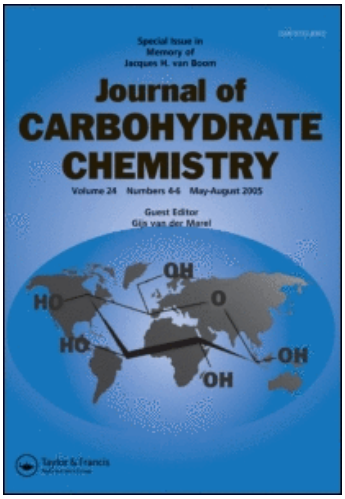

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IODONIUM-PROMOTED GLYCOSYLATIONS WITH PHENYL SELENOGLYCOSIDES

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ABSTRACT

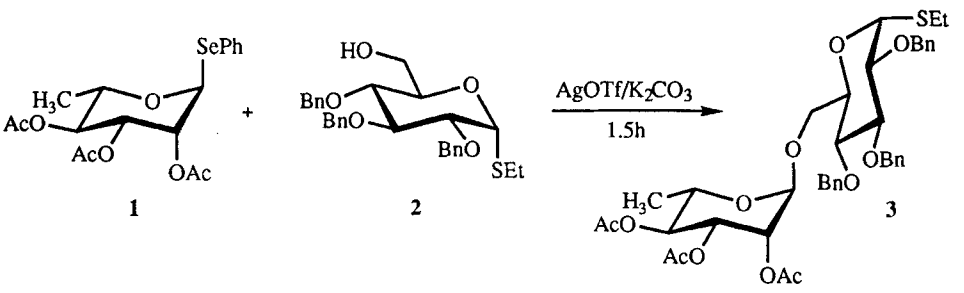
Fully benzylated or benzoylated phenyl selenoglycosides can be activated by the promoters iodonium di-*sym*-collidine perchlorate (IDCP) or *N*-iodosuccinimide and catalytic triflic acid (NIS/TfOH). The potential of the iodonium ion-mediated glycosylations with phenyl selenoglycosides is illustrated in the chemoselective synthesis of 1,2-*cis*- and 1,2-*trans* linked disaccharides.

INTRODUCTION

Recently, Pinto *et al.*[1] reported *inter alia* that phenyl 2,3,4-tri-*O*-acetyl-1-seleno-α-L-rhamnopyranoside (**1**) could be condensed (see Scheme 1) selectively under the agency of silver triflate with ethyl 2,3,4-tri-*O*-benzyl-1-thio-α-D-glucopyranoside (**2**) giving disaccharide **3** in 80% yield. It occurred to us that the importance of this interesting phenomenon had not fully been recognised and the subtle difference in that reactivity earlier observed in closely related iodonium ion-mediated glycosidations of "armed" or "disarmed" thioglycosides[2] had not been exploited.

We here report in detail[3] that iodonium ions generated from *N*-iodosuccinimide and catalytic triflic acid (NIS/TfOH) or iodonium di-*sym*-collidine perchlorate (IDCP) are effective agents to probe in depth the glycosylating properties of phenyl selenoglycosides.

Scheme 1

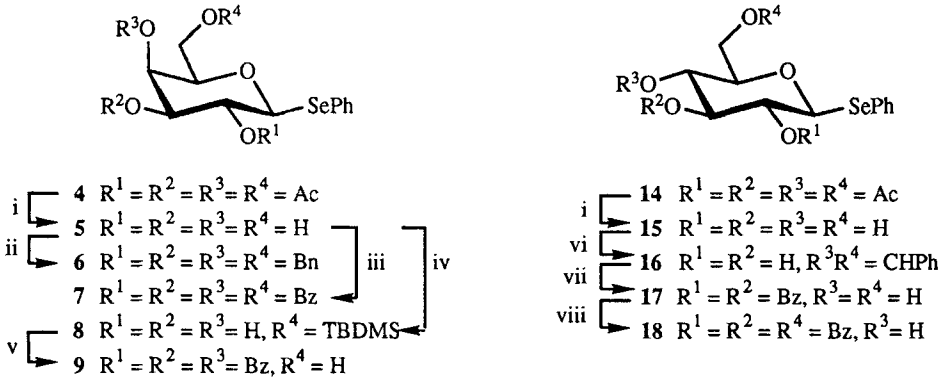


RESULTS AND DISCUSSION

In order to evaluate in detail the scope of phenyl 1-selenoglycosides in oligosaccharide synthesis, we first examined glycosylations using the fully benzylated phenyl 1-seleno-β-D-galactopyranoside **6** ("armed" donor) with terminal[4] (compounds **10-12**) and non-terminal acceptors (compounds **9**, **13** and **18**) using the weak thiophilic promoter IDCP.

The requisite "armed" donor **6** was readily accessible (see Scheme 2) by Zemplén deacetylation of fully acetylated phenyl 1-seleno-β-D-galactopyranoside **4**, obtained by

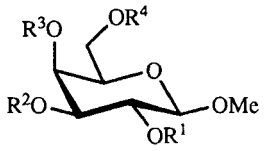
Scheme 2[a]



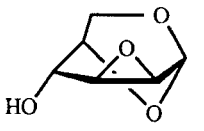
a. Reagents and conditions: (i) KO*t*Bu, MeOH; (ii) BnBr, NaH, DMF (75% based on **5**); (iii) BzCl, C_5H_5N (83% based on **5**); (iv) TBDMSCl, C_5H_5N (65% based on **5**); (v) BzCl, C_5H_5N, then *p*-TsOH, CH_3CN/H_2O [4:1] (82%); (vi) $PhCH(CH_3O)_2$, *p*-TsOH, DMF (57% based on **14**); (vii) BzCl, C_5H_5N, then $HOAc/H_2O$ [5:1], 50°C (82%); (viii) BzCl, C_5H_5N (79%).

treatment of penta-*O*-acetyl-β-D-galactopyranose with boron trifluoride etherate complex in the presence of phenylselenol,[1] followed by benzylation of **5** with benzyl bromide and sodium hydride.

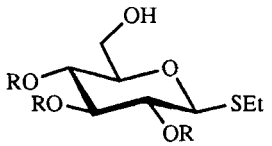
The IDCP-mediated glycosylation of the acceptors **9-13** and **18** are summarized in Table 1. Thus, IDCP-assisted glycosylation with "armed" donor **6** with the primary hydroxyl of the galactopyranosyl acceptor **10**[5] to give dimer **19** (entry 1) proceeds in a good yield but with poor stereoselectively. A similar result (entry 2), although with a higher preference for the formation of the 1,2-*cis* linked dimer **20**, was observed by condensing **6** with the equatorial hydroxyl group of the galactosyl acceptor **11**.[6] On the other hand, coupling of **6** with the axially oriented hydroxyl group of 1,6:2,3-dianhydro-β-D-mannopyranose **12**[7] was a high-yielding and rather stereoselective process (entry 3)



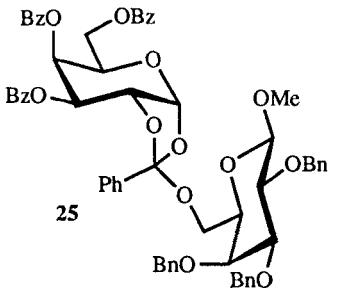
10 $R^1 = R^2 = R^3 = Bn$, $R^4 = H$
11 $R^1 = H$, $R^2 : R^3 = C(Me)_2$, $R^4 = Tr$



12



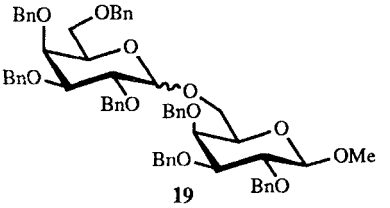
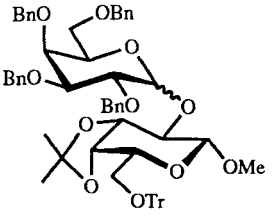
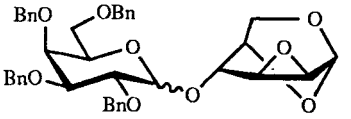
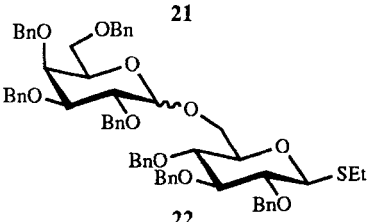
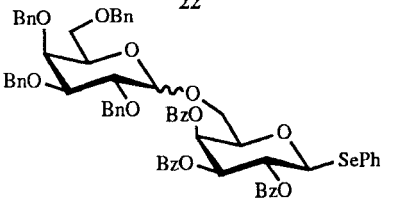
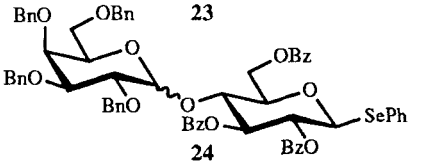
13 R = Bn
29 R = Bz



25

leading predominantly to the α-linked dimer **21**. Apart from these results, it is also of interest to note that the glycosylations mediated by the weak thiophilic promoter IDCP all proceeded[8] with a faster rate than similar condensations using an "armed" ethyl 1-thioglycoside as the donor. It might therefore be anticipated that donor **6** would react in a chemospecific manner with the "armed" and non-terminal thio-acceptor **13**. Indeed, it can be seen in entry 4 that IDCP-mediated condensation of **6** with **13**[9] leads to the isolation of dimer **22** in a good yield. Furthermore, the high reactivity of donor **6** towards IDCP was further illustrated by its chemoselective condensation (entry 5) with the non-terminal and "disarmed" phenyl 1-seleno-β-D-galactosyl acceptor **9**, which was

Table 1 Results of IDCP-promoted glycosylations using "armed" phenyl selenoglycoside donor **6** with acceptors **9-13** and **18**

Entry	Donor	Acceptor	Time (min)	Disaccharide	Yield(%) (α/β ratio)[a]
1	**6**	**10**	10	 **19**	82 (2.5/1)
2	**6**	**11**	20	 **20**	81 (6/1)
3	**6**	**12**	20	 **21**	90 (9/1)
4	**6**	**13**	15	 **22**	79 (5/1)
5	**6**	**9**	25	 **23**	87 (4/1)
6	**6**	**18**	15	 **24**	45 (9/1)

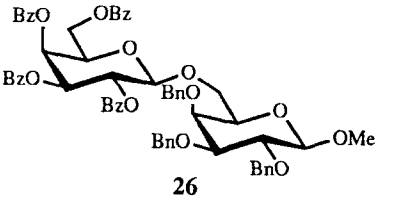
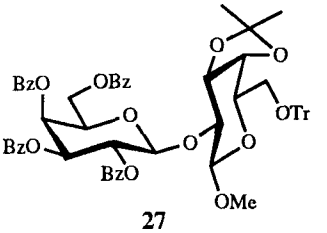
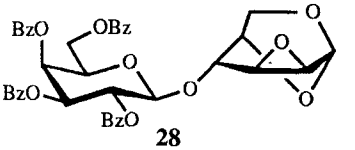
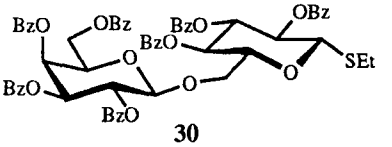
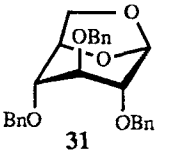
a. Estimated by ^{13}C NMR spectroscopy.

obtained (see Scheme 2) by regioselective silylation of **5** (→8) with *t*-butyldimethylsilyl chloride (TBDMS-Cl) followed by benzoylation and then acidic hydrolysis of the TBDMS group from the fully protected intermediate. On the other hand, glycosylation of the secondary hydroxyl of the phenyl selenoglycosyl acceptor **18**, prepared in five steps [Scheme 2: deacetylation of **14** (→**15**), benzylidenation (→**16**) followed by benzoylation and acid hydrolysis of the benzylidene group (→**17**), and then regioselective benzoylation], with donor **6** proceeded with a high degree of stereoselectively (mainly α-linked dimer **24**) but in a low yield.

At this stage, we focussed our attention on iodonium-promoted glycosylations with "disarmed" phenyl 1-seleno-β-D-galactopyranosyl donor **7**, readily accessible by benzoylation of **5**, with terminal (compounds **10-12**) and non-terminal acceptors (compounds **13** and **29**). First of all, it was established that donor **7** was not inert, in contrast[8] with the corresponding fully benzoylated ethyl 1-thioglycosyl donor, towards the promoter IDCP. For example, condensation of **7** with the terminal galactosyl acceptor **10** was a slow process (reaction was complete after 60 min: *cf.* entry 1 in Table 1), resulting in the 1,2-orthoester derivative **25** which could be isolated in 60% yield. As expected, glycosylation of the terminal acceptors **10-13** with donor **7** occurred rapidly under the agency of the strong thiophilic promoter NIS/TfOH providing the respective 1,2-*trans* linked dimers **26-28** (see entries 1-3 in Table 2). However, it is evident that the yield of the NIS/TfOH-promoted condensations in entries 1-3 is strongly affected by the reactivity of the acceptor. The latter finding is in sharp contrast with the IDCP-promoted glycosidation of the "armed" donor **6** with the same acceptors (see entries 1-3 in Table 1). Furthermore, it is also of interest to note that the condensation of **7** with the "disarmed" ethyl thioglycosyl acceptor **29**[10] yielding dimer **30** (entry 4) proceeds with the same degree of chemoselectively as the IDCP-assisted coupling of **6** with the corresponding "armed" ethyl thioglycoside acceptor **13** (see entry 4 in Table 1). Interestingly, glycosylation of **7** with the same acceptor **13** resulted in the rapid and exclusive formation of the 1,6-anhydro derivative **31** (entry 5), indicating that the cyclisation of **13** is a highly competitive process. In contrast, the α-anomer of **13** (*i.e.*, compound **2** in Scheme 1) could be condensed in a highly chemocontrolled manner with the "disarmed" rhamnosyl donor **1** using AgOTf as a promoter.

In conclusion, iodonium and (or) silver triflate activation of phenyl 1-selenoglycosides presents a valuable asset to future synthesis of complex oligosaccharides.

Table 2 Results of NIS/TfOH-promoted glycosylations using "disarmed" phenyl selenoglycoside **7** donor with acceptors **10-13** and **29**

Entry	Donor	Acceptor	Time (min)	Disaccharide	Yield(%)
1	**7**	**10**	2	 **26**	91
2	**7**	**11**	10	 **27**	67
3	**7**	**12**	15	 **28**	50
4	**7**	**29**	2	 **30**	79
5	**7**	**13**	5	 **31**	65

EXPERIMENTAL

General methods and materials. Pyridine and acetonitrile were dried by refluxing over CaH_2 (5 g/L) and then distilled. 1,2-Dichloroethane and toluene were distilled from P_2O_5. DMF was stirred with CaH_2 at room temperature and distilled under reduced pressure. Ether was distilled from $LiAlH_4$. Pyridine, acetonitrile and DMF were stored

over molecular sieves 4Å (Aldrich). Toluene and ether were stored over sodium wire and 1,2-dichloroethane over alumina. Schleicher and Schüll DC Fertigfolien F 1500 LS 254 were used for TLC analysis. Compounds were detected by charring with 20% sulfuric acid in methanol. Optical rotations were recorded at 20 °C with a Perkin-Elmer 241 polarimeter for solutions in $CHCl_3$, unless stated otherwise. Column chromatography was performed on silica gel 60, 230-400 mesh (Merck). Gel filtration was performed on Sephadex LH20 (Pharmacia). ^1H NMR spectra (300 MHz) were recorded at 25 °C with a Brucker WM 300 spectrometer. ^{13}C NMR spectra (50 MHz) were recorded with a Jeol JNM-FX 200 spectrometer. ^1H and ^{13}C chemical shifts (δ) are given in ppm relative to that of Me_4Si ($CDCl_3$).

Preparation of selenoglycosides. Phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-β-D-galactopyranoside and phenyl 2,3,4,6-tetra-*O*-acetyl-1-seleno-β-D-glucopyranoside were prepared from the corresponding β-acetates with phenylselenol (1.2 equiv.) and $BF_3{\cdot}OEt_2$ (3.5 equiv.). After 3 h at room temperature, the reaction mixture was diluted with CH_2Cl_2, washed with 0.9M $NaHCO_3$, water, dried ($MgSO_4$), and concentrated *in vacuo*. Purification of the residue was effected by chromatography on silica gel [1:0 to 0:1 light petroleum (bp 40-60 °C)-ether] to furnish the pure phenyl selenoglycosides.

Phenyl 2,3,4,6-Tetra-*O*-acetyl-1-seleno-β-D-galactopyranoside (4). Prepared as described above in a yield of 92%, $[\alpha]_D$ +8° (*c* 1). ^1H NMR ($CDCl_3$) δ 1.97, 2.04, 2.08, 2.10 (4 x s, 12H, CH_3COO), 3.91 (t, 1H, H-5, $J_{5,6}$ 7.0 Hz, $J_{5,6'}$ 6.2 Hz), 4.13 (m, 2H, H-6, H-6'), 4.91 (d, 1H, H-1, $J_{1,2}$ 10.0 Hz), 5.03 (dd, 1H, H-3, $J_{3,4}$ 3.4 Hz), 5.32 (t, 1H, H-2, $J_{2,3}$ 10.0 Hz), 5.41 (d, 1H, H-4), 7.21-7.70 (m, 5H, $H_{arom.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 20.4, 20.7 (CH_3COO), 61.5 (C-6), 67.2, 67.9, 71.7, 75.3 (C-2, C-3, C-4, C-5), 81.7 (C-1), 127.5-134.7 ($CH_{arom.}$, $C_{arom.}$), 168.9, 169.0 (CH_3COO).

Phenyl 1-Seleno-β-D-galactopyranoside (5). Potassium *tert*-butoxide (150 mg) was added to a solution of compound **4** (46 mmol, 22.4 g) in MeOH (200 mL) and the mixture was stirred for 2 h at room temperature. The reaction was neutralised with Dowex (H^+ form), filtered and concentrated to afford **5** which was sufficiently pure for further processing.

Phenyl 2,3,4,6-Tetra-*O*-benzyl-1-seleno-β-D-galactopyranoside (6). Compound **5** (10 mmol, 3.2 g) was dissolved in DMF (50 mL). Sodium hydride (52 mmol, 2.1 g 60% suspension) and benzyl bromide (48 mmol, 8.2 g) were added at 0 °C and the reaction mixture was stirred for 4 h at room temperature. Excess sodium hydride was destroyed by addition of MeOH (5 mL) and the mixture was concentrated, redissolved in CH_2Cl_2 (50 mL), washed twice with water (2 x 25 mL), dried ($MgSO_4$), and concentrated to give crude **6**. The residue was chromatographed on silica gel [1:0 to 0:1 light petroleum (bp

40-60 °C)-ether] to afford **6** (5.0 g, 75%), $[\alpha]_D$ -4° (*c* 1). ^1H NMR ($CDCl_3$) δ 3.64 (m, 4H, H-3, H-5, H-6, H-6'), 3.90 (t, 1H, H-2, $J_{2,3}$ 9.8 Hz), 4.45 (d, 1H, H-4, $J_{3,4}$ 2.6 Hz), 4.81 (AB, 8H, OCH_2Ph), 4.89 (d, 1H, H-1, $J_{1,2}$ 9.8 Hz), 7.16-7.67 (m, 25H, $H_{arom.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 68.5 (C-6), 72.5, 73.5, 74.4, 75.4 (OCH_2Ph), 73.6, 77.7, 78.2, 83.6 (C-2, C-3, C-4, C-5), 84.1 (C-1), 127.3-133.8 ($CH_{arom.}$, $C_{arom.}$).

Phenyl 2,3,4,6-Tetra-*O*-benzoyl-1-seleno-β-D-galactopyranoside (7). Compound **5** (10 mmol, 3.2 g) was dissolved in pyridine (50 mL) and treated with benzoyl chloride (48 mmol, 6.7 g) in pyridine (50 mL). The reaction was quenched, after 3 h at room temperature, by the addition of water. The mixture was concentrated under reduced pressure and the residue redissolved in CH_2Cl_2 (100 mL). The organic layer was washed with 0.9M $NaHCO_3$ (50 mL), water (50 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography [1:0 to 0:1 light petroleum (bp 40-60 °C)-ether) to furnish pure **7** (6.1 g, 83%), $[\alpha]_D$ +27° (*c* 1). ^1H NMR ($CDCl_3$) δ 4.40 (m, 2H, H-6', H-6'), 4.62 (m, 1H, H-5), 5.23 (t, 1H, H-1, $J_{1,2}$ 10.0 Hz), 5.61 (dd, 1H, H-3, $J_{3,4}$ 3.4 Hz), 5.75 (t, 1H, H-2, $J_{2,3}$ 10.0 Hz), 6.12 (d, 1H, H-4), 7.23- 8.64 (m, 25H, $H_{arom.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 62.3 (C-6), 68.3, 68.4, 72.5, 75.8 (C-2, C-3, C-4, C-5), 80.4 (C-1), 124.0-135.8 ($CH_{arom.}$, $C_{arom.}$), 164.9, 165.1, 165.2, 165.7 (PhCOO).

Phenyl 6-*tert*-Butyldimethylsilyl-1-seleno-β-D-galactopyranoside (8). To a solution of **5** (10 mmol, 3.2 g) in pyridine (50 mL) was added *t*-TBDMSCl (12 mmol, 1.8 g). After stirring for 4 h at room temperature, the reaction mixture was diluted with CH_2Cl_2 (100 mL), washed successively with water (50 mL), 0.9M $NaHCO_3$ (50 mL), water (50 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on silica gel in 95:5 CH_2Cl_2-MeOH to give pure **8** (2.8 g, 65%), $[\alpha]_D$ -25° (*c* 1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ –5.4 ($SiCH_3$), 17.9 ($C(CH_3)_3$) , 25.8 ($C(CH_3)_3$), 63.2 (C-6), 69.5, 70.5, 74.7, 79.1 (C-2, C-3, C-4, C-5), 85.4 (C-1), 128.1-134.6 ($CH_{arom.}$, $C_{arom.}$).

Phenyl 2,3,4-Tri-*O*-benzoyl-1-seleno-β-D-galactopyranoside (9). Benzoyl chloride (25.4 mmol, 3.6 g) was added to a stirred solution of **8** (6.5 mmol, 2.8 g) in pyridine (40 mL). After 4 h, water (5 mL) was added and the reaction mixture was concentrated. The residue was redissolved in CH_2Cl_2 (50 mL), washed with water (25 mL), 0.9M $NaHCO_3$ (25 mL), dried ($MgSO_4$) and concentrated. To a solution of the residue in acetonitrile (20 mL) and water (5 mL) was added *p*-TsOH (32.5 mmol, 5.6 g). After 0.5 h at room temperature, the reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with 0.9M $NaHCO_3$ (25 mL), water (25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification of the crude product by silica gel chromatography [1:0 to 1:2 light petroleum (bp 40-60 °C)-ether] furnished **9** (3.3 g, 82%), $[\alpha]_D$ +78° (*c* 1). ^1H NMR ($CDCl_3$) δ 3.63-3.83 (m, 2H, H-6, H-6'), 4.10 (m, 1H, H-5), 5.25 (d, 1H, H-1, $J_{1,2}$ 9.8

Hz), 5.60 (dd, 1H, H-3, $J_{3,4}$ 3.1 Hz), 5.82 (t, 1H, H-2, $J_{2,3}$ 9.8 Hz), 5.83 (d, 1H, H-4), 7.17-8.00 (m, 15H, $H_{arom.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 60.5 (C-6), 68.5, 72.8, 78.6 (C-2, C-3, C-4, C-5), 80.2 (C-1), 124.1-135.9 ($CH_{arom.}$, $C_{arom.}$), 164.8, 165.3, 165.8 (PhCOO).

Phenyl 2,3,4,6-Tetra-*O*-acetyl-1-seleno-β-D-glucopyranoside (14). Prepared as described above in a yield of 78%, $[\alpha]_D$ -5° (*c* 1); ^1H NMR ($CDCl_3$) δ 1.99, 2.02, 2.07 (4 x s, 12H, CH_3COO), 3.69 (m, 1H, H-5), 4.18 (m, 2H, H-6, H-6'), 4.88 (d, 1H, H-1, $J_{1,2}$ 10.0 Hz), 4.98-5.24 (3 x t, 3H, H-2, H-3, H-4, $J_{2,3} \approx J_{3,4} \approx J_{4,5} \approx$ 10.0 Hz), 7.26-7.63 (m, 5H, $H_{arom.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 19.7, 19.9 (CH_3COO), 61.3 (C-6), 67.5, 70.1, 72.9, 75.9 (C-2, C-3, C-4, C-5), 79.9 (C-1), 126.5 ($C_{arom.}$), 127.7-134.2 ($CH_{arom.}$), 168.3, 168.5, 169.0, 169.4 (CH_3COO).

Phenyl 4,6-Benzylidene-1-seleno-β-D-glucopyranoside (16). Compound **14** (3.0 mmol, 1.5 g) was dissolved in MeOH and potassium *tert*-butoxide (110 mg) was added. After stirring for 3 h, the reaction mixture was neutralised with Dowex (H^+ form), filtered and concentrated to give crude **15**, which was redissolved in DMF and treated with benzaldehyde dimethyl acetal (30 mmol, 4.6 g) and *p*-TsOH (50 mg). The resulting mixture was stirred at 50 °C for 17 h, the reaction quenched by addition of triethylamine (3 mL) and concentrated. The residue was dissolved in CH_2Cl_2 (50 mL) and washed with 0.9M $NaHCO_3$ (25 mL), water (25 mL), dried ($MgSO_4$), and concentrated once more. Silica gel chromatography [0:1 to 1:2 light petroleum (bp 40-60 °C)-ethyl acetate yielded **16** (0.7 g, 57% based on **14**), $[\alpha]_D$ +78° (*c* 1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 69.2 (C-6), 72.4, 74.6, 75.5, 81.4 (C-2, C-3, C-4, C-5), 85.7 (C-1), 102.5 (PhCH), 127.1-135.7 ($CH_{arom.}$, $C_{arom.}$).

Phenyl 2,3-Di-*O*-benzoyl-1-seleno-β-D-glucopyranoside (17). Benzoyl chloride (4.1 mmol, 0.6 g) was added to a stirred solution of **16** (1.7 mmol, 0.7 g) in pyridine (10 mL) After 4 h at room temperature, water (5 mL) was added and the reaction mixture was concentrated, taken up in CH_2Cl_2 (50 mL), washed with water (25 mL), 0.9M $NaHCO_3$ (25 mL), dried ($MgSO_4$), and concentrated. The residue was dissolved in acetic acid (50 mL) and heated to 70 °C. Water (10 mL) was added dropwise and stirring was continued for 10 h. The reaction mixture was concentrated and toluene (3 x 50 mL) was evaporated from the residue. Purification of the residue by chromatography on a column of silica gel (1:0 to 97:3 CH_2Cl_2-MeOH) yielded pure **17** (0.7 g, 82%), $[\alpha]_D$ -12° (*c* 1). ^1H NMR ($CDCl_3$) δ 3.57 (m, 1H, H-5), 3.90 (m, 3H, H-6, H-6', H-4), 5.16 (d, 1H, H-1, $J_{1,2}$ 10.2 Hz), 5.45 (m, 2H, H-2, H-3), 7.23-7.96 (m, 15H, $H_{arom.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 61.5 (C-6), 68.4, 71.7 (C-4, C-5), 76.9, 81.4 (C-2, C-3), 81.8 (C-1), 127.7-134.4 ($CH_{arom.}$, $C_{arom.}$), 165.5, 166.5 (PhCOO).

Phenyl 2,3,6-Tri-*O*-benzoyl-1-seleno-β-D-glucopyranoside (18). To a solution of compound **17** (1.4 mmol, 740 mg) in pyridine (10 mL) was added benzoyl chloride (1.5

mmol, 216 mg). After stirring for 2 h at room temperature, the reaction was quenched by the addition of water (5 mL). Evaporation of the solvent gave a residue which was redissolved in CH_2Cl_2 (50 mL), washed with water (25 mL), 0.9M $NaHCO_3$ (25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification of the residue by chromatography on silica gel with 1:0 to 1:2 light petroleum (bp 40-60 °C)-ether gave **18** (0.7 g, 79%), $[\alpha]_D$ -39° (*c* 1) . ^1H NMR ($CDCl_3$) δ 3.84 (m, 1H, H-5), 4.72 (m, 3H, H-4, H-6, H-6'), 5.16 (d, 1H, H-1, $J_{1,2}$ 9.2 Hz), 5.29-5.46 (2 x t, H-2, H-3, $J_{2,3} \approx J_{3,4}$ 9.0 Hz), 7.08-8.08 (m, 20H, $H_{arom.}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 63.7 (C-6), 68.8, 71.2, 79.3 (C-2, C-3, C-4, C-5), 81.2 (C-1), 128.2-134.8 ($CH_{arom.}$), 134.8 ($C_{arom.}$), 165.4 (PhCOO).

General procedure for IDCP-mediated glycosylations. A mixture of phenyl selenoglycoside donor **6** (0.3 mmol) and an alcohol (0.25 mmol for a primary alcohol and 0.2 mmol for a secondary alcohol) in 1:5 1,2-dichloroethane-ether (v/v, 6 mL) was stirred for 15 min with powdered molecular sieves (4Å, 0.5 g). Then, IDCP[11] (0.6 mmol, 280 mg) was added, while stirring was continued, until TLC analysis (97:3 CH_2Cl_2-acetone) showed the reaction to be complete. The reaction mixture was filtered and diluted with CH_2Cl_2 (30 mL). The organic layer was washed with M $Na_2S_2O_3$ (15 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed on Sephadex LH 20 (eluents: 1:1 CH_2Cl_2-MeOH) or silica gel to give the condensation products.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetrabenzyl-α/β-D-galactopyranosyl)-β-D-galactopyranoside (19). Prepared as described above, starting from donor **6** and acceptor **10** in a yield of 82% (α/β = 2.5/1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) (α-anomer) δ 56.8 (OCH_3), 67.2, 68.6 (C-6, C-6'), 69.2, 73.8, 76.2, 78.8, 79.4, 81.9 (C-2-C-5, C-2'-C-5'), 72.6, 72.3, 72.9, 73.4, 74.3, 74.6, 75.0 (OCH_2Ph), 98.2 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 170 Hz), 104.7 (C-1); (β-anomer) δ 103.6 (C-1'), 104.7 (C-1).

Methyl 3,4-*O*-Isopropylidene-2-*O*-(2,3,4,6-tetrabenzyl-α/β-D-galactopyranosyl)-6-*O*-triphenylmethyl-β-D-galactopyranoside (20). Prepared as described above, starting from donor **6** and acceptor **11** in a yield of 81% (α/β = 6/1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) (α-anomer) δ 26.3, 27.8 ($C(CH_3)_2$), 56.4 (OCH_3), 62.6, 67.5 (C-6, C-6'), 68.2, 71.9, 73.6, 74.5, 75.8, 76.1, 78.0, 78.8 (C-2-C-5, C-2'-C-5'), 72.4, 72.8, 73.2 (OCH_2Ph), 86.6 ($(C_6H_5)_3C$), 96.7 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 171 Hz), 103.7 (C-1), 109.5 ($C(CH_3)_2$), 126.9-138.8 ($C_{arom.}$, CH_{arom}) ; (β-anomer) δ 103.0 (C-1'), 103.7 (C-1).

1,6:2,3-Dianhydro-4-*O*-(2,3,4,6-tetrabenzyl-α/β-D-galactopyranosyl)-β-D-mannopyranoside (21). Prepared as described above, starting from donor **6** and acceptor **12** in a yield 90% (α/β = 9/1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) (α-anomer) δ 48.0, 54.2 (C-2, C-3), 65.6, 69.9 (C-6, C-6'), 70.1, 72.2, 74.8, 76.1, 76.8, 78.6 (C-2'-C-5', C-4-C-5) 73.1, 73.2, 73.5, 74.6 (OCH_2Ph), 97.3 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 171 Hz), 99.8 (C-1), 127.3-138.5 ($C_{arom.}$, $CH_{arom.}$); (β-anomer) δ 103.7 (C-1), 99.8 (C-1).

Ethyl 2,3,4-Tri-*O*-benzyl-6-*O*-(2,3,4,6-tetrabenzyl-α/β-D-galactopyranosyl)-1-thio-β-D-glucopyranoside (22). Prepared as described above, starting from donor **6** and acceptor **13** in a yield of 79% (α/β = 5/1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) (α-anomer) δ 15.2 (SCH_2CH_3), 24.8 (SCH_2CH_3), 68.9, 72.3 (C-6, C-6'), 69.1, 75.1, 76.6, 77.7, 78.1, 79.0, 81.6, 84.8 (C-2-C-5, C-2'-C-5'), 72.3, 72.9, 73.2, 74.7, 74.9, 75.4 (OCH_2Ph), 86.4 (C-1), 97.8 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 170 Hz), 127.2-128.9 ($CH_{arom.}$); (β-anomer) δ 86.4 (C-1), 103.6 (C-1').

Phenyl 2,3,4-Tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetrabenzyl-α/β-D-galactopyranosyl)-1-seleno-β-D-galactopyranoside (23). Prepared as described above, starting from donor **6** and acceptor **9** in a yield of 87% (α/β = 4/1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) (α-anomer) δ 66.9, 68.9 (C-6, C-6'), 69.5, 72.6, 74.8, 76.1, 76.8, 78.6, 78.6 (C-2-C-5, C-2'-C-5'), 72.9, 72.9, 73.1, 74.5, 76.4 (OCH_2Ph), 80.3 (C-1), 98.4 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 170 Hz), 127.1-135.8 ($CH_{arom.}$), 126.1, 128.8, 129.1, 137.8, 138.1, 138.3, 138.6 ($C_{arom.}$), 164.8, 165.1 (PhCOO); (β-anomer) δ 86.4 (C-1), 103.6 (C-1').

Phenyl 2,3,6-Tri-*O*-benzoyl-4-*O*-(2,3,4,6-tetrabenzyl-α/β-D-galactopyranosyl)-1-seleno-β-D-glucopyranoside (24). Prepared as described above, starting from donor **6** and acceptor **18** in a yield of 45% (α/β = 9/1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) (α-anomer) δ 65.3, 68.5 (C-6, C-6'), 72.9, 73.1, 73.3, 74.6 (OCH_2Ph), 70.7, 71.5, 74.9, 75.0, 75.2, 75.5, 78.4, 78.6 (C-2-C-5, C-2'-C-5'), 81.0 (C-1), 99.5 (C-1', $J_{C\text{-}1',H\text{-}1'}$ 170 Hz), 127.4-135.2 ($CH_{arom.}$), 129.4 ($C_{arom.}$).

3,4,6-Tri-*O*-benzoyl-α-D-galactopyranose 1,2-(methyl 2,3,4-tri-*O*-benzyl-l-β-D-galactopyranose-6-yl) Orthobenzoate (25). Prepared as described above from donor **7** and acceptor **10** in a yield of 60%. $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 56.9 (OCH_3), 62.2 (C-6, C-6'), 72.9, 74.4, 75.0 (OCH_2Ph), 92.9 (C-1'), 104.8 (C-1), 120.1 (PhCOOO), 125.8-133.7 ($CH_{arom.}$), 129.2 ($C_{arom.}$), 165.8 (PhCOO).

General procedure for NIS/TfOH (cat.)-promoted glycosylations. A mixture of phenyl selenoglycoside **7** (0.3 mmol), acceptor (0.25 mmol for a primary alcohol and 0.2 mmol for a secondary alcohol) and powdered molecular sieves (4Å, 0.5 g) in 1:1 1,2-dichloroethane/ether (v/v, 5 mL) was stirred for 15 min at room temperature. A solution of NIS and TfOH, freshly prepared by ultrasonic pulverisation of NIS (0.33 mmol, 74 mg) in 1:1 1,2-dichloroethane-ether (v/v, 3.3 mL) and subsequent addition of TfOH (0.33 μmol, 3.0 μL), was added. After 2 min, the reaction was filtered, diluted with CH_2Cl_2 (30 mL), washed successively with M $Na_2S_2O_3$ (15 mL), 0.9M $NaHCO_3$ (15 mL), dried ($MgSO_4$) and concentrated. The residue was chromatographed on Sephadex LH 20 (eluents: 1:1 CH_2Cl_2-MeOH) or silica gel to give the glycosylation products.

Methyl 6-*O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-2,3,4-tri-*O*-benzyl-β-D-galactopyranoside (26). Prepared as described above, starting from donor **7** and

acceptor **10** in a yield of 91%, $[\alpha]_D$ 58° (*c* 1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 56.5 (OCH_3), 61.7 (C-6'), 68.6 (C-6), 67.9, 69.8, 71.1, 71.4, 73.4, 79.2, 81.7 (C-2-C-5, C-2'-C-5'), 72.8, 74.3, 74.8 (OCH_2Ph), 101.4 (C-1'), 104.6 (C-1), 127.3-133.4 ($C_{arom.}$), 128.8, 129.0, 129.1, 138.1, 138.5 ($CH_{arom.}$), 165.0, 165.3, 165.8 (PhCOO).

Methyl 2-*O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-3,4-*O*-isopropylidene-6-*O*-triphenylmethyl-β-D-galactopyranoside (27). Prepared as described above, starting from donor **7** and acceptor **11** in a yield of 67%, $[\alpha]_D$ 61° (*c* 1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 25.8, 27.2 ($C(CH_3)_2$), 56.5 (OCH_3), 62.0, 62.5 (C-6, C-6'), 68.1, 70.1, 71.4, 71.6, 71.8, 73.4, 78.3, 81.6 (C-2-C-5, C-2'-C-5'), 86.5 ($(C_6H_5)_3C$), 101.6 (C-1'), 102.3 (C-1), 109.7 ($C(CH_3)_2$), 126.8-133.4 ($C_{arom.}$), 128.9, 143.7 ($C_{arom.}$), 165.0, 165.2 (PhCOO).

1,6:2,3-Dianhydro-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-β-D-mannopyranose (28). Prepared as described above, starting from donor **7** and acceptor **12** in a yield of 50%, $[\alpha]_D$ +78° (*c* 1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 48.1, 54.5 (C-2, C-3), 62.0 (C-6'), 65.7 (C-6), 68.0, 69.6, 71.6, 72.0, 75.5 (C-2'-C-5', C-4-C-5), 97.4 (C-1), 101.4 (C-1'), 128.2-133.6 ($C_{arom.}$), 165.4 (PhCOO).

Ethyl 2,3,4-Tri-*O*-benzoyl-6-*O*-(2,3,4,6-tetrabenzoyl-β-D-galactopyranosyl)-1-thio-β-D-glucopyranoside (30). Prepared as described above, starting from donor **7** and acceptor **29** in a yield of 79%, $[\alpha]_D$ 49° (*c* 1). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 14.6 (SCH_2CH_3), 23.7 (SCH_2CH_3), 61.8 (C-6'), 68.4 (C-6), 68.0, 69.5, 69.6, 70.3, 71.2, 71.6, 73.9, 77.9 (C-2-C-5, C-2'-C-5'), 83.1 (C-1), 101.4 (C-1'), 128.1-133.4 ($CH_{arom.}$), 126.6, 128.8, 128.9, 129.1 ($C_{arom.}$), 165.4 (PhCOO).

REFERENCES AND NOTES

1. S. Mehta and M. Pinto, *Tetrahedron Lett.*, **32**, 4425 (1991).

2. D.R. Mootoo and B. Fraser-Reid, *J. Am. Chem. Soc.*, **110**, 2662 (1988).
   G.H. Veeneman, S.H. van Leeuwen and J.H. van Boom, *Tetrahedron Lett.*, **31**, 1331 (1990).
   G.H. Veeneman and J.H. van Boom, *Tetrahedron Lett.*, **31**, 275 (1990).
   H.M. Zuurmond, S.C. van der Laan, G.A. van der Marel and J.H. van Boom, *Carbohydr. Res.*, **215**, C1 (1991).

3. H.M. Zuurmond, P.A.M. van der Klein, P.H. van der Meer, G.A. van der Marel and J.H. van Boom, *Recl. Trav. Chim. Pays-Bas*, **111**, 365 (1992).

4. A terminal acceptor contains, in contrast with a non-terminal one, an anomeric group which cannot be activated *in situ* by a promoter.

5. P.J. Garegg and C.G. Swahn, *Acta Chem. Scand.*, **26**, 3895 (1972).

6. V.I. Betaneli, A.Y. Ott, O.V. Brukhanova and N.K. Kochetkov, *Carbohydr. Res.*, **179**, 37 (1988).

7. J. Stanek and M. Cerny, *Synthesis*, 698 (1972).

8. G.H. Veeneman, *PhD. Thesis*, Leiden, (1991).

9. A.K. Ray and N. Roy, *Carbohydr. Res.*, **196**, 95 (1990).

10. A.F. Bochkov, V.I. Snuatkova, Ya. V. Voznyi and N.K. Kochetkov, *J. Gen. Chem. USSR*, **41**, 2808 (1971).

11. R.U. Lemieux and A.R. Morgan, *Can. J. Chem.*, **43**, 2190 (1965).