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THREE DIMENSIONAL QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIPS OF 3-[3-(N-4-FLUROBENZYL-N-2 PYRIDYLAMINO) PROPYLAMINO]-4-ETHYLAMINO-1, 2, 5- THIAZOLE-1-OXIDE (HISTAMINE H_1 RECEPTOR ANTAGONIST) AS AN ANTI-ULCER AND ANTI-ALLERGY

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ABSTRACT

This computer aided drug design based conformational and potential energy quantitative structure activity relationship established to find out best fit conformations with minimum potential energy, active structural and molecular sites for strong binding of 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5- thiazole-1-oxide ($C_{19}H_{23}FN_6OS$) as Histamine H_1 receptor antagonist which is previously derived from Cimetidine and extracted by leaves of *Espinheria santa.* Potential energy calculated for lower limit by Kitagorodasky potential energy function and in-silico approaches. This compound crystalline in monoclinic system, with unit cell dimensions a = 6.686 A˚, b = 14.717 A˚ and c = 20.850 A˚, β = 97.83˚. Present work find out new bond pair (N_{21}--C_{15}) with strong bonding site and suggests that 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5- thiazole-1-oxide has shown minimum potential energy -0.00000983 Kcal/mole as Histamine H_1 receptor antagonist at $\omega_1 = 280^\circ$ and $\omega_2 = 340^\circ$ (Figure-9). It would supports stable and strong binding of antihistaminic compound to their receptors in allowed active region. The compound ($C_{19}H_{23}FN_6OS$) in this active conformation would be helpful for the treatment of allergy and different kind of ulcers such as stomach and duodenum ulcers.

Key words: ($C_{19}H_{23}FN_6OS$), Histamine H_1 receptor antagonist, Allergy, Ulcer, Coordinate, Monoclinic and rectangular unit cell system, Receptor, Conformational and quantitative analysis.

INTRODUCTION

Drug discovery leads to the concept of computer aided drug design (Florence *et al*., 2002; James *et al*., 2004; Michael Williams, 2004 and Tommy Liljeforl, 2004). It is use to identify drugs, drug-like compounds and assist clinical testing (Weerasak Samee *et al*., 2004). It is dependent on the flexibility, lowest energy conformers of the most rigid compounds and superimpose. This may use to develop new compounds of minimum energy conformer, desired positions functional groups and most favorable binding mode within active sites of receptor (Munikumar Reddy Doddareddy *et al*., 2004 and Gupta, 1989).

Histamine (2, 4-imidazolyl ethylamine) (Fig. 1) is a natural, dibasic, vasoactive amine; neuromodulator and neurotransmitter that stimulate stomach cells to produce acid (Abbas *et al*., 1994 and Bannister *et al*., 1994). It is located in most of body tissues and gastrointestinal tract (Abbas *et al*., 1994; Bach, Jean-Francois, 1982; Froese, 1980 and Gallin, *et al*., 1980). This single polypeptide chain produced by histamine decarboxylation and stored in effectors cell (Goldie, 1990; Jawetz Melnick *et al*., 2002; Metcalfe *et al*., 1997 and Monroe *et al*., 1997). Release of histamine causes hay fever, bronchial infection, initial phase of asthma, (Bach, Jean-Francois, 1982 and Paul, William, 1984), urticaria (Rang *et al*., 1995), gastrointestinal tract, suffocation and massive degranulation of mast cells (Abbas *et al*., 1994, Bach, 1982, Sompayrac, Lauran, 1999, Spiegelberg, 1989). Its deficiency leads to lower levels of melatonin and decreased fat metabolism in the brain that can cause stress (Sompayrac, Lauran, 1999). It is used to treat different kinds of ulcers and allergies (Abbas *et al*., 1994 and Bach, Jean-Francois, 1982).

This paper describes computer aided drug design based conformational and potential energy quantitative structure activity relationship analysis of 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5- thiazole-1-oxide, $C_{19}H_{23}FN_6OS$ (Bannister *et al*., 1994). It is histamine H_1 receptor antagonist, (Fig. 2), previously derived from cimetidine (histamine H_2 receptor, Fig. 3) (Bannister *et al*., 1994 and Patrícia Maria Ferreira *et al*., 2004), extracted by *Maytenus aquifolium* and *Maytenus ilicifolia* (*Espinheria santa*) leaves (Fig. 4) (Patrícia Maria Ferreira *et al*., 2004). The data has been taken from literature (Bannister *et al*., 1994). This current research also correlates and compares with previous study (Bannister *et al*., 1994) for determination of minimum potential energy, bond lengths, bond angles, new molecular and structural sites by using potential energy function and *in-sillico* approaches. The $C_{19}H_{23}FN_6OS$ contains a heterocyclic head linked by a four-atom chain to a dipolar tail (Bannister *e.t al*., 1994), (Fig. 3). It has anti-allergy and anti-ulcer properties (Abbas *et al*., 1994; Bach,

Jean-Francois.,1982; Bannister *et al*., 1994; Froese, 1980; Gallin *et al*., 1980; Sompayrac, Lauran, 1999 and Spiegelberg, 1989). It can suppresses the histamines-induced wheal (swelling), flare (vasodilatation) (Abbas *et al*., 1994; Bach, Jean-Francois., 1982; Sompayrac, Lauran, 1999 and Spiegelberg, 1989), motion sickness (Abbas, *et al*., 1994; Goldie, 1990; Jawetz Melnick *et al*., 2002, and Metcalfe *et al*., 1997), certain types of headaches, Cohn's disease, acute multiple sclerosis and some stomach secretary conditions (Abbas *et al*., 1994; Bach, Jean-Francois., 1982 and Sompayrac, Lauran, 1999), response by blocking the binding of histamine to its receptors. It is available as over-the-counter drugs, such as, Azatadine (Optimine), carbinoxamine/pseudoephedrine (cardec), cetrizine (zyrtec), cyproheptadine (periactin), fexofenadine (allegra) and loratadine (Bach, Jean-Francois, 1982; Monroe *et al*., 1997 and Paul William, 1984). The search for histamine receptor antagonists by structural modification has lead to discovery of several new antihistaminic for clinical use (Abbas *et al*., 1994; Bach, Jean-Francois, 1982; Gallin *et. al*., 1980; Jawetz Melnick *et al*., 2002; Sompayrac, Lauran, 1999 and Spiegelberg, 1989).

METHODS

This work is not only describes the conformational analysis, (Lingling Shen., 2003 and Manuel *et. al*., 1992) potential energies determination and optimization of (*3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5- thiazole-1-oxide)* but also helpful to design potent candidate for medicinal use. It's based on quantitative predictions and action mechanism of a drugs (Munikumar *et al*., 2004; Gupta, 1989; Tommy Liljeforl., 2004 and*;* Weerasak Samee *et al*., 2004).

The structure of (*3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5- thiazole-1-oxide)* was constructed on gaussian-98 (Gaussian 98, Gaussian, Inc., Pittsburgh PA, 2003 USA). Structural modification, minimization and charges were calculated by sybyl 6.9 (SYBYL 6.9. Tripose Inc., 1699). Molden and Kitaigorodskii potential energy function (Kitaigorodskii, 1961 and Ramakrishan *et al*., 1965) ware used to optimizations and calculate potential energy respectively. The bond lengths, bond angles, rotation of coordinates and potential energy ware calculated by in-sillico approaches GW-Basic 3.0, Statistica 0.5. Gaussian 98 and Molden. In order to determine allowed conformation, the contact distances between the atoms in adjacent residues have to be examined by using the criteria for the minimum Vander Waals contact distance. X, Y, Z Cartesian coordinates on X, Y, Z-axis collected from literature (Bannister *et al*., 1994). The fractional coordinates X_f, Y_f, Z_f ware multiplied by Unit Cell dimensions a = 6.686 A˚, b = 14.717 A˚ and c = 20.850 A˚, converted into monoclinic and rectangular system by formula such as,

$X_r = Y_m + Z_m \cos \beta\ (97.83°)$
$Y_r = Y_m$
$Z_r = Z_m \text{ Sin } \beta\ (97.83°)$

Where,
X_m, Y_m and Z_m (mono-clinic coordinates) on X, Y and Z axis.
X_r, Y_r, and Z_r (rectangular coordinates) on X, Y and Z axis,

Contact distance between atoms can be calculated by the following relationship,
$r_{ij} = (X_2 - X_1)^2 + (Y_2 - Y_1)^2 + (Z_2 - Z_1)^2$
X_1, Y_1, Z_1 (coordinates of first atom in molecule)
X_2, Y_2, Z_2 (coordinates of second atom in molecule)
r_{ij} = distance between non-bonded interaction

Bond angles can be calculated by given below formula,

$$\text{Cos}\theta = - \frac{L_3 - L_1 - L_2}{2 L_1 * L_2}$$

L = Bond length

Coordinates after rotation:
$L = X_1 - X_2/l$
$M = Y_1 - Y_2/l$
$N = Z_1 - Z_2/l$

L, M, N (the direction of cosines on the axis of rotation with respect to the chosen system of coordinates).

$a = \cos \omega/2$
$b = L \sin \omega/2$
$c = M \sin \omega/2$
$d = N \sin \omega/2$

Where,
ω (Angle of rotation 0° to 360°)
a, b, c, d (Variables)

$X' = (a^2 + b^2 - c^2 - d^2) X + 2 (bc - ad) Y + 2 (bd + ac)Z$
$Y' = 2 (bc + ad) X + (a^2 - b^2 + c^2 - d^2)Y + 2 (cd - ab) Z$
$Z' = 2 (bd - ac) X+2 (cd + ad) Y + (a^2 - b^2 - c^2 + d^2) Z$
(X', Y' Z' are the coordinates after rotation)
Potential energies can be calculated by potential energy function (Kitaigorodskii, 1961 and Ramakrishan *et al*., 1965),
$V = 3.5 [8600 e^{-13z} - .04 / z^6$
$Z = r_{ij}/r_\circ$
$r_\circ$ = equilibrium distance
r_{ij} = distance between non-bonded interaction
Z = variable

RESULTS AND DISCUSSION

In present work, atomic coordinates were converted into fractional, monoclinic and rectangular coordinate systems by gaussion-98, Molden and GW-Basic (Tables 1, 2 and 3). The bond lengths (Table 4) and bond angles (Table 6) were calculated newly by gaussion-98 and molden and correlated with previously calculated study bond lengths (Table 5) and bond angles (Table 7) where no above-mentioned computational approaches were used. The $C_{18,}$ N_{19}, $C_{8,}$ - $C_{9,}$ N_{21}-$C_{15,}$ S_{22}-$C_{14,}$ O_{23}-$C_{15,}$ C_{20}-$C_{10,}$ N_{24}-$C_{12,}$ N_{26}-$C_{12,}$ C_{27}-$F_{13,}$ C_{28}-F_{13}, N_{21}-$C_{15,}$ S_{22}-$C_{14,}$ and O_{23}-C_{15} were selected as active bio-conformers in pairs for structural minimization, optimization (figures-5, 6), charges and energy calculation (Fig. 13, 14, 15). But during charges and optimization stage these pairs C_{20}-$C_{10,}$ N_{24}-$C_{12,}$ N_{26}-$C_{12,}$ C_{27}-$F_{13,}$ C_{28}-F_{13} were found no active atomic interaction with their base pairs The $C_{18,}$ N_{19}, $C_{8,}$ - C_{9}. So the $C_{18,}$ N_{19}, $C_{8,}$ - C_9 and N_{21}-$C_{15,}$ S_{22}-$C_{14,}$ O_{23}-$C_{15,}$ were selected as base and interacting pairs respectively for study and energy calculations. The potential energies and rotation of coordinates (Fig. 7, 8, 9, 10, 11, 12) were calculated by using gaussion-98, molden, Statistica and Kitagorodasky potential energy function.

At first stage, potential energy was calculated for pair N_{21}-C_{15} after rotating N_{21} atom about the bond C_{18}-N_{19} (ω_1) and C_{15} atom about the bond C_8-C_9 (ω_2). The minimum potential energy (-0.00000938 Kcal/mole at ω_1 = 280˚and ω_2 = 340˚) and maximum potential energy (10.1 Kcal/mole at ω_1 = 60˚and ω2 = 140˚) were found respectively (Figure-16). In second stage, S_{22}--C_{14} were selected for energy calculation after rotating S_{22} atom about the bond C_{18}-----N_{19} (ω_1) and C_{14} atom about the C_8-----C_9 (ω_2) bond (Fig. 17). The minimum potential energy (-0. 0001009 Kcal /mole at ω_1 = 360˚ and ω_2 = 340˚) and maximum potential energy (87.3 Kcal /mole at ω_1 = 60˚ and ω_2 = 140˚) were found respectively (Fig. 17). At third stage of energy calculation O_{23}--C_{15} were selected after rotating O_{23} about the bond C_{18} ---N_{19} (ω_1) and C_{15} about C_8--C_9 (ω_2) bond. The minimum potential energy (-0. 00001773 Kcal/mole at ω_1 = 300˚ and ω_2 = 300˚) and maximum potential energy (408.3 Kcal/mole at ω_1 = 60˚ and ω_2 = 160˚) were found respectively (Fig. 18). Finally, total potential energy calculated by taking sum of potential energies of all individual pairs. The minimum total potential energy (-0.000108 Kcal/ mole at ω_1 = 0˚ and ω_2 = 140˚) and maximum total potential energy (417.6 Kcal/mole at ω_1 = 60˚ and ω_2 = 160˚) were found (Fig. 18).

These results shown that 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5-thiazole-1-oxide **(**Histamine H_1 receptor antagonist) has shown maximum potential energy (10.1 Kcal/mole at ω_1 = 60˚and ω2 = 140˚) and minimum potential energy (-0.00000983 Kcal/mole at ω_1 = 280˚ and ω_2 = 340˚) for pair N_{21}--C_{15} (Fig. 16). The positive marked area shows non-allowed or disfavored region where $C_{19}H_{23}FN_6OS$ would not interact with its receptor because of rigidity, short contacts and clops between atoms. While negative marked area shows allowed or favored region (no short contacts and clops found) where $C_{19}H_{23}FN_6OS$ would show its anti-allergy and anti-ulcer properties by interact or bind strongly with its specific receptors. These kinds of analysis are beneficial for discovery of new antihistamines and would helpful for the treatment of allergy, different kind of ulcer such as stomach and duodenum ulcers and medicinal search.

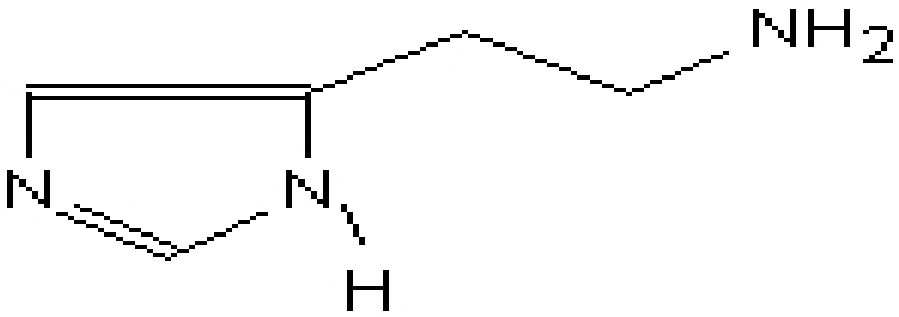

Fig.1. Histamine (2, 4-imidazolyl ethylamine).

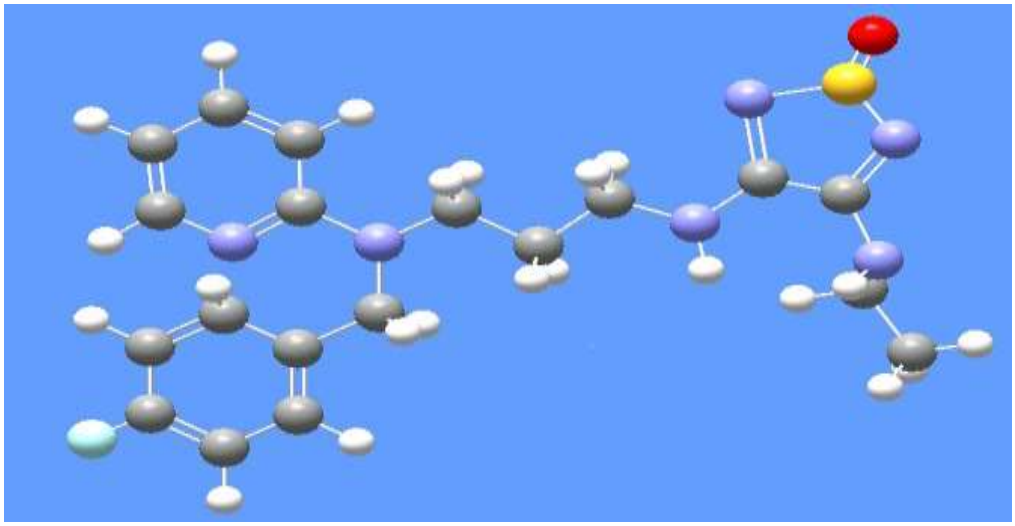

Fig.2. Structure of 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5- thiazole-1-oxide ($C_{19}H_{23}FN_6OS$) by Gaussian.

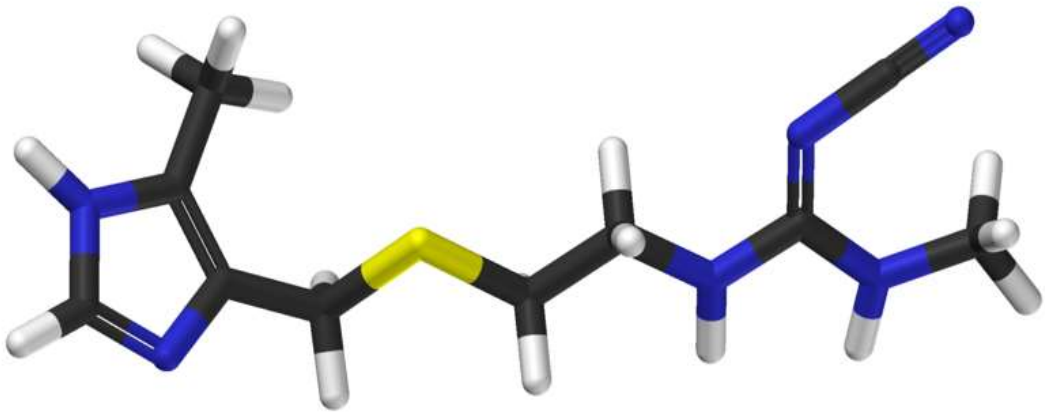

Fig.3. Structure of Cimetidine (Histamine H_2 receptor).

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Fig.4. *Espinheria santa* leaves.

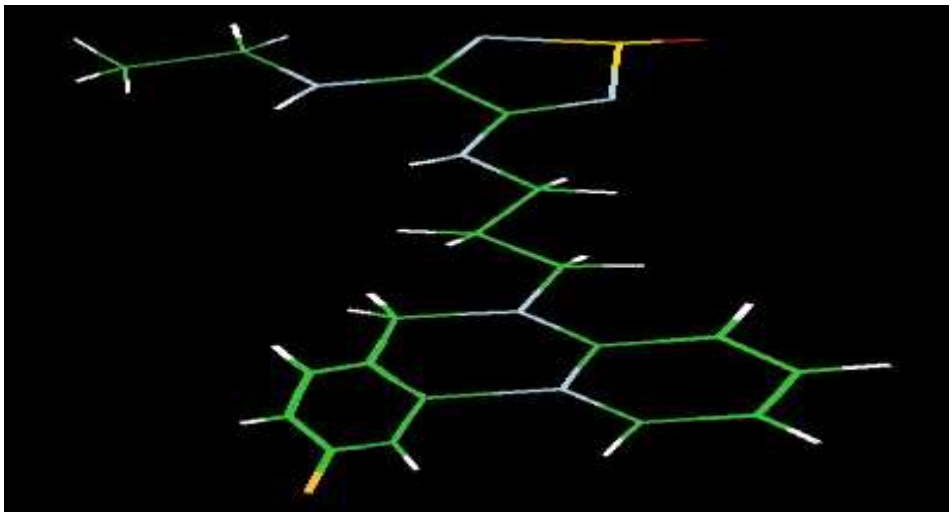

Fig.5. stereo view of $C_{19}H_{23}FN_6OS$ (before optimization) through Molden.

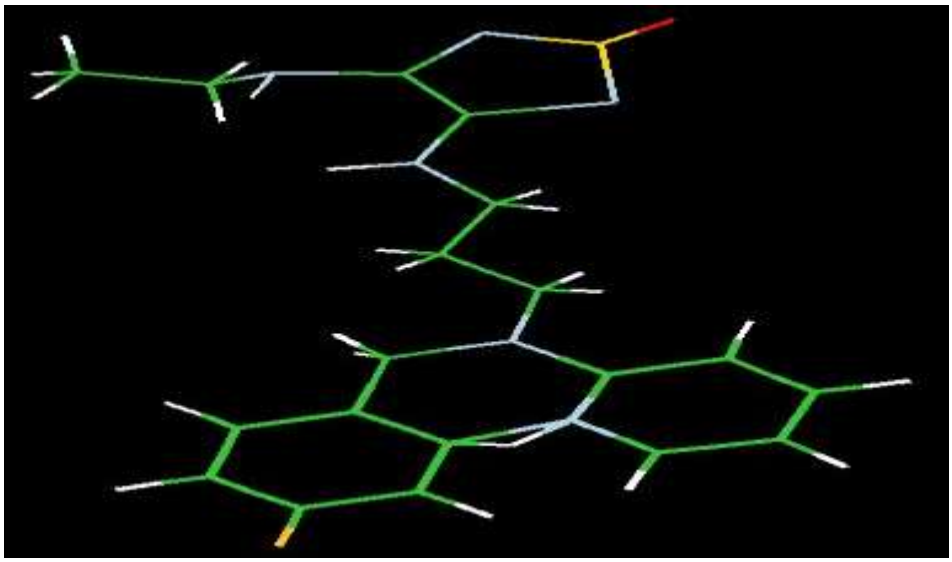

Fig.6. stereo view of $C_{19}H_{23}FN_6OS$ (after optimization) through Molden.

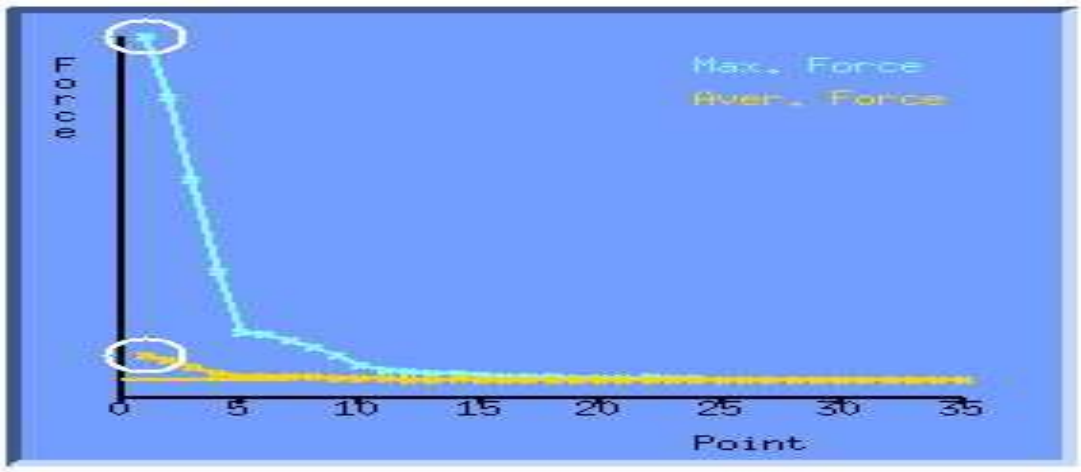

Fig.7. Compound $C_{19}H_{23}FN_6OS$ shown Maximum force (cyne) and average force (yellow) at initial stage.

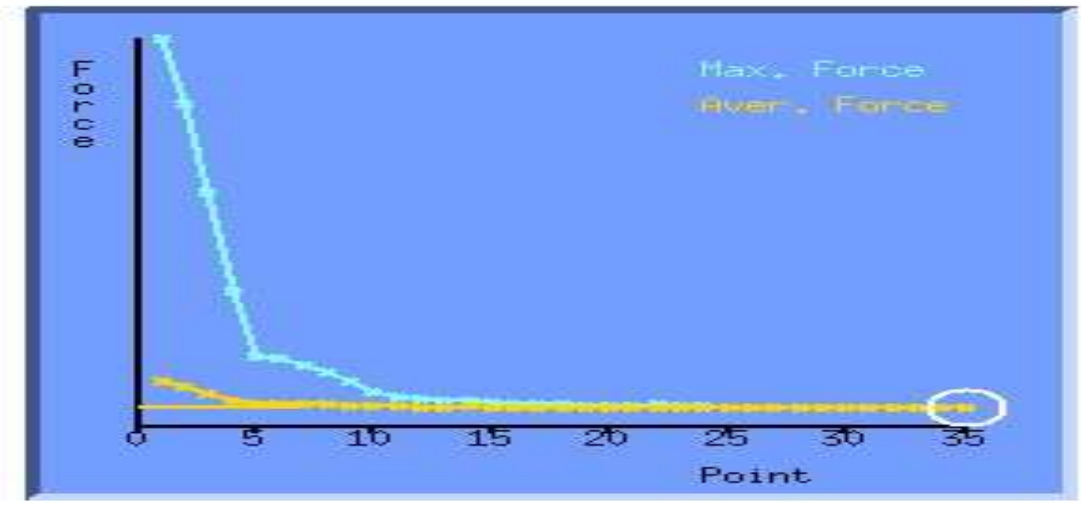

Fig.8. Compound $C_{19}H_{23}FN_6OS$ shown maximum force (cyne) and average force (yellow) at end stage.

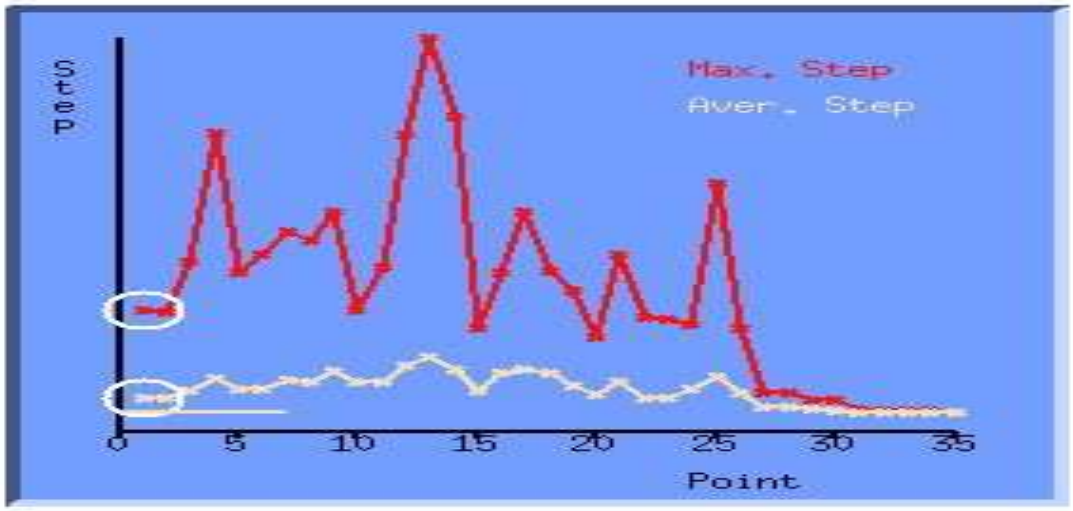

Fig.9. Compound $C_{19}H_{23}FN_6OS$ shown maximum steps (red) and average steps (yellow) involved in energy minimization at initial stage.

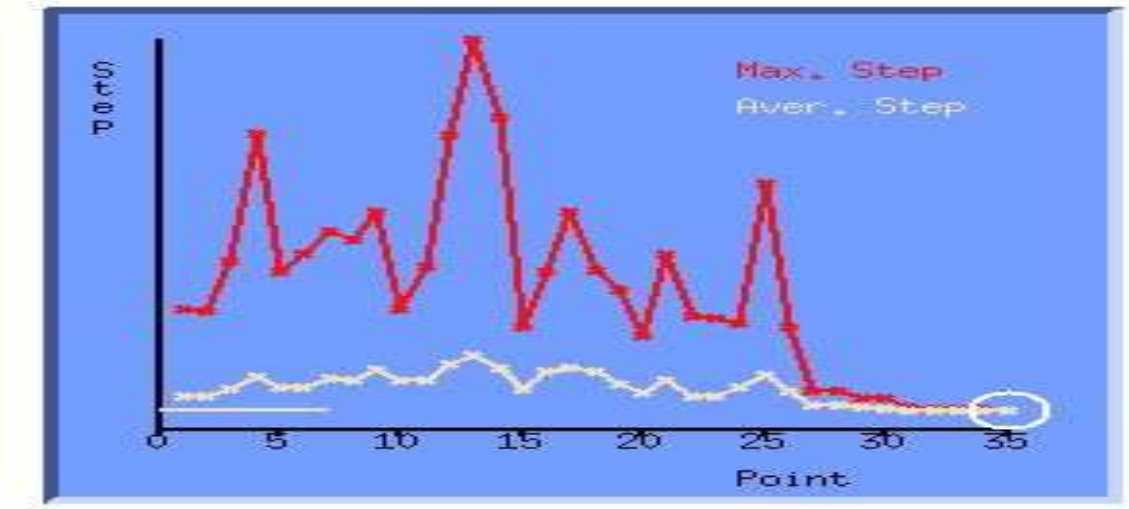

Fig.10. Compound $C_{19}H_{23}FN_6OS$ shown maximum steps (red) and average steps (yellow) involved in energy minimization at end stage.

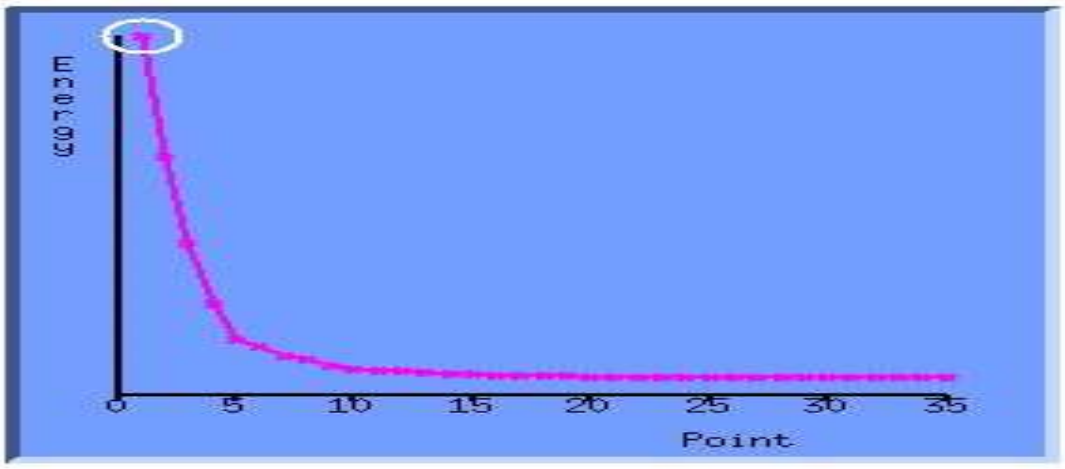

Fig.11.Compound $C_{19}H_{23}FN_6OS$ shown maximum energy (purple) at initial stage.

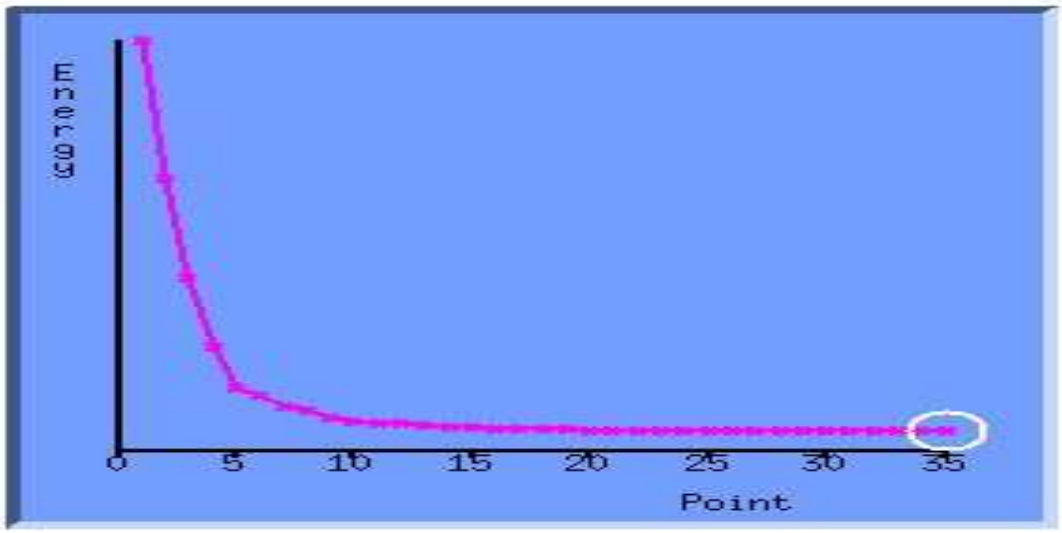

Fig.12. Compound $C_{19}H_{23}FN_6OS$ shown minimum energy (purple) at end stage.

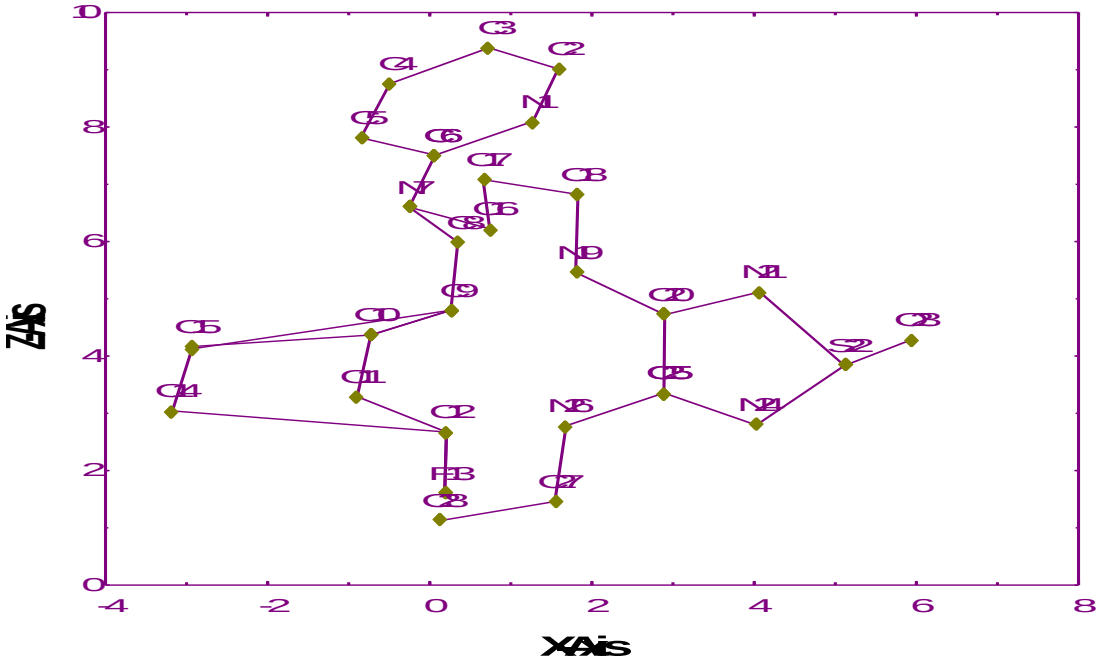

Fig-13. 010 projection of Histamine H1 receptor antagonist (3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5-thiazole-1-oxide) on ZX- axis.

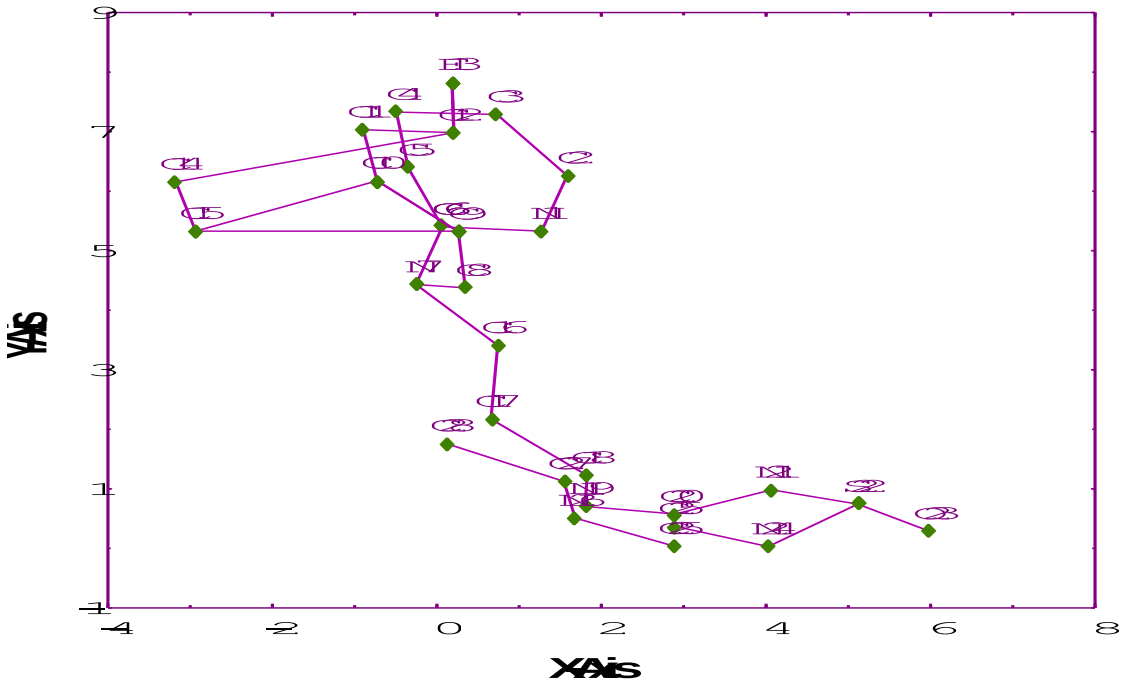

Fig-14. 001 projection of Histamine H1 receptor antagonist (3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5-thiazole-1-oxide) on YX- axis.

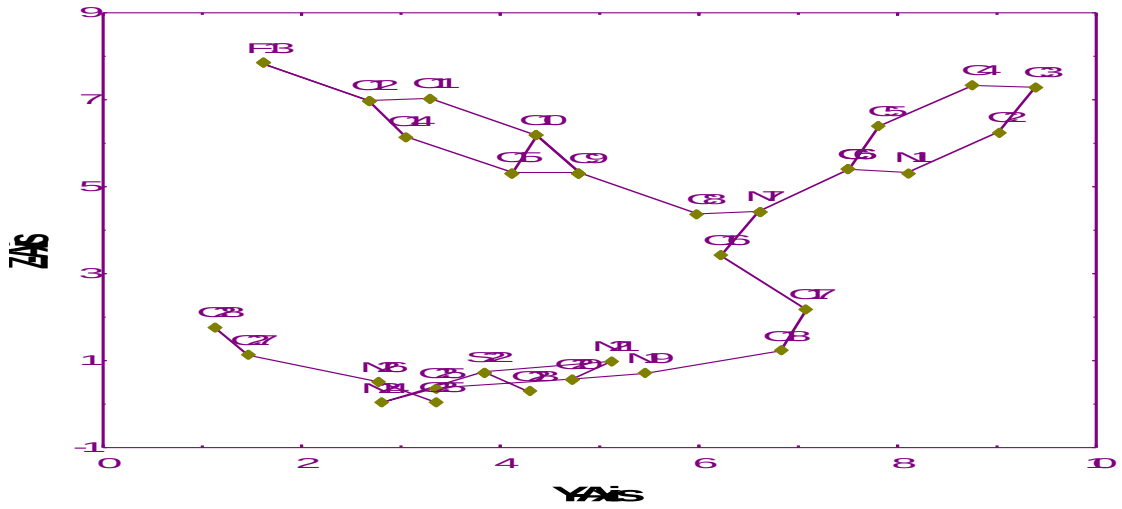

Fig-15. 100 projection of Histamine H1 receptor antagonist (3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino]-4-ethylamino-1, 2, 5-thiazole-1-oxide) on ZY- axis.

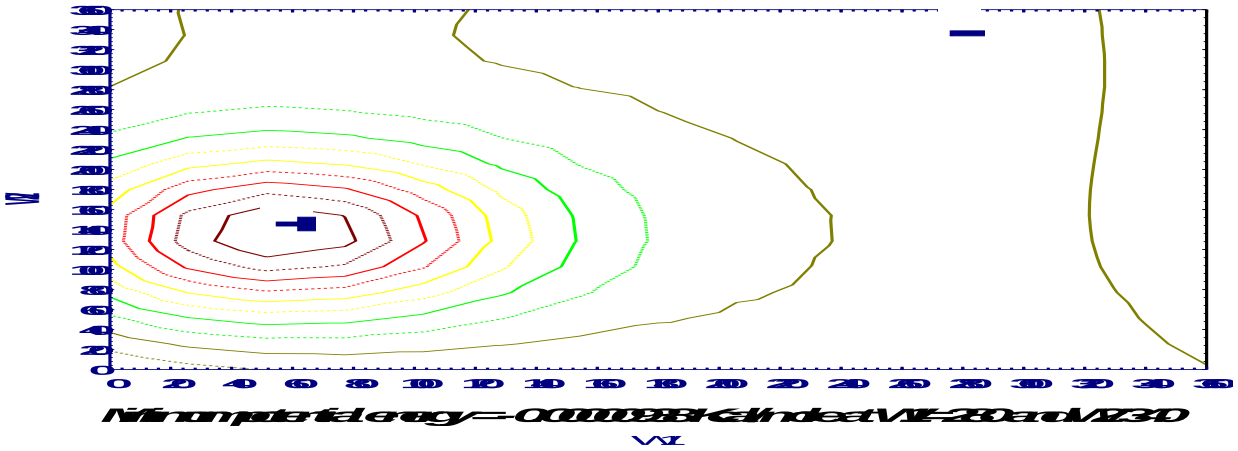

Fig-16. Potential energy calculated for pair N_{21}-$C_{15;}$ minimum potential energy (-0.00000938 Kcal/mole at ω_1 = 280˚and ω_2 = 340˚) and maximum potential energy (10.1 Kcal/mole at ω_1 = 60˚and ω2 = 140˚) were found.

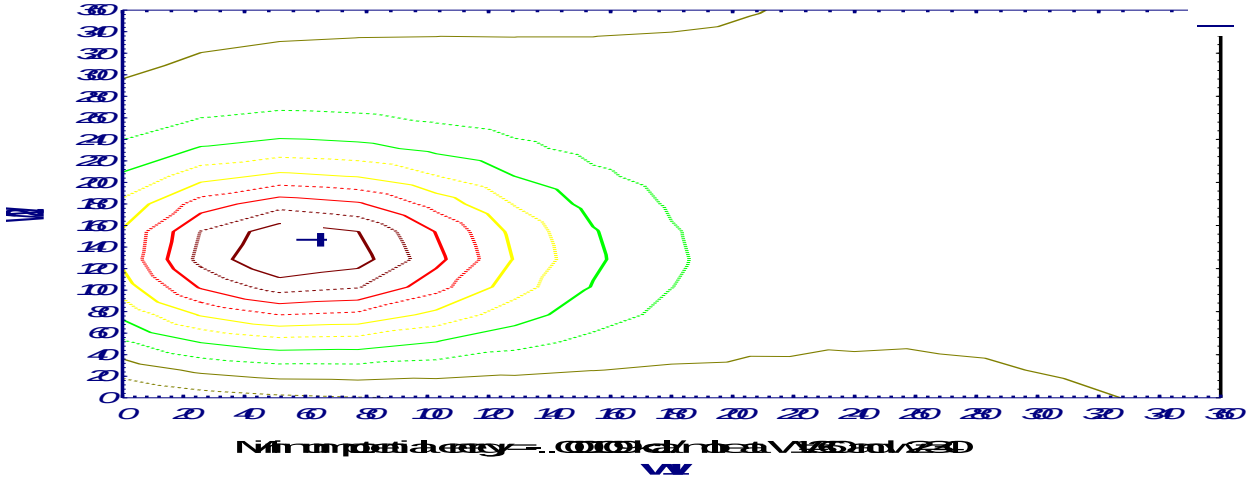

Fig-17. Potential energy calculated for pair S_{22}--$C_{14;}$ minimum potential energy (-0. 0001009 Kcal /mole at ω_1 = 360˚ and ω_2 = 340˚) and maximum potential energy (87.3 Kcal /mole at ω_1 = 60˚ and ω_2 = 140˚) were found respectively.

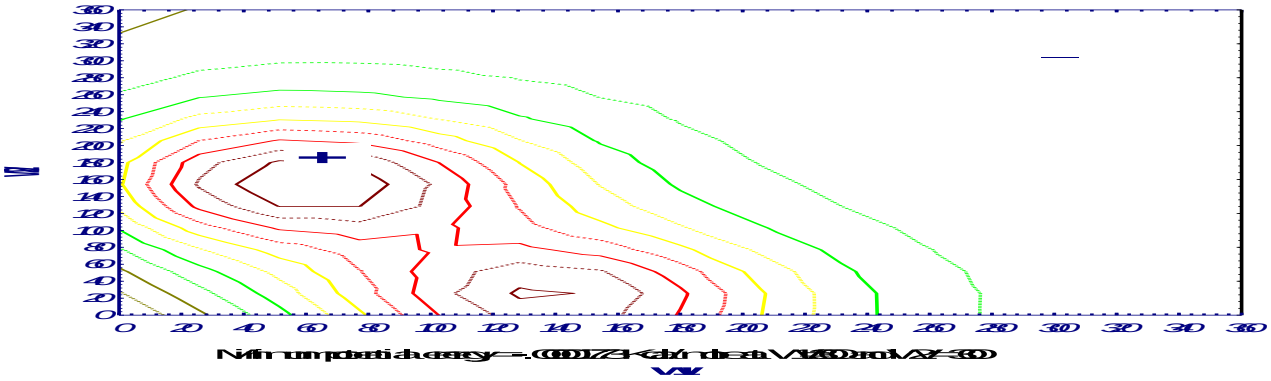

Fig-18. Potential energy calculated for pair O_{23}--$C_{15;}$ minimum potential energy ((-0. 00001773 Kcal/mole at $\omega_1 = 300^\circ$ and $\omega_2 = 300^\circ$) and maximum potential energy (408.3 Kcal/mole at $\omega_1 = 60^\circ$ and $\omega_2 = 160^\circ$) were found respectively.

Table1. Fractional coordinates of 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino] 4-ethylamino-1, 2, 5- thiazole-1-oxide, $C_{19}H_{23}FN_6OS$.

Serial	Atoms	Fractional Coordinates On X-axis	Fractional Coordinates On Y-axis	Fractional Coordinates On Z-axis
1	N_1	0.3001	0.5504	0.2580
2	C_2	0.3655	0.6127	0.3032
3	C_3	0.2592	0.6376	0.3528
4	C_4	0.0770	0.5951	0.3548
5	C_5	0.0042	0.5309	0.3095
6	C_6	0.1210	0.5103	0.2615
7	N_7	0.0530	0.4486	0.2146
8	C_8	0.1419	0.4070	0.2118
9	C_9	0.1484	0.3263	0.2576
10	C_{10}	0.0184	0.2969	0.2990
11	C_{11}	0.0109	0.2237	0.3405
12	C_{12}	0.1746	0.1816	0.3380
13	F_{13}	-0.1884	0.1091	0.3792
14	C_{14}	-0.3481	0.2067	0.2981
15	C_{15}	-0.3290	0.2804	0.2580
16	C_{16}	0.1805	0.4229	0.1653
17	C_{17}	0.1431	0.4812	0.1052
18	C_{18}	0.2986	0.4636	0.0593
19	N_{19}	0.2836	0.3711	0.0342
20	C_{20}	0.4453	0.3210	0.0279
21	N_{21}	0.6288	0.3479	0.0477
22	S_{22}	0.7803	0.2604	0.0366
23	O_{23}	0.9024	0.2913	0.0138
24	N_{24}	0.6087	0.1899	0.0015
25	C_{25}	0.4325	0.2280	0.0018
26	N_{26}	0.2622	0.1891	0.0247
27	C_{27}	0.3540	0.0992	0.0545
28	C_{28}	0.053	0.0763	0.0853

Table 2. Monoclinic coordinates of 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino] 4-ethylamino-1, 2, 5- thiazole-1-oxide, $C_{19}H_{23}FN_6OS$.

Serial	Atoms	Monoclinic Coordinates On X-axis	Monoclinic Coordinates On Y-axis	Monoclinic Coordinates On Z-axis
1	N_1	2.600	8.100	5.379
2	C_2	2.443	9.017	6.321
3	C_3	1.733	9.383	7.355
4	C_4	0.514	8.758	7.397
5	C_5	0.028	7.813	6.453
6	C_6	0.809	7.510	5.452
7	N_7	0.354	6.602	4.474
8	C_8	0.948	5.989	4.416
9	C_9	0.992	4.802	5.370
10	C_{10}	0.123	4.369	6.234
11	C_{11}	0.072	3.292	7.099
12	C_{12}	1.167	2.672	7.047
13	F_{13}	-1.259	1.605	7.906
14	C_{14}	-2.327	3.042	6.215
15	C_{15}	-2.199	4.126	5.379
16	C_{16}	1.206	6.223	3.446
17	C_{17}	0.956	5.461	2.193
18	C_{18}	1.996	7.081	1.236
19	N_{19}	1.896	5.461	0.713
20	C_{20}	2.977	4.724	0.581
21	N_{21}	4.204	5.120	0.994
22	S_{22}	5.217	3.832	0.763
23	O_{23}	6.033	4.287	0.287
24	N_{24}	4.06	2.794	0.031
25	C_{25}	2.89	3.355	0.037
26	N_{26}	1.753	2.782	0.514
27	C_{27}	1.698	1.459	1.136
28	C_{28}	0.354	1.122	1.778

Table 3. Rectangular coordinates of 3-[3-(N-4-Flurobenzyl-N-2 pyridylamino) propylamino] 4-ethylamino-1, 2, 5- thiazole-1-oxide, $C_{19}H_{23}FN_6OS$.

Serial	Atoms	Rectangular Coordinates On X-axis	Rectangular Coordinates On Y-axis	Rectangular Coordinates On Z-axis
1	N_1	1.273	8.1	5.329
2	C_2	1.582	9.017	6.262
3	C_3	0.73	9.383	7.287
4	C_4	-0.492	8.758	7.328
5	C_5	-0.851	7.813	6.392
6	C_6	0.066	7.51	5.401
7	N_7	-0.255	6.602	4.432
8	C_8	0.347	5.989	4.374
9	C_9	0.26	4.802	5.32
10	C_{10}	-0.072	4.369	6.176
				Cont'd……

11	C_{11}	-0.894	3.292	7.033
12	C_{12}	0.207	2.672	6.981
13	F_{13}	0.182	1.605	7.632
14	C_{14}	-3.174	3.042	6.157
15	C_{15}	-2.932	4.126	5.329
16	C_{16}	0.737	6.223	3.414
17	C_{17}	0.657	7.081	2.172
18	C_{18}	1.827	6.822	1.224
19	N_{19}	1.799	5.461	0.706
20	C_{20}	2.898	4.724	0.576
21	N_{21}	4.068	5.12	5.114
22	S_{22}	5.114	3.832	0.743
23	O_{23}	5.994	4.287	0.285
24	N_{24}	4.065	2.782	0.03
25	C_{25}	2.886	3.355	0.037
26	N_{26}	1.683	2.782	0.51
27	C_{27}	1.543	1.459	1.125
28	C_{28}	0.112	1.122	1.761

Tables 4-5. Calculated bonds length.

Present work

Atomic Pairs	Calculated Bonds Length (A°)
N_1 ..... C_2	1.343
N_1 ..... C_6	1.345
C_2 ..... C_3	1.382
C_3 ..... C_4	1.374
C_4 ..... C_5	1.382
C_5 ..... C_6	1.382
C_6 ..... N_7	1.365
N_7 ..... C_8	0.861
N_7 ..... C_{16}	1.471
C_8 ..... C_9	1.521
C_8 ..... C_{16}	1.063
C_9 ..... C_{10}	1.375
C_{10} ..... C_{11}	1.387
C_{11} ..... C_{12}	1.265
C_{14} ..... C_{15}	1.386
C_{16} ..... C_{17}	1.511
C_{17} ..... C_{18}	1.528

Previous work

Atomic Pairs	Calculated Bonds Length (A°)
N_1 ..... C_2	1.345
N_1 ..... C_6	1.346
C_2 ..... C_3	1.381
C_3 ..... C_4	1.375
C_4 ..... C_5	1.377
C_5 ..... C_6	1.385
C_6 ..... N_7	1.367
N_7 ..... C_8	1.434
N_7 ..... C_{16}	1.472
C_8 ..... C_9	1.528
C_8 ..... C_{16}	1.384
C_9 ..... C_{10}	1.385
C_9 ..... C_{15}	1.388
C_{10} ..... C_{11}	1.381
C_{12} ..... C_{14}	1.382
C_{14} ..... C_{15}	1.386
C_{16} ..... C_{17}	1.509

Tables 6-7. Calculation for bond angles.

Present work

Atomic Bonds Angles	Calculated Bonds Angles (°)
C_2 – N_1 - C_6	117.8
N_1 – C_2 - C_3	123.6
C_2 – C_3 - C_4	116.8
C_3 – C_4 - C_5	121.5
C_4 – C_5 - C_6	117.4
N_1 – C_6 - C_5	122.7
N_1 – C_6 - N_7	117.6
C_5 – C_6 - N_7	119.6
C_6 – N_7 - C_8	110.8
C_6 – N_7 - C_{16}	120.2
C_8 – N_7 - C_{16}	225.4
N_7 – C_8 - N_9	118.3
N_7 – C_8 - C_{16}	99.29
C_9 – C_8 - C_{16}	139.0
C_8 – C_9 - C_{10}	132.3
C_9 – C_{10} - C_{11}	135.6
C_{10} – C_{11} - C_{12}	104.4

Previous work

Atomic Bonds Angles	Calculated Bonds Angles (°)
C_8 – N_7 - C_6	121.7
C_{16} – N_7 - C_6	120.2
C_{16} – N_7 - C_8	118.1
C_9 – C_8 - N_7	114.2
C_{17} – C_{16} - N_7	112.8
C_{18} – C_{17} - C_{16}	111.9
C_{17} – C_{18} - N_{19}	111.3
S_{22} – N_{21} - C_{20}	106.5
N_{21} – S_{22} - O_{23}	105.3
N_{21} – S_{22} - N_{24}	98.90
N_{24} – S_{22} - O_{23}	105.2
S_{22} – N_{24} - C_{25}	107.3
N_{26} – C_{25} - N_{24}	123.8
C_{20} – C_{25} - C_{24}	112.9
C_{18} – N_{19} - C_{20}	122.4
N_{19} – C_{20} - N_{21}	122.9
C_{25} – C_{20} - N_{21}	114.0
C_{25} – C_{20} - N_{19}	123.0

C_{18}----------N_{19}	1.456
N_{19}----------C_{20}	1.330
C_{20}----------N_{21}	1.301
C_{20}----------C_{25}	1.470
S_{22}----------O_{23}	1.097
N_{24}----------C_{25}	1.305
C_{25}----------N_{26}	1.414
N_{26}----------C_{27}	1.466

C_{17}----------C_{18}	1.529
C_{18}----------N_{19}	1.458
N_{19}----------C_{20}	1.330
C_{20}----------N_{21}	1.301
C_{20}----------C_{25}	1.500
S_{22}----------O_{23}	1.487
N_{24}----------C_{25}	1.304
C_{25}----------N_{26}	1.306
N_{26}----------C_{27}	1.459

N_{7-} C_{16-} C_8	215.2
N_{7-} C_{16-} C_{17}	112.8
C_{8-} C_{16-} C_{17}	148.0
C_{16-} C_{17-} C_{18}	111.9
C_{17-} C_{18-} N_{19}	111.3
C_{18-} N_{19-} C_{20}	122.4
N_{19-} C_{20-} N_{21}	122.9
N_{19-} C_{20-} C_{25}	123.0
N_{21-} C_{20-} C_{25}	113.8
C_{20-} C_{25-} N_{24}	113.2
C_{20-} C_{25-} N_{26}	105.1
N_{24-} C_{25-} C_{26}	126.6
C_{25-} C_{26-} C_{27}	125.9

C_{20-} C_{25-} N_{26}	123.3
C_{27-} N_{26-} C_{25}	122.2
N_{26-} C_{27-} C_{28}	112.2

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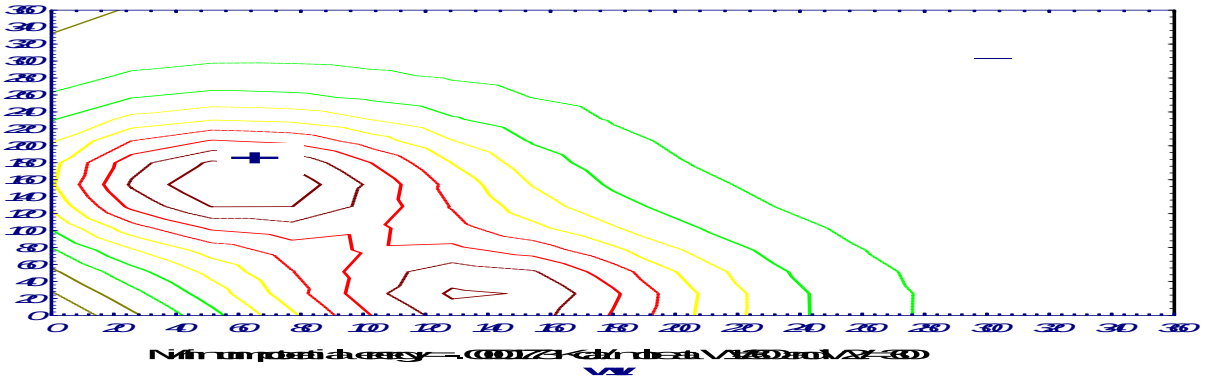

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