ELECTROPHILIC AROMATIC SUBSTITUTION

Aromatic Electrophilic substitution:

- The arenium ion mechanism.
- Orientation and reactivity, energy profile diagram.
- The ortho / para ratio, ipso attack, orientation in other ring system, quantitative treatment of reactivity in substrates and electrophiles.
- Diazonium coupling
- Vilsmeir reaction
- Gatterman-Koch reaction

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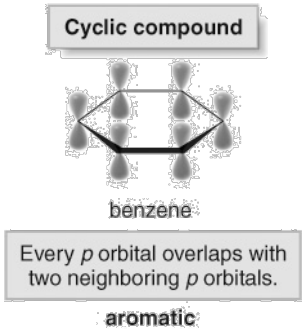
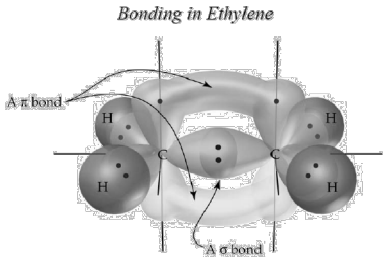
ELECTROPHILIC AROMATIC SUBSTITUTION

Both BENZENE and ALKENE are susceptible to E^+ attack due to their exposed π electrons





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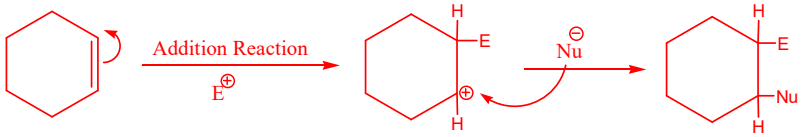
ELECTROPHILIC ADDITION IN ALKENE



WHY ELECTROPHILIC ATTACK IN BENZENE?

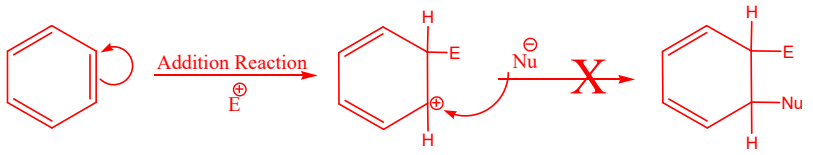
Theory The high electron density of the ring makes it open to attack by electrophiles

HOWEVER...

Because the mechanism involves an initial disruption to the ring, electrophiles will have to be more powerful than those which react with alkenes.

4

A fully delocalised ring is stable so will resist ELECTROPHILIC ADDITION.



STABLE DELOCALISED SYSTEM

DOES NOT FORM THIS PRODUCT SINCE LESS STABLE THAN STARTING MATERIAL DUE TO LOSS OF AROMATICITY

ELECTRONS ARE NOT DELOCALISED AROUND THE WHOLE RING - LESS STABLE

THEREFORE, BENZENE UNDERGOES SUBSTITUTION REACTION RATHER THAN ADDITION REACTION

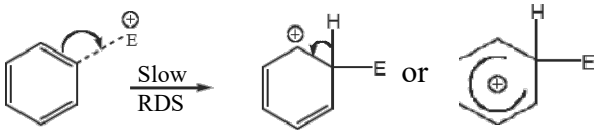
5

ARENIUM ION, ITS MECHANISM, S_E2 REACTION

The general equation for this reaction is:

Generation of E^+

STEP I

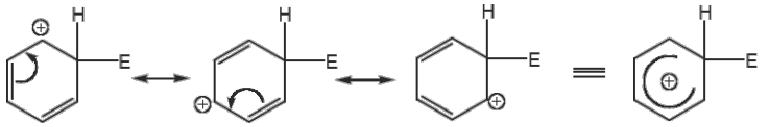


Arenium ion, Wheland intermediate or σ Complex

Carbocation, Sp_3 Hybridized due to new σ bonded electrophile

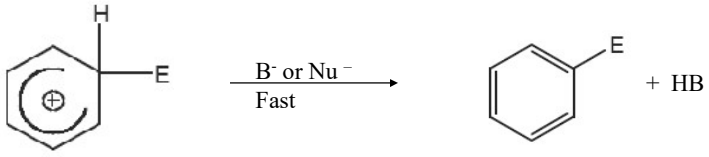
6

Although the Wheland intermediate is stabilized by resonance



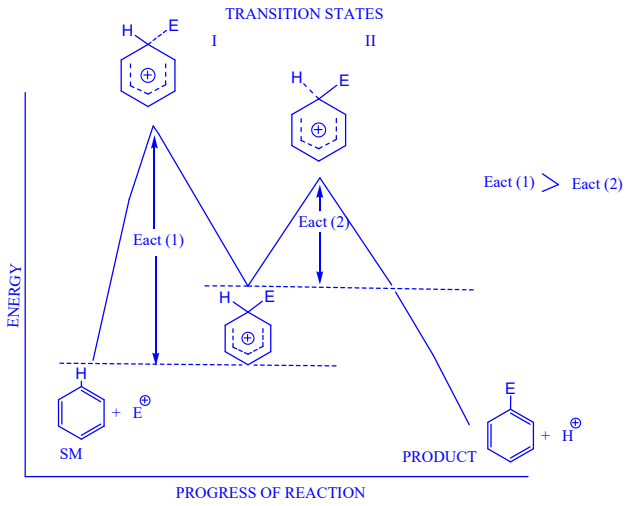
•we have clearly lost the aromatic stabilization of the starting material and hence the addition of the electrophile is going to be the slow step (rds = rate determining step).
•The second step will be fast since we regenerate the aromatic system by loss of the proton.

STEP II



7

ENERGY PROFILE DIAGRAM OF ARENIUM ION



SUBSTITUTION ELECTROPHILIC BIMOLECULAR (S_E2)

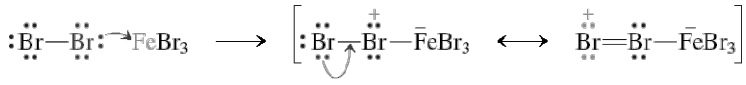
8

Halogenation of Benzene: the Need for a Catalyst

Benzene is normally unreactive to halogens because they are not strong enough to disrupt its aromaticity.

However, halogens can be activated by Lewis acid catalysts, such as ferric halides (FeX_3) or aluminum halides (AlX_3), to become much more powerful electrophiles.

Activation of Bromine by the Lewis Acid $FeBr_3$

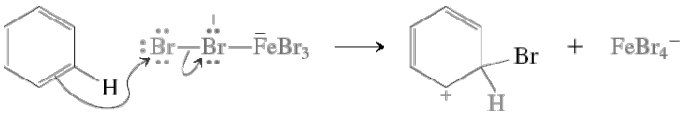


Bromine/Chlorine is non polar so is not a good electrophile. The halogen carrier is required to polarise the halogen.

9

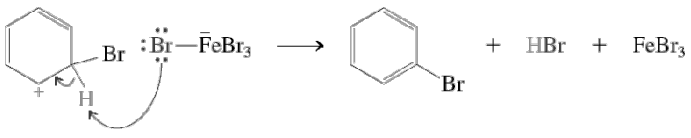
This activated bromine complex can attack the benzene molecule, allowing the other bromine atom to depart with the good leaving group $FeBr_4^-$

Electrophilic Attack on Benzene by Activated Bromine



The $FeBr_4^-$ next abstracts a proton from the cyclohexadienyl cation intermediate, and in the process regenerates the original $FeBr_3$ catalyst.

Bromobenzene Formation



Kinetic data shows that the:

Rate = K [Benzene] [Halogen] [catalyst $FeCl_3$]

10

Bond energy calculations show that the electrophilic bromination of benzene is exothermic:

Phenyl-H	+112 kcal mol^{-1}
Br-Br	+46 kcal mol^{-1}
Phenyl-Br	-81 kcal mol^{-1}
H-Br	-87.5 kcal mol^{-1}
Reaction	-10.5 kcal mol^{-1}

Fluorination of benzene is very exothermic (explosive).

Chlorination and bromination require an activating catalyst.

Iodination is endothermic and does not occur.

11

ELECTROPHILIC SUBSTITUTION REACTIONS - NITRATION

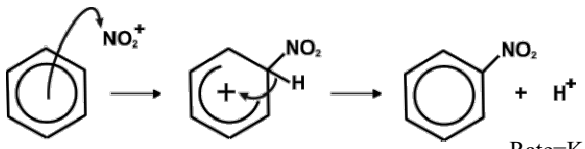
Reagents **conc. nitric acid** and **conc. sulphuric acid** (catalyst)

Conditions **reflux at 55°C**

Equation $C_6H_6 + HNO_3 \longrightarrow C_6H_5NO_2 + H_2O$

nitrobenzene

Mechanism



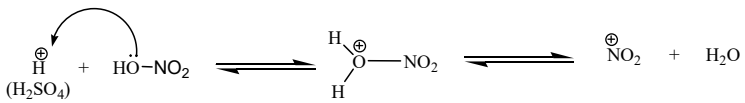
(resonance stabilized)

Rate=K[Substrate][NO_2^+]

Electrophile NO_2^+, **nitronium ion** or **nitryl cation**; it is generated in an acid-base reaction...

$2H_2SO_4 + HNO_3 \rightleftharpoons 2HSO_4^- + H_3O^+ + NO_2^+$

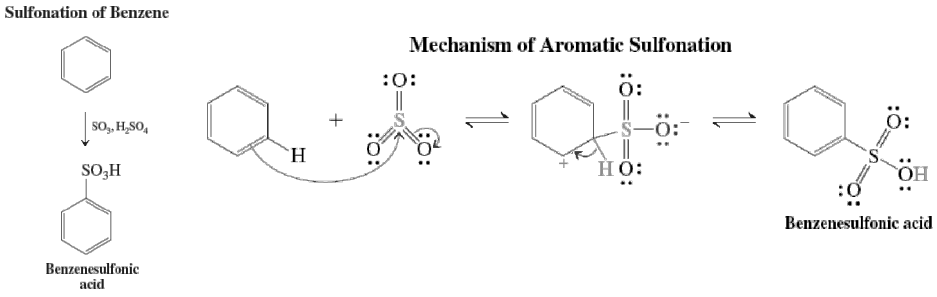
acid base



12

Sulfonation (a reversible reaction).

Fuming sulfuric acid (8% SO_3 in concentrated H_2SO_4) reacts with benzene to form benzenesulfonic acid.



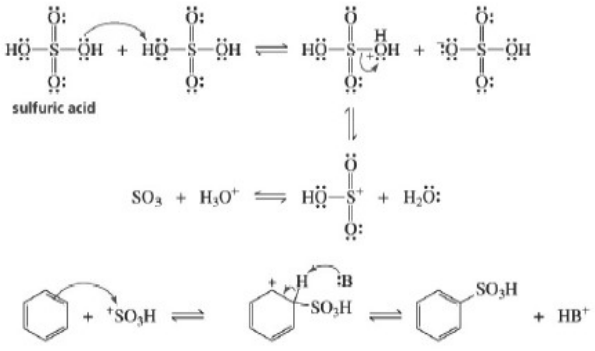
Because the reaction of SO_3 with water is so exothermic, the sulfonation of benzene can be reversed by heating benzenesulfonic acid in dilute aqueous acid.

Because sulfonation is reversible, it can be used as a blocking group to control further aromatic substitution and then later removed.

13

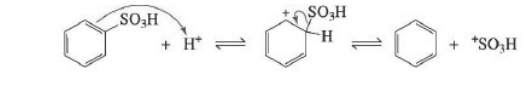
First H_2SO_4 donates a proton to SO_3 to produce HSO_3^+ (the reactive species)

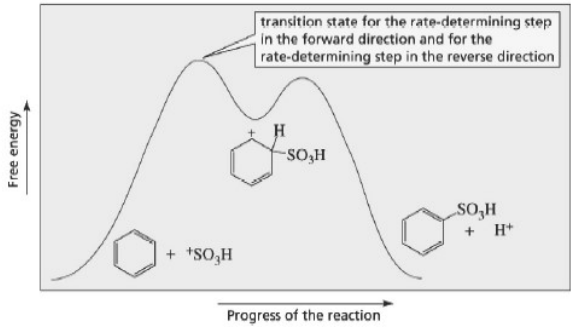
- **Mechanism for sulfonation**



14

- **Mechanism for desulfonation**





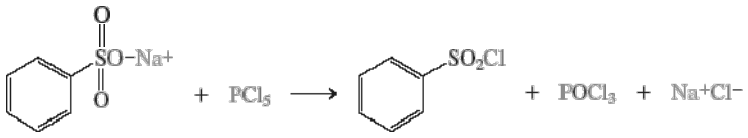
Here, H_2SO_4 is acting both as acid & base.

Rate = K [Benzene] [SO_3] NOT H_2SO_4

15

Sulfonyl chlorides can be prepared by reaction of the sodium salt of the acid with PCl_5 or $SOCl_2$.

Preparation of Benzenesulfonyl Chloride

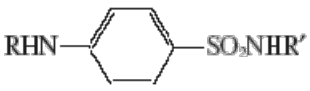


Sulfonyl chlorides are frequently used in synthesis, for example to convert the hydroxy group of an alcohol into a good leaving group.

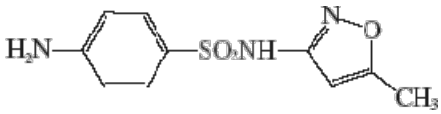
16

Sulfonamides are derived from the reaction of a sulfonyl chloride with an amine. An important class of sulfonamides, its derivatives are known as sulfa drugs:

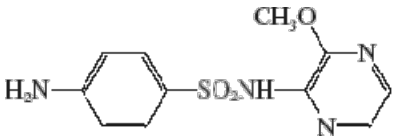
Sulfa Drugs



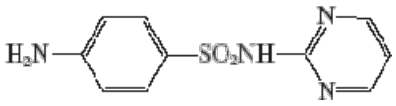
General structure



Sulfamethoxazole
(Gantanol)
(Antibacterial, used to treat urinary infections)



Sulfalene
(Kelfizina)
(Antiparasitic)



Sulfadiazine
(Antimalarial)

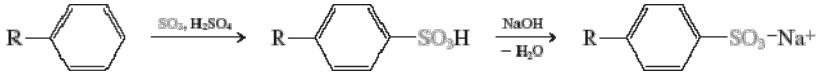
17

Benzenesulfonic acids have important uses.

Long chain-branched alkylbenzenes can be sulfonated to the corresponding sulfonic acids.

After conversion to their sodium salts, these compounds can be used as synthetic detergents.

Aromatic Detergent Synthesis



R = branched alkyl group

Sulfonate detergents have now been replaced by more biologically friendly, biodegradable detergents.

Sulfonation is often used to impart water solubility to organic compounds, as in the manufacture of certain dyes.

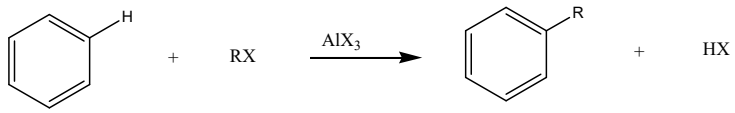
18

Friedel-Crafts Alkylation

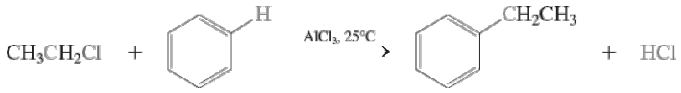
Carbon-carbon bonds to benzene can be created using a sufficiently electrophilic carbon based electrophile.

To create the necessary electrophilic carbon atom, a Lewis acid such as $AlCl_3$ is employed.

A alkyl halide reacts with benzene in the presence of an aluminum halide to form an alkylbenzene and a hydrogen halide.



Friedel-Crafts Alkylation of Benzene with Chloroethane



28%
Ethylbenzene

19

Reactivity of the alkyl halides increases in the order:

RI < RBr < RCl < RF (increasing bond polarity)

Typical Lewis acids are:

BF_3, $SbCl_5$, $FeCl_3$, $AlCl_3$ and $AlBr_3$

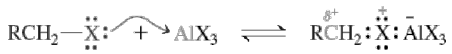
A catalyst is used to increase the positive nature of the electrophile and make it better at attacking benzene rings. $AlCl_3$ acts as a Lewis Acid and helps break the C—Cl bond.

20

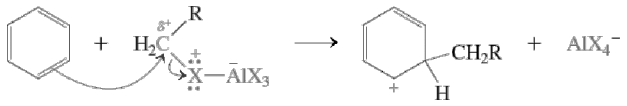
The mechanism of the Friedel-Crafts alkylation with primary haloalkanes (alkyl halides) involves coordination of the Lewis acid to the halogen atom:

Mechanism of Friedel-Crafts Alkylation with Primary Haloalkanes

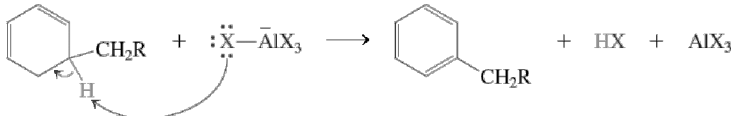
STEP 1. Haloalkane activation



STEP 2. Electrophilic attack



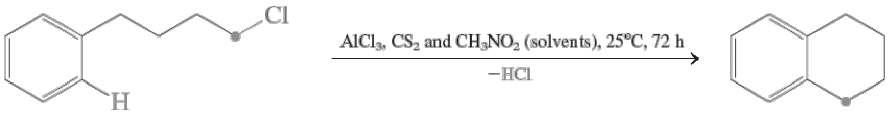
STEP 3. Proton loss



With secondary and tertiary alkyl halides, free carbocations are usually formed, which attack the benzene ring in the same way as the cation NO_2^+.

A new ring can be fused onto the benzene nucleus by means of an intramolecular Friedel-Crafts alkylation:

An Intramolecular Friedel-Crafts Alkylation



31%

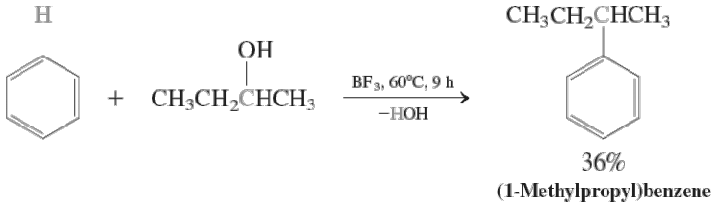
Tetralin

(Common name)

22

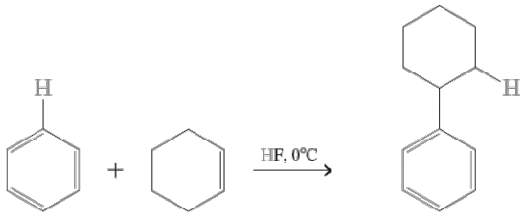
Any starting material that functions as a precursor to a carbocation can be used in a Friedel-Crafts alkylation:

Friedel-Crafts Alkylations Using Other Carbocation Precursors



36%

(1-Methylpropyl)benzene



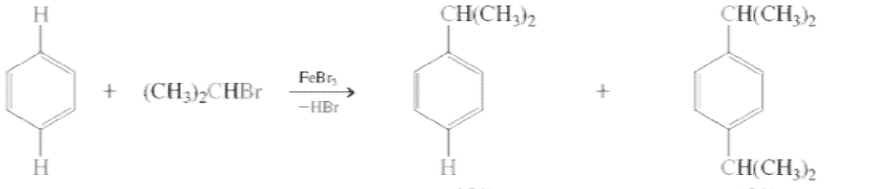
62%

Cyclohexylbenzene

23

Limitations of Friedel-Crafts Alkylations

Polyalkylation and carbocation rearrangement may cause the yield of desired products to diminish and lead to mixtures that may be difficult to separate:



25%

(1-Methylethyl)benzene (Isopropylbenzene)

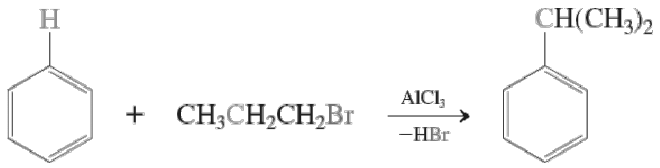
15%

1,4-Bis(1-methylethyl)benzene (*p*-Diisopropylbenzene)

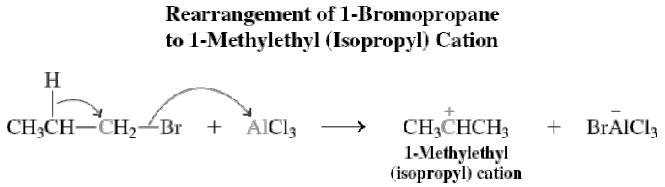
Polyalkylation occurs because the alkylbenzene first formed is electron-rich and activates the ring towards further substitution. This is in contrast to bromination, nitration and sulfonation, as they deactivate the ring towards further substitution (electron withdrawing substituents).

24

Skeletal rearrangement of the carbocation is the second unwanted side-reaction in aromatic alkylation. The desired 1-propylbenzene is not obtained when benzene is alkyated using 1-bromopropane:



In the presence of the Lewis acid, the starting haloalkane rearranges to the secondary carbocation by a hydride shift:



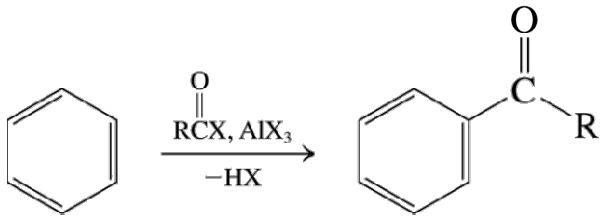
Because of polysubstitution and rearrangement reactions, Friedel-Crafts alkylations are rarely used in synthesis.

25

Friedel-Crafts Acylation (Alkanoylation)

An alternate route to C-C bond formation to the aromatic nucleus that does not have the problems encountered with alkylations is the Friedel-Crafts **acylation** or **alkanoylation**.

These reactions proceed through an acylium cation intermediate ($RC{=}O^+$).

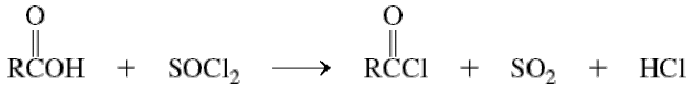


26

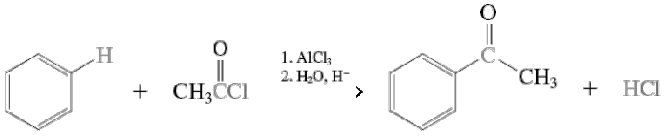
Friedel-Crafts acylation employs acyl chlorides

Benzene reacts with alkanoyl halides in the presence of aluminum halide to give 1-phenylalkanones (phenyl ketones).

Preparation of an Alkanoyl (Acyl) Chloride



Friedel-Crafts Alkanoylation of Benzene with Acetyl Chloride



61%

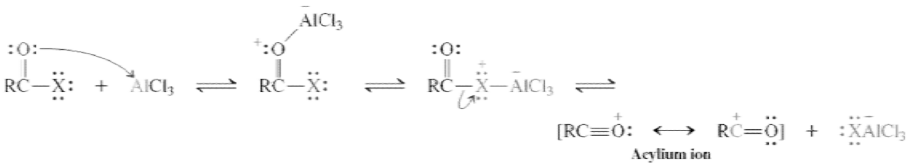
1-Phenylethanone (Acetophenone)

27

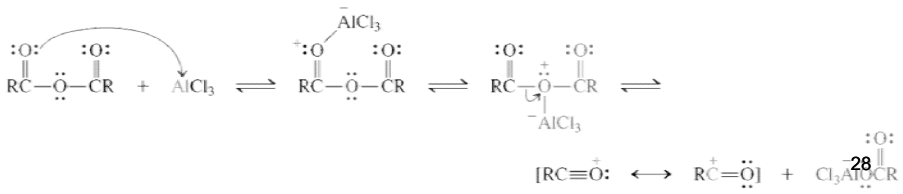
Acyl halides react with Lewis acids to produce acylium ions.

The acylium cation can be formed from either an acyl halide or a carboxylic anhydride:

Acylium Ions from Alkanoyl Halides

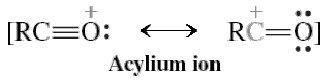


Acylium Ions from Carboxylic Anhydrides

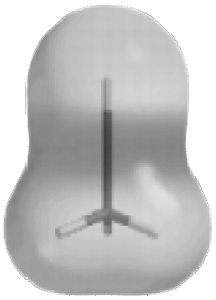


28

The acylium cation is stabilized by resonance and is not prone to rearrangement.



Acylium ion



Acetyl cation

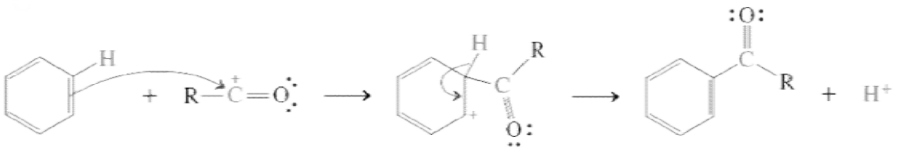
Most of the positive charge resides on the carbon atom (blue).

29

Acylium ions undergo electrophilic aromatic substitution.

An acylium ion is capable of attacking benzene by the usual aromatic substitution mechanism:

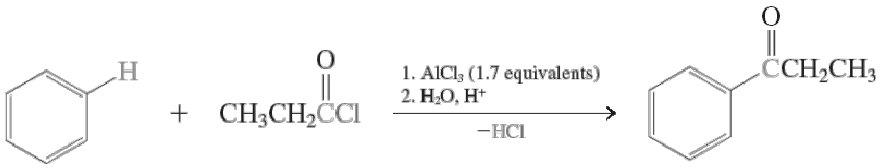
Electrophilic Alkanoylation



The acyl substituent is electron withdrawing which deactivates the ring and protects it from further substitution.

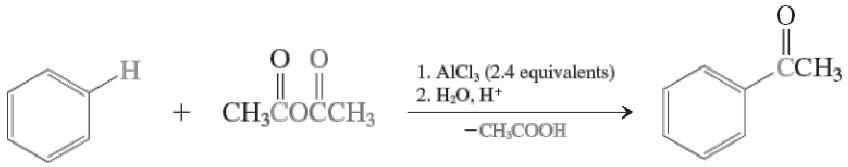
30

An aqueous work-up is required to liberate the final ketone from the aluminum chloride complex:



84%

1-Phenyl-1-acetone (Propiophenone)



85%

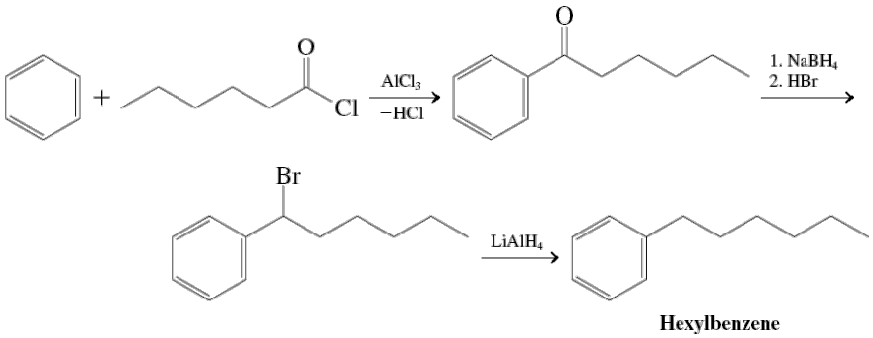
1-Phenylethanone (Acetophenone)

31

The ketone product of the Friedel-Crafts Acylation can be converted into an alcohol by hydride reduction.

The resulting hydroxyl can be converted into a good leaving group that can be further reduced by hydride leading to the corresponding hydrocarbon.

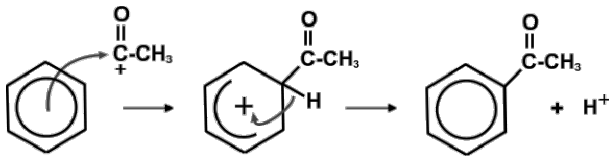
Preparation of Hexylbenzene by Hexanoylation–Reduction of Benzene



Hexylbenzene

32

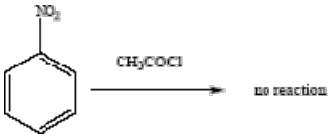
FRIEDEL-CRAFTS REACTIONS OF BENZENE - ACYLATION

Overview	**Acylation involves substituting an acyl (methanoyl, ethanoyl) group**
Reagents	**an acyl chloride (RCOX) and anhydrous aluminium chloride $AlCl_3$**
Conditions	**reflux 50°C; dry inert solvent (ether)**
Electrophile	**$RC^+=O$ (e.g. CH_3C^+O)**
Equation	**$C_6H_6 + CH_3COCl \longrightarrow C_6H_5COCH_3 + HCl$**
Mechanism	
Product	**A carbonyl compound (aldehyde or ketone)**

33

Limitation of FC Alkylation and FC Acyltion:

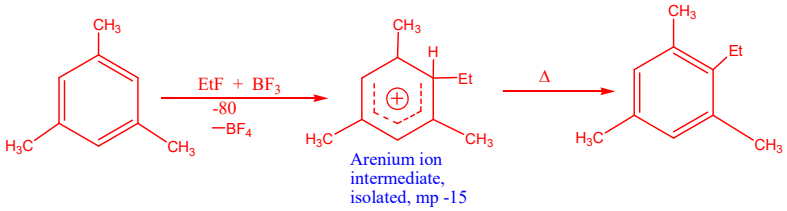
- Deactivated benzenes are not reactive to Friedel-Crafts Reaction



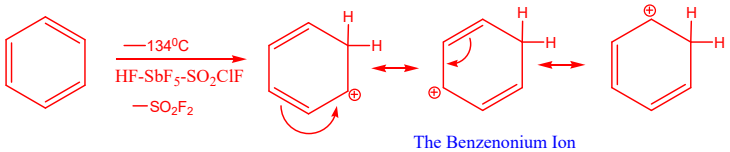
- Over alkylation can be a problem since the product is more reactive than the starting material

34

EVIDENCE OF ARENIUM ION FORMATION OR ISOLATION OF ARENIUM ION INTERMEDIATE

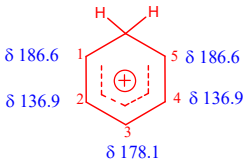


Arenium ion intermediate, isolated, mp -15



The Benzenonium Ion

δ 52.2



13C NMR Chemical Shifts
(Comparision of C-1, 3, 5 and C-2, 4)

35

Activation or Deactivation by Substituents on a Benzene Ring

The electronic influence of any substituent is determined by two factors, **inductance** and **resonance**.

Inductance occurs through the σ framework, tapers off rapidly with distance and is governed mostly by the relative electronegativity of the atoms.

Resonance takes place through π bonds, is longer range and is particularly strong in charged systems.

36

Inductive donors and acceptors:

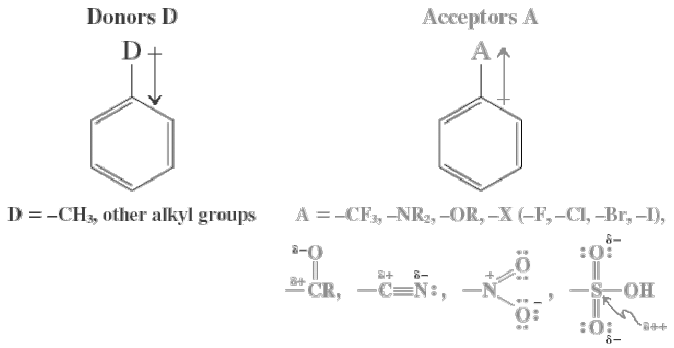
Simple alkyl groups are donating due to hyperconjugation.

The trifluoromethyl group is electron-withdrawing due to its electronegative fluorines.

Directly bound heteroatoms (N, O, halogens) are electron-withdrawing due to their electronegativities.

Positively polarized atoms (carbonyl, cyano, nitro and sulfonyl) are also electron-withdrawing.

Inductive Effects of Some Substituents on the Benzene Ring

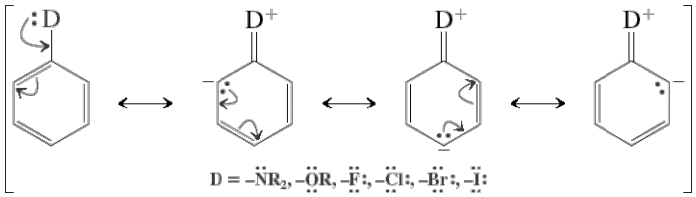


37

Resonance Effect

Substituents capable of resonance with the ring: Resonance donors bear at least one electron pair capable of delocalization into the benzene ring. This category contains groups such as $–NR_2$, -OR, and the halogens.

Resonance Donation to Benzene



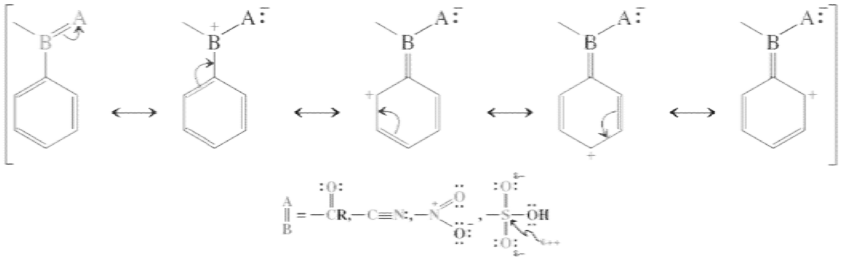
Inductance and resonance oppose each other. The effect that wins out depends upon the relative electronegativity of the heteroatoms, and the ability of their respective p-orbitals to overlap the π system. Resonance overrides induction for amino and alkoxy groups, while induction is more important for the halogens, making them weak electron acceptors.

38

Groups such as carbonyl, cyano, nitro and sulfonyl are all electron withdrawing through resonance.

They all contain a polarized double or triple bond whose partially positive end is attached to the benzene nucleus.

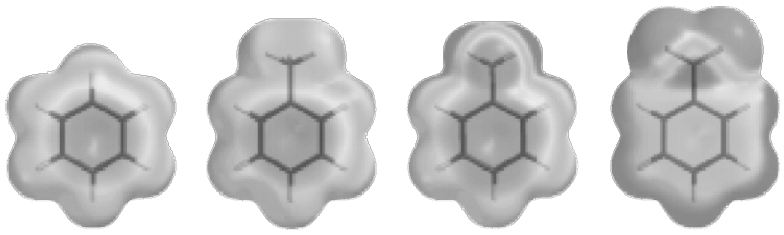
Resonance Acceptance from Benzene



In these cases, resonance reinforces induction.

39

Electron-donating groups increase the electron density in the benzene ring (red) while electron-withdrawing groups decrease the electron density in the ring (blue).



Benzene | **Methylbenzene (Toluene)** | **Benzenamine (Aniline)** | **Nitrobenzene**

Since the attacking species is an electrophile, the more electron rich the arene, the faster the reaction. Electrons donors activate the ring: Electron acceptors deactivate the ring.

Relative Rates of Nitration of C_6H_5X

X =	OH	> CH_3 >	H	> Cl >	$CO_2CH_2CH_3$ >	CF_3 >	NO_2
	1000	25	1	0.033	0.0037	2.6×10^{-5}	6×10^{-8}

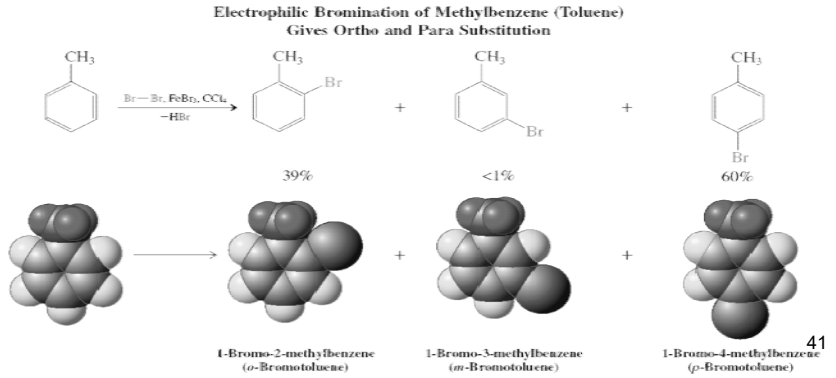
40

Directing Inductive Effects of Alkyl Groups

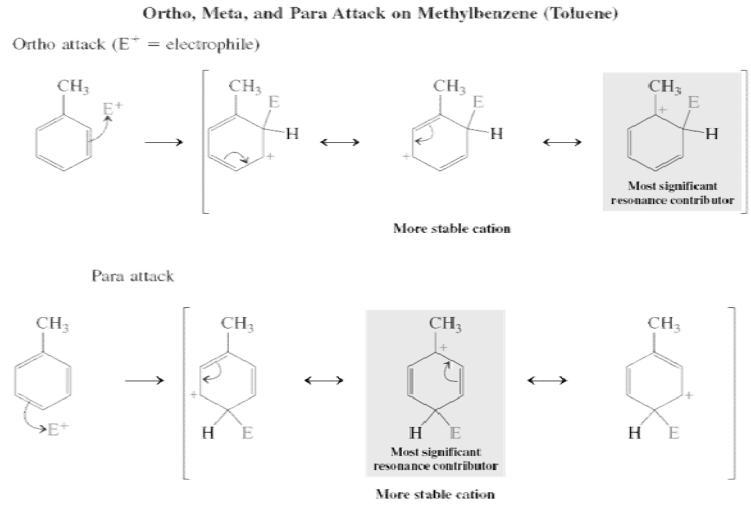
Groups that donate electrons by induction are activating and direct ortho and para.

The electrophilic bromination of methylbenzene is considerably faster than the bromination of benzene itself.

The reaction is also regioselective: Virtually no meta product is formed.

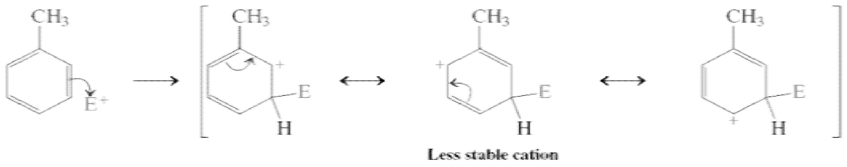


The transition states for addition at the ortho, meta and para positions account for the differences in regioselectivity:



In ortho and para attack, the transition state is stabilized by a resonance form having the positive charge on a tertiary carbon atom.

Meta attack



Less stable cation

In meta attack, all of the resonance forms of the transition state place the positive charge on the secondary carbon atom.

Ortho and para isomers are often not obtained in equal amounts, primarily due to steric effects. Para products often predominate over their ortho isomers.

43

Groups that withdraw electrons inductively are deactivating and meta-directing.

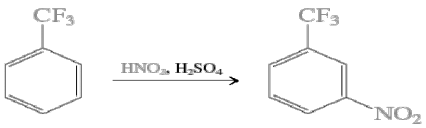
The trifluoromethyl group is electron-withdrawing due to its strongly electronegative fluorine atoms.

When carrying this substituent, the benzene ring becomes deactivated and reaction with electrophiles becomes very sluggish.

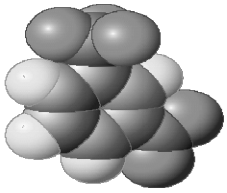
When substitution does occur (stringent conditions, such as heating), substitution occurs only at the meta positions.

The trifluoromethyl group is both deactivating and **meta-directing**.

Electrophilic Nitration of (Trifluoromethyl)benzene Gives Meta Substitution



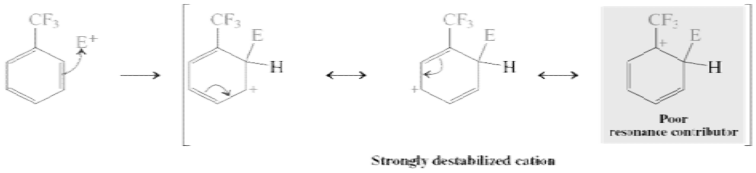
Only product



44

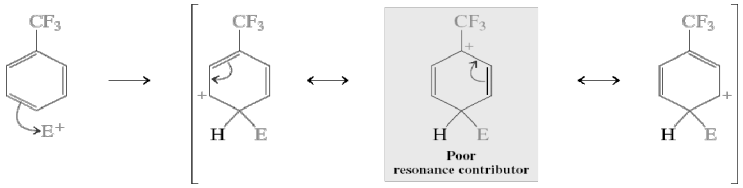
The transition states for addition at the ortho, meta, and para positions account for the differences in regioselectivity:

Ortho attack



Strongly destabilized cation

Para attack

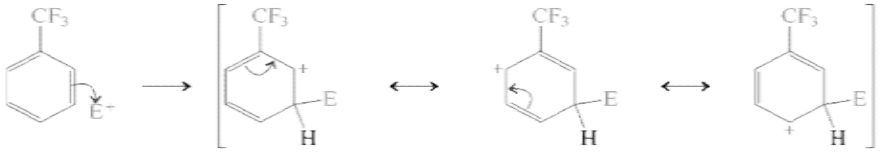


Strongly destabilized cation

Ortho and para attack place positive charge next to the electron withdrawing CF_3 group.

45

Meta attack



Less destabilized cation

Meta attack results in a transition state, which is more stable than either the ortho or para isomer since it does not place positive charge directly on the carbon atom bearing the electron-withdrawing group.

The meta transition state, although lower in energy than that of the para or ortho isomer, is still of higher energy than the transition states in the case of an activating substituent.

The trifluoromethyl group is both deactivating and meta-directing.

46

Directing Effects of Substituents in Conjugation with the Benzene Ring

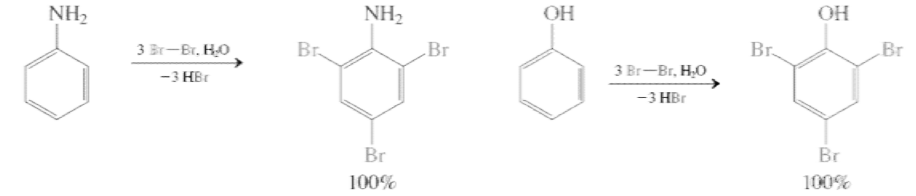
Groups that donate electrons by resonance activate and direct ortho and para.

The groups $-NH_2$ and –OH strongly activate the benzene ring.

Halogenations of aniline and phenol take place in the absence of a catalyst and are difficult to stop at single substitution.

Substitution occurs exclusively at the ortho and para positions.

Electrophilic Brominations of Benzenamine (Aniline) and Phenol Give Ortho and Para Substitution

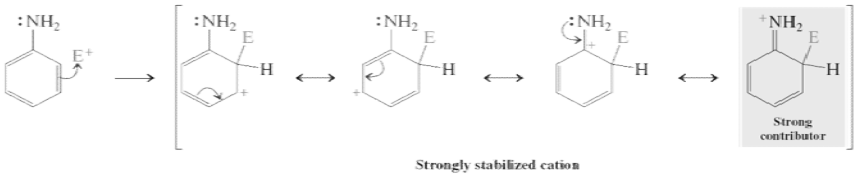


Benzenamine (Aniline) | 2,4,6-Tribromobenzenamine (2,4,6-Tribromoaniline) | Phenol | 2,4,6-Tribromophenol

47

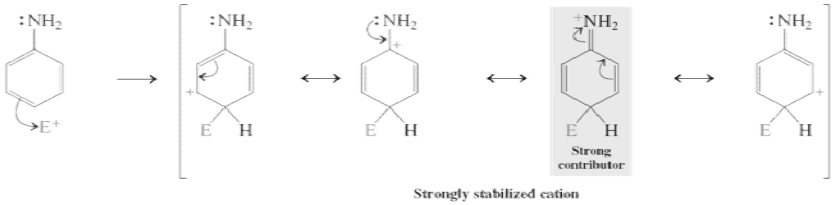
The activation and regioselectivity of aromatic electrophilic substitution by the amino group can be explained by examining the resonance forms for the intermediate cations:

Ortho attack



Strongly stabilized cation

Para attack

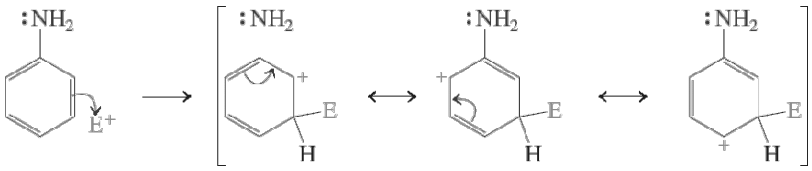


Strongly stabilized cation

The ortho or para transition state is stabilized through resonance (compared to benzene).

48

Meta attack



The transition state for meta attack is not resonance-stabilized by the amino group and the electronegative nitrogen atom withdraws electrons from the ring (deactivates).

Little meta product is formed.

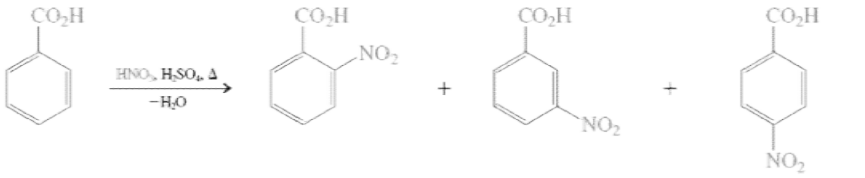
49

Groups that withdraw electrons by resonance deactivate and direct meta

An example of a group that deactivates the benzene ring by resonance is the carboxy group.

Nitration of benzoic acid, $C_6H_5CO_2H$, occurs at 1/1000th the rate of benzene nitration and gives predominately the meta isomer.

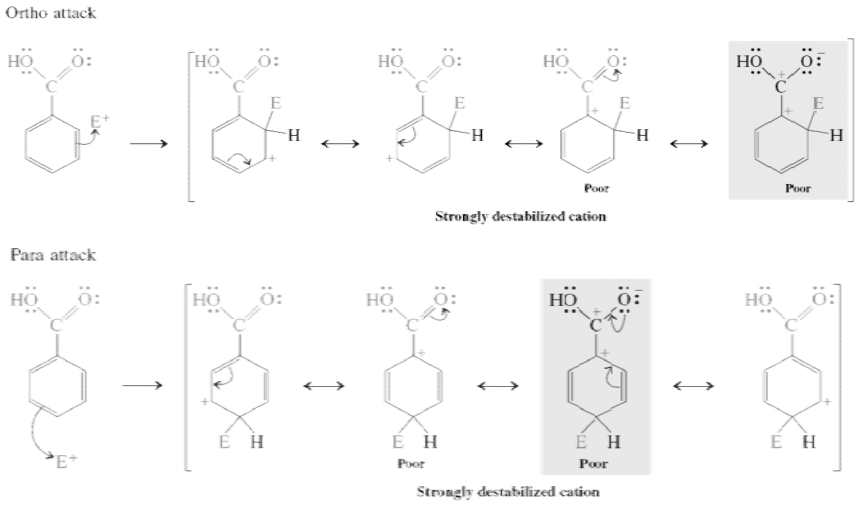
Electrophilic Meta-Nitration of Benzoic Acid



The CO_2H group is deactivating and meta directing.

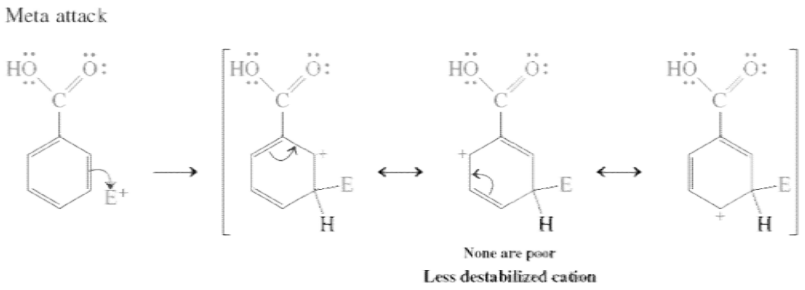
50

The resonance structures of the intermediate cations show why the meta isomer is favored.



The ortho and para transition states each have only two important resonance structures.

51



The meta transition state has three important resonance structures.

The carboxy group is therefore a deactivator (the carboxy group is electron-withdrawing) and a meta director (it deactivates the meta cation intermediate less than the ortho or para).

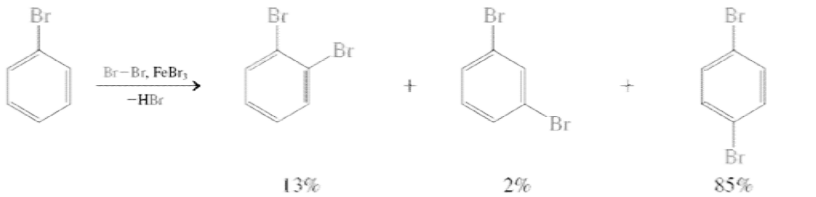
52

There is always an exception: Halogen substituents, although deactivating, direct ortho and para.

Halogen atoms are capable of donating electrons to the benzene ring through resonance and withdrawing electrons inductively (electronegativity).

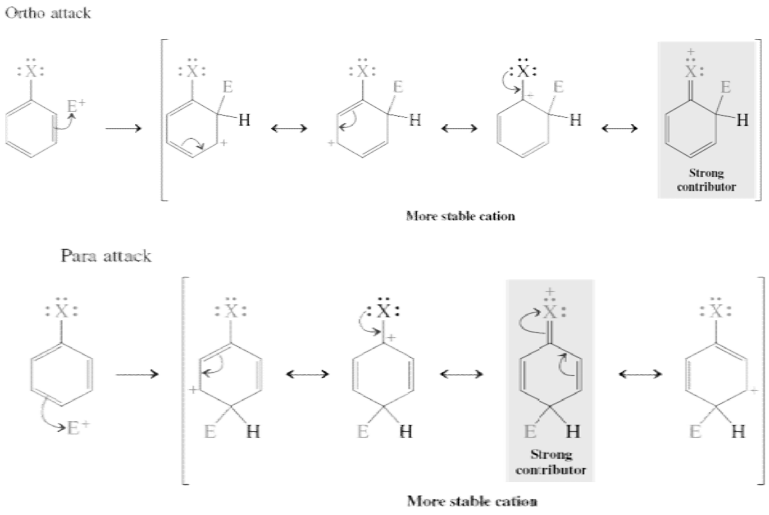
The overall effect is that halogens are deactivating but ortho- and para-directing.

Electrophilic Bromination of Bromobenzene Results in *ortho*- and *para*-Dibromobenzene



53

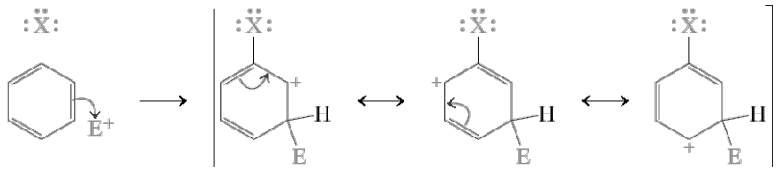
The competition between induction and resonance explains this unexpected result.



Ortho and para attack allow the positive charge of the transition state to be delocalized on the halogen. This outweighs the electron-withdrawing effect.

54

Meta attack



In the case of meta attack, the positive charge cannot be delocalized.

The inductive effect of the halogen is strong enough to make all three cations less stable than that derived from benzene itself.

A halogen atom is deactivating, yet ortho- and para-directing.

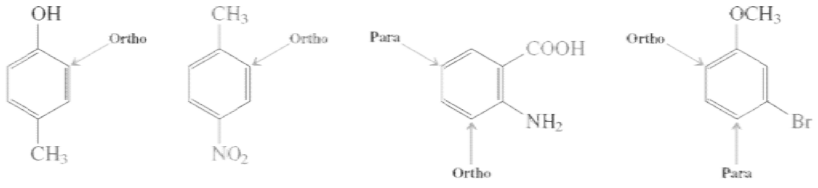
55

Electrophilic Attack on Disubstituted Benzenes

The strongest activator wins out.

A set of simple guidelines allows the product of electrophilic attack on a disubstituted benzene to be predicted:

The most powerful activator controls the position of attack (indicated by yellow arrows).



(There are two equivalent ortho positions to OH, attack at only one of which is marked.)

56

The sense of the directing power of substituents can be changed.

The simplest way to introduce a nitrogen substituent into an arene is by nitration.

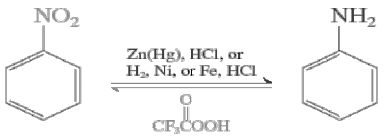
The nitro group (meta-directing, deactivating) can be easily converted into the amino group (ortho, para-directing, activating) by reduction:

Catalytic hydrogenation or

Exposure to acid in the presence of active metals (iron or zinc amalgam)

Oxidation of the amino group back to a nitro group can be accomplished using trifluoroperacetic acid.

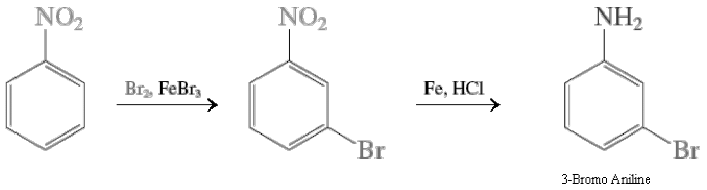
Interconversion of Nitro (Meta Director) with Amino (Ortho, Para Director)



58

To prepare 3-bromoaniline, direct bromination of aniline leads to ortho and para substitution.

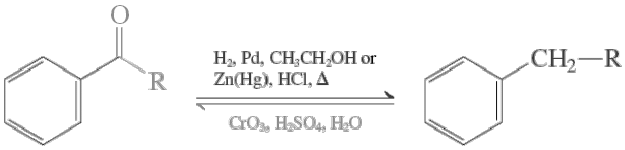
If nitrobenzene is used instead:



59

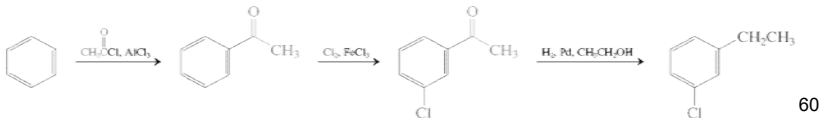
A similar conversion strategy can be used for alkanoyl alkyl

Interconversion of Alkanoyl (Meta Director) with Alkyl (Ortho, Para Director)



In the synthesis of 1-chloro-3-ethylbenzene from benzene, neither chlorobenzene nor ethylbenzene is suitable as the immediate precursor to the product; each is ortho-, para-directing.

Ethanoyl benzene is a meta director which can subsequently be reduced to the ethyl functional group.



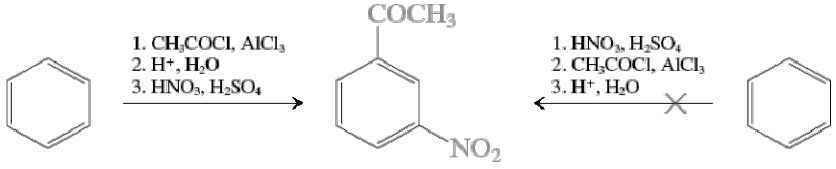
1-Chloro-3-ethylbenzene

60

Friedel-Crafts electrophiles do not attack strongly deactivated benzene rings

Only one of the two synthetic paths below to 1-(3-nitrophenyl)ethanone actually succeeds.

Successful and Unsuccessful Syntheses of 1-(3-Nitrophenyl)ethanone (*m*-Nitroacetophenone)



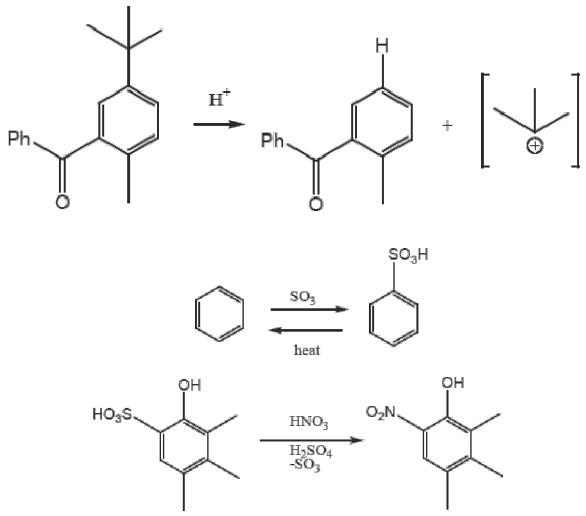
The second route fails primarily due to the extreme deactivation of the nitrobenzene ring. Another factor is the low electrophilicity of the acylium ion compared to other electrophiles in aromatic electrophilic substitution.

As a general rule, neither Friedel-Crafts alkylations nor alkanoylations take place with benzene derivatives strongly deactivated by meta-directing groups.

61

Ipso-Substitution

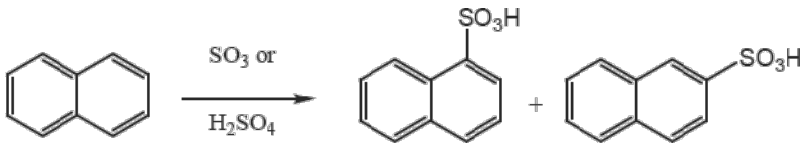
Ipso-substitution usually occurs either with tert–alkyl substituents which can form stable carbocations after attack by the electrophile or in reversible electrophilic substitution reactions such as sulphonation:



62

Reversible sulphonation: thermodynamic *versus* kinetic control.

When we have a reversible attack on a substituted benzene the prediction of the final position of the electrophile is more complicated. To illustrate this we will look at the sulphonation of naphthalene:



naphthalene-1-(or α)-sulphonic acid

naphthalene -2-(or β)-sulphonic acid

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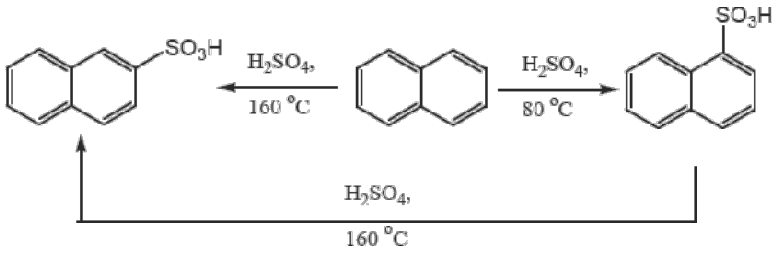
The two isomeric sulphonic acids are formed under different conditions, with the 1-sulphonic acid predominating at lower temperature and the 2-sulphonic acid predominating at higher temperature. Moreover the 1-sulphonic acid is converted into the 2-sulphonic acid at the higher temperature. The 1-sulphonic acid is, therefore, called the **kinetic** product (or the product of kinetic control) since it is formed faster at lower temperatures whereas the 2-sulphonic acid is called the **thermodynamic** product (or the product of thermodynamic control) since it is more stable at higher temperatures:



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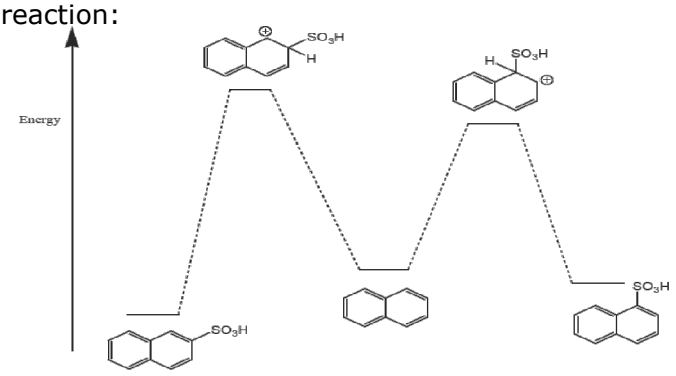
We can understand this behavior if we look at an energy level diagram for the reaction:



- notice that the 2-sulphonic acid is lower in energy than the 1-sulphonic acid i.e. the 2-sulphonic acid is the more stable (thermodynamic) product, as noted above.
- the Wheland intermediate to the 1-sulphonic acid is lower in energy than that to the 2-sulphonic acid i.e. there is a lower activation energy to the former than to the latter leading to faster production of the former i.e. the 1-sulphonic acid is the kinetic product, again as noted above.

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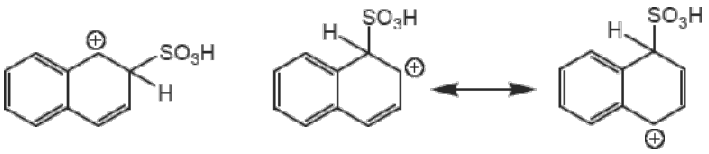
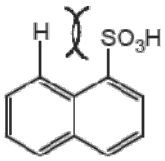
The answer to the first question is that the Wheland intermediate to



the 1-sulphonic acid has two contributing resonance forms whereas that to the 2-sulphonic acid has only one and therefore the Wheland intermediate (and hence the transition state) to the 1-sulphonic acid is more stable:

The answer to the second question is that the 1-sulphonic acid is destabilised by a repulsive force between the sulphonic acid group and a hydrogen on the so-called peri-position. This interaction is absent in the 2-sulphonic acid making this acid more stable:



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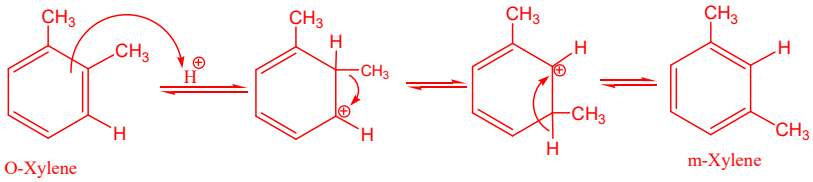
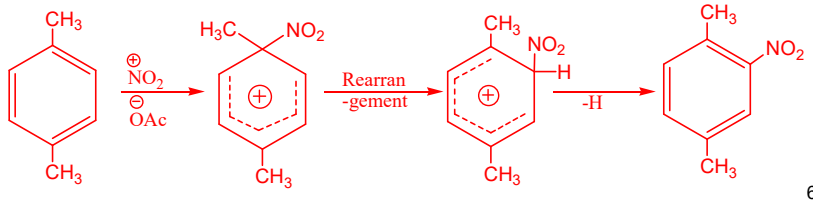
REARRANGEMENT AFTER *IPSO* ATTACK

An alkyl group migrates from one carbon atom on the ring to another one



When the substituent already present on the ring is not a good cationic leaving group, *IPSO* addition will provide a better leaving group after rearrangement.



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DIAZONIUM COUPLING

Preparation

The reaction between aniline and nitrous acid - particularly its reaction at temperatures of less than 5°C to produce diazonium salts.

Nitrous acid decomposes very readily and is always made *in Situ*. In the case of its reaction with aniline, the aniline is first dissolved in hydrochloric acid, and then a solution of sodium or potassium nitrite is added.

$$H^+_{(aq)} + NO_2^-{}_{(aq)} \rightleftharpoons HNO_{2(aq)}$$

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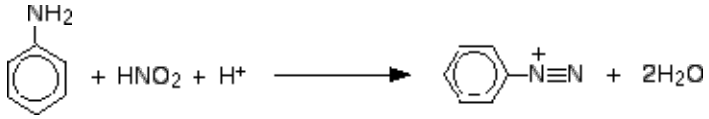
The reaction at low temperatures

The solution of aniline in hydrochloric acid (phenylammonium chloride solution) is stood in a beaker of ice. The sodium or potassium nitrite solution is also cooled in the ice. The solution of the nitrite is then added very slowly to the phenylammonium chloride solution - so that the temperature never goes above 5°C.



If the mixture is warmed, you get a black oily product which contains phenol (amongst other things), and nitrogen gas is given off.

$$C_6H_5NH_2 + HNO_2 \longrightarrow C_6H_5OH + H_2O + N_2$$

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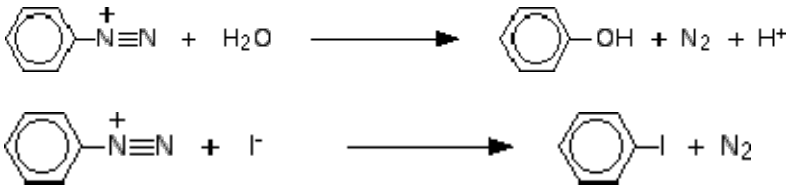
Substitution Reactions of Diazo Compound

Substitution of NN Group



Coupling reactions of diazonium ions

In the substitution reactions above, the nitrogen in the diazonium ion is lost.
In the Azo coupling, the nitrogen is retained and used to make a bridge between two benzene rings.

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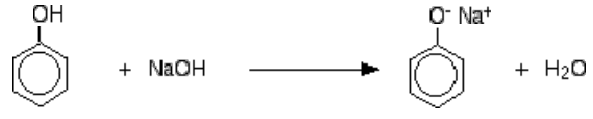
The diazonium ion is an electrophile as there is positive charge on terminal nitrogen.

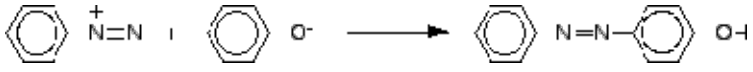
It can react with nucleophlic aromatic compounds (Ar - H) activated by electron - donating groups (-OH and -NH_2) which as strong nucleophiles react with aromatic diazonium salts to give coloured azo compounds in which two benzene rings are linked by a nitrogen bridge.

The nitrogen of the diazonium group is retained in the product. This reaction called coupling and is an electrophilic substitution reaction.

Reaction with Phenol -



sodium phenoxide



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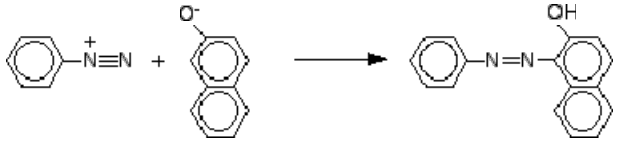
Coloured Azo Compounds

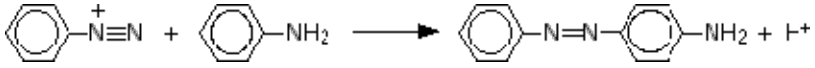
The reaction with β-Naphthol

Solution of β-Naphthol & NaOH is cooled and mixed with the benzenediazonium chloride solution to yield intense orange-red precipitate - another azo compound.



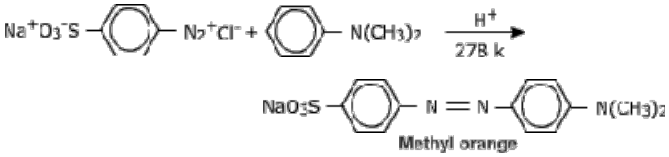
The reaction with aniline

Some liquid aniline is added to a cold solution of benzenediazonium chloride, and the mixture is shaken vigorously. A yellow solid is produced.



These strongly coloured azo compounds are frequently used as dyes known as ***azo dyes***. The one made from aniline is known as "aniline yellow". Azo compounds account for more than half of modern dyes.

Acid base indicator methyl orange is obtained by coupling of diazonium salt of sulphanilic acid and N,N-dimethylaniline.



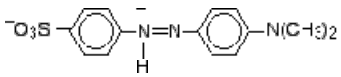
The use of an azo dye as an indicator - methyl orange

Azo compounds contain a highly delocalized system of electrons which takes in both benzene rings and the two nitrogen atoms bridging the rings.

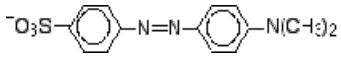
If white light falls on one of these molecules, some wavelengths are absorbed by these delocalized electrons.
The colour you see is the result of the non-absorbed wavelengths.

The groups which contribute to the delocalization (and so to the absorption of light) are known as a ***chromophore***.

Modifying the groups present in the molecule can have an effect on the light absorbed, and so on the colour you see. You can take advantage of this in indicators.
Methyl orange is an azo dye which exists in two forms depending on the pH: (Methyl orange in acidic medium, yellow in basic medium)



red form of methyl orange



yelow form of methyl orange

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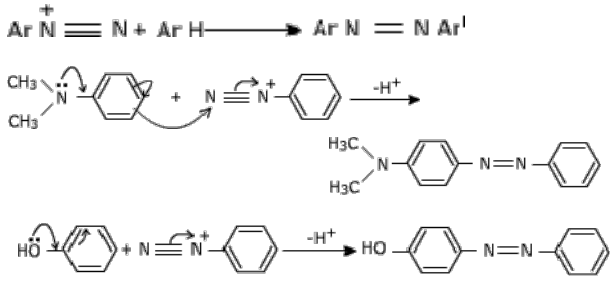
Mechanism of the reaction



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VILSMEIER-HAACK FORMYLATION

'The Vilsmeier aldehyde synthesis' or 'The Vilsmeier-Haack formylation' is a typical aldehyde synthesis employing a formylating agent derived from a formamide and $POCl_3$.

It is a special type of Friedel-crafts reaction, which involves electrophilic substitution of an activated aromatic ring with a halomethyleniminium salt.

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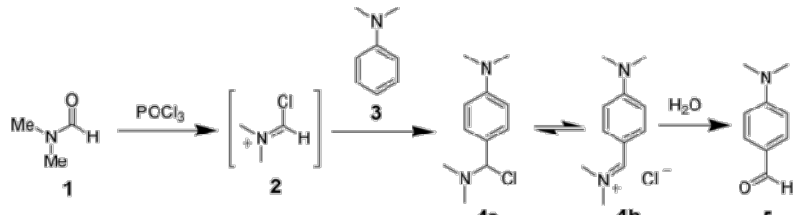
The **Vilsmeier-Haack reaction** (also called the **Vilsmeier reaction**) is the chemical reaction of a substituted amide (**1**) with phosphorous oxychloride and an electron rich arene (**3**) to produce an aryl aldehyde or ketone (**5**).



N:N-DMF

Chloroiminium ion
(Vilsmeier reagent)

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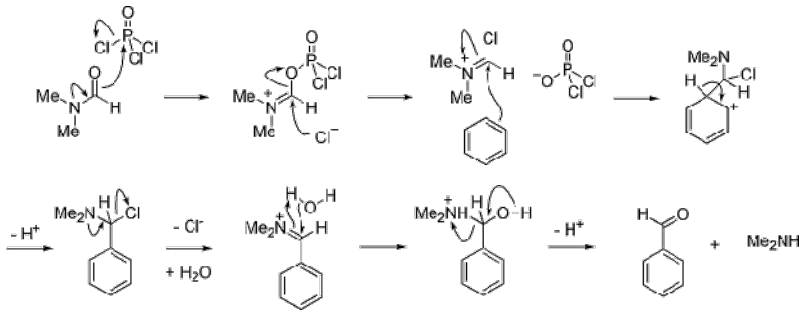
Reaction mechanism



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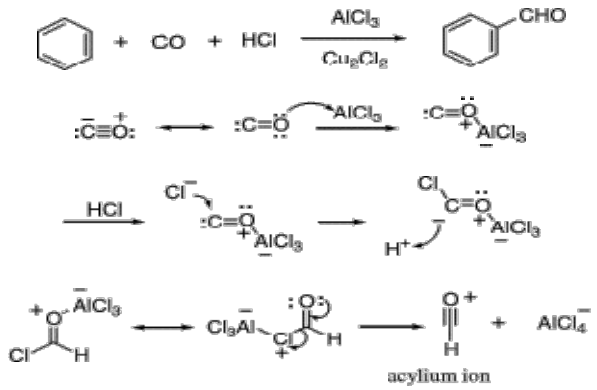
GATTERMANN KOCH REACTION

It refers to a Friedel Crafts acylation reaction in which Carbon monoxide and hydrochloric acid are used in-situ with Friedel Craft catalyst, namely $AlCl_3$ to produce a benzaldehyde derivative from a benzene-derivative in one step.

Benzaldehyde and many aromatic aldehyde are conveniently synthesized by this reaction.



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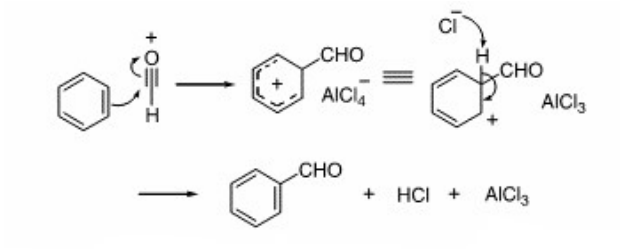

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