ORBITAL SYMMETRY (COURSE) SELECTION RULES:

ALLOWED PROCESSES: You may consult: your class notes, handouts, and problem sets; the textbook for this course; the 1990 exam and answers; and any of the standard textbooks on orbital symmetry (listed on pp. 3-5 of Books and Review Articles). You should also feel free to consult me when you run into difficulties; although I will not "give away" any answers, I will try to guide you to find the solution on your own. Once the exam has been distributed, I will only answer questions related to it; I will no longer answer questions on study materials.

FORBIDDEN PROCESSES: You may not search the primary literature (syllabus) or secondary review literature (pp. 5-46 of Books and Review Articles) for answers to your questions, nor may you seek assistance from classmates, other students, faculty (except for "yr obdt srvt"), faith healers, or anyone else, living or dead, real or imaginary.

There is no time limit (except for the very generous deadline shown at the top of this page). Although the exam could be answered in a single sitting, it’s advisable to spread it out over several sessions. You ought to begin work on it fairly soon; it would be a terrible mistake to wait until near the due-date before beginning. Once you have begun work on the exam, be careful not to violate the "selection rules" listed above. [The literature references on which these questions are based will be distributed after the exams have been turned in, so that you won’t be tempted to take "just a little peek."]

"Good people cannot do good things with bad mechanisms." Richard M. Nixon

"Nothing is ever created by two men. There are no good collaborations whether in music, in art, in poetry, in mechanics, in philosophy." John Steinbeck (1962 Nobel Laureate, who could not know of future Laureates Woodward and Hoffmann)

"A theory is something nobody believes except the person proposing the theory, whereas an experiment is something everybody believes except the person doing the experiment." Albert Einstein

"Every attempt to employ mathematical methods in the study of chemical questions must be considered profoundly irrational and contrary to the spirit of chemistry. If mathematical analysis should ever hold a prominent place in chemistry - an aberration which is happily impossible - it would occasion a rapid and widespread degeneration of the science." August Comte (1830)

I. (90 points)

A. Consider the supra/supra mode of cycloaddition of allyl cation with 1,3-butadiene.

1. Construct the electronic state correlation diagram for this reaction. Your answer should include these features:
   a. pictures of the reacting orbitals of reactants and product and their symmetry with respect to the appropriate symmetry element(s); you may do this for either the endo or exo mode of cycloaddition;
   b. the orbital correlation diagram;
   c. the electronic state correlation diagram for the ground states and first excited states of reactants and product; assume that the first excited state of reactants involves butadiene and that of product involves the C=C.
   d. your decision (with a brief justification) as to whether the concerted reaction is thermally or photochemically allowed.

2. As in the Diels-Alder reaction, both endo and exo modes for the above cycloaddition are possible. Using appropriate orbital drawings for the endo transition state, decide whether it will be stabilized or destabilized relative to the exo.

3. For the unsubstituted case (see above) one cannot distinguish between endo and exo modes. Design an experiment that would allow you to determine whether endo or exo cycloaddition is favored; assume that any reagents you need are available or can be easily made. State specifically what reaction(s) you would run and what quenching products you would analyze.

At this point in Question I, we pause for a brief interlude to consider the words of Wolfgang Roth in a 2001 article that had nothing to do with allyl cation cycloadditions but everything to do with clear thinking: "The vast majority of concerted reactions are found in the pericyclic reactions, and the two terms ‘concerted’ and ‘orbital symmetry allowed’ are therefore frequently used synonymously, as these latter reactions have to be concerted in nature, in contrast to those reactions that are not directed by orbital symmetry. However, this usage is unfortunate, because nonpericyclic reactions can be concerted as well ... Because of this equating of ‘concerted’ with ‘allowed’ processes,
the former reaction channel became considered to be thermodynamically favored. However, this assumption is questionable. We have to take into account that, among nonpericyclic reactions, the concerted pathway is the exception and not the rule.” In other words, just because a reaction is symmetry-allowed, this doesn’t mean that it is necessarily faster than various stepwise competitors. With that in mind, let us return to Question I.

4. Recent *ab initio* calculations, just a "tad" more sophisticated than our simple orbital symmetry correlations, have led to the conclusion that the two new σ bonds in the thermal reaction (on p. 1) are formed in separate steps. Unlike a stepwise Diels-Alder reaction (e.g., of 1,3-butadiene + ethene) that must produce a zwitterion or a diradical, the stepwise mechanism in the present case is not so disfavored. Using the curved arrow notation, show a "one σ-bond at a time" mechanism and explain (in not too many words) why it looks fairly reasonable.

B. trans-7,8-Dimethyl-1,3,5-cyclooctatriene can, in principle, ring-open or ring-close in a variety of electrocyclic processes. Without going through a detailed analysis, use the selection rules from orbital symmetry to decide the stereochemical fate expected for each of the potential thermal reactions to the right. Which, if any of them, are unlikely thermal processes because of excessive strain? (The reactant is racemic.)

C. In the *Dark Ages*, BWH (before Woodward-Hoffmann), curved arrows were used to show the "mechanism" of so-called "no-mechanism reactions." Consider the case of the thermal equilibrium between bicyclic triene 1 and Z,Z,Z,Z-1,3,5,7-cyclooctatetraene 2.

1. In orbital symmetry terms, what sort of reaction is (a)? Is the formation of all Z tetraene 2 allowed?

2. In orbital symmetry terms, what sort of reaction is (b)? Is the formation of all Z tetraene 2 allowed?

3. It turns out that Z,Z,Z,Z-cyclooctatetraene is a non-planar compound, preferring the tub-like structure shown to the right. What reason(s) can you provide to explain why it is not planar like its lower homolog 1,3,5-cyclohexatriene (i.e., benzene)?

4. Numerous studies have established a "bond-shift" process in which a compound like a 1,2-dialkyl-1,3,5,7-cyclooctatetraene is in equilibrium with the 1,8-dialkyl isomer. The energy barrier for this sort of reaction is surprisingly high (ca. 30 kcal/mol). Speculate on how this bond-switch occurs and why it is so slow.

5. In light of this, how might 7,8-dialkylbicyclo[4.2.0]-2,4,7-octatriene (shown to the right and numbered in accord with Parts 1 and 2) help decide whether (a) or (b) is the preferred mode of ring-opening.

D. Also in the *Dark Ages*, some seven years BWH, it was reported that the separation of stereoisomers A and B by distillation, followed by treatment with AgNO₃/H₂O gave the following results. Although inexplicable at the time, you (with the advantages gained from
your Chem. 650 course) should be able to explain what is going on. In your explanation, assign structures to A and B and explain the difference in behavior.
II. (40 points)

A. Although the vast majority of orbital symmetry-controlled reactions are performed in the laboratory, there are some that take place in Nature. There is a set of seven natural products that we'll refer to as Ponndorf A-G. [Ponndorf is a substitute for the real name so that you won't be tempted to try to look up these compounds.] To test a biosynthetic scheme that had been proposed for the formation of these materials in Nature, chemists synthesized some key intermediates and observed their behavior on thermolysis. When highly unsaturated ester 1 was hydrogenated over Lindlar catalyst (known to reduce alkynes to cis-CH=CH-) and the resulting mixture was heated to 100°C, Ponndorf B and C were produced. Your job is to write reasonable mechanisms for these spectacular transformations. To assist you, I've drawn the doubly hydrogenated derivative of 1 and, also, Ponndorf F and G which are presumed intermediates on the path to B and C. [In fact, when the doubly hydrogenated material is warmed at 25°C, Ponndorf F and G can be isolated; upon heating to 100°C, they are transformed, respectively, into Ponndorf B and C.]

B. After some 15 years of studying the photolysis of cyclobutenes, Canadian chemists seem finally to have reached an understanding of these reactions. In earlier work, the photolysis of cis-2 or trans-2 at 193 nm gave non-stereospecific ring-opening reactions. (That is, a mixture of stereoisomeric dienes was produced.) In contrast, when
the reactions were performed with less energetic light (228 nm) a stereospecific cleavage and a stereospecific ring-opening were found.

1. Consider, first, the cleavage into 2-butyne plus 2-butene. Are the results shown here what you would have expected for this sort of reaction? Justify briefly.

2. Now consider the ring-opening to the dienes. Are the results shown here what you would have expected for this sort of reaction? Justify briefly.

3. For a mere $6.02 \times 10^{23}$ of EXTRA CREDIT points, devise a convincing (and not too wordy) explanation for what is going on in the ring-opening.

C. Cyclobutadiene is a molecule with a fascinating history. One author has described it as "the Mona Lisa of organic chemistry in its ability to elicit wonder, stimulate the imagination, and challenge interpretative instincts." Resonance theory would predict that Kekulé-like structures $3a$ and $3b$ would result in resonance hybrid $3c$. But Hückel molecular orbital theory notes that, with four $\pi$ electrons, the perfect square would be anti-aromatic. It can avoid such a destabilization by distorting to a rectangular structure in which $3d$ and $3e$ may be in chemical equilibrium or by remaining square but having two unpaired electrons, a diradical ($3f$). This question concerns experiments that were designed to establish the structure of this elusive species.

1. One route to cyclobutadiene is through oxidation of an iron complex like $4$. If cyclobutadiene were rectangular, equal amounts of $5a$ and $5b$ would be formed; these isomers might or might not be in equilibrium. If cyclobutadiene were a square, it would be represented by structure $5c$. The cyclobutadiene from $4$ was trapped with $Z-\beta$-cyanoacrylate. Assuming that $5a$ and $5b$ behave like ordinary Diels-Alder dienes, show the structures of the two regiosymmetric adducts from $5a$ and of the two regiosymmetric adducts from $5b$. In what proportions would you expect these four adducts to be produced? Explain briefly. (Note that product $6$ is exclusively endo, so one needn't worry about different stereoisomers in this reaction.)

2. If square planar structure $5c$ were correct, all four isomers shown for $6$ in Part 1 could result from attack of the acrylate at any of the four bonds. In what proportions would you expect them to be formed, if $5c$ were correct.

3. In fact, the reaction produced exactly equal amounts of all four regioisomers. If you've done Parts 1 and 2 correctly, you'll realize that this experiment doesn't establish what the structure of $C_4H_4$ is. Right? Right. To decide, an alternative route to cyclobutadiene-$d_2$ was investigated. Azo compound $7$ was generated and found to decompose rapidly to $C_4H_2D_2 + N_2$ at $< 10^\circ C$. Two modes of decomposition, (a) and (b), are possible. One of these is much more likely than the other. Which one is it? Justify your choice.

4. In fact, when $7$ was generated in the presence of $Z-\beta$-cyanoacrylate, only two adducts, those formed from $5b$ in Part 1, were formed. What does this say about the structure of cyclobutadiene (square vs. rectangular)? If rectangular, what does this say about the barrier to equilibrium of the type shown for $3d$ and $3e$?

5. Finally, when $7$ was generated in the presence of a less reactive dienophile, methyl acrylate (H$_2$C=CH-COOMe), an equal mixture of four regiosymmetric adducts (analogous to those in Part 1) is formed. How do you reconcile this with the behavior discussed in Part 4?
III. (70 points)

A. Can benzene (either by itself or as part of a larger molecule) act as the dienophile in a Diels-Alder reaction? Ordinarily, No. But perhaps one could enhance the possibility by doing the reaction intramolecularly with a nearby diene.

1. A system that has been investigated is shown here. As the equilibrium arrows suggest, the potential Diels-Alder adduct 2 (shown from two perspectives) is much less stable than the reactant. Give at least two reasons why this should be true.

2. Adduct 2 will seek to shed its excess energy by doing a reverse Diels-Alder reaction. But note: in addition to the cyclohexene unit denoted by the numbered carbons 1...6, there is another cyclohexene unit that could cleave. Draw the reverse Diels-Alder product from this other cyclohexene.

3. If you’ve done Part 2 correctly, you’ve found that both modes of reverse Diels-Alder reaction give 1! [If you didn’t come to this conclusion, re-do Part 2.] Since 2 is too unstable to be isolated and since 1 is produced by both retro reactions, your job is to devise a method by which you could show that the forward reaction 1 -> 2 and the reverse reaction 2 -> 1 occur.

B. Here’s another case of a benzene moiety taken part in a Diels-Alder reaction, although these benzene units are very strained. (The drawing, for convenience sake, has the benzene rings planar, but in fact they are both tub-shaped; check any standard text for a discussion of the structure of [2,2]paracyclophane.)

1. Thermal reaction of

   

   ![Diagram](image)

   with dicyanoacetylene at 120°C gives a 1:1 adduct which reacts further at 170°C to give a 1:2 adduct. We’ll start with an easy task: use the curved arrow notation (and Kekulé structures) to show how these products are formed.

2. The chemists who did this work were surprised when they found that mono cyanoacetylene reacted with cyclophane 3 quite differently. In benzene solution at 160°C, the 1:2 adducts had the structures 4, 5, 6, and 7. In addition, small amounts of trimers (8 and 9) of the alkyne are formed. The structures are shown on the next page.

   a. Adducts 4 and 5 could have been formed by an initial Diels-Alder reaction (as in Part 1, above) followed by a [2+2] cycloaddition to another cyanoacetylene molecule from either the right or the left. Show how this would work.

   b. But such a mechanism could never explain the formation of 6 and 7, and for that reason may well be wrong for 4 and 5 as well. To explain the formation of all four 1:2 adducts, the authors suggested an initial [2+2] cycloaddition of two cyanoacetylenes giving an equilibrating mixture of cyclobutadienes (reminiscent of what we observed in Question IIC). Note that the cyclobutadienes have, between them, three different kinds of C=C bonds. Show how these could react in Diels-Alder fashion with cyclophane 3 to produce all four 1:2 adducts.

   c. Note that 8 and 9 are trimers of cyanoacetylene. It's likely that they're produced by further reaction of each of the cyclobutadienes (above) with another molecule of the alkyne. Show how this occurs.
C. 1. Furan is a very good diene in Diels-Alder reactions but isobenzofuran is far better. It reacts with dienophiles at lower temperatures and gives adducts that are more stable. Rationalize this behavior.

2. Consider, now, the reaction of isobenzofuran with N-methylmaleimide at 132°C. Two products are formed in high yield but in very different proportions depending on how long the reaction is allowed to run. Explain, in general terms, what is going on here.

D. The dimerization of 1,3-butadiene at 100°C and 1 atm pressure gives 94% of 4-vinylcyclohexene and 6% of trans-1,2-divinylcyclobutane. To elucidate the mechanism, the behavior of (Z,Z)-1,3-butadiene-1,4-d2 was examined. The results are shown here; all products are, of course, racemic.

1. For the two major products (94%), note that the protons at C3 and C6 are cis; note also that the protons at C4 and C5 are cis. What does this tell you about the nature of the reaction (supra/antara, concerted/stepwise, etc.)?

2. Note that the major product is a mixture of stereoisomers 10a and 10b. What conclusions can you draw from this?

3. For the minor product (6%), note that 11a, 11b, and 11c have unchanged Z stereochemistry for the two vinyl groups. Note, also, the 1:2:1 distribution of stereoisomeric products at the CHD sites of the ring. Suggest a detailed mechanism that will produce this result. [It would be helpful if you’d use the same analytical method employed for acrylonitrile dimerization in Handout V, pp 7a-7d.] Use a mixture of drawings and words in your


