RESEARCH ARTICLE

Synthesis and Characterization of Some Novel γ-Lactams, and Study of Their Antioxidant and Biological Activities

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ABSTRACT

Background: This review focuses on the synthesis, classification, and the examined behaviors of antioxidants and the biological activity of γ-lactams (2a-3d). In this reaction, succinic Anhydride interacts with different Schiff bases to synthesize γ-lactams (all of which have high yields). FT-IR, ^{1}H-NMR,^{13}C-NMR, and CHN spectral analysis formed the foundation for spectral analyses of γ-lactam structures. The antimicrobial activity was checked on the γ-lactams (2a-3d), resulting in successful findings on both staphylococcus aureus and Escherichia coli. Additionally, the behaviors of the antioxidants (2a-3d) were investigated by examining how "2,2-diphenyl-1-picrylhydrazyl" [DPPH] was influenced by the compound (2a-3d).

Keywords: Auccinic anhydride, Heterocyclic**,** γ-Lactams, Phenyl succinic Anhydride.

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INTRODUCTION

Organic compounds are containing more than one or hetero atoms called the heterocyclic ring. In heterogenous rings, there are widely known atoms such as oxygen, nitrogen, and sulfur. The lactams ring are known as 2-oxopyrrolidines, γ-lactams or Five-membered ring lactams. In many biological fields, alternative γ-lactams is used to synthesize drugs due to their activity in multiple diseases. Chlorophyll, hemoglobin, vitamins are biological molecules that contain the heterocyclic ring in the primary skeleton.[1]

In several diseases, heterocyclic compounds, for example, herbal anti-microbicides, have remained used as triazine derivatives, anti-inflammatory agents and urine antiseptics. Other reports include several bio-activities, including antibacterial, antifungal, antiviral and anthelmintic, for instance, benzimidazole derivatives.[2]

Natural molecules comprising a strong Ś-lactam ring structure with a stereo-centre[3,4] Significant in chemistry and biology A significant function for C5 involves μ-lactam, many examples of the antibiotic family Oxazolum mycin many examples from shielding other antagonists, dysibetaine, lactacystine and salinosporeamide.[5,6]

Preventing or treating infections due to bacteria is by inhibiting or killing the bacterial growth, called antibacterial agents. The chemical composition of antibiotics consists of heterocyclic aromatic derivatives that form an essential part of them, such as the derivatives of γ-lactam. Several compounds have been synthesized and established on numerous kinds of bacteria by chemists.[7,8]

Cell damage is caused by free radicals produced by a chain reaction resulting from a chemical reaction called oxidative stress. Some new heterocyclic complexes of organo-nitrogen, organo-sulfur, and organo-selenium derived derivatives with 5-replaced 1,3,4-oxadiazole-2-thiols. The substances have significant antioxidant effects in applicable methodologies.[9]

Examination of drug candidates requires developing effective and simple artificial methods for synthesizing many γ-lactam derivatives in a direct and effective technique by stereo-selective to γ-lactam skeleton addition. However, the cyclization or cycloaddition of N-containing originators are common methods for γ-lactam synthesizing, which are stereo-selective synthesized, and there are restricted readings on stereo-selective additions to skeletons γ-lactam.[10-12]

EXPERIMENTAL:

Materials and Instrumentation

All chemicals and solvents were commercially obtained and used without distillation or purification. The ^{1}H-NMR spectra were recorded using a Bruker ultra shield spectrophotometer (300 MHz). The ^{13}C-NMR spectra were recorded using a Bruker

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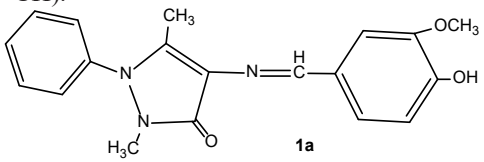
Ultra shield spectrophotometer (300 MHz). By using apparatus from Shimadzu company, FTIR γ-lactams was detected. The FTIR spectrum was obtained in the frequency range of 4000 to 400 cm^{-1}. The antimicrobial activities of compounds (2a-3d) were carried out by the disc diffusion method.

Synthesis of Schiff Bases

Preparation of Mono-imines

4-((4-hydroxy-3-methoxybenzylidene)amino)-2,5-dimethyl-1-Mono-imine 1a was prepared[9] by refluxing (0.005 mol, 0.7606 gm) of vanillin (0.005 mol, 1.0161 gm) of 4-amino antipyrine and 4 drops of glacial acetic acid in ethanol (25 mL). The reaction mixture was reflexed for 10 minutes in the microwave with stirring. TLC monitored the reaction development. The solvent was evaporated and the solid product was recrypted using ethanol until a continuous melting point was achieved after completion of the reaction. The physical data of mono-imine (1a) and the reactants are given in table 1. Yield = 86%, m.p. = 201°C. IR (KBr disk): 1622 cm^{-1}(C=N).

^{1}H-NMR [DMSO-d6,TMS]: δ (ppm) =2.26 ppm (s, 3H, CH3), 3.26 ppm (s, 3H, N -CH_3), 3.86 ppm (s, 3H, alphalic) for methyl (OCH3), 6.83 ppm (s, H, ArH) for the ring, 7.34 -7.56) ppm (7H, ArH) for the ring, 9. 13 ppm (s, 1H, CH=N imine), 9.73 ppm (s, 1H, O-H); ^{13}C-NMR [$CDCl_3$, δppm] :, 12.7(CH_3), 32. 06(N-CH_3), 56.28(OCH_3), 107.04 - 145.49(Aromatic C), 164.1(N=CH).

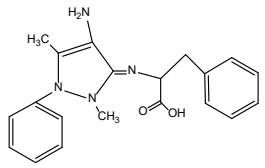


1a

(Z)-2-((4-amino-2,5-dimethyl-1-phenyl-1,2-dihydro-3H-pyrazol-3-ylidene)amino)-3-phenylpropanoic acid (1b)

Mono-imine 1b was prepared [7,13] by refluxing (0.005 mol, 1.0161 gm) of tyrosin, (0.005 mol, 1.0161 gm) of 4-amino antipyrine and 6 drops of glacial acetic acid in ethanol alcohol (20 mL). The mixture of reaction was reflexed for about 15 minutes in microwave 300 W. with stirring. TLC monitored the development of the reaction. Solvent evaporation and encryption of solid substance-using ethanol until a continuous melting point were achieved after completion of the reaction. Mono-imine (1b) and reactor physical details are given in Table 1. Yield =78%, m.p. = 198°C. IR (KBr disk): 1625 cm^{-1} (C=N).

^{1}H-NMR [DMSO-d6,TMS]: δ (ppm) =2.24 ppm (s, 3H, CH3), δ (ppm) =2.82 ppm (d, 1H, CH-COOH), 2.98 ppm (2H, CH2-Ar), 3.21 ppm (s, 3H, N -CH3, 6.83 ppm (s, H, ArH) for the ring, 7.14 -7.56) ppm (7H, ArH) for the ring, 4. 83 ppm (s, 2H, H2N amine), 12.83 ppm (s, 1H, COO-H); **^{13}C-NMR [$CDCl_3$, δppm]:** 8.3 (CH_3), 36.92 (CH), 68.55 (CH), 122.7-129.04(Aromatic C), 177.10 (COOH).



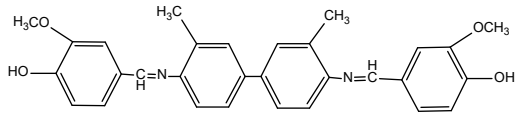
1b

Preparation of Bis-imines

4,4'-(((3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(azaneylylidene)) bis(methanelylid ene)) bis(2-methoxyphenol).[1c].

Vanillin (0.01 mol, 1.52 gm) and o-tolidine (0.005 mol, 1.061 gm) were dissolved in ethanol (40 mL) with five drops of glacial acetic acid.[7] The reaction mixture was reflexed for 10 min in microwave 300 W. TLC monitored the reaction development. The evaporation of the solvent was finished after the reaction ended. The solid product was filtered, washed several times with diethyl ether, dried in the vacuum oven at 80°C, and then recrystallized using ethanol until a constant melting point was obtained. The percentage yields and analytical dates of the title compounds are tabulated in table1. Yield = 89%, m.p. = 264°C. IR (KBr disk): 1619 cm^{-1} (C=N).

^{1}H-NMR [DMSO-d6,TMS]: δ (ppm) =2.2 ppm (s, 6H, CH_3), 3.75 ppm (s, 6H, alphalic) for methyl (OCH_3), 6.73 ppm (s, 2H, ArH) for the ring, 7.24 ppm (d, 2H, ArH) for the ring, 7.17 ppm (d, 2H, ArH) for the ring, 7.42 ppm(d, 2H, ArH) for the ring 7.73 (s, 2H, ArH) for the ring, 8. 75 ppm (s, 2H, CH=N imine), 9.67 ppm (s,2H,O-H); ^{13}C-NMR [$CDCl_3$, **δppm]:** 31.51(Ar-$\underline{C}H_3$) 56.2(O$\underline{C}H_3$), 117.64- 151.13(Aromatic C), 160.2(C=N imines).

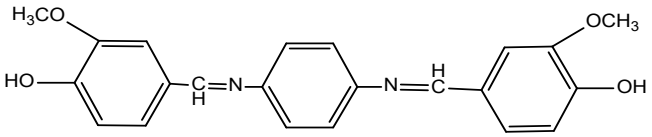


1c

4,4'-((1,4-phenylenebis(azaneylylidene))bis(methaneylylidene)) bis(2-methoxyphenol)[1d].

Bis-imine 1d was prepared by refluxing (0.04 mol, 6.08 gm) of vanillin, (0.02 mol, 1.62 gm) of 1,4-diamino benzene and 4 drops of phosphoric acid in ethanol (20 mL).[9] The reaction mixture was reflexed for 10 min in microwave 300W with stirring. TLC controlled the reaction production. Once the reaction was over, the solvent was drained and recrystallated with ethanol up to a steady melting point. The physical data of Bis-imine (1d) is given in Table 1. Yield =73%, m.p. = 198°C. IR (KBr disk): 1621 cm^{-1}(C=N).

^{1}H-NMR [DMSO-d6,TMS]: δ (ppm) = 3.85ppm (s, 6H, alphalic) for methyl (OCH_3), 6.83–7.73 (aromatic-H), 8.57 ppm (s, 2H, CH=N imine), 9.47 ppm (s,2H,O-H); ^{13}C-NMR [$CDCl_3$, **δppm]:** 58.2(OCH_3), 112.07–150.93 (Aromatic C), 161.02 (C=N imines).



1d

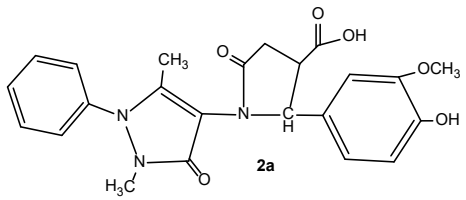
General Procedure of Mono and Bis Γ-Lactams (2a-3b]:

Preparation of mono γ-lactams [2a,2b,3a, and 3b]. In general, the mono γ-lactam [2a,2b,3a, and 3b]) were prepared.[8] by refluxing for 20 minutes in microwave 300W. 0.01 mol

of mono-imine [2a,2b,3a, and 3b] and 0.01 mol of phenylsuccinic anhydride or succinic Anhydride in 25 mL of dimethylformamide (DMF) with stirring. TLC monitored the development of the reaction. After the reaction was finished, the solution was evaporated and recrypted from a solution. Mono-gloomyrmeal (2a) and reactant physical evidence are given in Table 2.

1-(2,5-dimethyl-3-oxo-1-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-(4-hydroxy-3-methoxyphenyl)-5-oxopyrrolidine-3-carboxylic acid[2a]:

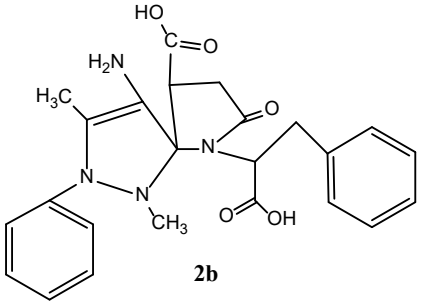
^{1}**H-NMR [DMSO-d6,TMS**]: δ (ppm) =2.27 ppm (s, 3H, CH_3), 3.06 ppm (s, 3H, N -CH_3), 3.71 ppm (s, 3H, alphalic) for methyl (OCH_3), 2. 67–2.97 ppm with J = 6 Hz, 6 Hz for one proton (dd, 1H, C4-H), 5.96 - 7.52 (m, Aromatic -H), 9. 52 ppm (OH), 11.31 ppm (s, 1H, COO-H)**;** ^{13}**C-NMR [CDCl$_3$, δppm]:** 35.64 (CH_2 -Pyrolidine), 172.55 (C =O pyrolidine), 101. 2-149. 72 (Aromatic C),172.3 (N-C=O), 178.15 (COOH).



2a

4-amino-6-(1-carboxy-2-phenylethyl)-1,3-dimethyl-7-oxo-2-phenyl-1,2,6-triazaspiro[4.4]non-3-ene-9-carboxylic acid.[2b].

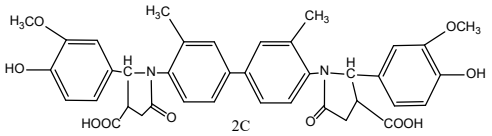
^{1}**H-NMR [DMSO-d^{6},TMS]:** δ (ppm) =2.21ppm (s, 3H, CH_3), δ (ppm) =3.17 ppm (d, 1H, CH-COOH), 2.74 ppm and 2.56 (2H, CH, pyrolidine), 2.71 ppm (s, 3H, N -CH3),), 7.15 - 7.58 (m, 10H,Aromatic), 6. 87 ppm (s, 2H, H_2N amine), 12.13 ppm (s, 1H, COO-H), 12.91 ppm (s, 1H, COO-H) ; ^{13}**C-NMR [CDCl$_3$, δppm]:** 31.36 (CH), 36.15 (CH), 124.52-131.1 (Aromatic C), 171.03(COOH) and 176.1(COOH).



2b

1,1'-(3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(2-(4-hydroxy-3-methoxyphenyl)-5-oxopyrrolidine-3-carboxylic acid)[2c].

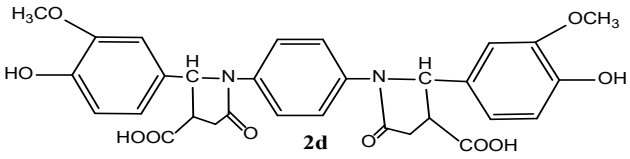
^{1}**H-NMR [DMSO-d^{6},TMS]:** δ (ppm) =2.17ppm (s, 6H, CH_3), 3.61ppm (s, 6H, alphalic) for methyl (OCH_3), 6.83 ppm (s, 2H, ArH) for the ring, 7.24 ppm (d, 2H, ArH) for the ring, 7.19ppm (d, 2H, ArH) for the ring, 7.42 ppm(d, 2H, ArH) for the ring 7.83 (s, 2H, ArH) for the ring, 5. 365 ppm (s, 2H, CH-N), 2.81 (d, 1H, CH_2),2.94 (d, 1H, C4-H), 3.31, (d, 1H, CH pyrolidine), 10.03 ppm (s,2H,O-H) 10.93 ppm (s,2H,COO-H); ^{13}**C-NMR [CDCl$_3$, δppm]:** 18.31(Ar-CH_3) 56.2(OCH_3), 110.94-150.2(Aromatic C), 179.26 (COO-H).



2C

1,1'-(1,4-phenylene)bis(2-(4-hydroxy-3-methoxyphenyl)-5-oxopyrrolidine-3-carboxylic acid)[2d].

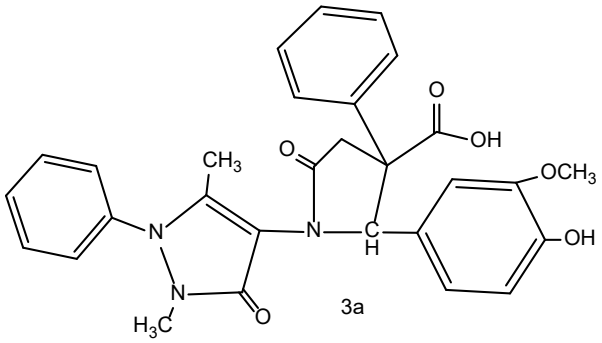
^{1}**H-NMR [DMSO-d6,TMS]:** 3.91ppm (s, 6H, alphalic) for methyl (OCH_3), 6.43-6.87 (m, 10H, ArH) for the ring, 5.9 ppm (s, 2H, CH-N), 2.88 (d, 1H, CH2),3.14 (d, 1H, C4-H), 3.37, (d, 1H, CH pyrolidine), 9.73 ppm (s,2H,O-H) 10.52 ppm (s,2H,COO-H); ^{13}**C-NMR [CDCl$_3$, δppm]:** 54.1(OCH_3), 111.04- 146.2(Aromatic C), 178.03 (COO-H).



2d

1-(2,5-dimethyl-3-oxo-1-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-2-(4-hydroxy-3-methoxyphenyl)-5-oxo-3-phenylpyrrolidine-3-carboxylic acid.[3a]:

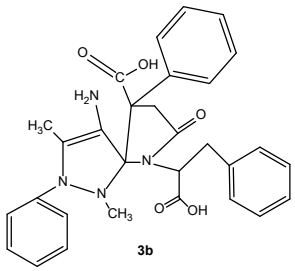
^{1}**H-NMR [DMSO-d^{6},TMS]:** δ (ppm) =2.27ppm (s, 3H, CH3), 3.05ppm (s, 3H, N -CH3), 3.77ppm (s, 3H, alphalic) for methyl (OCH3), 3. 07 (d, J= 9Hz, 1H, CH2),3.24 (d, J= 9Hz, 1H, C4-H), 5.71 (s, 1H, CH-N), 6.85 - 7.12 (m, ^{13}H,Aromatic), 9. 91 ppm (OH), 12.36 ppm (s, 1H, COO-H); ^{13}**C-NMR [CDCl$_3$, δppm]:** 46.5 (CH2 -Pyrolidine), 53.07 (C-Pyrolidine), 171.3 (C =O pyrolidine), 111. 82 – 146 02 (Aromatic C),162.71 (N-C=O), 177.85 (COOH).



3a

4-amino-6-(1-carboxy-2-phenylethyl)-1,3-dimethyl-7-oxo-2,9-diphenyl-1,2,6-triazaspiro[4.4]non-3-ene-9-carboxylic acid.[3b].

^{1}**H-NMR [DMSO-d^{6},TMS]:** δ (ppm) =2. 21ppm (s, 3H, CH_3), 2.58ppm (s, 3H, N -CH_3), 2. 98 (d, J= 9Hz, 1H, CH_2),3.04 (d, J= 9Hz, 1H, C4-H), 3.41, (d, J= 9Hz, 2H, CH2), 7.14 - 7.57 (m, 15H,Aromatic), 12.76 ppm (s, 1H, COO-H), 12.93 ppm (s, 1H, COO-H)**;** ^{13}**C-NMR [CDCl$_3$, δppm]:** 44.53 (C -Pyrolidine), 50.01 (C-Pyrolidine), 174.3 (C =O pyrolidine), 127. 42–136.75 (Aromatic C),172.71 (COO-H), 178.04 (COOH).

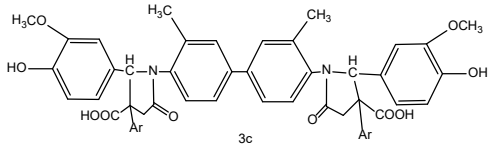


3b

Preparation of Bis γ-lactams (2c,3c,2d, and 3d). In general, the β-lactam (2c,3c,2d, and 3d) is prepared by 20 mL DMF for 20 minutes in the microwave at 300 W with stirring. TLC accompanied the success of the reactions with refluxation of 0.01 mol bis-imine and 0.02 mol phenyl succinic anhydride/ setinic anhydride. Once the reaction has been finished. A good solvent recrystalled the solid component. Bis α-lactam (2c) External evidence and the reactants are given Table 1.

1,1'-(3,3'-dimethyl-[1,1'-biphenyl]-4,4'-diyl)bis(2-(4-hydroxy-3-methoxyphenyl)-5-oxo-3-phenylpyrrolidine-3-carboxylic acid)[3c].

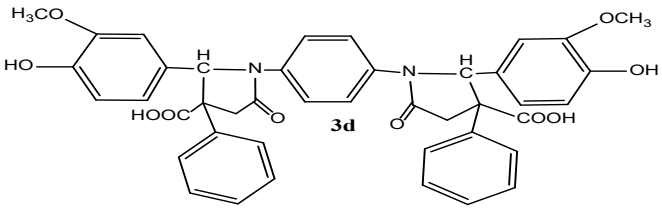
^{1}H-NMR [DMSO-d6,TMS]: δ (ppm) =2.07ppm (s, 6H, CH_3), 3.71ppm (s, 6H, alphalic) for methyl (OCH_3), 6.82-7.83 (m, 12H, ArH) for the ring, 5. 75 ppm (s, 2H, CH-N), 2.91 (d, 1H, CH_2), 3.04 (d, 1H, C4-H),, 9.93 ppm (s,2H,O-H) 11.83 ppm (s,2H,COO-H); **^{13}C-NMR [$CDCl_3$, δppm]:** 19.01(Ar-CH_3) 55.12(OCH3), 115.34- 147.2(Aromatic C), 177.37 (COO-H).



3c

1,1'-(1,4-phenylene)bis(2-(4-hydroxy-3-methoxyphenyl)-5-oxo-3-phenylpyrrolidine -3-carboxylic acid)[3d].

^{1}H-NMR [DMSO-d^6,TMS]: 3.71ppm (s, 6H, alphalic) for methyl (OCH_3), 6.73-7.36 (m, 20H, ArH) for the ring, 5.63 ppm (s, 2H, CH-N), 2.72 (d, 1H, CH_2),2.94 (d, 1H, C4-H),, 9.94 ppm (s, 2H, O-H) 11.32 ppm (s, 2H,COO-H); **^{13}C-NMR [$CDCl_3$, δppm]:** 56.71(OCH_3), 118.34- 151.1(Aromatic C), 176.63 (COO-H).



3d

Antibacterial Activity Test:

The antibacterial studies of all γ-lactam compounds were assayed using three types of bacterial: S*taphylococcus aureus coli and Salmonella typhi*. by Technique of Disc Diffusion were isolated.[14] Using a sterilized swab, the suspension of microorganisms was wiped on Petri dishes containing solidified nutrient agar. Three different concentrations (0.1M, 0.001 M, 0.00001 M) Preparation and positioning on the culture media until incubation by a disk of DMSO research compounds at 37°C for 24 hours, and by measuring the distance of the zone viewing complete inhibition.

Antioxidant Activity Test

According to the method described by Lu *et al.,* 2013[15], who studied the activity of free radical scavenging of the lactam against radicals of samples compound 2,2-diphenyl-1-picrylhydrazyl (DPPH). About (1mg/mL) of test compounds of stock solution were diluted to 500 and 100 µg/mL as a final concentration.[25] The sample fluid was applied to a minimum of 50µM DPPH methanolic fluid 3.8 mL (0.1 mL each) and allowed 30 minutes in darkness at room temperature. Absorption in 517 nm has been calculated and antioxidants can be obtained. Inhibition of DPPH radical (1%) was calculated using the relation.

$$\text{DPPH radical seavenging activity (\%)} \frac{\text{Abs}_{\text{control - Abs}_{\text{sample}}}}{\text{Abs}_{\text{control}}} \times 100$$

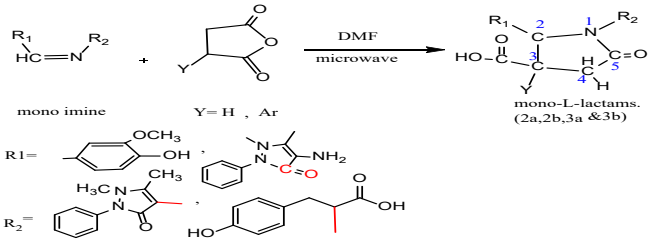
Where: Abs control - Absorbance of DPPH radical + methanol: DMSO(80:20).

"Abs sample - Absorbance of DPPH radical + sample[test samples /standard]".

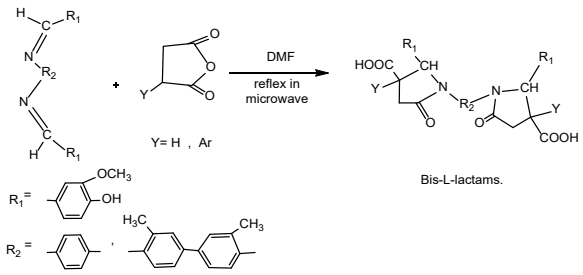
Ascorbic acid as (antioxidant standardization) were the values obtained are compared.[16]

RESULTS AND DISCUSSION

Among natural products, The γ-Lactams compounds are wildly established. After the reactions of Schiff bases with phenyl succinic anhydride or succinic anhydride, important lactams are obtained to give pure γ-lactams. The treatment of the mono or di imines (Schiff bases 1a-1c) with phenyl succinic Anhydride and succinic Anhydride in DMF to afford γ-lactams (2a-3d)afford and this considered the main mono and bis γ-lactams(2a-3d) synthesis as shown in Schemes I and II.



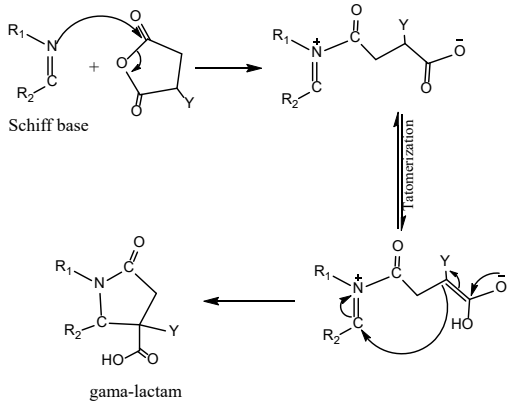
Scheme I: Synthesis of Mono- γ -Lactams



Scheme II: Synthesis of Bis- γ -Lactams

The mechanism[17,18] of formation of γ-lactams (**Scheme III**) involve form cyclo anhydride; a zwitterionic enolate was

formed. The enolate is favoured to form delocalization of negative charge to be formed by the suitably positioned aromatic ring. The formation of the lactam rings by the enolate zwitterions.



Scheme III: Mechanism of formation of γ -Lactams

on the basis «fourier transform infrared spectroscopy (FTIR), ^{1}H-NMR «, and ^{13}C-NMR spectral data, the established structures of γ-lactams of both mono and bicyclic.

Isolated compounds are readily soluble coloured powder in chloroform, DMSO and DMF. all the compounds before dissolution are decomposed, and this indicated by melting points. The analytical data Table 1 indicate that all γ-lactams. There is a good agreement between the primary evidence of Schiff base and its γ-lactams with the calculated results from the empirical formula for each compound.

Spectroscopic Study FTIR Spectrum

The Schiff bases (1a-1d) by the FT-IR spectrum, in KBr disc, showed absorption bond at 1612–1625 cm^{-1} equivalent to the imine compounds of azomethine(CH=N) group (Figure 1). The γ-lactams (2a-3d) by FT-IR spectrum have the vibrating stretching characteristic of the aliphatic(C-H), aromatic (C-H), carboxylic carbonyl group, aromatic (C=C) and (C-N)"bands and replaced ring within ranges occurs. The analytical data Table 2 indicate that all Schiff bases and γ-lactams.

^{1}H-NMR Spectral Analysis

Tthe γ-lactams of ^{1}H-NMR are presented in Figure 2, the spectrum of ^{1}H-NMR spectra (2a) inpyrrolidine-2-one at dual signal of one ring at δ (2.57 ppm) with (J= 6 Hz) for proton a (1H,C_4-H), signal at δ (3.14ppm) with (J= 6 Hz) for proton b (1H, C_4-H) and signal at δ (3.84 ppm) with (J= 6 Hz) for proton (1H, C_2-H)". The chemical shift of the signal protons of the synthesized compounds (1a-3d) showed in the experimental part.[21]

^{13}C-NMR Spectral Analysis

The spectrum ^{13}C-NMR of 2b, are shown in pyrrolidine-2-one ring diagonal sign at δ 29.27 ppm of one carbon (C_4-H **)" F**igure 3.

Table 1: Chemical and physical characterizations data for Schiff bases and γ-lactams[19]

Comp.	*Empirical*	*M. Wt.*	*Color*	*(%) Yield*	*%(Found) Calc.* C	H	N	*Mp. °C*
1a	$C_{19}H_{19}N_3O_3$	337.38	yellow	86	(67.53) 67.64	(5.60) 5.68	(12.39) 12.46	201
1b	$C_{20}H_{22}N_4O2$	350.4	white	78	(67.89) 68.55	(6.36) 6.33	(15.05) 5.99	198
2a	$C_{23}H_{23}N_3O_6$	437.4	yellow	89	(63.23) 63.15	(5.21) 5.30	(9.54) 9.61	231
3a	$C_{29}H_{27}N_3O_6$	513.5	white	73	(66.12) 67.83	(4.89) 5.30	(7.98) 8.18	223
2b	$C_{24}H_{26}N_4O_5$	450.5	white	68	(63.78) 63.99	(5.02) 5.82	(12.76)12.44	191.7
3b	$C_{30}H_{30}N_4O_5$	526.5	white	62	(68.54) 68.43	(5.91) 5.74	(10.09) 10.64	187.3
1c	$C_{30}H_{28}N_2O_4$	480.56	green	90	(74.71) 74.98	(5.83) 5.87	(5.82) 5.83	185
1d	$C_{22}H_{20}N_2O_4$	376.41	brown	89	(69.43) 70.20	(5.01) 5.36	(7.31) 7.44	187
2c	$C_{38}H_{36}N_2O_{10}$	680.7	green	78	(67.04) 67.05	(5.21) 5.33	(3.96) 4.12	189.5
3c	$C_{50}H_{44}N_2O_{10}$	832.9	Dark brown	83	(71.87) 72.10	(5.34) 5.32	(3.17) 3.36	195.1
2d	$C_{30}H_{28}N_2O_{10}$	576.56	brown	65	(62.28) 62.50	(4.83) 4.90	(4.78) 4.86	193.2
3d	$C_{42}H_{36}N_2O_{10}$	728.75	brown	75	(70.1) 69.22	(5.02) 4.98	(3.90) 3.84	197

Diagonal signal at δ64.33 ppm is for one-carbon (C2-H) can be seen in the spectrum in Figure 4. "The ^{13}C-NMR of the 2b displays sign of aromatic carbons at δ 120.46, 120.47, 127.16, 127.11, 127.53, 127.70, 128.53, 128.58, 138.03, 138.17, 138.97 and 139.34ppm".[22] The spectrum can be seen in Figure 5.

The spectrum (Figure 6) shows a diagonal sign of the COOH group at δ 171.03 ppm, and another diagonal sign of the" amide carbonyl group carbon at 176.1 ppm". The diagonal sign of the amide carbonyl group carbon at 174.12 ppm (equivalent carbon).

Compound 2,2-diphenyl-1-picrylhydrazyl (DPPH) Method for Antioxidant Activity

The activity of antioxidant of γ-lactams compounds (2a-2d) is determined by using a free radical "2,2-diphenyl-1-

Table 2: FTIR data of Schiff bases and γ-lactams[13,20]

Comp.	*C-H aromatic*	*C-H alphatic*	*C=C*	*C=N*	*COOH*
1a	3110	2835	1463	1622	–
1b	3274	2912	1416–1463	1625	1730(C=O)
1c	3073	2981	1584	1619	–
1d	3005	2983	1516	1612	–
2a	3150	2832	1578	–	1603.5(-N-C=O),1740 (HO-C=O)
3a	3210	2843	1522	–	1724 (-N-C=O), 1791 (HO- C=O)
2b	3274	2933	1590–1464	–	1676 (-N-C=O),1724 (HO-C=O)
3b	3137	2886	1584–1487	–	1683 (N-C=O),1725 (HO-C=O)
2c	3134	2290,2792	1561	–	1681 (-N–C=O),1715 (HO–C=O)
3c	3129	2843	1494	–	1690 (–N–C=O), 1705 (HO–C=O)
2d	3201	2912	1504	–	1676.7 (–N-C=O),1715 (HO-C=O)
3d	3190	2941	1487	–	1680.5(–N–C=O), 1731 (HO–C=O)

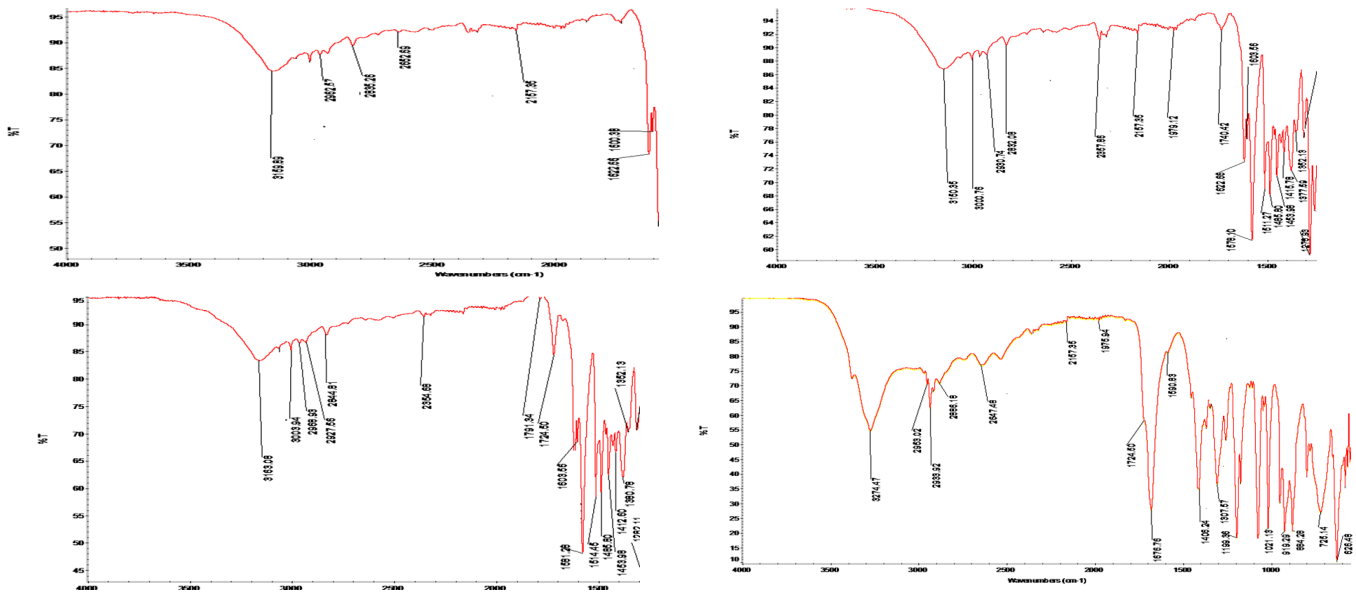


Figure 1: FTIR spectra of compounds 1a,2a 3a and 2d.

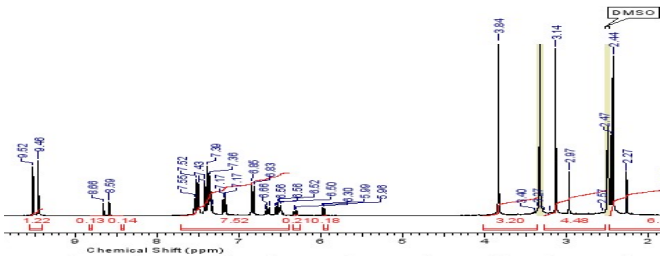


Figure 2: Selected ^{1}H NMR signals of 2a

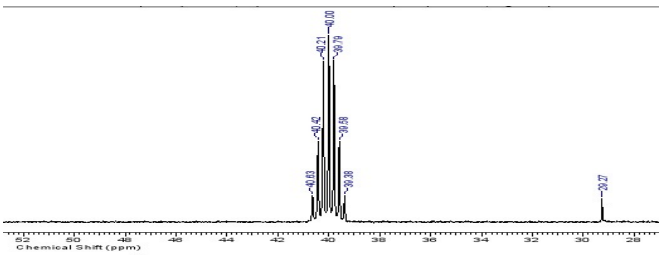


Figure 3: Pyrrolidine-2-one ring ^{13}CNMR signals of the 2b

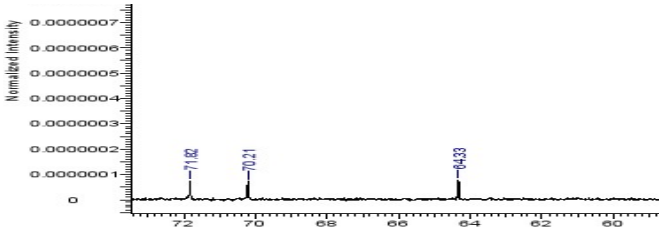


Figure 4: C2-H type ^{13}C –N MR signals of the 2b

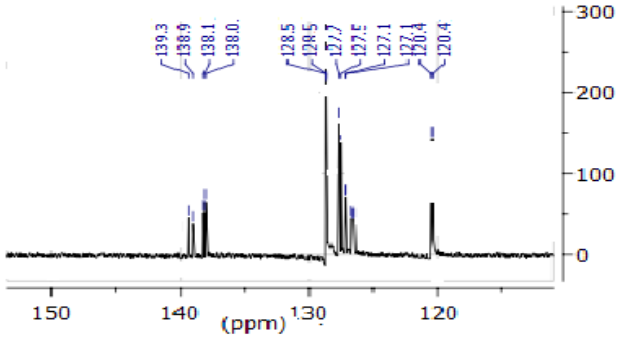


Figure 5: Aromatic ^{13}C-NMR signals of the 2b.

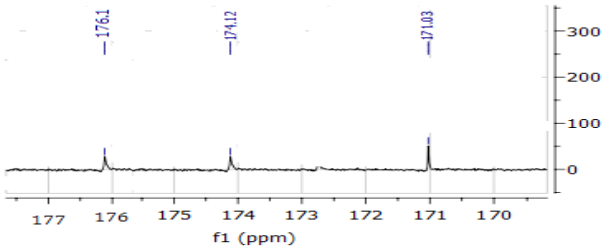


Figure 6: Selected ^{13}C -NMR signals of 2b.

Table 3: Power antioxidant activity of γ-lactams compounds against ascorbic acid at concentration 500 µg/mL and 100 µg/mL.

Sample	*500 µg/mL*	*100 µg/mL*
2a	91.56	15
3a	88.93	76.93
2b	-	-
3b	-	-
2c	86	40.23
3c	93	19.76
2d	77.14	19.01

pycrylhydrazyl (DPPH)".[23] This technique was based on the loss of DPPHradical violet color after reaction with samples(2a-2d). The activities of antioxidants of the synthesized samples (2a-3d) be present in Table 3 and Figure 5. The following points have been noticed:

1. The results revealed that all γ-lactams compounds except 2b and 3b were found to be potent in concentration 500 µg/mL.
2. The compounds 3a and 2c (100 µg/mL) were found to be a moderate activity (RPAA).
3. Compounds 2a, 3c and 2d (100 µg/mL) were found to be weak, reducing power antioxidant activity (RPAA).

Table 4: Antimicrobial activities of γ-lactams.

	staphylococcus aureus			*Escherichia coli*		
	Conc.			*Conc.*		
Comp.	1×10^{-1} *M*	1×10^{-3} *M*	1×10^{-5} *M*	1×10^{-1} *M*	1×10^{-3} *M*	1×10^{-5} *M*
2a	-	-	12	12	19	23
3a	-	-	18	15	20	18
2b	27	20	18	15	10	19
3b	30	23	21	19	15	20
2c	10	15	20	15	13	10
3c	30	25	27	15	20	18
2d	10	21	-	-	31	45
3d	34	42	39	23	39	41

4. The 2b and 3b compounds don't have reducing power antioxidant activity (RPAA).

Antibacterial Activity

The prepared γ-lactams were studied for their biological activity against two different types of bacteria (*S. aureus* and *E.coli)* at the concentrations of [1 × 10^{-5}, 1 × 10^{-3}, 1 × 10^{-1}] M and compared with original γ-lactams the inhibitory effect to same bacteria (Table 4).[24,25] The inhibitory effect of the prepared di γ-lactams was significantly higher than their original Schiff bases when they had been tested on the two types of bacteria. E.coli bacteria illustrated the most responsibility at the Schiff bases and its γ-lactams were tested in the plantation of this bacteria.

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