

Amit

General anesthetics:

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①

Inhalation anesthetics: Halothane*, Methoxyflurane, Enflurane, Sevoflurane, Isoflurane, Desflurane.

Ultra short acting barbiturates: Methohexital sodium*, Thiamylal sodium, Thiopental sodium.

Dissociative anesthetics: Ketamine hydrochloride.*

②

Narcotic and non-narcotic analgesics

Morphine and related drugs: SAR of Morphine analogues, Morphine sulphate, Codeine, Meperidine hydrochloride, Anilerdine hydrochloride, Diphenoxylate hydrochloride, Loperamide hydrochloride, Fentanyl citrate*, Methadone hydrochloride*, Propoxyphene hydrochloride, Pentazocine, Levorphanol tartarate.

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Narcotic antagonists: Nalorphine hydrochloride, Levallorphan tartarate, Naloxone hydrochloride.

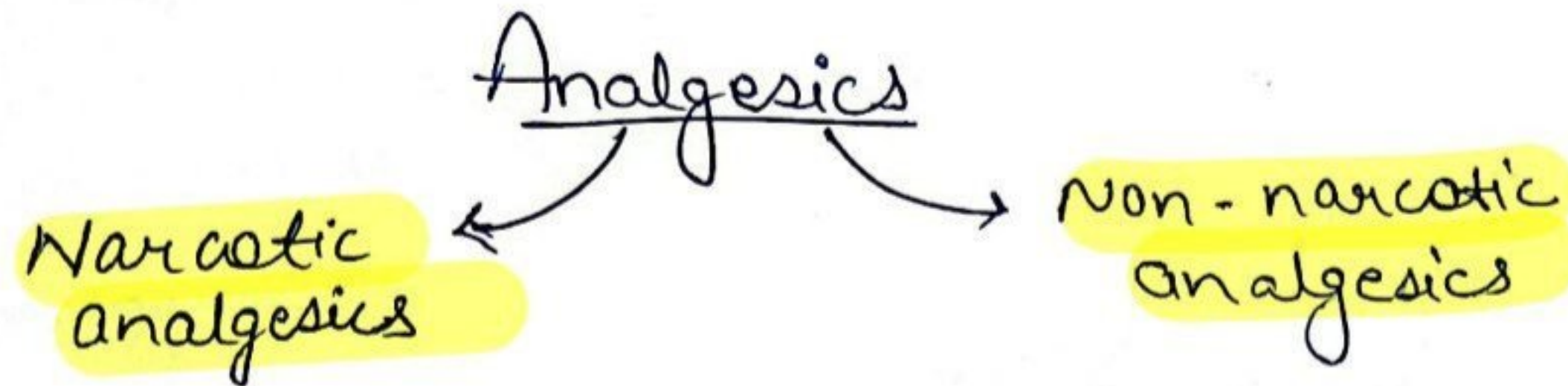
X

Anti-inflammatory agents: Sodium salicylate, Aspirin, Mefenamic acid*, Meclofenamate, Indomethacin, Sulindac, Tolmetin, Zomepirac, Diclofenac, Ketorolac, Ibuprofen*, Naproxen, Piroxicam, Phenacetin, Acetaminophen, Antipyrine, Phenylbutazone.

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Opioid analgesics ÷

Analgesics - a drug that selectively **relieves pain** by acting in **CNS** or on peripheral pain mechanism



1) Narcotic analgesics - Also known as **opioid pain** **relievers**. **Use in severe pain.**

→ Opioids - Any drug which binds to opioid receptor in CNS and antagonized by Naloxone.

Narcotics - Drugs derived from opium or opium like compounds, with potent effects associated with significant alteration of mood & behavior.

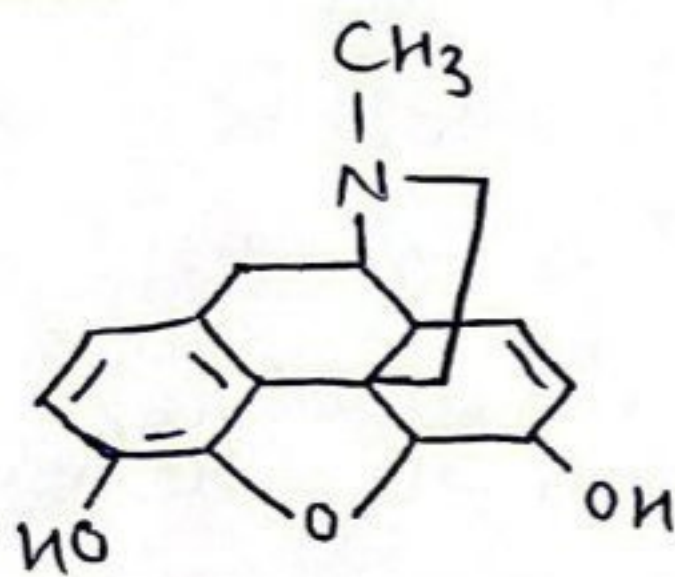
Opium → a dark brown, resinous material obtained from Poppy [Papaver somniferum] capsules.

* Actions associated with narcotic analgesics are sedation and constipation.

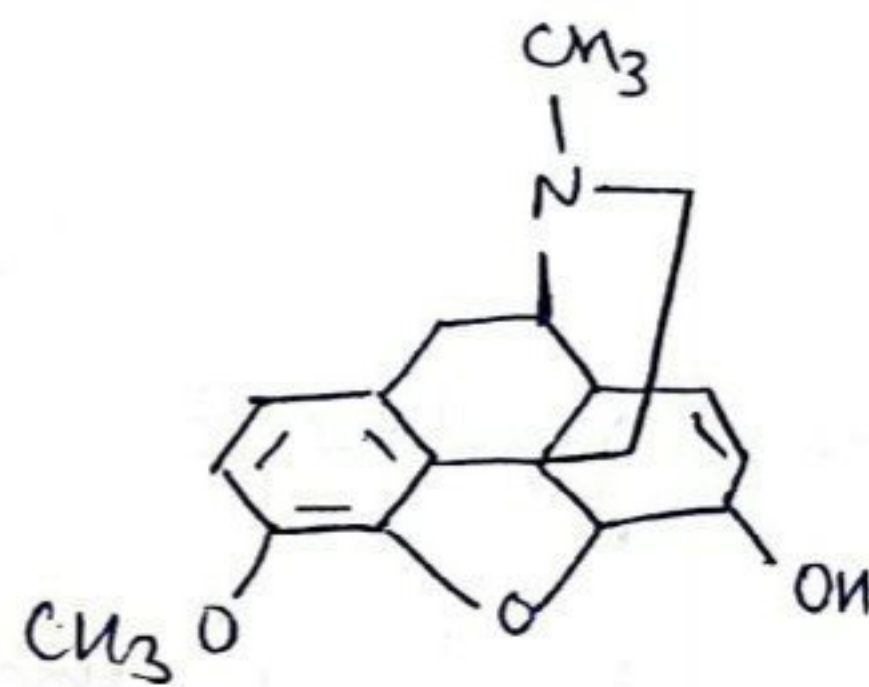
→ In therapeutic doses, morphine sometimes produce nausea or vomiting.

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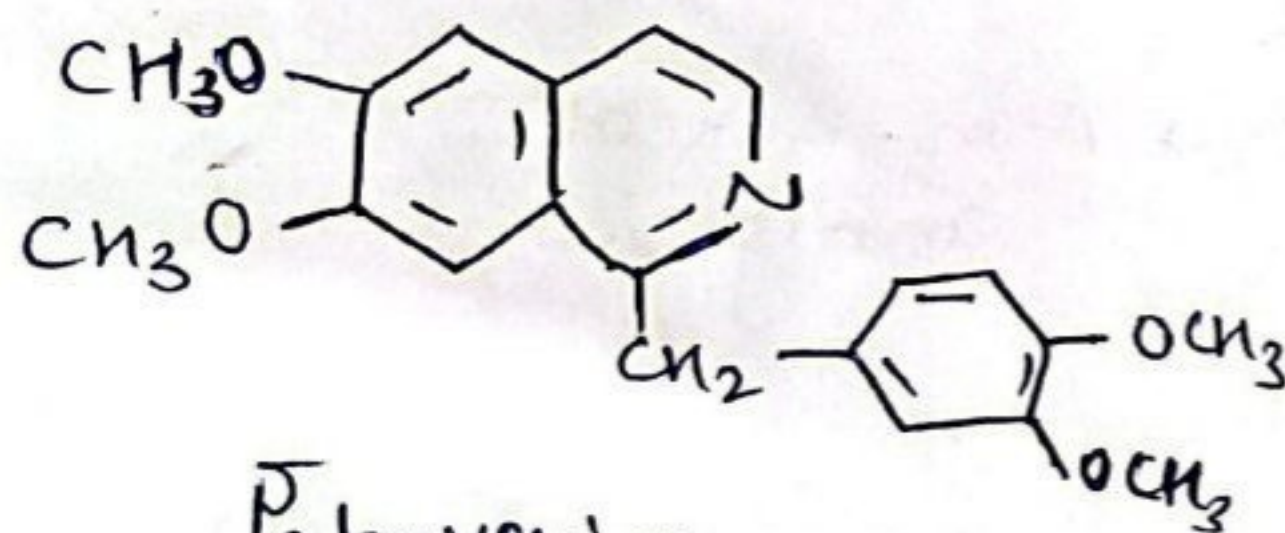
Opium alkaloids ÷



morphine



Codeine



Papaverine

(Change in mood, feeling behaviour)

affect the
↑ Brainwork.

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* Morphine is a potent opiate analgesic psychoactive drug.

- It relieves pain by directly acting on CNS.

- It is high potential for addiction.

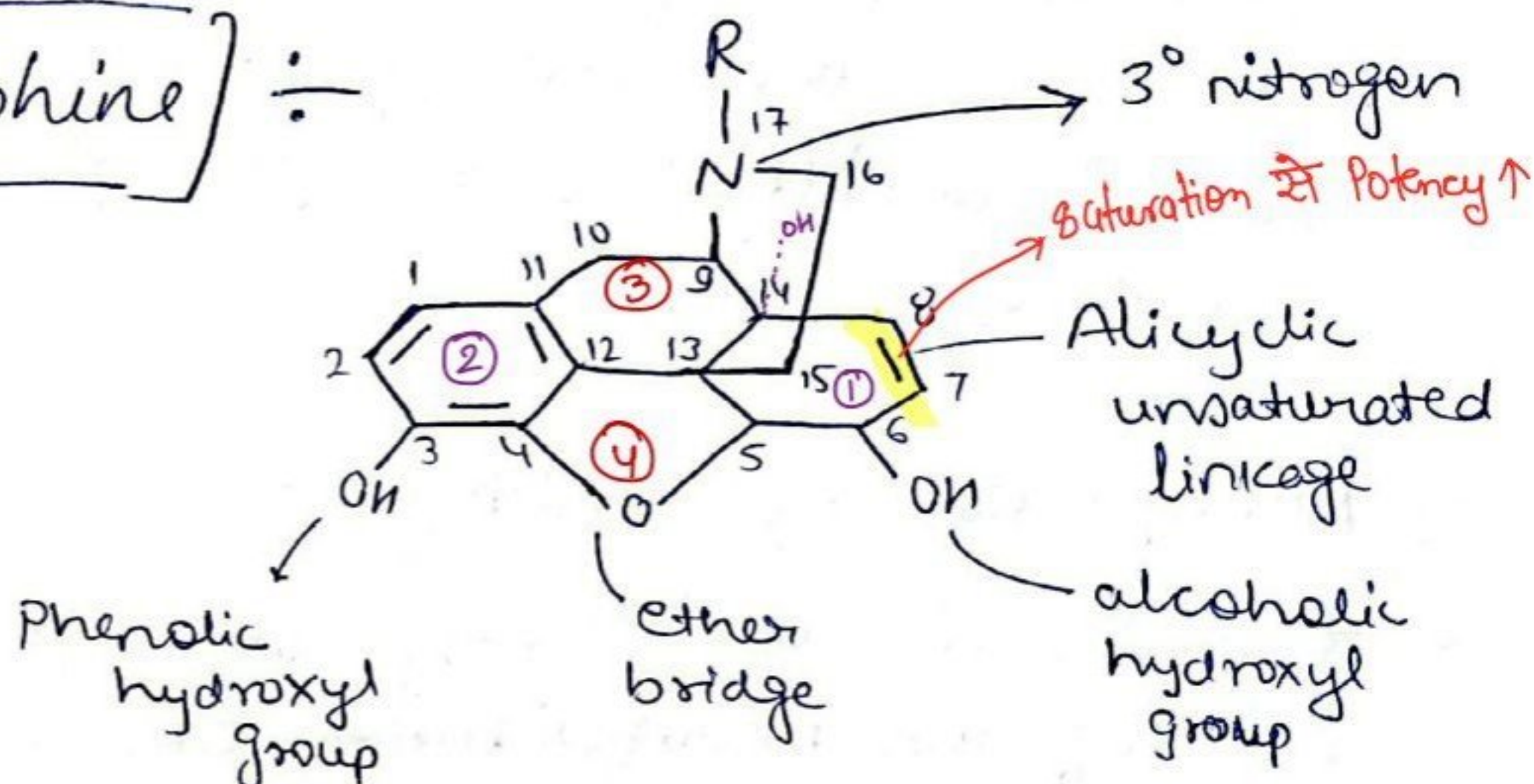
- Morphine analogues are closely related to morphine structure & are even synthesized from it.

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- * Morphine uses - analgesia, diarrhoea, relief cough, anaesthesia & pre-anaesthesia

[SAR of morphine] ÷

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1] Modification in alicyclic ring ⇒

- C₆ = alcoholic hydroxyl group at C-6 when esterified, oxidized, methylated, removed or replace by halogen then analgesic activity and toxicity of compound increased.
- C₆ - reduction of keto group to hydroxyl group in Oxymorphone gives Nalbuphine. Oxymorphone at reduction of keto group into OH group give Nalbuphine.
- C₇ = saturation of double bond gives Potent compound

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eg - Dihydromorphine

- The 14β-hydroxyl group generally enhance agonistic properties and decrease antitussive activity.
- Bridging of C₆ and C₄ through ethylene linkage gives potent derivative.

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2] Modification of phenyl ring

- Aromatic phenyl ring is essential for activity
- Phenolic hydroxyl group modification leads to decrease the activity.
- Any substitution on phenyl ring diminishes activity.

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3] Modification of 3° nitrogen →

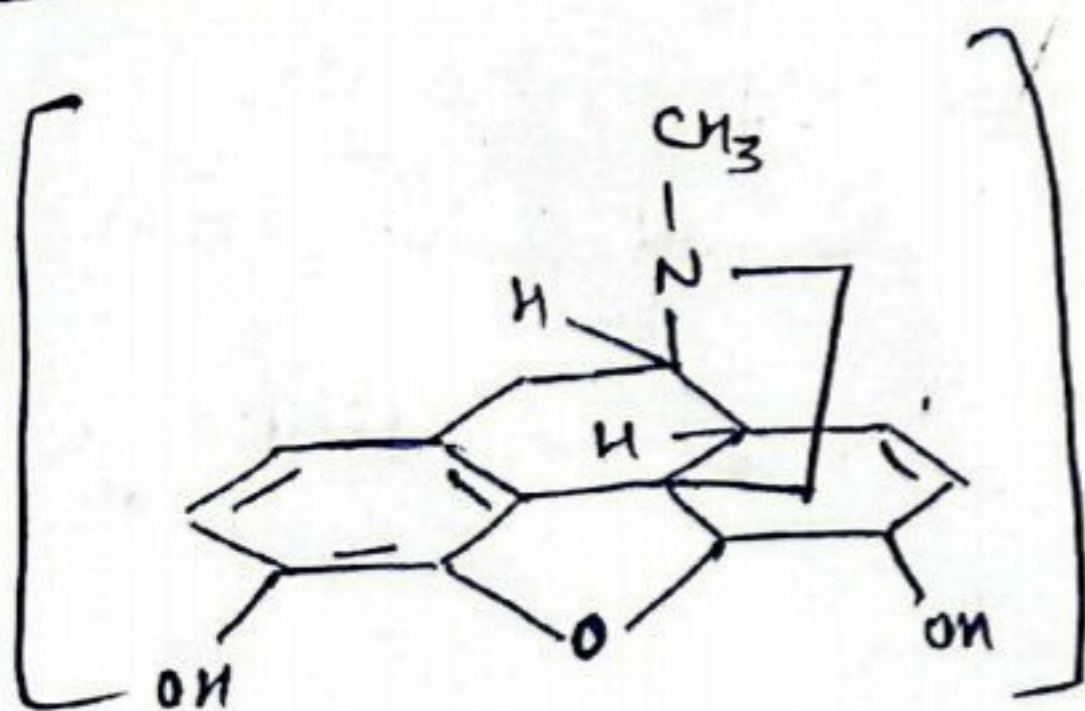
- 3° amine is necessary for good activity.
- Size of the N substitution can dictate the compounds potency and its agonist and reverse antagonist activity.
- N-methyl substitution is having good agonistic property
- Size increase by 3-5 carbon results in antagonistic activity.

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4] Epoxide bridge →

- Removal of 4,5 epoxide bridge in morphine structure results in the compound that is morphinans.
- morphinans prepared synthetically.

Morphine sulphate →

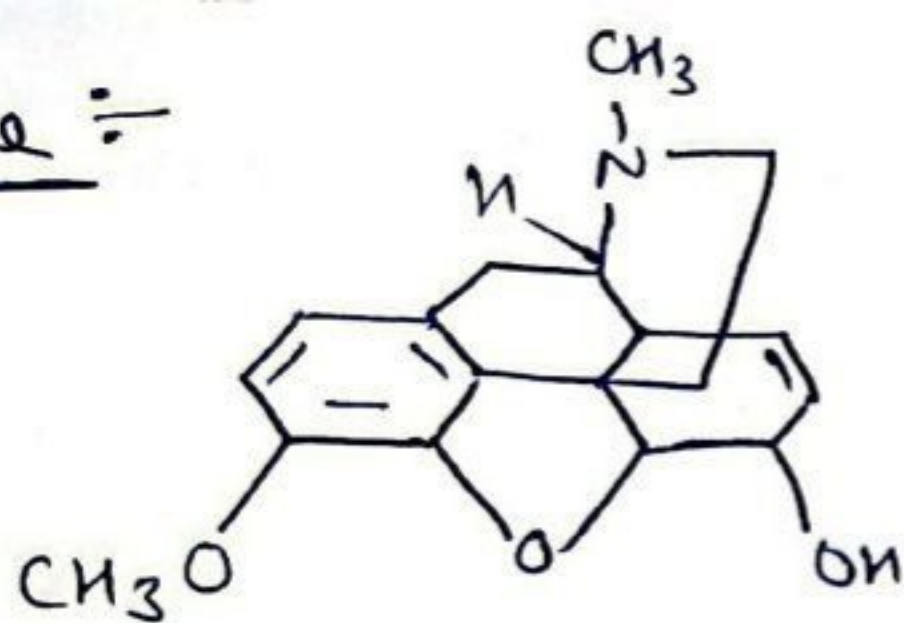


uses → to treat severe pain

→ inhibition of cough reflex.

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Codeine :-



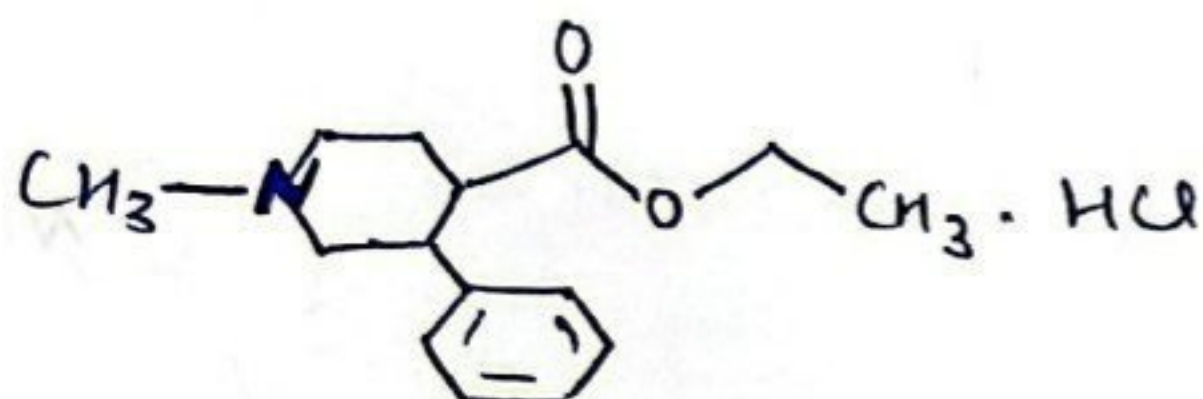
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uses - for treating and managing pain

→ antidiarrheal and cough suppressant

Meperidine hydrochloride -

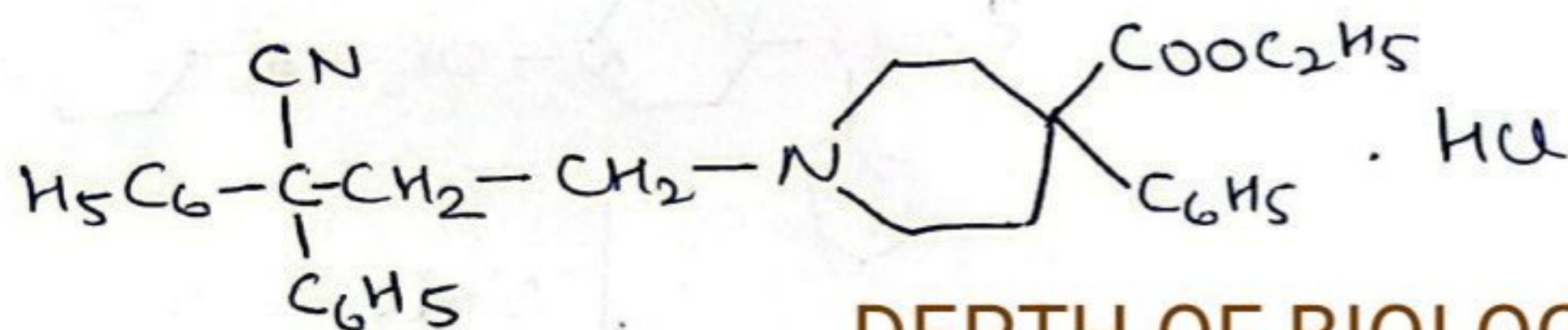
It is narcotic analgesic



uses ⇒ for controlling moderate to severe pain

Diphenoxylate hydrochloride

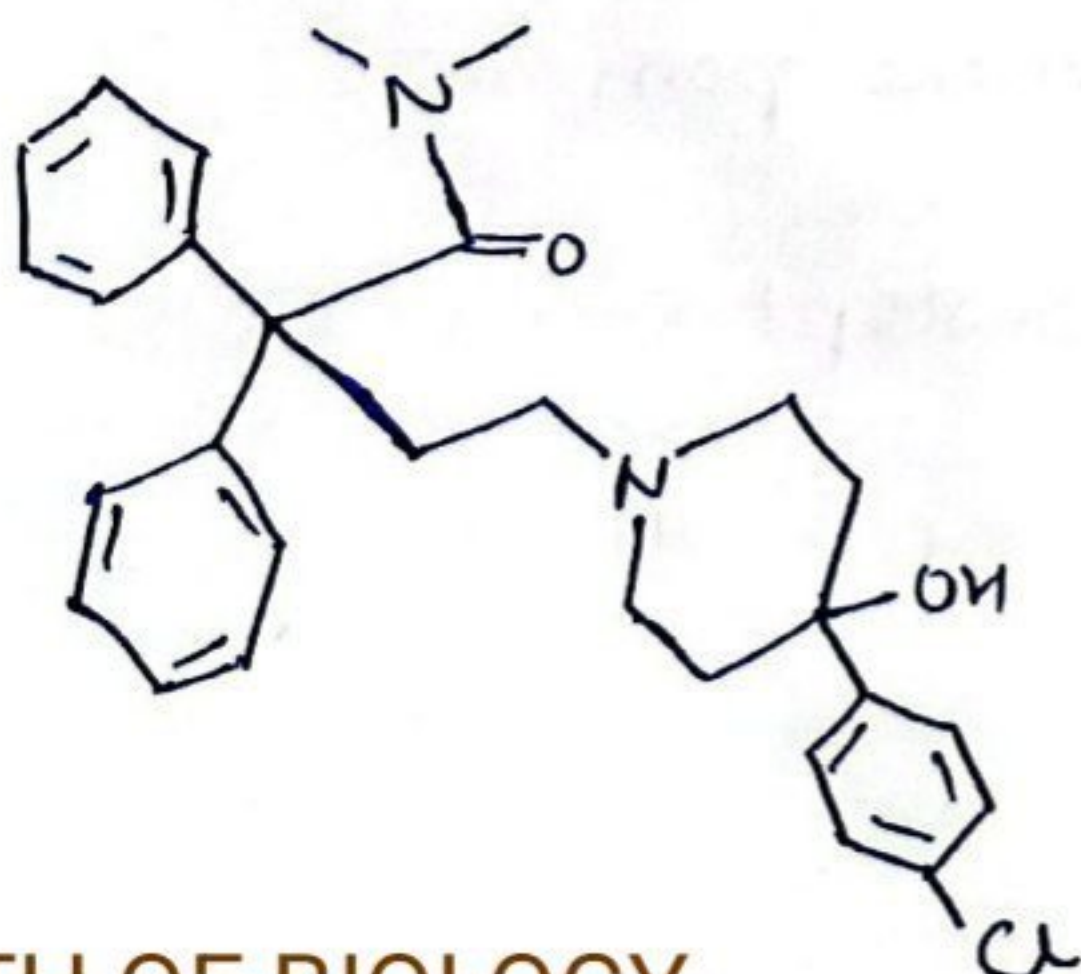
→ it acts like morphine in higher dose



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uses ⇒ use in managing diarrhoea

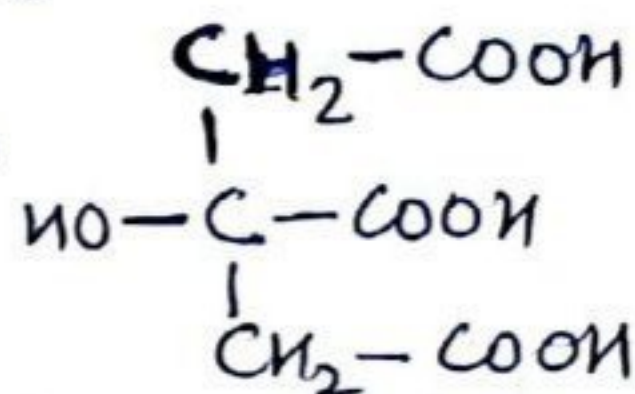
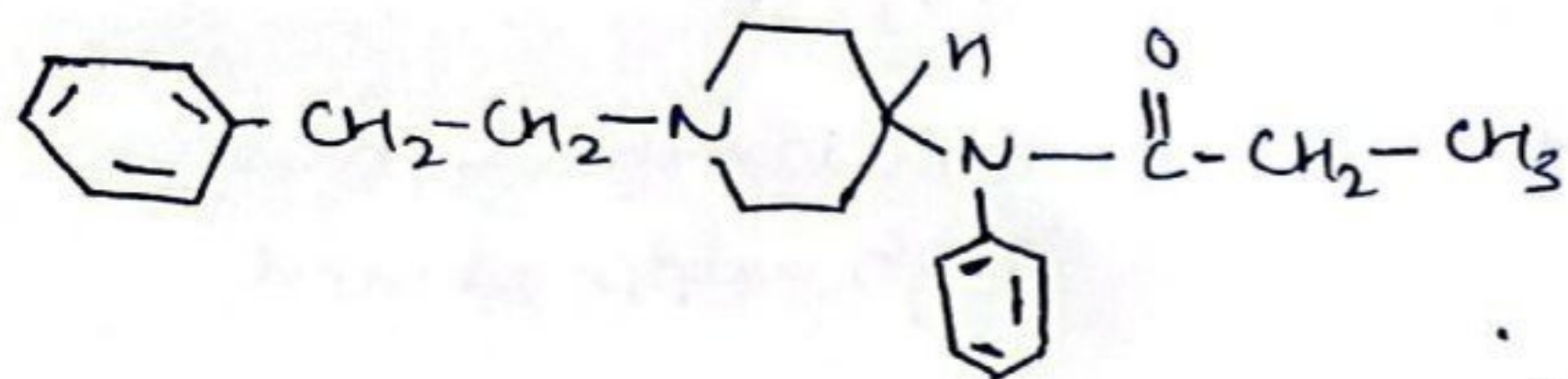
Loperamide HCl → It is a long acting synthetic antidiarrheal which is not absorbed in gut



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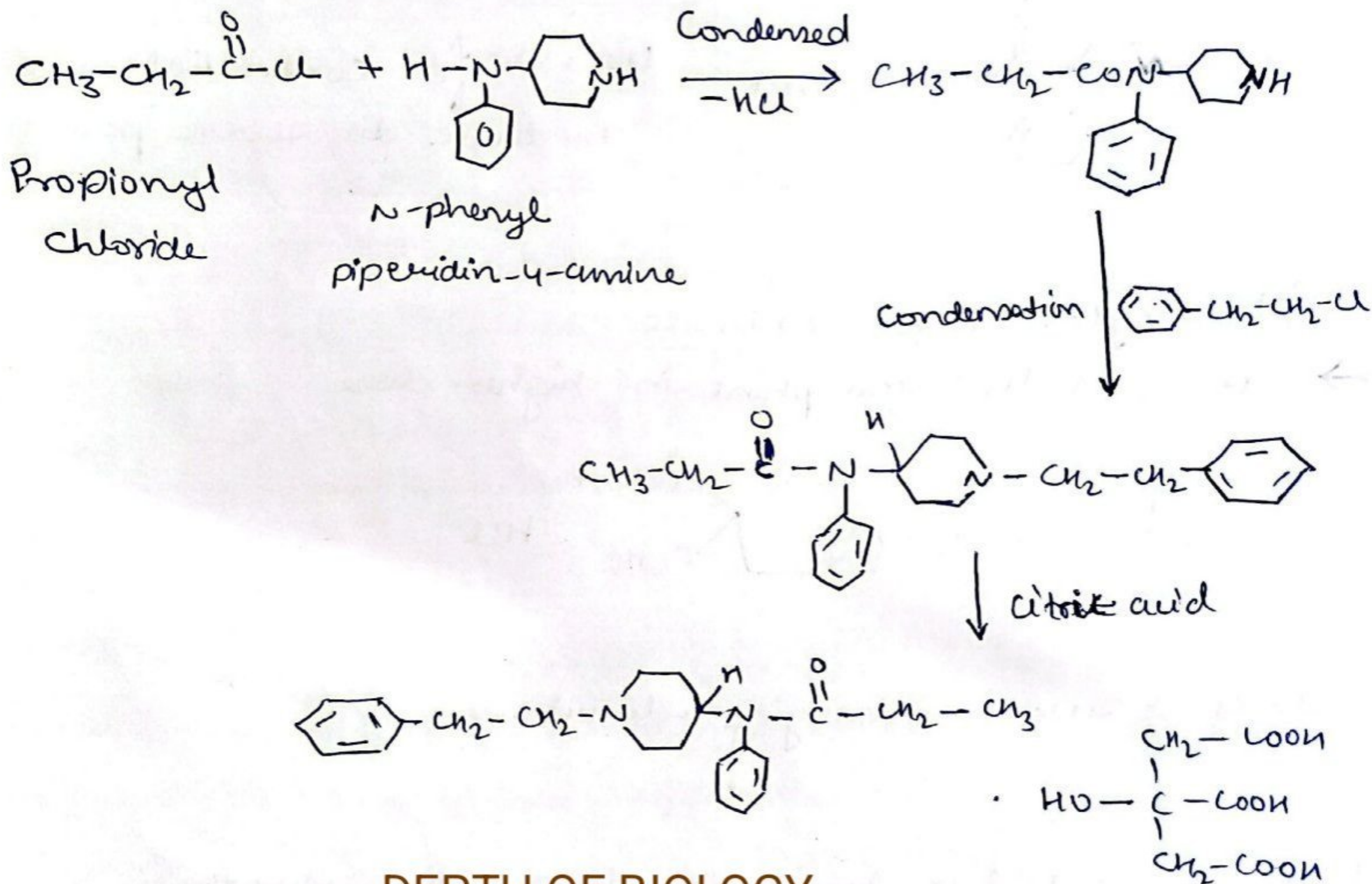
uses ⇒ for controlling the symptoms of diarrhoea

Fentanyl citrate $\Rightarrow$ potent narcotic analgesic



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Synthesis $\rightarrow$



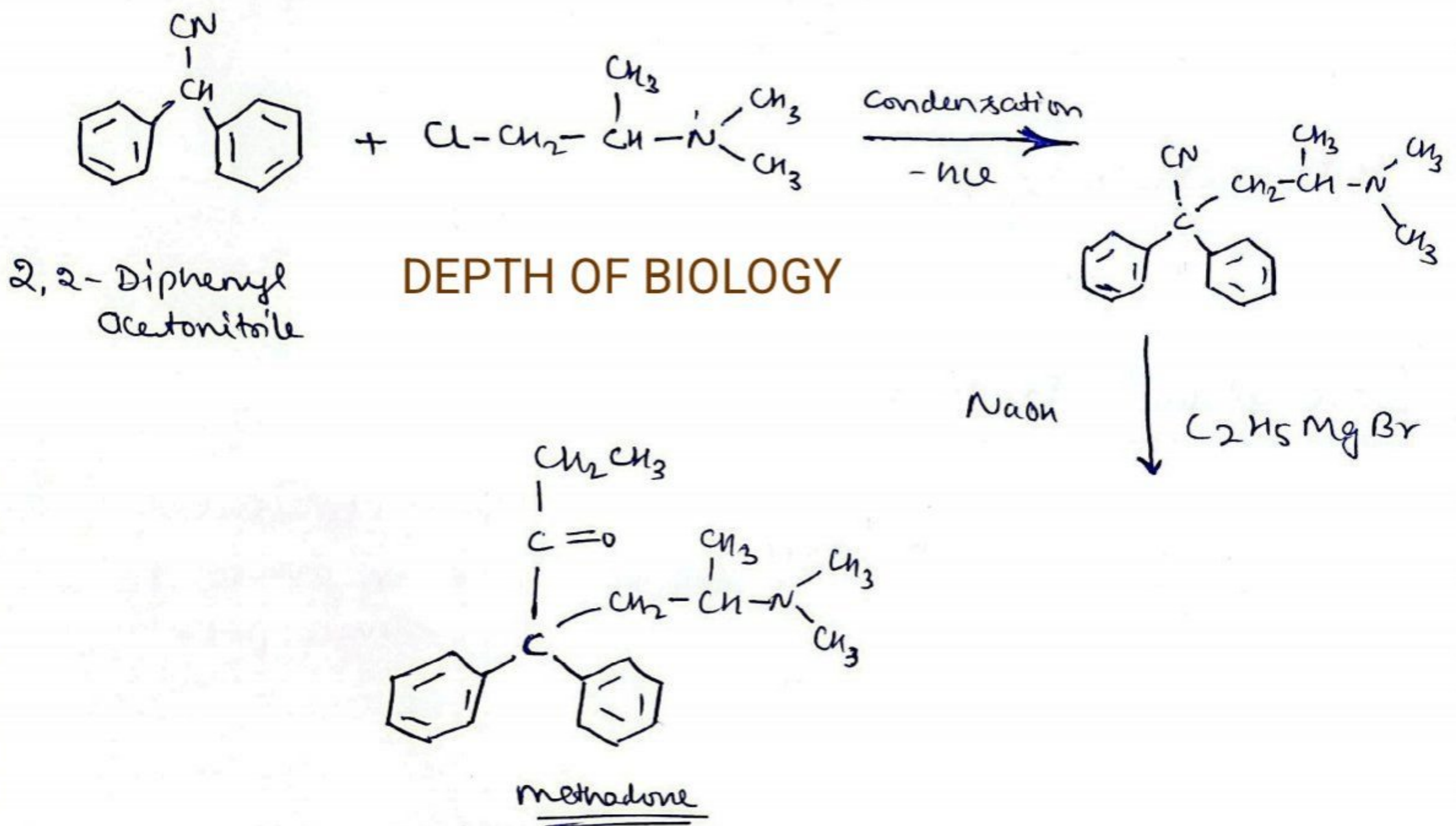
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Uses - in regular narcotic therapy for treating cancer patients having severe pain

- It binds to the opioid receptor in CNS.
- It is also used during anesthesia for surgery

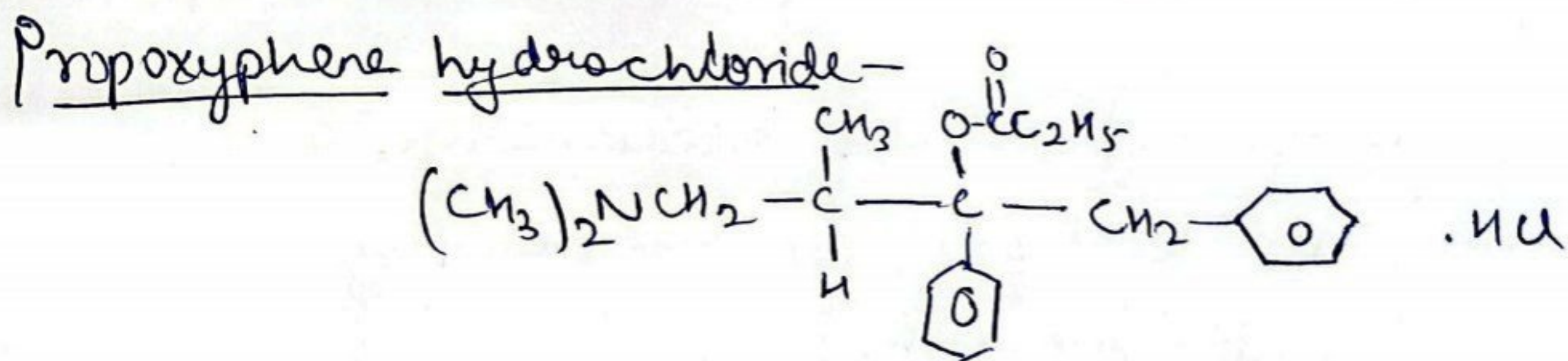
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Methadone HCl — Synthesis



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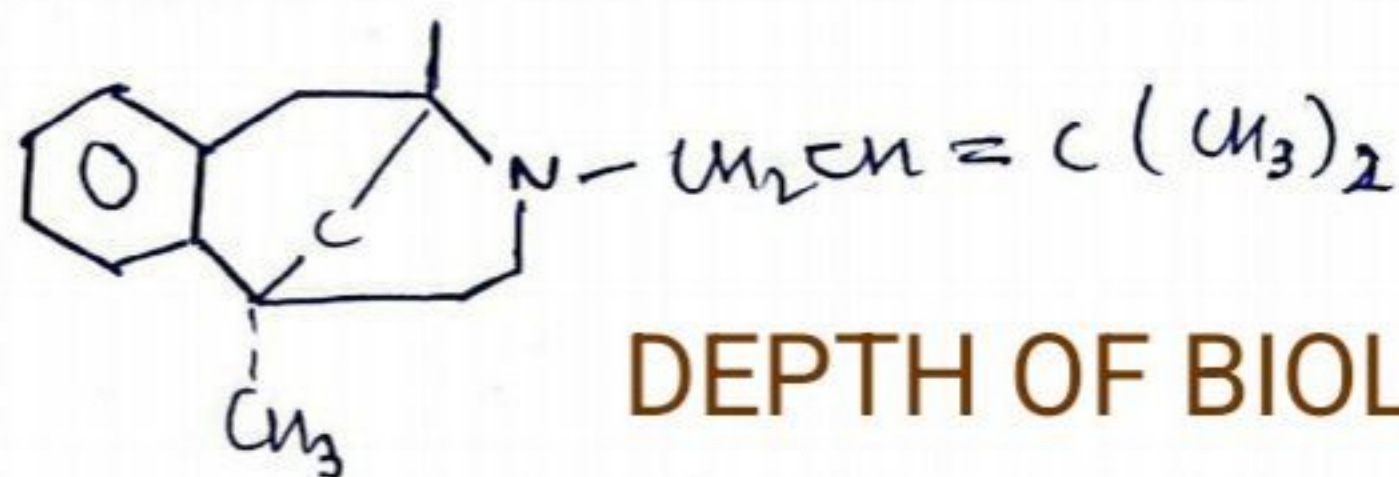
Uses $\Rightarrow$ use to treat dry cough, pain, drug withdrawal syndrome and opioid drug dependence



uses — relieving mild to moderate pain

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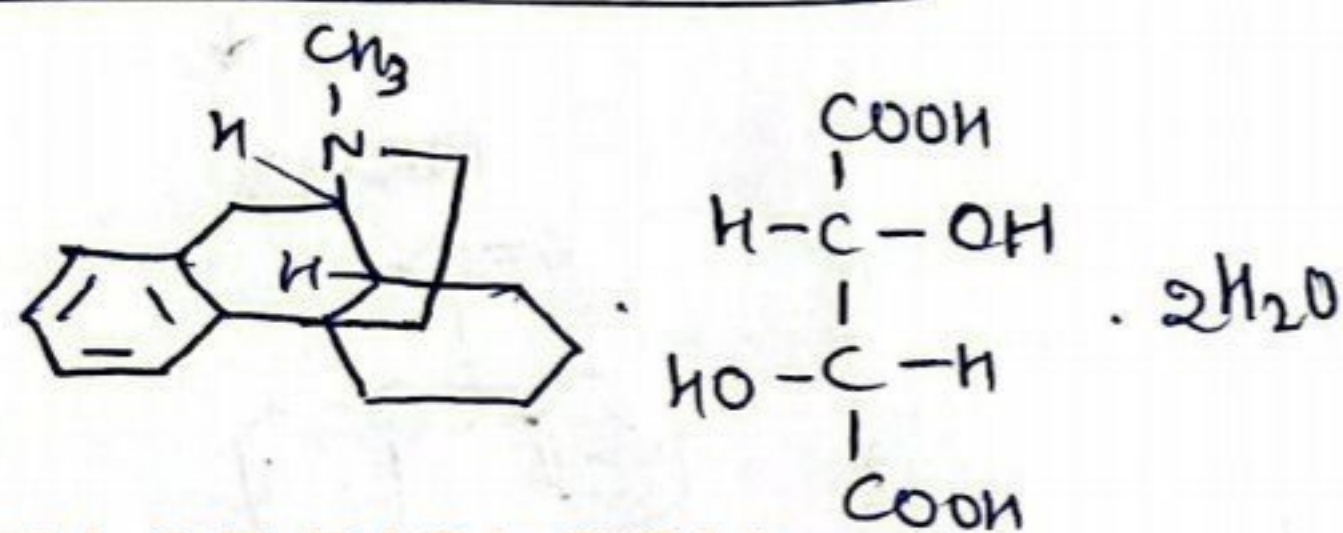
Pentazocine -



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Uses - relieving moderate to severe pain

Leverphanol tartrate -



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Use - to treat moderate to severe pain

Narcotic antagonists -

Drugs that are competitive antagonists that bind to opioid receptors with higher affinity than agonists but do not activate the receptor.

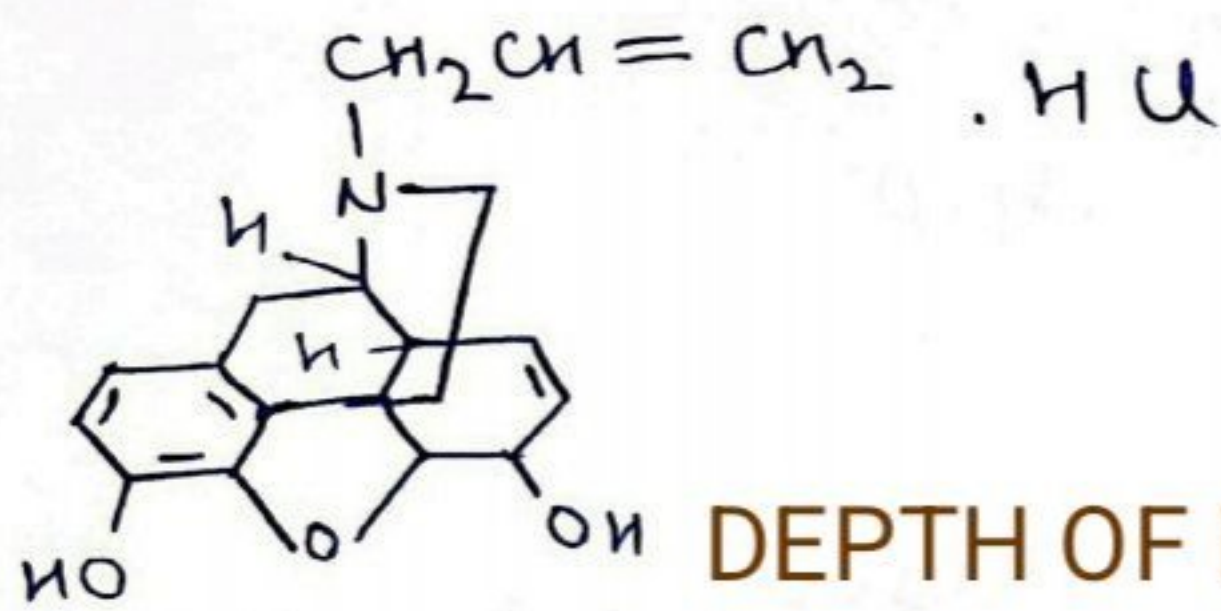
→ These drugs effectively blocks the receptor preventing the body from responding to opioids and endorphins.

eg - Nalorphine HCl
Naloxone HCl

(Hormone / Chemical)
↓
release at time of
pain & stress.
(reduce stress)
(pain relief).

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1) Nalorphine hydrochloride

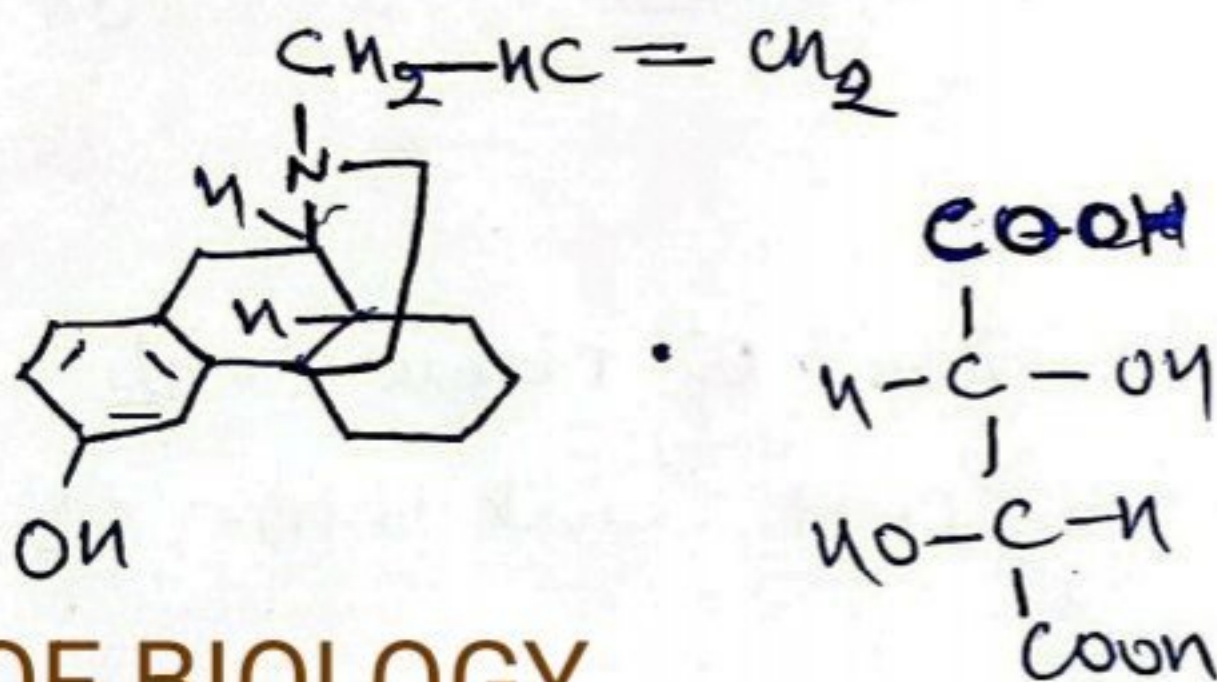


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Use - to reverse opioid overdose and in challenge test to determine opioid dependence.

→ It is effective against morphine, methadone, meperidine etc.

2) Lorazepam tartarate

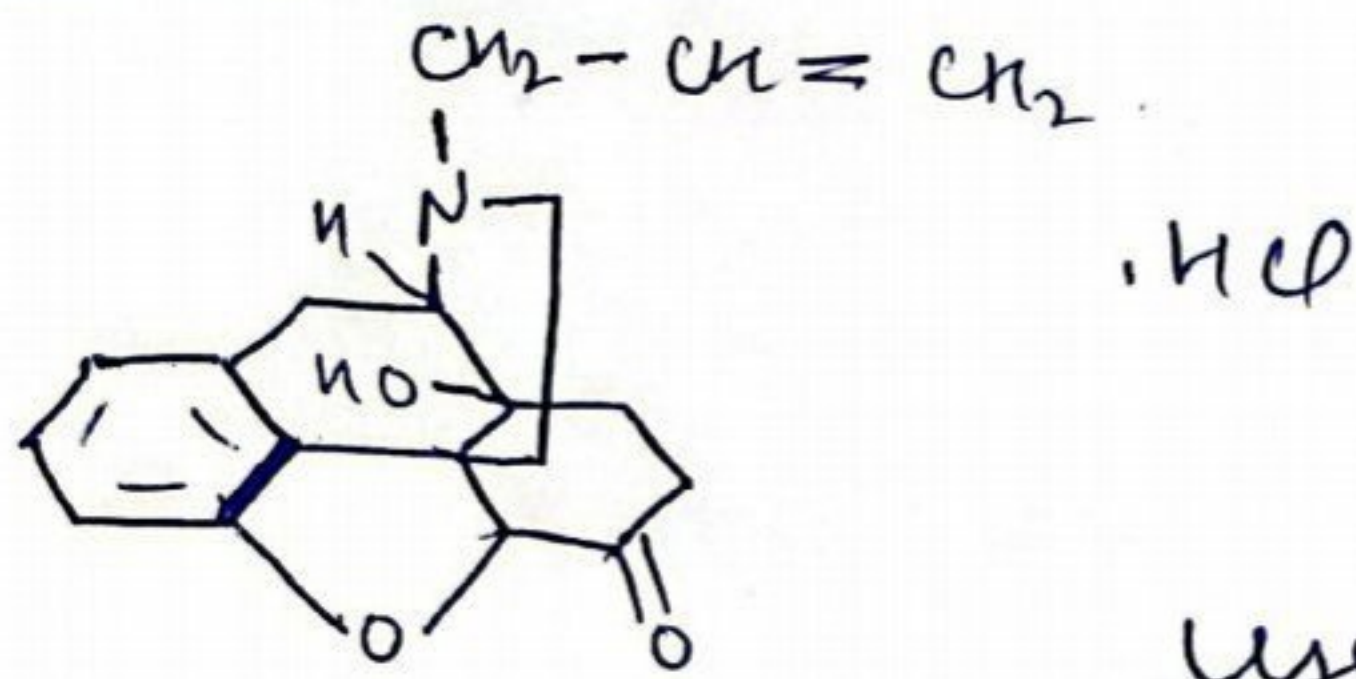


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Use - Treatment of respiratory depression due to narcotic overdose.

→ It reverses the effects of opioid including respiratory depression, sedation & hypotension

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3) Naloxane hydrochloride

Uses - it reverse the opioid overdose

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[MOA of Narcotics] → [morphine]

→ Morphine has an affinity delta, Kappa and Mu - opioid receptor. This drug produce most of its analgesic effects by binding to mu-opioid receptor.
Or we can say morphine direct work on opioid receptor in CNS.

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- Opioids cause hyperpolarisation of nerve cell lead to inhibition of neuronal firing and inhibition of neurotransmitter release.
- Opioids rising the pain threshold at the spinal cord level — and more importantly by altering the brain perception of pain

• Morphine

Agonistic

μ

Sedation.

Analgesia

Constipation

Resp. ↓

Miosis (constricted pupil.)

Euphoria

κ

Dysphoria (unhappiness)

Constipation

Analgesia

σ

• Spinal Analgesia

• Modf. of Hormone release.