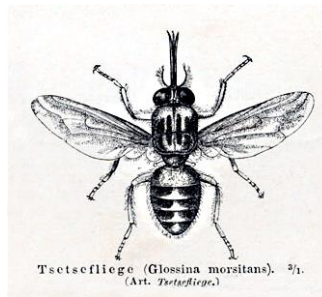


Sleeping Sickness (African trypanosomiasis)

- A parasitic disease caused by the protists *Trypanosoma brucei gambiense* (TbG) and *Trypanosoma brucei rhodesiense* (TbR), transmitted by the Tsetse fly of sub-saharan Africa
- Classified as a Neglected Tropical Disease by the CDC



Symptoms (Stage 1, Hemolympathic):

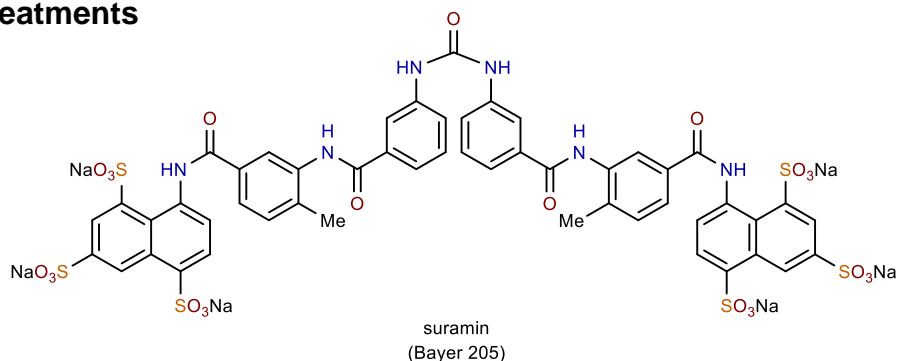
- Headaches, fatigue, intermittent fever (often confused with malaria)

Symptoms (Stage 2, Neurological):

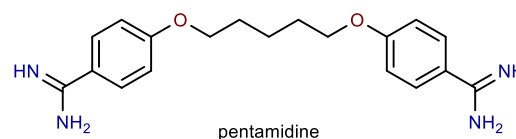
- Fragmented sleep patterns, with both insomnia and sudden sleepiness
- Tremors, weakness, muscle paralysis
- Psychosis, aggressiveness, hallucinations, delirium
- Without treatment, sleeping sickness is always fatal
- TbG causes death within years, while TbR kills within months

Steverding, D. *Parasites Vectors* **2010**, 3, 15. <https://doi.org/10.1186/1756-3305-3-15>

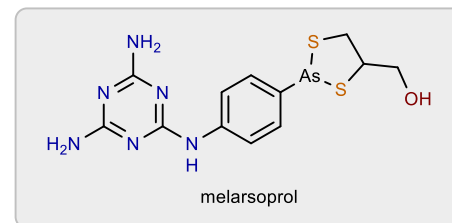
Treatments



- First synthesized in 1917, still first line of defense against Stage 1 TbR



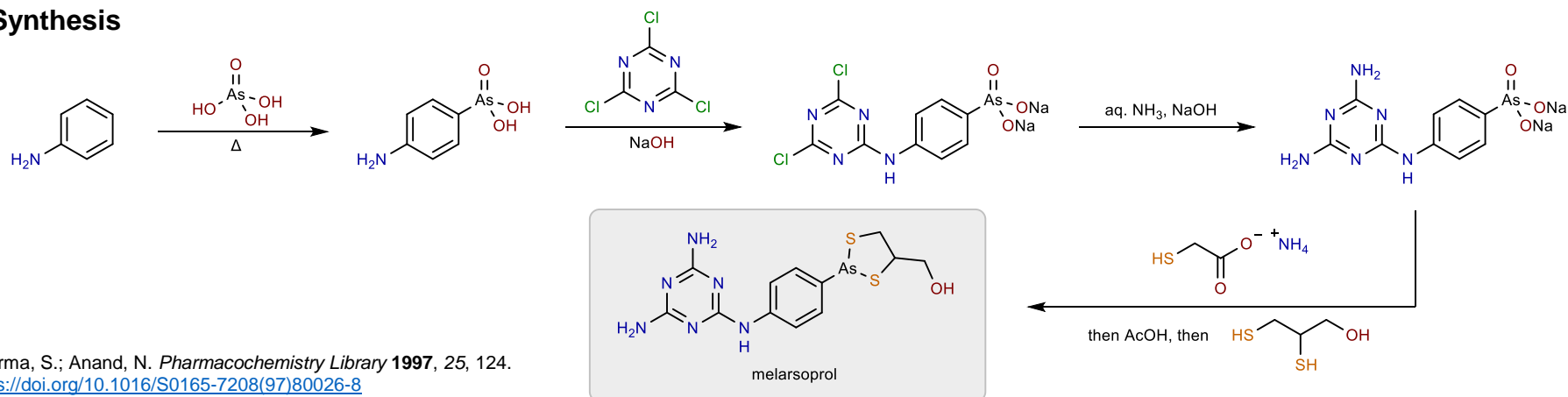
- First line of defense against Stage 1 TbG



- Only used for Stage 2 TbR infections

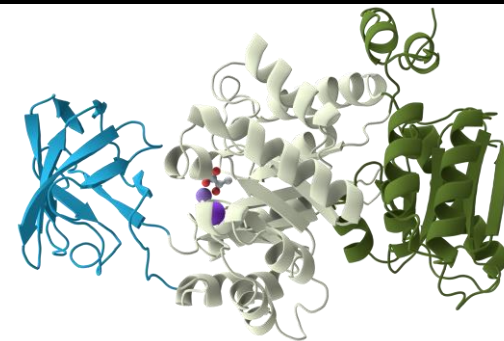
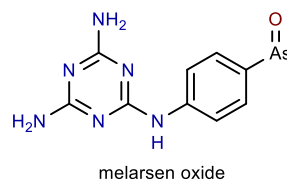
Fun Fact: Anti-sleeping sickness drugs were the first targets of early medicinal chemists at Bayer in the early 1900s

Synthesis



Mechanism of Action

- Melarsoprol is metabolized to melarsen oxide in vivo
- This irreversibly binds to pyruvate kinase (PK) thiols, shutting down glucose production
- However, there is no way for the drug to distinguish between parasite PK and patient PK enzymes



Side Effects May Include

- You die
- Melarsoprol treatment has a 95% success rate treating sleeping sickness, but there is roughly a 5% chance of encephalopathy and death
- Compound must be administered intravenously as a solution in propylene glycol
- Referred to as “arsenic in antifreeze”

