

Short Note

N-{[(4-Nitrophenyl)amino]methyl}benzamide

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Received: 30 December 2013 / Accepted: 3 March 2014 / Published: 11 March 2014

Abstract: We report the synthesis of *N*-{[(4-nitrophenyl)amino]methyl}benzamide from (benzamidomethyl)triethylammonium chloride and 4-nitroaniline in aqueous media. The structure of the newly synthesized compound was characterized on the basis of ¹H-NMR, ¹³C-NMR and FTIR spectroscopy.

Keywords: 4-nitroaniline; benzamidomethylation reaction; aqueous media

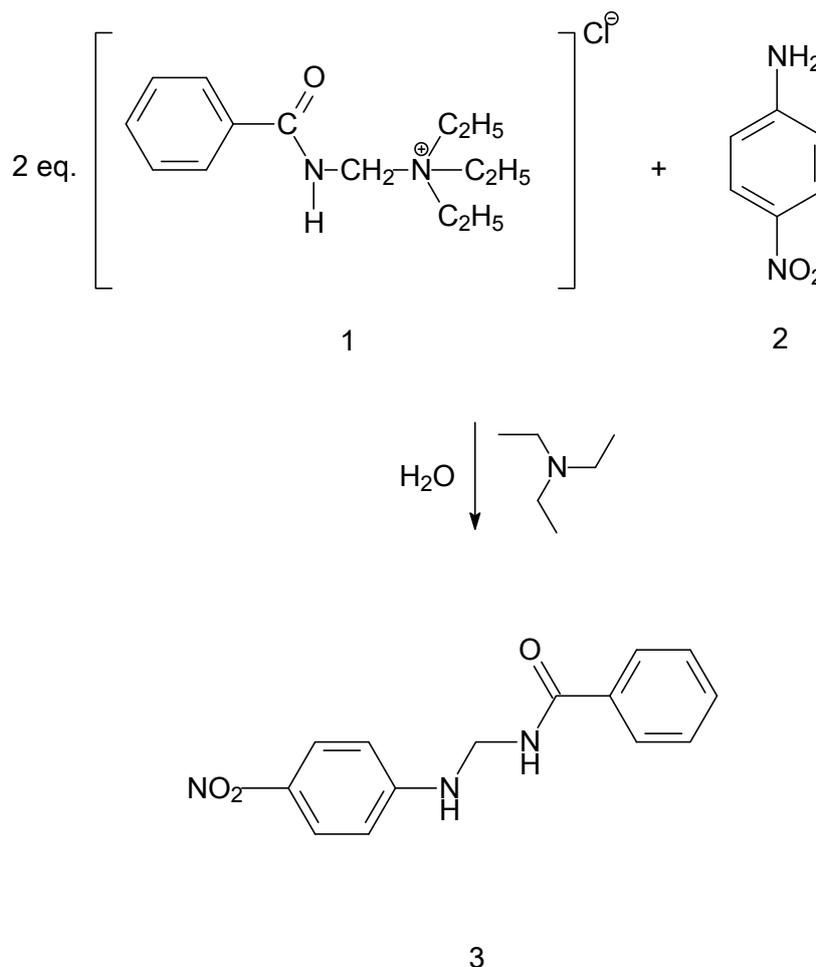
Introduction

In this study we report the synthesis of *N*-{[(4-nitrophenyl)amino]methyl}benzamide, that we have obtained in the course of our continuing study involving benzamidomethylation of N-containing compounds [1–3]. The incorporation of the benzamidomethyl moiety in various compounds has previously been reported due to its application in pro-drug design [4–6]. From the many methods for synthesis of a N-benzamidomethylated compound the most noted are the reaction of N-(chloromethyl)benzamide [7–9] or N-(hydroxymethyl)benzamide [10,11] with a primary or secondary amine or the Mannich-Einhorn reactions [12–14] that utilize benzamide, an aldehyde and a primary or secondary amine. A possible outcome when using a more reactive benzamidomethylating reagent, such as N-(chloromethyl)benzamide, is the formation of dibenzamidomethylated products [7,9]. The title compound we synthesized using (benzamidomethyl)triethylammonium chloride as the benzamidomethylating reagent.

Results and Discussion

The title compound was prepared by reacting 4-nitroaniline (Figure 1-2) and (benzamidomethyl)triethylammonium chloride (Figure 1-1) in an aqueous phase. The main obstacle that was needed to be overcome was the low reactivity of the amine, that is 4-nitroaniline (Figure 1-2), due to the presence of the nitro group in the para position. This problem was resolved with applying an excess of the (benzamidomethyl)triethylammonium chloride salt (Figure 1-1) in the aqueous phase. The low solubility of the amine in water resulted with a slow release in the reaction medium that further assured a monobenzamidomethylated product (Figure 1-3). The formation of a dibenzamidomethylated product was not observed, regardless of the quantity of (benzamidomethyl)triethylammonium chloride that was used. In the experimental protocols that were applied with ratios of up to 1:5, with favorance of the (benzamidomethyl)triethylammonium chloride salt, a dibenzamidomethylated product was not obtained. This can be explained with the very low reactivity of the title compound and its low solubility in water. After the reaction was completed (24 h), the product (Figure 1-3), was removed with vacuum filtration.

Figure 1. Reaction scheme for the title compound.



The structure of the newly synthesized compound was confirmed by ¹H-NMR, ¹³C-NMR, FTIR spectroscopy and HR-MS.

Experimental

Materials

All the reagents and solvents were obtained from commercial sources and used without further purification. The benzamidomethylation reagent, (benzamidomethyl)triethylammonium chloride, was prepared based on an already known method [2].

Instrumentation

Melting points were determined on a Mel-Temp II[®] and are uncorrected. The 1D (¹H, ¹³C{1H}, DEPT) and 2D (COSY, HMQC, HMBC) NMR spectra were recorded on a Bruker 600 MHz instrument in DMSO-*d*₆ as solvent and TMS as internal standard using standard sets of parameters. Infrared spectra (KBr pellets) were measured on a Perkin-Elmer System 2000 FT-IR. The HR mass spectra were made on FT-ICR Bruker Daltonics Apex II on ESI-MS High resolution mode.

Synthesis of *N*-{[(4-nitrophenyl)amino]methyl}benzamide

To an aqueous solution (50 mL) of 3.91 g (0.014 mol) of (benzamidomethyl)triethylammonium chloride and 0.2 mL of triethylamine, 1 g (0.0072 mol) of finely ground powder of 4-nitroaniline was added. The reaction mixture was left to stir at room temperature for 24 h. After the completion of the reaction a thick suspension of a yellow precipitate was observed. The precipitate (1.85 g, 94%) was removed from the solution via vacuum filtration. The product was purified with precipitation from ethanol with the addition of water.

The melting point of the purified product was 194–195 °C.

FTIR(KBr, cm⁻¹): $\nu(N-H)_{\text{amine}}$ 3412; $\nu(N-H)_{\text{amide}}$ 3327; Amide I 1664; Amide II 1530; $\nu(N=O)_{\text{asymmetric}}$ 1603; $\nu(N=O)_{\text{symmetric}}$ 1326.

¹H-NMR (600.13 MHz, DMSO-*d*₆) δ (ppm): 4.75 (dd, $J = 6.0$ Hz, 2H, **CH**₂), 6.87 (dd, $J = 9.0$ Hz, 2H, 4-**NO**₂-**ArH-2**), 7.45 (dd, $J = 8.0$ Hz, 2H, **ArH-3**), 7.52 (dd, $J = 8.0$ Hz, 1H, **ArH-4**), 7.85 (d, $J = 8.0$ Hz, 2H, **ArH-2**), 7.92 (t, $J = 8.0$ Hz, 1H, **Ar-NH**), 8.01 (d, $J = 9.0$ Hz, 2H, 4-**NO**₂-**ArH-3**), 9.22 (t, $J = 6.0$ Hz, 1H, **CO-NH**).

¹³C-NMR (150.91 MHz, DMSO-*d*₆) δ (ppm): 47.8 **CH**₂, 112.0 (4-**NO**₂-**ArC-2**), 126.1 (4-**NO**₂-**ArC-3**), 127.4 (**ArC-2**), 128.5 (**ArC-3**), 131.7 (**ArC-4**), 133.9 (**ArC-1**), 136.7 (4-**NO**₂-**ArC-4**), 153.5 (4-**NO**₂-**ArC-1**), 166.8 (**C=O**).

HRMS (ESI, pos) m/z calcd for C₁₄H₁₃N₃NaO₃ ([M+Na]⁺): 294.0849. Found: 294.0851.

Acknowledgments

This work was supported by the National Science Fund of Bulgaria (grant DRNF02/13).

Conflicts of Interest

The authors declare no conflict of interest.

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