Studies Directed Towards the Synthesis of (–)-Ebelactone-A

Colin Foster

This thesis describes work concerning the total synthesis of ebelactone-a **16**, and in particular the synthesis of one of the retrosynthetic fragments (fragment A **20**) and its coupling to the combined fragment BC **115** formed from the other two. We repeated the synthesis of enantiomerically enriched **20** devised by Williams, employing a Mukaiyama aldol reaction directed by Oppolzer's sultam to establish the *anti-anti* stereotriad of the fragment. We modelled the coupling of this to **115** using isobutyraldehyde in place of **20** and vinyl iodide **133** in place of **115**, and verified that the Nozaki-Kishi method using chromium(II) chloride and catalytic nickel(II) chloride was effective. By this method, we successfully coupled **133** to **20**. Model work was unsuccessful in establishing a methodology for removing the hydroxy group from alcohols **188**/**189** without disrupting either the position or geometry of the adjacent C=C bond.

We also established a completely new route to fragment A, utilising the features of organosilicon chemistry to control the stereochemistry. An intermediate **213** containing two different silyl groups, in which we hoped to transform one selectively into a hydroxy group with retention of configuration by Fleming's method, proved too unstable for synthesis, but we were able to modify the route and produce alcohol **254** in enantiomerically pure form (Oppolzer's sultam was once again used as the chiral auxiliary), and we expect future workers to be able to take this through to fragment A.