Hydrogen Bonds of RNA Are Stronger than Those of DNA, but NMR Monitors Only Presence of Methyl Substituent in Uracil/Thymine

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Supporting Information for

Hydrogen Bonds of RNA Are Stronger than Those of DNA, But NMR Monitors Only Presence of Methyl Substituent in Uracil/Thymine.

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Contents:

NMR shielding versus isotope effect

The experimental evidence consists of changes in deuterium isotope effects, which are defined as:

$$\Delta^{13}\mathrm{C2} = \delta^{13}\mathrm{C2}\left\{^{1}\mathrm{H3}\right\} - \delta^{13}\mathrm{C2}\left\{^{2}\mathrm{H3}\right\}$$

H/D isotope substitution affects only the average N–^{1,2}H distance which, in turn, influences the chemical shift linearly. We have tested this explicitly in a numerical experiment with an A:T (A:U) base pair designated "A:T H3 displaced" ("A:U H3 displaced"), in which we have placed the H3 atom of the pyrimidine base at a distance from N3 that it has in A:U (A:T). This simulates a change in average N3–H3 distance. Thus, we compute adenine C2 chemical shielding constants of 32.438 (A:T), 32.445 (A:T H3 displ.), 32.538 (A:U) and 32.531 ppm (A:U H3 displ.). The resulting *change* in chemical shift of adenine C2 appears to be proportional to the chemical shift: $\delta^{13}\mathrm{C2}\left\{^{AT\ H3\ displ}\mathrm{H3}\right\} / \delta^{13}\mathrm{C2}\left\{^{AT}\mathrm{H3}\right\}$ = 1.000216 and $\delta^{13}\mathrm{C2}\left\{^{AU}\mathrm{H3}\right\} / \delta^{13}\mathrm{C2}\left\{^{AU\ H3\ displ}\mathrm{H3}\right\}$ = 1.000215. Note that the change in N3–H3 distance we use in this simulation is not equal to the change in average N3–^{1,2}H3 distance due to the H/D isotope substitution but, within this regime of changes in (average) bond lengths, the linear behavior should not be influenced by the actual step size. Thus, we find the *change* in chemical shift due to the H/D isotope effect to be proportional to the chemical shift itself: $\delta^{13}\mathrm{C2}\left\{^{1}\mathrm{H3}\right\} - \delta^{13}\mathrm{C2}\left\{^{2}\mathrm{H3}\right\} = f \cdot \delta^{13}\mathrm{C2}\left\{^{1}\mathrm{H3}\right\}$. Therefore, the experimentally observed H/D isotope effect results from the larger chemical shift of adenine C2 in A:U vs. A:T: $\Delta^{13}\mathrm{C2}_{RNA} - \Delta^{13}\mathrm{C2}_{DNA} = f\left(\delta^{13}\mathrm{C2}_{RNA} - \delta^{13}\mathrm{C2}_{DNA}\right)$.

Atomic Cartesian coordinates (Å)

A:T

N	-2.804619	2.870483	0.000000
C	-1.500876	3.214866	0.000000
N	-0.436204	2.409711	0.000000
C	-0.804028	1.117367	0.000000
C	-2.109100	0.608355	0.000000
C	-3.155707	1.559337	0.000000
N	0.016004	0.006202	0.000000
C	-0.828525	-1.087949	0.000000
N	-2.108613	-0.774157	0.000000
N	-4.456964	1.227537	0.000000
H	-1.312320	4.289149	0.000000
C	1.471397	0.024194	0.000000
H	-0.434849	-2.099777	0.000000
H	-4.704639	0.247632	0.000000
H	-5.185612	1.959427	0.000000
N	-4.723472	4.924934	0.000000
C	-4.220413	6.210505	0.000000
N	-5.204958	7.213582	0.000000
C	-6.545550	6.899802	0.000000
C	-7.027132	5.629209	0.000000
C	-6.057292	4.540684	0.000000
O	-6.374784	3.337976	0.000000
O	-3.018553	6.460244	0.000000
C	-8.488872	5.291927	0.000000
H	-3.991273	4.149302	0.000000
C	-4.774321	8.612272	0.000000
H	-7.213616	7.761549	0.000000
H	-8.749389	4.687478	0.879911
H	-9.106892	6.198386	0.000000
H	-8.749389	4.687478	-0.879911
H	-5.143900	9.126706	0.896477
H	-3.681447	8.616543	0.000000
H	-5.143900	9.126706	-0.896477
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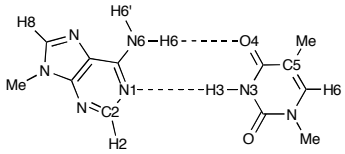

A:U

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C	4.356960	-6.040419	0.000000
C	3.560947	-4.871500	0.000000
N	6.283294	-7.121418	0.000000
C	5.206927	-7.988536	0.000000
N	4.035272	-7.384948	0.000000
N	2.218160	-4.890153	0.000000
H	5.990952	-2.647319	0.000000
C	7.702992	-7.442780	0.000000
H	5.353927	-9.064300	0.000000
H	1.747954	-5.784873	0.000000
H	1.680618	-4.008860	0.000000
N	2.830798	-1.232657	0.000000
C	3.623592	-0.103534	0.000000
N	2.908273	1.114507	0.000000
C	1.536644	1.129477	0.000000
C	0.783813	0.001582	0.000000
C	1.439433	-1.290395	0.000000
O	0.847443	-2.382075	0.000000
O	4.848979	-0.142812	0.000000
H	-0.300700	0.039112	0.000000
H	3.359756	-2.160814	0.000000
C	3.666046	2.367470	0.000000
H	1.088273	2.122365	0.000000
H	3.431973	2.955384	0.896752
H	4.727233	2.106351	0.000000
H	3.431973	2.955384	-0.896752
H	7.971531	-8.016593	-0.895645
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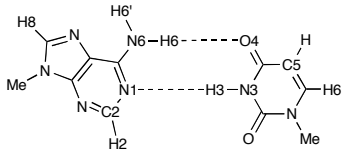
H	7.971531	-8.016593	0.895645



Atomic Cartesian coordinates (Å) ***continued***

A:T//A:U

N	-3.549974	-3.559427	0.000000
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N	-5.778735	-4.483422	0.000000
C	-5.160424	-5.676384	0.000000
C	-3.779970	-5.914810	0.000000
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N	-5.742538	-6.928541	0.000000
C	-4.696804	-7.832366	0.000000
N	-3.504975	-7.269660	0.000000
N	-1.602668	-4.839202	0.000000
H	-5.295636	-2.467229	0.000000
C	-7.172501	-7.200611	0.000000
H	-4.880921	-8.902403	0.000000
H	-1.163687	-5.749649	0.000000
H	-1.034969	-3.977027	0.000000
N	-2.088447	-1.162706	0.000000
C	-2.841716	-0.006840	0.000000
N	-2.084699	1.185733	0.000000
C	-0.713373	1.153257	0.000000
C	0.000000	0.000000	0.000000
C	-0.699911	-1.268530	0.000000
O	-0.146030	-2.380030	0.000000
O	-4.067728	-0.003715	0.000000
C	1.503511	-0.026989	0.000000
H	-2.649188	-2.072014	0.000000
C	-2.798686	2.464154	0.000000
H	-0.230932	2.130044	0.000000
H	-2.544420	3.043621	0.896752
H	-3.868268	2.239892	0.000000
H	-2.544420	3.043621	-0.896752
H	-7.460725	-7.764793	-0.895645
H	-7.689662	-6.235904	0.000000
H	-7.460725	-7.764793	0.895645
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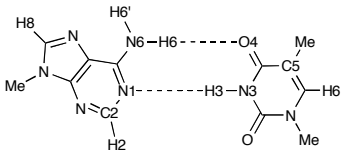
H	1.921663	0.987273	0.000000
H	1.884142	-0.564329	0.879742



A:U//A:T

N	4.244228	3.637454	0.000000
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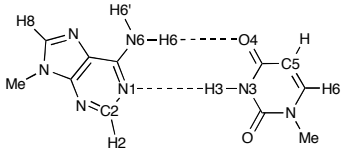
N	6.448409	4.618926	0.000000
C	5.799441	5.795483	0.000000
C	4.413340	5.998041	0.000000
C	3.607341	4.836095	0.000000
N	6.348652	7.062570	0.000000
C	5.279745	7.938830	0.000000
N	4.102981	7.345266	0.000000
N	2.264800	4.866835	0.000000
H	6.017283	2.590627	0.000000
C	7.770829	7.372258	0.000000
H	5.435850	9.013264	0.000000
H	1.803151	5.765967	0.000000
H	1.719360	3.989860	0.000000
N	2.836410	1.204181	0.000000
C	3.615628	0.064628	0.000000
N	2.881814	-1.134125	0.000000
C	1.504997	-1.129787	0.000000
C	0.750074	0.000000	0.000000
C	1.450348	1.278708	0.000000
O	0.870576	2.379241	0.000000
O	4.842867	0.091501	0.000000
H	-0.333865	-0.018084	0.000000
H	3.375476	2.124577	0.000000
C	3.615897	-2.400184	0.000000
H	1.047784	-2.119674	0.000000
H	3.371441	-2.984540	-0.896477
H	4.681751	-2.158632	0.000000
H	3.371441	-2.984540	0.896477
H	8.044020	7.943917	0.895642
H	8.313306	6.421560	0.000000
H	8.044020	7.943917	-0.895642



Atomic Cartesian coordinates (Å) ***continued***

A:T

N	2.75039	-2.32710	0.00000
C	3.37555	-3.52195	0.00000
N	4.68772	-3.76621	0.00000
C	5.39189	-2.62274	0.00000
C	4.88888	-1.31564	0.00000
C	3.48050	-1.18344	0.00000
N	6.76126	-2.46285	0.00000
C	7.00648	-1.10412	0.00000
N	5.90878	-0.37908	0.00000
N	2.85002	0.00142	0.00000
H	2.71044	-4.38645	0.00000
H	7.44291	-3.21216	0.00000
H	8.01709	-0.71046	0.00000
H	3.40748	0.84466	0.00000
H	1.81845	0.04774	0.00000
N	-0.05701	-2.28833	0.00000
C	-0.67704	-3.52147	0.00000
N	-2.07067	-3.43857	0.00000
C	-2.76521	-2.25240	0.00000
C	-2.13984	-1.04792	0.00000
C	-0.67692	-1.04295	0.00000
O	-0.00181	0.00013	0.00000
O	-0.08692	-4.59487	0.00000
C	-2.86066	0.26727	0.00000
H	1.01032	-2.30578	0.00000
H	-2.55357	-4.32998	0.00000
H	-3.85016	-2.34630	0.00000
H	-2.58306	0.86358	0.88018
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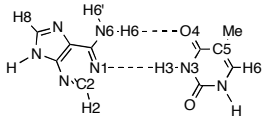
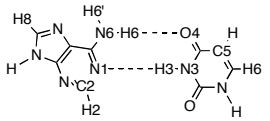
H	-2.58306	0.86358	-0.88018



A:U

N	2.74845	-2.32276	0.00000
C	3.37110	-3.51911	0.00000
N	4.68248	-3.76608	0.00000
C	5.38916	-2.62415	0.00000
C	4.88902	-1.31590	0.00000
C	3.48089	-1.18048	0.00000
N	6.75875	-2.46750	0.00000
C	7.00709	-1.10931	0.00000
N	5.91105	-0.38179	0.00000
N	2.85293	0.00571	0.00000
H	2.70422	-4.38223	0.00000
H	7.43861	-3.21848	0.00000
H	8.01864	-0.71801	0.00000
H	3.41190	0.84800	0.00000
H	1.82197	0.05488	0.00000
N	-0.05409	-2.28295	0.00000
C	-0.67240	-3.51596	0.00000
N	-2.07292	-3.44273	0.00000
C	-2.76908	-2.26297	0.00000
C	-2.13059	-1.06848	0.00000
C	-0.67730	-1.03457	0.00000
O	-0.00491	0.00785	0.00000
O	-0.08437	-4.58894	0.00000
H	-2.67145	-0.12782	0.00000
H	1.01509	-2.30035	0.00000
H	-2.54810	-4.33868	0.00000
H	-3.85332	-2.35428	0.00000



Atomic Cartesian coordinates (Å) *continued*

A:U^{Me6}

N	-2.801177	2.871617	0.000000
C	-1.497133	3.213587	0.000000
N	-0.433813	2.406737	0.000000
C	-0.804415	1.115131	0.000000
C	-2.110347	0.608180	0.000000
C	-3.155673	1.561105	0.000000
N	0.014089	0.002939	0.000000
C	-0.831932	-1.090058	0.000000
N	-2.111598	-0.774403	0.000000
N	-4.457599	1.233282	0.000000
H	-1.306610	4.287506	0.000000
C	1.469452	0.020063	0.000000
H	-0.439600	-2.102407	0.000000
H	-4.707929	0.253993	0.000000
H	-5.185269	1.967572	0.000000
N	-4.717825	4.923261	0.000000
C	-4.225799	6.207727	0.000000
N	-5.207845	7.228494	0.000000
C	-6.560655	6.933511	0.000000
C	-6.991343	5.639136	0.000000
C	-6.054343	4.541143	0.000000
O	-6.372305	3.338753	0.000000
O	-3.024562	6.459617	0.000000
C	-7.523643	8.091664	0.000000
H	-3.982596	4.150305	0.000000
C	-4.718593	8.609746	0.000000
H	-8.051503	5.404391	0.000000
H	-7.384024	8.728719	0.886434
H	-8.553589	7.717130	0.000000
H	-7.384024	8.728719	-0.886434
H	-5.058484	9.145499	0.895403
H	-3.627167	8.557542	0.000000
H	-5.058484	9.145499	-0.895403
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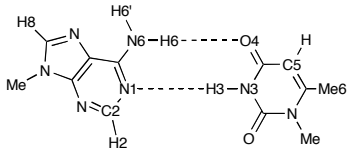

A:U^{Me6}//A:U

N	-5.481554	0.456349	0.000000
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C	-7.695247	-0.380488	0.000000
C	-6.302306	-0.624874	0.000000
N	-9.473258	0.930236	0.000000
C	-9.820539	-0.407618	0.000000
N	-8.788229	-1.227027	0.000000
N	-5.766663	-1.856341	0.000000
H	-5.275332	2.505179	0.000000
C	-10.350437	2.091861	0.000000
H	-10.861470	-0.716391	0.000000
H	-6.388574	-2.653112	0.000000
H	-4.742237	-1.983538	0.000000
N	-2.685431	0.207298	0.000000
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C	0.000000	0.000000	0.000000
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O	-2.522777	2.495171	0.000000
H	-0.237553	-2.123275	0.000000
H	-3.749035	0.307385	0.000000
C	0.251898	2.450210	0.000000
C	1.512848	-0.108636	0.000000
H	0.884048	2.478844	0.896752
H	-0.422827	3.309888	0.000000
H	0.884048	2.478844	-0.896752
H	-10.983921	2.100442	-0.895645
H	-9.714498	2.982757	0.000000
H	-10.983921	2.100442	0.895645
H	1.840430	-0.671984	-0.885168
H	2.035448	0.850364	0.000000
H	1.840430	-0.671984	0.885168

Atomic Cartesian coordinates (Å) *continued*

A^{Me8}:U

N	-4.407829	-0.405988	0.000000
C	-4.257671	0.933794	0.000000
N	-3.120725	1.633699	0.000000
C	-2.049610	0.823174	0.000000
C	-2.047459	-0.575389	0.000000
C	-3.310718	-1.206463	0.000000
N	-0.717140	1.185536	0.000000
C	0.011901	0.001170	0.000000
N	-0.758721	-1.073501	0.000000
N	-3.471118	-2.541180	0.000000
H	-5.190387	1.498821	0.000000
C	-0.220616	2.552281	0.000000
C	1.502089	-0.014517	0.000000
H	-2.646356	-3.125119	0.000000
H	-4.415087	-2.957018	0.000000
N	-7.011773	-1.441712	0.000000
C	-8.022606	-0.503072	0.000000
N	-9.327117	-1.045683	0.000000
C	-9.529097	-2.402353	0.000000
C	-8.514212	-3.301550	0.000000
C	-7.144677	-2.828015	0.000000
O	-6.144628	-3.564074	0.000000
O	-7.817709	0.705820	0.000000
H	-8.698813	-4.370940	0.000000
H	-6.018764	-1.043019	0.000000
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H	-11.079231	-0.275510	-0.897332
H	-10.060459	0.891511	0.000000
H	-11.079231	-0.275510	0.897332
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H	-1.091319	3.216095	0.000000
H	0.383852	2.750333	-0.894876
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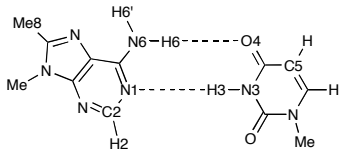

A^{Me8}:U//A:U

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N	-3.116975	1.634156	0.000000
C	-2.046139	0.822505	0.000000
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C	0.000000	0.000000	0.000000
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H	-4.420456	-2.955037	0.000000
N	-7.015376	-1.439580	0.000000
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C	-9.530974	-2.402011	0.000000
C	-8.515389	-3.300615	0.000000
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O	-7.821947	0.707572	0.000000
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C	-10.469271	-0.124605	0.000000
H	-10.575425	-2.711828	0.000000
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H	-10.066884	0.891458	0.000000
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H	0.402096	2.735350	0.895645
H	-1.065830	3.220233	0.000000
H	0.402096	2.735350	-0.895645
H	1.862953	-0.573021	-0.885605
H	1.935387	0.970299	0.000000
H	1.862953	-0.573021	0.885605

Atomic Cartesian coordinates (Å) ***continued***

Microsolvated A:T

N	-2.775960	2.894499	0.000000
C	-1.470004	3.223084	0.000000
N	-0.415681	2.403887	0.000000
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N	-4.458848	1.289868	0.000000
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H	1.785634	1.061663	0.000000
H	1.860630	-0.482858	0.895841
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H	-4.763242	0.311881	0.000000
H	-5.147892	2.053017	0.000000
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N	-4.968236	7.324622	0.000000
C	-6.323130	7.087145	0.000000
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C	-5.972297	4.710408	0.000000
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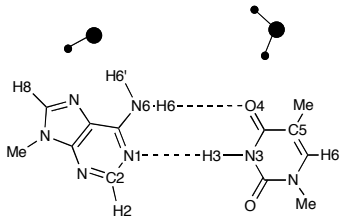
H	-4.362512	-1.730719	0.747496



Microsolvated A:U

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C	-0.833370	-1.087738	0.000000
N	-2.113444	-0.765249	0.000000
N	-4.460152	1.290714	0.000000
H	-1.266227	4.293684	0.000000
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H	1.859483	-0.483352	-0.895884
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H	1.859483	-0.483352	0.895884
H	-0.446871	-2.102082	0.000000
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H	-5.149697	2.053314	0.000000
N	-4.598622	5.024550	0.000000
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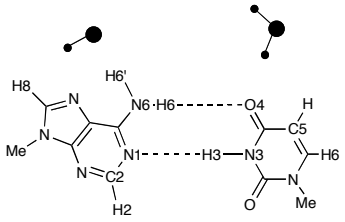

C	-6.837533	5.862323	0.000000
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H	-4.776452	9.250585	0.896745
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H	-8.146566	3.386804	0.000000
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O	-4.978440	-1.649363	0.000000
H	-4.358619	-1.732644	0.747410
H	-4.358619	-1.732644	-0.747410

Microsolvated A:U^{Me6}

N	-5.482770	0.551410	0.000000
C	-5.954756	1.812212	0.000000
N	-7.227814	2.214095	0.000000
C	-8.065172	1.164383	0.000000
C	-7.728874	-0.195729	0.000000
C	-6.342266	-0.503386	0.000000
N	-9.446895	1.200653	0.000000
C	-9.862982	-0.112065	0.000000
N	-8.870657	-0.982650	0.000000
N	-5.843695	-1.746148	0.000000
H	-5.187350	2.587322	0.000000
C	-10.261950	2.407362	0.000000
H	-10.893511	2.448711	-0.895900
H	-9.578410	3.262138	0.000000
H	-10.893511	2.448711	0.895900
H	-10.917411	-0.369795	0.000000
H	-6.474780	-2.552873	0.000000
H	-4.823320	-1.880132	0.000000
N	-2.696348	0.251020	0.000000
C	-1.978656	1.426645	0.000000
N	-0.573142	1.271628	0.000000
C	0.020149	0.020606	0.000000
C	-0.741755	-1.112350	0.000000
C	-2.177732	-1.030759	0.000000
O	-2.950732	-2.017024	0.000000
O	-2.516306	2.529814	0.000000
H	-0.282144	-2.097102	0.000000
H	-3.759074	0.361256	0.000000
C	0.223069	2.502370	0.000000
C	1.522241	-0.035590	0.000000
H	1.941674	0.463760	-0.886542
H	1.852824	-1.080206	0.000000
H	1.941674	0.463760	0.886542
H	0.854911	2.557783	0.895307
H	-0.482985	3.336085	0.000000
H	0.854911	2.557783	-0.895307
O	-1.382464	-4.330366	0.000000
H	-2.046503	-3.598588	0.000000
H	-1.906240	-5.145903	0.000000
O	-7.975118	-3.842696	0.000000
H	-8.392775	-3.376908	0.747233
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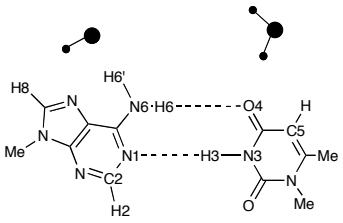


Table S1. NMR shielding constants, bond energy decomposition, and hydrogen bond lengths for the A:T, A:U, A:U//A:T,[a] A:T//A:U[b] and A:U^{Me6} base pairs (TZ2P basis)

	A:T	A:U	A:T//A:U	A:U//A:T	A:U^{Me6}
NMR shielding (SAOP; in ppm)					
N1-A	17.293	17.623	17.329	17.600	17.284
C2-A	32.438	32.538	32.454	32.526	32.499
H3-T/U	71.776	69.098	70.486	70.413	73.213
N3-T/U	-	-	-	-	-
Bond energy decomposition (BP86; in kcal/mol)[c]					
ΔE_{prep}	2.16	2.25	2.29	2.59	2.24
ΔE_{int}	-15.17	-15.44	-15.07	-15.54	-15.50
ΔE_{Pauli}	*38.49*	*38.55*	*38.60*	*38.45*	*39.09*
ΔV_{elstat}	*-31.82*	*-32.01*	*-31.79*	*-32.04*	*-32.36*
ΔE_{oi}	*-21.84*	*-21.98*	*-21.88*	*-21.95*	*-22.22*
ΔE_{σ}	*-20.20*	*-20.32*	*-20.24*	*-20.28*	*-20.54*
ΔE_{π}	*-1.64*	*-1.67*	*-1.64*	*-1.67*	*-1.68*
BSSE	0.67	0.68	0.69	0.68	0.71
ΔE_{total}	-12.33	-12.50	-12.10	-12.27	-12.55
Bond lengths (BP86; in Å)					
N6-O4	2.852	2.858	2.858	2.852	2.846
N1-N3	2.811	2.807	2.807	2.811	2.808
N3-H3	1.067	1.068	1.068	1.067	1.067

[a] A:U base pair at the A:T base pair geometry (see text). [b] A:T base pair at the A:U base pair geometry (see text). [c] $\Delta E_{total}=\Delta E_{prep} + \Delta E_{int}$ + BSSE. $\Delta E_{int}=\Delta E_{Pauli} + \Delta V_{elstat} + \Delta E_{oi}$; $\Delta E_{oi}=\Delta E_{\sigma} + \Delta E_{\pi}$.

Table S2. NMR shielding constants, bond energy decomposition, and hydrogen bond lengths for the A:T, A:U, A:U//A:T,[a] A:T//A:U[b] and A:U^{Me6} base pairs with scalar relativistic (ZORA)[c] effects taken into account (QZ4P basis)[d]

	A:T	A:U	A:T//A:U	A:U//A:T	A:U^{Me6}
NMR shielding (SAOP; in ppm)					
N1-A	9.447	9.779	9.489	9.766	9.441
C2-A	23.392	23.506	23.410	23.491	23.439
H3-T/U	63.286	61.004	61.987	62.391	65.242
N3-T/U	13.878	13.784	13.781	13.880	13.916
Bond energy decomposition (BP86; in kcal/mol)[e]					
ΔE_{prep}	2.18	2.38	2.30	2.69	2.25
ΔE_{int}	-15.25	-15.47	-15.15	-15.58	-15.67
ΔE_{Pauli}	*38.85*	*38.93*	*38.95*	*38.83*	*39.47*
ΔV_{elstat}	*-31.54*	*-31.73*	*-31.50*	*-31.77*	*-32.09*
ΔE_{oi}	*-22.56*	*-22.67*	*-22.60*	*-22.64*	*-23.05*
ΔE_{σ}	*-20.73*	*-20.81*	*-20.77*	*-20.78*	*-21.16*
ΔE_{π}	*-1.83*	*-1.86*	*-1.83*	*-1.86*	*-1.89*
BSSE	0.72	0.65	0.68	0.65	0.78
ΔE_{total}	-12.35	-12.44	-12.16	-12.24	-12.64

[a] A:U base pair at the A:T base pair geometry (see text). [b] A:T base pair at the A:U base pair geometry (see text). [c] Zeroth-order regular approximation, see Ref. 6. [d] BP86/TZ2P geometries. [e] $\Delta E_{total}=\Delta E_{prep} + \Delta E_{int}$ + BSSE. $\Delta E_{int}=\Delta E_{Pauli} + \Delta V_{elstat} + \Delta E_{oi}$; $\Delta E_{oi}=\Delta E_{\sigma} + \Delta E_{\pi}$.

Table S3. NMR shielding constants (ppm), bond energy decomposition (kcal/mol) and hydrogen bond lengths (Å) for the A:U^{Me6}, A:U^{Me6}//A:U, A^{Me8}:U, A^{Me8}:U//A:U, and H3 displaced A:T and A:U base pairs (TZ2P basis)

	A:U^{Me6}	A:U^{Me6}//A:U	A^{Me8}:U	A^{Me8}:U//A:U	A:T H3 displ.[a]	A:U H3 displ.[a]
NMR shielding (SAOP; in ppm)						
N1-A	17.284	17.180	17.289	16.978	17.358	17.558
C2-A	32.499	32.489	33.577	33.871	32.445	32.531
H3-T/U	73.213	72.891	68.802	68.989	71.591	69.284
N3-T/U	-	25.907	13.783	13.905	13.996	13.985
Bond energy decomposition (BP86; in kcal/mol)[b]						
ΔE_{prep}	2.24	5.18	2.34	3.43	2.23	2.18
ΔE_{int}	-15.50	-15.44	-15.49	-15.44	-15.24	-15.37
ΔE_{Pauli}	*39.09*	*38.71*	*38.96*	*38.68*	*38.59*	*38.45*
ΔV_{elstat}	*-32.36*	*-32.14*	*-32.20*	*-32.04*	*-31.88*	*-31.95*
ΔE_{oi}	*-22.22*	*-22.01*	*-22.25*	*-22.07*	*-21.95*	*-21.88*
ΔE_{σ}	*-20.54*	*-20.36*	*-20.58*	*-20.40*	*-20.30*	*-20.22*
ΔE_{π}	*-1.68*	*-1.65*	*-1.67*	*-1.66*	*-1.65*	*-1.66*
BSSE	0.71	0.69	0.69	0.70	0.67	0.68
ΔE_{total}	-12.55	-9.57	-12.46	-11.31	-12.33	-12.50
Bond lengths (BP86; in Å)						
N6-O4	2.846	2.858	2.863	2.858	2.852	2.858
N1-N3	2.808	2.807	2.802	2.807	2.811	2.807
N3-H3	1.067	1.068	1.070	1.068	1.068	1.067

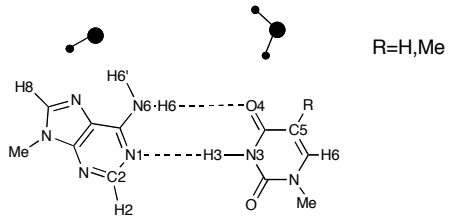
[a] A:T with r(N3-H3) adjusted to the value it has in A:U and vice versa [b] $\Delta E_{total}=\Delta E_{prep} + \Delta E_{int}$ + BSSE; $\Delta E_{int}=\Delta E_{Pauli} + \Delta V_{elstat} + \Delta E_{oi}$; $\Delta E_{oi}=\Delta E_{\sigma} + \Delta E_{\pi}$

Table S4. Computational results for the A:T, A:U, A:T//A:U, A:U//A:T, A:U^{Me6} base pairs, with two water molecules at the available major-groove positions, fully geometry-optimized (see illustration below, left), computed at SAOP/TZ2P, and without solvent (see illustration below, right) computed at the *ab initio* Hartree-Fock level with a mixed basis set[a,b]

	A:T	A:U	A:T//A:U	A:U//A:T	A: U^{Me6}
Microsolvated base pairs					
C2-A NMR shielding (in ppm)	31.579	31.735	31.618	31.706	31.695
HF/mixedbasis[b]					
C2-A NMR shielding (in ppm)	-21.271	-31.385	-21.116	-31.481	-18.606
ΔE_{total} (in kcal/mol)[c]	-7.44	-7.63	-7.04	-7.55	-7.58

[a] All calculations based on BP86/TZ2P geometries. [b] Hartree-Fock calculations carried out with NWChem 4.6, using 6-31G** on following atoms (N1(A), C2(A), H2(A), N6(A), H6(A), N3(T/U), H3(T/U), C4(T/U), O4(T/U), C5(T/U), H5/C(T/U)), 6-31G on others; limitation to 255 orbitals in NMR code. [c] $\Delta E_{total}=\Delta E_{prep} + \Delta E_{int}$ + BSSE.

solvents



model system used in HF calculations

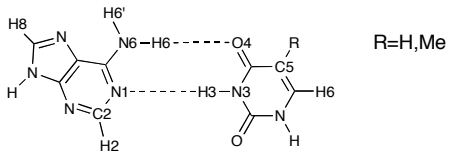
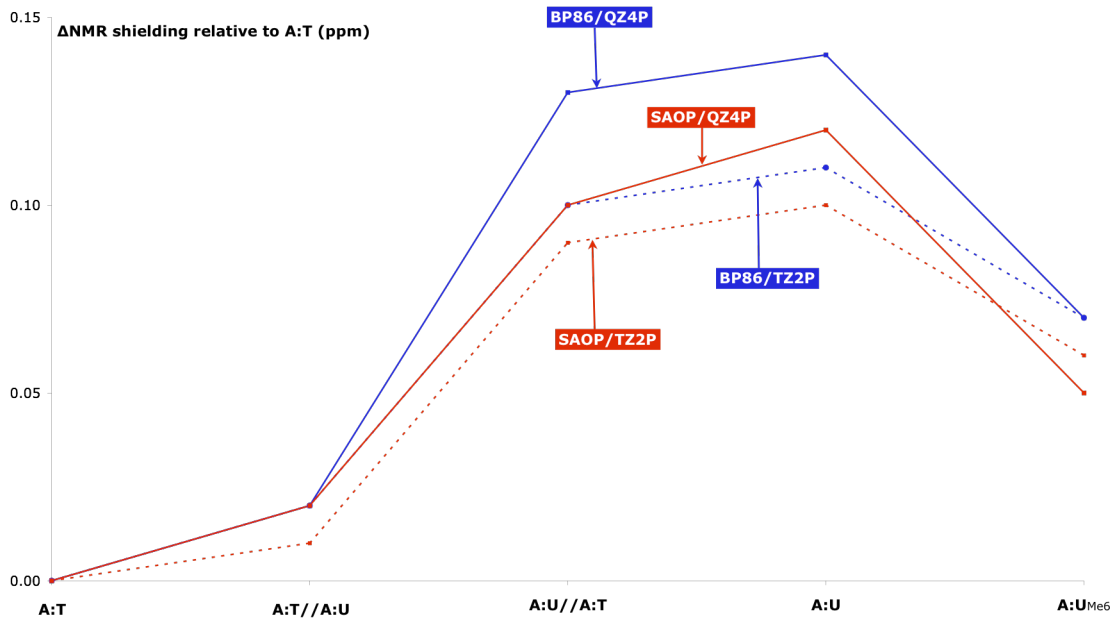


Figure S1. Influence of basis set size cq. DFT functional on C2-A NMR shielding



Definition of coordinate axes for variations of base pair geometry

Interaction energy and C2(A) NMR shielding constant as function of the base pair geometry parameters is plotted in Figures S2 through S5, using the following definition of the x- and y-axis:

- the x-axis goes through the adenine C6 and thymine/uracil C4 atoms
- the y-axis is perpendicular to the x-axis, exactly in the middle of these two atoms

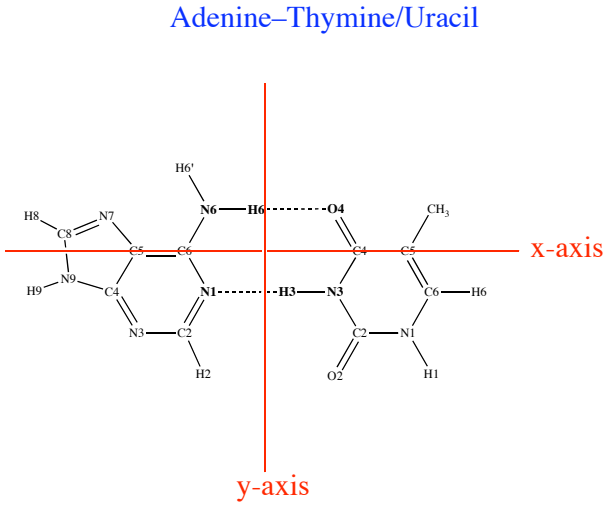
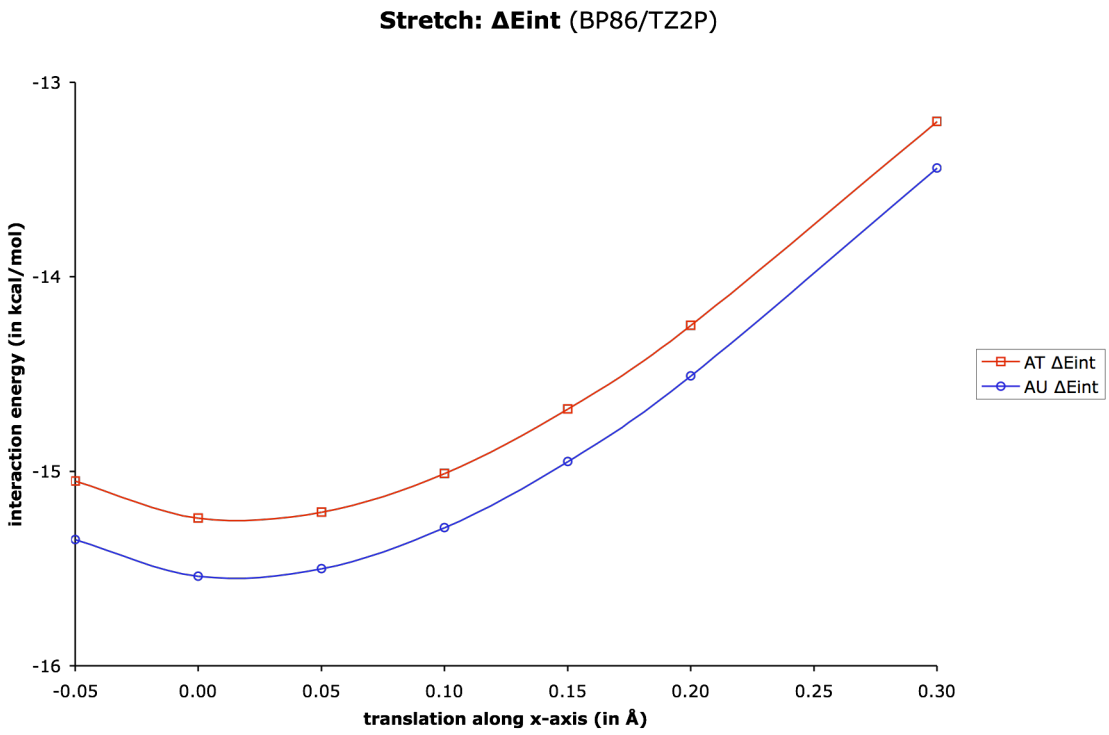


Figure S2. Variations of base pair geometry: **Stretch**



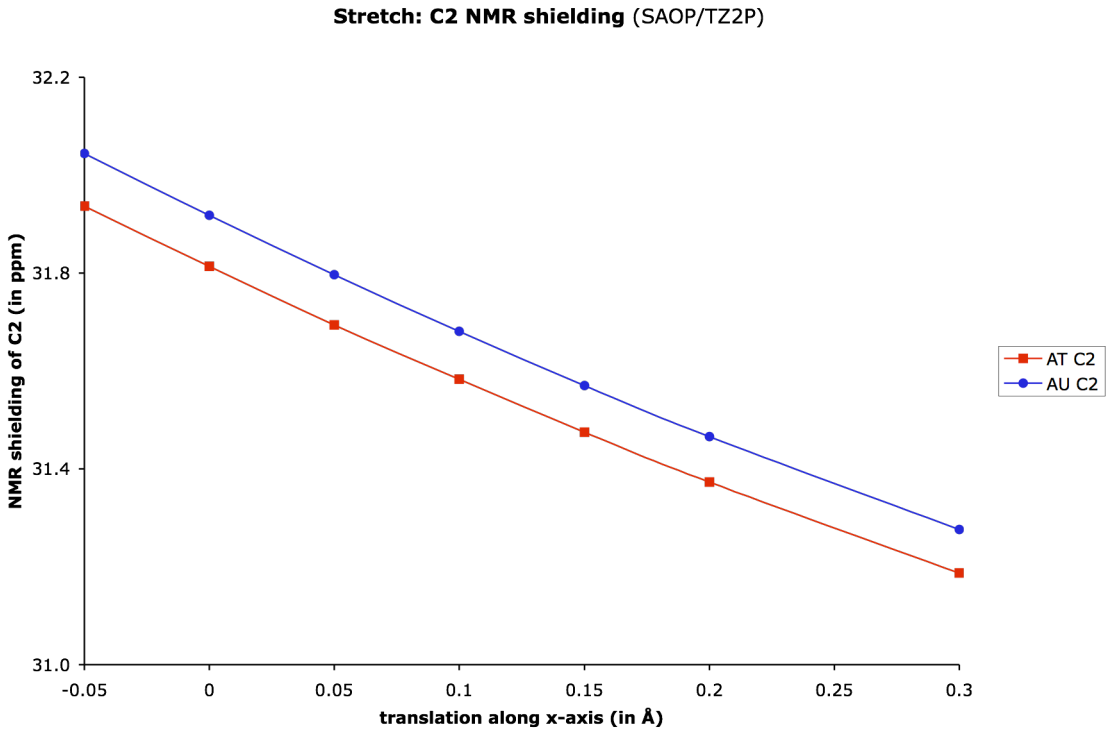
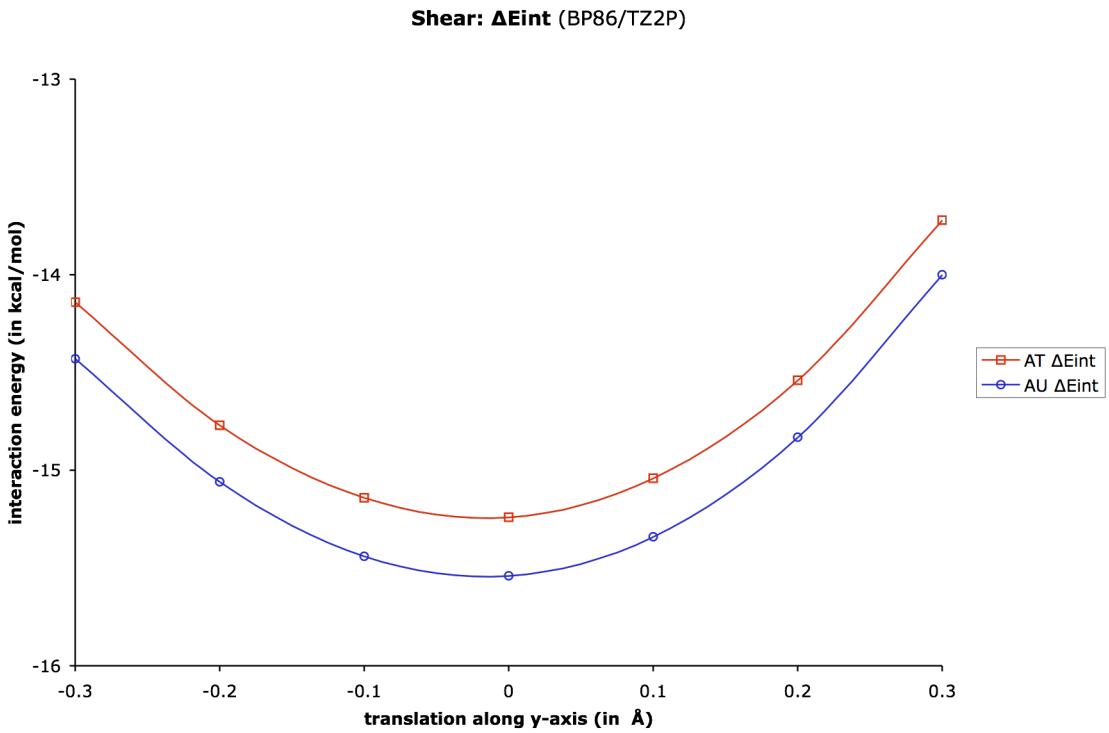


Figure S3. Variations of base pair geometry: **Shear**



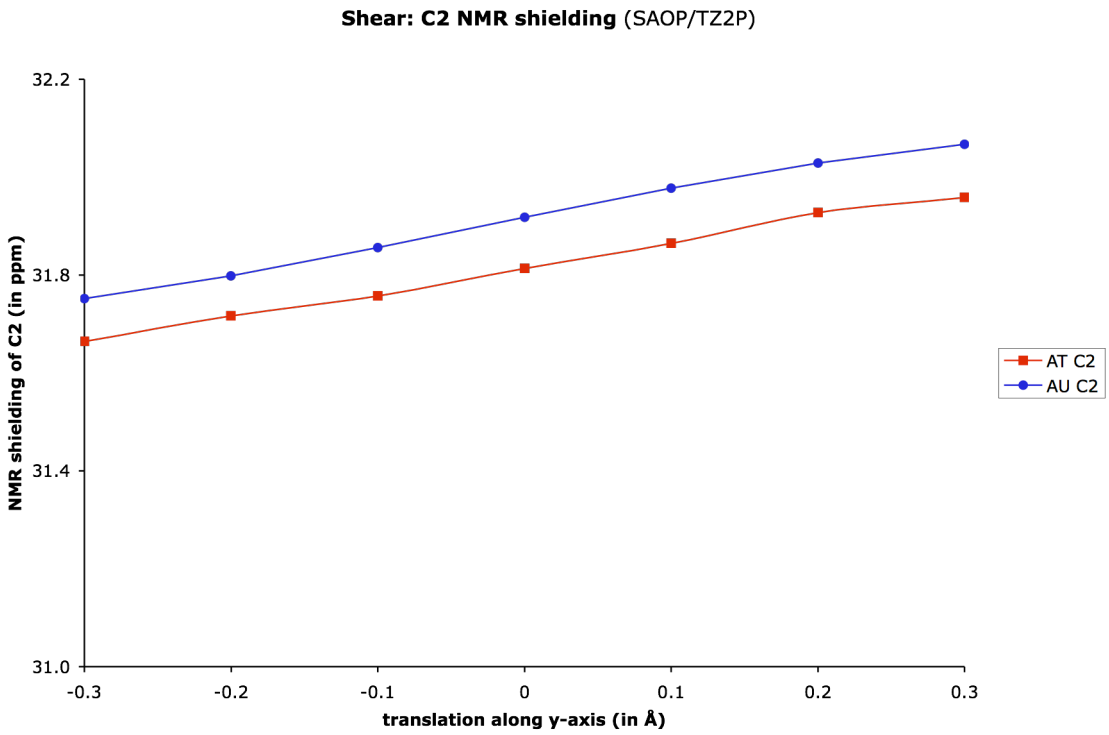


Figure S4. Variations of base pair geometry: **Propellor Twist**

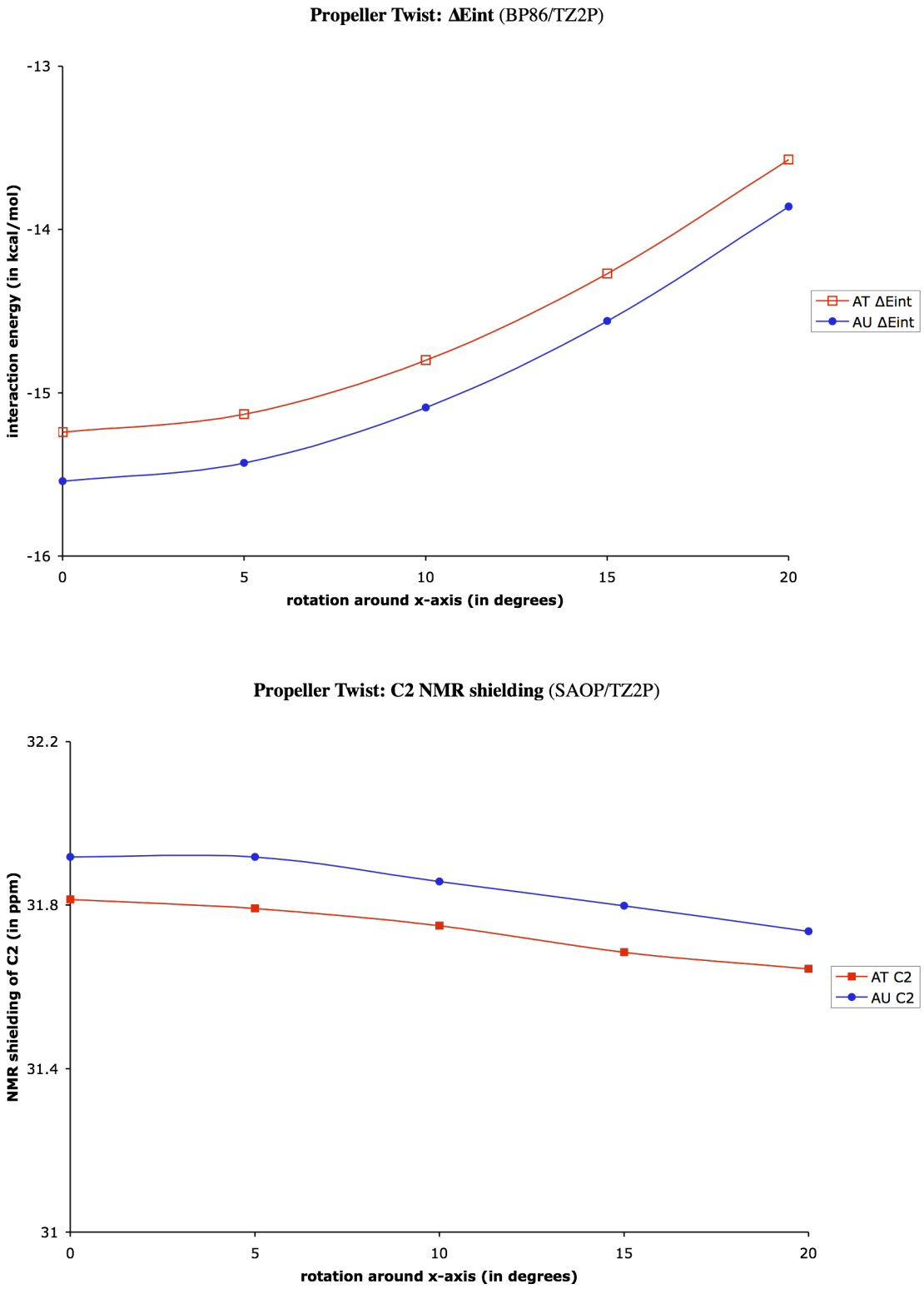


Figure S5. Variations of base pair geometry: **Buckle**