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Synthesis Process Optimization of Rebaudioside A and R

Ning Cao[1, 2], Shenghua Cao[1, *], Zehong Li[2], Jianbin Zhang[2], Zhizhuang Ye[2], Dan Lu[2], Xiangdong Meng[2], Minyi Ye[2], Ziwei Zhu[2], Zekun Zhai[2]

[1]Sichuan Industrial Institute of Antibiotics, Chengdu, China

[2]Guangzhou Baihua Flavours and Fragrgances Co., Ltd., Guangzhou, China

Email address:

cnyjscd@163.com (Ning Cao), 2726908321@qq.com (Shenghua Cao)

[*]Corresponding author

Abstract

Rebaudioside A and R have attracted widespread attention in the food and pharmaceutical fields due to their unique physiologically active core structure and the ability to finely regulate sweetness, especially the aftertaste of traditional steviol glycosides. The quality of their extracts is affected by the natural conditions of the growing areas of stevia, which has greatly limited further research of Rebaudioside A and R. Hence, efficient synthetic paths for these potentially useful natural products are required. We herein reported that Synthesis process optimization of Rebaudioside A and R, which was synthesized from Steviol via esterification at boththe C-13 and C-19 positions respectively using Yamaguchi reagent and a glycosyl donor. The C-13 sulfonic acid group was removed. Consequently, activation of the hydroxyl group at C-13 through utilization of a Lewis acid enables nucleophilic interaction with a glycosyl donor. The results showed that trimethylsilyl trifluoromethyl sulfonate was used as Lewis acid and the reaction was carried out at -20 ℃ for 2 hours, the yield of intermediate 13-O-[2,3-bis-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)-β-D-furanosyl] Stevia (2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside) ester was 97%. Then cleavage of all acetyl groups by $NaOCH_3$ to afford target compounds. After the improvement of the process, the total yield of Rebaudiside A and Rwere 71.6~68.8%, and the purity of product were 99.99~99.97%. The structures of intermediates and products were confirmed by MS and NMR. In summary, process optimization of Rebaudioside A and R has been developed. New synthetic methods to synthesize key intermediate were also developed from cheap commercially available materials. All reaction steps were carried out by conventional reagents. The syntheses solve the problems of availability of Rebaudioside A and R for potential applications, as they are also excellent raw materials for the synthesis of other potential bioactive molecules.

Keywords

Rebaudiside A, Rebaudiside R, Glycochemistry, Process Optimization, Drug Materials