Metabolites of Proteaceae. Part 9.[1] Eximin (6-*O*-Benzoylarbutin) and the Synthesis of Aryl Glycoside Esters

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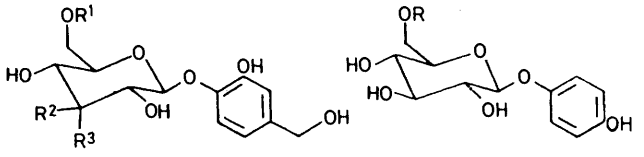
Eximin, obtained from the leaves of *Protea eximia* (Salisb. ex Knight) Fourcade, is shown to be 6-*O*-benzoylarbutin, and the synthesis of its tetra-acetate from arbutin is described. A synthesis of aryl glucoside esters by glucoside formation between tetra-*O*-acyl-1-α-D-glucopyranosyl bromides and phenols is shown to succeed only with phenols carrying electron-withdrawing substituents. Under the same conditions phenols with electron-donating substituents promote elimination reactions leading to the corresponding glucals.

MEMBERS of the genus *Protea* of the family Proteaceae have been shown to contain aromatic esters of aryl glycosides as typical leaf constituents. Thus *P. laticolor* was found [2] to contain the glucoside ester laticolorin (1), while *P. rubropilosa* contained [3] the alloside esters rubropilosin (2) and pilorubrosin (3). The leaves of *Protea eximia* (Salisb. ex Knight) Fourcade have now been found to contain 6-*O*-benzoylarbutin (eximin, 4). The structure of eximin (4) was demonstrated as in



(1) R^1 = Bz, R^2 = OH, R^3 = H
(2) R^1 = PhCH = CHCO, R^2 = H, R^3 = OH
(3) R^1 = Bz, R^2 = H, R^3 = H
(4) R = Bz
(5) R = H

previous instances [2,3] by its degradation to (+)-D-glucose (characterised as its osazone and by the g.l.c. characteristics of its products of trimethylsilylation), hydroquinone, and benzoic acid, and by spectral analysis of the native compound and of its tetra-acetate. A detailed exposition is available.[4]

Eximin, $C_{19}H_{20}O_8$, m.p. 199—202°, $[\alpha]_D$ −48°, gave a clearly resolved n.m.r. spectrum at 220 MHz (see Experimental section); the anomeric proton resonated at δ 4.74 as a doublet whose coupling constant (7 Hz) indicated the axial orientation [5,6] of H-1 of the glucose unit and hence the β-configuration for the glucoside. Its mass spectrum showed a strong peak at *m/e* 267 for a benzoylglucose oxonium ion, so that the ester group may be located on the pyranose system. This was confirmed by the mass spectrum of eximin tetra-acetate, m.p. 135—138°, where the corresponding ion, *m/e* 393, was again prominent; this mass spectrum also specifically afforded indication of the location of the ester group on C-6 through the relative abundance [7] of the ion, *m/e* 231, whose formation from the ion, *m/e* 393, is favoured when the three acetate groups on the pyranose ring are at C-2, C-3, and C-4.[7] This at the same time indicated [8,9] the pyranose nature of the sugar ring.

Structure (4) for eximin was furthermore supported [10] by the comparison of its ^{13}C n.m.r. characteristics with those of arbutin (5) observed under the same conditions, when the pyranose carbon resonances showed the changes expected [11] to result from acylation of 6-OH: the resonance position of C-6 is shifted downfield by 2.6 p.p.m. while that of C-5 is shifted upfield by a similar amount (assignments in Table 1).

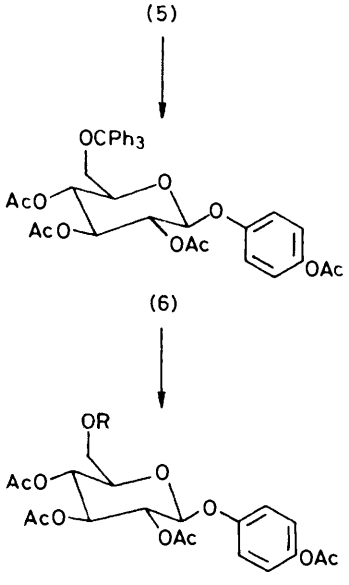
TABLE 1

^{13}C n.m.r. line positions for pyranose carbon atoms (δ in p.p.m. relative to Me_4Si in CD_3COCD_3 solution)

	C-1	C-2	C-3	C-4	C-5	C-6
Arbutin (5)	102.7	74.0	77.2 [a]	70.7	76.9 [a]	62.0
Eximin (4)	102.5	73.9 [a]	77.1	70.9	74.3 [a]	64.6

[a] These values may be alternatively assigned in both cases.

Structure (4) for eximin was confirmed by the 'partial' synthesis of its tetra-acetate (8) from arbutin (5). The

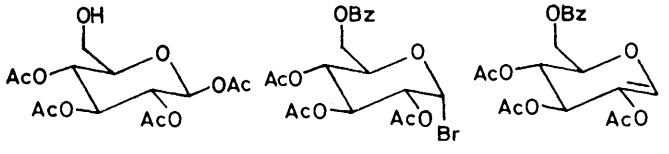


(7) R = H
(8) R = Bz

primary alcoholic function at C-6 was protected by forming the trityl ether and acetylation afforded its tetra-acetate (6). The latter was smoothly hydrogenolysed to the free primary alcohol (7) which on benzoyl-

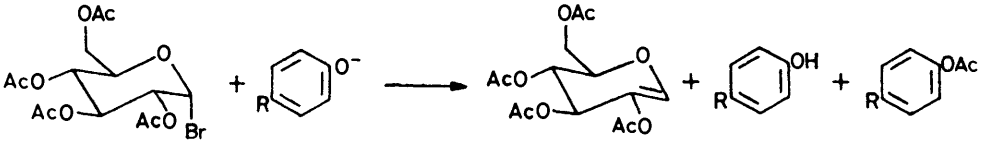
ation afforded eximin tetra-acetate (8), identical with the tetra-acetate of the natural product.

A study of a 'total' synthesis of eximin through formation of the glycosidic link was undertaken in view of our interest in glycoside esters as plant metabolites; it illustrated some problems of nucleophilic substitution at C-1 of fully acylated 1-α-bromo-glucose derivatives, given that strongly basic or acidic conditions would have to be avoided and that suitable protection would be required on the diphenolic aglycone. For this purpose the monoacetate and the monobenzyl ether of hydroquinone were selected as potential nucleophiles. A reaction of hydroquinone monoacetate with acetobromoglucose in quinoline with silver oxide, following the synthesis of arbutin by Robertson and Waters, which



(9) (10) (11)

succeeded with hydroquinone monobenzoate but not with hydroquinone itself,[12] was as unsuccessful as in the latter case and further approaches were therefore explored.



(12) (13) (14) (15)

2,3,4-Tri-*O*-acetyl-6-*O*-benzoyl-1-α-D-glucopyranosyl bromide (10) was prepared by benzoylation and bromination of 1,2,3,4-tetra-*O*-acetyl-D-glucose (9) (see Experimental section). The bromo-derivative (10) was treated with *p*-acetoxyphenoxide ion (prepared from hydroquinone monoacetate with sodium hydride) in dimethylformamide. The product, obtained in 70% yield, was, however, the elimination product, 2-acetoxy-3,4-di-*O*-acetyl-6-*O*-benzoylglucal (11), and not the desired substitution product (8). The *p*-acetoxyphenoxide ion here therefore acts as a base rather than as a nucleophile. Similarly, when it was allowed to react with acetobromoglucose in the presence of silver salicylate,[13] the only product isolated was 2,3,4,6-tetra-*O*-acetyl-1-*O*-salicyloyl-β-D-glucopyranose.

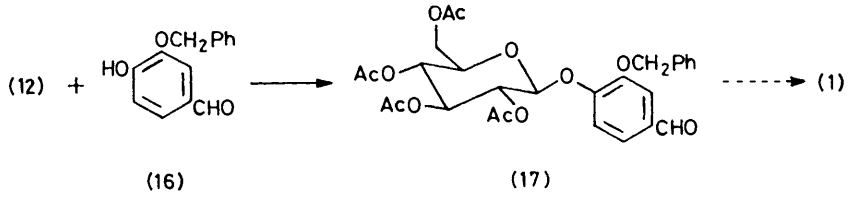
Acetobromoglucose (12), when treated with *p*-benzyloxyphenoxide ion (and also with phenoxide ion) in various dipolar aprotic solvents, gave the results in Table 2, again showing that these ions act as bases under these conditions, with the corresponding glucal[14] (13) as the only glucose-derived product. The intrinsic ability of the bromine atom of (10) to act as a good leaving group under these conditions was confirmed by its reaction with water in dimethylformamide solution when the expected hydroxy-compound was obtained in 80% yield and was characterised as 2,3,4-tri-*O*-acetyl-6-*O*-benzoyl-D-glucopyranose (see Experimental section).

TABLE 2

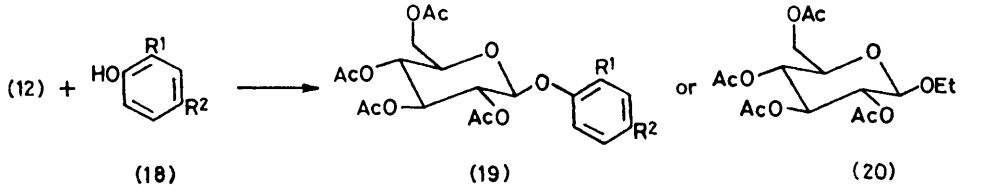
Elimination reactions in various dipolar aprotic solvents

R in (14)	Base used to generate anion	Solvent	Yield (%) (13)	(14)	(15)
H	NaH	Dimethylformamide	62	20	—
H	NaH	Dioxan	—	80	—
$PhCH_2O$	NaH	Pyridine	36	68	30
$PhCH_2O$	Bu^nLi	Tetrahydrofuran	18	43	22

During the course of this study successful syntheses of the related glucoside ester lacticolorin[2] (1) were reported,[15] based on similar earlier[16,17] condensation reactions of vanillin. The glycoside formation step was effected between acetobromoglucose (12) and 3-benzyloxy-4-hydroxybenzaldehyde (16) to accord the required glucoside ester (17) in acceptable yield using potassium hydroxide as the base in a mixture of chloroform and ethanol. Similar condensation reactions of acetobromoglucose (12) with a series of variously substituted phenols



(16) (17) (1)



(18) (19) (20)

(18) were carried out under these conditions. The results (Table 3) show that successful formation of the aryl glucosides (19) came about only when electron-withdrawing substituents were present on the phenol; with electron-donating substituents or hydrogen in the *para*-position the derived aryloxide anions were, under these conditions, weaker nucleophiles than ethanol and the ethyl glucoside ester (20) was the only coupling product obtained.

TABLE 3

Substitution *versus* elimination reactions recovery of chromatographed products (%) based on acetobromoglucose

R^1	R^2	Arylglucoside ester (19)	Ethyl glucoside ester (20)	Recovered phenol (18)
H	NO_2	57	—	45
OMe	CHO	44 [a]	—	40
H	CHO	24	—	70
H	OCH_2Ph	—	37	85
H	Me	—	30	80
H	H	—	25	80
H	OAc [b]	—	19	—
H	OMe	—	15	45
H	OH [b]	—	7	—

[a] Lit. 50% (ref. 16); 66% (ref. 15). [b] In de-aerated solvents.

These results are seemingly in conflict with the general effect of electron-donating substituents in increasing the nucleophilic strength of phenolate anions,[18] and also in conflict with the linear relationship found [19] between S_N2 reaction rates of phenacyl bromide with *para*-substituted phenolate anions, and the pK_a values of the corresponding phenols. In the case of glycoside formation from a substrate such as acetobromoglucose the substitution mechanism is not uniform, however.[20] It is furthermore to be expected that in a protic solvent such as is used here, nucleophiles with anionic sites of increased electron density would be more strongly solvated than corresponding phenolate anions under the influence of electron-withdrawing groups. Any projected general synthesis of aryl glycoside esters where the aglycone carries effective electron-donating substituents will therefore have to allow for these effects.

EXPERIMENTAL

Instruments used routinely were Kofler micro hot-stage (m.p.), Jasco IRA-1 and Perkin-Elmer 521 (i.r.), Varian-MAT CH5 (m.s.), Hitachi–Perkin-Elmer R20 (n.m.r., 60 MHz), and Pye Series 105 model 15 chromatograph (g.l.c.). I.r. spectra were recorded for potassium bromide dispersions. N.m.r. data are δ values relative to tetramethylsilane and approximate coupling constants are recorded as the separations (S in Hz) read from the spectra. T.l.c. was on precoated plates of silica gel (Merck F254), paper chromatography (p.c.) was on Whatman No. 1 sheets impregnated with glycerol and run in water-saturated n-butanol–toluene (1 : 1 v/v) after equilibration for 13—16 h, and results are quoted as hR_F (= 100 × R_F) values. Column chromatography was over silica gel (Merck, 0.05—0.20 mm). Analytical g.l.c. was over GE-SE 52 (5% on Supelcoport, 0.005 × 1.5 m) with nitrogen as the carrier gas at 10 lb in^{-2} inlet pressure. Reactions were at room temperature unless indicated otherwise.

Milled air-dried leaves (1 kg) of *Protea eximia* were extracted (Soxhlet) with methanol for 72 h. The dark oily extract (340 g) on p.c. showed (Pauly's reagent) three strong phenolic spots at hR_F 86 (purple, as for authentic hydroquinone), 72 (red, eximin), and 13 (plum red, as for authentic arbutin). The extract (316 g) was adsorbed on to 350 g of silica gel and was chromatographed over silica gel (1.6 kg) in benzene–ethyl acetate–methanol mixtures of gradually increased polarity; the progress of the elution was followed on t.l.c.

The fractions containing hydroquinone (10.74 g) from ethyl acetate directly yielded pure hydroquinone, m.p. and mixed m.p. with authentic hydroquinone, *m/e* 110 (M^+; 100%), 82 (M − CO; 31), and 81 (M − CO − H; 71), δ(C_2D_6SO) 8.48 (2 H, s, OH) and 6.50 (4 H, s, ArH).

The material (101 g) from fractions containing arbutin was (65 g) rechromatographed over silica gel (800 g) in ethyl acetate–methanol mixtures as above to give arbutin (5.3 g), m.p. 199—200°, from ethanol–chloroform, after intermediate melting at 164° and resolidification as for authentic arbutin [21] (Found: C, 52.5; H, 6.2. Calc. for $C_{12}H_{16}O_7$: C, 52.9; H, 5.9%); $\nu_{max.}$ 3 330s (OH), 1 605w, 1 510s and 1 442m (ArCH), 1 210s (ArOH), 1 060s (COH), and 823 cm^{-1} (1,4-disubst. benzene); [22] *m/e* 272 (M^+; 2%), 162 (M − $C_6H_6O_2$; 28), and 110 (100); δ(C_2D_6SO) 9.0 (1 H, OH), 6.7 (4 H, dd, S 8 and 13 Hz, ArH), 5.2, 5.0, and 4.6 (4 H, exchanged with D_2O, OH), and no clearly resolved resonances for non-aromatic CH.

The material (17.6 g) from fractions containing eximin gave *eximin* (4) (12 g), from ethanol–water, m.p. 199—202°, $[\alpha]_D$ −48° (*c* 0.94, ethanol) (Found: C, 58.5; H, 5.2. $C_{19}H_{20}O_8$ requires C, 60.6; H, 5.4. $C_{19}H_{20}O_8,H_2O$ requires C, 57.9; H, 5.6%); $\nu_{max.}$ 3 400s (OH), 2 960w and 2 920w (CH), 1 705s (PhC=O), 1 600w, 1 510s, and 1 450m (Ar), 1 285s and 1 070s (PhCO–O),[23] 1 210s (ArOH), 830m (1,4-disubst. benzene), and 770m and 710s cm^{-1} (Ph); [22] *m/e* 376 (M^+; 9%), 267 (M − $C_6H_5O_2$, 48), 266 (36), 249 (32), 126 (60), 110 (98), and 105 (100); δ(220 MHz; C_2D_6SO) 9.05 (1 H, s, OH), 7.98 (2 H, dd, S 1.5 and 8 Hz, benzoate *ortho*-H), 7.75—7.55 (3 H, m, benzoate *meta*- and *para*-H), 6.86 and 6.57 (4 H, 2 × d, S 9 Hz, Ar A_2B_2), 5.36 (2 H, d, S 5 Hz) and 5.23 (1 H, d, S 4 Hz) (3 × OH on glucose), 4.74 (1 H, d, S 7 Hz, H-1), 4.61 (1 H, d, S 11 Hz, H-3), 4.27 (1 H, dd, S 7.5 and 11.5 Hz, H-2), 3.69 (1 H, t, S 7.5 Hz, H-4), and 3.27 (3 H, m, H-5, H-6, H-6').

Eximin tetra-acetate (8), obtained from eximin with acetic anhydride in pyridine followed by chromatography, had m.p. 135—138° (from ethanol), $\nu_{max.}$ 1 750s (acetate C=O), 1 715m (benzoate C=O), 1 605w, 1 510s, and 1 455w (Ar), 1 260, 1 220, and 1 200s (acyl–O), 1 080m (PhCO–O), 830m (1,4-disubst. benzene), and 710s cm^{-1} (Ph); [22,23] *m/e* 393 (M − $CH_3CO_2C_6H_4O$, 39%), 231 (45), 169 (38), 110 (45), 109 (43), 106 (42), 105 (100), 77 (43), and 43 (99); δ(100 MHz; $CDCl_3$) 8.05 (2 H, dd, S 2 and 8 Hz, benzoate *ortho*-H), 7.52 (3 H, m, benzoate *meta*- and *para*-H), 7.3 and 6.9 (4 H, 2 × d, S 8 Hz, Ar A_2B_2), 2.26 (3 H, s, aryl Ac), 2.06, 2.04, and 2.03 (9 H, 3 × s, Ac).

Synthesis of Eximin Tetra-acetate (8).—*p*-Acetoxyphenyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-β-D-glucopyranoside (6),[24] m.p. 194—198° (lit.,[24] 197—198°) (528 mg), in chloroform (15 ml) was hydrogenolysed to completion over palladium on charcoal (10%, 110 mg). The recovered product was chromatographed (benzene–ethyl acetate) to afford quanti-

tative yields of triphenylmethane and of *p*-acetoxyphenyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside, m.p. 155—160° (from ethanol) (lit.,[25] m.p. 147—148°), $\nu_{max.}$ 3 400s (OH), 1 750s (Ac), 1 210s (ArO), and 1 030s cm^{-1}; *m/e* 440 (M^+; 3%), 289 ($M - CH_3CO_2C_6H_4O$; 90), 229 (90), 169 (95), 127 (100), and 109 (97). The latter compound (135 mg) was treated (14 h) with benzoyl chloride (60 μl) in pyridine (1 ml), and the recovered product chromatographed (100 mg) and crystallised from ethanol, m.p. 134—136°. It was identical with eximin tetra-acetate by mixed m.p., t.l.c., and by i.r., m.s., and n.m.r. spectra.

2,3,4-*Tri*-O-*acetyl*-6-O-*benzoyl*-1-α-D-*glucopyranosyl Bromide* (10).—1,2,3,4-Tetra-*O*-acetyl-D-glucose (9) [26] was benzoylated (in pyridine), and the product was chromatographed (63% yield) and crystallised from ethanol to give 1,2,3,4-tetra-*O*-acetyl-6-*O*-benzoyl-D-glucose, m.p. 135° (lit.,[27] 136°); $\nu_{max.}$ 1 740s, 1 720s, 1 200s, 1 080s, and 1 020s cm^{-1}; δ($CDCl_3$) 7.95 (2 H, dd, *S* 3 and 8 Hz), 5.70 (1 H, d, *S* 7 Hz, H-1), 2.04 (3 H, s), and 1.98 (9 H, s) as expected. It (1.03 g) was treated [28] with the known brominating reagent [28] (1.8 ml), and the product chromatographed in light petroleum–diethyl ether (1 : 4 v/v) and crystallised from diethyl ether to afford 2,3,4-tri-*O*-acetyl-6-*O*-benzoyl-1-α-D-glucopyranosyl bromide (10) (52% yield), m.p. 137—138.5° (lit.,[29] 52—53° from chloroform–light petroleum) (Found: C, 48.5; H, 4.9. Calc. for $C_{19}H_{21}BrO_9$: C, 48.2; H, 4.5%), $\nu_{max.}$ 1 760s (acetate C=O), 1 730s (benzoate C=O), 1 608w, 1 585w, and 1 450m (Ar), 1 280s, 1 230s, 1 100s, and 1 040s (acyl–O), and 710s cm^{-1} (Ph); δ($CDCl_3$) 8.0 (2 H, dd, *S* 3 and 8 Hz, benzoate *ortho*-H), 7.5 (3 H, m benzoate *meta*- and *para*-H), 6.58 (1 H, d, *S* 4 Hz, H-1), and 2.09 (3 H, s) and 2.02 (6 H, s) (3 × Ac).

2-*Acetoxy*-3,4-*di*-O-*acetyl*-6-O-*benzoylglucal* (11).—Hydroquinone monoacetate, m.p. 60—61° (lit.,[30] 62—63°) (406 mg), and sodium hydride (96 mg) were stirred in dimethylformamide (6 ml) for 1 h under nitrogen at room temperature. The foregoing bromide (10) (1.000 g) in dimethylformamide (6 ml) was added and the mixture stirred under nitrogen at 80° for 20 h. The recovered product was chromatographed (579 mg, 70%) and gave 2-*acetoxy*-3,4-*di*-O-*acetyl*-6-O-*benzoylglucal* (11), m.p. 115—116° (from ethanol) (Found: C, 58.3; H, 5.1. $C_{19}H_{20}O_9$ requires C, 58.2; H, 5.1%); $\nu_{max.}$ 1 750s (acetate C=O), 1 730s (benzoate C=O), 1 240s and 1 220s (acyl–O), and 708m cm^{-1} (Ph); *m/e* 392 (M^+; 5%), 350 ($M - C_2H_2O$; 52), 168 (57), 126 (67), 113 (53), 106 (50), 105 (100), 77 (53), and 43 (85); δ($CDCl_3$) 8.0 (2 H, dd, *S* 2 and 8 Hz, benzoate *ortho*-H), 7.49 (3 H, m, benzoate *meta*- and *para*-H), 6.59 (1 H, s, H-1), 2.09 (6 H, s, 2 × Ac), and 2.00 (3 H, s, Ac).

2,3,4,6-*Tetra*-O-*acetyl*-1-O-*salicyloyl*-β-D-*glucopyranose*.—Acetobromoglucose (199 mg, 0.48 mmol), hydroquinone monoacetate (37 mg, 0.24 mmol), and silver salicylate (133 mg, 0.54 mmol) were stirred in dry ether under nitrogen in the dark for 3 h. The filtered solution was dried and the product chromatographed to yield 2,3,4,6-tetra-*O*-acetyl-1-*O*-salicyloyl-β-D-glucopyranose (42 mg, 19%), m.p. 170—177° (lit.,[31] 184°); $\nu_{max.}$ 3 400s and 3 240s (OH), 1 750s (acetate C=O), 1 730s, 1 690s (salicylate C=O), 1 365s, 1 310s, 1 220s, and 1 090s (acyl–O), 910m, 765m, 695s, and 615s cm^{-1} (Ar).

The Stability of p-*Acetoxyphenoxide Ion in Non-de-aerated Solvents*.—Sodium hydride (7.5 mg, 0.31 mmol) and hydroquinone monoacetate (53 mg, 0.35 mmol) were heated in dry dimethylformamide (1 ml) under nitrogen at 80° for 1 h. The reaction was quenched with 1M hydrochloric acid (0.35 ml) and the product chromatographed to yield hydroquinone monoacetate (26 mg, 49%), m.p. 58—59° (from light petroleum), and identical with the starting material by t.l.c. and by g.l.c. (ret. time 12.5 min at 182°).

Reaction of Acetobromoglucose with Phenoxide Ion.—Solutions containing phenoxide ion were generated with sodium hydride or with n-butyl-lithium under nitrogen at room temperature, and the solutions were added to acetobromoglucose dissolved in the same solvent and heated under nitrogen. Details were as follows (phenol used, solvent, total vol., base used, amount of base, time for generating phenoxide ion, acetobromoglucose added, reaction temp., time): (a) phenol, 46 mg, dimethylformamide, 10 ml, sodium hydride, 17 mg, 1 h, 240 mg, 62°, 22 h; (b) phenol, 93 mg, dioxan, 5 ml, sodium hydride, 35 mg, 1 h, 327 mg, 70°, 18 h; (c) *p*-benzyloxyphenol, 92 mg, pyridine, 4 ml, sodium hydride, 16.5 mg, 241 mg, 70°, 20 h; (d) *p*-benzyloxyphenol, 133 mg, tetrahydrofuran, 10 ml, n-butyl-lithium, 0.7 mmol, 20 min, 208 mg, 62°, 18 h. Solvents were evaporated off and the residues chromatographed to afford the products listed in Table 2 which were identified as follows. 2-Acetoxy-3,4,6-tri-*O*-acetylglucal was obtained as a syrup in all cases, even when prepared as previously reported [14] when it had been found to have m.p. 61—62°; hR_F 36 in benzene–ethyl acetate (5 : 1 v/v); $\nu_{max.}$ 1 745br,s (acetate and enol acetate C=O), 1 680sh (enol acetate C=C),[32] 1 210s and 1 150s (acyl–O), 1 020s, and 900m cm^{-1}; *m/e* 330 (M^+; 1%), 288 (36), 169 (53), 155 (46), 113 (70), 98 (74), 97 (61), 69 (51), and 43 (100); δ($CDCl_3$) 6.70 (1 H, s, H-1), 5.60 (1 H, d, *S* 4 Hz), 5.24 (1 H, m), and 4.4 (3 H, m) (pyranose H), 2.12 (9 H, s) and 2.09 (3 H, s) (Ac). *p*-Acetoxyphenyl benzyl ether had m.p. 104—108° (lit.,[33] 110—111°); $\nu_{max.}$ 1 750s (Ac), 1 580m, 1 500m, and 1 450w (Ar), 1 220s and 1 190s (C–O), 1 005s, 900m, 840m (1,4-disubst. benzene), 740m, and 690m cm^{-1} (Ph); δ($CDCl_3$) 7.41 (5 H, s, Ph), 7.0 (4 H, ArH), 5.05 (2 H, s, $PhCH_2O$), and 2.28 (3 H, s, Ac).

Hydrolysis of 2,3,4-*Tri*-O-*acetyl*-6-O-*benzoyl*-1-α-D-*glucopyranosyl Bromide*.—(a) The bromide (10) (50 mg), water (100 μl), and dimethylformamide (1.5 ml) were kept under nitrogen at 70° for 16 h; the dried residue was chromatographed and the hydroxy-compound obtained as a solid (35 mg, 81%), hR_F 31 in benzene–ethyl acetate (3 : 1 v/v), identical with the product obtained under (b) below by t.l.c. and i.r. spectroscopy, and by g.l.c. of its trimethylsilyl ether prepared in Tri-Sil Z at 58° for 45 min (retention time, 3.5 min for the single peak at column temp. 286°).

(b) In accord with the known procedure [34] the bromide (10) (334 mg), water (60 μl), silver carbonate (297 mg), and acetone (1 ml) were kept for 1 h, filtered, and dried. The residue was chromatographed and gave the hydrolysis product as a solid (225 mg, 78%) characterised as 2,3,4-*tri*-O-*acetyl*-6-O-*benzoyl*-D-*glucopyranose*, m.p. 125—128° (from benzene); $[\alpha]_D$ +109° (*c* 0.31, ethanol) (Found: C, 55.6; H, 5.3. $C_{19}H_{22}O_{10}$ requires C, 55.6; H, 5.4%); $\nu_{max.}$ 3 480w, 3 420s (OH), 2 960w (CH), 1 750s (MeC=O), 1 700s (PhC=O), 1 600, 1 580, and 1 455 (m, Ar), 1 370s, 1 290m (benzoate C–O), 1 230 and 1 035 (vs, acyl–O), 770m and 720s cm^{-1} (Ph); *m/e* 305 (M – PhCO; 13%), 304 (16), 262 (12), 261 (9), 244 (13), 220 (9), 219 (9), 202 (17), 157 (39), 122 (40), 115 (40), 105 (100), and 77 (49); δ($CDCl_3$) 7.97 (2 H, dd, *S* 2 and 7 Hz) and 7.43 (3 H, m) (benzoate H), 4.4 (3 H, m, pyranose H), 2.01 (6 H, s), and 1.99 (3 H, s) (CH_3CO).

Glycosidation of Acetobromoglucose with para-*Substituted*

Phenols in Chloroform–Ethanol.[15]—All reactions were carried out as in the following example and the results are summarised in Table 3. *p*-Nitrophenol (105 mg, 0.75 mmol) and potassium hydroxide (43 mg, 0.77 mmol) in dry ethanol (2.9 ml) were stirred under nitrogen for 1 h. Acetobromoglucose (272 mg, 0.66 mmol) in dry chloroform (8 ml) was added, and the mixture was stirred under reflux for 45 h, diluted with chloroform, and poured into ice–water. The recovered products were chromatographed over silica gel (40 g) and eluted with light petroleum–diethyl ether mixtures and with diethyl ether to give unchanged *p*-nitrophenol (45% recovery) and *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (19; $R^1 = H$, $R^2 = NO_2$ (176 mg, 57% yield), m.p. 161—170° (from ethanol) (lit.,[35] 174—175°); hR_F 25 in benzene–ethyl acetate (5 : 1 v/v); $\nu_{max.}$ 1 750s, 1 730s, 1 605m, 1 585m, 1 520s, 1 490m, 1 380m, 1 340s, 1 230s, 1 030m, 1 050s, 1 030s, 910m, and 860m cm^{-1}; *m/e* 331 ($M - NO_2C_6H_4O$; 47%), 271 (38), 170 (39), 169 (85), 145 (39), 139 (41), 110 (37), 109 (76), 81 (42), and 43 (100); δ($CDCl_3$) 8.22 (2 H, d, *S* 9 Hz, ArH *ortho* to NO_2), 7.19 (2 H, dd, *S* 7 and 9 Hz, ArH *meta* to NO_2), and 2.08 (12 H, s, 4 × Ac).

p-Formylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (19; $R^1 = H$, $R^2 = CHO$) had m.p. 144—147° (from ethanol) (lit.,[36] 144—145°); hR_F 11 in benzene–ethyl acetate (5 : 1 v/v); $\nu_{max.}$ 1 750s, 1 685m, 1 600m, 1 580m, 1 500m, 1 360m, 1 220s, 1 200s, and 840w cm^{-1}; *m/e* 331 ($M - OHCC_6H_4O$; 18%), 170 (42), 169 (100), 145 (43), 139 (52), 138 (43), 127 (78), 121 (47), 115 (52), 110 (70), 109 (100), 103 (51), 97 (63), 85 (52), 81 (70), and 43 (100); δ($CDCl_3$) 9.96 (1 H, s, CHO), 7.90 (2 H, *S* 8 Hz, ArH *ortho* to CHO), 7.20 (2 H, dd, *S* 6 and 8 Hz, ArH *meta* to CHO), and 2.09 (12 H, s, 4 × Ac).

o-Methoxy-*p*-formylphenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (19; $R^1 = MeO$, $R^2 = CHO$) [15] had m.p. 134—137° (lit.,[15] 135—137°); hR_F 14 in benzene–ethyl acetate (5 : 1 v/v); δ($CDCl_3$) 9.94 (1 H, s, CHO), 7.57—7.30 (3 H, m, ArH), 3.90 (3 H, s, ArOMe), and 2.09 (12 H, 4 × Ac).

Ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (20) had m.p. 105—109° (from ethanol) (lit.,[37] 106—107°); hR_F 30 in benzene–ethyl acetate (5 : 1 v/v); $\nu_{max.}$ 1 750s, 1 740s, 1 430w, 1 380m, 1 315m, 1 220s, and 1 030s cm^{-1}; *m/e* 331 ($M - C_2H_5O$; 56%), 169 (83), 127 (46), 109 (78), and 43 (100); δ($CDCl_3$) 5.5—4.8 (3 H, m) and 4.6—4.1 (4 H, m) (pyranose H), 3.67 (2 H, q, *S* 7 Hz, $MeCH_2O$), 2.08 (12 H, s, 4 × Ac), and 1.20 (3 H, t, *S* 7 Hz, $MeCH_2O$).

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