Heterocyclic Scaffolds via Photolysis of Vinyldiazo Compound

2024.7.26 Literature Seminar

M1 Yo Matsumoto

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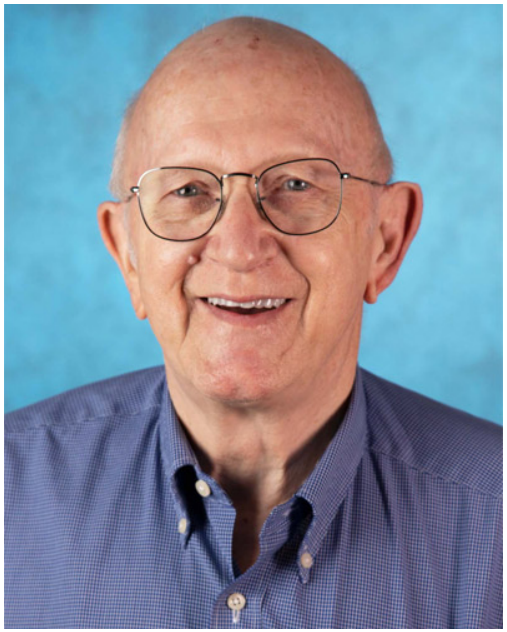
Introduction of Authors



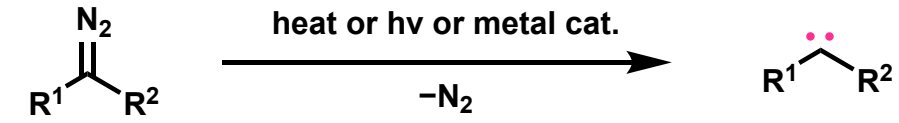
Prof. Michael P. Doyle

Career:
1964: B.S. @ University of St. Thomas
1968: Ph.D. @ Lowa State University (Prof. Walter S. Trahanovsky)
1968: Postdoc @ University of Illinois Chicago (Prof. Jan Rocek)
1968-1971: Assistant Professor @ Hope College
1971-1974: Associated Professor @ Hope College
1974-1984: Professor @ Hope College
1984-1997: Professor @ Trinity University
1997-2003: Professor @ University of Arizona
2003-2014: Professor @ University of Maryland
2015-present: Professor @ Univesity of Texas at San Antonio

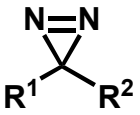
Research Topics:
Catalytic oxidation processes, Design and development of chiral catalysts, Diazo chemistry, Highly enantioselective catalytic reactions, Medicinal chemistry

https://sciences.utsa.edu/faculty/profiles/doyle-michael.html

Diazo-Compound and Carbene

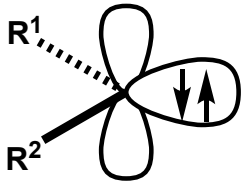


diazoalkane



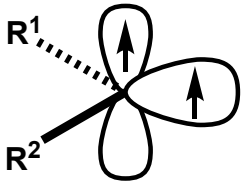
diazirine[1)]

Singlet Carbene



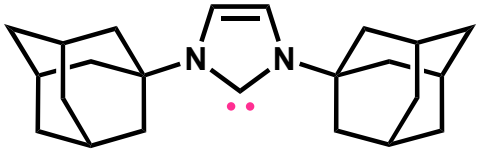
sp^2 : 2 electrons
p : 0 electrons

Triplet Carbene



sp^2 : 1 electron
p : 1 electron

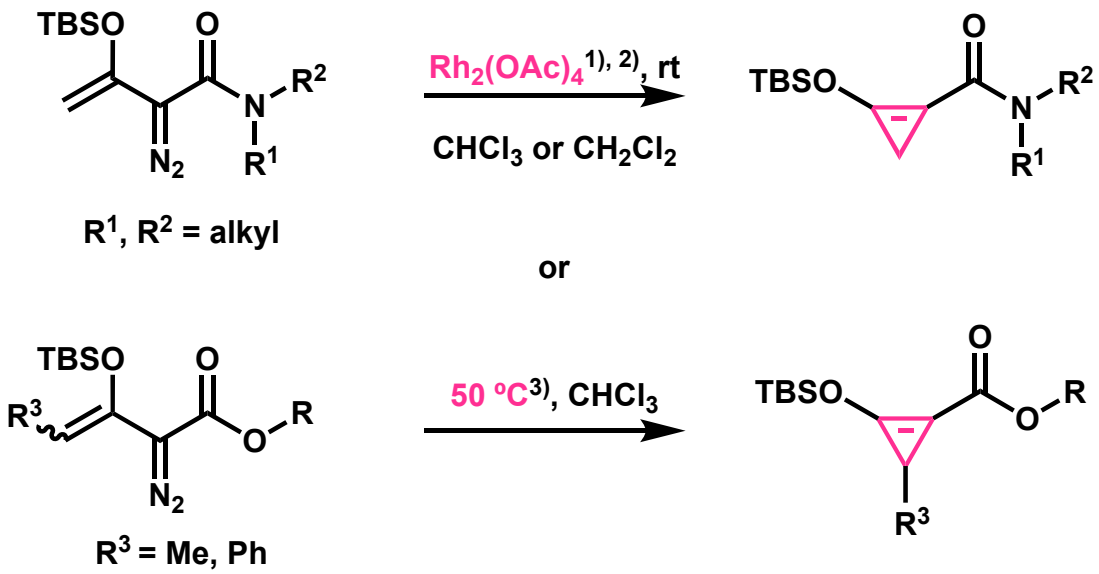
Application of singlet carbene
ex.) NHC (N-Heterocyclic Carbene)



relatively stable:
electron donation to the p-orbital of carbene by the lone pair of electrons of nitrogen atom

1) Diazirine was covered by 211203_LS_Lin_Yuanqi

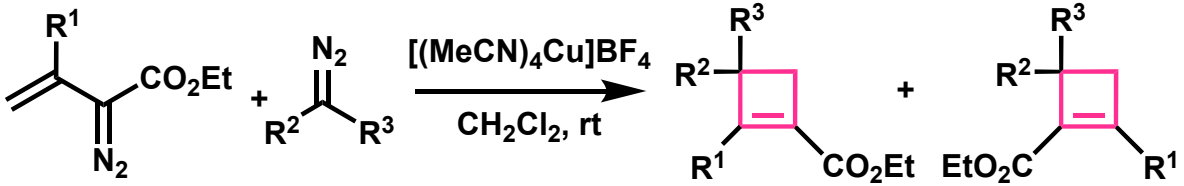
Intramolecular Cyclization of Vinyldiazo Compound



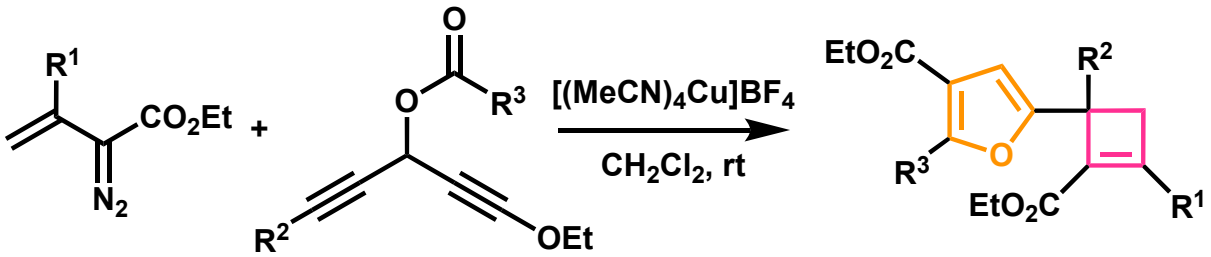
1) Davis, H. M. L.; Hu, B.; Saikali, E.; Bruzinski, P. R. *J. Org. Chem.* **1994**, *59*, 4535
2) Davis, H. M. L.; Houser, J. H.; Thornley, C. *J. Org. Chem*. **1995**, *60*, 7529
3) Deng, Y.; Jing, C.; Doyle, M. P. *Chem. Commun*. **2015**, *51*, 12924

Previous Research for Vinyldiazo Compound

Tomás's group (2009)[1)]

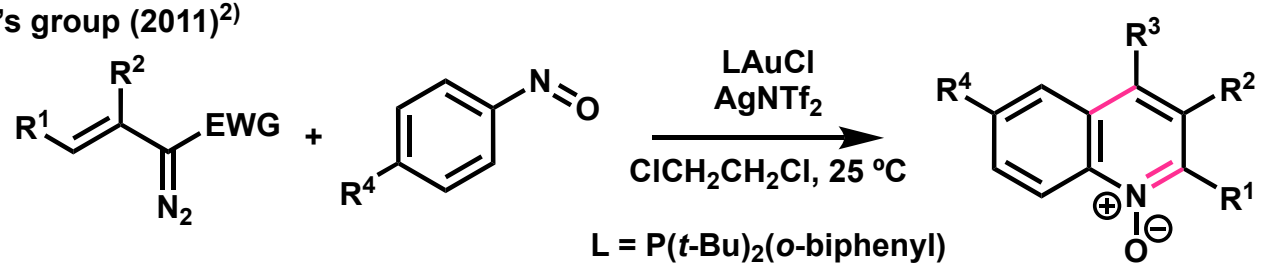


(R^1 = H or Me, R^2 = ester or Ph, R^3 = H or Ph or 4-$MeOC_6H_4$)



(R^1 = H or Me, R^2 = Ph or Cy or cyclopropyl, R^3 = Me or Et or Pr)

Liu's group (2011)[2)]

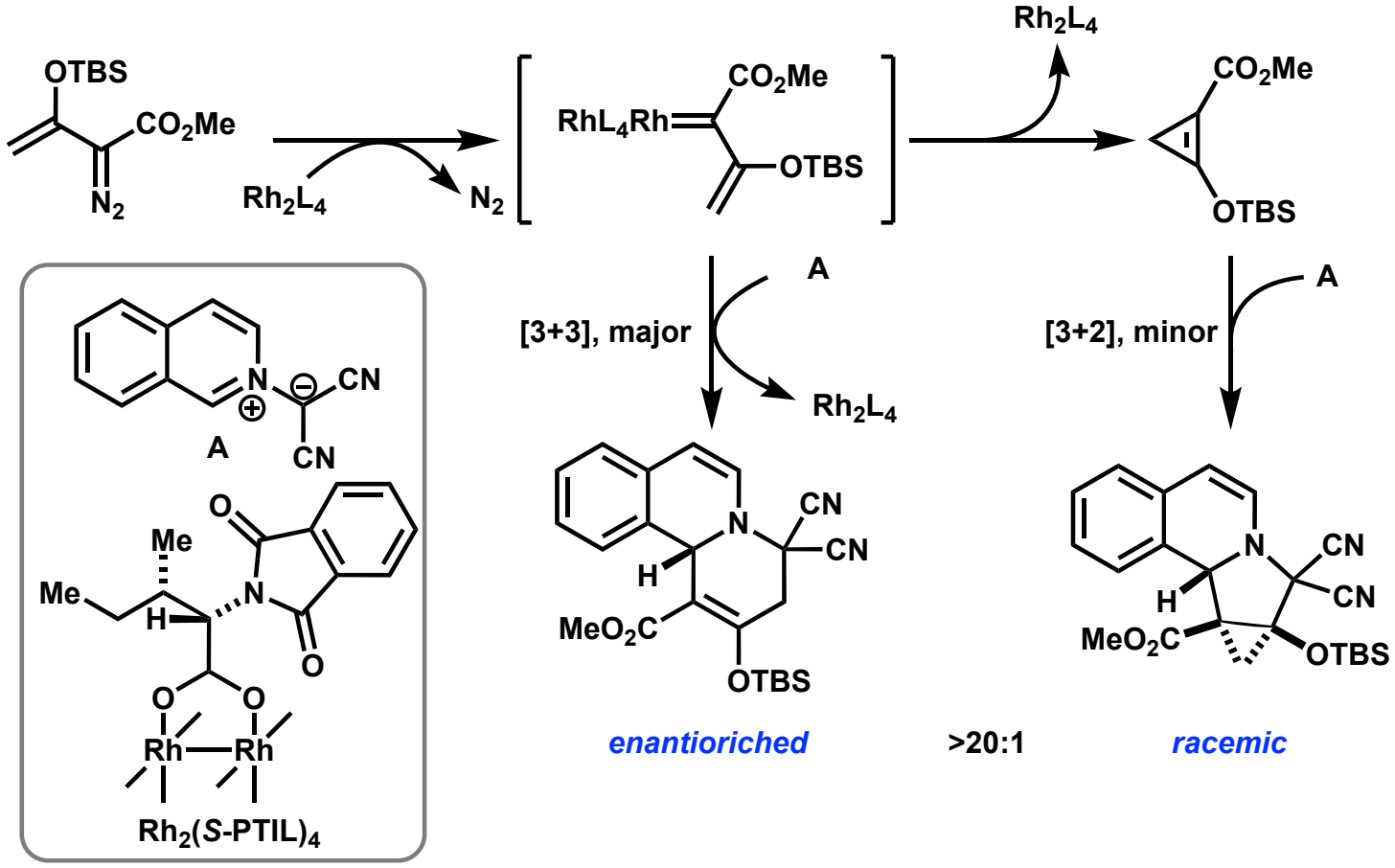


L = P(*t*-Bu)$_2$(*o*-biphenyl)

(R^1 = H or Me or Et or Cl or MeO, R^2 = H or Me or *n*-Bu or aryl, R^3 = ester)

1) Barluenga, J.; Riesgo, L.; López, L. A.; Rubio, E.; Tomás, M. *Angew. Chem.* **2009**, *121*, 7705
2) Pagar, V. V.; Jadhav, A. M.; Liu, R.-S. *J. Am. Chem. Soc.* **2011**, *133*, 20728

[3+3]-Cycloaddition of Isoquinolinium-dicyano-methylides and Enol Diazoacetates



Xu, X.; Zavalij, P. Y.; Doyle, M. P. *J. Am. Chem. Soc.* **2013**, *135*, 12439

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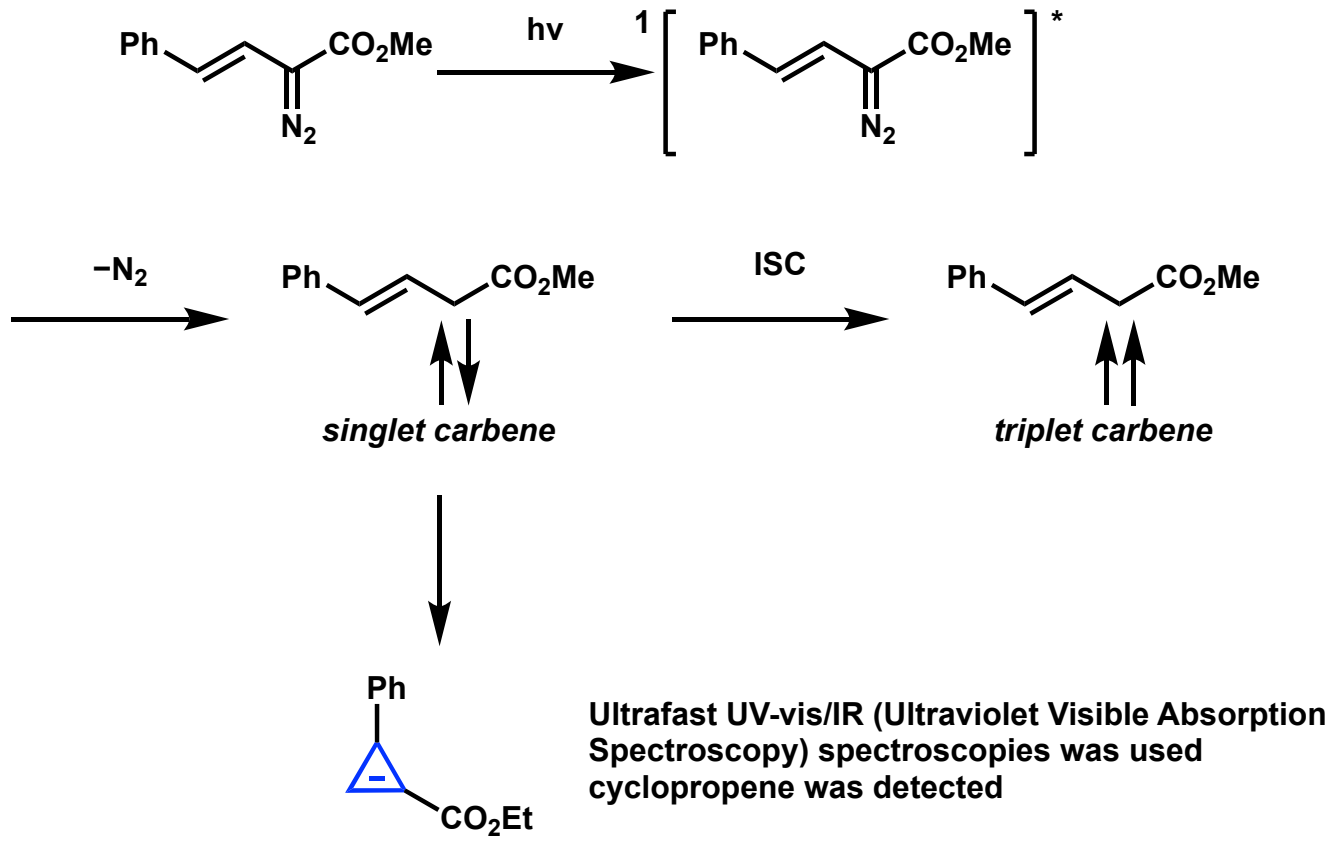
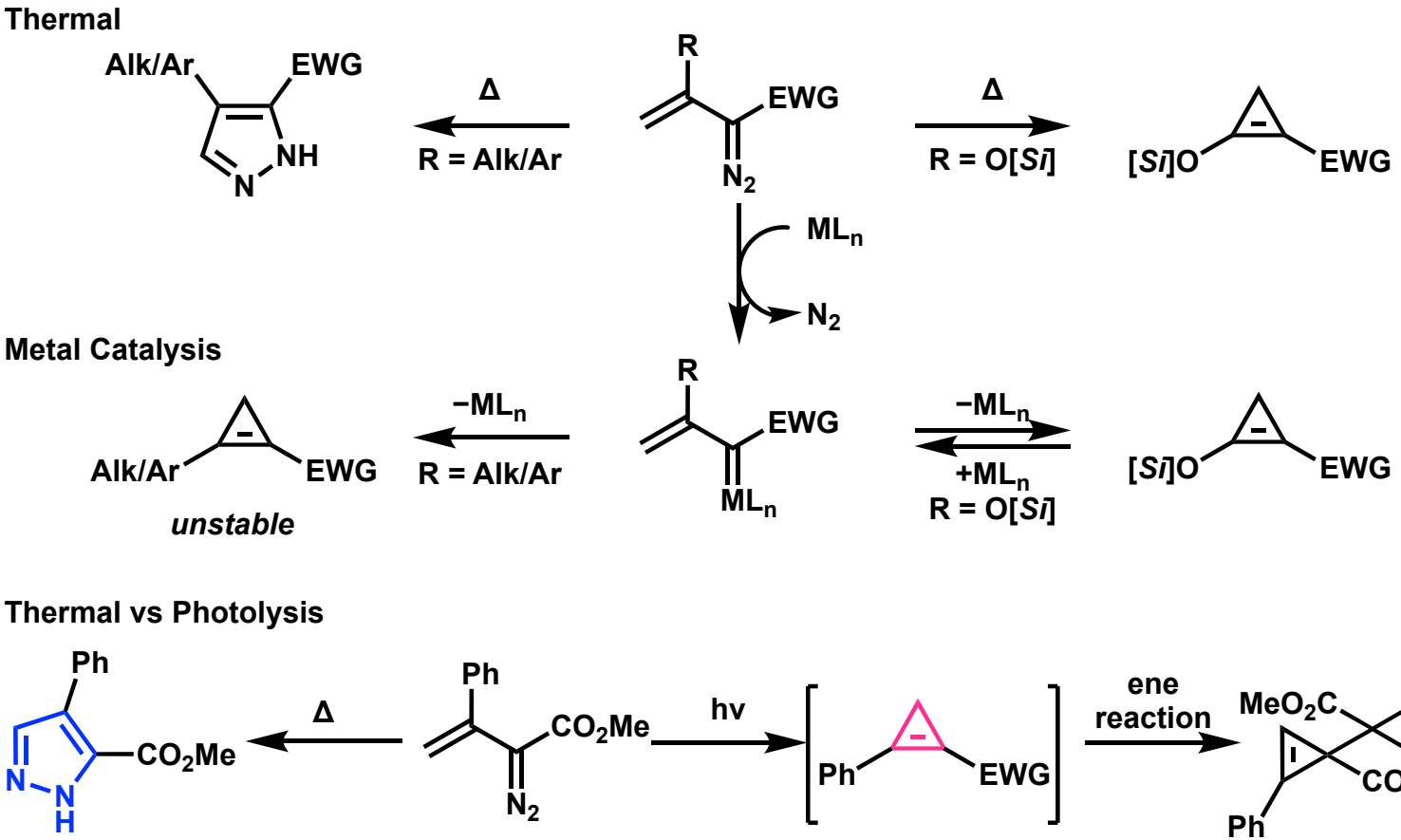
Reactivity of Vinyldiazo Compounds



Ultrafast UV-vis/IR (Ultraviolet Visible Absorption Spectroscopy) spectroscopies was used cyclopropene was detected

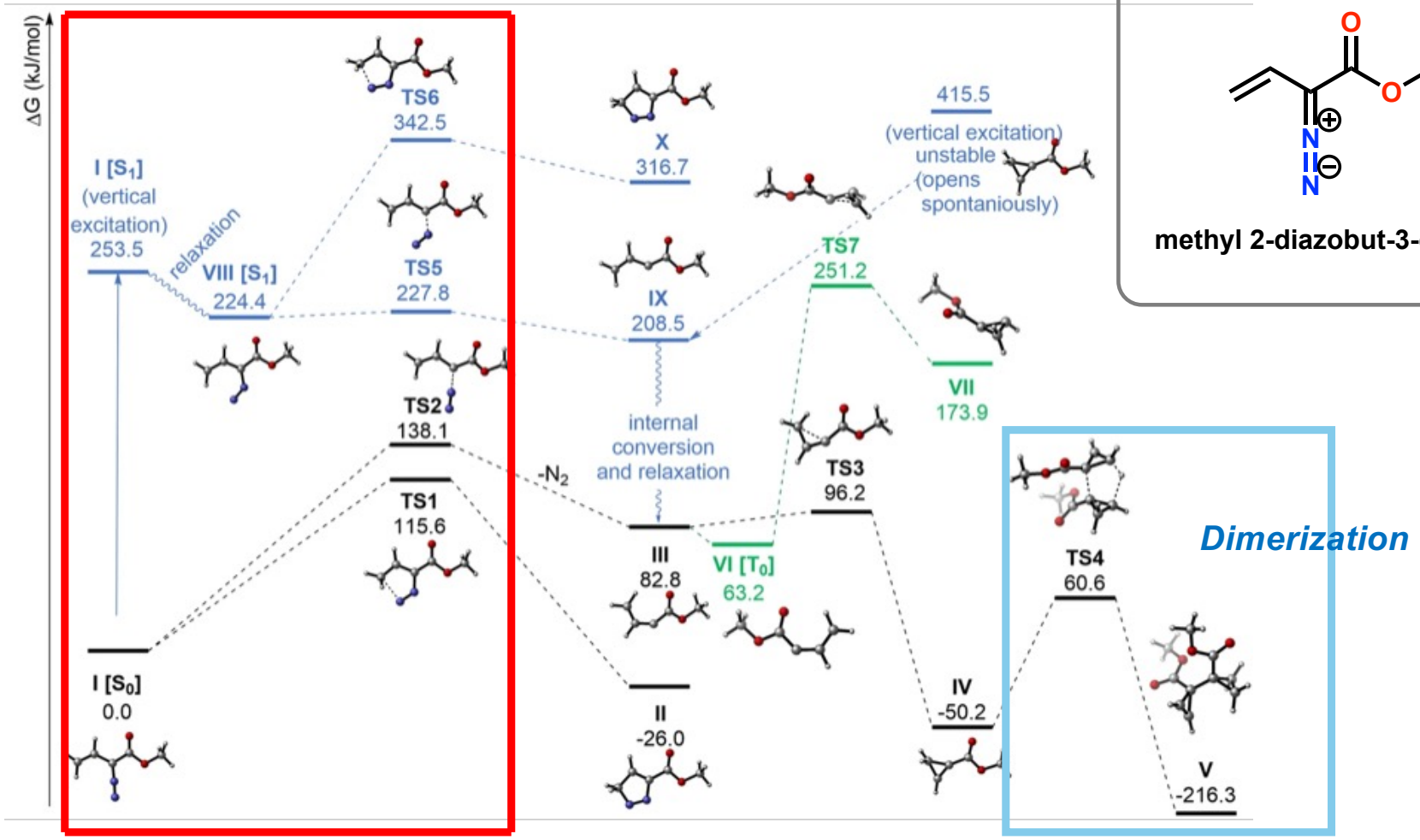
Zhang, Y.; Kubicki, J.; Platz, M. S. *J. Am. Chem. Soc.* **2009**, *38*, 13602

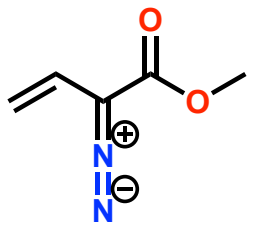
Reactivity of Vinyldiazo Compound



1) Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

DFT Study of Photolysis(1)

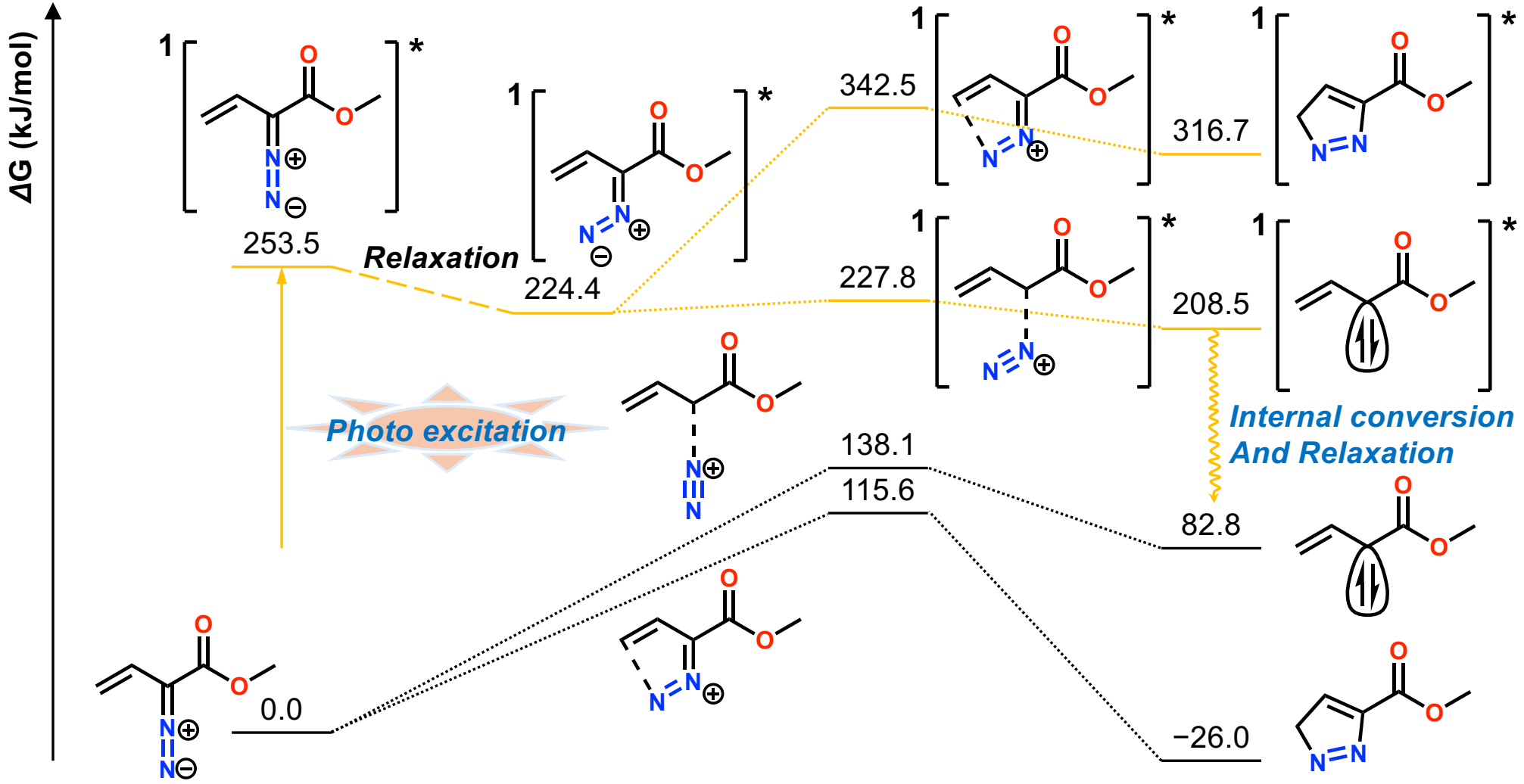




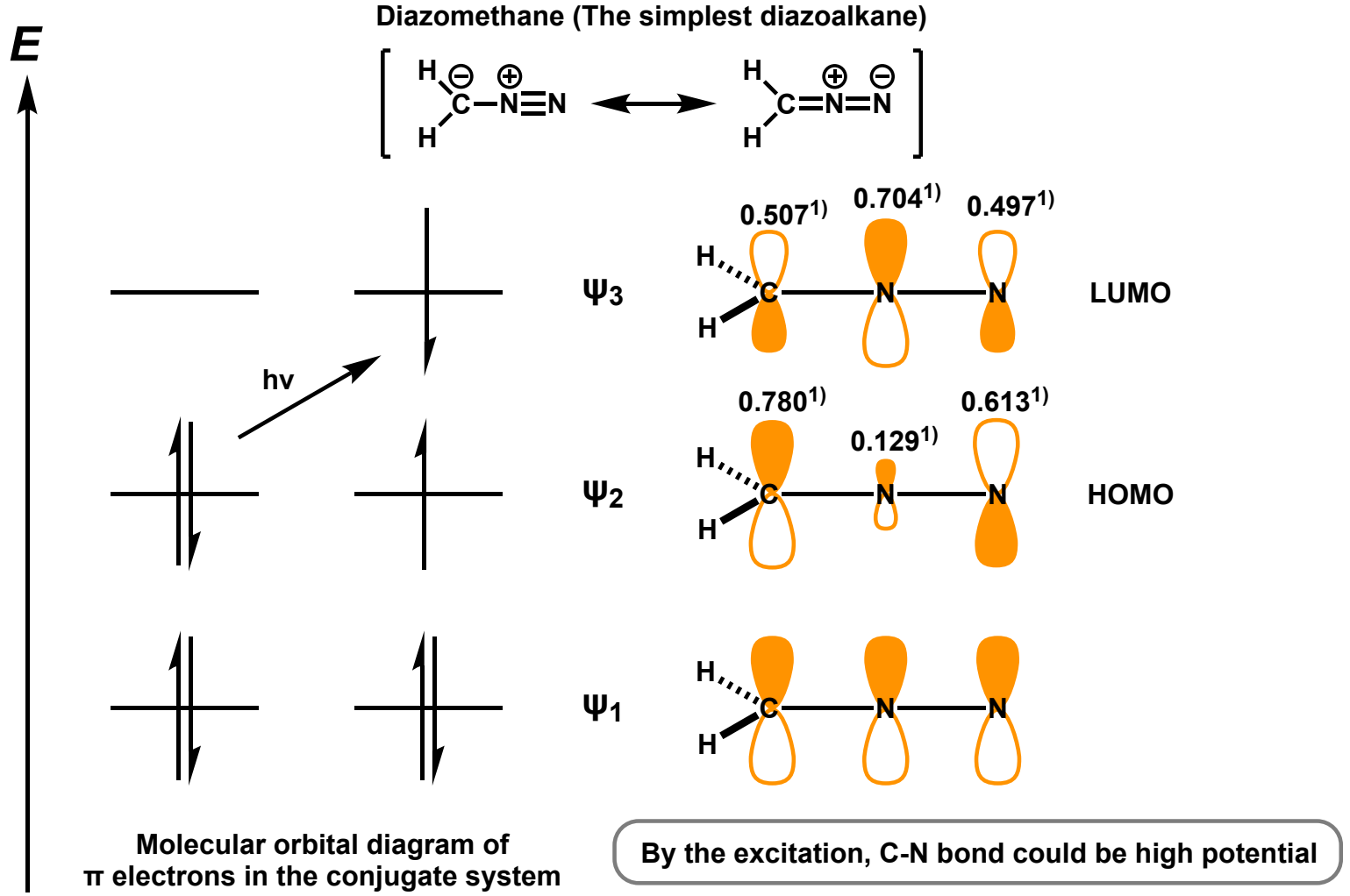
methyl 2-diazobut-3-enoate

Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

DFT Study of Photolysis(2)

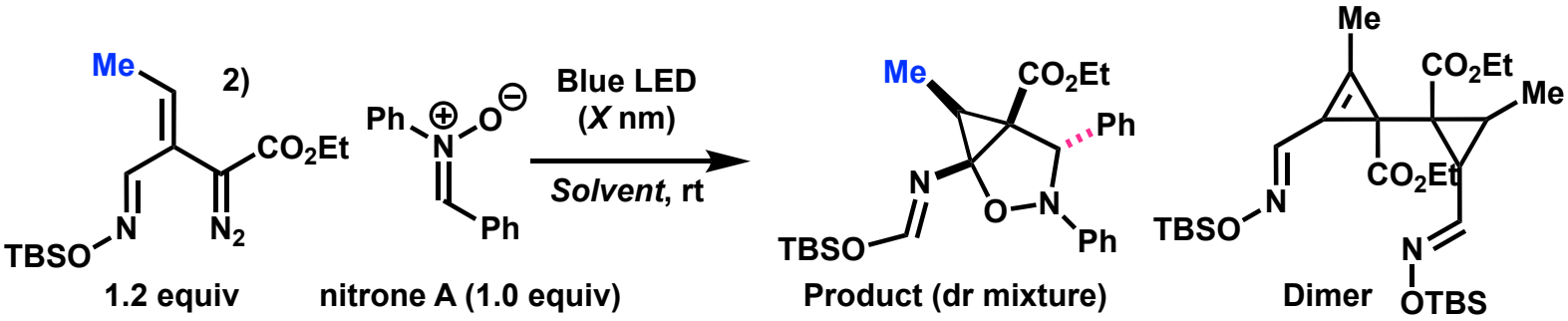


My Opinion about Photolysis of Diazo-Compound



1) Houk, K. N.; Sims, J.; Duke, Jr., R. E.; Strozier, R. W.; George, J. K. *J. Am. Chem. Soc.* **1973**, *22*, 7193

Model [3+2] Cycloaddition Reaction with Nitrones: Optimization of Experimental Conditions[1)]

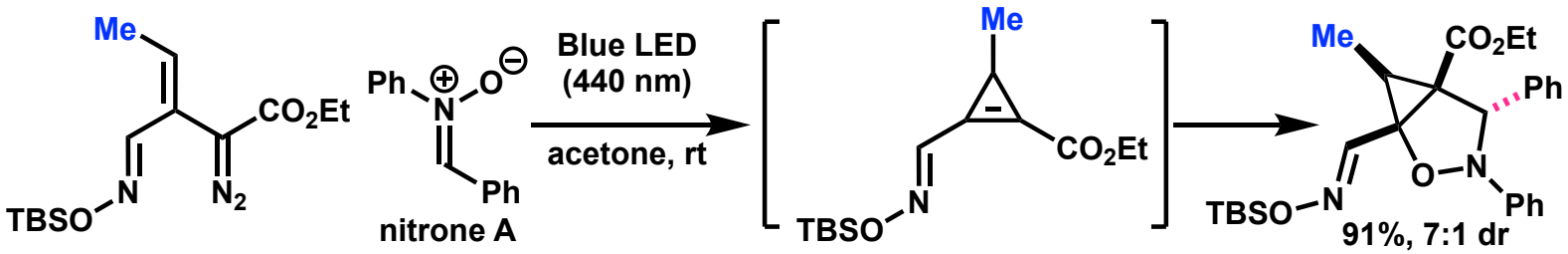


1.2 equiv | nitrone A (1.0 equiv) | Product (dr mixture) | Dimer

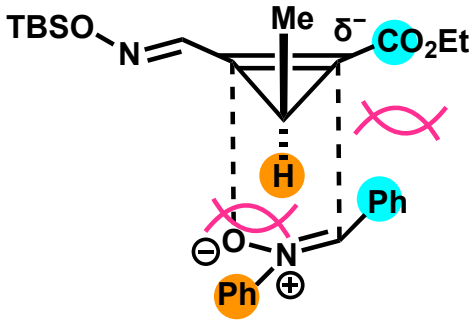
Solvent	*X*	*Product/Dimer Yields (%)*	*dr*
CH_2Cl_2	440	87/8	3:1
THF	440	80/15	5:1
MeCN	440	83/13	6:1
Acetone	440	90/<5	7:1
Acetone	400	30/65	5:1
Acetone	350	Not Detected/80	-

1) Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574
2) Bao, M.; Angelis, L. D.; Rada, M. S.; Baird, M.; Arman, H.; Wherritt, D.; Doyle, M. P. *Chem. Catalysis.* **2023,** *10*, 100778

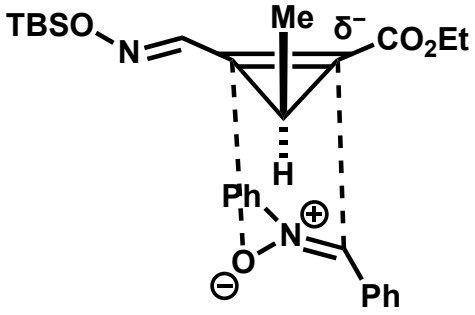
Model [3+2] Cycloaddition Reaction with Nitrones



Regioselectivity of [3+2] Cycloaddition



disfavored
$\Delta G^{\ddagger}$ = 90.0 kJ/mol

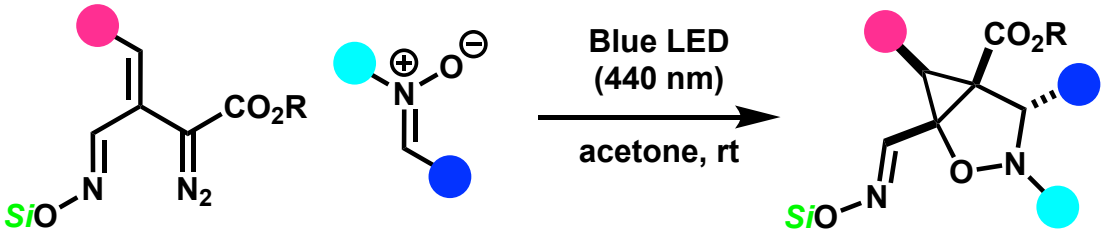


favored
$\Delta G^{\ddagger}$ = 85.2 kJ/mol

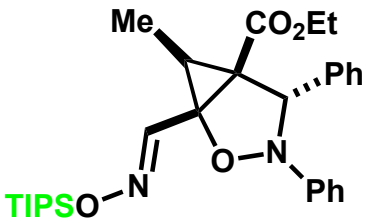
***DFT calculation was conducted by authors. Nitrone A is the standard for DFT calculation**

Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

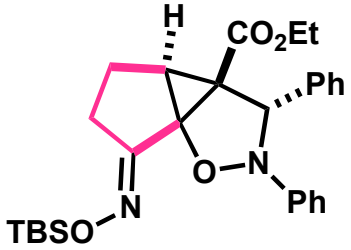
Substrate Scope of [3+2]-Cycloaddition of Nitrones



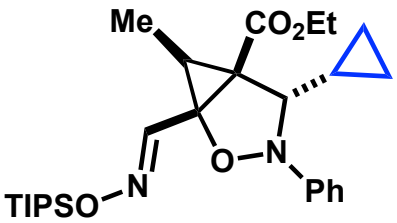
Oximidovinyldiazoacetates | **Nitrones**



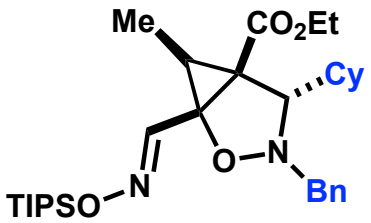
92%, 7:1 dr



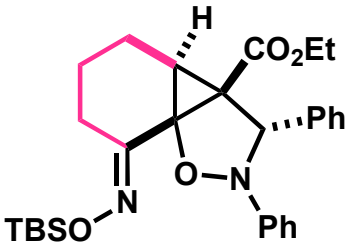
85%, 10:1 dr



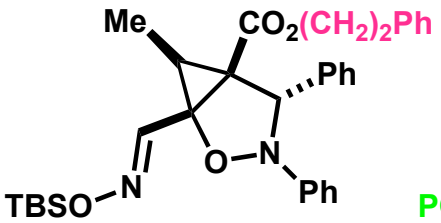
85%, 10:1 dr



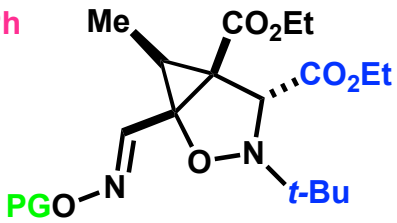
86%, 4:1 dr



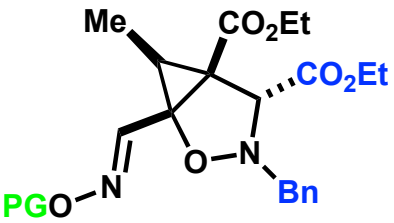
82%, 2:1 dr



84%, 8:1 dr



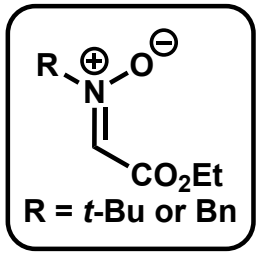
PG = TIPS: 53%, 99:1 dr
PG = H: 63%, 99:1 dr

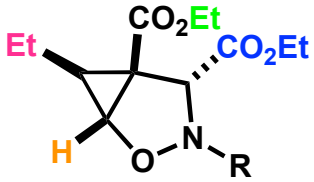


PG = TIPS: 33%, 2:1 dr
PG = H: 84%, 2:1 dr

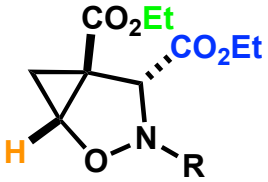
Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

[3+2]-Cycloaddition of Nitrones Via More Unstable Cyclopropene

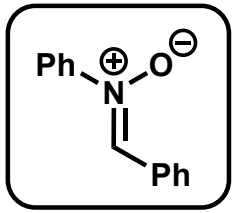


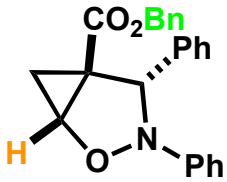


R = *t*-Bu: 49%, 99:1 dr
R = Bn: 48%, 1:1 dr

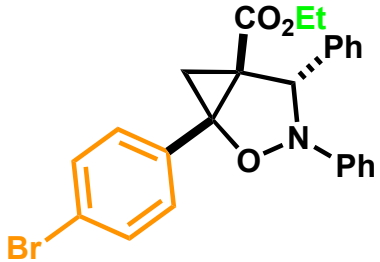


R = *t*-Bu: 40%, 99:1 dr
R = Bn: 30%, 1:1 dr





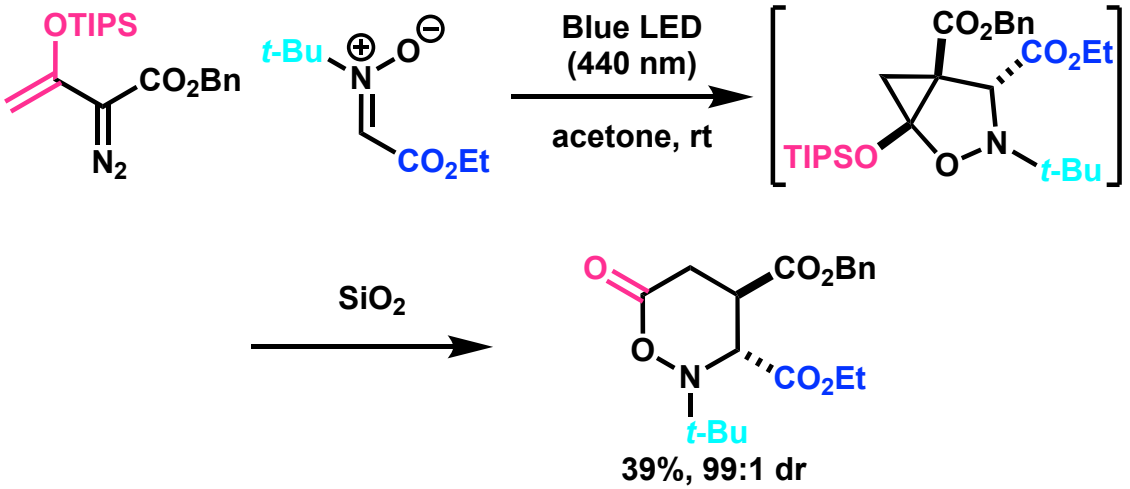
70%, 10:1 dr



78%, 15:1 dr

Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

[3+2]-Cycloaddition of Nitrones Via Relatively Stable Cyclopropene

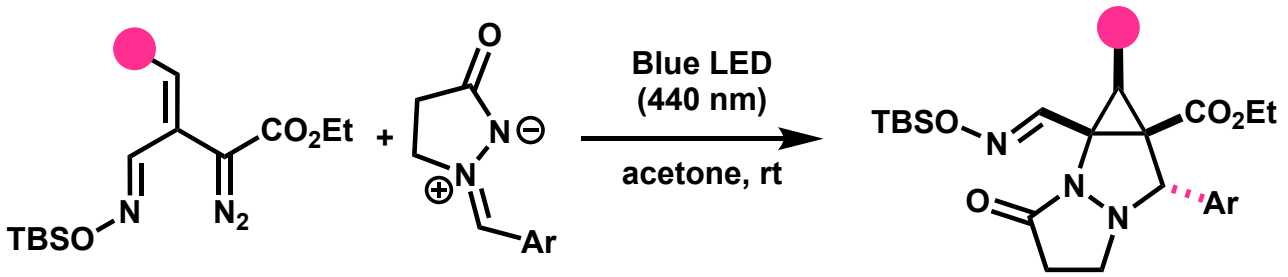


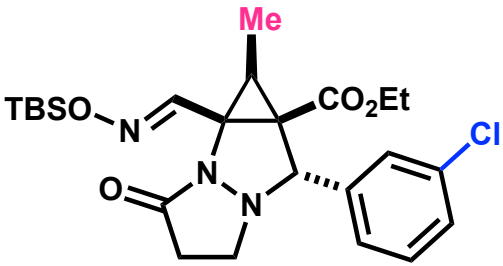
39%, 99:1 dr

- ring-opening of cyclopropane: its stalability of distorted ring
- disprotection of TIPS: acidity of silicagel

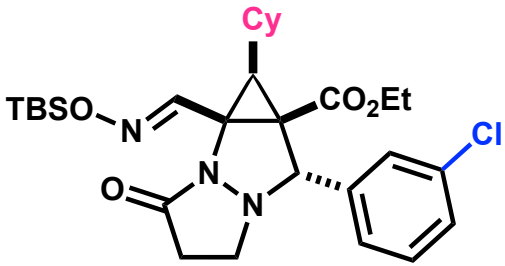
Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

[3+2]-Cycloaddition of Azamethine Imines

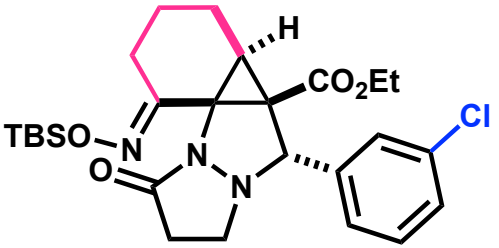




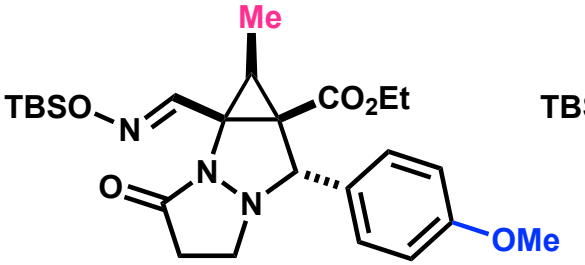
85%, 10:1 dr



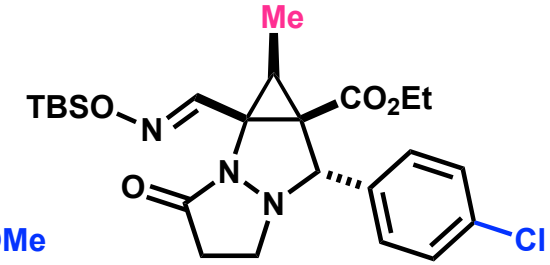
85%, 10:1 dr



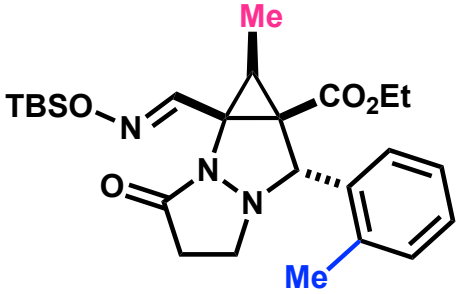
70%, 3:1 dr



73%, 10:1



75%, 5:1



79%, 8:1

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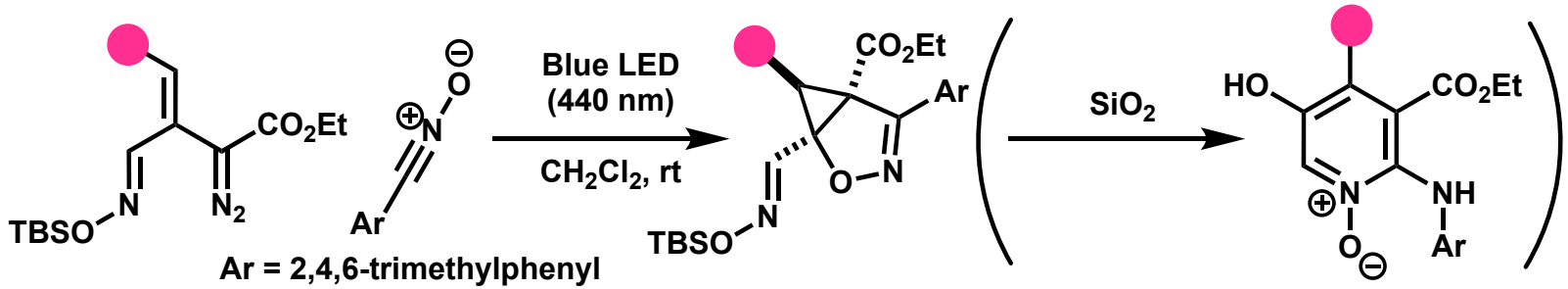
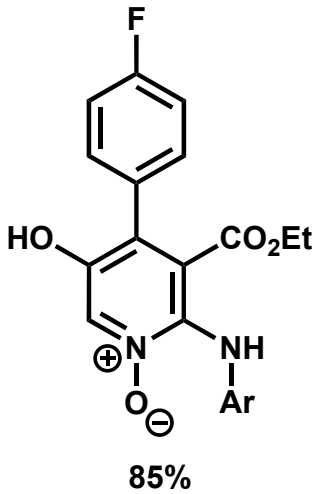
Substrate Scope of [3+2]-Cycloaddition of Nitrile Oxides



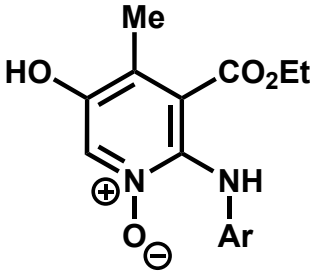
Ar = 2,4,6-trimethylphenyl

Rearrangement

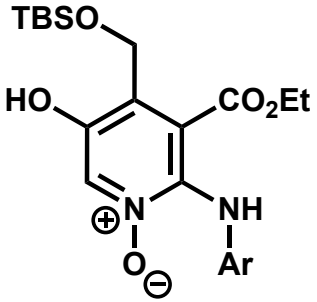


85%

pyridine-N-oxides

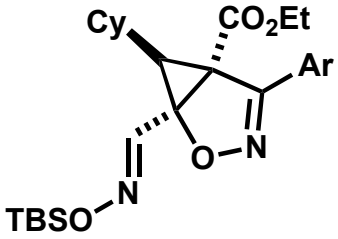


80%

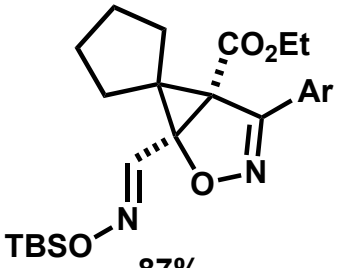


78%

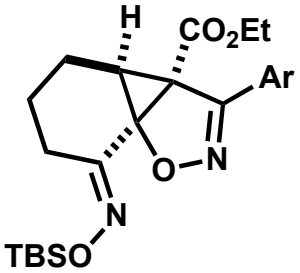
Without Rearrangement



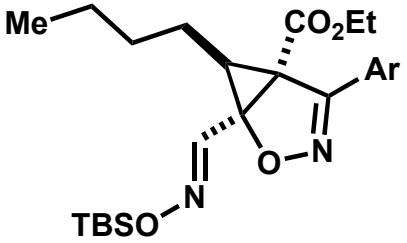
81%, >20:1 dr



87%



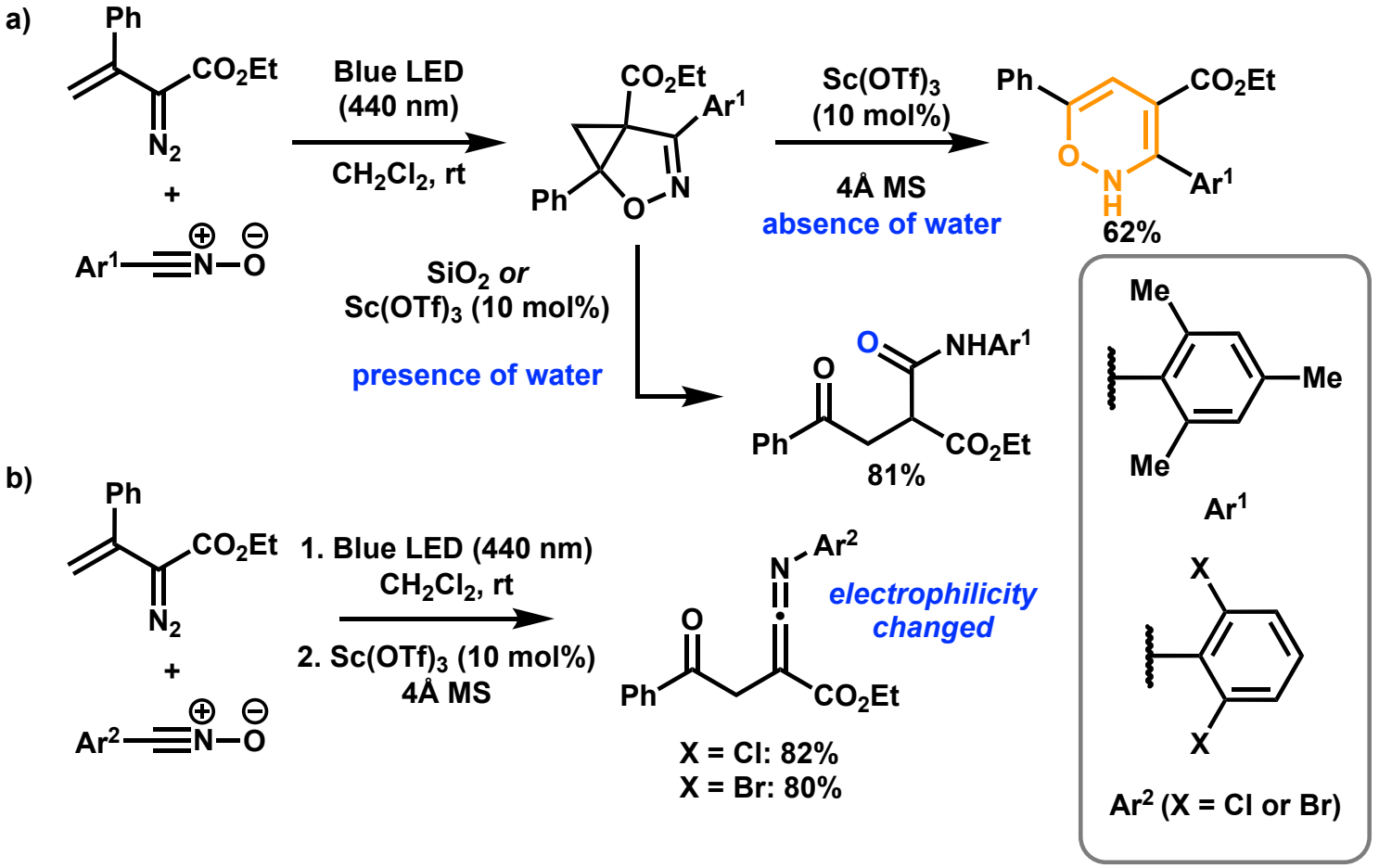
83%, 2:1 dr



80, >20:1 dr

Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

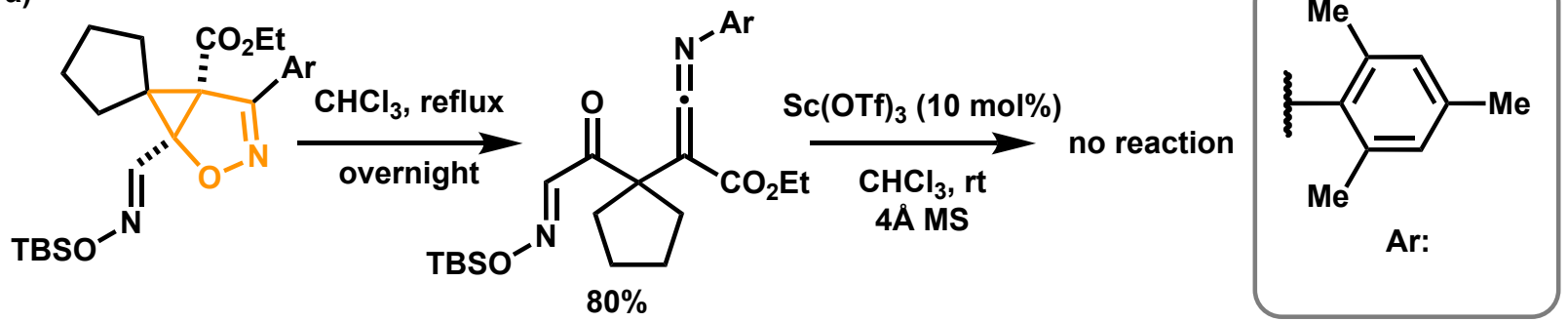
Mechanistic Experiment (1)



Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

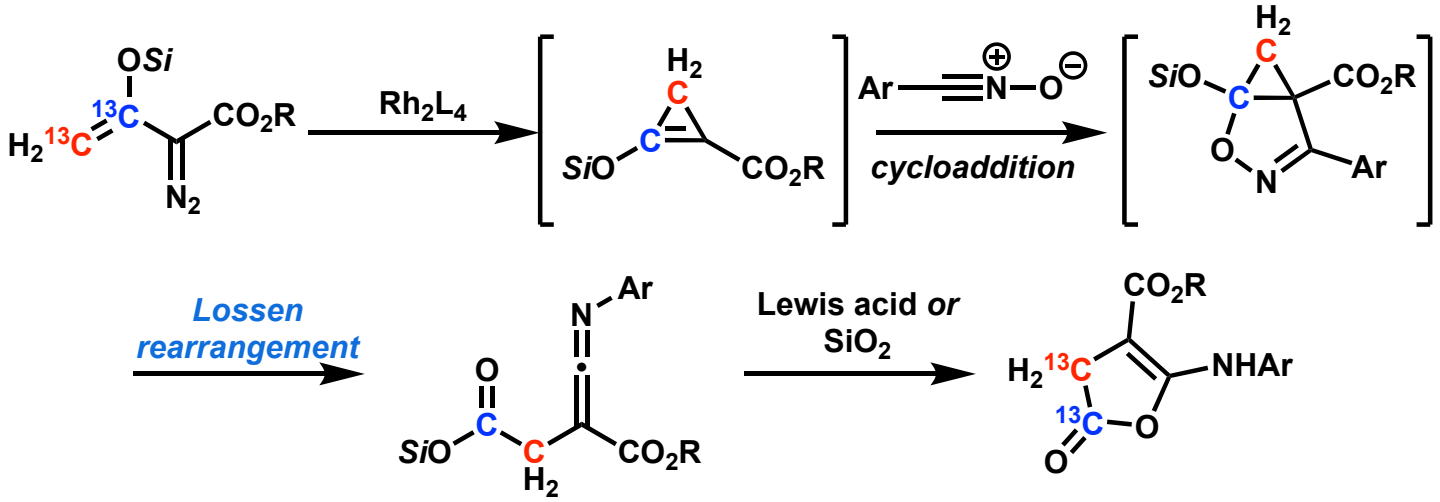
Mechanistic Experiment (2)

a)



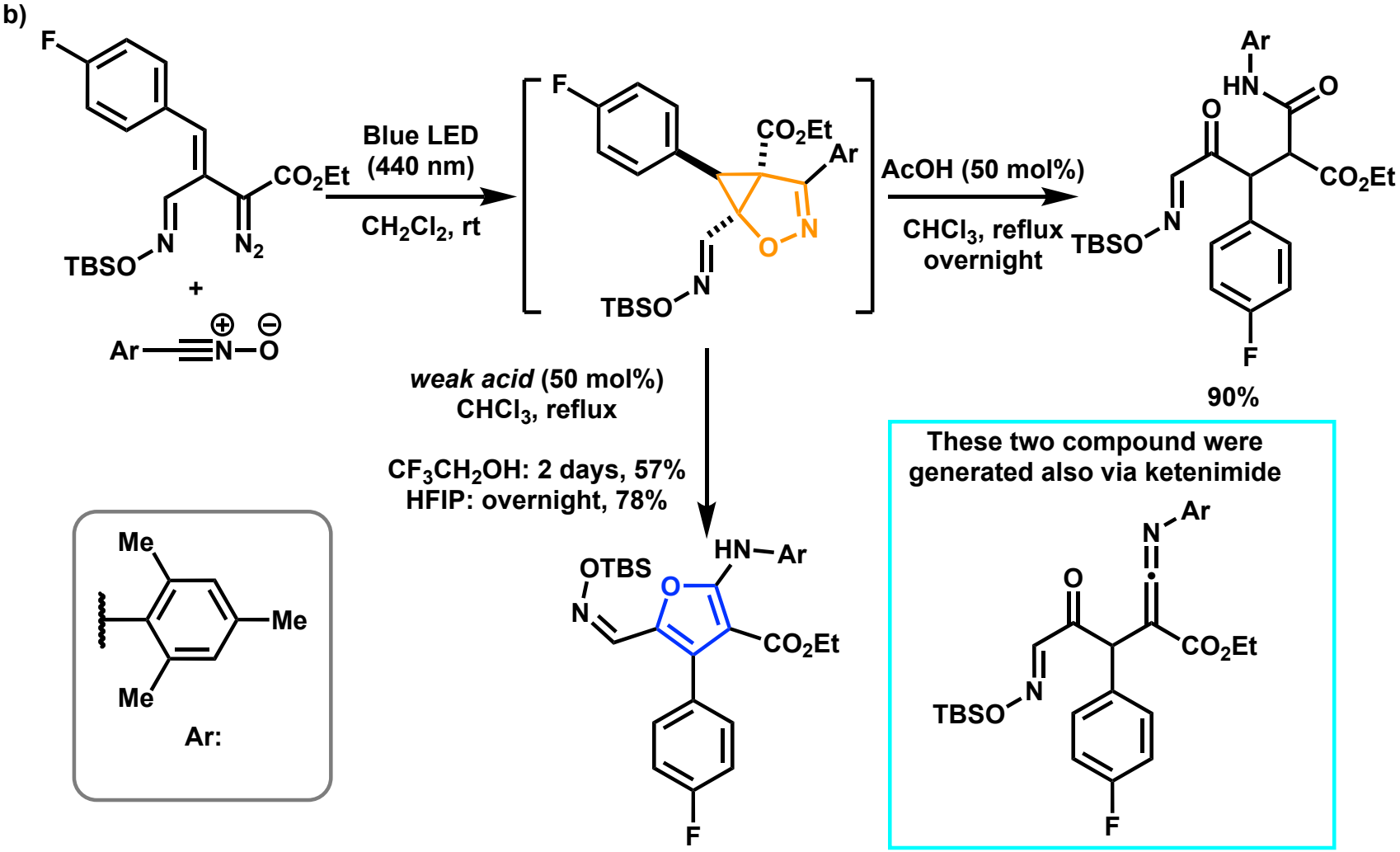
Previously reported by Doyle's group[2)]

Xu, X.; Shabashov, D.; Zavalij, P. Y.; Doyle, M. P. *Org. Lett.* 2012, *14*, 800



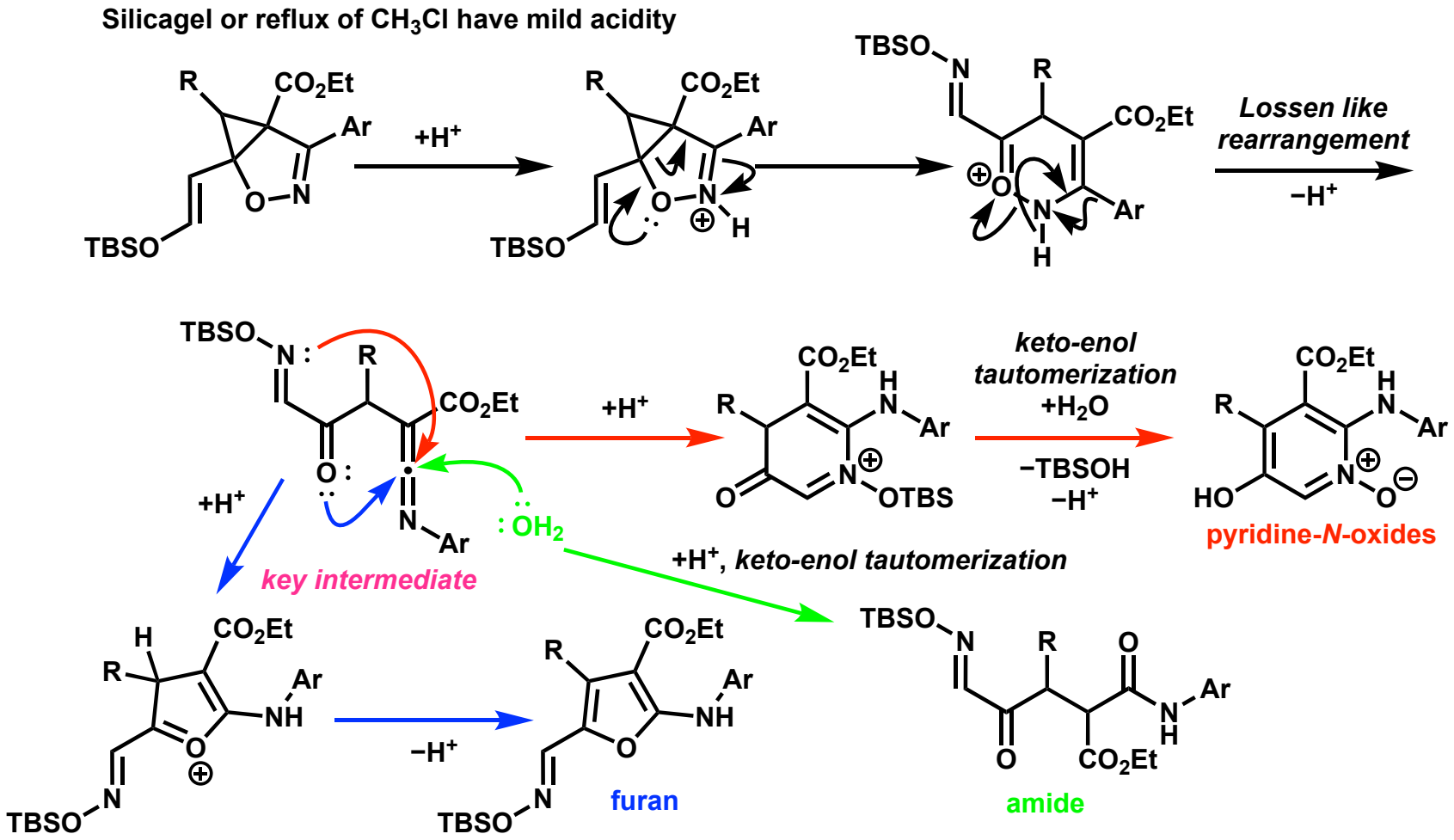
1) Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574
2) Xu, X.; Shabashov, D.; Zavalij, P. Y.; Doyle, M. P. *Org. Lett*. **2012**, *14*, 800

Mechanistic Experiment (3)



Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

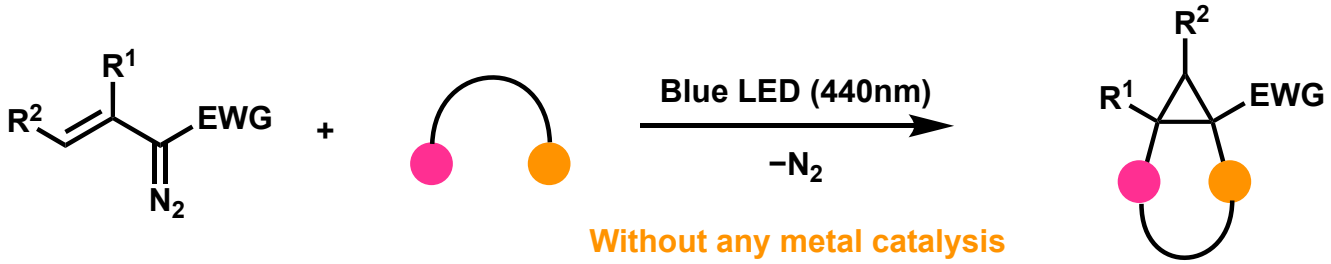
Proposed Mechanism for Furan, Pyridine-*N*-oxide, Amide



Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574

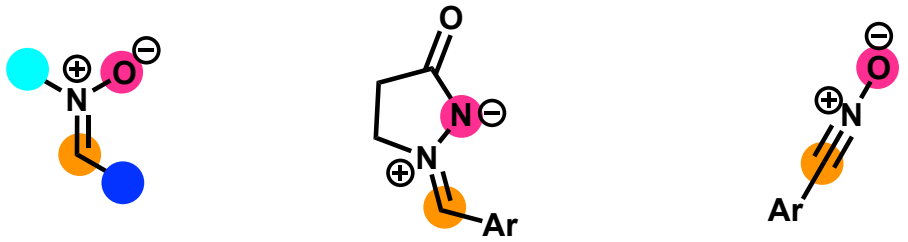
Summary

This work:
Development of tandem cycloaddition reaction of vinyldiazo compound in photo-irradation condition



Without any metal catalysis

Dipoles: Nitrones and *N,N*-Cyclic azamethine ylides, and Nitrile oxides



Nitrones | ***N,N*-Cyclic azamethine ylides** | **Nitrile oxides**

Bao, M.; Luczak, K.; Chatadaj, W.; Baird, M.; Gryko, D.; Doyle, M. P. *Nat. Commun.* **2024**, *15*, 4574