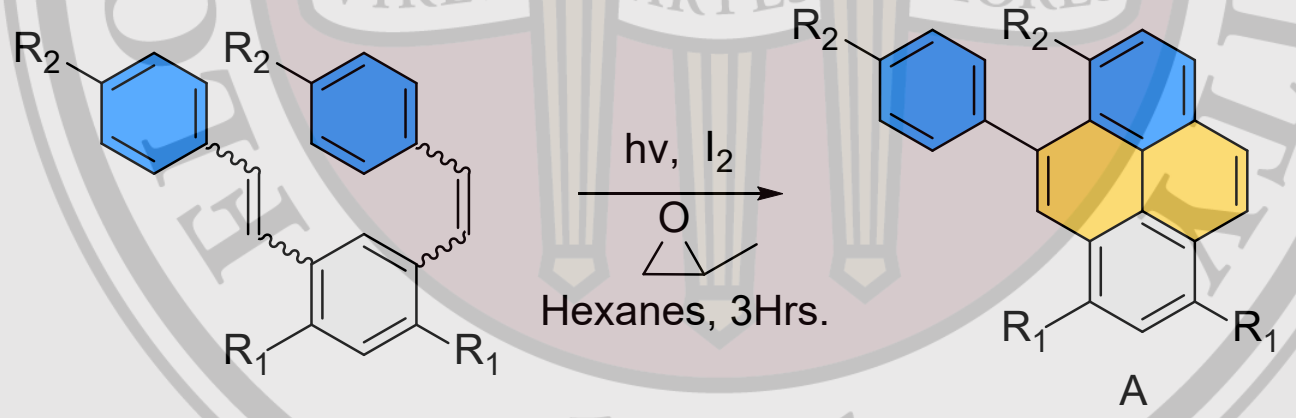
De Novo Photochemical Synthesis Of Non-Symmetric Pyrenes

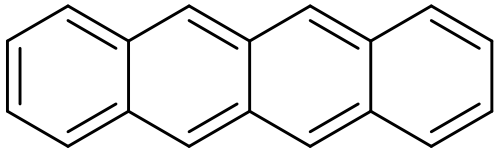
Nikolas R. Dos Santos
Dr. Igor Alabugin

4th Year Talk

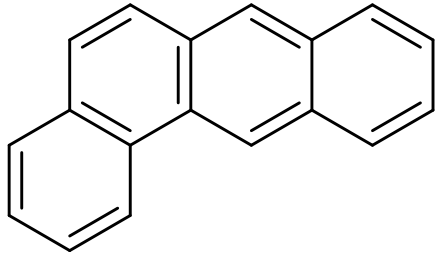
04.28.2022



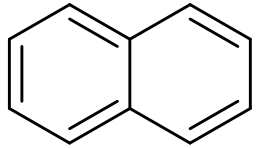
Aromatic fusions up to 4 rings



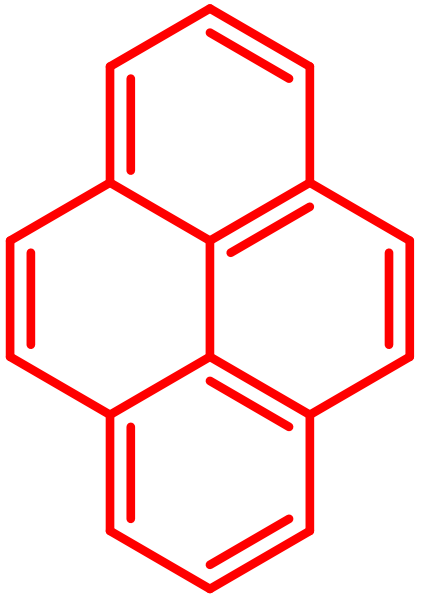
tetracene



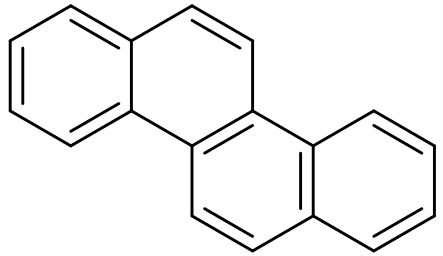
tetraphene



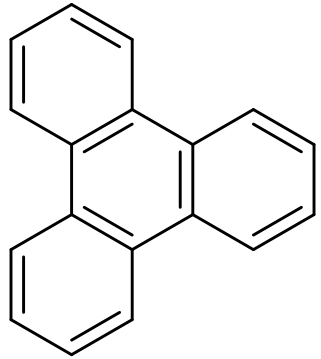
naphthalene



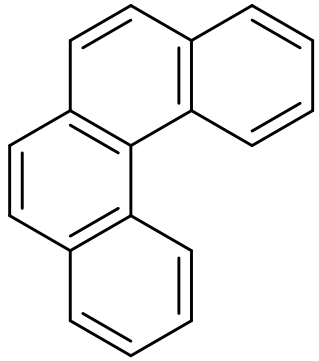
pyrene



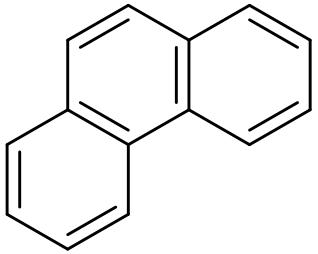
chrysene



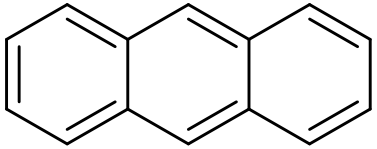
triphenylene



benzo[*c*]phenanthrene



phenanthrene



anthracene

Why is pyrene interesting?

-HOMO/LUMO gap- 3.8eV

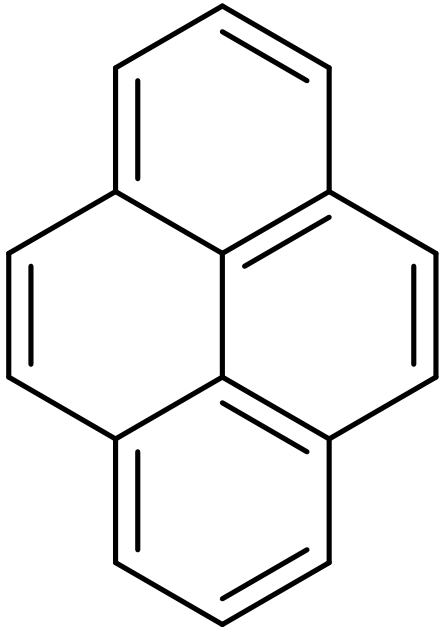
-Inherent emission at 375-410nm

-Long lived singlet, S_1, leading to high excimer formation (>100ns)

-Excimer Formation- changes emission to 425-550nm

-High Fluorescence Quantum Yield, ϕ_f=0.29

-Red. potential= 1.52V



-Fluorescent Probes

-Organic Field-Effect Transistors (OFETs)

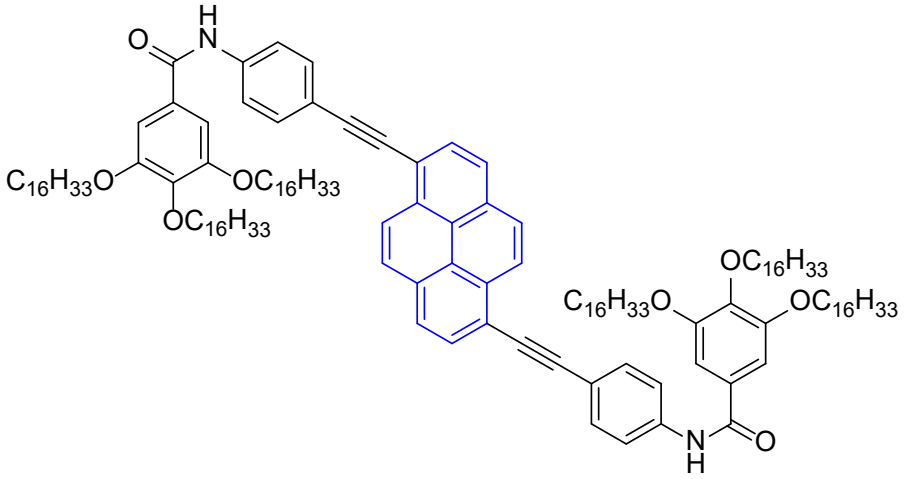
-Organic Light-Emitting Diodes (OLEDs)

-Organic Photovoltaic cells (OPV)

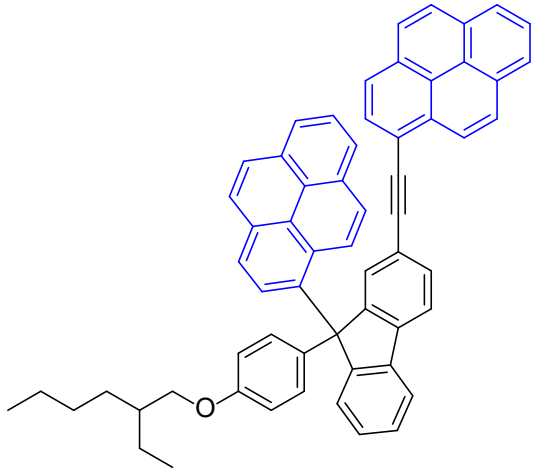
-Chemical Biology

Pyrene in materials

- Uses pyrene as the core for a semiconducting material in OFET due to its fluorescence.



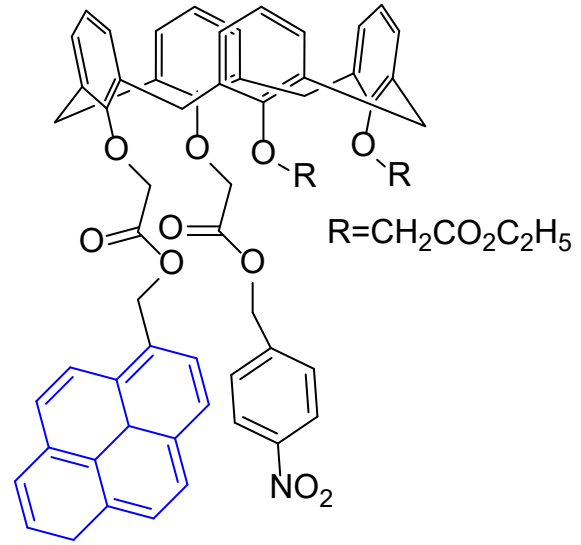
Diring et al., J. Am. Chem. Soc. 2009, 18177



Liu et al., Org. Electron. 2009, 256.

- Uses pyrene to tune fluorescence of the molecule in OLED.

- Uses the interaction between pyrene and NO_2 as an optical sensor for Na^+ detection.

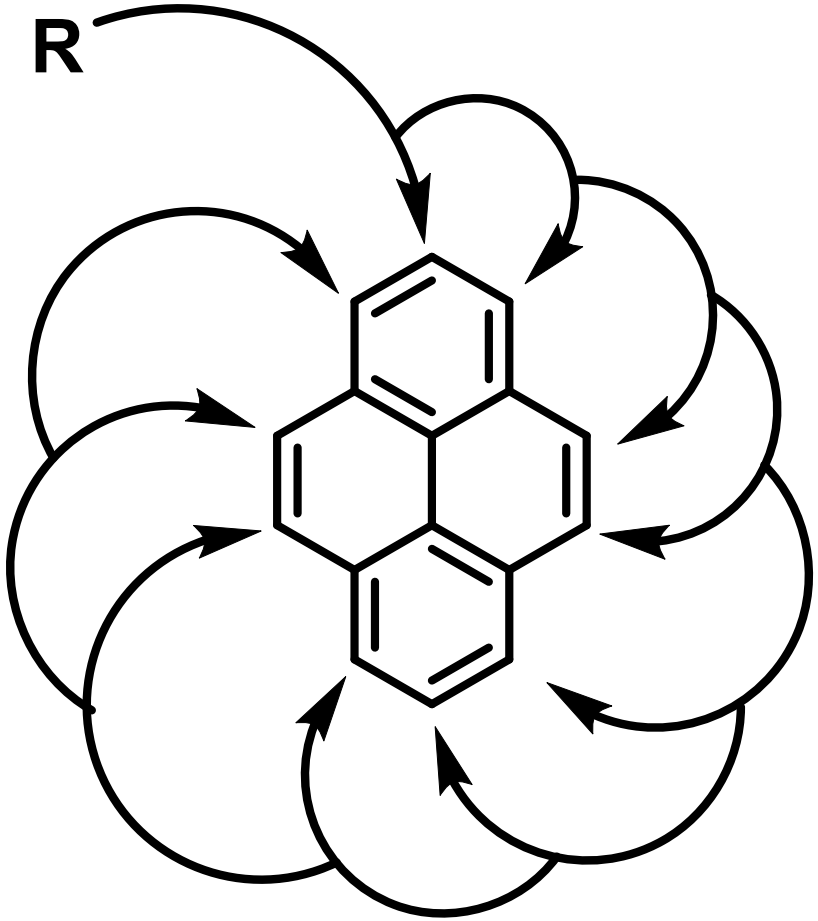


Aoki et al., Chem. Commun. 1992, 730

Strategies for synthesis of functionalized pyrenes

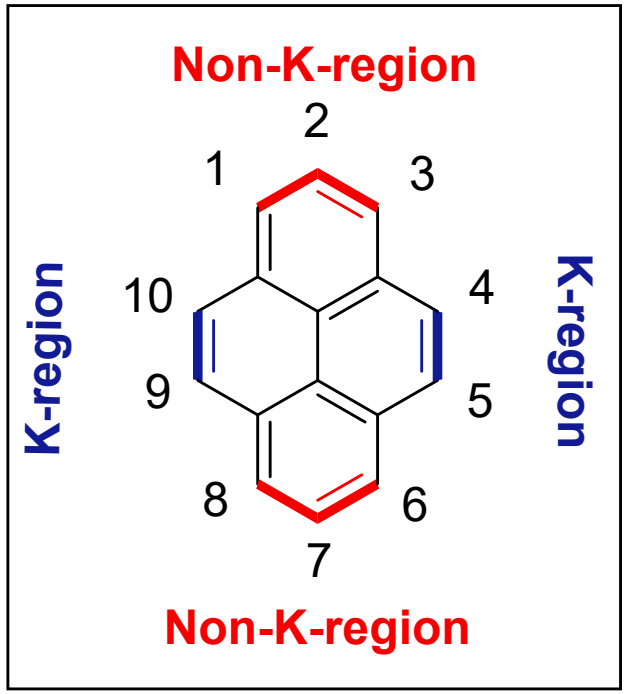
Strategy One

Functionalizing existing pyrene



R=alkyl, aryl, alkoxy, X

Summary of direct functionalization strategies



K-region

-Accessed **directly** through metal catalysis and EAS reactions when the Non-K-region is blocked with bulky substituents.

-Accessed **indirectly** through HHpy method.

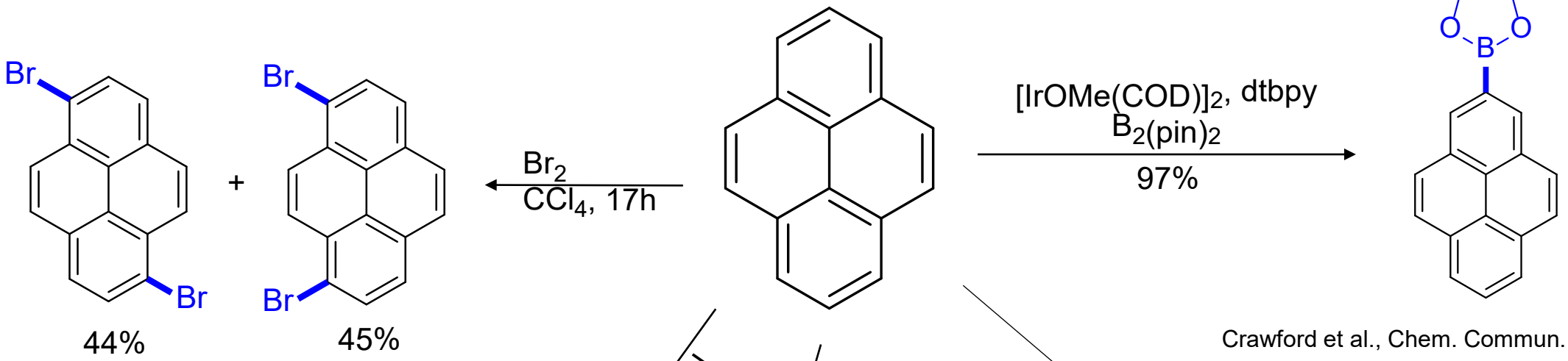
Non-K-region

-Acessed directly through EAS reactions and bulky electrophiles.

-Accessed indirectly through the THpy method.

- Difficulty or complex to selectively substitute any positions beyond first substitution.

Strategy one: direct functionalization



Grimshaw et al., *J. Chem. Soc., Perkin Trans.* 1972, 1622

Crawford et al., Chem. Commun. 2005, 2172

Streitwieser et al., J. Chem. Soc. Perkin Trans. 1 1997, 1201

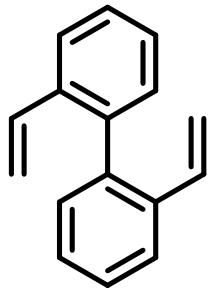
Filichev et al., Chem. Eur. J. 2008, 9968

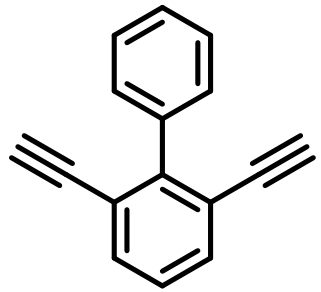
Mochida et al., *J. Am. Chem. Soc.* 2011, 10716

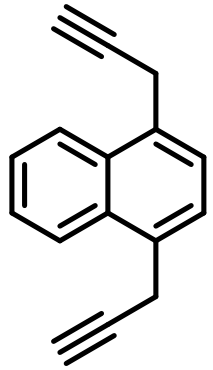
Strategies for synthesis of functionalized pyrenes

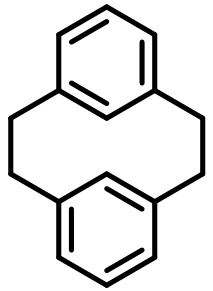
Strategy Two

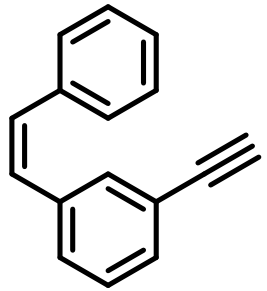
Assembling pyrene from smaller units
(de novo synthesis)



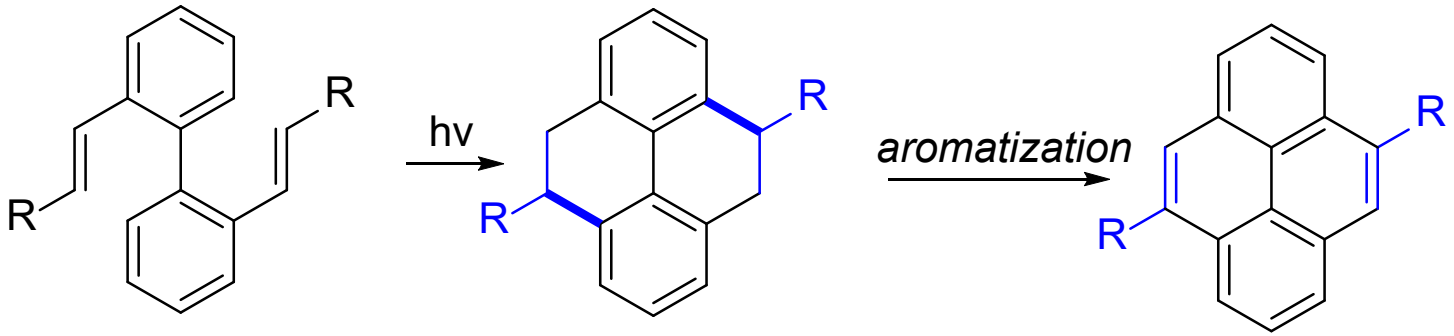




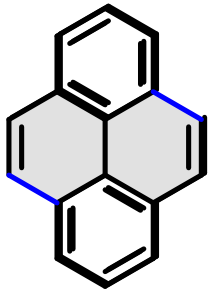




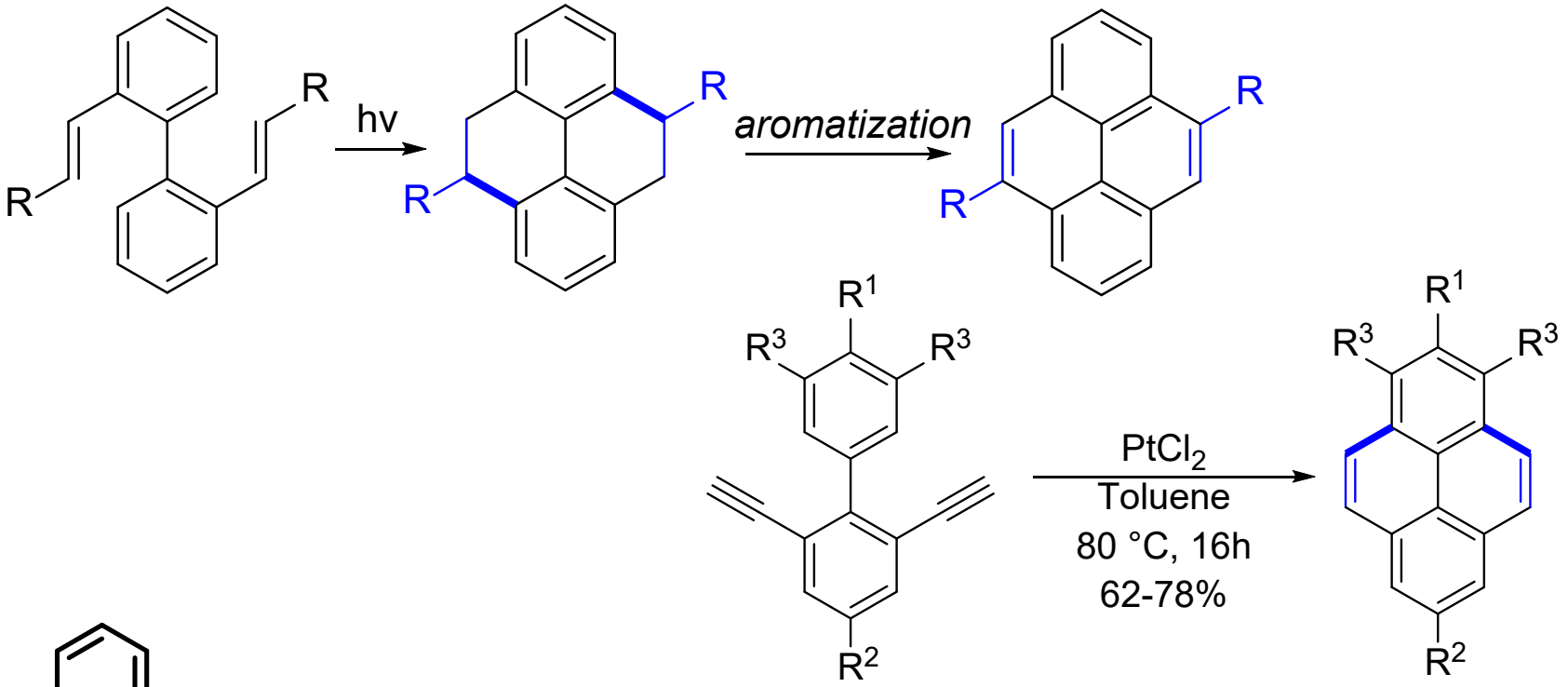
Biphenyl photocyclization



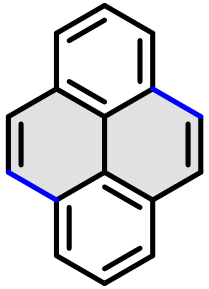
Laarhoven et al., J. Chem. Soc., Perkin Trans. 1972, 2074

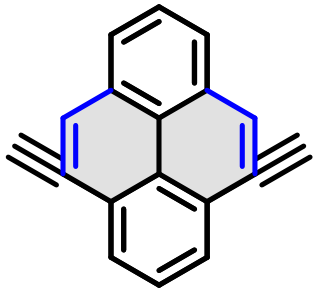


Bis-alkyne biphenyl cyclization

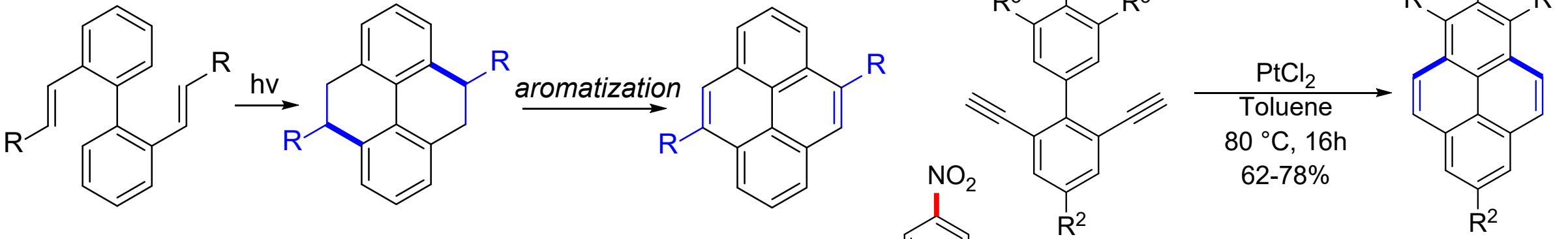


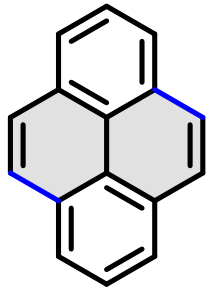
Walker et al., Synth. 2002, 8352

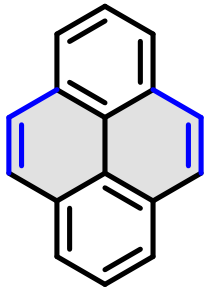


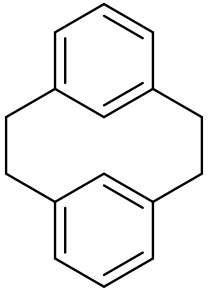


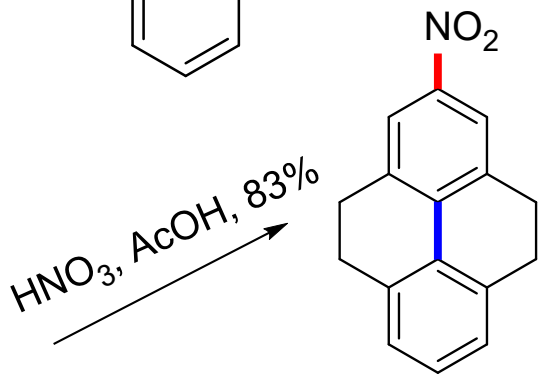
Transannular ring closure

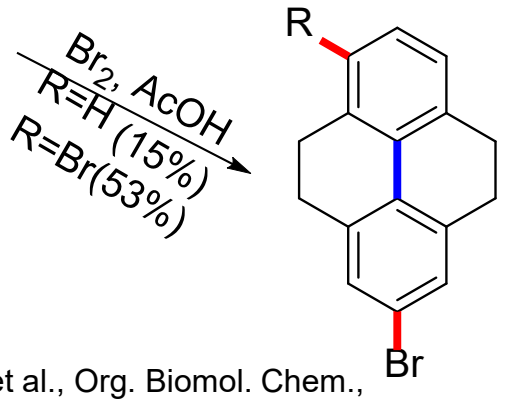


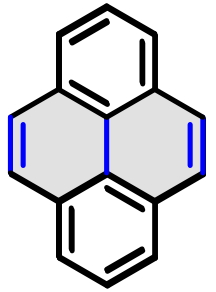






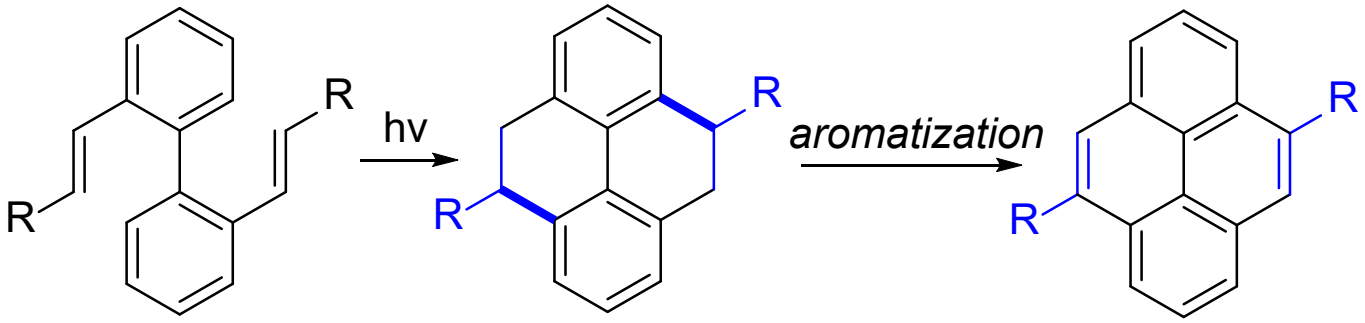


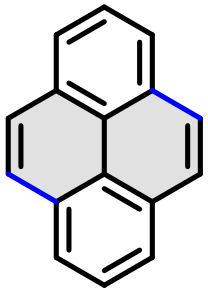


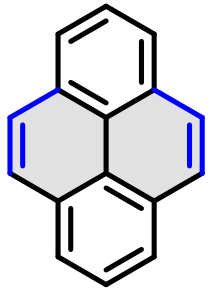


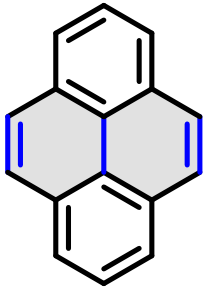
Casas-Solvas et al., Org. Biomol. Chem., 2014, 212

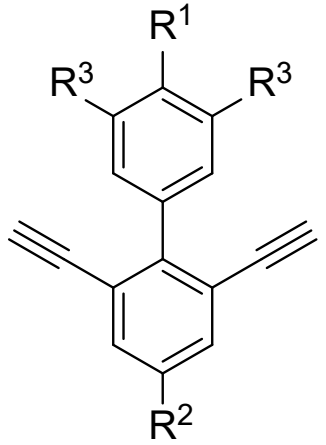
Summary of known strategies

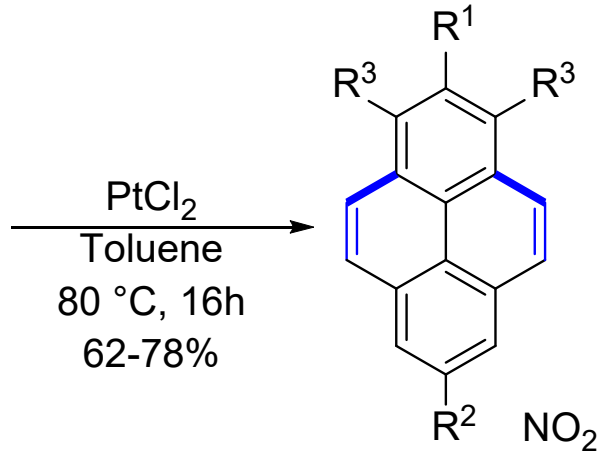


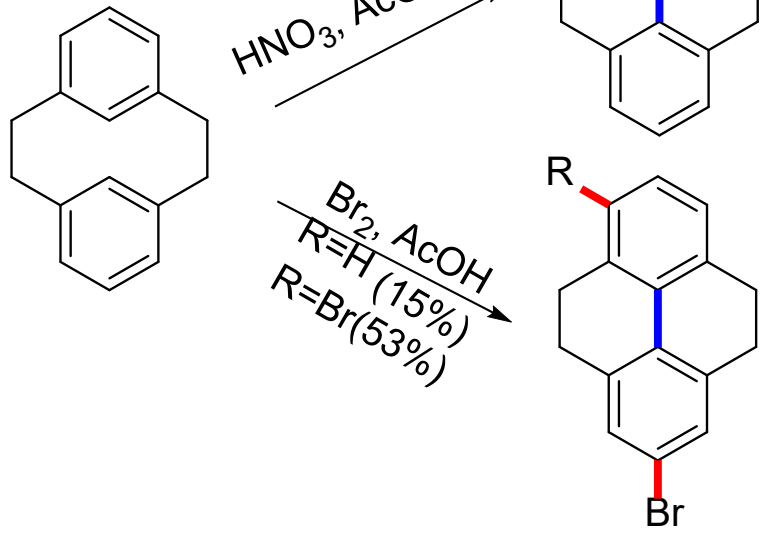








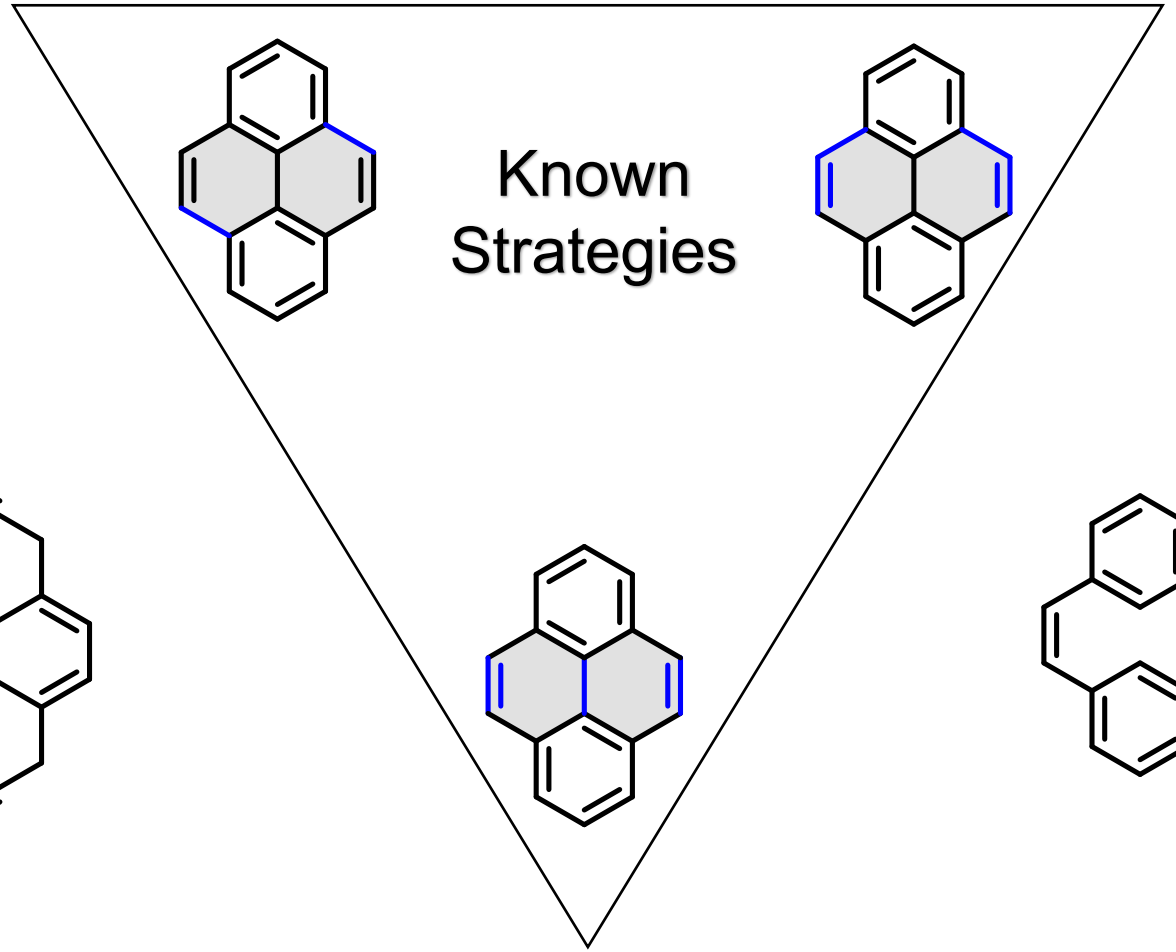




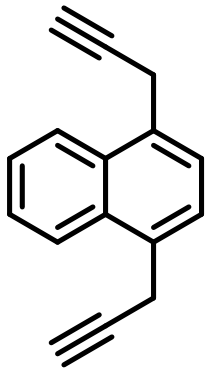
Out with the old, in with the new

Strategy Two

Assembling pyrene from smaller units
(de novo synthesis)

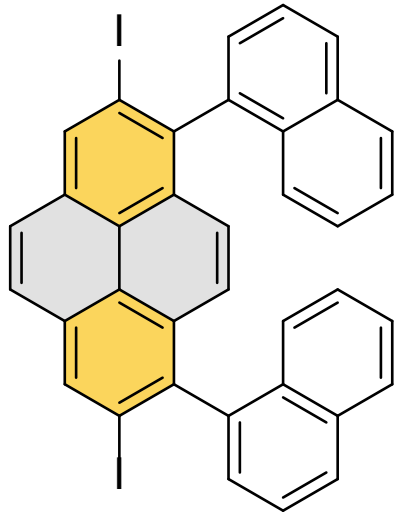


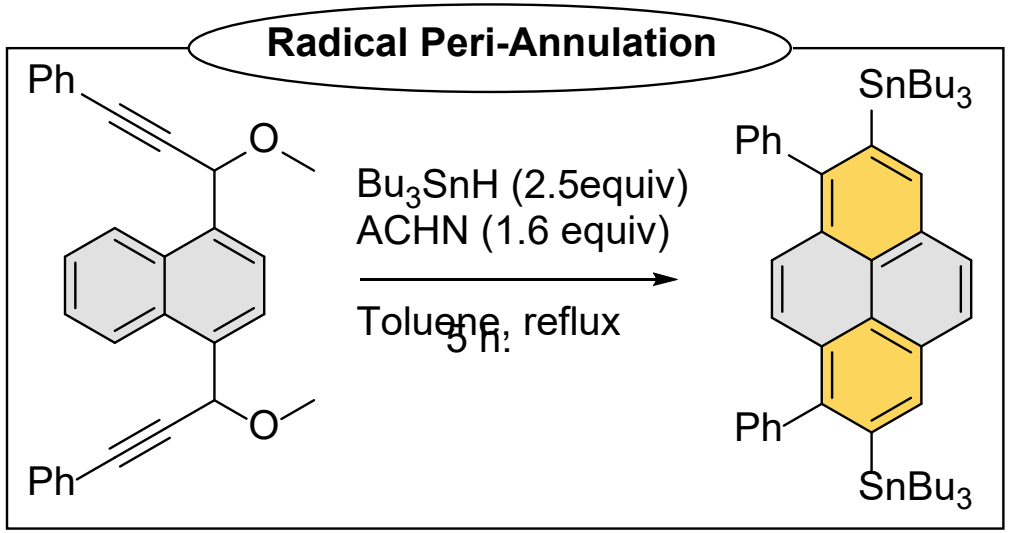
New Strategies

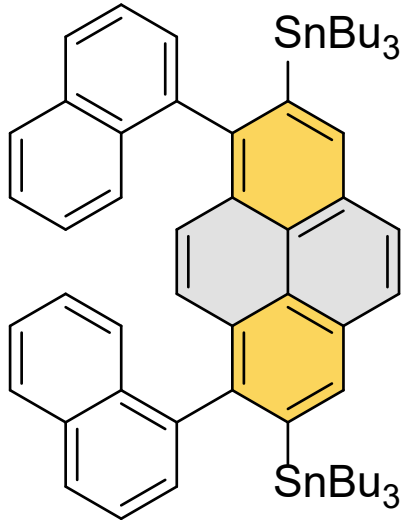


New Strategies

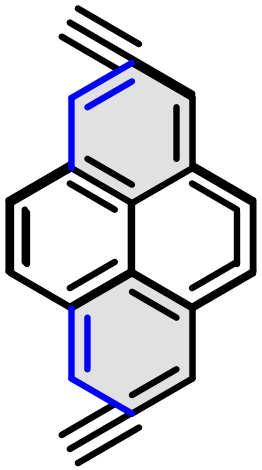
Strategy two: recent advances- beginning from naphthalene

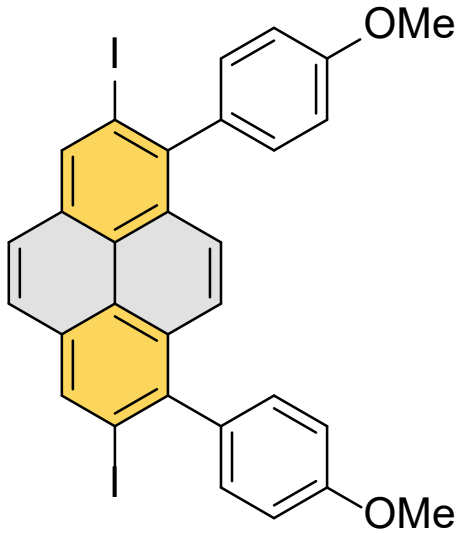


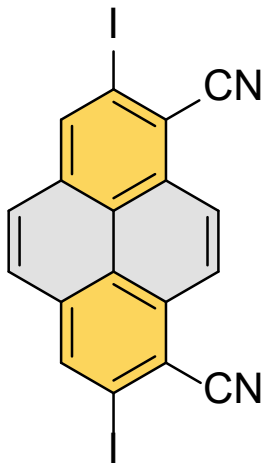


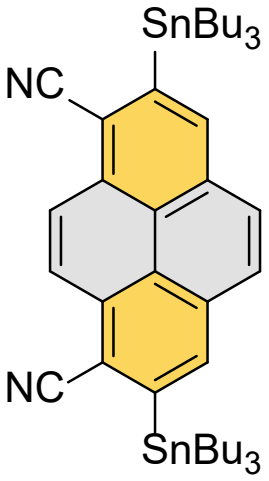


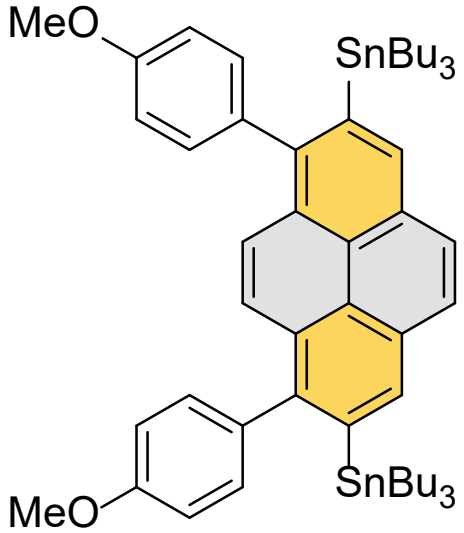
Gonzalez-Rodriguez et al., J. Am. Chem. Soc. 2020, 8352



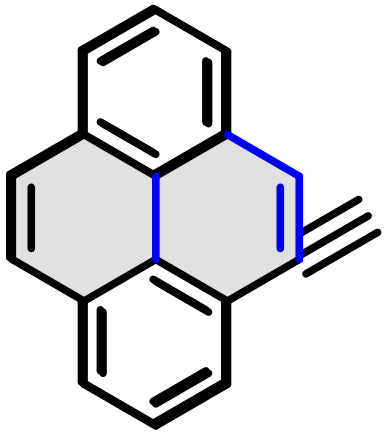


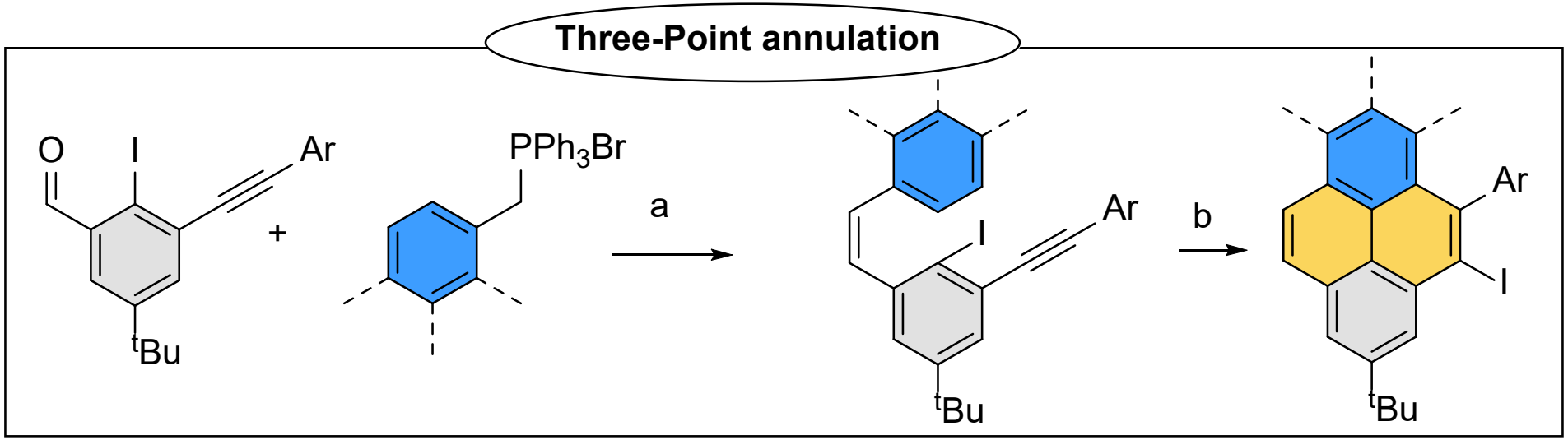




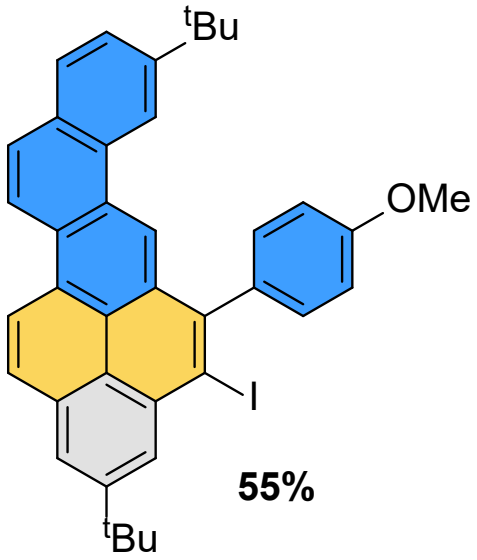


Strategy two: recent advances beginning from benzene.





Kawade et al., Angew. Chem. Int. Ed. 2020, 14352



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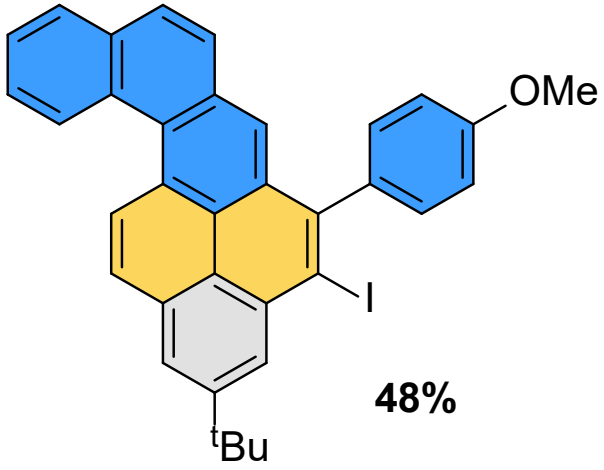

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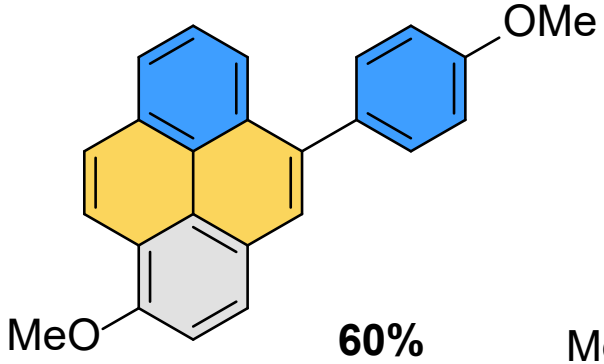
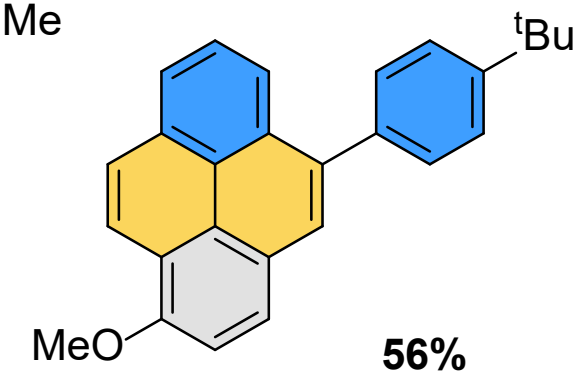


60%

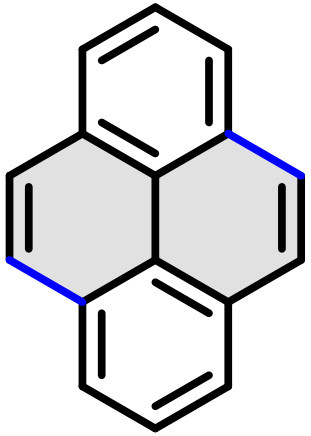


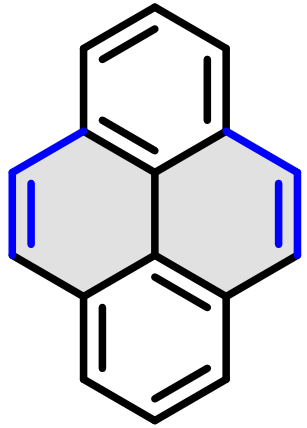
56%

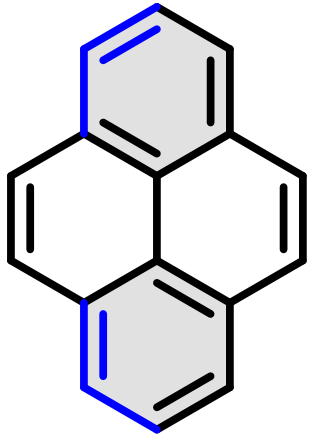
Summary of all current pathways to pyrene

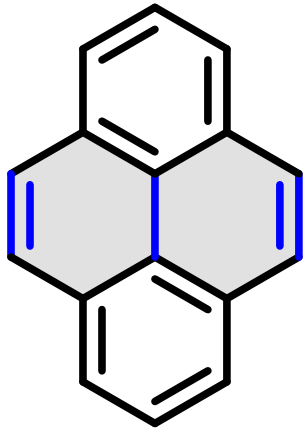
Strategy Two

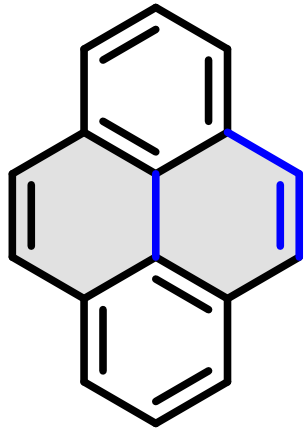
Assembling pyrene from smaller units
(de novo synthesis)







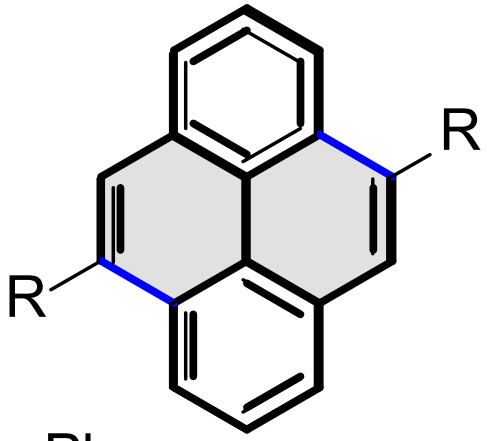


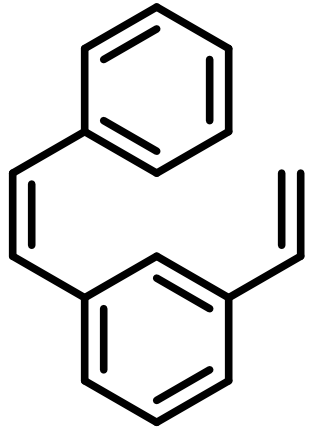


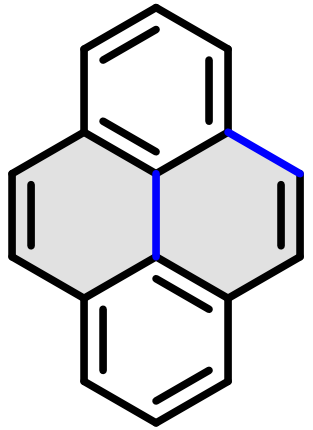
One missing approach

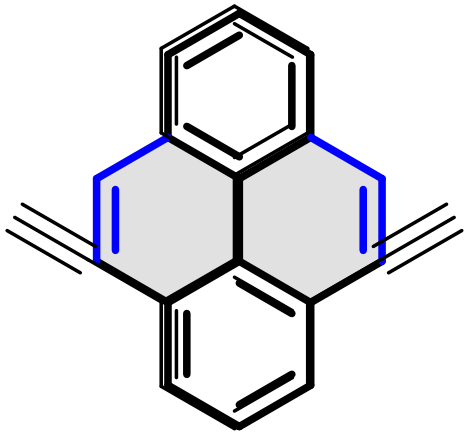
Strategy Two

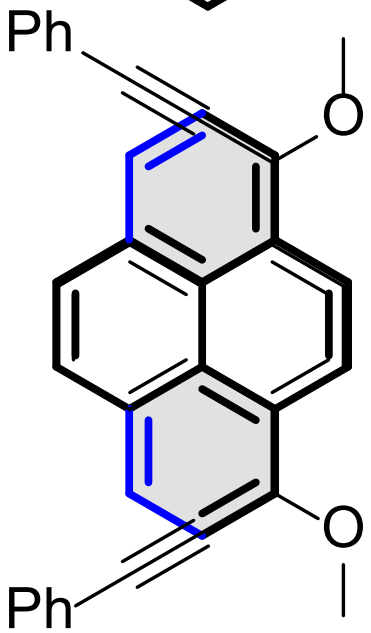
Assembling pyrene from smaller units
(de novo synthesis)

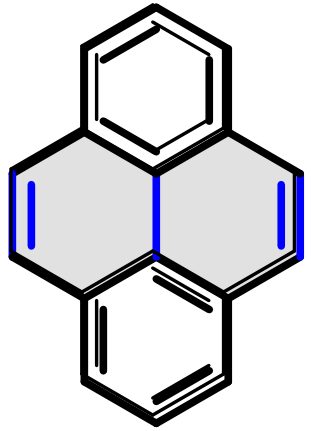


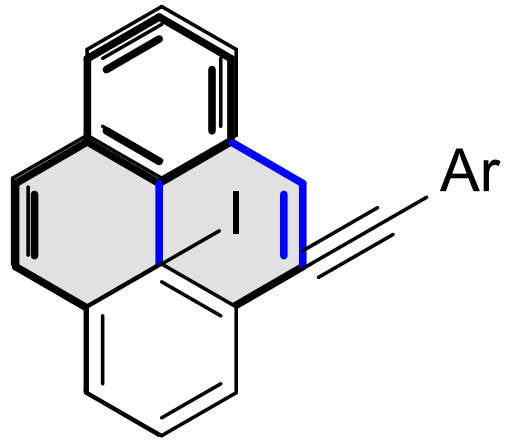






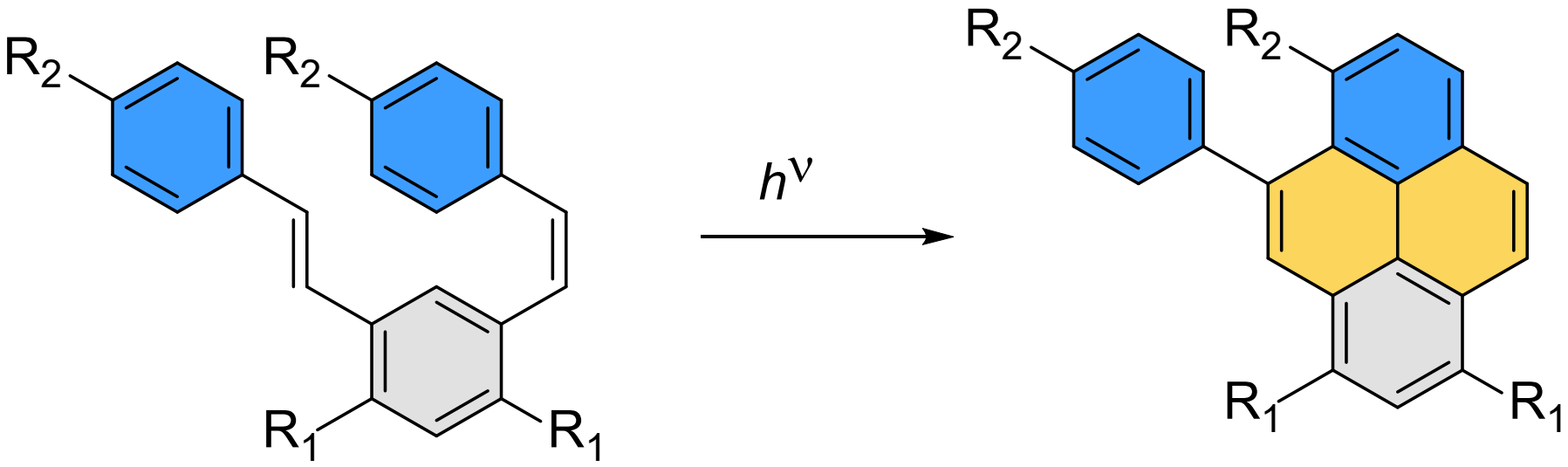




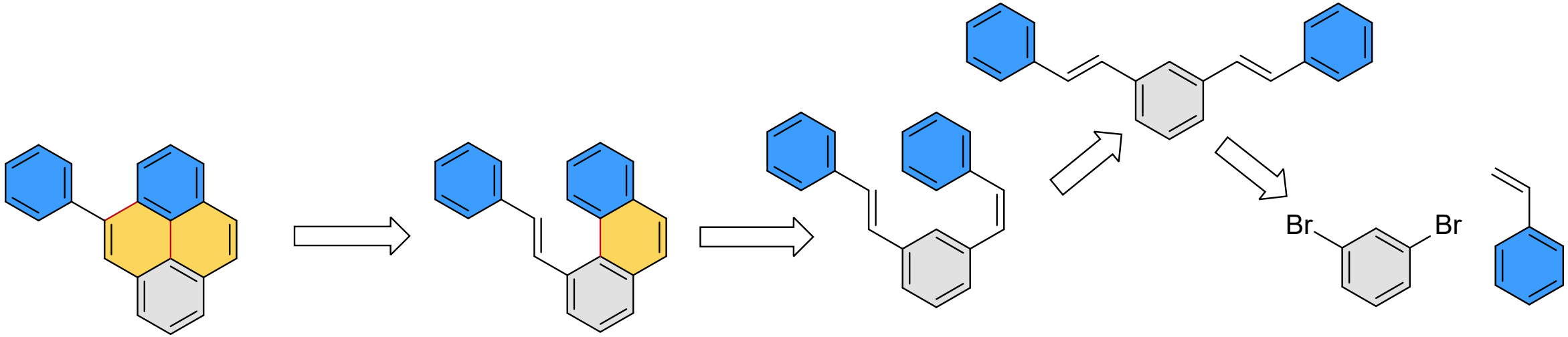


De novo photochemical synthesis of non-symmetric pyrenes

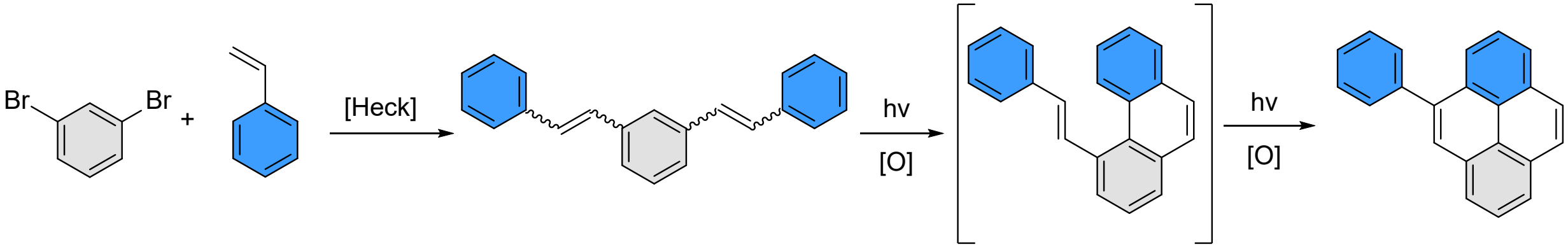
- Short synthesis



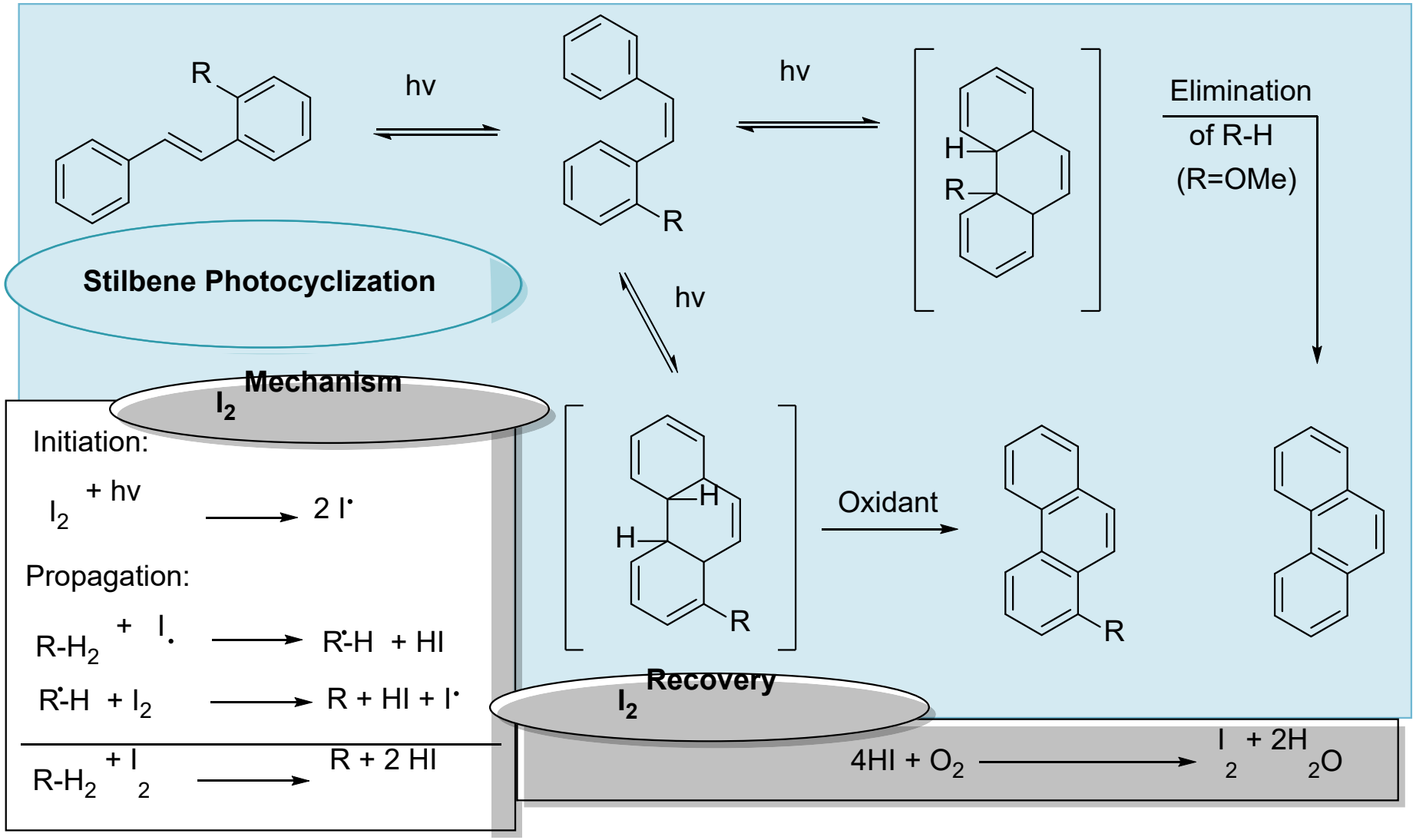
Retrosynthetic analysis



E and Z isomers interconvert under photochemical conditions

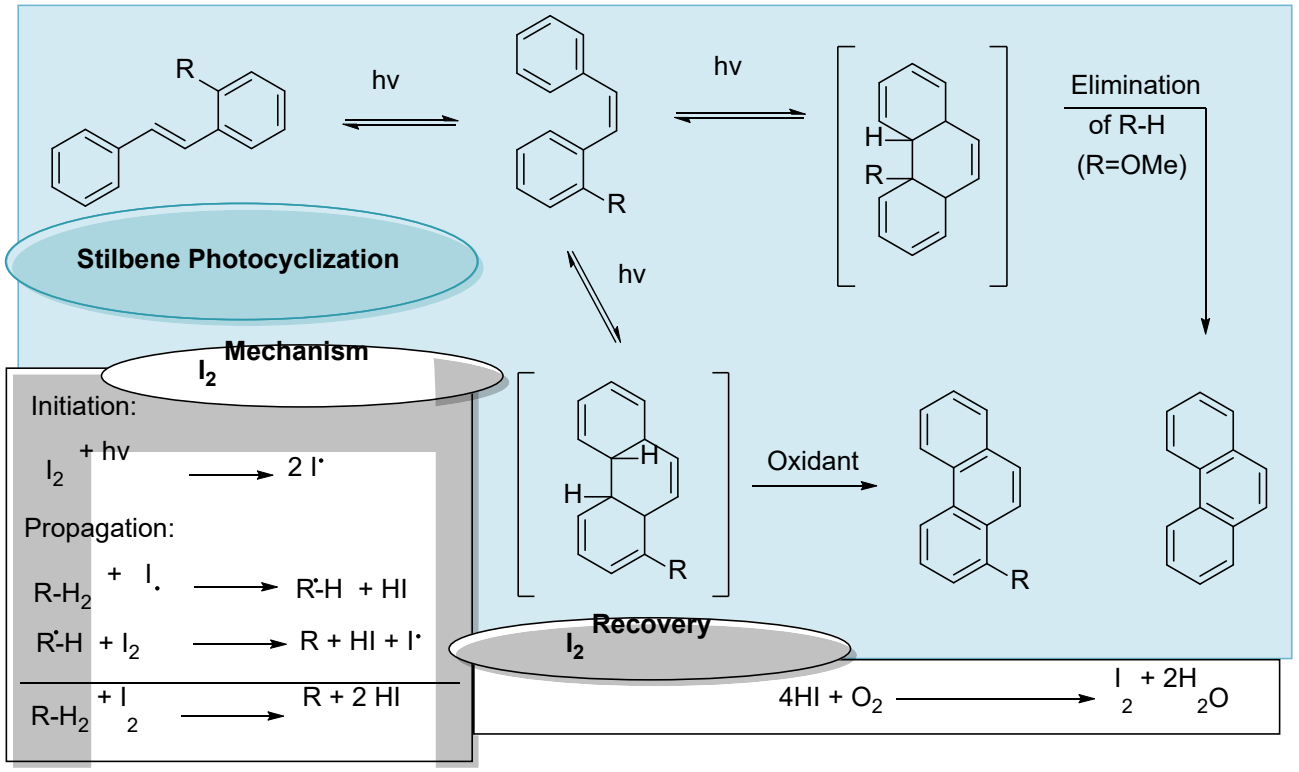


Precedents for the first step: the Mallory cyclization

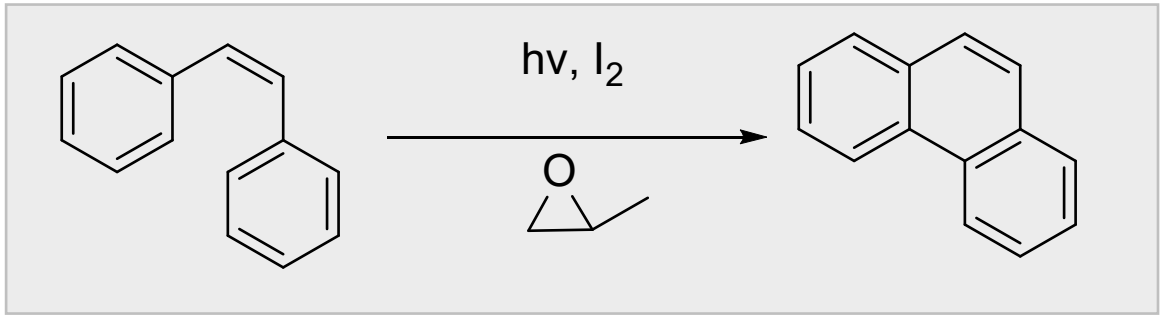


Mallory et al., Org. React. 1984, 30

The first step is easy: the Mallory cyclization



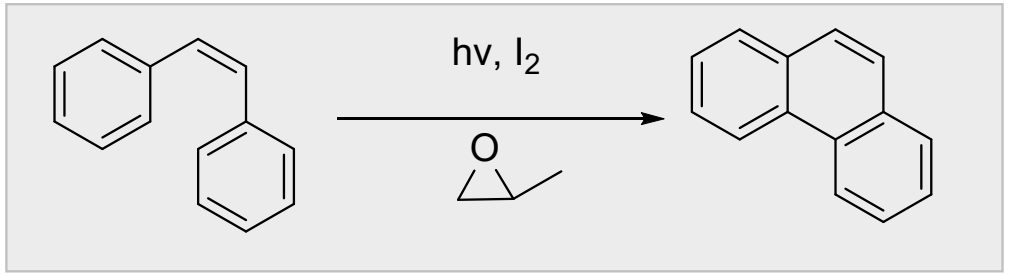
Mallory et al., Org. React. 1984, 30



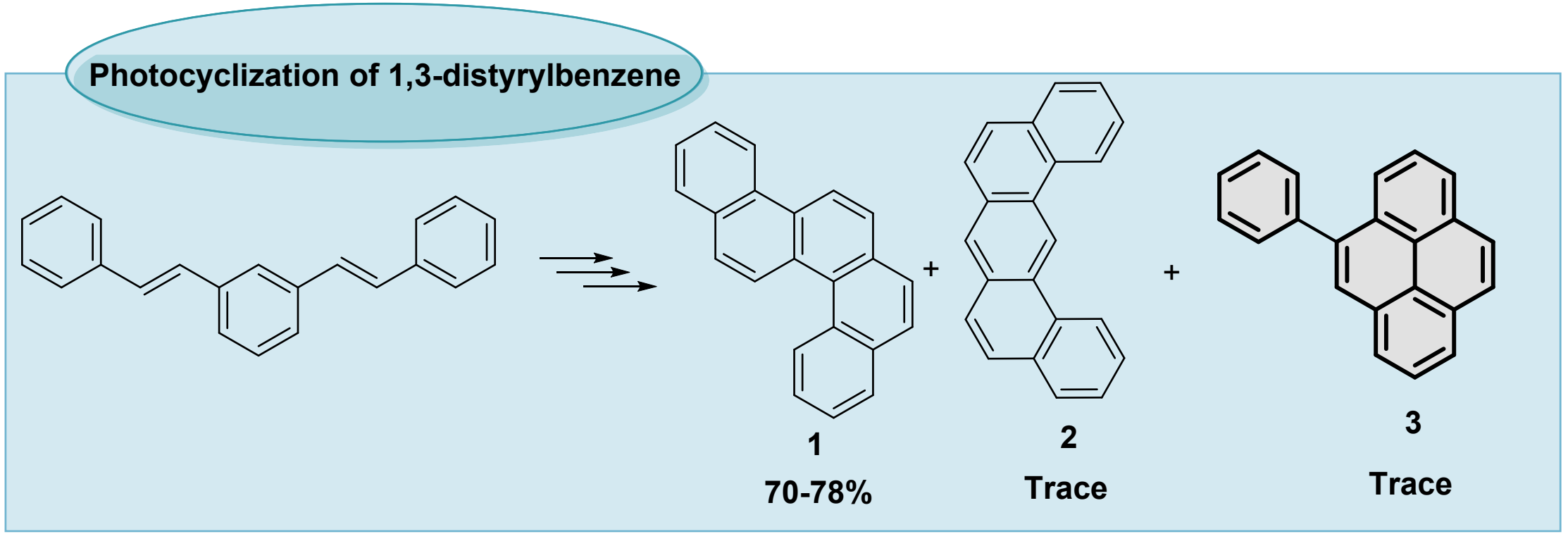
Katz and coworkers, Tetrahedron Lett. 1986, 2231.

- 100's of examples

Precedent for the second step, is it even possible?



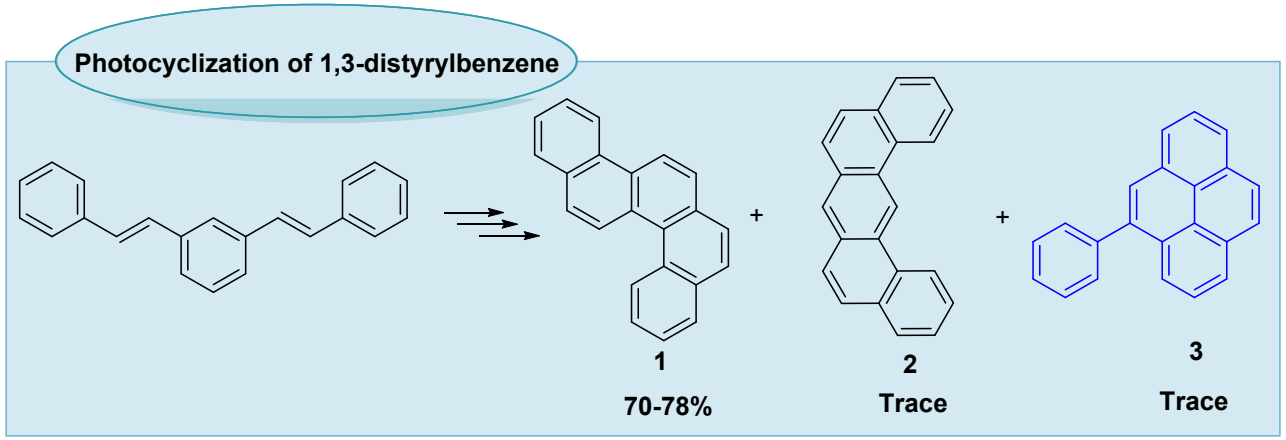
Katz and coworkers, Tetrahedron Lett. 1986, 2231.

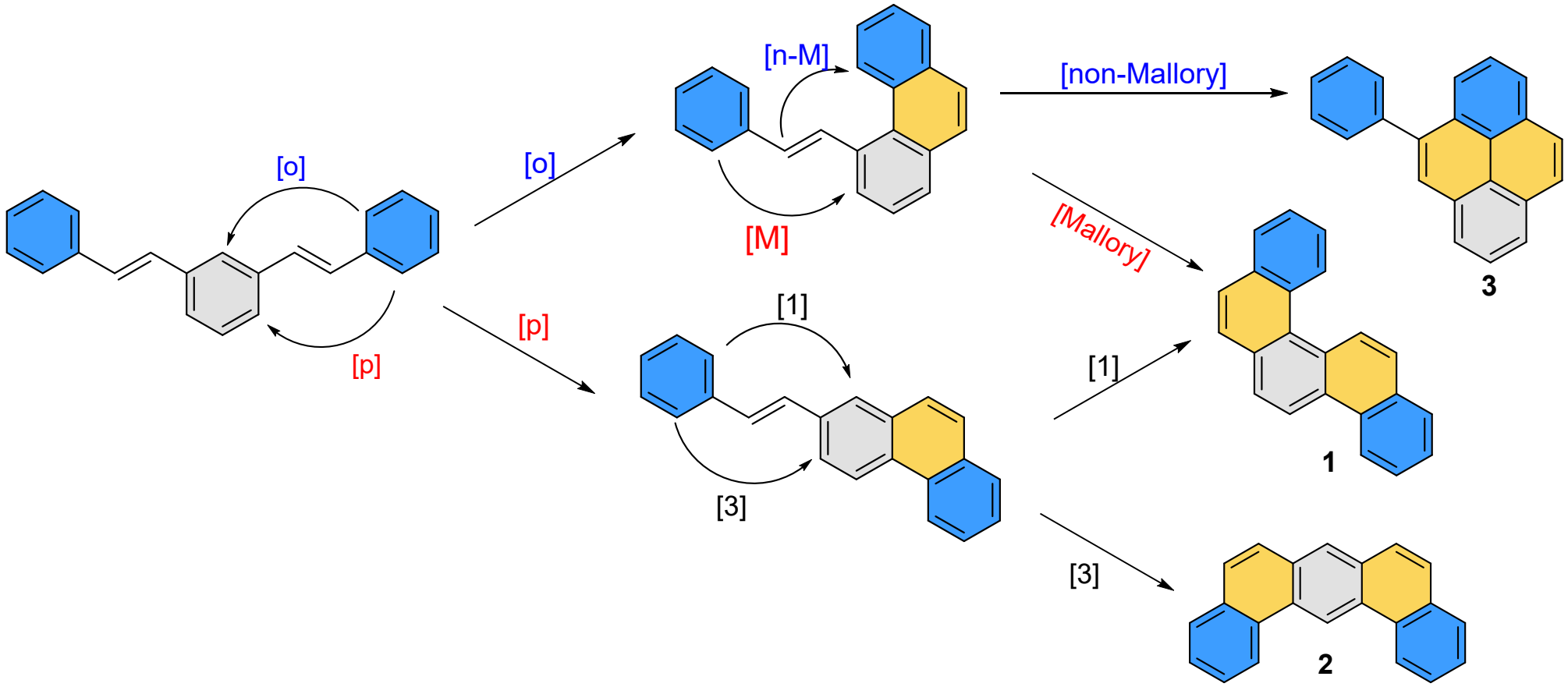


Laarhoven et al., Tetrahedron 1969, 1069

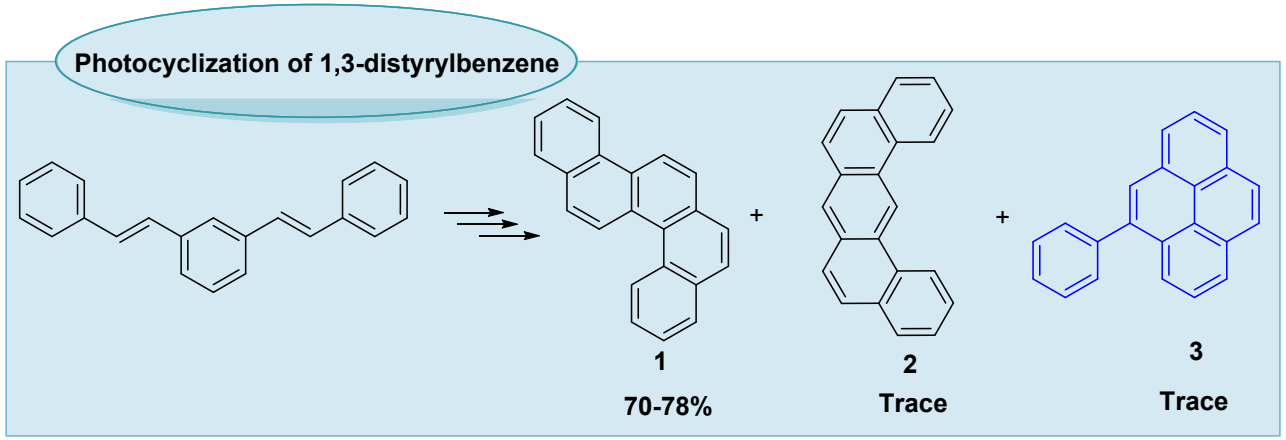
Morgan et al., Tetrahedron Lett. 1970, 4347

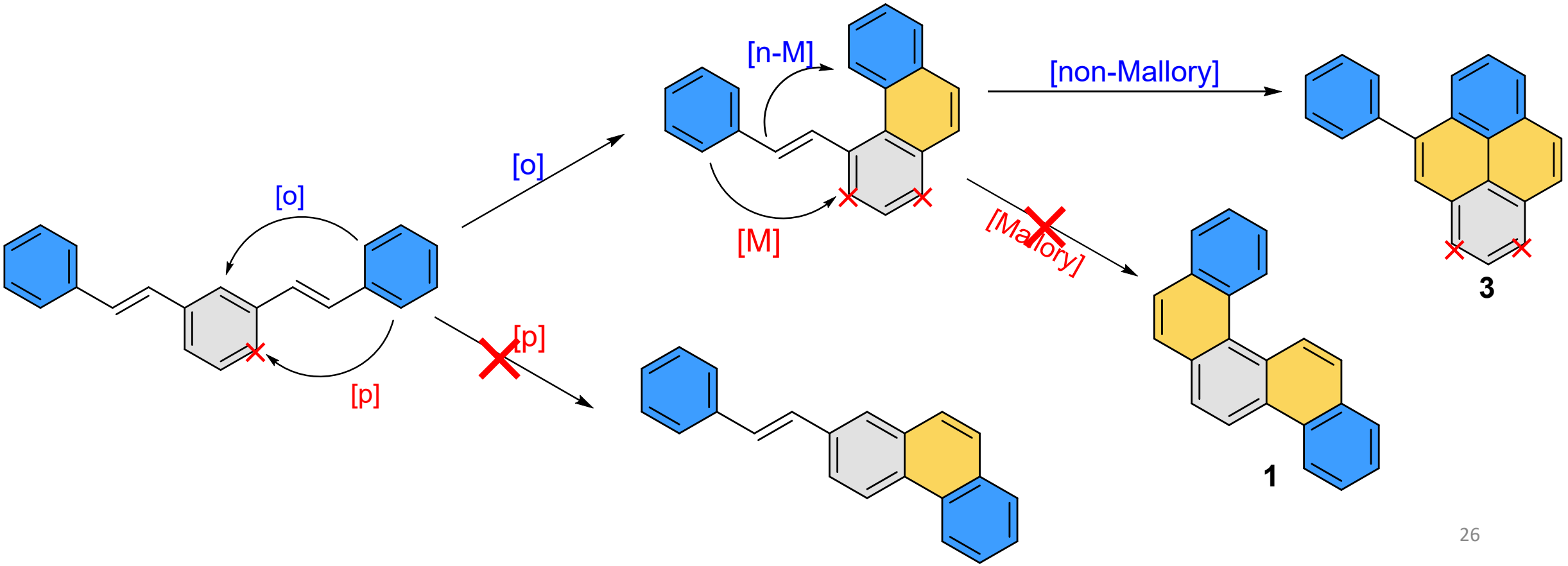
Why is pyrene the minor product?





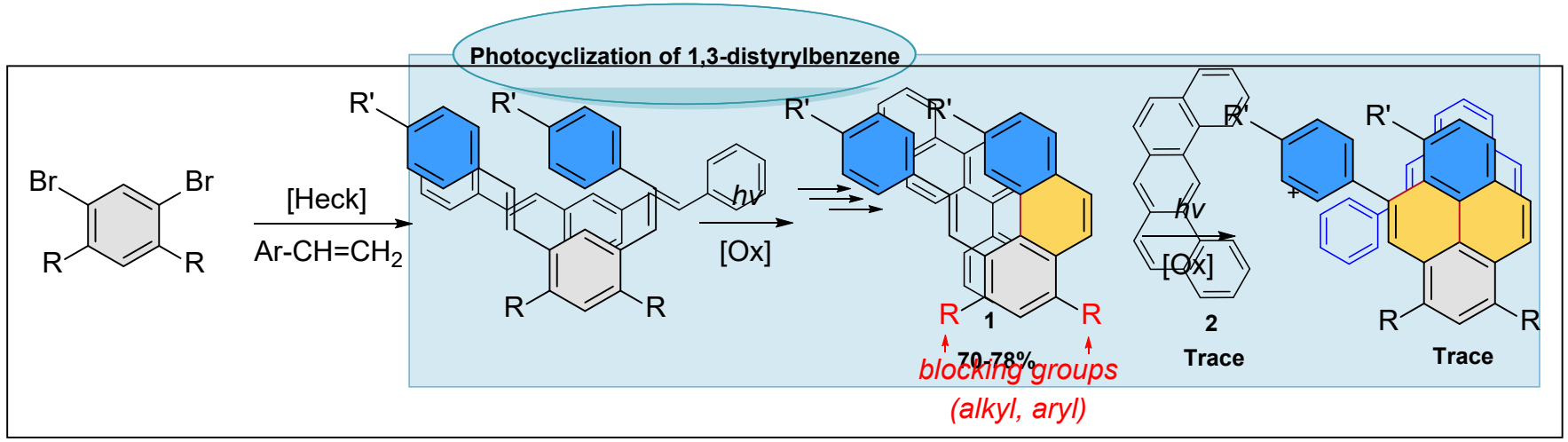
Redirecting reactivity: blocking a favorable reaction

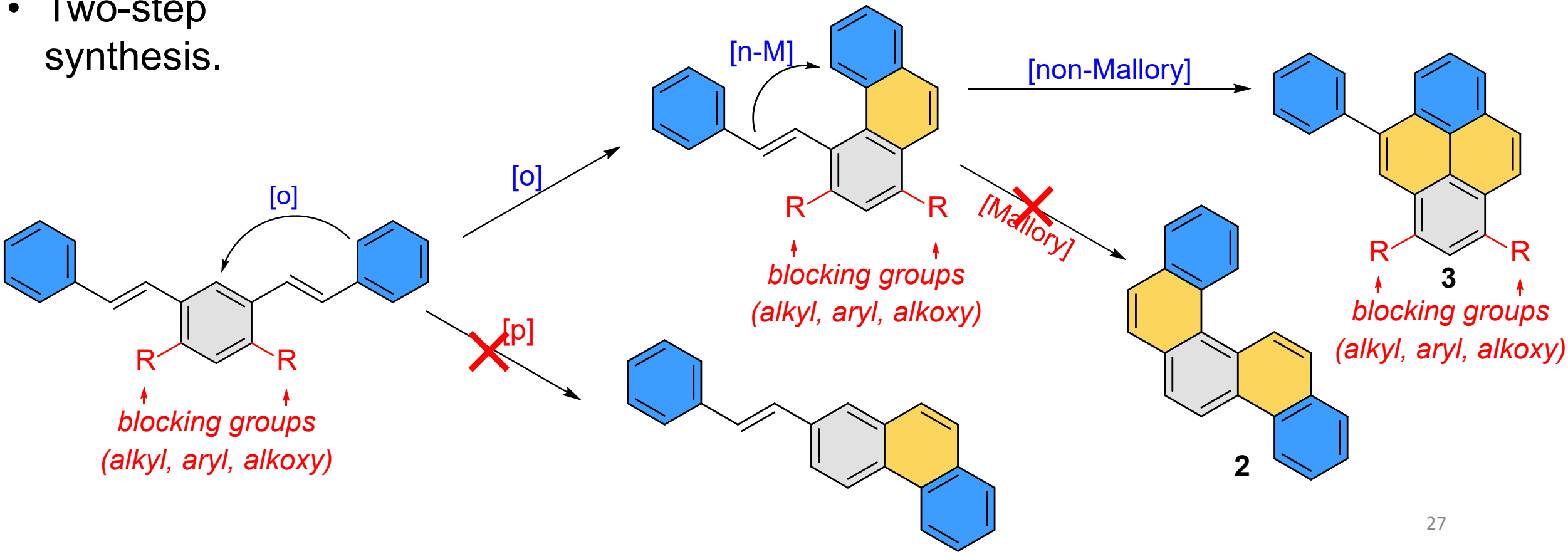




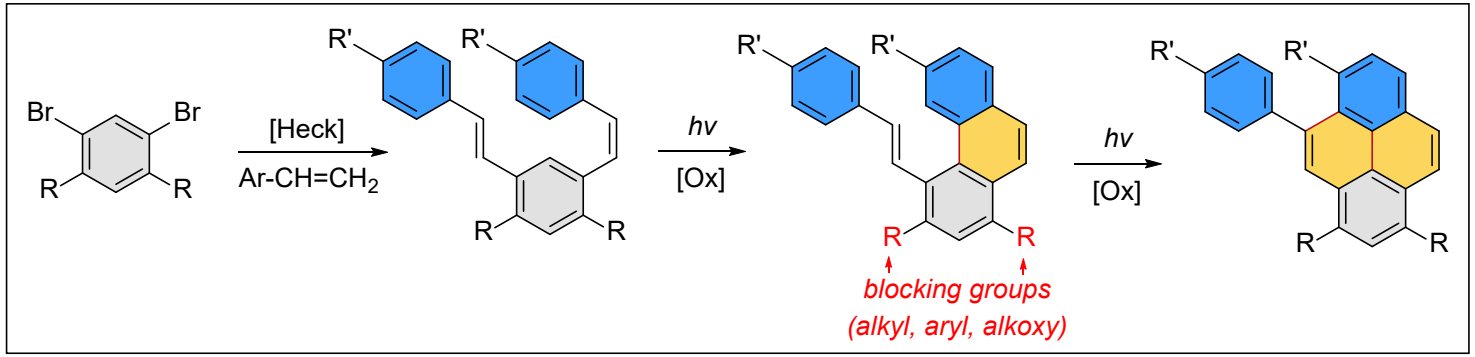
Solution: The blocking groups

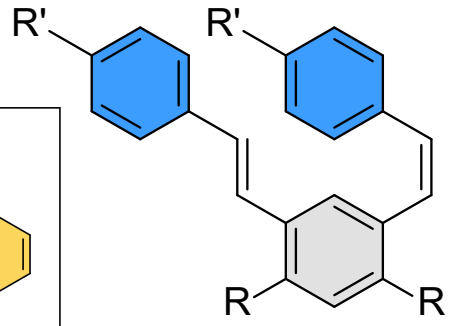
- Commercially available starting materials
- Two-step synthesis.

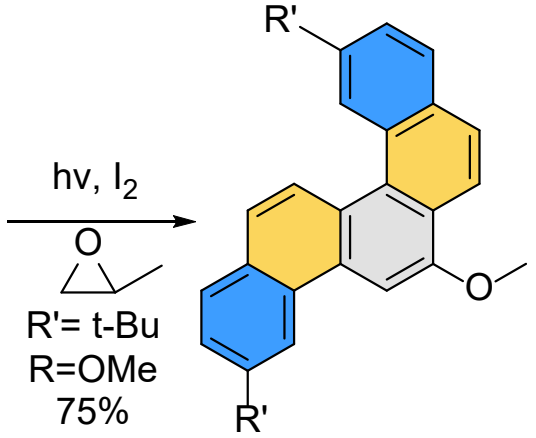


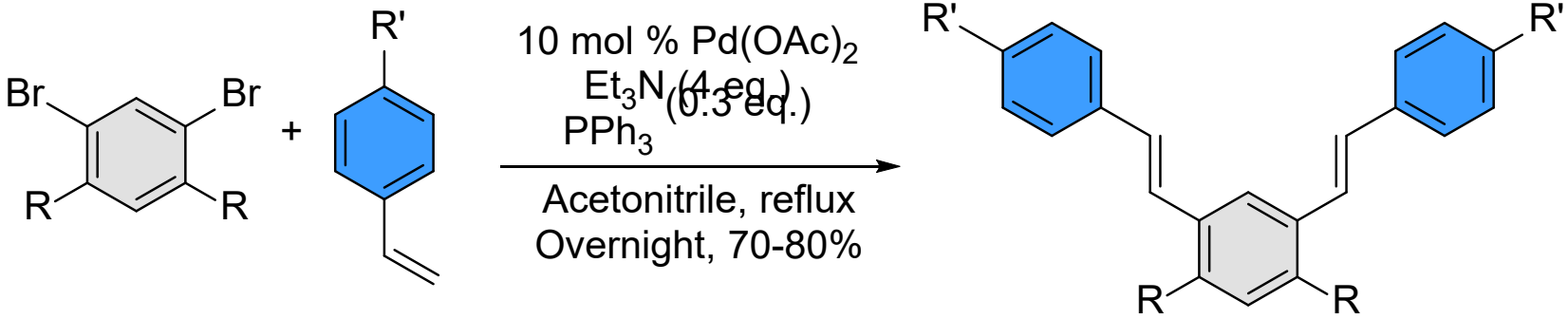


Initial studies





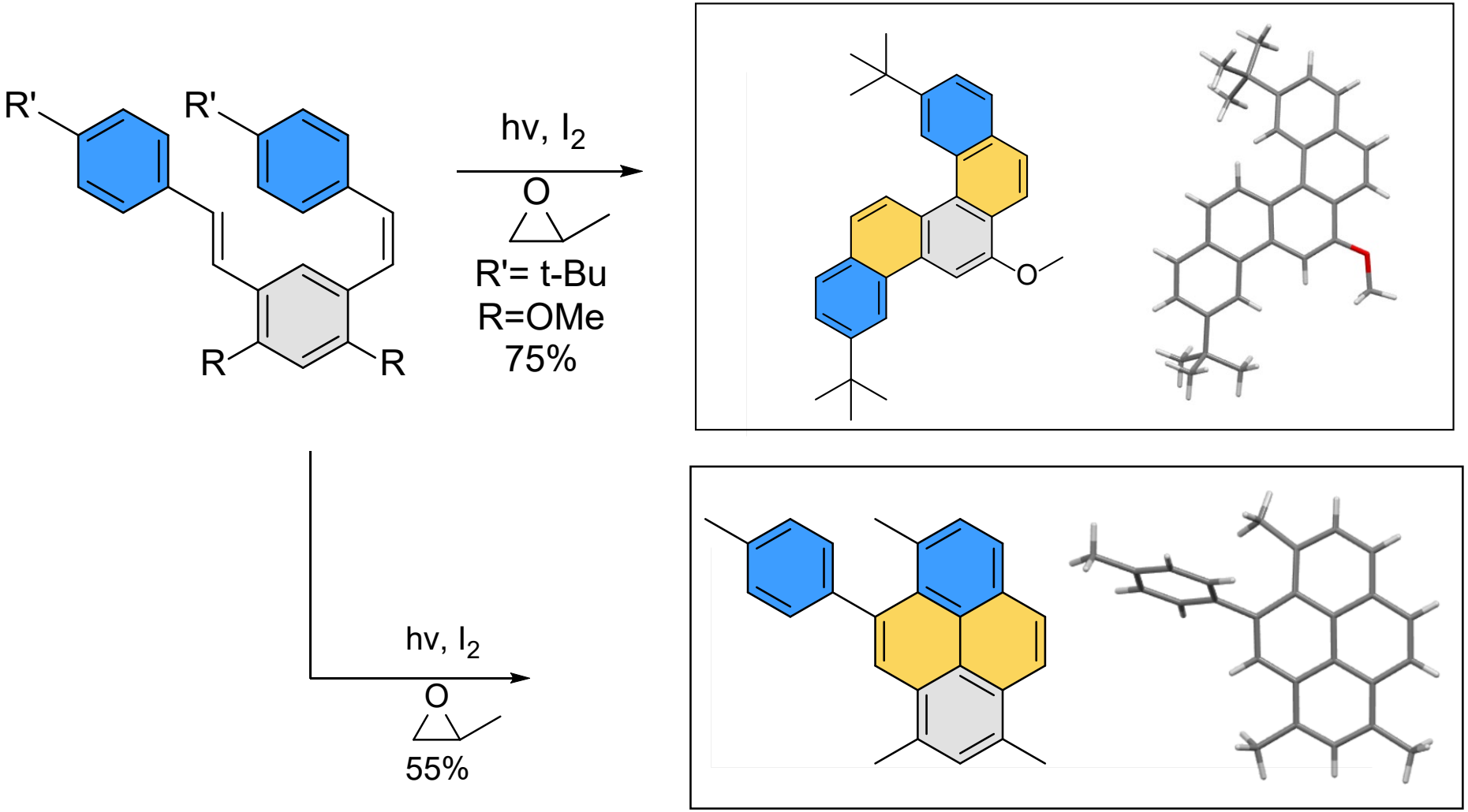




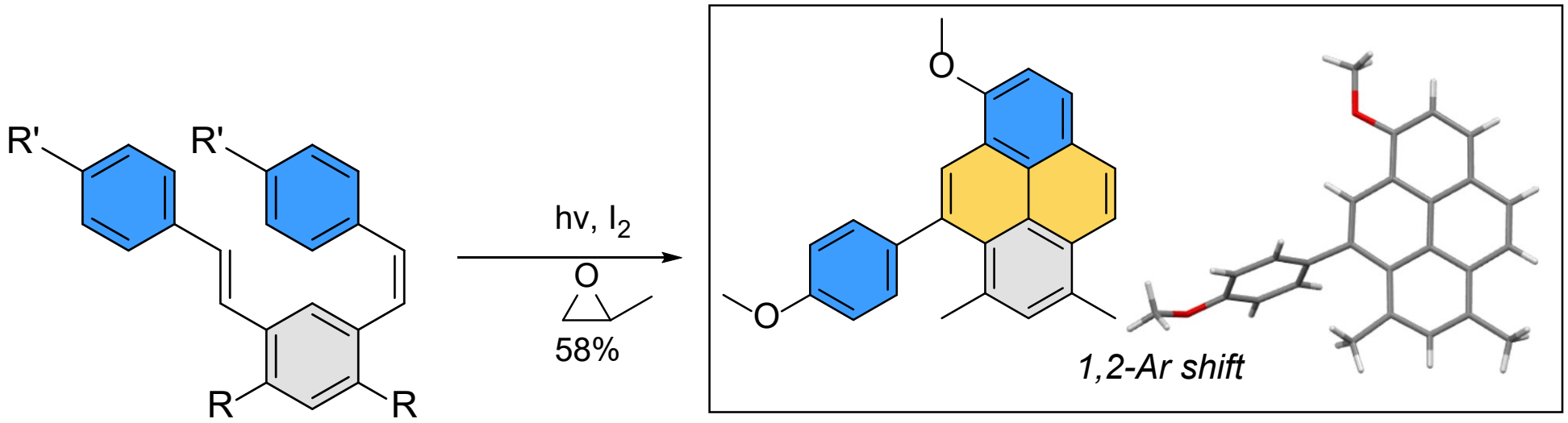
R'=Me, OMe, Cl, t-Bu

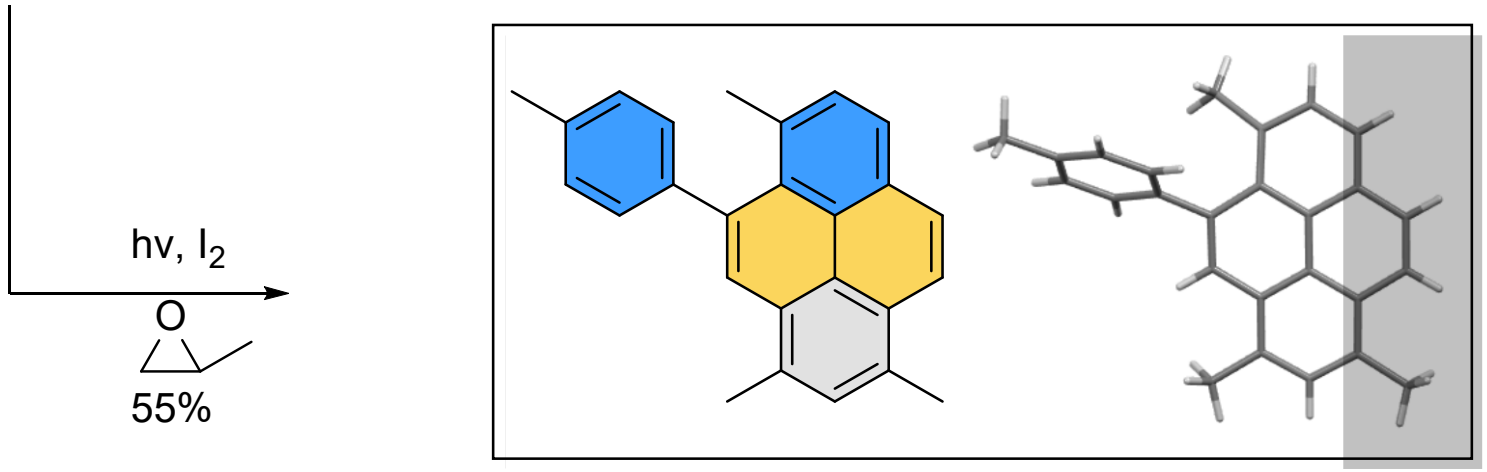
E- and Z-isomers interconvert under photochemical conditions

Not all blocking groups are equal

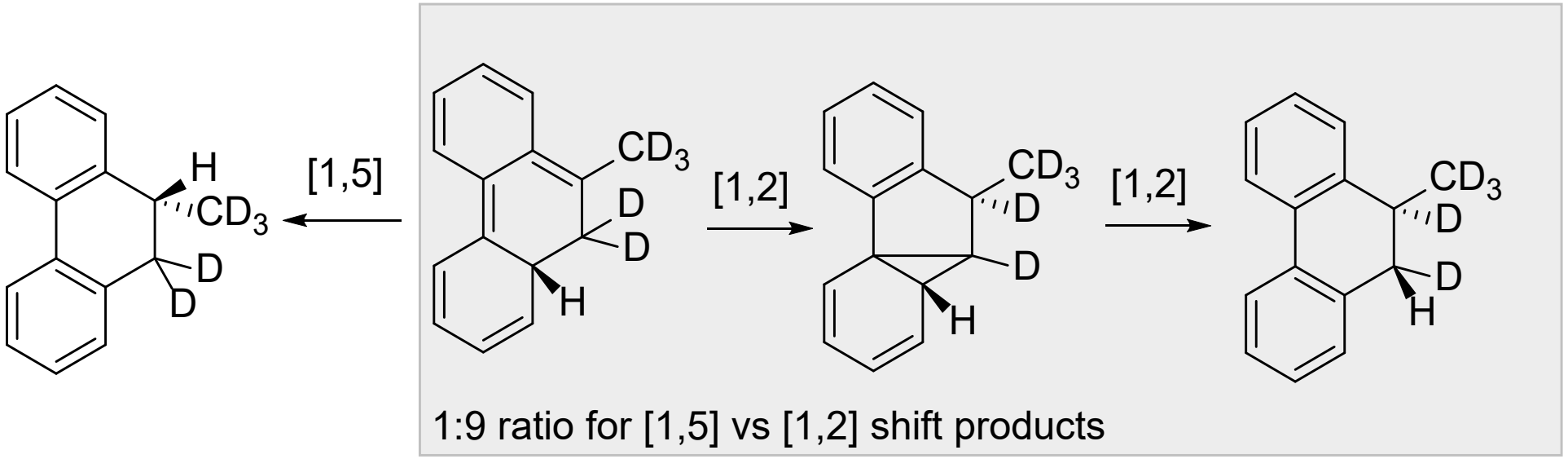


A new reaction- double photocyclization followed by Ar-shift





Mechanistic background for the aryl shift

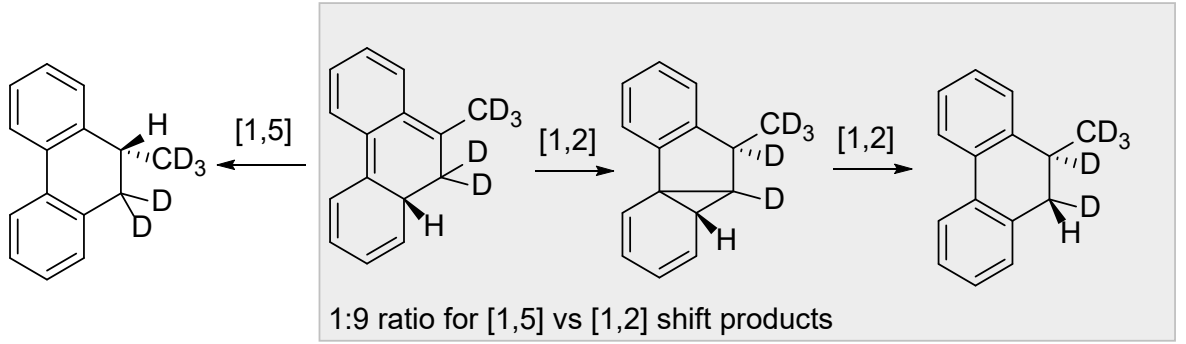


Cold

Lewis et al., J. Org. Chem. 2005, 10447

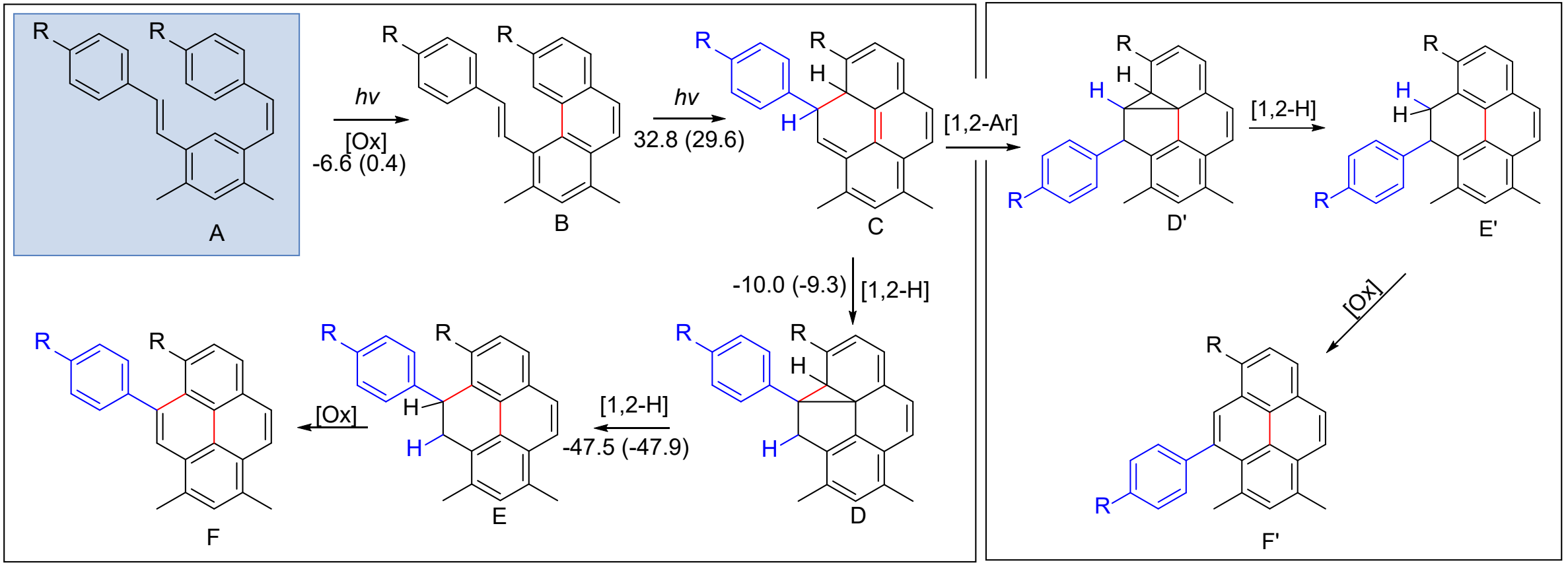
Room Temp.

Proposed mechanism

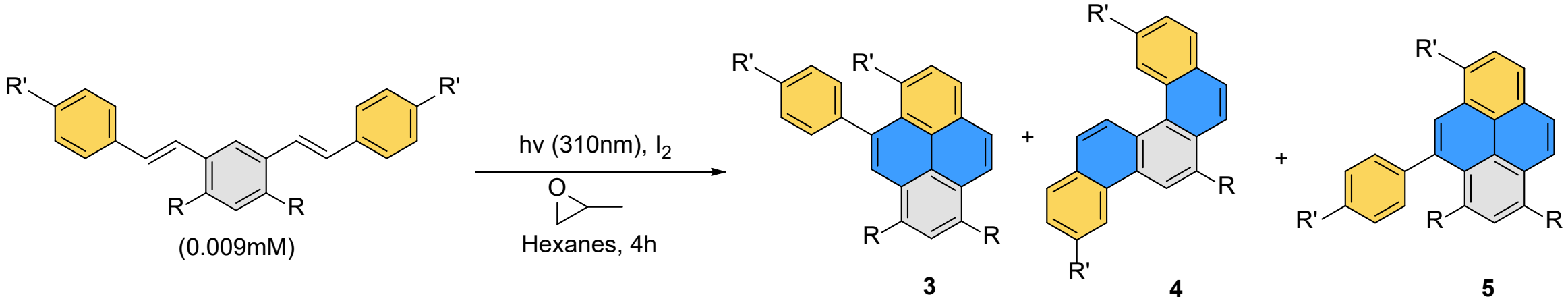


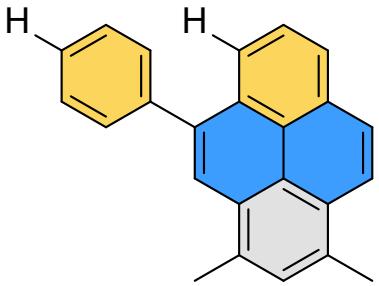
R=Me: ΔG (ΔH)

Energies in kcal/mol, M06-2X(D3)/6-311++G(d,p) Int=UF

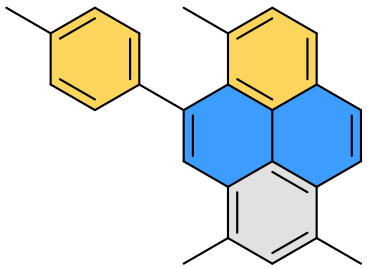


The blocking group is not perfect

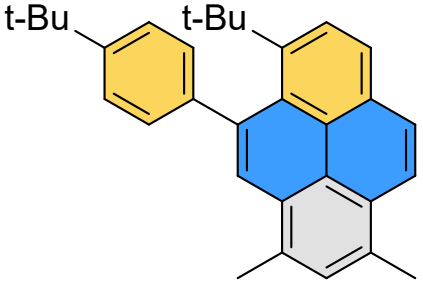




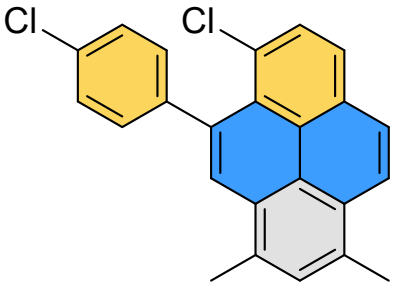
3a= 50%
3:4=5:2



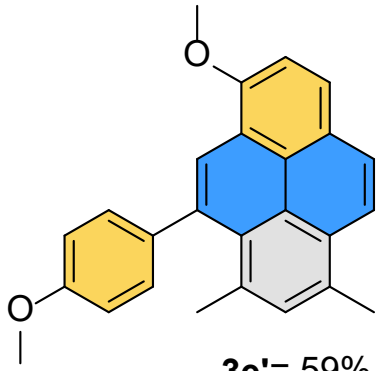
3b= 57%
3:4=5:2



3c= 25%
3:4=1:1

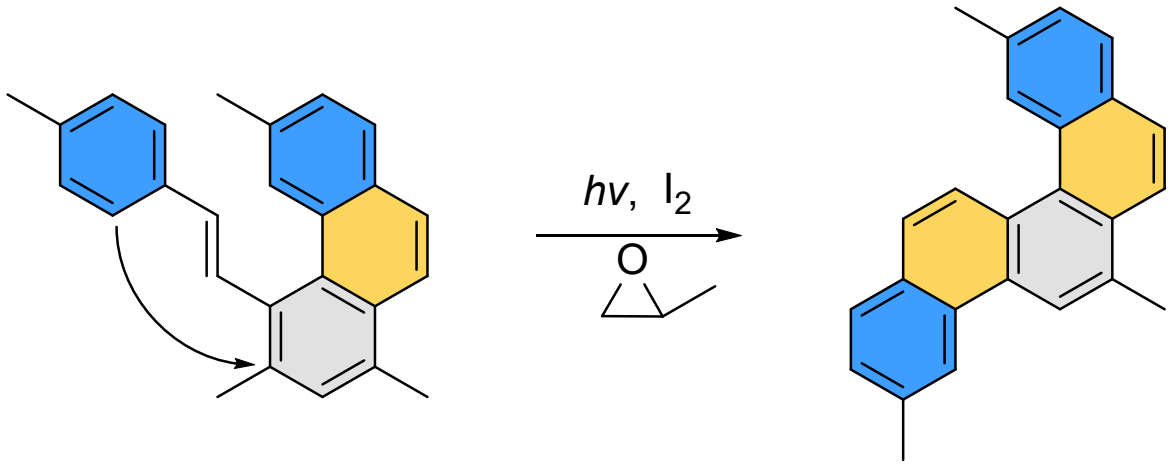


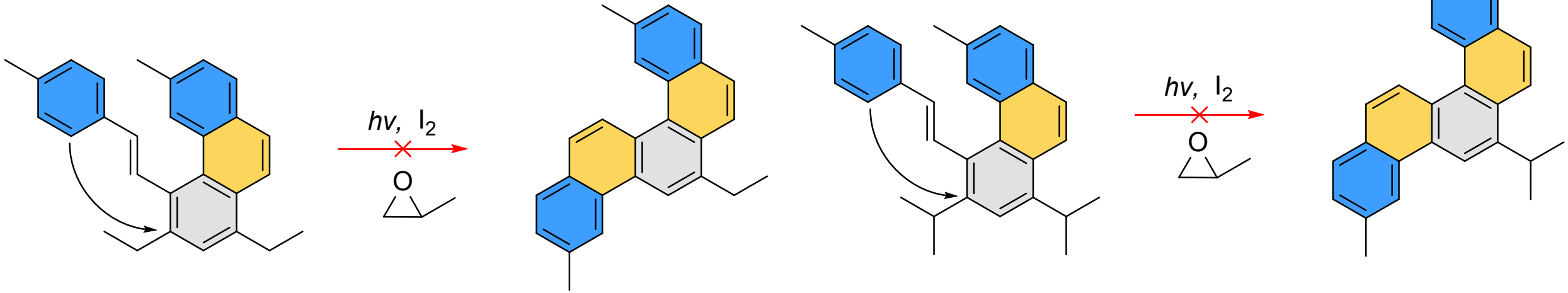
3d= 28%
3:4=1:1



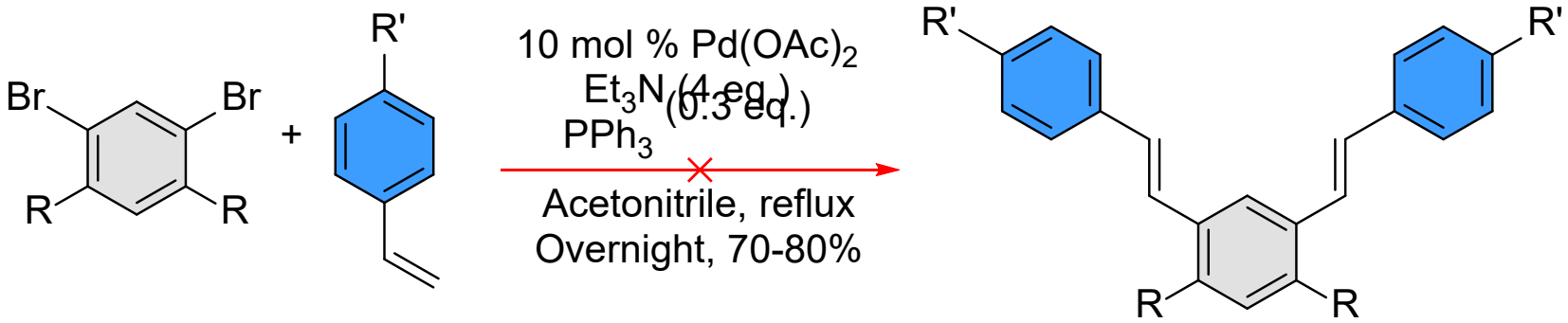
3e'= 59%
5:4=5:1

Is sterics the solution?

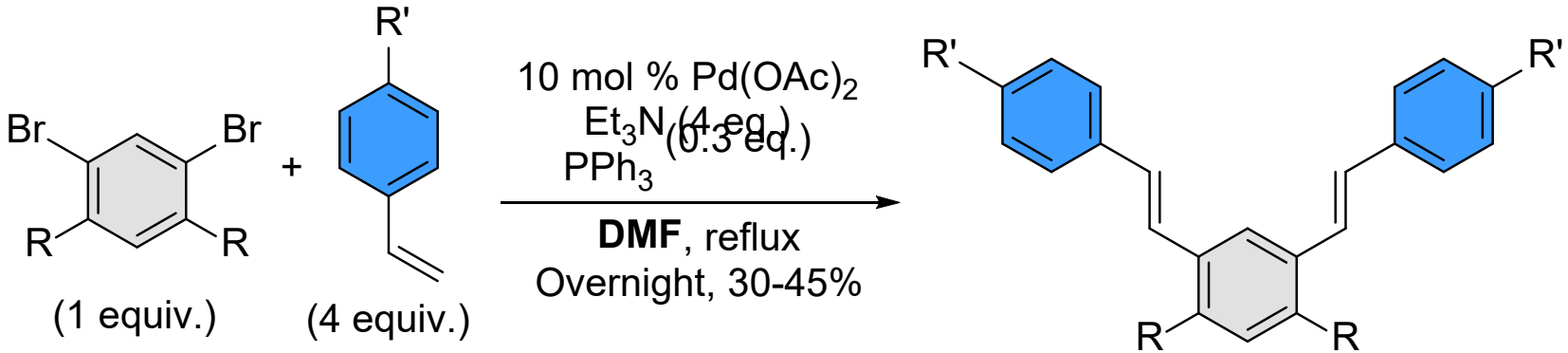




New problem: the starting material is unfavorable to make— re-optimization



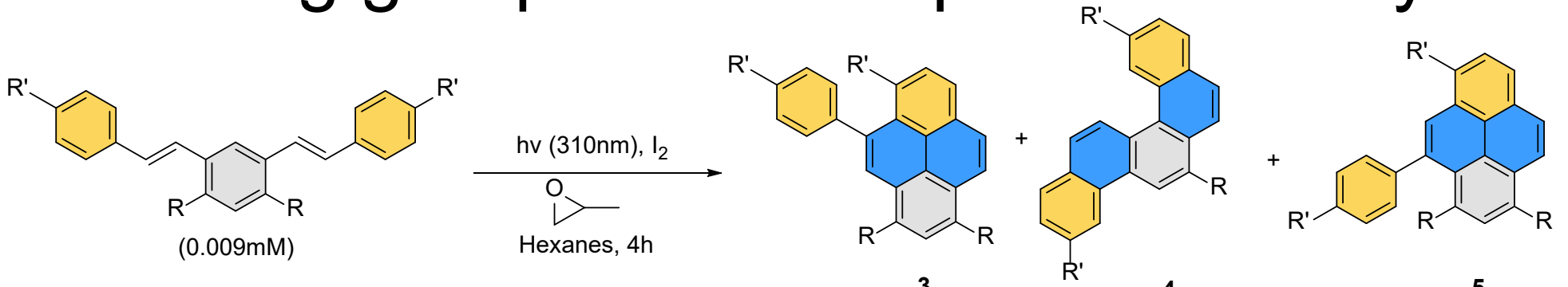
R'=Me, OMe, Cl, t-Bu
R=Et, i-Pr

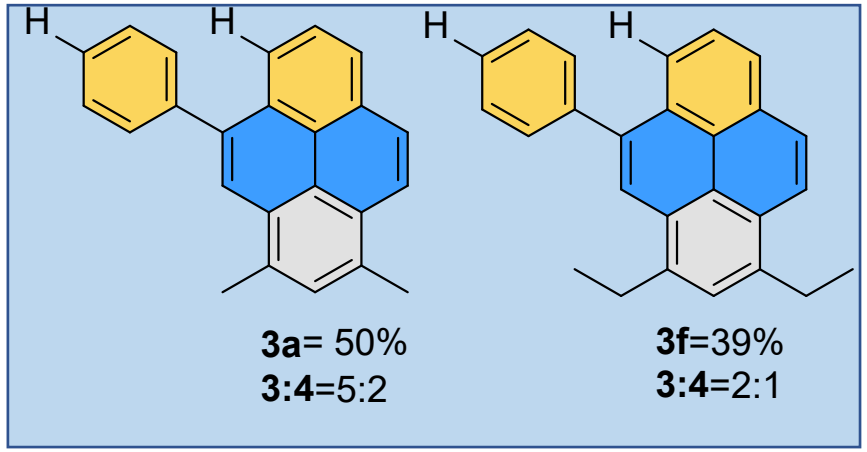


(1 equiv.) (4 equiv.)

R'=Me, OMe, Cl, t-Bu
R=Et, i-Pr

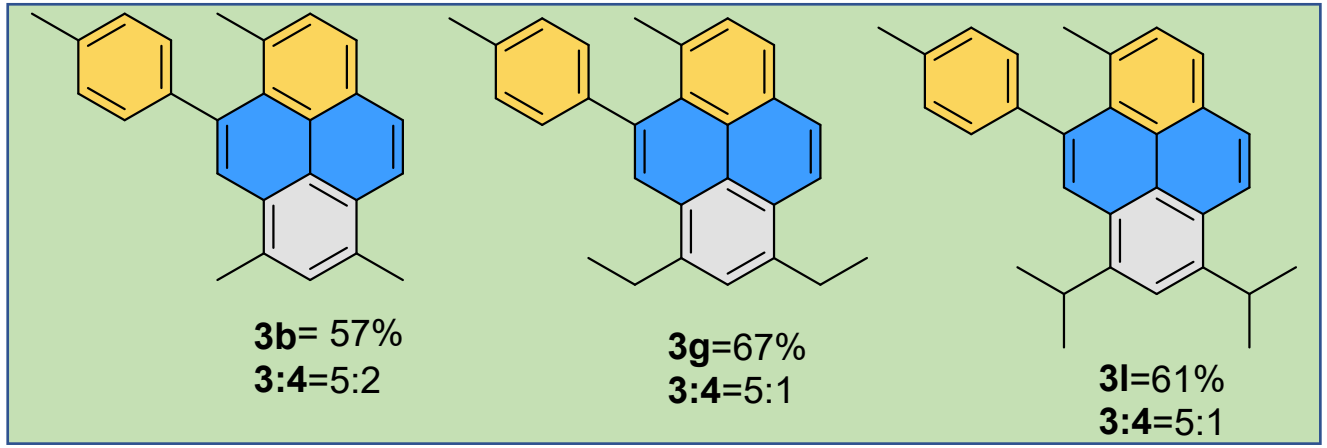
Larger blocking groups do not impact selectivity





3a= 50%
3:4=5:2

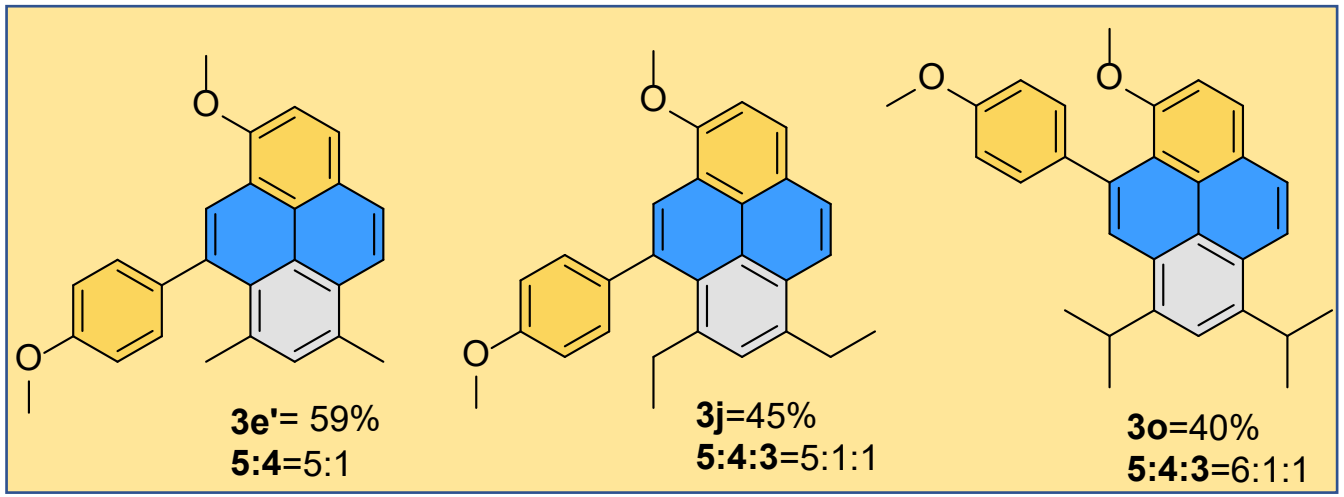
3f=39%
3:4=2:1



3b= 57%
3:4=5:2

3g=67%
3:4=5:1

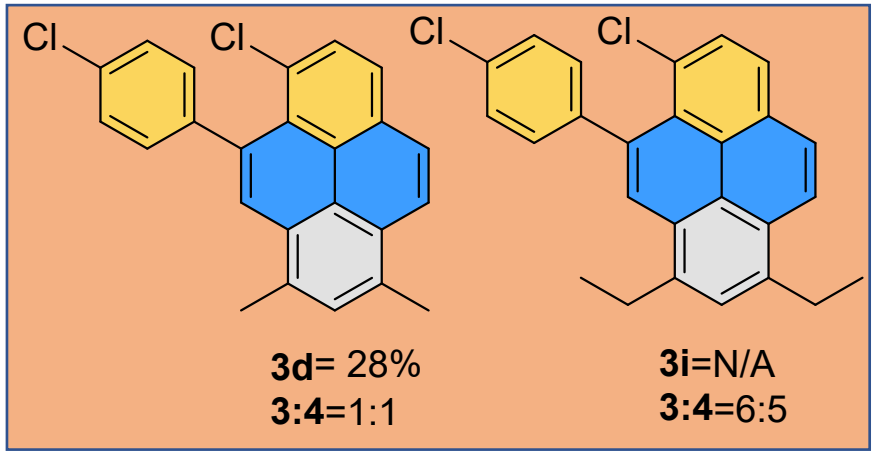
3l=61%
3:4=5:1



3e'= 59%
5:4=5:1

3j=45%
5:4:3=5:1:1

3o=40%
5:4:3=6:1:1

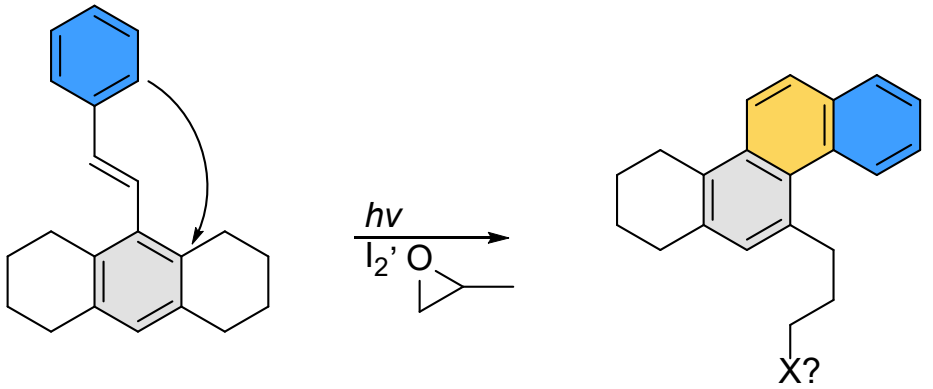


3d= 28%
3:4=1:1

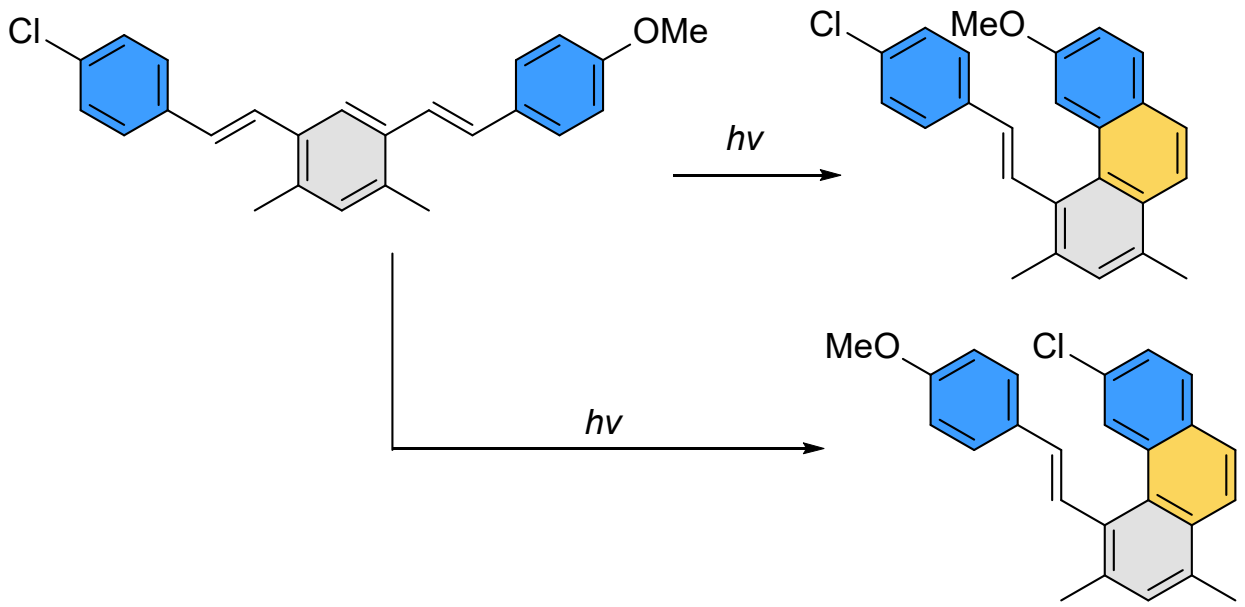
3i=N/A
3:4=6:5

Things to explore

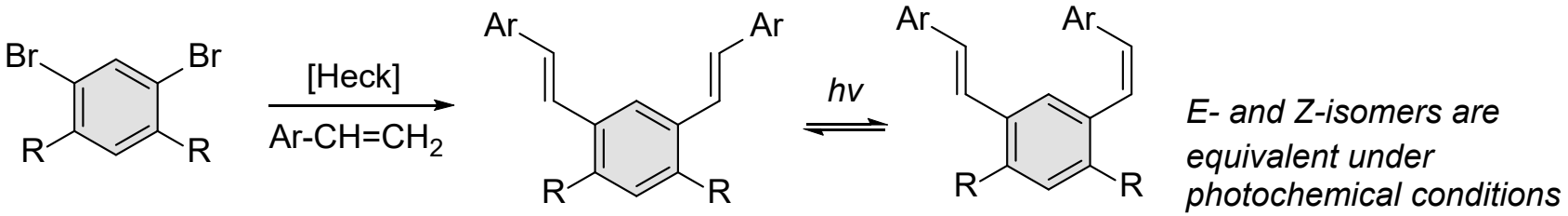
- Find what happens with the eliminated blocking group

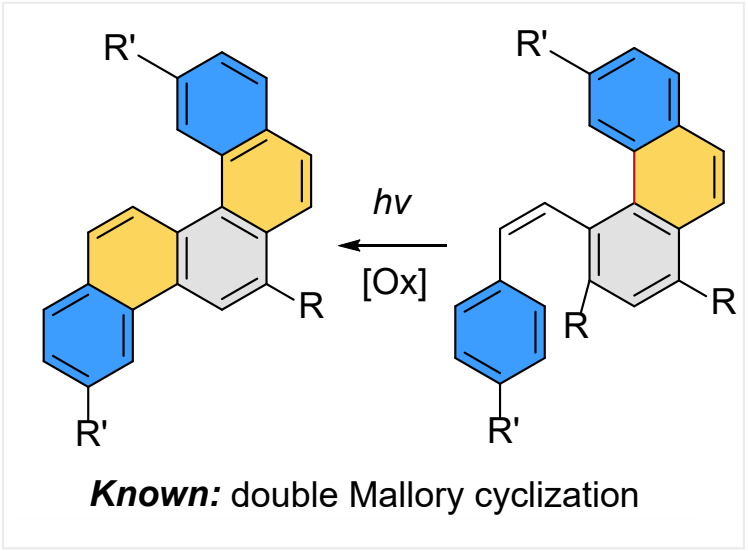


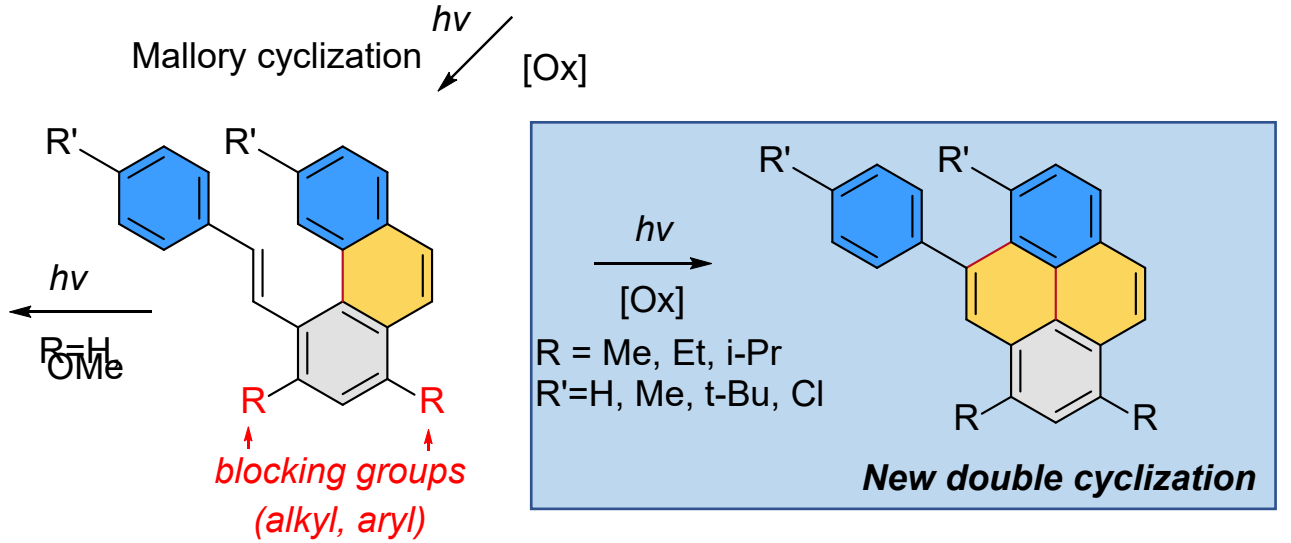
- Comparing relative reactivity of styryl groups

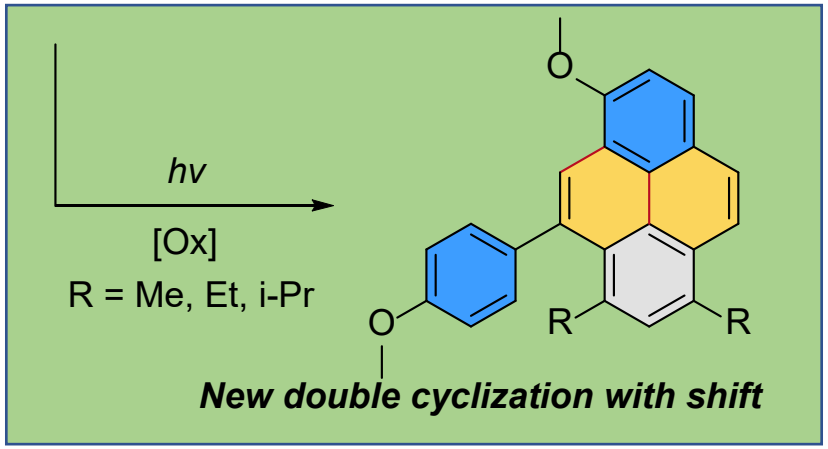


Conclusion


Br
Br
R
R
[Heck]
Ar-CH=CH2
Ar
Ar
R
R
hv
Ar
Ar
R
R
E- and Z-isomers are equivalent under photochemical conditions

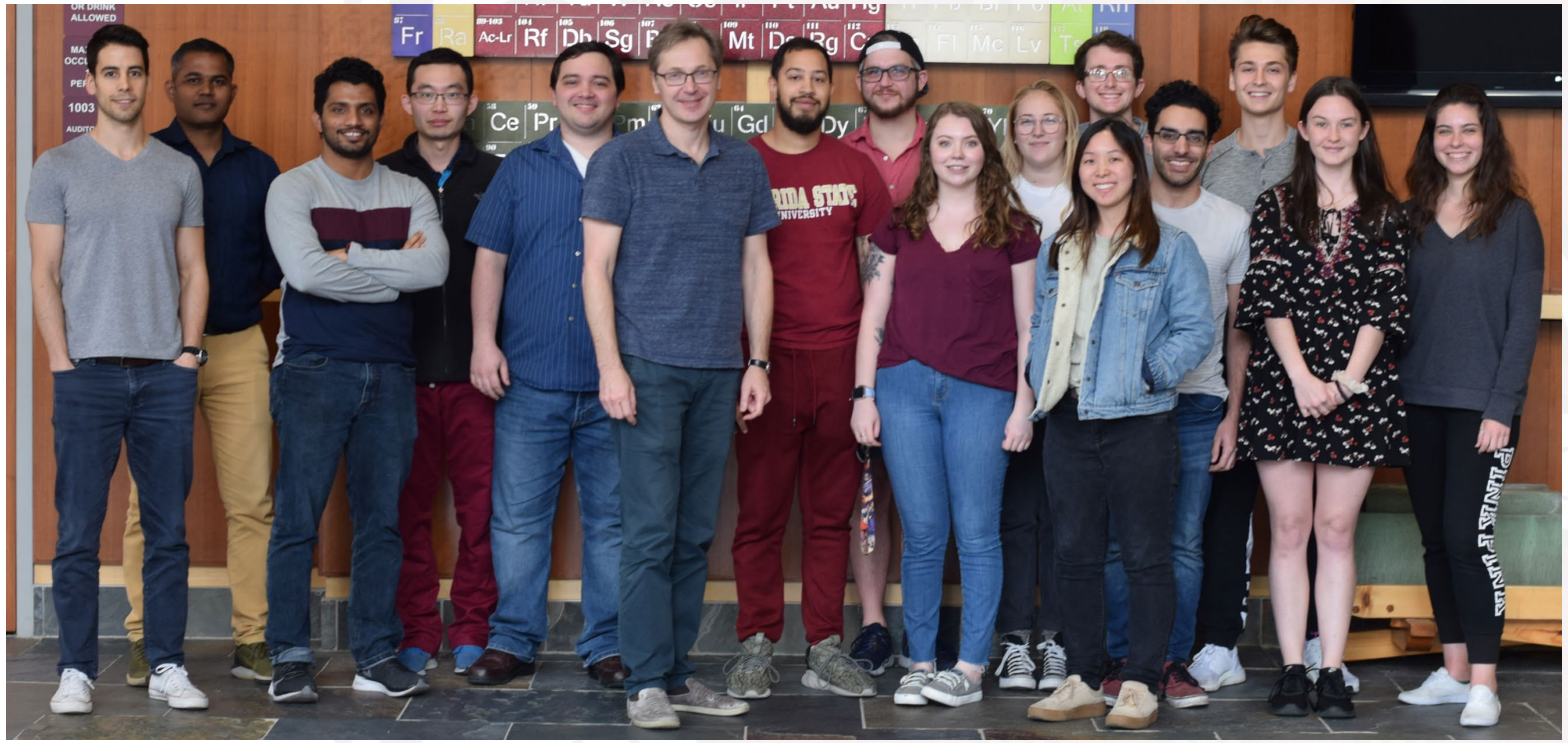

R'
R
R'
hv
[Ox]
R'
R
R
R'
Known: double Mallory cyclization

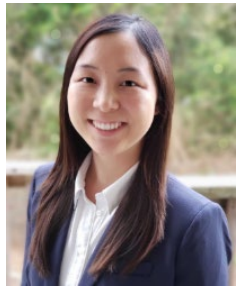

Mallory cyclization
hv
[Ox]
R'
R'
hv
R=H
OMe
R
R
blocking groups
(alkyl, aryl)
hv
[Ox]
R = Me, Et, i-Pr
R'=H, Me, t-Bu, Cl
R'
R'
R
R
New double cyclization


hv
[Ox]
R = Me, Et, i-Pr
O
O
R
R
New double cyclization with shift

Acknowledgements

Alabugin Group





Team Dos Santos
-Angel Chu
-Alexandria Palazzo
-Josef Maselli

Principal Investigator
-Dr. Igor Alabugin
Post-Doctorate
-Rahul Kawade
Graduate (left to right)
-Edgar Gonzalez-Rodriguez
-Febin Kuriakose
-Chaowei Hu
-Adam Campbell
-Michael Maxwell
-Leah Kuhn
-Quintin Elliott (not in picture)
Undergraduates (left to right)
-Morgan Skala
-Curtis DeShong
-Miguel Abdo
-Jordan Suarez
-Patricia Mehaffy

Crystallography
-Xinsong Lin