

Short Note

## ***N*-(2-Phenoxy-4-(3-phenoxyprop-1-ynyl)phenyl)methane Sulfonamide**

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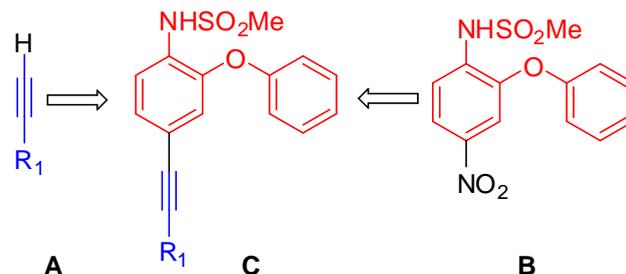
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**Abstract:** The title compound, *N*-(2-phenoxy-4-(3-phenoxyprop-1-ynyl)phenyl) methanesulfonamide was synthesized in high yield by Sonogashira cross coupling of *N*-(4-iodo-2-phenoxyphenyl)methanesulfonamide with 3-phenoxyprop-1-yne. The structure of the compound was fully characterized by IR, <sup>1</sup>H and <sup>13</sup>C NMR, Mass spectra and elemental analysis.

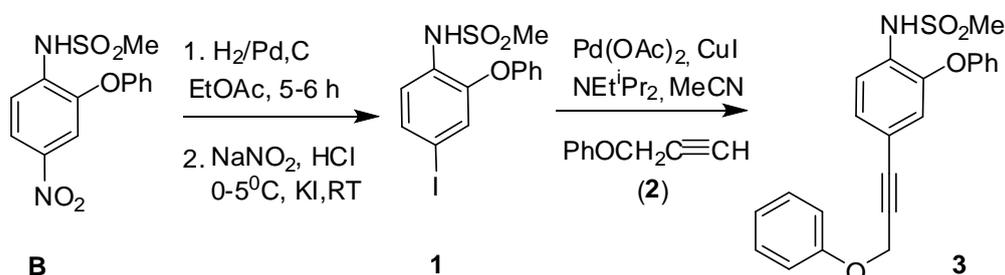
**Keywords:** Sonogashira coupling; alkyne; sulphonamide

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The disubstituted alkynes have long been of interest because of their numerous applications and uses in synthetic organic chemistry, molecular electronics and pharmacology. They mainly exhibit anti bacterial and anti cancer activities [1]. On the other hand, compounds containing sulfonamide moiety e.g., 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl]benzenesulfonamide (SC236) showed enhanced cytotoxic effects of doxorubicin on HKESC-1 and HKESC-2 cells [2]. Nimesulide **B** (Figure 1), a sulfonamide based well known antiinflammatory agent, is presently in patient's use in certain countries. Because of their common cytotoxic properties and our interest in nimesulide (*N*-(4-nitro-2-phenoxy phenyl)methane sulfonamide) derivatives [3–10] as potential cytotoxic agents, we designed the appropriately functionalized hybrid molecule **C** containing structural features of both **A** and **B** (Figure 1).

**Figure 1.** Design of hybrid molecule **C** from alkyne **A** and nimesulide **B**.

The alkylation of iodoarenes via C-C bond forming reaction under Pd-Cu catalysis (the Sonogashira coupling) [11] has found wide applications in organic synthesis [12]. The methodology offers a very convenient, mild and one-step process for the direct coupling of terminal alkynes with iodoarene to provide the desired internal alkynes. This methodology was adopted for the preparation of our target molecule **C** (or **3**) and the corresponding synthesis is shown in Scheme 1.

**Scheme 1.** Synthesis of the title compound **C** (or **3**).

The starting compound **1** required for our study was prepared in quantitative yield from nimesulide (**B**) *via* reduction of its nitro group to primary amine followed by conversion of the amine moiety to an iodo group under a Sandmeyer reaction condition. The Sonogashira cross-coupling was then employed to form a carbon-carbon bond between the aryl iodide (**1**) and the terminal alkyne (**2**). The reaction was carried out under mild conditions.

In the  $^1\text{H-NMR}$  spectrum (DMSO- $d_6$ ) of compound **3**, two characteristic singlets appeared at 3.03 and 4.97 ppm were due to the methyl and methylene group respectively. The singlet of NH group appeared at 9.59 ppm, which was confirmed by its disappearance during  $\text{D}_2\text{O}$  exchange experiment. Moreover, the two characteristic signals of acetylenic carbon atoms appeared in the  $^{13}\text{C-NMR}$  spectrum of compound **3** at 85.8 and 84.5 ppm. The fact was also supported by the mass spectrum of compound **3** which showed molecular ion peak ( $\text{M}^+$ ) at  $m/z$  394.1. The analytical data was in complete agreement with the molecular formula  $\text{C}_{22}\text{H}_{19}\text{NO}_4\text{S}$ .

*N*-(4-iodo-2-phenoxyphenyl) methane sulfonamide (**1**), (1.945 g, 5 mmol) in 20 mL acetonitrile was added diisopropylethyl amine (0.969 g, 7.5 mmol),  $\text{Pd}(\text{OAc})_2$  (125 mg, 0.5 mmol) and  $\text{CuI}$  (0.50 mmol). The mixture was stirred for 15 min at room temperature then added prop-2-ynoxybenzene (**2**, 0.792 mg, 6 mmol) followed by reflux for 10–12 h. The progress was confirmed by checking TLC in regular intervals. After completion of reaction, the crude was distilled under reduced pressure and the compound, **3** was purified by column chromatography by using cyclohexane:EtOAc = 9.5:0.5.

Description of the compound: Off white crystalline solid.

Yield: 80%.

Mp: 98–102 °C.

R<sub>f</sub>: 0.5 (Cyclohexane:EtOAc = 9.5:0.5).

IR  $\nu_{\max}$  (KBr  $\text{cm}^{-1}$ ): 3292, 2231, 1573, 1588, 1509, 1489.

Mass (ES): m/z 394.1(M+1, 100%).

<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  3.03 (s, 3H), 4.97(s, 2H), 6.81 (d, 1H, J 2 Hz), 7.00–6.94 (m, 3H), 7.08–7.06 (m, 2H), 7.31–7.19 (m, 4H), 7.46–7.41 (m, 3H), 9.59 (1H, NH, D<sub>2</sub>O exchangeable).

<sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  39.7 (CH<sub>3</sub>), 56.4 (OCH<sub>2</sub>), 84.5 (acetylenic C), 85.8. (acetylenic C), 114.8 (2CH), 119.0 (2CH), 119.1 (C), 120.2 (CH), 120.7 (CH), 121.4 (CH), 124.7 (CH), 127.7 (CH), 128.6 (C), 129.4 (2CH), 130.2 (2CH), 146.7 (C), 155.2 (C), 157.6 (C).

Anal. calc. for C<sub>22</sub>H<sub>19</sub>NO<sub>4</sub>S: C, 67.16; H, 4.87; N, 3.56, Found: C, , 67.38; H, 4.76; N, 3.39.

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