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Short Note

5-Bromo-*N′*-(2-oxoindolin-3-ylidene)furan-2-carbohydrazide

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Abstract: 5-Bromo-*N′*-(2-oxoindolin-3-ylidene)furan-2-carbohydrazide (**1**) was successfully synthesized in 79.4% yield by reaction of isatin with 5-bromofuran-2-carbohydrazide in acidic conditions under reflux. The structure of synthesized compound **1** was confirmed by ^{1}H and ^{13}C NMR, FTIR, and HRMS spectrometers. It is necessary to evaluate compound **1** as an anti-inflammatory agent.

Keywords: isatin; furan-2-carbohydrazide; reaction

1. Introduction

Inflammation is the immune system's response to harm and is an essential defense mechanism for health [1]. Notwithstanding, uncontrollable inflammation in different parts of the body contributes to the pathogenesis of numerous chronic diseases, including diabetes, neurodegenerative diseases like Alzheimer's, and cardiovascular diseases like atherosclerosis [2]. Thus, some studies have concentrated on developing novel drugs to counteract inflammatory damage to cellular components, but the efficacy and adverse effects of current medicines remain major issues [3].

Isatin-containing heterocycles possess favorable anti-inflammatory properties [4,5]. SAR analyses of in silico studies have indicated that the hydrazide moiety provides a hydrogen bonding domain that enables the structure to form a hydrogen bond, which is essential for the interaction with amino acid residues, appending the potential to be a potent anti-inflammatory agent [6]. Various furan-containing compounds naturally occur in plants, oils, fruits, and marine foods [7]; are reported to be biologically active, having an anti-inflammatory effect [8,9]; and are found in a variety of pharmaceutical medicines, such as furosemide [10]. Here, we report the synthesis of 5-bromo-*N′*-(2-oxoindolin-3-ylidene)furan-2-carbohydrazide (**1**).

2. Results and Discussion

The synthesis of 5-bromo-*N′*-(2-oxoindolin-3-ylidene)furan-2-carbohydrazide (**1**) has been successfully achieved by condensation of commercially available isatin (**2**) with 5-bromofuran-2-carbohydrazide (**3**) under acidic conditions, as shown in Scheme 1. The reaction of isatin (**2**) and 5-bromofuran-2-carbohydrazide (**3**) took place for 15 min under reflux, with ethanol as the solvent and sulfuric acid as the catalyst. The expected product was filtered and washed using dichloromethane to isolate compound **1** as a yellowish solid with 79.4% yield.

Structure identification of the synthesized compound **1** using an NMR spectrometer resulted in an ^{1}H NMR spectrum that corresponds to the structure of 5-bromo-*N′*-(2-oxoindolin-3-ylidene)furan-2-carbohydrazide (**1**). According to the ^{1}H NMR spectrum, the proton of the NH group of the hydrazide moiety showed up as a broad singlet signal at δ 13.72 ppm. This NH group vibration was recorded at υ 3233 cm^{-1} in the FTIR spectrum. Meanwhile, the NH of the isatin ring was detected as a singlet signal at

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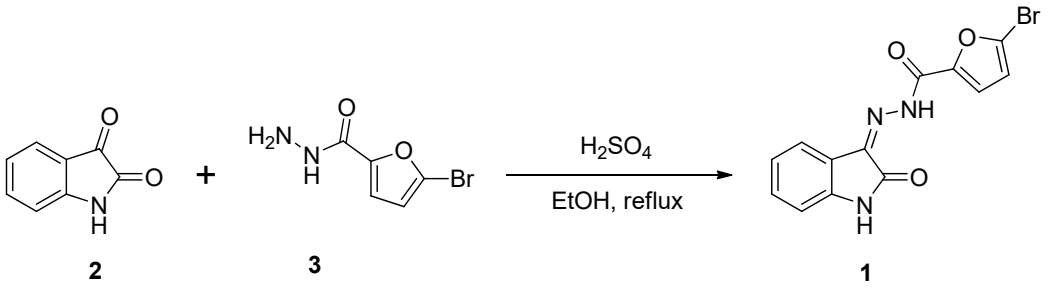
δ 11.30 ppm. In the ^{13}C NMR spectrum, the signal of hydrazide carbonyl carbon was detected at δ 153.62 ppm. The C=O absorption reinforced this at υ 1620 cm^{-1} in the FTIR spectrum, while the signal of isatin carbonyl carbon was observed at δ 163.4 ppm. Furthermore, the absorption at υ 1680 cm^{-1} showed the absorption of the C=N group (imine), indicating the successful condensation of isatin (**2**) and 5-bromofuran-2-carbohydrazide (**3**). In the HRMS spectrum, since the bromine atom has two isotopes in nature, namely ^{79}Br and ^{81}Br, the $[M+H]^+$ ions were recorded at *m/z* 333.9841 and 335.9813, which corresponds to the molecular formula for $C_{13}H_8{}^{79}BrN_3O_3$ and $C_{13}H_8{}^{81}BrN_3O_3$, respectively (calcd. 333.9822 ($C_{13}H_8{}^{79}BrN_3O_3$) and 335.9802 ($C_{13}H_8{}^{81}BrN_3O_3$)).



Scheme 1. Synthesis of 5-bromo-*N*′-(2-oxoindolin-3-ylidene)furan-2-carbohydrazide (**1**).

3. Materials and Methods

3.1. Materials

The materials utilized in this study were purchased from Tokyo Chemical Industry and Sigma-Aldrich and were not purified before use. Thin-layer chromatography (TLC) was used to monitor the reaction, which was seen under UV at 254 nm. The melting point was determined using Fisher-Johns melting point apparatus (Vernon Hills, IL, USA) and has not been corrected. The ^{1}H and ^{13}C NMR spectra were taken at 400 and 100 MHz on a Jeol JNM-ECS400 spectrometer (Tokyo, Japan) in DMSO-d_6, with tetramethylsilane (TMS) serving as an internal standard. Reports are given in parts per million (ppm) for the chemical shifts (δ) and in Hertz for the coupling constants (*J*). The FTIR spectrum was captured using a Shimadzu 8400S FTIR spectrometer (Kyoto, Japan). Mass spectra were recorded in a Xevo G2-S Qtof mass spectrometer with an ESI ionization in positive mode. The absorbance of the sample was measured using a Thermo Scientific Genesys 10S UV-VIS spectrophotometer (Milford, CT, USA).

*3.2. Synthesis of 5-Bromo-N′-(2-oxoindolin-3-ylidene)furan-2-carbohydrazide (**1**)*

A solution of isatin (**2**) (0.074 g, 0.50 mmol), 5-bromofuran-2-carbohydrazide (**3**) (0.10 g, 0.49 mmol), and a drop of sulphuric acid in ethanol (10 mL) was refluxed for 15 min (the reaction was monitored by TLC using ethyl acetate as an eluent). The mixture was cooled to room temperature. The precipitate was filtered off, washed with dichloromethane, and dried to yield the title compound as a yellowish solid (130 mg, 79.4%%); mp: 212–213 °C; FTIR (KBr) *υ* (cm^{-1}) 3233 (N-H), 1722 (C=O), 1680 (C=O), 1620 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.91–6.96 (m, 2H, ArH), 7.06–7.11 (m, 1H, ArH), 7.35–7.44 (m, 2H, ArH), 7.59 (t, *J* = 7.6 Hz, 1H, ArH), 11.31 (1H, s, NH), 13.72 (1H, bs NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 111.7, 115.7, 119.9, 120.2, 121.6, 123.2, 127.3, 132.4, 138.9, 143.1, 148.1, 153.6, 163.4. HRESIMS *m/z* (pos): 333.9841 ($C_{13}H_8{}^{79}BrN_3O_3$) and 335.9813 ($C_{13}H_8{}^{81}BrN_3O_3$) (calcd. 333.9827 ($C_{13}H_8{}^{79}BrN_3O_3$) and 335.9807 ($C_{13}H_8{}^{81}BrN_3O_3$)) (Supplementary Materials).

Supplementary Materials: The following supporting information can be downloaded online. Figure S1: IR spectrum of compound **1**; Figure S2: ^{1}H NMR spectrum of compound **1**; Figure S3: ^{13}C NMR spectrum of **1**; Figure S4: High-resolution mass spectrum of compound **1**.

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