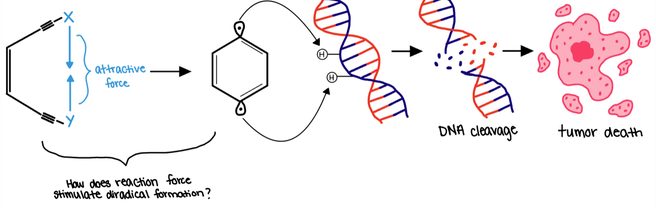
Exploring Non-covalent Driving Forces for the Bergman cyclization of Functionalized Enediynes

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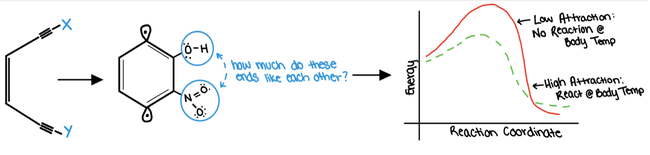
Project Overview

- **Diradicals**, with two unpaired electrons can be harnessed to kill cancer cells
- If **reaction** is **controlled *in cellulo***, DNA-attacking behavior could be enabled in *only* cancerous cells



Challenge: Determine if attraction felt between groups of atoms on ends of an enediyne precursor can lead to Bergman cyclization **at body temperature** and eventual tumor cell death

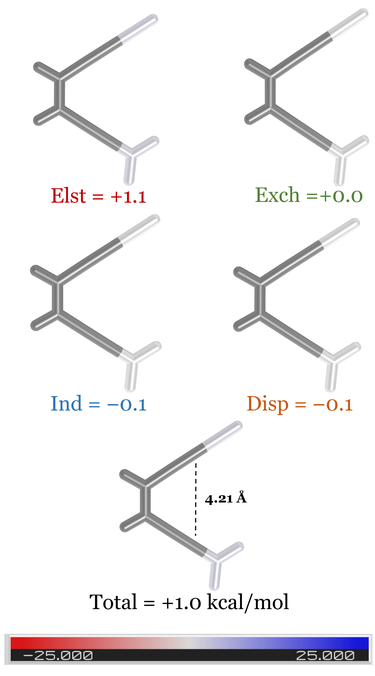
Objectives:



- Explore intramolecular functional group interactions w/ F-/ISAPT as a function of reaction progress

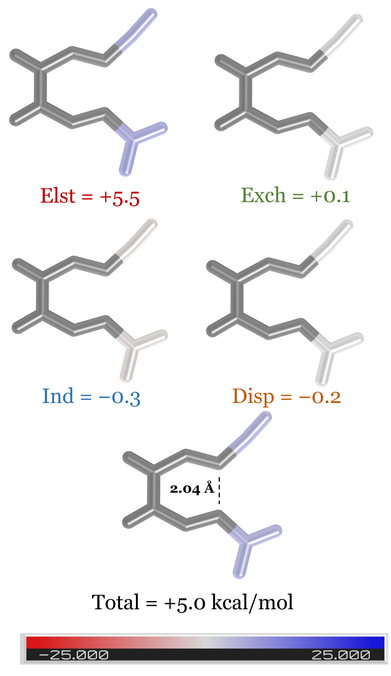
Our ?: Could optimal intramolecular interactions drive the Bergman cyclization for anti-tumor applications?

Reactant

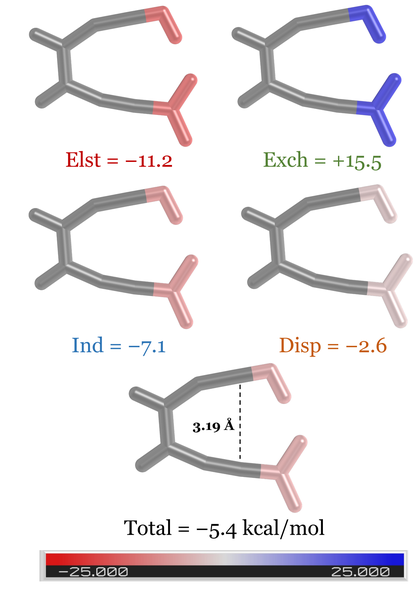


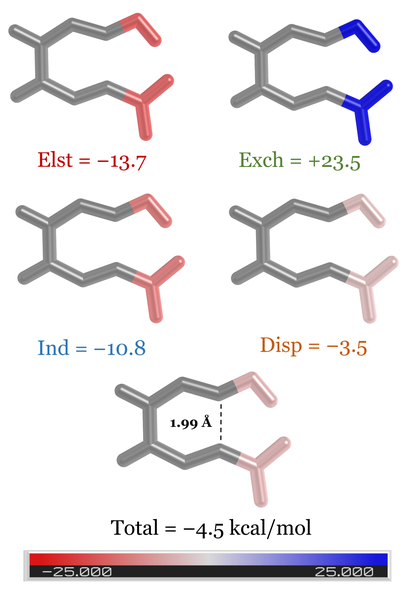
X=CN, Y=NO2

Top of Hill

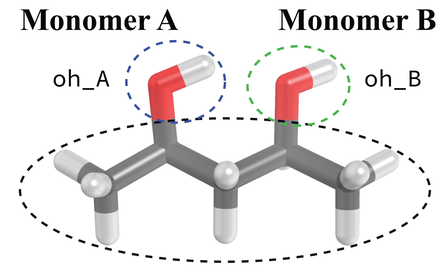


X=OH, Y=NO2





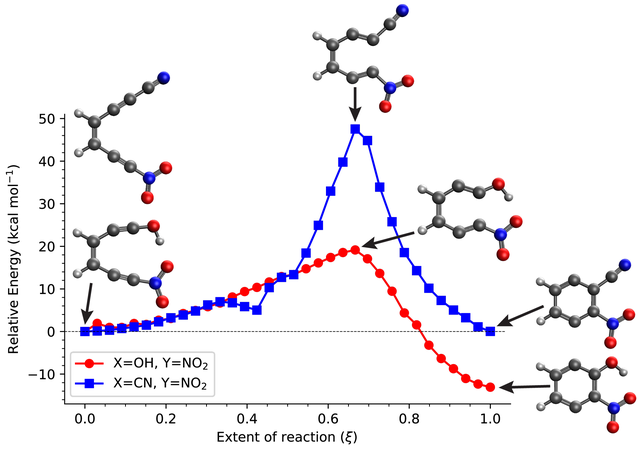
F-/ISAPT



$$\mathrm{IE}^{\mathrm{F-/ISAPT0}}_{\mathcal{A}\cdot\mathcal{B}} = E^{(10)}_{\mathrm{elst}} + E^{(10)}_{\mathrm{exch}} + E^{(20)}_{\mathrm{ind,resp}} + E^{(20)}_{\mathrm{exch-ind,resp}} + E^{(20)}_{\mathrm{disp}} + E^{(20)}_{\mathrm{exch-disp}} + \delta^{(2)}_{\mathrm{HF}}$$

$$\mathrm{IE}^{\mathrm{F-/ISAPT0}}_{f_i^{\mathcal{A}}\cdot f_j^{\mathcal{B}}} = E^{(10)}_{\mathrm{elst}} + E^{(10)}_{\mathrm{exch}} + E^{(20)}_{\mathrm{ind,resp}} + E^{(20)}_{\mathrm{exch-ind,resp}} + E^{(20)}_{\mathrm{disp}} + E^{(20)}_{\mathrm{exch-disp}}$$

Freezing String Trajectory



- Constructed at BS-UB3LYP/6-311++G**
- Canonical Bergman:[3] $\Delta E^{\ddagger}$ = +32.88 kcal/mol
- Use **reactant** and **top of hill** for F-/ISAPT analysis (minimal diradical nature)

Conclusions

- **X=CN, Y=NO2** fn'l group dipole moments parallel; d-d repulsion *inhibits* cyclization
- **X=OH, Y=NO2** formation of intramolecular H-bond *promotes* cyclization

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