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Potential usefulness of sugar 1,2 thio ortho esters in iodonium-promoted glycosidation

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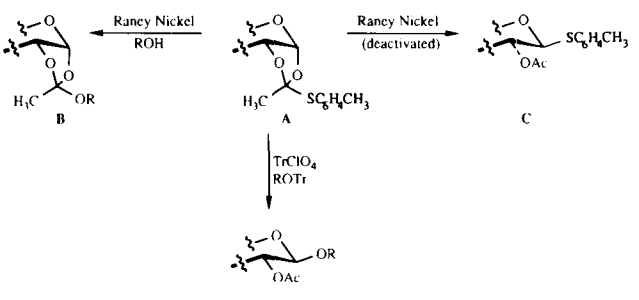
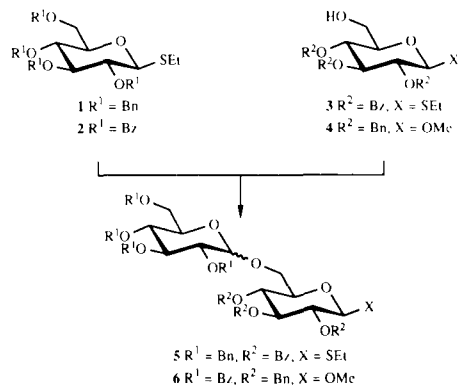
Abstract. Sugar 1,2 thio ortho esters can be condensed with terminal glycosyl acceptors using iodonium-ion sources (IDCP and NIS/TfOH) as activators. IDCP- or NIS/TfOH-assisted glycosidation of sugar 1,2 thio ortho esters with primary hydroxyl groups of "armed" or "disarmed" ethyl (phenyl) 1-thioglycosides gave the respective disaccharides having 1,2 ortho ester or 1,2 *trans* interglycosidic linkages.

Introduction

In 1977, *Magnusson* reported[1] that 4-methylphenyl 1,2 thio ortho esters (**A**) in the presence of primary and secondary alcohols could be transformed, by treatment with Raney nickel, into the 1,2 ortho ester **B**. In contrast[2], the use of deactivated Raney nickel led to 4-methylphenyl 1,2 *trans* 1-thioglycosides (**C**) in an excellent yield. Later *Kochetkov* et al.[3] showed that the reaction of 1,2 thio orthoester **A** with primary and secondary trityl ethers of monosaccharides (ROTr) in the presence of the catalyst triphenylmethylium perchlorate ($TrClO_4$) resulted in 1,2 *trans* disaccharides (**D**) in good to moderate yields.



Recent investigations[4] from this laboratory have revealed that "armed" or "disarmed" [a] alkyl 1-thioglycosides could be applied successfully for the introduction of 1,2 *cis* or *trans* interglycosidic linkages, respectively. For example, the fully benzylated "armed" thioglycoside **1** could be coupled chemoselectively with the partially benzoylated "disarmed" ethyl 1-thioglycosyl acceptor **3**, in the presence of iodonium di-*sym*-collidine [b] perchlorate (IDCP), to give predominantly the 1,2 *cis* disaccharide **5**. On the other hand, glycosylation of acceptor **4** by the fully benzoylated ethyl 1-thioglycoside **2** under the influence of *N*-iodosuccinimide (NIS) and catalytic triflic acid (TFOH) yielded exclusively 1,2-*trans*-linked disaccharide **6**. In addition, the above mentioned "armed-disarmed" approach showed great promise for synthesis of interesting oligosaccharides[6]. Despite this success, it is evident that disaccharide **6**, in contrast with disaccharide **5**, cannot be extended directly at the reducing end via the "armed-disarmed" principle.



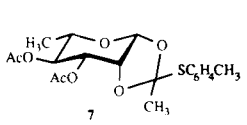
We here report in detail[7] that the latter limitation can be partially overcome by chemo- and stereoselective glycosidation of a sugar 1,2 thio ortho ester with "disarmed" or "armed" alkyl (aryl) 1-thioglycosides.

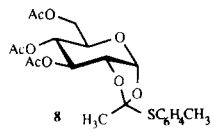
Results and discussion

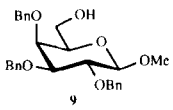
In order to widen the scope of 1,2 thio ortho esters in an "armed-disarmed" synthesis of oligosaccharides, we initially examined IDCP-mediated glycosidation of the easy accessible[8] thio ortho esters **7** and **8** (*exo / endo* mixtures) with the three glycosyl acceptors **3**, **9** and **10**. The results of these condensations are summarized in Table I. It is

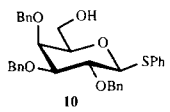
[a] This terminology was originally introduced by *Fraser-Reid* et al.[5] to differentiate between the reactivity of an *n*-pentenyl glycoside having either an ester or ether substituent at C-2 towards halonium ions. Thus, an *n*-pentenyl glycoside having an ether or ester substitutent on the C-2 oxygen is called "armed" or "disarmed", respectively.

[b] *Sym*-Collidine = 2,4,6-trimethylpyridine.









evident (entry 1) that glycosidation of rhamnosyl 1,2 thio ortho ester **7** with the methyl galactoside derivative **9**[9] under the influence of IDCP proceeds smoothly to yield the 1,2 ortho ester derivative **11** in excellent yield. On the basis of the foregoing result, it was to be expected that IDCP-assisted condensation of thio ortho esters **7** and **8** with the "disarmed" ethyl thioglucoside **3**[10] would proceed chemoselectively. Infact, IDCP-assisted glycosylation of acceptor **3** with donors **7–8** gave the respective orthoesters **12** and **13** (entries 2 and 3) in an acceptable yield. In this respect, it is of interest to note that condensation of donor **8** with the thioglycoside **3** using NIS as the promoter gave ortho ester **13** in an even higher yield (*cf.* 83% versus 77%). In order to assess further the above observed chemoselectivity, the "less armed"[11] phenyl thioglycoside **10**[12] was glycosylated by thio ortho ester **8** under the influence of NIS. It can be seen (entry 4) that the yield of ortho ester **14** resulting from NIS-promoted glycosidation is of the same order as observed earlier for ortho ester **13**. On the other hand, it was established that TfOH-catalysed rearrangement[13] of ortho ester **13** proceeded smoothly to give the corresponding 1,2-*trans*-linked dimer **17** in 65% yield. The latter result indicated that the glycosidation of thio ortho esters **7–8** in the presence of NIS and catalytic TfOH would result in the formation 1,2-*trans*-linked disaccharides. Infact, NIS/TfOH-mediated glycosidation of thio ortho ester **7** with acceptor **9** gave the α-linked disaccharide **15** in 71% yield (Table II, entry 1). Furthermore, the preferred formation of the 1,2-*trans*-linked disaccharide **16** (entry 2) shows that thio ortho ester donor **7** can be activated with an acceptable

Table I Results of IDCP (or NIS) promoted glycosidations of sugar 1,2 thio ortho ester 7 and 8 with acceptors 3, 9 and 10.

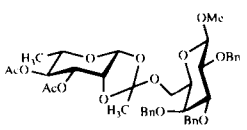
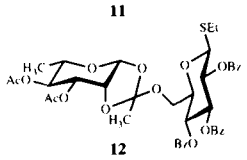
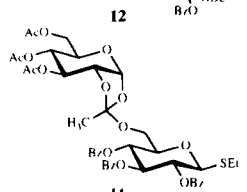
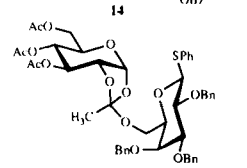
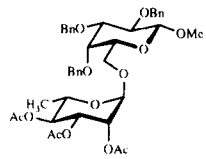
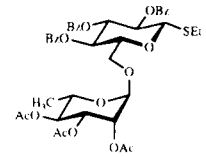
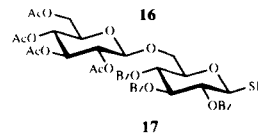
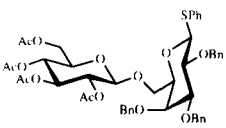
Entry	Donor	Acceptor	Promoter	Disaccharide	Yield(%)
1	7	9	IDCP	 **11**	92
2	7	3	IDCP	 **12**	73
3	8	3	IDCP (NIS)	 **14**	77 (83)
4	8	10	NIS	 **14**	79

Table II Results of NIS / TfOH-promoted glycosidations of sugar 1,2 thio ortho ester 7 and 8 with acceptors 3, 9 and 10.

Entry	Donor	Acceptor	Disaccharide	Yield(%)
1	7	9	 **15**	71
2	7	3	 **16**	75
3	8	3	 **17**	43 (65)[a]
4	8	10	 **18**	30 (47)[a]

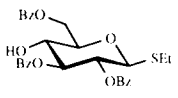
[a] Obtained by the one-pot two-step procedure

degree of selectivity over thioglycoside **3**. However, the chemoselectivity of the iodonium-promoted glycosidation of glucopyranosyl donor **8** with thioglycosyl acceptor **3** to give dimer **17** (entry 3) is less satisfactory than for the corresponding condensation of **7** with **3**. Similarly, addition of NIS and TfOH to a mixture of **8** and acceptor **10** provided dimer **18** in a poor yield (entry 4). The decrease in chemoselectivity of the last two couplings in Table II may be ascribed to the occurrence of NIS/TfOH-mediated self-coupling of the individual acceptors **3** and **10**.

We reasoned that the rather disappointing yield of the last two couplings (entry 3 and 4) could be improved by a one-pot two-step procedure involving the separate addition of NIS and TfOH. Thus, glycosylation of **3** with thio ortho ester **8** under the agency of NIS followed, after the formation of the ortho ester derivative **13** (see Table I), by the addition of catalytic TfOH, provided **17** in a much better yield (see entry 3). A similar increase in yield was also observed (entry 4) for disaccharide **18**.

At this stage, we were anxious to find out whether the *in-situ*-thio-ortho-ester-glycosidation approach could be extended to less reactive glycosyl acceptors. In a first experiment, ortho ester **8** and partially benzoylated thioglucosyl acceptor **19**[10] having a free secondary hydroxyl group were treated with NIS. Monitoring of the reaction by TLC revealed a rapid conversion of donor **8** into more polar products. Purification of the reaction mixture gave, apart from acceptor **19**, a major side-product, the structure of which was in accordance with the succinimide derivative **20**. In addition, it was also established that succinimide **20** was in every aspect identical with the compound obtained after treating donor **8** with the promoter NIS. The insertness of secondary hydroxyl groups was further illustrated in the failure to condense donor **8** with the relatively more reactive acceptor **21**[14] and using the promoters IDCP, NIS or NIS/TfOH. The formation of the succinimide adduct **20**, which concurs well with the occurrence[15,16] of similar succinimide adducts in iodonium ion-promoted glycosidations, indicates that the succinimide nucleophile generated in the NIS-promoted process is a more reactive species than the secondary

hydroxyls in acceptors such as **19** and **21**. In this respect, it is also worthwhile to mention that in the glycosylation of **21** with **8** the use of IDCP, instead of NIS, does not have a beneficial effect[16] on the coupling process.



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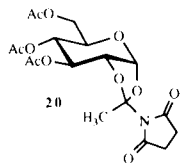

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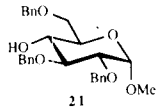

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In conclusion, iodonium-ion-mediated glycosidation of sugar 1,2 thio ortho esters may be a valuable asset for the chemoselective introduction of 1,2 *trans* glycosidic linkages via the "armed–disarmed" principle. However, it is evident that the extension of this principle is limited to glycosyl acceptors having primary hydroxyl groups.

Experimental

General methods and materials

1,2-Dichloroethane was distilled from P_2O_5 and stored over 1,2-dichloroethane over alumina. Diethyl ether was distilled from $LiAlH_4$ and stored over sodium wire. Schleicher and Schüll DC Fertigfolien F 1500 LS 254 were used for TLC. 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-permeation chromatography was performed on Sephadex LH 20 (Pharmacia). ^{1}H-NMR spectra (300 MHz) were recorded at 25°C with a Bruker WM 300 spectrometer. ^{13}C-NMR spectra (50 MHz) were recorded with a Jeol JNM-FX 200 spectrometer. ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to that of Me_4Si ($CDCl_3$).

General procedure for IDCP- or NIS-mediated glycosidations

Method A. A mixture of 1,2 thio ortho ester (0.3 mmol) and acceptor (0.25 mmol) in 1:1 1,2-dichloroethane/ether (v/v, 5 ml) was stirred with powdered molecular sieves 4Å (0.5 g) for 15 min at room temperature. IDCP[17] (0.6 mmol, 280 mg) was then 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, diluted with CH_2Cl_2 (30 ml), washed with M NaS_2O_3 (15 ml), dried $MgSO_4$, and concentrated. The residue was chromatographed on Sephadex LH 20 (eluent: 1:1 CH_2Cl_2/MeOH) or silica gel to give the glycosidation products.

Method B. A mixture of 1,2 thio ortho ester (0.3 mmol) and acceptor (0.25 mmol) in 1:1 1,2-dichloroethane/ether (v/v, 5 ml) was stirred with powdered molecular sieves 4Å (0.5 g) for 15 min at room temperature. NIS (0.3 mmol, 68 mg) was then added while stirring was continued until TLC analysis (97:3 CH_2Cl_2/acetone) showed the reaction to be complete. For further processing see method A.

1,2-(3,4-Di-O-acetyl-β-L-rhamnopyranose) 6-(methyl 2,3,4-tri-O-benzyl-β-D-galactopyranoside) orthoacetate (**11**). Compound **11** was prepared as described above (method A) starting from donor **7** and acceptor **9** in a yield of 92%. ^{13}C{^{1}H} NMR ($CDCl_3$) (*exo* isomer): δ 17.3 (C-6′), 20.6 ($\underline{C}H_3COO$), 25.0 ($\underline{C}H_3COOO$), 56.8 (OCH_3), 60.4 (C-6), 68.9, 70.2, 72.9, 76.9, 79.4, 82.0 (C-2–C-5, C-2′–C-5′), 72.8, 74.3, 74.9 (OCH_2Ph), 97.0, (C-1′), 104.8 (C-1), 123.9 ($CH_3\underline{C}OOO$), 127.3–128.1 ($CH_{arom.}$), 138.5, 138.7 ($C_{arom.}$), 170.1 ($CH_3\underline{C}OO$). Anal. calcd. for $C_{40}H_{48}O_{12}$: C 66.67, H, 6.67; found: C 66.61, H 6.71%.

1,2(3,4-Di-O-acetyl-β-L-rhamnopyranose) 6-(ethyl 2,3,4-tri-O-benzoyl-1-thio-β-D-glucopyranoside) orthoacetate (**12**). Compound **12** was prepared as described above (method A) starting from donor **7** and acceptor **3** in a yield of 73%. ^{13}C{^{1}H} NMR ($CDCl_3$) (*exo* isomer): δ 14.8 (SCH_2CH_3), 17.4 (C-6′), 20.5, 20.6 ($\underline{C}H_3COO$), 24.1 ($S\underline{C}H_2CH_3$), 24.5 ($\underline{C}H_3COOO$), 62.0 (C-6), 69.0, 69.8, 70.2, 70.5, 74.1, 76.6, 77.1 (C-2–C-5, C-2′–C-5′), 83.6 (C-1), 97.0 (C-1′), 123.9 ($CH_3\underline{C}OOO$), 128.1–133.1 ($CH_{arom.}$), 128.7, 128.9, 129.0 ($C_{arom.}$), 165.1, 165.6 (PhCOO), 169.6, 170.1 (CH_3COO). Anal. calcd. for $C_{41}H_{44}O_{15}S$: C 60.89, H 5.45; found: C 60.93, H 5.43%.

1,2-(3,4,6-TriO-acetyl-α-D-glucopyranose) 6-(ethyl 2,3,4-tri-O-benzoyl-1-thio-β-D-glucopyranoside)orthoacetate (**13**). Compound **13** was prepared as described above starting from donor **8** and acceptor **3** in a yield of 77% (method A) or 83% (method B). ^{13}C{^{1}H} NMR ($CDCl_3$) (*exo* isomer): δ 15.0 ($SCH_2\underline{C}H_3$), 20.2, 20.3, 20.7 ($\underline{C}H_3COO$, $\underline{C}H_3COOO$), 24.1 ($S\underline{C}H_2CH_3$), 62.8, 63.0 (C-6, C-6′), 66.9, 68.1, 69.6, 70.0, 70.4, 72.9, 74.2 (C-2-C-5, C-2′-C-5′), 83.6 (C-1), 97.0 (C-1′), 121.0 (CH_3COOO), 128.2–133.4 ($CH_{arom.}$), 165.1 (PhCOO), 168.2, 169.5, 170.7 (CH_3COO). Anal. calcd. for $C_{43}H_{46}O_{14}S$: C 63.08, H. 5.62; found: C 63.12, H. 5.72%.

1,2-(3,4,6-Trio-O-acetyl-α-D-glucopyranose) 6-(phenyl 2,3,4-tri-O-benzyl-1-thio-β-D-galactopyranoside) orthoacetate (**14**). Compound **14** was prepared as described above (method B) starting from donor **8** and acceptor **10** in a yield of 79%. ^{13}C{^{1}H} NMR ($CDCl_3$) (*exo* isomer): δ 20.6, 20.7, 20.9 ($\underline{C}H_3COO$, $\underline{C}H_3COOO$), 62.5, 63.0 (C-6, C-6′), 67.0, 68.0, 70.0, 73.1, 73.4, 76.8, 77.1, 84.0, 87.6 (C-2–C-5, C-2′–C-5′), 72.9, 74.3, 75.6 (OCH_2Ph), 87.0 (C-1), 97.0 (C-1′), 121.1 (CH_3COOO), 127.0–131.0 ($CH_{arom.}$), 134.2, 138.1, 138.5 ($C_{arom.}$), 168.9, 169.4, 170.5 (CH_3COO). Anal. calcd. for $C_{47}H_{52}O_{10}S$: C 69.80, H, 6.44; found: C 69.75, H 6.37%.

General procedure for NIS / TfOH-promoted glycosidations

Method A. A mixture of 1,2 thio ortho ester (0.3 mmol), acceptor (0.25 mmol) and powdered molecular sieves 4Å (0.5 g) in 1:1 1,2-dichloroethane/diethyl-ether (v/v, 5 ml) was stirred for 15 min at room temperature. A solution of NIS and TfOH, freshly prepared by ultrasonic pulvarisation of NIS (0.3 mmol, 68 mg) in 1:1 1,2-dichloroethane/diethyl-ether (v/v, 3 ml) and subsequent addition of TfOH (0.045 mmol, 4μl), was added to the reaction mixture. When TLC analysis (97:3 CH_2Cl_2/acetone) showed the reaction to be complete, the mixture was filtered, diluted with CH_2Cl_2 (20 ml), washed successively with M $Na_2S_2O_3$ (10 ml), 0.9M $NaHCO_3$ (10 ml), dried over $MgSO_4$ and concentrated. The residue was purified on Sephadex LH 20 (eluent: 1:1 CH_2Cl_2/MeOH) or silica gel to give the glycosidation products.

Method B. A mixture of 1,2 thio ortho ester (0.3 mmol), acceptor (0.25 mmol) and powdered molecular sieves 4Å (0.5 g) in 1:1 1,2-dichloroethane/diethyl-ester (v/v, 5 ml) was stirred for 15 min at room temperature. NIS (0.3 mmol, 68 mg) was added to the reaction mixture and, when TLC analysis showed the formation of the ortho ester disaccharide, a solution of TfOH (0.045 mmol, 4 μl) in 1:1 1,2-dichloroethane/diethyl-ether (v/v, 3 ml) was added to give the rearranged disaccharide. For further processing, see method A.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-β-D-galactopyranoside (**15**). Compound **15** was prepared as described above (method A) starting from donor **7** and acceptor **9** in a yield of 71%, $[\alpha]_D$ −36° (*c* 1). ^{1}H NMR ($CDCl_3$): δ 1.09 (d, 3H, H-6′, $J_{5,6}$ 6.3 Hz), 2.00, 2.03, 2.13 (3 s, 9H, CH_3COO), 3.54 (s, 3H, OCH_3), 3.50–3.56 (m, 3H, H-5, H-6^a, H-6^b), 3.57 (dd, 1H, H-3, $J_{3,4}$ 3.0 Hz), 3.62 (d, 1H, H-4), 3.70 (dq, 1H, H-5′), 3.81 (dd, 1H, H-2, $J_{2,3}$ 9.6 Hz), 4.28 (d, 1H, H-1, $J_{1,2}$ 7.7 Hz), 4.76 (s, 1H, H-1′), 4.58–5.09 (AB, 6H, OCH_2Ph), 5.02 (t, 1H, H-4, $J_{3,4} \approx J_{4,5}$ 9.8 Hz), 5.21–5.26 (m, 2H, H-2′, H-3′), 7.20–7.45 (m, 15H, $H_{arom.}$). ^{13}C{^{1}H} NMR ($CDCl_3$) δ: 17.1 (C-6′), 20.6 ($\underline{C}H_3COO$), 56.9 (OCH_3), 66.8 (C-6), 66.3, 68.9, 69.4, 70.8, 72.9, 73.6, 79.4, 82.0 (C-2–C-5, C-2′–C-5′), 73.1, 74.2, 74.9 (OCH_2Ph), 97.8 (C-1′), 104.8 (C-1), 127.4–128.2 ($CH_{arom.}$), 138.3 ($C_{arom.}$), 169.6, 169.8 (CH_3COO). Anal. calcd. for $C_{40}H_{48}O_{12}$: C 66.67, H, 6.67; found: C 66.73, H 6.62%.

Ethyl 2,3,4-tri-O-benzoyl-6-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-1-thio-β-D-glucopyranoside (**16**). Compound **16** was prepared as described above (method A) starting from donor **7** and acceptor **3** in a yield of 75%, $[\alpha]_D$ −16° (*c* 1). ^{1}H NMR ($CDCl_3$): δ 1.13 (d, 3H, H-6′, $J_{5,6}$ 6.3 Hz), 1.29 (t, 3H, SCH_2CH_3, *J* 7.4 Hz), 1.98, 2.03, 2.13 (3 s, 9H, CH_3COO), 2.78 (AB, 2H, $S\underline{C}H_2CH_3$), 3.82–3.90 (m, 3H, H-5, H-6, H-6′), 4.05 (m, 1H, H-5′), 4.84 (d, 1H, H-1, $J_{1,2}$ 9.9 Hz), 4.85 (d, 1H, H-1′, $J_{1,2}$ 1.8 Hz), 5.03 (t, 1H, H-4′, $J_{4,5}$ 9.9 Hz), 5.25 (dd, 1H, H-3′, $J_{3,4}$ 9.9 Hz), 5.29 (dd, 1H, H-2′, $J_{2,3}$ 3.5 Hz), 5.46 (t, 1H, H-2, $J_{2,3}$ 9.8 Hz) 5.52 (t, 1H, H-4, $J_{4,5}$ 9.5 Hz), 5.90 (t, 1H, H-3, $J_{3,4}$ 9.4 Hz), 7.10–8.00 (m, 15H, $H_{arom.}$). ^{13}C{^{1}H} NMR ($CDCl_3$) δ 14.8 (SCH_2CH_3), 17.2 (C-6′), 20.6 (CH_3COO), 24.3 (SCH_2CH_3), 66.4, 68.9, 69.3, 69.6, 70.5, 70.9, 74.0, 77.9 (C-2–C-5, C-2′–C-5′), 66.8 (C-6), 83.7 (C-1), 98.3 (C-1′), 128.1–133.4 ($CH_{arom.}$), 129.0 ($C_{arom.}$), 169.7 (CH_3COO). Anal. calcd. for $C_{41}H_{44}O_{15}S$: C 60.89, H, 5.45; found: C 60.79, H. 5.52%.

Ethyl 2,3,4-tri-O-benzoyl-6-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1-thio-β-D-glucopyranoside (**17**). Compound **17** was prepared as described above starting from donor **8** and acceptor **3** in a yield of 43% (method A) or 65% (method B), $[\alpha]_D$ +2° (*c* 1). ^{1}H NMR ($CDCl_3$): δ 1.29 (t, 3H, SCH_2CH_3, *J* 7.4 Hz), 1.99, 2.00, 2.01, 2.10 (4 s, 12H, CH_3COO), 2.79 (AB, 2H, $SC\underline{H}_2CH_3$), 3.62 (m, 1H, H-5'), 3.77 (dd, 1H, H-6^a, $J_{5,6a}$ 7.7 Hz, $J_{6a,6b}$ 11.5 Hz), 3.95–4.09 (m, 3H, H-5, H-6^b, H-6'^{b}), 3.77 (dd, 1H, H-6'^{a}, $J_{5,6'a}$ 5.0 Hz, $J_{6'a,6'b}$ 12.4 Hz), 4.61 (d, 1H, H-1', $J_{1,2}$ 7.9 Hz), 4.79 (d, 1H, H-1, $J_{1,2}$ 9.9 Hz), 4.99 (dd, 1H, H-2', $J_{2,3}$ 7.9 Hz), 5.03 (t, 1H, H-4', $J_{4,5}$ 9.9 Hz), 5.19 (t, 1H, H-3', $J_{3,4}$ 9.5 Hz), 5.37 (t, 1H, H-2, $J_{2,3}$ 9.7 Hz), 5.49 (t, 1H, H-4, $J_{4,5}$ 9.7 Hz), 5.87 (t, 1H, H-3, $J_{3,4}$ 9.5 Hz), 7.10–8.00 (m, 15H, $H_{arom.}$). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 14.6 ($SCH_2\underline{C}H_3$), 20.5, 20.6 ($\underline{C}H_3COO$), 24.1 (SCH_2CH_3), 66.0, 68.5 (C-6, C-6'), 68.2, 69.5, 70.5, 71.0, 71.7, 72.7, 74.0 (C-2–C-5, C-2'–C-5'), 83.6 (C-1), 100.7 (C-1'), 128.1–133.1 ($CH_{arom.}$), 129.0 ($C_{arom.}$), 165.0, 165.2 (PhCOO), 169.3, 170.1, 170.5 ($CH_3\underline{C}OO$). Anal. calcd. for $C_{43}H_{46}O_{14}S$: C 63.08, H, 5.62; found: C 63.02, H. 5.59%.

Phenyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-1-thio-β-D-galactopyranoside (**18**). Compound **18** was prepared as described above starting from donor **8** and acceptor **10** in a yield of 30% (method A) or 47% (method B), $[\alpha]_D$ +12° (*c* 1). ^{13}C {^{1}H} NMR ($CDCl_3$): δ 20.6 ($\underline{C}H_3COO$), 61.6, 68.6 (C-6, C-6'), 68.1, 71.3, 71.7, 73.5, 74.8, 77.2, 83.7 (C-2–C-5, C-2'–C-5'), 74.3 (OCH_2Ph), 87.9 (C-1), 100.5 (C-1'), 127.2–131.3 ($CH_{arom.}$), 138.1 ($C_{arom.}$), 169.4 ($CH_3\underline{C}OO$). Anal. calcd. for $C_{47}H_{52}O_{10}S$: C 69.80, H 6.44; found: C 69.82, H 6.49.

Rearrangement of ortho ester **13**

A catalytic amount of trifluoromethanesulfonic acid (0.045 mmol, 4 μl) was added to a cooled (0°C) solution of compound **13** (0.3 mmol, 136 mg) in 1,2-dichloroethane (5 ml). After 5 min at 0°C, the mixture was diluted with CH_2Cl_2 (10 ml), washed with 0.9M $NaHCO_3$ (5 ml), dried over $MgSO_4$ and concentrated. Purification of the residue on silica gel (97:3 CH_2Cl_2/acetone) gave pure **17** (164 mg, 65%).

1,2-(3,4,6-Tri-O-acetyl-α-D-glucopyranose) N-succinimide orthoacetate (**20**)

NIS (0.3 mmol, 68 mg) was added to a stirred solution of compound **8** (0.3 mmol, 136 mg) and molecular sieves 4Å (0.5 g) in 1:1 1,2-dichloroethane diethyl-ether (v/v, 5 ml). The mixture was stirred for 15 min at room temperature, filtered and the filtrate washed with M $Na_2S_2O_3$ (10 ml), dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel (97:3 CH_2Cl_2/acetone) to give **20** (32 mg, 25%). ^{13}C {^{1}H} NMR ($CDCl_3$: δ 20.6 ($\underline{C}H_3COO$), ($\underline{C}H_3COON$), 28.4 (CH_2CON), 63.0 (C-6), 67.3, 67.9, 69.6, 73.8 (C-2–C-5), 98.2 (C-1), 113.0 ($CH_3\underline{C}OON$), 169.6 ($CH_3\underline{C}OO$), 175.8 ($CH_2\underline{C}ON$). Anal. calcd. for $C_{18}H_{33}O_1N$: C 49.20, H, 7.52.; found: C 49.15, H 7.54%.

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