Communication

Synthesis, Spectroscopic Analysis, and In Vitro Anticancer Evaluation of 2-(Phenylsulfonyl)-2*H*-1,2,3-triazole

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Abstract: The 1,2,3-Triazole derivatives containing the sulfonyl group have proved their biological importance in medicinal chemistry and drug design. In this sense, we describe the regioselective synthesis of 2-(phenylsulfonyl)-2*H*-1,2,3-triazole **3** in good yield through a classical sulfonamidation reaction of 1*H*-1,2,3-triazole **1** with benzenesulfonyl chloride **2** in dichloromethane using a slight excess of triethylamine at 20 °C for 3 h. This procedure is distinguished by its short reaction time, high yield, excellent regioselectivity, clean reaction profile, and operational simplicity. The sulfonamide **3** was characterized by high-resolution mass spectrometry, FT–IR, UV–Vis, 1D and 2D NMR spectroscopy, and elemental analysis. The sulfonamide **3** exhibited moderate activity against UO-31 renal, SNB-75 central nervous system, HCT-116 colon, and BT-549 breast cancer cell lines, with growth inhibition percentages (GI%) ranging from 10.83% to 17.64%.

Keywords: 1,2,3-triazole; sulfonamidation; S–N bond formation; sulfonamide; cancer

1. Introduction

Triazoles are important five-membered heterocyclic scaffolds due to their extensive biological activities [1–3]. Compounds derived from this ring can be subdivided into three main classes, namely, monocyclic 1,2,3-triazoles, benzotriazoles, and 1,2,3-triazolium salts [1]. In particular, the 1,2,3-triazole has been successfully employed as an amide bioisostere in multiple therapeutic contexts [1–3]. As illustrated in Figure 1, an unsubstituted 1,2,3-triazole ring shows tautomeric forms depending on the hydrogen bonded to nitrogen atoms, namely, 1*H*- and 2*H*-1,2,3-triazole [2,3].

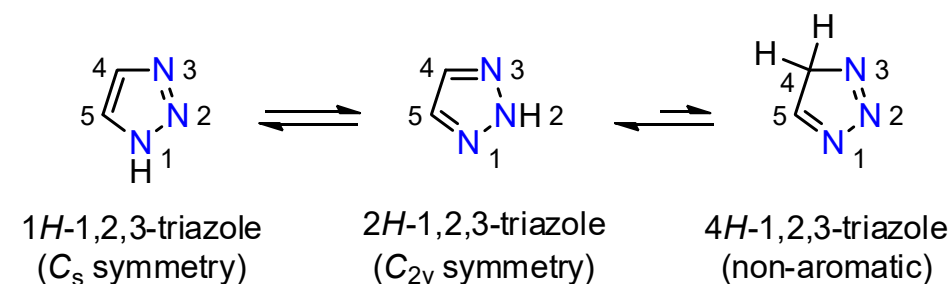**Figure 1.** Tautomeric forms of the unsubstituted 1,2,3-triazole ring.

^{1}H NMR spectroscopic study of 1*H*- and 2*H*-1,2,3-triazole in toluene solution showed that 1*H*-tautomer is predominant at −98 °C, while the 2*H*-tautomer increased more than 97% at 27 °C [4]. Four years later, the tautomeric equilibrium of gaseous 1,2,3-triazole was studied by microwave spectroscopy, finding that the dipole moment for

1*H*- and 2*H*-tautomers is 4.38 D and 0.218 D, respectively, while the relative abundance estimated from intensity measurements is ~1:1000 at room temperature [5]. In addition, theoretical calculations showed that the 2*H*-tautomer is the most stable compound ($\Delta E_{1H \to 2H} = -14.7$ kJ mol^{-1}). Shortly after, Elguero and colleagues reported that 2*H*-tautomer is more stable than 1*H*-tautomer in the gas phase by 18.8 kJ mol^{-1}, which is explained by the lone pair/lone pair repulsion of adjacent pyridine-type nitrogen atoms (N2 and N3 in l*H*-tautomer) [6].

The 1,2,3-triazole moiety plays an important role in medicinal chemistry because it is a well-known bioisostere of an amide [7]. Indeed, several properties of the 1,2,3-triazole, related to the planarity, dipole moment, hydrogen-bonding properties, and resistance to metabolic degradation, hydrolysis, reduction, and oxidation reactions, are comparable to those of an amide group [7]. As a result, 1,2,3-triazoles have been successfully used as a substitute for the amide linker synthesizing innumerable pharmacologically active compounds [1,8,9]. Although extensive studies have been performed on 1*H*-1,2,3-triazole-hybrids with significant anticancer activity [8–11], very few examples of isomeric 2*H*-1,2,3-triazole-hybrids as anticancer agents have been reported [12–14]. Among them, the *cis*-constrained analog of combretastatin A-4 (**I**) exhibited growth inhibition of 50% (GI$_{50}$) values of less than 10 nM against 80% of NCI-60 cancer cell lines, along with a GI$_{50}$ value of 10.3 nM against the Hs578T breast cancer cell line (Figure 2) [12]. In addition, the compound (**I**) was found to inhibit tubulin polymerization with the half maximal inhibitory concentration (IC$_{50}$) value of 1.7 μM. Moreover, the 4,5-disubstituted 2*H*-1,2,3-triazole (**II**) displayed GI$_{50}$ values of 10 nM against 95% of NCI-60 cancer cell lines and tumor growth inhibition (TGI) values of less than 10 nM against SF-539, MDA-MB-435, OVCAR-3, and A498 cancer cell lines [13]. The molecular docking studies of compounds (**I**) and (**II**) showed inhibition of tubulin polymerization by interaction with the colchicine binding site of tubulin [12,13]. Alternatively, the 2*H*-1,2,3-triazole-chalcone (**III**) significantly reduced cell viability and showed an IC$_{50}$ value of 15.6 μM against PC-3 prostate cancer cell line [14]. Moreover, the incorporation of a sulfonamide group in 1,2,3-triazole derivatives (**IVa–c**) showed IC$_{50}$ values ranging from 6 to 10 μM against A549 (lung), HepG2 (liver), HeLa (cervical), and DU145 (prostate) cancer cell lines [15]. Docking molecular compounds (**IVa–c**) against phosphodiesterase 4B (PDE4B) enzyme showed hydrogen bonding interactions between NH of the methanesulfonamide moiety and the active site. In the case of the highly functionalized 1,2,3-triazole (**V**), the sulfonamide moiety is part of the benzothiazine system, which exhibited a remarkable cytotoxicity against PC3 (prostate), HeLa (cervical), MDA-MB-231 (breast adenocarcinoma), and HepG2 (liver) cancer cell lines, with IC$_{50}$ values ranging from 9.5 to 11.9 μM [16]. Docking of the molecular compound (**V**) against interleukin-1*β* (IL-1*β*) displayed hydrogen bonding interactions between oxygen atoms of the sulfonamide moiety with the active site. It should be noted that the incorporation of the sulfonamide structural motif improves the chemical and metabolic stability of the 1,2,3-triazole ring; thus, it is highly appreciated in medicinal chemistry and drug design.

The classic approach towards synthesis of sulfonamides involves the reaction of sulfonyl chlorides with amines in the presence of a base, as well as the generation, in situ, of sulfonyl chlorides by the reaction of thiols with oxidizing and chlorinating agents [17,18]. Moreover, sulfonamides have been efficiently synthesized from arylboronic acids, amines, and 1,4-diazabicyclo[2.2.2]octane *bis*(sulfur dioxide) (DABSO) as a source of SO$_2$, and from copper as catalyst [19]. Recently, sulfonamides have been generated through an electrochemical oxidative coupling from thiols and amines and subsequent oxidation of the sulfur atom [20]. To date, versatile and practical methods for the synthesis of sulfonamides in high yields, easy workup procedure, and mild reaction conditions are still desirable.
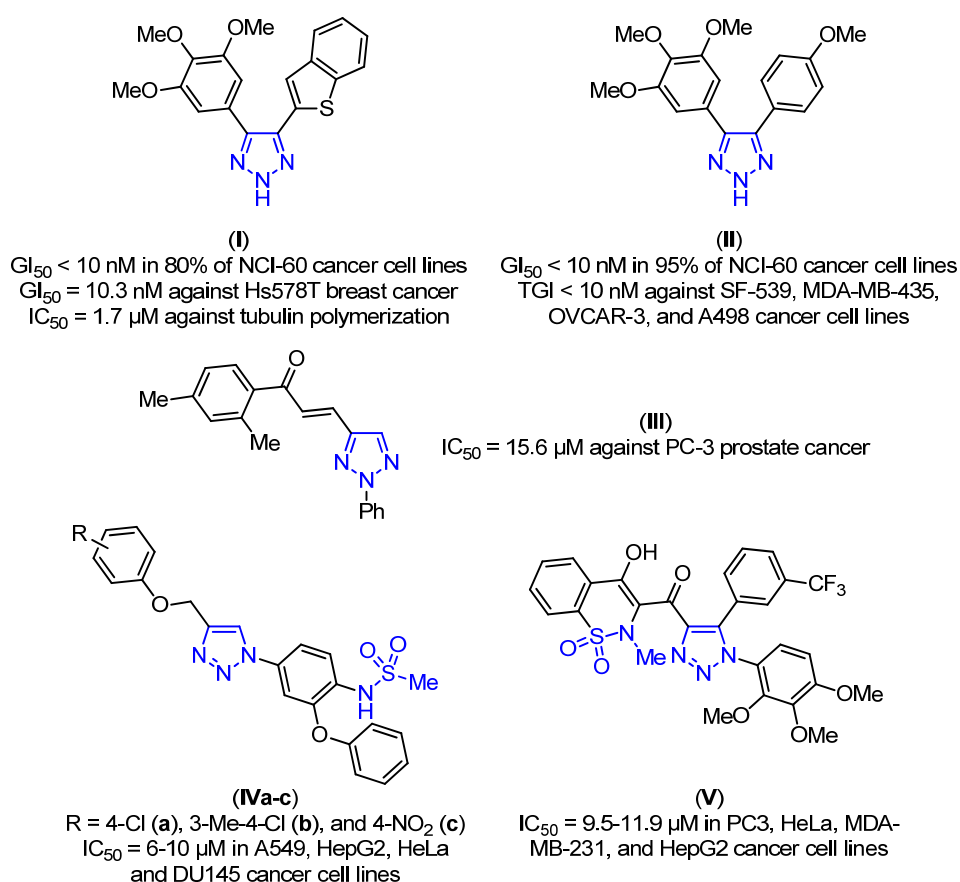
**Figure 2.** 2*H*-1,2,3-Triazole-containing hybrids with anticancer activity.

Herein, we describe the regioselective synthesis and characterization of new 2-(pheny lsulfonyl)-2*H*-1,2,3-triazole **3** through a classical sulfonamidation reaction of 1*H*-1,2,3-triazole **1** with benzenesulfonyl chloride **2** in the presence of triethylamine under mild reaction conditions. Ultimately, the in vitro anticancer activity of sulfonamide **3** was evaluated by the National Cancer Institute (NCI, USA) against 60 human cancer cell lines.

2. Results and Discussion

2.1. Chemistry

In connection with the ongoing development of efficient and simple protocols for the synthesis of azole heterocycles of biological interest [21–23], we report the regioselective synthesis of 2-(phenylsulfonyl)-2*H*-1,2,3-triazole **3** through a classical sulfonamidation reaction of 1*H*-1,2,3-triazole **1** with benzenesulfonyl chloride **2** in dichloromethane, using a slight excess of triethylamine with vigorous stirring at 20 °C for 3 h under normal atmospheric conditions (Scheme 1). After the specified reaction time, the solvent was removed under vacuum using a rotary evaporator. The resulting crude product was purified by column chromatography on silica gel using dichloromethane as an eluent to afford sulfonamide **3** in 65% yield. Although TLC showed a complete conversion of starting materials to the desired product, a moderate yield was obtained after purification by column chromatography. According to Katritzky et al., *N*-acyltriazoles are powerful acylating reagents, suitable for the acylation of different classes of proton-labile compounds, including alcohols, carboxylic acids, and amines, among others [24]. Thus, we thought that the *N*-sulfonyl-1,2,3-triazole **3** could be hydrolyzed during purification by column chromatography, owing to the acidity of the stationary phase (silica gel). Despite this drawback, the procedure is distinguished by its short reaction time, excellent regioselectivity, clean reaction profile, and operational simplicity. Surprisingly, the synthesis and characterization of sulfonamide **3** have not been reported on the Reaxys database. However, in 2010, Yamauchi et al. reported that the

1,2-rearrangement of a sulfonyl group occurs on treatment of 4-substituted 1-sulfonyl-1,2,3-triazoles with a catalytic amount of 4-dimethylaminopyridine (10 mol%) in acetonitrile at ambient temperature for 12–48 h, to afford predominantly 4-substituted 2-sulfonyl-2*H*-1,2,3-triazoles in 72–86% yields [25]. In the same year, Keith J.M reported on the *N*-sulfonylation of the 1,2,3-triazole (1.0 equiv) with toluensulphonyl chloride (1.4 equiv) using an excess of *N*,*N*-diisopropylethylamine (4.3 equiv) in dry dichloromethane at ambient temperature for 22 h to give predominantly 1-tosyl-1*H*-1,2,3-triazole in 83% yield and a small amount of the isomeric product 2-tosyl-2*H*-1,2,3-triazole [26]. As expected, the ^{1}H NMR spectroscopy analysis of the 1-tosyl-1*H*-1,2,3-triazole showed two doublets at 8.16 ppm (*J* = 0.6 Hz) and 7.69 ppm (*J* = 1.2 Hz), while the 2-tosyl-2*H*-1,2,3-triazole showed a singlet at 7.83 ppm assigned to the two magnetically equivalent protons of the 1,2,3-triazole ring. In 2018, Jie et al. reported that the *N*-sulfonylation of the 1,2,3-triazole (1.0 equiv) with *N*-fluorobenzenesulfonimide (1.5 equiv) was mediated by NaHCO$_3$ (50 mol%) in acetonitrile at 70 °C for 12 h to afford 1-(phenylsulfonyl)-1*H*-1,2,3-triazole in 55% yield [27]. However, Jie et al. wrongly concluded that the sulfonylation occurred in the N-1 position, because a singlet at 7.85 ppm integrating for two magnetically equivalent protons does not correspond with the expected symmetry of the 1,2,3-triazole ring. Taking into account the ^{1}H NMR spectroscopy analysis reported by Keith J.M, the incorporation of the toluensulphonyl group into N-1 and N-2 positions of the 1,2,3-triazole ring was confirmed by the presence of two doublets (8.16 and 7.69 ppm) and a singlet (7.83 ppm), respectively [26].
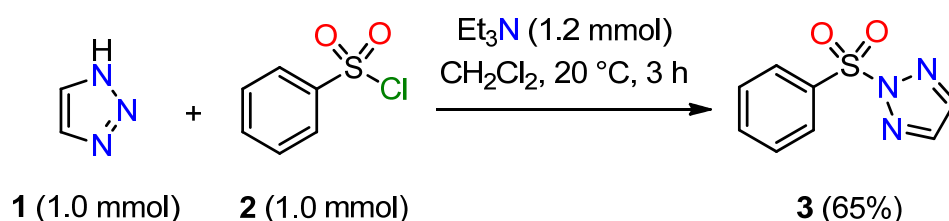
Scheme 1. Regioselective synthesis of 2-(phenylsulfonyl)-2*H*-1,2,3-triazole **3**.

To unequivocally confirm the position of the phenylsulfonyl group into the 1,2,3-triazole ring, a complete analytical and spectroscopic characterization was performed in this work (see Section 3). Initially, the structure of **3** was determined by high-resolution mass spectrometry, elemental analysis, FT–IR, UV–Vis, and 1D NMR spectroscopy (Figures S1–S7). Later, the analysis of 2D NMR spectra, including HMBC (Figure S8), HSQC (Figure S9), COSY (Figure S10), and NOESY (Figure S11), allowed the structural assignment without ambiguity.

2.2. NMR Analysis

^{1}H NMR spectrum of **3** recorded in CDCl$_3$ using TMS as an internal standard showed a triplet of triplets at 7.68 ppm (*J* = 7.8, 1.2 Hz) and two doublet of doublets at 7.56 ppm (*J* = 7.8, 7.8 Hz) and 8.10 ppm (*J* = 7.8, 1.2 Hz) for the benzene ring (Table 1). The signal of the 1,2,3-triazole ring is observed as a singlet at 7.85 ppm, indicating that the sulfonylation process is regioselective at the N-2 position, which is in good agreement with previously reported data by Keith J.M [26]. The ^{13}C{^{1}H} NMR and DEPT spectra of **3** showed five carbon signals, consisting of one quaternary carbon and four aromatic methines (Table 1 and Figure 3A). The HSQC spectrum recorded in CDCl$_3$ enabled the assignment of all protons to the directly bonded carbons. Thus, the signals of C-2′, C-3′, and C-4′ for the benzene ring are assigned at 128.8, 129.7, and 135.4 ppm, respectively. Moreover, the 1,2,3-triazole ring showed only one signal at 138.5 ppm, which is in good agreement with the regioselective sulfonamidation at the N-2 position. This signal appeared in the downfield region due to the π-deficient character in the 2*H*-1,2,3-triazole, because C-4 and C-5 carbon atoms are bonded to pyridine-type nitrogen atoms. The only quaternary carbon is assigned to C-1′ (136.1 ppm). The ^{1}H-^{1}H and ^{1}H-^{13}C correlations, observed in COSY and HMBC experiments, respectively, are illustrated in Table 1 and Figure 3B. As expected,

NOESY correlations are observed for aromatic protons of the benzene ring, which is in good agreement with the structure drawn. Ultimately, the accurate mass (m/z 210.0332) of the pseudo-molecular ion ([M + H]$^+$) and the elemental formula ($C_8H_8N_3O_2S^+$) is confirmed by HRMS measurements, obtaining an error mass of 1.43 ppm (Figure S1).

Table 1. ^{1}H and ^{13}C{^{1}H} NMR assignments, COSY, NOESY, and HMBC correlations of **3** [a].

Number	δ_H (mult, J in Hz)	δ_C (ppm)	COSY (^{1}H-^{1}H)	NOESY (^{1}H-^{1}H)	HMBC (^{1}H-^{13}C)
4 and 5	7.85 (s)	138.5	—	—	—
1'	—	136.1	—	—	H-3' (^3J)
2'	8.10 (dd, J = 7.8, 1.2)	128.8	H-3' (^3J)	H-3'	H-4' (^3J)
3'	7.56 (dd, J = 7.8, 7.8)	129.7	H-2' (^3J) H-4' (^3J)	H-2' H-4'	—
4'	7.68 (tt, J = 7.8, 1.2)	135.4	H-3' (^3J)	H-3'	H-2' (^3J)

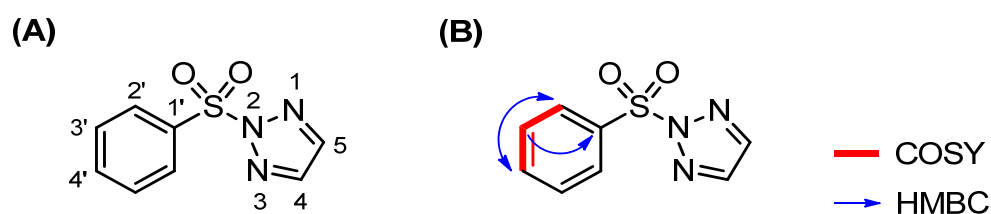[a] Measured at 400 MHz (^{1}H) and 101 MHz (^{13}C) in CDCl$_3$ at 25 °C.

Figure 3. (**A**) Structure of 2-(phenylsulfonyl)-2*H*-1,2,3-triazole **3**. (**B**) Connectivities of **3** based on COSY (bold red line) and HMBC (from H to C, blue arrow) data.

2.3. FTIR Analysis

2.3.1. SO$_2$ Vibrations

Tertiary sulfonamides of form RSO$_2$NR$_2$, where R is either CH$_3$ or aryl, show asymmetric and symmetric SO$_2$ stretching vibrations at 1324–1334 and 1142–1164 cm^{-1}, respectively, in the solid phase [28]. In the present work, compound **3** displayed strong absorption bands at 1388 and 1169 cm^{-1} associated to asymmetric and symmetric SO$_2$ stretching vibrations, respectively (Figures S2 and S3). Recently, Sambathkumar reported that scissoring and rocking vibrations related to in-plane bending vibrations of the SO$_2$ group in 2,4,6-trimethylbenzenesulphonyl chloride were observed at 700 and 558 cm^{-1}, respectively [29]. Moreover, the twisting and wagging vibrations related to out-of-plane bending vibrations of the SO$_2$ group were observed at 280 and 665 cm^{-1}, respectively [29]. In the present work, the scissoring, rocking, and wagging vibrations of the SO$_2$ group are observed in the range of 558–724 cm^{-1} (Figures S2 and S3).

2.3.2. S–N and S–C Vibrations

In the solid phase, the S–N stretching vibration of tertiary sulfonamides appears in the 770–815 cm^{-1} region, while the stretching vibration of the weaker S–C bond appears in the 700–749 cm^{-1} region [28]. In the current study, the S–N and S–C stretching vibrations are assigned at 847 and 759 cm^{-1}, respectively (Figures S2 and S3).

2.3.3. C=C Vibrations

The C=C stretching vibrations of the aromatic rings appear in the 1585–1600 cm^{-1} region [28]. Very recently, Gökce et al. reported that the C=C stretching vibration of 1*H*-1,2,3-triazole-4-carbohydrazide was observed at 1512 cm^{-1} [30]. In addition, measured and calculated fundamental frequencies of 2*H*-1,2,3-triazole were reported in the ranges of 1448–1522 and 1460–1496 cm^{-1}, respectively [31–33]. In the present work, the C=C stretching vibrations of 1,2,3-triazole and benzene rings are assigned at 1479/1522 and 1582 cm^{-1}, respectively (Figures S2 and S3).

2.3.4. N–N, C–N and C=N Vibrations

It should be mentioned that N–N, C–N, and C=N stretching vibrations can be difficult to assign because they have a diversity of band structures. Very recently, Gökce et al. reported that N–N stretching vibrations of 1*H*-1,2,3-triazole-4-carbohydrazide were observed at 978 and 1001 cm^{-1} [30]. In addition, the C–N stretching vibrations of 1*H*-1,2,3-triazole-4-carbohydrazide were assigned at 1035, 1183, 1213, 1279, 1365, and 1489 cm^{-1} [30]. In the current study, the N–N and C=N stretching vibrations of the 1,2,3-triazole ring are observed at 998 and 1610 cm^{-1}, respectively (Figures S2 and S3). Moreover, the C–N stretching vibrations in the triazole ring are assigned at 1053, 1141, 1183, 1274, 1340, and 1449 cm^{-1}.

2.3.5. C–H Vibrations

The presence of weak intensity bands in the range of 3000–3100 cm^{-1} corresponds to aromatic C–H stretching vibrations [28]. For instance, measured and calculated fundamental frequencies of 2*H*-1,2,3-triazole were reported in the range of 3088–3146 and 3078–3142 cm^{-1}, respectively [31–33]. The fundamental modes observed at 3121/3136 and 3068/3080 cm^{-1} in compound **3** are assigned to C–H stretching vibrations of 1,2,3-triazole and benzene rings, respectively (Figures S2 and S3). In addition, the out-of-plane ("oop") bending of aromatic C–H bonds is observed in the 675–900 cm^{-1} region [28]. In the present work, the mono-substitution of the benzene ring is confirmed by the presence of two out-of-plane C–H bending vibrations at 682 and 724 cm^{-1}. The other out-of-plane vibrations of the triazole ring appeared in the low-frequency zone. Furthermore, in-plane bending of aromatic C–H bonds is observed in the 1000–1300 cm^{-1} region [28]. In the current study, in-plane bending vibrations of hydrogen atoms on the benzene and triazole rings can appear at 953, 1089, 1200, 1287, and 1314 cm^{-1}.

2.4. UV–Vis Analysis

The UV–Vis spectrum of sulfonamide **3** measured in EtOH in the range of 200–400 nm is illustrated in Figure S4. The absorption spectrum of sulfonamide **3** shows six distinct bands, with variable intensity in the range of 200–280 nm. The weak bands at 205 nm (ε = 3670 L·mol^{-1}·cm^{-1}), 211 nm (ε = 4812 L·mol^{-1}·cm^{-1}), and 216 nm (ε = 6245 L·mol^{-1}·cm^{-1}) are assigned to $\pi \rightarrow \pi^*$ transitions of the 1,2,3-triazole ring and S=O bonds. In this sense, several authors have reported that the gas-phase UV absorption spectrum of the 1,2,3-triazole is dominated by a $\pi \rightarrow \pi^*$ transition at 205 nm [34,35]. Moreover, the highest extinction coefficient is observed at 236 nm (ε = 18750 L·mol^{-1}·cm^{-1}), attributed to the $\pi \rightarrow \pi^*$ transition of the benzene ring. Ultimately, the weak bands at 268 nm (ε = 1828 L·mol^{-1}·cm^{-1}) and 275 nm (ε = 1490 L·mol^{-1}·cm^{-1}) can be attributed to the n $\rightarrow \pi^*$ transition of the 1,2,3-triazole ring and S=O bonds.

2.5. In Vitro Anticancer Evaluation

The in vitro anticancer activity of the 2-(phenylsulfonyl)-2*H*-1,2,3-triazole **3** was evaluated by the National Cancer Institute (NCI, USA) against 60 human cancer cell lines representing nine tumor panels, including leukemia and melanoma, and cancers of the non-small cell lung, colon, central nervous system, ovarian, renal, prostate, and breast. The selected compound **3** with NCI code NSC D-829744/1 was screened at a single dose (10 µM) in the NCI 60-cell panel. These results are reported as a mean graph of the growth percentage (GP) of the treated cells compared to untreated control cells [36–38]. The one-dose mean graphs of compound **3** obtained from the NCI 60-cell line screening program are shown in Table S1. According to the data analysis of the one-dose mean graph, the reduction in the growth percentage (GP) increases the growth inhibition percentage (GI% = 100 − GP). Moreover, a negative value in the growth inhibition percentage means lethality; hence, more negative GI% values indicate higher activity of the tested compound. It is important to mention that low mean GP values are employed as a criterion for further screening at five different concentrations (0.01 to 100 µM) [36–38]. The most relevant growth inhibition

percentage of 2-(phenylsulfonyl)-2*H*-1,2,3-triazole **3** against a variety of human cancer cell lines is shown in Table 2.

Table 2. Mean growth, GI%, and lethality values for the most sensitive human cancer cell lines displayed by the compound **3**.

Mean Growth	Most Sensitive Cell Line	Growth Inhibition Percentage (GI%) [a]
	UO-31 (Renal Cancer)	10.83
	SNB-75 (CNS Cancer)	13.76
	HCT-116 (Colon Cancer)	17.37
100.60	BT-549 (Breast Cancer)	17.64
	RXF 393 (Renal Cancer)	−12.66 [b]
	OVCAR-3 (Ovarian Cancer)	−15.85 [b]
	HOP-92 (Non-Small Cell Lung Cancer)	−27.59 [b]

[a] GI% (growth inhibition percentage) = 100 − GP (growth percentage). [b] Negative values indicate lethality toward the respective human cancer cell line.

In light of the NCI 60-cell line screening results reported in Table 2 and Table S1, it can be observed that compound **3** shows moderate anticancer activity against UO-31 renal and SNB-75 central nervous system cell lines, with growth inhibition percentages of 10.83% and 13.76%, respectively. Moreover, compound **3** displays the better anticancer activity against HCT-116 colon and BT-549 breast cancer cell lines, with GI% of 17.37% and 17.64%, respectively. The antiproliferative activity could be explained by the presence of pharmacophores 2*H*-1,2,3-triazole and the phenylsulfonyl group in the structure of **3**, in accordance with previously reported data of analogous compounds [12–16]. The most relevant GI% values indicate that the compound **3** could be used as a preliminary lead molecule to discover promising anticancer agents.

3. Materials and Methods

3.1. General Information

The 1*H*-1,2,3-Triazole **1** (CAS 288-36-8, Saint Louis, MO, USA) and benzenesulfonyl chloride **2** (CAS 98-09-9, Saint Louis, MO, USA) were purchased from Sigma–Aldrich. The starting materials were weighed and handled in air at ambient temperature. The silica gel aluminum plates (Merck 60 F254, Darmstadt, Germany) were used for analytical TLC. The FTIR absorption spectrum was recorded at room temperature employing a Shimadzu FTIR 8400 spectrophotometer (Scientific Instruments Inc., Seattle, WA, USA) equipped with an attenuated reflectance accessory. The UV–Vis spectrum was obtained from an ethanol solution (5.0×10^{-5} M) in an Evolution 201 UV–Vis spectrophotometer (Thermo Fischer Scientific Inc., Madison, WI, USA). ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded at 25 °C on a Bruker Avance 400 spectrophotometer (Bruker BioSpin GmbH, Rheinstetten, Germany) operating at 400 MHz and 101 MHz, respectively. The concentration of the sample was approximately 16 mg/0.5 mL of $CDCl_3$. Chemical shifts of ^{1}H and ^{13}C{^{1}H} NMR experiments were referenced by tetramethylsilane (δ = 0.0 ppm). Chemical shifts (δ) are given in ppm, and coupling constants (J) are given in Hz. The 2D HMBC, HSQC, COSY, and NOESY experiments were performed using the standard Bruker pulse sequence. NMR data were analyzed using the MestReNova 12.0.0 (2017) software (Mestrelab, Escondido, CA, USA). Microanalysis was performed on a CHNS elemental analyzer (Thermo Fischer Scientific Inc., Madison, WI, USA), and the values are within ±0.4% of the theoretical values. The high-resolution mass spectrum (HRMS) was recorded using a Q-TOF 6520 spectrometer (Agilent Technologies Inc., Santa Clara, CA, USA) by electrospray ionization (ESI, 4000 V).

3.2. 2-(Phenylsulfonyl)-2H-1,2,3-triazole 3

A mixture of 1*H*-1,2,3-triazole **1** (69 mg, 1.0 mmol), benzenesulfonyl chloride **2** (128 μL, 1.0 mmol), and triethylamine (167 μL, 1.2 mmol) in dichloromethane (5.0 mL) was stirred

at 20 °C for 3 h (Scheme 1). After a complete disappearance of the starting materials, as monitored by thin-layer chromatography (TLC), the solvent was removed using a rotary evaporator under vacuum. The resulting crude product was purified by flash chromatography on silica gel, using dichloromethane as an eluent, to afford the title compound **3** (136 mg, 65%) as colorless needles, mp 92–93 °C; Rf 0.53 (CH_2Cl_2). FTIR–ATR: ν = (3136 and 3121 for ν C–H$_{triazole}$), (3080 and 3068 for ν C–H$_{benzene}$), 1610 (ν C=N$_{triazole}$), 1582 (ν C=C$_{benzene}$), 1522 (ν C=C$_{triazole}$), 1479 (ν C=C$_{triazole}$), 1449, 1388 (ν_a SO$_2$), 1340, 1314, 1287, 1274, 1200, 1183, 1169 (ν_s SO$_2$), 1141, 1089, 1053, 998 (ν N–N), 953, 847 (ν S–N), 759 (ν S–C), (724 and 682 δ_{op} C–H), 586, 558 cm^{-1}. UV–Vis (ethanol) λmax (ε, L·mol^{-1}·cm^{-1}): 205 (3670), 211 (4812), 216 (6245), 236 (18750), 268 (1828), 275 (1490) nm. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.56 (dd, *J* = 7.8, 7.8 Hz, 2H, H-3′), 7.68 (tt, *J* = 7.8, 1.2 Hz, 1H, H-4′), 7.85 (s, 2H, H-4 and H-5), 8.10 (dd, *J* = 7.8, 1.2 Hz, 2H, H-2′) ppm. ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ = 128.8 (CH, C-2′), 129.7 (CH, C-3′), 135.4 (CH, C-4′), 136.1 (Cq, C-1′), 138.5 (CH, C-4 and C-5) ppm. Anal. calcd. for $C_8H_7N_3O_2S$ (209.22): C, 45.92; H, 3.37; N, 20.08; S, 15.33. Found: C, 45.70; H, 3.34; N, 19.98; S, 15.26. HRMS (ESI+): calcd for $C_8H_8N_3O_2S^+$, 210.0332 [M + H]$^+$; found, 210.0329.

4. Conclusions

In summary, herein we describe the ambient-temperature synthesis of novel 2-(phenyl sulfonyl)-2*H*-1,2,3-triazole **3** through a regioselective sulfonamidation of 1*H*-1,2,3-triazole **1** with benzenesulfonyl chloride **2** in dichloromethane using a slight excess of triethylamine. This protocol is distinguished by its short reaction time, high yield, excellent regioselectivity, clean reaction profile, and operational simplicity. Importantly, the sulfonamide **3** displayed a moderate activity against UO-31 renal, SNB-75 central nervous system, HCT-116 colon, and BT-549 breast cancer cell lines, with GI% values ranging from 10.83% to 17.64%.

Supplementary Materials: The following are available online. Figure S1: HRMS spectrum of the compound **3**; Figure S2: FTIR spectrum of the compound **3**; Figure S3: Expansion FTIR spectrum of the compound **3**; Figure S4: ^{1}H NMR spectrum of the compound **3**; Figure S5: ^{13}C{^{1}H} NMR and DEPT-135 spectra of the compound **3**; Figure S6: Expansion ^{13}C{^{1}H} NMR and DEPT-135 spectra of the compound **3**; Figure S7: HMBC 2D C–H correlation spectrum of the compound **3**; Figure S8: HSQC 2D C–H correlation spectrum of the compound **3**; Figure S9: COSY 2D C–H correlation spectrum of the compound **3**; Figure S10: NOESY 2D H–H correlation spectrum of the compound **3**; Figure S11: UV–Vis spectrum of the compound **3**; Table S1: Mean growth, GI%, and lethality values displayed by the tested compound **3** against 60 NCI human cancer cell lines at 10 μM.

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