Synthesis of functionalized 2-Cyanobenzothiazoles via Pd-catalyzed Intramolecular C-S Bond Formation to access to Thiazole-fused Tricyclic Quinazolinone Alkaloids.

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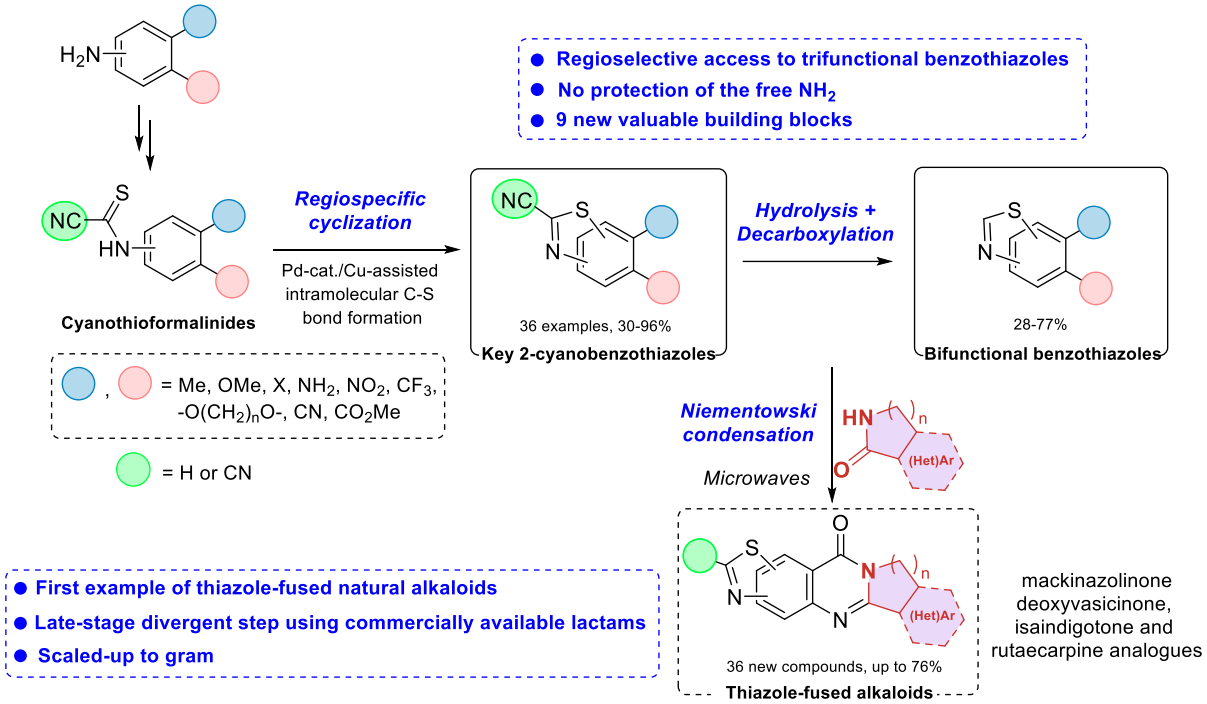
Benzothiazole backbones, widely found in marine natural molecules, pharmaceuticals, and natural products, have emerged as a privileged structure due to their wide-ranging biological activities.[1] The development of innovative synthesis of functionalized benzothiazole derivatives is still required for organic and medicinal chemists. In this context, we developed a Pd-catalyzed regiospecific C-H functionalization/intramolecular C-S bond formation reaction, starting from *N*-arylcyanothioformamides, allowing the synthesis of a wide range of various substituted 2-cyanobenzothiazole derivatives.[2] These new compounds could be seen as valuable building blocks for the design of more complex heterocyclic systems.



The synthesis of thiazole-fused quinazolinones, derived from bioactive natural alkaloids, hitherto undescribed was successfully achieved starting from polyfunctionalized benzothiazoles using a variant of the Niementowski reaction under microwave irradiation. This work demonstrates the synthetic interest of polyfunctionalized benzothiazoles providing convenient access to structures with high biological potential, opening the chemical space around naturally occurring tricyclic quinazolinones. [3]

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[1] a) Kamal, A.; Syed, M. A. H.; Mohammed, S. M. *Expert Opin. Ther. Pat*. **2015**, *25*, 335. b) Ammazzalorso, A.; *et. al*. *Eur. J. Med. Chem.* **2020**, *207*, 112762. c) Law, C. S. W.; Yeong, K. Y. *Expert Opin. Ther. Pat*. **2022**, *32*, 299.

[2] a) Broudic, N.; Pacheco-Benichou, A.; Fruit, C.; Besson, T. *Molecules* **2022**, *27,* 8426. b) Broudic, N.; Pacheco-Benichou, A.; Fruit, C.; Besson, T. *Synthesis* **2023**, *55*, 3263.

[3] a) Broudic, N.; Layec, C.; Fruit, C.; Besson, T. *Synthesis* **2024**, *56*, 1485. b) Fruit, C.; Besson, T.*et al. Pharmaceuticals* **2024**, *17*, 1452.