Vinyl Cations

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Outline

- Introduction
- Generation of Vinyl Cations
- Reaction of Vinyl Cations
- Summary
- Acknowledgement

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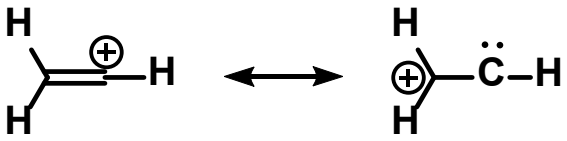
Selected Milestones of Vinyl Cation

First proposed by Jacobs and Searles

1944

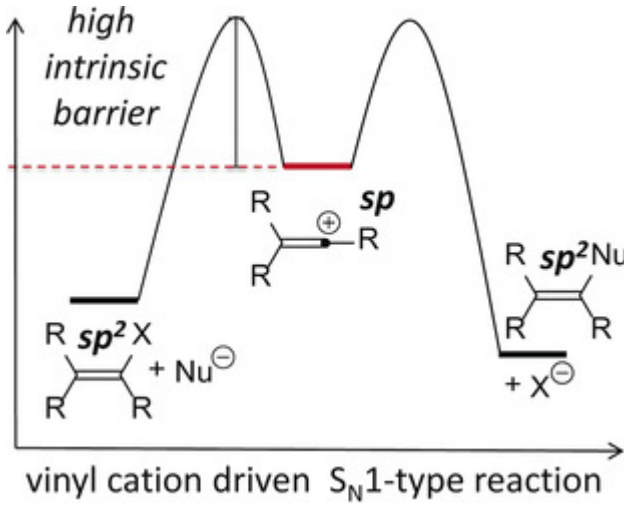


Kollmar and Smith first predicted its carbene-like reactivity

1972

1964

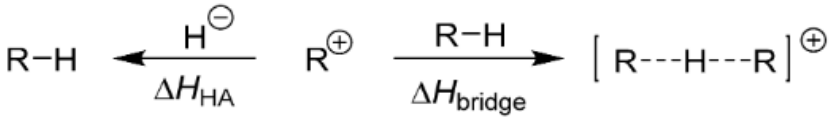
Grob and co-workers provided the first proof for vinyl cations with a solvolysis of aryl vinyl halides

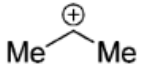
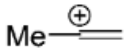
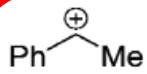
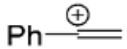
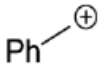
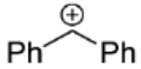


2017

Mayr and co-workers revealed that vinyl cations are sluggish electrophiles

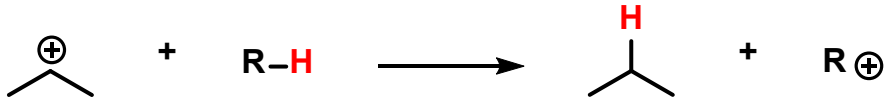
Stability of Vinyl Cation

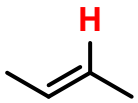
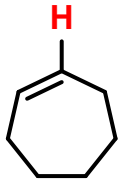
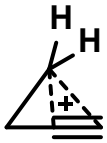
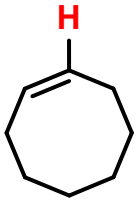
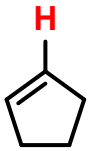
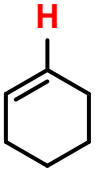
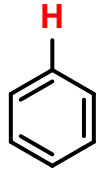


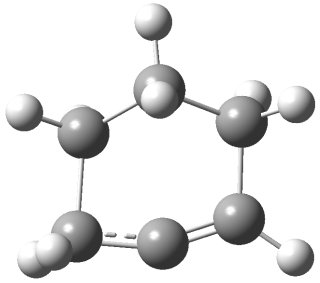
Entry	R^+	Experimental ΔH_{HA} [a]	Calculated Quantities [b]			
			ΔH_{HA} [b]	ΔG_{HA} [b]	ΔH_{bridge} [b]	ΔG_{bridge} [b]
1		−251.8	−259.3	−251.8	−18.5	−8.1
2		−264.9	−272.4	−264.2	−14.9	−2.9
3		−225.1	−234.5	−228.0	−12.2	+0.3
4		−239.7	−247.5	−240.1	−3.8	+8.2
5		−239.3	−246.8	−240.6	−12.9	−1.9
6		-	−220.9	−212.8	−8.0	+3.3

Bryne, P. A. *et al. J. Am. Chem. Soc.* **2017**, *139*, 1499.

Ring Tension of Cyclic Vinyl Cations

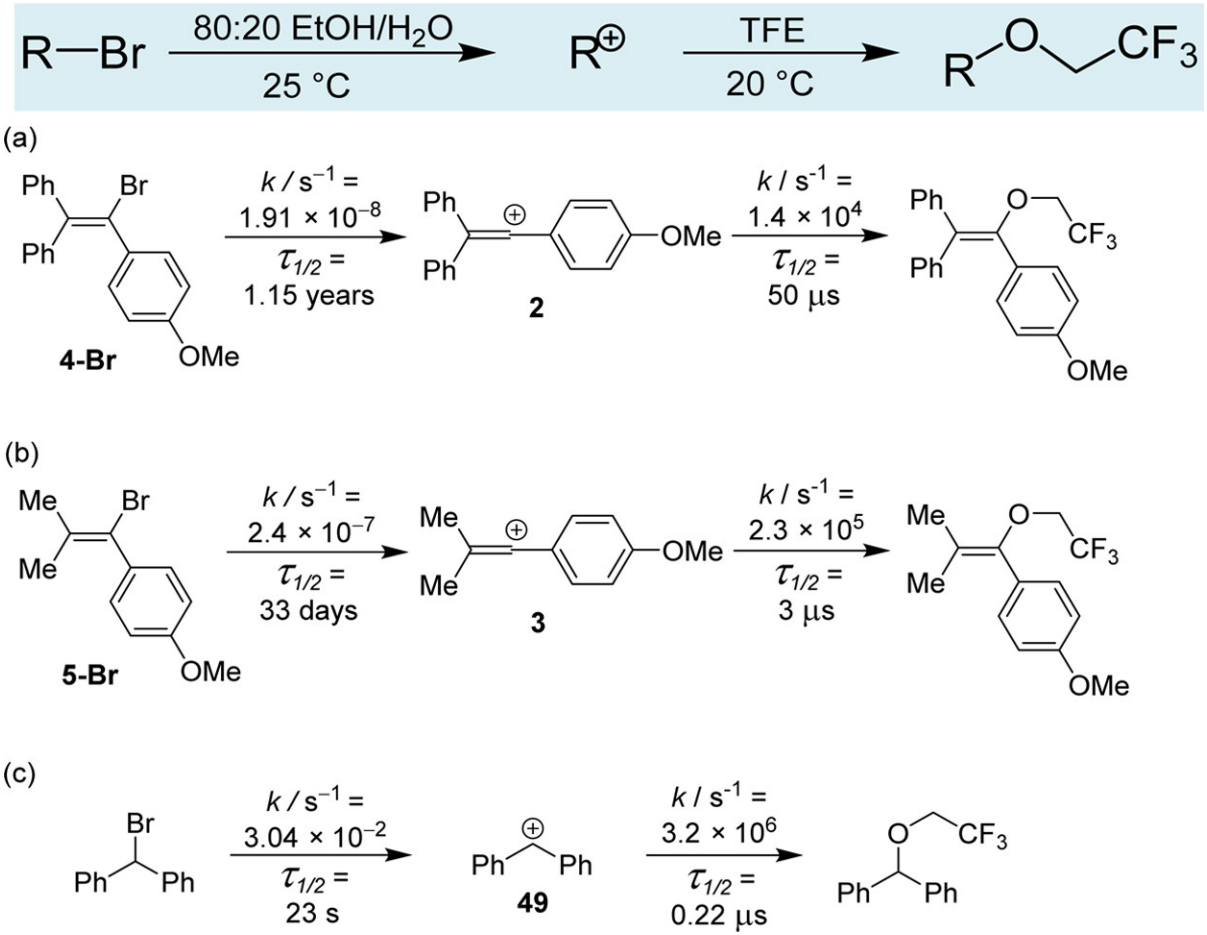


R–H	ΔG (kcal/mol)	R–H	ΔG (kcal/mol)
	5.4		1.7
 	2.2		3.3
	20.8		
	8.6		35.7



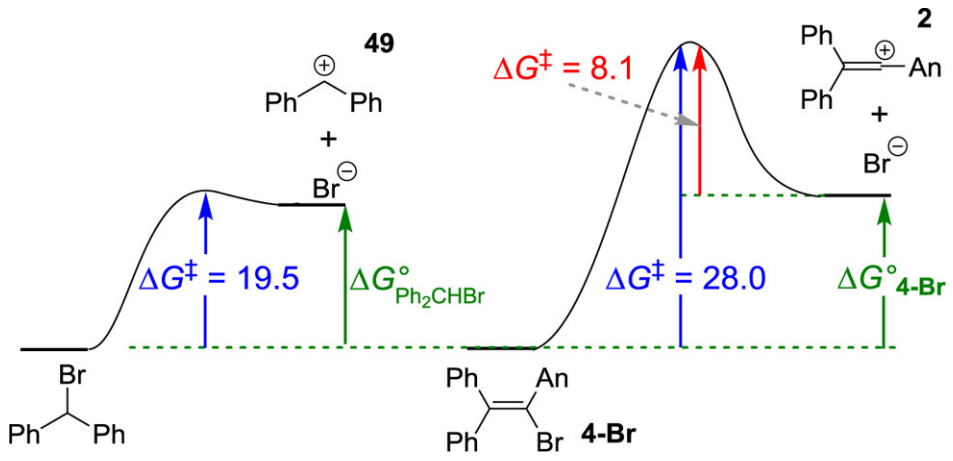
M06-2X-D3/def2-TZVP/SMD(benzene)//M06-2X-D3/def2-SVP

Solvolysis Reactions of Vinyl Cations



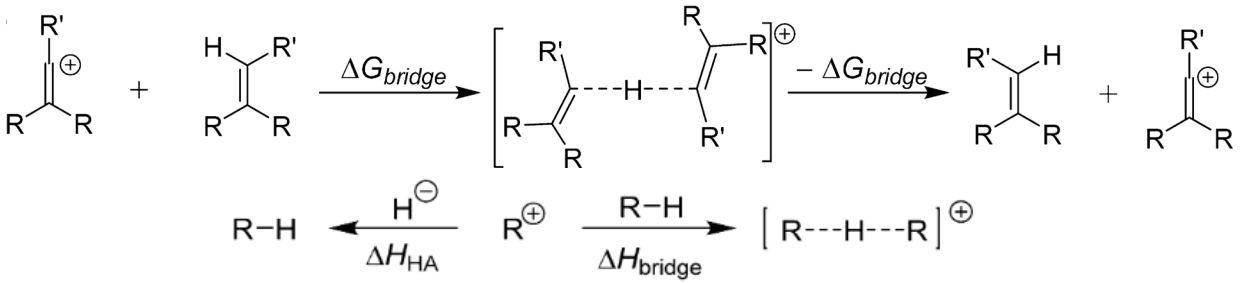
Bryne, P. A. *et al. J. Am. Chem. Soc.* **2017**, *139*, 1499.
Cozens, F. L. *et al*. *Can. J. Chem*. **1999**, *77*, 2069.

Addition to Vinyl Cation: Activation Control



Bryne, P. A. *et al. J. Am. Chem. Soc.* **2017**, *139*, 1499.

High Intrinsic Barrier



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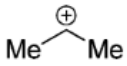
1		−251.8	−259.3	−251.8	−18.5	−8.1
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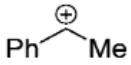
3		−225.1	−234.5	−228.0	−12.2	+0.3
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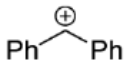
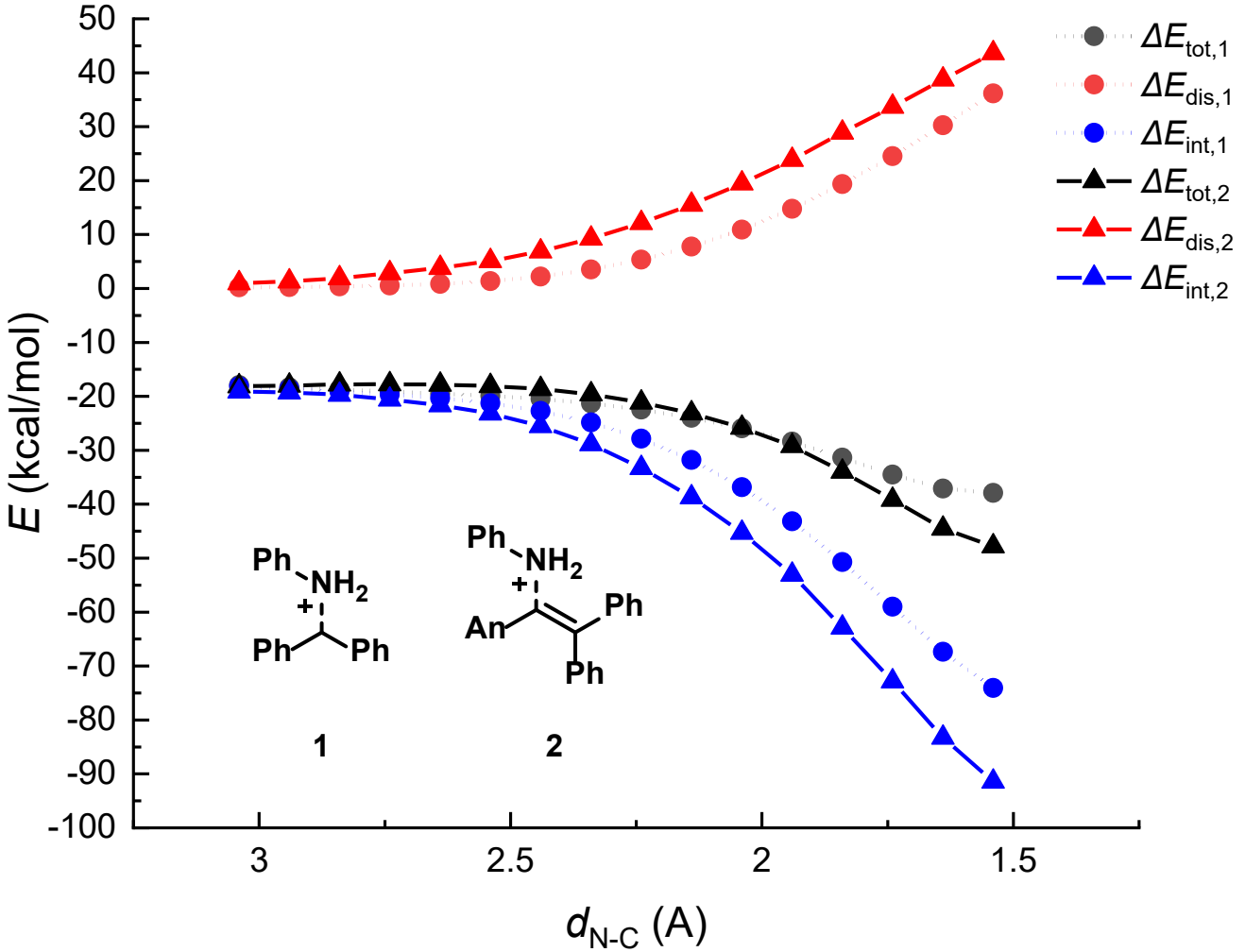
6		-	−220.9	−212.8	−8.0	+3.3

Bryne, P. A. *et al. J. Am. Chem. Soc.* **2017**, *139*, 1499.

Distortion-Interaction Analysis



Electronic energy at M06-2X-D3/def2-SVP
//M06-2X-D3/def2-SVP/SMD(trifluoroethanol)

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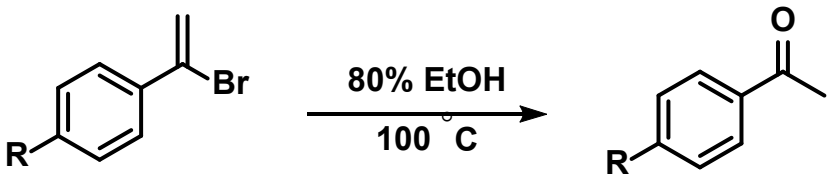
Direct Solvolysis: First Attempt

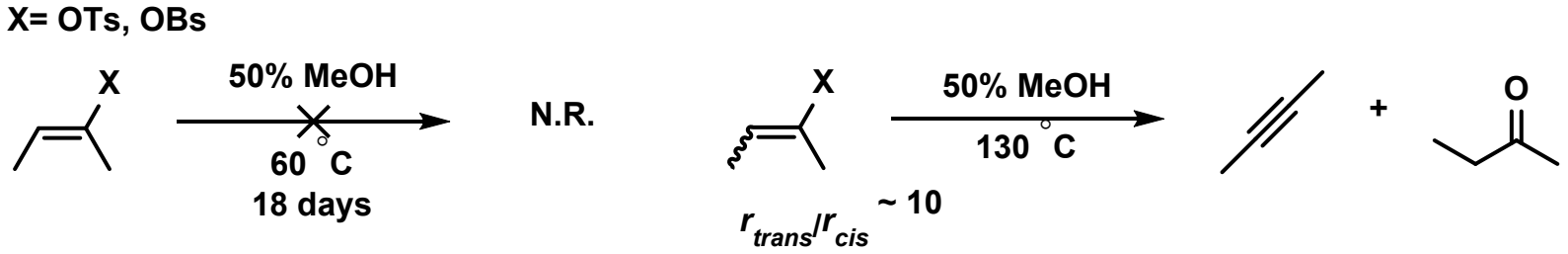


-R	k_{rel}
-H	1.0
$-NH_2$	5.5×10^8
-OMe	8.5×10^3
$-NO_2$	*I*

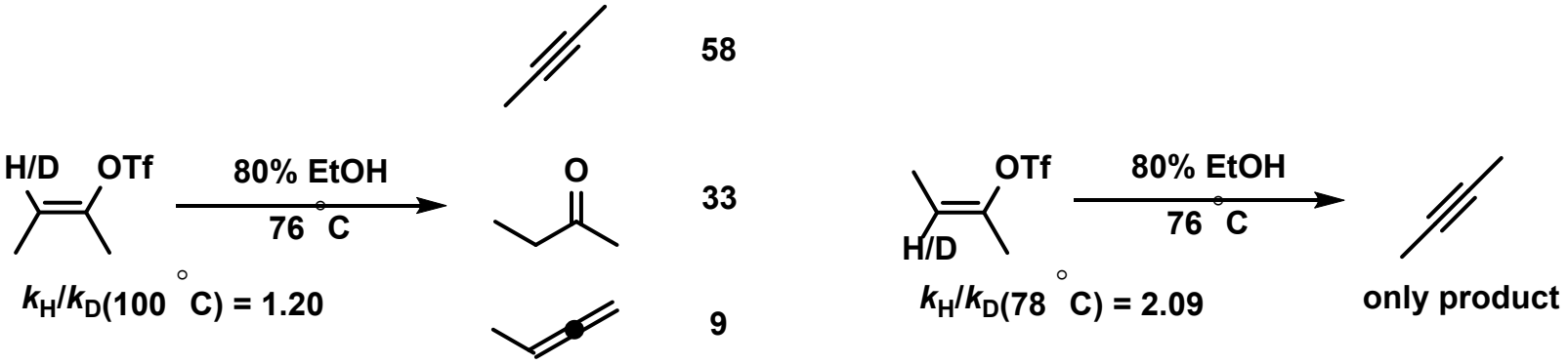
Grob, C. A. and Cseh, G. *Helv. Chim. Acta*, **1964**, *47*, 194.

Direct Solvolysis: Harsh and Not Useful

For alkyl substituted substrate, direct solvolysis of vinyl halides/sulfonates require highly polar solvents(usually protic solvents) and relatively high temperature.

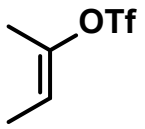
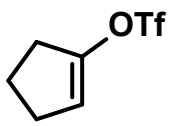
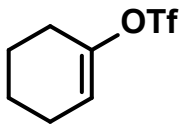
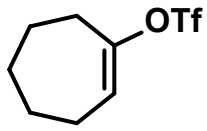
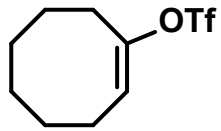


Peterson, P. E. and Indelicate, J. M. *J. Am. Chem. Soc.* **1968**, *90*, 6515.
Peterson, P. E. and Indelicate, J. M. *J. Am. Chem. Soc.* **1969**, *91*, 6194.



Stang, P. J. *J. Am. Chem. Soc*. **1969**, *91*, 4600.
Hanack, M. *Acc. Chem. Res*. **1970,** *3*, 209.

Cyclic Enol Triflate

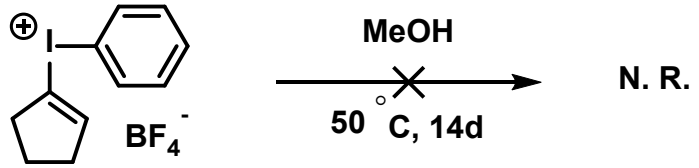
					
$k^{100\,^{\circ}C}$(50% EtOH)	1.77×10^{-3}	10^{-7} - 10^{-8}	1.90×10^{-5}	5.8×10^{-4}	4.7×10^{-3}
k_{rel}	1.0	10^{-4} - 10^{-5}	0.011	0.32	2.7

Hanack, M. *Acc. Chem. Res.* **1970,** *3*, 209.

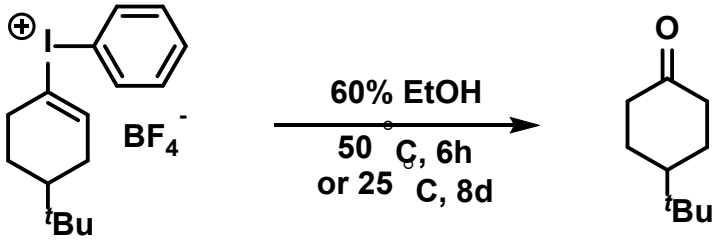
Strained Vinyl Cations: Stronger Leaving Group

Relative Leaving Ability

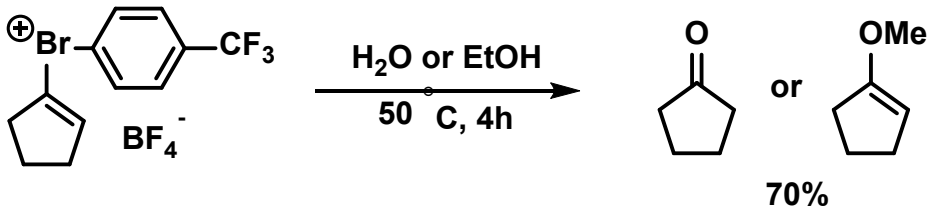
nucleofuge	relative leaving ability
—$^{+}SMe_2$	1
—OTs	7×10^5
—OTf	6×10^{11}
—^{+}IPh	5×10^{17}



M. Ochiai in *Chemistry of Hypervalent Compounds* (Ed.: K.-y. Akiba), Wiley-VCH, New York, **1999**, 359.



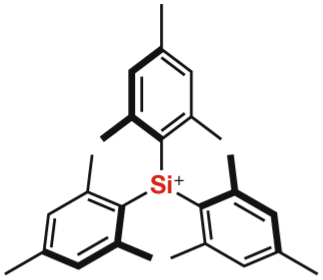
Okuyama, T. *et al. J. Am. Chem. Soc.* **1995**, 117, 3360.



Miyamoto, K. *et al. Angew. Chem., Int. Ed.* **2009**, *48*, 8931.

Silylium Ions: Eager for Coordination

b Free silylium ions

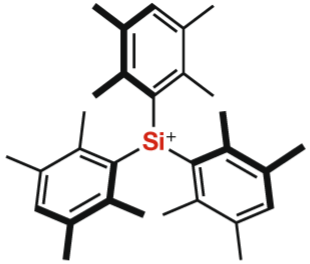


$B(C_6F_5)_4^-$

1

$\delta(^{29}Si)$ 225.5 ppm

Lambert et al.[8,11]

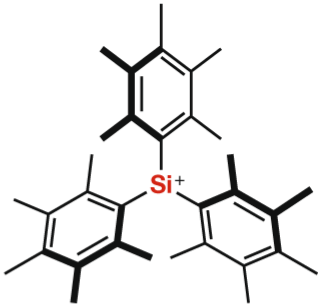


$B(C_6F_5)_4^-$

2

$\delta(^{29}Si)$ 226.8 ppm

Lambert and Lin[12]



$1/2B_{12}Cl_{12}^{2-}$

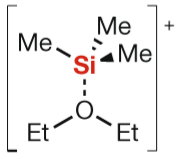
3

$\delta(^{29}Si)$ 216.4 ppm

Müller et al.[13]

c σ-Donor-stabilized silylium ions

Intermolecular stabilization



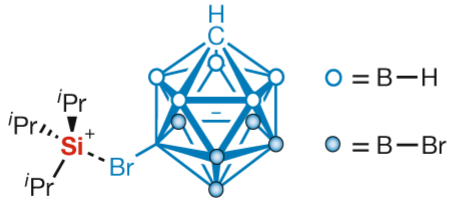
$BAr^F{}_4^-$

4

Ether

$\delta(^{29}Si)$ 66.9 ppm

Kira, Sakurai et al.[14]

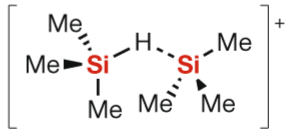


5

Halogen

$\delta(^{29}Si)$ 109.8 ppm

Reed et al.[18]



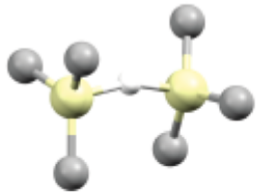
$CHB_{11}Cl_{11}^-$

6

Hydrosilane

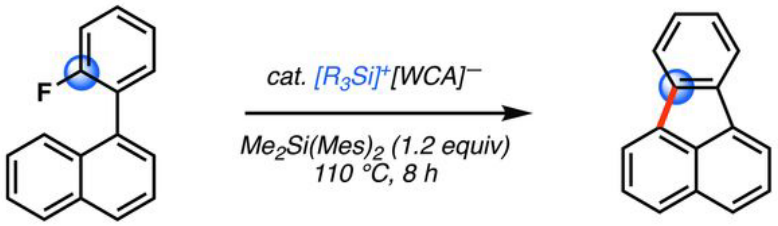
$\delta(^{29}Si)$ 85.4, 82.2 ppm

Reed et al.[23]

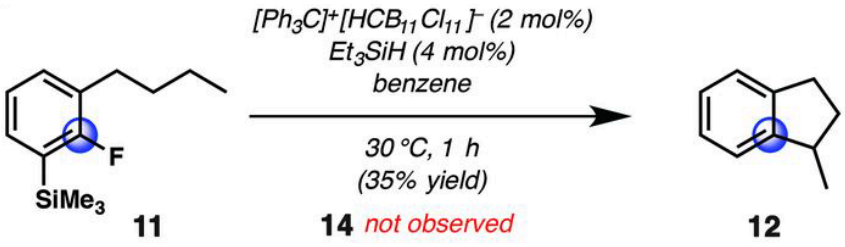


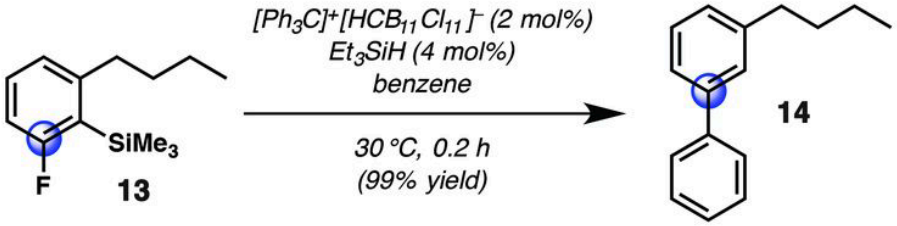
Walker, J. C. L. *et al. Nat. Rev. Chem.* **2020**, *4*, 54.

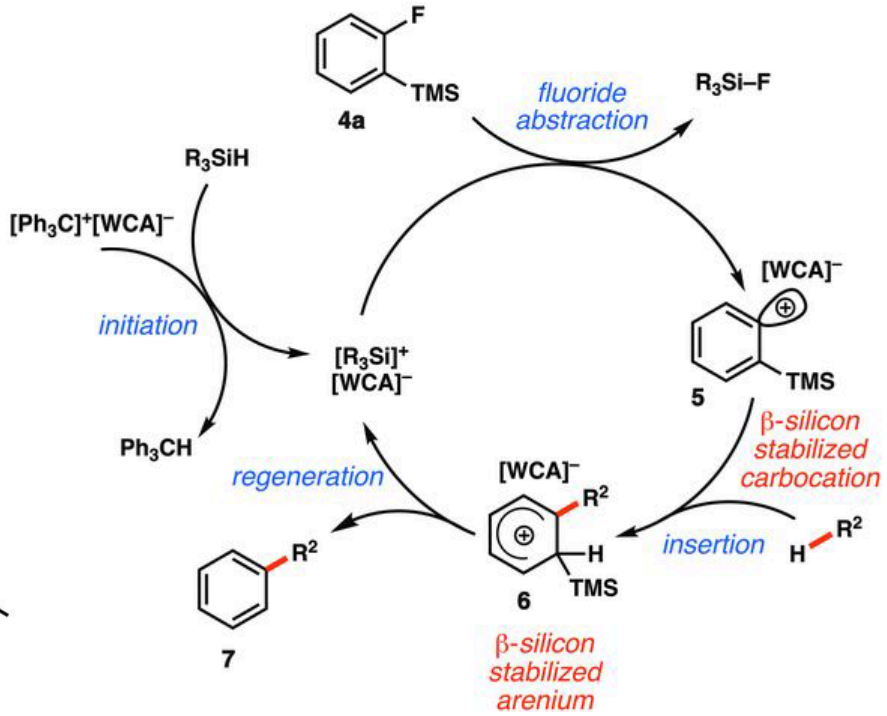
R_3Si^+-WCA Strategy for Aryl Fluoride



Allemann, O. *et al. Science* **2011**, 334, 574.

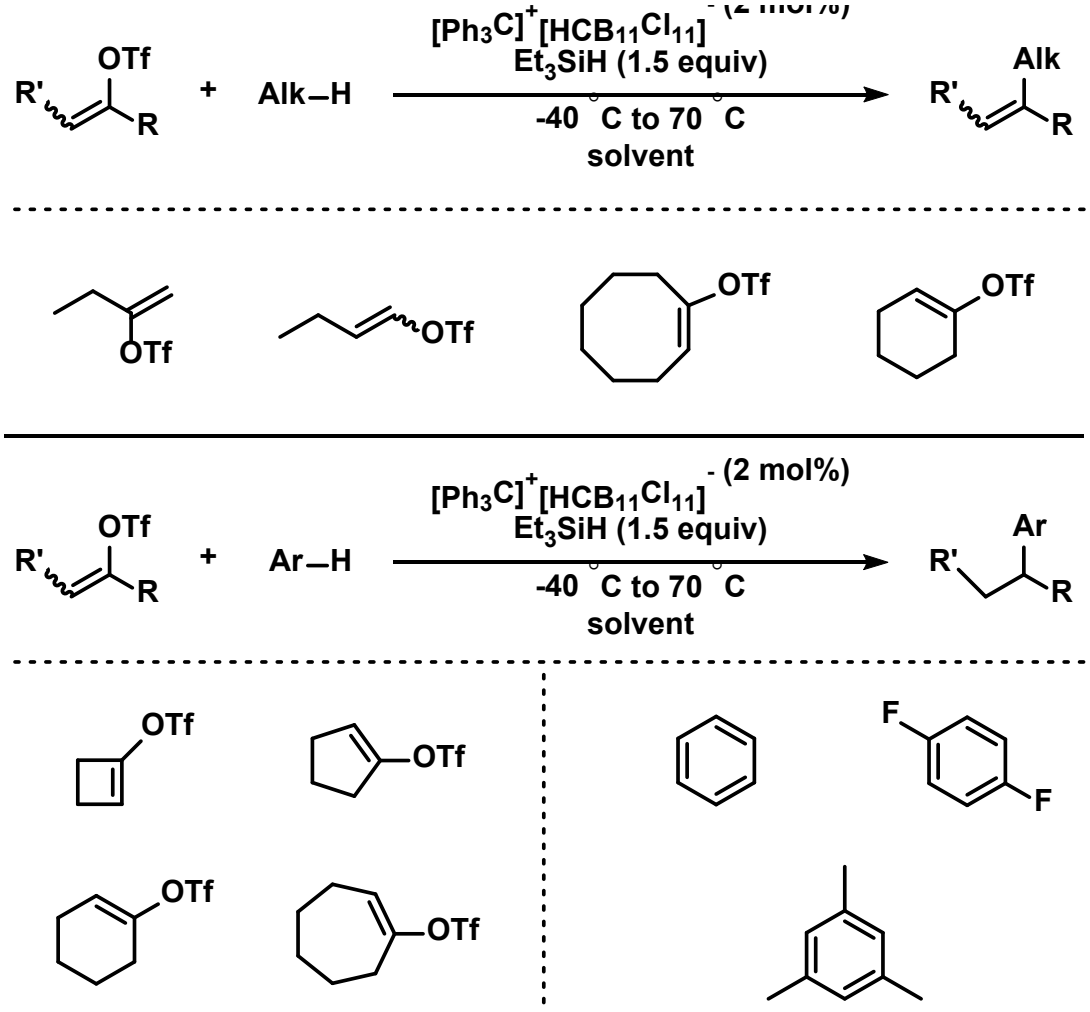






Shao, B. *et al. Science* **2017**, 355, 1403.

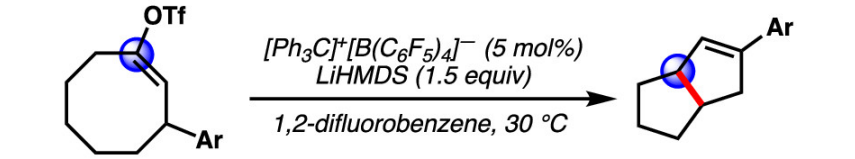
R_3Si^+-WCA^- System for Vinyl Triflate

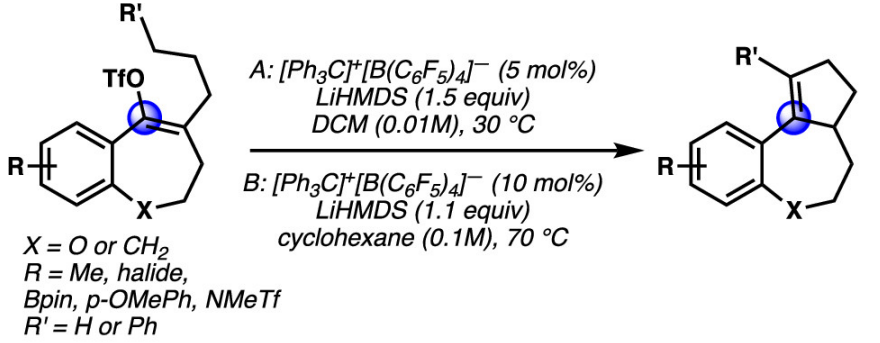


Popov, S. *et al. Science* **2018**, 361, 381.

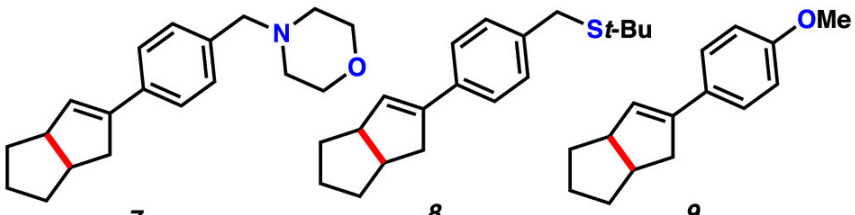
Li^+-WCA^- : Higher Compatibility

Using weaker LA Li^+ instead of silylium Ions, higher compatibility of functional group can be achieved, but strained vinyl cations cannot be generated.





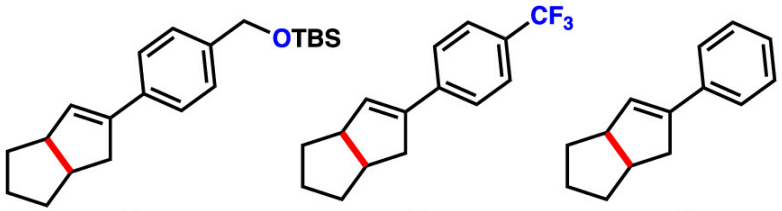
X = O or CH_2
R = Me, halide, Bpin, p-OMePh, NMeTf
R' = H or Ph



7
42% yield[a,b,c]
ca. 79% yield of olefin isomers[d]

8
38% yield
ca. 57% yield of olefin iosmers[e]

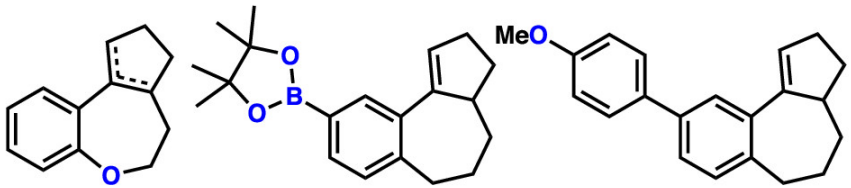
9
38% (29%[f]) yield
ca. 48% yield of olefin iosmers[d]



10
60% (46%[f]) yield[g]
97% yield of olefin isomers

11
50% (45%[f]) yield
ca. 88% yield of olefin isomers[d]

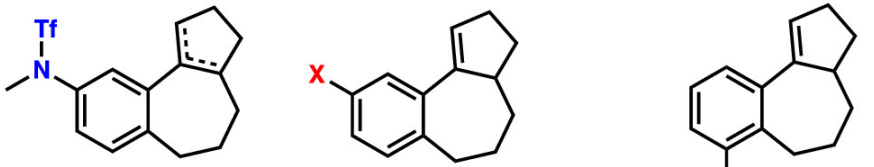
12
46% (35%[f]) yield
ca. 75% yield of olefin isomers[d]



15
84% yield
(3.3:1 tetra:tri)
B

16
68%[b] (58%) yield[a]
B

17
48%[b] (44%) yield
B



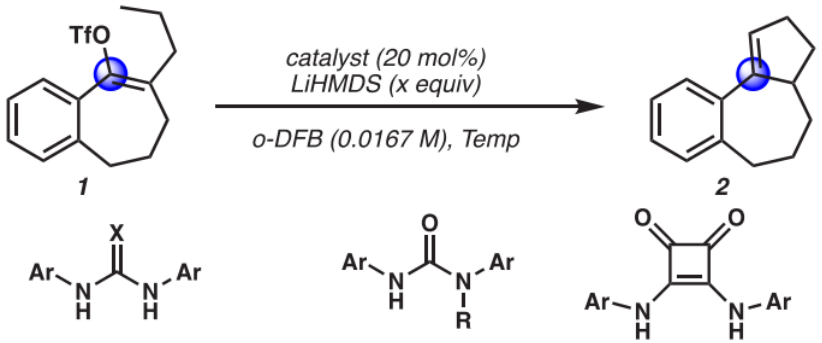
18
66% yield
(8:1 tri:tetra)
B

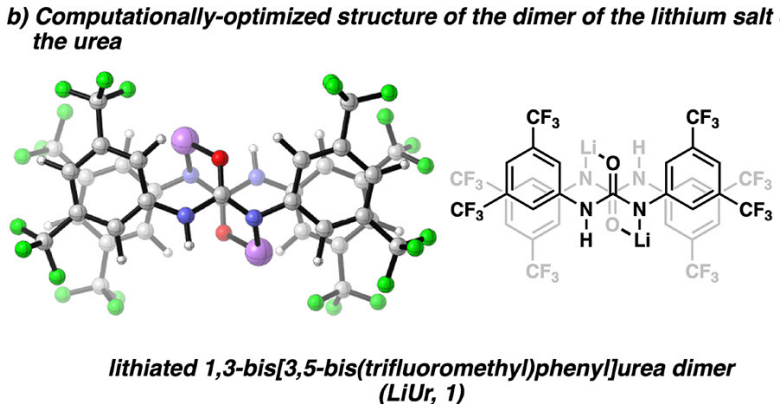
19, X = F, 72% yield[b]
20, X = Cl, 82% yield[b]
B

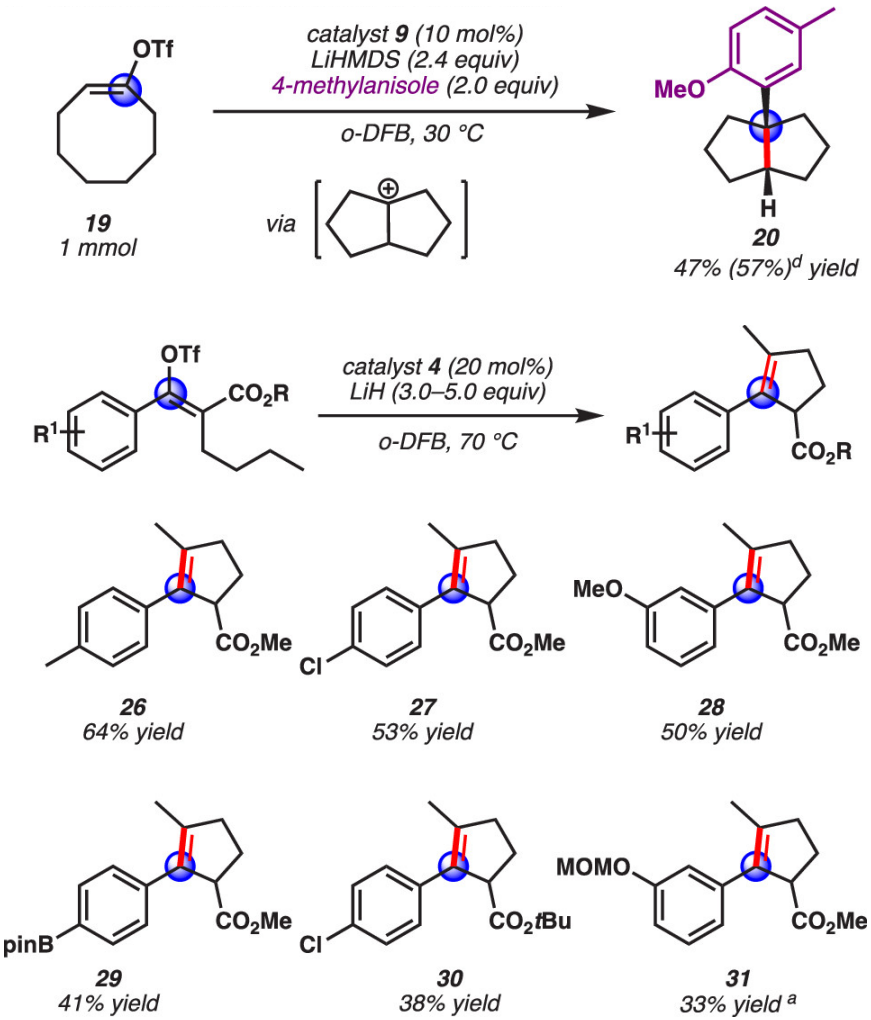
21
96%[b] (90%) yield
A

Wigman, B. *et al. J. Am. Chem. Soc.* **2019**, *141*, 9140.

Lithiated Ureas: Also Work, even Better

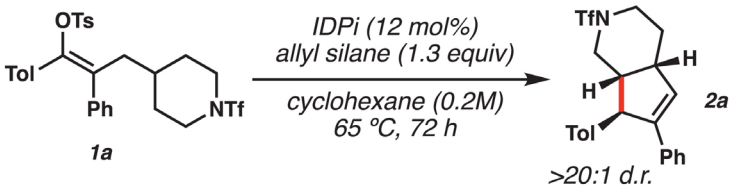




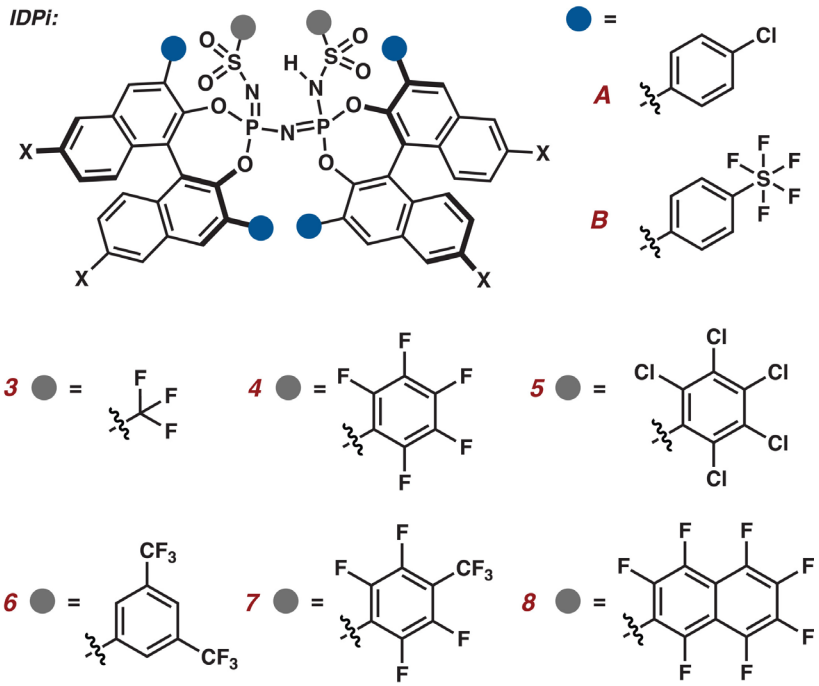


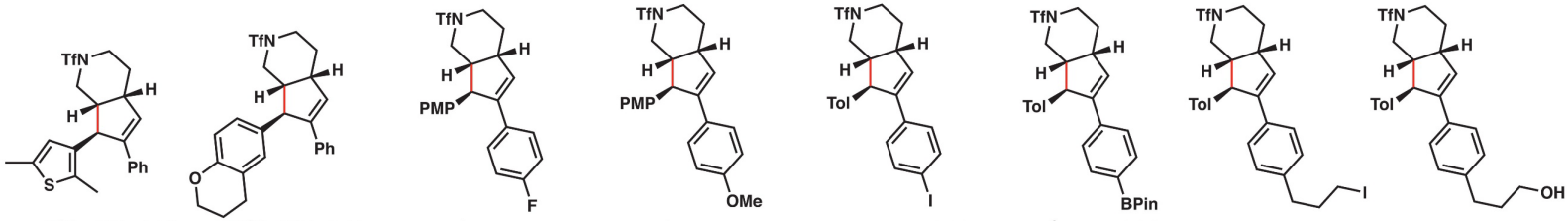
Bagdasarian, A. L. *et al. Org. Lett.* **2020**, *22*, 7775.
Lee, W. *et al. J. Org. Chem.* **2023**, *88*, 3403.

IDPi: Milder for Phenyl Aryl Tosylate



Entry	IDPi	X	Silane	Conv.	Yield	%ee
1	3A	H	allyl TIPS	70%	56%	52%
2	4B	CF_3	allyl TIPS	89%	79%	85%
3	5B	CF_3	allyl TIPS	95%	72%	60%
4	6B	CF_3	allyl TIPS	13%	11%	84%
5	7B	CF_3	allyl TIPS	93%	84%	85%
6	8B	CF_3	allyl TIPS	81%	72%	91%
7	8B	CF_3	allyl TMS	38%	34%	89%
8	8B	CF_3	allyl $Si(TES)_3$	full	91% (81%)*	91%
9	8B	CF_3	none	0%	0%	—





2j‡,§, 40% yield, >20:1 d.r., 90% ee

2k‡,¶, 65% yield, >20:1 d.r., 88% ee

2n‡, 78% yield, >20:1 d.r., 91% ee (>99% ee)*

2o‡, 60% yield, >20:1 d.r., 93% ee (>99% ee)*

2p, 54% yield, >20:1 d.r., 90% ee

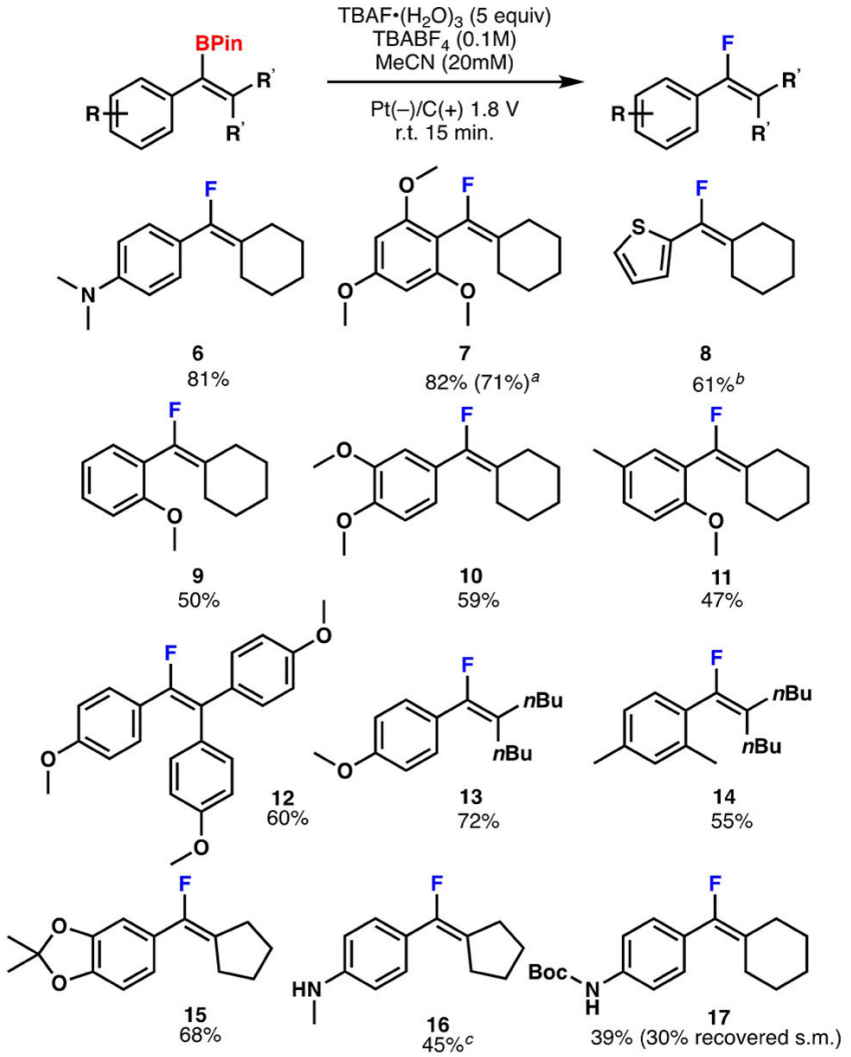
2q§, 60% yield, >20:1 d.r., 90% ee

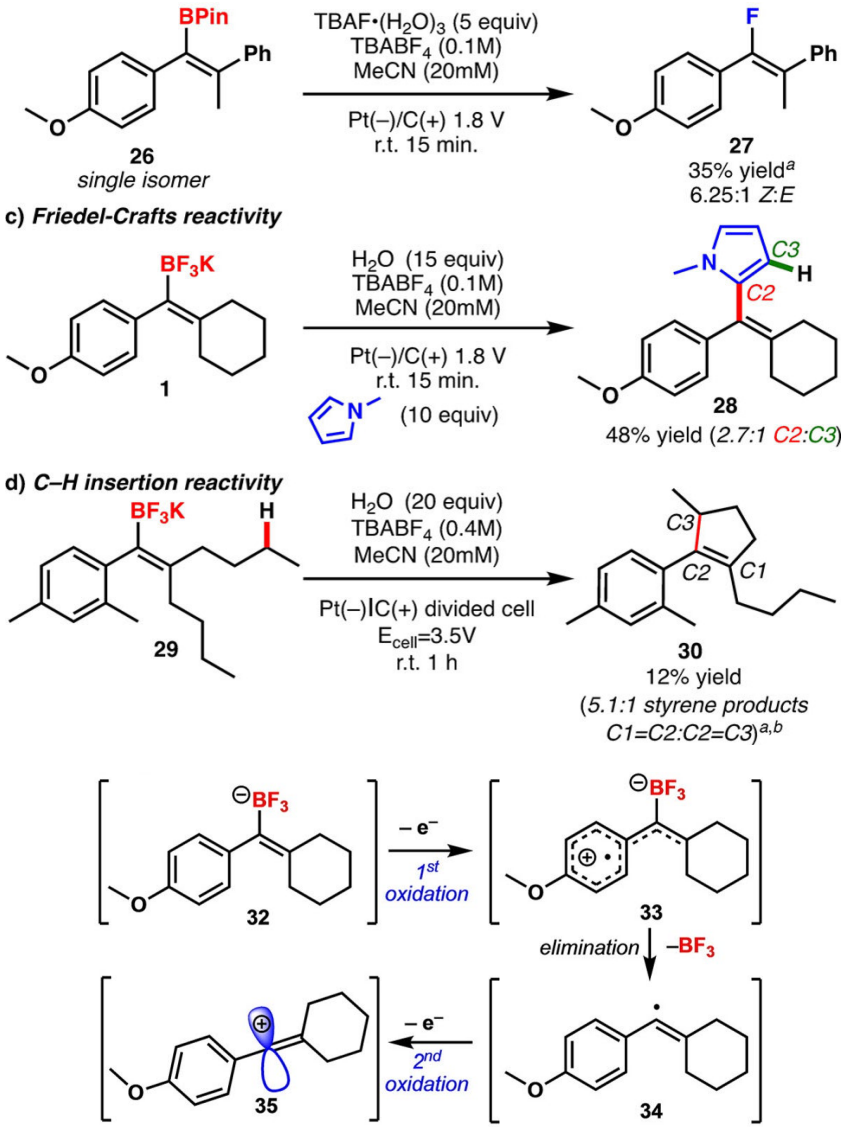
2r, 66% yield, >20:1 d.r., 91% ee

2s#, 64% yield, >20:1 d.r., 87% ee

Sepand, K. N. *et al. Science* **2022**, 378, 1085.

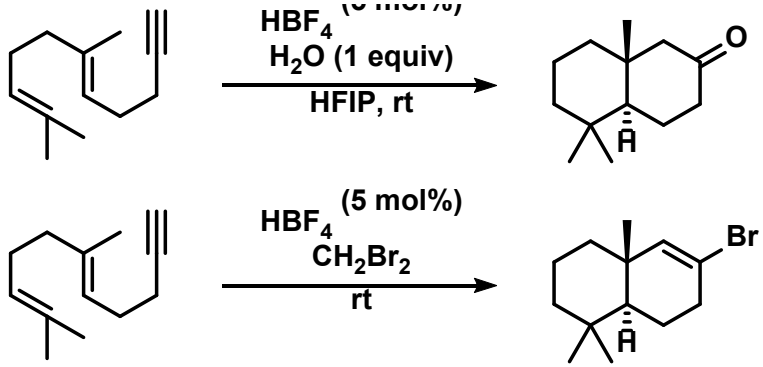
Electrochemical Approach



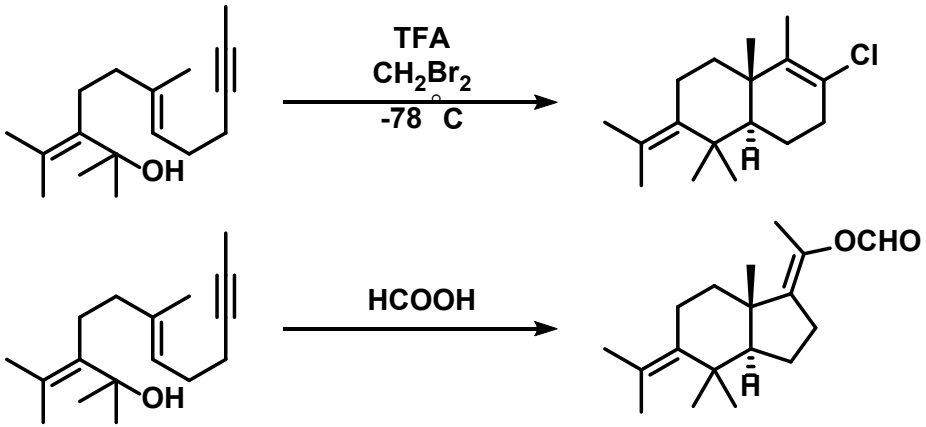


Wigman, B. *et al. Angew. Chem. Int. Ed.* **2022**, e202113972.

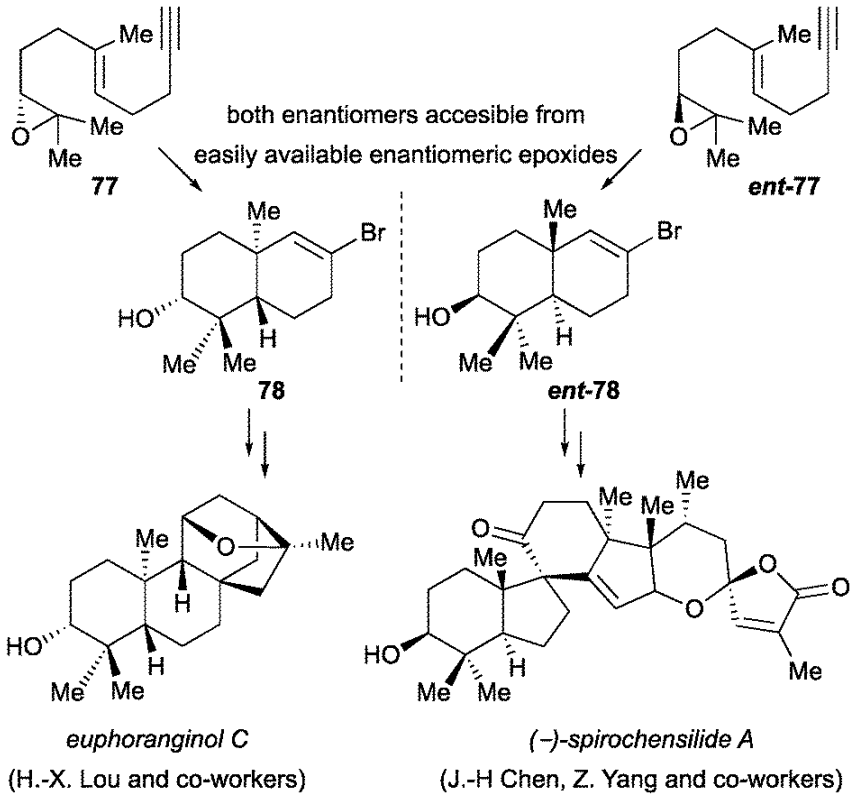
Electrophilic Addition to Alkyne by Carbocation



Alonso, P. *et al. Org. Lett.* **2018**, *20*, 1659.
Fontaneda, R. *et al. Org. Lett.* **2016**, *18*, 4626.

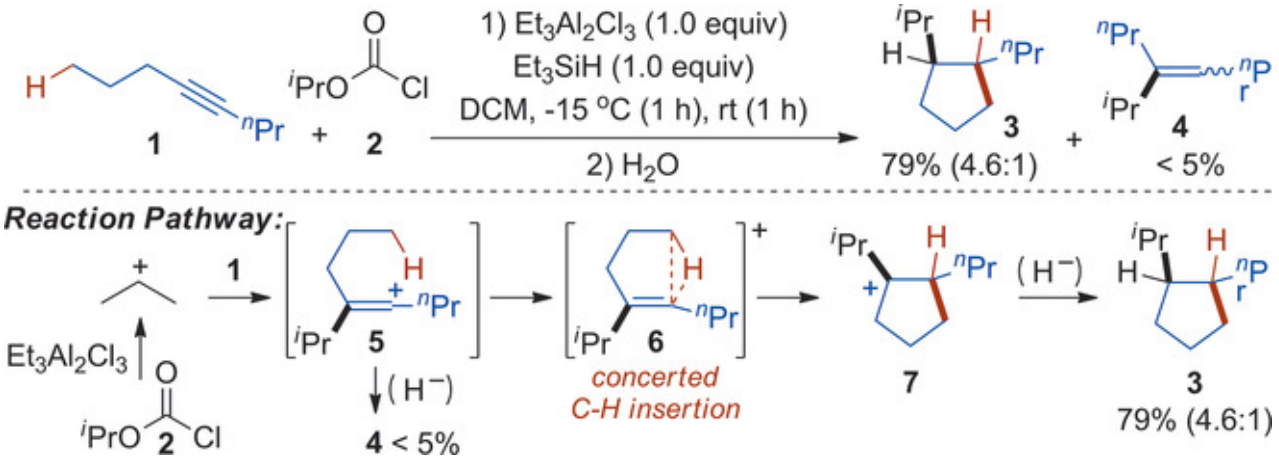


Lansbury, P. T. *et al. J. Am. Chem. Soc.* **1975**, *97*, 394.

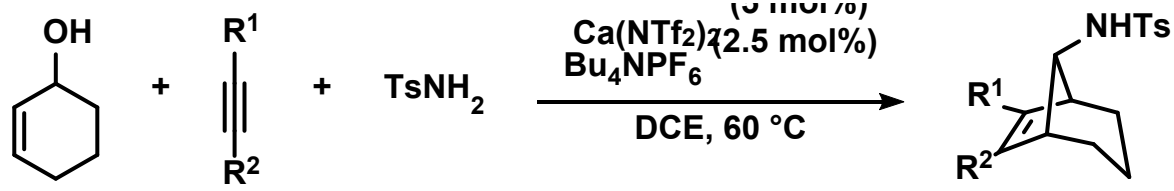


Xu, Z. *et al. Angew. Chem. Int. Ed.* **2020**, *59*, 19919.
Liang, X. *et al. J. Am. Chem. Soc.* **2020**, *142*, 8116.
Garcia-Pedrero, O. *et al. Chem. Commun.* **2022**, *58*, 1089

Intermolecular Capture

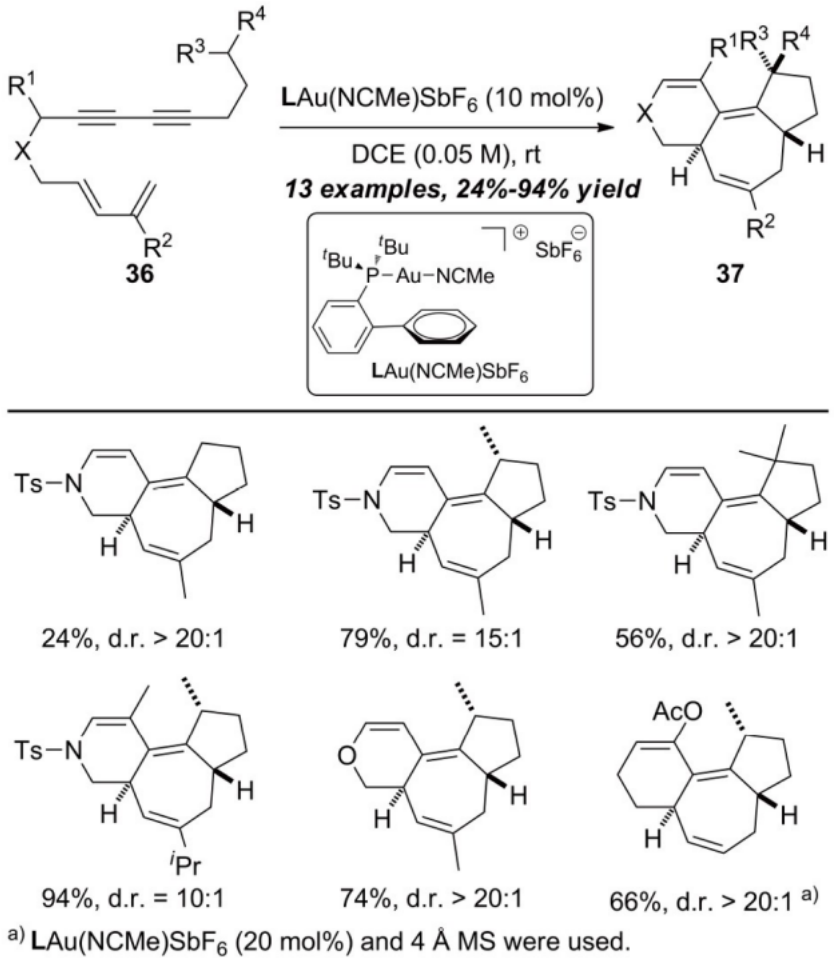


Biermann, U. *et al. Angew. Chem. Int. Ed.* **2006**, *45*, 3076.
Niggemann, M. and Gao, S. *Angew. Chem., Int. Ed.* **2018**, *57*, 16942

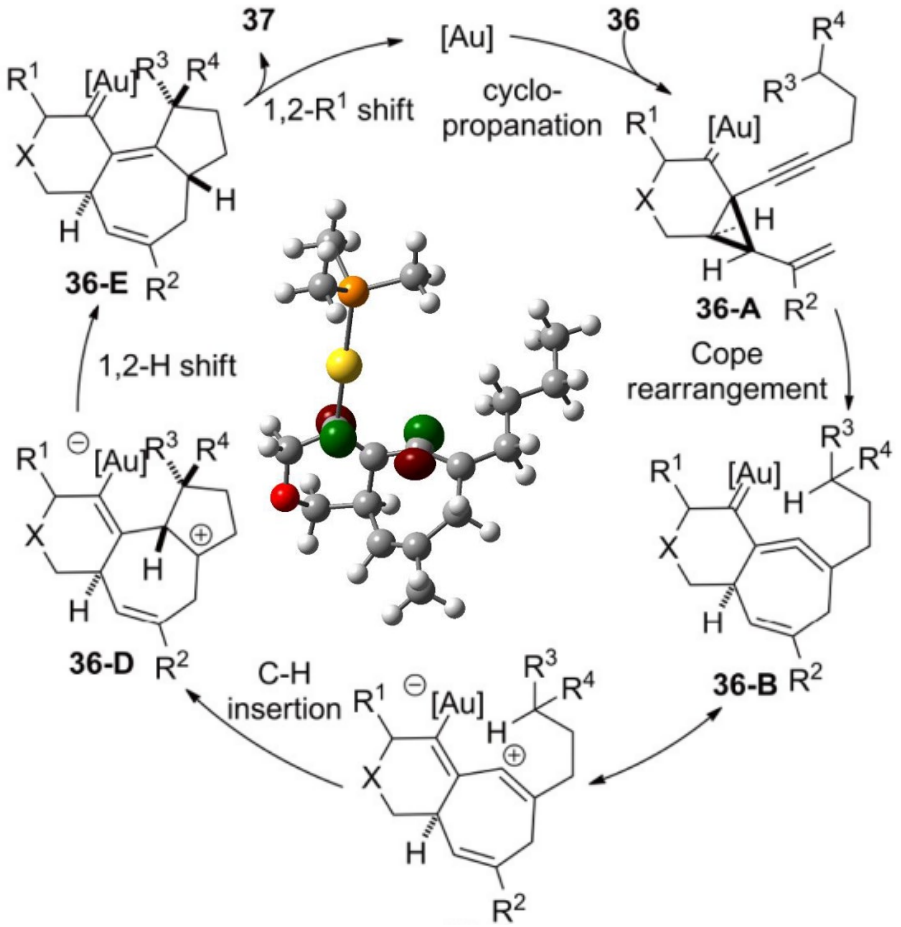


Gao, S. *et al. Org. Lett.* **2015**, *17*, 5080.

Gold Catalysts



Cai, P. *et al. Org. Lett.* **2014**, *16*, 5898.



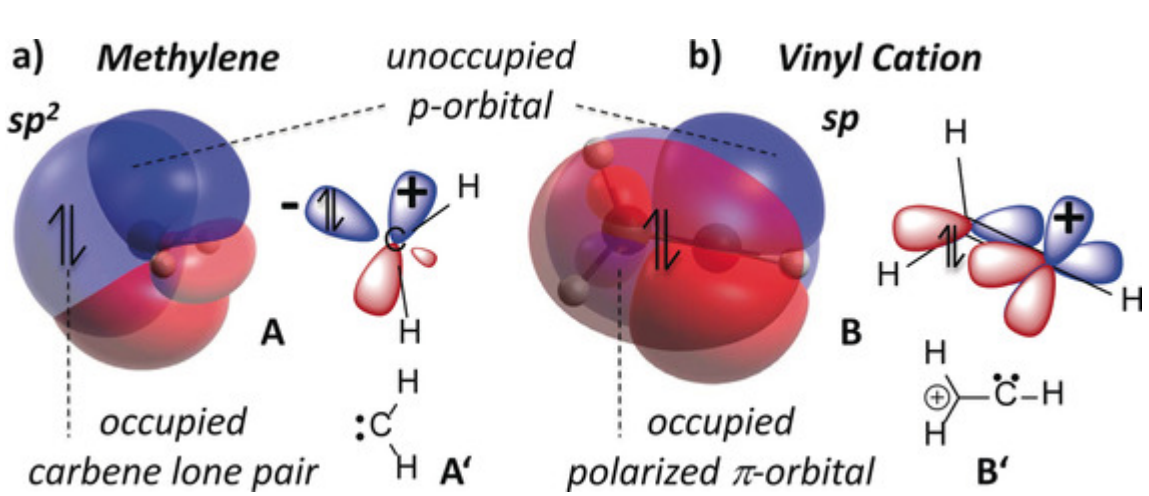
Wang, Y. *et al. J. Am. Chem. Soc.* **2020**, *142*, 2777.

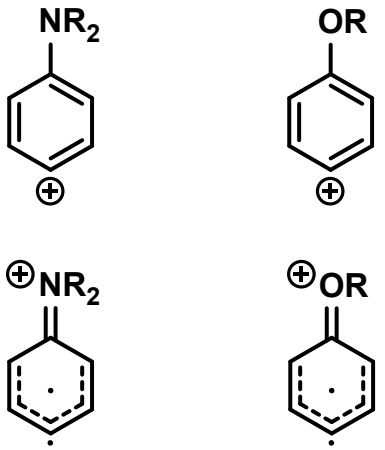
Liu, X. *et al. Sci. China Chem.* **2022**, *65*, 20.

Outline

- Introduction
- Generation of Vinyl Cations
- Reaction of Vinyl Cations
- Summary
- Acknowledgement

Carbene-like Reactivity

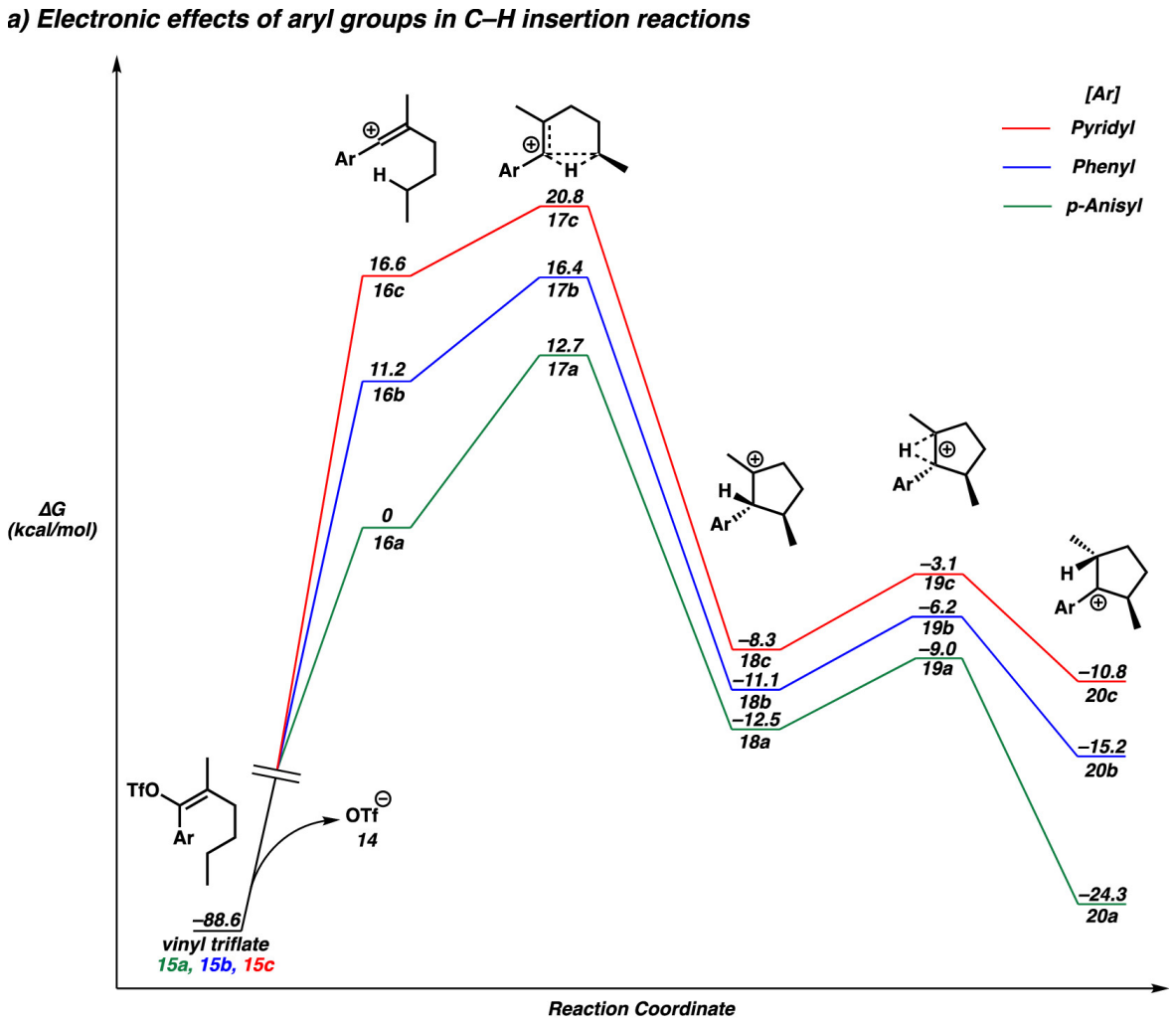




ground state triplet

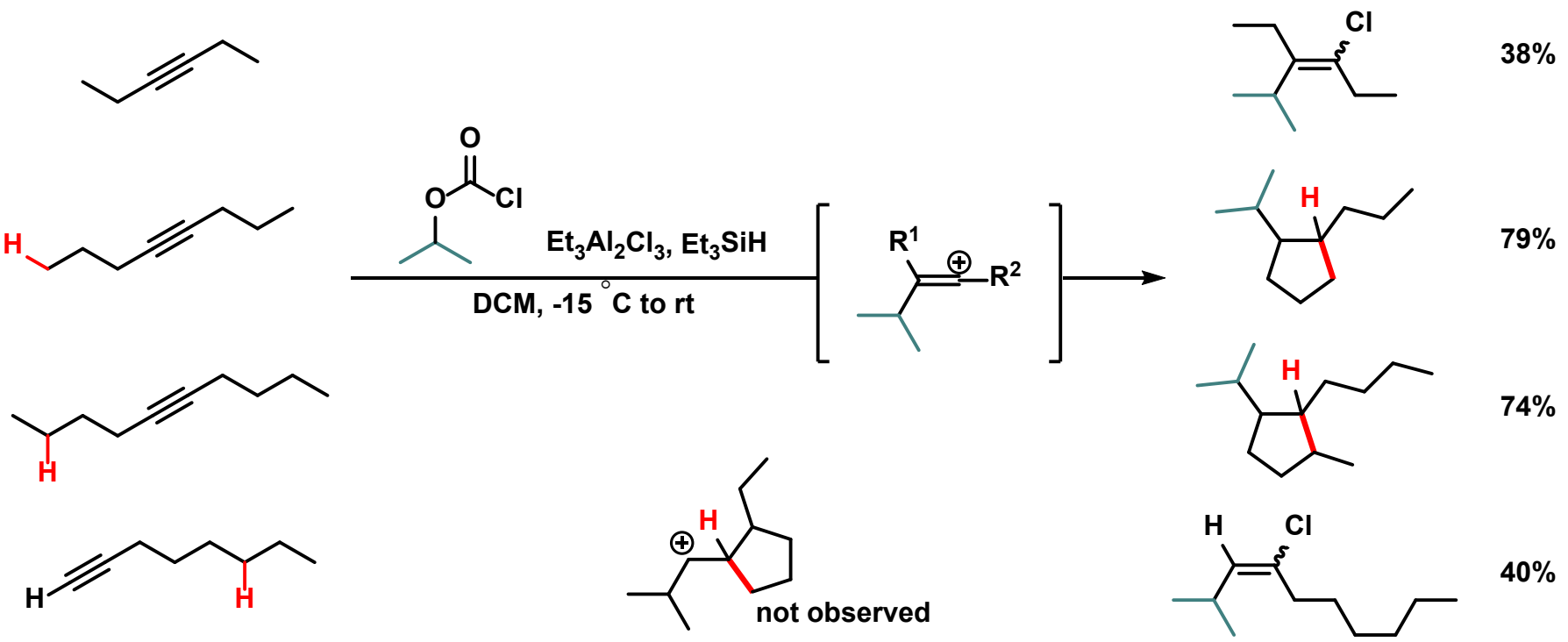
Niggemann, M. and Gao, S. *Angew. Chem., Int. Ed.* **2018**, *57*, 16942

C-H Insertion: Electrophilic Process



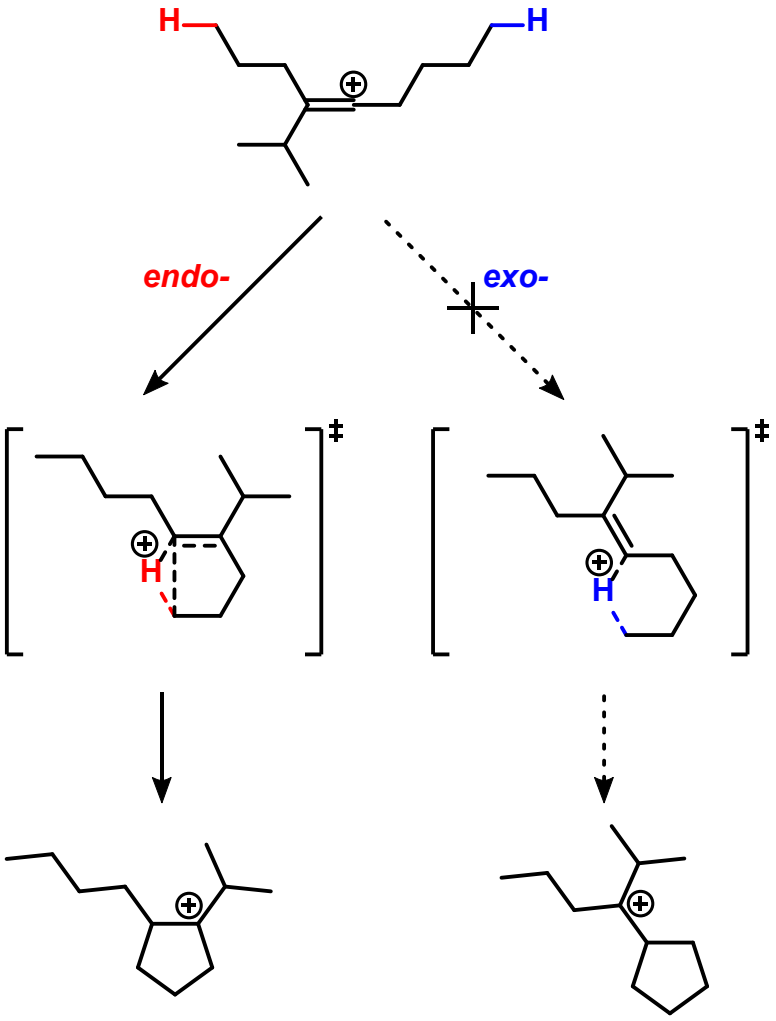
Lee, W. *et al. J. Org. Chem.* **2023**, *88*, 3403.

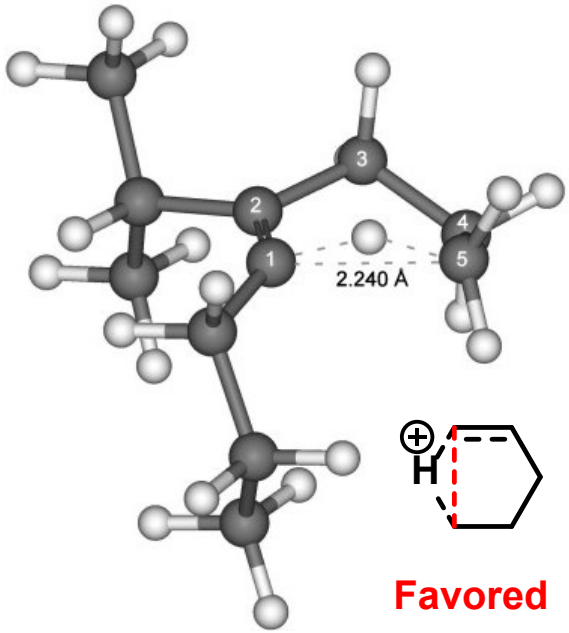
Intramolecular C-H Insertion: Only for *endo-*



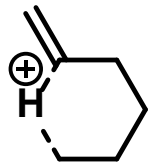
Biermann, U. *et al. Angew. Chem. Int. Ed.* **2006**, *45*, 3076.

Intramolecular C-H Insertion: Only for *endo-*

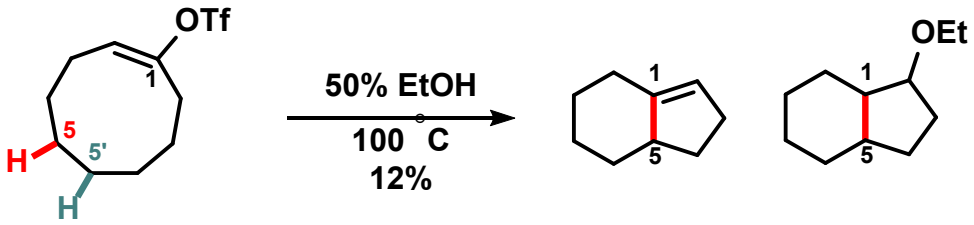




Favored



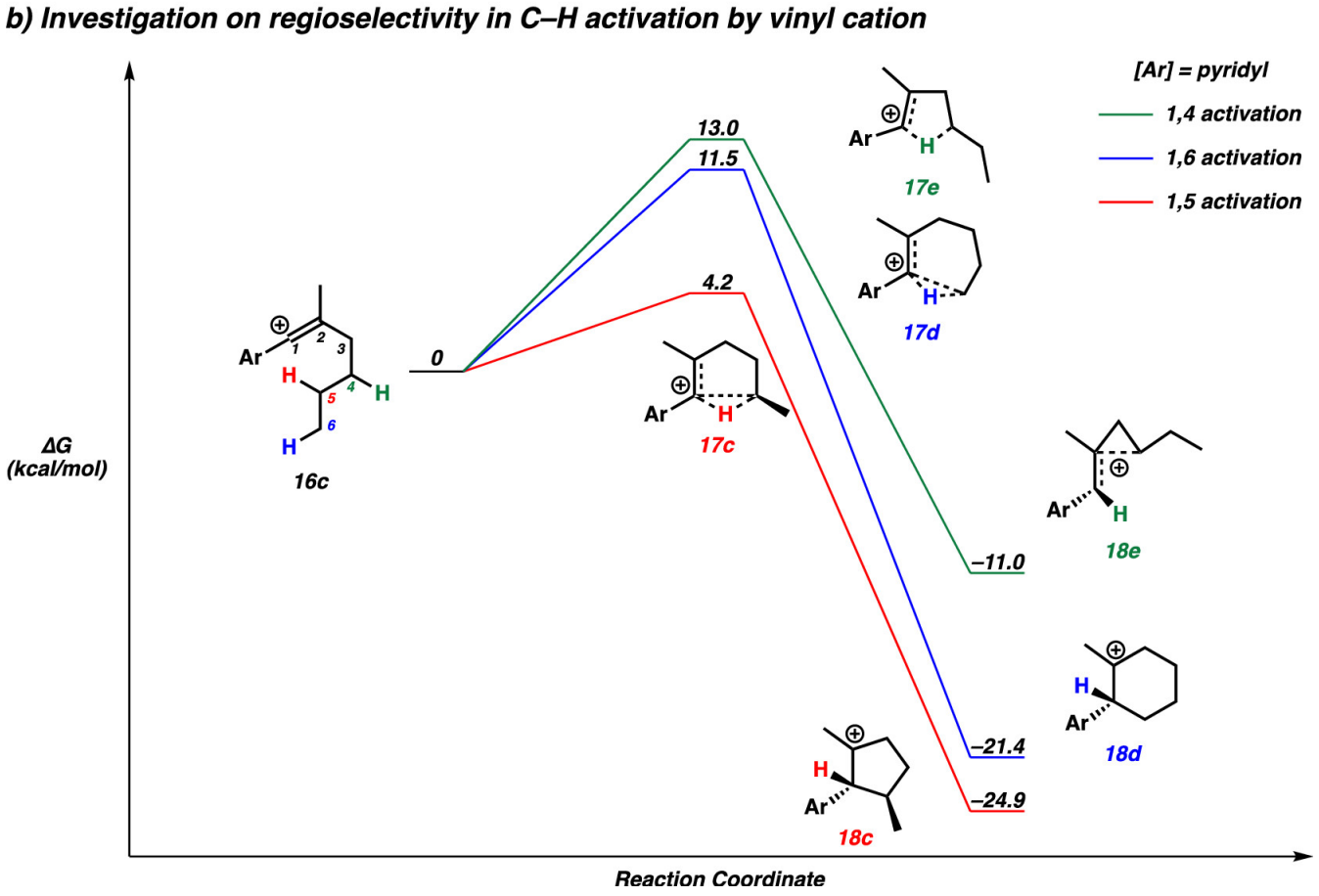
Disfavored



Biermann, U. *et al. Angew. Chem. Int. Ed.* **2006**, *45*, 3076.

Lamparter, E. *et al. Eur. J. Inorg. Chem.* **1972**. *105*, 3789.

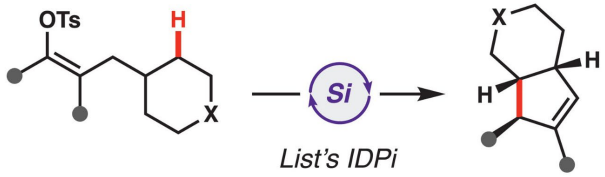
Regioselectivity: 1,5-Insertion Favored



Lee, W. *et al. J. Org. Chem.* **2023**, *88*, 3403.

Asymmetric Intramolecular C-H Insertion

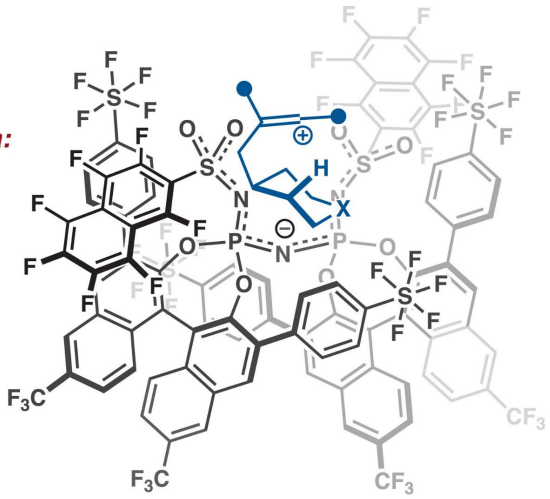
C ***This work: enantioselective vinyl cation C–H insertion reactions***



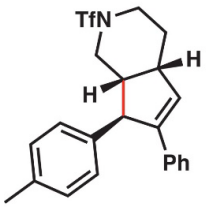
>20 examples

up to 95% yield, >20:1 d.r. & 93% ee

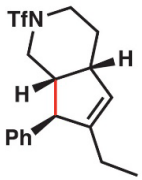
via:



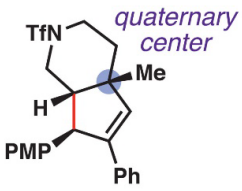
- *enantiocontrol over a dicoordinated vinyl carbocation*
- *organocatalytic asymmetric functionalization of unactivated C(sp^3)–H bonds*



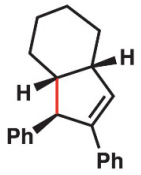
***2a**, 81% yield*
>20:1 d.r.
*91% ee (>99% ee)**



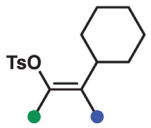
***2t**§, 40% yield*
>20:1 d.r.
75% ee



***2u**‡,§, 81% yield*
>20:1 d.r.
55% ee



2v*, 72% yield*
3.5:1 d.r.
57% ee



15

*IDPi (**3A**) (15 mol%)*
allyl Si(TES)$_3$ (1.3 equiv)
cyclohexane (0.025M)
65 °C, 72 h

16

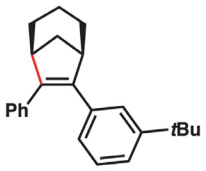
[3.2.1] bicycles

common natural product motifs

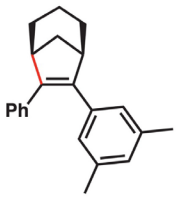
strained bicyclic ring systems

chiral if ● ≠ ●

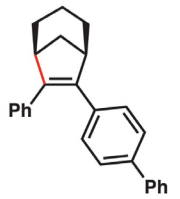
Preliminary studies



***16a**, 48% yield*
77% ee



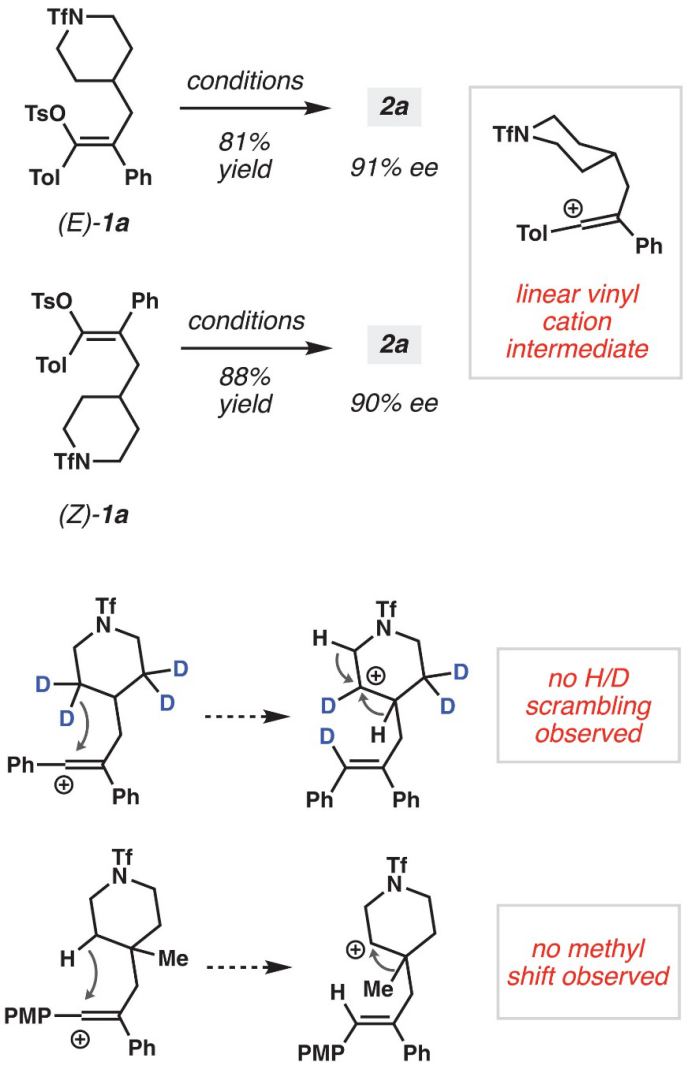
***16b**, 46% yield*
73% ee

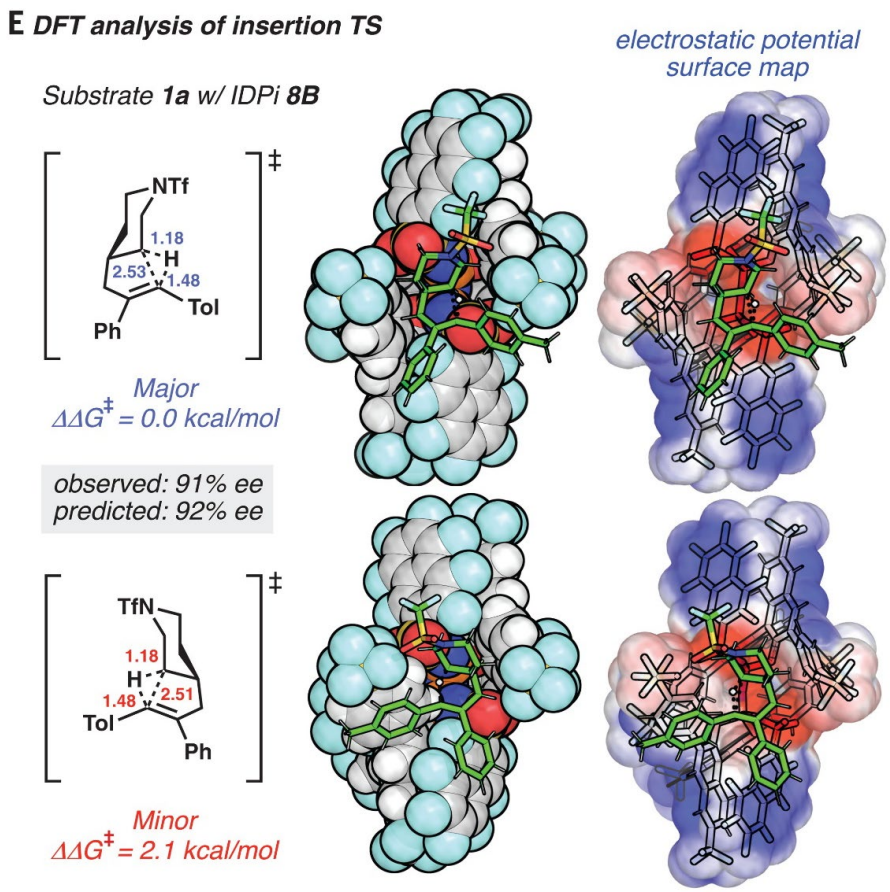


***16c**, 55% yield*
73% ee

Nistanaki, S. K. *et al. Science* **2022**, 378, 1085.

Asymmetric Intramolecular C-H Insertion

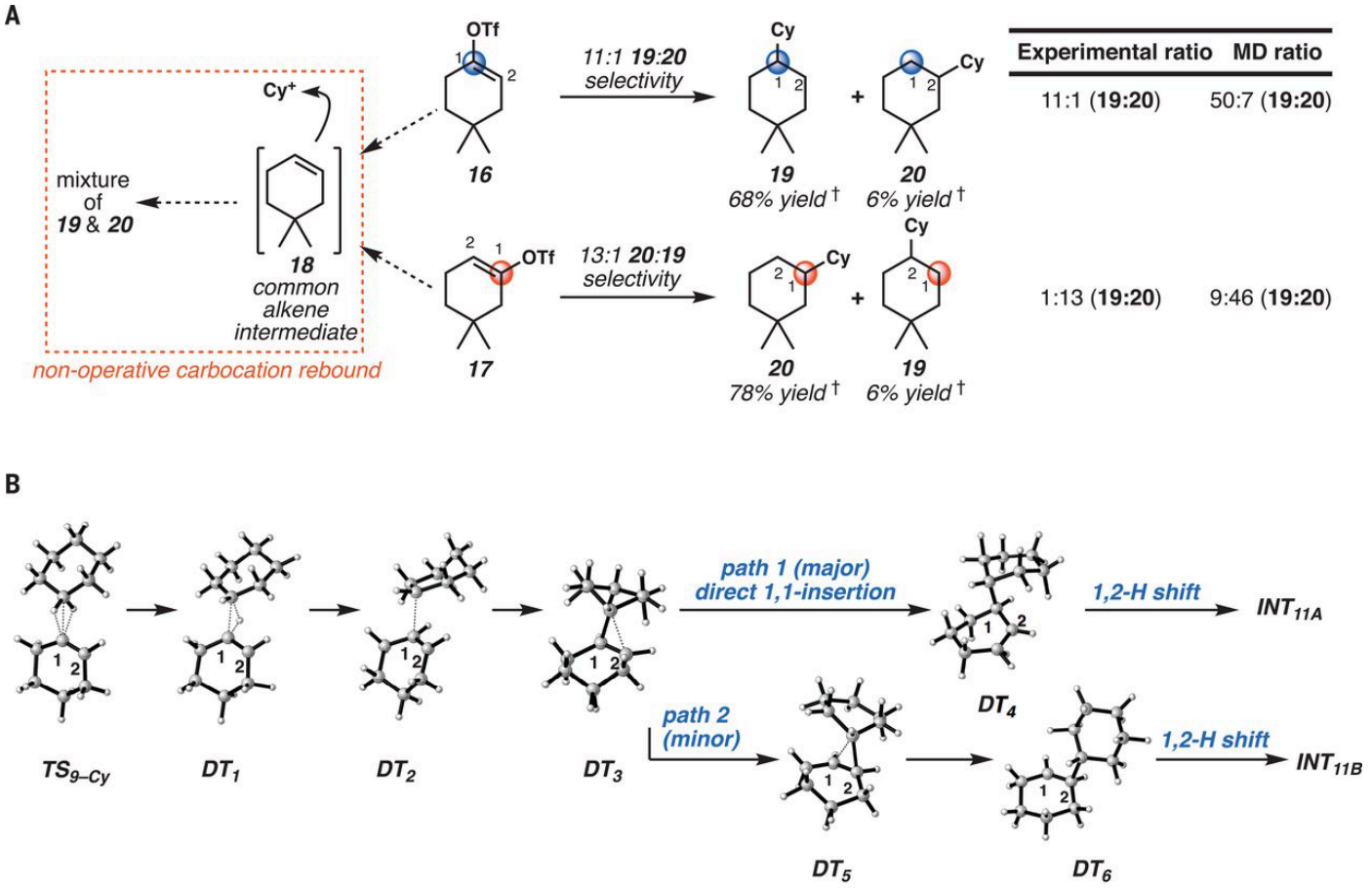




Nistanaki, S. K. *et al. Science* **2022**, 378, 1085.

Intermolecular C-H Insertion

In nonpolar solvents, there's little solvation stabilization for carbocations, so non-classical carbocations are preferred.

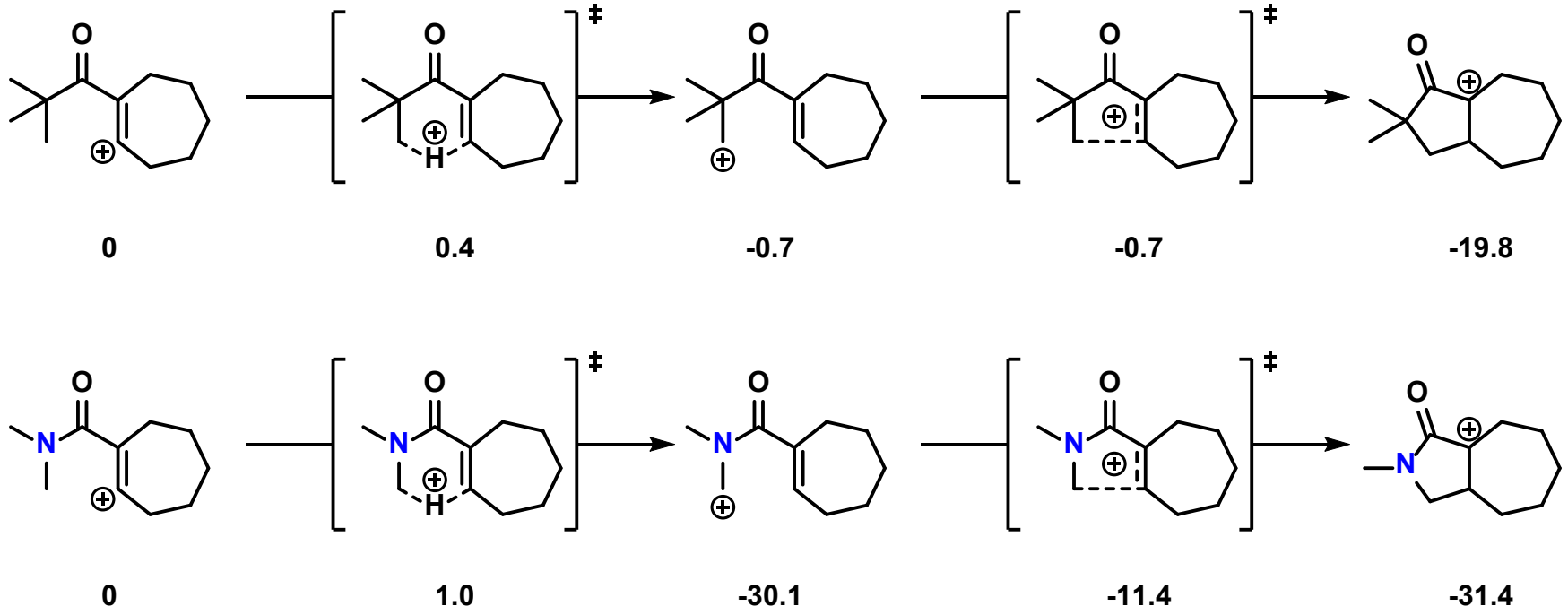


Popov, S. *et al. Science* **2018**, 361, 381.

C-H Insertion vs. Hydride Shift

For C-H bond: electron-rich C-H bonds prefer hydride shift

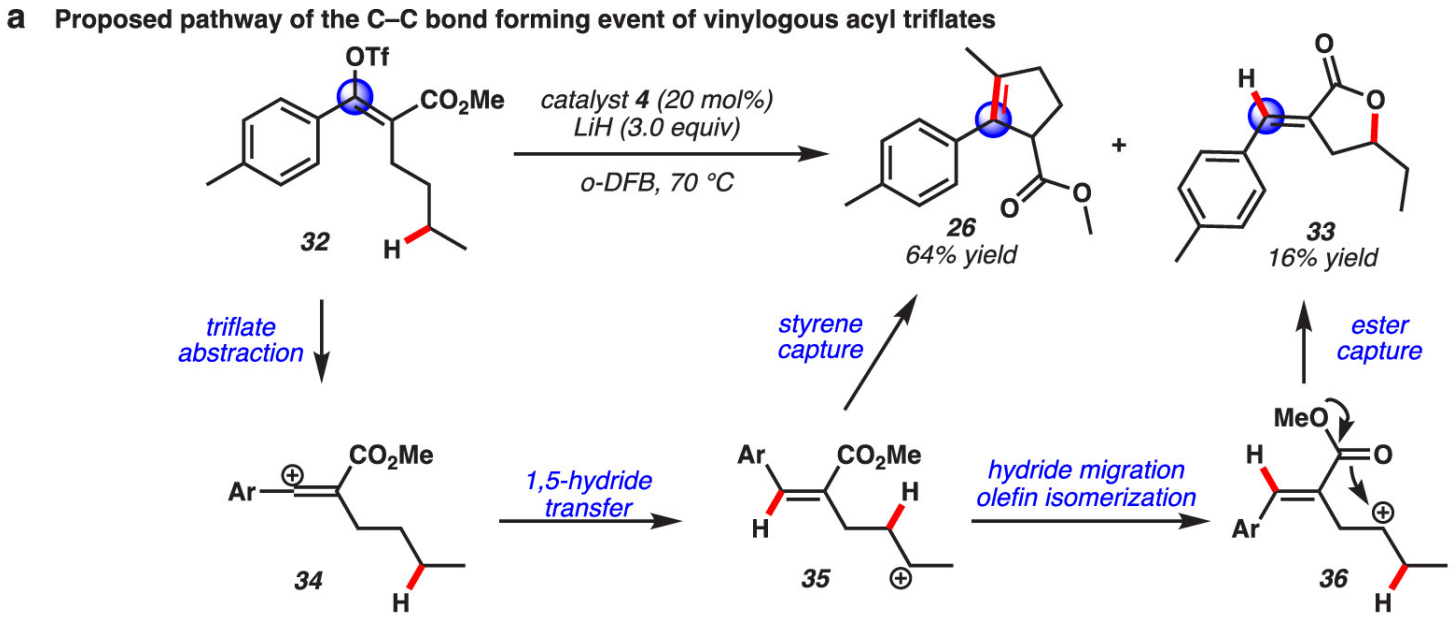
G_{rel} in kcal/mol; B3LYP-D3/6-311+G** //PCM(DCM)//B3LYP-D3/6-311+G** /PCM(DCM)



Cleary, S. E. *et al. J. Am. Chem. Soc.* **2019**, *141*, 3558.

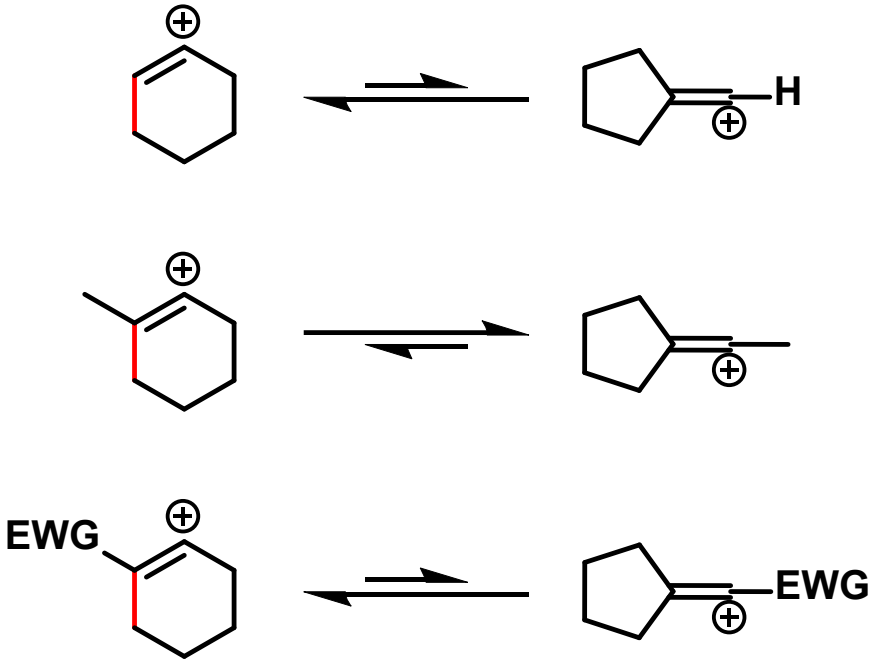
C-H Insertion vs. Hydride Shift

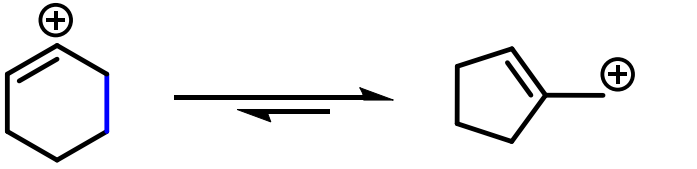
For vinyl cation: when the carbene-like resonance is disfavored, the concerted C-H insertion is not preferred



Bagdasarian, A. L. *et al. Org. Lett.* **2020**, *22*, 7775.

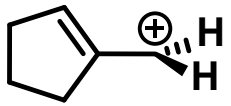
Rearrangement: General Law



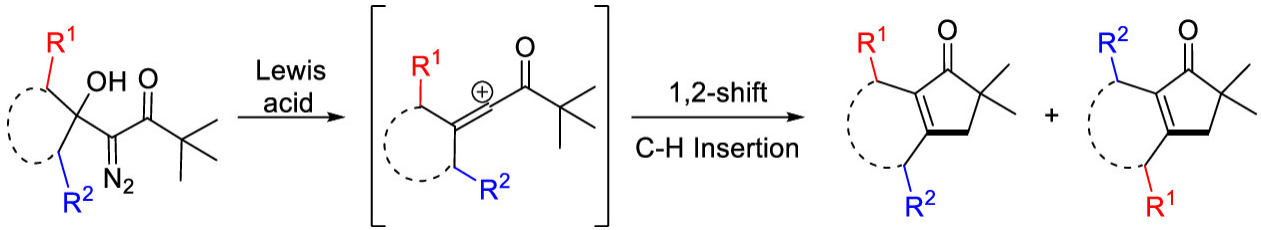


strongly favored

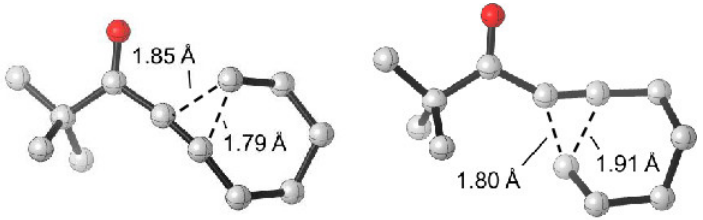
slow due to

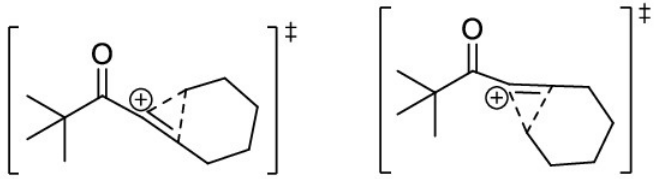


Migration in Destabilized Vinyl Cation



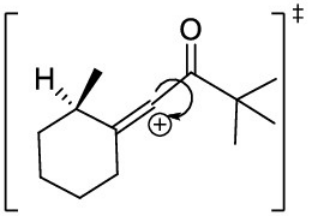
ΔG_{sol}(kcal/mol), B3LYP-D3/6-311+G(d,p)-PCM(DCM)
//B3LYP-D3/6-311+G(d,p)-PCM(DCM)



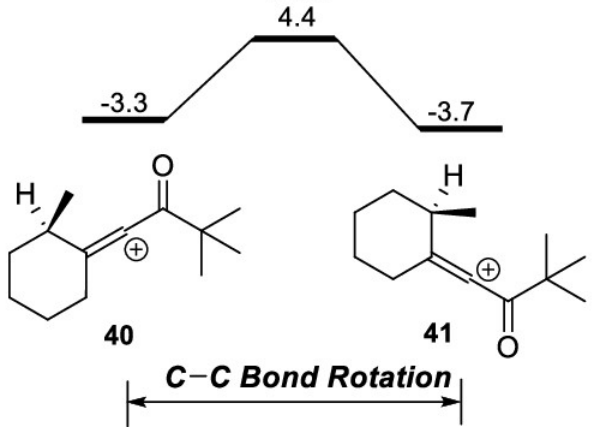


TS1
$\Delta\Delta G^{‡}$ = 0.0 kcal/mol

TS2
$\Delta\Delta G^{‡}$ = 6.9 kcal/mol



TS61



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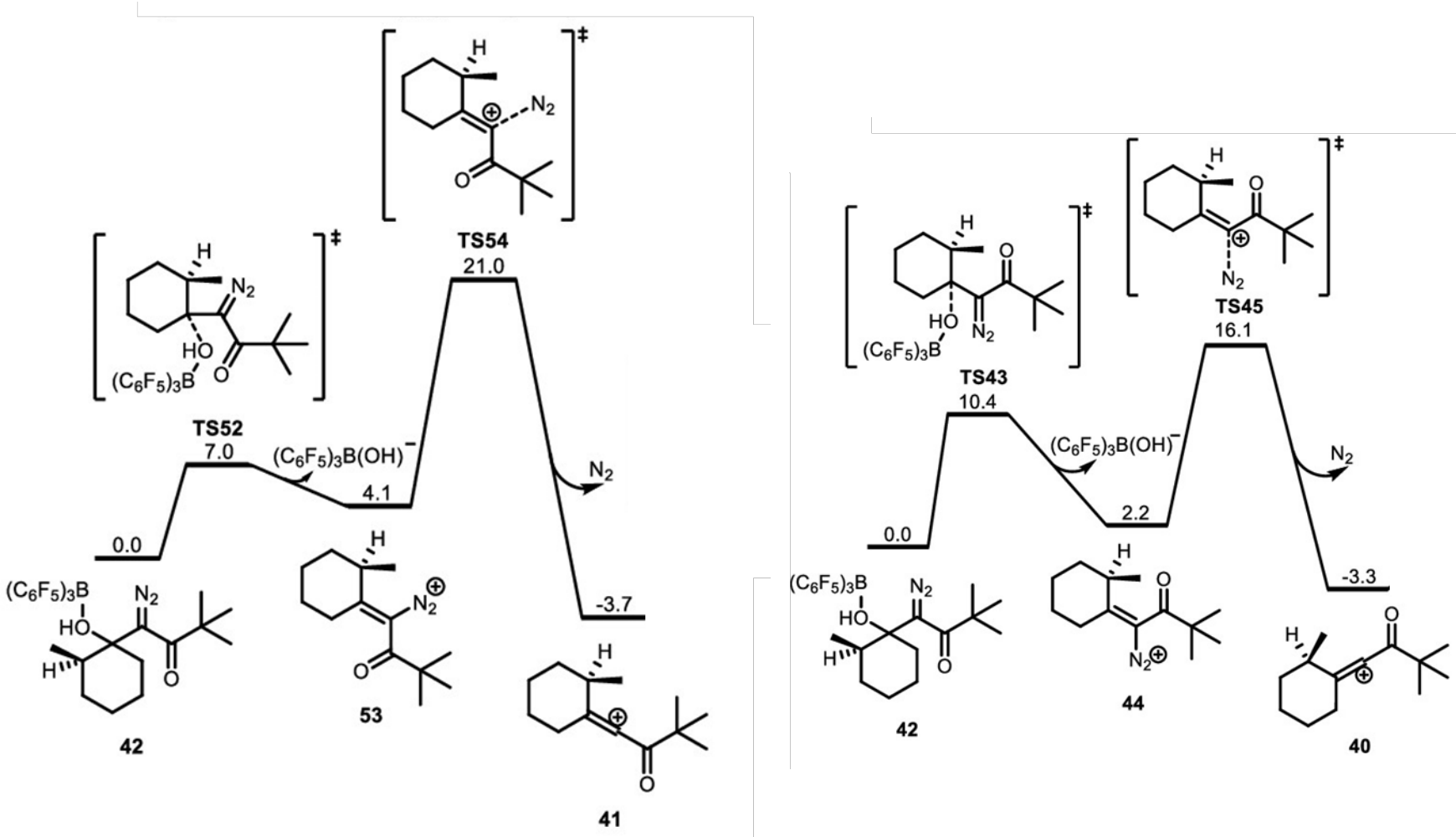
Migration in Destabilized Vinyl Cation



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Outline

- Introduction
- Generation of Vinyl Cations
- Reaction of Vinyl Cations
- Summary
- Acknowledgement

Summary and Outlook

- Stability: no significantly more labile than normal trisubstituted carbocations, albeit harder in generation
- Carbene-like reactivity: spatial controlled C-H insertion
- Generation of vinyl cation: need for mild condition with better functional group compatibility