

Research Topic for the ParisTech/CSC PhD Program

Field: Chemistry, Physical Chemistry and Chemical Engineering

Subfield: Chemistry

ParisTech School: LSO, Ecole Polytechnique

Title: A Unified Route to Polycyclic Terpenes

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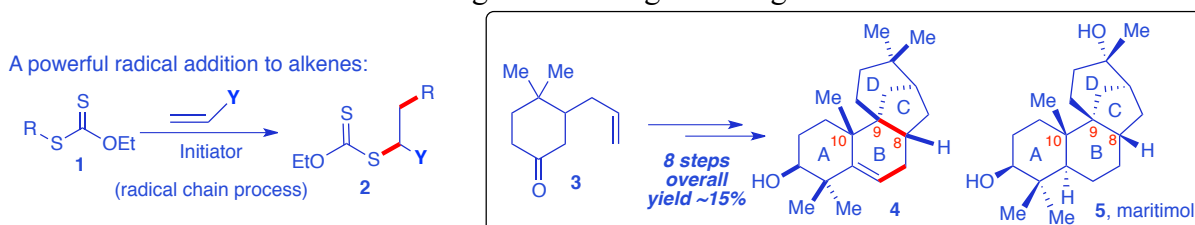
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Short description of possible research topics for a PhD:

Of all the natural products, terpenes offer the greatest skeletal variety and complexity. Several members, either in native form or as simple derivatives, are already in clinical use (e. g. taxol, Taxotere[®], Ingenol mebutate or Picato[®], pleuromutilin). Many contain fused or bridging 4, 5, 6, 7- and even 8-membered rings and constitute major synthetic challenges.

Our group has discovered a remarkably powerful reaction involving a xanthate transfer with a *unique ability to store reactive radicals in a dormant form* and thereby to enhance their lifetime in a concentrated medium, while at the same time regulating their absolute and relative concentrations. It allows *intermolecular* radical additions even to unactivated alkenes (**1** → **2**) and promotes otherwise sluggish processes such as 5-*endo*, 6-*exo*, 6-*endo*, 7-*endo* and 8-*endo* cyclizations. In the present proposal, we would like to develop a unified and particularly concise approach to polycyclic terpenes. Preliminary results are extremely promising, as demonstrated by the synthesis of maritimidol (**5**) analog **4** from simple allylcyclohexanone **3** in *only 8 steps*. This is by far the shortest route to such complex terpenoids. It is hoped to extend this powerful strategy to numerous other terpene structures with various combinations and arrangement of rings and ring sizes.



Required background of the student: General Organic Chemistry

A list of representative publications of the group:

1. *A Highly Stereoselective, Modular Route to (E)-Vinylsulfones and to (Z)- and (E)-Alkenes.* Braun, M.-G.; Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2011**, *133*, 15954-15957.
2. *From a Remarkable Manifestation of Polar Effects in a Radical Fragmentation to the Convergent Synthesis of Highly Functionalized Ketones.* Debien, L.; Zard, S. Z. *J. Am. Chem. Soc.* **2013**, *135*, 3808-3811.
3. *Radical Instability in Aid of Efficiency. A Powerful Route to Highly Functional MIDA Boronates.* Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **2015**, *137*, 6762-6765.
6. *A Radical Bidirectional Fragment Coupling Route to Unsymmetrical Ketones.* Anthore-Dalio, L.; Liu, Q.; Zard, S. Z. *J. Am. Chem. Soc.* **2016**, *138*, 8404-8407.
5. *The Xanthate Route to Ketones. When the Radical is Better than the Enolate.* Zard, S. Z. *Acc. Chem. Res.* **2018**, *51*, 1722-1733.