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."]

"A red dragonfly hovers above a backwater of the stream, its wings moving so fast that the eye sees not wings in movement but a probability distribution of where the wings might be, like electron orbitals: a quantum-mechanical effect that maybe explains why the insect can apparently teleport from one place to another, disappearing from one point and reappearing a couple of meters away, without seeming to pass through the space in between." — Neal Stephenson

"To me, any committee is a complete waste of time. Either the other members of the committee think the same way I do, in which case I might just as well not be there, or they disagree, in which case I have to waste time arguing with a bunch of obstinate idiots." — Michael J. S. Dewar

"Theoretical efforts to elucidate the thermal behavior of the pristinely, unsubstituted, archetypal cyclobutane in the gas phase have been extensive. At the experimental level, intrepid purists have explored these questions with deuterium as a minimal perturbation, while soldiering pragmatists have introduced more drastic perturbations in the hope of achieving answers." — William von E. Doering

"Curious, though, isn't it that the number six should be embodied in one of the most beautiful shapes in all of nature; I refer, needless to say, to the benzene ring with its single and double bonds. But is it truly symmetrical or asymmetrical? Or asymmetrically symmetrical, perhaps, not really like the rather unsatisfactory petals of an iris. Curious, wouldn't you say?" — Vikram Seth in "A Suitable Boy" (with all "ums" and "ers" mercifully removed to aid comprehension)

I. (75 points) PSYCHO ADDITION REACTIONS

A. 1. Pyrolysis of hydrocarbon 1 at 80°C gives a quantitative yield of benzene and cyclopentadiene. When the pyrolysis is performed in the presence of excess N-phenylmaleimide, only 2 is produced; the rate of formation of 2 is independent of the concentration of trapping agent. Write plausible mechanisms for these two reactions of 1.

2. In contrast to the behavior of 1, pyrolysis of isomeric hydrocarbon 3 does not lead to fragmentation. Instead, a tricyclic isomer 4, whose UV spectrum indicates the presence of a conjugated diene, is produced. Suggest a structure for 4 and a mechanism for its formation.
B. An unstable 1,3-dipole (only one contributing structure is shown on the next page) is generated in the presence of various trapping agents. Consider the following data about these reactions and answer questions 1 to 3 about them.

![Reaction Scheme]

1. Account for the fact that reaction with dimethyl fumarate is >99.97% stereoselective, whereas that with dimethyl maleate gives a small, but measurable, formation of the trans diester.

2. Account for the much greater loss of stereochemistry in the reactions with dicyanofumarate and -maleate. Also speculate on why the loss of stereochemistry is greater for the dicyanofumarate.

3. The compound in brackets is formed reversibly. Its presence is detected by trapping it with water (not shown). How do you account for its formation?

C. 1. Using clear conformational drawings for the reactants, explain clearly why decomposition of azo compound 5 gives exclusively EZ diene, whereas that of 6 gives EE diene (but no ZZ).

2. Analogously, use clear drawings to explain why decomposition of 7 gives exclusively EZ diene, whereas that of 8 gives ZZ (but no EE).

3. Although the activation parameters for azo compounds 7 and 8 have not been determined experimentally, they have been calculated to be $E_a = 27.2$ and $30.7$ kcal/mol, respectively. Speculate on why this difference exists.
II. (95 points) **SHIFTY AND SHIFTLESS ATOMS**

A. Is it possible that a student could gain a Ph.D. in organic chemistry without having learned the Reimer-Tiemann reaction? Surely not! So as a public service, I will now teach you the fundamentals of this reaction; for further detail, see Smith/March p. 716ff. In the Reimer-Tiemann reaction (to the right), the conjugate base of salicylaldehyde is formed in high yield using CHCl₃ as the source of the aldehyde carbon. Extensive mechanistic studies have led to the following postulated sequence:

\[
\text{CHCl₃} + \text{HO}^- \xrightarrow{\alpha\text{-elimination}} \text{Cl}^- + \text{H₂O} + :\text{CCl₂} \xrightarrow{\text{ClO}^-} \text{PhO}^- \xrightarrow{\text{H₂O}} \text{CHCl₃} + \text{HO}^- \]

1. For the step A --> B, what does orbital symmetry have to say about the likelihood of such a concerted [1,2] H transfer? Formulate your answer in terms of the type of orbital analysis devised by Woodward and Hoffmann.

2. Consider, now, the following experiments. What do they have to say about the possibility of an intramolecular A --> B reaction? [In the second experiment, the 2, 4, and 6 positions of phenoxide ion are not even close to being 100% tritiated, but it's important to know that tritium is present only at those positions.]

3. [FOR NO CREDIT, JUST FOR FUN] Although only one part of this reaction mechanism falls under the control of orbital symmetry, there are other interesting facets. Most texts (e.g., Smith/March) imply that the CHCl₂ group of B is simply hydrolyzed to the aldehyde, presumably by S_N2 displacement of one Cl by HO⁻ followed by elimination of the second chlorine. The mechanism cannot possibly be this simple, but in order to understand why you know have to learn something about the abnormal Reimer-Tiemann reaction. When the ortho and para positions of the phenoxide are substituted, the final product is the dichloromethyl derivative, not the aldehyde. Your challenge is to suggest a mechanism that explains why B does give aldehyde, whereas the trimethyl compound doesn't.

B. Pyrolysis of optically active compound 1 gives a mixture of 2 (major) and 3.
(minor). Use conformational drawings and orbital symmetry considerations to explain how these products are formed. Then, use this knowledge to predict the structures of 2d and 3d from the pyrolysis of stereospecifically deuterium-labeled 1d (to the right).

C. The prudent student (oh, how I love that term!) should, right now, review the brilliant experiment by Wolfgang Roth on the stereochemistry of the thermal [1,5] shift of H. As an essential element in establishing the primacy of orbital symmetry for such reactions, this experiment is unparalleled; but as a method for making stereospecifically labeled deuteriated compounds, it has two failings: (1) about 27% of the reactant remains after 2 hr at 250°C, but heating at higher temperatures leads to decomposition products; (2) although each of the products is stereospecifically labeled, the overall optical yield of degradation product CH₃-CHD-CH₂OH is low because the initial E and Z dienes are formed with opposite configuration at the newly created asymmetric carbon. With these limitations in mind, consider, now, the following experiment, initially performed with racemic reactant.

1. In contrast to the Roth experiment, none of the reactant in the reaction to the right remains at equilibrium; the two products are formed in 100% yield. Provide a rationalization for this.

2. Using suitable drawings of the conformations and transition states involved in the reaction, explain why EE diene predominates in all cases; and explain why it amounts to 100% of the reaction mixture when R = t-Bu.

3. By a series of well-precedented stereospecific steps, an enantiomerically pure reactant with Z stereochemistry at the isotopically labeled double bond (to the right) was prepared. On the basis of your analysis, above, show the structure of the single product that is expected from this reaction.

4. [FOR NO CREDIT, JUST FOR FUN] The product was subjected to the following sequence of steps: (1) O₃; (2) CF₃-CO-OOH; (3) KOH/H₂O. Show the three-dimensional structure of the enantiomerically pure two-carbon carboxylate that is produced; in doing so, explain what each synthetic step accomplishes.

D. Although the beautifully conceived Berson experiment for the stereochemistry of ring walk in norcaradienes (Handout IX, pp. 5ff) remains just that (a conception), other chemists have succeeded in using isotopic labels as a minimal perturbation to a substrate. For example, 9,9-dicyanobicyclo[6.1.0]nonatriene has been prepared with heavy isotope¹⁵N exclusively in the exo nitrile. After heating this substrate to various temperatures between 120 and 170°C, there is no evidence that the two cyano groups interchange their roles, a result that is perfectly in accord with Klärner’s observations on such [1.7] shifts (Handout, p. 9). However, a competing irreversible reaction does take place, yielding two "isotopomers" in a constant 2.7:1.0 ratio at every temperature over this 50-degree range. This rearrangement can be viewed as either a [1,5] shift of C₉ from C₁ to C₅ or (a little harder to see) a [1,3] shift of C₉ from C₆ to C₆ or from C₁ to C₃.
1. If this rearrangement were under the control of orbital symmetry, which of the two products would be expected if the reaction were a [1,5] shift and which if it were a [1,3] shift? Use lots of words and drawings in your answer.

2. If you've done things correctly, you should have concluded that the same product is expected from either orbital symmetry controlled route (no surprise!). [If you didn't reach this conclusion, go back to Part 1 and find your error.] Now the question is this: does this expected product correspond to the major product actually observed? And, regardless of your answer to that, how do you account for a significant presence (either 73% or 27%) of the symmetry-fordbidden product in the mixture?

3. What does the unchanging product ratio as temperature is varied from 120 to 170°C reveal about the nature of this reaction? Give a clear discussion in your answer.

III. (35 points) **COPING WITH ADVERSITY**

**A.** The famous Doering/Roth experiment established the stereochemistry of the Cope rearrangement through a study of the rearrangement of dl or meso 3,4-dimethyl-1,5-hexadiene. Now consider a stereochemical study of the related Claisen rearrangement, which is performed in the "reverse" direction (i.e., stereospecifically synthesized E or Z substrates are prepared and are rearranged to various RR, RS, SR, SS products).

1. Explain, clearly, why the Cope rearrangement has its equilibrium far on the side of 2,6-octadiene whereas the Claisen proceeds essentially irreversibly to the γ,δ unsaturated aldehyde.

2. Pyrolysis of E,E and E,Z isomers 1 and 2, respectively, proceeds as shown to the right. Using clear drawings, decide whether chair or boat transition states are involved. Do a full analysis for I only, but be sure to show the formation of both enantiomers of 3 and 4 in your mechanism. Then write a brief discussion of the relative importance of chair and boat transition states for 2; it is not necessary to draw additional pictures.

3. Predict the structure (with words or pictures) of the major product from reaction of the other two stereoisomers of reactant: the Z,E and the Z,Z. Give a brief justification.

**B.** 1. Consider the Cope equilibrium between isomeric hydrocarbons 5 and 6. Which isomer should predominate at equilibrium? Justify your answer.

2. Diene 5 has two stereo centers and can, therefore, exist in diastereomeric forms (meso 7 and dl 8). Both 7 and 8 rearrange to 6, but at vastly different rates. For 7 → 6, ΔH‡ = 41.8 kcal/mol and ΔS‡ = -0.4 cal deg⁻¹ mol⁻¹; for 8 → 6, ΔH‡ = 28.0 kcal/mol and ΔS‡ = -11.4 cal deg⁻¹ mol⁻¹. To explain this rate difference, carefully draw the conformations of 7 and 8 needed for rearrangement to 6; use molecular models to guide you. Which leads to a chair transition state and which to a boat? Can you now rationalize both the ΔH‡ and ΔS‡ data?
IV. (95 points) **A STATE OF FLUX**

A. The fluxional nature of bullvalene was established by its showing only one sharp signal in both the $^1H$ and $^{13}C$ NMR spectra at 100°C. Consider, now, two other compounds with similar properties.

1. Compound 1, a (CH)$_{10}$ like bullvalene, shows sharp, well defined multiplets at $\delta$ 6.1 and $\delta$ 3.2 in an area ratio 1:1.5 in the $^1H$ NMR spectrum at room temperature. An effort to see if these coalesced into a single peak at higher temperatures was thwarted by an irreversible decomposition that occurred. Thus an alternative method of looking for fluxion was needed. When labeled compound 1$d_2$ was synthesized at low temperature and its NMR spectrum measured at -40°C, it showed resonances at $\delta$ 6.1 and $\delta$ 3.2 in an area ratio 1:3. Upon warming to +35°C, the relative areas of the peaks changed, eventually reaching 1:1.5 after which there was no further change.

   a. Consider the NMR spectrum of 1. Is it what you'd expect for this structure? Is there any evidence that 1 is undergoing rapid Cope rearrangements? Justify your answer.

   b. Consider, now, 1$d_2$. Compare the spectrum at -40°C with that at +35°C and, using words and drawings, give a complete explanation of what is going on.

2. Consider, now, hydrocarbon 2, C$_{13}$H$_{16}$, in which three CH$_2$ groups have been inserted into three of the bonds of 1. Unlike 1 and 1$d_2$, compound 2 is chiral and can be resolved at low temperature into enantiomers. When warmed to temperatures ranging from 39 to 57°C, (+)-2 was found to racemize with a relatively low $E_a = 28.9$ kcal/mol. Using words and drawings, explain how racemization occurs.

B. 1. Consider the remarkable transformation to the right (E = ester). Take a deep breath, then rationally try to write a mechanism for this reaction using various types of symmetry-controlled processes. [Hint: the tetrazine acts as an electron-deficient "diene" in cycloadditions with electron-rich dienophiles.]

2. The $^1H$ NMR spectrum of the product shows sharp singlets at $\delta$ 4.79 (rel. area 2), $\delta$ 3.17 (3) and $\delta$ 1.17 (3). How do you account for such a simple spectrum?

C. 1. For a bullvalene with two identical substituents (e.g., Br), there are twelve distinct isomers (not counting enantiomers). Trust me on this!! Of these, four have the substituents on adjacent carbons. Draw these four.

   ![Diagram of Bullvalene Isomers](image)

   1. Which, if any, of these four dibromo compounds is/are chiral? Explain. [Be careful, here.]

   2. When the two substituents are part of a relatively small ring, only those same four isomers with substituents in a 1,2-relationship are possible.

   a. Explain why compound 3 exists entirely as a single isomer.

   b. Show clearly how the four possible isomers for compound 4 interconvert.

   ![Diagram of Isomer Interconversion](image)

4. Consider the case of furobullvalene (5). The low temperature and high temperature $^1H$-NMR spectra are shown to the right. Assign all of the peaks in the low temperature spectrum. Explain the

   \[\begin{array}{ccc}
   \text{δ at -60°C} & \text{δ at +100°C} \\
   7.62 (s, 1) & 7.46 (s, 2) \\
   7.30 (s, 1) & 5.77 (m, 2) \\
   5.93 (m, 2) & 4.06 (m, 4) \\
   5.77 (m, 2) & 3.10 (t, J = 8 Hz, 2) \\
   3.28 (t, J = 8 Hz, 1) & 2.92 (t, J = 8 Hz, 1) \\
   2.92 (t, J = 8 Hz, 1) & 2.19 (m, 2) \\
   \end{array}\]

   NOTE: s = singlet, t = triplet, m = multiplet. The number to the right of s, t, or m is the relative area.
change in spectrum as the temperature is increased. Be specific in your answer.

CHEMISTRY 650-25584  EXAM II  LITERATURE CITATIONS


