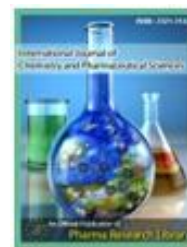




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### RESEARCH ARTICLE

## Synthesis of 2-benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetic acid and 2-benzamido-2-[(tetrahydro-furan-2-ylmethyl) amino] acetic acid

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### ABSTRACT

We reported here the synthesis of new  $\alpha$ ,  $\omega$ -diamino acid derivatives, as 2-benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetic acid and 2-benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino] acetic acid through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl  $\alpha$ ,  $\omega$ -diamino esters. The structure of these products were established on the basis of NMR spectroscopy ( $^1\text{H}$ ,  $^{13}\text{C}$ ), and MS data.

**Keywords:**  $\alpha$ ,  $\omega$ -Diamino esters;  $\alpha$ ,  $\omega$ -diamino acids; alkaline hydrolysis reaction.

### ARTICLE INFO

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### CONTENTS

1. Introduction .....	115
2. Experimental .....	116
3. Results and Discussion .....	116
4. Conclusion .....	117
5. Acknowledgements .....	117
6. References .....	117

### 1. Introduction

Heterocyclic compounds have a wide spectrum activities, including antimicrobial [1,2] and antibacterial properties [3,4], anticancer agents [5], antiviral [6], antitumor activity [7], and in agricultural science as potent fungicides, herbicides and insecticides [8]. Amino acids containing the 1,2,4-triazole moiety and their derivatives represent a well-known group of organic compounds also presenting biological activity [9-11]. Considering the interest in these

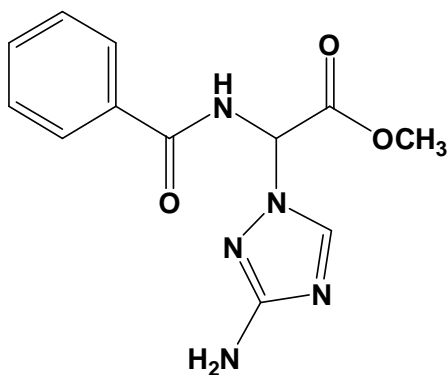
heterocyclic amino acids, several structurally related nonproteinogenic amino acids and their derivatives have been the subject of various investigations [12-14]. We present herein a convenient and easy procedure for the preparation of new racemic carboxylic  $\alpha$ ,  $\omega$ -diamino acid derivatives with the aim to have access to new active biomolecule with a good yield.

## 2. Experimental

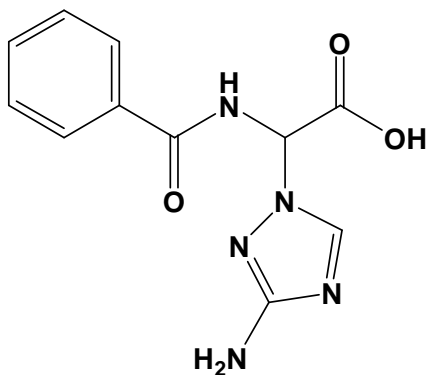
### Deprotection of acid function: Synthesis of *N*-benzoylated, -diamino acids derivatives 3 - 4

To a solution of the *N*-benzoylated, -diamino ester derivative (1 mmole) in 10 mL of dioxane/water mixture (8/2), one adds 1.5 mmole of NaOH (0,5N) with stirring and at 0°C. The stirring is maintained at room temperature until disappearance of the starting material. The reaction is always followed by TLC. The solvent is then evaporated and the pH of the aqueous phase is adjusted to 6 using a solution of sulfuric acid or hydrochloric acid (0,5N). One extracts with ethyl acetate and the organic layers recovered, are dried and concentrated under vacuum. The product is recrystallized from ether/hexane.

**Methyl 2-benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetate 1:** Yield: 77.5%; mp 214–216 °C (ether/hexane); R<sub>f</sub>: 0.3 (ether) <sup>1</sup>H NMR (CDCl<sub>3</sub>): ppm: 3.9 (s, 3H, OCH<sub>3</sub>); 5.6 (br s, 2H, NH<sub>2</sub>); 6.45 (d, 1H, J = 7.2 Hz, Ha); 7.47–8.05 (3 m, 7H, Ar + H<sub>triazol</sub> + NH<sub>amid</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): ppm: 54.04 (OCH<sub>3</sub>); 60.67 (–CH–); 106.42, 127.42, 128.92, 133.01, 149.92, 155.70, (C<sub>6</sub>H<sub>5</sub> aromatic carbons); 165.62, 168.16 (2CO). M.S.-E.I: m/z = 275.8 [M]; C<sub>12</sub>H<sub>13</sub>N<sub>5</sub>O<sub>3</sub>.

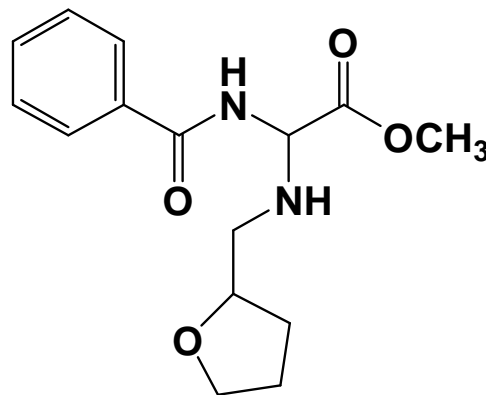


**2-Benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetic acid 2:** Yield: 90%; <sup>1</sup>H NMR (CDCl<sub>3</sub>): ppm: 5.4 (br s, 2H, NH<sub>2</sub>); 6.4 (d, 1H, J = 7Hz, H<sub>a</sub>); 7.4–8.1 (3 m, 7H, Ar + H<sub>triazol</sub> + NH<sub>amid</sub>), 11.02 (s, 1H, H<sub>acid</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): ppm: 61.12 (–CH–); 107.22, 127.86, 129.02, 133.18, 149.64, 155.92 (C<sub>6</sub>H<sub>5</sub> aromatic carbons); 164.80, 168.75 (2CO). M.S.-E.I: m/z = 261.7 [M]; C<sub>11</sub>H<sub>11</sub>N<sub>5</sub>O<sub>3</sub>.

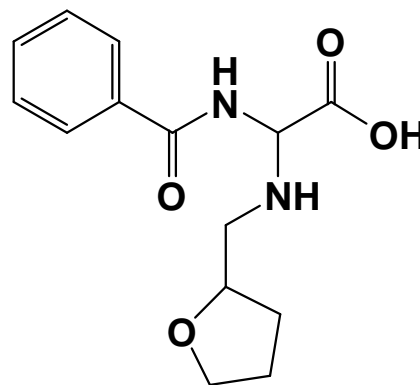


**Methyl 2-benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino] acetate 3:** Yield: 72%; m.p.: 130–132 °C (ether/hexane); R<sub>f</sub>: 0.6 (ether); <sup>1</sup>H NMR (CDCl<sub>3</sub>): ppm:

1.2–1.75 (2 m, 5H, H<sub>T.H.F</sub>); 2.9 (m, 2H, NCH<sub>2</sub>); 3.75 (s, 3H, OCH<sub>3</sub>); 4.1–4.45 (2 m, 3H, H<sub>T.H.F</sub> + NH); 5.6 (br s, 1H, Ha); 7.4–8.02 (3 m, 5H, Ar + N-H<sub>amid</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): ppm: 4. (CH<sub>2</sub>) 24.13, 27.07, 50.25, 66.12; 54.49 (OCH<sub>3</sub>); 71.32 (–CH–); 77.23 (OCH); 128.34, 129.54, 131.33, 135.77 (C<sub>6</sub>H<sub>5</sub> aromatic carbons); 169.07, 171.98 (2CO). MS (electrospray) m/z = 293.3 [M+1]; 292.3 [M]; C<sub>15</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>.



**3.5. 2-Benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino] acetic acid 3:** Yield: 88%; R<sub>f</sub>: 0.7 (ether); <sup>1</sup>H NMR (CDCl<sub>3</sub>): ppm: 1.25–1.80 (2 m, 5H, H<sub>T.H.F</sub>); 2.85 (m, 2H, NCH<sub>2</sub>); 4.20–4.50 (2 m, 3H, H<sub>T.H.F</sub> + NH); 5.5 (br s, 1H, H<sub>a</sub>); 7.45–8.00 (3 m, 5H, Ar + N-H<sub>amid</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>): ppm: 4. (CH<sub>2</sub>) 25.45, 27.18, 52.05, 66.42; 72.12 (–CH–); 77.26 (OCH); 127.84, 129.34, 131.72, 135.68 (C<sub>6</sub>H<sub>5</sub> aromatic carbons); 169.12, 171.92 (2CO). MS (electrospray) m/z = 279.2 [M+1]; 278.2 [M]; C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O<sub>4</sub>.



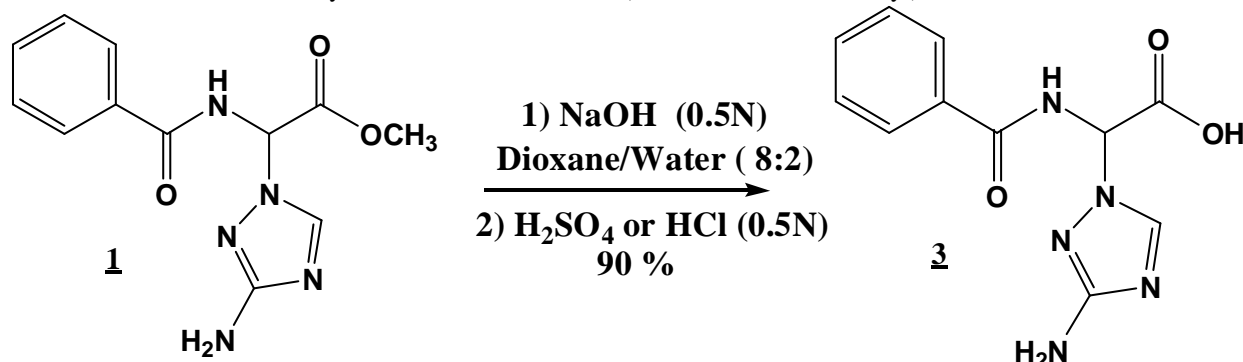
## 3. Results and Discussions

In continuation of our research interest in amino esters [15,16], we will present in this work, our results concerning the synthesis of new, -diamino acids derivatives, as 2-benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetic acid and 2-benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino] acetic acid through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl, -diamino esters [16]. After the obtaining of the *N*-protected methyl, -diamino esters **1-2**, we proceeded to the cleavage of the protecting groups to obtain the corresponding, -diamino acids **3-4**. The hydrolysis reaction of the, -diamino ester methyl 2-benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetate **1** in a basic medium is carried out for approximately 30 minutes

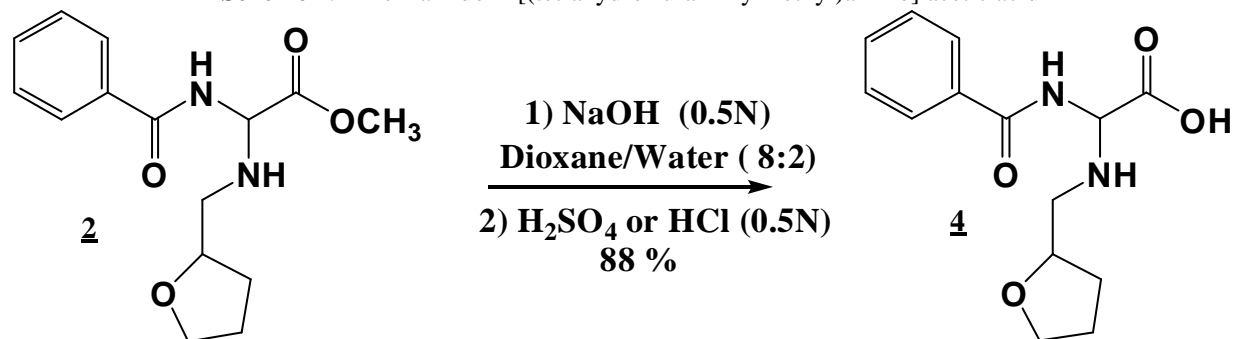
and leads, after acidification of the reaction medium with sulfuric acid or hydrochloric acid, to the corresponding  $\alpha$ ,  $\omega$ -diamino acid 2-benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetic acid **2** in good yield (scheme 1). By adopting the same approach and using the same operating conditions, the

hydrolysis of the  $\alpha$ ,  $\omega$ -diamino ester methyl 2-benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino]acetate **2** leads to  $\alpha$ ,  $\omega$ -diamino acid 2-benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino] acetic acid **4** with a very satisfactory yield (scheme 2).

**Scheme 1:** Synthesis of 2-benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetic acid **2**



**Scheme 2:** 2-Benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino] acetic acid **4**



#### 4. Conclusion

2-Benzamido-2-(3-amino-1,2,4-triazol-1-yl) acetic acid and 2-benzamido-2-[(tetrahydro-furan-2-ylmethyl)amino] acetic acid were synthesized through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl  $\alpha$ ,  $\omega$ -diamino esters. This method provides an easy procedure for the preparation of new carboxylic  $\alpha$ ,  $\omega$ -diamino acids in very satisfactory yields.

#### 5. Acknowledgements

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