



# Synthesis, biological investigation, calf thymus DNA binding and docking studies of the sulfonyl hydrazides and their derivatives



Shahzad Murtaza <sup>a,\*</sup>, Saima Shamim <sup>a</sup>, Naghmana Kousar <sup>a</sup>, Muhammad Nawaz Tahir <sup>b</sup>, Muhammad Sirajuddin <sup>c</sup>, Usman Ali Rana <sup>d,\*\*</sup>

<sup>a</sup> Department of Chemistry, University of Gujrat, Gujrat 50700, Pakistan

<sup>b</sup> Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan

<sup>c</sup> Department of Physics, University of Sargodha, Sargodha, Pakistan

<sup>d</sup> Sustainable Energy Technologies Center, College of Engineering, PO-Box 800, King Saud University, Riyadh 11421, Saudi Arabia

## ARTICLE INFO

### Article history:

Received 4 September 2015

Received in revised form

17 November 2015

Accepted 19 November 2015

Available online 29 November 2015

### Keywords:

Sulfonyl hydrazide

Crystal structure

Enzyme inhibition

DNA interaction

Molecular docking

DPPH radical scavenging activity

## ABSTRACT

The present study describes the syntheses and biological investigations of sulfonyl hydrazides and their novel derivatives. The detailed investigations involved the characterization of the newly synthesized compounds using FTIR, NMR, mass spectrometry and by single crystal X-Ray diffraction (XRD) analysis techniques. The binding tendencies of these compounds with CT-DNA (calf thymus DNA) have been explored by electronic absorption (UV) spectroscopy and viscosity measurement. The binding constant (K) and Gibb's free energy ( $\Delta G$ ) values were also calculated accordingly. In addition, we also investigated the biological activities such as antioxidant, antibacterial, enzyme inhibition and DNA interactions. The antioxidant activity was assayed by 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity, while antibacterial activity was investigated against four bacterial strains (*viz.* *Escherichia coli*, *Crynobacteria bovis*, *Staphylococcus aureus* and *Bacillus anthracis*) by employing the common disc diffusion method. Enzyme inhibition activity of the synthesized compounds was examined against butyrylcholinesterase. The results of enzyme inhibition activity and the DNA binding interaction studies were also collected through molecular docking program using computational analysis. Our study reveals that the newly synthesized compounds possess moderate to good biological activities.

© 2015 Elsevier B.V. All rights reserved.

## 1. Introduction

The advancement of research reveals many hidden areas that have the potential to address several known problems of modern era. In medical science, many life threats have been efficiently removed, a matter of great satisfaction for our future generation. The strategy to control diseases with synthetic drugs is a remarkable achievement of the combined efforts of the chemists, biologists and medical specialists. The major challenges in medical science are the ability of the pathogens to develop resistance against the medicine, the lack of antibiotic to kill bacteria and the emergence of the new pathogens. It is imperative to develop new materials to solve the health problems [1]. Intensive work has been

done since long and the successful approach is the chemical combination of biologically active moieties to develop new derivatives with subsequent screening of the biological activities.

In this research work, sulfonyl hydrazides have been explored to synthesize new Schiff bases, as it consists of two chemically as well as biologically important moieties *viz.* sulfonyl group and the hydrazine. These compounds also have similarity to some other important chemical classes; a sulfonamide ( $O_2S-N$ ) and azomethine ( $C=N$ ).

Sulfonyl hydrazides display diverse pharmacological activities such as anti-inflammatory [2], antidiabetic [3], anticancer [4], antitumour and analgesic activities [5]. Sulfonyl hydrazide and sulfonyl semicarbazide derivatives exhibit wide range of bacteriostatic activity [6]. Isoniazid (isonicotinohydrazide) is an antituberculosis drug [7], while Iproniazid (N'-isopropylisonicotinohydrazide) possesses antidepressant activity [8]. Phenelzine ((2-phenylethyl) hydrazine) is a good chemical to be used as muscle relaxant. Similarly, Hydralazine is used to treat

\* Corresponding author.

\*\* Corresponding author.

E-mail addresses: [shahzad.murtaza@uog.edu.pk](mailto:shahzad.murtaza@uog.edu.pk) (S. Murtaza), [urana@ksu.edu.sa](mailto:urana@ksu.edu.sa) (U.A. Rana).

hypertension [9]. Sulfonyl hydrazide derivatives act as DNA modifying agents and have antitumor activities against murine tumors, including the B16 melanoma, M109 lung carcinoma, L1210 leukemias, P388 and M5076 reticulum cell sarcoma [4]. Derivatives of sulfonyl hydrazines also act as cancer chemotherapeutic agents such as 1,2-bis(methylsulfonyl)-1-2(methylamino) carbonyl-hydrazine (Cloretazine), which exhibits wide spectrum anticancer activity. Cloretazine was found to inhibit enzymes containing thiols, such as glutathione reductase [10]. Sulfonyl hydrazide derivatives of safrole have potent analgesic action [5].

In view of wide range biological applications of hydrazine derivatives, the present study focused on the synthesis of Schiff bases of sulfonyl hydrazides in addition to evaluating their biological activities such as antibacterial, antioxidant, enzyme inhibition and DNA binding studies.

## 2. Materials and methods

### 2.1. Reagents

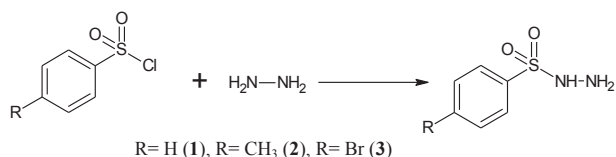
Analytical grade Hydrazine hydrate, benzenesulfonyl chloride, 4-bromobenzenesulfonyl chloride, 4-toluensulfonyl chloride and ethylacetoacetate were purchased from Aldrich (USA) and were used as received. Sodium salt of calf thymus DNA (Arcos) was used without any further process. Various solvents used in the present study (E. Merck, Germany) were employed after drying following the procedures described in literature [11].

### 2.2. Physical measurements

Gallenkamp electrothermal melting point apparatus (U.K) was used to determine the melting points of the synthesized compounds using capillary tube and were uncorrected. Bruker-300 MHz FT-NMR Spectrometer was used to record the NMR ( $^1\text{H}$  and  $^{13}\text{C}$ ) and  $\text{CDCl}_3$  [ $^1\text{H} = 7.25$  and  $^{13}\text{C} = 77$ ] was used as an internal reference. Shimadzu 1800 UV–Visible Spectrophotometer was used to collect the absorption spectra of all newly synthesized compounds. Bruker KAPPA APEX CCD diffractometer was used to collect the single crystal data, from which the structures of compounds were resolved using the SHELXL program. All structural data was collected at room temperature. A sealed ceramic diffraction tube (SIEMENS) was used to generate the graphite monochromated Mo- $\text{K}\alpha$  radiation for intensity measurements. Generator was set to generate 50 kV/35 mA of current. Direct methods were employed to solve the crystal structures. Ultimate tuning on  $F^2$  was done by using SHELXL-97 full-matrix least squares techniques. The packing of structures were analyzed by the program PLUTO and PLATON.

### 2.3. General procedure for the synthesis of Sulfonyl hydrazide

Sulfonyl hydrazides were prepared following the Scheme 1. Weighed amount of aromatic sulfonyl chloride was first dissolved in tetrahydrofuran (5 mL) in a round bottom flask and cooled to below 5 °C. Excess amount of Hydrazine hydrate (4:1) was appended to the solution of aromatic sulfonyl chloride in the form



Scheme 1.

of drops and maintained at temperature < 5 °C during addition. This mixture was stirred for half an hour after the complete addition of hydrazine hydrate and was later transferred to a separating funnel to obtain two separate layers. The upper layer containing organic solvent (tetrahydrofuran) and the product (sulfonyl hydrazide) was separated and stirred vigorously with cold distilled water, which precipitated out fluffy white crystalline needles of sulfonyl hydrazide (1–3) that were later washed with distilled water and dried at room temperature.

### 2.4. General procedure for the synthesis of Schiff bases of Sulfonyl hydrazide

Schiff bases of sulfonyl hydrazides were prepared following the Scheme 2. Stoichiometric amounts of ethyl acetoacetate and sulfonyl hydrazides (1–3) prepared earlier (Scheme 2) were dissolved in ethanol (10 mL). The concoction of reactants was refluxed for 4 h at 78 °C, followed by the removal of solvent under reduced pressure. This process yield white solid crystalline product that was washed with distilled water and recrystallized from ethanol to get colourless crystals of Schiff bases of sulfonyl hydrazide (4–6) [12].

The spectral data for the compounds (4–6) is given below:

#### 2.4.1. Ethyl (3E)-3-[(phenylsulfonyl)hydrazono]butanoate (4)

Yield: 82%, Melting point: 108 °C ± 1 °C, IR (KBr): 3341 (NH, st), 3070 (CH, st), 2994 (CH, st), 1632 (–C=O–, st), 1579 (–CH=N–, st), 1433 (–SO<sub>2</sub>, symm), 1360 (–SO<sub>2</sub>, asymm), 1167 (–SO<sub>2</sub>, asymm), 1033 (In plan CH, bend), 773 (out of plan CH, bend)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 1.19$  (3H, t,  $J = 7.0$  Hz,  $\text{CH}_3$ ), 1.86 (3H, s,  $\text{CH}_3$ ), 3.25 (2H, s,  $\text{CH}_2$ ), 4.14 (2H, q,  $J = 7.0$  Hz,  $\text{CH}_2$ ), 7.3 (1H, m, CH), 7.54 (2H, m, 2CH), 7.93 (2H, m, 2CH),  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ , ppm): 13.7, 14.2, 49.2, 61.1, 127.3, 129.1, 132.0, 139.7, 153.9, 168.4, MS ( $\text{ES}^+$ ):  $m/z$  (%) = ( $\text{M}^+$ ) 284 (15), 239 (37), 173 (42), 141 (90), 115 (15), 77 (100).

#### 2.4.2. Ethyl (3E)-3-[(4-methylphenyl)sulfonyl]hydrazono]butanoate (5)

Yield: 85%, Melting point: 105 °C ± 1 °C, IR (KBr): 3342 (NH, st), 3010 (Aromatic CH, st), 2971 (CH, st), 1630 (–C=O–, st), 1576 (–CH=N–, st), 1431 (–SO<sub>2</sub>, symm), 1365 (–SO<sub>2</sub>, asymm), 1171 (–SO<sub>2</sub>, asymm), 1039 (In plan CH, bend), 763 (out of plan CH, bend)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 1.18$  (3H, t,  $J = 7.0$  Hz,  $\text{CH}_3$ ), 1.84 (3H, s,  $\text{CH}_3$ ), 2.39 (3H, s,  $\text{CH}_3$ ), 3.22 (2H, s,  $\text{CH}_2$ ), 4.08 (2H, q,  $J = 7.0$  Hz,  $\text{CH}_2$ ), 7.26–7.80 (4H, m, 4CH),  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ , ppm): 13.4, 13.9, 24.3, 49.7, 61.3, 127.2, 129.4, 136.7, 141.6, 153.2, 167.9, MS ( $\text{ES}^+$ ):  $m/z$  (%) = ( $\text{M}^+$ ) 298 (15), 253 (30), 187 (35), 155 (60), 115 (15), 91 (100), 77 (62), 65 (35).

#### 2.4.3. Ethyl (3E)-3-[(4-bromophenyl)sulfonyl]hydrazonobutanoate (6)

Yield: 81%, Melting point: 116 °C ± 1 °C, IR (KBr): 3341 (NH, st), 3011 (Aromatic CH, st), 2968 (CH, st), 1631 (–C=O–, st), 1570 (–CH=N–, st), 1431 (–SO<sub>2</sub>, symm), 1364 (–SO<sub>2</sub>, asymm), 1169 (–SO<sub>2</sub>, asymm), 1029 (In plan CH, bend), 763 (out of plan CH, bend), 517 (C–Br)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , ppm):  $\delta = 1.20$  (3H, t,  $J = 7.0$  Hz,  $\text{CH}_3$ ), 1.85 (3H, s,  $\text{CH}_3$ ), 3.24 (2H, s,  $\text{CH}_2$ ), 4.12 (2H, q,  $J = 7.0$  Hz,  $\text{CH}_2$ ), 7.64–7.79 (4H, m, 4CH),  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ , ppm): 13.6, 14.1, 49.4, 61.0, 126.3, 129.5, 132.0, 138.7, 153.6, 168.1; MS ( $\text{ES}^+$ ):  $m/z$  (%) = ( $\text{M}^+$ ) 363 (15), 318 (40), 290 (20), 252 (40), 220 (96), 156 (100), 77 (70).

### 2.5. Antioxidant activity

Free radical scavenging activities of the newly synthesized compounds (1–6) were determined by using 2,2-diphenyl-1-

Download English Version:

<https://daneshyari.com/en/article/1401435>

Download Persian Version:

<https://daneshyari.com/article/1401435>

[Daneshyari.com](https://daneshyari.com)