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Research article

Synthesized novel chromogenic reagent and sensor: Detection and identification of dichlorvos

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ABSTRACT

We developed a novel chromogenic reagent and sensor by selective approach, for the detection and identification of dichlorvos, which we tested with the thin layer chromatography method. For the first time, we reported in situ-generated glyoxal as a hydrolysis product, which then interacts with isoniazid to produce a yellow-colored cyclic compound. We used well-known spectroscopic techniques to confirm the chemical identity of the final product. We initially investigated the reaction using a variety of approaches, followed by attempts to establish the reaction mechanism using Density Functional Theory by Gaussian software.

1. Introduction

Dichlorvos is the common term for 2,2′-dichlorovinyl-dimethyl phosphate (DDVP) (Fig. 1). It belongs to the organophosphate (OP) contact insecticide family. It has been widely used to protect greenhouse plants, fruits, and vegetables from mushroom flies, aphids, spiders, mites, caterpillars, thrips, and white flies, as well as to control sucking, chewing, and boring insects and spider mites on a very wide range of crops [1–6]. Both domestic and agricultural fields widely use dichlorvos, a highly effective and low-toxic insecticide, to enhance global agricultural production, maintain hygienic conditions [7–12], and treat livestock infections [13–15]. However, the World Health Organization states that dichlorvos has hazardous properties [5,16]. Chronic exposure to DDVP increases the risk of diabetes or liver failure in humans, while acute exposure can lead to breathing difficulties or even death [17–20]. Prolonged exposure to DDVP has been associated with significant repercussions, including liver and kidney deterioration [21–23]. People widely recognize that DDVP, widely used in underdeveloped nations, negatively affects the central nervous system and increases the risk of cancer [24, 25].

Thin layer and gas chromatographic methods are generally the most accurate and sensitive techniques for determining DDVP reactions from different sources of samples. Thin-layer chromatography is a straightforward qualitative analysis approach, whereas

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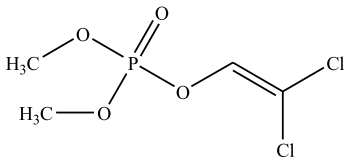
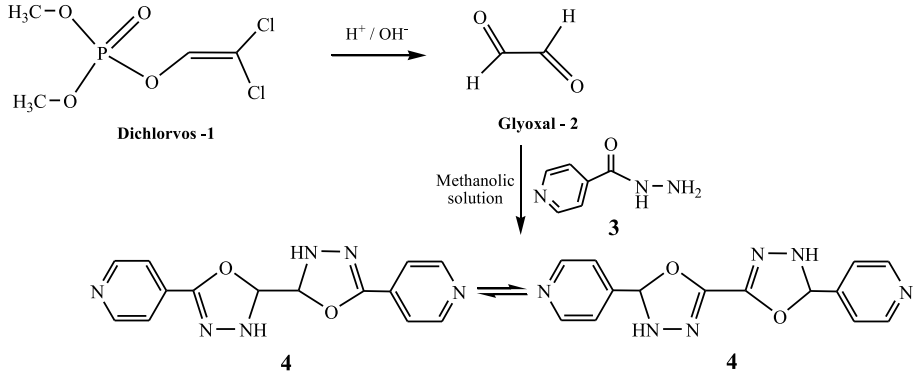


Fig. 1. Molecular structure of Dichlorvos.



Scheme- 1. Reaction pathways of dichlorvos.

gas chromatography is highly valuable for qualitative as well as quantitative on-site investigation of various DDVP mechanistic reaction pathways. Previous studies have reported the use of dangerous chemical reagents in thin-layer chromatography to detect DDVP.

This process commonly uses reagents such as bromine-fluorescein-silver nitrate [26], palladium chloride [27], alcoholic o-toluidine or *o*-dianisidine with UV light exposure [28], Congo red [29], zinc chloride-diphenyl amine [30,31], mercuric nitrate followed by diphenyl carbazone [32], mercurous nitrate [33], and 3,3′,5,5′-tetramethylbenzidine [34]. Researchers have described the detection of DDVP using thin-layer chromatography [35]. This detection method uses sodium hydroxide and sodium sulfide as reagents. Additionally, a color appears at 401 nm, indicating spectrophotometric detection within a concentration range of 20–100 μg/mL. Researchers have utilized a novel TLC spray reagent to detect and spectrophotometrically quantify DDVP in bluish-tinged maize grains [2]. Researchers have documented multiple chromogenic reagents and instrumentation approaches for identifying dichlorvos, such as 4-(*p*-nitrobenzyl) pyridine, in an alkaline solution at a temperature range of 175–180 °C [36]. Furthermore, researchers have developed a colorimetric method to detect organophosphate pesticides [37].

Based on our extensive review of the existing literature, we further investigations on these chromogenic reagents. Our results reveal that these substances can cause severe and immediate negative health effects through different pathways, including inhalation, skin contact, and ingestion. A compound's concentration and reactivity determine its nature and intensity of toxicity. The alveoli in the lungs are the primary absorption sites. The extensive surface area of the alveoli and the high blood flow contribute to the enhanced absorption [38]. Individuals who have inhaled those substances may experience damage to their respiratory tract, which can lead to tracheitis and bronchiolitis, ultimately resulting in pulmonary edema. High concentrations of palladium compounds can lead to skin sensitization and bronchial asthma. We have observed irritation of the skin and eyes as the main adverse effects of palladium salts. Palladium and its compounds possess the capacity to impede enzymatic activities. It is possible for palladium ions to form strong complexes with both organic and inorganic ligands, which could upset the balance of cells. The palladium compound has low oral toxicity due to its limited absorption [39]. Exposure to silver nitrate causes vertigo. Soluble silver compounds exhibit greater absorption rates compared to metallic or insoluble silver. Prolonged exposure to silver typically causes skin pigmentation, known as argyria, and can also affect the eyes, causing argyrosis [40]. Bromine inhalation can have adverse effects on the human body, including nervous system dysfunction and genetic material disruption. Additionally, it can cause damage to organs such as the liver, kidneys, lungs, and gastrointestinal system. Organic bromine compounds, like ethylene bromide, have the potential to induce cancer [41].

Mercury is present in organic compounds, including elemental mercury, mercurous, and mercuric, as well as inorganic salts that have distinct oxidative states. When mercuric compounds are present, they can do a lot of damage. They can cause protein precipitation, enzyme inhibition, ataxia, memory and sensory problems, tremors, muscle weakness, and kidney damage [42]. Worldwide, mercury (Hg) poses serious health threats [43]. Oral inhalation of toxic substances induces acute poisoning, leading to manifestations such as nausea, vomiting, hematemesis, and abdominal pain. The World Health Organization (WHO) ranks mercury among the top ten significant diseases.

Hence, excessive use of harmful chemicals in chromogenic reagents poses a significant disadvantage in insecticide identification. Researchers have developed a sensor that uses a green chromogenic reagent for on-site screening to detect dichlorvos. According to the literature, dichlorvos has the potential to undergo hydrolysis when exposed to aqueous sodium hydroxide, resulting in the formation of dichloroacetaldehyde [1,2,35]. Previous reports indicate that dichlorvos reacts with aqueous sodium hydroxide to produce

dichloroacetaldehyde as a hydrolysis product. However, there have been no reports of other hydrolysis products using the same reagent. In this report, dichlorvos undergoes a reaction with aqueous sodium hydroxide to produce glyoxal 2 as a hydrolysis outcome and confirmed by gas chromatography (GC) and mass spectroscopy (MS). A methanolic solution of isoniazid and the compound glyoxal 2 reacted, a dark yellow product was obtained. We aim to present a concise and highly efficient novel chromogenic reagent, along with its application as a sensor for detecting dichlorvos. Thin-layer chromatography monitored the progress of all reactions. Gas chromatography confirmed the purity of the final product, and highly sensitive spectroscopic techniques like 1H, 13C NMR, and high-resolution mass spectroscopy characterized it (Scheme 1). Computational calculations, using Density Functional Theory at the B3LYP/6-31G(d,p) basic set and Gaussian software, have supported the mechanism of the synthesized molecule [44].

2. Material and methods

2.1. General method

The reaction was monitored by TLC, and the purity of the reaction product was checked by gas Chromatographic technique is used starting at 80 °C to 280 °C; ramp rate is 20 °C/min; column flow is 1 ml/min; injection temperature is 250 °C; and injection volume is 1 μl. We recorded 1H and 13C NMR spectra on a Bruker Advance spectrometer. We recorded the HRMS (ESI) spectra using a SYNAPT-XS mass spectrometer. We performed thin layer chromatography (TLC) with E. Merck pre-coated TLC aluminum silica gel 60 F254 and used ultraviolet (UV) light to locate the spots.

2.2. Experimental method

2.2.1. Extraction of dichlorvos 1 from industrial materials [2,35]

We mixed the 25-mL industrial sample, containing DDVP, with 10 mL of diethyl ether and stirred it for 30 min using a magnetic stirrer. We collected the organic extract, specifically the ether layer, in a round bottom flask (RB) using a separating funnel. We then performed multiple re-extractions by adding diethyl ether (5 × 10 mL) to the aqueous phase and stirring for 30 min using the same protocol. We obtained the extract in the RB flask and then evaporated it using a rotary evaporator under vacuum conditions. This extracted product subsequently use for a hydrolysis reaction.

2.2.2. Hydrolysis of dichlorvos 1

We combined the solution containing 2.2 g of extracted DDVP 1 (10 mmol) and sodium hydroxide solution (1.5 mL, 1 M). We stirred the resulting mixture at room temperature for 10 min. The reaction was monitored using thin-layer chromatography (TLC), and a change in color from dark blue to bluish green was observed, with a maximum wavelength (λ-max) of 420 nm. After complete hydrolysis, we extracted the resulting glyoxal 2 using the same method and used it for subsequent reactions.

2.2.3. Reaction of glyoxal 2 and isoniazid 3

A mixture of glyoxal 2 (10 mmol) and isoniazid 3 (20 mmol) was stirred in methanol (5 mL) at room temperature, yellow colour shining solid was obtained instantly. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluents, and a single spot was observed. The final product was isolated by simple filtration and purified by recrystallization. Yellow solid; M. P. 229–230 °C. ^{1}H NMR 400 MHz, (DMSO-d_6): δ 7.611–7.591 (d, J = 8.0 Hz, 2H, C_3–C_5 Py-H), 7.385 (s, 1H, CH═N), 7.359 (s, 1H, NH), 6.971–6.951 (d, J = 8.0 Hz, 2H, C_2–C_6 Py-H). ^{13}C NMR 125 MHz (DMSO-d_6): δ 149.55, 122.51, 79.64. GCMS 6.701 with m/z 213.2; HRMS (m/z), 297.1095 $[M+H]^+$. Calcd. 297.1055 $[M+H]^+$. Anal. Calcd. for $C_{14}H_{13}N_6O_2$.

2.2.4. Chalk, ordinary and whatman filter papers as a sensor for detection of dichlorvos

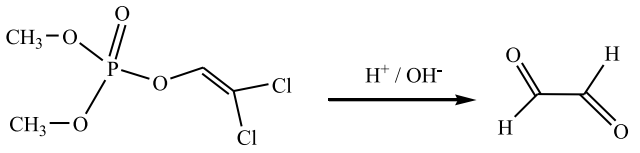
The drops of a methanolic solution containing the hydrolyzed product of dichlorvos were poured onto a dust-free chalk made of harmless calcium carbonate or onto filter papers made of glass fibers, both of which are effective absorbents. The solution was quickly absorbed and allowed to dry for a few minutes. Then, drops of a methanolic solution containing isoniazid were added. This resulted in a rapid color change from light yellow to dark greenish yellow. Chalk or filter papers are highly cost-effective and environmentally friendly sensors for detecting dichlorvos. They not only reduce environmental pollution but also prevent the release of toxic vapors from chemical reagents absorbed by the papers. Chalk or filter papers are highly effective chromogenic sensors due to their strong affinity for absorbing aqueous or organic solutions.

3. Result and discussion

3.1. Optimization of glyoxal 2

While stirring at room temperature, we investigated the reaction between dichlorvos 1 (used as a representative substrate) and aqueous solution of H_2SO_4/NaOH. Consequently, we produced glyoxal 2 as an intermediate product, as illustrated in Scheme 1. We optimized the reaction conditions by using a molar solution of NaOH, which resulted in significant hydrolysis product formation and outcome reported in Table 1. Initially, we treated the reactant in an aqueous medium without adding any reagent observed and no reaction was initiated (Table 1, Entry 1). Afterwards, we modified the ratio of reactant and reagent in an acid-catalyzed environment. However, despite prolonging the reaction time, we were unable to achieve either a complete reaction or the formation of the hydrolysis

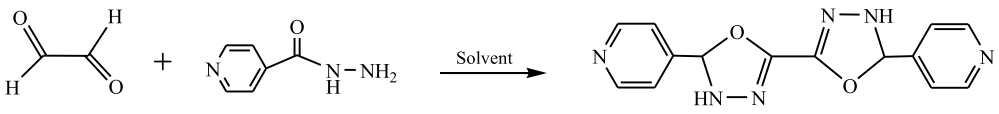
Table 1
Optimization of **2**.



1 **2**

Entry	1 (mmol)	Reagent	Proportion (1:Reagent)	Solvent	Time (Min)	Yield %
1	1	Neat	Neat	H_2O	45 min	0
2	1	0.1 M H_2SO_4	1:1	H_2O	15 min	0
3	1	0.1 M H_2SO_4	1:2	H_2O	45 min	0
4	1	0.1 M NaOH	1:1	H_2O	15 min	65
5	1	0.1 M NaOH	1:2	H_2O	30 min	75
6	**1**	**1M NaOH**	**1:2**	**H_2O**	**30 min**	**95**

Table 2
Optimization of **4**.



2 **3** **4**

Entry	2 (mmol)	3 (mmol)	Mol Ratio (1 : 2)	Solvent	Time (Min)	Yield %
1	5	5	1:1	Water	45	0
2	5	10	1:2	Water	45	0
3	5	5	1:1	Acetone	30	25
4	5	10	1:2	Acetone	45	45
5	5	15	1:3	Acetone	30	45
6	5	5	1:1	Ethanol	25	30
7	5	10	1:2	Ethanol	30	50
8	5	15	1:3	Ethanol	30	52
9	5	5	1:1	Methanol	20	48
10	**5**	**10**	**1:2**	**Methanol**	**20**	**97**
11	5	15	1:3	Methanol	30	80

product (Entry 2–3). Our findings indicate that the acid-catalyzed reaction is not suitable for hydrolysis, even when there are changes in the molar concentration of the reactant and reagent. We explored an alternative reagent for hydrolysis reaction and screened further reaction using various proportions of 0.1 M of NaOH solution for 15–30 min resulting in a relatively good yield (Entry 4–5). Ultimately, a 1 M solution of NaOH was identified as an effective reagent for hydrolysis reaction yielding remarkable results (Table 1, Entry 6).

When a basic medium was present, the first step of dichlorvos hydrolysis went smoothly, creating glyoxal 2 as an intermediate product. We concluded that the hydrolysis of dichlorvos involves the base-catalyzed cleavage of both the phosphate and dichloro vinyl bonds. This is made easier by a base catalyst. The phosphorus atom being electron-deficient is more susceptible to nucleophilic attack in the hydrolysis reaction. Based on empirical evidence, we have determined that hydrolysis in situ produces glyoxal 2, resulting in a decrease in the toxicity of dichlorvos.

3.2. Optimization of chromogenic reagent 4

Glyoxal 2 has two aldehyde groups that react strongly with hydrazine even when there is no solvent or catalyst present. Without isolation of 2, we proceeded to carry out the reaction with isoniazid 3 in the presence of various solvent systems, including protic, aprotic aqueous, and organic solvents and results are summarized in Table 2. Initially, we tested the molar ratio of glyoxal 2 and isoniazid 3 in an aqueous medium at room temperature with stirring. However, no reaction occurred because isoniazid is not soluble in water (Table 2, Entries 1–2). Therefore, an aqueous medium is unsuitable for optimizing the reaction. The slightly altered pathway is a superior alternative for optimizing the reaction, necessitating the use of an organic solvent instead of an aqueous one. Initially, we used acetone as a polar aprotic solvent to mix reactants 2 and 3 in different molar ratios ranging from 1:1 to 1:3. However, when we stirred

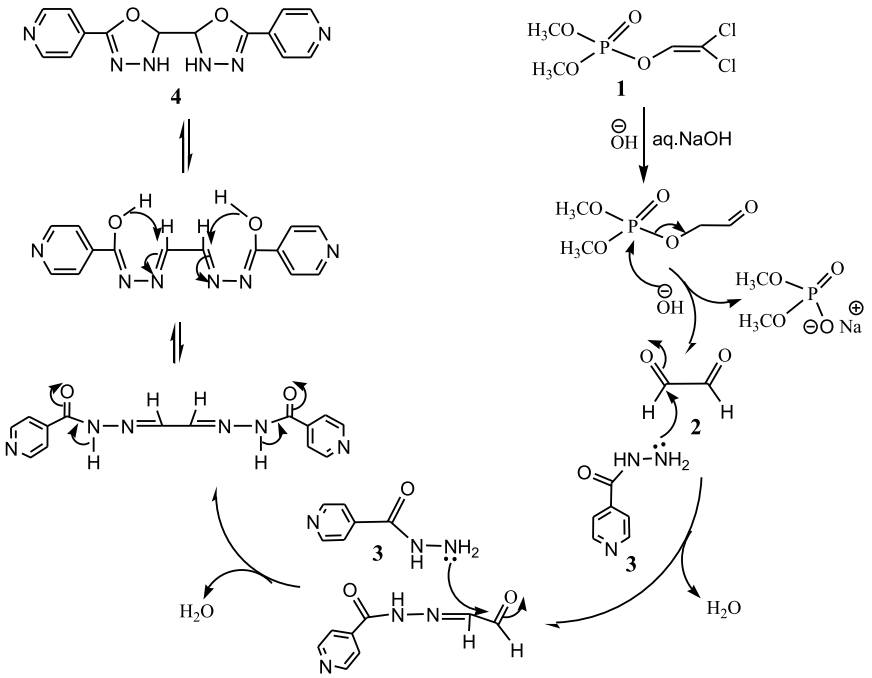
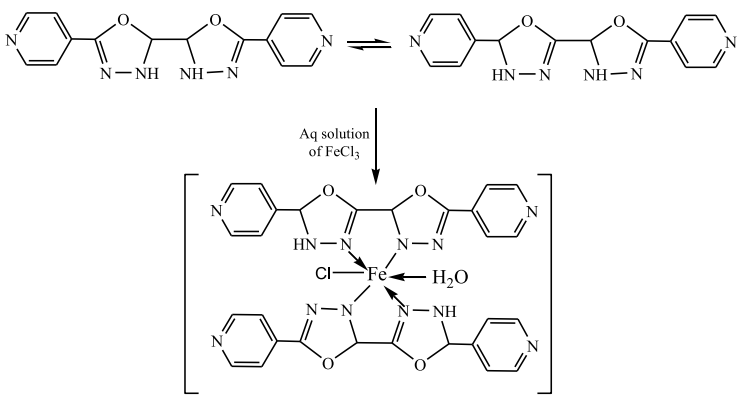


Fig. 2. Mechanistic Reaction pathway for the Glyoxal and Isoniazid.



Scheme-2. Complexometric study by Job's method.

the mixture at room temperature, we did not obtain a comparable yield of the desired product (Entries 3–5). Continuing the progressive screening, we utilized the ethanol as a polar protic solvent with variable molar proportion (1:1–1:3) of compounds 2 & 3, no significant impact on the yield of products was establish after 25–30 min (Entries 6–8).

Therefore we concluded that the limited solubility of isoniazid in organic medium was one of the rational restrictions for the completion of the reaction. Therefore, we achieved successful optimization of the reaction by substituting ethanol with methanol as the medium, resulting in an ideal possible yield of 4, (Entry 10).

Therefore methanol was identified as a best choice of solvent because starting materials dissolved quickly, and caused a shift in absorption towards longer wavelengths, resulting in the formation of an intense rose-red color. The desired product was easily isolated by filtration. The purity of the final product was confirmed by GCMS analysis. The progress of reaction was monitored by TLC using the appropriate eluent. The structure of product 4 was established and verified through spectral characterization like 1H, 13C NMR, and HRMS techniques. Finally, the cyclization reaction has been significantly investigated and the progress of mechanistic pathway depicted in Fig. 2.

3.3. Complexometric analysis by Job's methods

The reaction between intermediate glyoxal and isoniazid further confirmed its presence, leading to the formation of a Schiff base

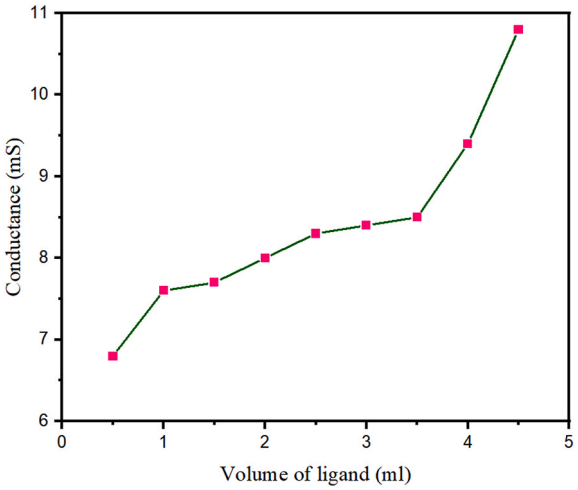


Fig. 3. Plot of absorbance against volume of Ligand (ml).

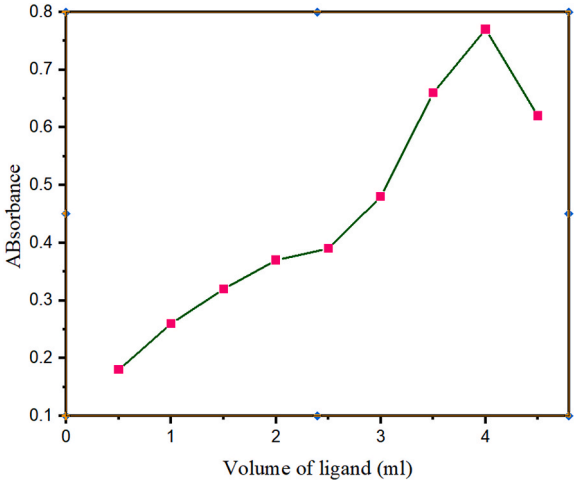


Fig. 4. Plot of Conductance (mS) against volume of Ligand (ml).

through condensation. We further verify the presence of Schiff bases through 1H NMR and GCMS analysis. Also, it is found that the Schiff base acts as monobasic bidentate ligand when treated with aqueous solution of neutral $FeCl_3$. Job's method confirmed the formation of chelate of Schiff base with Fe^{3+} ions in a 1:2 metal:ligand ratio. The study of simultaneous molar conductance suggests that the release of highly conducting H^+ ions during the chelation of the ligand with Fe^{3+} ions in the solution may be responsible for a slight increase in conductance (Scheme 2; Fig. 3 and Fig. 4).

3.4. Computational study

In order to support the synthesis and their mechanistic pathways of the examined reaction, we carried out the theoretical quantum chemical calculation using density functional theory by Gaussian software. We conduct the optimization of all geometries using the B3LYP functional and 6-31G(d,p) basis set in the Gaussian 09 software, utilizing Becke's three-parameter hybrid functional. This report focuses on optimizing concerned computational calculations and exploring the stepwise mechanism for the preparation of green chromogenic reagent based on energy calculations.

In the first step, Dichlorvos (1719.32 a. u.) reacts with 2 molecules of sodium hydroxide (−238.12) to produce an unstable compound with two hydroxy groups (−955.58) by removal of two molecules of sodium chloride (−622.56 a. u.). Then it will be converted into unstable compound three hydroxy ethene (−304.25 a. u.), followed by the formation of glyoxal (−227.82 a. u.) by removal of a water molecule (−76.42 a. u.). Therefore, in the first step we propose the base-catalyzed hydrolysis of dichlorvos by separating the phosphate and dichloro vinyl bonds. This results in the formation of glyoxal, an intermediate product.

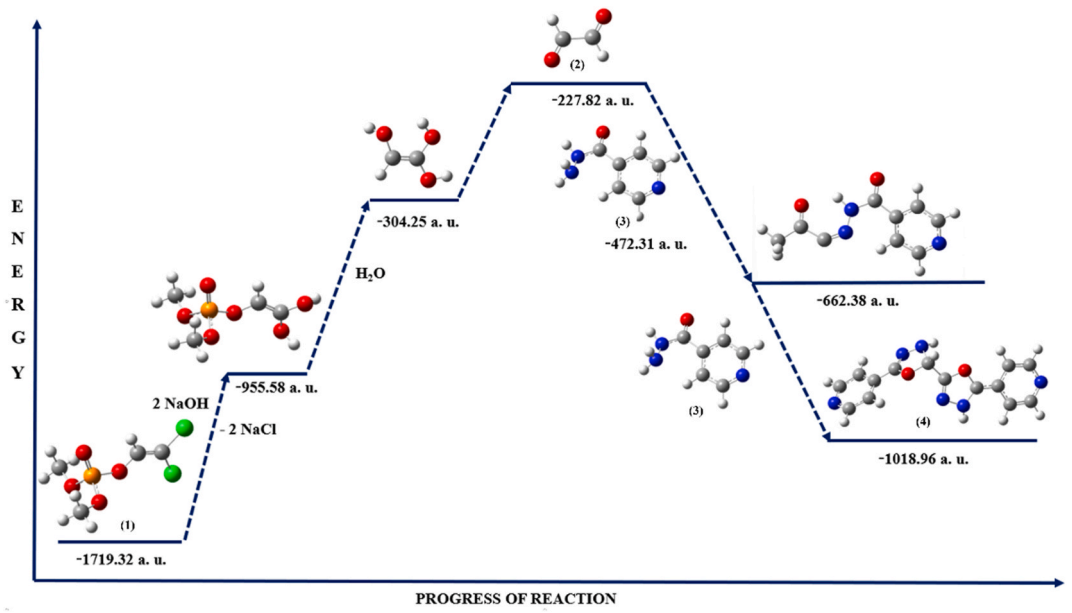


Fig. 5. Schematic representation of reaction pathways by DFT analysis.

In the second step, when glyoxal (−227.82 a. u.) reacts with Isoniazid (−472.31), which has a hydrazo linkage, first it gives the unstable intermediate glyoxazide (−662.38 a. u.) then further treated with second molecule of isoniazid, resulting the formation of stable cyclic product. This cyclic product has the potential to undergo C–C bond rotation. We have reported the energy profile diagram with progress of reaction in Fig. 5. Based on the energy calculation, we determined that bis-cyclic product is more stable. The results obtained from theoretical quantum chemical calculation by using Gaussian software has been strongly correlated with the synthesis and mechanistic pathways of the proposed green chromogenic reagent.

4. Conclusion

We developed the methodology to synthesize a novel chromogenic reagent using glyoxal, an in *situ* hydrolysis product. In this protocol, we also describe the role of chromogenic reagent as an absorption sensor, which is a crucial factor for the success of innovative synthetic methods. We used the manifest TLC method to detect the chromogenic reagent and sensor. The implemented methodology is highly straightforward, efficient, environmentally friendly, and facilitates the rapid isolation and purification of the product. We have employed the theoretical quantum chemical calculation using Gaussian software in order to support the synthesis and mechanistic pathway of the examined reaction.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Ashwin D. Gedam: Methodology, Formal analysis, Conceptualization. **Manish M. Katiya:** Formal analysis, Data curation. **Madhukar G. Dhonde:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Kapil S. Ganorkar:** Software. **Vijay J. Thakare:** Validation. **Prashant R. Mandlik:** Methodology. **Nitin L. Jadhao:** Investigation. **Jayant M. Gajbhiye:** Writing – review & editing, Supervision. **Ravi Kumar:** Investigation. **Nayana Vaval:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e31217.

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