STUDY OF PEPTIDE BOND DEFORMATION IN MODEL DIPEPTIDES BY THE SEMIEMPIRICAL QUANTUM CHEMISTRY METHODS

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The relationship between spatial structure and electron-conformational properties of the L-Arg-L-Pro and D-Arg-L-Pro model di-peptides has been carried out by the CNDO/2, CNDO/m and MINDO/3 semi-empirical methods. The effects of the peptide bond deformation at the scanning energy along C-N bond were investigated. The low-energy conformational states of the di-peptides were found, the values of dihedral angles of the backbone and side chains of the amino acid residues in chemical structure of the di-peptides and the energies of intra- and inter-residues interactions were calculated. The main electronic parameters such as electron density distribution, electron and nuclear forces, total dipole moments and dipole moments of individual bonds in dependence of low-energy conformational states were analyzed. The calculation results showed that the D-izomerization of the arginine residue in the positions 1 and 2 was accompanied by the large changes of the scanning energy along C-N peptide bond. In result the following conclusion was made: C-N peptide bond in L-Arg-L-Pro dipeptide is more stable in comparison with other model dipeptide molecules.

INTRODUCTION

There are great numbers of investigations dedicated to comparative study of the dynamical properties of the amino acids and other elementary molecules formed macromolecules. The main aim of such investigations is to establish general physical and chemical principles or rules which determine the functional activity of peptides and proteins. The conformational flexibility of such molecules on an example of modified di-peptide molecules was studied in detail by Shaitan and co-authors. The relationship between chemical structure and internal dynamical mobility as well as correlation of fluctuations between side chain effective size and the length of the peptide chain in di-peptide molecules was studied in depth in these works [1-5]. The conclusion was made that there is dynamical isomorphism or similarity of the correlation functions for different torsion angles in various peptide molecules. Such investigations were carried out for L-amino acids only. But presence of D-amino acids in peptide molecules and proteins may serve several purposes. First, new three-dimensional structures can be formed that cannot be built from L-amino acids only. It was founded that D-residues may modulate the biological activity of a peptide in a subtle way, thereby increasing the biological diversity encoded by a single gene.

In this report quantum chemical calculations for the model dipeptide molecules, composed of L- and D-stereoisomers of arginine and proline amino acids, i.e. for L-Arg-L-Pro and D-Arg-L-Pro were carried out by the CNDO/2, CNDO/m and MINDO/3 semiempirical methods. At first, theoretical conformational analysis was used to study the spatial structure and conformational properties of mentioned above dipeptide molecules. The low-energy conformations of these molecules were found, the values of dihedral angles of the backbone and side chains of the amino acid residues and the energies of intra- and inter-residual interactions were calculated. Calculation models were constructed on the base of coordinates of atoms in accordance with results of theoretical conformational analysis. The main electronic parameters such as electron density distribution, electron and nuclear forces, total dipole moments and dipole moments of individual bonds in dependence of low-energy conformational state were analyzed.

MODELS AND CALCULATION METHODS

The investigations were carried out using the theoretical conformational analysis as described in [6]. The conformational potential energy of the di-peptide molecule is given as the sum of the independent contributions of nonvalent (E_{nv}), electrostatic (E_{el}), torsional interactions (E_{tor}) and hydrogen bonds (E_{hb}). The energy of nonvalent interactions was described by the Lennard-Jones 6-12 potential with the parameters proposed by Scott and Sheraga. The contribution of electrostatic interactions was taken into account in a monopole approximation corresponding to Coulomb's law with partial charges of atoms as suggested by Scott and Sheraga. The effective dielectric constant ε was taken to be equal to ten, as described by Lipkind et al. A torsion energy was calculated using the value of internal rotation barriers given by Momany et al. Hydrogen bonding energy was calculated based on Morze potential and dissociation energy of the hydrogen bond was taken to be 6.3kJ/mol. A rigid valence scheme of the molecule was assumed, namely, the searches were made only on torsion angles. The nomenclature and conventions adopted are those recommended by IUPAC-IUB. Low-energy conformational states for L-Arg-L-Pro and D-Arg-L-Pro di-peptide molecules constructed by using program package [7] were shown on fig.1. In order to reduce the edge effect the *N*-terminus was modified by acetyl (ACE) and C-termius was modified by M-methylamine (NME) resulted in formation of two additional peptide bonds (fig.1). The detail study of such modification effects on the effective atomic charges in peptides had been carried out in [8].

Quantum chemical calculations were carried out by the CNDO/2, CNDO/m and MINDO/3 semi empirical methods on the base of the complex program LEV. The program worked out at the Institute named after Vernadsky at the Russian Academy of Sciences [9-14]. Calculation models were constructed on the base of coordinates of atoms in accordance with results of theoretical conformational analysis (fig.2).

At applying to big biological systems and other compounds the semi empirical methods due to correctly choosing parameters (holding for little range molecules) give more correct results in comparison to *ab initio* methods. Such parameters have not physical mean, but they correctly can

reproduce explicit properties of the molecular systems. For example, parameters choosen for CNDO/2 method can reproduce correctly the orbital energies difference for main state of the system. Coefficients of expansion of molecular orbital (MO) as combination of atomic orbital also coincide with results of *ab initio* calculations at the same basis (in this case the electron density is parameter).

Table 1.

Dihedral angles (in degree) in low-energy conformations of L-Arg-L-Pro and D-Arg-L-Pro di-peptides using in quantum chemical calculations

	L-Arg-L-Pro									
	ω_1	φ_1	χ_1	χ_2	χ_3	χ_4	Ψ_1	ω_2	Ψ_2	Energy, kJ/mol
	179	-132	187	272	200	187	75	181	-55	-5.86
	180	-130	190	278	200	189	89	179	146	-10.89
	179	-137	-82	195	168	200	125	200	138	6.70
	180	51	-77	236	188	195	88	171	162	21.35
	180	-133	186	273	202	189	81	180	-55	-7.95
	180	-137	-78	193	168	198	118	192	-71	-2.93
	D-Arg-L-Pro									Energy, kJ/mol
	ω_1	φ_1	χ_1	χ_2	χ_3	χ_4	Ψ_1	ω_2	Ψ_2	
	182	50	69	165	178	167	67	189	-64	-5.44
	179	-210	86	165	171	178	-106	180	155	-9.21
	182	49	68	166	180	168	69	189	124	-1.67

*Note: Conformations with minimal value of conformational energy are in gray.

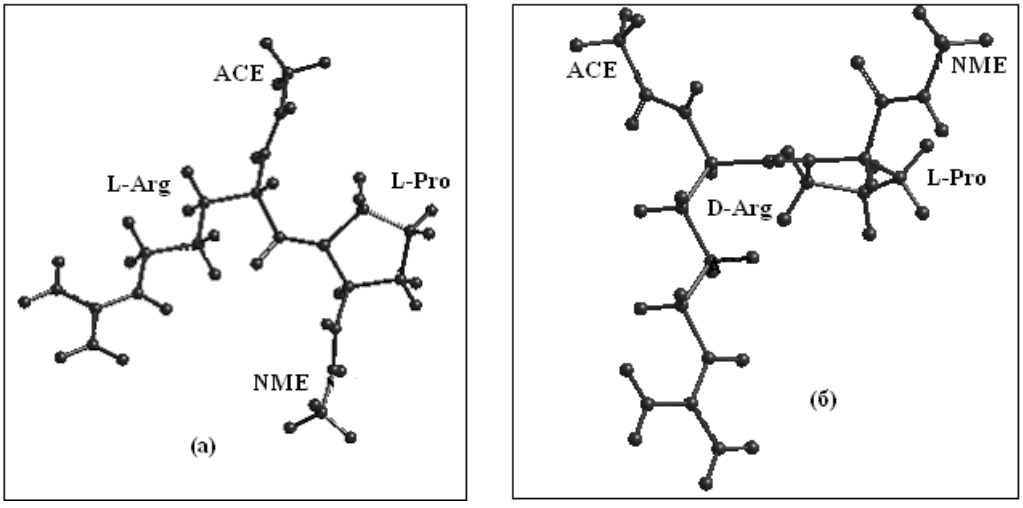

Fig.1. Low-energy conformational states of L-Arg-L-Pro and D-Arg-L-Pro calculated by the theoretical conformational analysis method

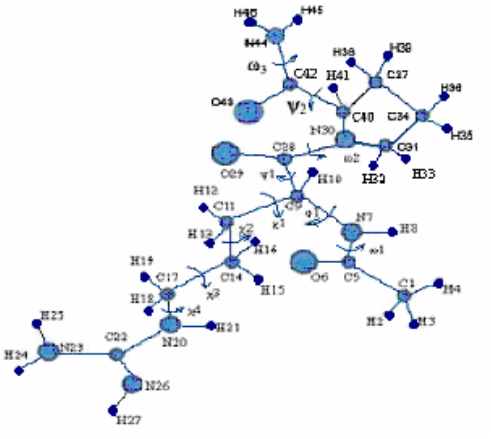

Fig.2. Calculation model with atoms numbering

At calculations of the main state of systems with open and closed shells for geometry and total energy minimization preferably must be used the method MINDO/3. In this method heat energy is considered as parameter which depends on atoms properties and their pair combination. Furthermore, the orbital exponential factors using for integral calculations also are parameters in the MINDO/3 method. In result, the accuracy of the calculated heat energy is ~16.7 kJ/mol, and ionization potential is ~0.35 eV. At the same time the spectral parameters, hydrogen bonds parameters and repulsion of the unshared electron pair were described unsatisfactorily in this method.

RESULTS AND DISCUSSION

Electron energy and changing limit of charges on several atoms of the peptide group in different conformational states of the Arg-L-Pro and D-Arg-L-Pro di-peptide molecules calculated by various semi empirical methods are shown in Table 2 and 3. According to calculation results the charge distribution on atoms slowly depends on conformational changes in spatial structures of di-peptides. Considerable differences observed for atoms of the peptide group at which the changing in absolute value of charges for atoms of the peptide group connected arginine and proline residue into L-Arg-L-Pro dipeptide were more greater than that in the D-Arg-L-Pro dipeptide (Table 3).

Table 2.

Partial charges and change limit (in units of electron charge) for several atoms of the L-Arg-L-Pro and D-Arg-L-Pro di-peptides according to quantum chemical calculations

CNDO/2 calculations											
Atom number	L-Arg-L-Pro di-peptide conformations							D-Arg-L-Pro di-peptide conformations			
	VR1	VR2	VR3	VR4	VR5	VR6	Δq	VR1	VR2	VR3	Δq
O6	-0.369	-0.370	-0.374	-0.360	-0.370	-0.373	0.014	-0.365	-0.374	-0.369	0.009
N7	-0.198	-0.198	-0.207	-0.206	-0.198	-0.207	0.009	-0.221	-0.207	-0.219	0.014
H8	0.124	0.124	0.127	0.106	0.126	0.129	0.023	0.104	0.127	0.107	0.023
C9	0.083	0.076	0.091	0.078	0.084	0.093	0.017	0.102	0.089	0.097	0.013
H10	0.003	0.006	-0.004	0.007	0.003	-0.004	0.011	0.014	-0.005	0.008	0.019
C11	0.002	0.004	0.006	0.005	0.003	0.009	0.007	0.005	0.012	0.005	0.007
C28	0.298	0.314	0.296	0.320	0.299	0.290	0.030	0.298	0.303	0.305	0.007
O29	-0.323	-0.338	-0.334	-0.304	-0.326	-0.320	0.034	-0.315	-0.322	-0.328	0.013
N30	-0.180	-0.171	-0.165	-0.184	-0.179	-0.172	0.019	-0.172	-0.174	-0.166	0.008
C31	0.115	0.117	0.119	0.122	0.116	0.117	0.007	0.117	0.119	0.120	0.003
H41	-0.001	-0.018	-0.020	-0.009	0.001	0.002	0.018	0.005	-0.015	-0.020	0.025
C42	0.352	0.356	0.358	0.355	0.352	0.351	0.007	0.351	0.355	0.356	0.005
O43	-0.353	-0.365	-0.366	-0.367	-0.352	-0.346	0.020	-0.347	-0.358	-0.372	0.025
N44	-0.245	-0.242	-0.241	-0.243	-0.245	-0.246	0.005	-0.248	-0.244	-0.239	0.009
CNDO/m calculations											
Atom number	L-Arg-L-Pro di-peptide conformations							D-Arg-L-Pro di-peptide conformations			
	VR1	VR2	VR3	VR4	VR5	VR6	Δq	VR1	VR2	VR3	Δq
O6	-0.642	-0.642	-0.647	-0.610	-0.642	-0.647	0.037	-0.621	-0.649	-0.628	0.028
N7	-0.606	-0.606	-0.633	-0.658	-0.605	-0.632	0.053	-0.685	-0.634	-0.682	0.051
H8	0.282	0.282	0.288	0.253	0.285	0.290	0.037	0.260	0.290	0.264	0.030
C9	0.139	0.125	0.157	0.146	0.140	0.159	0.034	0.185	0.151	0.177	0.008
H10	0.094	0.100	0.092	0.097	0.094	0.092	0.008	0.118	0.093	0.110	0.025
C11	-0.138	-0.140	-0.119	-0.115	-0.139	-0.125	0.025	-0.142	-0.117	-0.129	0.025
C28	0.605	0.630	0.603	0.668	0.604	0.597	0.071	0.648	0.626	0.656	0.030
O29	-0.593	-0.612	-0.596	-0.567	-0.594	-0.571	0.045	-0.586	-0.588	-0.615	0.029
N30	-0.541	-0.519	-0.524	-0.549	-0.541	-0.542	0.030	-0.531	-0.533	-0.515	0.018
C31	0.096	0.100	0.099	0.109	0.096	0.097	0.013	0.102	0.103	0.105	0.002
H41	0.087	0.059	0.055	0.072	0.089	0.091	0.036	0.096	0.057	0.059	0.039
C42	0.701	0.704	0.712	0.705	0.700	0.696	0.016	0.695	0.700	0.708	0.013
O43	-0.594	-0.607	-0.614	-0.623	-0.593	-0.574	0.049	-0.579	-0.583	-0.635	0.056
N44	-0.706	-0.705	-0.701	-0.707	-0.707	-0.721	0.020	-0.724	-0.709	-0.694	0.030

MINDO/3 calculations											
Atom number	L-Arg-L-Pro di-peptide conformations							D-Arg-L-Pro di-peptide conformations			
	VR1	VR2	VR3	VR4	VR5	VR6	Δq	VR1	VR2	VR3	Δq
O6	-0.591	-0.592	-0.597	-0.573	-0.592	-0.597	0.024	-0.587	-0.598	-0.593	0.011
N7	-0.182	-0.178	-0.191	-0.212	-0.180	-0.192	0.034	-0.233	-0.192	-0.228	0.041
H8	0.103	0.103	0.109	0.074	0.106	0.112	0.038	0.075	0.111	0.079	0.036
C9	0.084	0.071	0.097	0.079	0.086	0.096	0.025	0.103	0.090	0.098	0.013
H10	-0.004	0.001	-0.015	0.002	-0.005	-0.014	0.016	0.033	-0.014	0.024	0.047
C11	0.034	0.034	0.042	0.047	0.032	0.052	0.020	0.036	0.056	0.036	0.020
C28	0.542	0.566	0.541	0.590	0.541	0.537	0.053	0.569	0.565	0.579	0.010
O29	-0.566	-0.584	-0.582	-0.531	-0.568	-0.560	0.053	-0.553	-0.572	-0.581	0.028
N30	-0.226	-0.193	-0.185	-0.219	-0.224	-0.211	0.041	-0.217	-0.197	-0.196	0.021
C31	0.155	0.158	0.164	0.169	0.158	0.160	0.014	0.163	0.163	0.167	0.004
H41	0.011	-0.037	-0.044	-0.027	0.012	0.011	0.056	0.018	-0.030	-0.040	0.058
C42	0.600	0.603	0.609	0.606	0.599	0.599	0.010	0.598	0.601	0.604	0.008
O43	-0.558	-0.584	-0.584	-0.592	-0.558	-0.547	0.045	-0.546	-0.575	-0.600	0.054
N44	-0.216	-0.206	-0.204	-0.208	-0.217	-0.218	0.014	-0.222	-0.210	-0.194	0.028

Table 3.

Partial charges and change limit (in units of electron charge) several atoms of the L-Arg-L-Pro and D-Arg-L-Pro di-peptides according to quantum chemical calculations

Atom	CNDO/2		CNDO/m		MINDO/3	
	L-Arg-L-Pro	D-Arg-L-Pro	L-Arg-L-Pro	D-Arg-L-Pro	L-Arg-L-Pro	D-Arg-L-Pro
O_6	-0.360÷ -0.374	0.365 ÷-0.374	-0.610÷-0.647	-0.621÷-0.649	-0.573÷-0.597	-0.587÷-0.593
N_7	-0.198÷ -0.207	-0.207 ÷-0.219	-0.605÷-0.632	-0.634÷-0.685	-0.178÷-0.212	-0.192÷-0.233
O_{29}	-0.304÷ -0.338	-0.315 ÷-0.328	-0.567÷-0.612	-0.586÷-0.615	-0.531÷-0.584	-0.553÷-0.581
N_{30}	-0.165÷ -0.184	-0.166÷ -0.174	-0.519÷-0.549	-0.515÷-0.531	-0.185÷-0.226	-0.196÷-0.217
O_{43}	-0.346÷ -0.367	-0.347 ÷-0.372	-0.574÷-0.623	-0.579÷-0.635	-0.547÷-0.592	-0.546÷-0.600
N_{44}	-0.241÷ -0.246	-0.239÷ -0.248	-0.701÷-0.721	-0.694÷-0.724	-0.204÷-0.218	-0.194÷-0.222

*Note: Peptide bond atoms connected arginine and proline amino acids marked out by gray color

For comparison the values of the partial atomic charges and bonds dipole moments in the dipeptide molecules having identical values amino acids main and side chains dihedral angles are represented in table 4 and 5. It is well known that dipole moment and polarizability are the most important characteristics of the molecules. Dipole moment strongly effects on the electric and optic properties of the molecules. Due to this additive property the dipole moment can be represented as a sum of separate valence bonds dipole moments. As shown from Table 4 the dipole moments of the peptide bonds are sensible to conformational changes (in range of 0.2÷0.4D). As followed from comparison the greatest difference was observed for peptide group bonds, particularly for $C_{28}O_{29}N_{30}$, C_9-C_{11} and C_{11}-C_{14} bonds (Table 5). Conformation VR4 of the L-Arg-L-Pro dipeptide has minimal value of the $C_{28}O_{29}$ dipole moment and maximal value of the bond dipole moment difference was observed for $C_{28}N_{30}$ at the same conformational state. At comparison of the bonds dipole moments for conformation VR4 in L-Arg-L-Pro and conformation VR3 in D-Arg-L-Pro (Table 1), it was shown that all peptide groups in D-Arg-L-Pro have greater absolute value of the dipole moments. A big difference in CN bond peptide dipole moment also was observed.

Table 4.

Bond dipole moment (in debay) and its change limits in L-Arg-L-Pro and D-Arg-L-Pro di-peptides according to quantum chemical calculations

CNDO/2											
Bond	L-Arg-L-Pro							D-Arg-L-Pro			
	VR1	VR 2	VR3	VR4	VR 5	VR 6	Δ	VR1	VR 2	VR 3	Δ
C1C5	+0.069	+0.089	+0.113	+0.094	+0.071	+0.090	0.044	+0.096	+0.102	+0.104	0.008
C5O6	-2.180	-2.184	-2.207	-2.128	-2.184	-2.204	0.079	-2.159	-2.208	-2.180	0.049
C5N7	+0.094	+0.118	+0.165	+0.076	+0.100	+0.142	0.089	+0.103	+0.154	+0.130	0.051
N7H8	+0.597	+0.595	+0.611	+0.509	+0.606	+0.619	0.110	+0.501	+0.612	+0.512	0.111
N7C9	+0.617	+0.642	+0.736	+0.780	+0.613	+0.696	0.163	+0.925	+0.725	+0.925	0.200

C9C11	+0.037	+0.054	+0.236	+0.130	+0.037	+0.139	0.199	+0.125	+0.155	+0.242	0.117
C11H12	-0.011	-0.020	+0.069	+0.088	-0.007	+0.076	0.108	+0.093	-0.023	+0.135	0.158
C11H13	+0.067	+0.048	+0.083	+0.092	+0.061	-0.026	0.118	-0.034	+0.057	+0.044	0.091
C11C14	-0.057	-0.013	-0.024	-0.160	-0.057	+0.006	0.166	+0.008	+0.021	-0.044	0.065
C9C28	-0.025	+0.020	-0.101	+0.067	-0.026	-0.054	0.168	+0.003	-0.009	-0.037	0.040
C28O29	-1.908	-1.995	-1.975	-1.799	-1.927	-1.889	0.196	-1.860	-1.900	-1.936	0.076
C28N30	+0.141	+0.174	+0.164	-0.042	+0.153	+0.144	0.216	+0.114	+0.115	+0.116	0.002
N30C31	+0.755	+0.759	+0.730	+0.671	+0.756	+0.721	0.088	+0.698	+0.729	+0.702	0.031
C37C40	-0.134	-0.213	-0.211	-0.135	-0.133	-0.095	0.118	-0.082	-0.168	-0.194	0.112
C40N30	-0.654	-0.622	-0.598	-0.573	-0.659	-0.632	0.086	-0.624	-0.613	-0.584	0.040
C40H41	-0.004	-0.094	-0.107	-0.047	+0.003	+0.009	0.116	+0.025	-0.080	-0.105	0.130
C40C42	+0.072	+0.051	+0.069	+0.018	+0.071	+0.093	0.075	+0.061	+0.070	+0.046	0.024
C42O43	-2.083	-2.155	-2.160	-2.165	-2.081	-2.045	0.120	-2.048	-2.115	-2.196	0.148
C42N44	+0.063	+0.098	+0.106	+0.091	+0.060	+0.048	0.058	+0.025	+0.080	+0.137	0.112
CNDO/m											
Bond	L-Arg-L-Pro							D-Arg-L-Pro			
	VR1	VR2	VR3	VR4	VR5	VR6	Δ	VR1	VR2	VR3	Δ
C1C5	-0.142	-0.099	-0.064	-0.019	-0.143	-0.112	0.124	-0.038	-0.101	-0.013	0.088
C5O6	-3.791	-3.794	-3.825	-3.602	-3.794	-3.822	0.223	-3.671	-3.833	-3.712	0.161
C5N7	-0.649	-0.609	-0.548	-0.729	-0.645	-0.588	0.181	-0.694	-0.577	-0.635	0.117
N7H8	+1.354	+1.353	+1.382	+1.216	+1.370	+1.391	0.175	+1.251	+1.394	+1.267	0.143
N7C9	+1.544	+1.589	+1.803	+2.016	+1.519	+1.736	0.497	+2.194	+1.759	+2.217	0.458
C9C11	+0.322	+0.321	+0.612	+0.539	+0.297	+0.419	0.315	+0.258	+0.387	+0.512	0.254
C11H12	+0.437	+0.434	+0.511	+0.584	+0.446	+0.524	0.150	+0.611	+0.379	+0.662	0.283
C11H13	+0.564	+0.522	+0.600	+0.634	+0.549	+0.440	0.194	+0.346	+0.488	+0.476	0.142
C11C14	-0.067	+0.007	-0.073	-0.324	-0.078	-0.017	0.331	-0.043	+0.032	-0.138	0.170
C9C28	-0.399	-0.298	-0.535	-0.203	-0.410	-0.427	0.332	-0.167	-0.326	-0.283	0.159
C28O29	-3.504	-3.616	-3.519	-3.352	-3.507	-3.370	0.264	-3.462	-3.474	-3.632	0.170
C28N30	-0.432	-0.384	-0.520	-0.836	-0.431	-0.553	0.452	-0.555	-0.541	-0.518	0.037
N30C31	+1.780	+1.769	+1.700	+1.607	+1.776	+1.707	0.173	+1.669	+1.713	+1.674	0.044
C37C40	-0.230	-0.387	-0.364	-0.286	-0.227	-0.170	0.217	-0.177	-0.298	-0.386	0.209
C40N30	-1.538	-1.453	-1.407	-1.338	-1.544	-1.490	0.206	-1.449	-1.439	-1.370	0.079
C40H41	+0.455	+0.309	+0.291	+0.377	+0.465	+0.474	0.183	+0.502	+0.300	+0.310	0.202
C40C42	-0.205	-0.274	-0.227	-0.391	-0.212	-0.209	0.186	-0.300	-0.162	-0.329	0.167
C42O43	-3.511	-3.586	-3.629	-3.678	-3.505	-3.392	0.286	-3.422	-3.442	-3.754	0.332
C42N44	-0.851	-0.849	-0.814	-0.858	-0.861	-0.953	0.139	-0.995	-0.885	-0.746	0.249
MINDO/3											
Bond	L-Arg-L-Pro							D-Arg-L-Pro			
	VR1	VR2	VR3	VR4	VR5	VR6	Δ	VR1	VR2	VR3	Δ
C1C5	+0.122	+0.156	+0.193	+0.192	+0.121	+0.148	0.072	+0.172	+0.167	+0.190	0.023
C5O6	-3.490	-3.495	-3.528	-3.383	-3.497	-3.524	0.145	-3.467	-3.531	-3.506	0.064
C5N7	+0.030	+0.076	+0.143	+0.009	+0.040	+0.095	0.131	+0.043	+0.115	+0.107	0.072
N7H8	+0.493	+0.492	+0.525	+0.354	+0.510	+0.539	0.185	+0.360	+0.531	+0.379	0.171
N7C9	+0.585	+0.606	+0.725	+0.976	+0.558	+0.658	0.418	+1.145	+0.696	+1.154	0.458
C9C11	+0.174	+0.162	+0.387	+0.407	+0.143	+0.203	0.264	+0.112	+0.240	+0.349	0.237
C11H12	-0.081	-0.091	+0.019	+0.046	-0.071	+0.033	0.137	+0.084	-0.155	+0.176	0.331
C11H13	+0.072	+0.034	+0.051	+0.148	+0.056	-0.185	0.333	-0.211	-0.018	-0.064	0.193
C11C14	-0.061	-0.005	-0.022	-0.213	-0.073	+0.037	0.250	+0.025	+0.069	-0.072	0.141
C9C28	-0.147	-0.051	-0.227	+0.030	-0.149	-0.111	0.257	+0.094	-0.059	-0.027	0.153
C28O29	-3.343	-3.452	-3.439	-3.137	-3.354	-3.306	0.146	-3.268	-3.378	-3.430	0.162
C28N30	+0.025	+0.074	+0.070	-0.359	+0.040	+0.052	0.432	-0.021	-0.009	-0.012	0.012
N30C31	+0.856	+0.811	+0.775	+0.634	+0.856	+0.807	0.222	+0.773	+0.761	+0.750	0.023
C37C40	-0.113	-0.289	-0.285	-0.159	-0.112	-0.051	0.238	-0.013	-0.215	-0.248	0.235
C40N30	-0.749	-0.620	-0.596	-0.512	-0.753	-0.724	0.241	-0.725	-0.608	-0.610	0.117
C40H41	+0.056	-0.195	-0.229	-0.143	+0.065	+0.056	0.294	+0.094	-0.159	-0.208	0.302
C40C42	+0.231	+0.183	+0.255	+0.142	+0.227	+0.299	0.157	+0.249	+0.204	+0.209	0.045
C42O43	-3.296	-3.448	-3.453	-3.498	-3.294	-3.232	0.266	-3.226	-3.395	-3.542	0.316
C42N44	-0.065	+0.035	+0.063	+0.038	-0.069	-0.072	0.135	-0.114	+0.008	+0.153	0.267

Table 5.

Bonds dipole moments change limits in L-Arg-L-Pro and D-Arg-L-Pro di-peptides according to quantum chemical calculations

Bond	CNDO/2		CNDO/m		MINDO/3	
	L-Arg-L-Pro	D-Arg-L-Pro	L-Arg-L-Pro	D-Arg-L-Pro	D-Arg-L-Pro	L-Arg-L-Pro
C_5-O_6	-2.184 ÷ -2.204	-2.180÷-2.159	-3.602÷ -3.825	-3.671÷ -3.833	-3.383÷ -3.528	-3.467÷ -3.531

C_5-N_7	0.094÷ 0.165	0.103÷0.154	-0.548÷ -0.729	-0.577÷ -0.694	+0.009÷+0.143	+0.043÷+0.115
C_{28}-O_{29}	-1.799÷ -1.995	-1.86÷-1.94	-3.352÷ -3.616	-3.462÷ -3.632	-3.137÷ -3.452	-3.268÷ -3.430
C_{28}-N_{30}	-0.042÷ +0.174	+0.114÷+0.116	-0.384÷ -0.836	-0.518÷ -0.555	-0.359÷ +0.074	-0.009÷ -0.021
C_{42}-O_{43}	-2.045÷ -2.165	-2.048÷ -2.196	-3.392÷ -3.678	-3.422÷ -3.754	-3.232÷ -3.498	-3.226÷ -3.395
C_{42}-N_{44}	0.048÷ 0.106	0.025÷ 0.137	-0.814÷ -0.953	-0.746÷ -0.995	-0.072÷ +0.063	-0.114÷ +0.153

In general, the conclusion was made that CNDO/m and MINDO/3 methods are more sensible to charge changing and dipole moments variations in dipeptides in comparison with CNDO/2 method. Total dipole moments of the investigated dipeptides are shown in Table 6.

Table 6.

Total dipole moments of the L-Arg-L-Pro and D-Arg-L-Pro di-peptides in different conformational states (in debay)

Method	L-Arg-L-Pro						D-Arg-L-Pro		
	VR 1	VR 2	VR 3	VR 4	VR 5	VR 6	VR 1	VR 2	VR 3
CNDO/2	5.47	9.77	10.22	9.42	5.02	5.05	9.17	8.59	7.17
CNDO/m	8.61	13.71	13.27	13.14	7.88	7.03	13.05	11.01	10.70
MINDO/3	4.81	8.69	9.09	8.74	4.36	4.20	9.12	7.16	6.57

The total dipole moment for conformation VR4 in L-Arg-L-Pro and for conformation VR3 in D-Arg-L-Pro totally differs one from another. The value of the dipole moment in D-Arg-L-Pro is smaller than that in L-Arg-L-Pro. Obviously it is resulted from contributions of the side chains different conformational states.

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Table 7 summarized the result of the total electron energy calculations of the investigated dipeptide molecules. The calculation results are coinciding with conformational analysis data. Conformation VR2 has minimal value of the conformational energy due to calculations by both semiempirical methods and conformational search.

Table 7.

Total electron energy of L-Arg-L-Pro and D-Arg-L-Pro di-peptides in different conformational states (in kJ/mol)

Method	L-Arg-L-Pro di-peptide low-energy conformational states					
	VR 1	VR 2	VR 3	VR 4	VR 5	VR 6
CNDO/2	-619959.3	-619985.7	-619941.8	-619944.4	-619963.7	-619917.9
CNDO/m	-404276.7	-404321.4	-404284.8	-404238.8	-404289.3	-404259.7
MINDO/3	-394597.0	-394634.6	-394603.1	-394589.1	-394602.5	-394555.6
Method	D-Arg-L-Pro di-peptide low-energy conformational states					
	VR 1		VR 2		VR 3	
CNDO/2	-619899.0		-619924.2		-619922.4	
CNDO/m	-404179.0		-404269.1		-404190.7	
MINDO/3	-394515.2		-394604.8		-394554.8	

*Note: Conformation numbering corresponds to Table 1.

Quantum-chemical part of the LEV program allows to calculate potential curves, corresponded to the given bond deformation. Changing of the atomic partial charges at the bond dissociation and other parameters also can be calculated. The scanning was made along C_{28}-N_{30} bond increasing in length. Initial value of the bond length corresponded to the peptide bond length in dipeptide was choose as 1.36Å. The following step includes moving of the segment connected to flexible atom N_{30}, which recessive from fixed C_{28} atom by the step 0.1Å. The final bond length was 1.4Å. The energy minimal values and energy value corresponded to the dissociation limit at the scanning along $C_{28}N_{30}$ bond by the various quantum chemical calculations are shown in Table 8. Changing in total energy and partial charges of the peptide group atoms at the scanning along $C_{28}N_{30}$ bond as well as energy at each iteration step in the identical conformational states of the dipeptides also are given in Table 9 and 10. (Table 10 describes changing in charges at the bond deformation but not their absolute values).

Table 8.

Energy minimum *(E_{min})* and dissociation limit *(E_{lim})* of the $C_{28}N_{30}$ bond in L-Arg-L-Pro and D-Arg-L-Pro dipeptides (in kJ/mol)

		CNDO/2		CNDO/m		MINDO/3	
		L-Arg-L-Pro	D-Arg-L-Pro	L-Arg-L-Pro	D-Arg-L-Pro	L-Arg-L-Pro	D-Arg-L-Pro
VR1	E_{min}	-1892.4	-1902.4	-272.4	-207.0	-592.3	-524.7
	E_{lim}	-6180671.1	-617996.4	-404812.3	-404834.7	-394004.9	-393990.6
VR2	E_{min}	-1874.9	-1851.1	-206.3	-166.5	-606.1	-593.1
	E_{lim}	-618111.4	-618072.6	-404915.6	-404939.5	-394028.8	-394011.3
VR3	E_{min}	-1874.3	-16.95.6	-194.2	-242.1	-576.5	-530.7
	E_{lim}	-618068.4	-618226.4	-404941.0	-404848.1	-394026.8	-394023.7
VR4	E_{min}	-1911.6		-313.7		-579.0	
	E_{lim}	-618032.6		-404798.3		-394010.0	
VR5	E_{min}	-1896.2		-275.6		-501.5	

	E_{lim}	-618067.3		-404813.6		-394100.8	
VR6	E_{min}	-1860.4		-252.1		-557.8	
	E_{lim}	-618057.5		-404851.1		-393997.7	

Table 9.

Changing in total energy (in kJ/mol) at the energy scanning along C_{28}-N_{30} bond for identical conformations of di-peptide molecules

L-Arg-L-Pro dipeptide					D-Arg-L-Pro dipeptide				
CNDO/2									
Dissociation energy limit……..-618032.6					Dissociation energy limit .....-618226.4				
Minimal energy ..... -1911.6					Minimal energy .....-1695.6				
-1911.6	-1899.4	-1777.1	-1639.8	-1478.6	-1695.6	-1676.2	-1566.8	-1391.9	-1225.0
-1297.4	-1137.0	-987.5	-871.8	-750.9	-1066.3	-897.4	-736.8	-601.0	-486.0
-660.2	-573.1	-511.1	-459.6	-418.7	-391.2	-316.1	-252.8	-210.4	-174.4
-384.8	-356.7	-367.3	-356.5	-357.6	-149.7	-131.8	-161.4	-151.2	-144.0
- 331.4	-364.1	-344.4	-325.8	-344.3	-141.8	-137.1	-133.6	-131.8	-116.7
-337.1	-326.7	-334.8			-122.5	-116.1	-115.6		
CNDO/m									
Dissociation energy limit …….-404798.3					Dissociation energy limit ……-404848.1				
Minimal energy..... -313.7					Minimal energy ……. -242.1				
559.6	225.5	14.3	-129.7	-217.5	657.2	323.9	97.5	-47.5	-139.1
-270.3	-297.3	-310.7	-313.7	-311.8	-193.4	-223.4	-238.3	-242.1	-240.8
-306.0	-300.3	-292.2	-283.5	-278.3	-236.8	-231.5	-226.1	-221.7	-216.1
-271.3	-283.5	-253.8	-247.7	-242.4	-207.9	-204.2	-194.9	-191.6	-187.4
-232.8	-227.2	-223.0	-218.1	-213.8	-186.7	-183.6	-180.6	-178.0	-175.2
-209.4	-209.8	-206.4			-172.7	-174.0	-174.4		
MINDO/3									
Dissociation energy limit ……..-394010.0					Dissociation energy limit ……-394023.7				
Minimal energy.....-579.0					Minimal energy.....-530.7				
-578.4	-579.0	-554.8	-531.6	-465.5	-530.3	-530.7	-505.6	-466.0	-419.3
-424.8	-378.4	-332.8	-291.8	-258.8	-372.0	-332.4	-287.1	-249.6	-217.8
-229.4	-206.3	-187.4	-181.0	-160.1	-189.1	-168.4	-149.7	-132.9	-124.8
-159.5	-152.3	-146.8	-142.9	-136.3	-110.5	-101.3	-94.7	-89.9	-83.3
-132.2	-127.6	-124.8	-120.5	-117.6	-78.8	-74.7	-70.5	-67.1	-63.9
-109.5	-107.3	-107.8			-61.1	-58.8	-56.0		

*Note: In table the values of the bond energy are corresponded to each step of iteration.

Table 10.

Changing in partial charges of the peptide group atoms at the energy scanning along C_{28}-N_{30} bond for identical conformations of di-peptide molecules

U (kJ/mol)											
L-Arg-L-Pro (Conformation VR4, table 1)						D-Arg-L-Pro (Conformation VR3, table 1)					
CNDO/2											
C28	0.611	0.597	0.585	0.574	0.567	C28	0.272	0.257	0.243	0.231	0.221
0.562	0.559	0.558	0.560	0.562	0.563	0.212	0.207	0.204	0.200	0.199	0.201
0.564	0.566	0.567	0.568	0.571	0.574	0.198	0.193	0.187	0.175	0.159	0.140
0.492	0.469	0.445	0.410	0.398	0.417	0.057	0.025	0.021	0.045	0.040	0.042
0.339	0.382	0.378	0.364	0.384		0.034	0.008	0.021	0.022	0.034	
O29	0.070	0.103	0.128	0.148	0.164	O29	-0.139	-0.105	-0.079	-0.059	-0.044
0.176	0.186	0.196	0.208	0.215	0.227	-0.029	-0.019	-0.012	-0.002	0.009	0.021
0.235	0.244	0.252	0.260	0.268	0.275	0.030	0.037	0.046	0.049	0.048	0.045
0.242	0.235	0.227	0.213	0.210	0.221	0.012	0.000	0.000	0.013	0.012	0.015
0.184	0.205	0.205	0.201	0.208		0.012	-0.001	0.006	0.007	0.015	
N30	-0.383	-0.400	-0.411	-0.423	-0.433	N30	-0.023	-0.041	-0.054	-0.063	-0.072
-0.442	-0.453	-0.465	-0.481	-0.492	-0.506	-0.082	-0.093	-0.099	-0.110	-0.124	-0.140
-0.516	-0.527	-0.537	-0.545	-0.554	-0.562	-0.149	-0.154	-0.159	-0.154	-0.143	-0.128
-0.480	-0.459	-0.435	-0.404	-0.390	-0.408	-0.044	-0.014	-0.012	-0.038	-0.033	-0.037
-0.329	-0.376	-0.374	-0.361	-0.380		-0.029	-0.003	-0.018	-0.019	-0.032	
CNDO/m											
C28	0.313	0.297	0.281	0.267	0.255	C28	0.328	0.311	0.293	0.277	0.262
0.244	0.236	0.228	0.222	0.216	0.210	0.249	0.238	0.228	0.220	0.209	0.201
0.204	0.193	0.186	0.176	0.166	0.101	0.194	0.186	0.178	0.168	0.159	0.149
0.156	0.148	0.141	0.140	0.135	0.128	0.141	0.132	0.123	0.113	0.104	0.095
0.122	0.117	0.113	0.099	0.094		0.086	0.077	0.069	0.054	0.045	
O29	-0.288	-0.260	-0.236	-0.215	-0.198	O29	-0.287	-0.258	-0.233	-0.213	-0.196
-0.183	-0.170	-0.158	-0.148	-0.138	-0.129	-0.182	-0.169	-0.158	-0.147	-0.140	-0.131
-0.121	-0.115	-0.110	-0.106	-0.103	-0.119	-0.123	-0.115	-0.109	-0.105	-0.102	-0.100

-0.096	-0.094	-0.093	-0.090	-0.089	-0.088	-0.098	-0.097	-0.096	-0.096	-0.096	-0.097
-0.088	-0.087	-0.087	-0.090	-0.091		-0.098	-0.100	-0.102	-0.107	-0.109	
N30	0.084	0.064	0.048	0.033	0.020	N30	0.080	0.060	0.043	0.029	0.017
0.007	-0.006	-0.019	-0.030	-0.041	-0.050	0.005	-0.006	-0.018	-0.029	-0.032	-0.041
-0.057	-0.055	-0.058	-0.054	-0.049	0.026	-0.048	-0.053	-0.055	-0.052	-0.048	-0.043
-0.049	-0.045	-0.040	-0.042	-0.038	-0.033	-0.037	-0.032	-0.025	-0.017	-0.009	-0.000
-0.029	-0.025	-0.021	-0.006	-0.002		0.009	0.017	0.026	0.044	0.054	
MINDO/3											
C28	0.254	0.252	0.249	0.244	0.239	C28	0.241	0.239	0.235	0.229	0.222
0.234	0.229	0.225	0.221	0.217	0.214	0.215	0.208	0.202	0.195	0.189	0.181
0.210	0.184	0.162	0.179	0.137	0.135	0.157	0.164	0.159	0.149	0.142	0.136
0.128	0.120	0.121	0.117	0.113	0.107	0.128	0.120	0.146	0.143	0.140	0.137
0.105	0.101	0.082	0.076	0.072		0.135	0.133	0.131	0.124	0.122	
O29	-0.165	-0.135	-0.110	-0.087	-0.069	O29	-0.183	-0.153	-0.127	-0.104	-0.084
-0.051	-0.037	-0.023	-0.012	-0.002	0.008	-0.067	-0.052	-0.039	-0.027	-0.016	-0.007
0.015	0.015	0.015	0.026	0.018	0.020	-0.004	0.007	0.013	0.017	0.019	0.022
0.021	0.022	0.024	0.025	0.026	0.025	0.023	0.024	0.038	0.040	0.042	0.043
0.026	0.025	0.020	0.019	0.018		0.044	0.045	0.046	0.045	0.045	
N30	-0.057	-0.099	-0.133	-0.162	-0.183	N30	-0.029	-0.072	-0.107	-0.135	-0.157
-0.202	-0.217	-0.229	-0.238	-0.244	-0.249	-0.174	-0.189	-0.200	-0.208	-0.213	-0.214
-0.251	-0.220	-0.195	-0.221	-0.165	-0.163	-0.190	-0.208	-0.206	-0.197	-0.191	-0.187
-0.155	-0.145	-0.148	-0.142	-0.138	-0.130	-0.178	-0.169	-0.202	-0.199	-0.196	-0.192
-0.129	-0.123	-0.100	-0.093	-0.086		-0.190	-0.187	-0.185	-0.177	-0.174	

The greatest value in energy difference (about 181.2 kJ/mol) at the deformation of the $C_{28}N_{30}$ bond from 1.76Å to 1.86Å in the L-Arg-L-Pro dipeptide low-energy conformational states calculated by the CNDO/2 method was established. The maximum value corresponds to bond lengthening from 1.79Å to 1.80Å at the scanning energy by 0.01Å step. Lengthening the same bond from 1.56Å to 1.66Å in D-Arg-L-Pro dipeptide gives the same energy difference (174.9 kJ/mol). The conclusion was made that $C_{28}N_{30}$ bond in L-Arg-L-Pro dipeptide is more stable than that in D-Arg-L-Pro dipeptide. Energy scanning carried out by other quantum chemical methods shows that energy minimum and dissociation energy limit of the $C_{28}N_{30}$ bond in L-Arg-L-Pro dipeptide has smaller value than that in D-Arg-L-Pro. This result testified that L-Arg-L-Pro dipeptide is more stable than L-Arg-L-Pro dipeptide.

[1] *K.V.Shaitan*. Protein dynamics and new approaches to the molecular mechanisms of protein functioning. In: Stochastic Dynamics of Reacting Biomolecules (ed. *W. Ebeling, Yu. Romanovsky*, L. Schimansky-Geier), World Scientific, 2003, 283.

[2] *K.V. Shaitan, M.D. Ermolaeva and S.S. Saraikin*. Nonlinear dynamics of the molecular systems and the correlations of internal motions in the oligopeptides, Ferroelectrics, 220, 2000, 205.

[3] *A.S.Lemak, N.K.Balabaev*. On the Berendsen thermostat. Molecular Simulation, 13, 1994, 177.

[4] *K.V.Shaitan.* The topological structure of hypersurfaces of conformational energy levels and physical mechanisms of internal protein mobility, Macromolecular Symp. 106, 1996, 321.

[5] *K.V. Shaitan, A.B.Rubin.* Effect of isotope substitution on intermolecular electron transfer in biological systems, J.Theoret.Biol. 86, 1980, 203.

[6] *I.S. Maksumov, L.I. Ismailova, N.M. Godjaev.* The program for semiempirical calculation of conformations of the molecular complexes. J. Struc. Chem. (in Russian), 24, 1983, 147.

[7] *N.L.Allinger, V.Yuh*. QSPE-395,Quantum Chemistry Program Exhange, Indiana Univ., 1982.

[8] *M.Pudlak, K.V.Shaitan.* J. Biol. Phys., 19, 1993, 39.

[9] *L.A.Gribov, S.P.Mushtakova*. In: Quantum chemistry (in Russian) M.: Qardariki. 1999, 390.

[10] *L.A. Gribov*. Light elucidation of vibrations. The description of the program and instruction to the user, OOO «INLAN», 1995.

[11] *M.V.Volkenshtein, L.A.Gribov.* M.A.Elayashevich, V.I.Stepanov. Molecular vibration (in Russian), M: Nauka, 1972, 700.

[12] *L.A.Gribov, W.J.Orville–Thomas*. Theory and methods of calculation of molecular spectra. John Wiley and Sons, Chichester, New York, 1988, 636; Spectroscopy 6, No. 4, 1991, 48.

[13] *L.A.Gribov, M.E.Elyashberg*. Computer-aided identification of organic molecules by their molecular spectra. Critical reviews in analytical chemistry, 8, 1979, N 2, 111.

[14] *L.A.Gribov*. Intensity theory for infrared spectra of polyatomic molecules, Consultants bureau, New York, 1964, 113.

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KVANT-KİMYƏVİ ÜSULLARIN KÖMƏYİ İLƏ MODEL DİPEPTİDLƏRDƏ PEPTİD RABİTƏSİİNİN DEFORMASİYASININ TƏDQİQİ

CNDO/2, CNDO/m və MINDO/3 yarımempirik kvant-kimyəvi üsulların köməyi ilə L-Arg-L-Pro və D-Arg-L-Pro dipeptidlərin fəza quruluşlarının elektron xassələrinə təsiri tədqiq olunmuşdur. C-N kimyəvi rabitə üzrə uzunluğun dəyişməsinin peptid rabitənin deformasiyasına təsiri öyrənilmişdir. Dipeptidlərin kiçik enerjili konformasiyası halları müəyyən olunmuş, aminturşu qalıqlarının əsas və yan zəncirlərinin ikiüzlü bucaqlarının ədədi qiymətləri və qalıqlararası enerjilər hesablanmışdır. Dipeptidlərin müxtəlif konformasiya

hallarında elektron sıxlıqları, elektron buludunun və nüvələrin qarşılıqlı təsir qüvvələri, tam dipol momentləri və kimyavi rabitələrin dipol momentləri hesablanmışdır. Müəyyən olunmuşdur ki, 1 və 2 vəziyyətlərində arqinin amin turşusunun D-izomerlə əvəz olunması kəskin dəyişillərlə nəticələnir. J-N peptid rabitəsinin ən dayanıqlı halı L-Arg-L-Pro dipeptidində müəyyən edilmişdir.

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ИССЛЕДОВАНИЕ ДЕФОРМАЦИИ ПЕПТИДНОЙ СВЯЗИ В МОДЕЛЬНЫХ ДИПЕПТИДАХ ПОЛУЭМПИРИЧЕСКИМИ МЕТОДАМИ КВАНТОВОЙ ХИМИИ

Полуэмпирическими методами квантовой химии CNDO/2, CNDO/m и MINDO/3 исследована взаимосвязь между пространственной структурой и электронно-конформационными свойствами модельных дипептидов L-Arg-L-Pro и D-Arg-L-Pro. Исследовано влияние эффекта сканирования вдоль связи C-N на деформацию пептидной связи. Найдены низкоэнергетические конформационные состояния дипептидов, проведена количественная оценка величин двугранных углов основной и боковых цепей аминокислотных остатков, вычислена энергия внутри- и межостаточных взаимодействий. Проанализированы электронные параметры, такие как распределение электронной плотности, электронные и ядерные силы, полные дипольные моменты и дипольные моменты отдельных связей в зависимости от конформационных состояний дипептидов. Результаты показали, что D-изомеризация остатка аргинина в положениях 1 и 2 сопровождается большими изменениями при сканировании вдоль пептидной связи C-N. C-N пептидная связь в L-Arg-L-Pro дипептиде более стабильна по сравнению с другими модельными дипептидами.

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