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Note

A simple method for the synthesis of ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-rhamnopyranoside

TSUYOSHI FUJIWARA AND KIYOSHI ARAI
Laboratory of Chemistry, Institute for Natural Science, Nara University, Horai-cho 1230, Nara (Japan)
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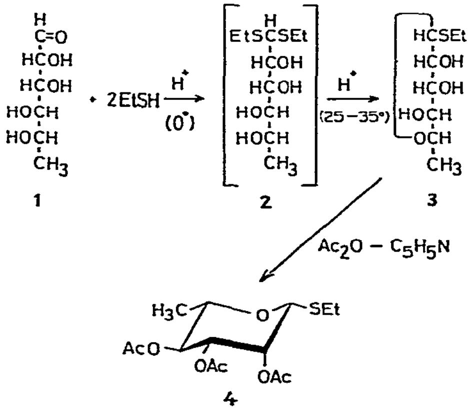
Peracylated alkyl 1-thioaldosides react with bromine in acetic acid to give per-*O*-acylaldosyl bromides that may or may not have the same anomeric configuration, and the bromide may be isolated in high yield if an inert solvent such as carbon tetrachloride is used[1,2]. Consequently, 1-thioaldosides serve as valuable intermediates for the synthesis of peracetylated aldosyl bromides that are difficult to synthesize by the usual method of using an aldose peracetate and hydrogen bromide. Tri-*O*-acetyl-α-L-rhamnopyranosyl bromide is difficult to synthesize from L-rhamnose, and hence, alkyl 1-thio-β-L-rhamnopyranosides are good intermediates for the synthesis of tri-*O*-acetyl-α-L-rhamnopyranosyl bromide. The method for preparing alkyl 1-thioaldopyranosides *via* the dialkyl dithioacetals (which involves their equilibration with the 1-thioaldosides) is simple and convenient. For L-rhamnose, dialkyl dithioacetals are readily formed in quantitative yield, and the reaction has been used for the determination of L-rhamnose[3]. Despite the availability of the dithioacetals, 1-thio-L-rhamnosides have been little studied.

We now report a simple and convenient method for the synthesis of ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-rhamnopyranoside (4) by the method of Wolfrom and Karabinos[3] (frequently used for the synthesis of dithioacetals), with a slight modifi-



cation. L-Rhamnose (**1**; 500 mg) was dissolved in conc. hydrochloric acid (5 ml), ethanethiol (5 ml) was added, and the mixture was stirred for 1 h at 25–35°. It was then made neutral with conc. ammonium hydroxide, and evaporated under diminished pressure. The residue (**3**) was dried by repeated addition and evaporation of ethanol, and acetylated with 1:1 acetic anhydride–pyridine for 24 h at room temperature. The mixture was poured onto ice and extracted with chloroform; the extract was washed successively with water, 10% hydrochloric acid, water, saturated sodium hydrogencarbonate, and water, dried, and evaporated to a pale-yellow syrup. Addition of ethanol to the syrup gave needle-like crystals, and recrystallization from absolute ethanol gave crystals of pure **4** (445 mg, 43.7%), m.p. 108.3–108.8°, $[\alpha]_D^{17}$ +57.8° (*c* 2.0, chloroform); t.l.c. R_F 0.73 (4:1 benzene–acetone); for the n.m.r. spectrum of **4**, see Fig. 1.

Anal. Calc. for $C_{14}H_{22}O_7S$: S, 9.86; mol. wt. 334. Found: S, 10.04; mol. wt. 334 (mass spectroscopy).

In the n.m.r. spectrum of **4**, the methylene signal at ~2.7 p.p.m. (2 H), the acetyl signals at ~2 p.p.m. (9 H), and the methyl signals at ~1.3 p.p.m. (6 H) showed that **4** was an ethyl tri-*O*-acetyl-1-thiorhamnoside. The $J_{3,4}$ value was unclear, but, as the $J_{4,5}$ value was 9.8 Hz, and H-4 shifted towards lower field (~5.0–5.1 p.p.m.), in contrast to the shift of H-5 (3.55 p.p.m.), **4** was in the pyranoside form and had the $^1C_4$(L) conformation. The acetyl signals indicated the presence of one axial acetoxyl group and two equatorial acetoxyl groups, supporting the $^1C_4$(L)

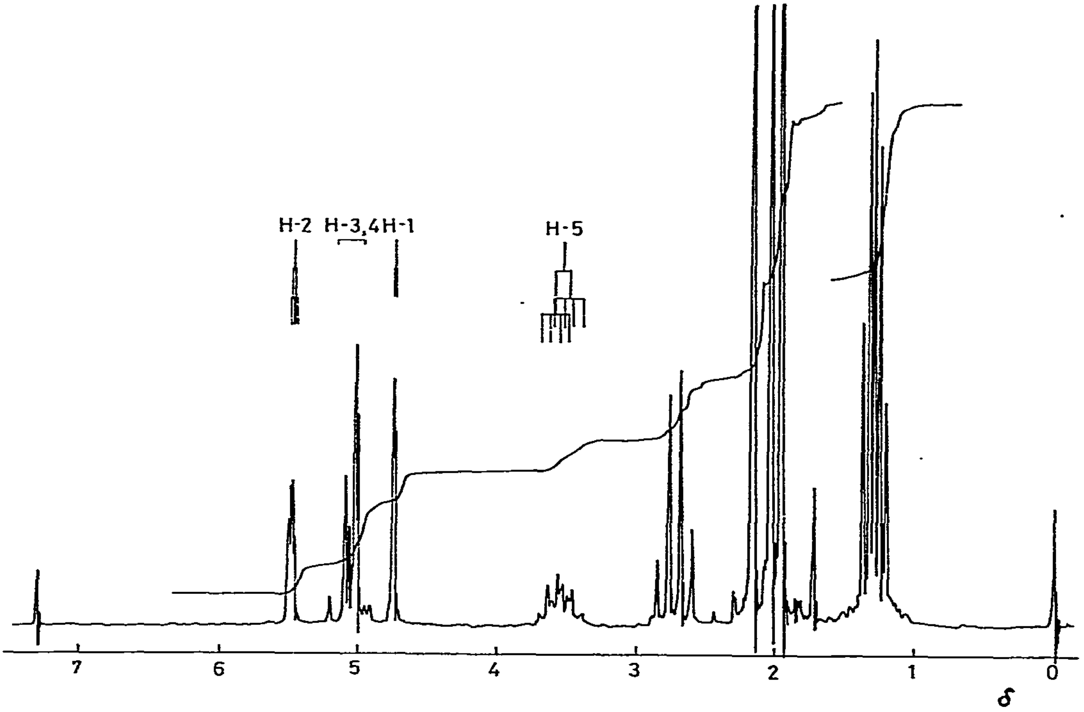


Fig. 1. N.m.r. spectrum of ethyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-rhamnopyranoside (**4**).

conformation. Hence, **4** was an ethyl 2,3,4-tri-*O*-acetyl-1-thio-L-rhamnopyranoside. The anomeric configuration was not determined from the n.m.r. data, but the positive specific rotation ($[\alpha]_D^{17}$ +57.8°) showed that **4** had the *β*-L configuration.

The structure of **4** was also supported by its i.r. and mass spectra. The i.r. spectrum of **4** (in KBr) showed absorptions due to SCH_2 (1414, 710, and 705 cm^{-1}) and acetic ester (1750, 1739, 1378, 1250, 1235, 1207, and 1058 cm^{-1}). The mass spectrum of **4** showed the parent peak at *m/e* 334 (M^+, 0.9%) and several peaks at *m/e* 273 (M^+ − SEt, 8.5%), 214 (M^+ − 2 AcOH, 5.2%), 153 (M^+ − 2 AcOH − SEt, 31.4%), 111 (M^+ − 2 AcOH − $CH_2{=}C{=}O$ − SEt, 27.3%), 83 (20.1%), and 43 (CH_3CO, 100%).

It is known that the dithioacetal **2**, and the 1-thioaldoside **3** are present in equilibrium in the reaction mixture, and that increase of the reaction temperature precedes the formation of the 1-thioaldoside[4]. Usually, the reaction for synthesizing the dithioacetal **2** is performed[3] at 0°, but, in the present work, the reaction was conducted at about room temperature. Therefore, the formation of the ethyl 1-thioaldoside (**3**) predominated.

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REFERENCES

1 F. Weygand, H. Ziemann, and H. J. Bestmann, *Chem. Ber.*, 91 (1958) 2534–2537.
2 C. Pederson and H. G. Fletcher, Jr., *J. Org. Chem.*, 26 (1961) 1255–1257.
3 M. L. Wolfrom and J. V. Karabinos, *J. Am. Chem. Soc.*, 67 (1945) 500–501.
4 D. Horton and D. H. Hutson, *Adv. Carbohydr. Chem.*, 18 (1963) 123–199.