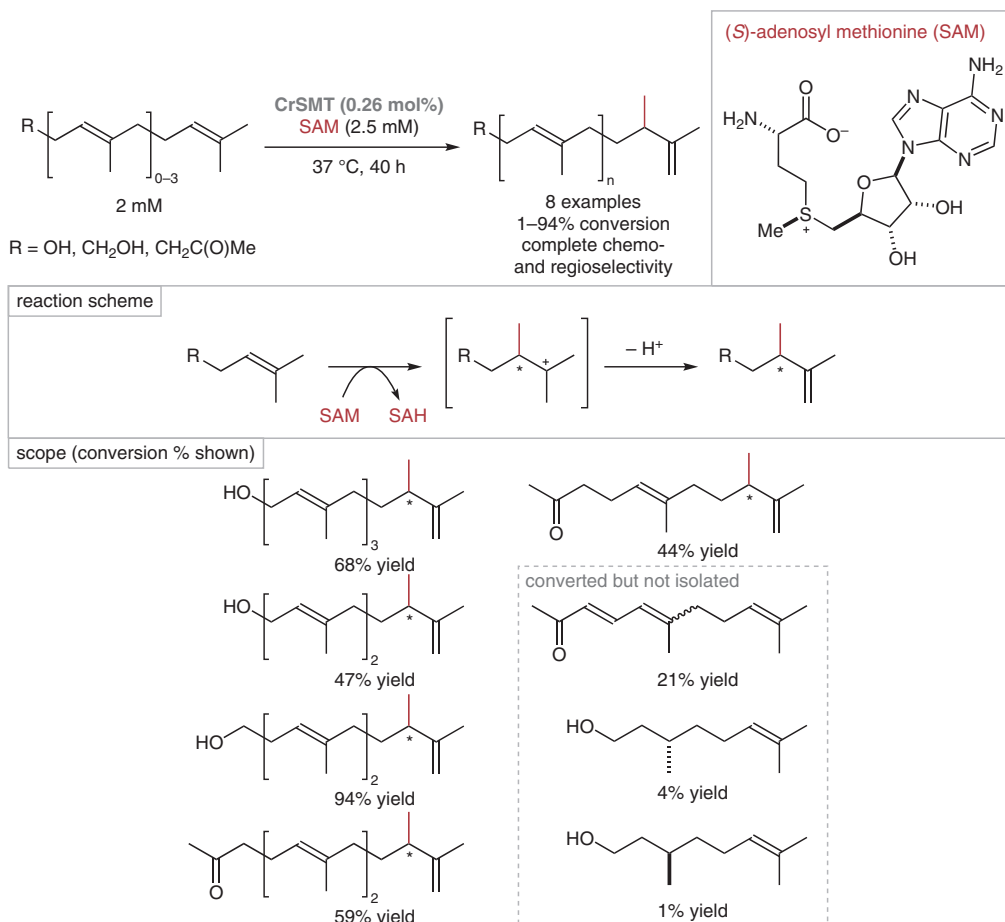


## Engineered Methyltransferase-Catalyzed Terminal Prenyl Group Tail Methylation of Linear Terpenoids



**Significance:** Hauer and co-workers report an engineered methyltransferase-catalyzed methylation of terminal prenyl groups on the tail end of linear terpenoids. The methyltransferase selected for this transformation came from *Chlamydomonas reinhardtii* and was subjected to three rounds of site-saturation mutagenesis in the optimization of the methylation of (*E,E*)-farnesol. In total, five terpenoids of various sizes were methylated with good to excellent conversions, all with complete chemo- and regioselectivity. Methylation was observed in three more terpenoids. However, low conversion did not allow for isolation or structural determination of the corresponding products.

**Comment:** The selectivity for the terminal prenyl group of the reported reaction is remarkable and was thus far not achievable through small-molecule catalysis. The authors report that the obtained methylated non-natural terpenoids are optically active. However, the absolute configuration of the products and the enantioselectivity of the reactions were not determined (although the authors suggest (*S*)-selectivity based on the reactivity of sterol). Chirality is of vital importance when considering the potential bioactivity-related applications of these molecules, and we hope that the authors will examine these factors in potential follow-up studies.