

*Short Note*

## 1-(1*H*-Benzimidazol-2-yl)-3-[5-(trichloromethyl)-1,3,4-oxadiazol-2-yl]propan-1-one

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**Abstract:** The title compound, 1-(1*H*-benzimidazol-2-yl)-3-[5-(trichloromethyl)-1,3,4-oxadiazol-2-yl]propan-1-one (**2**) was synthesized successfully from 4-(1*H*-benzimidazol-2-yl)-4-oxobutanehydrazide (**1**) under microwave irradiation in good yield by reacting with trichloroacetic acid, and the structure of title compound was confirmed on the basis of IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, MS and CHN analyses results.

**Keywords:** Benzimidazole; oxadiazole; trichloroacetic acid

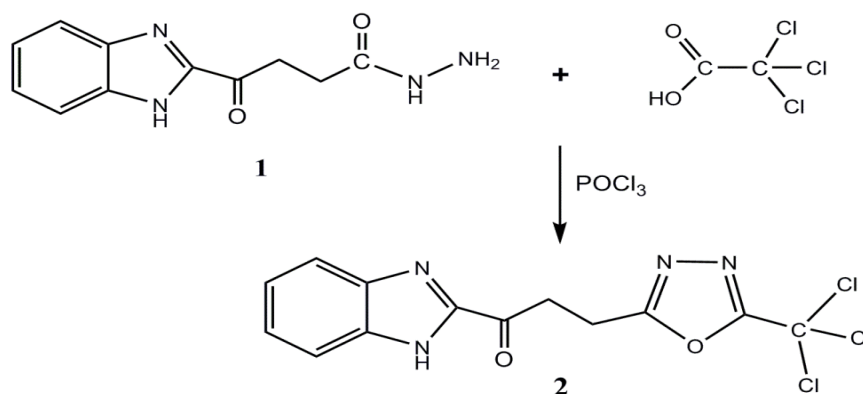
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The search for new anticancer agents having a heterocyclic nucleus continues worldwide at various laboratories [1] and from the reported literature, it can be concluded that benzimidazole heterocycles are of great importance in their biological as well as synthetic aspects of medicinal chemistry. Various substituted derivatives of the benzimidazole nucleus showed remarkable biological activity such as antitumor/antiproliferative/anticancer [2–6], anti-inflammatory [7], antiviral including anti-HIV [8], antibacterial [9], antifungal [10] antioxidant [11] and cysticidal activities [12]. Similarly, 1,3,4-oxadiazole is a class of heterocyclic compounds that have attracted significant interest in medicinal chemistry as they have a wide range of pharmaceutical and pharmacological applications including potential antitumor/antiproliferative/anticancer activities [13,14]. In view of these points, it was thought worthwhile to prepare a new type of compound that comprises both benzimidazole and 1,3,4-oxadiazole ring systems in the hope to obtain a promising anticancer agent.

The purity of the compound was checked by single-spot TLC [using silica gel G (Merck No. 5554) as stationary phase] with T/E/F (toluene/ethyl acetate/formic acid, 5:4:1) as the eluent and spots located by means of iodine vapors/UV light. The melting point was determined in an open capillary tube and is uncorrected. The final product was purified by recrystallization from ethanol. The spectral data of the title compound were found to be in full agreement with its postulated structure. Nuclear magnetic resonance spectra were recorded on a Bruker Spectrospin DPX-300 in DMSO- $d_6$ , chemical shift ( $\delta$ ) values are reported in parts per million (ppm) and coupling constants ( $J$ ) in Hz using tetramethylsilane as internal reference. The mass spectrum was recorded on a LCMS/MS (Perkin-Elmer and LABINDIA, Applied Biosystem), model no. API 3000 presented as  $m/z$ . The IR spectrum was recorded on a FT/IR (Jasco, Japan), model No. 410. Elemental analyses were performed on a Perkin-Elmer 240 analyzer and values were found in the range of  $\pm 0.4\%$  for each element analyzed (C, H and N).

The new compound was prepared as outlined in Figure 1. The IR spectrum of the compound showed a band at  $3336\text{ cm}^{-1}$  for N-H. In the  $^1\text{H-NMR}$  spectrum, an exchangeable singlet signal appeared at  $\delta\ 12.10$  ppm corresponding to the N-H proton. The observed bands in the IR spectrum at around  $1728$  and  $1666\text{ cm}^{-1}$  account for C=O and C=N. The chemical shift in the  $^{13}\text{C-NMR}$  spectrum at  $\delta\ 173.47$  and  $155.8$  could be accounted for C=O and C=N. The characteristic band at around  $1342\text{ cm}^{-1}$  for N=N=C is indicative for the formation of the oxadiazole ring. The title compound showed two triplets at appropriate chemical shifts in the  $^1\text{H-NMR}$  spectrum at around  $\delta\ 3.20$  ( $J = 6.9\text{ Hz}$ ) and  $\delta\ 2.80$  ( $J = 6.9\text{ Hz}$ ) and the  $^{13}\text{C-NMR}$  spectrum shows signals at around  $\delta\ 29.8$  and  $28.1$  which could be assigned to two methylene groups ( $-\text{CH}_2-\text{CH}_2-$ ) forming a linker chain through which the benzimidazole nucleus is attached to the oxadiazole ring, thus representing the back bone of this compound. The presence of doublet, triplet and double doublet signals at around  $\delta\ 7.70$ ,  $7.40$  and  $7.20$  ( $J = 8.1\text{ Hz}$ ,  $J = 8.1\text{ Hz}$  and  $J = 8.1\text{ Hz}$ ,  $J = 7.2\text{ Hz}$ ) indicated three benzimidazole hydrogens. The signals in the  $^{13}\text{C-NMR}$  spectrum which appear at around  $\delta\ 160.0$  could be assigned to the oxadiazole ring carbons. The mass spectrum (ESI-MS) shows the presence of molecular ion peaks at  $358$  ( $\text{M}^+$ ),  $360$  ( $[\text{M}+2]^+$ ),  $362$  ( $[\text{M}+4]^+$ ),  $364$  ( $[\text{M}+6]^+$ ) due to the presence of three chlorine atoms. The starting material 4-(1H-benzimidazol-2-yl)-4-oxobutanoic acid hydrazide (**1**) was synthesized based on our previous work [15].

**Figure 1.** Synthetic route to the title compound **2**.



*Synthesis of 1-(1H-benzimidazol-2-yl)-3-[5-(trichloromethyl)-1,3,4-oxadiazol-2-yl]propan-1-one (2)*

A mixture of 4-(1H-benzimidazol-2-yl)-4-oxobutanoic acid hydrazide (**1**) (0.001 mol, 0.232 g), trichloroacetic acid (0.001 mol, 0.163 g) and POCl<sub>3</sub> (5 mL) was placed into a microwave reaction vessel equipped with a magnetic stir bar. The reaction vessel was placed into the scientific microwave synthesizer and irradiated at a power level of 6 (60%, 420 W) for 9 min. After completion of reaction, checked by single-spot TLC (eluent: toluene/ethyl acetate/formic acid, 5:4:1), the reaction mixture was cooled and poured slowly onto crushed ice, then neutralized with sodium bicarbonate solution. A solid mass precipitated, which was filtered and washed with excess water to remove the inorganic components. The product was purified by recrystallization from ethanol.

Yield: 91%; m.p. 244–245 °C; R<sub>f</sub> = 0.45; greenish amorphous solid.

IR (KBr)  $\nu_{\max}$  (cm<sup>-1</sup>): 3336 (NH), 3105 (CH), 2974 (CH<sub>2</sub>), 1728 (C=O), 1666 (C=N), 1569 (C=C), 1342 (N-N=C), 1180 (C-O-C, asymmetric), 1029 (C-O-C, symmetric), 759 (C-Cl). <sup>1</sup>H-NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  12.10 (s, 1H, NH, D<sub>2</sub>O exchangeable), 7.71 (d, 1H, *J* = 8.1 Hz, H-4-benzimidazole), 7.41 (t, 1H, *J* = 8.1 Hz, H-7-benzimidazole), 7.29 (dd, 2H, *J* = 8.1 Hz, *J* = 7.2 Hz, H-5,6-benzimidazole), 3.23 (t, 2H, *J* = 6.9 Hz, CH<sub>2</sub>), 2.87 (t, 2H, *J* = 6.9 Hz, CH<sub>2</sub>CO). <sup>13</sup>C-NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  173.47 (C=O), 160.00 (C, oxadiazole), 155.86 (C=N), 133.29, 132.05, 129.69, 128.43, 123.14, 116.45 (Ar-C), 79.66 (CCl<sub>3</sub>), 29.83 (CH<sub>2</sub>, CH<sub>2</sub>CO), 28.13 (CH<sub>2</sub>). ESI-MS (*m/z*): 358 (M<sup>+</sup>), 360 ([M+2]<sup>+</sup>), 362 ([M+4]<sup>+</sup>), 364 ([M+6]<sup>+</sup>).

Anal. calcd. for C<sub>13</sub>H<sub>9</sub>Cl<sub>3</sub>N<sub>4</sub>O<sub>2</sub>: C, 43.42; H, 2.52; N, 15.58. Found: C, 43.45; H, 2.56; N, 15.63.

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