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Design and Synthesis of 23-Amino-24,25,26,27-tetrakisnorlanosterolacetate and Derivatives as New Antimycotic Agents

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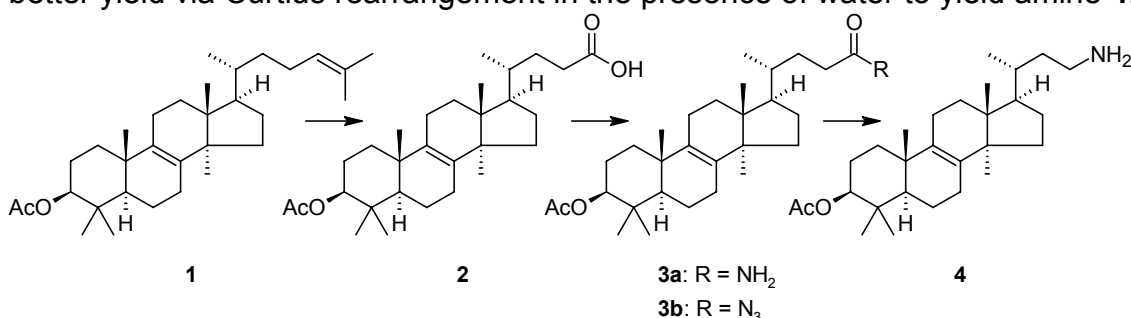
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In search of new antimycotic agents acting as ergosterol biosynthesis inhibitors we investigated widely new and optimized reaction pathways for preparing different types of triazasteroids [1, 2]. The various mono-, bi-, tri- and tetracyclic triazasteroidal compounds are designed as stable aza-analogues of carbocationic high energy intermediates (HEIA) of fungal enzymes [1, 2].

23-amino-24,25,26,27-tetrakisnorlanosterolacetate (**4**) and 24,26,27-triazalano-sterols derived of **4**, were prepared to act as inhibitors of Δ^{24} -methyltransferase catalyzing the introduction methyl in the side chain during the formation of lanosterol [3].

Two synthetic routes to generate 23-aminotetrakisnorlanosterolacetate **4** starting from lanosterolacetate **1** are described in this contribution. The common intermediate for both ways was 3-acetoxy-25,26,27-trinor-8-lanosten-24-acid (**2**), which was transformed into the carboxamide **3a** and carbonyl azide **3b**, respectively. Subsequently, various conditions were tried for the Hofmann rearrangement of amide **3a** but all of them gave amine **4** in only poor yield. 3-Acetoxy-25,26,27-trinor-8-lanosten-24-oyl azide (**3b**) was finally converted in better yield via Curtius rearrangement in the presence of water to yield amine **4**.



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