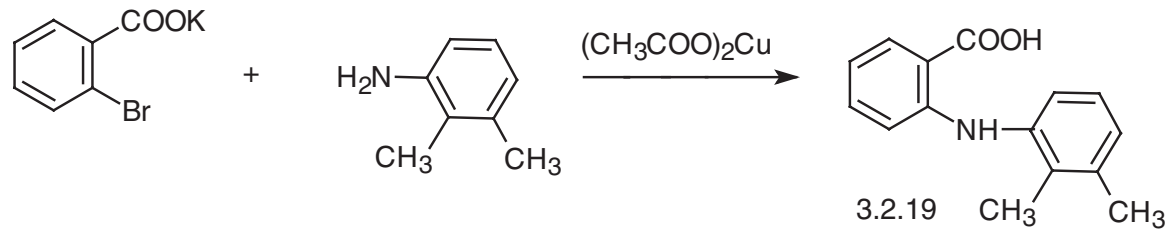
Synonym: arlef, flexocutan, and romazal



Mefenamic acid:

Its action is similar to flufenamic acid.

Synonym: parkemed, ponstan, and ponstel



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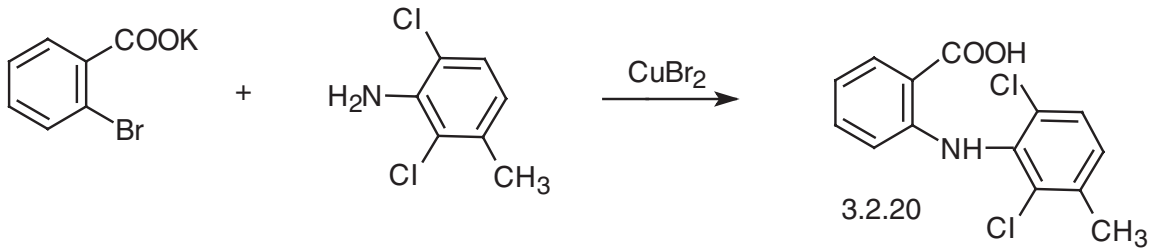
Meclofenamic acid:

Its action is similar to flufenamic acid.

Synonym: movens



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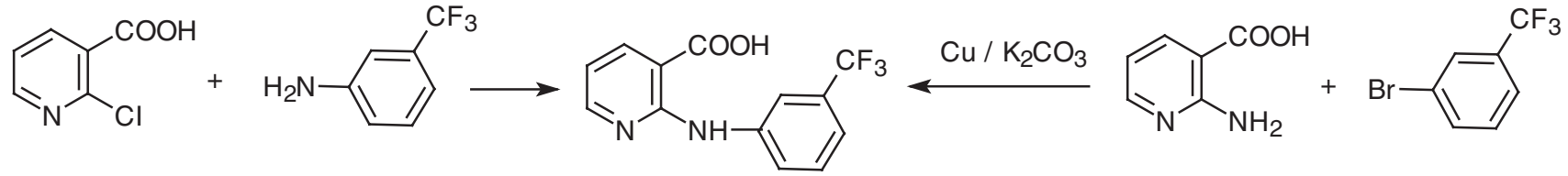
Niflumic acid:

Its action is similar to flufenamic acid.

Synonyms: actol, flunir, and nifluril



3.2.5 Propionic acid derivatives

This series of anti-inflammatory, analgesic, and fever-reducing compounds (ibuprofen, naproxene, ketoprofen, fenprofen) can be equally identified as both propionic acid derivatives as well as phenylpropionic acid derivatives.

The mechanism of their action has been suggested that it is also connected with the suppression of prostaglandin synthetase activity.

Ibuprofen:

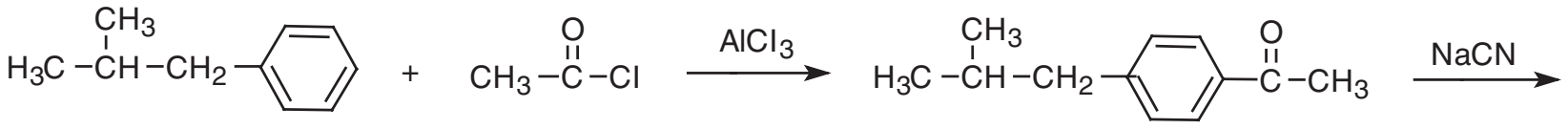
Ibuprofen is the first drug of the propionic acid derivatives that was permitted for clinical use. Ibuprofen exhibits analgesic, fever-reducing, and anti-inflammatory action comparable to, and even surpassing that of aspirin and acetaminophen.

It is tolerated better than aspirin, and side effects are rarely observed. It is used in treating rheumatoid arthritis, in various forms of articular and nonarticular rheumatoid diseases, as well as for pain resulting from inflammatory peripheral nerve system involvement, exacerbation of gout, neuralgia, myalgia, ankylosing spondylitis, radiculitis, traumatic soft-tissue inflammation, and in the musculoskeletal system.

It is used as an auxiliary drug in infections, inflammatory diseases of the ENT organs, adnexitis, dysmenorrhea, and for headaches and toothaches. It is not recommended for patients with stomach ulcers.

Synonyms: brufen, ibufen, motrin, and rebugen

Method 1



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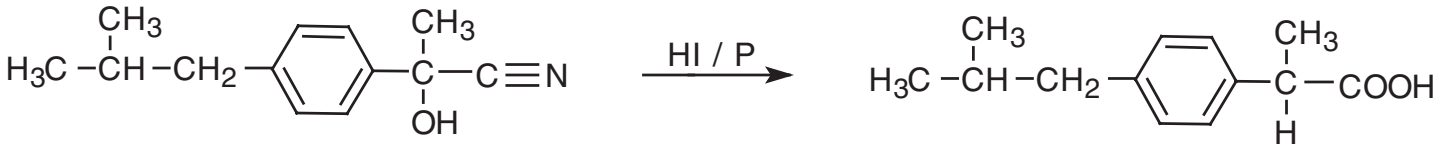

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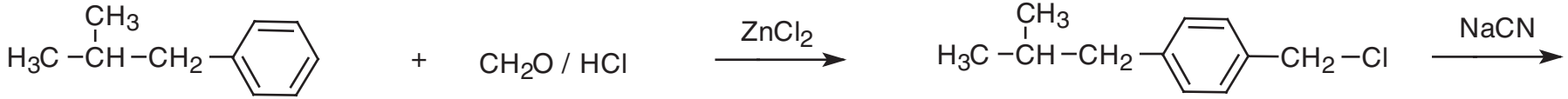
Method 2



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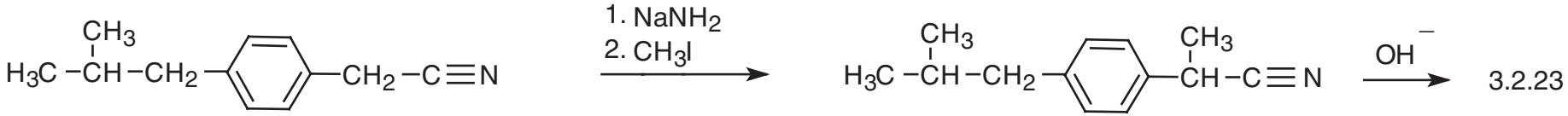

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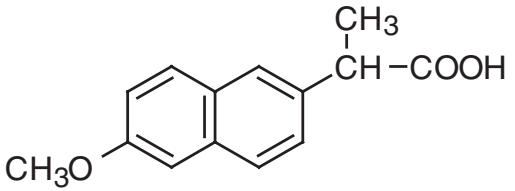
Naproxene:

It exhibits analgesic, fever-reducing, and long-lasting anti-inflammatory action.

It causes reduction and removal of painful symptoms including joint pain, stiffness, and swelling in the joints. It is used in the same indications as ibuprofen.

Synonyms: naprosyn, pronaxen, and apotex



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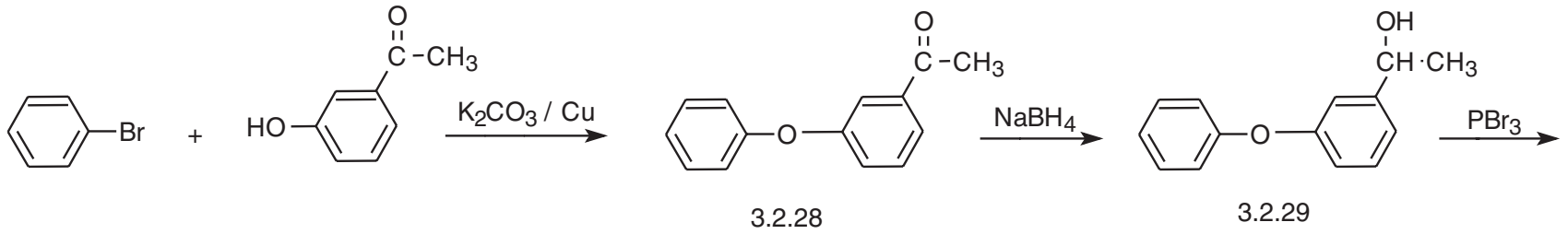
Fenoprofen:

It is used in treating symptoms of rheumatoid arthritis and osteoarthritis; however, fenoprofen exhibits a number of undesirable side effects.

Synonym: dista



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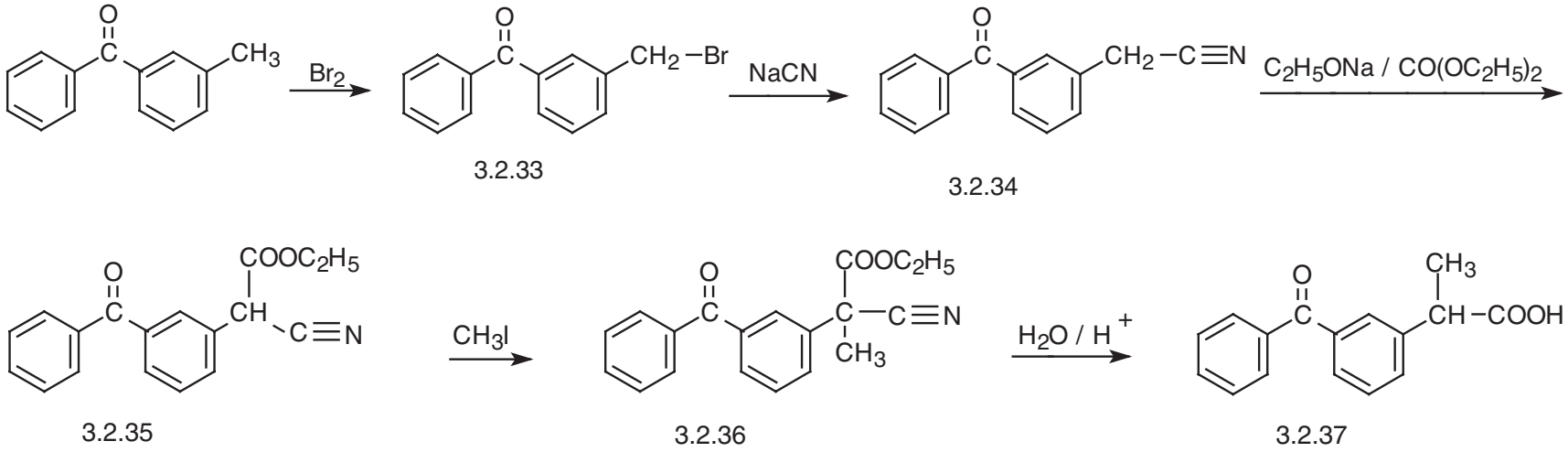
Ketoprofen:

Ketoprofen is used for relieving weak to moderate pain in rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, gout, back pain, neuralgia, and myalgia.

It is also used for mild trauma; in particular, in sporting injuries such as sprains or ligament and muscle ruptures.

It displays a number of undesirable side effects on hepatic and renal functions as well as on the gastrointestinal tract.

Synonyms: alrheumat, fastum, ketalgin, and reuprofen

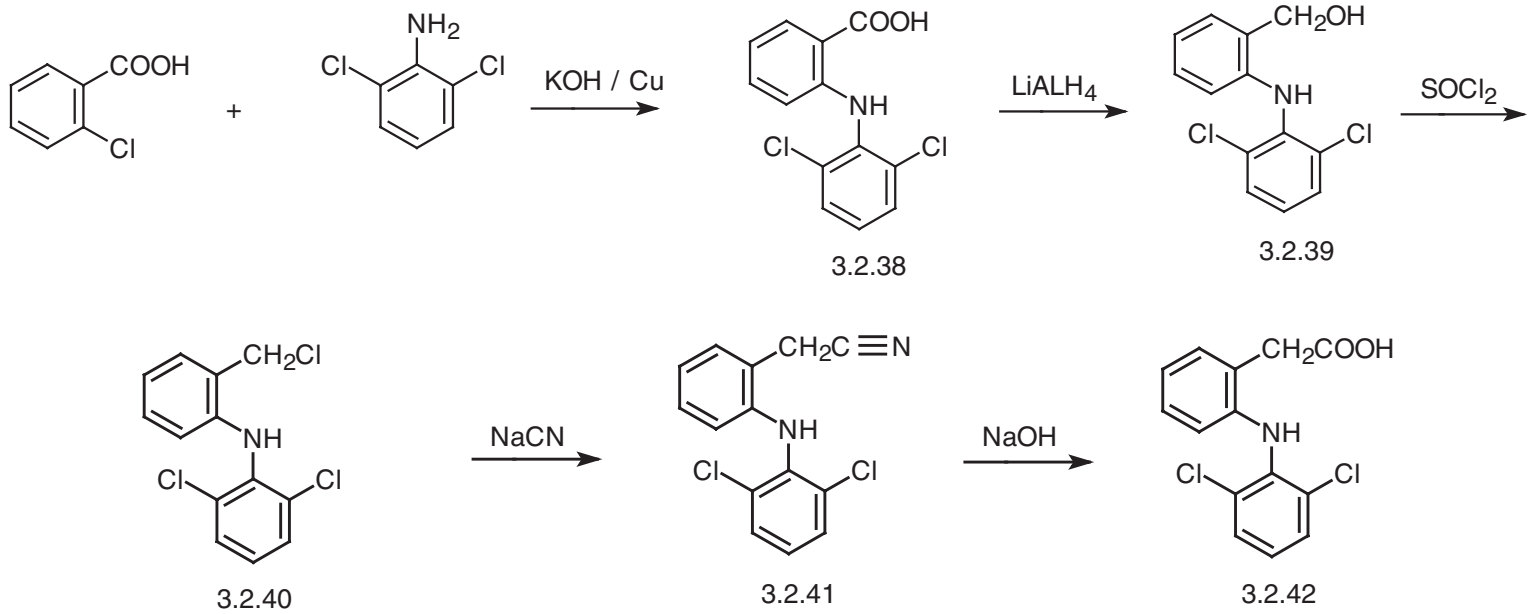


3.2.6 Acetic acid derivatives

There are acetic acid derivatives in particular (diclofenac, feclofenac, alclofenac) that are very widely used as anti- inflammatory, analgesic, and fever-reducing compounds.

Diclofenac:

Diclofenac possesses all of the properties unique to the series of propionic acid drugs, yet in terms of anti-inflammatory and analgesic strength it exceeds that of aspirin, analgin, and ibuprofen.



It is used in acute rheumatism, rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, arthrosis, back pain, neuralgia, and myalgia.

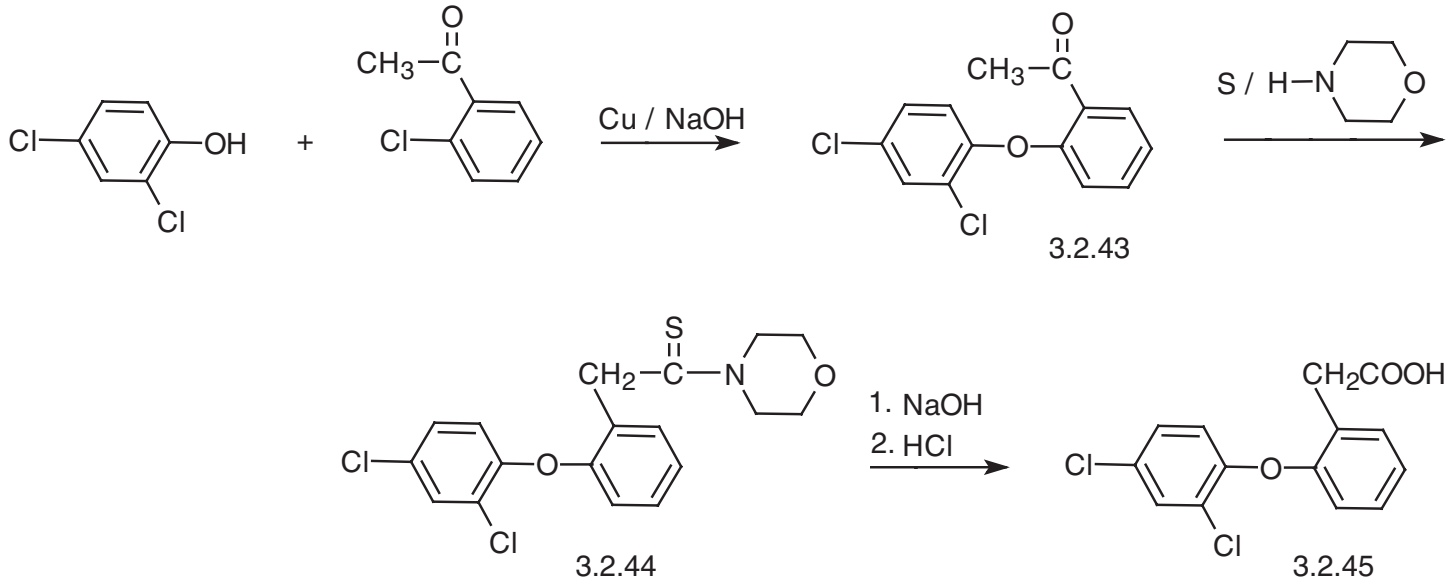
It rarely causes side effects.

Synonym: voltaren

Fenclofenac:

This drug is used for the same indications as diclofenac.

Synonym: flenac



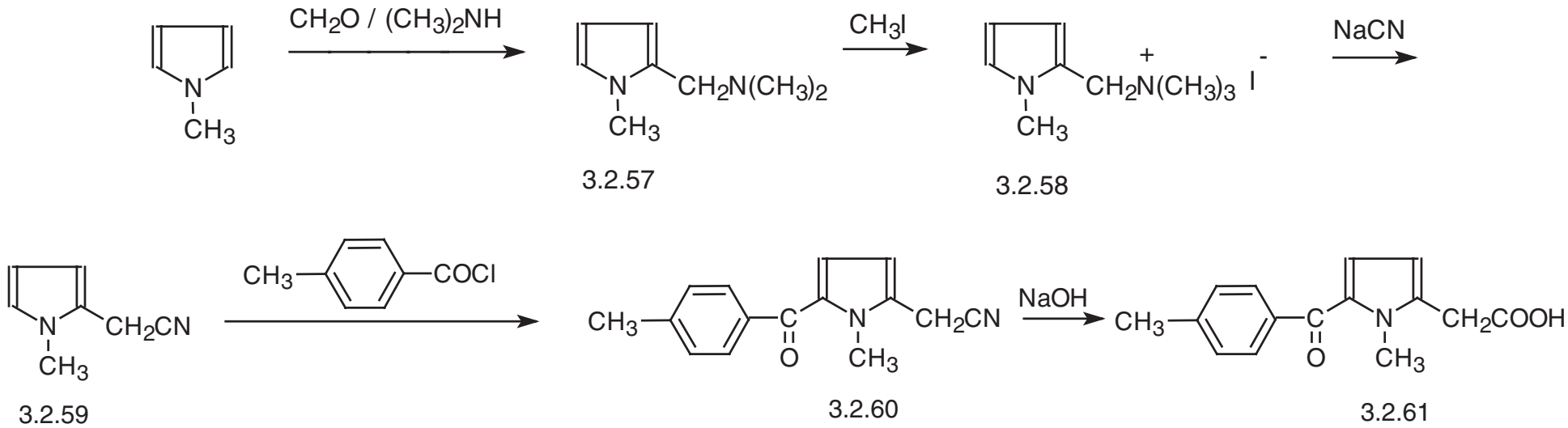
3.2.7 Indolyl/indeneacetic acids

Drugs of this series, indomethacin, tolmetin, sulindac, and others are very effective nonsteroidal anti-inflammatory drugs with strongly expressed analgesic action. They are strong inhibitors of prostaglandin biosynthesis.

Tolmetin:

It is used for relieving weak to moderate pain in rheumatoid arthritis and osteoarthritis.

Synonyms: tolectin and tolmex



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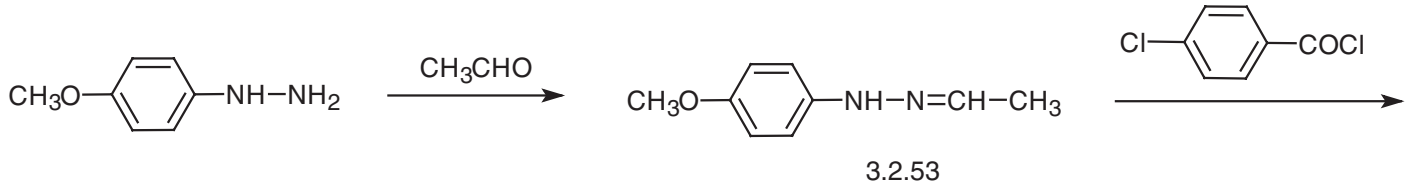
Indomethacin:

It is used in rheumatoid arthritis, nonspecific infectious polyarthritis, gouty arthritis, osteoarthritis, ankylosing spondylitis, arthrosis, back pain, neuralgia, myalgia, etc.



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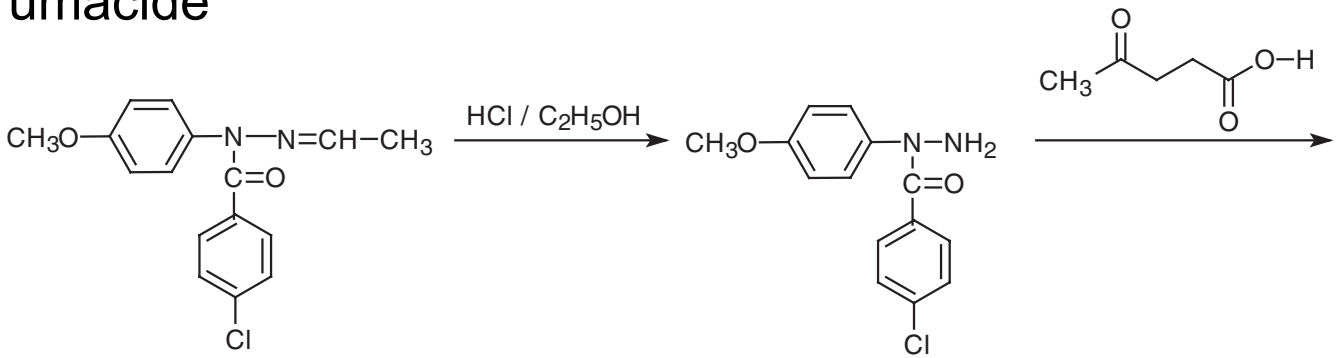
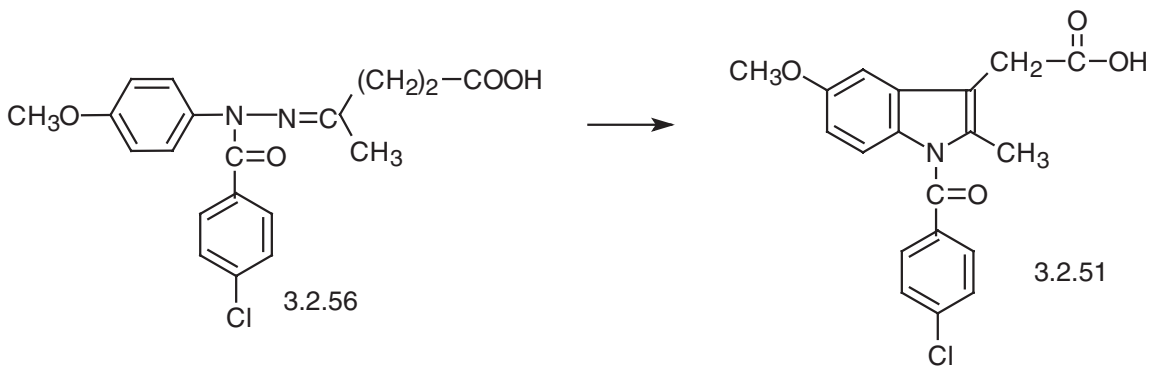
Synonyms: metindol, indacide, and rumacide





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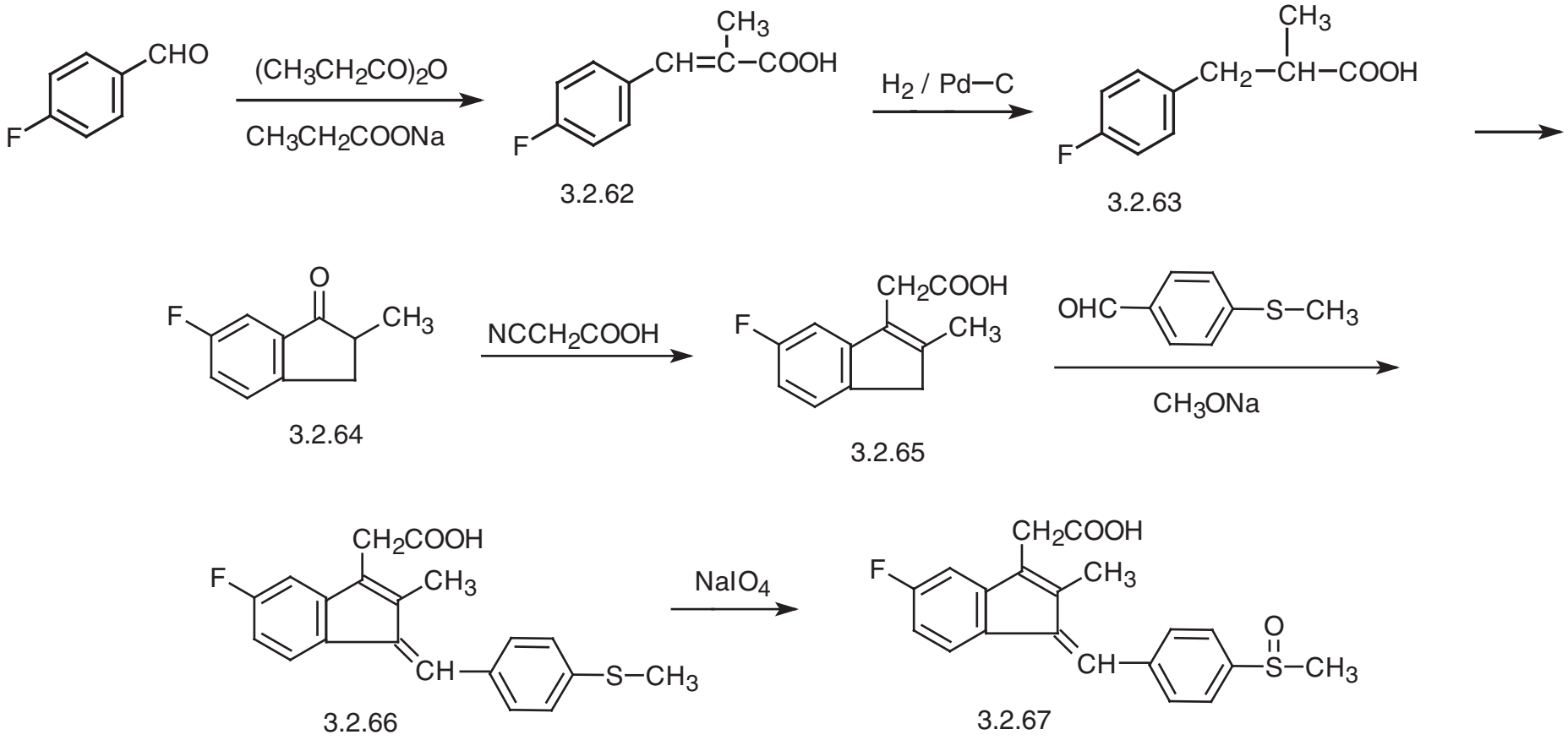
Sulindac:

It is used for relieving weak to moderate pain in rheumatoid arthritis and osteoarthritis.

Synonyms: suprol and imbaral

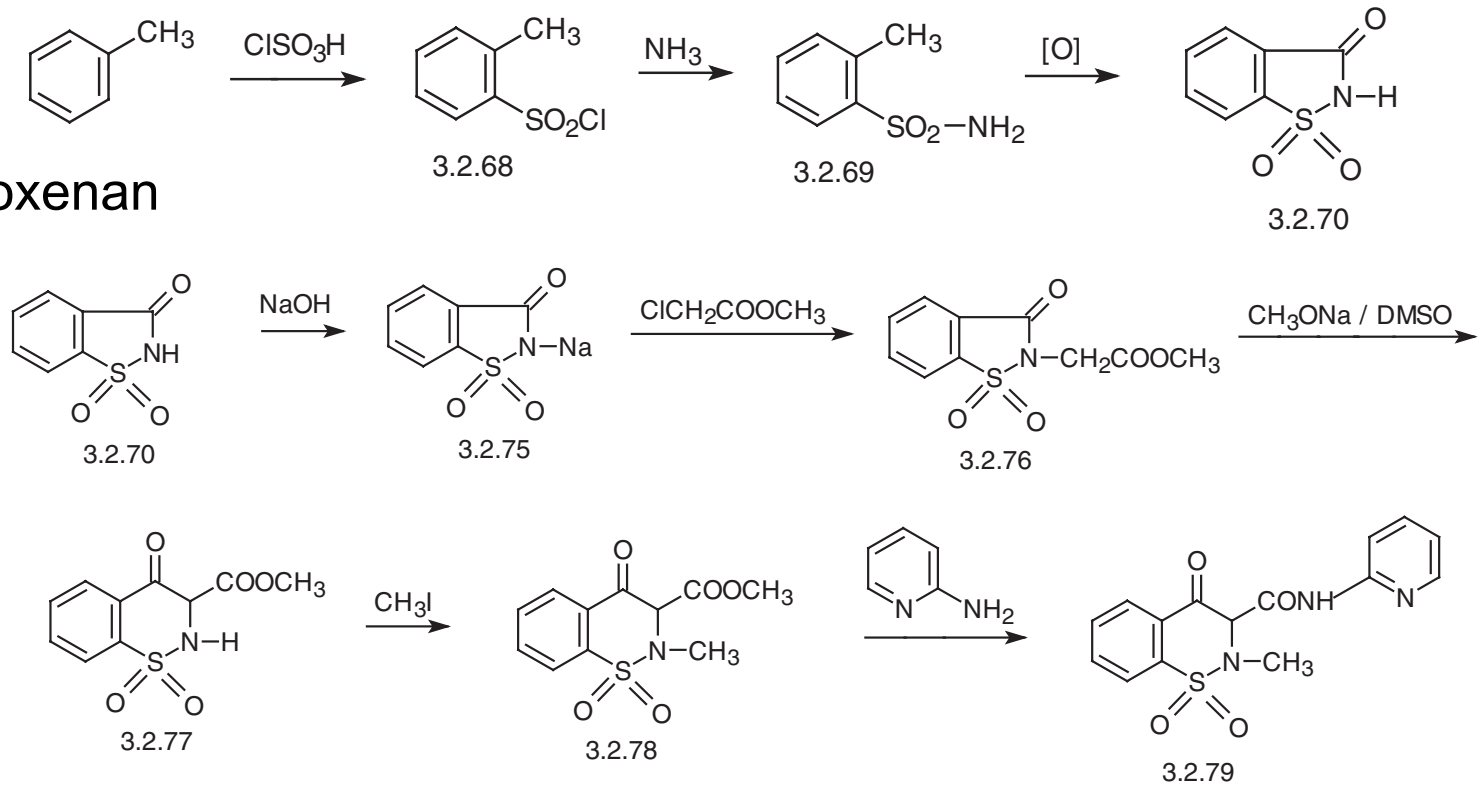


3.2.8 Oxicames

Oxicames are another series of anti-inflammatory, analgesic, and fever-reducing compounds whose mechanisms of action are most likely the suppression of prostaglandin synthesis. These drugs are capable of relieving painful symptoms of medium intensity.

Piroxicam:

Synonyms: feldene, dexicam, and roxenan



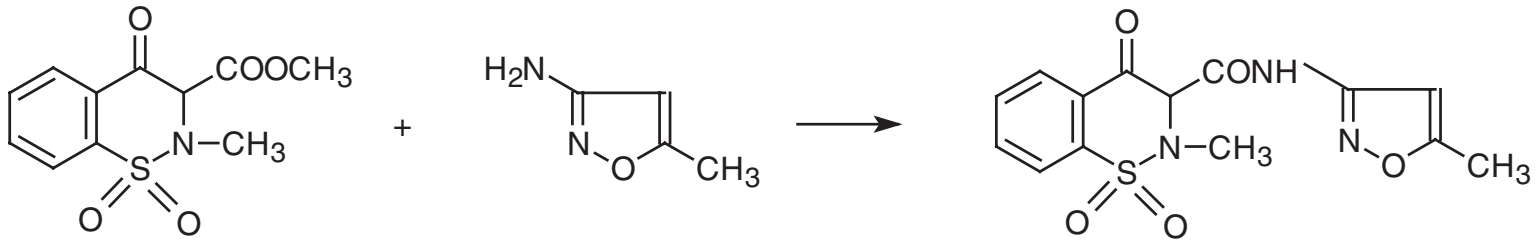
It is used in inflammatory and degenerative diseases of the musculoskeletal system that are accompanied by painful symptoms.

It is used for rheumatic heart disease, nonspecific infectious polyarthritis, gouty arthritis, rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, arthrosis, back pain, neuralgia, myalgia, and other diseases associated with inflammation.

Isoxicam:

It is used for the same indications as piroxicam.

Synonyms: floxicam and maxicam



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