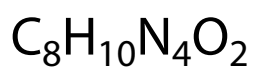
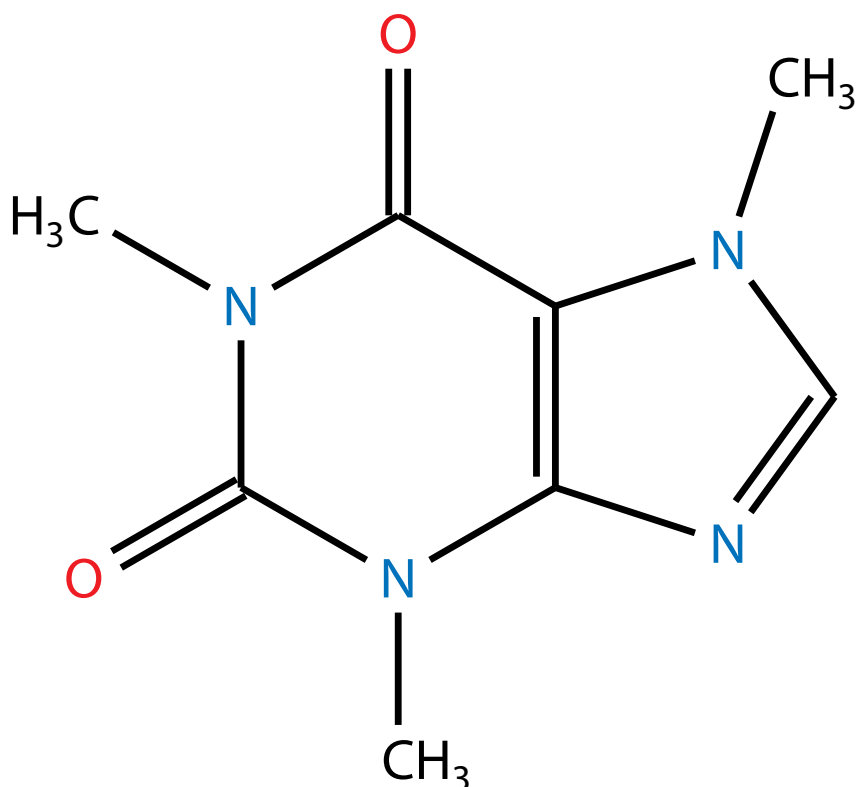


Organic Chemistry



1,3,7-trimethylpurine-2,6-dione

compiled: 2019-05-18

git: e4ff492f05ab7c31e6278dbe0845570d7f46e7f2

Contents

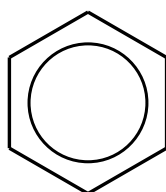
I. Arenes

1. Benzene	1
1.1 Physical Properties	2
2. Substituted Benzenes	2
2.1 Effect of Reactivity	2
2.2 Effect on Positions of Further Substituents	3
2.3 Directing Mechanism	4
2.3.1 Electron-withdrawing Groups	4
2.3.2 Electron-donating Groups	4
2.3.3 Halogen Substituents	4
3. Arene Reactions	5
3.1 Nitration of Benzene	5
3.2 Halogenation of Benzene	6
3.3 Alkylbenzene Reactions	6
3.3.1 Nitration	6
3.3.2 Halogenation	7
3.3.3 Free Radical Substitution	7
3.3.4 Side-chain Oxidation	8

Arenes

1 Benzene

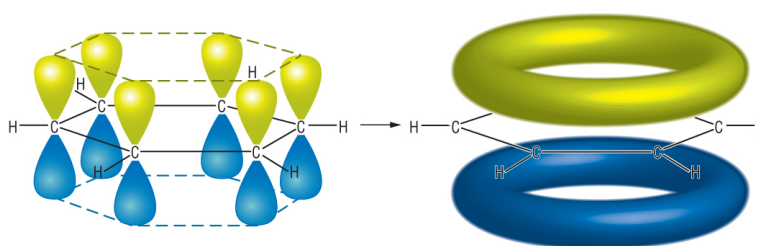
Benzene is simplest possible aromatic compound, or arene. The first known and isolated arene compounds had pleasant smells, such as benzaldehyde. Unfortunately, even though most known arenes now smell terrible and are carcinogenic, the name stuck.



The structural representation of benzene.

The most common form of arene is the benzene ring, or phenyl functional group. Note that aromatic rings with other configurations and structures can also form, such as with nitrogen.

Its basic structure consists of 6 carbon atoms, arranged in a hexagonal fashion. However, unlike cyclohexane, benzene is a flat, planar molecule. All 6 carbon atoms are sp^2 hybridised, giving the following structure:



The trigonal sp^2 hybrid orbitals gives an angle of 120° between each orbital, which is the internal angle of a regular hexagon. Each carbon atom has one bonded hydrogen, making the molecular formula of benzene C_6H_6 .

The carbon atoms are bonded to each other through π -bonds with their unhybridised p-orbitals, while external bonds are done with the sp^2 orbitals. Furthermore, the 6 π -bond electrons are delocalised in the ring, which increases stability.

1.1 Physical Properties

Since benzene is a regular hexagon, each C=C bond is the same length. As a non-polar molecule, it has relatively low melting and boiling points (5.5 °C and 80.1 °C), as well as low solubility in water. Of course, it is soluble in non-polar solvents, and in fact can be used as a solvent in its own right.

Benzene is a volatile, flammable and carcinogenic liquid. Don't drink it. Don't eat it. Don't touch it. It also happens to be colourless, with a distinct 'aromatic' odour.

2 Substituted Benzenes

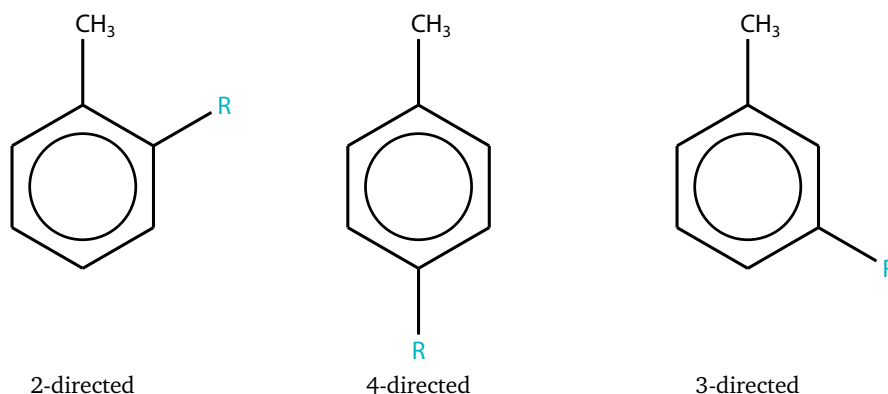
The primary reaction mechanism of benzenes is electrophilic substitution, which involves the electrophiles attacking the electron-rich π -system of the benzene ring. As mentioned previously, certain groups and atoms have the ability to withdraw or donate electrons (induction and resonance), which can affect the characteristics of the benzene ring.

2.1 Effect of Reactivity

If a benzene has electron-donating substituents, (such as CH_3) it will be more reactive, since it would increase the electron density of the π -system and make it a more appealing target for electrophiles. Thus, the ring is said to be *activated*. Conversely, electron-withdrawing substituents (such as $-\text{NO}_2$ or $-\text{CO}_2\text{H}$) *deactivate* the benzene, which decreases the reactivity of the benzene ring by making it less susceptible to electrophilic attacks.

2.2 Effect on Positions of Further Substituents

The main way substituents affect the benzene ring is through the distortion of its π -system electrons, and this distortion can affect the positions of additional substituents on the ring. For instance, an electrophilic substitution of an electrophile R on methylbenzene can produce 3 possible products:



In this case, the CH_3 is considered to be attached to carbon 1.

The exact reasoning for this directing behaviour is complex, and has to deal with the resonance structures of the intermediate benzene, and the distribution of electrons within the π -system. Furthermore, there are only two types of substituents: *2,4-directing* and *3-directing*. Also note that this is similar in concept to major and minor products; both will be produced, except one in much larger quantities.

Substituent	Electron Effect	Directing Effect
Alkyl/aryl groups (eg. $-\text{CH}_3$)	Weakly Activating	2,4-directing
$-\text{OH}$, $-\text{NH}_2$, $-\text{OCH}_3$	Strongly Activating	2,4-directing
$-\text{Cl}$, $-\text{Br}$	Weakly Deactivating	2,4-directing
$-\text{CHO}$, $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}_2\text{H}$	Strongly Deactivating	3-directing

Electronegative atoms (O, N, halogens, etc.) are electron withdrawing (deactivating) when they are indirectly attached to the benzene ring, but are generally electron donating (activating) when directly attached to the benzene ring.

This can be explained by the fact that, when directly attached, there is the possibility of a p-orbital overlap with the π -electron cloud of the benzene, allowing for the electron density to be added to the benzene ring.

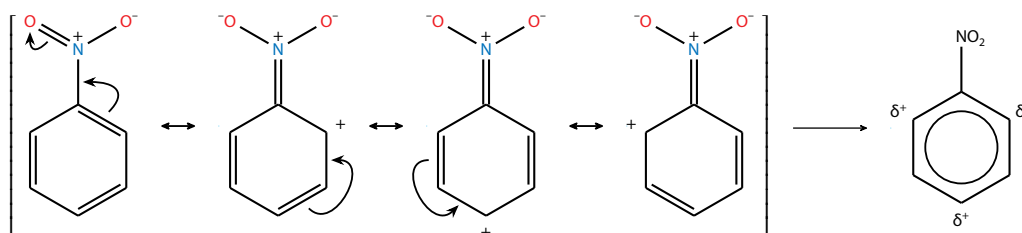
Conversely, when indirectly attached, the effect of electronegativity generally *pulls* the electron density through the σ -bonds. For example, even though N can have its p-orbital overlap with the π -electron cloud, $-\text{NO}_2$ substituents are still strongly deactivating, as the two highly electronegative O atoms can still act to retract electron density away from the benzene ring, *through* the N atom.

2.3 Directing Mechanism

The exact mechanism behind the directing effects of substituents can be explored through the resonance structure of the substituted ring. (The 2, 3, and 4 positions are also called *ortho*, *meta*, and *para* respectively).

2.3.1 Electron-withdrawing Groups

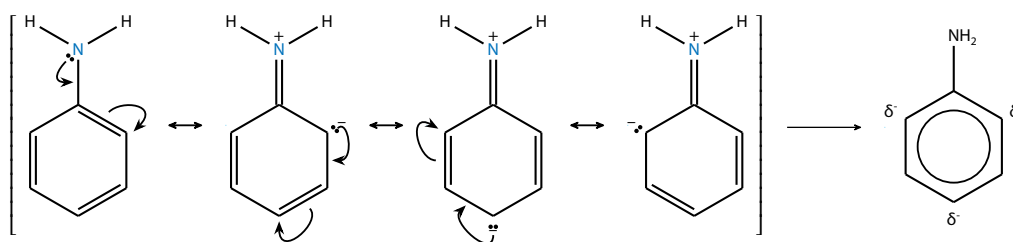
In nitrobenzene, the attached NO_2 group is electron-withdrawing; based on the resonance structure of the π -system below, there will be three points with a partial positive charge (δ^+). Since the substitution requires the attack of an *electrophile*, these positions are *less favourable*. Hence, the electrophile will tend to target the meta (or 3-directed) position, and the NO_2 group is said to be 3-directing.



The δ^+ positions represent areas of low electron density.

2.3.2 Electron-donating Groups

For an electron-donating group such as NH_2 , the reverse is true: there will be 3 areas of *high electron density* that *attract* electrophiles, and as such favours substituting further groups on the ortho/para, or 2,4, positions. Thus, NH_2 is said to be 2,4-directing.



The δ^- positions represent areas of high electron density.

2.3.3 Halogen Substituents

Halogens are a special case, since they can donate electrons through resonance, but can also withdraw electrons through the induction effect due to their substantial electronegativity difference compared to carbon.

The overall effect is that halogens are *ortho/para* (2,4) directors, and they are weakly electron-withdrawing.

3 Arene Reactions

Benzene undergoes substitution reactions rather than addition reactions, since adding atoms to the ring would destroy the delocalised π -system of the ring, which is energetically unfavourable. Instead, the H atoms on the ring are substituted.

The main mechanism for this is electrophilic substitution, the details of which can be found in *the appendix*.

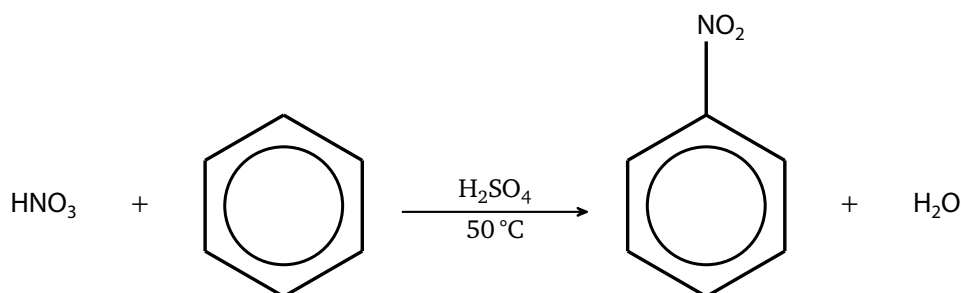
3.1 Nitration of Benzene

The nitration of benzene involves the substitution of one of the H atoms on the benzene with a nitro ($-\text{NO}_2$) group. Note that if there are electron-donating substituents, the benzene ring is said to be *activated*, and it is *deactivated* if there are electron-withdrawing groups.

This affects the reactivity of the benzene ring, and thus the temperatures at which the reaction should be carried out.

Conditions: Concentrated HNO_3 , concentrated H_2SO_4 catalyst.
Constant temperature of 50°C . (activated: 30°C , deactivated: above 50°C)

Observations: *Pale yellow* oily liquid, nitrobenzene.



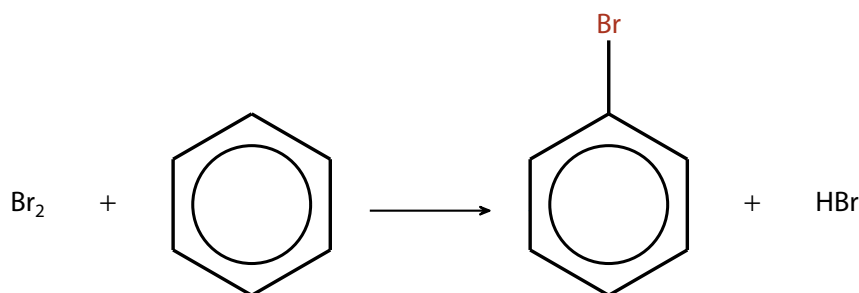
3.2 Halogenation of Benzene

The halogenation of benzene requires Lewis-acid catalysts (FeBr_3 or FeCl_2), and a warm environment. Aluminium-based analogues of these catalysts (AlBr_3 , AlCl_3) can also be used, as can pure metal filings, in which case the catalyst will be generated *in-situ* ($2 \text{ Fe (s)} + 3 \text{ Br}_2 \text{ (l)} \rightarrow 2 \text{ FeBr}_3$).

An in-depth explanation about the need for an anhydrous catalyst can be found [here](#).

Conditions: Warm, anhydrous FeBr_3 , AlBr_3 , or Fe / Al filings (for bromine),
Anhydrous FeCl_3 , AlCl_3 , or Fe / Al filings (for chlorine)

Observations: **Reddish-brown** Br_2 / **yellowish-green** Cl_2 decolourises.
Formation of white fumes of HX gas.



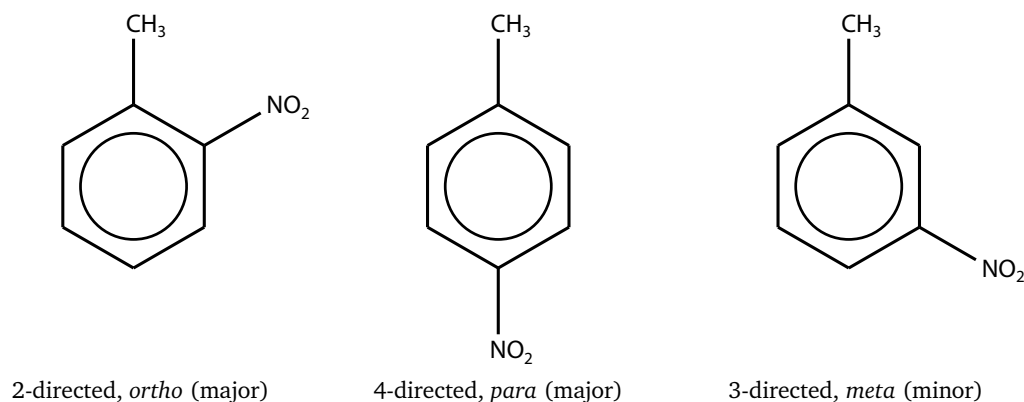
3.3 Alkylbenzene Reactions

3.3.1 Nitration

The nitration of alkylbenzenes gives two major products and one minor product, due to the 2,4-directing nature of alkyl substituents. Note that the required temperature is lower, due to the activating effect of the CH_3 substituent.

Conditions: Concentrated HNO_3 , concentrated H_2SO_4 catalyst.
Constant temperature of 30°C .

Observations: **Pale yellow** oily liquid, nitrobenzene.

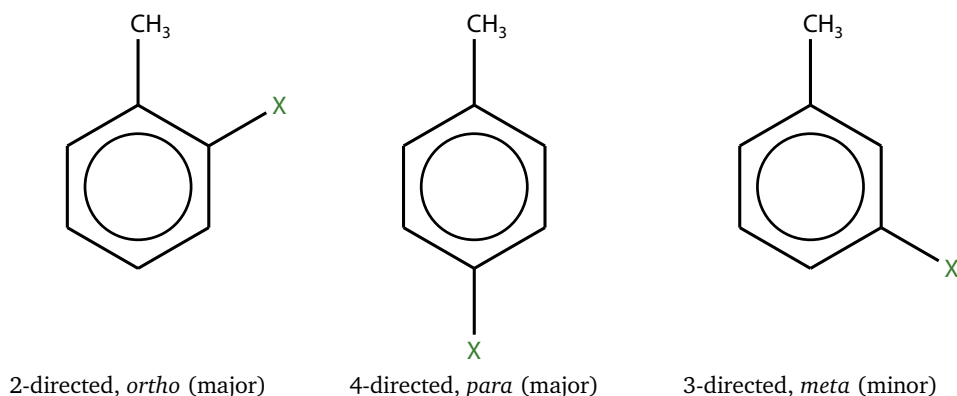


3.3.2 Halogenation

The reagents and conditions for the halogenation of alkylbenzenes are similar to that of normal, unsubstituted benzenes. Again, there are two major products and one minor product, due to the 2,4-directing nature of the alkyl groups

Conditions: Warm, anhydrous FeBr_3 , AlBr_3 , or Fe / Al filings (for bromine),
Anhydrous FeCl_3 , AlCl_3 , or Fe / Al filings (for chlorine)

Observations: **Reddish-brown** Br_2 / **yellowish-green** Cl_2 decolourises.
Formation of white fumes of HX gas.

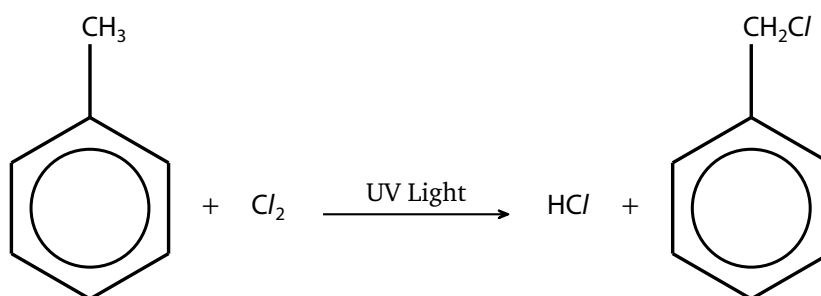


3.3.3 Free Radical Substitution

In the absence of Lewis-acid catalysts, halogens will not react with the benzene ring. In this case, the halogens will react with the side-chain of the alkylbenzene, with UV light.

Conditions: UV Light, Br_2 / Cl_2 gas

Observations: **Reddish-brown** Br_2 / **yellowish-green** Cl_2 decolourises.



Naturally, the alkyl side-chain can also undergo multiple substitutions.

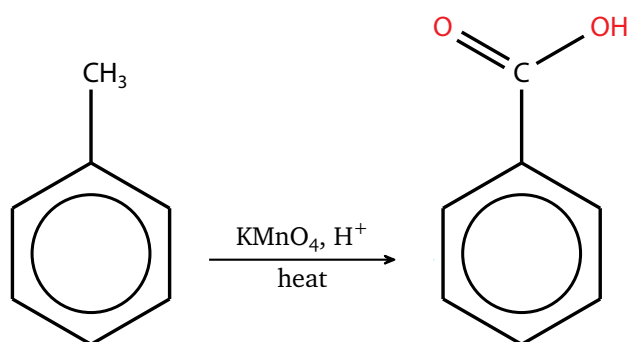
3.3.4 Side-chain Oxidation

When reacted with the strong oxidising agent KMnO_4 and heated, the alkyl chain attached to the benzene will be oxidised; regardless of the length of the chain, benzoic acid is always formed.

Note that the carbon attached to the benzene ring *must* have *at least 1* hydrogen atom (ie. it cannot be a tertiary carbon) for this oxidation to occur.

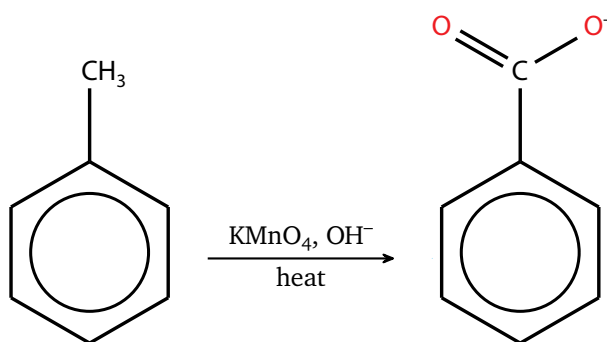
Conditions: Heat, KMnO_4 , dilute acid or alkali.

Observations: **Purple** KMnO_4 decolourises, forming Mn^{2+} (*acid*), or forms **brown** precipitate of MnO_2 (*alkali*).

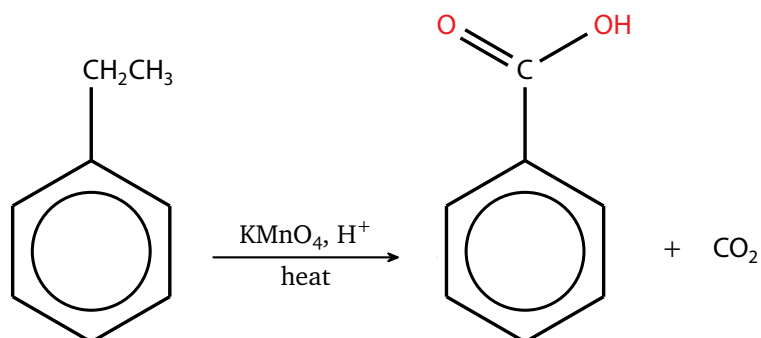


In this case, an acidic medium is used, hence H^+ .

Alternatively, an alkali medium can be used, for instance with $\text{NaOH}_{(\text{aq})}$. Instead of forming benzoic acid however, the benzoate ion is formed.



If the alkyl chain is 2-long, (ie. ethylbenzene), then CO_2 will be formed from the oxidation of the second carbon, in addition to benzoic acid.



If the chain is 3 or longer, then the rest of the chain (apart from the first) will be oxidised to form a carboxylic acid.

