

Lecture 27

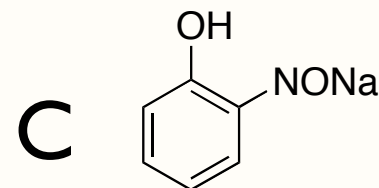
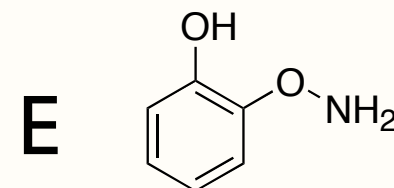
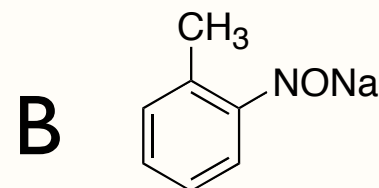
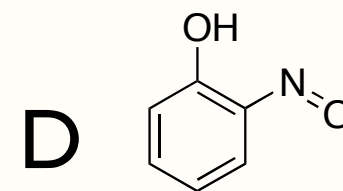
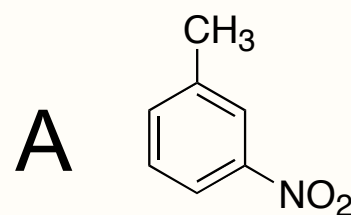
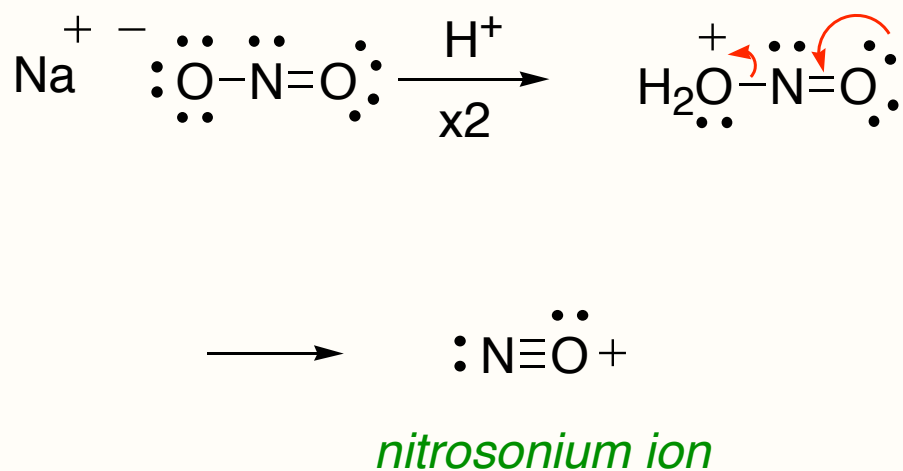
Organic Chemistry 1

Professor Duncan Wardrop

April 20, 2010

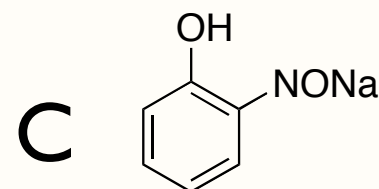
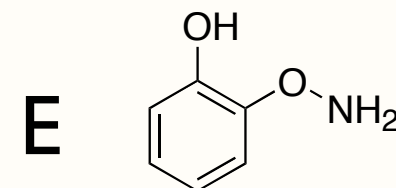
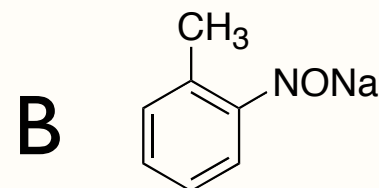
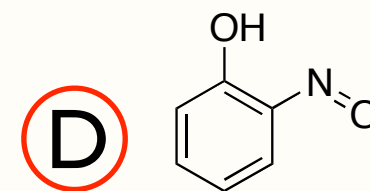
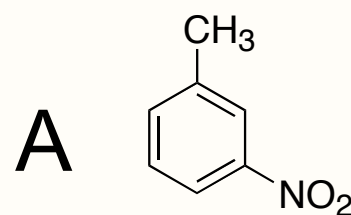
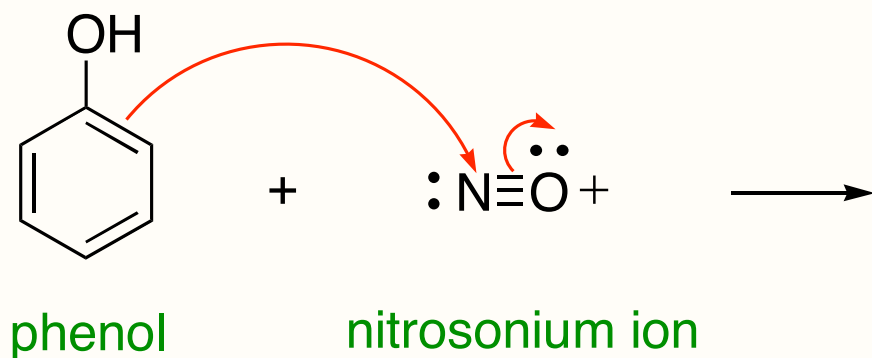
Self Test Question

Nitrosonium (not nitronium) cations can be generated by treating sodium nitrite (NaNO_2) with a strong acid. This relatively weak electrophile can undergo $\text{S}_{\text{E}}\text{Ar}$ with phenol. What is the *major* product when phenol reacts with a nitrosonium ion?



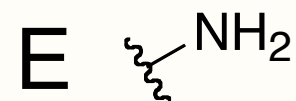
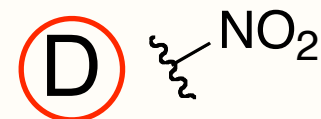
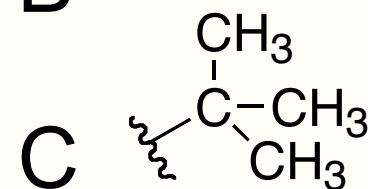
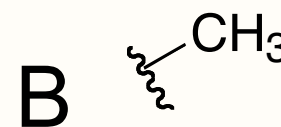
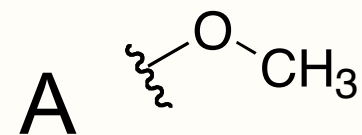
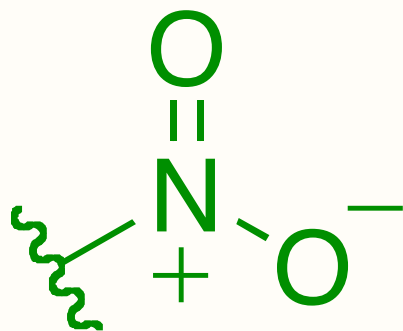
Self Test Question

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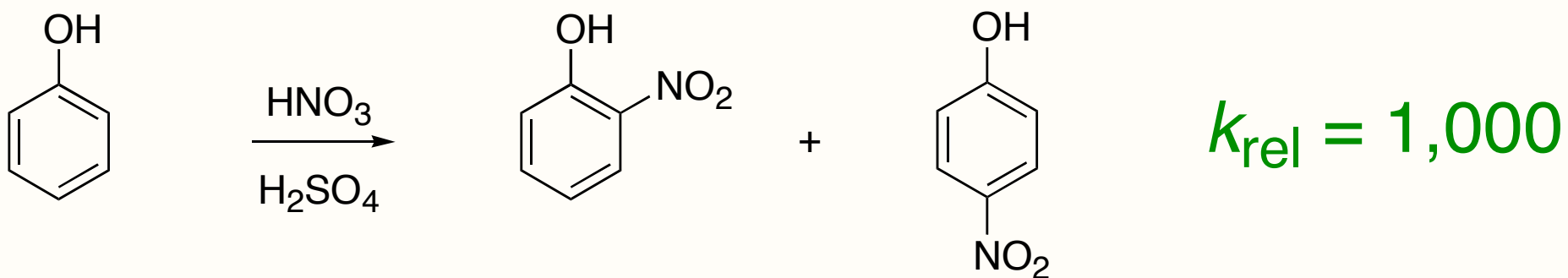
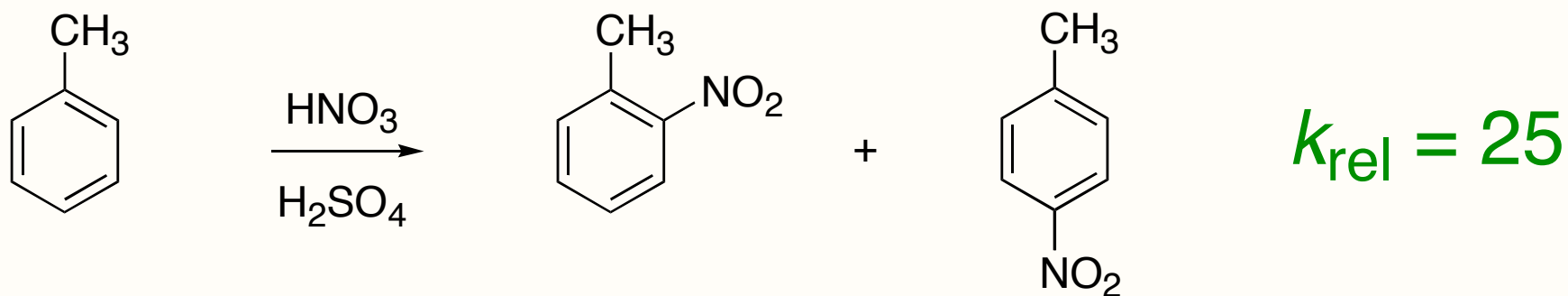
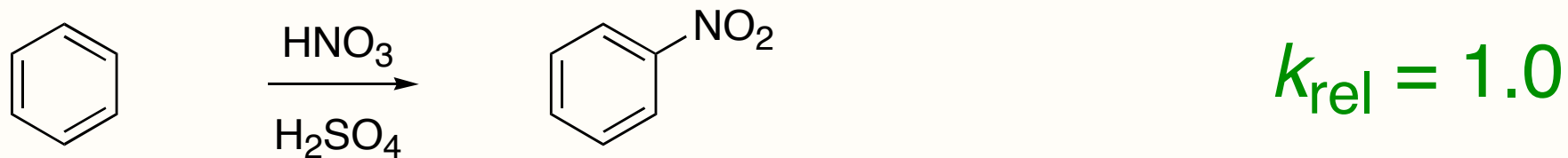


Self Test Question

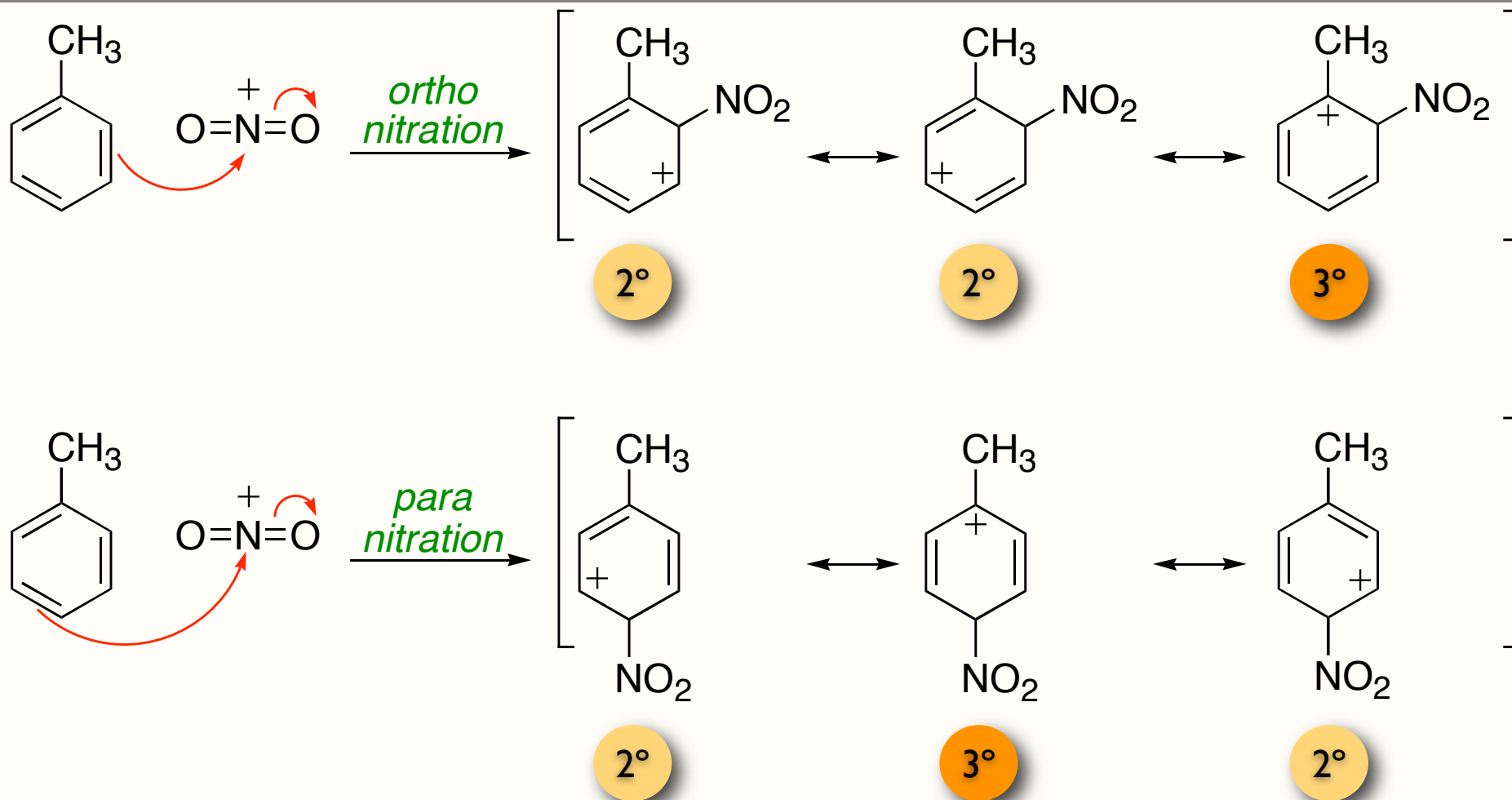
Which substituent would *not* activate an aromatic ring toward S_EAr (i.e. is not an electron donating group)?



Strongly Activating Substituents

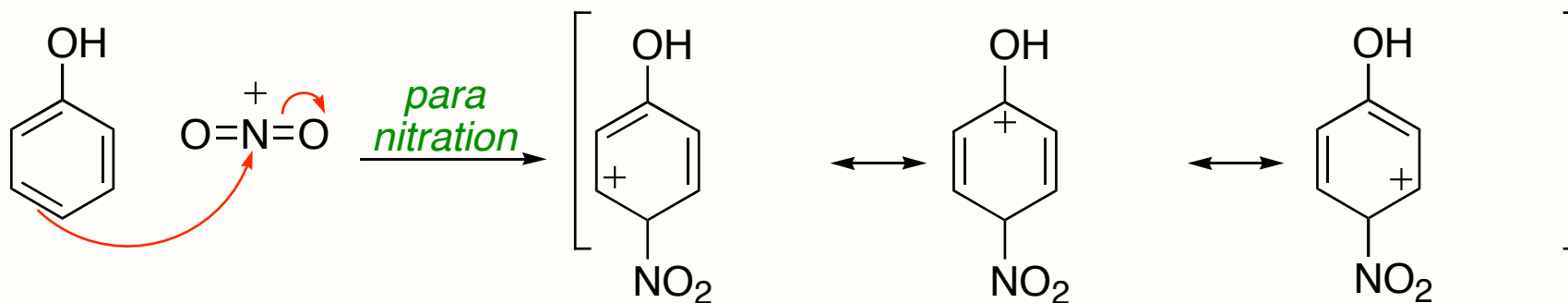
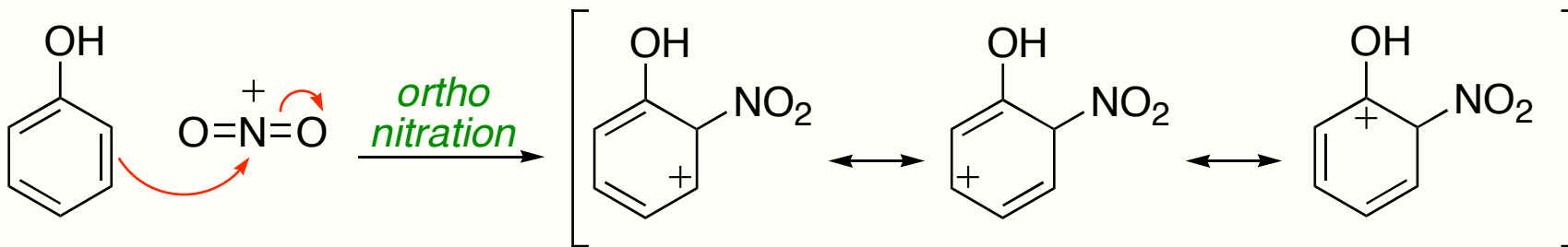


Review: Alkyl Groups are Activating and *Ortho/Para* Directing



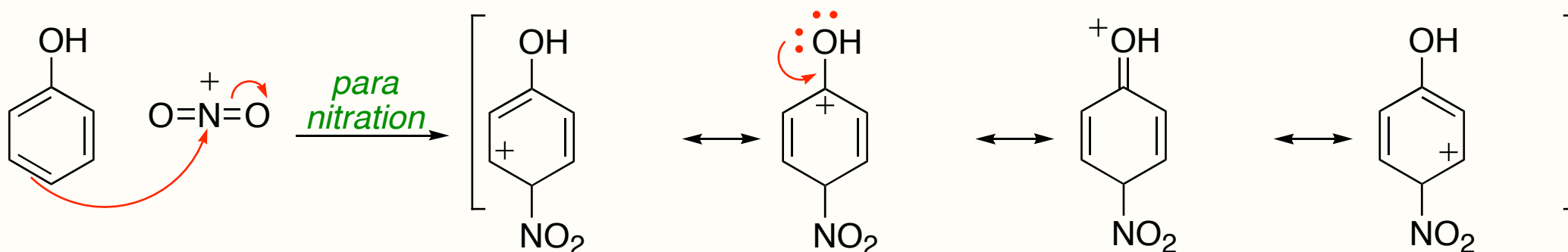
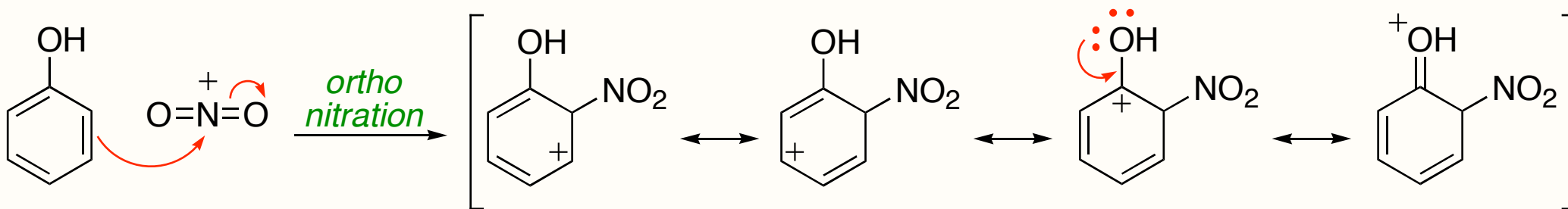
Both *ortho* nitration and *para* nitration provide an arenium ion with a 3° carbocation contributor.

Strongly Activating Substituents



Why is a hydroxyl group (-OH) more electron donating and thus more activating than a methyl group?

Strongly Activating Substituents



Additional resonance structure for *ortho* & *para* $\text{S}_{\text{E}}\text{Ar}$ when substituent has a lone pair of electrons = more stable arenium ion = faster $\text{S}_{\text{E}}\text{Ar}$ (more activated)

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

Activating

Standard = H

Deactivating

Strongly Deactivating

Very strongly deactivating

Activating:
greater electron donation =
more stable arenium ion =
faster S_EAr

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

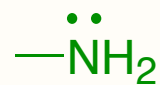
Activating

Standard = H

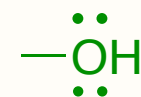
Deactivating

Strongly Deactivating

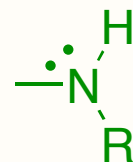
Very strongly deactivating



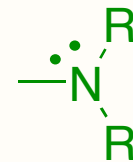
1° amine
(amino)



alcohol
(hydroxyl)



2° amine
(alkylamino)



3° amine
(dialkylamino)

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

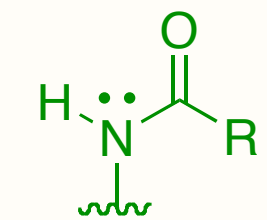
Activating

Standard = H

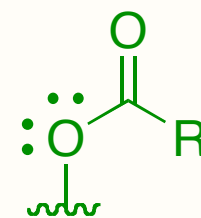
Deactivating

Strongly Deactivating

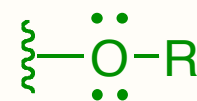
Very strongly deactivating



amide
(acylamino)



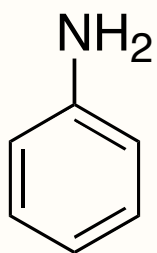
ester
(acyloxy)



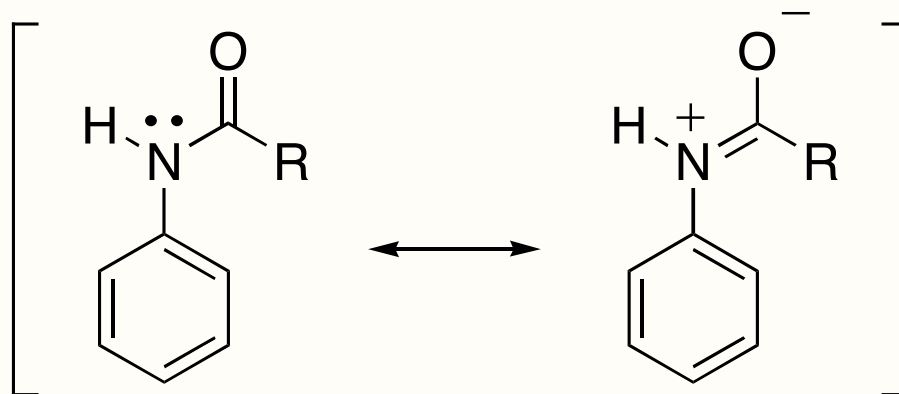
ether
(alkoxy)

Degree of Electron Donation

The acyl group on nitrogen increases the delocalization of the lone pair of electrons, thus decreasing its ability to be donated to the aromatic ring.



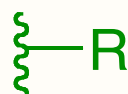
vs.



Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

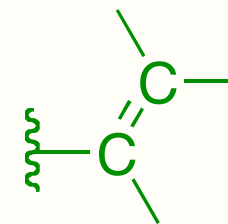
Very strongly activating
Strongly activating
Activating
Standard = H
Deactivating
Strongly Deactivating
Very strongly deactivating



alkane
(alkyl)



aromatic
(aryl)



alkene
(alkenyl)

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

Activating

Standard = H

Deactivating

Strongly Deactivating

Very strongly deactivating

All are also *ortho/para* directors

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

Activating

Standard = H

Deactivating

Strongly Deactivating

Very strongly deactivating

Deactivating
greater electron withdrawal =
less stable arenium ion =
slower S_EAr

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

Activating

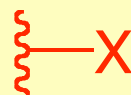
Standard = H

Deactivating

Strongly Deactivating

Very strongly deactivating

ortho/para directors

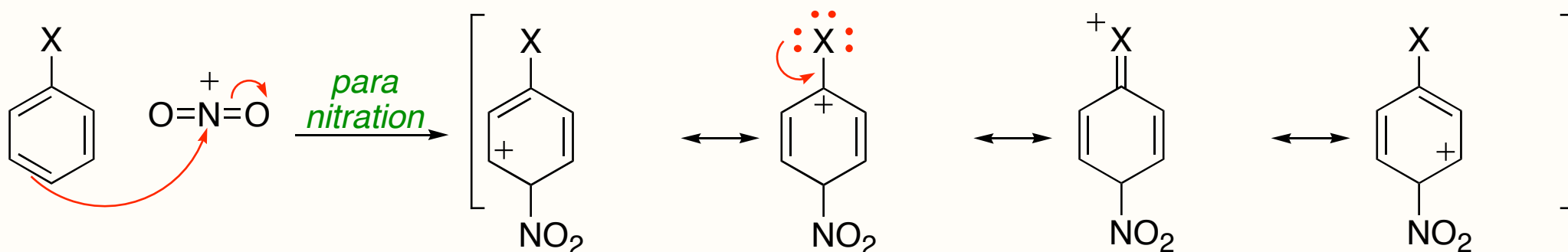
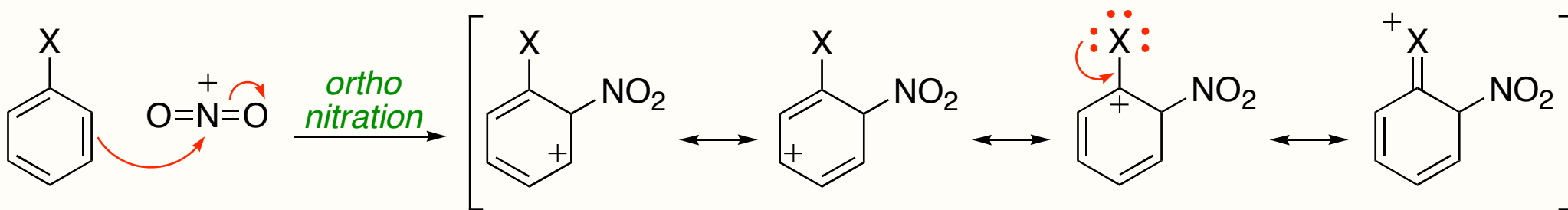


halogen
(halo)



halomethyl

Summary of Reactivity & Directing Effects



Although halogens deactivate aromatic rings through inductive effect, they are still *ortho/para* directors since they have lone pairs.

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

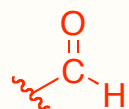
Activating

Standard = H

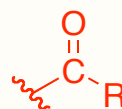
Deactivating

Strongly Deactivating

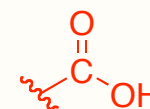
Very strongly deactivating



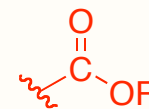
aldehyde
(formyl)



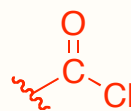
ketone
(acyl)



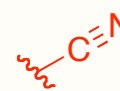
carboxylic acid
(carboxyl)



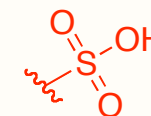
ester
(alkyl carboxylate)



acid chloride
(acyl chloride)



nitrile
(cyano)



sulfonic acid
(sulfonyl)

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

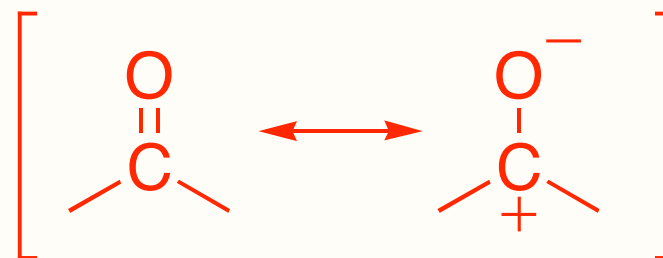
Activating

Standard = H

Deactivating

Strongly Deactivating

Very strongly deactivating



Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

Very strongly activating

Strongly activating

Activating

Standard = H

Deactivating

Strongly Deactivating

Very strongly deactivating



trifluoromethyl



nitro

Summary of Reactivity & Directing Effects

Classification of Substituents in Electrophilic Aromatic Substitution (S_EAr)

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Strongly activating

Activating

Standard = H

Deactivating

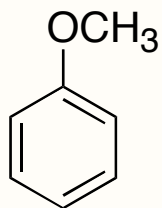
Strongly Deactivating

Very strongly deactivating

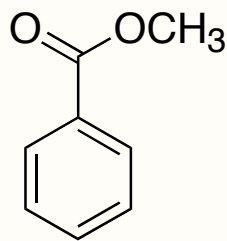
All are also *meta* directors

Self Test Question

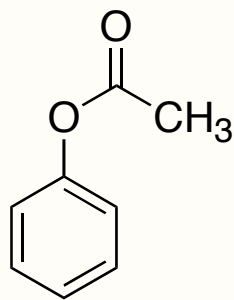
List the aromatic compounds below in order of *increasing* rate of S_EAr .



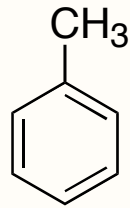
a



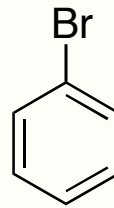
b



c



d



e

A. a,b,c,d,e

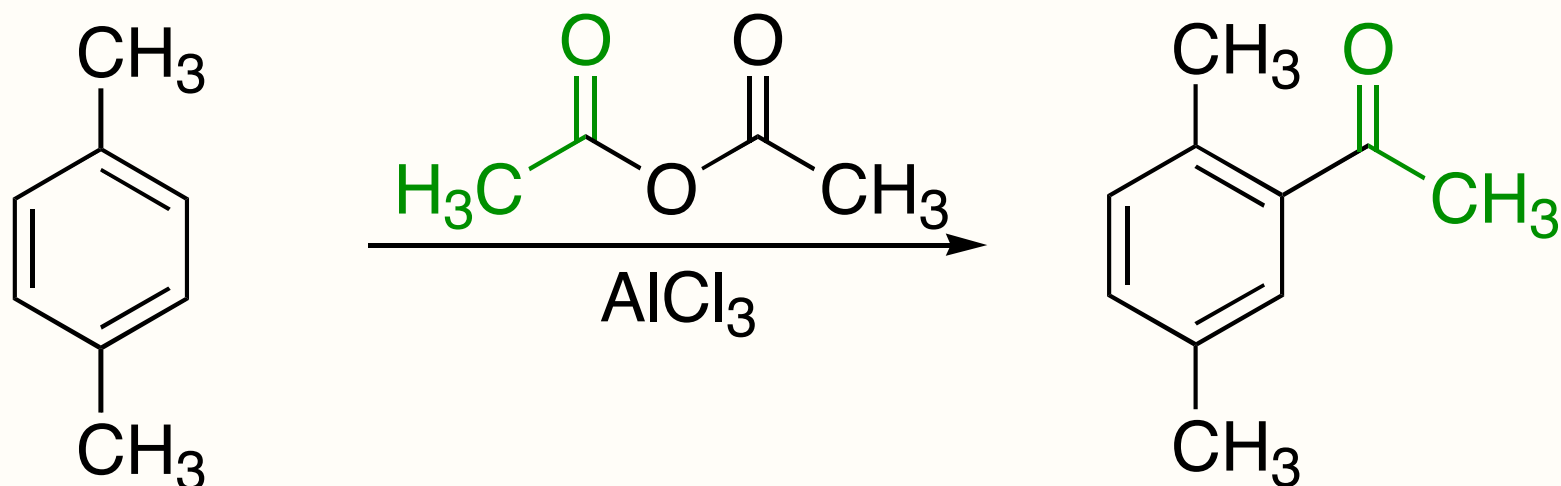
B. e,d,c,b,a

C. b,e,d,c,a

D. d,e,c,b,a

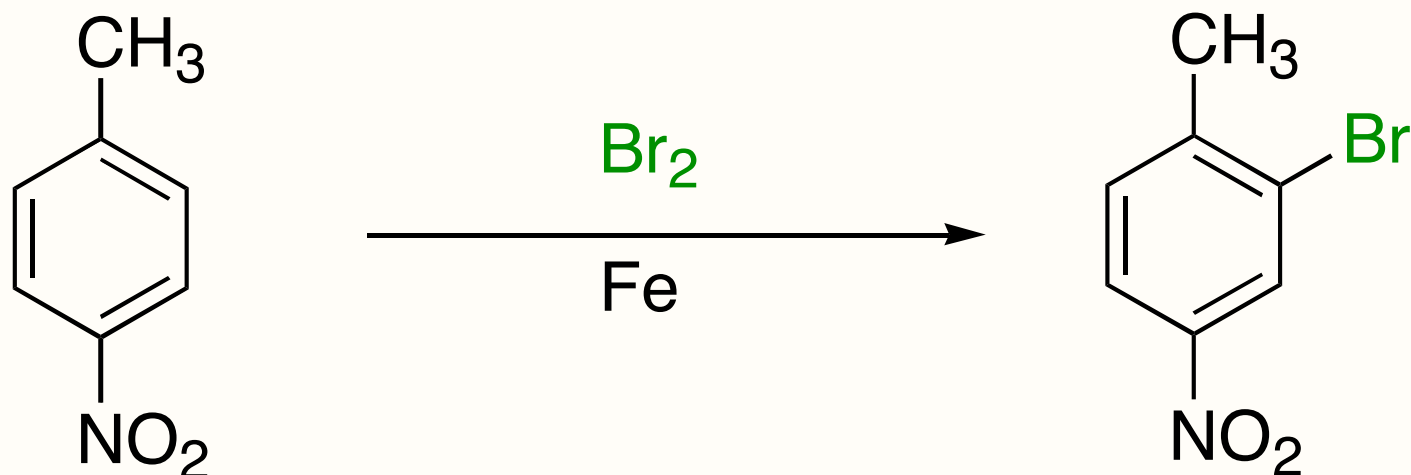
E. c,a,b,d,e

Multiple Substituent Effects



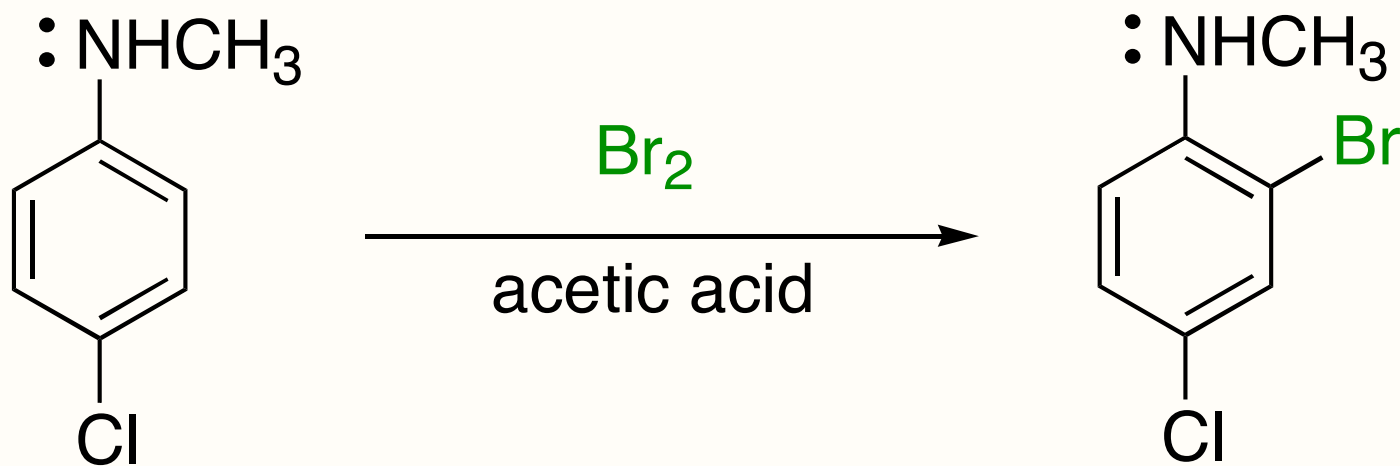
All positions on the aromatic ring are equivalent.

Multiple Substituent Effects



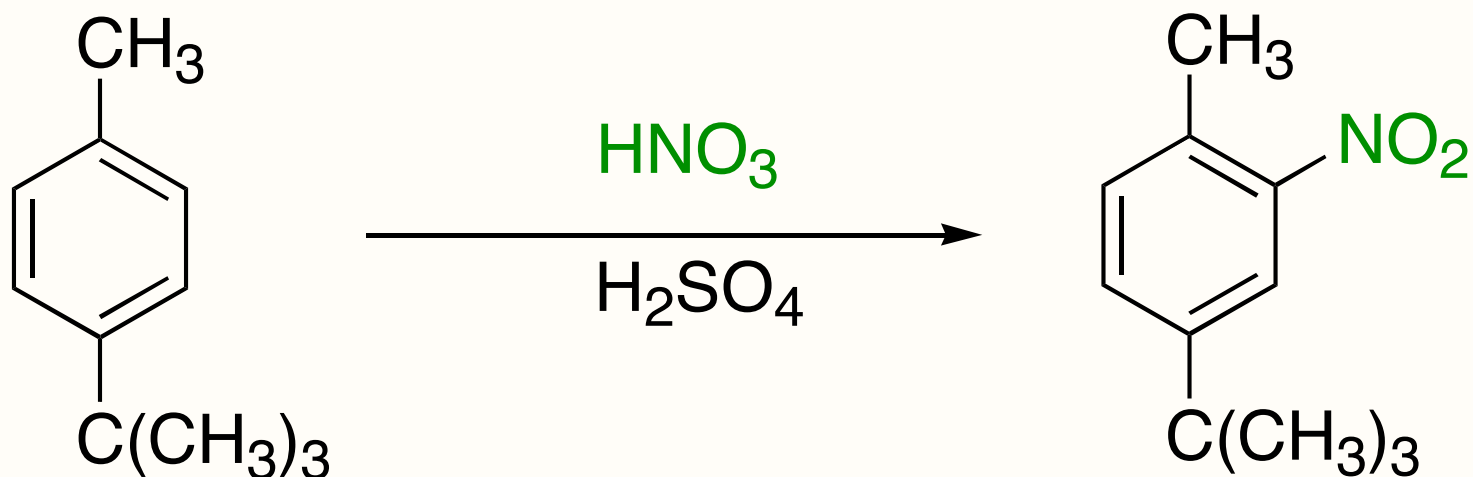
Directing effects reinforce each other; substitution here takes place *ortho* to the methyl group and *meta* to the nitro group.

Multiple Substituent Effects



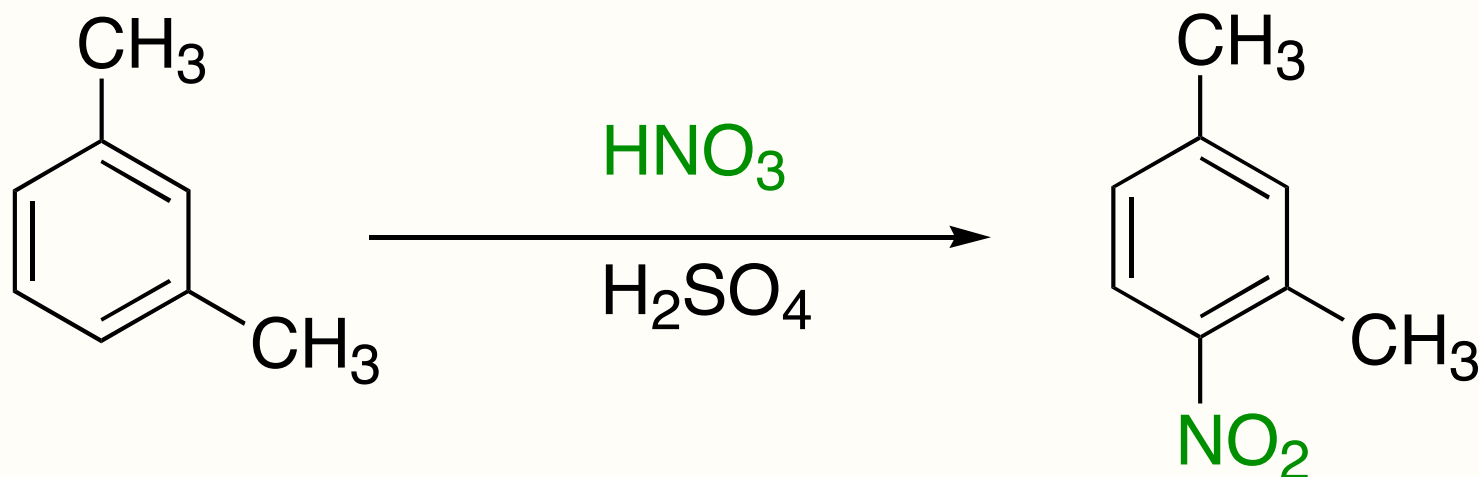
Regioselectivity is controlled by most activating substituent.

Multiple Substituent Effects



When activating effects are similar, substitution occurs *ortho* to smallest substituent (least sterics)

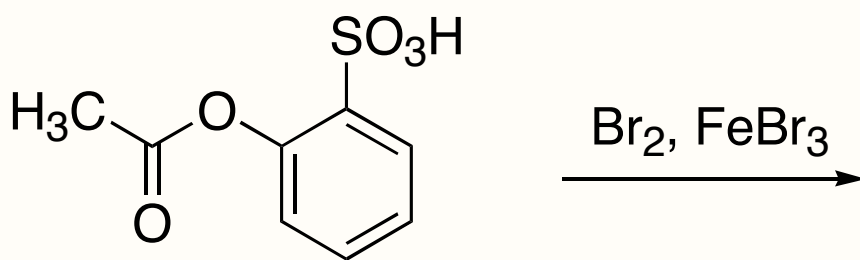
Multiple Substituent Effects



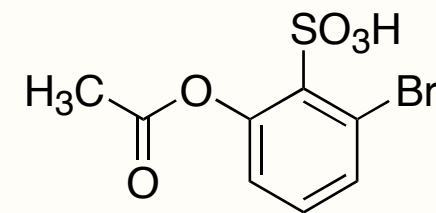
When electronic effects are similar/same, steric effects control regioselectivity; here substitution occurs at least sterically hindered *ortho* position.

Self Test Question

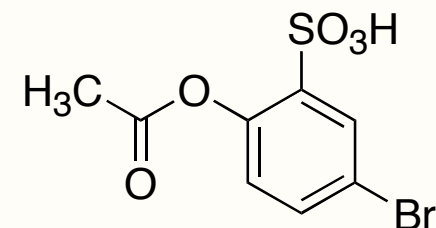
Predict the
major product.



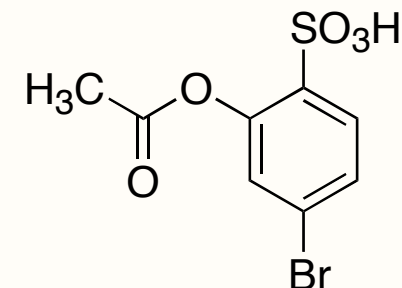
A



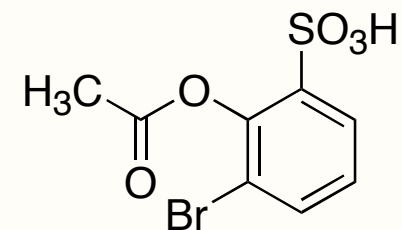
B



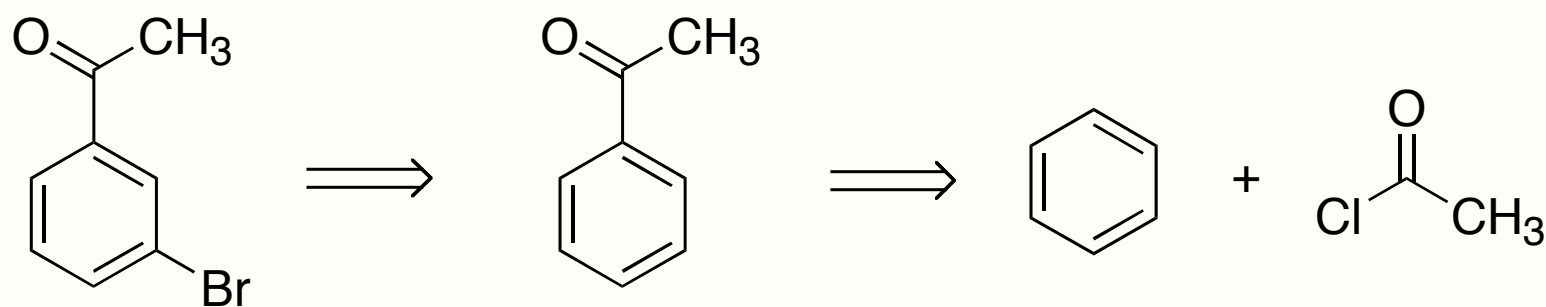
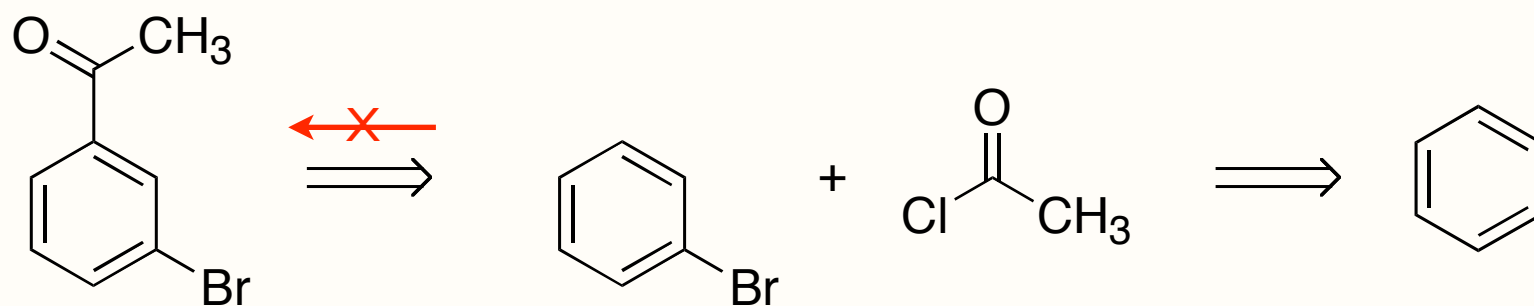
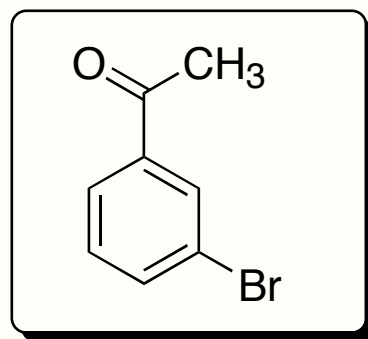
C



D

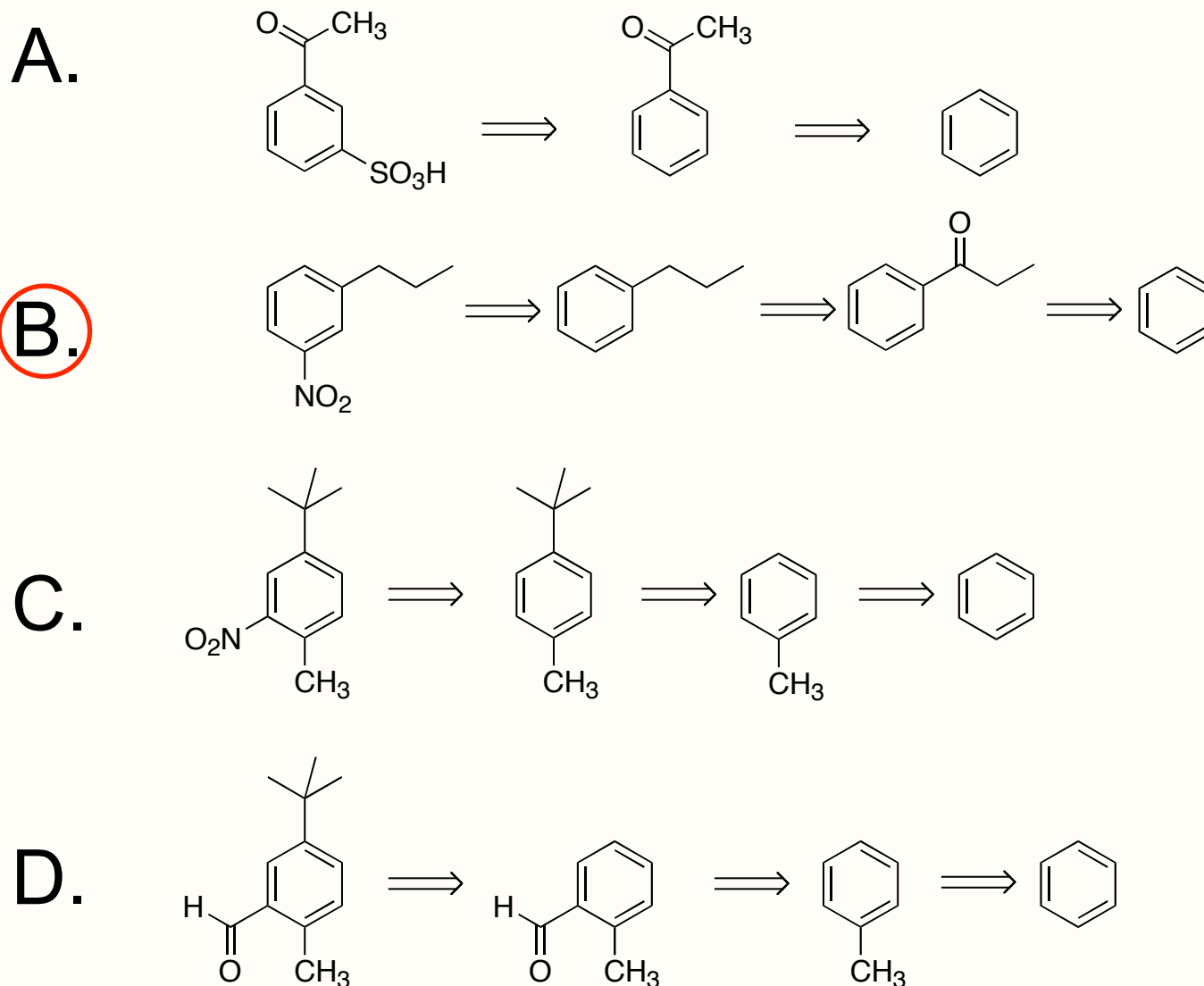


S_EAr in Synthesis



Self Test Question

Which retrosynthesis is *not* feasible?



Quiz This Week. . .

Synthesis Problem

Chapters 11 & 12