Synthesis of 2, 4-Dinitrophenoxyacetic Acid, Pyridylglycine and 2-Methoxy-5-Nitrophenylglycine as Intermediates for Indigo Dyes

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Abstract *: The preparation of indigo dye intermediates was carried out using 2, 4-dinitrophenol, 2-aminopyridine and 2-methoxy-5-nitroaniline as starting materials or reactants in the search for new indigo dye intermediates. Approximately 0.5 mole of 2, 4-dinitrophenol, 0.42 mole of 2- aminopyridine and 0.2 mole of 2-methoxy-5-nitroaniline, were treated separately with appropriate quantity of chloroacetic acid and sodium hydroxide pellets using nitrobenzene a high boiling liquid as solvent. The products that resulted: 2, 4-dinitrophenoxyacetic acid, pyridylglycine and 2-methoxy-5-nitrophenylglycine were purified using solvent extraction, activated carbon and column chromatography to reveal different amorphous powders in each case. Their structures were established by spectral analysis: ultraviolet spectroscopy (UV), infrared spectroscopy (IR), mass spectrometry (MS), proton nuclear magnetic resonance spectroscopy (^{1}H-NMR) and carbon- 13 magnetic resonance spectroscopy (^{13}C-NMR).*
Keywords: *Analysis, Dye, Extraction, Intermediates, Precursors, Solvent*

I. Introduction

The sources of organic raw materials for the synthetic dyes are mainly coal tar distillate from petroleum industry. These primary raw materials are benzene, toluene, o-, m- and p- xylenes naphthalenes anthracene etc [1]. A great variety of inorganic chemicals are also used as well. In some cases, laboratory preparation of the required compound may act as the sources of the raw material. The primaries are never used directly in the synthesis; they are first converted into a large number of derivatives, which are in turn made into dyes. The derivatives are generally known as dye intermediates because they act as intermediates between the primaries and the final dye [2]. They are produced by reactions involving substitution such as nitration, sulphonation and halogenations; rearrangement reactions involving intramolecular cyclization and other reactions in which reduction, oxidation, and condensation are involved.

By definition, dyes are intensely coloured substances which when applied to a substrate imparts colour to it by a process which at least temporarily destroys the crystal structure of the coloured substance [3]. Indigo occurs naturally as a glucoside, indican in the leaves and stalk of *Indigofera tinctoria* and *Lonchocarpus cynascens* found in many parts of Eastern Nigeria. Other sources are the woad plant *Isatis tinctoria*, sea snail, *Murex brandis* and *Rothmania hospidia* known as "uri igbo" in Igbo speaking area of Nigeria in West Africa [4-5].

Synthetically, Indigo had been prepared from isatin, o-nitrocinnamic acid, aniline, anthranilic acid, o-, m- and p-toluidines [6].

In this article, indigo dye intermediates: 2, 4-dinitrophenoxyacetic acid, pyridylglycine and 2-methoxy-5-nitrophenylglycine were synthesized from 2, 4-dinitrophenol 2-aminopyridine and 2-methoxy-5-nitroaniline.

2.0 General Experimental Procedures

All reagents were of analytical grades, purchased from Aldrich, USA and BDH England. All melting points were determined on Gallenkamp melting point instrument model MFB 595 and Electrothermal Digital melting point apparatus model IA9100 using open capillary tubes and were uncorrected. All weighing was done on Mettler P2010 and AE balances. Thin layer chromatography was performed on Kieslgel F_{254} (E.Merck) precoated plates and were visualized by spraying with 10 % H_2SO_4 or iodine vapour. Column chromatography was run on neutral alumina and this was used as a purification procedure. The infrared spectra was recorded on a Perkin-Elmer model 337 grating infracord spectrophotometer as KBr discs or as a solution using deuterated Dimethylsulphoxide (DMSO). Ultra violet and visible spectroscopy was done on UVI spectrophotometer model 061408, the GC-MS spectrophotometer were carried out on GC-6890N coupled with MS-5973N. Nuclear magnetic resonance spectra (^{13}C-NMR and ^{1}H-NMR) were determined on Fourier Transform (FT) model 6853 in deuterated DMSO at ambient temperature using Trimethylsilane as internal standard unless otherwise stated.

2.1 Synthesis of 2, 4-dinitrophenoxyacetic acid.

The reactant 2, 4-dinitrophenol 92.0 g (0.5 mol) was added into a two necked round bottomed 1000 mL flask and placed on a stirrer heater. Chloroacetic acid (47.25 g, 0.5 mol), sodium hydroxide pellets (20.0 g, 0.5 mol) followed by 200 mL of nitrobenzene were also added to the the reactant. The mixture was left to reflux for about 6 h; at the end of the reaction time, the contents were transferred to a 500 mL beaker to cool. Nitrobenzene which floated on top of the mixture was removed by decantation and the filtrate was washed severally in generous portions of acetone, a dark-brown powder was recovered and this was recrystallized from methanol- acetone solvent system to give a dirty white amorphous powder, this dissolved in water and methanol.

2.2 Synthesis of Pyridylglycine.

The substituted pyridine; 2-aminopyridine was the substrate. About 63.0 g (0.42 mole) of it, 39.69 g (0.42 mole) of chloroacetic acid and 20.0 g (0.5 mole) of sodium hydroxide were introduced into a 500 mL round bottomed flask already having 200 mL of nitrobenzene which was used as the solvent for the reaction. The reaction was under reflux for 5 h, dark slurry was recovered which was washed exhaustively in 5 x 200 mL of methanol, passed through alumina packed column to yield a creamy powder. The compound was soluble in water and sparingly soluble in acetone, methanol and dichloromethane.

2.3 Synthesis of 2-methoxy-5-nitrophenylglycine.

Into a 500 mL round bottomed flask were introduced 100 mL of nitrobenzene, 33.6 g (0.2 mole) 2-methoxyl-5-nitroaniline, 28.35 g (0.3 mole) chloroacetic acid and 20.0 g (0.5 mole) sodium hydroxide. The mixture was heated on a magnetic stirrer heater and refluxed for 6 h at a temperature of 320°C; the reaction was monitored by thin layer chromatography [7]. After 6 h, the mixture was transferred to a 1000 mL beaker and allowed to cool. The brown coloured solution was separated by filtration from the precipitate that formed [8-10]. The residue was washed with 5 x 100 mL acetone and finally recrystallized from 150 mL methanol treated with activated carbon to reveal a creamy powder. The yield was calculated and the purity determined by the melting point. The spectral analysis was carried out on this compound.

II. Results

The reaction of 2-methoxyl-5-nitroaniline, 2, 4-dinitrophenol and 2-aminopyridine when treated with chloroacetic acid in nitrobenzene under anhydrous condition at a temperature of above 300°C were summarized in Tables 1, 2 and 3 while their spectral results are given in Tables 4, 5 and 6.

Table 1 Data of the Reaction of 2, 4-dinitrophenol

Factors	Properties/ Results
Limiting Reagent	2,4-dinitrophenol
Product	2,4-dinitrophenoxyacetic acid
Theoretical yield	121 g
Actual yield	66 g
Percent yield	54.5 %
Melting point	196-197 $\pm$ 2
Colour	Dirty white powder
Solubility	Soluble in water and methanol

Table 2 Data of the Reaction of 2-Aminopyridine

Factors	Properties/ Results
Limiting Reagent	2-aminopyridine
Product	2-pyridylglycine
Theoretical yield	63.84
Actual yield	43.6
Percent yield	68.3 %
Melting point	179-180 $\pm$ 2
Colour	Dirty white
Solubility	Soluble in water

Table 3 Data of the Reaction of 2-methoxy-5-nitroaniline

Factors	Properties/ Results
Limiting Reagent	2-methoxy-5-nitroaniline
Product	2-methoxy-5-nitrophenylglycine
Theoretical yield	45.2 g
Actual yield	34.4 g
Percent yield	76.1 %
Melting point	194-195 $\pm$ 1
Colour	creamy powder
Solubility	Soluble in water and methanol

Table 4 Spectral Results of 2, 4-dinitrophenoxyacetic acid

Spectral Analysis	Solvent used	Results
UV/VIS	DMSO	ʎ max nm: 381
IR	DMSO, KBr dics	υ cm^{-1} 4197.4, 3896.6, 2810.2 2368.2, 1766.9, 1346.7
^{1}HNMR	DMSO-d$_6$	ꭤ ppm 3.4, 4.8, 8,8, 10.2, 10.8
^{13}C-NMR	DMSO-d$_6$	ꭤ ppm 177.0, 163.2, 146.3, 130.9, 128.0, 116.0, 66
MS		m/z 32, 77, 91, 152, 243(M$^+$)

Table 5 Spectral Results of 2-Pyridylglycine

Spectral Analysis	Solvent used	Results
UV/VIS	DMSO	ʎ max nm:338, 398, 460
IR	DMSO, KBr dics	υ cm^{-1} 3786.1, 3322.0, 3160.1, 2920.7, 2036.8, 1664.2, 1613.5, 1481.6, 1386.6
^{1}HNMR	DMSO-d$_6$	ꭤ ppm 3.8, 4.0, 5.2, 6.8, 7.0, 7.6, 7.8, 8.1
^{13}C-NMR	DMSO-d$_6$	ꭤ ppm 174.7, 144.6, 143.1, 137.8, 130.3, 123.7
MS		m/z 32, 44, 63, 152(M$^+$)

Table 6 Spectral Results of 2-methoxy-5-nitrophenylglycine

| Spectral Analysis	Solvent used	Results
UV/VIS	DMSO	ʎ max nm:328, 336, 381
IR	DMSO, KBr dics	υ cm^{-1} 3422, 2990.62, 2448.08, 2319.18, 1655.99, 1421.14, 1315.56.
^{1}HNMR	DMSO-d$_6$	ꭤ ppm 2.4, 3.3, 4.0, 6.4, 7.4, 8.8, 9.4, 10.0
^{13}C-NMR	DMSO-d$_6$	ꭤ ppm 173.10, 147.0, 139.1, 132.0, 129.0, 120.91, 114.0, 62.10.
MS		m/z 32,93, 152, 167, 226 (M$^+$)

III. Discussion

The reactant 2, 4-dinitrophenol 92.0 g, Chloroacetic acid 47.25 g and sodium hydroxide pellets 20.0 g yielded 66 g of 2, 4-dinitrophenoxyacetic acid with a melting point of about 196 ^{o}C. The UV analysis showed an absorption maxima at 381 nm. The IR spectrum indicated the presence of hydroxyl group of an acid at cm^{-1} 4197.4 and cm^{-1} 3896.6; aromatic methines at 2810.2 cm^{-1}, 2368.2 cm^{-1}; carbonyl band at 1766. 9 cm^{-1} and ether presence at 1346.7 cm^{-1} respectively. The ^{1}H-NMR showed a peak at ꭤ 10.2 and at ꭤ 10.8 for the proton of the carboxylic acid group; aromatic peak at ꭤ 8.8 and methylene peaks at ꭤ 3.4 and ꭤ 4.8. ^{13}C-NMR showed peaks at ꭤ 177.0 and ꭤ 163.2 for carbonyl carbon of acid; methine protons at ꭤ 146.3, ꭤ 130.9, ꭤ 128.0, ꭤ 116.0 and ꭤ 66 for CH$_2$ group. The mass spectrometry showed peaks at m/z 32 for HOCH$_3$; 77 for tropinium cation and 243 (m$^+$+ 1) which was the molecular peak plus proton and was in agreement with the molecular formular of the compound C$_8$H$_6$N$_2$O$_7$ [11-14].

The substituted pyridine; 2-aminopyridine 63.0 g reacted with 39.69 g of chloroacetic acid using 20.0 g of sodium hydroxide to produce 43.6 g of 2-pyridylglycine. The resulting dirty white compound which was soluble in water melted between 179-180 ^{o}C. The IR spectra at υ cm^{-1} 3786.1, 3322.0, 3160.1, 2920.7, 2036.8, 1664.2, 1613.5, 1481.6, 1386.6 were consistent with OH group of organic acids, N-H group (3322.0), C=C bond, carbonyl group and aromatic ring system. ^{1}H-NMR and ^{13}C-NMR showed consistent bands characteristic of the presence of carboxylic acid proton and carbon, aromatic methine groups and the molecular peak at m/z 152 confirmed the molecular formular C$_7$H$_8$N$_2$O$_2$.

The actual yield recovered when 33.6 g of 2-methoxy-5-nitroaniline was reacted with 28.35 g of chloroacetic acid and 20 g of NaOH was 34.4 g approximately over 70%, a pure intermediate compound that melted between 194-195 ^{o}C. This compound was soluble in water and methanol. The UV/VIS in DMSO showed absorption at 328, 336 and 381 nm respectively. The IR   absorption bands in cm^{-1} using KBr discs showed absorption frequencies at 3422 for an OH group of a carboxylic acid, 2990.6 for NH of ammonium salt of a carboxylic acid, 2448.08 and 2319.18 for an aromatic methine group,   1655.99 indicated the presence of a carbonyl group while   1421.14 and 1315.56 bands were for C-O overtone stretches. The proton NMR performed in deuterated DMSO on the delta scale in parts per million showed peaks at 2.4, 3.3 for the protons of OCH$_3$ of the ether functional group, multiplet peaks at 6.4, 7.4, 8.0 and 9.0 for aromatic protons and a peak at 10.0 for the carboxylic acid proton. The ^{13}C-NMR showed peaks at ꭤ 173.1 for carbonyl carbon; ꭤ 147.0, ꭤ 139.1, ꭤ 132.0, ꭤ 129.0, ꭤ 120.91, ꭤ 114.0 for aromatic carbon atoms and a peak at ꭤ 62.10 for the ether carbon atom. The mass peak at m/z 226 was consistent with the molecular formular C$_9$H$_{10}$N$_2$O$_5$.

The proposed reactions and their mechanisms are outlined in schemes 1, 2 and 3 below [15-18]. In the substitution nucleophilic bimolecular reactions, 2, 4-dinitrophenol, 2-aminopyridine and 2-methoxy-5-nitroaniline were the nucleophiles because they had oxygen and nitrogen atoms which supplied the electrons while chloroacetic acid as far as these reactions were concern was the substrate- the alkyl halide. The electron rich atoms attacked the electron deficient carbon in the alkyl halide to yield the quaternary ammonium
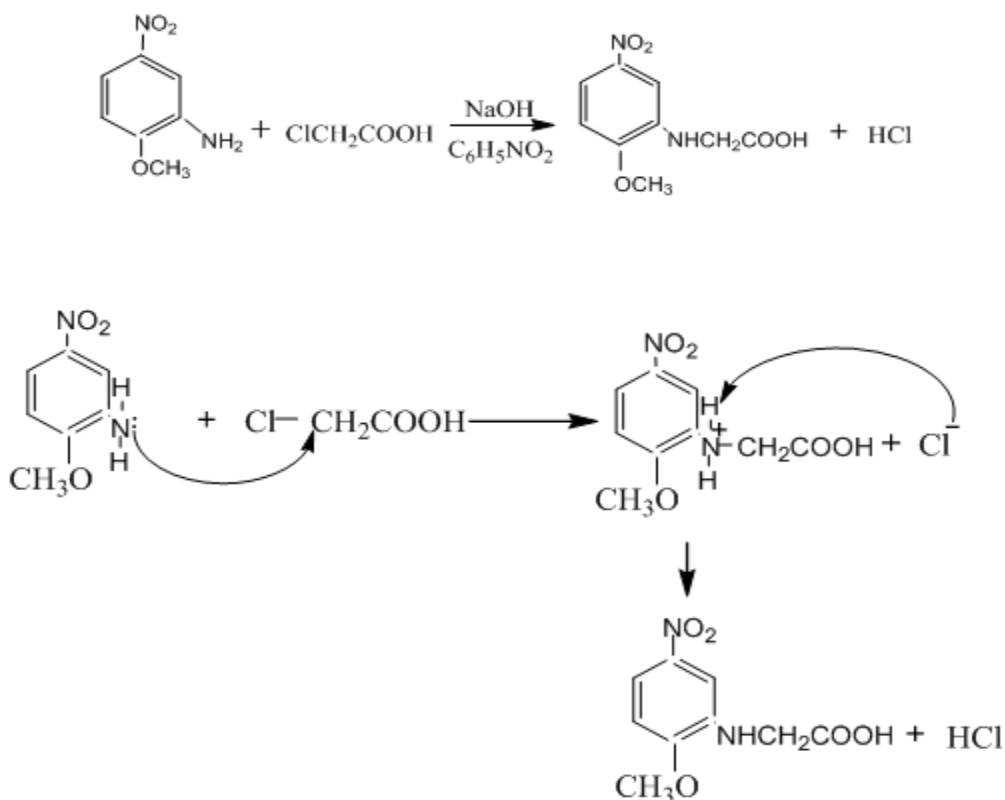
compounds or salts. Abstraction of protons from the nitrogen atoms gave the final product schemes 2 and 3. In scheme 1, the oxygen atom of the phenol was rich in electrons and attacked the alkyl halide.
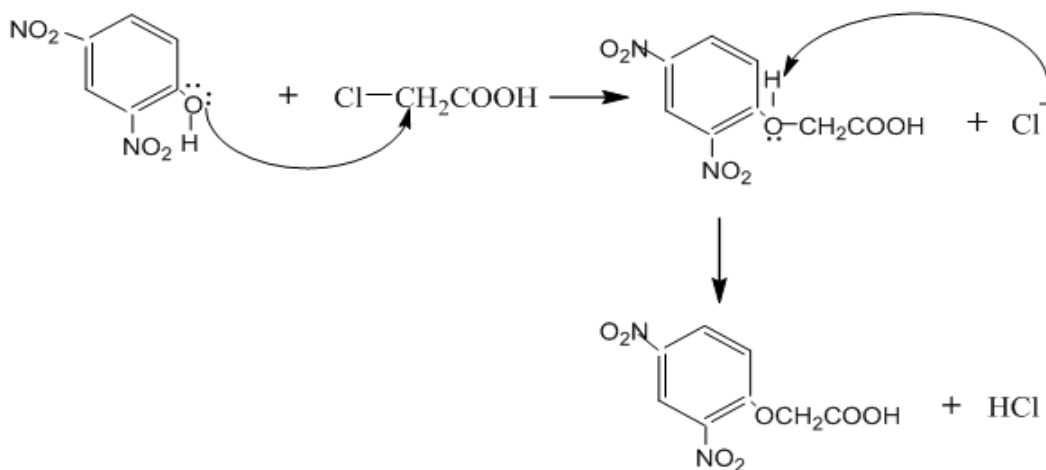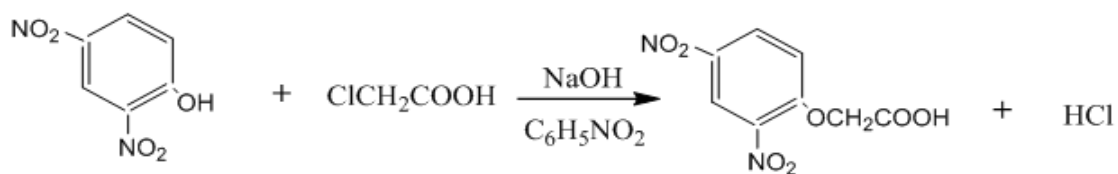
Scheme 1
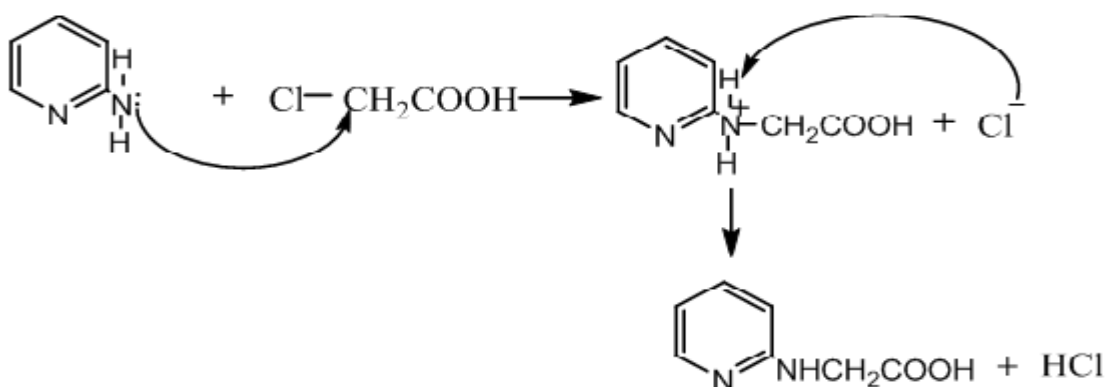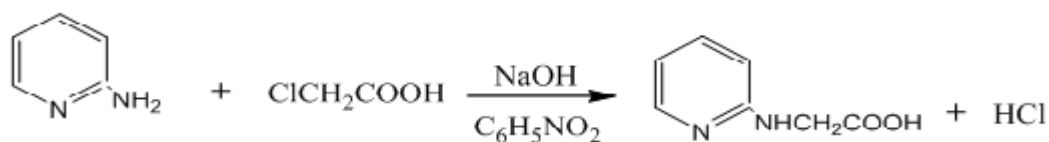
Scheme 2

Scheme 3

Summary

These three intermediate compounds proved to be excellent precursors to indigo dyes and 2-aminopyridine was probably the first heterocyclic compound that had been used as a substrate for the synthesis of indigo dye. Further work will focus on the use of these intermediates in the synthesis of indigo dye.

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