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Theoretical study of Some Anesthesia *Derivatives by using RHF method*

دراسة نظرية لبعض مشتقات Anesthesia ***بأستخدام طريقة*** **(RHF)**

Manal. A. Mohammad Shathaa A. Gawad
Dep. Of chemistry , college of Education for pure Science , university of Karbala, Iraq.

Abstract:-

In the present work , the adoption of the program (Gaussian 09) to use the method of calculation the total (Ab initio of method) according to the Hartree – Fock method (RHF) , for the purpose of the expense of dimensional geometric (lengths and angles bond) when the geometry of a balanced, functions thermodynamic, some physical properties, charges for Anesthesia [Thiazol derivative] mono & bicyclic compounds.

The results study Heat formation(ΔH_f^0 (in kJ/mole) by using (semi-empirical method PM3 model in MOPAC) for these molecules and the results showed that the compound **$C_7H_8N_2O_3S$(B)** has less value which means high thermal stability than the other's.

Calculation results have shown that the compound **$C_7H_6N_2O_2S_9$(D)** is more activity because it has the lower value of ΔE and hardness η and has high value of ($G\omega$ Electrophilicity) .

Also the results have shown that the compound **$C_7H_8N_2O_3S$(B)** has highest value of thermodynamic functions (E^0 , H^0 , G^0 , A^0 , C_V , C_P ,S^0) The difference in results come according to the difference of substituted groups. The calculations were held in Karbala university.

Key words: RHF study , Anesthesia, Diazepam ,Electrophilicity.

الخـــلاصـــــة:-

تضمنت هذه الدراسة اعتماد برنامج كاوس (Gaussian 09) لاستخدام طريقة الحساب التام على وفق طريقة هارتري فوك (RHF), وذلك لغرض حساب الأبعاد الهندسية (أطوال و زوايا التاصر)عند الشكل الهندسي المتوازن , الدوال الثرموديناميكية (G^0,H^0,S^0,A^0,E^0) وكذلك تم حساب السعة الحرارية (C_p ,C_V), بعض الخصائص الفيزيائية وكذلك الشحنات لمشتقات حلقة الثاياديازول.

تم اعتماد برنامج **MOPAC** لاستخدام الطريقة الشبه تجريبية **PM3** لحساب حرارة التكوين للمركبات (ΔHf^0 in kJ/mole). وقد أظهرت النتائج الحساب أن المركب **$C_7H_8N_2O_3S$(B)** اكثر استقرارحراري لكونه يمتلك اقل قيمة في حرارة التكوين.

وقد أظهرت نتائج الحساب أن المركب **$C_7H_6N_2O_2S$ (D) اكثر المركبات فعالية لكونه يمتلك اقل قيمة** ΔE واقل قيمة للصلابة η وأعلى قيمة في الالكتروفيلية $G\omega$.كذلك تم حساب الدوال الثرموديناميكية حيث بينت الحسابات أن المركب **$C_7H_8N_2O_3S$(B)** يمتلك أعلى قيمة للدوال (E^0 , H^0 , G^0 , A^0 , C_V , C_P ,S^0) , أن هذا التغاير بالنتائج يعزى بصورة عامة لتأثير اختلاف المجموعة المعوضة على المركبات المدروسة في هذا البحث. تمت هذة الحسابات في جامعة كربلاء.

Introduction.

The mono & bicyclic compounds are class of compounds well known for along time as anesthetic drugs in surgery such as diazepine compounds[1,2] which were first introduced for the treatment of anxiety [3,4] .

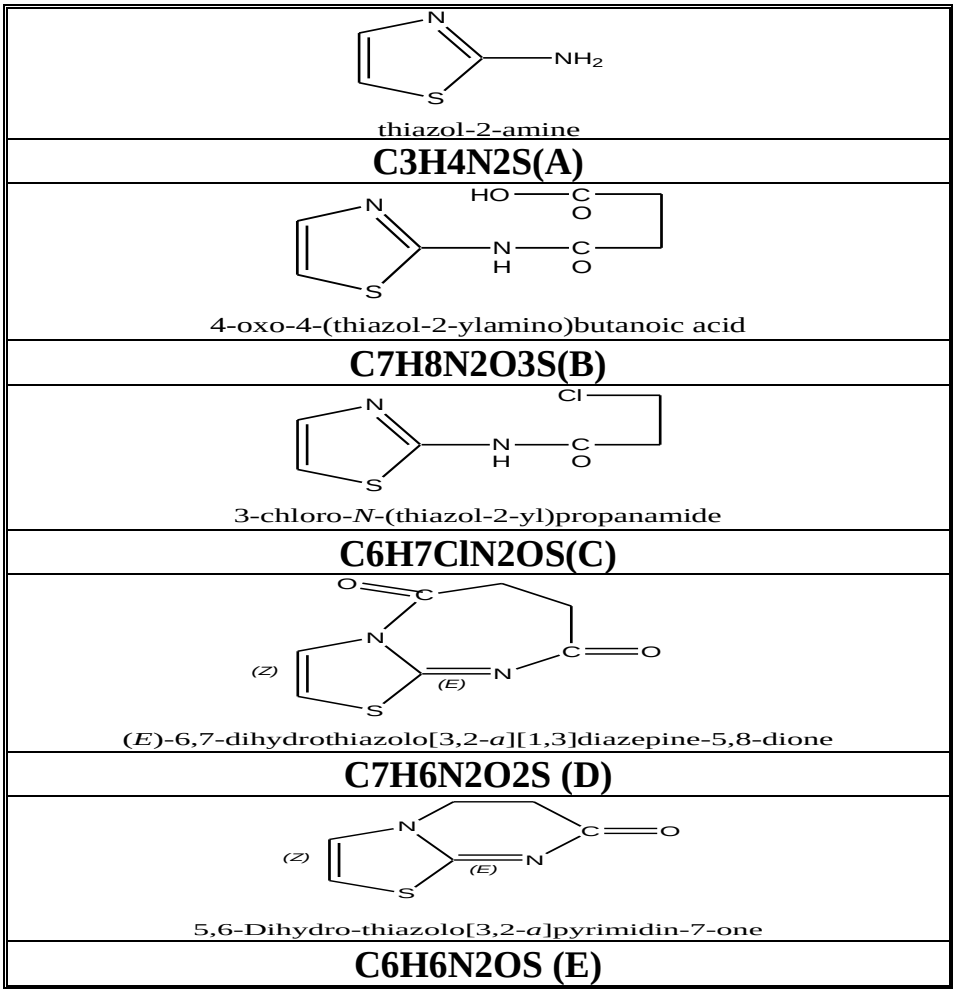
Diazepam (valium) is a class of drugs used as relaxants , minor tranquilizers , hypnotics and muscle relaxant because it is often seen in fortensic and clinical cases . It introduced in 1969 under brand name valium [5].

Diazepam (valium) is used to relive anxiety tension associated with anxiety disorder and muscle spasms as well as alcohol with drawl [6] , and other clinically uses [7-10].

The activity of thio compounds due to the presence of sulphur atom in there structure , it has a wide spectrum of uses as a : selected HIV mutants [11], antibiotic [12], antitumor , dyes and in synthesis of polymers in thermal mold ability [13].

Many examples belonging to oxazepines , diazepines are documented ,but very little is known about thiazepine. 1,4 –Benzothiazepine derivatives are of considerable interest because of their biological activity as a muscle relaxants [14,15].

Thiazepine contains two hetroatoms (nitrogen and sulphur) in seven membered ring [16].



Computational details

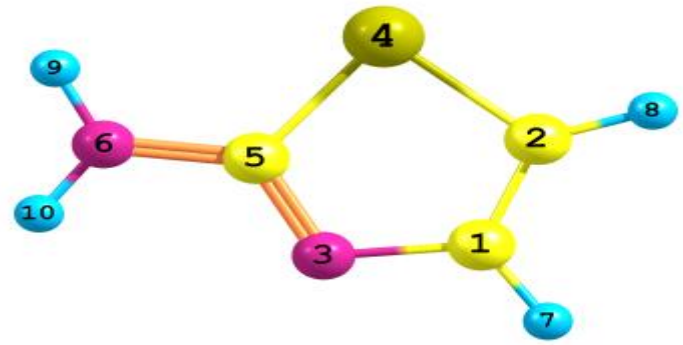
Calculations of the title compound were carried out with(Gaussian09) software program using RHF/6-31G B3LYP basis sets to predict the molecular structure Calculations were carried out with Becke's three parameter hybrid model using the Lee–Yang– Parr correlation functional (B3LYP) method. Molecular geometries and physical properties.

Results and Discussion.

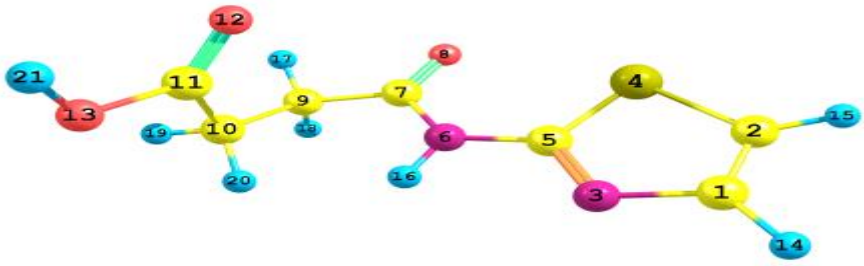
Geometrical parameter.

In this research calculated the geometry (bond lengths and bond angels) of the five molecules of derivatives **Anesthesia.** According to the results calculated and recorded in the (**table 1**and **fig. 1)** . Show that each the bond C_5-N_6 in compound **C** has high value compared to other compounds studies it may be due to high electro – negative of N_6 atom with substituted group, whereas for the same bond length for the compound **D** has less value , may be caused by the difference of electro – negative of (N) with substituted groups . Also the bond C_5-N_3 in compound **D** has high value compared to other compounds studies it may be due to high electro – with drawing electron of carbonyl group and its single bond in this compound compare with other's.

Also the change of the group substituted had effect on the value of the angles of the compounds studied in this research , have shown calculation in the (**table 1**and **fig. 1).** That the angles ∠ $S_4C_5N_5$ in compound **C** has high value , May be due to the big size of substitution groups of Chloride on the angles . Also the angle ∠ $\mathbf{C_2\ S_4C_5}$ the results showed that in compound **D** has high value may by to the seven- membered ring.

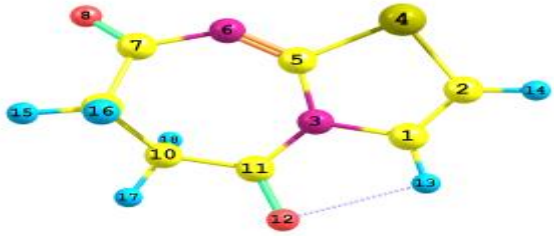


C3H4N2S(A)



C7H8N2O3S(B)

C6H7ClN2OS(C)



C7H6N2O2S (D)

C6H6N2OS (E)

Fig.(1): The geometric equilibrium of **Anesthesia** derivatives

Table 1 : Geometric structure of Anesthesia derivatives calculated by RHF method

$C_3H_4N_2S$(A)		$C_7H_8N_2O_3S$(B)		$C_6H_7ClN_2OS$(C)		$C_7H_6N_2O_2S$ (D)		$C_6H_6N_2OS$ (E)	
Para. Geo.	**Bond length and Angle**	Para. Geo.	**Bond length and Angle**	Para. Geo.	**Bond length and Angle**	Para. Geo.	**Bond length and Angle**	Para. Geo.	**Bond length and Angle**
R(3-5)	1.286	R(3-5)	1.284	R(3-5)	1.282	R(3-5)	1.402	R(3-5)	1.364
R(4-5)	1.812	R(4-5)	1.794	R(4-5)	1.794	R(3-11)	1.404	R(3-9)	1.463
R(5-6)	1.349	R(5-6)	1.379	R(5-6)	1.380	R(4-5)	1.820	R(4-5)	1.803
R(6-9)	0.986	R(6-7)	1.368	R(6-7)	1.361	R(5-6)	1.259	R(5-6)	1.279
R(6-10)	0.989	R(6-16)	0.990	R(6-14)	0.992	R(6-7)	1.393	R(6-7)	1.396
A(2-1-3)	117.0	R(7-8)	1.218	R(7-8)	1.220	R(7-8)	1.210	R(7-8)	1.515
A(2-1-7)	125.0	R(7-9)	1.509	R(7-9)	1.508	R(7-9)	1.501	R(7-10)	1.212
A(1-2-4)	109.6	R(9-10)	1.526	R(9-10)	1.511	R(9-10)	1.533	R(8-9)	1.526
A(1-2-8)	130.1	R(9-17)	1.077	R(9-15)	1.079	R(9-15)	1.076	R(8-13)	1.076
A(3-1-7)	117.9	R(9-18)	1.084	R(9-16)	1.085	R(9-16)	1.083	R(8-14)	1.083
A(1-3-5)	112.4	R(10-11)	1.495	R(10-17)	1.071	R(10-11)	1.497	R(9-15)	1.078
A(4-2-8)	120.3	R(10-19)	1.082	R(10-18)	1.070	R(10-17)	1.076	R(9-16)	1.083
A(2-4-5)	86.8	R(10-20)	1.082	A(2-1-3)	115.8	R(10-18)	1.084	A(2-1-3)	114.9
A(3-5-4)	114.2	R(11-12)	1.207	A(2-1-12)	126.0	R(11-12)	1.215	A(2-1-11)	126.6
A(3-5-6)	124.5	R(11-13)	1.347	A(1-2-4)	110.5	R(12-13)	2.296	A(1-2-4)	111.0
A(4-5-6)	121.3	R(13-21)	0.950	A(1-2-13)	129.3	A(2-1-3)	115.4	A(1-2-12)	128.5
A(5-6-9)	122.5	A(2-1-3)	115.9	A(3-1-12)	118.2	A(2-1-13)	127.8	A(3-1-11)	118.5
A(5-6-10)	118.0	A(2-1-14)	126.0	A(1-3-5)	112.4	A(1-2-4)	111.9	A(1-3-5)	115.5
A(9-6-10)	119.	A(1-2-4)	110.5	A(4-2-13)	120.2	A(1-2-14)	127.4	A(1-3-9)	125.4
		A(1-2-15)	129.3	A(2-4-5)	86.5	A(3-1-13)	116.9	A(4-2-12)	120.5
		A(3-1-14)	118.1	A(3-5-4)	114.8	A(1-3-5)	114.2	A(2-4-5)	89.1
		A(1-3-5)	112.4	A(3-5-6)	120.1	A(1-3-11)	117.8	A(5-3-9)	118.6
		A(4-2-15)	120.3	A(4-5-6)	125.2	A(1-13-12)	97.8	A(3-5-4)	109.4
		A(2-4-5)	86.6	A(5-6-7)	127.3	A(4-2-14)	120.7	A(3-5-6)	127.0
		A(3-5-4)	114.7	A(5-6-14)	112.9	A(2-4-5)	89.9	A(3-9-8)	108.7
		A(3-5-6)	120.0	A(7-6-14)	119.8	A(5-3-11)	127.9	A(3-9-15)	108.8
		A(4-5-6)	125.3	A(6-7-8)	122.5	A(3-5-4)	108.6	A(3-9-16)	109.2
		A(5-6-7)	127.2	A(6-7-9)	115.8	A(3-5-6)	133.3	A(4-5-6)	123.6
		A(5-6-16)	112.3	A(8-7-9)	121.6	A(3-11-10)	120.0	A(5-6-7)	119.3
		A(7-6-16)	120.5	A(7-9-10)	112.2	A(3-11-12)	118.6	A(6-7-8)	116.5
		A(6-7-8)	121.6	A(7-9-15)	111.7	A(4-5-6)	118.1	A(6-7-10)	122.0
		A(6-7-9)	117.2	A(7-9-16)	106.8	A(5-6-7)	131.5	A(8-7-10)	121.4
		A(8-7-9)	121.1	A(10-9-15)	110.5	A(6-7-8)	120.3	A(7-8-9)	111.3
		A(7-9-10)	117.9	A(10-9-16)	108.1	A(6-7-9)	118.1	A(7-8-13)	108.9
		A(7-9-17)	105.5	A(9-10-17)	112.2	A(8-7-9)	121.6	A(7-8-14)	108.0
		A(7-9-18)	107.0	A(9-10-18)	112.2	A(7-9-10)	110.4	A(9-8-13)	111.0

Physical properties.

Depending on the Ab initio of method of calculation according to the Hartree Fock (HF) is calculate some physical properties of the molecules studied in this research; Dipole moments (μ in Debye) , energies (e V) of the high Occupied Molecular Orbital (E_{HOMO}) and the Lower Unoccupied Molecular Orbital (E_{LUMO}) and according Koopmans theorem (the negative E_{HOMO} is equal to the ionization potential) the calculation has been ionization energies (e V) , Also calculated the energy difference (ΔE , e V), And finally calculated (Molecular Hardness)Hardness(η) = ½(E_{HOMO} - E_{LUMO}) , (Electron Affinity) EA = - E_{LUMO} according Koopmans theorem for N system of electrons**[17-20].** that compound **$C_7H_6N_2O_2S$ (D)** is more activity because it has the lower value of ΔE and hardness η and has high value of (GO Electrophilicity) and(E_{LUMO})this means that this compound has more ability to lose electrons and be easier ionization compared to other compounds

Also ,The MOPAC computational packages (semi-empirical method , PM3 model) employed to compute physical properties; heats of formation (ΔHf, kJ.mol-1)**[21,22]**. the results showed **(Table 2)** for the compound **$C_7H_8N_2O_3S$(B)** has less value which means high stability than the other's.

Table 2: Energetic properties of Anesthesia derivatives calculated by(RHF) method

Comp.	ΔH_f KJ/Mol	μ Debye	E_{HOMO} *eV*	E_{LOMO} *eV*	ΔE *eV*	IP *eV*	EA *eV*	η *eV*	*X* *eV*	$G\mathcal{D}$ *eV*
$C_3H_4N_2S$(A)	737.065	1.333	-8.660	3.487	12.487	8.660	-3.487	6.074	2.586	0.551
$C_7H_8N_2O_3S$(B)	140.762	4.392	-9.097	2.921	12.018	9.097	-2.921	6.009	3.088	0.793
$C_6H_7ClN_2OS$(C)	476.499	3.637	-9.275	2.635	11.911	9.275	-2.635	5.955	3.319	0.925
$C_7H_6N_2O_2S$ (D)	694.746	4.514	-9.266	1.757	11.024	9.266	-1.757	5.512	3.754	1.278
$C_6H_6N_2OS$ (E)	524.102	8.798	-8.774	2.651	11.425	8.774	-2.651	5.712	3.062	0.820

Thermodynamics functions

The fundamental vibration frequencies for five compound of ***Anesthesia*** molecules along with the rotational constants, obtained in this study, where used to calculate the vibration and rotation contributions to the thermodynamic functions .

Thermodynamics functions standard and heat capacity for the studied molecules listed **Table: 3** looking at the calculation results show that each of the thermodynamic functions (G^0, A^0, E^0, H^0) and (C_V , C_P)have the same gradient values (different the group substitutes),

B > C > D > E > A

Table 3: Standard thermodynamics functions at 298.15oK of Anesthesia derivatives calculated by (RHF)

Comp.	E^0 KJ/Mol	H^0 KJ/mol	G^0 KJ/mol	S KJ/mol.deg	A^0 KJ/mol	Cp KJ/mol.deg	Cv KJ/mol.deg
$C_3H_4N_2S$(A)	215.894	218.422	127.016	0.307	35.603	0.088	0.079
$C_7H_8N_2O_3S$(B)	466.554	469.032	328.842	0.470	188.652	0.183	0.174
$C_6H_7ClN_2OS$(C)	395.153	397.632	254.878	0.437	112.136	0.157	0.149
$C_7H_6N_2O_2S$ (D)	384.400	386.879	266.396	0.404	145.914	0.155	0.146
$C_6H_6N_2OS$ (E)	352.025	354.504	245.858	0.364	137.211	0.127	0.119

The Charges

The Calculated for all charges atoms of the molecules studied according to the method (HF) have shown calculation results of the charges **(Table: 4)** are each of the (N_6, N_3) has high value of charge (the lowest density electronic) , Perhaps the reason for this difference in electrical negative and molecular weight which increase the electronic density on nitrogen atom (N_6, N_3) As in the case of compound (**A , B**).

This scientific fact indicates that the compound (**A , B**) can be use as a strong legend when it linked to metal complex formation ,

C > B > E > D

Table:4 Charge of Anesthesia derivatives calculated by (RHF)method

$C_3H_4N_2S$(A)		$C_7H_8N_2O_3S$(B)		$C_6H_7ClN_2OS$(C)		$C_7H_6N_2O_2S_9$(D)		$C_6H_6N_2OS$ (E)	
Atom	Charge	Atom	Charge	Atom	Charge	Atom	Charge	Atom	Charge
1 C	0.1775	1 C	0.1563	1 C	0.1546	1 C	0.313251	1 C	0.3442
2 C	-0.5394	2 C	-0.5537	2 C	-0.5499	2 C	-0.553151	2 C	-0.5744
3 N	-0.5094	3 N	-0.5004	3 N	-0.4908	3 N	-0.891027	3 N	-0.8093
4 S	0.2586	4 S	0.4225	4 S	0.4185	4 S	0.343841	4 S	0.3477
5 C	0.3427	5 C	0.3003	5 C	0.2960	5 C	0.359626	5 C	0.3666
6 N	-0.8991	6 N	-0.8741	6 N	-0.8789	6 N	-0.502807	6 N	-0.5254
7 H	0.2068	7 C	0.7912	7 C	0.8113	7 C	0.6257	7 C	0.5986
8 H	0.2209	8 O	-0.5269	8 O	-0.5375	8 O	-0.4378	8 C	-0.5295
9 H	0.3678	9 C	-0.4742	9 C	-0.5004	9 C	-0.5011	9 C	-0.0879
10 H	0.3737	10 C	-0.5219	10 C	-0.4089	10 C	-0.5326	10 O	-0.4675
		11 C	0.7705	11 Cl	-0.1203	11 C	0.8107	11 H	0.2326
		12 O	-0.4858	12 H	0.2126	12 O	-0.4988	12 H	0.2337
		13 O	-0.7084	13 H	0.2256	13 H	0.2779	13 H	0.2251
		14 H	0.2095	14 H	0.3952	14 H	0.24007	14 H	0.2270
		15 H	0.2229	15 H	0.2230	15 H	0.24037	15 H	0.1998
		16 H	0.3849	16 H	0.2449	16 H	0.21484	16 H	0.21872
		17 H	0.2512	17 H	0.2334	17 H	0.2532	1 C	0.3442
		18 H	0.227333			18 H	0.2378	2 C	-0.5743
		19 H	0.250750						
		20 H	0.219931						

Conclusion

Energetic properties with Standard thermodynamic functions have been investigated using quantum mechanics result by using RHF method with 6-31G B3LYP as basis sets, showed each of compounds (D,E) have heat of formation (694.746 , 524.102)kJ .mol^{-1} that's mean these cyclic compounds more stable and it can use as drug than the others.

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