

This Week's Citation Classic

Dennis D T, Upper C D & West C A. An enzymic site of inhibition of gibberellin biosynthesis by Amo 1618 and other plant growth retardants. *Plant Physiol.* 40:948-52, 1965.

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Cyclization of trans-geranylgeranyl pyrophosphate to form kaurene is the first step unique to gibberellin biosynthesis. Several plant growth retardants, which were thought to act by inhibiting gibberellin biosynthesis *in vivo*, are shown in this paper to specifically inhibit this step. [The *SCI*[®] indicates that this paper has been cited over 130 times since 1965.]

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"The most interesting results are often obtained by good fortune and by performing experiments which logically should stand little chance of success. Similarly, the best ideas are often generated in the most unlikely of places. This paper was an example of the above principles.

"I arrived at UCLA on November 23, 1963, a rather unfortunate day for a foreigner, to work with Charlie West on the biosynthesis of gibberellins, a class of plant growth regulators. For sometime, Charlie had been studying gibberellin biosynthesis in the endosperm of the seeds of the wild cucumber which contains large amounts of gibberellins. These cucumbers grow in the Santa Monica Mountains just north of Los Angeles and every spring Charlie and his group disappear into these mountains to collect them. It is a hazardous occupation, for not only are they armed with large spines but the area is also infested with rattlesnakes which often make their presence known. According to Charlie, no one has been lost so far.

"Jan Graebe, a graduate student, had already demonstrated the conversion of mevalonic acid, a terpene precursor, into a series of lipids in the endosperm and it was my good fortune to identify one of these

lipids as kaurene which had been postulated to be the first compound unique to gibberellin biosynthesis. We were particularly excited when Chris Upper further demonstrated the conversion of fransgeranylgeranyl pyrophosphate to kaurene, catalysed by kaurene synthetase, the first enzyme of the gibberellin pathway.

"A series of plant growth retardants were known at the time, and Anton Lang had evidence that they acted by inhibiting gibberellin biosynthesis. Over a beer, Charlie and I thought how exciting it would be if they inhibited our enzyme, kaurene synthetase. Now the chance of this happening was small, since there are at least 20 enzymes in the pathway, but much to our delight and amazement, when I added one of them, Amo 1618, into the reaction the enzyme was specifically and completely inhibited.

"The day after this result, I was due to leave on a vacation with my wife, Marjory, but I was determined to repeat the experiment before I left. I worked late, and, in my rush to leave, managed to drop a tray of vials on the floor of the scintillation room, discovering to my horror that toluene rapidly dissolves floor tiles. I have often wondered if the results of this 'classic' experiment are still visible at UCLA.

"It was a pleasure and privilege to work with Charlie at UCLA and I know of no one who is looked upon with so much respect and affection as he is by graduate students and postdocs. He has continued to extend our knowledge of this area of terpene metabolism. Upper is now working on plant diseases in Madison and I have attempted to become a plant enzymologist.

"I assume that the paper has been cited frequently because it is of general interest, not only to those in terpene metabolism, but also to those working on plant growth regulators and also those in horticulture and industry. The paper was first submitted to *Science* but was rejected because it was not of great interest. One should not always take reviewers too seriously."