

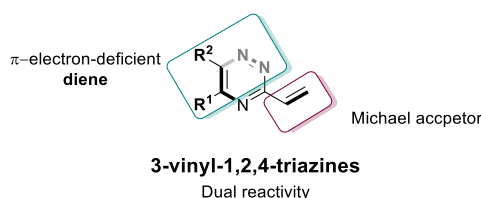
USE OF 3-VINYL-1,2,4-TRIAZINES AS VERSATILE PLATFORMS TO ACCESS NEW FUSED SATURATED AND UNSATURATED HETEROCYCLES

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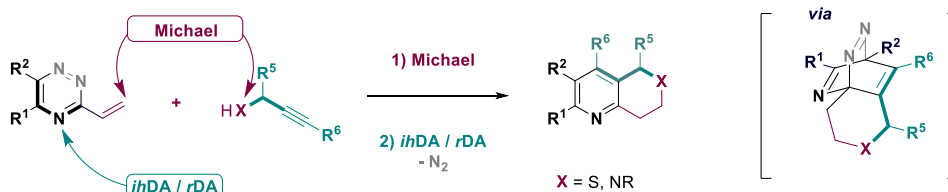
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In order to increase both the diversity of heterocyclic architectures and the opportunity to discover original druggable scaffolds, the development of new heterocyclic systems highly functionalized remains a major objective of modern organic chemistry. This approach is more and more considered by pharmaceutical industry especially if the structures concern chiral fused saturated and aromatic cycles in order to explore new chemical spaces and to 'escape from flatland'.^[1]

Within this context, we are currently exploiting the high synthetic potential of 3-vinyl-1,2,4-triazine as a dual heterocyclic platform able to act as a Michael acceptor and as π -electron-deficient *aza*-diene. Nitrogen containing heteroaromatic compounds, such as di-, tri- and tetrazines are indeed known to undergo in *inverse*-electron-demand *hetero*-Diels-Alder (*ihDA*) / *retro*-Diels-Alder (*rDA*) reactions with a wide range of electron-rich dienophile partners.^[2]



So far, we have evaluated the reactivity of 3-vinyl-1,2,4-triazines with N and S nucleophiles bearing a triple bond as dienophile partner in a Michael addition / *ihDA* / *rDA* sequence.^[3]



This synthetic strategy opens new straightforward routes to highly substituted saturated-unsaturated scaffolds,^[4] which are poorly described in literature such as 7,8-dihydro-5*H*-thiopyrano[4,3-*b*]pyridines or 1,6-tetrahydronaphthyridines.

^[1] (a) Lovering, F.; Bikker, J.; Humblet, C. *J. Med. Chem.* **2009**, *52*, 6752-6756. (b) Lovering, F. *Med. Chem. Commun.*, **2013**, *4*, 515-519.

^[2] For review on *ihDA/rDA* to azines, see: R. A. A. Foster, M. C. Willis, *Chem. Soc. Rev.* **2012**, *42*, 63-76.

^[3] For reviews on conjugated addition to vinyl arenes, see: (a) D.A. Klumpp, *Synlett* **2012**, 1590-1604. (b) D. Best, H.W. Lam, *J. Org. Chem.* **2014**, *79*, 831-845.

^[4] a) M. Lorion, G. Guillaumet, J.-F. Brière, F. Suzenet, *Org. Lett.* **2015**, *17*, 3154-3157. b) J. Jouha, F. Buttard, M. Lorion, C. Berthonneau, M. Khouili, M. A. Hiebel, G. Guillaumet, J. F. Briere, F. Suzenet *Org. Lett.* **2017**, *19*, 4770-4773. c) C. Berthonneau, F. Buttard, M. A. Hiebel, F. Suzenet J. F. Briere *Adv. Synth. Catal.* **2017**, *10.1002/adsc.201700831.*