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### JACS **1987**, 109 (26)

Evolution of Modern
Homoenolate Chemistry

### 2. Evolution of Modern C-F Bond Functionalization Chemistry

December 1<sup>st</sup>, 1987 On this day in history:

#### **Events**

- Digging begins to link England and France under the English Channel.
- NASA announces the names of four companies who were awarded contracts to help build Space Station Freedom: Boeing Aerospace, General Electric's Astro-Space Division, McDonnell Douglas, and the Rocketdyne Division of Rockwell.

#### **Famous Birthday**

- Grégoire Leprince-Ringuet
- Vance Joy: Rock Singer.
- Simon Dawkins: English footballer.
- Tabarie Henry: Virgin Islander sprinter.
- Brett Williams: English footballer.
- Ian Hecox: Comedian.

### Carbon-Carbon Bond-Forming Reactions of Zinc Homoenolate of Esters. A Novel Three-Carbon Nucleophile with General Synthetic Utility

Eiichi Nakamura,\* Satoshi Aoki, Kouichi Sekiya, Hiroji Oshino, and Isao Kuwajima\*

Contribution from the Department of Chemistry, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan. Received March 26, 1987



#### Scheme I



"In the present work, we describe the versatile reactivities of zinc homoenolate... to demonstrate for the first time the great potential of homoenolate chemistry in organic synthesis."

- 1. Copper-catalyzed Conjugate Addition Reactions
- 2. Allylation Reactions
- 3. Arylation and Vinylation Reactions
- 4. Carbonyl Addition: Homo-Reformatsky Reactions
- 5. Acylation Reactions
- 6. Silylation Reactions



Undesirable competition with internal electrophile

1. Copper-catalyzed Conjugate Addition Reactions



63 - 93% 10 examples

2. Allylation Reactions



3. Arylation and Vinylation Reactions

4.

2



5. Acylation Reactions



6. Silylation Reactions



### Modern Homoenolate Reagents



### Modern Homoenolate Reagents



Org. Lett. 2018, 20, 554 - 557

## Modern Applications of Homoenolates: Cross-Coupling Reactions





#### Activation of Carbon-Fluorine Bonds by Oxidative Addition

Thomas G. Richmond,\* Carolyn E. Osterberg, and Atta M. Arif





Salt Lake City, Utah 84112

Received September 21, 1987

### Modern Strategies for C-F Bond Activation



## Modern Strategies for C-F Bond Activation

Ichikawa 2017

Loh 2015



For a helpful review: Angew. Chem. Int. Ed. 2019, 58, 390

## Modern Strategies for *sp*<sup>3</sup> C-F Bond Activation



Scheme 5. Mechanistic hypothesis.

### Modern Strategies for *sp*<sup>3</sup> C-F Bond Activation

Hilmersson 2013





Scheme 2. Mechanistic proposal for the F/I substitution.

## Modern Strategies for *sp*<sup>3</sup> C-F Bond Activation



## Summary

#### Homoenolate Chemistry

#### 1987

- A new homoenolate reagent was developed that facilitated some of the first synthetic applications
- However, the substituents on the homoenolate reagent were limited

#### Present

- A variety of homoenolate reagents have been developed to for cross-coupling applications

#### C-F Bond Activation

#### 1987

 Aromatic C-F bond activation was demonstrated but the strategy did not have synthetic applications

#### Present

 Strategies for C-F bond activation have been expanded to aliphatic C-F bonds and