



Diels-Alder Reactions of 2-Cycloalkenylthiophenes and 2-Cycloalkenylbenzo[*b*]thiophenes

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Abstract

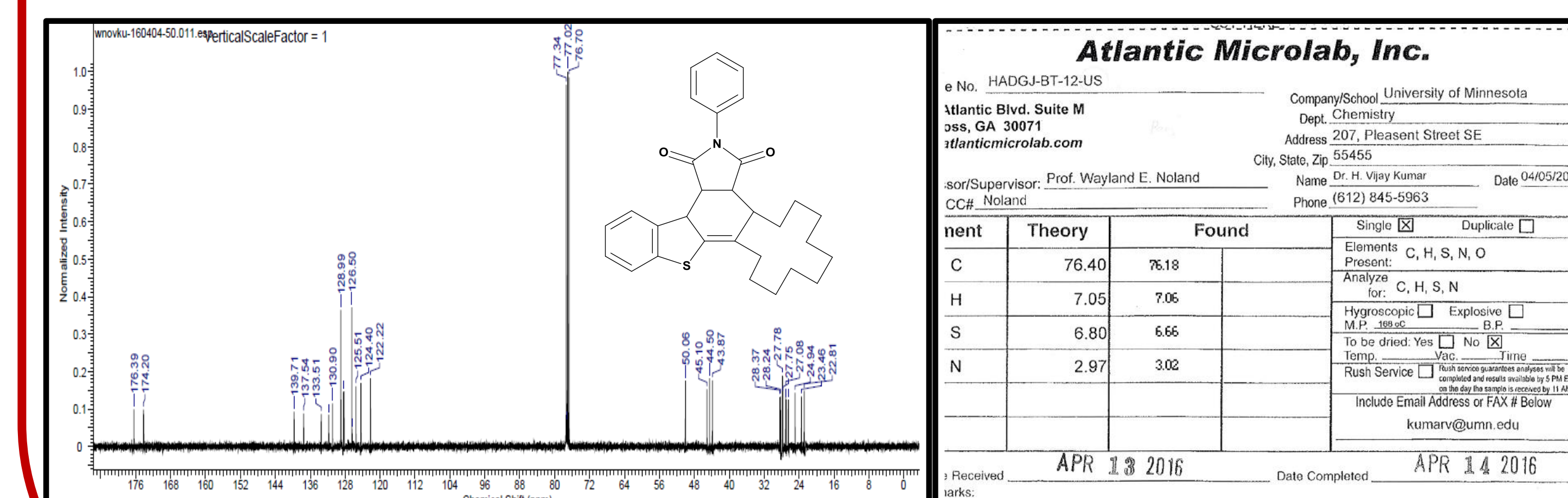
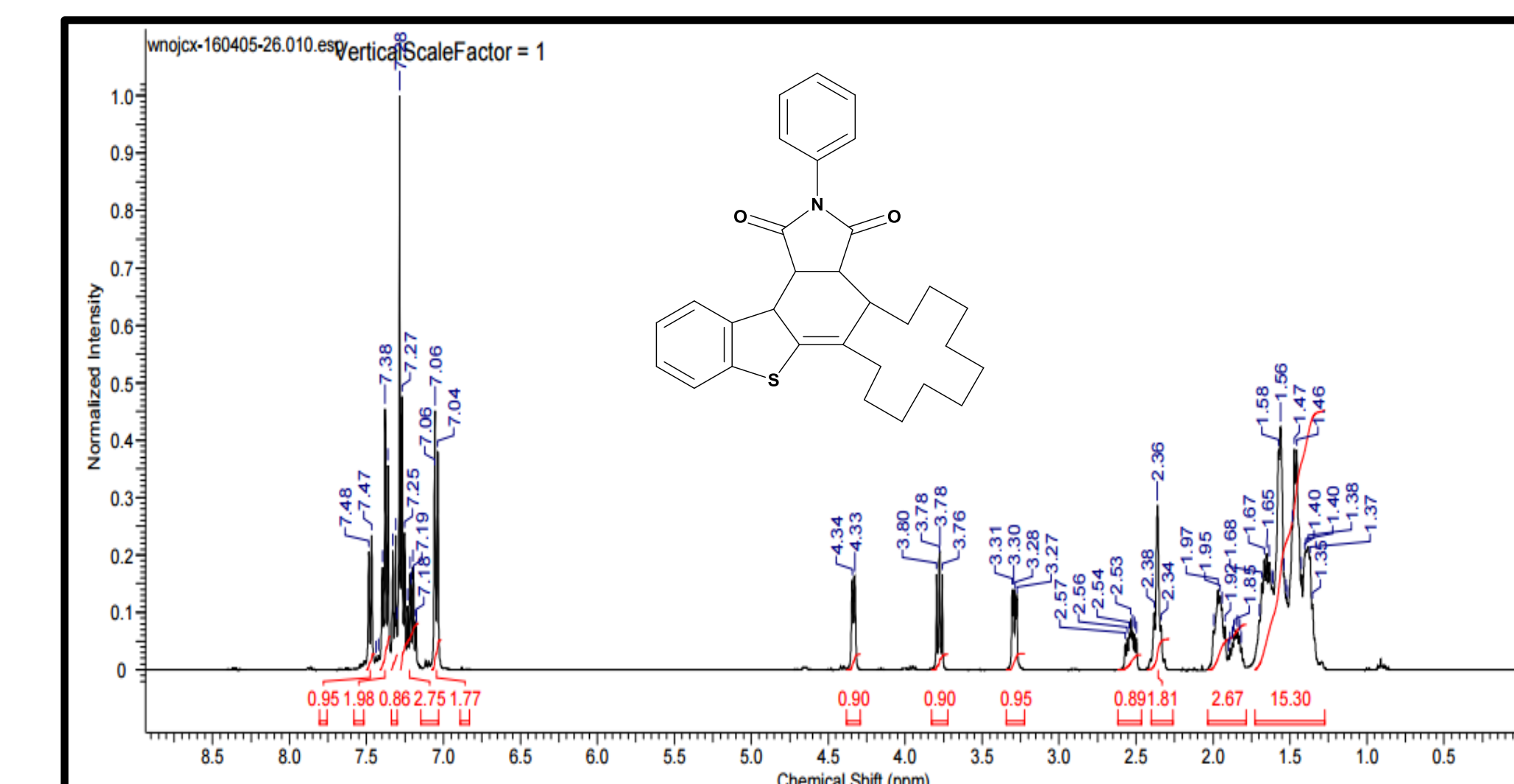
2-vinylthiophene **1** and 2-vinylbenzo[*b*]thiophene **2**-based heteroaromatic dienes with the vinyl groups fused to five-, six-, and seven-membered cycloalkene rings, underwent [4+2] cycloaddition reactions with substituted *N*-phenyl maleimides, gave isomerized *endo*-addition Diels-Alder adducts **6a-d** (36-98%). Also isolated fully aromatized Diels-Alder adducts **4a-d** (15-25%), and a highly diastereospecific ($\geq 98\%$ de) Michael-addition intermediates **5a-d** (25-55%). This route to annulated thiophenes and benzo[*b*]thiophenes is versatile, and the starting materials are easily prepared. The newly synthesized compounds will be offered to the National Institute of Health (NIH) to explore their anti-cancer activities.

Keywords: Diels-Alder, 2-Cycloalkenylthiophenes, 2-Cycloalkenylbenzo[*b*]thiophenes, [4+2] cycloaddition.

Introduction

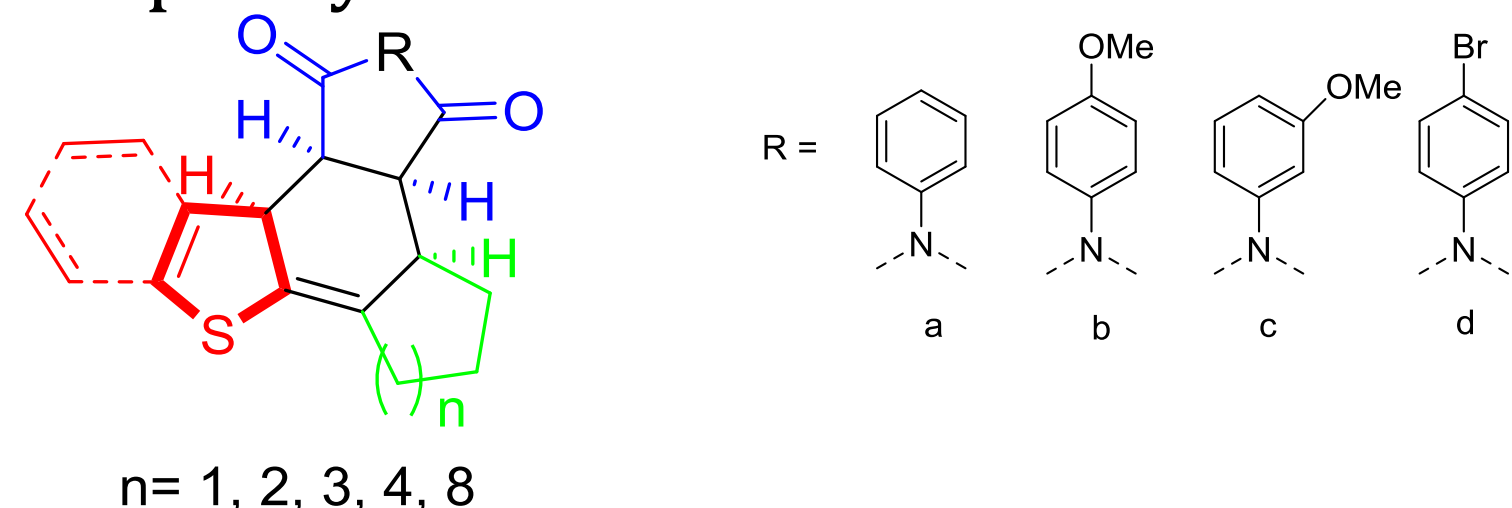
- Diels-Alder reactions of both vinylindoles¹ and vinylpyrroles² were extensively studied in our laboratory and some of the nitrogen based heterocyclic compounds showed anti-tumor and anti-HIV properties.
- Nitrogen and sulfur based heterocyclic compounds displayed an array of biological activities like antioxidant³⁻⁴, antibacteria⁵, anti-inflammatory⁶.
- Exploring sulfur based heterocyclic compounds for better biological properties.

Results

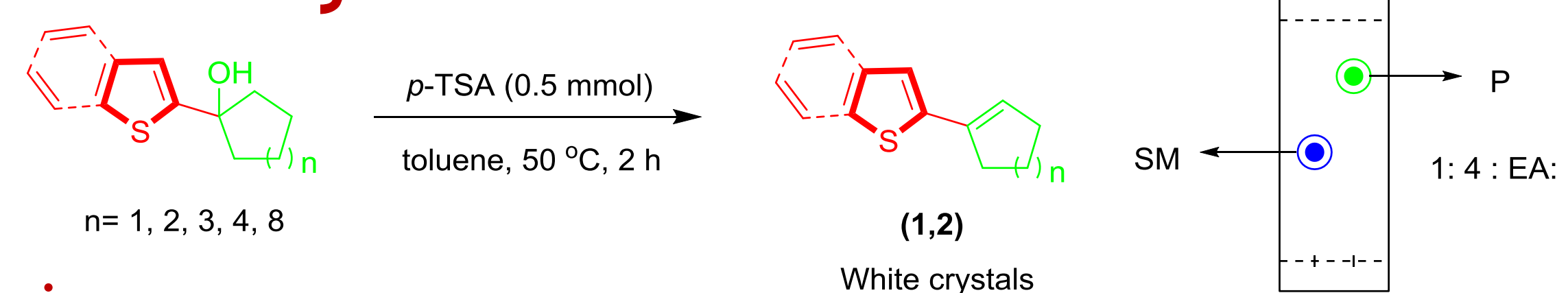


Purpose of the Study

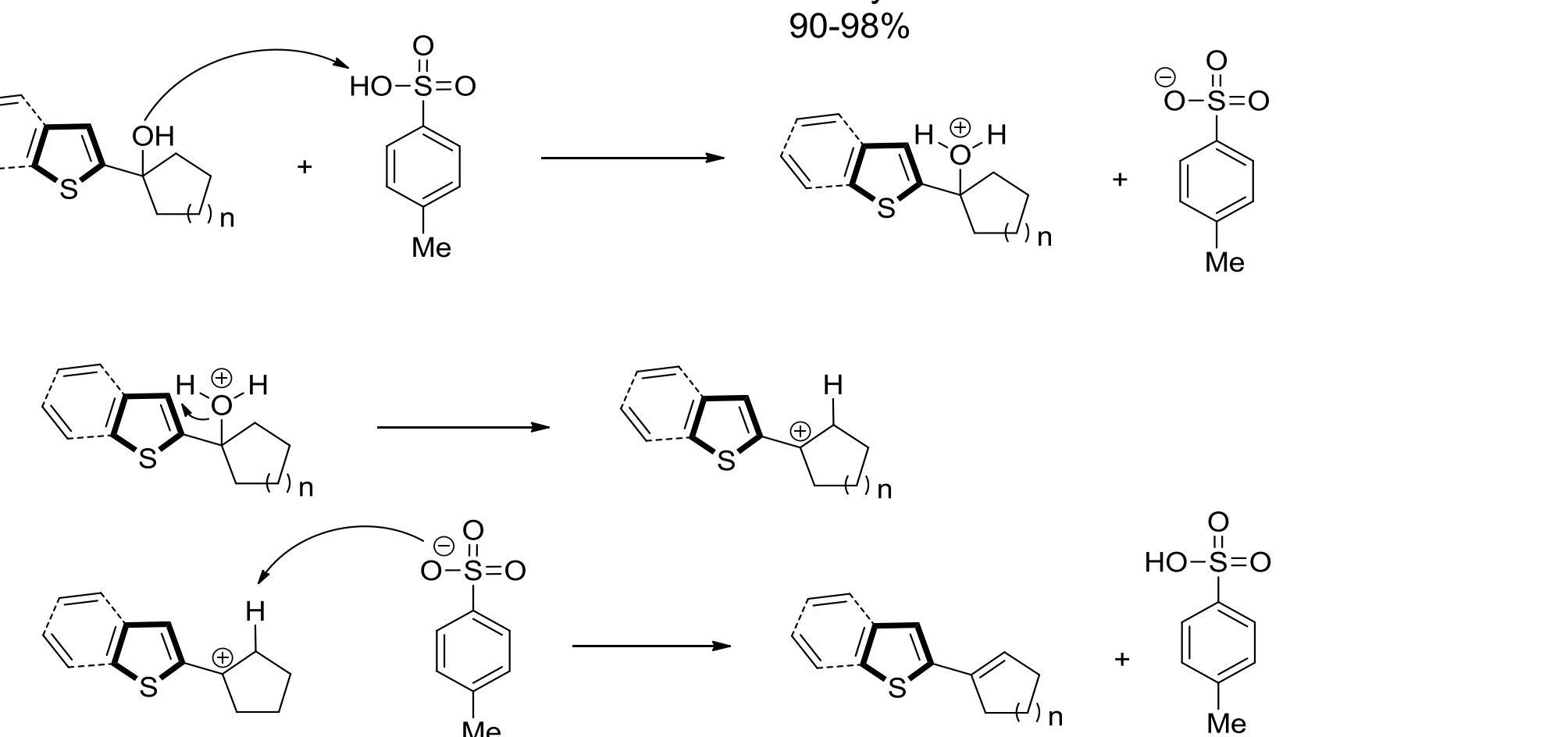
- ❖ Synthesize Diels-Alder adducts using Benzothiophene and Thiophene with various cyclic alkene rings (5, 6, 7, 8 and 12) and substituted *N*-phenylmaleimides.



Synthesis of Dienes



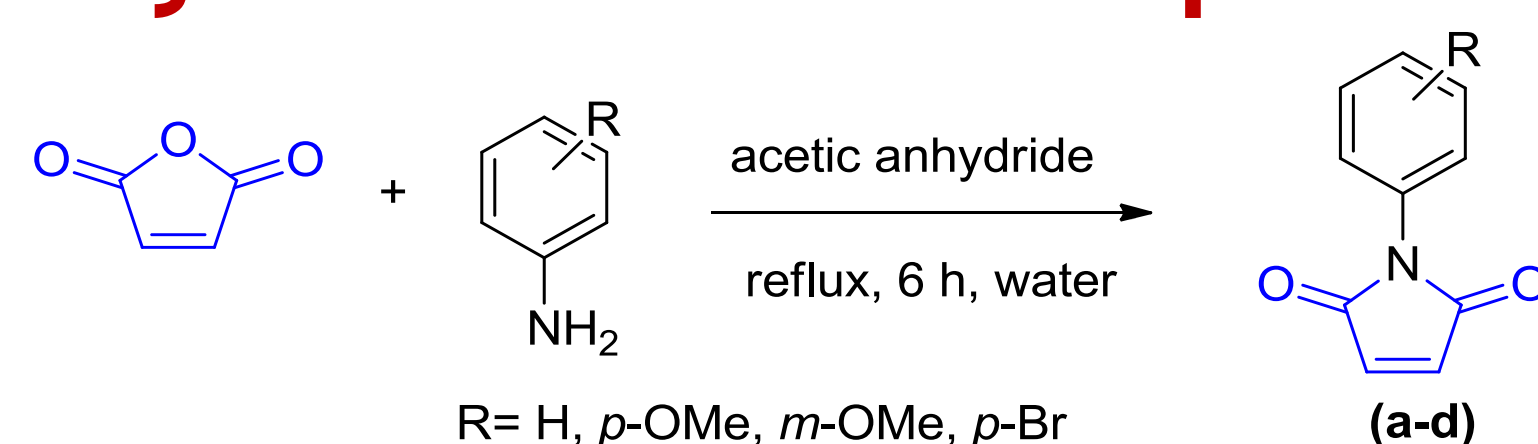
Mechanism



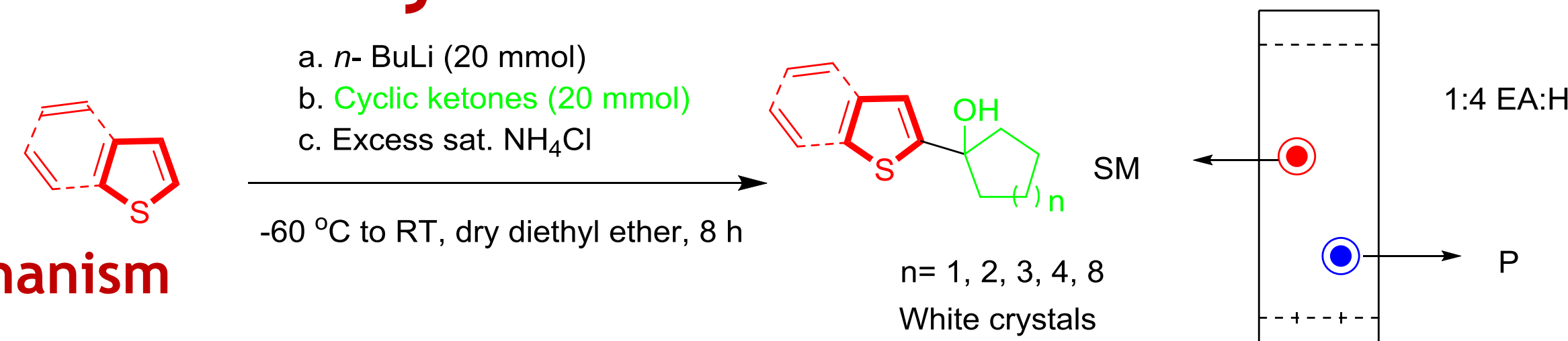
Conclusion/Outcome

- The route to prepare annulated thiophenes and benzo[*b*]thiophenes are versatile, and the starting materials were easily prepared.
- These research findings afforded finding the new thiophene and benzo[*b*]thiophene based Diels-Alder adducts.
- The newly synthesized compounds will be offered to the National Institutes of Health (NIH) to explore their anticancer activities.

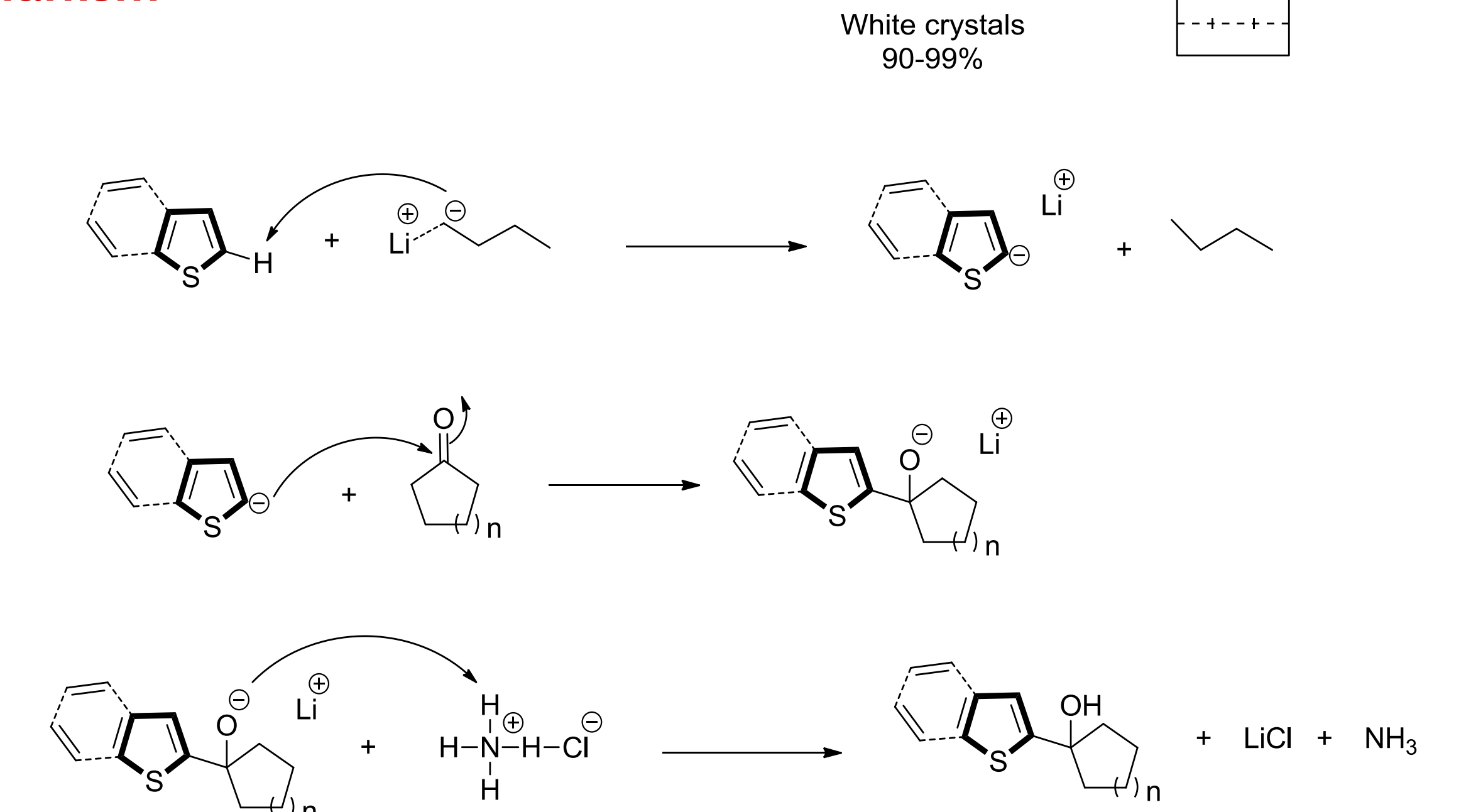
Synthesis of Dienophiles



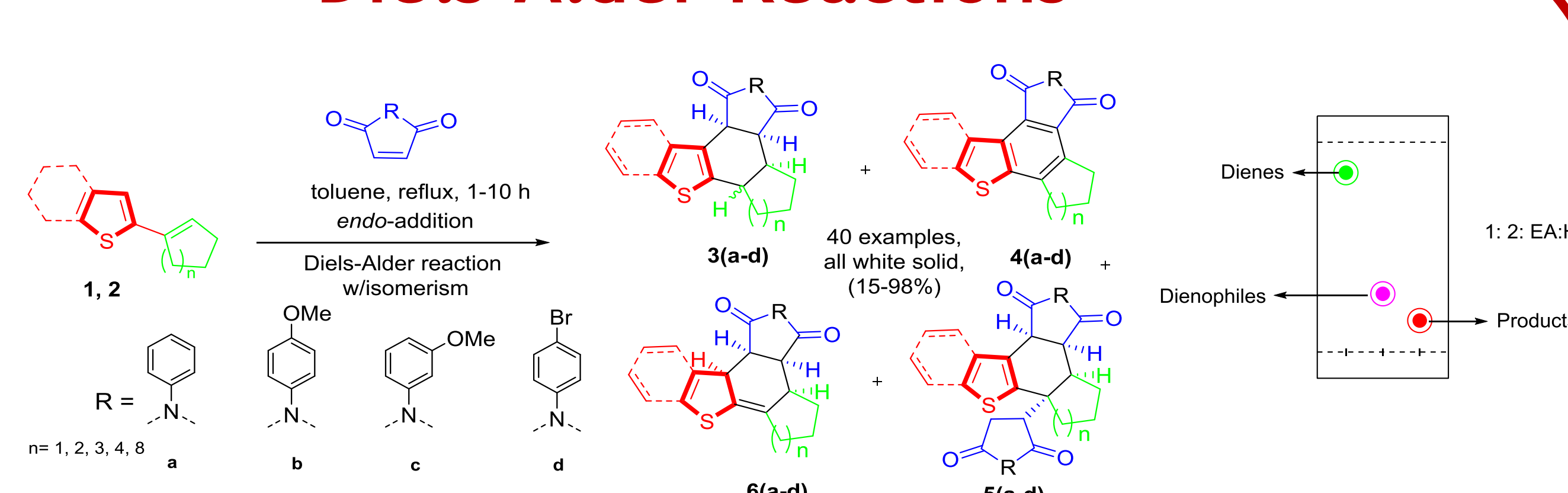
Synthesis of Alcohols



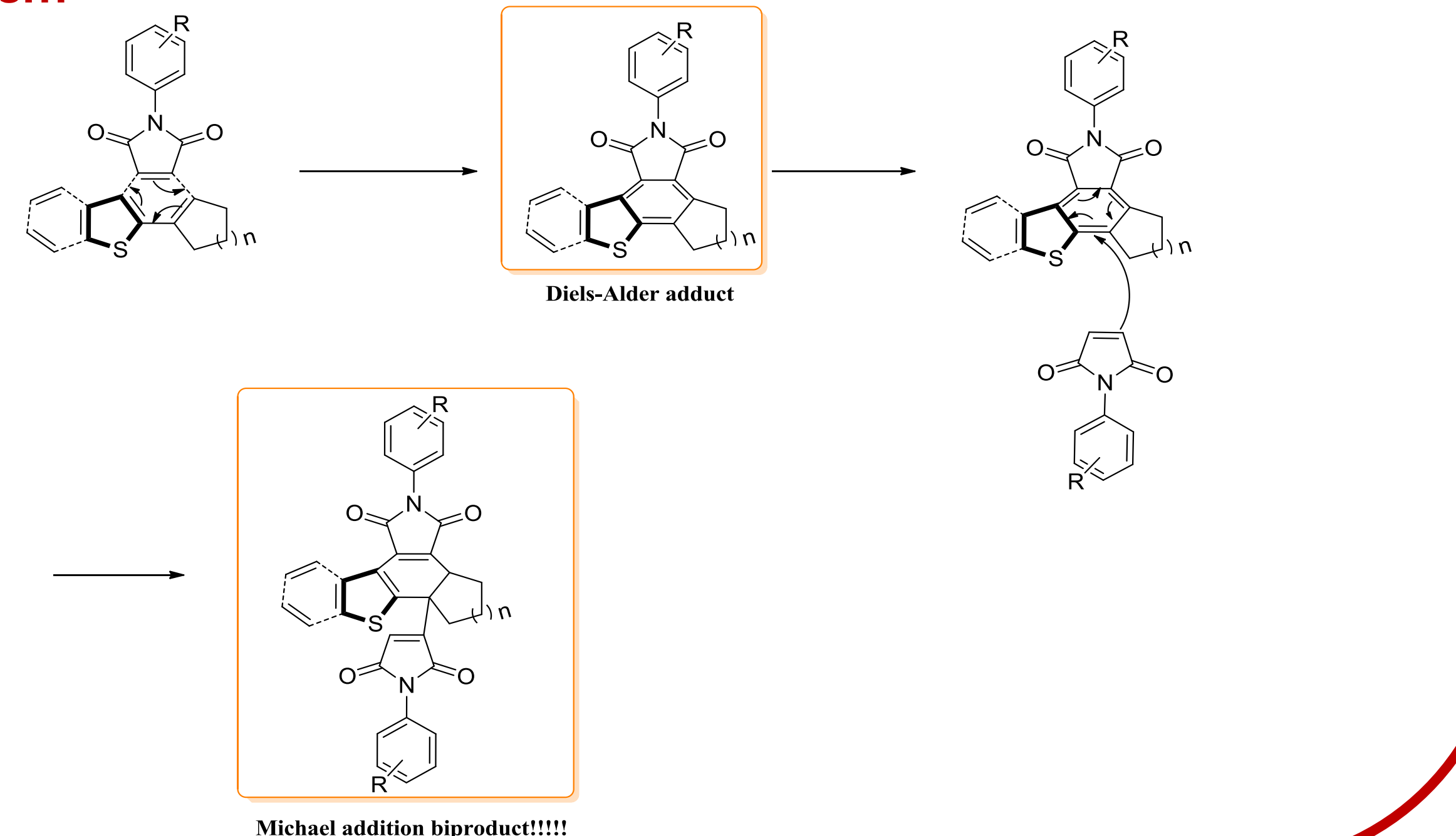
Mechanism



Diels-Alder Reactions



Mechanism



References

- Noland, W. E.; Kuryla, W. C.; Lange, R. F. *J. Am. Chem. Soc.* **1959**, *81*, 6010.
- (b)Noland, W. E.; Sundberg, R. J. *J. Org. Chem.* **1963**, *28*, 884-885.
- Noland, W. E.; Wahlstrom, M. J.; Konkel, M. J.; Brigham, M. E.; Trowbridge, A. G.; Konkel, L. M. C.; Gourneau, R. P.; Scholten, C. A.; Lee, N. H.; Condoluci, J. J.; Gac, T. S.; Mostafaei Pour, M.; Radford, P. M. *J. Heterocycl. Chem.* **1993**, *30*, 81-85.
- Helal, M. J.; Salem, M. A.; Gouda, M. A.; Ahmed, N. S.; El-sherif, A. A. *Spectrochimica Acta Part A: Molecular Biomolecular Spectroscopy.* **2015**, *147*, 73-83.
- Kumar, K. P.; Mohan, S.; Saravanan, K. V.; Prakash, N. A.; Raju, J. V.; Rao, Int. *J. Chem. Sci.* **2007**, *5*, 1284-1290.
- Kemnitzer, W.; Sirisoma, C.; May, B.; Tseng, J.; Drewe, S.X.; Cai, Bioorg. *Med. Chem. Lett.* **2009**, *19*, 3536-3540.
- Fakhr, I. M. I.; Radwan, M. A. A.; El-Batran, S.; Omar, M. E.; El-Salam, A.; El-shenawy, S. M. Eur. *J. Med. Chem.* **2009**, *44*, 1718-1725.

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