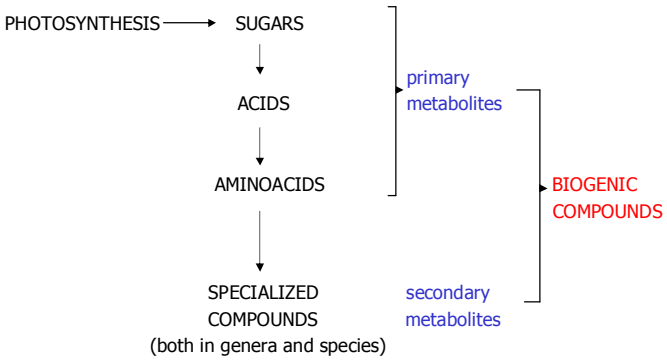
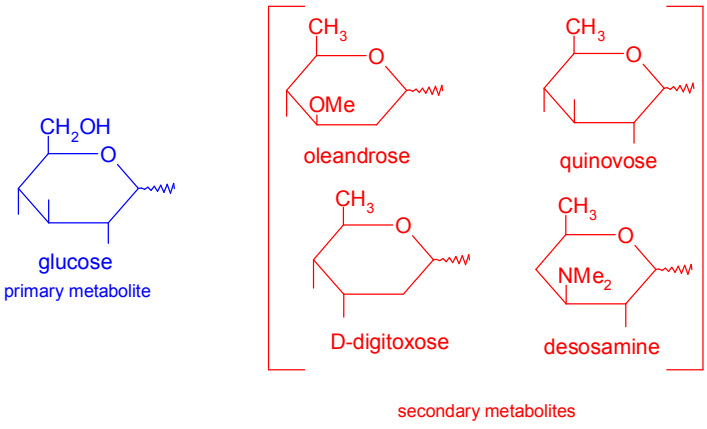
BIOGENESIS OF NATURAL COMPOUNDS



BETWEEN PRIMARY AND SECONDARY METABOLITES IS NOT ALWAYS EASILY DISTINGUISHED BORDER



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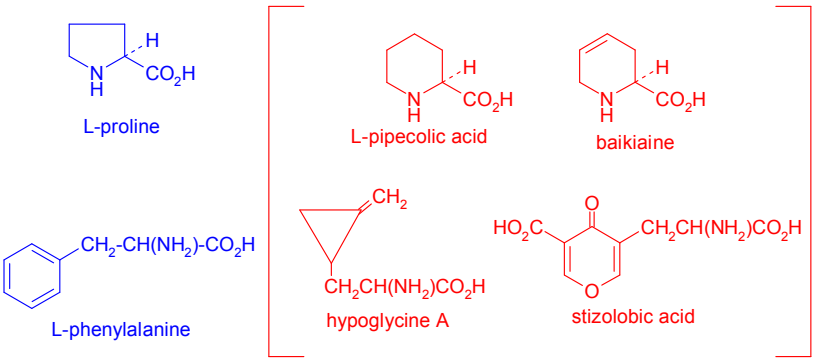
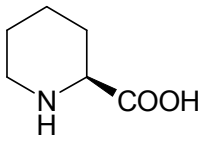


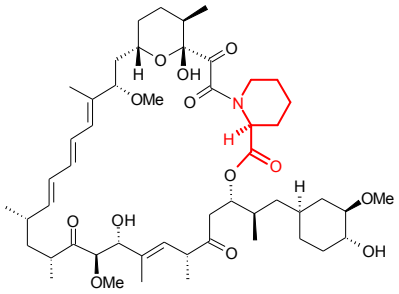
L-PIPECOLIC ACID

(S)-2-piperidinecarboxylic acid; L-homoproline

Widely dispersed in plants: apples, date,
hops *(Humulus lupulus),*
beans (*Phaseolus vulgaris*)
white clover (*Trifolium repens*).
Part of some macrolide antibiotics, for example RAPAMYCINE.



RAPAMYCINE (SIROLIMUS, RAPAMUNE)



31-membered peptide lactone, chain of carboxlic acid is cyclised with L-pipecolic acid as a bridge.

Produced by *Streptomyces hygroscopicus*.
Posses antifungal, antineoplastic and immunosuppressive activity.

In combination with cyclosporine and tacrolimus in transplantation medicine.

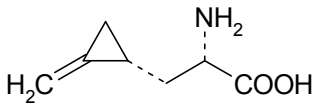
HYPOGLYCINE

Blighia sapida Kon. – ackee (unripe fruits)

West Africa → Jamaica (intoxications)

α-amino-β-(2-methylencyclopropyl)propionic acid. Hypoglycemic and teratogennic effect. It decreases blood glucose levels 3-4 hours after administration.

Active metabolite is (methylencyclopropyl)phormyl-CoA, impacts on metabolism of fatty acids, disrupts their β-oxidation. In DM therapy did not find its place, its biological activity is intensively studied from toxicological and experimental point of view (studies of fatty acids metabolism).

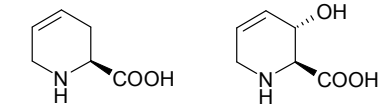


BAIKIAINE

Baikiaea plurijuga (Fabaceae), *Caesalpinia tinctoria,* red algae

Baikianine inhibits the neurotransmittory activity of glutamic acid.

3-Hydroxybaikianine is highly concentrated found in fruiting bodies of toxic fungus *Russula subnigricans.*



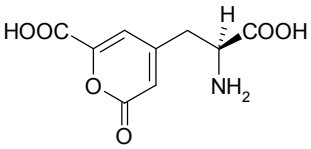
Baikiaine

(1,2,3,6-tetrahydropyridine--2-carboxylic acid)

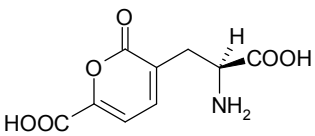
STIZOLOBIC ACID

Stizolobium hassjoo (Fabaceae)
Amanita pantherina, A. muscaria, A. gemmata

Toxicological importance.



Stizolobic acid



Stizolobinic acid

All life forms contain the same molecules of organic and anorganic compounds. Differences are found their inter-ratio.

BIOPOLYMERS

are built up from many identical or similar sub-units

Basic biopolymers:

- Proteins made of 21 different aminoacids. Function: catalytic (enzymes), regulatory (chosen hormones), nutrition, structural. Combined glycoproteins (prevalence of monosaccharide units)
- Polysaccharides – linear or branched chains (starch, cellulose, glycogen). At plants basic building and storage material. Metabolic changes of these bring „chemical“ energy.
- Lipids made biological membranes (phospholipids), storage compounds. Combined are lipopolysaccharides and lipoproteins.
- Nucleic acids composed of nucleotides (nitrogenous base, monosaccharide (Rib, deRib) a phosphoric acid.

  RNA: A, G, C, U; DNA: A, G, C, T

A X I O M E S

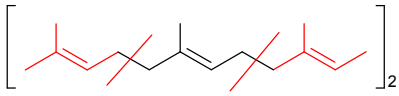
PRIMARY METABOLISM POSSESES BASIC IMPORTANCE,
on which has variability of organic systems very low influence.

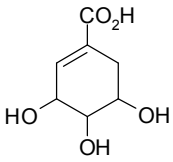
SECONDARY METABOLITES

1. They posses limited taxonomical occurrence.
2. They are produced under specific conditions.
3. Their biochemical function is not fully elucidated.

One of the basic characteristics of secondary metabolism is that they use only limited selection of precursors and these precursors have special importance in primary metabolism.

PRECURSORS

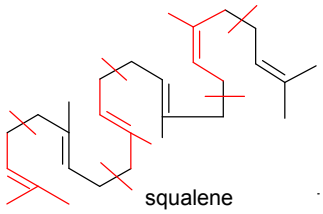




shikimic acid

Ilicium religiosum

Star anyse



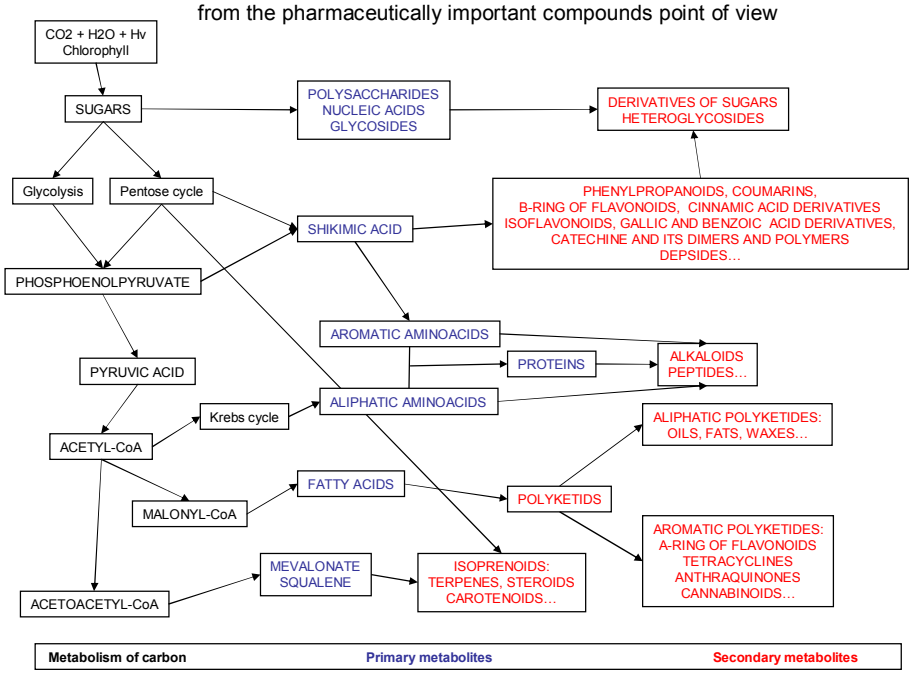
squalene

IMPORTANCE OF PRIMARY METABOLISM FOR PRODUCTION OF NATURAL COMPOUNDS

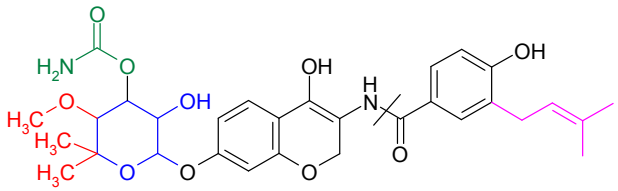
IN REGARDS TO INTER SOUVISLOSTI AND CONSEQUENTIONAL RELATIONS OF METABOLIC PROCESSES IN LIVING PLANTS, IT IS NOT POSSIBLE TO NADŘAZOVAT FROM THE POINT OF VIEW OF NATURAL COMPOUNDS PRODUCTION ON PROCESS OF PRIMARY METABOLISM UPON ANOTHER ONE.

CONSEQUNTIONALLY IT WILL BE TARGETED ON CHOSEN BIOSYNTHETIC MECHANISMS WITH DURECT IMPORTANCE FOR PRODUCTION OF SECONDARY METABOLITES.

Important inter-relations in plant metabolism
from the pharmaceutically important compounds point of view



NOVOBIOCIN
from the „biogenetic parents" point of view

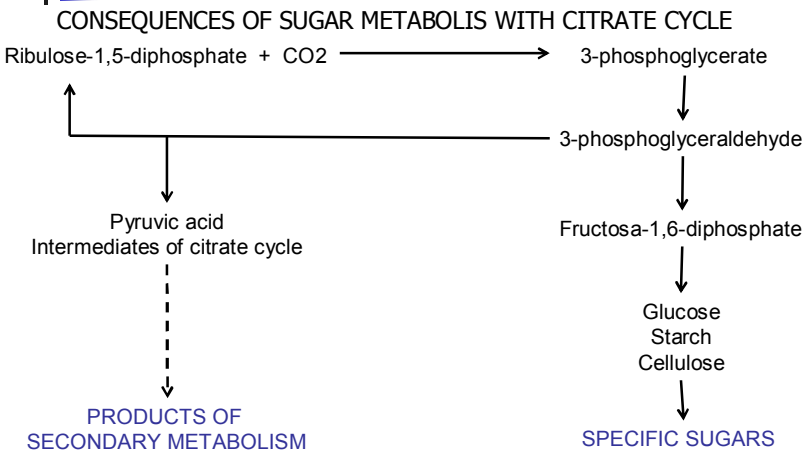


novobiosa – sugar derived from glucose
carbonamid- group – derived from nitrogen metabolism
C-methyl, *O*-methyl – several C1 sources (phormyl, hydroxymethyl, it is a pathway of methionine, glycine and serine)
3-amino-4-hydroxycoumarin – from shikimic acid via tyrosine
p-hydroxybenzyl – from shikimic acid
isopentenyl – via mevalonate

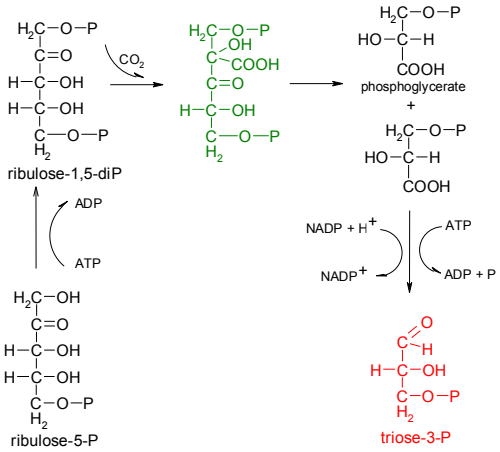
FIVE CATEGORIES OF NATURAL COMPOUNDS ACCORDING TO THEIR BIOSYNTHETIC ORIGIN

1. Specific sugars, polysaccharides, sugar part of glycosides
2. Shikimates
3. Metabolites derived from aminoacids
4. Polyketides
5. Isoprenoids

METABOLISM OF SUGARS



PHOTOSYNTHESIS – ABSORPTION OF CO_2 AND A REDUCTION TO SUGAR

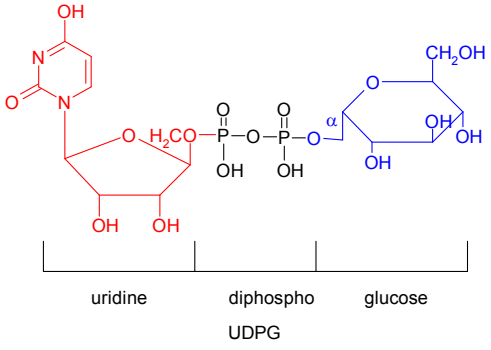


PRODUCTION OF GLYCOSIDES

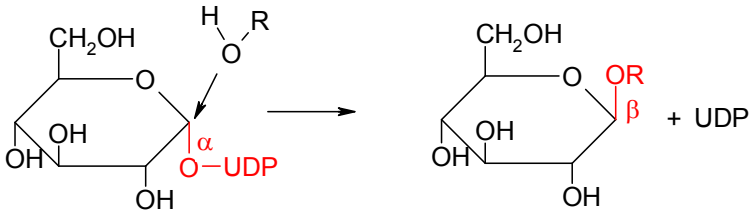
(transglycosylation)

1. Production of aglycones
2. Connection to sugar residues

CONNECTION OF SUGAR TO AN OXYGEN OF FURTHER SUGAR OR TO A OXYGEN ATOM OF ALCOHOLIC HYDROXYL, SULPHUR, NITROGEN, OR CARBON IS MOST OFTEN ARRANGED BY URIDINEDIPHOSPHOGLUCOSE (UDPG)

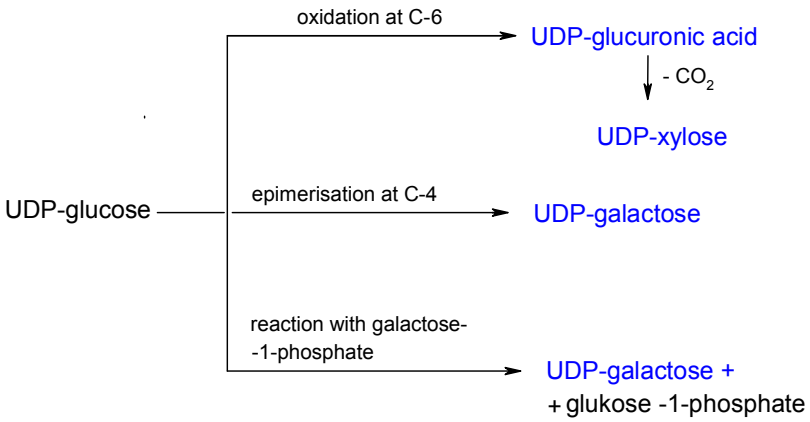


CHANGES OF C-1 CONFIGURATION



Release of UDP by nucleophil atack at C-1 of sugar residue shows as a consequence **A CHANGE OF CONFIGURATION AT C-1** and a production of **ß-glucopyranoside**

FUNCTION OF SUGAR NUKLEOTIDES DURING THE SUGAR CHANGES

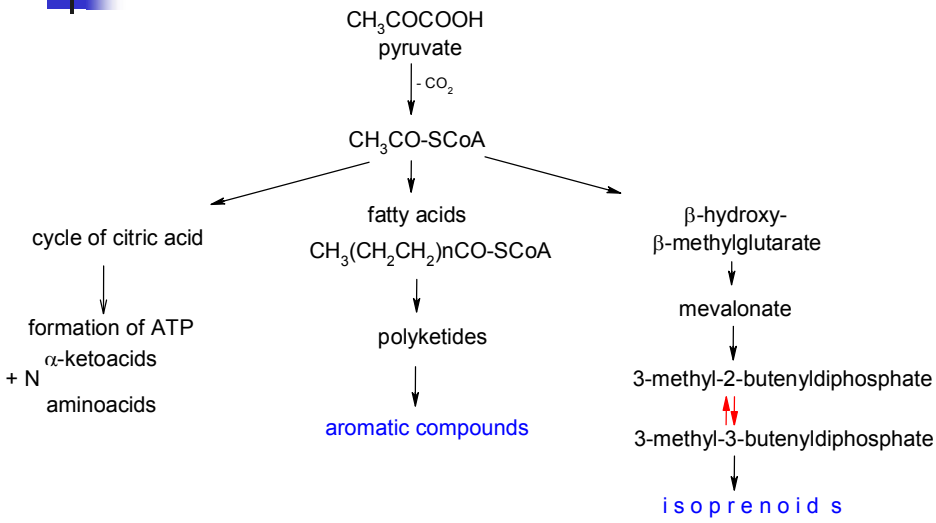


THREE-CARBON COMPOUNDS OF PRIMARY METABOLISM

Key compounds of primary metabolism – sugars entering CO_2 fixation
(triosophosphate, phosphoglycerate, sugars of pentose cycle).
→→→ pyruvate, phosphoenolpyruvate, acetylcoenzyme A.
These are building blocks of majority of natural compounds.

phosphoenolpyruvate + erythroso-4-phosphate → C_7 acid → shicimic acid →
→ chorismic acid → phenylpyruvic acid → phenylalanine →
→ cinnamic acid

ACETYLCOENZYME A



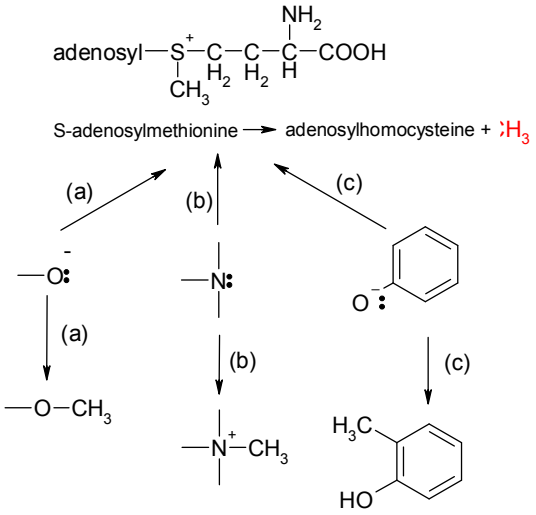
„ONE-CARBON METABOLISM"

METHYL GROUPS TRANSFERS TO A NUCLEOPHILLIC CENTRE MOSTLY S-ADENOSYLMETHIONINE, WORKING AS ALKYLATION REAGENT.

AT NATURAL COMPOUNDS:

- FORMATION OF PHENOLIC ETHERS
- FORMATION OF N-METHYL AMINES
- FORMATION OF C-METHYLATED PHENOLS AND KETONES

TRANSFER OF C_1 GROUP



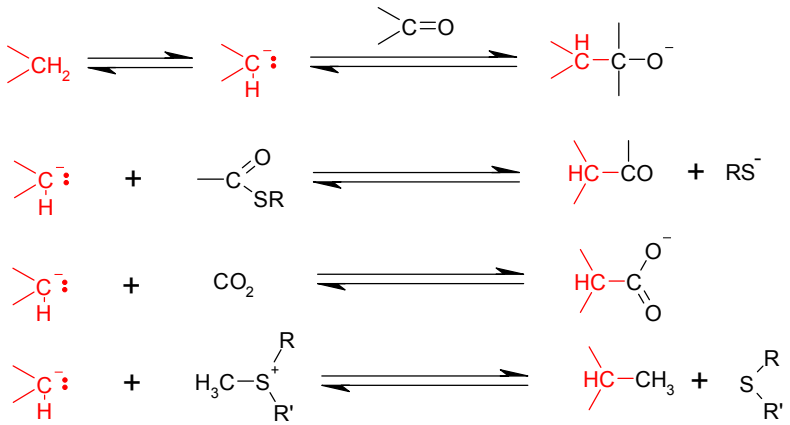
BASIC BIOSYNTHETIC REACTIONS

- Living organisms posses extraordinary diverse composition.
- Catalytic operation of enzymes
- Limited number of precursors

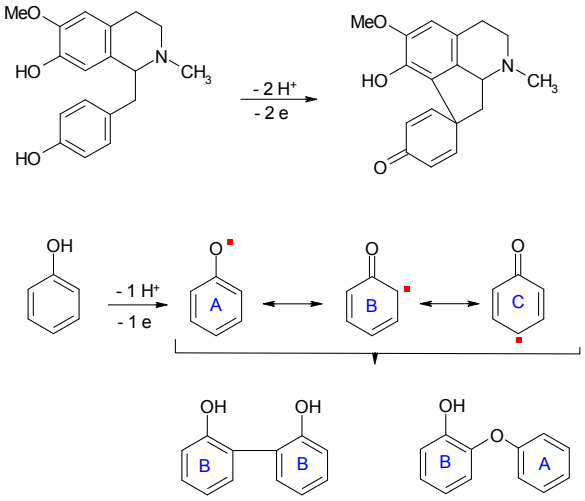
- Small number of reactions which find place in metabolism.
- Simple and known reactions.

FORMATION OF CARBON – CARBON BOND

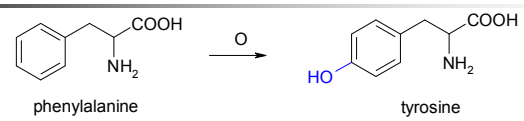
Nucleophillic methylene grouping + electrophillic C-atom of ketone, ester …



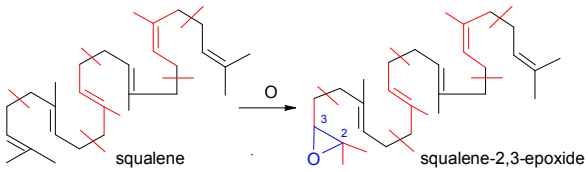
FORMATION OF C-C OR C-O-C BOND *VIA* OXIDATION



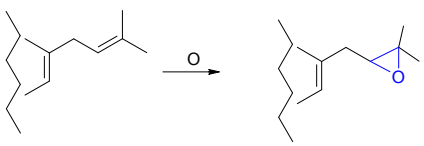
INTRODUCTION OF OXYGEN GROUP VIA OXIDATION OF C-H BOND, OR VIA DIRECT EPOXIDATION C=C



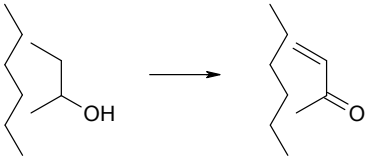
phenylalanine tyrosine



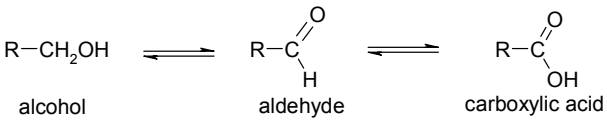
squalene squalene-2,3-epoxide



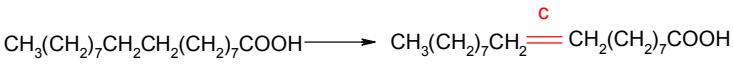
OXIDATION AND REDUCTION OF C-O OR C-C BOND
(FORMATION OF CARBONYL AND UNSATTURATED COMPOUNDS)



formation of carbonyl compounds

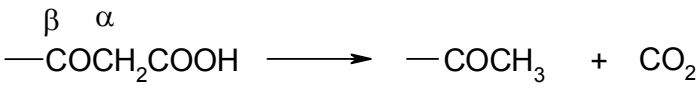


alcohol aldehyde carboxylic acid

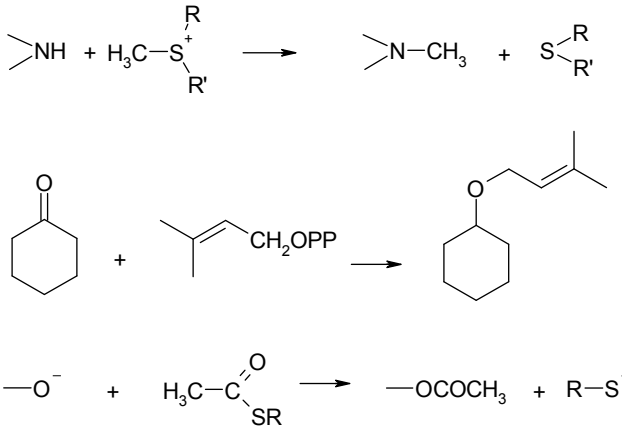


stearic acid $C_{18}H_{36}O_2$ oleic acid $C_{18}H_{34}O_2$

DECARBOXYLATION OF β-KETOCARBOXYLIC ACIDS



ALKYLATION AND ACYLATION OF NUCLEOPHILLIC ATOMS OF NITROGEN AND OXYGEN



SPONTANEOUS REACTIONS

(ALDOL CONDENSATION, FORMATION OF LACTONES AND LACTAMS)