

Short Note

## 2-[(1-Benzamido-2-methoxy-2-oxoethyl)amino]benzoic Acid

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Received: 10 October 2012 / Accepted: 6 January 2013 / Published: 11 January 2013

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**Abstract:** The carboxylic  $\alpha,\alpha$ -diaminoester 2-[(1-benzamido-2-methoxy-2-oxoethyl)amino]benzoic acid is obtained by *N*-alkylation of methyl  $\alpha$ -azido glycinate *N*-benzoylated with 2-aminobenzoic acid.

**Keywords:**  $\alpha$ -amino esters; *N*-alkylation; methyl  $\alpha$ -azidoglycinate; 2-aminobenzoic acid

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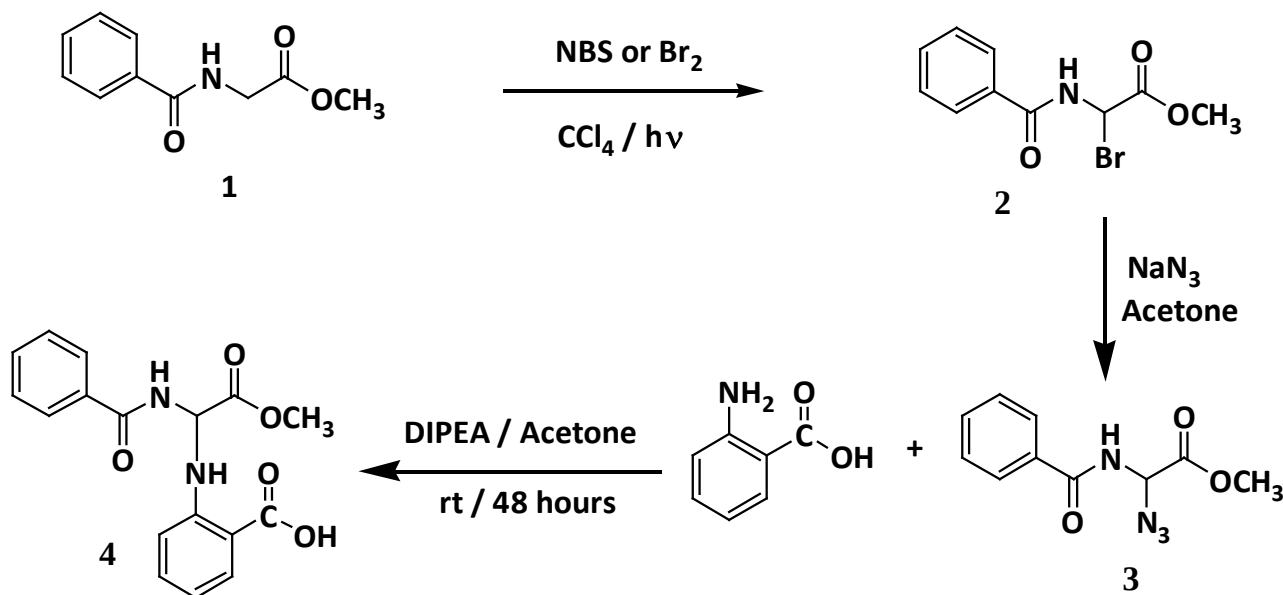
### 1. Introduction

Amino acids are the fundamental building blocks of peptides and proteins and play essential roles in living organisms. Because of the physiological importance of  $\alpha$ -amino acids, innumerable studies for their chemistry and synthesis have been published [1].

Since the end of last century, the studies of amino acids have changed into focusing on their biochemistry, physiology and medical activities such as apoptosis inducing, platelet aggregation-inhibiting/inducing, antimicrobial, anti-HIV...

The chemistry of amino acids has undergone a very important development. Their applications make themselves currently in several domains: biochemistry, enzymology [2], medicine (antibiotics, antiviral, antiprotozoal, cardiovascular tissues, neuroexcitatory [3–6]), industry agrochemical (herbicides, fungicides, regulating of plant growth) in addition of their important utility in asymmetric synthesis [7].

Following the research done on the synthesis of new carboxylic  $\alpha,\alpha$ -diaminoesters [8] we reported in this paper another part of our investigations concerning the preparation of 2-[(1-benzamido-2-methoxy-2-oxoethyl)amino]benzoic acid. The product synthesized with a satisfactory yield was characterized by nuclear magnetic resonance and mass spectrometry (Scheme 1).

**Scheme 1.** *N*-alkylation of 2-aminobenzoic acid with methyl  $\alpha$ -azidoglycinate.

## 2. Results and Discussion

Our strategy is based on the *N*-alkylation of 2-aminobenzoic acid with methyl  $\alpha$ -azidoglycinate *N*-benzoylated **3** (Scheme 1). Azide derivative **3** was prepared using Steglich method [9] and Achamlale's procedure [10].

Methyl  $\alpha$ -azido glycinate *N*-benzoylated **3** was obtained by the reaction [10] of sodium azide with the methyl  $\alpha$ -bromo glycinate **2**. The title compound is stable and can be stored for an unlimited time without any signs of decomposition. The methyl  $\alpha$ -bromo glycinate **2** can also be used and gives satisfactory results; the azide **3** is used especially for its stability.

The reaction was carried out in dry acetone at room temperature for 48 h in the presence of base such as diisopropylethylamine (DIPEA).

As shown in Scheme 1, the reaction of 2-aminobenzoic acid on azide **3** result in formation of the new racemic carboxylic  $\alpha,\alpha$ -diaminoester **4**: 2-[(1-benzamido-2-methoxy-2-oxoethyl)amino]benzoic acid.

The product **4** was obtained in 72% overall yield from **3** and was characterized by MS,  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectroscopy.

## 3. Experimental

To a stirred solution of 2.86 mmoles of amine (nitrogen compound) and 3.12 mmoles of DIPEA in 10 mL of dry acetone, 2.6 mmoles of  $\alpha$ -azido glycinate were added. The mixture was stirred at room temperature and the reaction was followed by TLC (Kiesegel Merck 60F524). The solvent was evaporated under reduced pressure. The residue was quenched with saturated aqueous solution of ammonium chloride (20 mL) and extracted with dichloromethane (20 mL  $\times$  3). The organic phase was dried over sodium sulfate ( $\text{Na}_2\text{SO}_4$ ) and the solvent was removed under reduced pressure. The product **4** was purified by column chromatography on silica gel using ether/hexane mixture with an increasing gradient of polarity as eluant to afford pure *N*-alkylated product.

Liquid: yield = 72%;  $R_f$  = 0.7 (ether).

$^1\text{H}$ -NMR (Bruker, 300.13 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 3.83 (s, 3H,  $\text{OCH}_3$ ), 4.85 ( $s_{\text{br}}$ , 1H, NH), 5.85 (d,  $^3J$  = 8.2 Hz, 1H,  $\text{H}_\alpha$ ), 6.7 (d,  $^3J$  = 8.4 Hz, 2H,  $\text{H}_{\text{arom}}$ ), 7.3 (d,  $^3J$  = 7.2 Hz, 1H,  $\text{H}_{\text{arom}}$ ), 7.46 (m, 3H,  $\text{H}_{\text{arom}}$ ), 7.8 (dd,  $^3J$  = 7.4 Hz,  $^4J$  = 1.5 Hz, 2H,  $\text{H}_{\text{arom}}$ ), 7.88 (dd,  $^3J$  = 8.4 Hz,  $^4J$  = 1.5 Hz, 1H,  $\text{H}_{\text{arom}}$ ), 7.95 (d,  $^3J$  = 7.8 Hz, 1H,  $\text{NH}_{\text{amid}}$ ), 11.02 (s, 1H, COOH).

$^{13}\text{C}$ -NMR (75.47 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) = 53.57 ( $\text{OCH}_3$ ), 59.45 ( $-\text{CH}-$ ), 111.9, 116.0, 122.0, 128.18, 128.8, 132.2, 133.4, 133.46, 134.9, 148.29 ( $\text{C}_6\text{H}_5$  aromatic carbons), 167.22 (CO), 169.92 (CO), 170.08 (CO).

MS (electrospray)  $m/z$ : 329 ( $\text{M}+\text{H}^+$ , 100%).

Anal Calcd. for  $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_5$ : C, 62.19%; H, 4.91%; N, 8.53%. Found: C, 62.15%; H, 4.86%; N, 8.42%.

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