Synthesis of 2-Phenylethyl α-Glucoside

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2-Phenylethyl α-glucoside was synthesized from 2-phenylethanol and α-D-glucose in the presence of *p*-toluenesulfonic acid monohydrate at 75 °C and was isolated by continuous extraction, during which hexane was used to remove the excess 2-phenylethanol and then ethyl acetate was used to isolate the product. The spectral data including IR, ^{1}H NMR, ^{13}C NMR, and MS of this compound are presented.

Keywords: *2-Phenylethanol; 2-phenylethyl α-glucoside; α-D-glucose; p-toluenesulfonic acid*

INTRODUCTION

Recently the occurrence of glycosides has been extensively studied in a variety of fruits and vegetables (Buttery et al., 1990; Krammer et al., 1991; Schwab and Schreier, 1990; Wu et al., 1991; Ackermann et al., 1989; Kodama et al., 1984). It has been generally considered that the glycoside plays an important role in the release of aroma-bearing compounds, such as alcohols and phenols, during the ripening and aging of fruits and other plants. To support research in this area, different glycosides have been synthesized (Ishag et al., 1985; Schwab and Schreier, 1988; Mastelic et al., 1989; Leong et al., 1989; Voirin et al., 1990).

Methods to synthesize β-glucosides including 2-phenylethyl β-glucoside have already been reported in the literature, although the methods reported use adaptations of the Koenigs–Knorr method (Williams et al., 1983; Schwab et al., 1990). Other methods for the synthesis of 2-phenylethyl α-glucoside are not well documented. As both 2-phenylethyl α-glucoside and 2-phenylethyl β-glucoside thermally release the roselike aroma compound 2-phenylethanol, an attempt was made to synthesize 2-phenylethyl α-glucoside. In this paper we present a simple one-step method for such a preparation.

EXPERIMENTAL PROCEDURES

Preparation of the Reaction Mixture. Into a reaction vessel equipped with a mechanical stirrer, a thermometer, a condenser, and a powder additional funnel were charged 44 g of 2-phenylethanol (0.36 mol), 21.6 g of α-D-glucose (0.12 mol), and 2.4 g of *p*-toluenesulfonic acid monohydrate. The reaction was carried on with stirring at 75 °C for 24 h, after which time 2.8 g of Na_2CO_3 was added to the reaction vessel (at 70 °C); the reaction mixture was stirred for 1 h and then cooled to room temperature.

Extraction. The reaction mixture obtained was dissolved in 150 mL of water, and the solution was subjected to continuous extraction using hexane to remove the excess 2-phenylethanol (in 24 h), after which time ethyl acetate was used to isolate 2-phenylethyl α-glucoside (also in 24 h). The ethyl acetate extract was dried over anhydrous $MgSO_4$ and filtered. Ethyl acetate was removed from this extract by a rotary evaporator. A solid was crystallized during concentration. After air-drying, 9 g of the title compound was obtained.

Acetylation of the Title Compound. A small portion of the title compound (0.2 g) was mixed with 2 mL of pyridine and 0.3 mL of acetic anhydride. The solution was kept at room temperature for 2 h prior to the GC/MS analysis.

GC/MS Analysis. The acetylated sample was analyzed on a DB-5 fused silica column (30 m × 0.32 mm, 0.15-μm-thick film). The oven temperature was programmed from 50 to 120 °C at 3 °C/min and then to 240 °C at 15 °C/min. A mass selective detector (HP 5970B) was used.

IR Analysis. The title compound was analyzed on a Mattson Polaris microscope.

NMR Analysis. The title compound was analyzed on a 360-MHz spectrometer. Dimethyl-d_6 sulfoxide was used as ^{13}C NMR solvent, and acetone-d_6 and methanol-d_4 were separately used as proton NMR solvents.

RESULTS AND DISCUSSION

From this reaction, 9 g of white fine needles of the title compound was obtained. The melting point was 53–55 °C, and the yield from this reaction was calculated as 27%.

The IR spectrum obtained shows strong absorption bands between 3500 and 3200 and 1022 cm^{-1}, which are characteristic for the hydroxy group and the C–O–C moiety, respectively.

The proton NMR spectrum obtained from acetone-d_6 or from methanol-d_4 shows a doublet signal for the anomeric proton at 4.80 ppm with the coupling constant $J = 3.8$ Hz. As for the corresponding β-glucoside, the chemical shift of the anomeric proton was reported to be at 4.82 ppm, $J = 7$ Hz, from $CDCl_3$ (Umehara et al., 1988) and at 4.92 ppm, $J = 7.5$ Hz, from pyridine-d_5 (Miyase et al., 1988).

A comparison between the ^{13}C NMR spectrum of the α-glucoside obtained from this study and that of the β-glucoside reported earlier (Umehara et al., 1988) is compiled in Table 1. From the data it can be seen that the chemical shifts of the alcohol moiety are similar for the α-glucoside and the β-glucoside and that the chemical shifts of the glucose moiety from the α-glucoside are lower than those from the β-glucoside, especially for the anomeric carbon (98.6 vs 104.8 ppm).

The GC/MS analysis of the acetylated final product showed that the α-glucoside was 95% and the β-glucoside was 5%. Both sets of mass spectral data are very similar, as shown in Table 2.

The method to prepare alkyl α-glucoside was initially developed by Dean and Pyle (1953) using an acid catalyst to couple an alkyl alcohol and glucose. The workup procedure from their method was to use vacuum distillation or steam distillation to remove the excess alcohol. This limited their method to the synthesis of

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Table 1. ^{13}C NMR Chemical Shifts (Parts per Million) of 2-Phenylethyl Glucoside

	α glucoside[a]	β glucoside[b]
	Alcohol Moiety	
C-1	138.9	139.3
C-2/6	128.2	128.6
C-3/5	128.9	129.3
C-4	126.1	126.4
C-α	35.6	36.6
C-β	68.0	71.6
	Glucose Moiety	
C-1′	98.6	104.8
C-2′	72.0	75.2
C-3′	72.8	78.6
C-4′	70.3	71.8
C-5′	73.3	78.6
C-6′	60.9	63.0

[a] From this study. [b] From the literature (Umehara et al., 1988).

Table 2. Mass Spectral Data of 2-Phenylethyl 2,3,4,6-Tetra-*O*-acetylglucoside

isomer	*m*/*z* (%)
α	43 (100), 81 (12), 103 (12), 104 (41), 105 (74), 109 (19), 169 (23), 287 (8), 347 (7), 412 (M^+, 0)
β	43 (100), 44 (12), 81 (13), 103 (12), 104 (44), 105 (81), 109 (12), 115 (9), 169 (14), 287 (6), 347 (6), 412 (M^+, 0)

α-glucosides of low boiling point alkyl alcohols. The synthetic method described here for the preparation and isolation of 2-phenylethyl α-glucoside using an adaptation of the Dean and Pyle procedure for high boiling point alcohols is both simple and efficient.

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