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Facile synthesis, single crystal analysis, and computational studies of sulfanilamide derivatives

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ABSTRACT

Antibacterial resistance is a worldwide problem. Sulfanilamide is widely used antibacterial. For the first time, we report here a simple method for the derivative synthesis of the title drugs, single crystal XRD and density functional theory (DFT) studies. The optimized molecular structure, natural bond orbital (NBO), frontier molecular orbitals (FMOs) molecular electrostatic potential studies (MEP) and Mulliken population analysis (MPA) have been performed using M06-2X/6-31G(d, p). The FT-IR spectra and thermodynamic parameters were calculated at M06-2X/6-311 + G(2d,p) and B3LYP/6-31G(d, p) levels respectively, while, the UV–Vis analysis was performed using TD-DFT/B3LYP/6-31G(d, p) method. The experimental FT-IR spectra of both compounds were also carried out to reconfirm –H···O– hydrogen bonds. The DFT optimized parameters exhibiting good agreement with the experimental data. NBO analysis explored the hyper conjugative interaction and stability of title crystals, especially, reconfirmed the existence of –H···O– hydrogen bonds between the dimers. The FT-IR, thermodynamic parameters, MEP and MPA also revealed the hydrogen bonding detail is harmonious to XRD data. As a matter of the fact, the hydrogen bonding is a significant parameter for the understanding and design of molecular crystals, subsequently; it can also play a vital role in the supramolecular chemistry. Moreover, the global reactivity descriptors suggest that title compounds might be bioactive.

1. Introduction

Menace of bacterial resistance [1] for antibiotics poses a great hurdle [2] for the treatment of infections. This situation urges the development of new active compounds. Sulfonamide functional groups are popular for their wide range pharmaceutical role [3]. These well-known compounds are being administered as antibacterial, antifungal, antiviral, and anti-tumor drugs [4–11]. The pharmacological and toxicological properties can be boosted if sulfonamides with amide moiety are used as drugs. Domagk was the first who discovered sulfonamides as the active chemotherapeutic ingredient and his work was acknowledged by awarding him the *Nobel Prize* in medicine for the year of 1939 [12].

Sulfanilamide, an aniline derivative of sulfonamide family is a low priced drug having chemotherapeutic properties popular in developing countries with serious bacterial resistance problem [13,14] https://en.wikipedia.org/wiki/Sulfanilamidecite_note-10Sulfanilamide was popularized because of its role in reducing infection rates during 2nd world war (WWII) [15]. Sulfanilamide functions by competing with para amino benzoic acid (PABA) in folic acid biosynthesis hence suppressing the key growth metabolic factor essential for bacterial growth [16]. In past the structure of sulfanilamide derivatives [17–19] and their characterization have been studied [20–22].

However, according to the best of our knowledge, neither experimental technique like XRD, nor the computational studies regarding the (E)-4-oxo-4-[(4-sulfamoylphenyl) amino] but-2-enoic acid and 4-oxo-4-[(4-sulfamoylphenyl) amino] butanoic acid employing famous DFT [23,24]have been reported so for. Detailed structure-activity studies reveal important information regarding biological and pharmacological properties to design potential drug molecules [25]. Moreover, hydrogen bond is also a

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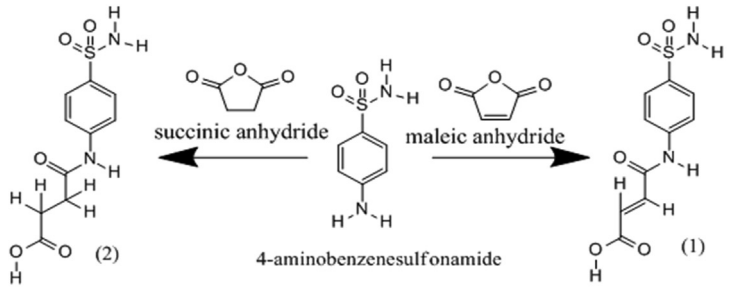

4-oxo-4-((4-sulfamoylphenyl)amino)butanoic acid (*E*)-4-oxo-4-((4-sulfamoylphenyl)amino)but-2-enoic acid

Scheme 1. Schematic representation of the synthesis of reported derivatives.

Table 1
Single crystal XRD data of **1** and **2**.

Compounds	**1**	**2**
Chemical formula	$C_{10}H_{10}N_2O_5S$	$C_{10}H_{12}N_2O_5S$
M_r	270.26	272.28
Crystal system, space group	Monoclinic, *Cc*	Triclinic, *P*1
Temperature (K)	296	296
a, *b*, *c* (Å)	24.529 (3), 5.1692 (7), 9.4722 (12)	5.1309 (4), 11.3811 (11), 11.7458 (10)
α, *β*, *γ* (°)	90.0, 106.858(7), 90.0	62.623 (4), 85.940 (4), 77.247 (4)
V (Å^3)	1149.4 (3)	593.68 (9)
Z	4	2
Radiation type	Mo *Kα*	Mo *Kα*
μ (mm^{-1})	0.30	0.29
Crystal size (mm)	0.40 × 0.20 × 0.16	0.34 × 0.26 × 0.22
Data collection		
Diffractometer	Bruker Kappa APEXII CCD	Bruker Kappa APEXII CCD
Absorption correction	Multi-scan (*SADABS*; Bruker, 2005)	Multi-scan (*SADABS*; Bruker, 2005)
T_{min}, T_{max}	0.892, 0.956	0.911, 0.943
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	4664, 2019, 1689	7816, 2323, 2021
R_{int}	0.043	0.024
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.639	0.617
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.048, 0.114, 1.05	0.034, 0.095, 1.05
No. of reflections	2019	2323
No. of parameters	172	170
No. of restraints		3
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement	
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.31, −0.28	0.27, −0.33

Table 2
Hydrogen bond distances in **1** and **2**.

Compounds	*D*—H···*A*	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	*D*—H···*A* (°)
1	N1—H1A···O2^{i}	0.86	2.05	2.850 (6)	154.2
	N2—H2A···O4^{ii}	0.72 (8)	2.31 (8)	3.022 (8)	170 (8)
	N2—H2B···O5^{iii}	0.89 (7)	2.42 (7)	3.035 (7)	127 (5)
	C3—H3···N2^{iv}	0.93	2.68	3.494 (7)	146.1
	C10—H10···O3	0.93	2.25	2.853 (7)	121.9
2	C10—H10···O3	0.93	2.26	2.860 (2)	121.6
	N1—H1A···O2^{i}	0.86	2.05	2.9110 (19)	176.2
	N2—H2C···O3^{ii}	0.843 (9)	2.074 (10)	2.909 (2)	171 (2)
	N2—H2D···O1^{iii}	0.842 (9)	2.196 (10)	3.025 (2)	168 (2)
	O1—H1···O5^{iv}	0.82	1.92	2.7003 (18)	159.8
	O1—H1···S1^{iv}	0.82	2.84	3.4443 (13)	132.1

For **1**: Symmetry code(s): (i) *x*, *y*+1, *z*; (ii) *x*, *y*−1, *z*; (iii) *x*, −*y*, *z*+1/2; (iv) *x*+1/2, −*y*+1/2, *z*+1/2.
For **2**: Symmetry code(s): (i) −*x*+3, −*y*, −*z*; (ii) −*x*+1, −*y*+1, −*z*; (iii) *x*−1, *y*, *z*+1; (iv) *x*+2, *y*, *z*−1.

significant parameter for the understanding and design of molecular crystals and biological activities [26]. Therefore, it is very essential and need of hour to synthesize, exploration of the hydrogen bond details, electronic structures and molecular features of sulfanilamide derivatives.

To fulfill this research gap regarding the sulfanilamide derivatives, we synthesized two derivatives by simple reaction of drug with maleic anhydride and with succinic anhydride (Scheme 1). Derivatives were characterized using the XRD and computational studies. The detailed analysis of NBO, FMOs, MEP, MPA, FT-IR, UV–Vis, and thermodynamic parameters to explore electronic and non-covalent interactions (NCIs) of sulfanilamide derivatives. They are helpful for a deep understanding of structure-property relation.

2. Experimental and calculations

2.1. Experimental section

Analytical grade chemicals were used as received without