Hindawi Publishing Corporation
Journal of Chemistry
Volume 2016, Article ID 2739832, 7 pages
http://dx.doi.org/10.1155/2016/2739832

Research Article

Synthesis and Bacteriostatic Activities of Bis(thiourea) Derivatives with Variable Chain Length

Ainaa Nadiah Abd Halim and Zainab Ngaini

Department of Chemistry, Faculty of Resources Science and Technology, Universiti Malaysia Sarawak, 94300 Kota Samarahan, Sarawak, Malaysia

Correspondence should be addressed to Zainab Ngaini; nzainab@unimas.my

Received 1 September 2016; Revised 18 November 2016; Accepted 24 November 2016

Academic Editor: Radhey Srivastava

A series of 1,4-bis(decoxyphenyl)carbamothioyl-terephthalamide derivatives was successfully synthesised by reaction of benzene-1,4-dicarbonyl isothiocyanate intermediates with long alkyl chain. The alkylation was performed via Williamson etherification of 4-acetamidophenol with bromoalkanes. The synthesised bis(thiourea) derivatives differed in the chain length, C_nH_{2n+1}, where $n = 10$, 12, and 14. The structures of all compounds were characterised by elemental CHN analysis, IR, ^{1}H, and ^{13}C NMR spectroscopies. Bacteriostatic activities of bis(thiourea derivatives which consisted of two folds of N-H, C=O, and C=S and long alkyl chain substituents were carried out against Gram-negative bacteria (*Escherichia coli*, ATCC 25922) via turbidimetric kinetic method. Bis(thiourea) derivatives with $n = 10$ and $n = 12$ displayed excellent activity against *E. coli* with MIC of 135 μg/mL and 145 μg/mL, respectively, while bis(thiourea) derivatives with $n = 14$ acted as cutoff point with no antibacterial properties. Similar trend was observed in binding affinity to the active site of enoyl ACP reductase (FabI), which demonstrated binding free energy of −5.3 Kcal/mol and −4.9 and −4.8 Kcal/mol, respectively.

1. Introduction

Thiourea which is also known as thiocarbamide is a white crystalline solid compound that consists of sulphur and nitrogen atoms. Thiourea moiety has become intensely synthesised due to its ability to undergo structural modifications [1]. The existing of two units of reactive primary amine groups has made thiourea a suitable precursor for a synthesis of many new compounds [2]. Thiourea derivatives are well known to display a broad spectrum of applications in pharmaceutical industry due to their biological properties such as antiparasitic [3], anticancer [4], antioxidant [5, 6], antibacterial [7–10], antifungal [11], and anti-HIV [12, 13] properties.

The synthesis and antibacterial studies of monothiourea derivative are progressing at the considerable rate while bis(thiourea) compounds are relatively less reported [14]. The presence of two or more thiourea moieties, for example, bis(thiourea), was envisaged to possess better antibacterial activity [15]. This is due to the ability of C=S and N-H groups in thiourea moieties which can be easily protonated under acidic condition and reacted with the carboxyl and phosphate groups of the bacterial surface and thus enhanced the activity [16].

Incorporation of alkyl chain as substituents in thiourea derivatives has been reported for significant biological properties [17, 18]. The presence of long alkyl chains was reported to enhance the biological activity of thiourea derivatives [19]. Alkyl chains have the ability to increase lipophilicity and promote the ability of the compound to disrupt microorganism cell wall [20–22].

In this paper, we report on the synthesis of novel 1,4-bis(decoxyphenyl)carbamothioyl-terephthalamide derivatives (**2a–c**) bearing alkyl chain of different length (C_{10}, C_{12}, and C_{14}). The compounds were demonstrated for antibacterial activities against Gram-negative bacteria (*Escherichia coli*, ATCC 25922) where the effects of different length of alkyl chains were evaluated.