

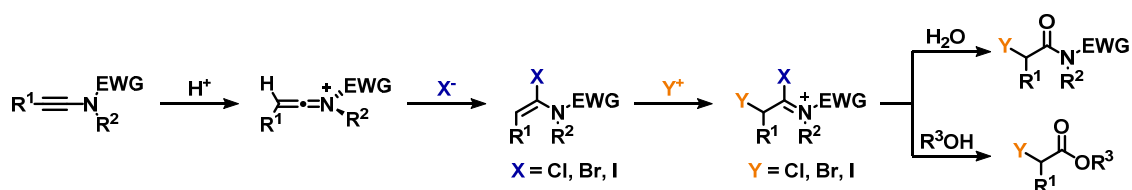
DOUBLE ELECTROPHILIC ACTIVATION OF YNAMIDES: A STRAIGHTFORWARD ENTRY TO α -HALO-CARBOXYL DERIVATIVES

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α -Halo-carboxyl derivatives are versatile synthetic intermediates in organic synthesis. However, the synthesis of such derivatives is not that trivial and often requires multiple steps and harsh reaction conditions while only showing variable selectivity. Additionally, due to steric bulk and good leaving group ability, α -iodo-carboxyl derivatives have only scarcely been described to date. With this in mind, and in continuation to our work on ynamides^[1] and keteniminium ions,^[2] we recently developed a novel route to α -chlorinated-, brominated- and iodinated-carboxyl derivatives based on the double electrophilic activation of ynamides.

More precisely, upon acid-mediated generation and trapping of activated keteniminium ions with hydrogen halides,^[3] we have shown that the resulting electron-deficient halo-enamides could be activated by various electrophilic halogenation reagents. *In-situ* hydrolysis or alcoholysis of the resulting halo-iminium intermediates could subsequently yield the desired α -halo-carboxyl derivatives.



Moreover, we successfully developed a one-pot process based on the stepwise addition of trimethylsilyl halides and *N*-halosuccinimides giving the desired carboxyl-derivatives in good to excellent yields. The scope and limitations of this process will be discussed.

[1] For a recent review on the chemistry of ynamides, see: Evano, G.; Theunissen, C.; Lecomte, M. *Aldrichimica Acta* **2015**, *48*, 59.

[2] For a recent review on the chemistry of keteniminium ions, see: Evano, G.; Lecomte, M.; Thilmany, P.; Theunissen, C. *Synthesis* **2017**, *49*, 3183.

[3] (a) Mulder, J. A.; Kurtz, K. C. M.; Hsung, R. P.; Coverdale, H.; Frederick, M. O.; Shen, L.; Zifcsak, C. A. *Org. Lett.* **2003**, *5*, 1547. (b) Compain, G.; Jouvin, K.; Martin-Mingot, A.; Evano, G.; Marrot, J.; Thibaudeau, S. *Chem. Commun.* **2012**, *48*, 5196. (c) Métayer, B.; Compain, G.; Jouvin, K.; Martin-Mingot, A.; Bachmann, C.; Marrot, J.; Evano, G.; Thibaudeau, S. *J. Org. Chem.* **2015**, *80*, 3397. (d) Ohashi, K.; Mihara, S.; Sato, A. H.; Ide, M.; Iwasawa, T. *Tetrahedron Lett.* **2014**, *55*, 632.