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ORIGINAL ARTICLE

# Design and synthesis of two triazonine-carbaldehyde derivatives using several chemical tools

**Lauro Figueroa-Valverde [a,*], Francisco Díaz-Cedillo [b], Elodia García-Cervera [a], Eduardo Pool-Gómez [a], Marcela Rosas-Nexticapa [c], María López-Ramos [a], Maria Isabel Vera-Escobedo [a]**

[a] *Laboratory of Pharmaco-Chemistry at the Faculty of Chemical Biological Sciences from the University Autonomous of Campeche, Av. Agustín Melgar s/n, Col Buenavista, C.P. 24039 Campeche Cam., Mexico*
[b] *Escuela Nacional de Ciencias Biológicas del Instituto Politécnico Nacional, Prol. Carpio y Plan de Ayala s/n, Col. Santo Tomas, México D.F. C.P. 11340, Mexico*
[c] *Facultad de Nutrición, Universidad Veracruzana, Médicos y Odontólogos s/n, C.P. 91010 Xalapa, Veracruz, Mexico*

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**KEYWORDS**

Triazonine;
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**Abstract** Several triazonine-carbaldehyde derivatives have been prepared using different protocols; however, some require special reagents and conditions. The aim of study involved the synthesis of two triazonine-carbaldehyde derivative using testosterone or OTBS-testosterone as chemical tool. Triazonine-carbaldehyde derivatives were prepared by a series of reactions that involve the following: (1) synthesis of two nitrobenzamide derivatives by reaction of testosterone or OTBS-testosterone with *p*-nitrobenzoyl azide using Copper(II) as catalyst; (2) reaction of the nitrobenzamides with ethylenediamine to form two triazonine derivatives using boric acid as catalyst; (3) preparation of hexynyl-triazonine derivatives by the reaction of two triazonines 6-chlorohex-1-yne in basic medium; (4) reaction of hexynyl-triazonine derivatives with benzaldehyde to form two triazoninol analogs; (5) preparation of triazoninynal derivatives through oxidation of triazoninol analogs with dimethyl sulfoxide; and (6) synthesis of triazonine-carbaldehyde derivatives by the reaction of triazoninynal derivatives with hexyne-1 using Copper(II) as catalyst.

* Corresponding author.
E-mail address: lauro_1999@yahoo.com (L. Figueroa-Valverde).
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The chemical structure of compounds was determined by spectroscopic and spectrometric methods. In conclusion, in this work were prepared two triazoninone derivatives using several chemical techniques, which are simple procedures and easy to handle.



## 1. Introduction

Since some years ago, have been developed several aldehydes derivatives which are used as precursors for the conversion from other functional groups [1]. For example, there is a study that showed the preparation of a carbaldehyde derivative by the reaction of glycine methyl ester with methylpentanimidoate [2]. Another data showed the formylation of pyrroles with $POCl_5$ to form a pyrrol-2-carbaldehyde [3]. In addition, a report showed that the TiCl4/t-$BuNH_2$ complex produces hydroamination/annulation of δ-keto-acetylenes to form the pyrrolo[1,2-a]indol-2-carbaldehyde [4]. Also, other data [5] showed the synthesis of 10-hydroxyphenanthrene-9-carbaldehyde by the reaction of boron trifluoride etherate with Spiro [9-Hydro-10-oxo-phenanthrene-9-oxirane]. Additionally, the compound 2-chloro-quinoline-3-carbaldehyde derivatives were prepared by the condensation of acetanilide derivatives with *N,N*-dimethylformamide in the presence of phosphorusoxychloride [6]. Another report [7] indicates the synthesis of 3-substituted-1*H*-pyrazole-4-carbaldehydes by the reaction of (2E)-2-(1-arylethylidene)hydrazinecarboxamide with $POCl_3$. Another study showed the synthesis of pyrimidine-5-carbaldehydes from α-formylaroylketene dithioacetals [8]. In addition, a study showed an acid-catalyzed acetal deprotection of benzimidazole derivatives to give some carbaldehyde analogs [9]. Another study indicated the preparation of 2-butyl-5-chloro-3H-imidazole-4-carbaldehyde by the reaction of glycine with imidate in basic conditions [10]. In addition, a study shown that $TiCl_4$/*t*-$BuNH_2$-promoted hydroamination/annulation of δ-keto-acetylenes to form the compound pyrrolo[1,2-a]indol-2-carbaldehydes [4]. Another data indicate the synthesis of indol-carbaldehyde by the reaction of an indol-nitrile analog with diisobutylaluminium hydride [11]. All these experimental results show several procedures that are available for synthesis of some carbaldehyde derivatives; nevertheless, expensive reagents and special conditions are required. Therefore, the aim of study involved the synthesis of a two triazonine-carbaldehyde derivatives using testosterone and its derivative as chemical tool.

## 2. Materials and methods

### 2.1. Protection of hydroxyl group from testosterone

The compound 17-(tert-butyldimethylsilanyloxy)-10,13-dimethyl-1,2,6,7,8, 9,10,11,12,13,14,15,16,17-tetradecahydro-cyclopenta[a]phenanthren-3-one (OTBS-Testosterone) was prepared mainly previously reported [12]. The other compounds evaluated in this study were purchased from Sigma–Aldrich Co., Ltd. The melting point for the testosterone derivative was 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 (nuclear magnetic resonance) spectra were recorded on a Varian VXR-300/5 FT NMR spectrometer at 300 and 75.4 MHz (megahertz) in $CDCl_3$ (deuterated chloroform) using TMS (tetramethylsilane) as an internal standard. Electron impact mass spectroscopy (EIMS) spectra were obtained with a Finnigan Trace Gas Chromatography Polaris Q Spectrometer. Elementary analysis data were acquired from a Perkin Elmer Ser. II CHNS/0 2400 elemental analyzer.

### 2.2. General method for synthesis of nitrobenzamide derivatives

A mixture of testosterone (100 mg, 0.34 mmol) or OTBS-testosterone (100 mg, 0.24 mmol), p-nitrobenzoyl azide (100 mg, 0.52 mmol), Copper(II) chloride anhydrous (80 mg, 0.60 mmol) in 5 mL of methanol was stirred for 72 h at room temperature. The organic phase was evaporated to dryness under reduced pressure; the residue was subjected to $SiO_2$ column chromatography with the methanol–hexane–acetone solvent system to afford the steroid derivatives.

#### 2.2.1. *N-((Z)-((3aR,5As,6S)-6-hydroxy-3a,5a-dimethyl-2-oxotetradecahydrodicyclopenta [a,f]naphtalen-1(2H)-ylidene) methyl)-4-nitrobenzamide (**2**)*

The product yield was of 65% of product, m.p. 88–90 °C; IR ($V_{max}$, $cm^{-1}$): 3400, 1712, 1644 and 1380; $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.78 (s, 3H), 0.92–0.96 (m, 2H), 1.08 (s, 3H), 1.09–1.40 (m, 6H), 1.48–1.64 (m, 3H), 1.80–1.96 (m, 4H), 2.24–3.60 (m, 4H), 4.86 (d, 1H, $J$ = 3.20 Hz), 8.00–8.22 (m, 4H), 8.30 (broad, 2H) ppm. $^{13}$C NMR (75.4 Hz, $CDCl_3$) $\delta_C$: 11.88 (**C**-18), 12.84 (**C**-17), 22.08 (**C**-15), 23.60 (**C**-10), 23.72 (**C**-8), 30.80 (**C**-7), 34.82 (**C**-11), 35.62 (**C**-3), 37.25 (**C**-16), 44.00 (**C**-5), 44.02 (**C**-9), 44.32 (**C**-1), 50.40 (**C**-12), 51.14 (**C**-4), 56.02 (**C**-2), 81.50 (**C**-6), 124.26 (**C**-26, **C**-30), 129.22 (**C**-14), 129.30 (**C**-27, **C**-29), 136.12 (**C**-25), 149.32 (**C**-21), 150.63 (**C**-28), 164.22 (**C**-23), 205.12 (**C**-13) ppm. EI-MS $m/z$: 452.23. Anal. Calcd. for $C_{26}H_{32}N_4O_5$: C, 69.01; H, 7.13; N, 6.19; O, 17.68. Found: C, 68.94; H, 7.06.

#### 2.2.2. *N-((E)-((3aR,5As,6S)-6-hydroxy-3a,5a-dimethyl-2-oxotetradecahydrodicyclopenta [a,f]naphtalen-1(2H)-ylidene) methyl)-4-nitrobenzamide (**3**)*

The product yield was of 12% of product, m.p. 98–100 °C; IR ($V_{max}$, $cm^{-1}$): 3400, 1710, 1640 and 1382; $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.78 (s, 3H), 0.92–1.10 (m, 4H), 1.12 (s, 3H), 1.18–1.42 (m, 4H), 1.48–1.64 (m, 3H), 1.80–1.96 (m, 5H), 2.50–3.60 (m, 3H), 4.44 (d, 1H, $J$ = 3.20 Hz), 7.76–8.10 (m, 4H), 8.80 (broad, 2H) ppm. $^{13}$C NMR (75.4 Hz, $CDCl_3$) $\delta_C$: 11.88 (**C**-18), 12.84 (**C**-17), 22.08 (**C**-15), 23.60 (**C**-10), 23.72 (**C**-8), 30.80 (**C**-7), 34.82 (**C**-11), 35.62 (**C**-3), 37.25 (**C**-16), 41.00 (**C**-9), 44.02 (**C**-5), 44.32 (**C**-1), 50.40 (**C**-12), 51.14 (**C**-4), 56.02 (**C**-2), 81.50 (**C**-6), 122.86 (**C**-26, **C**-30), 129.22 (**C**-14), 129.30 (**C**-27, **C**-29), 138.32 (**C**-25), 150.63 (**C**-28), 151.70 (**C**-21), 161.62 (**C**-23), 205.12 (**C**-13) ppm. EI-MS $m/z$:

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452.23. Anal. Calcd. for $C_{26}H_{32}N_4O_5$: C, 69.01; H, 7.13; N, 6.19; O, 17.68. Found: C, 68.94; H, 7.06.

#### *2.2.3. N-((Z)-((3aR,5aS)-6-((isopropyldimethylsilyl)oxy) 3a,5a-dimethyl-2-oxotetradecahydro dicyclopenta[a,f] naphtalen-1(2H)-ylidene)methyl)-4-nitrobenzamide (**5**)*

The product yield was of 64% of product, m.p. 112–114 °C; IR ($V_{max}$, $cm^{-1}$): 1710, 1646, 1378; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.07 (s, 6H), 0.70 (m, 1H), 0.90 (s, 3H), 0.92–1.05 (m, 3H), 1.06 (s, 3H), 1.10–1.40 (m, 5H), 1.60–1.92 (m, 7H), 2.24–3.50 (m, 4H), 4.86 (d, 1H, $J$ = 3.20), 8.00–8.22 (m, 4H), 10.34 (broad, 1H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: −4.60 (**C**-21, **C**-27), 11.42 (**C**-18), 12.90 (**C**-17), 18.00 (**C**-28), 22.08 (**C**-15), 23.50 (**C**-8), 23.64 (**C**-10), 25.50 (**C**-29, **C**-36, **C**-37), 31.00 (**C**-7), 34.82 (**C**-11), 35.62 (**C**-3), 36.72 (**C**-16), 43.30 (**C**-5), 44.00 (**C**-9), 44.32 (**C**-1), 50.40 (**C**-12), 51.94 (**C**-4), 56.02 (**C**-5), 81.70 (**C**-6), 124.26 (**C**-31, **C**-36), 129.22 (**C**-14), 129.30 (**C**-32, **C**-34), 136.12 (**C**-30), 149.32 (**C**-23), 150.65 (**C**-33), 164.22 (**C**-25), 205.12 (**C**-13) ppm. EI-MS $m/z$: 566.31. Anal. Calcd. for $C_{32}H_{46}N_2O_5Si$: C, 67.81; H, 8.18; N, 4.94; O, 14.11; Si, 4.96. Found: C, 67.70; H, 8.02.

#### *2.2.4. N-((E)-((3aR,5aS)-6-((tert-buthyldimethylsilyl)oxy) 3a,5a-dimethyl-2-oxotetradecahy drodicyclopenta[a,f] naphtalen-1(2H)-ylidene)methyl)-4-nitrobenzamide (**6**)*

The product yield was of 14% of product, m.p. 120–122 °C; IR ($V_{max}$, $cm^{-1}$): 1712, 1648, 1372; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.07 (s, 6H), 0.70 (s, 3H), 0.86 (s, 9H), 0.92–1.08 (m, 4H), 1.10 (s, 3H), 1.16–1.60 (m, 7H), 1.76–1.94 (m, 5H), 2.54–3.52 (m, 3H), 4.44 (*d*, 1H, $J$ = 3.20), 7.72–8.10 (m, 4H), 11.30 (broad, 1H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: −4.60 (**C**-21, **C**-27), 11.42 (**C**-18), 12.90 (**C**-17), 18.00 (**C**-28), 22.06 (**C**-15), 23.50 (**C**-8), 23.64 (**C**-10), 25.50 (**C**-29, **C**-36, **C**-37), 31.00 (**C**-7), 34.82 (**C**-11), 35.62 (**C**-3), 36.72 (**C**-16), 41.00 (**C**-9), 43.30 (**C**-5), 44.32 (**C**-1), 50.40 (**C**-12), 51.94 (**C**-4), 56.02 (**C**-2), 81.70 (**C**-6), 122.86 (**C**-31, **C**-35), 129.22 (**C**-14), 129.30 (**C**-32, **C**-34), 138.32 (**C**-30), 150.65 (**C**-33), 151.72 (**C**-23), 161.72 (**C**-25), 205.12 (**C**-13) ppm. EI-MS $m/z$: 566.31. Anal. Calcd. for $C_{32}H_{46}N_2O_5Si$: C, 67.81; H, 8.18; N, 4.94; O, 14.11; Si, 4.96. Found: C, 67.72; H, 8.06.

### *2.3. General method for synthesis from triazonine derivatives*

A solution of **2** (200 mg, 0.44 mmol) or **5** (200 mg, 0.36 mmol), ethylenediamine (80 µl, 0.74 mmol), and boric acid (40 mg, 0.65 mmol) in 5 mL of methanol was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure. Thereafter, the residue was purified by crystallization from methanol:water (4:1).

#### *2.3.1. (2aS,7bZ,10Z,14Z,15aR)-2a-15a-dimethyl-10-(4-nitrophenyl)-2,2a,3,4,5,5a,5b,6,7,7a,9, 12,13,15,15a,15b-hexadecahydro-1H-indeno[5′,4′:4,5]indeno[2,1-g][1,3,6]triazonin-3-ol (**7**)*

The product yield was of 66% of product, m.p. 172–174 °C; IR ($V_{max}$, $cm^{-1}$): 3402, 3320, 1580 and 1554; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.78 (s, 3H), 0.92–1.16 (m, 5H), 1.22 (s, 3H), 1.36–1.60 (m, 6H), 1.70–1.94 (m, 5H), 2.50–3.60 (m, 3H), 4.34–4.60 (m, 4H), 7.40 (d, 1H, $J$ = 1.64), 7.40 (m, 2H), 7.44 (broad, 4H), 8.22 (m, 2H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: 12.34 (**C**-25), 16.74 (**C**-24), 22.00 (**C**-22), 23.80 (**C**-14), 23.82 (**C**-20), 30.86 (**C**-13), 33.30 (**C**-9), 34.70 (**C**-21), 37.26 (**C**-23), 44.00 (**C**-11), 46.90 (**C**-7), 49.97 (**C**-19), 48.62 (**C**-6), 51.70 (**C**-10), 51.94 (**C**-3), 52.96 (**C**-8), 53.12 (**C**-2), 81.50 (**C**-12), 125.02 (**C**-18), 127.30 (**C**-29, **C**-31), 130.42 (**C**-28, **C**-32), 135.30 (**C**-17), 142.38 (**C**-27), 148.92 (**C**-30), 150.65 (**C**-15), 161.82 (**C**-5) ppm. EI-MS $m/z$: 476.27. Anal. Calcd. for $C_{28}H_{36}N_4O_3$: C, 70.56; H, 7.61; N, 11.76; O, 10.07. Found: C, 70.48; H, 7.52.

#### *2.3.2. (2aS,7bZ,10Z,14Z,15aR)-3-((isopropyldimethylsilyl-oxy)-2a,15a-dimethyl-10-(4-nitro phenyl)-2,2a,3,4,5,5a,5b,6,7,7a,9,12,13,15,15a,15b-hexadecahydro-1H-indeno[5′,4′:4,5] indeno[2,1-g][1,3,6]triazonine (**8**)*

The product yield was of 56% of product, m.p. 112–114 °C; IR ($V_{max}$, $cm^{-1}$): 3322, 1558 and 1380; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.07 (s, 6H), 0.80 (m, 1H), 0.90 (s, 3H), 0.92–0.93 (m, 2H), 1.00 (s, 6H), 1.04–1.18 (m, 3H), 1.22 (s, 3H), 1.34–1.60 (m, 6H), 1.70–1.94 (m, 5H), 2.50–3.60 (m, 3H), 4.34–4.60 (m, 4H), 7.40 (d, 1H, $J$ = 1.64), 7.42–8.22 (m, 4H), 8.50 (broad, 1H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: −4.08 (**C**-28, **C**-35), 11.42 (**C**-25), 15.60 (**C**-36), 16.66 (**C**-24), 16.90 (**C**-37, **C**-40), 22.00 (**C**-22), 23.50 (**C**-14), 23.82 (**C**-20), 31.00 (**C**-13), 33.32 (**C**-9), 34.70 (**C**-21), 36.72 (**C**-23), 43.30 (**C**-11), 46.90 (**C**-7), 46.98 (**C**-19), 48.60 (**C**-6), 51.85 (**C**-3), 51.94 (**C**-10), 52.96 (**C**-8), 53.12 (**C**-2), 80.90 (**C**-12), 125.02 (**C**-18), 127.30 (**C**-31, **C**-33), 130.42 (**C**-30, **C**-34), 135.30 (**C**-17), 142.38 (**C**-29), 148.92 (**C**-32), 150.65 (**C**-15), 161.82 (**C**-5) ppm. EI-MS $m/z$: 576.34. Anal. Calcd. for $C_{33}H_{48}N_4O_3Si$: C, 68.71; H, 8.39; N, 9.71; O, 8.32; Si, 4.87. Found: C, 68.66; H, 8.30.

### *2.4. General method for synthesis of hexynyl-triazonine derivatives*

A solution of **7** (200 mg, 0.41 mmol) or **8** (200 mg, 0.35 mmol), 6-chlorohex-1-yne (77 µl, 0.69 mmol), and sodium hydroxyde (20 mg, 0.50 mmol) in 5 mL of MetOH/$CHCl_3$ (2:3) was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure. Thereafter, the residue was purified by crystallization from methanol:water (4:1).

#### *2.4.1. (2aS,7bZ,10Z,14Z,15aR)-9-(hex-5-yn-1-yl)-2a,15a-dimethyl-10-phenyl-2,2a,3,4,5,5a, 5b,6,7,7a,9,12,13,15,15a, 15b-hexadecahydro-1H-indeno[5′,4′:4,5]indeno[2,1-g][1,3,6] triazonin-3-ol (**9**)*

The product yield was of 67% of product, m.p. 186–188 °C; IR ($V_{max}$, $cm^{-1}$): 3400 and 3318, 2138 and 1580; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.78 (s, 3H), 0.92–1.16 (m, 5H), 1.22 (s, 3H), 1.36–1.48 (m, 4H), 1.52 (t, 2H, $J$ = 6.00 Hz), 1.57–1.60 (m, 2H), 1.62 (t, 2H, $J$ = 6.50 Hz), 1.70–1.88 (m, 4H), 1.90 (s, 1H), 1.96 (m, 1H), 2.18 (t, 2H, $J$ = 7.18 Hz) 2.50–3.60 (m, 3H), 3.80 (t, 2H, $J$ = 6.80 Hz) 4.30–4.48 (m, 4H), 6.40 (broad, 1H), 7.04–7.34 (m, 4), 7.42 (d, 1H, $J$ = 1.00), 7.50 (m, 1H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: 12.30 (**C**-25), 16.68 (**C**-24), 18.00 (**C**-36), 22.00 (**C**-22), 23.80 (**C**-14), 23.86 (**C**-20), 25.72 (**C**-37), 27.66 (**C**-34), 30.80 (**C**-13), 33.02 (**C**-9), 34.70 (**C**-21), 37.30 (**C**-23), 44.00 (**C**-11), 46.90

(**C**-7), 48.08 (**C**-19), 48.60 (**C**-6), 51.70 (**C**-10), 52.00 (**C**-3), 52.96 (**C**-8), 53.72 (**C**-2), 54.24 (**C**-33), 68.56 (**C**-38), 81.50 (**C**-12), 84.00 (**C**-37), 122.80 (**C**-18), 128.44 (**C**-28, **C**-32), 129.38 (**C**-29, **C**-31), 129.66 (**C**-30), 139.60 (**C**-27), 142.32 (**C**-17), 154.26 (**C**-17), 162.52 (**C**-5) ppm. EI-MS *m*/*z*: 511.35. Anal. Calcd. for $C_{34}H_{45}N_3O$: C, 79.80; H, 8.86; N, 8.21; O, 3.13. Found: C, 79.72; H, 8.78.

*2.4.2. (2aS,7bZ,10Z,14Z,15aR)-9-(hex-5-yn-1-yl)-3-((isopropyldimethylsilyl)oxy)-2a,15a-dimethyl-10-phenyl-2,2a,3,4,5,5a,5b,6,7,7a,9,12,13,15,15a,15b-hexadecahydro-1H-indeno[5′,4′:4,5] indeno[2,1-g][1,3,6]triazonine (**10**)*

The product yield was of 45% of product, m.p. 204–206 °C; IR ($V_{max}$, $cm^{-1}$): 3318, 2138 and 1558; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.07 (s, 6H), 0.80 (m, 1H), 0.89 (s, 3H), 0.92–0.93 (m, 2H), 1.00 (s, 6H), 1.04–1.18 (m, 3H), 1.22 (s, 3H), 1.32–1.38 (m, 4H), 1.52 (t, 2H, $J$ = 6.00 Hz), 1.57–1.59 (m, 1H), 1.64 (t, 2H, $J$ = 6.50 Hz), 1.65–1.88 (m, 5H), 1.90 (s, 1H), 2.18 (t, 2H, $J$ = 7.18 Hz) 2.50–3.60 (m, 3H), 3.80 (t, 2H, $J$ = 6.80 Hz) 4.30–4.48 (m, 4H), 7.04–7.34 (m, 4), 7.42 (d, 1H), 7.50 (m, 1H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: −4.08 (**C**-28, **C**-41), 11.40 (**C**-25), 15.60 (**C**-42), 16.66 (**C**-24), 16.94 (**C**-43, **C**-44), 18.04 (**C**-38), 22.00 (**C**-22), 23.50 (**C**-14), 23.82 (**C**-20), 25.72 (**C**-37), 27.66 (**C**-36), 31.00 (**C**-13), 33.30 (**C**-9), 34.70 (**C**-21), 36.72 (**C**-23), 43.30 (**C**-11), 46.84 (**C**-7), 48.02 (**C**-19), 48.60 (**C**-6), 51.94 (**C**-3), 51.96 (**C**-10), 52.96 (**C**-8), 53.72 (**C**-2), 54.20 (**C**-35), 68.56 (**C**-40), 80.90 (**C**-12), 84.00 (**C**-39), 122.80 (**C**-18), 128.42 (**C**-30, **C**-34), 129.38 (**C**-31, **C**-33), 129.62 (**C**-32), 139.60 (**C**-29), 142.28 (**C**-17), 154.18 (**C**-17), 162.52 (**C**-5) ppm. EI-MS *m*/*z*: 611.42. Anal. Calcd. for $C_{39}H_{57}N_3OSi$: C, 76.54; H, 9.39; N, 6.87; O, 2.61; Si, 4.59. Found: C, 76.46; H, 9.30.

*2.5. General method for synthesis of triazoninol derivatives*

A solution of **9** (0.39 mmol) or **10** (0.32 mmol) and benzaldehyde (100 µl, 0.98 mmol) was added to 10 ml of potassium hydroxide (20 mg, 0.50 mmol) in 7 ml of EtOH/MetOH/$CHCl_3$ (2:2:3) was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure. Thereafter, the residue was purified by crystallization from methanol:water (4:1)

*2.5.1. (7bZ,10Z,14Z)-9-(7-hydroxy-7-phenylhept-5-yn-1-yl)-2a,15a-dimethyl-10-phenyl-2,2a,3,4,5,5a,5b,6,7,7a,9,12,13,15,15a,15b-hexadecahydro-1H-indeno[5′,4′:4,5]indeno [2,1-g][1,3,6]triazonin-3-ol (**11**)*

The product yield was of 48% of product, m.p. 80–82 °C; IR ($V_{max}$, $cm^{-1}$): 3400, 3320, 2158 and 1558; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.80 (s, 3H), 0.92–1.18 (m, 5H), 1.22 (s, 3H), 1.32–1.48 (m, 5H), 1.53 (t, 2H, $J$ = 6.78 Hz), 1.60 (m, 1H), 1.64 (t, 2H, $J$ = 6.80 Hz), 1.72–1.92 (m, 5H), 2.22 (m, 2H), 2.50–3.60 (m, 3H), 3.80 (t, 2H, $J$ = 13.60 Hz), 4.26 (m, 4H), 4.32 (broad, 2H), 4.44 (m, 2H), 5.52 (s, 1H), 7.04–7.40 (m, 7H), 7.42 (d, 1H, $J$ = 1.64 Hz), 7.50–7.52 (m, 3H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: 12.26 (**C**-25), 18.70 (**C**-36), 19.12 (**C**-24), 22.00 (**C**-22), 23.70 (**C**-14), 24.12 (**C**-20), 26.22 (**C**-35), 27.66 (**C**-34), 30.78 (**C**-13), 33.08 (**C**-9), 34.70 (**C**-21), 36.67 (**C**-23), 43.54 (**C**-11), 46.60 (**C**-6), 47.10 (**C**-7), 48.92 (**C**-19), 51.00 (**C**-10), 51.96 (**C**-3), 52.96 (**C**-8), 53.76 (**C**-2), 54.20 (**C**-33), 63.40 (**C**-39), 80.38 (**C**-38), 81.50 (**C**-12), 84.28 (**C**-37), 122.80 (**C**-18), 126.32 (**C**-42, **C**-46), 128.20 (**C**-43, **C**-45), 128.25 (**C**-44), 129.45 (**C**-28, **C**-32), 129.40 (**C**-29, **C**-31), 129.72 (**C**-30), 139.58 (**C**-27), 141.20 (**C**-41), 142.28 (**C**-17), 154.25 (**C**-15), 162.62 (**C**-5) ppm. EI-MS *m*/*z*: 617.39 Anal. Calcd. for $C_{41}H_{51}N_3O_2$: C, 79.70; H, 8.32; N, 6.80; O, 5.18. Found: C, 79.62; H, 8.26.

*2.5.2. 7-((2aS,3S,7bZ,10Z,14Z,15aR)-3-((terbutyldimethylsilyl)oxy)-2a,15a-dimethyl-10-phenyl-1,2,2a,3,4,5,5a,5b,6,7,7a,12,13,15,15a,15b-hexadecahydro-9H-indeno[5′,4′:4,5] indeno[2,1-g][1,3,6]triazonin-9-yl)-phenylhept-3-yn-2-ol (**12**)*

The product yield was of 67% of product, m.p. 94–96 °C; 3320, 2158 and 1558; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.08 (s, 6H), 0.70 (s, 3H), 0.86 (s, 9H), 0.92–1.18 (m, 5H), 1.22 (s, 3H), 1.32–1.38 (m, 3H), 1.53 (t, 2H, $J$ = 6.78 Hz), 1.57–1.59 (m, 2H), 1.62 (t, 2H, $J$ = 6.80 Hz), 1.63–1.90 (m, 6H), 2.18 (m, 2H). 2.24 (broad, 1H), 2.50–3.50 (m, 3H), 3.80 (t, 2H, $J$ = 13.60 Hz), 4.26–4–44 (m, 4H), 5.52 (s, 1H), 7.04–7.40 (m, 7H), 7.43 (d, 1H, $J$ = 1.64 Hz), 7.50–7.52 (m, 3H) ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: −4.40 (**C**-28, **C**-43), 11.40 (C-25), 16.70 (C-24), 18.00 (C-44), 18.70 (C-38), 22.00 (C-22), 23.50 (C-14), 23.88 (C-20), 25.56 (C-45, C-52, C-53), 26.22 (C-37), 27.68 (C-36), 31.08 (C-13), 33.32 (**C**-9), 34.72 (**C**-21), 36.72 (**C**-23), 43.28 (**C**-11), 46.90 (**C**-7), 47.10 (**C**-7), 48.12 (**C**-19), 48.60 (**C**-6), 51.96 (**C**-3), 52.00 (**C**-10), 52.96 (**C**-8), 53.72 (**C**-2), 54.20 (**C**-35), 63.40 (**C**-41), 80.35 (**C**-40), 81.70 (**C**-12), 84.28 (**C**-39), 122.80 (**C**-18), 126.32 (**C**-47, **C**-51), 128.22 (**C**-48, **C**-50), 128.26 (**C**-49), 128.40 (**C**-30, **C**-34), 129.40 (**C**-31, **C**-33), 129.70 (**C**-32), 139.60 (**C**-29), 141.15 (**C**-46), 142.28 (**C**-17), 154.25 (**C**-15), 162.62 (**C**-5) ppm. EI-MS *m*/*z*: 731.48 Anal. Calcd. for $C_{47}H_{65}N_3O_2Si$: C, 77.10; H, 8.95; N, 5.74; O, 4.37; Si, 3.84. Found: C, 77.04; H, 8.87.

*2.6. General method for synthesis of triazonin-aldehyde derivatives*

A solution of **11** (200 mg, 0.32 mmol) or **12** (200 mg, 0.27 mmol) and Dimethyl sulfoxide (68 µl, 0.58 mmol) was stirred 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, and the residue was purified by crystallization from methanol: water (4:2).

*2.6.1. (2aS,3S,7bZ,10Z,14Z,15aR)-2a,15a-dimethyl-9-(8-oxo-7-phenyloct-5-yn-1-yl)-10-phenyl-2,2a,3,4,5,5a,5b,6,7,7a,9,12,13,15,15a,15b-hexadecahydro-1H-indeno[5′,4′:4,5] indeno [2,1-g][1,3,6] triazonine-3-carbaldehyde (**13**)*

The product yield was of 87%; m.p. 104–106 °C; 3320, 2158, 1725 and 1558; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.74 (s, 3H), 0.88–1.20 (m, 3H), 1.22 (s, 3H), 1.24–1.54 (m, 6H), 1.56–1.64 (m, 4H), 1.68–1.98 (m, 6H), 2.10 (m, 2H) 2.14–3.20 (m, 4H), 3.80 (t, 2H, $J$ = 13.60 Hz), 4.26 (m, 2H), 4.40 (s, 1H), 4.44 (m, 2H), 7.04–7.34 (m, 7H), 7.43 (d, 1H, $J$ = 1.64 Hz), 7.50–7.60 (m, 3H), 9.70 (d, 1H, $J$ = 2.00 Hz), 9.82 (d, 1H, $J$ = 1.75 Hz), ppm. $^{13}C$ NMR (75.4 Hz, $CDCl_3$) $\delta_C$: 14.50 (**C**-25), 16.70 (**C**-24), 18.90 (**C**-35), 22.33 (**C**-13), 23.44 (**C**-22), 23.82 (**C**-19), 24.34 (**C**-21), 26.22 (**C**-34), 27.68

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(**C**-33), 34.72 (**C**-20), 35.50 (**C**-9), 38.00 (**C**-12), 39.00 (**C**-38), 42.90 (**C**-11), 46.86 (**C**-7), 48.08 (**C**-18), 48.58 (**C**-6), 52.00 (**C**-3), 53.80 (**C**-2), 54.20 (**C**-32), 54.40 (**C**-8), 54.42 (**C**-10), 55.00 (**C**-23), 79.80 (**C**-37), 81.75 (**C**-36), 122.80 (**C**-17), 125.90 (**C**-44, **C**-48), 127.00 (**C**-46), 128.40 (**C**-27, **C**-31), 129.45 (**C**-28, **C**-30), 129.72 (**C**-29), 131.50 (**C**-45, **C**-47), 135.34 (**C**-43), 139.60 (**C**-26), 142.28 (**C**-16), 154.25 (**C**-14), 162.60 (**C**-5), 191.78 (**C**-39), 204.10 (**C**-41) ppm. EI-MS *m*/*z*: 641.39 Anal. Calcd. for $C_{43}H_{51}N_3O_2$: C, 80.46; H, 8.01; N, 6.55; O, 4.99. Found: C, 80.38; H, 7.96.

#### *2.6.2. 8-((2aS,3S,7bZ,10Z,14Z,15aR)-3-((terbutyldimethylsilyl)oxy)-2a,15a-dimethyl-10-phenyl-1,2,2a,3,4,5,5a,5b,6,7,7a,12,13,15,15a,15b-hexadecahydro-9H-indeno[5′,4′:4,5] indeno[2,1-g][1,3,6]triazonin-9-yl)-2-phenyloct-3-ynal (**14**)*

The product yield was of 66% of product, m.p. 116–118 °C; 3318, 2158, 1724 and 1558; $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.08 (s, 6H), 0.70 (s, 3H), 0.86 (s, 9H), 0.92–1.18 (m, 5H), 1.22 (s, 3H), 1.36–1.38 (m, 3H), 1.53 (t, 2H, $J$ = 6.00 Hz), 1.56 (s, 3H), 1.58–1.60 (m, 2H), 1.62 (t, 2H, $J$ = 6.50 Hz), 1.63–1.90 (m, 6H), 2.14 (m, 2H), 2.50–3.54 (m, 3H) 3.80 (t, 2H, $J$ = 13.60 Hz), 4.26 (m, 2H), 4.40 (s, 1H), 4-44 (m, 2H), 7.04–7.34 (m, 7H), 7.43 (d, 1H, $J$ = 1.64 Hz), 7.50–7.58 (m, 3H), 9.72 (d, 1H, $J$ = 1.75 Hz) ppm. $^{13}$C NMR (75.4 Hz, $CDCl_3$) $\delta_C$: −4.42 (**C**-28, **C**-44), 11.40 (**C**-25), 16.70 (**C**-24), 18.04 (**C**-45), 18.90 (**C**-38), 22.00 (**C**-22), 23.50 (**C**-14), 23.88 (**C**-20), 25.56 (**C**-46, **C**-53, **C**-54), 26.22 (**C**-37), 27.68 (**C**-36), 31.08 (**C**-13), 33.38 (**C**-9), 34.72 (**C**-21), 36.72 (**C**-23), 38.96 (**C**-41), 43.28 (**C**-11), 46.90 (**C**-7), 48.10 (**C**-19), 48.62 (**C**-6), 51.96 (**C**-3), 52.00 (**C**-10), 52.96 (**C**-8), 53.82 (**C**-2), 54.20 (**C**-35), 79.78 (**C**-40), 81.65 (**C**-12), 81.76 (**C**-39), 122.80 (**C**-18), 125.92 (**C**-48, **C**-52), 127.00 (**C**-50), 128.40 (**C**-30, **C**-34), 129.45 (**C**-31, **C**-33), 129.72 (**C**-32), 131.48 (**C**-49, **C**-51), 135.28 (**C**-47), 139.60 (**C**-29), 142.30 (**C**-17), 154.25 (**C**-15), 162.60 (**C**-5), 191.80 (**C**-42) ppm. EI-MS *m*/*z*: 743.48 Anal. Calcd. for $C_{48}H_{65}N_3O_2Si$: C, 77.47; H, 8.80; N, 5.65; O, 4.30; Si, 3.77. Found: C, 77.38; H, 8.73.

### *2.7. General method for synthesis of formyl-triazonin-carbaldehyde derivatives via alkynylation/cyclization*

A solution of **13** or **14** (0.50 mmol), hexyne (100 µl, 0.88 mmol), and Copper(II) (100 mg, 0.72 mmol) in 3 ml of MetOH was stirred for 72 h at room temperature. The reaction mixture was evaporated to dryness under reduced pressure. Thereafter, the residue was purified by crystallization from methanol:water (4:1)

#### *2.7.1. (2aS,3S,7bZ,10Z,14Z,15aR)-9-(4-(5-butyl-2-formyl-3-phenylcyclopenta-1,4-dien-1-yl) butyl)-2a,15a-dimethyl-10-phenyl-2,2a,3,4,5,5a,5b,6,7,7a,9,12,13,15,15a,15b-hexadecahydro-1H-indeno[5′,4′:4,5]indeno[2,1-g][1,3,6] triazonine-3-carbaldehyde (**15**)*

The product yield was of 56% of product, m.p. 120–122 °C; 3318, 2158, 1724, 1558 and 1510; $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.74 (s, 3H), 0.84 (m, 1H), 1.00 (s, 3H), 1.10–1.20 (m, 2H), 1.22 (s, 3H), 1.24–1.44 (m, 5H), 1.45 (m, 2H), 1.46 (m, 2H), 1.52 (m, 2H), 1.54 (m, 1H), 1.62 (t, 2H, $J$ = 6.80 Hz), 1.70–2.24 (m, 8H) 2.32 (t, 2H, $J$ = 13.80.80 Hz), 2.46 (t, 2H, $J$ = 13.80 Hz), 2.50–3.20 (m, 2H), 3.68 (t, 2H, $J$ = 13.60 Hz), 4.00 (s,1H), 4.26–4.44 (m, 4H), 6.70 (d, 1H, 1.58 Hz), 7.04–7.34 (m, 7H), 7.43 (d, 1H, $J$ = 1.64 Hz), 7.50–7.56 (m, 3H), 9.20 (d, 1H, $J$ = 0.90 Hz), 9.80 (d, 1H, $J$ = 1.75 Hz) ppm. $^{13}$C NMR (75.4 Hz, $CDCl_3$) $\delta_C$: 14.00 (**C**-56), 14.50 (**C**-25), 16.68 (**C**-24), 22.30 (**C**-13), 22.56 (**C**-53), 23.40 (**C**-22), 23.88 (**C**-19), 24.36 (**C**-21), 26.40 (**C**-34), 28.18 (**C**-33), 28.68 (**C**-35), 30.88 (**C**-52), 32.08 (**C**-51), 34.72 (**C**-20), 35.52 (**C**-9), 38.00 (**C**-12), 42.90 (**C**-11), 46.90 (**C**-7), 48.04 (**C**-18), 48.62 (**C**-6), 51.58 (**C**-38), 52.00 (**C**-3), 53.30 (**C**-32), 53.80 (**C**-2), 54.40 (**C**-8), 54.42 (**C**-10), 55.00 (**C**-23), 122.80 (**C**-17), 126.76 (**C**-46, **C**-50), 127.64 (**C**-48, **C**-50), 127.65 (**C**-39), 128.40 (**C**-27, **C**-31), 128.80 (**C**-47, **C**-49), 129.45 (**C**-28, **C**-30), 129.72 (**C**-29), 135.00 (**C**-45), 139.62 (**C**-26), 141.30 (**C**-37), 142.28 (**C**-16), 152.70 (**C**-40), 154.25 (**C**-14), 162.60 (**C**-5), 165.74 (**C**-36), 186.30 (**C**-43), 204.10 (**C**-41) ppm. EI-MS *m*/*z*: 723.47 Anal. Calcd. for $C_{49}H_{61}N_3O_2$: C, 81.28; H, 8.49; N, 5.80; O, 4.42. Found: C, 81.18; H, 8.40.

#### *2.7.2. 3-butyl-2-(4-((2aS,3S,7bZ,10Z,14Z,15aR)-3-((terbutyldimethylsilyl)oxy)-2a,15a-dimethyl-10-phenyl-1,2,2a,3,4,5,5a,5b,6,7,7a,12,13,15,15a,15b-hexadecahydro-9H-indeno[5′,4′:4,5]indeno[2,1-g][1,3,6]triazonin-9-yl)-butyl)-5-phenylcyclopenta-1,3-diene-1-carbaldehyde (**16**)*

The product yield was of 68% of product, m.p. 142–144 °C; 3320, 2158, 1724, 1558 and 1512; $^1$H NMR (300 MHz, $CDCl_3$) $\delta_H$: 0.07 (s, 6H), 0.68 (s, 3H), 0.84 (s, 9H), 0.90–0.94 (m, 2H), 1.00 (s, 3H), 1.06–1.18 (m, 3H), 1.22 (s, 3H), 1.34–1.38 (m, 3H), 1.46 (t, 2H, $J$ = 7.00 Hz), 1.47–1.52 (m, 4H), 1.58–1.60 (m, 2H), 1.62 (t, 2H, $J$ = 0.25 Hz), 1.64–1.88 (m, 6H), 2.30 (t, 2H, $J$ = 0.90 Hz), 2.44 (t, 2H, $J$ = 0.90 Hz), 2.50–3.50 (m, 3H), 3.68 (t, 2H, $J$ = 13.60 Hz), 4.00 (d, 1H, 2.00 Hz), 4.26–4-44 (m, 4H), 6.70 (d, 1H, 1.40 Hz), 7.04–7.34 (m, 7H), 7.43 (d, 1H, $J$ = 0.99 Hz), 7.50–7.56 (m, 3H), 9.20 (d, 1H, $J$ = 0.90 Hz) ppm. $^{13}$C NMR (75.4 Hz, $CDCl_3$) $\delta_C$: −4.60 (**C**-28, **C**-44), 11.40 (**C**-25), 14.00 (**C**-58), 16.68 (**C**-24), 18.00 (**C**-45), 22.00 (**C**-22), 22.50 (**C**-57), 23.50 (**C**-14), 23.88 (**C**-20), 25.50 (**C**-46, **C**-59, **C**-60), 26.40 (**C**-37), 28.18 (**C**-36), 28.68 (**C**-38), 30.88 (**C**-56), 31.00 (**C**-13), 32.00 (**C**-55), 33.30 (**C**-9), 34.72 (**C**-21), 36.73 (**C**-23), 43.30 (**C**-11), 46.90 (**C**-7), 48.04 (**C**-19), 48.62 (**C**-6), 51.60 (**C**-41), 51.96 (**C**-3), 52.00 (**C**-10), 53.00 (**C**-8), 53.30 (**C**-35), 53.80 (**C**-2), 81.60 (**C**-12), 122.80 (**C**-18), 126.76 (**C**-50, **C**-54), 127.60 (**C**-42, **C**-52), 128.40 (**C**-30, **C**-34), 128.80 (**C**-53), 129.45 (**C**-31, **C**-33), 129.72 (**C**-32), 134.98 (**C**-49), 139.66 (**C**-29), 141.30 (**C**-40), 142.28 (**C**-17), 152.70 (**C**-43), 154.25 (**C**-15), 162.60 (**C**-5), 165.78 (**C**-39), 186.30 (**C**-47) ppm. EI-MS *m*/*z*: 825.26 Anal. Calcd. for $C_{54}H_{75}N_3O_2Si$: C, 78.49; H, 9.15; N, 5.09; O, 3.87; Si, 3.40. Found: C, 78.40; H, 9.04.

## *3.* Results and discussion

### *3.1. Nitrobenzamide derivatives*

The triazonine-carbaldehyde derivatives were synthesized using several methods; the first stage involves the reaction of an azide with the unsaturated ketone to form two nitrobenzamide derivatives. It is noteworthy, that there are several protocols which indicate that some azide groups react with saturated ketones upon treatment with Lewis acids to afford ring-expansion products through the azido-Schmidt reaction

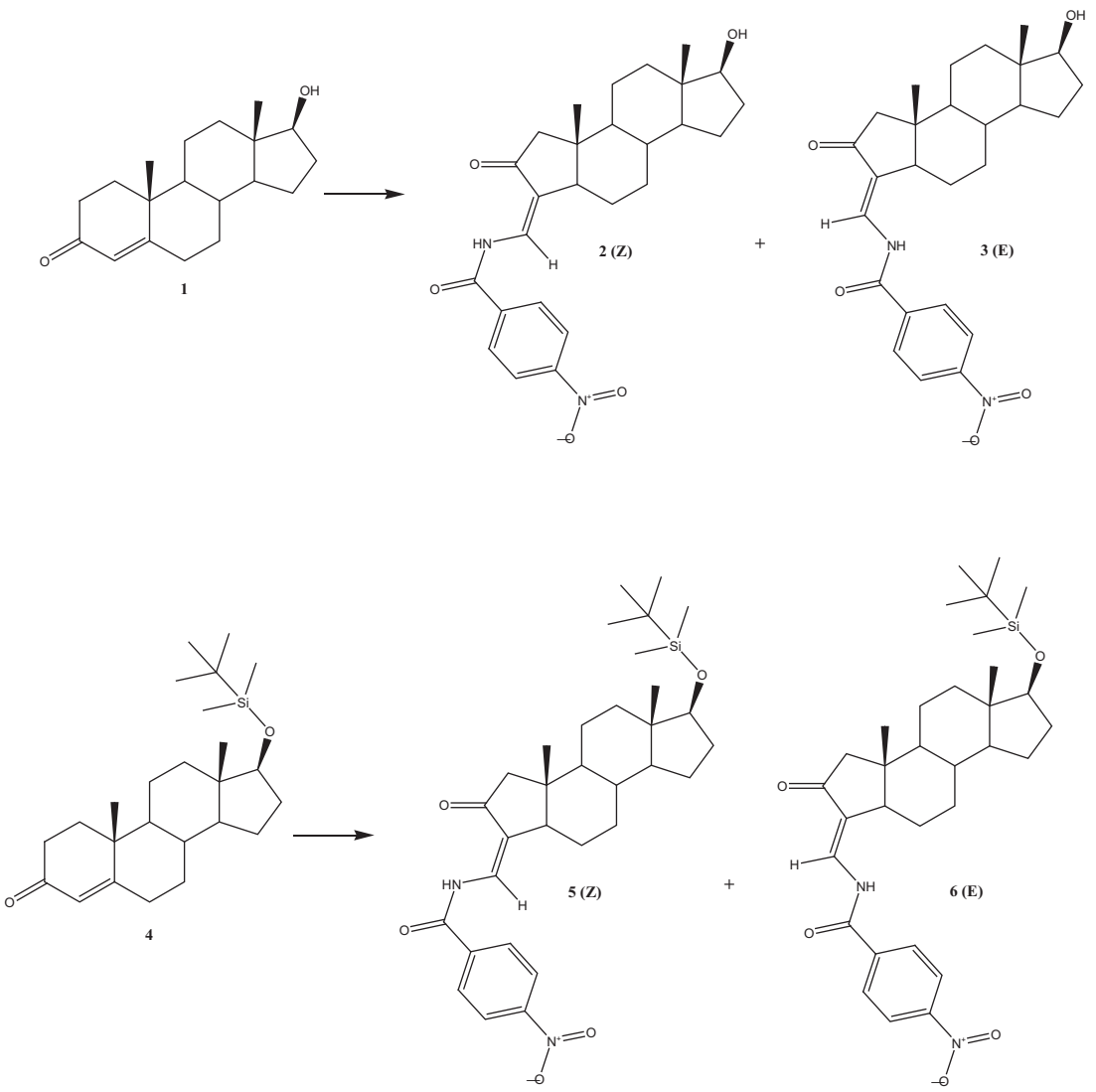


**Figure 1** Synthesis of nitrobenzamide derivatives (**2**, **3**, **5** and **6**) by reaction of testosterone (**1**) or OTBS-testosterone (**3**) with *p*-nitrobenzoyl azide using Copper(II) as catalyst (i).

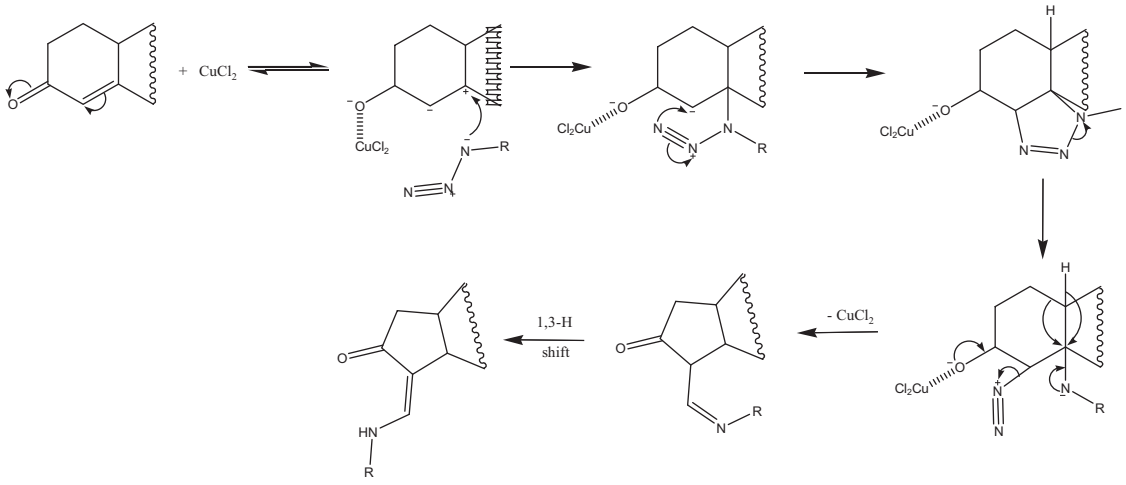


**Figure 2** Mechanism of reaction involved in the synthesis of nitrobenzamide derivatives.

[13,14]. However, other studies indicate that the amines react with unsaturated cyclic ketones which can lead to the contraction of the ring in the presence of a Lewis acid [15]. This hypothesis is available by the reports of Reddy and coworkers which showed that azide reacts with unsaturated ketones in the presence of TMSOTf or BF3-Et2O to form enaminones [16]. Therefore, in this investigation the compound **2** was prepared by the reaction of *p*-nitrobenzoyl azide with testosterone using Copper(II) reagent (Fig. 1). The mechanism of reaction involves (1) 1,3-dipolar cycloaddition of the Copper(II) reagent to the unsaturated ketone; (2) electrophilic attack of the azide to $\mathbf{C_5}$ of the steroid derivative for producing a triazoline as intermediary; and (3) elimination of nitrogen followed by a contraction of the A ring from steroid nucleus to form a cyclopentanone (Fig. 2).

The $^{1}$H NMR spectrum of **2** showed several signals at 0.78 and 1.08 ppm for methyl groups; at 0.92–0.96 and 1.08–3.60 ppm for hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 4.86 ppm for proton of alkene group; at 8.00–8.22 ppm for phenyl group; and at 8.30 ppm for both amide and hydroxyl groups. The $^{13}$C NMR spectra display chemical shifts at 12.28–12.84 ppm for methyl groups; at 22.08–81.50 and 129.22 ppm for hexadecahydrodicyclopenta[*a*,*f*]naphthalene fragment; at 124.26, 129.30–136.12 and 150.63 ppm for phenyl group; at 149.32 ppm for alkene group; at 164.22 ppm for amide group; and at 2015.12 ppm for ketone group. Finally, the presence of compound **2** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 452.23. Moreover, the $^{1}$H NMR spectrum of compound **3** showed significantly differences in comparison with **2** at 4.46 ppm for alkene group and 8.80 ppm for amide group.

On the other hand, the compounds **5** and **6** were synthesized using the same route involving reaction from **2** or **3** with *p*-nitrobenzoyl azide in the presence of Copper (II) reagent. The $^{1}$H NMR spectrum of **5** shows signals at 0.07 and 0.90 ppm for the protons involved in the *tert-butyldimethylsilane* fragment; at 0.70 and 1.06 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 0.92–3.50 ppm for hexadecahydro-dicyclopenta [*a*,*f*]naphthalene fragment; at 4.86 ppm for alkene group; at 8.00–8.22 ppm for phenyl group; and at 10.30 ppm for amide group. The $^{13}$C NMR spectra displays chemical shifts at −4.60, 18.00 and 25.50 ppm for carbons involved in the *tert-butyldimethylsilane* fragment; at 11.42 and 12.90 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]-naphthalene fragment; at 22.08–23.64, 31.00–81.70 and 129.22 ppm for hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 124.26, 129.30–136.12 and 150.65 ppm for phenyl group; at 149.32 ppm for alkene group; at 164.22 ppm for amide group; and at 205.12 ppm for carbonyl group. Finally, the presence of compound **5** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 566.31. In addition, it is important to mention that the $^{1}$H NMR spectrum of compound **6** shows significantly differences in comparison with **5** at 4.44 ppm for alkene group and 11.30 ppm for amide group.

All these data show a high stereoselectivity on compounds **2** (*Z*) and **5**(*Z*) in comparison with their steroisomers-E. The regioselectivity must be a function of the Lewis acid used in these reactions and not an inherent selectivity of the substrate. Therefore, it is important to mention that the compounds **2** and **5** were used in following reaction.

### 3.2. Synthesis of triazonine derivatives

Several triazonine derivatives have been prepared using different protocols which involve the use of special reagents such as $H_2SO_4$ [17], MeI [18], tetrabutylammonium [19] and others. In this study, two triazonine derivatives (**7** or **8**) were synthesized by the reaction of **2** or **5** with ethylenediamine using boric acid as catalyst (Fig. 3). The mechanism of reaction involves (Fig. 4): (1) addition of boric acid to the ketone group; (2) electrophilic attack of amino group to the carbon which is bound to phenyl group; and (3) elimination of boric acid adduct and formation of the imino group. This premise is supported by other studies involved in the synthesis of some imino derivatives [19]. The $^{1}$H NMR spectrum of **7** shows signals at 0.78 and 1.22 ppm for methyl groups; at 0.90–1.16 and 1.36–3.64 ppm for hexadecahydrodicyclopenta[*a*,*f*]naphthalene fragment; at 4.34–4.60 ppm for methylene groups bound to both imino groups; at 7.40 ppm for alkene group; at 7.42 and 8.22 ppm for phenyl group; and at 7.44 ppm for both amino and hydroxyl groups. The $^{13}$C NMR spectra display chemical shifts at 12.34 and 16.74 ppm for methyl groups; at 22.00–51.70, 52.96 and 81.50–125.02 ppm for hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 51.94 and 53.12 ppm for methylene groups bound to both imino groups; at 127.30–130.42 and 142.38–148.92 ppm for phenyl groups; at 135.30 ppm for alkene group; and at 150.65–161.82 ppm for imino groups. Finally, the presence of compound **7** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 476.27.

Another data showed several signals involved in $^{1}$H NMR spectrum for compound **8** at 0.07–0.80 and 1.00 ppm for protons involved in the *tert*-butyldimethylsilane fragment; at 0.90 and 1.22 ppm for methyl groups bound to cyclohexane rings; at 0.92–0.93, 1.04–1.18, and 1.34–3.60 ppm for hexadecahydro-dicyclopenta[a,f]naphthalene fragment; at 4.34–4.60 ppm for methylene groups bound to both imino groups; at 7.40 ppm for alkene group; at 7.42–8.22 ppm for phenyl groups; and at 8.50 ppm for amino group. The $^{13}$C NMR spectra display chemical shifts at −4.08, 15.60 and 16.90 ppm for carbons involved in the *tert*-butyldimethylsilane fragment; at 11.42 and 16.66 ppm for methyl groups bound to cyclohexane rings; at 22.00–48.60, 52.96 and 80.90–125.02 ppm for hexadecahydrodicyclopenta[*a*,*f*] naphthalene fragment; at 51.85 and 53.12 ppm for methylene groups; at 127.30–130.42 and 142.38–148.92 ppm for phenyl groups; at 135.30 ppm for alkene group; and at 150.65–161.82 ppm for imino groups. Finally, the presence of compound **8** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 576.34.

### 3.3. Hexynyl-triazonines derivatives

There are studies which show the reaction of chloro-hexyne derivatives with secondary amines: for example, the preparation of *β*-Alkynyl-*β*-amino esters through Ag-catalyzed asymmetric Mannich reactions of silylketene acetals and alkynyl imines [20]. Another data indicate the preparation of 1-hex-5-ynyl-1*H*-indole-3-carboxylic acid amide by the reaction of 5-chloro-1-pentyne or 6-chloro-1-hexyne with indole-3-acetamide in basic medium [21]. Therefore, in this investigation the compound **7** or **8** was reacted with 6-chloro-1-hexyne in basic conditions to form the compound **9** or **10** through a

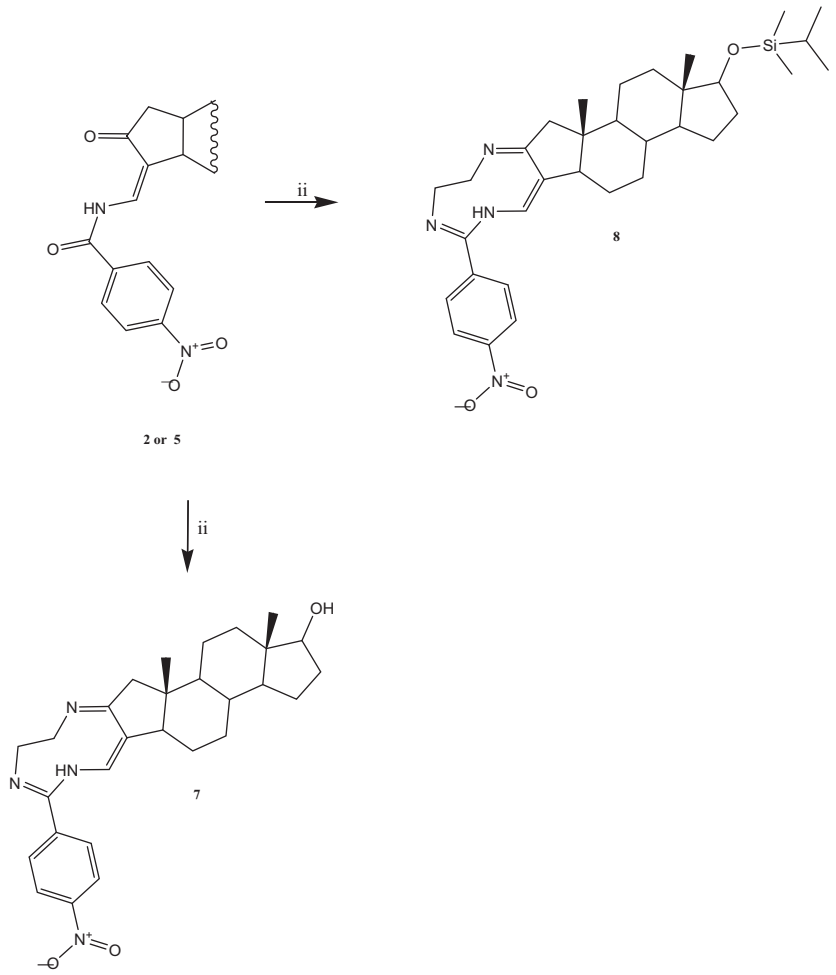


**Figure 3** Synthesis of triazonine derivatives (**7** and **8**). Reaction of nitrobenzamide analogs (**2** or **5**) with ethylenediamine to form the compound **7** or **8**. ii = Boric acid/rt.

$SN_2$ mechanism (Figs. 5 and 6). The $^1$H NMR spectrum of **9** shows signals at 0.78 and 1.22 ppm for methyl groups; at 0.92–1.16, 1.36–1.48, 1.57–1.60, 1.70–1.88 and 2.50–3.60 ppm for hexadecahydrodicyclopenta [a,f]naphthalene fragment; at 1.90 ppm from alkyne group; at 1.52, 1.62, 2.48 and 3.80 ppm for methylene groups bound to both amino and alkyne groups; at 4.30–4.80 ppm for methylene bound to imino groups; at 6.40 ppm for hydroxyl group; at 7.42 ppm for alkene group; and at 7.04–7.34 and 7.50 for phenyl groups. The $^{13}$C NMR spectra display chemical shifts at 12.30 and 16.70 ppm for methyl groups; at 18.00, 25.72–27.66 and 54.24 ppm for methylene groups bound to both alkyne and amine groups; at 22.00–23.86, 30.80–52.96, 81.50 and 122.80 ppm for hexadecahydrodicyclopenta[a,f]naphthalene fragment; at 52.00 and 53.72 ppm for methylene bound to imino groups; at 68.56 and 84.00 ppm for carbons of alkyne group; at 128.44–139.60 ppm for phenyl group; at 142.32 for alkene; and at 154.26–162.52 for imino groups. Finally, the presence of compound **9** was confirmed with mass spectrum which showed a molecular ion at $m/z$ 511.35.

The $^1$H NMR spectrum for compound **10** showed signals at 0.89 and 1.22 ppm for methyl groups; at −0.07–0.80 and 1.00 ppm for protons involved in the *tert*-butyldimethylsilane fragment; at 0.92–0.93, 1.04–1.18, 1.32–1.38, 1.57–1.59, 1.65–1.88 and 2.50–3.60 ppm for hexadecahydro-dicyclopenta [a,f]naphthalene fragment; at 1.52, 1.62, 2.18 and 3.80 ppm for methylene bound to both amino and alkyne groups; at 1.90 ppm for proton of alkyne; at 4.30–4.48 ppm for methylene bound to imino groups; at 7.42 ppm for alkene group; and at 7.04–7.34 and 7.50 ppm for phenyl groups. The $^{13}$C NMR spectra display chemical shifts at 11.40 and 16.66 ppm for methyl groups; at −4.08, 15.60 and 15.94 ppm for carbons involved in the *tert*-butyldimethylsilane fragment; at 18.04, 25.72–27.66 and 54.20 ppm for methylene bound to both amino and alkyne groups; at 22.00–23.82, 31.00–48.60, 51.96–52.96, 80.90 and 122.80 ppm for hexadecahydro-dicyclopenta[a,f]na phthalene fragment; at 51.94 and 53.72 ppm for methylene bound to imino groups; at 68.56 and 84.00 ppm for carbons of alkyne group; at 128.42–139.60 ppm for phenyl group; at 142.28 for alkene; and at 154.26–162.52 ppm for imino groups. Finally, the presence of compound **10** was confirmed with mass spectrum which showed a molecular ion at $m/z$ 611.42.

### *3.4. Propargylic-alcohols derivatives via reaction of terminal alkynes with aldehydes*

Several propargylic alcohols have been developed by the reaction of terminal alkynes with aldehyde groups using some

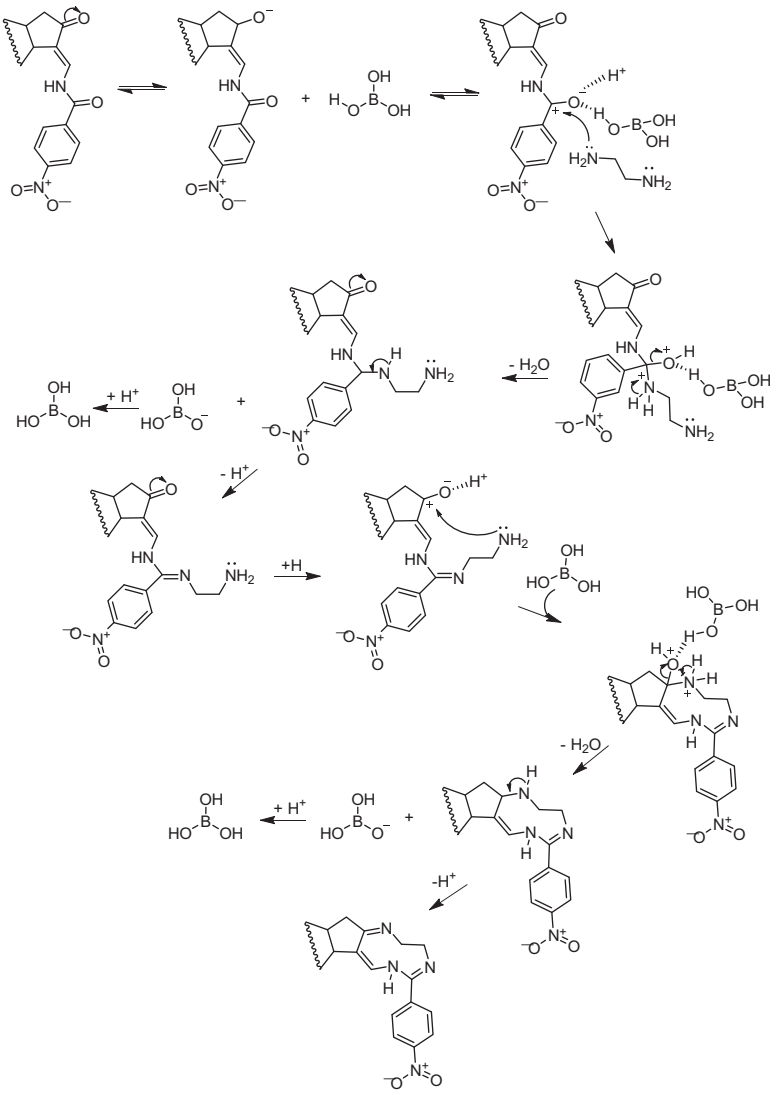

**Figure 4** Mechanism of reaction involved in the synthesis of triazonine derivatives.

reagents such as *N*-methyl-ephedrine [22] Zn(OTf)2 [23], Ti(O-i-Pr)4-BINOL [24] and others [25]; however, some of these reagents are difficult to handle required and special conditions. Therefore, in this study, the compound **9** or **10** was reacted with benzaldehyde in basic conditions to form the compound **11** or **12** (Figs. 7 and 8). The $^{1}$H NMR spectrum for compound **11** showed signals at 0.80 and 1.22 ppm for methyl groups bound to hexadecahydrodicyclo-penta[*a*,*f*]-naphthalene fragment; at 0.92–1.18, 1.32–1.48, 1.72–1.92 and 2.50–3.60 ppm for hexadecahydrodicyclopenta[a,f] naphthalene fragment; at 1.53, 1.64, 2.20 and 3.80 ppm for methylene groups bound to both amino and alkyne groups; at 4.26 and 4.44 ppm for methylene groups bound to imino groups; at 4.32 ppm for hydroxyl groups; at 7.04–7.40 and 7.50–7.52 ppm for phenyl groups; and at 7.44 ppm for alkene group. The $^{13}$C NMR spectra display chemical shifts at 12.26–19.12 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 22.00–24.12, 30.78–51.00, 52.96, 81.50 and 122.80 ppm for hexadecahydrodi cyclopenta[a,f] naphthalene fragment; at 18.70, 26.22–27.66 and 54.20 ppm for methylene groups bound to both amino and alkyne groups; at 51.96 and 53.76 ppm for carbons bound to imino groups; at 63.40 ppm for carbon bound to both hydroxyl and phenyl groups; at 82.38 and 84.28 ppm for alkyne group; at 126.32–141.20 ppm for phenyl groups; at 142.28 ppm for alkene group; and at 154.25–162.62 ppm for imino groups. Finally, the presence of compound **11** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 617.39.

Another data showed several signals involved in the $^{1}$H NMR spectrum for compound **12** at 0.08 and 0.86 ppm for protons involved in the *tert*-butyldimethylsilane fragment; at 0.70 and 1.22 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 0.92–1.18, 1.57–1.59, 1.63–1.90 and 2.50–3.50 ppm for hexadecahydrodicyclo-penta[*a*,*f*]naphthalene fragment; at 1.53, 1.62, 2.18 and 3.80 ppm for methylene groups bound to both amino and alkyne groups; at 2.24 ppm for hydroxyl group; at 4.26–4.40 ppm for methylene groups bound to imino groups; at 5.52 ppm for methylene group bound to both hydroxyl and phenyl groups; at 7.04–7.40 and 7.50–7.52 ppm for phenyl groups; and at 7.43 ppm for alkene group. The

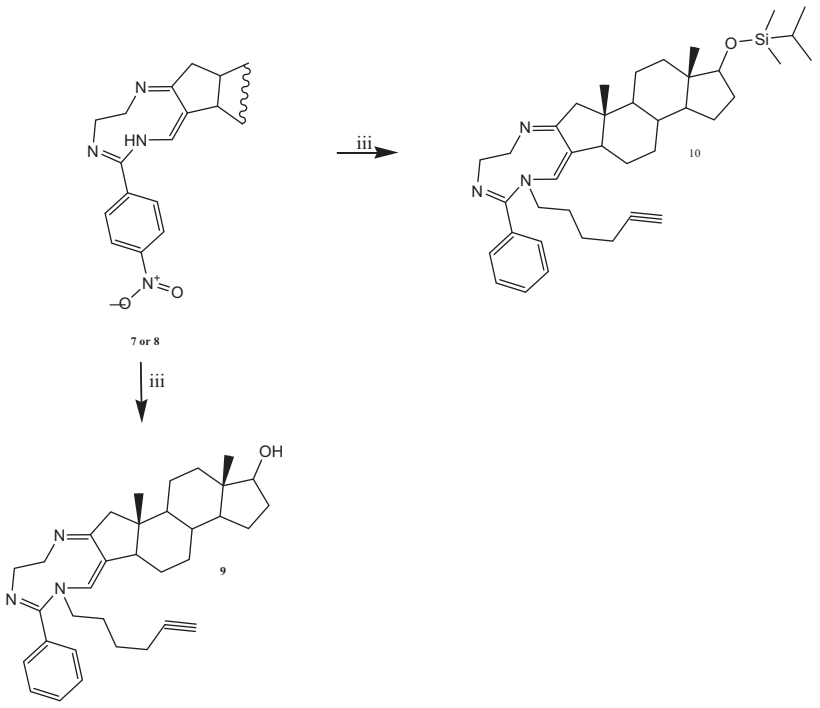


**Figure 5** Reaction of the triazonine (**7** or **8**) with 6-chloro-1-hexyne to form two hexynyl-triazonine derivatives (**9** or **10**). iii = Boric acid.

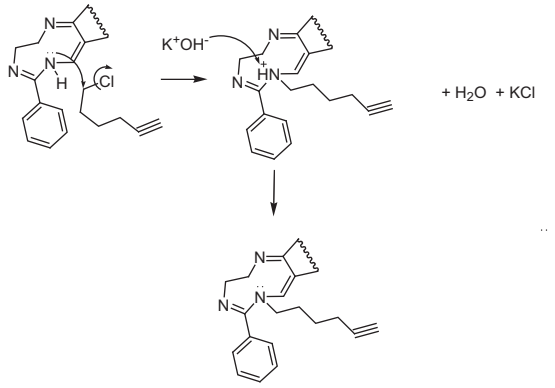


**Figure 6** Mechanism of reaction involved in the preparation of hexynyl-triazonine derivatives.

$^{13}$C NMR spectra display chemical shifts at −4.40, 18.00 and 25.56 for carbons of the *tert*-butyldimethylsilane fragment; at 11.40 and 16.70 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 18.70, 26.22–27.68 and 54.20 ppm for methylene groups bound to both amino and alkyne groups; at 22.00–23.88, 31.08–48.60, 52.00–52.96, 81.70 and 122.80 ppm hexadecahydrodicyclopenta[*a*,*f*]naphthalene fragment; at 51.96 and 53.72 ppm for methylene groups bound to imino groups; at 63.40 ppm for carbon bound to both hydroxyl and phenyl groups; at 80.35 and 84.28 ppm for alkyne group; at 126.40–141.15 ppm for phenyl groups; at 142.28 ppm for alkene group; and at 154.25–162.62 ppm for imino groups. Finally, the presence of compound **12** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 731.48.

### *3.5. Preparation of triazonine-aldehyde derivatives via oxidation of alcohol groups*

It is noteworthy that there are several reports on the oxidation of primary alcohols to form the corresponding aldehydes. These compounds can be prepared with some techniques which are accomplished by stoichiometric amounts of metallic oxidants such as chromium(VI) palladium, rhodium or ruthenium and hydrogen peroxide reagents [26]. However, these reagents may induce risks of toxicity by generation of several substances involved on some reaction mixtures. Therefore, in this study a method previously reported [27] for oxidation of hydroxyl groups was used for formation of **13** and **14** by the reaction of **11** or **12** with DMSO (Fig. 9). The $^{1}$H NMR spectrum for compound **13** showed signals at 0.78 and 1.22 ppm for methyl groups bound to hexadecahydrodicyclopenta[*a*,*f*] naphthalene fragment; at 0.88–1.20, 1.24–1.54, 1.68–1.98 and 2.14–3.20 ppm for hexadecahydrodicyclopenta[*a*,*f*] naphthalene fragment; at 1.56–1.64, 2.10 and 3.80 ppm for methylene groups bound to both amino and alkyne groups; at 4.26 and 4.44 ppm for methylene groups bound to imino groups; at 4.40 ppm for methylene group bound to both aldehyde and phenyl groups; at 7.04–7.34 and 7.50–7.60 ppm for phenyl groups; at 7.43 ppm for alkene group; and at 9.70–9.82 ppm for aldehyde groups. The $^{13}$C NMR spectra display chemical shifts at 14.50 and 16.70 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 22.33–24.34, 34.72–38.00, 42.90–48.58, 54.40–55.00 and 122.80 ppm for hexadecahydro-dicyclopenta[a,f]naphthalene fragment; at 18.90, 26.22–27.68 and 54.20 ppm for methylene groups bound to both amino and alkyne groups; at 39.00 ppm for carbon bound to both aldehyde and phenyl

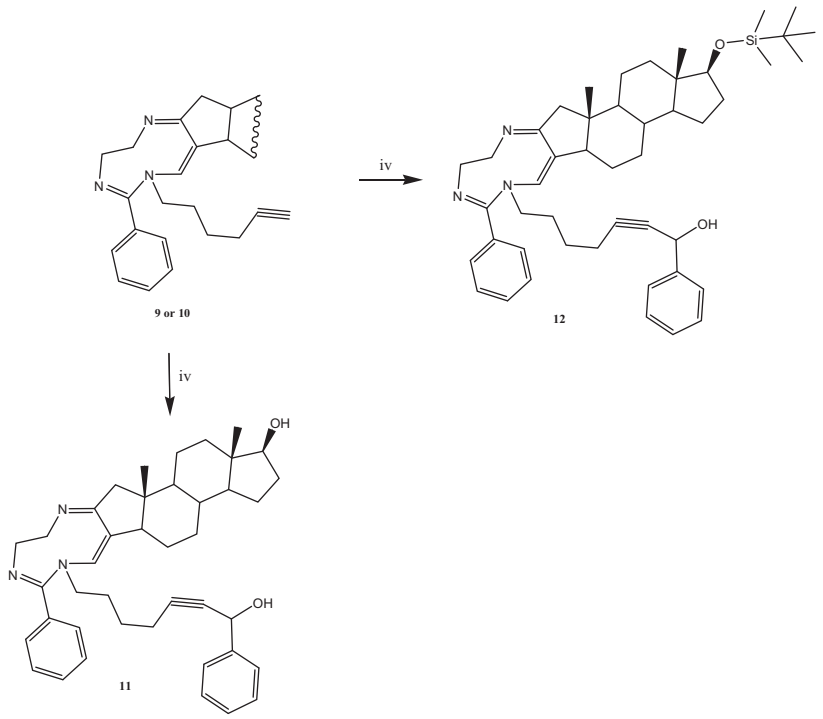


**Figure 7** Preparation of triazoninol derivatives (**11** or **12**) by the reaction of hexynyl-triazonine derivatives (**8** or **10**) with benzaldehyde (iv).

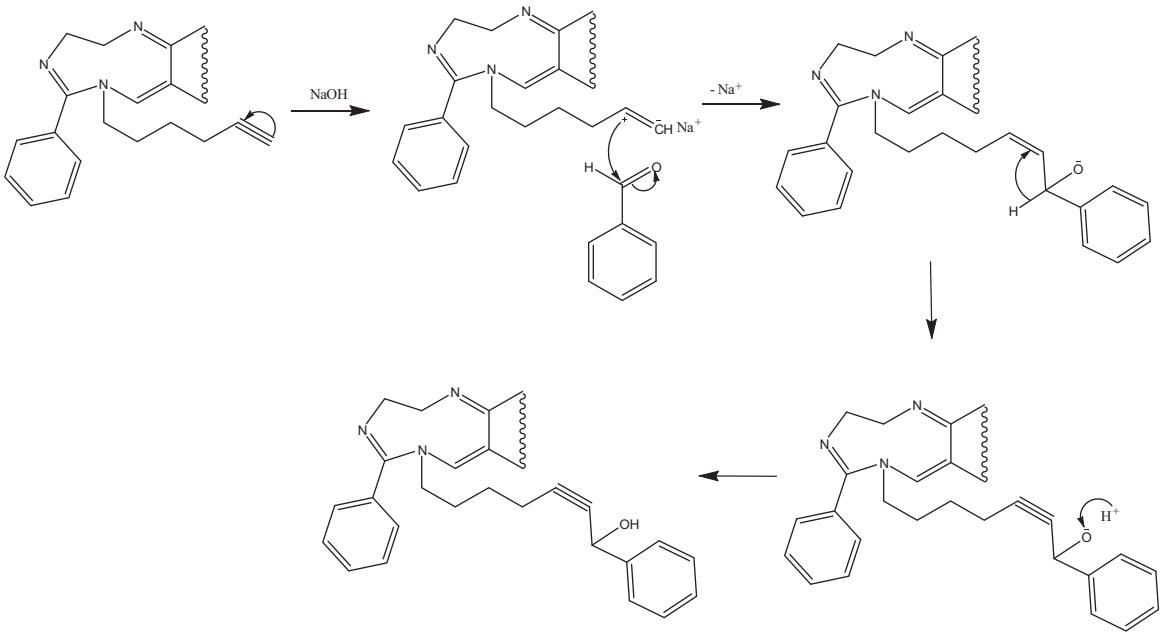


**Figure 8** Mechanism of reaction involved in the preparation of triazoninol derivatives.

groups; at 512.00 and 53.80 ppm for carbons bound to imino groups; at 79.80–81.75 ppm for alkyne group; at 125.90–139.60 ppm for phenyl groups; at 142.28 ppm for alkene group; at 154.25–162.60 ppm for imino groups; and at 191.78–204.10 ppm for aldehyde groups. Finally, the presence of compound **13** was confirmed with mass spectrum which showed a molecular ion at $m/z$ 641.39.

Another data showed several signals involved in the $^{1}$H NMR spectrum for compound **14** at 0.08 and 0.86 ppm for protons involved in the *tert*-butyldimethylsilane fragment; at 0.70 and 1.22 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 0.92–1.18, 1.36–1.38, 1.58–1.60, 1.63–1.90 and 2.50–3.54 ppm for hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at

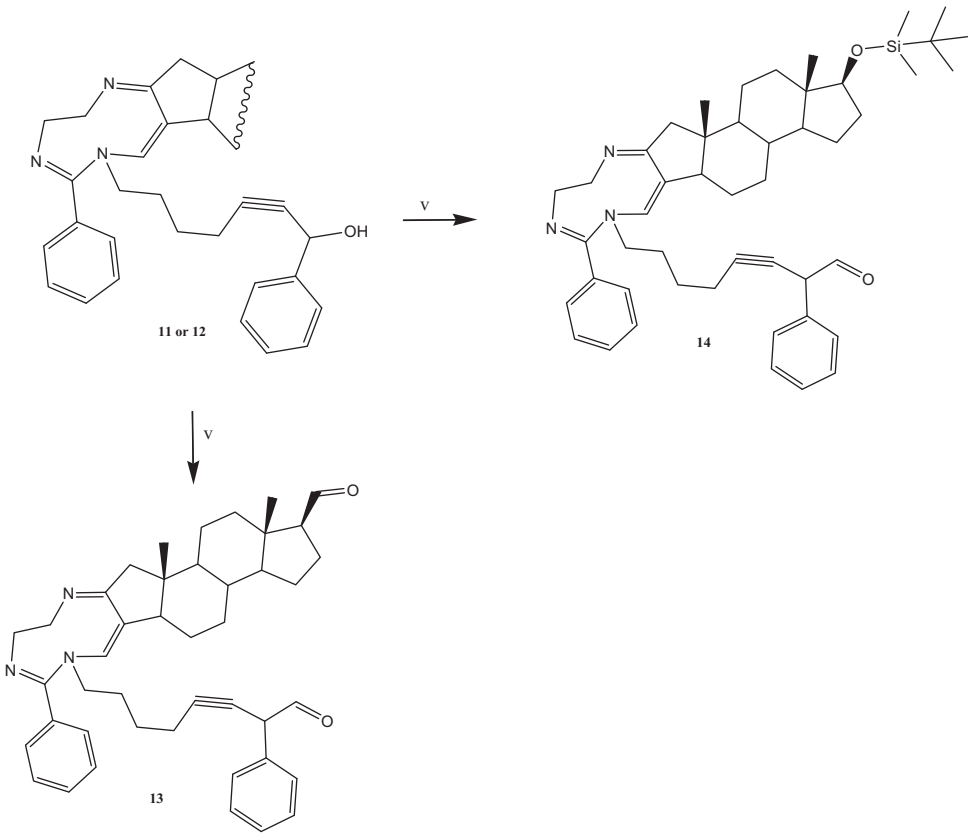


**Figure 9** Synthesis of triazonine-aldehyde derivatives (**13** or **14**). Oxidation of the triazoninol analogs (**11** or **12**) with dimethyl sulfoxide (v).

1.53, 1.62, 2.14 and 3.80 for methylene groups bound to both amino and alkyne groups; at 4.40 ppm for methylene group bound to aldehyde group; at 4.26 and 4.44 ppm for methylene groups bound to imino groups; at 7.04–7.34 and 7.50–7.58 ppm for phenyl groups; at 7.43 ppm for alkene group; and at 9.72 ppm for aldehyde group. The $^{13}$C NMR spectra display chemical shifts at −4.42, 18.04 and 25.56 ppm for carbons of the *tert*-butyldimethylsilane fragment; at 11.40 and 16.70 ppm for methyl groups bound to hexadecahydro-dicyclo penta[a,f]naphthalene fragment; at 18.90, 26.22–27.68 and 54.20 ppm for methylene groups bound to both amino and alkyne groups; at 22.00–23.88, 31.08–36.72, 43.28–48.62, 52.00–52.96, 81.65 and 122.80 ppm hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 38.96 ppm for methylene group bound to both aldehyde and phenyl groups; at 51.96 and 53.82 ppm for methylene groups bound to imino groups; at 79.78 and 81.76 ppm for alkyne group; at 125.92–139.60 ppm for phenyl groups; at 142.30 ppm for alkene group; at 154.25–162.60 ppm for imino groups; and at 191.80 ppm for aldehyde group. Finally, the presence of compound **14** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 743.48.

### *3.6. Triazonin-carbaldehyde derivatives via alkynylation/cyclization of terminal alkynes*

Several protocols have been used for the alkynylation-cyclization of terminal alkynes; however, some reagents are hazardous and difficult to handle such as In(OTf)3 [28], AuCl(PPh3) [29], Au-Ph3 [30], AgPh3 [31]. The mechanism of reaction involves the cupric catalyzed aldehyde-alkyne cyclization for preparation of cyclopentadiene-carbaldehyde derivative (Figs. 10 and 11). The $^{1}$H NMR spectrum for compound **15** showed signals at 0.74 and 1.22 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 1.00 for methyl involved in the arm which is bound to cyclopentadiene ring; at 0.84, 1.10–1.20, 1.24–1.44, 1.54, 1.70–2.24 and 2.50–3.20 ppm for hexadecahydrodicyclo-penta[*a*,*f*]naphthalene fragment; at 1.45, 1.62, 2.46 and 3.68 ppm for methylene groups bound to both amino and cyclopentadiene rings; at 1.46–1.50 and 2.32 ppm for methylene groups involved in the arm bound to cyclopentadiene ring; at 4.26–4.44 ppm for methylene groups bound to imino groups; at 4.00 and 6.70 ppm for cyclopentadiene ring; at 7.04–7.34 and 7.50–7.56 ppm for phenyl groups; at 7.43 ppm for alkene group; and at 9.20–9.80 ppm for aldehyde groups. The $^{13}$C NMR spectra display chemical shifts at 14.50–16.68 ppm for methyl groups bound to hexadecahydro-dicyclo penta[a,f]naphthalene fragment; at 14.00 ppm for methyl involved in the arm which is bound to cyclopentadiene ring; at 22.30, 23.40–24.36, 34.72–48.62 54.40 and 122.80 ppm for hexadecahydrodicyclopenta[*a*,*f*] naphthalene fragment; at 22.56 and 30.38–32.08 ppm for arm bound to cyclopentadiene ring; at 26.40–28.68 and 53.30 ppm for methylene groups involved in the arm bound to cyclopentadiene ring; at 52.00–53.80 ppm for methylene groups bound to both imino groups;

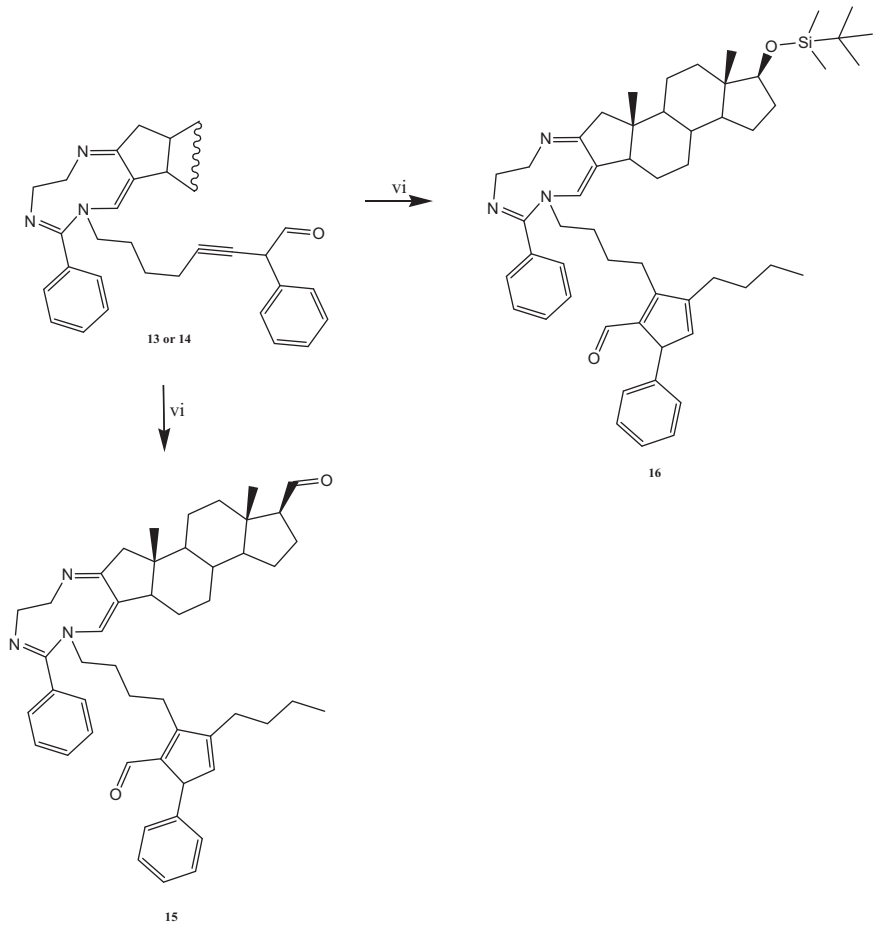


**Figure 10** Synthesis of triazinone-carbaldehyde (**15** or **16**) by the reaction of triazoninynal derivatives with hexyne (vi).

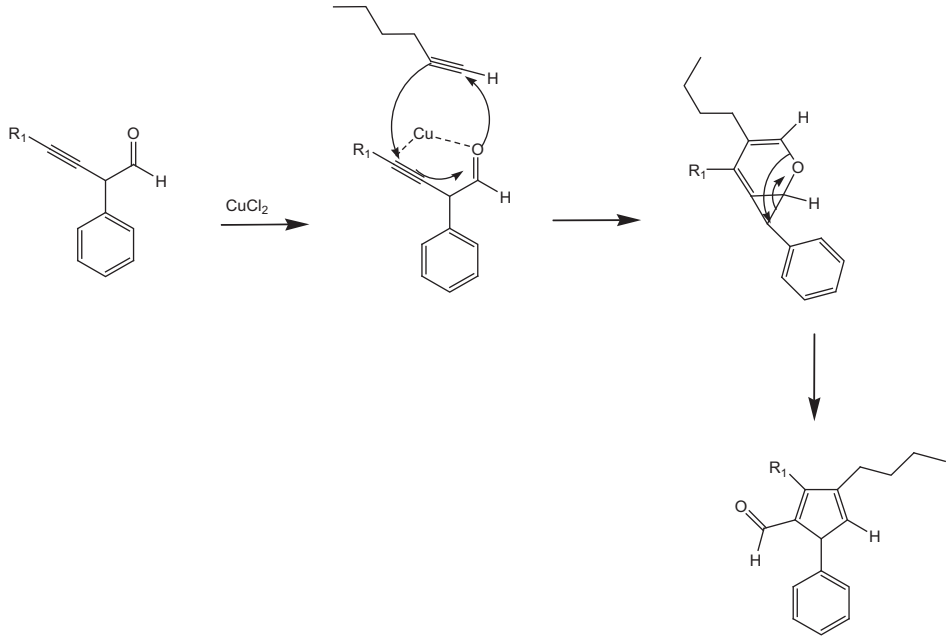


**Figure 11** Mechanism of reaction involved in the preparation of triazoninynal derivatives.

at 51.58, 127.65, 141.30, 152.70 and 165.74 ppm for cyclopentadiene ring; at 126.76–127.64 and 128.40–139.62 ppm for phenyl groups; at 142.28 ppm for alkene group; at 154.25–162.60 ppm for imino groups; and at 186.30–204.10 for aldehyde groups. Finally, the presence of compound **15** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 723.43.

The $^{1}$H NMR spectrum for compound **16** showed signals at 0.07 and 0.84 ppm for protons involved in the *tert*-butyldimethylsilane fragment; at 0.68 and 1.22 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 1.00 for methyl group involved in the arm bound to cyclopentadiene ring; at 0.90–0.94, 1.06–1.18, 1.34–1.38, 1.58–1.60, 1.64–1.88 and 2.50–3.50 ppm for hexadecahydro-dicyclopenta[*a*,*f*]naphthalene fragment; at 1.46, 1.62, 2.44 and 3.68 ppm for methylene groups bound to both amino and cyclopentadiene rings; at 1.47–1.52 and 2.30 ppm for methylene groups involved in the arm bound to cyclopentadiene ring; at 4.00 and 6.70 ppm for cyclopentadiene ring; at 4.26–4.44 ppm for methylene groups bound to imino groups; at 7.04–7.34 and 7.50–7.56 ppm for phenyl groups; at 7.43 ppm for alkene group; and at 9.20 ppm for aldehyde group. The $^{13}$C NMR spectra display chemical shifts at −4.60, 18.00 and 25.50 ppm for carbons of the *tert*-butyldimethylsilane fragment; at 11.40 and 16.68 ppm for methyl groups bound to hexadecahydro-dicyclopenta[*a*,*f*]-naphthalene fragment; at 14.00 ppm for methyl involved in the arm which is bound to cyclopentadiene ring; at 22.00, 23.50–23.88, 31.00, 33.30–48.62, 52.00 and 81.60–122.80 ppm for hexadecahydro-dicyclopenta[*a*,*f*] naphthalene fragment; at 22.48 and 30.88 and 32.00 ppm for methylene group involved in the arm bound to cyclopentadiene ring; at 26.40–28.68, 53.30 ppm for arm bound to both amino group and cyclopentadiene rings; at 51.96 and 53.80 ppm for methylene groups bound to both imino groups; at 51.60, 141.30, 152.70 and 165.78 ppm for cyclopentadiene ring; at 126.76–139.66 ppm for phenyl groups; at 142.28 ppm for alkene group; at 154.25–162.60 ppm for imino groups; and at 186.30 for aldehyde group. Finally, the presence of compound **16** was confirmed with mass spectrum which showed a molecular ion at *m*/*z* 825.26.

## 4. Conclusions

In conclusion, in this work were prepared two triazonine-carbaldehyde derivatives using several chemical techniques, which are simple procedures and easy to handle.

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