

Cover Picture

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The cover picture shows a new concept in protecting-group chemistry termed unichemo protection (UCP). This strategy only requires a single chemical process for all deprotection reactions. The UCP protecting groups are derived from a repetitive unit that permits their controlled and efficient step-wise removal. Functional-site selectivity is achieved by varying the degree of oligomerization at each site, and, after each deprotection cycle, only the newly liberated functional site is available for derivatization. The UCP strategy does not impose a restriction on the possible number of selectively protected sites in a molecule. The low-energy conformer of the pentalysine scaffold assembled with *N*-*sec*-butylglycyl protecting-group units is shown bottom left. By using the UCP approach the five protecting groups were sequentially removed and the exposed amino acid groups functionalized with five different organic acids. UCP facilitates an orthogonal process that is not dependent on a range of finely tuned and differently compatible processes. Moreover, since UCP is based on uniform deprotection reactions, the requirement of reaction compatibility with other parts of a molecule only increases linearly with the degree of polyfunctionalization (graph, bottom right). That is, after the initial requirement of parent-molecule stability is satisfied, only the sequential requirements towards each newly introduced group is an issue. In contrast, a quadratic increase in complexity with respect to the number of protected functional groups, even in the simplest cases, accompanies existing orthogonal protection strategies. More about the UCP strategy is reported by L. P. Miranda and M. Meldal on p. 3655ff.

