12.9

Rate and Regioselectivity in Electrophilic Aromatic Substitution

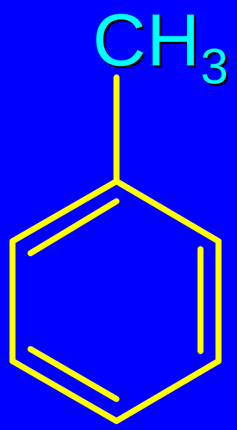
A substituent already present on the ring can affect both the *rate* and *regioselectivity* of electrophilic aromatic substitution.

Effect on Rate

Activating substituents increase the rate of EAS compared to that of benzene.

Deactivating substituents decrease the rate of EAS compared to benzene.

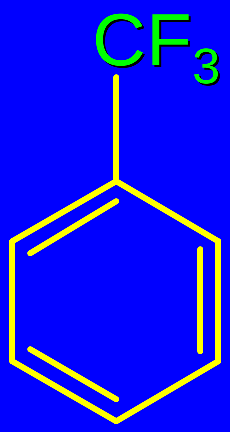
Methyl Group



Toluene undergoes nitration 20-25 times faster than benzene.

A methyl group is an activating substituent.

Trifluoromethyl Group



(Trifluoromethyl)benzene undergoes nitration 40,000 times more slowly than benzene .

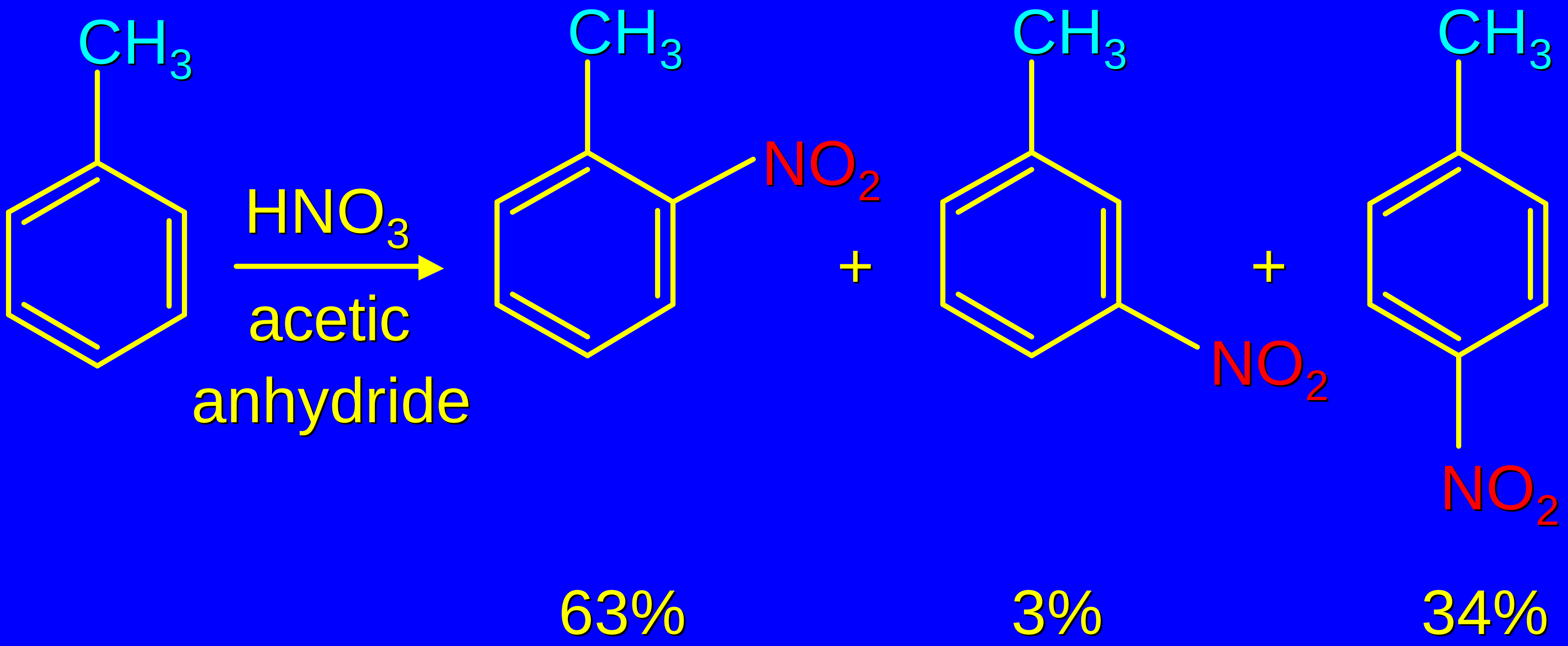
A trifluoromethyl group is a deactivating substituent.

Effect on Regioselectivity

Ortho-para directors direct an incoming electrophile to positions ortho and/or para to themselves.

Meta directors direct an incoming electrophile to positions meta to themselves.

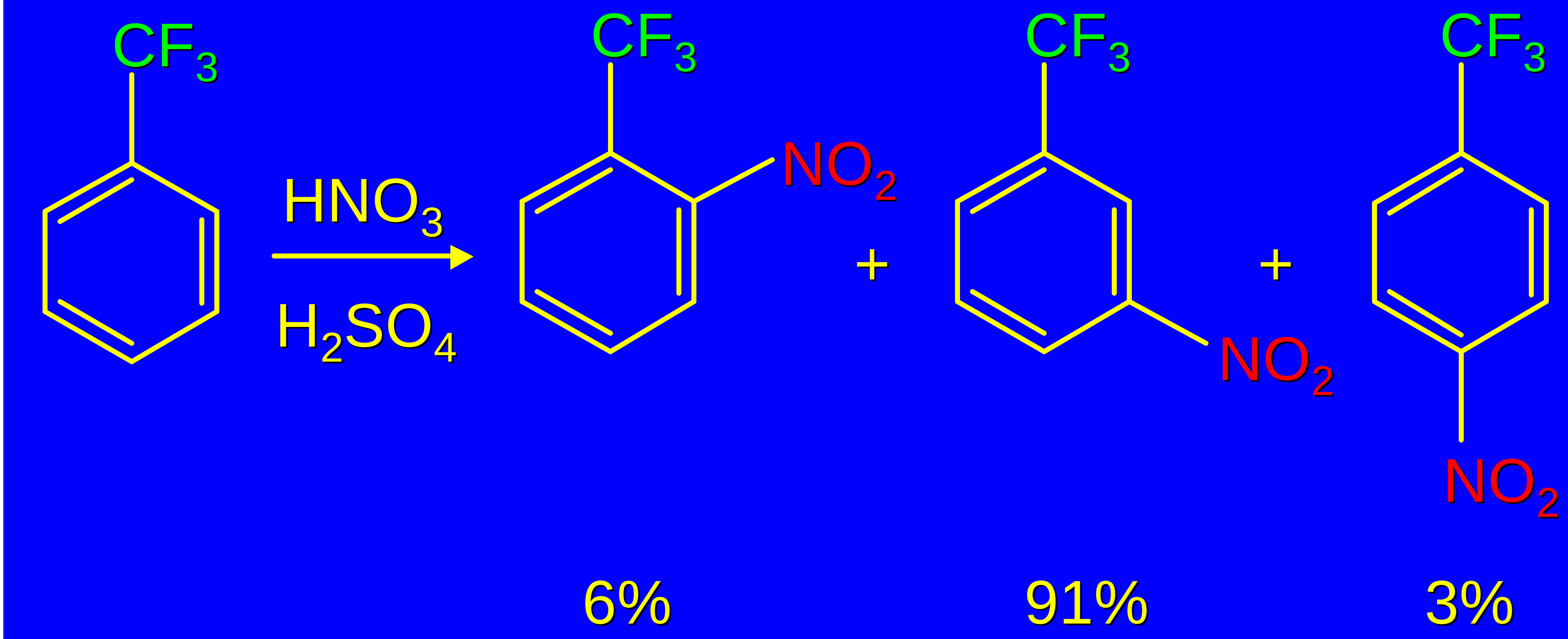
Nitration of Toluene



o- and *p*-nitrotoluene together comprise 97% of the product

a methyl group is an ortho-para director

Nitration of (Trifluoromethyl)benzene



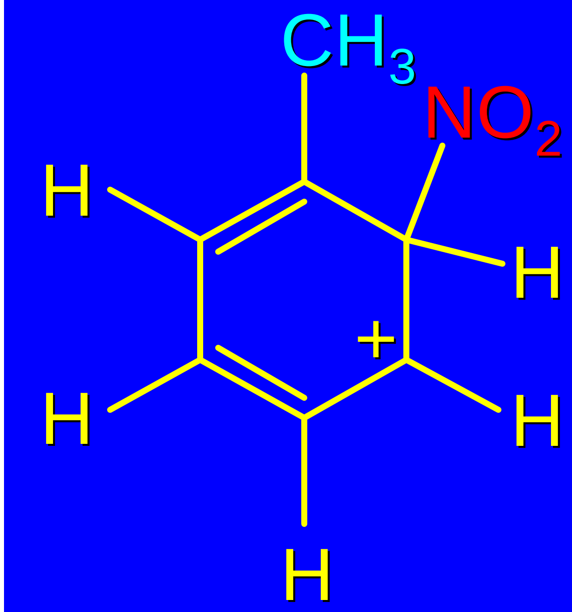
m-nitro(trifluoromethyl)benzene comprises 91% of the product

a trifluoromethyl group is a meta director

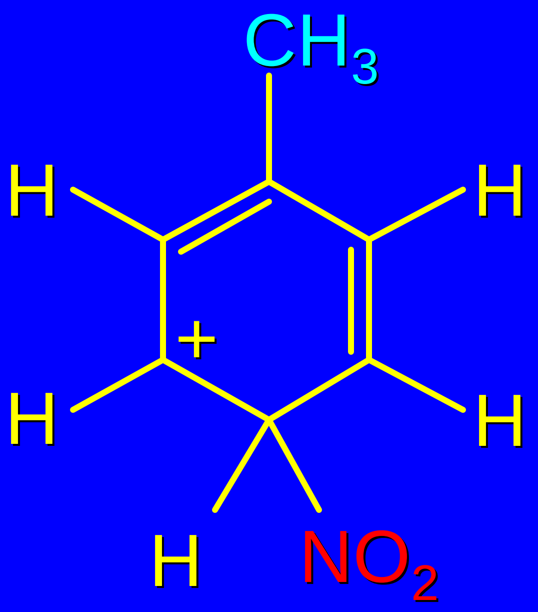
12.10

Rate and Regioselectivity in the Nitration of Toluene

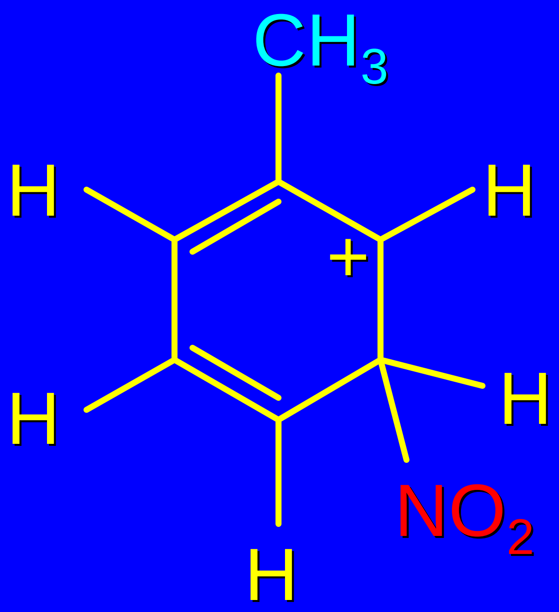
Carbocation Stability Controls Regioselectivity



gives ortho

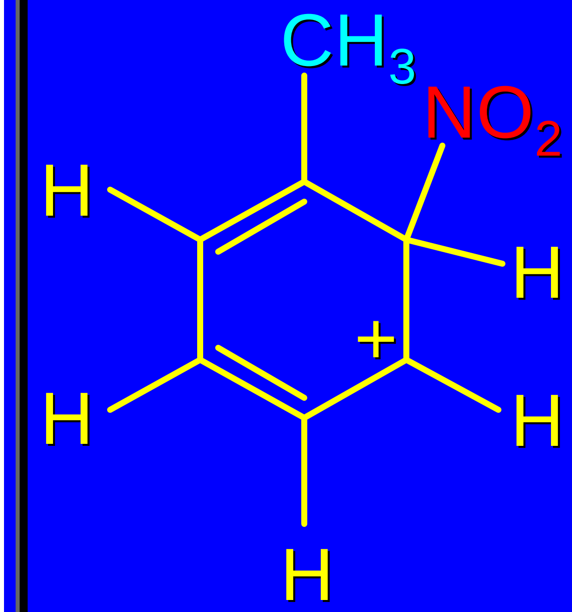


gives para

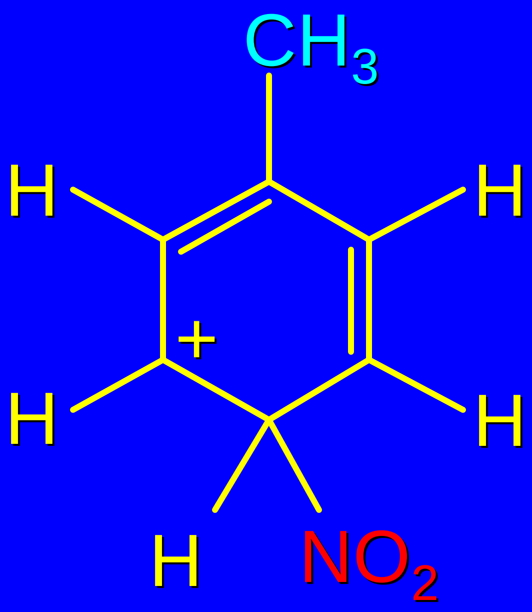


gives meta

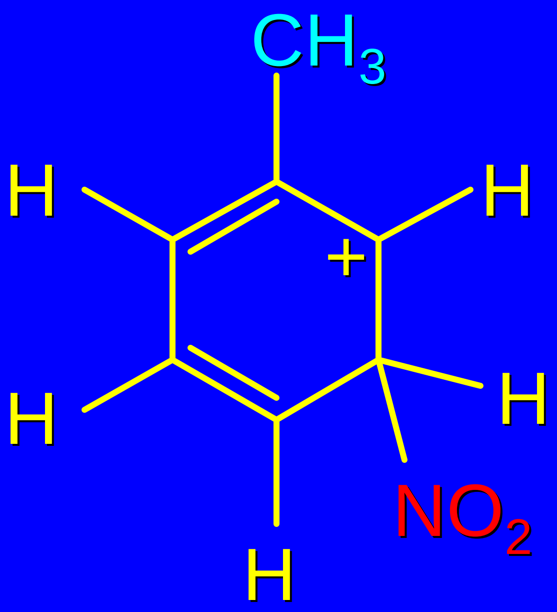
Carbocation Stability Controls Regioselectivity



gives ortho



gives para

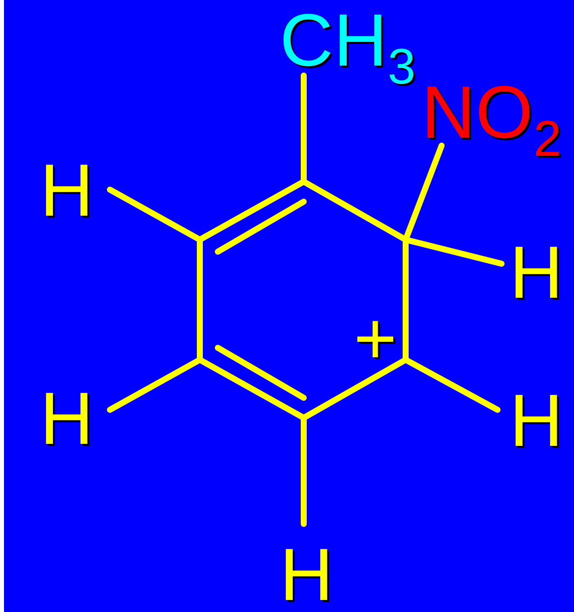


gives meta

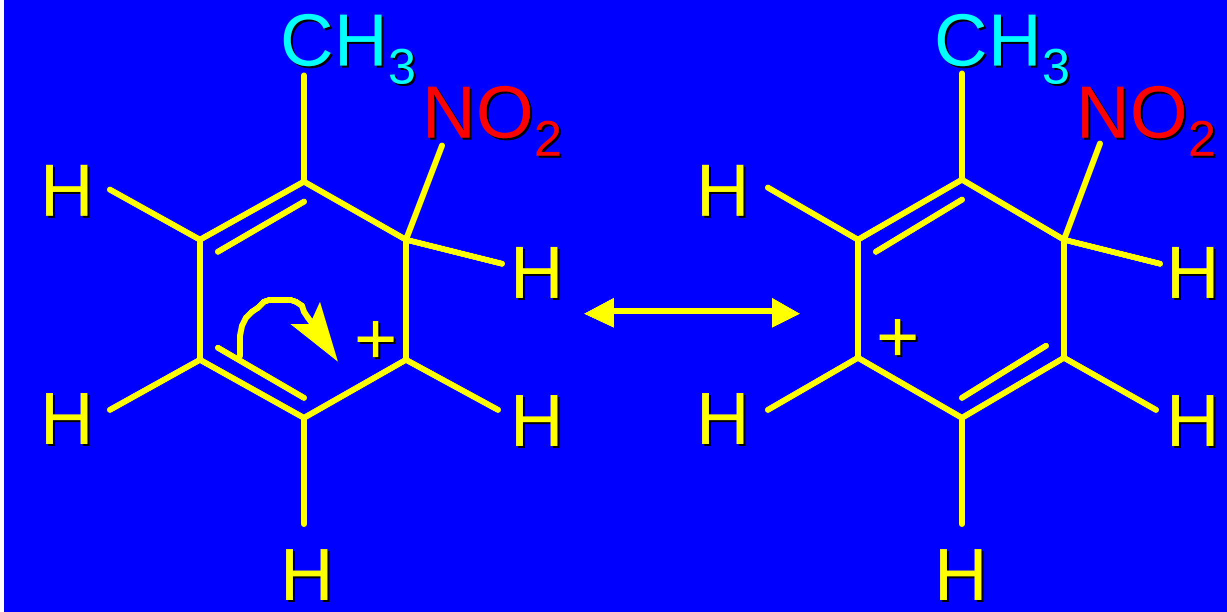
more stable

less stable

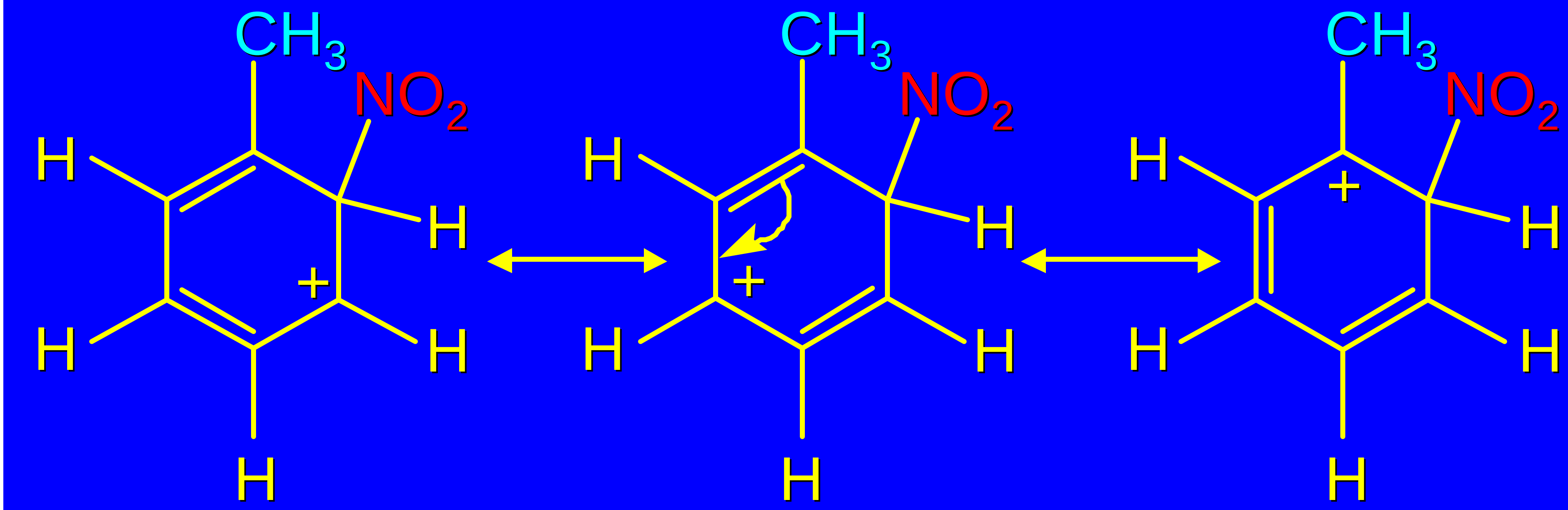
ortho Nitration of Toluene



ortho Nitration of Toluene

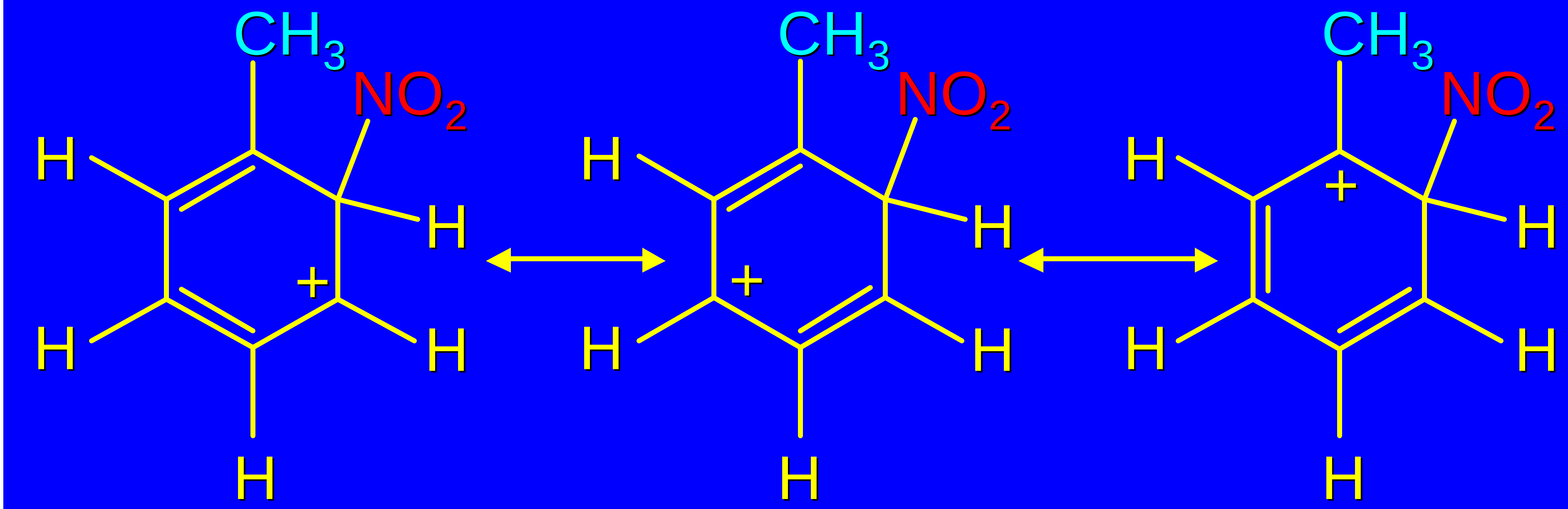


ortho Nitration of Toluene



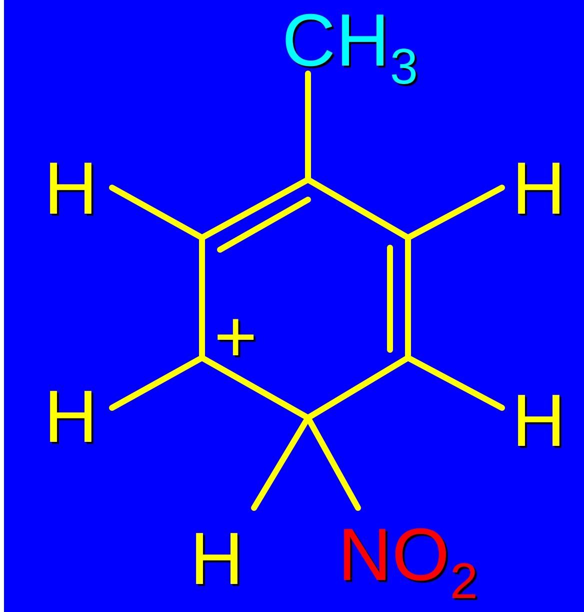
this resonance
form is a
tertiary
carbocation

ortho Nitration of Toluene

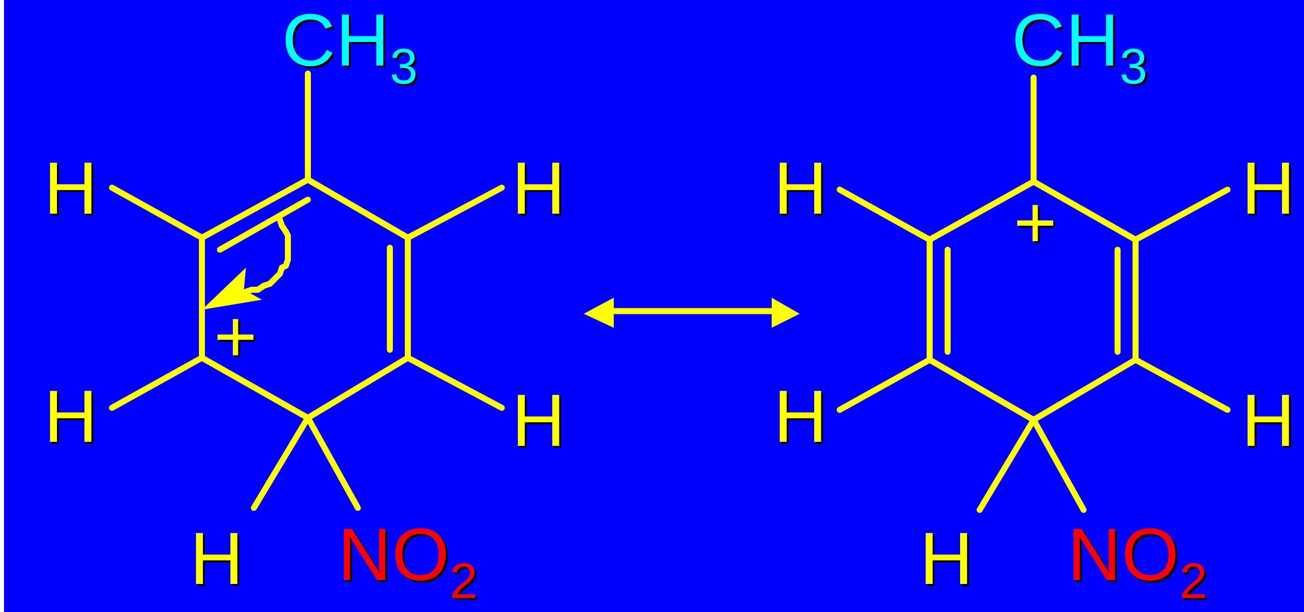


the rate-determining intermediate in the ortho nitration of toluene has tertiary carbocation character

para Nitration of Toluene

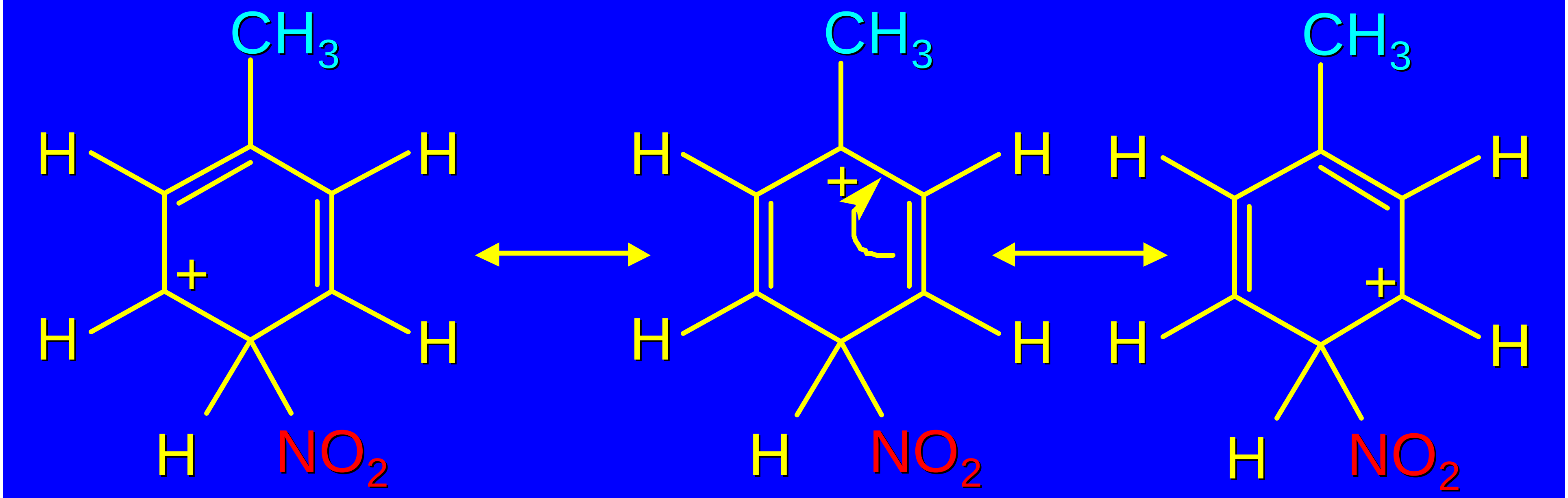


para Nitration of Toluene



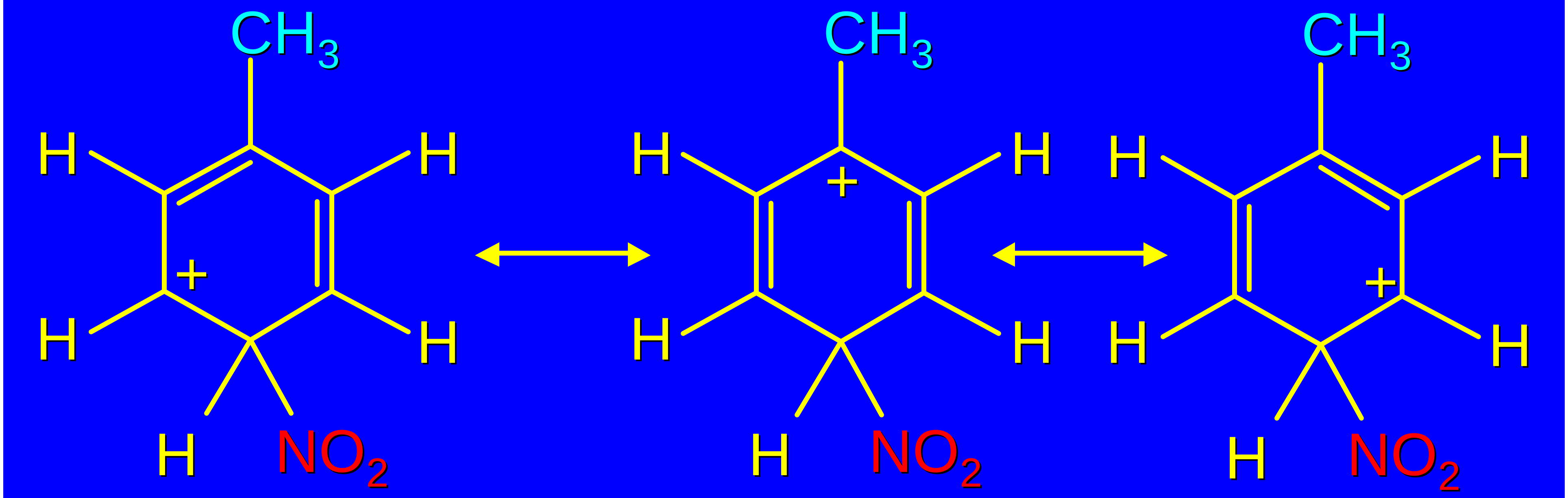
this resonance
form is a tertiary
carbocation

para Nitration of Toluene



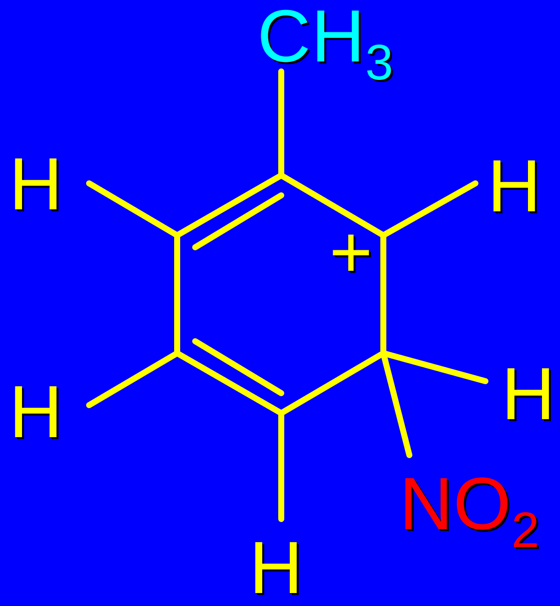
this resonance
form is a tertiary
carbocation

para Nitration of Toluene

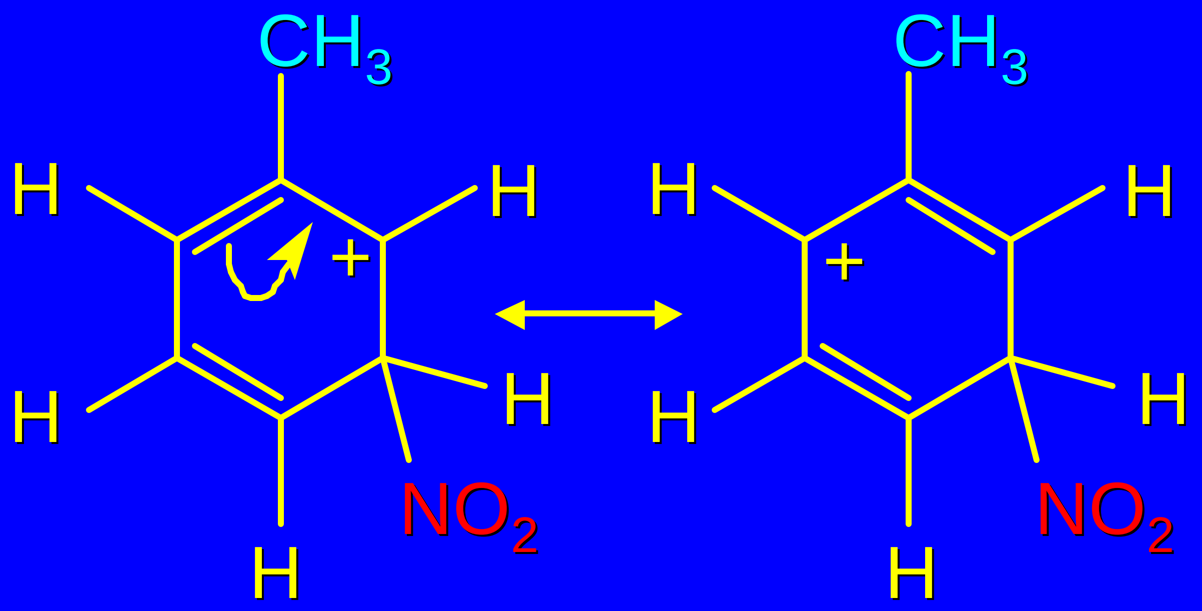


the rate-determining intermediate in the para nitration of toluene has tertiary carbocation character

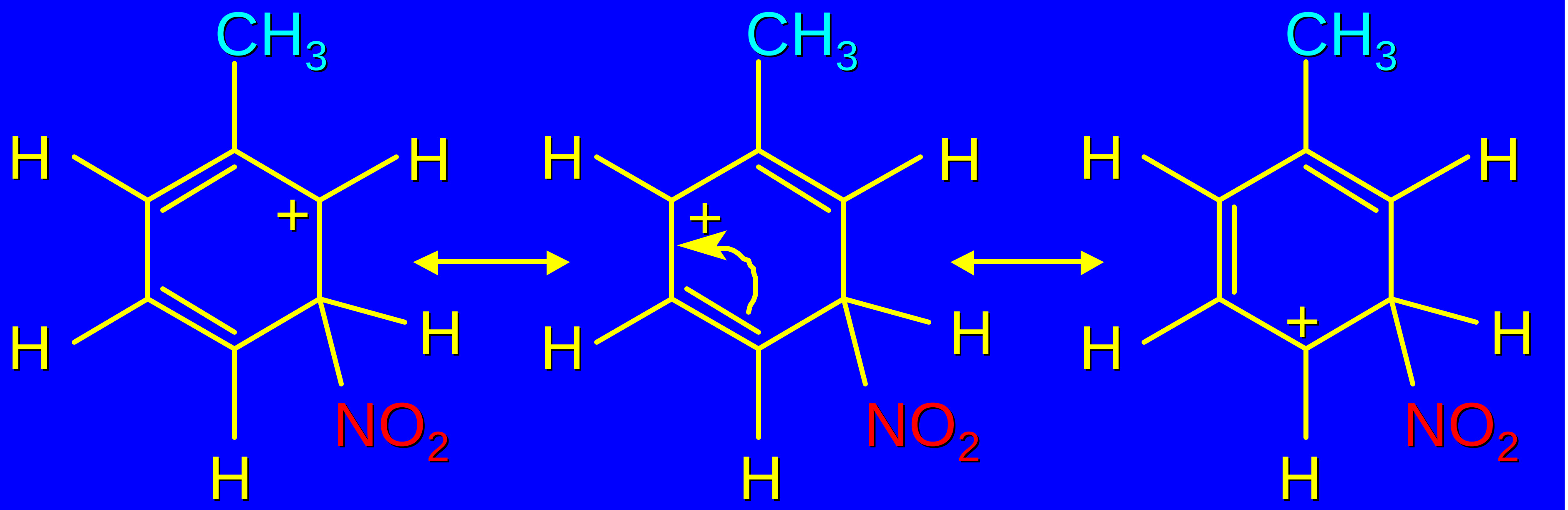
meta Nitration of Toluene



meta Nitration of Toluene



meta Nitration of Toluene



all the resonance forms of the rate-determining intermediate in the meta nitration of toluene have their positive charge on a secondary carbon

Nitration of Toluene: Interpretation

- The rate-determining intermediates for ortho and para nitration each have a resonance form that is a tertiary carbocation. All of the resonance forms for the rate-determining intermediate in meta nitration are secondary carbocations.
- Tertiary carbocations, being more stable, are formed faster than secondary ones. Therefore, the intermediates for attack at the ortho and para positions are formed faster than the intermediate for attack at the meta position. This explains why the major products are *o*- and *p*-nitrotoluene.

Nitration of Toluene: Partial Rate Factors

- The experimentally determined reaction rate can be combined with the ortho/meta/para distribution to give *partial rate factors* for substitution at the various ring positions.
- Expressed as a numerical value, a partial rate factor tells you by how much the rate of substitution at a particular position is faster (or slower) than at a single position of benzene.

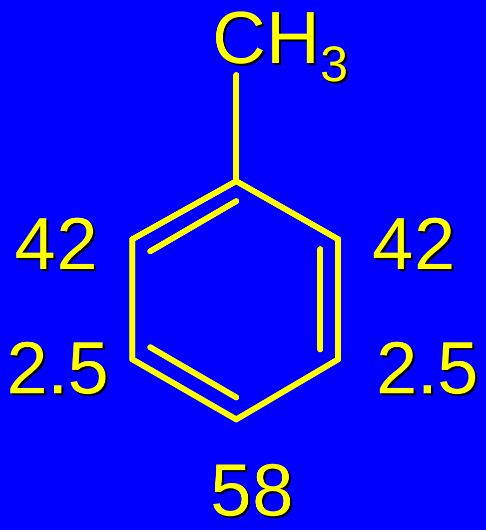
Nitration of Toluene: Partial Rate Factors

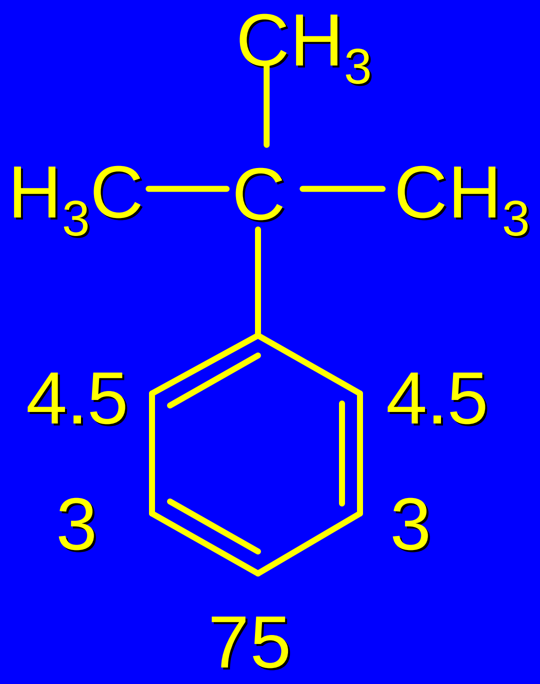
All of the available ring positions in toluene are more reactive than a single position of benzene.

A methyl group activates all of the ring positions but the effect is greatest at the ortho and para positons.

Steric hindrance by the methyl group makes each ortho position slightly less reactive than para.

Nitration of Toluene vs. tert-Butylbenzene





tert-Butyl is activating and ortho-para directing

tert-Butyl crowds the ortho positions and decreases the rate of attack at those positions.

Generalization

all alkyl groups are activating and
ortho-para directing

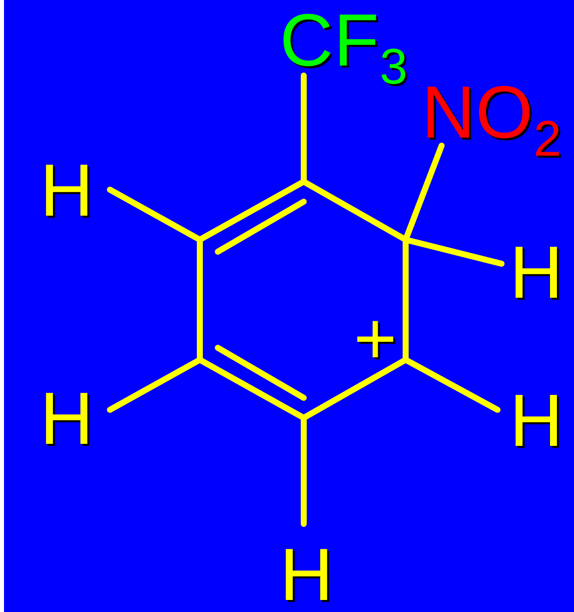
12.11
Rate and Regioselectivity in the Nitration of (Trifluoromethyl)benzene

A Key Point

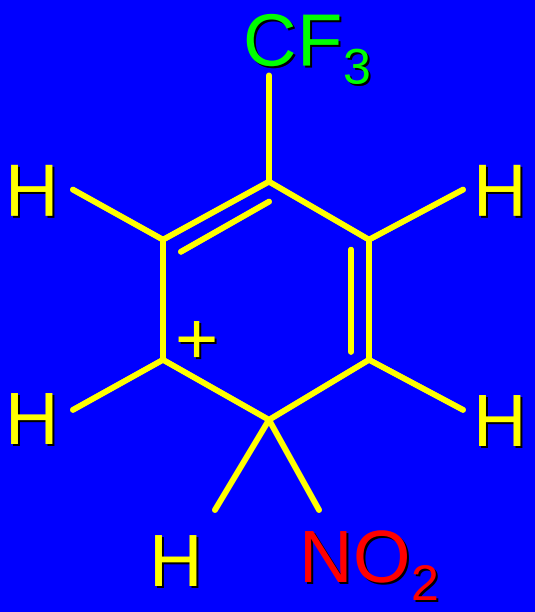
A methyl group is electron-donating and stabilizes a carbocation.

Because F is so electronegative, a CF_3 group destabilizes a carbocation.

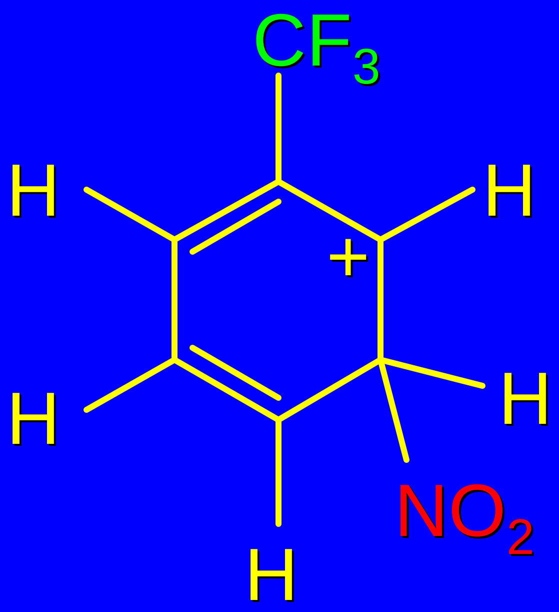
Carbocation Stability Controls Regioselectivity



gives ortho

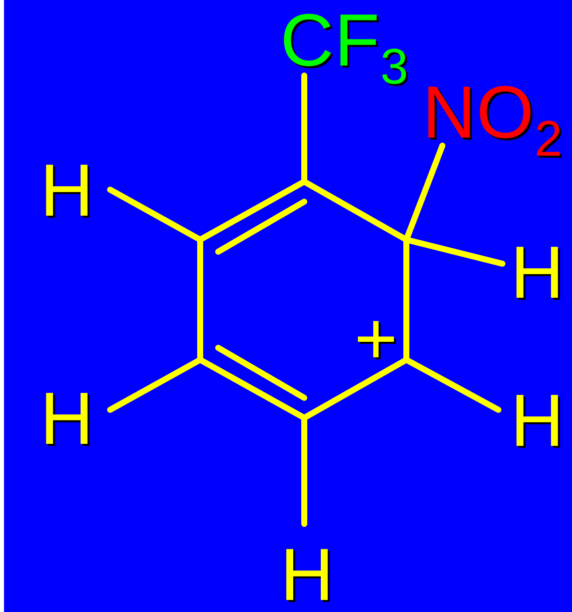


gives para

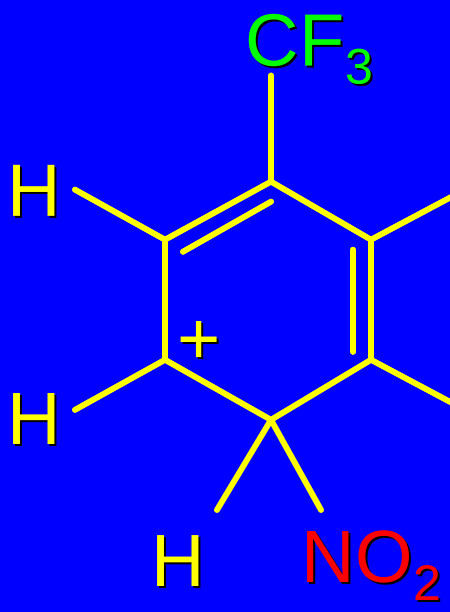


gives meta

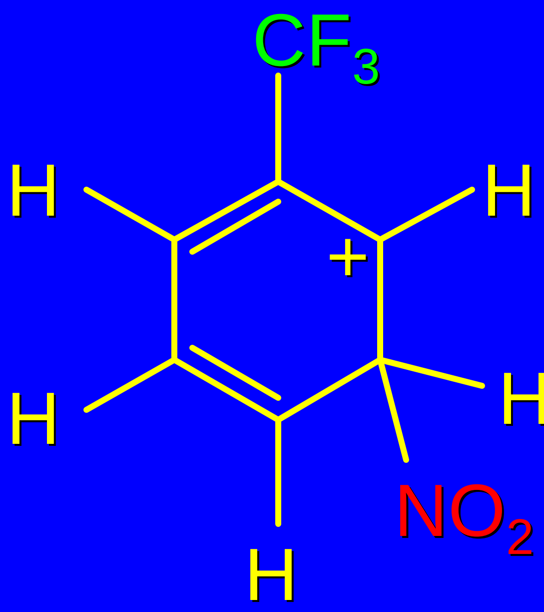
Carbocation Stability Controls Regioselectivity



gives ortho



gives para

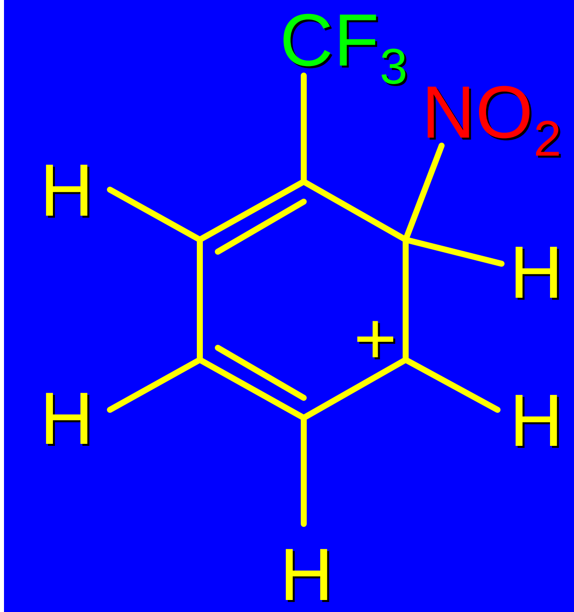


gives meta

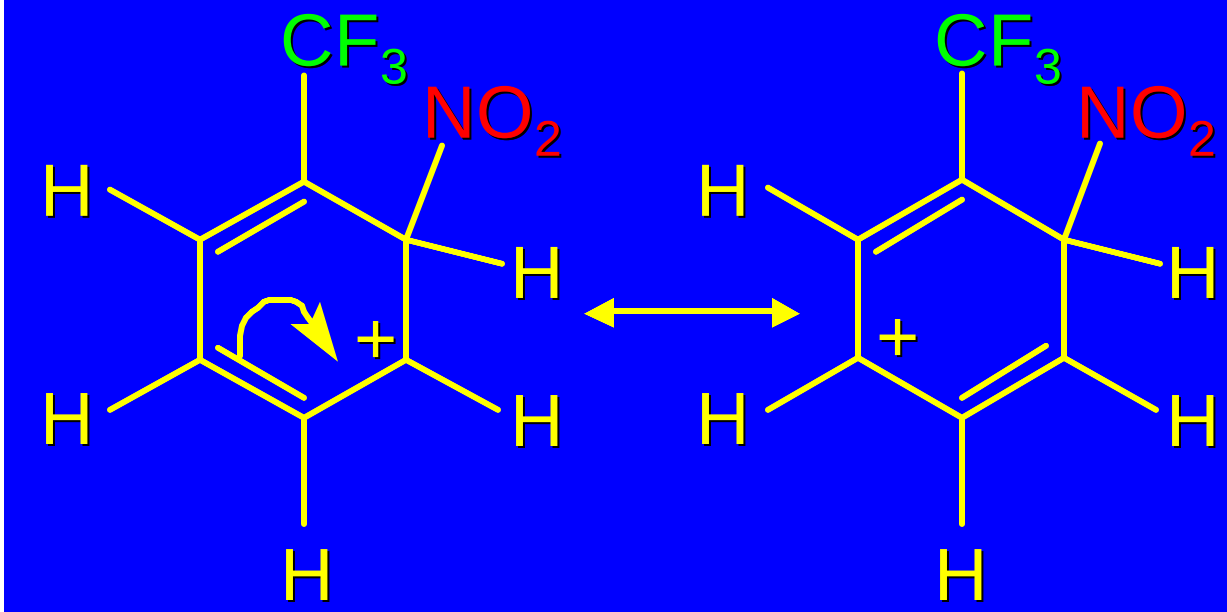
less stable

more stable

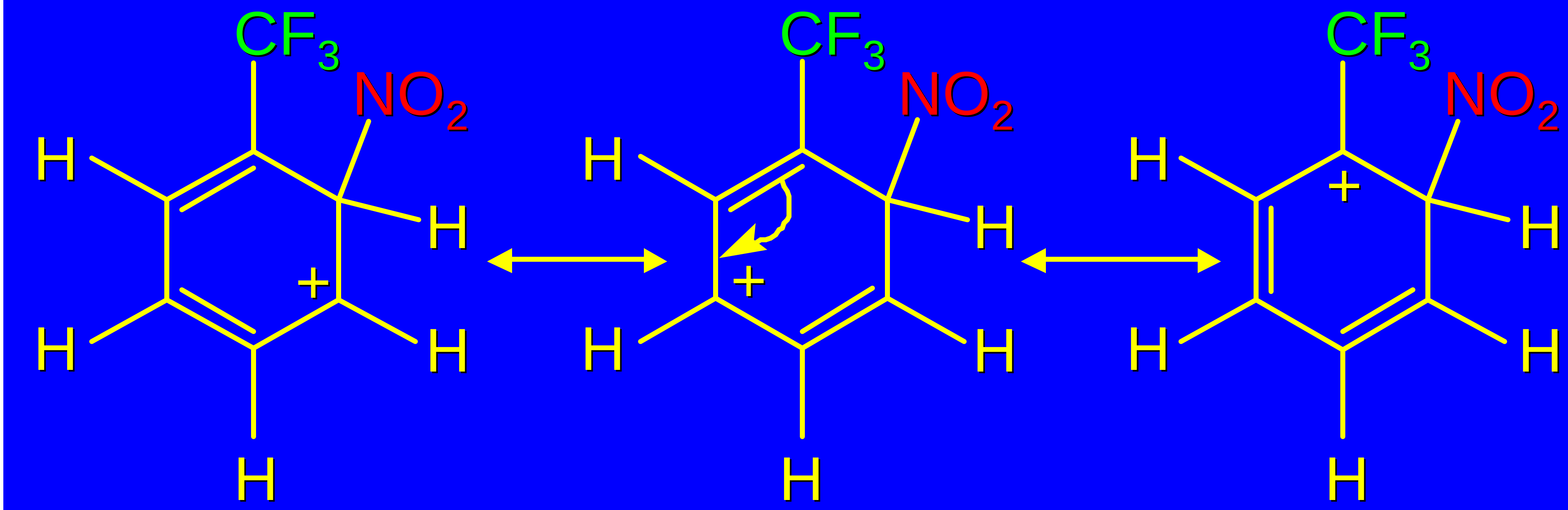
ortho Nitration of (Trifluoromethyl)benzene



ortho Nitration of (Trifluoromethyl)benzene

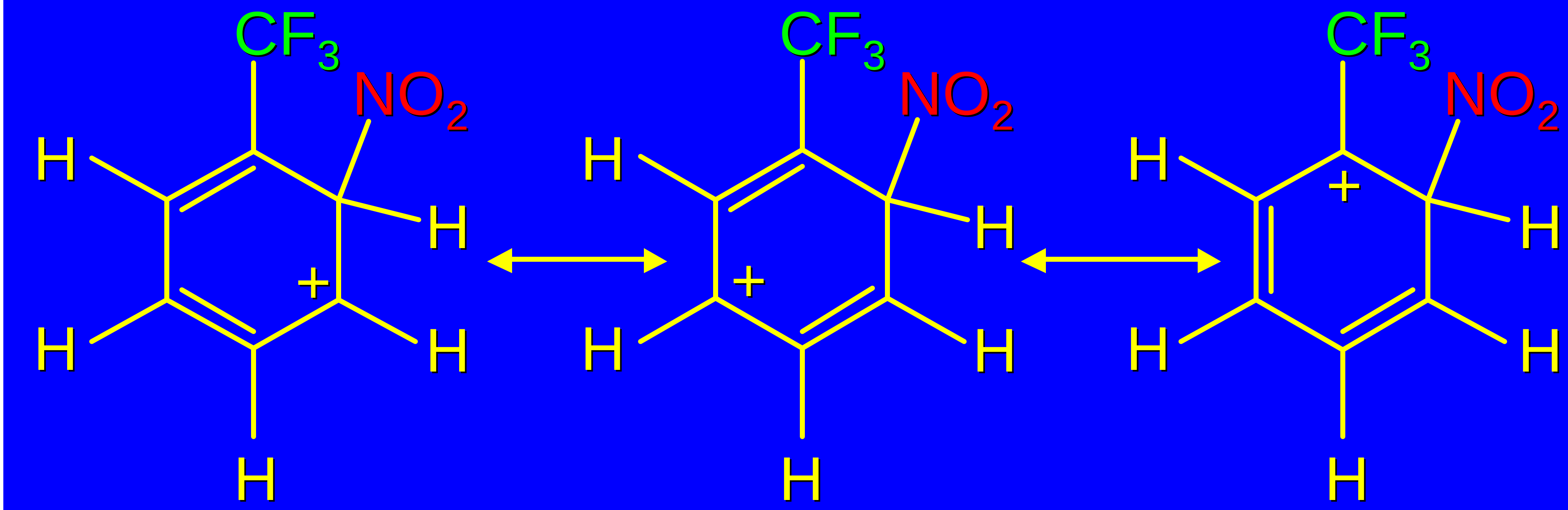


ortho Nitration of (Trifluoromethyl)benzene



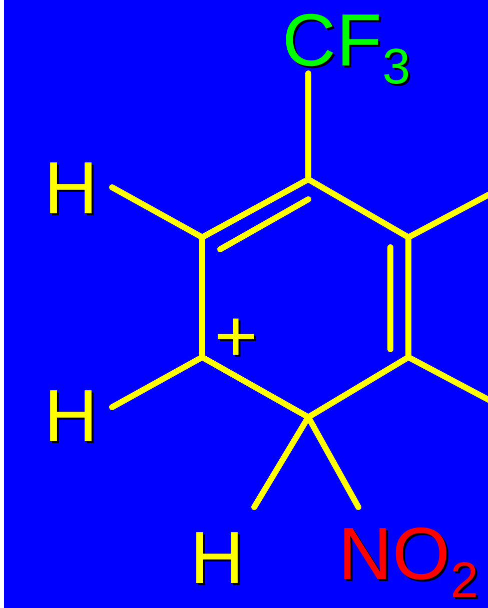
this resonance
form is
destabilized

ortho Nitration of (Trifluoromethyl)benzene

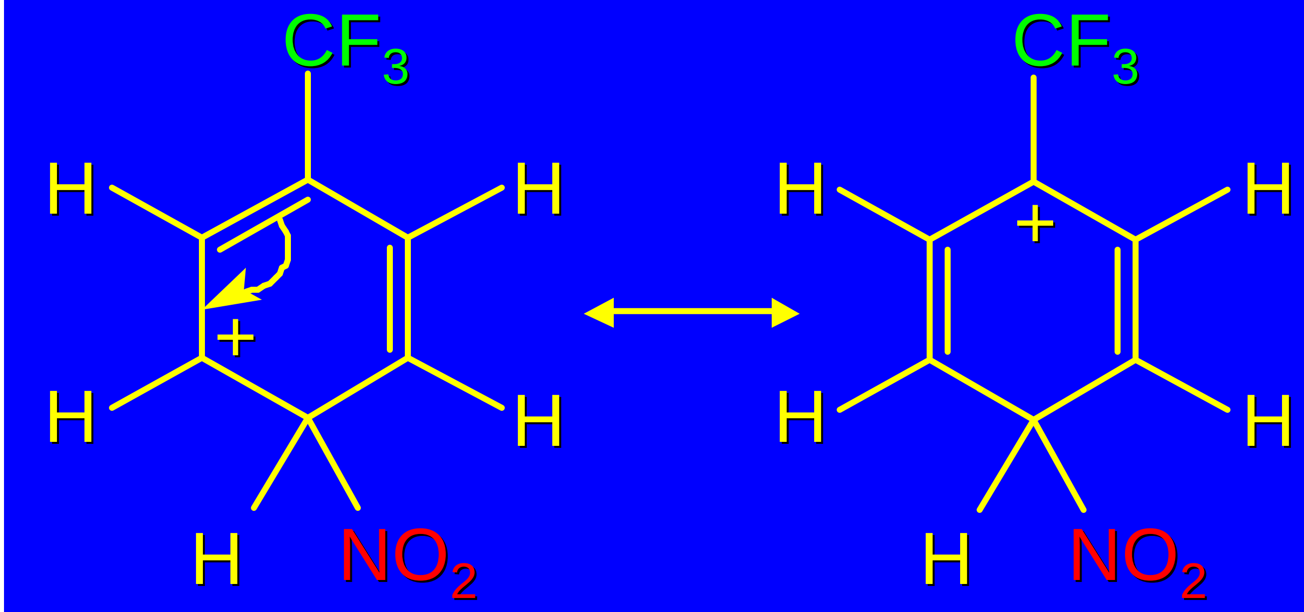


one of the resonance forms of the rate-determining intermediate in the ortho nitration of (trifluoromethyl)benzene is strongly destabilized

para Nitration of (Trifluoromethyl)benzene

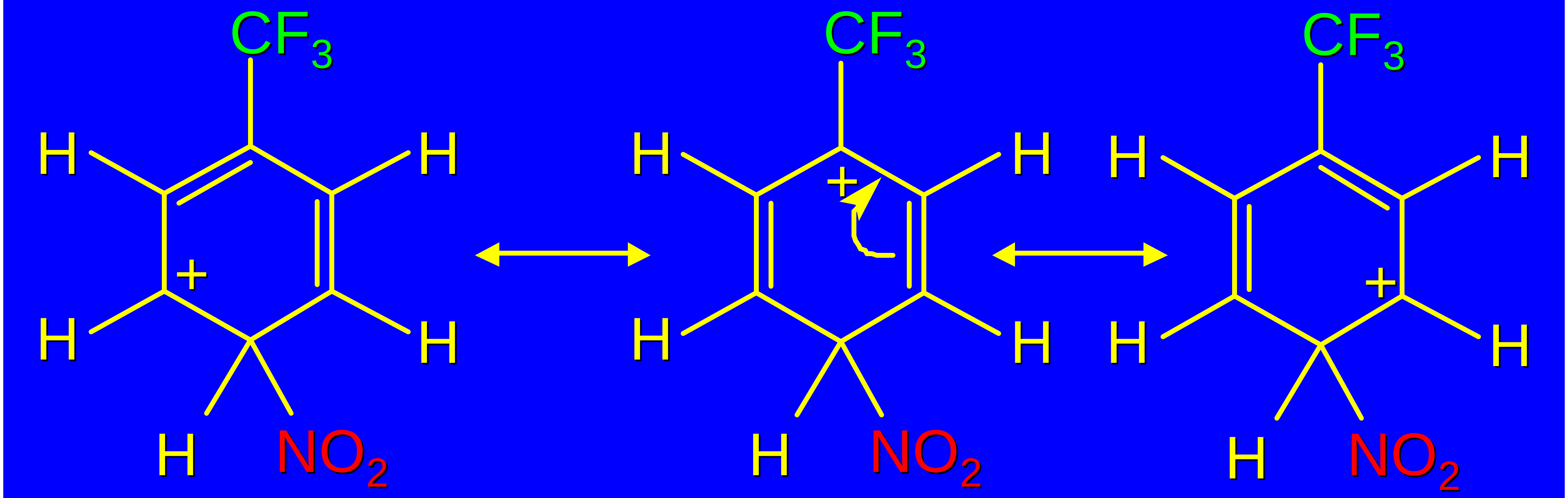


para Nitration of (Trifluoromethyl)benzene



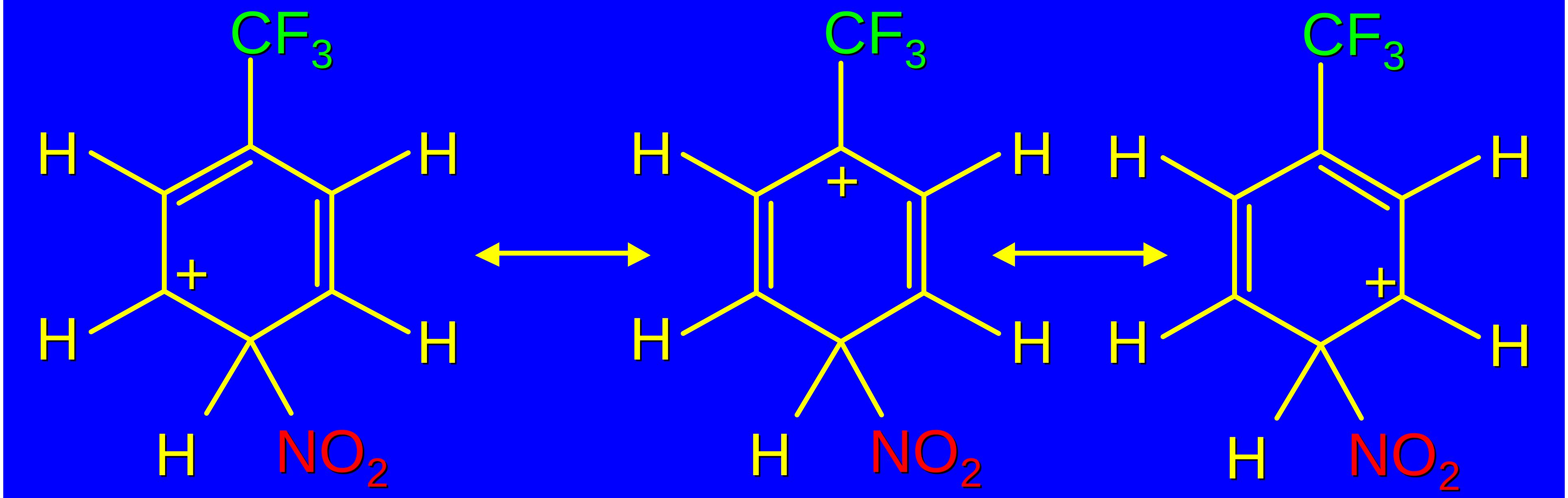
this resonance
form is destabilized

para Nitration of (Trifluoromethyl)benzene



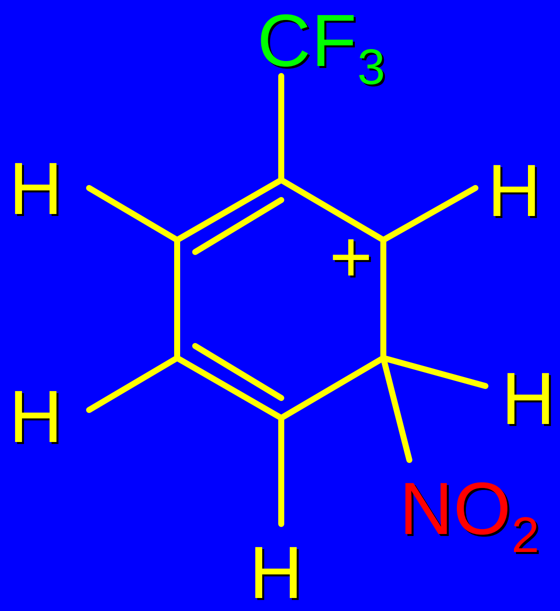
this resonance
form is destabilized

para Nitration of (Trifluoromethyl)benzene

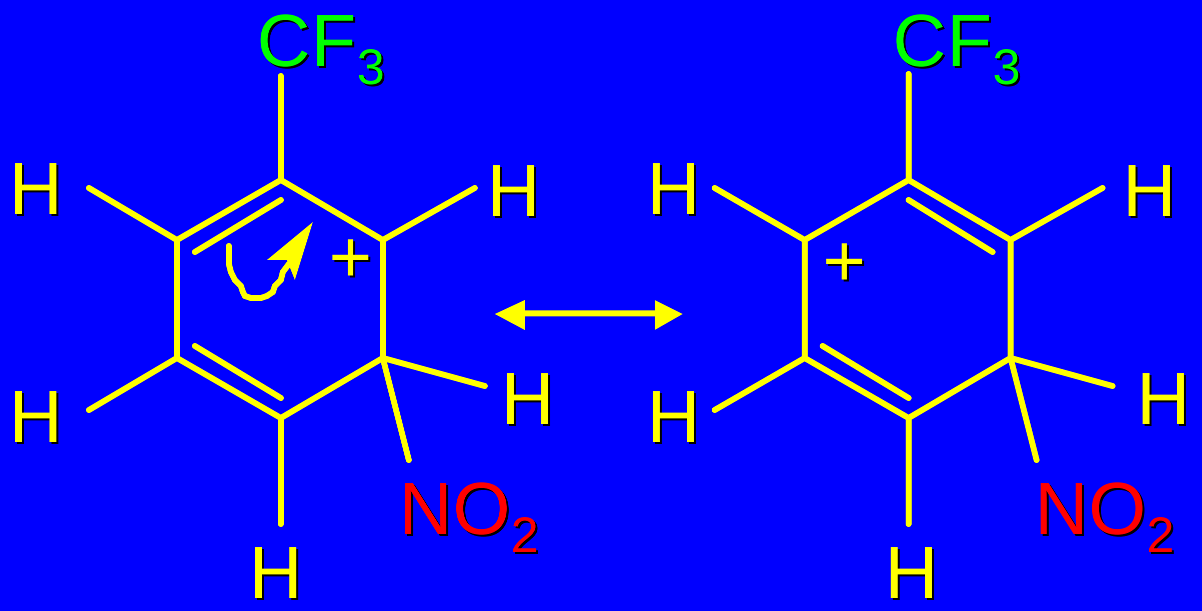


one of the resonance forms of the rate-determining intermediate in the para nitration of (trifluoromethyl)benzene is strongly destabilized

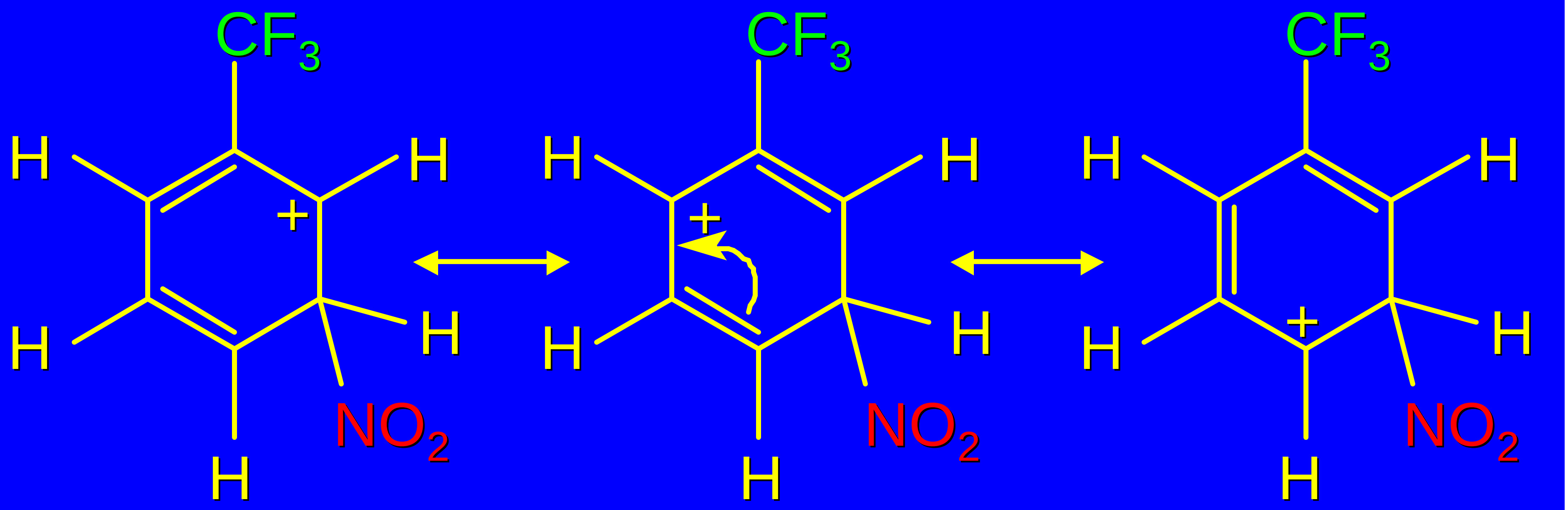
meta Nitration of (Trifluoromethyl)benzene



meta Nitration of (Trifluoromethyl)benzene



meta Nitration of (Trifluoromethyl)benzene

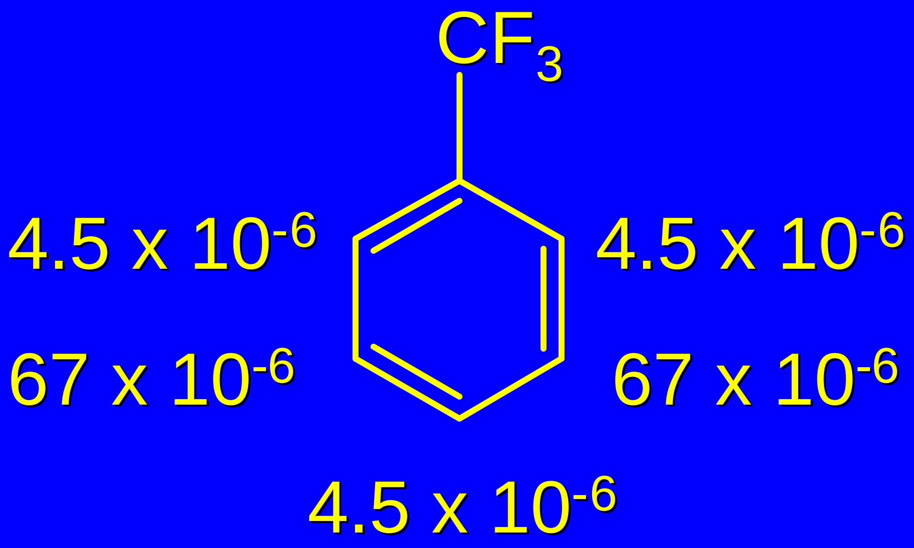


none of the resonance forms of the rate-determining intermediate in the meta nitration of (trifluoromethyl)benzene have their positive charge on the carbon that bears the CF_3 group

Nitration of (Trifluoromethyl)benzene: Interpretation

The rate-determining intermediates for ortho and para nitration each have a resonance form in which the positive charge is on a carbon that bears a CF_3 group. Such a resonance structure is strongly destabilized. The intermediate in meta nitration avoids such a structure. It is the least unstable of three unstable intermediates and is the one from which most of the product is formed.

Nitration of (Trifluoromethyl)benzene: Partial Rate Factors



All of the available ring positions in (trifluoromethyl)benzene are much less reactive than a single position of benzene.

A CF_3 group deactivates all of the ring positions but the degree of deactivation is greatest at the ortho and para positons.