

## Photochemical Cleavage of Leader Peptides

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The recent explosion of fully sequenced genomes has resulted in the discovery of over a dozen different classes of peptide-derived natural products that are DNA encoded. Extensive posttranslational modifications morph these peptides into their active form. In almost all known examples, an N-terminal leader peptide guides at least part of the posttranslational modifications, but the leader peptide must be removed from the core peptide in the final step of maturation to produce the active natural product. *In vitro* reconstitution of the activities of a growing number of the biosynthetic enzymes of these natural products has started to be exploited, however, the final removal of the leader peptide usually poses a major hurdle. We report the development of photolabile compound **1** capable of linking the leader and unmodified core peptides of the lantibiotic lactacin 481. *In vitro* reconstitution of the activity of the bifunctional enzyme LctM, followed by photoirradiation affords the C-terminal modified core peptide, lactacin 481.

