

ABSTRACT

SYNTHESIS OF ANALOGUES OF KUANONIAMINE A

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Marine secondary metabolites, and in particular the alkaloids, have been of interest to both medicinal and synthetic chemists due to the range of biological activity they demonstrate, and the synthetic challenge posed. In this thesis, the work undertaken to synthesise novel thiazolo[4,5,6-ij][2,7]naphthyridine analogues of a pyridoacridine alkaloid - kuanoniamine A, is described.

In chapter one, the total synthesis of a number of pyridoacridine marine alkaloids is outlined. This work is categorised on the basis of the key reactions employed in construction of the condensed aromatic systems.

2-Phenyl-thiazolo[4,5-g]quinoline 5,8-dione was recognised as the key intermediate in our synthesis of analogues of kuanoniamine A. Beginning with the readily available 2,5-dimethoxyaniline, a series of reactions towards the synthesis of this key intermediate is explored. Reactions which do not include a Diels-Alder reaction, and which produce the novel 2-phenyl-thiazolo[5,4-g]quinoline-5,8-dione are presented in chapter two.

A review of the literature on the development of 1-aza-1,3-dienes as 4π fragments for and the advantages derived in hetero Diels-Alder reactions is contained in chapter three.

In chapter four, the preparation of the novel dienophiles - 4,7-dioxo-2-phenylbenzothiazoles, their reactions with 1-azadiene by hetero Diels-Alder cycloaddition towards the synthesis of 2-phenylthiazolo[4,5-g]quinoline-5,8-dione, and the eventual formation of the new benzothiazolo[4,5,6-ij][2,7]naphthyridine analogue of kuanoniamine A is detailed. The results of anti-growth studies with radish seeds var. Scarlet Globe, and calcium release activity studies of selected intermediates and the above-mentioned analogue, are also outlined in this chapter.