UNIVERSITI TEKNOLOGI MARA

SYNTHESIS OF 3,5-DIACETOXY-12-BENZYLOXYSTILBENE

AZYYATI MOHD SUHAIMI

Dissertation submitted in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons)

Faculty of Pharmacy

October 2005

ACKNOWLEDGEMENTS

First and foremost, I wish to express my appreciation to Allah the almighty, for without his permission I could not have completed the research in time. Along the way, a lot of people have helped me to make sure this research project possible.

I would like to acknowledge my supervisor, Prof. Dr. J.F.F. Weber for his kindness, praiseworthy supervision, thoughtful suggestions and without whose perseverance this thesis would have never been accepted in the first place.

I am also indebted to Dr. Ibtisam Abdul Wahab and Miss Saraswati Velu for their valuable generosity, patience and tolerance in helping me during both good and hard times. They were there at the beginning to get things going.

I also owe a debt of gratitude to my friends, Nor Hayati, Nafiza and Fariz whom I had worked with in the same laboratory and also my housemates for their whole-hearted support and cooperation throughout the research.

Finally, but by no means last in my thoughts, I would like to particularly thank my beloved family for their understanding and never-ending encouragement. They provided the love, the help and the fulfillment required for me to keep going and helped me to put this project into its proper perspective.

TABLE OF CONTENTS

			Page
	PAGE		
APPROVAL FORM			ii
ACKNOWLEDGEMENTS TABLE OF CONTENTS			iii
TABLE OF CONTENTS			
LIST OF TABLES			V
LIST OF FIGURES LIST OF SCHEMES			vi
			vii
		BREVIATIONS	viii
ABSI	RACT		X
CHAF	TER O	NE (INTRODUCTION)	1
CHAF	TER T	WO (LITERATURE REVIEW)	3
CHAF	TER TI	HREE (MATERIALS AND METHODS)	
3.1		and materials	8
3.2	Genera	al instrumentation	8
3.3.		natographic techniques	8
3.4.		imental methods	
	3.4.1.	Protection of para-iodophenol 9	9
		Protection of 3,5-dihydroxybenzaldehyde 12	10
	3.4.3. Attempted preparation of 3,5-diacetoxystyrene 15 (Wittig reaction)		
	3.4.4.	Attempted preparation of 3,5-dimethoxy-12-benzyloxystilbene 1	17 12
		(Heck coupling)	
CHA	PTER F	OUR (RESULTS)	
4.1.	Protec	tion of para-iodophenol 9	13
4.2.		tion of 3,5-dihydroxybenzaldehyde <u>12</u>	13
4.3.	Attem	pted preparation of 3,5-diacetoxystyrene <u>15</u> (Wittig reaction)	14
4.4.		pted preparation of 3,5-dimethoxy-12-benzyloxystilbene 17	15
	(Heck	coupling)	
СНА	PTER F	IVE (DISCUSSION)	
5.1.		anism of reaction in stilbene synthesis	
	5.1.1.	Protection of para-iodophenol 9	18
	5.1.2.	Protection of 3,5-dihydroxybenzaldehyde 12	19
		Wittig reaction	20
5.2.	Characterization of synthesized compounds		
	5.2.1.		22
		Spectroscopic evidence for 1-benzyloxy-4-iodobenzene 11	23
	5.2.3.		24
	524	Spectroscopic evidence for 3.5.12-trimethoxystilbene 27	25

ABSTRACT

A large number of stilbene derivatives which have been widely known for various therapeutic values have been isolated from various plants. Nevertheless, only a minute amount of them can be obtained naturally. Therefore the synthesis of its derivatives can provide access to unnatural analogues as well as enabling further studies on their structure-activity relationships. The aim of the research was to produce a stilbene derivative, 3,5-diacetoxy-12-benzyletherstilbene to be used by other researches for synthesis of more complex compounds and further investigation on structure-activity relationships. The preparation of the compound has been performed through four established reactions. The first reaction was the synthesis of protected iodophenol to be used as a starting material for Heck coupling. The second reaction involved synthesis of protected 3,5-dihydroxybenzaldehyde to be used as a starting material in the Wittig reaction. Both protected compounds were successfully synthesized and extracted. Next the Wittig reaction was performed to synthesize 3,5-diacetoxystyrene as another starting material for Heck coupling. However, the reaction failed to produce the desired styrene. To execute the final reaction, 3,5-dimethoxystyrene, synthesized and donated by another researcher, was used as a replacement of 3,5-diacetoxystyrene. Heck coupling was performed but failed to produce the desired stilbene. In each reaction, the products were analyzed using TLC and extracted using ethyl acetate or hexane. In the Wittig reaction and Heck coupling, the reaction products were attempted to be purified by column chromatography but separation did not occur. Each compound was sent for NMR analysis for structure characterization. The spectra were recorded using ¹H-NMR spectrometer in order to elucidate the structure of the compounds.

CHAPTER 1

INTRODUCTION

Stilbenoids form one minor class of phenolic compounds in plants which has a basic skeleton of C_6 - C_2 - C_6 1. A large number of derivatives have been isolated from various plants. Nevertheless, only a minute amount of them can be obtained from these natural sources. For this reason, the need of synthesizing stilbene derivatives is important in enabling further investigation on their structure-activity relationships as well as providing opportunity to access to unnatural analogues.

Figure 1.1: Structures of stilbene skeleton $\underline{1}$ and compound to be synthesized $\underline{2}$

The main objective this research was to synthesize large quantities (gramme scale) of stilbene derivative, 3,5-diacetoxy-12-benzyloxystilbene 2. The compound was to be synthesized through four established reactions, purified by standard chromatographic techniques and characterized by spectroscopic techniques. The obtained 2 will be used