Supporting information

Cross-Modulation of Physico-Chemical Character of Aglycones in Dinucleoside (3'→5') monophosphates by the Nearest Neighbor Interaction in the Stacked State

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Legends for Figure S1:

Figure S1a: pH dependant ^{1}H chemical shift of aromatic protons (H8A, H2A, H8G) of ApG within the pH values of $0.03 \leq pH \leq 7.56$. Chemical shift variations at 63 different pH values ($0.03 \leq pH \leq 7.56$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH8A,δH2A and δH8G are shown in the respective graphs.

Figure S1b: pH dependant ^{1}H chemical shift of aromatic protons (H8A, H2A, H8G) of ApG within the pH values of $7.56 \leq pH \leq 11.63$. Chemical shift variations at 30 different pH values ($7.56 \leq pH \leq 11.63$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH8A,δH2A and δH8G are shown in the respective graphs.

Figure S1c: pH dependant ^{1}H chemical shift of aromatic protons (H8A, H2A, H8G) of GpA within the pH values of $0.12 \leq pH \leq 7.29$. Chemical shift variations at 61 different pH values ($0.12 \leq pH \leq 7.29$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH8A,δH2A and δH8G are shown in the respective graphs.

Figure S1d: pH dependant ^{1}H chemical shift of aromatic protons (H8A, H8G) of GpA within the pH values of $6.93 \leq pH \leq 10.70$. Chemical shift variations at 35 different pH

values ($6.93 \leq pH \leq 10.70$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH8A and δH8G are shown in the respective graphs. H2A of GpA did not show any significant change in chemical shift with pH hence plot for H2A is not shown.

Figure S1e: pH dependant ^1H chemical shift of aromatic protons (H6U, H5U, H6C, H5C) of CpU within the pH values of $1.87 \leq pH \leq 6.92$. Chemical shift variations at 35 different pH values ($1.87 \leq pH \leq 6.92$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH6U, δH5U, δH6C and δH5C are shown in the respective graphs.

Figure S1f: pH dependant ^1H chemical shift of aromatic protons (H6U, H5U, H6C, H5C) of CpU within the pH values of $6.92 \leq pH \leq 11.32$. Chemical shift variations at 25 different pH values ($6.92 \leq pH \leq 11.32$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH6U, δH5U, δH6C and δH5C are shown in the respective graphs.

Figure S1g: pH dependant ^1H chemical shift of aromatic protons (H5U, H6C, H5C) of UpC within the pH values of $1.97 \leq pH \leq 6.79$. Chemical shift variations at 25 different pH values ($1.97 \leq pH \leq 6.79$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH5U,δH6C and δH5C are shown in the respective graphs. H6U of UpC did not show any significant change in chemical shift with pH hence plot for H6U is not shown.

Figure S1h: pH dependant ^1H chemical shift of aromatic protons (H6U, H5U, H6C, H5C) of UpC within the pH values of $6.79 \leq pH \leq 11.42$. Chemical shift variations at 30 different pH values ($6.79 \leq pH \leq 11.42$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of δH6U, δH5U, δH6C and δH5C are shown in the respective graphs.

Figure S1i: pH dependant ^{1}H chemical shift of aromatic protons (H8A, H2A, H6U, H5U) of UpA within the pH values of $1.11 \leq pH \leq 6.98$. Chemical shift variations at 43 different pH values ($1.11 \leq pH \leq 6.98$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of H8A, H2A, H6U and H5U are shown in the respective graphs.

Figure S1j: pH dependant ^{1}H chemical shift of aromatic protons (H6U, H5U) of UpA within the pH values of $6.6 \leq pH \leq 11.10$. Chemical shift variations at 47 different pH values ($6.6 \leq pH \leq 11.10$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of H6U and H5U are shown in the respective graphs. H8A and H2A of UpA did not show any significant change in chemical shift with pH hence plots for H8A and H2A are not shown.

Figure S1k: pH dependant ^{1}H chemical shift of aromatic protons (H8A, H2A, H6U, H5U) of ApU within the pH values of $1.35 \leq pH \leq 6.99$. Chemical shift variations at 36 different pH values ($1.35 \leq pH \leq 6.99$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of H8A, H2A, H6U and H5U are shown in the respective graphs.

Figure 1l: pH dependant ^{1}H chemical shift of aromatic protons (H8A,H2A,H6U,H5U) of ApU within the pH values of $6.99 \leq pH \leq 10.96$. Chemical shift variations at 39 different pH values ($6.99 \leq pH \leq 10.96$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves in all cases. pK_a values obtained from Hill plot of H8A, H2A, H6U and H5U are shown in the respective graphs.

Figure S1m: pH dependant ^{1}H chemical shift of aromatic protons (H8A, H2A) of ApEt within the pH values of $1.62 \leq pH \leq 6.38$. Chemical shift variations at 18 different pH values ($1.62 \leq pH \leq 6.38$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of H8A and H2A are shown in the respective graphs.

Figure S1n: pH dependant ^{1}H chemical shift of aromatic proton (H8G) of GpEt within the pH values of $6.89 \leq pH \leq 11.00$. Chemical shift variations at 15 different pH values ($6.89 \leq pH \leq 11.0$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curve. pK_a value obtained from Hill plot of H8G is shown in the respective graph.

Figure S1o: pH dependant ^{1}H chemical shift of aromatic protons (H6U, H5U) of UpEt within the pH values of $6.65 \leq pH \leq 11.44$. Chemical shift variations at 23 different pH values ($6.65 \leq pH \leq 11.44$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of H6U and H5U are shown in the respective graphs.

Figure S1p: pH dependant ^{1}H chemical shift of aromatic protons (H6C, H5C) of CpEt within the pH values of $1.66 \leq pH \leq 6.39$. Chemical shift variations at 22 different pH values ($1.66 \leq pH \leq 6.39$) have been measured in an interval of 0.1 – 0.2 pH units to obtain the sigmoidal curves. pK_a values obtained from Hill plot of H6C and H5C are shown in the respective graphs.

Legends for Figure S2:

Figure S2a: The Hill plots for δH8A, δH2A, δH8G of ApG in the $0.03 \leq pH \leq 7.56$. Δ_T for H8A ($0.03 \leq pH \leq 7.56$) = 0.297 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope =1.34 ($\sigma = 0.04$) and $pK_a = 2.88(\sigma = 0.02)$. Δ_T for H2A ($0.03 \leq pH \leq 7.56$) = 0.322 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope =1.36($\sigma = 0.04$) and $pK_a = 2.83$ ($\sigma = 0.02$). Δ_T for H8G ($0.03 \leq pH \leq 7.56$) = 1.124 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope =0.92 ($\sigma = 0.04$) and $pK_a = 1.64$ ($\sigma = 0.02$). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8A, δH2A, δH8G are shown in the respective graphs.

Figure S2b: The Hill plots for δH8A, δH2A, δH8G of ApG in the 7.56 ≤ pH ≤ 11.63. Δ_T for H8A (7.56 ≤ pH ≤ 11.63) = 0.009 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 0.97 (σ = 0.04) and pK_a = 9.71 (σ = 0.02). Δ_T for H2A (7.56 ≤ pH ≤ 11.63) = 0.032 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 0.98 (σ = 0.04) and pK_a = 9.65 (σ = 0.02). Δ_T for H8G (7.56 ≤ pH ≤ 11.63) = 0.068 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 1.00) with a slope =0.92 (σ = 0.03) and pK_a = 9.42 (σ = 0.01). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8A, δH2A, δH8G are shown in the respective graphs.

Figure S2c: The Hill plots for δH8A, δH2A, δH8G of GpA in the 0.12 ≤ pH ≤ 7.29. Δ_T for H8A (0.12 ≤ pH ≤ 7.29) = 0.205 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 1.02 (σ = 0.02) and pK_a = 3.22 (σ = 0.01). Δ_T for H2A (0.12 ≤ pH ≤ 7.29) = 0.301 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 1.00) with a slope = 1.26 (σ = 0.02) and pK_a = 2.94 (σ = 0.01). Δ_T for H8G (0.12 ≤ pH ≤ 7.29) = 1.184 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 1.00) with a slope = 1.03 (σ = 0.03) and pK_a = 1.68 (σ = 0.01). The values of correlation coefficient R, pKa obtained from Hill plot analysis, and the Hill slope values of δH8A, δH2A, δH8G are shown in the respective graphs.

Figure S2d: The Hill plots for δH8A and δH8G of GpA in the 6.93 ≤ pH ≤ 10.7. Δ_T for H8A (6.93 ≤ pH ≤ 10.7) = 0.056 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 0.96 (σ = 0.04) and pK_a = 9.16 (σ = 0.02). Δ_T for H8G (6.93 ≤ pH ≤ 10.7) = 0.141 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 1.00 (σ = 0.04) and pK_a = 9.17 (σ = 0.02). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8A, δH2A, δH8G are shown in the respective graphs. H2A of GpA did not show any significant change in log((Δ_T – Δ)/Δ) with pH, hence Hill plot for H2A was not done.

Figure S2e: The Hill plots for δH6U, δH5U, δH6C, δH5C of CpU in the 1.87 ≤ pH ≤ 6.92. Δ_T for H6U (1.87 ≤ pH ≤ 6.92) = 0.013 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.97) with a slope = 0.96 (σ = 0.07) and pK_a = 3.48 (σ = 0.03). Δ_T for H5U (1.87 ≤ pH ≤ 6.92) = 0.073 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.05 (σ = 0.03) and pK_a = 3.58 (σ = 0.02). Δ_T for H6C (1.87 ≤ pH ≤ 6.92) = 0.289 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 0.99 (σ = 0.03) and pK_a = 3.56 (σ = 0.01). Δ_T for H5C (1.87 ≤ pH ≤ 6.92) = 0.262 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.01 (σ = 0.03) and pK_a = 3.58 (σ = 0.01). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH6U, δH5U, δH6C, δH5C are shown in the respective graphs.

Figure S2f: The Hill plots for δH6U, δH5U, δH6C, δH5C of CpU in the 6.92 ≤ pH ≤ 11.32. Δ_T for H6U (6.92 ≤ pH ≤ 11.32) = 0.162 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.06 (σ = 0.05) and pK_a = 9.21 (σ = 0.02). Δ_T for H5U (6.92 ≤ pH ≤ 11.32) = 0.059 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.01 (σ = 0.05) and pK_a = 9.25 (σ = 0.02). Δ_T for H6C (6.92 ≤ pH ≤ 11.32) = 0.078 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.98) with a slope = 1.08 (σ = 0.07) and pK_a = 9.18 (σ = 0.03). Δ_T for H5C (6.92 ≤ pH ≤ 11.32) = 0.053 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.07 (σ = 0.06) and pK_a = 9.18 (σ = 0.03). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH6U, δH5U, δH6C, δH5C are shown in the respective graphs.

Figure S2g: The Hill plots for δH5U, δH6C, δH5C of UpC in the 1.97 ≤ pH ≤ 6.79. Δ_T for H5U (1.97 ≤ pH ≤ 6.79) = 0.033 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 0.82 (σ = 0.04) and pK_a = 3.71 (σ = 0.02). Δ_T for H6C (1.97 ≤ pH ≤ 6.79) = 0.242 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 0.81 (σ = 0.04) and pK_a = 3.71 (σ = 0.02). Δ_T for H5C (1.97 ≤ pH ≤ 6.79) = 0.247 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 0.82 (σ = 0.04) and pK_a = 3.71 (σ = 0.02). The values of

correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH5U, δH6C, δH5C are shown in the respective graphs. H6U of UpC did not show any significant change in $\log((\Delta_T - \Delta)/\Delta)$ with pH, hence Hill plot for H6U was not done.

Figure S2h: The Hill plots for δH6U, δH5U, δH6C, δH5C of UpC in the $6.79 \leq pH \leq 11.42$. Δ_T for H6U ($6.79 \leq pH \leq 11.42$) = 0.244 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.16 (σ = 0.02) and pK_a = 9.06 (σ = 0.01). Δ_T for H5U ($6.79 \leq pH \leq 11.42$) = 0.068 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.16 (σ = 0.02) and pK_a = 9.04 (σ = 0.01). Δ_T for H6C ($6.79 \leq pH \leq 11.42$) = 0.037 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.16 (σ = 0.03) and pK_a = 9.14 (σ = 0.02). Δ_T for H5C ($6.79 \leq pH \leq 11.42$) = 0.021 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.17 (σ = 0.03) and pK_a = 9.06 (σ = 0.02). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH6U, δH5U, δH6C and δH5C are shown in the respective graphs.

Figure S2i: The Hill plots for δH8A, δH2A, δH6U, δH5U of UpA in the $1.11 \leq pH \leq 6.98$. Δ_T for H8A ($1.11 \leq pH \leq 6.98$) = 0.188 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.17 (σ = 0.02) and pK_a = 3.07 (σ = 0.01). Δ_T for H2A ($1.11 \leq pH \leq 6.98$) = 0.219 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.18 (σ = 0.03) and pK_a = 3.06 (σ = 0.01). Δ_T for H6U ($1.11 \leq pH \leq 6.98$) = 0.094 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.27 (σ = 0.02) and pK_a = 3.12 (σ = 0.01). Δ_T for H5U ($1.11 \leq pH \leq 6.98$) = 0.052 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.17 (σ = 0.03) and pK_a = 3.01 (σ = 0.01). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8A, δH2A, δH6U and δH5U are shown in the respective graphs.

Figure S2j: The Hill plots for δH6U, δH5U of UpA in the $6.6 \leq pH \leq 11.1$. Δ_T for H6U ($6.6 \leq pH \leq 11.1$) = 0.226 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.07 (σ = 0.02) and pK_a = 9.09 (σ = 0.01). Δ_T for H5U ($6.6 \leq pH$

≤ 11.1) = 0.117 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 1.00) with a slope = 1.06 (σ = 0.02) and pK_a = 9.09 (σ = 0.01). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH6U, and δH5U are shown in the respective graphs. H8A and H2A of UpA did not show any significant change in $\log((\Delta_T - \Delta)/\Delta)$ with pH, hence Hill plots for H8A and H2A were not done.

Figure S2k: The Hill plots for δH8A, δH2A, δH6U, δH5U of ApU in the 1.35 ≤ pH ≤ 6.99. Δ_T for H8A (1.35 ≤ pH ≤ 6.99) = 0.216 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.98) with a slope = 0.97 (σ = 0.05) and pK_a = 2.95 (σ = 0.02). Δ_T for H2A (1.35 ≤ pH ≤ 6.99) = 0.242 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.98) with a slope = 0.96 (σ = 0.06) and pK_a = 2.95 (σ = 0.02). Δ_T for H6U (1.35 ≤ pH ≤ 6.99) = 0.089 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.98) with a slope = 0.92 (σ = 0.05) and pK_a = 2.98 (σ = 0.02). Δ_T for H5U (1.35 ≤ pH ≤ 6.99) = 0.159 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.98) with a slope = 0.96 (σ = 0.05) and pK_a = 2.95 (σ = 0.02). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8A, δH2A, δH6U and δH5U are shown in the respective graphs.

Figure S2l: The Hill plots for δH8A, δH2A, δH6U, δH5U of ApU in the 6.99 ≤ pH ≤ 10.96. Δ_T for H8A (6.99 ≤ pH ≤ 10.96) = 0.021 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.04 (σ = 0.03) and pK_a = 9.35 (σ = 0.02). Δ_T for H2A (6.99 ≤ pH ≤ 10.96) = 0.007 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 0.99 (σ = 0.05) and pK_a = 9.33 (σ = 0.02). Δ_T for H6U (6.99 ≤ pH ≤ 10.96) = 0.126 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 0.99 (σ = 0.03) and pK_a = 9.36 (σ = 0.02). Δ_T for H5U (6.99 ≤ pH ≤ 10.96) = 0.017 ppm. The plot of $\log((\Delta_T - \Delta)/\Delta)$ vs. pH gave a straight line (R = 0.99) with a slope = 1.13 (σ = 0.04) and pK_a = 9.42 (σ = 0.02). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8A, δH2A, δH6U and δH5U are shown in the respective graphs.

Figure S2m: The Hill plots for δH8A, δH2A, of ApEt in the 1.62 ≤ pH ≤ 6.38. Δ_T for H8A (1.62 ≤ pH ≤ 6.38) = 0.228 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.98) with a slope = 0.97 (σ = 0.1) and pK_a = 3.11 (σ = 0.04). Δ_T for H2A (1.62 ≤ pH ≤ 6.38) = 0.206 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.98) with a slope = 0.98 (σ = 0.1) and pK_a = 3.10 (σ = 0.04). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8A and δH2A are shown in the respective graphs.

Figure S2n: The Hill plots for δH8G of GpEt in the 6.98 ≤ pH ≤ 11.00. Δ_T for H8G (6.98 ≤ pH ≤ 11.00) = 0.149 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 0.95 (σ = 0.05) and pK_a = 9.25 (σ = 0.02). The value of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH8G is shown in the respective graph.

Figure 2o: The Hill plots for δH6U, δH5U, of UpEt in the 6.65 ≤ pH ≤ 11.44. Δ_T for H6U (6.65 ≤ pH ≤ 11.44) = 0.198 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 1.03 (σ = 0.05) and pK_a = 9.44 (σ = 0.02). Δ_T for H5U (6.65 ≤ pH ≤ 11.44) = 0.091 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 0.99) with a slope = 1.04 (σ = 0.04) and pK_a = 9.43 (σ = 0.02). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH6U and δH5U are shown in the respective graphs.

Figure S2p: The Hill plots for δH6C, δH5C, of CpEt in the 1.66 ≤ pH ≤ 6.39. Δ_T for H6C (6.65 ≤ pH ≤ 11.44) = 0.321 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 1.00) with a slope = 1.01 (σ = 0.04) and pK_a = 3.83 (σ = 0.02). Δ_T for H5C (1.66 ≤ pH ≤ 6.39) = 0.190 ppm. The plot of log((Δ_T – Δ)/Δ) vs. pH gave a straight line (R = 1.00) with a slope = 1.02 (σ = 0.04) and pK_a = 3.82 (σ = 0.02). The values of correlation coefficient R, pK_a obtained from Hill plot analysis, and the Hill slope values of δH6C and δH5C are shown in the respective graphs.

Legends for Figure S3:

Figure S3a: pH dependant fraction protonation (f_P) of aromatic protons (H8A, H2A, H8G) of ApG within the pH values of $0.3 \leq pH \leq 7.56$. $\delta_{neutral}$ (8.261 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.297 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (8.153 ppm) of H2A is substracted from δ_{obs} at each pH values of H2A and divided by the total change $\Delta\delta$ (0.322) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (7.933 ppm) of H8G is substracted from δ_{obs} at each pH values of H8G and divided by the total change $\Delta\delta$ (1.124) in going from neutral to protonated state to get the value of f_P. pK_a values obtained from Hill plot of H8A, H2A and H8G are shown in the respective graphs.

Figure S3b: pH dependant fraction deprotonation (f_D) of aromatic protons (H8A, H2A, H8G) of ApG within the pH values of $7.56 \leq pH \leq 11.63$. $\delta_{neutral}$ (8.261 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.009 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (8.153 ppm) of H2A is substracted from δ_{obs} at each pH values of H2A and divided by the total change $\Delta\delta$ (0.032 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (7.933 ppm) of H8G is substracted from δ_{obs} at each pH values of H8G and divided by the total change $\Delta\delta$ (0.068 ppm) in going from neutral to deprotonated state to get the value of f_D. pK_a values obtained from Hill plot of H8A, H2A and H8G are shown in the respective graphs.

Figure S3c: pH dependant fraction protonation (f_P) of aromatic protons (H8A, H2A, H8G) of GpA within the pH values of $0.12 \leq pH \leq 7.29$. $\delta_{neutral}$ (8.344 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.205 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (8.206 ppm) of H2A is substracted from δ_{obs} at each pH values of H2A and divided by the total change $\Delta\delta$ (0.301 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (7.904 ppm) of H8G is substracted from δ_{obs} at each pH values of H8G and divided by the total change $\Delta\delta$ (1.184 ppm) in going from neutral to protonated state to get the value of

f_P. pK_a values obtained from Hill plot of H8A,H2A and H8G are shown in the respective graphs.

Figure S3d: pH dependant fraction deprotonation (f_D) of aromatic protons (H8A, H8G) of GpA within the pH values of $6.93 \leq pH \leq 10.70$. $\delta_{neutral}$ (8.345 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.056 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (7.906 ppm) of H8G is substracted from δ_{obs} at each pH values of H8G and divided by the total change $\Delta\delta$ (0.141 ppm) in going from neutral to deprotonated state to get the value of f_D. pK_a values obtained from Hill plot of H8A and H8G are shown in the respective graphs. H2A of GpA did not show any significant change in fraction deprotonation (f_D) with pH, hence pH dependant fraction deprotonation (f_D) of aromatic proton H2A was not done.

Figure S3e: pH dependant fraction protonation (f_P) of aromatic protons (H6U, H5U, H6C, H5C) of CpU within the pH values of $1.87 \leq pH \leq 6.92$. $\delta_{neutral}$ (δ 7.930) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.013 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (5.816 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change $\Delta\delta$ (0.073 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (7.902 ppm) of H6C is substracted from δ_{obs} at each pH values of H6C and divided by the total change $\Delta\delta$ (0.289 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (5.969 ppm) of H5C is substracted from δ_{obs} at each pH values of H5C and divided by the total change $\Delta\delta$ (0.262 ppm) in going from neutral to protonated state to get the value of f_P. pK_a values obtained from Hill plot of H6U, H5U, H6C and H5C are shown in the respective graphs.

Figure S3f: pH dependant fraction deprotonation (f_D) of aromatic protons (H6U, H5U, H6C, H5C) of CpU within the pH values of $6.92 \leq pH \leq 11.32$. $\delta_{neutral}$ (7.930 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.162 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (5.816 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the

total change Δδ (0.059ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (7.902 ppm) of H6C is substracted from δ_{obs} at each pH values of H6C and divided by the total change Δδ (0.0.078 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (5.969 ppm) of H5C is substracted from δ_{obs} at each pH values of H5C and divided by the total change Δδ (0.053 ppm) in going from neutral to deprotonated state to get the value of fraction deprotonation f_D. pK_a values obtained from Hill plot of H6U,H5U, H6C and H5C are shown in the respective graphs.

Figure S3g: pH dependant fraction protonation (f_P) of aromatic protons (H5U, H6C, H5C) of UpC within the pH values of 1.97 ≤ pH ≤ 6.79.$\delta_{neutral}$ (5.858 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change Δδ (0.033ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (7.936 ppm) of H6C is substracted from δ_{obs} at each pH values of H6C and divided by the total change Δδ (0.242 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (6.026 ppm) of H5C is substracted from δ_{obs} at each pH values of H5C and divided by the total change Δδ (0.247 ppm) in going from neutral to protonated state to get the value of f_P. pK_a values obtained from Hill plot of H5U, H6C and H5C are shown in the respective graphs. H6U of UpA did not show any significant change in fraction protonation (f_P) with pH, hence pH dependant fraction protonation (f_P) of aromatic proton H2A was not done.

Figure S3h: pH dependant fraction deprotonation (f_D) of aromatic protons (H6U, H5U, H6C, H5C) of UpC within the pH values of 6.79 ≤ pH ≤ 11.42. $\delta_{neutral}$ (7.918 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change Δδ (0.244 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (5.858 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change Δδ (0.068ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (7.936 ppm) of H6C is substracted from δ_{obs} at each pH values of H6C and divided by the total change Δδ (0.037ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (6.026 ppm) of H5C is substracted from δ_{obs} at each pH values of H5C and divided by the total change Δδ (0.021 ppm) in going from neutral to

deprotonated state to get the value of f_D. pK_a values obtained from Hill plot of H6U, H5U, H6C and H5C are shown in the respective graphs.

Figure S3i: pH dependant fraction protonation of aromatic protons (H8A, H2A, H6U, H5U) of UpA within the pH values of $1.11 \leq pH \leq 6.60$. $\delta_{neutral}$ (8.435 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.188 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (8.256 ppm) of H2A is substracted from δ_{obs} at each pH values of H5U and divided by the total change $\Delta\delta$ (0.219 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (7.748 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.094 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (5.785 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change $\Delta\delta$ (0.052 ppm) in going from neutral to protonated state to get the value of f_P. pK_a values obtained from Hill plot of H8A, H2A H6U and H5U are shown in the respective graphs.

Figure S3j: pH dependant fraction deprotonation (f_D) of aromatic protons (H6U, H5U) of UpA within the pH values of $6.60 \leq pH \leq 11.10$. $\delta_{neutral}$ (7.918 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.226 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (5.731 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change $\Delta\delta$ (0.117 ppm) in going from neutral to deprotonated state to get the value of f_D. pK_a values obtained from Hill plot of H6U and H5U are shown in the respective graphs. H8A and H2A of UpA did not show any significant change in fraction deprotonation (f_D) with pH, hence pH dependant fraction deprotonation (f_D) of aromatic protons H8A and H2A were not done.

Figure S3k: pH dependant fraction protonation (f_P) of aromatic protons (H8A, H2A, H6U, H5U) of ApU within the pH values of $1.35 \leq pH \leq 6.99$. $\delta_{neutral}$ (8.362 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.216 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$

(8.222 ppm) of H2A is substracted from δ_{obs} at each pH values of H2A and divided by the total change $\Delta\delta$ (0.242 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (7.767 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.089 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (5.639 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change $\Delta\delta$ (0.159 ppm) in going from neutral to protonated state to get the value of f_P. pK_a values obtained from Hill plot of H8A, H2A, H6U and H5U are shown in the respective graphs.

Figure S3l: pH dependant fraction deprotonation (f_D) of aromatic protons (H8A, H2A, H6U, H5U) of ApU within the pH values of $6.99 \leq pH \leq 10.96$. $\delta_{neutral}$ (8.362 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.021 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (8.222 ppm) of H2A is substracted from δ_{obs} at each pH values of H2A and divided by the total change $\Delta\delta$ (0.007 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (7.767 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.126 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (5.638 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change $\Delta\delta$ (0.017 ppm) in going from neutral to deprotonated state to get the value of f_D. pK_a values obtained from Hill plot of H8A, H2A, H6U and H5U are shown in the respective graphs.

Figure S3m: pH dependant fraction protonation (f_P) of aromatic protons (H8A, H2A) of ApEt within the pH values of $1.62 \leq pH \leq 6.38$. $\delta_{neutral}$ (8.354 ppm) of H8A is substracted from δ_{obs} at each pH values of H8A and divided by the total change $\Delta\delta$ (0.228 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (8.270 ppm) of H2A is substracted from δ_{obs} at each pH values of H2A and divided by the total change $\Delta\delta$ (0.206 ppm) in going from neutral to protonated state to get the value of f_P. pK_a values obtained from Hill plot of H8A and H2A are shown in the respective graphs.

Figure S3n: pH dependant fraction deprotonation (f_D) of aromatic proton (H8G) of GpEt within the pH values of $6.89 \leq pH \leq 11.00$. $\delta_{neutral}$ (8.010 ppm) of H8G is substracted from δ_{obs} at each pH values of H8G and divided by the total change $\Delta\delta$ (0.149 ppm) in going from neutral to deprotonated state to get the value of f_D. pK_a value obtained from Hill plot of H8G is shown in the respective graph.

Figure S3o: pH dependant fraction deprotonation (f_D) of aromatic protons (H6U, H5U) of UpEt within the pH values of $6.65 \leq pH \leq 11.44$. $\delta_{neutral}$ (7.884 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.198 ppm) in going from neutral to deprotonated state to get the value of f_D. $\delta_{neutral}$ (5.918 ppm) of H5U is substracted from δ_{obs} at each pH values of H5U and divided by the total change $\Delta\delta$ (0.091 ppm) in going from neutral to deprotonated state to get the value of f_D. pK_a values obtained from Hill plot of H6U and H5U are shown in the respective graphs.

Figure S3p: pH dependant fraction protonation (f_P) of aromatic protons (H6C, H5C) of CpEt within the pH values of $1.66 \leq pH \leq 6.39$. $\delta_{neutral}$ (7.848 ppm) of H6U is substracted from δ_{obs} at each pH values of H6U and divided by the total change $\Delta\delta$ (0.321 ppm) in going from neutral to protonated state to get the value of f_P. $\delta_{neutral}$ (6.069 ppm) of H5C is substracted from δ_{obs} at each pH values of H5C and divided by the total change $\Delta\delta$ (0.190 ppm) in going from neutral to protonated state to get the value of f_P. pK_a values obtained from Hill plot of H6C and H5C are shown in the respective graphs.

Legends for Figure S4:

Panels (A1) – (E2) show the chamical shift change over the pH-range, $\Delta\delta$ [$\delta_N - \delta_{P/D}$, in ppm; N, P, D stands for neutral, protonated and deprotonated state], as a basis for atom-$\pi\sigma$ interaction[12,16] between nearest neighbor nucleobases in **1** – **6**. $\Delta\delta$ corresponds to the relative shielding (upfield shift, $\Delta\delta > 0$) or deshielding (downfield shift, $\Delta\delta < 0$) as a function of pH (see Figure S1). $\Delta\delta$ of nucleotide-3'-ethylphosphate and nucleoside have

been used for mimicking 3'-nucleotidyl unit (Np) and 5'-nucleotidyl unit (pN') for corresponding dinucleotide monophospahte (NpN').

The electrostatic interaction between the partial charge distribution of a nucleobase (depending upon its pseudoaromatic character) and the π-electron density corresponding to the next base constitutes charge transfer through atom-πσ interaction[12,16,43]. The protonation/deprotonation at nucleobase changes the conformational characteristics of pentose moieties as well as the partial charge distribution of aglycone (particularly for heteroatoms), in ground state, which in turn, causes a differential electrostatic interaction between neighboring nucleobases.

Panel (**A1**) shows the pH-dependent Δδ of following aromatic protons of ApG in alkaline range (pH ~7.0 – 11.0; ApG^-): H8A and H2A of ApG [(**H8A**)pG^-: -0.009ppm and (**H2A**)pG^-: -0.032ppm] and ApEt [no change of (**H8A**)pEt and (**H2A**)pEt, as adenosine does not have any deprotonation site]; H8G of ApG [Ap(**H8G**$^-$): 0.068ppm] and G [**H8G**: 0.138ppm]. Panel (**A2**) shows the pH-dependent Δδ of following aromatic protons of GpA in alkaline range (pH ~7.0 – 11.0; G^-pA): H8G of GpA [(**H8G**$^-$)pA: 0.141ppm] and GpEt [(**H8G**$^-$)pEt: 0.149ppm]; H8A and H2A of GpA [G^-p(**H8A**): -0.056ppm and G^-p(**H2A**): -0.004ppm] and A [no change of **H8A** and **H2A** as adenosine does not have any deprotonation site].

Panel (**B1**) shows the pH-dependent Δδ of following aromatic protons of ApU in acidic range (pH ~2.0 – 7.0; $A^{H+}pU$): H8A and H2A of ApU [(**H8A**)$^{H+}$pA: -0.216ppm and (**H2A**)$^{H+}$pA: -0.242ppm] and ApEt [(**H8A**)$^{H+}$pEt: -0.321ppm and (**H2A**)$^{H+}$pEt: -0.19ppm]; H6U and H5U of ApU [A^{H+}p(**H6U**): -0.089ppm, A^{H+}p(**H5U**): -0.159ppm] and U [no change of **H6U** and **H5U** as uridine does not have any protonation site]. Panel (**B2**) shows the pH-dependent Δδ of following aromatic protons of ApU in alkaline range (pH ~7.0 – 11.0; CpU^-): H8A and H2A of ApU [(**H8A**)pU^-: 0.021ppm and (**H2A**)pU^-: -0.007ppm] and ApEt [no change of (**H8A**)pEt and (**H2A**)pEt, as adenosine does not have any deprotonation site,]; H6U and H5U of ApU [Ap(**H6U**$^-$): 0.126ppm, Ap(**H5U**$^-$): 0.017ppm] and U [**H6U**: 0.176ppm and **H5U**: 0.084ppm].

Panel (**C1**) shows the pH-dependent Δδ of following aromatic protons of UpA in acidic range (pH ~1.0 – 7.0; UpA^{H+}): H6U and H5U of UpA [(**H6U**)pA^{H+}: -0.094ppm, (**H5U**)pA^{H+}: -0.052ppm] and UpEt [no change of (**H6U**)pEt and (**H5U**)pEt as uridine

does not have any protonation site]; H8A and H2A of UpA [Up(**H8A**)$^{H+}$: -0.188ppm and Up(**H2A**)$^{H+}$: -0.219ppm] and A [**H8A**$^{H+}$: -0.216ppm and **H2A**$^{H+}$: -0.198ppm]. Panel (**C2**) shows the pH-dependent Δδ of following aromatic protons of UpA in alkaline range (pH ~7.0 – 11.0; U^{-}pA): H6U and H5U of UpA [(**H6U**$^{-}$)pA: 0.226ppm, (**H5U**$^{-}$)pA: -0.117ppm] and UpEt [(**H6U**$^{-}$)pEt: 0.198ppm and (**H5U**$^{-}$)pEt: 0.091ppm]; H8A and H2A of UpA [almost no change, U^{-}p(**H8A**): -0.003ppm and U^{-}p(**H2A**): -0.002ppm] and A [no change of **H8A** and **H2A** as adenosine does not have any deprotonation site].

Panel (**D1**) shows the pH-dependent Δδ of following aromatic protons of UpC in acidic range (pH ~2.0 – 7.0; UpC^{H+}): H6U and H5U of UpC [(**H6U**)pC^{H+}: 0.002ppm, (**H5U**)pC^{H+}: -0.033ppm] and UpEt [no change of (**H6U**)pEt and (**H5U**)pEt as uridine does not have any protonation site]; H6C and H5C of UpC [Up(**H6C**)$^{H+}$: -0.242ppm and Up(**H5C**)$^{H+}$: -0.247ppm] and C [**H6C**$^{H+}$: -0.309ppm and **H5C**$^{H+}$: -0.19ppm]. Panel (**D2**) shows the pH-dependent Δδ of following aromatic protons of UpC in alkaline range (pH ~7.0 – 11.0; U^{-}pC): H6U and H5U of UpC [(**H6U**$^{-}$)pC: 0.068ppm, (**H5U**$^{-}$)pC: 0.033ppm] and UpEt [(**H6U**$^{-}$)pEt: 0.198ppm and (**H5U**$^{-}$)pEt: 0.091ppm]; H6C and H5C of UpC [U^{-}p(**H6C**): 0.037ppm and U^{-}p(**H6C**): -0.021ppm] and C [no change of **H6C** and **H5C** as cytidine does not have any deprotonation site].

Panel (**E1**) shows the pH-dependent Δδ of following aromatic protons of CpU in acidic range (pH ~2.0 – 7.0; C^{H+}pU): H6C and H5C of CpU [(**H6C**)$^{H+}$pU: -0.289ppm and (**H5C**)$^{H+}$pU: -0.262ppm] and CpEt [(**H6C**)$^{H+}$pEt: -0.321ppm and [(**H5C**)$^{H+}$pEt: -0.19ppm]; H6U and H5U of CpU [C^{H+}p(**H6U**): 0.013ppm, C^{H+}p(**H5U**): -0.073ppm] and U [no change of **H6U** and **H5U** as uridine does not have any protonation site]. Panel (**E2**) shows the pH-dependent Δδ of following aromatic protons of CpU in alkaline range (pH ~7.0 – 11.0; CpU^{-}): H6C and H5C of CpU [(**H6C**)pU^{-}: 0.078ppm and (**H5C**)pU^{-}: 0.053ppm] and CpEt [no change of (**H6C**)pEt and (**H6C**)pEt, as cytidine does not have any deprotonation site]; H6U and H5U of CpU [Cp(**H6U**$^{-}$): 0.013ppm, Cp(**H5U**$^{-}$): 0.073ppm] and U [**H6U**: 0.176ppm and **H5U**: 0.084ppm].

^{1}H NMR (at 500MHz with δ_{DSS} = 0.015 ppm as internal standard) for nucleoside adenosine (**A**), Guanosine (**G**), Uridine (**U**) and Cytidine (**C**) [with sample concentration of 1 mM] have been studied at acidic (pH = 1.9), neutral (pH = 6.6) and alkaline (pH = 10.3) state to compare with the 5'-nucleotidyl moieties of dimer, **1** – **6**. The pH-dependent chemical

shifts (δ, in ppm) of aromatic protons are as follows: δ_{H8A} = 8.555 (at pH = 1.9) and 8.339 (at pH = 6.6); δ_{H2A} = 8.458 (at pH = 1.9) and 8.260 (at pH = 6.6) for **A**. δ_{H8G} = 8.591 (at pH = 1.9), 8.002 (at pH = 6.6) and 7.864 (at pH = 10.3) for **G**. δ_{H5U} = 5.901 (at pH = 6.6) and 5.817 (at pH = 10.3); δ_{H6U} = 7.871 (at pH = 6.6) and 7.695 (at pH = 10.3) for **U**. δ_{H5C} = 6.054 (at pH = 1.9) and 6.244 (at pH = 6.6); δ_{H6C} = 7.84 (at pH = 1.9) and 8.149 (at pH = 6.6) for **C**.

Legends for Figure S5:

Panels (**A**) – (**F**) show the dimerisation shift[31-33] ($\delta_{\mathbf{Np}Et} - \delta_{\mathbf{Np}N'}$, in ppm) of the aromatic protons of 3' nucleotidyl unit of **1** – **6** at neutral (pH = 6.6), acidic (pH = 1.9) and alkaline (pH = 10.4) state. Due to base-base stacking interaction in dinucleoside monophosphates, **1** – **6**, the aromatic protons are shifted upfield compared to their monomeric counterparts, **7** – **10**. [except for δ_{H8A} of ApU at neutral pH, δ_{H5U} of UpA in alkaline pH and δ_{H6U} of UpC as well as δ_{H6C} of CpU at both neutral and acidic pH - where different partial charges between the nearest neighbor neucleobases cause these aromatic proton to get deshielded on dimerisation.]

Panel (**A**) shows dimerisation shift for H8A and H2A of ApG compared to H8A and H2A of ApEt at neutral (pH = 6.6), acidic (pH = 1.9) and alkaline (pH = 10.4) state. Panel (**B**) shows dimerisation shift for H8G of GpA compared to H8G of GpEt at neutral (pH = 6.6), acidic (pH = 1.9) and alkaline (pH = 10.4) state. Panel (**C**) shows dimerisation shift for H8A and H2A of ApU compared to H8A and H2A of ApEt at neutral (pH = 6.6), acidic (pH = 1.9) and alkaline (pH = 10.4) state. Panel (**D**) shows dimerisation shift for H5U and H6U of UpA compared to H5U and H6U of UpEt at neutral (pH = 6.6), acidic (pH = 1.9) and alkaline (pH = 10.4) state. Panel (**E**) shows dimerisation shift for H5U and H6U of UpC compared to H5U and H6U of UpEt at neutral (pH = 6.6), acidic (pH = 1.9) and alkaline (pH = 10.4) state. Panel (**F**) shows dimerisation shift for H5C and H6C of CpU compared to H5C and H6C of CpEt at neutral (pH = 6.6), acidic (pH = 1.9) and alkaline (pH = 10.4) state. See Table S3 for details.

Figures S1a - S1p

Figure S1a : ApG

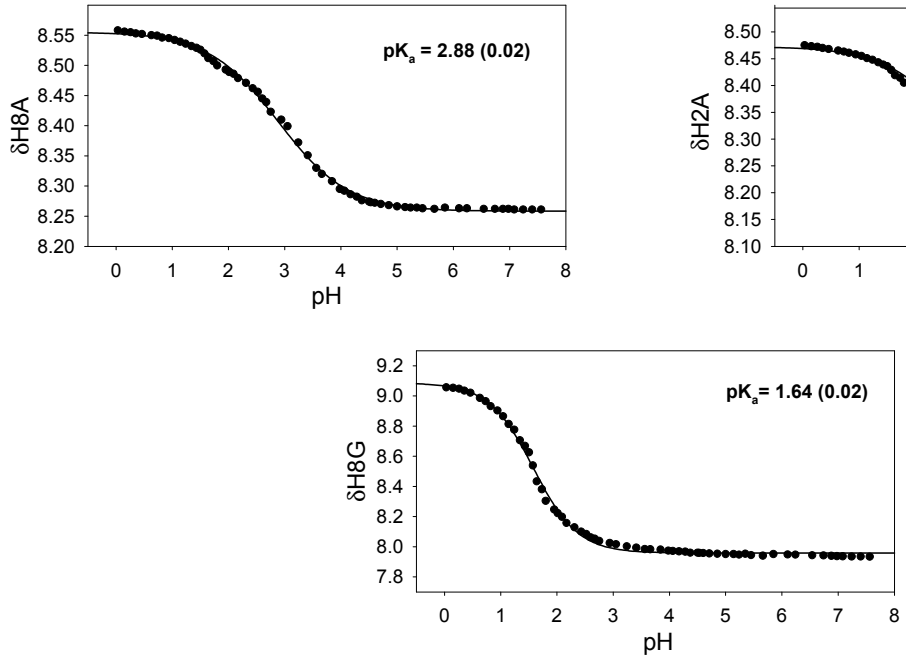
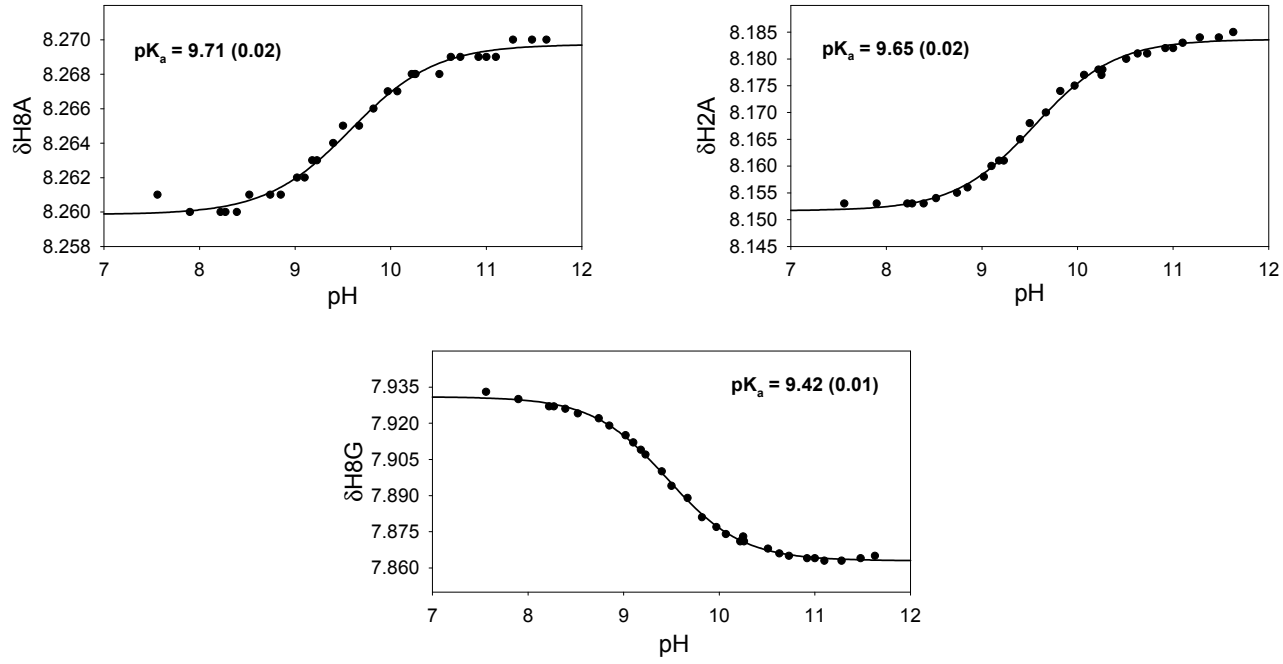


Figure S1b : ApG



Figures S1a - S1p

Figure S1c : GpA

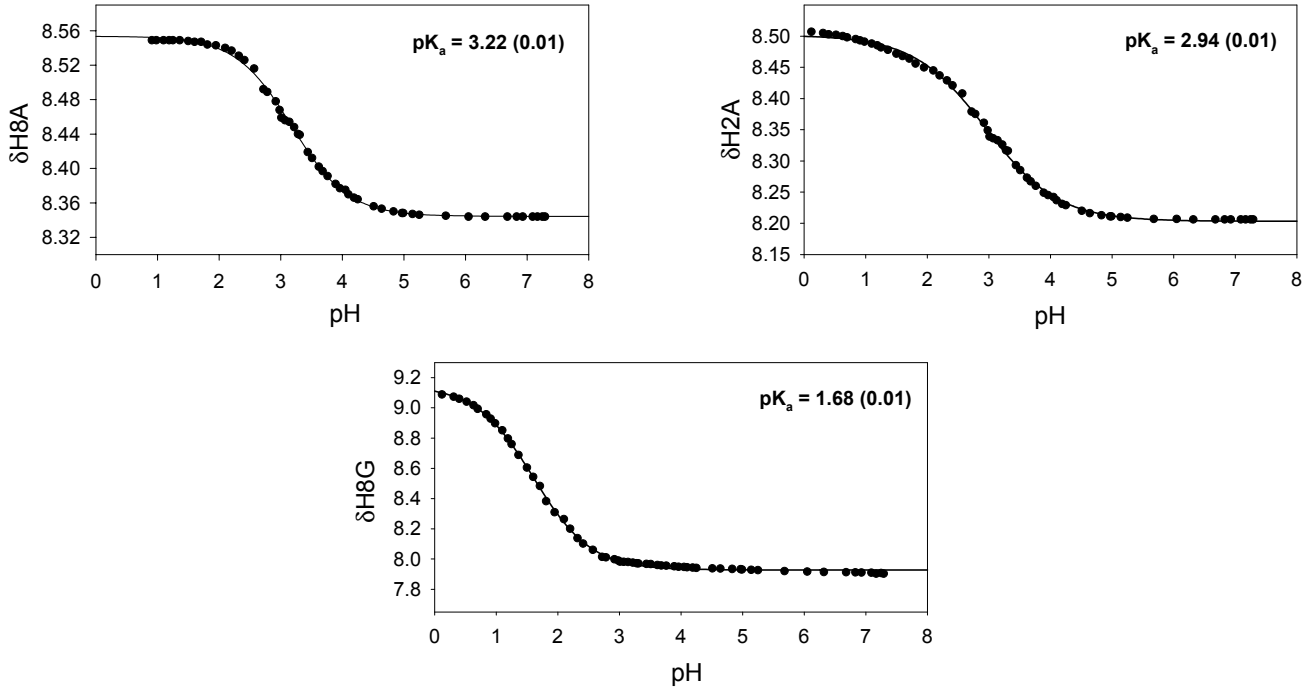
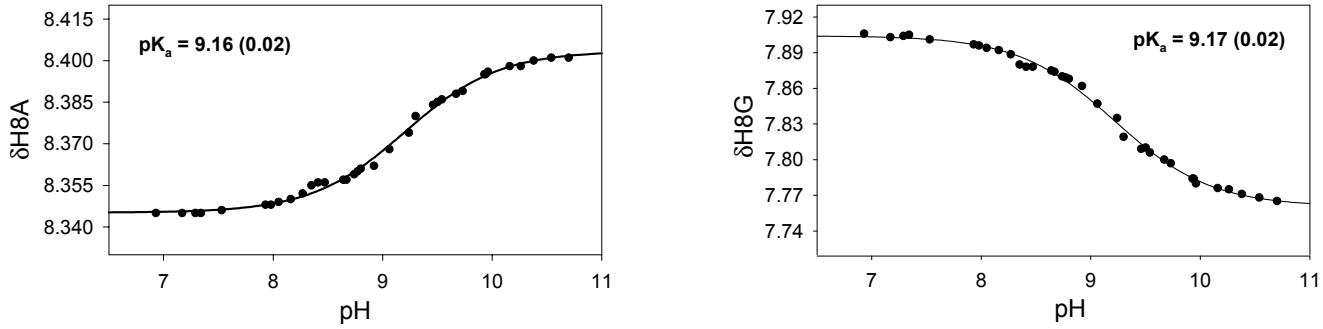


Figure S1d : GpA



Figures S1a - S1p

Figure S1e : CpU

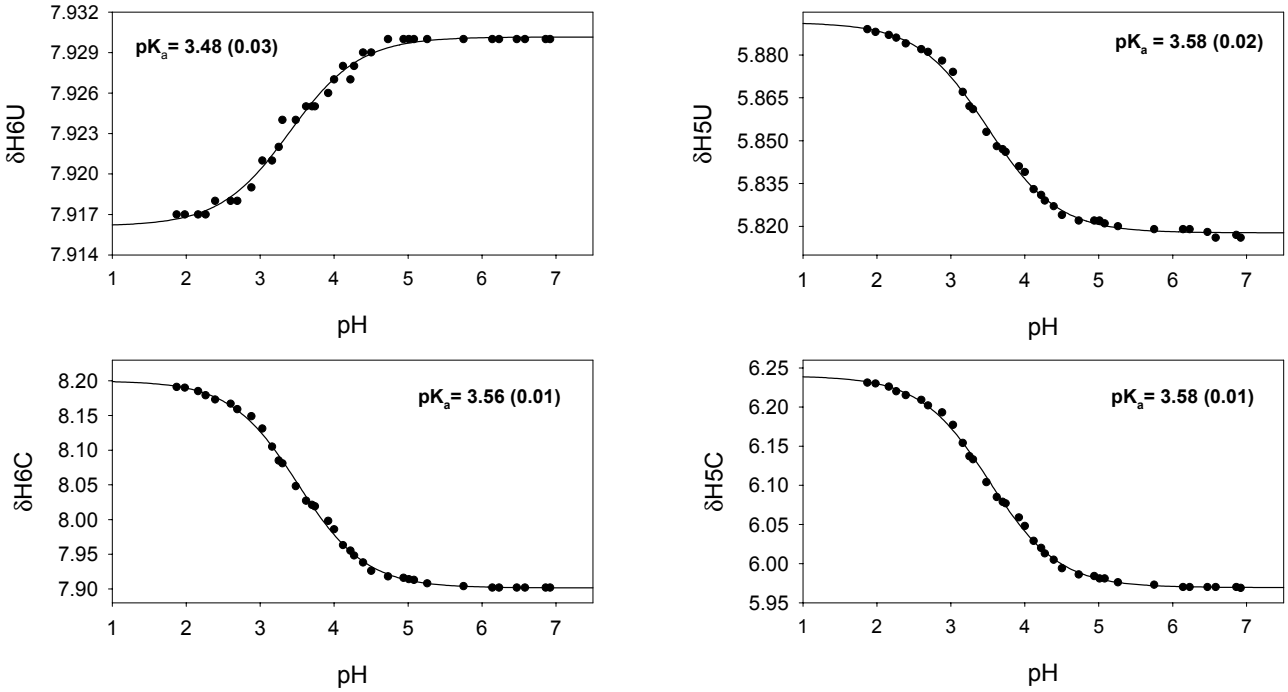
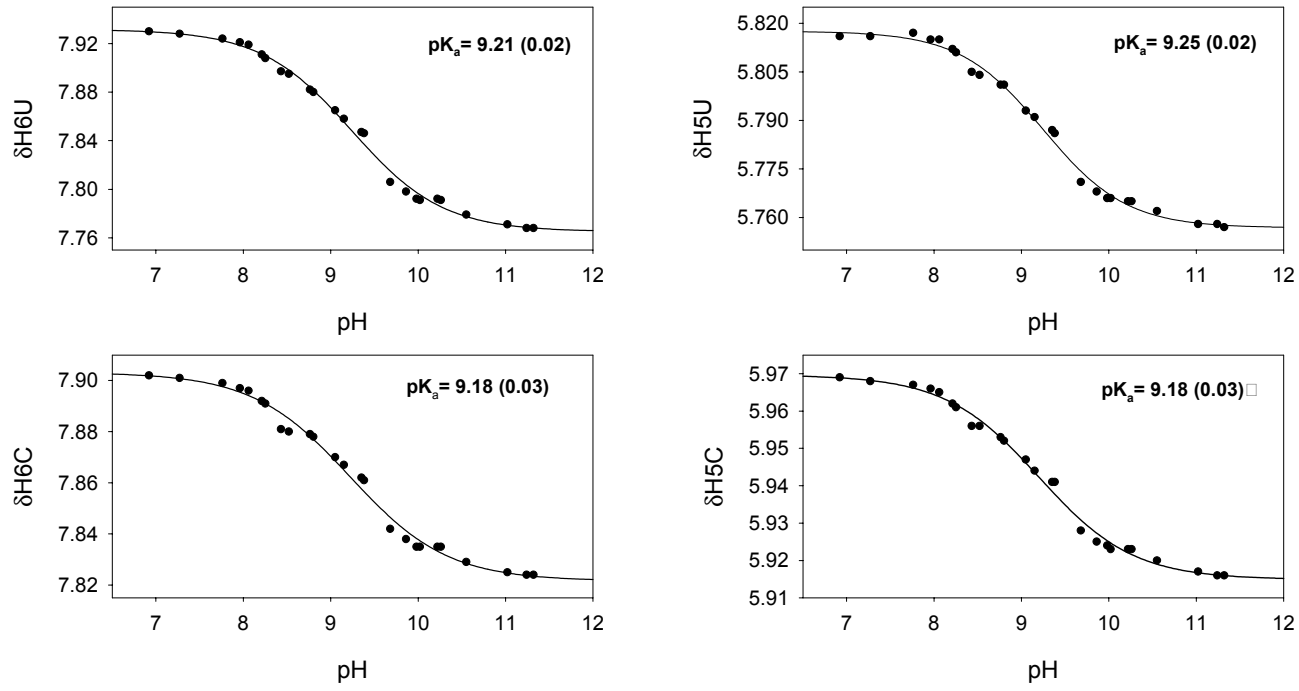


Figure S1f : CpU



Figures S1a - S1p

Figure S1g : UpC

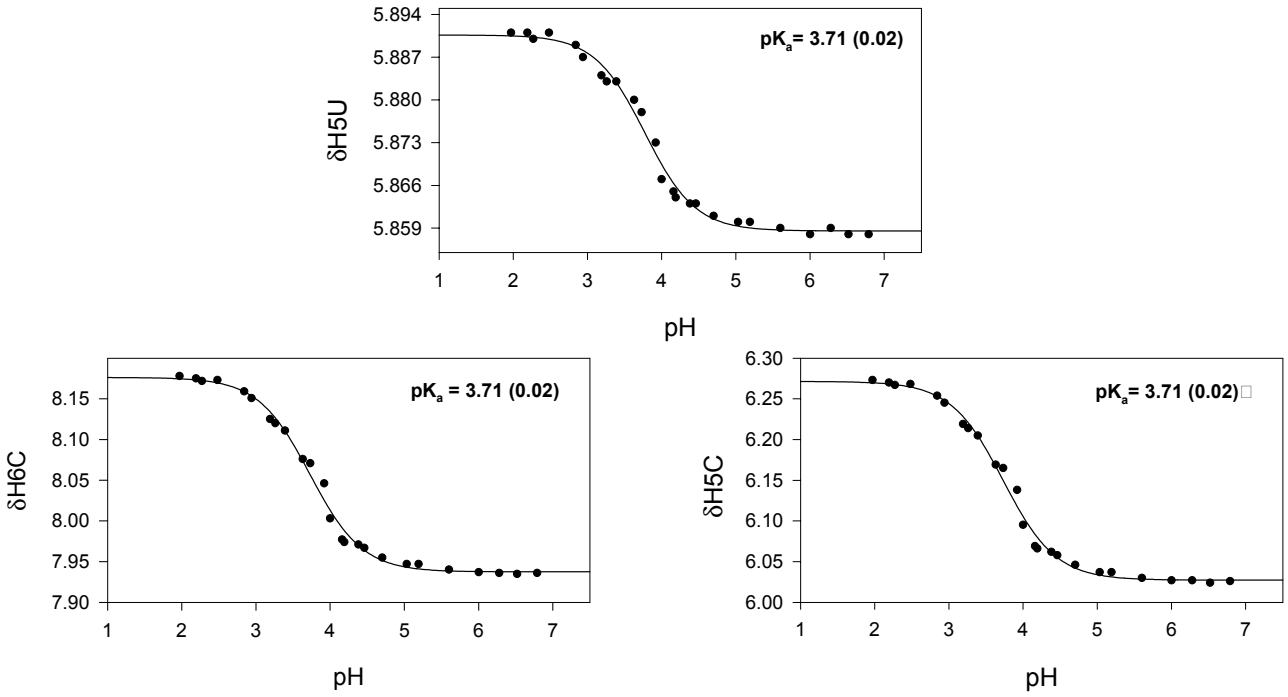
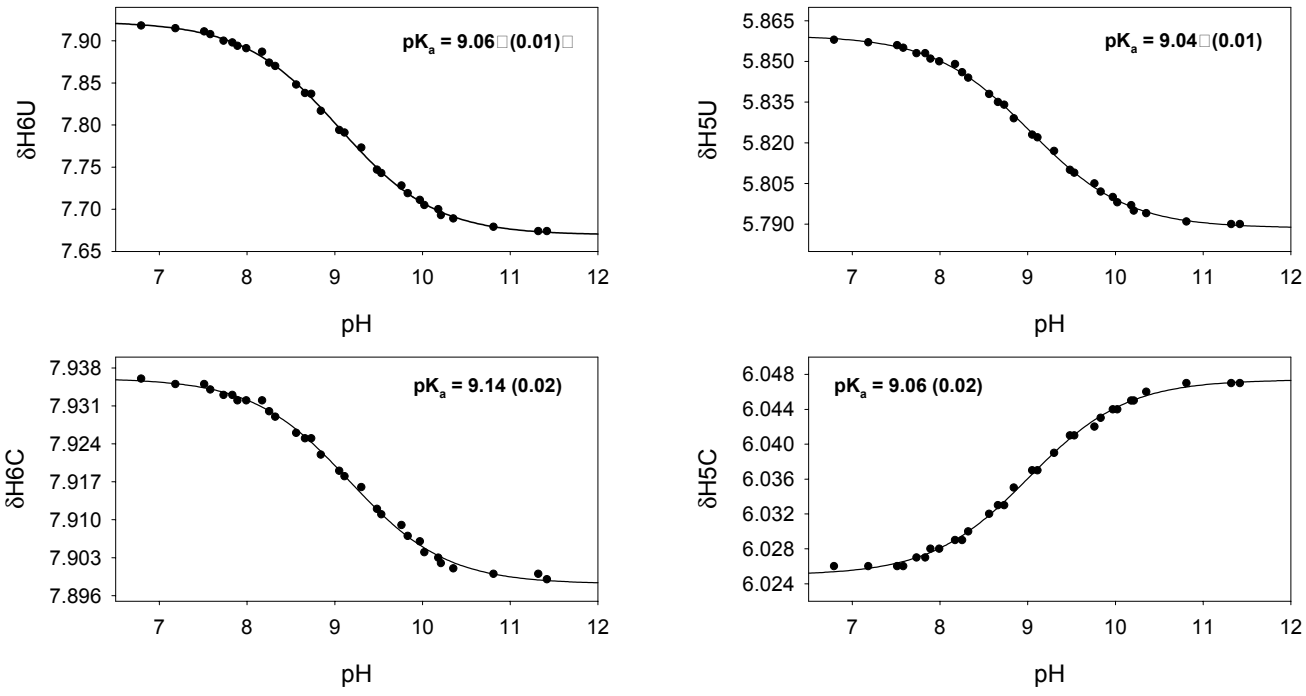


Figure S1h : UpC



Figures S1a - S1p

Figure S1i : UpA

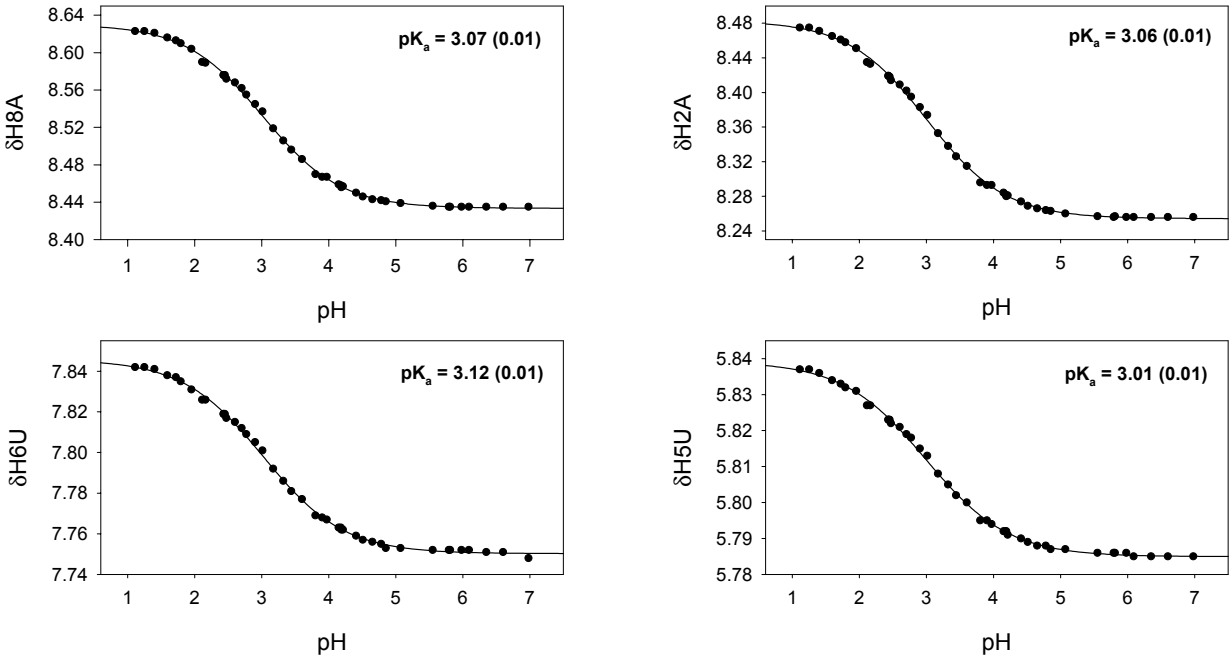
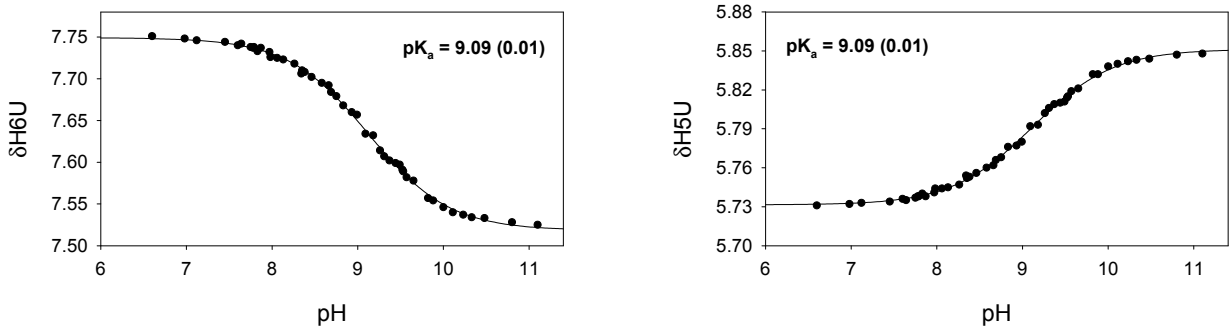


Figure S1j : UpA



Figures S1a - S1p

Figure S1k : ApU

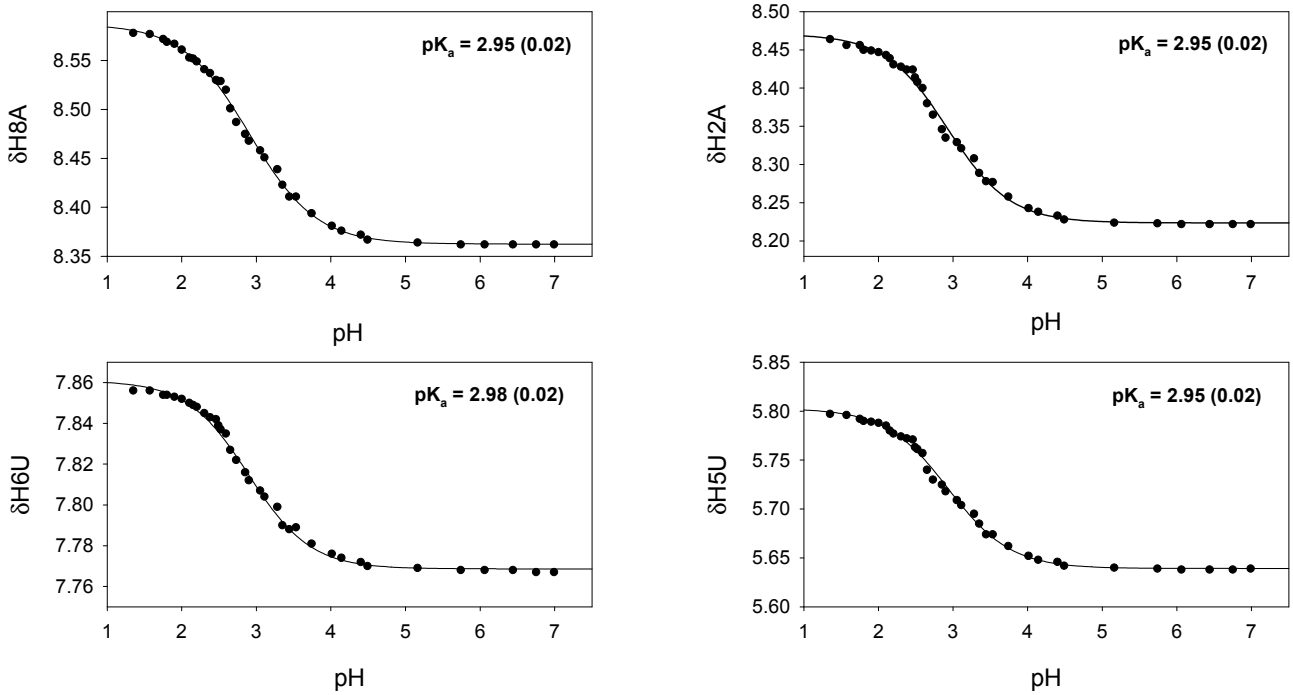
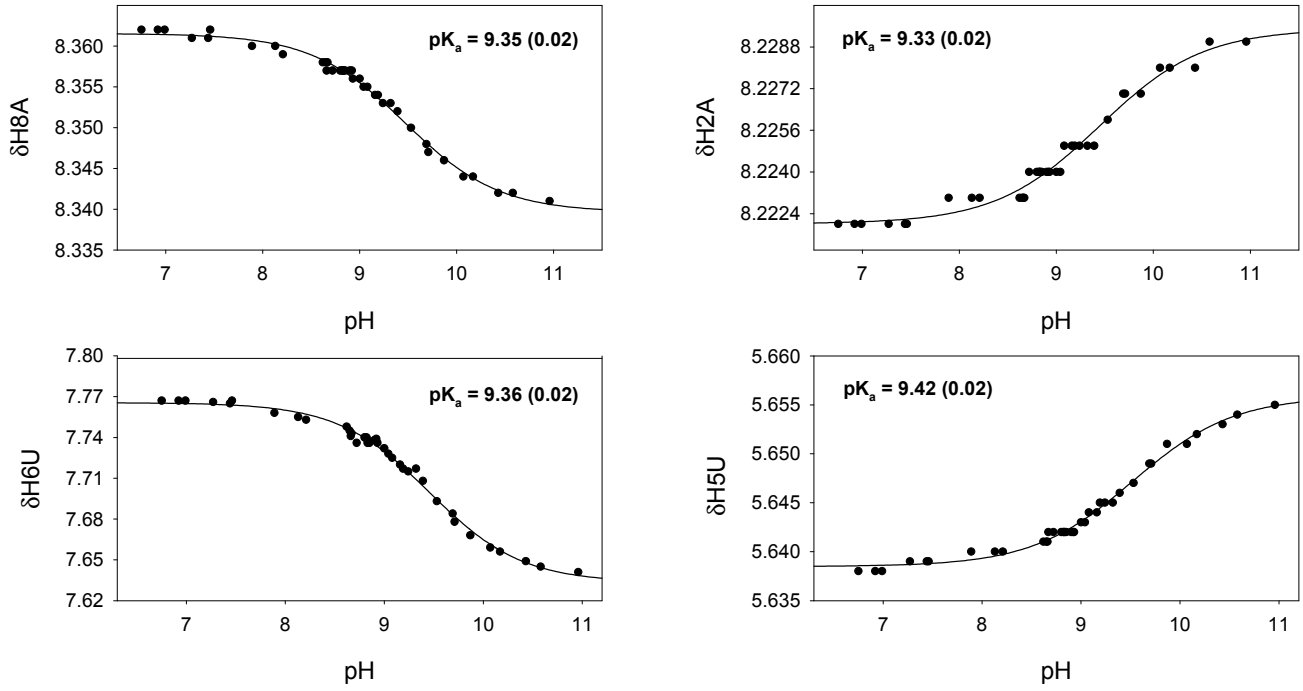


Figure S1l : ApU



Figures S1a - S1p

Figure S1m : ApEt

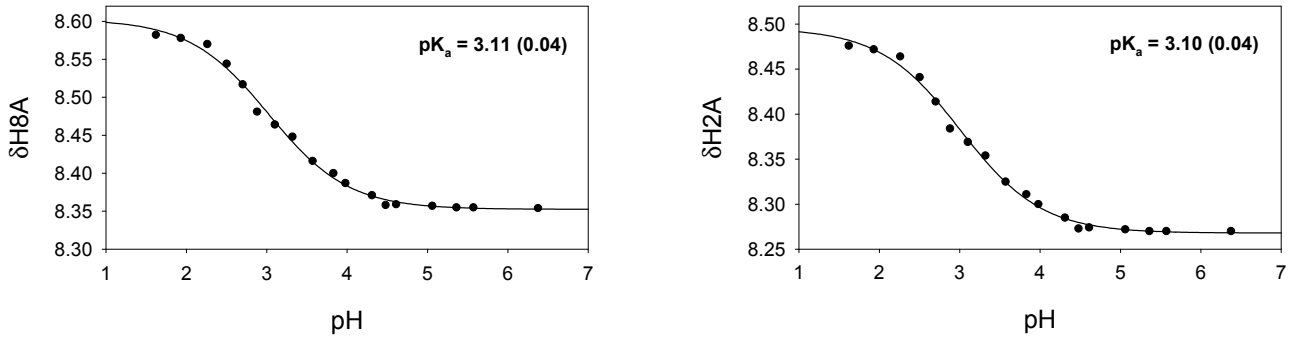


Figure S1n : GpEt

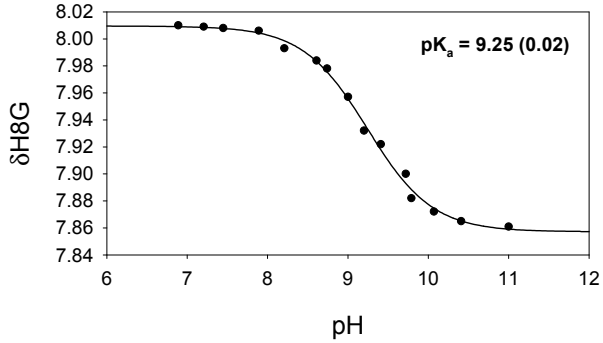


Figure S1o : UpEt

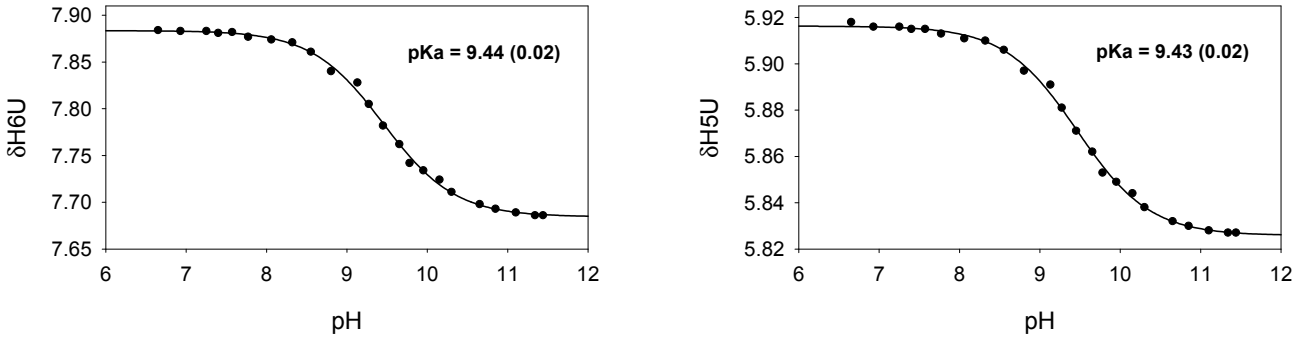
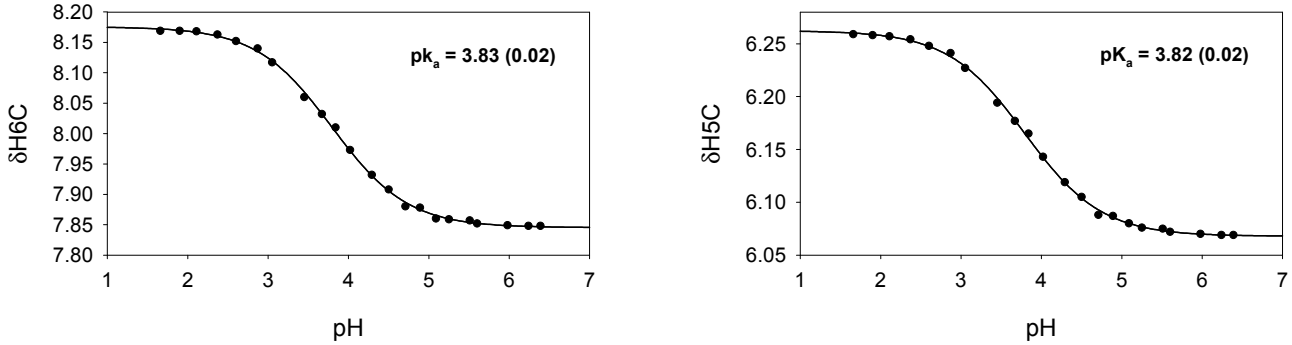


Figure S1p : CpEt



Figures S2a - S2p

Figure S2a : ApG

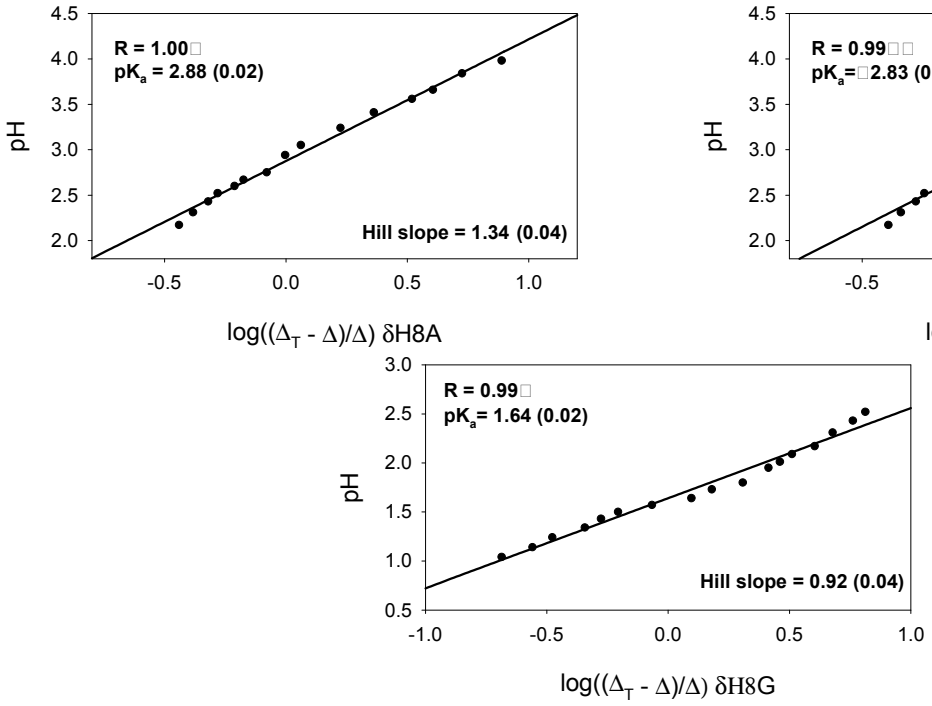
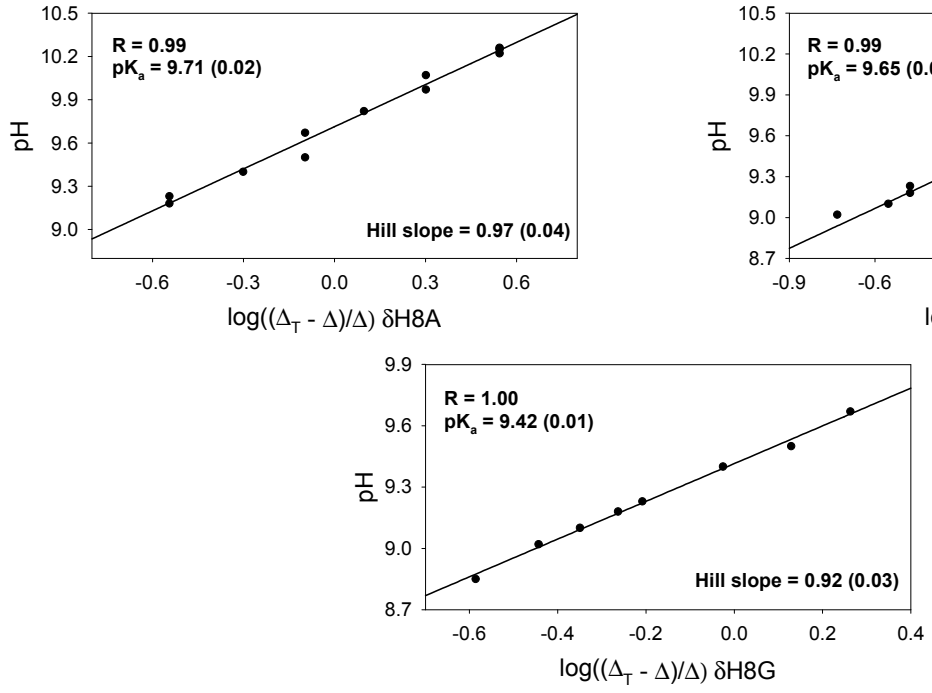
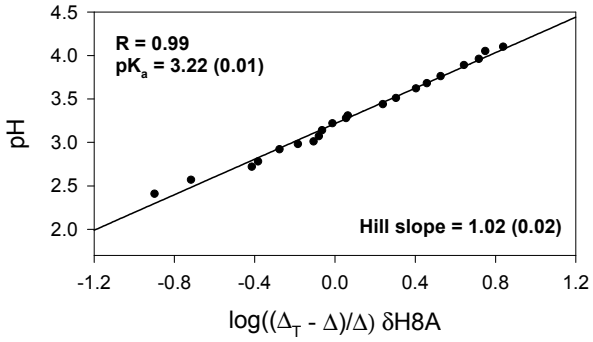


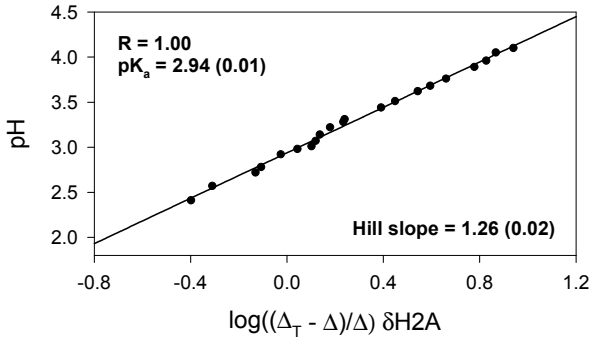
Figure S2b : ApG



Figures S2a - S2p

Figure S2c : GpA





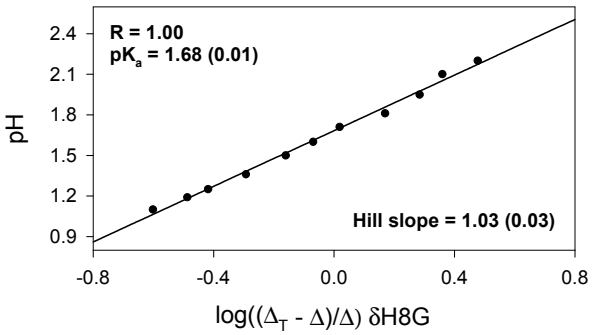
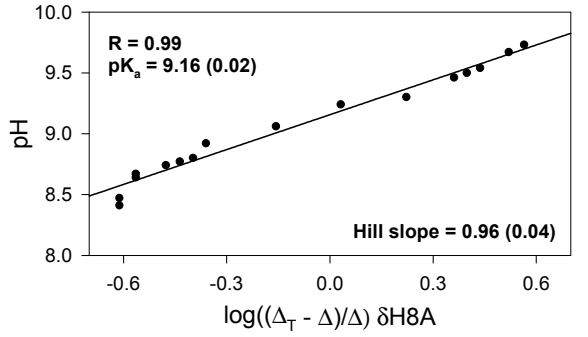
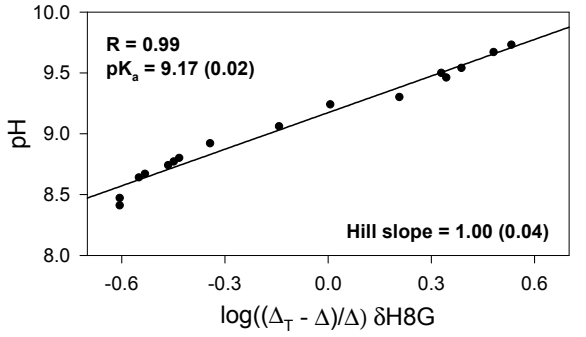


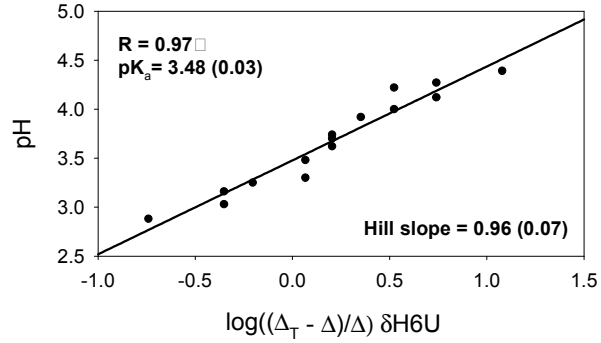
Figure S2d : GpA

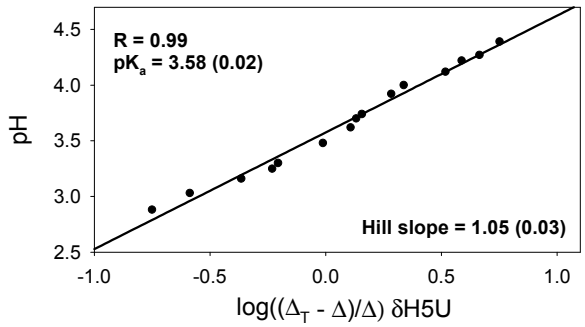


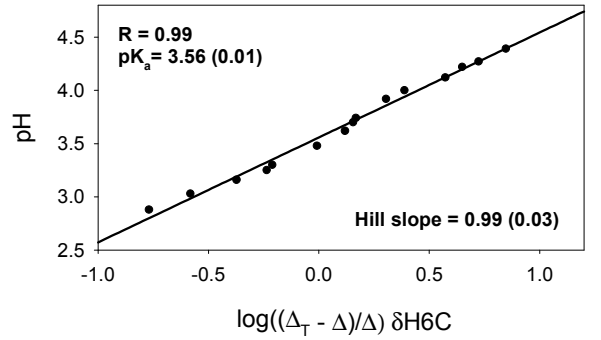


Figures S2a - S2p

Figure S2e : CpU







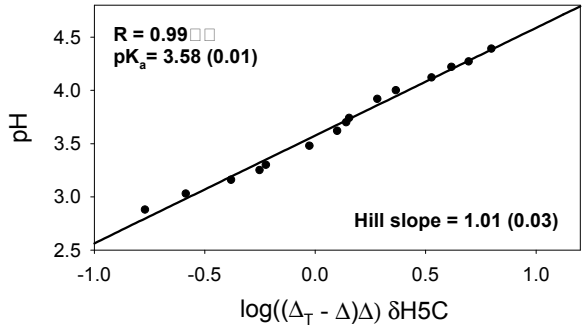
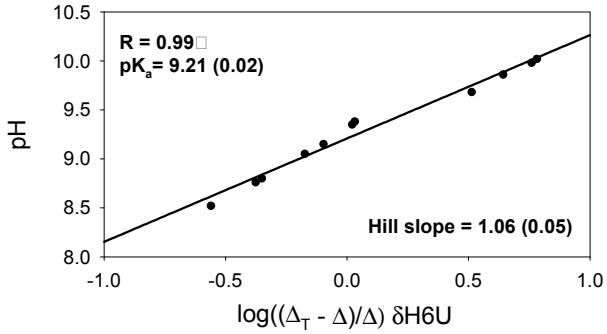
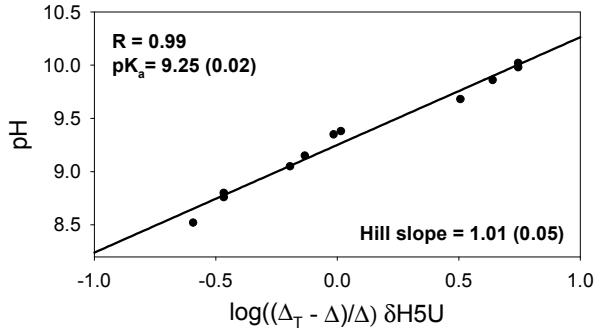
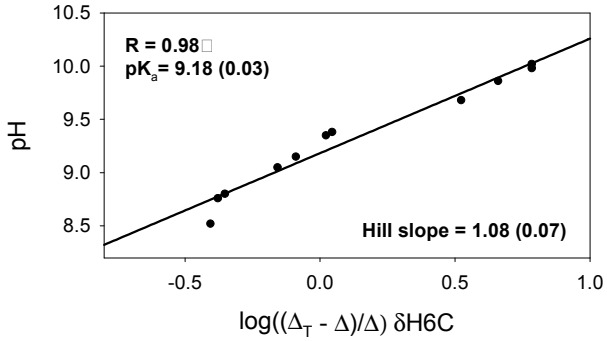
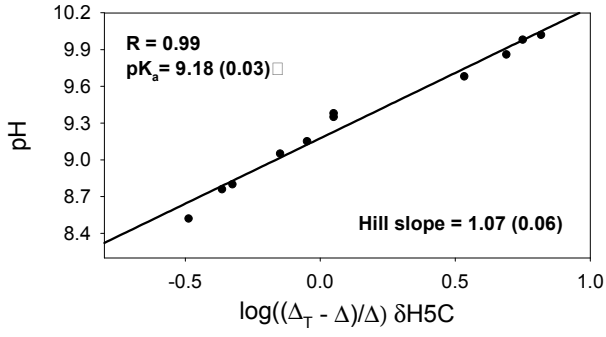


Figure S2f : CpU



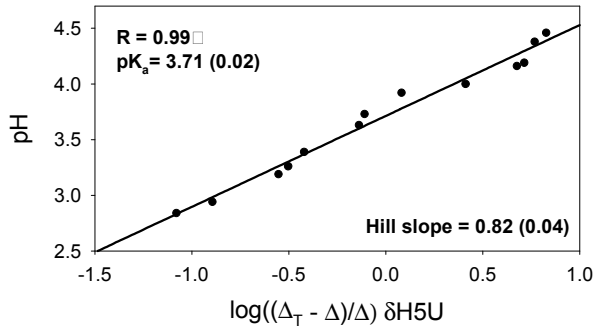


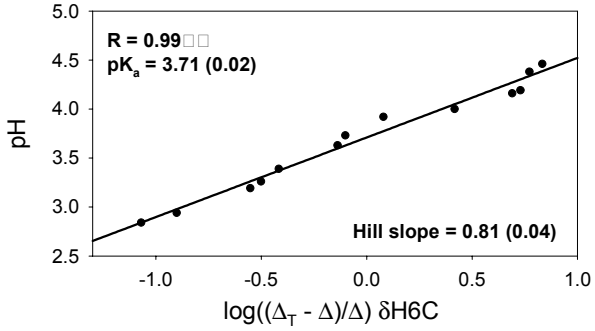




Figures S2a - S2p

Figure S2g : UpC





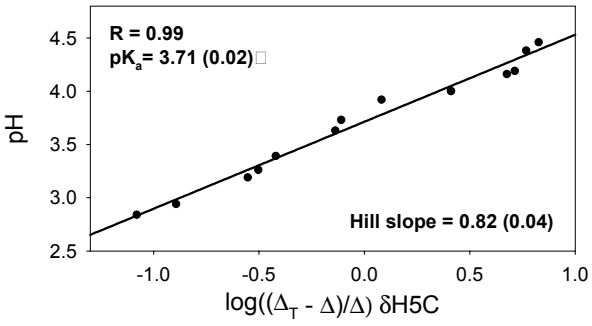
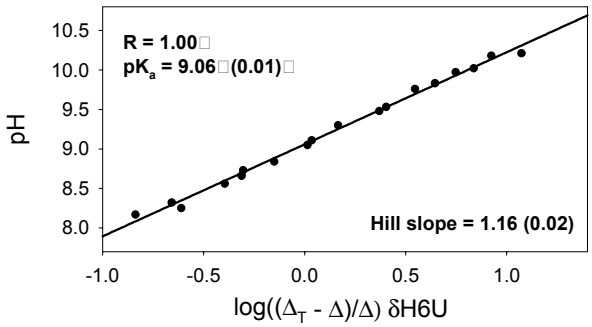
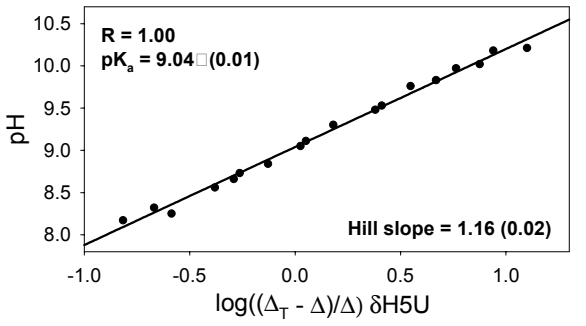
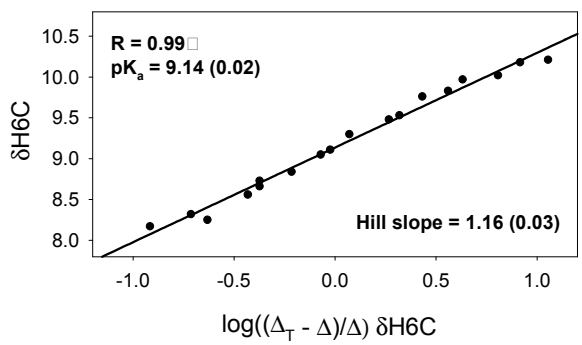
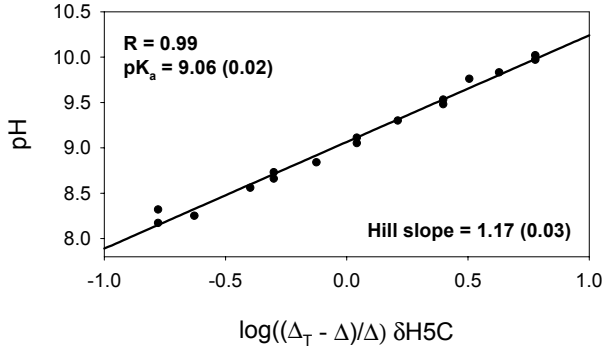


Figure S2h : UpC









Figures S2a - S2p

Figure S2i : UpA

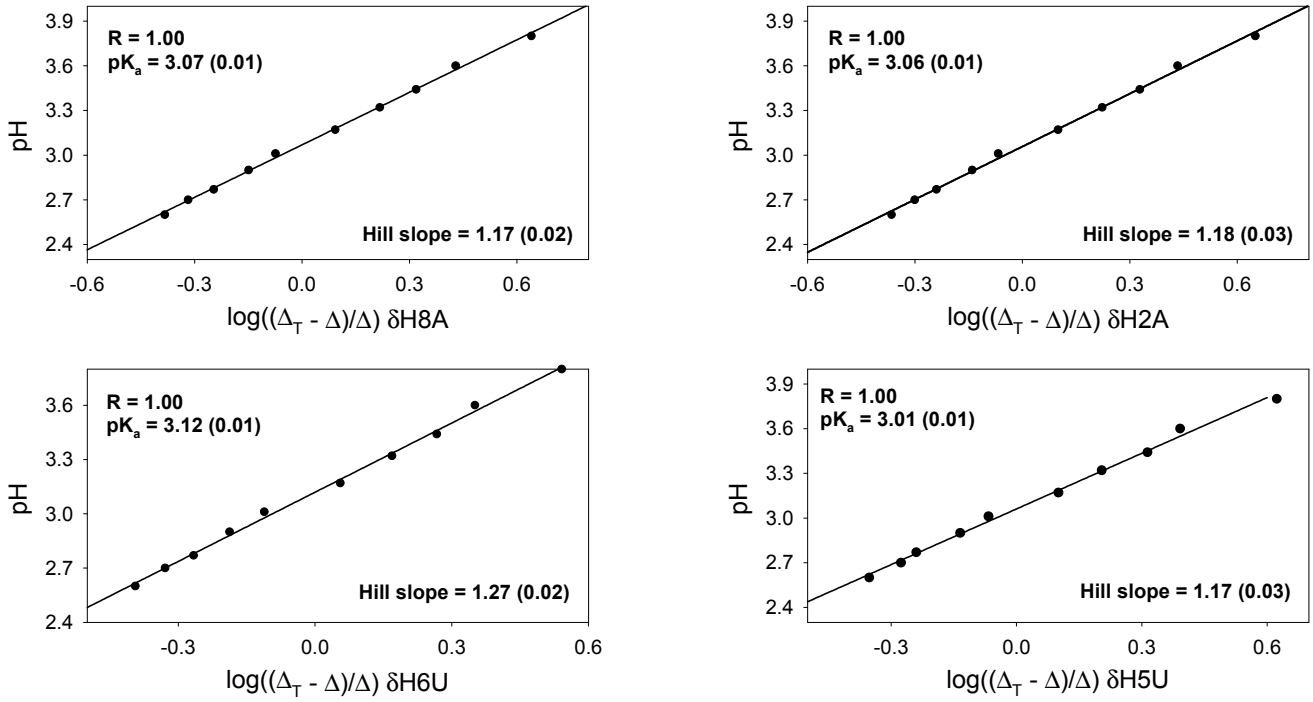
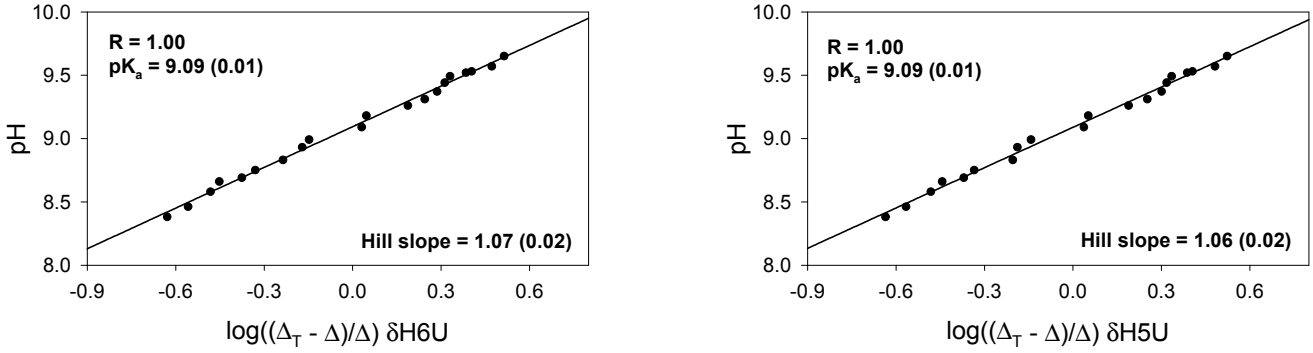


Figure S2j : UpA



Figures S2a - S2p

Figure S2k : ApU

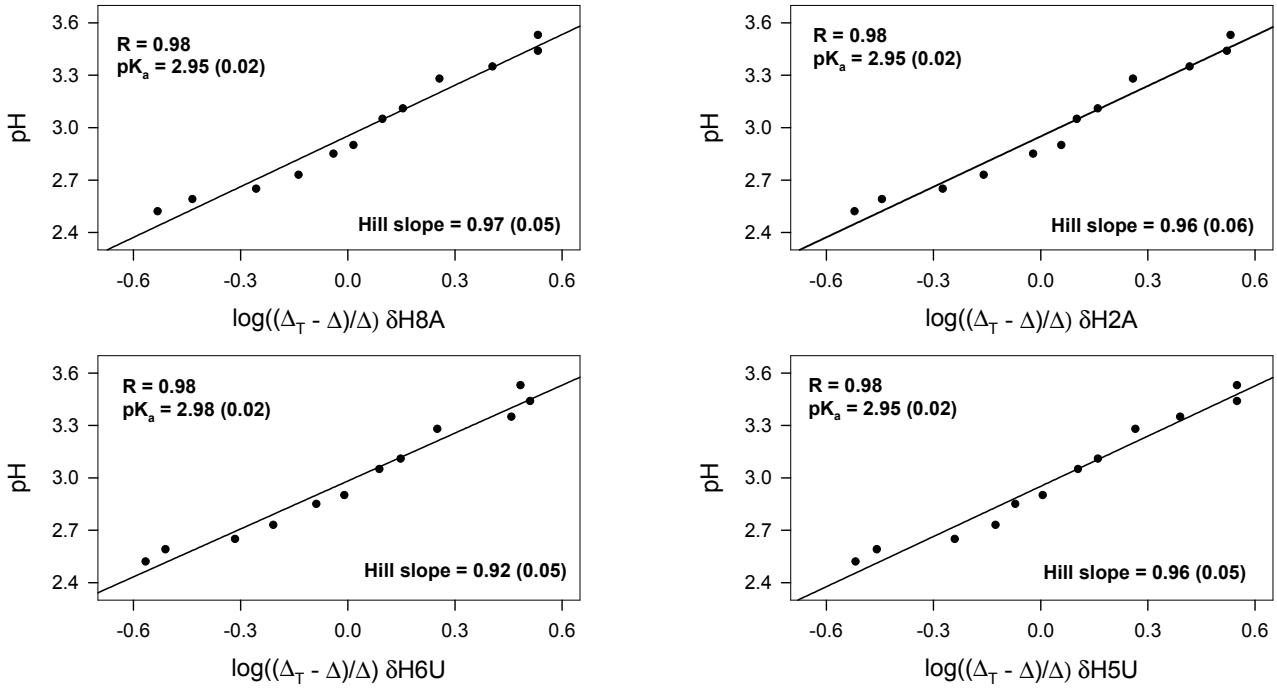
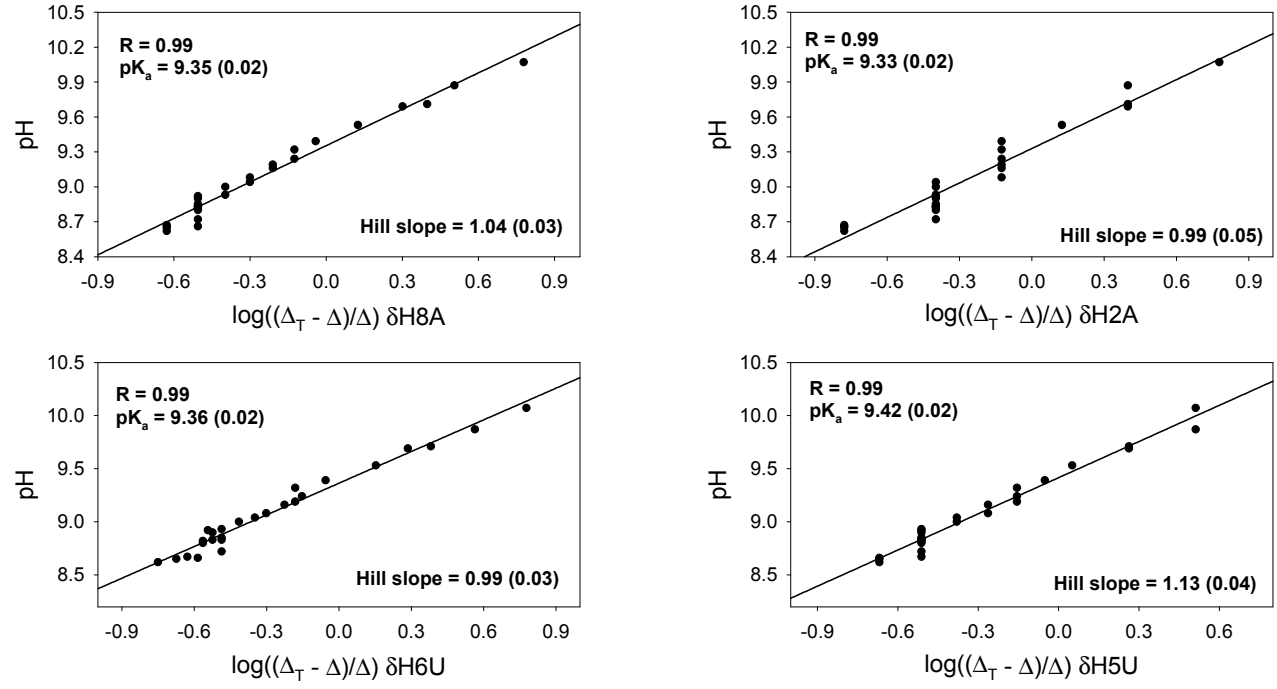
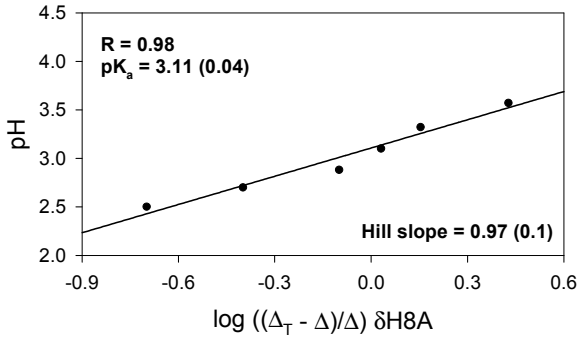


Figure S2l : ApU



Figures S2a - S2p

Figure S2m : ApEt



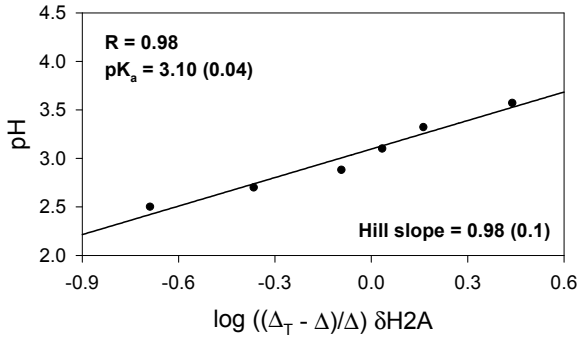


Figure S2n : GpEt

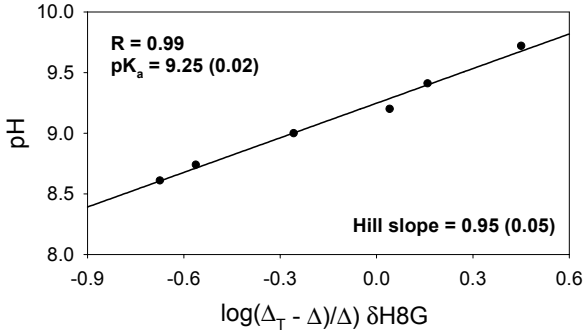
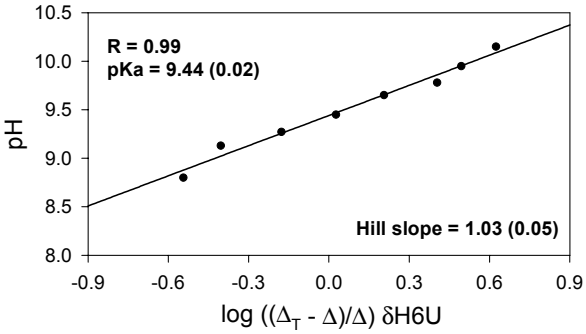


Figure S2o : UpEt



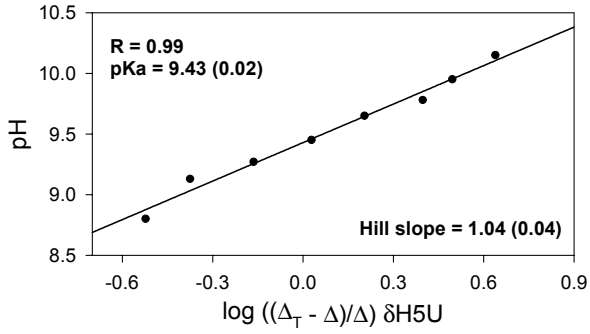
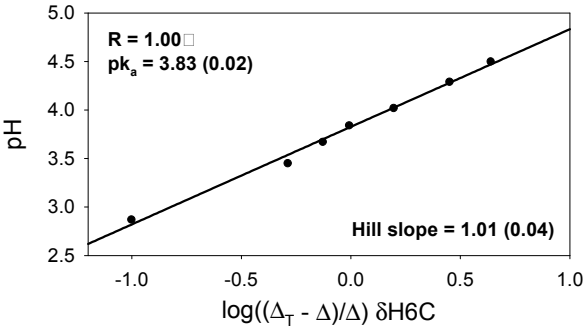
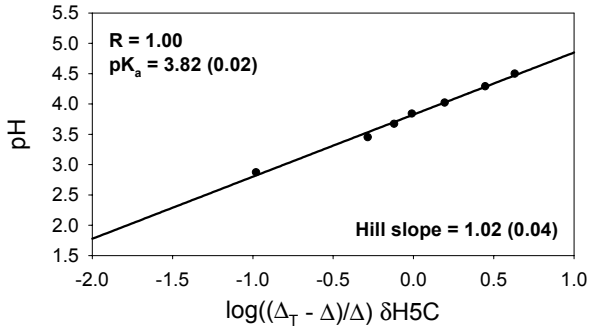


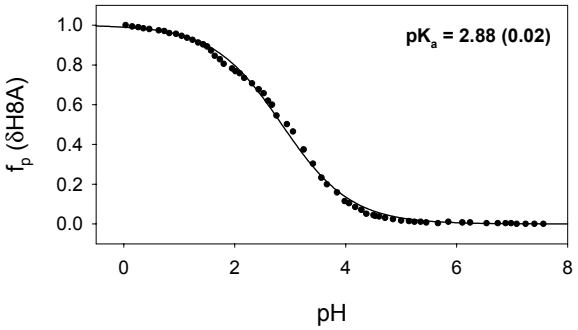
Figure S2p : CpEt

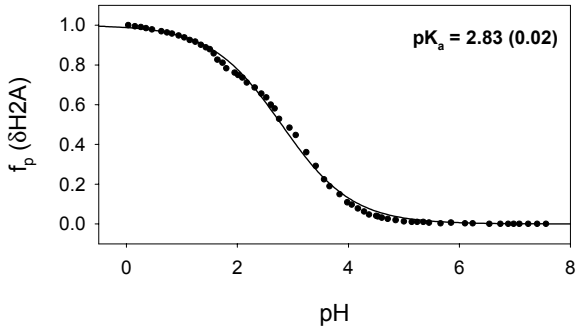


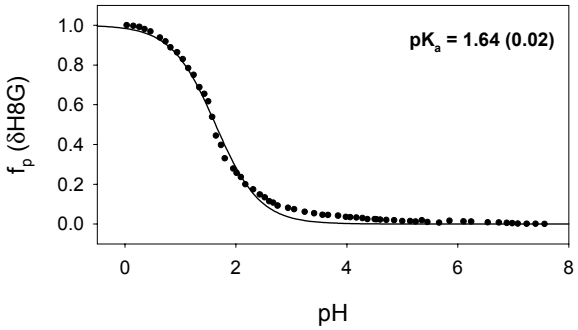


Figures S3a - S3p

(3a): ApG







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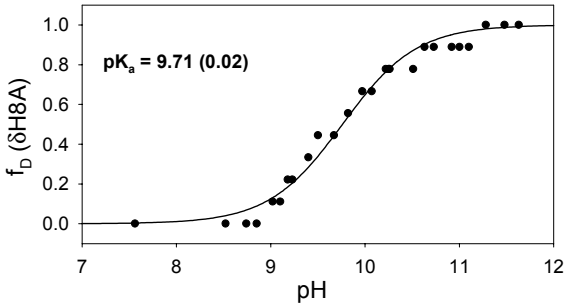

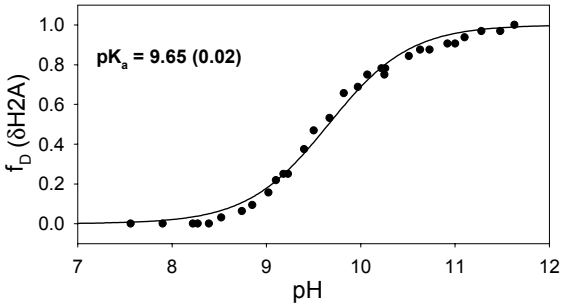

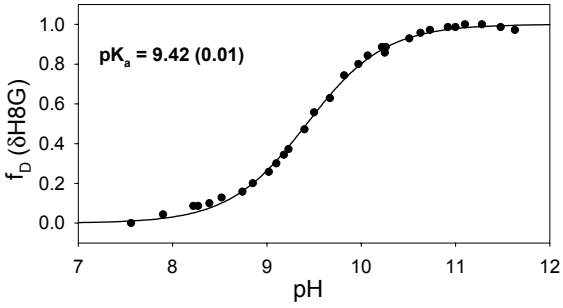

Figures S3a - S3p

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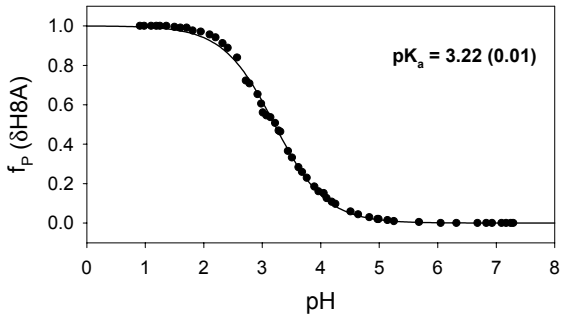

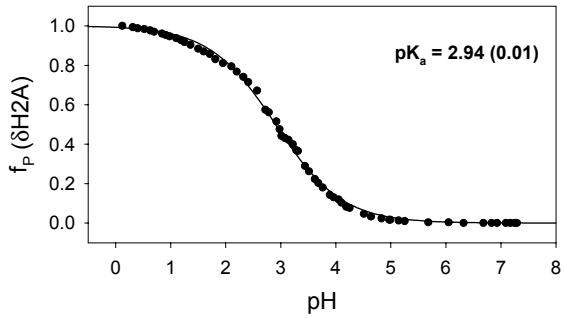

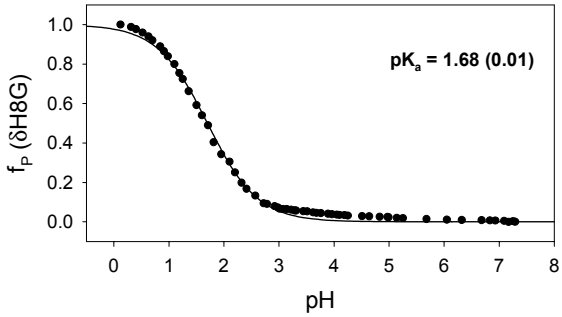

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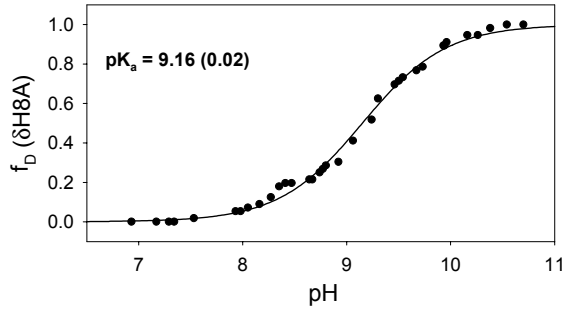

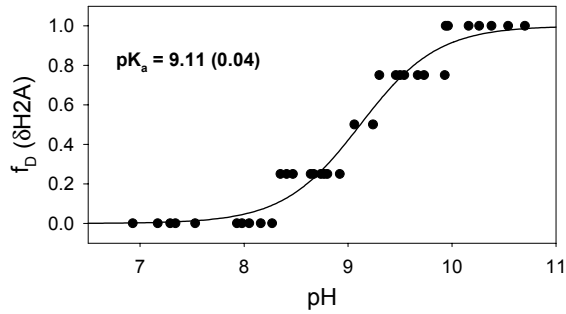

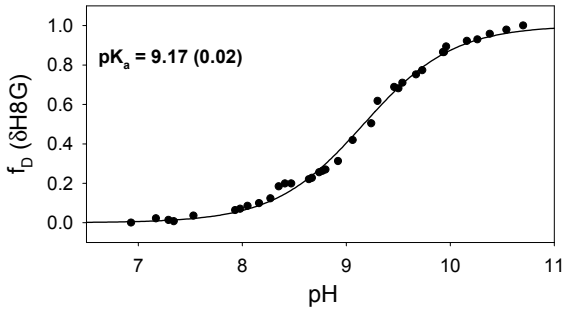

Figures S3a - S3p

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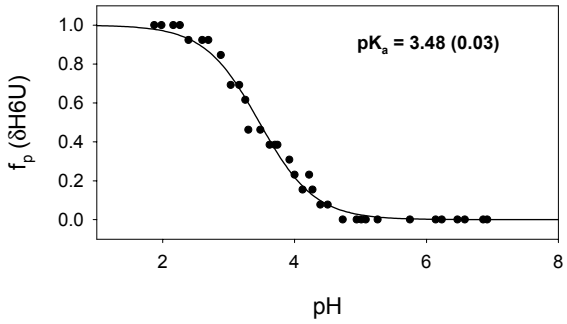

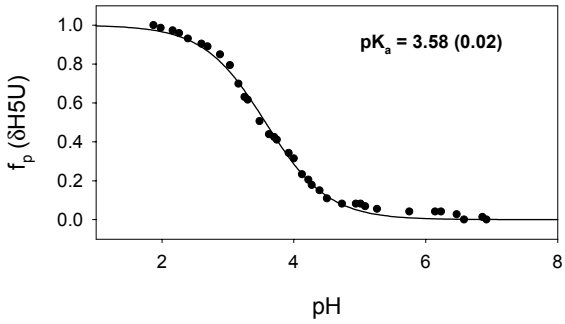

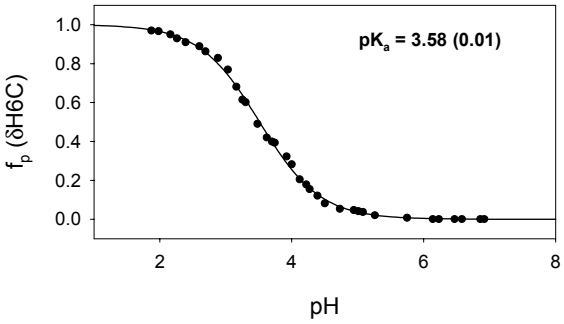

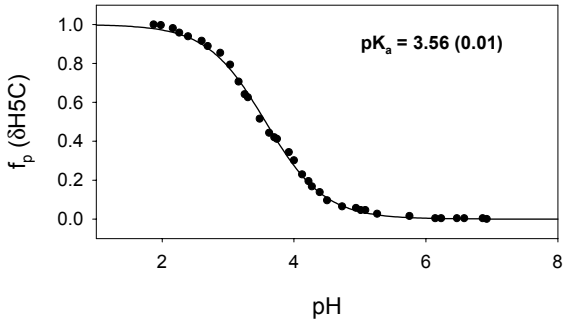

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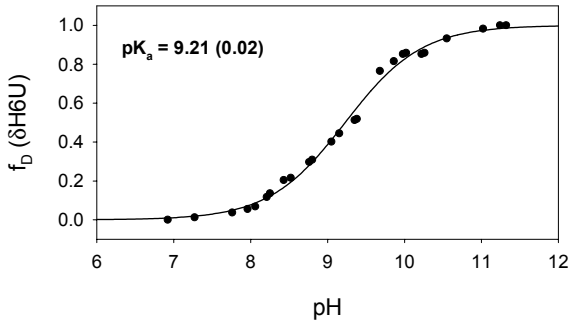

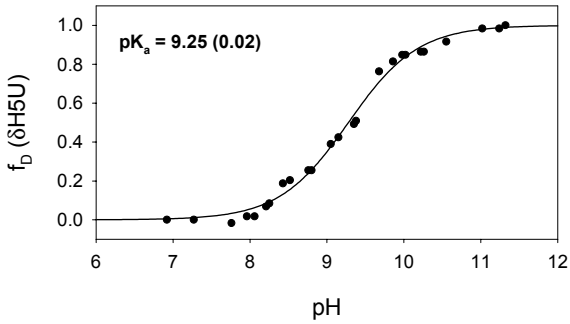

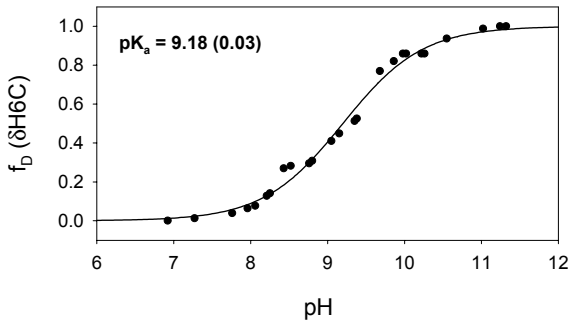

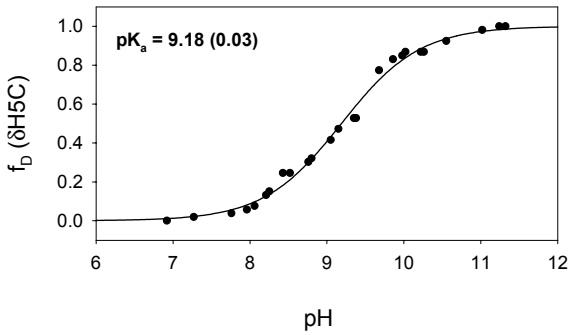

Figures S3a - S3p

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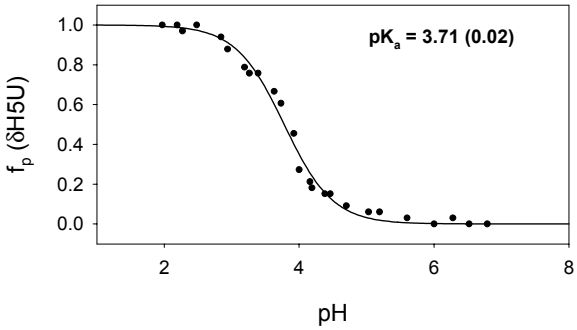

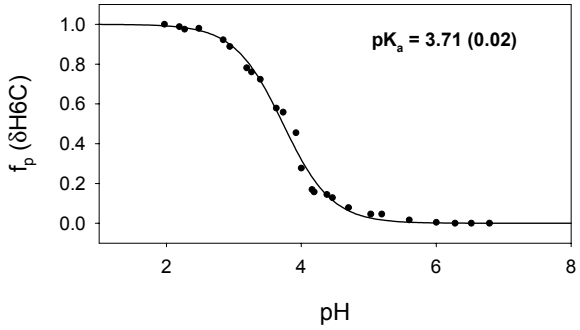

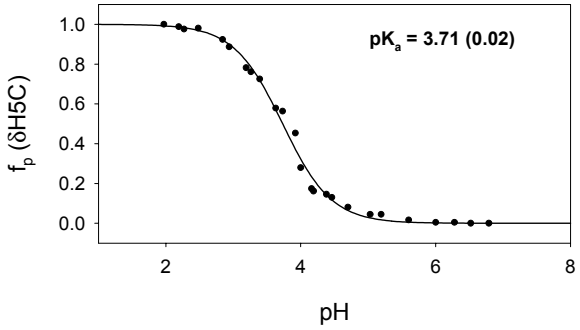

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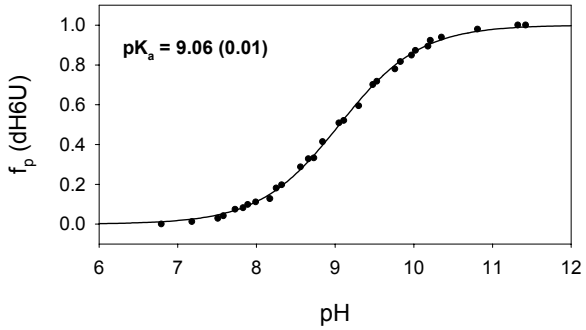

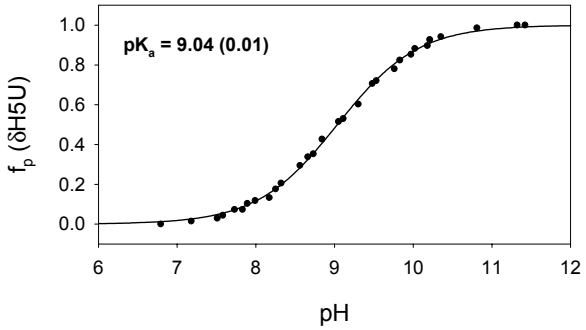

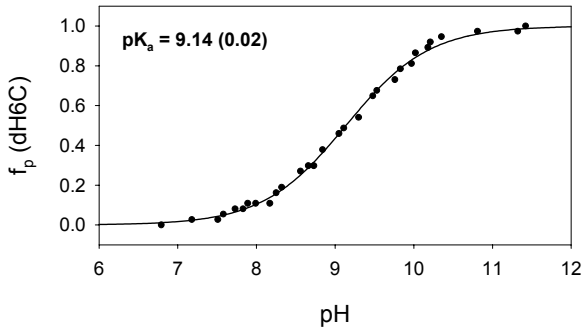

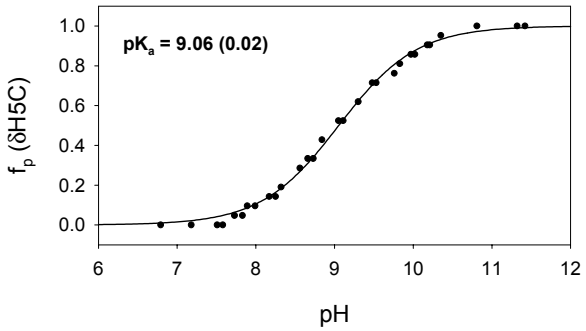

Figures S3a - S3p

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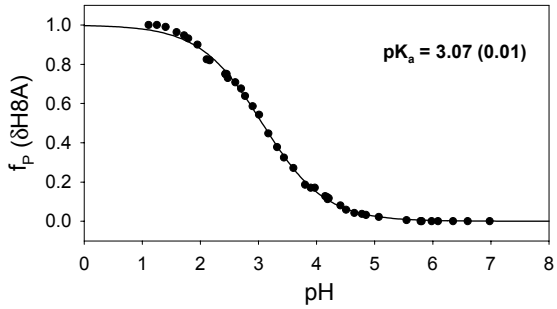

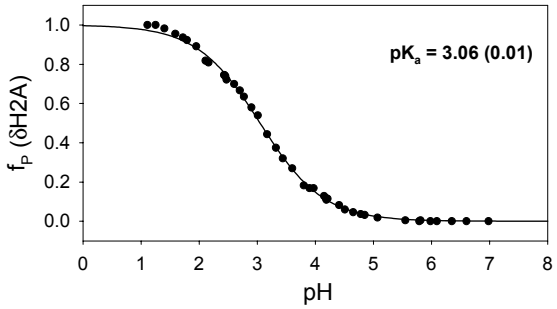

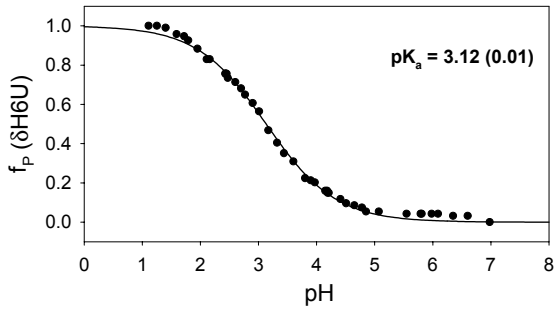

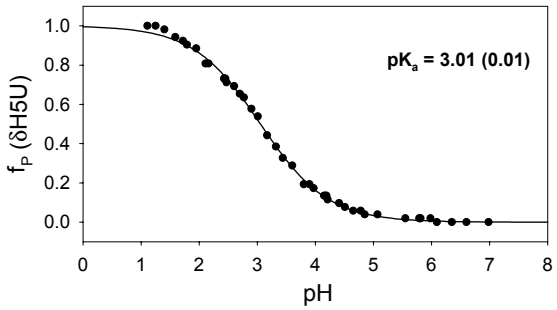

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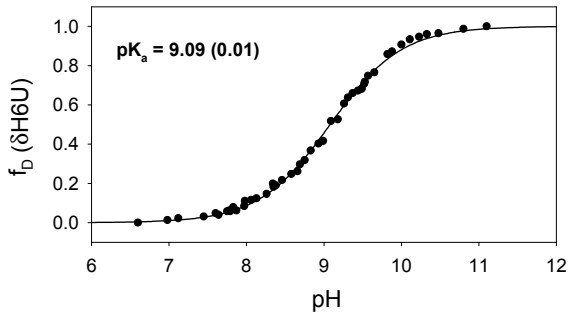

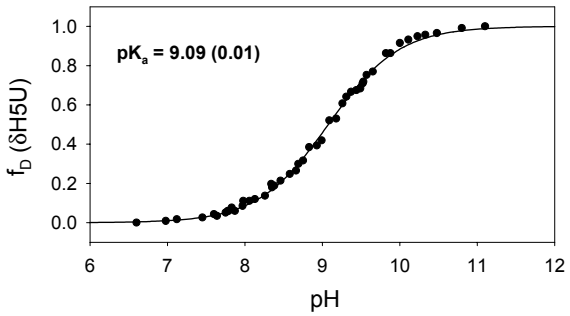

Figures S3a - S3p

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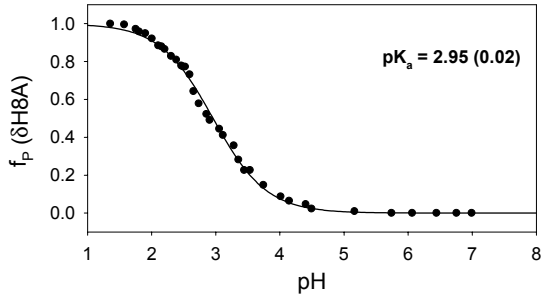

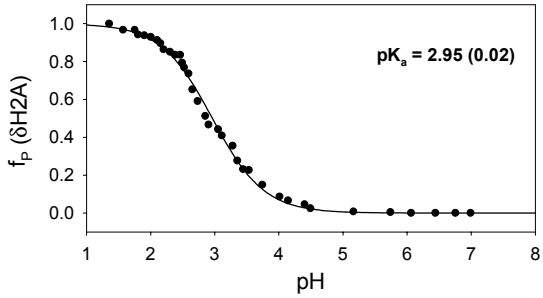

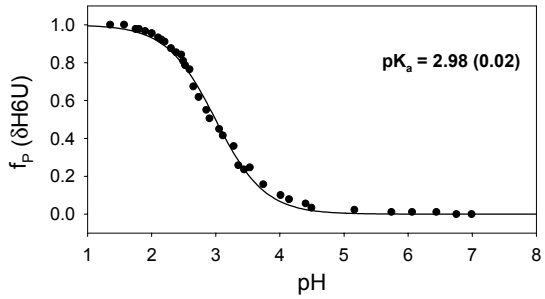

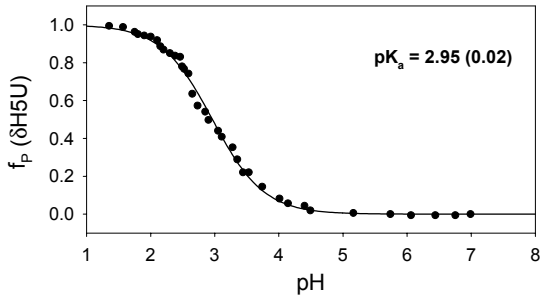

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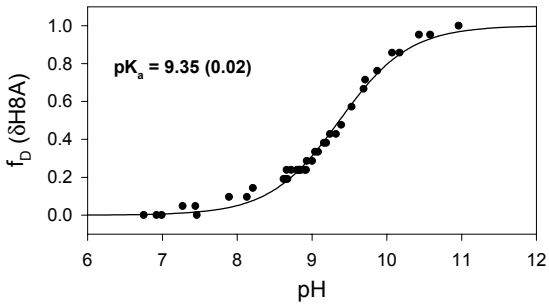

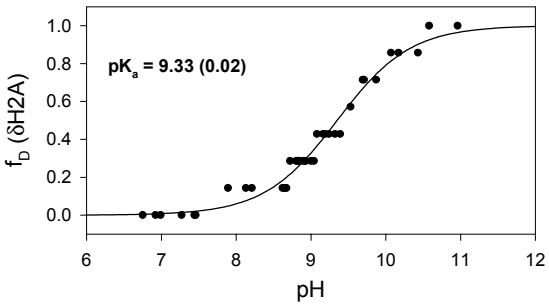

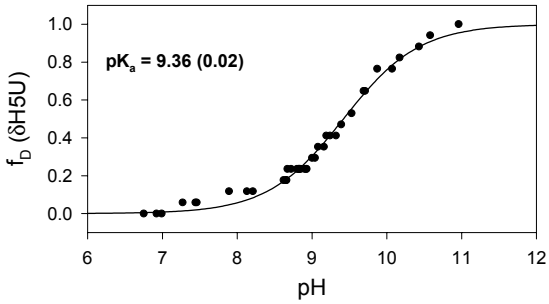

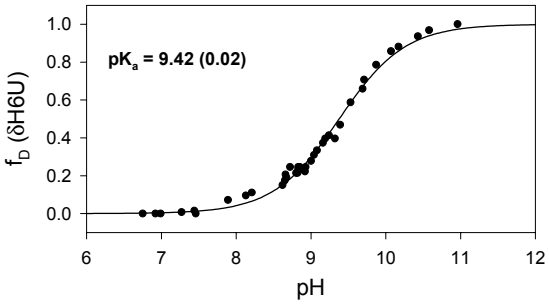

Figures S3a - S3p

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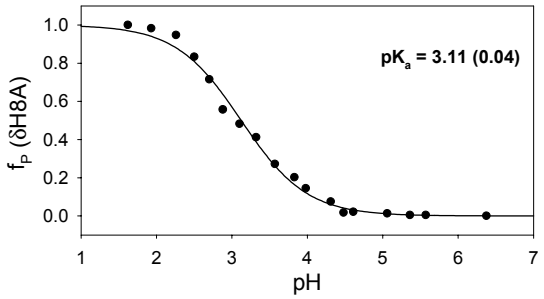
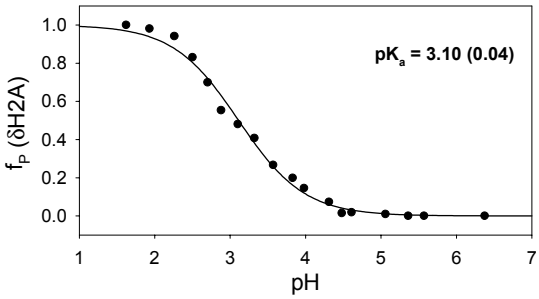
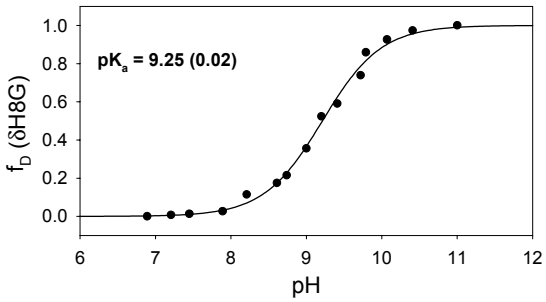
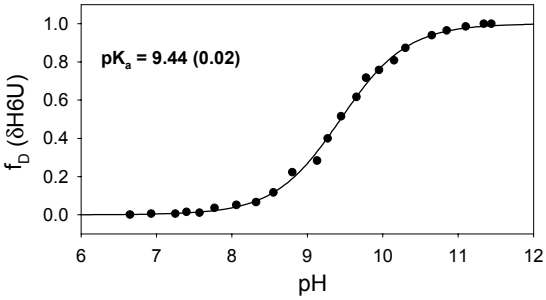


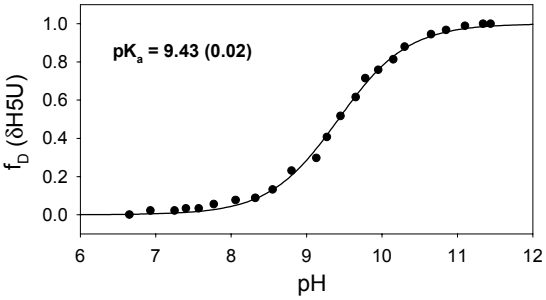


(3n): GpEt

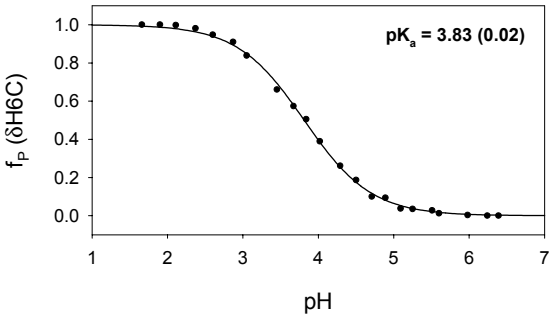


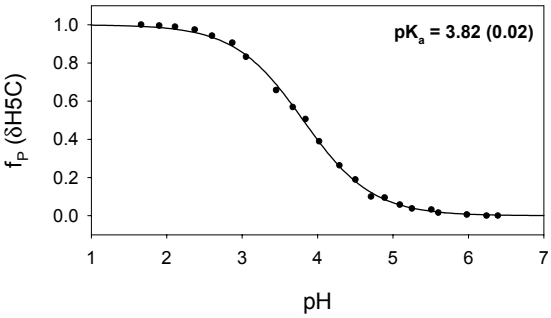
(3o): UpEt





(3p): CpEt





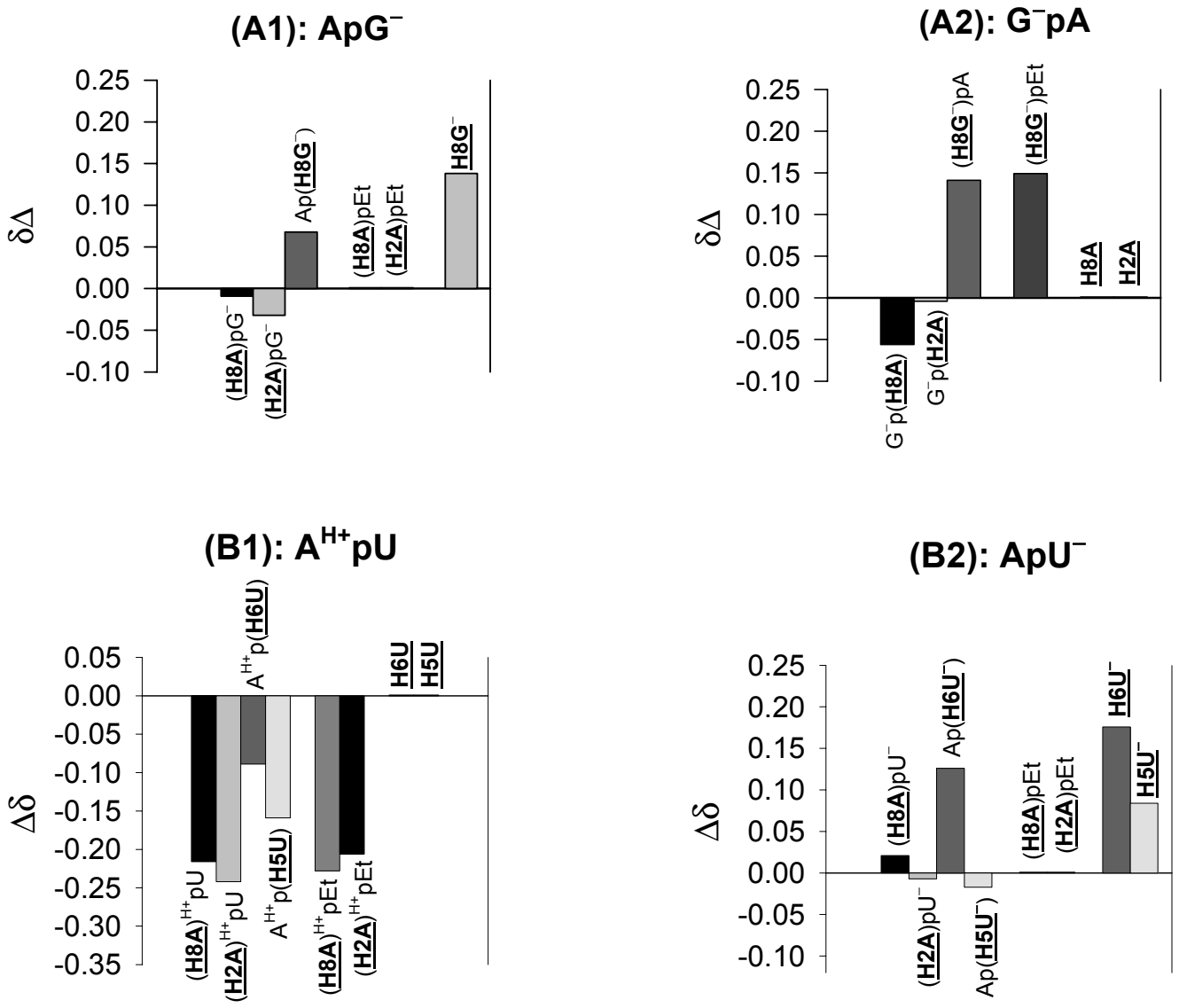

(A1): ApG⁻
δΔ
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
(H8A)pG⁻
(H2A)pG⁻
Ap(H8G⁻)
(H8A)pEt
(H2A)pEt
H8G⁻
(A2): G⁻pA
δΔ
G⁻p(H8A)
G⁻p(H2A)
(H8G⁻)pA
(H8G⁻)pEt
H8A
H2A
(B1): A^H+pU
ΔΔ
0.05
0.00
-0.05
-0.10
-0.15
-0.20
-0.25
-0.30
-0.35
(H8A)^H+pU
(H2A)^H+pU
A^H+p(H6U)
A^H+p(H5U)
(H8A)^H+pEt
(H2A)^H+pEt
H6U
H5U
(B2): ApU⁻
Δδ
0.25
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
(H8A)pU⁻
(H2A)pU⁻
Ap(H6U⁻)
Ap(H5U⁻)
(H8A)pEt
(H2A)pEt
H6U⁻
H5U⁻

Figure S4

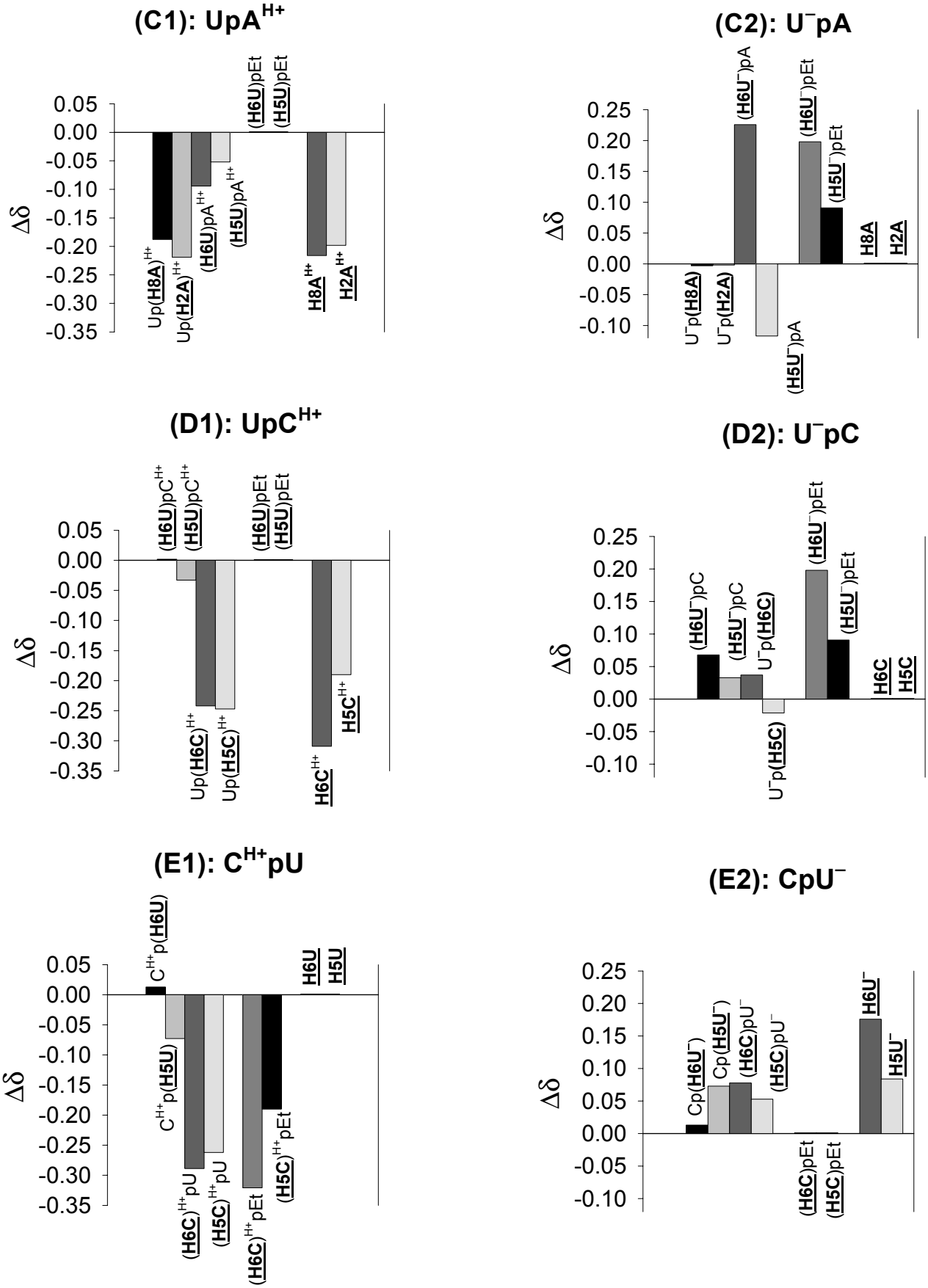


Figure S4

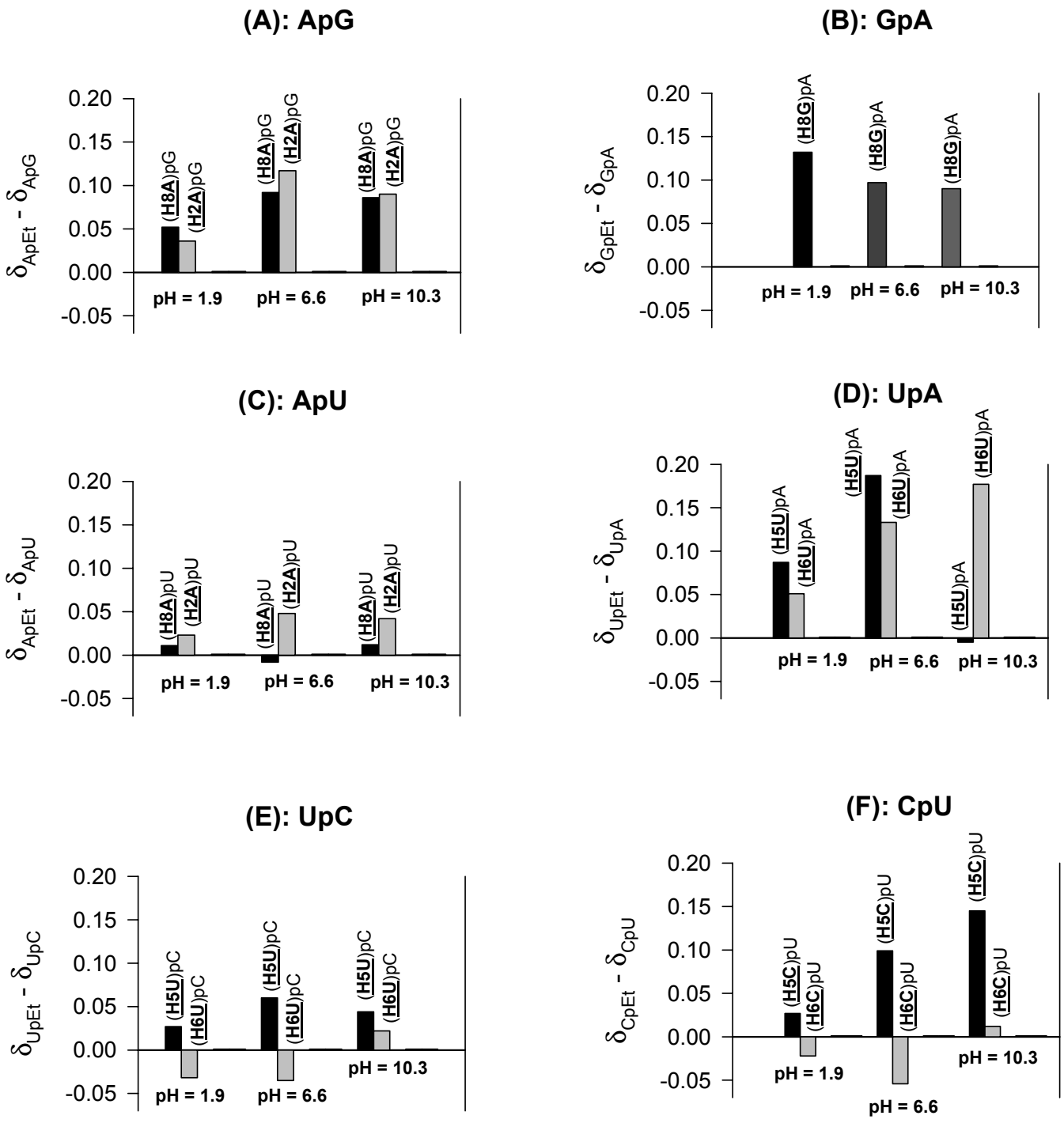


Figure S5

Table S1. pH-dependent $^3J_{HH}$ (± 0.1)[a], percentage population of N-type pseudorotamer[6] (% N) and corresponding free energy ($\Delta G^{o}_{N/S\,(298\,K)}$)[b] and Stacking free energy ($\Delta\Delta G°$)[c] from ^{1}H NMR at 298 K for **1** – **10** in D_2O.

Compd.		pH = 1.9 (± 0.1)						pH = 6.6 (± 0.1)						pH = 10.3 (± 0.1)					
		$^3J_{1'2'}$	$^3J_{2'3'}$	$^3J_{3'4'}$	% N	$\Delta G°$	$\Delta\Delta G°$	$^3J_{1'2'}$	$^3J_{2'3'}$	$^3J_{3'4'}$	% N	$\Delta G°$	$\Delta\Delta G°$	$^3J_{1'2'}$	$^3J_{2'3'}$	$^3J_{3'4'}$	% N	$\Delta G°$	$\Delta\Delta G°$
ApG (**1**)	**A**p	4.4	- [h]	- [h]	51[g]	-0.1	-1.4	4.6	4.6	4.7	54	-0.4	-3.6	5.2	5.0[d]	4.2	46	0.4	-2.8 [k]
	p**G**	4.8	5.1	5.1	49	0.1		4.5	5.1	5.3	53	-0.3		4.7	5.3	5.0	49	0.1	
GpA (**2**)	**G**p	4.0	5.0[d]	5.4	59	-0.9	-0.9 [k]	4.4	5.0	5.3	56	-0.6	-3.2	6.2	5.0[d]	2.6	25	2.7	-1.7
	p**A**	4.1	5.2	5.3	56	-0.6		4.5	5.0	5.5	53	-0.3		5.1	5.3	4.7	43	0.7	
ApU (**3**)	**A**p	4.8	5.0	4.7	46	0.4	-0.9	4.2	4.9	5.3	54	-0.4	-3.6	5.2	5.1	5.2	46	0.4	-2.8 [k]
	p**U**	3.7	- [h]	- [h]	61[g]	-1.1		3.5	- [h]	- [h]	64[g]	-1.4		3.9	- [h]	- [h]	58[g]	-0.7	
UpA (**4**)	**U**p	5.0	5.2	5.0	45	0.5	-0.3 [k]	4.6	5.3	5.4	50	0.0	-0.8	5.5	4.8	5.4	45	0.5	-0.7
	p**A**	4.6	5.0	5.1	53	-0.3		4.8	5.2	5.0	51	-0.1		5.2	4.8	4.9	47	0.3	
UpC (**5**)	**U**p	4.9	5.2	5.2	47	0.3	-0.5 [k]	3.9	5.3	5.7	57	-0.7	-1.5	4.8	5.3	5.5	49	0.1	-1.1
	p**C**	3.2	- [h]	- [h]	68[g]	-1.8		3.4	5.3	- [h]	65[g]	-1.5		3.8	5.4	5.5	59	-0.9	
CpU (**6**)	**C**p	3.8	5.2	6.2	67	-1.7	-1.1	3.5	5.1	6.0	67	-1.7	-1.9	3.5	5.2	6.4	70	-2.1	-2.3 [k]
	p**U**	3.7	5.1	- [h]	61[g]	-1.1		2.6	5.0	- [h]	77[g]	-3.0		2.5	4.9	6.3	78	-3.1	
ApEt (**7**)		5.7	5.3	3.9	37	1.3	-	6.8	5.3	2.7	21	3.2	-	- [e]	- [e]	- [e]	- [e]	- [e]	-
GpEt (**8**)		- [e]	- [e]	- [e]	50[f]	0.0[f]	-	6.5	5.3	3.1	26	2.6	-	7.3	5.3	2.1	14	4.4	-
UpEt (**9**)		- [e]	- [e]	- [e]	- [e]	- [e]	-	5.3	5.3	4.8	42	0.8	-	5.6	5.4	4.6	38	1.2	-
CpEt (**10**)		4.1	5.2	5.7	56	-0.6	-	4.8	5.3	5.3	48	0.2	-	- [e]	- [e]	- [e]	- [e]	- [e]	-

[a] calculated using DAISY simulation program package (supplied by Bruker Spectrospin, Germany) of the experimental ^{1}H NMR spectra. [b] calculated using PSEUROT[4-6] (see the experimental section for details). The negative $\Delta G^{o}_{N/S\,(298\,K)}$ implies relatively more N-type conformational population, so more stabilization due to stacking. [c] The stacking free energy [$\Delta\Delta G° \cong \Delta G^{o}_{Stacking}$, in kJ mol^{-1}] has been calculated by [$\Delta G^{o}_{N/S\,(298\,K)}$]$_{dimer}$ - [$\Delta G^{o}_{N/S\,(298\,K)}$]$_{monomer}$ (see Experimental section for details). [d]Due to the spectral overlap with HOD signal at these pH, we have taken values by extrapolation from nearest available pH. [e] No NMR experiments have been performed as there is no pronation/deprotonation site at such pH range. [f] value for EtpGpEt (see ref. 5) has been used as 5'-ethylphosphate has very little conformational effect on sugar geometry[6], so can be ignored. [g] %N (± 3.0) has been calculated by %N = 100*(7.9 - $^3J_{1'2'}$)/6.9] due to unavailability of all $^3J_{HH}$ no PSEUROT could be performed. [h] No simulation of the spectra could be performed due to either spectral overlapping or overlap with HOD signal. [k] $\Delta\Delta G°$ has been calculated using [$\Delta G^{o}_{N/S\,(298\,K)}$]$_{monomer}$ at pH = 6.6.

Table S2. PSEUROT (v5.4) calculations[a] based on $^3J_{HH}$ at acidic (pH = 1.9), neutral (pH = 6.6) and alkaline (pH = 10.3) state for **1** – **10** in D_2O.

Compd.		pH = 1.9 (± 0.1)						pH = 6.6 (± 0.1)						pH = 10.3 (± 0.1)					
		P_N	$[\Psi_m]_N$	P_S	$[\Psi_m]_S$	%S	rms[d]	P_N	$[\Psi_m]_N$	P_S	$[\Psi_m]_S$	%S	rms[d]	P_N	$[\Psi_m]_N$	P_S	$[\Psi_m]_S$	%S	rms[d]
ApG (**1**)	**A**p	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-15	40	141	40	46	±0.1	-15	40	141	40	54	±0.1
	p**G**	-11	39	131	39	51	±0.1	-11	39	131	39	47	±0.1	-11	39	131	39	51	±0.1
GpA (**2**)	**G**p	34	36	175	36	41	±0.1	34	36	175	36	44	±0.1	34	36	175	36	75	±0.1
	p**A**	7	36	138	36	45	±0.1	7	36	138	36	47	±0.1	7	36	138	36	57	±0.1
ApU (**3**)	**A**p	5	37	139	37	54	±0.1	5	37	139	37	46	±0.1	5	37	139	37	54	±0.1
	p**U**	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]
UpA (**4**)	**U**p	15	37	135	37	55	±0.1	15	37	135	37	50	±0.1	15	37	135	37	55	±0.1
	p**A**	-16	41	131	41	47	±0.1	-16	41	131	41	49	±0.1	-16	41	131	41	53	±0.1
UpC (**5**)	**U**p	15	36	135	36	53	±0.1	15	36	135	36	43	±0.1	15	36	135	36	51	±0.1
	p**C**	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]
CpU (**6**)	**C**p	39	35	180	37	33	±0.1	39	35	180	37	33	±0.1	39	35	180	37	30	±0.1
	p**U**	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]	-[b]
ApEt (**7**)		23	35	152	35	63	±0.1	23	35	152	35	79	±0.1	-[c]	-[c]	-[c]	-[c]	-[c]	-[c]
GpEt (**8**)		-[c]	-[c]	-[c]	-[c]	-[c]	-[c]	23	35	154	35	74	±0.1	23	35	154	35	86	±0.1
UpEt (**9**)		-[c]	-[c]	-[c]	-[c]	-[c]	-[c]	10	37	135	37	58	±0.1	10	37	135	37	62	±0.1
CpEt (**10**)		13	36	134	36	44	±0.1	13	36	134	36	52	±0.1	-[c]	-[c]	-[c]	-[c]	-[c]	-[c]

[a] pH-dependent $^3J_{HH}$ at 298 K. See the experimental section for details of PSEUROT methodology. Geometries of the pentose moieties have been defined by puckering amplitudes and pseudorotational angle[6] for N-type (P_N and $[\Psi_m]_N$) and S-type conformer (P_S and $[\Psi_m]_S$). During several PSEUROT optimizations $[\Psi_m]_N$ and $[\Psi_m]_S$ were initially kept fixed to identical values in the range from 27° to 45° for **1** – **10** and surveyed the conformational hyperspace for N- and S-type pseudorotamers, in 1° steps. For **7** – **9** at neutral and alkaline pH, P_N and $[\Psi_m]_N$ (minor conformers, mole fraction ≤ 70%) were kept fixed. [b] Due to the non-availability of endocyclic $^3J_{HH}$, PSEUROT could not be performed. [c] No NMR experiments have been performed (See Table S1). [d] The overall rms of the PSEUROT calculations. The error estimates have been assessed in terms of ΔJ_{max} and r.m.s. (see experimental section for details) having ΔJ_{max} and r.m.s. values ≤ 0.4 and ≤ 0.3 Hz respectively.

Table S3. ^{1}H chemical shifts[a] as well as the dimerisation shifts[b] (shown in parenthesis) for aromatic protons of compounds **1** – **10** at three different pHs as specified below.

Compd.		pH = 1.9 (± 0.1)				pH = 6.6 (± 0.1)				pH = 10.3 (± 0.1)			
		δH8	δH2	δH5	δH6	δH8	δH2	δH5	δH6	δH8	δH2	δH5	δH6
ApG (**1**)	**A**p	8.526 (**0.052**)[b]	8.436 (**0.036**)[b]	-	-	8.262 (**0.092**)[b]	8.153 (**0.117**)[b]	-	-	8.268 (**0.086**)[b,c]	8.180 (**0.09**)[b,c]	-	-
	p**G**	8.626	-	-	-	7.942	-	-	-	7.868	-	-	-
GpA (**2**)	**G**p	8.382 (**0.132**)[b]	-	-	-	7.913 (**0.097**)[b]	-	-	-	7.775 (**0.09**)[b]	-	-	-
	p**A**	8.544	8.456	-	-	8.344	8.206	-	-	8.399	8.210	-	-
ApU (**3**)	**A**p	8.567 (**0.011**)[b]	8.449 (**0.023**)[b]	-	-	8.362 (**-0.008**)[b]	8.222 (**0.048**)[b]	-	-	8.342 (**0.012**)[b,c]	8.228 (**0.042**)[b,c]	-	-
	p**U**	-	-	5.789	7.853	-	-	5.638	7.767	-	-	5.653	7.649
UpA (**4**)	**U**p	-	-	5.831 (**0.087**)[b,c]	7.833 (**0.051**)[b,c]	-	-	5.731 (**0.187**)[b]	7.751 (**0.133**)[b]	-	-	5.843 (**-0.005**)[b]	7.534 (**0.177**)[b]
	p**A**	8.604	8.451	-	-	8.435	8.256	-	-	8.438	8.258	-	-
UpC (**5**)	**U**p	-	-	5.891 (**0.027**)[b,c]	7.916 (**-0.032**)[b,c]	-	-	5.858 (**0.06**)[b]	7.919 (**-0.035**)[b]	-	-	5.794 (**0.044**)[b]	7.689 (**0.022**)[b]
	p**C**	-	-	6.273	8.178	-	-	6.024	7.935	-	-	6.046	7.901
CpU (**6**)	**C**p	-	-	6.231 (**0.027**)[b]	8.191 (**-0.022**)[b]	-	-	5.970 (**0.099**)[b]	7.902 (**-0.054**)[b]	-	-	5.924 (**0.145**)[b,c]	7.836 (**0.012**)[b,c]
	p**U**	-	-	5.889	7.917	-	-	5.816	7.930	-	-	5.767	7.792
ApEt (**7**)		8.578	8.472	-	-	8.354	8.270	-	-	-	-	-	-
GpEt (**8**)		8.514	-	-	-	8.010	-	-	-	7.865	-	-	-
UpEt (**9**)		-	-	-	-	-	-	5.918	7.884	-	-	5.838	7.711
CpEt (**10**)		-	-	6.258	8.169	-	-	6.069	7.848	-	-	-	-

[a] In ppm. [b] The values in parenthesis with bold, indicate the dimerisation shifts (δ_{NpEt} - $\delta_{NpN'}$) of the corresponding protons (See Figure S5). [c] dimerisation shifts (δ_{NpEt} - $\delta_{NpN'}$) at this pH have been calculated using δ_{NpEt} of neutral pH assuming that there will be no change of chemical shift over the pH due to the absence of any protonation/deprotonation site at that particular pH range.