Synthesis and Characterization of 2-Hydroxy-1,4-Naphthoquinone as a Prerequisite for C-Alkylation and O-Acylation Products

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ABSTRACT

2-Hydroxy-1,4-naphthoquinone and its derivatives are used in many industries due to their biological activities and their ability to be used as intermediates in the synthesis of drugs and other compounds. In this study, a four-step synthesis of 2-Hydroxy-1,4-naphthoquinone from 2-naphthol as the starting material was detailed. Additionally, a number of 2-Hydroxy-1,4-naphthoquinone C-alkylation and O-acylation products were synthesized and studied. FTIR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy were used to characterize the synthesized 2-Hydroxy-1,4-naphthoquinone. The results of this study provide useful information on the synthesis and characterization 2-Hydroxy-1,4-naphthoquinone and its derivatives, which could be used in the pharmaceutical and other industries.

***Keywords**: 2-Hydroxy-1,4-Naphthoquinone, Synthesis, Characterization, Pharmaceutical Industry, C-Alkylation, O-Acylation.*

INTRODUCTION

Natural quinone compounds like 2-hydroxy-1,4-naphthoquinone (2-HNQ) and its derivatives are used in several pharmaceutical businesses [1]. It is an aromatic chemical with two hydroxy groups and a ring structure, one of which is joined to the naphthoquinone nucleus' 1-position. Many biological activities, including antioxidant, anti-inflammatory, antibacterial, and antifungal capabilities, are possessed by 2-HNQ [2]. Moreover, it serves as a starting point for the synthesis of a number of medications and other substances, including the malaria medicine quinine.

In the pharmaceutical industry, 2-HNQ and its derivatives are used as intermediates in the synthesis of drugs such as quinine, quinidine, and other antimalarial drugs. They are also used as active ingredients in various cosmetic products. 2-HNQ and its derivatives are used in the pharmaceutical industries for the manufacture of a variety of products, including drugs, cosmetics, and medical devices [3].

Antioxidants, such as 2-HNQ and its derivatives, are also utilized to protect the body from oxidation and free radical damage. They serve as antioxidants in a variety of food and drink items, including beer, wine, fruit juices, and soft beverages. Moreover, they serve as preservatives in cosmetic products like sunscreen and lipstick. Moreover, they are used as active components in anti-cancer medications.

2-HNQ and its derivatives can also be used as dyes, pigments and fluorescent agents in a variety of products, such as paints, printing inks and plastics. They are also used as precursors for the synthesis of various organic compounds,

such as vitamins and amino acids. In addition, they are used as intermediates for the synthesis of various drugs, such as antimalarials, antibiotics, anti-inflammatory drugs and antifungal drugs [3, 4].

In this study, we detailed a four-step synthesis of 2-hydroxy-1,4-naphthoquinone from 2-naphthol as the starting material. We further tested the synthesized 2-hydroxy-1,4-naphthoquinone using FTIR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy [5]. Additionally, we provided a number of 2-hydroxy-1,4-naphthoquinone C-alkylation and O-acylation products. In summary, 2-HNQ and its derivatives have many uses in the pharmaceutical and other industries due to their biological activities and their ability to be used as intermediates in the synthesis of drugs and other compounds. They are also utilized as antioxidants, dyes, pigments, and fluorescent agents in a range of products, as well as precursors for the synthesis of various organic compounds. As such, they are important compounds in the pharmaceutical industry, and have numerous applications.

EXPERIMENTAL

Chemicals and materials

Sigma-Aldrich provided the 2-Naphthol, Hydrazine hydrate, and Acetic Anhydride, while SRL Limited provided the analytical-grade potassium permanganate, sodium hydroxide, sodium nitrite, and ammonium chloride. The HPLC grade solvents, including sulfuric acid, ethanol, glacial acetic acid, and hydrochloric acid, were supplied by Merck India Limited Company. As a last step, Double Distilled Water was employed.

Synthesis of 2-Hydroxy-1,4-naphthoquinone

2-Hydroxy-1,4-naphthoquinone can be synthesized by carrying out four steps. In the first step, 4-amino-3-hydroxynaphthelene-1-sulphonic acid is synthesized from 2-naphthol by heating it in an 80°C water bath for 30 minutes followed by the addition of sodium nitrite and sodium hydroxide. In the second step, the 4-amino-3-hydroxynaphthelene-1-sulphonic acid is converted to ammonium 1,2-naphthoquinone sulphonate by heating the solution in an 80°C water bath for 1 hour with the addition of NaOH and HCl. In the third step, the ammonium 1,2-naphthoquinone sulphonate is converted to methoxynaphthoquinone by heating the solution in a water bath for 1 hour with the addition of sulfuric acid and methanol. Finally, in the fourth step, the methoxynaphthoquinone is converted to 2-Hydroxy-1,4-naphthoquinone by heating the solution in a water bath for 1 hour with the addition of acetic acid, hydrazine hydrate, and hydrogen peroxide. The synthesis scheme was shown in Figure 1.

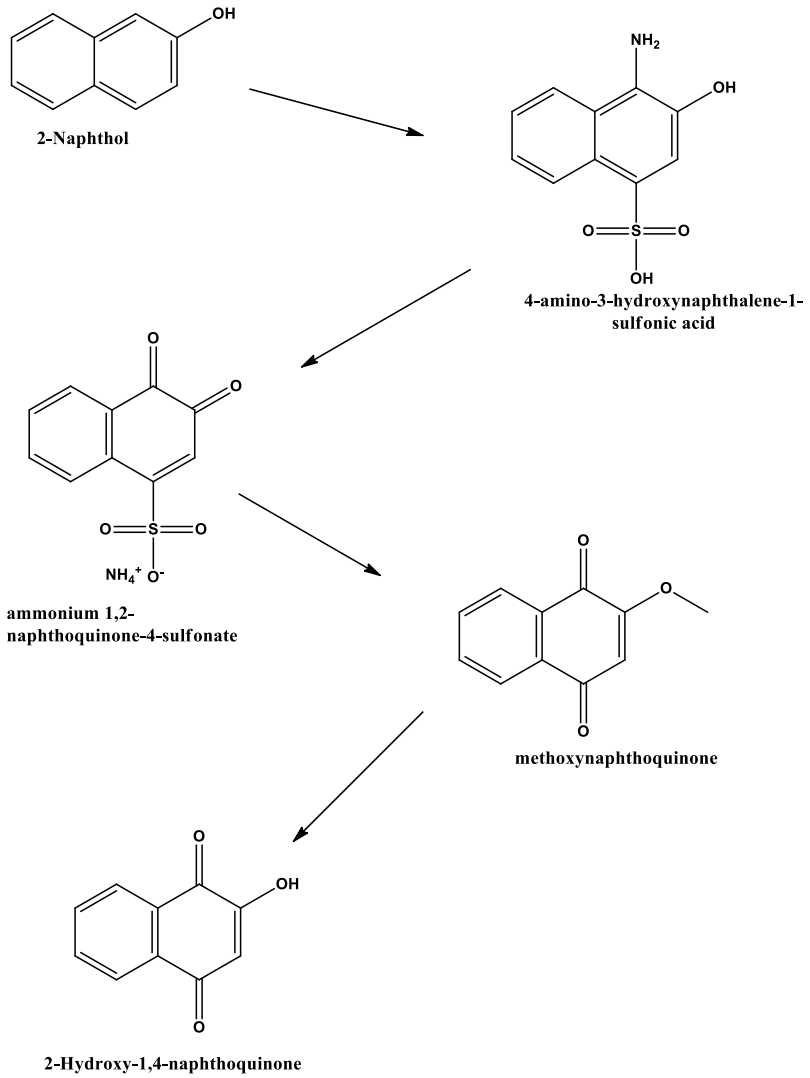

Figure 1. Synthesis of 2-Hydroxy-1,4-naphthoquinone.

Characterization

The structure of the as-synthesized 2-Hydroxy-1,4-naphthoquinone was confirmed by 1H NMR (300 MHz), FTIR, and Powder XRD. The Powder XRD pattern was recorded on Philips (Xpert) X-ray diffractometer using Cu K-α radiation having wavelength 1.540 Å at room temperature. The ^{1}H-NMR (300 MHz) spectra were collected on Bruker AVANCE spectrometer. The FTIR spectra of the 2-Hydroxy-1,4-naphthoquinone were recorded on 3000 Hyperion Microscope with vertex 80 FTIR using KBr pellets in the range of 400 to 4000 cm^{-1}.

C-alkylation and O-acylation of 2-hydroxy-1,4-naphthoquinone

The as-produced 2-hydroxy-1,4-naphthoquinone served as an essential precursor for a variety of processes. Figure 2 displays several 2-hydroxy-1,4-naphthoquinone C-alkylation and O-acylation products.

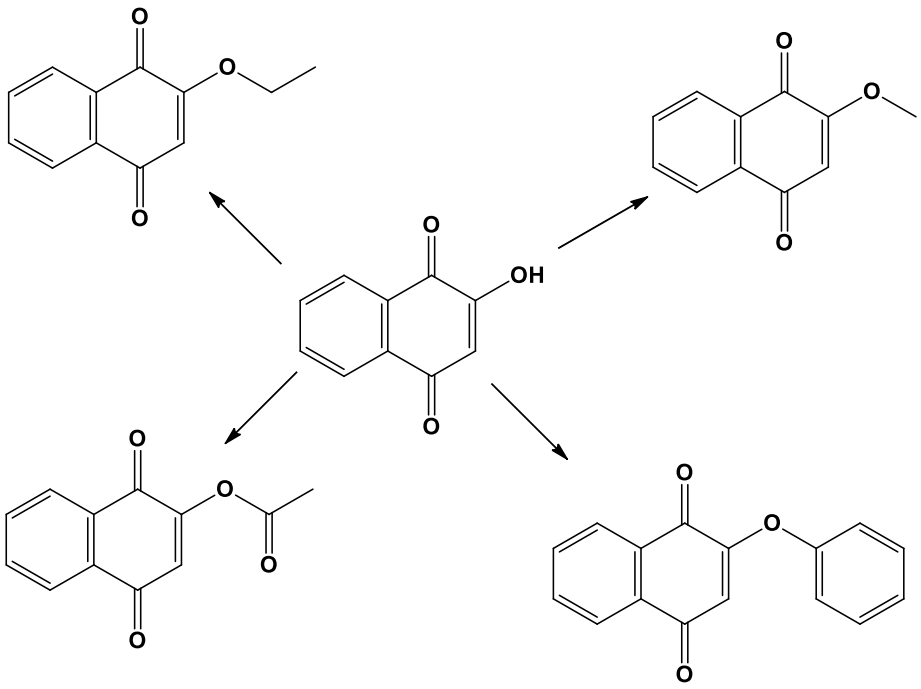

Figure 2. C-alkylation and O-acylation products of 2-hydroxy-1,4-naphthoquinone.

In the current study, we show a number of 2-hydroxy-1,4-naphthoquinone C-alkylation and O-acylation products. When 2-hydroxy-1,4-naphthoquinone is subjected to C-alkylation or O-acylation, an acid catalyst is used to add either aliphatic or aromatic acyl groups to the compound's molecule. The end results can be employed as starting materials for subsequent reactions or in the synthesis of other compounds. The alkylation and acylation products of 2-hydroxy-1,4-naphthoquinone are verified using FTIR spectroscopy.

RESULTS AND DISCUSSION

FTIR, ^{1}H-NMR, and ^{13}C-NMR study

FTIR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy can be used to identify 2-hydroxy-1,4-naphthoquinone. The hydroxyl group of the 2-hydroxy group is one of the distinctive functional groups that can be found using FTIR, along with any other functional groups that may be present. The number of protons present and their relative chemical shifts can be determined using ^{1}H-NMR. The number of carbon atoms present and their relative chemical shifts can be determined using ^{13}C-NMR. With computer-aided techniques like 2D-NMR, the structural data can be further improved.

The synthesized 2-Hydroxy-1,4-naphthoquinone spectroscopic data are as follows:
Name: 2-Hydroxy-1,4-naphthoquinone
Molecular Formula: $C_{10}H_6O_3$
Colour: Orange-red
Yield: 65.25%

^{1}H-NMR (300 MHz, DMSO) δ /ppm:
H-8= 7.98 (dd, J=7.2 and 1.4), H-7=7.82 (dt, J=7.2 and 1.4), H-6= 7.81 (dt, J=7.2 and 1.4), H-5= 8.01 (dd, J=7.2 and 1.4), and H-3= 6.12 (s).

^{13}C-NMR (DMSO-d6, 500 MHz) δ /ppm:

184.7, 181.9, 160.3, 134.05, 133.8, 132.3, 131.4, 126.8, 125.3, and 110.7.

FTIR (cm^{-1}):
3145, 2937, 1750, 1600, 1570, 1420, 1380, 1160, 1120, 990, 900, 820, 690, 610,520.

2-Hydroxy-1,4-naphthoquinone, also known as 2-hydroxy-1,4-naphthoquinone, is an organic compound belonging to the quinone class of compounds. It is an orange-red solid substance that melts at approximately 113 °C. Its chemical formula is $C_{10}H_6O_3$ and its molar mass is 178.14 g/mol. This compound is slightly soluble in water and soluble in organic solvents.
The ^{1}H-NMR spectra of 2-hydroxy-1,4-naphthoquinone shows a doublet of doublets at 7.98 ppm for H-8, a doublet of triplets at 7.82 ppm for H-7, a doublet of triplets at 7.81 ppm for H-6, a doublet of doublets at 8.01 ppm for H-5, and a singlet at 6.12 ppm for H-3. The ^{13}C-NMR spectra show the presence of 10 different chemical shifts at 184.7, 181.9, 160.3, 134.05, 133.8, 132.3, 131.4, 126.8, 125.3, and 110.7 ppm. The FTIR spectra of 2-hydroxy-1,4-naphthoquinone shows absorption bands at 3145, 2937, 1750, 1600, 1570, 1420, 1380, 1160, 1120, 990, 900, 820, 690, 610, and 520 cm^{-1}.

Synthesis of o-alkylation and o-acylation products

2-Hydroxy-1,4-naphthoquinone is an organic compound which has multiple applications in the synthesis of organic products. It is used as a reagent for the synthesis of various organic products such as dyes, pigments, heterocycles, and pharmaceuticals. It is also used as a catalyst in the oxidation of organic compounds. For example, it has been used in the synthesis of anthraquinone and its derivatives, which have applications as dyes and pigments in the textile industry. Additionally, it is used in the synthesis of pharmaceuticals such as antimalarial drugs, and as an intermediate in the synthesis of dyes and pharmaceuticals. It can also be used as an oxidizing agent in the synthesis of heterocyclic compounds and as a catalyst for the synthesis of amines. Furthermore, it is used in the synthesis of polymers, including polyurethanes and polyesters, and in the synthesis of polyurethane-based resins.
As synthesized 2-Hydroxy-1,4-naphthoquinone was used as starting material for synthesis of various acylation, sulfonation and alkylation products. These products used for different applications.

1. **Alkylation of 2-Hydroxy-1,4-naphthoquinone**

The 2-methoxynaphthalene-1,4-dione was synthesized using 2-hydroxy-1,4-naphthoquinone as the starting ingredient. The alkylation of 2-Hydroxy-1,4-naphthoquinone is the procedure that results in 2-methoxynaphthalene-1,4-dione. During the synthesis, 2-Hydroxy-1,4-naphthoquinone and methyl alcohol were combined in the presence of sulfuric acid as a catalyst, and this reaction mixture was continuously refluxed for 5 hours to produce 2-methoxynaphthalene-1,4-dione. This is a description of the alkylation reaction that synthesized 2-methoxynaphthalene-1,4-dione.

The 2-ethoxynaphthalene-1,4-dione was synthesized using 2-hydroxy-1,4-naphthoquinone as the starting ingredient. The alkylation of 2-Hydroxy-1,4-naphthoquinone is the procedure that results in 2-ethoxynaphthalene-1,4-dione. During the synthesis, 2-Hydroxy-1,4-naphthoquinone and ethyl alcohol were combined in the presence of sulfuric acid as a catalyst, and this reaction mixture was continuously refluxed for 5 hours to produce 2-methoxynaphthalene-1,4-dione. This is a description of the alkylation reaction that synthesized 2-methoxynaphthalene-1,4-dione.
The starting material for the 2-phenoxynaphthalene-1,4-dione synthesis was 2-hydroxy-1,4-naphthoquinone. The technique that results in 2-phenoxynaphthalene-1,4-dione is alkylation of 2-Hydroxy-1,4-naphthoquinone. 2-Hydroxy-1,4-naphthoquinone and benzoyl chloride were mixed in the presence of DAMP as a catalyst during the synthesis, and the reaction mixture was continuously stirred at room temperature for 45 hours to yield 2-phenoxynaphthalene-1,4-dione. This is an explanation of the alkylation reaction that resulted in the formation of 2-phenoxynaphthalene-1,4-dione.

2. Acylation of 2-Hydroxy-1,4-naphthoquinone

Acylation of 2-hydroxy-1,4-naphthoquinone is the addition of an acyl group (a functional group containing a carbon-oxygen double bond) to the molecule of 2-hydroxy-1,4-naphthoquinone. This is referred to as acylation. The acyl group can be either aliphatic or aromatic, such as acetyl, benzoyl, or propionyl. Generally, an acid catalyst, such as sulfuric acid or hydrochloric acid, is used in the acylation of 2-hydroxy-1,4-naphthoquinone. The process produces an acylated product, which can be utilized in subsequent reactions or as a starting material for the synthesis of other chemicals.

The starting material for the 1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate was 2-hydroxy-1,4-naphthoquinone. The acylation of 2-Hydroxy-1,4-naphthoquinone produces 1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate. During the synthesis, 2-Hydroxy-1,4-naphthoquinone and acyl anhydride were mixed with sulfuric acid as a catalyst, and the reaction mixture was agitated continuously at room temperature for 6 hours to yield 1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate. The acylation procedure that produced 1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate is described below. The characteristic peaks in the IR spectrum that correspond to the distinct functional groups that are being added were recorded using FTIR to confirm the alkylation and acylation products of 2-hydroxy-1,4-naphthoquinone. For instance, the existence of C-H and C-C stretching at 1300–1450 cm^{-1} and 2800–3000 cm^{-1}, respectively, would indicate alkylation. C=O and C-O stretching at 1710–1790 cm^{-1} and 1000–1300 cm^{-1}, respectively, would indicate acylation.

CONCLUSIONS

This study detailed the synthesis of 2-hydroxy-1,4-naphthoquinone from 2-naphthol as the starting material and further tested the synthesized compound using FTIR, ^{1}H-NMR, and ^{13}C-NMR spectroscopy. Additionally, derivatives of 2-hydroxy-1,4-naphthoquinone such as acylation, sulfonation and alkylation products were synthesized and studied. The results from this study provide useful information on the synthesis and characterization of 2-hydroxy-1,4-naphthoquinone and its derivatives, which could be used in the pharmaceutical and other industries.

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