

Year 2, Organic Chemistry, Chapter 26:

Organic Synthesis

- In Organic Synthesis what you are asking is “How do I get from somewhere to somewhere else?”. The example that I used in an earlier Chapter (and, for those of you are applying to one of the prestigious Universities in London) this time I will insert the Universities to which I was alluding “How do I get to South Ken (**Imperial**) / Euston Square (**UCL**) / Denmark Hill (**King’s**) from Gerrards Cross?”.

- In essence, for Organic Synthesis you need to construct an Info Tree or Table showing the route into and out of every major compound that you are required to have a knowledge of at ‘A’ Level viz.

- Alkanes	Saturated Carbon compounds (C_nH_{2n+2})
- Alkenes	Species with one or more double bonds
- Alcohols	Compounds with one or more “–OH” substituents
- Halogenoalkanes	Compounds with one or more “–Hal” substituents
- Benzene (and its sister Arenes)	C_6H_6 derived compounds
- Aldehydes	“ $R.C=O(H)$ ” or “ $RCHO$ ”
- Ketones	“ $R.C=O(R')$ ”
- Carboxylic Acids	“ $R.COOH$ ”

and for Organic Synthesis purposes you would be well-advised to have small Info Trees of some of the compounds that I have mentioned as species that will take you from one compound into another e.g.

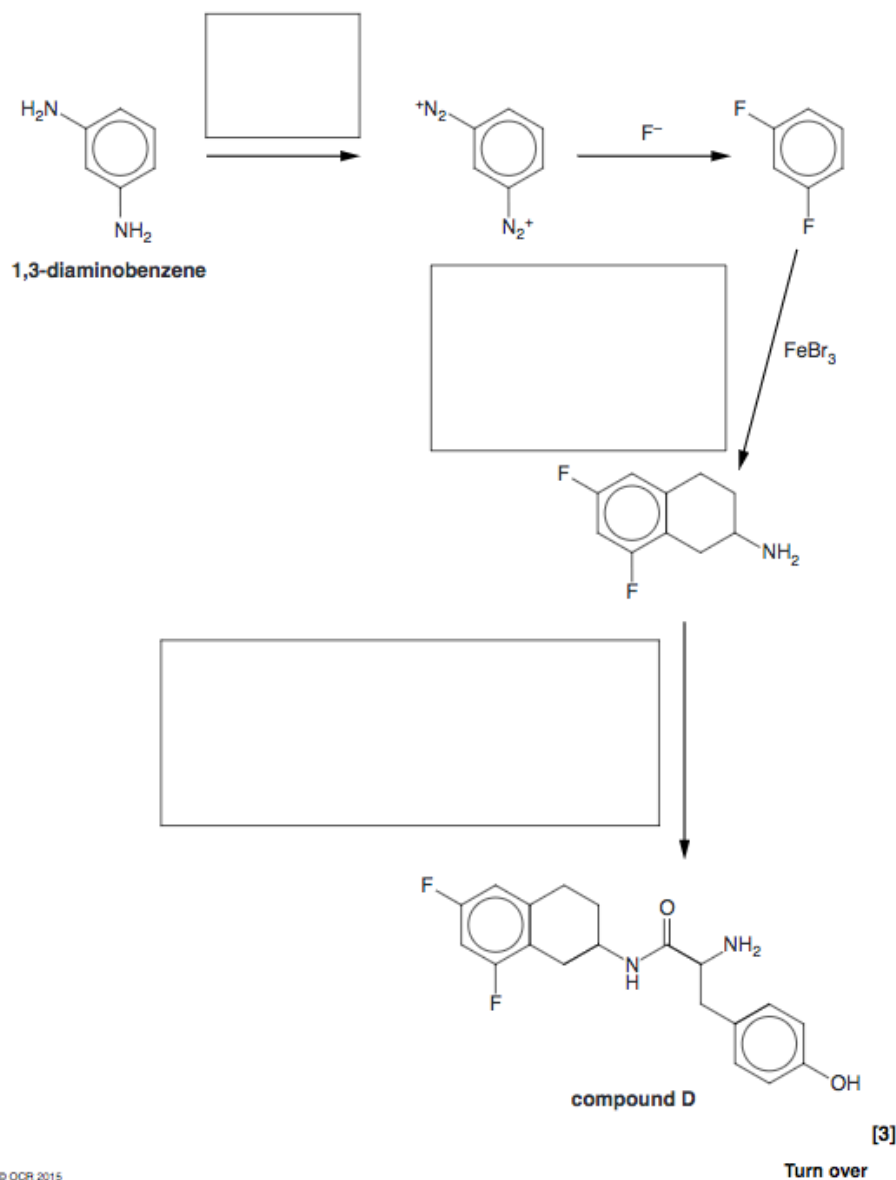
- Amines	“ $R.NH_2$ ”
- Amides	“ $R.C=O(NH_2)$ ”
- Nitriles	“ $R-C\equiv N$ ”

- Where possible, in both my First Year and Second Year books I have endeavoured to provide you with an Information Tree or Table for every one of the Organic substances above, and it is up to you to memorise them. When I was doing my ‘A’ Levels, I used to get through every one of my info trees in my head in 30 minutes. In the weeks leading up the exams I did that every night – not just for Chemistry but for every ‘A’ Level that I was doing.¹
- Let me start by showing you Question 2(d) from the OCR Rings, Polymers and Analysis exam paper of June 2015.

¹ In later life I had a modestly successful career in the City from 1970 to 1990 because I then prepared meticulously for everything that I did before I did it.

(d) The types of reaction in (b) and (c) can be used to synthesise compound D, as shown in the flowchart below.

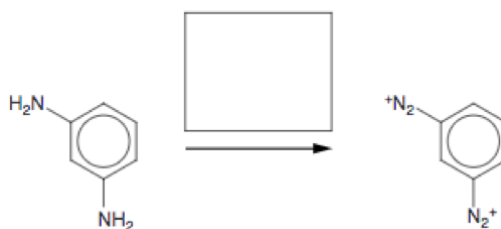
- (i) Complete the boxes below to suggest formulae for the reactants involved in the synthesis of compound D.
Give structures for organic compounds.



I teach 'A' Level Chemistry, and I do not for the life of me know what Compound D is (and luckily, neither do you need to know what it is)!

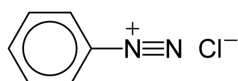
Now can you see why this Chapter is quite important?

- In the first part of the synthesis, you are going from $C_6H_4(NH_2)_2$ to a double diazo phenyl compound. It looks daunting, but keep your cool.



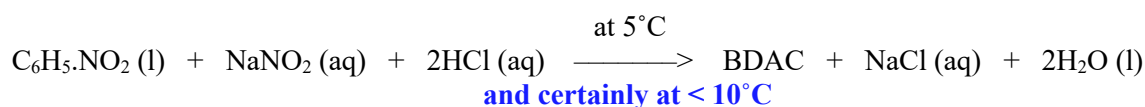
- In Chapter 16 of “Year 2, Organic Chemistry, Chapter 16, Azo Reactions”, you will see the following

Stage 1 Benzene (C_6H_6) \longrightarrow Nitrobenzene ($C_6H_5.NO_2$)
 Stage 2 Nitrobenzene ($C_6H_5.NO_2$) \longrightarrow Phenylamine ($C_6H_5.NH_2$)
 Stage 3 Phenylamine ($C_6H_5.NH_2$) \longrightarrow Benzenediazoniumchloride ($C_6H_5.N^+ \text{triple bond N}$)

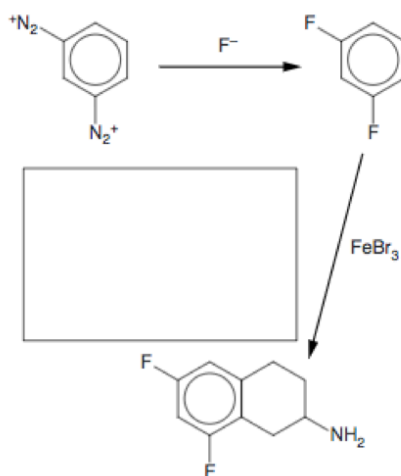


and that is the $C_6H_4(N^+_2)_2$ at the right hand of the diagram above, and in Chapter 16 I told you that with regard to going from Phenylamine to Benzenediazoniumchloride (BDAC)

BDAC can easily be obtained by reacting Nitrobenzene with “Nitrous acid” (HNO_2)
 – but nitrous acid is very unstable and it decomposes very quickly, therefore the nitrous acid has to be made and used on-the-spot (*in situ*) by reacting $NaNO_2(aq)$ with 2 $HCl(aq)$ and we would thus get

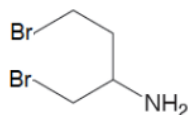


- As you can see therefore, you **do** know how to make the first conversion in Question 2(d) from the OCR Rings, Polymers and Analysis exam paper of June 2015, and all that the examiners in fact required from you was to state that you had to use “ HNO_2 ” (and they did not even require you to explain that it had to be created ‘in situ’ and how it could be so created). They just wanted you to write “ HNO_2 ” in the box provided.
- Now, as it happens, in the next bit of the question



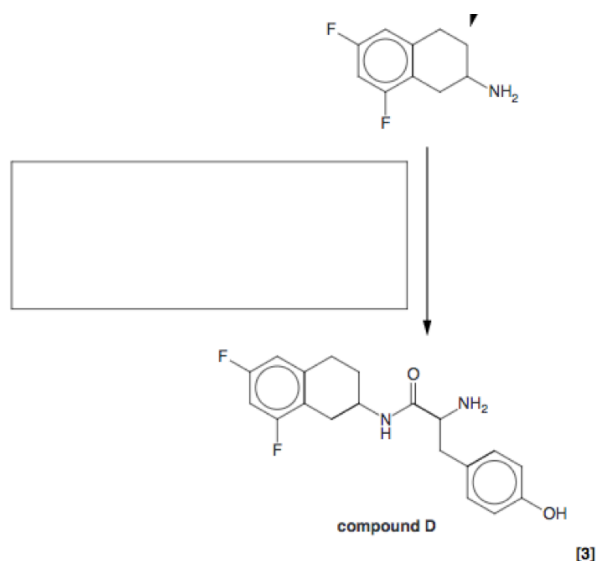
they did not ask you about the conversion of the double diazo compound to $C_6H_4F_2$ (which is not part of the ‘A’ Level Syllabus). The question was actually about the conversion into the molecule at the bottom of the above diagram.

- However, they gave you a massive hint because they showed you FeBr_3 , and **if you see FeBr_3 or AlCl_3 then you know that you are dealing with a Friedel-Crafts' catalyst** – and in Chapter 05, I told you all about Friedel-Crafts' catalysts/Halogen carriers. The only thing that you had to work out therefore was what to add to FeBr_3 in order to get $\text{C}_6\text{H}_2\text{F}_2\cdot\text{C}_4\text{H}_7\text{NH}_2$, and I have to admit that I think that the answer is not within the remit of the 'A' Level Syllabus, but the answer was



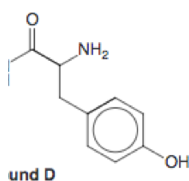
and I would not have expected any of my students to get that answer because the compound above is a most unusual one.

- The last bit of the question then wanted you to make the following conversion

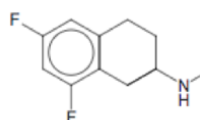


and I have to say that I teach 'A' Level Chemistry and I have not the faintest idea what compound D is – and I do not suppose that you do either!

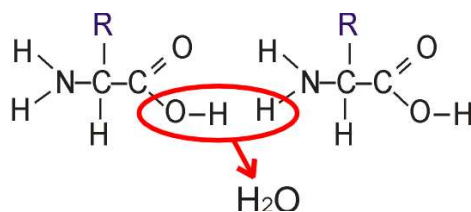
- However, I hope that you can see that what they have done is to add



onto

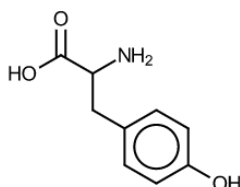


and I hope that you will also have seen that this involves the classic Amide/polypeptide Condensation link between an Amine and a Carboxylic Acid viz.



and I told you about this in “Year 2, Organic Chemistry, Chapter 25, Zwitterions and Polymers”.

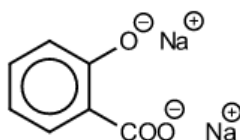
- The answer that they wanted you to give them therefore was the molecule with an ‘acid’ (–COOH) at one end and a Phenol at the other end viz.



- Now, I personally believe that this was an unfair question, not in the sense that it asked for material that is not in the ‘A’ Level Syllabus (because it clearly is in the Syllabus because I have taught you all this), but **I think that it was unfair in the sense that the context in which the Syllabus was being tested was too challenging**. A few of my students were competent enough to answer the question, **but not one of them was able to get it right in the time allowed**² – the time given to answer Section (d) of the question being 3 minutes and **that IS unfair!**
- OK, now you have an idea of the sort of the *extremely challenging questions* that you could be asked in Organic Synthesis – and I have to say that if you get an A* in this sort of Chemistry paper, then you genuinely are of outstanding calibre and you have every chance of going on and getting a First in whatever subject you choose to read at any of the most prestigious Universities in the world. **Well done if you can do that sort of advanced Chemistry. You really do have a good brain!**
- Let me do for you another question – this one being Question 1 from the “Rings, Polymers and Analysis” paper of June 2014.

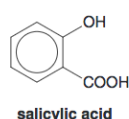
² ... including the ones who were offered places at either Oxford or Cambridge.

- In the first part of the Question (about Salicylic Acid) all that they wanted was for you to recognise (as I told you in the Chapter on Phenols, Chapter 15) that in a Phenol the locking of the electrons in the unhybridised 'p' orbital on the Oxygen atom into the delocalised π ring of the $-C_6H_5$ means that the " $-OH$ " bond is weakened and the proton becomes more easily dissociable. Phenol is therefore a weak acid (with a pK_a of 10.0), and in the diagram given, there are therefore **two** Protons that can be dissociated (one from the Acid and one from the Alcohol bit) each of which will react with an alkali (in this case " $NaOH$ ") to form a Sodium salt. **That is what they wanted you to recognise** – and you got only one mark for doing so.



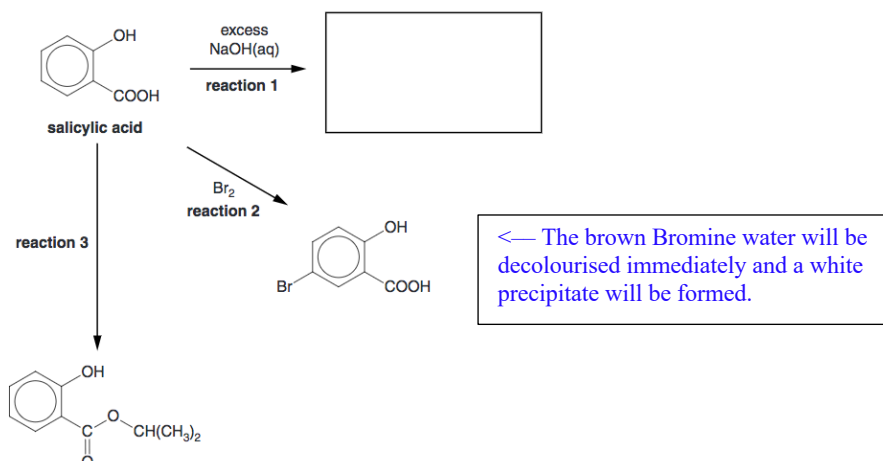
- The question then said

1 Salicylic acid is a naturally occurring carboxylic acid, widely used in organic synthesis.

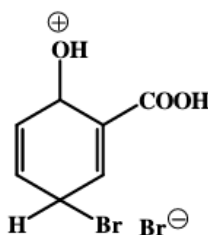


(a) The flowchart below shows some reactions of salicylic acid.

(i) In the box below, draw the structure of the organic compound formed by **reaction 1**. [1]

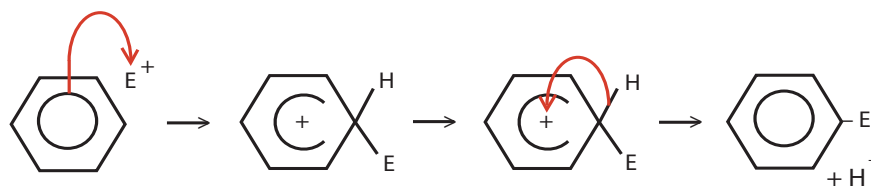


- In the classic reaction between an unsaturated C species (in this case a Phenol derivative, Salicylic Acid) and a Halide molecule (here Br_2), the Br_2 takes on a partial separation of charge as it approaches the area of high electron density (the delocalised π ring), and this causes it to break heterolytically as it crashes into the Salicylic Acid. At one stage in the reaction mechanism the delocalised π ring is temporarily interrupted and you get

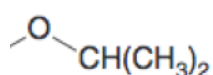


until the H atom breaks away as a Proton (leaving behind its electron to re-establish the delocalised π ring) and one of the Br atoms on the Salicylic Acid. The Proton and the Br^- now form HBr. The reaction of Salicylic Acid thus is very like that of Phenol (except that bromination takes place at position 4, and not at 2,4,6).

- The way that I taught you to draw this reaction was



- In the third part of the Question they wanted to know the reagents and the reaction conditions for Reaction 3.
- If you now concentrate on the “-COOH” bit of the Salicylic Acid and then look at the bottom bit of the above diagram, then you will see that all that has happened is that an Alcohol has reacted with an acid in an Esterification reaction



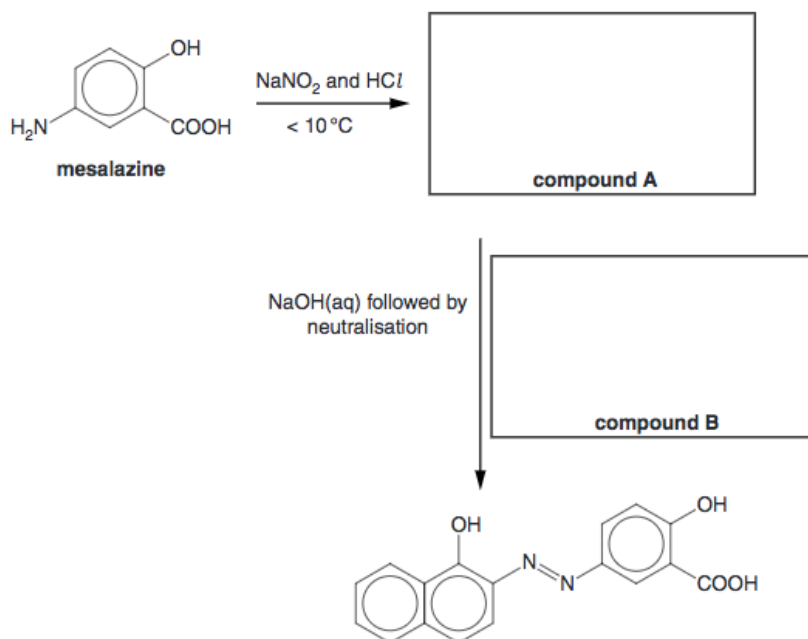
and from the information tree in the Chapter on Alcohols (Chapter 6, First Year Organic Chemistry) you will see that you need to reflux the Carboxylic Acid and the Alcohol in the presence of concentrated Sulphuric Acid.

- I think that it is fair to say that whilst the Questions in the OCR papers often look very complicated, in reality the answers that they require are not very sophisticated ones (*and they often command just one mark*).
- If you keep your cool and have done your revision, then you should be able to answer almost any question that comes up in the exam.
- Let me do one more bit of the Question on Salicylic Acid and you will see what I mean. However, you ought to revise Chapter 16 to know what is going on (and all the reaction conditions involved in the next bit e.g. when you need to keep the reaction temperature at about 5°C, and certainly below 10°C). Please do make sure that you understand the workings of BDAC! It really is rather important.
- The next bit asked

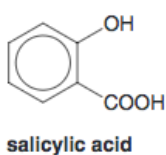
(iii) Mesalazine reacts in another two-stage process as shown below.

In the boxes, draw the structures of organic compounds **A** and **B**.

[2]



(d) Salicylic acid can be used to form a condensation polymer similar to Terylene®.



(i) Explain what is meant by the term *condensation polymer*.

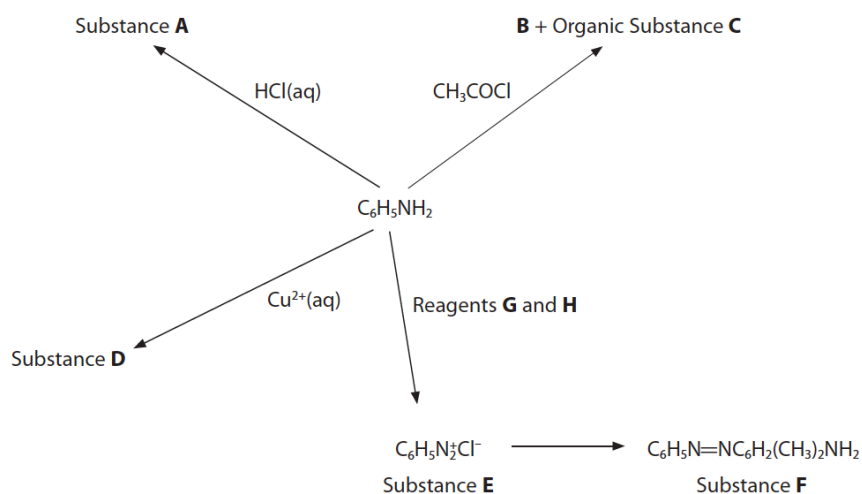
.....
 [1]

and all that they were asking about is in Chapter 16.

- Let me now do Question 24 from the 2015 Edexcel paper for you. It was a lovely question that tested a large amount of your comprehension of both Organic and Inorganic Chemistry.
- Q24(b) contained the following. (NB Just in case you did not recognise “C₆H₅” and the Phenyl element of a Benzene ring, they actually tell you that the substance in the middle of the diagram is Phenylamine (or as it is also called “Aniline”)³.

³ The “A” in the name of the huge German chemicals company BASF comes from “Aniline” because the name of the company used to be “Badische Anilin und Soda Fabrik”.

(b) Some reactions of phenylamine are shown below.



and then asked questions about the substances/compounds A to H, so let us look at the reactions involved in each case.

Substance A : this is an acid/base reaction

(The lone pair on the N atom makes Phenylamine into a Lewis base and HCl is an acid.)

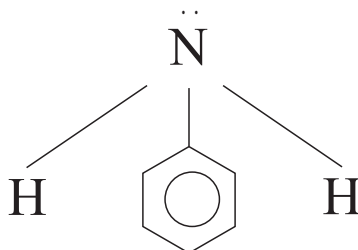
- The N atom in Phenylamine / Aniline has its required three bonds (one to “C₆H₅”, and one each to the two H atoms), but the N atom still has a lone pair of electrons and it uses that lone pair to form a dative bond with the H⁺ in the HCl(aq) to form the cation “C₆H₅.NH₃⁺”. (Please draw it, and you will follow what I have just said.) This cation and the anion “Cl⁻” then form a straightforward ionic substance **C₆H₅NH₃⁺ Cl⁻**.

Substance B and an Organic Substance, C : this is the Acylation of Phenylamine

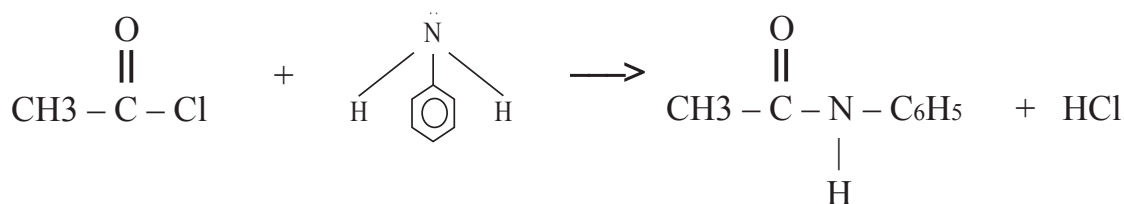
(A Friedel-Crafts’ catalyst is not needed because Phenylamine is 2,4,6-activated whereas Benzene is not.)

- On my interpretation of the Edexcel Syllabus, strictly speaking the Acylation reactions of Phenylamine are not in the syllabus; but, as I have pointed out elsewhere the Examining Boards make the rules and they mark your exam papers, so my job is to teach you enough Chemistry, and your job is to remain cool/calm/collected and use the stuff that I have taught you and the brains that you were born with, **and you will be able to answer this question.**
- Once again I want to draw your attention to the fact the N atom in Phenylamine has its required three bonds (one to “C₆H₅”, and one each to the two H atoms), but the N atom still has a lone pair of electrons and it uses that lone pair to form a dative bond.
- Let me draw it for you and you will see the point that I am making.

Don't look at the "Phenyl" bit, **concentrate on the AMINE bit**



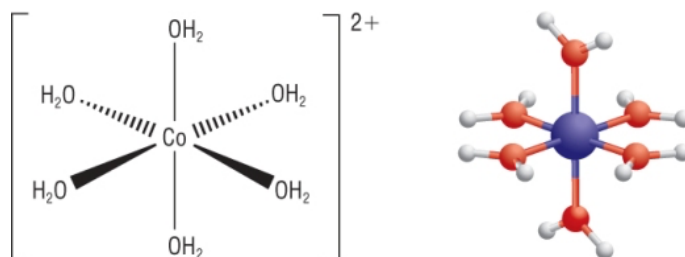
- What is going to happen in this reaction is that the "Cl" in the Acetyl Chloride will break away heterolytically as "Cl⁻" thus leaving the Acetyl bit as a positively charged cation " $\text{CH}_3\text{C}=\text{O}^+$ " (and since it has a positive charge, it is *short* of electron density). On the other hand, Phenylamine has the lone pair of electrons that I have talked about therefore it is *long* on electron density. This therefore is going to lead to the classic "electrophile reacting with a nucleophile" reaction.
- One of the H species in the Phenylamine will break away as a proton and bond with the Cl⁻ to form HCl and we thus get the following.



Substance D : This is all about the complexes formed by aqueous Transition Metals

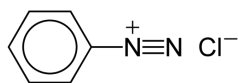
(Cu²⁺ is the cyan coloured complex formed by Cu²⁺ and six molecules of Water: [Cu(H₂O)₆]²⁺)

- In Chapter 12 of Year 2, Inorganic Chemistry I showed you the following complex. It was for Cobalt, but all that you need to do is substitute Cu²⁺ for Co²⁺.



- In the exam, I know that a number of candidates were cursing and swearing wondering how many of the (big) Phenylamine molecules they could fit in round the central Copper atom – and the examiners were **EXTRAORDINARILY** remiss in not doing their job properly by not having foreseen this problem but, as it happens, all that the examiners wanted was for candidates to say that a Copper complex would be formed.

Substance E : Phenylamine ($\text{C}_6\text{H}_5\text{NH}_2$) \longrightarrow Benzenediazoniumchloride ($\text{C}_6\text{H}_5\text{N}^+$ *triple bond N*)
(Using NaNO_2 and 2HCl : Chapter 16, Year 2, Organic Chemistry, Azo reactions.)



This compound is called **BenzenediazoniumChloride, BDAC**

- If you go back to Chapter 16 you will see that the conversion of Phenylamine to BDAC is achieved via Nitrous Acid ‘in situ’ and below 10°C (because Nitrous Acid decomposes above that temperature). I put the diagram from Knockhardy here to remind you of the whole process of the reaction from Benzene to Phenol,

PHENOL

Structure phenol is an aromatic alcohol with formula $\text{C}_6\text{H}_5\text{OH}$ the OH group is attached directly to the benzene ring it is an almost colourless crystalline solid

Preparation You cannot put an OH group directly onto a benzene ring by electrophilic substitution, so phenol has to be synthesised in a multi-stage process

Step 3 - Diazotisation of phenylamine

reagents nitrous acid and hydrochloric acid (use sodium nitrite)

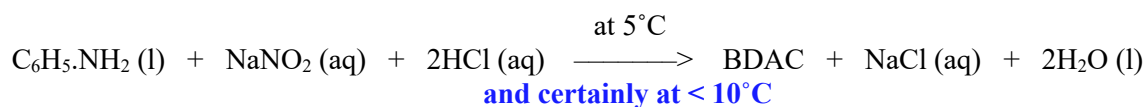
conditions keep below 10°C

equation $\text{C}_6\text{H}_5\text{NH}_2 + \text{HNO}_2 + \text{HCl} \longrightarrow \text{C}_6\text{H}_5\text{N}_2^+ \text{Cl}^- + 2\text{H}_2\text{O}$

reaction type diazotisation

and this is what I had to say about this bit of the reaction

- Please do not be put off by the look of BDAC. After all, what conceptual difference is there between the salt that you have on your dining table (Na^+Cl^-) and any other salt? *None whatsoever*. The salt above is just more complex than (but conceptually no different from) table salt.
- BDAC can easily be obtained by reacting Nitrobenzene with “Nitrous acid” (HNO_2) – **but nitrous acid is very unstable and decomposes very quickly**, therefore the nitrous acid has to be made and used on-the-spot (*‘in situ’*) by reacting $\text{NaNO}_2(\text{aq})$ with $2\text{HCl}(\text{aq})$ and we would thus get



NB Please remember that in Organic Chemistry it is permissible to omit non-organic products in reaction equations (and that is why Organic equations sometimes do not balance).

- Textbooks quote different temperatures ranging from 0°C to 10°C , and one of the reasons for keeping the temperature down is that Nitrous Acid is unstable and decomposes at higher temperatures – and it is the Nitrous Acid that is being made *in situ* and being utilised as soon as it is made. The table below shows the process of creating the benzenediazonium chloride (BDAC) diagrammatically, but please remember that I have told you the positive charge is on the N atom that is closer to the C_6H_5 species.

Substance F : BDAC to something else

(Here from $\text{C}_6\text{H}_5\text{N}\equiv\text{N}^+\text{Cl}^-$ to $\text{C}_6\text{H}_5\text{-N=N-C}_6\text{H}_2\text{.}(\text{CH}_3)_2\text{.NH}_2$)

- Now, please could **YOU** draw a Benzene ring with
 - one bond to the outside “N” in BDAC
 - one bond to an “NH₂” species (the amine bit of Phenylamine)
 - two bonds: one each to a Methyl group, and
 - two bonds: one each to an H atom.
- Now could you count all the bonds on your Benzene ring. If you do not have six bonds (one at each of the 6 vertices) then you have not drawn your Benzene ring correctly.
- Now can I ask you to check to see **where** you have drawn your Methyl additions – and please remember that the Amine species in Phenylamine activates the Benzene ring at 2, 4, and 6 and that at position “4” there is a bond to the outside “N” in BDAC.⁴
- I would not like to even attempt to name the molecule $\text{C}_6\text{H}_5\text{-N=N-C}_6\text{H}_2\text{.}(\text{CH}_3)_2\text{.NH}_2$, nor to tell you the reaction conditions for the reaction – but, as it happens, **all that the examiners wanted you to tell them was that the substance was an “azo dye” or a “diazo compound”**.

Substances G and H

- We have already dealt with this above. You need to form Nitrous Acid “in situ” from Sodium Nitrite and Hydrochloric Acid and keep the temperature around 5°C.

I have already said this elsewhere but I will say it again.

In the modern (post Mr Gove) ‘A’ Level Chemistry exams, the examiners are using **fearsome** looking examples to try to draw out from you some basic ‘A’ Level Chemistry principles. There is nothing wrong with this. What is unfair in my opinion is that you are given a disproportionately short period of time to answer the questions and a ridiculously small number of marks for unravelling the complicated examples that they have used in the exam. Even so, by doing example after example after example during the year, you will become very familiar with spotting what they want within seconds of reading an exam question.

The Department for Education and the Examining Boards make the rules, and every year there are candidates who sit the exams and get very high marks (As and A*s) and if you want to get such a grade, then you have to play by the rules of the game **set by the examining authorities**. **I have every confidence that those of you who work your socks off (instead of spending time on social media) will achieve a grade that is commensurate with both your intellectual abilities and with the work that you put in.**

⁴ Please remember that the electron density of the unhybridised ‘p’ orbitals on the N atom in the Amine in Phenylamine gets locked into the ‘frying-pan handle’ of $\text{C}_6\text{H}_5\text{NH}_2$ by the positive mesomeric effect.

I have written my two books, and I write my Blogs each week for **'A' Level students** who (by definition) must have the brain power to give a good account of themselves intellectually. I can therefore confidently say if you want to achieve a really high grade and get into the University/Med School/Law Firm/Accountancy Partnership/whatever of your choice, then the best advice that I can give you is **“dig a big hole in your garden and put your mobile phone in it while you are doing your 'A' Levels”** – and leave it there until you have finished your degree.

It is extremely rare to find a job that pays well because you know how to use 'facebook' / 'snapchat' / or whatever. In contrast, if you get a First in (alphabetically) Biology / Chemistry / Maths / Physics, then you will have no reason to have any money problems for the remainder of your life.

However, please remember that being well-off is not the same as being happy. Happiness is something that comes from inside you and not from outside you.

Happiness springs from the actualisation of YOUR own potential.

Good luck. Work hard and your hard work will serve you in good stead all your life.