Reductive Cleavage as a Route to Carbohydrate Enolates. Applications to the Synthesis of C-Linked Disaccharides

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The carbohydrate-derived α-bromo ketones 4 and 5 undergo reductive cleavage using either Zn–Cu or CeCl₃–NaI and the resulting enolates are trapped by carbohydrate-based aldehydes 6, 7 and 14 to give C-disaccharide derivatives.

The C-1 alkylation of a nucleophilic sugar to give a C-glycoside provides an attractive entry to this important class of carbohydrate derivatives and several approaches towards this objective have been described. However, current solutions do not readily accommodate the presence of a functional group providing an attractive entry to this important class of carbohydrate derivatives.

The reactivity of enolates obtainable from the sterically more demanding 3,6-anhydro-bridged ulosyl bromide 52 have also been examined. Accordingly, cerium-mediated activation of 5 (a procedure that proved to be more efficient than use of zinc) and trapping with aldehydes 6 and 7 gave aldol adducts 10 (as a 4:1 mixture of diastereomers at C-6, 46% from 6) and 11 (as a 10:1 mixture of diastereomers at C-5, 40% from 7), respectively (Scheme 2). While it was possible to separate these diastereomeric mixtures, dehydration of the crude product in each case gave a single enone 12 (62% from 10) and 13 (34% from 11), respectively. Enone 13 has recently been used in the synthesis of the C₁₁-glycosyl component of the herbicides and, as part of this study, we have also examined the nucleoside-based aldehyde 14 as an aldol substrate. The extreme sensitivity of aldehyde 14 towards basic conditions precluded the use of enolates derived from 3a, but reaction of the cerium enolate obtained from bromide 5 gave a 1:1 diastereomeric mixture of aldol adducts which were immediately dehydrated to give enone 15 (20% overall from 14).

Scheme 1 Reagents and conditions: i, 4, Zn–Cu, THF, −35 °C; ii, 4, CeCl₃, NaI, THF, room temp.
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References


6. The reaction of the zinc enolate derived from 4 towards simple aldehydes, together with the stereoselective reduction (using NaBH₄/CH₃CN) of the resulting 2-keto-1,3-α-glycosides to give the corresponding 2-hydroxy-1-C-glycosides has been described: F. W. Lichtenthaler, S. Schwidetzky and K. Nakamura, Tetrahedron Lett., 1990, 31, 71.


12. NHBz

Footnotes

† The structures of 9a,b and 9a,b are based on 1H NMR analysis, assignment of the C-glycosyl ‘anomeric’ configuration (α vs. β) was established by NOE studies, and in the case of 9a, also by CD data of the corresponding enolone ester, readily formed by base-induced 9,10-elimination of benzoic acid.