Sequential Michael Addition and Enamine-Promoted Inverse Electron Demanding Diels-Alder Reaction upon 3-Vinyl-1,2,4-Triazine Platforms

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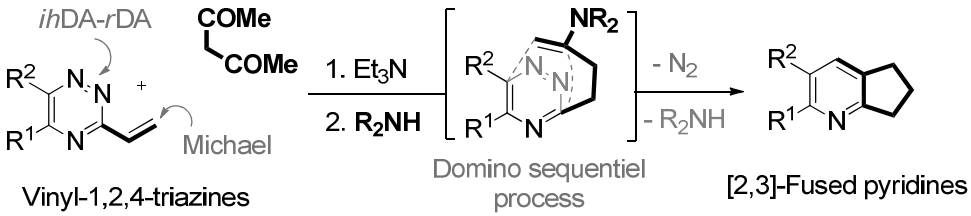
1,2,4-Triazine derivatives belong to an important class of heterocycles encompassing applications in medicine and agrochemistry, but also as useful building blocks in organic synthesis.[1] The □-electron-deficient triazine, flanked by a suitable leaving group, is well known to undergo aromatic nucleophilic substitution (S_NAr) reactions to give functionalized products. Furthermore, these heterocyclic platform are capable to undergo domino inverse-electron-demand hetero-Diels–Alder (*ih*DA)/retro-Diels–Alder (*r*DA) reactions with various dienophiles that allow for a straightforward access to substituted pyridine derivatives, which are ubiquitous derivatives in pharmaceutical ingredients.[2]

In this project, we aim to study a new reactivity of 1,2,4-triazines as Michael acceptor and capitalize on a subsequent intramolecular cycloaddition reaction. Thus, an original one-pot Michael addition-*ih*DA/*r*DA sequence was achieved from 3-vinyl-1,2,4-triazine platforms. This sequence provides a novel access to functionalized [2,3]-fused pyridine derivatives *via* a unique enamine promoted intramolecular *ih*DA reaction of 1,2,4-triazine intermediates to access saturated-unsaturated heterocycles.



(1) Neunhoeffer, H. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 6, p 507. (b) Lindsley, C. W.; Layton, M. E. In *Science of Synthesis*; Weinreb, S. M., Eds.; Thieme: Stuttgart, 2003; Vol. 17, p 357. (2) (a) Boger, D. L. *Chem. Rev.* **1986**, *86*, 781. (b) Boger, D. L. *Tetrahedron* **1983**, *39*, 2869. (d) Raw, S.A.; Taylor, R. J. K. In *Advances in Heterocyclic Chemistry*; 2010, 100, 76. (c) Fosterand, R. A. A.; Willis, M. C. *Chem. Soc. Rev.* **2013**, *42*, 63.