Experiment

Various Synthetic experiments with cinnamaldehyde

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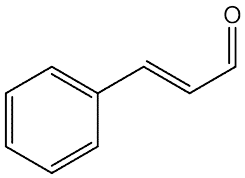
PURPOSE OF THE EXPERIMENT

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

BACKGROUND INFORMATION

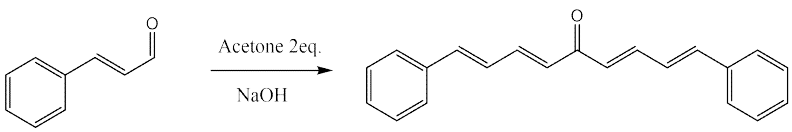


Cinnamaldehyde

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.

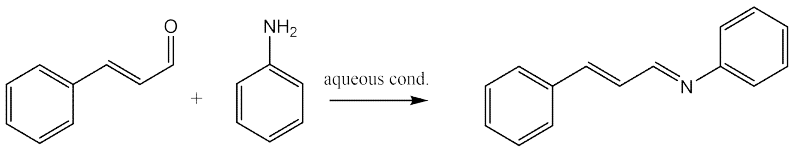
Aldol condensation

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.



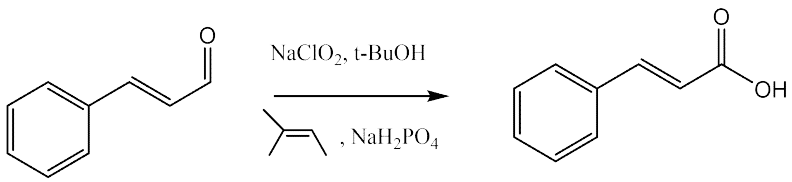
Shiff base reaction

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 water 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).



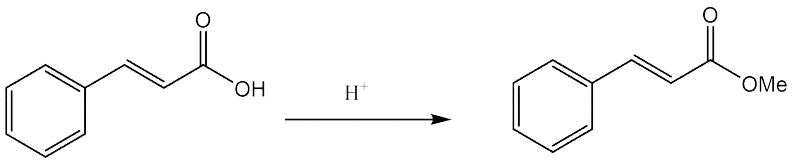
Pinnick oxidation

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.



Reagents and Properties

substance	*quantity*	*molar mass* (*g/mol*)	mmol*	*mp* (*°C*)	bp (*°C*)	*density* (*g/mL*)
Cinnamaldehyde		132.16				
Acetone		58.08		-95	56	0.7845
EtOH	~2ml					
Aniline	0.93ml	93.1	10			
2M NaOH	1.2ml					
t-BuOH	25ml					
2-Methyl-2-butene	11ml	70.1329			38.5	0.662
NaClO2	0.995g	90.44	11			
NaH2PO4·H2O	1.145g	137.98	8.3			
0.2M MeOH	9ml					
H2SO4	~0.1ml					
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. Schiff base reaction

Dissolve 0.93ml of aniline at 10ml of distilled water in 100ml round bottom flask(RBF) and add 1.26ml of cinnamaldehyde.

Stir the mixture about 30 minutes under room temperature. Be sure that aniline is stirring within solvent(Aniline is insoluble at water, so it can attach inside wall), vigorously.

You can use TLC analysis to confirm reaction completion (Eluent: 1:1 mixture of Ethyl acetate and n-hexane).

Vacuum filtrate the reaction media and wash it with distilled water. Dry the product and calculate the yield and do 1H NMR analysis.

2. Aldol condensation

Add 2.3mmol(0.3ml) of cinnamaldehyde into a vial and mix with 2.0ml of EtOH. Add 1.2ml of 2M NaOH solution and 0.08ml of acetone to vial and stir under room temperature about 15 minutes.
(Put the vial beside the reaction 1's RBF for saving space.)

Vacuum filtrate precipitate and wash it with water followed by EtOH. Dry the product and calculate percentage yield and do 1H NMR analysis.

3. Pinnick oxidation

※***Oxidation reaction needs longer time, so it recommended that running oxidation reaction first before other reactions.***

Place 0.32g of cinnamaldehyde, 25ml of t-BuOH, 6ml of 2-methyl-2-butene in 100ml RBF. In other beaker, dissolve 1g of $NaClO_2$, 1.14g of NaH_2PO_4 with 10ml of distilled water.
Add this solution to RBF, dropwisely.

After 1.5~2 hour, transfer the reaction solution to separatory funnel.

Add 30ml of ethyl ether to separatory funnel and mix the funnel several times. Separate aqueous layer and organic layer into two different beaker.

Move the aqueous layer to separatory funnel again, and repeat the washing with ethyl ether two times(Gather separated organic layer in one beaker).

Wash combined organic layer(ethyl ether) with 30ml of brine(saturated NaCl solution), and dry with Na_2SO_4.

Filter the drying agent(Na_2SO_4) and pour the ether in pre-weighed 250ml RBF. Evaporate ethyl ether with rotary

evaporator and gain white solid product. Check the after weigh of RBF and calculate the reaction yield.

4. Fischer esterification

Add 9ml 0.2M MeOH and 0.1ml of H_2SO_4 into reaction 3' 250ml RBF. Connect 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, add 10ml of saturated $NaHCO_3$ solution for neutralization.

Move the reaction solution to separatory funnel and add 10ml of ethyl ether. Wash the aqueous layer with ethyl ether two more times.

Wash the combined organic layer with 10ml of brine and then dry with Na_2SO_4.

Filter the drying agent and remove the solvent with rotary evaporator. Calculate the reaction yield and do NMR analysis.

Pre-Laboratory Questions

1. Summarize all MSDS's of chemicals used in this experiment.
2. What is the key role of 2-methyl-2-butene during Pinnick oxidation? Explain with reaction mechanism.

Post-Laboratory Questions

1. Assign peaks in 1H NMR spectrum to confirm the product(Shiff base product, aldol product, and methyl cinnamate).

2. Draw the mechanism of the aldol reaction of acetone and cinnamaldehyde.