STUDIES TOWARDS THE SYNTHESIS OF BIO-LACTONES: PHOSTRIECIN, PORTENTOL AND THERMOLIDES

Phostriecin (**1)** is attracting much attention as a total synthesis target because of its potent biological activities and complex molecular architecture. Given the scarcity of Phostriecin (**1**) coupled with its antibiotic, antitumor activity and our long-standing interest in the synthesis of a hydroxyvinyl *δ*-lactone moiety containing molecules we thus embarked on the total synthesis of Phostriecin (**1**) to enable additional biological evaluation. Herein, we describe the synthetic studies of Phostriecin (**1**).

In conclusion we have achieved the pivotal C1 **-** **C**13 and **C**14 **-** **C**22 fragments of the antitumor natural product phostriecin from readily available starting materials with good yields. The key steps involved are Crimmin's non-Evans *syn* aldol, Wittig reaction, Browns' alkoxyallylboration, alkyne coupling, CBS reduction, ring-closing metathesis, Corey - Fuchs protocol and Stork's protocol.

Thermophilic fungi are eukaryotes, growing optimally above 40 °C, represent a potential reservoir of thermostable enzymes for industrial applications and could be developed into cell factories to support the production of chemicals and materials at elevated temperatures.[1] However, very few of them have been screened for their production of structurally and biologically novel secondary metabolites.

Thermolides **1** and **2** display potent inhibitory activity against three difficult nematodes, such as rootknot nematode (*Meloidogyne incognita*), pine-wood nematode (*Bursaphelenchus xylophilus*), and free-living nematode (*Panagrellus redivevus*) with LC_{50} values 0.5–1 μg/mL by using avermectins as standard.[4] Compounds **3** and **4** shows medium and slight nematicidal activity against above three nematodes and compounds **5-7** biological activities are not reported due to low amount of material was isolated.

A concise and highly stereoselective approach for C12-C21 fragment of thermolides **1-5** were achieved by employing desymmetrization strategy, Barton-McCombie reaction, Brown's asymmetric allylation, Wacker oxidation and *anti*-reduction as key steps. The synthesis involved 13 steps starting from bicylic lactone **9** with a 20.1% overall yield.