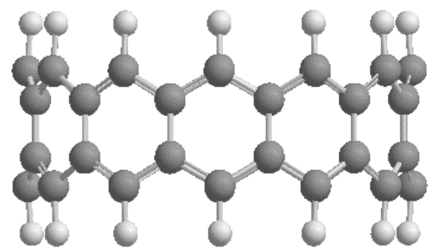
Studies into the Synthesis of [12]Cyclacene



Zhuoran Zhang

Douglas Research Group

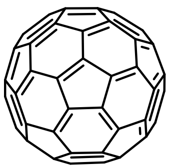
University of Minnesota – Twin Cities

Graduate Research Symposium

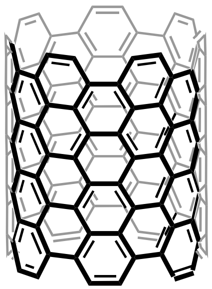
07/20/2017

Interesting Theoretical Molecules

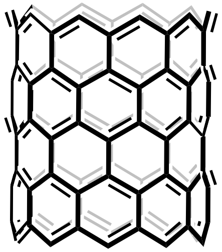
- Fullerenes and carbon nanotubes



C_{60}



Armchair CNT

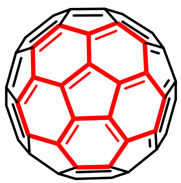


Zig-zag CNT

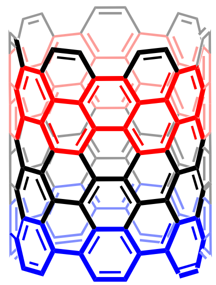
- ❖ Sphere vs tube
- ❖ Materials science applications
- ❖ Curved conjugation

Interesting Theoretical Molecules

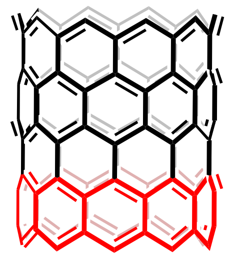
- Fullerenes and carbon nanotubes



C_{60}



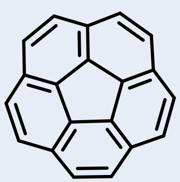
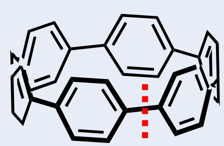
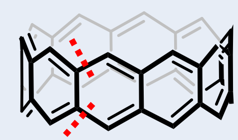
Armchair CNT



Zig-zag CNT

❖ Sphere vs tube
❖ Materials science applications
❖ Curved conjugation

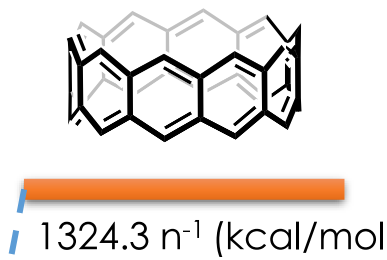
- Fragment structures

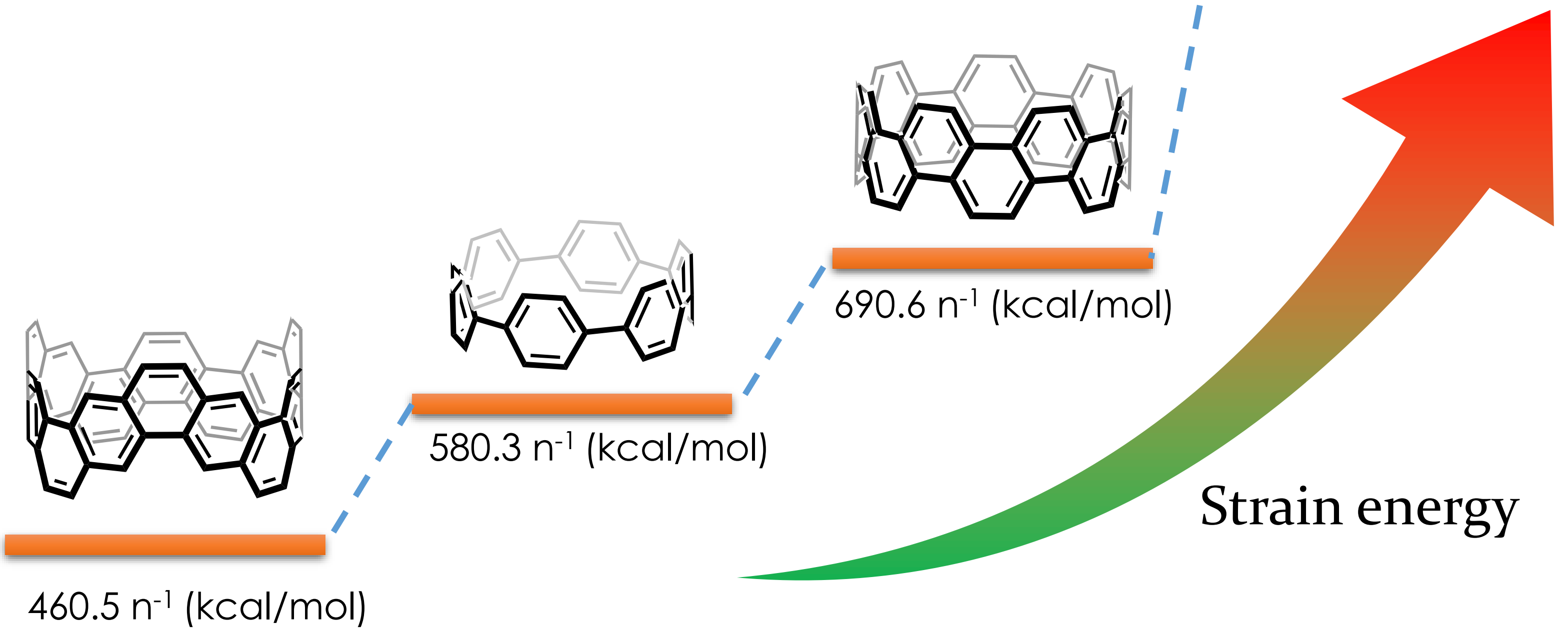
Buckybowl	Carbon nanorings	Carbon nanobelts	
 Corannulene	 Cycloparaphenylene	 Cyclophenacene isomer	 Cyclacene
synthesized in 1966	*synthesized in 2008*	*synthesized in 2017*	*proposed in 1954* *not synthesized*

1. Barth, W. E.; Lawton, R. G. *J. Am. Chem. Soc.* **1966**, *88*, 380–381.
2. Jasti, R.; Bhattacharjee, J.; Neaton, J. B.; Bertozzi, C. R. *J. Am. Chem. Soc.* **2008**, *130*, 17646-17647.
3. Povie, G.; Segawa, Y.; Nishihara, T.; Miyauchi, Y.; Itami, K. *Science*, **2017**, *356*, 172–175.

General challenges in Carbon Nanobelt Synthesis

- Strain energy
- Product stability (diradical character)
- Separation

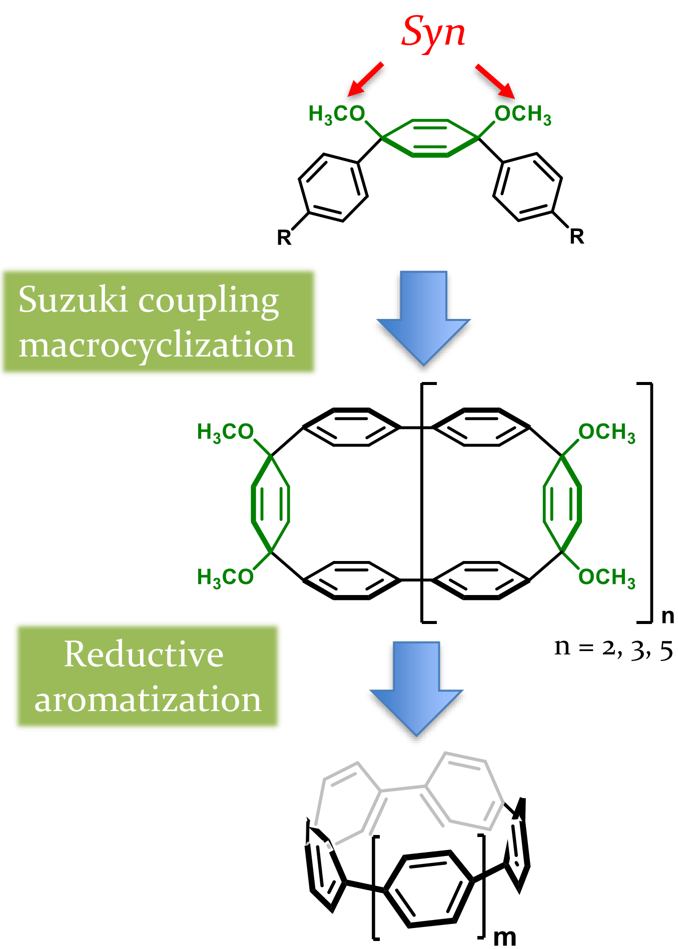




1. Segawa, Y.; Yagi, A.; Ito, H.; Itami, K. *Org. Lett.* **2016**, *18*, 1430–1433.

Synthetic Strategies for Carbon Nanorings and Nanobelts

Cycloparaphenylenes



Curved/unstrained synthons

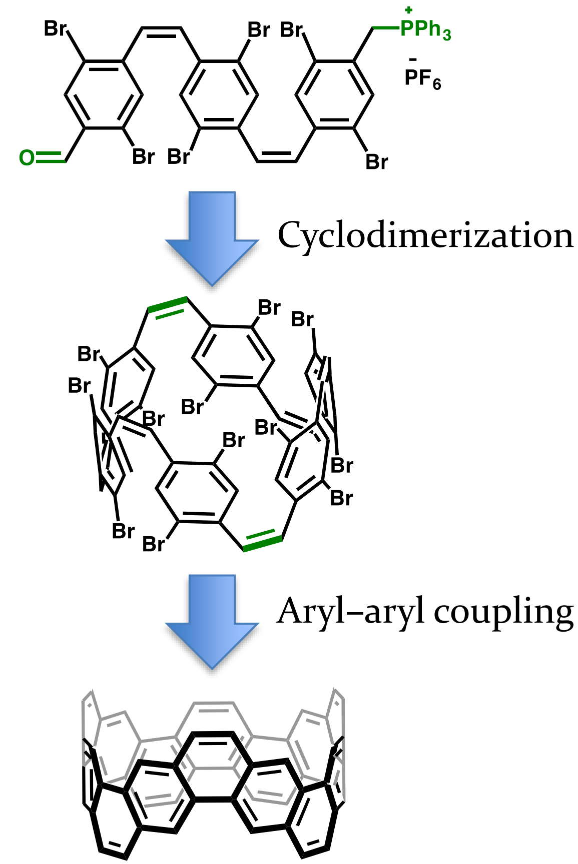
↓

Macrocycle

↓

End-game (aromatization)

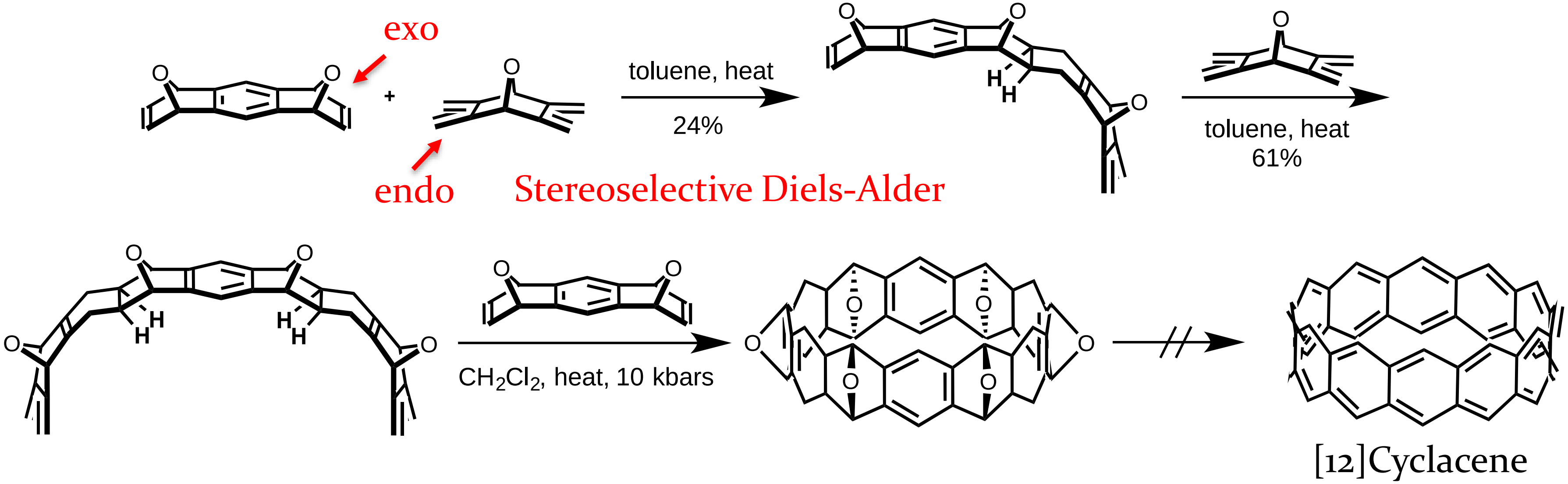
Chiral CNB



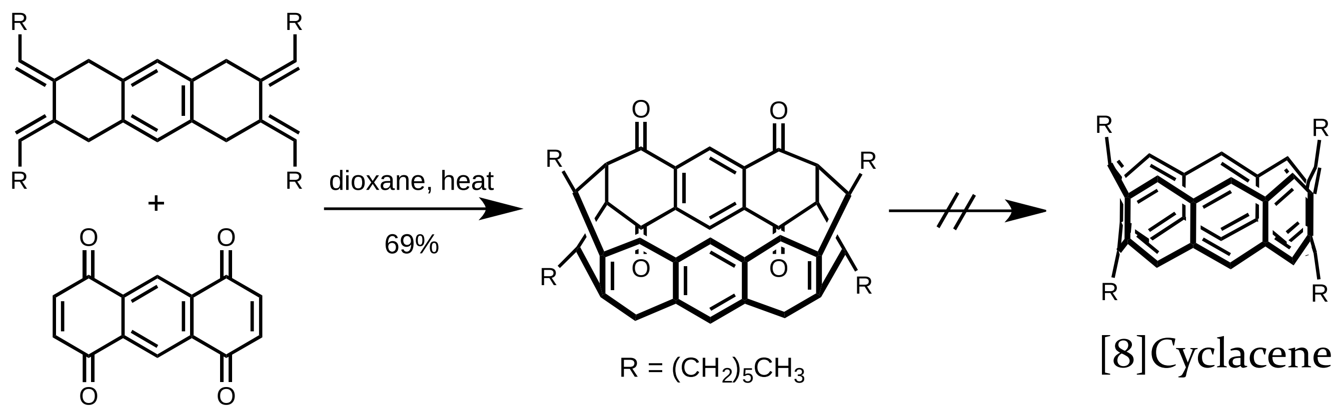
(1) Jasti, R.; Bhattacharjee, J.; Neaton, J. B.; Bertozzi, C. R. *J. Am. Chem. Soc.* **2008**, *130*, 17646-17647.
(2) Povie, G.; Segawa, Y.; Nishihara, T.; Miyauchi, Y.; Itami, K. *Science*, **2017**, *356*, 172–175.
(3) Yamago, S.; Watanabe, Y.; Iwamoto, T. *Angew. Chem., Int. Ed.* **2010**,*49*, 757–759.
(4) Takaba, H.; Omachi, H.; Yamamoto, Y.; Bouffard, J.; Itami, K. *Angew. Chem., Int. Ed.* **2009**,*48*, 6112–6116.

Synthetic precedence to [n]Cyclacene derivatives

- Stoddart's approach to [12]cyclacene



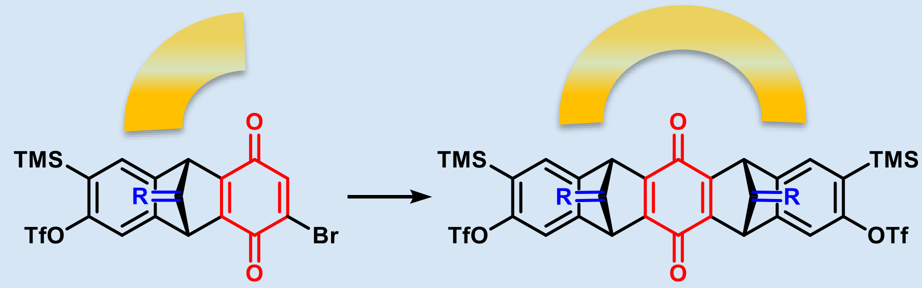
- Cory's approach to [8]cyclacene



(1) Kohnke, F. H.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed.* **1987**, *26*, 892-894
(2) Girreser, U.; Giuffrida, D.; Kohnke, F. H.; Mathias, J. P.; Philp, D.; Stoddart, J. F. *Pure Appl. Chem.* **1993**, *65*, 119-125.
(3) Cory, R. M.; McPhail, C. L.; Dikmans, A. J.; Vittal, J. J. *Tetrahedron Lett.* **1996**, *37*, 1983-1986.

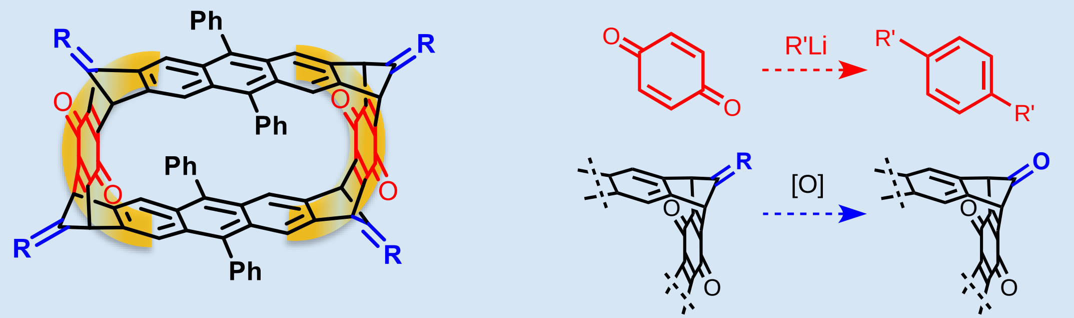
The Strategy for Macrocycle Synthesis– The Douglas Approach

Curved/unstrained synthons



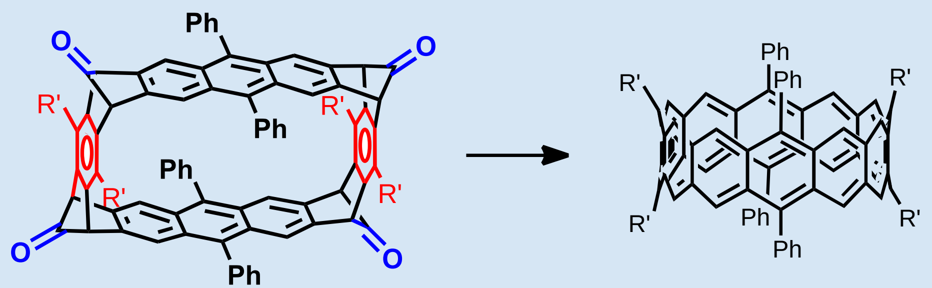
Stereoselective Diels–Alder reaction

Macrocycle



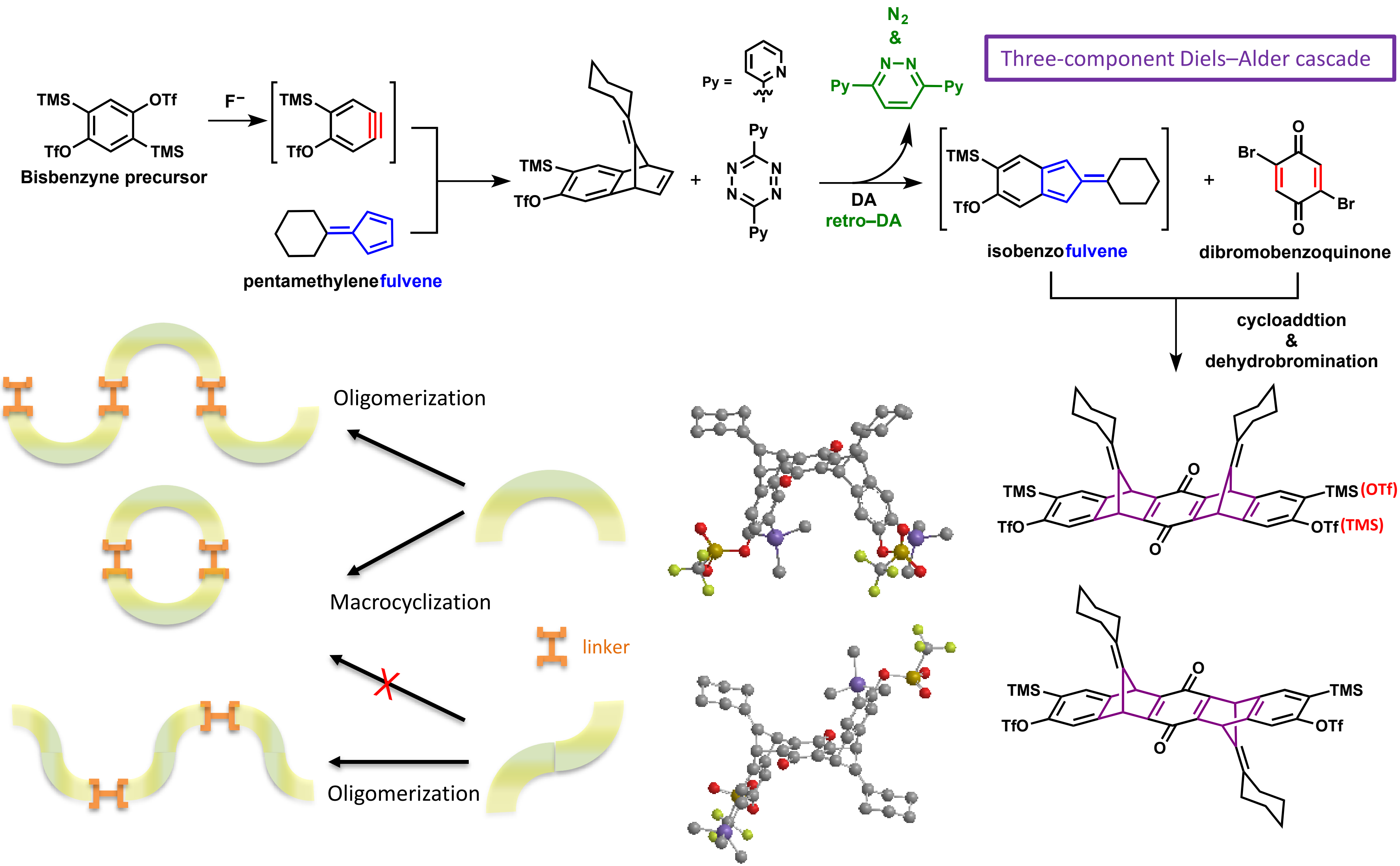
Dehydrogenation
Quinone reduction
decarbonylation

End-game (aromatization)



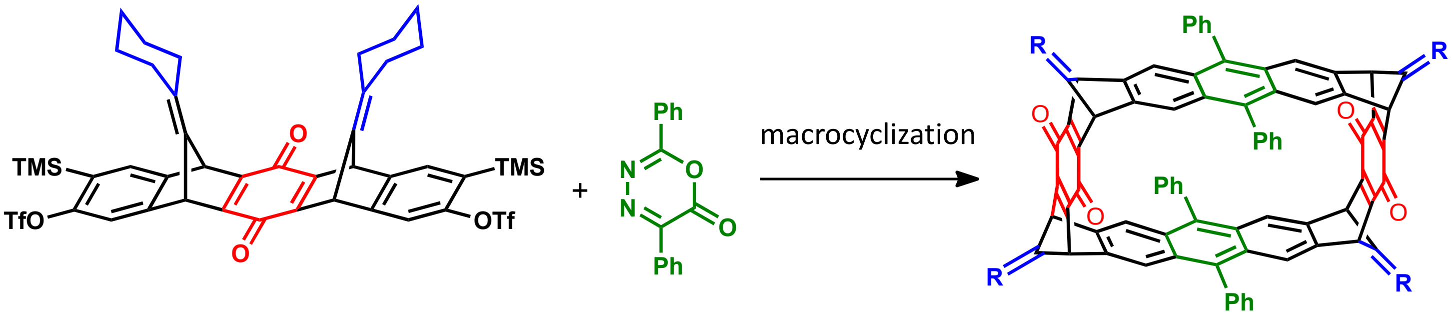
Proposed Synthesis and Predicted Challenges

➢ Challenge I: Stereoselective synthesis of cyclization precursor (half cycle)

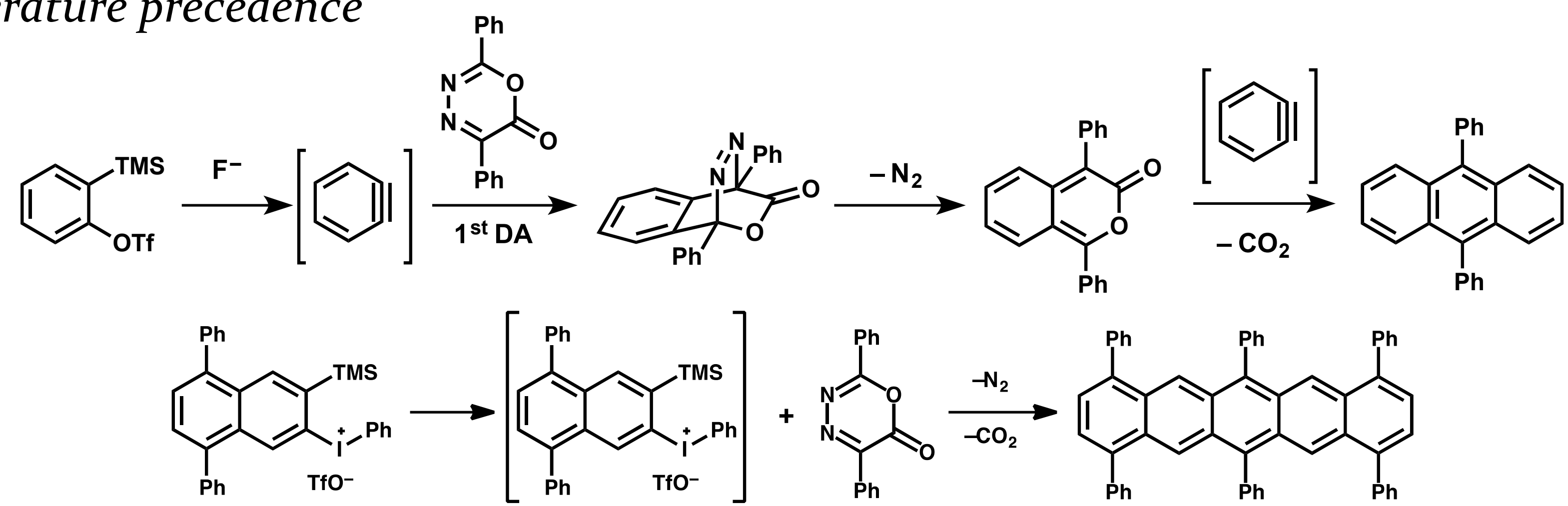


Proposed Synthesis and Predicted Challenges

- Challenge II: macrocyclization and late-stage functionalization



Literature precedence



Steglich, W.; Buschmann, E.; Gansen, G.; Wilschowitz, L. *Synthesis* **1977**, 1977(*4*), 252-253.
Miao, Q.; Chi, X.; Xiao, S.; Zeis, R.; Lefenfeld, M.; Siegrist, T.; Steigerwald, M. L.; Nuckolls, C. *J. Am. Chem. Soc.* **2006**, *128*, 1340–1345.

Proposed Synthesis and Predicted Challenges

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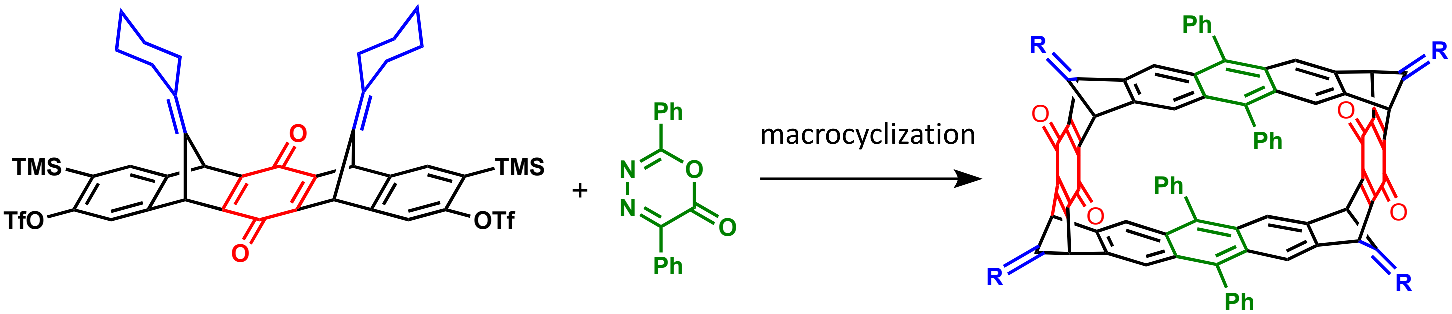
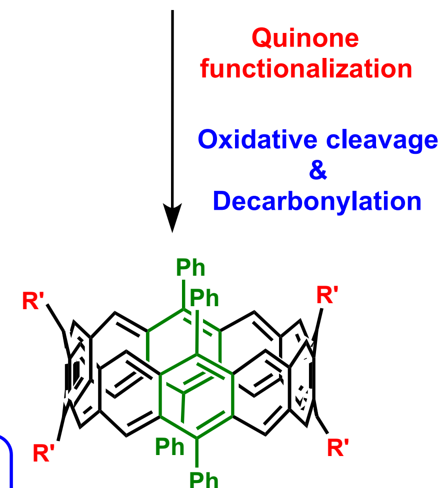
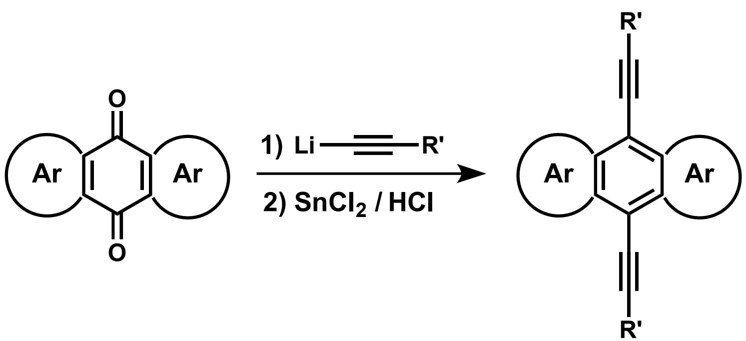
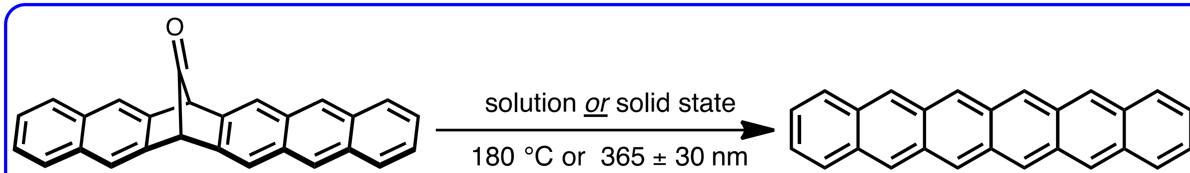






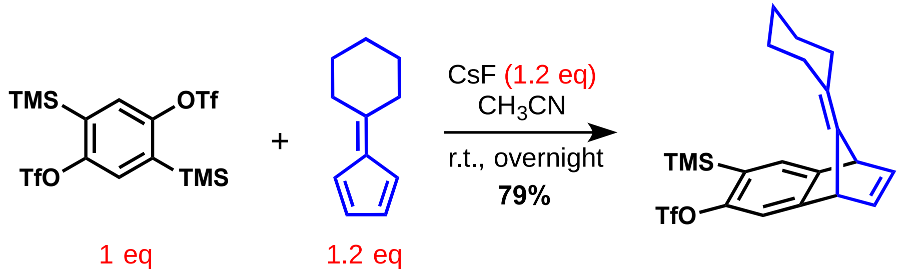
Anthony, J. E.; Eaton, D. L.; Parkin, S. R. *Org. Lett.* **2002**, *4(1)*, 15-18.

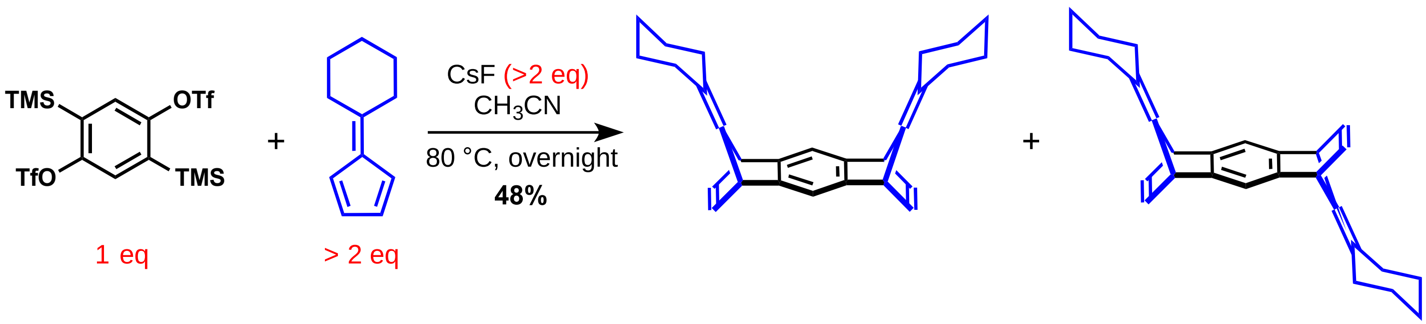


Watanabe, M. et al. *Nat. Chem.* **2012**, *4*, 574-578.

Synthesis of Mono-bridged Precursor (1/4 cycle)

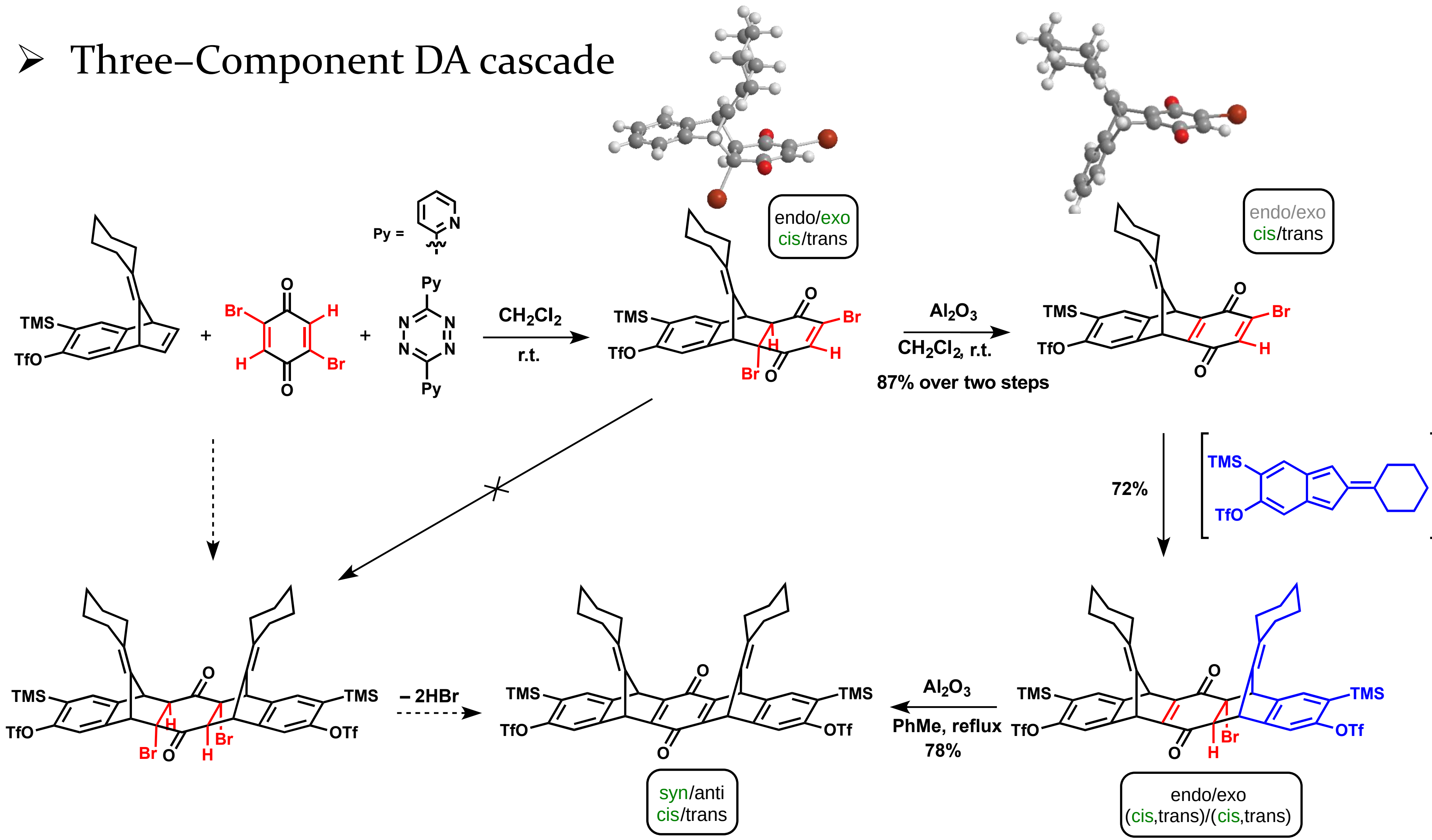
- Controlled benzyne Diels–Alder reaction





Synthesis Attempts toward Syn-isomer

- Three–Component DA cascade



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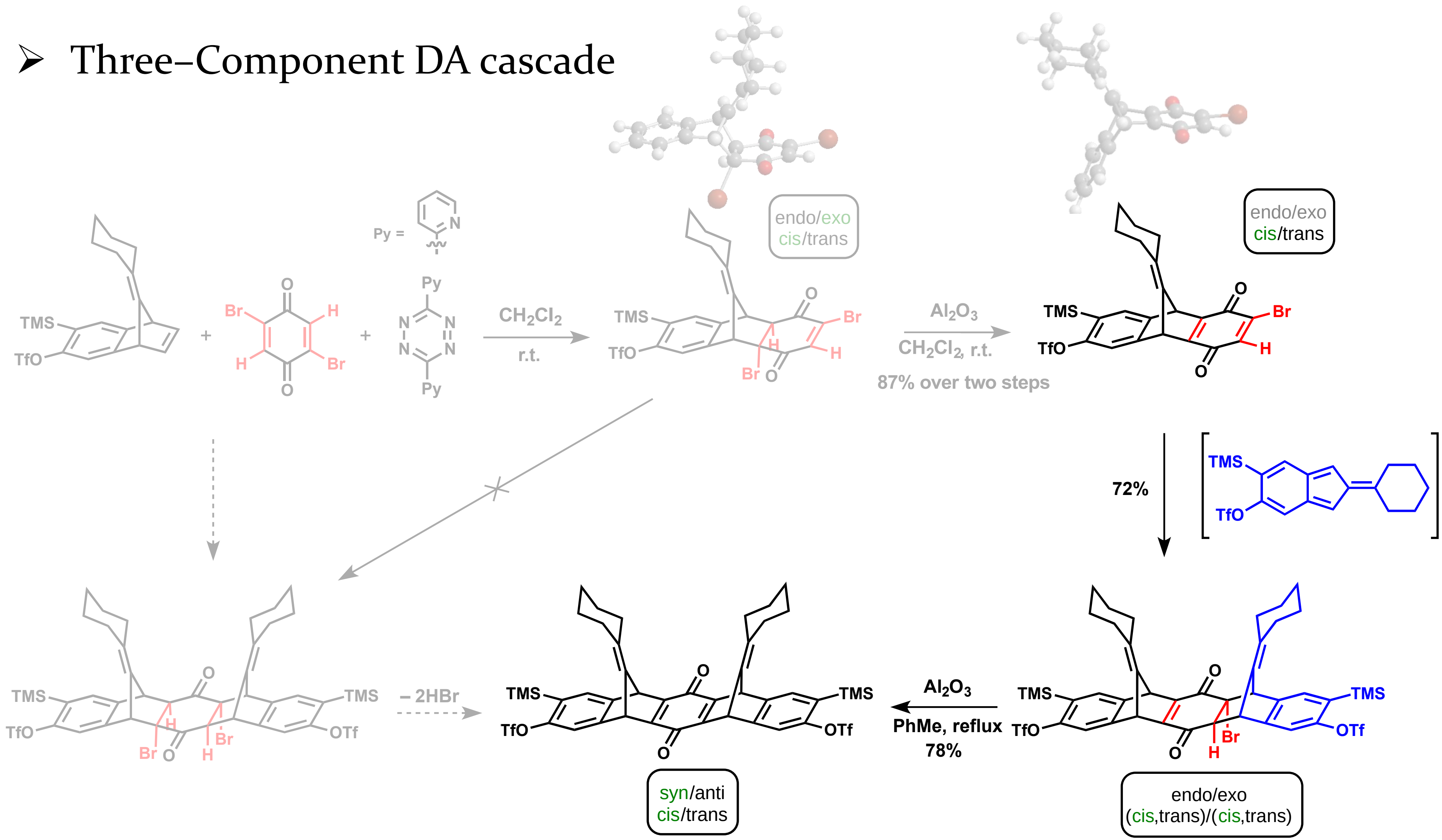
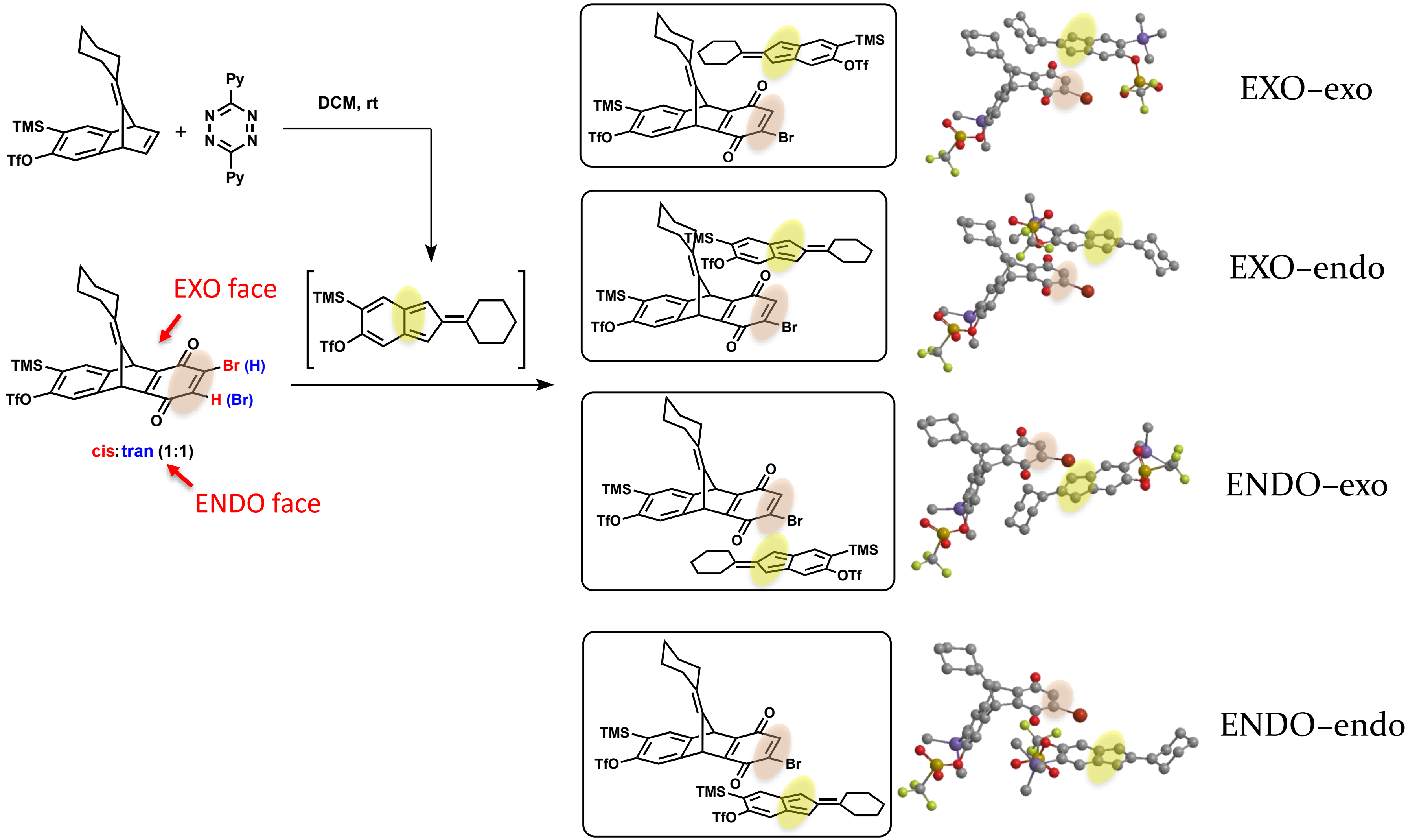


Steric Analysis

- Stereoselective Diels–Alder reactions –– "*EXO–exo* selectivity"



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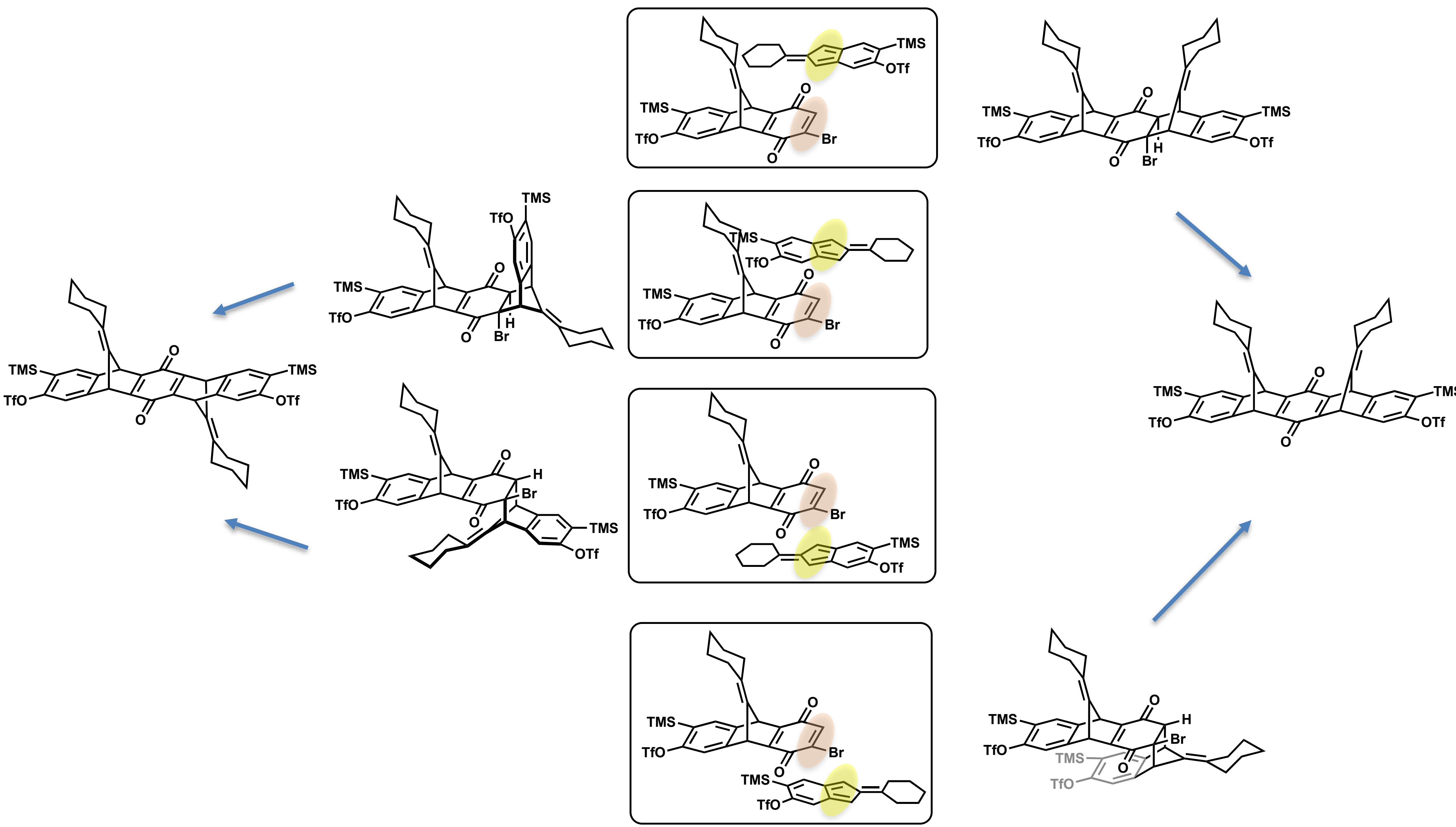
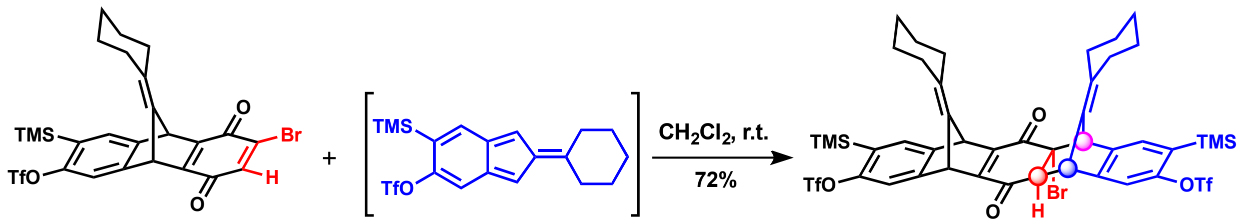
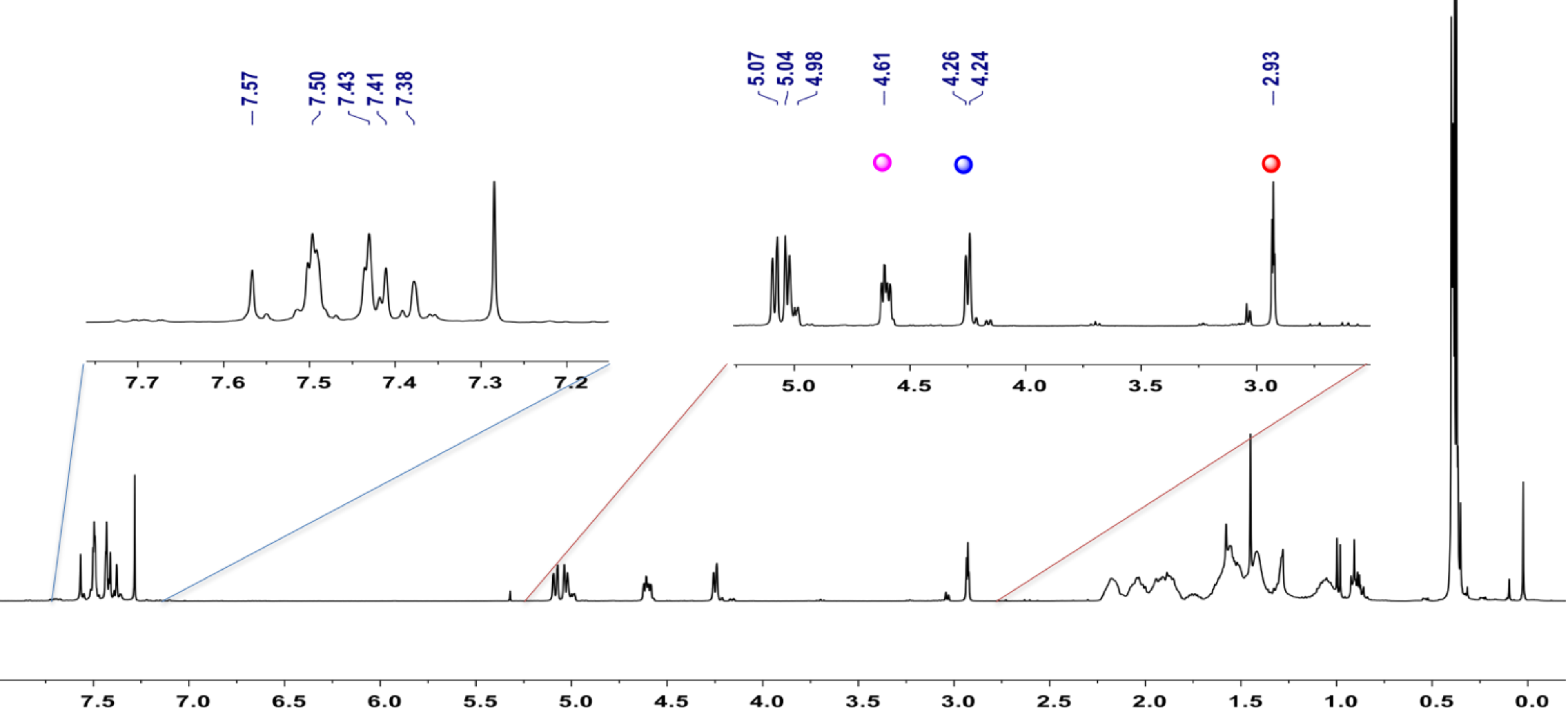


Stereoselective Diels–Alder Reaction

- Stereoselectivity observed in ¹H–NMR spectrum!

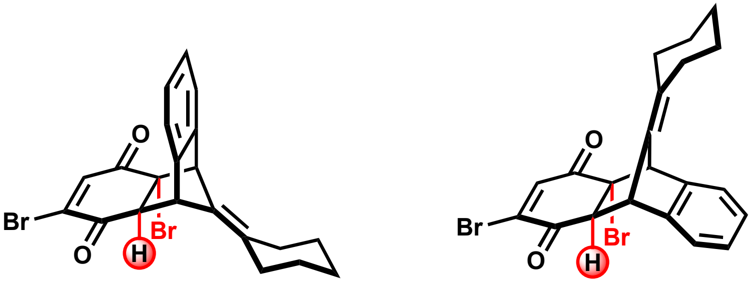


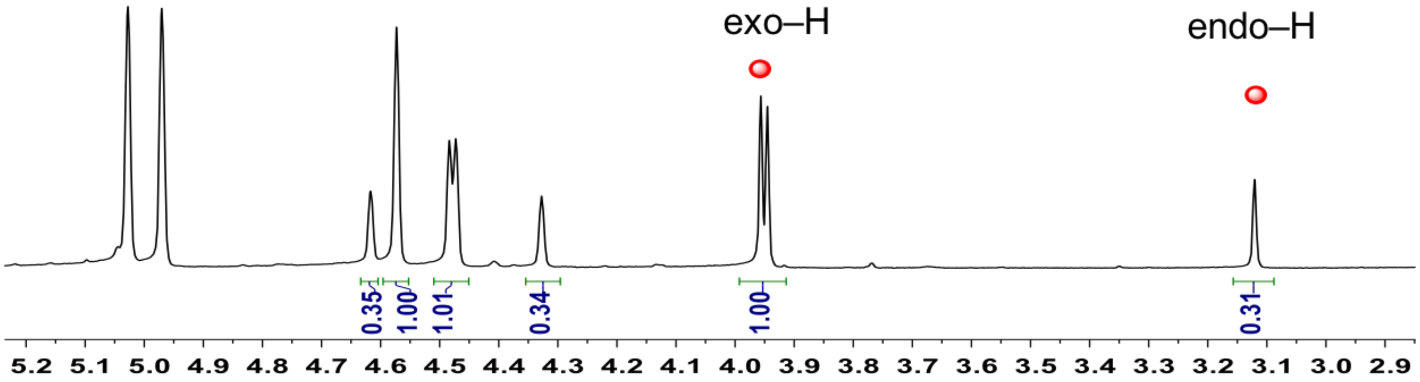


Stereoselective Diels–Alder Reaction

- Model study

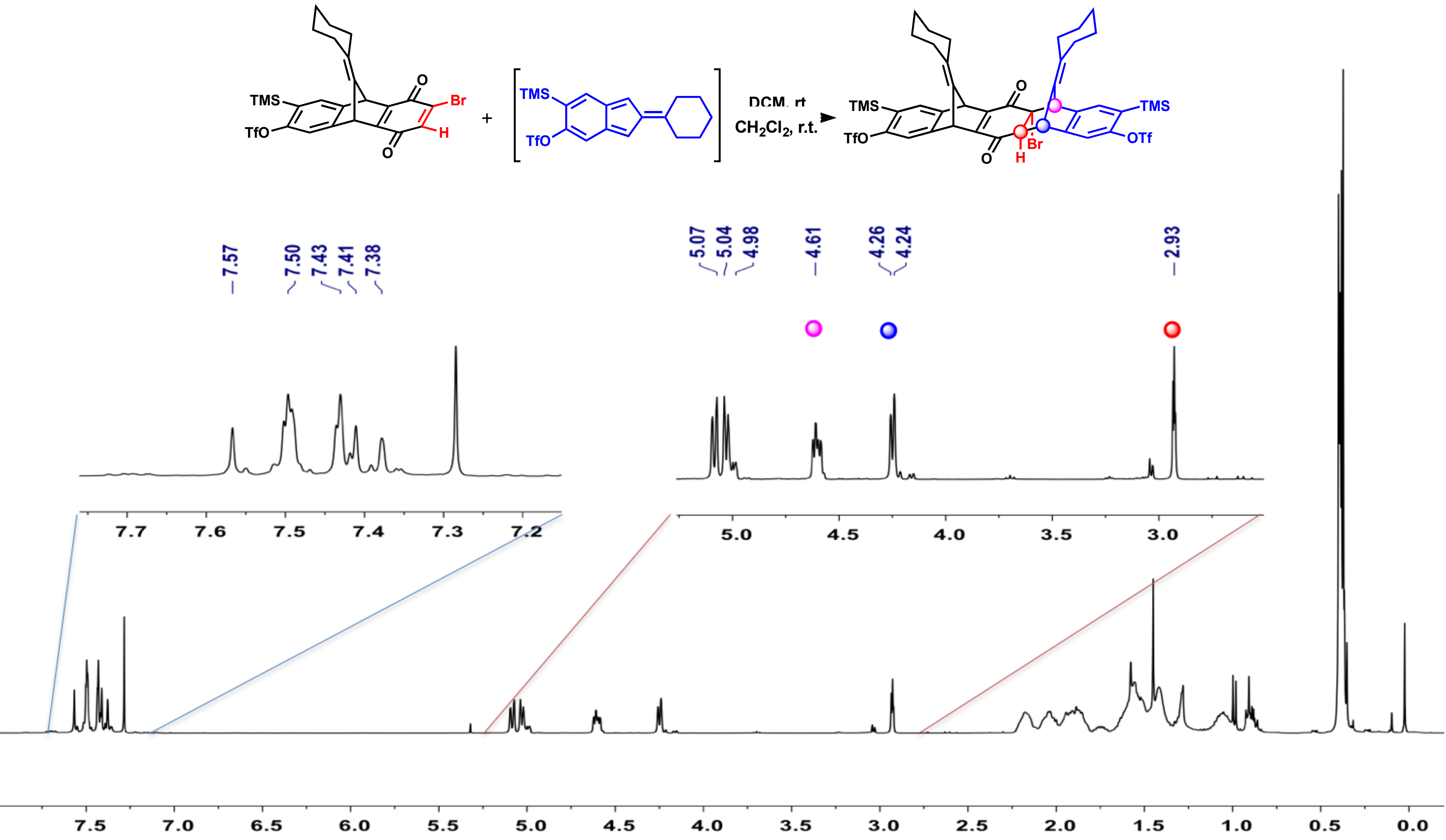
Sarah Wegwerth





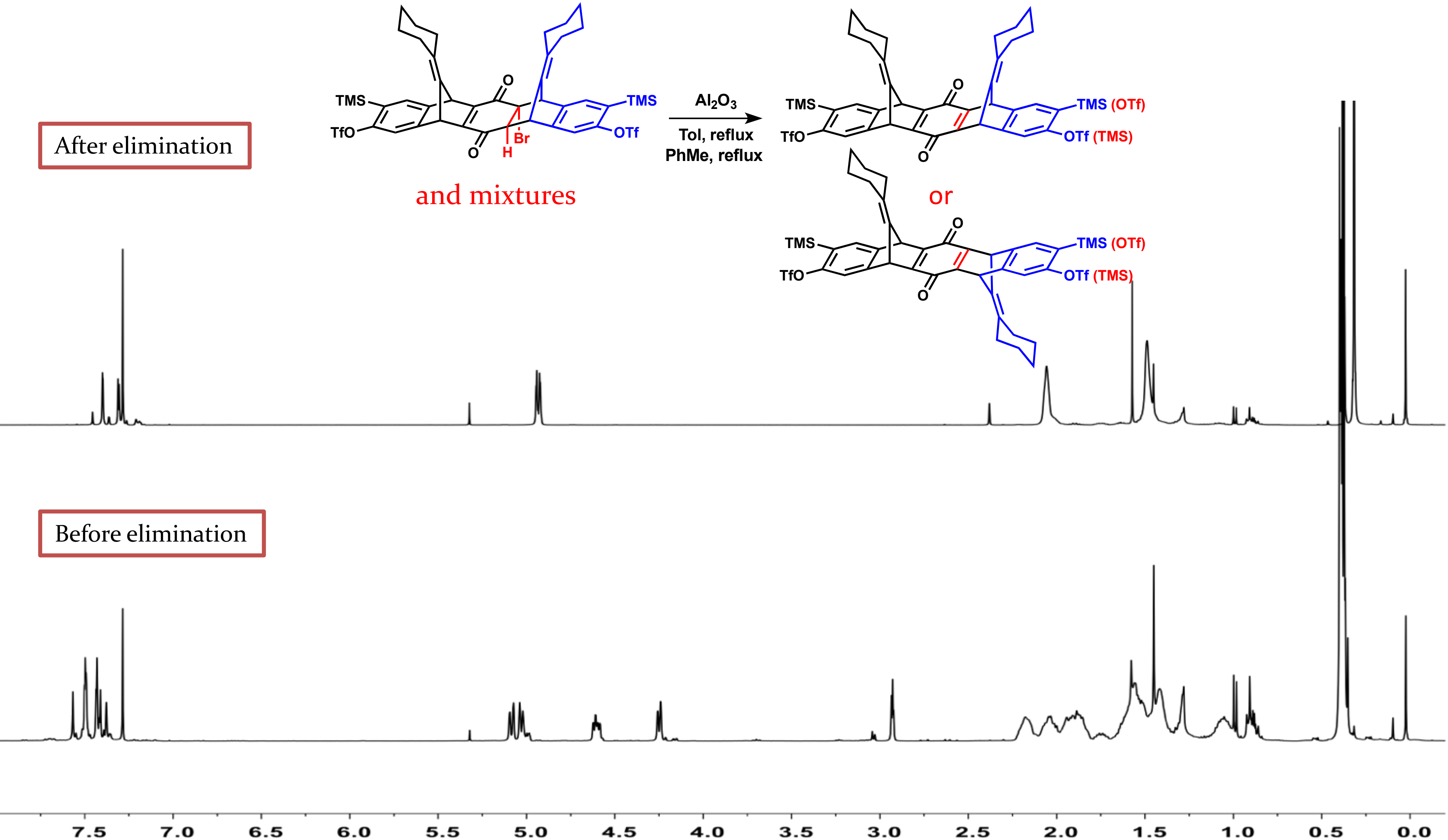
Stereoselective Diels–Alder Reaction

➢ Stereoselectivity observed in ^{1}H–NMR spectrum!



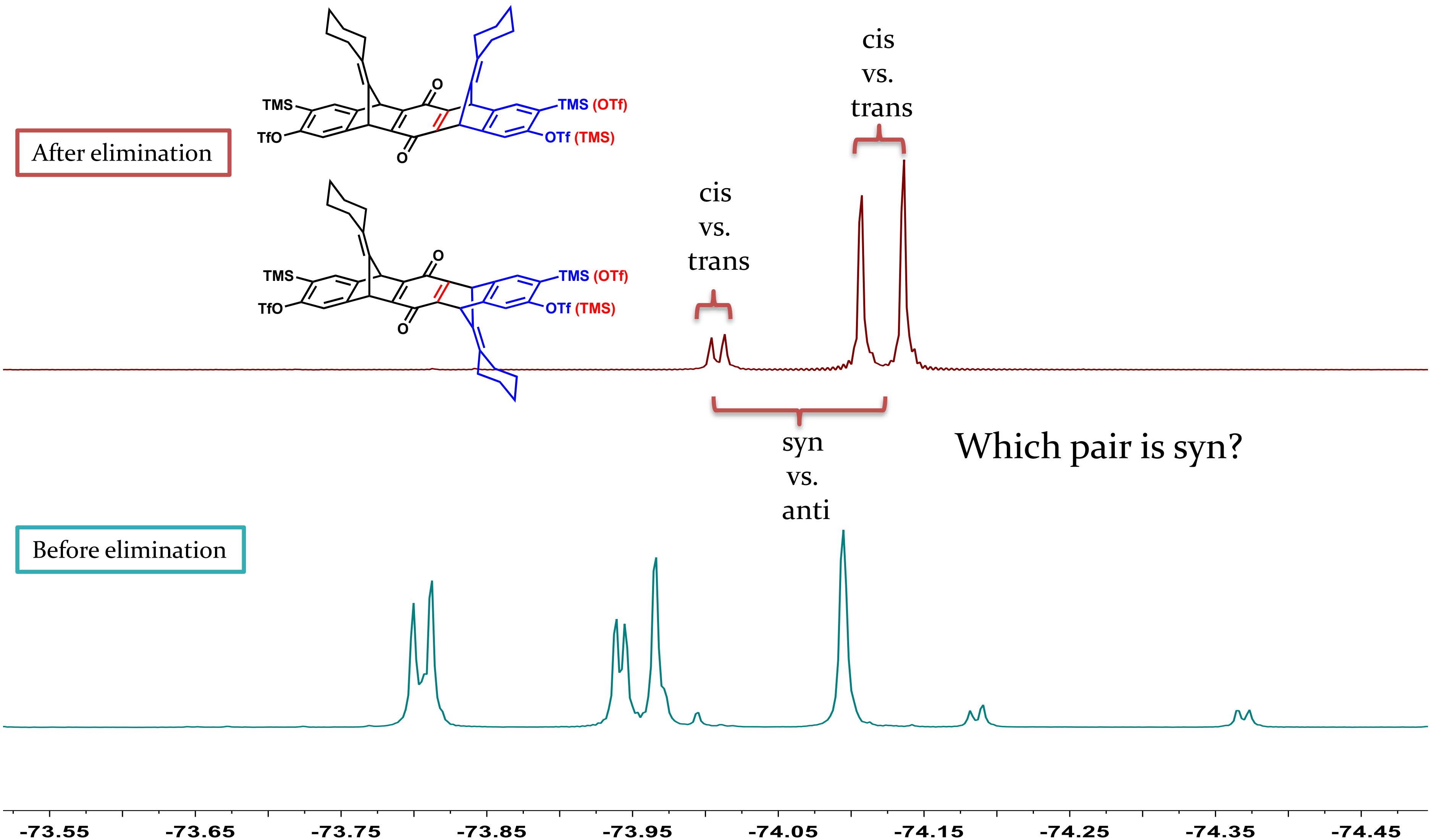
Synthesis Attempts toward Syn-isomer

➢ Dehydrobromination of stereoisomers



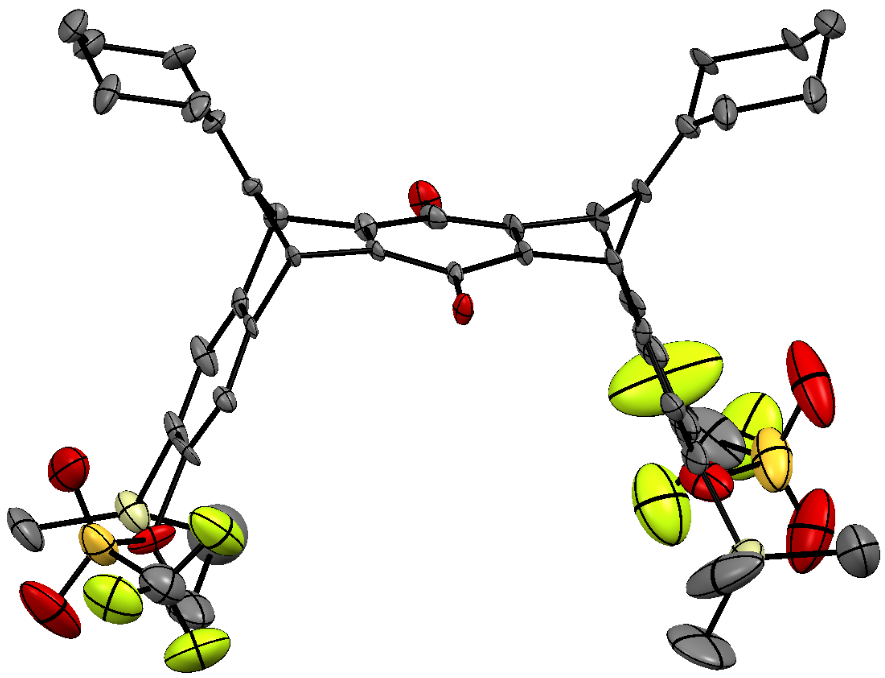
Synthesis Attempts toward Syn-isomer

- Dehydrobromination of stereoisomers by ^{19}F–NMR



Crystal Structure of *Syn*-isomer

- *Syn*-isomer as the major product!

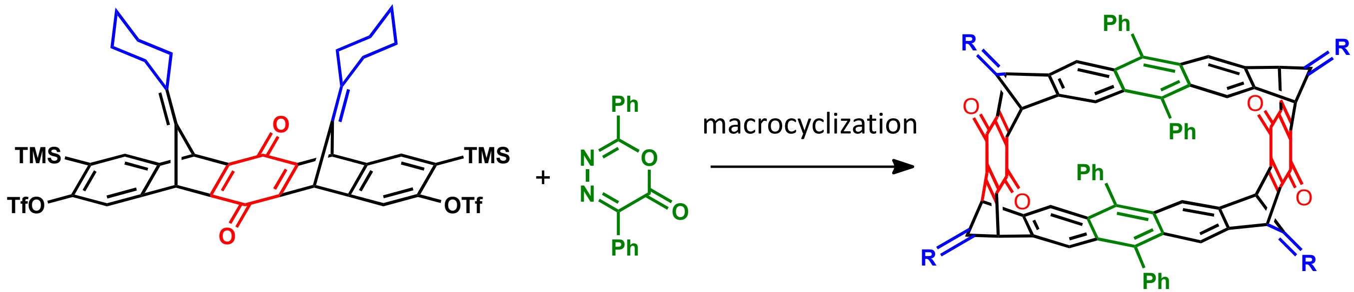


Steven Underwood

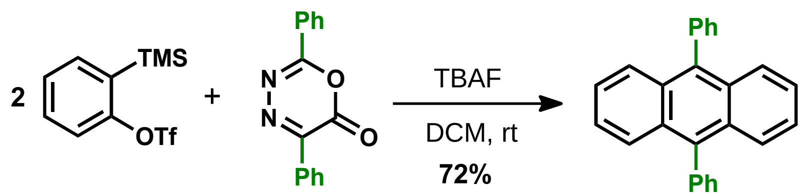
Dr. Victor Young

Future Work – Advance to the Macrocycle

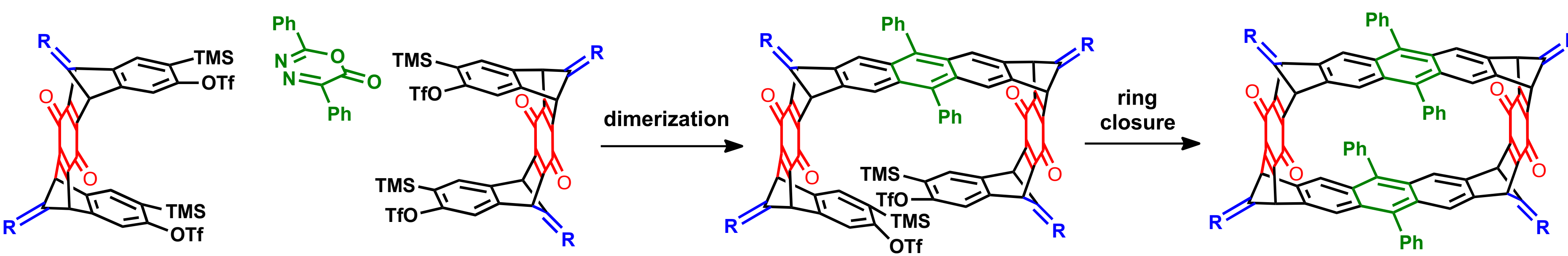
➢ Macrocyclization and late-stage functionalization



Model reaction

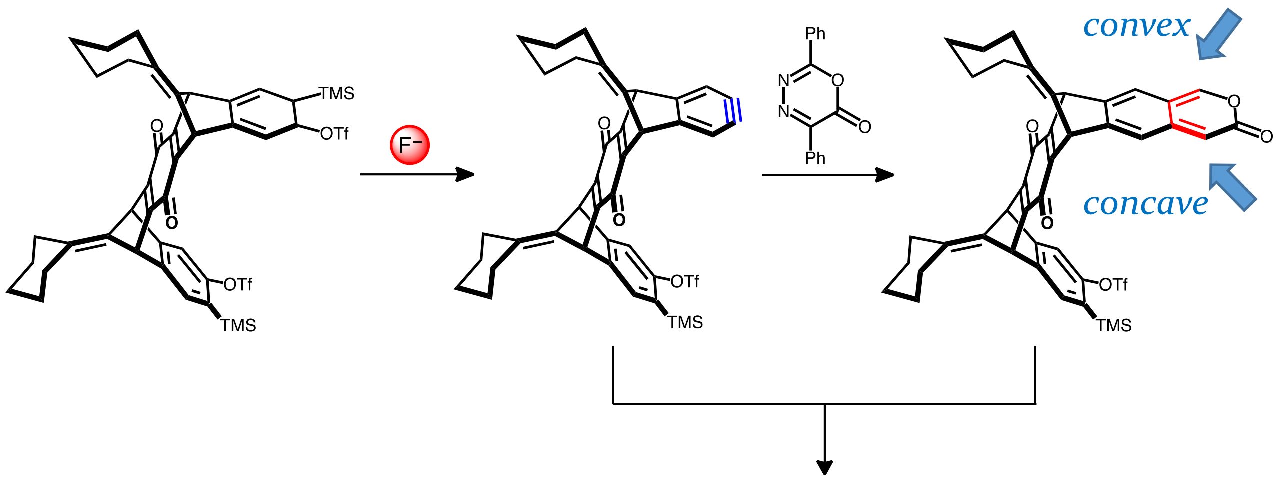


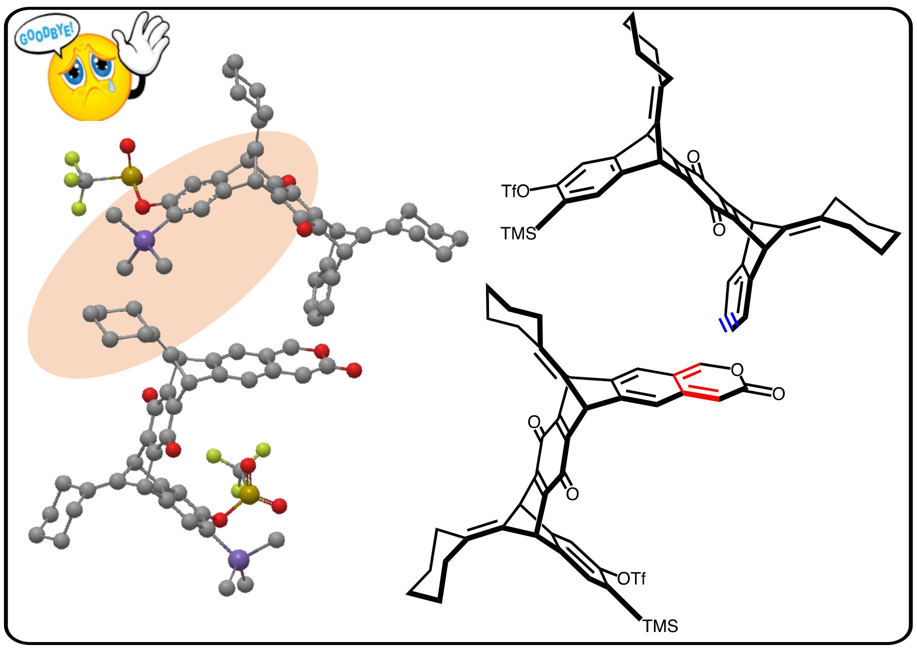
Real system –– "AA + BB"

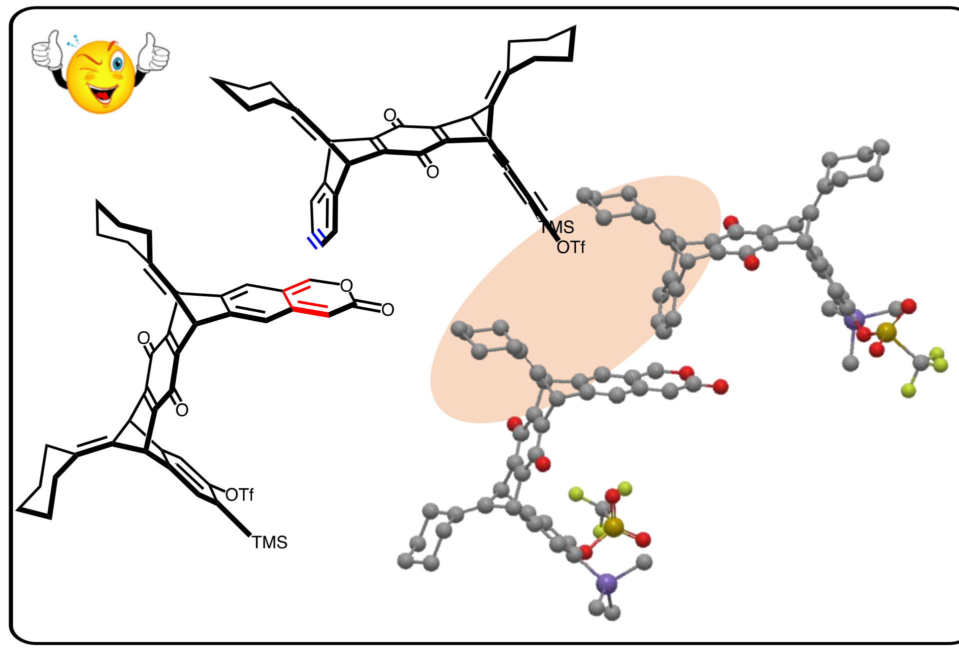


Steglich, W.; Buschmann, E.; Gansen, G.; Wilschowitz, L. *Synthesis* **1977**, *1977(4)*, 252-253.

Vision into the Dimerization Intermediate







Acknowledgements

- Prof. Chris Douglas
- Team Cyclacene (Sarah Wegwerth, Steve Underwood)
- NMR lab and XCL @ University of Minnesota