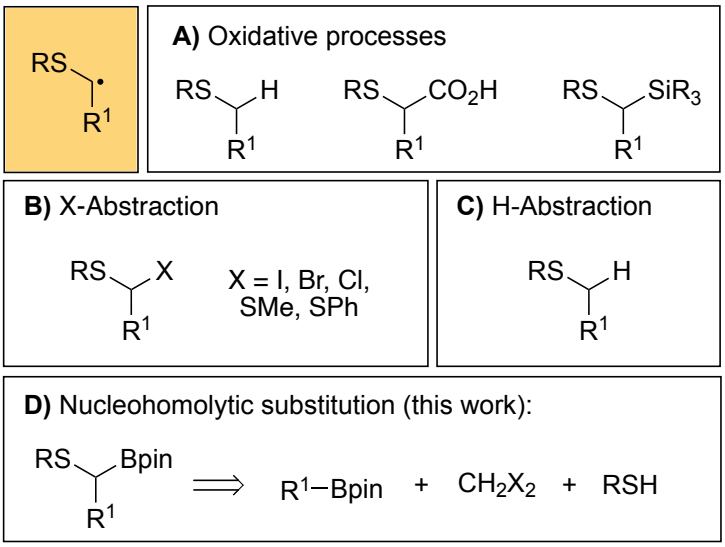
Generation of α-Thioalkyl Radicals from Pinacol Boronic Ester Precursors

Lise Benoist, Fabrice Dénès and Phillipe Renaud.
Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, 3012 Bern (Switzerland)
lise.benoist@unibe.ch

Dialkyl thioethers are widely present in biologically active natural products[1] and are also found across a broad spectrum of fields including the pharmaceutical[2] and agrochemical industries[3] as well as organic functional materials.[4] Consequently, the ubiquity of sulfur-containing molecules has long motivated synthetic chemists to develop efficient strategies towards their synthesis. Over the last decades, the generation of α-thioalkyl radicals has emerged as a powerful strategy for the functionalization of thioethers. Notably, α-thioalkyl radicals can be generated through oxidative processes,[5] X-abstraction[6] and H-abstraction.[7]



Scheme 1. Generation of α-thioalkyl radicals.

Organoboron derivatives have proven over the years to be an efficient source of alkyl radicals.[8] Herein, we report a novel protocol for the generation of α-thioalkyl radicals starting from α-thioalkyl pinacol boronic ester precursors, readily prepared by Matteson homologation of commercially available boronic esters and subsequent 1,2-metalate shift with diverse sodium thiolates.

(1) Morikawa, T.; Ninomiya, K.; Tanabe, G.; Matsuda, H.; Yoshikawa, M.; Muraoka, O. *J. Nat. Med.* **2021**, *75* (3), 449–466.
(2) Scott, K. A.; Njardarson, J. T. *Top. Curr. Chem. (Z)* **2018**, *376* (1), 5.
(3) Devendar, P.; Yang, G.-F. *Top. Curr. Chem. (Z)* **2017**, *375* (6), 82.
(4) Boyd, D. A. *Angew. Chem. Int. Ed.* **2016**, *55* (50), 15486–15502.
(5) Alfonzo, E.; Hande, S. M.; *ACS Catal.* **2020**, *10* (21), 12590–12595.
(6) Arya, P.; Samson, C.; Lesage, M.; Griller, D. *J. Org. Chem.* **1990**, *55* (26), 6248–6250.
(7) Le, C.; Liang, Y.; Evans, R. W.; Li, X.; MacMillan, D. W. C. *Nature* **2017**, *547* (7661), 79–83.
(8) Ollivier, C.; Renaud, P. *Chem. Rev.* **2001**, *101* (11), 3415–3434.