AN INTRAMOLECULAR CYCLOADDITION APPROACH TO THE KAURANOID FAMILY OF DITERPENE METABOLITES

Brenda Callebaut, Jan Hullaert, and Johan M. Winne

Department of Organic and Macromolecular Chemistry, Ghent University, S4 Krijgslaan 281, 9000 Ghent, Belgium

One of the most diverse and, at the same time, structurally intriguing subfamily of plant diterpenes is formed by the ent-kauranes, which are biosynthetically related to the huge family of gibberellin plant hormones. Over a thousand kaurene metabolites are known, which continue to attract considerable interest from both a synthetic and a biological point of view.[1] Drawing on the arguments of biology-oriented synthesis, or natural product inspired synthesis, the kauranoid skeleton can thus be regarded as a highly privileged scaffold.[2] To date, however, general and concise synthetic approaches to this intriguing tetracyclic ring system are still rare, mainly due to the presence of an intricate bridged seven-membered ring system.

Our research group has already successfully developed multiple concise and modular synthesis routes towards complex natural terpene scaffolds containing a seven-membered ring, employing a dehydrative (4+3) cycloaddition between a furfurylcation and a 1,3-diene.[3]

We now report our own synthetic studies in this field, aiming at a direct elaboration of the [3.2.1]bicyclic system via an intramolecular (4+3) cycloaddition.[4] We have achieved a remarkably short, and also scalable entry into the wide class of kaurene metabolite-type scaffolds. Six different bromo-aldehyde starting compounds were implemented in the synthesis route generating a library of unnatural kauranoid analogues, which allows for a rapid exploration of the kauranoid chemical space.