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Synthesis, and studying effect of a solvent on the ^{1}H-NMR chemical shifts of 4-Azido-N-(6-chloro-3-pyridazinyl)benzenesulfonamide

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ABSTRACT

The compound 4-Azido-N-(6-chloro-3-pyridazinyl)benzenesulfonamide was synthesized and studied using FTIR, and 1H-NMR . The influence of a solvent on the experimental 1H-NMR chemical shifts of title compound is discussed. Small chemical shift $\Delta\delta < 0.1$ ppm were observed when switching from DMSO-d6 to CD3OD. Record a marked change in chemical shifts valeues $\Delta\delta > 0.3$ ppm when transform from high-polar solvents (DMSO-d6,and CD3OD) to low-polar solvent (CDCl3). The 1H-NMR chemical shifts of C2-H and C6-H were shown to have excellent linear correlation with the dielectric constants of the solvents DMSO-d6, CD3OD,and CDCl3 (r = 0.995). The 1H-NMR chemical shifts of C18-H shows a perfect relationship with solvatochromic parameter β (r = 0.999).

1. Introduction

Organic azides play a distinct role in organic chemistry, they are highly effective compounds that have a major role in many organic chemical reactions such as Curtius rearrangement [19,23], aza-Wittig reaction [14,24], and Staudinger reduction [15, 16] synthesis of triazoles and tetrazoles through 1,3 dipolar cycloaddition reaction to alkynes [4,12] and nitriles [28], as well in natural product synthesis [30].

As reactive molecules, organic azides exhibit many interesting properties such as cross-linkers [29] and photoaffinity labels [17,18]. Using azidonucleosides as a treatment of Acquired immunodeficiency syndrome (AIDS) has attracted specialist in this field, and azidothymidine (AZT) is one of the first treatments for AIDS [5]. Furthermore, AZT gold (I) complex has been shown to act as an anti-inflammatory agent, and as an inhibitor to HIV-1, as well [26].

A number of studies have been carried based on practical and theoretical usefulness of organic azides. Najafi et al synthesis and characterization of performed DFT calculations at B3LYP/6-31G* level on 4-(Sulfonylazide)phenyl-1-azide, and they compared the spectral properties that have been calculated

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with the practical results [31]. Zhu et al use IR absorption, Raman scattering, and synchrotron angle-dispersive X-ray diffraction (ADXRD) measurements to study the behavior of the azide group and the structure evolution of 4-acetamidobenzenesulfonyl azide at high pressure [13]. Zeng et al had been using a combined of matrix-isolation IR spectroscopy and quantum chemical calculations to study the thermal and photo-decomposition of benzenesulfonyl azide [10] .

In the present study, we report preparation 4-Azido-N-(6-chloro-3-pyridazinyl)benzenesulfonamide (Figure 1) and effect of solvents on chemical shifts in ^{1}H-NMR. Since the chemical shifts in the ^{1}H-NMR spectrum are affected by a number of factors, including concentration [2] , anisotropic [3] , substituents [33], temperature [32], and solvent effects [25].

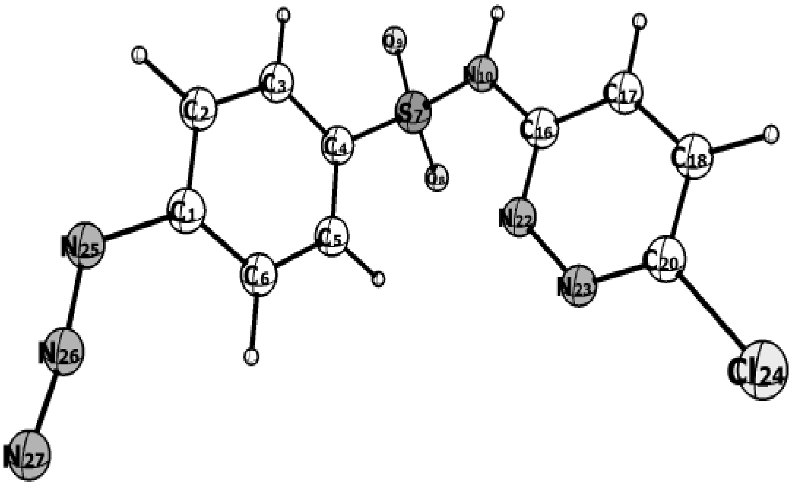

Figure 1. Shows the structure of 4-Azido-N-(6-chloro-3-pyridazinyl)benzenesulfonamide.

2. Experimental

2.1 Materials and Measurements

All chemical reagents employed in this study used were of analytical grade and have not been purified more. The chemicals and solvents were provided by Sigma-Aldrich and Romell. Thermal Scientific melting point equipment was used to measure and record the melting point of utilized at the Chemistry Department, College of Education for Pure Sciences, University of Basrah, Iraq. Fourier-transform infrared (FTIR) spectra were recorded as KBr discs in the 4000-400 cm-1 range using a JASCO-4200 FTIR spectrophotometer at Polymer Research Center, University of Basrah – IRAQ. Varian-INOVA 500MHz spectrometer instrument in Tehran University central lab was used to measure 1HNMR spectra in DMSO-d_6, $CDCl_3$, and CD_3OD as solvents. All chemical shifts were measured relative to tetramethylsilane (TMS), which used as an internal reference.

2.2 Synthesis of 4-Azido-N-(6-chloro-3-pyridazinyl)benzenesulfonamide

(0.002 mol) was dissolved in conc. HCl (2 ml) from Sulfachloropyridazine. The solution was cooled to 0 °C using an ice bath, and then sodium nitrite (0.002 mole) that dissolved in 10 ml of water was slowly added at 0 °C while stirring. Aqueous sodium azide NaN_3 solution (0.002 mole dissolved in 10 ml water) was added dropwise to the previous solution and stirred for 30 minutes at 5°C. The solid product was filtered , dried, and recrystallized from THF-hexane (8:2) give pale yellow powder. Yield: 82 % ; mp 122–124 °C. FTIR (ν, cm–1): 3177 (NH), 2132 (N3), 3080 (C-Harom), 1584 (C=C).

3. Results and Calculations

3.1 Infrared Spectroscopic

The chemical structure of 4-Azido-N-(6-chloro-3-pyridazinyl)benzenesulfonamide was determined using spectroscopic data. The IR spectra revealed a huge band at 2132 cm-1 owing to asymmetric N3 stretching [34], as well as disappearing absorption bands in the area 3490-3390 cm-1 due to asymmetric and symmetric stretching vibrations of the NH2 group.

3.2 ^{1}H-NMR Spectroscopic

3.2.1 Assignment of Chemical Shifts

The structure of 4-Azido-N-(6-chloro-3-pyridazinyl)benzenesulfonamide was determined using ^{1}H-NMR in several deuterated solvents DMSO-d_6, CD_3OD, and $CDCl_3$. Table 1 shows the ^{1}HNMR chemical shifts of compound under study in various deuterated solvents. Note that the resonant signal of C2-H ,and C6-H in all solvents is shown in the region 7.10 - 7.29 ppm, while resonance signal of C3-H and C5-H appears in highly deshielded area at 7.91-7.98 ppm in agreement with the study of Refs. [31, 21]. pyridazine C17-H showed as a singlet at 7.58 ppm in DMSO-d_6, while appearing as a doublet signal in CD_3OD and $CDCl_3$ at 7.65, and 7.36 ppm respectively. On the other hand, C18-H has a doublet resonance signal in the three solvents under study, and it is highly deshielded compared with signal of C17-H, and that is the result of an effect of the electronic withdrawal of the chlorine atom attached in C20 adjacent to C18. The resonant signal of -NH group did not appear this is due to the rapid exchange with the water residue in the sample.

3.2.2 Solvent Effect on Chemical Shifts

In this study, three different polar solvents were selected for the purpose of studying their on chemical shifts in the compound under study. These solvents included DMSO-d_6 and CD_3OD as polar solvent, and $CDCl_3$ as nonpolar solvent. Table 1 shows the experimental results. The results show that there is no significant change in the chemical shifts of all protons (C-H bond type), and that is when going in from DMSO-d_6 as high-polar solvent to CD_3OD which is less polar solvent. However, when shifting from DMSO-d_6 and CD_3OD to $CDCl_3$, there are obvious changes in the chemical shifts values, these results are consistent with that of Abraham et al [1], and Mari et al [20] **.**

There is a noticeable difference in chemical shifts for C18-H, C17-H, C2-H, and C6-H. Considerable (0.36 and 0.32 ppm) values have been found for C18-H. A plot of chemical shift values for C2-H, C6-H protons *vs*. dielectric constant (ε) values of solvents is shown in Figure 2. The chemical shift value for C2-H, and C6-H has an excellent linear relationship (correlation coefficient r = 0.995) with the dielectric constant values of solvents, while the chemical shift value for C18-H has less linear relationship (r = 0.972) with the dielectric constant values of solvents (see Figure 3).

The resonance signal of C17-H has shifted significantly with CD_3OD solvent being the most downfield (7.65 ppm) compared with DMSO-d_6 solvent, which are the most polar, but it suffers a displacement towards highfield region when moving from DMSO-d_6 and CD_3OD to $CDCl_3$ solvent. In this case, the correlation between chemical shift values and the dielectric constant values of solvents is 0.842 (see Figure 4) . Finally, the chemical shift of C3-H, and C5-H is influenced by the change of the solvent polarity, but the effect of the change in solvent polarity on the chemical shift values of these protons is small. In addition, there is a weak correlation between the polarity of solvents and the chemical shift value of these protons, with correlation coefficients equal -0.093.

Table 1. Experimental chemical shifts (ppm) in DMSO-d_6, CD_3OD, and CD_3Cl, and their differences.

Position	δ(DMSO-d6)	δ(CD_3OD)	δ($CDCl_3$)	Δδ(DMSO-d6- CD_3OD)	Δδ(DMSO-d6-CDCl3)	Δδ(CD_3OD -CDCl3)
C2-H, and C6-H	7.29 (8.75 Hz)	7.21 (8.65Hz)	7.10 (8.75Hz)	0.08	0.19	0.11
C17-H	7.58 (singlet)	7.65 (9.4Hz)	7.36 (9.55Hz)	0.07	0.22	0.29
C18-H	7.78 (9.5Hz)	7.74 (9.4Hz)	7.42 (9.55Hz)	0.04	0.36	0.32
C3-H, and C5-H	7.91 (8.60Hz)	7.98 (8.65Hz)	7.93 (8.8Hz)	0.07	-0.02	0.05

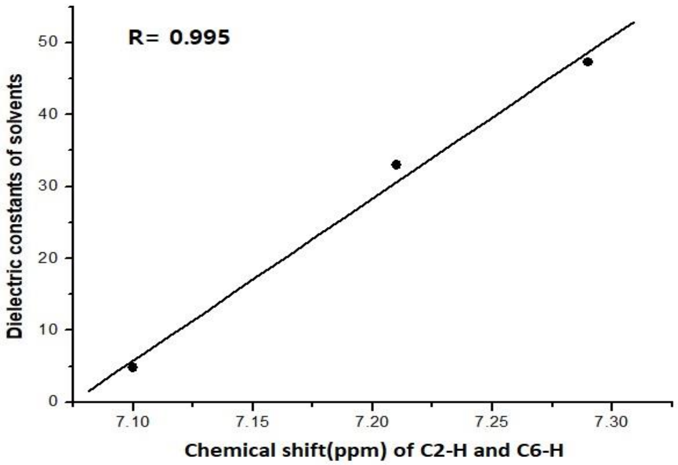

Figure 2. Plot of the dielectric constants values of solvents *vs.* ^{1}H NMR chemical shift (ppm) of C2-H , and C6-H protons.

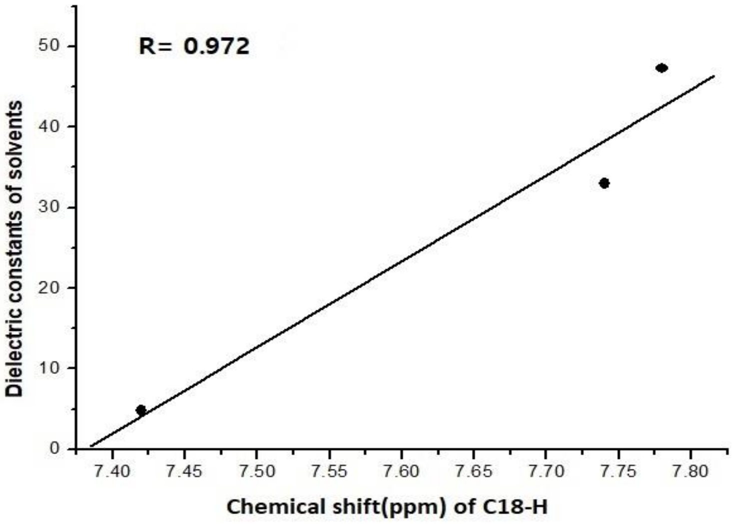

Figure 3. Plot of the dielectric constants values of solvents *vs.* ^{1}H NMR chemical shift (ppm) of C18-H proton.

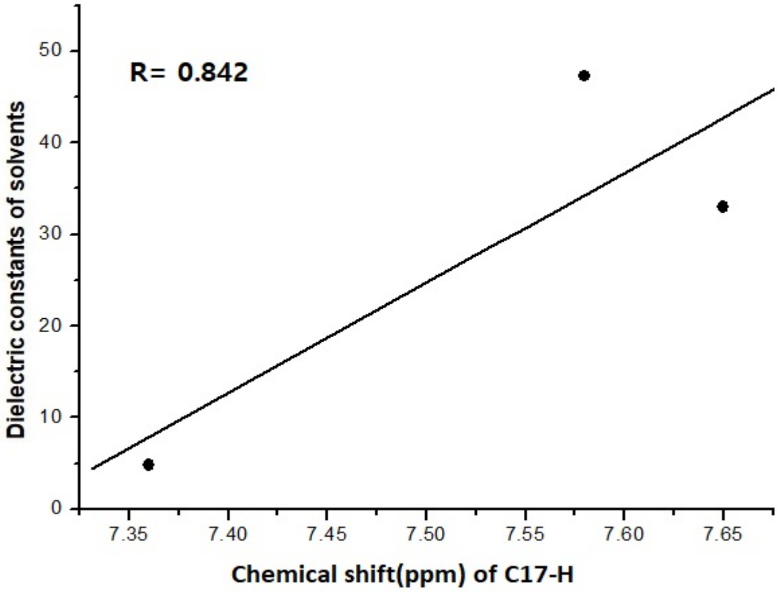

Figure 4. Plot of the dielectric constants values of solvents *vs.* ^{1}H NMR chemical shift (ppm) of C17-H proton.

3.2.3 Correlation between chemical shifts and solvatochromic parameters

The relationship between ^{1}H-NMR chemical shifts values of compounde under study in three deuterated solvent and solvatochromic parameters of solvents was evaluated. These parameters included scale of solvent hydrogen-bond acceptor basicities (β), solvent acidity (SA), solvent basicity (SB), solvent dipolarity and polarizability scale (SPP), solvent dipolarity (SdP), and acceptor number scale (AN). The dielectric constant, and solvatochromic parameters values for the solvents tested are listed in Table 2.

Table 3 gives the correlation coefficient values for relationship between the ^{1}H chemical shifts values recorded in solvents under discussed (see Table 1) and the parameters relating to these solvents. From this table, it can be seen that the ^{1}H chemical shifts values of positions C2-H, and C6-H , C17-H, and C18-H in the title compound have an excellent linear relationship with the β values, similar results were too gained by Hashimoto and Sakata. (28). Maximum linear relation with β values shown by resonant signal of position C18-H (Figure 5). This result is consistent with practice, where the resonance signal of C18-H is clearly affected by solvent change (see Table 1). In contrast, the chemical shift of C3-H, and C5-H shows a weak relationship with β values. This result is consistent with practical results, as the chemical shift of C3-H, and C5-H shows random variable as the solvent changes.

Table 2. Dielectric constant, and solvatochromic parameters values of three solvents studied

Parameter / Solvent	ε[a]	β[b]	SA[c]	SB[d]	SdP[e]	SPP[f]	AN[g]
DMSO-d_6	47.24	0.76	0.072	0.647	1	1	19.3
CD_3OD	33.00	0.66	0.605	0.545	0.904	0.857	41.3
$CDCl_3$	4.80	0.1	0.047	0.071	0.614	0.786	4

a. Values taken from reference [9], b. from reference [27], c,d, and e from reference [6], f. from reference [8], and g. from reference [7].

Table 3. Correlation coefficient values for relationship between the 1H chemical shifts parameters values of three solvents studied

Parameter / Position	ε	β	SA	SB	SdP	SPP	AN
C2-H, and C6-H	0.995	0.957	0.130	0.964	0.981	0.960	0.489
C17-H	0.842	0.930	0.715	0.921	0.889	0.582	0.923
C18-H	0.972	0.999	0.445	0.997	0.990	0.817	0.746
C3-H, and C5-H	-0.093	0.101	0.949	0.075	0.001	-0.455	0.764

From Table 3, the chemical shift value of C3-H and C5-H has a good linear relationship with the SA value (r = 0.949). This is an indication that the chemical shift of these positions is sensitive to the solvent acidity value for those solvents, while the correlation for δ C17-H with SA is moderate. In opposition, the chemical shifts of C18-H, C2-H and C6-H exhibit poor relationships with SA. The chemical shift of C2-H, and C6-H, C17-H, and C18-H protons exhibit an excellent linear correlation with SB (r = 0.964, 0.924, and 0.997 respectively). On the other hand, ^{1}H chemical shift of C3-H, and C5-H does not exhibit an acceptable linear relationship with SB values. This shows that it is insensitive to the solvent basicity.

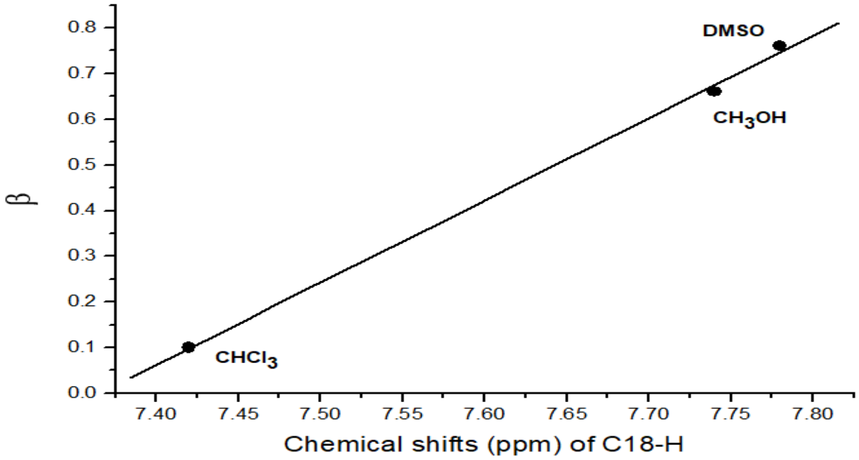

Figure 5. Plot of β values of solvents *vs.* 1H NMR chemical shift (ppm) of C18- proton.

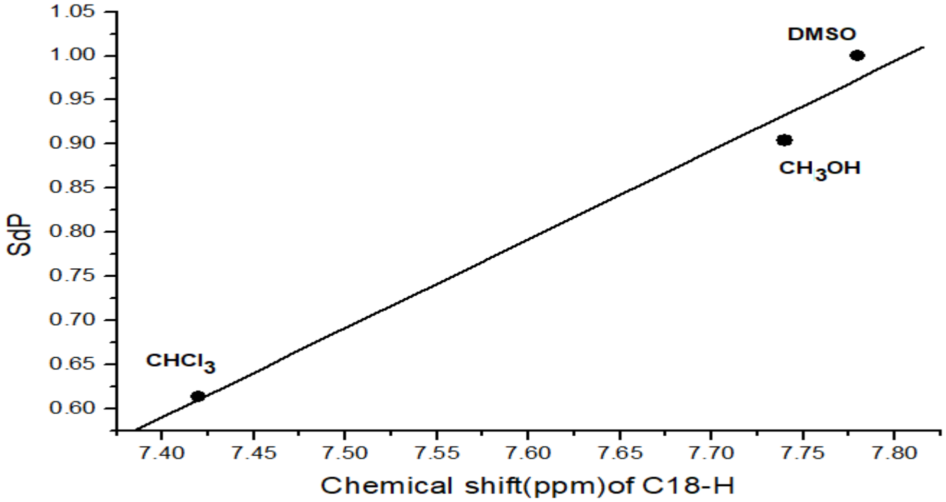

Figure 6. Plot of SdP values of solvents *vs.* ^{1}H NMR chemical shift (ppm) of C18-H proton.

Figure 6. shows the correlation between SdP data and ^{1}H NMR chemical shift of C18-H proton. The correlation is excellent (r = 0.990). It's also worth mentioning that DMSO and MeOH have a minor deviation from line. Similarly, SdP give a good linear relationship with chemical shift of C2-H and C5-

H, and C17-H protons. In contrast, SdP exhibit a weak relationship with chemical shift of C3-H and C5-H. As can be noticed from Table 3, ^{1}H chemical shift of C2-H and C5-H protons give a good linear relationship with SPP of solvents under discussed. In contrast, SPP exhibit a weak relationship with ^{1}H chemical shift of C17-H, C3-H, and C5-H. This is a sign that this chemical shifts are not affected by SPP values, while the chemical shift of C18-H has a good relationship with SPP values (r = 0.889). Finally, from Table 3, we can observe the correlation coefficient for ^{1}H chemical shifts with acceptor number (AN) derived by Mayer *et a1* [22] based on the ^{31}P NMR chemical shifts . This provides an indication of the solvents electrophilic characteristics. The ^{1}H chemical shift of C17-H shows good relationships with AN values (r = 0.923). Whereas chemical shifts of other protons gives a lower correlation coefficient with AN values comparison with chemical shift of C17-H.

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