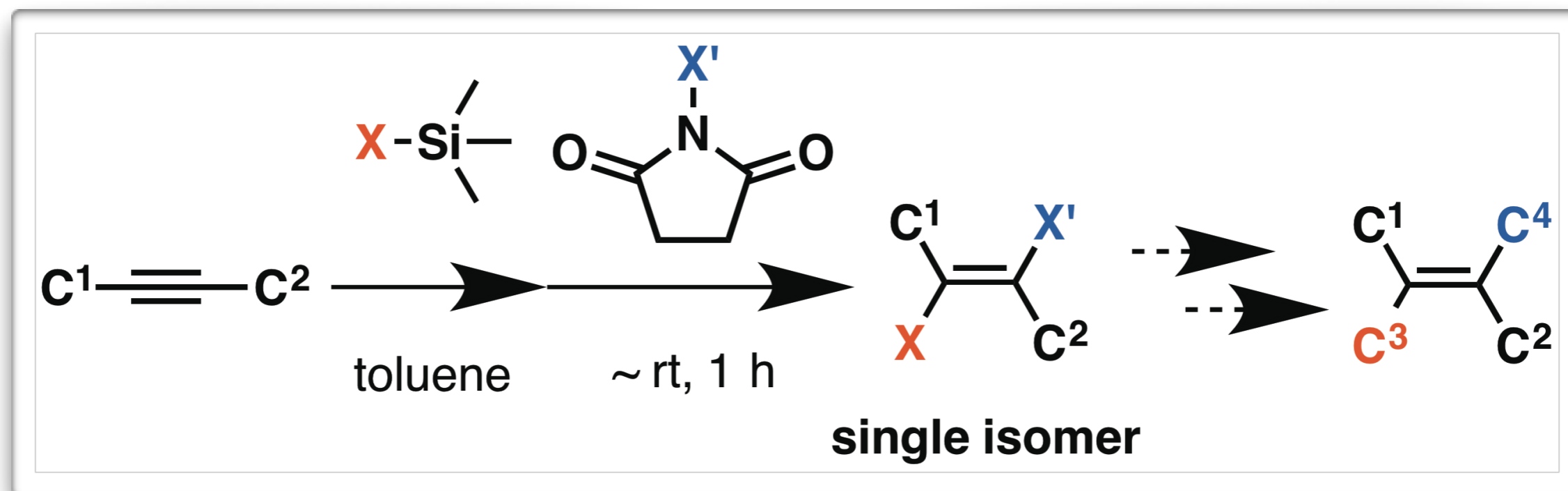


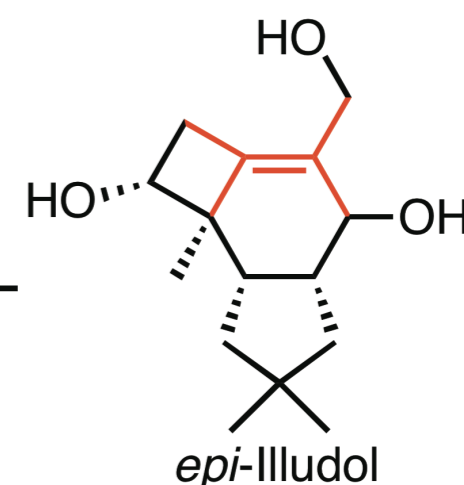
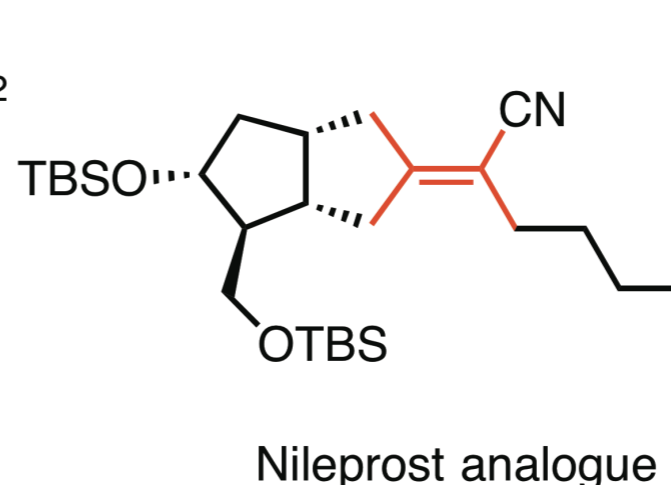
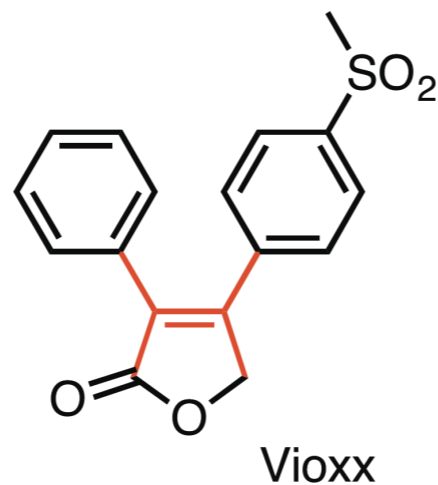
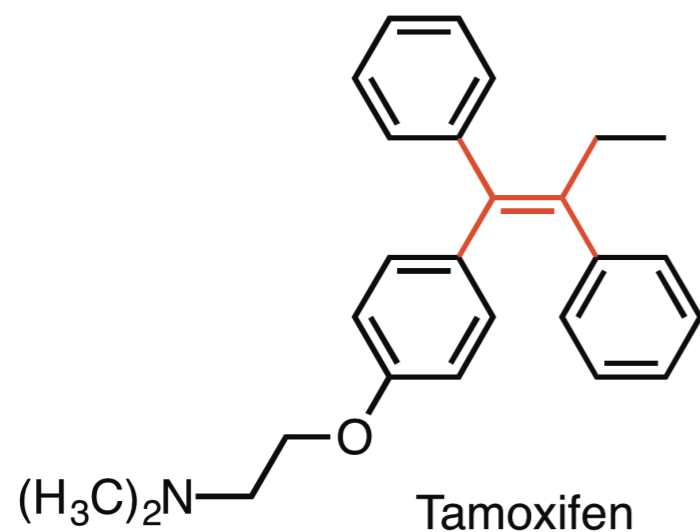
# 汎用試薬を利用した 四置換アルケンのテンプレート合成



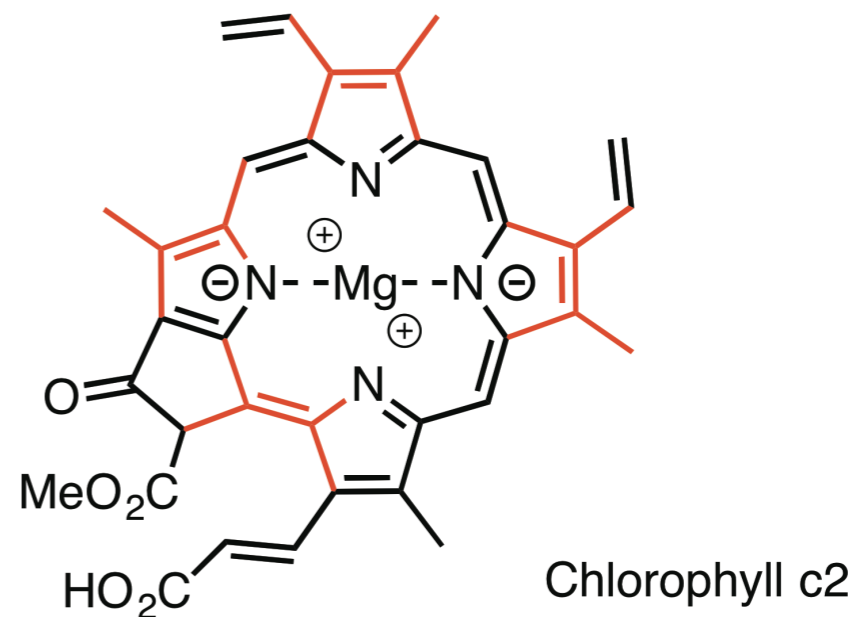
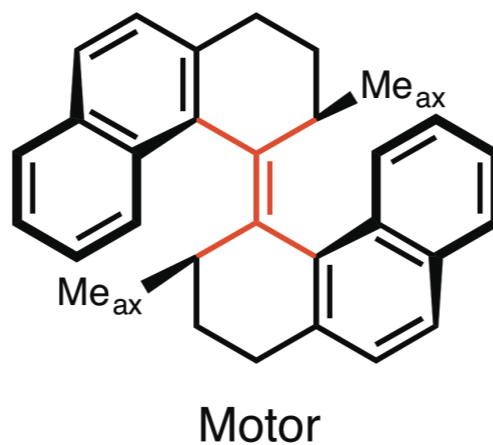
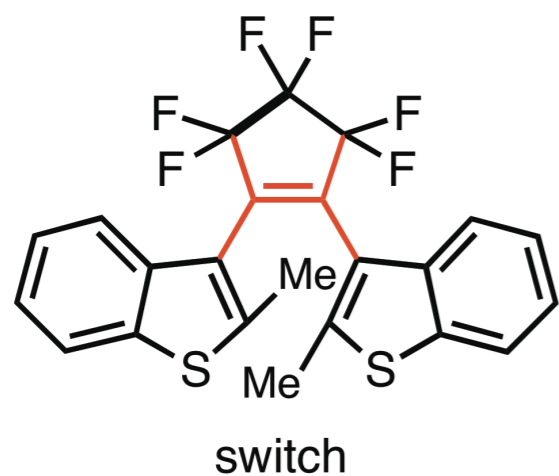
龍谷大学 理工学部 物質化学科  
岩澤 哲郎

# 背景：四置換アルケンの価値

## For Therapeutics

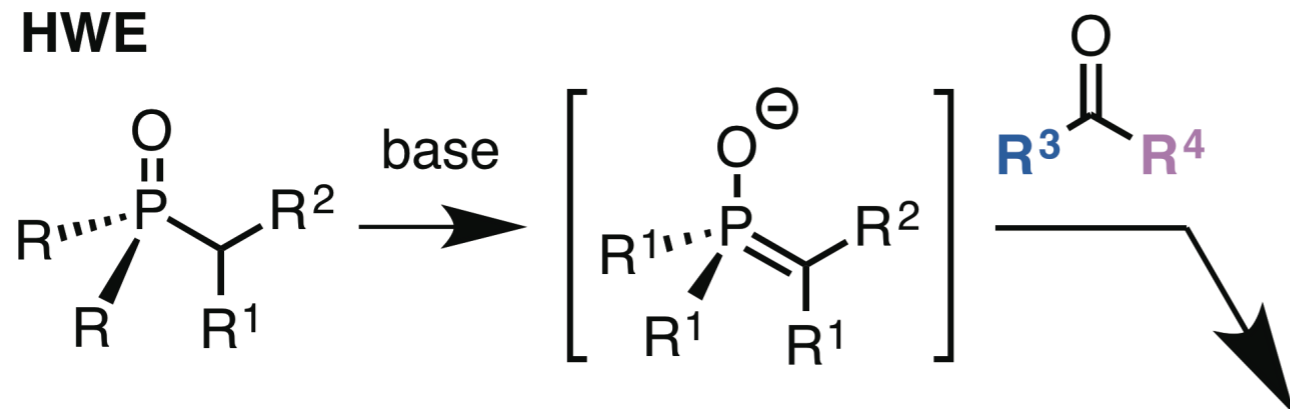


## For Materials



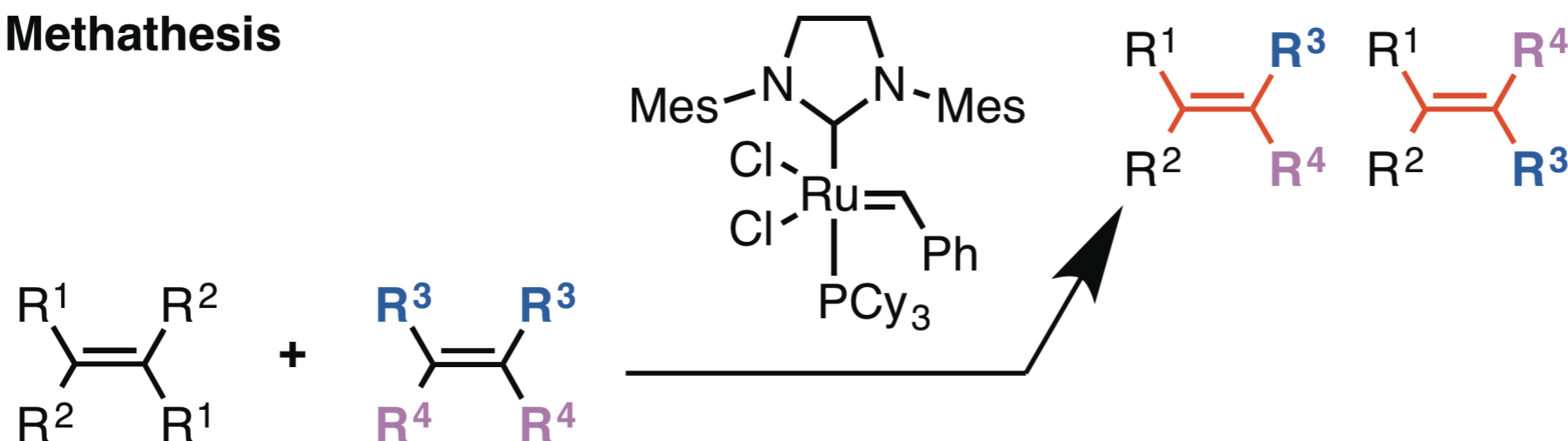
# 従来技術とその問題点

## HWE

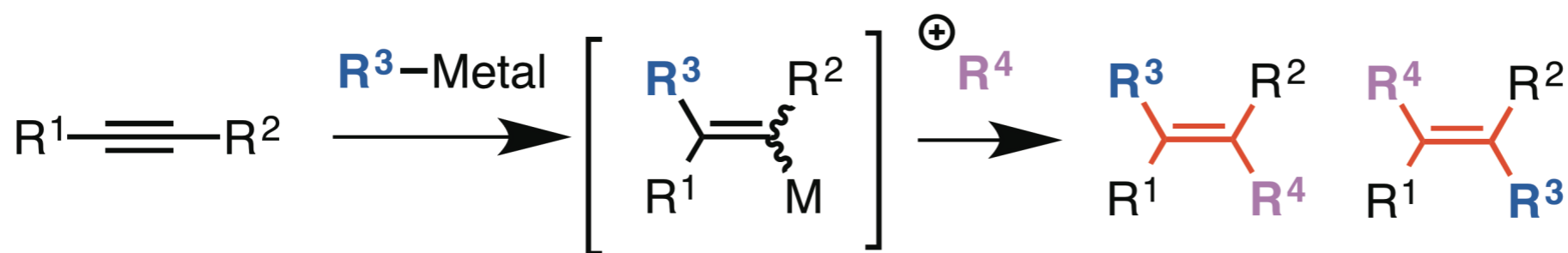


鎖状には無力  
異性体の混じりに

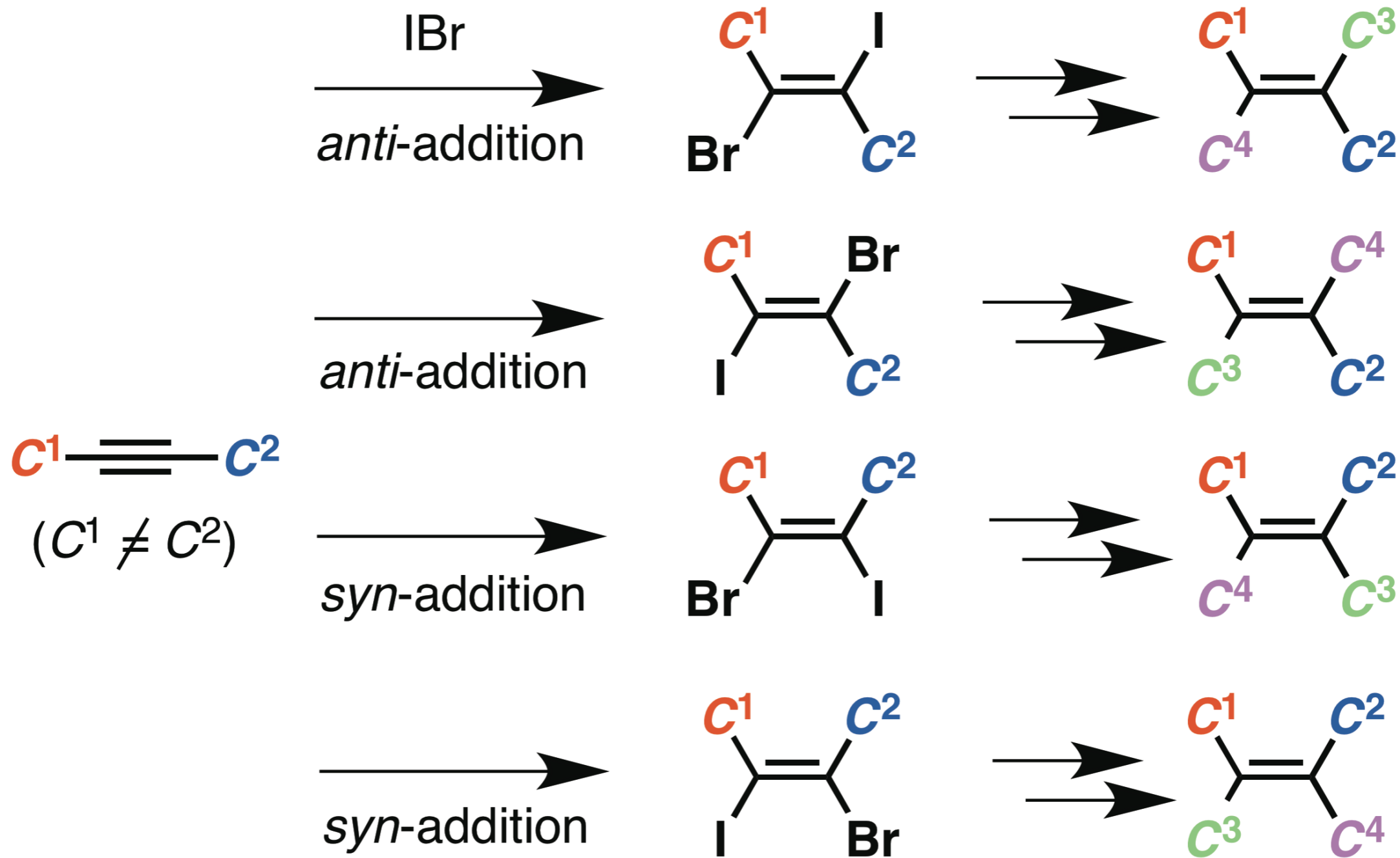
## Methathesis



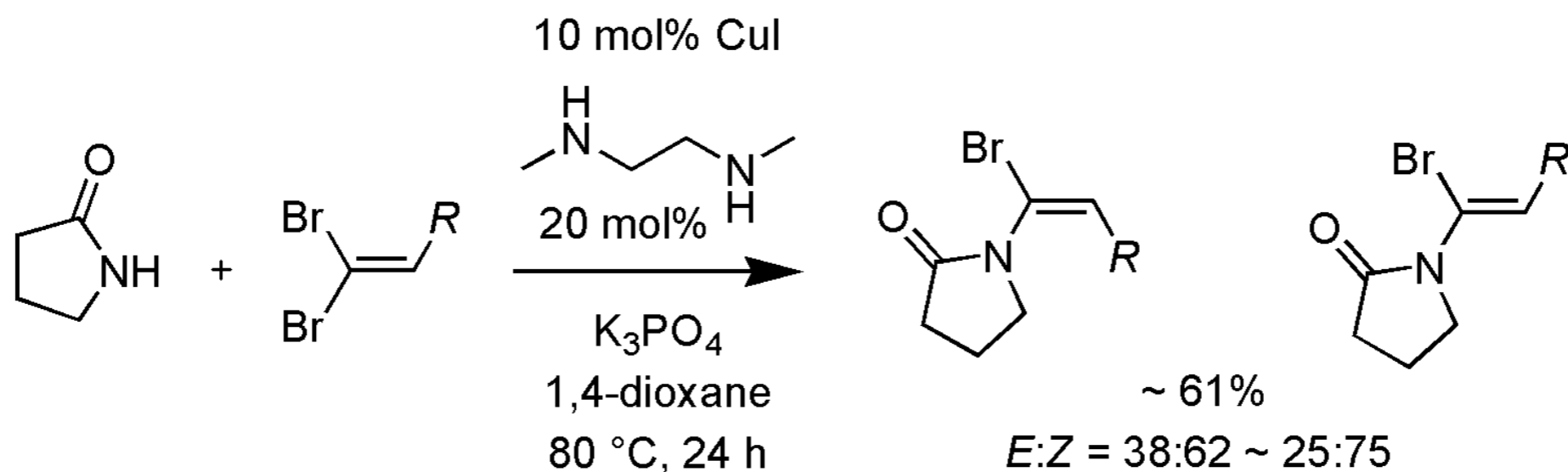
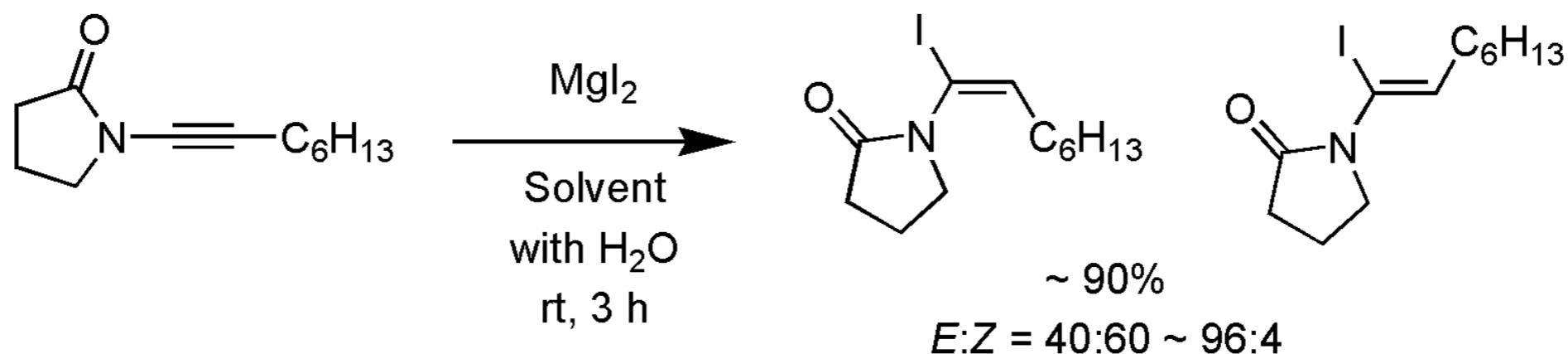
## Carbometallation



# 世界の研究動向



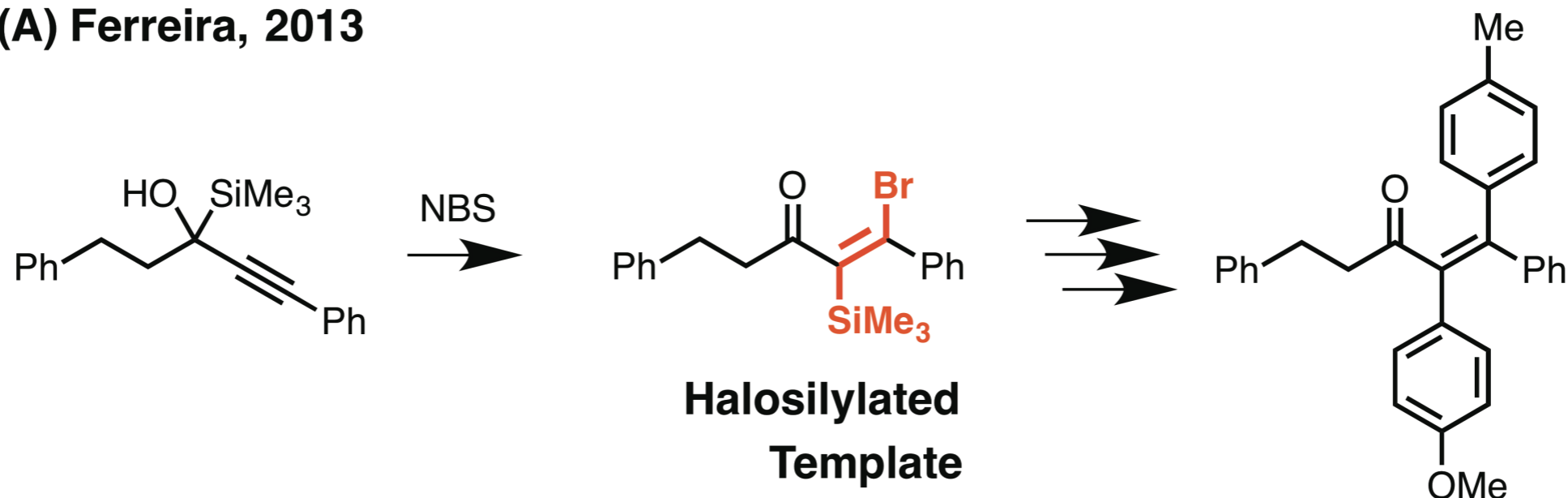
# 実際はまだまだ



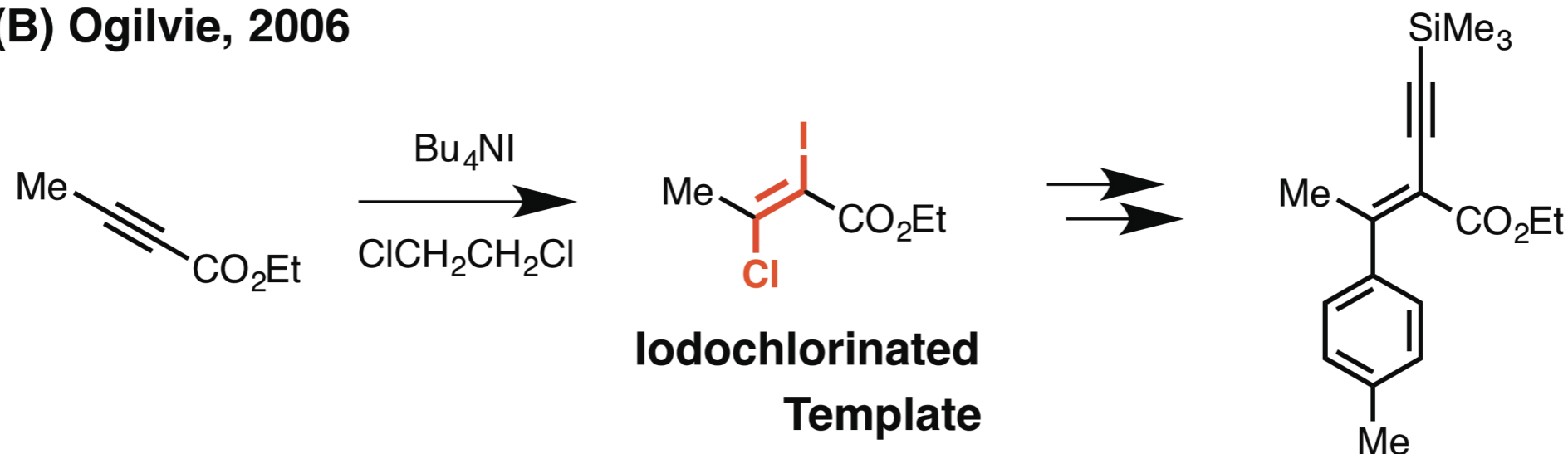
1. Mulder, J. A.; Kurtz, K. C. M.; Hsung, R. P.; Coverdale, H.; Frederick, M. O.; Shen, L.; Zificsak, C. A. *Org. Lett.* **2003**, 5, 1547-1550.
2. Jouvin, K.; Coste, A.; Bayle, A.; Legrand, F.; Karthikeyan, G.; Tadiparthi, K.; Evano, G. *Organometallics* **2012**, 31, 7933-7947.

# そんな中でも、過去に2例

## (A) Ferreira, 2013



## (B) Ogilvie, 2006



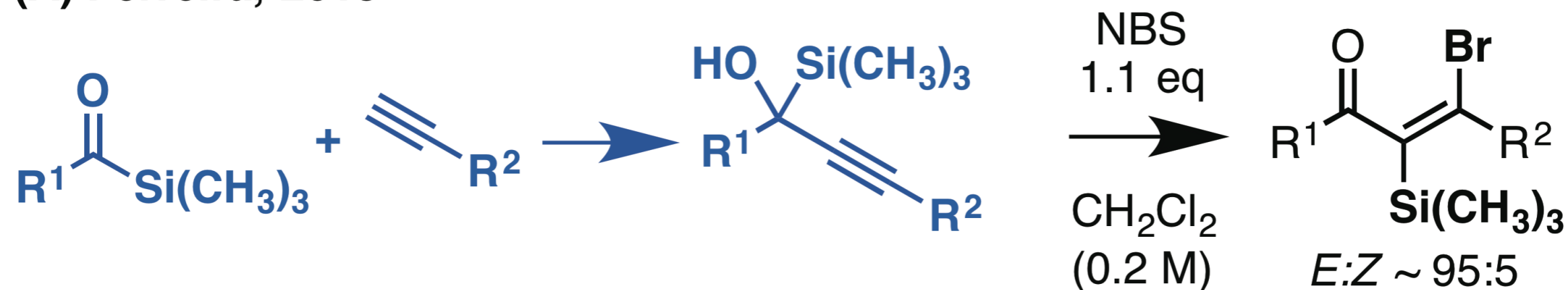
A. N. T. Barczak, D. A. Rooke, Z. A. Menard, E. M. Ferreira, *Angew. Chem. Int. Ed.* **2013**, 52, 7579-7582

B. a) A. B. Lemay, K. S. Vulic, W. W. Ogilvie, *J. Org. Chem.* **2006**, 71, 3615;

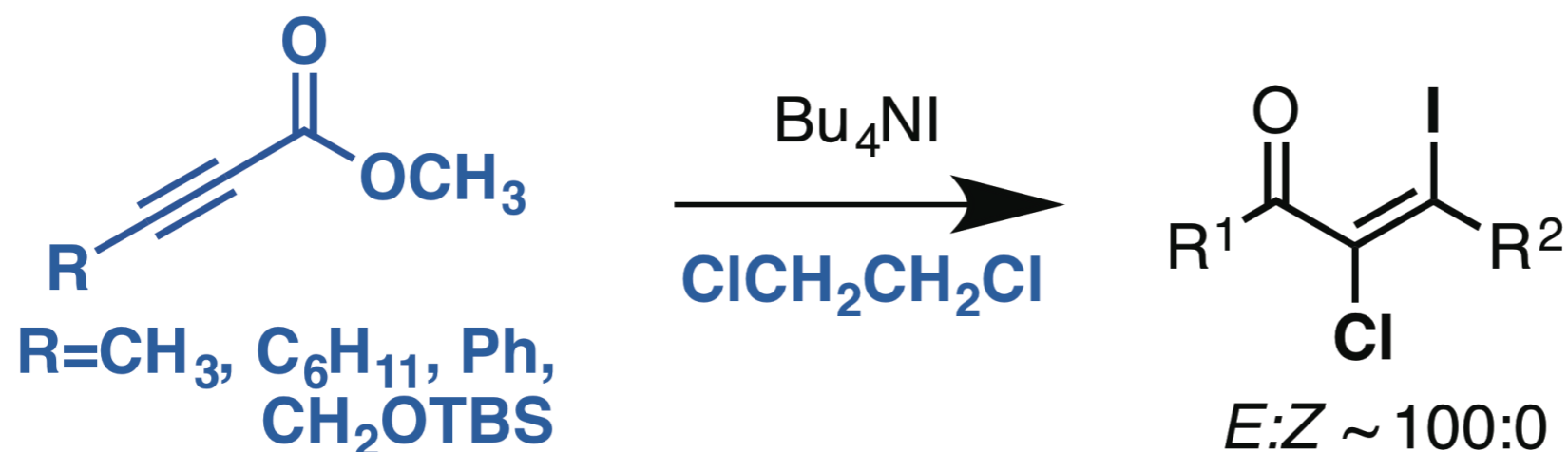
b) M. N. Ho, A. B. Lemay, W. W. Ogilvie, *J. Org. Chem.* **2007**, 72, 977.

# 問題点：原料が限定的、広がらず

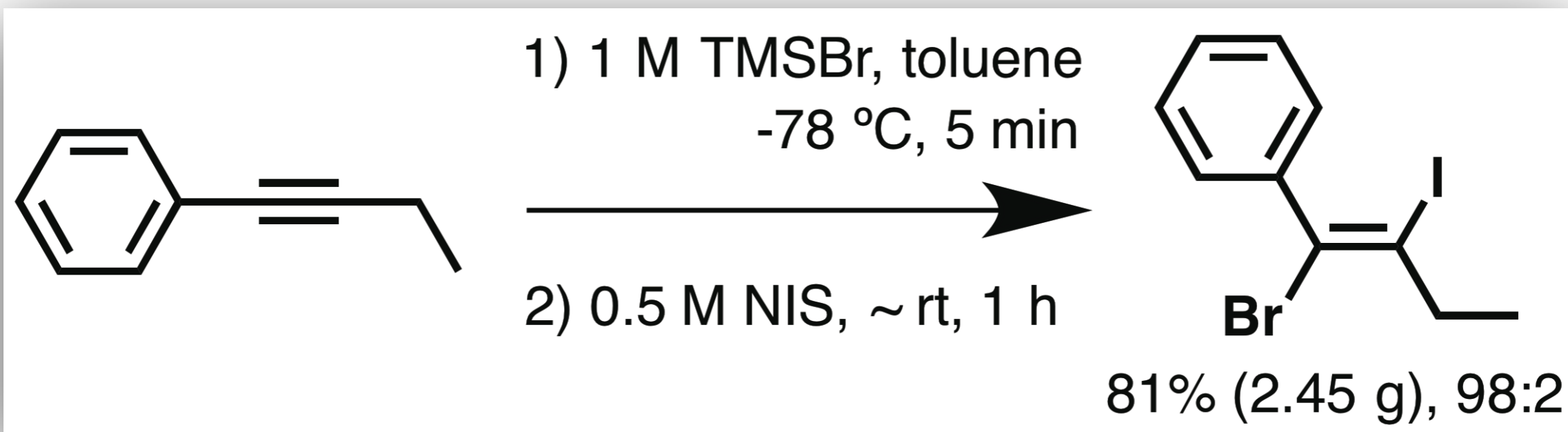
(A) Ferreira, 2013



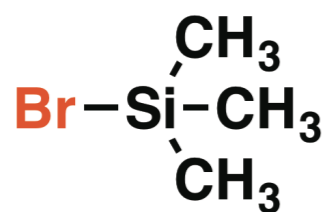
(B) Ogilvie, 2006



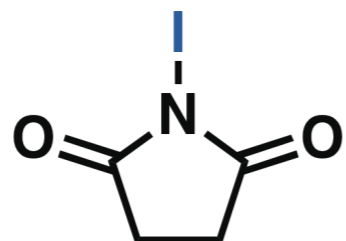
# 我々の開発した手法



TMSBr  
25 mL ¥3000



NIS  
25 g, ¥ 9000



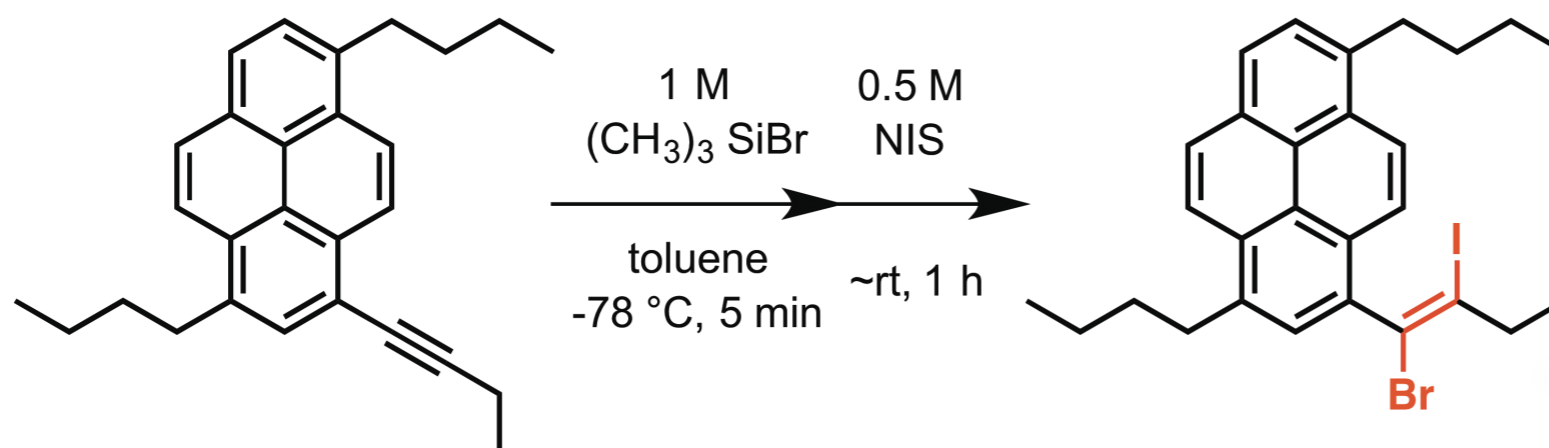
単純な炭化水素鎖に有効  
汎用な市販試薬を使うだけ

■ Ide, M.; Yauchi, Y.; Shiogai, R.; Iwasawa, T. *Tetrahedron* **2014**, *70*, 8532-8538.

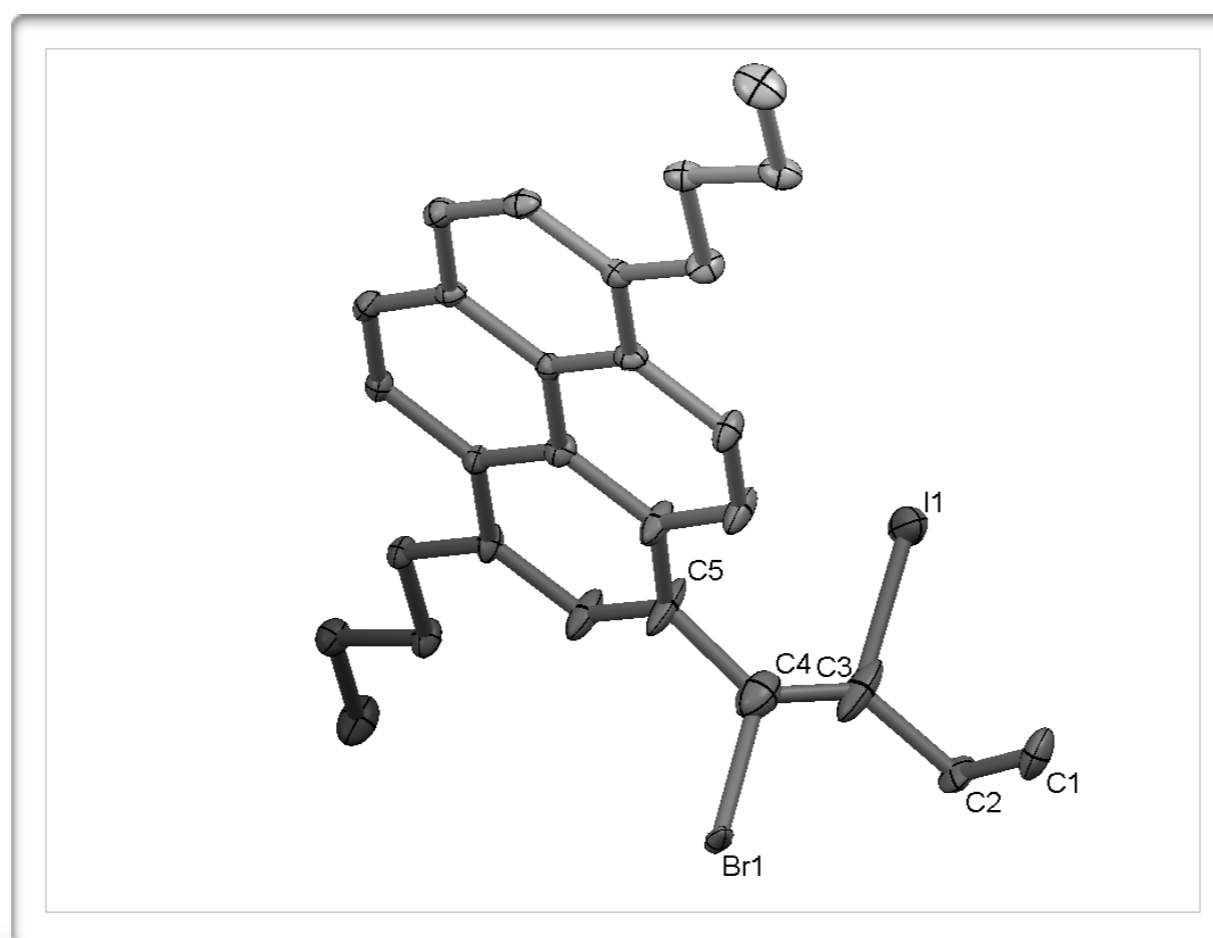
■ 特願 2014-153644 (2014年7月29日 出願)



# 構造決定

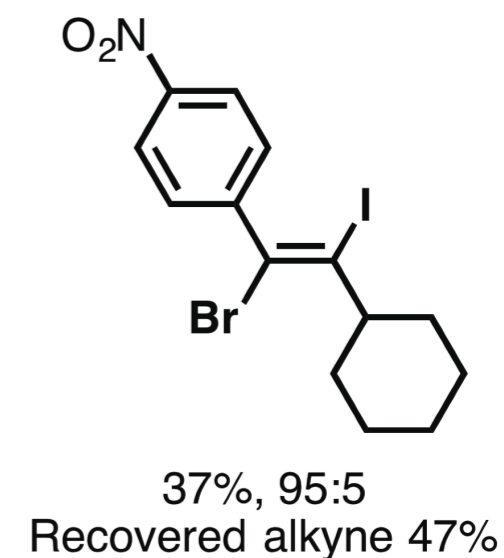
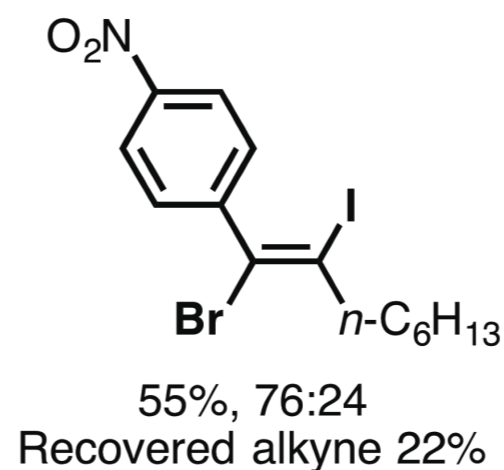
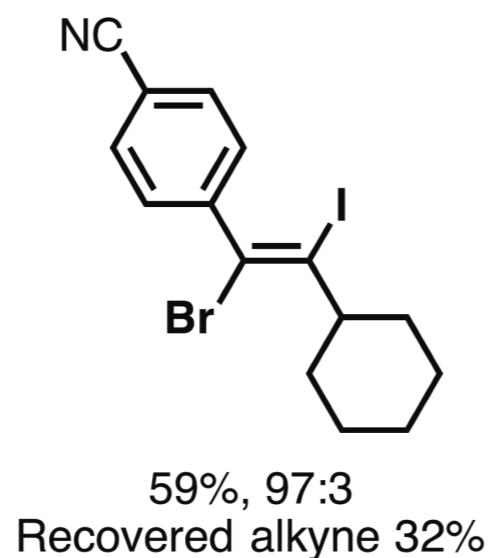
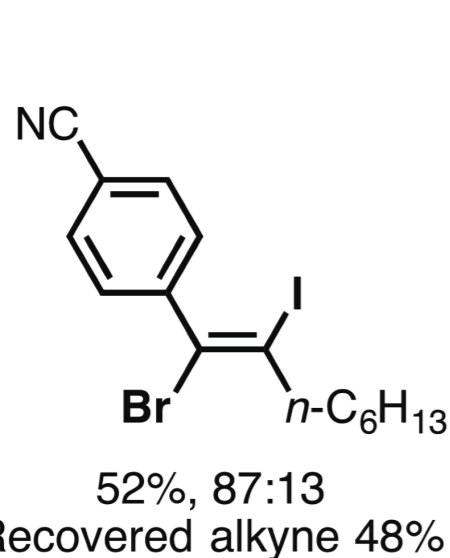
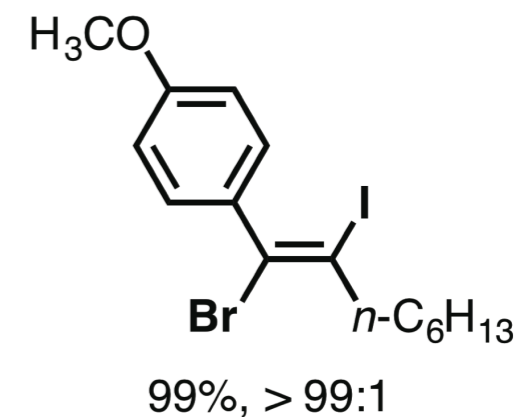
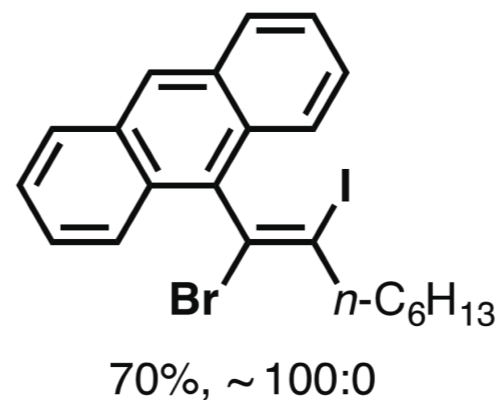
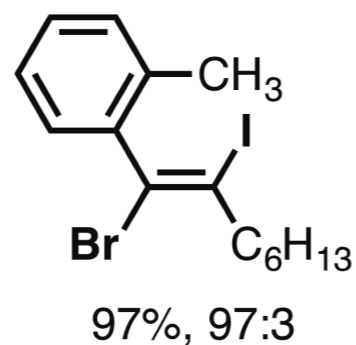
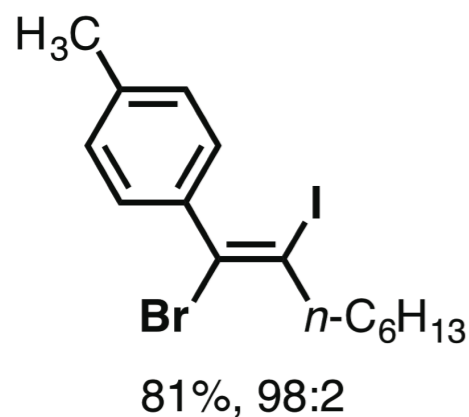
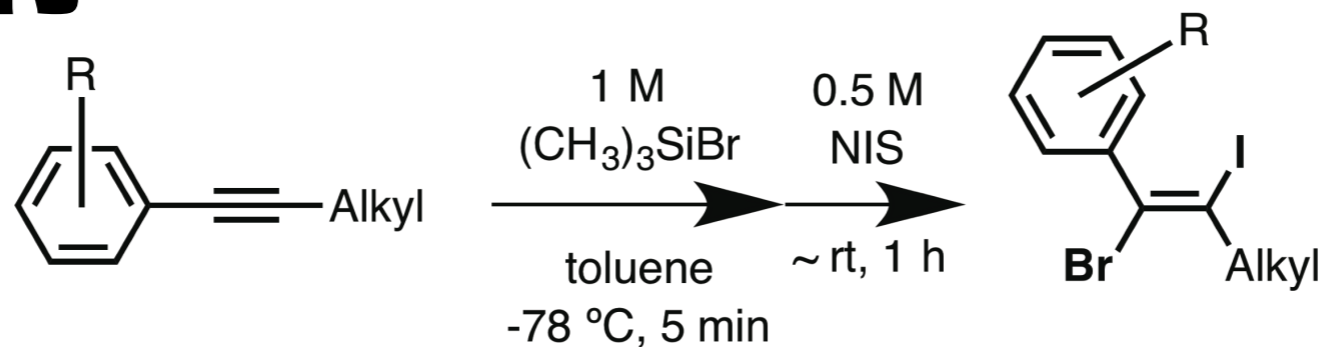


77% (443 mg)  
94:6  
(*E*)-, 1-bromo-2-iodo

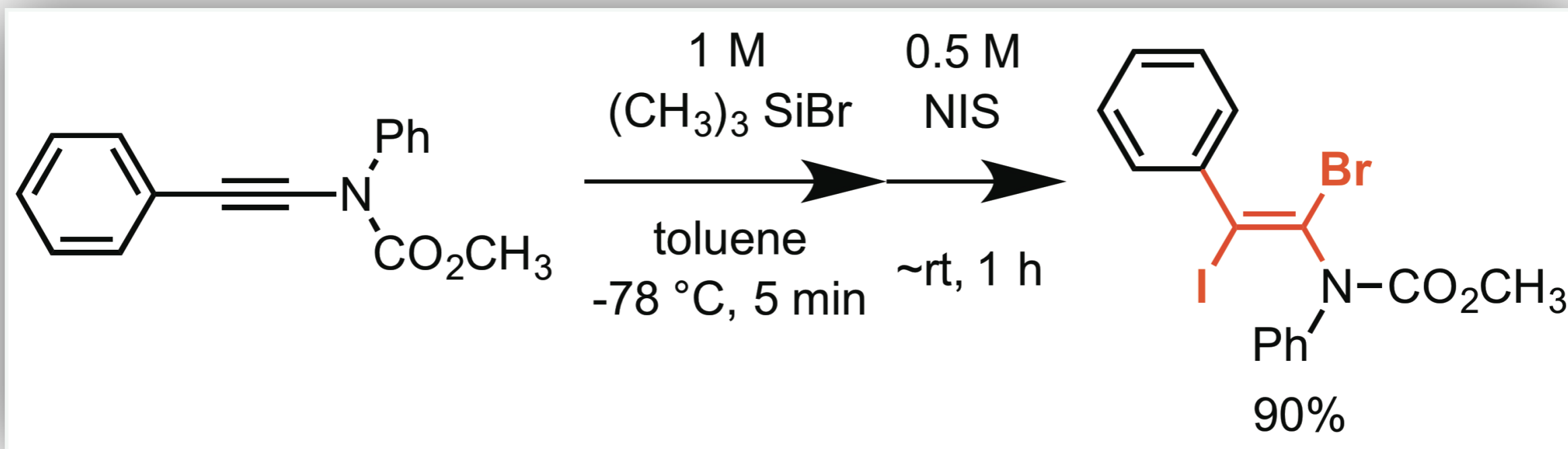


(Å): C(2)-C(3) = 1.507  
C(3)-I(1) = 2.168  
C(3)-C(4) = 1.267  
C(4)-Br(1) = 1.905  
C(4)-C(5) = 1.501

# 基質検討



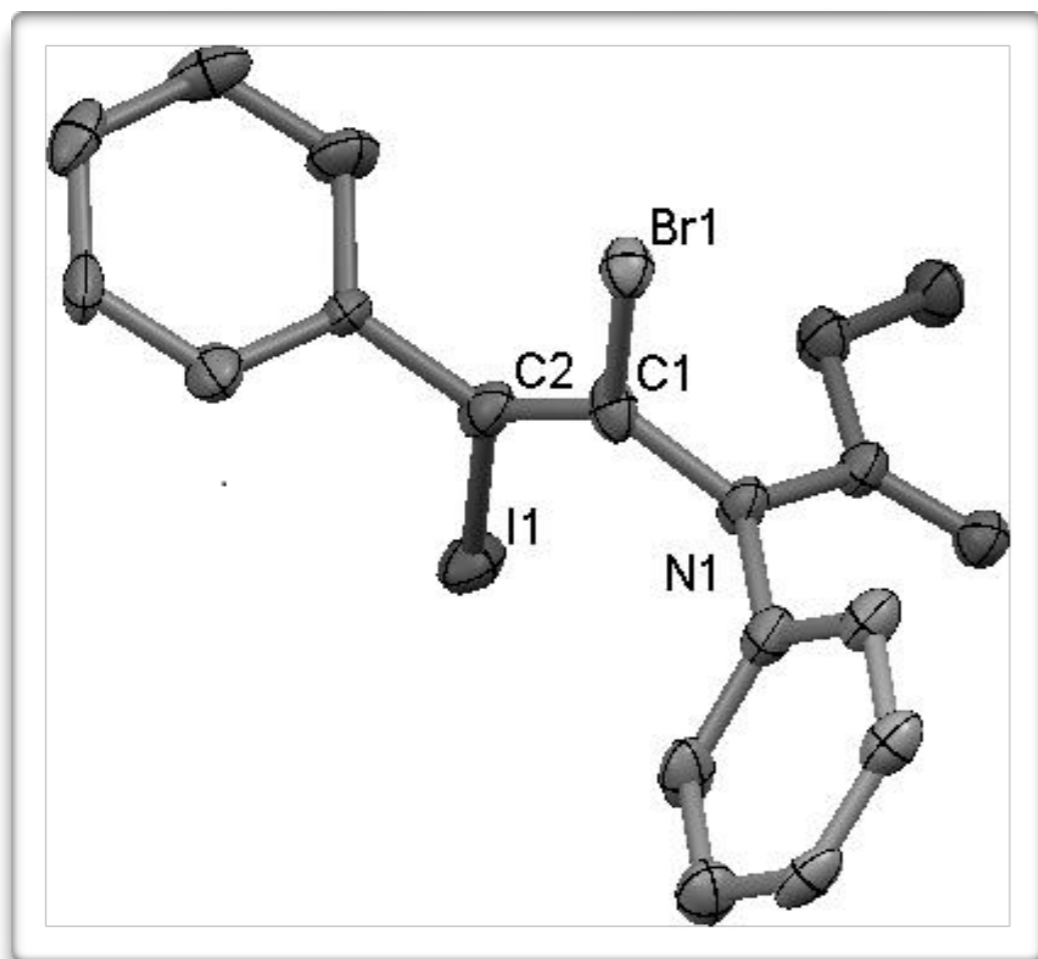
# 含窒素の鎖状分子にも有効



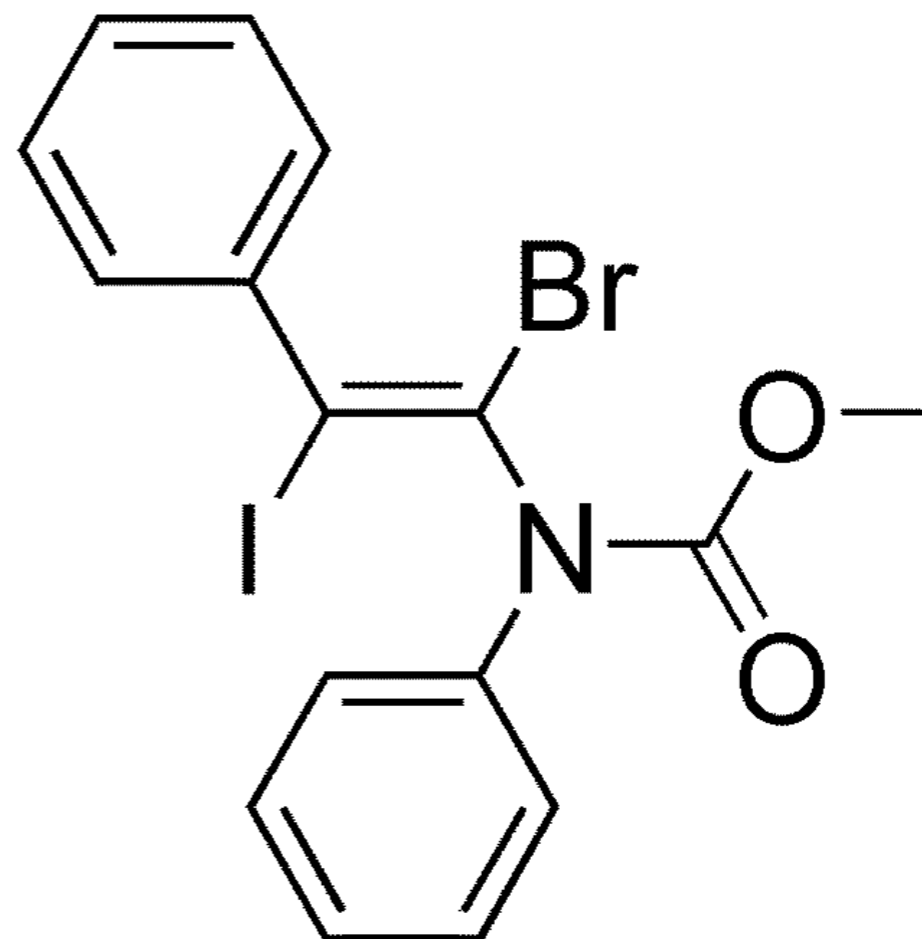
単一化合物として得られる  
異性体の混合物にはならない

1. Ide, M.; Yauchi, Y.; Iwasawa, T. *Eur. J. Org. Chem.* **2014**, 3262-3267.
2. 特願 2014-014060

# 構造決定

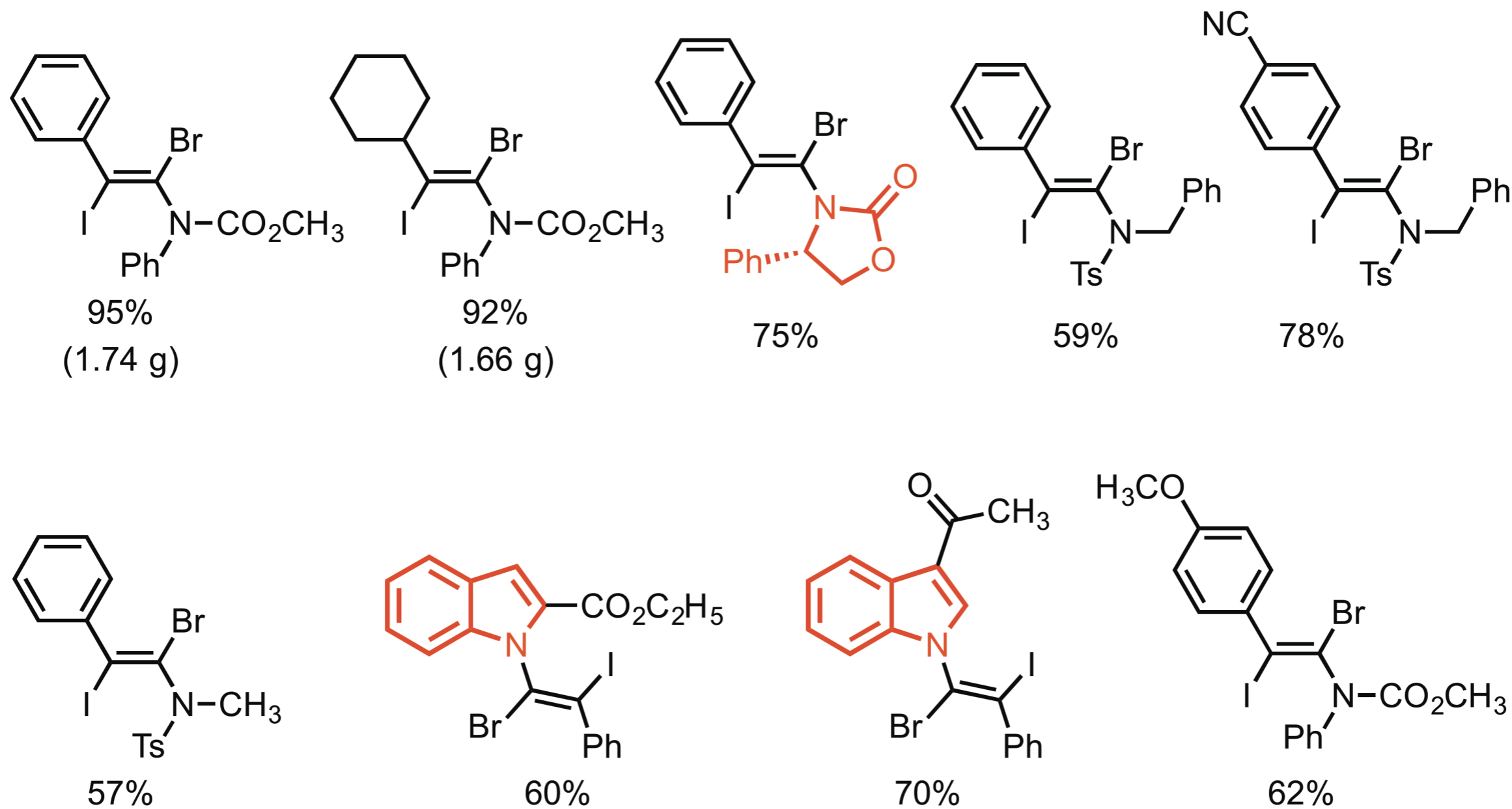


(Å): N(1)-C(1)=1.417,  
C(1)-Br(1)=1.934,  
C(2)-I(1)=2.114,  
C(1)-C(2)=1.304.

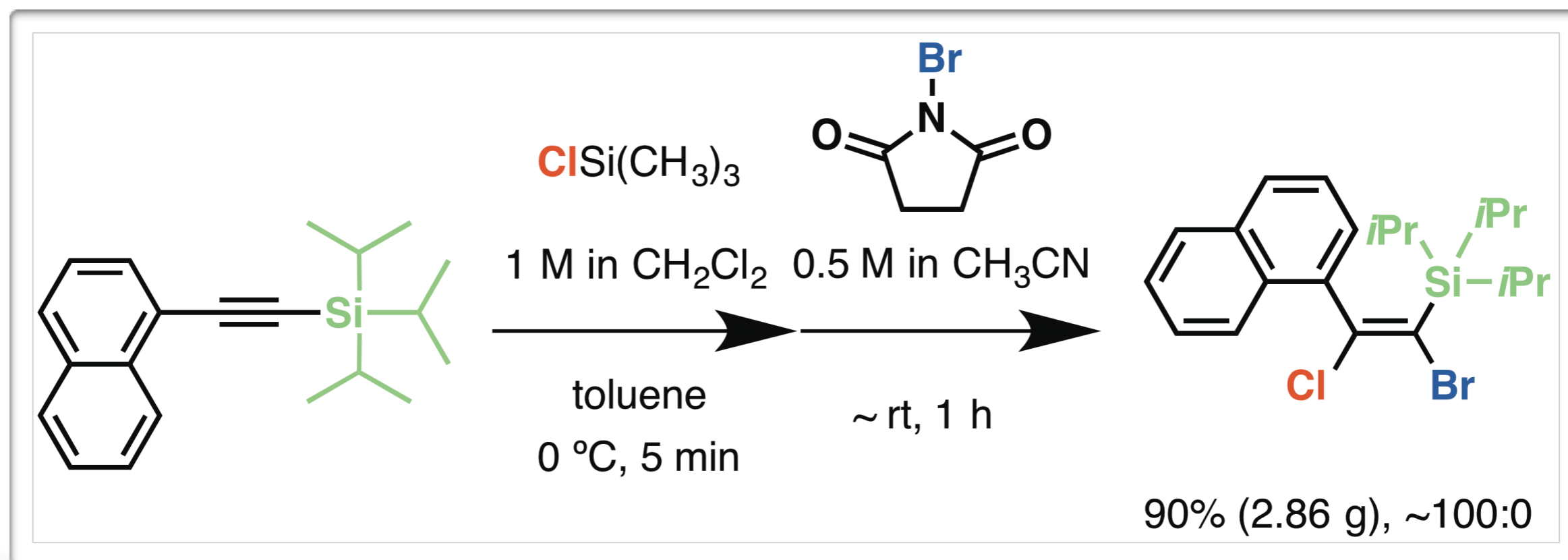


**Decomposed in 2 d  
(solution state)**

# 基質検討



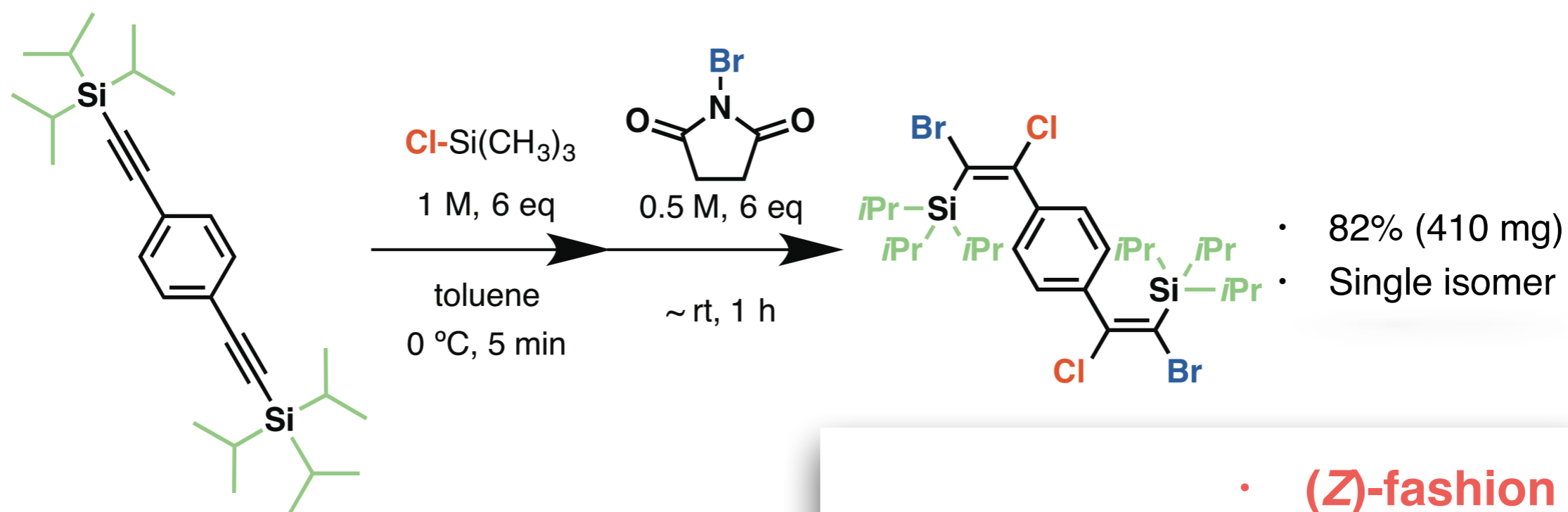
# 3つのビニル位がチューニング可



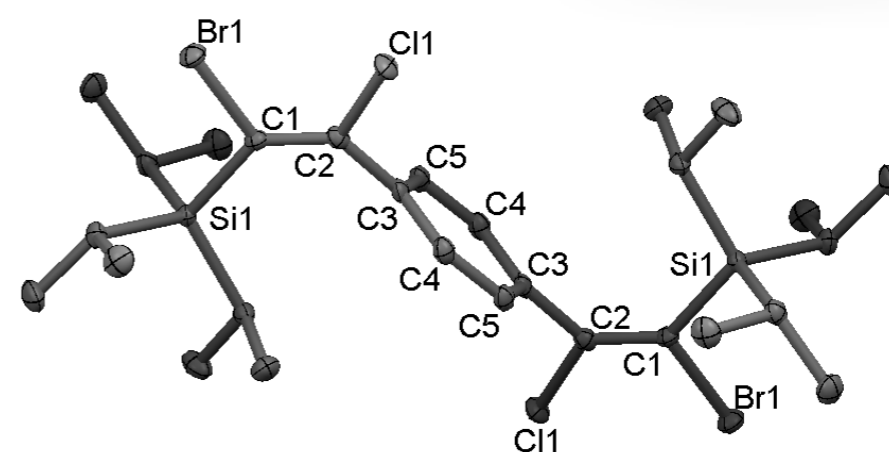
■ Ide, M.; Yauchi, Y.; Chikugo, T.; Iwasawa, T. *Eur. J. Org. Chem.* **2015**, xxxx-xxxx.

■ 特願 2014-247030 (2014年12月5日 出願)

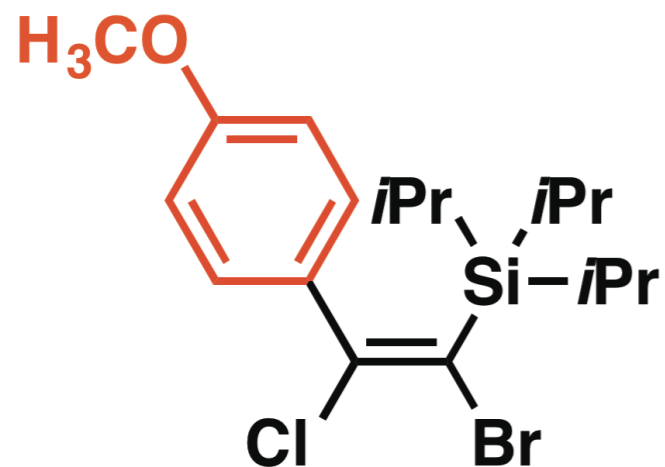
# 構造決定、シン付加！？



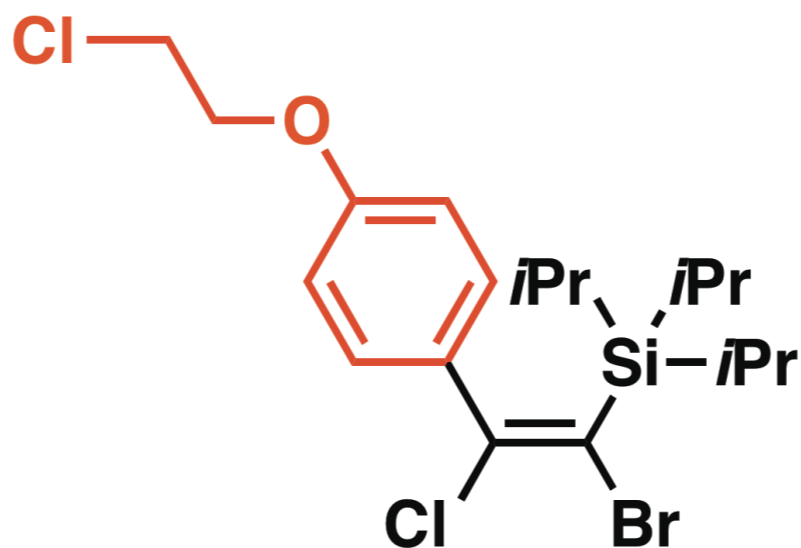
• **(Z)-fashion**



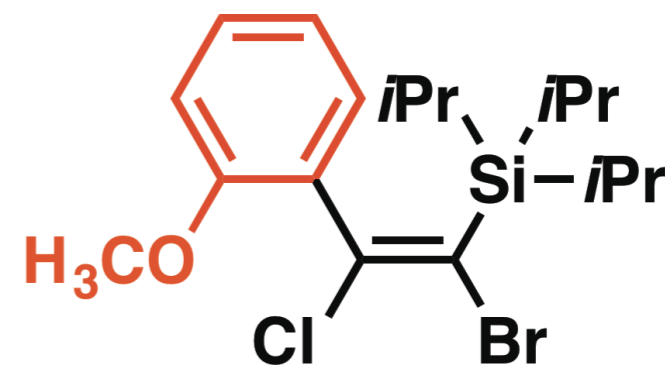
# 基質検討



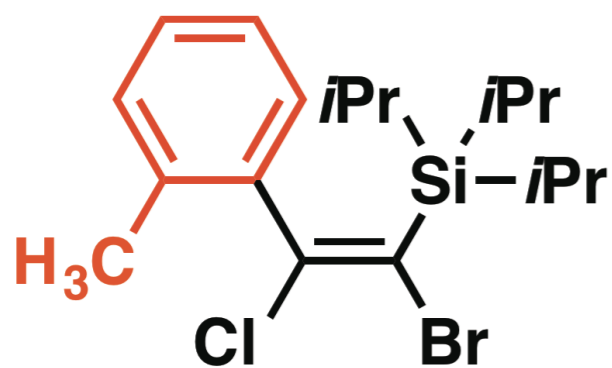
98%, 397 mg



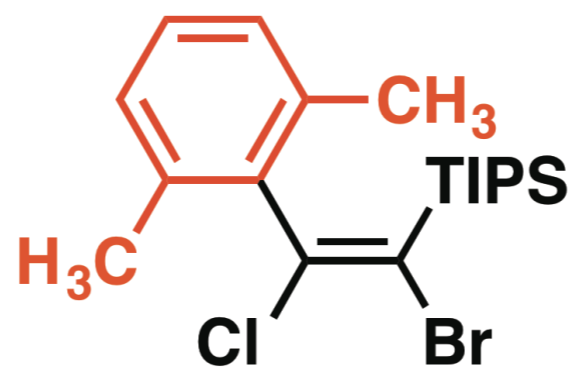
92%, 10.0 g



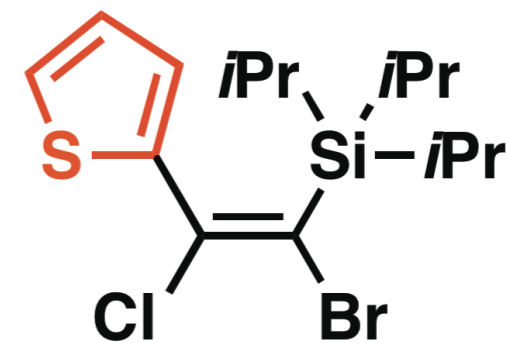
88%, 356 mg



95%, 369 mg



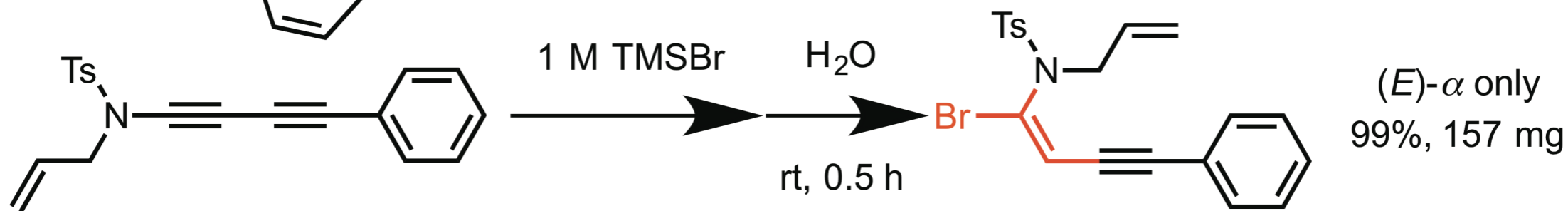
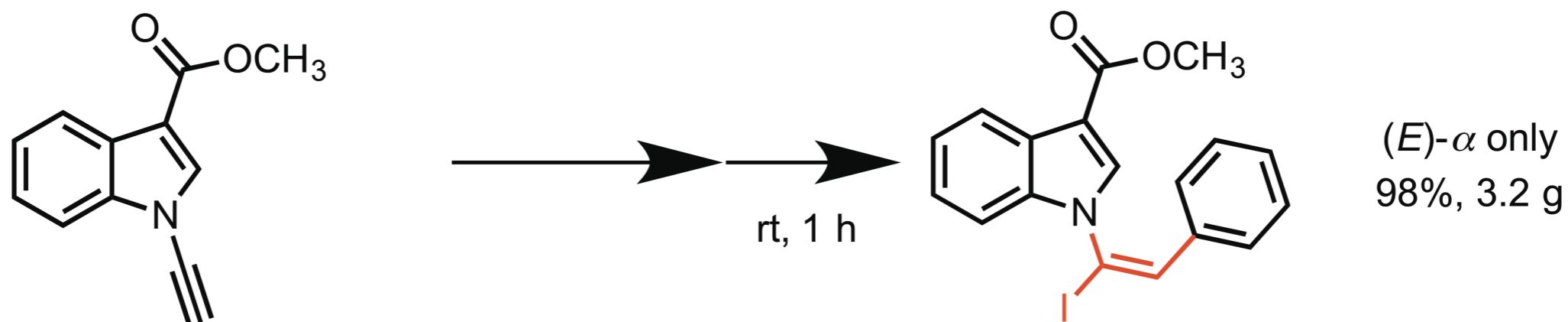
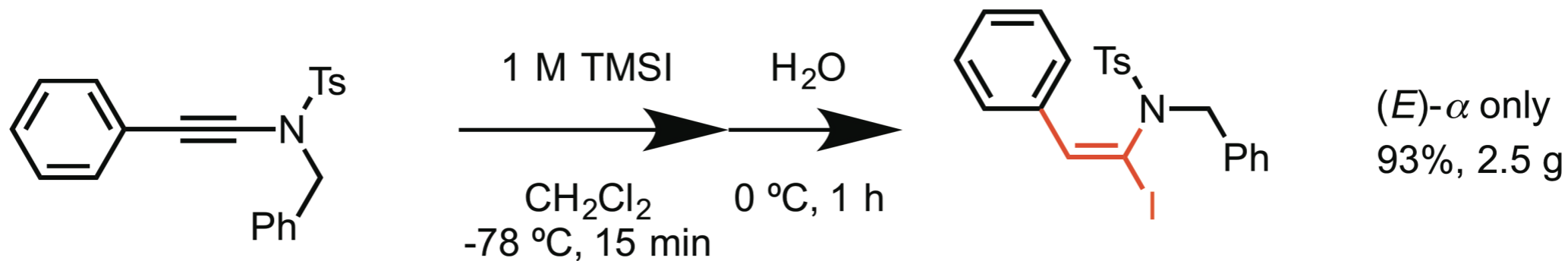
80%, 161 mg



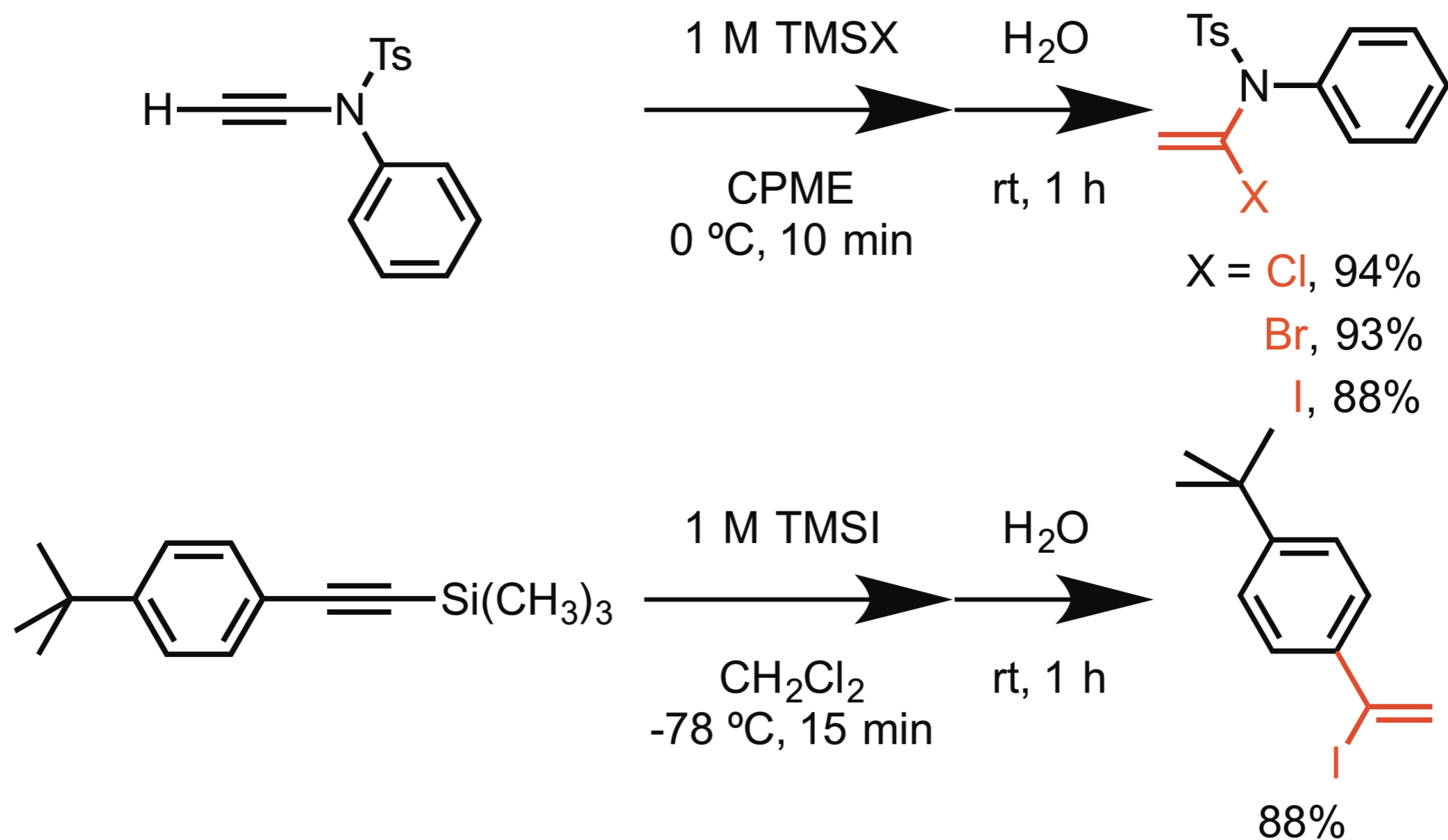
38%, 143 mg



# ヒドロハロゲン化もできる

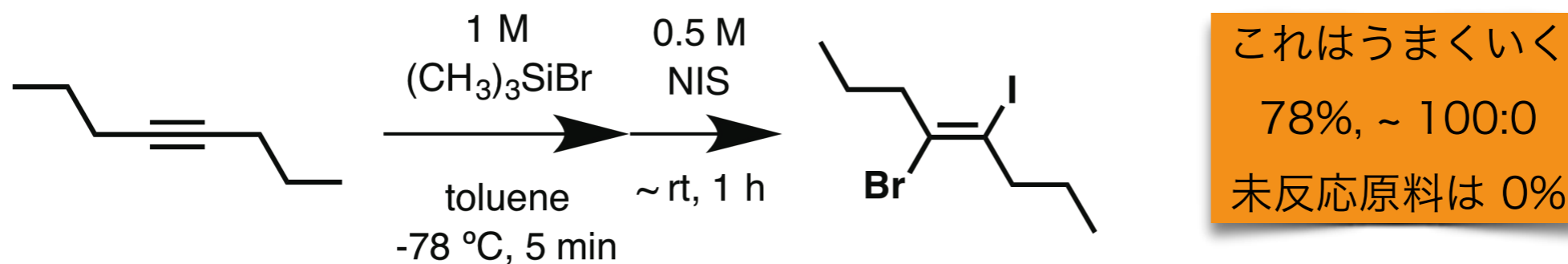


# こんなヒドロハロゲン化も

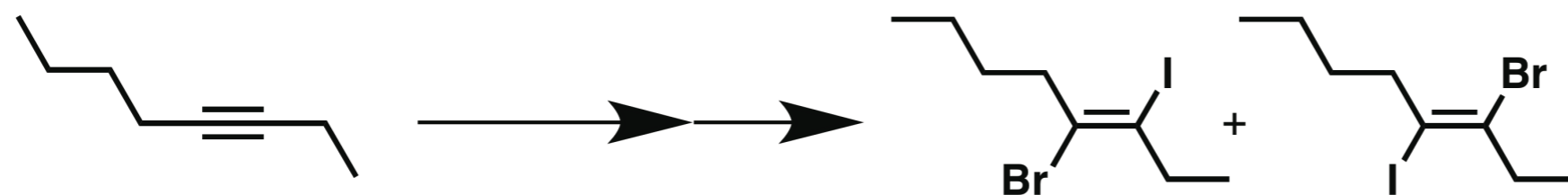


特願2013-33888; 特願2012-278613; 特願2012-170680

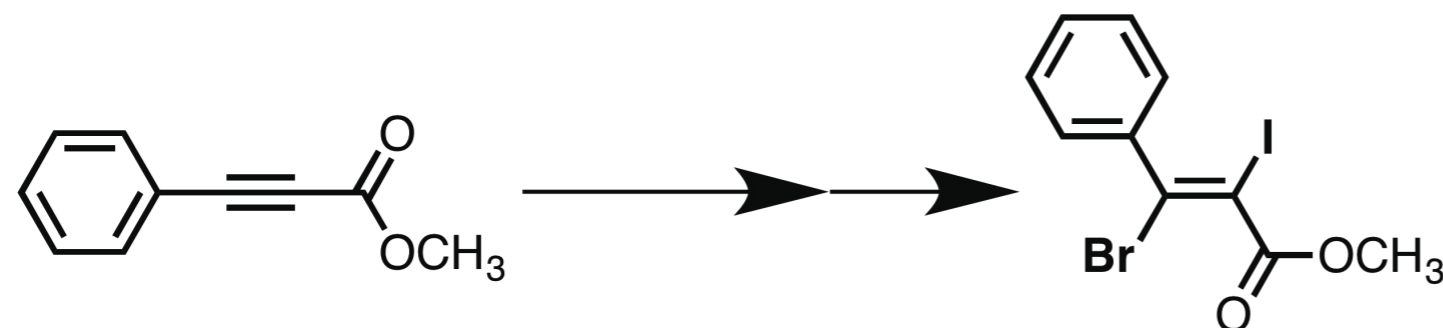
# うまくいかない基質は



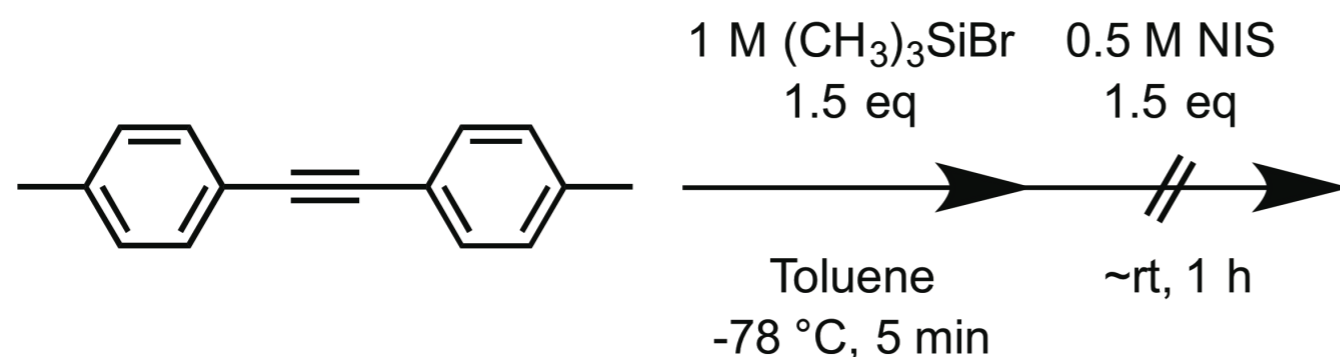
これはうまくいく  
78%, ~ 100:0  
未反応原料は 0%



75 %, 50:50, 混じりに  
未反応原料は 0%

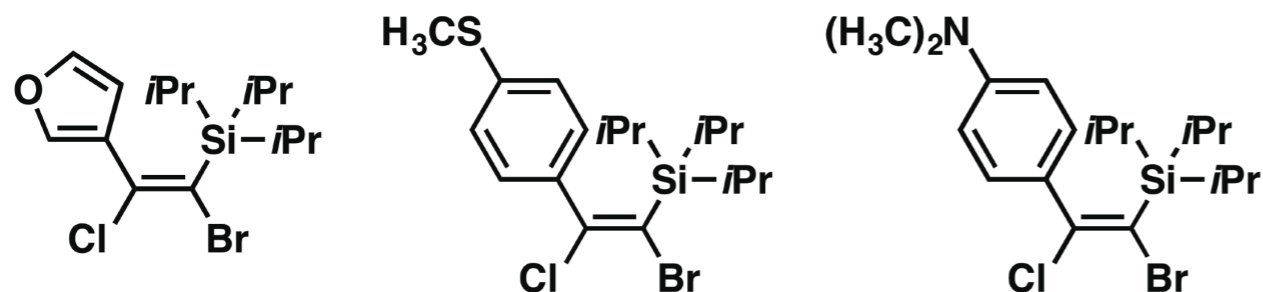


34%, ~ 91:9, 混じりに  
未反応原料が 66%も残ってしまう

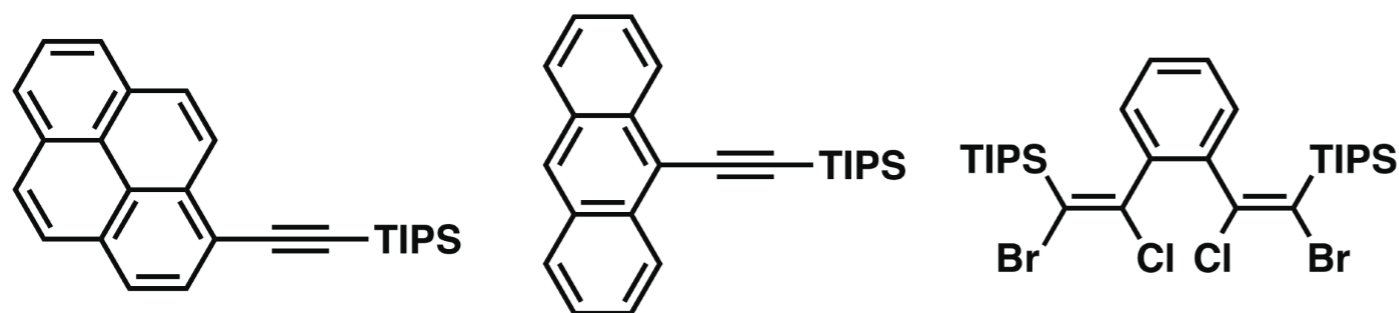


目的物は全くできない  
グチャグチャの混合物に  
未反応原料 ~ 41%

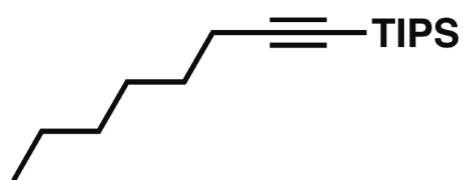
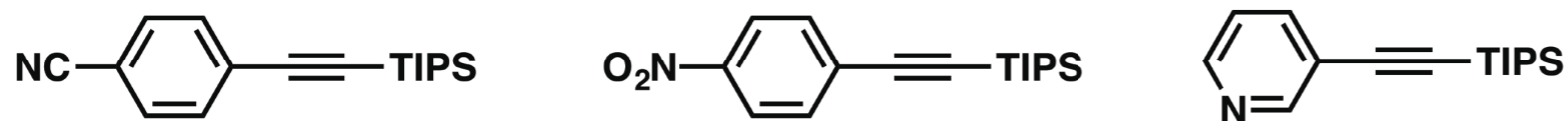
# うまくいかない基質は



would be formed,  
but too labile to isolate in pure form



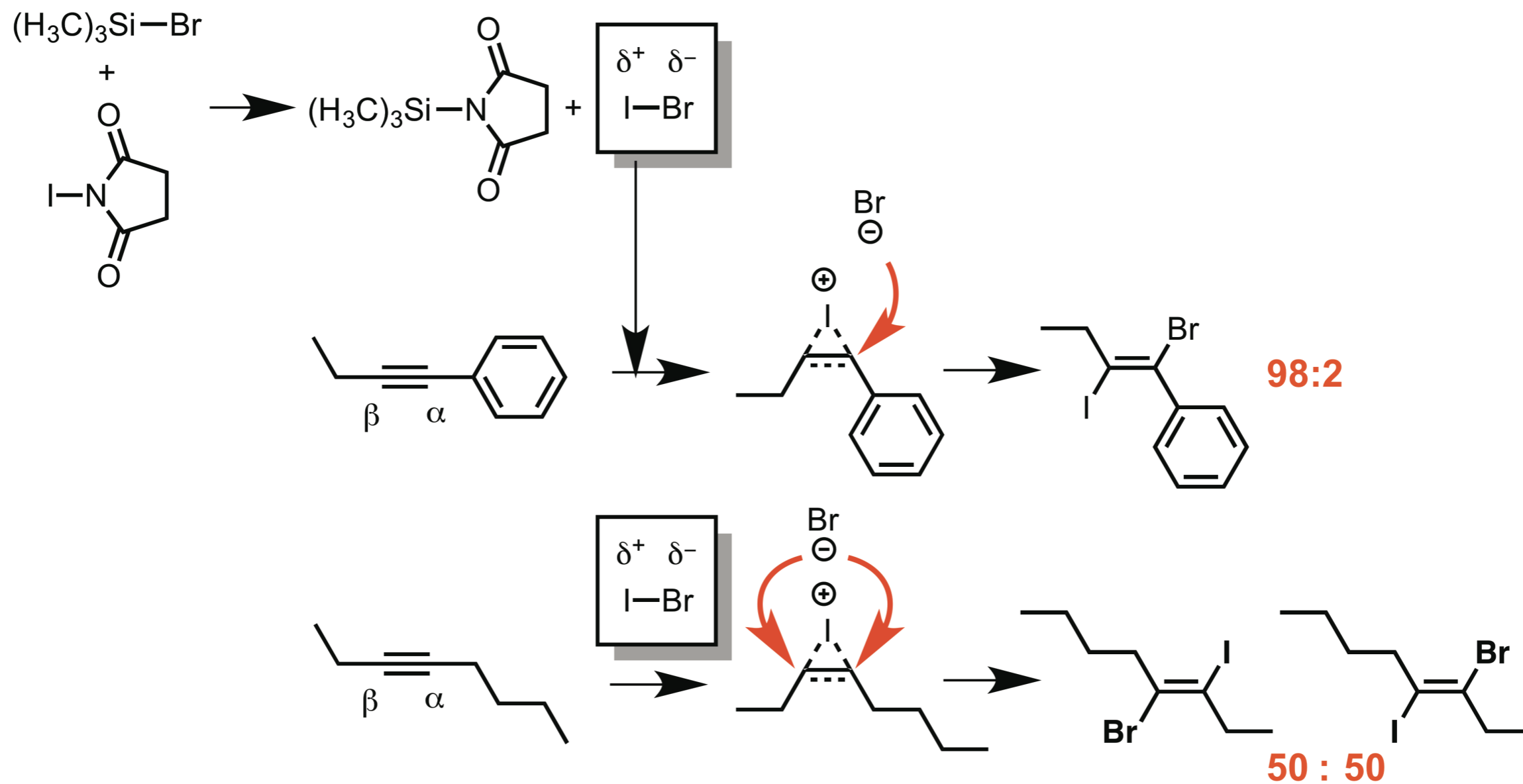
alkyne ~ 0%;  
messy NMR spectrum in the crude states



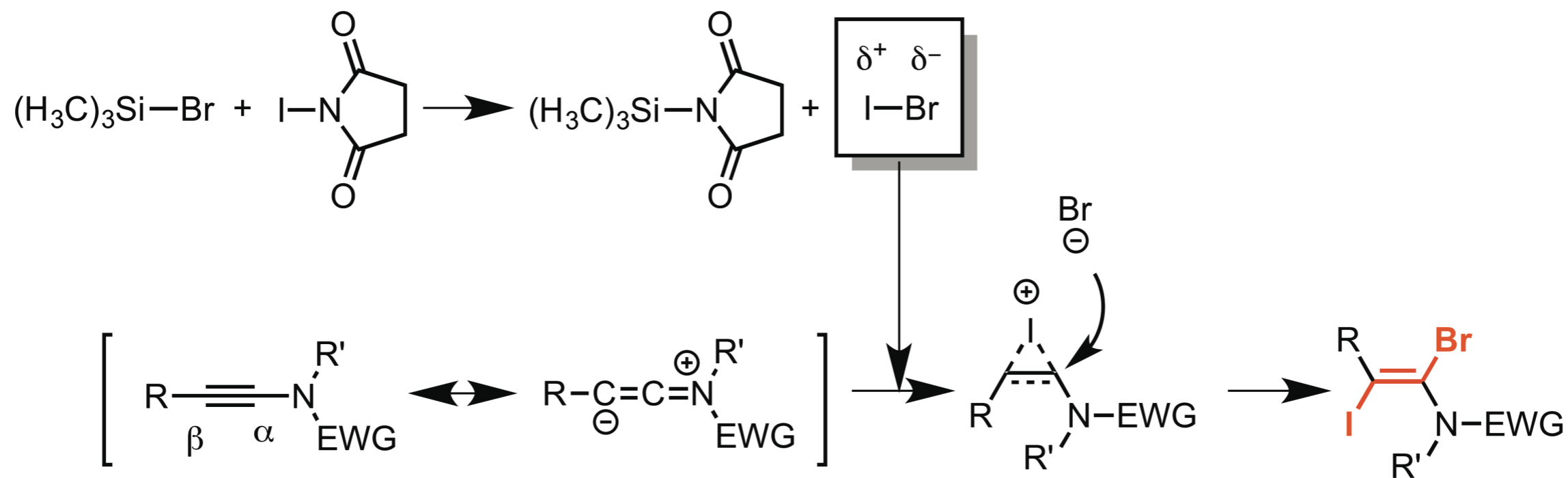
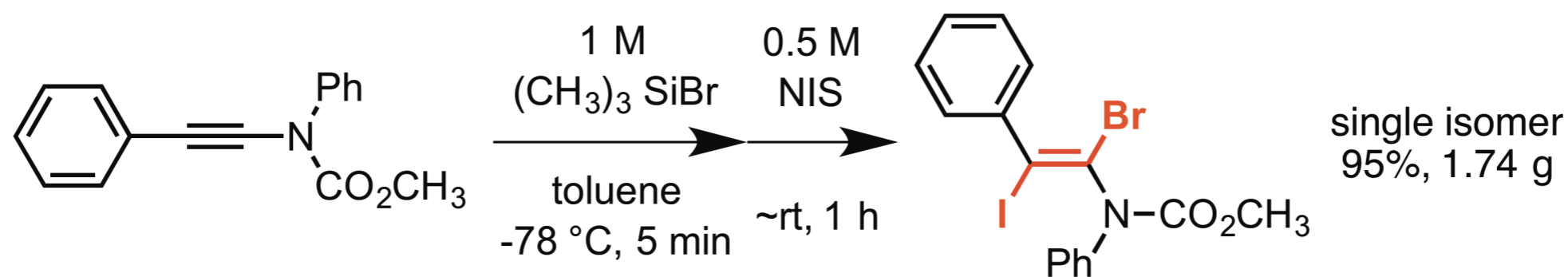
alkyne ~ 100%  
~ 1 eq of PhCH<sub>2</sub>Br was observed.

- Over-reactive: Fused-aromatics
- Less reactive: EWG-group, Alkyl groups
- **Covering the limitations by transformation of Br, Cl, & Si**

# 反応機構



# 反応機構



# 新技術の特徴・従来技術との比較

- 生成物はほとんど**単一異性体**、混じりでないので精製操作がととても簡便、グラムスケールも可
- **単純な脂肪族内部アルキン**に対して選択的にハロゲン元素をビニル位に導入できる  
(従来は高い選択性を出すためにキレート可能な元素が原料に付いている必要があった)
- **市販アルキン**や**汎用試薬TMSX**や**NXS**を使用
- 金属試薬を使う必要がない

# 本技術に関する知的財産権



- 発明の名称：
  - ①(E)-ブロモヨードアルケン誘導体及びその製造方法
  - ②(E)-1-ブロモ-2-ヨードエナミド誘導体及びその製造方法
- 出願番号：
  - ①特願2014-153644、②特願2014-014060
- 出願人：学校法人 龍谷大学
- 発明者：岩澤哲郎、井手将貴(大学院生)



# お問い合わせ先



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**Shiogai, R.**



**Ide, M.**



**Yauchi, Y.**

- 知的財産本部 弁理士 櫻井 雄三 先生
- REC コーディネータ 筒井 長徳 様

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- Ryukoku University
- MEXT-Supported Program for the Strategic Research Foundation at Private University
- Grant-in-Aid for Scientific Research (C)