Supplementary material

Understanding the DNA binding of novel non–symmetrical guanidinium/2–aminoimidazolinium derivatives

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Circular Dichroism results for compounds 1, 2, 6 and 8

CD titrations were performed not only for all asymmetric derivatives by increasing the compound to DNA Bp/D ratio from 22.4 to 0.56. The maximum absorption occurred at around 280 nm for compounds **8** and **6**, and 260 nm for compounds **2** and **1**. Upon increasing addition of compounds **8**, **6**, **2** and **1** to DNA a growth in the bands at 280 nm and at 260 nm, respectively, is observed corresponding to λ_{max}. we have observed that, in the cases studied, the strength of binding to the AT oligonucleotide, as calculated in the thermal denaturation experiments with poly(dA•dT)$_2$,[14] is related to the amount of incremental growth in the induced CD signal and thus, compound **1** which is the one that most weakly binds to DNA according to the ΔT_m values, shows the smallest increment.

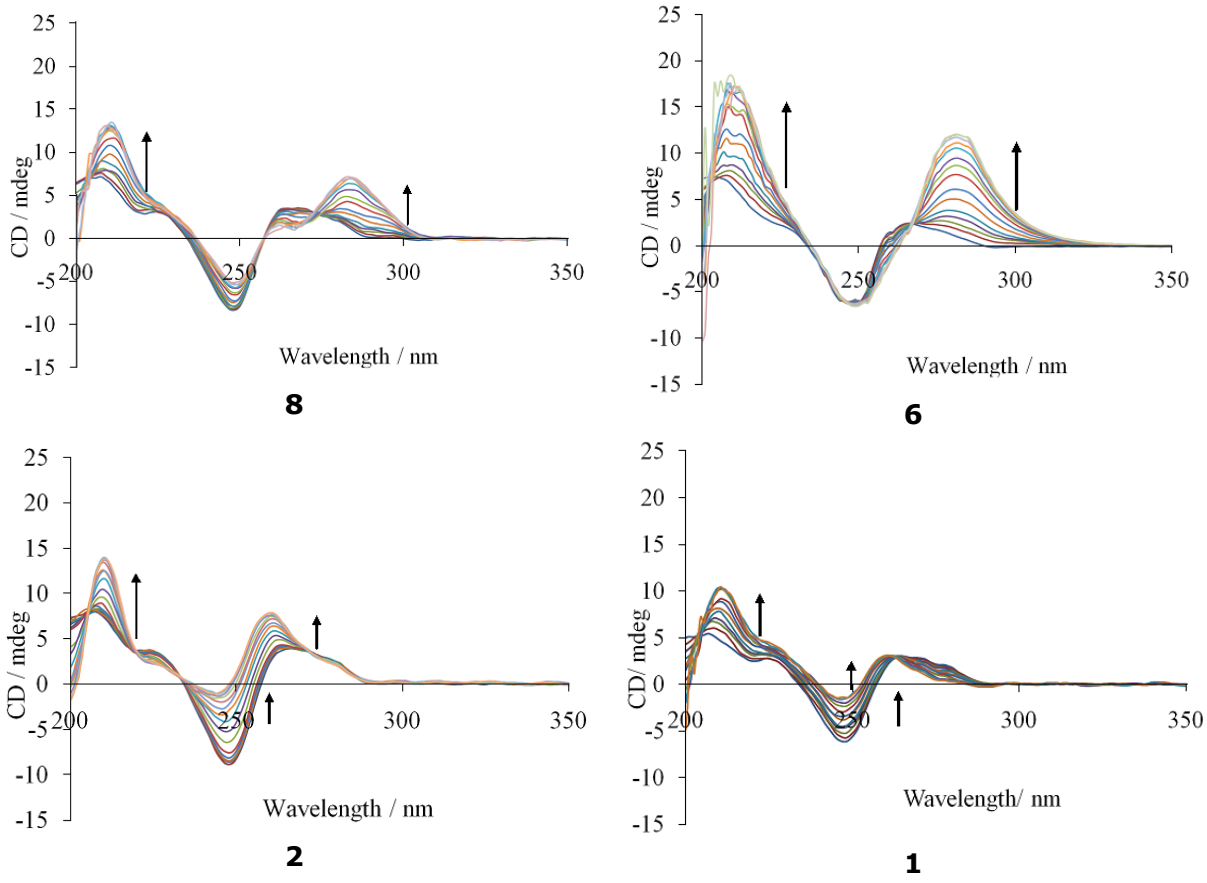

Figure I.– CD spectra obtained for compounds **8** (upper left, urea), **6** (upper right, piperazine), **2** (bottom left, CH_2CH_2) **1** and (bottom right, CH_2) titrated with poly(dA•dT)$_2$ in a concentration of 37.5 μM varying the Bp/D ratio from 1.12 to 44.8 through ten additions.

Comparative Docking

Different docking experiments were carried out for comparative proposes with ArgusLab,[i] AutoDock-4.2[ii] and AutodockVina.[iii] All compounds were docked using a rigid DNA template and in a rigid and flexible approach for the ligand. Considering that these compounds are asymmetrical, both approaches (*normal* and *inverted*) were considered and the final energies used are an average of both types of interactions. The binding scores obtained for AutoDock-4.2 and AutodockVina using rigid and flexible ligands are presented in Table I.

Table I.- Binding scores obtained using AutoDock-4.2 and AutodockVina in rigid and flexible ligand approaches.

		AVERAGE DOCKING			
		(Normal + inverted)/2 [kcal/mol]			
linker		**ad4flexi**	**ad4rigid**	**vinaflexi**	**vinarigid**
CH2	**1**	-5.945	-10.810	-8.700	-8.900
CH2CH2	**2**	-7.190	-10.295	-9.100	-8.550
O	**3**	-7.355	-11.060	-8.400	-8.500
S	**4**	-6.170	-10.965	-9.100	-8.800
NH	**5**	-6.465	-10.460	-8.300	-8.750
Piperazine	**6**	-6.380	-10.365	-8.200	-8.600
CO	**7**	-6.675	-11.535	-9.000	-9.250
Urea	**8**	-5.650	-11.210	-8.950	-9.100

Different correlations were tested with the energy corresponding to the conformational penalty ($E_{conf.penalty}$) and the increment in denaturation energy (ΔT_m) but the only significant model obtained was the one presented in the main manuscript.

References

i. ArgusLab 4.01: Planaria Software LLC, Seatle, WA, 2004)

ii. Autodock 4.2: G. M. Morris, R. Huey, W. Lindstrom, M. F. Sanner, R. K. Belew, D. S. Goodsell, A. J. Olson, *J. Comput. Chem*. 2009, **30**, 2785–2791.

iii. AutodockVina: O. Trott, A. J. Olson, *J. Comput. Chem.*, 2010, **31**, 455-461.