School of Engineering
Institute of Materials
Laboratory of Macromolecular
and Organic Materials

Organic Chemistry (MSE 211)

Synthesis and Purification of *p*-Iodonitrobenzene

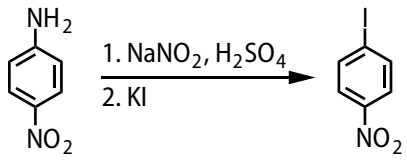
1. Introduction

The regiochemistry in electrophilic aromatic substitution reactions is strongly influenced by the substituents already present on the aromatic ring. However, certain substitution patterns, particularly those involving aryl iodides, are difficult to access directly, since iodine is a relatively unreactive electrophile toward aromatic systems. A convenient alternative is to introduce iodine through **nucleophilic aromatic substitution** of a diazonium salt, a transformation commonly known as the Sandmeyer reaction. This strategy often exploits the versatility of the nitro group: it can be introduced by electrophilic substitution, reduced to the corresponding amine, and then converted into a diazionium ion, which can undergo substitution with a wide variety of nucleophiles, including iodide.

Reading Recommendation: *Clayden*, Chapters 21 and 22

2. General Principle of the Synthesis

The transformation of *p*-nitroaniline into *p*-iodonitrobenzene proceeds via a diazonium-mediated nucleophilic aromatic substitution. In the first step, the amino group is converted into the corresponding diazonium salt under strongly acidic conditions. This diazionium intermediate is then displaced by iodide in a Sandmeyer-type reaction, yielding the desired aryl iodide.



3. Required Equipment

- two 100 mL round bottom flasks, 50 mL and 100 mL beakers, 1 L Erlenmeyer flask
- 50 mL graduated cylinder
- DrySin©, heating plate, magnetic stirrer
- reflux condenser
- Büchner funnel
- spatula
- TLC chamber, TLC silica gel on aluminum foil

4. Experimental Procedure

p-Nitroaniline (5 g) is mixed with concentrated sulfuric acid (96 %, 4.1 mL) in water (30 mL) in a 100 mL round bottom flask. The mixture is stirred until the compound is dissolved. In parallel, a solution of sodium nitrite (2.5 g) in water (10 mL) and a solution of potassium iodide (10 g) in water (30 mL) are prepared. After the starting aniline is dissolved, the round bottom flask is immersed in an ice bath to keep the temperature below 5 °C. The sodium nitrite solution is then slowly added with continuous vigorous stirring and the mixture is stirred for 15 min. The potassium iodide solution is transferred into a 1 L Erlenmeyer flask. The cold diazonium solution is then very slowly poured into the potassium iodide solution upon vigorous stirring to minimize diazonium decomposition, which can lead to gas evolution. The precipitated crude product is filtered over a Büchner funnel and washed thoroughly with cold water.

5. Purification

The crude product is purified by recrystallization from ethanol (~75 mL).

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Note: Add at least 50 mL of ethanol before you start to heat! The purified product should then be thoroughly washed with cold ethanol.

6. Control of the Purity

6.1 Thin-Layer Chromatography (TLC)

The purity of the product should be checked by thin layer chromatography (TLC). Compare the R_f values of the product and the starting compounds.

6.2 Melting Point Determination

The melting point of the dry product is measured and compared with the literature value (171–173 °C).

6.3 NMR Spectroscopy

Analyze the ^{1}H-NMR spectrum of the starting and target compound dissolved in $CDCl_3$ and compare them.

7. End of the Manipulation

1/ The product is weighed in a sample vial labelled with compound name, student name, and date. Then, it is trashed as halogenated organic solvent waste.

2/ All starting materials are put back into the retention trays.

3/ The glassware is cleaned, dried, and put back in place:

- Remaining traces of organic chemical compounds are removed by rinsing the flask with a minimum of solvent (for example acetone), which is subsequently disposed as non-halogenated organic solvent waste in case of the starting compound and as halogen containing organic solvent waste in case of the product.

- Being free of any chemical contamination, the dirty glassware is washed with a conventional detergent and rinsed thoroughly. It is then rinsed

Learning Objective: **Thin Layer Chromatography (TLC)**

Chromatographic methods are widely applied in organic chemistry, particularly for compound isolation, analysis, or following the progress of a reaction.
Chromatography is based on the continuous exchange of chemical compounds between a mobile phase (solvent) and a stationary phase (most common: silica gel). Depending on the distribution coefficient, compounds move with a different rate along the direction of flow. Adsorption, i.e. an interaction between a stationary phase and a compound, is fundamental for thin layer chromatography (TLC). The chemical structure, in particular differences in polarity and hydrogen bonding capability, has a major impact on the adsorption behavior of a compound, which in turn is also strongly influenced by the solvent.

Given a defined solvent composition, a compound can accordingly be characterized by the so-called retention factor (RF-value) that is the ratio of migration distance of the compound and migration distance of the solvent front. In practice, the sample of interest is dissolved in a solvent of low polarity and placed as a small spot on the lower corner of the TLC plate. The TLC plate is placed into a chamber that contains the eluent. Capillary forces move the eluent from the bottom to the top of the TLC plate. When finished, the solvent front is marked and the RF-value determined. UV-light is the most common source for sample detection. Commercial TLC plates are often coated with a fluorescence indicator and fluoresce upon UV-irradiation. Compounds that absorb the incoming UV-light (for example, aromatic compounds) appear as dark spots on the plate. Using shortwave UV-light, the compound may inherently fluoresce itself.

TLC is highly suitable for following the progress of a reaction. Comparing the RF-value of starting compounds, potential intermediates, and products allows to qualitatively determine the degree of the chemical conversion.

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with deionized water to avoid the presence of limestone. It is possible to dry the glassware with acetone.

- All the glassware used is placed back into its original location. Any defective part is signaled to the assistant.

4/ The fume hood is tidied up. All electrical appliances are unplugged. Ventilation and lighting of the hood are switched off.

5/ The sink is cleaned.

6/ All waste contaminated with chemicals (absorbent paper, etc.) is collected in specific recovery cans, according to the indications of the assistants.

Be sure you have also completed the prelab protocol with the relevant safety information (**BEFORE** the lab course).

8. To be Addressed in the Protocol

1.) Give a detailed reaction mechanism including the elementary steps. Comment on the potential side product formation and show its mechanism.

2.) Where does the gas evolution that might occur upon mixing the diazonium salt with the potassium iodide solution come from?

3.) Which compounds are separated during the recrystallization?

4.) Why is it important to add only 1 equivalent of sodium nitrite in the system? What is the potential side reaction that can occur upon adding potassium iodide if there is excess of sodium nitrite?

5.) Can HCl be used as a strong acid instead of sulfuric acid? Explain your answer.

Learning Objective: **Recrystallization – Principle and Practical Realization**

The crude product is purified by recrystallization. This technique is very practical on an industrial scale, typically resulting in compounds in a very pure form.

A product obtained by a chemical reaction always contains "impurities", such as solvents, traces of starting materials, decomposition products, or side products. Several techniques have been developed to remove these impurities, among which recrystallization is of utmost importance for the purification of *solid products.*

Recrystallization is based on the different solubility of a compound at different temperatures. The solubility increases with increasing temperature and becomes disproportionately high towards the boiling point. Accordingly, a compound is typically recrystallized from a solvent referred to as "bad solvent" at room temperature, whereas it provides sufficient solubility close to its boiling point.

A recrystallization is performed as follows:

a) Dissolving of the impure solid in the minimum volume of an appropriate solvent at the solvent boiling temperature (ideally forming a saturated solution at boiling temperature). In some cases, binary solvent mixtures can be applied instead of a single solvent.

b) A slow cooling of this solution is required for the success of recrystallization, particularly at temperatures close to the boiling point when nucleation of the crystals is initiated. During further temperature decrease, the decreasing solubility promotes the formation of product crystals

Although the purity of the crystalline product is improved by means of recrystallization, exclusion of the impurities is not complete. Some impurities still co-crystallize with the target compound, their concentration being a function of their initial amount, their chemical nature, the cooling rate, and the solvent. If the degree of purity achieved by recrystallization is not considered as sufficient, it can be improved by a second (or even third) recrystallization. In current practice, a purity of 98-99% is acceptable for most applications.

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