*Heterocyclic Letters*
*Vol. 12| No.2|243-251|February -April|2022*
*ISSN : (print) 2231–3087 / (online) 2230-9632*
*CODEN: HLEEAI*
***http://heteroletters.org***

# SYNTHESIS OF TWO AMIDE DERIVATIVES WITH BIOLOGICAL ACTIVITY AGAINST SOME BACTERIA STRAINS

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## Abstract
Several amide derivatives have been prepared as antibacterial agents; however, some methods used involve different reagents which can be dangerous and require special conditions such as different pH and higher temperatures. The aim of this study was synthesize two amide derivatives (compounds **7** and **8**) using some chemical strategies to evaluate their biological activity against some bacteria. The chemical structure of compounds involved in this studywas confirm with both $^{1}H$ and $^{13}C$ NMR spectra. Other data showed that compound **7** decreased bacterial growth of all bacterial strains compared to compound **8**;. These data suggest that the biological activity depends on the functional groups involved in the chemical structure of **7**.

**Keywords**. Synthesis, amide, derivatives, antibacterial.

## Introduction
For several years, there has been a growing interest in the development of new amide derivatives by the chemical and pharmaceutical industry. In this way, different amide derivatives have been prepared to evaluate their biological activity against some clinical pathologies such as infectious[i-iv], pain[v, vi], cancer[vii-ix], heart failure[x, xi] and others. for example, the synthesis of an amide derivative from salinomycin and N-N´-dicyclohexylcarbodiimideas antibacterial agent against both Gram negative and Gram positivebacteria[xii]. In addition, one study demonstrated the reaction of of (phenyl)ethylamine with a ketone derivative to form a pyridine-carboxamide analog which can decrease human papilloma growth[xiii]. Besides, a series of fatty acid amides were prepared from fatty acids derivatives and cyclic amines as antibacterial agents against *Mycobacterium tuberculos*[xiv]. Other report showed that N-(2,3-diphenylquinoxalin-6-yl)carbamoyl chloride reacted with 4-Oxo-2-thioxopyrimidine to

synthesis of N-(2, 3-diphenylquinoxalin-6-yl) acetamidewith antibacterial effect on both Gram-positive and Gram-negative bacteria[xv]. All these studies indicate the preparation of several amide derivatives; however, some protocols use different reagents which require special conditions such different pH and higher temperatures. Analyzing all data, the aim of this was synthesize two amide derivatives using some chemical strategies to evaluate their biological activity against*Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli* and *Klebsiella pneumoniae* using minimum inhibitory concentration method.

## Materials and Methods

*General methods.*

Starting materials were purchased from commercial suppliers (Sigma-Aldrich and AKos Consulting & Solutions). NMR spectra were recorded on a Varian VXR300/5 FT apparatus (300 MHz/$CDCl_3$) using tetramethylsilane as an internal standard. Electron Ionization mass spectrometry (EIMS) was recorder on a Finnigan PolarisQ ion trap mass spectrometer. Melting-point (m.p.) was determined on an electrothermal-900 model apparatus. The infrared spectrum (IR) was determined on a thermo-scientific iSOFT/IR device. Elemental analysis was determined using a PerkinElmer apparatus (Ser. II CHNS / 02400).

*Chemical synthesis.*

**N-(4-ethynylphenyl)-4-hydroxy-benzamide (2).**

In a round bottom flask (10 ml), 4-hydroxybenzoic acid (100 mg, 0.72 mmol), 3-ethynyl aniline (100 µl, 0.94 mmol) and N,N´-Dicyclohexylcarbodiimide (160 mg, 0.77 mmol) in methanol (5 ml) was stirring for 72 h at room temperature. Then the solvent is evaporated on a rotary evaporator and the product is separated using the chloroform:hexane (3:1) system. yielding 76% of product; m.p. 54-56ºC; IR ($V_{max}$, $cm^{-1}$) 3400, 1712, 1602 and 1070: $^1$H NMR (300 MHz, $CDCl_3$-*d*) $\delta_H$: 3.02 (s, 1H), 6.20 (broad, 2H), 7.06 (m, 2H), 7.40-7.50 (m, 4H), 7.70 (m, 2H) ppm. $^{13}$C NMR (300 Hz, $CDCl_3$) $\delta_C$: 82.00-82.10, 115.10, 118.06, 120.40, 125.90, 130.26, 130.30, 139.60, 160.22, 164.44 ppm. EI-MS m/z: 237.07. Anal. Calcd. for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90; O, 13.49. Found: C, 75.91; H, 4.64.

**4-hydroxy-N-[4-(3-oxo-3-phenyl-prop-1-ynyl)phenyl]benzamide (3)**

In a round bottom flask (10 ml), compound **2** (200 mg, 0.84 mmol), benzoyl bromide (100 µl, 0.84 mmol) and Copper(II) chloride anhydrous (120 mg, 0.89 mmol) in methanol (5 ml) was stirring for 72 h at room temperature. Then the solvent is evaporated on a rotary evaporator and the product is separated using the chloroform:water (4:1) system. yielding 76% of product; m.p.88-90ºC; IR ($V_{max}$, $cm^{-1}$) 3400, 1712, 1602 and 1070: $^1$H NMR (300 MHz, $CDCl_3$-*d*) $\delta_H$: 6.20 (broad, 2H), 7.06 (m, 2H), 7.50-7.58 (m, 4H), 7.62 (m, 2H), 7.69 (m, 1H), 7.74 (m, 2H), 8.25 (m, 2H) ppm. $^{13}$C NMR (300 Hz, $CDCl_3$) $\delta_C$: 87.20, 91.72, 115.10, 117.50, 119.96, 125.90, 128.34, 129.20, 130.26, 130.44, 133.22, 137.90, 140.70, 160.22, 164.44, 176.22 ppm. EI-MS m/z: 341.10. Anal. Calcd. for $C_{22}H_{11}NO_3$: C, 77.41; H, 4.43; N, 4.10; O, 14.06. Found: C, 77.38; H, 4.40.

**4-hydroxy-N-[4-(5-phenyl-2,3-dihydro-1H-1,4-diazepin-7-yl)phenyl]benzamide (4)**

In a round bottom flask (10 ml), compound **3** (200 mg, 0.58 mmol), ethylenediamine (50 µl, 0.92 mmol) and boric acid (120 mg, 0.89 mmol) in methanol (5 ml) was stirring for 72 h at room temperature. Then the solvent is evaporated on a rotary evaporator and the product is separated using the chloroform:water:hexane (4:1:1) system. yielding 76% of product; m.p.108-110ºC; IR ($V_{max}$, $cm^{-1}$) 3400, 1712, 1602 and 1070: $^1$H NMR (300 MHz, $CDCl_3$-*d*) $\delta_H$: 3.22-3.60 (m, 4H), 5.28 (broad, 4H), 7.10 (m, 2H), 7.38 (m, 2H), 7.40 (m, 2H), 7.44 (m, 1H),

7.54 (m, 2H), 7.70 (m, 2H), 7.80 (m, 2H) ppm.$^{13}$C NMR (300 Hz, $CDCl_3$) $\delta_C$: 41.80, 54.00, 80.80, 98.26, 115.10, 120.20, 120.60, 125.90, 127.50, 129.82, 130.26, 130.28, 130.44, 135.86, 140.72, 160.22, 160.60, 164.44 ppm. EI-MS m/z: 383.16. Anal. Calcd. for $C_{24}H_{21}N_3O_2$: C, 75.18; H, 5.52; N, 10.96; O, 8.35. Found: C, 75.15; H, 5.50.

**4-hydroxy-N-[4-(5-phenyl-2,3-dihydro-1H-1,4-diazepin-7-yl)phenyl]benzamide (5)**

In a round bottom flask (10 ml), compound **4** (200 mg, 0.52 mmol) andboric acid (40 mg, 65 mmol) in methanol (5 ml) was stirring for 72 h at room temperature. Then the solvent is evaporated on a rotary evaporator and the product is separated using the chloroform:water (4:1) system. yielding 76% of product; m.p. 136-140 $^oC$; IR ($V_{max}$, $cm^{-1}$) 3400, 1712, 1602 and 1070: $^1$H NMR (300 MHz, $CDCl_3$-*d*) $\delta_H$: 3.30-3.50 (m, 4H), 5.66 (m, 1H), 6.22 (broad, 3H), 7.06 (m, 2H), 7.30 (m, 2H), 7.50 (m, 2H), 7.70 (m, 1H), 7.76 (m, 2H), 7.82 (m, 2H), 7.94 (m, 2H) ppm. $^{13}$C NMR (300 Hz, $CDCl_3$) $\delta_C$: 46.00, 53.20, 96.52, 115.10, 119.20, 125.90, 126.60, 126.88, 127.40, 130.10, 130.26,133.10, 139.40, 139.62, 151.90,160.22, 160.92, 164.44 ppm.EI-MS m/z: 383.16. Anal. Calcd. for $C_{24}H_{21}N_3O_2$: C, 75.18; H, 5.52; N, 10.96; O, 8.35. Found: C, 75.15; H, 5.49.

**4-[4-(cyanomethyl)phenoxy]-N-[4-(5-phenyl-2,3-dihydro-1H-1,4-diazepin-7-yl)phenyl]benzamide (6)**

In a round bottom flask (10 ml), compound **5** (200 mg, 0.52 mmol), 2-(4-nitrophenyl)acetonitrile(85 mg, 0.52 mmol), dimethyl sulfoxide and sodium carbonate anhydrous (70 mg, 0.50 mmol) was stirring for 48 h to reflux (at 80 $^oC$). Then the solvent is evaporated on a rotary evaporator and the product is separated using the chloroform:water (4:1) system. yielding 76% of product; m.p.112-114$^oC$; IR ($V_{max}$, $cm^{-1}$) 3400, 1712, 1602 and 1070: $^1$H NMR (300 MHz, $CDCl_3$-*d*) $\delta_H$: 3.30-3.50 (m, 4H), 3.64 (m, 2H), 5.66 (m, 1H), 6.96 (m, 2H), 7.00 (m, 2H), 7.30 (m, 2H), 7.36 (m, 2H), 7.50 (m, 2H), 7.58 (broad, 2H), 7.70 (m, 1H), 7.82 (m, 2H), 7.96 (m, 2H), 8.02 (m, 2H) ppm. $^{13}$C NMR (300 Hz, $CDCl_3$) $\delta_C$: 23.42, 45.00-98.54, 117.02, 117.40, 117.44, 119.20, 122.50, 126.52, 126.87, 127.36, 127.42, 128.24, 130.10, 130.30, 133.12, 139.44, 139.62, 151.90, 154.62, 160.90, 161.81, 164.44 ppm. EI-MS m/z: 498.20. Anal. Calcd. for $C_{32}H_{26}N_4O_2$: C, 77.09; H, 5.26; N, 11.24; O, 6.42. Found: C, 77.06; H, 5.24.

**N-[4-[(3Z)-3-[2-[(3-chloro-2-oxo-propyl)amino]ethylimino]-3-phenyl-prop-1-ynyl]phenyl]-4-hydroxy-benzamide (7)**

In a round bottom flask (10 ml), compound **6** (200 mg, 0.40 mmol), chloroacetyl chloride (130 µl, 1.63 mmol) and triethylamine (200µl, 1.43 mmol) in methanol (5 ml) was stirring for 72 h at room temperature. Then the solvent is evaporated on a rotary evaporator and the product is separated using the chloroform:benzene:water (4:1:1) system. yielding 76% of product; m.p.108-110$^oC$; IR ($V_{max}$, $cm^{-1}$) 3400, 1712, 1602 and 1070: $^1$H NMR (300 MHz, $CDCl_3$-*d*) $\delta_H$:3.60-3.70 (m, 4H), 4.00 (m, 2H), 6.60 (broad, 3H), 7.06 (m, 2H), 7.36 (m, 3H), 7.40 (m, 2H), 7.42 (m, 1H), 7.50 (m, 2H), 7.70 (m, 2H), 7.82 (m, 2H) ppm.$^{13}$C NMR (300 Hz, $CDCl_3$) $\delta_C$: 41.00, 41.96, 54.24, 80.80, 98.27, 115.10, 120.22, 120.64, 125.90, 127.50, 129.80, 130.26, 130.28, 130.44, 136.12, 140.72, 160.22, 160.60, 162.12, 164.44 ppm.EI-MS m/z: 459.13. Anal. Calcd. for $C_{26}H_{22}ClN_3O_3$: C, 67.90; H, 4.82; Cl, 7.71; N, 9.14; O, 10.44. Found: C, 67.88; H, 4.80.

**N-[2-[(Z)-[3-[4-[(4-hydroxybenzoyl)amino]phenyl]-1-phenyl-prop-2-ynylidene]amino]ethyl]-3-(2-hydro-xy-1-naphthyl)oxirane-2-carboxamide;methane (8)**

In a round bottom flask (10 ml), compound **7** (180 mg, 0.39 mmol), 2-hydroxy-1-naphthaldehyde (68 mg, 0.40 mmol), and sodium hydroxide (10 mg, 0.25 mmol) in 5 ml of ethanol was stirred for 72 h at room temperature. Then the solvent is evaporated on a rotary evaporator and the product is separated using the chloroform:water (4:1) system. yielding 76% of product; m.p. 136-140 $^oC$; IR ($V_{max}$, $cm^{-1}$) 3400, 1712, 1602 and 1070: $^1$H NMR (300 MHz,

$CDCl_3$-*d*) $\delta_H$: 3.60-3.70 (m, 4H), 3.94-4.22 (m, 2H), 7.06 (m, 2H), 7.10 (broad, 4H), 7.22-7.30 (m, 2H), 7.36 (m, 2H), 7.40 (m, 2H), 7.42 (m, 2H), 7.44 (m, 1H), 7.50 (m, 2H), 7.70 (m, 2H), 7.74 (m, 2H), 7.82 (m, 2H), 7.90 (m, 1H) ppm. $^{13}$C NMR (300 Hz, $CDCl_3$) $\delta_C$: 41.60, 53.66, 54.22, 59.56, 80.80, 98.22, 115.10, 118.84, 120.22, 120.60, 121.44, 122.62, 123.40, 125.90, 126.84, 127.53, 128.00, 129.22, 129.76, 130.26, 130.28, 130.38, 130.44, 134.34, 136.10, 140.70, 152.74, 160.22, 160.60, 164.44 ppm. EI-MS m/z: 595.21. Anal. Calcd. for $C_{37}H_{29}N_3O_5$: C, 74.61; H, 4.91; N, 7.05; O, 13.43. Found: C, 74.58; H, 4.90.

***Biological evaluation*.**

*Staphylococcus aureus* (ATCC 33591), *Streptococcus pneumoniae* (ATCC 6303) *Escherichia coli* (ATCC 14035), and *Klebsiella pneumoniae* (ATCC 4352) were acquired from the strain bank from Laboratory of Pharmacochemistry, Faculty of Chemical-Biological Sciences of the Autonomous University of Campeche.

***Antimicrobial activity*.**

This stage was carried out using a previously reported technique[xvi] [21]; in this way, 12 tubes containing 2 mg/2 ml of culture medium (soybean trypticase) were prepared. Then, to the first tube, an aliquot of either of the compounds 2 to 7 (1 mg/ml) was added and was shaken to homogenize the mixture. Then, in the next 11 tubes, different dilutions of either of compounds (2 to 7) at a dose of 0.5 to 0.0004 mg/ml were added with constant stirring (Table 1). Following, each tube was inoculated with 0.1 ml of bacterial suspension, whose concentration corresponded to McFarland scale ($9 \times 10^8$ cells/ml), and all the tubes were incubated at 37$^o$C for 24 h. Finally, a sample of any of the compounds was taken with a sterile loop to inoculate them in specific cultures for each bacterial organism at 37 $^o$C for 24 h.

**Results and Discussion**

There are reports which show the synthesis of several amide derivatives; however, some methods involve reagents that are expensive and difficult to handle[xii-xv]. Therefore, aim of this study was to prepare two amide derivatives using some chemical strategies as follows:In the firststagethe compound *N*-(4-ethynylphenyl)-4-hydroxy-benzamide was prepared using a previously reported method[xvii]; in this way, 4-hydroxylbenzoic acid reacted with 3-ethynylaniline in the presence of N,N´-Dicyclohexylcarbodiimide to form the benzamide derivative (**2**). The $^1$H NMR spectrum of **2** showed several signals at 3.02 ppm for alkyne group; at 6.20 ppm for both hydroxyl and amino groups; at 7.06 and 7.70 ppm for phenyl bound to both amide and hydroxyl groups; at 7.40-7.50 ppm for phenyl group linked to both amide and alkyne groups. The $^{13}$C NMR spectra display chemical shifts at 82.00-82.10 ppm for alkyne group; at 115.10, 125.90-130.36 and 160.22 ppm for phenyl group bound to both hydroxyl and amide groups; at 118.06-120.40 and 130.30-139.60 ppm for phenyl group linked to both alkyne and amide groups; at 164.44 ppm for amide group. In addition, the mass spectrum from **2** showed a molecular ion (m/z) at 237.07.

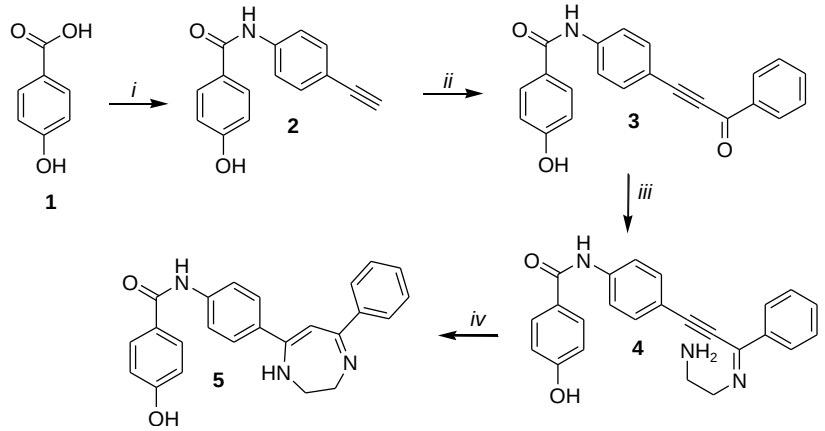


**Figure 1**. Synthesis of a diazepin-benzamide derivative (**5**). *Reagents and conditions*.*i*= 3-ethynyl aniline; N,N´-Dicyclohexylcarbodiimide; MeOH, 72 h, rt; *ii* = benzoyl bromide, Copper(II) chloride anhydrous, MeOH, 72 h, rt; *iii* = ethylenediamine, boric acid, MeOH, 72 h, rt;*iv* = boric acid, MeOH, 72 h, rt.
rt = room temperature.

The second stage was synthesized a benzamide derivative **(3**) using a previously reported method for coupling aryl bromide with a terminal alkyne[xviii]. In this way, the compound **2**reacted with benzoyl bromide using in the presence of Copper(II) chloride to form **3**(Figure 1). The$^{1}$H NMR spectrum of **3** showed several signals at 6.20 ppm for both hydroxyl and amino groups; at 7.06 and 7.74 ppm for phenyl group bound to both hydroxyl and amide groups; at 7.50 and 7.62 ppm for phenyl group linked to both alkyne and amide groups; at 7.58, 7.69 and 8.25 ppm for phenyl group bound to ketone group. The $^{13}$C NMR spectra display chemical shifts at 87.20-91.72 ppm for alkyne group; at 115.10, 125.90, 130.26 and 160.22 ppm for phenyl group bound to both amide and hydroxyl groups; at 117.50-119.96, 130.44 and 140.70 ppm for phenyl group linked to both alkyne and amide groups; at 128.34-129.20 and 133.22-137.90 ppm for phenyl group bound to ketone group; at 164.44 ppm for amide group; at 176.22 ppm for ketone group. Besides, the mass spectrum from **3** showed a molecular ion (m/z) at 341.10.

On the other hand, an imino derivative (compound **4**) was prepared by reacting **3** with ethylenediamine using boric acid as a catalyst (Figure 1); it should be noted that this catalyst does not require special conditions and is easy to handle[xix] .The $^{1}$H NMR spectrum of **4** showed several signals at 3.22-3.60 ppm for methylene groups linked to both amino groups; at 5.28 ppm for both hydroxyl and amino groups; at 7.10 and 7.70 for phenyl group lined to both amide and hydroxyl groups; at 7.40 and 7.54 ppm for phenyl group bound to both alkyne and amide groups; at 7.38, 7.44 and 7.80 ppm for phenyl group linked to imino group. The $^{13}$C NMR spectra display chemical shifts at 41.80-54.00 for methylene groups bound to both amino groups; at 80.80-98.26 ppm for alkyne group; at 115.10, 125.90, 130.26 and 160.22 ppm for phenyl group bound to both amide and hydroxyl groups; at120.20-120.60, 130.44 and 140.72 ppm for phenyl group linked to both amide an alkyne groups; at 127.50-129.82, 130.28 and 135.86 ppm for phenyl group bound to imino group; at 160.60 ppm for imino group; at 164.40 ppm for amide group. Additionally, the mass spectrum from **4** showed a molecular ion (m/z) at 383.16.

The following stage was achieved a via intramolecular reaction of alkyne with amino group of compound **4** to form a 2,3-Dihydro-1H-[1,4]diazepine ring involved in the chemical structure of compound **5**(Figure 1). The $^{1}$H NMR spectrum of **5** showed several signals at 3.30-3.50 ppm for 2,3-Dihydro-1H-[1,4]diazepine fragment; at 6.22 ppm for both hydroxyl and amino groups; at 7.06 and 7.76 ppm for phenyl group bound to both hydroxyl and amide groups; at 7.30, 7.70 and 7.94 ppm for phenyl group linked to 2,3-Dihydro-1H-[1,4]diazepine fragment; at 7.50 and

7.82 ppm for phenyl group bond to amide and 2,3-Dihydro-1H-[1,4]diazepine fragment. The $^{13}$C NMR spectra display chemical shifts at46.00-96.52 151.90 and 160.92 ppm for 2,3-Dihydro-1H-[1,4]diazepine fragment; at 115.10, 125.90 and 160.22 ppm for phenyl group bound to both amide and hydroxyl group; at 119.20, 126.60 and 33.10-139.40 ppm for phenyl group linked to 2,3-Dihydro-1H-[1,4]diazepine fragment; at 126.80-130.10 and 139.62 ppm for phenyl group bound to imino group; at 164.44 for amide group. Besides, the mass spectrum from **5** showed a molecular ion (m/z) at 383.16.

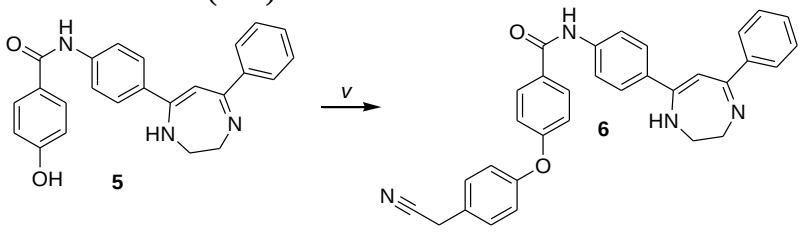


**Figure 2**. Synthesis of and ether derivative (**6**). *Reagents and conditions*. *v*=2-(4-nitrophenyl)acetonitrile, dimethyl sulfoxide, sodium carbonate anhydrous, 48 h, reflux.

Following, an etherification reaction was carried out using a previously reported method[xx]; in this way, **5**reacted with dimethyl sulfoxide in middle conditions to form an ether derivative (compound **6**, Figure 2). The $^{1}$H NMR spectrum of **6** showed several signals at 3.30-3.50 and 5.66 ppm for 2,3-Dihydro-1H-[1,4]diazepine fragment; at 3.64 for methylene group bound to cyanide group; at 6.96 and 8.02 ppm for phenyl group linked to both amide and ether groups; at 7.00 and 7.36 ppm for phenyl group bound to both ether and acetonitrile groups; at 7.30. 7.70 and 7.96 ppm for phenyl group linked to 2,3-Dihydro-1H-[1,4]diazepine fragment; at 7.50 and 7.80 for phenyl group bound to both amide and 2,3-Dihydro-1H-[1,4]diazepine fragment; at 7.58 ppm for both amino and amide groups.The $^{13}$C NMR spectra display chemical shifts at 23.42 ppm for methylene group bound to cyanide group; 45.00-98.54 ppm for alkyne 2,3-Dihydro-1H-[1,4]diazepine fragment; at 117.02, 122.50, 128.24 and 154.62 ppm for phenyl group bound to both ether and amide groups; at 117-40 ppm for nitrile group; at 117.44, 127.42, 130.30 and 161.81 ppm for phenyl group bound to both ether and amide groups; at 119.20, 126.87-127.36, 130.10 and 139.62 ppm for phenyl group linked to both amideand 2,3-Dihydro-1H-[1,4]diazepine fragment; at 126.52, 133.12-139.44, 151.90 and 160.90 ppm for phenyl group linked to both amide and 2,3-Dihydro-1H-[1,4]diazepine fragment; at 164.44 ppm for amide group. In addition, the mass spectrum from **6** showed a molecular ion (m/z) at 498.20.
The following stage was achieved by the synthesis of a chloroamide derivative; it is important mention that several methods have been used to prepare some amide analogs[xxi], however, some these techniques require special conditions such as different Ph and higher temperatures. In this study, **4**reacted with chloroacetyl chloride in the presence of triethylamine to form a chloroamide derivative (compound **7**, Figure 3). The $^{1}$H NMR spectrum of **7** showed several signals at 3.30-3.70 for methylene groups bound to both amino groups; at 4.00 ppm for chloroamide; at 6.60 for amide, hydroxyl, and amino groups; at 7.06 and 7.70 ppm for phenyl group bound to both hydroxyl and amide groups; at 7.36, 7.42 and 7.82 ppm for phenyl group linked to imino group; at 7.40 and 7.50 ppm for phenyl group linked to both alkyne and amide groups. The $^{13}$C NMR spectra display chemical shifts at 41.00 and 54.24 ppm for methylene groups bound to both amino groups; at 41.96 ppm for chloroamide; at 80.80-98.27 ppm for alkyne group; at 115.10, 125.90, 130.26 and 180.22 ppm for phenyl group bound to both hydroxyl and amide groups; at 120.22-120.64, 130.44 and 140.72 ppm for phenyl group linked to both amide and alkyne group; at 127.50-129.80, 130.28, 136.12 and 160.60 ppm for phenyl group bound to imino group; at 162,12-164.44 ppm for amide groups. Besides, the mass spectrum from **7** showed a molecular ion (m/z) at 459.13.

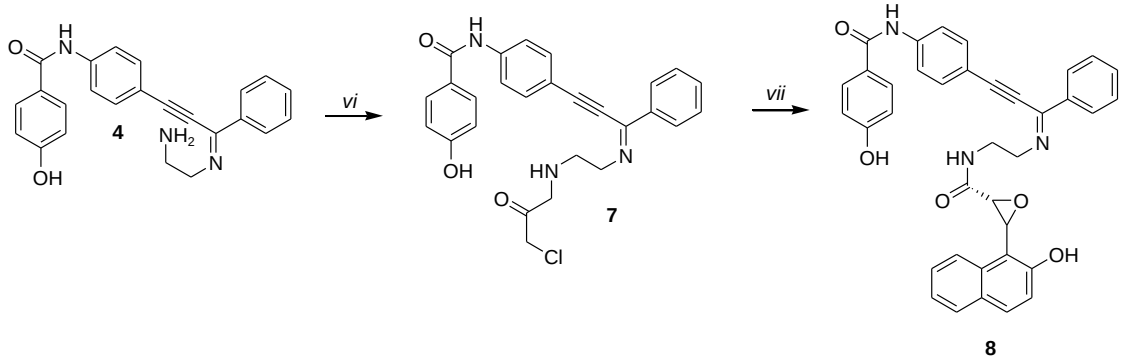


**Figure 3**. Synthesis of and epoxide derivative (**8**). *Reagents and conditions*. *v*=chloroacetyl chloride, triethylamine,MeOH, 72 h, rt; 2-hydroxy-1-naphthaldehyde, sodium hydroxide, MeOH, rt.
rt = room temperature.

Finally, a epoxide derivative (compound **8**, Figure 3); it is important to mention that some epoxide derivatives have been prepared using some methods; however, these protocols require special reagents such as Co(III), and Cr(III)[xxi]. In this investigation, a previously method reported[xxii] was used to preparation of the compound **8**via reaction of **7**with 2-hydroxy-1-naphthaldehyde in basic medium. The $^{1}$H NMR spectrum of **8** showed several signals at 3.30-3.70 for methylene groups bound to both amino groups; at 3.94-4.22 ppm for oxirane ring; at 7.06 and 7.74 ppm for phenyl group bound to both amide and hydroxyl groups; at 7.10 ppm for hydroxyl, amide and amino groups; at 7.22-7.32, 7.42, 7.70 and 7.90 ppm for naphtalene group; at 7.36, 7.44 and 7.82 ppm for phenyl group bound to imino group; at 7.40 and 7.50 ppm for phenyl group bound to both alkyne and amide groups. The $^{13}$C NMR spectra display chemical shifts at 41.00 and 54.24 ppm for methylene groups bound to both amino groups; at 41.60 and 54.22 ppm for methylene groups bound to both amino groups; at 53.66 and 59. 56 ppm for oxirane ring; at 80.80-98,22 ppm for alkyne group; at 115.10, 125.90 130.26-130.28 and 160.22 for phenyl group bound to both amide and hydroxyl groups; at 118.84, 12.44-125.40, 126.84, 128.00-129.22 and 130 ,38 ppm for naphtalene group; at 120.22, 120.60, 130.44 and 140.70 ppm for phenyl group bound to both alkyne and amide groups; at 127.53, 129.76 and 136.10 ppm for phenyl group bound to imino group; at 160.60 ppm for imino group; at 164.44 ppm for amide group. Finally, the mass spectrum from **8** showed a molecular ion (m/z) at 595.21.

### *3.4. Antibacterial activity*

There are some studies which indicate that several amide derivatives can exert biological activity on some bacterial strains[xii-xv]; in this way, biological activity of compounds **7** to **8** against *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli* and *Klebsiella pneumoniae* was evaluated, using he compounds **1** to **6** as control with minimum inhibitory concentration method (MIC). The data observed (Table 1) showed that bacterial growth of either Gram-negative or Gram-positive bacteria only was inhibited by the compounds**7**; however, the bacterial growth of *Staphylococcus aureus* and *Streptococcus pneumoniae* was inhibited by compound**8**. All these data suggest that bacterial activity of compounds **7** and **8** depend onfunctional groups involved in their chemical structure. In this way, it is noteworthy that antibacterial activity produced by **7** on either Gram-negative or Gram-positive bacteria could be due to nitrile linked to phenyl group, which could result as a hydrophobic interaction with some biomolecule present in the bacteria.

**Table 1**. Antibacterial activity of compounds **7** and **8** against four bacterial strains

| Compound | Staphylococcus aureus (mg) | Streptococcus pneumoniae (mg) | Escherichia coli (mg) | *Klebsiella pneumoniae (mg)* |
|---|---|---|---|---|
| **1** to**6**(controls) | - | - | - | - |
| 7 | 0.5 | 0.5 | 0.5 | 0.5 |
| 8 | 1.0 | 1.0 | - | - |

## CONCLUSIONS

In this study an easy method for the preparation of two amide derivatives (compounds **7** and **8**) using some chemical strategies is reported; It should be noted that the performance obtained is good. On the other hand, the antibacterial activity produced by compound **7** on bacteria depends on the functional groups involved in the chemical structure of **7** in comparison with compound 8.

## ACKNOWLEDGEMENT

None

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Received on February 5, 2022.