# Regioselective One Pot Approach to Aminodeoxy Sugars *via* Aminosilanes

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A novel one-step synthesis of regioisomerically pure aminodeoxy sugars (**6**)—(**11**) has been achieved by *trans*-diaxial cleavage of the oxirane ring in 2,3-anhydro sugars (**1**)—(**5**) with *N,N*-diethyltrimethylsilylamine or its *N,N*-dimethyl analogue, using $AlCl_3$ as catalyst; the reagents work under mild conditions and avoid the difficulties which sometimes are encountered in ring-opening reactions of epoxy sugars.

Aminodeoxy sugars are extremely important owing to their occurrence as essential parts of a large variety of highly effective antibiotics.[1] The biochemical interest attached to these compounds has led us to investigate the possibilities of synthesis in this group. One method employed, amongst others, for the synthesis of monoamino sugars involves cleavage of the oxirane ring in anhydro sugars by nitrogen nucleophiles.[2a] The epoxides of monocyclic sugars have a flexible half-chair conformation[3] and exist in two forms $^5H_o$ and $^oH_5$.[4] *trans*-Diaxial epoxide cleavage in these leads in general to a binary mixture of isomeric aminodeoxy sugars.[2b] Moreover, most of these reactions often require forcing reaction conditions which adversely affect the yields of the desired compounds. In this communication we report *trans*-diaxial ring-opening in 2,3-anhydro sugars *via* aminosilanes, and our results demonstrate the potential of this synthetically attractive strategy and show the possibility of controlling the regioselectivity. *N,N*-Diethyltrimethylsilylamine (TMSDEA) and *N,N*-dimethyltrimethylsilylamine (TMSDMA), which are readily available versatile reagents, were employed in the presence of anhydrous aluminium chloride as catalyst. We found that epoxide ring-opening with these reagents results in partial transformation to give the aminodeoxy sugars. The product in each case arises from the more stable predominant

**Table 1.** Reactions of 2,3-anhydro sugars (**1**)—(**5**) (see text for details) with aminosilanes.

| Starting compound | Reagent | Reaction time/h | Product | % Yield[d] | $[\alpha]_D^{20}$ ($CHCl_3$) | M.p./°C | F.d.m.s.[e] ($M^+$) |
|---|---|---|---|---|---|---|---|
| (**1**) | TMSDEA | 96 | Methyl 2-diethylamino-4.6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (**6**) | 46 | +30° | Oil | 337 |
| (**2**) | TMSDEA | 96 | Methyl 3-diethylamino-4,6-*O*-benzylidene-3-deoxy-α-D-altropyranoside (**7**) | 48 | +120.48° | Oil | 337 |
| (**3**) | TMSDEA | 72 | Benzyl 3-diethylamino-3-deoxy-β-L-xylopyranoside (**8**) | 53 | +33° | Oil | 295 |
| (**4**) | TMSDEA | 48 | Methyl 3-diethylamino-3-deoxy-α-D-glucopyranoside (**9**)[b] | 41 | +106° | 102 | 249 |
| (**4**) | TMSDMA | 48 | Methyl 3-dimethylamino-3-deoxy-α-D-glucopyranoside (**10**)[b,c] | 43 | +122° | 81 | 221[f] |
| (**5**) | TMSDMA | 48 | Methyl 3-dimethylamino-3,6-dideoxy-α-D-glucopyranoside (**11**)[c] | 43 | +122° | 81 | 205 |

[a] All the products gave correct elemental analyses. [b] Characterized as the hydrogen chloride. [c] Ref. 12. [d] Yields are given for the isolated products after column chromatography. [e] Field desorption mass spectrometry. [f] Free base.

conformation of the epoxy sugar. Other isomers of the aminodeoxy sugars were either absent or formed in trace amounts and could be eliminated easily by column chromatography over silica gel. Apart from the amino sugars, the unchanged anhydro sugars could also be recovered and recycled.

The scope of the reaction was demonstrated by employing a variety of 2,3-anhydro sugars including methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**1**),[5] methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside (**2**),[6] benzyl 2,3-anhydro-β-L-ribopyranoside (**3**),[7] methyl 2,3-anhydro-α-D-allopyranoside (**4**),[8] and methyl 2,3-anhydro-6-deoxy-α-D-allopyranoside (**5**).[9] In each case, to a solution of the compound (**1**)—(**5**) (4 mmol) and aminosilane (4 mmol) at 0 °C in dry dichloromethane, $AlCl_3$ (4 mmol) was rapidly added and the mixture refluxed for the times recorded in Table 1. Further heating results in the formation of a complex mixture of side products. The product and the unchanged epoxy sugar were separated by column chromatography over silica gel using chloroform–methanol (23.5 : 1.5) as solvent.

The anhydro sugars (**1**) and (**2**) exist in fixed $^oH_5$ conformation owing to *trans*-fused 4,6-*O*-benzylidene formation, and TMSDEA cleavage gives the diaxial products (**6**) and (**7**) according to the Furst–Plattner rule.[10] The conformation of (**3**) on the other hand, is dynamic but $^1$H n.m.r. spectroscopy[4] has shown it to exist almost entirely in the favoured half-chair conformation $^oH_5$ and *trans*-diaxial cleavage with TMSDEA gives the 3-substiuted product (**8**). The attack by the reagent at position 3 is also favoured by steric considerations as position 2 is comparatively blocked by the bulky substituent at C-1, explaining the absence of 2-substituted products from the reaction mixture. The anhydro sugars (**4**) and (**5**) undergo *trans*-diaxial cleavage with TMSDEA and TMSDMA to yield the corresponding dialkylamino sugars, of which the diethylamino product from (**5**) was extremely susceptible to aerial oxidation and could not be obtained in a pure form for characterization. In these epoxy sugars the conformation during the reaction is evidently $^5H_o$, which is stabilized in the transition state by hydrogen bonding between the 4-hydroxy group and the ring oxygen atom. The participation of a $^5H_o$ conformation has already been described in the literature[11] to explain the persistent formation of glucopyranoside derivatives from this epoxy sugar. The structures of the products were fully supported by microanalytical results and spectroscopic data. The conformations were assigned on the basis of chemical shift correlations and the relative coupling constants in 300 MHz $^1$H n.m.r. spectra. The compounds (**6**), (**7**), (**9**), (**10**), and (**11**) were shown to exist wholly in the *C*1 chair form while the 1*C* form could be assigned to (**8**).

The absence of a trimethylsilyl ether moiety in the products suggests the formation of a stable salt intermediate with aluminium chloride. Hydrolysis of this intermediate finally provides the desired unsilylated aminodeoxy sugars. The participation of such an intermediate has already been observed by us during Lewis-catalysed epoxide ring-openings with trimethylsilyl azide. In conclusion, TMSDEA and TMSDMA can serve as reagents of choice for the direct introduction of amino-functions in carbohydrate systems. The one-step procedure has the added advantage of allowing the recovery and recycling of unreacted sugars, and 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.

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