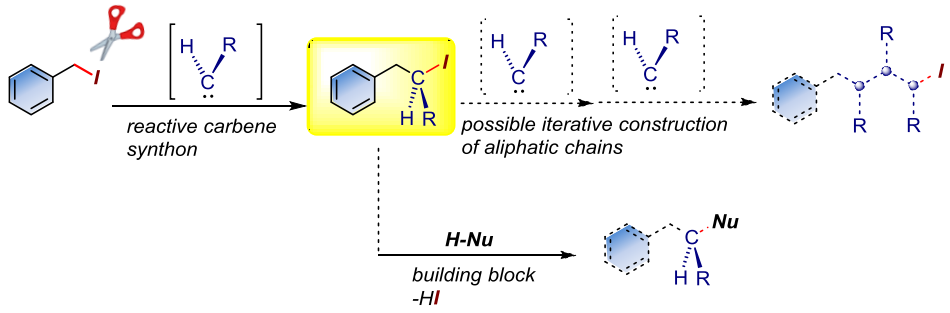
PERSONA CIÈNCIA EMPRESA
UNIVERSITAT RAMON LLULL

Halogen-directed construction of molecular complexity: testing the concept

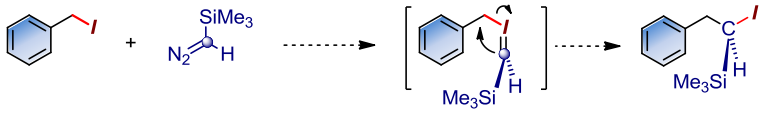
Prof.: Dra. Ana B. Cuenca. Dept. Organic Chemistry
http://www.iqs.edu/es/dra-ana-belen-cuenca-gonzalez

Organic synthesis relies heavily on the use of halogenated compounds. Indeed, several of the key synthetic transformation, including substitution (S_N1 and S_N2) and elimination reactions, the formation of organo-magnesium reagents and a variety of cross-coupling reactions require the use of organohalogens. In virtually all applications, however, the halogen acts a good leaving group, and is, therefore, eliminated.

We now wish to test a radically different methodology in which a halogen (especially: iodine) can act as a directing group in a new class of reactions which would allow an efficient way to access a range of biologically relevant targets. This proposal is based upon our recent work in inserting carbene synthons into activated B-X bonds,[1] as well some preliminary results made possible by the ability of halogens to expand its shell beyond the "octet rule".[2] Specifically, through the insertion of carbenes into a carbon-iodine bond of aliphatic and benzylic species a series of complex and valuable structures might be obtained in a highly efficient manner.



As part of the mechanistic rationale, we envisage that a carbene equivalent, obtained through the decomposition of TMS-CHN_2[1] might form a transient halonium ylide[3] structure which would then undergo a [1,2] shift, thus extending the carbon chain by 1 C.



iodonium ylide
(hypervalent)

A unique feature of the new approach is the ability to retain the halogen in the product, opening the door to a wide range of biologically relevant targets, either through iterative chain extension or through classical halogen substitution approaches.

---

[1] a) Civit, M. G.; Royes, J.; Vogels, C.; Wescott, S.; Cuenca, A. B.*; Fernández, E. * *Org. Lett*. **2016**, *18*, 3830; b) E. La Cascia, A. B. Cuenca*, E. Fernández*, *Chem. A. Eur. J.* **2016**, DOI: 10.1002/chem.201604782.

[2] Yoshimura, A.; Zhdankin, V. V. Chem. Rev. 2016, 116, 3328.

[3] For related allyliodine chemistry, see: a) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094; b) Xu, B.; Tambar, U. K. *J. Am. Chem. Soc.* **2016**, 138, 12073.