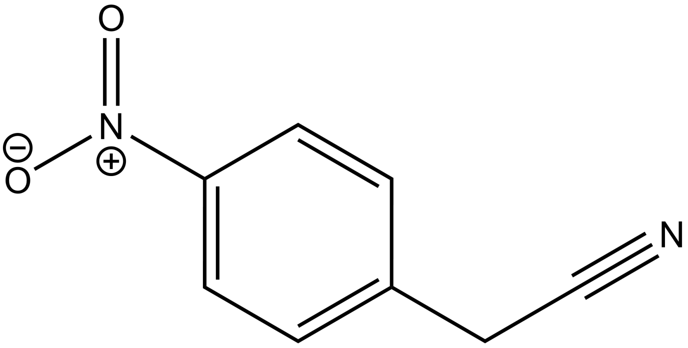
ETH zürich

Laboratory Course OACP I
Spring Semester 2024

The Synthesis of (4-Nitrophenyl)acetonitrile by Electrophilic Aromatic Substitution



Loganathan Visva vloganathan@student.ethz.ch
Interdisciplinary Sciences Biochemical-Physical Major

Teaching Assistant
Neves Vieira Adriana adriana.vieira@org.chem.ethz.ch

Abstract The objective of this experiment is to synthesize (4-Nitrophenyl)acetonitrile and analyze the yield of the product. The synthesis is performed by the electrophilic aromatic substitution through mixing concentrated sulfuric and nitric acid and the drop wise addition of benzyl cyanide into the mixture. The substance was purified by recrystallization. The success of the experiment is determined by thin layer chromatography, a melting point analysis and an infrared spectrum measurement.

Zürich, May 9, 2024

V. Loganathan
Loganathan Visva

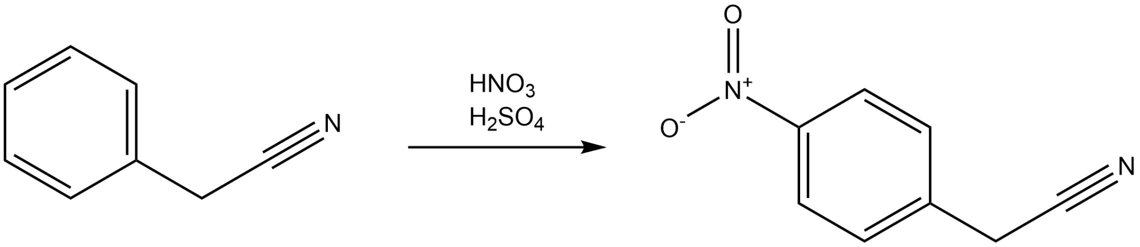
Ariana

Introduction

(4-Nitrophenyl)acetonitrile consists of a cyano group and a carbamate group joined to a phenyl ring. At room temperature it typically appears as a white to pale yellow solid crystalline powder [1]. As a result of its molecular structure, it demonstrates moderate solubility in organic solvents like ethanol and ether, while its solubility in water remains relatively low. It has been identified as a sensitive reagent for the detection of quinones, hydroquinone, and pyrocatechol, indicating its utility in analytical chemistry applications [2].

Material Properties

For the synthesis of (4-Nitrophenyl)acetonitrile electrophilic aromatic substitution was used. Benzyl cyanide and concentrated nitric acid reacted together to form the product. Sulfuric acid acted as a catalyst to the reaction.



Substance	GHS Hazard Pictogram	H and P Phrases
Benzyl cyanide [3]		H301, H330, H311-P260, P264, P271, P280, P302, P352, P312, P304, P340, P310
Sulfuric acid [4]		H290, H314, H318, H315, H319-P234, P280, P303, P361, P353, P304, P340, P310, P305, P351, P338, P363
Nitric acid [5]		H272, H290, H331, H314, H318, H319, H315-P210, P220, P280, P303, P361, P353, P304, P340, P310, P305, P351, P338
(4-Nitrophenyl)acetonitrile [6]		H301, H302, H311, H312, H315, H319, H331, H332,P233, P261-P265, P270, P271, P280, P301 + P316, P317, P302 + P352, P304 + P340, P305, P321, P330, P332, P337, P351, P361-P364, P388, P403, P405, P501

Substance	Molar Mass [g/mol]	Density [g/mL]	Melting Point [°C]	Boiling Point [°C]
Sulfuric acid	98.079	1.8	10.31	290 (approx)
Nitric acid	63.01	1.55	-41.6	83
Benzyl cyanide	117.15	1.020	-23.8	233.5
(4-Nitrophenyl)acetonitrile	162.15	1.3	117	373

Safety Assessment

In the lab, each chemical demands specific safety measures. Benzyl cyanide can cause skin and eye irritation, and its vapors may be harmful if inhaled. It is acutely toxic, that means it has an immediate and severe toxic effect. Sulfuric acid is corrosive to metals and tissue, leading to severe burns upon contact. Nitric acid shares similar hazards with sulfuric acid, being highly corrosive and potentially causing deep burns. It can also release toxic fumes. (4-Nitrophenyl)acetonitrile is also acutely toxic, just like benzyl cyanide and ingestion or skin contact should be avoided.

The entire reaction should be conducted in a well ventilated fume hood to avoid exposure to any harmful vapors, particularly from benzyl cyanide and nitric acid. The reaction can be exothermic, so adding the benzyl cyanide slowly to control the reaction rate is important. The internal temperature should not exceed 20 °C.

The handling of each requires appropriate personal protective equipment, cautious storage, and clear protocols for exposure response and spill management. Always adhere to detailed guidelines as provided by their respective Safety Data Sheets for safe laboratory practices.

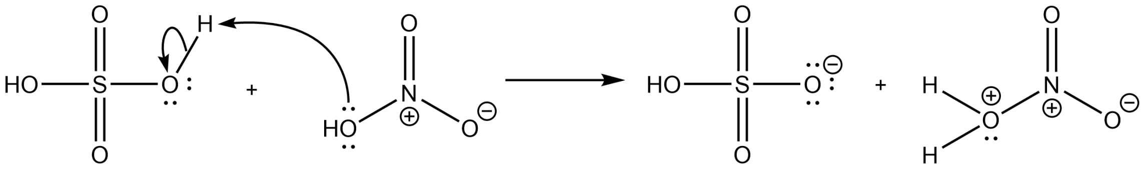
For avoiding any health issues that could be caused by the chemicals, gloves and safety googles should be worn in the laboratory. In a case of an accident the emergency number should be called. With the internal ETH-phones it would be 888, on personal mobile phones the number would be 044 342 11 88. If something get's into the eye, an eye shower has to be performed for at least 15 minutes and then the eye clinic from the university hospital Zurich has to be visited. If sulfuric acid gets spilled on the skin, the clothing over it has to be removed and the contaminated area on the skin has to be rinsed with running water for several minutes. Afterwards a doctor must be seen. All incidents should always be reported.

Waste Disposal

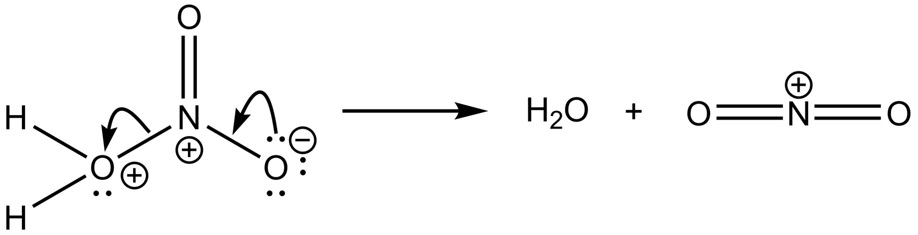
Nitric acid and sulfuric acid should be disposed into the aqueous acidic waste. Benzyl cyanide and (4-nitrophenyl)acetonitrile should be disposed of in to the non chlorinated organic solvent waste.

Reaction Mechanism

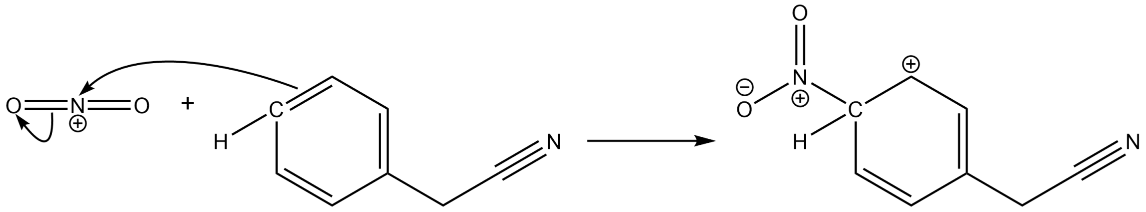
Both the nitric acid and the sulfuric acid are really strong Brønsted–Lowry acids. But the nitric acid has a pK_a of -1.3 and the sulfuric acid has a pK of -3.0, what means the nitric acid acts as a Brønsted base together with the sulfuric acid. The sulfuric acid protonates the nitric acid what turns the nitric acid into a nitrooxonium ion and the sulfuric acid into a hydrogensulfate ion.



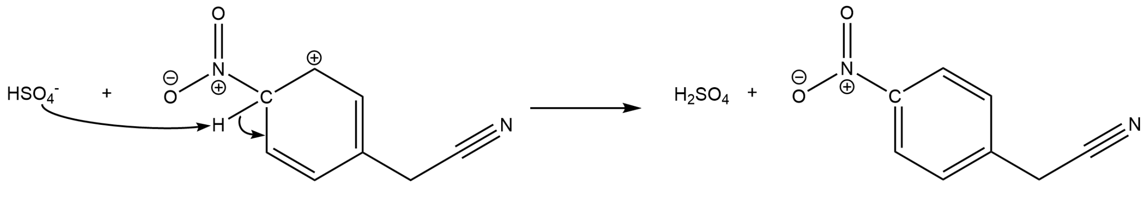
The nitrooxonium ion breaks up into a water molecule and a nitronium ion.



The nitronium ion is very electrophilic. The Carbon from the benzyl cyanide does an nucleophilic attack with the electron pair from it's double bond on the nitrogen of the nitronium ion. This builds a bond between the carbon and the nitrogen.



The carbon ring is now not aromatic anymore because it lost two electrons from it's aromatic system for the building of the C-N bond. The hydrogensulfate ion can act as Brønsted base and deprotonate the H from the carbon connected to the carbamate group. Now the hydrogensulfate turned back into it's initial form, sulfuric acid. That means the sulfuric acid is considered as a catalyst to the reaction. The two electrons from the C-H bond are now free to be integrated into the carbon ring, what restores the aromaticity. This creates the product (4-nitrophenyl)acetonitrile and marks the end of the reaction.



Atom Economy

Atom economy refers to the efficiency of a chemical reaction and it is calculated with the equation below. The atom economy of the reaction is approximately 90%. This reaction is extremely atom efficient. The molar mass of the product is 162.15 g/mol and the cummulative molar masses of the educts are 180.16 g/mol. So a substance with 6 g/mol leaves this reaction. This could be the water molecule that leaves when the nitrooxonium ion breaks up.

$$\mathrm{AE} = \frac{M_{\text{Product}}}{M_{\text{Reagents}}} = \frac{162.15\ \text{g/mol}}{63.01\ \text{g/mol} + 117.15\ \text{g/mol}} \approx 90.00\%$$

Experimental

Procedure

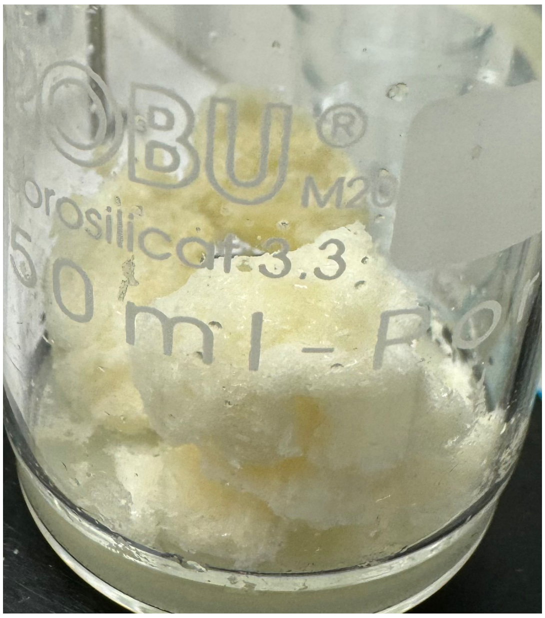
The synthesis is performed by the electrophilic aromatic substitution. Concentrated sulfuric acid and concentrated nitric acid is cooled to 10 °C. Over the course of an hour benzyl cyanide is cautiously inserted drop wise to the reaction, ensuring the temperature remains below 20 °C. Following the complete addition, the mixture is stirred at room temperature for an additional hour. The reaction is then quenched with crushed ice, followed by filtration, and the resultant product is subsequently dried using a vacuum. The product was a faint yellowish solid that looked like vanilla ice cream. The yield would be a yield of 138.8%. The substance wasn't put under a vacuum, so the additional weight should come from the ethanol that is still contained in it.

Observation

The synthesis was conducted by mixing concentrated nitric acid (7.0 mL, 120.54 mmol, 5.61 equiv.) and concentrated sulfuric acid (7.00 mL, 128.47 mmol, 5.98 equiv.) in a two necked round bottom flask with a thermometer and a magnetic stirr bar. The flask is put into an ice bath to reach a temperature of under 10 °C. Benzyl cyanide (2.5 mL, 21.5 mmol, 1.00 equiv.) is added really slowly with a syringe into the mixture. Adding benzyl cyanide causes the mixture to heat up, because the reaction is exothermic. The benzyl cyanide was added so slowly that the temperature of the mixture didn't exceed 20 °C. After the whole benzyl cyanide was added the mixture was left to stirr for one hour. The liquid became clear faint yellowish.

A 300 mL Erlenmeyer flask was filled with 30 g crushed ice. Then the faint yellowish liquid was poured into the Erlenmeyer flask with the ice. Then after the ice melted, the liquid was filtrated with a frit and a vacuum and was washed with distilled water. Then the residue solid on the frit was put into a one necked round bottom flask and that was connected to a rotarotory evaporator. The settings of the rotarotory evaporator were 50 mBar and 60 °C, so that the water could evaporate completely from the solid residue. After 15 minutes, the round bottom flask was taken away from the rotarotory evaporator.

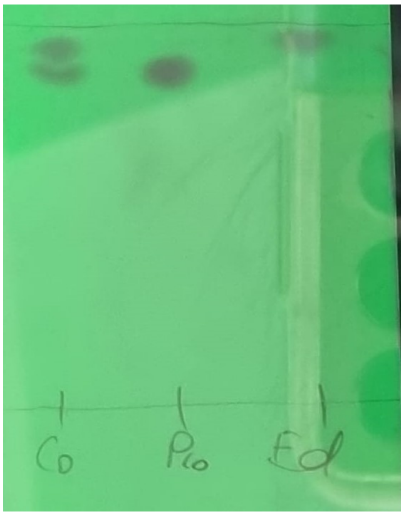
Then some Ethanol was heated up until boiling. A little bit of this hot Ethanol was poured into the round bottom flask with the residue and the flask was shaken until all the solid dissolved. Then later the round bottom flask was let to cool down until it reached room temperature. After that the round bottom flask was put into an ice bath for some minutes. Then the liquid with the recrystallized solid was poured into a frit under a vacuum. The faint yellowish solid residue in the frit is the product (4-nitrophenyl)acetonitrile (4.8389 g, 29.842 mmol, 1.39 equiv.).



Characterisation

Thin Layer Chromatography

A little bit of the solid yellowish product was dissolved in ethanol and benzyl cyanide was also dissolved in ethanol for the TLC. In this TLC, a silicate plate was used and there were three columns. The first column (Co) had a mixture of both the benzyl cyanide and the product solution on it. The second column (Pro) only had the product solution on it and the third column (Ed) only had the educt benzyl cyanide solution on it. The solvent the author used consisted of 1:10 n-hexane to ethylacetate. This solution didn't result in a good TLC, so the TLC from a lab partner was used instead, that had a solvent of 1:1 n-hexane to ethylacetate.



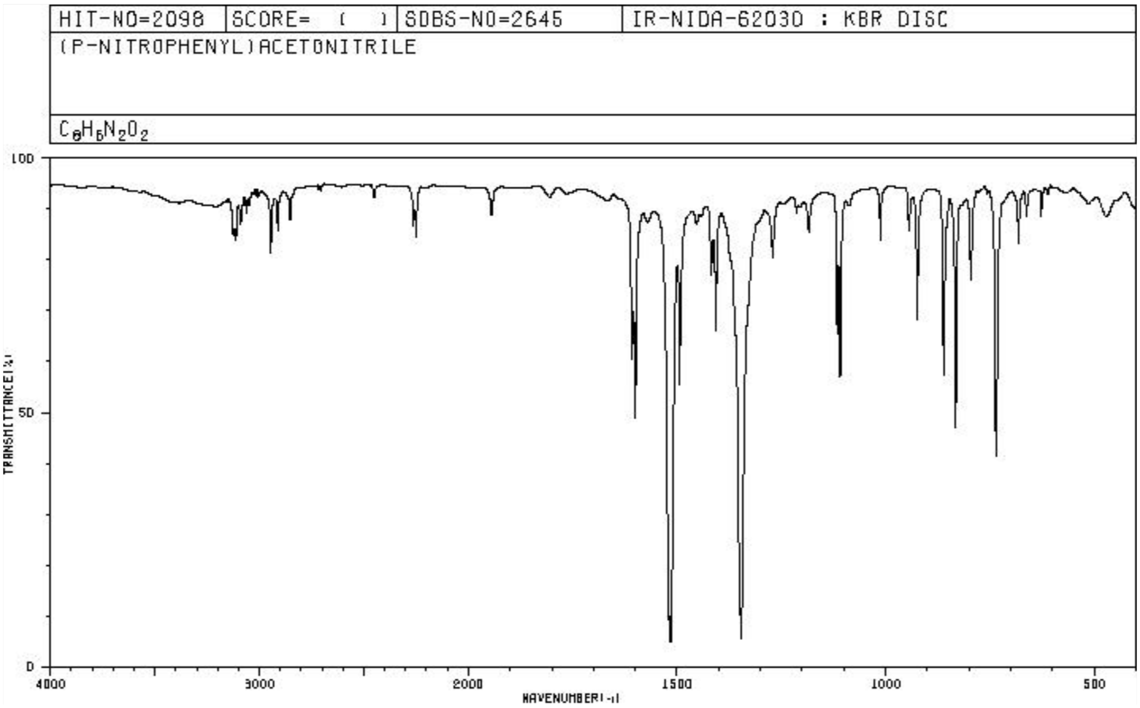
The difference in the rise of the product and the benzyl cyanide are really small. That could maybe be explained with the fact that the product and the Educt are really similar and only have a carbamate group difference.

Melting Point Analysis

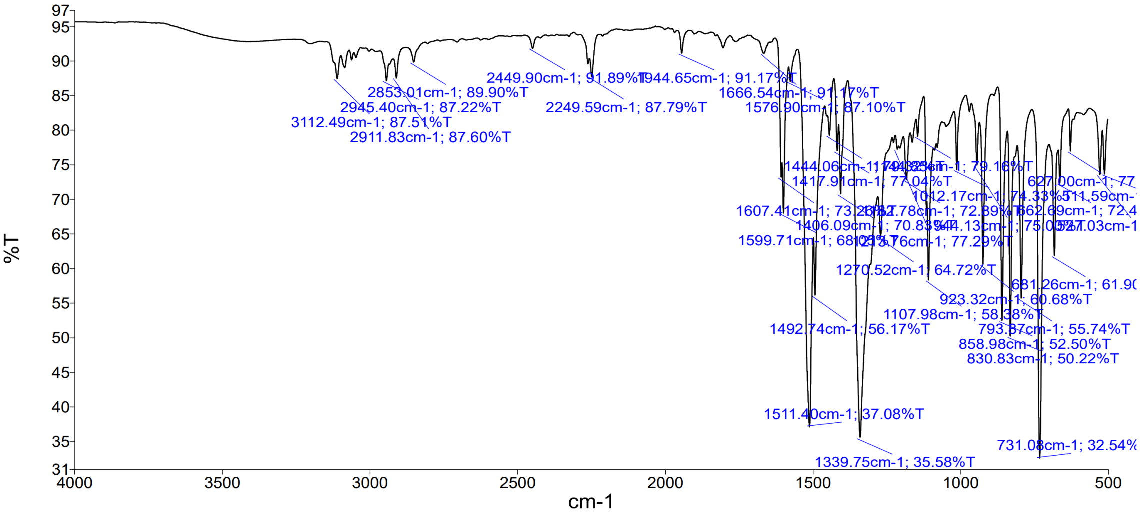
The melting point was at around 100 °C. Many other lab partners who did the same experiment had similar observations. Normally the melting point should be around 117 °C, but some impurities could have brought it down to 100 °C.

IR Spectrum

This would be the literature values of the infrared spectrum of (4-nitrophenyl)acetonitrile [7].



And this would be the measured infrared spectrum of the synthesized (4-nitrophenyl)acetonitrile from the author.



Wavenumber (cm^{-1})	Bond	%T
3112.49	Aromatic C-H stretch	87.51%
2945.40	Aliphatic C-H stretch	87.22%
2911.83	Aliphatic C-H stretch	87.60%
2853.01	Aliphatic C-H stretch	89.90%
2249.59	CN stretch	87.79%
1944.65	NO_2 asymmetric stretch	91.17%
1666.54	C=C stretch (Aromatic)	91.17%
1576.90	N-O symmetric stretch	87.10%
1444.06	C-H bending (Aliphatic)	79.32%
1417.91	C-H bending (Aliphatic)	77.04%
1406.09	C-N stretch	70.83%
1270.52	C-N stretch	64.72%
1213.76	C-N stretch	77.29%
1144.85	C-N stretch	79.16%
1012.17	C-O stretch	74.33%
944.13	C-O stretch	75.00%
858.98	C-H out-of-plane bend	52.50%
830.83	C-H out-of-plane bend	50.22%

In the spectral analysis, the observed peaks mostly align with those documented in the literature, although they are weaker in intensity [8]. The wavelengths are accurate, but the absorption rates are lower, indicated by the T%, potentially due to the presence of impurities, variations in sample concentration, or the influence of the instrument's sensitivity and configuration.

References

[1] Sigma-Aldrich. Safety data sheet for (4-nitrophenyl)acetonitrile. `https://www.sigmaaldrich.com/CH/en/sds/ALDRICH/151572?userType=anonymous`, 2024. Accessed on 29 March 2024.

[2] Chemdad. p-nitrophenylacetonitrile. `https://chemdad.com/index.php?c=article&id=9479`, 2024. Accessed on 29 March 2024.

[3] Sigma-Aldrich. Safety data sheet for benzyl cyanide. `https://www.sigmaaldrich.com/CH/en/sds/SIAL/12608`, 2024. Accessed on 29 March 2024.

[4] Sigma-Aldrich. Safety data sheet for sulfuric acid. `https://www.sigmaaldrich.com/CH/en/sds/SIGALD/258105`, 2024. Accessed on 29 March 2024.

[5] Sigma-Aldrich. Safety data sheet for nitric acid. `https://www.sigmaaldrich.com/CH/de/sds/SIGALD/438073?userType=anonymous`, 2024. Accessed on 29 March 2024.

[6] Pubchem. Compound summary for (4-nitrophenyl)acetonitrile. `https://pubchem.ncbi.nlm.nih.gov/compound/4-Nitrophenylacetonitrile`, 2024. Accessed on 29 March 2024.

[7] Chemical Book. p-nitrophenylacetonitrile(555-21-5) ir2. `https://www.chemicalbook.com/SpectrumEN_555-21-5_IR1.htm`.

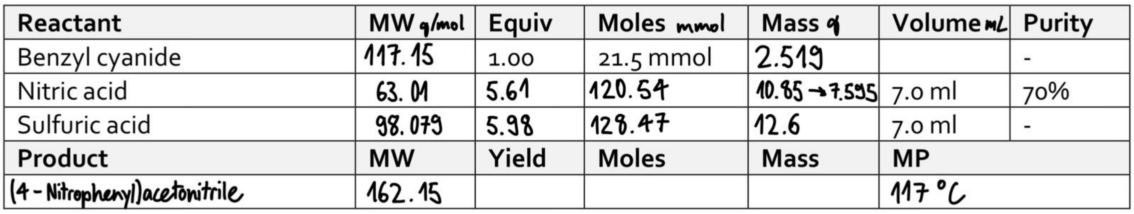
[8] Infrared spectroscopy absorption table. `https://chem.libretexts.org/Ancillary_Materials/Reference/Reference_Tables/Spectroscopic_Reference_Tables/Infrared_Spectroscopy_Absorption_Table`. Accessed on 02.03.2024.

Appendix

List of H and P Phrases

- **H301**, **H330**: Toxic if swallowed, fatal if inhaled.
- **H311**: Toxic in contact with skin.
- **H314**: Causes severe skin burns and eye damage.
- **H315**: Causes skin irritation.
- **H318**: Causes serious eye damage.
- **H319**: Causes serious eye irritation.
- **H331**: Toxic if inhaled.
- **H332**: Harmful if inhaled.
- **H335**: May cause respiratory irritation.
- **H336**: May cause drowsiness or dizziness.
- **H351**: Suspected of causing cancer.
- **H372**: Causes damage to organs through prolonged or repeated exposure.
- **H290**: May be corrosive to metals.
- **P210**: Keep away from heat, sparks, open flames, hot surfaces. — No smoking.
- **P220**: Store away from clothing/combustible materials.
- **P233**: Keep container tightly closed.
- **P234**: Keep only in original container.
- **P260**: Do not breathe dust/fume/gas/mist/vapours/spray.
- **P264**: Wash skin thoroughly after handling.
- **P271**: Use only outdoors or in a well-ventilated area.
- **P280**: Wear protective gloves/protective clothing/eye protection/face protection.
- **P301**, **P316**, **P317**: IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell.
- **P302** + **P352**: IF ON SKIN: Wash with plenty of water.
- **P304** + **P340**: IF INHALED: Remove person to fresh air and keep comfortable for breathing.
- **P305**, **P351**, **P338**: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
- **P321**: Specific treatment (see ... on this label).
- **P330**: Rinse mouth.
- **P332**, **P337**: If skin irritation occurs: Get medical advice/attention.
- **P361-P364**: Take off contaminated clothing and wash it before reuse.
- **P388**: Do not mix with other chemicals.
- **P403**, **P233**, **P405**: Store in a well-ventilated place. Keep container tightly closed. Store locked up.
- **P501**: Dispose of contents/container in accordance with local/regional/national/international regulations.

Table from the Experiment Manual



Reactant	**MW** g/mol	**Equiv**	**Moles** mmol	**Mass** g	**Volume** mL	**Purity**
Benzyl cyanide	117.15	1.00	21.5 mmol	2.519		-
Nitric acid	63.01	5.61	120.54	10.85 → 7.595	7.0 ml	70%
Sulfuric acid	98.079	5.98	128.47	12.6	7.0 ml	-
Product	**MW**	**Yield**	**Moles**	**Mass**	**MP**	
(4-Nitrophenyl)acetonitrile	162.15				117 °C	

Infrared Spectroscopy Absorption Table

The following table lists **infrared spectroscopy absorptions** by frequency regions.

4000-3000 cm^{-1}

3700-3584	medium	sharp	O-H	stretching	alcohol	free
3550-3200	strong	broad	O-H	stretching	alcohol	intermolecular bonded
3500- 3400	medium	-	N-H	stretching	primary amine	-
3400-3300 3330-3250	medium	-	N-H	stretching	aliphatic primary amine	-
3350-3310	medium	-	N-H	stretching	secondary amine	-
3300-2500	strong	broad	O-H	stretching	carboxylic acid	usually centered on 3000 cm^{-1}
3200-2700	weak	broad	O-H	stretching	alcohol	intramolecular bonded
3000-2800	strong	broad	N-H	stretching	amine salt	-

3000-2500 cm^{-1}

3333-3267	strong	sharp	C-H	stretching	alkyne	-
3100-3000	medium	-	C-H	stretching	alkene	-
3000-2840	medium	-	C-H	stretching	alkane	-
2830-2695	medium	-	C-H	stretching	aldehyde	doublet
2600-2550	weak	-	S-H	stretching	thiol	-

2400-2000 cm^{-1}

2349	strong	-	O=C=O	stretching	carbon dioxide	-
2275-2250	strong	broad	N=C=O	stretching	isocyanate	-
2260-2222	weak	-	C≡N	stretching	nitrile	-
2260-2190	weak	-	C≡C	stretching	alkyne	disubstituted
2175-2140	strong	-	S-C≡N	stretching	thiocyanate	-
2160-2120	strong	-	N=N=N	stretching	azide	-
2150	-	-	C=C=O	stretching	ketene	-
2145-2120	strong	-	N=C=N	stretching	carbodiimide	-
2140-2100	weak	-	C≡C	stretching	alkyne	monosubstituted
2140-1990	strong	-	N=C=S	stretching	isothiocyanate	-
2000-1900	medium	-	C=C=C	stretching	allene	-
2000	-	-	C=C=N	stretching	ketenimine	-

2000-1650 cm^{-1}

2000-1650	weak	-	C-H	bending	aromatic compound	overtone

1870-1540 cm^{-1}

1818 1750	strong	-	C=O	stretching	anhydride	-
1815-1785	strong	-	C=O	stretching	acid halide	-
1800-1770	strong	-	C=O	stretching	conjugated acid halide	-
1775 1720	strong	-	C=O	stretching	conjugated anhydride	-
1770-1780	strong	-	C=O	stretching	vinyl / phenyl ester	-
1760	strong	-	C=O	stretching	carboxylic acid	monomer
1750-1735	strong	-	C=O	stretching	esters	6-membered lactone
1750-1735	strong	-	C=O	stretching	δ-lactone	γ: 1770
1745	strong	-	C=O	stretching	cyclopentanone	-
1740-1720	strong	-	C=O	stretching	aldehyde	-
1730-1715	strong	-	C=O	stretching	α,β-unsaturated ester	or formates
1725-1705	strong	-	C=O	stretching	aliphatic ketone	or cyclohexanone or cyclopentenone
1720-1706	strong	-	C=O	stretching	carboxylic acid	dimer
1710-1680	strong	-	C=O	stretching	conjugated acid	dimer
1710-1685	strong	-	C=O	stretching	conjugated aldehyde	-
1690	strong	-	C=O	stretching	primary amide	free (associated: 1650)
1690-1640	medium	-	C=N	stretching	imine / oxime	-
1685-1666	strong	-	C=O	stretching	conjugated ketone	-
1680	strong	-	C=O	stretching	secondary amide	free (associated: 1640)
1680	strong	-	C=O	stretching	tertiary amide	free (associated: 1630)
1650	strong	-	C=O	stretching	δ-lactam	γ: 1750-1700 β: 1760-1730

1670-1600 cm^{-1}

1678-1668	weak	-	C=C	stretching	alkene	disubstituted (trans)
1675-1665	weak	-	C=C	stretching	alkene	trisubstituted
1675-1665	weak	-	C=C	stretching	alkene	tetrasubstituted
1662-1626	medium	-	C=C	stretching	alkene	disubstituted (cis)
1658-1648	medium	-	C=C	stretching	alkene	vinylidene
1650-1600	medium	-	C=C	stretching	conjugated alkene	-
1650-1580	medium	-	N-H	bending	amine	-
1650-1566	medium	-	C=C	stretching	cyclic alkene	-
1648-1638	strong	-	C=C	stretching	alkene	monosubstituted
1620-1610	strong	-	C=C	stretching	α,β-unsaturated ketone	-

1600-1300 cm^{-1}

1550-1500 1372-1290	strong	-	N-O	stretching	nitro compound	-
1465	medium	-	C-H	bending	alkane	methylene group
1450 1375	medium	-	C-H	bending	alkane	methyl group
1390-1380	medium	-	C-H	bending	aldehyde	-
1385-1380 1370-1365	medium	-	C-H	bending	alkane	gem dimethyl

1400-1000 cm^{-1}

1440-1395	medium	-	O-H	bending	carboxylic acid	-
1420-1330	medium	-	O-H	bending	alcohol	-
1415-1380 1200-1185	strong	-	S=O	stretching	sulfate	-
1410-1380 1204-1177	strong	-	S=O	stretching	sulfonyl chloride	-
1400-1000	strong	-	C-F	stretching	fluoro compound	-
1390-1310	medium	-	O-H	bending	phenol	-
1372-1335 1195-1168	strong	-	S=O	stretching	sulfonate	-
1370-1335 1170-1155	strong	-	S=O	stretching	sulfonamide	-

1350-1342 1165-1150	strong	-	S=O	stretching	sulfonic acid	anhydrous hydrate: 1230-1120
1350-1300 1160-1120	strong	-	S=O	stretching	sulfone	-
1342-1266	strong	-	C-N	stretching	aromatic amine	-
1310-1250	strong	-	C-O	stretching	aromatic ester	-
1275-1200 1075-1020	strong	-	C-O	stretching	alkyl aryl ether	-
1250-1020	medium	-	C-N	stretching	amine	-
1225-1200 1075-1020	strong	-	C-O	stretching	vinyl ether	-
1210-1163	strong	-	C-O	stretching	ester	-
1205-1124	strong	-	C-O	stretching	tertiary alcohol	-
1150-1085	strong	-	C-O	stretching	aliphatic ether	-
1124-1087	strong	-	C-O	stretching	secondary alcohol	-
1085-1050	strong	-	C-O	stretching	primary alcohol	-
1070-1030	strong	-	S=O	stretching	sulfoxide	-
1050-1040	strong	broad	CO-O-CO	stretching	anhydride	-

1000-650 cm^{-1}

995-985 915-905	strong	-	C=C	bending	alkene	monosubstituted
980-960	strong	-	C=C	bending	alkene	disubstituted (trans)
895-885	strong	-	C=C	bending	alkene	vinylidene
850-550	strong	-	C-Cl	stretching	halo compound	-
840-790	medium	-	C=C	bending	alkene	trisubstituted
730-665	strong	-	C=C	bending	alkene	disubstituted (cis)
690-515	strong	-	C-Br	stretching	halo compound	-
600-500	strong	-	C-I	stretching	halo compound	-

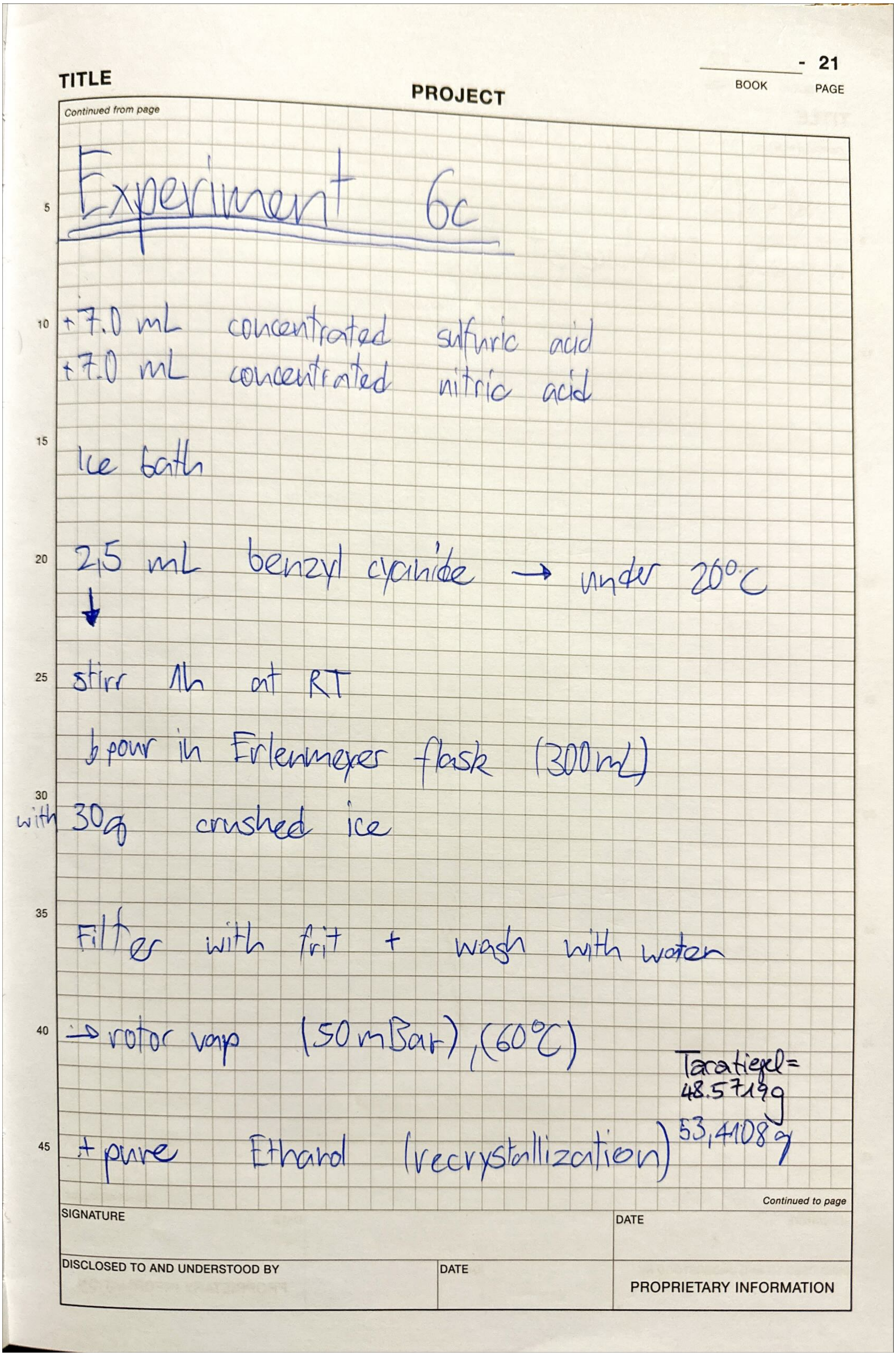
900-700 cm^{-1}

880 ± 20 810 ± 20	strong	-	C-H	bending	1,2,4-trisubstituted	-
880 ± 20 780 ± 20 (700 ± 20)	strong	-	C-H	bending	1,3-disubstituted	-

810 ± 20	strong	-	C-H	bending	1,4-disubstituted or 1,2,3,4-tetrasubstituted	-
780 ± 20 (700 ± 20)	strong	-	C-H	bending	1,2,3-trisubstituted	-
755 ± 20	strong	-	C-H	bending	1,2-disubstituted	-
750 ± 20 700 ± 20	strong	-	C-H	bending	monosubstituted benzene derivative	-

Contributors and Attributions

- OChemOnline



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Experiment 6c

+7.0 mL concentrated sulfuric acid
+7.0 mL concentrated nitric acid

Ice bath

2,5 mL benzyl cyanide → under 20°C
↓

stirr 1h at RT

↳ pour in Erlenmeyer flask (300mL)
with 30g crushed ice

Filter with frit + wash with water

→ rotor vap (50 mBar), (60°C)

Taratiegel =
48.5719g

+ pure Ethanol (recrystallization) 53,4108 g

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SIGNATURE		DATE
DISCLOSED TO AND UNDERSTOOD BY	DATE	PROPRIETARY INFORMATION

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1 : 1
n-Hexan || Ethylacetat