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Synthesis of 2-Methoxy-5-Nitro-2-(Phenylamino) Ethanoic Acid; 2, 4-Dinitrophenoxyethanoic Acid and Pyridyl-2-Aminoethanoic Acid

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Abstract : In organic synthesis, use is made of appropriate starting materials that would give high yield of the desired products. 2-methoxy-5-nitroaniline (0.2 mol), 2,4-dinitrophenol (0.5 mol) and 2-aminopyridine (0.42 mol) were used as starting materials or reactants in the preparation of 2-methoxy-5-nitro-2-(phenylamino)ethanoic acid; 2, 4-dinitrophenoxyethanoic acid and pyridyl-2-aminoethanoic acid. These substrates were treated with appropriate quantities of chlorinated acetic acid with a base, preferably sodium hydroxide in the presence of nitrobenzene, which was an inert organic solvent. The resulting products 2- Methoxy-5-nitro-2-(phenylamino) ethanoic acid (0.17 mol); 2, 4-Dinitrophenoxyethanoic acid (0.27 mol) and Pyridyl-2-aminoethanoic acid(0.29 mol) were purified by crystallization and elution by column chromatography packed with silica gel and alumina using dichloromethane. Pure amorphous powders were obtained respectively. These compounds proved to be useful precursors for indigo blue dyes when they were fused with admixture of sodium hydroxide, potassium hydroxide and sodamide. These compounds were very good starting materials/substrates or precursors for indigo dyes. The structures of these compounds were established by spectral analysis.

Keywords : analysis, dye, extraction, intermediates, precursor.

Introduction

There are many possible reasons for carrying out laboratory synthesis of an organic molecule from simple substrates, precursors or compounds. These new organic compounds are prepared with the expectation that some might be useful drugs, colourants etc. In chemical industry, synthesis is done with the aim to device more economical routes to known / new compounds [1]. Raw materials for organic synthetic compounds could be from natural products such as plants, animals (*indigofera tinctoria*, *lonchocarpus cyanescens*, etc) or coal tar distillate from petroleum industry. These primary raw materials may be aromatic such cyclopentadiene, benzene, toluene, o-, m- and p- xylenes naphthalenes anthracene etc [1-2]. A great variety of inorganic chemicals is 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 some syntheses; they are first converted into a large number of derivatives, which are in turn made into the desired compounds, which could be colourants or dyes. These derivatives are generally known as intermediates because they act as intermediates between the primaries and the final product[3]. They are produced by reactions such as substitution, which involves nitration, sulphonation, and halogenations; rearrangement reactions involving intramolecular cyclization and other reactions in which reduction, oxidation, and condensation are involved. When the intermediate is a precursor to a colourant as in this case where the products of these syntheses were blue indigo dye substrates, a dye is regarded as an intensely coloured substance which when applied to a substrate/fabrics imparts colour to it by a process which at least temporarily destroys its crystal structure [4]. Indigo dye

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 "uriigbo" in Igbo speaking area of Nigeria in West Africa[5-6]. Synthetically, Indigo had been prepared from isatin, o-nitrocinnamic acid, aniline, anthranilic acid, o-,m- and p-toluidines [7].

In this article, 2-Methoxy-5-nitro-2-(phenylamino) ethanoic acid; 2, 4-Dinitrophenoxyethanoic acid and pyridyl-2-aminoethanoic acid were prepared from 2-methoxy-5-nitroaniline, 2, 4-dinitrophenol and 2-aminopyridine.

General Experimental Procedures

All reagents used 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 F₂₅₄ (E.Merck) precoated plates and were visualized by spraying with 10 % H₂SO₄ or iodine vapour. Column chromatography was run on silica gel and 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 (¹³C-NMR and ¹H-NMR) were determined on Fourier Transform (FT) model 6853 in deuterated DMSO at ambient temperature using Trimethylsilane as internal standard unless otherwise stated.

Synthesis of 2-Methoxy-5-nitro-2-(phenylamino) ethanoic acid

Exactly 33.6 g (0.2 mol) 2-methoxy-5-nitroaniline, 28.35 g (0.3 mol) chloroacetic acid and 20.0 g (0.5 mol) sodium hydroxide were put into a 500 mL round bottomed flask containing 100 mL of nitrobenzene. The mixture was brought to boil, and refluxed on a magnetic stirrer heater for 6 h at a temperature range between 320 -350°C; the reaction was monitored by thin layer chromatography [8]. The mixture was transferred into a 1000 mL beaker and allowed to cool; the dark nitrobenzene solution was separated by filtration from the precipitate that formed [8-11]. The residue was washed exhaustively with 5 x 100 mL acetone and finally recrystallized from hot activated carbon treated 150 mL methanol to reveal a creamy powder. The yield was calculated and the purity determined by the melting point. The spectral analysis was determined.

Synthesis of 2, 4-Dinitrophenoxyethanoic 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 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.

Synthesis of Pyridyl-2-aminoethanoic acid

The substituted pyridine; 2-aminopyridine was used as the substrate. Exactly 63.0 g (0.42mol) of it, 39.69 g (0.42 mol) of chloroacetic acid and 20.0 g (0.5 mol) of sodium hydroxide were into a 500 mL round bottomed flask already having 200 mL of nitrobenzene which was used as the solvent medium for the reaction. The reaction was under reflux for 5 h, dark slurry was obtained which was washed severally 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.

Results

The reaction of 2-methoxy-5-nitroaniline, 2, 4-dinitrophenol and 2-aminopyridine when treated with chloroacetic acid in nitrobenzene under anhydrous condition at a temperature 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-methoxy-5-nitroaniline

Factors	Properties/ Results
Product	2-Methoxy-5-nitro-2-(phenylamino) ethanoic acid
Limiting Reagent	2-methoxy-5-nitroaniline
Melting point	194-195 ± 1
colour	creamy powder
Solubility	Soluble in water and methanol
Theoretical yield	45.2 g
Actual yield	34.4 g
Percent yield	76.1 %

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

Factors	Properties/ Results
Product	2, 4-Dinitrophenoxyethanoic Acid.
Limiting Reagent	2,4-dinitrophenol
Melting point	196-197 ± 2
colour	Dirty white powder
Solubility	Soluble in water and methanol
Theoretical yield	121 g
Actual yield	66 g
Percent yield	54.5 %

Table 3 Data of the Reaction of 2-Aminopyridine

Factors	Properties/ Results
Product	Pyridyl-2-aminoethanoic acid
Limiting Reagent	2-aminopyridine
Melting point	179-180 ± 2
colour	Dirty white
Solubility	Soluble in water
Theoretical yield	63.84
Actual yield	43.6
Percent yield	68.3 %

Table 4 Spectral Results of 2-Methoxy-5-nitro-2-(phenylamino) ethanoic acid

Spectral Analysis	Solvent used	Results
MS		m/z 32,93, 152, 167, 226 (M ⁺)
¹³ C-NMR	DMSO-d ₆	δ ppm 173.10, 147.0, 139.1, 132.0, 129.0, 120.91, 114.0, 62.10.
¹ HNMR	DMSO-d ₆	δ ppm 2.4, 3.3, 4.0, 6.4, 7.4, 8.8, 9.4, 10.0
IR	DMSO, KBr discs	ν cm ⁻¹ 3422, 2990.62, 2448.08, 2319.18, 1655.99, 1421.14, 1315.56.
UV/VIS	DMSO	λ max nm:328, 336, 381

Table 5 Spectral Results of 2, 4-Dinitrophenoxyethanoic Acid

Spectral Analysis	Solvent used	Results
MS		m/z 32, 77, 91, 152, 243(M ⁺)
¹³ C-NMR	DMSO-d ₆	δ ppm 177.0, 163.2, 146.3, 130.9, 128.0, 116.0, 66
¹ HNMR	DMSO-d ₆	δ ppm 3.4, 4.8, 8.8, 10.2, 10.8
IR	DMSO, KBr discs	ν cm ⁻¹ 4197.4, 3896.6, 2810.2, 2368.2, 1766.9, 1346.7
UV/VIS	DMSO	λ max nm: 381

Table 6 Spectral Results of Pyridyl-2-aminoethanoic acid

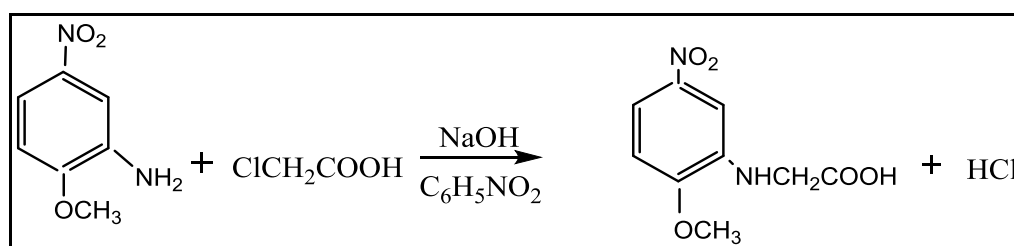
Spectral Analysis	Solvent used	Results
MS		m/z 32, 44, 63, 152(M ⁺)
¹³ C-NMR	DMSO-d ₆	δ ppm 174.7, 144.6, 143.1, 137.8, 130.3, 123.7
¹ HNMR	DMSO-d ₆	δ ppm 3.8, 4.0, 5.2, 6.8, 7.0, 7.6, 7.8, 8.1
IR	DMSO, KBr discs	ν cm ⁻¹ 3786.1, 3322.0, 3160.1, 2920.7, 2036.8, 1664.2, 1613.5, 1481.6, 1386.6
UV/VIS	DMSO	λ max nm:338, 398, 460

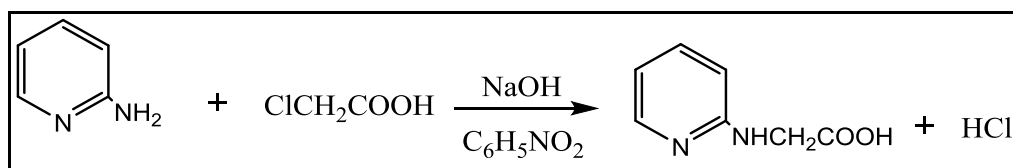
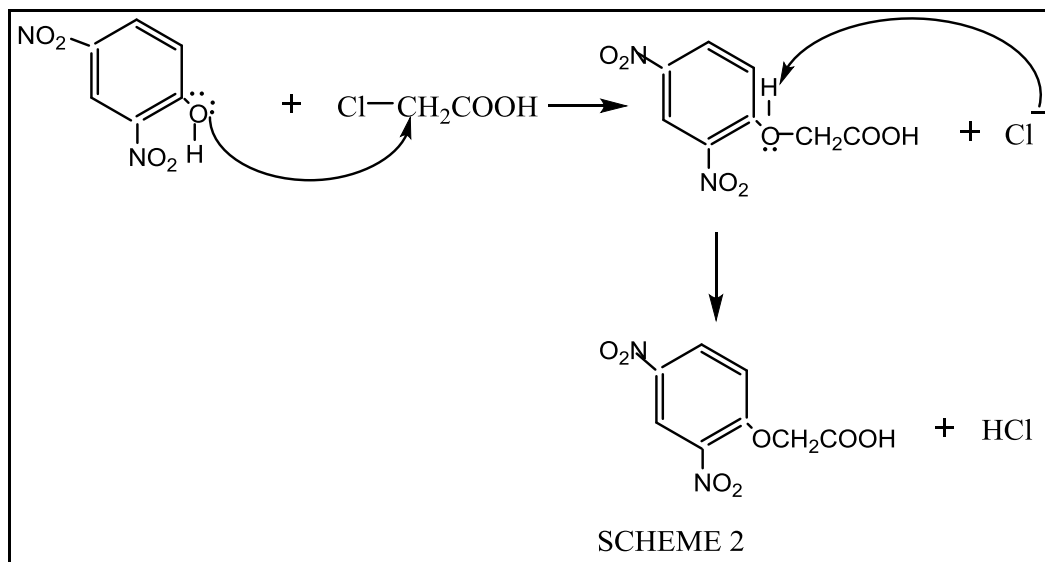
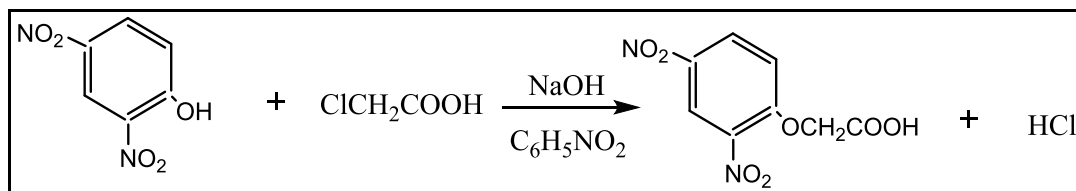
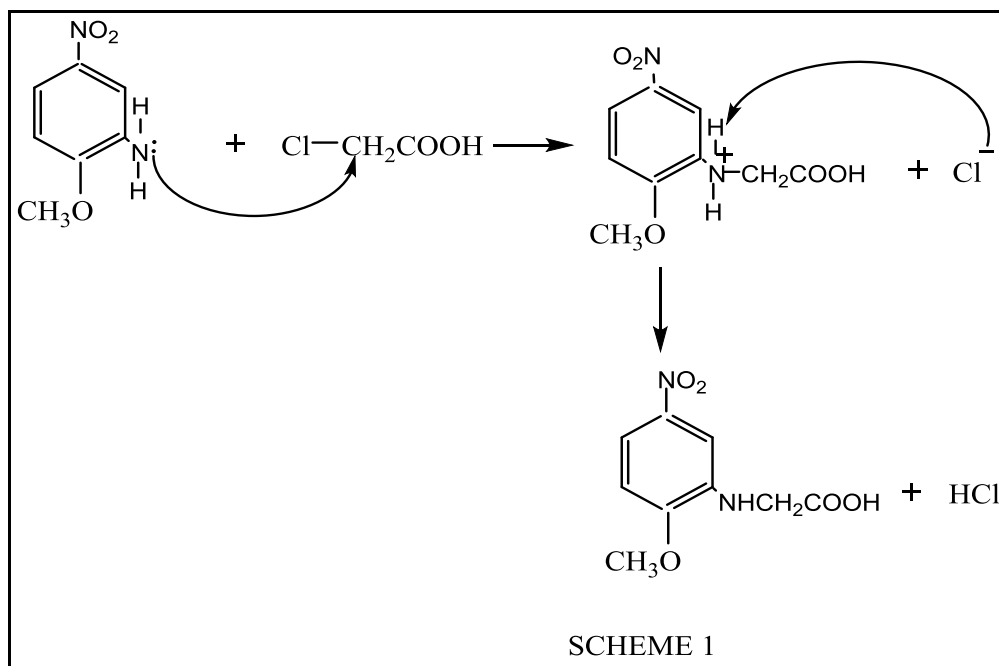
Discussion

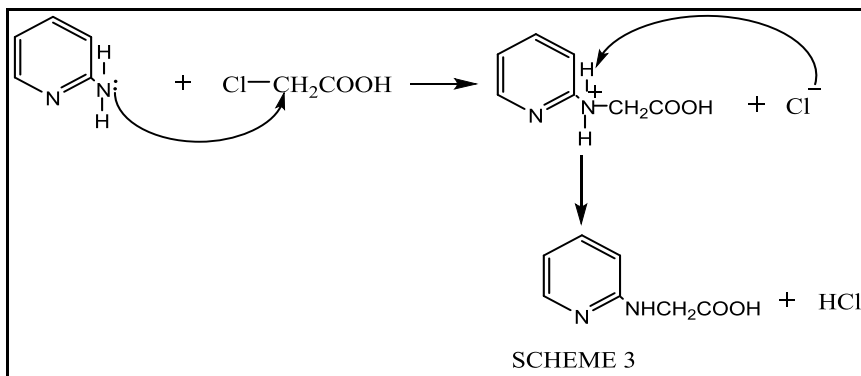
The actual yield 2-Methoxy-5-nitro-2-(phenylamino) ethanoic acid recovered when 33.6 g of 2-methoxy-5-nitroaniline was reacted with 28.35 g of chloroacetic acid and 20 g of NaOH was 34.4 g approximately over 70%, a pure intermediate compound that melted between 194-195°C. This compound was soluble in water and methanol. The mass peak at m/z 226 was consistent with the molecular formula C₉H₁₀N₂O₅. The ¹³C-NMR

spectroscopy showed peaks at δ 173.1 for carbonyl carbon; δ 147.0, δ 139.1, δ 132.0, δ 129.0, δ 120.91, δ 114.0 for aromatic methane carbon atoms and a peak at δ 62.10 for the ethereal carbon atom. 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 IR absorption bands measured 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 UV/VIS in DMSO showed absorption at 328 nm, 336 nm and 381 nm respectively. The reaction of 2, 4-dinitrophenol 92.0 g, chloroacetic acid 47.25 g and sodium hydroxide pellets 20.0 g yielded 66 g of 2, 4-Dinitrophenoxyethanoic acid with a melting point of approximately 196°C . 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 formula of the compound $\text{C}_8\text{H}_6\text{N}_2\text{O}_7$. The ^{13}C -NMR spectroscopy showed peaks at δ 177.0 and δ 163.2 for carbonyl carbon of acid; methine protons at δ 146.3, δ 130.9, δ 128.0, δ 116.0 and δ 66 for CH_2 group. The ^1H -NMR spectroscopy showed a peak at δ 10.2 and at δ 10.8 for the proton of the carboxylic acid group; aromatic peak at δ 8.8 and methylene peaks at δ 3.4 and δ 4.8. The IR spectra indicated the presence of hydroxyl group of an acid at cm^{-1} 4197.4 and cm^{-1} 3896.6; aromatic methines at 2810.2cm^{-1} , 2368.2cm^{-1} ; carbonyl band at 1766.9cm^{-1} and ether presence at 1346.7cm^{-1} respectively. The UV analysis showed absorption maxima at 381 nm [12-15].

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 Pyridyl-2-aminoethanoic acid. The resulting dirty white compound which was soluble in water melted between $179\text{-}180^\circ\text{C}$. The molecular formula was in agreement with the molecular peak at m/z 152; molecular formula $\text{C}_7\text{H}_8\text{N}_2\text{O}_2$. ^1H -NMR and ^{13}C -NMR showed consistent bands characteristic of the presence of carboxylic acid proton and carbon, aromatic methine groups. The IR spectra at ν 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. The proposed reactions and their mechanisms were outlined in schemes 1, 2 and 3 below [16-19]. In the substitution nucleophilic bimolecular reactions, 2-methoxy-5-nitroaniline, 2, 4-dinitrophenol and 2-aminopyridine were the nucleophiles because they had nitrogen and oxygen atoms which supplied the electrons while chloroacetic acid as far as these reactions were concerned 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 atom gave the final product schemes 1 and 3. In scheme 2, the oxygen atom of the phenol was rich in electrons and attacked the carbon of the alkyl halide.







Summary

These three intermediate compounds were used in the synthesis of blue indigo dyes and 2-aminopyridine, a heterocyclic compound had probably not been used as a substrate for the synthesis of indigo dye. Further work would focus on the use of these intermediates in the synthesis of indigo blue dye.

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