Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics




# Stability and iron coordination in DNA adducts of anthracycline based anti-cancer drugs

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## Supplementary Data

## (A total of seven pages)

**Figure S1.** Structure of the [Anthracycline-DNA]Fe(III) complex. The Anthracycline drug is presented in blue and DNA is presented in element-coloured stick model.

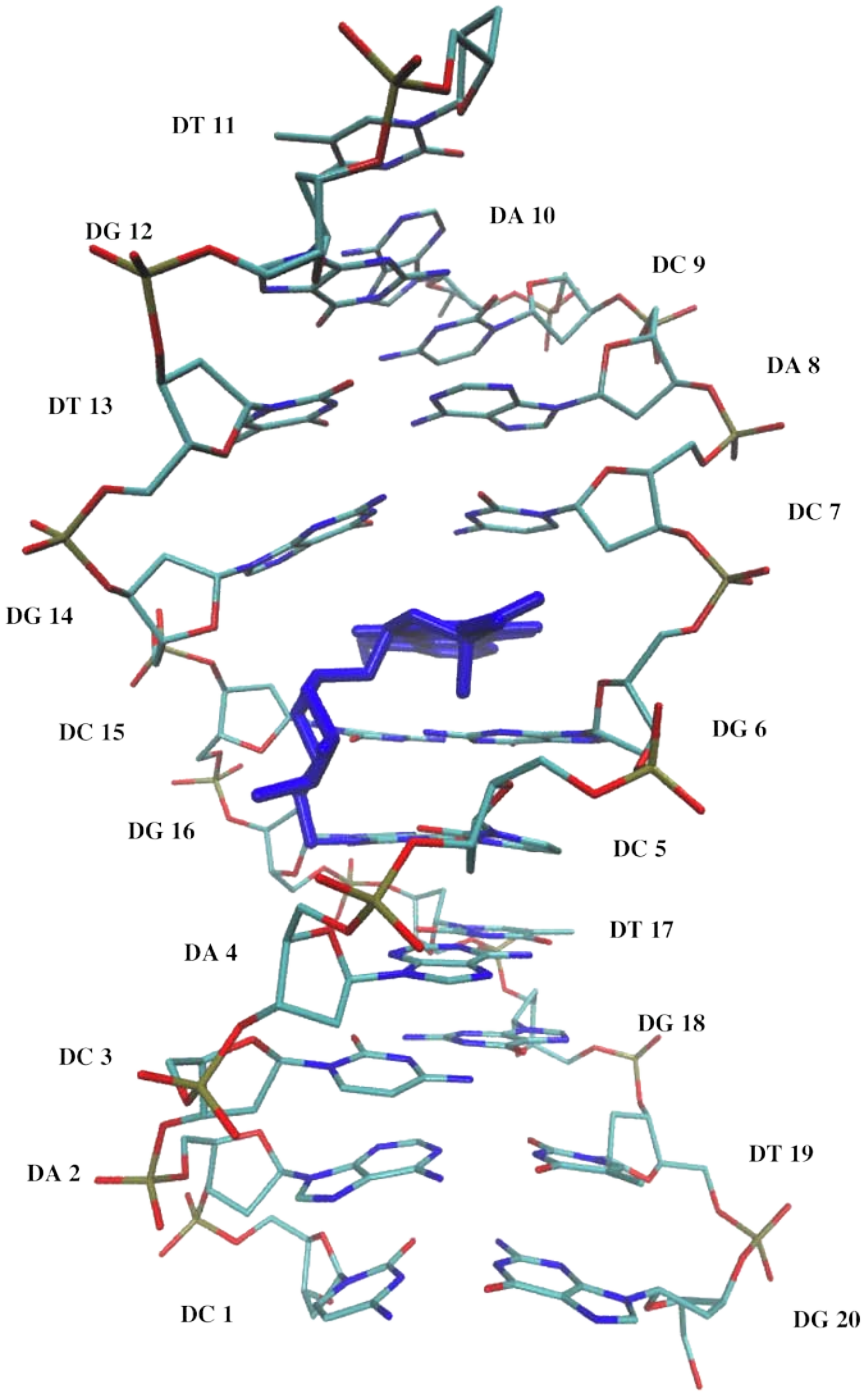


**Figure S2**. Atom numbering of the nucleotides.

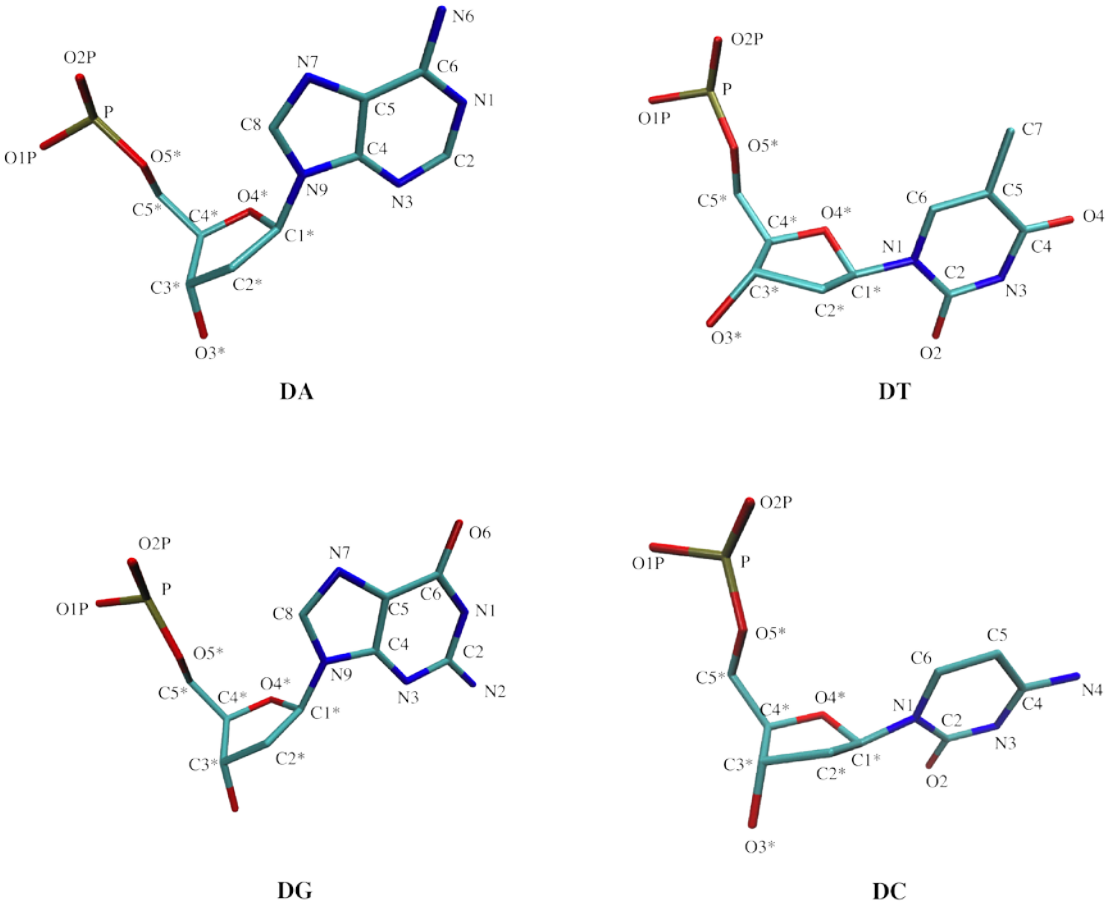
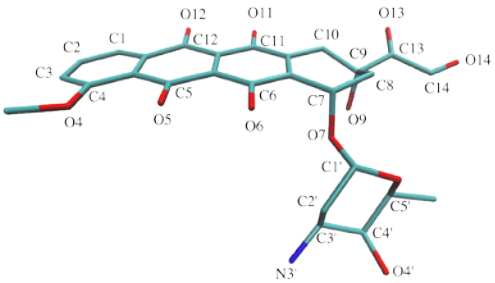
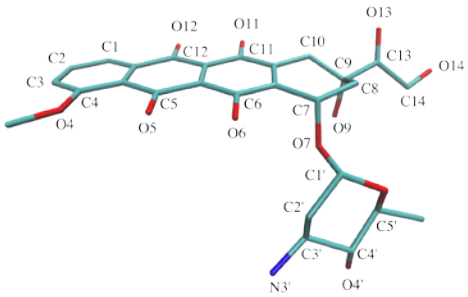


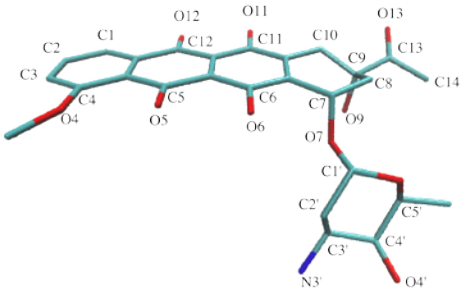
**Figure S3.** Atom numbering of the Anthracycline drugs.



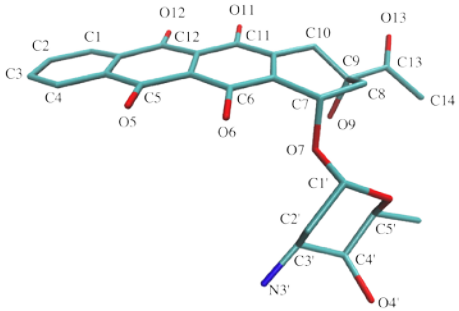

**DOXORUBICIN**



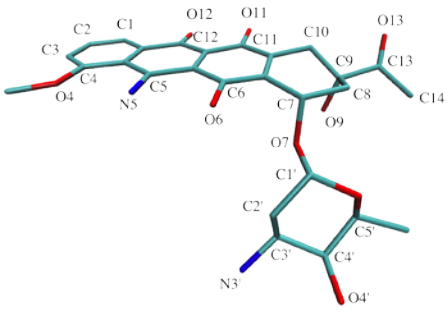

**EPIRUBICIN**




**DAUNORUBICIN**




**IDARUBICIN**




**5-IMINODAUNOMYCIN**

**Table S1**. H-bond distances (in Å) in the final structures of the [Anthracycline-DNA] and [Anthracycline]Fe(III) systems. O9H-N3 corresponds to the H-bond formed between the O9 atom belonging to the drug and the N3 atom belonging to DG 6. N2H-O7 is the H-bond generated between the O7 atom of the drug and the N2 atom of the DG 6 nucleotide. N3'H-O2 is the H-bond between the O2 atom of DC 15 and the N3' atom of the drug. N3'H-O4* is the H-bong generated between the N3' atom of the drug and the O4* atom of the DC 15. O4'H-O2 represents the H-bond between the O4' atom of the Epirubicin drug and the O2 atom of DC 5. O14H-O5* is the H-bond formed between the O14 of Doxorubicin and the O5* atom belonging to the DT 13 nucleotide.

| | O9H-N3 | N2H-O7 | N3'H-O2 | N3'H-O4* | O4'H-O2 | O14H-O5* |
|---|---|---|---|---|---|---|
| DOX-DNA | 1.817 | 2.016 | 1.976 | | | |
| EPI-DNA | 1.907 | 2.095 | 2.010 | | 1.590 | |
| DNR-DNA | 1.825 | 2.052 | - | | | |
| IDA-DNA | 1.786 | 2.026 | 2.121 | | | |
| 5-IMINO-DAU-DNA | 1.765 | 1.967 | 2.008 | | | |
| [DOX-DNA]Fe(III) | 1.765 | 2.088 | - | 2.337 | | 2.006 |
| [EPI-DNA]Fe(III) | 2.020 | 1.887 | 2.084 | | 1.628 | |
| [DNR-DNA]Fe(III) | - | - | - | | | |
| [IDA-DNA]Fe(III) | 1.836 | 1.927 | 2.115 | | | |
| [5-IMINO-DAU-DNA]Fe(III) | 1.870 | 1.899 | - | | | |

**Figure S4.** Superposition of [Anthracycline-DNA]Fe(III) systems. The equilibrated and final structures are represented in red and black respectively. a) [EPI-DNA]Fe(III) system. b) [DNR-DNA]Fe(III) system. c) [IDA-DNA]Fe(III) system. d) [5-IMINO-DAU-DNA]Fe(III) system.

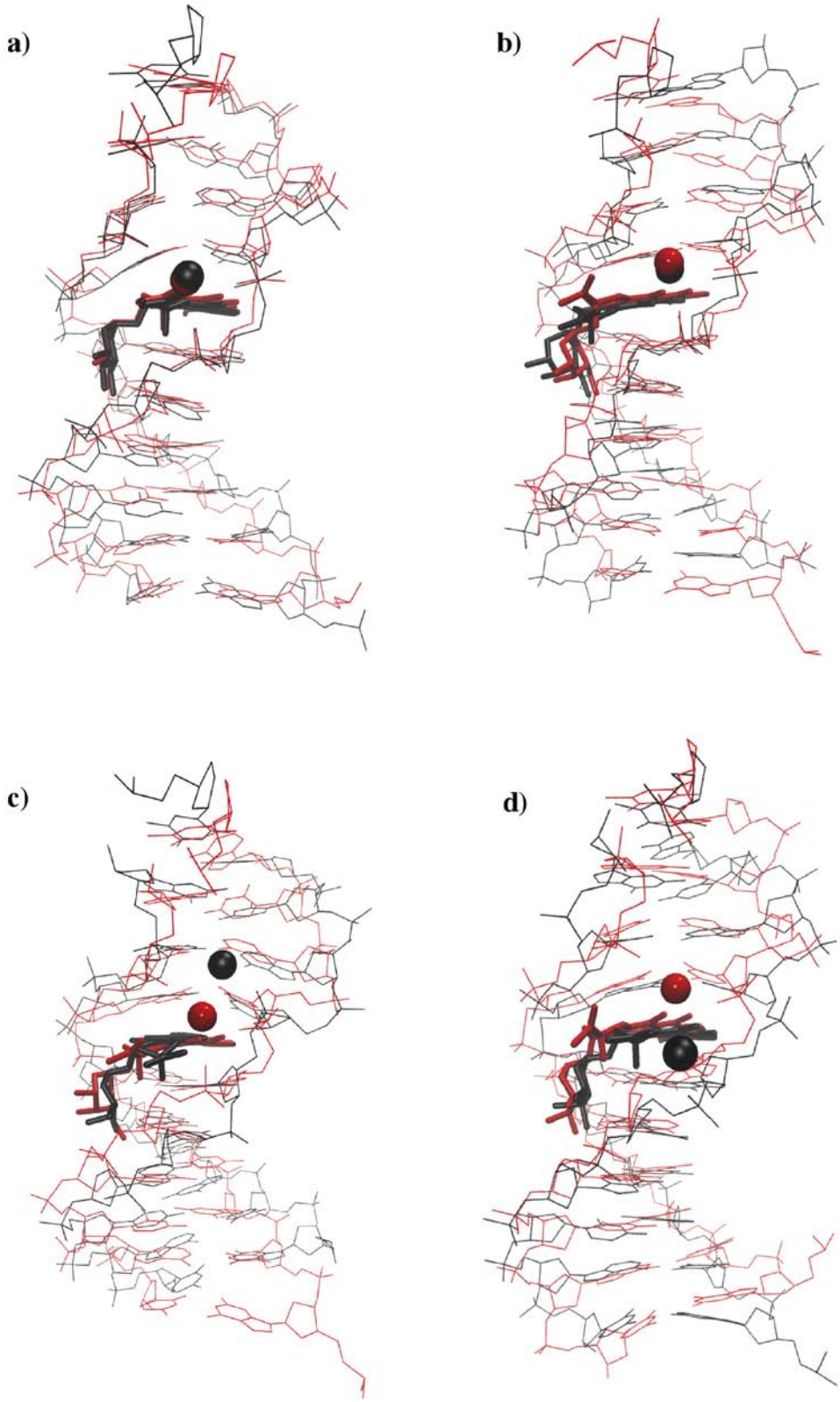



**Figure S5.** Initial structures of the Fe-containing systems after minimazation. a) The [DOX-DNA]Fe(III) system, where the Fe-OA, Fe-OB, Fe-OC, Fe-O14 and Fe-O13 distances are 2.924, 2.612, 2.753, 3.056 and 2.921 Å, respectively. b) The [EPI-DNA]Fe(III) system, where the Fe-OA, Fe-OB, Fe-OC, Fe-O14 and Fe-O13 distances are 2.711, 2.694, 2.633, 2.903 and 4.770 Å, respectively. c) The [DNR-DNA]Fe(III)

system, where the Fe-OA, Fe-OB, Fe-OC, Fe-C14 and Fe-O13 distances are 2.672, 2.617, 2.683, 4.280 and 4.783 Å, respectively. d) The [IDA-DNA]Fe(III) system, where Fe-OA, Fe-OB, Fe-OC, Fe-C14 and Fe-O13 distances are 2.626, 2.627, 2.676, 4.470 and 4.762 Å, respectively. e) The [5-IMINO-DAU-DNA]Fe(III) system, where Fe-OA, Fe-OB, Fe-OC, Fe-C14 and Fe-O13 distances are 2.624, 2.614, 2.633, 4.249 and 3.239 Å, respectively.