Synthesis of Calystegine A(3) from Glucose by the Use of Ring-Closing Metathesis

A synthesis of the nortropane alkaloid calystegine A(3) is described from D-glucose. The key step employs a zinc-mediated tandem reaction where a benzyl-protected methyl 6-iodo glucoside is fragmented to give an unsaturated aldehyde, which is then transformed into the corresponding benzylimine and allylated in the same pot. The functionalized nona-1,8-diene, thus obtained, is converted into the seven-membered carbon skeleton in calystegine A(3) by ring-closing olefin metathesis. Subsequent deoxygenation by the Barton-McCombie protocol, hydroboration and oxidative workup followed by hydrogenolysis affords calystegine A(3). The synthesis uses a total of 13 steps from glucose and confirms the absolute configuration of the natural product.