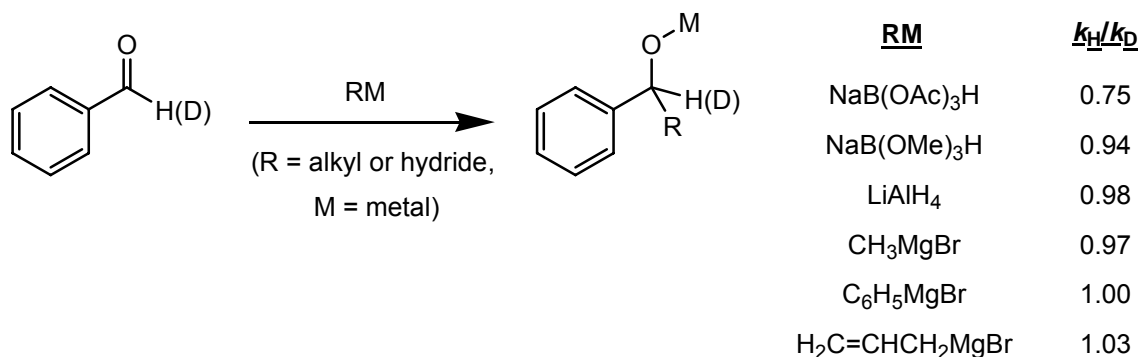


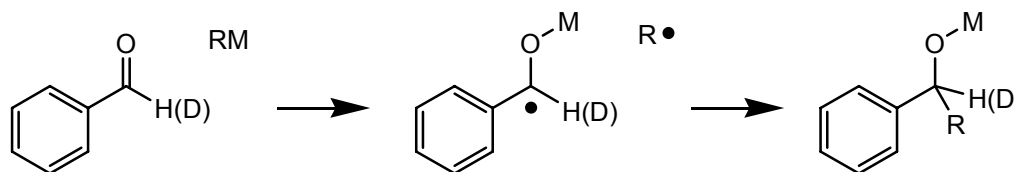
Problem Set 7

Due: In class, Monday, November 27
(after Thanksgiving)

1. The kinetic isotope effect observed for addition of organometallic and hydride reagents to benzaldehyde depends on the specific reagent. In most cases, $k_H/k_D < 1$, but in a few instances, no kinetic isotope effect is observed.

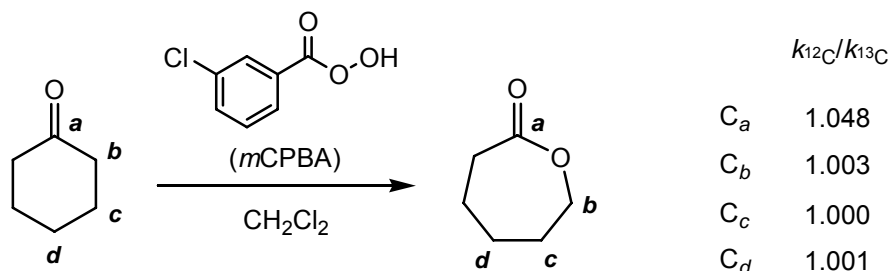


- a) In the cases where $k_H/k_D < 1$, the (inverse) kinetic isotope effect has been justified by changes in hybridization at the aldehyde carbon. Explain why this change would lead to the kinetic isotope effect observed. Support your case with both vibrational frequencies and a potential energy diagram.
- b) The magnitude of the inverse isotope effects correlate, to some extent, with the reactivity of the reagents. For example, very reactive LiAlH₄ and CH₃MgBr show smaller inverse kinetic isotope effects than the less reactive NaB(OAc)₃H. Why?
- c) Gajewski has argued that isotope effects near $k_H/k_D \approx 1$ would also be observed if rate-determining, single electron transfer from RM to benzaldehyde preceded alkyl addition.¹ Does this make sense in terms of the observed kinetic isotope effects? Why or why not?

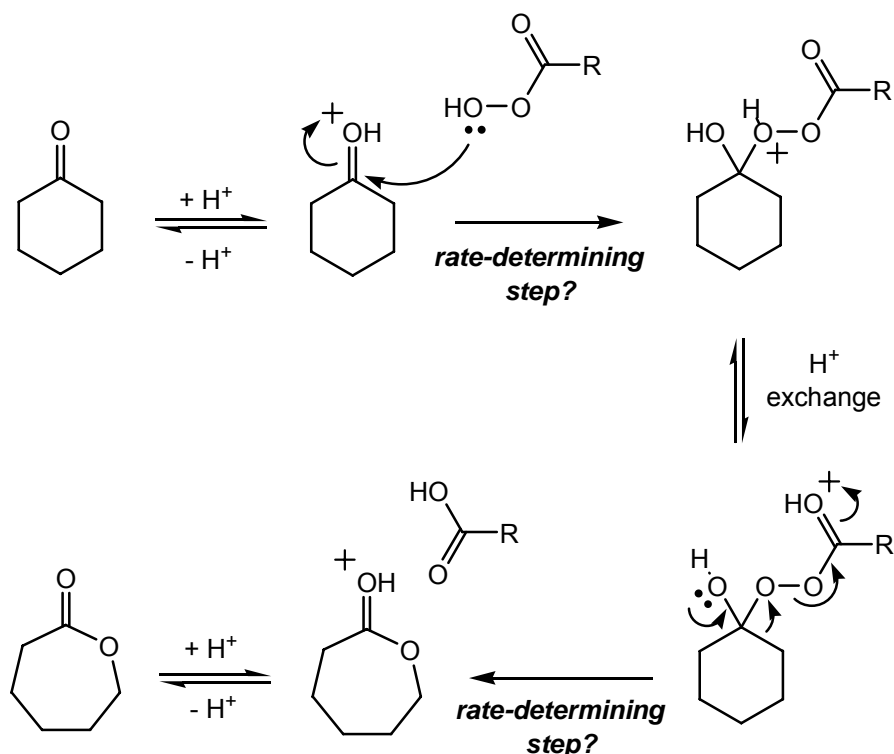


¹ Gajewski, J. J.; Bocian, W.; Harris, N. J.; Olson, L. P.; Gajewski, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 326.

2. Singleton and coworkers have measured natural-abundance, ^{13}C kinetic isotope effects for the Baeyer-Villiger oxidation of cyclohexanone to caprolactone:²



Singleton analyzed this data in the context of the mechanism for the reaction, which could have one of two rate-determining steps.



- a) In the first potential rate-determining step shown above, carbon **a** could exhibit isotope effects for both bond-forming and bond-breaking ($\text{C}=\text{O}$ to $\text{C}-\text{O}$) processes. What should bond making and bond breaking contribute to the overall kinetic isotope effect for this step? Answer as mathematically as you can, and assume that $\text{C}=\text{O}$ stretching frequencies are the only contributors to the observed isotope effect.

² Singleton, D.; Szymanski, M. *J. Am. Chem. Soc.* **1999**, *121*, 9455.

- b) Draw the transition state for the second potential rate-determining step. What carbons are experiencing changes in bonding? Which of these might you imagine to exhibit kinetic isotope effects, and why?
- c) Given the observed kinetic isotope effects and your answers to parts (a) and (b), what do you think is the rate-determining step for the Baeyer-Villiger oxidation of cyclohexanone?

Problems to try on your own:

MPOC, Chapter 8: Problems 19.

L&R,