Honors Cup Synthetic Proposal

Section: 270-V
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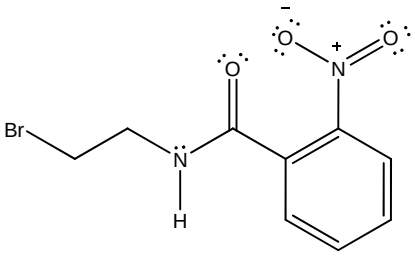
Title: Synthesis of indigo from N-(2-bromoethyl)-2-nitrobenzamide

Introduction: Indigo has been used as a dye in clothing for over a thousand years. It was first painstakingly extracted from a plant called woad, which produced a chemically identical dye to the one used today. Around 1900, chemical syntheses of indigo were discovered and replaced natural sources. Indigo is especially useful as a dye because the hydrogen atoms bonded to the nitrogen atoms can migrate to the carboxyl groups, creating hydroxyl groups and making the dye water soluble. After fabric is soaked in the reduced indigo solution, it is allowed to oxidize in air and the indigo becomes insoluble again; thus, the fabric will remain blue when it is washed.

Overall synthetic reaction scheme:

A

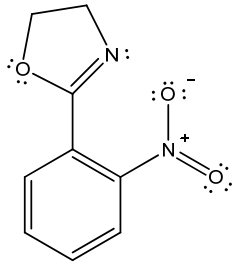


N-(2-bromoethyl)-2-nitrobenzamide

CAS number: 63004-24-0
Chemical Formula: $C_9H_9BrN_2O_3$
Molecular Weight: 273.09

1) NaOH in ethanol
2) HCl

B



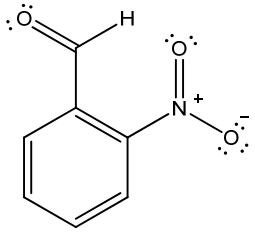
2-(2-nitrophenyl)-4,5-dihydrooxazole

CAS number: 88186-34-9
Chemical Formula: $C_9H_8N_2O_3$
Molecular Weight: 192.174

1) $NiCl_2$, $NaBH_4$
2) 5% HCl

Both in methanol

C

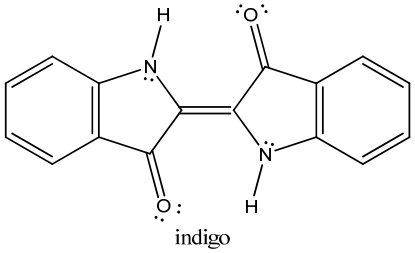


2-nitrobenzaldehyde

CAS number: 552-89-6
Chemical Formula: $C_7H_5NO_3$
Molecular Weight: 151.12
Melting Point: 43.5 °C

1) Acetone
2) NaOH

X



indigo

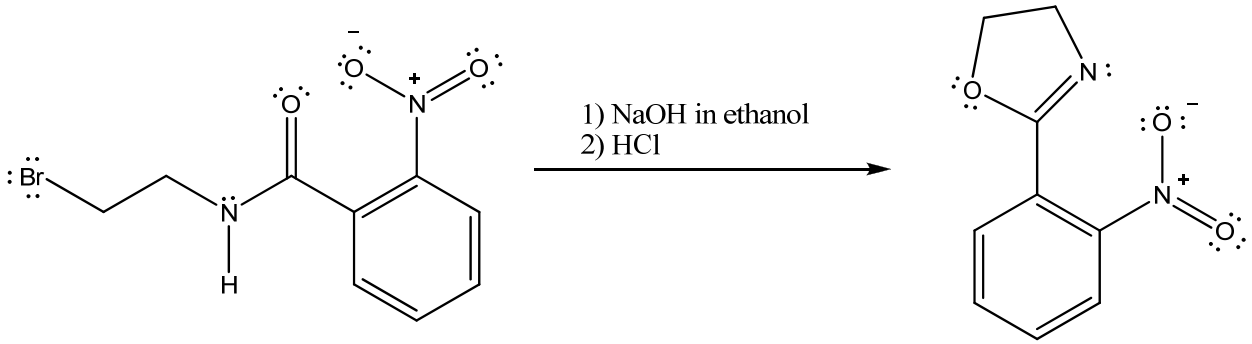
CAS number: 482-89-3
Chemical Formula: $C_{16}H_{10}N_2O_2$
Molecular Weight: 262.2676
Melting Point: 300 °C

Prelab:

Synthesize at least 0.005 mol (1.37 grams) of N-(2-bromoethyl)-2-nitrobenzamide using 2-nitrobenzoyl chloride with 2-bromoethylamine hydrobromide (for use in experiment). Use an aqueous solution of 0.010 mole (2.049 grams) of 2-bromoethylamine hydrobromide in 150 mL of distilled water; to this, add a solution of 0.011 mole (2.041 grams) of 2-nitrobenzoyl chloride in 50 mL of warm benzene. Shake and cool the emulsion in running water during the gradual addition of a 5% aqueous solution of 0.023 mole of sodium hydroxide. Shake mixture mechanically for two hours, then filter the solid amide out with suction and wash in dilute sodium carbonate solution. Recrystallize the amide from benzene.

Step 1

Synthetic transformation 1:



N-(2-bromoethyl)-2-nitrobenzamide

2-(2-nitrophenyl)-4,5-dihydrooxazole

Experimental 1:

0.005 mol (1.37 grams) of N-(2-bromoethyl)-2-nitrobenzamide are dissolved in 100 mL of hot (70-75°C) ethanol. Create a warm 80% alcohol solution with 0.0051 mol (0.204 grams) of sodium hydroxide, and add slowly to the first solution while stirring. Maintain the reaction mixture at the initial temperature for 30 seconds, and then pour rapidly with stirring, into approximately 400 grams of ice water. Filter with suction, and then dissolve in 15% cold (below 15°C) hydrochloric acid. To store, make the solution alkaline with cold dilute aqueous ammonia.

Expected Yield 1:
.0046 mol (.884 grams) 2-(2-nitrophenyl)-4,5-dihydrooxazole, 92% yield

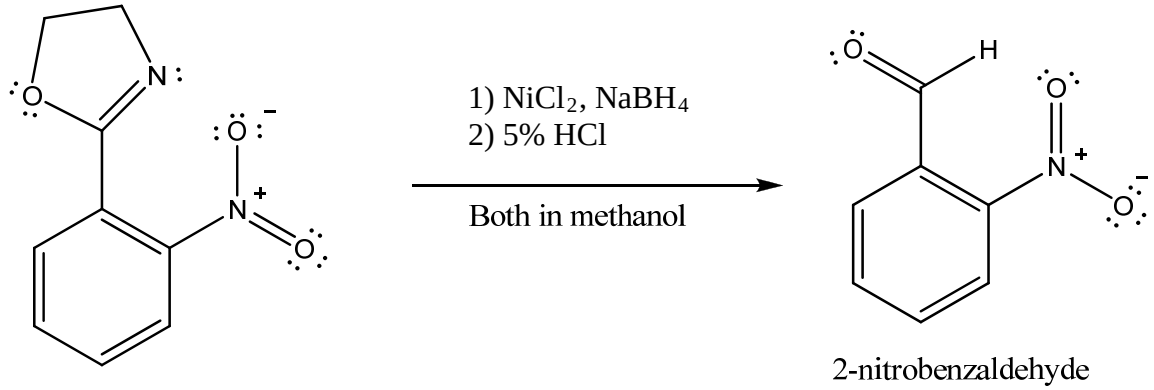
Safety 1:
Acids and acidic solutions, such as hydrochloric acid, can cause burns. Handle with care and avoid skin contact with HCl.

Bases and basic solutions, such as sodium hydroxide, can cause burns. Handle with care and avoid skin contact with NaOH.

Be sure to dispose all materials into proper waste containers.

Step 2

Synthetic transformation 2:



2-(2-nitrophenyl)-4,5-dihydrooxazole

2-nitrobenzaldehyde

Experimental 2:

First, 2-(2-nitrophenyl)-4,5-dihydrooxazole, the organic product from the previous step, (0.0046 mol, .884 grams) and $NiCl_2$ (0.0092 mol, 1.192 grams) were dissolved in methanol and cooled to -10°C using an ice bath. Add sodium borohydride (0.0184 mol, .678 grams) in small amounts over 30 minutes while maintaining the temperature at 10°C. Continue to the keep the temperature of the mixture at 10°C for 30 minutes to allow the reaction to complete. Filter the reaction mixture by gravity filtration. Now, evaporate the solvent under vacuum. Treat the residue with 5% HCl (10 mL) at 40°C for 10–15 minutes. Allow the mixture to cool to room temperature. Extract the organic product with diethyl ether (25 mL). Wash the organic layer with water, dry over anhydrous sodium sulfate and evaporate under a vacuum to give 2-nitrobenzaldehyde as a colorless oily liquid.

Expected yield 2:
.00414 mol (.626 grams) 2-nitrobenzaldehyde, 90% yield

Safety 2:
Acids and acidic solutions, such as hydrochloric acid, can cause burns. Handle with care and avoid skin contact with HCl

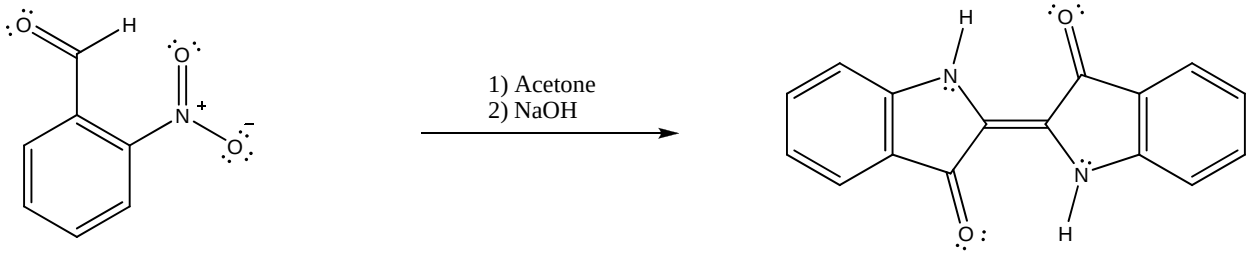
Sodium borohydride is corrosive. Causes burns to any area of contact. Harmful if swallowed, inhaled or absorbed through skin.

Nickel salts are carcinogenic. Be careful not to inhale any dust fumes.

Be sure to dispose all materials into proper waste containers.

Step 3

Synthetic transformation 3:



2-nitrobenzaldehyde

indigo

Experimental 3:

0.00414 mol (.626 grams) of 2-nitrobenzaldehyde and 7.825 mL of acetone are combined in an appropriately sized flask, placed in an ice bath, and slowly stirred with a magnetic stirring rod. 7.825 mL of 1.0 M sodium hydroxide are slowly added to the solution. The mixture is stirred slowly for five minutes after the sodium hydroxide is added. Indigo forms as a blue precipitate and can be isolated by vacuum filtration.

Expected Yield 3:
.532 grams indigo, 86% yield*

Safety 3:
Bases and basic solutions, such as sodium hydroxide, can cause burns. Handle with care and avoid skin contact with NaOH.

Be sure to dispose all materials into proper waste containers.

*The journal article, from 1882, did not contain percent yield information. The expected yield is based on stoichiometric calculations.

Overall budget:

Chemical	Purity	Supplier	Cost	Amt. Needed	Total
2-nitrobenzoyl chloride	.97	Aldrich	$81.50/25 grams	2.049 grams	$6.68
2-bromoethylamine hydrobromide	>.97	Fluka	$70.90/100 grams	2.041 grams	$1.45
$NiCl_2$	.98	Aldrich	$26.80/50 grams	1.192 grams	$0.64
$NaBH_4$	>.985	Aldrich	$25.10/25 grams	0.678 grams	$0.68
				Total Cost:	**$9.45**

Notes: The prices for common laboratory materials were excluded from the calculations of total cost. These excluded materials include NaOH and HCl (which must be prepared to solutions of various molarities), methanol, ethanol, and acetone.

References:

(Prelab, 1) Leffler, M. T.; Adams, R. *J. Am. Chem. Soc.* **1937**, *59*, 2252-2258.

(2) Babu, M. S.; Rai, K. M. L. *Tetrahedron Lett.* **2004**, *45*, 7969-7970.

(3) Baeyer, A.; Drewson, V.; *Ber. Dtsch. Chem. Ges.* **1882**, *15*, 2856-2864.