



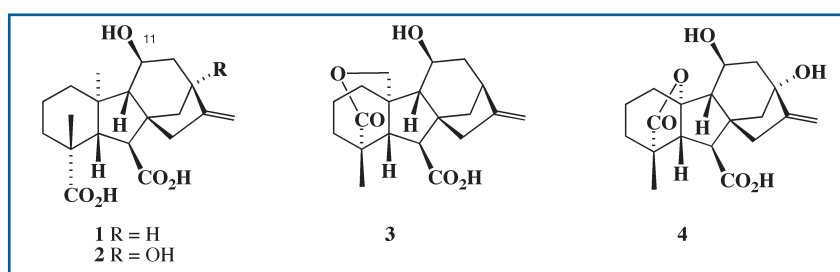
Organic Synthesis

Professor Lew Mander

Our research interests are concerned primarily with methods and strategies for the synthesis of complex natural products that have interesting biological properties. Within this context, members of the group have successfully completed syntheses of numerous complex natural products and developed a number of useful synthetic procedures. We are also interested in the molecular basis of plant growth regulation, using organic synthesis as an enabling technology, with special reference to the gibberellins (GAs). GAs affect numerous aspects of plant growth and development, including for example, germination, induction of stem growth and flowering, and there are several commercially valuable applications. Studies pursued in collaboration with groups in the CSIRO and the University of Calgary have led to the discovery of semi-synthetic derivatives that interfere with the plant's natural production of phytohormones, thereby inhibiting growth.

Structural and Synthetic Studies on New Gibberellins

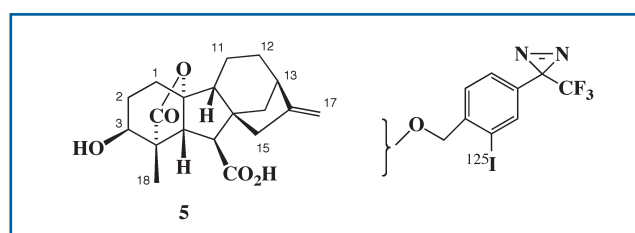
As part of a continuing program directed at the identification of new naturally occurring gibberellins, we have found four new 11 β -hydroxy variants in the immature seeds of loquat fruit, namely compounds 1–4. Their structures were confirmed by synthesis of the methyl esters from gibberellic acid. (*With T V Hau, T P Le, B Twitchin*)



See also: <http://www.plant-hormones.info/gibberellins.htm>

Preparation of Photo-affinity Probes for Labelling of Gibberellin Receptors

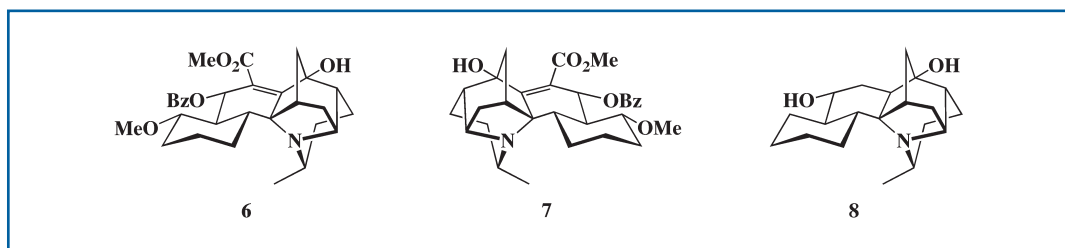
In order to understand more fully the molecular basis of gibberellin bioactivity, we are presently undertaking the synthesis of gibberellins with attached groups designed to crosslink to binding sites in receptors and other gibberellin ("GA")-binding proteins. Trifluoromethyl aryl diazirines have been



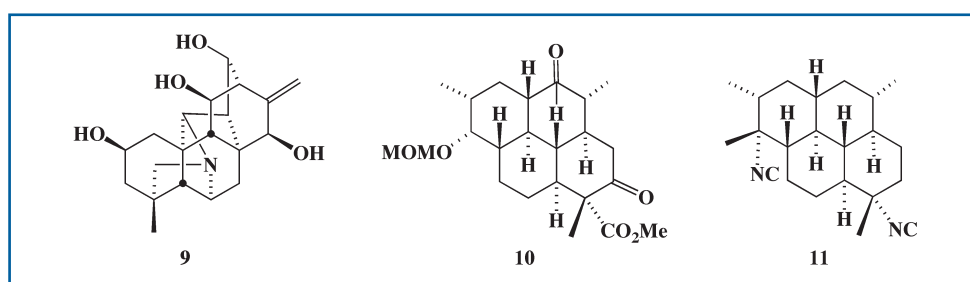
shown to be some of the most effective auxiliaries for photo-affinity labelling, but their steric bulk may interfere with binding. Before attempting to prepare a fully elaborated probe, we have made and tested a series of benzyloxy substituted GAs and evaluated their bioactivity. Substituents at C-1, C-2, C-11, C-12, C-13, C-15, C-17 and C-18 (see structure 5 for numbering) have been screened in leaf-growth and the barley endosperm bioassays with those substituted at C-2 α , C-11 and C-12 shown to retain acceptable levels of bioactivity. Current efforts are being directed at the elaboration of the "fully equipped" probes which will then be tested for bioactivity. (With J R Crow, M J McDonough)

Total Synthesis of Natural Products

Synthetic studies are being directed towards the assembly of several highly caged natural products. They include members of a group of 28 novel alkaloids isolated from the Northern Australian rain forest species, *Galbulimima belgraveana*. Recent X-ray crystallographic studies have revealed the absolute configuration of the more complex alkaloids to be antipodal to the structures that were originally assigned in the mid-60's. For example, himandrine possesses structure 6, not 7. Recent studies have culminated in the assembly of the hexacyclic skeleton 8 while current efforts based on elaboration of the original approach are expected to afford the complete structure 6.



Preliminary studies on the construction of the heptacyclic family of diterpenoid alkaloids typified by hetisine 9 have been undertaken. A number of promising leads have been developed, culminating in a tetracyclic intermediate, while the advanced tetracyclic diester 10 has been prepared *en route* to the total synthesis of the anti-malarial diterpenoid, diisocyanoadociane 11. (With G Del Signore, O E Hutt, K A Fairweather, P D O'Connor, A C Willis)



<http://rsc.anu.edu.au/research/mander.php>