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RESEARCH ARTICLE

ONE POT SYNTHESIS OF SOME NEW AMINO SUGARS

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Abstract

A mild one pot synthesis of some new 3-amino-3-deoxy sugars is reported. The method involved the classical S_N2 displacement of trifluoromethanesulfonyloxy group in a suitably protected glucose moiety (1) through a variety of secondary heterocyclic bases (2 – 6) which afforded corresponding heterocyclic amino sugars (7 – 11) in good yield. The difficulties which, sometimes, are encountered during displacement reactions in carbohydrates are absent. The method provides not only an easy route for the syntheses of these potential compounds but also a possible entry into new types of alkaloidal N-glycosides.

Keywords: 3-amino-3-deoxy sugars, trifluoromethanesulfonyloxy group, alkaloidal N-glycosides.

Experimental

Preparation of Heterocyclic amino sugars (7 – 11) (General Procedure)

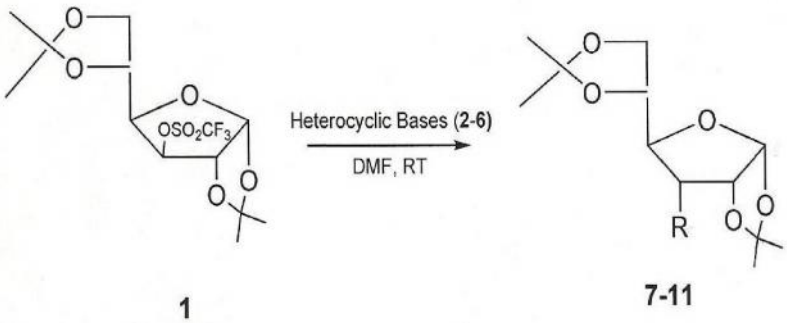
In each case the sugar triflate **1** (1 mmol) was dissolved in dimethylformamide (5 ml) and added the corresponding heterocyclic amine **2** - **6** (4 mmols) at –20 °C under nitrogen. After 15 minutes the reaction mixture was gradually warmed to room temperature and continue stirring for 18 hours. Dried in vacuo and the products were isolated through column chromatography over silica gel using toluene-methanol (8.5:1.5) as the eluent. The compounds **7** - **11** were identified by their elemental analyses and spectral data. The percentage yields and physical constants are described in Table-1.

Results and Discussions

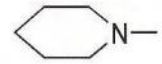
The relative reactivities of the methanesulfonate (mesylate), p-toluenesulfonate (tosylate) and trifluoromethanesulfonate (triflate), 1.00, 0.70 and 56,000, respectively, indicated that triflate is the leaving group of choice in many displacement reactions (Stang et al., 1982). The high selectivity observed during these reactions has prompted us to carry out substitution of triflyl group in a suitably protected sugar triflate with different heterocyclic bases.

A new class of heterocyclic amino sugars was reported by one of us 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 (Ahmed et al., 1988). These reactions demonstrated the high selectivity, reactivity and clear advantage of triflyl group over its common counterparts and thus prompted us to further investigate the C-N coupling reactions between sugars and heterocyclic bases in relatively hindered secondary sugar triflates. These studies have now resulted in one pot synthesis of new pharmacologically interesting heterocyclic amino sugars through a smooth displacement of triflyl group in 1,2:5,6-Di-O-isopropylidene-3- triflyl- α-D-

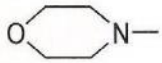
Scheme-1

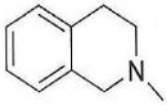


1 7-11

(7) R = 

(8) R = 

(9) R = 

(10) R = 

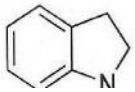
(11) R = 

Table-1

Physical constants and yields of compounds **7** – **11**

S. No.	Product[a]	Yield[b]	$[a]_D^{20}$ [c] (o)	FDMS [M^+]
1	1,2:5,6-Di-O-isopropylidene-3-piperidino-α-D-allofuranose (**7**)	57	-47.21	3270.53
2	1,2:5,6-Di-O-isopropylidene-3-(4-methylpiperidino)-α-D-allofuranose (**8**)	65	-61.37	3410.58
3	1,2:5,6-Di-O-isopropylidene-3-morpholino-α-D-allofuranose (**9**)	69	-49.28	3290.56
4	1,2:5,6-Di-O-isopropylidene-3-(1,2,3,4-tetrahydroisoquinolino) -α-D--allofuranose (**10**)	57	17.25	3750.45
5	1,2:5,6-Di-O-isopropylidene-3-indolino-α-D-allofuranose (**11**)	48	-57.21	3610.47

a: All products gave correct elemental analyses.
b: The isolated yield.
c: chloroform
d: Toluene-methanol (8:2)

glucofuranose with a variety of heterocyclic bases. The heterocyclic bases used in these reactions form part of different classes of alkaloids indicating the reaction pathway may also have an access to new types of alkaloidal N-glycosides.

1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose was prepared by previously published method (Schmidt, 1963) from D-glucose. Reaction with trifluoromethanesulfonic anhydride in the presence of pyridine at 0 °C afforded corresponding triflate (**1**)[4]. On the other hand piperidine (**2**), 4-methyl piperidine (**3**), morpholine (**4**), 1,2,3,4-tetrahydroisoquinoline (**5**) and indoline (**6**) were used to demonstrate the scope of reaction (Scheme-1). The substitution in **1** is known to be difficult (Freudenberg et al. 1926; Nayar et al., 1968) 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 to afford the corresponding heterocyclic amino sugars **7** - **11** which were purified by column chromatography over silica gel. Their structures were assigned on the basis of analytical and spectral data. 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 3.12 Hz with H-4 but it does not couple with H-2 which appeared as doublet owing to coupling with H-1 ($J_{1,2}$ = 3.71 Hz). On the other hand, in products **7** – **11**, H-2 gives a triplet due to coupling of the same magnitude (3.71 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 amines, suggested the operation of an S_N2 mechanism rather than a unimolecular process. In the light of the foregoing observations it may be concluded that the displacement reactions of the secondary triflyl group by various heterocyclic amines provide a better approach to these types of potential compounds.

References

1. Stang, P. J., Hanack M. and Subramanian, L. R. 1982, *Synthesis*, 85.
2. Ahmed, Z., Kazmi, S. N. H., Ahmed, S. S., Khan, A. Q. and Malik, A., 1988, *Synthetic Commun.* 18(5)**,** 501.
3. Schmidt, O. T., 1963, *Methods Carbohydr. Chem.*, 320.
4. Hall, L. D. and Miller, D. C., 1975, *Carbohydr. Res.*, *C1*, 40.
5. Freudenberg, K., Burkhart, G. and Braun, E., 1926, *Ber. Dtsch. Chem. Ges.*, 59, 714.
6. Nayar, U. G. and Whistler, R. L., 1968, *J. Org. Chem.*, 34, 3819.