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Photodetachment of Zwitterions: Probing Intramolecular Coulomb Repulsion and Attraction in the Gas Phase Using Pyridinium Dicarboxylate Anions

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Abstract: Zwitterions are critically important in many biological transformations and are used in numerous chemical processes. The consequences of electrostatic effects on reactivity and physical properties, however, are largely unknown. In this work, we report the results of negative ion photoelectron spectra of nine isomeric pyridinium dicarboxylate zwitterions and three nonzwitterionic methoxycarbonylpyridine carboxylate isomers ($^{-}O_2CPyrCO_2CH_3$). Information about the intramolecular electrostatic interactions was directly obtained from the photoelectron spectra. The adiabatic and vertical detachment energies were measured and understood in terms of intramolecular Coulombic forces. Calculations at the B3LYP and CCSD(T) level were performed and compared to the experimental electron binding energies. Structures, relative stabilities, and the electron detachment sites also were obtained from the calculations.

Introduction

Zwitterions are compounds with oppositely charged centers and are often referred to as dipolar ions, salt-bridge-containing molecules, and inner salts. This diverse nomenclature is a reflection of the extraordinary importance of these species in biological transformations, organic synthesis, the preparation of novel materials, and as chromatographic supports.[1−6] In aqueous solutions, all 20 essential amino acids exist in their zwitterionic form (e.g., $^{+}NH_3CH_2CO_2^{-}$, glycine) over a wide pH range (∼2−10). The resulting forces generated by the charged centers play a critical role in determining the structure and function of proteins and enzymes.[7−9] A detailed understanding of the chemical consequences of electrostatic effects, however, is largely lacking.[10−13] Given that the dielectric constant and physical environment of an enzyme's active site often are closer in nature to those in the gas phase than in bulk solution, fundamental insights of biological significance can be obtained from gas-phase investigations of dipolar ions.[14]

Peptides, proteins, and enzymes are commonly assumed to form salt bridges in the gas phase.[15−19] The presence of these zwitterionic interactions, undoubtedly, impacts the mass spectroscopic analysis of biological samples, but their ramifications are largely unknown. Recently, we reported the first preparation and characterization of a gas-phase zwitterionic ion (*D*(3,5)) and its nonzwitterionic counterpart (*3C-5E-Pyr*) (Figure 1),[20]

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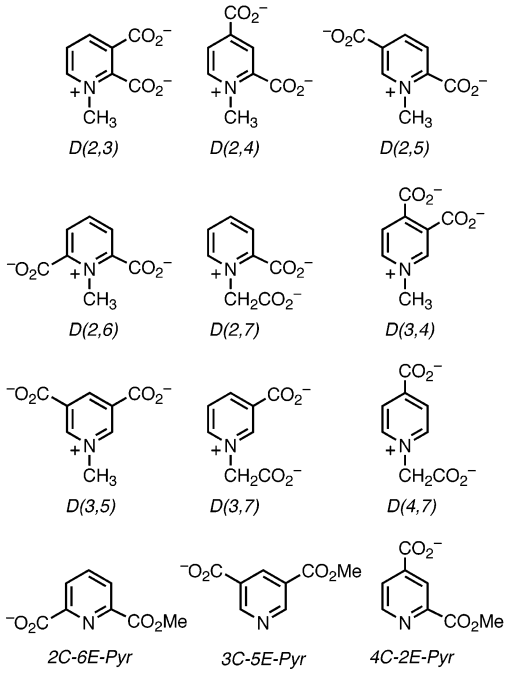

Figure 1. Anionic species studied in this work and their abbreviations.

and the first spectroscopic characterization of such species via negative ion photoelectron spectroscopy.[21] To gain a better understanding of dipolar anions, and as a prelude to investigating biological decarboxylation reactions, we report herein on nine zwitterionic dicarboxylates (*D*(*x*,*y*)) and three "neutral" reference ions (*2C-6E-Pyr*, *3C-5E-Pyr*, and *4C-2E-Pyr*), all of which are shown in Figure 1.

Experimental Section

Methods and Materials. Picolinic, nicotinic, and isonicotinic acids (*o*-, *m*-, and *p*-pyridinecarboxylic acids), 2,3-, 2,4-, 2,5-, 2,6-, 3,4-, and 3,5-pyridinedicarboxylic acids, and 2,6-dimethoxycarbonylpyridine were purchased from Sigma-Aldrich or Lancaster Synthesis and used as received. Solvents were dried by standard methods, and all other reagents were used as received. ^{1}H and ^{13}C NMR spectra were recorded on Varian VAC-200, VAC-300, or VI-500 spectrometers and are reported in ppm (δ). Combustion analyses were carried out by M-H-W Laboratories (Phoenix, AZ).

General Procedure for the Preparation of Dimethoxycarbonylpyridines.[22] The desired dimethoxycarbonylpyridines were prepared according to standard literature procedures.[20,23] In particular, the selected pyridinedicarboxylic acid (~0.02 mol) was dissolved in a solution containing 20 mL of methanol and ~6 mL of concentrated sulfuric acid, and was heated at reflux for 24−48 h under an argon atmosphere. Upon being cooled to room temperature, the reaction mixture was neutralized with a saturated sodium carbonate solution and concentrated to dryness at aspirator pressure. The solid residue was dissolved in water and chloroform, and the organic layer was washed with water until the aqueous layer had a pH of 7. It was then dried with $MgSO_4$, and the solvent was removed with a rotary evaporator.

General Procedure for the Preparation of Dimethoxycarbonyl-1-methylpyridinium Methyl Sulfates.[24] Following literature procedures,[20,22] a solution containing the appropriate dimethoxycarbonylpyridine (0.04 mol) and dimethyl sulfate (0.24 mol) in 10 mL of dry benzene was heated under an argon atmosphere at reflux for 6−24 h. The solvent and the excess alkylating reagent were removed under high vacuum (~1×10^{-7} Torr) to afford oils, except in the case of the 2,3-bis-ester which crystallized, and these crude materials were taken on without further purification.

General Procedure for the Preparation of Dicarboxy-1-methylpyridinium Chlorides. The selected dimethoxycarbonyl-1-methylpyridinium methyl sulfate (~4 mmol) was added to 4 mL of a 10 M HCl solution and heated at reflux for 4 h. Concentration of the reaction mixture under aspirator pressure afforded a solid product which was recrystallized from hot water.

2,3-Dicarboxy-1-methylpyridinium Chloride.[25] This compound was obtained in a nonoptimized overall yield of 8% starting from 2,3-dimethoxycarbonylpyridine (mp 250−254 °C (dec)). ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.30 (s, 3H), 8.21 (br t, J = 7.5 Hz, 1H), 8.94 (d, J = 8.1 Hz, 1H), 9.17 (d, J = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 47.0, 127.4, 128.3, 145.4, 147.1, 149.6, 162.5, 163.7.

2,4-Dicarboxy-1-methylpyridinium Chloride.[22,25] This compound was obtained in a nonoptimized overall yield of 18% starting from 2,4-dimethoxycarbonylpyridine (mp 208−210 °C (dec)). ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.49 (s, 3H), 8.43 (d, J = 5.7 Hz, 1H), 8.49 (s, 1H), 9.15 (d, J = 6.0 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 48.3, 127.3, 127.4, 140.1, 146.3, 149.2, 161.5, 163.9 (lit.[5b] (H_2O) 50.1, 130.6, 147.1, 147.2, 151.0, 161.8, 164.75, 164.82).

2,5-Dicarboxy-1-methylpyridinium Chloride.[22a,25] This compound was obtained in a nonoptimized overall yield of 45% starting from 2,5-dimethoxycarbonylpyridine (mp 168−170 °C (dec)). ^{1}H NMR (300 MHz, D_2O): δ 4.27 (s, 3H), 7.98 (d, J = 8.1 Hz, 1H), 8.82 (d, J = 8.1 Hz, 1H), 9.12 (s, 1H) [lit.[22a] 4.31 (s, 3H), 8.02 (d, J = 8.0 Hz, 1H), 8.86 (dd, J = 8.0 and 2.0 Hz, 1H), 9.16 (d, J = 2.0 Hz, 1H)]. ^{13}C NMR (75 MHz, NaOD/D_2O, pH = 4): δ 46.8, 125.8, 131.7, 146.1, 147.0, 153.9, 165.0, 165.4.

3,4-Dicarboxy-1-methylpyridinium Chloride.[22a] This compound was obtained in a nonoptimized overall yield of 13% starting from 3,4-dimethoxycarbonylpyridine (mp 223−225 °C (dec)). ^{1}H NMR (300 MHz, D_2O): δ 4.27 (s, 3H), 7.86 (d, J = 6.3 Hz, 1H), 8.77 (d, J = 6.3 Hz, 1H), 9.13 (s, 1H) [lit.[2a] 4.21 (s, 3H), 7.90 (br d, J = 7.0 Hz, 1H), 8.75 (br d, J = 7.0 Hz, 1H), 9.11 (br s, 1H)]. ^{13}C NMR (75 MHz, NaOD/D_2O, pH = 3): δ 48.1, 125.3, 128.3, 147.4, 147.8, 153.4, 164.7, 170.4.

2,6-Dimethoxycarbonyl-1-methylpyridinium Trifluoromethanesulfonate.[26] 2,6-Dimethoxycarbonylpyridine (1.95 g, 10 mmol) was dissolved in 10 mL of methylene chloride (freshly distilled from CaH_2) and methylated at 40 °C by adding 30 mL of a 1.0 M methylene chloride solution of methyl trifluoromethanesulfonate in three equal portions over a 2 week period. The reaction mixture was then cooled to room temperature, diluted with 150 mL of diethyl ether, and placed in a refrigerator for 24 h. Small needlelike crystals of 2,6-dimethoxycarbonyl-1-methylpyridinium trifluoromethanesulfonate precipitated out of solution and were recrystallized from ethyl acetate to afford 1.72 g (53%) of the desired product (mp 75−79 °C (dec), lit.[26a] 97−99 °C). ^{1}H NMR (200 MHz, DMSO-d_6): δ 4.05 (s, 6H), 4.58 (s, 3H), 8.64 (d, J = 8.1 Hz, 2H), 8.91 (t, J = 8.1 Hz, 1H). ^{13}C NMR (50 MHz, DMSO-d_6): δ 46.5, 55.3, 131.6, 146.3, 148.6, 160.4.

2,6-Dicarboxy-1-methylpyridinium Chloride.[25] 2,6-Dimethoxycarbonyl-1-methylpyridinium trifluoromethanesulfonate was hydrolyzed

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by reacting it with 5 mL of 0.5 M HCl at reflux for 2 h. After the reaction mixture was cooled, it was concentrated with a rotary evaporator and diluted with 10 mL of diethyl ether. Upon refrigeration, 2,6-dicarboxy-1-methylpyridinium chloride slowly crystallized from solution, and 0.32 g (12%) was collected by filtration (mp 152−155 °C). ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.41 (s, 3H), 8.33 (d, J = 8.0 Hz, 2H), 8.68 (t, J = 8.0 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 45.2, 128.7, 147.5, 149.6, 162.1.

4-Carboxy-2-methoxycarbonylpyridine.[23,27] Partial hydrolysis of 2,4-dimethoxycarbonylpyridine (0.5 g, 2.6 mmol) with 1 equiv of potassium hydroxide (0.14 g) in 25 mL of methanol was carried out at 0 °C over 2 h. The solvent was removed with a rotary evaporator, and the resulting solid was washed with ethyl acetate and collected by vacuum filtration. The resultant salt was dissolved in water, acidified with concentrated HCl, and extracted three times with 4 mL portions of chloroform. Removal of the solvent after drying with $MgSO_4$ afforded 0.13 g (27%) of the half ester-half acid (mp 244−246 °C (dec)). ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.91 (s, 3H, NOE with 8.37 (strong) and 8.90 (weak)), 8.03 (dd, J = 1.5 and 4.9 Hz, 1H, NOE with 8.90 (strong)), 8.37 (dd, J = 0.6 and 1.5 Hz, 1H, NOE with 3.91 (strong) and 8.90 (weak)), 8.90 (dd, J = 0.6 and 4.9 Hz, 1H, NOE with 3.91 (weak), 8.03 (strong), and 8.37 (weak)). ^{13}C NMR (75 MHz, DMSO-d_6): δ 53.2, 124.1, 126.8, 140.1, 149.0, 151.6, 165.2, 165.9.

2-Carboxy-6-methoxycarbonylpyridine.[23,27] Partial hydrolysis of 2,6-dimethoxycarbonylpyridine (0.5 g, 2.6 mmol) was carried out as described for the 2,4-isomer to afford 0.21 g (51%) of the half ester-half acid (mp 141−144 °C [lit. 148−150 °C][23]). ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.06 (s, 3H), 8.15 (t, J = 7.8 Hz, 1H), 8.38 (dd, J = 1.2, 7.8 Hz, 1H), 8.44 (dd, J = 1.1, 7.7 Hz, 1H) [lit. ($CDCl_3$) δ 4.04 (s, 3H), 8.14 (t, J = 7.8 Hz, 1H), 8.37 (d, J = 6.8 Hz, 1H), 8.42 (d, J = 7.8 Hz, 1H)]. ^{13}C NMR (75 MHz, DMSO-d_6): δ 53.2, 128.2, 128.4, 139.6, 148.1, 149.3, 165.3, 166.2.

2-Carboxy-1-carboxymethylpyridinium Hydroxide, Inner Salt. *o*-Pyridinecarboxylic acid (2.0 g, 16.3 mmol) and chloroacetic acid (2.0 g, 21.2 mmol) were added to a stirred solution containing 50 mL of water and 4% NaOH by weight, and the mixture was refluxed for 96 h. After the solution was allowed to cool to room temperature, 50 mL of 2 N HCl was added with stirring. The resulting mixture was evaporated to dryness, and the solid residue was dissolved in 1 mL of H_2O and diluted with 50 mL of methanol. This solution was refluxed for 15 min, and the resulting precipitate was filtered from the hot liquid. After the solvent was removed with a rotary evaporator, the product was crystallized from H_2O−EtOH to afford 0.52 g (18%) of 2-carboxy-1-carboxymethylpyridinium hydroxide, inner salt (mp 157−158 °C (dec), lit.[28]162 °C (dec)). To obtain the sodium salt of this compound, the inner salt was dissolved in aqueous sodium bicarbonate, and ethanol was added to precipitate out the product. Free acid, ^{1}H NMR (300 MHz, D_2O): δ 5.59 (s, 2H), 8.07 (t, J = 6.9 Hz, 1H), 8.29 (d, J = 7.8 Hz, 1H), 8.65 (t, J = 7.8 Hz, 1H), 8.75 (d, J = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, D_2O): δ 60.9, 128.2, 128.3, 147.1, 147.9, 150.8, 164.7, 169.8. Na salt, ^{1}H NMR (300 MHz, D_2O): δ 5.34 (s, 2H), 7.99 (t, J = 6.9 Hz, 1H), 8.13 (d, J = 8.1 Hz, 1H), 8.55 (t, J = 7.5 Hz, 1H), 8.64 (d, J = 6.3 Hz, 1H). ^{13}C NMR (75 MHz, D_2O): δ 62.2, 127.4, 127.5, 146.2, 146.8, 151.8, 165.4, 171.3. Anal. Calcd for $C_8H_7NO_4$: C, 53.04; H, 3.90; N, 7.73. Found: C, 52.61; H, 4.11; N, 7.53.

3-Carboxy-1-carboxymethylpyridinium Hydroxide, Inner Salt. To a stirred suspension of 2.0 g (16.3 mmol) of *m*-pyridinecarboxylic acid and 2.0 g (21.2 mmol) of chloroacetic acid in 30 mL of methanol was added 2.8 g (33.3 mmol) of sodium bicarbonate, and the resulting mixture was refluxed for 48 h. After being heated for 1−2 h, all of the solid material was dissolved, and thereafter a white precipitate formed. This material was filtered, washed with methanol, and then dissolved in 20 mL of hot water. Next 2 N HCl (20 mL) was added to the aqueous solution, and then 90% of the liquid volume was removed at reduced pressure using a rotary evaporator. Crystalline product was obtained from the residual methanol−water solution and was dried in a vacuum pistol (mechanical pump pressures) at 100 °C over P_2O_5 to afford 2.15 g (73%) of 3-carboxy-1-carboxymethylpyridinium hydroxide, inner salt (mp 180−185 °C (dec), lit.[28] 190 °C (dec)). Free acid, ^{1}H NMR (300 MHz, D_2O): δ 5.42 (s, 2H), 8.20 (dd, J = 6.3 and 8.1 Hz, 1H), 8.95 (d, J = 6.3 Hz, 1H), 9.02 (d, J = 8.1 Hz, 1H), 9.31 (s, 1H). ^{13}C NMR (75 MHz, D_2O): δ 63.0, 128.2, 133.7, 146.3, 147.0, 147.9, 165.9, 170.1. Na salt, ^{1}H NMR (300 MHz, D_2O): δ 5.27 (s, 2H), 8.10 (dd, J = 6.3 and 8.1 Hz, 1H), 8.80 (d, J = 6.3 Hz, 1H), 8.88 (d, J = 8.1 Hz, 1H), 9.10 (s, 1H) [lit.[29] 5.18 (s, 2H), 8.02 (dd, J = 5.8 and 8.1 Hz, 1H), 8.72 (d, J = 5.8 Hz, 1H), 8.80 (d, J = 8.1 Hz, 1H), 9.00 (br s, 1H)]. ^{13}C NMR (75 MHz, D_2O): δ 63.7, 127.8, 137.1, 145.5, 146.3, 146.5, 168.1, 171.0 [lit.[29] 64.2, 128.3, 137.6, 146.0, 146.8, 147.0, 168.5, 171.5].

4-Carboxy-1-carboxymethylpyridinium Hydroxide, Inner Salt. To a stirred suspension of 2.0 g (16.3 mmol) of *p*-pyridinecarboxylic acid and 2.0 g (21.2 mmol) of chloroacetic acid in 30 mL of methanol was added 2.82 g (33.5 mmol) of sodium bicarbonate, and the resulting mixture was refluxed for 48 h. After being heated for 3−4 h, all of the solid material was dissolved, and thereafter a white precipitate formed. This material was filtered, washed with methanol, and then dissolved in 20 mL of hot water. Next 2 N HCl (20 mL) was added to the aqueous solution, and then 90% of the liquid volume was removed at reduced pressure using a rotary evaporator. Crystalline product was obtained from the residual methanol−water solution and was dried in a vacuum pistol (mechanical pump pressures) at 100 °C over P_2O_5 to afford 1.97 g (67%) of 4-carboxy-1-carboxymethylpyridinium hydroxide, inner salt (mp 270 °C (dec), lit.[28] 262 °C (dec)). To obtain the sodium salt of this compound, the inner salt was dissolved in aqueous sodium bicarbonate, and methanol was added to precipitate out the product. Free acid, ^{1}H NMR (300 MHz, D_2O): δ 5.38 (s, 2H), 8.39 (d, J = 6.3 Hz, 2H), 8.90 (d, J = 6.3 Hz, 2H). ^{13}C NMR (75 MHz, D_2O): δ 62.8, 126.8, 127.3, 142.5, 146.7, 149.9, 167.2, 170.0. Na salt, ^{1}H NMR (300 MHz, D_2O): δ 5.25 (s, 2H), 8.27 (d, J = 6.9 Hz, 2H), 8.81 (d, J = 6.9 Hz, 2H). ^{13}C NMR (75 MHz, D_2O): δ 63.5, 126.8, 146.2, 152.8, 169.4, 171.0. Anal. Calcd for $C_8H_7NO_4$: C, 53.04; H, 3.90; N, 7.73. Found: C, 53.17; H, 3.94; N, 7.79.

Photodetachment Photoelectron Spectroscopy (PES). The PES experiments were performed with a magnetic-bottle time-of-flight photoelectron analyzer coupled with an electrospray ion source and an ion-trap mass spectrometer. Details of this apparatus have been described elsewhere.[30] Briefly, nine zwitterionic anions ($D(x,y)$) and three nonzwitterions (*2C-6E-Pyr*, *3C-5E-Pyr*, *4C-2E-Pyr*), as shown in Figure 1, were sprayed into the gas phase using 10^{-3} M solutions of their corresponding salts dissolved in a 30:70 (v/v) water/methanol mixture. Anions produced from the electrospray source were transported into a quadrupole ion trap where they were accumulated for 0.1 s before being pulsed out for mass-to-charge ratio analyses with a time-of-flight mass spectrometer. The main ion signals were the $D(x,y)$ anions and the conjugate bases of the substituted pyridinecarboxylic acids. The ions of interest were mass-selected and decelerated before being detached by a laser beam in the interaction zone of the magnetic-bottle photoelectron spectrometer. Two photon energies from an excimer laser (157 and 193 nm) were used for photodetachment in this study: 193 nm (6.424 eV) and 157 nm (7.866 eV). The electron kinetic energy resolution was $\Delta E/E \approx 2\%$, that is, ~10 meV for 0.5 eV electrons, as measured from the spectrum of I^- at 355 nm.

Computational Details. Full geometry optimizations were carried out using the B3LYP mixed-hybrid density functional and the 6-31+G-(d) basis set.[31] All of the resulting structures were analyzed in terms of

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their second derivatives (Hessian matrices) to ensure that each species is a minimum on the potential energy surface and to provide their zero-point energies (ZPEs). Radicals were computed using the spin-unrestricted formulism (i.e., UB3LYP), and their spin contamination, as assessed by the expectation value of S^2, is small in each case. Adiabatic electron affinities (EAs) of the radicals were calculated at 0 K by taking the difference in the ZPE-corrected electronic energies of the anions and their corresponding radicals. Isogyric reactions also were used for the dicarboxylates to account for the average error in the calculated adiabatic dissociation energies (ADEs = EAs) of the conjugate bases of *o*-, *m*-, and *p*-pyridinecarboxylic acid. Vertical dissociation energies (VDEs) in which the geometry of the anion was used for the corresponding radical were computed too, although in this case no ZPE correction was applied.

In one instance, *D*(3,4), single-point energy calculations were carried out at the B3LYP/6-311+G(2df,2pd), MP2/6-31G(d), MP2/6-311+G-(3df,2p), and CCSD(T)/6-31G(d) levels.[32,33] Again, the spin-unrestricted method was used for the radical calculations except for a R(U)CCSD-(T) energy which was obtained using MOLPRO.[34] An effective CCSD-(T)/6-311+G(3df,2p) energy was subsequently obtained by taking the difference in the MP2 energies and adding it to the CCSD(T)/6-31G-(d) result (eq 1).

$$\text{CCSD(T)/6-311+G(3df,2p)} = \text{CCSD(T)/6-31G(d)} + [\text{MP2/6-311+G(3df,2p)} - \text{MP2/6-31G(d)}] \quad (1)$$

This approach and one where diffuse functions are included in the small basis set (i.e., 6-31+G(d) instead of 6-31G(d)) also were used to compute the electron binding energy (EBE, EBE = ADE = EA) of benzoate. The results, 3.57 (6-31G(d)) and 3.55 (6-31+G(d)), are virtually the same and are in good accord with the experimental value of 3.70 ± 0.10 eV.[35] This additivity approach is analogous to G2-(MP2) and G3(MP2) theory,[36,37] gives the same electron affinity for phenyl radical as the full blown CCSD(T)/6-311+G(3df,2p) calculation to within 0.07 eV, and reproduces the experimental EAs of a number of related monocarboxylate species.[38]

All of the DFT and MP2 calculations were carried out using Gaussian 98[39] on IBM and SGI workstations at the Minnesota Supercomputer Institute (MSI). CCSD(T) computations were carried out using MOLPRO[34] also at the MSI because these energies are computed more efficiently with this program.

Results

Photoelectron Spectra. Figure 2 shows the photoelectron spectra of the nine *D*(*x*,*y*) zwitterion anions at 157 nm. Data were also obtained at 193 nm (not shown here) with slightly better resolution. The broad feature at the low binding energy side (2.3−4.0 eV) of the *D*(3,4) spectrum is due to an unknown impurity with the same mass-to-charge ratio as the *D*(3,4) anion. The intensity of this feature was dependent on the photon energies used and the age of the solution. Overall, the spectral patterns of all of the *D*(*x*,*y*) zwitterions are similar. They all consist of a strong broad band with several discernible features below about 6.5 eV and much weaker features above 6.5 eV. The spectra of *D*(2,6) and *D*(3,5), which are more symmetric (Figure 1), seem to have well-resolved threshold features. Except for those of *D*(3,7) and *D*(4,7), the spectra of the other *D*(*x*,*y*) species also exhibited a discernible feature near the threshold. Because no vibrational structures were resolved, the ADEs were estimated from the threshold of each PES spectrum by drawing a straight line along the leading edge and then adding a constant to the intersection with the binding energy axis to take into account the instrumental resolution and a finite thermal effect. The VDEs were estimated from the maxima of the threshold features and have relatively large uncertainties for those species where the threshold features are not well resolved. All of the ADEs and VDEs were measured from the 193 nm spectra, which yielded more accurate values because of the slightly better instrumental resolution. The obtained ADEs and VDEs for all nine zwitterions are given in Table 1. We note that the lowest ADE is for *D*(3,4) (4.17 eV) and the highest one is for *D*(3,7) (5.14 eV), consistent with intramolecular electrostatic interactions.

The 157 nm spectra of nonzwitterions *2C-6E-Pyr*, *3C-5E-Pyr*, and *4C-2E-Pyr* are shown in Figure 3a and are compared with their corresponding *D*(2,6), *D*(3,5), and *D*(2,4) zwitterions. All three nonzwitterions have similar spectra, each with numerous well-resolved spectral features. The strong low binding energy features are similar to those of the corresponding *D*(*x*,*y*) species, but the higher binding energy features are all much stronger in the "neutral" ions. The ADEs and VDEs of the three nonzwitterionic isomers also are given in Table 1, and they are smaller than those of their dipolar analogues.

Computational Results. Geometry optimizations at the B3LYP level with the 6-31+G(d) basis set were carried out on all nine *D*(*x*,*y*) zwitterionic species, the three nonzwitterions (*4C-2E-Pyr*, *2C-6E-Pyr*, *3C-5E-Pyr*), benzoate, *o*-, *m*-, and *p*-pyridinecarboxylate, and all of their corresponding radicals. A summary of the structural parameters for the *D*(*x*,*y*) anions is given in Table 2, and their three-dimensional geometries are illustrated in Figure 4. More complete structural and energetic data (*xyz* coordinates, absolute energies, and ZPEs) can be found in the Supporting Information.

The ADEs and VDEs were also computed at the B3LYP/6-31+G(d) level for all 16 anions noted above and are given in Table 1. In one case, single-point energy calculations were carried out to provide the ADE for the *D*(3,4) anion at the B3LYP/6-311+G(2df,2pd) and CCSD(T)/6-311+G(3df,2p) levels; the latter result was obtained via an additivity scheme as described in the Experimental Section. These calculations using the larger basis set improved upon the agreement with the measured electron binding energies by a mere 0.02 and 0.14

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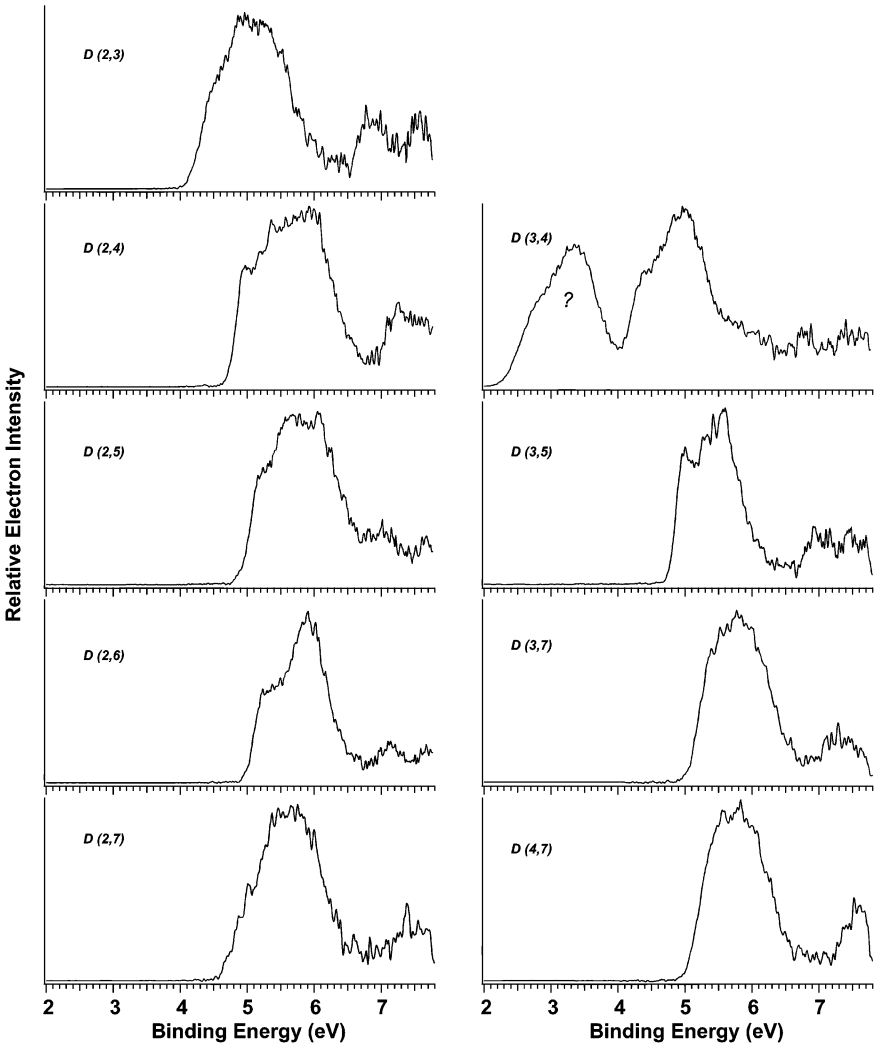

Figure 2. Photoelectron spectra at 157 nm (7.866 eV) for zwitterionic dicarboxylates $D(x,y)$. The lowest binding energy feature (labeled ?) in the spectrum of $D(3,4)$ is due to an unknown impurity.

eV, respectively. Consequently, similar calculations were not carried out for the other dipolar ions.

Discussion

General Comments Pertaining to the PES Detachment Features. The strong broad bands in all of the spectra are due to detachment from the carboxylate groups. As a result, the general characteristics of these spectra are similar to those for benzoate and the benzenedicarboxylates, which also showed detachment features from the carboxylate group at low binding energies (3.6−5.0 eV), as well as a broad feature around 5.5 eV attributed to detachment from the benzene ring π orbitals.[35] In fact, the low binding energy features of the three nonzwitterions below 5.5 eV (Figure 3a) are almost identical to that of benzoate. Accordingly, the strong band near 6 eV in the nonzwitterion spectra (Figure 3a) is due to detachment from the pyridine ring π orbitals. The higher binding energy features are likely due to detachment from the N lone pairs or the O lone pairs on the neutral ester groups.

The strong low binding energy features in all of the $D(x,y)$ zwitterions also are due to detachment from the carboxylate groups. The apparently more complicated and broader bands of the $D(x,y)$ ions are due to the fact that there are two carboxylate groups which can both contribute to these features. It is interesting to note that the features in the spectra of $D(2,6)$ and $D(3,5)$ are narrower and better resolved. They also are more similar to those features in the corresponding nonzwitterions (Figure 3). This is because the two carboxylate groups are equivalent in these two species (Figure 1). Among all of the $D(x,y)$ anions, the threshold band in the spectrum of the $D(2,4)$ ion appears to be the broadest. Presumably, this is due, in part, to the large difference in the electronic environments of the two carboxylate groups; one is close to the positive charge center, and the other is far away. It is also significant to note that the strong features attributed to the pyridine ring π electrons are missing in all of the spectra of the $D(x,y)$ species because the positive charge on N must have a large stabilizing effect on these orbitals.

Electron Binding Energies and Intramolecular Electrostatic Interactions of the *D*(*x*,*y*) Zwitterions and the *2C-6E-Pyr*, *3C-5E-Pyr*, and *4C-2E-Pyr* Nonzwitterions. The electron binding energies of *o*-, *m*-, and *p*-pyridinecarboxylate anions range from 3.70 to 4.05 eV.[40] Substitution of a methyl ester group for a hydrogen atom in these ions leads to an increase of ∼0.2 eV, on average, in the ADEs, and EBEs for *2C-6E-Pyr*,

(40) Wang, X. B.; Wang, L. S., unpublished results.

Table 1. Adiabatic (ADE) and Vertical (VDE) Electron Detachment Energies and Relative Stabilities for Zwitterionic *D*(*x*,*y*) Anions and Related Species[a]

	ADE (eV)		VDE (eV)		rel stability (kcal/mol)		
cmpd	B3LYP	expt	B3LYP	expt	B3LYP	AM1	Coul. law
D(2,3)	3.99	4.25 ± 0.05	4.29	4.50 ± 0.10	20.6	26.3	57.6
D(2,4)	4.77	4.83 ± 0.05	4.85	4.98 ± 0.08	4.7	9.2	37.7
D(2,5)	4.87	5.02 ± 0.05	4.96	5.23 ± 0.10	0.0	2.8	24.6
D(2,6)	4.88	5.08 ± 0.05	4.88	5.32 ± 0.10	1.9	0.0	0.0
D(3,4)	3.70	4.17 ± 0.10	4.33	4.42 ± 0.10	26.1	33.6	99.5
	(3.84)[b]						
D(3,5)	4.67	4.85 ± 0.05	4.72	5.02 ± 0.05	7.9	14.8	62.8
D(2,7)	4.65	4.75 ± 0.05	4.79	5.03 ± 0.10	8.6	5.4	11.0
D(3,7)	4.88	5.14 ± 0.05	4.94	5.40 ± 0.10	3.0	3.5	25.9
D(4,7)	4.87	5.12 ± 0.05	4.93	5.57 ± 0.10	3.3	4.7	31.3
2C-6E-Pyr	3.86	3.85 ± 0.05	4.55	4.10 ± 0.08	−0.8	−9.1	
3C-5E-Pyr	4.13	4.17 ± 0.07	4.46	4.36 ± 0.06	8.2	−20.6	
4C-2E-Pyr	4.21	4.25 ± 0.05	4.47	4.46 ± 0.10	6.6	−15.7	
o-PyrCO_2^-	3.39	3.70 ± 0.10[c]	3.91	4.00 ± 0.10	8.8	5.9	
m-PyrCO_2^-	3.69	3.95 ± 0.10[c]	4.22	4.30 ± 0.10	1.4	0.2	
p-PyrCO_2^-	3.79	4.05 ± 0.10[c]	4.32	4.35 ± 0.10	0.0	0.0	
PhCO_2^-	3.43	3.70 ± 0.10[d]	4.10	3.98± 0.07[d]			
	(3.57)[b]						

[a] Computed energies are at the B3LYP/6-31+G(d) level. ADEs for the *D*(*x*,*y*) and *rC-sE-Pyr* anions have been corrected by adding 0.28 eV to account for the average error in the computed values for *o*-, *m*-, and *p*-pyrCO_2^- and PhCO_2^-. Likewise, the VDEs have been adjusted by adding 0.06 eV. [b] CCSD(T)/6-311+G(3df,2p)//B3LYP/6-31+G(d) energy (see text for further details) corrected for the calculated error in the ADE of benzoate anion (0.13 eV too small) using the same computational procedure. [c] See ref 40. [d] See ref 35.

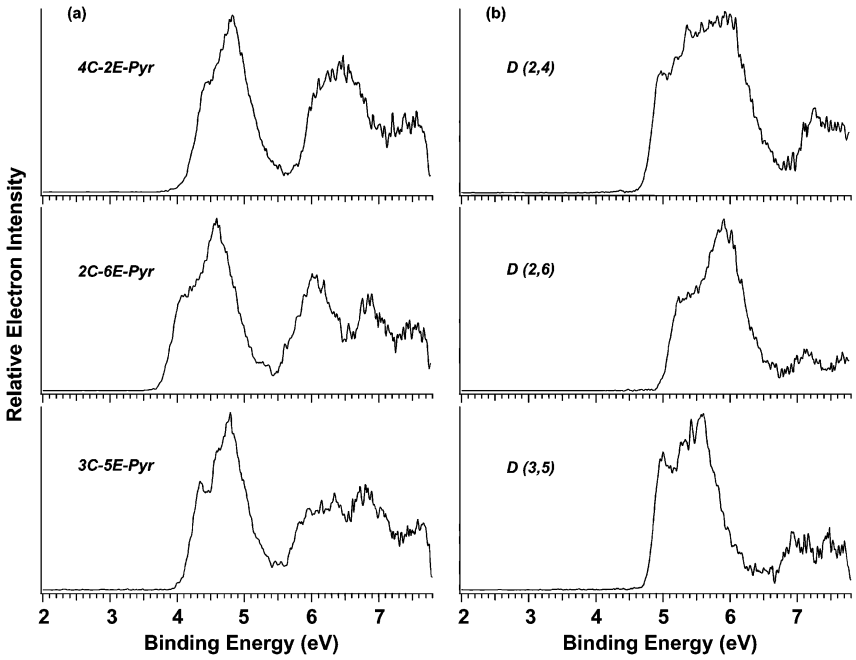

Figure 3. Photoelectron spectra at 157 nm for (a) *4C-2E-Pyr*, *2C-6E-Pyr*, and *3C-5E-Pyr* and (b) the corresponding zwitterions.

3C-5E-Pyr, and *4C-2E-Pyr* of 3.85 to 4.25 eV (see Table 1). This increase in the ADEs of the latter species is due to the electron-withdrawing nature of the methyl ester group (CO_2-CH_3). In comparison, the electron binding energies of the corresponding *D*(2,6), *D*(3,5), and *D*(2,4) zwitterionic anions are even higher than their nonzwitterionic analogues (Table 1). These differences and the ADEs of all of the dipolar *D*(*x*,*y*) anions can be understood in terms of the electrostatic interactions within each molecule. In particular, the electron binding energies of the zwitterions are mainly determined by the combined effects of the mutual Coulomb repulsion between the two negative charges on the carboxylates and their attraction to the positively charged nitrogen-atom center.[41]

One can model the charge−charge interactions and the stability of the *D*(*x*,*y*) anions from a simple perspective by considering the number of bonds between the charged centers, and comparing the value for the repulsive term to the sum for the attractive interactions. For example, the *D*(2,6) and *D*(2,5) anions are predicted to be equally stable. In the former case, both carboxylates are adjacent to the positively charged nitrogen atom and are meta to each other, whereas in the latter species, the carboxylate at C5 is one bond further away from the N-atom (less favorable) and one bond more distant from the carboxylate at C2 (more favorable). In a similar manner, the following

(41) See ref 21 for a description of the point charge model that we employed.

Table 2. Geometric Parameters for Zwitterionic $D(x,y)$ Anions[a]

	compounds								
	D(2,3)	D(2,4)	D(2,5)	D(2,6)	D(2,7)	D(3,4)	D(3,5)	D(3,7)	D(4,7)
					Bonds				
N1−C2	1.371	1.364	1.364	1.369	1.362	1.361	1.358	1.357	1.356
C2−C3	1.416	1.400	1.397	1.392	1.402	1.383	1.385	1.388	1.386
C3−C4	1.391	1.392	1.391	1.392	1.387	1.419	1.404	1.398	1.400
C4−C5	1.404	1.410	1.403	1.392	1.400	1.423	1.404	1.396	1.403
C5−C6	1.374	1.372	1.380	1.394	1.382	1.370	1.385	1.387	1.380
C6−N1	1.364	1.367	1.363	1.370	1.361	1.366	1.358	1.356	1.359
$CH_{2(3)}$−N	1.479	1.475	1.479	1.485	1.486	1.464	1.471	1.482	1.477
$C_{(a)}$−CO_2[b]	1.546	1.544	1.550	1.546	1.550	1.570	1.560	1.557	1.557
$C_{(b)}$−CO_2[b]	1.558	1.559	1.555	1.554	1.589	1.527	1.560	1.591	1.593
r_1	2.411	2.403	2.297	2.631	2.451	2.214	2.354	2.286	2.454
r_2	2.448	2.415	2.425	2.155	2.715		2.603	2.446	2.481
r_3		2.520	2.508	2.704	2.256			2.472	2.453
					Angles				
OCCC	76.4	113.0	50.8	63.3	120.0	172.2	0.4	0.0	1.3
	(−111.0)[c]	(−67.9)[e]	(−127.9)[c]	(−114.9)[c]	(−56.2)[c]	(−7.0)[j]	(−179.5)[j]	(−179.5)[e]	(−179.2)[k]
OCCC	35.4	178.5	1.4	55.0	175.4	98.9	179.5	168.2	163.5
	(−148.0)[d]	(−1.6)[f]	(−178.6)[g]	(−122.6)[h]	(−6.3)[i]	(−89.4)[f]	(−0.4)[g]	(−14.0)[i]	(−18.9)[i]

[a] All distances and angles are in angstroms and degrees, respectively. Atomic labels are as shown in Figure 4; carboxylate carbons are C8 and C9, where the former is closer to the nitrogen atom. [b] For $D(x,y)$ anions, $a = x$ and $b = y$. [c] OC8C2C3 dihedral angles. [d] OC9C3C2 dihedral angles. [e] OC8C3C2 dihedral angles. [f] OC9C4C3 dihedral angles. [g] OC9C5C4 dihedral angles. [h] OC9C6C5 dihedral angles. [i] OC9C7N1 dihedral angles. [j] OC8C3C2 dihedral angles. [k] OC8C4C3 dihedral angles.

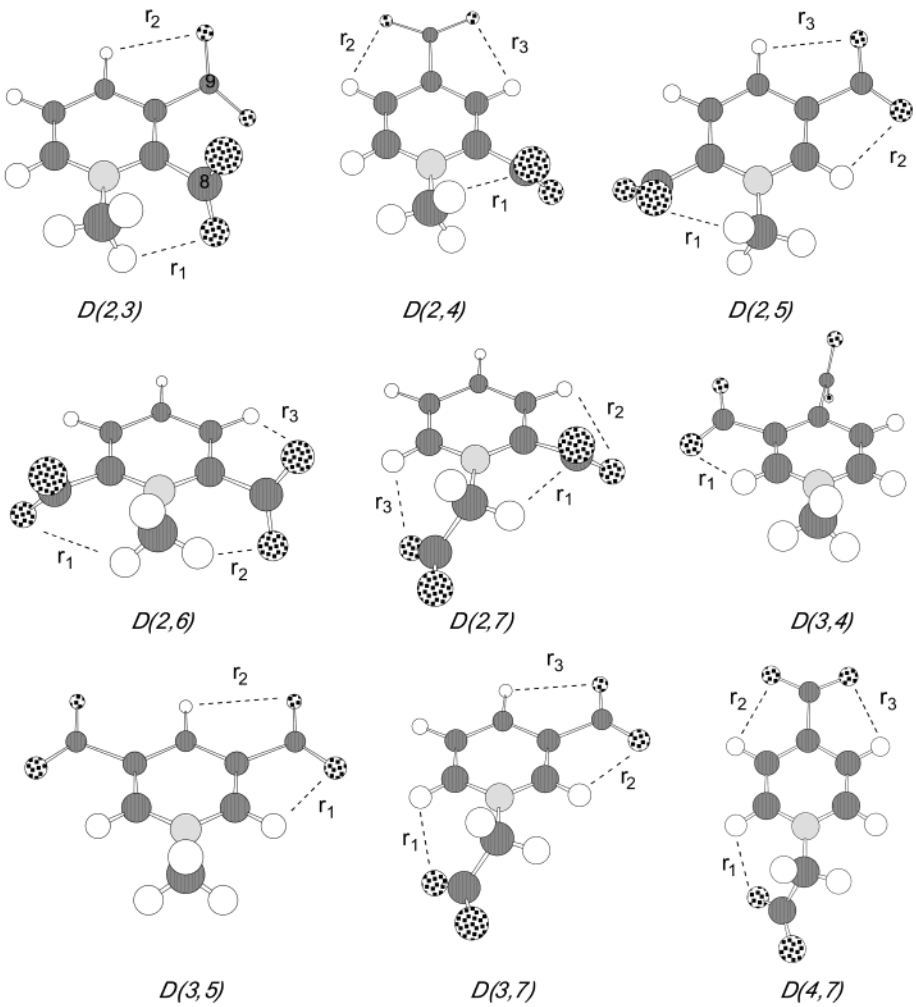

Figure 4. Computed B3LYP/6-31+G(d) geometries for the zwitterionic dicarboxylates $D(x,y)$.

stability order is obtained: D(2,6), D(2,5) > D(2,4), D(3,5), D(2,3) > D(3,4). This ordering also might be expected to reflect the ADEs. In accord with this expectation, the D(2,6) and D(2,5) anions have the largest ADEs in this group, and their values are the same within the experimental uncertainty (i.e., 5.08 ± 0.05 and 5.02 ± 0.05 eV, respectively). The D(2,4) and D(3,5)

ions have nearly identical ADEs (4.83 ± 0.05 and 4.85 ± 0.05 eV, respectively), which are ~0.2 eV smaller than those for the more stable *D*(2,6) and *D*(2,5) isomers. As predicted, the *D*(3,4) anion has the smallest ADE of the group (4.17 ± 0.10 eV). The *D*(2,3) isomer is anomalous, however, as its ADE (4.25 ± 0.05 eV) is similar to that for the *D*(3,4) anion (4.17 ± 0.10 eV). This failing of the model presumably is due to either the particularly unfavorable interaction between two adjacent carboxylate groups or a diminished electrostatic interaction between the C3-carboxylate and the positively charged N-center as a result of shielding brought about by the C2-carboxylate.

Further application of this model indicates that the *D*(2,7), *D*(3,7), and *D*(4,7) anions are equally stable and that their electron binding energies should be similar to those for the *D*(2,6) and *D*(2,5) zwitterions. This expectation is borne out for the latter two isomers (ADE = 5.14 ± 0.05 and 5.12 ± 0.05 eV, respectively), but not for the *D*(2,7) ion which has an ADE of 4.75 ± 0.05 eV, ~0.25 eV smaller than anticipated. This observation suggests that the Coulomb repulsion between the two negatively charged carboxylate groups plays a more important role in determining the stability of the *D*(*x*,*y*) dipolar ions because these two groups are much closer in *D*(2,7) (4.31 Å) than in *D*(3,7) and *D*(4,7) (6.18 and 6.66 Å, respectively).[42] The distances between the two carboxylate groups in the latter two anions are in fact very close to each other, as shown in Figure 4.

Structures of the *D*(*x*,*y*) Zwitterions. Our computational studies showed that all of the *D*(*x*,*y*) anions have C_1 symmetry except for the 3,5-isomer, which has a mirror plane perpendicular to the aromatic ring. The most notable structural feature, however, is the orientation of the carboxylate groups, which vary from compound to compound. This is a result, in part, of the small rotation barrier (4.0 kcal/mol) for benzoate anion (Ph−CO_2^-). Some trends in their orientation emerge nevertheless. Carboxylates in the 2-position are found to be closer to being perpendicular to the aromatic ring than planar to it. Presumably, this is the result of a steric interaction between the carboxylate and the N-substituted substituent. Carboxylates in the 3- and 4-position do not suffer from such an interaction and tend to adopt a pseudo-planar orientation with the aromatic ring because this results in increased conjugation between the π-system of the pyridine ring and the carboxylate group. The one exception to this generalization is for the *D*(3,4) ion where the carboxylate at C4 rotates so as to accommodate the one at C3. A second striking characteristic in these zwitterions are the intramolecular hydrogen bonds between the oxygen atoms of the carboxylates and the available aryl and methyl hydrogen atoms. These interactions are shown in Figure 4, and the distances, which span from 2.155 to 2.715 Å, are given in Table 2.

Comparison of the Computed Electron Binding Energies to Experiment. ADEs calculated at the B3LYP level with the 6-31+G(d) basis set generally are in excellent accord with experiment, but for $PhCO_2^-$, *o*-, *m*-, and *p*-$PyrCO_2^-$ the electron binding energies are too low by 0.26−0.31 eV. As a result, all of the other computed ADEs were corrected for the average error (0.28 eV) in these four ions (Table 1); this is equivalent to using four isogyric reactions to determine the EAs. The resulting values for *2C-6E-Pyr*, *3C-5E-Pyr*, and *4C-2E-Pyr* are in excellent accord with experiment (within 0.01−0.04 eV) as anticipated given their structural similarities to the reference compounds. As for the zwitterionic species, their ADEs are improved by the 0.28 eV isogyric correction, but the results are still systematically too low by anywhere from 0.06 to 0.47 eV; the average error is 0.21 eV.[43] This means that the directly computed values for the zwitterionic dicarboxylates are too small by ~0.5 eV or 11 kcal/mol. Employing the larger 6-311+G-(2df,2pd) basis set has little impact (<0.05 eV) on the monodecarboxylated zwitterions (i.e., *D*(*x*,*y*) − CO_2) and the one *D*(*x*,*y*) anion we tested. Coupled cluster theory at the CCSD-(T)/6-311+G(3df,2p) level also was explored. Because these calculations are too large to carry out on the ions of interest directly, an additivity scheme similar to those in G2(MP2) and G3(MP2) theory was carried out. Excellent results for the *D*(*x*,*y*) − CO_2 anions were obtained, but there is only a modest improvement (0.14 eV) for the ADE of the *D*(3,4) ion after correcting for the computed error in the electron binding energy of benzoate. This method is size-limited from a practical standpoint and currently is unsuitable for molecules that are larger than those in this study by more than one or two heavy atoms.

The relative stabilities of the *D*(*x*,*y*) zwitterions were analyzed not only by counting bonds but also via density functional theory, AM1 semiempirical calculations, and the application of Coulomb's law (Table 1).[41] In general, there is reasonable qualitative agreement between the different methods, but the AM1 and Coulomb's law results are not useful from a quantitative standpoint. This is not surprising, but the fact that AM1 and Coulomb's law give reasonable relative stabilities should prove useful when dealing with larger zwitterionic species.

Mulliken Population Analyses. We also examined the Mulliken population analyses (Table 3) to confirm the origin of the threshold detachment features of the *D*(*x*,*y*) anions. Both the spin densities and the atomic charges of the carboxyl groups indicate that the ejected electron largely comes from the carboxylate further away from the positively charged nitrogen

Table 3. Mulliken Population Spin Densities and Atomic Charges on the CO_2 Groups of the Radicals Derived from the *D*(*x*,*y*) Anions[a]

	C(*x*)–CO_2		C(*y*)–CO_2	
D(*x*,*y*)	spin	charge	spin	charge
D(2,3)	0.31	−0.46	0.62	−0.20
D(2,4)	0.01	−0.46	0.97	0.02
D(2,5)	0.17	−0.33	0.80	−0.11
D(2,6)	0.41	−0.30	0.41	−0.30
D(3,4)	0.49	−0.28	0.50	−0.22
D(3,5)	0.50	−0.27	0.50	−0.27
D(2,7)	0.22	−0.45	0.75	−0.03
D(3,7)	0.63	−0.43	0.34	−0.26
D(4,7)	0.64	−0.42	0.26	−0.24

[a] Computed structures are at the B3LYP/6-31+G(d) level. Combined spin densities and atomic charges for the CO_2 group attached to C(*x*) or C(*y*).

(42) It is somewhat surprising that this model works so well because electron binding energies correspond to an energy difference, and the stability of the zwitterionic radical is ignored. An alternative model in which the focus is on the attractive and repulsive interactions that are lost upon electron detachment, consequently, was considered. This was done by counting bonds and leads to the following predicted order for the ADEs: *D*(2,6), *D*(2,5), *D*(2,7), *D*(3,7), *D*(4,7) > *D*(3,5) > *D*(2,4), *D*(2,3) > *D*(3,4). These results are similar to the first model, but there is an additional anomaly (i.e., the ordering of the *D*(2,4) isomer), and thus this method does not do quite as well.

(43) Similar problems are found for the computed VDEs.

center, which is consistent with our assignments of the spectra. This is as expected, because the attractive interaction between the oppositely charged centers is diminished as they become farther apart. The only exception to this is for the *D*(3,4) isomer. In this case, the resulting radical has C_S symmetry, and the odd electron is delocalized over both CO_2 groups. One can view this species as a radical anion of a diacyl peroxide (i.e., R(CO)O−O(CO)R), as the O−O distance is 2.16 Å. It also is interesting to note that in the *D*(2,7) ion where both carboxylates are adjacent to the N-atom, it's the carboxylate at C7 that has the bulk of the spin density. Presumably, this is because the π-system of the carboxylate at C2 can conjugate with the aromatic ring, and this provides more stabilization in the anion than in the radical. In summary, the Mulliken population analyses verify that the threshold features in all of the *D*(*x*,*y*) dipolar ions are due to detachment from the carboxylate groups, and they provide further confirmation of the importance of the intramolecular electrostatic interactions.

Conclusions

Nine isomeric pyridinium dicarboxylate zwitterions were examined by photoelectron spectroscopy and compared to their nonzwitterion counterparts. Information about the intramolecular electrostatic interactions was directly obtained from the PES data. The adiabatic electron binding energies of the nine dipolar ions span a relatively wide range of 1.0 eV from 4.17 (*D*(3,4)) to 5.14 eV (*D*(3,7)) largely because of electrostatic effects. As expected, the zwitterions with the two carboxylates close to the formal positive charge center (i.e., the nitrogen atom) and far apart from each other [i.e., *D*(2,5), *D*(2,6), *D*(3,7), and *D*(4,7)] have the largest adiabatic electron binding energies. In contrast, the least favorable zwitterions are *D*(2,3) and *D*(3,4), in which the two adjacent carboxylate groups result in considerably lower electron binding energies. In the nonzwitterion analogues, we observed that the Coulomb repulsion between the negative charge on the carboxylate group and the N lone pair also is significant: the isomer where the carboxylate is closest to N (*2C-6E-Pyr*) has the lowest ADE (3.85 eV), whereas the one where the carboxylate is farthest from N (*4C-2E-Pyr*) has the highest ADE (4.25 eV).

Theoretical calculations were carried out to obtain the optimized structures and electron binding energies of the nine dipolar ions. A simple structural model, Coulomb's law calculations based upon point charges, and AM1 energies were found to be qualitatively useful for predicting the relative stabilities of the *D*(*x*,*y*) ions, but for quantitative results full blown ab initio or density functional theory computations are required. B3LYP electron affinities for $PhCO_2^{\cdot}$, *o*-$PyrCO_2^{\cdot}$, *m*-$PyrCO_2^{\cdot}$, and *p*-$PyrCO_2^{\cdot}$ were used as benchmarks and are systematically too low by 0.26−0.31 eV. Upon correcting for this deficiency, the *D*(*x*,*y*) ADEs are uniformly improved, but they still are too small relative to experiment by 0.06−0.47 eV; the direct computations are in error by 0.34−0.75 eV. Mulliken population analyses confirm that the lower binding energy detachment features in all of the anions largely come from the carboxylate remote from the positively charged nitrogen atom.

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Supporting Information Available: Computed structures and energetics (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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