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SYNTHETIC STUDIES OF CARBOHYDRATE DERIVATIVES WITH PHOTOCHEMICAL REACTION. VII.[1]

PHOTOCHEMICAL ADDITION OF ETHANETHIOL AND 1-PROPANETHIOL TO ENOSES

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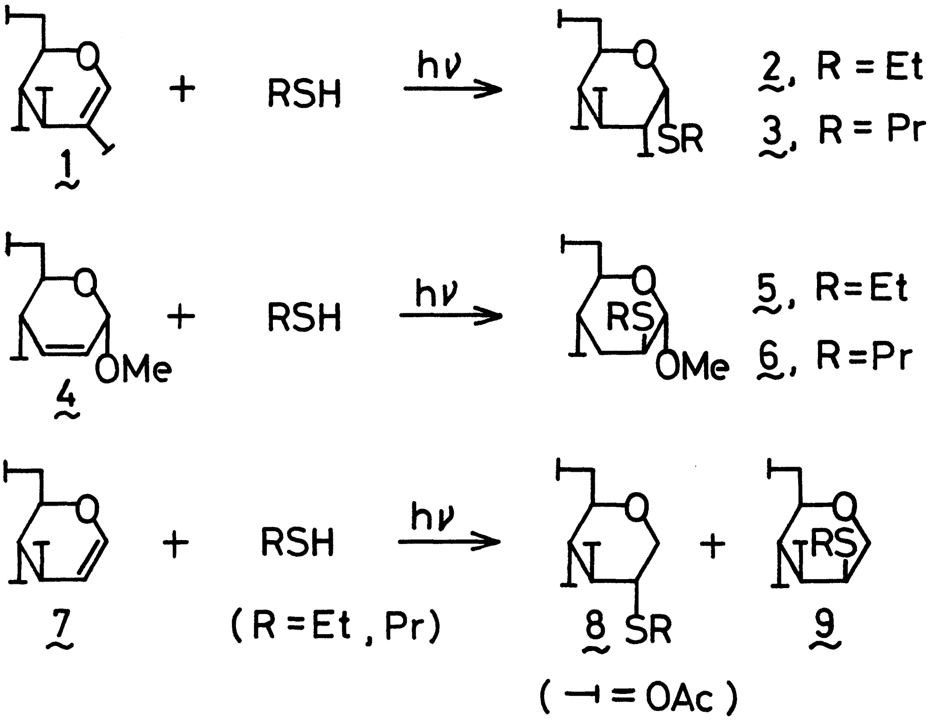
Acetone-sensitized photochemical addition of ethanethiol and 1-propanethiol to 2,3,4,6-tetra-O-acetyl-2-hydroxy-D-glucal gave the corresponding α-thioglucopyranosides in 77.1% and 79.3% yields, respectively. Similar addition reactions of thiols to methyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside and 3,4,6-tri-O-acetyl-D-glucal were also described.

In the series of this investigation, photochemistry with respect to carbohydrate derivatives has been reported,[2] and the utility of the photochemical reaction in the field of carbohydrate chemistry was exhibited. The present authors wish to report a useful photochemical addition of ethanethiol and 1-propanethiol to some carbohydrate derivatives having an endocyclic double bond in their structures.

Olefins have been shown to afford the corresponding sulfides by the photochemical addition of thiols[3]; however, such an addition reaction has never been known in the field of carbohydrate chemistry except the addition of thioacetic acid to 5,6-dideoxy-1,2-O-isopropylidene-α-D-*xylo*-hex-5-enofuranose.[4] Moreover, photochemical addition of thioacetic acid and phenylmethanethiol to methyl 5-deoxy-2,3-O-isopropylidene-β-D-*erythro*-pent-4-enofuranoside has been reported to give methyl 5-acetylthio- and 5-benzylthio-2,3-O-isopropylidene-β-D-ribofuranoside in 68% and 69% yields, respectively; however, 3,4,6-tri-O-acetyl-D-glucal was recovered almost quantitatively[5] under the same condition.[2a] Such a remarkable difference in the photochemical reactivity between endocyclic and exocyclic double bonds can be stated to be an interesting problem in the field of carbohydrate chemistry and photochemistry. Thus, the photochemical addition of ethanethiol and 1-propanethiol to some enoses involving endocyclic double bonds was undertaken in this investigation.

A solution of 2,3,4,6-tetra-O-acetyl-2-hydroxy-D-glucal(**1**)(0.500 g) in a mixture of ethanethiol(18 ml) and acetone(2 ml) was irradiated with a UV lamp[6] at room temperature under nitrogen atmosphere for 25 hr. GLC[7] of the resultant solution exhibited that **1** was no longer remained at all and the formation of a new single product. Evaporation of the resultant solution *in vacuo* followed by a successive recrystallization of the residual crystals from ethanol gave ethyl 2,3,4,6-tetra-O-acetyl-1-thio-α-D-glucopyranoside(**2**)[8][0.458 g, 77.1%] as colorless crystals, mp



96 – 97°C, $[\alpha]_D^{22}$ +192°(c 1.0, Me_2CO).[9] NMR spectral data(Table 1, $J_{1,2}$ = 5.8Hz and $J_{2,3}$ = 10.2Hz) indicate the α-D-*gluco* structure. A similar treatment of 1 in a mixture of 1-propanethiol(18 ml) and acetone(2 ml) afforded propyl 2,3,4,6-tetra-O-acetyl-1-thio-α-D-glucopyranoside(3)[0.488 g, 79.3%] as colorless needles, mp 105 – 106°C, $[\alpha]_D^{22}$ +185°(c 1.0, Me_2CO). The α-D-*gluco* structure of this product was confirmed from its NMR spectrum having the same trend as that of 2(Table 1). It is of quite interest to note the stereoselective formation of α-D-*gluco* type product in high yields, considering the difficulty in the preparation of α-D-thioglucopyranoside by the usual procedure.[10]

Photochemical addition reaction of the thiols to methyl 4,6-di-O-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside(4) was also found to proceed with high stereo- and regioselectivity giving methyl 4,6-di-O-acetyl-2-S-ethyl-3-deoxy-2-thio-α-D-*erythro*-L-*glycero*-hexopyranoside(5) and methyl 4,6-di-O-acetyl-2-S-propyl-3-deoxy-2-thio-α-D-*erythro*-L-*glycero*-hexopyranoside(6) as a sirup, respectively. 5 and 6 were easily purified by a chromatography of the resultant sirup, which was obtained by the concentration of the reaction mixture, on a column of silica gel by the use of a solvent system of benzene-acetone(98 : 2) for the elution. 5: 87.4 % yield, $[\alpha]_D^{22}$ +61.9°(c 1.4, Me_2CO). 6: 93.7% yield, $[\alpha]_D^{22}$ +42.5°(c 1.9, Me_2CO). The structures of 5 and 6 were confirmed by their NMR spectra(Table 1); both $J_{1,2}$ (= 1.8Hz) imply that H-1 and H-2 are in the equatorial orientation.

In addition, the photochemical addition of the thiols also took place in the

Table 1. NMR Spectral Data.

Protons	2	3	5	6
H-1	5.70 ppm	5.56 ppm	4.68 ppm	4.67 ppm
H-2	5.03	5.01	2.99	2.95
H-3	5.39	5.38	1.9 – 2.2	1.9 – 2.25
H-3′	——	——		
H-4	5.05	5.05	5.04	5.05
H-5	4.00 – 4.55	4.00 – 4.55	3.89	3.89
H-6,6′			4.18	4.18
$\mathrm{OCOC\underline{H}_3}$	2.02 2.04 2.07 2.09	2.02 2.04 2.07 2.09	2.03 2.08	2.04 2.07
$\mathrm{O\underline{CH}_3}$	——	——	3.39	3.39
$\mathrm{SC\underline{H}_2}$(α)	2.59	2.52 2.55	2.61	2.56
$\mathrm{CC\underline{H}_2}$(β)	——	1.64	——	1.61
$\mathrm{CC\underline{H}_3}$	1.29	0.98	1.25	0.98
J-values				
H-1 – H-2	5.8 Hz	6.0 Hz	1.8 Hz	1.8 Hz
H-2 – H-3	10.2	9.8	4.0	4.0
H-2 – H-3′	——	——	4.0	4.0
H-3 – H-4	9.0	9.0	7.0	6.8
H-3′– H-4	——	——	7.8	8.0
H-4 – H-5	9.3	9.5	9.6	9.6
H-5 – H-6	——	——	4.8	4.8
H-5 – H-6′	——	——	3.6	3.6
CH_3 – CH_2	7.3	7.2	7.2	7.0
CH_2 – CH_2	——	7.0 7.4	——	7.0

These data were taken with a Varian HA-100 spectrometer in $CDCl_3$ by the use of trimethylsilane as the internal standard.

case of 3,4,6-tri-O-acetyl-D-glucal(7) to give 1 : 1 mixture[11] of 1,5-anhydro-3,4,6-tri-O-acetyl-2-S-ethyl(or propyl)-2-thio-D-glucitol(8) and -D-mannitol(9) in an 87.3%(or 94.6%) yield after purification of the crude products by the column chromatography.[12] The site where the addition took place was established by the NMR spectroscopy; 1) Signals with a 1H area were detected at ca. δ 3.35 and 3.65 ppm, respectively. 2) No signals were observed at ca. δ 2.00 and 4.65 ppm.[13]

In view of the results of this investigation, it can be concluded that the photochemical addition of alkanethiols to enoses involving endocyclic double bond proceeds with a considerable easiness and high regio- and stereoselectivity, and that it is feasible for the synthesis of a variety of sulfur containing sugar derivatives. An extention of this reaction is now in progress in order to elucidate the correlation between the properties of thiols and the reactivity of enoses arising from their structural differences.

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5) Traces of the corresponding addition products were detected by GLC.

6) A high pressure mercury lamp(450 W) of Ushio Electric Inc. was applied to the irradiation, and Pyrex-glass test tubes were used as the reaction vessel.

7) Conditions: See ref. 2c.

8) Elemental analyses of all the products in this communication were consistent with the expected structures.

9) These data were consistent with the data{Mp 95°C, $[\alpha]_D^{20}$ +194.1°(c 1.6, $CHCl_3$)} reported by E. Pacsu and E. J. Wilson, Jr.[J. Amer. Chem. Soc., 61, 1450(1939)].

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11) The relative content retios were calculated from their NMR spectra by means of the area ratios of the S-methylene proton signals observed at ca. δ 2.55 - 2.60 ppm.

12) Chromatographic separation of these epimeric mixtures requires further examinations since they showed almost the same chromatographic behavior.

13) Assuming the products to be the corresponding 2-deoxy-thioglycosides, which might be formed by the attack of thio radicals at C-1 of **7**, NMR signals of their H-2,2′ and H-1 are expected to appear in these regions, respectively.

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