Synthesis and Characterization of New Compounds Derived from Pyrrolidine-2-One and Evaluation of their Biological Activities

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Abstract
New derivatives of pyrrolidine-2-one have been prepared by lactamization of γ-butyrolactone GBL with hydrazine hydrate (NH2NH2 (80%)) to afford (1-aminopyrrolidin-2-one) which undergo many reactions to prepare the other derivatives. The prepared derivatives were determined by utilizing their FT-IR, 1H-NMR and some by Mass spectrum. These derivatives were evaluated biologically against (Staphylococcus aureus and E. coli). Some of these derivatives exhibited good biological activity against one or both kind of bacteria while some exhibited no biological activity at all.

Keywords:
Lactamization
Pyrrolidine-2-one
Biological activity

1. Introduction
2-Pyrrolidinones are lactams of 5-membered ring with biological interest. Pyrrolidine-2-one is the simplest 2-pyrrolidinones, see Figure 1; it is a colorless liquid that show miscibility with water and most organic solvents [1]. Pyrrole referred to pyrrolidine-2-one in natural products [2]. When γ-butylactone (GBL) treated with NH3, pyrrolidine-2-one would produce and this process is used to prepare it industrially which is a straight process because reactants may not be pre-functionalized. However process needs harsh pressure or high temperature [3]. Pyrrolidine-2-one is an important component in several active natural products and pharmaceuticals [4]. Cotinine, an alkaloid found in tobacco considered to be biochemically important 2-pyrrolidinones which is the predominant metabolite of nicotine [5]. N-Substituted Pyrrolidine-2-one can be rapidly synthesized by condensation of GBL with primary amines that stand up to the temperatures range (200-300 °C) which is necessary to eliminate water molecule and cyclize the hydroxyl butyl amide intermediate. A wide range of amines can be utilized [6]. Pyrrolidine-2-one could be the monomers of various synthetic polymers, like poly (1-vinylpyrrolidin-2-one) derivatives [7].

Figure 1. Structure of pyrrolidine-2-one.

2. Experimental Parts
2.1 Instruments
Melting points were recorded and left uncorrected in open capillary tubes using Gallenkamp melting point apparatus. FT-IR spectrum was determined using a Perkin-Elmer 1600 series FT-IR spectrometer. 1H-NMR spectrum of synthesized derivatives was determined using CDCl3 as solvent and the other using DMSO with TMS as internal standard utilizing Varian-Mercury 300 MH Spectrometer. Peak at 7.2 ppm that belong to CDCl3 and the peaks at 2.5 and 3.3 ppm that belong to DMSO and water impurities respectively may appear in these spectra. Mass spectra determined using (SHIMADZU model QP 1000EX using (SCI) mode

2.2 Synthesis
Synthesis of 1-aminopyrrolidin-2-one (N1) [8]: (0.01 mol) of hydrazine hydrate (80%) was mixed with (0.01 mol.) of GBL and heated to 220 °C for (24 hrs.) in an oil bath under reflux. Afterwards a white precipitate was obtained and washed with petroleum ether and acetone and then recrystallized from absolute C2H5OH. Yield (68%), color (white), m.p. (85-87 °C), M.Wt. (100), FT-IR ν (cm⁻¹): (3294, 3203) attribute to sym. and asym. stretching vibration of (–NH2), (2964, 2877) attribute to (CH aliph.), (1703) attribute to stretching vibration of (C=O) of lactam ring, 1635 attribute to bending vibration of (NH), 1H-NMR spectrum (ppm), (1.03) (m, 2H, CH aliph.) far from carbonyl and nitrogen of lactam ring, (1.52) (t, 2H, CH aliph.) near nitrogen atom of lactam ring, (2.50) (t, 2H, CH aliph.) near carbonyl group of lactam
ring. (2.16) (s, 2H, NH₂), Mass, the molecular ion peak (M+, m/z) = 100.

Synthesis of dimethyl (2-oxyopyrrolidin-1-yl) carbonodithioimidate (N₉) [9]: (5ml) of 20 M–NaOH, (0.02 mol.) of Cs₂ and (0.01 mol.) of CH₃I were added to stirred cold solution of (0.01 mol.) of compound (N₁) in (25 ml) DMF. The stirring was continued for (4 hrs.). The mixture was poured onto cold water and the obtained solid recrystallized from benzene. Yield (54%), color (dark yellow), m.p. (108-110 °C), M.Wt. (204), FT-IR ν (cm⁻¹): (2862) belong to (CH aliph.), (1678, 1660) belong to stretching vibration of (C=O) of lactam and of (C=N) respectively. ¹H-NMR spectrum (ppm), (1.10) (m, 2H, CH₂ aliph.), (1.55) (t, 4H, 2CH₂ aliph.), (2.50) (s, 6H, 2CH₃ aliph.).

Synthesis of 2,6,7,8-tetrahydropyrrolo[1,2-b] [1,2,4,5] tetrazine-3(4H)-thione (N₅) [10]: (0.01 mol.) of compound (N₁) was added to a solution of (0.01 mol.) KOH in C₂H₅OH at (0 °C) then (0.01 mol.) of CS₂ was gradually add to this solution with stirring for an hour and then add (0.1 mol.) of 99% hydrazine and stirring continued for another hour with raising temperature to (45 °C-55 °C). The obtained solid filtered and washed with water and recrystallized from C₂H₅OH. Yield (70%), color (white), m.p. (172-174 °C), M.Wt. (156), FT-IR ν (cm⁻¹): (3549, 3408) belong to stretching vibration of (−NH) of six membered ring, (2918, 2852) belong to stretching vibration of (CH aliph.), (1610) belong to stretching vibration of (C=N), ¹H-NMR spectrum (ppm), (1.60) (m, 2H, CH₂ aliph.), (2.09) (t, 4H, 2CH₂ aliph.) singlet at (8.42) due to (−NH) bonded to (C=S).

Synthesis of compound 2-chloro-N (2-oxyopyrrolidene-1-yl) (N₈) [11]: (0.01 mol.) of CICH₂COCI was added drop wise to (20 ml) of benzene (C₆H₆) containing (0.01 mol.) of compound (N₁), the solution was refluxed for (4 hrs.). Afterwards, the reaction mixture was cooled to room temperature and solvent evaporated under reduced pressure, the formed precipitate was filtered off and recrystallized from C₂H₅OH, yield (73%), color (creamy white), m.p. (128-130 °C), M.Wt. (176), FT-IR ν (cm⁻¹), (3344) attribute to stretching vibration of (−NH), (2931, 2833) attribute to stretching vibration of (CH aliph.), (1693) attribute to stretching vibration of (C=O) of lactam ring, (1678) attribute to stretching vibration of (C=O) of amide group. ¹H-NMR spectrum (ppm) (2.11) (m, 2H, CH₂ aliph.), (2.65) (t, 2H, CH₂ aliph.), (3.32) (s, 2H, CH₂ aliph.), (4.44) (s, 2H, CH₂ between NHCO and chloride atom), (5.69) (s, 1H, NHCO).

Synthesis of 2-amino-3-(2-oxyopyrrolidin-1-yl)-1, 3-thiazolidin-4-one (N₉) [12]: Solution of (0.01 mol.) of compound (N₁) and (0.01 mol.) of NH₄SCN in (25 ml) C₂H₅OH was refluxed for (15-16 hrs.). The solution was cooled and poured onto crushed ice with continuous stirring. The obtained solid washed with cold water, dried and recrystallized from CH₃OH. Yield (83%), color(light yellow), m.p. (332-334 °C), M.Wt. (199), FT-IR ν (cm⁻¹), (3346) belong to stretching vibration of (−NH), (2926, 2854) belong to stretching vibration of (CH aliph.), (1699, 1674) attribute to stretching vibration of two carbonyl groups (C=O) of lactam rings, (1575) belong to stretching vibration of (C=N), ¹H-NMR spectrum (ppm) (1.62) (m, 2H, CH₂ aliph.), (2.14) (t, 2H, CH₂ aliph.), (2.67) (t, 2H, CH₂ aliph.), (5.69) (s, 1H, NH) and (3.40) (s, 2H, CH₂ aliph.) next to carbonyl group of lactam ring containing sulfur atom.

Synthesis of 1-{(2-amino-1, 3-thiazol-4-yl) amino} pyrroloidin-2-one (N₈) [13]: A mixture of (0.01 mol.) of compound (N₁) with (0.01 mol.) of NH₂CSNH₂ in (20 ml) of absolute C₂H₅OH were refluxed for (12 hrs.), afterwards the mixture was cooled and then poured onto ice /water mixture. The formed precipitate was filtered, washed with 2% NaHCO₃ solution and then with H₂O, and recrystallized from absolute C₂H₅OH. Yield (63%), color (yellowish white), m.p. (194-196 °C), M.Wt. (198), FT-IR ν (cm⁻¹), (3396, 3358) and (3265) due to stretching vibration of (−NH₂) and (−NH), (1699) due to stretching vibration of (C=O) of lactam ring. Mass, the molecular ion peak (M+, m/z) = 198.

General synthesis of compounds (N₅-N₉) [14]: (0.01 mol.) of compound (N₁) with (0.01 mol.) of phthalic anhydride or maleic anhydride / (0.01 mol.) of compound (N₈) with (0.01 mol.) of phthalic anhydride in (15 ml) of (gla. CH₃COOH) were refluxed for (3 hrs.). Afterwards (25 ml) of cold water has been added to the reaction mixture and the formed precipitate was dried and recrystallized from absolute C₂H₅OH.

2-(2-oxyopyrrolidin-1-yl)-1H-isioindole-1,3(2H)-dione (N₉): yield (69%), color (white), m.p. (310-312 °C), M.Wt.(230), FT-IR ν (cm⁻¹), (3034, 3014) due to stretching vibration of (CH arom.), (2953) due to stretching vibration of (CH aliph.), (1739) belong to stretching vibration of two carbonyl groups of imide ring, (1718) belong to stretching vibration of (C=O) of lactam ring, (1600) belong to stretching vibration of (C=C arorn.), ¹H-NMR spectrum (ppm) (0.89) (m, 2H, CH₂ aliph.), (1.27) (t, 2H, CH₂ aliph.), (1.64) (t, 2H, CH₂), (7.88-8.25) (m, aromatic protons).

1-(2-oxyopyrrolidin-1-yl)-1H-pyrrol-2,5-dione(N₉): yield (81%), color (light yellow), m.p. (237-239 °C), M.Wt. (180), FT-IR ν (cm⁻¹), (2937, 2879) belong to stretching vibration of (CH aliph.), (1739) belong to stretching vibration of two carbonyl groups of (C=O) of imide ring, (1714) belong to stretching vibration of (C=O) of lactam ring, (1651) belong to stretching vibration of (C=C arorn.), ¹H-NMR spectrum (ppm) (1.64) (m, 2H, CH₂ aliph.), (2.14) (t, 4H, 2CH₂ aliph.), (4.44) (d, 2 vinyl protons).

2-[(2-oxyopyrrolidin-1-yl)amino]-1,3-thiazole-2-yl]-1H-isioindole-1,3(2H)-dione (N₉): yield (73%), color (creamy), m.p. (304-306 °C), M.Wt. (328) FT-IR ν (cm⁻¹), (3263) due to stretching vibration of (−NH), (2993) due to (CH aliph.), (1716) due to stretching vibration of two carbonyl groups (C=O) of imide ring, (1662) due to
stretching vibration of (C=O) of lactam ring, (1539) due to stretching vibration of (C=N), \(^1\)H-NMR spectrum (ppm), (0.63) (m, 2H, CH\(_2\) aliph.), (1.24) (m, 4H, CH\(_2\) aliph.), (7.31-7.68) (m, aromatic protons and 1H (~NH) of thiazol ring).

**General synthesis of compounds (N\(_{10}\), N\(_{11}\)) [15]:** (0.01 mol) of aromatic aldehydes (p-chloro benzaldehyde or p-nitro benzaldehyde) was added to a solution of (0.01 mol) of compound (N\(_{1}\)) in (20 ml) absolute C\(_2\)H\(_2\)OH in presence of (4 drops) of glacial CH\(_3\)COOH. The mixture was refluxed for (3-6 hrs.). Afterwards, the mixture was cooled, filtered and the obtained solid recrystallized from C\(_2\)H\(_2\)OH to afford the wanted compounds.

1-[(2-[[4-(chlorophenyl)methylidene] amino]-3-thiazol-4-yl) amino] pyrrolidin-2-one (N\(_{10}\)): yield (79%), color (yellow), m.p. (188-190 °C), M.Wt. (317) \(^1\)H-NMR ν (cm\(^{-1}\)), (3033) due to stretching vibration of (CH arom.), (2953, 2852) due to stretching vibration of (CH aliph.), (1683) due to stretching vibration of (C=O) of lactam ring, (1668) belong to stretching vibration of (C-N).

1-[(2-[[4-(nitrophenyl)methylidene] amino]-3-thiazol-4-yl) amino] pyrrolidin-2-one (N\(_{11}\)): yield (72%), color (yellow), m.p. (219-221 °C), M.Wt. (331), \(^1\)H-NMR ν (cm\(^{-1}\)), (3043) due to stretching vibration of (CH arom.) (2922, 2852) due to stretching vibration of (CH aliph.), (1693) due to stretching vibration of (C=O) of lactam ring, (1666) due to stretching vibration of (N=O), \(^1\)H-NMR spectrum (ppm) (0.85) (m, 2H, CH\(_2\) aliph.), (1.34) (t, 4H, 2CH\(_2\) aliph.), (6.73), (7.71) (d, d, Para sub. Benzene), (7.49) (s, proton of thiazole ring), (7.52) (s, 1H, NH), (8.75) (s, 1H, (N=CH)).

**Synthesis of 1-naphthalen-1-yl-3-(2-oxopyrrolidin-1-yl) urea (N\(_{12}\)) [16]:** (0.01 mol) of naphthyl isocyanate was added to a solution of (0.01 mol) of compound (N\(_{1}\)) dissolved in (20 ml) DMF and then refluxed for (7 hrs.). A precipitate then formed immediately when (20 ml) of diethyl ether was added to the solution, a mixture of ethanol: water (1:1) was used for recrystallization. Yield (80%), color (light pink), m. p. (132-134 °C), M.Wt. (269), \(^1\)H-NMR ν (cm\(^{-1}\)), (3282, 3203) due to stretching vibration of (N=O) of lactam ring and (1701,1651) due to stretching vibration of (CH) aromatic, (2955, 2879) due to stretching vibration of (C=O) groups of lactam ring and (1615) due to stretching vibration of (NH) of (NH=C=O=NH), (3037) due to stretching vibration of (CH) aromatic, (2955, 2879) due to stretching vibration of (C=O) groups of lactam ring and (NH=ONH) respectively, \(^1\)H-NMR spectrum (ppm), (0.87) (m, 2H, CH\(_2\) aliph.), 1.78 (t, 4H, 2CH\(_2\) aliph.), 7.47-7.64 (m, aromatic protons and protons of (NCHCONH)).

**Synthesis of compound 1-(2-oxopyrrolidin-1-yl)-3-phenylthiourea (N\(_{13}\)) [17]:** to a solution of (0.01 mol) of compound (N\(_{1}\)) in (25 ml) of DMF, (0.01 mol) of Phenyliothiocyanate was added and refluxed for (10-12 hrs.). The solution was poured onto ice/water mixture. The obtained precipitate was filtered and recrystallized from C\(_2\)H\(_2\)OH:H\(_2\)O mixture (10:1), yield (68%), color (light brown), m.p. (150-152 °C), M.Wt. (235), \(^1\)H-NMR ν (cm\(^{-1}\)): (3371, 3203) due to stretching vibration of (NH) of (NH=C=S~NH), (3043) due to stretching vibration of (CH) aromatic, (2965, 2875) due to stretching vibration of (CH) aliph., (1693) due to stretching vibration of (C=O) of lactam ring, (1338) due to stretching vibration of (C=S), \(^1\)H-NMR spectrum (ppm) (1.56) (m, 6H, CH\(_2\) aliph.), 7.88-8.23 (m, aromatic protons), (8.49, 9.16) (s, 2H, NH=SNH).

**General synthesis of compounds (N\(_{14}\), N\(_{15}\)) [18]:** (0.01 mol) of compound (N\(_{12}\)) or (0.01 mol) of compound (N\(_{13}\)) was mixed with (0.01 mol) N, N-dimethyl benzaldehyde or P-nitro benzaldehyde respectively and then add (0.01 mol.) of ethyl aceacetate and (0.005 mol.) LiBr. The mixture was heated in an oil bath with stirring at 90 °C for (3 hrs.). Afterwards, the mixture was cooled and then poured in ice/water mixture and the obtained solid was collected by filtration, washed with distilled H\(_2\)O, dried and recrystallized from C\(_2\)H\(_2\)OH to afford the pure product.

**Methyl 4-((dimethylamino)-1-(naphthalene-1-yl)-6-methyl-2-oxo-3-(2-oxopyrrolidin-1-yl)1,3,4-tetrahydropyrimidine-5-carboxylate (N\(_{14}\))**: yield (61%), color (bright yellow), m.p. (190-192 °C), M.Wt. (498), \(^1\)H-NMR ν (cm\(^{-1}\)): (3059, 3026) attribute to stretching vibration of (CH arom.), (2972,2879) attribute to stretching vibration of (CH aliph.), (1730,1716 and 1701) attribute to stretching vibrations of carbonyl groups of ester, lactam and urea moiety, respectively, (1651) attribute to stretching vibration of (C=C) atoms, \(^1\)H-NMR spectrum (ppm) (1.54) (m, 2H,CH\(_2\) aliph.), (2.01) (t, 2H, 2CH\(_2\) aliph.), (2.11) (t, 2H, 2CH\(_2\) aliph.), (2.72) (s, 6H, N(CH\(_2\))\(_2\)), (2.85) (s, 3H,CH\(_3\)) attached to six membered ring, (4.52) (s, 5H, CH\(_2\)CH\(_3\)) of ester group and (7.32-8.67) (m, aromatic proton).

**Methyl 6-methyl-4-((nitrophenyl)-3-(2-oxopyrrolidin-1-yl)-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (N\(_{15}\))**: yield (57%), color (dark yellow), m.p. (118-120 °C), M.Wt. (389), \(^1\)H-NMR ν (cm\(^{-1}\)): (3072, 3030) belong to vibration of (CH arom.), (2966, 2831) belong to vibration of(CH) aliph. (1728) (ester), (1708) (lactam), (1344) due to vibration of (C=S), \(^1\)H-NMR spectrum (ppm) (0.84) (m, 2H,CH\(_2\) aliph.), (2.17) (t, 4H, 2CH\(_2\) aliph.), (2.87) (s, 4H,CH benzyl,CH\(_2\) aliph. attached to six membered ring), (4.01) (m, 5H, CH\(_2\)CH\(_3\) of ester group) and (7.26-7.64) (m, aromatic protons).

### 2.3 Biological activities [19]

In vitro antimicrobial testing effects of pyrrolidine-2-one derivatives were estimated against two kinds of bacteria (Staphylococcus aureus and Escherichia Coli). Agar well diffusion was the method to determine the Antimicrobial activity. DMSO (Dimethyl sulfide) acted as a control and the test was set at (1000, 500) μg/ml concentration using (DMSO) as solvent. The bacteria were sub cultured in agar. The plates were incubated at 37 °C and checking after 24 hrs.
3. Results and Discussion

3.1 Spectra

The synthesis of compound (N₁) by lactamation of GBL with NH₂NH₂ (80%) was approved by FT-IR, ¹H-NMR and Mass spectroscopy, FT-IR (cm⁻¹) spectrum of compound (N₁) exhibited disappearance of stretching vibration of (C=O) at (1760) that was belong to GBL see Figure 2 and appearance of new band at (1703) which belong to carbonyl group (C=O) of lactam ring beside appearance of new bands at (3294, 3203) that attribute to symmetric and asymmetric stretching vibration of (−NH₂) group, see Figure 3. Spectra of ¹H-NMR spectrum (ppm) for compound (N₁) exhibited multiplate at (1.03) attribute to (2H, CH₂ aliph.), triplet at (1.52) attribute to (2H, CH₂ aliph.), and a triplet at (2.50) due to (2H, CH₂ aliph.) next to carbonyl group of lactam ring, a singlet at (2.16) due to (2H, NH₂), see Figure 4. Mass spectra of compound (N₁) showed the molecular ion peak (M⁺, m/z) = 100, which correspond to its molecular weight. Compound (N₁) was characterized using FT-IR (cm⁻¹) and ¹H-NMR spectrum (ppm) techniques, the disappearance of (−NH₂) stretching vibration bands that belong to compound N₁ and appearance of new bands at (1600) that belong to (C=N) and appearance of band at (1678) due to lactam ring in FT-IR spectrum of compound (N₂), see Figure 5, indicates its formation, the ¹H-NMR spectrum (ppm) of this compound showed the following signals: - multiplate at (1.10) attribute to (2H, CH₂ aliph.), triplet at (1.55) attribute to (4H, 2CH₂ aliph.), singlet at (2.50) attribute to (6H, 2CH₃ of −C(SCH₂)₃) and disappearance of (−NH₂) singlet peak that was at (2.16) in spectra of compound (N₁). Compound (N₃) was characterized using FT-IR (cm⁻¹), ¹H-NMR and Mass techniques, the disappearance of stretching vibration of (−NH₂) and (C=O) bands that belong to lactam ring of compound (N₁) and appearance of new bands at (3549, 3408) that belong to new (−NH) bands of six membered and appearance of new bands at (1610) that belong to (C=N) in FT-IR spectrum, see Figure 6, indicate the formation of this compound. The ¹H-NMR spectrum (ppm) of this compound has the following signals: - multiplate at (1.60) attribute to (2H, CH₂ aliph.), triplet at (2.09) attribute to (4H, 2CH₂ aliph.), singlet at (8.42) attribute to (2−NH) bonded to (C=S). Mass spectrum of the compound (N₃) showed the molecular ion peak (M⁺, m/z) = 156 which corresponded to its molecular weight. The formation of compound (N₃) was confirmed by FT-IR and ¹H-NMR spectroscopy, FT-IR(cm⁻¹) spectrum showed disappearance of stretching vibration of (−NH₂) of lactam ring of compound (N₁) and appearance of new band at (3344) attribute to stretching vibration of (−NH) of amide group besides a band at (1693) and (1678) attribute to stretching vibration of (C=O) of lactam ring and amide group respectively and appearance of band at (812) attribute to (C−Cl), ¹H-NMR spectrum (ppm) exhibited multiplate at (2.11) attribute to (2H, CH₂ aliph.), triplet at (2.65) attribute to (2H, CH₂ aliph.), triplet at (3.32) attribute to (2H, CH₂ aliph.), singlet at (4.44) attribute to (2H, CH₂−Cl) and singlet at (5.69) attribute to (1H, −NCOH) which is a proof to formation of this compound. The formation of compound (N₄) was characterized using FT-IR and ¹H-NMR techniques, the FT-IR (cm⁻¹) spectrum of compound (N₄) exhibited bands at (3346) attribute to stretching vibration of (−NH) group, band at (1699) attribute to stretching vibration of (C=O) group of lactam ring, band at (1674) attribute to (C=O) stretching vibration absorptions of new lactam ring with sulfur atom. The ¹H-NMR (ppm) spectrum of compound (N₅), see Figure 7, showed multiplate at (1.62) attribute to (2H, CH₂ aliph.), triplet at (2.14) attribute to (2H, CH₂ aliph.), triplet at (2.67) attribute to (2H, CH₂ aliph.), and singlet at (5.69) attribute to (1H, NH) and singlet at (3.40) attribute to (2H, CH₂ aliph.) next to carbonyl group of lactam ring containing sulfur atom. Compounds (N₅) was confirmed by its FT-IR, and Mass spectroscopy, FT-IR (cm⁻¹) spectrum showed new bands at (3396, 3358) and (3265) belong to vibration of (−NH) and (−NH−N₂H). Mass spectra showed molecular ion peak (M⁺, m/z) = 198, which correspond to its molecular weight. Compounds (N₅−N₆) were characterized using FT-IR, ¹H-NMR and some by Mass techniques, the disappearance of stretching vibration (−NH₂) bands at (3294, 3203) and (3358, 3265) that belong to compounds (N₁, N₃) respectively and appearance of new bands belong to new carbonyl groups (C=O) of inside rings in the range (1716-1739) in FT-IR spectrum of these compounds indicate their formation. Figure 8 showed the mass spectrum of the compound N₅, the molecular ion peak (M⁺, m/z) = 230 was corresponded to its molecular weight. The ¹H-NMR spectrum (ppm) of compound N₅ has the following signals: - multiplate at (1.64) attribute to (2H, CH₂ aliph.), triplet at (2.14) due to (4H, 2CH₂ aliph.) aliphatic protons doublet at (2.16) attribute to (two vinyl protons). Compounds (N₁₀, N₁₁) were characterized using FT-IR and ¹H-NMR techniques, the disappearance of the (−NH₂) stretching vibration bands that was at (3358, 3265) of compound (N₆) and appearance of new stretching vibration at (1668 and 1666) that belong to (C=N, imine group) indicates formation of Schiff bases.¹H-NMR spectrum (ppm) of compound (N₁₁) shows doublet at (6.73) and doublet at (7.71) attribute to Para sub. Benzene and singlet at (8.75) attribute to (N=CH) group which indicate its formation, see Figure 9. The formation of compounds (N₁₂, N₁₃) has been proved by their FT-IR and ¹H-NMR, FT-IR (cm⁻¹) spectrum showed disappearance of sym. Vibrations bands at (3294, 3203) that belong to stretching vibration of (−NH₂) group of compound (N₁) and appearance of new bands at (3282, 3203) and at (3371, 3203) that belong to vibration of (−NH) in (NHC=ONH) and (NH−C=S−NH) moieties, respectively and appearance of band at (1651) and (1338) due to stretching vibration of C=O and C=S of (NH−C=O−NH and NH−C=S−NH) in compound (N₁₂, N₁₃), respectively, see Figure 10. ¹H-NMR spectrum (ppm)
of compound (N₁₁₃) has multiplate at (7.88-8.23) due to aromatic protons and two singlet peaks at (8.49) and at (9.16) due to protons of (NH–C=S–NH) which considered to be a proof for its formation. Compounds (N₁₁₂, N₁₁₃) were characterized using FT-IR, ¹H-NMR techniques, the disappearance of (∼NH) stretching vibration bands at (3282, 3203) and at (3371, 3203) of urea and thiourea moieties of compounds (N₁₁₂, N₁₁₃), respectively and appearance of new bands at (1730, 1728) that belong to new carbonyl groups (C=O) of ester attached to six membered ring in FT-IR spectrum of these compounds indicate their formation, the ¹H-NMR spectrum (ppm) of compound (N₁₁₃), see Figure 11, show disappearance of singlet peaks at (8.49, 9.16) that belong to (2H, NH–C=S–NH) of compound (N₁₁₃) and appearance of singlet peaks at (2.87) and (4.01) due to (4H, CH benzylic, CH₃ attached to six membered ring) and due to (5H, CH₂CH₃ of ester group) respectively, indicate its formation.

Scheme 1. Preparation steps for compounds N₁⁻N₉ compounds.

Scheme 2. Preparation steps for compounds N₁₀⁻N₁₅.
Figure 3. FT-IR spectrum of compound N₁.

Figure 4. ¹H-NMR spectrum of compound N₁.

Figure 5. FT-IR spectrum of compound N₂.

Figure 6. FT-IR spectrum of compound N₃.

Figure 7. ¹H-NMR spectrum of compound N₅.

Figure 8. Mass spectrum of compound N₇.
3.2. Biological activity

We see from Table 1 that Compounds N_2, N_3, N_6, N_8, N_11, N_12 and N_13 showed biological activity for both kinds of bacteria (E. coli and St. aure.). Compound N_4 and N_10 show no biological activity at all. Compounds N_7, N_14 show biological activity against E.coli. only. Compound N_15 show biological activity against St. aur. only.

Table 1. biological activity for prepared compounds toward E.coli and St.aur.

| Comp. no. | Escherichia Coli Conc. (µg/ml) | Inhibition zone diameter (mm) | Staphylococcus aureus Conc. (µg/ml) | Inhibition zone diameter (mm) |
|-----------|-------------------------------|------------------------------|-----------------------------------|------------------------------|
| N_1       | 1000                          | 500                          | 1000                              | 500                          |
| N_2       | 17                            | 23                           | 12                                | 17                           |
| N_3       | 23                            | 10                           | 15                                | 13                           |
| N_4       |                                | 7                            |                                    | 15                           |
| N_5       | 16                            | 10                           | 15                                | 13                           |
| N_6       | 13                            | 7                            | 17                                | 15                           |
| N_7       | 7                             | 10                           |                                    | 18                           |
| N_8       |                                | 14                           | 17                                | 18                           |
| N_9       |                                | 20                           | 15                                | 22                           |
| N_10      |                                | 20                           |                                    | 18                           |
| N_11      | 14                            | 20                           | 15                                | 18                           |
| N_12      | 15                            | 20                           |                                    | 11                           |
| N_13      | 14                            | 20                           |                                    | 11                           |
| N_14      | 15                            | 14                           |                                    | 11                           |

4. Conclusion

As conclusion, this work includes synthesis of new pyrrolidin-2-one derivatives by lactamization of GBL with amines derivatives with full characterization of the compounds by ¹H-NMR, FT-IR, and Mass spectroscopies. This indicates very good nucleophilic activities with using high temperature or pressure. It also has proved that these derivatives showed excellent biological activities against both E. coli and St. aur. bacteria.

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