

Short Note

N'-(1,3-Dithiolan-2-ylidene)-3-(phenylamino)propanehydrazide

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Abstract: A synthesis of *N'*-(1,3-dithiolan-2-ylidene)-3-(phenylamino)propanehydrazide from 3-(phenylamino)propanehydrazide, carbon disulfide and 1,2-dibromoethane is reported. The title compound was characterized by ¹H NMR, ¹³C NMR, ESI/MS, and elemental analysis.

Keywords: 1,3-dithiolane; propanehydrazide; amino acid

1. Introduction

N-Substituted β -amino acids and their derivatives are structural units of various natural compounds, such as alkaloids, antibiotics, and co-enzymes. Carboxylic acid hydrazides and hydrazones exhibit a broad spectrum of biological activity [1].

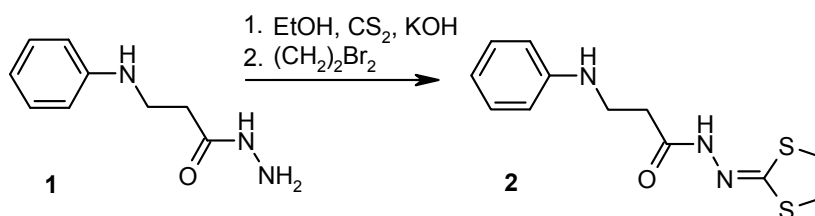
1,3-Dithiolane is an attractive scaffold for the synthesis of heterocyclic compounds possessing valuable properties. It is embodied by many widely used compounds. Among them, an important place is taken by the compounds containing the 1,3-dithiolan-2-ylidene moiety. Such compounds can be used for selective sorption [2]. 2-Alkylidene-1,3-dithiolanes containing the sulfoxide group form dinuclear iron(0) complexes [3], whereas 2-salicylichydrazono-1,3-dithiolane derivatives form complexes with cobalt [4] and manganese [5] ions. A facile method for functionalization of thioamides involves ring fragmentation of 2-acetylmethylene-1,3-dithiolane in the presence of amine [6].

An interesting method for the synthesis of 2-imino-1,3-dithiolane derivatives by the treatment of allyl dithiocarbamates with iodine in methylene chloride has been reported in [7]. A simple synthesis method of *N'*-(1,3-dithiolan-2-ylidene)isonicotinehydrazide involves reaction of isonicotinehydrazide with carbon disulfide in alkali solution followed by the treatment with dibromoethane [8]. A similar procedure was employed for preparation of 1,3-dithiolane-2-ylidenhydrazidebenzoic acid [9].

In the search for new potentially biologically active compounds and in light of the data listed above, we report the synthesis of a compound containing both β -amino acid and 1,3-dithiolane moieties.

2. Results and Discussion

N'-(1,3-Dithiolan-2-ylidene)-3-(phenylamino)propanehydrazide **2** was synthesized according to the synthesis protocol described in [8] by stirring 3-(phenylamino)propanehydrazide **1** [10] with carbon disulfide in ethanolic KOH solution and subsequent heating at reflux after addition of 1,2-dibromoethane (Scheme 1). The obtained residue was recrystallised from methanol.



Scheme 1. Synthesis of *N'*-(1,3-dithiolan-2-ylidene)-3-(phenylamino)propanehydrazide **2**.

The formation of the dithiolane moiety has been confirmed by the ¹H NMR resonances in the range of 3.49–3.54 ppm and 3.59–3.72 ppm attributable to the methylene group protons of *s-E/s-Z* isomers. These isomers are formed in the DMSO solution owing to the restricted rotation around the amide bond. Signals attributable to the COCH₂ and NH groups protons are also observed in two line sets in the ¹H NMR spectrum. Usually, the most information about the existing isomers can be obtained from the NH group resonances [11]. The NH group singlets are present down-field at 10.13 ppm (*s-Z*) and 10.30 ppm (*s-E*) and the intensity ratio is 0.3:0.7.

The presence of the carbon resonance at 162.52 ppm attributable to the C=N group and the spectral line at 35.12 ppm attributable to the CH₂ group in the ¹³C NMR spectrum indicate the formation of the target product as well.

3. Experimental Section

3.1. General

All the reagents and chemicals were obtained from commercial sources and used without further purification. Melting points were measured on a B-540 Melting Point Analyzer and are uncorrected (Büchi Corporation, New Castle, DE, USA). ¹H and ¹³C NMR spectra were recorded at ambient temperature on a Varian Unity Inova (300 MHz) spectrometer (Palo Alto, CA, USA). Chemical shifts (δ) are reported in parts per million (ppm) calibrated from TMS (0 ppm) as an internal standard for ¹H NMR, and DMSO-*d*₆ (39.5 ppm) for ¹³C NMR. The *J* constants are given in Hz. Mass spectrum

was recorded on a Waters Micromass ZQ 2000 instrument (Milford, MA, USA). Elemental analysis was performed on a CE-440 elemental analyzer (Exeter Analytical Inc., North Chelmsford, MA, USA). TLC was performed using Silica gel 60 F254 (Kieselgel 60 F254) (Merck, Darmstadt, Germany) plates.

3.2. Experimental Procedure for the Preparation of *N'*-(1,3-Dithiolan-2-ylidene)-3-(phenylamino)propanehydrazide (**2**)

To a mixture of KOH (1.2 g, 20 mmol) and ethanol (10 mL), hydrazide **1** (1.79 g, 10 mmol) was added with stirring. Afterwards, CS₂ (0.6 mL, 10 mmol) was added dropwise followed by 1,2-dibromoethane (0.86 mL, 10 mmol). The reaction mixture was refluxed for 0.5 h. After cooling it to room temperature, water (50 mL) was added. Precipitate formed was filtered off, washed with water, and recrystallized from methanol.

Yield: 0.65 g (80%), white, m.p. 133–134 °C.

¹H NMR (300 MHz, DMSO-*d*₆), δ: 2.50 (t, 1.4H, *J* = 7.2 Hz, *s*-Z COCH₂); 2.69 (t, 0.6H, *J* = 7.2 Hz, *s*-E COCH₂); 3.22–3.33 (m, 2H, NHCH₂); 3.49–3.54 (m, 2H, *s*-Z SCH₂CH₂); 3.59–3.72 (m, 2H, *s*-E SCH₂CH₂); 5.57 (s, 1H, NHCH₂); 6.56 (t, 1H, *J* = 7.5 Hz, H_{ar4}); 6.60 (d, 2H, *J* = 7.5 Hz, H_{ar2,6}); 7.09 (t, 2H, *J* = 1.2 Hz; *J* = 7.5 Hz, H_{ar3,5}); 10.13 (s, 0.3H, *s*-Z NH); 10.30 (s, 0.7H, *s*-E NH).

¹³C NMR (75 MHz, DMSO-*d*₆), δ: 33.41 (C-8); 35.12 (C-11,12); 38.60 (C-7); 112.03 (C-2,6); 115.72 (C-4); 128.82 (C-3,5); 148.44 (C-1); 162.52 (C-10); 166.71 (C-9).

MS (ESI, 20 V) *m/z* (%): 282 ([M + H]⁺, 80).

Anal. Calcd. (%) for C₁₂H₁₅N₃OS₂: C, 51.22; H, 5.37; N, 14.93., found: C, 51.09; H, 5.37; N, 14.67.

¹H NMR (Figure S1) and ¹³C NMR (Figure S2) spectra for the title compound **2** are available in the Supplementary Information.

Author Contributions

Ingrida Tumosienė performed the synthesis and spectral analysis; Kristina Kantminienė contributed to the data analysis and prepared the manuscript; Zigmuntas J. Beresnevičius designed the synthesis and supervised the work. All authors read and approve the final manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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