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Conference paper

QUANTUM CHEMICAL CALCULATION OF GEOMETRY AND ELECTRON PARAMETERS OF RIBOFLAVIN ANION RADICAL

Boško JOVANOVIĆ[1*], Ljubica VUJISIĆ[2] and Ivan JURANIĆ[3]

[1]Center for Multidisciplinary Studies, Belgrade University,
[2]Institute of Nuclear Sciences "Vinča", Belgrade,
[3]Faculty of Chemistry, University of Belgrade, Yugoslavia.

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The semiempirical quantum chemical method AM1 (version 7.10) was applied to established the geometry, as well as the electron and spin densities of the riboflavin anion radical.

The results obtained show that the ribityl chain has a minor influence on planarity and π-electron distribution of isoalloxazine structure. Thus, the unpaired electron is predominantly localized on the isoalloxazine structure. This is substantiated by the agreement of the spin densities calculated in this paper and the experimental EPR spectroscopy data.

Key words: AM1, electron and spin densities, EPR, geometry, riboflavin anion radical

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[*] Corresponding author: Boško Jovanović, Center for Multidisciplinary Studies, University of Belgrade, 29.Novembra 142, 11000 Belgrade, F.R.Yugoslavia; fax (+381) 11 761 433; e-mail: *bole@ibiss.bg.ac.yu*

INTRODUCTION

Flavoproteins are a large group of molecules with great biological, biophysical and biochemical importance. The functioning of flavin containing enzymes is based on changes of the redox state and the structure of the flavin coenzyme, and very often different forms of flavin free radicals are appearing as an intermediary stage. Riboflavin (vitamin B2) is the basic molecular structure of some important flavin coenzymes (flavin adenine dinucleotide and flavin mononucleotide).

In order to gain information about geometry and properties of the riboflavin anión radical we performed quantum chemical calculations. Then, we compared the calculated spin densities with experimental EPR spectroscopy data to verify the established geometry and other calculated radical properties.

MATERIAL AND METHODS

Molecular geometry and electron and spin densities of the anionic riboflavin free radical were calculated by the AM1 method (version 7.10). AM1 is a semi- empirical method based on a SCF MO approximation. Semi-empirical methods are now well established procedures for calculating molecular properties and molecular geometry optimization. The only exceptions in the earlier semi-empirical methods were anion radicals, but the problem has been mostly overcome in the AM1 model (Dewar and Dieter, 1986). Generally, for the anion radicals the errors of the latest versions of AM1 calculations are in the range of the errors of very complex *ab initio* studies (except for some molecular properties such as H(1s) electron and spin densities), so we used it in our investigation of the riboflavin anion radical.

RESULTS AND DISCUSSION

Results of molecular geometry optimization and calculations of electron parameters are summarized on Fig. 1 and in Table 1. It is shown that the ribityl chain has a minor influence on planarity and π-electron distribution of the aromatic heterocyclic isoalloxazine structure. Only the N(8) atom is out of plane to some degree. So, the unpaired electron is predominantly localized on isoalloxazine structure while the ribityl chain is almost orthogonal to the aromatic heterocyclic part of a molecule. This result is in concordance with NMR and X-ray crystallographic data (Moonen *et al.*, 1984 and references cited therein).

It is well known that hyperfine coupling constants obtained from an EPR spectra are proportional to adequate H(1s) spin densities and in the case of π-electron radicals to the spin densities of a closest atomic p_z orbital included in the π system (McConnell and Chesnut, 1958; Wertz and Bolton, 1972). As pointed out by other authors (Clark, 1985), AM1 is a very good method for molecular geometry optimization, but the prediction of coupling constants from H(1s) non annihilated and annihilated calculated spin densities can fail, which is what happened in the case of the considered radical. Nevertheless, estimation of hyperfine couplings using calculated p_z spin densities (Table 2) gives good results. The range of values for the spin densities derived from the EPR spectroscopy data (Table 2), is determined by the limits of spin polarization para-

Table 1. Calculated parameters and optimized geometry of the riboflavin anion radical.

atom number	chemical symbol	bond length (angstroms)	bond angle (degrees)	twist angle (degrees)				electron density	total spin density
I		NA:I	NB:NA:I	NC:NB:NA:I	NA	NB	NC		
1	C							-4.155	0.1266511
2	C	2.808			1			-4.149	0.0270310
3	C	1.405	61.511		2	1		3.983	0.0974978
4	C	1.433	61.659	-2.799	1	2	3	-4.017	0.0185237
5	N	1.356	119.662	-176.647	4	1	2	-5.106	0.2056652
6	C	1.365	117.058	176.928	5	4	1	-4.233	0.1424805
7	C	1.454	124.037	3.091	6	5	4	3.812	0.3869800
8	N	1.407	122.388	-177.001	3	2	1	-5.194	0.0736987
9	C	1.469	118.691	-176.781	6	5	4	3.640	0.0236880
10	N	1.402	116.521	177.045	9	6	5	-5.399	0.0016149
11	C	1.416	122.721	0.382	10	9	6	3.646	0.0127940
12	N	1.351	124.201	-176.225	7	6	5	-5.355	0.0206783
13	O	1.251	126.155	-3.042	9	6	5	-6.397	0.0307842
14	O	1.259	116.725	-178.469	11	10	9	-6.429	0.0134059
15	C	1.442	120.731	12.856	8	3	2	3.997	0.0006450
16	C	1.542	116.001	-97.301	15	8	3	3.974	0.0044051
17	C	1.549	110.933	-176.153	16	15	8	-4.002	0.0003434
18	C	1.542	110.238	152.814	17	16	15	-4.006	0.0001270
19	C	1.534	110.904	172.039	18	17	16	-4.063	0.0000326
20	C	1.389	60.205	177.071	1	2	3	-4.067	0.0002197
21	C	1.401	59.861	-177.707	2	1	3	-4.147	0.1478123
22	C	1.479	119.778	-179.363	21	2	1	-4.147	0.0000462
23	C	1.482	120.109	179.828	20	1	2	-4.164	0.0000066
24	O	1.418	108.158	66.437	16	15	8	-6.328	0.0001165
25	O	1.416	108.739	32.435	17	16	15	-6.303	0.0000087
26	O	1.419	107.096	52.593	18	17	16	-6.333	0.0000017
27	O	1.419	106.357	-175.357	19	18	17	-6.334	0.0000062
28	H	1.101	179.419	-82.569	1	2	3	0.860	0.0000183
29	H	1.102	175.935	116.877	2	1	3	0.865	0.0000027
30	H	0.993	118.802	-179.351	10	9	6	0.771	0.0000013
31	H	1.126	109.013	25.391	15	8	3	0.907	0.0005639
32	H	1.131	108.564	142.812	15	8	3	0.868	0.0013839
33	H	1.124	110.304	-54.975	16	15	8	0.876	0.0000190
34	H	1.126	108.726	-87.486	17	16	15	0.914	0.0000036
35	H	1.125	109.704	-66.829	18	17	16	0.884	0.0000000
36	H	1.122	110.338	-56.018	19	18	17	0.929	0.0000000
37	H	1.122	110.495	65.438	19	18	17	0.934	0.0000002
38	H	0.966	106.845	-163.836	24	16	15	0.789	0.0002156
39	H	0.964	106.725	-173.538	25	17	16	0.814	0.0000309
40	H	0.966	106.338	-176.938	26	18	17	0.780	0.0000022
41	H	0.963	106.728	175.511	27	19	18	0.800	0.0000043
42	H	1.119	110.159	-116.449	22	21	2	0.943	0.0059357
43	H	1.117	111.438	3.851	22	21	2	0.935	0.0000310
44	H	1.119	110.469	124.392	22	21	2	0.940	0.0047959
45	H	1.117	111.414	3.463	23	20	1	0.923	0.0000000
46	H	1.119	110.324	124.016	23	20	1	0.945	0.0000063
47	H	1.119	110.208	-125.932	23	20	1	0.933	0.0000031

meters (Q) found in literature (McConnell and Chesnut, 1958; Eriksson and Ehrenberg, 1964; Wertz and Bolton, 1972) and by the precision of EPR spectra analysis. Q is proportionality constant, connecting hyperfine coupling with an adequate ρ, spin

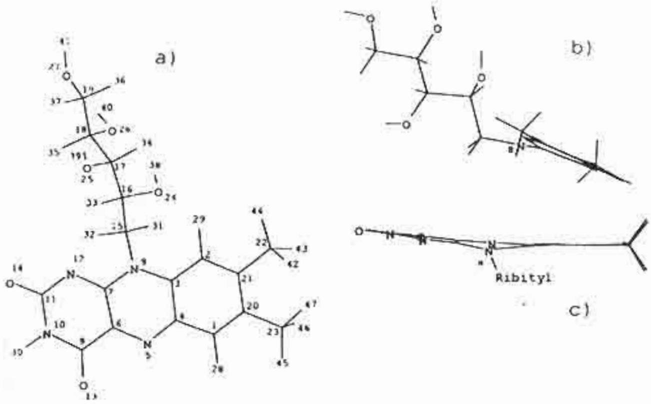

Fig. 1. **a.** *Optimized geometry of the riboflavin anion radical with atom numeration.* **b,c.** *Figures showing planarity of the heterocyclic isoalloxazine structure and the outplane position of the N(8) atom*

density.

According to literature data (Moonen *et al.*, 1984), the outplane position of the N(8) atom and its hyperfine coupling constant is independent of the substituent at N(8), but it strongly depends on the polarity of the solution. This explains why only at the N(8) atom some discrepancy appears between EPR and calculated values. EPR spectra are recorded in the aqueous solution with pH around 12, while radical properties are calculated independently of the environment.

Table 2. *Spin densities: p_z calculated and derived from EPR spectroscopy data.*

atom number and chemical symbol	1 C	2 C	5 N	8 N	10 N	12 N	20 C	21 C
AM1 calculated p_z spin densities	0.13	0.03	0.21	0.07	0	0.02	0	0.15
spin densities derived from EPR data	0.11-0.15	0.03-0.04	0.19-0.29	0.09-0.14	0	0	0.02-0.03	0.13-0.19

Good agreement of calculated spin densities with literature (Eriksson and Ehrenberg, 1964; Wertz and Bolton, 1972) and our experimental EPR spectroscopy data (Jovanović *et al.*, 1998) are proving established geometry and other calculated riboflavin anion radical properties. Moreover, all these results are in a concordance with results of our similar study (Jovanović and Vujisić, 1998) of the lumiflavin anion radical.

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