

## 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**

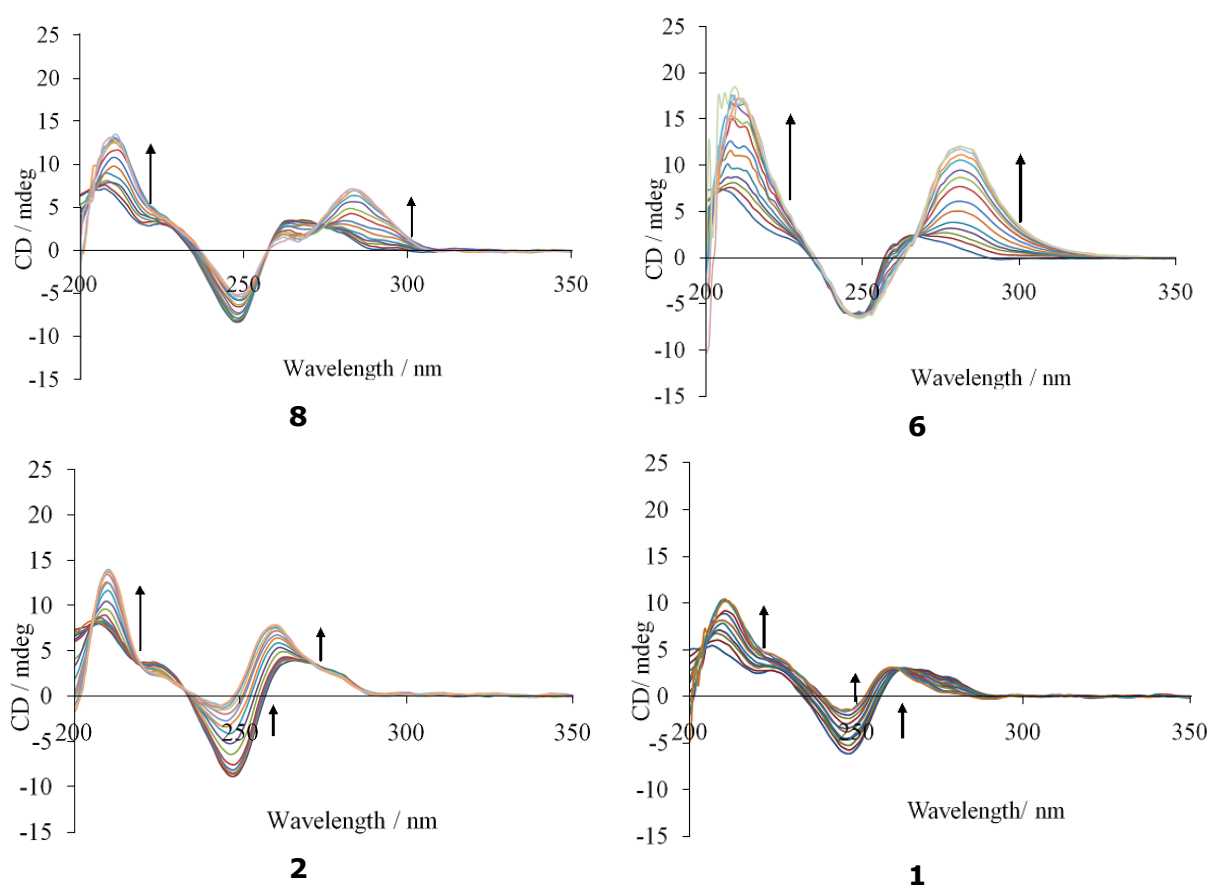
**II**

**Comparative docking**

**III**

## 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  $\lambda_{\max}$ . 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)<sub>2</sub>,<sup>14</sup> 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  $\Delta T_m$  values, shows the smallest increment.



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

## Comparative Docking

Different docking experiments were carried out for comparative purposes with ArgusLab,<sup>i</sup> AutoDock-4.2<sup>ii</sup> and AutodockVina.<sup>iii</sup> 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.

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

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

## References

- i. ArgusLab 4.01: Planaria Software LLC, Seattle, 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.