Communications to the Editor

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SYNTHESIS OF SOME DEOXY, UNSATURATED, AND DIDEOXY SUGARS VIA REGIOSELECTIVE THIOACYLATION OF GLYCOPYRANOSIDES BY THE DIBUTYLTIN OXIDE METHOD[1)]

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Treatment of non-protected glycopyranosides (Me α-D-Glc, Me β-D-Glc, Me α-D-Xyl, and Me β-D-Xyl) with dibutyltin oxide followed by thioacylation with phenoxythiocarbonyl chloride gave the mono-thionocarbonates regioselectively in high yields. Acetylation of the latter followed by deoxygenation with Bu_3SnH smoothly gave the corresponding deoxy derivatives except for the 6-O-thionocarbonate derivatives. Similar treatment of the pyranosides that have a cis-vicinal glycol (Me α-D-Gal, Me β-D-Gal, Me β-L-Ara, and Ph α-L-Ara) leads to the formation of cyclic thionocarbonates which on acetylation followed by olefination with trimethylphosphite afforded the unsaturated derivatives in satisfactory yields. On deacetylation and subsequent hydrogenation over platinic oxide, they gave the corresponding dideoxy compounds quantitatively.

KEYWORDS——glycopyranoside; regioselective thioacylation; dibutyltin oxide; deoxygenation; cis-vicinal glycol; cyclic thionocarbonate; deoxy sugar; unsaturated sugar; dideoxy sugar

Thiocarbonyl esters of the secondary alcohols are reduced by Bu_3SnH to give the deoxygenated products usually in high yields.[2)] These products when combined with regioselective thioacylation leads to the regioselective deoxygenation of carbohydrates that provides useful intermediates for the synthesis of natural products from easily available sugars. We succeeded in regioselective acylation[3)] by using the dibutylstannylene intermediates of some non-protected sugars.

This communication describes the results of thioacylation of some non-protected glycopyranosides by the dibutyltin oxide method and their modification to deoxy, unsaturated, and dideoxy derivatives.

Among the reagents tested for thioacylation, phenoxythiocarbonyl chloride[4)] was found to be the most suitable for preparation of the mono-thionocarbonates by the Bu_2SnO method. Usually glycopyranosides that do not have cis-vicinal glycol system (Me α-D-Glc, Me β-D-Glc, Me α-D-Xyl, and Me β-D-Xyl), on stannylation followed by thioacylation, produced the mono-thionocarbonates regioselectively in high yields. These on acetylation followed by reduction with Bu_3SnH gave the corresponding deoxy derivatives. These results are summarized in Table I. The

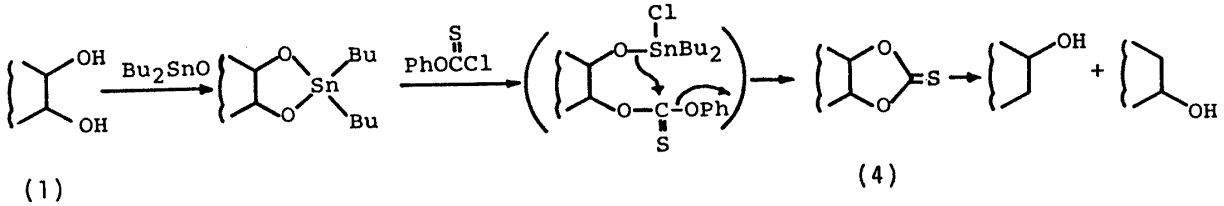
structures of the resulting thioesters and deoxy sugars (as acetates) were confirmed on the basis of ^{13}C-NMR spectra after chromatographical isolation of each product. The secondary thionocarbonates were smoothly deoxygenated to the corresponding deoxy derivatives. However, the primary thionocarbonates produced the deoxy compounds in poor yields, obviously due to the lesser stability of the primary relative to the secondary carbon radicals.[5]

Chart 1

Table I. Yields and Percentage Composition of the Mono-thionocarbonates and the Deoxy Derivatives of the Glycopyranosides That Do Not Have cis-Vicinal Glycol System

Starting material	Mono-thionocarbonate Yield (%)	Composition		mp (°C)	Deoxy derivative	Yield (%)	Acetate
Me α-D-Glc	83.0	2-Ester	93.5	128-129	2-Deoxy	75.6	Syrup
		6-Ester	6.5	Syrup	-----		
Me β-D-Glc	84.8	6-Ester	100.0	Amorphous	-----		
Me α-D-Xyl	76.3	2-Ester	54.0	130-131	2-Deoxy	91.6	Syrup
		4-Ester	46.0	115-116	4-Deoxy	83.2	Syrup
Me β-D-Xyl	97.4	4-Ester	100.0	136-137	4-Deoxy	82.6	Syrup

Stannylation followed by thioacylation of the pyranosides that possess a cis-vicinal glycol with phenoxythiocarbonyl chloride produced the cyclic thionocarbonates in good yields. The direct preparation of cyclic thionocarbonates from non-protected sugars by other reagents such as thiocarbonyl diimidazole[6] or thiophosgen[7] gave poor results. So the above method offers a facile and simple alternative procedure to obtain the cyclic thionocarbonates without protecting the other hydroxyl groups. The formation of cyclic thionocarbonates, however, reduces the regioselectivity of deoxygenation. On acetylation followed by reduction with Bu_3SnH, they gave two deoxy sugars in the yields and selectivities shown in Table II.



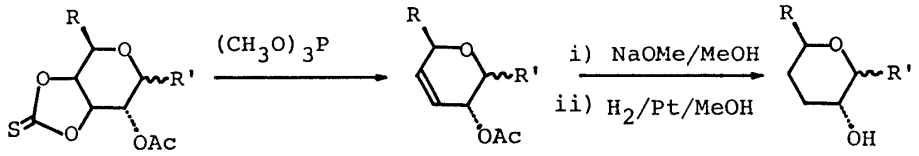
(1) (4)

Chart 2

Table II. Yields and Percentage Composition of the Cyclic Thionocarbonates and the Deoxy Derivatives of the Pyranosides That Possess cis-Vicinal Glycol

Starting material	3,4-Thionocarbonate Yield (%)	mp °C	(mp of acetate)	Deoxy compound Yield (%)	3-Deoxy/4-deoxy
Me α-D-Gal	62.6	Syrup	(131-132)	56.6	67 : 33
Me β-D-Gal	85.3	Syrup	(94- 96)	56.0	57 : 43
Me β-L-Ara	83.2	Syrup	(120-121)	57.3	50 : 50
Ph α-L-Ara	94.9	202-203	(118-120)	73.6	74 : 26

On the other hand, those cyclic thionocarbonates would serve as useful intermediates for the synthesis of unsaturated and dideoxy sugars. On olefination of their acetates (**5**) according to Corey-Winter method,[8] they gave the unsaturated sugars (**6**) in satisfactory yields. Deacetylation followed by hydrogenation over PtO_2 resulted in the formation of the dideoxy compounds (**7**) quantitatively. These results are given in Table III.



5 a: R=CH_2OAc, R'=α-OMe
b: R=CH_2OAc, R'=β-OMe
c: R=H, R'=β-OMe
d: R=H, R'=α-OPh

6 a: R=CH_2OAc, R'=α-OMe
b: R=CH_2OAc, R'=β-OMe
c: R=H, R'=β-OMe
d: R=H, R'=α-OPh

7 a: R=CH_2OH, R'=α-OMe
b: R=CH_2OH, R'=β-OMe
c: R=H, R'=β-OMe
d: R=H, R'=α-OPh

Chart 3

Table III. Yields and the ^1H- and ^{13}C-NMR Data of the Unsaturated and Dideoxy Derivatives of 3,4-Thionocarbonates

3,4-Thionocarbonate	Unsaturated sugar (acetate) Yield (%)	δH-3	δH-4	3,4-Dideoxy sugar Yield (%)	δC-3	δC-4
5a	55	5.84	5.73	100	27.1	26.0
5b	66	5.91	5.85	96	29.0	26.0
5c	65	4.66	5.95	99	27.5	24.0
5d	76	4.96	6.17	99	27.7	22.3

In conclusion, the glycopyranosides whose all-hydroxyl groups are trans oriented are regioselectively mono-thioacylated by the Bu_2SnO method. But in the

cases of pyranosides possessing a cis-vicinal glycol system, this method produces the cyclic thionocarbonates which are smoothly reduced to the dideoxy sugars through their unsaturated derivatives. The deoxy, unsaturated, and dideoxy sugars obtained should be useful intermediates for the synthesis of complex molecules having chiral centers.

Example: Deoxy Sugar——Me α-D-Glc (200 mg) and Bu_2SnO (1.5 eq) in dry methanol (10 ml) were heated under reflux for 3 h. The solvent was evaporated in vacuo to leave a glassy solid which was dissolved in dioxane (10 ml) and phenoxythiocarbonyl chloride (1.1 eq) was added dropewise on the stirred mixture at room temperature. After 1.5 h, the mixture was concentrated and the residue was chromatographed on silica gel to yield the 2-O-phenyl thionocarbonate (264 mg), mp 128-129°C, and the 6-O-phenyl thionocarbonate (18 mg), syrup. The 2-O-phenyl thionocarbonate was acetylated in a usual manner to yield the tri-O-acetate as a syrup. This was heated in toluene (5 ml) at 100°C with Bu_3SnH (1.1 eq) and a catalytic amount of AIBN for 2.5 h, then the solvent was evaporated in vacuo. Chromatography of the residue gave the 3,4,6-tri-O-acetyl-2-deoxy derivative (104 mg) as a syrup. Alkaline hydrolysis of this compound gave 2-deoxy Me α-D-Glc, mp 89-90°C.

Unsaturated and Dideoxy Sugar——Me α-D-Gal (200 mg) was thioacylated as described above to yield the 3,4-thionocarbonate (207 mg) as a syrup, which gave the di-O-acetate, mp 94-96°C, on acetylation. The diacetate (20 mg) in trimethylphosphite (3 ml) was heated at 110-120°C for 70 h. After addition of saturated Na_2CO_3 aq, the cooled mixture was extracted with CH_2Cl_2 and worked up as usual to yield the unsaturated derivative (10 mg) as a syrup. This was deacetylated with NaOMe in methanol to give a syrup, which was hydrogenated over PtO_2 in methanol for 5 h to give the dideoxy derivative (syrup) quantitatively.

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