INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

ISSN:2320-2831

IJPAR |Vol.5 | Issue 2 | April- June -2016

Journal Home page: www.ijpar.com

Research article *Open Access*

Synthesis, characterization and in silico studies of some schiff's bases derived from amino acids

E. Mohana Roopa

Department of Pharmaceutical Chemistry, Holy Mary College of Pharmacy, Bogaram, Hyderabad, India

***Corresponding Author: Mohana R**

Email Id: mohanarupa.e@gmail.com

ABSTRACT

The project is aimed at the synthesis of some schiff bases derived from some aldehydes with amino acids such as glycine and alanine. This method is applied successfully to the synthesis of six imines from compounds. The structures of these Schiff bases are confirmed by using physical methods, namely, melting point or boiling point, UV and IR spectra. The physicochemical properties and possible biological activities are predicted using i lab 2 and PASS softwares.

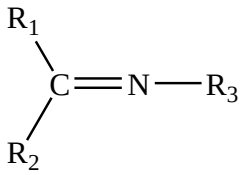
Key words: Schiff bases, Amino acids, physicochemical properties

INTRODUCTION

Drugs are chemicals that prevent disease or assist in restoring health to the diseased individuals as such they play an indispensable role in modern medicine. Medicinal chemistry is the branch of science that provides these drugs either through discovery or through design. In the last century, the classical drugs were primarily discovered either by alteration of natural substances or entirely by chemical synthesis. In the recent years, an ever-increasing understanding of pathophysiology of disease has increasingly led to novel opportunities to deliberate design synthesis and evaluation of candidate drug molecules[1].

Schiff's bases

Hugo Schiff, a German Chemist discovered Schiff's bases and other imines, and was responsible for research into aldehydes and had the Schiff's test named after him. Compounds containing an azomethazine group (-CH=N) are known as Schiff bases.



R_1,R_2,R_3-alkyl or aryl groups

General structure of Schiff's base

Schiff's bases are usually formed by condensation of a primary amine with a carbonyl compound according to the following scheme:

$$R\text{-}CHO + H_2NR \longrightarrow RCH{=}NR + H_2O$$

Schiff bases of aliphatic aldehydes are relatively unstable and are readily polymerizable while those of aromatic aldehydes, have an effective conjugation system, are more stable. Condensation of amines with aldehydes and ketones has numerous applications which include preparative use, identification, detection and determination of aldehydes or ketones, purification of carbonyl or amino compounds or protection of these groups during complex action or sensitive reactions[2,3].

General methods of preparation of imines

Imines are typically prepared by the condensation of primary amines and aldehydes and less commonly ketones. In terms of mechanism, such reactions proceed via the nucleophilic addition giving hemiaminal –C(OH)(NHR)- intermediate, followed by an elimination of water to yield the imine. The equilibrium in this reaction usually favours of the carbonyl compound and amine, so that azeotropic distillation or use of a dehydrating agent such as molecular sieves is required to push the reaction in favour of imine formation[4].

Synthetic importance of Schiff's bases

Schiff's bases have a large number of synthetic uses in organic chemistry. Acylation of Schiff's base by acid anhydrides, acid chlorides and acyl cyanides is initiated by attack at the nitrogen atom and leads to net addition of the acylating agent to the carbon-nitrogen double bond. Reactions of this type have been put to good use in natural product synthesis. Also the base-catalyzed condensation of acetyl chlorides with N-arylaldimines occurs by initial acylation at the nitrogen atom and leads to β-lactams of interest in penicillin chemistry[5-8].

Biological importance of Schiff's bases

Schiff bases appear to be important intermediates in a number of enzymatic reactions involving interaction of an enzyme with an amino or a carbonyl group of the substrate. One of the most prevalent types of catalytic mechanisms in biochemical processes involves condensation of primary amine in an enzyme, usually that of a lysine residue, with a carbonyl group of the substrate to form imines or Schiff's bases.[9-12]

Stereochemical investigations carried out with the aid of molecular models showed that Schiff's bases formed between methylglyoxal and the amino groups of the lysine side chains of proteins can bend back in such a way towards the nitrogen atoms of peptide groups that a charge transfer can occur between these groups and the oxygen atoms of the Schiff's bases. [13-16]

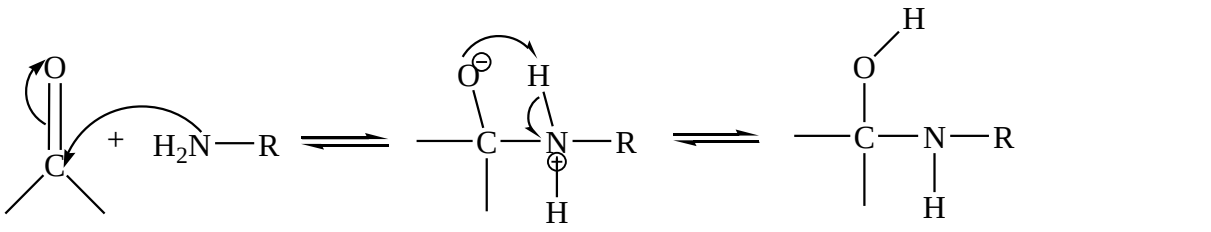
Synthetic Methodology

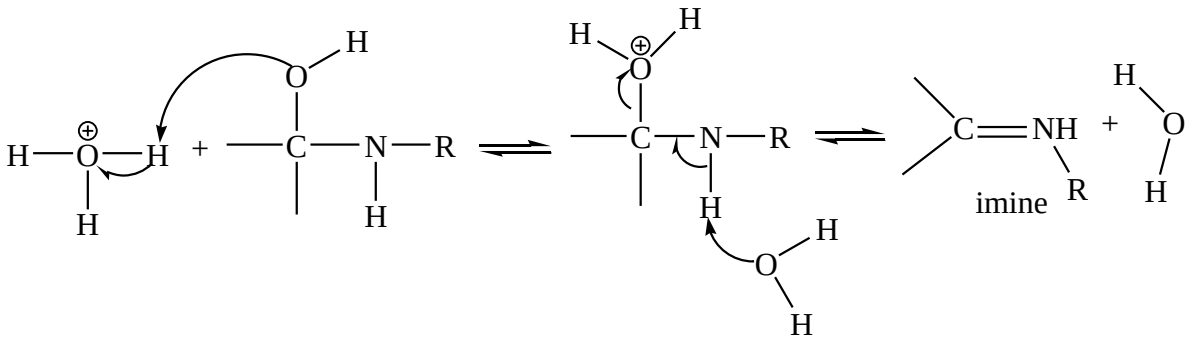
Scheme of the reaction

$$R\text{-}CHO + H_2NRCHCOOH \longrightarrow RCH{=}NRCHCOOH + H_2O$$

Aldehyde Amino acid Imine

Reaction Mechanism





Schiff's base can be synthesized from an amine and a carbonyl compound by nucleophilic addition forming a hemiaminal, followed by a dehydration to generate an imine.[17-21]

General Synthetic Procedure

A mixture of 30 mmole aldehyde and 30 mmole amino acid is to be taken in a RBF. To this, 15 ml of ethanol is to be added. A small amount of potassium hydroxide (KOH) should be added which serves as a catalyst. The condensation reaction has to be carried out for 60-180 min. The mixture is cooled, product is collected and dried.[22-25]

Synthesis of {[Phenylmethylidene]amino} acetic acid: (SB-1)

A mixture of 30 mmole benzaldehyde and 30 mmole glycine is to be taken in a round bottomed flask. To this, 15 ml of ethanol is to be added. A small amount of potassium hydroxide (KOH) should be added which serves as a catalyst. The condensation reaction has to be carried out for 60-180 min. The mixture is cooled, product is collected and dried.

The UV spectrum has revealed that the compound exhibits absorbance value of 0.48 at a wavelength of 235 nm.

The IR (cm^{-1}) spectra has shown characteristic bands at 1398 [C-H def ($-CH_2-$)], 1498 [C=O str (Acid)], 1574 (C=N str), 2591(O-H str), 2914 (C-H str), 3145(Ar-H str).

Synthesis of 2-{[(Phenylmethylidene]amino} propanoic acid: (SB-2)

A mixture of 30 mmole benzaldehyde and 30 mmole alanine is to be taken in a round bottomed flask. To this, 15 ml of ethanol is to be added. A small amount of potassium hydroxide (KOH) should be added which serves as a catalyst. The condensation reaction has to be carried out for 60-180min.The mixture is cooled, product is collected and dried.

The UV spectrum has revealed that the compound exhibits absorbance value of 0.035 at a wavelength of 230 nm.

The IR (cm^{-1}) spectra has shown characteristic bands at 1451[C-H def ($-CH_3$)], 1508 [C=O str (Acid)], 1581 (C=N str), 2598 (O-H str), 2843 (C-H str), 2917 (Ar-H str).

Synthesis of 2-(5-Oxopentylideneamino) acetic acid: (SB-3)

A mixture of 30 mmole gluteraldehyde and 30 mmole glycine is to be taken in a round bottomed flask. To this, 15 ml of ethanol is to be added. A small amount of potassium hydroxide (KOH) should be added which serves as a catalyst. The condensation reaction has to be carried out for 60-180min.The mixture is cooled, product is collected and dried.

The UV spectrum has revealed that the compound exhibits absorbance value of 0.934 at a wavelength of 230 nm.

The IR (cm^{-1}) spectra has shown the characteristic bands at 1490 [C=O str (Acid)], 1573 (C=N str), 1742 [C=O str (Aldehyde)], 2868 (C-H str), 3094 (O-H str).

Synthesis of 2-{[5-Oxopentylidene]amino}propanoic acid : (SB-4)

A mixture of 30 mmole gluteraldehyde and 30 mmole alanine is to be taken in a round bottomed flask. To this, 15 ml of ethanol is to be added. A small amount of potassium hydroxide (KOH) should be added which serves as a catalyst .The condensation reaction has to be carried out for 60-180min.The mixture is cooled, product is collected and dried.

The UV spectrum has revealed that the compound exhibits absorbance value of 0.955 at a wavelength of 230 nm.

The IR (cm^{-1}) spectra has shown the characteristic bands at 1451[C-H def ($-CH_3$)], 1511 [C=O str (Acid)], 1584 (C=N str), 1737 [C=O str (Aldehyde)], 2847 (C-H str), 2922 (O-H str).

Synthesis of 2-(4-Methoxybenzylidene amino) acetic acid: (SB-5)

A mixture of 30 mmole anisaldehyde and 30 mmole glycine is to be taken in a round bottomed flask. To this, 15 ml of ethanol is to be added. A small amount of potassium hydroxide (KOH) should be added which serves as a catalyst. The condensation reaction has to be carried out for 60-180min.The mixture is cooled, product is collected and dried.

The UV spectrum has revealed that the compound exhibits absorbance value of 2.678 at a wavelength of 240 nm.

The IR (cm^{-1}) spectra has shown the characteristic bands at 1169 ($-OCH_3$ str), 1602 (C=N str), 1642 [C=O str (Acid)], 2834 (O-H str), 2932 (C-H str), 2998 (Ar-H str).

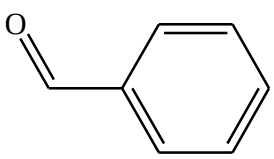
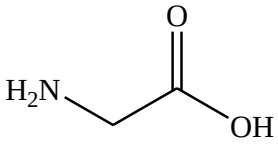
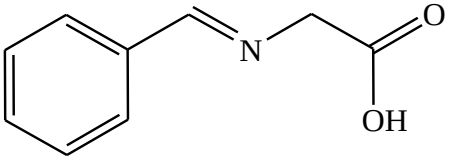
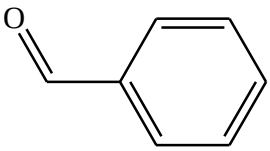
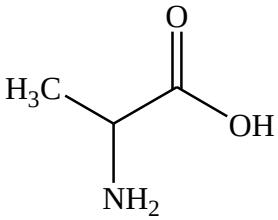
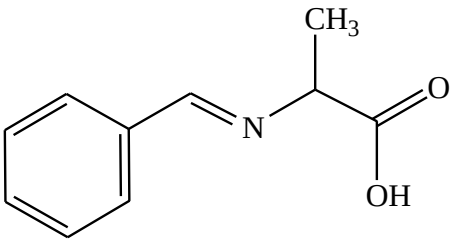
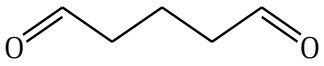
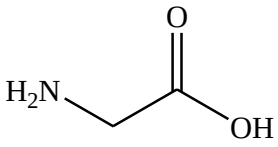
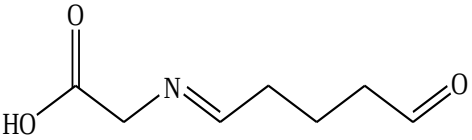
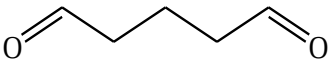
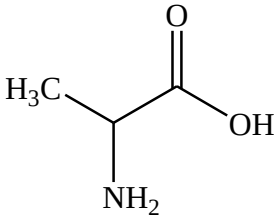
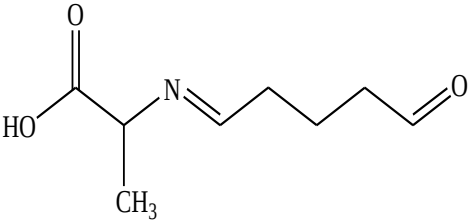
Synthesis of 2-(4-methoxybenzylideneamino) propanoic acid: (SB-6)

A mixture of 30 mmole anisaldehyde and 30 mmole alanine is to be taken in a round bottomed flask. To this, 15 ml of ethanol is to be added. A small amount of potassium hydroxide (KOH) should be added which serves as a catalyst .The condensation reaction has to be carried out for 60-180min. The mixture is cooled, product is collected and dried.

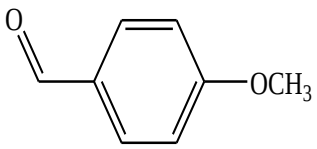
The UV spectrum has revealed that the compound exhibits absorbance value of 2.051at a wavelength of 225 nm.

The IR (cm^{-1}) spectra has shown the characteristic bands at 1108 ($-OCH_3$ str), 1602 (C=N str), 1505 [C=O str (Acid)], 2919 (C-H str), 3002 (Ar-H str), 3365 (O-H str).

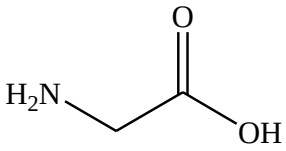
Table no 1: List of synthesized Schiff's bases

CODE	ALDEHYDE	AMINOACID	SCHIFF'S BASE
SB-1	 BENZALDEHYDE	 GLYCINE	
SB-2	 BENZALDEHYDE	 ALANINE	
SB-3	 GLUTERALDEHYDE	 GLYCINE	
SB-4	 GLUTERALDEHYDE	 ALANINE	

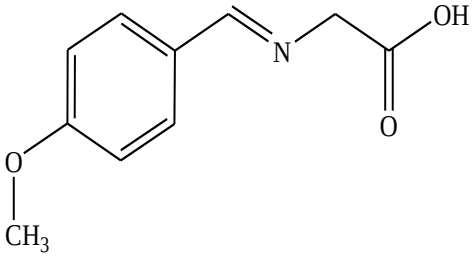
SB-5



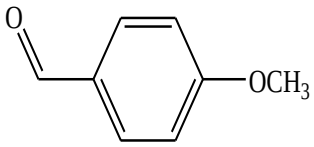
ANISALDEHYDE



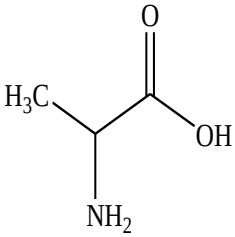
GLYCINE



SB-6



ANISALDEHYDE



ALANINE

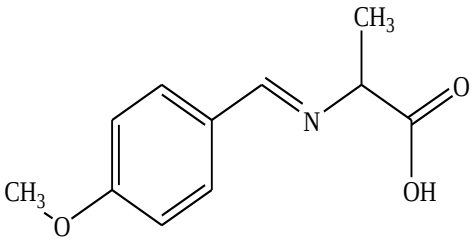
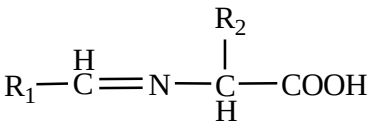


Table no 2: IUPAC names of the synthesized compounds

SB-01	{[Phenylmethylidene]amino}acetic acid
SB-02	2-{[Phenylmethylidene]amino}propanoic acid
SB-03	2-(5-Oxopentylideneamino) acetic acid
SB-04	2-{[5-Oxopentylidene]amino}propanoic acid
SB-05	2-(4-Methoxybenzylideneamino)acetic acid
SB-06	2-(4-Methoxybenzylideneamino)propanoic acid

Table no 3: Physical characterisation data for the synthesized schiff's bases



S. No	Code	R_1	R_2	Molecular formula	Molecular weight	Yield (%)	R_f values
1	SB-01	C_6H_5	H	$C_9H_9NO_2$	163.17	79	0.56
2	SB-02	C_6H_5	CH_3	$C_{10}H_{11}NO_2$	177.19	74	0.53
3	SB-03	$(CH_2)_3CHO$	H	$C_7H_{11}NO_3$	157.16	77	0.59

4	SB-04	$(CH_2)_3CHO$	CH_3	$C_8H_{13}NO_3$	171.19	75	0.57
5	SB-05	$C_6H_5OCH_3$	H	$C_{10}H_{11}NO_3$	193.19	74	0.52
6	SB-06	$C_6H_5OCH_3$	CH_3	$C_{11}H_{13}NO_3$	207.22	72	0.58

Table no 4: IR Spectral data for the synthesized schiff's bases

Compound	IR (KBr disc) position of absorption band (cm^{-1})
SB-01	1398 [C-H def (-CH_2-)], 1498 [C=O str (Acid)], 1574 (C=N str), 2591(O-H str), 2914 (C-H str), 3145(Ar-H str).
SB-02	1451[C-H def (-CH_3)], 1511 [C=O str (Acid)], 1584 (C=N str), 1737 [C=O str (Aldehyde)], 2847 (C-H str), 2922 (O-H str)
SB-03	1490 [C=O str (Acid)], 1573 (C=N str), 1742 [C=O str (Aldehyde)], 2868 (C-H str), 3094 (O-H str)
SB-04	1451[C-H def (-CH_3)], 1511 [C=O str (Acid)], 1584 (C=N str), 1737 [C=O str (Aldehyde)], 2847 (C-H str), 2922 (O-H str)
SB-05	1169 (-OCH_3 str), 1602 (C=N str), 1642 [C=O str (Acid)], 2834 (O-H str), 2932 (C-H str), 2998 (Ar-H str)
SB-06	1108 (-OCH_3 str), 1602 (C=N str), 1505 [C=O str (Acid)], 2919 (C-H str), 3002 (Ar-H str), 3365 (O-H str)

Table no 5: UV Spectral data for the synthesized schiff's bases

CODE	ABSORBANCE	WAVE LENGTH (nm)
SB-1	0.48	235
SB-2	0.035	230
SB-3	0.934	230
SB-4	0.955	230
SB-5	2.678	240
SB-6	2.051	225

IN SILICO STUDIES

PASS (Prediction of Activity Spectra of Substances) Software

PASS (Prediction of Activity Spectra for Substances) is a software product designed as a tool for evaluating the general biological potential of an organic drug-like molecule. PASS provides simultaneous predictions of many types of biological activities based on the structure of organic compounds. Thus, PASS can be used to estimate the biological activity profiles for virtual molecules, prior to their chemical synthesis and biological testing.

Pa (probability "to be active") estimates the chance that the studied compound is belonging to the sub-class of active compounds (resembles the structures of molecules, which are the most typical in a sub-set of "actives" in PASS training set).

Pi (probability "to be inactive") estimates the chance that the studied compound is belonging to the sub-class of inactive compounds (resembles the structures of molecules, which are the most typical in a sub-set of "inactives" in PASS training set).

PASS RESULTS

Table no 6: Predicted Biological Activity Spectra of title compounds

SB-1	**Pa**	**Pi**	**Activity**
	0.914	0.003	Phospholipase inhibitor
	0.913	0.002	Carboxypeptidase inhibitor
	0.885	0.004	Amino peptidase inhibitor
	0.878	0.003	Aldehyde dehydrogenase inhibitor
	0.868	0.002	Biotin COA ligase inhibitor
SB-2	**Pa**	**Pi**	**Activity**
	0.901	0.004	Anti-ulcer
	0.902	0.006	Aplasia
	0.883	0.005	Beta-adrenergic receptor kinase inhibitor
	0.883	0.005	G protine-coupled recptor kinase inhibitor
	0.873	0.003	Transaminase inhibitor
SB-3	**Pa**	**Pi**	**Activity**
	0.890	0.003	Carboxypeptidase inhibitor
	0.835	0.004	Contact dermatitis
	0.834	0.007	Glutathione inhibitor
	0.832	0.008	Dipeptidase inhibitor
	0.796	0.003	Aldehyde –dehydrogenase inhibitor
SB-4	**Pa**	**Pi**	**Activity**
	0.873	0.005	Dipeptidase inhibitor
	0.842	0.006	Glutathione inhibitor
	0.824	0.005	Contact dermatitis
	0.809	0.006	Carboxypeptidase inhibitor
	0.791	0.020	Anti-ulcer
SB-5	**Pa**	**Pi**	**Activity**
	0.837	0.004	Fibrosis
	0.833	0.004	Aldehyde dehydrogenase inhibitor
	0.809	0.012	Phospholipase inhibitor
	0.795	0.008	Carboxy peptidase inhibitor
	0.735	0.007	Transaminase inhibitor
SB-6	**Pa**	**Pi**	**Activity**
	0.862	0.007	Anti-ulcer
	0.858	0.009	Anti-seborrheic
	0.854	0.008	Beta -adrenergic receptor kinase inhibitor
	0.854	0.008	G-protein-coupled recepyor kinase inhibitor
	0.729	0.011	Fibrosis

I-Lab 2.0

I-Lab 2.0 software provides structure-based predictions for the compounds from five modules: (1) PHYSIOCHEMICAL PROPERTIES, (2) ADME (Adsorption-Distribution-Metabolism-Excretion), (3) TOXICITY, (4) NMR (Nuclear Magnetic Resonance), and (5) NAMING.

I-LAB 2.0. RESULTS

Table no 7: Physical and Lipinski properties predicted using I-LAB 2.0

Code	Physical properties	Lipinski-type properties
SB-01	Molar Refractivity: 46.22 ± 0.5 cm3 Molar Volume: 148.1 ± 7.0 cm3 Parachor: 378.1 ± 8.0 cm3 Index of Refraction: 1.536 ± 0.05 Surface Tension: 42.4 ± 7.0 dyne/cm Density: 1.10 ± 0.1 g/cm3 Polarizability: 18.32 ± 0.5 10-24cm3	Molecular Weight: 163.17 No. of Hydrogen Bond Donors: 1 No. of Hydrogen Bond Acceptors: 3 TPSA: 49.66 No. of Rotatable Bonds: 3
SB-02	Molar Refractivity: 50.65 ± 0.5 cm3 Molar Volume: 163.4 ± 7.0 cm3 Parachor: 409.2 ± 8.0 cm3 Index of Refraction: 1.532 ± 0.05 Surface Tension: 39.3 ± 7.0 dyne/cm Density: 1.08 ± 0.1 g/cm3 Polarizability: 20.08 ± 0.5 10-24cm3	Molecular Weight: 177.2 No. of Hydrogen Bond Donors: 1 No. of Hydrogen Bond Acceptors: 3 TPSA: 49.66 No. of Rotatable Bonds: 3
SB-O3	Molar Refractivity: 40.41 ± 0.5 cm3 Molar Volume: 141.6 ± 7.0 cm3 Parachor: 361.3 ± 8.0 cm3 Index of Refraction: 1.482 ± 0.05 Surface Tension: 42.3 ± 7.0 dyne/cm Density: 1.10 ± 0.1 g/cm3 Polarizability: 16.02 ± 0.5 10-24cm3	Molecular Weight: 157.17 No. of Hydrogen Bond Donors: 1 No. of Hydrogen Bond Acceptors: 4 TPSA: 66.73 No. of Rotatable Bonds: 6
SB-04	Molar Refractivity: 44.83 ± 0.5 cm3 Molar Volume: 156.9 ± 7.0 cm3 Parachor: 392.4 ± 8.0 cm3 Index of Refraction: 1.483 ± 0.05 Surface Tension: 39.0 ± 7.0 dyne/cm Density: 1.09 ± 0.1 g/cm3 Polarizability: 17.77 ± 0.5 10-24cm3	Molecular Weight: 171.19 No. of Hydrogen Bond Donors: 1 No. of Hydrogen Bond Acceptors: 4 TPSA: 66.73 No. of Rotatable Bonds: 6
SB-05	Molar Refractivity: 52.04 ± 0.5 cm3 Molar Volume: 169.9 ± 7.0 cm3 Parachor: 428.3 ± 8.0 cm3 Index of Refraction: 1.524 ± 0.05 Surface Tension: 40.3 ± 7.0 dyne/cm Density: 1.13 ± 0.1 g/cm3 Polarizability: 20.63 ± 0.5 10-24cm3	Molecular Weight: 193.2 No. of Hydrogen Bond Donors: 1 No. of Hydrogen Bond Acceptors: 4 TPSA: 58.89 No. of Rotatable Bonds: 4
SB-06	Molar Refractivity: 56.46 ± 0.5 cm3 Molar Volume: 185.2 ± 7.0 cm3 Parachor: 459.4 ± 8.0 cm3 Index of Refraction: 1.521 ± 0.05 Surface Tension: 37.8 ± 7.0 dyne/cm Density: 1.11 ± 0.1 g/cm3 Polarizability: 22.38 ± 0.5 10-24cm3	Molecular Weight: 207.23 No. of Hydrogen Bond Donors: 1 No. of Hydrogen Bond Acceptors: 4 TPSA: 58.89 No. of Rotatable Bonds: 4

Table no 8: Toxicity properties predicted using I-LAB 2.0

CODE	LD50
SB-01	> 500 mg/kg

SB-02	> 300 mg/kg
SB-03	> 400 mg/kg
SB-04	> 300 mg/kg
SB-04	> 700 mg/kg
SB-06	> 500 mg/kg

Table no 9: ADME properties predicted using I- LAB 2.0

CODE	Log P	Vd
SB-1	1.65	0.27 L/kg
SB-2	0.92	0.26 L/kg
SB-3	0.52	0.27 L/kg
SB-4	0.83	0.26 L/kg
SB-5	2.02	0.28 L/kg
SB-6	2.46	0.28 L/kg

RESULTS AND DISCUSSION

This work relates to the Synthesis, Characterization and *in silico* studies of synthesized Schiff's bases. The physical parameters such as Molecular formula, Molecular weight and Percentage yield for the synthesized compounds were determined (Table 3). The compounds were characterized by using thin layer chromatography and the R_f values were calculated (Table 3). From the UV spectroscopic data, considerable absorbance values at specific wavelengths for the synthesized compounds have been observed (Table 5). From the IR spectroscopic data, the groups such as C=N, COOH, $-CH_3$, $-OCH_3$, Aromatic ring etc, were confirmed by the position of absorption bands (Table 4). Using PASS software, the possible biological activities of the compounds were predicted (Table 6). Using I Lab-2.0, physical and lipinski properties, toxicity profile and ADME properties were predicted (Tables 7-9).

CONCLUSION

By following the mentioned synthetic procedure, a series of six schiff's base compounds were synthesized and obtained in good yields. The synthesized compounds were physically characterized by performing thin layer chromatography. They were structurally characterized by UV and IR analytical techniques. The IR spectroscopic data confirmed the presence of adequate functional groups in the respective title compounds. UV spectroscopic data revealed that the synthesized compounds exhibited adequate absorbance. From the results of PASS computerized program, it was found that the title compounds possessed useful biological activities. From the results of i lab 2.0 software, it was found that the synthesized compounds could be good drug candidates regarding ADME aspects and also found to be less toxic.

BIBLIOGRAPHY

[1]. H. Schiff. (1864) Justus Liebigs Ann. *Chem*. Vol 131, 118.
[2]. D.N. Dhar and C.L. Taploo (1982) J. Sci. Ind. Res. Vol 41, 501.
[3]. P. Przybylski, A. Huczynski, K. Pyta, and B. Bartl (2009) *Curr. Org. Chem*. Vol 13, 124.
[4]. W. J. Middleton and H. D. Carlson (1988), *"Hexafluoroacetone imine", Org. Synth.*; Coll. Vol. 6: 664.
[5]. C. F. H. Allen and James Van Allan, "m-Tolylbenzylamine", *Org. Synth.:* 827; Coll. Vol. 3.

[6]. Sithambaram Karthikeyan. M, Jagadesh Prasad. D, Poojary. B, Subramanya Bhat. K., Bioorg. *Med.chem*.2006.14.7482.
[7]. K.N.Campbell, H.Sommers and B.K.Campbell, *J.Am. chem. Soc*., 1944, 66, 82.
[8]. Y. Zheng, K. Ma, H. Li, J. Li, J. He and X. Sun (2009) Catal. *Lett Vol* 128, 465.
[9]. R.B. Moffett and N. Rabjohn (1963) *Organic syntheses*, vol. 4. New York (USA): John Wiley & Sons, Inc.; 4, 605.
[10]. K. Taguchi and F.H. Westheimer (1971) *J. Org. Chem*. Vol 36, 1570.
[11]. S.Arulmurugan, Helen P. Kavitha1 and B.R. Venkatraman *RASAN J.CHEM* Vol.3, (2010), 385-410 ISSN: 0974-1496.
[12]. A.P. Mishra and Monika Soni Received November 12, 2007; Revised March 1, 2008; Accepted April 9, 2008.
[13]. Alagarsamy V, Muthukumar V, Pavalarani N., Synthesis, analgesic and anti-inflammatory activities of some novel 2,3-disubstituted quinazoline-4(3H)-ones, *Biol. Pharm. Bull*,. 2003; 26(4):557-559.
[14]. Sham M sondhi, Monica Dinodia, Shubhi Jain and Ashok kumar, *Indian Journal of chemistry,* vol. 48B, August 2009, pp. 1128-1136.
[15]. J. J. Vora, S. B. Vasava, K. C. Parmar,S. K. Chauhan and S.S. Sharma *E-Journal of Chemistry* 2009, 6(4), 1205-1210.
[16]. F.M. Morad, M.M.EL.ajaily, S. Ben Gweirif, *Journal of Science and Its Application* Vol. 1, No. 1, pp 72-78, February 2007.
[17]. Shalin kumar, Durga nath dhar, P.N.Saxena, Applications of complexes of sciff's bases, *Journal of scientific and industrial research*, Vol. 68, March 2009, 181-187.
[18]. S.Arulmurugan, Helen P. Kavitha1 and B.R. Venkatraman *RASAN J.CHEM* Vol.3, (2010), 385-410 ISSN: 0974-1496.
[19]. Hai Jian YANG, Wen Hua SUN*, Zi Long LI, Zhi MA, The Rapid Synthesis of Schiff-Base without Solvent under Microwave Irradiation, *Chinese Chemical Letters* Vol. 13, No. 1, pp 3 – 6, 2002.
[20]. Cleiton M. Silva, Daniel L. Silva, Schiff bases: A short review of their antimicrobial activities, *Journal of Advanced Research* (2011) 2, 1–8.
[21]. Gehad Geindy MOHAMED, Mohamed Mohamed OMAR, Metal Complexes of Schiff Bases: Preparation,Characterization, and Biological Activity, *Turk J Chem* 30 (2006) , 361 – 382.
[22]. Muhammad Aqeel Ashraf, Karamat Mahmood, Abdul Wajid, Synthesis, Characterization and Biological Activity of Schiff Bases, *2011 International Conference on Chemistry and Chemical Process*, IPCBEE vol.10.
[23]. Robina Aman and Garima Matela, Tin (IV) Complexes of Schiff Base Derived from Amino Acid: Synthesis and Characteristic Spectral Studies, *Journal of Chemistry* Volume 2013.
[24]. K. Mounika, B. Anupama, J. Pragathi, and C. Gyanakumari, Synthesis¸ Characterization and Biological Activity of a Schiff Base Derived from 3-Ethoxy Salicylaldehyde and 2-Amino Benzoic acid and its Transition Metal Complexes, *J. Sci. Res*. 2 (3), 513-524 (2010).
[25]. Joao Costa Pessoa , Maria J. Calhorda , Isabel Cavaco, Molecular modelling studies of N-salicylideneamino acidato complexes of oxovanadium(IV), *J. Chem. Soc., Dalton Trans.*, 2002, 4407-4415.