



Synthesis of a remarkable new Schiff bases series via an amino-1, 3-diol substrate

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ABSTRACT

Piperidine catalysed In chemistry, 2-amino-2-methyl-1,3-propanediol's reaction with various aromatic aldehydes, generating Schiff bases and the corresponding 1,3-dioxane. The combination of Schiff bases and 1,3-dioxane compounds were practically separated. The data were then identified utilising relevant Spectroscopic Imaging in the infrared spectrum and nuclear magnetic resonance are only two examples of the ¹H-HNR, and ¹³C-NMR spectroscopy, in addition to the GC-MS methodology.

Keywords: 1,3-Propanediol; Imine compounds; Piperidine catalysed; Amino alcohol

INTRODUCTION

Schiff bases are regarded as "fortunate ligands" due to the simplicity with which they may be synthesised through aldehyde-amine condensation reactions [1]. Hugo Schiff was the first chemist and scientist to combine amine and carbonyl to produce compounds with an azomethine [C=N-] functional group, which he called Schiff bases, and then, they were used to design and manufacture a variety of physiologically active compounds[2]. Carbon and nitrogen atoms joined by Several compounds have been found to benefit from a double bond for their biological characteristics. Azomethine's nitrogen atom may form hydrogen bonding with cell components' active centers, which disrupts cell activity [3, 4]. Because the nitrogen atom has one lone pair, the double bond is electron-donating, and nitrogen has a low electronegativity, the N of the azomethine family [C=N] functions as an efficient donor site, activating Schiff bases' biological potential [5-7] to combat yeast infections, free radicals, malaria, viruses, cancer, and bacteria, anti-inflammatory, and antipyretic agents [6-9]. Schiff bases are an organic molecule class that finds use throughout

the chemical sciences. [1,2]. Imines' stability, chelation capacity, and a wide variety of biological applications have made the existence of the azomethine (-CH=N-) connection in them a topic of interest [10]. Due to their direct synthesis, crystalline characteristics, biological activity, and redox and catalytic properties, Imines' compounds are attracting attention [11-13]. Furthermore, Imines have undergone extensive development and research for their unique properties, which include their outstanding biological activities, adaptable synthesis, thermal stability, unique structural characteristics, and therapeutic effectiveness [14]. In the sphere of therapeutic research, the structural activity technique is anticipated to provide an efficient platform for locating powerful medications [11]. For the logical development of fresh scaffolds that rely on therapeutics already found in the skeletal framework of imine molecules. These prototypes were recently improved using a variety of strategies [15, 16]. Further Schiff bases have several applications outside of biology, pigments, stabilizers for polymers, corrosion inhibitors,

dyes, and intermediates in chemical synthesis. [6, 17]. Some researchers were inspired to develop novel heterocyclic or aryl Schiff bases allowing the widespread use of Schiff base derivatives in numerous processes, which will allow for the creation of new ecologically friendly technologies [18].

Recently, one study investigated the effective interaction of bioactive metal ions in the domain of related drugs (L1 and L2), and the first and second ligands were synthesised by reacting the substrate 2-amino-2-methyl-1,3-propanediol with the corresponding carbonyl compounds [12].

Another study revealed that when drug candidates 1 and 2 are synthesised in the presence of the ligand produced from the reaction of 2-amino-2-methyl-1,3-propanediol with salicylaldehyde, can serve as potential anticancer agents and call for more biological research [19]. Furthermore, sphingosine and sphinganine lipids are among the exceptionally bioactive compounds that, despite changes in size, show a pattern similar to that of 2-amino-2-methyl-1,3-propanediol (Figure 1). Both belong to the class of amino alcohols [20].

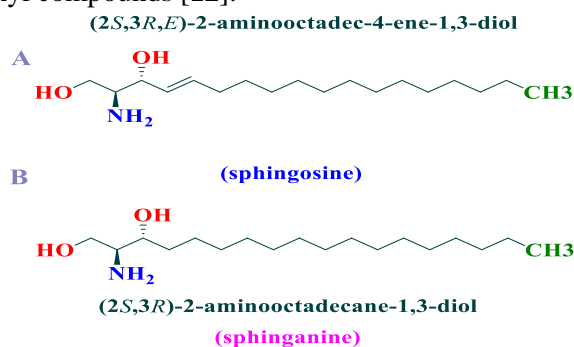


Figure 1. Structure of sphingosine (A) and sphinganine (B).

As a result, from our perspective, the problem is that occasionally you could need to alter the fluorescent detector and the o-phthalaldehyde employed in the quality of extraction and measurement of sphingosine and sphinganine, respectively while tracking various diseases linked to those lipids.

The major goal of the current study is to create novel short-chain aliphatic Schiff bases that are easier to prepare in the lab and identify spectroscopically using standard spectroscopic

techniques. Whereas new design concepts focused on Schiff's bases and demanded that, they have functional groups resembling those in sphingolipid derivatives like sphingosine and sphinganine. Because it possesses the identical functional groups in sphingosine and sphinganine with the aliphatic short chain as opposed to the equivalent aliphatic long chain in sphingosine and sphinganine, the molecule 2-amino-2-methyl-1,3-diol was chosen for this purpose; see Figure 2.

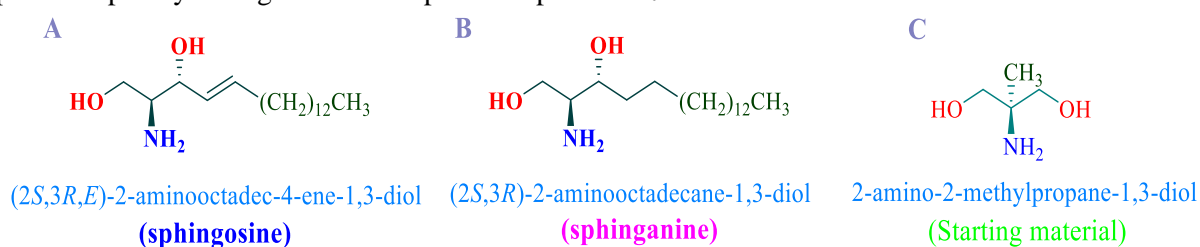


Figure 2. Structure of sphingosine (A), Sphinganine (B) and Starting material (C).

The natural resources are difficult to deal with for sphingosine and sphinganine, as well as the organic identification of their derivatives. In addition, compared to the alternate molecule in our study, their industrial sources are more expensive. These factors are the main drivers behind this approach to scientific research. Additionally, the substance picked as a target fat substitute throughout development guarantees

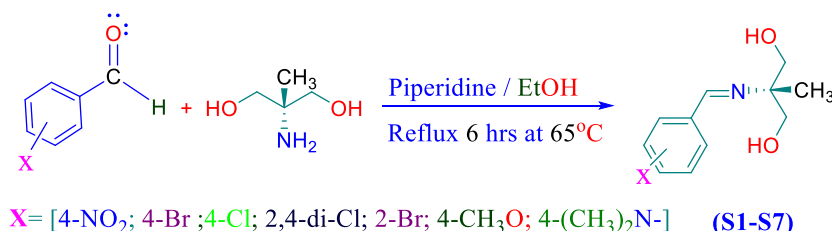
that we will successfully complete the task and adhere to the QSAR standards. In addition to the aforementioned, this study offers a fundamental building block for estimating the fats involved in the study, as well as a fundamental building block for developing alternative medical treatments and exploring the potential for creating anti-cancer medications using the intended fats in the current study.

RESULTS AND DISCUSSION

Chemistry of Schiff bases derivatives

All new Schiff bases were created using a combination of selected benzaldehyde substitutes and 2-amino-2-methyl-1,3-propanediol. Several aldehydes that undergo 1,3-diol derivative treatment undergo a carbonyl group protection reaction when piperidine is present. The remaining component, however, makes the

proper even though some aldehydes do not respond well to the carbonyl group protection procedure and have a high potential to produce Schiff base derivatives. Examples of aldehyde derivatives that do not completely undergo the carbonyl group protection procedure include 4-methylbenzaldehyde, 4-methoxybenzaldehyde, and 4-(CH₃)₂N-benzaldehyde.



Scheme 1: The general reaction to the synthesis of the new Schiff base series'

Characterization of Schiff bases derivatives

Infrared spectra IR: Using the compounds' infrared spectra, the functional groups included in the newly synthesized compounds were mapped (400–4000 cm⁻¹). The infrared spectra of the covalent bonds (S1–S7) indicated a significant region because of the stretching vibration of aliphatic -OH (3230–3390 cm⁻¹). The spectra also showed two absorption stretching bands of Aliphatic (-CH₂ and -CH₃)_{Al} at (2918–2966 cm⁻¹) and (2845–2885 cm⁻¹) respectively, and absorption stretching bands (C–H)_{Ar} at (3007–3045 cm⁻¹). A strong new intensity range (1600–1653 cm⁻¹) was linked to the existence of the azomethine group (-CH=N-), verifying the creation of the suggested imine bonds. All spectra furthermore displayed two bands of absorption stretching (C=C)_{Ar} at wave numbers (1448–1477 cm⁻¹) and (1520–1598 cm⁻¹) respectively [21, 22]. The removal of the carbonyl and amino groups was another characteristic shared by all infrared spectra and all manufactured Schiff bases. pertaining to the primary reactants and the emergence of the aforementioned imine bond bundles.

¹H-NMR and ¹³C-NMR: Using DMSO-d₆, the ¹H-NMR¹ spectra of novel Schiff bases (S1-S7)

were recorded. The ¹H-NMR spectra of Schiff bases (S1-S7) revealed a singlet at¹ (8.64–8.19) ppm¹(Table 2), confirming the existence of the (-CH=N-) connection and ultimately the synthesis of Schiff base compounds. Both ligand moieties have aliphatic -CH₂ and -CH₃ families. could be seen in the peaks at (3.58–3.36) and (1.10–1.18) ppm. Doublet signals in the (8.08–7.70) ppm and (8.29–7.56) ppm ranges, respectively, showed the existence of 2,4, and 3,5 phenyl ring protons with para replacements [21, 22].

On the other hand, the spectrum information for the diagnosis of atomic family of imines, which is the fundamental class of uses in the Schiff bases, can be condensed (S1-S7). In which spectroscopic information was used to determine how Schiff bases were arranged. The recognized azomethine proton (H-C=N) emerged in the ¹H-NMR spectra at its expected value (8.64–8.19 ppm), whereas the azomethine carbon echoed at range 157.75–157.01 ppm in the ¹³C-NMR spectra [12]. The structures [23] were supported by the (H-C=N) stretching absorption in the IR spectra, which took place at its typical area of 1653 cm⁻¹. The IR and ¹H-NMR data are shown in Tables 1 & 2.

Table 1: IR data of new Schiff bases series, S1-S7

Comp No.	Ar-Group	v(-OH) Ring	v(C-H) Ar	v(C-H) Al	v(C=N)	v(C=C) Ar	Others
S1		3237	3011	2966, 2875	1604	1520, 1457	-NO ₂ : 1347, 1485

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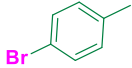
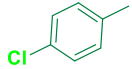
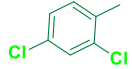
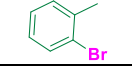
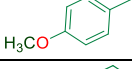
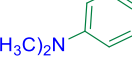
S2		3230	3032	2925, 2885	1630	1598, 1477	
S3		3233	3023	2924, 2883	1635	1598, 1478	
S4		3358	3007	2935, 2879	1600	1589, 1463	
S5		3385	3033	2933, 2877	1635	1593, 1448	
S6		3390	3040	2918, 2845	1645	1562, 1460	
S7		3355	3045	2941, 2884	1653	1595, 1456	

 Table 2: ¹H-NMR data of new Schiff bases series, S1-S7

Structure	Chemical Shift (δ) ppm	Signal Features	No. Protons	Type of Protons
S1	8.49	s	1H	imine proton
	8.29	(d, J=8.9 Hz)	2H	aromatic proton
	8.04	(d, J=8.8 Hz)	2H	aromatic proton
	3.45-3.56	m	4H	CH ₂
	1.18	s	3H	CH ₃
S2	8.36	s	1H	imine proton
	7.80	(d, J=8.5 Hz)	2H	aromatic proton
	7.49	(d, J=8.6 Hz)	2H	aromatic proton
	3.41-3.54	m	4H	CH ₂
	1.15	s	3H	CH ₃
S3	8.37	s	1H	imine proton
	7.80	(d, J=8.5 Hz)	2H	aromatic proton
	7.46	(d, J=8.5 Hz)	2H	aromatic proton
	3.45-3.58	m	4H	CH ₂
	1.18	s	3H	CH ₃
S4	8.64	s	1H	imine proton
	8.03	(dd, J=2.1, 7.4 Hz)	1H	aromatic proton
	7.67	(d, J=2.1, Hz)	1H	aromatic proton
	7.57	(d, J=8.5 Hz)	1H	aromatic proton
	3.45-3.55	m	4H	CH ₂
	1.17	s	3H	CH ₃
S5	8.62 ⁴	s	1H	imine proton
	8.00	(t, J= 7.2 Hz)	2H	aromatic proton
	7.67	(dd, J=1.3, 7.8 Hz)	1H	aromatic proton
	7.43	(dd, J=2.0, 7.6 Hz)	1H	aromatic proton
	3.45-3.55	m	4H	CH ₂
	1.17	s	3H	CH ₃
S6	8.30	s	1H	imine proton
	7.71	(d, J=8.8 Hz)	2H	aromatic proton
	6.97	(d, J=8.8 Hz)	2H	aromatic proton
	3.40-3.54	m	4H	CH ₂
	1.14	s	3H	CH ₃
S7	8.19	s	1H	imine proton
	7.56	(d, J=8.9 Hz)	2H	aromatic proton
	6.70	(d, J=8.8 Hz)	2H	aromatic proton

	3.36-3.49	m	4H	CH ₂
	2.95	s	6H	(CH ₃) ₂ -N
	1.10	s	3H	CH ₃

EXPERIMENTAL

3.1. Chemicals and instruments

Chemicals: All of the compounds were synthesised utilising the ingredients and reagents listed below: 4-nitrobenzaldehyde (98% BDH, England), 4-bromobenzaldehyde (99% BDH, England), piperidine (99% Sigma-Aldrich, Germany), dimethyl sulfoxide (Merck), 2-amino-2-methyl-1,3-propanediol (Sigma, China), 4-chlorobenzaldehyde (BDH, England), 2-bromobenzaldehyde (BDH, England), 2,4-d (BDH, England); TLC silica gel 60 F254 aluminum sheets, 20 cm × 20 cm (Merck, Germany).

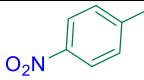
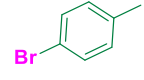
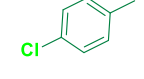
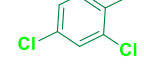
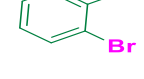
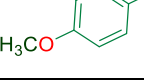
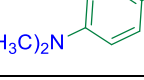
Instruments: The College of Applied Sciences at the University of Samarra is home to all the instruments needed In order to identify the elements that make up compounds, with the exception of a Bruker Advance. Radiation-free magnetic resonance imaging (¹H-NMR) and ¹³C-NMR spectra were measured at Basra University's College of Education, Department of Chemistry, using a Bruker Advance (400 MHz) and DMSO-d₆ solvent. A Fourier Transform

Infrared Spectrometer was used to get the IR data. /FTIR-8400S supplied by the Shimadzu Japanese Company; samples were formed onto (KBr) discs. Using the Shimadzu GC-MS-QP 2010 Ultra mass spectrometer, mass spectra were collected. Sartorius' delicate Balance from Germany was employed. The Stuart-United Kingdom provided the Melting Point Digital Advanced SMP30, and all melting points of samples are uncorrected.

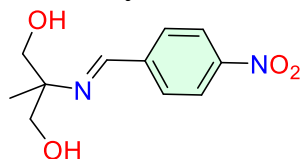
3.2. Generic Synthesis Methodology of Schiff bases derivatives

Piperidine (0.5 ml) was combined with equimolar amounts of 2-amino-2-methyl-1,3-propanediol (0.001 mol) and one of the aromatic aldehyde derivatives to produce a novel series of Schiff bases (S1-S7). For 5–6 hours, the reaction's components were stirred and refluxed to 65°C. After then, it is allowed to gradually cool. The reaction products were then transferred to a beaker and left in the fume hood for the ethanol to evaporate and a dry precipitate to develop.

Table 3: physical properties data of new Schiff bases series

Comp No	Ar-Group	Molecular Weight	Melting Point	Color	Yield%
S1		238.1	(87-89)°C	Yellow Orange	73.5
S2		271.0	(95-97)°C	Golden	94.1
S3		227.1	(85-87)°C	Off White	60.3
S4		261.0	(78-81)°C	Beige Yellow	71.3
S5		271.0	(66-68)°C	Apricot	75.6
S6		223.1	(94-96)°C	Light Hazel	56.5
S7		236.2	(73-75)°C	Lemon yellow	54.2

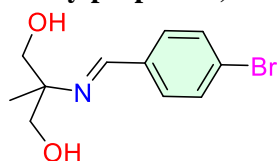
(E)-2-methyl-2-((4-nitrobenzylidene)amino)propane-1,3-diol, S1



¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.18 (s, 3H), 3.45 – 3.56 (m, 4H), 8.04 (d, J = 8.9 Hz, 2H), 8.29 (d, J = 8.8 Hz, 2H), 8.49 (s, 1H).

¹³C NMR (101 MHz, DMSO-*d*₆) δ 18.73, 65.60, 65.97, 124.19, 129.32, 142.95, 148.71, 157.04.

(E)-2-((4-bromobenzylidene)amino)-2-methylpropane-1,3-diol, S2

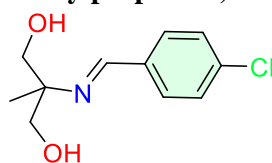


¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.15 (s, 3H), 3.41 – 3.54 (m, 4H), 7.49 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.6 Hz, 2H), 8.36 (s, 1H).

¹³C-NMR (101 MHz, DMSO-*d*₆) δ 18.86, 65.36, 65.50, 128.96, 129.95, 135.29, 136.22, 157.21.

DEPT135_ ¹³C NMR (101 MHz, DMSO-*d*₆) δ 18.86, 65.49, 128.96, 129.95, 157.21.

(E)-2-((4-chlorobenzylidene)amino)-2-methylpropane-1,3-diol, S3



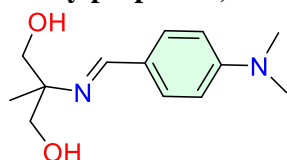
¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.18 (s, 3H), 3.45 – 3.58 (m, 4H), 7.46 (d, J = 8.5, 2H), 7.80 (d, J = 8.5 Hz, 2H), 8.37 (s, 1H).

¹³C-NMR (101 MHz, DMSO-*d*₆) δ 18.82, 65.35, 65.45, 128.95, 129.94, 135.34, 136.18, 157.24.

DEPT135_ ¹³C NMR (101 MHz, DMSO-*d*₆) δ 18.82, 65.44, 128.95, 129.95, 157.25.

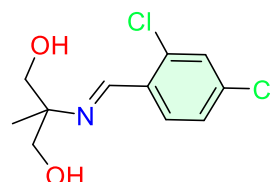
(E)-2-((2,4-dichlorobenzylidene)amino)-2-methylpropane-1,3-diol, S4

(E)-2-((4-(dimethylamino)benzylidene)amino)-2-methylpropane-1,3-diol, S7



¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.10 (s, 3H), 2.95 (s, 6H), 3.36 – 3.49 (m, 4H), 6.70 (d, J = 8.9 Hz, 2H), 7.56 (d, J = 8.8 Hz, 2H), 8.19 (s, 1H).

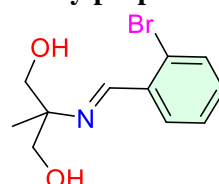
(E)-2-((2,4-dichlorobenzylidene)amino)-2-methylpropane-1,3-diol, S3



¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.17 (s, 3H), 3.45 – 3.55 (m, 4H), 7.57 (dd, J = 2.1, 7.4 Hz, 1H), 7.67 (d, J = 2.1 Hz, 1H), 8.03 (d, J = 8.5 Hz, 1H), 8.64 (s, 1H).

¹³C-NMR (101 MHz, DMSO-*d*₆) δ 18.74, 65.37, 65.56, 128.07, 129.53, 129.79, 132.86, 133.64, 135.35, 153.67.

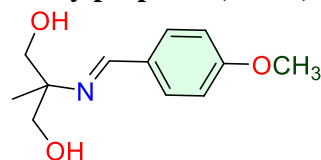
(E)-2-((2-bromobenzylidene)amino)-2-methylpropane-1,3-diol, S5



¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.17 (s, 3H), 3.45 – 3.54 (m, 4H), 7.43 (t, J = 7.2, 7.2 Hz, 2H), 7.67 (dd, J = 1.5, 7.8 Hz, 1H), 8.00 (dd, J = 2.0, 7.6 Hz, 1H), 8.62 (s, 1H).

¹³C-NMR (101 MHz, DMSO-*d*₆) δ 18.75, 65.93, 66.03, 125.10, 128.34, 128.44, 132.54, 133.34, 135.13, 157.01.

(E)-2-((4-methoxybenzylidene)amino)-2-methylpropane-1,3-diol, S6



¹H-NMR (400 MHz, DMSO-*d*₆) δ 1.14 (s, 3H), 3.40 – 3.54 (m, 4H), 3.79 (s, 3H), 6.97 (d, J = 8.8 Hz, 2H), 7.71 (d, J = 8.8 Hz, 2H), 8.30 (s, 1H).

¹³C-NMR (101 MHz, DMSO-*d*₆) δ 18.96, 55.67, 64.76, 65.43, 114.23, 129.87, 130.32, 157.53, 161.39.

DEPT135_ ¹³C NMR (101 MHz, DMSO-*d*₆) δ 18.95, 55.66, 65.42, 114.23, 129.88, 157.53.

¹³C-NMR (101 MHz, DMSO-*d*₆) δ 19.07, 40.29, 64.32, 65.44, 111.80, 125.49, 129.57, 152.09, 157.75.

CONCLUSION

All new Schiff bases created in lab work for this study had their structure confirmed using a variety of important and cutting-edge organic identification methods. These Schiff bases may have anticancer properties against some cancer types.

By comparing the essential structural components of these compounds with a study of the literature from a few studies, one of which was issued as a patent with the title (Synthesis and application of 3,5-dibromosalicylaldehyde 2-amino-2-meth--1,3-propanediol Schiff base with antitumor activity). The fundamental components of the substances matched their function in the development of future anti-cancer medications. Additionally, techniques for quantifying the quantity of certain classes of spongy lipids, such as sphingosine and sphinganine, throughout the production process may be developed.

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