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A theoretical study on methamphetamine: geometry, energies, NMR and NBO

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ABSTRACT

The methamphetamine has been studied theoretically at the MP2 [1]/6-31G[2] level in gas phase. Methamphetamine has been investigated Via NMR, Frequencies Calculation and NBO analysis. The structure of methamphetamine was designed primarily using of Chem. Bio Draw and it geometry has been optimized at the MP2/6-31G computational level. The present work consists the study of the methamphetamine reported in Fig1. Frequencies calculations have been carried out to confirm that the structure obtained correspond to energetic minima. The all calculations have been performed with the Gaussian-03 program [3].

Keywords: Methamphetamine; Theoretical; NBO; NMR

INTRODUCTION

Methamphetamine is a cationic lipophilic molecule with potent action on the sympathetic and central nervous systems and it is a chiral center with two enantiomers. Methamphetamine a variant of amphetamine has been synthesized in Japan in 1893 by Nagayoshi Nagai from the precursor chemical ephedrine and it has a methyl group more than amphetamine [4, 5]; it is a stimulant and addictive substance that is a stronger central nervous system stimulant than amphetamines [6, 7]. Animal studies show that increasing the concentration of injected methamphetamine decreased dopamine release from the striatum. Methamphetamine effects on abuser depend on the dose and duration of its use [8].

During the World War II by the Japanese, American and German soldiers used to relieve fatigue and increase energy [9]. In recent decades, an increase in methamphetamine use has been associated with increased disability and death

COMPUTATIONAL METHODS

The structure of methamphetamine was designed primarily using of Chem. Bio Draw 12.0 (Scheme1). All the calculations of all systems were done by density functional theory (DFT) using MP2 method and the standard 6-31G basis set, by Gaussian03 suit of programs [3] and

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was done in the gas phase. The total energy, electronic and nuclear energies were calculated for the methamphetamine, as well as HOMO, LUMO energies and the difference between then (ΔE) and they are listed in Table 1. Mullikan charges on the atoms and the dipole moments, and geometry parameters such as bond lengths were also determined.

RESULTS AND DISCUSSION

Geometry

Optimized geometrical parameters of methamphetamine Obtained by MP2/6-31G density functional calculations (Table 1). The optimized molecular structure along with the numbering atom of methamphetamine is as shown in Fig.1. The optimization and NBO calculation of all systems are done by density functional theory (DFT) using MP2 method and the standard 6-31G basis set, by Gaussian03 suit of programs were done in the gas phase.

Energies

We report in Table 1 the energies corresponding to methamphetamine. The reported geometry and molecular properties, such as the equilibrium energy, HOMO-LUMO band gap, dipole moment etc. The basic electronic parameters related to the frontier orbitals in a molecule are the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) and their resulting energy gap. Both the HOMO and LUMO are the main orbital take part in chemical stability [10].

NBO

Population analysis is a mathematical way of partitioning a wave function or electron density into charges on the nuclei, bond orders, and other related information. A full NBO analysis is obtained in Gaussian when using the POP=NBO keyword.

NBOs are an orthonormal set of localized "maximum occupancy" orbitals whose leading N/2 members (or N members in the open-shell case) give the most accurate possible Lewis-like description of the total N-electron density [11, 12].

Table 1 lists the calculated occupancies of natural orbitals. The calculated Natural bond hybrids and are also given in this table.

For each donor (*i*) and acceptor (j), the stabilization energy $E(2)$ associated with the delocalization $i \rightarrow j$ is estimated as

$$\Delta E^{(2)}_{i\rightarrow j^*} = -n_\sigma \frac{\langle \sigma_i | \hat{F} | \sigma_j^* \rangle^2}{\varepsilon_{j^*} - \varepsilon_i} \qquad (1)$$

where $\hat{F}$ is the effective orbital Hamiltonian and $\langle \sigma_i | \hat{F} | \sigma_j^* \rangle^2$ is the Fock matrix element i and j NBO orbitals, ε_{j^*} and ε_i are the energies of i and j* NBOs and n_σ is the population of the donor σ orbital.

Table. 2 lists the selected values of the calculated second order interaction the bond hybridization and the bond order of various chemical bonds can also be derived from NBO analysis based on DFT/MP2 calculations. The natural bond hybrid orbital, bond occupancies, and natural bond hybrid orbital energy are listed in Table 1. The results of second order perturbation theory analysis of Fock matrix at MP2/6-31G level of theory. Table 2 lists the selected values of the calculated second order interaction energy (E2) between donor–acceptor orbitals in methamphetamine. The strongest interactions are the electron donations from a π_{C-C} to the antibonding acceptor π^*_{C-C} orbitals.

NMR

Chemical shielding tensors are calculated for the optimized structure at MP2/6-31G level of theory by means of the gauge included atomic orbital method (GIAO). Quantum chemical calculations yield chemical shielding tensors in the principal axis system (PAS) with the order of $\sigma_{33} > \sigma_{22} > \sigma_{11}$; hence, Eqs. (1) and (3) are used to convert the calculated chemical shielding tensors to the absolute isotropic (σ_{11}) and anisotropic ($\Delta\sigma$) chemical shielding parameters:

$$\sigma_{iso} = (\sigma_{11} + \sigma_{22} + \sigma_{33})/3 \qquad (1)$$

$$\Delta\sigma = \sigma_{33} - (\sigma_{11} + \sigma_{22})/2 \qquad (2)$$

The shielding tensor asymmetry parameter (η) which is given by:

$$\eta = \frac{|\sigma_{22} - \sigma_{11}|}{|\sigma_{33} - \sigma_{iso}|} \qquad (3)$$

Table 3 presents the computed chemical shift for selected hydrogen, nitrogen and carbon atoms. The graphs of calculated isotropic shielding values, anisotropic chemical shift tensor ($\Delta\sigma$), asymmetry parameter (η) and total atomic charge versus the atomic number are also drawn in Figure 2a to d, respectively.

As shown in Figure 2, the N nucleus has more negative total atomic charge and a larger isotropic chemical shift tensor (σiso) and anisotropic chemical shift tensor (Δσ) for the N atom (Fig 2a, b).

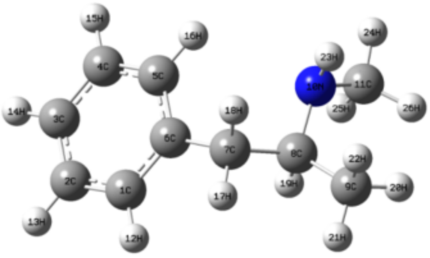

Fig. 1. The structure of Methamphetamine.

CONCLUSION

The optimized structure of molecular that studied in this work, have been shown in Fig 1. Dipole moment, E, HOMO, LUMO, band gap, ΔG and ΔH reported in Table 1. The strongest interactions are the electron donations from a π_{C-C} to the antibonding acceptor π^*_{C-C} orbitals. The chemical shifts of these molecules have been simulated using quantum mechanics.

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Table 1. Occupancy of natural orbitals (NBOs), hybrids, geometry and molecular properties of methamphetamine calculated by the MP2 method with 6-31G(d) basis

Symbol	charge of nitrogen (a.u)	ΔG (kcal/mol)	ΔH (kcal/mol)	Energy of band gap (kcal/mol)	E (kcal/mol)	Dipole Moment(D)	NBO [a]	Occupancy	Hybrides	Energy (hartree)
$H - Mta$*	-0.733586	121.29689	153.048689	-34.7199	-288.62	1.8026	$\sigma_{C_8-N_{10}}$	1.98698	$0.63(sp^{3.28})_{C8}+0.77(sp^{2.10})_{N10}$	-0.92443
							$\sigma_{N_{10}-C_{11}}$	1.99244	$0.77(sp^{2.26})_{N10}+0.62(sp^{3.02})_{C11}$	-0.92104
							$\sigma_{N_{10}-H_{23}}$	1.98244	$0.83(sp^{3.45})_{N10}+0.55s_{H23}$	-0.78029
							CR(1) N_{10}	1.99947	s	-11.12596
							LP (1) N_{10}	1.94561	$sp^{5.87}$	-0.42710

[a] LP(n)A is a valence lone pair orbital (n) on A atom and CR is 1c core.

* $H - Mta$ = methamphetamine

Table 2. Second-order interaction energy (E2, kcal/mol) between donor and acceptor orbitals (π→ π *) in methamphetamine.

Donor NBO (i)	Acceptor NBO (j)[a]	E(2) [b]	E(j)-E(i)[c] a.u.	F(i,j)[d] a.u.
πC1-C6	π *C2-C3	44.18	0.46	0.128
πC1-C6	π *C4-C5	39.23	0.47	0.122
πC2-C3	π *C1-C6	38.08	0.48	0.120
πC2-C3	π *C4-C5	41.90	0.47	0.125
πC4-C5	π *C1-C6	42.87	0.47	0.127
πC4-C5	π *C2-C3	42.04	0.46	0.125

[a] Starred label (*) denotes antibonding NBO orbital

[b] E (2) means energy of hyper conjugative interaction (stabilization energy)

[c] Energy difference between donor and acceptor i and j NBO orbitals

[d] F (i, j) is the Fock matrix element between i and j NBO orbitals

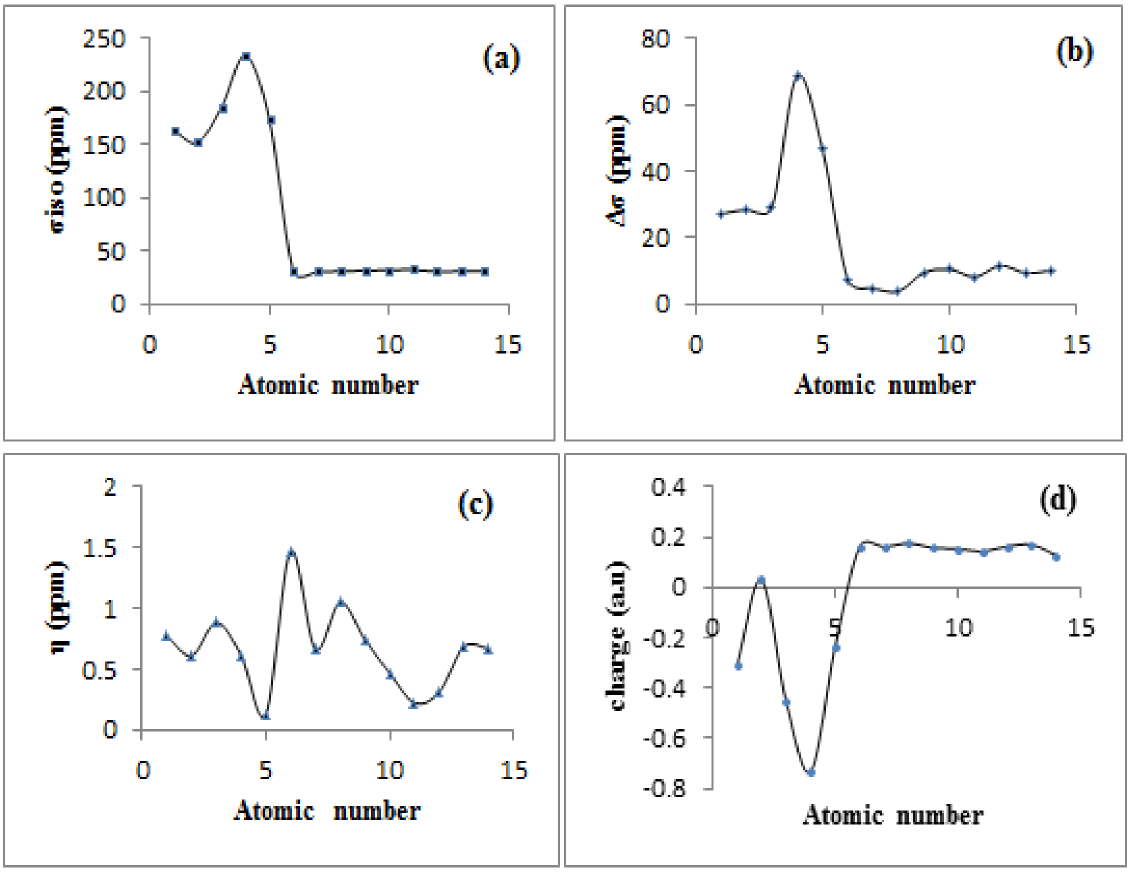

Fig. 2. Graphs of the isotropic shielding values (σ_{iso}) versus atomic number; (a) anisotropic shielding value(Δσ) versus atomic number; (b) η versus atomic number; (c) total atomic charge (a.u) versus atomic number; (d) for selected atoms of methamphetamine at the level of MP2/6-31G theories in GIAO method.

Table 3. Computed chemical shifts for selected atoms

atom number	σiso(ppm)	Δσ(ppm)	η(ppm)	Charge (a.u)
C7	162.9957	27.12495	0.770805	-0.31273
C8	152.1214	28.5115	0.609133	0.02915
C9	185.368	28.91185	0.883843	-0.45397
N	233.8801	68.69795	0.61002	-0.73359
C11	173.2191	46.6549	0.134121	-0.23831
H17	30.79367	7.4381	1.469125	0.161477
H18	30.6145	4.78425	0.661765	0.160793
H19	30.91833	3.93565	1.049903	0.174737
H20	31.58077	9.4982	0.74054	0.157462
H21	32.14153	10.50115	0.466278	0.153787
H22	32.4925	8.2095	0.222949	0.143134
H24	30.59553	11.6149	0.309688	0.162492
H25	31.0788	9.3915	0.683597	0.169746
H26	30.8365	10.14975	0.668366	0.127256

The isotropic chemical shielding σiso parameters are average of parameters, σ_{11}, σ_{22} and σ_{33}.

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