

Short Note

1,1,2,2-Tetrakis[(benzoylamino)methyl]hydrazine

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Abstract: We report herein the synthesis of 1,1,2,2-tetrakis[(benzoylamino)methyl]hydrazine from (benzamidomethyl)triethylammonium chloride and hydrazine monohydrate in the presence of triethylamine in ethanol/aqueous media. The structure of the newly synthesized compound was characterized on the basis of ¹H-NMR, ¹³C-NMR, IR and mass spectral data.

Keywords: hydrazines; benzamidomethylation reaction

1. Introduction

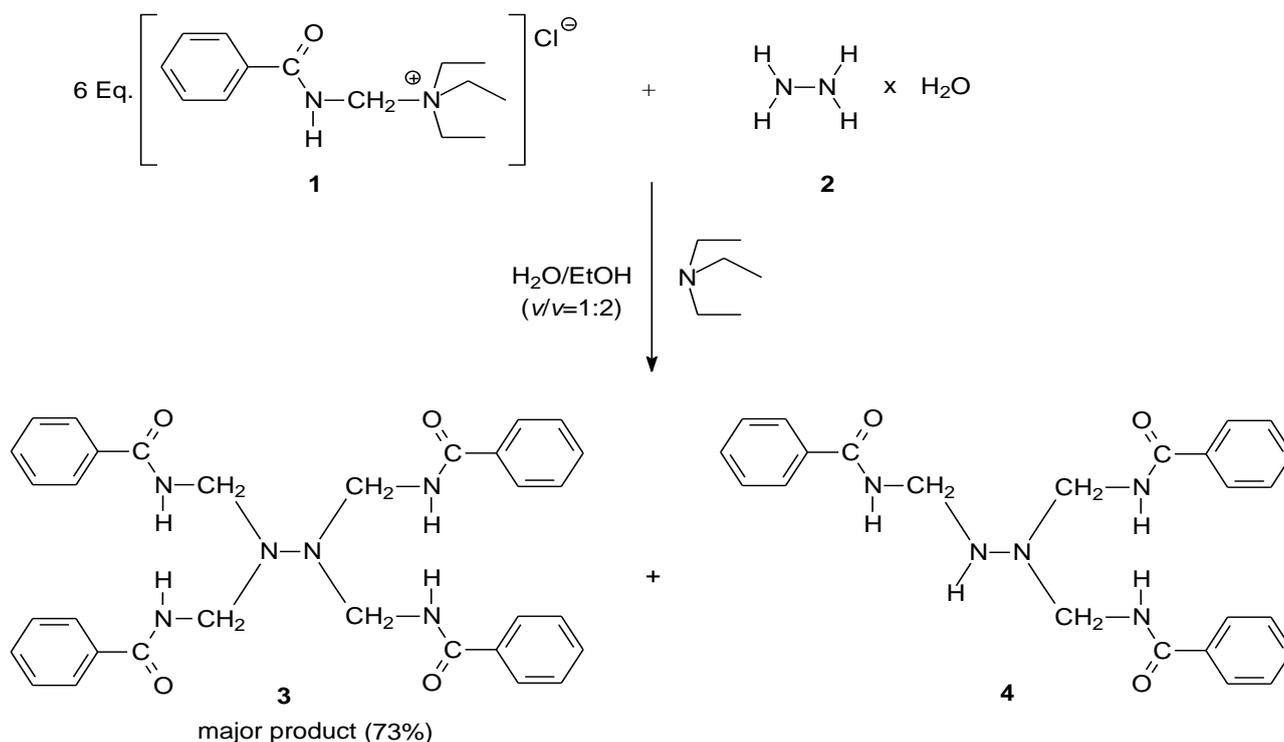
The promising usefulness of the benzamidomethyl derivatives as biologically active products [1-3] and their implication for pro-drug design [4-7] have been previously reported. On the other hand, many hydrazine derivatives are known to exhibit significant biological activity and several compounds with hydrazine moiety were shown to be effective for treatment of tuberculosis, Parkinson's disease, hypertension and widely used as antidepressant drugs [8,9]. The hydrazine moiety has been used for modification of peptides as well. For example, novel building blocks for peptide modification have been designed and synthesized to obtain β -sheet tripeptide mimics that comprise the azapeptide modification at one end [10]. Azapeptides, hydrazine-based peptidomimetics, were found to be potent agents against hepatitis [11], AIDS [12] and SARS [13]. In addition, hydrazines, particularly when they are tetrasubstituted, are an excellent source of radical cations [14-18]. Tetraalkylhydrazines are also employed in the study of single-electron transfer reactions [15-18], and as charge-transfer quenchers of singlet oxygen [14].

In the course of our continuous study on the benzamidomethylation reactions of *N*-containing compounds [19-22], we report herein the synthesis and spectral characterization of the novel 1,1,2,2-tetrakis[(benzoylamino)methyl]hydrazine.

2. Results and Discussion

The title compound was prepared by the reaction of a hydrazine monohydrate (**2**) in ethanol/aqueous ($v/v = 2:1$) solution with (benzamidomethyl)triethylammonium chloride (**1**) in the presence of a small quantity of triethylamine ($\text{pH} > 9$) at room temperature. In fact, hydrazine in the presence of a large excess of **1**, leads to formation of two compounds in aqueous media in an overall yield of 93%. The ratio of the formed products, tetrakis[(benzoylamino)methyl]hydrazine (**3**) and 1,1,2-tris[(benzoylamino)methyl]hydrazine (**4**), was 1.2:1. In order to improve the yield of **3**, the effect of the mole proportion of reactants and solvents was investigated. It was found that the corresponding tetrabenzamidomethylated product was obtained predominantly by increasing the amount of **1** and utilizing an ethanol-aqueous solution as solvent. Thus, large excess of the reagent **1** (at least 6 equivalents) and the use of ethanol-aqueous ($v/v = 2:1$) solvent was required to obtain the optimum yield (73%) of the desired product **3**. After the reaction was completed (2 h), an additional amount of water was added slowly to the reaction mixture until a precipitate occurred. Compound **3** was easily isolated from reaction mixture by vacuum filtration due to its complete insolubility in water. In contrast, compound **4** is slightly soluble in water, and appeared as white amorphous precipitate after remaining one day in the filtrate.

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



The structure of the newly synthesized compound **3** was characterized on the basis of $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, IR and mass spectral data. The $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra of **3** showed only a few signals, implying the presence of a highly symmetrical compound. Seven of the signals in the $^{13}\text{C-NMR}$ spectrum of **3** were recognized (1 C, 1 CH_2 , 5 CH), which were assigned to a carbonyl (δ 166.88), a methylene (δ 56.36) and an aromatic group (δ 127.20–134.11), and therefore indicated for the presence of benzamidomethyl group. Moreover, in the $^1\text{H-NMR}$ of **3** revealed the absence of the hydrazine protons, which indicates that all of the hydrazine protons have been substituted. Mass spectrometric analysis of compound **3** using ESI technique indicated a molecular ion ($m/z = 587.2$; $[\text{M}+\text{Na}]^+$) which is consistent with the molecular formula of a 1,1,2,2-tetrakis[(benzoylamino)methyl]hydrazine ($\text{C}_{32}\text{H}_{32}\text{N}_6\text{O}_4$, calc. 564). The values are in complete agreement with the structure assigned.

The spectral characterization of **4** was reported by our group previously [22].

3. Experimental

The starting material (benzamidomethyl)triethylammonium chloride **1** was synthesized based on a literature method [21].

3.1. Synthesis of 1,1,2,2-tetrakis[(benzoylamino)methyl]hydrazine (**3**)

To a solution of (benzamidomethyl)triethylammonium chloride (1.576 g, 5.82 mmol) in 10 mL of water and 0.2 mL of triethylamine, a solution of hydrazine monohydrate (48.56 mg, 0.97 mmol) in 20 mL of ethanol was added. The resulting mixture was stirred for 2 h at room temperature. Afterwards, water was added slowly to the reaction mixture until a precipitate occurred. The product **3** was obtained by vacuum filtration as a white amorphous solid (0.4 g, 73%). The purification was performed by dissolving the product in ethanol and precipitation with water. The same isolation and purification procedure was followed for the formed precipitate **4** in the filtrate from the first filtration step.

Melting point: 99–101 °C (uncorrected);

FTIR (KBr, cm^{-1}): 3303 $\nu(\text{N-H})$, 1650 (C=O, Amide I), 1533 (N-H, Amide II);

$^1\text{H-NMR}$ (250 MHz, $\text{DMSO-}d_6$): δ/ppm 8.90 (t, $J = 5.0$ Hz, 1(4)H, CONH), 7.41–7.90 (m, 5(20)H, ArH), 4.55 (d, $J = 5.0$ Hz, 2(8)H, CH_2);

$^{13}\text{C NMR}$ (62.9 MHz, CDCl_3): δ/ppm 166.88 C=O; 56.36 CH_2 ; Ar: 134.11, 131.43, 128.31, 127.27;

MS (ESI, pos) m/z : 587.2 ($\text{M}+\text{Na}$) $^+$.

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