Abstract

In this PhD thesis, we report for the first time, new methodology for the synthesis of angucycline antibiotic natural products. In particular, for the synthesis of 1,8-dihydroxy-3-methyltetraphene-7,12-dione, commonly known as tetrangulol. We also report on the synthesis of 1,10,12-trimethoxy-8-methylbenzo[*c*]phenanthridine in our quest to synthesise phenanthroviridone from an intermediate product in the synthesis of tetrangulol.

The Suzuki-Miyaura coupling reaction between 1,4,5-(trimethoxynaphthalen-2-yl)boronic acid and 2-iodo-3-methoxy-5-methylbenzaldehyde afforded intermediate, 3-methoxy-5-methyl-2-(1,4,5-trimethoxynaphthalen-2-yl)benzaldehyde. Conversion of this benzaldehyde into the alkyne, 2-(2-ethynyl-6-methoxy-4-methylphenyl)-1,4,5-trimethoxynaphthalene was accomplished utilizing the Corey-Fuchs reaction. Exposure of the derived acetylene to a catalytic platinum(II)-mediated ring closure yielded the required tetracyclic aromatic product, 1,7,8,12-tetramethoxy-3-methyltetraphene which was converted into tetrangulol. Exposure of the related 3-methoxy-5-methyl-2-(1,4,5-trimethoxynaphthalen-2-yl)benzaldehyde *O*-phenyl oxime to microwave irradiation in an ionic liquid yielded 1,10,12-trimethoxy-8-methylbenzo[*c*]phenanthridine, instead of the desired natural product phenanthroviridone.

We also report on the unexpected synthesis of the benzonaphthopyranone core found in other classes of angucycline antibiotics from oxygen analogs of 2-naphthylbenzyl alcohols when exposed to *N*-bromosuccinimide. Treatment of (2-(1,4-dimethoxynaphthalen-2-yl)phenyl)methanol and related analogues with *N*-bromosuccinimide under an oxygen atmosphere afforded 12-methoxy-6*H*-dibenzo[*c*,*h*]chromen-6-one, 2-Methoxy-6*H*-benzo[*c*]chromen-6-one and of 6*H*-benzo[*c*]chromen-6-one. An investigation into possible mechanisms for this transformation was also conducted.