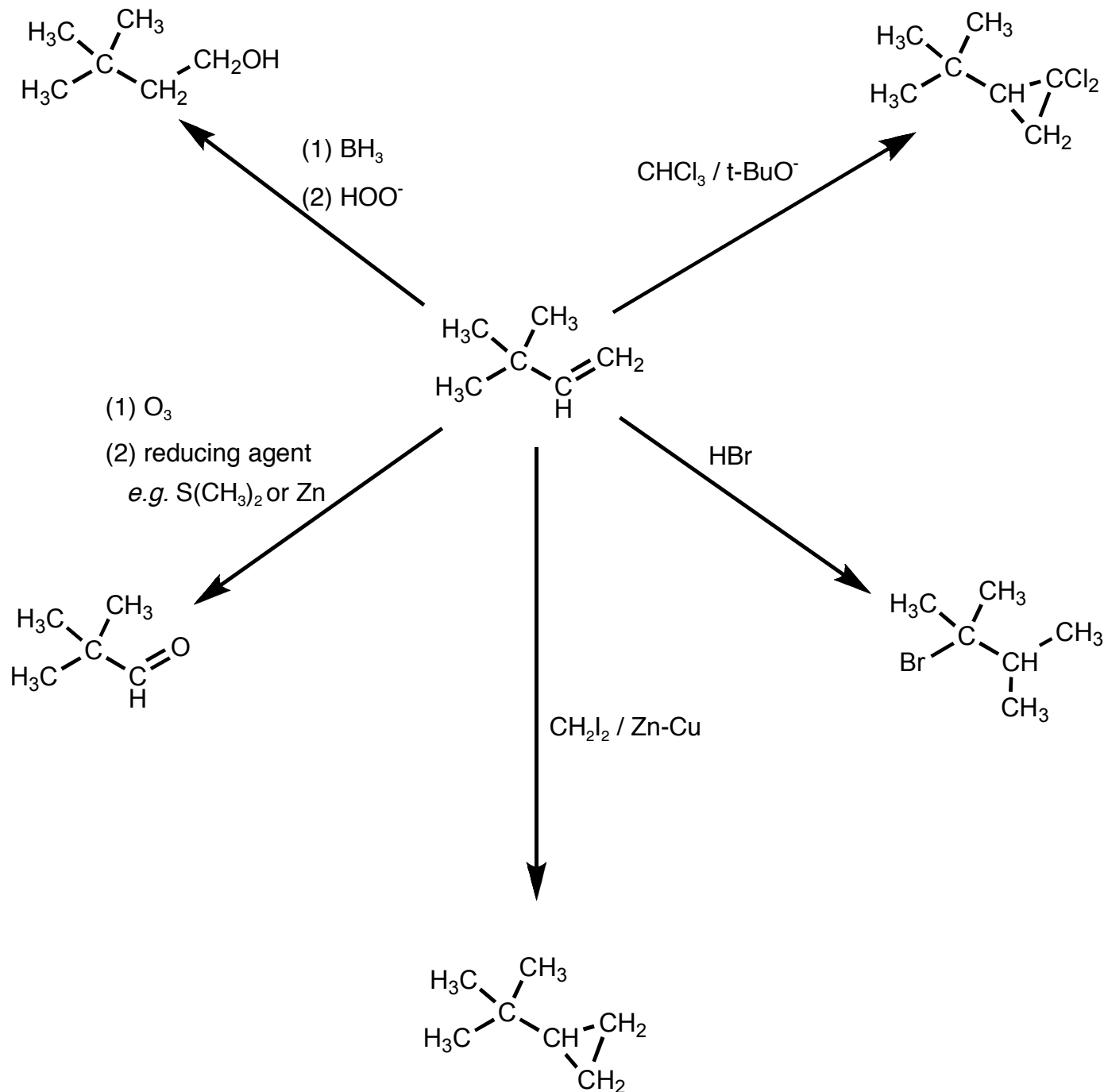


Statistics: Average 56.5 1/3 > 65 2/3 > 48

1. (10 min) Complete this scheme by supplying a reagent (or reagents) for achieving each of the following five conversions in good yield.

No mechanisms or curved arrows are required, just the reagents, but do indicate if two successive treatments are required by writing (1) reagent 1 (2) reagent 2.



2. (5 min) Consider these three **pairs** of C_4 isomers - radicals, cations, and alkenes. In two cases the energy difference between the members of a pair is about 2.5 kcal/mole, but in the other case it is estimated to be 21 kcal/mole.

Circle the more stable isomer in **each pair**, and provide a plausible **explanation** for the difference in each case, indicating why the difference is so much larger for one of the pairs.



(1) **Hybridization**: In all three cases the isomer in which the sp^2 -hybridized carbon forms more bonds to C is favored. This is because C-C bonds are more sensitive to hybridization change than C-H bonds are.



(2) **Hyperconjugation**: Electrons in out-of-plane bonds projecting from the next-adjacent carbon should be stabilized by mixing with a low vacant orbital (or SOMO) on an sp^2 -hybridized carbon. This effect should be much **more important for the cation**, where the vacant p-orbital is especially low in energy because of the positive charge. It is not so important when the orbital is higher in energy (π^* of C=C) or already singly occupied (radical).



3. Consider the chlorination reaction : $i\text{-Pr}_2\text{NCl} + \text{RH} \rightarrow i\text{-Pr}_2\text{NH} + \text{RCl}$

and these approximate bond dissociation energies (kcal/mole): N-Cl (46), R-Cl (85), N-H (92), R-H (100).

- A. (3 min) Estimate the equilibrium constant for the transformation at room temperature:

$$\text{Lose } 46 + 100 = 146 \text{ kcal/mole} \quad \text{Gain } 85 + 92 = 177 \text{ kcal/mole} \quad K \sim 10^{3/4 \times 31} = 10^{23}$$

- B. (3 min) The transformation requires light (or added free-radical initiators). If you doubled the amount of light (or initiator) would you expect the rate of transformation to (a) increase about 50%, (b) double, (c) quadruple, (d) stay the same, or (e) decrease? Why?

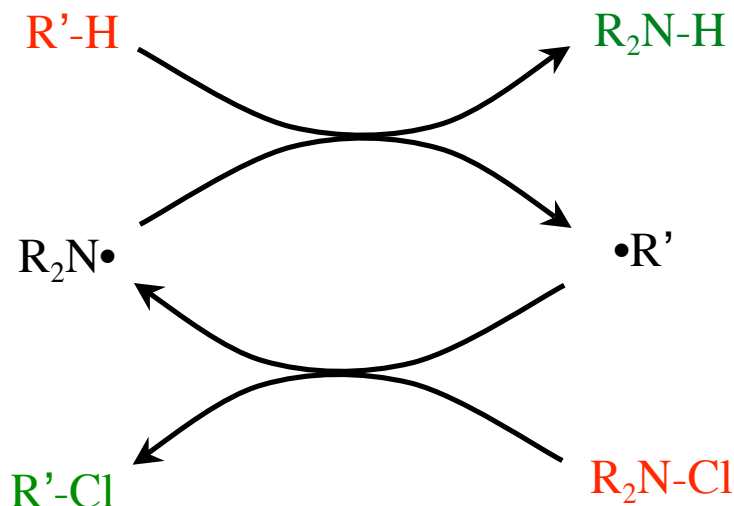
The rate of a radical chain process is proportional to the concentration of radicals (the number of "machines" operating). At steady-state the rate of production of radicals by initiation is equal to their rate of disappearance by termination, which is second-order in radical concentration:

$$\begin{aligned} \text{initiation rate} &= \text{termination rate} \propto [\text{R}\cdot]^2 \\ [\text{R}\cdot] &\propto (\text{initiation rate})^{1/2} \end{aligned}$$

Thus the rate of the chain process is $1/2$ order in the rate of initiation. Doubling the initiation rate would increase the chain rate by a factor of $\sqrt{2} = 1.4$, so about a 50% increase.

Question 3 (cont)

C. (5 min) Write a plausible mechanistic scheme for the chlorination of R'H by R₂NCl.



(These are the propagation steps, we could also include initiation to make radicals and termination to destroy them.)

D. (5 min) One might change the rate of product formation by changing R or R'. Explain whether this rate should be more sensitive to changes in the strength of the R'-Cl bond, or to changes in the strength of the R₂N-H bond.

(1) Hammond Postulate

The first propagation step loses R'-H (100 kcal/mole) and gains R₂N-H (92 kcal/mole). It is 8 kcal uphill in energy, so by the Hammond postulate the transition state should be late and the activation energy should be relatively sensitive to the strength of the R₂N-H bond being formed.

By contrast, the second propagation step loses R₂N-Cl (46 kcal/mole) and gains R'-Cl (85 kcal/mole), and is thus 39 kcal/mole downhill. By the Hammond postulate its transition state should come very early, when the R'-Cl bond has not formed very much. So the rate should be relatively insensitive to changes in the R'-Cl bond strength.

(2) Rate-Limiting Step

Even neglecting the differing sensitivity of rate constants to changes in alkyl groups described above, the rate of such a chain reaction is relatively insensitive to the rate constant of the faster process, because its increase shifts very little of the radical population to the pool waiting for the slower step. (By contrast, increasing the rate constant for the slower step shifts substantial population to the pool awaiting the faster step.)

Again the rate of product formation should be much more sensitive to the rate constant for the slower step.

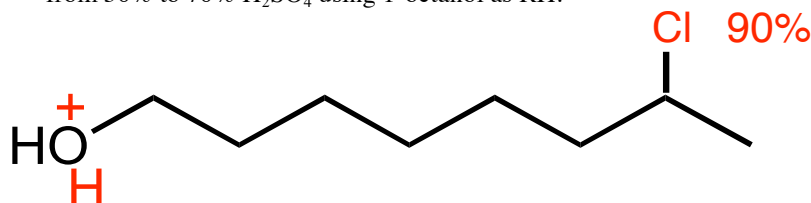
Question 3 (cont)

- E.** (3 min) Explain why the reaction fails unless the solution is made acidic.

The chain reaction fails when the propagation steps are slow compared to the rate of termination. No radicals – no chain reaction. In this case there are many more $R_2N\cdot$ radicals waiting for the slow step than there are $\cdot R'$ radicals waiting for the fast step, so most of the termination involves reaction between two $R_2N\cdot$ radicals (by $H\cdot$ transfer).

Adding acid converts the $R_2N\cdot$ radicals to $R_2HN\cdot^+$ cation radicals, which repel one another electrostatically and are thus much slower to react with one another. This allows the propagation steps to compete successfully with termination

- F.** (5 min) Explain **how and why** the reaction's regioselectivity changes dramatically as the medium is changed from 50% to 70% H_2SO_4 using 1-octanol as RH.



In 50% H_2SO_4 the $R_2HN\cdot^+$ cation radical, as expected, shows very little selectivity in abstracting H from the various secondary C-H bonds along the chain, so that yields of the individual chlorinated isomers range from 10 to 20%.

In 70% H_2SO_4 the OH group of the alcohol becomes very extensively protonated so that the $R_2HN\cdot^+$ cation radical is forced to react with the alcohol in its protonated form. When the two cations are forced to react with one another, the centers of positive charge stay as far as possible, so the last secondary C-H group in the alcohol is attacked 90% of the time to give the product shown.

- G.** (3 min) Why should the BDEs of N-Cl and R-Cl be so different, when those for N-H and R-H are so similar?

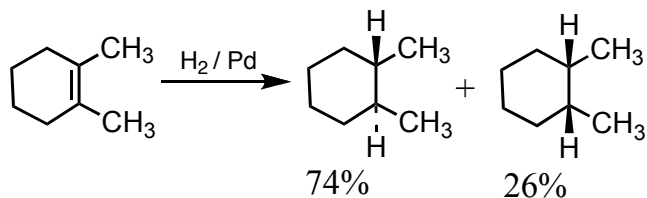
Like the O-O bond, the N-Cl bond is weakened by mixing between lone pairs of the two atoms. Also there is better energy match between N and Cl than between C and Cl. For comparable overlap, BDEs are increased by poor energy match (*cf.* the high strength of the H-F bond).

Several people mentioned bonds being strengthened by electronegativity (EN) difference between the bonded atoms. This constitutes an interesting tautology, because in 1932 Pauling **defined** his scale of EN such that the difference between EN of two atoms X and Y would be the difference between the BDE of XY and the average of the BDEs of XX and YY.* His idea was that X-Y should be stabilized by "resonance" with the ionic structure $X^+ Y^-$.

The physical **reason** that X-Y is strengthened is because of poor energy match. Saying that strengthening is due to a difference in EN confuses cause with effect.

.*) Actually he used the square root of the BDE difference $XY - \frac{1}{2}(XX + YY)$.

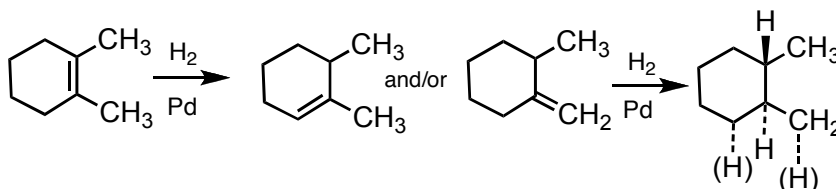
4. (8 min) What is surprising about the yields of isomeric products from this catalytic hydrogenation?



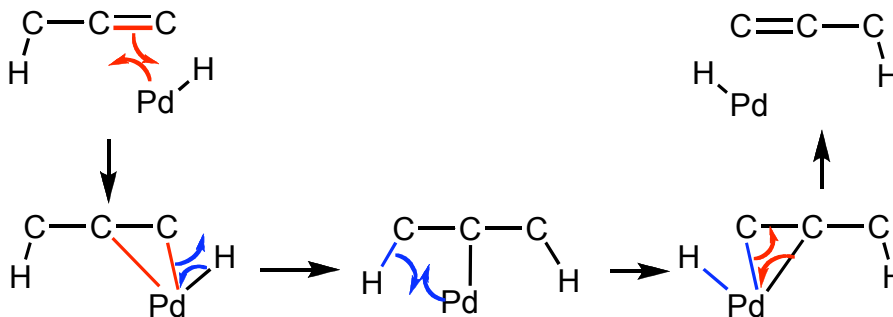
Catalytic hydrogenation of alkenes is usually said to give *syn* addition. In this case most of the product has the new hydrogen atoms *trans* to one another, apparently the result of *anti* addition.

Draw several key mechanistic steps with curved arrows to explain the yields. (You may abbreviate the structure to simplify your drawings.)

If the alkene undergoes “allylic rearrangement”, it gives an isomer that would give the “*trans* product” by normal *syn* addition.



Mechanism of allylic rearrangement by Pd insertion (or reverse) into π bond (red) and into σ bond (blue):



ALSO suggest an experiment with a different starting material to test your explanation.

If the *trans*-1,2-dimethylcyclohexane results from initial isomerization of the 1,2-dimethylcyclohexene to 1,6-dimethylcyclohexene or 1-methyl-2-methylenecyclohexane, then hydrogenation of these proposed intermediates should give (at least) as much of the *trans*-product as observed above (depending on whether any of the product is formed by direct *syn* addition without intervention of the proposed intermediate).

[Another good test is to add D_2 and show that it enters non-tertiary positions.]

In fact Nishimura, Sakimoto, and Ozawa also reported the yields shown at the right. (*Chemistry Letters*, **1979**, 855-858)

Although they reported their yields to tenths of %, their experimental accuracy was almost surely much lower, so that they seem consistent with the above isomerization mechanism.

With other metal catalysts they found much less of the surprising *trans* product: Pt (21%), Rh (12%), Ru (7%), Ir (0.8%). Pd is a bad actor.

