APPROACHES TO THE SYNTHESIS OF THIAZOLO AND THIAZINO PYRIDOACRIDINES: ELUCIDATING THE MECHANISM OF THIOBENZAMIDE CYCLISATIONS

A THESIS

Submitted in Partial Fulfilment of the Requirement for the Degree of

Doctor of Philosophy in Chemistry

of

The University of the West Indies

by

Nadale Kimberley Downer-Riley

February 2007

Department of Chemistry

Faculty of Pure and Applied Sciences

Mona.

ABSTRACT

APPROACHES TO THE SYNTHESIS OF THIAZOLO AND THIAZINO PYRIDOACRIDINES: ELUCIDATING THE MECHANISM OF THIOBENZAMIDE CYCLISATIONS

Nadale Kimberley Downer-Riley

Pyridoacridines represent a class of marine alkaloids which exhibit a range of biological properties including antitumor and antiviral activity. Pyridoacridines have therefore become prime synthetic targets and possess great potential as lead compounds for combinatorial synthesis.

In Chapter 1, the pharmacological activity as well as the chemical synthesis and biosynthesis of pyridoacridines are outlined. The Chapter also focuses on one method which is commonly employed in pyridoacridine synthesis: the hetero Diels-Alder reaction.

The synthesis of the immediate precursor to an analogue of kuanoniamine A is described in Chapter 2. The key reaction was a hetero Diels-Alder cycloaddition of a bromoquinone to a novel cyclic azadiene. The Jacobson cyclisation of an *o*-methoxythiobenzamide with the unlikely loss of the *ortho* methoxy group is also introduced in this chapter.

Different approaches to the synthesis of a tetracyclic shermilamine B analogue are discussed in Chapter 3. The challenging step in this synthesis has proven to be annelation of a methylquinolone bearing a thiazinone ring. The approaches taken towards obtaining the target molecule are discussed.

In Chapter 4, a detailed investigation into the cyclisation of *o*-methoxythiobenzamides is presented. The cyclisation of *o*-methoxythiobenzamides using AIBN, DDQ, iodine, PIDA and PIFA is described. This represents the first report of use of some of these reagents for this purpose. The various products obtained from these reactions have led to a tentative proposal for the mechanistic pathway of thiobenzamide cyclisation.

The novel reaction of thiobenzamides with iodine to produce benzothiazoles and benzoxazoles is explored in Chapter 5. The mechanism by which these reactions are thought to occur is investigated and discussed.