

Enantioselective Synthesis of *Epi*-Emetine Analogues: Control of the Facial Selectivity in a Three-Component Domino *Knoevenagel-Hetero-Diels-Alder* Reaction*

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The domino *Knoevenagel-hetero-Diels-Alder* reaction of the aldehyde *rac*-**8**, *Meldrum's* acid **2** and enol ether **3** leads to the cycloadduct *rac*-**17** as the main product which in a second domino process was transformed into the benzoisoquinolizidine *rac*-**18** by solvolysis, hydrogenolysis, condensation and hydrogenation; *rac*-**18** was used as a substrate for the synthesis of the two diastereomeric epimetine analogues **9** and **10** with > 96% *ee* (**9**) and 80% *ee* (**10**), respectively, by condensation with the phenylethylamine **23**, *Bischler-Napieralski* reaction and “enantioselective” hydrogenation using the chiral catalyst (*R,R*)-**26**.

Key words: Alkaloids, *Bischler-Napieralski* Reaction, Enantioselective Hydrogenation, Domino Reactions, Iminium Ions, Multicomponent Reactions