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ORIGINAL ARTICLE

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

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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.

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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, $CDCl_3$) δ_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, $CDCl_3$) δ_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, $CDCl_3$) δ_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, $CDCl_3$) δ_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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