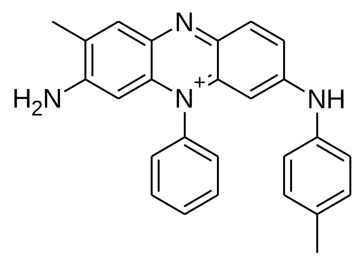
The history of indigo

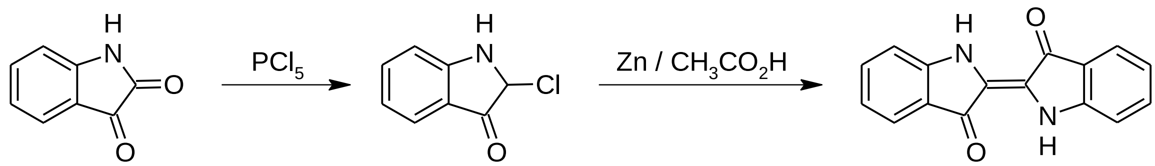
Blue jeans may the current fashion, but the dye used in coloring them has a long history in which chemistry is very much involved. Blue jeans are made of cotton denim, and the substance responsible for the blue color, indigo, has been known for at least 4000 years. The indigo plant (*Indigofera tinctoria*) was grown mainly in India. 1.7 million acres were required which yielded 8000 tons of indigo annually, worth $100 M. The dye was obtained by extraction of the plant's leaves.

In 1856, William Henry Perkin at the age of 17 discovered the synthesis of Mauveine (a mixture of 4 compounds, one of which is shown below). He was working as a lab assistant at the Royal College of Chemistry in London, England, conducting experiments in his apartment over the Easter holiday. The era of synthetic dyes was born.



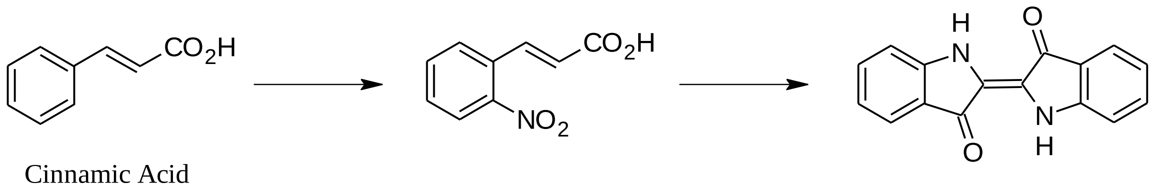
Structure of Mauveine A

Starting in 1865, recognizing the potential of synthetic dyes, Adolph von Baeyer (Professor in Munich, Germany) researched the synthesis of indigo and determined its structure in 1870. The same year he prepared indigo from isatin:



Isatin   Indigo

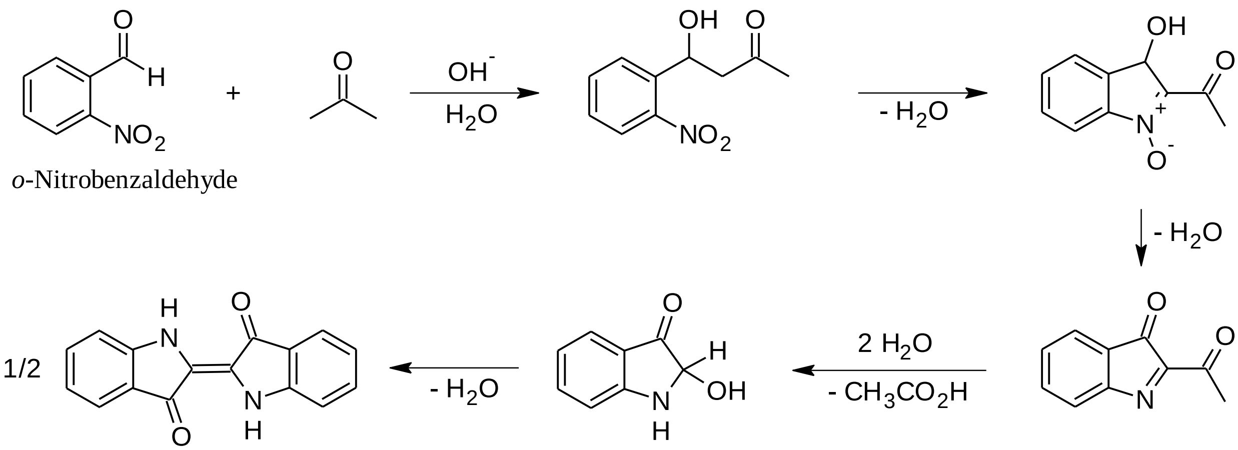
Isatin unfortunately was rare and extremely expensive, unsuitable for industry. In 1878 Baeyer completed the laboratory synthesis of indigo starting from phenylacetic acid (Ph-CH_2CO_2H). Baeyer spent another five years improving the process and informed his friend Heinrich Caro in 1883 about his findings. Caro was the head of research at BASF and immediately recognized two of Baeyer's synthetic routes to be potentially useful for industrial scale up:



Cinnamic Acid

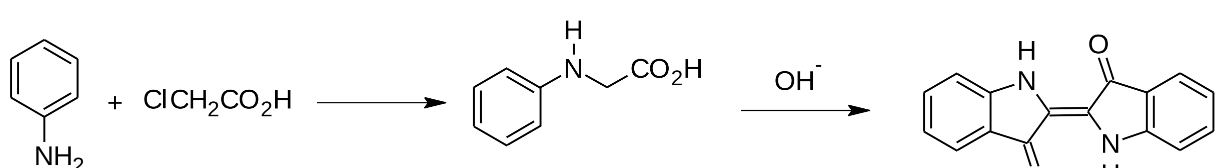
Baeyer patented this synthetic route and sold it to BASF for $100,000. In the end it proved too expensive.

A second route, developed in 1882 by Baeyer and Drewson turned out to be impractical at the time because the starting material was very difficult to make. However, *o*-Nitrobenzaldehyde is readily available these days and we will use this route in the lab today:



o-Nitrobenzaldehyde

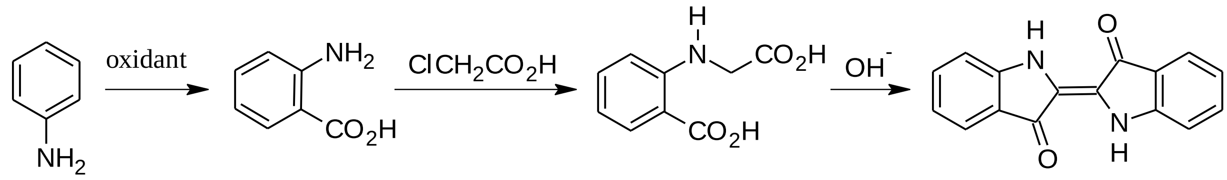
The only two industrial players in indigo research, BASF and Hoechst, joined forces but researchers in both companies spent another decade developing a viable route to indigo that could compete with the natural product. A major breakthrough was achieved in 1890 when Karl Heumann (Professor in Zurich, Switzerland) discovered two routes starting from the readily available Anilin:



Anilin

A major setback was the fact that the reaction gave poor yields when scaled up and was never used industrially.

His second synthesis however was fruititious and both companies built factories for multi-ton preparation of synthetic indigo:

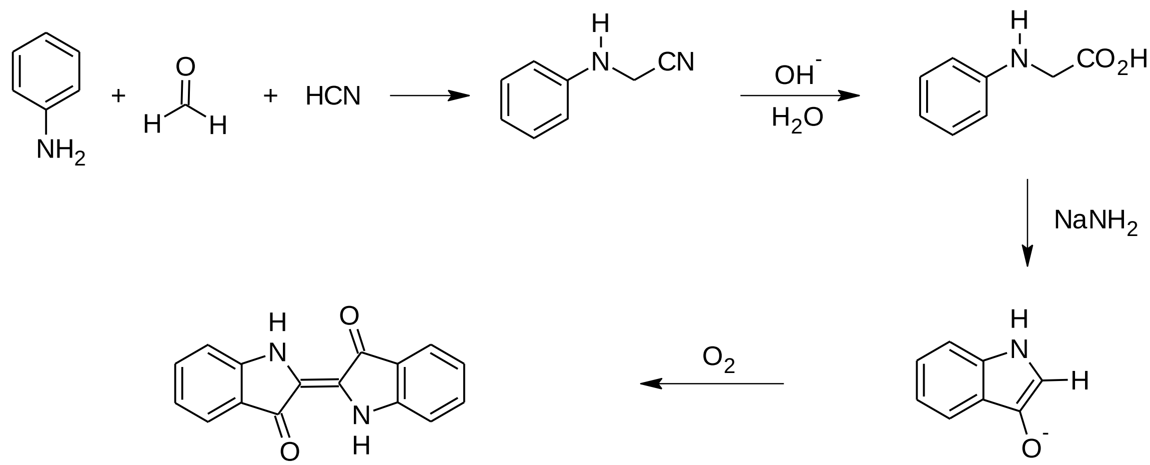


oxidant = Cr(III) (Hoechst)

Hg, H_2SO_4 (BASF)

One of the most remarkable chapters of industrial synthesis happened at Hoechst where construction of an entire indigo factory was stopped just before its completion when Johannes Pfleger recognized that yields in the first Heumann synthesis could be improved dramatically if $NaNH_2$ was added to OH^- in the final step. Retrofitting the factory cost over $250 M but the gamble paid off.

In 1897 the first synthetic indigo was sold by BASF, Hoechst followed 5 years later. The development of large scale industrial synthesis of indigo went mainly unnoticed worldwide and the sensational announcement by BASF was met with skepticism. BASF had to hire an independent company to verify their production. It was quickly recognized that because of the low price and superior purity, the dye could not originate from plant material. By 1913 BASF sold 4900 tons of indigo annually while Hoechst sold 4500 tons. The production has of course been improved, the synthetic routes tweaked to ensure the most competitive product. The most current synthesis was introduced in 1925 by BASF based on work by Baeyer and is still in use today:



Current annual production is about 5000 tons, almost all of it for the dying of jeans. For every pair of jeans, 10 g of indigo is required.

Synthesis of Indigo

Safety

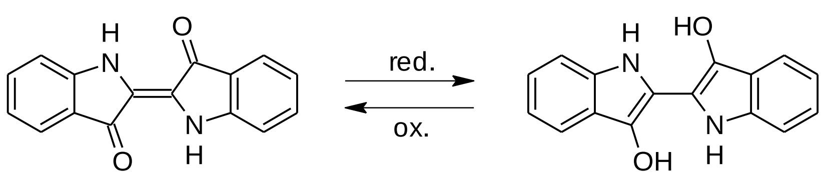
Personal protective equipment including safety goggles, gloves and a lab coat must be worn at all times during the experiment. Long pants must be worn along with close-toed shoes. No food or drink is allowed in the lab. Acetone is flammable. Acetone is a skin irritant and is toxic by ingestion or inhalation. o-Nitrobenzaldehyde is a mutagen. Sodium hydroxide is a caustic agent. Ethyl alcohol is flammable. Indigo is a mild irritant. Indigo will be absorbed by the skin, and it causes a blue coloration.

Procedure

1. In a test tube, dissolve 0.5 g of o-nitrobenzaldehyde in 5 mL of acetone.
2. Add 5 mL of water and stir using a stir rod.
3. Add 2.5 mL of 1 M NaOH dropwise and observe the blue color of indigo form. Let the reaction stand for 5 minutes.
4. Collect the precipitated indigo by vacuum filtration using a Buchner funnel. Wash with 10 mL of water then 10 mL of ethanol.

Synthesis of Leucoindigo and Dying

One of the major problems encountered early on in the use of indigo as a dye is the fact that it is not very soluble in water. While this is good news for washing fabrics, it makes it very difficult to get it into the material in the first place. Indigo can be reduced to leucoindigo which is water soluble, adheres well to fabric and is almost colourless. Simple air oxidations converts it back to the blue indigo.



Indigo Leucoindigo

Formally, leucoindigo is hydrogenated indigo and the simple equation for its conversion is:

Indigo + 2 H· → Indigo-H_2, where H· is a hydrogen atom

We will produce hydrogen *in situ*:

$Na_2S_2O_4 + 4\ H_2O \rightarrow 2\ NaHSO_4 + 6\ H\cdot$

Once applied to the fabric, indigo is regenerated:

$\text{Indigo-}H_2 + \frac{1}{2}\ O_2 \rightarrow \text{Indigo} + H_2O$

Procedure

1. Place the indigo precipitate in a 25 mL RBF with 10 mL of water, 3 pellets of NaOH, and a magnetic stirbar.
2. Heat the solution to boiling using a thermowell.
3. Add 2 mL of 10% sodium dithionite.
4. Add additional sodium dithionite dropwise until the indigo dissolves and a clear, yellowish leucoindigo solution forms.
5. Place 100 mL of cool water into a 250 mL beaker and add the leucoindigo solution.
6. Place a piece of cotton cloth into the beaker and work into the dye solution with a heavy glass rod.
7. After a few minutes, remove the cloth and allow to air dry. As the cloth dries, the blue indigo color will appear.

References used:

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The birth of the pharmaceutical industry

The discovery and industrial exploitation of the indigo synthesis was a major step forward in the chemical industrial revolution. Some of the companies involved in the dye industry are still around today but their main products have changed. The story below highlights how important observations taken during a lab session are.

A medical student, Paul Ehrlich, had been impressed with the ability of certain dyes to stain tissues selectively. Ehrlich believed that staining was a result of a chemical reaction between the dye and the tissue, so he sought dyes that had an affinity for micro-organisms, hoping that the dye could be modified to become specifically lethal to the micro-organisms. Ehrlich discovered in 1907 the curative properties of the dye, Trypan Red I, when used as a remedy for syphilis. Through these discoveries he invented the term “chemotherapy”. His research was looking for “magic bullets” – chemicals that would be toxic to infectious microorganisms but harmless to humans.

In 1935, the daughter of Gerhard Domagk, a doctor employed by a German dye manufacturer (I. G. Farbenindustrie), contracted a streptococcal infection (strep) from a pin prick. As his daughter neared death, her father decided to give her an oral dose of a dye called Pronstil, which had been developed by the company. Tests had shown that it inhibited the growth of streptococci in mice. Within a short time the little girl recovered. Domagk’s gamble not only saved his daughter’s life, but it initiated a new and wonderful productive phase in modern chemotherapy.