

## Samir Zard

Director of Research - Exceptional Class in the CNRS  
Professor of Organic Chemistry at École polytechnique

- 1955 born in Ife, Nigeria  
1973 - 1975 BSc in American University of Beirut, Lebanon  
(interrupted by Lebanese civil war)  
1976 - 1978 BSc in Imperial College London, UK  
1978 - 1983 PhD in Université Paris-Sud, France  
(Supervisor: Prof. Sir Derek Barton)  
1981 - 1986 Attaché de Recherche in CNRS (in Barton group)  
1986 - now École polytechnique, France

Research field: radical chemistry, organosulfur chemistry (xanthates), heterocycle synthesis, total synthesis, RAFT/MADIX for block polymers

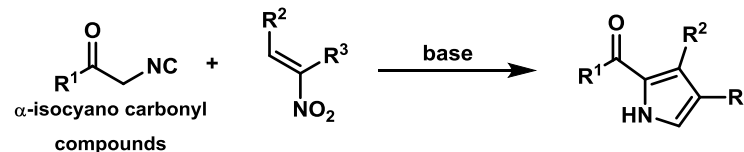
## Selected awards and honors:

- Chevalier dans l'Ordre de la Légion d'Honneur (2007)  
Silver Medal of the CNRS (2007)  
Grignard-Wittig Award of the German Chemical Society (2008)  
Woodward Distinguished Lectureship - Harvard University (2010)  
Grand Prix Joseph-Achille Le Bel of the French Chemical Society (2012)  
Inaugural Barton Distinguished Lectureship in Creativity in Organic Synthesis Imperial College (2012)  
Birch Distinguished Lectureship at the Australia National University (2015)

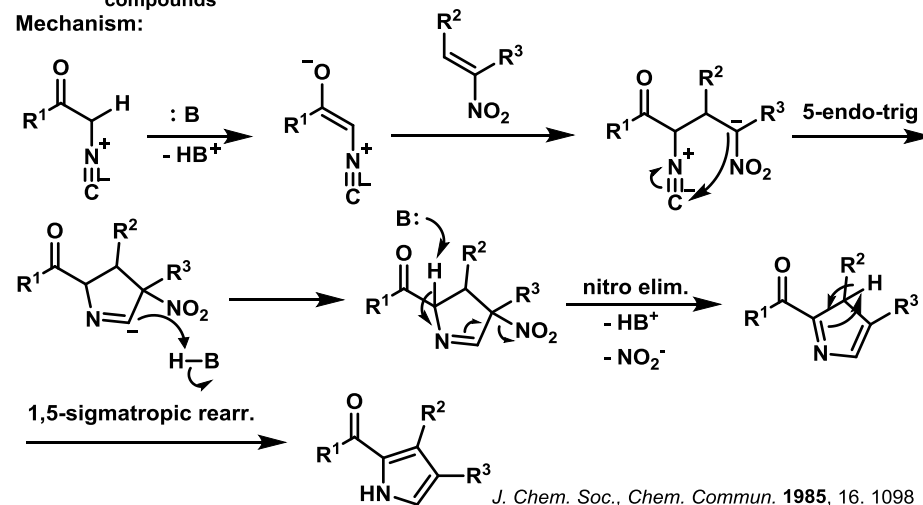
Publications: ~ 350 papers, ~5 book chapters, 35 patents



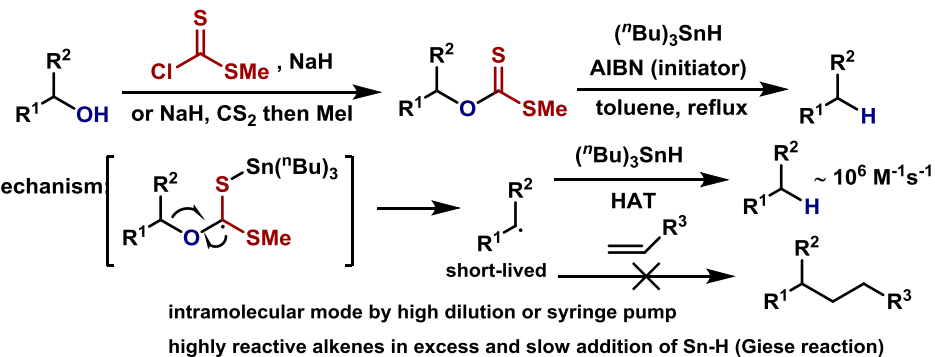
## 1985 Barton-Zard pyrrole synthesis



## Mechanism:

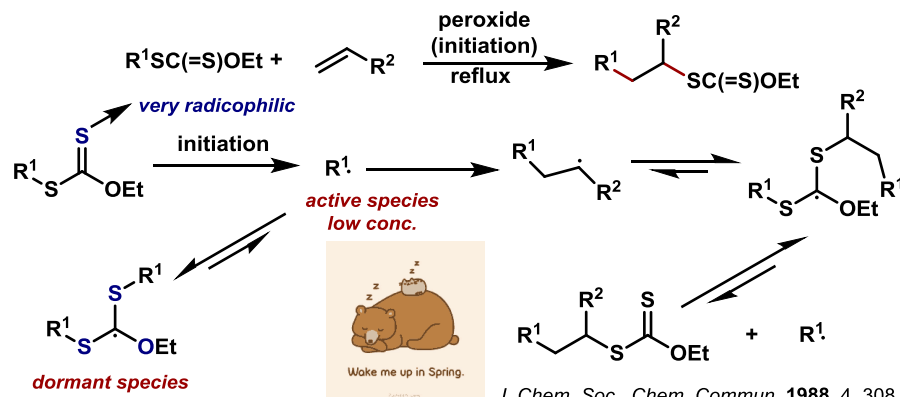


## 1975 Barton-McCombie deoxygenation



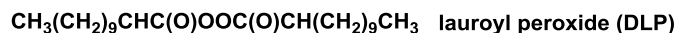
Prof. Zard began his independent career on the trail of Xanthates

### The degenerative radical system of Xanthates



J. Chem. Soc., Chem. Commun. 1988, 4. 308

1. Active radical gets captured by xanthate precursor **very rapidly and reversibly**, the dormant radical is **very stable**;
2. Self-regulation: the equilibrium between active and dormant radicals favors the later, thus the **conc. of active radical is very low** in the system (prevents radical-radical coupling);
3. **Extended lifetime** of active radical enables inter- / intra-molecular addition to **unactivated alkenes**;
4. Initiator: mainly peroxide, such as **lauroyl peroxide (DLP)**
5. R on O of xanthates (mainly Et) should be less or similar stable than R1 on S;
6. Solvents: EA, DCE, PhCl, etc.



Other advantages:

- reagents are available, cheap, stable *but smelly* • no heavy metals
- under **high conc.** (typically 1-2 M, even neat) • safe and easily scalable
- mild and neutral conditions • **broad tolerance for polar FGs and protection free**
- radical-polar crossover reactions

For reviews, see:

*ACIE*, 1997, 36, 672; *Chem. Eur. J.* 2006, 12, 6002; *Pure. Appl. Chem.* 2010, 83, 519; *CHIMIA*, 2012, 66, 404.

For book chapters, see:

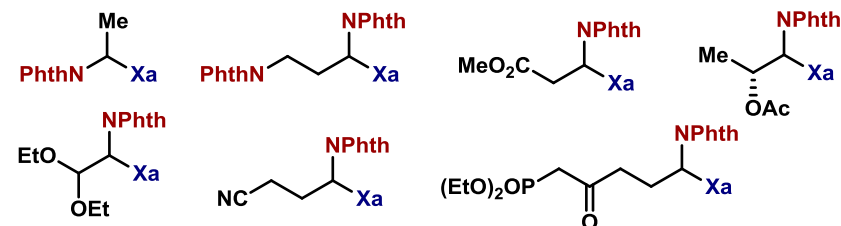
*Top. Curr. Chem.* 2006, 264, 201; *Handbook of RAFT Polymerization*, 2008, 151

### Selectivity issue:

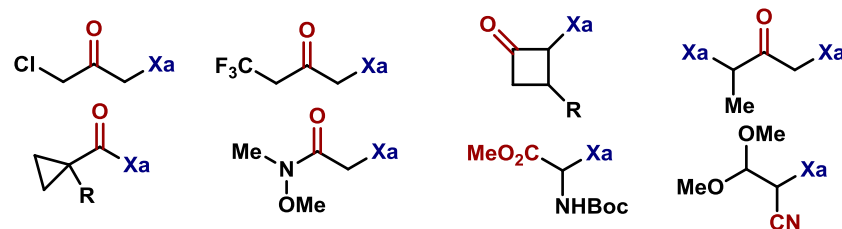
1. **Reactant radical should be more stable than product radical** to prevent oligomerization (2 kcal/mol difference in energy results in **100-fold** difference in their relative concentration).
  2. **Terminal alkenes** are normally required for regio-selectivity and high reaction rate
- Selected array of xanthates

#### • Stabilized by phthalimide:

> 100 xanthates > 2000 additions



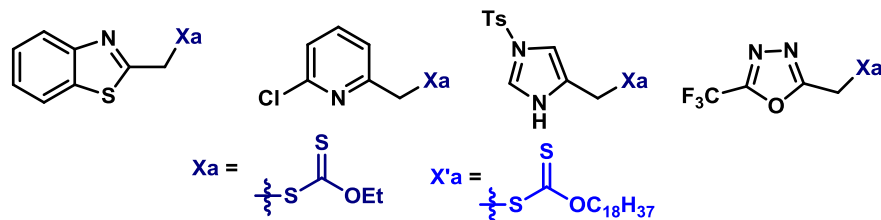
#### • Stabilized by ketone, amide, ester, nitrile, etc.:



#### • Organofluorine compounds:



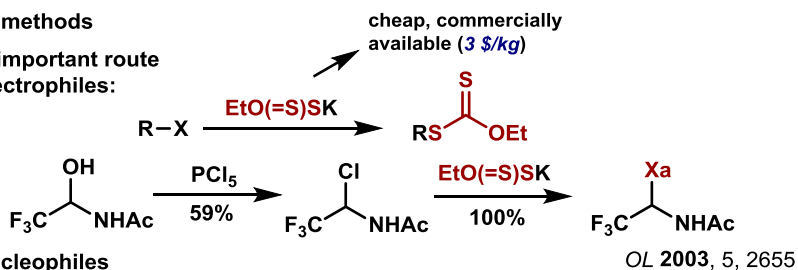
#### • Stabilized by heterocycles:



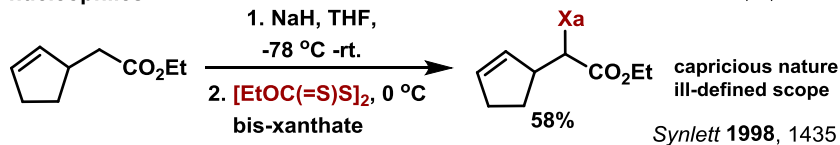
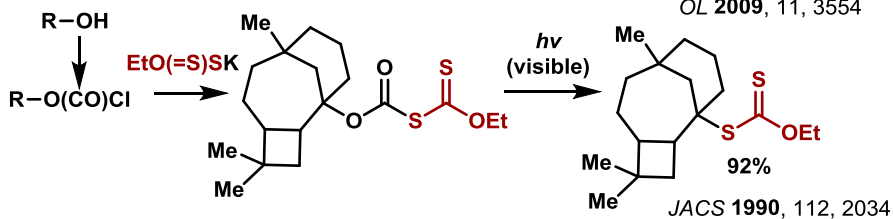
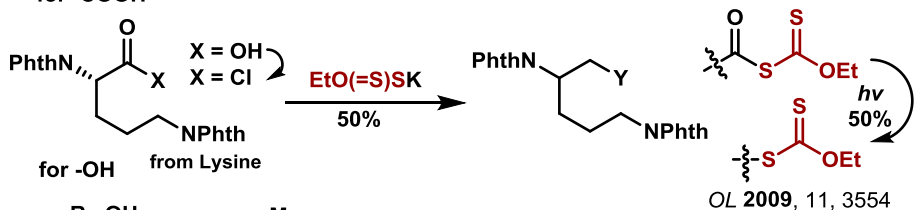
## Introduction of xanthate

## • ionic methods

most important route  
for electrophiles:

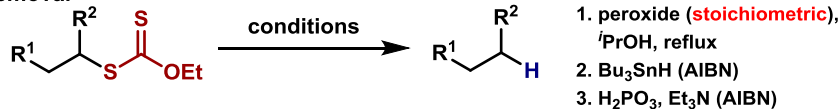


## for nucleophiles

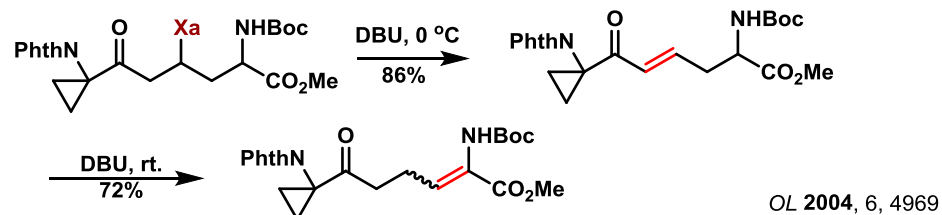
• radical methods  
for -COOH

## Transformations of xanthate

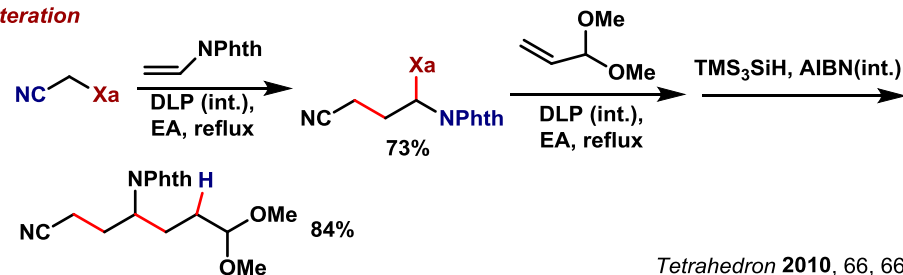
## removal



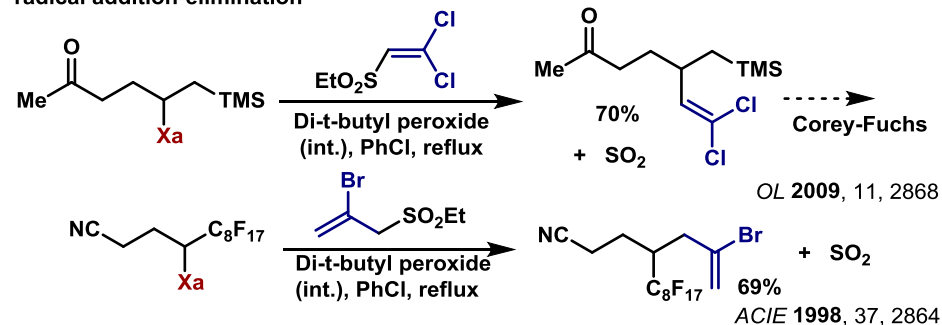
## alkene formation



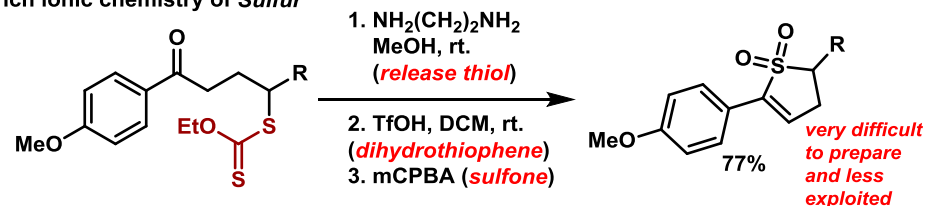
## iteration

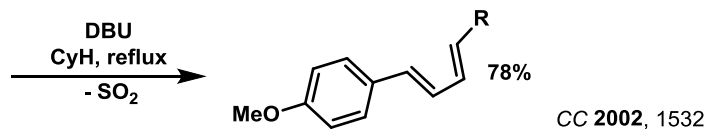


## radical addition-elimination



## rich ionic chemistry of Sulfur

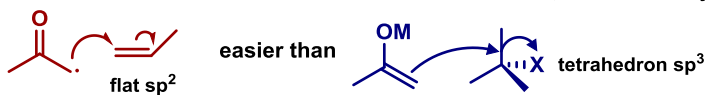
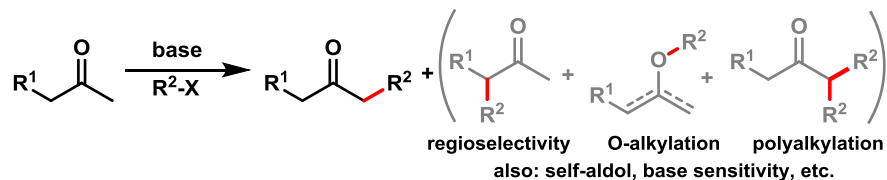




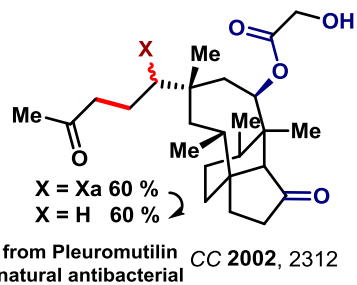
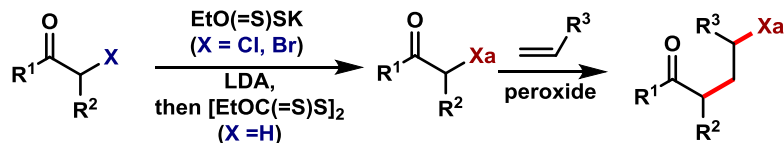
## The application on organic synthesis

- Alternative to alkylation of enolate For review, see: *ACR*, 2018, 51, 1722

Enolate chemistry is key to organic synthesis but can be difficult to control

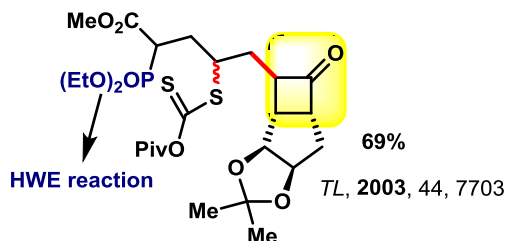


lack of generally applicable methods for  $\alpha$ -ketonyl radical generation

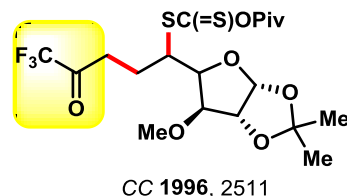


troublesome ketones:

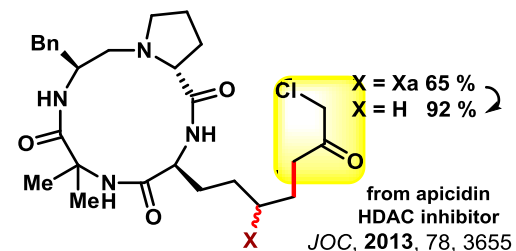
- cyclobutanone (prone to self condense, hydrazone or imine used)



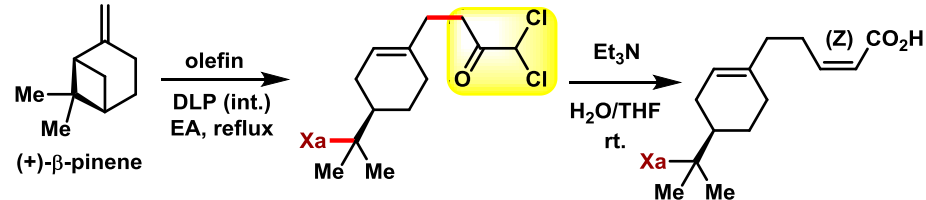
- trifluoroketone (self-condensation)



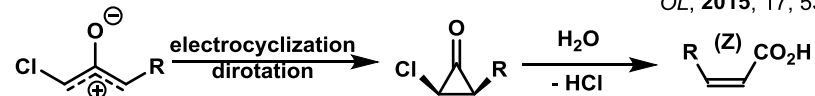
- chloroacetone (base sensitive)



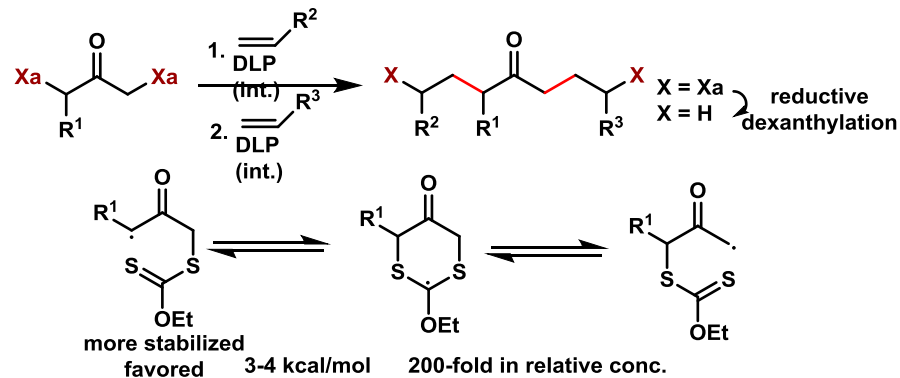
- 1,1-dichloroacetone (more base sensitive)

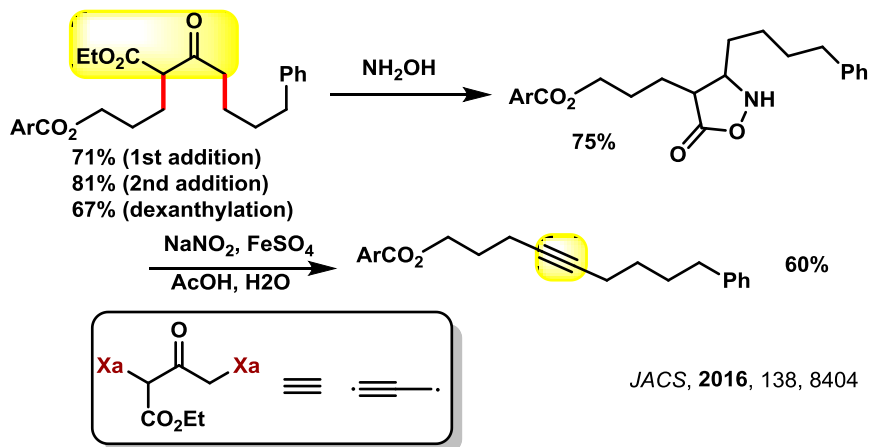


Favorskii rearr.

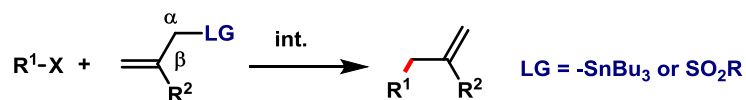
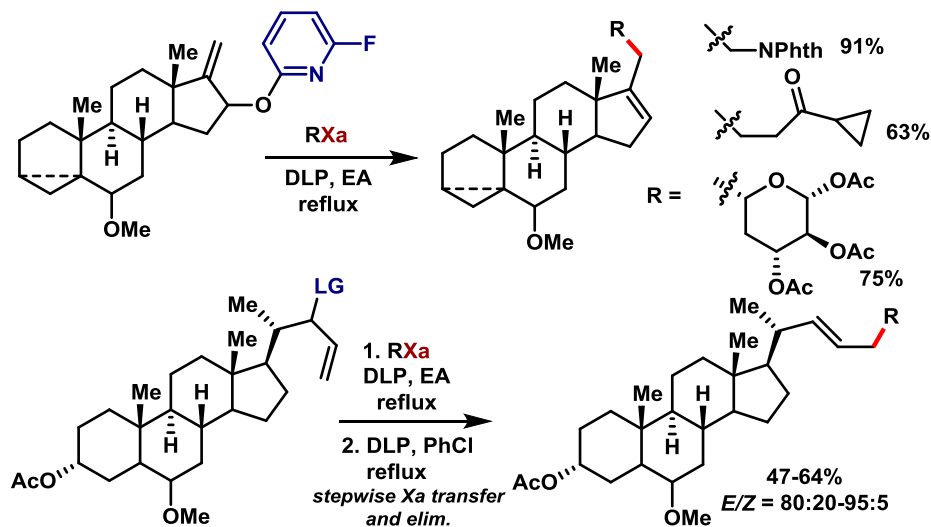
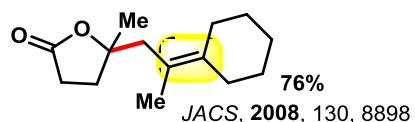
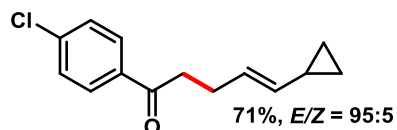
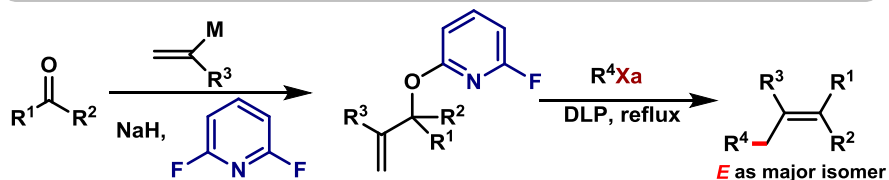
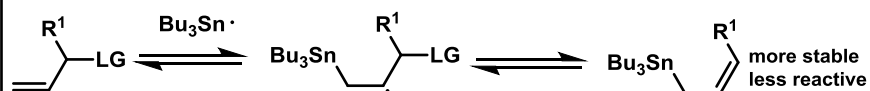


unsymmetric ketone synthesis

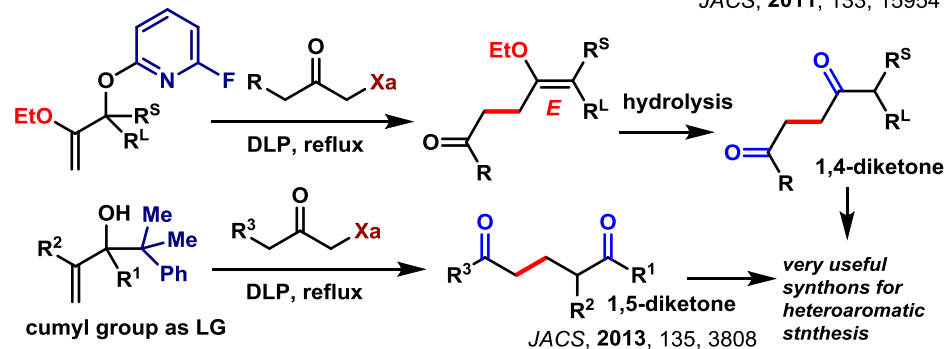
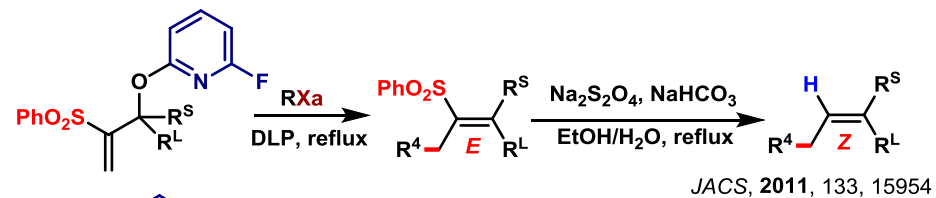




## Radical allylation using allylic alcohols

complications associated with  $\alpha$ -substituted precursors

to better control Z/E

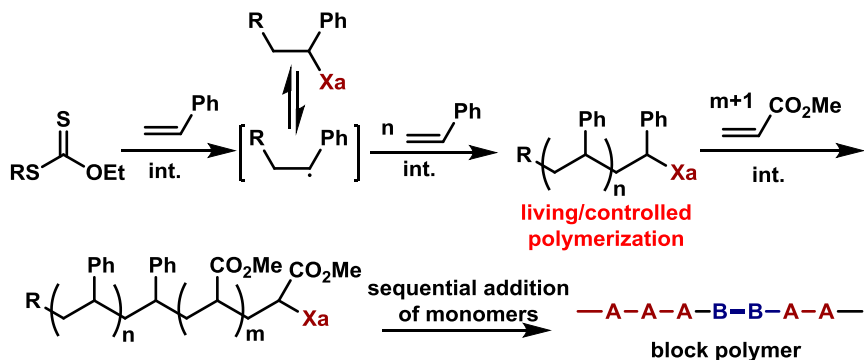






## RAFT/MADIX process for block polymer manufacture

**Block copolymers:** two or more homopolymer subunits linked by covalent bonds



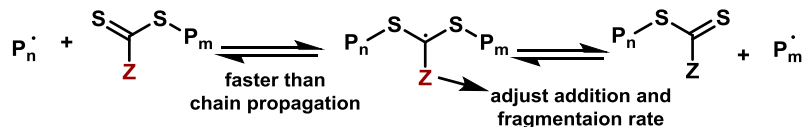
**RAFT** (reversible-addition-fragmentation chain-transfer) named by CSIRO (Australia)

IUPAC definition: Degenerate-transfer radical polymerization in which chain activation and chain deactivation involve a degenerative chain-transfer process which occurs by a two-step addition-fragmentation mechanism.

**MADIX** (macromolecular design by interchange of xanthate) coined by Rhodia (France, now owned by Solvay)

Original patents on RAFT/MADIX:  
Rhodia and CNRS: WO 9858974 (1998)  
CSIRO: *Int. Pat.* 9801478 (1998)

**MW. distribution of RAFT/MADIX is excellent**



For book chapter, see: *Handbook of RAFT Polymerization*, 2008, 373

commercial block polymers:

**Rhodibloc®** (Rhodia-Solvay) and **Asteric®** (Lubrizol)

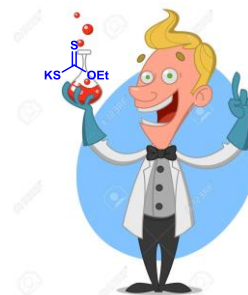
- Rhodibloc® FL: cementing additives for the oilfield
- Rhodibloc® FL-A/D/X: fluid loss block polymer additives (retaining water within slurries over a wide range of temperatures)
- Rhodibloc® GC: gas migration control agent

For review, see: *Poly.Chem.* 2018, 9, 4947



>100 other companies: DuPont, Arkema, Henkel, 3 M, etc.

*By the end of 2018, all the RAFT foundation patents have expired and RAFT will be free to use by anyone on a commercial basis!*



*"It is an amusing twist of fate that potassium ethyl xanthate was one of the first organic compounds I prepared as a teenager in a small room next to the kitchen, to my mother's utter disgust. It is perhaps only fair that I should also thank her and the rest of my family for putting up with such smelly activity for a good many years."*

*ACIE*, 1997, 36, 672