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Short Note

5,6-Dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione

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Abstract: 1,2,5-Chalcogenadiazoles fused with electron-withdrawing heterocycles have been actively investigated for the preparation of organic photovoltaic materials. [1,2,5]Oxadiazolo[3,4-d]pyridazines are much less studied than other chalcogenadiazolopyridazines due to their low availability. In this communication, we report our study showing that 5,6-dihydro-[1,2,5]oxadiazolo[3,4-d]pyridazine-4,7-dione, a key precursor for the synthesis of 4,7-dihalo-[1,2,5]oxadiazolo[3,4-*d*]pyridazines, is formed via the cyclization of 1,2,5-oxadiazole-3,4-dicarbohydrazide in hydrochloric acid. The structure of the newly synthesized compound was established by means of elemental analysis; high-resolution mass spectrometry; ^{1}H and ^{13}C NMR; IR spectroscopy, and mass spectrometry.

Keywords: [1,2,5]oxadiazolo[3,4-d]pyridazines; ring closure; 5,6-dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione

1. Introduction

The oxadiazolopyridazine heterocyclic system has been of interest to organic chemists for the past 50 years. The main attention is paid to various *N*-oxide derivatives of this heterocycle, including 1,2,5-oxadiazole *N*-oxides and pyridazine-di-*N*-oxides, which have been actively investigated as nitric oxide donors [1,2] and as high-energy compounds [1,3,4]. [1,2,5]Oxadiazolo[3,4-*d*]pyridazines are much less studied since the methods for their synthesis are limited by the deoxygenation of the corresponding 1,2,5-oxadiazole *N*-oxides. Meanwhile, these compounds have been studied for photovoltaic applications [5,6]. 4,7-Dihalogen-substituted 2,1,3-benzoxadiazoles are important precursors for the synthesis of organic solar cell (OSC) and organic light-emitting diode (OLED) components [7]. The sulfur-containing analog of the oxadiazolopyridazine, 4,7-dibromo-[1,2,5]thiadiazolo pyridazine, has previously been shown to be a key precursor for a number of photovoltaic materials [8–10]. 4,7-Dihalo-[1,2,5]oxadiazolo[3,4-*d*]pyridazines can also act as useful compounds for the preparation of such materials. The key intermediate for the synthesis of these heterocycles is 5,6-dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione **1**, which can be obtained from 1,2,5-oxadiazole-3,4-dicarbohydrazide **2** [11] via a procedure similar to the synthesis of 5,6-dihydro-[1,2,5]thiadiazolo[3,4-*d*]pyridazine-4,7-dione [12]. Herein, we report a study on the cyclization reaction of 1,2,5-oxadiazole-3,4-dicarbohydrazide **2** to 5,6-dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione **1**.

2. Results and Discussion

We studied the reaction of closing the pyridazine ring in 1,2,5-oxadiazole-3,4-dicarboxylic acid dicarbohydrazide **2** under the action of hydrochloric acid in order to obtain 5,6-dihydro-[1,2,5]oxadiazolo [3,4-*d*]pyridazine-4,7-dione **1**. Previously, we showed [12] that the closure of the pyridazine ring into dicarbohydrazide 1,2,5-thiadiazole-3,4-dicarboxylic acid proceeded successfully by refluxing in a 2N HCl solution for 6 h. However, attempts

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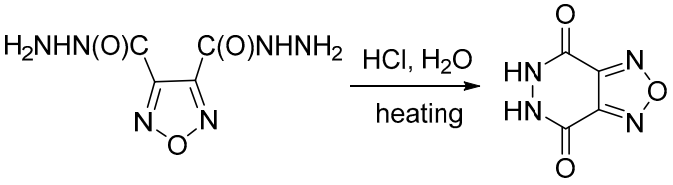
to apply this method to dicarbohydrazide 1,2,5-oxadiazole-3,4-dicarboxylic acid **2** were unsuccessful. Instead of the precipitation of compound **1**, a clear brown solution was formed. Using thin-layer chromatography, it was shown that bis-hydrazide **2** completely reacted with 2N hydrochloric acid for 3 h at 75 °C. However, the yield of the target dihydropyridazindione **1** isolated via extraction with ethyl acetate was only 15% (Table 1, entry 1). It has been established that the reason for the low yield of dione **1** is its decomposition into a mixture of unidentifiable compounds when heated in 2N hydrochloric acid; thus, complete decomposition of dione **1** was observed upon heating for 6 h. The best yield of [1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione **1** (41%) was obtained by heating the reaction mixture for 1 h at 75 °C (Table 1, entry 3). A decrease in the temperature of the reaction mixture from 75 °C to 60 °C, as well as an increase in the temperature to 90 °C, did not lead to an increase in the yield of the target product **1** (Table 1, entries 4 and 5).

Table 1. Reaction of 1,2,5-oxadiazole-3,4-dicarbohydrazide **2** with hydrochloric acid.



2 **1**

Entry	Temperature, °C	Time, h	Yield, of 1, %
1	75	3	15
2	75	2	25
3	75	1	41
4	60	1	39
5	90	1	28

The structure of 5,6-dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione **1** was confirmed by means of elemental analysis; high-resolution mass spectrometry; ^{1}H and ^{13}C NMR; IR spectroscopy, and mass spectrometry.

In conclusion, 5,6-dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione **1** was synthesized via the ring closure reaction of 1,2,5-oxadiazole-3,4-dicarbohydrazide **2** with hydrochloric acid. The compound obtained may serve as a precursor for the preparation of 4,7-dihalo-[1,2,5]oxadiazolo[3,4-*d*]pyridazines.

3. Materials and Methods

1,2,5-Oxadiazole-3,4-dicarbohydrazide **2** was prepared according to the published method [11]. The solvents and reagents were purchased from commercial sources and used as received. Elemental analysis was performed using a 2400 Elemental Analyzer (Perkin ElmerInc., Waltham, MA, USA). The ^{1}H and ^{13}C NMR spectra were obtained with a Bruker AM-300 machine (Bruker AXS Handheld Inc., Kennewick, WA, USA) (at frequencies of 300 and 75 MHz) in an acetone-d_6 solution, with TMS as the standard. The MS spectrum (EI, 70 eV) was obtained with a Finnigan MAT INCOS 50 instrument (Hazlet, NJ, USA). The high-resolution MS spectrum was measured using a Bruker micrOTOF II instrument (Bruker Daltonik Gmbh, Bremen, Germany) with electrospray ionization (ESI). The IR spectrum was measured with a Bruker "Alpha-T" instrument in KBr pellet.

5,6-Dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione **1** (CAS 898057-22-2) was commercially available from Aurora Fine Chemicals LLC (San Diego, CA, USA).

Synthesis of 5,6-dihydro-[1,2,5]oxadiazolo[3,4-*d*]pyridazine-4,7-dione **1** (Supplementary Materials).

1,2,5-Oxadiazole-3,4-dicarbohydrazide **2** (100 mg, 0.53 mmol), H_2O (20 mL), and conc. HCl (0.6 mL) were added to a 50 mL three-necked flask. The mixture was stirred for 1 h at

75 °C and then cooled to room temperature; water (10 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was separated using silica gel column chromatography (eluent: CH_2Cl_2/EtOH = 10:1). The yield was 33 mg (41%), as a yellow solid, and R_f = 0.1 (CH_2Cl_2). Mp = 240–243 °C. IR spectrum, ν, cm^{-1}: 3109, 3038, 2931, 2850, 1725, 1679, 1324, 1120, 1023, 828, 722, 641, and 511. ^{1}H NMR (ppm): δ 10.1 (2H, s, NH). ^{13}C NMR (ppm): δ 146.3 and 148.9. HRMS (ESI-TOF), m/z: calcd. for $C_4H_3N_4O_3$ $[M + H]^+$ 155.0200 and found 155.0203. MS (EI, 70eV), m/z (I, %): 154 ($[M]^+$, 40), 70 (20), and 30 (100). Anal. calcd. for $C_4H_3N_4O_3$ (288.2952): C, 30.96; H, 1.95; and N, 36.13%. Found: C, 31.25; H, 2.04 %; and N, 36.47%.

Supplementary Materials: The following are available online: copies of the ^{1}H, ^{13}C NMR, IR, and LR and HR mass-spectra for the compound **1**.

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Sample Availability: Samples of compound **1** are available from the authors.

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