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Multicomponent 1,3-dipolar cycloadditions of azomethine ylides

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Multicomponent reactions (MCRs) are important processes from atom and step economy point of view. 1,3-Dipolar cycloadditions (1,3-DC) involving azomethine ylides and electrophilic alkenes are good examples for this type of transformation but are not so frequently described. In this lecture, the thermal and silver mediated multicomponent 1,3-DC between α-amino esters, dipolarophiles and aldehydes will be considered. This 1,3-DC allows the synthesis of highly substituted pyrrolidines under conventional or MW heating. In general, 4,5-endo diastereoselectivity was mainly observed and 2,5-cis-cycloadducts are formed according to a W-shaped dipole. When this MCR was performed with 2-oxoaldehydes, the 1,3-DC takes place under silver acetate catalysis at rt [3b]. On the other hand, the multicomponent 1,3-dipolar cycloaddition between different proline esters, aldehydes and dipolarophiles afford highly substituted pyrrolizidines will also be described. The corresponding highly substituted pyrrolizidines are obtained in all cases with 2,5-trans-relative configuration between two electron-withdrawing groups and major endo-selectivity with 2,4-cis-relative configuration. The use of (2S,4R)-4-hydroxyproline methyl ester hydrochloride allowed the synthesis of enantiomerically enriched pyrrolizidines. When pipecolic acid alkyl esters are used the corresponding indolizidines can be prepared under thermal reaction conditions.

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