

SELECTIVE MONO-/DIFUNCTIONALIZATION OF PIPERAZINE WITH FATTY ACIDS RESIDUES AS WAY TO NEW PSEUDOCERAMIDES

Ballou Y.⁽¹⁾, Sadieva L.K.⁽¹⁾, Kopchuk D.S.^(1,2), Kovalev I.S.^(1,2), Zyryanov G.V.^(1,2)

⁽¹⁾ Ural Federal University

620002, Yekaterinburg, Mira St., 19

⁽²⁾ Postovsky Institute of Organic Synthesis UB RAS

620990, Yekaterinburg, S. Kovalevsky St., 22

The surface of human skin is protected by the stratum corneum (the outermost layer of the epidermis), and the lipids of the last one in its components form a layered structure to contribute to maintaining the skin's basic function. Keratinocyte intercellular lipids are composed of ceramide as a main component, which plays a central role in the maintenance of moisture and barrier function of the stratum corneum. And the reducing of ceramide (for instance, upon aging) results in reducing the protective barrier function of the stratum corneum and results in various skin diseases, including skin cancer. Therefore, there is high demand for research and development of a synthetic ceramides having a natural ceramide-like structure (so called pseudo-ceramides), which are easy to synthesize, and having improved physical properties. In this regard, in a frame of this work we have studied an approach to new pseudo-ceramides, constructed by the modification of piperazine by fatty or natural acid residues.

Initial attempts, based on the selective mono-acylation of piperazine this (Fig. 1) failed as resulted in a mixture of mono- and di-acylated products with poor selectivity. To overcome this, a tert-butoxycarbonyl (Boc) protection–deprotection strategy was (Fig. 2). As a result, several N-BOC and N-acyl derivatives were obtained, which are considered as new pseudo-ceramides.

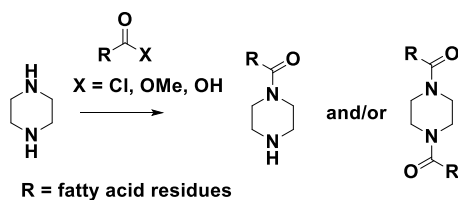


Figure 1. Non-selective acylation of piperazine

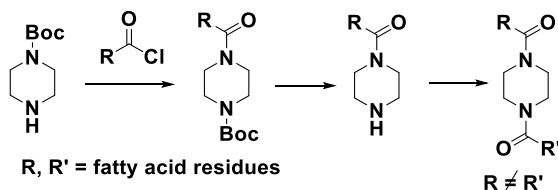


Figure 2. Selective mono-acylation of piperazine via Boc protection

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