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A NEW SYNTHETIC METHOD FOR 1-O-ACYL-β-D-GLUCOPYRANOSES USING TRI-O-TRIFLUOROACETYL-1,6-ANHYDROGLUCOSE. SYNTHESIS OF TULIPOSIDE-A.

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Summary: Tri-O-trifluoroacetyl-1,6-anhydroglucose 1 was proved to be an useful precursor of 1β-O-acylglucoses. Treatment of 1 with $TiBr_4$ in boiling CF_3COOH afforded 2,3,4,6-tetra-O-trifluoroacetyl-α-D-glucopyranosyl bromide, which on reaction with a silver carboxylate in benzene gave the 1β-O-acyl derivative. The TFA group was removed either by contact the compound with methanol or by alumina chromatography yielding 1β-O-acyl-D-glucopyranose. By this method tuliposide-A, 1-O-(γ-hydroxy-α-methylenebutyroyl)-β-D-glucopyranose, was synthesized.

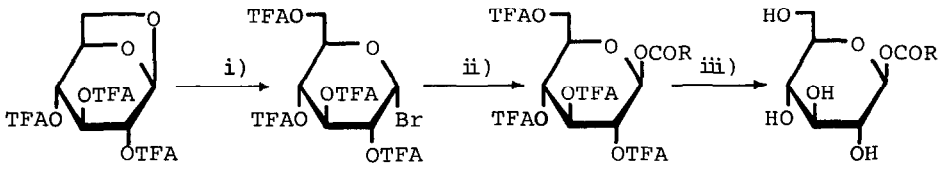
Synthesis of 1-O-acyl-β-D-glucoses carrying unsaturation at the acyl moiety such as tuliposide-A (4b)[1] by usual methods is difficult because they are sensitive both to solvolysis and hydrogenation which are general procedures for removal of protecting groups. This communication describes a new synthetic method applicable to those vulnerable 1β-O-acylglucoses with use of tri-O-trifluoroacetyl-1,6-anhydro-D-glucose.

It is believed that trifluoroacetyl (TFA) group has little synthetic value for protecting hydroxyl groups, since O-TFA group is so weak to be readily solvolysed. However, this disadvantage of TFA group may be avoided by performing all synthetic procedures in non-solvolytic conditions, when its instability turned to an advantage as a protecting group since it can be removed under very mild conditions at the final stage of synthesis.

Tri-O-TFA-1,6-anhydroglucose 1 was prepared by trifluoroacetylation of 1,6-anhydroglucose with $(CF_3CO)_2O$ and CF_3COONa as colorless needles, mp 62-64°C. This compound resisted to opening of 1,6-anhydro ring by $TiBr_4$ in $CHCl_3$, whereas tri-O-acetyl-1,6-anhydroglucose readily undergo the ring opening, on a similar treatment, to yield 2,3,4-tri-O-acetyl-α-D-glucopyranosyl bromide.[2] There are several precedents of such stabilization of C1-O6 linkage by an electronegative substituent at C-2.[3] This problem was solved by use of trifluoroacetic acid as a solvent. Thus, treatment of 1 with $TiBr_4$ in boiling trifluoroacetic acid (5 h) opened the 1,6-anhydro ring to furnish 2,3,4,6-tetra-O-TFA-α-D-glucopyranosyl bromide 2 (gum) in 69% yield. Evidently, attack of TFA cation formed from $TiBr_4$ and trifluoroacetic acid on O-6 caused irreversible cleavage of C1-O6 linkage by trifluoroacetylation with accompanied introduction of Br^- at C-1.

The structure of 2 was supported by the spectral data; IR: 1800, 890, 872. ^{1}H-NMR($CDCl_3$): δ 6.67(1H, d, J=4.1 Hz, C_1-H), 5.91(1H, t, J=9.7 Hz, C_3-H), 5.41 (1H, t, J=9.5 Hz, C_4-H), 5.13(1H, dd, J=4.1 and 9.7 Hz, C_2-H), 4.49-4.68(3H, $C_{5,6}$-H).

Treatment of 2 with silver butyrate in dry benzene for 4 days at room temp. gave 1-O-butyroyl-2,3,4,6-tetra-O-TFA-β-D-glucopyranose 3a, mp 98-99°C (96%). TFA group was removed either by dissolving 3a in dry methanol (5 min) with suspension of Amberlite-IRA-400(HCO_3^-) or by passing in acetone through a short alumina column (solvolytic cleavage of 1β-O-acyl group was thus minimized) yielding 1-O-butyroyl-β-D-glucopyranose 4a (gum, 88%) [δ 6.34(1H, d, J=7.7 Hz, C_1-H], which was identified by converting to the tetraacetate.[4]



1 2 3a,b 4a,b

TFA=$-COCF_3$, a: R=$-CH_2CH_2CH_3$, b: R=$-\underset{\underset{CH_2}{\|}}{C}-CH_2CH_2OH$

i) $TiBr_4$ in boiling CF_3COOH ii) RCOOAg in dry benzene iii) MeOH, r.t. or alumina

Similarly, reaction of the bromide 2 with silver γ-hydroxy-α-methylene-butyrate in dry benzene for a week at room temp. yielded 3b as a gum (87%). TFA group was removed as described above, yielding 1-O-(γ-hydroxy-α-methylene-butyroyl)-β-D-glucopyranose (tuliposide-A) 4b (83%) as a gum, whose structure was identified by the following spectral data [IR(film): 3350, 1728, 1680, 1550, 970. ^{1}H-NMR(Py-d_5): δ 6.39(1H, d, J=7.6 Hz, C_1-H), 6.46 and 5.82(each 1H, s, CH_2=C<), 3.91-4.46(6H, $C_{2,3,4,5,6}$-H), 4.02(2H, t, J=6.6 Hz, $-CH_2\underline{CH_2}OH$), 2.82 (2H, t, J=6.6 Hz, $-\underline{CH_2}CH_2OH$). ^{13}C-NMR(Py-d_5): δ 166.3(C=O), 138.2($CH_2=\underline{C}<$), 127.8 ($\underline{CH_2}$=C<), 96.3(C_1), 79.4(C_5), 78.3(C_3), 74.0(C_2), 70.9(C_4), 62.0(C_6), 60.9 ($-CH_2\underline{CH_2}OH$), 36.0($-\underline{CH_2}CH_2OH$)], and by converting to the pentaacetate.[5] The compound 4b was proved to be unstable on solvolysis; for example, in pyridine-d_5 it completely decomposed to D-glucose and α-methylene-γ-butyrolactone when being kept for 30 h at room temp.

References

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