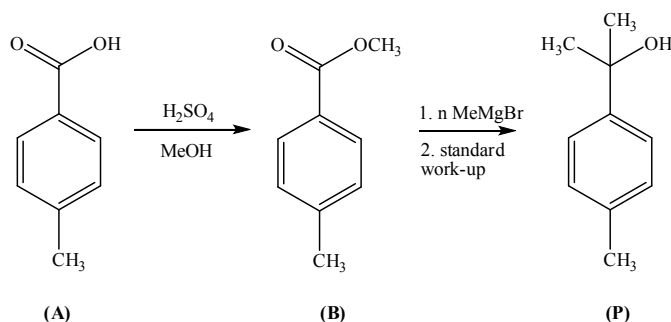
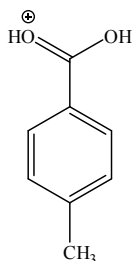


1. a. The first reaction is an esterification leading to a methyl ester. The second reaction is a Grignard reaction that affords a tertiary alcohol. Note that two equivalents of MeMgBr are added here!



b. Sulfuric acid is used as catalyst in the Fischer esterification. It protonates the carbonyl group of the carboxylic acid and not the hydroxyl function. The resulting cation is resonance stabilized.



c. In order to calculate the yield, first the limiting reagent has to be identified.

$$n_A = 2.45 \text{ g} / 136.15 \text{ g/mol} = 18.0 \text{ mmol}$$

$$n_{\text{MeOH}} = 3.0 \text{ mL} \cdot 0.792 \text{ g/mL} / 32.04 \text{ g/mol} = 74.2 \text{ mmol}$$

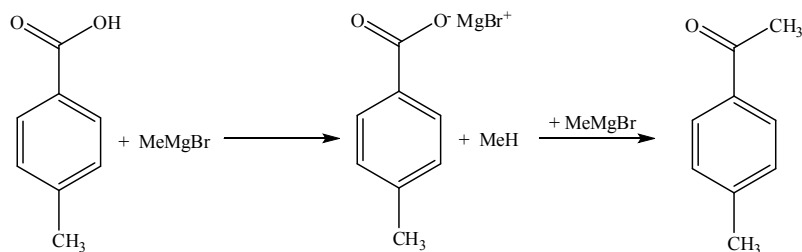
$$n_{\text{ester}} = 2.22 \text{ g} / 150.17 \text{ g/mol} = 14.8 \text{ mmol}$$

Since the reaction is a 1:1 reaction (carboxylic acid:alcohol), the carboxylic acid is the limiting reagent. This makes sense since the acid is a solid (see below). Methanol serves as reactant and as solvent in this reaction like in the lab.

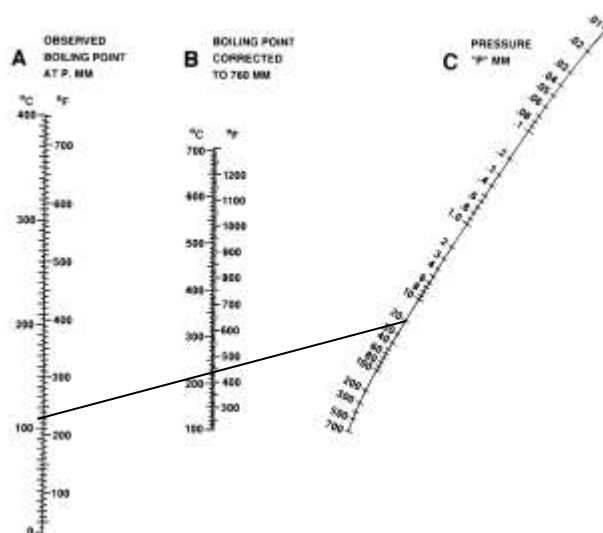
The reaction should yield 18.0 mmol of the methyl ester, but 14.8 mmol of the product are isolated. Thus, the yield is 82.2%, which is pretty decent for an esterification.

$$\text{Yield} = 14.8 \text{ mmol} / 18.0 \text{ mmol} \cdot 100\% = \mathbf{82.2\%}$$

d. If the formation of the ester is skipped, *reaction 2* would afford a different product (ketone instead of tertiary alcohol). The first equivalent of Grignard reagent is consumed in an acid-base reaction. The second equivalent performs the nucleophilic attack, but the resulting tetrahedral intermediate cannot eliminate spontaneously. As a result, only one methyl group is added to the molecule.



e. The boiling point for the compound is $T_b = 110^\circ\text{C} \pm 5^\circ\text{C}$ at $p = 20$ torr. The graph below illustrates how to get there. The scale in the middle (B) is used for the given boiling point of $T_b = 220^\circ\text{C}$ at 760 mmHg, the graph on the right (C) for the pressure $p = 20$ mmHg. The line is then extrapolated to scale (A) to obtain the boiling point under these conditions.

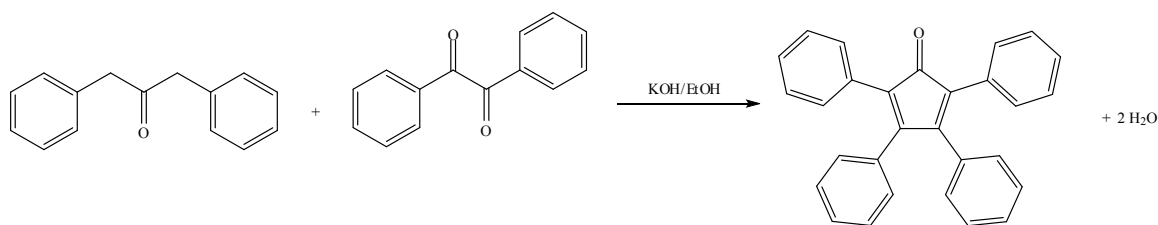


f. The higher melting point of compound **A** compared to compound **B** is a result of the stronger intermolecular forces in compound **A**. The carboxylic acid group causes relatively stronger intermolecular hydrogen bonds, which increases the melting point. Compound **B** is an ester, which only exhibits a dipole moment. Since dipole-dipole interactions are much weaker than hydrogen bonds, a significantly lower melting point is observed.

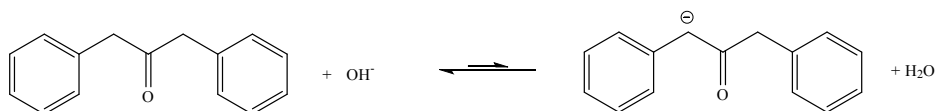
g. If $X = \text{NHMe}$ instead several complications would arise in both reactions. In the first reaction, much more sulfuric acid would be required because the mineral acid would react with the amine function in an acid-base reaction first before it can catalyze the esterification. In addition, the pH-value has to be better controlled during the work-up to minimize the solubility of the ester in the aqueous layer. In *reaction 2*, an addition equivalent of Grignard would be needed since the first equivalent would react with the secondary amine function in an acid-base reaction.

h. The peak at $m/z = 119$ amu is due to $[\text{CH}_3\text{C}_6\text{H}_4\text{C}=\text{O}]^+$, which is obtained after the loss of a methoxy group from the ester.

2. a. The reaction requires one mole dibenzylketone and one mole of benzil as reactants, absolute ethanol as solvent and potassium hydroxide as catalyst. It yields one mole of tetraphenylcyclopentadiene and two moles of water.



b. The initial step of the reaction is the formation of the enolate ion. The problem is that the equilibrium even under normal conditions lies on the left side. Additional water pushes it even further to the left (Le Châtelier Principle), which would decrease the enolate concentration even further and slow down the reaction dramatically.



Water is excluded from the reaction by the using *absolute ethanol* for the reaction and by using dry glassware.

c. The product is highly conjugated, which is the thermodynamic driving force. The second step of the reaction is intramolecular because the electrophile and the nucleophile are in the same molecule. The third driving force is entropy, because two reactant molecules are converted into three product molecules.

d. The color change is a result of the increased conjugation. A yellow color indicates absorption at the edge of ultraviolet and visible light. Conjugation decreases the energy gap between the π/n -orbital and the π^* -orbital. Radiation with larger wavelength is sufficient to cause the excitation.

3. a. In order to obtain 4.5 g of the crude benzoin, the procedure has to be downscaled by a factor 100. This means that 5 g of benzaldehyde and 0.5 g of sodium cyanide are dissolved in 6.25 mL of 95% ethanol and 5 mL of water.

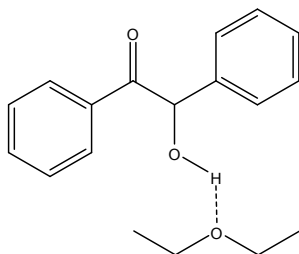
b. Benzaldehyde is often contaminated by benzoic acid due to aerial oxidation. The presence of benzoic acid would lower the yield because less benzaldehyde is present in the reactant, and also lower the pH-value. This poses a problem because hydrocyanic acid can be formed that is very volatile and also very toxic!

c. The larger amount of water in 50% ethanol means that the product is less soluble in the solvent, but also the impurities. Both precipitate in larger amount, which means that the yield of the crude is higher. But the crude is also more contaminated by benzaldehyde and other compounds, which results in a more yellowish color.

4. a. Dichloromethane is used as solvent for extraction because it is poorly miscible with most aqueous solutions, which allows for a clean phase separation. In addition, it has a low polarity, which means that it dissolves a broad variety of organic compound relatively well (large distribution coefficient) and it is relatively inert towards most solutions used for extraction. It also exhibits a low boiling point, which makes it easy to remove from the product.

b. Ethyl acetate is the best solvent for this TLC problem to start with since it has a weak-medium polarity. Ethanol is too polar for this particular problem because neither benzil nor benzoin is extremely polar, which means that they would exhibit very high R_f -values. Hexane would be too non-polar, and cause very little migration of the compounds. In both cases poor separation would be observed.

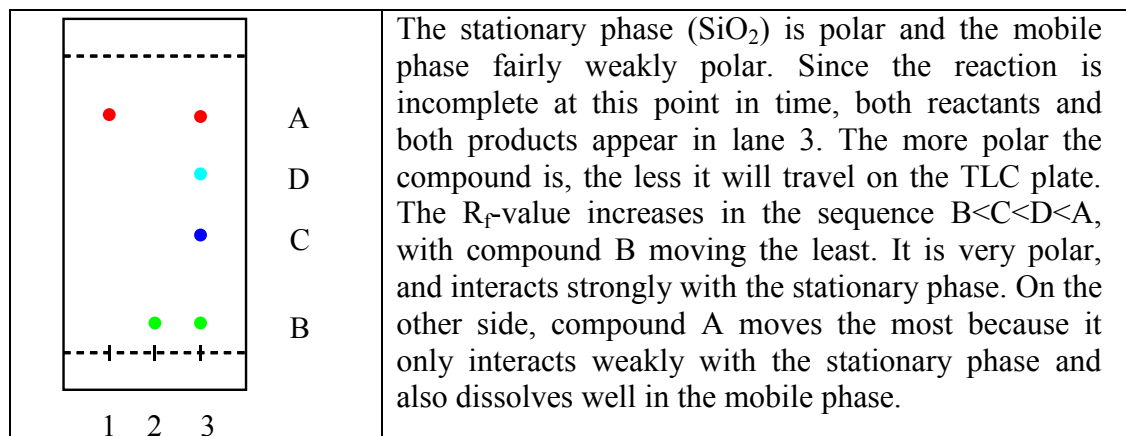
c. Benzoin dissolves better than benzil in diethyl ether because it interacts stronger with the solvent. While benzil mainly forms dipole-dipole interactions, benzoin can also form hydrogen bonds, which are stronger.



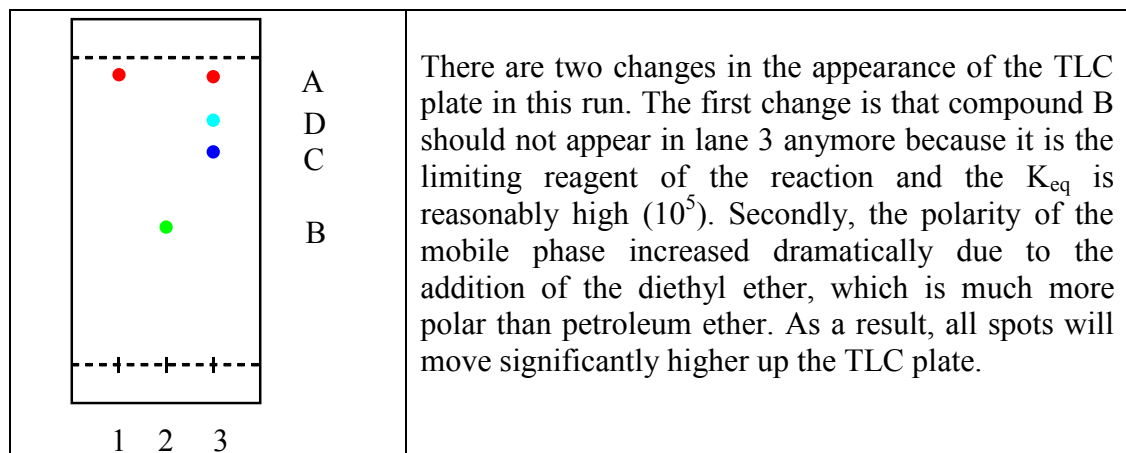
Despite the solubility difference, diethyl ether is not suitable to purify benzoin since it dissolves better in the solvent than benzil, which would precipitate out first.

d. The solvent in the Diels-Alder reaction, 1,2-dimethoxyethane, is more polar than diethyl ether. Thus, it is a better solvent for the very polar anthranilic acid. In addition, it has a boiling point that is about 50 °C, which is an advantage as well because the reaction is highly entropy driven.

5.a.

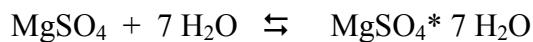


b.



c. Propanol has a relatively high boiling point (b.p. = 97°C), which makes it very difficult to evaporate it. If it stays on the plate it will cause the spots to look crescent-shaped because most of the compounds will be absorbed on the edge of the spot and not where the compound is applied to the plate. This will complicate the separation because often times tailing is observed in addition.

6. a. The drying process itself is reversible. At low temperatures, the forward reaction is favored because the process is slightly exothermic. At higher temperatures, the reaction reverses because the entropy term increases.



In terms of the use of drying agents, this means that the drying agent has to be removed before the solution is heated i.e. to remove the solvent from a solution or the crude product is distilled.

b. Even though the drying agent can be removed by vacuum filtration in some cases, in this particular case it is not the good approach. The boiling point of diethyl ether (solvent at this point) is too low, which means that it would evaporate as soon as vacuum is applied. The product precipitates in the filter flask and on the inside of the Hirsch funnel. The final yield would be fairly low since it will be extremely difficult to collect all of this material.

c. The C=O stretching frequencies for the given compounds are: 1806 cm^{-1} for CH_3COCl , 1715 cm^{-1} for CH_3COCH_3 and 1681 cm^{-1} for CH_3CONH_2 .



3

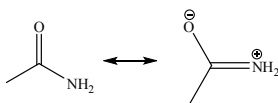


2



1

The differences can be explained by the importance of different resonance structures. In the acyl chloride, the high electronegativity of the chlorine causes the C=O bond to be stronger to compensate for the electron-pulling effect of the chlorine atom. The chlorine is not able to donate electron density back (resonance) because it is much bigger than the carbon atom, which results in a poor overlap of the p-orbital with the π^* -orbital. The situation entirely changes in the amide, where the nitrogen is less electronegative than the oxygen atom and therefore much more able to donate its lone pair to form a partial double bond.



d. Signals in the GC can be assigned in two different ways. Both methods require the compound to be available as an authentic compound. The first method would be an external reference in which the authentic compound is run under identical conditions as the sample mixture. If the retention times match up, the compounds are most likely identical. The second method is referred to as “spiking”. Here, the sample is run without and with the authentic sample added (“spike”). If the authentic sample is in the sample mixture, the integration of the peak to be identified should increase in comparison to all other peaks.

e. In order to assess the purity of the sample, the observed refractive index has to be corrected for the temperature (not the other way around!).

$$n_D^{20} = n_D^{24} + (24-20)*0.00045 = 1.4470 + 4*0.00045 = \mathbf{1.4488} \text{ (corr.)}$$

This value is way outside the window of $\Delta n_D^{20} = \pm 0.001$ of the literature value of $n_D^{20} = 1.4460$ (1.4450...1.4470). The higher refractive index indicates the presence of significant amounts of cyclohexanol in the final product.

f. It is very important to know the exact concentration of the first solution (stock) in order to perform the dilutions to the proper concentration level afterwards. If only part of the compound is dissolved, this concentration is unknown and all other concentrations as well. As a result, the absorbance readings are too low, which also results in ϵ -values that are much lower than the literature values independent from the sample purity.

g. Azeotropic distillations are usually used to remove water from a reaction mixture. However, this only works if the reactants have a significantly higher boiling point than the azeotropic mixture. In the esterification low boiling alcohols are used as reactants, which would distill before most azeotropes. This makes this technique less useful for the esterification carried out in the lab.

h. The effect that the student is observing is called “supersaturation”, where the solution dissolves more solute than it should at a given set of conditions i.e. temperature. This often happens if impurities interfere with the crystallization process or like in this case a new flask is used which has a very smooth surface. The problem can be solved by seeding the solution or by scratching the inside of the flask to provide nucleation sites.

7. a. The compound dissolves poorly in petroleum ether (non-polar), a little better in ethyl acetate (medium polar) and by far the best in isopropanol. This means that compound **V** is fairly polar itself (polarity scale: 4).

b. The solubility of compound **V** doubles in isopropanol, increases by a factor six in petroleum ether and by a factor nine in ethyl acetate. The impurity is medium polar which would make it fairly soluble in ethyl acetate as well. Based on this, ethyl acetate would be the best solvent to be used for recrystallization.

c. In order to dissolve 5.4 g of compound **V**, 60 mL of hot ethyl acetate (80 °C) are needed (=5.4 g/(9.0 g/100 mL)). After cooling, 0.6 g of the compound (=60 mL* (1.0 g/100 mL)) remain in solution and 4.8 g (=5.4 g - 0.6 g) precipitate out at 0 °C.

d. The rinsing step after the filtration is necessary to remove the mother liquor from the crystals. Usually a small amount of a cold solvent is used here to minimize the loss of product in this step.

8. Spectrum 1: *Compound D*

Characteristic peaks at cm^{-1} : 3200-3600 (OH, alcohol), 2870-2950 (CH, sp^3), 1347, 1453 (CH_2 , bend), 1036 (C-OH, alcohol)

Spectrum 2: *Compound F*

Characteristic peaks at cm^{-1} : 3014-3027 (CH, sp^2), 2863, 2974 (CH, sp^3), 1741 (C=O, ester), 1677 (C=C, alkene), 1337, 1448 (CH_2 , CH_3 , bend), 1024, 1234 (COC, ester)

Spectrum 3: *Compound L*

Characteristic peaks at cm^{-1} : 3293, 3374 (NH_2 , prim. amine), 2852-2921 (CH, sp^3), 1609 (NH_2 , bending), 1388, 1450 (CH_2 , bend)

Spectrum 4: *Compound B*

Characteristic peaks at cm^{-1} : 2876-2962 (CH, sp^3), 1751, 1819 (C=O, anhydride), 1382, 1466 (CH_2 , CH_3 , bend), 1037 (COC, anhydride)

Spectrum 5: *Compound A*

Characteristic peaks at cm^{-1} : 2500-3500 (OH, acid), 2871-2971 (CH, sp^3), 1708 (C=O, acid), 1452 (CH_2 , bend), 1297 (C-OH, acid)

Spectrum 6: *Compound G*

Characteristic peaks at cm^{-1} : 3072-3089 (CH, sp^2), 2754, 2869 (CHO, aldehyde), 1698 (C=O, conj. aldehyde), 1484, 1593 (C=C, aromatic), 825 (C-Cl), 758 (oop, ortho subst.)

Spectrum 7: *Compound J*

Characteristic peaks at cm^{-1} : 3314 (CH, sp, alkyne), 2872-2961 (CH, sp^3), 2121 ($\text{C}\equiv\text{C}$, alkyne), 1368, 1470 (CH_2 , CH_3 , bend), 629 (H-C \equiv C, bend)

Spectrum 8: *Compound I*

Characteristic peaks at cm^{-1} : 2859-2955 (CH, sp^3), 1717 (C=O, ketone), 1378, 1448, (CH_2 , CH_3 , bend)

9. a. Degree of unsaturation: $D.U. = (2 \cdot C + 2 - H + N) / 2 = (2 \cdot 9 + 2 - 11 + 1) / 2 = 5$

b. The most important peaks are at (in cm^{-1}): 3374, 3461 (NH_2 , prim. Amine), 3069 (CH , sp^2), 2873-2982 (CH , sp^3), 1708 ($\text{C}=\text{O}$, conj. ester), 1604 (NH_2 , bending), 1493, 1588 ($\text{C}=\text{C}$, aromatic), 1368, 1462 (CH_2 , CH_3 , bend), 683, 755, 880 (oop, meta-subst.)

c. The carbon spectrum shows nine signals for a total of nine carbon atoms in the structure. This means that there is no symmetry in the molecule.

d. The ^1H -NMR spectrum shows seven signals. The signal group between $\delta = 6.82$ to 7.41 ppm (d, s, t, d; 1H each) can be attributed to a meta substituted benzene ring. The quartet at $\delta = 4.32$ ppm and the triplet at $\delta = 1.35$ ppm are part of an ethyl group that is attached to an oxygen atom. The broad singlet at $\delta = 4.79$ ppm is due to the primary amine group.

e. The ^{13}C -NMR spectrum exhibits nine signals. The signals at $\delta = 131$, 147 and 167 ppm (ester) are due to quaternary carbon atoms. The signals at $\delta = 116$, 119.4 , 119.5 and 129 ppm are due to CH functions from the benzene ring. The signal at $\delta = 61$ ppm is a methylene group and the signal at $\delta = 14$ ppm is due to a methyl group.

f. Based on the discussion above, compound **W** is **ethyl m-aminobenzoate**.

