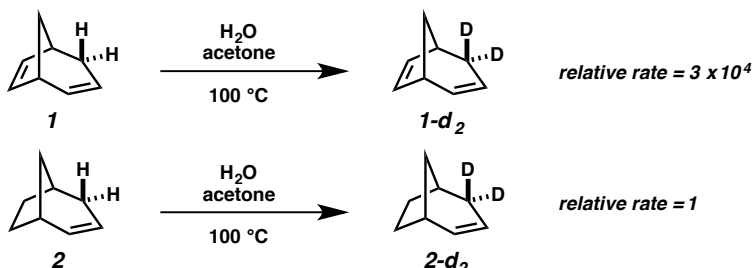
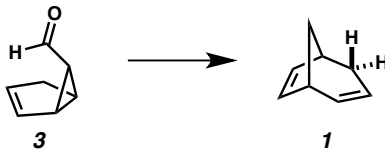


Attempt all questions. Present your answers **clearly** and **legibly** in the order that they appear below. Label each section in your answer book according to the problem numbering. **(100 total points)**

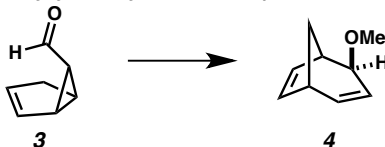
1. Hydrocarbon **1** and related congeners have been studied extensively due to several notable observations of their reactivity. Among these, Brown and co-workers discovered that H/D exchange occurs approximately 30,000 times (3×10^4) more rapidly in diene **1** than in the related olefin **2**. (*Chem. Commun.* **1965**, 376)



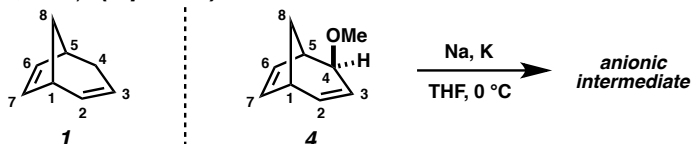
- a. Provide a detailed arrow-pushing mechanism for the deuterium exchange reaction in diene **1**. Your mechanism should account for the observed reactivity difference relative to alkene **2**. **(8 points)**
- b. The bicyclic diene used in these studies is accessible using the readily available cyclopropane **3**. Suggest conditions for the conversion of **3** into diene **1** (you may use multiple steps, although it is possible to achieve this in a two-step, one pot operation). (*Tetrahedron Lett.* **1964**, 5, 2503) **(10 points)**



- c. Suggest how you would modify your synthesis in part b to access the related ether **4**. **(5 points)**

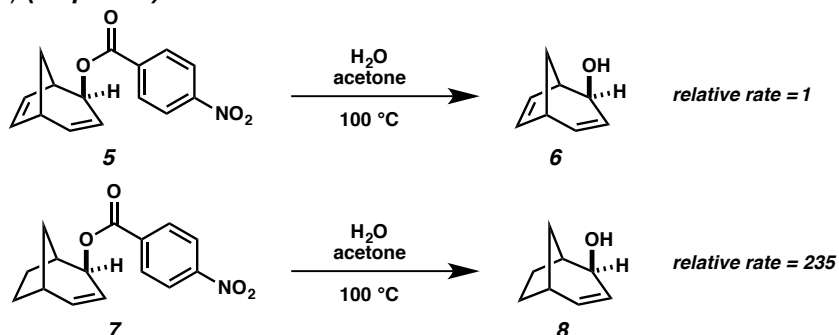


- d. NMR provides remarkable evidence for the origin of the accelerated deuterium exchange. The table below indicates the observed resonances for hydrocarbon **1** and those of the anion derived from *reduction* of allylic ether **4** to simulate the anionic intermediate presumed in the deuterium exchange reaction in part a. Provide an interpretation of the NMR data and explain how this informs your understanding of the intermediate. (*J. Am. Chem. Soc.* **1967**, 89, 3656 and *Chem. Commun.* **1967**, 638) **(8 points)**



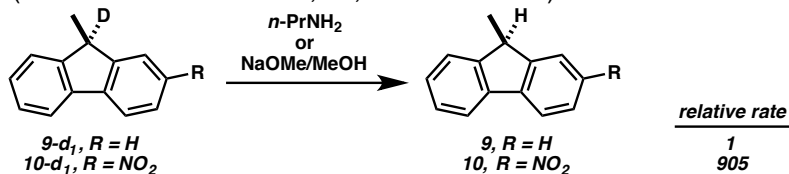
Proton	Chemical Shift (δ , ppm)		
	compound 1	compound 4	anionic intermediate
H(1) & H(5)	2.57	2.74	2.45
H(2)	5.92	6.10	2.84
H(3)	5.15	5.28	5.39
H(4)	2.17, 1.79	3.3	2.84
H(6)	5.65	5.82	3.67
H(7)	6.18	6.43	3.67
H(8)	1.90, 1.66	1.8 (2H)	0.87, 0.42

- e. In a different study, the *exo-p*-nitrobenzoates **5** and **7** were subjected solvolysis reactions with water as a nucleophile, leading to the corresponding *exo*-alcohols **6** and **8** as the major products. In these experiments overall first-order kinetics were observed. With this in mind, provide a detailed arrow-pushing mechanism for the conversion of benzoate **5** to alcohol **6**. (*J. Am. Chem. Soc.* **1970**, *92*, 7477) (10 points)

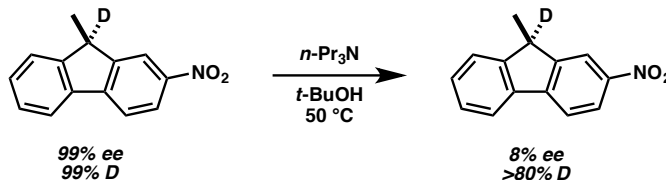


- f. Explain the preferential formation of the *exo*-alcohol isomers in the solvolysis reactions in part e. (6 points)
- g. In these systems a different reactivity trend is observed in the solvolysis reactions of diene **5** and *mono*-alkene **6** (part e), with the diene **5** reacting 235 times *slower* than the *mono*-olefin **6**. This result was, in fact, expected based on theoretical calculations. Suggest a mechanistic explanation for this difference in reactivity and explain why the presence of an additional alkene is *deactivating* in this case, but *activating* in the exchange experiment in part a. (HINT: Consider the quantity of electrons involved in the presumed intermediates). (10 points)

2. The rate of deuterium exchange in fluorenyl systems is affected dramatically by substitutions on the system. For instance, the relative rate of H/D exchange in fluorene itself (**9**) is 905 times slower than in 2-nitrofluorene (**10**). (*J. Am. Chem. Soc.* **1968**, *90*, 2598 and 2606)

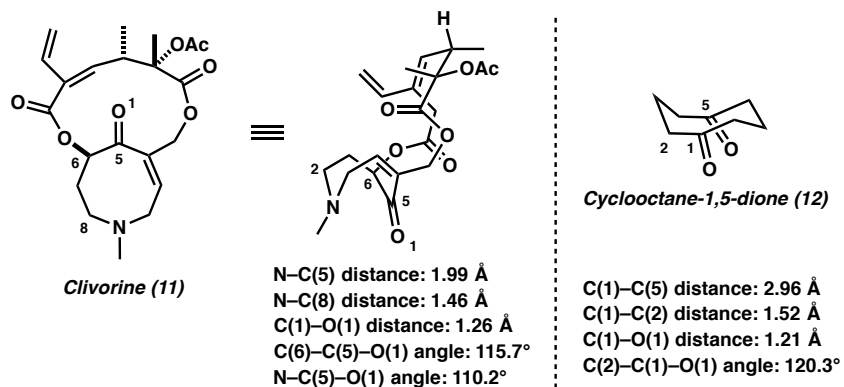


- a. Suggest an explanation for the difference in rate of H/D exchange. (6 points)
- b. An intriguing result from a related experiment is shown below. Draw a scheme to correspond with your expected outcome from this experiment and explain what is unusual about the actual result. (8 points)



- c. The result shown in part b is sensitive to the nature of the reaction medium. If the amine concentration is increased, then the overall dielectric constant for the reaction mixture is decreased. As a result, the relative rate of H/D exchange and racemization is *decreased*. Explain how this change dielectric constant informs your understanding of how the racemization and H/D exchange reactions occur. (5 points)
- d. Suggest a detailed arrow-pushing mechanism that is consistent with the observations above. (8 points)

3. The structure of the alkaloid natural product clivorine **11** has been of great importance to the development of physical organic chemistry. A key observation can be made from evaluation of the X-ray crystal structure, where the nitrogen-containing eight membered ring is found to adopt a tub-like shape. (*Tetrahedron* **1974**, *30*, 1563 and *Acta Cryst.* **1972**, *B28*, 2825). This structure differs significantly from the X-ray structure of cyclooctane-1,5-dione (**12**) which adopts a chair-boat conformation. Calculations suggest that cyclooctanone also prefers this conformation. Some potentially useful structural data are included as well. For the purposes of this question, you may ignore the effects of the 13-membered bis(lactone) ring in **11**. (*J. Chem. Soc., Perkin Trans. 2* **1979**, 1527)



- Provide a potential explanation for the difference in conformational preference shown. **(5 points)**
- Using your knowledge of frontier molecular orbital theory, provide a drawing that rationalizes the preference for the conformation of the eight membered ring. **(8 points)**
- The analysis of this crystallographic observation and the extension to general carbonyl reactivity is strongly associated with two researchers. What are the names that are commonly referred to with respect to this fundamental carbonyl chemistry concept? **(3 points)**