Preparation, Characterization, Biological Evaluation and Assess Laser Efficacy for New Derivatives of Imidazolidin-4-one

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Abstract: In this study, new Imidazolidin-4-one [A1-A5] compounds were prepared by the reaction of schiff base compounds with alanine in ethanol. The prepared compounds were characterized by physical properties, UV-Vis, FT-IR and 1H-NMR spectral and C.H.N analysis. TLC checked the purity for these compounds. All compounds [A1-A5] were prepared by the traditional method (reflux) and microwave technology. It was found that using the microwave method gives better results in terms of less time and, higher yield. Antibacterial behaviors were investigated against a variety of bacteria, including Escherichia coli and Klebsiella pneumonia Gram (-) ve, Staphylococcus aureus, and Staphylococcus epidermidis Gram (++) ve. The laser efficacy of the compounds [A1-A5] was evaluated after they were radiated by laser for (10, 20, 30) seconds. As the melting point and color of the substances were determined, it was discovered that they were unaffected and did not disintegrate or polymerize. Using the Chem Draw Specialist 19.0 program, the stereoisomers of the prepared compounds [A1-A5] were examined at the lowest layer stage. Using the Chem3D 19.0 program, the heat of the formulation of the compounds [A1-A5] was also investigated.

Keywords: Imidazolidin-4-one, Biological Activity, Laser Effectiveness.

1. Introduction

Imidazolidin-4-one is one of the five-ring heterocyclic compounds which have a vital application in biological as well as nonlinear optical applications and that contain four nitrogen atoms and a carbon atom in addition to hydrogen atoms [1]. The simplest of them is the compound (imidazolidin-4-one) with the formula CH2N4 [2]. These compounds are considered one of the most effective cyclic compounds because they possess four free pairs of electrons for four nitrogen atoms of the electron propellant compounds [3]. This Imidazolidin-4-one is prepared by cyclic addition between Schiff base compounds and alanine [4]. Imidazolidin-4-one compounds and their derivatives possessed great importance, especially in the biological field, as the prepared compounds showed anti-bacterial, anti-fungal, and anti-viral efficacy [5]. They were also used in the preparation of medicinal drugs to treat chronic diseases, as well as used as anti-hypertension, showing antibacterial and anti-fungal effectiveness, anti-cancer efficacy, and anti-spasmodic efficacy [6,7]. They play important roles in coordination chemistry, in the photographic industry, or as components of special explosives [8, 9]. As a result of their acidities, 5-monosubstituted Imidazolidin-4-ones are also used as activators in oligonucleotide synthesis [10]. However, the most important use of Imidazolidin is to be found in medicinal chemistry [11]. The first compound containing an imidazolidin ring to have been prepared is thought to be 2-phenyl-2H-imidazolidin-4-one-5-carbonitrile, which was prepared and characterized in 1885 [12, 13].

2. Experimental details
2.1. Material and Device’s instrument:

Both chemicals were used precisely as they were given by the producer (Alfa Aesar and Aldrich). The melting points were measured using the Electrothermal Melting Apparatus 9300 in uncorrected free capillary tubes. The reaction was tracked, and purity was tested using thin-layer chromatography (TLC). Microwave synthesis workstation MAS-II. The FT-IR spectra were captured using a Shimadzu FT-IR 8400S spectrophotometer with a scale of (400-4000) cm⁻¹. The UV-Vis spectra were calculated using a Shimadzu 800UV in the range (200-400) nm in ethanol.
Chloroform-d6 as solvents were used to capture 1H-NMR
600 MHZ. C.H.N research was used to evaluate the
spectrophotometer components’ quantitative analysis. A
1-milliwatt helium-neon laser beam (visible laser) with a
wavelength of 600-700 nanometers was used to
irradiate the prepared compounds.

2.2. Prepare of Imidazolidin-4-one [A1–A5] in the
traditional methods:

In 45 ml of ethanol, Schiff bases prepared [14]
(0.001 mol) are combined with (0.002 mol, 0.18 gm) of
alanine and refluxed for (3-7) hours. The residue was
extracted, and acetone was used to re-crystallize it [15].
Table (1) describes the physical properties.

2.3. Prepare of Imidazolidin-4-one [A1–A5] in the
microwave methods:

In 15 ml of ethanol, Schiff bases prepared [15]
(0.001 mol) are combined with (0.002 mol, 0.18 gm) of
alanine and microwaved for (4-8) minutes (ability 600
W). The residue was extracted, and acetone was used to re-crystallize it [15].

3. Results and Discussion

In this research, five compounds were prepared
including Imidazolidin-4-one [A1-A5] as in the scheme (1)
and characterized by UV-Vis, FT-IR, 1H-NMR Spectra
and C.H.N analysis.

3.1. Characterization Of Imidazolidin-4-One
Derivatives [A1–A5]

The reaction of 2 moles of alanine with Schiff
bases in ethanol yielded Imidazolidin-4-one derivatives

Table 1. Physical properties and elemental analysis of prepared compounds [A1–A5]

| Comp. No. | Ar | Molecular Formula M. Wt. | Color | M.P (C°) | Ref. (hr.) | R.f. MeOH | found / (calc.) % |
|-----------|----|------------------------|-------|----------|-----------|-----------|-----------------|
| A1        |    | C44H33NaO4 742.84       |       | 250-252  | 3         | 6         | 14.97 (15.08)   |
| A2        |    | C44H33N10O8 832.83      | Red   | 210-212  | 3         | .82       | 16.75 (16.82)   |
| A3        |    | C40H34N12O4 746.79      | Orange| 291-292  | 6         | .77       | 22.60 (22.51)   |
| A4        |    | C44H33NaO8 774.84       | Yellow| 270-271  | 7         | .40       | 14.53 (14.46)   |
| A5        |    | C50H68N12O10S2 1063.13  | Gray  | 258-260  | 3         | 0.9       | 15.88 (15.81)   |

The FT-IR spectrum revealed the
disappearance of the band azomethine (HC=N) group,
as well as the emergence of bands at (3402-3454) cm⁻¹
due to the (OH), and appearances of bands at (3231-
3278) cm⁻¹ due to the (NH), and appearances of bands
at (3052-3091) cm⁻¹ due to the (CH) aromatic, as well as
appearances of bands at (2937-2991) cm⁻¹ due to the
(CH) aliphatic. Aside from the bands at (1581-1598) cm⁻¹
and (1481-1506) cm⁻¹ due to the (C≡C) aromatic ring,
and at (1425-1442) cm⁻¹ for (N=N) azo group, there are
other bands at (1213-1250) cm⁻¹ due to the (C-N) group
and (1067-1093) cm⁻¹ due to the (N-N) group [16],
as seen in figures (1-3). Table (2) shows the UV and FT-IR
continuum.

In addition, the 1H-NMR (400 MHz, Chloroform-d) δ/ppm to the
[A1] Compound: (1.22 & 1.23) (d, 6H, 2CH3); (3.51, 3.52
& 3.53) (t, 2H, 2NH Imidazolidin-4-one); (3.91-3.95) (f,
2H, 2CH Imidazolidin-4-one); (6.21 & 6.22) (d, 2H, 2CH
Imidazolidin-4-one); (6.99-7.55) (m, 22H, Aromatic
benzene); 7.53 (s, Chloroform-d); 8.31 (s, 2H, 2OH). As
shown in figure (4).

In the UV spectra, the transition n-π* and π-π* which
confirmed the presences of the un-bonded
pair electrons on nitrogen, oxygen atoms and aromatic
system (double bond) as seen in figures (12). UV & IR
absorbance spectra are given in table (2).
Scheme 1. Route of prepared compounds [A1-A5]

Table 2. FT-IR and UV/Vis data of prepared compounds [A1-A5]

| Comp. No. | Ar | max₁ (O-H) | max₂ (N-H) | v(C-H) | v(C=O) | v(N=N) | v(N=O) | Others |
|-----------|----|------------|------------|--------|--------|--------|--------|--------|
| A₁        |        | 234        | 3232       | 3078   | 1693   | 1591   | 1402   | .......... |
| A₂        |        | 255        | 3190       | 3077   | 1675   | 1596   | 1434   | 1245   | v(NO₂) asy.(1559), sym.(1382) |
| A₃        |        | 216        | 3215       | 3058   | 1650   | 1585   | 1417   | 1263   | v(C=N) (1687) |
| A₄        |        | 239        | 3265       | 3074   | 1666   | 1585   | 1419   | 1294   | .......... |
| A₅        |        | 242        | 3212       | 3082   | 1656   | 1591   | 1432   | 1210   | v(SO₂) asy.(1368), sym.(1147) |

Figure 1. FT-IR spectrum of compound [A1]
Figure 2. FT-IR spectrum of compound [A2]

Figure 3. FT-IR spectrum of compound [A4]

Figure 4. 1H-NMR spectrum of compound [A1]
3.2. Solubility Test for Prepared Compounds [A1-A5]

The prepared compounds are thermally stable at normal temperatures, as it is noticed that Imidazolidin-4-one derivatives [A1-A5] are completely dissolved in methanol, THF, DMSO, DMF, CHCl3 and mix 1,4-dioxane with EtOH, as well as not soluble in solvents EtOH, H2O, acetone, benzene, 1,4-dioxane, and are poorly soluble in solvents CCl4, ether, hexanol as shown in the table (3).

3.3. Discuss Difference Between Preparing Compounds Using Traditional Method (Reflux) And Microwave Method

All compounds [A1-A5] were prepared by the traditional method (reflux) and then prepared by microwave technology to compare the two methods in terms of using the solvent and, the time taken for the reaction, the percentage of the yield, the degree of melting, the color and the solubility, as it was found that using the microwave method to prepare the organic compounds gives better results where they are used. The amount of solvent is less than in the traditional method (reflux). The yield ratio is higher, the byproducts are very little or no, and the time taken for the reaction is very short compared to the time taken by the traditional method (reflux), as well as the ease of isolating the products prepared by microwave technology compared to the traditional method (reflux). As for the physical properties of the compounds prepared by the microwave method, the melting point, color and solubility are identical to the compounds prepared by the traditional method (reflux) [18], as shown in table (4).
3.4. Antibacterial Activity

The antibacterial function of compounds [A₁₋₅] was evaluated using the disk diffusion system against four bacteria: *Escherichia coli* and *Klebsiella Pneumonia* Gram (-) ve., *Staphylococcus aureus*, and *Staphylococcus epidermidis* Gram (+) ve. The disks were then immersed in DMSO and dried in an incubator before being used in bacteria cultures. The plates were incubated for two days at 37°C. Maximum inhibition zone diameter (IZD) was observed and calculated. At three doses, *ampicillin*, *amoxicillin*, and *Ciprofloxacin* were used as monitoring samples. The findings revealed that certain of the compounds had antibacterial activity. Compound [A₁ & A₂] showed weak and moderate activity against the bacterial species used. Compounds [A₃, A₄ & A₅] gave strong efficacy and high inhibition, reaching (5) cm at a concentration of (100) mg/ml and reached (4) cm at Concentration (50) mg/ml against all bacterial species used in the study [19-23]. Table (5), and scheme (2–5) demonstrate the effects of the inhibition zone diameter (IZD) in millimeters.

3.5. Lasers’ Impact on Prepared Compounds [A₁₋₅]

A laser with a (5) milliwatt power emits laser rays in the visible spectrum with a wavelength of (600-700) nm in continuous waves. The laser was used to irradiate the compounds [A₁₋₅] for (10, 20, 30) seconds. The substances were discovered to be untouched. When the melting point and color were determined, they did not disintegrate or polymerize. This indicates that the substances were untouched by the laser beams. They are secure, as shown by table (6) [24].

3.6. Influence of Stereochemistry and Heat of Formation of Compounds [A₁₋₅]

The compounds [A₁₋₅] were also investigated at the lowest energy level with the Chem Draw Specialist 19.0 package (2019 version), as seen in figures (6-10). The heat of formulation of the prepared compounds [A₁₋₅] was also examined using the Chem3D 19.0 program, with positive heat formation for compounds [A₁ and A₃], suggesting that the reactions of their preparation are endothermic, which is compatible with the functional findings. In comparison, the compound [A₄] had a negative formation temperature, meaning that their preparation reactions are exothermic, which contradicts the realistic findings. The compounds [A₂, A₅] did not show the temperature of formation. As shown in table (7).

### Table 4. Comparison between preparing compounds using the traditional method (reflux) and the microwave method

| Comp. No. | Traditional method (reflux) | Microwave method |
|-----------|-----------------------------|------------------|
|           | T.Ref. (hr.) | Yield(%) | Solvent(ml) | Color | T.Ref.(min.) | Yield(%) | Solvent(ml) | color |
| A₁        | 3            | 80       | 45        | Green  | 4            | 90       | 15        | Green  |
| A₂        | 3            | 55       | 45        | Red    | 8            | 80       | 15        | Red    |
| A₃        | 6            | 76       | 45        | Orange | 4            | 92       | 15        | Orange |
| A₄        | 7            | 43       | 45        | Yellow | 5            | 77       | 15        | Yellow |
| A₅        | 3            | 60       | 45        | Gray   | 7            | 93       | 15        | Gray   |

### Table 5. Antibacterial activity of the prepared compounds [A₁₋₅] and control antibiotic

| Comp. No. | E. Coil | K. Pneumonia | S. Aureus | S. Epidermidis |
|-----------|---------|--------------|-----------|---------------|
|           | Conc. mg/ml | Conc. mg/ml | Conc. mg/ml | Conc. mg/ml |
|           | 25 50 100 | 25 50 100 | 25 50 100 | 25 50 100 |
| A₁        | 1 2 5 | 1 2 3 | 0 1 3 | 1 3 4 |
| A₂        | 0 1 3 | 1 2 4 | 1 2 2 | 1 3 4 |
Table 6. The results of the irradiation of the prepared compounds [A1-A5] by laser beams

| Comp. No. | 10 S    | 20 S    | 30 S    |
|-----------|---------|---------|---------|
|           | M.P. °C | Color   | M.P. °C | Color   | M.P. °C | Color   |
| A1        | 250-252 | Green   | 250-252 | Green   | 250-252 | Green   |
| A2        | 210-212 | Red     | 210-212 | Red     | 210-212 | Red     |
| A3        | 291-292 | Orange  | 291-292 | Orange  | 291-292 | Orange  |
| A4        | 270-271 | Yellow  | 270-271 | Yellow  | 270-271 | Yellow  |
| A5        | 258-260 | Dark gray | 258-260 | Dark gray | 258-260 | Dark gray |

Table 7. Heat of formation Kcal/mol of synthesized compounds [A1-A5]

| Comp. No. | Heat of Formation KJ/mol |
|-----------|--------------------------|
| A1        | 189.51                   |
| A2        | -----                    |
| A3        | 403.23                   |
| A4        | -165.11                  |
| A5        | -----                    |

**Scheme 2.** Evaluation of inhibitory activity of [A1-A5] for *E. Coli*

**Scheme 3.** Evaluation of inhibitory activity of [A1-A5] for *K. Pneumonia*
### Biological activity of *S. Aureus*

| Comp. No. | 25 mg/ml | 50 mg/ml | 100 mg/ml |
|-----------|-----------|-----------|-----------|
| A1        | 0         | 1         | 3         |
| A2        | 0.5       | 2         | 2         |
| A3        | 1         | 3         | 4         |
| A4        | 1.5       | 4         | 5         |
| A5        | 2         | 2         | 5         |

### Biological activity of *S. Epidermidis*

| Comp. No. | 25 mg/ml | 50 mg/ml | 100 mg/ml |
|-----------|-----------|-----------|-----------|
| A1        | 1         | 1         | 1         |
| A2        | 0.5       | 5         | 5         |
| A3        | 1         | 3         | 3         |
| A4        | 1.5       | 4         | 4         |
| A5        | 2         | 2         | 5         |

**Scheme 4.** Evaluation of inhibitory activity of [A1−A5] for *S. Aureus*

**Scheme 5.** Evaluation of inhibitory activity of [A1−A5] for *S. Epidermidis*

**Figure 6.** Stereochemistry of [A1]

**Figure 7.** Stereochemistry of [A2]

**Figure 8.** Stereochemistry of [A3]

**Figure 9.** Stereochemistry of [A4]

**Figure 10.** Stereochemistry of [A5]

**Figure 11.** TLC spots and *R* of [A1−A5]
4. Conclusions

The precision of the substances prepared is shown by spectroscopic measurements. It was found that using the microwave method gives better results than the traditional method (reflux) in terms of less time, higher productivity, and no catalyst. The prepared compounds [A₁⁻A₅] also showed good solubility in many solvents. Compound [A₁ and A₂] showed weak and moderate activity against the bacterial species used. Compounds [A₃, A₄ and A₅] gave strong efficacy and high inhibition, reaching (5) cm at a concentration of (100) mg/ml and reached (4) cm at Concentration (50) mg/ml against all bacterial species used in the study. At the lowest energy stage, the stereoisomers and heat of creating the prepared compounds [A₁⁻A₅] were also investigated. Positive heat formation was found in the Imidazolidin-4-one derivatives, suggesting that their preparation reactions are endothermic. The laser was used to irradiate the compounds [A₁⁻A₅] for (10, 20, 30) seconds. The substances were discovered to be untouched. When the melting point and color were determined, they did not disintegrate or polymerize. This indicates that the imports were unaffected by the laser beams. And they are dependable. The prepared compounds' thermal efficiency and optical stability were examined, and the findings revealed that they were stable.

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Conflict of interest
None of the authors have any conflicts of interest to declare.

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