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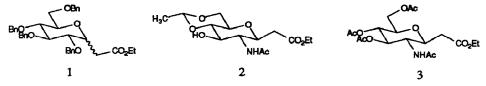
## SYNTHESIS OF C-GLYCOSIDES OF N-ACETYLGLUCOSAMINE BY DIRECT ALKYLATION OF 2-AMINO-2-DEOXY-2,3,4,6-TETRA-O-ACETYL GLUCOPYRANOSYL CHLORIDE

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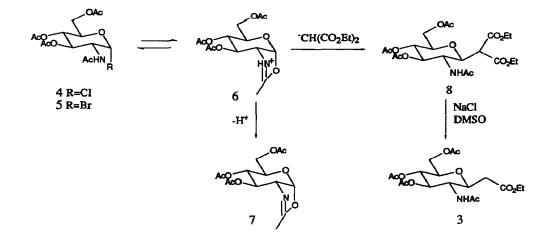
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ABSTRACT. The  $\beta$ -isomer of C-glycoside, ethyl 2-acetamino-2-deoxy-3,4,6-tri-O-acetyl- $\beta$ -D-glucopyranosylacetate(3) was prepared stereoselectively in two steps by reaction of 2-acetamino-2-deoxy-3,4,6-tri-O-acetyl- $\alpha$ -D-glucopyranosyl chloride(4) with potassium diethylmalonate and 18-crown-6, followed by decarboxylation.

C-Glycoside formation of carbohydrates becomes more interesting to carbohydrate chemists and biochemists, not only for the preparation of useful synthetic intermediates but also for the synthesis of carbohydrate biological probes which are inert to O-glycosidic bond cleavage by glycosidases. Though syntheses of N-acetylglucosamine C-glycosides such as 1 and 2 have been reported<sup>1,2</sup> for use in the preparation of lipid A analogues, their use has been limited because multistep routes are required for their preparation. We report here a more simple and convenient preparative method, with high stereoselectivity, which yields the  $\beta$ -isomer 3 exclusively.



To a solution of 60% KH in mineral oil(2.67gr, 40mmole), was added anhydrous dichloromethane(20ml). Diethyl malonate(6.4gr, 40mmole) and 18-crown-6(5.3gr, 20mmole) were added to this solution while maintaining it at 0°C. After additional stirring at 0°C for 15 min.,  $\alpha$ -D-acetochloroglucosamine <u>4</u> (3.66gr, 10mmole) was added to the solution in one portion. After additional stirring at room temperature for 20 min., acetic acid(2.4gr) was added to quench the reaction. The solution was washed with 5% aqueous sodium hydrogencarbonate(100ml), dried over anhydrous magnesium sulfate, filtered and concentrated. The product<sup>5</sup> was purified by silica gel flash column chromatography(eluent: CH<sub>2</sub>Cl<sub>2</sub>/MeOH=30/1). The first purified oily product was dissolved in DMSO(24ml) with NaCl(2.0gr, 34mmole). After refluxing for 16 hrs., DMSO was removed by



column chromatography(eluent: CH2Cl2/MeOH=30/1). 0.88gr(21%) pure oily product 36 was obtained.

Attempt of direct alkylation of acetobromogalactose and acetobromoglucuronic acid methylester by this method were both unsuccessful. It has been reported<sup>3</sup> that treatment of the acetobromoglucosamine 5 with pyridine at room temperature for 20 min. gave the oxazoline 6 in high yield(90%). It was therefore necessary to maximize the effective concentration of the nucleophile(malonate) for the formation of § to dominate over that of 7. Moisture in the reaction mixture also seemed to accelerate the formation of 7. As a result, it was important to add the minimum amount of the solvent and keep the reaction mixture anhydrous.

## **REFERENCES AND NOTES**

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2) A. Giannis; K. Sandhoff, Carbohydrate Res., 1987, 171, 201. and references cited therein.

 (a) M. Imoto; M. Yoshimura; M. Yamamoto; T. Shimamoto; S. Kusumoto; T. Shiba, <u>Bull. Chem. Soc. Jpn.</u>, 1987, 60, 2197.; (b) M. Imoto; H. Yoshimura; T. Shimamoto; N. Sakaguchi; S. Kusumoto; T. Shiba, <u>Bull.</u> <u>Chem. Soc. Jpn.</u>, 1987, 60, 2205.

4) Silica (Kieselgel 60 F254 Merck) eluent: CH2Cl2/MeOH= 20/1.

5) Diethyl 2-acetamino-2-deoxy-3,4,6-tri-O-acetyl- $\beta$ -D-glucopyranosylmalonate:  $R_F^4$  0.37; <sup>1</sup>H-n.m.r. (CDCl<sub>3</sub>, TMS, J in Hz)  $\delta$ =1.26(3H, t, J=8.0, CH<sub>3</sub>), 1.27(3H, t, J=8.0, CH<sub>3</sub>), 1.87(3H, s, CH<sub>3</sub>), 2.03(3H, s, CH<sub>3</sub>), 2.04(3H, s, CH<sub>3</sub>), 2.06(3H, s, CH<sub>3</sub>), 3.69(1H, m, H-5), 3.72(1H, d, J=8.0, CH), 4.06-4.35(8H, m, H-1, H-2, H-6, H-6' and O<u>CH<sub>2</sub>CH<sub>3</sub></u>), 5.09(2H, m, H-3 and H-4).

6) Ethyl 2-acetamino-2-deoxy-3,4,6-tri-O-acetyl-β-D-glucopyranosylacetate:  $R_F^4$  0.35;  $[\alpha]_D^{20}$ -1.94 (c 0.09, CHCl<sub>3</sub>); <sup>1</sup>H-n.m.r. (CDCl<sub>3</sub>, TMS, J in Hz) δ=1.23(3H, t, J=7.0, CH<sub>3</sub>), 1.90(3H, s, CH<sub>3</sub>), 2.00(3H, s, CH<sub>3</sub>), 2.01(3H, s, CH<sub>3</sub>), 2.04(3H, s, CH<sub>3</sub>), 2.58(2H, d, J=6.0, CH<sub>2</sub>), 3.62(1H, m, H-5), 3.79(1H, dt, J=10.0 & 6.0, H-1), 4.01-4.22(4H, m, H-2, H-6, H-6' and O<u>CH<sub>2</sub>CH<sub>3</sub>), 4.98(1H, dd</u>, J=10.0 & 10.0, H-4), 5.06(1H, dd, J=10.0 & 10.0, H-3). ;<sup>13</sup>C-n.m.r. (CDCl<sub>3</sub>, TMS) 37.70(C-2).; M.S. (Neg. FAB, matrix: NBA) 416.2(M-1).

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