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Iodocyclisations reactions of Boc- and Cbz-protected *N*-allylguanidines

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ABSTRACT

The cyclisation of mono-protected and bis-protected guanidines **8a–j** under standard iodocyclisation conditions (I_2/K_2CO_3) gave the guanidine heterocycles **9–25** via either a direct cyclisation or by a cyclisation/ring-contraction process, which could be controlled by careful selection of conditions.

1. Introduction

We have previously reported[1–3] on the iodocyclisation[5–11] of allyl substituted guanidines as part of a synthetic approach to a variety of natural products including the hepatotoxin cylindrospermopsin **1**[12,13] the unusual amino acid enduracididine **2**,[14] the cytotoxin nitensidine E **3**,[15] the β-carboline guanidine derivative tiruchanduramine **4**[16] a potent α-glucosidase inhibitor and the cytotoxic guanidine trachycladindole G[17] (Fig. 1).

As part of this work we have studied the cyclisation of a range of mono- and bis-protected allylic and homoallylic substituted guanidines, which have led to the formation of a range of five- and six-membered guanidine heterocycles with a predictable protecting group substitution pattern. We take this opportunity to report our findings in full.

2. Results and discussion

We initially prepared a series of *N*-allyl and *N*-homoallyl guanidines **8a–j** via the reaction between the protected pyrazolecarboxamidines[18–20] **6a–d** and the amines **7** resulting in the synthesis of the corresponding guanidine in high yields (Scheme 1, Table 1).

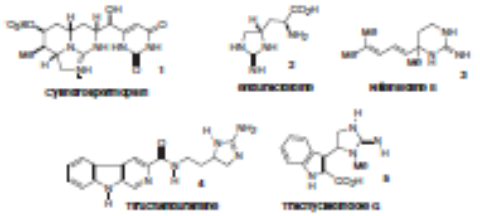

Fig. 1. Target natural products 1–5.

Our initial investigations focused on the formation of five- and six-membered guanidine heterocycles from the bis-protected guanidines and the outcome of this work was much as expected. For example, cyclisation of the guanidine **8a** with iodine in the presence of potassium carbonate gave the corresponding five-membered heterocycle **9a** in 86% yield and similarly the bis-Cbz-protected allyl guanidine **8b** gave **9b** in a 79% yield (Scheme 2).

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