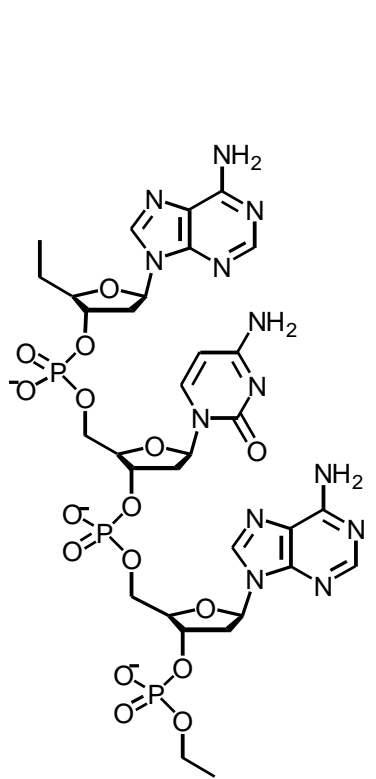
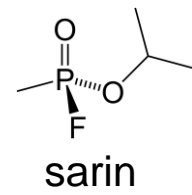
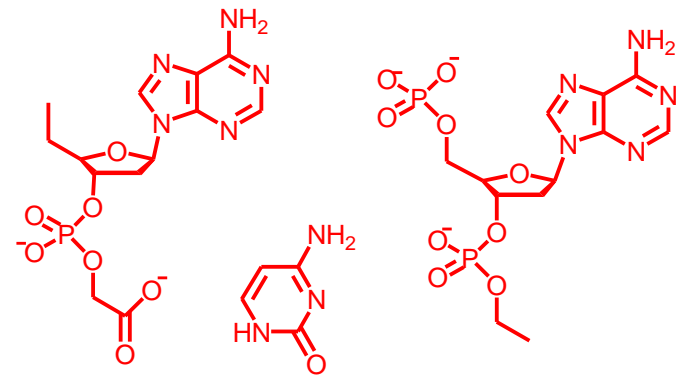


Why artificial phosphates or nucleases?

- ✓ Enzyme models
- ✓ Chemical weapons destruction
- ✓ DNA manipulation and study
- ✓ Antitumor, antibiotic and antiviral drugs

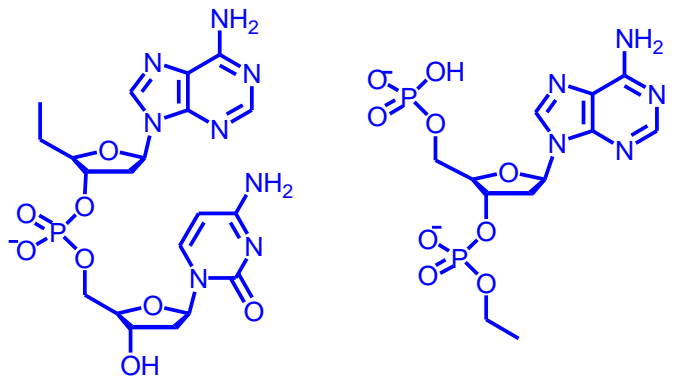
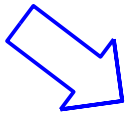


Oxidative cleavage



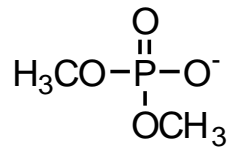
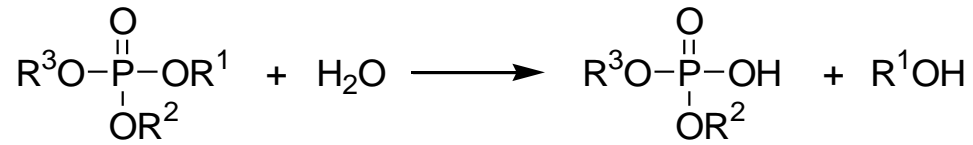
- ⇒ Efficient
- ⇒ Need cofactors
- ⇒ Nucleotides damage

Hydrolytic cleavage

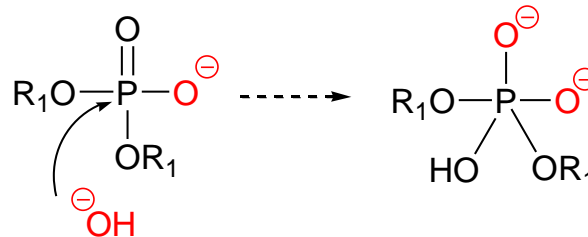
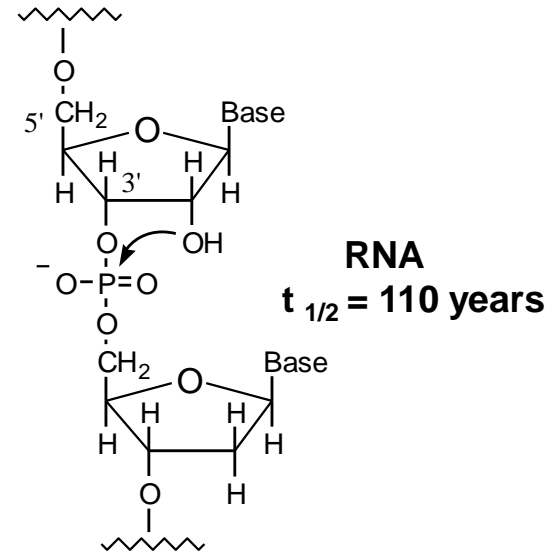
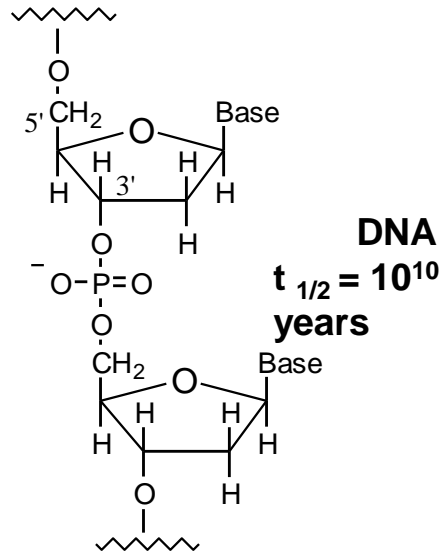


- ⇒ Enzyme like cleavage
- ⇒ No cofactors
- ⇒ Still not efficient

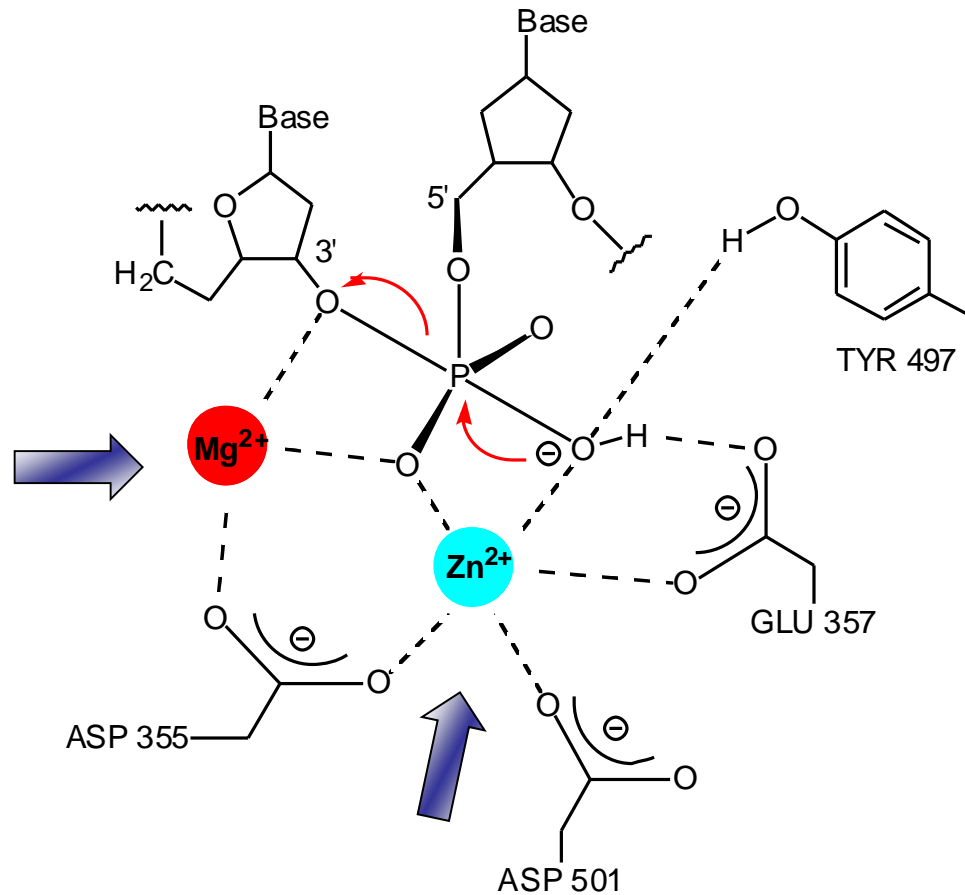
Phosphate Esters Hydrolysis



$t_{1/2} = 10^{10}$ years
(pH = 7, 25 °C)

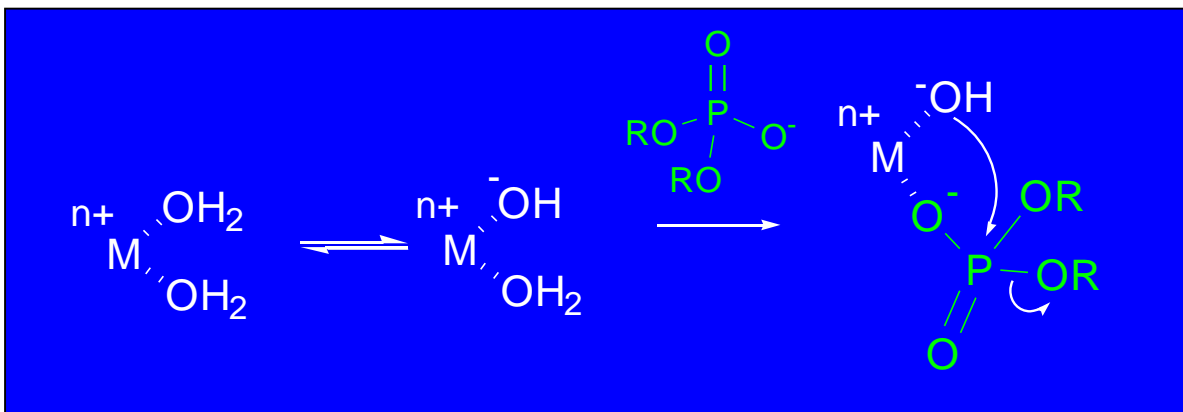


METALLONUCLEASES



DNA polymerase I

Metal-based hydrolytic agents

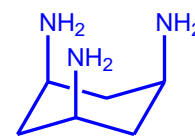


- ⇒ Template effect (neutralization of electrostatic repulsion)
- ⇒ Nucleophile Lewis acid activation
- ⇒ Substrate Lewis acid activation

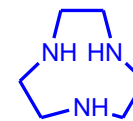
Lanthanide ions (Ce(IV))
 (Efficient, Toxic
 Undefined coordination
 chemistry)

Cu(II) ions

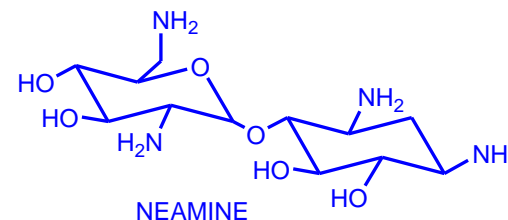
(Efficient
 Redox chemistry)



TACH



[9]aneN₃



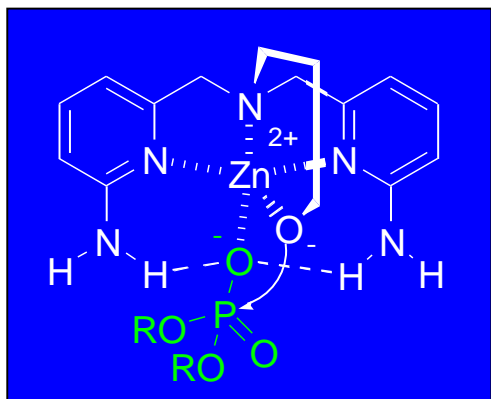
NEAMINE

Zn(II) ions

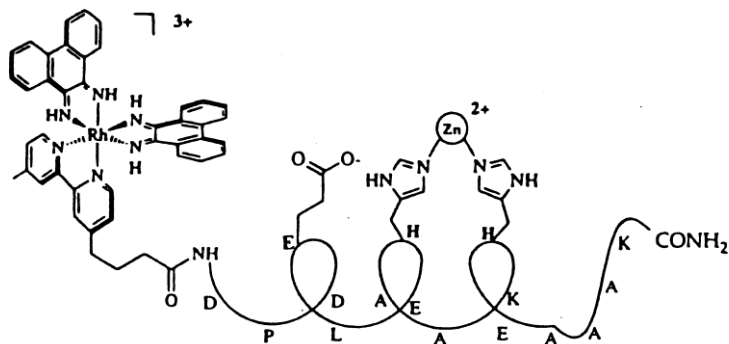
- ⇒ Poorly efficient
- ⇒ No redox chemistry

Increasing the efficiency of Zn(II)-based system

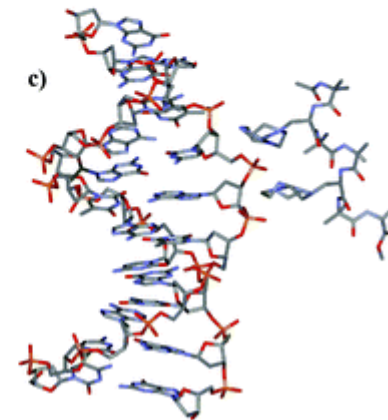
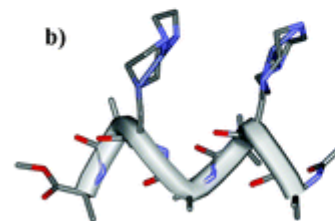
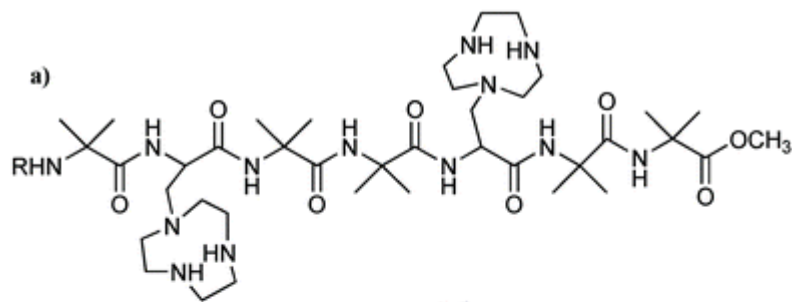
Ligand structure modification



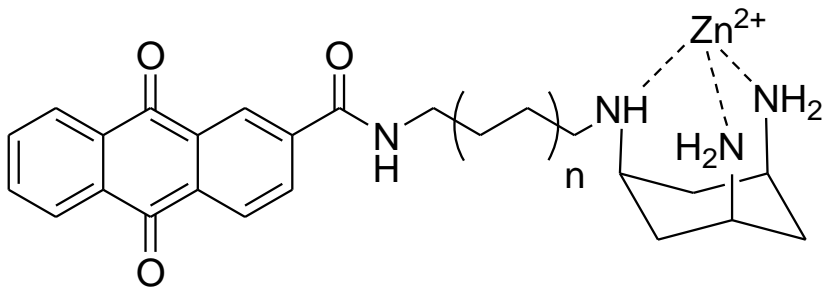
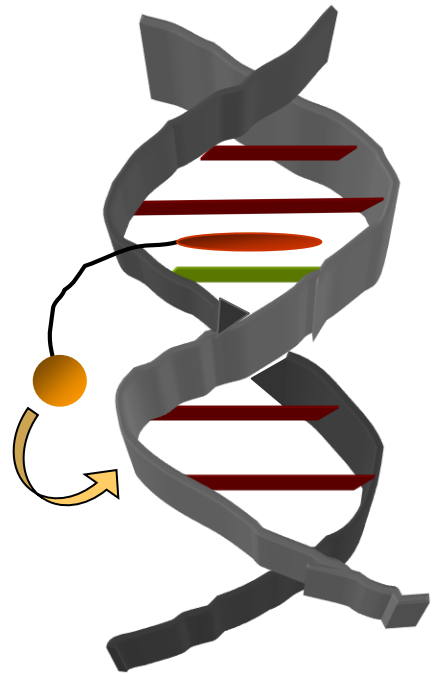
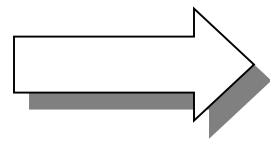
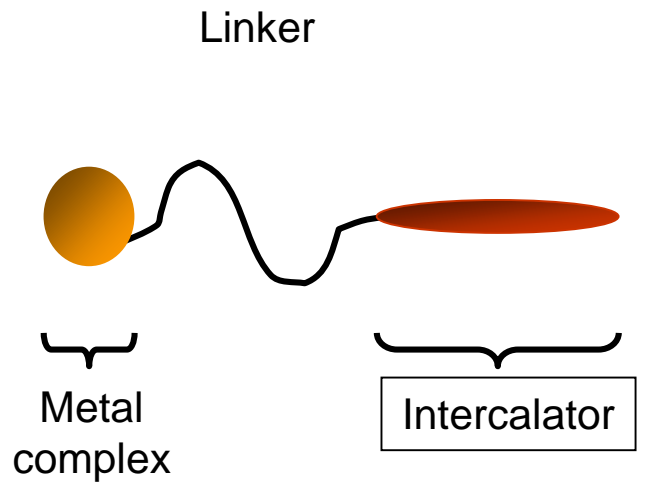
Conjugation with DNA binders



Bimetallic systems

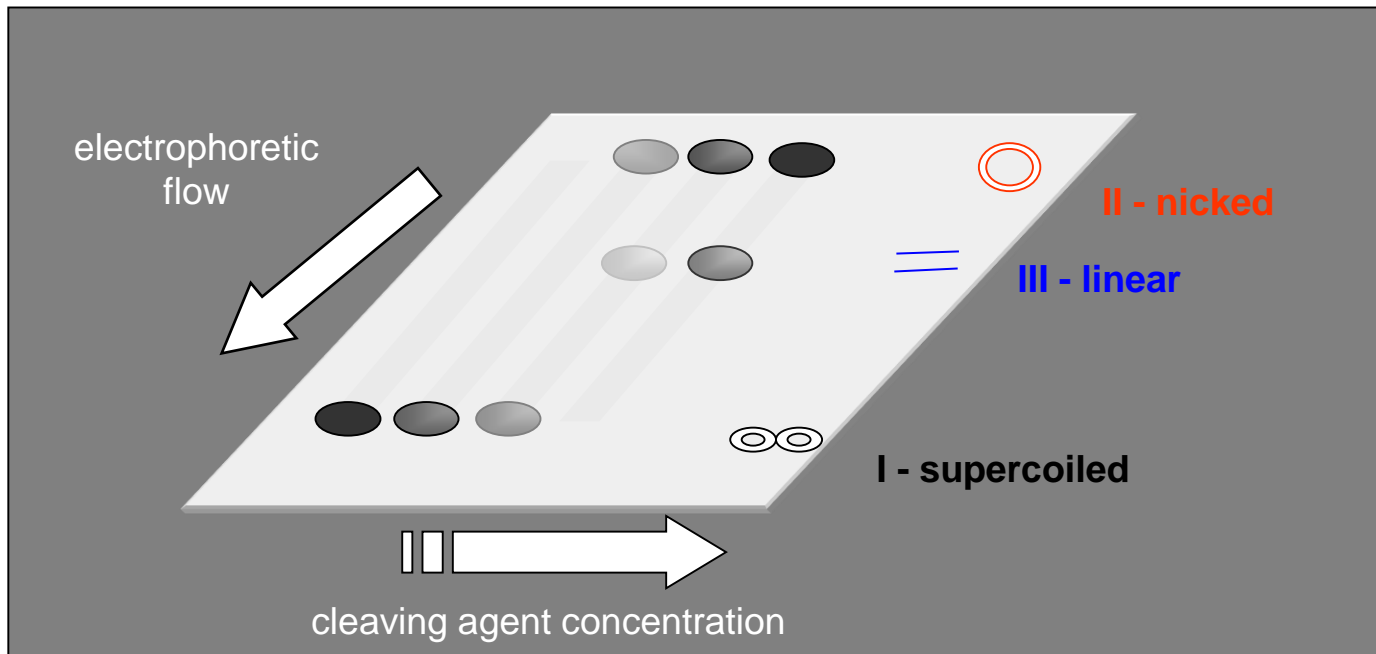
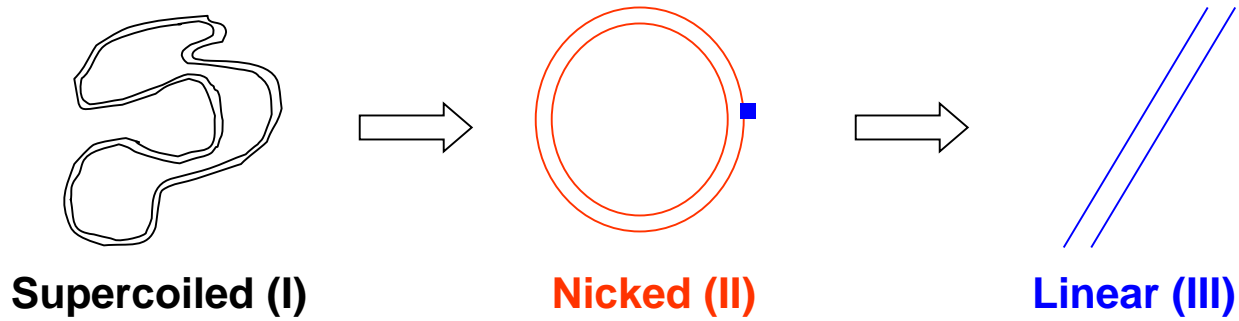


Anthraquinone Zn(II) complexes conjugates

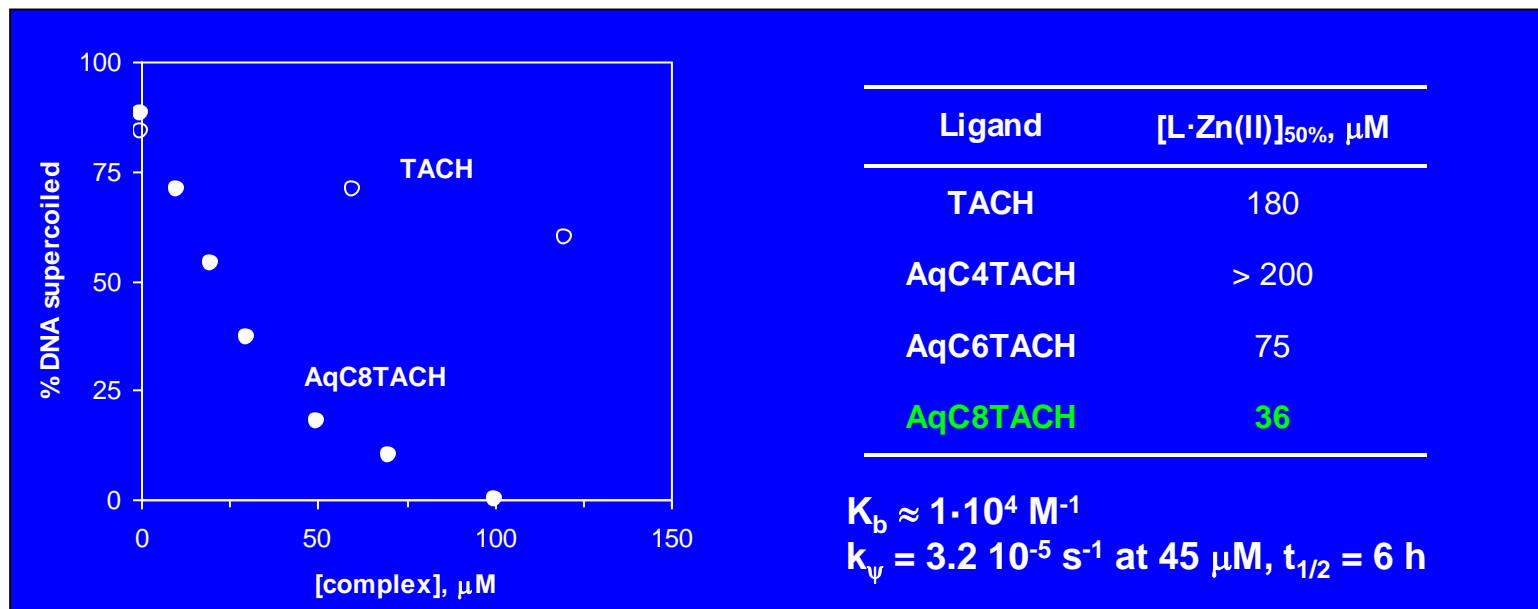
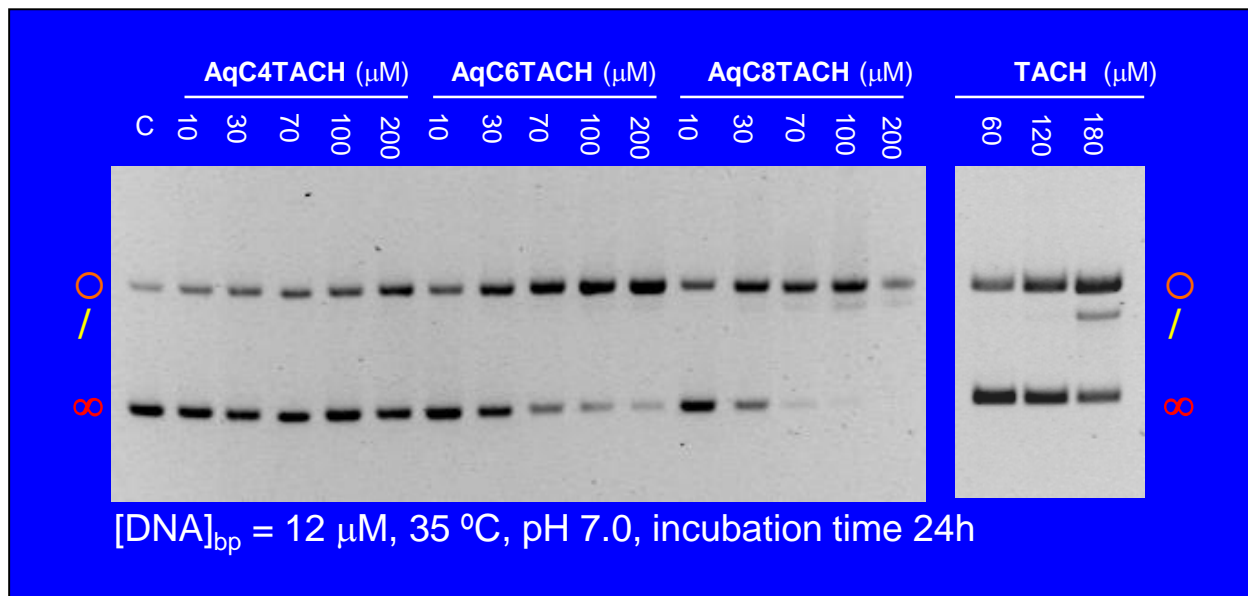


- AqC4TACH : n =1**
- AqC6TACH : n =2**
- AqC8TACH : n =3**

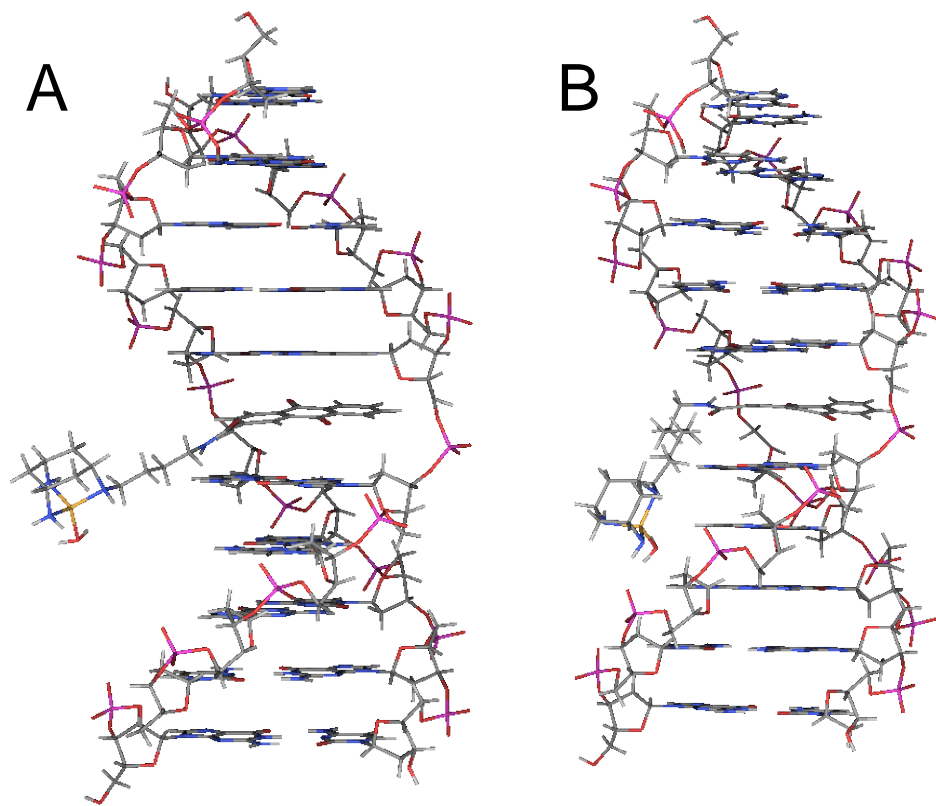
Plasmid DNA cleavage



Anthraquinone Zn(II) complexes conjugates



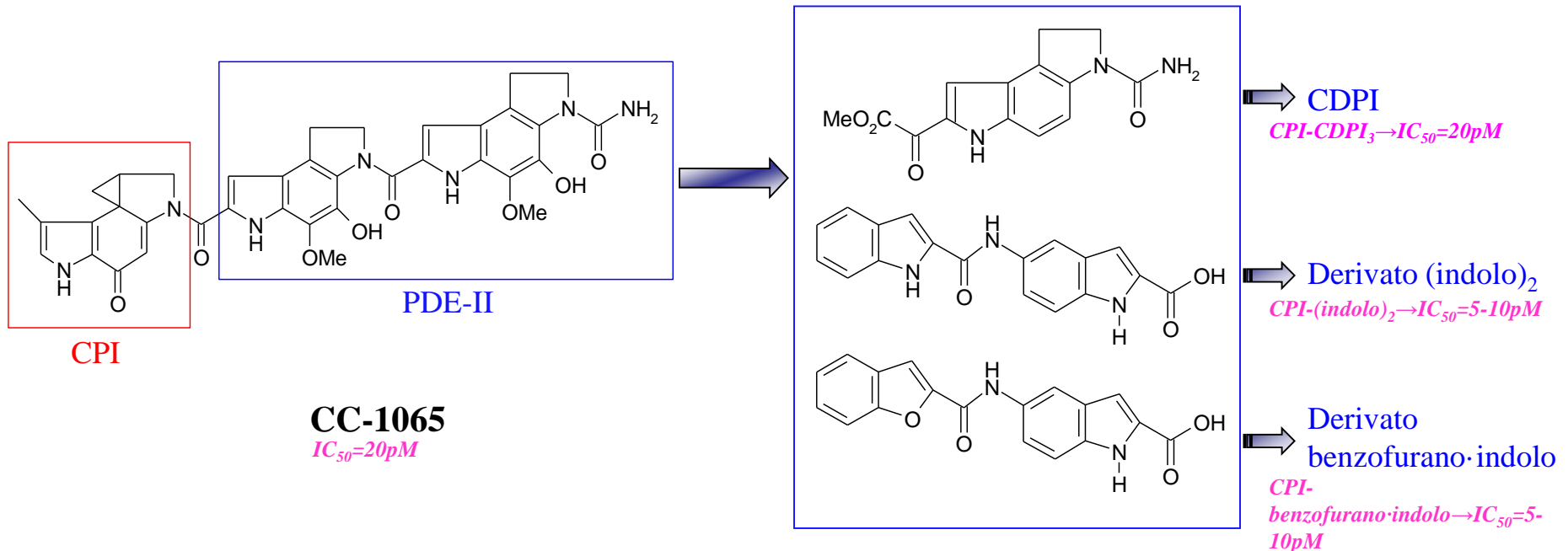
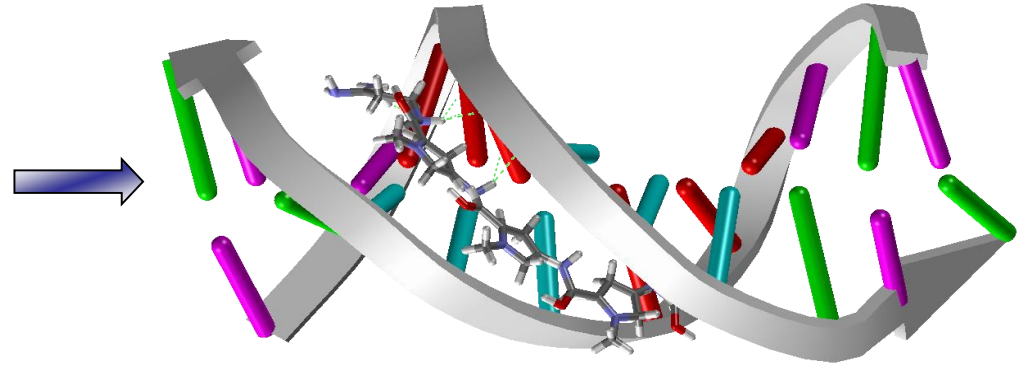
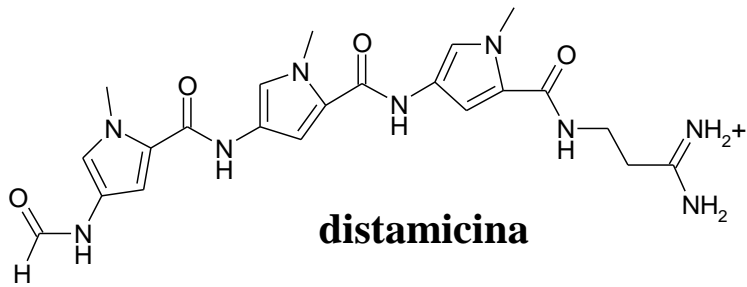
Anthraquinone Zn(II) complexes conjugates



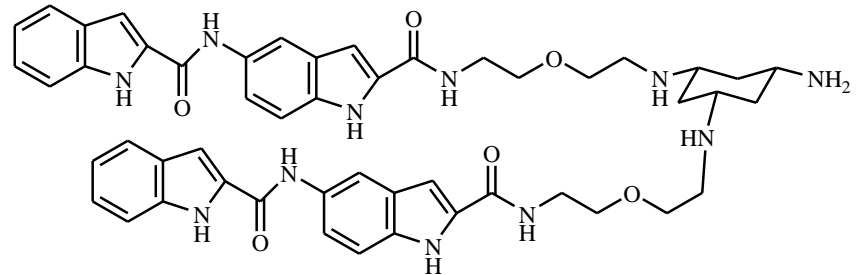
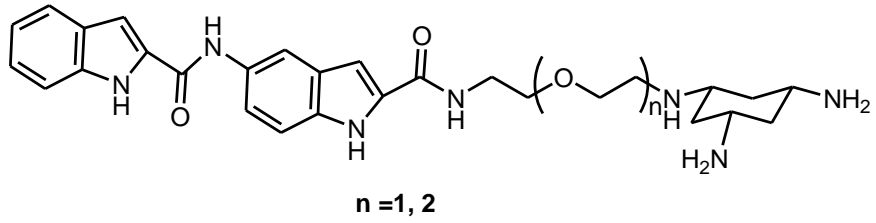
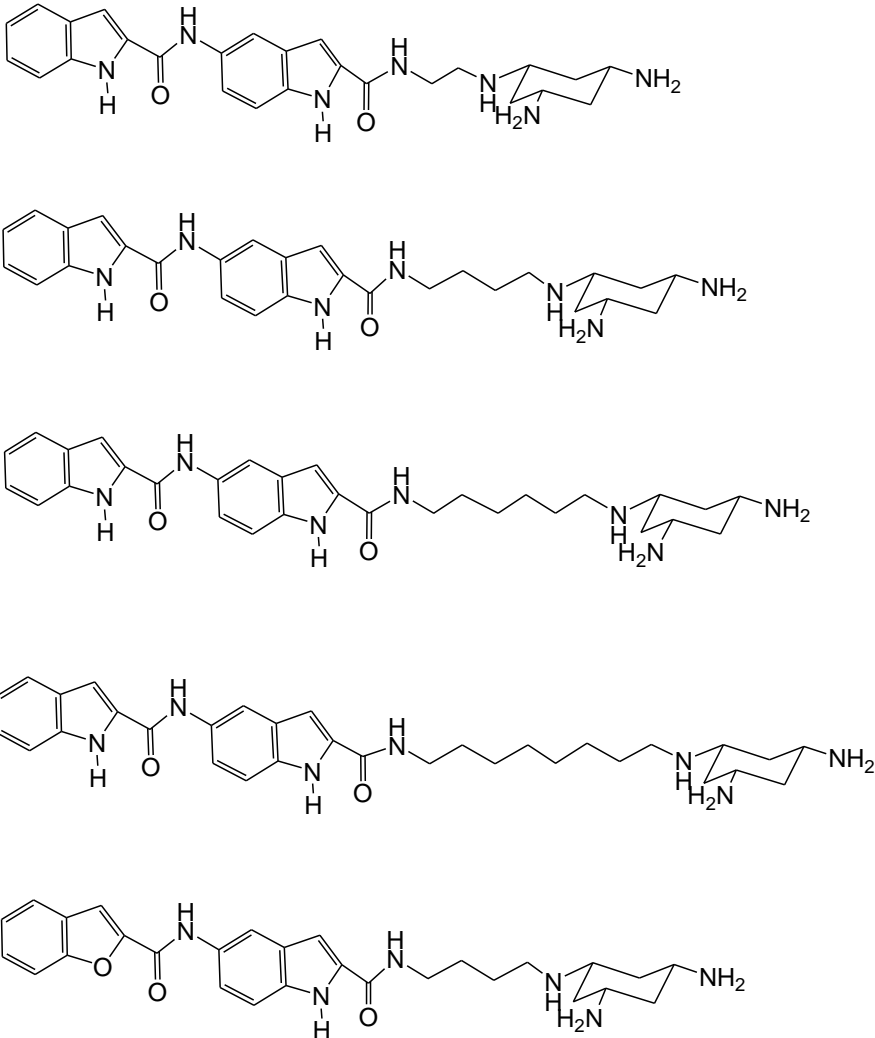
Calculated structures (MMFF94)

MINOR GROOVE BINDERS

- High DNA affinity
- Selective for A-T reach sequences

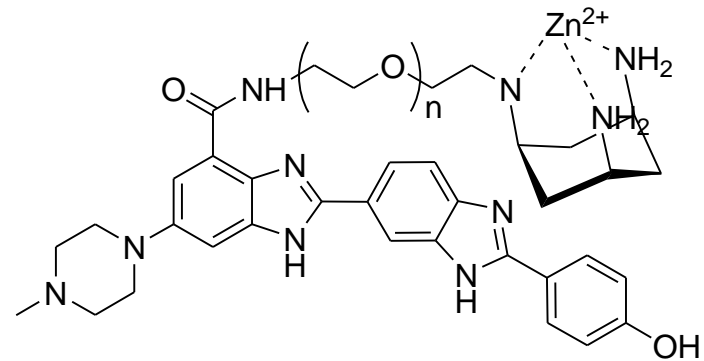
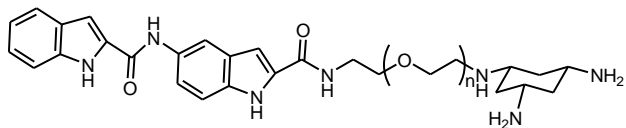
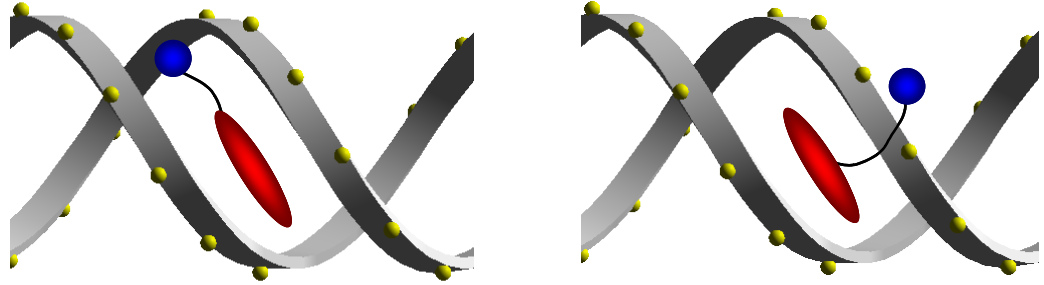
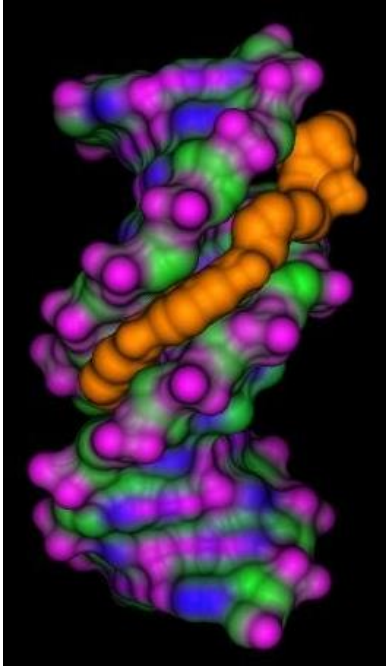


Minor groove binders Zn(II) complexes conjugates



BINDING YES
ACTIVITY NO

Minor groove binders Zn(II) complexes conjugates



Hoechst 33258