

Diels–Alder Stereochemistry Notes

John Terhorst

May 9, 2010

Contents

1	Introduction	1
2	Example Reactions	2
2.1	Diene <i>trans/trans</i> and Dienophile <i>cis</i>	2
2.2	Diene <i>trans/cis</i> and Dienophile <i>cis</i>	3
2.3	Diene <i>trans/trans</i> and Dienophile <i>trans</i>	4
2.4	Diene <i>trans/cis</i> and Dienophile <i>trans</i>	5
3	Summary	6

1. Introduction

Let's look at a 1,4-disubstituted diene undergoing a Diels-Alder reaction with a 1,2-disubstituted dienophile. In such an event, there are many possible outcomes, depending on the stereochemistry of the diene (*trans/trans*, *trans/cis*, *cis/trans*, *cis/cis*) and the stereochemistry of the dienophile (*cis*, *trans*), as well as the orientation of the dienophile with respect to the diene (endo, exo) as the reaction proceeds. This amounts to a total of 16 possible outcomes, with 32 possible *enantiomers* (depending of course upon the symmetry of the products). Fortunately the endo product predominates, so we can pretty much ignore the exo product as a major product. These examples should help you sort through the patterns.

2. Example Reactions

2.1. Diene *trans/trans* and Dienophile *cis*

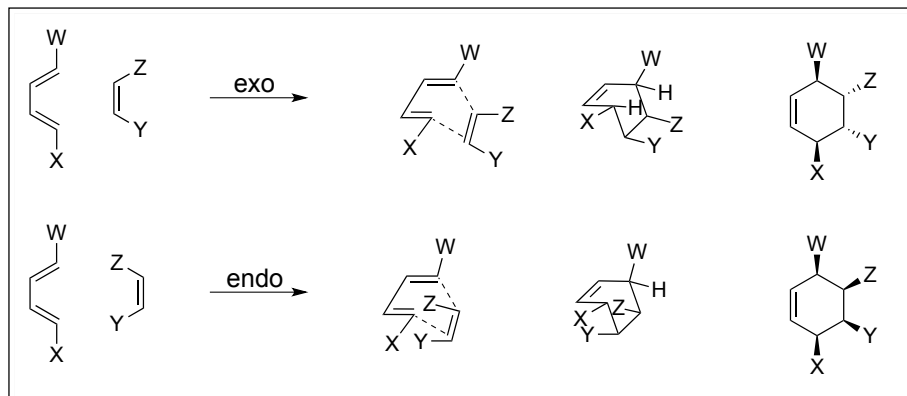


Figure 1: Diene *trans/trans* and dienophile *cis*.

Here we have a *trans/trans* diene and a *cis* dienophile. This is the most common Diels-Alder reaction you'll see. It is also the simplest system to visualize. I actually find it easiest to envision the *exo* *transition state* leading to the *exo* product. In the *exo* *transition state*, the dienophile approaches the diene with its substituents positioned outside of the reaction coordinates. As it approaches (from the underside of the diene as drawn here), it pushes the substituents of the diene up. The *endo* *transition state* gives rise to the opposite stereochemistry on the dienophile carbons with respect to the diene carbons, which is evident by carefully drawing the respective *transition states*. Notice that the product of a *trans/trans* + *cis* reaction yields *syn* stereochemistry between W and X (the substituents of the diene) and *syn* stereochemistry between Y and Z (the substituents of the dienophile). The *exo* reaction gives *anti* stereochemistry between the substituents of the diene and dienophile (W/Z, X/Y), whereas the *endo* reaction gives *syn* stereochemistry.

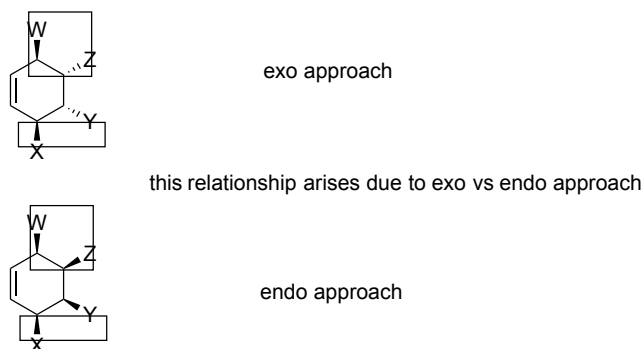


Figure 2: Diene *trans/trans* and dienophile *cis* endo/*exo* outcomes.

2.2. Diene *trans/cis* and Dienophile *cis*

Once we are comfortable with the above two reactions, working through the various permutations becomes fairly trivial. Let's start by inverting the stereochemistry of one of the substituents on the diene, to give us a *trans/cis* + *cis* reaction.

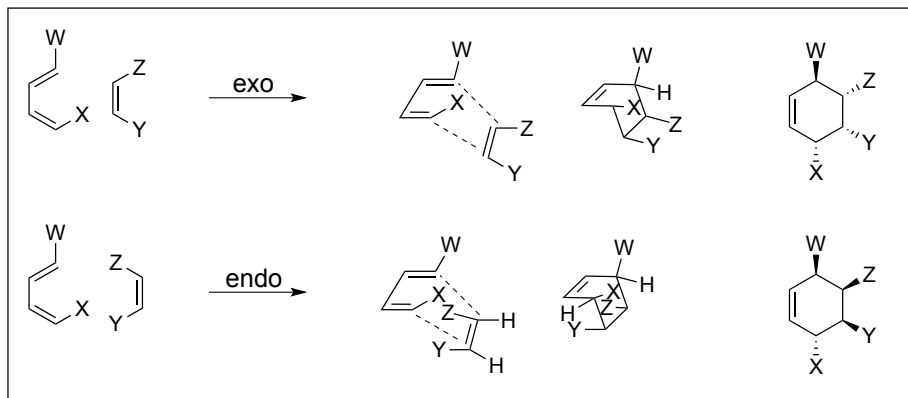


Figure 3: Diene *trans/cis* and dienophile *cis*.

We can work through the *transition* states, but essentially all we're doing is taking both the products from the first example and inverting the stereochemistry at X. All other stereochemistry remains unchanged. The big picture here is that a *trans/cis* relationship between the two alkenes in the diene leads to an *anti* relationship between the diene substituents (W and X) in the product.

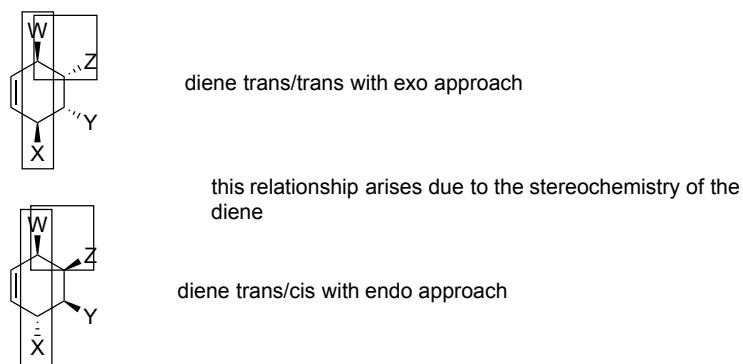


Figure 4: Diene *trans/cis* and dienophile *cis* endo/exo outcomes.

2.3. Diene *trans/trans* and Dienophile *trans*

Let's now take a look at what happens when we have a *trans* dienophile. To stay consistent, let's take the reactions from the first example and invert the stereochemistry at one of the carbons on the dienophile, giving us a *trans/trans* + *trans* reaction.

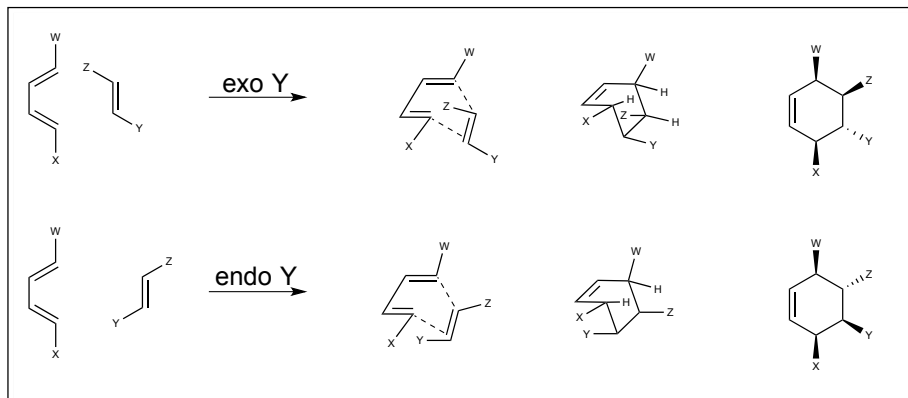
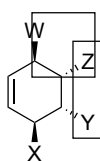


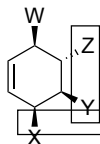
Figure 5: Diene *trans/trans* and dienophile *trans*.

Now, in this case, we could have the dienophile approach with Y exo or with Y endo. Again, we could work through the *transition* states, but all we're doing as far as the big picture is concerned is we're taking the products from the first example and we're inverting the stereochemistry at either carbon on the dienophile. Notice that a *trans* dienophile gives rise to *anti* stereochemistry between the two dienophile carbons in the product. All other stereochemical relationships remain unchanged.



dienophile cis with exo approach by Y to X (X and Y anti)

this relationship arises due to the stereochemistry of the dienophile



dienophile trans with endo approach by Y to X (X and Y syn)

Figure 6: Diene *trans/trans* and dienophile *trans* endo/exo outcomes.

2.4. Diene *trans/cis* and Dienophile *trans*

Lastly, let's consider a *trans/cis* + *trans* reaction. In this case we'd have to take the products from the first example and invert two carbons, or take any of the products from the second and third examples and invert one carbon. Let's take the products from the third example and invert the carbon at X.

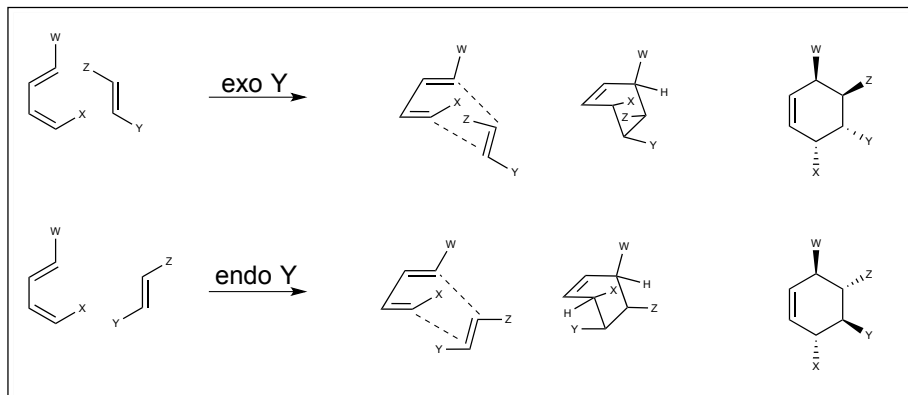


Figure 7: Diene *trans/cis* and dienophile *trans*.

Notice again that the relationships between W and Z, and X and Y, arise from the exo vs endo approach. The stereochemistry between W and X arises from the stereochemistry of the two alkenes in the diene, and the stereochemistry between Y and Z arises from the stereochemistry of the dienophile.

3. Summary

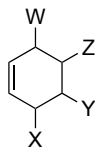


Table 1: Summary of diene and dienophile stereochemistry with endo/exo outcomes.

Reaction partner	Stereochemistry	Outcome
Diene	<i>trans/trans</i>	W,X <i>syn</i>
	<i>cis/trans</i>	W,X <i>anti</i>
	<i>cis/cis</i>	W,X <i>syn</i>
Dienophile	<i>trans</i>	Y,Z <i>anti</i>
	<i>cis</i>	Y,Z <i>syn</i>
Approach	exo	W,Z / X,Y <i>anti</i> unless dienophile is <i>trans</i> , in which case only the endo atom is <i>anti</i> .
	endo	W,Z / X,Y <i>syn</i> unless dienophile is <i>trans</i> , in which case only the endo atom is <i>anti</i> .