Chemistry 4321/8321	Midterm Examination I 6:00 – 8:00 PM	October 12, 2022
Organic Synthesis	0.00 0.00 1 W	T. R. Hoye

Name: Answer Key	Part I	<u>14 / 14</u>
<u> </u>	Part II	<u>12 / 12</u>
Please clearly print your name above.	Part III	<u>12 / 12</u>
There are 101 points and five questions on the exam.	Part IV	<u>10</u> / 10
Answer all questions directly in the space provided on the five exam pages.	Part V	<u>53</u> / 53
You may not use books, notes, phones, etc.	Total	<u>101 /101</u>

A copy of our diamond lattice is attached as a final page in the case that you would find that useful.

I. (14 points) For parts **a** and **b** indicate (circle the word) whether the two structures are the *same*, a pair of *enantiomers*, or a pair of *diastereomers*. *If* they are diastereomers, indicate the number of stereogenic centers that are different in the two structures. Ignore differences in conformation. For part **c** indicate (circle the word) whether the indicated pairs of atoms or groups are *homotopic*, *diastereotopic*, or *enantiotopic*.

II. (12 points) Decide whether each of the following *equilibria* lies predominantly to the **left** or to the **right** as a solution in an organic solvent such as, e.g., THF. Circle the species on the side that is more stable (i.e., lower in energy and more highly populated).

III. (12 points) Provide the structure for the major product expected from each of the reactions a)-c). The molecular formula of the missing product is given in the lower right corner of each box.

IV. (10 points) The Hofmann elimination of quaternary ammonium hydroxide salts results in preferential formation of the <u>less</u> highly substituted (and thermodynamically <u>less</u> stable) alkene. That is to say, the product distribution is under kinetic rather than thermodynamic control. As you know, the preferred geometry for an E2 elimination involves an antiperiplanar relationship between the vicinal (or β) proton that is lost and the leaving group. On the partial diamond lattice below, provide a carefully drawn representation of the most stable conformation of the tetra-alkylammonium hydroxide (*R*)-1 and use it to rationalize (with accompanying text you add <u>within the blank box</u>) why the pyrolysis of (*R*)-1 yields mostly 1-butene with only a minor amount of the (more stable) 2-butenes.

One of the C1 (Me) protons is **always anti** to the C2–N⁺ bond (see circled hydrogen atom). The only way to avoid a syn-pentane (or 1,7-H/H) interaction (note, 1,6-H/H interactions shown by magenta arrows) between the C4 methyl protons and one of the three equivalent methyl groups on the nitrogen is to adopt the conformation/rotamer along the C2–C3 bond as shown in the structure to the left. Neither of the boxed C3 protons is anti to the C2–N bond in that dominant conformation, so elimination is favored across the C1-C2 bond [a rate is a rate constant times a concentration, and there is a very low concentration of a reactive conformation required for formation of either of the 2-butenes].

- **V.** (53 pts) Provide a *detailed mechanism* to account for each of the following six reactions. Show *ALL* intermediates, equilibria, and bond-making and -breaking steps. For species that have more than one significant resonance contributor, you only need to show one of them.
- a) (6) The use of dimethylformamide dimethyl acetal to make methyl esters from carboxylic acids.

b) (12)

HO OH
$$\rho$$
-TsOH (cat.)

PhH, reflux

HO
H
 θ
H

c) (6)

d) (9)

OHOH NaOH (cat.)
$$H_2O$$
, THF, rt

OHHOH

e) (14)

f) (**6**)