Molbank **2011**, M712; doi:10.3390/M712

OPEN ACCESS

molbank

ISSN 1422-8599

www.mdpi.com/journal/molbank

Short Note

Methyl 4-[(Benzoylamino)methoxy]benzoate

Emil Popovski [1,*], Kristina Mladenovska[2] and Ana Poceva Panovska [2]

[1] Institute of Chemistry, Faculty of Natural Sciences & Mathematics, Ss. Cyril and Methodius University, Arhimedova 5, PO Box 162, 1000 Skopje, Macedonia

[2] Department of Drug Design and Metabolism, Faculty of Pharmacy, Ss. Cyril and Methodious University, Vodnjanska 17, 1000 Skopje, Macedonia

* Author to whom correspondence should be addressed; E-Mail: popovski.emil@gmail.com.

Received: 1 December 2010 / Accepted: 21 December 2010 / Published: 24 December 2010

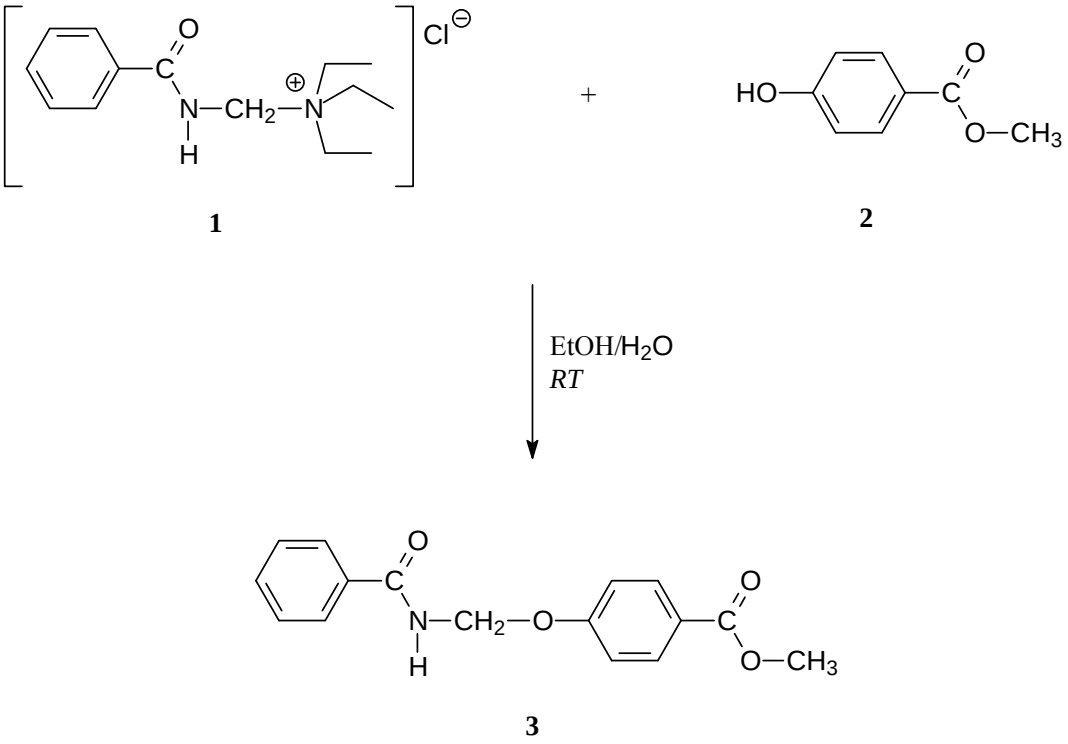
Abstract: Methylparabene **(2)** was simply benzamidomethylated with (benzamidomethyl)-triethylammonium chloride (**1**) in aqueous medium to afford methyl 4-(benzamido-methoxy)benzoate (**3**) in high yield. The title compound was characterized by elemental analysis, FT-IR, ^{1}H-NMR and ^{13}C-NMR 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 (benzamidomethyl)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 (νNH), 1,718 (νOC=O), 1,663 (Amide I), 1,555 cm^{-1} (Amide II)

^{1}H-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-CH_2-O); 3.81 (s, 3H, CH_3)

^{13}C-NMR (63 MHz, DMSO-d_6): δ/ppm 167.0 (C=O); 165.9 (C=O); 68.7 (CH_2); 51.9 (CH_3); *Ar*: 160.8, 133.3, 132.1, 131.2, 128.6, 127.5, 122.3, 115.2.

Anal. Calcd. (found) for $C_{16}H_{15}NO_4$: C, 67.36 (67.55); H, 5.30 (5.41); N, 4.91 (5.07).

References

1. Wang, H.; Pullambhatla, M.; Guilarte, T.R.; Mease, R.C.; Pomper, M.G.; Synthesis of [125I]iodoDPA-713: A new probe for imaging inflammation. *Biochem. Biophys. Res Commun.* **2009**, *389*, 80–83.
2. Perriot, R.; Breme, K.; Meierhenrich, U.J.; Carenini, E.; Ferrando, G.; Baldovini, N. Chemical composition of French mimosa absolute oil. *J. Agric. Food Chem.* **2010**, *58*, 1844–1849.
3. Panda, H. *Perfumes and Flavours Technology Handbook*; Asia Pacific Business Press Inc: Delhi, India, 2010.
4. Rapior, S.; Breheret, S.; Talou, T.; Pélissier, Y.; Bessière, J.-M. The anise-like odor of Clitocybe odora, Lentinellus cochleatus and Agaricus essettei. *Mycologia* **2002**, *94*, 373–376.
5. Binder, R.G.; Flath, R.A. Volatile components of pineapple guava. *J. Agric. Food Chem*. **1989**, *37*, 734–736.
6. Hardy, P.J.; Michael, B.J. Volatile components of *feijoa* fruits. *Phytochemistry* **1970**, *9*, 1355–1357.
7. Shaw, J.G.; Ellingham, P.J.; Birch, E.J. Volatile constituents of feijoa-headspace analysis of intact fruit. *J. Sci. Food Agric.* **1983**, *34*, 743–747.
8. Ceballos, L.; Pino, J.A.; Quijano-Celis C.E.; Dago A. Optimization of a HS-SPME/GC-MS Method for determination of volatile compounds in some Cuban unifloral honeys. *J. Food Quality* **2010**, *33*, 507–528.
9. Popovski, E.; Klisarova, L.; Vikic-Topic, D. Simple method for benzamidomethylation of phenols in water solution. *Synth. Commun.* **1999**, *29*, 3451–3458.
10. Popovski, E.; Mladenovska, K. (Benzoylamino)methyl 4-hydroxybenzoate. *Molbank* **2010**, *2010*, M658.
11. Popovski, E.; Klisarova, L.; Vikic-Topic, D. Benzamidomethylation with (benzamidomethyl)-triethylammonium chloride 2. A simple method for benzamidomethylation of thiols, amines and carboxylic acids. *Molecules* **2000**, *5*, 927–936.