

The discovery and synthesis of new HIV-1 inhibitors

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Aims

- To synthesise one of the potential biologically active leading chemicals and characterise the new substance
- Analysis of the physiochemical properties of one of the detected leads by the past virtual screening programme

Introduction

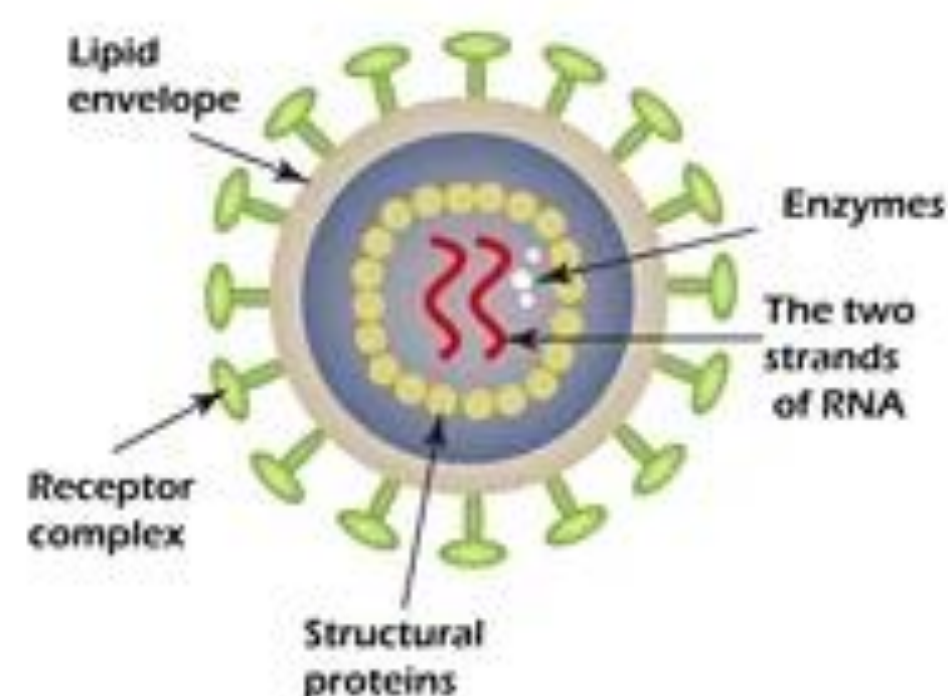
There is presently no vaccination available to protect against HIV infection. Antiretroviral (ARV) drugs can prevent the immune system of an HIV-positive individual from deteriorating.

Consequently, the majority of HIV-infected people, particularly those in low- and middle-income countries, lack regular access to antiretroviral medications and other health-care services.

The emergence of drug-resistant HIV, an unavoidable by-product of increased antiretroviral medicine use, poses a substantial threat to the effectiveness of antiretroviral therapy. Access to ARV drugs must continue to expand in order to aid with HIV management.

Antiretroviral medication classes have been approved and are under development for HIV prevention, and drug resistance may restrict their effectiveness for both prevention and treatment. In the absence of a feasible HIV vaccine and treatment, new classes of HIV inhibitors active against treatment-resistant strains must be added to the antiretroviral medicine pathway.

The structure of the HIV virus



Methods

- Dichloromethane (17ml) was added to a suspension of sulfonyl chloride (1.0 equivalent)
- Then Polymer supported Hunigs (1.2 equivalent) was added to the mixture.
- The required amine (1.2 equivalent) was added to the mixture
- Finally, Deoxyadenosine monophosphate (DMAP), (0.1 equivalent) was added
- The mixture was heated and stirred and heated under reflux overnight
- Then, the product was cooled and filtered under a vacuum and then evaporated and finally weighed.

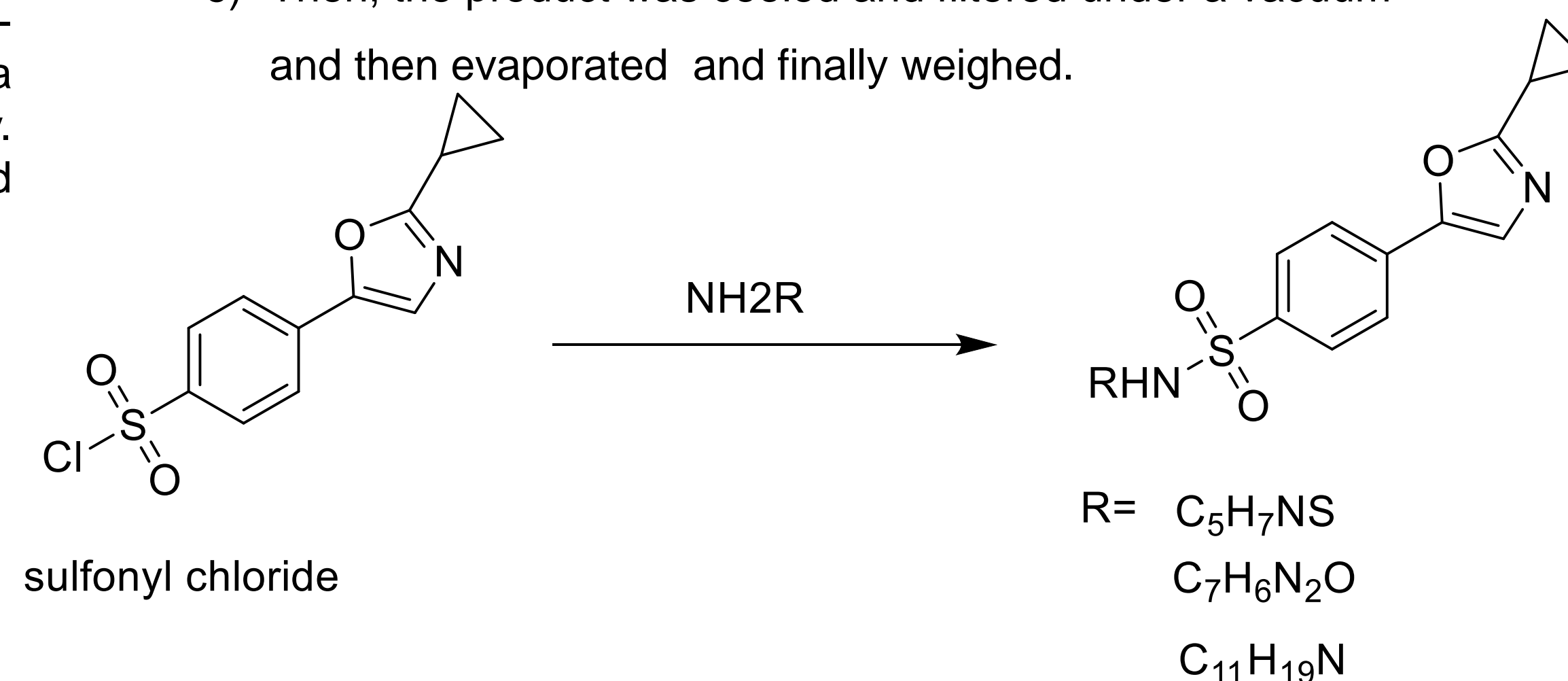


Figure 1- Synthesis of the lead compound reaction

Results

- The findings revealed that the substance identified as having promising chemical characteristics for a potential medication, shown in *Figure 2*.
- The properties included: Not blood-brain barrier permanent which is not preferred, high gastrointestinal absorption moderate solubility, bioavailability of 0.55.
- A logP of 3.42 (Lipophilicity of an organic compound can be described by a partition coefficient, logP)

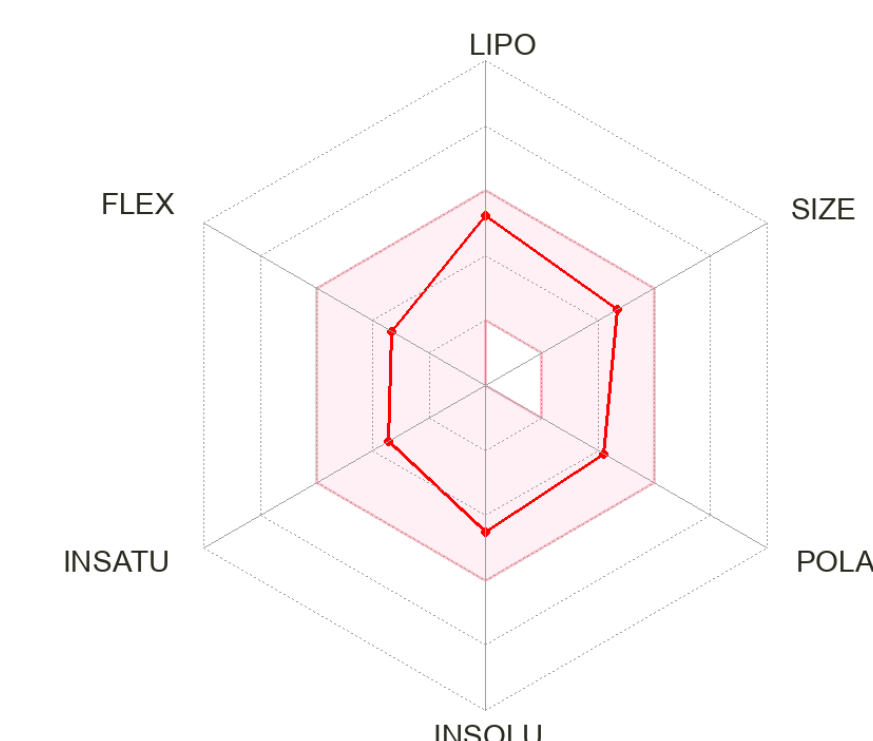


Figure 2- Bioavailability Radar of lead compound produced

The results of the synthetic approach described in Figure 1 were inconclusive as to whether the lead molecule had been successfully produced. Due to time restrictions and a limited quantity of starting materials, the final product was tested using 1H NMR spectroscopy, which produced ambiguous and varied data.

Conclusions

- A new synthetic pathway analogue molecule that has been successfully assessed and advances to bio screening.
- Developed approaches for compound purification

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