Pergamon

Tetrahedron Letters 41 (2000) 225–227

TETRAHEDRON LETTERS

C-Glycosylation via radical cyclization: synthetic application to a new *C*-glycoside

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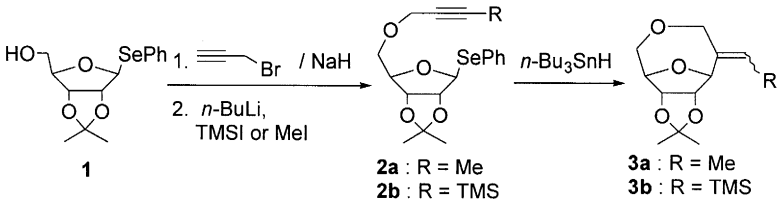
Received 13 September 1999; revised 18 October 1999; accepted 22 October 1999

Abstract

Radical cyclization of ribo-phenylselenoglycoside tethered with propargyl moieties on C-5 hydroxyl group afforded new potential intermediates for the synthesis of *C*-nucleside derivatives.

New routes to *C*-glycosides have been developed over recent years due to their structural attraction as well as useful biological activities.[1] Most of the approaches have concerned the stereoselective *C*-glycosylation reaction at the first stage. Several selective methods involving connecting the necessary functional groups to the adjacent one such as an alcohol have been explored recently and proved to be an insured way to achieve the desired stereochemistry.[2] In this paper, we report a new radical cyclization reaction of phenylselenofuranoside tethered with propargyl moieties on C-5 hydroxyl group and a synthetic application. After the cyclization reaction, the carbon–oxygen bond of the tether is expected to be oxidatively cleaved for further manipulation (Scheme 1).



Scheme 1.

Propargyl intermediates **2** have been prepared by using the known intermediate **1**[2d] via a two-step sequence, treating with propargyl bromide/NaH and deprotonation with *n*-BuLi followed by addition of electrophiles such as TMSCl or MeI, providing **2a** or **2b** with the same yield of 78% in two steps. Under the conventional radical reaction condition, Bu_3SnH/AIBN in toluene (80°C), **2** afforded the desired products, 93% for **3a** and 82% for **3b**, respectively.[3] The radical cyclization of propagyl ether without

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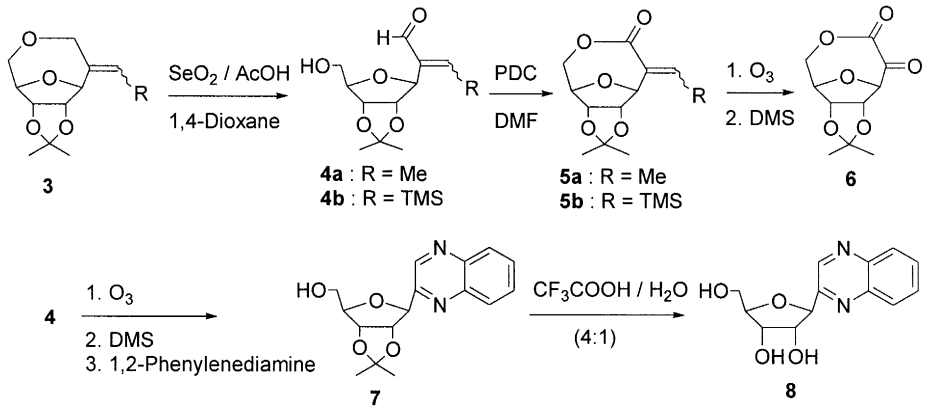
0040-4039/00/$ - see front matter
PII: S0040-4039(99)02011-0

TMS or methyl protecting groups of **2** suffered from low yield due to competative hydrostannylation of the triple bond.

Allylic oxidation of **3** with SeO_2 in 1,4-dioxane in the presence of acetic acid gave out aldehyde **4** (29% for **4a** and 69% for **4b**) presumably through hemiacetal intermediate (Scheme 2). When treated with pyridinium dichromate in DMF, the aldehydes **4** were further oxidized to lactones **5**[4] (30% and 74%, respectively), through hemiacetal intermediate also,[5] which could be converted to **6** in 19% yield, the known precursor of showdomycin syntheses,[6] under ozonolysis and reductive cleavage.



Scheme 2.

Transformation of the aldehyde intermediates **4** to a pyrazine *C*-glycoside derivative was performed by ozonolysis and reductive cleavage to yield α-keto aldehyde intermediate, which was reacted with 1,2-phenylenediamine without purification. Compound **7**[4] was obtained in 21% yield from **4a** and 52% from **4b**, respectively. Deprotection of **7** in a 4:1 mixture of CF_3CO_2H and H_2O provided **8**[4] in 41% yield.

In summary, the radical cyclization reaction of ribofuranose intermediate **2** suggests a new *C*-glycosylation route for *C*-glycoside derivatives.

Acknowledgements

This research was financially supported by the Ministry of Education through the Basic Science Research Institute Program (BSRI-98-3433).

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3. The products are mixtures of *E/Z* isomers in a ca. 1:1 to 4:3 ratio. Following reactions were carried out with the mixtures.
4. Compound **5a** (one isomer): IR ($CDCl_3$) 1732, 1379, 1371,1251 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 6.49 (s, 1H), 4.91 (*d*, 1H, *J*=5.7 Hz), 4.65 (*d*, 1H, *J*=5.7 Hz), 4.55 (*s*, 1H), 4.37 (*m*, 1H), 4.15–4.21 (*m*, 2H), 1.49 (*s*, 3H), 1.30 (*s*, 3H), 0.14 (*s*, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) 169.1, 151.3, 146.3, 112.3, 87.4, 83.4, 81.8, 81.5, 71.5, 25.9, 24.2, −1.2 (×3); *m/z* 283 (M^+-CH_3). **7**: ^1H NMR (300 MHz, $CDCl_3$) 8.91 (*s*, 1H), 8.02–8.16 (*m*, 2H), 7.75–7.83 (*m*, 2H), 5.38 (*d*, 1H, *J*=3.4 Hz), 4.92–4.98 (*m*, 2H), 4.56 (*dt*, 1H, *J*=2.4, 2.3 Hz), 4.04 (*dd*, *J*=12.4, 2.4 Hz), 3.75 (*dd*, 1H, *J*=12.4, 2.7 Hz), 1.60 (*s*, 3H), 1.40 (*s*, 3H); *m/z* 287 (M^+-CH_3); $[\alpha]_D^{25}=-7.89$ (c=0.015, MeOH). Compound **8**: ^1H NMR (400 MHz, CD_3OD) 9.12 (s, 1H), 8.07–8.10 (*m*, 2H), 7.81–7.87 (*m*, 2H), 5.10 (*d*, 1H, *J*=5.6 Hz), 4.31 (*dd*, 1H, *J*=5.6, 5.2 Hz), 4.20 (*dd*, 1H, *J*=5.20, 5.20 Hz),

4.13 (*m*, 1H), 3.91 (*dd*, 1H, *J*=12.0, 3.2 Hz), 3.77 (*dd*, 1H, *J*=12.0, 3.0 Hz); *m/z* 226 ($M^+ - 2H_2O$); $[\alpha]_D^{25}$=5.48 (c=0.006, MeOH).

5. Every protection condition of the hydroxyl group of **4** provided acetal intermediates. It is assumed that hemiacetal formation is dominated in the presence of base due to proximity between hydroxyl and aldehyde groups, although the groups exist separated in neutral condition.
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