

Lecture 7

The effect of a benzene ring on substituents: Acidity, free radicals, carbocation stability and The Benzylic Carbon

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Reference textbook

- “Organic Chemistry” by Paula Yurkanis Bruice, 8th Edn.
- This lecture – **Chapter 8**, in particular **8.9, 8.10, 8.11**

Learning Objectives – Lecture 7

Section 5– The effects of aromatic rings on substituents

Account for the enhanced acidity of phenol, relative to that of aliphatic alcohols

Discuss and account for the factors affecting the acidity of substituted phenols and carboxylic acids

Discuss and account for the factors affecting the basicity of substituted aromatic amines

Account for the relative ease with which benzyl halides undergo nucleophilic substitution reactions compared to aliphatic halides

Describe and account for the ease of chlorination and bromination of benzylic carbon atoms

Recall the reagents required to effect a range of functional group interconversions, to include: oxidation of alkyl side-chains to give aromatic carboxylic acids (to include an appreciation of the features required in the aromatic substrate in order for oxidation to occur)

Lecture Outline: L7

1. Introduction

2. Acidity

2a. Acids

2b. Bases

3. Substituent effects on pKa

4. The benzylic position

4a. Addition to benzylic alkenes

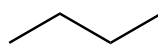
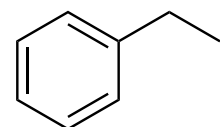
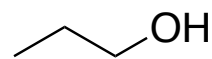
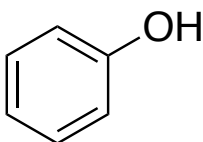
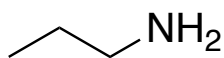
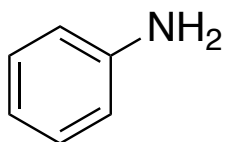
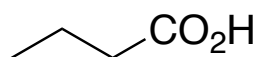
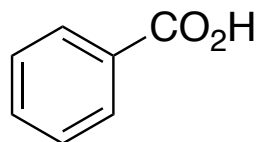
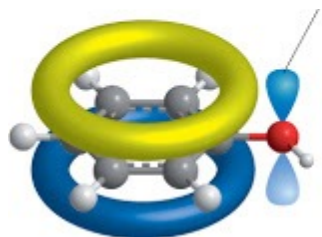
4b. Free radicals at the benzylic position

4c. Benzylic halogen substitution

4d. Oxidation of benzylic carbon

1. Introduction

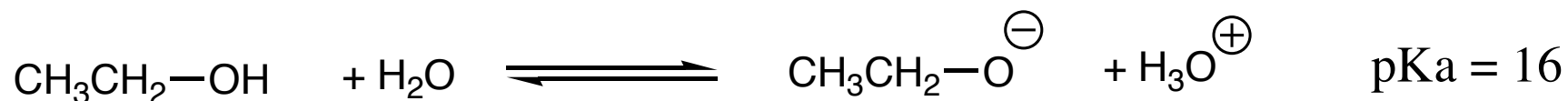
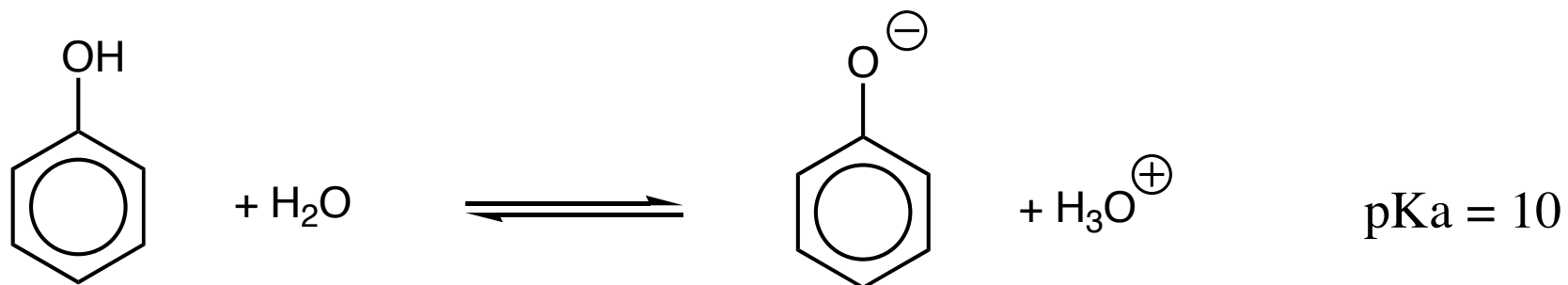
- We have spent most of this module discussing the perspective of how substituents *influence* the reactivity of an *aromatic ring*.
- Of course, the **converse** also true – **aromatic rings also influence the reactivity/properties of a substituent**



- In this lecture we will look at examples of acidic and basic FGs attached to Ar.
- And then we will look at how **substituents** on the aromatic ring can also influence pKa.

2a. Acids - phenol

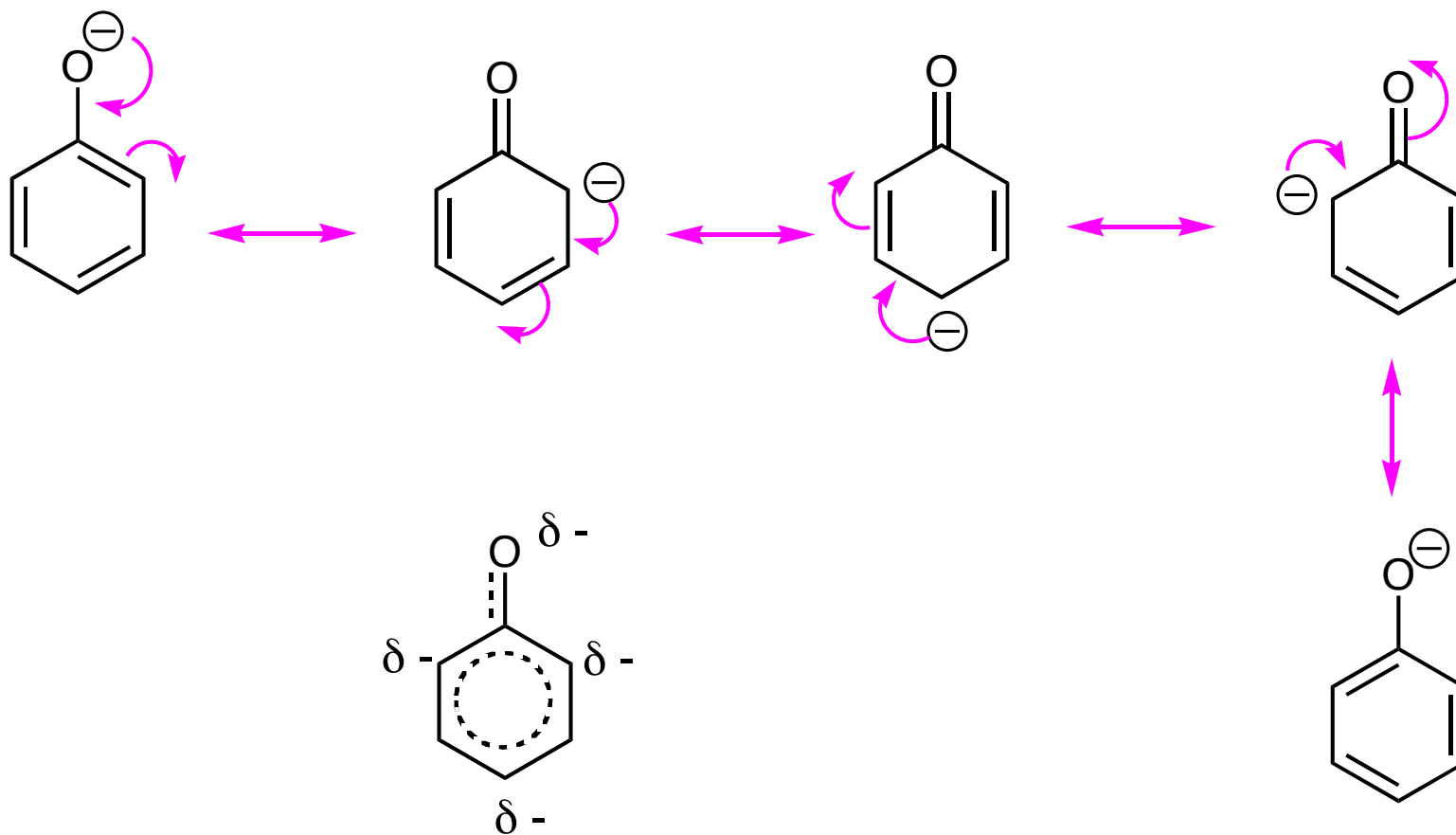
- **Phenol** is a weak acid... but it is **comparatively a stronger acid** than an alkyl alcohol



- the phenolate (phenoxide) ion is resonance stabilised
- the alkoxide is not
- Rephrased - the conjugate base of the phenol is more stable than the conjugate base of the alkyl alcohol

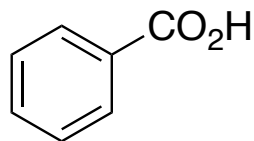
2a. Acids - phenol

- The phenolate (phenoxide) ion is resonance stabilised (**exact slide from lecture 1**)

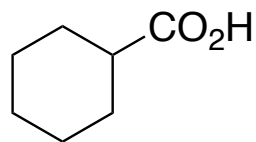


2a. Acids – carboxylic acids

- Benzoic acid is **slightly** more acidic than cyclohexylcarboxylic acid

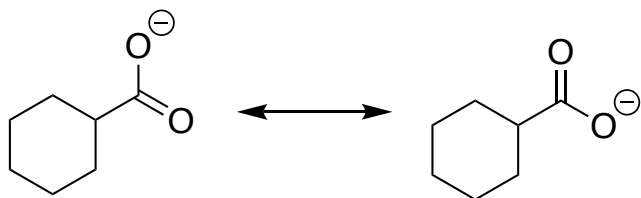
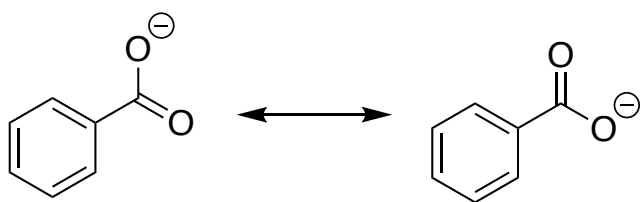


pKa = 4.20

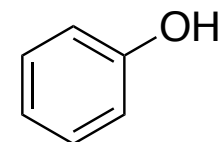


pKa = 4.90

- Why hardly any difference in acidity?
 - Because the carboxylate **can not be** stabilised via **resonance** by the aromatic ring



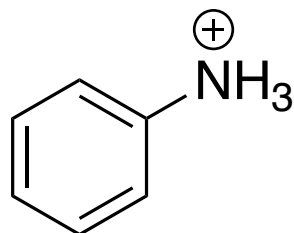
Conjugate base stabilisation by the aromatic ring isn't always the biggest contributor to acidity, e.g. remember benzoic acid is still a **much stronger acid than phenol**, despite phenol's conjugate base being resonance stabilised by the Ar ring



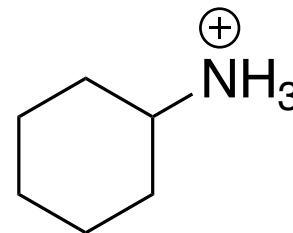
pKa = 10

2b. Bases – aniline

- Protonated aniline is a much stronger acid than protonated cyclohexylamine

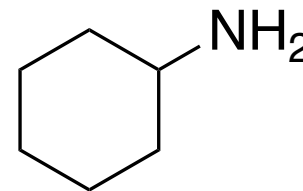
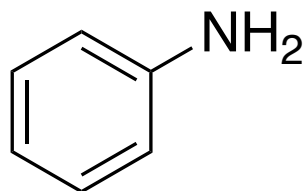


pKa = 4.58



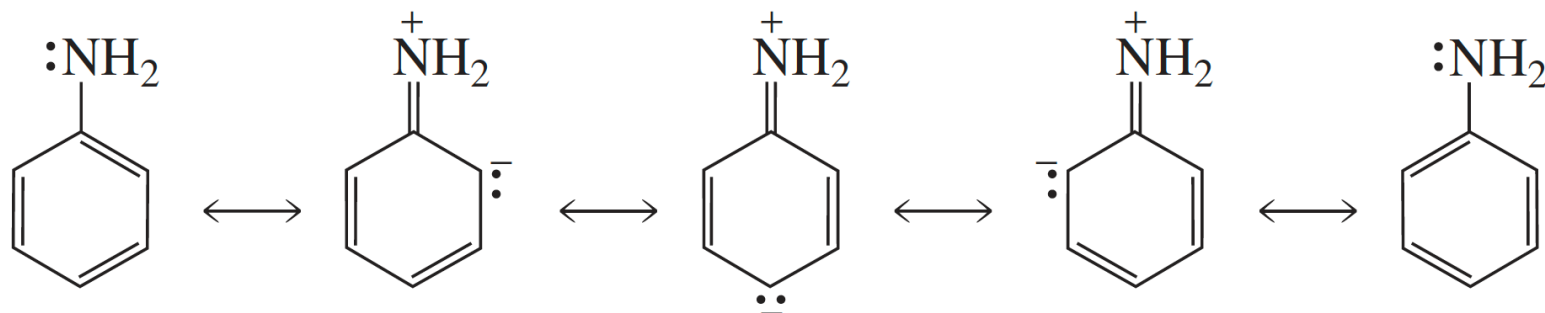
pKa = 11.2

- i.e. cyclohexylamine is a much **stronger base** than aniline



2b. Bases – aniline

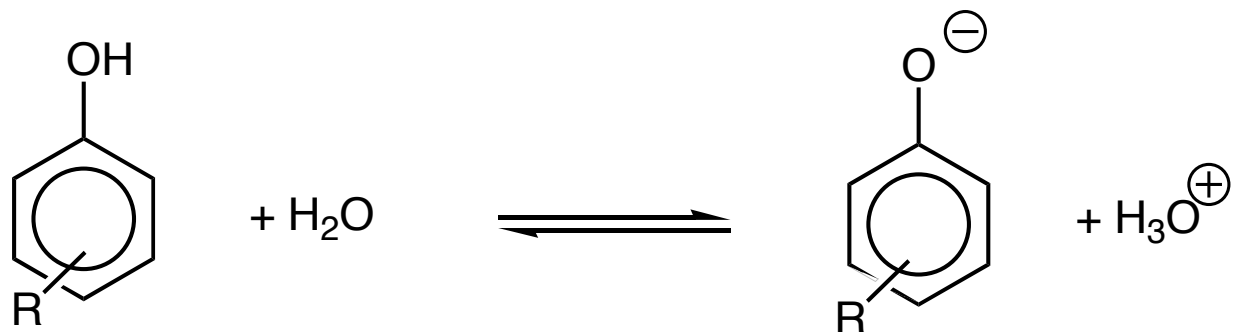
- The lone pair of electrons on aniline's nitrogen is delocalised via resonance



- Cyclohexylamine does not have any **resonance** stabilisation

3. Substituent effects on pKa

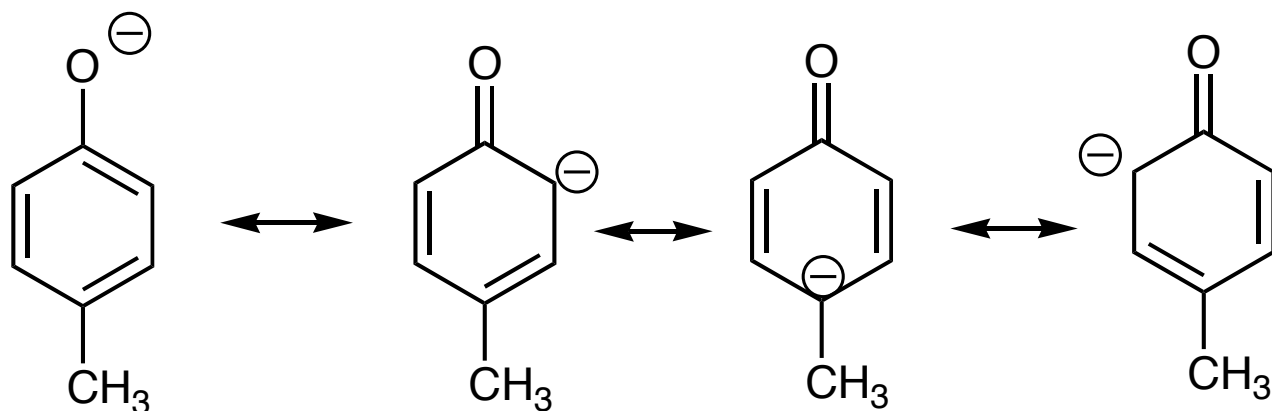
- Electron donation and electron withdrawal by another substituent can influence pKa
- This can be via resonance (+M, -M) and/or via induction (+I, -I)



R	pKa	I/M
H	10	n/a
p-CH ₃	11	
p-Cl	9	
p-OCH ₃	12	
p-NO ₂	7	
m-NO ₂	8	
2,4-(NO ₂) ₂	4	
2,4,6-(NO ₂) ₃	0.4	

3. Substituent effects on pKa

- Showing effects using resonance diagrams...
- 4-Methylphenol (also called *para*-cresol) is **LESS** acidic than phenol because the conjugate base is less stable

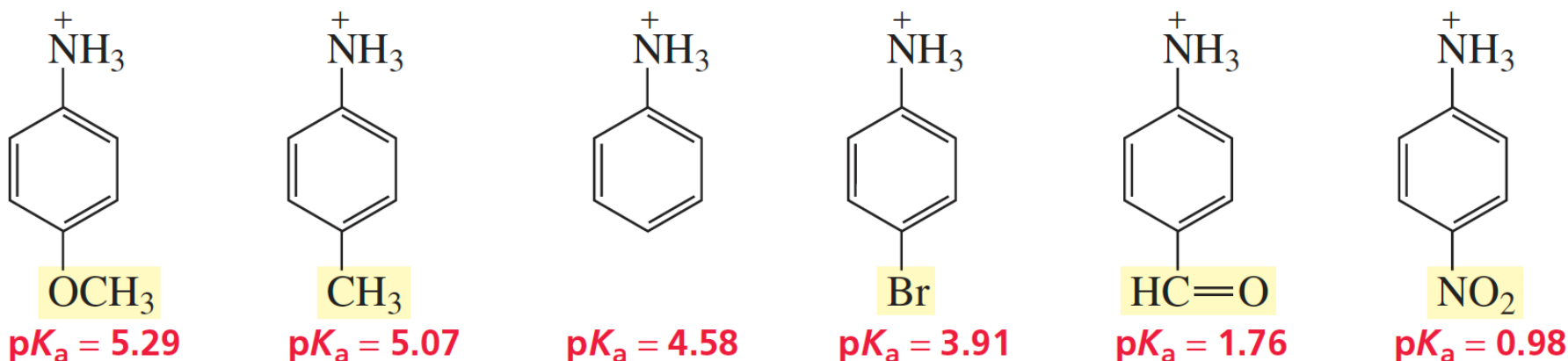


- Whereas 2,4,6-trinitrophenol is **MORE** acidic than phenol

Have a go yourselves - Show using resonance structures why 2,4,6-trinitrophenol is much more acidic than phenol

3. Substituent effects on pKa

- Now using substituted **aniline** as an example...
- Same occurs – EWG substituents increase acidity.

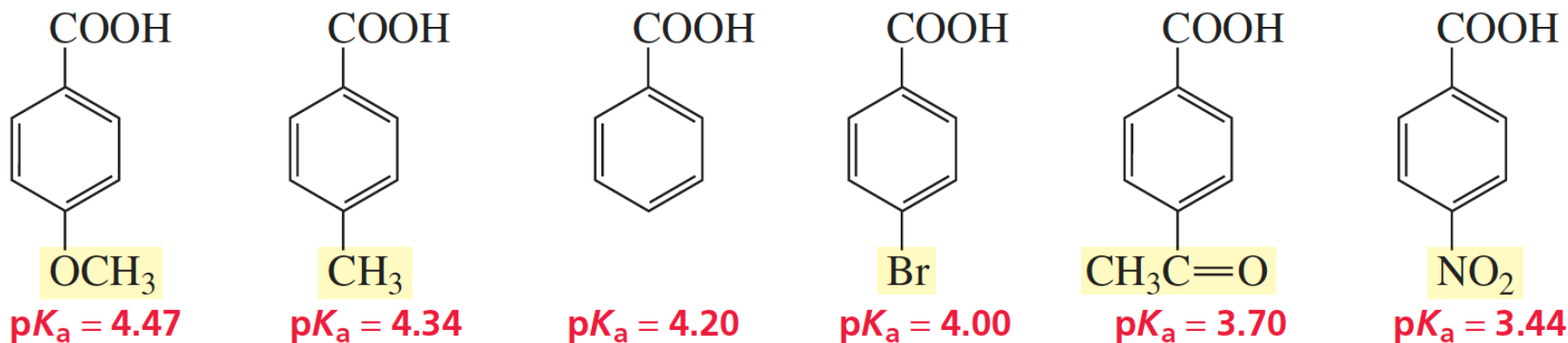


- i.e., the nitrogen of *p*-nitroaniline is less nucleophilic than the nitrogen of *p*-methoxyaniline,
rephrased - '*p*-methoxyaniline is a stronger base when compared to *p*-nitroaniline.'

Have a go yourselves - Show this using resonance structures

3. Substituent effects on pKa

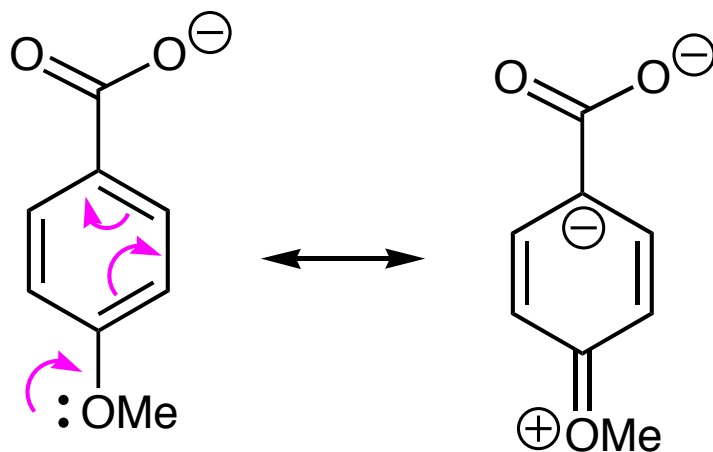
- Now using substituted **carboxylic acid** as an example...
- Same occurs – EWG substituents increase acidity.



- The effect of different substituents (i.e. the difference in pka) is not as profound for benzoic acid. **Why?**

3. Substituent effects on pKa

- As we saw earlier, the carboxylate negative charge **can not be shared by resonance** with the aromatic ring, but substituents can destabilise the carboxylate via their own 'resonance' contributions.



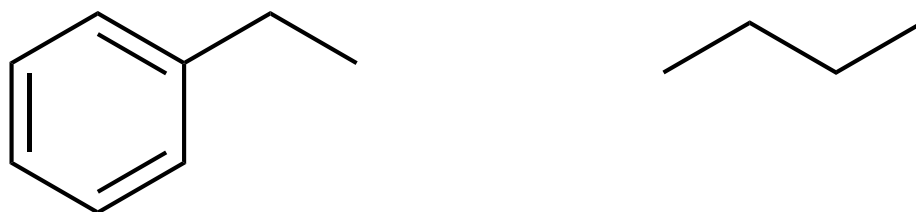
A high energy contributor.
Two -ve charges close to each other are destabilising

*para-Methoxybenzoic acid is a **slightly weaker acid** ($pK_a = 4.47$) than benzoic acid ($pK_a = 4.20$) because its conjugate base is destabilised by the methoxy group's resonance contribution.*

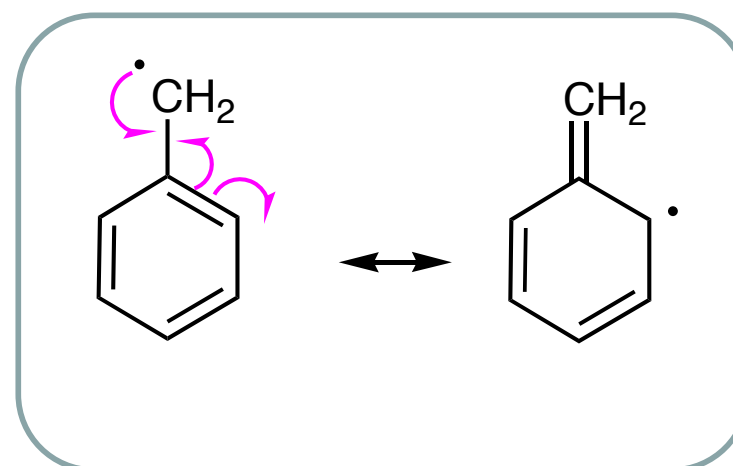
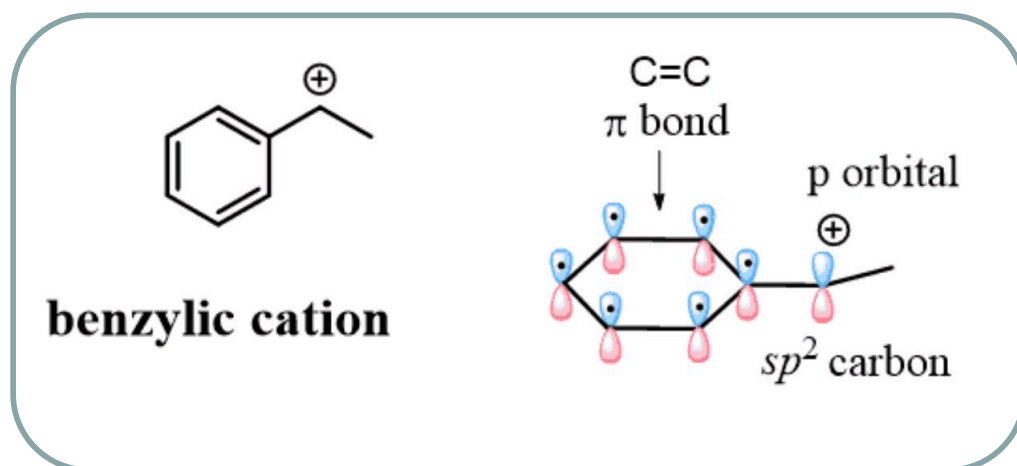
- BREAK

4. Reactivity of the benzylic position

- What's so special about the benzylic position?



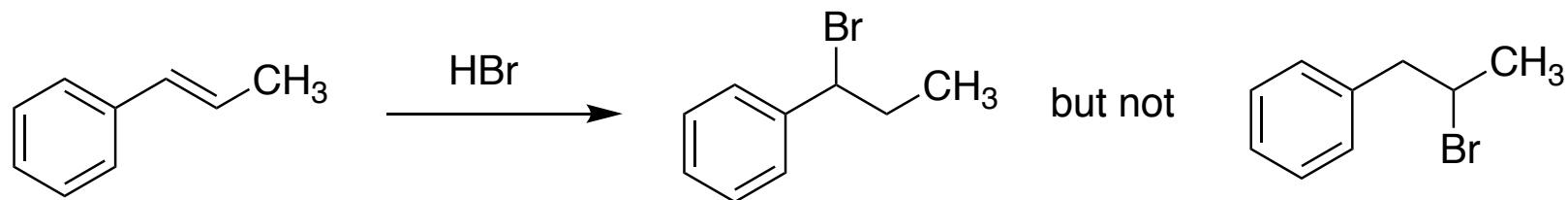
- The benzylic C-H bond is **WEAKER** than a 'normal' alkyl C-H bond
- Charges or a radical on the benzylic carbon can be **resonance stabilised** by the aromatic ring.



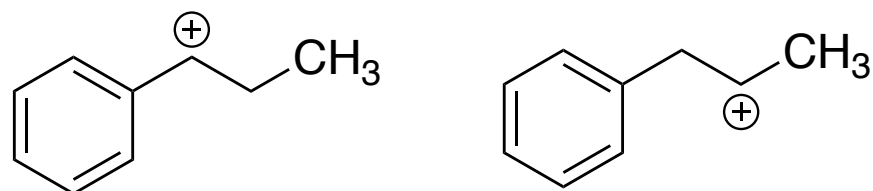
Now let's look at some reactions that can occur at the benzylic position

4a. Benzylic alkenes

- Reactivity of benzylic alkenes:

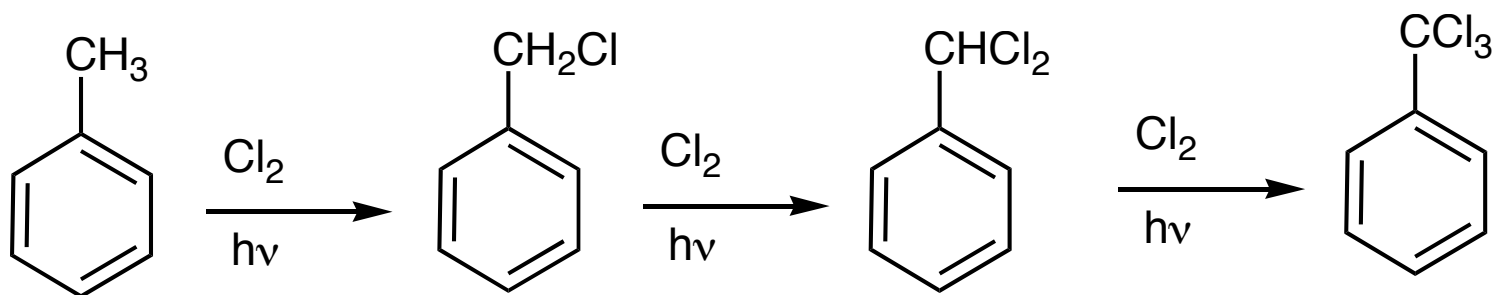


- But both are secondary carbocations.... So what is the most stable carbocation intermediate?



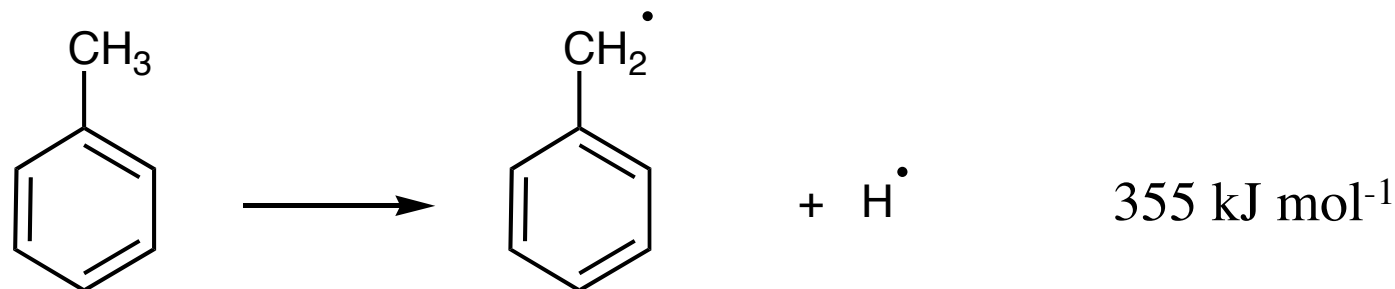
4b. Halogenation of the benzylic carbon

- A benzylic carbon can be easily chlorinated or brominated via a free radical mechanism because of the stability of benzyl radical

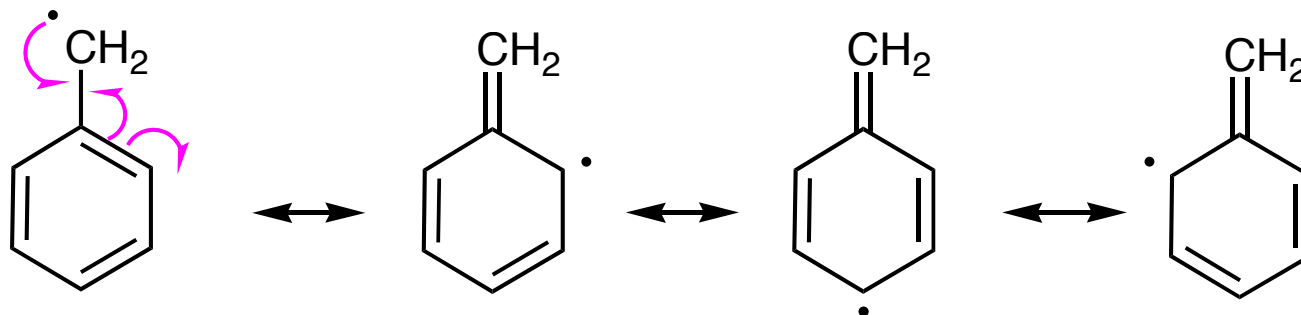


4b. Halogenation of the benzylic carbon

Compare:



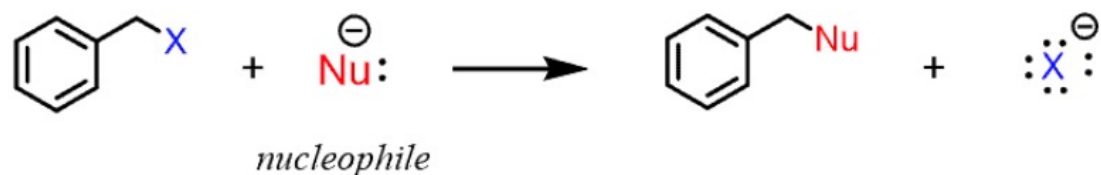
Why is this bond weaker? Examine the radical intermediate. The benzene ring is affecting the C—H bond strength.



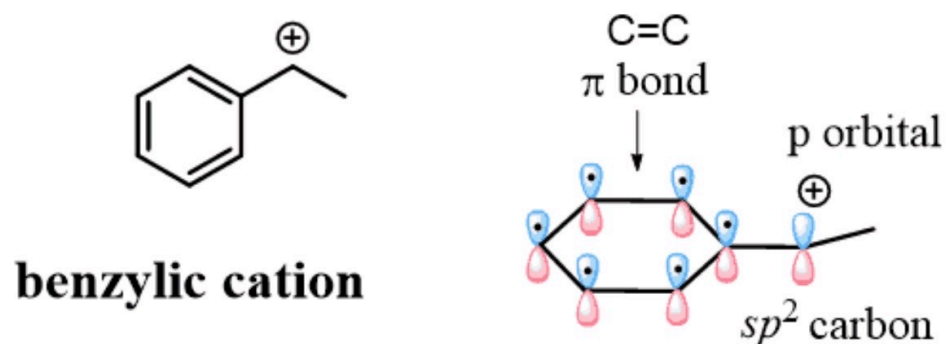
The radical is stabilised by resonance. Therefore the transition state leading to the radical is also stabilised. Lower ΔE_a for the bond breaking.

4c. Benzylic halogen substitution

- Benzylic halides can undergo nucleophilic substitution reactions **more readily** than alkyl halides



- WHY?** Again, because the carbocation is resonance stabilised

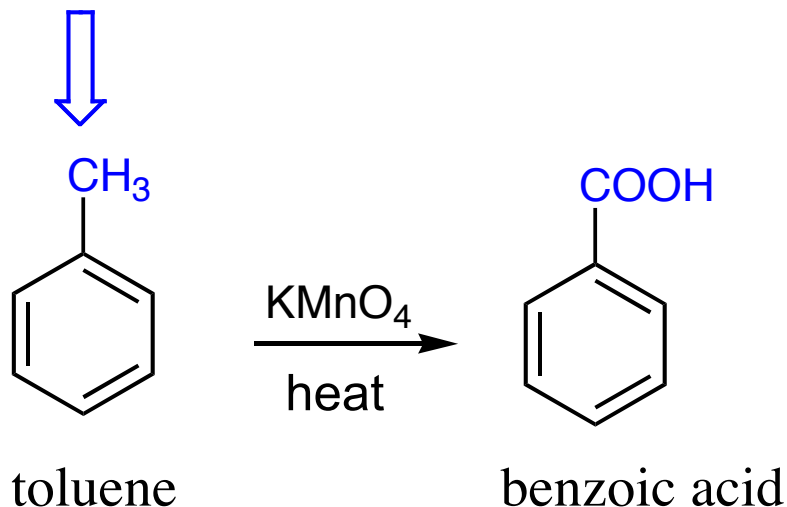


4d. Oxidation of benzylic carbon

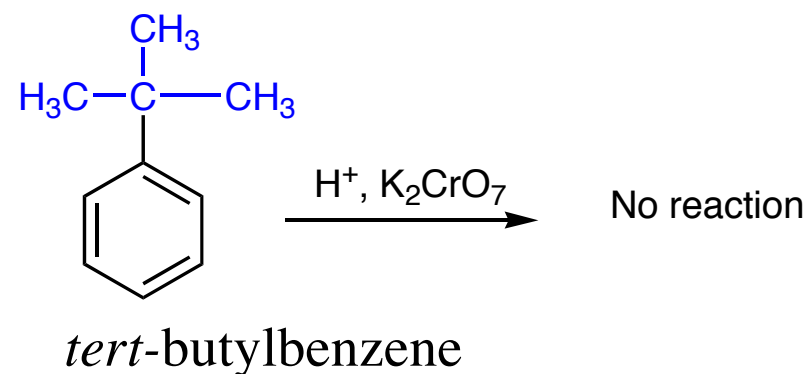
Aromatic carboxylic acids (i.e. CO_2H attached directly to Ar ring) can be prepared by oxidation of alkyl side chains.

- the **benzylic carbon** is oxidised.
- the aromatic ring itself is resistant to oxidation (*under these conditions*)
- the carbon bound to benzene ring **must be bonded to 1 hydrogen or more**.

this carbon atom
is easily oxidised

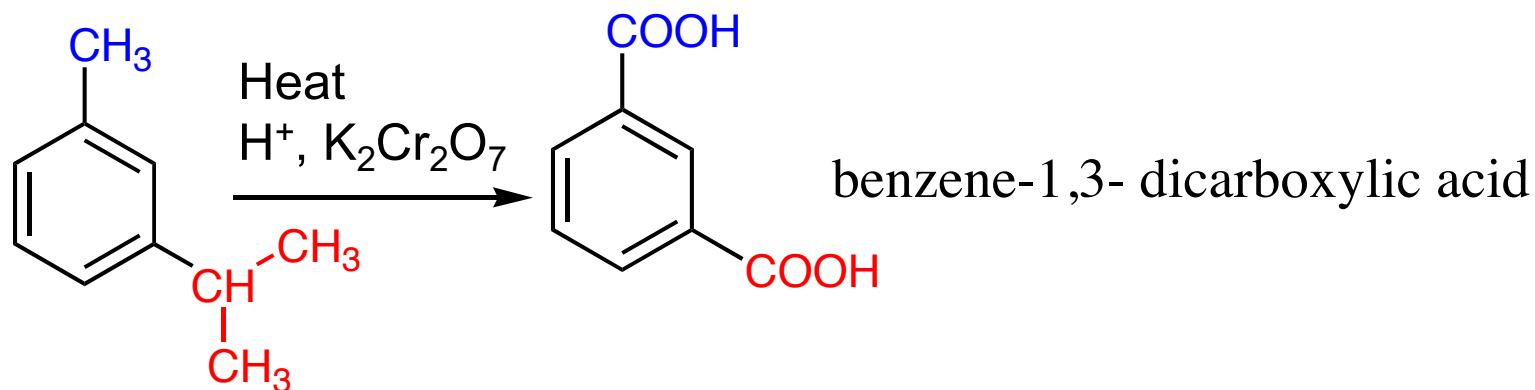


But without a benzylic hydrogen -



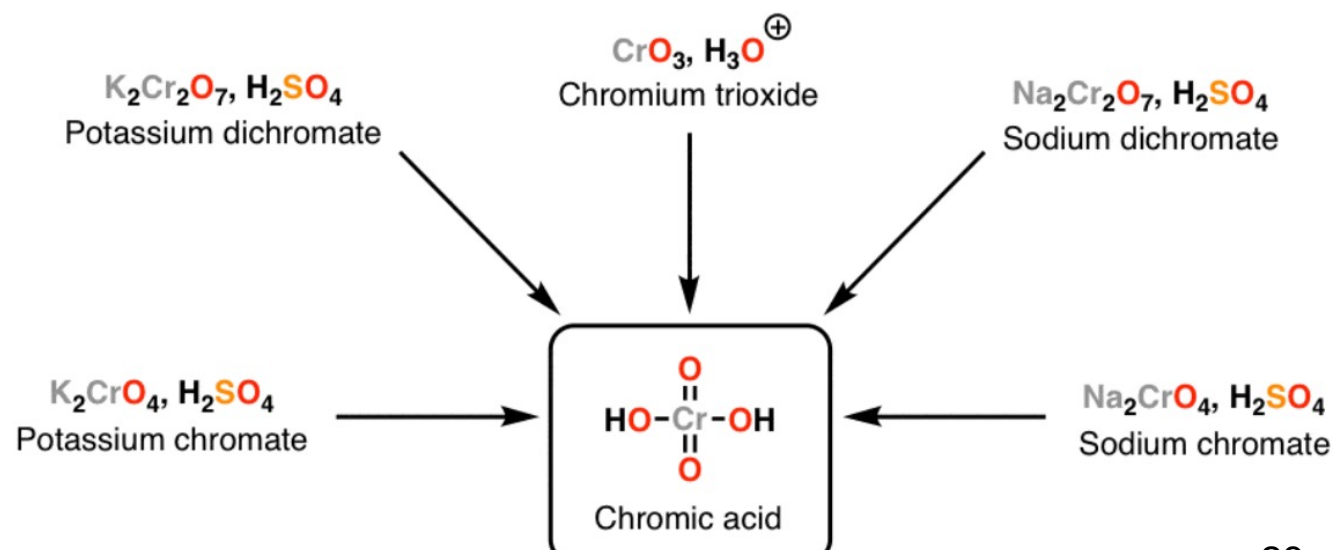
4d. Oxidation of benzylic carbon

Regardless of the length of the alkyl substituent, it is oxidised to Ar-CO₂H (provided there is a hydrogen on the starting material's benzylic carbon)



Chromic acid H_2CrO_4
generated *in situ*

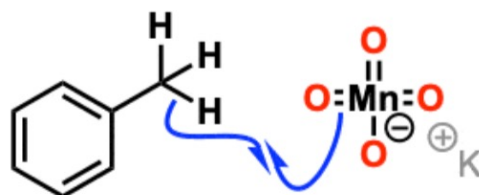
There are several
ways to do this



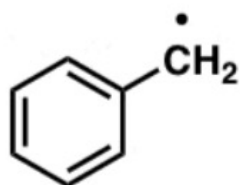
4d. Oxidation of benzylic carbon

Why does oxidation at the **benzylic** position occur more readily than e.g. a 'normal' alkane carbon?

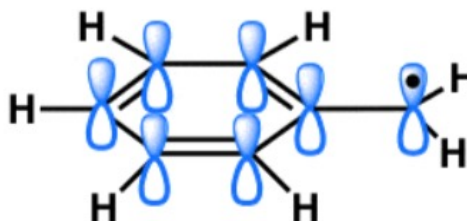
- The benzylic **C-H bond is weaker** than a normal alkyl C-H bond, the free radical intermediate is **resonance stabilised** by the aromatic ring



The benzyl radical IS stabilized by resonance, since the p-orbital is aligned with the neighboring pi system:



Benzyl radical



Benzyl radical
(side view)

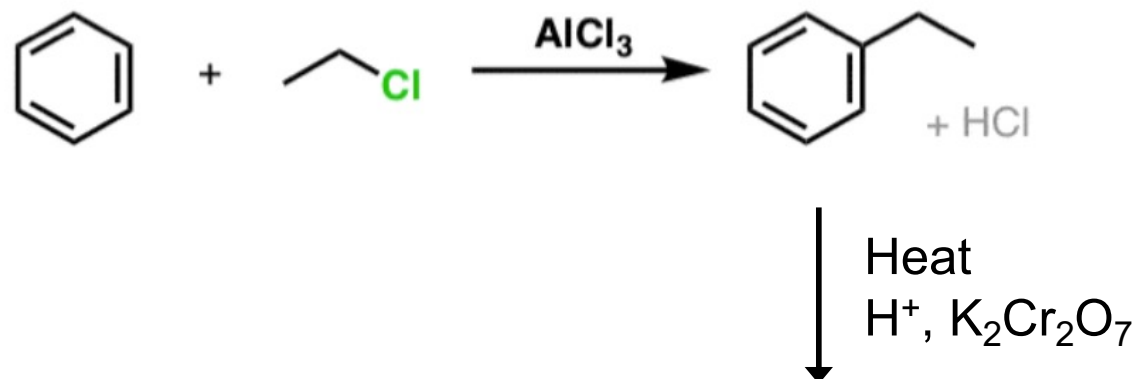
p- orbital aligned with
pi system of benzene ring

stabilized by resonance!

4d. Oxidation of benzylic carbon

Why is this reaction so useful?

- It is difficult to directly attach (from 'H') CO_2H onto an Ar ring.
- E.g. can't place CO_2H directly on Ar using Friedel Crafts Acylation, so FC alkylation followed by oxidation is a good alternative.....



Oxidation of alkyl chains **NOT** attached to an Ar ring can be achieved using different reagents in multiple steps, but it is very hard to **selectively** oxidise a non-benzylic aliphatic C-H bond..... (!)