Progress toward the Synthesis of an Antiviral Phenylpropenoid & Derivatives

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TBIOMD495

Introduction

Target Molecule - Phenylpropenoid

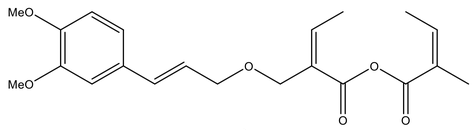


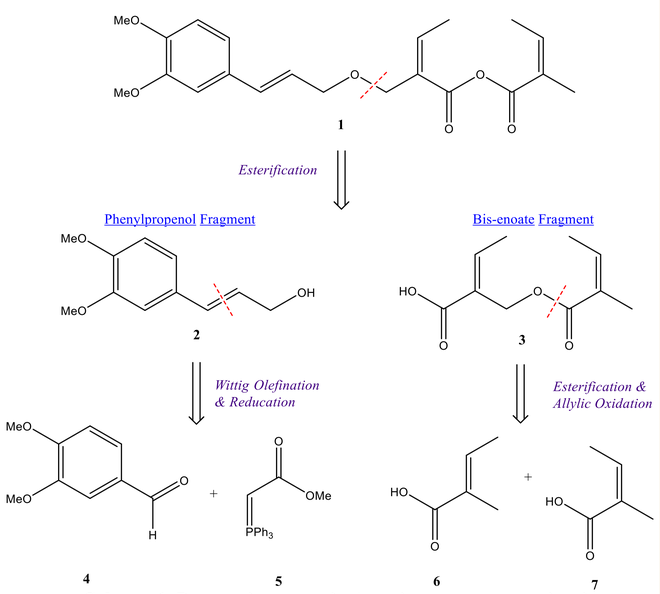
Figure 1. Target bioactive molecule

- Naturally occurring compound found in *Bupleurum fruticosum.*[1]
- Anti-inflammatory properties and potential to be an effective capsid binder for Human Rhinovirus (HRV).[2]
- Potential for further study of antiviral properties.

Project Goal

Develop a synthesis for **1** to use for preparation of derivatives and future structure-activity relationship studies.

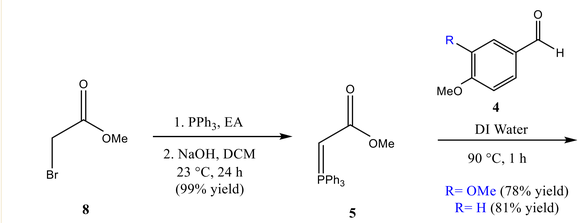
Synthetic Pathway



Scheme 1. Proposed retrosynthetic pathway to target molecule

Results

Phenylpropenol Fragment



Scheme 2. Synthesis of phenylpropenol fragment (**2**) via Ylide synthesis[3], Wittig reaction[4], and DIBAL reduction[5]

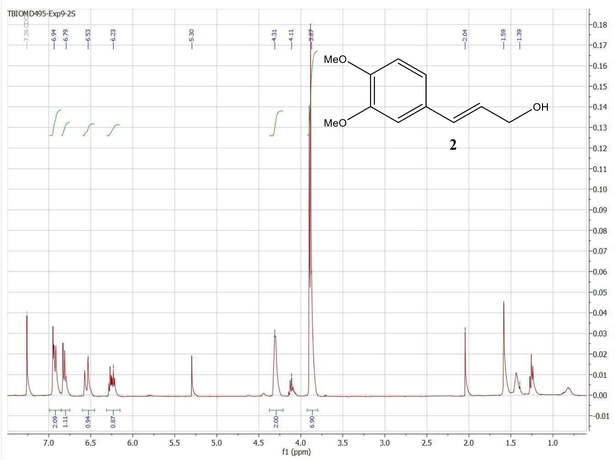
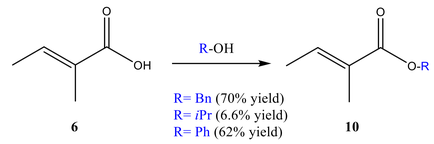


Figure 2. ^{1}H NMR of phenylpropenol fragment **2** (400 MHz, $CDCl_3$)

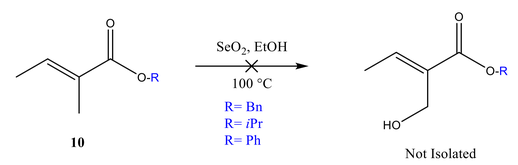
Key Signal Changes:
- Loss of OMe signal near 3.78 ppm
- New 2H signal at 4.30 ppm
- Signal at 3.87ppm for 6H

Bis-enoate Fragment

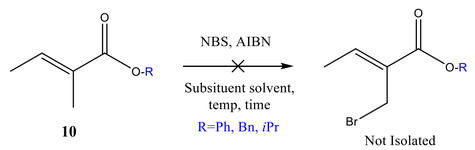


Scheme 3. Esterification of tiglic acid[6]

- Efforts Towards Allylic Functionalization



Scheme 4. Efforts toward oxidation using selenium dioxide[7]



Entry	R	Solvent	Temperature	Time
1	Bn	CCl_4	80 °C	22 h
2	Bn	CCl_4	80 °C	2.5 h
3	*i*Pr	CCl_4	90 °C	5 h
4	*i*Pr	CCl_4	90 °C	2 h
5	*i*Pr	Ac_2O	120 °C	1 h
6	*i*Pr	Ac_2O	120 °C	0.5 h
7	*i*Pr	Ac_2O	120 °C	0.5 h
8	Ph	Ac_2O	120 °C	0.5 h

Table 1. Conditions explored for allylic bromination [8, 9]

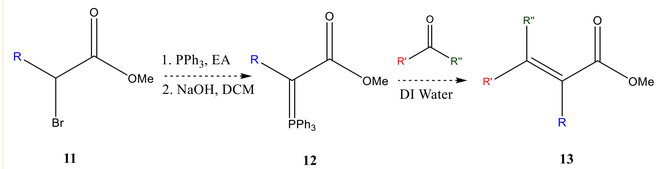
- Reactions show conversion of starting material via TLC analysis
- Products inseparable on silica gel column

Conclusion

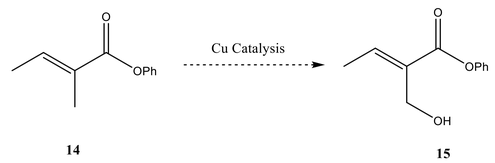
- Phenylpropenol fragment of target molecule synthesized
- Tiglate esters prepared in good yield
- Efforts toward allylic functionalization of tiglic esters underway

Current Focus and Future Directions

Progress towards Bis-enoate Fragment



Scheme 5. Alternative substrate synthesis



Scheme 6. Alternative strategy for allylic oxidation

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References

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