

Computational Investigation into the Diastereoselectivity of Photoredox Hydroalkylation Reaction

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I. Introduction

Diastereomers are molecules where the connectivity of the bonds is the same, but the atoms are arranged differently in three-dimensional space, and the molecules are not mirror images. A reaction may form more than one diastereoisomer, which is important because diastereomers have different chemical properties. Diastereoselectivity refers to how much a reaction prefers to form one diastereomer over another.

Photoredox catalysis has become a major topic for research in the field of organic chemistry over the last decade. It uses low energy visible light and a catalyst to perform reactions with little byproducts and waste.

This investigation is about the diastereoselectivity of the photoredox hydroalkylation reaction of 1,3-dicarbonyls (Scheme 1). Our lab has shown this reaction to proceed with excellent yields but consistently poor diastereoselectivity. In this study we used computational methods to examine why this was the case.

Scheme 1 — Established reaction conditions

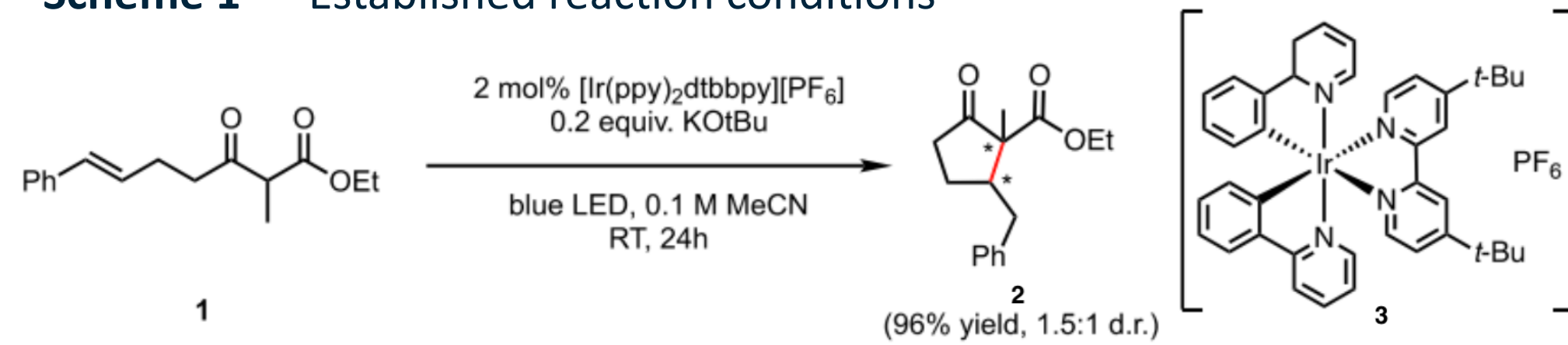


Table 1— Relative energies of molecules in reaction

Molecule	Starting Material (1)	(<i>R,R</i>) transition state	(<i>R,S</i>) transition state	(<i>R,R</i>) product (6)	(<i>R,S</i>) product (7)
Relative Energy	0 kcal/mol	7.88779 kcal/mol	8.1388 kcal/mol	-10.75552 kcal/mol	-10.64257 kcal/mol

II. Methods

For this investigation we chose to use computational methods that rely only on computers rather than performing experiments in a lab. Computational chemistry not only allowed us to conduct research remotely, but also to get better insights on the details of the reaction. These computations were done using Density Functional Theory (DFT) at the B3LYP/6-311+G(2d,p) level.

III. Results

There is a small difference in energy between the two diastereomeric transition states and also between the two diastereomeric products. The lower energy of the (*R,R*) transition state and product suggests that is both thermodynamically and kinetically favored, but only slightly. It also explains why we have observed such poor diastereoselectivity in the reaction.

Scheme 2 — Proposed mechanism for photoredox reaction

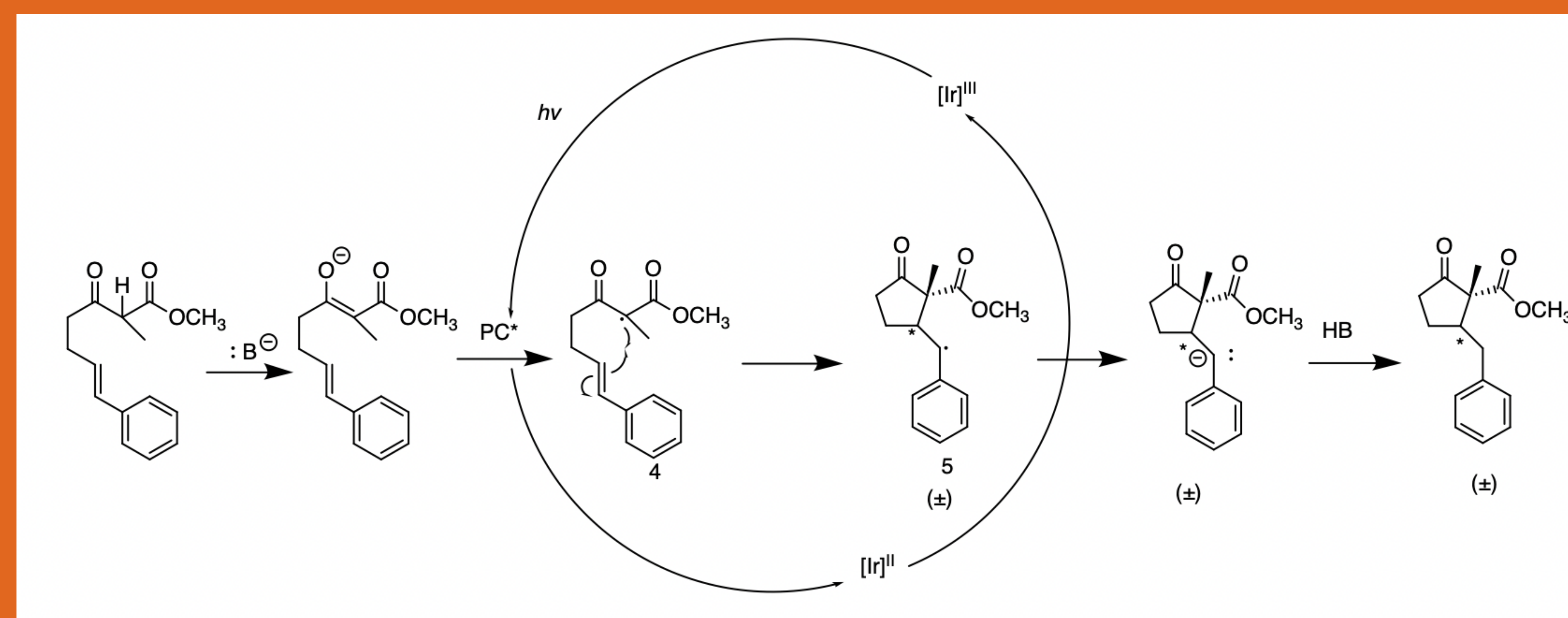
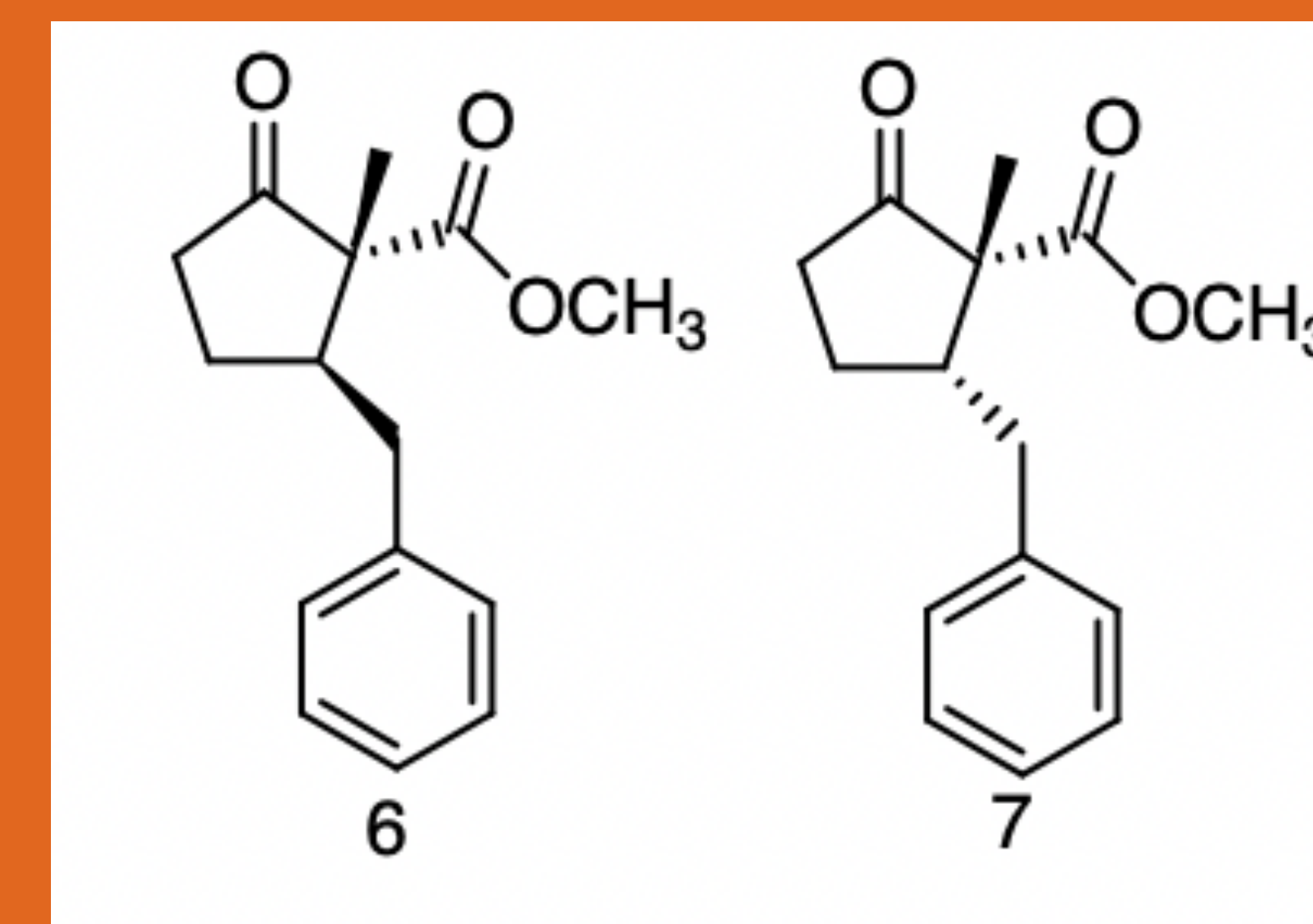


Figure 1 — (*R,R*) product (6) and (*R,S*) product (7)



IV. Conclusions & Future Work

Based on the results, the (*R,R*) diastereomer is both kinetically and thermodynamically favored as the low energy diastereomer. However, the difference in energy is not large enough to produce a good diastereomeric ratio.

Future investigations could be done on how to synthesize the desired diastereomer in this reaction. We will continue to use computational studies to investigate ways to control diastereoselectivity in this reaction. For example, we can determine the effects of using certain additives or modifying the structure will have on the reaction.

