Experiment 8

Various Synthetic experiments with cinnamaldehyde

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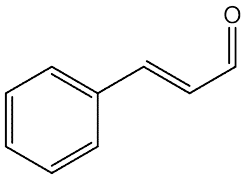
PURPOSE OF THE EXPERIMENT

Deal with various synthetic skills and reaction;
Aldol condensation reaction, Schiff's base reaction, Pinnick oxidation reaction, and Fischer esterification.

BACKGROUND INFORMATION

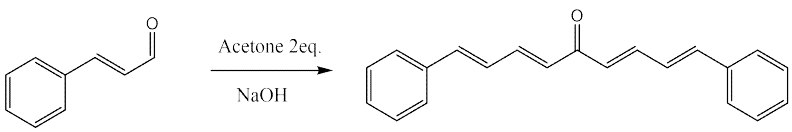


Cinnamaldehyde

Cinnamaldehyde is natural product that can be easily extracted from cinnamon bark by steam-distillation. Also cinnamaldehyde has the characteristic smell associated with cinnamon. Because of its specific structure that is α-β unsaturated carbonyl compounds, cinnamaldehyde was chosen for reaction materials of various synthetic experiments.

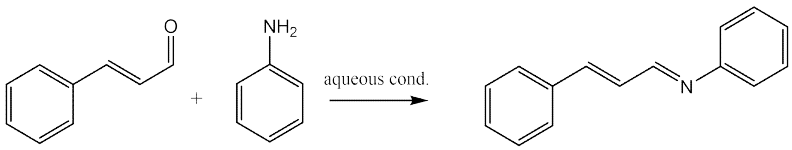
Aldol condensation

Aldol condensation is one of the most important reactions for new C-C bond formation. Aldol reaction requires two carbonyl compounds; One can be enolizable and the other have to be non-enolizable and much more electrophilic. We go through crossed aldol condensation with two different starting materials, cinnamaldehyde and acetone. Because We choose cinnamaldehyde, α-β unsaturated carbonyl compounds, so we have to keep considering that β-carbon of cinnam--aldehyde also electrophilic. Two α-carbon of acetone can react with cinnamaldehyde, as a result, final product would be dicinnamalacetone(1,9-Diphenyl-1,3,6,8-nonatetraen-5-one) Product material can be used for sunscreening.



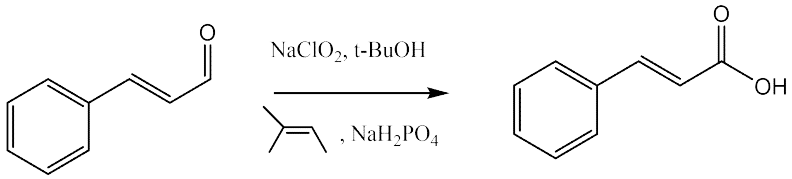
Shiff base reaction

Schiff base is sub-class of imines, but its general structure is [R1R2C=NR3] when R3 is not hydrogen. Schiff bases are known as important biologically active compounds with antibacterial, anticancer, antiviral, antioxidant, and anti-inflammatory. Typically, Schiff base reaction are carried out in organic solvents, which are volatile and toxic. However, cinnamaldehyde-derived Schiff bases have been created in no solvent conditions. We go through Schiff base reaction with cinnamaldehyde and aniline. Reaction completion can be decided monitoring aniline consumption by TLC analysis(Eluent as EtOAc or diethyl ether).



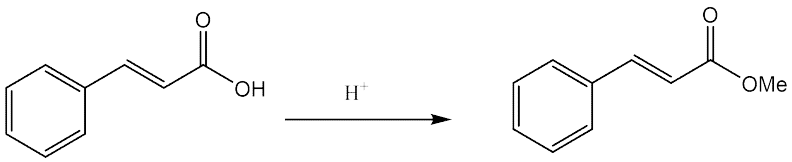
Pinnick oxidation

There are many different reaction methods for oxidizing aldehyde, however, only few methods can be applied to specific functional group(α-β unsaturated aldehyde). The Pinnick oxidation is a better effective method for sensitive functionalities and also capable of reacting with sterically hindered group. During the Pinnick oxidation reaction, HOCl produces as a byproduct and HOCl can react with so 2-methyl-2-butene, a scavenger is added. β-aryl substituted α-β unsaturated aldehyde works well with the reaction conditions. So we go through the Pinnick oxidation reaction of cinnamaldehyde to cinnamic acid.



Fischer esterification

Fischer esterification is acid-catalyzed esterification. Fischer esterification is one of simple reaction for synthesizing ester. Because of the simplicity of Fischer esterification reaction, it still widely use for synthesizing simple ester. Pinnick oxidation followed by Fischer esterification will be carried out.



EXPERIMENTAL PROCEDURE

Reagents and Properties

substance	*quantity*	*molar mass* (*g/mol*)	mmol*	*mp* (*°C*)	bp (*°C*)	*density* (*g/mL*)
Cinnamaldehyde						
Acetone						
EtOH						
NaOH						
t-BuOH						
2-Methyl-2-butene						
$NaClO_2$						
NaH_2PO_4						
MeOH						
H_2SO_4						
Aniline						
Ethyl acetate						
Diethyl ether						

PROCEDURE

Caution: Wear lab coats and safety goggles at all times while in the lab. Many chemicals are potentially harmful. Prevent contact with your eyes, skin, and clothing. Wearing contact lens is strictly prohibited.

Caution:

Experiment should be performed under fume hood. Ethyl acetate, diethyl ether, and t-BuOH is flammable liquid and can cause skin and eye irritant. 2-Methyl-2-butene is also flammable liquid and skin irritation, and high aspiration hazardous.

1. Aldol condensation

Add 2.3mmol of cinnamaldehyde into a vial and mix with 2.0ml of 95% EtOH. Add 1.2ml of 2M NaOH solution. Add 1.13mmol of acetone to cinnamaldehyde solution and stir under room temperature about 15 minutes. Vacuum filtrate bright yellow precipitate. Wash it with water followed by EtOH.

2. Schiff base reaction

Dissolve 0.93ml(10mmol) of aniline in 10ml of water and add 10mmol of cinnamaldehyde. Stir the mixture about 30 minutes under room temperature. Use TLC analysis to confirm reaction completion. Calculate the yield and do 1H NMR analysis

3. Pinnick oxidation

1.2mmol cinnamaldehyde, t-BuOH 25ml, 6ml 2-methyl-2-butene in one r.b.f.

10ml of water solution with 11mmol of $NaClO_2$, 8.3mmol of NaH_2PO_4, dropwisely add into aldehyde solution.

8 hour reaction?

*Pre-test should be needed

4. Fischer esterification

Weigh 0.25g of cinnamic acid and place in 25ml r.b.f with stirring. Add 9ml 0.2M MeOH followed by 0.07ml of 75 mol% H_2SO_4(p-TSA can be replaced). Connect to reflux condensor and heat the reaction mixture for 1 hour. To monitor the reaction completion, run TLC(eluent for 1:4 mixture of EtOAc:hexane, Rf value is 0.1 for cinnamic acid and 0.74 for methyl cinnamate).

After completion of reaction, add 10ml of saturated $NaHCO_3$ solution for neutralization followed by 10ml ether. Extract organic layer through seperatory funnel and wash the aqueous layer with 10ml of ether one more time. Combine two extracted organic layer and wash with 10ml of saturated NaCl solution and dry with $MgSO_4$. Filter the dry agent and remove the solvent by evaporation. Calculate the reaction yield and do NMR analysis.

Pre-Laboratory Questions

1. Summarize all MSDS's of chemicals used in this experiment.
2. Set your reaction order that can complete the entire reaction as fast as you can.

Post-Laboratory Questions

1. Assign peaks in 1H NMR spectrum to confirm the product(Shiff base, aldol product, and .
2. Draw the mechanism of the aldol reaction of acetone and cinnamaldehyde.