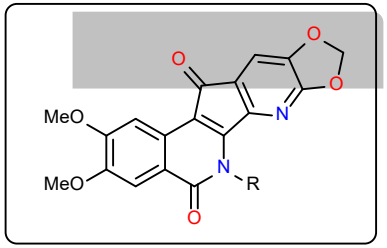
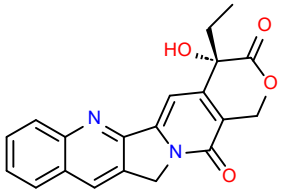
7-Azaindenoisoquinolines



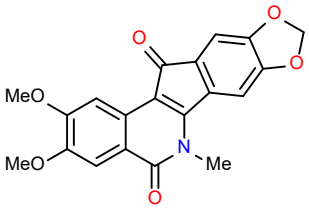
- Indenoisoquinolines are a class of potential anticancer drugs dual-targeting MYC G-quadruplex and Topoisomerase I, therefore inhibiting DNA transcription process.
- MYC is a general transcription “amplifier” and a super enhancer overexpressed in most cancers.
- Several indenoisoquinoline derivatives have completed phase 1 clinical trials, while more recent and potent 7-azaindenoisoquinolines are still under investigation.

Han, Y.; Buric, A.; Chintareddy, V.; DeMoss, M.; Chen, L.; Dickerhoff, J.; De Dios, R.; Chand, P.; Riggs, R.; Yang, D.; Cushman, M. *J. Med. Chem.* **2024**, *67*, 7006–7032. https://doi.org/10.1021/acs.jmedchem.3c02303.
Kiselev, E.; DeGuire, S.; Morrell, A.; Agama, K.; Dexheimer, T. S.; Pommier, Y.; Cushman, M. *J. Med. Chem.* **2011**, *54*, 6106–6116. https://doi.org/10.1021/jm200719v.
Nagarajan, M.; Morrell, A.; Fort, B. C.; Meckley, M. R.; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M. *J. Med. Chem.* **2004**, *47*, 5651–5661. https://doi.org/10.1021/jm040025z.

MOA study & structure investigation

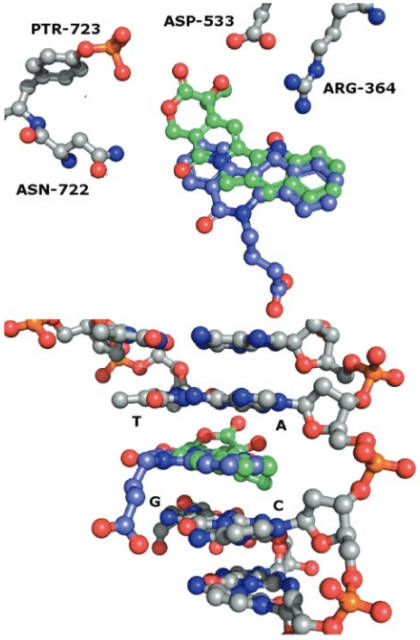


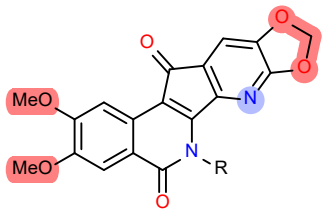
camptothecin



NSC 314622

- Byproduct of nitidine chloride synthesis
- Target more specifically
- Enhanced chemical stability



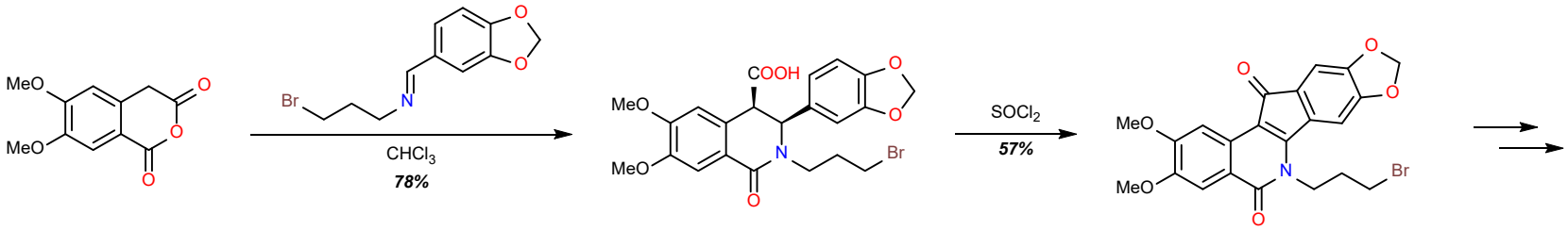


7-Azaindenoisoquinolines

- Electronegative nitrogen atomenhance charge transfer complex formation
- 2,3-dimethoxy and8,9-methylenedioxy substituents silghtly enhanceanticancer activity

7-Azaindenoisoquinolines

indenoisoquinolines



7-Azaindenoisoquinolines