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Synthesis of aryl D-gluco- and D-galacto-pyranosides and 1-*O*-acyl-D-gluco- and -D-galacto-pyranoses exploiting the Mitsunobu reaction. Influence of the pK_a of the acid on the stereoselectivity of the reaction*

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ABSTRACT

Glycosides (α- and β-D-glucosides and -D-galactosides) derived from three pesticides, 2-*tert*-butyl-2,4-dinitrophenol, 2,6-dibromo-4-cyanophenol, and 5-(2,4-dichlorophenoxy)-2-nitrobenzoic acid, were synthesized from 2,3,4,6-tetra-*O*-chloroacetyl-D-gluco- and -D-galactopyranose by use of the Mitsunobu reaction. It was shown that selectivity for the β-D anomer increases with the pK_a of the acid component.

INTRODUCTION

Dinoterbe (2-*tert*-butyl-2,4-dinitrophenol, **1**), Bromoxynil (3,5-dibromo-4-hydroxybenzonitrile, **2**), and Bifenox [5-(2,4-dichlorophenoxy)-2-nitrobenzoic acid **3**] are three commonly used non-systemic pesticides that are slightly soluble in water. Since sugars are the major form of transported carbon in many plant species[1], it was of interest to link D-glucose and D-galactose to these pesticides in order to increase their water solubility and to improve their biological properties, especially the recognition by the proteins responsible for sucrose transport. For example, some α-D-glucosides are known to be good inhibitors of sucrose influx into protoplasts from developing soybean cotyledons[2]. To measure the influence of the structure and the anomeric configuration of the sugar, the three pesticides were coupled with D-glucose and D-galactose in α and β configuration. We also report the coupling of 2,6-dibromo-4-cyanophenol (**2**) to D-glucose, through a linear spacer, to decrease the steric hindrance near the sugar residue.

RESULTS AND DISCUSSION

The β-D-glucoside and -D-galactoside of Dinoterbe (**1**) and Bromoxynil (**2**) were prepared from the peracetylglycosyl bromides under phase-transfer catalysis[3] in dichlo-

* Dedicated to Professor Serge David on the occasion of his 70th birthday.
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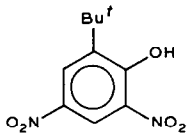
romethane in the presence of 1.25M sodium hydroxyde and benzyltriethylammonium bromide, but removal of the protecting acetyl groups required extremely mild conditions to prevent glycosidic bond cleavage. Indeed, the acidic or basic conditions generally used in the case of nitrophenyl glycosides[4] led, in our case, to extensive hydrolysis of the glycosidic bond, especially in the case of the more labile Dinoterbe glycosides. The unprotected β-D-glycosides **6**, **7**, **12**, and **13** were obtained in better yields by use of triethylamine in water–methanol at 0°. Aryl α-D-glycosides may be prepared[5] from the β anomers by Lewis acid catalysis ($ZnCl_2$, $AlCl_3$, or $TiCl_4$), or by the action of a strong base in the case of the nitro substituted phenols[6]. They can also be prepared directly by acid fusion[7] ($ZnCl_2$) to afford a mixture of anomers. Alternatively, nucleophilic substitution onto a protected β-glycosyl halide in polar aprotic solvent is known to give aryl α-D-glycosides in moderate yield[8]. All these methods proved to be unsuccessful. The pK_a of the carboxylic acid, Bifenox (**3**), is not very different from that of the two substituted phenols, Dinoterbe (**1**) and Bromoxynil (**2**), because of the presence of electron-withdrawing substituents in **1** and **2**. This makes them good candidates for a



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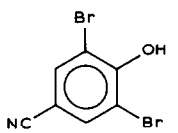

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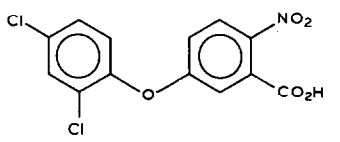

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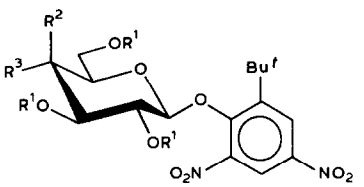
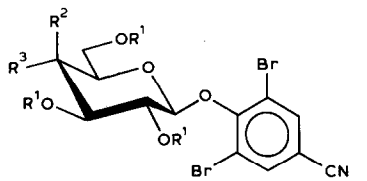
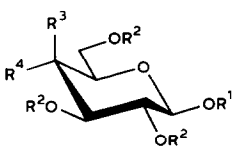


4 R^1 = Ac, R^2 = H, R^3 = OAc
5 R^1 = Ac, R^2 = OAc, R^3 = H
6 R^1 = R^2 = H, R^3 = OH
7 R^1 = R^3 = H, R^2 = OH
8 R^1 = $COCH_2Cl$, R^2 = H, R^3 = $OCOCH_2Cl$
9 R^1 = $COCH_2Cl$, R^2 = $OCOCH_2Cl$, R^3 = H



10 R^1 = Ac, R^2 = H, R^3 = OAc
11 R^1 = Ac, R^2 = OAc, R^3 = H
12 R^1 = R^2 = H, R^3 = OH
13 R^1 = R^3 = H, R^2 = OH
14 R^1 = $COCH_2Cl$, R^2 = H, R^3 = $OCOCH_2Cl$
15 R^1 = $COCH_2Cl$, R^2 = $OCOCH_2Cl$, R^3 = H



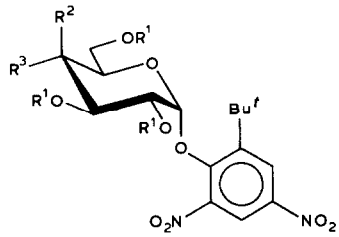
16 R^1 = R^2 = $COCH_2Cl$, R^3 = H, R^4 = $OCOCH_2Cl$
17 R^1 = R^2 = $COCH_2Cl$, R^3 = $OCOCH_2Cl$, R^4 = H
18 R^1 = R^3 = H, R^2 = $COCH_2Cl$, R^4 = $OCOCH_2Cl$
19 R^1 = R^4 = H, R^2 = $COCH_2Cl$, R^4 = $OCOCH_2Cl$

Mitsunobu synthesis[9] [diethyl or diisopropyl azodicarboxylate (DIAD) and triphenylphosphine] and this type of synthesis was selected for the preparation of the α-D-glucosides and α-D-galactosides of Dinoterbe, Bromoxynil, and Bifenox. This reaction, commonly used for acylation of primary hydroxyl groups, has already been used[10] for the acylation of anomeric OH and the preparation of aryl glycosides in moderate to good yields[11]. Owing to the extreme lability of glycosyl esters under the conditions used for *O*-acetyl group removal, the monochloroacetyl group was selected for protection because it is known to be cleaved under nearly neutral conditions[12]. Thus, the required 2,3,4,6-tetra-*O*-chloroacetyl-D-glycopyranoses (**18** and **19**) were obtained from D-glucose and D-galactose in two steps by treating the free sugar with chloroacetyl chloride in dichloromethane in the presence of triethylamine, followed by regioselective hydrazinolysis of $ClCH_2CO$-1 (overall yield, 80% for D-glucose and 77% for D-galactose). Compound **18** has been prepared by a more complicated method from benzyl β-D-glucopyranoside[13,14]. The Mitsunobu conditions afforded the desired glycosides as a mixture of α and β anomers. Table I shows the ratio of α to β anomer and the total yields of some D-glucopyranosides. For comparison, the reactions with acrylic acid[15] and with acid **36**, which was prepared from azelaic acid (nonandioic acid) and Bromoxynil, are included. The data show clearly that the ratio of α to β anomer decreases with the increase of the pK_a of the acid component. The same tendency was observed for the D-galactose derivatives. Starting from a mixture of α to β of 7:3 in the case of the most acidic compound, Bifenox (pK_a 3.4), the less acidic compound, **36** (pK_a 4.8), gave nearly exclusively the β anomer. This could result from a modification of the mechanism of the Mitsunobu reaction, extensively studied previously[16], or from a change in the ratio of anomers of the starting 2,3,4,6-tetra-*O*-chloroacetyl-D-glycopyranose, catalyzed by the acidic component of the reaction. The temperature of the reaction medium also modified the ratio of α to β anomer. Whereas the reaction between Bromoxynil (**2**) and 2,3,4,6-tetra-*O*-chloroacetyl-D-glucopyranose (**18**) conducted at room temperature led

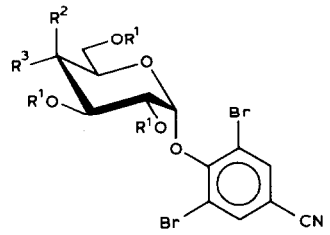
TABLE I

Yields and proportions of α-to-β-anomers in the reaction of various compounds with 2,3,4,6-tetrachloroacetyl-D-glucopyranose under the conditions of the Mitsunobu reaction

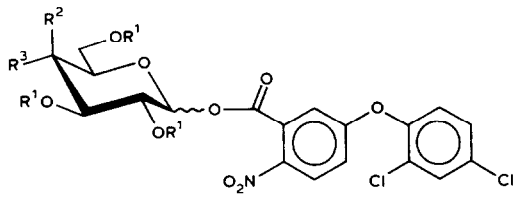
Reagent	*pK_a of reagent*	*Ratio of α-to-β anomer*	*Yield (%)*
3	3.4	7:3	70
2	4	3:2	70
1	4	7:13	51
Acrylic acid	4.25	1:9	54
36	4.8	<1:100	60



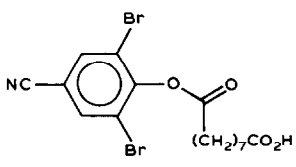
20 $R^1 = COCH_2Cl, R^2 = H, R^3 = OCOCH_2Cl$
21 $R^1 = COCH_2Cl, R^2 = OCOCH_2Cl, R^3 = H$
22 $R^1 = R^2 = H, R^3 = OH$
23 $R^1 = R^3 = H, R^2 = OH$



24 $R^1 = COCH_2Cl, R^2 = H, R^3 = OCOCH_2Cl$
25 $R^1 = COCH_2Cl, R^2 = OCOCH_2Cl, R^3 = H$
26 $R^1 = R^2 = H, R^3 = OH$
27 $R^1 = R^3 = H, R^2 = OH$



28 (α anomer), **29** (β anomer) $R^1 = COCH_2Cl, R^2 = H, R^3 = OCOCH_2Cl$
30 (α anomer), **31** (β anomer) $R^1 = COCH_2Cl, R^2 = OCOCH_2Cl, R^3 = H$
32 (α anomer), **33** (β anomer) $R^1 = R^2 = H, R^3 = OH$
34 (α anomer), **35** (β anomer) $R^1 = R^3 = H, R^2 = OH$



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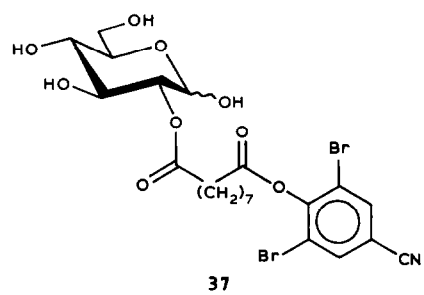

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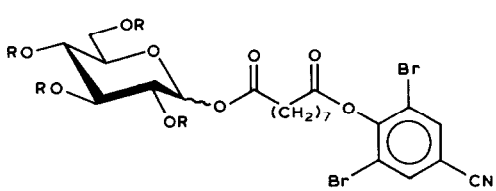

38 (β anomer), **39** (α anomer) $R = COCH_2Cl$
40 (β anomer) **41** (α anomer) $R = H$

to a 3:2 α to β ratio, the reaction conducted at −50° led to a 3:7 ratio. Nevertheless, the reaction conditions allowed the preparation of the α-D-glucosides and α-D-galactosides from Dinoterbe (**1**), Bromoxynil (**2**), and Bifenox (**3**), but not from acid **36**. In this last case, the synthesis of the α anomer was best carried out by use of dicyclohexylcarbodiimide in acetonitrile in the presence of a catalytic amount of 4-(dimethylamino)-pyridine[17] to give the α anomer **39** as the major compound. The aryl glycosides **9**, **14**, **15**, **20**, **21**, **24**, and **25** were deprotected by use of triethylamine in water–methanol within 5 min at 0°, whereas, in the case of acyl glycosides these contitions led to extensive hydrolysis, one exception being **40** which withstood the basic conditions. Consequently, the acyl glycosides were prepared under the almost neutral conditions described by van Boeckel and Beetz[12] giving the labile unprotected glycosyl esters **32**–**35** and **41** from compounds **28**–**31** and **39**, respectively. It is of interest that deprotection of **39** with triethylamine in water–methanol, even at 0°, led to the migration* of the ester group from C-1 to C-2 to give **37**, isolated by flash chromotography.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Roussel–Jouan electronic digital micropolarimeter. ^{1}H-N.m.r. spectra were recorded with a Bruker AM 250 or AM 200 (where specified) spectrometer, the chemical shifts being given relative to the signal of tetramethylsilane as internal standard for solution in organic solvents, and as external reference for solution in D_2O. The reactions were monitored by t.l.c. on Silica gel 60 F_{254} (Merck) with detection by charring with H_2SO_4. Silica gel flash chromatography was performed on Chromagel 6–35μ (S.D.S. Chemical Co.). Solvents were dried and distilled just before use. Pyridine, dichloromethane, triethylamine, and acetonitrile were distilled from CaH_2, ether and oxolane from sodium benzophenone.

*2-*tert*-Butyl-4,6-dinitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside* (**4**) *and -galactopyranoside* (**5**). — A solution of the acetylglycosyl bromide (1.13 g, 4.9 mmol) in dichloromethane (10 mL) was vigorously stirred with benzyltriethylammonium bromide (0.5 g, 2 mmol) in 1.25M aqueous NaOH (5 mL). After two days at 40°, the mixture was diluted with water, the two phases were separated, and the organic layer was washed successively with 1.25M aqueous NaOH and water, and then evaporated. Flash chromatography of the residue (1:1:1 ether–hexane–dichloromethane) gave the corresponding glycoside.

Compound (**4**). Yield 0.55 g (40%), m.p. 156–158° (ethanol), $[\alpha]_D^{20}$ −114° (*c* 1, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 8,50 (d, 1 H, *J* 2.5 Hz, arom.), 8,49 (d, 1 H, *J* 2.5 Hz, arom.), 5.40 (dd, 1 H. $J_{1,2}$ 8, $J_{2,3}$ 9 Hz, H-2), 5.27 (t, 1 H, $J_{2,3} = J_{3,4}$ 9 Hz, H-3), 5.16 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.16 (t, 1 H, $J_{3,4} = J_{4,5}$ 9 Hz, H-4), 4.10 (dd, 1 H, $J_{5,6a}$ 4, $J_{6a,6b}$ 12 Hz, H-6a), 4.00 (dd, 1 H, $J_{5,6a}$ 2, $J_{6a,6b}$ 12 Hz, H-6b), 3.64 (ddd, 1 H, $J_{4,5}$ 9, $J_{5,6a}$ 4, $J_{5,6b}$ 2 Hz, H-5), 2.20–2.00 (4 s, 12 H, 4Ac), and 1.45 (s, 9 H, Bu^t).

* For migration of ester group from C-1 to C-2, see ref. 18.

Anal. Calc. for $C_{24}H_{30}N_2O_{14}$: C, 50.52; H, 5.30; N, 4.91; O, 39.26. Found: C, 50.73; H, 5.10; N, 5.00; O, 39.44.

Compound **5**. Yield 0.79 g (58%), m.p. 142–144° (ethanol), $[\alpha]_D^{20}$ −144° (*c* 1, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 8.50 (d, 1 H, *J* 2.5 Hz, arom.), 8.49 (d, 1 H, *J* 2.5 Hz, arom.), 5.58 (dd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 10 Hz, H-2), 5.39 (d, 1 H, $J_{3,4}$ 3 Hz, H-4), 5.15 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.05 (dd, 1 H, $J_{3,4}$ 3, $J_{2,3}$ 10 Hz, H-3), 4.10–3.90 (m, 2 H, H-6a,6b), 3.85 (t, 1 H, $J_{5,6a} = J_{5,6b}$ 7 Hz, H-5), 2.20–2.00 (4s, 12 H, 4 Ac), and 1.50 (s, 9 H, Bu^t).

Anal. Calc. for $C_{25}H_{30}N_2O_{14}$: C, 50.52; H, 5.30; N, 4.91; O, 39.26. Found: C, 50.35; H, 5.35; N, 5.10; O, 39.21.

2,6-Dibromo-4-cyanophenyl 2,3,4,6-tetra-O-*acetyl-β*-D-*glucopyranoside* (**10**) *and -galactopyranoside* (**11**). — Starting from 2,3-dibromo-4-cyano-phenol (1.36 g, 4.9 mmol), the same procedure gave the corresponding glycosides.

Compound **10**. Yield 1.32 g (91%), m.p. 179–180° (ethanol), $[\alpha]_D^{20}$ −7° (*c* 1, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 7.72 (s, 2 H, arom.), 5.50–5.25 (m, 3 H, H-1,1,3), 5.20 (t, 1 H, $J_{3,4} = J_{4,5}$ 9 Hz, H-4), 4.20 (dd, 1 H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 12 Hz, H-6a), 4.05 (dd, 1 H, $J_{5,6b}$ 3.5, $J_{6a,6b}$ 12 Hz, H-6b), 3.65 (ddd, $J_{5,6b}$ 3.5, $J_{5,6a}$ 4.5, $J_{4,5}$ 9 Hz, H-5), and 2.15–2.05 (4s, 12 H, 4 Ac).

Anal. Calc. for $C_{21}H_{21}Br_2NO_{10}$: C, 41.54; H, 3.48; Br, 26.32; N, 2.30; O, 26.35. Found: C, 41.30; H, 3.28; Br, 26.20; N, 2.47; O, 26.26.

Compound **11**. Yield 1 g (70%), amorphous, $[\alpha]_D^{20}$ + 2° (*c* 1.3, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 7.80 (s, 2 H, arom.), 5.60 (t, 1 H, $J_{1,2} = J_{2,3}$ 8 Hz, H-2), 5.41 (d, 1 H, $J_{3,4}$ 3 Hz, H-4), 5.35 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.12 (dd, 1 H, $J_{3,4}$ 3, $J_{2,3}$ 8 Hz, H-3), 4.10 (dd, 1 H, $J_{5,6a}$ 7, $J_{6a,6'b}$ 12 Hz, H-6a), 4.07 (dd, 1 H, $J_{5,6b}$ 7, $J_{6a,6b}$ 12 Hz, H-6b), 3.88 (t, 1 H, $J_{5,6a} = J_{5,6b}$ 7 Hz, H-5), and 2.20–1.90 (4 s, 12 H, 4Ac).

Anal. Calc. for $C_{21}H_{21}Br_2NO_{10}$: C, 41.54; H, 3.48; Br, 26.32; N, 2.30; O, 26.35. Found: C, 41.15; H, 3.67; N, 2.59; O, 26.80.

Deblocking of glycosides **4**, **5**, **10**, *and* **11**. — A 1:8:1 (v/v) mixture of triethylamine, methanol, and water (10 mL) was added to a cooled (0°) solution of the protected glycoside (1 mmol) in dichloromethane (1.5 mL). After 3 days at 0°, the base was carefully neutralized with cold aqueous M HCl, and the mixture was extracted with ethyl acetate. Flash chromatography (9:1 ethyl acetate–hexane) of the residue obtained, after concentration of the organic phase, afforded the unprotected glycoside.

2-tert-*Butyl-4,6-dinitrophenyl β*-D-*glucopyranoside* (**6**). — Yield 0.161 g (40%), pale yellow, amorphous, $[\alpha]_D^{20}$ −103° (*c* 1, methanol); ^{1}H-n.m.r. (CD_3OD): δ 8,50 (s, 2 H, arom.), 5.00 (d, $J_{1,2}$ 7 Hz, H-1), 3.72 (dd, 1 H, $J_{5,6a}$ 2, $J_{6a,6b}$ 12 Hz, H-6a), 3.62 (dd, $J_{5,6b}$ 4, $J_{6a,6b}$ 12 Hz, H-6b), 3.59 (t, 1 H, $J_{1,2} = J_{2,3}$ 7 Hz, H-2), 3.40 (m, 2 H, H-3,4), 3.15 (m, 1 H, H-5), and 1.50 (s, 9 H, Bu^t).

Anal. Calc. for $C_{16}H_{22}N_2O_{10}\cdot H_2O$: C, 45.70; H, 5.76; N, 6.67; O, 41.88. Found: C, 45.77; H, 5.70; N, 7.01; O, 41.72.

2-tert-*Butyl-4,6-dinitrophenyl β*-D-*galactopyranoside* (**7**). — Yield 0.21 g (30%), pale yellow, amorphous, $[\alpha]_D^{20}$ −188° (*c* 1, methanol); ^{1}H-n.m.r. (CD_3OD): δ 8.50 (bs, 2 H, arom.), 4.95 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.94 (t, 1 H, $J_{2,3} = J_{1,2}$ 7.5 Hz, H-2), 3.92 (d, 1 H, $J_{3,4}$ 3 Hz, H-4), 3.60 (m, 2 H, H-6a,6b), 3.52 (dd, 1 H, $J_{2,3}$ 7.5, $J_{3,4}$ 3 Hz, H-3), 3.38 (t, 1 H, $J_{5,6a} = J_{5,6b}$ 6.5 Hz, H-5), and 1.60 (s, 9 H, Bu^t).

Anal. Calc. for $C_{16}H_{22}N_2O_{10}\cdot H_2O$: C, 45.70; H, 5.76; N, 6.67; O, 41.88. Found: C, 45.87; H, 5.65; N, 6.84; O, 41.64.

*2,6-Dibromo-4-cyanophenyl β-*D*-glucopyranoside* (**12**). — Yield 0.26 g (60%), m.p. 145–146° (water–methanol), $[\alpha]_D^{20}$ 0° (*c* 0.55, methanol); ^{1}H-n.m.r. (CD_3OD): δ 8.00 (s, 2 H, arom.), 5.38 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 3.75 (dd, 1 H, $J_{5,6a}$ 2, $J_{6a,6b}$ 11 Hz, H-6), 3.63 (t, 1 H, $J_{1,2} = J_{2,3}$ 8 Hz, H-2), 3.58 (dd, 1 H, $J_{5,6a}$ 5, $J_{6a,6b}$), 11Hz, H-6b), 3.45 (t, 1 H, $J_{2,3} = J_{3,4}$ 8 Hz, H-3), 3.33 (m, 1 H, H-4), and 3.23 (ddd, 1 H, $J_{5,6a}$ 2, $J_{5,6b}$ 5, $J_{4,5}$ 9 Hz, H-5).

Anal. Calc. for $C_{13}H_{13}Br_2NO_6$: C, 35.56; H, 2.98; N, 3.19; O, 21.86. Found: C, 35.18; H, 3.12; N, 2.60; O, 22.63.

*2,6-Dibromo-4-cyanophenyl β-*D*-galactopyranoside* (**13**). — Yield 0.30 g (70%), m.p. 138–140° (water–methanol), $[\alpha]_D^{20}$ + 10° (*c* 0.58, methanol); ^{1}H-n.m.r. (CD_3OD): δ 7.95 (s, 2 H, arom.), 5.29 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.98 (dd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 10 Hz, H-2), 3.90 (dd, 1 H, $J_{3,4}$, 3.5, $J_{4,5}$ 1 Hz, H-4), 3.75–3.55 (m, 3 H, H-3,6a,6b), and 3.45 (dt, 1 H, $J_{4,5}$ 1, $J_{5,6a} = J_{5,6b}$ 6 Hz, H-5).

Anal. Calc. for $C_{13}H_{13}Br_2NO_6$: C, 35.56; H, 2.98; N, 3.19; O, 21.86. Found: C, 35.46; H, 3.14; N, 3.12; O, 22.13.

*1,2,3,4,6-Penta-*O*-chloroacetyl-α,β-*D*-glucopyranose* (**16**) *and* -D-*galactopyranose* (**17**). — A solution of chloroacetyl chloride (24 mL, 300 mmol) in dichloromethane (200 mL) was added dropwise over 8 h to a vigorously stirred suspension of D-glucose or D-galactose (9 g, 50 mmol) in a mixture of pyridine (26 mL, 300 mL) and dichloromethane (250 mL). The mixture was then diluted with dichloromethane, washed successively with cold aq. M HCl, cold 3% aq. $KHCO_3$, and dil. NaCl. After evaporation of the organic layer, the residue was directly used for hydrazinolysis. For analytical purpose, flash chromatography (dichloromethane) afforded pure **16** and **17**.

Compound **16**. — Yield 27.86 g (99%), amorphous, $[\alpha]_D^{20}$ +49° (*c* 1.1, dichloromethane); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 6.45 (d, 0.6 H, $J_{1,2}$ 3.2 Hz, H-1α), 5.84 (d, 0.4 H, $J_{1,2}$ 8 Hz, H-1β), 5.60 (t, 0.6 H, $J_{2,3} = J_{3,4}$ 10 Hz, H-3α), 5.23 (t, 0.4 H, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3β), 5.32–5.20 (m, 2 H, H-2,4), 4.50–4.25 (m, 3 H, H-5,6a,6b), and 4.93–4.25 (multiple s, 10 H, 5 $COCH_2Cl$); lit.[13] α anomer: $[\alpha]_D^{20}$ +64.2° (*c* 1.1, chloroform).

Anal. Calc. for $C_{16}H_{17}Cl_5O_{11}$: C, 34.16; H, 3.05; O, 31.26. Found: C, 34.42; H, 2.98; O, 31.04.

Compound **17**. — Yield 27.16 g (96.5%), amorphous, $[\alpha]_D^{20}$ +63° (*c* 2.7, dichloromethane); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 6.50 (d, 0.9 H, $J_{1,2}$ 3 Hz, H-1α), 5.84 (d, 0.1 H, $J_{1,2}$ 8 Hz, H-1β), 5.62 (m, 1 H, H-4), 5.48 (m, 2 H, H-2,3), 4.50 (bt, $J_{5,6a} = J_{5,6b}$ 7 Hz, H-5), 4.30 (bd, 2 H, $J_{5,6a} = J_{5,6b}$ 7 Hz, H-6a,6b), and 4.50–4.00 (multiple s, 10 H, 5 $COCH_2Cl$); lit.[13] α anomer: $[\alpha]_D^{20}$ +74.4° (*c* 1.6, chloroform).

Anal. Calc. for $C_{16}H_{17}Cl_5O_{11}$: C, 34.16; H, 3.05; O, 31.26. Found: C, 34.37; H, 3.05; O, 31.54.

*2,3,4,6-Tetra-*O*-chloroacetyl-*D*-glucopyranose* (**18**) *and* -D-*galactopyranose* (**19**). — Hydrazine acetate (5.52 g, 60 mmol) was added to a solution of the crude perchloroacetylated sugar (28 g, 50 mmol) in *N,N*-dimethylformamide (200 mL). After 10 min at room temperature, the mixture was extracted with ether. Solvent removal gave a residue which was purified by flash chromatography (1:1 hexane–ethyl acetate) to afford **18** and **19**.

Compound **18**. — Yield 19.5 g (80%), m.p. 104–105° (ether–hexane), $[\alpha]_D^{20}$ + 75° (*c* 0.9, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 6.32 (d, 0.1 H, $J_{1,OH\beta}$ 7 Hz, OHβ), 6.18 (d, 0.9 H, $J_{1,OH\alpha}$ 4 Hz, OHα), 5.69 (t, 0.9 H, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3α), 5.50 (t, 0.9 H, $J_{1,2} = J_{1,OH\alpha}$ 4 Hz, H-1α), 5.40 (t, 0.1 H, $J_{2,3} = J_{3,5}$ 9.5 Hz, H-3β), 5.20 (m, 1 H, H-4α,1β), 5.05 (t, 0.1 H, $J_{3,4} = J_{4,5}$ 9.5 Hz, H-4β), 4.96 (m, 1 H, H-2), 4.45–4.25 (m, 3 H, H-5,6a,6b), and 4.20–4.05 (multiple s, 8 H, 4 $COCH_2Cl$); lit.[14] m.p. 104–106°, $[\alpha]_D^{20}$ + 72.5° (*c* 1, chloroform containing one drop of pyridine per mL); lit.[13] m.p. 115–116° (ether–hexane), $[\alpha]_D^{20}$ + 73.2° (*c* 0.8, chloroform containing one drop of pyridine per mL).

Compound **19**. — Yield 19.5 g (80%), amorphous, $[\alpha]_D^{20}$ + 36° (*c* 0.6, dichloromethane); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 5.60 (m, 3 H, H-1,2,4), 5.25 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 4 Hz, H-3), 4.55 (bt, 1 H, $J_{5,6a} = J_{5,6b}$ 8 Hz, H-5), 4.40 (bd, 2 H, $J_{5,6a} = J_{5,6b}$ 8 Hz, H-6a,6b), 4.20–4.00 (4 s, 8 H, 4 $COCH_2Cl$), and 3.20 (bs, 1 H, OH).

Anal. Calc. for $C_{14}H_{16}Cl_4O_{10}$: C, 34.57; H, 3.31; O, 32.89. Found: C, 34.66, H, 3.32; O, 32.94.

*2-*tert*-Butyl-4,6-dinitrophenyl 2,3,4,6-tetra-*O*-chloroacetyl-β-* (**8**) and *-α-*D*-glucopyranoside* (**20**), *and-β-* (**9**) *and -α-*D*-galactopyranoside* (**21**). — Diisopropyl azodicarboxylate (0.4 mL, 2.2 mmol) was added dropwise to a solution of 2,3,4,6-tetra-*O*-chloroacetyl-D-glucopyranose or -galactopyranose (0.5 g, 1.13 mmol), 2-*tert*-butyl-4,6-dinitrophenol (0.311 g, 1.35 mmol), and triphenylphosphine (0.524 g, 2.2 mmol) in oxolane (10 mL). After 15 min at room temperature, t.l.c. (11:6:3 hexane–dichloromethane–ethyl acetate) showed complete disappearance of the starting material. The solvent was evaporated and the residue was purified by flash chromatography (6:2:1 hexane–dichloromethane–ethyl acetate) to provide, in the order of elution, the pure α and β glycopyranosides.

Compound **8**. Yield 0.26 g (33%), amorphous, $[\alpha]_D^{20}$ − 43° (*c* 1,2, acetone); ^{1}H-n.m.r. ($CDCl_3$): δ 8.50 (d, 1 H, *J* 2.5 Hz, arom.), 8.49 (d, 1 H, *J* 2.5 Hz, arom.), 5.49 (dd, 1 H, $J_{1,2}$ 7, $J_{2,3}$ 9 Hz, H-2), 5.40 (dd, 1 H, $J_{2,3}$ 9, $J_{3,4}$ 9.5 Hz, H-3), 5.25 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 9 Hz, H-4), 5.17 (d, 1 H, $J_{1,2}$ 7 Hz, H-1), 4.25–4.00 (m, 10 H, H-6a,6b, 4 $COCH_2Cl$), 3.79 (ddd, 1 H, $J_{5,6a}$ 2, $J_{5,6b}$ 2.5, $J_{4,5}$ 9.5 Hz, H-5), and 1.50 (s, 9 H, Bu^t).

Anal. Calc. for $C_{24}H_{26}Cl_4N_2O_{14}$: C, 40.68; H, 3.69; N, 3.95; O, 31.61. Found: C, 41.58; H, 3.73; N, 4.09; O, 31.50.

Compound **20**. Yield 0.14 g (18%), amorphous, $[\alpha]_D^{20}$ + 251° (*c* 0.9, dichloromethane); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 8.54 (d, 1 H, *J* 3.5 Hz, arom.), 8.47 (d, 1 H, *J* 3.5 Hz, arom.), 6.11 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 5.85 (t, 1 H, $J_{2,3} = J_{3,4}$ 10 Hz, H-3), 5.34 (dd, 1 H, $J_{1,2}$ 4, $J_{2,3}$ 10 Hz, H-2), 5.25 (t, 1 H, $J_{3,4} = J_{4,5}$ 10 Hz, H-4), 4.32 (dd, 1 H, $J_{5,6a}$ 5, $J_{6a,6b}$ 13 Hz, H-6a), 4.15–4.00 (m, 9 H, H-6b, 4 $COCH_2Cl$), 3.81 (ddd, 1 H, $J_{5,6b}$ 2, $J_{5,6a}$ 5, $J_{4,5}$ 10 Hz, H-5), and 1.65 (s, 9 H, Bu^t).

Anal. Calc. for $C_{24}H_{26}Cl_4N_2O_{14}$: C, 40.68; H, 3.69; N, 3.95; O, 31.61. Found: C, 41.03; H, 3.76; N, 3.69; O, 31.48.

Compound **9**. Yield 0.26 g (30%), amorphous, $[\alpha]_D^{20}$ − 26° (*c* 1.5, acetone); ^{1}H-n.m.r. ($CDCl_3$): δ 8.50 (m, 2 H, arom.), 5.67 (dd, 1 H, $J_{1,2}$ 7.5, $J_{2,3}$ 10.5 Hz, H-2), 5.47 (d, 1 H, $J_{3,4}$ 3 Hz, H-4), 5.23 (dd, 1 H, $J_{3,4}$ 3, $J_{2,3}$ 10.5 Hz, H-3), 5.18 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.15–4.00 (m, 11 H, H-5,6a,6b, 4 $COCH_2Cl$), and 1.50 (s, 9 H, Bu^t).

Anal. Calc. for $C_{24}H_{26}Cl_4N_2O_{14}$: C, 40.68; H, 3.69; N, 3.95. Found: C, 41.48; H, 3.96; N, 3.91.

Compound **21**. Yield 0.20 g (25%), amorphous $[\alpha]_D^{20}$ +294° (*c* 1.1, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 8.50 (d, 1 H, *J* 2.5 Hz, arom.), 8.42 (d, 1 H, *J* 2.5 Hz, arom.), 6.20 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.75 (dd, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 5.55 (m, 2 H, H-2,4), 4.25–3.95 (m, 11 H, H-5,6a,6b, 4 $COCH_2Cl$), and 1.55 (s, 9 H, Bu^t).

Anal. Calc. for $C_{24}H_{26}Cl_4N_2O_{14}$: C, 40.68; H, 3.69; N, 3.95; O, 31.61. Found: C, 41.03; H, 3.76; N, 3.69; O, 31.48.

2,6-Dibromo-4-cyanophenyl 2,3,4,6-tetra-O-*chloroacetyl-β-* (**14**) *and -α-*D-*glucopyranoside* (**24**), *and -β-* (**15**) *and -α-*D-*galactopyranoside* (**25**). — Starting from 2,6-dibromo-4-cyanophenol (0.374 g, 1.35 mmol) and following the same procedure described above, flash chromatography (11:2:3 hexane–dichloromethane–ethyl acetate) afforded, in the order of elution, the pure α and β glycopyranosides.

Compound **14**. Yield 0.23 g, (28%), m.p. 180–182° (ether–hexane), $[\alpha]_D^{20}$ +28° (*c* 1, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 7.90 (s, 2 H, arom.), 5.50–5.40 (m, 3 H, H-1,2,3), 5.32 (dd, 1 H, $J_{4,5}$ 9.5, $J_{3,4}$ 9 Hz, H-4), 4.30 (bd, 2 H, $J_{5,6a} = J_{5,6b}$ 3 Hz, H-6a,6b), 4.20–4.00 (4s, 8 H, 4 $COCH_2Cl$), and 3.78 (dt, 1 H, $J_{4,5}$ 9.5, $J_{5,6a} = J_{5,6b}$ 3 Hz, H-5).

Anal. Calc. for $C_{21}H_{17}Br_2Cl_4NO_{10}$: C, 33.85; H, 2.30; N, 1.88; Br, 21.45; O, 21.47. Found: C, 34.09; H, 2.32; N, 1.89; Br, 21.43; O, 21.65.

Compound **24**. Yield 0.35 g (42%), amorphous $[\alpha]_D^{20}$ +88° (*c* 1,dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 7.90 (s, 2 H, arom.), 6.28 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.95 (t, 1 H, $J_{2,3} = J_{3,4}$ 10 Hz, H-3), 3.51 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 10 Hz, H-2), 5.30 (t, 1 H, $J_{3,4} = J_{4,5}$ 10 Hz, H-4), 4.85 (ddd, 1 H, $J_{4,5}$ 10, $J_{5,6a}$ 4, $J_{5,6b}$ 2.5 Hz, H-5), 4.39 (dd, 1 H, $J_{5,6a}$ 4, $J_{6a,6b}$ 12 Hz, H-6a), 4.31 (dd, 1 H, $J_{5,6b}$ 2.5, $J_{6a,6b}$ 12 Hz, H-6b), and 4.10–4.00 (4 s, 8 H, 4 $COCH_2Cl$).

Anal. Calc. for $C_{21}H_{17}Br_2Cl_4NO_{10}$: C, 33.85; H, 2.30; N, 1.88; O, 21.47. Found: C, 34.11; H, 2.36; N, 1.89; O, 21.49.

Compound **15**. Yield 0.23 g, (28%), amorphous, $[\alpha]_D^{20}$ +3° (*c* 1, dichloromethane); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 7.90 (s, 2 H, arom.), 5.69 (dd, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 10 Hz, H-2), 5.50 (dd, 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 1 Hz, H-4), 5.45 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 5.30 (dd, 1 H, $J_{3,4}$ 3.5, $J_{2,3}$ 10.5 Hz, H-3), and 4.35–3.95 (m, 11 H, H-5,6a,6b, 4 $COCH_2Cl$).

Anal. Calc. for $C_{21}H_{17}Br_2Cl_4NO_{10}$: C, 33.85; H, 2.30; N, 1.88; Br, 21.45; O, 21.47. Found: C, 34.06; H, 2.14; N, 1.82; Br, 21.53; O, 21.77.

Compound **25**. Yield 0.35 g, (42%), amorphous $[\alpha]_D^{20}$ +85° (*c* 1, dichloromethane); ^{1}H-n.m.r. ($CDCl_3$): δ 7.90 (s, 2 H, arom.), 6.39 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 5.82 (dd, 1 H, $J_{3,4}$ 3, $J_{2,3}$ 11 Hz, H-3), 5.70 (bd, 1 H, $J_{3,4}$ 3 Hz, H-4), 5.57 (dd, 1 H, $J_{1,2}$ 4, $J_{2,3}$ 11 Hz, H-2), 5.08 (bt, 1 H, $J_{5,6a} = J_{5,6b}$ 7 Hz, H-5), and 4.30–4.10 (m, 10 H, H-6a,6b, 4 $COCH_2Cl$).

Anal. Calc. for $C_{21}H_{17}Br_2Cl_4NO_{10}$: C, 33.85; H, 2.30; N, 1.88; O, 21.47. Found: C, 34.18; H, 2.08; N, 1.88; O, 22.21.

Deblocking of 2,3,4,6-tetra-O-*chloroacetyl-α-*D-*glycopyranosides.* — A mixture of 8:1:1 methanol–triethylamine–water (10 mL) was added dropwise to a cooled (0°) solution of the perchloroacetylated α-D-glycoside (1 mmol) in dichloromethane. After 5 min, t.l.c. (8:2:1 ethyl acetate–2-propanol–water) indicated complete conversion of the starting material. The mixture was then diluted with M phosphate buffer (pH 7) and

extracted with ethyl acetate (4 × 50 mL). After solvent removal, flash chromatography (ethyl acetate) of the residue gave the pure α-D-glycoside.

2-tert-Butyl-4,6-dinitrophenyl α-D-glucopyranoside (**22**). — Yield 0.217 g (54%), pale yellow, amorphous, $[\alpha]_D^{20}$ + 306° (*c* 0.9, acetone); ^{1}H-n.m.r. (200 MHz, CD_3OD): δ 8.45 (s, 2 H, arom.), 5.83 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 3.91 (dd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 9 Hz, H-3), 3.70 (dd, 1 H, $J_{1,2}$ 4, $J_{2,3}$ 9.5 Hz, H-2), 3.60 (m, 2 H, H-6a,6b), 3.50 (dd, 1 H, $J_{3,4}$ 9, $J_{4,5}$ 10 Hz, H-4), 3.10 (dt, $J_{4,5}$ = $J_{5,6a}$ 10, $J_{5,6b}$ 3 Hz, H-5), and 1.45 (s, 9 H, Bu^t).

Anal. Calc. for $C_{16}H_{22}N_2O_{10}\cdot 0.5H_2O$: C, 46.72; H, 5.64; N, 6.81; O, 40.84. Found: C, 46.11; H, 5.91; N, 6.25; O, 40.41.

2-tert-Butyl-4,6-dinitrophenyl α-D-galactopyranoside (**23**). — Yield 0.161 g (40%), pale-yellow, amorphous, $[\alpha]_D^{20}$ + 122° (*c* 0.5, methanol); ^{1}H-n.m.r. (CD_3OD): δ 8.50 (d, 1 H, *J* 2.5 Hz, arom.), 8.40 (d, 1 H, *J* 2.5 Hz, arom.), 5.45 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.36 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 9.5 Hz, H-2), 4.21 (dd, 1 H, $J_{2,3}$ 9.5, $J_{3,4}$ 3 Hz, H-3), 4.08 (dt, 1 H, $J_{4,5}$ 1, $J_{5,6a}$ = $J_{5,6b}$ 7 Hz, H-5), 3.82 (dd, 1 H, $J_{4,5}$ 1, $J_{3,4}$ 3 Hz, H-4), 3.68 (d, 2 H, $J_{5,6a}$ = $J_{5,6b}$ 7 Hz, H-6a,6b), and 1.55 (s, 9 H, Bu^t).

Anal. Calc. for $C_{16}H_{22}N_2O_{10}\cdot 0.5H_2O$: C, 46.72; H, 5.64; N, 6.81; O, 40.84. Found: C, 46.99; H, 5.54; N, 6.06; O, 40.88.

2,6-Dibromo-4-cyanophenyl α-D-glucopyranoside (**26**). — Yield 0.430 g (98%), m.p. 175–176° (water–methanol), $[\alpha]_D^{20}$ + 91° (*c* 0.36, methanol); ^{1}H-n.m.r. (CD_3OD): δ 8.00 (s, 2 H, arom.), 6.31 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.17 (dt, 1 H, $J_{4,5}$ 10, $J_{5,6a}$ = $J_{5,6b}$ 3 Hz, H-5), 4.05 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ 9 Hz, H-3), 3.72–3.60 (m, 3 H, H-2,6a,6b), and 3.50 (dd, 1 H, $J_{3,4}$ 9, $J_{4,5}$ 10 Hz, H-4).

Anal. Calc. for $C_{13}H_{13}Br_2NO_6$: C, 35.56; H, 2.98; N, 3.19; O, 21.86. Found: C, 35.41; H, 3.23; N, 3.02; O, 21.97.

2,6-Dibromo-4-cyanophenyl α-D-galactopyranoside (**27**). — Yield 0.430 g (98%), m.p. 138–140° (water–methanol). $[\alpha]_D^{20}$ + 122° (*c* 0.5, methanol); ^{1}H-n.m.r. (CD_3OD): δ 8.00 (s, 2 H, arom.), 6.38 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.39 (t, 1 H, $J_{5,6a}$ = $J_{5,6b}$ 6 Hz, H-5), 4.15 (dd, 1 H, $J_{2,3}$ 11, $J_{3,4}$ 3 Hz, H-3), 4.05 (m, 2 H, H-2,4), 3.68 (dd, 1 H, $J_{5,6a}$ 6, $J_{6a,6b}$ 11.5 Hz, H-6a), and 3.59 (dd, 1 H, $J_{5,6a}$ 6, $J_{6a,6b}$ 11.5 Hz, H-6b).

Anal. Calc. for $C_{13}H_{13}Br_2NO_6$: C, 35.56; H, 2.98; N, 3.19; O, 21.86. Found: C, 35.01; H, 2.70; N, 2.92; O, 22.95.

1-O-[5-(2,4-Dichlorophenoxy)-2-nitrobenzoyl]-α- and -β-D-glycopyranoses (**32–35**). — Diisopropyl azodicarboxylate (3.24 mL, 16.5 mmol) was added dropwise to a solution of 2,3,4,6-tetra-*O*-chloroacetyl-D-glycopyranose (4 g, 8.23 mmol), 5-(2,4-dichlorophenoxy)-2-nitrobenzoic acid (4.04 g, 12.35 mmol), and triphenylphosphine (4.33 g, 16.5 mmol) in oxolane (50 mL). After 15 min at room temperature, the mixture was concentrated and the residue was purified by flash chromatography (4:1 hexane–ethyl acetate) to afford, in each case (D-glucose or D-galactose), an inseparable mixture of α and β anomers (**28–31**), (4.6 g, 70%), in a 7:3 ratio in favor of the α anomer. The mixture was dissolved in dichloromethane (6 mL) and treated with a freshly prepared solution of hydrazine dithiocarbonate [23 mmol in 7:2 ethanol–water (25 mL)]. After 20 min at room temperature, t.l.c. (19:1 ethyl acetate–methanol) showed complete disparition of the starting material. After solvent removal, the residue was purified by flash

chromatography (7:19:1 hexane–ethyl acetate–methanol) to provide first the pure α, followed by the β anomer.

1-O-[5-(2,4-Dichlorophenoxy)-2-nitrobenzoyl]-α-D-glucopyranose (**32**). — Yield 1.18 g (29%), amorphous $[\alpha]_D^{20}$ +72° (*c* 0.9, acetone); ^{1}H-n.m.r. (200 MHz, CD_3OD): δ 8.10 (d, 1 H, *J* 9 Hz, arom.), 7.69 (d, 1 H, *J* 2 Hz, arom.), 7.48 (dd, 1 H, *J* 2 and 9 Hz, arom.), 7.35 (d, 1 H, *J* 2 Hz, arom.), 7.31 (d, 1 H, *J* 9 Hz, arom.), 7.11 (dd, 1 H, *J* 2 and 9 Hz, arom.), 6.35 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 3.82 (dd, 1 H, $J_{5,6a}$ 3, $J_{6a,6b}$ 12 Hz, H-6), 3.74 (dd, 1 H, $J_{5,6a}$ 3.5, $J_{6a,6b}$ 12 Hz, H-6b), and 3.70–3.48 (m, 4 H, H-2,3,4,5).

Anal. Calc. for $C_{19}H_{17}Cl_2NO_{10}$: C, 46.53; H, 3.49; N, 2.89; O, 32.62. Found: C, 47.16; H, 3.89; N, 2.80; O, 31.95.

1-O-[5-(2,4-Dichlorophenoxy)-2-nitrobenzoyl]-β-D-glucopyranose (**33**). — Yield 0.508 g (13%), amorphous, $[\alpha]_D^{20}$ +26° (*c* 1, acetone); ^{1}H-n.m.r. (200 MHz, CD_3OD): δ 8.10 (d, 1 H, *J* 9 Hz, arom.), 7.68 (d, 1 H, *J* 2 Hz, arom.), 7.47 (dd, 1 H, *J* 2 and 9 Hz, arom.), 7.35 (d, 1 H, *J* 2 Hz, arom.), 7.30 (d, 1 H, *J* 9 Hz, arom.), 7.13 (dd, 1 H, *J* 2 and 9 Hz, arom.), 5.68 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 3.80 (dd, 1 H, $J_{5,6a}$ 1.5, $J_{6a,6b}$ 12 Hz, H-6a), 3.72 (dd, 1 H, $J_{5,6b}$ 4, $J_{6a,6b}$ 12 Hz, H-6b), and 3.45 (m, 4 H, H-2,3,4,5).

Anal. Calc. for $C_{19}H_{17}Cl_2NO_{10}$: C, 46.53; N, 3.49; N, 2.85; O, 32.62. Found: C, 46.85; H, 3.75; N, 2.76; O, 31.78.

1-O-[5-(2,4-Dichlorophenoxy)-2-nitrobenzoyl] α-D-*galactopyranose* (**34**). — Yield 1.18 g (29%), amorphous, $[\alpha]_D^{20}$ +81° (*c* 1, acetone); ^{1}H-n.m.r. (200 MHz, CD_3OD): δ 8.05 (d, 1 H, *J* 9 Hz, arom.), 7.65 (d, 1 H, *J* 2 Hz, arom.), 7.42 (dd, 1 H, *J* 2 and 9 Hz, arom.), 7.37 (d, 1 H, *J* 2 Hz, arom.), 7.25 (d, 1 H, *J* 9 Hz, arom.), 7.10 (dd, 1 H, *J* 2 and 9 Hz, arom.), 6.35 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.05 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 10 Hz, H-2), 3.96 (dd, 1 H, $J_{3,4}$ 3, $J_{4,5}$ 1 Hz, H-4), 3.90 (dt, 1 H, $J_{4,5}$ 1, $J_{5,6a} = J_{5,6b}$ 6 Hz, H-5), 3.72 (d, 2 H, $J_{5,6a} = J_{5,6b}$ 6 Hz, H-6a,6b), and 3.95 (dd, 1 H, $J_{2,3}$ 10, $J_{3,4}$ 3 Hz, H-3).

Anal. Calc. for $C_{19}H_{17}Cl_2NO_{10}$: C, 46.53; H, 3.49; N, 2.85; O, 32.62. Found: C, 46.81; H, 4.07; N, 2.61; O, 32.07.

1-O-[5-(2,4-Dichlorophenoxy)-2-nitrobenzoyl]-β-D-galactopyranose (**35**). — Yield 0.51 g (13%), amorphous, $[\alpha]_D^{20}$ +31° (*c* 1, acetone); ^{1}H-n.m.r. (200 MHz, CD_3OD): δ 8.10 (d, 1 H, *J* 9 Hz, arom.), 7.68 (d, 1 H, *J* 2 Hz, arom.), 7.45 (dd, 1 H, *J* 2 and 9 Hz, arom.), 7.35 (d, 1 H, *J* 2 Hz, arom.), 7.30 (d, 1 H, *J* 9 Hz, arom.), 7.15 (dd, 1 H, *J* 2 and 9 Hz, arom.), 5.62 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 3.90 (d, 1 H, $J_{3,4}$ 3 Hz, H-4), 3.80–3.50 (m, 4 H, H-2,5,6a,6b), and 3.60 (dd, $J_{3,4}$ 3, $J_{2,3}$ 9.5 Hz, H-3).

Anal. Calc. for $C_{19}H_{17}Cl_2NO_{10}$: C, 46.53; H, 3.49; N, 2.89; O, 32.62. Found: C, 46.80; H, 4.02; N, 2.74; O, 32.46.

1-O-[8-(2,6-Dibromo-4-cyanophenoxycarbonyl)octanoyl]-2,3,4,6-tetra-O-monochloroacetyl-β-D-glucopyranose (**38**). — Bromoxinil (**2**; 5.54 g, 20 mmol) and dicyclohexylcarbodiimide (6.18 g, 30 mmol) were added to a solution of nonane-1,9-dioic acid (azelaic acid) (11.34 g, 60 mmol) in acetonitrile (200 mL) heated at 60°. After 2 h at this temperature, the mixture was filtered to remove dicyclohexylurea and the filtrate concentrated. Flash chromatography (4:1 hexane–ethyl acetate) afforded 8-(2,6-dibromo-4-cyanophenoxycarbonyl)octanoic acid (**36**; 6.8 g, 76%), m.p. 82–83° (ether–hexane); ^{1}H-n.m.r. ($CDCl_3$): δ 11.00 (bs, 1 H, CO_2H), 7.90 (s, 2 H, arom.), 2.68 (t, 2 H, *J* 7

Hz, CH_2CO_2R), 2.35 (t, 2 H, *J* 7 Hz, CH_2CO_2H), and 1.81–1.40 (m, 10 H, $-(CH_2)_5-$). Acid **36** (6.8 g, 13.6 mmol) was added to a cold (0°) solution of 2,3,4,6-tetra-*O*-monochloroacetyl-D-glucopyranose (2.20 g, 4.53 mmol) and triphenylphosphine (3.56 g, 13.6 mmol) in oxolane (35 mL), and diisopropyl azodicarboxylate (2.67 mL, 13.6 mmol) was added dropwise. The mixture was filtered 5 min after the end of the addition, and the filtrate concentrated. Flash chromatography of the residue afforded **38** (2.27 g 55%) as a colorless gum, $[\alpha]_D^{20}$ + 5° (*c* 1, dichloromethane); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 7.90 (s, 2 H, arom.), 5.84 (d, 1 H, $J_{1,2}$ 9 Hz, H-1), 5.44 (t, 1 H, $J_{2,3} = J_{3,4}$ 9 Hz, H-3), 5.26 (t, 1 H, $J_{1,2} = J_{2,3}$ 9 Hz, H-2), 5.25 (t, 1 H, $J_{3,4} = J_{4,5}$ 9 Hz, H-4), 4.40 (dd, 1 H, $J_{5,6a}$ 4, $J_{6a,6b}$ 11 Hz, H-6), 4.30 (dd, 1 H, $J_{5,6a}$ 2, $J_{6a,6b}$ 11 Hz, H-6b), 4.15–4.00 (4s, 8 H, 4 $COCH_2Cl$), 2.70 (t, 2 H, *J* 7 Hz, CH_2CO), 2.40 (t, 2 H, *J* 7 Hz, CH_2CO), and 1.85–1.35 [m, 10 H, $(CH_2)_5$].

Anal. Calc. for $C_{30}H_{18}Br_2Cl_4NO_{13}$: C, 39.37; H, 3.41; N, 1.53; O, 22.72. Found: C, 40.34; H, 3.45; N, 1.63; O, 22.59.

*1-O-[8-(2,6-Dibromo-4-cyanophenoxycarbonyl)octanoyl]-2,3,4,6-tetra-*O*-monochloroacetyl-α-D-glucopyranose* (**39**). — 4-Dimethylaminopyridine (10 mg) was added to a cold (0°) solution of 2,3,4,6-tetra-*O*-monochloroacetyl-D-glucopuranose (2 g, 4 mmol), acid **36** (3 g, 6.3 mmol), and dicyclohexylcarbodiimide (1.3 g, 6.3 mmol) in acetonitrile (40 mL). After 20 min at 0°, the mixture was filtered to remove dicyclohexylurea and the filtrate was concentrated. Flash chromatography (4:8:5 hexane–dichloromethane–ethyl acetate) of the residue afforded first the α anomer **39** (2 g, 51%), followed by the β anomer **38** (0.67 g, 17%).

Compound **39**. Colorless gum, $[\alpha]_D^{20}$ + 45° (*c* 1, dichloromethane); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 7.90 (s, 2 H, arom., 6.39 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.60 (t, 1 H, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3), 5.24 (t, 1 H, $J_{3,4} = J_{4,5}$ 9.5 Hz, H-4), 5.20 (dd, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 9.5 Hz, H-2), 4.40–4.20 (m, 3 H, H-5,6a,6b), 4.15–4.00 (4 s, 8 H, 4 $COCH_2Cl$), 2.70 (t, 2 H, *J* 7 Hz, CH_2CO), 2.45 (t, 2 H, *J* 7 Hz, CH_2CO), and 1.80–1.40 [m, 10 H, $(CH_2)_5$].

1-O-[8-(2,6-Dibromo-4-cyanophenoxycarbonyl)octanoyl]-β-D-glucopyranose (**40**). — 1:8:1 (v/v) Triethylamine–methanol–water (10 mL) was added to a cold (0°) solution of **38** (0.91 g, 1 mmol) in dichloromethane (2 mL). After 5 min at 0° M phosphate buffer (pH 7) was added and the mixture was extracted with ethyl acetate. The combined organic layers were concentrated and flash chromatography of the residue afforded **40**, amorphous (0.484 g, 80%), $[\alpha]_D^{20}$ + 3.5° (*c* 0.8, methanol); ^{1}H-n.m.r. [200 MHz, $(CD_3)_2CO$]: δ 8.24 (s, 2 H, arom.), 5.50 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 3.85 (m, 5 H, 4 OH, H-6a), 3.70 (dd, 1 H, $J_{5,6a}$ 4.5, $J_{6a,6b}$ 12 Hz, H-6b), 3.60–3.32 (m, 4 H, H-2,3,4,5), 2.80 (t, 2 H, *J* 7 Hz, CH_2CO), 2.43 (t, 2 H, *J* 7 Hz, CH_2CO), and 1.85–1.45 [m, 10 H, $(CH_2)_5$].

Anal. Calc. for $C_{22}H_{24}Br_2NO_9$: C, 43.36; H, 4.46; N, 2.23; O, 23.63. Found: C, 43.73; H, 4.51; N, 2.36; O, 23.88.

1-O-[8-(2,6-Dibromo-4-cyanophenoxycarbonyl)octanoyl)]-α-D-glucopyranose (**41**). — A freshly prepared solution of hydrazine dithiocarbonate [3.13 mmol in 3:5:1 ethanol–water (3.5 mL)] was added to a solution of **39** (0.70 g, 0.07 mmol) in dichloromethane (3 mL). After 20 min at room temperature, the mixture was concentrated. Flash chromatography (19:1 ethyl acetate–methanol) of the residue afforded **41** (0.255

g, 55%), amorphous, $[\alpha]_D^{20}$ +47° (*c* 1.7, methanol); ^{1}H-n.m.r. [200 MHz, $(CD_3)_2CO$–D_2O]: δ 8.25 (s, 2 H, arom.), 6.12 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 3.80–3.45 (m, 6 H, H-2,3,4,5,6a,6b), 2.80 (t, 2 H, *J* 7 Hz, CH_2CO), 2.45 (t, 2 H, *J* 7 Hz, CH_2CO), and 1.83–1.40 [m, 10 H, $(CH_2)_5$].

*2-O-[8-(2,6-Dibromo-4-cyanophenoxycarbonyl)octanoyl]-*D*-glucopyranose* (**37**). — 1:8:1 (v/v) Triethylamine–methanol–water (10 mL) was added to a cold (0°) solution of **39** (0.915 g, 1 mmol) in dichloromethane (2 mL). After 5 min at 0°, M phosphate buffer (pH 7) was added and the mixture was extracted with ethyl acetate. The combined organic layers were concentrated and flash chromatography (3:1 ethyl acetate–acetone) afforded **37** (0.484 g, 80%), amorphous, $[\alpha]_D^{20}$ +41° (*c* 0.85, acetone); ^{1}H-n.m.r. [200 MHz, $(CD_3)_2CO$–D_2O): δ 8.25 (s, 2 H, arom.), 5.25 (d, 0.6 H, $J_{1\alpha,2\alpha}$ 3.5 Hz, H-1α), 4.65 (d, 0.4 H, $J_{1\beta,2\beta}$ 7 Hz, H-1β), 4.58 (dd, 0.6 H, $J_{1\alpha,2\alpha}$ 3.5, $J_{2\alpha,3\alpha}$ 9 Hz, H-2α), 4.10–3.40 (m, 5.4 H, H-2β,3α,β,4α,β,5α,β,6a,α,β,6b,α,β), 2.81 (t, 2 H, *J* 7 Hz, CH_2CO α,β), 2.40 (t, 2 H, *J* 7 Hz, $CH_2CO\alpha$,β), and 1.83–1.45 [m, 10 H, $(CH_2)_5\alpha$,β].

Anal. Calc. for $C_{22}H_{24}Br_2NO_9$: C, 43.36; H, 4.46; N, 2.23; O, 23.63). Found: C, 43.49; H, 4.59; N, 2.17; O, 23.73.

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