SUPPORTING INFORMATION

Formation and Stability of Peptide Enolates in Aqueous Solution

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Table S1. First-order Rate Constants, k_{ex}, for Exchange for Deuterium of the First Proton of the α-Methyl and α-Methylene Groups of *N*-Acetylglycine Anion (**1**) in Alkaline D_2O at 25 ˚C and *I* = 1.0 (KCl), Determined by Monitoring the Incorporation of Deuterium into **1** by ^1H NMR Spectroscopy.

$[DO^-]$/M	k_{ex} (s^{-1}) **1-H_α'**	k_{ex} (s^{-1}) **1-H_α**
0.04	1.9×10^{-7}	7.8×10^{-8}
0.08	3.3×10^{-7}	1.44×10^{-7}
0.12	5.1×10^{-7}	2.26×10^{-7}
0.16	7.5×10^{-7}	3.04×10^{-7}
0.20	8.8×10^{-7}	3.76×10^{-7}

Table S2. First-order Rate Constants, k_{ex}, for Exchange for Deuterium of the First Proton of the α-Methyl and α-Methylene Groups of *N*-Acetylglycinamide (**2**) in D_2O at 25 ˚C and I = 1.0 (KCl), Determined by Monitoring the Incorporation of Deuterium into **2** by ^{1}H NMR Spectroscopy.

Buffer System	$[B]_T$/M [a]	pD	$[DO^-]$/M [b]	k_{ex} (s^{-1}) **2-H_α'**	k_{ex} (s^{-1}) **2-H_α**
CF_3CD_2OD	0.02	12.57	6.34×10^{-3}	1.32×10^{-7}	1.62×10^{-5}
	0.05	12.58	6.49×10^{-3}	1.38×10^{-7}	1.70×10^{-5}

[a] Total buffer concentration. [b] Concentration of deuteroxide ion at the pD of the experiment calculated using $[DO^-] = (10^{pD-pK_w})/\gamma_{OL}$ with pK_w = 14.87 and γ_{OL} = 0.79 [Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 3129-3141].

Table S3. First-order Rate Constants, k_{ex}, for Exchange for Deuterium of the First Proton of the *N*-Terminal α-Methylene Group of Glycylglycine (**3**) in D_2O at 25 ˚C and I = 1.0 (KCl), Determined by Monitoring the Incorporation of Deuterium into **3** by ^1H NMR Spectroscopy.

Buffer System	pK_{BD} [a]	$[B]_T$/M [b]	f_B [c]	pD	f_{N+} [d]	$[DO^-]$/M [e]	k_{ex} (s^{-1}) **3-H_α^+**
$HP_2O_7^{3-}$	8.5	0.02	0.85	9.16	0.31	2.47×10^{-6}	2.7×10^{-8}
			0.70	8.79	0.51	1.05×10^{-6}	1.9×10^{-8}
			0.55	8.51	0.67	5.52×10^{-7}	1.4×10^{-8}
			0.35	8.15	0.82	2.41×10^{-7}	7.4×10^{-9}

[a] Apparent pK_a of pyrophosphate in D_2O at 25 ˚C and I = 1.0 (KCl) given by pK_{BD} = pD – log ([B]/[BD^+]), determined as described in the Experimental Section. [b] Total buffer concentration. [c] Fraction of the buffer in the basic form. [d] Fraction of glycylglycine present in the reactive *N*-protonated form, calculated from the solution pD and pK_{BD} = 8.81 for the terminal amino group in D_2O (25 ˚C, I = 1.0, KCl). [e] Concentration of deuteroxide ion at the pD of the experiment calculated using $[DO^-] = (10^{pD-pK_w})/\gamma_{OL}$ with pK_w = 14.87 and γ_{OL} = 0.79 [Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 3129-3141].

Table S4. First-order Rate Constants, k_{ex}, for Exchange for Deuterium of the First Proton of the *N*-Terminal and Internal α-Methylene Groups of Glycylglycylglycine (**4**) in D_2O at 25 ˚C and I = 1.0 (KCl), Determined by Monitoring the Incorporation of Deuterium into **4** by ^1H NMR Spectroscopy.

Buffer System	pK_{BD} [a]	$[B]_T$/M [b]	pD	$[DO^-]$/M [c]	k_{ex} (s^{-1}) **4-H_α^+**	k_{ex} (s^{-1}) **4-H_α'**	f_{N+} [d]	$(k_{ex})_o$ (s^{-1}) [e] **4-H_α^+**	$(k_{ex})_o$ (s^{-1}) [e] **4-H_α'**
$(CF_3)_2CHOD$	9.9 [f]	0.05	11.00	1.71×10^{-4}	1.3×10^{-7}	8.6×10^{-8}	5.2×10^{-3}	1.3×10^{-7}	8.1×10^{-8}
		0.20	11.11	2.20×10^{-4}	1.3×10^{-7}	1.0×10^{-7}			
Quinuclidine	12.1 [g]	0.05	11.33	3.65×10^{-4}	1.5×10^{-7}	1.6×10^{-7}	2.2×10^{-3}	1.5×10^{-7}	1.5×10^{-7}
		0.20	11.33	3.65×10^{-4}	1.5×10^{-7}	2.0×10^{-7}			
		0.10	11.82	1.13×10^{-3}	1.9×10^{-7}	5.7×10^{-7}	7.2×10^{-4}	1.9×10^{-7}	5.4×10^{-7}
		0.30	11.81	1.10×10^{-3}	1.7×10^{-7}	6.4×10^{-7}			
		0.05	12.37	4.00×10^{-3}	1.7×10^{-7}	1.7×10^{-6}	2.1×10^{-4}	1.6×10^{-7}	1.6×10^{-6}
		0.20	12.41	4.39×10^{-3}	2.0×10^{-7}	1.9×10^{-6}			
		0.05	12.86	1.24×10^{-2}	2.0×10^{-7}	4.9×10^{-6}	6.8×10^{-5}	1.9×10^{-7}	4.7×10^{-6}
		0.20	12.89	1.32×10^{-2}	2.2×10^{-7}	5.4×10^{-6}			

[a] Apparent pK_a of the acidic form of the buffer in D_2O at 25 ˚C and I = 1.0 (KCl) given by pK_{BD} = pD – log ([B]/[BD^+]). [b] Total buffer concentration. [c] Concentration of deuteroxide ion at the pD of the experiment calculated using [DO^-] = (10^{pD-pK_w})/γ_{OL} with pK_w = 14.87 and γ_{OL} = 0.79 [Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 3129-3141]. [d] Fraction of glycylglycylglycine present in the reactive *N*-protonated form, calculated from the solution pD and pK_{BD} = 8.68 for the terminal amino group in D_2O (25 ˚C, I = 1.0, KCl). [e] Rate constant for solvent-catalyzed exchange, determined by extrapolation of the values of k_{ex} to zero buffer concentration. [f] Data from: Rios, A.; Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 9373-9385. [g] Data from: Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1996**, *118*, 3129-3141.