SIDE CHAIN AZASTEROLS AS ERGOSTEROL BIOSYNTHESIS INHIBITORS

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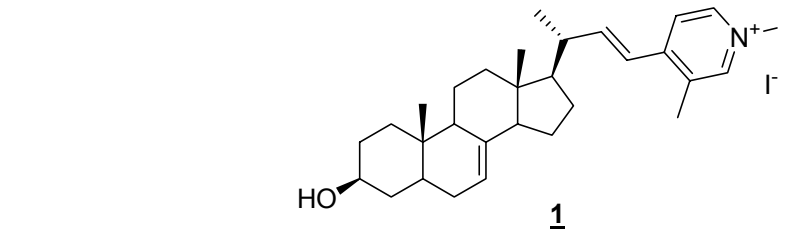
The increase in the incidence of fungal infections together with gradual rise in drug resistance highlight the need to find novel drugs. Amphotericine B and 5-fluorocytosine are the oldest ones [1]. Because of their pour selectivity and their great toxicity, new types of inhibitors of ergosterol biosynthesis have been developed: allylamines as inhibitors of squalene epoxidase, azoles as inhibitors of *C-14*α demethylase and morpholines as inhibitors of Δ^{14}-reductase and Δ^{8},Δ^{7}-isomerase [1,2].
Previous work on the synthesis of the marine steroid alkaloid plakinamine B **1** led to the identification of azasterols which inhibit the fungal enzyme *C-24* methyltransferase [3]. Taking these results in account, we decided to investigate structure-activity relationships in this new class of inhibitors. Starting from the aldehyde **2**, various aminosteroids were synthesised. They were obtained using reductive amination as crucial step. The so obtained compounds were screened for antifungal activityand their ability to inhibit selected enzymes in ergosterol biosynthesis.



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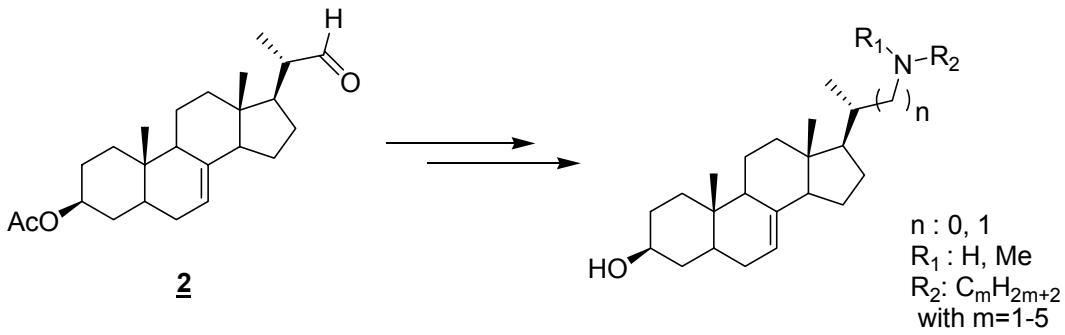

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[1] P.G Hartmann, D. Sanglard, *Current Pharmaceutical Design*, **1997**, 3, 177-208.
[2] D. Berg, M. Plempel, *Sterol Biosynthesis Inhibitors*, Wiley VCH, **1988**.
[3] Dissertation M. Gans, Ludwig-Maximilians University, Munich, **2003**.