Communications to the Editor

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REGIOSELECTIVE INTRODUCTION OF p-COUMAROYL GROUP TO α-L-ARABINOPYRANOSIDES. TOTAL SYNTHESES OF INUNDOSIDE-G AND INUNDOSIDE-D_1[1)]

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Stannylation of cholesteryl α-L-arabinopyranoside with Bu_2SnO followed by p-coumaroylation gave the 3′-O-p-coumarate, which on heating in pyridine rearranged to the 4′-O-p-coumarate. Similarly inundoside-A was converted to its 3′-O-p-coumarate and then 4′-O-p-coumarate, which were identical with inundoside-G and inundoside-D_1, respectively, thus providing their total syntheses.

KEYWORDS —— dibutyltin oxide; regioselective acylation; p-coumaroylation; acyl migration; inundoside-G; inundoside-D_1; triterpenoid glycoside; α-L-arabinopyranoside; Lycopodium inundatum; cholesteryl α-L-arabinopyranoside

Synthesis of naturally occurring acylated poly-hydroxy compounds such as acylated glycosides requires introduction of an acyl group regioselectively to a desired position in non-acylated substrates; that is, the differentiation of one hydroxyl group from the others.

This communication treats the above problem for α-L-arabinopyranosides, choosing cholesteryl α-L-arabinopyranoside (1a)[2)] and serratenediol 3-α-L-arabinopyranoside (1b: inundoside-A)[3)] as substrates. p-Coumaroyl group, one of the common acyl groups of shikimate origin, was selected as an acyl moiety. Introduction of p-coumaroyl group to 4′-OH of 1b would lead to the synthesis of inundoside-D_1, an acylated glycoside isolated from Lycopodium inundatum.[3)] 2′-O-Acylation may be acheived via an O,O-isopropylidene derivative and 3′-O-acylation can be done regioselectively by using either Bu_2SnO or $(Bu_3Sn)_2O$ method.[4)] However, 4′-O-acylation can not be done regioselectively, since 4′-OH of arabinopyranosides is least reactive. We thought this can be done by acyl migration of the 3′-O-acyl group.

Stannylation of cholesteryl α-L-arabinopyranoside (1a) with Bu_2SnO (1.5 eq) in boiling dioxane for 7.5 h followed by acylation with freshly prepared p-acetoxycinnamoyl chloride (1.5 eq) at room temperature for 3 h yielded 3′-O-p-acetoxycinnamate (2a) (50.5%), mp 279-281°C, and 4′-O-p-acetoxy-cinnamate (3a) (13.5%), mp 157-160°C. The phenolic acetyl group of the former was easily removed solvolytically on treatment with boiling methanol to yield 3′-O-p-coumarate (4a), mp 289-290°C. The 3′-O-acyl group in 2a, when heated in pyridine at 130°C for 3 h, migrated to 4′-O-position, giving rise to an equilibrium mixture of 4′-O- (3a) and 3′-O-ester (2a) in a ratio of 3 : 2. The structures of these products and the ratio were estimated by ^{13}C-NMR spectra. Chromatographic separation of the product effected the isolation of 4'-O-ester (3a), mp 275-278°C, in a pure form. Treatment of 3a with $NaBH_4$ in THF smoothly gave the deacetylated compound (5a), mp 289-290°C. 3'-O-p-Coumarate (4a) also migrated, on heating in pyridine at 130°C for 3 h, giving rise to a 2 : 3 mixture of 4a and 5a. Crystallization of the reaction mixture from $CHCl_3$-MeOH gave 5a in a pure form.

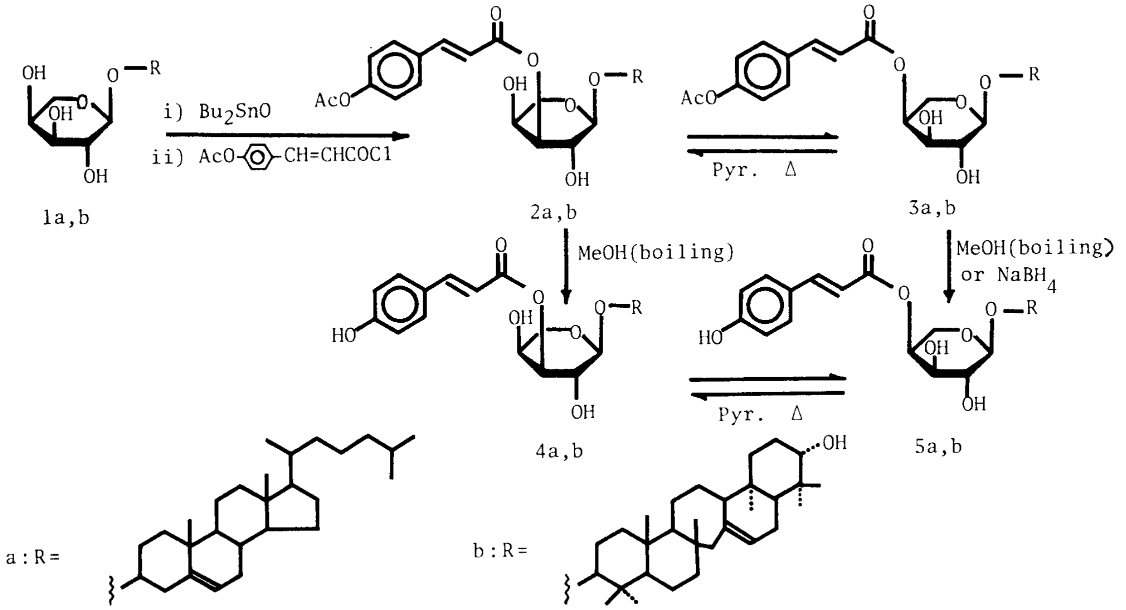

Table I. ^{13}C-NMR δ_C of the Arabinose Moiety for the non-Acylated and Acylated α-L-Arabinopyranosides, 1a, 2a, 3a, 4a, 5a, 1b, 4b, and 5b, and Their Acylation Shift Values (in Parentheses) in Pyridine-d_5

Carbon No.	1a	2a	3a	4a	5a	1b	4b	5b
1'	103.1	103.0	103.3	103.0	103.3	106.8	106.9	106.6
		(-0.1)	(+0.2)	(-0.1)	(+0.2)		(+0.1)	(-0.2)
2'	72.5	69.7	72.7	69.7	72.7	72.8	69.9	72.8
		(-2.8)	(+0.2)	(-2.8)	(+0.2)		(-2.9)	(0)
3'	74.6	77.2	72.7	76.9	72.3	74.4	76.7	73.3
		(+2.6)	(-1.9)	(+2.3)	(-2.3)		(+2.3)	(-1.1)
4'	69.5	67.1	72.9	67.2	72.9	69.0	66.9	72.3
		(-2.4)	(+3.4)	(-2.3)	(+3.4)		(-2.1)	(+3.3)
5'	66.8	66.8	64.6	66.9	64.7	66.1	66.2	64.5
		(0)	(-2.2)	(+0.1)	(-1.9)		(+0.1)	(-1.6)

Similarly stannylation of inundoside-A (1b) with Bu_2SnO (3.0 eq) in boiling dioxane followed by acylation with p-acetoxy-cinnamoyl chloride and crystallization of the product from hot $CHCl_3$-MeOH gave, with concomitant loss of acetyl group, 3'-O-p-coumarate (4b), mp 297-299°C. Acetylation of this gave the tetraacetate, mp >300°C. This tetraacetate was found to be identical with inundoside-G tetraacetate (lit. mp >300°C) (^{1}H-NMR, IR, and TLC comparisons), for which the position of the p-coumaroyl group had not been established.[3)]

Heating of 3'-O-p-coumarate (4b) in pyridine at 110°C for 3 h gave ca. 1 : 1 equilibrium mixture of 3'-O- and 4'-O-p-coumarate (4b and 5b) with slight excess of the latter (estimated from ^{13}C-NMR). Preparative TLC and several crstallizations of the mixture from $CHCl_3$-MeOH afforded 4'-O-p-coumarate (5b), mp 285-287°C, in a pure form, which was identical with inundoside-D_1 (lit. mp 286-290°C)[3)] (NMR, IR, and TLC comparisons). Acetylation of this gave the tetraacetate, mp 275-276°C, identical with inundoside-D_1 tetraacetate (lit. mp 272-274°C)[3)] (NMR, IR, and TLC comparisons).

The above syntheses provide not only the rigid proofs of the structures of inundoside-D_1 and inundoside-G but also the total syntheses of these acylated triterpenoid glycosides in a formal sence, since total synthesis of inundoside-A has already been accomplished.[5)]

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