Journal of Physical & Theoretical Chemistry
Islamic Azad University of Iran 2 (3)
(2005)
Science and Research Campus
ISSN: 1735-2126

Ab initio study , Investigation of NMR ShieldingTensors and Vibrational frequency of 5-S-cysteinyldopamine

D.M.Boghaei[1*] and A.Bagheri[2]

[1] Deparrtment of Chemistry,Sharif University of Technology,P.O.Box 11365-9516 Tehran,Iran
[2] Chemistry Department,Science and Research Campus, Islamic Azad University, Tehran, Iran

ABSTRACT

The interaction of dopamine and cysteine for formation of 5-S-cysteinyldopamine are investigated at the Hartree-Fock level theory. The structural and vibrational properties of 5-S-cysteinyldopamine are studied at level of HF/6-31G*.Interaction energy (ΔE) is calculated -771.6923 Kcal/mol Rotational energy and thermodynamic parameters around two bond have been determined using HF/3-21G. Changes of entropy during rotation around of two atom is from 119.252 to 133.016 cal/mol.K and in the case of another bond is from 111.439 to 123.55 cal/mol.K . Vibrational frequencies and isotropic shifts are interpreted

Keywords: Dopamine; Hartree-Fock; Thermodynamic parameters

INTRODUCTION

There is a considerable distance between a transmitter molecule and its effects on behavior. Neurotransmitters have been divided into there categories:a)some of simple amino acids b) classical transmitters acetylcholine c) neuropeptides.Neurotransmitter receptors and hormones both act by binding to receptors.Neurotransmitter receptors are exclusively located on the plasma membrane. Dopamine systems have been found to be important memory function [1-7]

In 1991 the pigment neuromelanine was isolated.It is interesting that neuromelanine is formed by a complex of the amino-acid cysteine with dopamine.The complex called 5-S-cysteinyldopamine carbon ring.It was identified as an intermediate in the biosynthesis of sulfur containing phenomelanine,the pigments of hen detected in the urine of normal humans irrespective of their skin and hair colours.The levels of the compound in urine of melanoma patients were significantly higher than healthy controls in particular those having metastases of malignant melanoma.It showed antitumour activity against several tumour cell lines such as murine.L1210 Leukemia and B-16 melanoma *invitro* and *invivo* [8-10].The mechanism of antitumour activity was proposed to be partly caused by hydrogen peroxide generated in the cells.

In the present exploratory theoretical study, we investigated interaction between dopamine and cysteine where is formed 5-S-cysteinyldopamine.Vibrational frequency and isotropic shift are reported.

* Corresponding author: <dboghaei@sharif.edu>

METHODS

All the calculations reported here are carried out using the Gaussian 98[11,12].The system studied by using geometry optimization consisted of dopamine and cysteine. The optimization are done with HF functional, using basis set 6-31g* and the Gaussian 98 .Structure of optimized are given in figure 1. The rotation around two bonds and Freq calculation are performed with basis set 3-21g. All NMR [13] analysis have been performed using 6-31g* basis set and HF level.GIAO [14-16] methods are used to calculate the isotropic NMR shielding at the HF/6-31G* of theory.

Interaction energy (ΔE) are calculated due to the difference between the total energies of the adduct with the sum of the component[17]:

$$\Delta E=E_{CX}-(E_{BC}-E_{AC})$$

Where ΔE is the energy of interaction, E_{CX} the complex energy, E_{BC} the energy of proton-donor component (i.e. Brönsted acid), E_{AC} the energy of proton acceptor component(i.e. Brönsted base)

RESULTS

The energies of 5-S-cysteinyldopamine and their components are listed in a summarized way in table 1

Table 1. Energies (kcal/mol) obtained for 5-S-cysteinyldopamine and their components

Compound	Energy(kcal/mol)
Dopamine	-390.15
Cysteine	-645.85
5-S-cysteinyldopamine	-1027.39

Results of the optimized structure of 5-S-cysteinyldopamine are reported.

The bond lenght of sulfur and ring carbon(number 9) is 1.7808A°.Angle of sulfur with two neighbouring carbon (number 9,21) is 98.9772°.Angle of sulfur with ring carbon binding to sulfur and the carbon binding to OH (number 9,5) is 118.513°.

Results of freq calculations are given in table 2 (in temperature 298.15°K)

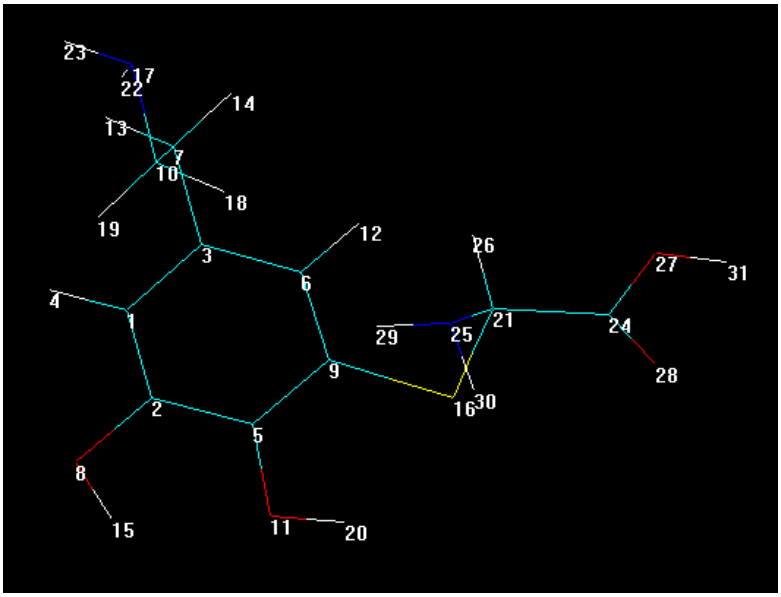

Figure 1. Optimized structure of 5-S-cysteinyldopamine.

Table 2. Thermodynamic parameters of 5-S-cysteinyldopamine

Δ G(kcal/mol)	Δ H(kcal/mol)	Δ S(cal/mol K)	Δ E(kcal/mol)
-135.42	-176.52	138.53	-771.69

Table 3. Thermochemical data during rotatation

Degree of rotation	ΔG(kcal/mol)	ΔH(kcal/mol)	ΔS(cal/mol K)	ΔE(kcal/mol)
1	-136.85	-172.64	120.64	-1023.44
2	-139.58	-173.33	113.76	-1021.86
3	-140.72	-173.78	111.44	-1021.19
4	-137.90	-174.56	123.55	-1021.80
5	-137.64	-174.29	123.53	-1022.20

Table 4. Thermochemical data during rotation

Degree of rotation	ΔG(kcal/mol)	ΔH(kcal/mol)	Δ S(cal/mol K)	ΔE(kcal/mol)
1	-134.66	-174.12	133.02	-1022.99
2	-138.12	-174.19	121.59	-1021.77
3	-138.39	-174.11	120.39	-1021.85
4	-138.63	-174.01	119.25	-1022.15
5	-136.74	-174.52	127.38	-1021.95

Energy of molecule is -1027.3873 kcal/mol . Interaction energy is -771.6923 kcal/mol.

The conformational study of 5-S-cysteinyldopamine are performed by ab initio using instruction S 5 36.0.Results of the rotation of 180° around carbon binding to N and carbon of carboxyl group(atoms of 21,24) are reported in table 3.Changes of entropy is 120.636,113.764, 111.439,123.55 and 123.527 cal/mol.K during of rotation.The lowest energy and the most enthalpy and gibss free energy are obtained with rotation of number 1.

Results of rotation about bond of sulfur and carbon binding to N (atoms of 16,21) using instruction S 5 18.0 was reported in table 4.

Changes of entropy during rotation is 133.016, 121.593, 120.386, 119.252, 127.380 cal/molK , respectively. Changes of enthalpy is insignificant. Gibss free energy with rotation of number 4 is the lowest and number 1 most,-138.631,-134.658 kcal/mol ,respectively.Energy of molecule with rotation of number 1 is the lowest and number 5 most,-1022.988,-1021.9498 kcal/mol, respectively.

Some of the frequency assignments for these compound are given in table 5.

Isotropic spectroscopic shielding for all atoms are reported in table 6.

The chemical shifts of anisotropy of C and H are calculated and isotropic shifts of atoms are decreased from isotropic shift of TMS (table 7) .

DISCUSSION

pK_1,pK_2(thiol group)pK_3 and pK of isoelectric of cysteine with ionic side chain are given in table 8.

Cysteine is binding to dopamine from direction of thiol group.Thermochemical parameters are given in table 9 when cysteine with dopamine are binding from side of carboxylat factor.Entropy and ΔE of 5-S-cysteinyldopamine is 138.532 cal/mol K and -771.6921 kcal/mol, therefore it is more stable than cysteinyldopamine.

The mechanism of formation of 5-S-cysteinyldopamine ,a putative index of oxidative stree in dopaminergic reactions of the brain,was investigated by comparing the ability of a number of neurochemically relevant oxidizing system to promote the conjugation of dopamine with cysteine in vitro[18]

In table 3 are shown that the most stable structure compaired by the most free gibss energy.

In table 4 are shown that the lowest energy and the most entropy and gibss free energy are obtained with rotation of number 1.

In table 5 a very strong band at 1815 cm^{-1} is assigned to C=O stretching vibration. Peaks of ~2800-2900 cm^{-1} are assigned to stretching vibration of CH aromatic ring. Peaks of strong intensity at ~3600-3640 cm^{-1} are assigned to phenol stretching vibration of $-NH_2$ group is observed in ~3400 cm^{-1}.

In table 6 are shown that oxygens of carboxylat group (27,28) have lower shifts than hydroxyls (8,11) . Nitrogens of amine group binding to dopamine (17) and cysteine (25) have positive shifts.Carbons of number 9 belong to ring have more shift than other carbons (1,2,3,5,6) of ring because it is binding to sulfur.

Carbons binding to OH group have Δδ of more positive than carbon binding to sulfur.

Table 5. Frequencies (cm^{-1}) of 5-S-cysteinyldopamine

Frequency (cm^{-1})	Intensity	Frequency (cm^{-1})	Intensity
3639	130	1815	413.6
3601	163	1634	2.18
3430	9.6	1618	4.32
3390	9.6	1477	193
2908	36	1425	100
2850	32.1	1159	149
2803	72.64		

Table 6. Isotropic shifts in ppm for atoms in 5-S-cysteinyldopamine

Number	Atom	Isotropic shift	Number	Atom	Isotropic shift
1	C	83.07	17	N	246.92
2	C	61.29	18	H	30.42
3	C	68.87	19	H	30.27
4	H	25.71	20	H	28.14
5	C	62.67	21	C	141.89
6	C	75.42	22	H	32.63
7	C	165.91	23	H	33.03
8	O	280.25	24	C	39.60
9	C	87.40	25	N	238.63
10	C	159.1	26	H	28.92
11	O	284.86	27	O	187.31
12	H	25.62	28	O	-21.28
13	H	30.59	29	H	31.99
14	H	30.15	30	H	31.92
15	H	28.46	31	H	27.5
16	S	549.22			

Table 7. Relatve (to TMS) shifts in ppm and parameters of $\Delta\delta$ and η for 5-S-cysteinyldopamine

number	atom	S_{iso}TMS-S_{iso} atom	$\Delta\delta$	η
1	C	118.64	-173.55	-0.79
2	C	140.42	-102.68	10.73
3	C	132.84	-157.39	0.75
4	H	7.2	-23.38	-0.28
5	C	139.04	-130.65	-0.139
6	C	126.29	-107.16	3.25
7	C	35.8	-152.7	30.78
9	C	114.31	-171.54	0.75
10	C	42.61	-139.04	0.116
12	H	7.29	-16.99	0.49
13	H	2.32	-31.18	0.029
14	H	2.76	-26.48	-0.03
15	H	4.45	-19.01	-0.0005
18	H	2.45	-29.22	0.15
19	H	2.64	-26.79	-0.069
20	H	4.77	-20.26	0.18
21	C	59.82	-147.65	-0.108
22	H	0.26	-32.4	0.14
23	H	-0.12	-29.76	0.23
24	C	162.11	-46.82	1.82
26	H	3.95	-30.13	-0.16
29	H	0.92	-26.01	0.22
30	H	0.99	-26.48	0.024
31	H	5.41	-22.99	-0.0017

Table 8. pK and pH of isoelectric of Cysteine

pK_1	pK_2(thiol group)	pK_3	$pH_{isoelectric}$
1.96	8.18	10.28	5.07

Table 9. Thermodynamic parameters of cysteinyldopamine

ΔG(kcal/mol)	Δ H(kcal/mol)	Δ S(cal/mol K)	Δ E(kcal/mol)
-149.54	-191.18	63.18	-720.52

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