American Journal of Organic Chemistry 2015, 5(4): 116-124
DOI: 10.5923/j.ajoc.20150504.02

Design and Synthesis of Two New Epoxides

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Abstract In this study is reported a straightforward route for synthesis of two new epoxides using some strategies. The first stage was achieved by the synthesis of the cyclohexylimino-azetidin-benzoic acid (3) by the reaction of 4-hydroxy benzoic acid with a nitrobenzamide derivative. Following, 3 was reacted with ethylenediamine using boric acid as catalyst to form a phenoxy-carboxamide analog (4). In addition, **4** was used to react with chloroacetyl chloride in presence of triethylamine for preparation of a chloroamide derivative (**5**). Then, **5** was reacted with 2-hydroxy-1-naphthaldehyde in basic medium for the synthesis of an epoxide-benzamide analog (**6**). The second stage was developed by the synthesis of an enone-derivative (10) using the three component system (cinnamaldehyde, 4-aminoantipyrine and alkyne-1) in presence of cupric chloride. In addition 10 was reacted with ethylenediamine in presence of boric acid to form an phenylcyclopentamine derivative (11). After, **11** was reacted with chloroacetyl chloride using treiethylamine as catalyst to form a chloroacetamide analog (**12**). Following, **12** was reacted with 2-hydroxy-1-naphthaldehyde in basic medium for preparation of an epoxide-amide derivative (**13**). The structure of the compounds obtained was confirmed using elemental analysis and NMR spectra. The proposed method offers some advantages such as simple procedure and ease of workup.

Keywords Epoxide, Naphthaldehyde, Derivative, Enone

1. Introduction

Since years ago several epoxide derivatives have been prepared using protocols different; for example, the synthesis of 1-[(Ethoxycarbonyl)methyl]tetrahydrothiophen ium Bromide by the reaction of tetrahydrothiophene with ethyl bromoacetate [1]. Other data showed the preparation of 3-oxyranil-chlorophyll by the reaction of Methyl pyropheophorbide with a chlorophyll derivative [2]. In addition the compound methyl 4-(3-hydroxycyclohex-1-en-1-yl)buta- noate was reacted with *m*-chloroperoxybenzoic acid (*m*CPBA) to form the epoxide derivative (methyl 4-(5-hydroxy-7-oxabicyclo[4.1.0]hept-1-yl)butanoate) [3]. Other study shown the synthesis of 1,1-Bis(2,3-epoxy-cyclohexyloxymethyl)-3,4-epoxycyclohexane by the reaction of 1,1-Bis(2-cyclohexenyloxymethyl)-3-cyclohexe ne (I) with *m*CPBA [4]. Another report indicate preparation of the compound phenyl [(2*S*,4*R*)-4-phenyloxetan-2-yl] methanone by the reaction of (2*E*)-1,3-bis(4-methoxyphenyl) prop-2-en-1-one with potassium hydroxide [5]. In addition, a study showed the synthesis of a vinyl carbamate-epoxide by reaction of vinyl carbamate with dimethyldioxirane [6]. Recently was synthesized the compound (2*R*,3*S*)-*N*-(3-(5-*H*-dibenzo[*b*,*f*]azepin-5-yl)-2,5-dihydro-1,2,4-thiadiazol-5-yl)-3-phenyloxirane-2-carboxamide by the reaction of *N*-[3-(5*H*-diben-zo[*b*,*f*]azepin-5-yl)-2,5-dihy-dro-1,2,4-thiad iazol-5-yl] propanamide with sodium hydroxide [7]. All these experimental results show several procedures which are available for synthesis of several epoxide-derivatives; nevertheless, expensive reagents and special conditions are required. Therefore, in this study two new epoxide-derivatives were synthesized using several strategies.

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Published online at http://journal.sapub.org/ajoc

2. Experimental

General methods

The compound **1** (*N*-(3-Butyl-1-cyclohexyl-4-ciclohexyl-imino-azetidin-2-ylidene)-4-nitro-benzamide) was prepared with methods previously reported [8]. In addition, all the reagents used in this study were purchased from Sigma-Aldrich Co. Ltd. The melting points for the different compounds were determined on an Electrothermal (900

model). Infrared spectra (IR) were recorded using KBr pellets on a Perkin Elmer Lambda 40 spectrometer. ^{1}H and ^{13}C NMR and 2D-COSY spectra were recorded on a Varian VXR-300/5 FT NMR spectrometer at 300 and 75.4 MHz in $CDCl_3$ using TMS as internal standard. EIMS spectra were obtained with a Finnigan Trace GCPolaris Q. spectrometer. Elementary analysis data were acquired from a Perkin Elmer Ser. II CHNS/0 2400 elemental analyzer.

4-[4-(3-Butyl-1-cyclohexyl-4-cyclohexylimino-azetidin-2-ylidenecarba- moyl)-phenoxy]-benzoic acid (3)

A solution of **1** (200 mg, 0.44 mmol), 4-hydroxybenzoic acid (70, 0.50 mmol) potassium carbonate anhydrous (42 mg, 0.30 mmol) in 5 ml of Dimethyl sulfoxide was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (3:1) yielding 80% of product, m.p. 222-224°C; IR (V_{max}, cm^{-1}): 1680, 1722 and 1224; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.86 (s, 3H), 1.08-1.20 (m,7H), 1.30-1.44 (m, 7H), 1.46 (m, 2H), 1.50-1.54 (m, 3H), 1.58 (t, 2H, J = 6.0 Hz), 1.62-1.66 (m, 3H), 1.80-1.90 (m, 2H), 3.18-3.20 (m, 2H), 4.80 (m, 1H), 6.94 (m, 2H), 7.00-8.10 (m, 4H), 8.44 (m, 2H), 10.80 (broad, 1H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 14.16, 23.00, 23.08, 24.40, 25.36, 26.00, 26.28, 29.10, 29.66, 32.20, 38.70, 57.88, 59.68, 116.70, 117.22, 124.18, 131.00, 132.60, 133.84, 134.46, 157.10, 164.09, 165.08, 168.40, 175.94 ppm. EI-MS *m/z*: 543.30 (M^+ 9). Anal. Calcd. for $C_{33}H_{41}N_3O_4$: C, 72.90; H, 7.60; N, 7.73; O, 11.77. Found: C, 72.84; H, 7.55.

***N*-(2-aminoethyl)-4-(4-(((2*Z*,4*Z*)-3-butyl-1-cyclohexyl-4-(cyclohexylimino)azetidin-2-ylidene)carbamoyl)phenoxy)benzamide (4)**

A solution of **3** (200 mg, 0.37 mmol), ethylenediamine (80 µl, 0.74 mmol), and boric acid (40 mg, 0.60 mmol) in 5 ml of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (4:1) yielding 65% of product, m.p. 268-270°C; IR (V_{max}, cm^{-1}):3378, 3320 and 1686; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.86 (s, 3H), 1.08-1.20 (m, 7H), 1.32-1.44 (m, 7H), 1.46 (m, 2H), 1.50-1.54 (m, 3H), 1.58 (t, 2H, J = 6.96 Hz), 1.60-1.64 (m, 3H), 1.80-1.90 (m, 2H), 3.12 (t, 2H, J = 6.44 Hz), 3.18-3.22 (m, 2H), 3.50 (t, 2H, J = 6.44 Hz), 4.62 (broad, 3H), 4.80 (m, 1H), 6.82 (m, 2H), 6.98 (m, 2H), 7.64 (m, 2H), 8.36 (m, 2H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 14.16, 23.00, 23.10, 24.40, 25.46, 26.00, 26.30, 29.12, 29.68, 32.20, 38.66, 43.28, 43.66, 57.90, 59.68, 116.64, 117.38, 128.700, 130.88, 131.00, 132.60, 134.37, 160.92, 163.21, 164.10, 169.64, 175.88 ppm. EI-MS *m/z*: 585.36 (M^+ 10). Anal. Calcd. for $C_{35}H_{47}N_5O_3$: C, 71.76; H, 8.09; N, 11.96; O, 8.19. Found: C, 71.70; H, 8.00.

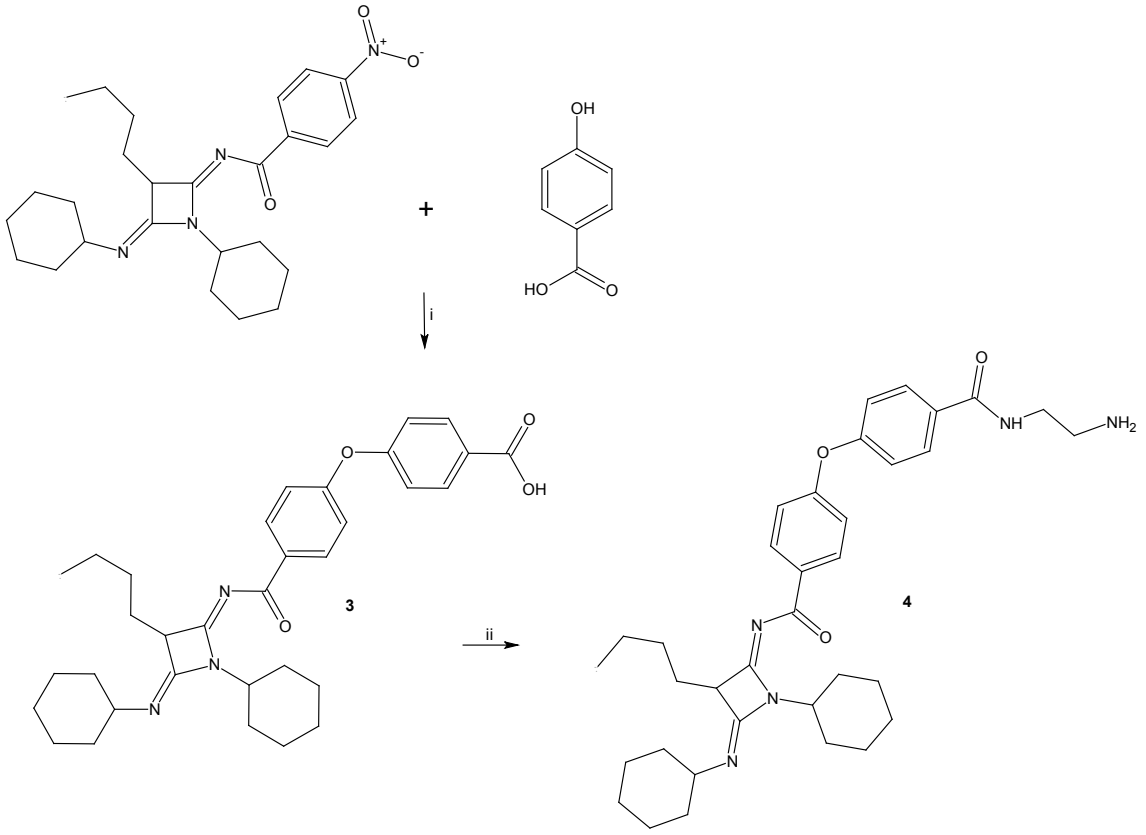

Figure 1. Synthesis of a phenoxy-carboxamide derivative (**4**). Reaction of a nitrobenzamide analog (**1**) with 4-hydroxy benzoic acid (**2**) to form the cyclohexylimino-azetidin-benzoic acid derivative (**3**). Following, **3** was reacted with ethylenediamine (ii) in presence of boric acid to form **4**. i = K_2CO_3/rt

***N*-((2*Z*,4*Z*)-3-butyl-1-cyclohexyl-4-(cyclohexylimino)azetidin-2-ylidene)-4-(4-((2-(2-chlroacetamido)ethyl)carbamoyl)phenoxy)benzamide (5)**

A solution of **4** (200 mg, 0.34 mmol), triethylamine (100 µl, 1.50 mmol) and chloroacetyl chloride (128 µl, 1.60 mmol) in 5 ml of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water:hexane (4:1:2) yielding 44% of product, m.p. 280-282°C; IR (V_{max}, cm^{-1}):3380, 1684 and 1226; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.88 (s, 3H), 1.08-1.20 (m, 7H), 1.30-1.46 (m, 7H), 1.48 (m, 2H), 1.50-1.54 (m, 3H), 1.58 (t, 2H, *J* = 6.96 Hz), 1.62-1.66 (m, 3H), 1.80-1.90 (m, 2H), 3.18-3.22 (m, 2H), 3.50 (m, 4H), 4.00 (t, 2H, *J* = 13.62 Hz), 4.80 (m, 1H), 6.82 (m, 2H), 6.98 (m, 2H), 7.64 (m, 2H), 8.02 (broad, 2H), 8.38 (m, 2H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 14.18, 23.00, 23.10, 24.40, 25.36, 26.00, 26.30, 29.22, 29.67, 32.24, 38.70, 38.80, 38.84, 42.40, 57.88, 59.82, 116.82, 117.34, 128.90, 130.88, 131.00, 132.70, 134.48, 161.04, 162.30, 162.58, 163.32, 164.13, 176.00 ppm. EI-MS *m/z*: 661.33 (M^+ 12). Anal. Calcd. for $C_{37}H_{48}ClN_5O_4$: C, 67.10; H, 7.31; Cl, 5.35; N, 10.57; O, 9.66. Found: C, 67.03; H, 7.24.

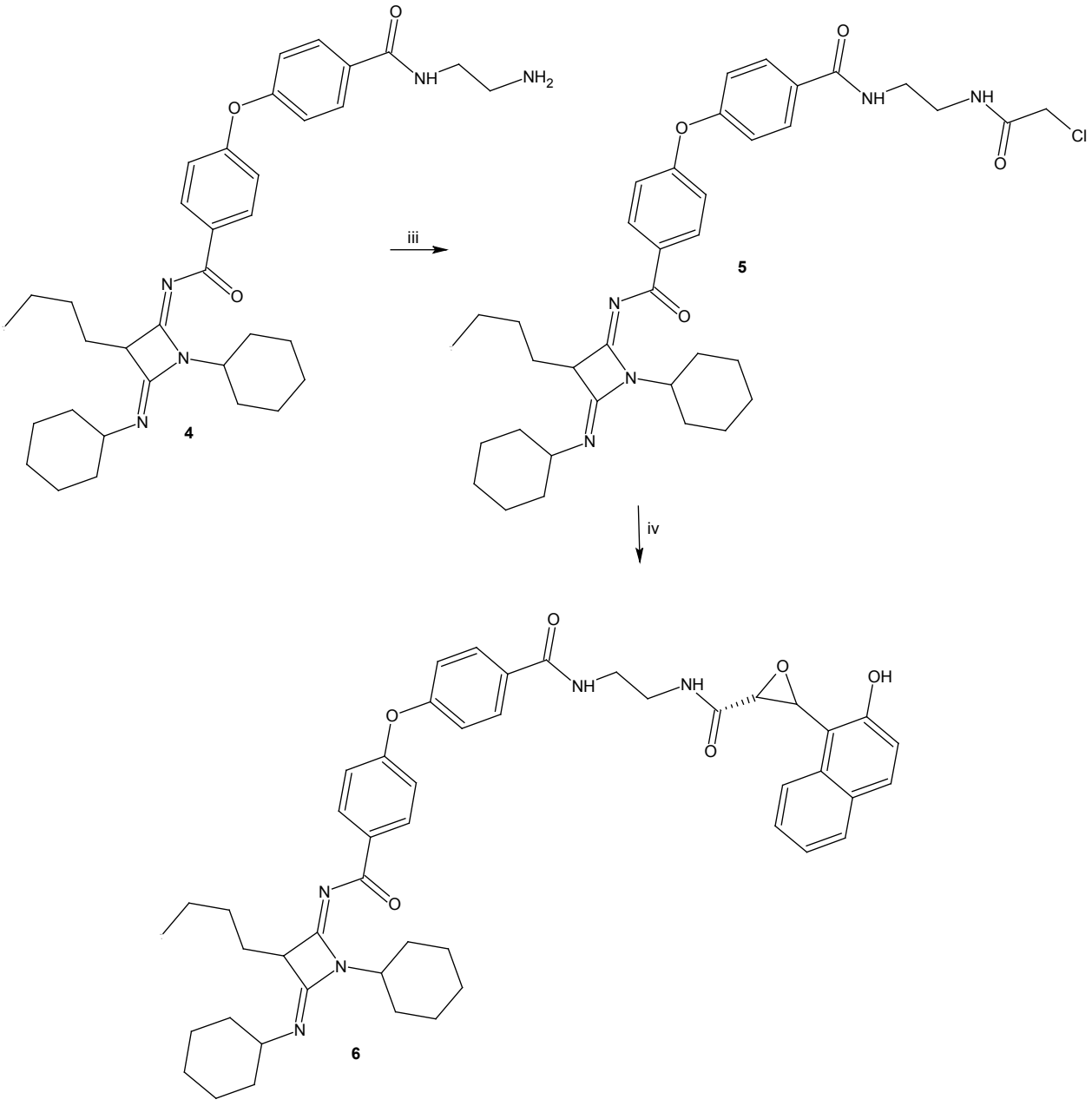

Figure 2. Synthesis of an epoxide-benzamide derivative (**6**). Reaction of compound **4** with chloroacetyl chloride in presence of triethylamine (iii) to form a chloroamide derivative (**5**). After, **5** was reacted with 2-hydroxy- 1-naphthaldehyde (iv) in basic medium to form **6**

N-((2Z,4Z)-3-butyl-1-cyclohexyl-4-(cyclohexylimino)azetidin-2-ylidene)-4-(4-((2-(2-(3-(2-hydroxynaphthalen-1-yl)oxiran-2-yl)acetamido)ethyl)carbamoyl)phenoxy)benzamide (6)

A solution of **5** (200 mg, 0.30 mmol), 2-hydroxy-1-naphthaldehyde (68 mg, 0.40 mmol), and sodium hydroxide (20 mg, 0.50 mmol) in 5 ml of ethanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol: water: hexane (4:1:2) yielding 38% of product, m.p. 180-182°C; IR (V_{max}, cm^{-1}):3380, 3222, 1680, and 1220; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 0.88 (s, 3H), 1.04-1.20 (m, 7H), 1.30-1.44 (m, 7H), 1.48 (m, 2H), 1.50-1.53 (m, 3H), 1.56 (t, 2H, J = 6.96 Hz), 1.60-1.64 (m, 3H), 1.78-1.90 (m, 2H), 3.18-3.22 (m, 2H), 3.50 (t, 2H, *J* = 13.62 Hz), 3.54 (t, 2H, *J* = 13.62 Hz), 3.90-4.20 ppm (m, 2H), 4.70 (m, 1H), 6.82 (m, 2H), 6.98 (m, 2H), 7.20-7.40 (m, 4H), 7.64 (m, 2H), 7.70-7.90 (m, 2H), 8.20 (broad, 3H), 8.38 (m, 2H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 14.16, 23.00, 23.10, 24.40, 25.40, 26.00, 26.38, 29.18, 29.80, 32.22, 38.70, 38.86, 39.16, 53.66, 57.90, 59.52, 59.74, 116.70, 117.38, 118.80, 121.36, 122.58, 123.40, 126.78, 128.00, 129.00, 129.24, 130.26, 130.96, 131.04, 132.70, 134.28, 134.40, 152.80, 161.00, 162.28, 163.32, 164.10, 172.22, 176.01 ppm. EI-MS *m/z*: 797.41 (M^+ 11). Anal. Calcd. for $C_{48}H_{55}N_5O_6$: C, 72.25; H, 6.95; N, 8.78; O, 12.03. Found: C, 72.18; H, 6.90.

2-[Hex-1-ynyl-(3-phenyl-allyl)amino]-3,4-dimethyl-5-phenyl-cyclopent-2-enone (10)

A solution of cinnamaldehyde (87 µl, 0.69 mmol), 4-aminoantypirine (100 mg, 0.50 mmol), hexyn-1 (56 µl, 0.50 mmol) and cupric chloride anhydrous (100 mg, 0.74 mmol) in 5 ml of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (4:1) yielding 60% of product, m.p. 98-100°C; IR (V_{max}, cm^{-1}): 2264, 1720 and 1170; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 0.90 (s, 3H), 1.24 (s, 3H), 1.42 (t, 2H, J = 7.13 Hz), 1.50 (t, 2H, J, 6.00 Hz), 1.78 (s, 3H), 2.30 (t, 2H, J = 6.00 Hz), 2.50 (m, 1H), 3.80 (m, 2H), 4.08 (m, 1H), 5.80-6.80 (m, 2H), 7.20 (m, 5H), 7.30-7.40 (m, 5H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 13.58, 15.00, 16.28, 16.88, 21.94, 32.00, 39.58, 62.00, 62.80, 65.20, 89.48, 126.48, 126.66, 127.10, 127.87, 128.55, 128.80, 130.00, 134.28, 135.68, 137.92, 143.70, 145.74, 198.44 ppm. EI-MS *m/z*: 397.24 (M^+ 10). Anal. Calcd. for $C_{28}H_{31}NO$: C, 84.59; H, 7.86; N, 3.52; O, 4.02. Found: C, 84.50; H, 7.80.

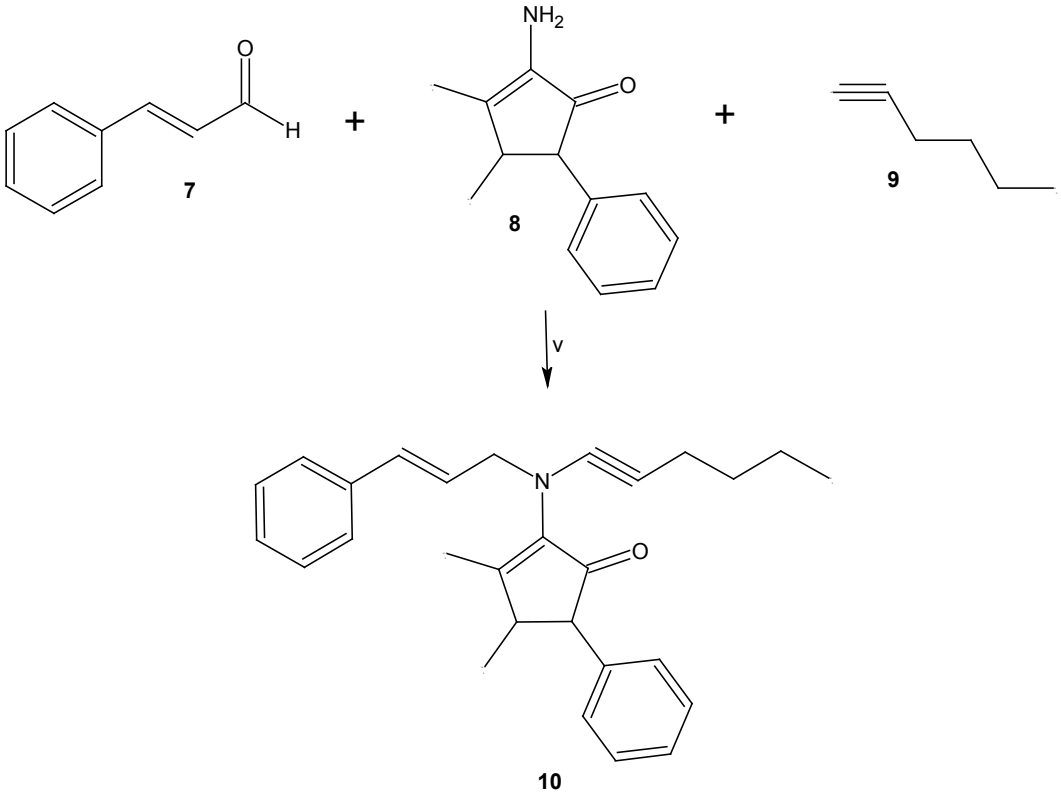

Figure 3. Synthesis of an enone derivative (**10**). Reaction of cinnamaldehyde (**7**), 4-aminoantipyrine (**8**) and alkyne-1 (**9**) to form **10**. v = cupric chloride anh./MeOH/rt

(*E*)-5-((2-aminoethyl)imino)-*N*-cinnamyl-*N*-(hex-1-yn-1-yl)-2,3-dimethyl-4-phenylcyclopent-1-en-1-amine (11)

A solution of **10** (200 mg, 0.50 mmol), ethylenediamine (80 µl, 0.74 mmol), and boric acid (40 mg, 0.60 mmol) in 5 ml of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (4:1) yielding 54% of product, m.p. 76-78°C; IR (V_{max}, cm^{-1}):3382, 3320 and 2260; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.90 (s, 3H), 1.14 (s, 3H), 1.46-1.50 (m, 4H), 1.70 (s, 3H), 2.36 (m,2H), 3.10 (t, 2H, *J* = 6.44 Hz), 3.48 (m, 1H), 3.56 (t, 2H, J = 6.44 Hz), 3.60 (m, 1H), 3.84 (m, 2H), 4.30 (broad, 2H), 5.90-6.80 (m, 2H), 7.00-7.14 (m, 5H), 7.20-7.40 (m, 5H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 13.59, 16.48, 16.60, 16.88, 22.00, 32.00, 40.80, 49.62, 50.44, 54.00, 62.28, 62.50, 89.84, 121.44, 126.18, 126.48, 126.64, 127.80, 128.58, 128.92, 128.85, 130.00, 136.02, 136.54, 139.08, 140.95, 149.56 ppm. EI-MS *m/z*: 439.29 (M^+ 10). Anal. Calcd. for $C_{30}H_{37}N_3$: C, 81.96; H, 8.48; N, 9.56. Found: C, 81.90; H, 8.40.

2-Chloro-*N*-(2-{2-[hex-1-ynyl-(3-phenyl-allyl)-amino]-3,4-dimethyl-5-phenyl-cyclopent-2-enylideneamino}-ethyl-acetamide (12)

A solution of **11** (200 mg, 0.45 mmol), triethylamine (100 µl, 1.50 mmol) and chloroacetyl chloride (128 µl, 1.60 mmol) in 5 ml of methanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (4:1) yielding 77% of product, m.p. 115-117°C; IR (V_{max}, cm^{-1}): 3378, 2264 and 1680; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 0.90 (s, 3H), 1.14 (s, 3H), 1.44-1.50 (m, 4H), 1.70 (s, 3H), 2.32 (m, 2H), 3.50 (m, 1H), 3.60 (t, 2H, J =6.54 Hz), 3.62 (m, 1H), 3.66 (t, 2H, *J* =6.54 Hz), 3.90 (m, 2H), 4.00 (m, 2H), 6.00-6.80 (m, 2H), 7.00 (broad, 1H), 7.04-7.15 (m, 5H), 7.20-7.40 (m, 5H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 13.60, 16.46, 16.62, 16.94, 21.98, 32.00, 34.80, 42.47, 49.62, 50.38, 54.32, 62.22, 62.50, 89.70, 121.50, 126.20, 126.52, 126.64, 127.90, 128.63, 128.82, 130.00, 135.88, 136.54, 139.04, 140.82, 149.56, 162.70 ppm. EI-MS *m/z*: 515.27 (M^+ 11). Anal. Calcd. for $C_{32}H_{38}ClN_3O$: C, 74.47; H, 7.42; Cl, 6.87; N, 8.14; O, 3.10. Found: C, 74.40; H, 7.36.

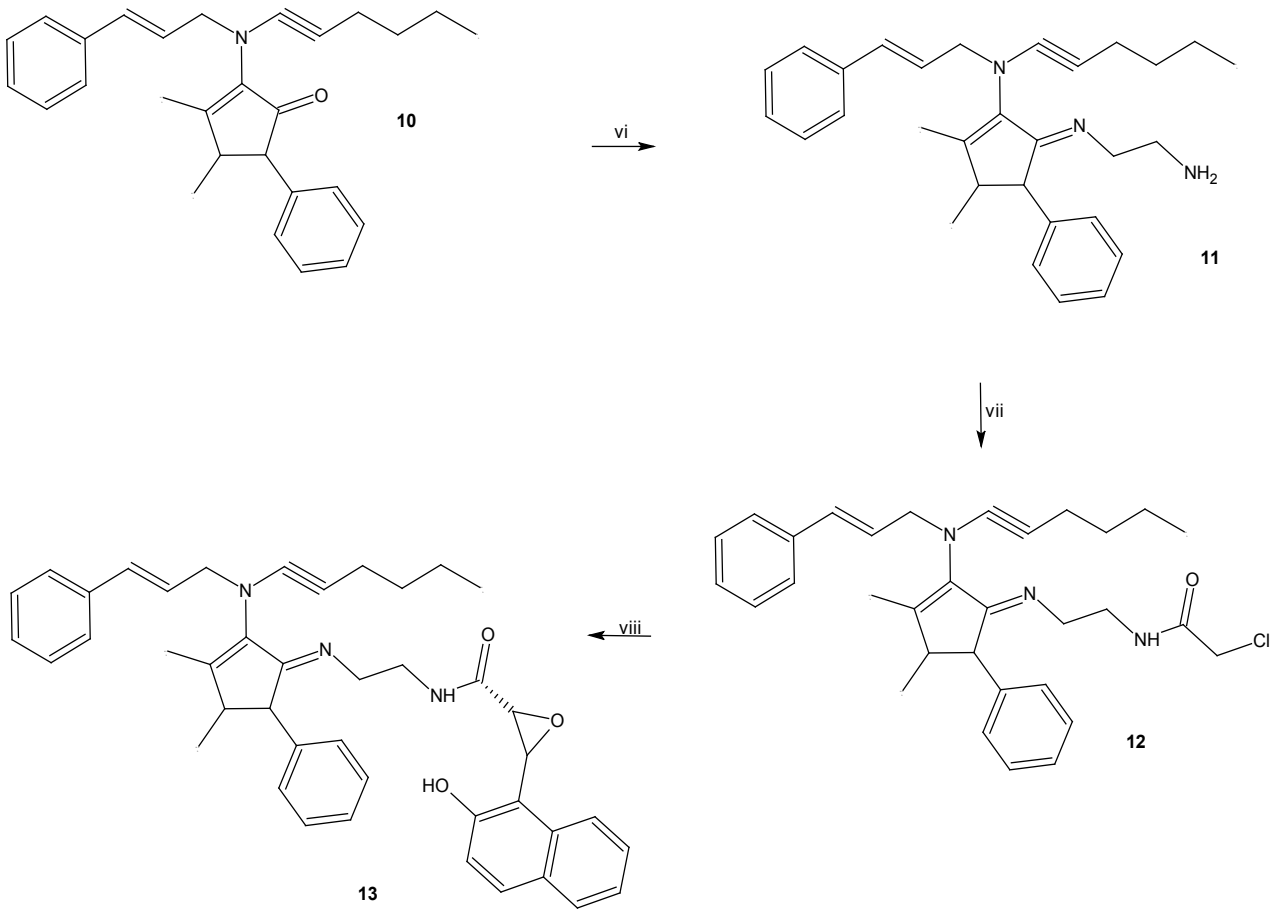

Figure 4. Synthesis of an epoxide-amide derivative (**13**). Reaction of **10** with ethylenediamine in presence of boric acid (vi) to form an phenylcyclopentamine derivative (**11**). After, **11** was reacted with chloroacetyl chloride using treiethylamine as catalyst (vii) to form a chloroacetamide analog **(12**). Following, **12** was reacted with 2-hydroxy-1-naphthaldehyde (vii) in basic medium for preparation of **13**

3-(2-Hydroxy-naphtalen-yl)-oxirane-2-carboxyl acid (2-{2-[hex-1-ynyl-(3-phenyl-allyl)-amino]-3,4-dimethyl-5-phenyl-cyclopent-2-enylideneamino}-ethyl)-amide (13)

A solution of **12** (200 mg, 0.39 mmol), 2-hydroxy-1-naphthaldehyde (68 mg, 0.40 mmol), and sodium hydroxide (20 mg, 0.50 mmol) in 5 ml of ethanol was stirring for 72 h at room temperature. The reaction mixture was evaporated to a smaller volume. After the mixture was diluted with water and extracted with chloroform. The organic phase was evaporated to dryness under reduced pressure, the residue was purified by crystallization from methanol:water (4:1) yielding 65% of product, m.p. 104-106°C; IR (V_{max}, cm^{-1}): 3380, 2262, 1684 and 690; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 0.90 (s, 3H), 1.12 (s, 3H), 1.46-1.50 (m, 4H), 1.70 (m, 3H), 2.34 (m, 2H), 3.50 (m,1H), 3.54 (t, 2H, J = 6.54 Hz), 3.60 (m, 1H), 3.66 (t, 2H, *J* = 6.54 Hz), 3.90 (m, 2H), 3.98-4.30 (m, 2H), 6.00-6.80 (m, 2H), 7.00-7.20 (m, 7H), 7.26-7.34 (m, 2H), 7.36-7.40 (m, 3H), 7.44-7.70 (m, 3H), 7.80 (broad, 2H), 7.90 (m, 1H) ppm. ^{13}C NMR (75.4 Hz, $CDCl_3$) δ_C: 13.60, 16.48, 16.66, 16.90, 22.00, 32.00, 35.51, 49.62, 50.38, 53.72, 54.28, 59.55, 62.20, 62.62, 89.70, 118.80, 121.36, 121.50, 122.62, 123.40, 126.26, 126.48, 126.58, 126.80, 127.90, 128.00, 128.56, 128.85, 129.18, 130.00, 130.42, 134.40, 135.90, 136.52, 139.08, 140.92, 149.60, 152.82, 172.12 ppm. EI-MS *m/z*: 651.34 (M^+ 10). Anal. Calcd. for $C_{43}H_{45}N_3O_3$: C, 79.23; H, 6.96; N, 6.45; O, 7.36. Found: C, 79.18; H, 6.90.

3. Results and Discussion

In this study several straightforward routes are reported for synthesis of two new epoxide-derivatives using some strategies; the first stage (Figure 1 and 2) was achieved by the synthesis of an ether group involved in the chemical structure of compound 4-[4-(3-Butyl-1-cyclohexyl-4-cycloh e-xylimino-azetidin-2-ylidenecarbamoyl)-phenoxy]-benzoic acid (**3**). It is noteworthy that there are many procedures for preparation of several ether derivatives; however, despite its broad scope, they have some drawbacks; For example, several reagents used are hazardous and expensive such as Iodophenol [9], 1,4-diazabicyclo[2.2.2]octane [10], 2,2,6,6-tetramethyl-heptane-3,5-dione [11] aryltrifluorobora te salts [12]. Another data indicate that formation of ether groups via displacement of nitro groups with hydroxyl groups using a dipolar aprotic solvent; In general, dipolar solvents are used to attain high yield of ether groups [7]. Therefore, in this study, the compound **3** was synthetized by the reaction of **1** with 4-hydroxybenzoic acid in presence of dimetyhylsulfoxide at mild conditions. The ^1H NMR spectrum of **3** shows signals at 0.86 ppm for methyl group; at 1.08-1.44, 1.50-1.54, 1.62-1.66 and 3.17-3.20 ppm for cyclohexane ring; at 1.44, 1.58 and 1.78-1.90 ppm for me thylene groups of arm bound to cyclobutane ring; at 4.80 ppm for proton of cyclobutane ring; at 6.94-8.44 for phenyl groups; at 10.80 ppm for carboxyl group. The ^{13}C NMR spectrum of **3** contains peaks at 14.16 for methyl group; at 23.00, 24.40-26.28, 32.20 and 57.88-59.68 ppm for hexane ring; at 23.08 and 29.10-29.69 ppm for methylene groups of arm bound to cyclobutane ring; at 38.70, 134.46 and 164.09 ppm for carbons of cyclobutane ring; at 116.70, 133.84, 152.10 and 165.08 ppm for phenyl groups; at 168.40 ppm for carboxyl group; at 175.95 ppm for amide group. Finally, the presence of compound **3** was confirmed with the mass spectrum which showed a molecular ion at *m/z* 543.30.

The second stage was achieved by formation of an amide group involved in the compound **4**. There are several reports for the preparation of amide groups, the most widely used one employs carboxyl acid chlorides as electrophile which react with the amino groups in the presence of an acid scavenger. Despite its wide scope, this protocol suffers from several drawbacks; limited stability of many acid chlorides and hazardous reagents needed for their preparation (e.g., thionyl chloride) [13]. Another data indicate that boric acid is a good catalyst to formation of amide group [14]; in this sense, **3** was reacted with ethylenediamine in presence of boric acid to form the compound **4**. The ^1H NMR spectrum of **4** shows signals at 0.86 ppm for methyl group; at 1.08-1.44 and 1.50-1.54 ppm for cyclohexane ring; at 1.46, 1.58, 1.80-1.90 and 3.18-3.22 ppm for methylene groups of arm bound to cyclobutane ring; at 1.60-1.64 ppm for cyclohexane ring; at 3.12 and 3.50 ppm for methylene groups of arm bound to amino group; at 4.62 ppm for both amide and amino groups; at 4.78 ppm for cyclobutane ring; at 6.82-8.36 ppm for phenyl groups. The ^{13}C NMR spectrum of **3** contains peaks at 14.16 ppm for methyl group; at 23.00, 24.40-26.30, 32.20 and 57.90-59.68 ppm for cyclohexane ring; at 23.10 and 29.12-29.68 ppm for me- thylene groups of arm bound to cyclobutane ring; at 38.66 ppm for cyclobutane ring; at 43.28-43.66 ppm for me- thylene groups bound to amino group; at 116.64-132.60 and 160.92-163.21 ppm for phenyl groups; at 134.37 and 164.10 ppm for imino group; at 169.64 and 175.88 ppm for amide group. In addition, the presence of compound **4** was confirmed with the mass spectrum which showed a molecular ion at *m/z* 585.36.

The third stage was achieved by the formation of a chloroamide group involved in the chemical structure of the compound **5.** There are many procedures for the formation of chloroamides that are known in the literature, for example the reaction of an amine with trichloroisocyanuric Acid [15] or an amide secondary with *N*-chlorobenzotriazole to form a chloroamide derivative [16]; in addition, have been prepared some chloroamide groups using chloroacetyl chloride [17]. Analyzing these data, in this study, the compound **4** was reacted with chloroacetyl chloride to form the compound **5** using triethylamine as catalyst. The ^1H NMR spectrum of **5** shows signals at 0.88 ppm for methyl group; at 1.08-1.46, 1.50-1.54, 1.62-1.66 and 3.18-3.22 ppm for cyclohexane ring; at 1.48, 1.58 and 1.80-1.90 ppm for cyclobuatane ring; at 3.50 for methylene group bound to amide groups; at 4.00 for methylene group of chloroamide group; at 4.80 for cyclobutane ring; at 6.82-7.64 and 8.38 ppm for phenyl groups; at 8.02 for amide group. The ^{13}C NMR spectrum of **5** contains peaks at 14.18 ppm for methyl group; at 23.00, 24.40-26.30, 23.24 and 59.82-57.88 ppm for cyclohexane

ring; at 23.10 and 29.22-29.67 ppm for methylene groups of arm bound to cyclobutane ring; at 36.87 ppm for cyclobutane ring; at 38.80-38.84 ppm for methylene bound to amide group; at 42.40 ppm for methylene group of chloroamide group; at 116.82-132.70, 161.04 and 163.32 ppm for phenyl groups; at 134.48 and 164.16 ppm for imino group; at 162.30-162.58 and 176.00 ppm for amide group. Finally, the presence of compound **5** was confirmed with the mass spectrum which showed a molecular ion at *m/z* 661.33.

The fourth stage involved the formation of an epoxide derivative (**6**); it is noteworthy that several epoxides have been prepared using protocol different; nevertheless, expensive reagents and special conditions are required [1-7]. For example, the most widely practiced methods employs some reagents such as Co(III) [18] and Cr(III) [19]. Therefore, in this study the compound **6** was prepared by the reaction of **5** with sodium hydroxide to form the compound **6**. The ^{1}H NMR spectrum of **6** shows signals at 0.88 ppm for methyl group; at 0.88 for methyl group; at 1.04-1.44, 1.50-1.53, 1.60-1.64 and 3.18-3.22 ppm for cyclohexane ring; at 1.48, 1.58 and 1.78-1.90 ppm for methylene group of arm bound to cyclobutane ring; at 3.50-3.54 ppm for methylene bound to amide groups; at 3.90-4.20 ppm for oxirane ring; at 4.70 ppm for cyclobutane ring; at 6.80-7.90 and 8.38 ppm for phenyl groups; at 8.20 for amide groups. The ^{13}C NMR spectrum of **6** contains peaks at 14.16 ppm for methyl group; at 23.00, 24.40-26.38, 32.22, 57.90 and 59.74 ppm for cyclohexane ring; at 23.10 and 29.18-29.80 ppm for methylene groups of arm bound to cyclobutane ring; at 38.70 ppm for cyclobutane ring; at 38.86-39.16 ppm for methylene groups bound to amide group; at 53.66 and 59.52 ppm for oxirane ring; at 116.70-134.28, 152.80-161.00 and 163.32 ppm for phenyl groups; at 162.28, 172.22 and 176.01 ppm for amide groups; at 134.40 and 164.10 ppm for imino groups. In addition, the presence of compound **4** was confirmed with the mass spectrum which showed a molecular ion at *m/z* 797.41.

The fifth stage was performed using the three component system for the synthesis of an enone derivative (**10**). There are many procedures which use a three component system for the synthesis of several compounds. The most widely practiced method employs boric acid [20], silica sulfuric acid [21], poly(4-vinylpyridinecodivynylbenzene)- Cu(II) complex [22], sulfuric acid [23], silica triflate [24] and phosphorus pentoxide [25]. Nevertheless, despite their wide scope, the protocols mentioned suffer from several drawbacks owing to the limited stability of some reagents. Analyzing these data and the reports which indicate that the copper(II) reagent has been found to be an efficient catalyst for an enantioselective one-pot three-component synthesis [26, 27]. In this study, the synthesis of **10** (Fig. 3) was achieved by the reaction of cinnamaldehyde (**7**), 4-aminoantipyrine (**8**) and alkyne-1 using cupric chloride as catalyst. The ^{1}H NMR spectrum of **10** shows signals at 0.90 for methyl group; at 1.24 and 1.78 ppm for methyl groups bound to cyclopentene ring; at 1.42-1.50 and 2.30 ppm for methylene groups bound to alkyne group; at 2.50 and 4.08 ppm for cyclopentene ring; at 3.80 for methylene bound to both amino and alkene groups; at 5.80-6.80 for protons of alkene group; at 7.207.40 for phenyl groups. The ^{13}C NMR spectrum of **10** contains peaks at 13.58 ppm for methyl group of alkyne group; at 15.00-16.28 ppm for methyl groups of cyclopentene ring; at 16.88-32.00 of methylene groups bound to alkyne group; at 39.58-62.00, 143.70 and 145.74 ppm for carbons of cyclopentene ring; at 65.20-89.48 ppm for alkyne group; at 126.48-128.80 and 136.68-137.92 ppm for phenyl groups; at 130.00-134.28 for carbons of alkene group; at 198.44 ppm for ketone group. Finally, the presence of compound **10** was confirmed with the mass spectrum which showed a molecular ion at *m/z* 397.24.

The following stage was achieved by the reaction of **10** with ethylenediamine to form an imino group involved in the chemical structure of the compound **11.** It is important to mention that many procedures for the synthesis of imino groups which are described in the literature [28]; nevertheless, in this study boric acid was used as a catalyst, because it is not an expensive reagent and no special conditions for its use are required [29]. The ^{1}H NMR spectrum of **11** shows signals at 0.90 ppm for methyl group of arm bound to alkyne; at 1.14 and 1.70 ppm for methyl groups bound to pentene ring; at 1.46-1.50 and 2.36 ppm for methylene groups bound to alkyne; at 3.10 and 3.56 ppm for me- thylene groups bound to both imino and amino groups; at 3.48 and 3.60 for protons of pentene ring; at 3.84 ppm for methylene group bound to both amino and alkene groups; at 4.30 for amino group; at 5.90-6.80 ppm for hydrogens of alkene group; at 7.00-7.40 ppm for phenyl groups. The ^{13}C NMR spectrum of **11** contains peaks at 13.59 for methyl group of arm bound to alkyne group; at 16.52-16.60 ppm for methyl groups bound to pentene ring; at 16.88-32.00 for methylene groups bound to alkyne group; at 40.80 and 54.00 ppm for methylene groups bound to both imino and amino groups; at 49.62-54.00, 121.44 and 139.08 ppm for carbons of pentene ring; at 62.28 ppm for methylene group bound to both amino and alkene groups; at 62.50 and 89.84 ppm for alkyne group; at 126.18-128.92 and 136.02-136.54 for phenyl groups; at 130.00 and 140.95 ppm for alkyne group. In addition, the presence of compound **11** was confirmed with the mass spectrum at *m/z* 439.29.

The seventh stage (Fig. 4) was achieved by synthesis of a chloroamide derivative group involved in the chemical structure of the compound **12.** It is noteworthy, that there are many procedures for the formation of chloroamides which are known in the literature, for example the reaction of amine with trichloroisocyanuric Acid [30] or amide secondary with *N*-chlorobenzotriazole to form a chloroamide derivative [31]; in addition, have been prepared some chloroamide groups using chloroacetyl chloride [32]. In this study, **11** was reacted with chloroacetyl chloride in presence of triethylamine to form the compound **12**. The ^{1}H NMR spectrum of **12** shows signals at 0.90 ppm for methyl group of arm bound to alkyne group; at 1.14 and 1.70 ppm for methyl groups bound to cyclopentene ring; at 1.44-1.50 and 2.32 ppm for methylene groups bound to alkyne; at 3.50 and

3.62 for protons involved in the cyclopentene ring; at 3.60 and 3.66 ppm for methylene groups bound to both amino and imino groups; at 3.90 ppm for methylene group bound to both amino and alkene groups; at 4.00 ppm for methylene group bound to amide; at 6.00-6.80 ppm for hydrogens of alkene group; at 7.00 for amide group; at 7.04-7.40 ppm for phenyl groups. The ^{13}C NMR spectrum of **12** contains peaks at 13.60 ppm for methyl of arm bound to alkyne group; at 16.46-16.62 ppm for methyl groups bound to cyclopentene ring; at 16.94 and 21.98-32.00 ppm for of arm bound to alkyne group; at 34.80 and 54.32 ppm methylene groups bound to both imino and amino groups; at 42.47 ppm for methylene group bound to amide; at 49.62-50.38, 121.50 and 139.04 ppm for cyclopentene ring; at 62.22 ppm for methylene group bound to both alkene and amino groups; at 62.50 and 89.70 ppm for alkyne group; at 126.20-128.82 and 135.88-136.54 ppm for phenyl groups; at 130.00 and 140.82 ppm for carbons of alkene group; at 149.56 ppm for imino group; at 162.70 ppm for amide group. In addition, the presence of compound **12** was confirmed with the mass spectrum at *m/z* 515.27.

Finally, the compound **12** was used in the synthesis of an of epoxide derivative (**13**). In this study, the formation of epoxide was made by the reaction of **12** with 2-hydroxy-1-naphthaldehyde in basic medium to form **13**. The ^{1}H NMR spectrum of **13** shows signals at 0.90 ppm for methyl of arm bound to alkyne group; at 1.12 and 1.70 ppm for methyl groups bound to cyclopentene ring; at 1.46-1.50 and 2.34 ppm for methylene groups bound to alkyne group; at 3.50 and 3.60 for the protons of cyclopentene ring; at 3.54 and 3.60 ppm for methylene groups of arm bound to imino and amide groups; at 3.90 ppm for methylene group bound to both alkene and amino groups; at 3.98 and 4.30 ppm for oxirane ring; at 6.00-6.80 for protons of alkene group; at 7.00-7.70 and 7.90 ppm for phenyl groups; at 7.80 ppm for both amide and hydroxyl groups. The ^{13}C NMR spectrum of **13** contains peaks at 13.60 ppm for methyl group of arm bound to alkyne; at 16.48 and 16.66 ppm for methyl groups bound to cyclopentene ring; at 16.90 and 22.00-32.00 ppm for methylene groups of arm bound to alkyne; at 35.51 and 54.28 ppm for methylene groups of arm bound to both imino and amide groups; at 49.62, 50.38, 121.50 and 139.08 ppm for cyclopentene ring; at 53.72 and 59.28 ppm for carbons of oxirane ring; at 62.20 ppm for methylene bound to alkene group; at 62.62 and 89.70 ppm for alkyne group; at 118.80-121.30, 122.62-129.18 and 130.42-136.56 and 152.82 ppm for phenyl groups; at 130.00 and 140.92 ppm for alkyne group; at 149.60 for imino group; at 172.12 for amide group. Furthermore, the presence of compound **13** was confirmed from mass spectrum at *m/z* 651.34.

4. Conclusions

In this study was reported the synthesis of two new epoxide derivatives. The proposed method offers some advantages such as simple procedure and ease of workup.

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