

STUDY OF REACTIVITY ENERGY AND STRUCTURE OF BENZOAZOLES, INDAZINE, PYRAZEPINES AND DIAZOAZOLES ON THE BASIS OF QUANTUM CHEMICAL METHOD

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ABSTRACT

We choose computational methods to solve chemical problem depends upon the properties. Quantum chemical methods are expensive for large systems. But it give more information about reactivity, structure and reaction co-ordinates.

Some computational methods like MNDO, AM1, PM3 and semi-empirical have been used due to their accuracy of results.

Experimental heat of formation is difficult to measure but by computational methods we can easily measure.

The numbering schemes in the figures reflect that Benzoazoles and Pyrines are similar in structure to cyclopentadiene, Indene and Benzene.

Benzoazoles are indicated with a 'B' before the number reflecting the ring, for example Indole is Benzo – Fused Pyrrole (51). So Indol is numbered B51. The numbering scheme was introduced to facilitate balancing the isobaric reaction schemes used to generate the ab-initio heat of formation.

Keywords – MNDO, AM1, PM3.

INTRODUCTION

Chemistry based on atoms, molecules and their different phenomena and properties. Atom obeys the laws of quantum mechanics. It depends upon wave – function. Wave – function depend upon particle and time.

Quantum Chemistry or Theoretical Chemistry applies calculating a wide range of electronic, thermodynamic properties of interest of a chemist or physicist.

Computational technologies are embodied in nearly every aspect chemical research development, design and manufacture. They have a broad range of applications from molecular modelling to the simulation and control of chemical process.

All quantum mechanical methods solve the schrodinger wave equation to give the total molecular energy and wave function of the system. The total wave function in principle, allows calculation of all properties related to molecular structure, such as spectra, dipole moments, polarizability and thermodynamic properties are many quantum mechanical approaches to molecular structures from simple Huckel Mo based theories to extensive ab-initio and density functional methods.

Semi – empirical methods depend on using experimental and theoretical data to parameterize and approximate certain integrals in the fock matrix. This approach reduces the computational time and cost of a Hartree-Fock calculation.

Overview of Compound

The quantum-mechanical or computational methods used in this work project describe the structure, reactivity and energies of some pharmacologically interesting chemical compounds like Benzoazoles, Diazoazoles, Azolyidenes.

Benzoazole

A Bezoazole is an aromatic organic compound with a molecular formula C_7H_5NO , a benzene-fused oxazol ring structure, and an odor similar to pyridine. Benzoxazole is used primarily in industry and research, and has no household use. Being a heterocyclic compound; benzoxazole finds use in research as a starting material for the synthesis of larger, usually bioactive structures. It is found within the chemical structures of pharmaceutical drug such as flunoxapfen. Its aromaticity makes it relatively stable, although as a heterocycle, it has reactive sites which allow for functionalization.

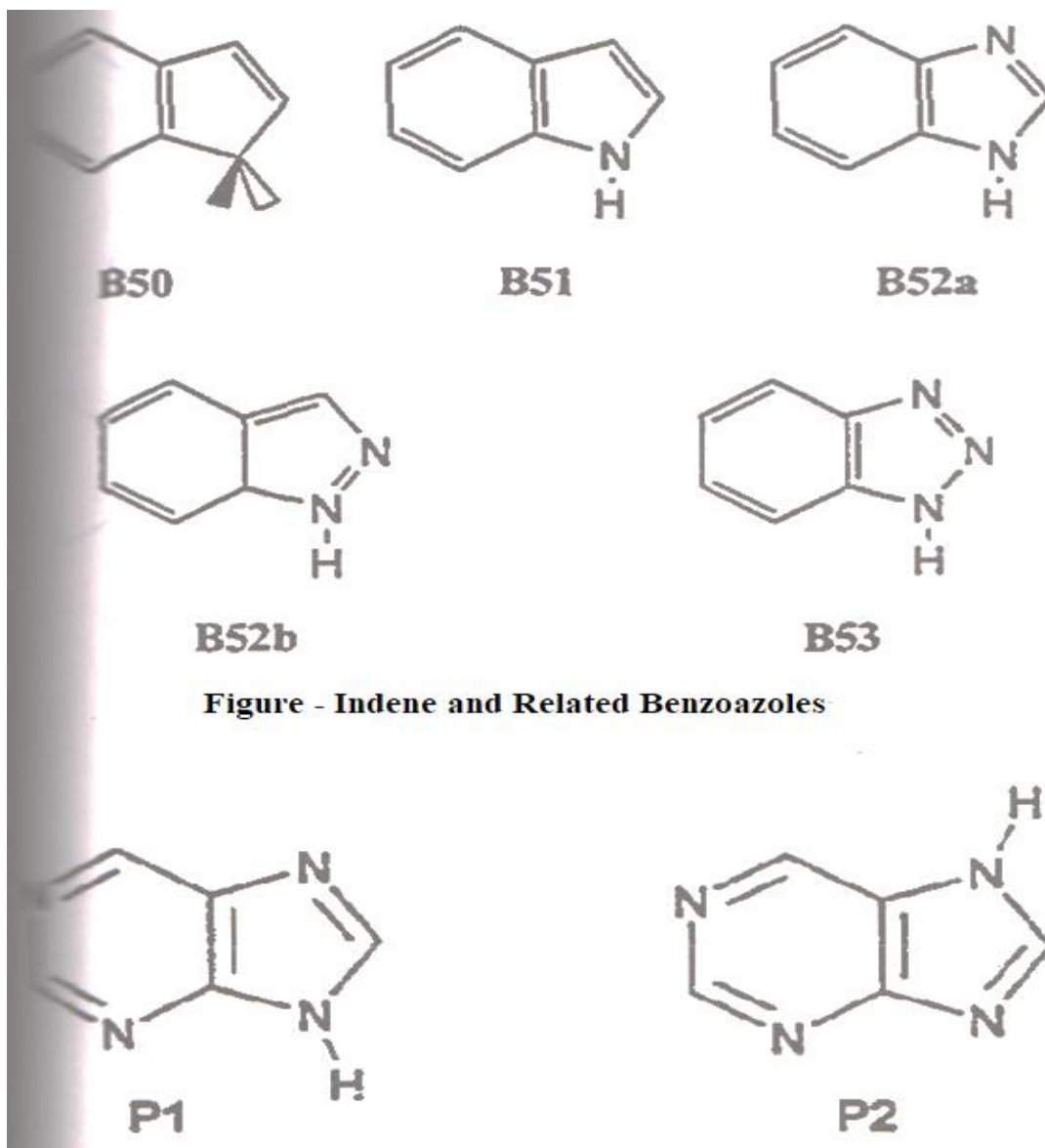


Figure - Indene and Related Benzoazoles

Figure - Purines

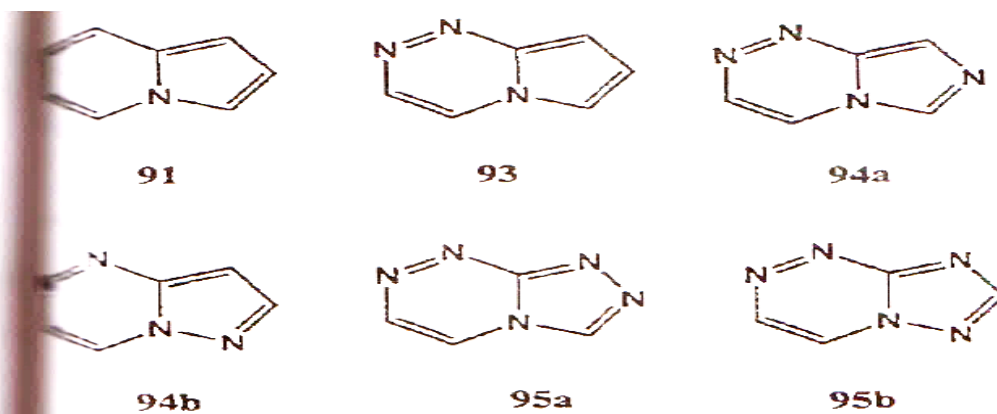


Figure - Indazine and Some Related Azolotriazines

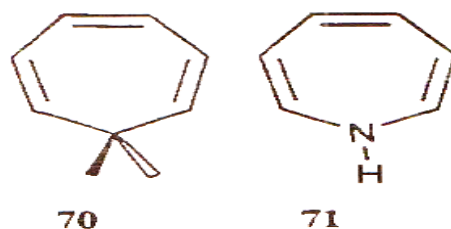
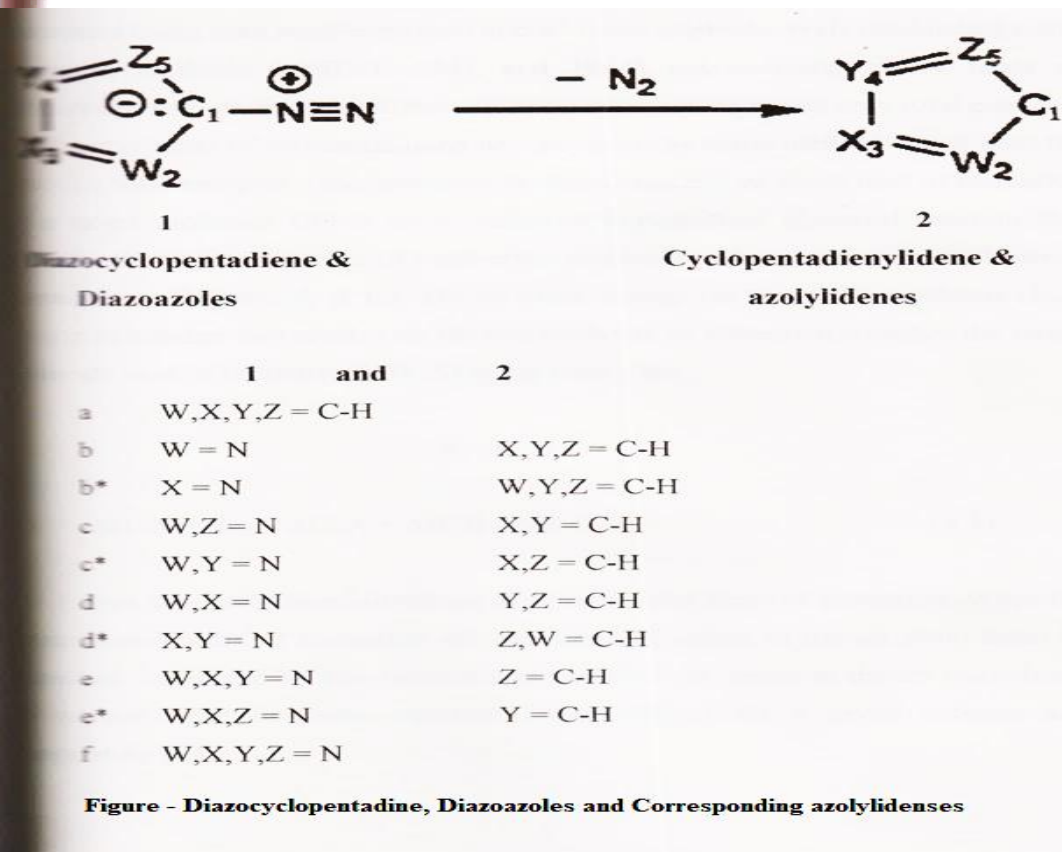


Figure - Pyrazepines



Results and Discussion

Benzo – Fused Compounds and Purines

Ab initio heats of formation of benzoazoles and purines were calculated with both isolobal and benzofusion reaction schemes. Reaction schemes, heats of reaction and subsequent heats of formation are in Table – 1.2. The isolobal and benzofusion 4-31G** reaction energies are very close to each other, indicating that basis set and electron correlation errors almost completely cancel; therefore, these are excellent schemes for heats of formation calculation. Semi – empirical and ab initio benzoazole and purine heats of formation are compared with available experimental data in Table – 5.6. The ab initio heats of formation are the best fit to experiment. PM3, which perform well on azoles, also performs well on benzoazoles to MNDO and AMI errors in azole heats of formation.

Table – 1.1

Semi – Empirical and Ab initio Heats of Formation of Benzofused Azoles

Compound	ΔH_f (kcal/mol)			This work ab initio A	expt.
	MNDO	AMI	PM3		
B50 Indene	38.3	45.8	40.7	37.5	39.0*
B51 Indole	44.2	55.2	42.6	40.8	37.4*
B52 a					
Benzoimidazole	45.9	67.1	47.8	48.9	--
B52b					
Benzopyrazole	58.4	82.3	65.7	62.4	--
B53					
Benzotriazole	64.0	104.2	85.6	81.1	83.0*
P1 purine (1)	59.5	90.0	62.3	68.3	--
	69.9	--	69.5		
P2 Purine (2)	64.0	94.0	65.8	73.2	--
	74.4	--	73.0		

A = average of 4-31G and 6-31G** values

a = ref. 16

italics = corrected semi-empirical

Table – 1.2

Reaction Schemes for Benzoazoles and Purines

Target Compound Reaction Schemes (e= ethene)	ΔH_{rxn} (kcal/mol)		ΔH_f	
	4-31G	6-31G**	4-31G	6-31G**
Indene (B50)				
60 + 50 → B50 + e	-0.2	0.05	39.0	39.3
B51 + 50 → B50 + 51	-7.8	-7.4	35.5	35.9
			37.3	37.6
Indole (B51)				
60 + 51 → B51 + e	7.6	7.4	40.9	40.7
B50 + 51 → B51 + 50	7.8	7.4	40.9	40.5
			40.9	40.6
Benzoimidazole (B52a)				
60 + 52a → B52a + e	6.6	6.6	48.9	48.9
B50 + 52a → B52a + 50	6.8	6.6	48.9	48.7
			48.9	48.8
Benzopyrazole (B52b)				
60 + 52b → B52b + e	10.7	11.5	62.0	62.8
B50 + 52b → B52b + 50	10.9	11.5	62.0	62.6
			62.0	62.7
Benzotriazole				
B2 + 53a + 52b → B6 + 52a + 51	9.9	16.0	76.3	82.4
B1 + 52a + 54a → B6 + 50 + 53a	5.9	5.7	82.1	81.9
60 + 53c → B6 + e	10.3	11.6	81.5	82.8
			79.9	82.2
purine1 (p1)				
62b + 52a → p1 + e	3.7	3.1	73.2	72.6
62c + 52a → p1 + e	-1.1	-3.4	68.3	66.0
indole + 52a + 62b → p1 + 51 + 60	-3.9	-4.2	69.7	69.4
indole + 63c → p1 + 60	-9.2	-6.9	62.3	64.6
			68.4	68.2
purine2 (p2)				
62b + 52a → p2 + e	9.2	8.2	78.7	77.7
62c + 52a → p2 + e	4.3	1.7	73.1	71.2
indole + 52a + 62b → purine2 + 51 + 60	1.5	0.8	75.1	74.4
indole + 63c → p2 + 60	-3.7	-1.8	67.8	69.7
			73.7	73.3

Ethane ΔH_f kcal/mol (ref. 16)

Semi-empirical and ab initio purine heats of formation are not in good agreement because purines contain an azine moiety. However, by applying the previously developed semi-empirical azine heat of formation correction terms to MNDO and PM3 purine heats of formation improves the MNDO and PM3 results. Corrected PM3 and MNDO purine heats of formation agree well with the ab initio purine heats of formation. Azine correction terms do not help the AMI overestimates purine heats of formation by 20 – 30 kcal/mol, which is similar to the AMI overestimation of azole heats of formation.

Indazine and Azolotriazines

Indazine (91) and Azolotriazines (93-95b) are compounds similar to benzotriazoles and purines, except that a nitrogen atom is shared by both the five and six-membered rings.

Isolobal reaction schemes that generate indazine and azolotriazine from moles and azines could not be found, because all the reaction schemes considered violate one or more of the conditions set forth for isolobal reactions. However, since all the azolotriazines can easily be

generated from isolobal reactions involving indazine, the indazine heat of formation was calculated from the non-isolobal isomerization reaction :



The calculated indazine heat of formation was used as the ‘experimental’ indazine heat of formation in subsequent isolobal reaction schemes. The ab initio indazine heat of formation calculated by the isomerization reaction agrees with the corrected PM3 and MNDO indazine heats of formation, suggesting that the ab initio value is responsible, because MNDO and PM3 perform well on azoles and azines with one or two nitrogen heteroatomd. Reaction schemes used to generate azolotriazine heats of formation are in Table.

Table – 1.3

Semi-Empirical and AB initio Indazine and Azolotriazine Heats of Formation

Compound	ΔH_f (kcal/mol)			
	semi-empirical			ab initio
	MNDO	AM1	PM3	A
Indazine 91	55.7	72.3	50.5	54.5*
	<i>60.9</i>	--	<i>54.1</i>	
93	78.7	107.5	85.1	104.5
	<i>106.8</i>	--	<i>99.2</i>	
94a	81.4	120.7	91.8	115.5
	<i>109.5</i>	--	<i>105.9</i>	
94b	91.8	135.3	109.1	116.2
	<i>119.9</i>	--	<i>123.2</i>	
95a	93.0	148.5	117.4	138.5
	<i>121.1</i>	--	<i>131.5</i>	
95b	94.4	151.7	117.1	125.9
	<i>122.5</i>	--	<i>131.2</i>	

*Taken as the ‘experimental’ indazine ΔH_f in subsequent isolobal reaction schemes

Italics = corrected semi-empirical

A = average of 4-31G and 6-31G**results

Table – 1.4
Indazine and Azolotriazine Isolobal Reaction Schemes

Target Compound Reaction Schemes (e = ethene)	ΔH_{rxn} (kcal/mol)		ΔH_f°	
	4-31G	6-31G**	4-31G	6-31G**
*B50 → 91	18.2	15.9	53.3	55.6
93				
91 + 62a → 93 + 60	3.5	3.5	104.7	104.7
91 + 53a → 93 + 51	28.3	31.1	102.8	105.6
			103.8	105.2
94a				
91 + 62a + 52a → 94a + 60 + 51	8.7	8.7	118.9	118.9
91 + 53a + 52a → 94a + 2(51)	33.5	36.3	116.9	119.9
91 + 62a + 62b → 94a + 60 + 61	3.2	3.2	116.8	116.8
91 + 53a + 62c → 94a + 51 + 61	23.1	24.3	109.9	111.1
91 + 62a + 53c → 94a + 60 + 62b	3.4	6.1	111.5	114.2
			114.8	116.2
94b				
91 + 62a + 62a → 94b + 60 + 61	-14.3	-16.2	118.8	116.9
91 + 62a + 53a → 94b + 60 + 52a	4.1	2.7	116.3	114.9
91 + 53a + 53a + 94b + 51 + 52a	28.8	30.4	114.3	115.9
			116.5	115.9
95a				
91 + 62a + 53a → 95a + 60 + 51	18.9	16.1	140.1	137.3
91 + 2(53a) → 95a + 2(51)	43.6	43.7	138.1	138.2
			139.1	137.8
95b				
91 + 62a + 53a → 95b + 60 + 51	7.4	2.0	128.6	123.2
91 + 53a + 53a → 95b + 2(51)	32.1	29.6	126.6	124.1
91 + 62a + 62a → 95b + 2(60)	-17.4	-25.6	130.5	122.3
			128.6	123.2

As with azines, the MNDO and PM3 azolotriazine heats of formation are consistently lower than the ab initio values, because MNDO and PM3 underestimate the energy of the azine portion of the azolotriazine. However, applying the MNDO and PM3 azine heat of formation correction terms to the azolotriazine heats of formation brings their values closer to the ab initio result AM1 consistently gives azolotriazine heats of formation larger than the ab initio values, presumably because AM1 overestimates the energy of the azole portion of the azolotriazine.

Thus, as with purins, the AM1 azines heat of formation correction terms were not applied to AM1 azolotriazine heats of formation, as they would not improve the AM1 results. Unfortunately, there are no experimental azolotriazine heats of formation with which to compare with the results.

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