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Synthesis of a Novel Type of Glycophosphate Mimics

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Abstract: A series of novel type of glycophosphate mimics are synthesized by Todd reaction and their structure were determined on the basis of NMR, ESI-MS.

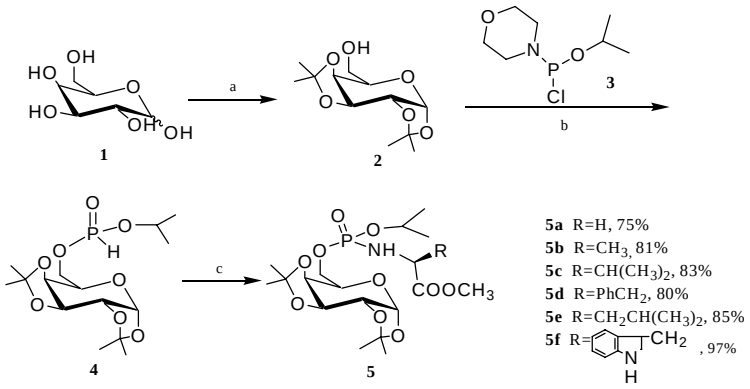
Keywords: Glycoconjugate, phosphate, *H*-phosphonate, amino acids.

The interest in "glycomimetic" is growing with the knowledge of the multifarious functions of carbohydrates, which are clarified in the biological process. Carbohydrate phosphates play very important roles in nature, such as components of nucleic acids and various coenzymes, and the donor in the biosynthesis and metabolism of sugar. Thus, the synthesis of phosphoglycose analogues is of great significance in investigation of the characteristic properties. There are many procedures reported[1]. In order to understand the influence of phosphate in the glycobiology and look for relationship between carbohydrate and amino acid, a series of novel type of glycophosphate are reported in this paper. Compounds **5a-f** are the minimized model compounds of carbohydrate -amino acid containing phosphorus.

The reaction of galactose **1** with 2, 2-dimethoxypropane in dry acetone in the presence of toluene-*p*-sulfonic acid as catalyst afforded the protected carbohydrate **2** in 70.5% yield[2]. Firstly, **2** was treated with tricoordinated compound **3**[3] in anhydrous dichloromethane. After the reaction was over, the mixture was evaporated the solvent and then hydrolyzed with 1*H*-tetrazole in CH_3CN-H_2O (10:1) to afford the key intermediate **4**[4]. Our strategy for the synthesis of compounds **5a-f** was based on the Todd reaction. And we have made some modifications on this reaction[5]. Thus, the reaction of carbohydrate *H*-phosphate **4** with L-amino acid methyl ester afforded the target molecule **5a-f** in good yield in CH_3CN /H_2O/Et_3N/CCl_4 system[5]. Compounds **4** and **5a-f** are all a pair of diastereomer with the ratio about 1:1 from ^{31}P NMR and ^{1}H NMR.

In conclusion, a series of novel type of glycophosphate mimics **5a-f** have been successfully synthesized in good yield. Their structures were established on the basis of NMR, MS spectral methods. In our knowledge, all of the compounds **5a-f** are reported as new compounds for the first time. The methodology described herein is currently being extended to other carbohydrates and will also be used to synthesize other novel glycopeptides containing phosphorus. We will report our progress in due course.

Scheme 1



Reagents and reaction conditions: (a) 2, 2-dimethoxypropane, toluene-*p*-sulfonic acid, acetone, RT, 4h; (b) ⅰ) 3,CH_2Cl_2, RT, 20 min., ⅱ) 1*H*-tetrazole, CH_3CN-H_2O(10:1), RT, 20 min; (c) CH_3CN/H_2O/Et_3N/CCl_4, RCH (NH_2)$COOCH_3$, 0°C, 30 min..

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References and Notes

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4. Spectral data of **4**: ^{31}P NMR (200 MHz, $CHCl_3$, δ ppm): 8.02, 7.18* (d, J_{P-H}=702 Hz), ^1H NMR (500 MHz, $CDCl_3$, δ ppm): 6.90, 6,89* (d, 1H, J_{P-H}= 702 Hz), 5.55, 5.54* (d, 1H, $J_{1,2}$=5.0 Hz), 4.64, 4.62* (t, 1H, $J_{2,3}$=2.5 Hz, $J_{3,4}$=8.0 Hz), 4.34 (dd, 1H, $J_{2,3}$=2.5 Hz, $J_{1,2}$=5.0 Hz), 4.25 (dd, 1H, $J_{4,5}$= 1.5 Hz, $J_{3,4}$=8.0 Hz), 4.03-4.23 (m, 3H), 1.54 (br, 3H), 1.45 (br, 3H), 1.37 (d, 3H, J_{P-H}=1.5 Hz), 1.36 (d, 3H, J_{P-H}=1.5 Hz), 1.33 (s, 6H); ESI-MS(+): *m/z* 367 (M+H), 389 (M+Na).
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