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Calculation of Proton-Transfer Energies and Electrostatic Lattice Energies of Various Amino Acids and Peptides Using CNDO/2 and ab Initio SCF Methods

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Abstract: The proton-transfer energies and the electrostatic lattice energies are calculated for 16 amino acids and peptides, using the semiempirical CNDO/2 method and the LCAO–MO–SCF ab initio method with four different basis sets of minimal, split valence, double-ζ, and polarized double-ζ quality. The proton-transfer energies were calculated as the SCF energy differences between the zwitterion in the crystal and the nonzwitterion in the gas phase. For CNDO/2 and the minimal basis the calculated proton-transfer energies were about 2–3 times as large as for the larger basis sets. For the polarized double-ζ basis the proton-transfer energies could only be calculated for the three modifications of glycine, and they were estimated for the remaining compounds. The proton-transfer energies vary from −88 to −114 kJ/mol for the heterocyclic α-amino acids with a NH_2^+ group, and from −133 to −178 kJ/mol for the aliphatic α-amino acids with a NH_3^+ group. For the dipeptide glycylglycine a proton-transfer energy was calculated of −242 kJ/mol, and for anthranilic acid I of −93 kJ/mol. The electrostatic lattice energies were calculated in the point-charge approximation, using gross Mulliken populations. A very different electrostatic lattice energy was obtained using either CNDO/2 or ab initio point charge—the former being smaller by about 100 kJ/mol for the zwitterionic structures and about 60 kJ/mol for the nonzwitterionic structures. The electrostatic lattice energy for a crystal of zwitterions is considerably larger than that for a crystal of nonzwitterions. However, most of this energy surplus is cancelled by the proton-transfer energy. This rationalizes why amino acids and peptides crystallize both as zwitterions and nonzwitterions.

I. Introduction

The work we describe here is part of a program to derive an intermolecular force field for amino acids and peptides. In order to calibrate this force field we have to calculate the lattice energies of these compounds.[1] These energies are closely related to the observed enthalpies of sublimation, which can be obtained directly by calorimetry or indirectly from the temperature dependence of the vapor pressure.[2]

For molecular crystals the lattice energy itself is a good approximation to the enthalpy of sublimation, if the geometries of the molecules in the crystal and in the gas phase are equal.[3] However, if these geometries are different, a molecular deformation energy has to be considered as well. This applies especially for those amino acids and peptides which crystallize as zwitterions, since the molecules in the gas phase usually exist as nonzwitterions. For glycine gas this has been shown experimentally by means of microwave spectroscopy.[4-6] Therefore for these crystals, in addition to the lattice energy, we must know the energy difference between the zwitterion and the nonzwitterion, which is called the proton-transfer energy. The proton-transfer energy is not known from experiment. Takagi[7] constructed an energy cycle in order to determine this contribution for glycine, but unfortunately the values for many of the steps involved are unknown. A few quantum-mechanical calculations for glycine have been made to estimate the proton-transfer energy, both on the CNDO and ab initio level.[8,9] In this paper we extend these calculations to a larger number of molecules and to more basis sets.

A remarkable feature of the observed enthalpies of sublimation of amino acids and peptides is that they differ little for crystals of zwitterions and crystals of nonzwitterions.[2] Since in the zwitterionic crystals there is a large proton-transfer energy (see section IV.1), this observation implies that the lattice energies for these crystals must be considerably more negative than that for the nonzwitterionic crystals, due to a large electrostatic lattice energy. As a first test of this hypothesis we here report the electrostatic lattice energies in a point-charge approximation, where the point charges are obtained from gross Mulliken populations from the CNDO/2 and ab initio wave functions. A more

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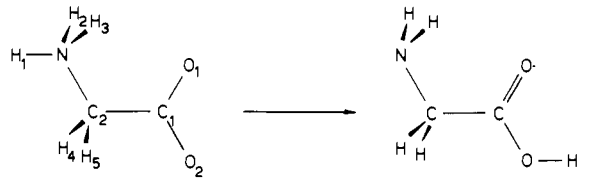

Figure 1. The proton transfer for glycine.

complete calculation of the lattice energies will be presented in a following paper, in which we derive a set of atom–atom potentials for amino acids and peptides.[1]

Momany, Carruthers, and Scheraga[10] have derived a set of intermolecular potentials, which they used to compute the minimum-energy packing configurations and lattice energies for crystals of various amino acids. More recently, Snir, Nemenoff, and Scheraga[11] have developed a new empirical potential, the EPEN model, based on the interactions of electrons and nuclei. Their model was used for conformational, intermolecular, and solvation anayses of several classes of compounds. In these papers[10,11] the proton-transfer energy contribution was completely ignored when deriving the potentials.

II. Theory

In this section we relate the lattice energy to the experimental enthalpy of sublimation. We give the expressions for the different energy contributions to the lattice energy, in particular the electrostatic lattice energy and the proton-transfer energy.

In order to compare the calculated lattice energy with the experimental enthalpy of sublimation we use an extension of the relation given by Warshel and Lifson:[12]

$$\Delta H_{sub} = H^{g} - H^{cr} = 4RT + (\epsilon_0{}^{g} - \epsilon_0{}^{cr}) + (U_{vibr}{}^{g} - U_{vibr}{}^{cr}) + (U_{el}{}^{g} - U_{el}{}^{cr}) - \Delta U_{lat} \quad (1)$$

where ϵ_0 is the zero-point vibrational energy, U_{vibr} is the additional energy of vibration at temperature T, U_{el} is the total (fixed-nuclei) molecular energy, ΔH_{sub} is the enthalpy of sublimation, and ΔU_{lat} is the lattice energy. We here adopt the usual approximation to this expression, given by Rae and Mason:[13]

$$\Delta H_{sub} \simeq -\Delta U_{lat} - 2RT + (U_{el}{}^{g} - U_{el}{}^{cr}) \quad (2)$$

In the atom–atom potential method[14] the lattice energy ΔU_{lat} is calculated as the sum of pairwise interactions between the molecules in the crystal, the interaction energy between a pair of molecules being represented by the interactions between the atoms of the molecules. In this method one usually distinguishes attraction, repulsion, hydrogen-bond, and electrostatic energy contributions,[15] as:

$$\Delta U_{lat} = V_{attr} + V_{rep} + V_{HB} + V_{elec} \quad (3)$$

The first three contributions will be considered in our following paper.[1]

The electrostatic part of the lattice energy is evaluated as:

$$V_{elec} = \tfrac{1}{2}\sum_i\sum_j 1389.3 q_i q_j / r_{ij} \quad (4)$$

Here the q's are the atomic point charges in units of e, r_{ij} is the distance between atoms i and j in angstroms, and the constant 1389.3 is a conversion factor to obtain V_{elec} in kJ/mol. The summation index i runs over all atoms of the independent molecules of the asymmetric unit and j runs over all atoms of the surrounding molecules in the crystal. This result has to be divided by the number of independent molecules in the asymmetric unit. Convergence of the lattice sums is ensured by application of Williams' method.[16] The electrostatic lattice energies will be calculated with the point charges obtained from gross Mulliken populations.

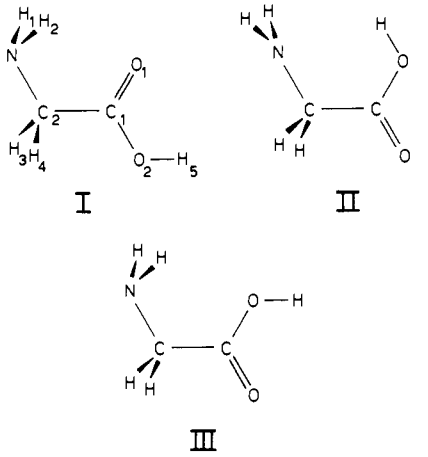

Figure 2. The three low-energy conformations of glycine.

The term $(U_{el}{}^{g} - U_{el}{}^{cr})$ is the difference of the molecular energies in the gas and in the crystal. For molecular crystals it is usually assumed that the geometries of the molecules in the gas phase and in the crystal are approximately equal, so this term is then neglected. This is legitimate for, e.g., hydrocarbons. However, for amino acids and peptides which crystallize as zwitterions, this energy contribution is very important, because in the gas phase the molecules are most probably present as nonzwitterions.[4-6] So during sublimation a proton has to be transferred from the NH_3^+ or NH_2^+ group to the COO^- group, which is represented schematically for glycine in Figure 1. This means that we have to take into account a proton-transfer energy:

$$\Delta U_{pr} = U_{el}{}^{g} - U_{el}{}^{cr} \quad (5)$$

The proton-transfer energies will here be calculated as the differences between the SCF energies for both geometries, using eq 5.

It is noticed that for amino acids and peptides which are nonzwitterionic in the crystal, another deformation energy, of about 7.5 kJ/mol, for the carboxylic group has to be taken into account, due to small changes in the geometry which occur in the transition from hydrogen-bonded molecules in the crystal to free molecules in the gas phase.[17]

III. Computational Details

1. Quantum-Mechanical Methods. The ab initio SCF calculations were performed with four different basis sets. In order of increasing quality the four Gaussian basis sets were, using Dunning's notation:[18] minimal basis, (6,3/3) contracted to 2,1/1; split valence, (6,3/3) contracted to 3,2/2; double-ζ, (9,5/4) contracted to 4,2/2; and polarized double-ζ, (9,5,1/4,1) contracted to 4,2,1/2,1. The exponents and contraction coefficients were taken from Van Duijneveldt.[19] As these exponents are "best atom" exponents, scaling factors were applied to the valence orbitals of the two smallest basis sets. (The scaling factors employed for minimal and split valence, respectively, were for the zwitterions (for the numbering of the atoms, see Figures 1 and 2): N 2s/0.97, 0.85; 2p/0.97, 0.97; O 2s/0.95, 0.85; 2p/1.01, 1.04; C_1 2s/1.05, 0.88; 2p/1.09, 0.94; C_2 2s/1.05, 0.84; 2p/1.09, 0.96; H_N 1s/1.40, 1.12; H_C 1s/1.32, 1.08. For the nonzwitterions the

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Table I. The Calculated Proton-Transfer Energies for CNDO/2 and ab Initio Basis Sets, and the Estimated Proton-Transfer Energy in the Polarized Double-ζ (DZP^{est}) Basis Set (kJ/mol)[a]

	CNDO/2	MB	SV	DZ	DZP	DZP^{est}
α-glycine	−389	−318	−167	−137	−156	
β-glycine	−413	−331	−167	−139	−152	
γ-glycine	−390	−318	−161	−133	−149	
L-alanine	−376	−309	−158	−126		−142
L-serine	−385	−353	−186	−162		−178
DL-serine	−370	−342	−180	−157		−173
DL-α-amino-*n*-butyric acid B	−371	−303	−138	−117		−133
L-azetidine-2-carboxylic acid	−341	−270	−123	−98		−114
L-proline	−297	−253	−115	−86		−102
4-hydroxy-L-proline	−336	−257	−99			−88
anthranilic acid I (zwitterion)	−324	−267	−104			−93
glycylglycine	−555	−429	−253			−242

[a] The abbreviations MB, SV, DZ, and DZP refer to the ab initio basis sets of respectively: minimal basis, split valence, double-ζ quality. For the references of the crystal structures we refer to Table II.

scaling factors for N, C_1, H_N and H_C are the same as for the zwitterions, while for the other atoms they are: O_1 2s/0.95, 0.85; 2p/1.00, 1.02; O_2 2s/0.95, 0.85; 2p/0.98, 1.01; C_2 2s/1.05, 0.88; 2p/1.09, 0.94; H_0 1s/1.46, 1.18.) Due to the inherent flexibility of the double-ζ basis sets, these were not scaled, except for the H 1s functions (ζ = 1.2). For the polarization functions the exponents were taken as 1.0.

The wave functions and total molecular energies were obtained using local versions of the IBMOLH[20] (for the ab initio calcualtions) and the CNDO/2 programs.[21] The IBMOLH program calculates integrals over GTO's; the default value for the integral threshold is 10^{-10} au. In calculations on large molecules, or in calculations with large basis sets, the number of integrals tends to exceed the mass-storage limit of our computer (CDC Cyber 175/100). To reduce the number of integrals to be stored, we then decreased the integral threshold to 10^{-5} au. We checked for α-glycine to see that this threshold has a negligible influence on the proton-transfer energy, providing that both zwitterion and nonzwitterion are calculated with the same integral threshold (the total energies for the zwitterion and the nonzwitterion being lowered by 0.50 and 0.25 kJ/mol respectively in the minimal basis). Its influence on the Mulliken populations was 10^{-4} e or less for both zwitterion and n onzwitterion. In larger molecules, where the total molecular energies are up to twice as large as for glycine, the errors will be proportionally larger.

2. Geometries. In order to calculate the proton-transfer energies, we need the geometries of the molecules both in the crystal and in the gas phase. We did not use optimized geometries for the basis sets chosen. Instead, for the zwitterions we used experimental crystal structures, as for our purpose optimization of the structures of zwitterions is not meaningful unless the crystalline surroundings are taken into account, which is computationally unfeasible. For consistency, we then had to use experimental geometries for the nonzwitterions as well, since it is anticipated that errors due to lack of optimization cancel for the greater part when experimental geometries are used for both the zwitterion and the nonzwitterion. Incidentally, we estimate the energy difference between experimental and optimized structures to be only of the order of 5–10 kJ/mol for the larger basis sets. The geometries of many amino acids and peptides in the crystal are known from diffraction data, but little is known about the molecular structure of amino acids and peptides in the gas phase. Recent microwave studies for glycine[4-6] confirmed the expectation that the molecules are nonzwitterions. Of the several conformations which are possible in the gas phase,[5] Figure 2 shows three low-energy conformations.[6] Experimentally it has been shown that conformation I has the lowest energy; this conformation has an energy which is about 6 kJ/mol lower than the energy of conformation II. This is in excellent agreement with recent quantum-mechanical ab initio studies;[22-25] both Vishveshwara and Pople[22] and Sellers and Schäfer[23] calculated I to be more stable than II by about 9 kJ/mol. Calculations on alanine[24] also showed that conformation I is more stable than II (about 6 kJ/mol). In this work we assume that in the gas phase all amino acids and peptides are nonzwitterions with conformation I. Therefore, we consider for each compound two geometries, namely, (A) the geometry of the molecule in the crystal (zwitter- or nonzwitterion) and (B) the geometry of the nonzwitterion in the gas phase, with conformation I. Details of each type of geometry will now be summarized.

(A): The geometries of the molecules in the solid state were obtained from the experimental X-ray or neutron diffraction data. The positions of all atoms, including the hydrogen atoms, must be accurately known. For the X-ray diffraction data we placed the hydrogen atoms in the following ways: the hydrogen atoms on nitrogen were placed tetrhedrally with N–H = 1.039 Å; the hydrogen atoms on carbon were placed at C–H = 1.090 Å with an angle C–C–H = 109.5° at aliphatic carbon atoms and an angle of 120.0° at aromatic ring carbons. For those molecules which are nonzwitterionic in the crystal, the hydrogen atoms of the carboxyl group were placed at O–H = 1.024 Å, with an angle C–O–H = 112.7°. For the X-ray structures of L-serine and L-proline the bond lengths and bond angles of the hydrogen atoms were taken from the corresponding atoms of DL-serine and 4-hydroxy-L-proline, respectively, as determined by neutron diffraction.

(B): The gas-phase geometry was constructed by transferring a proton from the NH_2^+ or NH_3^+ group to the COO^- group of the zwitterion. In this way a nonzwitterion with a neutral carboxylic group is obtained (see Figure 1). Except for this carboxyl group, the geometry of the nonzwitterion was taken to be the same as that for the corresponding zwitterion. For the geometry of the carboxyl group we chose the average bond distances and bond angles of a few compounds, measured by microwave spectrometry and electron diffraction: C=O = 1.196 Å, C—O = 1.351 Å, O—H = 0.984 Å, C—O=O = 125.6°, C—C—O = 110.4°, C—O—H = 107.0°, and an expansion of the C_α—C bond of 0.012 Å.[17,26] The geometry of this carboxylic group is in excellent agreement with the optimized geometries of glycine and alanine, as calculated by Sellers and Schäfer in a 4-21G basis set.[23,24]

IV. Results and Discussion

The amino acids and peptides for which calculations have been carried out were selected on the following criteria: (1) accurate crystal structures should be known; (2) the sample should contain both zwitterions and nonzwitterions, and aliphatic as well as heterocyclic and aromatic compounds; (3) the molecules may not be too large in view of the time-consuming quantum-mechanical

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Table II. The Electrostatic Lattice Energy V_{elec} (in kJ/mol) for Various Amino Acids and Peptides, Calculated with Mulliken Population Point Charges from Different CNDO/2 and ab Initio Wave Functions[a]

	ref	CNDO/2	MB	SV	DZ	DZP
			Zwitterionic Structures			
α-glycine	32	−144.0	−239.5	−206.5	−218.0	−205.5
β-glycine	33	−144.5	−235.0	−201.0	−211.5	−199.0
γ-glycine	34	−141.0	−231.5	−195.5	−209.5	−198.5
L-alanine	35	−139.0	−235.0	−193.5	−209.5	
L-serine	36	−143.5	−272.5	−226.0	−233.5	
DL-serine	37	−135.0	−300.5	−242.5	−237.5	
DL-α-amino-butyric acid B	38	−124.5	−201.5	−148.0	−175.0	
L-azetidine-2-carboxylic acid	39	−113.5	−198.5	−168.5	−185.5	
L-proline	40	−104.0	−171.0	−122.0	−147.5	
4-hydroxy-L-proline	41	−106.5	−213.0	−186.0		
glycylglycine	42	−284.5	−396.0	−353.5		
			Mixed Structure			
anthranilic acid I[b]	43	−50.5	−130.5	−110.0		
			Nonzwitterionic Structures			
anthranilic acid II	44	−10.5	−68.0	−75.5		
p-aminobenzoic acid[c]	45	−14.5	−66.0			
DL-5-oxoproline	46	−22.0	−91.5	−91.5		
N-acetylglycine	47	−23.0	−85.0	−83.0	−73.5	

[a] The abbreviation ref refers to the crystal structures, for the other abbreviations see Table I. [b] Anthranilic acid I has one zwitterion and one nonzwitterion in the asymmetric unit. [c] p-Aminobenzoic acid has two independent nonzwitterions in the asymmetric unit.

calculations, especially for the larger basis sets; (4) the enthalpies of sublimation should be known for most compounds, since in the next paper we will compare these with the lattice energies.[1]

1. Proton-Transfer Energy. Large proton-transfer energies were calculated for both CNDO/2 and the minimal basis (MB); these were in the range of −300 to −550 kJ/mol and of -250 to -430 kJ/mol, respectively (see Table I). In contrast with this, the proton-transfer energies obtained in the larger basis sets are only about half the MB values. The reason for this behavior is that CNDO/2 and the MB set lack the flexibility to describe the expanded orbitals of the negatively charged group in the zwitterion,[27,28] thereby causing the proton-transfer energy to be highly overestimated. The same explanation can be used to rationalize the (much smaller) decrease in the proton-transfer energy going from SV to DZ, the DZ basis being the better one to describe an anion. The DZ value for α-glycine (−137 kJ/mol) is in good agreement with the value of −131 kJ/mol obtained by Tse and co-workers[9] in a 4-31G set (which should be somewhat inferior to our DZ basis).

Unexpectedly, the use of polarization functions in the basis set (the DZP basis) leads to larger stabilization for the nonzwitterion than for the zwitterion, and thus the proton-transfer energy, is increased compared to the DZ calculation. The proton-transfer energy may be thought to be the difference between the gas-phase proton affinities of an amine and a carboxylic anion, corrected for the Coulomb attraction between the charge centers.[9] Since proton affinities of small molecules are generally well described at the DZP level, we may therefore expect that further enlargement of the basis would not significantly change the result.

An illustration of the dependence of the proton-transfer energies on the basis sets is given in Figure 3. For the sake of clarity the results of only six compounds have been plotted, but the other compounds show the same trends. This graph clearly demonstrates that the changes in the proton-transfer energy as a function of the basis are about the same for all compounds studied here. The average decrease in the proton-transfer energy going from the MB to the SV basis set is 158 kJ/mol, and from the SV to the DZ basis set it is 27 kJ/mol, with standard deviations of 10 and 4 kJ/mol, respectively. The average increase in the proton-transfer energy between the DZ and the DZP basis sets only could be calculated for the three modifications of glycine, viz., 16 kJ/mol.

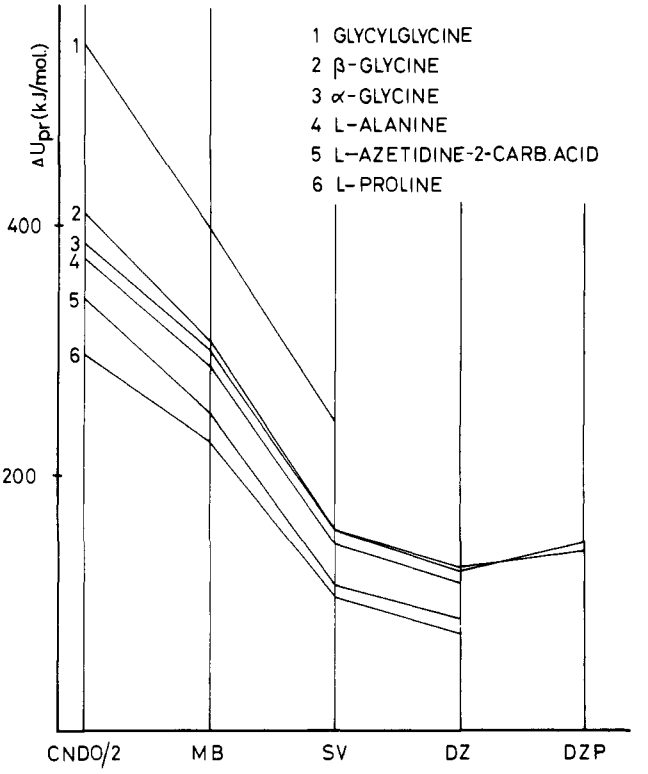

Figure 3. The calculated proton-transfer energies ΔU_{pr} (kJ/mol) for CNDO/2 and the ab initio basis sets. For the abbreviations we refer to Table I.

We used these average values to estimate the proton-transfer energies for those compounds which could not be calculated in the DZ and DZP basis sets. The estimated proton-transfer energies in the DZP basis have also been listed in Table I.

When comparing the estimated DZP^{est} proton-transfer energies of the various amino acids and peptides we can distinguish two main classes of compounds: (1) aliphatic α-amino acids with a NH_3^+ group with proton-transfer energies in the range of −133 to −178 kJ/mol and (2) heterocyclic α-amino acids with a NH_2^+ group with proton-transfer energies in the range of −88 to −114 kJ/mol. Two compounds lie outside these ranges, viz., glycylglycine and anthranilic acid I. The peptide glycylglycine has a proton-transfer energy of −242 kJ/mol. This large proton-transfer

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Table III. The Gross Mulliken Population (Electrons), the Electrostatic Lattice Energy V_{elec} (kJ/mol), the Dipole Moment $\langle\mu\rangle$ (D) Calculated from the Wave Functions, the Dipole Moment μ^{pc} (D) Calculated from the Partial Charges, and the Total Molecular Energy E (au) Calculated for α-Glycine (Neutron Diffraction Geometry) with CNDO/2 and ab Initio Basis Sets[a]

	CNDO/2	MB	SV	DZ	DZP
N	0.022	−0.810	−0.956	−0.772	−0.467
H_1	0.164	0.429	0.432	0.414	0.324
H_2	0.208	0.459	0.468	0.459	0.367
H_3	0.199	0.447	0.462	0.445	0.355
C_2	−0.021	−0.100	−0.360	−0.337	−0.204
H_4	0.033	0.179	0.284	0.246	0.166
H_5	0.030	0.180	0.285	0.251	0.170
C_1	0.374	0.484	0.766	0.486	0.493
O_1	−0.526	−0.656	−0.712	−0.628	−0.632
O_2	−0.483	−0.612	−0.669	−0.564	−0.572
V_{elec}	−144.0	−239.5	−206.5	−218.0	−205.5
$\langle\mu\rangle$	13.2	13.6	13.0	13.7	13.1
μ^{pc}	8.9	12.9	11.7	12.3	12.1
E	−66.31962	−281.60033	−281.92430	−282.69927	−282.84535

[a] For the other abbreviations we refer to Table I, for the numbering of the atom see Figure 1.

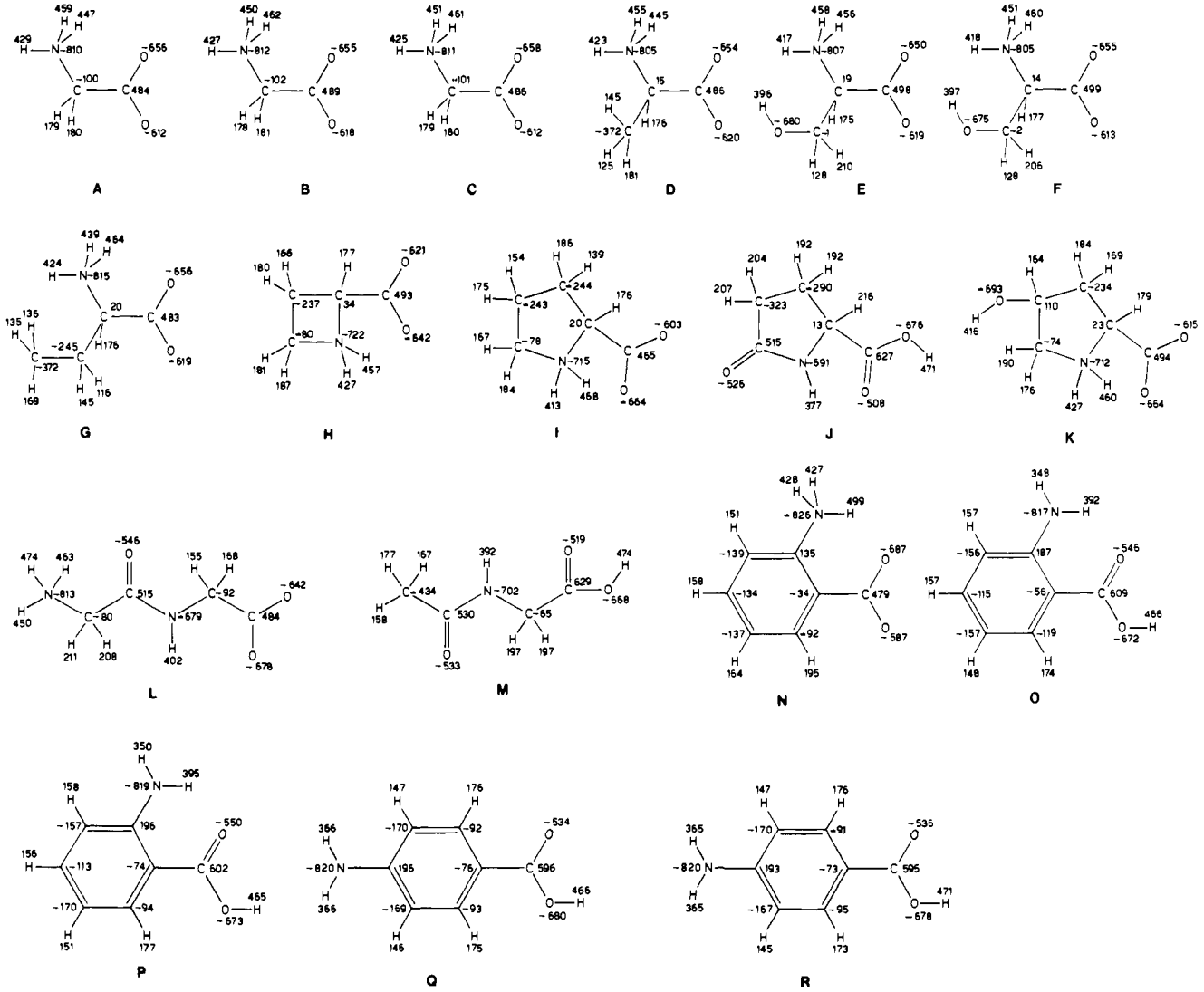

Figure 4. The structures and the minimal basis Mulliken point charges (in units of e × 1000) for the following molecules: (A) α-glycine, (B) β-glycine, (C) γ-glycine, (D) L-alanine, (E) L-serine, (F) DL-serine, (G) DL-α-amino-*n*-butyric acid, (H) L-azetidine-2-carboxylic acid, (I) L-proline, (J) DL-5-oxoproline, (K) 4-hydroxy-L-proline, (L) glycylglycine, (M) *N*-acetylglycine, (N) anthranilic acid I (zwitterion), (O) anthranilic acid I (nonzwitterion), (P) antranilic acid II, (Q) *p*-aminobenzoic acid (molecule A), (R) *p*-aminobenzoic acid (molecule B).

energy is clearly caused by the large charge separation between the NH_3^+ and the COO^- groups. Anthranilic acid I is the only aromatic compound in the series; the zwitterion has a proton-transfer energy of −93 kJ/mol.

The differences in the calculated proton-transfer energies between the two classes of compounds are caused at least in part by differences in the proton affinities. The proton affinities for alkyl-substituted amines were calculated by Umeyama and Mo-

Table IV. The Cancellation of the Electrostatic Lattice Energy and the Proton-Transfer Energy for the Zwitterionic Crystals[a]

zwitterionic structures	$V_{elec}^{MB} - \Delta U_{pr}^{DZP}$	$V_{elec}^{SV} - \Delta U_{pr}^{DZP}$	$V_{elec}^{DZ} - \Delta U_{pr}^{DZP}$	$V_{elec}^{DZP} - \Delta U_{pr}^{DZP}$
α-glycine	−84	−51	−62	−50
β-glycine	−83	−49	−60	−47
γ-glycine	−83	−47	−61	−50
L-alanine	−93	−52	−68	
L-serine	−95	−48	−56	
DL-serine	−128	−70	−65	
DL-α-amino-*n* butyric acid B	−69	−15	−42	
L-azetidine-2-carboxylic acid	−85	−55	−72	
L-proline	−69	−20	−46	
4-hydroxy-L-proline	−125	−98		
anthranilic acid I	−84	−64		
glycylglycine	−154	−112		

nonzwitterionic structures	V_{elec}^{MB}	V_{elec}^{SV}	V_{elec}^{DZ}
anthranilic acid II	−68	−76	
para-amino-benzoic acid	−66		
DL-oxoproline	−92	−92	
N-acetylglycine	−85	−83	−74

[a] For comparison the electrostatic lattice energies for the nonzwitterionic structures are also given.

rokuma[29] in a split valence 4-31G basis. They found that dimethylamine has a proton affinity which is about 24 kJ/mol larger than that of methylamine. So these calculations are consistent with our finding that aliphatic α-amino acids have significantly larger calculated proton-transfer energies than the heterocyclic α-amino acids.

2. Electrostatic Lattice Energies. Electrostatic lattice sums were calculated using Williams' convergence acceleration method,[16] with a summation limit of 6.0 Å in direct space and of 0.6 $Å^{-1}$ in reciprocal space, and a convergence constant $K = 0.3$. Derissen, Smit, and Voogd[30] showed for the three modifications of glycine that convergence is ensured in this way.

Large differences in the electrostatic lattice energies were calculated using the point charges obtained from gross Mulliken populations from either CNDO/2 wave functions or those from ab initio wave functions (see Table II). These differences are of the order of about 100 kJ/mol for the zwitterionic structures and about 60 kJ/mol for the nonzwitterionic structures. It appears that the CNDO/2 approximation leads to a severe underestimation of the electrostatic lattice energies. This effect is also observed in crystals of carboxylic acids.[31] The mutual differences in the electrostatic lattice energies within the ab initio basis sets are much smaller, up to 45 kJ/mol for the zwitterionic crystals and up to 12 kJ/mol for the nonzwitterionic crystals. The origin of these differences in the electrostatic lattice energies is the variation of the point charges with the basis set. In Table III this variation is demonstrated for glycine. Because of the somewhat arbitrary nature of the Mulliken populations a larger basis set does not necessarily lead to a more accurate set of point charges. For this reason it is not possible to say which of the values for the electrostatic lattice energies are most reliable. In Figure 4 we show the minimal basis Mulliken charges for all the molecules considered here. It is noticed that the point charges of a particular group of atoms (e.g., NH_3^+, COO^-, CH_2) are transferable to equivalent groups in other molecules (this holds for all basis sets studied here).

The first group of compounds of Table II are all zwitterionic structures, the last group of compounds of this table are nonzwitterionic structures, while anthranilic acid I is a "mixed" crystal structure, with one zwitterion and one nonzwitterion in the asymmetric unit. The electrostatic lattice energies of the zwitterionic crystals are much larger than the electrostatic lattice energies of the nonzwitterionic crystals. However, the difference is roughly cancelled by the proton-transfer energy as is apparent from Table IV. Thus in agreement with experiment[2] the result is that one obtains comparable enthalpies of sublimation for both types of crystals, assuming that the van der Waals and hydrogen-bond contributions to the lattice energies are approximately similar.

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