



Common Pain Killers
Miscellaneous Factoids and Information

Chemistry Inspired by Pain

February 16, 2007

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Aspirin™* - acetyl ester of naturally occurring salicylic acid



Tylenol™ - acetaminophen



*Trade make in Canada but this was lost in the US after WWI.



Ibuprofen

DOCTORS AND PHARMACISTS RECOMMEND ALEVE FOR SAFE, LONG-LASTING PAIN RELIEF



Aleve



Vioxx™



Vicodin™



OxyCotin™

Percodan™ - with aspirin

Pecoset™ - with acetaminophen



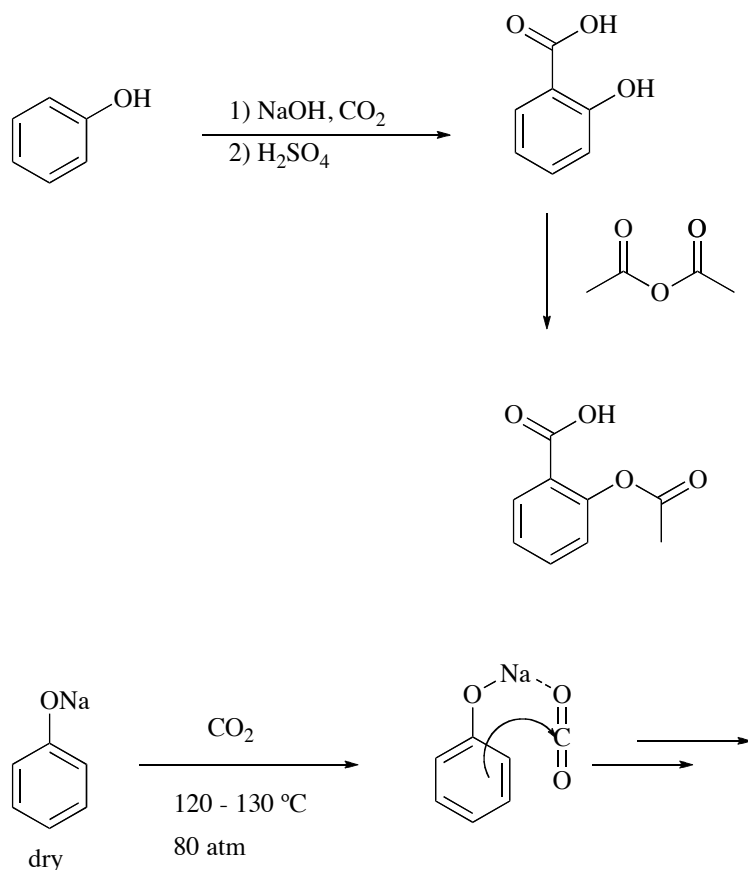
Fentanyl™



Aspirin



Kolbe-Schmit Reaction



- 5th Century BC willow bark extract
- Isolated in 1828 by Henri Leroux
- First Synthesis in 1853 by LaFont
- Kolbe first did this in 1860 at 1 atm, < 50 %
- Schmit ran it under pressure in quantitative yield.



Aspirin : New Crystal Structure

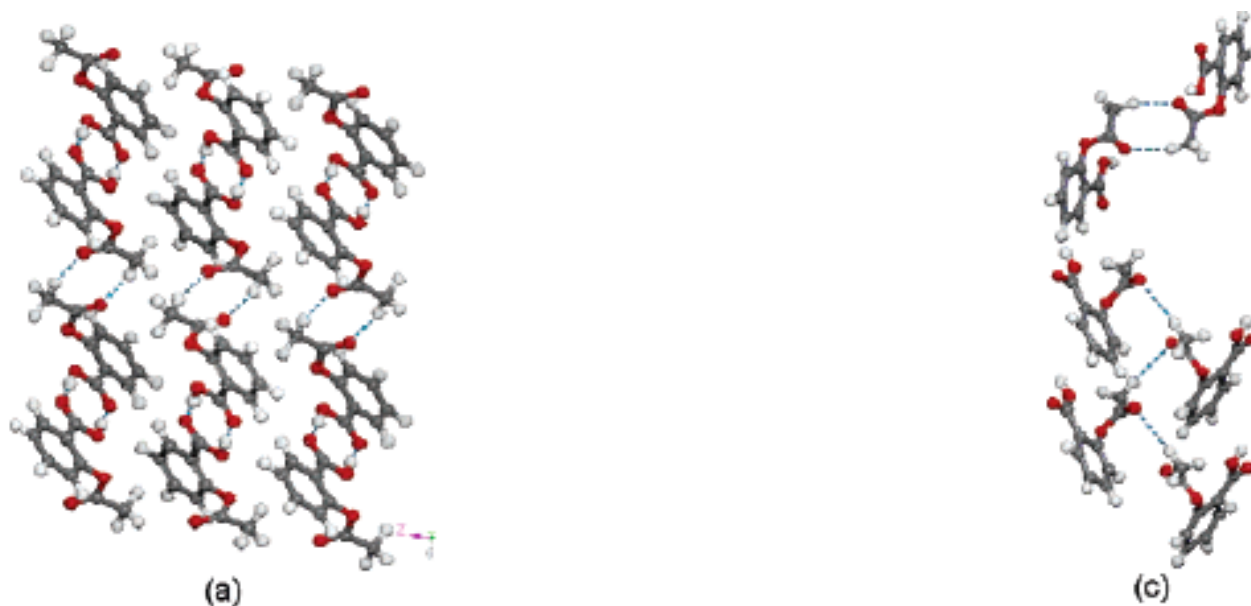


Figure 1. Crystal packing of aspirin forms I, II, and S. L. Price predicted form II. (a) Form I: 1D chains sustained by alternating carboxylic acid and acetyl group centrosymmetric dimers. (b) Form II: acid dimers are connected via catemeric methyl C–H...O and phenyl C–H...O (not shown) hydrogen bonds. (c) Acetyl group C–H...O dimers in form I and catemers in form II. (d) S. L. Price predicted form II. Note the similarity with the crystal packing of form II (b).



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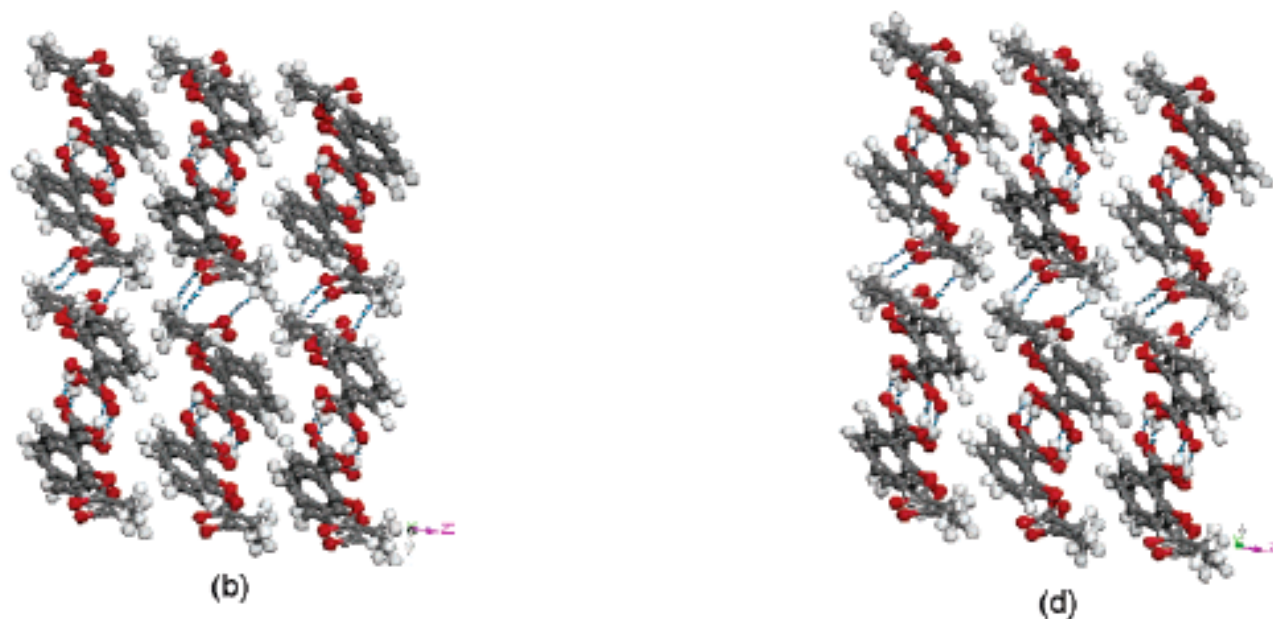
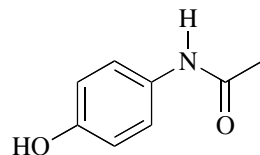


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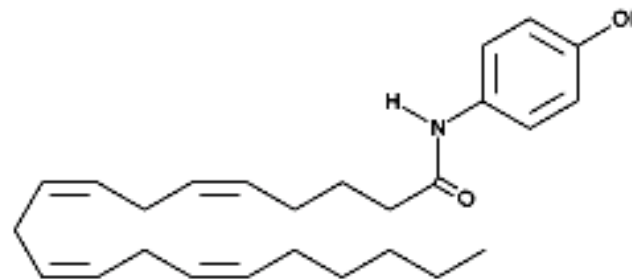


Tylenol™: Acetaminophen



- First made in 1874 by Harmon Morse
- Up for sale in 1955
- Cox-3 inhibitor which only is found in the brain and spin
- Converted to N-arachidonoylphenolamine which is a known CB1 activator
- Prostaglandin synthesis inhibitor

Over doses lead to liver toxicity

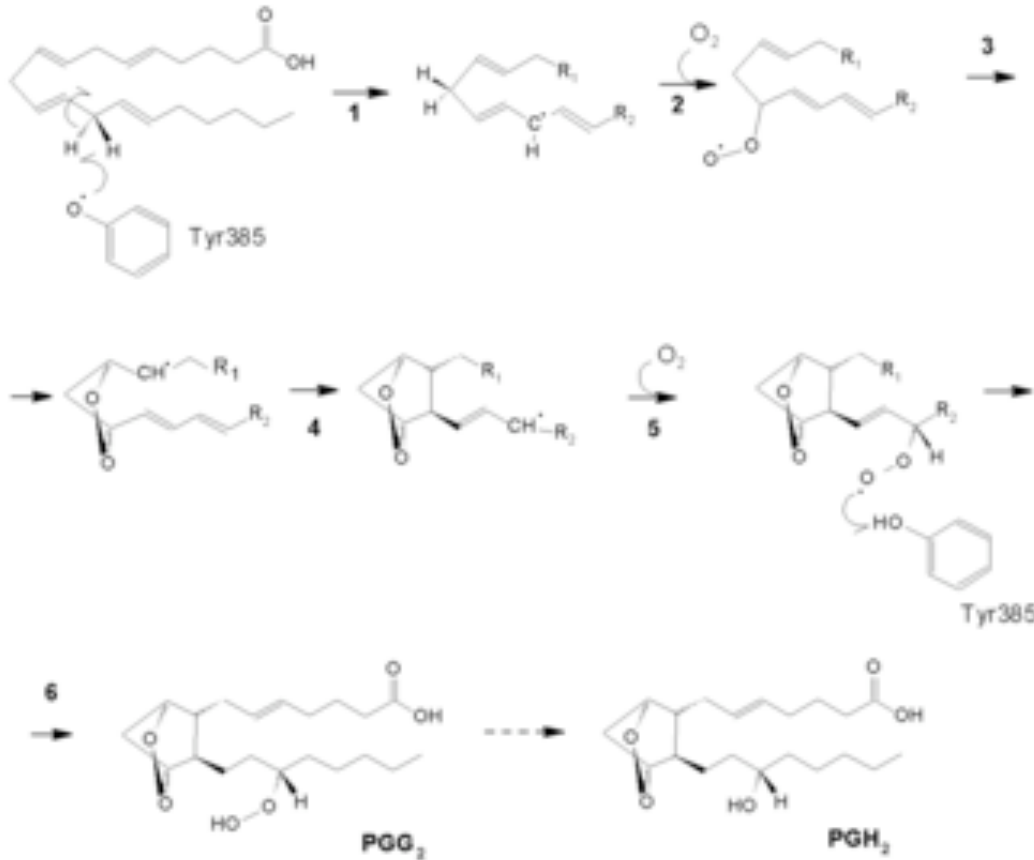




COX - Cyclooxygenase

S

arachidonic acid



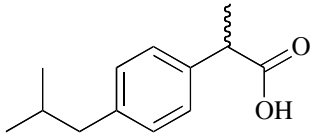
Prostaglandins
- responsible for
the perception
of pain



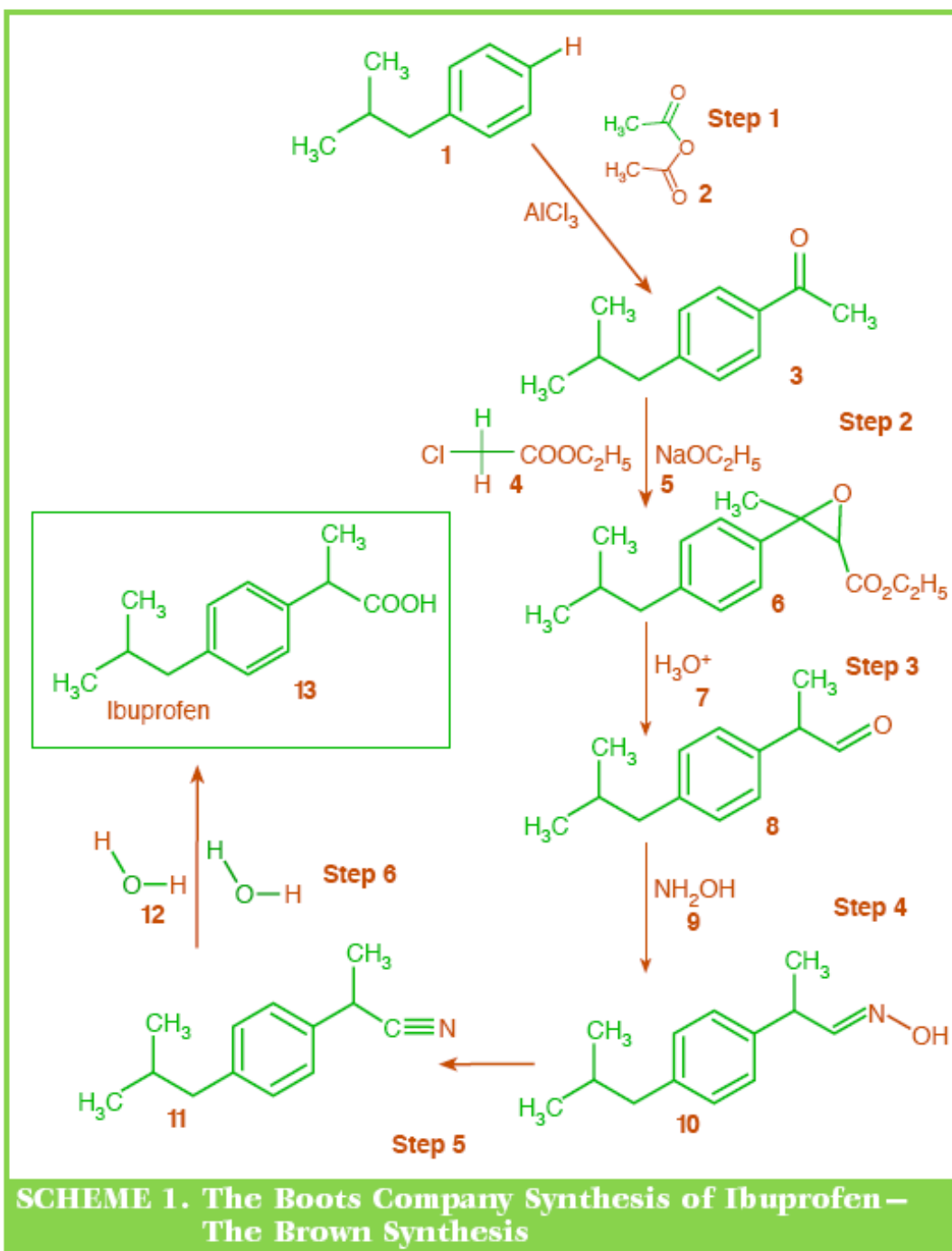
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- Prostaglandins work with cells to promote inflammation and other function.
 - COX-1 is continuously secreted in the stomach and is required for gastrointestinal health. They promote the excretion of mucus in the stomach.
 - COX-2 is associated with swelling injuries
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Ibuprofen



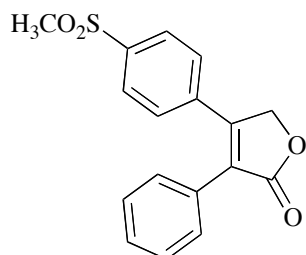
- Inhibits COX-1 and COX-2 (mostly)
- Heart failure issues
- Available by prescription in 1974 in the US
- Over the counter in 1984
- (S)-(+)-ibuprofen is the active form. The inactive can be converted in the body to the active form.



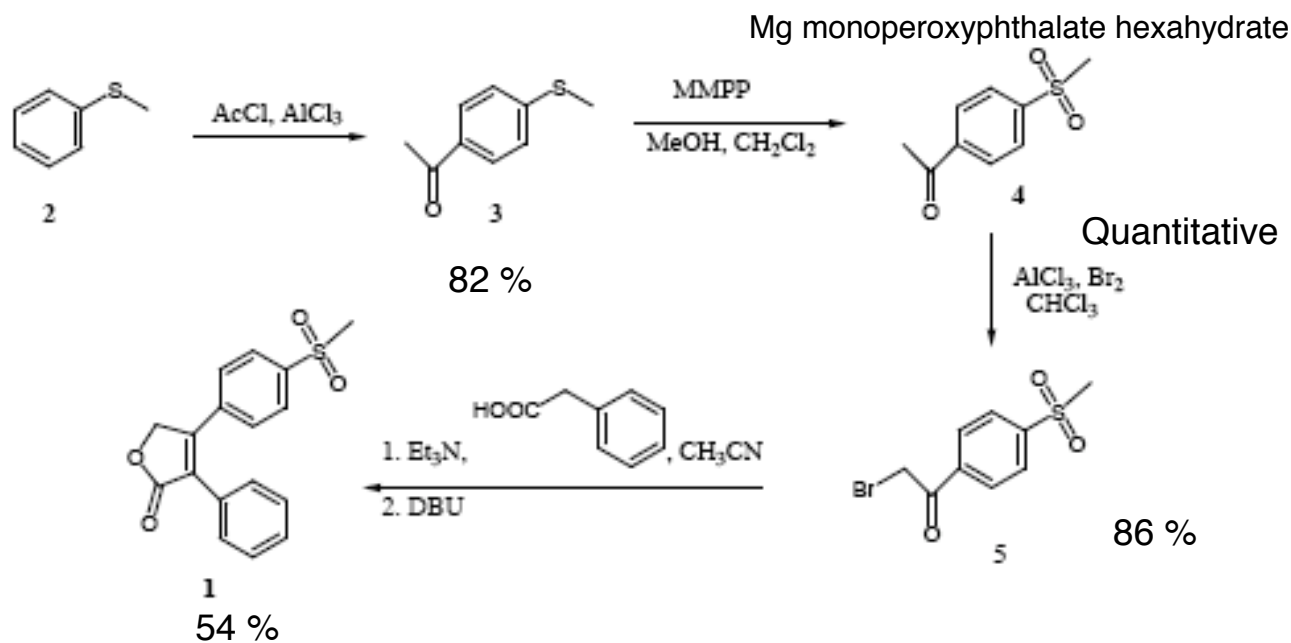


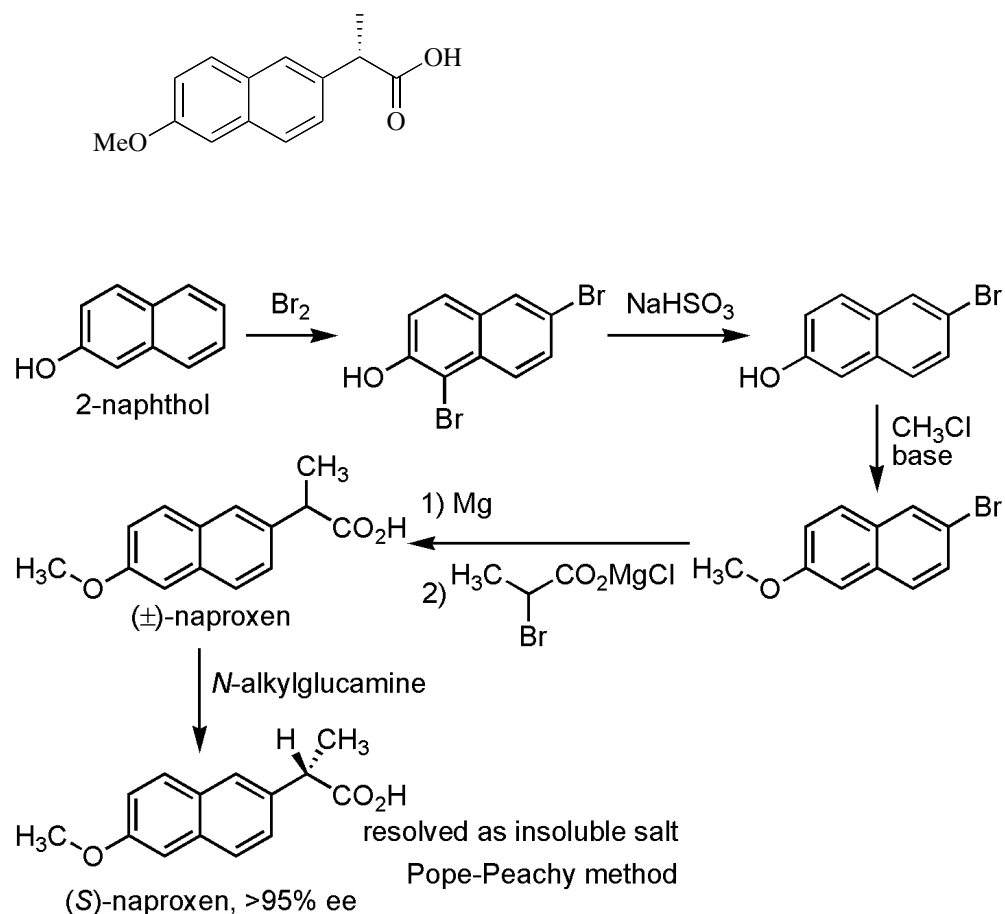
Vioxx™

S



- Vioxx (Rofecoxib)- 2.5 billion sales and withdrawn in September 30, 2004. The largest selling drug to be withdrawn.
- An apparent 4 x increase heart attack risk over Aleve™



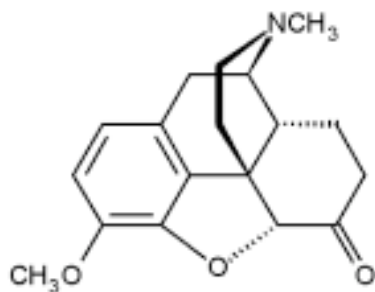


- Naproxen - introduced in 1976
- Over the counter in 1994
- Some data indicates an increase in heart attack risk and some states it decreases the risk.
- COX1 and COX2 inhibitor

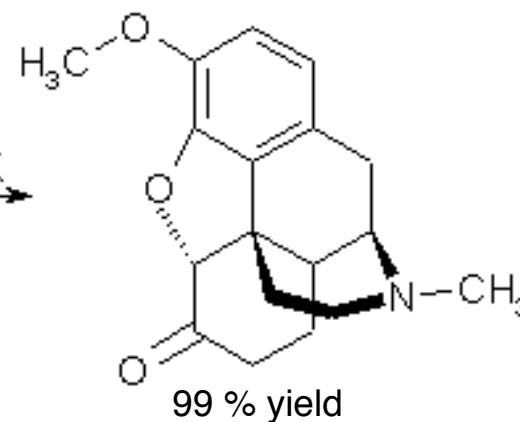
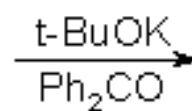
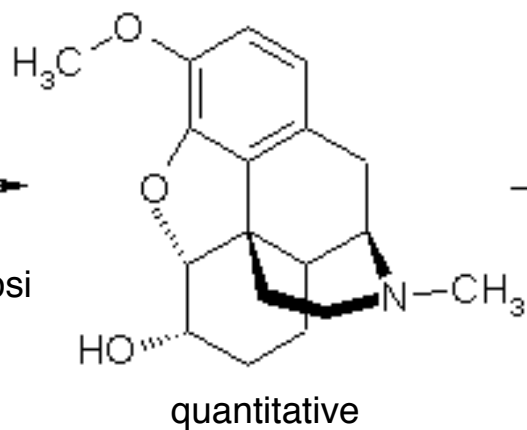
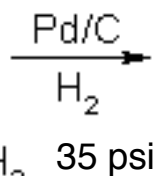
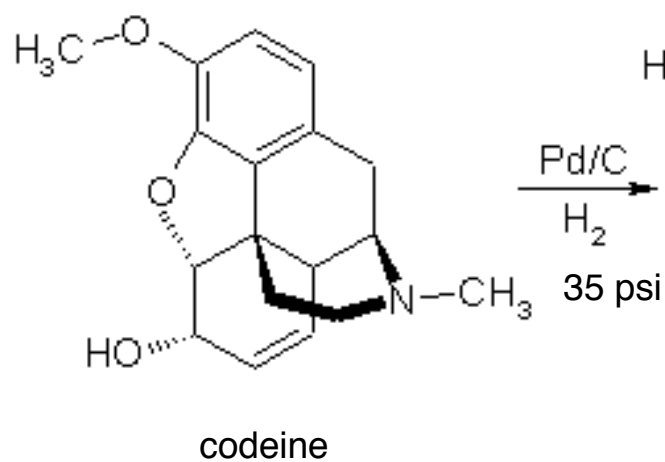


Vicodin

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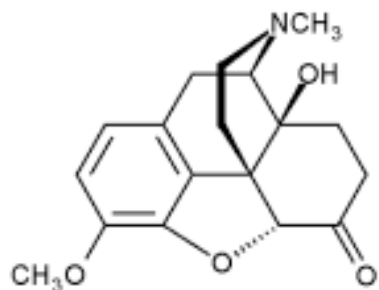
- Hydrocodone
- Opium derived
- Opium goes back at least 3400 BC



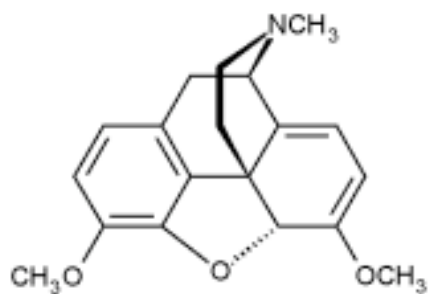
Meerwein-Ponndorf-Verley like



OxyCotin™

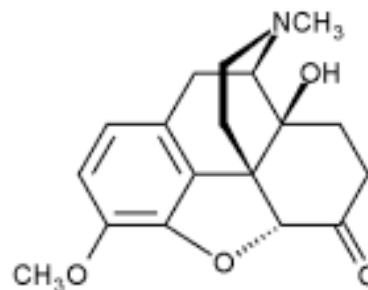


- Oxycodon
- Drug of choice for Russ Limbaugh
- Introduced in 1995
- 50 % more potent than Vicodin™
- Highly addictive
- From thebaine minor component of opium



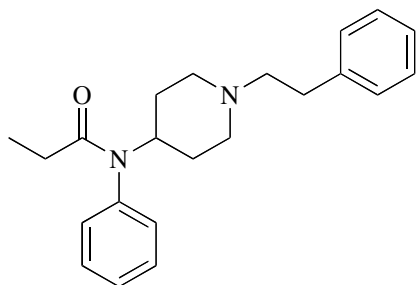
1) $\text{H}_2\text{O}_2, \text{CH}_3\text{CO}_2\text{H}$

2) $\text{Pd/C}, \text{H}_2$





Fentanyl™

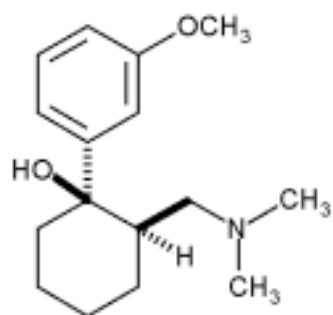


- Introduced in 1960's
- Sold as a "lollipop"
- Sold as a patch and more effective if absorbed through skin or tongue
- 80 times more potent than morphine
- Commonly mixed with cocaine or heroin for an extra "kick" or to dilute down cocaine or heroin

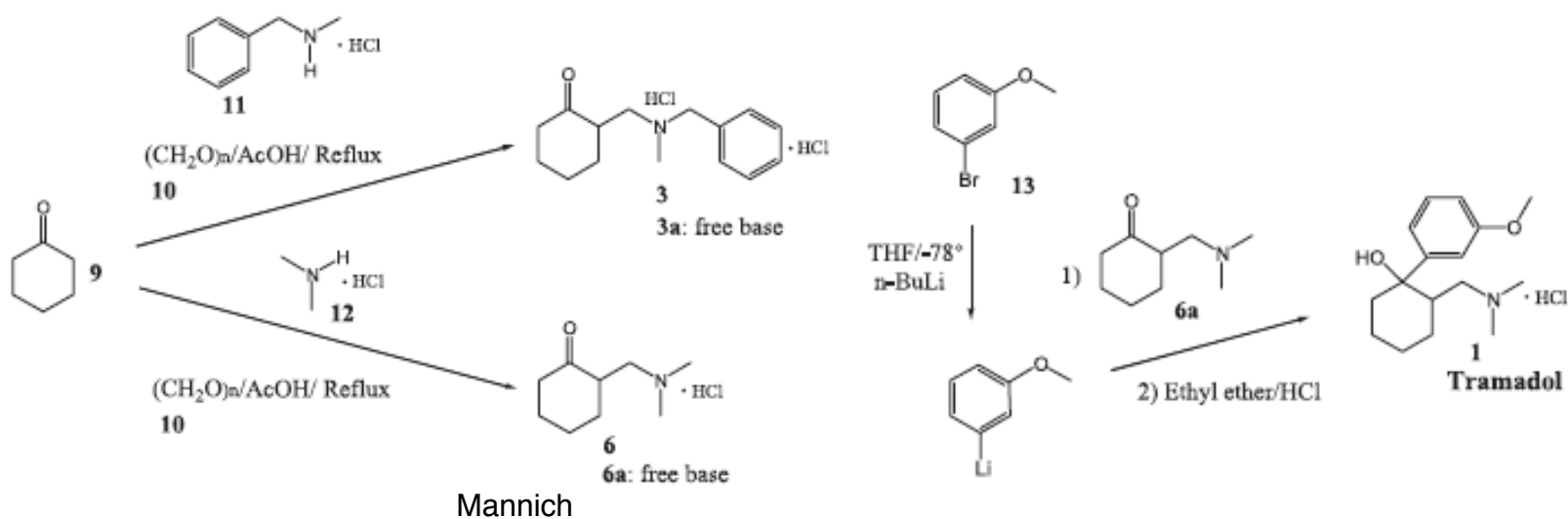


Ultam (Tramadol)

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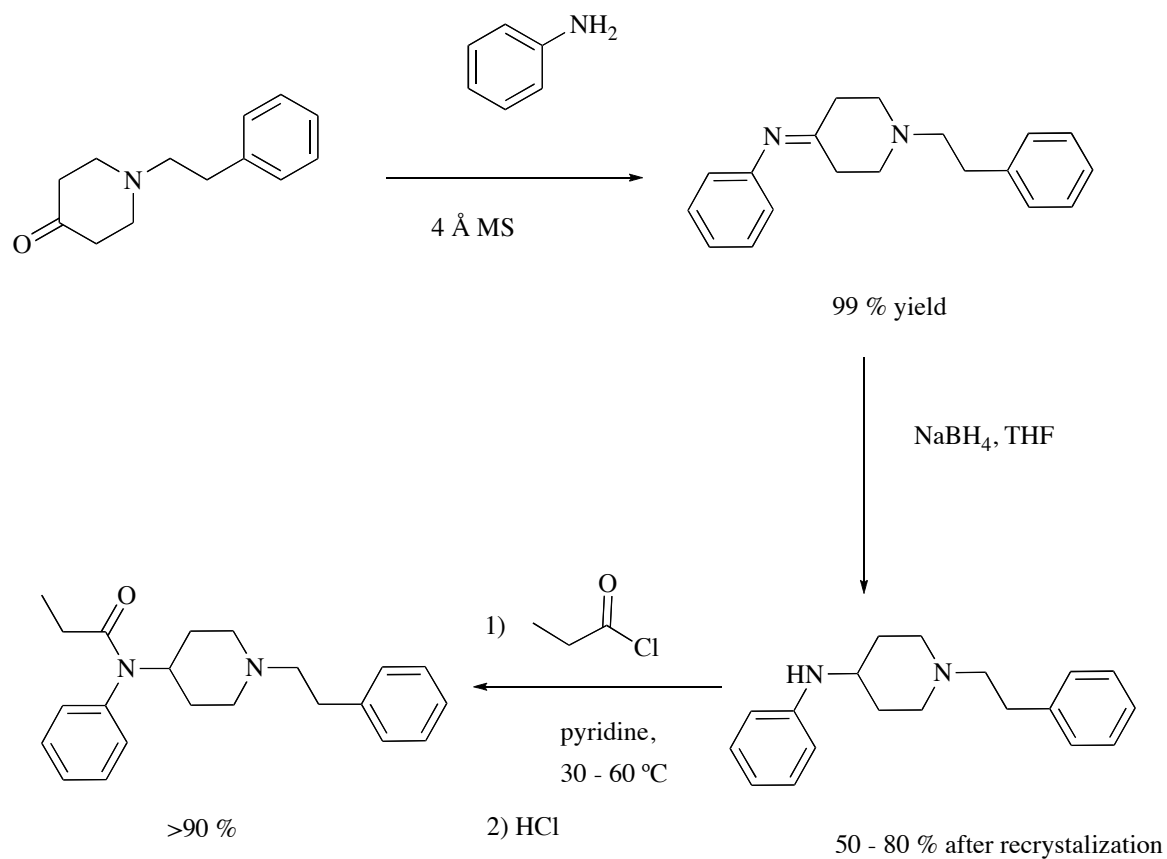
- 10 % as potent as morphine and it hits those receptors
- Mixture of enantiomers



Scheme 1



Could Not Find in Literature - But Found on Website to Make in your Garage





Keith's Evaluations of Pain Killers



- Aspirin - does not work well on my headaches, but if you have injuries that involves swelling, it works well
 - Acetaminophen - works ok on headaches - insufficient data on injury but little anti-inflammatory effects
 - Ibuprofen - works best on tooth pain and headaches, and it works ok on injuries involving swelling.
 - Vicodin™ - you still hurt badly but you just don't care!
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