Course Chem 345 Lecturer Gellman

Day Mon. Date 2/9/15

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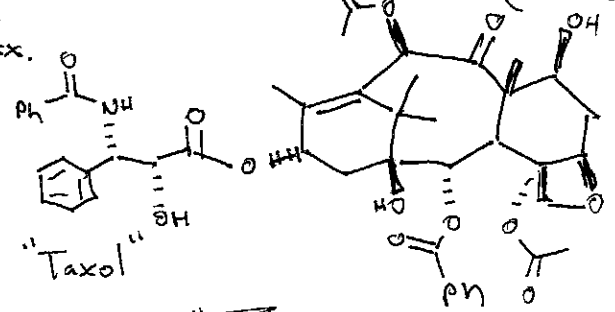
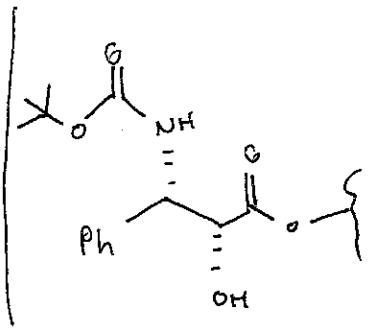
What do chemists do? (Pt. 2) → "Natural Product Discovery / New Drugs"

Ex.

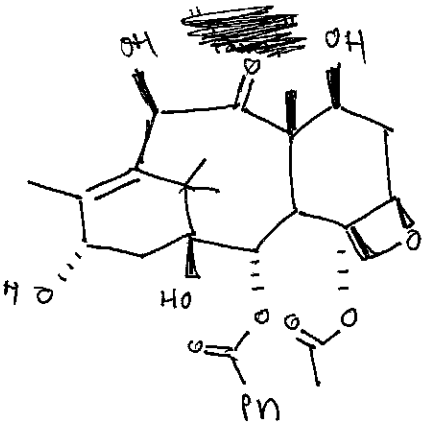


"Taxol"



"Taxotere"

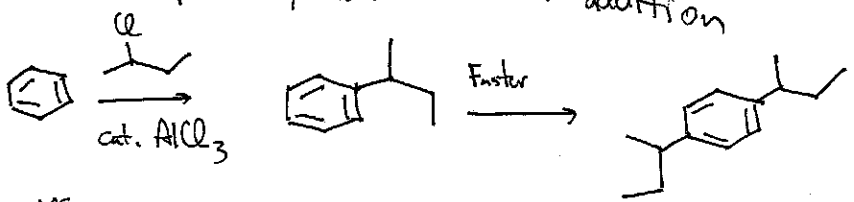
("precursor")



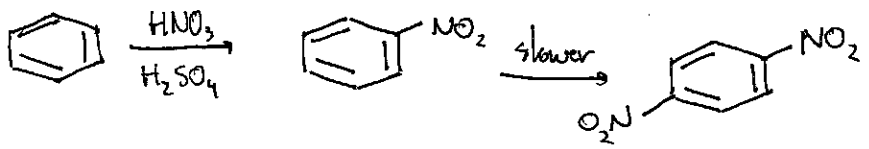
(Gif-sur-Yvette)

Recall: EAS...

Cannot stop alkylation after 1st addition



vs.



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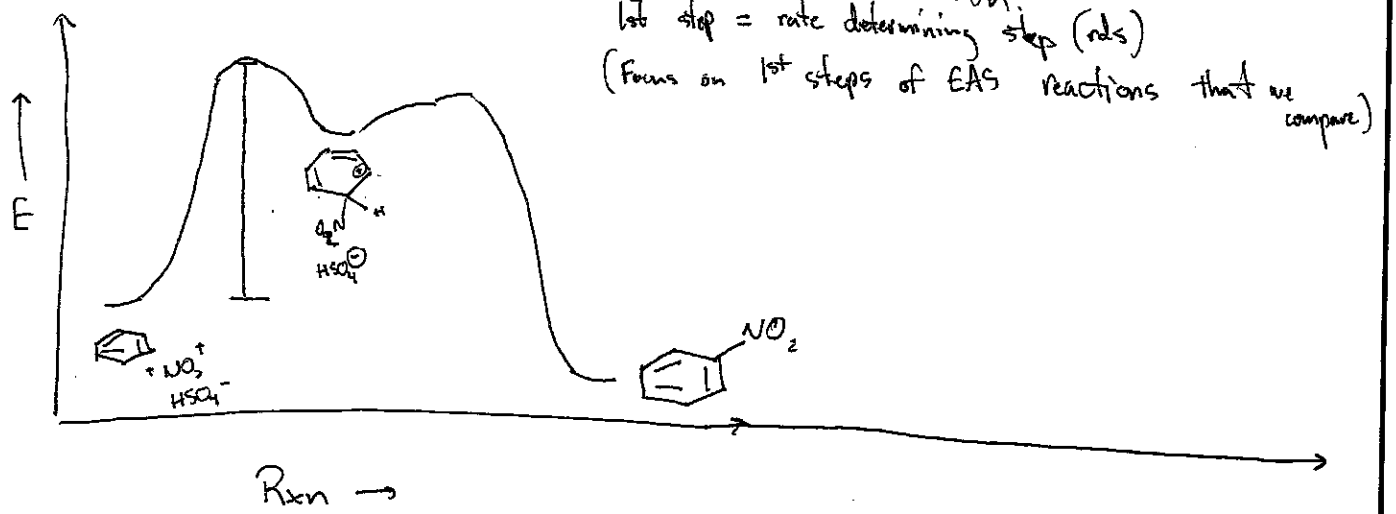
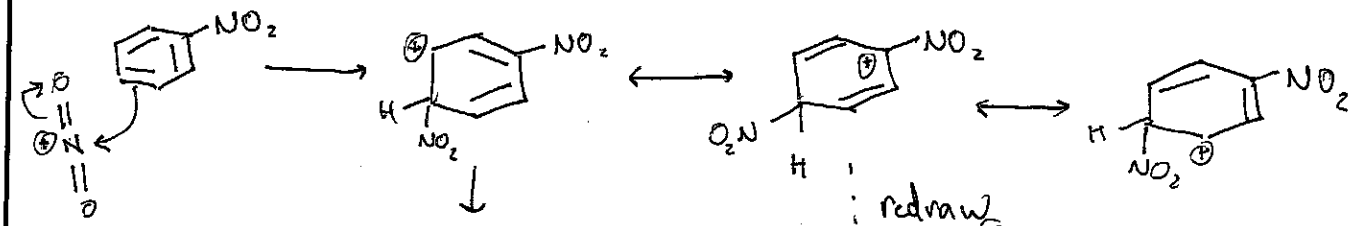
- Why is an alkyl group activating (w.r.t. EAS), while nitro is deactivating?

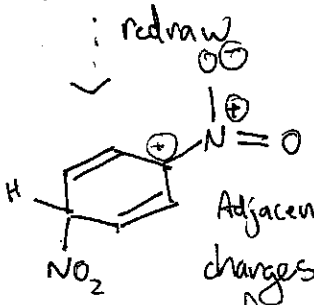
Begin analysis w/ rxn energy diagram for nitration.
1st step = rate determining step (rds)
(Focus on 1st steps of EAS reactions that we compare)



Thus:



redraw



Adjacent ⊕ charges very unfavorable!

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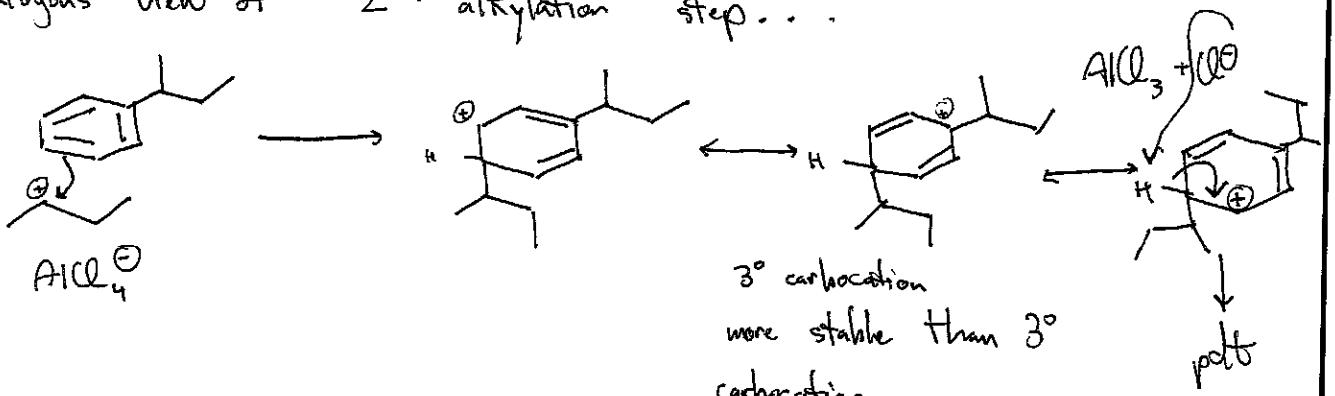
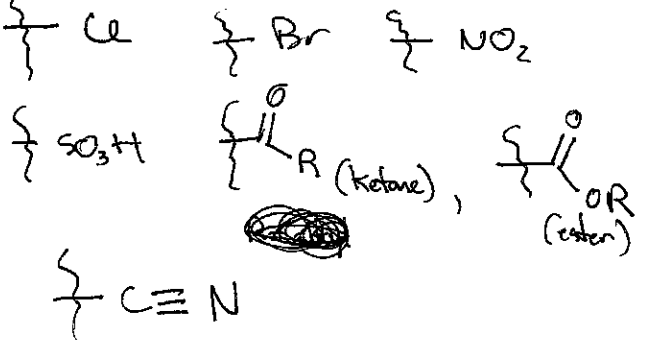
Thus, NO_2 on ring for nitration is "worse" than H, i.e., NO_2 is deactivating.

Analogous view of 2nd alkylation step...



Following this analysis, any ring substituent can be classified as either activating or deactivating wrt EAS reactions. Common deactivating substituents:



These are all "electron-withdrawing" substituents. In contrast, "electron-donating" substituents are activating for EAS rxns. Common ex: alkyl, OH, OR, NR_2

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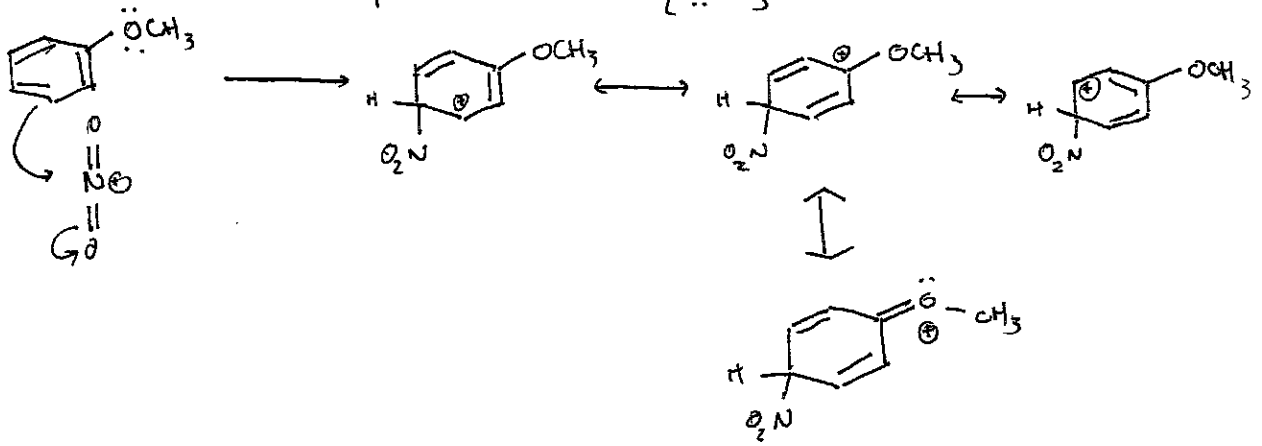
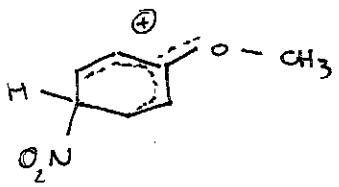
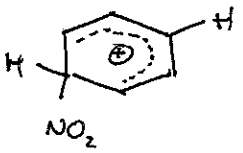
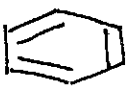
Rationale for a specific case, $\{\ddot{O}CH_3$



- extra resonance structure (rel. to other cases, esp. "H")
- extra resonce structure is very. favorable

Thus,  is more stable than 

∴  more reactive (EAS) than 

See text regarding halogens. - different outcomes for inductive vs. π-type electronic effects.