Int. J. Chem. Sci.: 13(1), 2015, 63-66
ISSN 0972-768X
www.sadgurupublications.com

GLYCOSIDATION OF SOME PHARMACEUTICALLY ACTIVE COMPOUNDS

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ABSTRACT

Glycosidation studies of some insecticidal compounds and pharmaceutically active bases have been reported. The method involved the classical S_N2 displacement of trifluoromethanesulfonyloxy group in a suitably protected glucose moiety **(1)** through a variety of insecticidal bases **(2-4)** and active bases **(5-7)**, which afforded corresponding glycosides **(8-13)** in good yield. The difficulties which, sometimes, are encountered during displacement reactions in carbohydrates are absent. The method provides an easy access for the syntheses of these potential compounds.

Key words: Glycosidation, Insecticides, Pyrrolines, Anabasine, Anatabine, Nornicotine

INTRODUCTION

The relative reactivities of the methanesulfonate (mesylate), p-toluenesulfonate (tosylate) and trifluoromethanesulfonate (triflate), 1.00, 0.70 and 56,000, respectively, indicated that triflate is the leaving group of choice in many displacement reactions[1]. The high selectivity observed during these reactions has prompted us to carry out substitution of triflyl group in a suitably protected sugar triflate with different pharmaceutically interesting bases.

A new class of heterocyclic amino sugars was reported by Ahmed et al.[2] in which the primary triflyl group in 1,2:3,4-di-O-isopropylidene-6-triflyl-α-D-galactopyranose was replaced with a variety of heterocyclic bases to afford the corresponding 6-amino-6-deoxy sugars. These reactions demonstrated the high selectivity, reactivity and clear advantage of triflyl group over its common counterparts and thus prompted us to further investigate such coupling reactions between sugar and pharmaceutically interesting bases using a relatively hindered secondary sugar triflate **(1)**.

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EXPERIMENTAL

Synthesis of glycosides (8-13) (General procedure)

In each case the sugar triflate **(1)** (1 mmol) was dissolved in dimethylformamide (5 mL) and added the corresponding bases **(2-7)** (4 mmols) at –20°C under nitrogen. After 15 minutes, the reaction mixture was gradually warmed to room temperature and continues stirring for over night. Dried in vacuo and the products were isolated through column chromatography over silica gel using toluene-methanol (8.0 : 2.0) as the eluent.

RESULTS AND DISCUSSION

The compounds **(8-13)** were identified by their elemental analyses and spectral data. The percentage yields and physical constants are described in Table 1.

Table 1: Physical constants and yields of Compounds (8-13)

S. No.	Product[a]	Yield[b] (%)	FDMS [M^+]	R_f [c]
1	1,2:5,6-Di-O-isopropylidene-3-anabasino-α-D-allofuranose **(8)**	53	404	0.46
2	1,2:5,6-Di-O-isopropylidene-3-nornicotino-α-D-allofuranose **(9)**	59	390	0.43
3	1,2:5,6-Di-O-isopropylidene-3-anatabino-α-D-allofuranose **(10)**	55	402	0.46
4	1,2:5,6-Di-O-isopropylidene-3-pyrrolidino-α-D-allofuranose **(11)**	62	313	0.42
5	1,2:5,6-Di-O-isopropylidene-3-(3-pyrrolino)-α-D-allofuranose **(12)**	67	311	0.44
6	1,2:5,6-Di-O-isopropylidene-3-(2,5-dimethyl-3-pyrrolino)-α-D-allofuranose **(13)**	65	339	0.45

a: All products gave correct elemental analyses

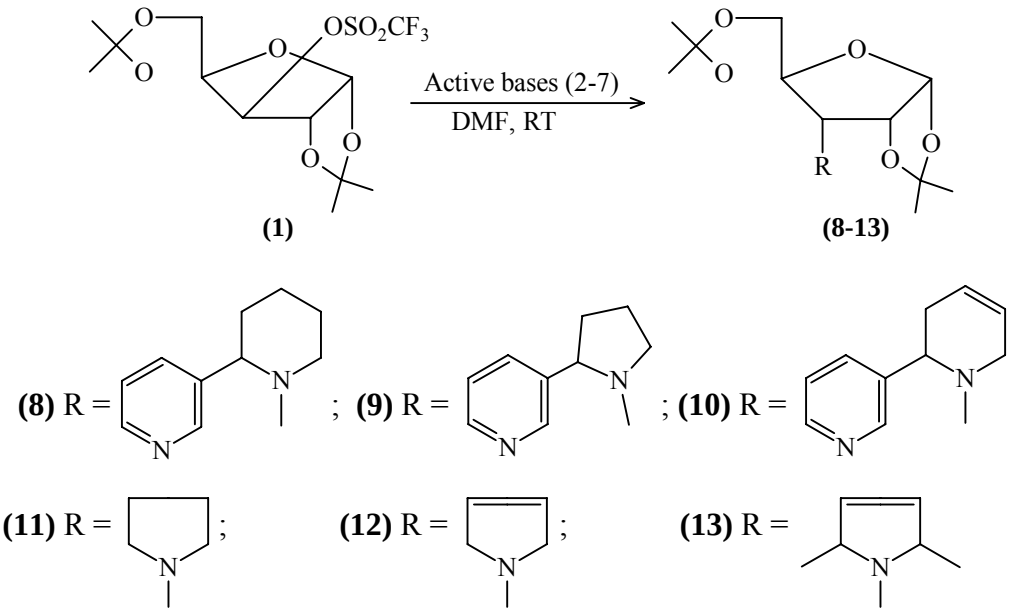
b: The isolated yield

c: Toluene : Methanol (8:2)

These studies have now resulted in one pot synthesis of new pharmacologically interesting glycosides **(8-13)** through a smooth displacement of triflyl group in 1, 2:5, 6-Di-

O-isopropylidene-3-triflyl-α-D-glucofuranose **(1)** with a variety of active bases. The active bases used in these reactions are precursors of some insecticides as well as reported insecticides.

1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose was prepared by previously published method[3] from D-glucose. Reaction with trifluoromethanesulfonic anhydride in the presence of pyridine at 0°C afforded corresponding triflate **(1)**[4]. On the other hand anabasine **(2)**, nornicotine **(3)**, anatabine **(4)**, pyrrolidine **(5)**, 3-pyrroline **(6)** and 2,5-dimethyl-3-pyrroline **(7)** were used to demonstrate the scope of reaction (**Scheme 1**). The substitution in **(1)** is known to be difficult[5-6] but the effectiveness of these reactions can be attributed to the unusual ease of displacement of the triflyl group. The reactions were carried out in dimethylformamide under the conditions described in the experimental part to afford the corresponding glycosides **(8-13)**, which were purified by column chromatography over silica gel. Their structures were assigned on the basis of analytical and spectral data.



Scheme 1

The reaction of **(1)** had led to the allo-products owing to stereochemical inversion at C-3. The key evidence to this effect was provided by the coupling constants in the ^{1}H-NMR spectra, particularly $J_{2,3}$ and $J_{3,4}$. In **(1)**, H-3 showed a coupling of 3.11 Hz with H-4 but it does not couple with H-2 which appeared as doublet owing to coupling with H-1 ($J_{1,2}$ = 3.70 Hz). On the other hand, in products **(8-13)**, H-2 gives a triplet due to coupling of

the same magnitude (3.70 Hz) with H-1 and H-3, while H-3 showed no coupling with H-4. The formation of allo-products can be rationalized by an S_N2 or ion-pair mechanisms. However, the observation that the reaction rates varied considerably with the nature and concentration of the bases, suggested the operation of an S_N2 mechanism rather than a unimolecular process. In the light of these observations, it may be concluded that the displacement reactions of the secondary triflyl group by various pharmaceutically interesting bases provide a better approach to these types of potential compounds which may have more pronounced insecticidal activities than the parent ones.

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Revised : 22.09.2014 *Accepted : 24.09.2014*