SmI_2-Catalyzed Reaction by Procter's Group

Literature Seminar

2022/7/23

Takahiro Watanabe

Contents

1. Introduction

2. Intramolecular cyclization

nature catalysis
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SmI_2-catalysed cyclization cascades by radical relay

Huan-Ming Huang, Joseph J. W. McDouall and David J. Procter*

3. Intermolecular coupling

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Article

SmI_2-Catalyzed Intermolecular Coupling of Cyclopropyl Ketones and Alkynes: A Link between Ketone Conformation and Reactivity

Soumitra Agasti, Nicholas A. Beattie, Joseph J. W. McDouall, and David J. Procter*

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Samarium Iodide (SmI_2)

Sm atom: one of lanthanoids

	atomic No.	electron configuration atom	Sm^{2+}	Sm^{3+}	Sm(0)/ Sm^{2+}	Sm^{2+}/ Sm^{3+}
Sm	62	[Xe] $4f^66s^2$	[Xe] $4f^6$	[Xe] $4f^5$	–2.41 V	–1.55 V

Benefit for organic synthesis:

1. strong redox potential
2. high oxophilicity
3. large ionic radius
4. high coordination number

SmI_2: One-electron reducing agent; firstly described in organic synthesis by Kagan in 1977:

- preparation:

- Dehalogenation, deoxygenation, and reduction of conjugated olefins were reported.

Effects of additives:

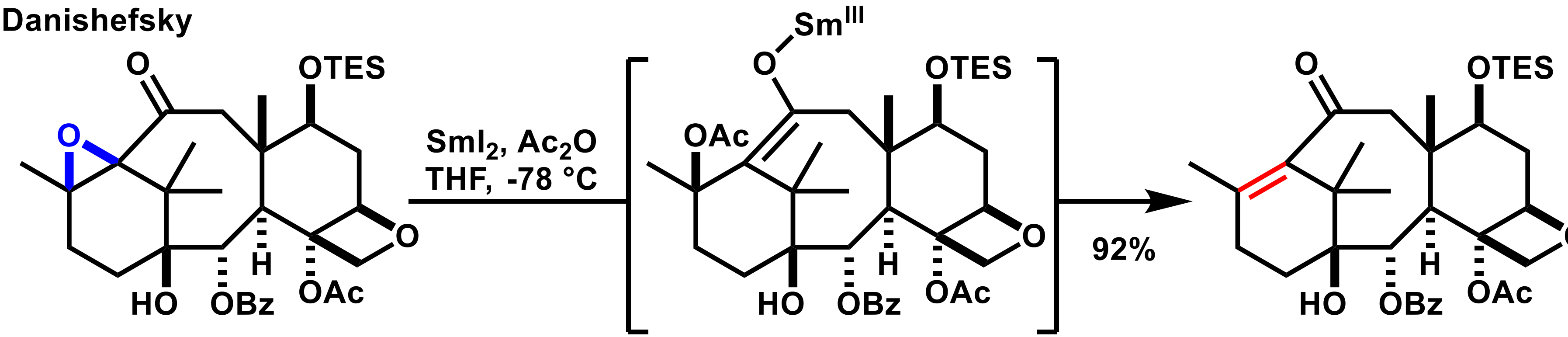
Additives change redox potential of SmI_2, and substrate scope has been expanded.

Entry	Reductant	$E_{1/2}$ [V]	Electrode	Solvent
1	SmI_2 in THF	-0.98 ± 0.04	SCE	THF
2	$SmI_2(TPPA)_{10}$	-1.45 ± 0.09	SCE	THF
3	$SmI_2(DMPU)_{30}$	-1.61 ± 0.01	SCE	THF
4	$SmI_2(HMPA)_4$	-1.75 ± 0.06	SCE	THF
5	$SmI_2(LiBr)_n$	-1.55 ± 0.07	SCE	THF
6	$SmI_2(LiCl)_n$	-1.78 ± 0.10	SCE	THF
7	$SmI_2(H_2O)_n$	-1.3 ± 0.1	SCE	THF
8	$Sm(HMDS)_2$	-1.5 ± 0.1	SCE	THF
9	SmI_2 in CH_3CN	-0.84 ± 0.05	SCE	CH_3CN
10	$SmI_2(DMPU)_{10}$ in CH_3CN	-1.48 ± 0.06	SCE	CH_3CN

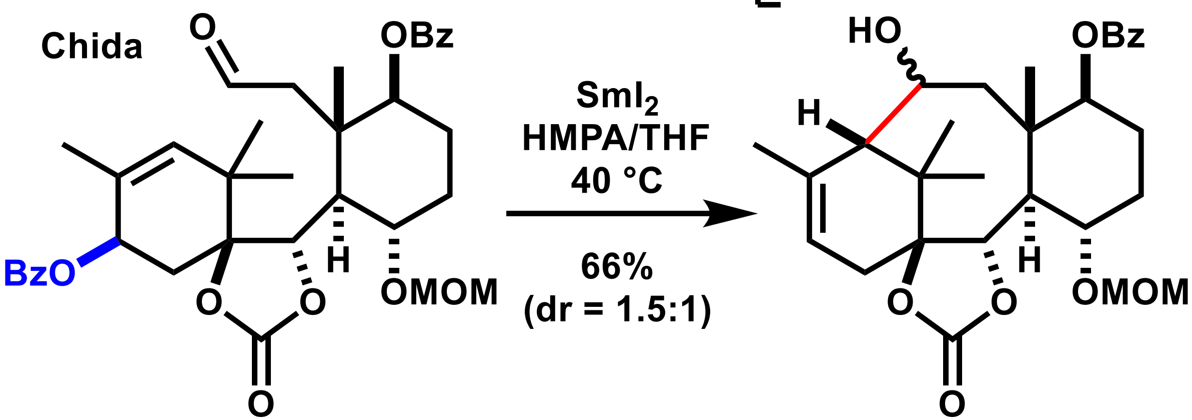
1) ランタノイドを利用する有機合成；日本化学会；季刊化学総説，1998, No 37. 2) (a) Namy, J. L.; Girard, P.; Kagan, H. B. *Nouv. J. Chim.* **1977**, *1*, 5. (b) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. 3) Szostak, M.; Spain, M.; Procter, D. J. *Chem. Soc. Rev.* **2013**, *42*, 9155.

Application of SmI_2 in Total Syntheses of taxol

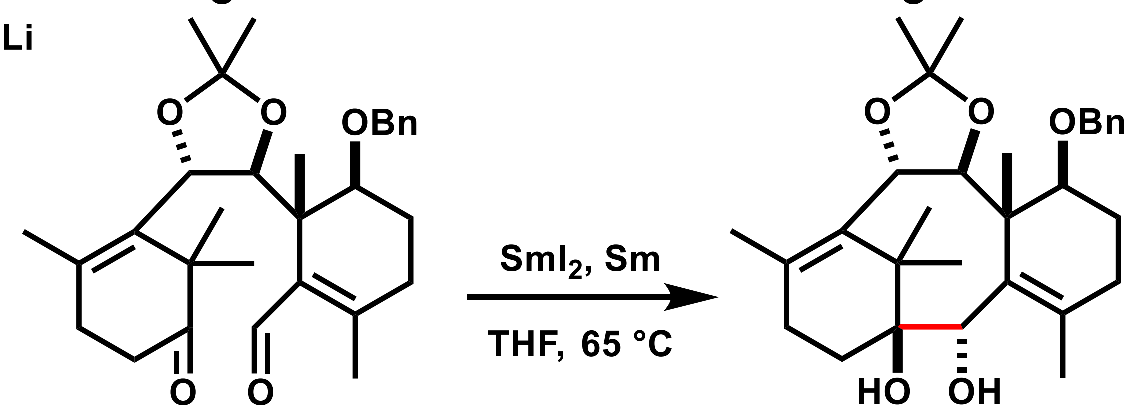
Danishefsky



Chida



Li



Other groups:

Holton
(elimination of α-OH group of ketone)
Mukaiyama
(intramolecular pinacol coupling)
Kuwajima
(cleavage of cyclopropane ring)

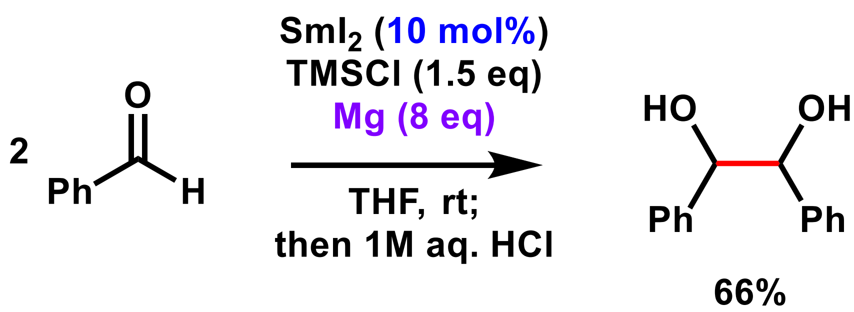
-> SmI_2 is so versatile that it has been used by many chemists.

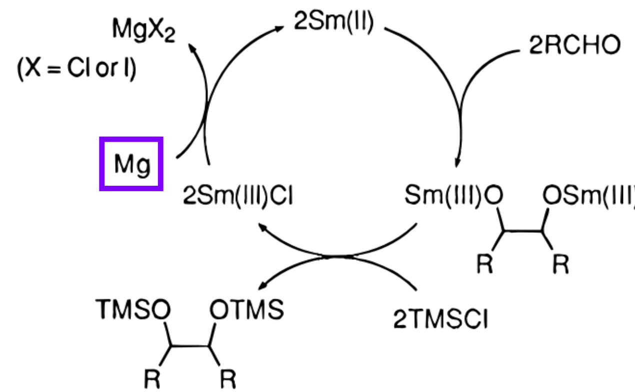
1) Danishefsky et al. *J. Am. Chem. Soc*. **1996**, *118*, 2843. 2) Chida et al. *Org. Lett.* **2015**, *17*, 2570.
3) Li et al. *J. Am. Chem. Soc*. **2021**, *143*, 17862.

Reaction with Catalytic Amount of SmI_2

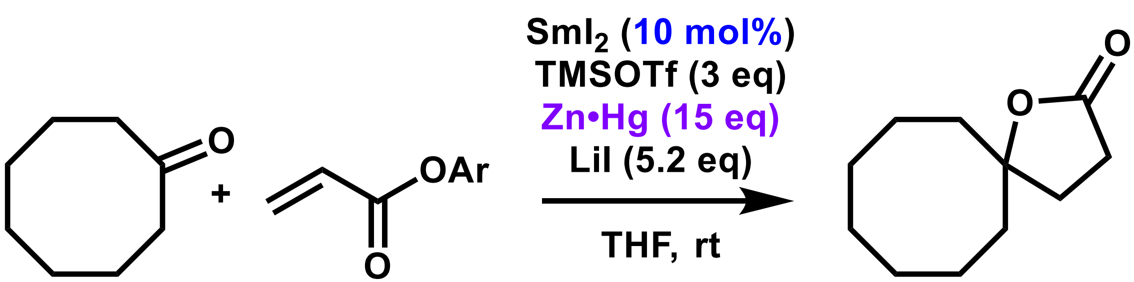
- Of the few reports of the use of catalytic SmI_2, all reactions of C-C bond formation require the use of superstoichiometric amounts of a metal coreductant to regenerate Sm(II).

- pinacol coupling [1)]





- intermolecular radical coupling [2)]



(Ar = 2,4,6-trimethylphenyl)

1) Nomura, R.; Matsuno, T.; Endo, T. *J. Am. Chem. Soc.* **1996**, *118*, 11666.
2) Corey, E. J.; Zheng, G. Z. *Tetrahedron Lett.* **1997**, *38*, 2045.

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Prof. David J. Procter

1995: PhD with Prof. Christopher Rayner @ the Univ. of Leeds

1995-1997: postdoc with Prof. Robert Holton @ Florida State Univ. in Tallahassee

1997-2004: Lecturer @ the Univ. of Glasgow in Scotland

2004: Senior lecturer @ the Univ. of Glasgow in Scotland

2004-2008: Reader @ the Univ. of Manchester

2008-: Professor @ the Univ. of Manchester

Research interest:

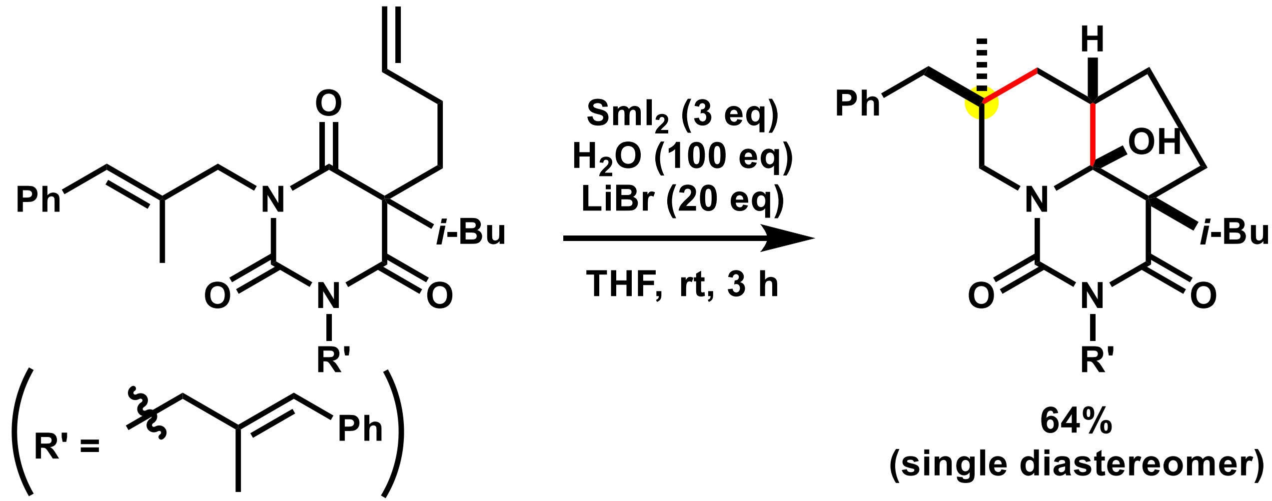
1. SmI_2-mediated radical cascades

2. Sulfonium-mediated C-H functionalization

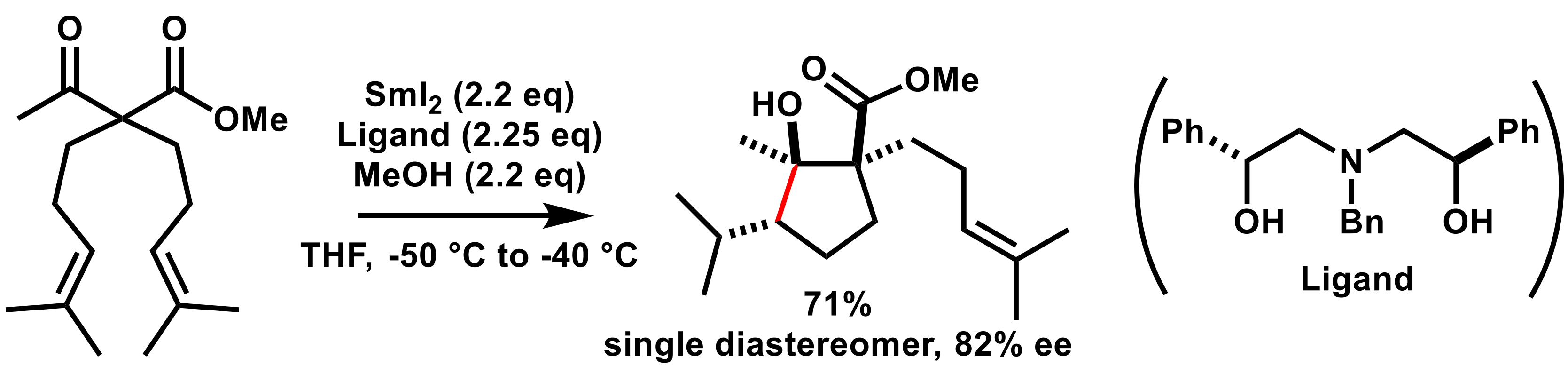
3. Asymmetric copper-catalyzed multicomponent reactions

Recent His Study about Application of SmI_2

Cyclization cascades with SmI_2-H_2O-LiBr system (*J. Am. Chem. Soc*. 2016, *138*, 7770; *Angew. Chem. Int. Ed*. 2018, *57*, 4995.):



Enantioselective cyclization cascades (*Nature Chem*. 2017, *9*, 1198.):



Radical Relay Cascade

Radical relay: a redox-neutral process in which radical character is regenerated and thus only a catalytic amount of radical-generating reagent is required

Key three steps:

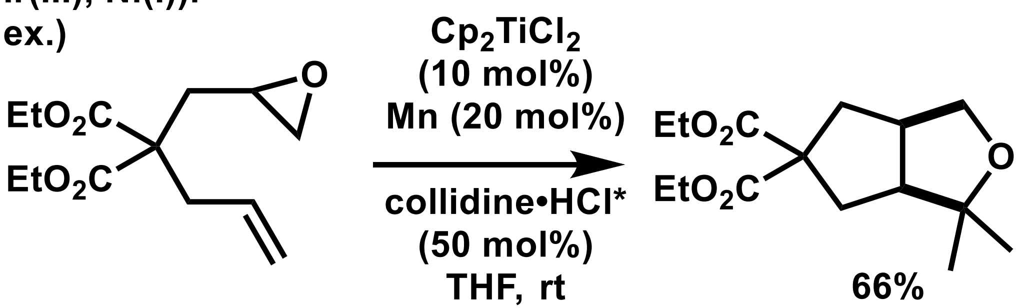
(1) **radical formation**: Radical character is generated by single-electron transfer (SET) or addition of a radical.

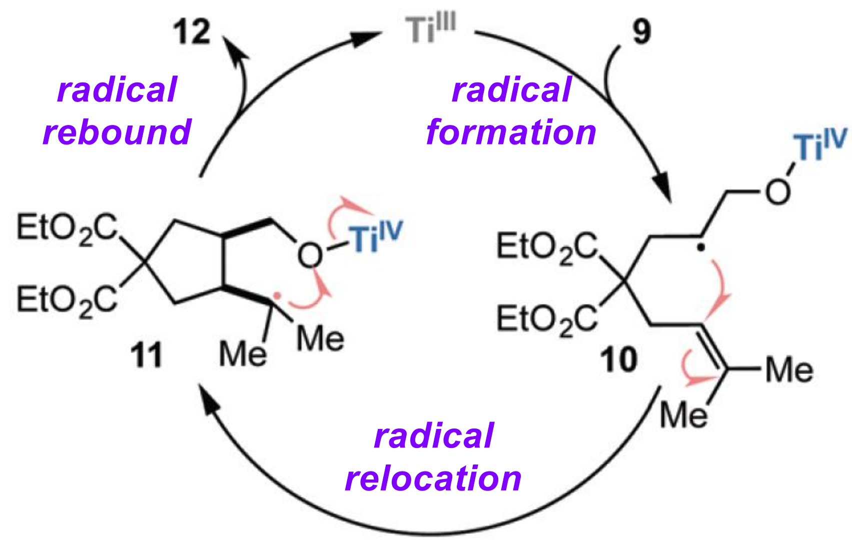
(2) **radical relocation**: Radical character is propagated during a bond-forming/breaking sequence;

(3) **radical rebound**: Radical character is recycled, typically by SET back to a metal catalyst or the expulsion of a radical that acts as a catalyst

To date, various metal catalysts have been used (e.g., Ti(III), Cu(I), Ru(II), Mn(III), Co(II), Rh(II), Fe(II), Ir(III), Ni(I)).

ex.)



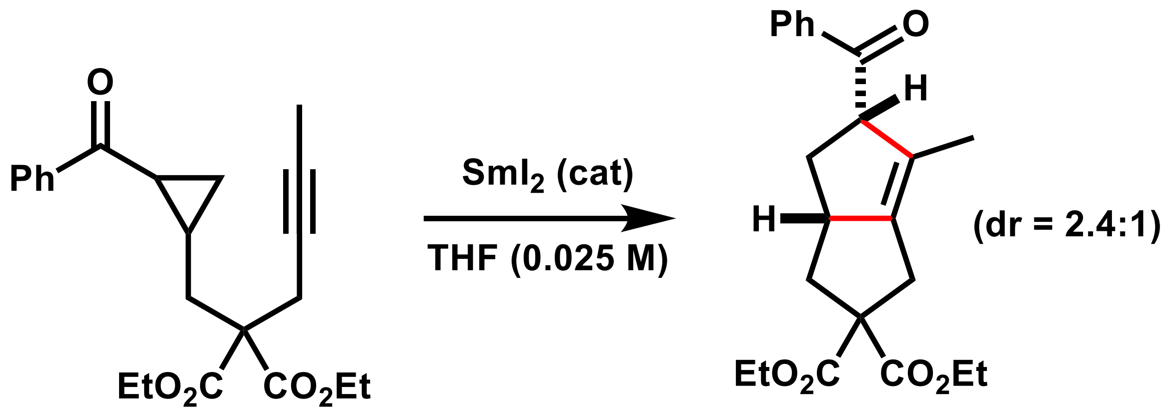


*Collidine•HCl is shown to be unnecessary in other entries.

-> **Can the radical relay be realized with SmI_2 ?**

(a) Huang, H-M.; Garduño-Castro, M. H.; Morrill, C.; Procter, D. J. *Chem. Soc. Rev.,* **2019**, *48*, 4626.
Gansäuer, A.; Rinker, B.; Pierobon, M.; Grimme, S.; Gerenkamp, M.; Mück-Lichtenfeld, C. *Angew. Chem.Int. Ed.*, **2003**, *42*, 3687.

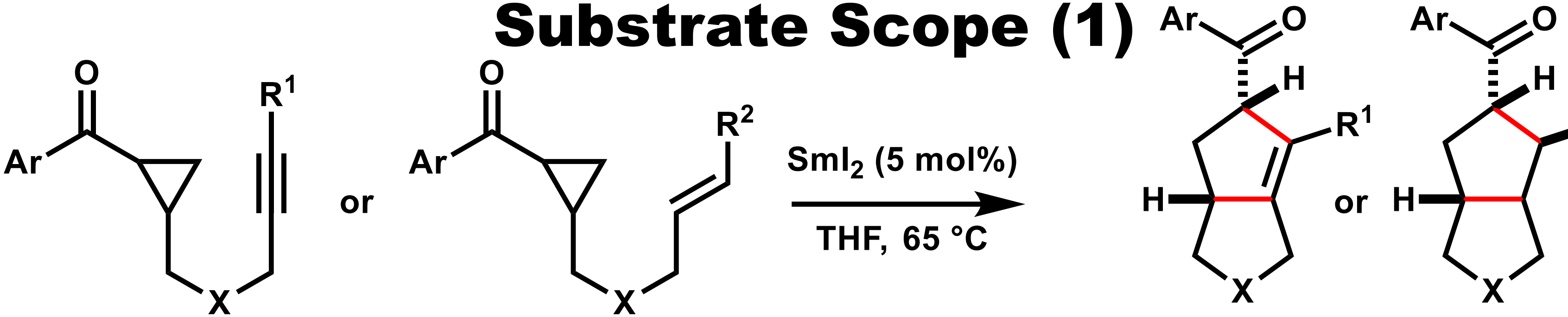
Optimization of Conditions

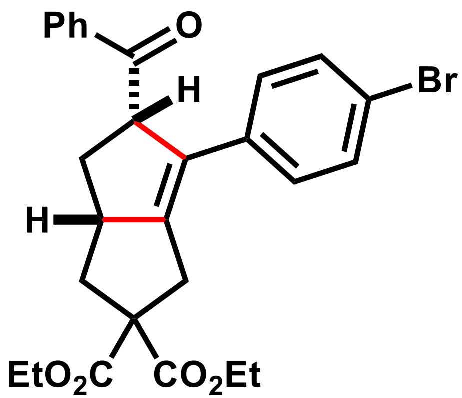


entry	temp. (°C)	SmI_2 loading	yield	recovery
1	rt	300%	76%	-
2	rt	30%	70%	-
3	rt	10%	56%	31%
4	50 °C	10%	79%	9%
5	65 °C	10%	89%	-
6	65 °C	5%	88%	-

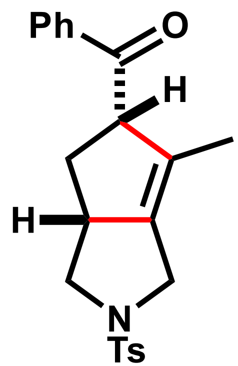
Huang, H. M.; McDouall, J. J. W.; Procter, D. J. *Nat. Chem.* **2019**, *2*, 211.

Substrate Scope (1)

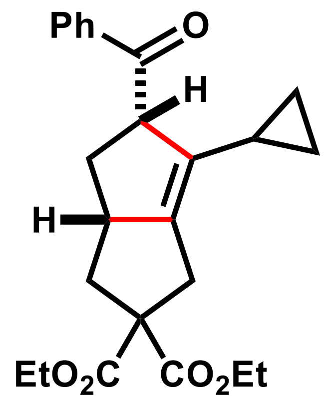




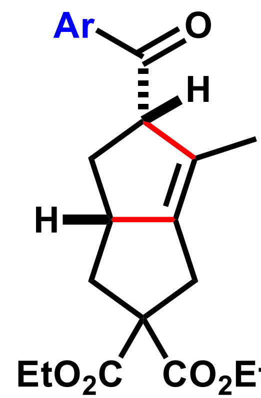
88%, dr = 1:0.34



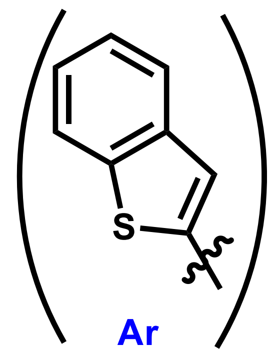
84%, dr = 1:0.37

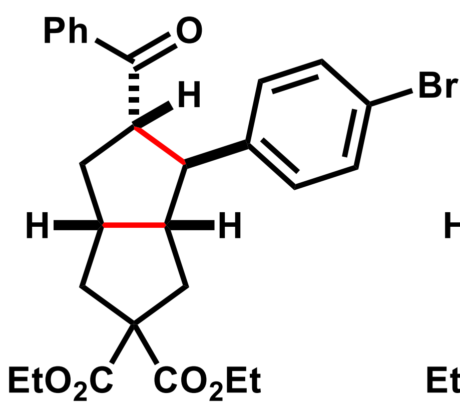


94%, dr = 1:0.42

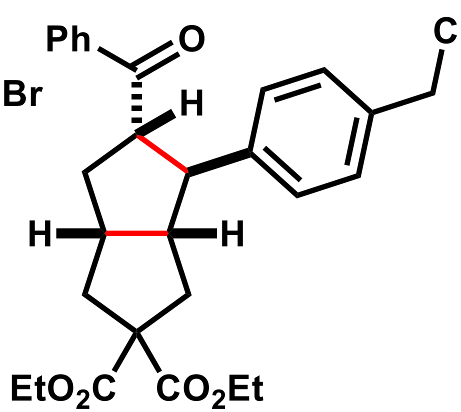


53%, dr = 1:0.53

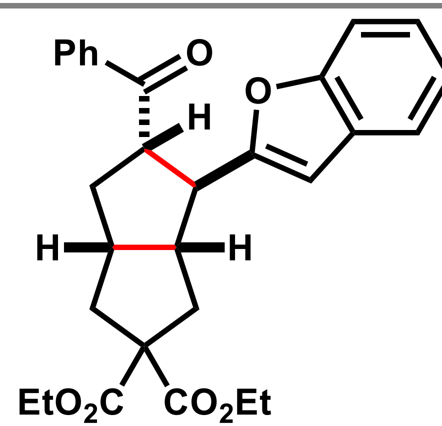




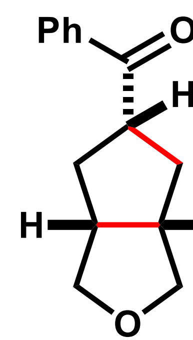
84%, dr = 1:0.18



73%, dr = 1:0.20
(with 10 mol% of SmI_2)

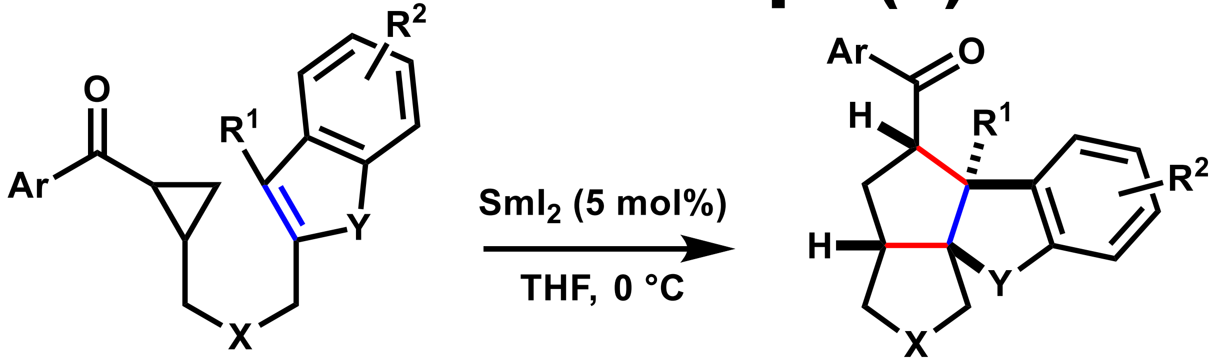


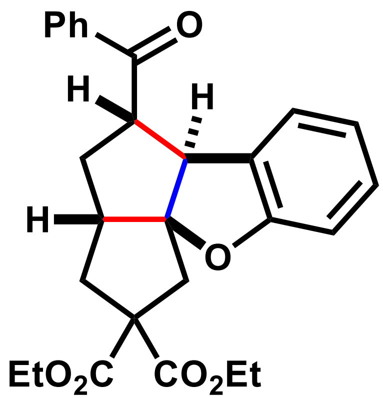
73%, dr = 1:0.18
(with 15 mol% of SmI_2)



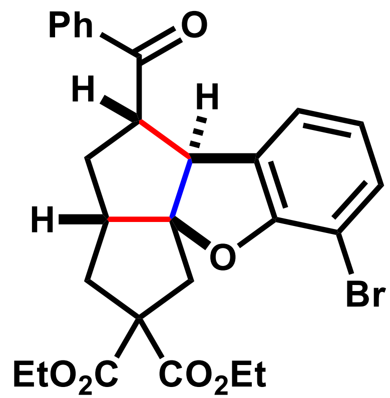
76%, dr = 1:0.60
(with 10 mol% of SmI_2)

Substrate Scope (2)

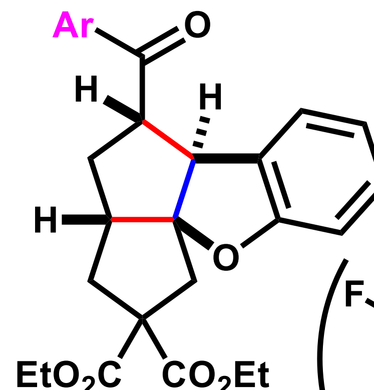




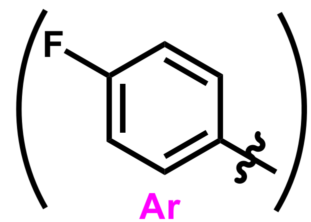
99%, dr = 1:0.07

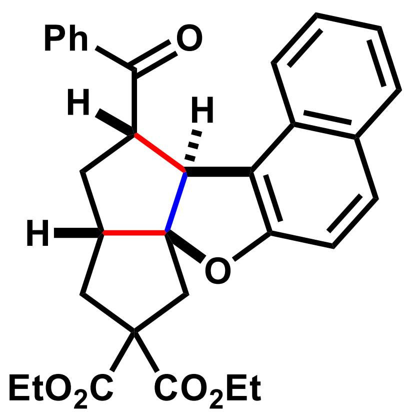


71%, dr = 1:0.16

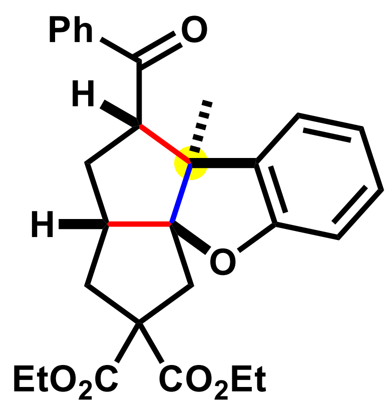


68%, dr = 1:0.16

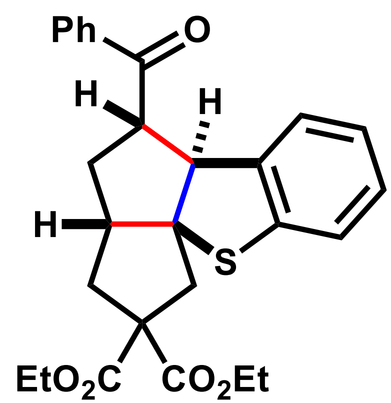




79%, dr = 1:0.20

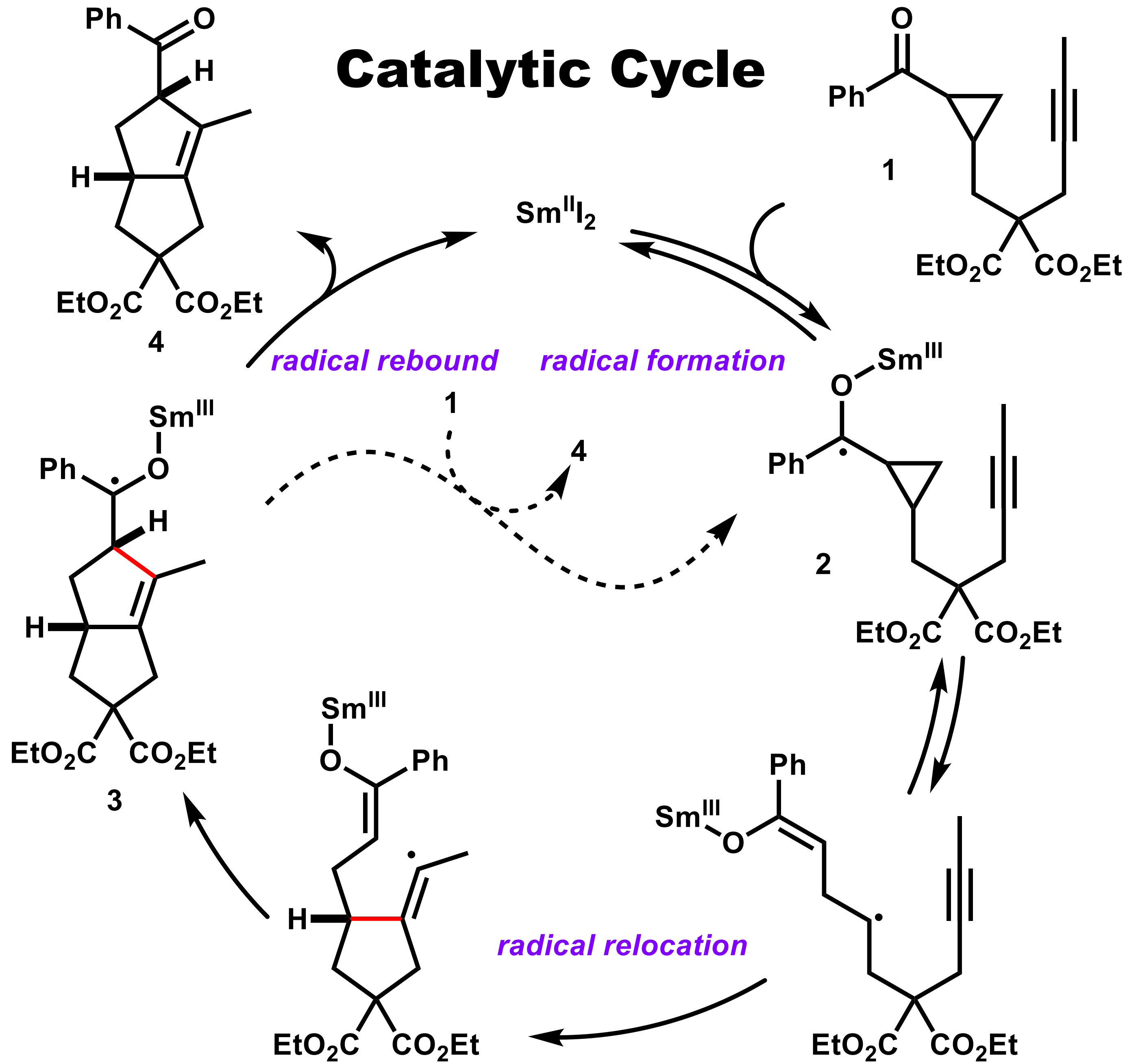


70%, single diastereomer



90%, dr = 1:0.23

Catalytic Cycle



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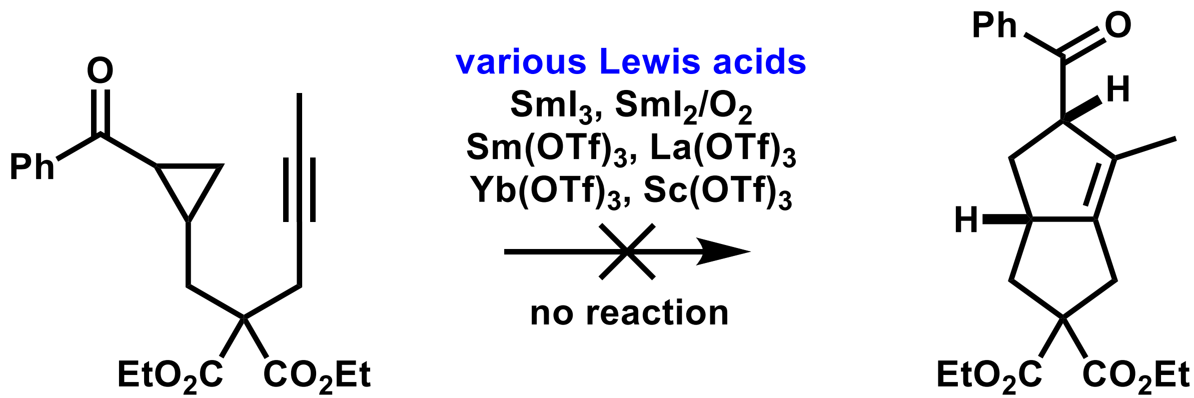
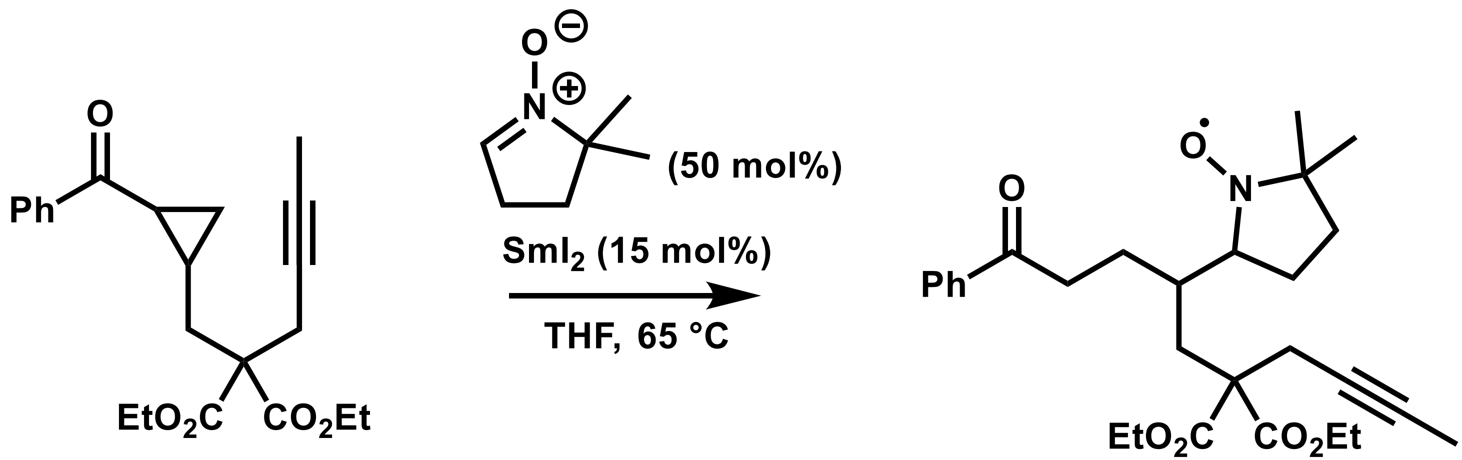
Mechanistic Studies (1)

- **Confirmation of radical mechanisms:**





observed with ESR and HRMS

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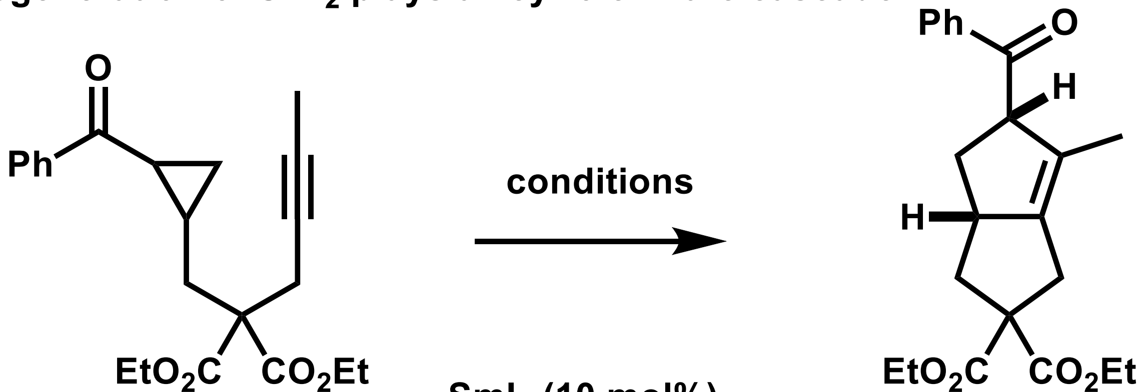
Mechanistic Studies (2)

- **Regeneration of SmI_2 plays a key role in the cascade:**

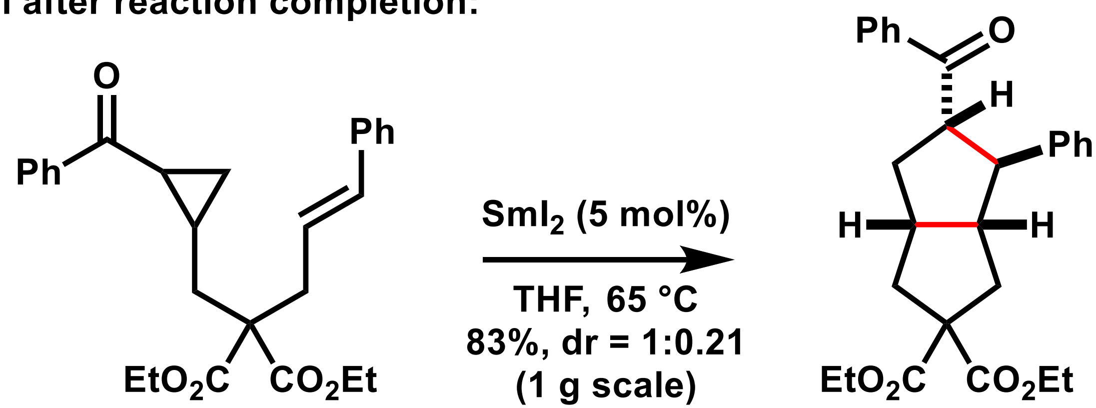


Conditions	
SmI_2 (10 mol%) TMSCl (200 mol%) THF, 65 °C	10%, 68%, rcv.
Cp*$TiCl_3$ (10 mol%) Zn (20 mol%) THF, 65 °C	18%

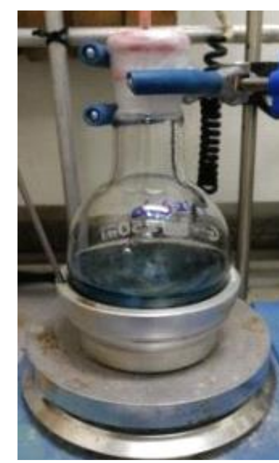
The catalytic cycle is prevented by trapping samarium enolates with TMSCl.

Chain-type process (shown in dashed curves in page 13) will be unlikely.

- **Observation of blue color of reaction mixture still after reaction completion:**



2 min
(reaction complete)



15 min

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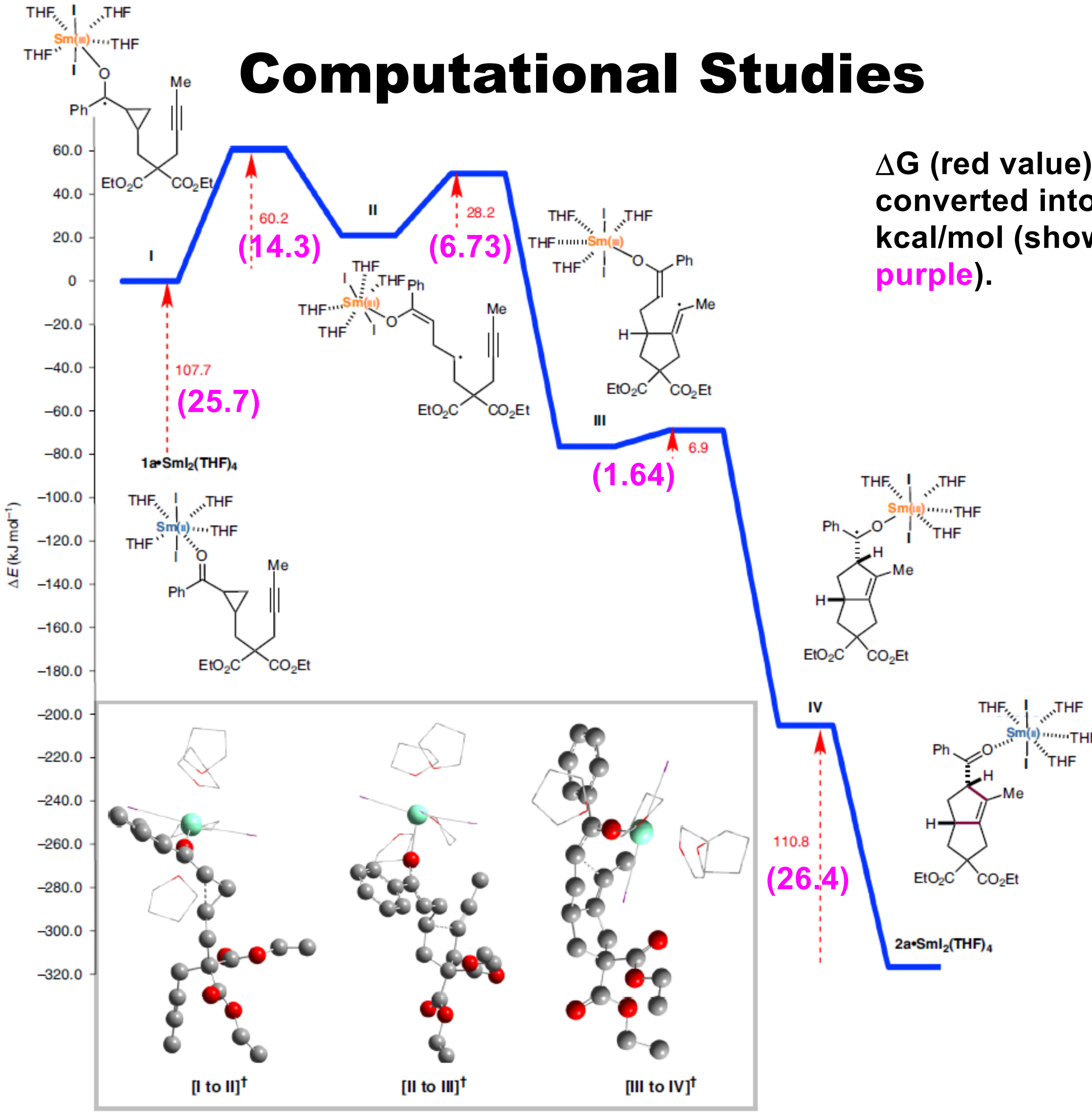
Computational Studies



ΔG (red value) is converted into kcal/mol (shown in purple).

Fig. 6 | Computational studies. Computed density functional theory free-energy profile for the SmI_2-catalysed cyclization cascades (PBE/Def2-SVP level).

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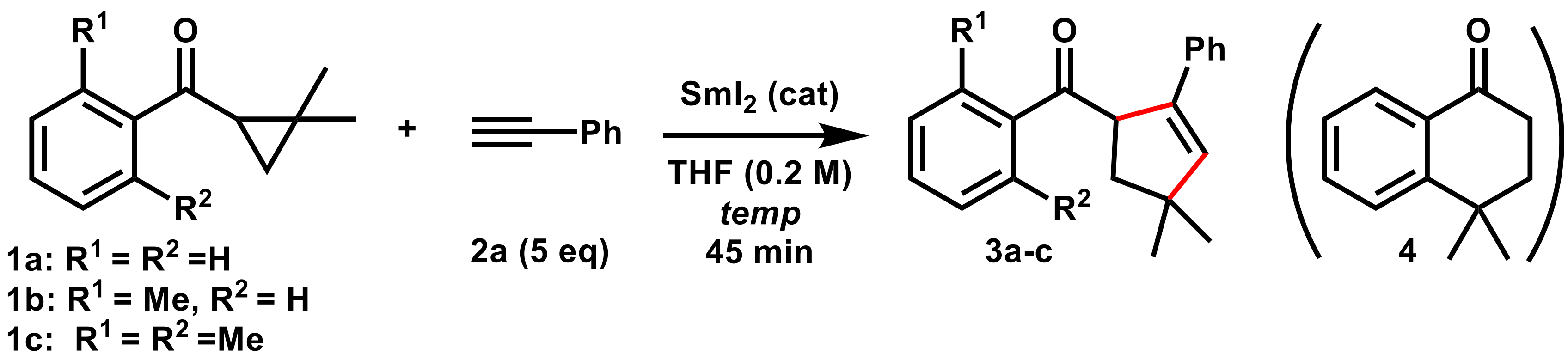
Screening of Catalytic Conditions

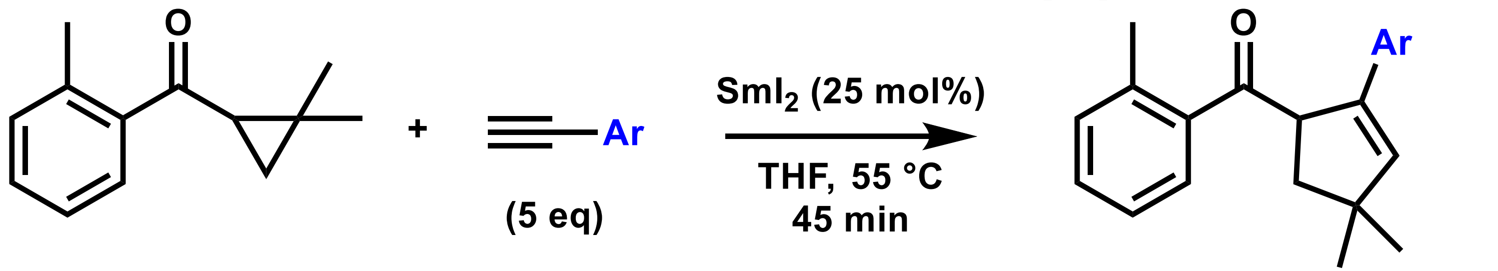


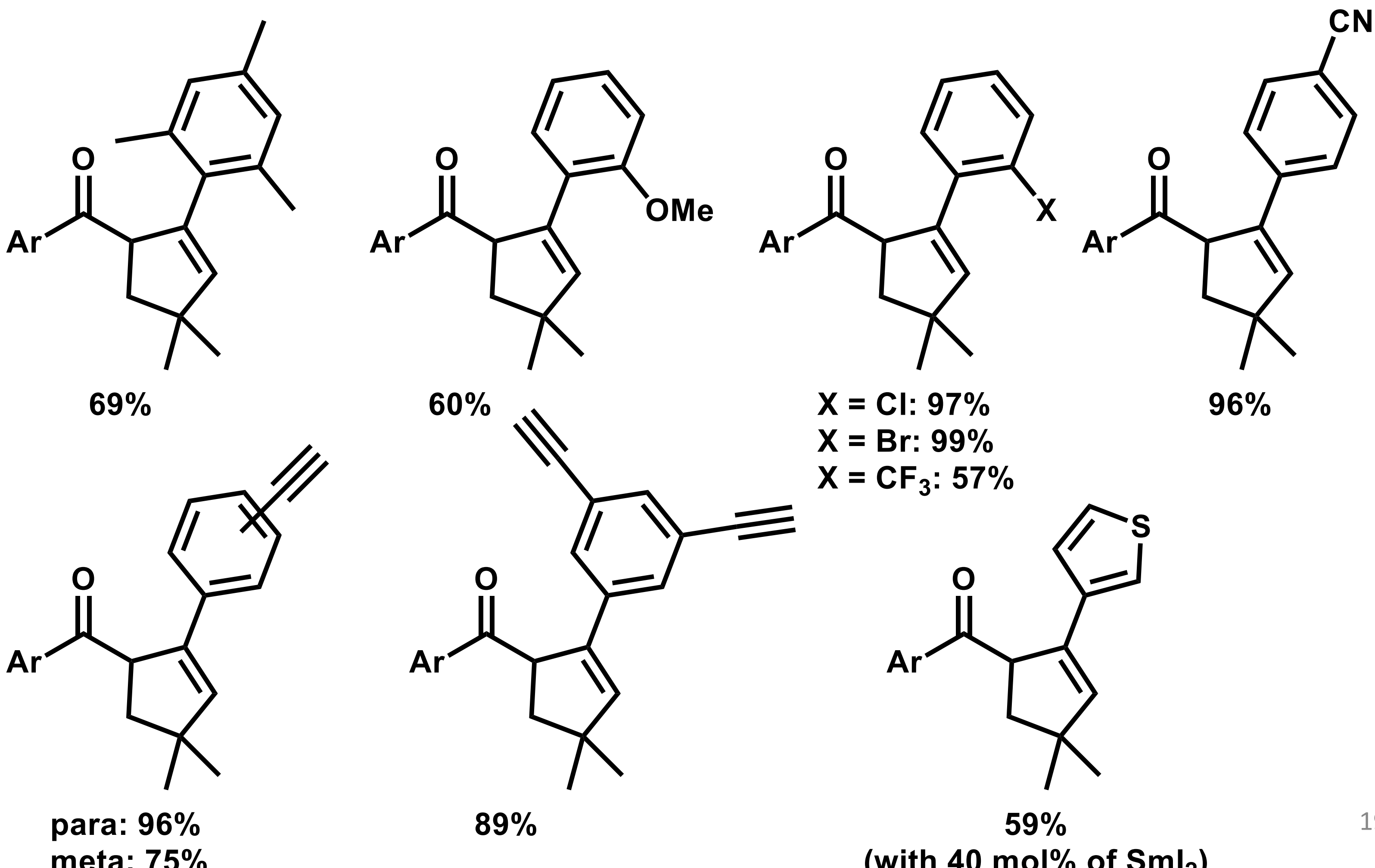
entry	ketone	temp. (°C)	SmI_2 loading	conversion	yield of 3
1	1a	55	25 mol%	40%	35%*
2	1b	55	25 mol%	100%	99%
3	1b	rt	25 mol%	85%**	82%
4	1b	55	20 mol%	85%	79%
5	1b	55	15 mol%	63%	50%
6	1c	55	15 mol%	89%	87%

*Byproduct 4 was also obtained (9%).**reaction time: 16 h

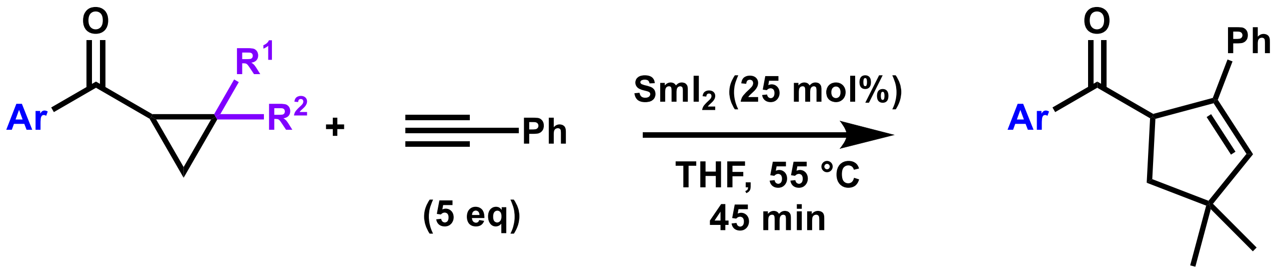
Agasti, S.; Beattie, N. A.; McDouall, J. J. W.; Procter, D. J. *J. Am. Chem. Soc.* **2021**, *143*, 3655.

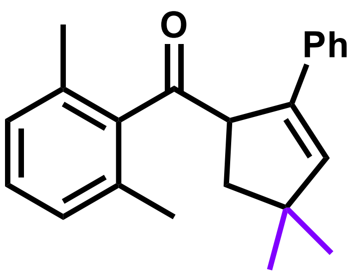
Substrate Scope (1)



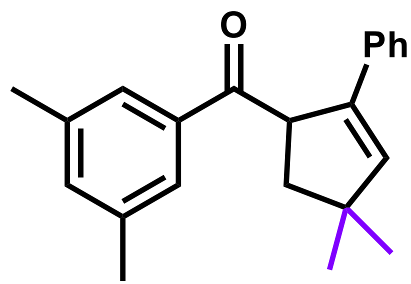


Substrate Scope (2)

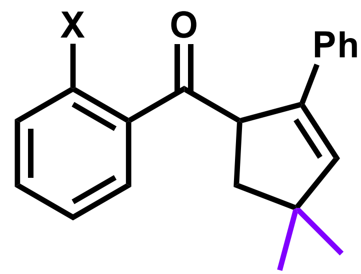




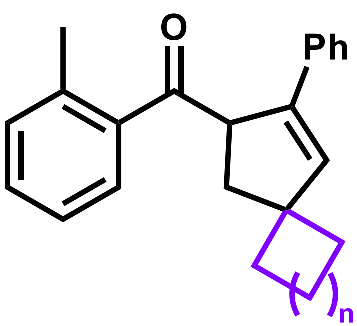
99%



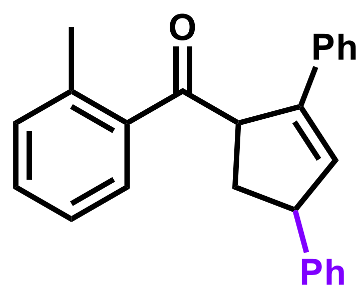
49%



X = F: 67%
X = I: 35%



n = 1: 52%
n = 3: 73%



0%

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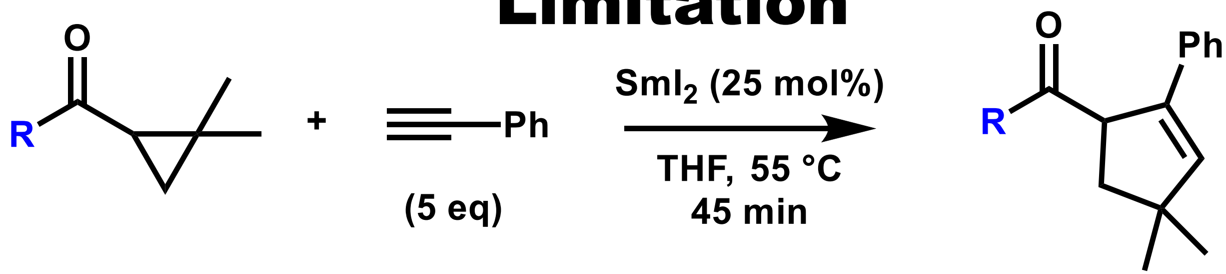
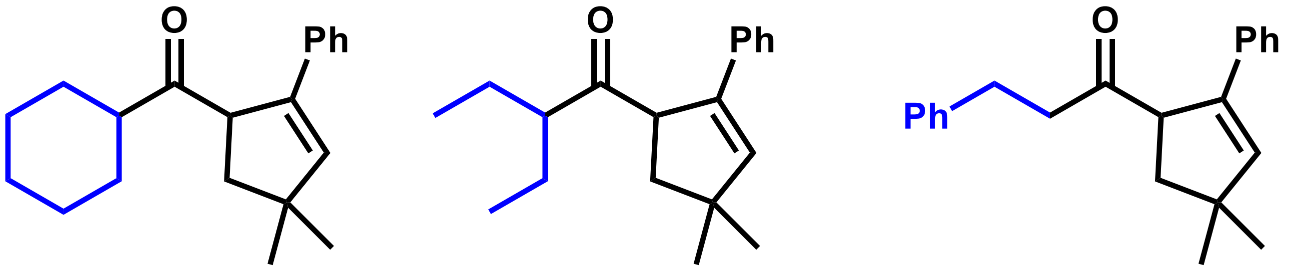
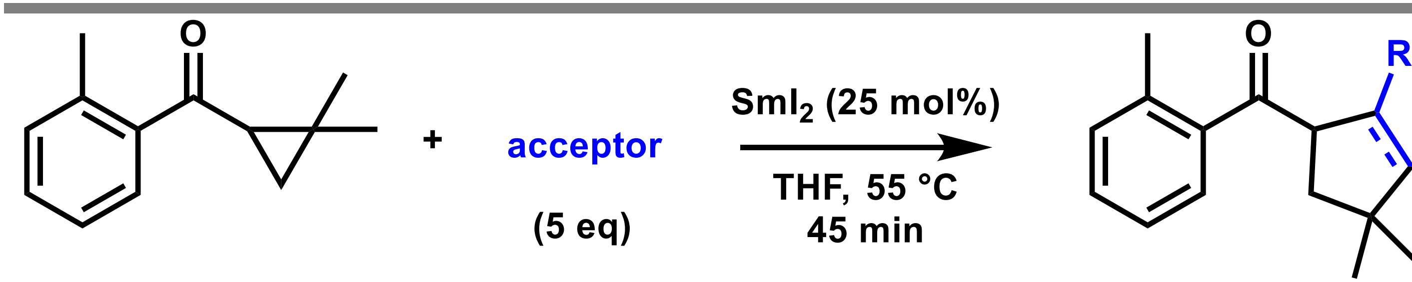
Limitation

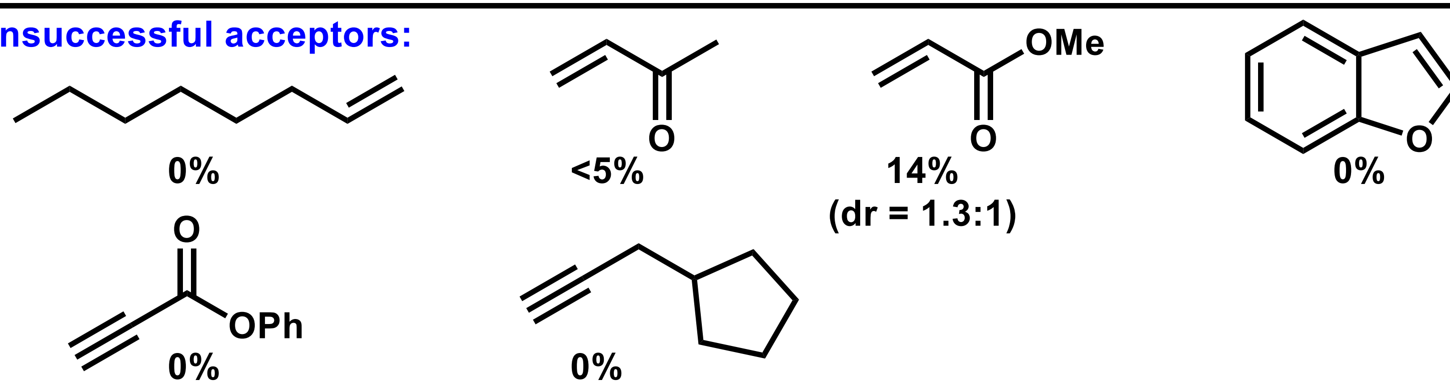




0% (SM rcv.) | <5% | 15% (81%, SM rcv.)



unsuccessful acceptors:



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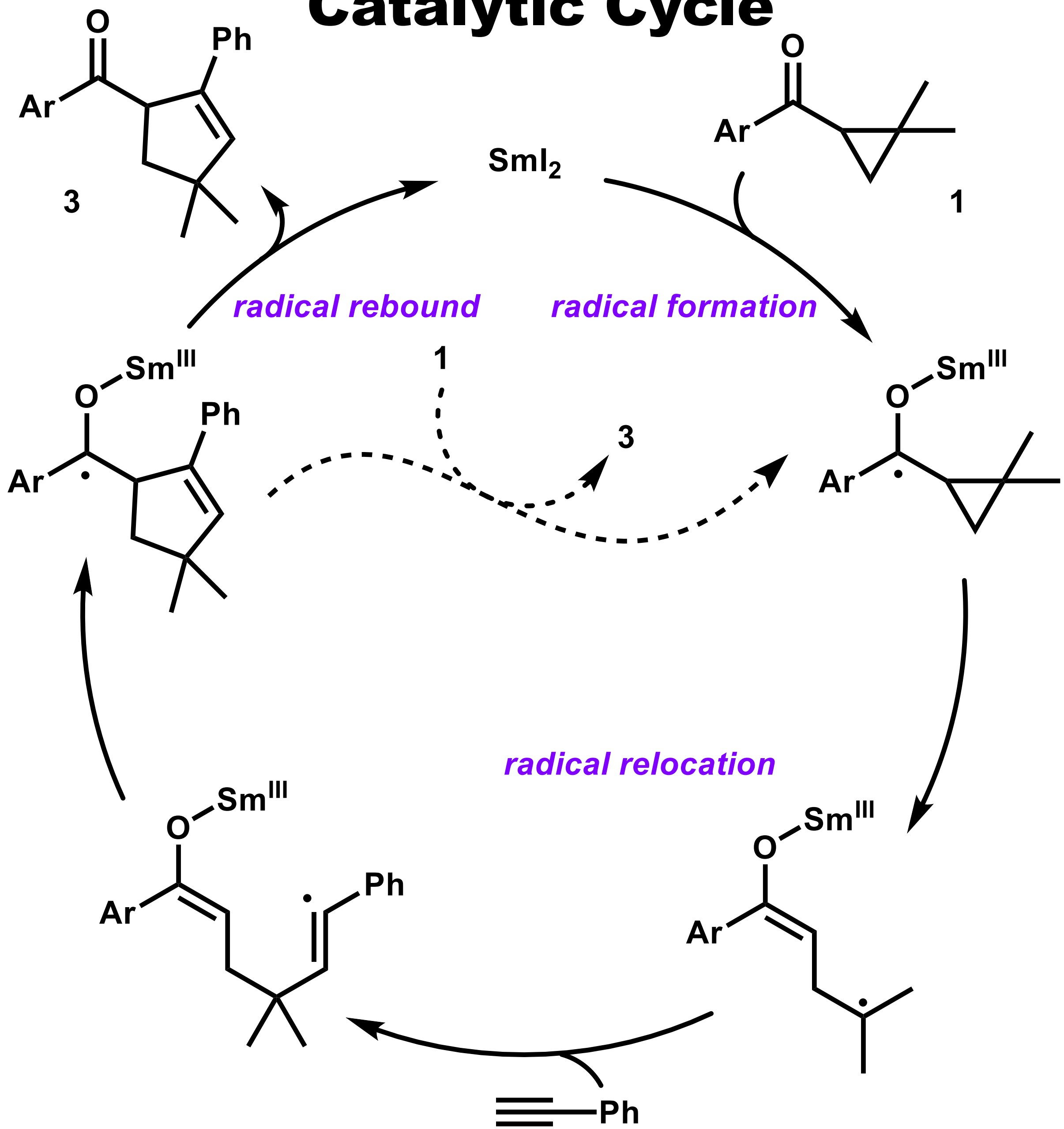
Catalytic Cycle



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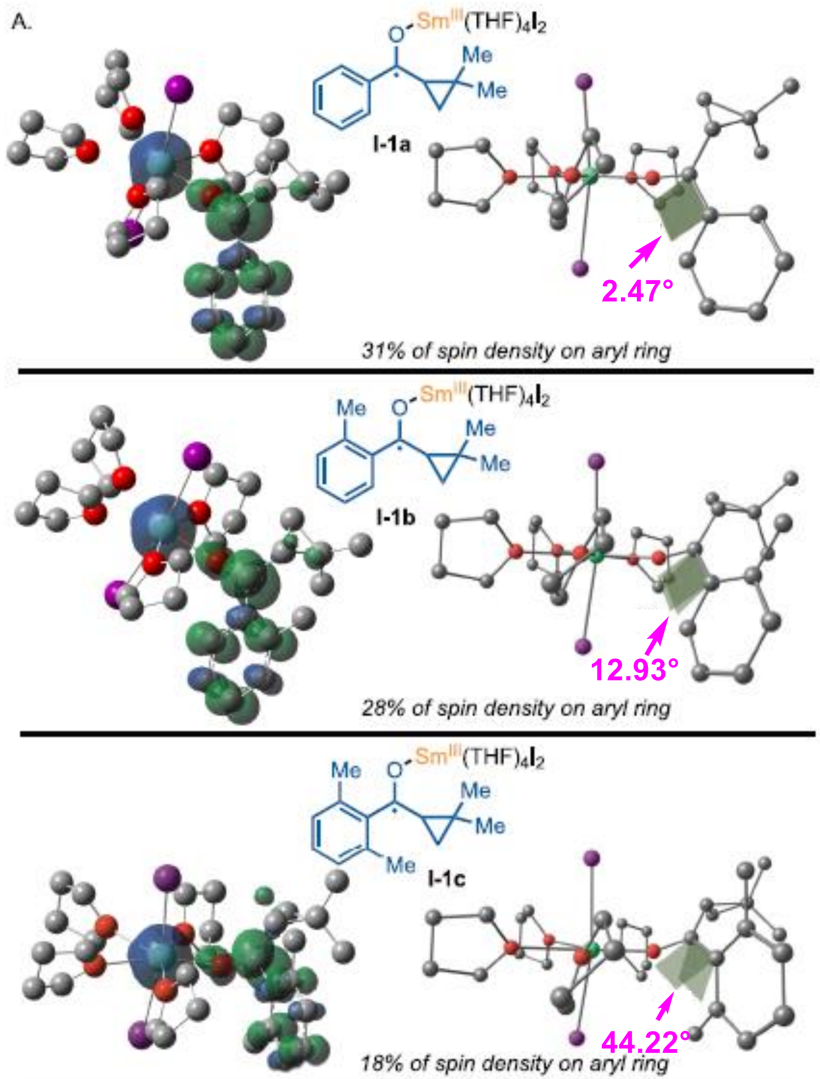
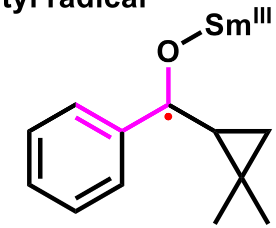
Probing the Importance of Ketyl Radical Stability

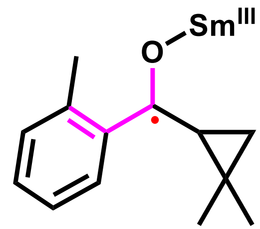


Coupling yield with phenylacetylene

less localized ketyl radical

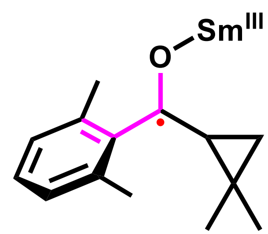


35%
(40% conv. with 25 mol% SmI_2)



99%
(100% conv. with 25 mol% SmI_2)

50%
(63% conv. with 15 mol% SmI_2)



more twisting

87%
(89% conv. with 15 mol% SmI_2)

more localized ketyl radical → facile cyclopropane opening

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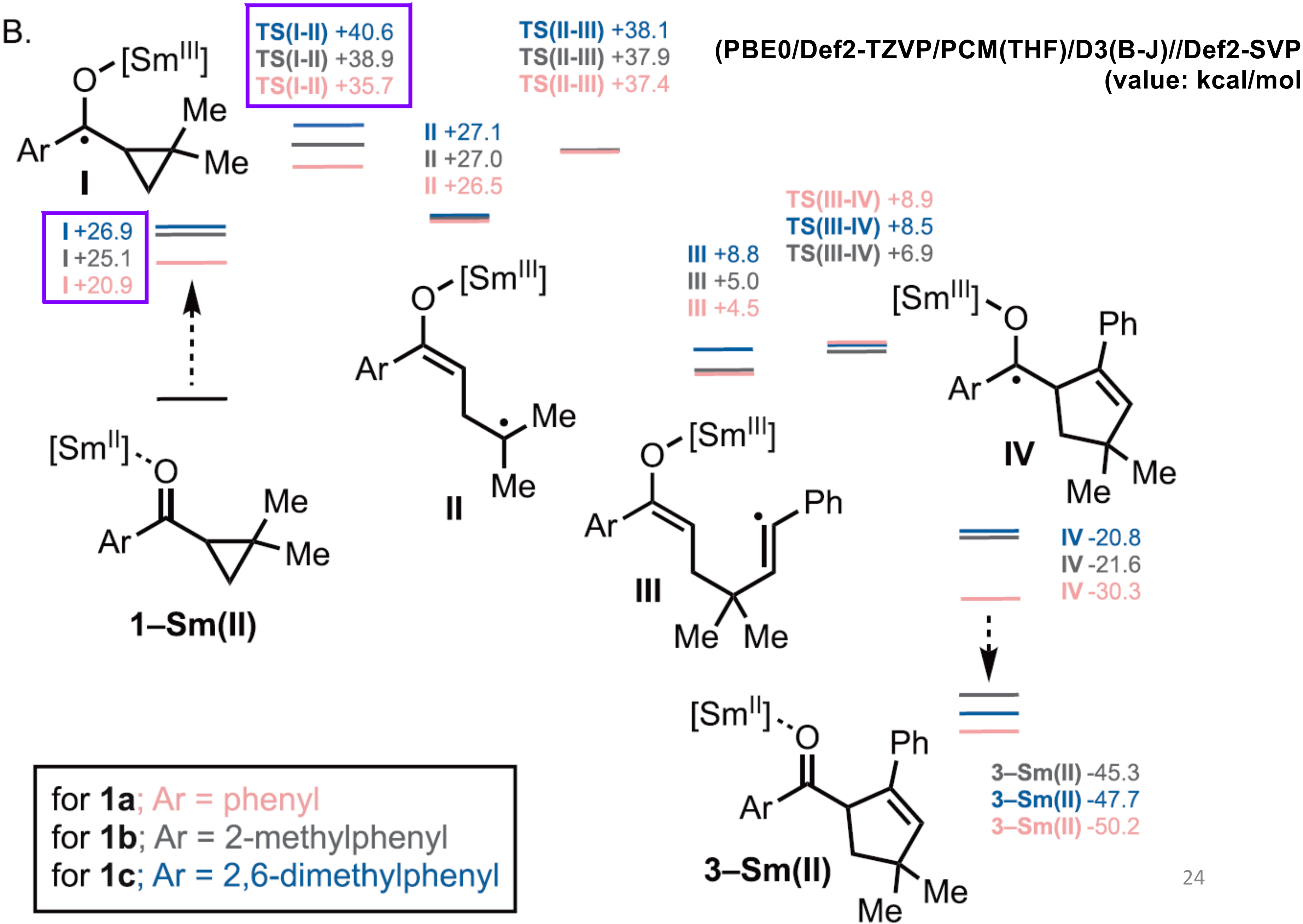
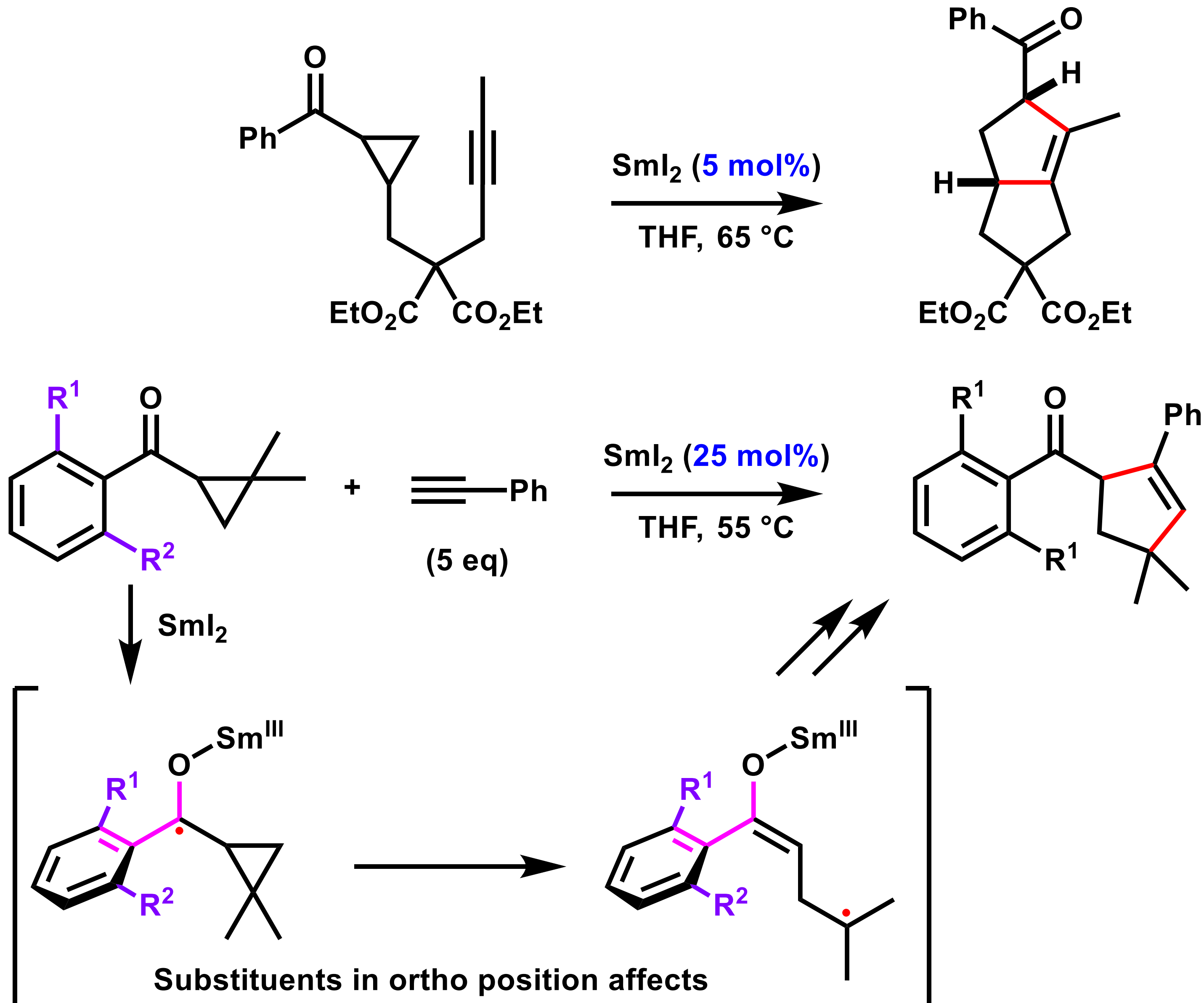
Computational Studies



Summary



Substituents in ortho position affects
ring-opening and efficiency of the coupling.