The study molecular structure of the implicit water stability and NMR-NQR tensors of mescaline

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Abstract

Mescaline or 3,4,5-trimethoxyphenethylamine is a naturally occurring psychedelic alkaloid of the phenethylamine category, known for its mind-altering effects similar to those of psilocybin. It is found in the peyote cactus, the San Pedro cactus and in the Peruvian torch and in small amounts in special members of the Fabaceae (bean) class. In this study, Density functional theory(DFT) was used to investigate the effects of implicit waters and intra-molecular interactions on the relative stability and NMR-NQR parameters of mescaline at the B3LYP/6-311++G** level of theory. Results represented that the stability and NMR-NQR tensors are affected by the implicit waters and the relative stability in the water phase is more than it is in gaseous former. Furthermore, nitrogen nucleus has higher value of chemical shielding(σ_{iso}) and NQR tensors ($\chi_{zz}$and q_{zz}) in the gas phase than water one. Natural bond orbital (NBO) analysis also showed that the lone pair electrons of nitrogen(LPN) have a higher occupancy and lower resonance energy in the water phase than the gas one. However, it can be concluded that water bulk leads to decrease of nitrogen contribution in intra-molecular interactions of mescaline. The probable reason of this phenomena can be participating of nitrogen atom in the hydrogen bond formation and inter-molecular interactions. However, the relative stability increases while NQR-NMR parameters decrease.

Keywords: mescaline, NMR-NQR tensors, implicit water molecules.

Introduction

Mescaline or 3,4,5-trimethoxyphenethylamine(see Fig.1) is a well-known member of Phenylalkylamines family. It is found in the peyote cactus, the San Pedro cactus and in the Peruvian torch and in small amounts in special members of the Fabaceae (bean) class *[1]*. Phenylalkylamines provide a category of hallucinogenic agents which are pharmacologically diverse [2]. Different properties of phenylalkylamine derivatives, (which were known to display hallucinogenic, central stimulant and …) have been studied using different fields [3]. Phenylalkylamines are one of the few types of psychotomimetic compounds whose structure–activity relationships (QSAR) have been studied [4]. Snyder and Merril first reported a correlation of hallucinogenic activity with a quantum index that was calculated using the Hückel molecular orbital theory [5].They understood that high

activity is associated with the highest occupied molecular orbital (HOMO) energy in a small number of phenylalkylamines. Moreover, some quantitative structure–activity relationship (QSAR) studies were reported recently on this class of structures [6–8].

The latest development in computer technology and software for electronic structure theory allows the calculation of quantum chemical descriptors at first principal levels, such as DFT, with a higher accuracy including some effective consideration of electron correlation effects DFT Methods are capable of calculating a variety of isolated molecular properties, such as ionization energies, dipole moment, electron affinities, electronegativities, hardness and softness, electrostatic potential *etc*., quite accurately[9-11]. since pharmacological activities are performed in solution medium. However, recognition of the electronic structure and how intra- molecular interactions is very important in these media.

In this work, we studied the effect of chemical medium(gaseous and aqueous media) on structural stability and NMR-NQR tensors of nitrogen and oxygen nuclei involved in hallucinogenic mescaline using DFT and NBO interpretation.

Computational details

Geometrical optimizations were performed at the B3LYP/6-311++G** level on mescaline. Bulk effects were modeled on the structure by using

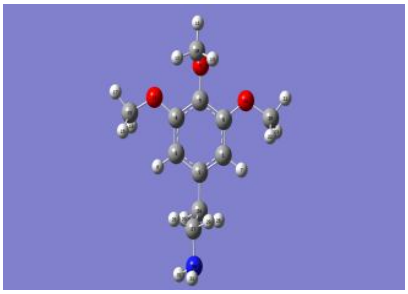

Fig.1.The optimized structure of Medazepam sedative.

Self-Consistent Reaction Field (SCRF) method which is based on a continuum model with uniform dielectric constant (ε). Tomasi's Polarized Continuum Model (PCM) defines the cavity as a union of a series of interlocking atomic spheres [12]. NBO analysis, gauge-independent atomic orbital (GIAO) and electric-field gradient (EFG)calculations were then performed at the B3LYP/6-311++G** level of theory on the optimized structure in the gas and aqueous phases [13-15].All calculations were performed by using the Gaussian program [16].

Results and discussion

In this study, effects of implicit waters and intra-molecular interactions on the relative stability of mescaline were investigated at the B3LYP/6-311++G** level of theory. The obtained results showed that the structural stability and NMR-NQR tensors are affected by the chemical media and the relative stability in the water phase is more than it is in the gaseous one(See Table 1). Also, Tables 2 represent that nitrogen nucleus has higher value of chemical shielding(σ_{iso}) and NQR tensors ($\chi_{zz}$and q_{zz}) in the gas phase than water one. Furthermore, The highest value of σ_{iso} among the considered atoms has O_9 atom in both water and gas phases. Natural bond orbital (NBO) analysis also showed that the lone pair electrons of nitrogen(LPN) have a higher occupancy and lower resonance energy in the water phase than the gas one However, it can be concluded that water bulk leads to decrease of nitrogen contribution in intra-molecular interactions of mescaline. The probable reason of this phenomena can be participating of nitrogen atom in the hydrogen bond formation and inter-molecular interactions. However, the relative stability increases while NQR-NMR parameters decrease.

Conclusion

The reported theoretical study made a suitable scheme from the important effects of water bulk and intra-molecular interactions on stability and NMR-NQR tensors of nitrogen and oxygen nuclei in hallucinogenic mescaline structure. The results showed that:

- the implicit water molecules cause to increasing the structural stability of mescaline.
- The highest value of σ_{iso} among the considered atoms has O_9 atom in both water and gas phases.

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Table 1. Calculated EFG tensors, the NQR parameters and related frequencies of ^{14}N nuclei for mescaline at the B3LYP/6-311++G**level of theory in the gas and water phases.

Dielectric constant (ε)	Nuclei	ν_+	ν_-	ν_0	χ_{zz}	η_Q	q_{zz}	q_{yy}	q_{xx}
E		10^{26}MHz					10^{20} V/m^2		
1.00	**N30**	**4.0893**	**3.7423**	**0.347**	**5.2211**	**0.1329**	**105.64**	**59.839**	**45.803**
	O9	**12.4922**	**6.7270**	**5.7651**	**12.8128**	**0.8999**	**207.1532**	**196.7893**	**10.3639**
	O14	**10.5774**	**6.7163**	**3.8611**	**11.5291**	**0.6698**	**186.3995**	**155.6264**	**30.7730**
	O19	**10.5672**	**6.7065**	**3.8607**	**11.5158**	**0.6705**	**186.1839**	**155.5136**	**30.6703**
78.39	**N30**	**3.8699**	**3.3966**	**0.4733**	**4.8443**	**0.1954**	**98.0174**	**58.5877**	**39.4297**
	O9	**12.3105**	**6.7146**	**5.5959**	**12.6834**	**0.8824**	**205.0616**	**193.0015**	**12.0600**
	O14	**10.4517**	**6.6072**	**3.8445**	**11.3726**	**0.6761**	**183.8698**	**154.0951**	**29.7747**
	O19	**10.4524**	**6.6021**	**3.8503**	**11.3697**	**0.6773**	**183.8218**	**154.1637**	**29.6582**

Table 2. **NMR chemical shielding (σ_{iso}) values calculated for nitrogen and oxygens atoms from the mescaline structure at the B3LYP/6-311++G** level of theory in the water and gaseous media.**

E	**1**	**2.023**	**4.9**	**7.58**	**20.7**	**32.63**	**38.2**	**46.7**	**78.39**
O_9									
σ_{iso}	279.7922	281.7273	283.6136	283.7808	285.1775	285.0164	284.9474	285.1192	285.4882
$\Delta\sigma_{dir}$	-	0.000	2.088	2.756	3.729	4.151	4.105	4.045	4.5952
$\Delta\sigma_{ind}$	-	0.000	-0.3426	-0.9349	-0.642	-1.213	-1.259	-1.089	-1.145
O_{14}									
σ_{iso}	233.0239	232.6436	232.5383	232.2291	232.6315	232.5757	232.5961	232.4471	232.9589
$\Delta\sigma_{dir}$	-	0.000	0.3302	0.4471	0.6553	1.0918	0.8155	0.6943	1.4309
$\Delta\sigma_{ind}$	-	0.000	-0.6001	-1.0819	-1.0853	-1.5286	-1.3733	-1.4339	-1.298
O_{19}									
σ_{iso}	*232.6900*	*232.2502*	*232.2142*	*232.0056*	*232.4466*	*232.3013*	*232.1990*	*232.2928*	*232.7518*
$\Delta\sigma_{dir}$	-	0.000	*0.333*	*0.459*	*0.721*	*0.97*	*0.879*	*0.778*	*1.439*
$\Delta\sigma_{ind}$	-	0.000	*-0.575*	*-0.922*	*-1.092*	*-1.390*	*-1.349*	*-1.326*	*-1.546*
N_{30}									
σ_{iso}	218.8706	*219.8963*	*220.8014*	*220.8679*	*221.4667*	*221.4379*	*221.4565*	*221.4094*	*221.7078*
$\Delta\sigma_{dir}$	-	0.000	*0.7074*	*2.2258*	*2.9183*	*3.0956*	*3.1204*	*3.1558*	*3.1868*
$\Delta\sigma_{ind}$	-	0.000	*-0.981*	*-1.5457*	*-1.7467*	*-2.0019*	*-1.9699*	*-2.1158*	*-1.9276*