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N-Isocyanodialkylamines Generated *In Situ* for the Joullié–Ugi reaction with Indolenines

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Abstract: *N*-Isocyanodialkylamines are rare isocyanide surrogates for the Ugi-type reactions. To avoid problems with instability and the obnoxious smell of these reagents, we optimized and employed a convenient protocol for *in situ* dehydration of *N,N*-dialkyl-*N'*-formyl hydrazines to give the respective *N*-isocyanodialkylamines which were utilized in the reaction with indolenines and acetic acid. The reaction was demonstrated to give modest to excellent yields of products incorporating the *N*-isocyanodialkylamine but not the carboxylic acid component.

Keywords: multicomponent reactions, Joullié–Ugi reaction, *in situ* dehydration, *N*-isocyanodialkylamines, Mumm rearrangement, *O*-deacylation.

The Ugi multicomponent reaction (Ugi MCR)¹ provides a facile entry into peptidomimetic bis-amides **1** by allowing incorporation of the four different reagents (an amine, a carbonyl compound, a carboxylic acid and an isocyanide) into the structure of **1** in a predictable and efficient manner (Fig. 1).

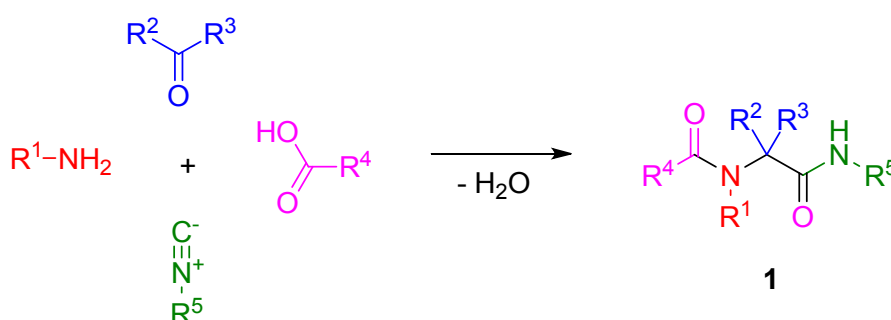


Figure 1. The Ugi multicomponent reaction.

The Ugi reaction undoubtedly occupies a central place in the toolbox of combinatorial chemistry² and has given rise to numerous compound libraries for biomedical research. Additionally, the use of post-condensational modifications³ of the Ugi reaction products as well

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