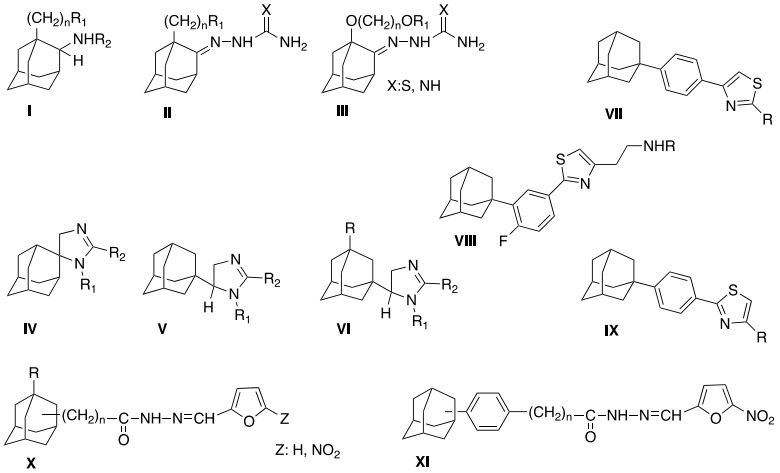
Synthetic routes of adamantane derivatives with a trypanocidal profile

Ioannis P. Papanastasiou

National and Kapodistrian University of Athens, Greece
papanastasiou@pharm.uoa.gr

The current drugs used against HAT and CD are suboptimal. The approved regimen presents many restrictions, such as serious adverse side effects, excessive toxicity, limited efficacy and increasing resistance [1]. This has led the World Health Organization (WHO) to coordinate public sector and private partnerships as part of a global effort to develop new and safer trypanocidal dugs. We have been exploring the chemical space of structurally different adamantane derivatives and their biological role against trypanosomes, over the last decade [2-6]. The structural modification comprising of the phenyl ring insertion between the adamantane core and the hydrazone side chain has improved the pharmacological properties, in terms of activity and toxicity. The most active adduct with the best selectivity is the phenylacetoxy hydrazone XIb (C1, n=1, Tb,IC_{50}=11 ± 0.9 nM and Tb,SI=770).



References

[1]V. Kourbeli, E. Chontzopoulou, K. Moschovou, D. Pavlos, T. Mavromoustakos, I. P. Papanastasiou, *Molecules* **2021**, 26(15), 4629.

[2]I. Papanastasiou, A. Tsotinis, N. Kolocouris, S. R. Prathalingam, J. M. Kelly, *J.Med.Chem.,* **2008**, *51,* 1496.

[3]A. Koperniku, I. Papanastasiou, G. B. Foscolos, A. Tsotinis, M. C. Taylor, J.M. Kelly, *MedChemComm*., **2013**, 4, 856.

[4]A.-S. Foscolos, I. Papanastasiou, G. B. Foscolos, A. Tsotinis, T. F. Kellici, T. Mavromoustakos, M. C. Taylor, J. M. Kelly, *MedChemComm*., **2016**, 7, 1229.

[5]A.-S. Foscolos, I. Papanastasiou, A. Tsotinis, M. C. Taylor, J. M. Kelly, *ChemMedChem*, **2019**, 14, 1227-1231.

[6]M.-O. Georgiadis, V. Kourbeli, I. P. Papanastasiou, A. Tsotinis, M. C. Taylor, J. M. Kelly, *RSC Med.Chem*., **2020**, *11(1)*, 72-84.