

Short Note

Methyl 4-[(benzoylamino)methoxy]benzoate

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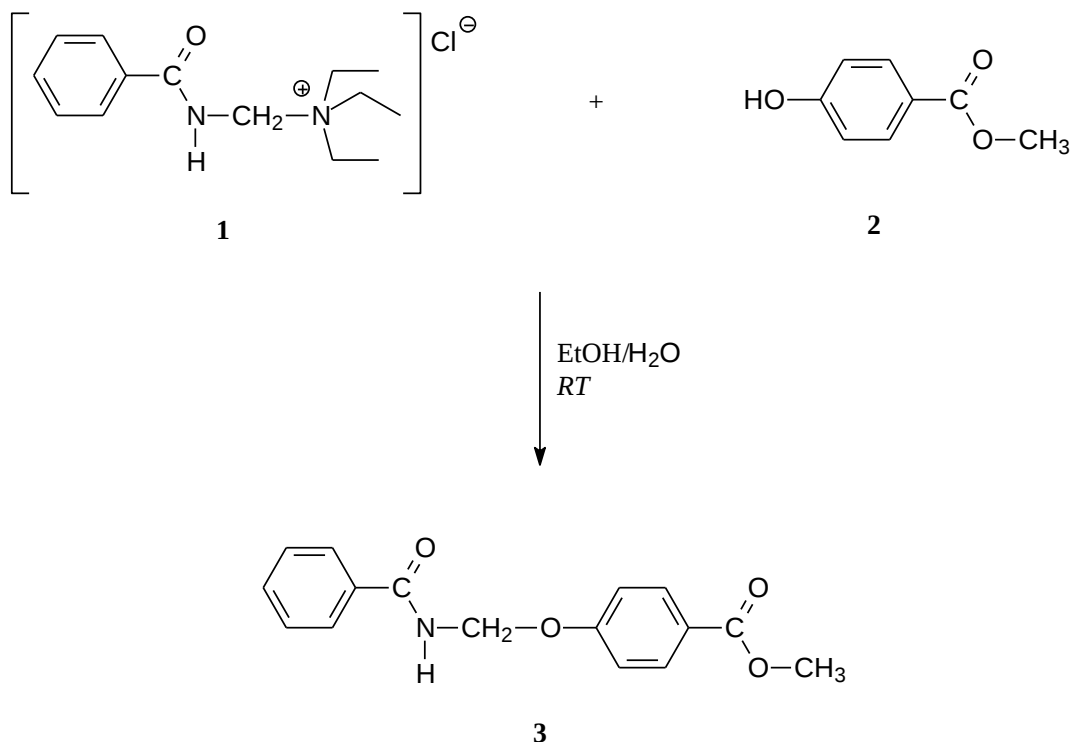
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Abstract: Methylparabene (**2**) was simply benzamidomethylated with (benzamido-methyl)-triethylammonium chloride (**1**) in aqueous medium to afford methyl 4-(benzamido-methoxy)benzoate (**3**) in high yield. The title compound was characterized by elemental analysis, FT-IR, ¹H-NMR and ¹³C-NMR spectroscopy.

Keywords: methylparabene; benzamidomethylation

This paper aims to present a compound similar to methyl 4-methoxybenzoate in which methyl from the methoxy group is replaced with a benzamidomethyl group. Methyl 4-methoxybenzoate, also known as methyl anisate, has been frequently used as pharmaceutical intermediate and in many organic syntheses [1] and in food as flavoring agent [2,3]. In addition, it can be found as volatile component in many plants and mushrooms [4–8].

Although (benzamido-methyl)triethylammonium chloride (**1**) is an excellent reagent for benzamido-methylation of phenols [9], in our previous work [10] we demonstrated that the phenol group at 4-hydroxybenzoic acid cannot be benzamidomethylated with **1** in aqueous media. The carboxylic group as a weak nucleophile in aqueous media does not react [11], but it deactivates the phenol group in the molecule of 4-hydroxybenzoic acid. Since in methylparabene (**2**) the carboxylic group is protected, the hydroxy group can be easily benzamidomethylated with **1** in aqueous media to give methyl 4-[(benzoylamino)methoxy]benzoate (**3**) (Scheme 1).

Scheme 1. Synthetic route to the title compound **3**.

Experimental

Compound **1** is not commercially available and it was synthesised as described previously [9].

Methyl 4-[(benzoylamino)methoxy]benzoate (**3**)

To a mixture of powdered **1** (1.058 g, 3.9 mmol), **2** (0.501 g, 3.3 mmol), ethanol (20 mL) and triethylamine (0.2 mL), water was continually added, drop by drop, until a clear solution was obtained. The mixture was stirred for 5 h at room temperature. Then, water was added to the mixture until occurrence of a precipitate. The typical yield of crude colorless crystals with mp of 133–140 °C was 80%. Purification was performed by dissolving the product in acetone followed by precipitation with water and subsequent recrystallization from toluene.

Melting point of pure crystals: 142–143 °C (uncorrected).

FT-IR (KBr): 3,290 (ν_{NH}), 1,718 (ν_{OC=O}), 1,663 (Amide I), 1,555 cm⁻¹ (Amide II)

¹H-NMR (250 MHz, DMSO-*d*₆): δ/ppm 9.64 (t, *J* = 6.6 Hz, 1H, NH); 7.93–7.15 (9H, Ar); 5.41 (d, *J* = 6.6 Hz, 2H, N-CH₂-O); 3.81 (s, 3H, CH₃)

¹³C-NMR (63 MHz, DMSO-*d*₆): δ/ppm 167.0 (C=O); 165.9 (C=O); 68.7 (CH₂); 51.9 (CH₃); Ar: 160.8, 133.3, 132.1, 131.2, 128.6, 127.5, 122.3, 115.2.

Anal. Calcd. (found) for C₁₆H₁₅NO₄: C, 67.36 (67.55); H, 5.30 (5.41); N, 4.91 (5.07).

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