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Electronic and vibrational polarizabilities of the twenty naturally occurring amino acids

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Abstract

The geometries, relative energies, gas-phase static and dynamic dipole polarizabilities of the two most stable neutral forms and of the zwitterionic form of the twenty naturally occurring amino acids have been obtained by Density Functional and conventional ab initio Hatree–Fock theories using correlation consistent basis sets. Mean electronic polarizabilities (<α^e>s) are encompassed in the 40–160 a.u. range and are little dependent on the amino acid framework conformation and structure. The relation between <α^e> and the number of electrons in the molecule makes to classify the amino acids as one of the most polarizable family of compounds. Calculated <α^e> values of the neutral forms linearly relate to the molecular volume and molecular hardness as well as, rather unexpectedly, with the experimental values in water solution, where amino acids are known to be in a zwitterionic form. Vibrational polarizabilities amount to 15–45 a.u.. They come essentially from the low-frequency angular deformation modes of the –OH and $-NH_2$ groups.

Keywords: Amino acids; Electronic polarizability; Vibrational polarizability; DFT; MP2 calculations

1. Introduction

The molecular polarizability is the response of the electronic structure of a system to an external electric field F, owing to the molecular dipole moment μ varies as

$$\mu_i(F) = \mu_i(0) + \alpha_{ij}F_j + 1/2!\beta_{ijk}F_jF_k + 1/3!\gamma_{ijkl}F_jF_kF_l\ldots$$

where $\mu(0)$ is the dipole moment value in the absence of field, and α, β and γ define polarizability, first and second hyperpolarizabilities, respectively. Thus the components of the polarizability tensor are obtained as $\alpha_{ij}=(\partial\mu_i/\partial F)_{F\to 0}$. Polarizability has a volume dimension and depends on the shape and size of the molecule. Three contributions determine α: an electronic contribution, α^e, due to the electronic polarization, a vibrational one, α^v, due to the molecular relaxation and, in a floppy molecule, a contribution due to the permanent dipole moment, $<\mu^2>_0/kT$, where $<\mu^2>_0$ is the average of the square of the projection of the permanent dipole moment on the axis of the electric field [1].

Experimentally the mean value $<\alpha>=1/3(\alpha_{xx}+\alpha_{yy}+\alpha_{zz})$is usually determined from the refractive index or from dielectric measurements [2], while α^v can be obtained from infrared intensities [2–4]. Theoretically <α> can be obtained accurately by means of Density Functional Theory (DFT) and wave function-based methods, provided that sufficiently flexible basis sets are used including diffuse and polarization functions, and that electron correlation corrections are taken into account. Owing to its intrinsic significance, α is an important factor which characterizes many physical–chemical properties such as dielectric properties [5,6], polarizable force field [7] and QSAR studies for chemical–biological interactions [8]. Relative α value is a descriptor of relative molecular stability. The present paper reports the results of gas phase theoretical determination

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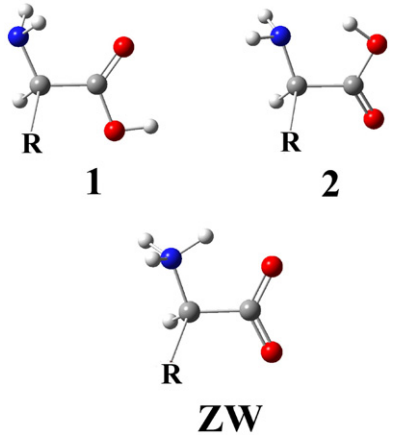

Fig. 1. Backbone conformations of the studied amino acids.

of dipole moments, electronic and vibrational static and dynamic (frequency-dependent) polarizabilities of the twenty naturally occurring amino acids, carried out by conventional ab initio Hartree–Fock (HF), DFT and second order Møller–Plesset Perturbation Theory (MP2) correlated methods. Neutral forms of the amino acid are considered, which are the stable ones in the gas phase. There are not many papers concerning the experimental and/or theoretical determination of the amino acids polarizability. Khanarian and Moore [9] obtained the molar Kerr constant and dipole moment of amino acids in water and deduced from the molar refraction R_m reported by Meekin et al. [10] the sum ($\alpha_{xx}+\alpha_{yy}+\alpha_{zz}$) of the α_{ij} components. Only very recently ab initio theoretical computations of amino acids polarizabilties have been addressed. Hansen et al. [11] reported the frequency-dependent polarizabilities of the twenty essential amino acids calculated by HF and point dipole interaction (PDI) models. Tulip and Clark [12] calculated polarizability tensors of alanine, leucine, isoleucine and valine using plane wave pseudopotential methods. Finally Swart et al. [13] used time-dependent DFT (TD-DFT) computations to obtain molecular polarizabilities of the twenty amino acids residues.

Table 1
Relative energy (kcal/mol) of form **2** *vs.* **1** of amino acids calculated on the B97-1/cc-pVDZ geometry

		HF/aug-cc-pVDZ	MP2/aug-cc-pVDZ	B97-1/aug-cc-pVDZ	B97-1/cc-pVDZ	B97-1/cc-pVDZ + ΔZPVE
1	Ala	2.95	0.34	−0.04	−0.74	−0.38
2	Arg	4.41	1.40	0.96	0.92	0.93
3	Asn	1.55	−2.42	−3.13	−4.13	−3.23
4	Asp	4.95	0.37	−1.18	−2.42	−2.00
5	Cys	3.49	1.28	0.88	−0.01	0.43
6	Gln	0.71	−1.94	−2.09	−2.10	−1.78
7	Glu	0.79	−0.95	−1.73	−2.80	−2.59
8	Gly	3.46	0.54	0.46	0.46	0.75
9	His	5.46	3.14	2.68	1.63	1.79
10	Ile	2.20	−0.49	−0.53	−0.94	−0.82
11	Leu	2.56	−0.32	−0.42	−0.87	−0.42
12	Lys	2.64	−0.16	−0.28	−0.60	−0.21
13	Met	2.07	−0.66	−0.75	−0.86	−0.62
14	Phe	4.64	2.03	1.61	1.05	1.23
15	Pro	2.22	−1.40	−1.22	−1.66	−1.27
16	Ser	0.19	−2.84	−3.72	−6.51	−5.7
17	Thr	1.72	−0.88	−1.47	−1.90	−1.56
18	Trp	4.86	1.91	1.36	0.33	0.53
19	Tyr	4.68	2.12	1.68	1.07	1.27
20	Val	2.26	−0.48	−0.48	−0.89	−0.57

Table 2
Geometries and relative energies of glycine forms

	Form 1		Form 2		
	B97-1/cc-pVDZ [a]	CCSD/DZP [b]	B97-1/cc-pVDZ [a]	CCSD/DZP [b]	Exp. [c]
r(O–H)	0.944	0.972	0.989	0.982	0.966
r(C–O)	1.353	1.359	1.341	1.347	1.354
r(C═O)	1.211	1.216	1.206	1.214	1.204
r(C–C)	1.526	1.525	1.541	1.533	1.529
r(C–H)	1.105	1.098			1.081
r(C–N)	1.452	1.458	1.471	1.475	1.466
r(N–H)	1.024	1.021	1.021	1.018	1.001
θ(H–O–C)	105.9	105.9	103.9	104.4	(112.3)
θ(O═C–C)	125.0	125.7	123.1	122.3	125.1
θ(O–C–C)	111.9	111.5	113.1	114.1	111.6
θ(C–C–N)	115.1	115.4	110.5	111.2	112.1
θ(H–N–C)	108.2	108.8	110.6	111.0	(113.2)
θ(H–N–H)	103.5	104.7	106.1	106.9	(110.3)
$\Sigma\theta$ [d]	319.9	322.3	328.2	328.9	333.9
E_R	0.00 (0.00) [e]	0.00	0.54 (0.84) [e]	1.43	1.4±0.4

Bond lengths in Å, bond angles in degrees, relative energies in kcal/mol.
[a] Present work.
[b] Ref. [20].
[c] Ref. [21].
[d] $\Sigma\theta = 2\theta$(H–N–C) + θ(H–N–H).
[e] Value corrected for the zero-point vibrational energy.

Table 3
Dipole moments (Debye) of amino acids

		Form 1			Form 2		
		HF	MP2	B97-1	HF	MP2	B97-1
1	Ala	1.52	1.39	1.44	5.80	5.25	5.35
2	Arg	1.95	2.04	1.96	7.93	7.14	7.34
3	Asn	4.32	4.01	4.10	3.80	3.24	3.40
4	Asp	2.09	1.82	1.94	6.96	6.25	6.41
5	Cys	0.66	0.46	0.56	6.71	6.05	6.16
6	Gln	5.20	4.66	4.82	2.34	2.16	2.15
7	Glu	1.78	1.73	1.71	4.65	4.23	4.28
8	Gly	1.38	1.29 (1.28) [a]	1.32	6.01	5.46 (5.46) [a]	5.57
9	His	2.45	2.53	2.45	8.50	7.95	7.99
10	Ile	1.68	1.52	1.58	5.59	5.05	5.15
11	Leu	1.68	1.56	1.59	5.43	4.88	4.98
12	Lys	0.67	0.68	0.64	6.42	5.82	5.92
13	Met	3.10	2.91	2.90	4.55	4.10	4.19
14	Phe	1.58	1.47	1.48	5.28	4.75	4.86
15	Pro	1.81	1.59	1.66	6.10	5.54	5.64
16	Ser	0.78	0.52	0.64	5.52	4.96	5.06
17	Thr	2.93	2.53	2.65	6.09	5.51	5.58
18	Trp	2.17	2.38	2.22	3.23	2.73	2.82
19	Tyr	1.43	1.64	1.54	6.44	5.79	5.86
20	Val	1.60	1.44	1.50	5.69	5.15	5.25

Basis set: aug-cc-pVDZ. Calculations are carried out on the B97-1/cc-pVDZ optimized geometry.
[a] From CCSD(T)/aug-cc-pVDZ calculations.

2. Computational procedure

The geometries of the investigated amino acids conformers were obtained by DFT computations using the B97-1 functional [14] with the cc-pVDZ correlation consistent basis set. Relative energies were obtained at HF, MP2 and DFT-B97-1 levels using cc-pVDZ and aug-cc-pVDZ basis sets, and were corrected for zero-point vibrational energy (ZPVE) contribution. Harmonic vibrational analysis, carried out at B97-1/cc-pVDZ level, showed that the reported structures are true minima in the potential energy surface. HF dipole moments and static dipole polarizabilities were computed analytically within the TD-HF using the aug-cc-pVDZ basis set. Electron correlation contributions were introduced by MP2 and DFT-B97-1 methods. Correlated polarizability values were computed by means of the finite field (FF) procedure following Kurtz at al. [15] using an electric field strength of 0.005 a.u.. The accuracy of this approach was checked at HF level by comparing α^e values obtained by both analytical and FF procedures. Frequency-dependent polarizabilities were evaluated at B97-1/aug-cc-pVDZ level at the experimental laser radiation energy of 0.0788 a.u. ($\lambda = 578$ nm). The vibrational contribution to α was evaluated under the double harmonic oscillator approximation with the sum-over-modes expression [16]:

$$\alpha_{ij}^{v} = \sum_{a}^{3N-6} \frac{\left(\frac{\partial \mu_i}{\partial Q_a}\right)_0 \left(\frac{\partial \mu_j}{\partial Q_a}\right)_0}{\omega_a^2} \quad (1)$$

where ω_a is the circular vibrational frequency of the ath normal mode Q_a and $\partial\mu_i/\partial Q_a$ is the partial derivative of the *i*-component of μ with respect to Q_a evaluated at the equilibrium geometry. Static α^v values were calculated at DFT-B97-1 level with the cc-pVDZ basis set. All computations were performed with GAUSSIAN-03 [17] and GAMESS [18] series of programs.

3. Results and discussion

3.1. Geometries and relative energies

Accurate α values require accurate molecular geometries. The molecular parameters of the investigated amino acids were optimized at DFT-B97-1/cc-pVDZ level. The complete set of the optimized geometrical parameters is available on request by the authors. Two molecular configurations of the $NH_2-CH-COOH$ backbone were taken into consideration, which, by reference to glycine molecule are (Fig. 1): form **1** which bears a bifurcated NH_2-----O═C hydrogen bonding, and form **2** which bears a single O–H-----NH_2 hydrogen bonding. Many previous studies have demonstrated that in the vapour forms **1** and **2** are the lowest energy, molecular conformations of amino acids [19]. The relative energies of these two forms obtained at various theoretical levels are shown in Table 1. Calculations indicate that the relative energy of the two forms depends on the amino acid, on the basis set and on the correlation energy. Significant contributions come also from the ZPVE. At HF level **1** is more stable than **2** for all compounds by up to about 5 kcal/mol. Electron correlation at both MP2 and DFT levels favours **2.** This in many cases determines **2** to be more stable than **1.** It is important to note that MP2 and DFT methods give the same order of stability, except for aspartic acid and, perhaps,

Table 4
Mean dipole polarizability (a.u.) of amino acids

		Form 1				Form 2				ZW-gas	
		HF	MP2	B97-1		HF	MP2	B97-1		B97-1	Exp.[a]
		$<\alpha^e>(0;0)$	$<\alpha^e>(0;0)$	$<\alpha^e>(0;0)$	$<\alpha^e>(-\omega;\omega)$	$<\alpha^e>(0;0)$	$<\alpha^e>(0;0)$	$<\alpha^e>(0;0)$	$<\alpha^e>(-\omega;\omega)$	$<\alpha^e>(0;0)$	
1	Ala	50.68	55.26	55.98	57.44	50.46	54.99	55.41	56.77	58.09	55.88
2	Arg	109.85	120.16	121.71	125.59	109.63	120.20	121.38	125.23	124.58	115.62
3	Asn	70.59	78.33	78.98	81.24	70.52	78.21	78.42	80.59	82.05	79.82
4	Asp	65.90	72.71	73.43	75.33	65.87	72.91	73.19	75.02	76.92	79.72
5	Cys	70.42	75.80	76.76	79.10	70.51	76.18	77.03	79.43	80.34	
6	Gln	82.40	90.80	91.85	94.44	81.86	90.26	90.93	93.40	94.19	
7	Glu	77.87	85.51	86.66	88.95	77.29	85.05	85.90	88.06	89.48	90.45
8	Gly	39.15	43.09 (42.98)[b]	43.57	44.70	39.22	43.18 (43.06)[b]	43.40	44.50	47.13	44.26
9	His	94.22	101.01	102.40	105.93	94.13	100.79	101.89	105.27	105.87	102.64
10	Ile	84.77	91.24	92.67	95.04	84.31	90.67	91.84	94.09	94.88	95.28
11	Leu	85.39	91.98	93.47	95.90	84.97	91.55	92.78	95.11	96.00	94.51
12	Lys	94.53	102.37	104.18	107.04	94.18	102.01	103.56	106.34	106.96	
13	Met	95.53	102.22	103.81	106.99	95.09	101.78	103.11	106.19	106.56	102.18
14	Phe	115.97	122.39	123.64	128.57	116.19	122.64	123.73	128.64	127.82	122.96
15	Pro	68.60	74.18	75.19	77.13	68.14	73.61	74.23	76.02	76.82	73.51
16	Ser	54.36	59.90	60.69	62.27	53.91	59.42	59.93	61.42	63.86	61.24
17	Thr	65.57	71.56	72.56	74.37	65.26	71.36	72.07	73.82	75.47	73.73
18	Trp	147.07	155.77	157.49	165.42	147.01	156.26	157.56	165.46	161.72	157.81
19	Tyr	120.00	128.26	129.76	135.17	120.36	128.68	130.04	135.49	134.43	
20	Val	73.16	79.03	80.19	82.26	72.75	78.5	79.39	81.34	82.31	81.51

Dynamic values at $\omega = 0.0788$ a.u.
Basis set: aug-cc-pVDZ. Calculations are carried out on the B97-1/cc-pVDZ optimized geometry.
[a] Water solution, Ref. [9].
[b] From CCSD(T)/aug-cc-pVDZ calculations.

for alanine. The effect of basis set was investigated at the correlated B97-1 level: the increase of the basis set size, by including diffuse functions, favours **1.** The correlation energy effect seems to be more important than the basis set effect. Any way, difference in the relative energy is encompassed within 3 kcal/mol, so in the gas the two forms probably coexist in all compounds. The ZPVE, evaluated at B97-1/cc-pVDZ level, favours **1** typically by 0.3–0.4 kcal/mol (0.9 kcal/mol in asparagine), but in no case it is able to change the order of stability of the two forms. Given the above results a strictly quantitative comparison with the previous theoretical estimates cannot be made. Accordingly in many cases our data differ significantly from literature data, recently reviewed by Dahereng and Dive [19]. The present work allows to compare geometries and relative energies of the two lowest-energy forms of amino acids on an homogeneous theoretical ground. Any way, to test our results, a quantitative comparison is made with literature data on glycine for which, owing to its small size, experimental and accurate theoretical data are available (Table 2). It is apparent that our theoretical geometrical parameters are in good agreement with experimental data and with the results of more sophisticated theoretical calculations such as CCSD/DZP ones [20]. The energy of **1** relative to **2** (−0.84 kcal/mol, when corrected for ZPVE) is somewhat overestimated with respect to the experimental value of −1.4 kcal/mol [21] and to the CCSD value of −1.43 kcal/mol [20]. Note that single point CCSD(T)/DZP calculations [20] gave $E_R = -1.06$ kcal/mol, while MP2/6311++G** calculations gave $E_R = -0.59$ [22–24] and −1.05 [25] kcal/mol *vs.* a DFT-B3LYP/6-311G** datum of −0.82 kcal/mol [25].

3.2. Dipole moments

HF, MP2 and B97-1 gas-phase dipole moments, μ_s, of amino acids obtained with the aug-cc-pVDZ basis set are reported in Table 3. B97-1 and MP2 results are very close with each other. To validate the results, μ of glycine was calculated also at the higher CCSD(T) level, using the same basis set. The obtained μ values for both **1** and **2** forms fully support the accuracy of MP2 and B97-1 methods in describing the electronic distribution in the amino acids. Correlated μ values are lower than HF ones, especially for form **2**. The amino acid polarity is, as expected, very dependent on the molecular conformation. This issue requires specific investigation and it is outside the aim of the present work, however data in Table 3 show that the simultaneous rotations around the C–C, C–O and C–N bonds in the amino-acidic framework, to pass from **1** to **2**, produce a remarkable increase of μ, as exemplified in glycine (Fig. 1). Exceptions are glutamine and asparagine, where dipole orientation of the $-CH_2-CH_2-CO-NH_2$ and $-CH_2-CO-NH_2$ residues makes $\mu(\mathbf{2}) < \mu(\mathbf{1})$. Experimental μ values of amino acids in the gas or in non-polar solvents are not known, but for glycine [26] and tryptophane [27]. Gas-phase dipole moments of glycine **1** and **2** conformers were obtained by microwave spectroscopy as 1.10 and 5.45 D, in excellent agreement with our MP2 and CCSD(T) previsions of 1.28 and 5.46 D, respectively. B97-1/aug-cc-PVDZ calculations produce a slight overestimation of ca. 0.1 D relative to the CCSD(T) figures.

From deflection measurements of a molecular beam in inhomogeneous electric field the gas-phase dipole moment of form **2** of tryptophane was inferred to be close to the calculated

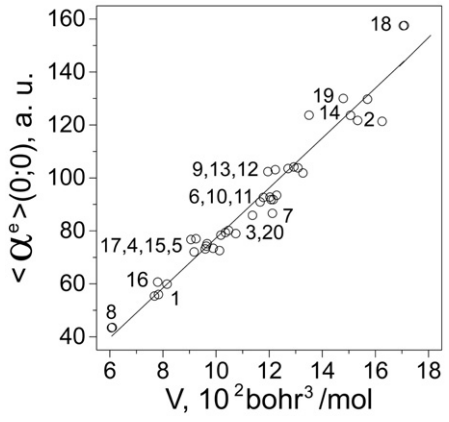

Fig. 3. Mean electronic dipole polarizability of amino acid **1** and **2** forms as a function of the molecular volume. The computed volume corresponds to the 0.001 a.u. density contour. $\langle\alpha^e\rangle(0;0) = 0.09\ V - 16.99$, $r^2 = 0.95$. B97-1/aug-cc-pVDZ results.

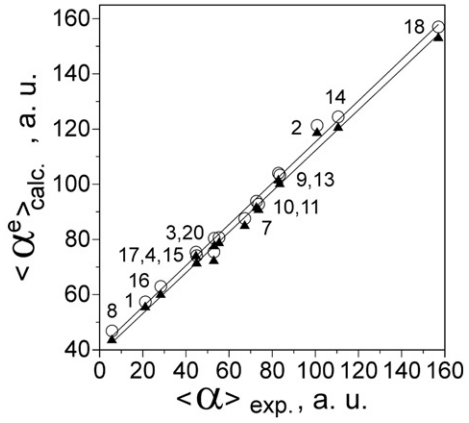

Fig. 2. Calculated *vs* experimental (H_2O) electronic dipole polarizabilities of amino acids. Triangles refer to a mean $\langle\alpha^e\rangle$ value of **1** and **2** forms, circles refer to the zwitterionic form. B97-1/aug-cc-pVDZ results.

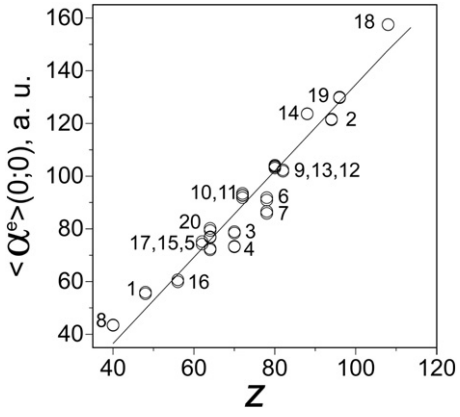

Fig. 4. Relation between mean electronic dipole polarizability and number of electrons of amino acid **1** and **2** forms. $\langle\alpha^e\rangle(0;0) = 1.64Z - 29.03$, $r^2 = 0.95$. B97-1/aug-cc-pVDZ results.

MP2/6-31G** value of 3.08-3.99 D [27]. Our MP2/aug-cc-PVDZ datum of 2.73 D is in partial agreement, suggesting that a more accurate search of the chain conformation is needed.

3.3. Electronic polarizabilities

HF, MP2 and B97-1 electronic dipole polarizabilities carried out with the aug-cc-pVDZ basis set are shown in Table 4, together with available experimental values in water solution for a tentative comparison; dynamic values were obtained at the 578 nm laser wavelength used in the experimental measurements in water solution [9]. To compare static and dynamic values in calculating static dipole polarizabilities we omitted contributions coming from the permanent dipole moment orientation of the floppy molecule, since they are absent in the dynamic regime at 578 nm. The results show:

a) MP2 and B97-1 data are very close with each other. The usually observed overestimation of the molecular polarizability by DFT methods is here not observed. The accuracy of the MP2 and B97-1 data has been successfully assessed, as for μ, by CCSD(T) calculations on glycine (Table 4). HF/aug-cc-pVDZ values are very close to the HF/POL-Sadlej ones reported by Hansen et al. [11]. Our correlated values are somewhat smaller than those reported by Tulip and Clark on alanine, isoleucine, leucine and valine [12], while they well correlate with the DFT-LB94/QZ4p polarizabilities of the amino acid residues reported by Smart et al. [13]. We consider the reported values as the most accurate dipole polarizability data of the present amino acids to date.
b) Correlation energy produces a significant increase of $<\alpha^e>$ of 6–10%.
c) Dynamic values at $\lambda = 578$ nm are greater than the static ones by 3–4%.
d) Quite important, $<\alpha^e>$ values of form **1** are almost equal to those of form **2**, despite a marked difference in the charge distribution, as indicated by the relative μ values.

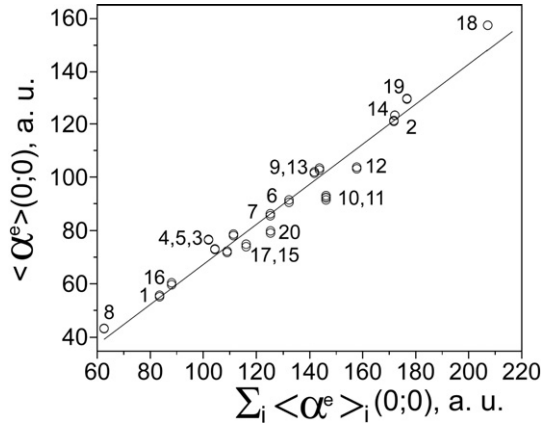

Fig. 5. Relation between mean electronic dipole polarizability of amino acid **1** and **2** forms and the sum of atomic contributions. $<\alpha^e>(0;0) = 0.75\ \Sigma_i <\alpha^e>_i(0;0) - 7.71$, $r^2 = 0.96$. Mean atomic polarizabilities (a.u.). H:4.60; N: 7.00; C: 11.72; O: 4.57; S: 18.47. B97-1/aug-cc-pVDZ results.

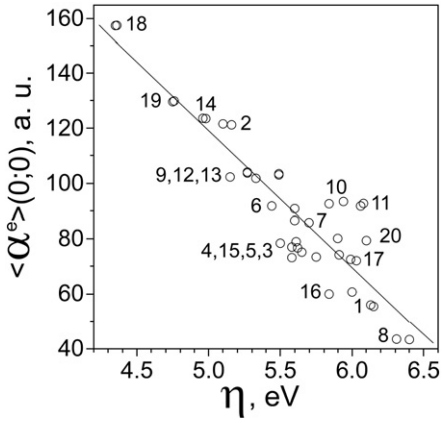

Fig. 6. Relation between mean electronic dipole polarizability of amino acid **1** and **2** forms and molecular hardness. $<\alpha^e>(0;0) = -49.73\ \eta + 367.91$, $r^2 = 0.84$. B97-1/aug-cc-pVDZ results.

e) Quite unexpectedly gas-phase $<\alpha^e>$ values are very close to the experimental values in water solution, where the amino acids are notoriously in a zwitterionic form. The following relations have been found:

$$<\alpha^e>_{B97-1/\text{aug-cc-pvdz}} = -2.61 + 1.02<\alpha>_{\text{exp}},\quad r^2 = 0.992$$

$$<\alpha^e>_{\text{MP2/aug-cc-pvdz}} = -2.72 + 1.01<\alpha>_{\text{exp}},\quad r^2 = 0.992$$

Dynamic data correlate similarly:

$$<\alpha^e>_{B97-1/\text{aug-cc-pvdz}} = -4.94 + 1.08<\alpha>_{\text{exp}},\quad r^2 = 0.990$$

Slopes are near to unit in all cases. These results induced us to carry out gas-phase dipole polarizability calculations on the

Table 5
Ionization potential, IP (eV), molecular hardness, η (eV), LUMO–HOMO energy difference, $\varepsilon_L - \varepsilon_H$ (eV) of amino acids. B97-1/cc-pVDZ results

		Form 1			Form 2		
		IP	η	$\varepsilon_L - \varepsilon_H$	IP	η	$\varepsilon_L - \varepsilon_H$
1	Ala	9.38	6.13	7.08	9.38	6.15	7.26
2	Arg	8.04	5.10	6.16	7.80	5.16	6.06
3	Asn	8.96	5.61	7.02	8.83	5.50	6.44
4	Asp	9.30	5.75	6.98	9.36	5.58	6.48
5	Cys	8.82	5.62	6.52	8.76	5.58	6.52
6	Gln	8.72	5.44	6.96	8.75	5.60	7.30
7	Glu	9.09	5.60	6.96	9.11	5.70	7.24
8	Gly	9.56	6.31	7.18	9.56	6.40	7.44
9	His	8.11	5.15	6.06	8.19	5.33	6.28
10	Ile	9.10	5.84	6.96	9.18	6.06	7.38
11	Leu	9.20	5.94	7.00	9.23	6.08	7.40
12	Lys	8.34	5.27	6.56	8.40	5.49	6.88
13	Met	8.19	5.27	6.02	8.27	5.49	6.36
14	Phe	8.39	4.98	6.44	8.36	4.96	6.38
15	Pro	8.59	5.65	6.44	9.10	5.91	7.16
16	Ser	9.24	6.00	7.08	9.33	5.84	7.06
17	Thr	9.11	5.99	7.06	9.15	6.03	7.26
18	Trp	7.24	4.35	5.20	7.25	4.36	5.18
19	Tyr	7.84	4.75	5.74	7.80	4.76	5.80
20	Val	9.17	5.90	6.98	9.22	6.10	7.38

Table 6
Main contributions to vibrational polarizabilities (a.u.) of **1** and **2** forms of amino acids

		Form 1					Form 2				
		ω (cm^{-1})	I_{IR} (km/mol)	Mode [a]	$<\alpha^v>$	$<\alpha^v>/<\alpha^e>$	ω (cm^{-1})	I_{IR} (km/mol)	Mode [a]	$<\alpha^v>$	$<\alpha^v>/<\alpha^e>$
1	Ala	218	37	ρ NH_2	7.08		1450	371	δ OH	1.58	
		599	64	τ OH	1.60		276	13	ρ CH_3	1.56	
		1151	211	δ OH	1.43		307	14	ρ NH_2	1.35	
				Total	17.74	0.32			Total	10.50	0.19
2	Arg	617	127	ω NH_2	2.99		324	41	ρ NH_2	3.5	
		237	18	ρ NH_2	2.91		294	28	ρ NH_2	2.86	
		776	159	γ NH	2.37		514	80	γ NH	2.72	
				Total	29.98	0.25			Total	29.19	0.24
3	Asn	277	187	ω NH_2	21.91		427	169	ω NH_2	8.32	
		229	34	ρ NH_2	5.71		208	13	ν NH–O	2.69	
		635	65	τ OH	1.44		1465	466	δ OH	1.95	
				Total	42.33	0.53			Total	25.76	0.33
4	Asp	220	33	ρ NH_2	6.20		225	15	ν NH–O	2.57	
		615	121	τ OH	2.87		257	15	ν NH–O	1.97	
		932	109	ω NH_2	1.13		892	144	τ OH	1.63	
				Total	22.80	0.31			Total	18.82	0.26
5	Cys	252	32	ρ NH_2	4.48		216	12	τ SH	2.35	
		618	83	τ OH	1.95		281	16	ρ NH_2	1.83	
		289	13	ρ NH_2	1.36		365	17	ρ NH_2	1.11	
				Total	16.09	0.21			Total	13.29	0.17
6	Gln	252	185	ω NH_2	26.28		286	15	ρ NH_2	1.63	
		237	30	ρ NH_2	4.75		359	23	ν OH–N	1.62	
		602	73	τ OH	1.81		1458	321	δ OH	1.35	
				Total	45.72	0.50			Total	13.62	0.15
7	Glu	234	38	ρ NH_2	6.24		291	18	ρ NH_2	1.88	
		608	92	τ OH	2.24		670	76	τ OH	1.52	
		946	143	ω NH_2	1.43		1446	345	δ OH	1.48	
				Total	23.23	0.27			Total	18.63	0.22
8	Gly	234	43	ρ NH_2	7.02		282	16	ρ NH_2	1.86	
		666	88	τ OH	1.77		326	21	ν OH–N	1.73	
		961	138	ω NH_2	1.34		1444	336	δ OH	1.45	
				Total	17.66	0.40			Total	9.53	0.22
9	His	508	61	γ NH	2.12		485	62	γ NH	2.37	
		329	23	ρ NH_2	1.87		301	23	ρ NH_2	2.26	
		648	86	τ OH	1.83		202	7	τ C–C	1.55	
				Total	18.27	0.18			Total	15.81	0.16
10	Ile	245	19	ρ NH_2	2.85		287	27	ρ NH_2	2.94	
		260	14	ρ NH_2	1.89		1439	359	δ OH	1.56	
		630	74	τ OH	1.67		337	13	ν OH–N	1.00	
				Total	16.26	0.18			Total	10.49	0.11
11	Leu	245	30	ρ NH_2	4.44		294	21	ρ NH_2	2.16	
		627	86	τ OH	1.95		346	17	ν OH–N	1.26	
		321	12	ρ NH_2	1.05		1453	215	δ OH	0.91	
				Total	15.62	0.17			Total	10.07	0.11
12	Lys	244	30	ρ NH_2	4.58		306	38	ρ NH_2	3.64	
		310	36	ρ NH_2	3.36		889	176	ω NH_2	2.00	
		629	96	τ OH	2.17		266	13	ρ NH_2	1.67	
				Total	22.16	0.21			Total	17.78	0.17
13	Met	228	19	ρ NH_2	3.32		281	17	ρ NH_2	1.91	
		624	99	τ OH	2.27		1438	416	δ OH	1.80	
		253	15	ρ NH_2	2.16		334	16	ν OH–N	1.28	
				Total	16.62	0.16			Total	11.31	0.11
14	Phe	322	29	ρ NH_2	2.49		291	18	ρ NH_2	1.92	
		257	13	ρ NH_2	1.75		1428	406	δ OH	1.78	
		649	66	τ OH	1.40		865	76	τ OH	0.92	
				Total	15.55	0.13			Total	11.56	0.09
15	Pro	660	80	τ OH	1.64		366	19	ν OH–N	1.28	
		1144	172	δ OH	1.18		215	5	τ ring	1.05	
		431	22	ν NH–O	1.05		1455	240	δ OH	1.02	
				Total	10.86	0.14			Total	9.03	0.12

Table 6 (*continued*)

		Form 1					Form 2				
		ω (cm^{-1})	I_{IR} (km/mol)	Mode [a]	$<\alpha^v>$	$<\alpha^v>/<\alpha^e>$	ω (cm^{-1})	I_{IR} (km/mol)	Mode [a]	$<\alpha^v>$	$<\alpha^v>/<\alpha^e>$
16	Ser	246	88	τ OH	13.08		636	110	τ OH	2.44	
		267	30	ρ NH_2	3.73		1440	508	δ OH	2.20	
		314	27	ρ NH_2	2.42		304	19	ρ NH_2	1.82	
				Total	30.87	0.51			Total	16.63	0.28
17	Thr	261	100	τ OH	13.16		214	55	τ OH	10.74	
		244	33	ρ NH_2	5.03		1457	441	δ OH	1.86	
		655	106	τ OH	2.22		370	28	ν OH–N	1.86	
				Total	32.56	0.45			Total	24.00	0.33
18	Trp	361	39	ρ NH_2	2.69		287	23	ρ NH_2	2.48	
		506	64	δ OH	2.25		1438	452	δ OH	1.96	
		411	32	γ NH	1.68		428	38	γ NH	1.86	
				Total	21.89	0.14			Total	19.40	0.12
19	Tyr	367	95	τ OH	6.36		364	96	τ OH	6.51	
		330	21	ρ NH_2	1.74		1436	395	δ OH	1.72	
		257	12	ρ NH_2	1.64		285	12	ρ NH_2	1.34	
				Total	25.20	0.19			Total	22.05	0.17
20	Val	219	13	ρ NH_2	2.43		289	20	ρ NH_2	2.12	
		275	19	ρ NH_2	2.26		1442	340	δ OH	1.47	
		248	11	ρ NH_2	1.58		338	13	ν OH–N	1.00	
				Total	16.61	0.21			Total	10.26	0.13

[a] ρ = rocking, γ = bending, δ = bending, τ = torsion, ν = stretching, ω = wagging.

zwitterionic structure, $<\alpha^e>_{zw}$ of the amino acids, which was obtained by geometry optimization procedures in water solution at B97-1/cc-pVDZ level by the Polarizable Continuum Method (PCM) [28]. The results are reported in Table 4. It can be seen that $<\alpha^e>_{zw}$ are very close to $<\alpha^e>$ of the neutral forms, being only 2–8% higher. Also $<\alpha^e>_{zw}$ can be linearly related to $<\alpha>_{exp}$ (Fig. 2) following the relation

$$<\alpha^e>_{B97-1/aug-cc-pvdz} = -0.75 + 1.04<\alpha>_{exp},$$
$$r^2 = 0.993.$$

The above behaviour suggests that the molecular polarization of the amino acid is not strictly dependent on the molecular structure and conformation, but it is rather governed by some other physical properties such as molecular volume (V), total number of electrons (Z) and atomic polarizabilty sum ($\Sigma_i<\alpha^e>_i$). Relations between $<\alpha^e>$ and these properties are reported in Figs. 3–5. The dependence is indeed linear with a good statistics. It is of interest to note that the $<\alpha^e>/Z$ correlation puts in evidence that amino acids constitute a family of very polarizable molecules having a $<\alpha^e>/Z$ ratio of 0.24 $Å^3$, comparable to that exhibited by non substituted hydrocarbons (saturated, unsaturated, aromatic, etc.) which show a $<\alpha^e>/Z$ ratio of 0.25 $Å^3$, what makes to classify them as the most polarizable molecules [4]. The $<\alpha^e>/\Sigma_i<\alpha^e>_i$ correlation has a slope (0.75) much smaller than unit. This suggests that a simple additive approach to the molecular polarizability of the amino acids can hardly be applicable. Indeed such a value indicates a considerable loss of polarizability, i.e. an increase of the molecular stability, in the molecule relative to the sum of the atomic contributions, along the series as Z increases. Accordingly a linear inverse correlation can be drawn between $<\alpha^e>$ and the chemical hardness η (Fig. 6), this property having been obtained from data in Table 5, as [29]

$$\eta = \frac{\varepsilon_L - \varepsilon_H}{2} + \varepsilon_H + \mathrm{IP} \quad (2)$$

where ε_L and ε_H are the energies of the lowest unoccupied, LUMO, and the highest occupied molecular orbitals, HOMO, respectively, and IP is the vertical ΔSCF ionization potential.

3.4. Vibrational polarizabilities

Total averaged vibrational polarizability, $<\alpha^v>$, and the main contributions from the individual vibrational modes of the amino acid **1** and **2** forms are reported in Table 6. In calculating $<\alpha^v>$ we omitted contributions coming from vibrational modes with frequency lower than 200 cm^{-1} which would give exceptionally high unrealistic $<\alpha^v>$ values. Indeed low-frequency modes are likely improperly described by the Bishop–Kirtman perturbation treatment [16,30]. The results show that $<\alpha^v>$ is an important part of the total polarizability showing values ranging from ca. 10 a.u. in proline to ca. 45 a.u. in asparagine and glutamine. Averaged vibrational polarizability of form **1** is greater than that of form **2** principally owing to rocking and wagging contributions of the NH_2 group. It follows that $<\alpha^v>/<\alpha^e>(\mathbf{1}) > <\alpha^v>/<\alpha^e>(\mathbf{2})$. According to Eq. (1), the most important vibrational contributions come from low-frequency angular deformation modes. Stretching modes, despite having higher intensity, do not significantly contribute. It is of interest to note that the δ(OH) contribution to $<\alpha^v>$ is negligible in form **1** of all compounds, whilst it is significant in form **2** because this mode produces a $\partial\mu_i^e/\partial Q_a$ in **2** greater than in **1**.

4. Summary and conclusions

We have calculated molecular dipole moments, μ, and polarizabilities, α, of two lowest-energy conformations of the twenty naturally occurring amino acids, using conventional ab initio and Density Functional Theory methods. The aim of the work was to investigate the effect on μ and α of the amino-acidic $NH_2-CH-COOH$ backbone conformation in the **1** and **2** forms, which bring NH_2-----O and O-H-----N type hydrogen bonds, respectively. The reliability of the reported data has been validated by performing CCSD(T)/aug-cc-pVDZ calculations of μ and α of the smallest amino acid glycine.

One has found that on passing from **1** to **2** intensity and direction of the dipole vector change noticeably, suggesting that μ might be a precious property in studying molecular conformation of amino acids.

Gas-phase dipole polarizabilities of the neutral **1** and **2** forms are in good agreement with each other and linearly correlate with the experimental data in water solutions where the amino acids are known to exist in a zwitterionic form. This is a rather unexpected result. However, gas-phase polarizabilities of zwitterionic structures, as obtained by geometry optimization in water, are also close to the polarizability values of the neutral forms. These results suggest that α-amino acid polarizabilities are not much dependent on molecular structure and conformations although the dependence of $<\alpha^e>$ on the atomic polarizability sum suggests that a simple additive model to the molecular polarizability of amino acids can hardly be supported. On the other hand $<\alpha^e>$ linearly correlates with the molecular volume, molecular hardness and total electron number. The latter correlation makes to classify α-amino acids as one of the most polarizable family of compounds.

Vibrational polarizability is an important fraction of the total polarizability. The most important contributions come from low-frequency angular deformation modes.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bpc.2007.11.003.

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