^{13}C NMR SPECTROSCOPIC STUDY FOR THE SYNTHESIS AND REARRANGEMENT OF A NOVEL HETEROCYCLIC THIOGLYCOSIDE

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INTRODUCTION

Alkyl and arylthioglycosides are very widely used in oligosaccharide synthesis[1]. However, heterocyclic thioglycosides have been given less attention in this respect although, it was reported that some heterocyclic thioglycosides are found to be exceptionally fast and efficient in the formation of glycosides by remote activation[2].

In the present investigation a novel thioglycoside, namely, 5-phenyl-1,3,4-thiadiazole-2-(1-thio-2,3,4,6-tetra-O-acetyl-ß-D-glucopyranoside) [3] was prepared by reacting acetobromoglucose[3] [2] with 5-phenyl-1,3,4-thiadiazole-2-thione[4] [1].

It was interesting to note that, methyl trifluoromethanesulfonate (methyltriflate, MeTf) treatment of [3] resulted in the migration of the sugar residue from the sulfur atom to the ring nitrogen of the thiadiazole ring, resulting in a thioglycoside nucleoside rearrangement.

RESULTS AND DISCUSSION

Sandstrom and Wennerbeck studied[4b] the equilibrium 1a ⇌ 1b using UV spectroscopy and LCAO-MO calculations, and their conclusions showed that 5-phenyl 1,3,4-thiadiazole-2-thione [1a] is the dominating structure rather than the thiol form 1b [Scheme 1].

In the present investigation 1a was prepared and the ^{13}C NMR spectrum (in DMSO) (Figure 1 A) was studied using TMS as an internal standard. The spectrum was in accordance with the proposed structure showing C=S at δ 177.55 ppm and C-5 at δ 160.53 ppm., together with the aromatic multiplet at δ 122 - 132.30 ppm. The spectrum did not show any traces of the 2b tautomer, which would have been indicated by a signal at δ 178 ppm for the C=C-SH.

Acetobromoglucose [2] reacted with 5-phenyl-1,3,5-thiadiazole-2-thione [1] in presence of potassium carbonate in acetone giving 5-phenyl-1,3,4-thiadiazole-2-(1-thio-2,3,4,6-tetra-O-acetyl-ß-D-glucopyranoside [3]. A study of the ^{13}C NMR spectrum in $CDCl_3$ (Figure 1 B) of the product 3, revealed, besides the sugar residue and aromatic carbons, the C-5 of the thiadiazole ring at δ 160.62 ppm. together with a signal at δ 166.51 ppm which is attributable to the =C-S-sugar carbon. Such a spectrum proves that acetobromoglucose reacts with the sodium salt of the thiol form 1b i.e. the sodium hydride shifts the equilibrium 1a ⇌ 1b to the thiol form 1b, prior to its reaction with the bromosugar.

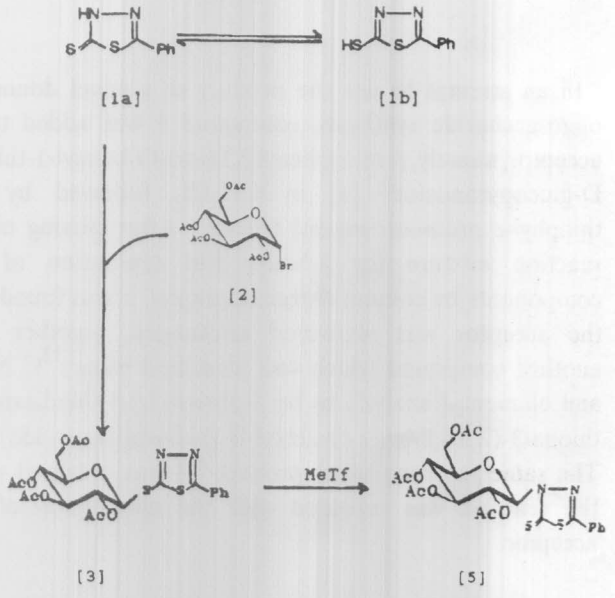

Figure 1-a. Please, if possible enlarge the scheme.

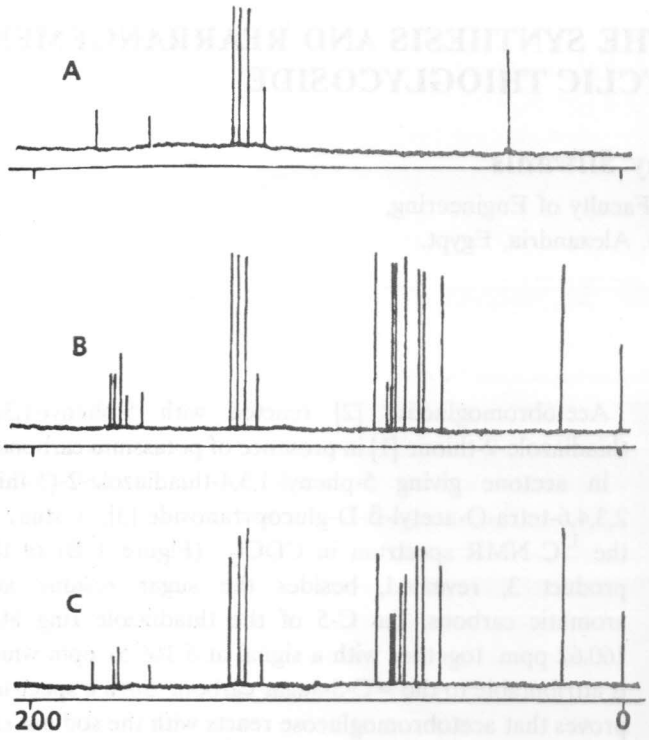

Figure 1. (a) ^{13}C NMR spectrum of compound [1]
(b) ^{13}C NMR spectrum of compound [3]
(c) ^{13}C NMR spectrum of compound [5].

In an attempt to use the product as a novel donor for oligosaccharide synthesis, compound 3 was added to an acceptor, namely, p-nitrophenyl 2,3,6-tri-O-benzyl-1-thio-ß-D-glucopyranoside[5] [4] in CH_2Cl_2 followed by the thiophylic promoter methyl triflate. After stirring of the reaction mixture for 2-hours and separation of the components by column chromatography, it was found that the acceptor was recovered unchanged, together with another compound which was identified using ^{13}C NMR and elemental analysis to be 5-phenyl-1,3,4-thiadiazole-2-thione-3-(2,3,4,6-tetra-O-acetyl-ß-D-glucopyranoside) [5]. The same rearrangement product [5] was obtained when the reaction was repeated with the elimination of the acceptor.

The ^{13}C NMR spectrum (Figure 1 C) of the product [5] was characterized by the appearance of the C=S carbon at δ 177.96 ppm and the C-5 carbon signal at δ 160.22 besides the aromatic and sugar residue carbon signals.

EXPERIMENTAL

General methods

Melting points are uncorrected. Concentrations were performed under reduced pressure at <40°C using a rotary evapourator. NMR spectra were recorded with a GX-270 instrument at 25°C for solutions in $CDCl_3$ using TMS as internal standard. T.l.c was performed on silica gel F_{254} (Merck) and detection by u.v. light and by charring with sulfuric acid. Column chromatography was performed using silica gel (0.040-0.063 mm, Merck) using 3:1 toluene - ethylacetate as eluent. Dichloromethane was distilled from phosphorus pentoxide. Dry solvents were stored over molecular sieves (4A°).

5-Phenyl 1,3,4-thiadiazole-2-thione[4] [1], *2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide*[3] [2] and *p-nitrophenyl 2,3,6-tri-O-benzyl-1-thio-ß-D-glucopyranoside*[5] [4] were prepared as mentioned in literature.

5-Phenyl-1,3,4-thiadiazole-2-(1-thio-2,3,4,6-tetra-O-acetyl-ß-D-glucopyranoside [3]: To acetobromoglucose (3.11 gm, 0.01 mol), and the thiadiazole [1] (1.94 gm, 0.01 mol) dissolved in acetone (50 ml), 1 gm potassium carbonate was added. The mixture was left to stir at room temperature for 48 hours. The resulting solution was poured over ice, extracted twice with methylene chloride, washed with water and dilute hydrochloric acid and concentrated under reduced pressure, to give a crystalline solid mass, 4.0 gm, 94 % yield, m.p. 132° C which was purified by recrystallization from methanol, m.p. 136°C.

^{13}C NMR data: δ 20.56 (CH_3CO); 61.58, 67.76, 69.81, 73.52, 76.50 (C-2,3,4,5,6); 83.40 (C-1); 123.30, 126.60, 129.16, 132.03 (aromatic); 160.62 (thiadiazole C-5); 166.51 (thiadiazole C-2); 169.34, 169.44, 169.94, 170.53 (acetyl C=O).
Calculated for $C_{22}H_{24}O_9N_2S_2$: C, 50.38; H, 4.58; N, 5.34 and S, 12.21. Found: C, 50.5; H, 4.5; N, 5.2.

5-Phenyl-1,3,4-thiadiazole-2-thione-3-(2,3,4,6-tetra-O-acetyl-ß-D-glucopyranoside) [5]: To 4.2 gm of [3] in methylene chloride (50 ml), 0.1 ml methyl triflate were added and the mixture was stirred for 2 hours at room temperature being monitored by t.l.c. After completion

of the reaction triethylamine (0.5 ml) was added to the reaction medium and stirring was continued for 5 minutes after which the solution was evapourated whereby a solid separated (4.1 gm; 98 % yield) m.p. 145°C. The product was purified by recrystallization from methanol, m.p. 148°C.

^{13}C NMR data: δ, 20.56 (CH_3CO); 61.57, 67.59, 69.26, 73.25, 74.74 (C-2,3,4,5,6); 83.02 (C-1); 121.95, 126.81, 129.18, 132.80 (aromatic); 160.12 (thiadiazole C-5); 168.93, 169.36, 170.06, 170.57 (acetyl C=O); 177.96 (thiadiazole C-2).

Calculated for $C_{22}H_{24}O_9N_2S_2$: C, 50.38; H, 4.58; N, 5.34 and S, 12.21. Found: C, 50.4; H, 4.4; N, 5.1.

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