A New Efficient Access to Aminodeoxy Sugars

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A mild and convenient synthesis of aminodeoxy sugars is described, involving the esterification of partially protected carbohydrates with trifluoromethanesulphonic anhydride and the reaction of the resulting trifluoromethanesulphonates with ammonia; the difficulties which sometines are encountered in displacement reactions in carbohydrate systems are absent.

Aminodeoxy sugars are widely distributed in nature in free or combined forms, and some of them constitute the essential parts of highly effective antibiotics.[1] Although several types of reaction have been useful in obtaining these compounds, displacement processes generally have been most effective.[2] Many displacement reactions, however, suffer from severe limitations[2—4] including competing elimination reactions, and the inability to effect displacement in certain situations, particularly when the leaving group is attached to a secondary carbon atom. A reaction which overcomes many of these

Table 1. Reactions of sugar triflates with a 2 M solution of ammonia in chloroform

Substrate	Reaction time/h	Product[a]	Yield[b] (%)	M.p. or b.p./°C (*p*/mmHg)	$[\alpha]_D^{20}$/°
Benzyl 2,3-anhydro-4-triflyl-α-D-ribopyranoside (**1**)[f]	5	Benzyl 2,3-anhydro-4-amino-4-deoxy-β-L-lyxopyranoside (**7**)	52.7 (75)[c]	37—38	+105[d]
Benzyl 2,3-anhydro-4-triflyl-β-L-ribopyranoside (**2**)[f]	5	Benzyl 2,3-anhydro-4-amino-4-deoxy-α-D-lyxopyranoside (**8**)[f]	75.7 (82)[c]	48—49	+91[d]
Benzyl 2,3-anhydro-4-triflyl-α-D-lyxopyranoside (**3**)[f]	5	Benzyl 2,3-anhydro-4-amino-4-deoxy-β-L-ribopyranoside (**9**)[f]	63.2 (77)[c]	55	+54.4[d]
1,2 : 3,4-Di-*O*-isopropylidene-6-triflyl-α-D-galactopyranose (**4**)[g]	7	1,2 : 3,4-Di-*O*-isopropylidene-6-amino-6-deoxy-α-D-galactopyranose (**10**)[h]	77	122—124 (0.7)	−70.85[d]
1,2 : 5,6-Di-*O*-isopropylidene-3-triflyl-α-D-allofuranose (**5**)[g]	14	1,2 : 5,6-Di-*O*-isopropylidene-3-acetamido-3-deoxy-α-D-glucofuranose (**11**)[i]	75	92—93	+40.5[e]
1,2 : 5,6-Di-*O*-isopropylidene-3-triflyl-α-D-glucofuranose (**6**)	36	1,2 : 5,6-Di-*O*-isopropylidene-3-amino-3-deoxy-α-D-allofuranose (**12**)[i]	35 (58)[c]	95—96	−36[d]

[a] All the compounds gave correct elemental analyses. [b] Yields refer to the isolated products after purification. [c] The figures in parentheses represent improved yields obtained under different reaction conditions. [d] $CHCl_3$. [e] $C_2H_2Cl_4$. [f] Ref. 7. [g] Ref. 9. [h] Ref. 10. [i] Ref. 11.

limiting factors is the displacement of the trifluoromethanesulphonyloxy (triflyl) group with ammonia. The effectiveness of this reaction can be attributed to the unusual ease of displacement of the triflyl group which permits facile introduction of amino-groups at both primary and secondary positions. The present one-step procedure is markedly superior to traditional methods employing intermediate azidodeoxy sugars, particularly for the introduction of amino-groups in the presence of highly reduction-sensitive functionalities.

The scope of the reaction was demonstrated by employing a variety of sugar trifluoromethanesulphonates (triflates) including the secondary triflate (**6**) for which the substitution is known to be difficult[5,6] (Table 1). In each case, compound (**1**)—(**6**) (3 mmol) was dissolved in absolute chloroform (20 ml), a 2 M solution (20 ml) of dry gaseous ammonia in absolute chloroform was added, and the mixture heated at 50 °C for the times recorded in Table 1. The products were isolated by conventional procedures and purified either through direct crystallization or column chromatography over silica gel. The aminodeoxy sugar obtained from (**5**) was, however, not stable at room temperature and could only be characterized *via* its crystalline *N*-acetyl derivative. Table 1 shows satisfactory yields for all the amines except (**12**). Different reaction conditions (1,2-dichloroethane, 70 °C, 48 h) could nevertheless be used to improve its yield to 58%. The structures were assigned to compounds (**7**)—(**12**) on the basis of analytical and spectral data, and were confirmed in each instance by comparison with an independently synthesized sample of the aminodeoxy sugar.

Since nucleophilic substitutions in secondary triflates invariably lead to products of inverted configuration, they probably involve an S_N2 mechanism. The evidence to this effect was also provided by the ease of displacements in compounds (**1**)—(**3**). In 2,3-anhydro sugars the formation of a transition state at C-4 is favoured not only by the neighbouring oxirane ring,[7,8] but also by the molecular geometry which shows a dipole moment in the direction of the C–O bond and not parallel to the newly forming C–N bond.[7] The combination of these two factors allowed the facile introduction of the amino group even at −10 °C by passing dry gaseous ammonia into acetone solutions of (**1**)—(**3**) for 1 h, resulting in the improved yields of the amines (**7**)—(**9**) given in parentheses in Table 1.

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