

Synthesis of methyl 2-benzamido-2-(phenoxy) acetate

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Abstract: The carboxylic α -amino ester methyl 2-benzamido-2-(phenoxy) acetate is obtained by *O*-alkylation of methyl α -azido glycinate *N*-benzoylated with phenol.

Keywords: α -amino ester; *O*-alkylation; methyl α -azido glycinate

1. Introduction

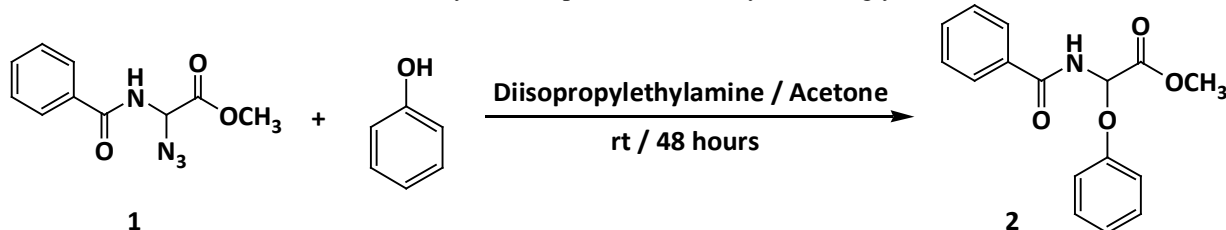
It is interesting to note that amino acids are obligatory for cellular functions and survival. They are of special importance among the other chemical substances since they form the basic constituents of living organisms and are precursors for protein formation. It is imperative to know the properties of amino acids [1–6] in order to understand and explain their behavior and the synthesis of peptides, proteins and enzymes in living organisms.

Several researchers have investigated the inhibitory potential of some amino acids and the results obtained from such

studies have given some hope for the use of amino acids as green corrosion inhibitors [7–10].

For this reason, we considered it interesting to synthesize new compounds of amino acid, in order to study their biological activities. Following the research done on the synthesis of new α -carboxylic amino esters [11], we reported in this paper another part of our investigations concerning the preparation of methyl 2-benzamido-2-(phenoxy) acetate. Our strategy is based on the *O*-alkylation of methyl α -azido glycinate *N*-benzoylated with phenol. The product synthesized with a satisfactory yield was characterized by nuclear magnetic resonance and mass spectrometry (Scheme 1).

Scheme 1. *O*-alkylation of phenol with methyl α -azido glycinate.



2. Results and Discussion

Our strategy is based on the *O*-alkylation of alcohol phenol with methyl α -azido glycinate **1** (scheme 1). Azide derivative **1** was prepared using Steglich method [12] and Achamlale's procedure [13].

Methyl α -azido glycinate *N*-benzoylated **1** was obtained by the reaction [13] of sodium azide with the methyl α -bromo glycinate. The title compound is stable and can be stored for an unlimited time without any signs of decomposition. The methyl α -bromo glycinate also can be used and gives satisfactory results; the azide **1** is used especially for its stability.

As shown in Scheme 1, the reaction of phenol on azide **1** results in formation of the new racemic α -carboxylic amino ester **2** carrying phenoxy group or substituent in position α . As a first step and to optimize the different reaction conditions (choice of base, solvent ...), we conducted several test reactions. For all these tests, the reactions were followed by TLC and ¹H-NMR. Yields are given as pure product after column chromatography on silica gel. After several attempts of reactions without base or in the presence of bases such as triethylamine, reaction with diisopropylethylamine (DIPEA) gave the best results. The reaction was carried out in dry acetone at room temperature for 48 h. Results are summarized in Table 1.

Table 1: Synthesis of Methyl 2-benzamido-2-(phenoxy) acetate **2**.

| Nu-H | Product | M.P. (°C) | Reaction Time (h) | -DCM | Et ₃ N DCM | Et ₃ N Acetone | DIPEA DCM | DIPEA Acetone |
|--------|---|-----------|-------------------|-----------|-----------------------|---------------------------|-----------|---------------|
| | | | | Yield (%) | Yield (%) | Yield (%) | Yield (%) | Yield (%) |
| Phenol | Methyl 2-benzamido-2-(phenoxy) acetate | 122–124 | 48 | 0 | 9 | 12.5 | 18 | 31 |

The product **2** was obtained in 31% overall yield from **1** and was characterized by MS, ¹H-NMR and ¹³C-NMR

spectroscopy. Comparing these results with the work done by our team [11,14,15], we see that we have obtained almost the same results.

3. Experimental

1. General

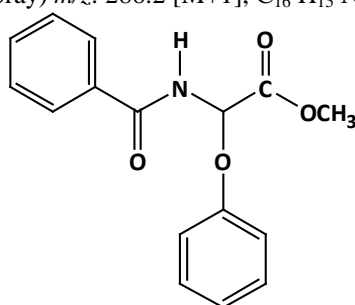
Melting points were determined with an Electrothermal melting point apparatus and are uncorrected. NMR spectra (^1H , ^{13}C) were recorded on a Bruker AM 300 (operating at 300.13 MHz for ^1H , at 75.47 MHz for ^{13}C) spectrometer (Centre Universitaire Régional d'Interface, Fès). NMR data are listed in ppm and are reported relative to tetramethylsilane (^1H , ^{13}C); residual solvent peaks being used as internal standard. All reactions were followed by TLC. TLC analyses were carried out on 0.25 mm thick precoated silica gel plates (Merck Fertigplatten Kieselgel 60F254) and spots were visualised under UV light or by exposure to vaporised iodine. Mass spectra were recorded by electrospray on a micromass ESI Platform II (Université Montpellier II, France).

2. Typical procedure

To a stirred solution of 2.86 mmol of alcohol (oxygen compound) and 3.12 mmol of diisopropylethylamine in 10 mL of dry acetone, 2.6 mmol of α -azido glycinate were added. The mixture was stirred at room temperature and the reaction was followed by TLC (Kieselgel Merck 60F254). 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 in sodium sulfate (Na_2SO_4) and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica gel using ether/hexane as eluant to afford pure *O*-alkylated product.

Methyl 2-benzamido-2-(phenoxy) acetate: White solide: Yield = 31 %. Mp = 122-124 °C (ether/ hexane). Rf = 0.6 (ether). ^1H NMR (300 MHz, CDCl_3): δ ppm = 3.82 (s, 3H, OCH_3); 6.1 (d, 1H, $J = 8.5\text{Hz}$, Ha); 6.96 (d, 1H, $J = 8.5\text{Hz}$, NH_{amid}); 7.3-7.8 (2m, 10H, H_{arom}). ^{13}C NMR (75.5 MHz, CDCl_3): δ ppm = 53.15 (OCH_3); 88.71 ($-\text{CH}-$); 116.23 (2C), 121.6, 127.07 (2C), 128.11 (2C), 130.5 (2C), 132.19, 133.22, 165.76 (C_6H_5 aromatic carbons); 169.16 (CO), 171.4 (CO).

MS (electrospray) m/z : 286.2 $[\text{M}+1]$, $\text{C}_{16}\text{H}_{15}\text{NO}_4$.



4. Acknowledgements

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