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Reply

Reply to the comment concerning the review article: The Diels-Alder reaction and biopolymer catalysis

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First, we would like to apologize for the mistake in Scheme 2. As the referee pointed out in his second critique of our paper, the double bond in the product should be on the opposite side of ring. Unfortunately, this error was not noticed during the revision and reviews of the paper. We think it is appropriate to print a correction and would like to provide the correct drawing.

As for the purpose of Schemes 1 and 2, we included these frontier molecular orbital (FMO) diagrams as a refresher and a point of reference for what we anticipated to be a largely biologically oriented group of readers. Unlike the Woodward-Hoffmann rules for pericyclic processes, which would include an analysis of all reactant and product molecular orbitals, FMO theory only requires the consideration of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). FMO theory predicts how orbital symmetry affects pericyclic reactions and is presented in virtually all organic textbooks. Our schemes are similar to those found in many texts and no reference was given since this information is widely available.

With regards to the Referee, his original criticism of our schemes seemed to center on the fate of the 6 pi electrons involved in the cycloaddition. Consequently, we explicitly stated in the text that two pairs were used to create the two new sigma bonds and the remainder occupied the new pi bond of the product. We did not want to state the obvious by detailing that these electron pairs resided in the bonding orbitals (two sigma and one pi) of the product and that there were three corresponding unoccupied antibonding molecular orbitals. Unfortunately, the Referee still has a ‘main issue’ which is a result of his misunderstanding of the FMO diagrams in Schemes 1 and 2. In these schemes there are no HOMO-LUMO pairs with A-symmetry. Indeed, by definition, a thermal [4 + 2] pi electron pericyclic reaction is a symmetry-allowed process. It does not matter whether one considers mixing of the diene HOMO with the dienophile LUMO or the diene LUMO with the dienophile HOMO, both are symmetry-allowed. A quote from the text Lowery and Richardson, Mechanism and Theory in Organic Chemistry, 2nd Ed.; Harper & Row; New York, New York, page 846, Figure 11.2’. ‘In the unsubstituted case, butadiene and ethylene (a), both HOMO-LUMO interactions are equally important’. The dotted lines in Scheme 1 are meant to point out this fact. For Scheme 2 we could have perhaps lowered the relative energy of the dienophile to indicate greater mixing of the diene HOMO with the dieneophile LUMO in relation to the mixing of the diene LUMO with the dienophile HOMO. In the published correction of Scheme 2 we can make that change. The Referee is mistaken if he thinks that any asymmetric mixing is depicted in any of our schemes.

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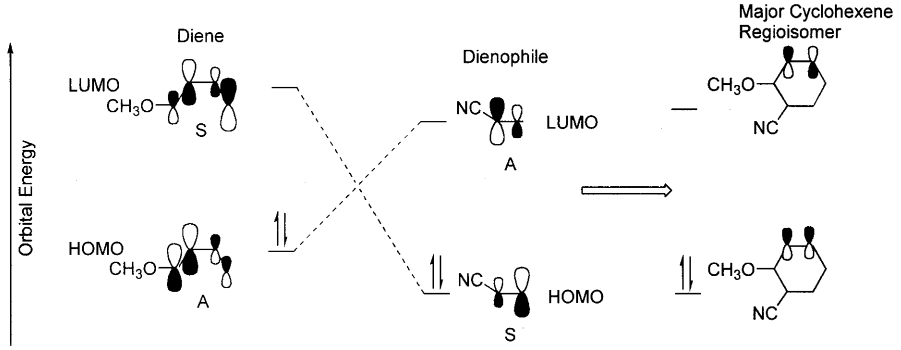

Scheme 2. The Diels-Alder cycloaddition between an unsymmetrical diene and dienophile. The optimum alignment of the polarized HOMO diene and LUMO dienophile orbitals gives the predominant regioisomer product as shown.