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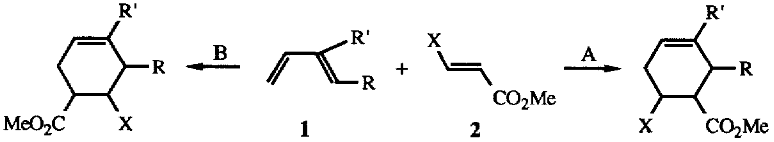
A NEW REGIOCHEMICAL CONTROL ELEMENT FOR DIELS-ALDER REACTIONS

George A. Kraus* and Spiros Liras
Department of Chemistry, Iowa State University, Ames, IA 50011

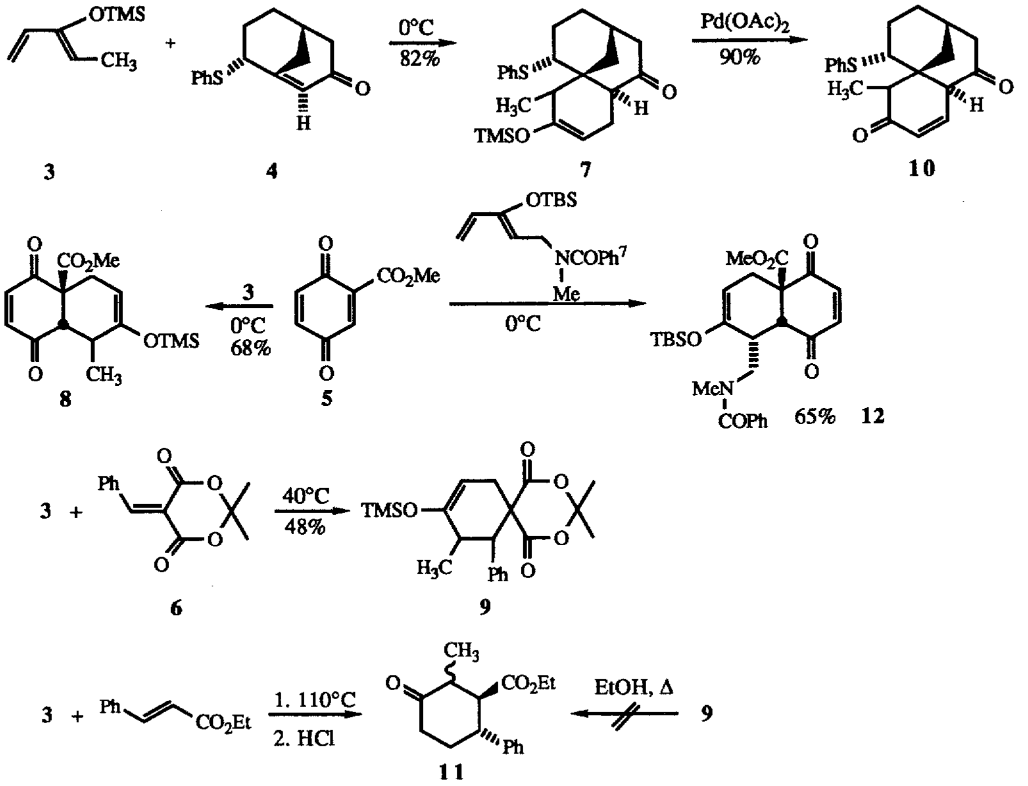
Summary: The regiochemistry exhibited by diene **3** in the Diels-Alder reaction is dependent on the dienophile.

The question of regiochemical control in the Diels-Alder reaction has been extensively examined from both a theoretical and an experimental perspective. Recently, Hehre has proposed a model for Diels-Alder regiochemistry whose predictions match experimental results more reliably than do those of FMO theory.[1] Experimentally, researchers have focused on ways to expand the applicability of the Diels-Alder reaction; in particular the reversal of the normal regiochemical outcome (path B rather than path A). Several researchers have demonstrated that dienes **1** with sulfur substituents can be manipulated to achieve this goal.[2]



Alternatively, Danishefsky has shown that dienophiles with removable activating groups (e.g., **2**: X = NO_2) can also be employed to simulate a path B reaction.[3] We now report that either path A or path B reactions can be obtained with certain dienes merely by enhancing the dienophile.

This result stemmed from an examination of possible mechanisms for Diels-Alder reactions of dienes with in situ generated bridgehead enones.[4] Unexpectedly, we had obtained exclusively exo adducts. Additionally, we observed that 1,1,3-trisubstituted dienes (normally poor dienes) form adducts in good yields with equally good stereoselectivity. Bridgehead enones are extremely reactive dienophiles. Their reactions with electron-rich dienes might proceed via a polarized transition state or even via an ionic one. In order to better understand the mechanism, we prepared diene **3**.[5] This diene had already been used in Diels-Alder reactions.[5] The product is one in which the methyl group directs the regiochemistry. If the transition state in the bridgehead enone case is polarized, we reasoned that the silyloxy group at C-2 might exert the dominant effect. The results of the reactions of dienes with **4**, **5** and **6** to give **7**, **8**, **9**, and **12** are depicted below. The structure of **7** was determined by treating the crude adduct with palladium acetate[6] and then analyzing the NMR spectrum of the resulting enone. The olefinic pattern clearly showed the



superposition of an AB quartet and a doublet, which is consistent with the structure of **10**. NMR decoupling experiments further supported the structure. The structures of adducts **8**, **9** and **12** also were verified directly by decoupling experiments. The reaction of **3** with ethyl cinnamate at 100°C produced a mixture of stereoisomeric adducts which could be hydrolyzed with 1N HCl to afford esters **11**. Ethanolysis of adduct **9** produced ketoesters which were different from **11** by both NMR and capillary gas chromatography. Adduct **12** represents an attractive intermediate for the synthesis of diterpene alkaloids.

Footnotes

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