



**Faculty of Resource Science and Technology**

**Synthesis and Characterization of Triazene and Thiourea Derivatives as  
Potential Antibacterial Agents**

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# Synthesis and Characterization of Triazene and Thiourea Derivatives as Potential Antibacterial Agents

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## DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Malaysia Sarawak. Except where due acknowledgements have been made, the work is that of the author alone. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.

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## ABSTRACT

Two different series of triazene **43a-i** and thiourea derivatives **45a-i** bearing acetanilide moiety with a total of 18 compounds have been successfully synthesized from 4'-aminoacetanilide as the core structure through azo coupling and nucleophilic substitution reaction, respectively. The structures were characterized by using Fourier-transform infrared (FTIR) spectroscopy, <sup>1</sup>H and <sup>13</sup>C nuclear magnetic resonance (NMR) analysis. The unexpected structural formation of **43a-i** instead of the initially proposed azo derivatives **42a-i** was confirmed by employing correlation spectroscopy (COSY). The antibacterial activity of **43a-i** and **45a-i** was tested against two types of bacteria which were *Staphylococcus aureus* (ATCC 25923), a Gram-positive bacterium and *Escherichia coli* (ATCC 25922), a Gram-negative bacterium. The antibacterial potential was utilized via turbidimetric kinetic method for **43a-i** and Kirby-Bauer disc diffusion method for **45a-i**. The study revealed that among the triazene series **43a-i**, **43c** bearing fluorine at *para* position was the most potent inhibitor against both bacteria with minimum inhibitory concentration (MIC) values of 68 ppm (*S. aureus*) and 84 ppm (*E. coli*), surpassing the standard ampicillin with the MIC values of 85 ppm (*S. aureus*) and 86 ppm (*E. coli*). The more nitrogen atoms on the triazene bridge along with the fluorine substituent were envisaged to promote greater hydrogen bond interactions with the bacterial receptors. On the other hand, another derivative of the 4'-aminoacetanilide called thiourea derivatives **45a-i** showed susceptible inhibition against those bacteria, particularly **45a** and **45f** with 7-8 mm of inhibition zone, comparable to the standard ampicillin. The similar aspect these compounds possessed was the low molecular weight which resulted in better bacterial membrane penetration.

**Keywords:** 4'-aminoacetanilide, antibacterial, spectroscopy, thiourea, triazene

## ***Sintesis dan Pencirian Terbitan Triazen dan Tiourea Sebagai Potensi Agen Antibakteria***

### **ABSTRAK**

Dua siri berbeza terbitan triazen **43a-i** dan tiourea **45a-i** menggalas moiety asetanilida berjumlah 18 sebatian telah berjaya disintesis daripada 4'-aminoasetanilida sebagai struktur teras melalui tindak balas gandingan azo dan penggantian nukleofilik. Struktur-struktur tersebut dicirikan menggunakan spektroskopi inframerah penukarganti Fourier (FTIR),  $^1\text{H}$  dan  $^{13}\text{C}$  resonan magnetik nukleus (NMR). Pembentukan **43a-i** dan bukannya terbitan azo **42a-i** yang tidak dijangka disahkan menggunakan spektroskopi korelasi (COSY). Aktiviti antibakteria **43a-i** dan **45a-i** diuji ke atas dua jenis bakteria iaitu Staphylococcus aureus (ATCC 25923), bakteria Gram-positif dan Escherichia coli (ATCC 25922), bakteria Gram-negatif. Kaedah yang digunakan ialah kaedah kinetik turbidimetrik bagi **43a-i** dan kaedah penyebaran cakera Kirby-Bauer bagi **45a-i**. Hasil-hasil menunjukkan **43c** yang mengandungi atom fluorin pada posisi para ialah perencat bakteria yang terbaik ke atas kedua-dua bakteria dengan jumlah kepekatan perencatan minimum (MIC) sebanyak 68 ppm (S. aureus) dan 84 ppm (E. coli), menandingi piawai ampisilin yang mempunyai jumlah MIC sebanyak 85 ppm (S. aureus) dan 86 ppm (E. coli). Jumlah atom nitrogen yang banyak pada titian triazen bersama dengan bahan ganti fluorin digambarkan menggalakkan lebih banyak interaksi ikatan hidrogen dengan reseptor-reseptor bakteria. Manakala, satu lagi terbitan 4'-aminoasetanilida dipanggil terbitan tiourea **45a-i** menunjukkan perencat bakteria yang rentan, terutamanya **45a** dan **45f** dengan zon perencatan sebanyak 7-8 mm, setanding dengan piawai ampisilin. Aspek serupa yang dimiliki sebatian-sebatian ini ialah berat molekul yang rendah menyebabkan penembusan membran bakteria yang lebih baik.

**Kata kunci:** 4'-aminoasetanilida, antibakteria, spektroskopi, tiourea, triazen

## TABLE OF CONTENTS

	<b>Page</b>
<b>DECLARATION</b>	i
<b>ACKNOWLEDGEMENT</b>	ii
<b>ABSTRACT</b>	iii
<b>ABSTRAK</b>	iv
<b>TABLE OF CONTENTS</b>	v
<b>LIST OF TABLES</b>	viii
<b>LIST OF FIGURES</b>	ix
<b>LIST OF SCHEMES</b>	xi
<b>LIST OF ABBREVIATIONS AND SYMBOLS</b>	xiii
<b>CHAPTER 1 INTRODUCTION</b>	1
1.1 Background of study	1
1.1.1 Azo	1
1.1.2 Triazene	3
1.2 Thiourea	5
1.3 Problem statement	8
1.4 Objectives	10
<b>CHAPTER 2 LITERATURE REVIEW</b>	12