Solution Thermochemistry of the Radicals of Glycine

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Using gas phase thermochemical data, the following Gibbs energies of formation in aqueous solution (in kJ mol^{-1}) have been estimated for radicals of glycine: $H_3N^+CH_2CO_2^{\bullet}$ −93, $H_2N^{\bullet +}CH_2CO_2H$ −163, $H_3N^+CH^{\bullet}CO_2H$ −198, $H_2NCH^{\bullet}C(OH)_2^+$ −268, $H_3N^+CH_2CO_2^-$ −371, $H_2NCH_2CO_2^{\bullet}$ −95, $H_2N^{\bullet +}CH_2CO_2^-$ −158, $HN^{\bullet}CH_2CO_2H$ −148, $H_2NCH^{\bullet}CO_2H$ −246, $HN^{\bullet}CH_2CO_2^-$ −147 and $H_2NCH^{\bullet}CO_2^-$ −208. The uncertainty in these values is estimated to be ±20 kJ mol^{-1}.

In accord with earlier EPR studies, the $H_2NCH^{\bullet}CO_2H$ and $H_2NCH^{\bullet}CO_2^-$ radicals are predicted to be the most stable. Non-equivalence of the NH protons of the latter can be rationalized by a strong internal $H \cdots {}^-OCO$ bond. Formation of the $H_3N^+CH_2CO_2^{\bullet}$ and $H_2NCH_2CO_2^{\bullet}$ acyloxyl species is expected to require very strong oxidants ($E^\circ > 3$ V). Production of $H_2N^{\bullet +}CH_2CO_2H$ and $H_2N^{\bullet +}CH_2CO_2^-$ is proposed as a better explanation of $H_2NCH_2^{\bullet}$ formation in $SO_4^{\bullet -}$ oxidations. The $H_2N^{\bullet +}CH_2CO_2^-$ radical, which is also susceptible to loss of CO_2, would lie above $H_2NCH_2CO_2^{\bullet}$ in the gas phase, but its Gibbs energy of formation in aqueous solution will be *ca.* 0.65 V less than that of $H_2NCH_2CO_2^{\bullet}$. $E^\circ(H_2N^{\bullet +}CH_2CO_2^-/H_2NCH_2CO_2^-)$ is estimated to be near 1.6 V. This is in keeping with observed one electron oxidations of $H_2NCH_2CO_2^-$ by triplet states of organic molecules with reduction potentials in the region of 1.5–1.8 V.

The –NH–CH–C(O)– arrangement of nuclei, which occurs in glycine, is a fundamental building block in the α-amino acids and in proteins derived from them.[1,2] Oxidative damage to those molecules frequently creates ionic or free radical species centred in this unit and is of importance in pharmacology, toxicology and radiation biology.[3–5] Glycine also serves as a simplified model of the aminopolycarboxylic acids, such as iminodiacetic [$HN(CH_2CO_2H)_2$, IDA], nitriloacetic acid [$N(CH_2CO_2H)_3$, NTA] and ethylenediaminetetraacetic acid (EDTA), which are frequently used as electron donors in redox studies[6,7] and in investigations of solar energy conversion.[8] Knowledge of the relative stabilities and thermodynamic properties of radicals produced from glycine-like species in an aqueous matrix is therefore of importance in understanding the reaction mechanisms in many areas.

Radicals of glycine and the aminopolycarboxylic acids are normally produced by strong oxidants, such as excited triplet states of organic molecules,[7,9] the $SO_4^{\bullet -}$ radical[10] or the $OH^{\bullet}$ radical.[11–13] In $R^1R^2NCH_2CO_2^-$ species, where R^1 and R^2 may be H or $CH_2CO_2^-$, the nitrogen centre has been cited as an important locus for oxidative damage.[7,13] For example, reactions with excited triplet states of acceptor molecules (A^T) are frequently interpreted as one electron transfers which produce a charge separated form, $R^1R^2N^{\bullet +}CH_2CO_2^-$, *viz*:

$$A^T + R^1R^2NCH_2CO_2^- \longrightarrow A^{\bullet -} + R^1R^2N^{\bullet +}CH_2CO_2^- \quad (1)$$

The evidence for this comes from the observation of $A^{\bullet -}$ in flash photolysis studies and from analyses of CO_2 and other degradation products.[7,14] Since there is a possibility that carboxyl-to-amino electron transfer may precede decarboxylation,[7] *viz*:

$$R^1R^2N^{\bullet +}CH_2CO_2^- \longrightarrow R^1R^2NCH_2CO_2^{\bullet} \quad (2)$$

$$R^1R^2NCH_2CO_2^{\bullet} \longrightarrow R^1R^2NCH_2^{\bullet} + CO_2 \quad (3)$$

knowledge of the relative stabilities of the two radical forms, if distinct, is a necessary prelude to understanding the thermochemistry of the oxidation-induced decarboxylation of these systems. It is also needed for glycine and other simple amino acids, where similar mechanisms have been postulated.[13]

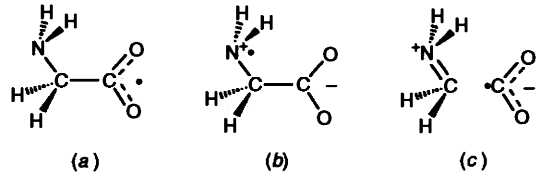
Fig. 1 Structures of $[H_2NCH_2CO_2]^{\bullet}$ radicals (*a*) O-centred acyloxyl form of ref. 15; (*b*) N-centred charge-separated radical resonance form of ref. 16; (*c*) delocalized form of ref. 32

The electronic structure of this most important glycine-derived radical species, $[H_2NCH_2CO_2]^{\bullet}$ requires special consideration, since it, like glycine itself, is commonly thought of as existing in a neutral and a zwitterionic form, as illustrated in Fig. 1(*a*) and (*b*), respectively. Unlike glycine, however, where the two forms are tautomeric, the two forms of the radical differ only in the electronic distribution and therefore must be considered as different electronic states of the same species, and/or as resonance structures, some superposition of which [along with other possible structures, *e.g.* Fig. 1(*c*)] describes the actual ground-state electron distribution of the species. The particular weight assigned to each resonance structure may depend strongly on the conditions in which the radical is found. It is clear from calculations[15] that in the gas phase, the electronic ground state is best described by the neutral structure [Fig. 1(*a*)]. Evidence that the ground state in an ionic matrix resembles the zwitterionic form [Fig. 1(*b*)] has been obtained from EPR studies of glycine crystals.[16] No data on the thermochemical properties of this or $[R^1R^2NCH_2CO_2]^{\bullet}$ radicals in aqueous solution appear to be available. Approximate information for amino acids of the general formula $R^1R^2N[CH_2]_nCO_2H$ may be gained by the following argument. The ionization potential of a typical amine (~9 eV[17]) is much larger than the electron affinity of an $RCO_2^{\bullet}$ radical (~3.4 eV[18,19]), so in the gas phase the neutral

Table 1 Thermodynamic properties of glycine and glycyl radical species at 298 K and 1 bar[a]

No. of H	Species	$\Delta_f H^0_{(g)}$ [b]	$\Delta_f G^0_{(g)}$ [b]	$\Delta G^0_{(soln)}$ [c]	$\Delta_f G^0_{(aq)}$ [d]
6	$H_3N^+CH_2CO_2H$	*249*	363	770	*−384*
5	$H_3N^+CH_2CO_2^{\bullet}$	547	642	782	−93
	$H_2N^{\bullet+}CH_2CO_2H$	502	599	755	−163
	$H_3N^+CH^{\bullet}CO_2H$	454	549	770	−198
	$H_2NCH^{\bullet}C(OH)_2^+$	399	494	755	−268
	$H_3N^+CH_2CO_2^-$	−310	−211	−160	*−371*
	$H_2NCH_2CO_2H$	*−392*	−295	−45	*−340*
4	$H_2NCH_2CO_2^{\bullet}$	−138	−62	−33	−95
	$H_2N^{\bullet+}CH_2CO_2^-$	−78	2	−160	−158
	$HN^{\bullet}CH_2CO_2H$	−181	−105	−43	−148
	$H_2NCH^{\bullet}CO_2H$	−279	−201	−45	−246
	$H_2NCH_2CO_2^-$	*−491*	−413	*−1419*	*−315*
3	$HN^{\bullet}CH_2CO_2^-$	−303	−245	−1419	−147
	$H_2NCH^{\bullet}CO_2^-$	−346	−287	−1438[e]	−208[e]

[a] Units are kJ mol^{-1}. Italicized values are based on experimental data. Others were calculated here or in ref. 15. [b] From ref. 15 unless otherwise stated. [c] For ions these follow the normal convention—see text and ref. 25. [d] Italicized values from ref. 25. Others calculated from $\Delta_f G^0_{(g)}$ and $\Delta_f G^0_{(soln)}$ and subject to ± 20 kJ mol^{-1} uncertainty. [e] Obtained from $\Delta_f G^0_{(aq)}$ of $H_2NCH^{\bullet}CO_2H$ using the experimental pK from ref. 12.

$R^1R^2N[CH_2]_nCO_2^{\bullet}$ structure is lower in energy.† Since solvation stabilizes the ionic forms of both the $-NR^1R^{2\bullet+}$/$-NR^1R^2$ and the $-CO_2^{\bullet}$/$-CO_2^-$ redox couple, the level of a charge-separated form $R^1R^2N^{\bullet+}[CH_2]_nCO_2^-$ relative to the neutral form $R^1R^2N[CH_2]_nCO_2^{\bullet}$ will drop in solution. The contribution to $\Delta_f G^0_{(aq)}$ from solvation of the ionic groups would increase with their average separation, and this would be expected to rise with increasing n. The ultimate difference for very large n can therefore be estimated from $[E^0(R^1R^2N^{\bullet+}$-/R^1R^2N-$) - E^0(-CO_2^{\bullet}/-CO_2^-)]$. $E^0(R^1R^2N^{\bullet+}$-/R^1R^2N-$)$ is typically 1.3 V for a low molecular weight aliphatic primary amine and it falls off for secondary and tertiary amines.[20,21] $E^0(RCO_2^{\bullet}/RCO_2^-)$ is *ca.* 2.0 V.[19,22,23] Thus for large n the $R^1R^2N^{\bullet+}[CH_2]_nCO_2^-$ form of the radical would be more stable in solution by ~0.7 V for $R^1 = R^2 = H$, and by more than this for the aminopolycarboxylic acids.

A recent publication from this laboratory reported an *ab initio* study[15] of the gas phase structures and thermochemical properties of the O-, N- and C-centred radical species which may be formed from glycine. Here we examine their Gibbs energies of solution and formation in water. At the same time we estimate pK_a values and reduction potentials, which can assist in the interpretation of acid–base and redox reactions of these species. We also examine the expected relative stabilities of the $H_2N^{\bullet+}CH_2CO_2^-$ and $H_2NCH_2CO_2^{\bullet}$ radical forms in aqueous solution and compare them with those of other glycyl radicals. Finally the present results are compared with experimental observations from the literature.

Calculations and Results

$\Delta_f H^0_{(g)}$ *and* $\Delta_f G^0_{(g)}$.—Thermochemical data at 298 K and 1 bar (1 bar = 10^5 Pa) for glycyl species, grouped according to the number of H atoms present, are given in Table 1. Gibbs energies of formation in solution, $\Delta_f G^0_{(aq)}$, were taken from the sources indicated or were calculated as explained below. The values of $\Delta_f H^0_{(g)}$ and $\Delta_f G^0_{(g)}$ were taken from our previous publications.[15,24] The gas-phase Gibbs energies of formation, $\Delta_f G^0_{(g)}$, were calculated from the heats of formation and from $T\Delta S$ data. Entropies of glycine species were derived from *ab initio* calculations[15] and those of the elements from standard tables.[25] In cases where $T\Delta S$ data obtained in this way can be compared with literature data the two agree to within ± 3 kJ mol^{-1}.[19] This is similar to the uncertainty in $\Delta_f H^0_{(g)}$ for parent molecules (< 2 kJ mol^{-1}),[26] but is smaller than that for radicals (10 kJ mol^{-1}).[15] Thus the values of $\Delta_f G^0_{(g)}$ are subject to absolute uncertainties of ± 5 and 13 kJ mol^{-1} for the parent molecule and radicals, respectively.

$\Delta_f G^0_{(aq)}$ *and* $\Delta G^0_{(soln)}$.—Note that for ions $\Delta_f G^0_{(aq)}$ corresponds to the Gibbs energy changes for reactions (4) and (5) for

$$\mathrm{ESSB(D^+)} + H^+ \longrightarrow D^+ + \tfrac{1}{2}H_{2(g)} \qquad (4)$$

$$\mathrm{ESSB(A^-)} + \tfrac{1}{2}H_{2(g)} \longrightarrow A^- + H^+ \qquad (5)$$

positive, (D$^+$), and negative, (A$^-$), species, respectively.[25] The term ESSB(X) means 'stoichiometric quantities of elements in their standard states at 1 bar required to produce one mol of X'. The subscript (g) indicates that a molecular species is present in the gas phase at 1 bar; absence of a subscript implies that it is present at a concentration of 1 mol dm^{-3} in aqueous solution. Use of the above convention (ref. 27, p. 244) makes it possible to calculate pK values (*i.e.* $\Delta G^0_{(ioniz)}$) and reduction potentials directly from the differences in $\Delta_f G^0_{(aq)}$ for different species.

Also note that the 'conventional' Gibbs energies of solution, $\Delta G^0_{(soln)}$, used for ions are defined as the free energy changes in reactions (6) and (7) for positive and negative ions, respectively.[25]

$$D^+_{(g)} + H^+ \longrightarrow D^+ + H^+_{(g)} \qquad (6)$$

$$A^-_{(g)} + H^+_{(g)} \longrightarrow A^- + H^+ \qquad (7)$$

For a given species the Gibbs energy of solution is related to $\Delta_f G^0_{(aq)}$ and $\Delta_f G^0_{(g)}$ by eqn. (8). $\Delta_f G^0(H^+)_{(g)}$ is the

$$\Delta G^0_{(soln)} = \Delta_f G^0_{(aq)} - \Delta_f G^0_{(g)} + k\Delta_f G^0(H^+)_{(g)} \qquad (8)$$

Gibbs energy of formation of the gaseous proton (1517 kJ mol^{-1})[17] and k has values of + 1, − 1 and 0 for positive, negative and neutral species, respectively.‡

Closed Shell Species.—The italicized values of $\Delta_f G^0_{(aq)}$ in Table 1 are well established experimental data[25] (uncertainty < 2 kJ mol^{-1}). The value for glycine $H_2NCH_2CO_2H$ has

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† The increase, ΔE, in energy of the charge separated $R^1R^2N^{\bullet+}$-$[CH_2]_nCO_2^-$ species above the neutral $R^1R^2N[CH_2]_nCO_2^{\bullet}$ form is $\Delta E = (9 - 3.4 - C)$ V, where C is the Coulombic interaction of the two charges. This is *ca.* 4.5 eV for glycine and thus ΔE for glycine will be ≈1 V.

‡ Note that the gas phase heats and free energies of formation for ions were computed on the basis of the ion convention.[17] The value of $\Delta_f G^0(H^+)_{(g)}$ is appropriate to that convention.

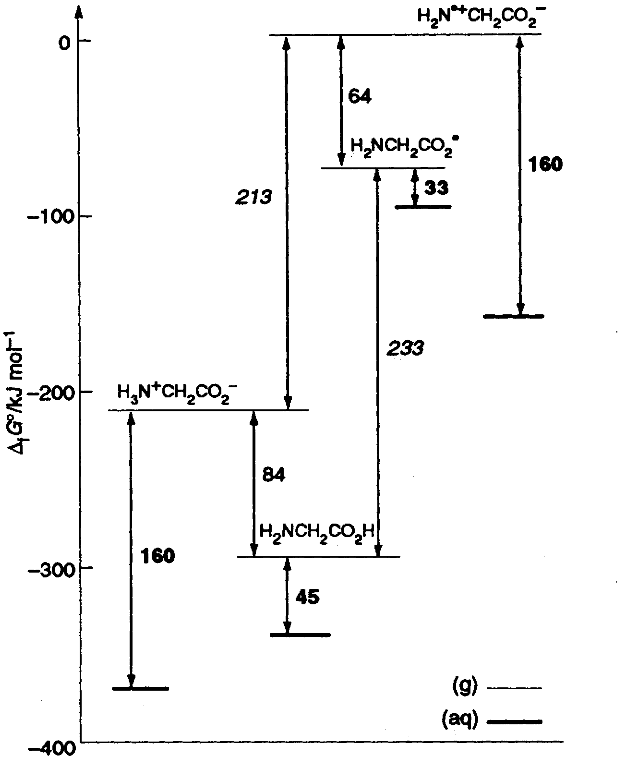

Fig. 2 Relative Gibbs energies of formation in the gas phase and aqueous solution for neutral and charge-separated parent species and radicals. The bold faced values are $\Delta G^0_{(soln)}$ and the italicized values are for loss of $\frac{1}{2}$ $H_{2(g)}$.

been based on an analysis of the microscopic ionization constants given by Daniels and Alberty.[28] The free energies of solution of the various glycine forms were computed with the aid of eqn. (8).

The zwitterion form $H_3N^+CH_2CO_2^-$ which prevails in aqueous solution does not exist in the gas phase.[15,24,29] However, two stationary points corresponding to different conformations of zwitterionic glycine can be found at the level of restricted Hartree–Fock theory with the 6-31 + G(D) basis set.[24] Their energies relative to neutral glycine $H_2NCH_2CO_2H$ were determined at high level[24] and were found to be 81 and 106 kJ mol^{-1} for the eclipsed and staggered orientations of the $-NH_3$ hydrogens, respectively. A later calculation[15] at the G2(MP2) level for the staggered conformation showed essentially no change in the 106 kJ mol^{-1} energy difference. In Table 1 we use the values of $\Delta_f H^0$ and $\Delta_f G^0$ for the hypothetical gas phase zwitterion in order to derive the solution properties.

The relationship between the gas and solution phase Gibbs energies of $H_2NCH_2CO_2H$ and $H_3N^+CH_2CO_2^-$ has been illustrated in Fig. 2. A similar diagram for enthalpies was given in ref. 29. As pointed out above, the $\Delta G^0_{(soln)}$ for ions are 'conventional' Gibbs energies of solution. Absolute free energies of solution of positive or negative ionic species can be obtained from them by respectively adding or subtracting the absolute Gibbs energy of solution of the proton (-1089 kJ mol^{-1}).[30] Thus for the $H_3N^+CH_2CO_2H$ ion, the absolute value would be $770 - 1089 = -319$ kJ mol^{-1}. A negative ion of the same size and charge would have a negative solvation energy of a similar magnitude. Since $\Delta G^0_{(soln)}$ for the $H_3N^+CH_2CO_2^-$ zwitterion is only -160 kJ mol^{-1} (Fig. 2 and Table 1), it is obvious that the proximity of the two charges drastically reduces the binding of water molecules from that for two separate ionic species (~ -600 kJ mol^{-1}). On the other hand $\Delta G^0_{(soln)}$ for the dipolar zwitterion is significantly greater than for $H_2NCH_2CO_2H$ (-45 kJ mol^{-1}). The increase is sufficient to reverse the relative stabilities for the two species (Fig. 2). Note that the values of $\Delta G^0_{(soln)}$ for $H_2NCH_2CO_2H$ and $H_3N^+CH_2CO_2^-$ in Table 1 are in reasonable agreement with values obtained by Cramer and Truhlar with their SM2 and SM3 procedures: -50 and -52 kJ mol^{-1}, respectively, for $H_2NCH_2CO_2H$ and -183 and -160 kJ mol^{-1}, respectively, for $H_3N^+CH_2CO_2^-$.[30]

In our earlier papers[15,24] it was noted that in the gas phase glycine tended to form 'rotamers' and internally hydrogen bonded conformations with energies differing by < 20 kJ mol^{-1}. Though in some cases results were obtained for the Boltzmann distribution of conformers at 298 K,[24] our present gas phase data were computed only for the most stable species. The effect of this approximation on $\Delta_f G^0_{(g)}$ is small. In solution hydrogen bonding interactions with H_2O molecules should dominate, since they are normally much stronger than differences in the energies of rotamers or of intramolecular hydrogen-bonding interactions to neutral groups. Thus conformations yielding greatest access to H_2O molecules may be expected to be the most important in solution.

C-Centred Radicals.—The Gibbs energies of solution of HCO_2H and CH_3CO_2H are both -22 kJ mol^{-1}.[19] Thus $\Delta G^0_{(soln)}$ for these species is not very sensitive to the size of the aliphatic group. The same was also true for the anions $CH_3CO_2^-$ and $^\bullet CH_2CO^-$, for which the $\Delta G^0_{(soln)}$ values differed by only 4 kJ mol^{-1};[19] this line of reasoning was used to obtain values of $-\Delta G^0_{(soln)}$ for $H_2NCH^\bullet CO_2H$ and $H_3N^+CH^\bullet CO_2H$. In each case $-\Delta G^0_{(soln)}$ was taken to be the same as that for the closed shell counterpart appearing in the group above it in Table 1, the geometries of the two differing only in the loss of a single H atom. The values of $\Delta_f G^0_{(aq)}$ for those radicals were then calculated from $\Delta_f G_{(aq)}$ with the aid of eqn. (8).

O-Centred Radicals.—Owing to the loss of an $OH \cdots O$ hydrogen bond the magnitude of $-\Delta G^0_{(soln)}$ will be reduced in going from a CO_2H form of glycine to an O-centred $CO_2^\bullet$ radical. For the case of acetic acid this difference was estimated to be 12 kJ mol^{-1} [19] and the same can be assumed to apply to O-centred radicals of glycine. Thus the $-\Delta G^0_{(soln)}$ values for $H_2NCH_2CO_2^\bullet$ and $H_3N^+CH_2CO_2^\bullet$ in Table 1 are 12 kJ mol^{-1} less than those for $H_2NCH_2CO_2H$ and $H_3N^+CH_2CO_2H$. The $\Delta_f G^0_{(aq)}$ values in Table 1 were calculated from these and the $\Delta_f G^0_{(g)}$ data.

N-Centred Radicals.—The species $HN^\bullet CH_2CO_2H$ and $HN^\bullet CH_2CO_2^-$ have geometries similar to those of the closed shell parents $H_2NCH_2CO_2H$ and $H_2NCH_2CO_2^-$. Based on our earlier work,[21] $-\Delta G^0_{(soln)}$ for the $HN^\bullet CH_2CO_2H$ radicals was taken to be 2 kJ mol^{-1} less than the corresponding value for the parent molecule, which is the estimated contribution of an $NH \cdots OH_2$ hydrogen bond to $-\Delta G^0_{(soln)}$ for a neutral species. For the negative species $HN^\bullet CH_2CO_2^-$ and $H_2NCH_2CO_2^-$ the difference was assumed to be zero, since the weak $NH \cdots OH_2$ interactions in both would be further reduced by the proximity of the negative charges.

As in the case of $H_3N^+CH_2CO_2H$, the charge in the $H_2N^{\bullet+}CH_2CO_2H$ radical cation is centred on the NH_2 group,[15] and the only significant difference in geometry is the greater planarity at that centre. In previous work[21,31] we have found that this planarity tends to make the magnitude of $-\Delta G^0_{(soln)}$ for amminium ions larger than those of the corresponding ammonium ions by *ca.* 30 kJ mol^{-1}. Here, because of the relatively large ions involved, we assume a smaller difference from $H_3{}^+NCH_2CO_2H$ ($\Delta G^0_{(soln)} = 770$ kJ mol^{-1} from Table 1) and take $\Delta G^0_{(soln)}$ of $H_2N^{\bullet+}CH_2CO_2H$ equal to 755 kJ mol^{-1}. From eqn. (8), this yields $\Delta_f G_{(aq)} = -163$ kJ mol^{-1} (Table 1).

As pointed out in the introduction, in the gas phase the $H_2N^{\bullet+}CH_2CO_2^-$ charge-separated radical is an excited

Table 2 Estimated standard reduction potentials, E^0

Half reaction process	E^0/V
$H^+ + e^-$ Transfer	
(*ia*) $H_3N^+CH_2CO_2^{\bullet} + H^+ + e^- \longrightarrow H_3N^+CH_2CO_2H$	3.0
(*ib*) $H_2NCH_2CO_2^{\bullet} + H^+ + e^- \longrightarrow H_2NCH_2CO_2H$	2.5 (2.4)[a]
(*iia*) $H_2N^{\bullet +}CH_2CO_2H + H^+ + e^- \longrightarrow H_3{}^+NCH_2CO_2H$	2.3 (1.9)[b]
(*iib*) $H_2N^{\bullet +}CH_2CO_2^- + H^+ + e^- \longrightarrow H_3{}^+NCH_2CO_2^-$	2.2
(*iiia*) $HN^{\bullet}CH_2CO_2H + H^+ + e^- \longrightarrow H_2NCH_2CO_2H$	2.0 (2.0)[b]
(*iiib*) $HN^{\bullet}CH_2CO_2^- + H^+ + e^- \longrightarrow H_2NCH_2CO_2^-$	1.7
(*iva*) $H_3N^+CH^{\bullet}CO_2H + H^+ + e^- \longrightarrow H_3N^+CH_2CO_2H$	1.9
(*ivb*) $H_3N^+CH^{\bullet}CO_2^- + H^+ + e^- \longrightarrow H_3N^+CH_2CO_2^-$	1.9
(*ivc*) $H_2NCH^{\bullet}CO_2H + H^+ + e^- \longrightarrow H_2NCH_2CO_2H$	1.0 (1.8),[a] (1.6)[b]
(*ivd*) $H_2NCH^{\bullet}CO_2^- + H^+ + e^- \longrightarrow H_2NCH_2CO_2^-$	1.1 (1.7)[a]
e^- Transfer	
(*va*) $H_3N^+CH_2CO_2^{\bullet} + e^- \longrightarrow H_3N^+CH_2CO_2^-$	2.9
(*vb*) $H_2NCH_2CO_2^{\bullet} + e^- \longrightarrow H_2NCH_2CO_2^-$	2.3 (2.1)[a]
(*via*) $H_2N^{\bullet +}CH_2CO_2H + e^- \longrightarrow H_2NCH_2CO_2H$	1.8 (1.3)[b]
(*vib*) $H_2N^{\bullet +}CH_2CO_2^- + e^- \longrightarrow H_2NCH_2CO_2^-$	1.6

[a] Analogous values for acetic acid from ref. 19. [b] Analogous values for methylamine acid from ref. 21.

electronic state of $H_2NCH_2CO_2^{\bullet}$ lying above the electronic ground state. Unfortunately the structure and energy of a $H_2N^{\bullet +}CH_2CO_2^-$ radical with the same symmetry as the ground state is very difficult to obtain by direct computation and we have not pursued this route. However, the species is reported to be stable in the polar matrix of the glycine crystal, where its structure resembles that of the glycine zwitterion with one of the H atoms of the NH_3^+ group removed and the $H_2N^{\bullet +}C$ geometry made planar [Fig. 1(*b*)].[16,32]

The values of $\Delta_fH^0_{(g)}$ and $\Delta_fG^0_{(g)}$ for $H_2N^{\bullet +}CH_2CO_2^-$ in Table 1 were calculated from the corresponding data for $H_3N^+CH_2CO_2^-$ and from ΔH^0 and ΔG^0 for reaction (9).

$$H_3N^+CH_2CO_2^-{}_{(g)} \longrightarrow H^{\bullet}_{(g)} + H_2N^{\bullet +}CH_2CO_2^-{}_{(g)} \qquad (9)$$

Thermodynamic data for $H^{\bullet}$ were taken from ref. 25. $\Delta H^0_{(9)}$ and $\Delta G^0_{(9)}$ for reaction (9) were taken to be the same as for reaction (10), where R is CH_3 or C_2H_5. $\Delta H^0_{(10)}$ is equal to $D_{N\text{-}H}$, which

$$H_3N^+R_{(g)} \longrightarrow H^{\bullet}_{(g)} + H_2N^{\bullet +}R_{(g)} \qquad (10)$$

from the data of Lias *et al.*,[17]§ is 450 ± 5 kJ mol^{-1} for both $H_3N^+CH_3$ and $H_3N^+C_2H_5$. From Table III in ref. 21, $T\Delta S_{(10)} = 34$ kJ mol^{-1}, the differences between R = CH_3 and CH_3CH_2 again being trivial. Thus one obtains $\Delta_fH^0_{(g)} = -78$ kJ mol^{-1} and $\Delta_fG^0_{(g)} = 2$ kJ mol^{-1} for $H_2N^{\bullet +}CH_2CO_2^-$ (see Table 1). More importantly, the difference in $\Delta_fG^0_{(g)}$ of $H_2N^{\bullet +}CH_2CO_2^-$ and $H_3N^+CH_2CO_2^-$ is 213 kJ mol^{-1}. Based on their similar structures and charges, $\Delta G^0_{(soln)}$ for the two species should be the same to within ± 10 kJ mol^{-1}. Hence this difference will be maintained in solution (see Fig. 2) and from $\Delta_fG^0_{(aq)} = -371$ kJ mol^{-1} for the primary closed shell $H_3N^+CH_2CO_2^-$ species one then obtains $\Delta_fG^0_{(aq)}$ $H_2N^{\bullet +}CH_2CO_2^- = -158$ kJ mol^{-1}.¶ It is important to note that, unlike the values of $\Delta_fH^0_{(g)}$ and $\Delta_fG^0_{(g)}$ for $H_2N^{\bullet +}CH_2CO_2^-$ in Table 1, this quantity does not depend on $\Delta_fH^0_{(g)}$ of $H_3N^+CH_2CO_2^-$.

The Gibbs energy differences between the $H_2N^{\bullet +}CH_2CO_2^-$ and $H_2NCH_2CO_2^{\bullet}$ radical structures are illustrated in Fig. 2, where direct comparisons with the closed shell systems can be made. In the gas phase, a structure corresponding to $H_2N^{\bullet +}CH_2CO_2^-$ is predicted to lie some 60 kJ mol^{-1} above $H_2NCH_2CO_2^{\bullet}$. The difference in the expected solvation energies, ~127 (= 160 − 33, Table 2), is in the opposite sense and substantially larger, so that the charge separated form of the radical would be the more stable in aqueous solution. The actual electronic structure of lowest energy in water will depend on the extent of the interaction between the internal charge distribution and the aqueous medium. The $H_2N^{\bullet +}CH_2CO_2^-$ structure represents maximum charge separation and maximum $-\Delta G^0_{(soln)}$, while $H_2NCH_2CO_2^{\bullet}$, in which there is minimal delocalization of electrons from the H_2N lone pair onto the carboxyl, corresponds to the extreme of minimum interaction and minimum $-\Delta G^0_{(soln)}$. Calculations which take into account the interaction with the medium and determine the structure more precisely are beyond the scope of this study. However, the much lower $\Delta_fG^0_{(aq)}$ for the charge separated form clearly indicates that it is closer to the minimum energy structure and it will dominate over the $H_2NCH_2CO_2^{\bullet}$ structure after solvent relaxation. For practical purposes it is therefore treated as the minimum energy state.

Relative Energies and pK_a *Values*.—The relative stabilities expressed as pK_as of the C-centred, N-centred and O-centred radicals, based on the data in Table 1, are presented in Fig. 3. The formulae have been placed at vertical positions correspond-

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§ The value of $D_{N\text{-}H}$ of H_3N^+R, is given by: $D_{N\text{-}H}$ = (E_i of H_2NR + E_p of H_2NR − E_i of $H^{\bullet}$). Note that more recent data (ref. 33) have confirmed the accuracy of the gas phase E_p scale in ref. 17.

¶ If one uses $D_{N\text{-}H}$ for $H_3N^+CH_2CO_2H$ = 471 kJ mol^{-1} from ref. 15 instead of the value for the small amines ($D_{N\text{-}H}$ = 450 kJ mol^{-1}) in the above procedure, one obtains $\Delta_fH^0_{(g)} = -57$ kJ mol^{-1}, $\Delta_fG^0_{(g)} = +23$ kJ mol^{-1} and $\Delta_fG^0_{(aq)} = -137 \pm 20$ kJ mol^{-1} for $H_2N^{\bullet +}CH_2CO_2^-$. As with the procedure in the main text, this approach assumes that the solution free energies for $H_2N^{\bullet +}CH_2CO_2^-$ and $H_3N^+CH_2CO_2^-$ are the same. However, it also assumes that the energies of the orbitals of the $H_2N^{\bullet +}$ centre in $H_2N^{\bullet +}CH_2CO_2H$ are similar to those in $H_2N^{\bullet +}CH_2CO_2^-$. In our view the significantly larger $D_{N\text{-}H}$ for $H_3N^+CH_2CO_2H$ is an indication that the radical centre in $H_2N^{\bullet +}CH_2CO_2H$ is destabilized by the protonated carboxylate group. This will not be the case in $H_2N^{\bullet +}CH_2CO_2^-$ because the CO_2^- group would tend to stabilize the $NH_2^{\bullet +}$ centre, leading in the limit to the $H_2NCH_2CO_2^{\bullet}$ form of the radical. The use of data for the small primary amines is in accord with minimal charge delocalization from the N centre and hence of minimum stabilization or destabilization.

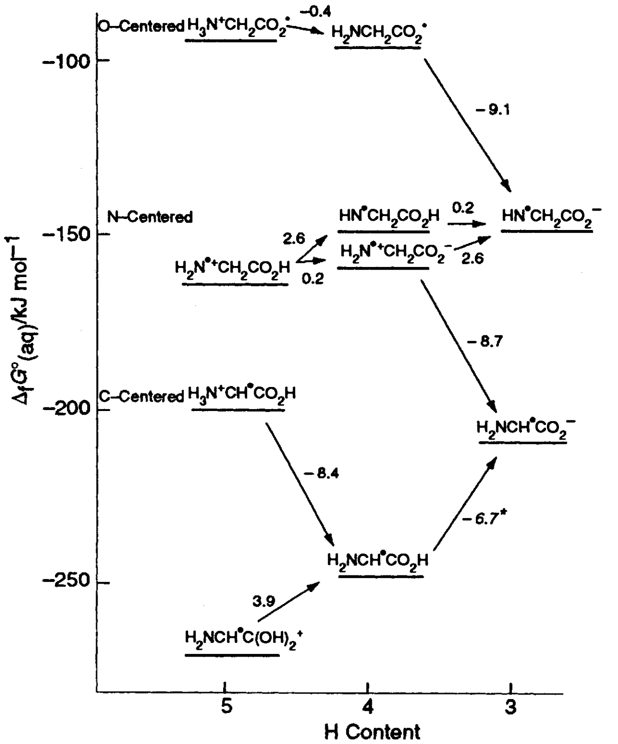

Fig. 3 Relative stabilities (pK_as) of aqueous glycine radical species. * Indicates experimental value from ref. 12.

ing to the values of $\Delta_fG^0_{(aq)}$. The pK_as have been given on interconnecting arrows. Apart from the single experimental value (in italics) they are subject to an uncertainty of ± 2pK_a units.

Reduction Potentials.—The reduction potentials for the cell reaction (11), where R′ is the H_2N or H_3N^+ group, can be

$$R'CH_2CO_2^{\bullet} + \tfrac{1}{2}H_{2(g)} \longrightarrow R'CH_2CO_2^- + H^+ \quad (11)$$

calculated from the values of $\Delta_fG^0_{(aq)}$ in Table 1 and the relation $E^0 = -\Delta G^0_{(11)}/F$, where F is the Faraday constant. These correspond to the values of $E^0(R'CH_2CO_2^{\bullet}/R'CH_2CO_2^-)$, the standard reduction potentials for the half reaction:

$$R'CH_2CO_2^{\bullet} + e^- \longrightarrow R'CH_2CO_2^- \quad (12)$$

Standard reduction potentials for any other half reactions can be calculated in a similar manner. Those of interest here are given in Table 2. Half reactions such as (12), which are appropriate for the consideration of electron-transfer reactions, have been grouped separately from those which are relevant to H-abstraction reactions, *e.g.*

$$RCH_2CO_2^{\bullet} + e^- + H^+ \longrightarrow RCH_2CO_2H \quad (13)$$

For comparison, reduction potentials for radicals of acetic acid and methylamine are also given.

Like the $H_3N^+CH_2CO_2^-$ zwitterion the $H_3N^+CH^{\bullet}CO_2^-$ radical does not exist as a stable structure in the gas phase, but is expected to be a stable form in aqueous solution. It was possible to obtain the C–H bond dissociation energy of H_3N^+-$CH_2CO_2^-$ (=415 kJ mol^{-1}) by calculating both structures with suitable constraints.[15] The value of E^0 in Table 2 for process (*ivb*) corresponds to E^0 for the half reaction (14). This

$$H_3N^+CH^{\bullet}CO_2^- + H^+ + e^- \longrightarrow H_3N^+CH_2CO_2^- \quad (14)$$

was derived from the above C–H bond dissociation energy by a standard thermochemical calculation,[34,35] assuming equal energies of solution of $H_3N^+CH^{\bullet}CO_2^-$ and $H_3N^+CH^{\bullet}CO_2^-$.

The reduction potentials can assist in interpreting formation reactions. Thus the E^0 values for the electron additions to O- and N-centred radicals with the H_2N and carboxylate deprotonated in processes (*vb*) and (*vib*) in Table 2, 2.3 and 1.6 V, are the minimum E^0 values required for an oxidant to create $H_2NCH_2CO_2^{\bullet}$ and $H_2N^{\bullet+}CH_2CO_2^-$, respectively, by electron transfer from $H_2NCH_2CO_2^-$. Similarly, based on the E^0 values for the half reactions (*ib*), (*iiia*) and (*ivc*) of Table 2, the E^0s required to create O-, N- and C-centred radicals by H atom removal from $H_2NCH_2CO_2H$ are 2.5, 2.0 and 1.0 V, respectively. Note that these decrease in the order O-centred > N-centred > C-centred, reflecting the order of increasing stability indicated in Fig. 3 and by the values of $\Delta_fG^0_{(aq)}$ in Table 1.

Discussion

The Gibbs energies of formation in solution of the closed shell species and their pK_as are highly reliable quantities. Hence the parent species from which radicals can be formed and their relative importance in different pH ranges can be stated with certainty. First it is important to note that at all pHs the concentration of $H_2NCH_2CO_2H$ is too low for it to be a viable source of radicals in water. However, this may not be so in apolar solvents. The other species and the pH ranges over which they dominate (in parentheses) are: $H_3{}^+NCH_2CO_2H$ (0–2.3), $H_3{}^+NCH_2CO_2^-$ (2.3–9.8) and $H_2NCH_2CO_2^-$ (≥9.8).

Radical reactions with the amino protonated forms of glycine have always been recognized as being more difficult and slower than attack on $H_2NCH_2CO_2^-$.[36,37] In particular the rate constant for the reaction of $OH^{\bullet}$ with $H_3N^+CH_2CO_2H$ and $H_3N^+CH_2CO_2^-$ in the pH range 1–6 is 1.7×10^7 dm^3 mol^{-1} s^{-1}. For reaction with $H_2NCH_2CO_2^-$ at pH 10 it rises to 5.3×10^9 dm^3 mol^{-1} s^{-1}.[36] The increase is in keeping with the reduction in the values of E^0 with decreasing protonation (see Table 2). This fall off is greatest for the C-centred radicals where E^0 of process (*iv*) falls from 1.9 V for the amino protonated species to 1.1 V for the unprotonated ones.

Apart from the rationalization of reaction rates, the present results can be useful in formulating mechanisms. Starting with the least stable radicals, in the following subsections, individual properties and formation mechanisms are discussed and compared with experimental observations. In this regard evidence from EPR observations on a ~ 1 ms timescale is likely to reflect relative stabilities of radicals with protonation–deprotonation equilibria established, while observations by kinetic spectroscopy on a timescale of 1 µs or less will give better information on primary processes. Inferences from product distributions are considered where relevant.

$H_3N^+CH_2CO_2^{\bullet}$ *and* $H_2NCH_2CO_2^{\bullet}$.—The values of E^0 for $H_2NCH_2CO_2^{\bullet}$ in processes (*ib*) and (*vb*) with the NH_2 group of glycine unprotonated (see Table 2) are fairly similar to those of acetic acid, 2.5 *vs.* 2.4, and 2.3 *vs.* 2.1 V, respectively. With H_3N^+ $CH_2CO_2^{\bullet}$ (*i.e.* with the NH_2 protonated) E^0 increases to 3.0 V for process (*ia*) and 2.9 V for process (*va*). This must be attributed to a reduction of electron density at the carboxyl group. These large E^0 values would preclude formation of $H_3N^+CH_2CO_2^{\bullet}$ in water by currently available oxidants. If $H_3N^+CH_2CO_2^{\bullet}$ were formed, the $\Delta_fG^0_{(aq)}$ values in Table 1 and data for CO_2 and methylamine species in the literature,[21,25] show that decarboxylation [reaction (15)] would be exergonic

$$H_3N^+CH_2CO_2^{\bullet} \longrightarrow H_3N^+CH_2^{\bullet} + CO_2 \quad (15)$$

by *ca.* 160 kJ mol^{-1}. Ionization to $H_2NCH_2CO_2^{\cdot}$ represents another mode of decay and it is interesting that the strong electron withdrawing power of the acyloxyl group causes the pK_a of the NH_3^+ group in this radical to be depressed from the typical value of 10.7 for methylamine and ethylamine to ≈ -0.4 (Fig. 3). Production of $H_2NCH_2CO_2^{\cdot}$ from $H_2NCH_2CO_2^-$ in alkaline solution requires one electron oxidants with $E^0 > 2.3$ V [process (*vb*)]. Hence $H_2NCH_2CO_2^{\cdot}$ is inaccessible with $OH^{\cdot}$ [$E^0(OH^{\cdot}/OH^-) = 1.8$ V[38]], but in principle it could be produced by $SO_4^{\cdot-}$ [$E^0(SO_4^{\cdot-}/SO_4^{2-}) = 2.4$ V[38]]. Decarboxylation [reaction (16)] is estimated to be exergonic by 119 kJ

$$H_2NCH_2CO_2^{\cdot} \longrightarrow H_2NCH_2^{\cdot} + CO_2 \qquad (16)$$

mol^{-1}. From Table 1 and Fig. 3 other decay channels of $H_2NCH_2CO_2^{\cdot}$ are: (*a*) formation of $H_2N^{\cdot+}CH_2CO_2^-$, $\Delta G^0 = -63$ kJ mol^{-1}; (*b*) deprotonation to form $H_2NCH^{\cdot}CO_2^-$, $\Delta G^0 = -113$ kJ mol^{-1} (p$K_a \sim -16$, not shown in Fig. 3) and (c) deprotonation to $HN^{\cdot}CH_2CO_2^-$ $\Delta G^0 = -52$ kJ mol^{-1} (p$K_a \approx -9.1$). All are strongly exergonic. However, because of charge formation they all require solvent reorganization and it is not clear whether they could compete with reaction (16), which should be subject to only a minimal solvent rearrangement.

Based on results for other aliphatic acyloxyl radicals,[39] reactions (15) and (16) are expected to be rapid ($t_{\frac{1}{2}} < 10^{-9}$ s) and it is not surprising that neither of the glycine acyloxyl radicals has been reported in EPR studies of aqueous systems.[10–12,40] On the other hand the finding of $H_3N^+CH_2^{\cdot}$ and $H_2NCH_2^{\cdot}$ by EPR spin trapping in the $SO_4^{\cdot-}$ oxidized systems[10] is in keeping with the present thermochemistry. However, as discussed below, the role of $H_2NCH_2CO_2$ is likely to be minor relative to that of $H_2N^{\cdot+}CH_2CO_2^-$.

$HN^{\cdot}CH_2CO_2H$ *and* $HN^{\cdot}CH_2CO_2^-$.—These radicals are next in terms of stability (Fig. 3). The reduction potential for $HN^{\cdot}CH_2CO_2H$ in processes (*iiia*) in Table 2 [*i.e.* $E^0(HN^{\cdot}CH_2CO_2H,H^+/HN^{\cdot}CH_2CO_2H)$] is identical to that calculated for methylamine (2.0 V), indicating little effect of the CH_2CO_2H group. With deprotonation of the carboxyl the E^0 is decreased [$E^0(HN^{\cdot}CH_2CO_2^-,H^+/H_2NCH_2CO_2^-) = 1.7$ V, process (*iiib*)]. Thus $CH_2CO_2^-$ has a greater stabilizing effect on the $HN^{\cdot}$ radical centre than does CH_2CO_2H. The $HN^{\cdot}CH_2CO_2H$ radical in principle could be formed by abstraction of H from $H_2NCH_2CO_2H$. As pointed out above, this is more likely in non-polar solvents. If it were formed in water, it is prone to deprotonation to $HN^{\cdot}CH_2CO_2^-$ (p$K_a \approx 0.2$, Fig. 3). Direct formation of $HN^{\cdot}CH_2CO_2^-$ from $H_2NCH_2CO_2^-$ requires 1.7 V [E^0 for process (*iiib*) in Table 2], but the process is less likely than H abstraction from CH (see below). Consequently these radicals are not expected to be very important in water and they have not been reported.[11,12] However, when H abstraction from the α-C is blocked by double methylation, the $HN^{\cdot}C(CH_3)_2CO_2^-$ radical is observed.[11]

$H_2N^{\cdot+}CH_2CO_2H$ *and* $H_2N^{\cdot+}CH_2CO_2^-$.—The former of these should in principle be accessible in strongly acid solutions by H abstraction from $H_3N^+CH_2CO_2H$. As shown by the E^0 value for process (*iia*) in Table 2, this requires 2.3 V. It could be achieved with $OH^{\cdot}$ [$E^0(OH^{\cdot},H^+/H_2O) = 2.7$ V[38]], but the abstraction from CH is far more likely (see below). Also any $H_2N^{\cdot+}CH_2CO_2H$ formed would be subject to deprotonation to $H_2N^{\cdot+}CH_2CO_2^-$, p$K_a \approx 0.2$ (Fig. 3). $H_2N^{\cdot+}CH_2CO_2H$ radicals are not therefore expected to play a major role and they have not been reported in EPR studies.[10–12,40] While largely of theoretical interest, note that, based on the data in Table 1, the radical centre at N lowers the carboxylate pK_a from 2.3 (in $H_3N^+CH_2CO_2H$) to ≈ 0.2. The NH pK_a of $H_2N^{\cdot+}CH_2CO_2H$ ($\approx$2.6) is similarly lowered below that of $H_3N^+CH_2CO_2H$, which is estimated to be 7.7.[28] A pK_a near to 2.6 is also predicted for the ionization of $H_2N^{\cdot+}CH_2CO_2^-$ to $HN^{\cdot}CH_2CO_2^-$ (see Fig. 3).

Much of the experimental information on $H_2N^{\cdot+}CH_2CO_2^-$ comes from the EPR studies of Iwasaki and co-workers,[16,32] who also cite references to earlier work on other radicals in glycine crystals. In their investigation of radicals of structural formula $H_2NCH_2CO_2$ they did not report signals for the purely O-centred $H_2NCH_2CO_2^{\cdot}$ form [see Fig. 1(*a*)]. However, at early stages in the irradiation of glycine crystals they observed a radical with spin densities as follows: N = 0.31; C_α = 0.18–0.26; O = 0.15–0.42. This corresponds to the delocalized structure which could be schematically characterized by Fig. 1(*c*). At later stages the initially formed radicals changed into the $H_2N^{\cdot+}CH_2CO_2^-$ species predominantly, [structure 1(*b*)], which was evidently more stable in a more relaxed matrix. This form was reported to have near planar H_2NC geometry and 0.7 spin density on N.

Stabilization of the charge separated $H_2N^{\cdot+}CH_2CO_2^-$ structure in the glycine crystal can be attributed to the highly polar environment which results from the fact that positive nitrogen centres, including those of the radical, are surrounded by negative carboxylate groups and *vice versa*.[16,32] The present thermochemical data indicate that $H_2N^{\cdot+}CH_2CO_2^-$ would also be strongly stabilized in water, and that it should dominate over structure (*a*) in Fig. 1.

The oxidation of $H_2NCH_2CO_2^-$ to $H_2N^{\cdot+}CH_2CO_2^-$ requires only 1.6 *vs.* 2.3 V for formation of $H_2NCH_2CO_2^{\cdot}$ (see E^0s for processes (*vib*) and (*vb*)]. Thus formation of the former radical by electron transfer should be much faster and production of the purely O-centred $H_2NCH_2CO_2^{\cdot}$ radical in water is less favoured. If formed by photoionization or rapid electron transfer from $H_2NCH_2CO_2^-$, it would decay by the channels discussed above.

The $H_2N^{\cdot+}CH_2CO_2^-$ species is also unstable. In the first place its ionization to the C-centred $H_2NCH^{\cdot}CO_2^-$ form:

$$H_2N^{\cdot+}CH_2CO_2^- \longrightarrow H_2NCH^{\cdot}CO_2^- + H^+ \qquad (17)$$

is exergonic by 50 kJ mol^{-1}, which corresponds to p$K_a \approx -8.7$ (Fig. 3). This and the CH pK_a of $H_2NCH_2CO_2^{\cdot}$ noted above resemble the negative CH pK_as of the $CH_3CO_2^{\cdot}$ and $HCO_2^{\cdot}$ radicals previously discussed.[19] Negative pK_as for CH hydrogens are highly abnormal[1] and only arise with very unstable species.

$H_2N^{\cdot+}CH_2CO_2^-$ is also unstable with respect to decarboxylation. For the specific case of $H_2N^{\cdot+}CH_2CO_2^-$ in glycine crystals the lifetime at room temperature is *ca.* 1 μs.[41] Specific information relating to the rates of reactions (17) and (18) in

$$H_2N^{\cdot+}CH_2CO_2^- \longrightarrow H_2NCH_2^{\cdot} + CO_2 \qquad (18)$$

water is lacking. However, based on the present values of $\Delta_fG^0_{(aq)}$ and data for $H_2NCH_2^{\cdot}$[21] and CO_2[25] reaction (18) is exergonic by 56 kJ mol^{-1}, *vs.* 50 kJ mol^{-1} for reaction (17). The latter also requires substantially more solvent reorganization and its rate may depend on the concentration of proton acceptors. It is therefore likely to be the slower.

The above discussion shows that the $H_2NCH_2^{\cdot}$ radicals seen by EPR[10] spin trapping in the $SO_4^{\cdot-}$ oxidation of $H_2NCH_2CO_2^-$ are best attributed to the production of $H_2N^{\cdot+}CH_2CO_2^-$ and its subsequent decarboxylation. Other evidence for the formation of $H_2N^{\cdot+}CH_2CO_2^-$ comes from photochemistry. The flavin triplet [$E^0(Fl^{Triplet}/Fl^{\cdot-}) = 1.8$ V[42]] is unreactive toward the $H_3N^+CH_2CO_2^-$ zwitterion,[43] but oxidation of $H_2NCH_2CO_2^-$ in reaction (1*a*), with $A^T = Fl^{Triplet}$, *viz*:

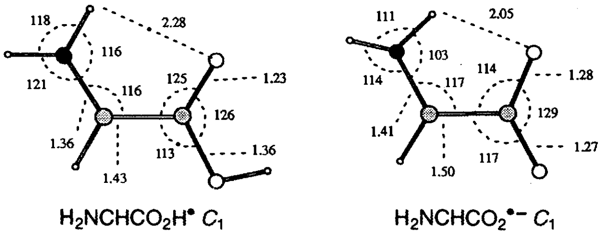

Fig. 4 MP2/6-31G(D) optimized structures of $H_2NCH^{\cdot}CO_2H$ and $H_2NCH^{\cdot}CO_2^-$ from ref. 15. Filled balls represent nitrogen atoms and shaded ones for carbon atoms. Large open balls are oxygen and small open balls are hydrogen. Bond lengths are in angstroms and angles in degrees.

$$A^T + H_2NCH_2CO_2^- \longrightarrow A^{\cdot -} + \text{glycine radical} \quad (1a)$$

occurs with close to 100% yield.[44] This reaction is in direct contrast to its lack of reactivity with anions of unsubstituted carboxylic acids,[45] which have $E^0(RCO_2^{\cdot}/RCO_2^-)$ similar to $E^0(H_2NCH_2CO_2^{\cdot}/H_2NCH_2CO_2^-) \approx 2.3$ V in Table 2.[19,22,23] Its occurrence implies that the glycine radical product is $H_2N^{\cdot +}CH_2CO_2^-$ and that $E^0(H_2N^{\cdot +}CH_2CO_2^-/H_2NCH_2CO_2^-)$ is near to or lower than 1.8 V. Further evidence for this comes from the fact that Battacharyya and Das[14] have observed the formation of the benzophenone anion in reaction (1*a*) between glycine and benzophenone triplet at pH 9.5 with $k_{1a} = 1.9 \times 10^7$ dm^3 mol^{-1} s^{-1}. The value of $E^0[(Ph)_2CO^{Triplet}/(Ph)_2CO^{\cdot -}]$ is ≈ 1.5 V.[46,47] The fairly low rate is an indication that the reduction potential of the glycine radical, which is formed, must be close to 1.5 V, and similar to the value of 1.6 V estimated for $E^0(H_2N^{\cdot +}CH_2CO_2^-/H_2NCH_2CO_2^-)$ in Table 2.

If $E^0(H_2N^{\cdot +}CH_2CO_2^-/H_2NCH_2CO_2^-)$ is indeed near 1.6 V, then $H_2N^{\cdot +}CH_2CO_2^-$ should be accessible by electron transfer from $H_2NCH_2CO_2^-$ to $OH^{\cdot}$ [$E^0(OH^{\cdot}/OH^-) = 1.8$ V[38]]. In fact at pHs above the amino pK_a of glycine high yields of CO_2 are produced on reaction with $OH^{\cdot}$. This has been cited as evidence for the decarboxylation of an $OH^{\cdot}$ adduct of $H_2NCH_2CO_2^-$ or a one-electron-oxidized-radical.[13] Since the decarboxylation of C-centred radicals is endoergonic (see later), the CO_2 formation is best attributed to reaction (18). To explain the fact that the EPR spectrum of the $H_2NCH_2^{\cdot}$ radical was not observed[11,12] under similar conditions it has been suggested[13] that on a ~1 ms timescale they may produce C-centred radicals by abstracting H atoms from the α-Cs of glycine. From the present data we note that reaction (19*a*) is endoergonic by

$$H_2NCH_2^{\cdot} + H_3N^+CH_2CO_2 \longrightarrow H_2NCH_3 + H_3N^+CH^{\cdot}CO_2^- \quad (19a)$$

28 kJ mol^{-1} and therefore unlikely. However, reaction (19*b*) is

$$H_2NCH_2^{\cdot} + H_2NCH_2CO_2^- \longrightarrow H_2NCH_3 + H_2NCH^{\cdot}CO_2^- \quad (19b)$$

exergonic by 45 kJ mol^{-1} and therefore removal of the $H_2NCH_2^{\cdot}$ radicals by this process is feasible above pH 9.8. At the same time, it is important to note that reaction (19*b*) cannot form the basis for a chain decomposition of glycine, since the decarboxylations of the C-centred radicals in reactions (20) and (21) are endoergonic by 55 and 33 kJ mol^{-1}, respectively.

$$H_2NCH^{\cdot}CO_2^- + H_2O \xrightarrow{pH\sim 10} H_2NCH_2^{\cdot} + OH^- + CO_2 \quad (20)$$

$$H_2NCH^{\cdot}CO_2H \longrightarrow H_2NCH_2^{\cdot} + CO_2 \quad (21)$$

C-Centred Radicals: $H_3N^+CH^{\cdot}CO_2H$, $H_2NCH^{\cdot}CO_2H$, $H_2NCH^{\cdot}C(OH)_2^+$ *and* $H_2NCH^{\cdot}CO_2^-$.—As shown in Table 2, E^0 for process (*ivc*) (= 1.0 V) is predicted to be significantly smaller than $E^0(H_2NCH_2^{\cdot},H^+/H_2NCH_3) = 1.6$ V and $E^0(CH_2^{\cdot}CO_2H,H^+/CH_3CO_2H) = 1.8$ V. This is due to the special stabilization of the $CH^{\cdot}$ radical centre by the H_2N and CO_2H groups in a 'captodative' effect.[15] When the CO_2H groups are deprotonated, as for process (*ivd*), E^0 is 1.1 V *vs.* $E^0(CH_2^{\cdot}CO_2^-/CH_3CO_2^-) = 1.7$ V. Thus the captodative effect in $H_2NCH^{\cdot}CO_2^-$ is lessened, but still significant. With the amino protonated [process (*ivb*)] and with both it and the carboxyl protonated [process (*iva*)] the captodative effect is lost and E^0 becomes 1.9 V. This is larger than $E^0(H_2NCH_2^{\cdot},H^+/H_2NCH_3)$ and $E^0(CH_2^{\cdot}CO_2H,H^+/CH_3CO_2H)$ (see Table 2), and implies destabilization of the $CH^{\cdot}$ radical centre by H_3N^+ similar to the case of the O-centred radicals noted above.

At low pH $H_3N^+CH^{\cdot}CO_2H$ is the only C-centred radical directly accessible by H abstraction from $H_3N^+CH_2CO_2H$. This process requires 1.9 V (see above) and could be achieved by $OH^{\cdot}$ [$E^0(OH^{\cdot},H^+/H2O) = 2.7$ V[38]]. The fact that $H_3N^+CH^{\cdot}CO_2H$ has not been confirmed in EPR studies[11,12,40] can be attributed to ionization to $H_2NCH^{\cdot}CO_2H$, which is exergonic by 48 kJ mol^{-1} at pH 0 (see p$K_a \approx -8.4$ in Fig. 3) and should be quite fast. As shown in Fig. 3, $H_2NCH^{\cdot}C(OH)_2^+$ is expected to be more stable at very low pH and reprotonation to that form, which cannot be produced directly from $H_3N^+CH_2CO_2H$, may occur. At present experimental evidence for this species appears to be lacking.

The fact that $H_2NCH^{\cdot}CO_2H$ and $H_2NCH^{\cdot}CO_2^-$ are the two important radicals with spectra identified in EPR experiments in aqueous solutions at room temperature[11,12] is in accord with the relative stabilities shown in Fig. 3. The pK_a reported[12] for the carboxylate of $H_2NCH^{\cdot}CO_2H$ is 6.7. Owing to the strong stabilization of the $CH^{\cdot}$ radical centre in the protonated $H_2NCH^{\cdot}CO_2H$ form (see above), this is larger than the pK_a of the $H_2NCH_2CO_2H$ parent (= 4.4[25,28]). Above pH 9.8 $H_2NCH^{\cdot}CO_2^-$ is accessible directly from $H_2NCH_2CO_2^-$ by H abstraction with $OH^{\cdot}$. Below this pH the equilibrium concentrations of radicals could be produced by H abstraction from the CH_2 of $H_3N^+CH_2CO_2H$ or $H_3N^+CH_2CO_2^-$, followed by proton redistribution.

Our gas phase structures[15] of $H_2NCH^{\cdot}CO_2H$ and $H_2NCH^{\cdot}CO_2^-$ are shown in Fig. 4. The fact that the NH protons of $H_2NCH^{\cdot}CO_2^-$ are non-equivalent in solution[11,12] is an indication that the NH ··· $^-$OCO hydrogen bond is maintained in solution. The NH ··· OCOH interaction in the gas phase $H_2NCH^{\cdot}CO_2H$ radical structure should also lead to non-equivalent NH protons, but for this species they are equivalent in solution.[11,12] While the intramolecular H-bond to the charged carboxylate in $H_2NCH^{\cdot}CO_2^-$ persists, evidently the hydrogen bonding interactions with H_2O molecules are strong enough to break down the weaker NH interaction with the neutral CO_2H in $H_2NCH^{\cdot}CO_2H$.

The value of $\Delta_f G^0_{(aq)}$ for $H_2NCH^{\cdot}CO_2^-$ in Table 1 was calculated from $\Delta_f G^0_{(aq)}$ for $H_2NCH^{\cdot}CO_2H$ and the experimental pK_a of 6.7.[12] As shown in Table 1, this leads to $\Delta G^0_{(soln)}$ of $H_2NCH^{\cdot}CO_2^- = -1438$ kJ mol^{-1}, which is 19 kJ mol^{-1} more negative than $\Delta G^0_{(soln)}$ of $H_2NCH_2CO_2^-$ (= −1419 kJ mol^{-1}). Owing to the more compact planar structure of $H_2NCH^{\cdot}CO_2^-$ the difference may be real. However, it is within the overall uncertainty arising from possible errors in $\Delta_f G^0_{(g)}$ of $H_2NCH^{\cdot}CO_2^-$ and $H_2NCH^{\cdot}CO_2H$.

Conclusions

The thermodynamic data derived here have been shown above to be largely consistent with existing experimental results. At the same time the present data shed new light on the mechanisms of oxidation of glycine. In particular in solution the radical of formula $H_2NCH_2CO_2$ exists primarily as the charge separated $H_2N^{\bullet +}CH_2CO_2^-$ form. It is predicted to have a much lower energy than the acyloxyl form, $H_2NCH_2CO_2^{\bullet}$. There is experimental as well as the present theoretical evidence that $E^0(H_2N^{\bullet +}CH_2CO_2^-/H_2NCH_2CO_2^-)$ is near 1.6 V. The role of this radical is therefore likely to be more important than hitherto considered. Also decarboxylation of $H_2N^{\bullet +}CH_2CO_2^-$ is best regarded as a concerted process, driven by the formation of the two C=O bonds of CO_2. Another important feature is the low value of the reduction potential for the carbon-centred $H_2NCH^{\bullet}CO_2^-$ radical. This means that in alkaline solutions the α-C centre may be more important as a site for oxidative damage by radicals with much lower reduction potentials than $OH^{\bullet}$. The overall picture of the relative stabilities of the radicals provided by the present results should assist in formulating reaction mechanisms and in the design of new experiments.

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