Honors Cup Synthetic Proposal

Section: 220
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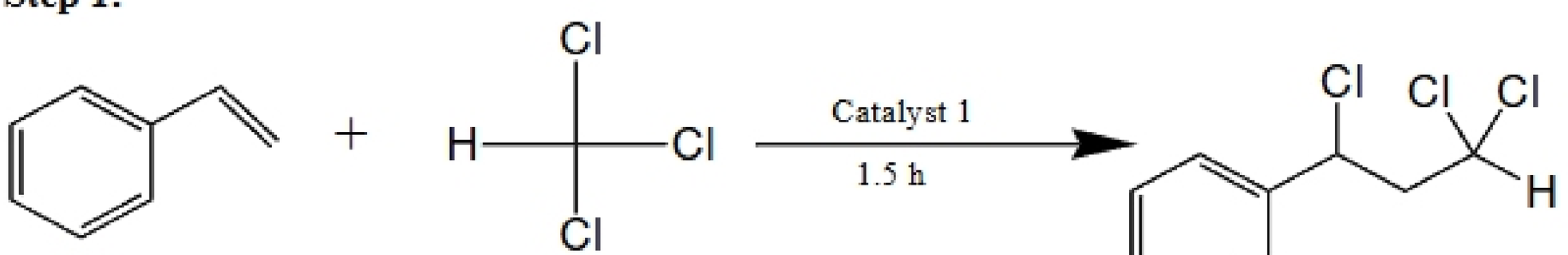
Title: Synthesis of Trans-Cinnamaldehyde using Nobel Prize winning Grubbs Catalyst, 1st Generation

Introduction:
Trans-Cinnamaldehyde, in its naturally occurring form, gives cinnamon its spice. Cinnamaldehyde is used for the flavoring in candy, ice cream, and chewing gum. Besides flavoring and scents, this compound has many other practical uses. Cinnamaldehyde is also used as a fungicide applied to the root systems of many crops. Because of its low levels of toxicity, it is perfect for agricultural applications. It is sometimes used as an insecticide, and its scent is used to repel certain animals such as cats and dogs. Clearly, this compound has many practical uses. This compound would be very interesting for the Chemistry 216H lab because the students would be producing a compound that they recognize by its distinct smell. Students feel more involved in the chemistry when they can identify with the compounds being produced, and everyone can identify with cinnamon flavoring and the great smell it produces. Everybody in the chemistry building will appreciate the lab rooms smelling like cinnamon candy! This method of synthesis is also particularly interesting because the catalyst used won the Nobel Prize this year. Both the compound being produced and the synthesis by which it is made are both tremendously interesting.

Overall synthetic reaction scheme:

Step 1:

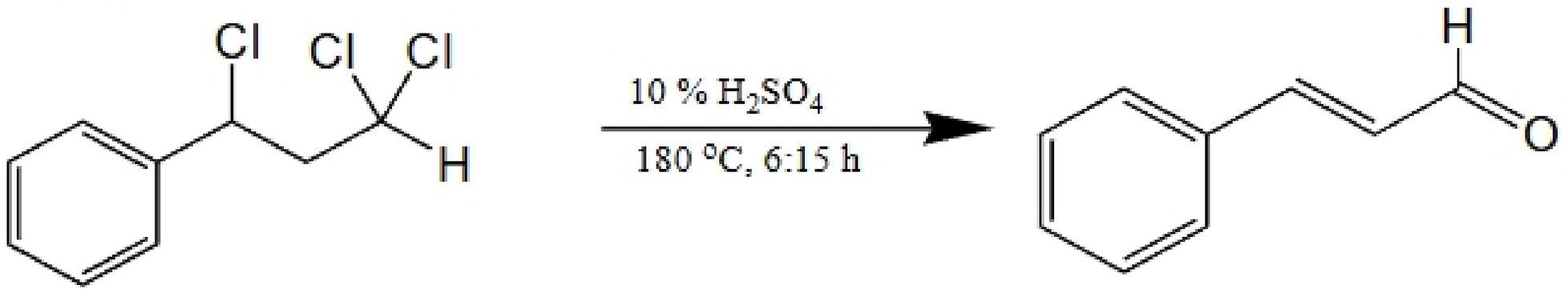


Styrene

1,1,1-Trichloromethane (Chloroform)

(1,3,3-trichloropropyl)benzene

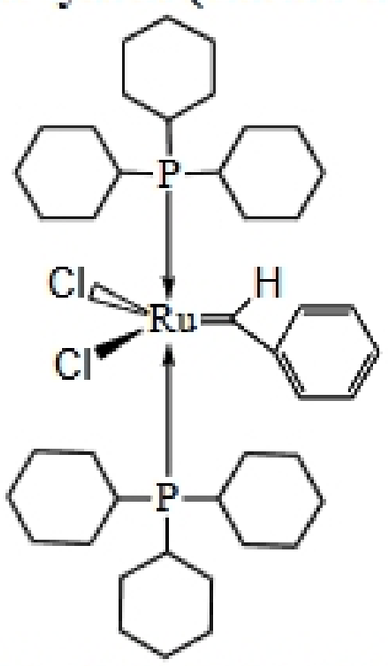
Step 2:



(1,3,3-trichloropropyl)benzene

Trans-cinnamaldehyde

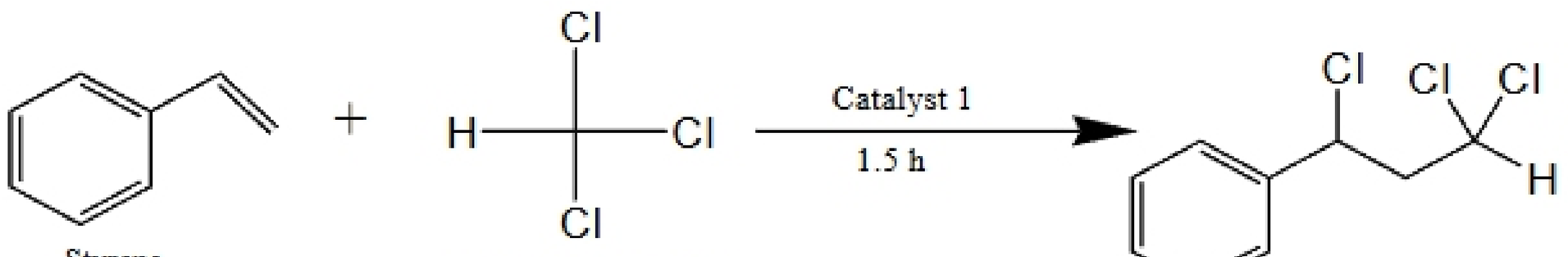
Catalyst 1: (Grubb's Catalyst 1st Generation)



Grubbs Catalyst, 1st Generation

Step 1

Synthetic transformation 1:



Styrene

1,1,1-Trichloromethane (Chloroform)

(1,3,3-trichloropropyl)benzene

- Catalyst on second page

Experimental 1

Product: (1,3,3-Trichloro-propyl)-benzene. To a Schlenk flask equipped with a reflux condenser was added catalyst 1 (210 mg, 0.247 mmol), 1,1,1-trichloromethane (10 mL) and styrene (2) (.531 g, 4.94 mmol). The reaction was heated to 75 8C under N2 atm. for 1.5 h. The reaction was concentrated and purified by silica gel chromatography (pentanes) to give (1,3,3-Trichloro-propyl)-benzene (1.15 g, 4.74 mmol, 96% yield) as a colorless oil.

*The molar values for the original reaction were divided by 1.94 in order to compensate for the desired intermediate yield.
*This step corresponds to the formation of a different compound, (1,3,3-Trichloro-butyl)-benzene, but we confirmed with Dr. Koreeda that this generic process applies to our molecules as well.

Expected yield: 96 % 1.1 g

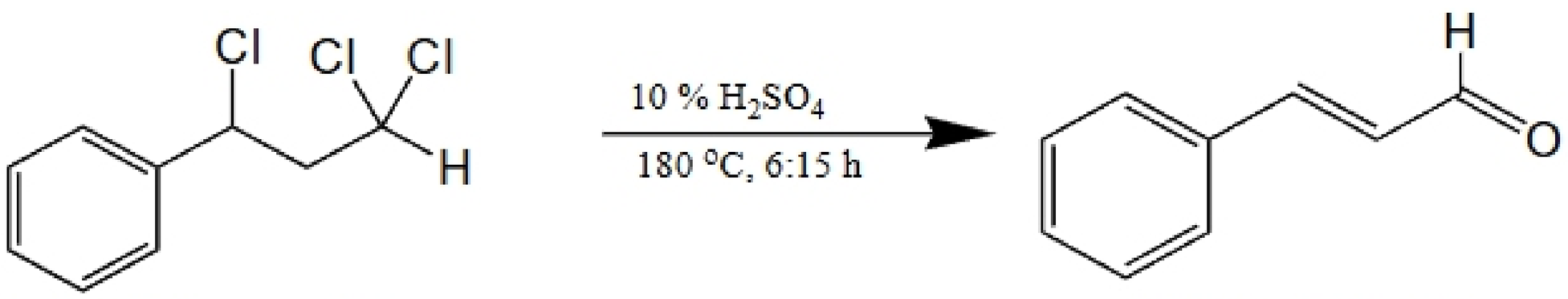
Safety, disposal and green issues 1:

Grubb's Catalyst is classified as an irritant to the eyes skin and respiratory system. Grubb's catalyst should also never come into contact with water and should be handled with care as it has a limited shelf life. However, it is a very effective catalyst in that it is less reactive than some others, including Shrock's catalysts. Grubb's catalyst should not under any circumstances be disposed of down a drain, but may be

disposed of in a regular waste container. Grubb's catalyst is significant to green chemistry because it enables reactions to be more efficient, thereby requiring fewer resources and creating less waste. It also allows for more environmentally nontoxic reactions by requiring less hazardous solvents and creating less hazardous waste. Styrene is classified as a harmful substance and as a possible carcinogen by the EPA. It is toxic through external contact with the skin, and inhalation or swallowing. It is also flammable and must be handled with extreme care under a hood to avoid inhalation. Styrene should be disposed of in a hazardous waste container. Styrene dissolves in most organic solvents, and should eventually be disposed of dissolved in a combustible solvent and then burned in a chemical incinerator containing an afterburner and scrubber. Proponents of green chemistry have been attempting to produce styrene via a more environmentally friendly route, which involves using xylenes instead of benzene, but styrene itself is still considered to be quite toxic. Chloroform is also a harmful substance in the same ways as styrene is, through contact with skin, eyes, and inhalation, and should never be handled without gloves. It should also be disposed of in a hazardous waste container and then through controlled incineration, preferably when mixed with another combustible material, such as styrene. Chloroform has some green issues. Currently there is a move to decrease its use in industry to limit exposure to it. During the procedure of this part of the experiment, precaution should be taken while heating the reactants, thus the inclusion of the reflux condenser to prevent overheating. The system should be kept closed from the air as two of the reactants are flammable. All procedures should be performed in a hood for safety purposes to minimize the risk of inhaling the catalyst. Groves and safety goggles should be worn at all times during the experiment.

Step 2

<u>Synthetic transformation 2</u>:



(1,3,3-trichloropropyl)benzene

Trans-cinnamaldehyde

<u>Experimental 2</u>

Alternative hydrolysis. To a heavy walled reaction tube was added compound 6 (1.1 g, 4.88 mmol), and H2SO4 (28% aq., 1.0 mL). The tube was sealed with a Teflone screw cap and heated to 180 8C (oil bath temp) for 6.5 h. The reaction was partitioned between Et2O and H2O. The organic layer was separated, concentrated, and purified by silica gel chromatography (pentanes/Et2O, 10:1) to give trans-cinnamaldehyde (14) (500 mg, 3.78 mmol, 77% yield) as a yellow oil.

*The molar values were multiplied by 15.75 to scale for desired product yield.

<u>Expected yield: 77% 0.5 g</u>