Applied Chemical Engineering (2026) Volume 9 Issue 4 ISSN: 2578-2010 (O)
doi: 10.59429/ace.v9i4.6040

ORIGINAL RESEARCH ARTICLE

Synthesis of new thioxoimidazolidine containing azide moiety derived from acetophenone catalyzed by CdO nanoparticles and study of their biological effect

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ABSTRACT

The co-precipitation approach was used in this work to create cadmium oxide nanoparticles (CdO NPs) from cadmium nitrate. Atomic force microscopy (AFM) and scanning electron microscopy (SEM) were used to assess the size and shape of the produced CdO NPs. As thioimidazolidine derivatives, new heterocyclic compounds with azide groups were created. Schiff bases were initially prepared using p-nitro, p-chloro, and p-bromo benzaldehydes with CdO. NPs as a catalyst. Filtration was used to successfully recover the catalyst. The target compounds (4a–c) were obtained by reacting these intermediates with ethyl chloroacetate, chloroacetyl chloride, and sodium azide. Spectroscopic methods such as FT-IR, ^{1}H-NMR, and ^{13}C-NMR were used to characterize the produced compounds. The spectral analyses indicated that the synthesized compounds were obtained in a pure form, as no significant impurity signals were observed. Characteristic absorption bands were visible in the FT-IR spectra, especially for the azide group (N_3) at about 2115 cm^{-1}. Additionally, the synthetic substances' biological activity were assessed. Preliminary data on their safety profile was obtained by estimating acute toxicity by computing LD50 values. Strong broad-spectrum antibacterial activity was shown by the compounds against both Gram-negative bacteria like Escherichia coli and Klebsiella spp. and Gram-positive bacteria like Staphylococcus aureus and Staphylococcus epidermidis. Additionally, encouraging antifungal efficacy against the pathogenic yeast Candida albicans was noted.

Keywords: thioimidazolidine; Azide; CdO. NPs; inflammation; LD50

ARTICLE INFO

Received: 27 May 2026
Accepted: 15 June 2026
Available online: 04 November 2026

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1. Introduction

Imidazolidine has the chemical formula $C_3H_2N_2$, making it a heterocyclic molecule. The original imidazolidine has not gotten much attention, but structurally similar compounds with one or both nitrogen centers replaced are more prevalent. These substances are typically polar, basic, and colorless. A saturated five-membered heterocyclic system is represented by the imidazolidine ring[1]. Aldehydes and 1,2-diamines are usually condensed to produce imidazolidines. Alkyl or benzyl groups are frequently used to replace one or both nitrogen centers, producing a wide range of derivatives with various characteristics[2]. Imidazolidine derivatives also show strong antibacterial activity[3,4]. Numerous biological activities, such as antiviral[5], antileishmanial[6,7], antimicrobial[8–12], anti-proliferative[13], anticancer [14], and anthelmintic qualities[15], have also been identified for imidazolidine-based compounds. Additionally, the imidazolidine ring system has shown significant anticancer effects along with anti-inflammatory and antioxidant properties[16,17]. Certain derivatives have

been studied for their anti-corrosion qualities in addition to their biological uses[18]. For more than 150 years, researchers have been studying azide chemistry. Peter Griess created phenyl azide for the first time in 1864. A well-known reaction in which acyl azides are rearranged to create the equivalent isocyanates is known as the Curtius rearrangement, which was initially reported by Curtius in 1890[19,20]. Hydrazoic acid (HN_3) was identified as a result of these early discoveries, which signaled the start of azide chemistry. Organic azides are compounds that have the generic formula RN_3. Azides have a propensity to undergo fast, highly exothermic breakdown processes that release molecular nitrogen (N_2) and generate reactive nitrene intermediates due to their highly polarized π-bond[21]. In the past ten years, nanoparticles have emerged as extremely promising materials due to their high surface area and smaller size, which provide higher catalytic activity than bulk materials. Because of its strong catalytic activity in chemical synthesis and biological applications like antioxidant, antibacterial, and anticancer properties, cadmium oxide nanoparticles (CdO-NPs) have a wide range of uses in nanotechnology[22,23].

2. Experimental

Sigma-Aldrich and Fluka supplied all of the starting ingredients and solvents, which were employed without additional purification. Melting points are uncorrected and were found using an electrothermal capillary device. A Bruker Alpha II spectrometer (Germany) was used to record the FT-IR spectra. Tetramethylsilane (TMS) was used as the internal standard and DMSO-d_3 as the solvent in a Bruker spectrometer running at 500 MHz to acquire ^{1}H NMR and ^{13}C NMR spectra.

2.1. The process of co-precipitation for the production of CdO NPs.

The co-precipitation approach, a straightforward, effective, and economical process that yields CdO. NPs with uniform particle size and large surface area, improving catalytic performance and product purity, was used to create cadmium oxide nanoparticles (CdO NPs). A 1:1 ethanol–water combination was used to dissolve 15 mmol of $Cd(NO_3)_2{\cdot}4H_2O$ in a 60 mL round-bottom flask. Dropwise additions of 1 mL of deionized water containing 0.004 mmol of threonine was added dropwise while continuously stirring. A 2 M aqueous solution of NaOH was used to bring the mixture's pH to 10. At room temperature, the resultant suspension was agitated for 12 hours. After that, the mixture was centrifuged for 25 minutes at 5000 rpm. Centrifugation was used to wash the precipitate using a 1:1 ethanol–deionized water mixture. The final product was obtained by drying the CdO NPs for 20 hours at 80 °C in an oven[22].

2.2. Synthesis of 1-{4-[(arylidene)amino]phenyl}ethanone 1a - c

After dissolving 0.02 mole of aryl aldehyde in 30 mL absolute ethanol, (0.2 gm) CdO. NPs was added with stirring 10 min. then (0.02 mole) 4-amino acetophenone was added. The reaction mixture was stirred for 2 hrs., after that CdO. NPs. was filtrated to recover the catalyst." And the filtrate put onto crushed ice and agitated for fifteen minutes. the product was filtrated off and purified by recrystallization from ethanol[21].

(1a): 1-{4-[(4-nitrobenzylidene)amino]phenyl}ethanone: Yield 65%, FT-IR (cm-1) for

: 3054 (C-H Ar), (2978,2850) (C-H aliphatic), 1670 (C=O) carbonyl ketone, 1594,1520 (C=C), 1576(C=N)

(1b): 1-{4-[(4-chlorobenzylidene)amino]phenyl}ethanone Yield 69%, FT-IR (cm-1) for

: 3080 (C-H Ar), (2985,2855) (C-H aliphatic), 1672 (C=O) carbonyl ketone, 1599,1527 (C=C), 1559(C=N)

(1c): 1-{4-[(4-bromobenzylidene)amino]phenyl}ethanone yield 72%, FT-IR (cm-1) for

: 3067 (C-H Ar), (2990,2860) (C-H aliphatic), 1675 (C=O) carbonyl ketone, 1593,1521 (C=C), 1580(C=N)

2.3. Synthesis of3-[(E)-(1-{4-[(4-arylidene)amino]phenyl}ethylidene)amino]-2-thioxoimidazolidin-4-one 2a - c

Cadmium oxide nanoparticles (0.4 g) was added with stirring for 10 min. to (0.01 mole,) (**1a – c**) after dissolving in 30 mL absolute ethanol, then (0.01 mole) thiosemicarbazide was added and the mixture was stirred at rt. for 60 min., then chloroethylacetate (0.01 mole). was added, The reaction mixture was stirred at room temperature for 2 hrs. , then mixture was filtered to remove CdO.NPs. and cold water was added to filtrate, the solid product was collected and recrystallization from ethanol: water (3:7)[21].

2a: 3-[(*E*)-(1-{4-[(4-nitrobenzylidene)amino]phenyl}ethylidene)amino]-2-thioxoimidazolidin-4-one: yield 79%, FT-IR (cm-1) for 3362 (NH), 3053 (C-H Ar), (2978,2856) (C-H aliphatic), 1738 (C=O) carbonyl of cyclic amide, 1589,1503 (C=C). finally 1652 (C=N)

2b: 3-[(*E*)-(1-{4-[(4-chlorobenzylidene)amino]phenyl}ethylidene)amino]-2-thioxoimidazolidin-4-one yield 81%, FT-IR (cm-1) for 3345 (NH), 3030 (C-H Ar), (2981,2863) (C-H aliphatic), 1738 (C=O) carbonyl of cyclic amide, 1607,1520, (C=C). finally 1655 (C=N)

2c: 3-[(*E*)-(1-{4-[(4-bromobenzylidene)amino]phenyl}ethylidene)amino]-2-thioxoimidazolidin-4-one yield 74%, FT-IR (cm-1) for 3250 (NH), 3033 (C-H Ar), (2921,2868) (C-H aliphatic), 1739 (C=O) carbonyl of cyclic amide, 1606,1526, (C=C). finally 1652 (C=N)

2.4. Synthesis of 1-(chloroacetyl)-3-[(E)-(1-{4-[(arylidene)amino]phenyl}ethylidene)amino]-2-thioxoimidazolidin-4-one 3a - c

Compounds (**2a - c**) (0.01 mole) and (0.5 mL) triethylamine were dissolved in dry dioxane (30 mL) and stirred for 20 minutes at r.t. Chloroacetyl chloride (0.01 mole,) was added drop wise, then reaction mixture, was stirred for an additional 2 hours. After that mixture was poured an appropriate amount of cold water and stirring 20 min. Precipitate was filtered, washed with small amount of water, and recrystallization from a (4:6) ethanol–water.

3a:1-(chloroacetyl)-3-[(*E*)-(1-{4-[(4-nitro benzy lid ene) amino] phenyl } ethyl idene)amino]-2-thioxoimidazolidin-4-one: yield 71% ,FT-IR (cm-1) for , 3088 (C-H Ar), (2921,2868) (C-H aliphatic), 1722 (C=O) carbonyl of cyclic amide, 1694 (C=O) carbonyl of amide, 1660 (C=N), 1599,1525 (C=C), 1565, 1333 (NO2).

3b:1-(chloroacetyl)-3-[(*E*)-(1-{4-[(4-chlorobenzylideneamino]phenyl}ethylidene) amino]-2-thioxoimidazolidin-4-one: yield 65% , FT-IR (cm-1) for, 3080 (C-H Ar), (2977,2880) (C-H aliphatic), 1733 (C=O) carbonyl of cyclic amide, 1697 (C=O) carbonyl of amide, 1652 (C=N), 1608,1523, (C=C),

3c:1-(chloroacetyl)-3-[(*E*)-(1-{4-[(4-bromobenzylidene)amino]phenyl}ethylidene) amino]-2-thioxoimidazolidin-4-one: yield 70%, FT-IR (cm-1) for , 3036 (C-H Ar), (2982,2834) (C-H aliphatic), 1730 (C=O) carbonyl of cyclic amide, 1688 (C=O) carbonyl of amide, 1640 (C=N), 1602,1502, (C=C).

2.5. Synthesis of 1-(azidoacetyl)-3-[(E)-(1-{4-[(arylidene) amino] phenyl} ethylidene) amino]-2-thioxoimidazolidin-4-one 4a - c

A stirred solution of [compounds 3a–c] ([0.01 mole]) in [acetone] ([15 mL]), potassium iodide ([0.01 mole]) was added. The solution kept stirring at ambient temperature for [2 hours]. Thereafter, an aqueous solution of sodium azide (0.01 mole in 10 mL of water) was added dropwise, and the stirring was continued for [60 min]. The reaction mixture was then quenched by pouring it into cold water. The precipitated solid was separated by filtration, rinsed with water, and purified by recrystallization from [dioxane].

4a: 1-(azidoacetyl)-3-[(*E*)-(1-{4-[(4-nitrobenzylidene) amino] phenyl } ethylidene) amino]-2-thioxoimidazolidin-4-one yield 83%, FT-IR (cm-1) for, 3066 (C-H Ar), (2981,2858) (C-H aliphatic), 2196 (N_3), 1741 (C=O) carbonyl of cyclic amide, 1679 (C=O) carbonyl of amide, 1603,1528, (C=C), 1551.1339

(NO_2). **Figure 1** ^{1}H-NMR (**4a**): (DMSO-d6), H2O (3.32 3.35 ppm); 2.28,2.44: 2.07 (CH3), 3.36 (CH_2-N_3), 4.19 (CH2) cyclic amide, 6.98-8.19 (H-Ar), 7.95 (CH=N) near imidazolidine ring, 8.27 another (CH=N), at para for NO2 group. ^{13}C-NMR (**4a**), **Figure 2**: 20.28 (CH3), 34.10 (CH2-N3), 56.37 (CH2) cyclic amide 122.28-157.56 (C-Ar), 162.37 (CH=N) near imidazolidine ring, 166.37 another (CH=N), at para for NO_2 group. 170.40 (C=O) carbonyl amide, 173.45 (C=O) carbonyl imidazolidine ring, 176.16 (C=S)

4b: 1-(azidoacetyl)-3-[(*E*)-(1-{4-[(4-chlorobenzylidene) amino] phenyl } ethylidene) amino]-2-thioxoimidazolidin-4-one yield 76%, FT-IR (cm-1) for, 3072 (C-H Ar), (2982,2838) (C-H aliphatic), 2115 (N3), 1703 (C=O) carbonyl of cyclic amide, 1665 (C=O) carbonyl of amide, 1605,1535, (C=C), 1H-NMR (**4b**) : (DMSO-d6), H2O (3.32 3.35 ppm); 2.28,2.44 : 2.09 (CH3), 3.42 (CH_2-N_3), 4.15 (CH2) cyclic amide, 6.92-8.17 (H-Ar), 7.99 (CH=N) near imidazolidine ring, 8.32 another (CH=N), at para for Cl group. ^{13}C-NMR (**4b**),

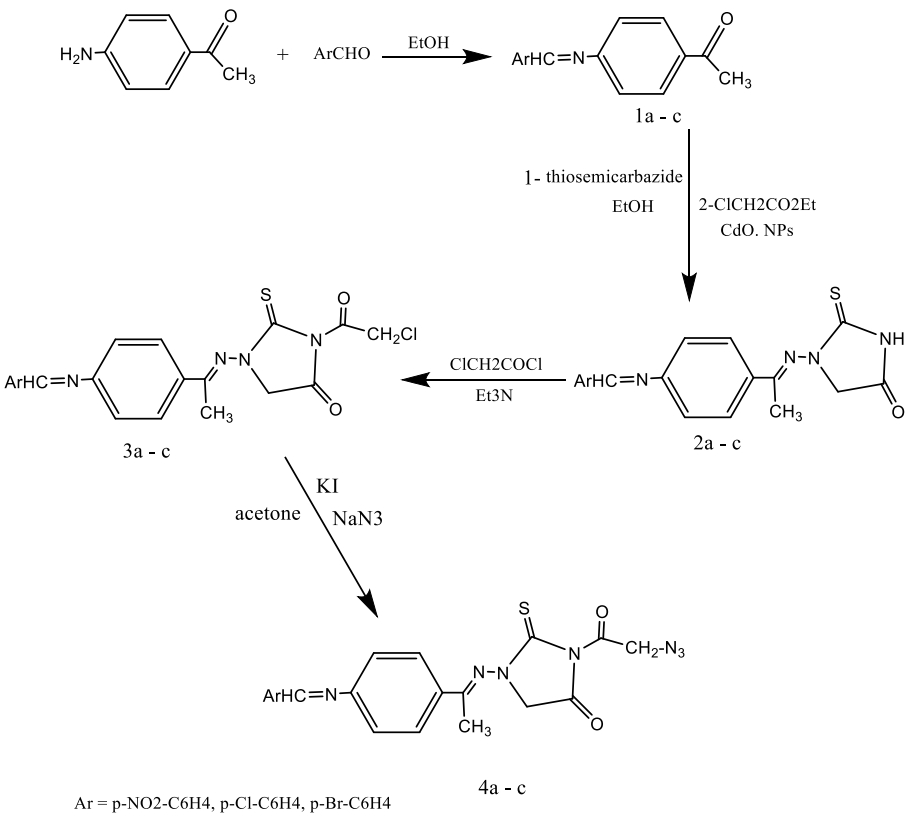
Figure 2 ^{13}C-NMR (**4b**): 20.25 (CH3), 34.19 (CH2-N3), 56.40 (CH2) cyclic amide 124.29-157.75 (C-Ar) ,161.31 (CH=N) near imidazolidine ring, 165.32 another (CH=N), at para for Cl group. 171.41 (C=O) carbonyl amide, 173.41(C=O) carbonyl imidazolidine ring, 175.21 (C=S)

4c: 1-(azidoacetyl)-3-[(*E*)-(1-{4-[(4-bromobenzylidene) amino] phenyl } ethylidene) amino]-2-thioxoimidazolidin-4-one yield 72%, FT-IR (cm-1) for, 3055 (C-H Ar), (2945,2852) (C-H aliphatic), 2156 (N3), 1709 (C=O) carbonyl of cyclic amide, 1661 (C=O) carbonyl of amide, 1601,1505, (C=C), ^{1}H-NMR (**4c**) : (DMSO-d6), H2O (3.32 3.35 ppm); 2.28,2.44: 2.05 (CH3), 3.40 (CH_2-N_3), 4.19 (CH2) cyclic amide, 6.82-8.25 (H-Ar), 7.93 (CH=N) near imidazolidine ring, 8.33 another (CH=N), at para for Br group. ^{13}C-NMR (**4a**),

Figure 2: 20.29 (CH3), 34.13 (CH2-N3), 55.49 (CH2) cyclic amide 122.29-157.70 (C-Ar), 162.32 (CH=N) near imidazolidine ring, 164.30 another (CH=N), at para for Cl group. 171.45 (C=O) carbonyl amide, 173.43(C=O) carbonyl imidazolidine ring, 176.29 (C=S).

3. Results and Discussion

Scheme 1 shows stages of reaction that leading to the synthesis of final products (**4a – c**). All of the steps in **Scheme 1** were carried out at room temperature.



Scheme 1. Shows the formation compounds 4a- c.

IR spectra of compounds **1a - c** exhibited show disappearance peaks of NH_2 and new peak was appeared of C=N at (1559-1580 Cm^{-1}) in additional to conjugated carbonyl of ketone between (1670 – 1675 Cm-1) and asymmetric & symmetric for CH3 at (2990 – 2850 Cm^{-1}). While spectra of compounds **2a – c** show an absorption band at (3250 - 3362 cm^{-1}) due to NH of imidazolidine ring and strong band at (1738 – 1739 cm^{-1}) for carbonyl of cyclic amide, a distinct band at (3030 - 3053 cm^{-1}) attributed to the aromatic (C–H) another bands at (1503 – 1606 cm^{-1}) return to C=C of aromatic ring. Furthermore, three spectra of FT-IR of compounds **3a – c** appeared tow carbonyl groups one for imidazolidine ring and another for new amide at (1722 – 1733 Cm^{-1}) and at (1688 – 1697 Cm^{-1}) respectively, Furthermore, band of CHAr at 3036 - 3088 Cm^{-1}) while two bands of C=C Ar appear at 1502- 1608 Cm-1). Finally products **4a – c** FT-IR spectrum of the compound **4a** shows 3066 Cm^{-1} for (C-H Ar), Asym. & sym. at (2981,2858 Cm^{-1}) due to (C-H aliphatic), new band at 2196 Cm^{-1} attributed to (N_3), azido group strong peak at 1741Cm^{-1} for (C=O) carbonyl of cyclic amide, while band at 1679 (C=O) carbonyl of amide, finally two bands at 1551.1339 Cm^{-1} (Asym. & sym.) of (NO_2) group. So ^{1}H-NMR (**4a**) **Figure 1**: (DMSO-d6), H2O (3.32 3.35 ppm); 2.28,2.44 : give signal at 2.07 ppm attributed to (CH3) group, and a singlet signal at 3.36 ppm for (CH_2-N_3), Additionally, a singlet observed at 4.19 due to (CH2) cyclic amide, The spectrum displayed a multiple signals at 6.98-8.19) ppm integrating for the (8H), which was attributed to the aromatic ring protons , and two singlet signals at 7.95 ppm for (CH=N) near imidazolidine ring and at 8.27 ppm due to another (CH=N), at para for NO_2 group respectively. ^{13}C-NMR spectrum of (**4a**), **Figure 2**: appear signal at 20.28 ppm due to (CH3) group, and signal at 34.10 ppm attributed to (CH2-N3) of side chain while another (CH2) cyclic amide appear at 56.37 ppm, multiple signals at 122.28-157.56 ppm for aromatic carbon, two signals at 162.37 and at 166.37 ppm for (CH=N) near imidazolidine ring, another (CH=N), at para for NO_2 group respectively. Finally three signals appear at 170.40 ppm for (C=O) carbonyl amide, at 173.45 ppm due to (C=O) carbonyl imidazolidine ring and at 176.16 ppm attributed to (C=S). FT-IR spectrum of the compound **4b** shows 3072 Cm^{-1} for (C-H Ar), Asym. & sym. at (2982,2838 Cm^{-1}) due to (C-H aliphatic), new band at 2115 Cm^{-1} attributed to (N_3), azido group strong peak at 1703Cm^{-1}

for (C=O) carbonyl of cyclic amide, while band at 1665 (C=O) carbonyl of amide. So ^{1}H-NMR (**4b**) (DMSO-d6), H2O (3.32 3.35 ppm); 2.28,2.44 : give signal at 2.09 ppm attributed to (CH3) group, and a singlet signal at 3.42 ppm for (CH_2-N_3), Additionally, a singlet observed at 4.15 due to (CH2) cyclic amide, The spectrum displayed a multiple signals at 6.92-8.17) ppm integrating for the (8H), which was attributed to the aromatic ring protons , and two singlet signals at 7.99 ppm for (CH=N) near imidazolidine ring and at 8.32 ppm due to another (CH=N), at para for Cl group respectively. ^{13}C-NMR spectrum of (**4b**): appear signal at 20.25 ppm dueto (CH3) group , and signal at 34.19 ppm attributed to (CH2-N3) of side chain while another (CH2) cyclic amide appear at 56.40 ppm , multiple signals at 124.29-157.75 ppm for aromatic carbon, two signals at 161.31 and at 165.32 ppm for (CH=N) near imidazolidine ring, another (CH=N), at para for Cl group respectively. Finally three signals appear at 171.41 ppm for (C=O) carbonyl amide, at 173.41 ppm due to (C=O) carbonyl imidazolidine ring and at 175.21 ppm attributed to (C=S). FT-IR spectrum of the compound **4c** shows 3055 Cm^{-1} for (C-H Ar), Asym. & sym. at (2945,2852 Cm^{-1}) due to (C-H aliphatic), new band at 2156 Cm^{-1} attributed to (N_3), azido group strong peak at 1709 Cm^{-1} for (C=O) carbonyl of cyclic amide, while band at 1661 (C=O) carbonyl of amide. So 1H-NMR (**4c**) (DMSO-d6), H2O (3.32 3.35 ppm); 2.28,2.44 : give signal at 2.05 ppm attributed to (CH3) group, and a singlet signal at 3.40 ppm for (CH_2-N_3), Additionally, a singlet observed at 4.19 due to (CH2) cyclic amide, The spectrum displayed a multiple signals at 6.82-8.25) ppm integrating for the (8H), which was attributed to the aromatic ring protons , and two singlet signals at 7.93 ppm for (CH=N) near imidazolidine ring and at 8.33 ppm due to another (CH=N), at para for Cl group respectively. ^{13}C-NMR spectrum of (**4c**): appear signal at 20.29 ppm due to (CH3) group, and signal at 34.13 ppm attributed to (CH2-N3) of side chain while another (CH2) cyclic amide appear at 55.49 ppm, multiple signals at 122.29-157.70 ppm for aromatic carbon, two signals at 162.32 and at 164.30 ppm for (CH=N) near imidazolidine ring, another (CH=N), at para for Cl group respectively. Finally three signals appear at 171.45 ppm for (C=O) carbonyl amide, at 173.43 ppm due to (C=O) carbonyl imidazolidine ring and at 176.29 ppm attributed to (C=S).

3.1. Biological activity

Both Gram-positive (*Staphylococcus epidermidis* and *Staphylococcus aureus*) and Gram-negative (*Escherichia coli* and *Klebsiella spp*.) bacteria were used to test the synthetic compounds' antibacterial properties. Additionally, the antifungal activity against Candida albicans was evaluated. The results are summarized in **Table 1**. As a control, DMSO was used to dissolve the produced compounds (4a, 4b, and 4c). By calculating the inhibition zones (mm) against particular microbial strains, their antibacterial and antifungal properties were assessed. Gram-positive bacteria (*Staphylococcus aureus and Staphylococcus epidermidis*), Gram-negative bacteria (*Escherichia coli and Klebsiella spp*.), and the fungus Candida albicans were among the microorganisms evaluated at different doses of 50, 100, 200, and 400 µg/mL. The inhibition zones grew with concentration for the majority of the chemicals. Compound 4a demonstrated zones of 19 mm, 19 mm, 19 mm, and 22 mm against S, exhibiting moderate to severe antibacterial activity with maximum inhibition seen at 400 µg/mL. *aureus, S. Epidermidis, E. Klebsiella spp.* and Coli, respectively. Particularly against Gram-negative bacteria, compound 4b exhibited inconsistent efficacy. The maximum inhibition was seen at 100 and 200 µg/mL, reaching up to 21 mm. Even at lower concentrations, 4c showed the greatest antibacterial activity of all the studied drugs, with high inhibition zones (up to 23 mm), particularly against Klebsiella spp. Flagyl, the usual medication, demonstrated superior antifungal action against C. albicans (up to 20 mm), although inhibition zones range from 10 to 13 mm, indicating reduced antibacterial action against the majority of bacterial species. In conclusion, the synthesized compounds demonstrated strong antibacterial action, especially compound 4c. The para-bromo substituent on the aromatic ring of compound 4c is responsible for its highest biological activity among the produced derivatives. The bromine atom makes the molecule more polarizable and lipophilic, which improves its capacity to cross biological membranes. Furthermore, the interaction between the azomethine and thiohydantoin moieties and biological targets may be enhanced by the electron-withdrawing effect of bromine. Compound 4c is probably more active than compounds 4a and 4b

because of these combined actions. These results imply that the compounds may be good candidates for additional investigation and development as antimicrobial agents.

Table 1. shows results of anti-bacterial activity.

Compounds		Inhibition zone				
		Stophy. aureus	*Stophy. empidermidis.*	*Esch. coli*	*Klebsiella sp.*	*Candida aeruginosa*
4a	50	12	15	11	15	13
4a	100	13	17	15	15	15
4a	200	17	20	20	21	14
4a	400	19	19	19	22	14
4b	50	13	15	17	17	15
4b	100	19	19	20	21	14
4b	200	18	19	19	20	14
4b	400	13	17	15	14	15
4c	50	20	20	20	23	14
4c	100	20	19	19	21	14
4c	200	17	17	15	19	15
4c	400	19	17	15	15	15
Flagyl	200	10	13	10	10	19
Flagyl	400	10	11	10	10	20

3.2. 2- LD50 of compounds (4a - c) in different concentration and animals used

The study used sixty mature male albino mice that were three months old and weighed between 25 and 35 grams. In the animal facility of the Iraqi Center for Cancer Research and Medical Genetics, Mustansiriyah University, Baghdad, the animals were kept in polypropylene cages under standard circumstances, which included controlled lighting, ventilation, a temperature of 25 ± 2°C, and 35–60% humidity. Standard food and water were given to them. Ten experimental groups (G1–G10), each with six mice (N = 6), were used to assess acute toxicity. To evaluate the safety profile of the synthesized compounds (4a, 4b, and 4c), various doses were given. Groups G1 and G2 were given 25 and 500 mg/kg of compound 4a, respectively; groups G3 and G4 were given 250 and 500 mg/kg of compound 4b; and groups G5 and G6 were given 250 and 500 mg/kg of compound 4c. In contrast, groups G7 and G8 received 200 and 400 mg/kg of the common medication Flagyl, respectively. Group G10 was given distilled water as a negative control, while group G9 was given a 10% DMSO–water mixture. Under the experimental conditions, it was discovered that the produced chemicals 4a, 4b, and 4c were harmless. It exceeds 500 mg/kg because the median lethal dosage (LD_{50}) was not obtained within the studied dose range. These findings point to a broad margin of safety, suggesting that the compounds are appropriate for additional pharmacological research.

Table 2. shows lethal dose for compounds (4a - c) in different concentration.

Groups	Com. code	Mortality (x/N)	Mortality (x/N)	symptom
G1	4a 250	0\6	0%	nil
G2	4a 500	0\6	0%	nil
G3	4b 250	0\6	0%	nil
G4	4b 500	0\6	0%	nil
G5	4c 250	0\6	0%	nil
G6	4c 500	0\6	0%	nil
G7	Flagyl 200	0\6	0%	nil
G8	Flagyl 400	0\6	0%	nil
G9	DMSO:H_2O 10%	0\6	0%	nil
G10	Dist. H2O	0\6	0%	nil

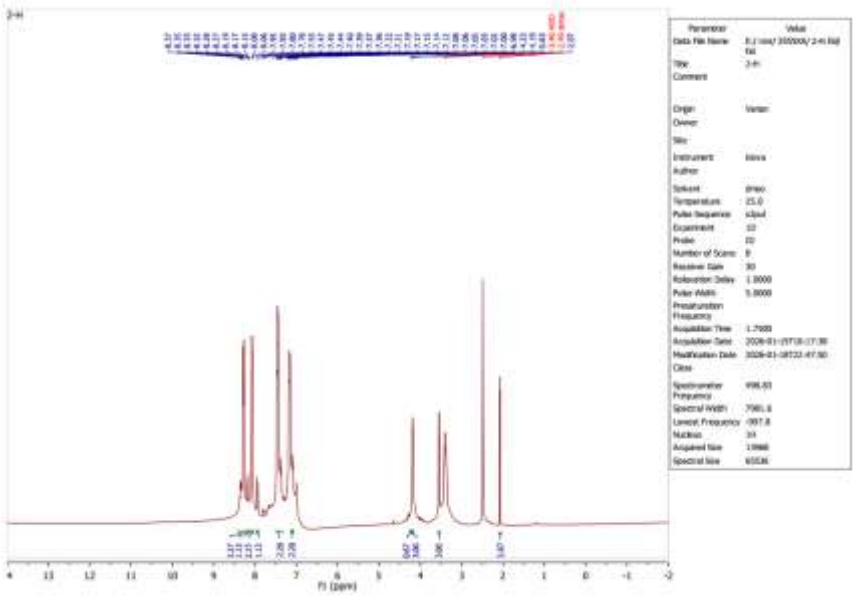


Figure 1. ^{1}H-NMR spectrum of the compound (4a).

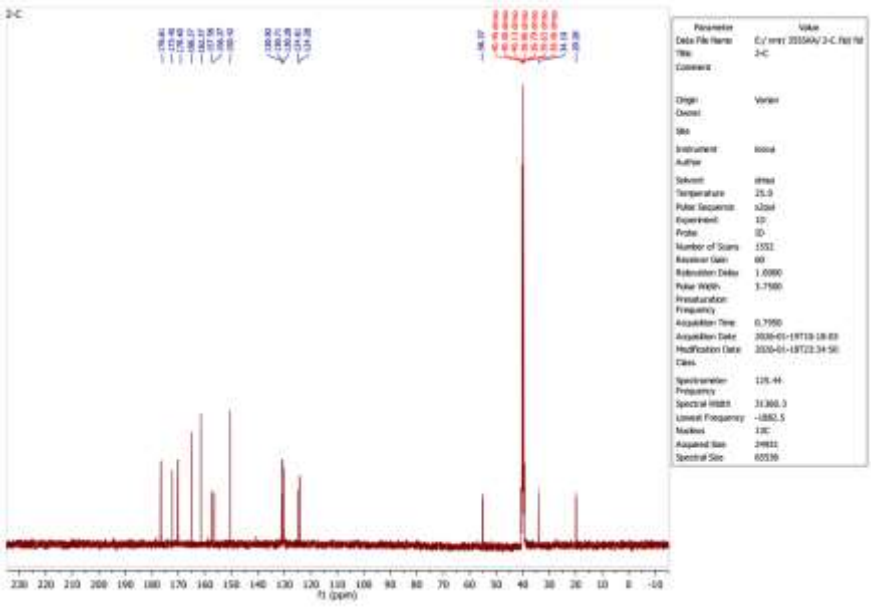


Figure 2. ^{13}C-NMR spectrum of the compound (4a).

4. Conclusion

Using CdO nanoparticles as an effective catalyst, a number of novel thioxoimidazolidine derivatives with an azide moiety were effectively produced from Schiff bases generated from acetophenone. FT-IR, ^1H NMR, ^13C NMR, and mass spectral studies were used to describe the produced compounds, confirming their purity and suggested structures. Good catalytic efficiency was demonstrated by the CdO nanoparticle catalyst, which was readily recovered by filtration and reused. The produced compounds have potential activity, according to biological evaluation, with compound 4c exhibiting the highest activity among the evaluated derivatives. The para-bromo substituent, which increases the molecule's lipophilicity and contact with biological targets, may be responsible for compound 4c's increased activity.

Acknowledgments

We thank Mustansiriyah University, College of Science, Department of Chemistry for their help.

Conflict of interest

The authors declare no conflict of interest.

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