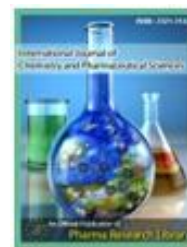




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RESEARCH ARTICLE

Synthesis of the new carboxylic , -diamino acids: 2-benzamido-2-(*N*-benzyl *N*-methylamino) acetic acid and 2-benzamido-2-(*N*-benzyl *N*-ethylamino) acetic acid

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ABSTRACT

We reported here the synthesis of new , -diamino acids derivatives, as 2-benzamido-2-(*N*-benzyl *N*-methylamino) acetic acid and 2-benzamido-2-(*N*-benzyl *N*-ethylamino) acetic acid through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl , -diamino esters. The structure of these products were established on the basis of NMR spectroscopy (^1H , ^{13}C), and MS data.

Keywords: , -Diamino esters; , -diamino acids; alkaline hydrolysis reaction.

ARTICLE INFO

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1. Introduction

Amino acids play critical roles in biological functions and protection against diseases [1]. They were investigated on serum biochemical variables, jejunal mucosal amino acid contents, and intestinal inflammation in weaned piglets [2]. Recently, it has become clear that dietary protein plays a key role in regulating both metabolic health and longevity, and that both the quantity and quality - the specific amino International Journal of Chemistry and Pharmaceutical Sciences

acid composition - of dietary protein mediates metabolic health [3,4]. Amino acids are essential components of plant metabolism, not only as constituents of proteins, but also as precursors of important secondary metabolites and as carriers of organic nitrogen between the organs of the plant [5]. Protein and amino acid supplements are very popular among athletes. There are different studies and scientific

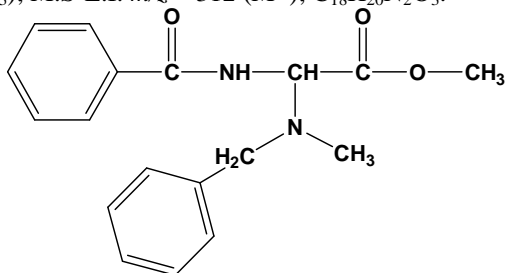
opinions on the benefit of these amino acids in sports performance and in different sports (stimulation of muscle protein synthesis, prevention of muscle protein breakdown and reduction of markers of exercise-induced muscle damage, reduction of feelings of fatigue, etc.) [6]. Peracetic acid (PAA) is a sanitizer with increasing use in food, medical and water treatment industries. Amino acids are important components in targeted foods for PAA treatment and ubiquitous in natural water bodies and wastewater effluents as the primary form of dissolved organic nitrogen [7]. We focused in the present study on the synthesis of new carboxylic, -diamino acids derivative with the aim to have access to new active biomolecule with a good yield.

2. Experimental

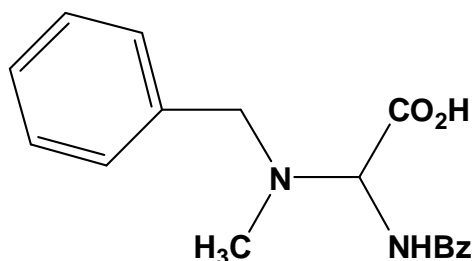
2.1. Deprotection of acid function: Synthesis of *N*-benzoylated, -diamino acids derivatives 3 - 4

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.

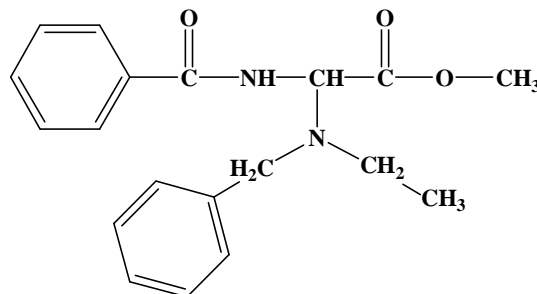
3.2. Methyl 2-benzamido-2-(*N*-benzyl *N*-methylamino) acetate 1: Yield 78 %; m.p.: 200–202°C (ether/hexane); Rf: 0.7 (ether); $^1\text{H NMR}$ (CDCl_3): ppm: 7.8 (d, 1H, NH_{amid} , 7.3 Hz), 7.5 (m, 10H, H_{arom}), 5.6 (d, 1H, H, 7.3 Hz), 4.0 (s. e, 2H, NCH_2), 3.8 (s, 3H, OCH_3); 2.4 (s, 3H, NCH_3); $^{13}\text{C NMR}$ (CDCl_3): ppm: 171.3, 168.02 (2CO), 137.8, 133.1, 132.0, 129.16, 128.7, 128.4, 128.2, 127.1 (C_6H_5 aromatic carbons), 68.94 ($-\text{CH}-$); 55.65 (CH_2), 52.7 (OCH_3); 36.1 (NCH_3); M.S.-E.I: $m/z = 312$ (M^+); $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_3$.



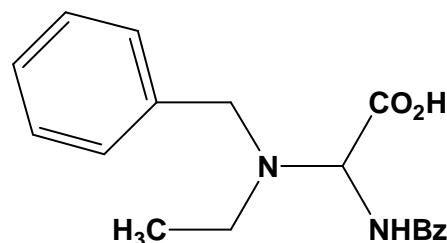
2.2. 2-Benzamido-2-(*N*-benzyl *N*-methylamino) acetic acid 3: Yield 84 %; $^1\text{H NMR}$ (CDCl_3): ppm: 10.9 (s, 1H, H_{acid}), 7.85 (d, 1H, NH_{amid} , 7.35 Hz), 7.54 (m, 10H, H_{arom}), 5.8 (d, 1H, H, 7.35 Hz), 4.15 (s. e, 2H, NCH_2), 2.6 (s, 3H, NCH_3); M.S.-E.I: $m/z = 298$ (M^+); $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_3$.



2.4. Methyl 2-benzamido-2-(*N*-benzyl *N*-ethylamino) acetate 2: Yield 80 %; m.p.: 218–220°C (ether/hexane); Rf: 0.75 (ether); $^1\text{H NMR}$ (CDCl_3): ppm: 7.8 (d, 1H, NH_{amid} , 7.3 Hz), 7.5 (m, 10H, H_{arom}), 5.55 (d, 1H, H, 7.3 Hz), 4.0 (s. e, 2H, NCH_2), 3.8 (s, 3H, OCH_3); 2.6 (q, 2H, NCH_2 , 7Hz), 1.3 (t, 3H, CH_3 , 7Hz); $^{13}\text{C NMR}$ (CDCl_3): ppm: 171.1, 168.2 (2CO), 137.7, 133.3, 132.1, 129.1, 128.74, 128.46, 128.25, 127.12 (C_6H_5 aromatic carbons), 68.7 ($-\text{CH}-$); 55.6 (CH_2), 52.8 (OCH_3); 42.1 (NCH_2); 14.03 (CH_3); M.S.-E.I: $m/z = 326$ (M^+); $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_3$.



3.5. 2-Benzamido-2-(*N*-benzyl *N*-ethylamino) acetic acid 4: Yield 78 %; $^1\text{H NMR}$ (CDCl_3): ppm: 10.25 (s, 1H, H_{acid}), 7.9 (d, 1H, NH_{amid} , 7.32 Hz), 7.58 (m, 10H, H_{arom}), 5.5 (d, 1H, H, 7.32 Hz), 4.2 (s. e, 2H, NCH_2), 2.8 (q, 2H, NCH_2 , 7.1Hz), 1.45 (t, 3H, CH_3 , 7.1Hz); M.S.-E.I: $m/z = 312$ (M^+); $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_3$.

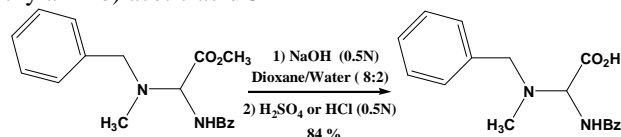


Solution was cooled and diluted to volume with mobile phase and filtered through 0.45 μm membrane filter. (Stock solution). Further pipette 0.25ml of Naloxone and Oxycodone of the above stock solution in to a 10ml volumetric flask and dilute up to the mark with diluent.

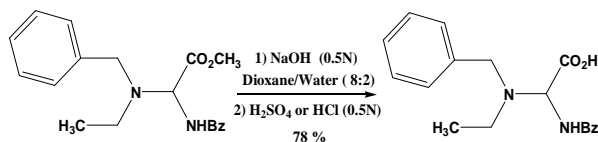
3. Results and Discussions

In continuation of our research interest in amino esters [8,9], we will present in this work, our results concerning the synthesis of new, -diamino acids derivatives, as 2-benzamido-2-(*N*-benzyl *N*-methylamino) acetic acid and 2-benzamido-2-(*N*-benzyl *N*-ethylamino) acetic acid through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl, -diamino esters. 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-(*N*-benzyl *N*-methylamino) 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, -diamino acid 2-benzamido-2-(*N*-benzyl *N*-methylamino) acetic acid **3** in good yield (scheme 1).

Scheme 1: Synthesis of 2-benzamido-2-(*N*-benzyl *N*-methylamino) acetic acid **3**



By adopting the same approach and using the same operating conditions, the hydrolysis of the α , ω -diamino ester methyl 2-benzamido-2-(*N*-benzyl *N*-ethylamino)acetate **2** leads to α , ω -diamino acid 2-benzamido-2-(*N*-benzyl *N*-ethylamino) acetic acid **4** with a very satisfactory yield (scheme 2).



Scheme 2: Synthesis of 2-benzamido-2-(*N*-benzyl *N*-ethylamino) acetic acid **4**

4. Conclusion

In summary, this method provides a convenient method and easy procedure for the preparation of new carboxylic α , ω -diamino acids in very satisfactory yields through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl α , ω -diamino esters.

5. Acknowledgements

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