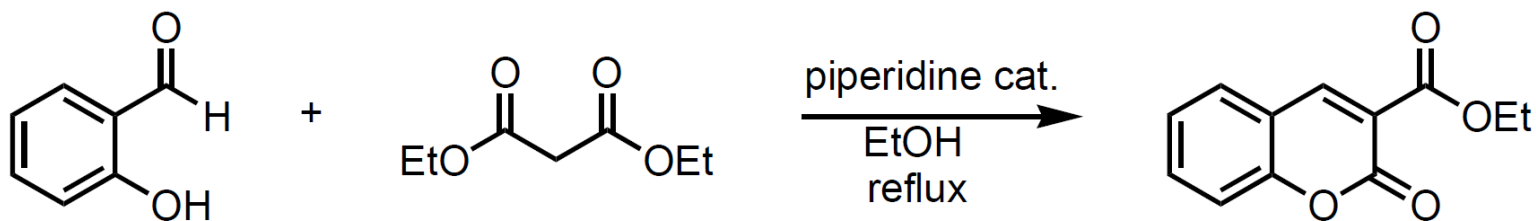


## Experiment 4:

# Synthesis of coumarins, Knoevenagel condensation

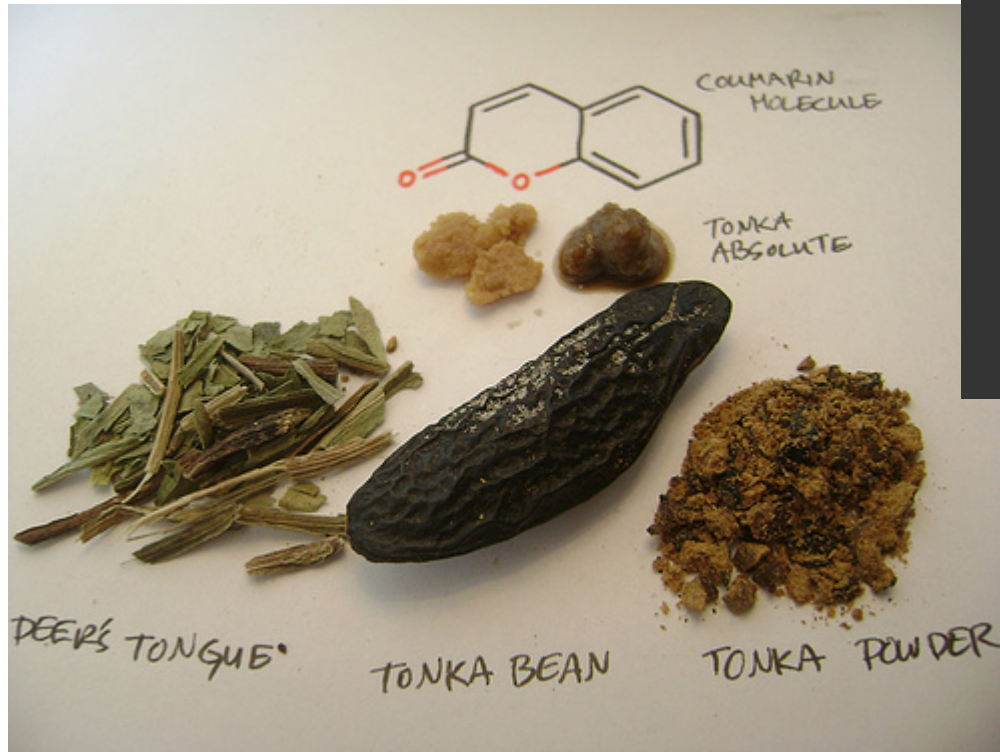
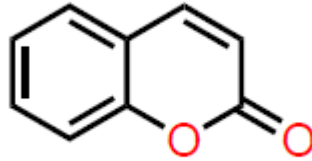
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- Synthesis of coumarins
- Chemistry of enolates: Knoevenagel condensation
- Techniques: reflux, cristallization
- Manipulation of toxic substances

# Coumarins

- Found in many plants



# Coumarins

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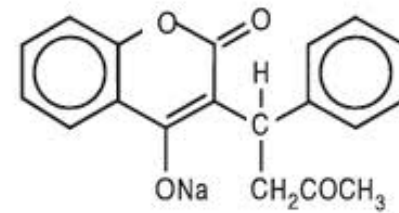
- Perfums



Among the most popular ingredients in perfumes coumarin takes pride of place being included in almost 90% of all perfumes! The pliability and versatility of this fragrance note is legendary, accounting for a sweet and fresh facet that rises up from the bottom onto the heart of the fragrance, lingering on the skin for hours and enriching a perfume composition via its scent magic.

# Coumarins

- Anticoagulants



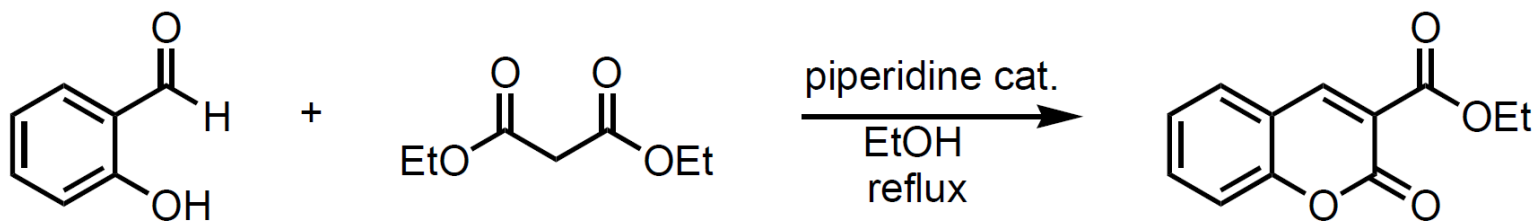
Warfarin sodium



## Experiment 5:

# Synthesis of coumarins, Knoevenagel condensation

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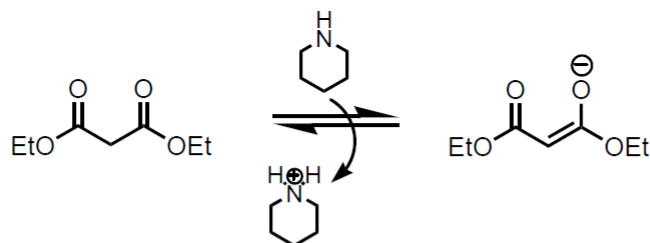


- Knoevenagel condensation + intramolecular transesterification
- **Knoevenagel condensation:** similar to the aldol reaction but now the nucleophile is the enolate of a compound with activated methylene protons

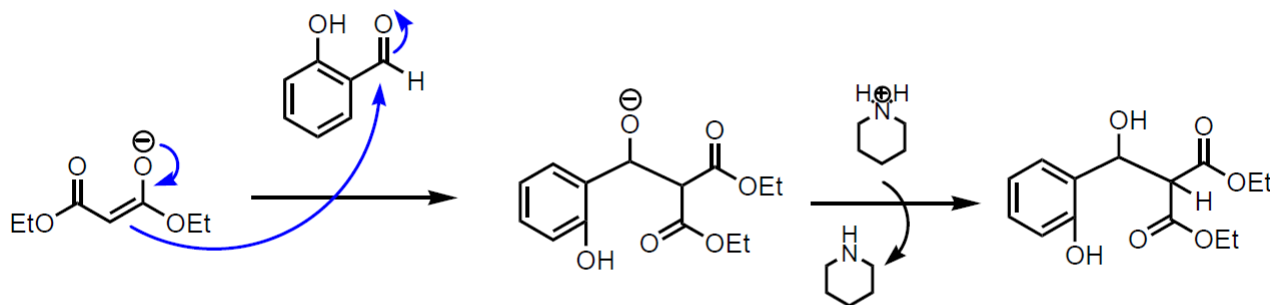
# Knoevenagel condensation

Heinrich Emil Albert Knoevenagel  
(18 June 1865 – 11 August 1921)

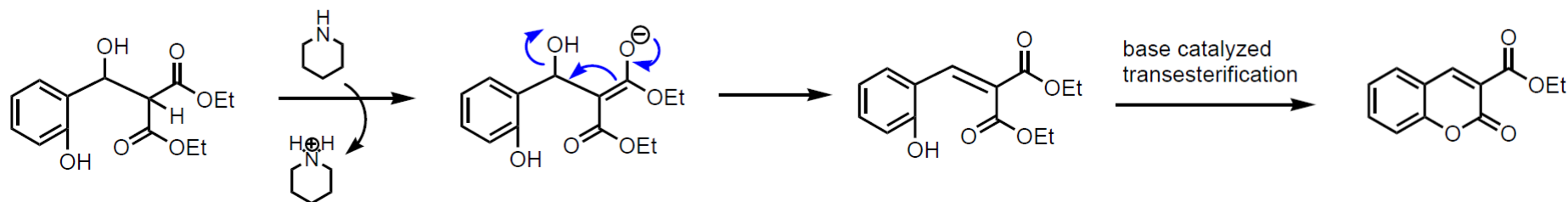
Knoevenagel, E. Condensation von Malonsäure mit Aromatischen Aldehyden durch Ammoniak und Amine. *Ber. Dtsch. Chem. Ges.* **1898**, 31, 2596-2619.



Enolate formation



Addition



## Experiment 5:

# Synthesis of coumarin, Knoevenagel condensation

|                           |                                                                                                                                                                                                                                                            |
|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Aldeide salicilica        |                                                                                       |
| Dietil malonate           |                                                                                                                                                                                                                                                            |
| Etanolo                   |                                                                                                                                                                          |
| Piperidina                |    |
| Cloruro di metilene       |                                                                                                                                                                          |
| 3-carboetossi<br>cumarina |                                                                                                                                                                                                                                                            |