International Journal of Chemistry and Pharmaceutical Sciences

Journal Home Page:www.pharmaresearchlibrary.com/ijcps

R E S E A E C H A R T I C L E

New carboxylic α,α-diamino acids: 2-benzamido-2-(benzylamino) acetic acid and 2-benzamido-2-(*N*,*N*-dibenzylamino) acetic acid

El Houssine Mabrouk*

Laboratory of Organic Chemistry, Faculty of Sciences Dhar El Mahraz, University Sidi Mohamed Ben Abdellah, B.P. 1796, Fez, Morocco

A B S T R A C T

New α,α-diamino acids derivatives, as 2-benzamido-2-(benzylamino) acetic acid and 2-benzamido-2-(*N*,*N*-dibenzylamino) acetic acid were synthesized in high yield through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl α,α-diamino esters. The structure of these products were established on the basis of NMR spectroscopy (^{1}H, ^{13}C), and MS data.

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

A R T I C L E I N F O

Corresponding Author
El Houssine Mabrouk
Laboratory of Organic Chemistry,
Faculty of Sciences Dhar El Mahraz,
University Sidi Mohamed Ben Abdellah,
B.P. 1796, Fez, Morocco
MS-ID: IJCPS3885

PAPER-QRCODE

A R T I C L E H I S T O R Y: Received 19 January 2019, **Accepted** 29 February 2019, **Available Online** 27 March 2019

Citation: El Houssine Mabrouk. *New carboxylic α,α-diamino acids: 2-benzamido-2-(benzylamino) acetic acid and 2-benzamido-2-(N,N-dibenzylamino) acetic acid*. *Int. J. Chem, Pharm, Sci.*, 2019, 7(3): 57-59.

C O N T E N T S

1. Introduction

Amino acids are essential for life as independent units that are structural units of peptides and proteins. They have become the focus of many researchers who study their synthesis and the structure-activity relationship thus allowing a better approach to understanding their mechanisms of action [1-4]. The synthesis of new carboxylic amino acids and their esters is attracting interest from research teams around the world given the broad spectrum of activity they present: biochemistry, enzymology, medicine (antibiotics, antiviral, antiprotozoal, cardiovascular tissues, neuroexcitatory) [5-8]. The functional role of amino acids as regulators of protein degradation was investigated using primary myogenic precursor cell culture as in vitro model of rainbow trout white muscle [9]. There is evidence for amino acids as both positive and negative regulators of protein turnover in rainbow trout muscle [10]. We focused in the present work on the synthesis of new carboxylic α,α-diamino acids

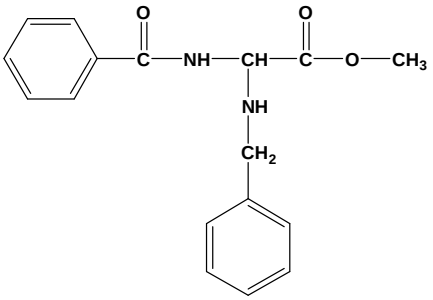
derivative with the aim to have access to new active biomolecule with a good yield.

2. Experimental

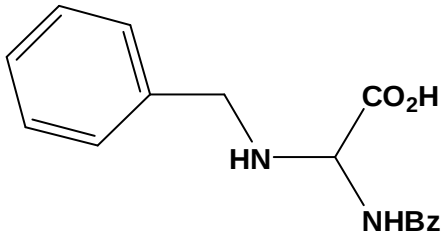
2.1. Deprotection of acid function: Synthesis of N-benzoylated α,α-diamino acids derivatives 6 - 9

To a solution of the *N-benzoylated* α,α-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 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.

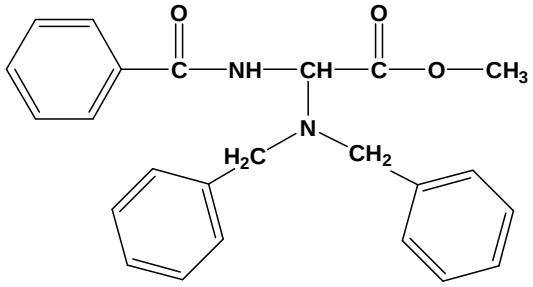
***2.2. Methyl 2-benzamido-2-(benzylamino)acetate* 1**: Yield 67 %; m.p.: 104-106 °C (ether/hexane); Rf: 0.54 (ether); **^{1}H NMR ($CDCl_3$): δppm**: 7.9-6.9 (4m, 12H, NH+ H_{arom}+ NH_{amid}), 5.5 (d, 1H, H_α, 7.5 Hz), 3.87 (d, 2H, CH_2, 9.8 Hz), 3.79 (s, 3H, OCH_3); **^{13}C NMR ($CDCl_3$):** δ ppm: 170.76, 167.37 (2CO), 139.17, 133.44, 132.06, 128.68, 128.53, 128.27, 127.30, 127.10 (C_6H_5 aromatic carbons), 64.98 (-CH-), 53.00 (OCH_3), 49.18 (CH_2); EIMS: *m/z* = 298.8 ($M^{+\cdot}$); $C_{17}H_{18}N_2O_3$.



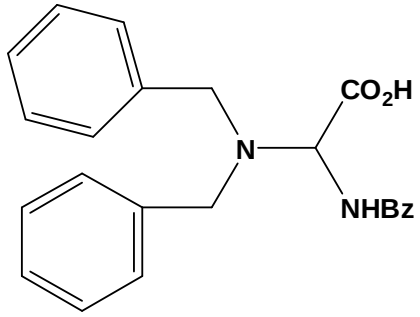
2.2. 2-Benzamido-2-(benzylamino) acetic acid 3: Yield 90 %; **^{1}H NMR ($CDCl_3$): δppm**: 11.02 (s, 1H, Hacid), 7.9-6.85 (4m, 12H, NH+ H_{arom}+ NH_{amid}), 5.8 (d, 1H, H_α, 7.6 Hz), 3.82 (d, 2H, CH_2, 9.83 Hz); EIMS: *m/z* = 284.8 ($M^{+\cdot}$); $C_{16}H_{16}N_2O_3$.



2.4. Methyl 2-benzamido-2-(N,N-dibenzylamino)acetate *2*: *Yield 84 %;* ***^{1}H NMR ($CDCl_3$): δppm****: 7.87 (d, 1H, NH_{amid}, 7.3 Hz), 7.5 (m, 15H, H_{arom}), 5.6 (d, 1H, H_α, 7.3 Hz), 4.0 (s. e, 4H, NCH_2), 3.8 (s, 3H, OCH_3);* ***^{13}C NMR ($CDCl_3$):*** *δ ppm: 170.44, 167.92 (2CO), 139.58, 133.21, 132.15, 128.96, 128.77, 128.64, 128.26, 127 (C_6H_5 aromatic carbons), 66.47 (-CH-); 54.05 (CH_2), 52.73 (OCH_3); M.S-E.I:* m/z = *388.9 ($M^{+\cdot}$); $C_{24}H_{24}N_2O_3$.*



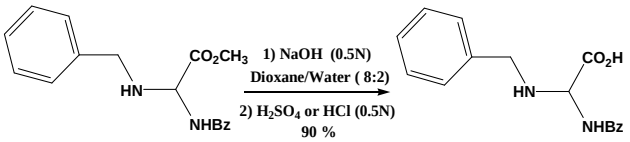
2.5. 2-Benzamido-2-(N,N-dibenzylamino) acetic acid 4: *Yield 70 %;* ***^{1}H NMR ($CDCl_3$): δppm****: 10.9 (s, 1H, Hacid), 7.8 (d, 1H, NH_{amid}, 7.3 Hz), 7.56 (m, 15H, H_{arom}), 5.8 (d, 1H, H_α, 7.3 Hz), 4.1 (s. e, 4H, NCH_2); M.S-E.I:* m/z = *374.9 ($M^{+\cdot}$); $C_{23}H_{22}N_2O_3$.*



3. Results and Discussions

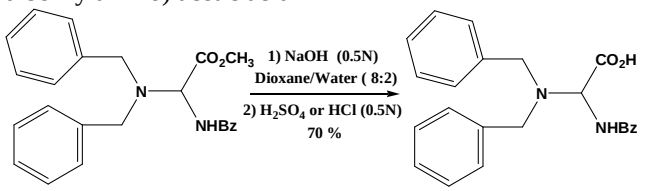
In continuation of our research interest in amino acids [11,12], we will present in this study, our results concerning the synthesis of new α,α-diamino acids derivatives, as 2-benzamido-2-(benzylamino) acetic acid and 2-benzamido-2-(*N*,*N*-dibenzylamino)acetic acid through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl α,α-diamino esters. After the obtaining of the *N*-protected methyl α,α-diamino esters **1-2**, we proceeded to the cleavage of the protecting groups to obtain the corresponding α,α-diamino acids **3-4**. The hydrolysis reaction of the α,α-diamino ester methyl 2-benzamido-2-(benzylamino) acetate **2** 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 α,α-diamino acid 2-benzamido-2-(benzylamino) acetic acid **3** in high yield (scheme 1).

Scheme 1: Synthesis of 2-benzamido-2-(benzylamino) acetic acid **3**



By adopting the same approach and using the same operating conditions, the hydrolysis of the α,α-diamino ester methyl 2-benzamido-2-(*N*,*N*-dibenzylamino) acetate **3** leads to α,α-diamino acid 2-benzamido-2-(*N*,*N*-dibenzylamino) acetic acid **4** with a very good yield (scheme 2).

Scheme 2: Synthesis of 2-benzamido-2-(*N*,*N*-dibenzylamino) acetic acid **4**



4. Conclusion

The preparation of 2-benzamido-2-(benzylamino) acetic acid and 2-benzamido-2-(*N*,*N*-dibenzylamino) acetic acid through alkaline hydrolysis reaction of corresponding *N*-benzoylated methyl α,α-diamino esters was carried out by cleavage of the protecting groups. This method provides a convenient method and easy procedure for the preparation of new carboxylic α,α-diamino acids in very satisfactory yields.

5. Acknowledgements

We thank the CNR for financial support of this work (PROTARS D13/03, Morocco).

6. References

[1] AM Remete, M Nonn, S Fustero, F Fülöp, L Kiss. Synthesis of fluorinated amino acid derivatives through late-stage deoxyfluorinations. Tetrahedron, 1 November 2018, 74: 44, 6367-6418.

[2] M Samel, K Tõnismägi, G Rõnnholm, H Vija, J Siigur, N Kalkkinen, E Siigur, L-Amino acid oxidase from Naja naja oxiana venom. Biochem. Physiol. *B* 2008, 149*:* 572–580.

[3] RS Rodrigues, JF Da Silva, J Boldrini-França, FPP Fonseca, AR Otaviano, F Henrique-Silva, AJ Magro, ASK Braz, JI Dos Santos, MI Homsi-Brandeburgo, MRM Fontes, AL Fuly, AM Soares, VM Rodrigues. Structural and functional properties of Bp-LAAO, a new L-amino acid oxidase isolated from Bothrops pauloensis snake venom. Biochimie, 2009, 91: 490–501.

[4] IC E Cátia, AMF Silva, MMR Manuela, PGC Susana. Unnatural benz-X-azolyl asparagine derivatives as novel fluorescent amino acids: synthesis and photophysical characterization. Tetrahedron, 2009, 65: 9373–9377.

[5] A Elmarrouni, M Güell, C Collell, M Heras. A simple approach for the synthesis of new pyrimidinyl α-amino acids. Tetrahedron, 2010, 66: 612–623.

[6] D Liu, EY Zong, PF Huang, JZ Yang, SL Yan, JZ Li, YL Li, XQ Ding, SP He, X Xiong, YL Yin. The effects of dietary sulfur amino acids on serum biochemical variables, mucosal amino acid profiles, and intestinal inflammation in weaning piglets. Livestock Science. February 2019, 220: 32-36.

[7] LG Cara, WL Dudley. Regulation of metabolic health by essential dietary amino acids. Mechanisms of Ageing and Development. January 2019, 177: 186-200.

[8] K Onishi, S Shibutani, N Goto, Y Maeda, H kiIwata. Amino acid starvation accelerates replication of Ibaraki virus. Virus Research, 15 January 2019, 260: 94-101.

[9] JMM Sanz, AN Navarro, ES García, IS López. Chapter 43 - An Overview on Essential Amino Acids and Branched Chain Amino Acids. Nutrition and Enhanced Sports Performance (Second Edition), Muscle Building, Endurance, and Strength, 2019, 509-519.

[10] BM Cleveland, LM. Radler. Essential amino acids exhibit variable effects on protein degradation in rainbow trout (Oncorhynchus mykiss) primary myocytes. Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology, March 2019, 229: 33-39.

[11] EH Mabrouk, A Elachqar, A Alami, A El Hallaoui. Synthesis of new racemic α,α-diaminocarboxylic ester derivatives. Molecules, 2010, 13: 9354–9363.

[12] EH Mabrouk, A Elachqar, A El Hallaoui, S El Hajji, J Martinez, V Rolland. Synthesis of new racemic α-heterocyclic α,α-diaminoesters and α-aminoester carboxylic. Arabian Journal of Chemistry, 2013, 6: 93–96.