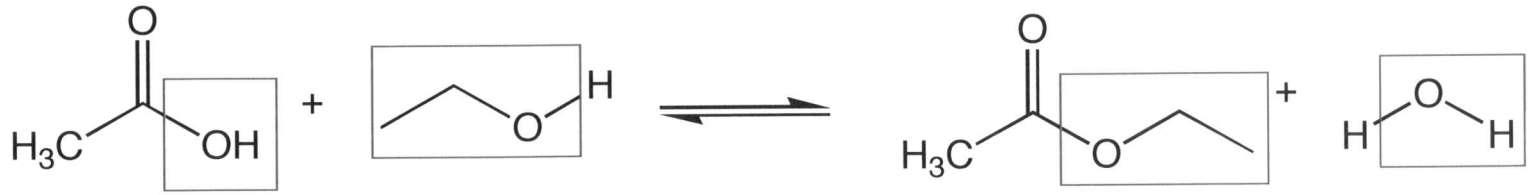
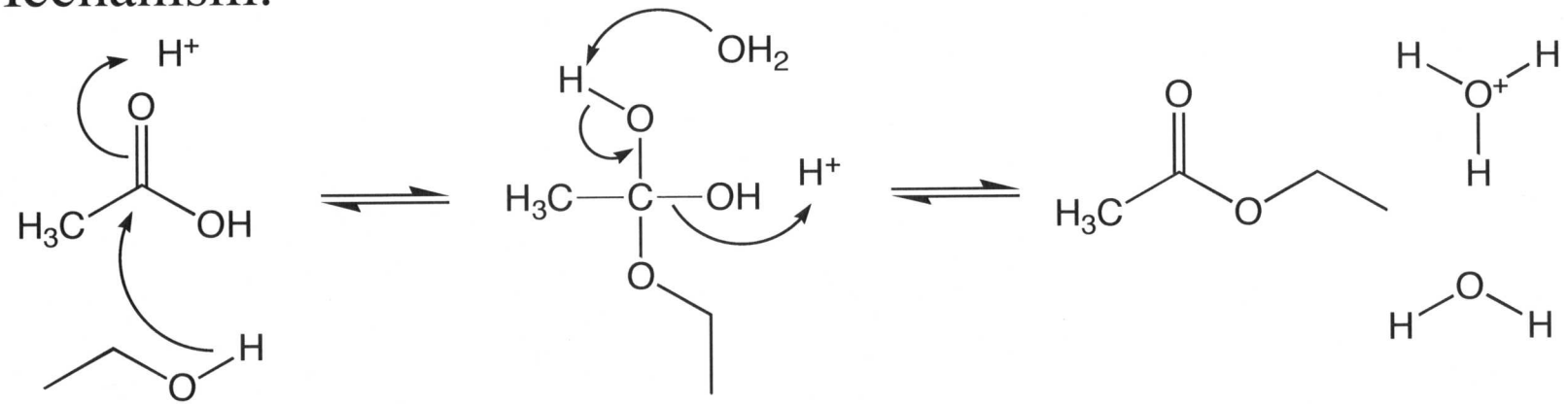
Conversion of Acids to Esters: requires acidic conditions

The following reaction occurs in bad wine (wine containing acetic acid).

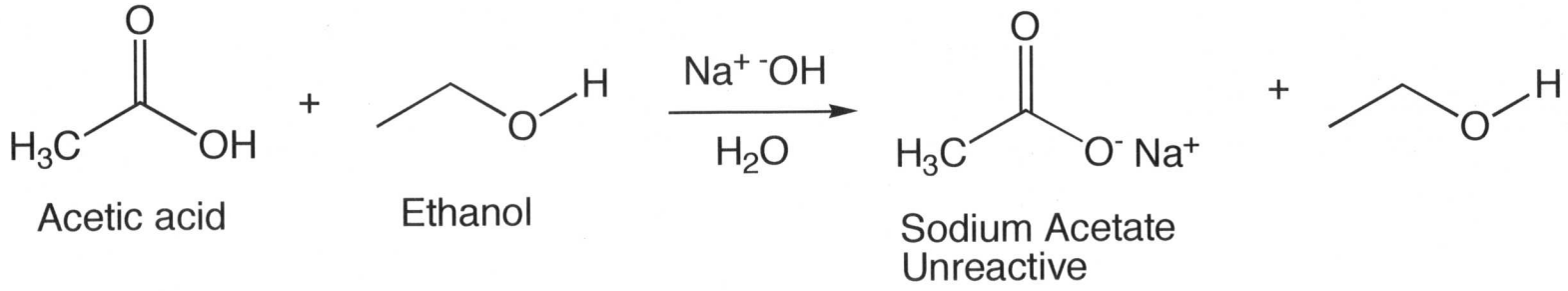


Acetic acid Ethanol Ethyl Acetate

Mechanism:



Would an ester be formed under basic conditions? **NO** get a salt instead

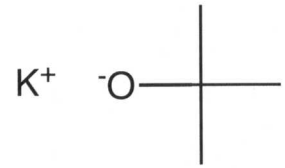


Acetic acid Ethanol

Sodium Acetate
Unreactive

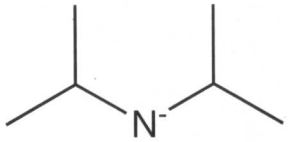
Reactions at the α Carbon - most common for esters

a base is needed that
will not attack the carbonyl



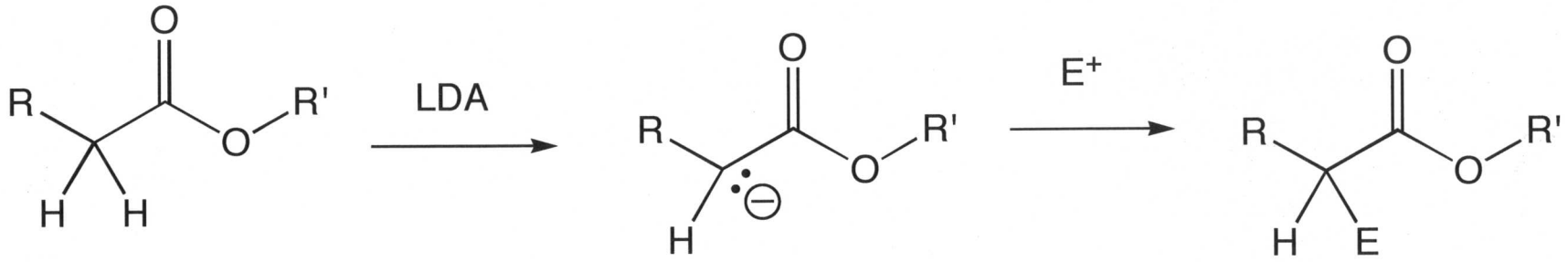
weak

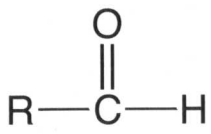
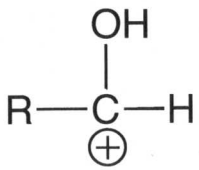
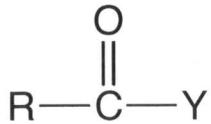
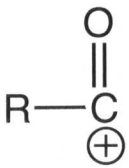
KOtBu



strong

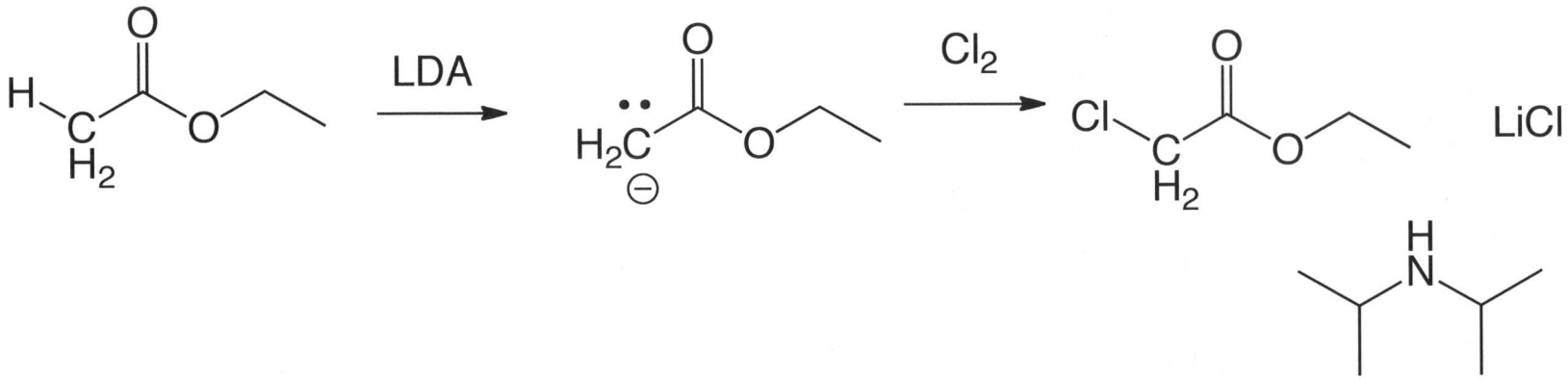
LDA



Reaction	Electrophile	Acts as 'E+'
Halogenation	X_2 X = Cl, Br, I	X^+
Alkylation	$R\text{-}CH_2\text{-}X$	RCH_2^+
Aldol		
Acylation		

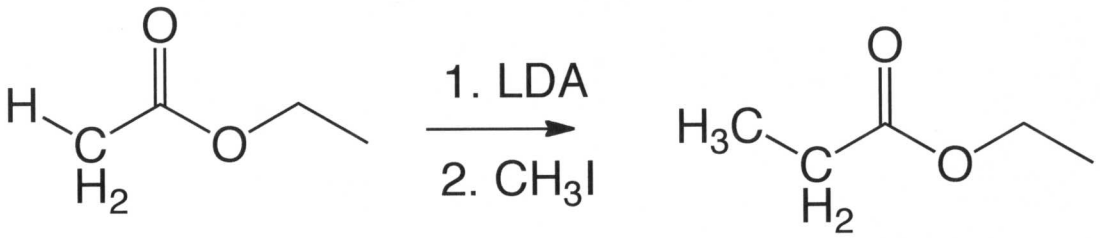
Reactions at the α Carbon - Examples

Halogenation



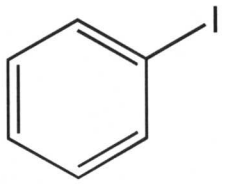
Reactions at the α Carbon - Examples

Alkylation

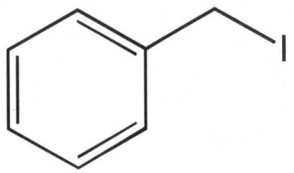


S_N2 substitution

What else could be used (instead of CH_3I) ? Many $1^o, 2^o$ halides

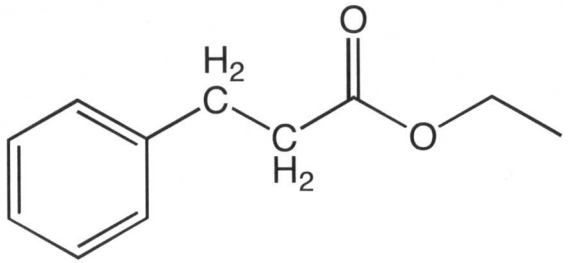


No, S_N2 reactions won't go with this reagent



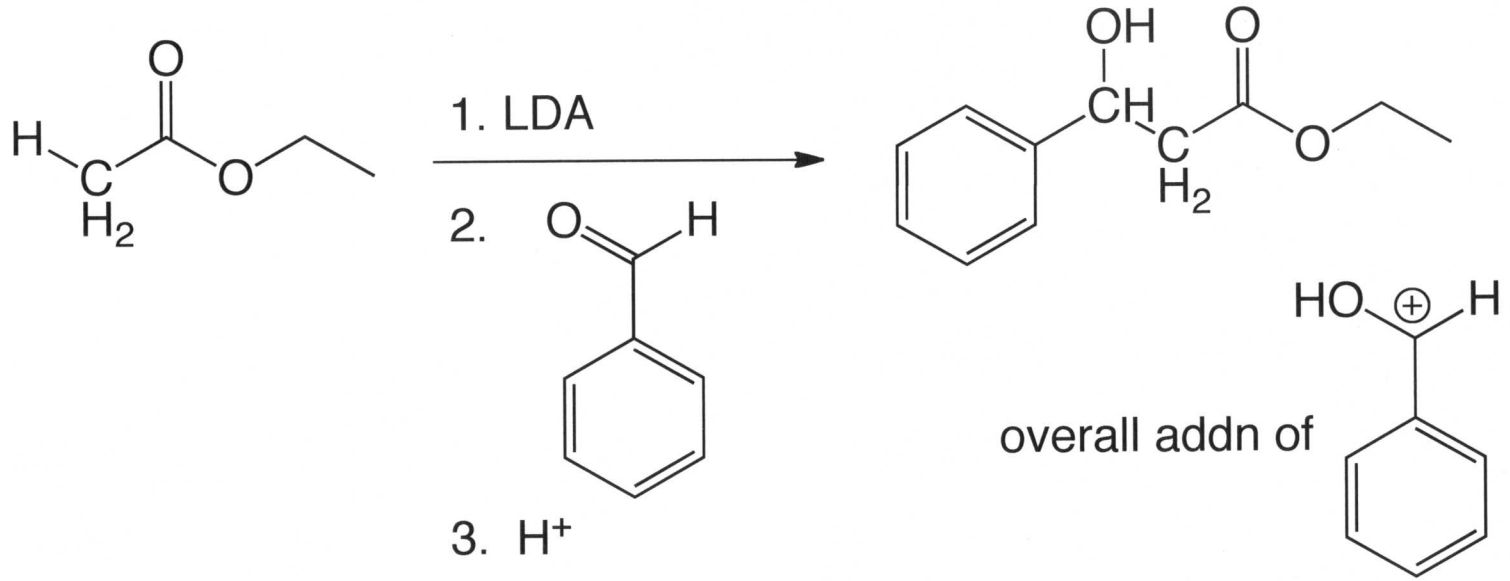
Benzyl iodide

Yes, in the above reaction the product would be



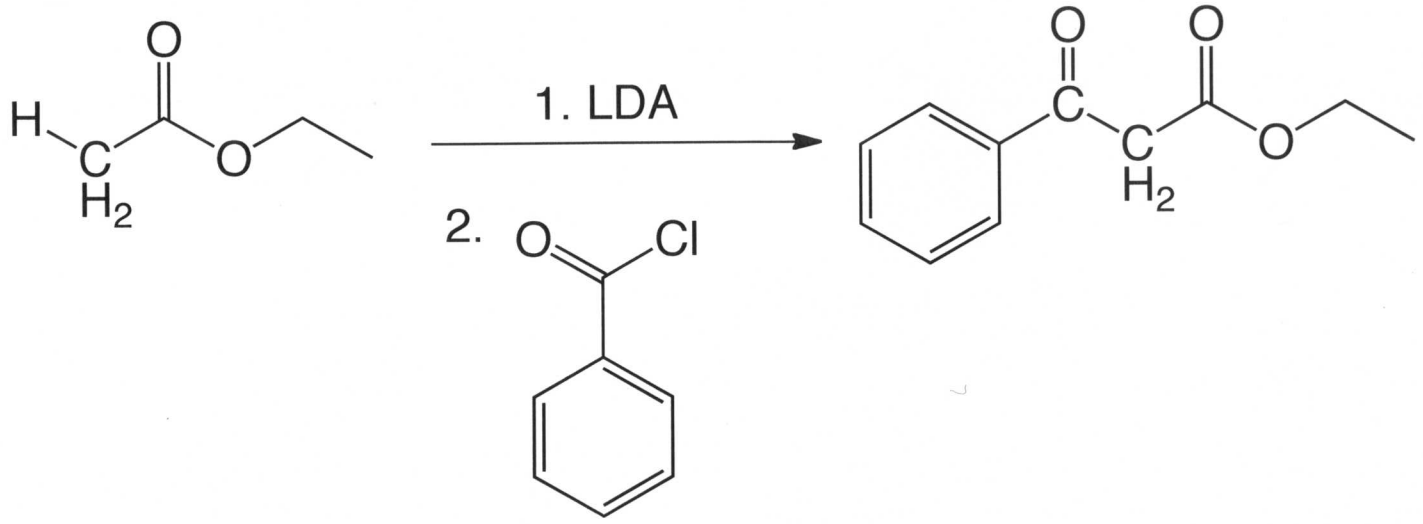
Reactions at the α Carbon - Examples

Aldol

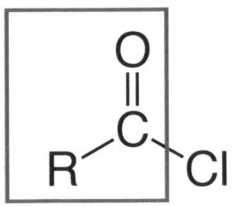


Reactions at the α Carbon - Examples

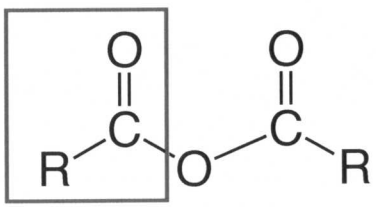
Acylation



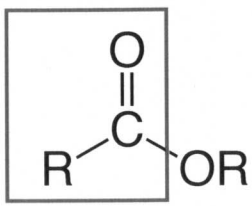
acylating agents: add acyl group = RCO



acyl halides

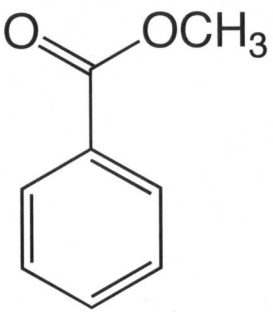


anhydrides



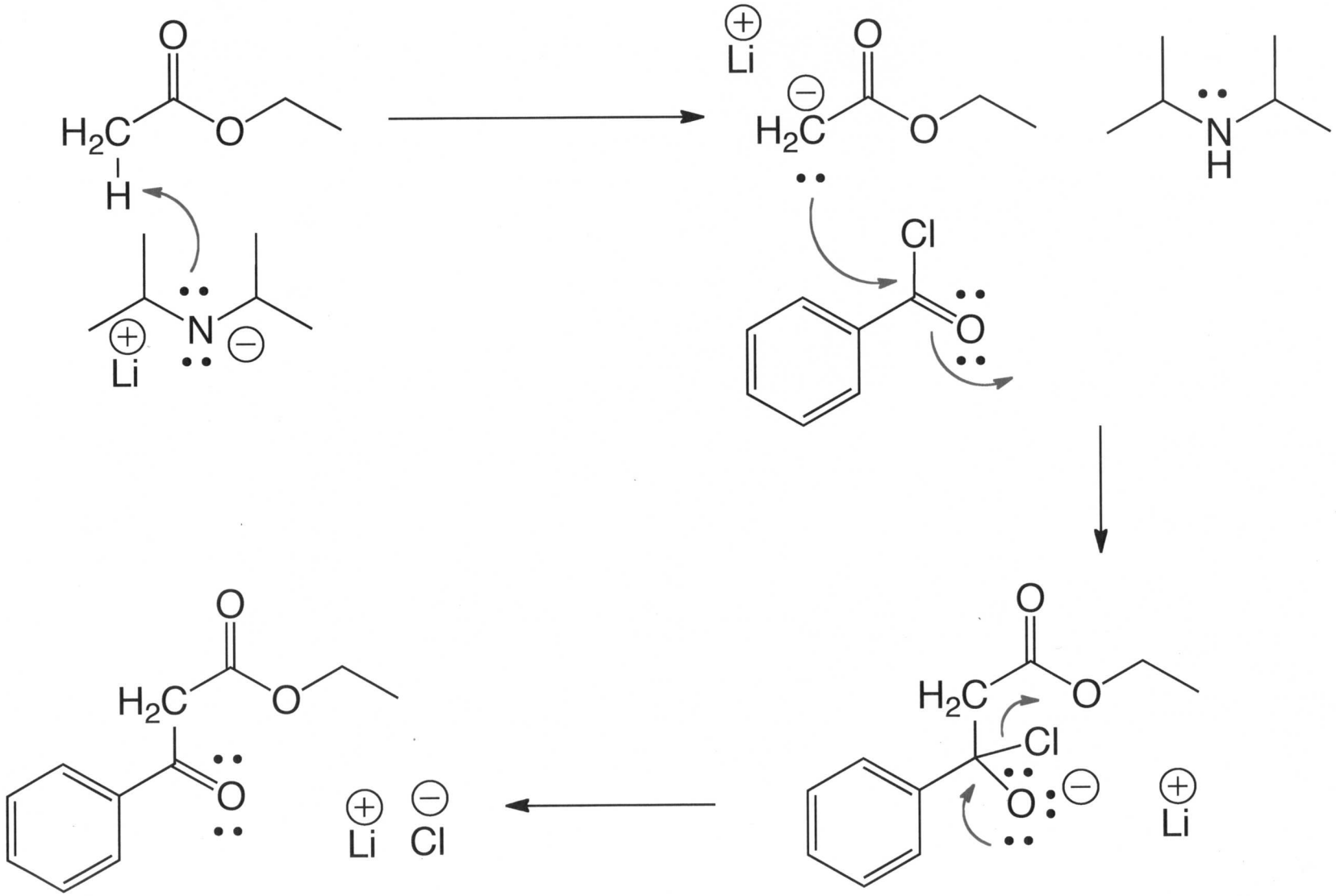
esters

could use as acylating agent for above reaction



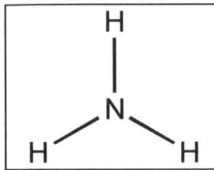
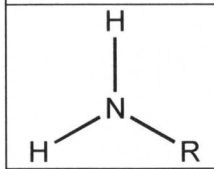
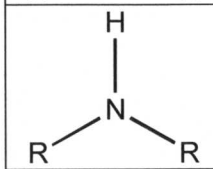
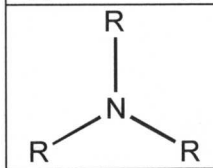
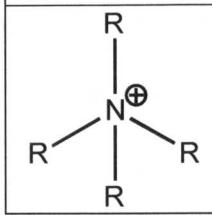
Reactions at the α Carbon - Examples

Acylation Mechanism



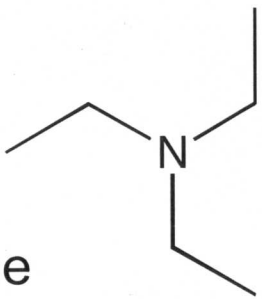
Amines: Lecture Outline 5

Nomenclature:

	Ammonia (simplest amine)
	Primary amine
	Secondary amine
	Tertiary amine
	Quaternary ammonium salt

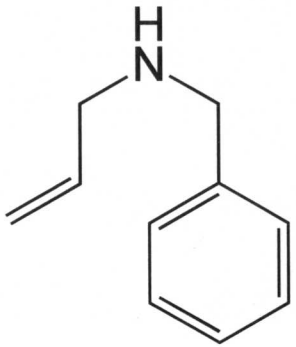
name the alkyl group (R), and add amine

CH_3NH_2 methylamine

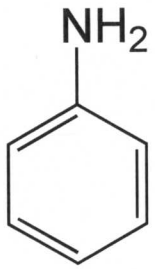


triethylamine

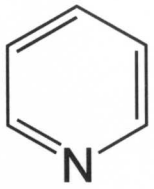
Amine Nomenclature:



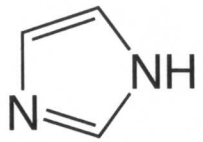
allylbenzylamine



aniline

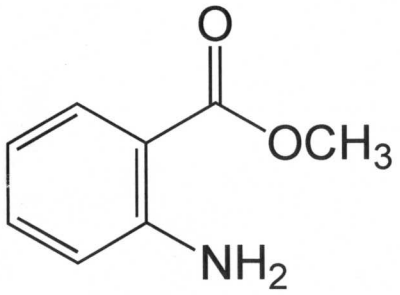


pyridine



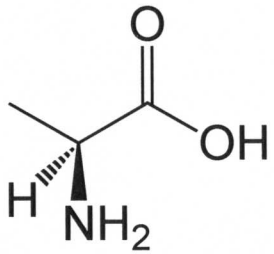
imidazole

group can be named as an amino or N-alkylamino:



methyl 2-aminobenzoate

grape flavour - repels geese



(S)-2-aminopropanoic acid
L-alanine

constituent of spider silk

Amine Properties:

Amines are polar, and have higher boiling point, melting point than hydrocarbons of similar molecular weight

Small amines are soluble in water, and larger ones are soluble in acid

amines have a lone pair and are bases and often nucleophiles

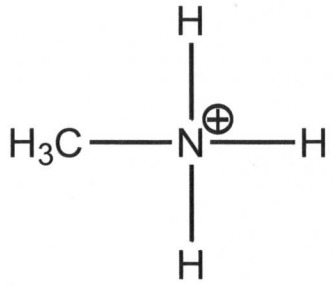
pKa for ammonia is about 36

amide anion

pKa for ammonium ion is about 9.4 - biochemists refer to this as "pKa for ammonia"

Amine Properties:

The pKa of protonated methylamine is about 10.5



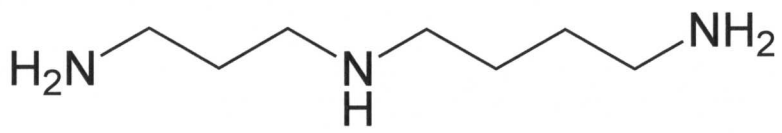
Is this more or less acidic than ammonium ion ?

less acidic. Higher pKa means less acidity
conjugate base (methylamine) is more basic
greater tendency to hold on to H+

Why is protonated methylamine less acidic than ammonium ?

alkyl group donates negative charge to the nitrogen (inductive)
stabilizes positive charge on nitrogen when protonated
makes parent amine more basic
(unprotonated nitrogen more negative)

Amine Properties: Example



spermidine

isolated from seminal fluid in males

but occurs in all cells

reacts with acetic acid that is present in females

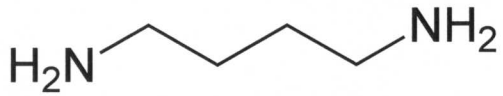
Which amine is protonated first?

secondary amine in the middle since it is the most basic nitrogen

2 alkyl groups donate negative charge through the inductive effect to nitrogen

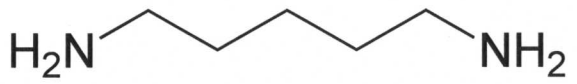
some diamines

1,3-diaminopropane



1,4-diaminobutane

putrescine



1,5-diaminopentane

cadaverine

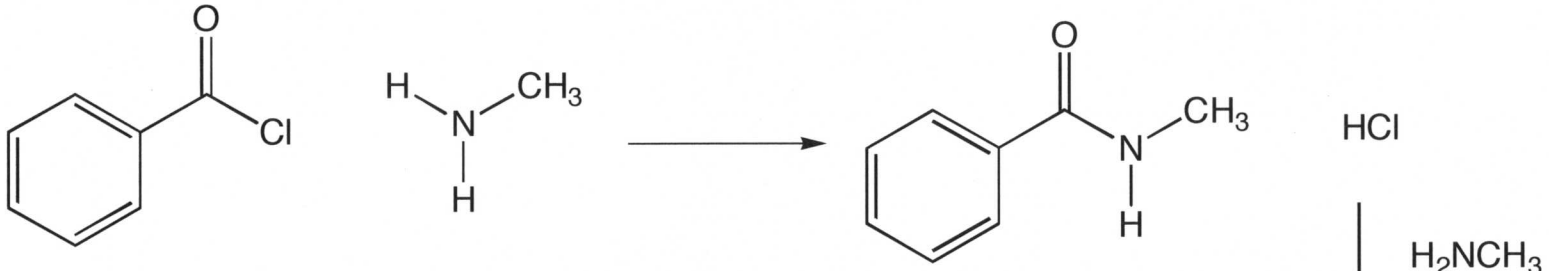
occur in decaying meat, the smell alerts you to not eat it.

Reactions of amines

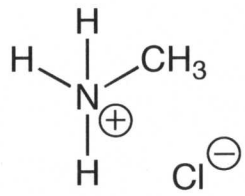
Halogenation: NH_3 and I_2 gives NI_3 (demo last time)

Aminal & imine formation with ketones & aldehydes reviewed later

Acylation:

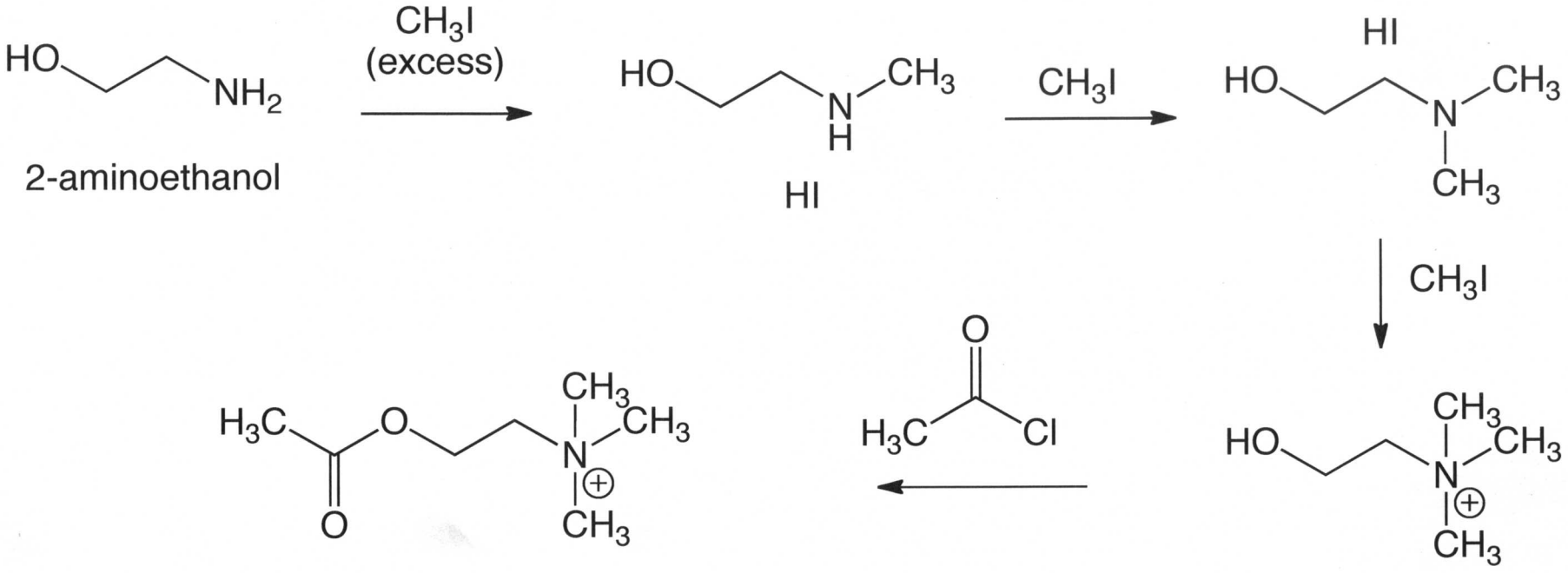


Note that 2 equivalents of the amine are needed,
1 for the acylation and the second forms a salt with the acid byproduct

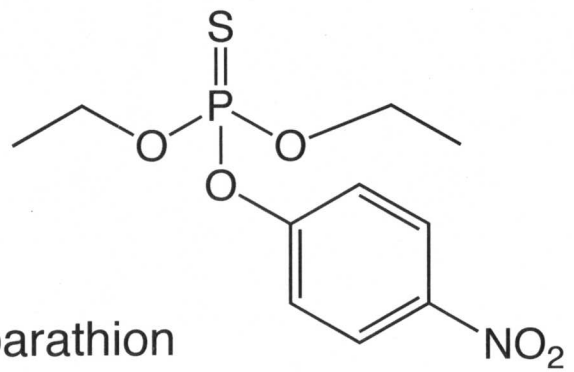


other carboxylic acid derivatives react, namely anhydrides & esters

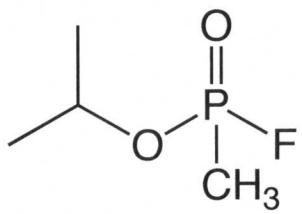
Reactions of amines Alkylation:



acetylcholinesterase inhibitors:

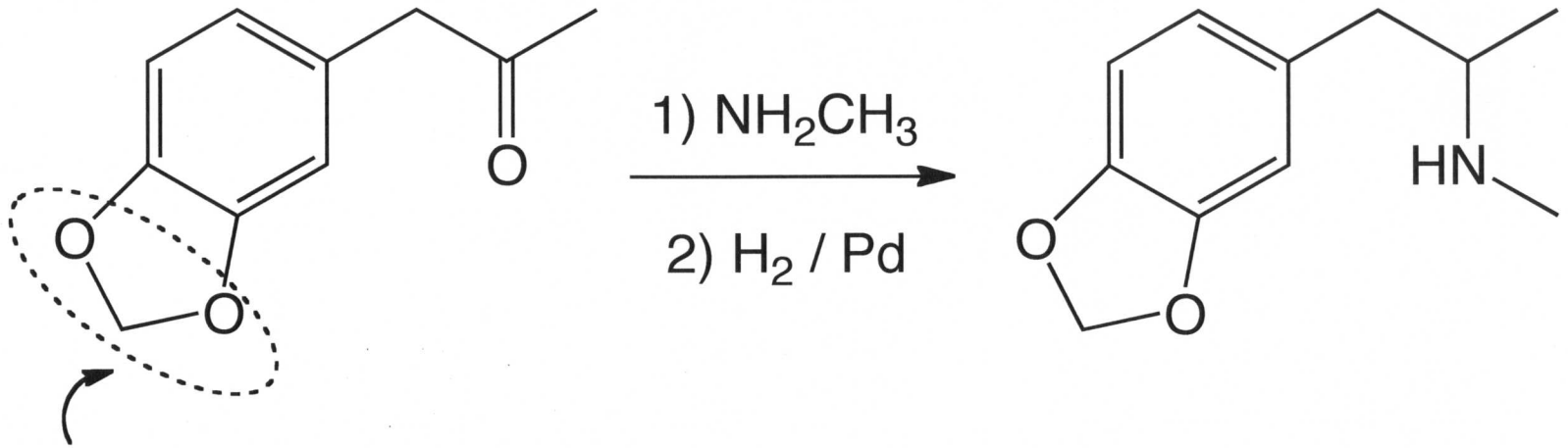


parathion



sarin

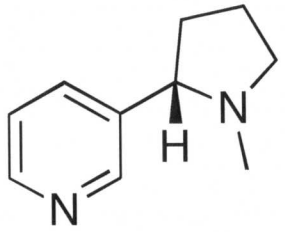
Reductive amination



methylene dioxy group

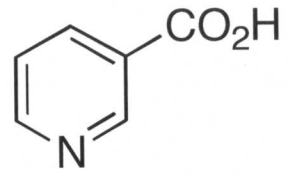
ecstasy

Alkaloids Solanaceae plant family
includes peppers, tobacco, potato, yams, tomato, nightshade

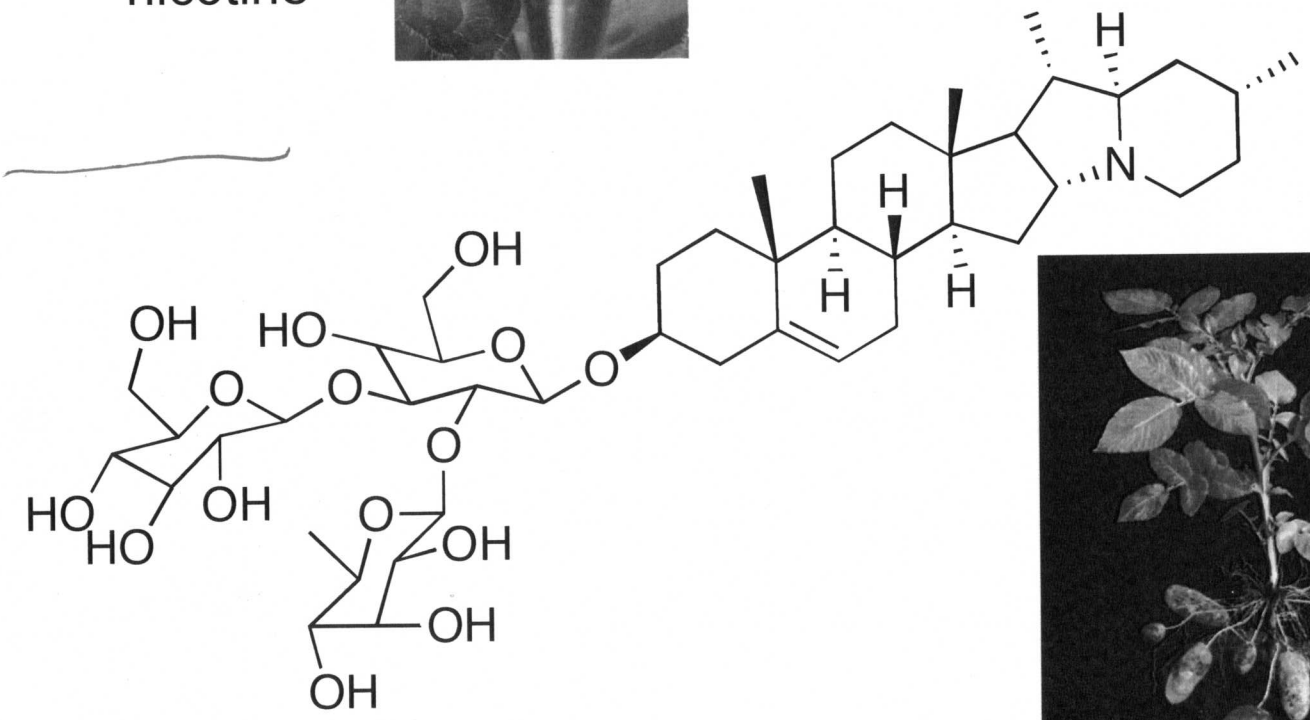


nicotine

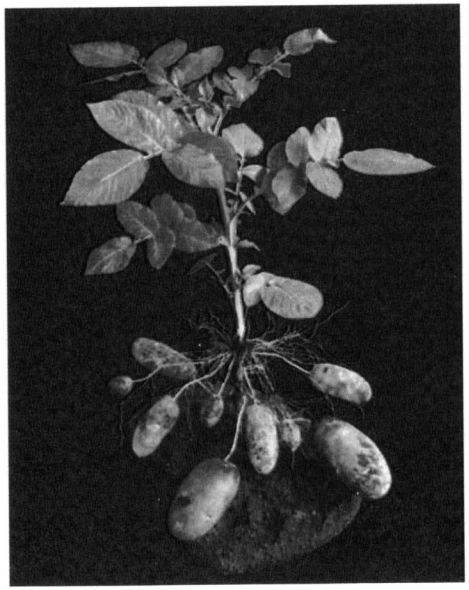
body →



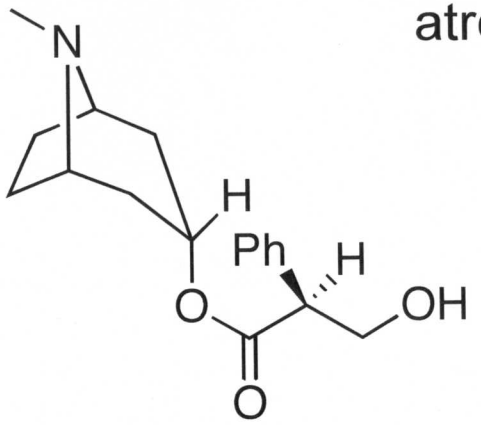
nicotinic acid niacin vitamin B3



solanine from green parts of potato

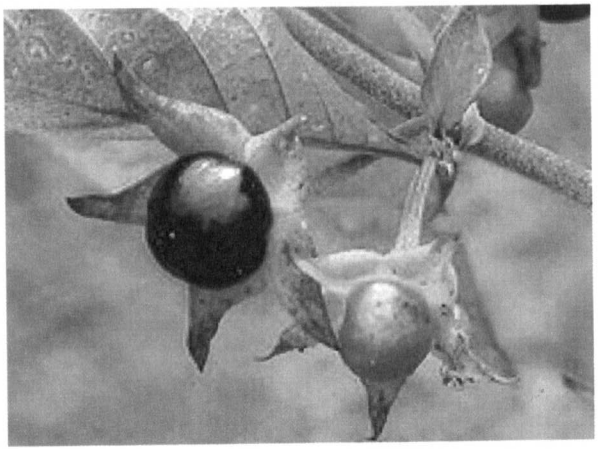


Alkaloids Solanaceae plant family



atropine from *Atropa belladonna* = deadly nightshade

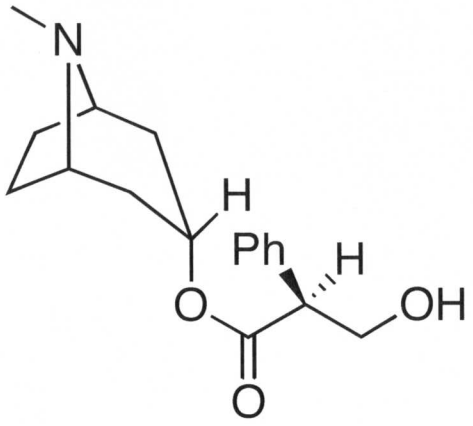
natural racemate = racemic mixture



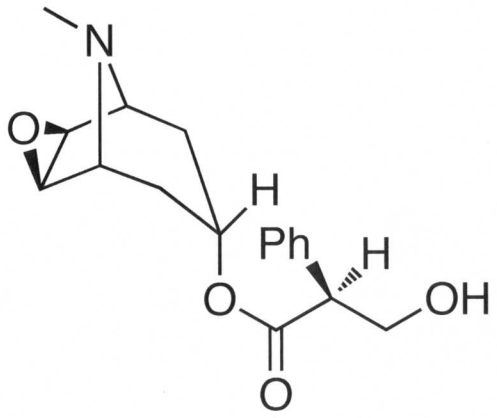
hyoscyamine from *Hyoscyamus niger*

the enantiomer shown above

Alkaloids Solanaceae plant family

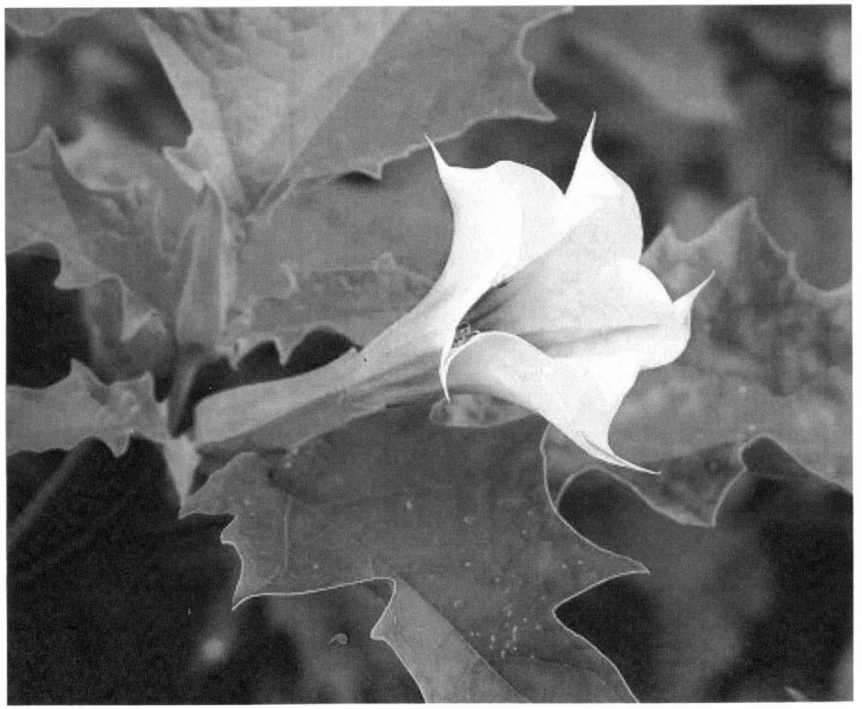


hyoscyamine from *Hyoscyamus niger*

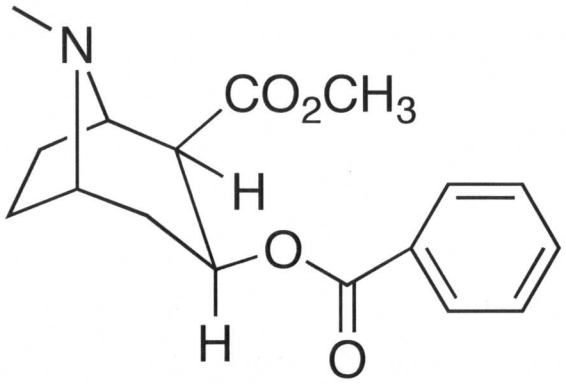


scopolamine from *Datura stramonium*

Jimson weed

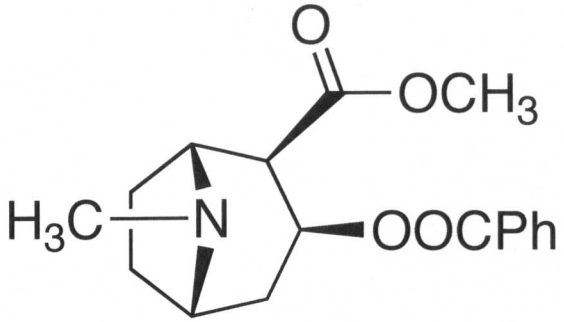


Alkaloids Erythroxylum coca

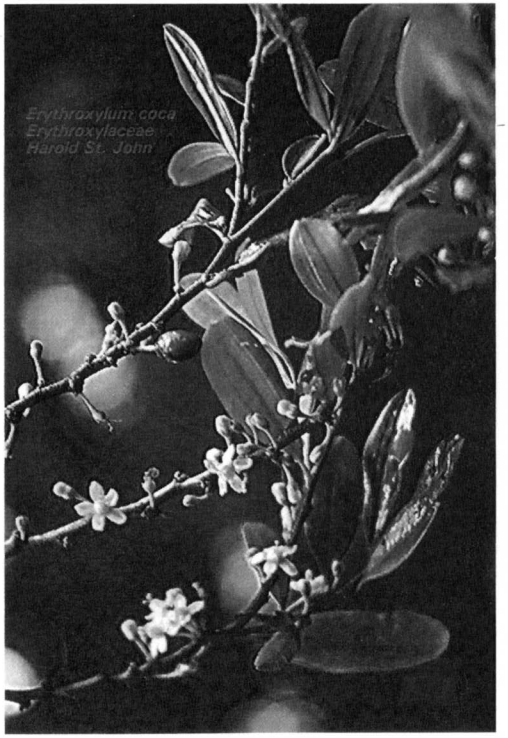


cocaine

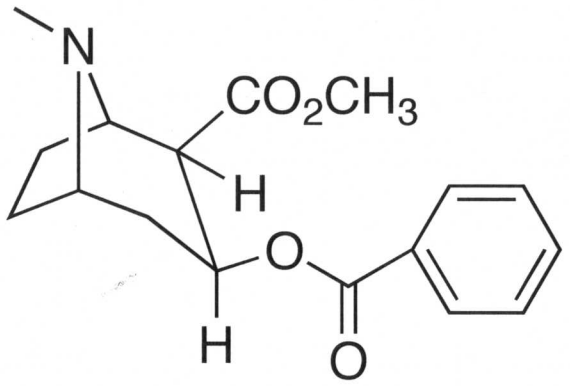
same as



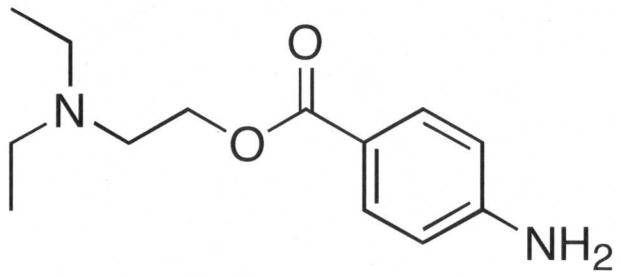
cocaine



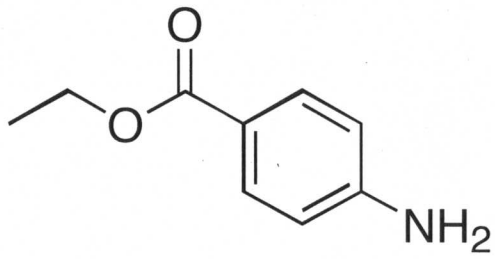
Alkaloids Erythroxylum coca



cocaine



novocaine



benzocaine