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Synthesis and study of quantitative structure-activity relationship of schiff bases containig electronegative groups

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ABSTRACT

Schiff bases were easily synthesized by condensation process. On the basis of QSAR study it easily explains the effect of electronegative group on drug active Schiff bases. When we introducing more electronegative group in Schiff base then it increase the biological activity of that drugs.

Keywords:- Schiff bases, QSAR, Electronegative group.

INTRODUCTION

New drug development is a costly affair. Trial and error methods become uneconomical. It requires considerations of rational drug [1,3] design i.e. prediction of pharmacokinetic, pharmacodynamic and toxic property before synthesis of chemical compounds. Synthesis of such compounds has to be carefully designed and tested on a suitable biological system. It is estimated that out of several thousand compounds synthesized and tested hardly one or none reach market. The understanding of drug potency in biological systems requires an understanding of chemical structure in terms of physical and chemical properties. In a drug design [15], the first step is variation of lead compound to derive some hypothesis of relationships between chemical structure and biological activity.

In recent years the advances made in organic chemistry, biology, biophysics etc have been helpful in designing new chemical leads and optimization of activities within the congeneric series of compounds. Computer aided technique have been useful in reducing random synthesis and screening of compounds. The introduction of Hansch model [2] in 1964 enabled medicinal/pharmaceutical chemists to formulate structure-activity relationship in quantitative terms and check the hypothesis by means of statistical methods. From such quantitative structure-activity relationship (QSAR) [14], it is possible to elucidate the influence of various physicochemical properties on drug potency and to predict activity values for new compounds with certain limits.

In that present work,we calculated in ProjectLeader are Connectivity Index (order 0, standard), Connectivity Index (order 1, standard), Connectivity Index (order 2, standard), Dipole Moment (debye), Electron Affinity (eV), Heat of Formation (kcal/mole), HOMO Energy (eV), Ionization Potential (eV), Log P, LUMO Energy (eV), Molar Refractivity, Molecular Weight, Shape Index (basic kappa, order 1), Shape Index (basic kappa, order 2), Shape Index (basic kappa, order 3), Solvent Accessibility Surface Area (angstromsquare), Valence Connectivity Index (order 0, standard), Valence Connectivity Index (order 1, standard), Valence Connectivity Index (order 2, standard) for various imines.

MATERIALS AND METHODS

The synthesis scheme show in fig.1 in this, the Schiff base is formed by the condensation process.

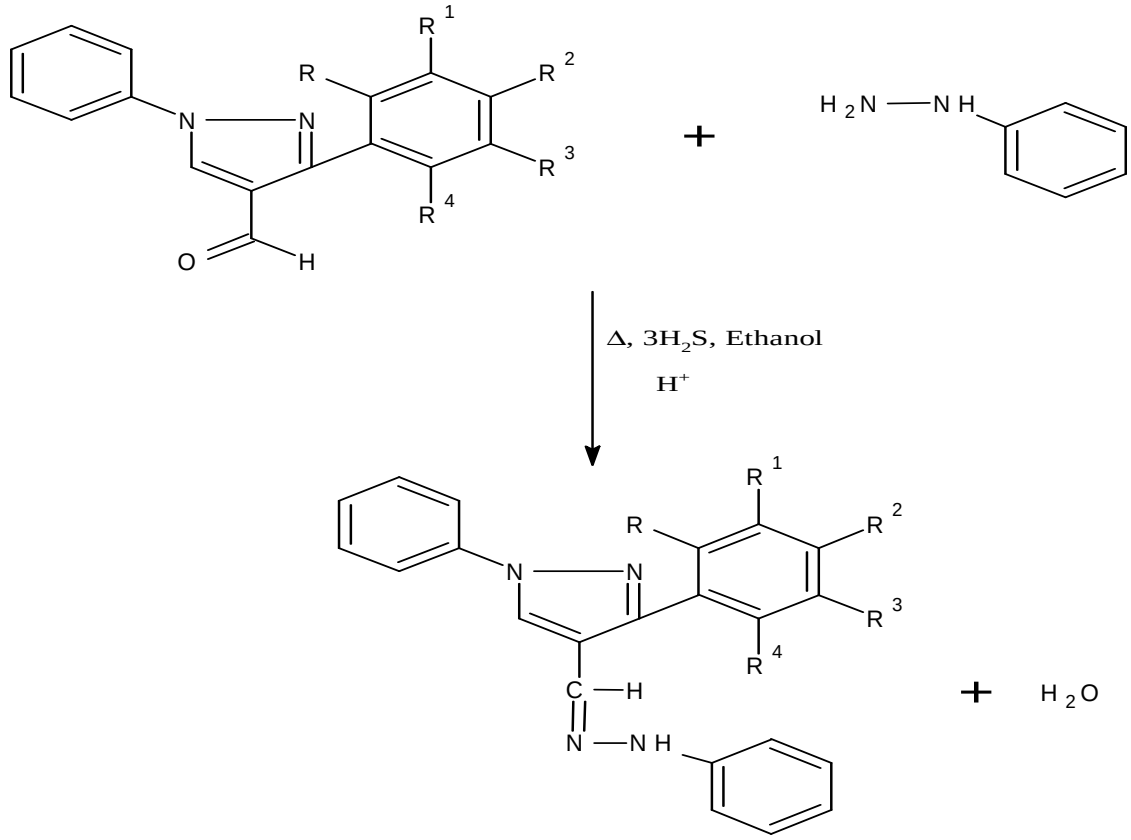


Fig.1.-scheme of synthesis of Schiff base.

All the structures were drawn in ISIS draw 2.4. The 2D structures were converted to 3D structures in **WORKSPACE** of BioMedCAChe 6.1.10. The structures were beautified comprehensively for valency, hybridization, ring, geometry, and hydrogens. The structures of the molecules are refined by performing an optimize geometry calculation in Mechanics using augmented MM3 parameters. Energy minimized and geometrically optimized structures were opened in **PROJECTLEADER** module. Various descriptors were calculated for the molecules.

RESULTS AND DISCUSSION

The compound formed in condensation of different aldehyde with diamine group was confirmed with the help spectral data which was given in table 1.

Development of QSAR model is summarized in Table 02. Electronic parameters dipole moment, vector x of dipole moment and ionization potential are found to be highly correlated with biological activity. These parameters have positive correlation with biological activity. From this QSAR study we can design new derivatives with improved dipole moment, ionization potential and vector x of dipole moment which ultimately improves the antimicrobial activity.

Table: 1. Structure and Spectral Data

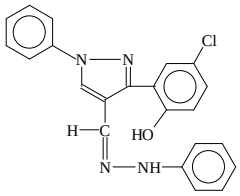
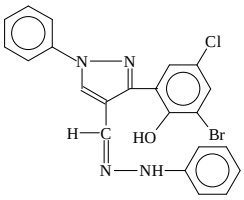
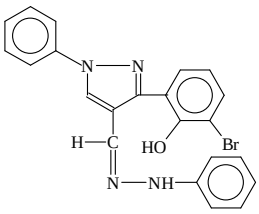
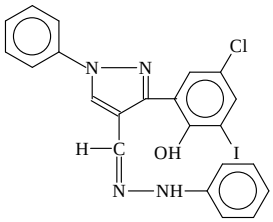
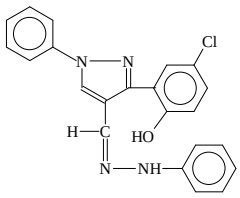
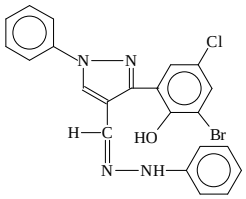
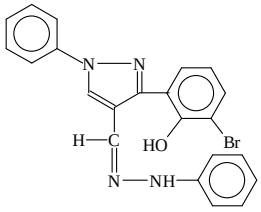
Sr.	R	R^1	R^2	R^3	R^4	Product	Spectral data
C1.	H	Cl	H	H	OH		**I.R.:-** 3130-3450 cm^{-1} – OH stretching vibrations, 1600-1620 cm^{-1} – C=N stretching vibrations **NMR:-** Azomethine proton gives singlet near at 8.4 – 9.4, NH proton gives singlet near at 8.5 to 10.5
C2.	H	Cl	H	Br	OH		**I.R.:-** 1600-1620 cm^{-1} – C=N stretching vibrations,3130-3450 cm^{-1} – OH stretching. **NMR:-** Azomethine proton gives singlet near at 8.4 – 9.4, NH proton gives singlet near at 8.5 to 10.5
C3.	H	H	H	Br	OH		**I.R.**:- 1600-1620 cm^{-1}– C=N stretching vibrations, 3130-3450 cm^{-1} – OH stretching. **NMR:-** Azomethine proton gives singlet near at 8.4 – 9.4, NH proton gives singlet near at 8.5 to 10.5
C4.	H	Cl	H	I	OH		**I.R.**:- 1600-1620 cm^{-1}– C=N stretching vibrations, 3130-3450 cm^{-1} – OH stretching. **NMR:-** Azomethine proton gives singlet near at 8.4 – 9.4, NH proton gives singlet near at 8.5 to 10.5

Table: 2. Structure and Their Biological activity

Sr. No.	Structure	Biological activity
C1.		**6**
C2.		**5.9586**
C3.		**5.8538**

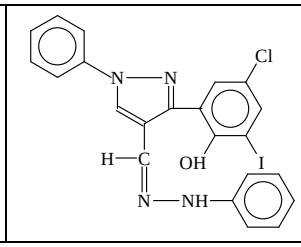
C4.		**6**

Table :3 Properties of training set molecules

Chemical Sample	Conformation Minimum Energy (kcal/mole)	Connectivity Index (order 0, standard)	Connectivity Index (order 1, standard)	Connectivity Index (order 2, standard)	Dipole Moment (debye)	Dipole Vector X (debye)	Dipole Vector Y (debye)	Dipole Vector Z (debye)	Electron Affinity (eV)	Dielectric Energy (kcal/mole)
C1	-6.323	19.347	13.704	12.048	2.499	1.099	-2.048	-0.918	0.581	-0.629
C2	-6.396	20.217	14.114	12.565	2.007	0.988	-1.724	-0.286	0.632	-0.565
C3	-9.005	18.476	13.293	11.508	2.1	0.374	-2.049	0.272	0.728	-0.466
C4	-6.454	20.217	14.114	12.565	1.131	0.553	-0.985	0.045	0.771	-0.578

Steric Energy (kcal/mole)	Heat of Formation (kcal/mole)	HOMO Energy (eV)	Ionization Potential (eV)	Log P	LUMO Energy (eV)	Molar Refractivity	Molecular Weight	Shape Index (basic kappa, order 1)	Shape Index (basic kappa, order 2)	Shape Index (basic kappa, order 3)	Ba
-6.323	118.144	-8.301	8.301	5.579	-0.581	110.084	388.856	21.24	10.347	5.587	6
-6.396	127.047	-8.366	8.366	6.371	-0.632	117.706	467.752	22.203	10.543	5.627	5.9586
-9.005	160.316	-8.349	8.349	5.864	-0.728	108.39	372.856	20.28	10.156	5.538	5.8538
-6.454	145.914	-8.332	8.332	6.837	-0.771	122.492	514.752	22.203	10.543	5.627	6

CONCLUSION

On the basis of above study the Schiff base containing Chlorine and iodine group are more biological activity then bromine group containing Schiff base. Hence when introducing Chlorine and iodine group in Schiff base then it increase the biological activity of that drugs.

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