



Identifying Biosynthetic Intermediates at the Microgram Scale

Many of today's drugs are based on compounds produced by plants and other organisms, and these natural products continue to inspire drug development. Elucidating the biosynthetic pathways that create this diverse chemistry is interesting both for basic discovery and to aid synthetic biology efforts to produce potential new drugs. Modern sequencing and bioinformatics approaches are revolutionizing investigators' ability to discover these pathways. However, testing the hypotheses generated by these methods still requires confirming the structures of chemical intermediates. In many cases, NMR is the best tool to differentiate a putative intermediate from related compounds including regioisomers and stereoisomers. Obtaining enough compound for NMR remains a challenge because the intermediates are often produced in low amounts and must be purified from a complex mixture. Sequoia's micro-scale purification and structure elucidation expertise is well suited to this problem. Using about 50 micrograms of compound, we have confirmed the structures of biosynthetic intermediates identified by collaborating researchers. In some cases, we have purified the intermediate of interest from expression host cell culture extracts.

Relevant Publications

Zerbe, P., Chiang, A., Dullat, H., O'Neil-Johnson, M., Starks, C., Hamberger, B., Bohlmann, J., "Diterpene Synthases of the Biosynthetic System of Medicinally Active Diterpenoids in *Marrubium vulgare*," *The Plant Journal*, **2014**, 79 (6), 914-927

Kilgore, M., Augustin, M., Starks, C., O'Neil-Johnson, M., May, G., Crow, J., Kutchan, T., "Cloning and Characterization of a Norbelladine 4'-O-Methyltransferase Involved in the Biosynthesis of the Alzheimer's Drug Galanthamine in *Narcissus sp. aff. pseudonarcissus*," PLoS ONE, **2014**, 9(7): e103223. doi:10.1371/journal.pone.0103223

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