A New Approach to Brassinolide and its Biosynthetic Precursors

Vladimir A. Khripach, Vladimir N. Zhabinskii, Nikolai D. Pavlovskii

Institute of Bioorganic Chemistry, National Academy of Sciences of Belarus, ul Kuprevicha, 5/2, 220141, Minsk, Belarus

Since 1979 synthesis of brassinolide has been a challenging goal for many chemists working in this field. The most difficult problem which has to be solved for preparation of brassinolide and congeners is construction of the side chain. A number of approaches to a solution of this problem made use of steroidal Δ²³-22-ketones, transformation of which into derivatives containing the side chain characteristic of brassinolide is well known.

Here we would like to report a new route to brassinolide 7. Many its biosynthetic precursors like teasterone 8 and 6-deoxobrassinolide 9 could be obtained also from the key intermediate 6. The proposed methodology is based on the 1,3-dipolar cycloaddition reaction of the steroidal nitrile oxide with low-molecular acetylene. The unstable nitrile oxide 3 was generated from the oxime 2 via successive steps of chlorination - dehydrochlorination, and without isolation it was reacted with propargyl bromide to give the bromoisoxazole 4. Hydrogenolysis of the latter proceeded with simultaneous debromination to afford the enaminoketone 5. Benzylation of 5 followed by hydride reduction and acid-catalysed rearrangement led to the enone 6. Its transformation into brassinosteroids and some analogues was carried out according to known methods.