Experiment 8

Multistep Synthesis (3)

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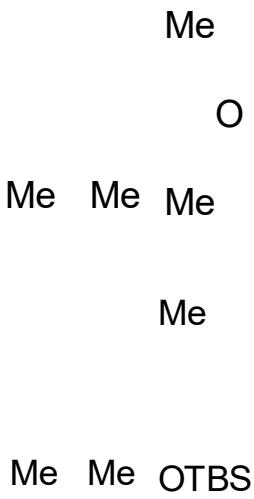
PURPOSE OF THE EXPERIMENT

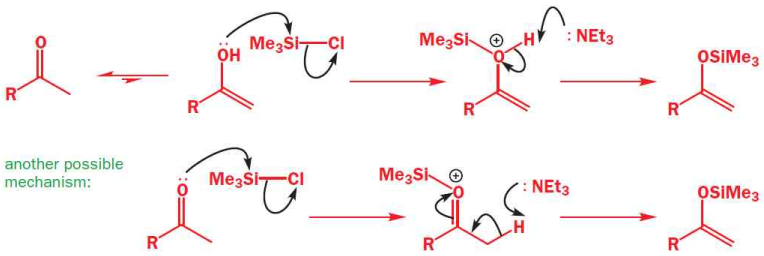
Conduct a multistep synthesis: Silyl enol ether synthesis by silylation

BACKGROUND INFORMATION

Synthesis of silyl enol ether

Silicon-oxygen bonds are so strong that silicon reacts with carbonyl compounds on oxygen even without a strong base to form the enolate. The reaction probably goes through the small amount of enol present in neutral solution, and just needs a weak base (Et3N) to remove the proton from the product. An alternative view is that the silicon reacts with oxygen first, and the base just converts to oxonium ion to the silyl enol ther. Both mechanisms are given below-either might be correct. This is one of the two best ways to make a stable enol derivative from virtually any enolizable carbonyl compound.





EXPERIMENT A

Synthesis of silyl enol ether

Reagents and Properties

substance	*quantity*	*molar mass (g/mol)*	mmol*	*mp (°C)*	bp (°C)	*density (g/mL)*

SM	1.0 g	166.26	6.015			
Et3N	2.5 mL	101.19	18.044	88.8	-115	0.726
TBSOTf	2.8 mL	264.34	12.029		65-67	1.151
THF	19 mL	72.11		-108	65-67	0.889

Et3N = Triethyl amine

TBSOTf = *tert*-Butyldimethylsilyl trifluoromethanesulfonate

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: Dichloromethane, ethyl acetate and hexane are toxic and irritating. Ultraviolet radiation can cause severe damage to the eyes. Do not look directly into the UV lamp.

1. Preparing TLC reference

Obtain standard samples of starting material and product from your TA. Prepare a developing chamber by adding proper amount of ethyl acetate and hexane. By performing TLC analysis, find appropriate separation condition. View the plate under UV light to visualize the spots.

Caution:

2. Setting Up the Apparatus

In the fume hood, dissolved 1.0 g of starting material in 50 mL Tetrahydrofuran in a 100 mL 1-neck round flask.
Et3N was added to a solution of ketone under dry ice/acetone cooling condition. TBSOTf was added dropwise under the same conditions. The mixture was allowed to warm to room temperature and stirred for 2 h. The reaction mixture was quenched by adding sat. $NaHCO_3$ 20 mL, and pentane 20 mL. The layers were separated and the organic layer was washed with diluted water 20 mL 3 times.
Organic layer dried over $MgSO_4$ and the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (silica 100% pentane) to afford the desired silyl enol ether product as a cololess oil. Rf 0.90 (100% pentane)

3. Characterizing the Product

Obtain the NMR spectrum as directed by your TA.

4. Post-Laboratory Questions

1. Calculate the percent yield of the reaction.
2. Use your TLC data to explain whether or not the acetylation reaction went to completion.

3. Assign peaks in 1H NMR spectrum to confirm the formation of the desired product.

5. Pre-Laboratory Questions

1. Write the MSDS of all reagents that is used in this experiment.

2. Search for the original research paper that discussed the use of silyl protection of alcohol. What are the journal name, year, volume, page, authors?