Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/16027
DOI URL: http://dx.doi.org/10.21474/IJAR01/16027

RESEARCH ARTICLE

CONVENIENT CONVERSION OF 2-HYDROXY-4-METHOXYBENZALDEHYDE FROM THE ESSENTIAL OIL OF *MONDIA WHITEI* (HOOK. F.) SKEELS INTO 2, 4-DINITROPHENYLHYDRAZONE: ACID-CATALYZED NUCLEOPHILIC ADDITION REACTION AND UV-VISIBLE SPECTROPHOTOMETRIC ANALYSIS.

Ndzeli Likibi Belline
Plant and Life Chemistry Unit, Faculty of Sciences and Technics, MarienNgouabi, University, Brazzaville, BP 69, Congo.

Manuscript Info

Manuscript History
Received: 15 November 2022
Final Accepted: 18 December 2022
Published: January 2023

Key words:-
Essential Oil, GC-SM Analysis, 2-Hydroxy-4-Methoxybenzaldehyde, 2,4-Dinitrophenylhydrazone, Nucleophilic Additionreaction, UV-Visible Spectrophotometric Analysis

Abstract

The beige essential oil, in the form of crystals at room temperature, was extracted from the dry roots of *Mondiawhitei* (Hook. f.) Skeels by hydrodistillation with a yield of 0.50%. Analysis by gas chromatography (GC) and gas chromatography coupled by mass spectrometry (GC/MS) revealed the presence of a single constituent, the aromatic aldehyde, 2-hydroxy-4-methoxybenzaldehyde, an isomer of vanillin representing (99.85%) of the total essential oil. 2-Hydroxy-4-methoxybenzaldehyde was instantly converted to the brick-red colored 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone by the addition of 2,4-dinitrophenylhydrazine on 2-hydroxy-4-methoxybenzaldehyde, nucleophilic addition reaction catalyzed by surfuric acid with a conversion rate of 93%. Analysis of hydrazone by UV-visible spectrophotometry shows a wavelength at the absorption maximum of 362 nm. The UV-visible spectrophotometric method used for the determination of this hydrazone is convenient, rapid and economical. This conversion allows the chemical structure of 2-hydroxy-4-methoxybenzaldehyde to be changed by providing the formed 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone with additional biological, chemical and physical properties while enhancing its economic value. The 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone formed opens up the prospects of its diversified use in the fields of pharmaceutical, electrochemical, catalytic, polymer chemistry, environmental, energy, materials, biology and engineering.

Copy Right, IJAR, 2023,. All rights reserved.

Introduction:-

Organic compounds can be of synthetic origin or come from natural resources (animal or vegetable). Among the organic compounds resulting from plants resources counted 2-hydroxy-4-methoxybenzaldehyde, the major constituent of the essential oil of *Mondiawhitei*(Hook. f.) Skeelswith proportions of almost 100 % [1; 2].

Corresponding Author:- Ndzeli Likibi Belline
Address:- Plant and Life Chemistry Unit, Faculty of Sciences and Technics, MarienNgouabi, University, Brazzaville, BP 69, Congo.

It is a chemical compound and isomer of vanillin belonging to the class of aromatic compounds known as methoxyphenols, a product of secondary metabolism. More precisely an aromatic aldehyde (carbonyl compound) substituted by hydroxyl and methoxyl groups respectively in positions 2 and 4.

This finds its interest in the food and cosmetics industries [3; 4; 5]; acts as a necessary chemical formulation for the pharmaceutical and nutraceutical industry [6].

It has antimicrobial and antioxidant properties [7], it is also recognized for its antifungal effects which result in remarkable activity against fumonisins, mycotoxins mainly produced by Fasariumvertilloides [8; 9]. At the same time, it has various chemical properties due to the presence of the carbonyl C=O double bond, giving rise to several nucleophilic and electrophilic addition reactions [10]. However, the main drawback or disadvantage of the latter is its instability which often leads to oxidations, hence the need to convert it into hydrazone, a crystalline compound more stable than its (carbonyl) precursor [11; 12].

Hydrazones are organic compounds with the general formula:
RR'C=N-N-R''R'''. 2, 4-dinitrophenylhydrazones are substituted hydrazones derived from the condensation of an aldehyde or ketone with 2,4-dinitrophenylhydrazine [13] (Figure 1); a reversible reaction subjected to acid catalysis [14]. They play an important role in the protection of carbonyl compounds [15]. They also participate in the isolation, purification and characterization of the carbonyl group [16] and acts as intermediates in organic synthesis [17]. In addition, hydrazones are used for the extraction or determination of transition metals such as iron [18], molybdenum [19] by formation of hydrazone metal complexes.Salicylaldehyde benzoyl hydrazone on its side is used for the determination of copper content in blood, urine, water, soil, environment and food[20].

2-Hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone in its case is the product of the condensation of 2-hydroxy-4-methoxybenzaldehyde (an aromatic aldehyde) with 2,4-dinitrophenylhydrazine.

A number of the pharmacological studies performed across the world claim that 2-hydroxy-4-methoxybenzaldehyde hydrazone possesses antiaflatoxigenic and antimicrobial properties [21]. Their complexes of metals such as nickel (II), copper (II) and organotin (IV) respectively exhibit antibacterial activities [22]; antimicrobial [23] and anticancer [24].

Furthermore, antioxidant and antimicrobial activities have been reported for 2-hydroxy-4-methoxybenzaldehyde-4-phenyl thiosemicarbazone and its palladium (II), nickel (II) and copper (II) complexes [25]. Interestingly, nitrobenzaldehydehydrazoneis endowed with antiamoebic potential [26]. In addition, 2-methoxyphenol has antibacterial properties [27].

To these biological properties are added complexing electrochemical properties with respect to metals such as [zinc (II), molybdenum (VI)] and [cobalt (II), nickel (II), copper (II)] with 2-hydroxy-4-methoxybenzaldehyde hydrazones derived from hydrazine and 2-amino-6-methylbenzothiazole, respectively [28; 29]. In addition, dioxidomolybdenum (VI) hydrazone complexes exhibit catalytic activity [30] while nitrobenzaldehydehydrazonedisplaysredox potency [26].

Several synthesesof 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitophenylhydrazone from marketed 2-hydroxy-4-methoxybenzaldehyde have been reported in the literature [31; 32; 33; 34].

Very few studies devoted to the formation of hydrazones derived from aromatic aldehydes of essential oils have been reported in the literature.

To our knowledge, the addition of2,4-dinitrophenylhydrazine on 2-hydroxy-4-methoxybenzaldehyde extracted from essential oils has not yet been reported in the literature.

Various analytical methods are involved in the determination of hydroxylated and methoxylated derivatives of benzaldehyde 2,4-dinitrophenylhydrazones, among others, HPLC-UV which is the method of choice [35;36], HPLC-DAD and MS/MS [37]. Also, RRLC-UV and RRLC-MS(/MS) [38]) and LC-UV/MS [39] are used for the analysis of 2-hyroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone, without forgetting GC-MS, a sensitive and reliable method for the simultaneous determination of carbonyls [40; 41; 42; 43].

In addition to these methods, there is UV-visible spectrophotometry which is widely used for the determination of 2-hydroxy-4-methoxybenzaldehyde hydrazones [44; 27; 45]. However, some of these analytical methods involve long analysis time, tedious sample pre-treatment and high product cost.

The aim of this present work is to extract the essential oil of *Mondiawhiteï*(Hook f.) Skeels, to convert the 2-hydroxy-4-methoxybenzaldehyde extracted from this essential oil into 2,4-dinitrophenylhydrazone and to characterize the hemi-synthesized 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazoneby UV-Visible spectrophotometry, simple, fast and economical method.

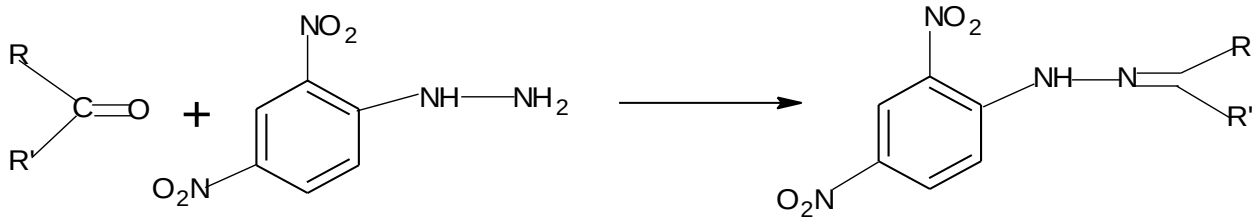

Figure 1:- Reaction of a carbonyl compound with 2,4-dinitrophenylhydrazine

Materials and methods:-

Plant material

The sample of *Mondiawhiteï*(figure 2) were purchased in february 2021 at the Brazzaville total market, from Kindamba, a locality locatedin the Pool department, in the south of Congo Brazzaville. These were identified by the botanists of the National Herbarium of Congo. Only the roots were selected for the study.

Figure 2:- Roots of *Mondiawhiteï* (Hook. f.) Skeels.

Extraction of essential oils:

After 16 days of drying at room temperature, in a ventilated room, *Mondiawhiteï*sample consisting of dry roots are subjected to hydrodistillation for four (4) hours using a standard extractor equipped with a two (2) liter balloon [46]. The condensate loaded with essential oil and hydrolat is recuperative. The essential oil is separated from the hydrosol by decantation. Extraction with diethyl ether is carried out to isolate the aqueous phase of the essential oil followed by drying of the ether phase with anhydrous sodium sulphate. Twenty-four (24) hours after evaporation of the diethyl ether in air, the essential oil is recovered. These operating conditions are summarized in Table I. The yield R of essential oil is calculated according to the following formula:

Table 1:- Operating conditions for the hydrodistillation of the roots of Mondiawhiteï (Hook f.)Skeels.

Matièrevégétale	***Mondiawhiteï*(Hook.f.) Skeels**
Organs	Roots
Quantity of dry matter (g)	409
Quantity of water (L)	1
Operation execution time (h)	4

Analysis of essential oils

Analysis by gas chromatography

The constituents were quantified using a Hewlett Packard HP 5890 type chromatograph equipped with a flame ionization detector equipped with HP ChemStation data acquisition software. The different constituents are separated using a DB5 capillary column (30 m x 0.25 mm), (thickness of the film 0.25 µm) under the following operating conditions: carrier gas helium (1 $mL.min^{-1}$), temperature injector temperature: 280°C, detector temperature: 280°C. The oven is programmed at 50°C for 5 minutes with a gradient of $5°C.min^{-1}$ from 50 to 300°C, 5 minutes at 300°C with a split mode injection of 1-20.

Analysis by gas chromatography-mass spectrometry

Analysis by gas chromatography-mass spectrometry was carried out using a Hewlett Packard HP 6890 brand chromatograph coupled with an HP 5973 mass spectrometer. of the various constituents is carried out using a DB5 capillary column (30 m x 0.25 mm), (thickness of the film 0.25 µm) under the following experimental conditions: carrier gas: (helium: 1 $mL.min^{-1}$), ionization energy (70 eV), injector temperature (280 °C), detector temperature (280 °C). The oven is programmed at 50°C for 5 minutes with a gradient of $5°C.min^{-1}$ from 50 to 300°C, 5 min at 300°C with a split mode injection 1-10.

Identification of constituents

The different constituents of the essential oil were identified on the basis of their retention indices and their mass spectra by comparison with data from the literature [47; 48; 49]

Hemi-synthesis of 2,4-dinitrophenylhydrazone

The reagent 2,4-dinitrophenylhydrazine and 2-hydroxy-4-methoxybenzaldehyde derived from the essential oil of *Mondiawhiteï*species are used for the preparation of hydrazone.

The method used was reported by [50]. It consists of dissolving 0.25 g of 2,4-dinitrophenylhydrazine in 5 mL of methanol, followed by the addition of 0.5 mL of concentrated sulfuric acid, then filtration of the lukewarm solution. To this solution are added 0.2 g of essential oil dissolved beforehand in a small volume of methanol. Aftera few seconds, the solid formed is filtered and washed in a small amount of methanol. The precipitate is then recrystallized from ethanol and then dried. These conditions are summarized in (Table 2).

Table 2:- Operating conditions for the hemi-synthesis of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone.

Essential oil	**Quantity of reagent**	**Quantity of essential oil**	**Quantity of MeOH (mL)**	**Quantity of H_2SO_4 (mL)**
Mondiawhiteï	0.25	0.2	5	0.5

Characterization of 2-hydroxy-4-methoxybenzaldehyde hydrazone

Determination of melting point

The melting temperature of the prepared hydrazone is measured using the Kofler bench.

The method consists in calibrating the apparatus with benzoic acid whose melting point is 122.35 °C. The carriage is moved horizontally until the cursor is at the boundary between solid and liquid. Then the mobile index is moved

vertically until it indicates the melting point of the standard. The melting point of the hydrazone is then taken by depositing it at the cold end of the kofler bench by bringing it towards the hot zone until the first drops of liquid appear. The carriage is then moved horizontally until the cursor is at the border between solid and liquid. The mobile index then indicates the melting point. Three tests are carried out.

Analysis by UV-visible spectrophotometry
The analysis of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone is made by a WPA Lightwawe II UV-visible spectrophotometer, connected to an HP computer.

Preparation of solutions
2,4-dinitrophenylhydrazine solution
A solution of 2,4-dinitrophenylhydrazine is prepared by dissolving 0.3 g of 2,4-dinitrophenylhydrazine in 100 mL of a 0.05 M sulfuric acid solution.

Essential oil solution
2-Hydroxy-4-methoxybenzaldehyde) (10 to 20 mg) is introduced into a 10 mL vial to which methanol is added up to the mark.

Spectral sweep
2-Hydroxy-4-methoxybenzaldehyde hydrazone sweep
0.5 mL of the 2,4-dinitrophenylhydrazine solution is added to 0.5 mL of the essential oil solution. A brick-red precipitate forms. The precipitate is allowed to stand for 10 minutes at room temperature and 5 mL of methanol is added to it: This is the solution of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone.

We put in the reference tank:

• 1 mL of 30% (V/V) water/ethanol solvent

and in the measuring tank:

• 1 mL of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone solution

Results and Discussion:-

Extraction and yield of essential oil
Extraction by hydrodistillation of the dry roots of Mondiawhiteï provides an essential oil in the form of beige crystals at room temperature (Table 3) with a yield of 0.50%. This yield is low compared to that obtained by [2], which was 1.40%.

Table 3:- Extraction yield of essential oil from the dry roots of Mondiawhiteï (Hook. f.)Skeels.

Species	**Yield(%)**	
	Our study	**Previousstudies / origin**
Mondiawhiteï(Hook. f.) Skeels	0.50	1.40 [2] / Congo

Figure 3:- Crystals of *Mondiawhiteï*(Hook.f.) Skeels essential oil at room temperature.

Chemical composition of *Mondiawhiteï*essential oil

The results of the chemical analysis of the essential oil extracted from the roots of *Mondiawhiteï* are shown in Table 4. Analysis by gas chromatography and by gas chromatography coupled to mass spectrometry allowed the identification of a single compound, the aromatic aldehyde, 2-hydroxy-4-methoxy-benzaldehyde representing 99.85 % of total essential oil.

Qualitative and quantitative similarities are observed with the results reported by Ouambain Congo [2], who describes an essential oil containing 99% 2-hydroxy-4-methoxybenzaldehyde.

However, there are also qualitative disparities with the extract from Togo which contains coumarinolignam[51], and also with the essential oil of South African origin which contains isovanillin (3-hydroxy- 4-methoxybenzaldehyde) [52].

Table 4:- Chemical composition of the essential oil extracted from the roots of *Mondiawhiteï*(Hook f.) Skeels.

N°	Compound	KI	%
1	2-hydroxy-4-methoxybenzaldehyde	1344	99.85

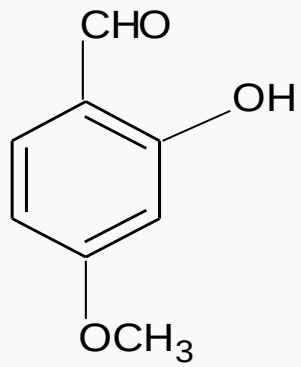

Figure 4:- Chemical structure of 2-hydroxy-4-methoxybenzaldehyde extracted from the essential oil of *Mondiawhiteï*(Hook f.) Skeels.

Hemi-synthesis of 2-hydroxy-4-methoxybenzaldehyde hydrazone

Physical characterization

Table 5 shows the results of the hemi-synthesis of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone and its measured melting point.

The reaction of 2,4-dinitrophenylhydrazine in the presence of sulfuric acid on the essential oil of *Mondiawhiteï*(2-hydroxy-4-methoxybenzaldehyde) gives rise to a precipitate of brick red color. This color is characteristic of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone.

2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone forms instantly, the reaction rate is fast so the kineticsis also fast. In addition, the yield of the formation of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone is 93%. This yield is high, and could result in the absence of discomfort or competition in the essential oil during the reaction. Indeed, the absence of other constituents than 2-hydroxy-4-methoxybenzaldehyde in the essential oil accelerates the speed of the reaction, resulting in rapid kinetics.

In addition, the melting point of the hydrazone derived from the crystals of the essential oil of *Mondiawhiteï*is 262 °C. This melting point is approximate to that of the literature [53], and corresponds to that of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone.

Table 5:- Yield and physical properties of hemi-synthesized 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone.

Compound of essential oil converted to 2,4-dinitrophénylhydrazone	**Aspect**	**Colour**	**Yield (%)**	**Melting Point measured (°C)**
2-hydroxy-4-methoxy-benzaldehyde 2,4-dinitrophenylhydrazone	Precipitate	Brick red	93	262

Characterization by UV-visible spectrophotometry

2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone

The peak wavelength of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone derived from essential oil of Mondiawhiteï recorded is 362 nm (Table 6). This value is characteristic of the C=N chromophore of 2,4-dinitrophenylhydrazones whose wavelength at absorption maximum is (λmax = 360-370 nm) [54; 55; 56].

Table 6:- Wavelength at maximum absorption of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone

2,4-dinitrophenylhydrazonederivative	**λmax (nm)**
2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone	362

Figure 5 shows the UV-visible spectrum of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone. It shows three essential bands:

1. A very weak band at 255 nm. This corresponds to the transition $\pi \rightarrow \pi^*$ relating to the substituted aromatic system;
2. A low intensity band at 288 nm relating to the anilin aromatic system;
3. Another weak band at 362 nm which is characteristic of the $n \rightarrow \pi^*$ transition of the C=N grouping of the hydrazone

The different absorption bands of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone, their transitions and their groups are shown in Table 7.

Table 7:- Different absorption bands of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone.

2,4-dinitrophenyl-Hydrazine derivative	**Absorption band λ(nm)**	**Transition and Chromophore**	**Group**

2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenyl-hydrazone	**255** Very weak band	π→π* (C=C)	Substituted aromatic system
	288 Low intensity band	n→σ* (C-NH-)	Anilin aromatic system
	362 Another weak band	n→π* (C=N)	Hydrazone

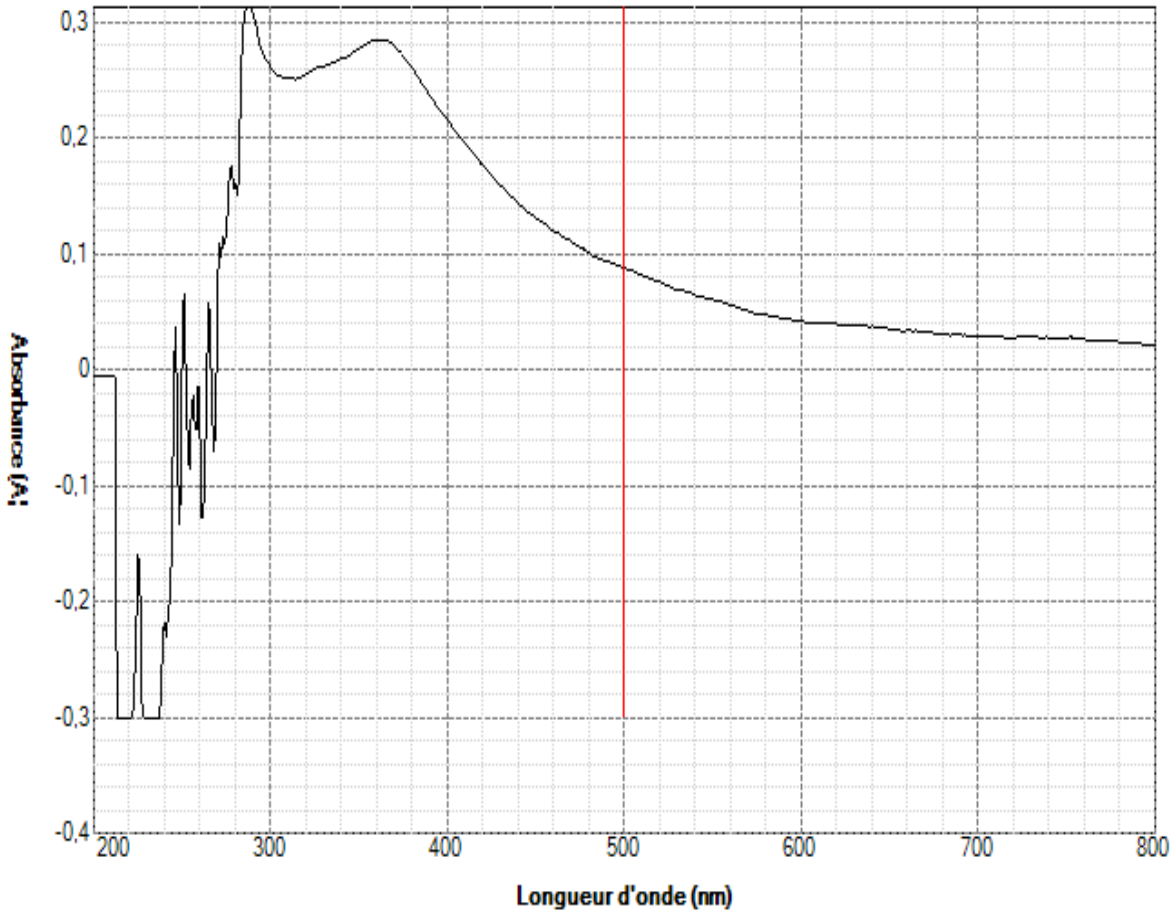

Figure 5:- UV-visible spectrum of 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone.

Dinitrophenylhydrazine

The UV-visible spectrum of 2,4-dinitrophenylhydrazine plotted in figure 6 shows three main bands at 346 nm, 360 nm and 377 nm due to C-N and NO_2chromophore groups substituted on the aromatic ring.

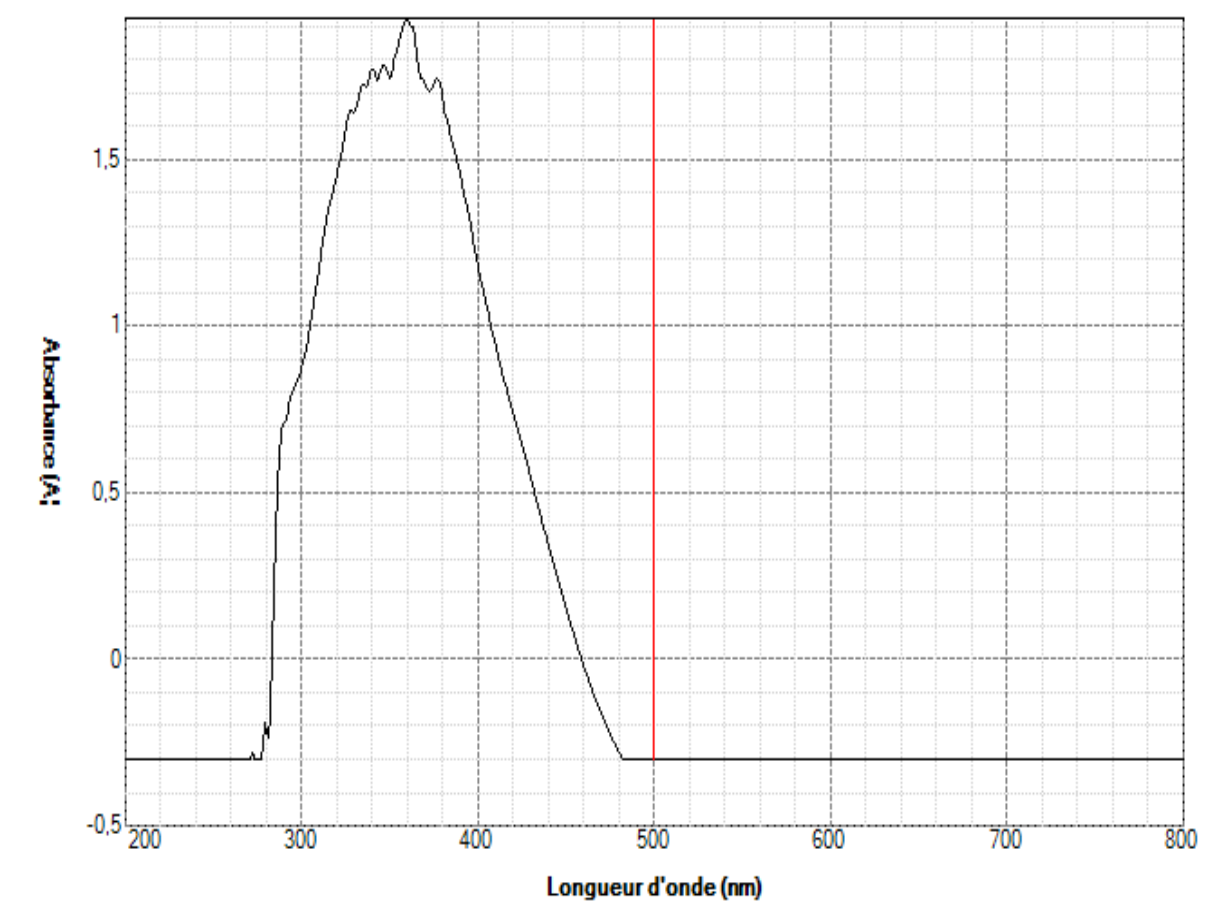

Figure 6:- UV-visible spectrum of 2,4-dinitrophenylhydrazine.

Conclusion:-

2-Hydroxy-4-methoxybenzaldehyde, a molecule of high added value, of great biological, pharmaceutical, nutraceutical, food and cosmetic interest, almost 100% extracted from the essential oil of *Mondiawhiteï*was simply and instantly transformed into 2-Hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone, a more stable molecule than its precursor (carbonyl) with a conversion rate of 93%. This transformation allows the chemical structure of 2-hydroxy-4-methoxybenzaldehyde to be changed by providing the formed 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone with additional biological, chemical and physical properties while enhancing its economic value. Analysis of hydrazone by UV-visible spectrophotometry shows a wavelength at the absorption maximum of 362 nm. The UV-visible spectrophotometric method used for the determination of this hydrazone is convenient, rapid and economical. The 2-hydroxy-4-methoxybenzaldehyde 2,4-dinitrophenylhydrazone hemi-synthesized opens up the prospects for its diversified use in the fields of pharmaceutical, electrochemical, catalytic, polymer chemistry, environmental, energy (photovoltaic, photophysics and optoelectronics), materials, biology and engineering [57].

References:-

1. NdzeliLikibi B. ; MadieleMabika A. M. ; MoutsamboténJ. M., NSikabaka S. ; Ouamba J. M. (2020).Cristal de l'huile essentielle de *MondiaWhiteï* (Hook. f.) Skeels : isomère de la vanilline (2-hydroxy-4-méthoxybenzaldéhyde). *International Journal of Innovation and AppliedStudies*, 28 : 586-570.

2.Ouamba J.M.(1991).Valorisation chimique des plantes aromatiques du Congo. Extraction et analyse des huiles essentielles. Oximation des aldéhydes naturels. Thèse de doctorat d'Etat. Université de Montpellier II, Montpellier, France.341p.

3. Anish K. And Adinpunya M. (2016).Méthoxybenzaldéhyde in plant: insight to the natural resources, isolation, application and biosynthesis. Current Science, 11(8): 1325-1334.

4.MCGeoch L. (2004).Plant ecology in a human context.MondiawhiteïinKakameja Forest, Kenya.Environnemental Science, Brown University. Providence, Rhode Island, USA, PP: 1-80.
5.KavakaMukonyi W. and LsaiahNdiegeO..(2001). 2-hydroxy-4-methoxybenzaldéhyde: Aromatic taste modifying compound from *Mondiawhitei*Skeels. *Bull. Chem. Soc. Ethiop*., 5(2): 137-141.
6.Rathi N.; Harwalkar K..; Jayashree V.; Sharma A.; Rao N. N. (2017).2-hydroxy-4-methoxy-benzaldehyde. An astounding food flavoring metabolite: A review. *Asian Journal of Pharmaceutical and Clinical Research*, 10(10): 105-110.
7.Jihua Wang; Hao Liu; Jianglin Zhao; HaifengGao; Ligang Zhou. (2010). Antimicrobial and antioxidant activities of essential oil of Periplocasepium and its main component 2-hydroxy-4-methoxybenzaldéhyde. *Molecules*, 15(8): 5808-5817.
8.SreeangegowdaTheppeswamy; RayasandraUmeshAbhishek ;KeragandurManjunath.(2015).Antifumonisin efficacy of 2-hydroxy-4-methoxybenzaldéhyde isolated from *Decalepsishamiltonii*.*International Journal of Food Properties*, 18(9): 2002-2008.
9.DevihalliChikkaiahMohana; SridharamurthySatish; KoteshwaraAnandaraoRaveesha.(2009).Antifongicalactivity of 2-hydroxy-4-methoxybenzaldehyde isolated from *Decalepsishamiltonii*(Wright &Arn.) on seed-borne fungi causing bio deterioration of paddy. *Journal of Plant Protection Research*, 49(3): 251-256.
10.Vollhard K.P.C.; Schore N. E. (1995). Traité de chimieorganique, 2ème éditionBruxelles: DeboeckUniversité. PP: 629-674.
11.Quédraogo I.W.;Boulvin M., Flammang R. ;Gerbaux P. and Bonzi-Coulibaly Y. L. (2009). Conversion of natural aldehydes from *Eucalyptus citriodora*, *Cymbopogoncitratus* and *Lippiamultiflora* into oximes: GC-MS and FT-IR analysis. *Molecules*., 14: 3275-3285.
12.Adjeroud Y. (2017). Synthèse et étude structurale d'une nouvelle famille de molécules hétérocycliques à visée médicale. Thèse de doctorat, Université BadjiMochtar Annaba, Annaba, Algérie),159p.
13.Hany S. I. ;Soha R. ;Abdelhadi et Haten A. A. (2015). Hydrolysis and hydrazinolysis of isatin-based-ald-and ketazines. *Journal of Chemistry*. 2015: 1-6.
14.Rauk A. Orbitale interaction of organic chemistry, 2nd édition, John wiley and sons, New York. (2001).
15.Greene T.W.;Wuts P.G.M. Protective groups in organic synthesis, 3rd éd. Wiley, New York. (1999). 355 pages
16.Shriner R.L.; Fuson R.C.; Curtin D.Y. &MorillT.C.The systematic identification of organic compounds, (John Wiley, New York).(1980), 6th éd.
17.Armbruster F.; Klingebiel U.; NoltemeyerM. and Naturforsch. (2006). 61b, 225.
18.Shobha B. (2911). Synthesis, caracterization and spectrophotometric determination of fer (II) complexe of 2,4-dihydroxybenzaldehydeisonicotinoylhydrazone(E)-N-(2,4-dihydroxybenzylidène)isonicotinohydrazide, it's application and biological activity. Pelagia Research Library. *Der ChemicaSinica*., 2 (4): 64-71.
19.Battula S.R.; Som S. D. and KIran B. (2012). Determination of molybdenium (VI) in Arnaranthus and patato by new extractive spectrophotometry method with isonitro p-isopropyl acetophenonephenylhydrazone.Research*Journal of Pharmaceutical, Biological and Chemical Sciences*, 3(1): 580-584.
20. Jamaluddin M. A. and Tasnima Z. (2012). A simple spectrophotometric method for the determination of copper in some real, environmental, biological, food and soil samples.Park. *J. Anal. Environ*, 13(1): 22-35.
21.Nanishankar V.; Harochally Chris C.; Praveena B. and AnuAppaiah K. A. (2017). Antiaflatoxigenic and antimicrobial activities of schiff base of 2-hydroxy-4-methoxybenzaldehyde, cinnamaldehyde and similar aldehydes. *J. Agric Food Chem*., 65(40): 8773-8778.
22.Pramod Kumar S., Kamalika Banerjee, Sangeeta S. (2016). Synthesis, spectroscopic characterization and in vitro bacterial evaluation of Ni (II) complexes of new tridentate aroylhydrazone ligands. *International Journal of Advanced Engineering Research and Science*, 3(12): 119-124.
23.Pahontu E.; Carolina Ilies D.; Shova S. (2015). Synthesis, characterization, crystal structure and antimicrobial activity of copper (II) complexes with the base Schiff derived from 2-hydroxy-4-methoxybenzaldehyde. *Molecules*, 20(4): 5771-5792.
24.SharifafNadhira Syed A.; NurulFarahana K., Normah A. and KokMeng Chan. (2021).Cellular basis of organotin (IV) derivatives as anticancer metallodrugs: *A review. Frontiers in Chemistry*, 9: 1-15.
25. Kumar Asha V.; Vedasree N.; M. Lavanya; S. Babu. (2017). Synthèse, caractérisation, activités antimicrobienne etantioxydante de la 2-hydroxy-4-methoxy-benzaldéhyde-4-phényl thiosémicarbazone et ses complexes Pd (II), Ni (II) et Cu (II) ayant des bases héterocycliques. *Journal Mondial des Sciences Pharmaceutiques*, 5(8): 152-164.
26. Toledano-Magaña Y.; Garcia-Ramos J. C. ; Navarro-Oliverria M. (2015). Potential amoebicidal activity of hydrazones derivatives: synthesis, characterization, electrochemical behavior, theorical study and evaluation of the biological activity. *Molecules*, 20(6): 9929-9948.

27.Ade A.; Amengor C. D. K.; AbenaBrobbey ; Ayensu I.; Harley B.K.; Duah and DuahBoakye Y.(2020).. Synthesis and antibacterial resistant modulatory activity of 2,4-dinitrophenylhydrazone derivatives as agents against some ESKAPE human pathogens. *Journal of Chemistry*, 2020:1-9
28. Usman H. A.; Garba A. B.; Sani M. A.; Yusul G. A. (2019). Synthesis and characterization of Schiff base and its metals (Zn (II) and Mo (VI) complexes derived from 2-hydroxy-4-methoxybenzaldehyde. *International Journal of Scientific Research in Multidisciplinary Studies*, 5(9): 01-07.
29.Madhurichaurasia, Deepak T. and Sulekh C. (2019).BSA-binding studies of Co(II), Ni(II) and Cu(II) metal complexes of Schiff base derived from 2-hydroxy-4-méthoxybenzaldéhyde and 2-amino-6-methoxybenzothiazole, *Egypt Journal of Chemistry*, 62(2): 357-372.
30. Bikas R.; Lippolis V.; Noshiranzadeh N. ; Farzaneh-Bonab H. ; Blake A. J.(2017). Effet électroniques des anneaux aromatiques sur l'activité catalytique des complexes dioxydomolybdenum-hydrazone. *European Journal of Inorganic Chemistry*,6 (2017): 999-1006.
31.Amrutha Kala A. L.; NanishankarHarohally V.; Naveen S., Ramegowda M. &Lokanath N. K. (2016). O-hydroxy Schiff bases derived from 2-hydroxy-4-methoxybenzaldehyde: synthesis, X-Ray studies and hydrogen bonding attributes. *Molecular Crystals and Liquid Crystals*, 629(1): 146-157.
32.Parvarinezhad S. and Salehi M. (2020). Synthesis, Characterization, crystal structure, hirshelfed surface analysis and DFT computational studies of new Schiff bases derived from phenylhydrazine. *Journal of Molecular Structure*, 1222(1): 128780.
33. Bessy Raj B. N.; M. PrathapachandraKureep and Suresh Eringathodi. (2008). Synthèse, caracterisation spectrale et structure crystalline de la N-2-hydroxy-4-méthoxybenzaldéhyde-N'-4-nitrobenzoylhydrazone et son complexe cu(II) plan carré. SpectrochimicaActaPartie A. *SpectroscopieMoleculaireetBiomoleculaire*, 71(4): 1253-1260.
34. Frey J.; Schneider F.; Schink B. ; Huhn T. (2018). Synthesis of the short chain hydroxyaldehydes and their 2,4-dinitrophénylhydrazones derivatives, and separation of their isomers by high-Performance liquid chromatography. *Journal of Chromatography A*, (1531): 143-150.
35.Sakuragawa A.; Yoneno T.; Inoue K. and Okutani T. (1999). Trace analysis of carbonyl compounds by liquid chromatography-spectrometry after collect as 2,4-dinitrophénylhydrazonederivatives. *Journal of Chromatography A*, 844(1-3):403-408.
36.Grosjean E.; Green P. G.; and Grosjean D. (1999). Liquid chromatography analysis of carbonyl (2,4-dinitrophenyl)hydrazone with detection by Diole Array ultraviolet spectroscopy and by atmospheric pressure negative ionization mass spectrometry. *Anal. Chem*., 71(9): 1851-1861.
37.Kovarikova P. Vavrona K.; Tomalova K.; Schőngut M. (2008). Analyse HPLC-DAD et MS/MS de nouveaux candidatsmédicaments du groupe des hydrazones aromatiques révélant la présence d'isomères géométriques. *Pharm. Biomed.Anal.*, 48(2): 295-302.
38. Soraya de M. Ochs; MairaFasciotti and Annibal D. P. N. (2015). Hydrazones of carbonyl compounds by RRLC-UV and RRLC-MS (/MS): A comparison of methods. Journal of Spectroscopy, 2015:1-11.
39. Bures J. ; Jansova H.; Stariat J.; Filipsky T. (2015).Méthodes LC-UV/MS pour l'analyse du prochelateurboronylsalcyaldehydeisonicotinoyhydrazone (BSIH) et son chelateuractifsalicyaldéhydeisonycotinoylhydrazone (SIH). *J. Pharm. Biomed. Anal*., (105) : 55-63.
40.XiaobingPang; Alastair C.L.; Hamilton J. F. (2011). Détermination des carbonyles en suspension dans l'air via la dérivation de la pentaflorophenylhydrazine par GC-MS et sa comparaison avec la méthode HPLC. *Talante*., 85(1) : 406-414.
41.JianLi ; Yan Li Feng ; Chun Juan Xie, Juan Huang. (2009).Determination of gaseous carbonyl compound by their pentafluorophenylhydrazones with gazchromatography, *Anal.Chen. Acta*. 635 (1): 84-93.
42. Yeh-Chung Chen and Ko-Ghun Yin. (2009). Détermination simultanée des carbonyles en suspension dans l'air et des hydrocarbures aromatiques à l'aide de la collecte de sorbants mixtes et l'analyse par chromatographie en phase gazeuse-désorption thermique/spectrométrie de masse. *J. Environ. Monit*., 11(5) : 1013-1019.
43. Ji-Zhou D. and Serban M. (2004). Gas chromatography-mass spectrometry of carbonyl compounds in cigarette mainstream smoke after derivatization with 2,4dinitrophenylhydrazine. *Journal of Chromatography A*, 1027(1-2):25-35.
44.Guo-Xu He and Ling-Wei Xue. (2021). Synthèsis, structures, and antibacterial activities of hydrazone compound derived from 4-dimethylaminobenzo-hydrazide.*ActaChim. Slov*.68: 567-574.
45.Dilek O. and Bane S. L. (2011). Synthesis and spectroscopic characterization of fluorescent boron dipyrromethene derived hydrazones. *J.Fluoresc*., 21(2): 347-354.
46.Clevenger J. F.(1928).Apparatus for the determinationof volatile oil. *Journal of the American Pharmaceutical Association*, 17(4): 45-349.

47.Adams R.P. (2001). Identification of essential oils by gaz chromatography quadrupole mass spectroscopy.Carol Stream. IL, USA: Allured Publishing Corporation, 101p.
48.Joulain D. &Köning W. A. (1998).The atlas of spectral data of sesquiterpene hydrocarbons. Hamburg Germany: EB-Verlag.
49. Davies NW. (1990). Gas Chromatographic retention indices of monoterpenesand sesquiterpenes on methyl silicone and carbo wax 20M phases. *J. Chromatogr*, 503: 1.
50.Leclercq. (2008). Détermination de la teneur en composés toxiques dégagés lors de la combustion d'encens et des bougies parfumées. Rapport du projet d'étude. Université de Rouen, Institut National des Sciences Appliquées, 52p.
51.Ramesh P.; Satya S. K.; KossiKoumaglo H. and Roy R.(2005). A chlorinatedcoumarinolignan from the African medicinal plant,*Mondiawhitei* (Hook f.).*Phytochemistry*, 66(6): 683-686.
52.Koorbanally N. A.; Mulholland D. A.; Crouch N. R. (2000).Isolation of isovanillin from aromatic roots of medicinal African lianeMondiawhitei.*Journal of Herbs, Spices and Medical Plants*, 7(3): 37-43.
53.Rappoport Z. CRC Handbook of tables for organic compound identification 3rd edition. (1967), P.147.
54. Zhou X., Mopper K.(1990).Measurement of sub-part-per-bilion levels of carbonyl compounds in marine air by a simple cartridge trapping procedure followed by liquid chromatography. *Environmental Science and Technology*, 24:1482-1485.
55.Pötter W., Lamotte S.; Engelhardt H., karst U. (1997).Non-porous silica ultrafast reversed phase high performance liquide chromatography separation of aldehydes and ketones 2,4-dinitrophénylhydrazones. *Journal of Chromatography A*, 786: 47-55.
56.Levart A., Veber M. (2001). Determination of aldehydes and ketones in air samples using criptrapping sampling. *Chemosphene*, 44:701-708.
57. Khan M.uhammad I.; Gul S. & Khan M. A. (2020).Schiff bases and their metallic derivatives: highly versatile molecules with biological and abiological perspective. Stability and application of coordination compounds.https://doi.org/10.5772 /intechopen.80799.