Design, Synthesis and Characterization of 2, 4-Dimethylphenyl Hydrazine based Chemosensors

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Design, Synthesis and Characterization of 2,4-Dimethylphenyl Hydrazine Based Chemosensors

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Abstract

Hydrazones are a unique division of compounds found in various syntheses. They have an important role in synthetic chemistry due to their different biological properties, such as antifungal, anticonvulsant, antibacterial, antimalarial, anti-inflammatory and anti-TB properties. This paper reports the syntheses of a series of 3 hydrazones based on the condensation of 2,4-dimethylphenyl hydrazine HCl with different aromatic carbonyl compounds. The structures of the synthesized compounds were confirmed by EIMS. These compounds can act as ideal candidates in chemosensor chemistry.

Keywords: chemosensors, hydrazone, sensors, 2,4-dimethylphenyl hydrazine HCL

Introduction

Sensors quantify a physical quantity converting it into a signal which can be examined through electronic equipment. For example, a glass thermometer filled with mercury measures the temperature range based on the contraction and expansion of liquid mercury, which can be calibrated on the glass tube. A thermocouple is an instrument that converts the measuring temperature into an outgoing current through a voltmeter. For the sake of precision, well-known standards are used to calibrate sensors. They are based on the principles of reflectance, absorbance, light scattering, fluorescence, luminescence, refractive index, and optothermal effect [1].

Depending on their principles, the sensors are classified as magnetic sensors, electrical sensors, electrochemical sensors, thermometric sensors, mass sensitive sensors and chemosensors. Chemical sensors are small devices that display actual time and give online information about the existence of particular ions and/or compounds in complex samples. Depending on their type, they are classified as direct and distance chemosensors. Olfaction receiving
neurons exemplify distance chemosensors which can detect chemicals in the gas state [2]. The design and synthesis of chemosensors for heavy and/or transition metal (HTM) ions with a high accuracy continues to be an active part of supramolecular chemistry. They are designed to incorporate three components: firstly, a chemical receptor that receives the guest of interest frequently with considerable selectivity; secondly, a transducer or signaling unit that converts the binding component into a measureable physical change; and lastly, a design of measuring that change and converting it into useful information [3]. The following is a schematic diagram of this type of chemosensors.

![Figure 1. Quantum dot sensor for the specific detection of the explosive 2, 4, 6-trinitrotoluene (TNT) in aqueous environments](image)

The identification and sensing of ionic species such as cations and anions have been an area of interest for many scientific research groups. Transition metal complexes of Schiff bases are the most extensively studied coordination compounds because they have a number of uses. The property that displays electronic relation and structural relation with Schiff bases also plays a vital role in catalysis [5].

Hydrazine (N₂H₄) is a very rigorous base and a reducing agent that plays an important role in pharmaceutical, chemical and agricultural industries [6, 7]. It is used in projectile propulsion methods such as maximum energy fuel and it is the primary material used in a variety of products including foaming agents for antioxidants, plastics and polymer. Still, it has been categorized as a possible human carcinogen with a threshold limit value (TLV) of 10 ppb by the U.S. Environmental Protection Agency (EPA). It also causes mutations and has a neurotoxic impact on the kidneys, liver and lungs [8]. Thus, numerous recognition methods for hydrazine have been devised lately. Analyzing techniques such as MS-Gas chromatography, MS-Liquid chromatography and
capillary electrophoresis are used for the detection of hydrazine [9, 10, 11].

Hydrazones are a form of organic compounds with the structural formula $R^1R^2C=NNH_2$ [12] and they are identified in many useful synthetic products. Due to their extensive biological properties including anti-inflammatory, antifungal, antimalarial, antituberculosis, antibacterial, and anticonvulsant properties, hydrazine-hydrazone have gain considerable importance [13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25]. This paper reports the synthesis, design and characterization of a series of 3 hydrazones based on the condensation of 2,4-dimethylphenyl hydrazine HCl with different aromatic carbonyl compounds. The structures of the synthesized compounds were confirmed by EIMS. These compounds can act as ideal candidates in chemosensor chemistry.

![Figure 2. Structure of hydrazone functional group](image)

Taking into consideration the significant roles that transition metal ions played in many biomedical and environmental researches, the growth of hydrazone derivative ligands as artificial receptors was used for selective sensing in the current research. The development of aromatic hydrazone derived is known for measuring the concentration of low molecular weight ketones and aldehydes, for instance in gas flowing. The process of elution and analyzing is further proceeded via high performance liquid chromatography using a UV detector. Hydrazone based coupling techniques are utilized in medical biotechnologies to couple drugs with the targeted antibodies (see ADC), such as the antibodies against a specific form of cancer cell [26].

2. Material and Method

Chemosensors are based on molecular recognition that is emerging as a very important research field in the area of supramolecular chemistry,
which permits the determination of guest by binding-induced modification in spectroscopic or electrochemical properties [27]. A typical chemosensor comprises two parts: a receptor site that selectively attaches an analyte and a signaling unit connected through a spacer. Receptor components vary from simple metal-chelating compounds to a synthetic host compound or to proteins or protein fragments in case of biosensors. By coupling these molecules to a sensitive fluorescent readout system, molecular sensors are devised for analytes ranging from metal ions to simple organic compounds [28].

![Figure 3. General scheme for the synthesis of chemosensors](image)

**2.1. Syntheses of Hydrazone Derivatives Acting as Chemosensors**

All compounds were synthesized by mixing hydrazine hydrochloride acid and various acetophenones or aldehydes in 1:1 molar ratios which is a straightforward approach to synthesize the series of hydrazones derivatives.

**2.1.1. Synthesis of 2, 4, 5-trimethoxybenzaldehyde-2, 4 dimethylphenyl hydrazine.** 113.63 mg (0.579 mmole) of 2, 4, 5-trimethoxybenzaldehyde was mixed in 20 ml of ethanol in a round bottomed flask. After heating the mixture for 10 minutes at 78°C, 5 droplets of acetic acid were added to it and the reaction mixture was heated to another 5 minutes. Then, 100 mg (0.579 mmole) of 2,4-dimethylphenyl hydrazine HCl was added and the mixture was refluxed for one hour. After refluxing, the reaction mixture was cooled down and 10 ml of sodium bicarbonate (1M) was added to it. Then, 10 ml of dichloromethane was added to separate the layers. The evaporation of the solvent resulted in fine crystals of compound 1 giving 90% yield.
Scheme 1: Synthesis of 2, 4, 5-trimethoxybenzaldehyde-2,4-dimethylphenyl hydrazone (I)

2.2.2. Synthesis of 3, 4, 5-trimethoxybenzaldehyde-2,4-dimethylphenyl hydrazone. 113.63 mg (0.579 mmole) of a 3, 4, 5-trimethoxybenzaldehyde was mixed in 20 ml of ethanol in a round bottomed flask. After heating the mixture for 10 minutes at 78°C, 5 droplets of acetic acid were added to it and the reaction mixture was heated to another 5 minutes. Then, 100 mg (0.579 mmole) of 2, 4-dimethylphenyl hydrazine HCl was added and the mixture was refluxed for one hour. After refluxing, the reaction mixture was cooled down and 10 ml of sodium bicarbonate (1M) was added to it. Then, 10 ml of dichloromethane was added to separate the layers. The evaporation of the solvent resulted in fine crystals of compound 2 giving 88% yield.

Scheme 2: Synthesis of 3, 4, 5-Trimethoxybenzaldehyde-2,4-Dimethylphenyl Hydrazone (2)
2.2.3. Synthesis of acetophenone-2,4-dimethylphenyl hydrazine. 0.1 ml of acetophenone was mixed in 20 ml of ethanol in a round bottomed flask. After heating the mixture for 10 minutes at 78°C, 5 droplets of acetic acid were added to it and the reaction mixture was heated to another 5 minutes. Then, 100 mg (0.579 mmole) of 2,4-dimethylphenyl hydrazine HCl was added and the mixture was refluxed for one hour. After refluxing, the reaction mixture was cooled down and 10 ml of sodium bicarbonate (1M) was added to it. Then, 10 ml of dichloromethane was added to separate the layers. The evaporation of the solvent resulted in fine crystals of compound 3 giving 92% yield.

\[
\text{Acetophenone-2,4-dimethylphenyl hydrazone}
\]

Scheme 3: Synthesis of acetophenone-2, 4-dimethylphenyl hydrazone (3)

3. Results and Discussion

Different types of hydrazones were synthesized by reacting a variety of aromatic aldehydes and ketones with 2,4-dimethylphenylhydrazine hydrochloride. The synthesized compounds were confirmed by mass spectrometry.

3.1. Compound 1

3.1.1. 2, 4, 5-trimethoxybenzaldehyde-2,4-dimethylphenyl hydrazine. Molecular mass of Compound 1 having the molecular formula C\textsubscript{18}H\textsubscript{22}N\textsubscript{2}O\textsubscript{3} was 314, which was found to be comparable with the calculated molecular mass. Molecular mass was determined using JEOL JMS 600-H. Compound 1 showed different fragment peaks such as 212, 157 and 312.
3.2. Compound 2

3.2.1. *3, 4, 5*-trimethoxybenzaldehyde-*2,4*-dimethylphenyl hydrazine. Molecular mass of Compound 2 having the molecular formula $\text{C}_{18}\text{H}_{22}\text{N}_{2}\text{O}_{3}$ was 314, which was found to be comparable with the calculated molecular mass. Molecular mass was determined using JEOL JMS 600-H. Compound 2 showed different fragment peaks such as 212, 157 and 312.

Figure 4. EIMS of compound (I)

Figure 5. EIMS of compound (2)
3.3. Compound 3

3.3.1. Acetophenone-2,4-dimethylphenyl hydrazine. Molecular mass of Compound 3 having the molecular formula C\textsubscript{16}H\textsubscript{18}N\textsubscript{2} was 238, which was found to be comparable with the calculated molecular mass. Molecular mass was determined using JEOL JMS 600-H. Compound 3 showed different fragment peaks such as 212, 147 and 128.

![Figure 6. EIMS of compound (3)](image)

4. Conclusion

Chemosensors are sensory receptors that transform a chemical signal into an active potential. Generally, they determine the chemical stimuli present in an environment. Chemosensors have a variety of applications in biological, medicinal and environmental sciences. Hydrazones can act as synthetic chemosensors. Hydrazones are mostly produced through the reaction of hydrazines with ketones or aldehydes. Hydrazones are a significant class of compounds present in many synthetic products. They also show variable biological properties including anticonvulsant, antibacterial, antifungal, antimalarial, anti-inflammatory, and anti-tuberculosis properties. In order to synthesize different hydrazones, a variety of aromatic aldehydes and ketones were refluxed with 2,4-dimethylphenyl hydrazine in the presence of acetic
acid acting as a catalyst and ethanol acting as a solvent. The reaction was quenched by adding 1M aqueous solution of NaHCO₃. The required compound was extracted by adding 10 ml dichloromethane. The evaporation of the solvent resulted in fine crystals of target molecules which were characterized by EIMS. The synthesized compounds can act as ideal candidates in chemosensor chemistry. Target molecules were synthesized by the condensation of 2,4-dimethylphenyl hydrazine with the following aromatic aldehydes and ketones (3, 4, 5-trimethoxybenzaldehyde, 2, 4, 5-trimethoxy-benzaldehyde, benzophenone). The synthesized compounds were obtained as fine crystals with good yield and were characterized by EIMS. These compounds are expected to act as chemosensors.

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