FLAVANOIDS

- Flavonoids are polyphenolic compounds that occur ubiquitously in foods of plant origin.
- Dietary intake of these natural compounds has a significant effect on preventing a variety of diseases.
- Different flavonoid derivatives act as antioxidants
- Most of the flavonoids are very potent antioxidants because they can chelate metal ions, scavenge oxygen free radicals and prevent the oxidation of low density lipoprotein (LDL).

Twelve basic classes (chemical types) of flavonoids have been recognized:

- flavones,
- isoflavones,
- flavans,
- flavanones,
- flavanols,
- flavanolols,
- aurones.
- catechins (including proanthocyanidins),
- leukoanthocyanidins,
- chalcones,
- dihydrochalcones,
- anthocyanidins,
  - *Anthocyanidins and closely related flavonoids such as proanthocyanidins may collectively be referred to as anthocyanosides.*

STRUCTURE

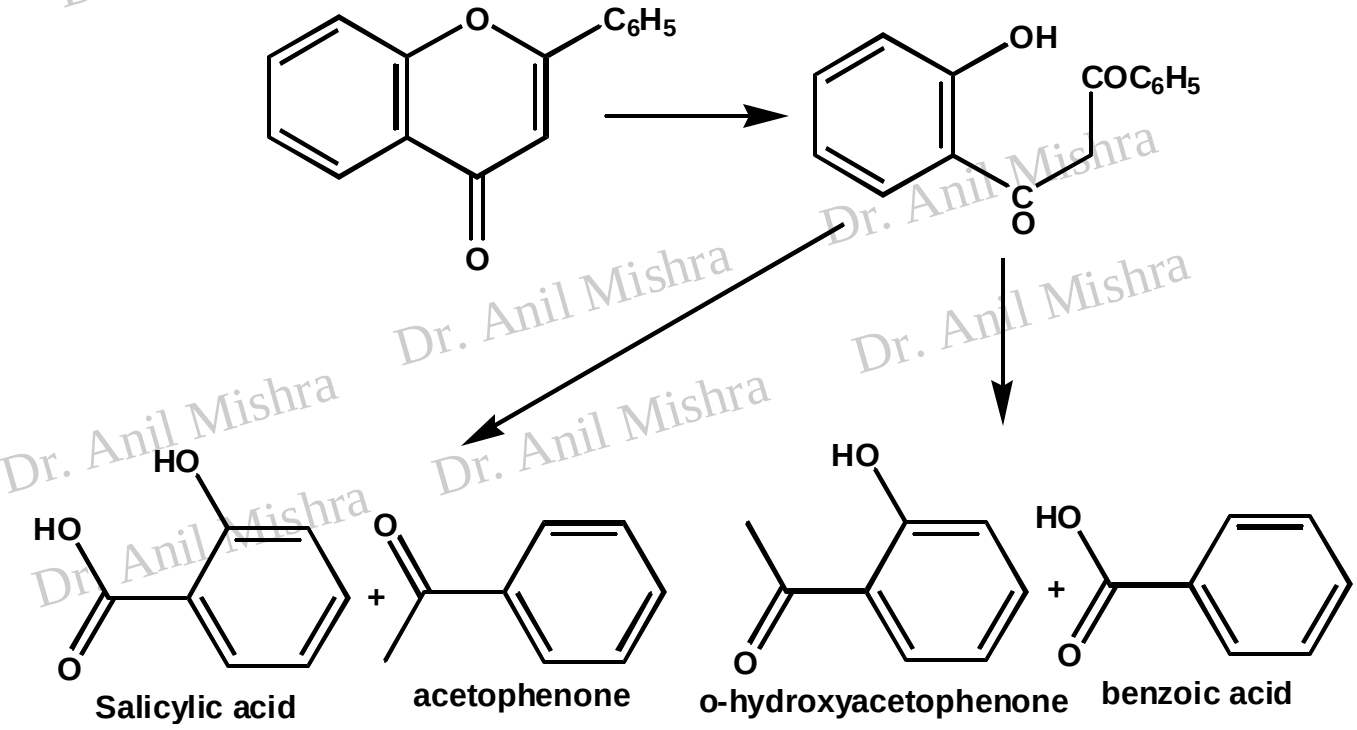
- Determine the number of free hydroxyl groups
- Determine the number of methoxyl groups
- Degradation studies
  - Fusion with alkali
  - Acid hydrolysis
- Structure confirmed by synthesis

Flavone

- These are yellow pigments found in plants.
- Flavones belong to the group of compounds known as flavonoids.
- Occurs as dust on flowers, leaves etc.
- Also known as ***anthoxanthins*** (anthoxanthinidin and glucose).
- Most flavones are soluble in water, ethanol, dilute acids and alkali.
- Oxonium salts are more coloured that free bases.

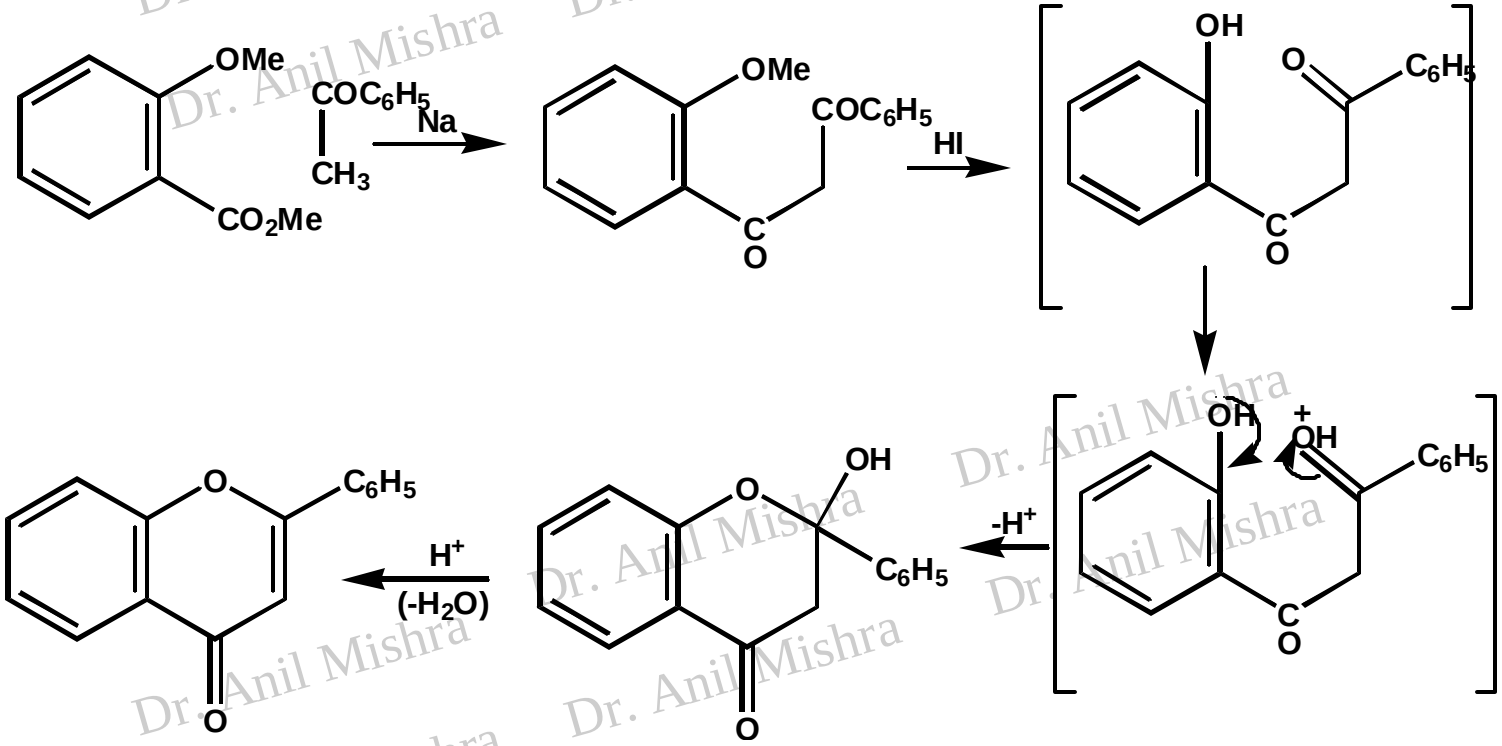
Structure of **Flavone**

- Contains no hydroxyl or methoxyl groups
- When boiled with KOH gives four products
  - Salicylic acid
  - Acetophenone
  - *o*-hydroxyacetophenone
  - benzoic acid



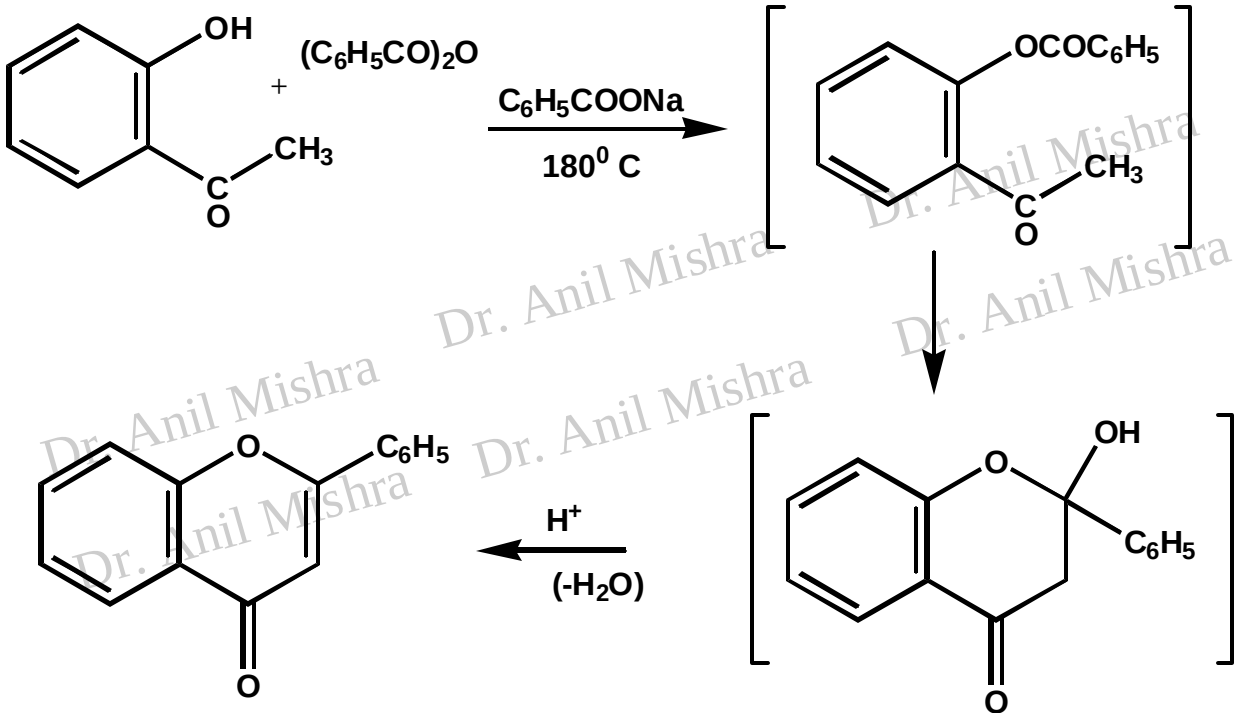
Kostanecki Synthesis

- Involves the condensation of the ester of an **alkylated salicylic acid** with **acetophenone** in the presence of sodium



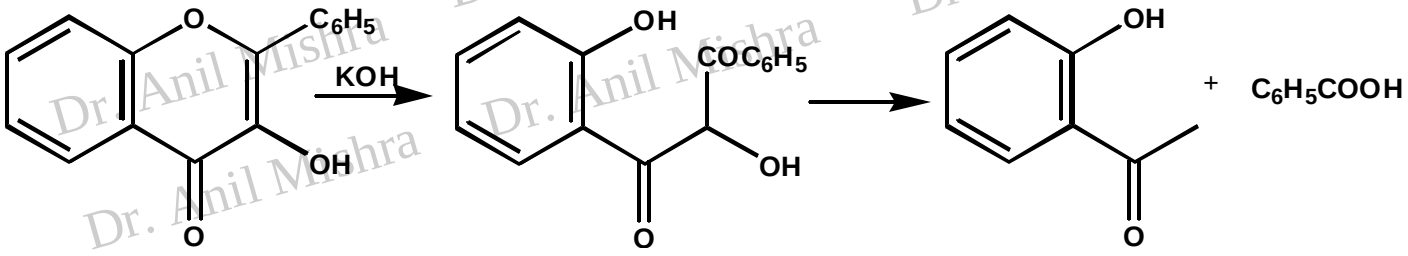
Robinson's Synthesis

- *o*-Hydroxyacetophenone is heated with the anhydride and sodium salt of a substituted benzoic acid

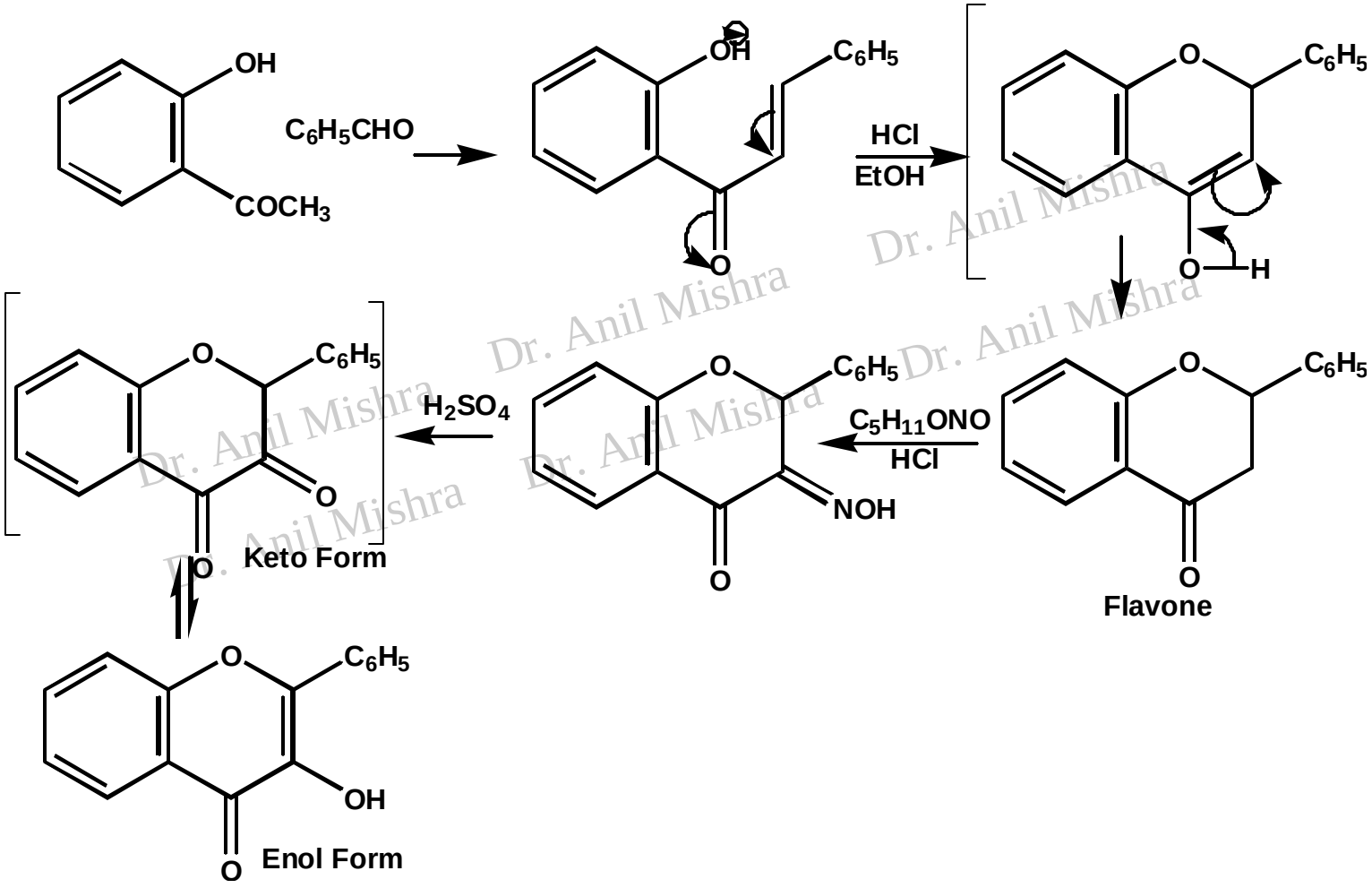


Flavanol

- widely distributed in plants in form of glycoside
- Contains one hydroxyl group
- When boiled with ethanolic KOH, it gives *o*-hydroxy-benzoylmethanol and benzioc acid
  - Flavanol therefore is 3-hydroxy flavone

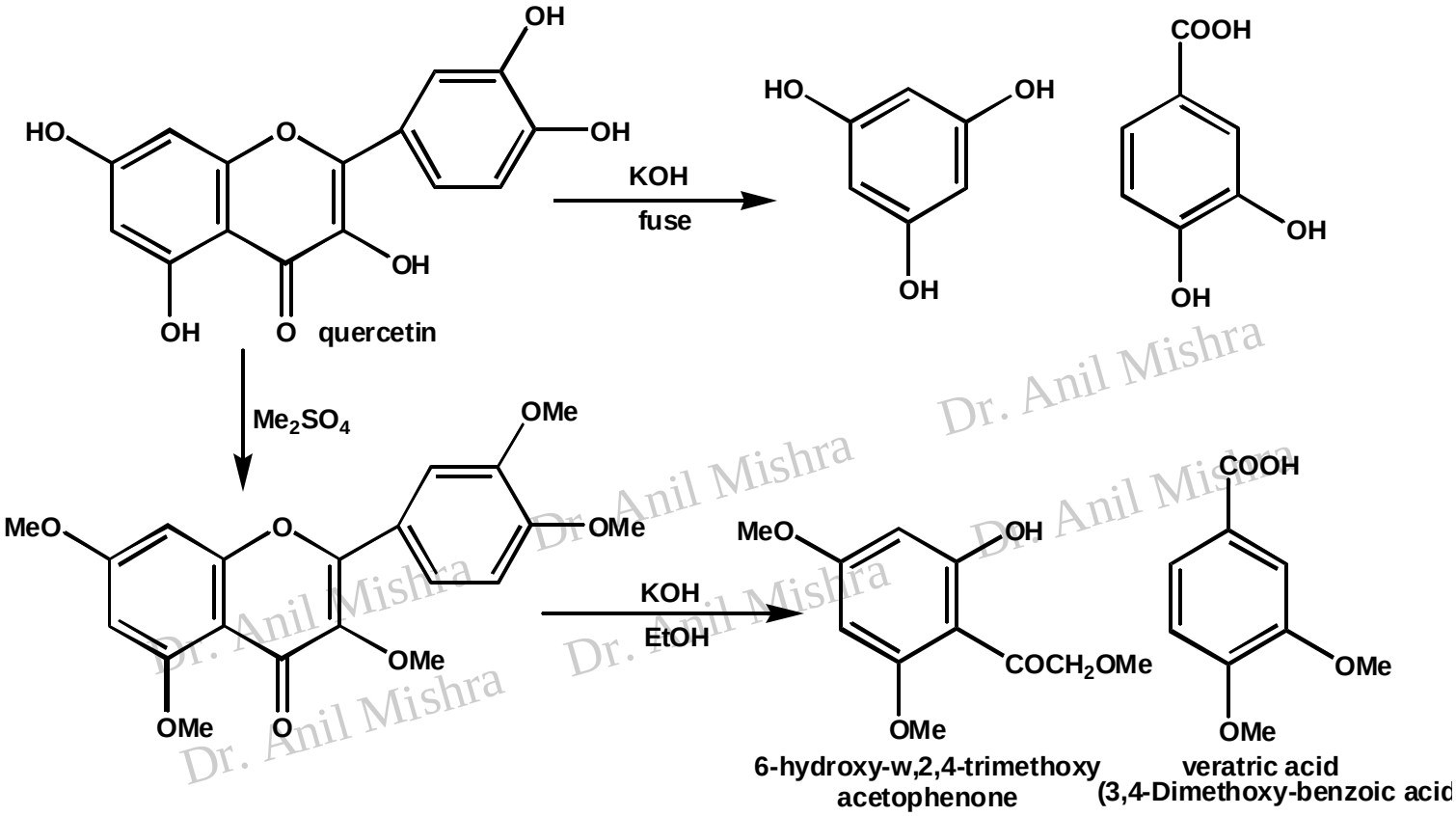


Kostanecki Synthesis



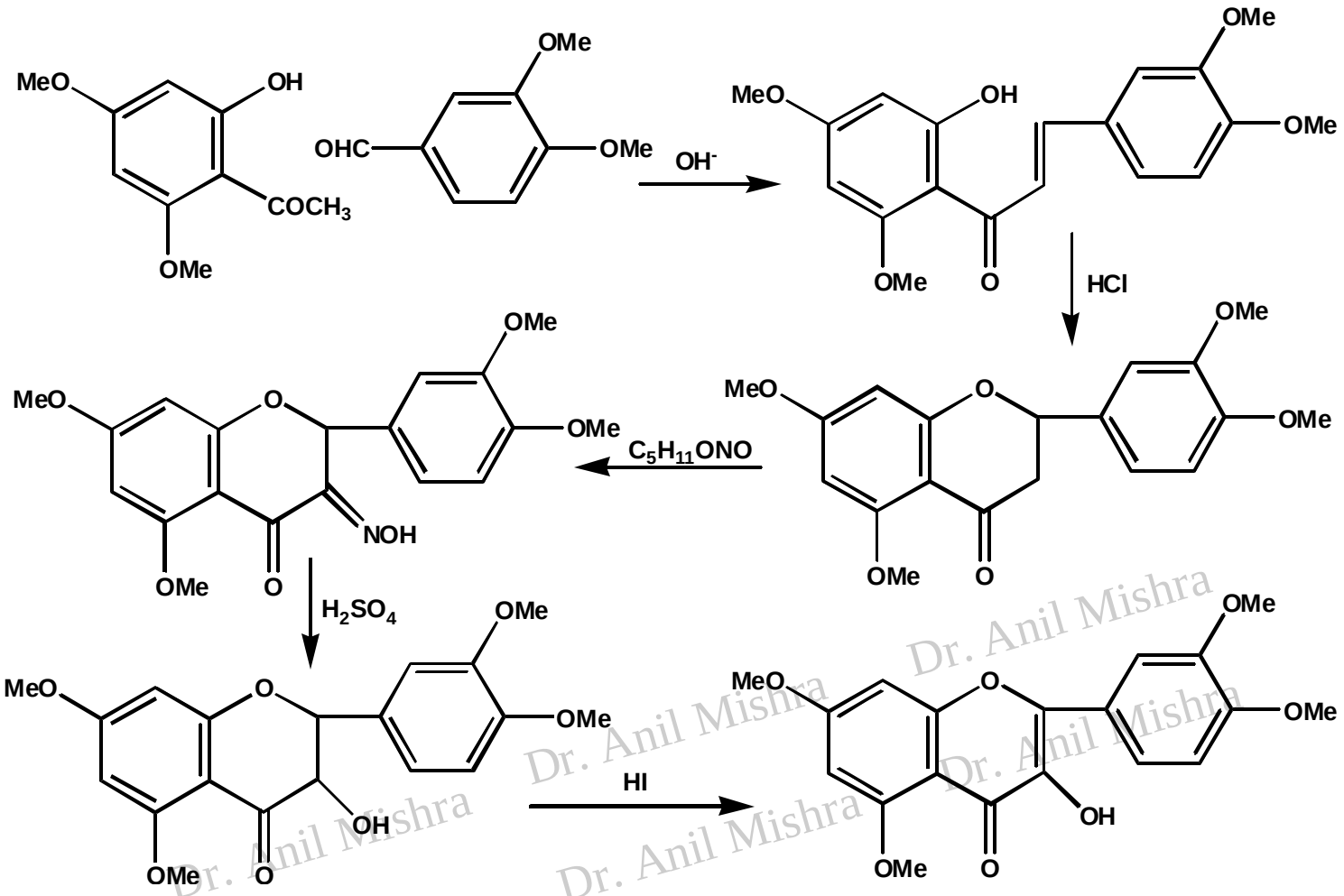
Quercetin

- Occurs as the glycoside *quercitrin* in the bark of *Quercus tinctoria*
- On hydrolysis with acid quercitrin forms quercetin and one molecule of rhamnose.
- The rahmnose moiety is attached to position 3.
- Contains five hydroxyl groups and no methoxyl group.
- Fusion with KOH gives phloroglucinol and protocatechuic acid.
- Methylation gives pentamethylquercetin, which on boiling with ethanolic KOH gives 6-hydroxy-ω,2,4-trimethoxyacetophenone and veratric acid

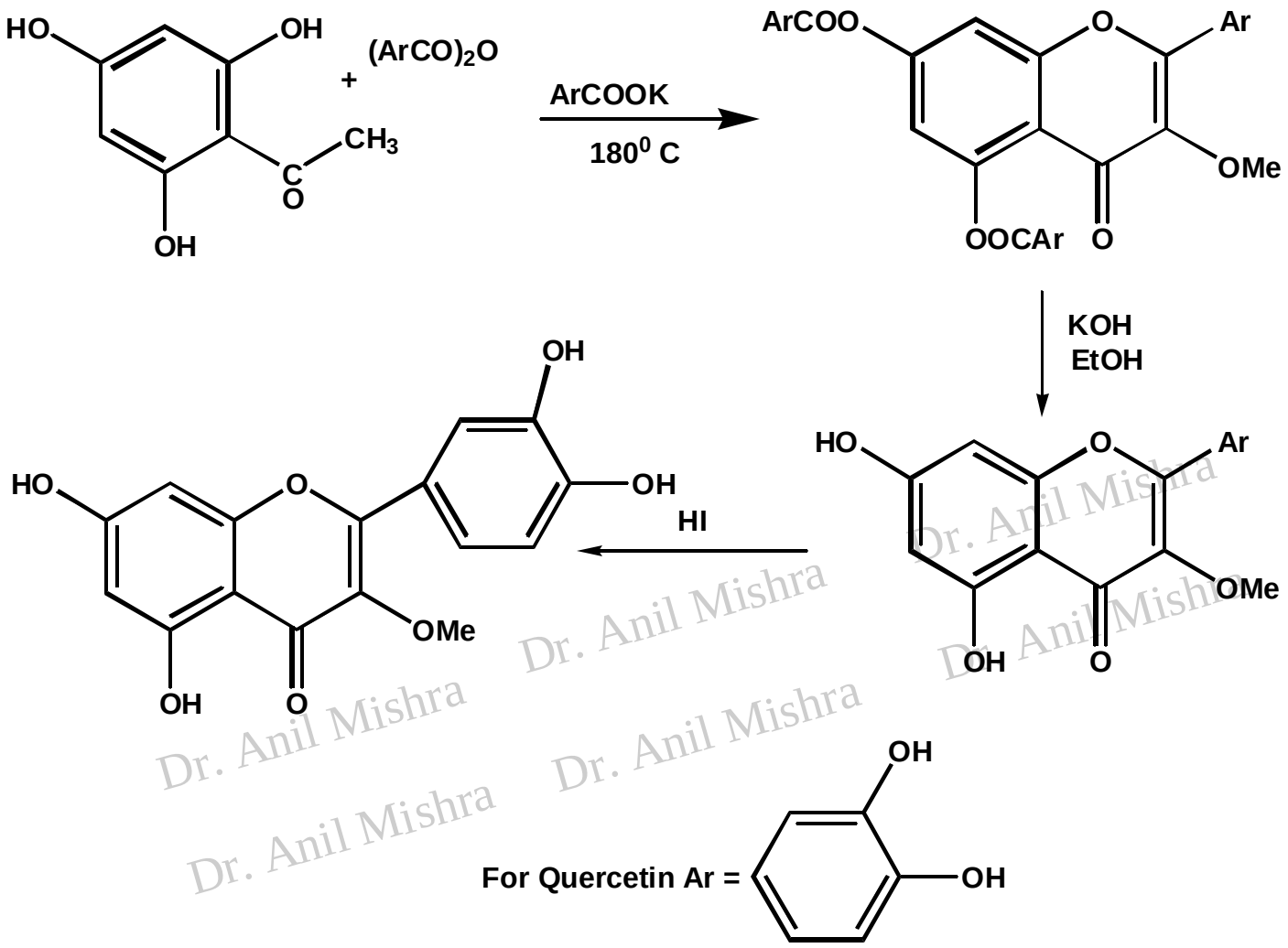


Thus quercetin is 3,3',4'5,7-pentahydroxyflavone

Kostanecki Synthesis

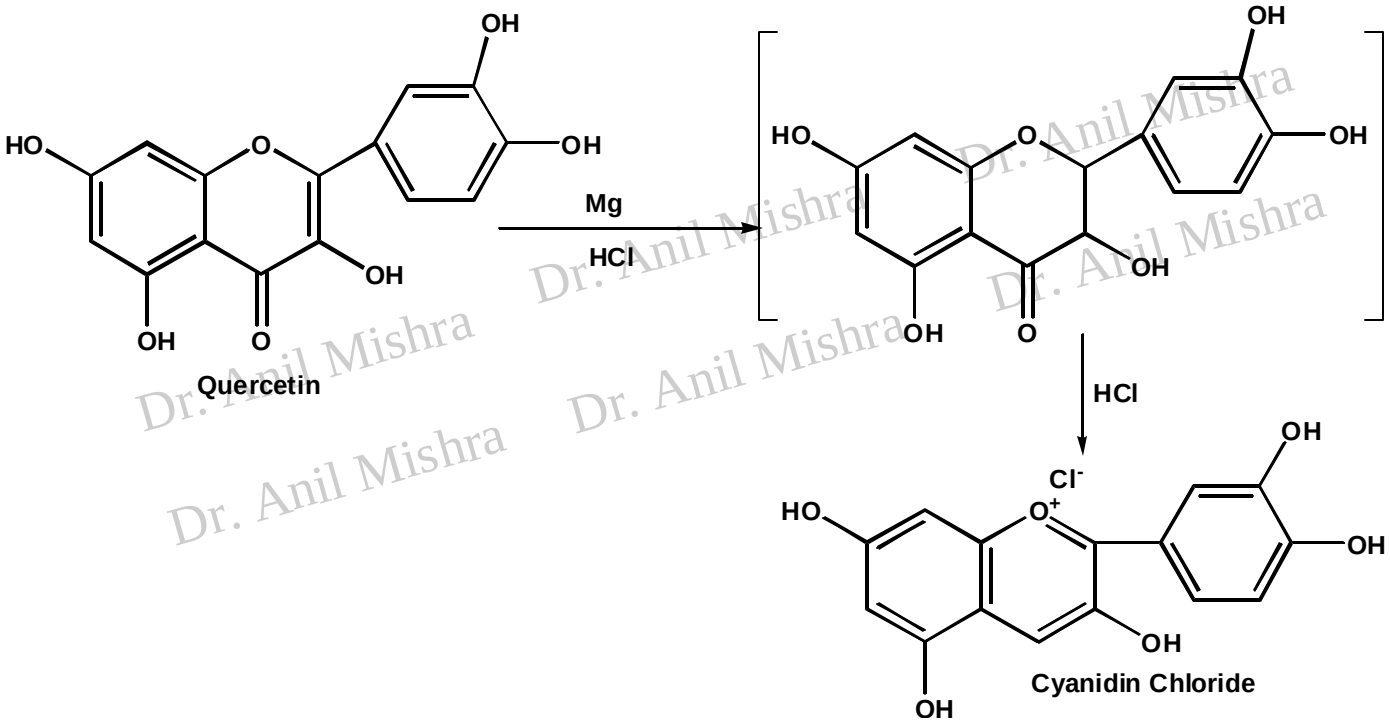


Robinson's synthesis



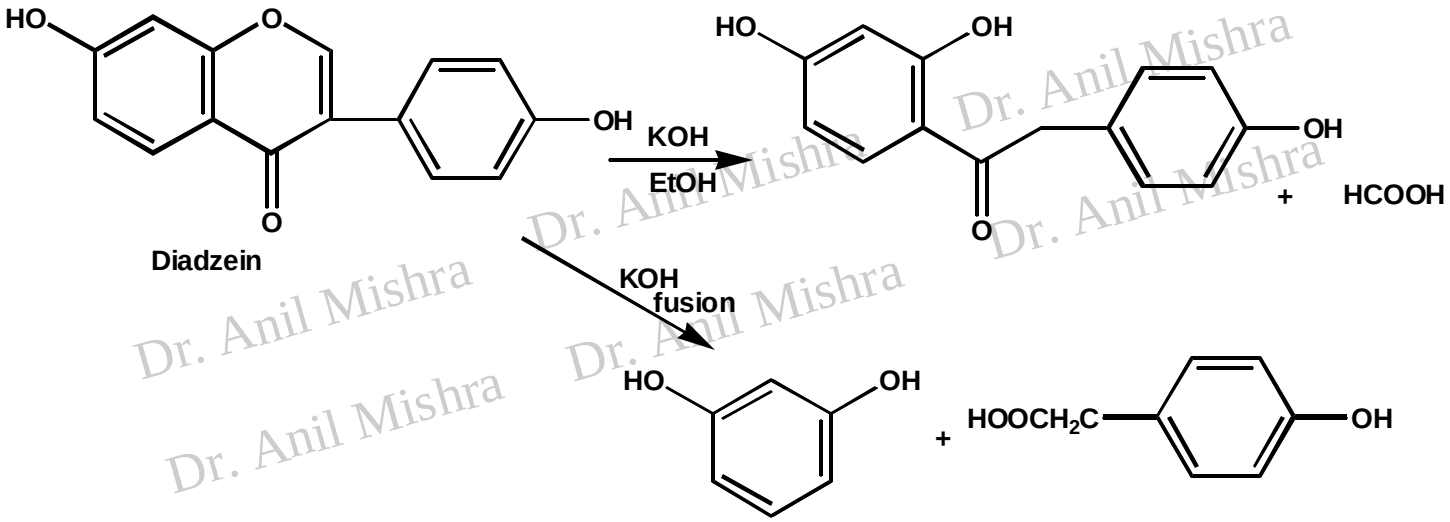
Relationship with Cyanidin Chloride

- **Both give phloroglucinol and protocatechuic acid on fusion with KOH.**
- **Quercetin can be converted to cyanidin chloride easily.**



Isoflavones

- Most of these (flavanones, flavones, flavonols, and anthocyanins) bear ring B in position 2 of the heterocyclic ring. In isoflavonoids, ring B occupies position 3.
- They occur in nature but are not as abundant as flavonones.
- They occur as free base or as glycosides.
- Structure is determined as was done for other compounds in the series.



Synthesis of isoflavones

Späth *et al.*

- This is a general method of synthesis of isoflavones starting from benzyl-*o*-hydroxyphenyl ketone and ethylformate
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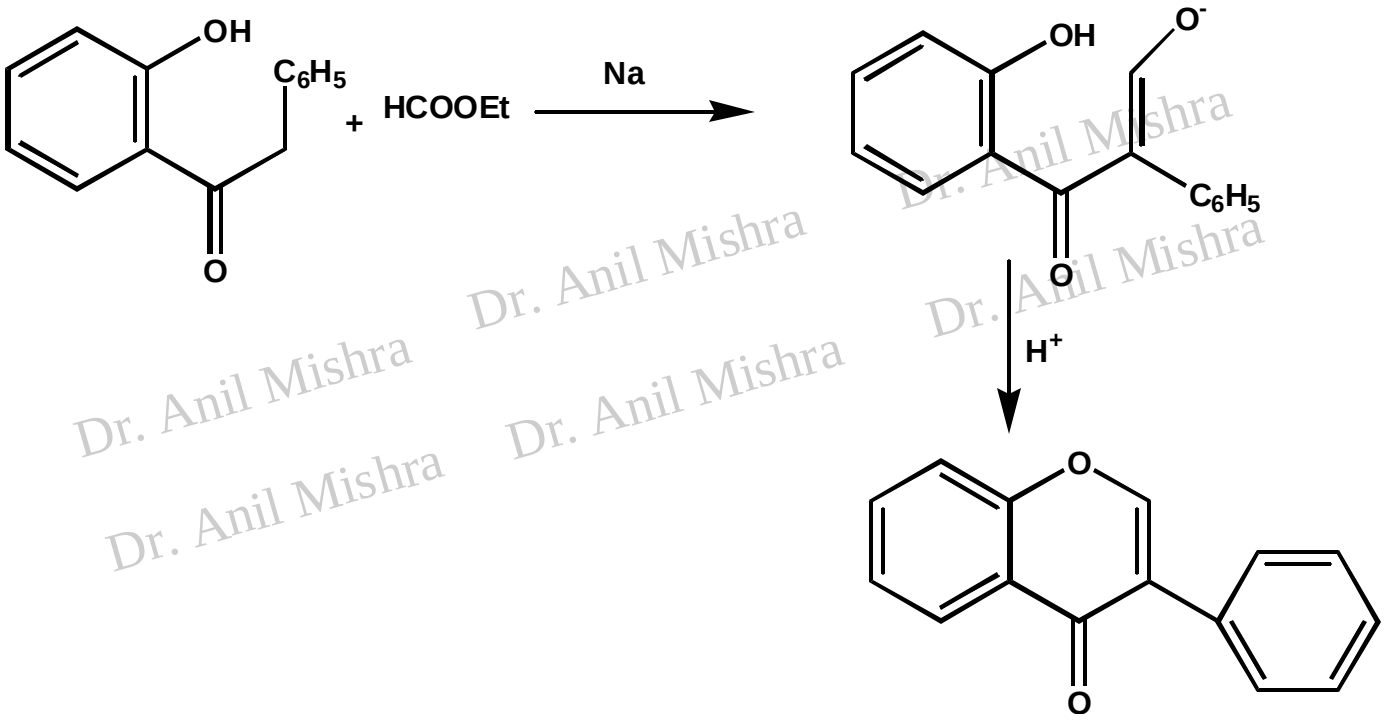

Various isoflavones can be synthesized using substituted ketones

- eg. Diadzein from 2,4-dihydroxyphenyl-*p*-hydroxybenzyl ketone
- Genistein from 2,4,6-trihydroxyphenyl-p-hydroxybenzyl ketone