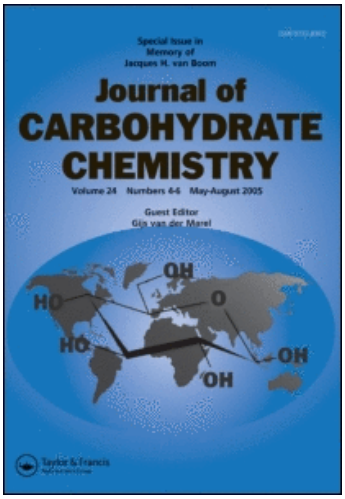

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4,6-*O*-Benzylidene Directed β-Mannosylation Without Intermediate Triflate Formation? Comparison of Trichloroacetimidate and DISAL Donors in Microwave-Promoted Glycosylations under Neutral Conditions

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4,6-*O*-Benzylidene Directed β-Mannosylation Without Intermediate Triflate Formation? Comparison of Trichloroacetimidate and DISAL Donors in Microwave-Promoted Glycosylations under Neutral Conditions

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4,6-Benzylidene-protected mannosyl donors have emerged as efficient tools for the formation of 1,2-*cis* β-mannosides, which otherwise are difficult to access. Previously studied sulfoxide and trichloroacetimidate mannosyl donors were activated with strong Lewis acids at low temperature and the glycosylations are believed to proceed through intermediate formation of an α-triflate. This paper describes the synthesis of new benzylidene-protected glucosyl and mannosyl methyl 3,5-dinitrosalicylate (DISAL) donors, their application in *O*-glycosylations, and comparison with a mannosyl trichloroacetimidate donor. In contrast to previous reports on torsionally "disarmed" donors, these glycosylations were performed in the absence of strong Lewis acids, but in the presence of lithium perchlorate or triflate, using either conventional heating to 40 to 60°C or precise microwave heating to 100 to 150°C. This approach aimed at addressing the question of whether mannosyl triflate intermediates are essential for high β-selectivity in 4,6-*O*-benzylidene directed mannosylations. We find, again, that precise microwave heating promoted glycosylations under very mild conditions.

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While a DISAL mannosyl donor gave higher β-selectivity in the presence of LiOTf than with $LiClO_4$, the corresponding trichloroacetimidate did not give any β-selectivity with LiOTf. Thus, under these conditions, the nature of the original leaving group, trichloroacetimidate vs. DISAL, still is important. However, our results point to the possibility of intermediate formation of a mannosyl triflate from a DISAL donor.

Keywords Mannosides, Microwave promotion, Glycosylations, Stereo-control

INTRODUCTION

Glycoconjugates play crucial roles in the development, growth, and proper function of an organism.[1] Mannose is found in many biologically important poly- and oligosaccharides (e.g., in glycans of *O*- and *N*-glycopeptides and proteins) and tumor-associated antigens. The synthesis of oligosaccharides of these glycoconjugates provides important tools for glycobiology (e.g. in neuroglycobiology).[2] Establishing the β-mannosidic linkage has for a long time been one of the major problems in glycosylation chemistry. One recent solution to this problem has been the use of torsionally deactivated 4,6-benzylidene mannosyl donors. Crich[3] and later Schmidt[4] showed that activation of, respectively, sulfoxide and trichloroacetimidate donors with strong Lewis acids form β-mannosides with good β-selectivity. Crich has ascribed this to intermediate formation of an α-configured glycosyl triflate, which as a contact ion pair gives preferred displacement from the β-face, as the 4,6-benzylidene moiety opposes rehybridization of the anomeric carbon.[3e] Schmidt has hypothesized that the 4,6-benzylidene moiety favors formation of a twist-boat-type intermediate, which is preferably attacked from the β-face, and thus it would be a conformational effect and not the displacement of an α-configured triflate that gives rise to the remarkable β-selectivity.[4] Bols and coworkers have indicated that the deactivating effect of a 4,6-benzylidene is due to not only "torsional disarmament" but also an electronic effect associated with locking the 6-OH in the *tg* conformation; their conclusion was based on a study of the hydrolysis of dinitrophenyl β-glucoside derivatives.[17] Thus, the question arose as to whether 4,6-O-benzylidene-directed β-mannosylation can occur without intermediate formation of a mannosyl triflate. Toshima and coworkers have very recently reported β-selective mannosylation with 2,3-di-*O*-benzyl-4,6-benzylidene mannosyl phosphite in the presence of the solid promoter montmorillonite K-10 without formation of a mannosyl triflate intermediate.[5]

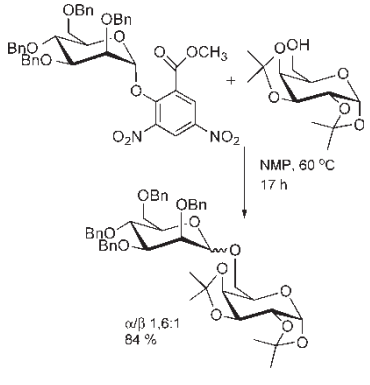
Novel methods for glycosylation in the absence of strong Lewis acids (i.e., under mild conditions) hold great promise (e.g., for combinatorial chemistry and solid-phase synthesis applications).[6] We have recently described a new, efficient method for glycosylation under strictly neutral, mildly basic, or very mildly acidic ($LiClO_4$) conditions.[7] In this glycosylation technique, the

anomeric leaving group on benzyl or benzoyl protected donors is methyl 3,5-dinitrosalicylate (DISAL) or its para regioisomer. The potential of DISAL glycosyl donors was demonstrated in their successful application to solution-d[7a,d] and solid-phase[7b] oligosaccharide synthesis, as well as intramolecular glycosylation via a novel 1,9-glycosyl shift.[7c]

DISAL glycosyl donors were prepared by a convenient and robust nucleophilic aromatic substitution protocol. DMAP-catalyzed formation of DISAL glycosides predominantly gave α-anomers, while dimethylpiperazine (DMP) predominantly gave β-anomers. Whereas *O*-benzyl (Bn)-protected DISAL donors could *O*-glycosylate simply by dissolution in *N*-methylpyrrolidinone (NMP) at 40 to 60°C with α-selectivity, the less reactive benzoyl (Bz) donors became efficient donors in CH_3NO_2 or $(CH_2Cl)_2$ in the presence of $LiClO_4$ providing 1,2-trans β-selectivity. Also, β-selective glycosylations with glucosamine donors have been achieved.[7f] These glycosylations are operationally simple and can be carried out in standard plastic vials.

We have previously shown that a per-*O*-benzyl-protected mannosyl DISAL donor can glycosylate in good yields and with a slight preference for formation of α-linkages (Sch. 1).[7a]

Here we describe the synthesis of three new, benzylidene-protected glucose and mannose DISAL donors, their use in *O*-glycosylations, and comparison with a trichloroacetimidate 4,6-benzylidene mannosyl donor. These glycosylations were performed with α-configured DISAL donors either (1) in the absence of added Lewis acids or (2) in the presence of $LiClO_4$, both thus proceeding without intermediate formation of glycosyl triflates, or (3) in the presence of LiOTf or TMSOTf, which could give rise to an intermediate glycosyl triflate. The question was whether β-selectivity could be achieved without the intermediate formation of a configurationally locked triflate.[3,4] In addition, we applied our new protocol for the precise microwave heating in *O*-glycosylations.[7g]



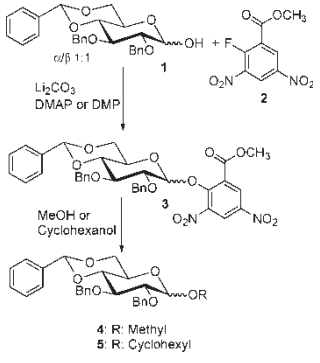
Scheme 1: Disaccharide synthesis with per-*O*-benzyl protected mannosyl DISAL donor.[7a]

RESULTS AND DISCUSSION

First, the 4,6-*O*-benzylidene glucose derivative **1**[8] was converted into DISAL donor **3**. Reaction of lactol **1** (α/β 1:1) with aryl fluoride **2** in the presence of DMAP gave DISAL donor **3** in 94% yield (α/β 1:2.7), while DMP catalysis gave 91% with good β-selectivity (α/β 1:14.3). Glycosylations of MeOH were solvolytic, while glycosylations of cyclohexanol were performed with 5 equiv. relative to donor **3**. The temperature was increased from 40 to 60°C to accelerate the reaction and to prevent hydrolysis of **3**, which was seen with prolonged reaction times. The 4,6-*O*-benzylidene-protected glucose donor **3** gave *stereospecific* glycosylation of the very reactive acceptor MeOH and α-selectivity in glycosylation of secondary alcohol cyclohexanol (Sch. 2, Table 1), and thus behaved similarly to the corresponding tetra-*O*-benzyl glucose DISAL donor. This is in accordance with previous findings on per-*O*-benzylated glucose DISAL donors.[7a] As the benzylidene di-*O*-benzyl-protected donor in our initial screen provided stereoselectivities similar to the tetra-*O*-benzyl-protected donor, we did not glycosylate more challenging acceptors.

The 4,6-*O*-benzylidene mannose lactol proved somewhat difficult to access, as benzylidenation of 4-methoxyphenyl[9] mannoside gave both the mono- and dibenzylidenated derivatives. However, with the 2,3:4,6-di-*O*-benzylidene-protected 4-methylphenyl derivative **6** at hand, it was converted to first the hemiacetal and then further to the DISAL donor **8**, the latter by DMAP catalysis, which gave the pure α-anomer in 91% yield (Sch. 3). Dibenzylidene derivative **8** was unreactive under our standard, very mild glycosylation conditions (solvolysis with MeOH, no added additive or activator). Most likely, this donor is too conformationally locked and was not chosen for further studies.

The (mono-) 4,6-benzylidenated mannose lactol **12** (Sch. 4) was accessed after some optimization, as changing the anomeric protection group from 4-methoxyphenyl to 4-methylphenylthio together with other changes in the protocol provided the mono-benzylidene thioglycoside derivative **11**. The



Scheme 2: Synthesis of benzylidene glucosyl DISAL donor **3** and its use in *O*-glycosylations.

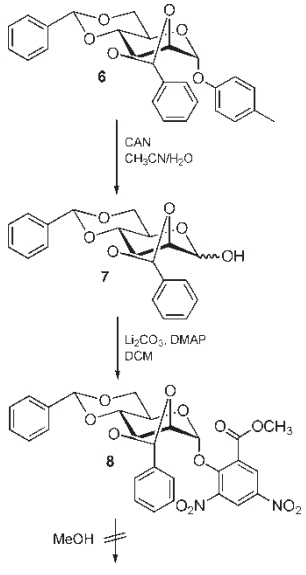
Table 1: Glycosylation with glucose DISAL donor **3**.

Entry	DISAL donor (α/β)	ROH (solvent)	Temp.[a] (°C)	Time	Product, yield (α/β ratio)
1	**3** (1:0)	MeOH	40	4d	**4β** 90% (0:1)
2	**3** (0:1)	MeOH	40	20 h	**4α** 95% (1:0)
3	**3** (1:0)	Cyclohexanol (NMP)	60	27 h	**5** 53% (1.7:1)
4	**3** (1:14.3)	Cyclohexanol (NMP)	60	24 h	**5** 63% (1.9:1)

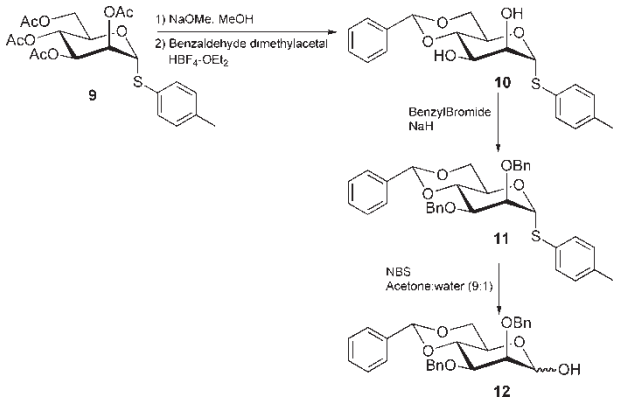
[a] Heating by heater shaker.

4-methylphenylthio moiety was introduced via either the nucleophilic reaction of thiocresol with per-acetylated mannose[10] or via phase-transfer catalyzed thiophenolysis[11] of a tetra-*O*-acetyl-mannosyl bromide.[12] The 4,6-*O*-benzylidene group was introduced using the method of Oshitari et al.,[13] which provided the 4,6-*O*-benzylidene derivative **10**, without formation of the analogous dibenzylidene derivative. Finally, **10** was benzylated followed by removal of the 4-methylphenylthiol group using NBS as described by Motawia et al.,[14] which easily led to the required lactol **12**.[13]

Mannose lactol **12** was converted to the DISAL donor **13** with DMAP catalysis, which gave the α-anomer in 92% yield. Initial studies of glycosylations with DISAL donor **13** under mild conditions revealed that it was relatively



Scheme 3: Synthesis of 2,3:4,6-di-*O*-benzylidene-protected mannosyl DISAL derivative.



Scheme 4: Synthesis of lactol **12**.

stable and less reactive; thus, we applied our previously described protocol[7g] for precise microwave heating to accelerate glycosylations. Microwave irradiation is an efficient source of energy, leading to a rapid rise in reaction temperature without heating the reaction vessel first. This in turn can lead to faster and cleaner reactions with precise temperature control.[15]

Solvolytic glycosylation of MeOH with DISAL donor **13** proceeded in 20 min at 130°C (Table 2, entry 1), giving the methyl mannoside in 80% yield with predominant β-configuration. Glycosylation of cyclohexanol (5 equiv.) with conventional heating in CH_3NO_2 required 42 h at 70°C (Table 2, entry 2) and provided no stereoselectivity. The same reaction but with microwave heating at 130°C took only 10 min (2 × 5 min) and had the added benefit of improved stereoselectivity (α/β 1:6). Increasing the reaction time to 60 min did increase the yield from the previous 50% to 67%

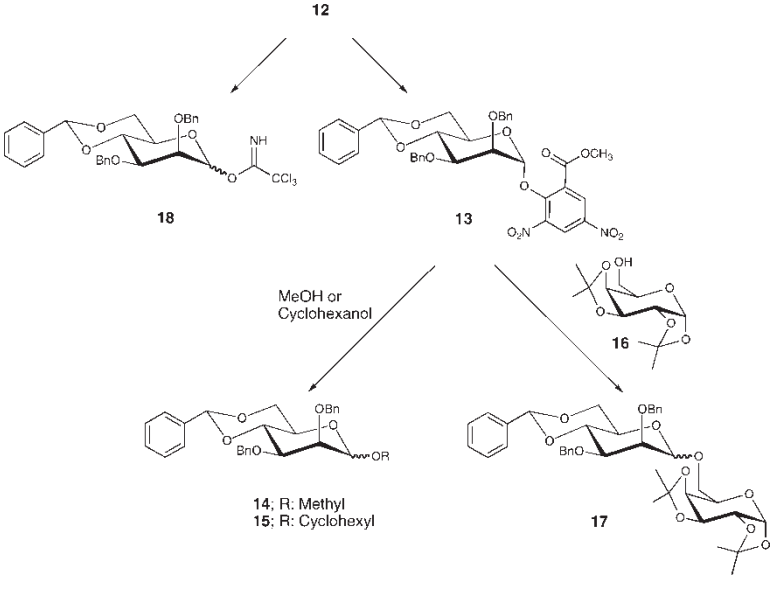
Table 2: Initial glycosylations with DISAL donor **13** (pure α-anomer); see Scheme 5.

Entry	Acceptor	Solvent (additive)	Time temp.[a]	Product, yield (α/β ratio)
1	MeOH	MeOH (none)	20 min 130°C#	**14** 80% (1:5)
2	Cyclohexanol	CH_3NO_2 ($LiClO_4$)	42 h 70°C*	**15** 50% (1:1)
3	Cyclohexanol	CH_3NO_2 ($LiClO_4$)	2 × 5 min 130°C#	**15** 50% (1:6)
4	Cyclohexanol	CH_3NO_2 ($LiClO_4$)	60 min 130°C#	**15** 67% (1:1)
5	Cyclohexanol	$(CH_2Cl)_2$ ($LiClO_4$)	15 min 150°C	**15** 44% (1:2)

[a] Symbol indicates means of heating. *Heater shaker. #Microwave heating.

but with the loss of stereoselectivity (Table 2, entry 3). Changing the solvent to the more apolar $(CH_2Cl)_2$ and increasing the reaction temperature to 150°C did not improve the yield (44%) or stereoselectivity (α/β 1:2) much (Table 2, entry 5). Though we have not previously observed trans-*O*-glycosylation of the product formed in glycosylations with microwave heating to 100 to 150°C, this possibility cannot be ruled out as the cause for the loss of stereoselectivity in the case of prolonged reaction times with excess of the acceptor (entry 3 vs. 4). Nishimura and coworkers have described transglycosylation of methyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside with 1-octanol with microwave heating to 120°C in the presence of $Yb(TfO)_3$ to give the octyl glucoside.[16]

Next, we tested glycosylations with DISAL donor **13** of the galactose acceptor **16** (Sch. 5, Table 3). Initial glycosylation of acceptor **16** with donor **13** in nitromethane and with $LiClO_4$ as additive and at 130°C did not produce any satisfactory results (not shown). A change of solvent to $(CH_2Cl)_2$ and an increase in glycosylation temperature to 150°C led to a yield of 74% but with the desired 1,2-*cis* β-mannoside as the minor anomer (Table 3, entry 1). Substituting $LiClO_4$ for LiOTf *could* give intermediate formation of the α-mannosyl triflate, which according to Crich's model should lead to preferred formation of the β-mannoside. Thus, would the addition of a very weak Lewis acid to a triflate counter-ion improve the β-selectivity? Indeed, LiOTf as additive gave the pure β-mannoside



Scheme 5: Synthesis of donors **13** and **18**; *O*-glycosylations of methanol and cyclohexanol with DISAL donor **13**.

Table 3: Glycosylation of acceptor **16** with DISAL mannosyl donor **13** (α-anomer); see Scheme 5.

Entry	Solvent (additive)	Time temp.[a]	Product 17, yield (α/β ratio)
1	$(CH_2Cl)_2$ ($LiClO_4$)	2 × 30 min 150°C	74% (2:1)
2	$(CH_2Cl)_2$ (LiOTf)	30 min 150°C	38% (0:1)
3	$(CH_2Cl)_2$ (LiOTf)	2 × 30 min 150°C	35% (1:3)
4	$(CH_2Cl)_2$ (TMSOTf, 0.3eq to **13**)	10 min 100°C	26% (1:1)

[a] All reactions were heated using microwave irradiation.

but in a low, 38% yield (Table 3, entry 2). Increasing the reaction time from 30 min to 60 min did not improve the yield, but lowered the perfect β-selectivity into a 1:3 α/β ratio (Table 3, entry 3). Somewhat surprisingly, a change to the strong Lewis acid, TMSOTf (Table 3, entry 4), at 100°C, gave poor yield and α/β ratio.

Weingart and Schmidt[4] have reported the β-selective mannosylation with 4,6-*O*-benzylidene-protected mannosyl trichloroacetimidate **18**. We have previously shown that glycosylation with trichloroacetimidates can be promoted by microwave heating in the presence of lithium salts.[7g]

The aim here was to investigate mannosylations with the trichloroacetimidate donor **18** in the presence of lithium perchlorate or triflate and with microwave heating. We now find that mannosylation with trichloroacetimidate donor **18** in the presence of lithium salts can be accelerated by microwave heating. Thus, mannosylation at 130°C for 25 min in $(CH_2Cl)_2$ (Table 4, entry 1) produced disaccharide **17** in 88% yield, unfortunately only with a α/β-ratio of 1:1. Changing the activator from $LiClO_4$ to LiOTf did not improve the α/β ratio or the yields (Table 4, entry 2). Glycosylation of acceptor **19** gave a yield of 44% with an α/β ratio of 1.3:1 (Table 4, entry 3).

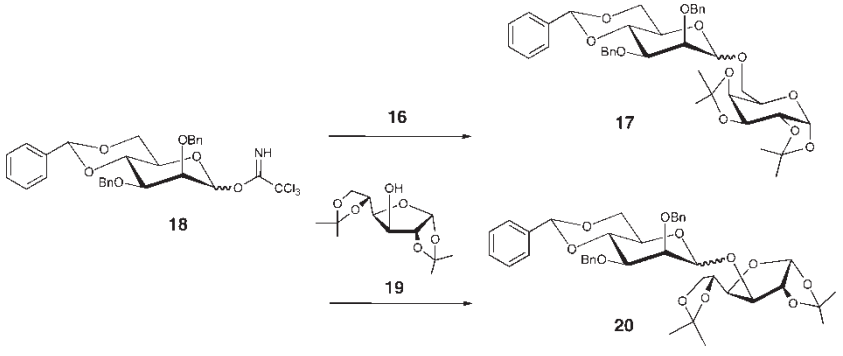
In conclusion, we have prepared three new benzylidene-protected mannose and glucose DISAL donors, and compared their glycosylating ability with that of a 4,6-*O*-benzylidene mannosyl trichloroacetimidate in *O*-glycosylations in the absence of a strong Lewis acid but in the presence of lithium perchlorate or triflate and with microwave heating. All benzylidene-protected donors in this study were found to be less reactive than comparable benzyl-protected donors. Microwave heating to 100 to 150°C again proved efficient for promoting sluggish glycosylations under mild conditions. The stereoselectivity provided by 4,6-benzylidene-protected DISAL glucosyl donor **3** was comparable to that of the corresponding benzyl-protected donor, even providing the same stereospecific glycosylation of methanol. That 4,6-*O*-benzylidene-protected glucose donors react similar to their benzyl-protected analogs has been shown previously for trichloroacetimidate and

Table 4: Initial glycosylations with trichloroacetimidate donor **18** (α/β 5:1); see Scheme 6.

Entry	Acceptor	Solvent (additive)	Time temp.[a]	Product, yield (α/β ratio)
1	**16**	$(CH_2Cl)_2$ ($LiClO_4$)	25 min 130°C	**17** 88% (1:1)
2	**16**	$(CH_2Cl)_2$ (LiOTf)	25 min 130°C	**17** 48% (1.6:1)
3	**19**	$(CH_2Cl)_2$ ($LiClO_4$)	25 min 130°C	**20** 44% (1.3:1)

[a]All reactions were heated using microwave irradiation; solvent $(CH_2Cl)_2$.

sulfoxide donors. The 4,6-benzylidene-protected mannosyl donor **13** glycosylated methanol with high β-selectivity, whereas mannosylation of cyclohexanol in the presence of $LiClO_4$ did proceed with some β-selectivity, albeit with low reactivity. Interestingly, mannosylation of monosaccharide **16** with DISAL donor **13** in the presence of $LiClO_4$ gave some α-selectivity, whereas LiOTf as additive gave β-selectivity. This could indicate that these relatively slow glycosylations to some extent can proceed through a α-mannosyl triflate contact ion pair. The analogous trichloroacetimidate mannosyl donor was able to glycosylate at 130 to 150°C in the presence of $LiClO_4$ or LiOTf, unfortunately without any β-selectivity but with somewhat improved yields. Thus, under these conditions, the nature of the original leaving group, trichloroacetimidate vs. DISAL, still is important. However, our results point to the possibility of intermediate formation of a mannosyl triflate from a DISAL donor. There are three scenarios for these particular mannosylations: (1) the reactive acceptor MeOH provides S_N2-type reactions with DISAL donors in the absence of additives, (2) the DISAL donor gives improved β-selectivity with LiOTf rather than $LiClO_4$ as additive, whereas (3) for the trichloroacetimidate donor the β-selectivity does not improve in the presence of LiOTf.



Scheme 6: *O*-Glycosylations with trichloroacetimidate donor **18**.

EXPERIMENTAL

General Methods

Molecular sieves (3 Å and 4 Å) were activated under high vacuum at 150°C for 24 h. Water contents (<20 ppm) were measured by Karl-Fischer titration. All other solvents were distilled and/or stored over 3 Å or 4 Å molecular sieves as appropriate. Analytical HPLC was performed on a Waters 600 system with a 996 diode array detector and a 717 Autosampler equipped with a 3.9 × 50 mm Nova-Pak C18 4 μm 60 Å column. The following solvents were used: 0.1% TFA/H_2O (A); 0.1% TFA/CH_3CN (B); H_2O (C); and CH_3CN (D). Analytical HPLC was performed on micro filtered or centrifuged 0.1% solutions in MeCN (for more hydrophilic compounds, solubility was improved by addition of water). The following programs were used:

Program A; 0.00 min: 1.00 mL/min, 95.0% C, 5.0% D; 7.00 min: 1.00 mL/min, 5.0% C, 95.0% D; 8.50 min: 1.00 mL/min, 5.0% C, 95.0% D; 9.00 min: 1.00 mL/min, 95.0% C, 5.0% D; 15.00 min: 1.00 mL/min, 95.0% C, 5.0% D.

Characteristic absorption maxima were: Bn: 256 to 257 nm, DISAL-OH: 220 nm and 286 nm.

Preparative HPLC was performed on a Waters 600 system with Waters 996 diode array detector and three consecutive columns (40 × 100 mm prep. NOVA Pak HR C18 6 μm 60 Å units). Linear gradients of CH_3CN (D) and water (MilliQ) (C) were used.

Program A; 0.00 min: 0.00 mL/min, 95.0% C, 5.0% D; 1.00 min: 20.00 mL/min, 95.0% C, 5.0% D; 20.00 min: 20.00 mL/min, 50.0% C, 50.0% D; 60.00 min: 20.00 mL/min, 5.0% C, 95.0% D; 75.00 min: 20.00 mL/min, 0.0% C, 100.0% D; 81.00 min: 0.00 mL/min, 0.0% C, 100.0% D.

^1H, ^{13}C, gHSQC, HMBC, and H,H-COSY NMR spectra were recorded on Varian Mercury 300, Bruker Avance 300, or Varian Unity Inova 500 spectrometers. The chemical shifts are referred to the residual solvent signal. Chemical shift (δ) values are in ppm; coupling constants (J) are in Hz. Mass determination (high-resolution MS, HR-MS) was performed on a Micromass LCT instrument with an ESI probe. For TLC Merck TLC Aluminium Sheets Silica Gel 60 F_{254} were used. Compounds containing UV-absorbing groups were visualized under UV light (254 nm), and carbohydrates were developed with 2M H_2SO_4 followed by charring with a heat gun. Vacuum liquid chromatography (VLC) was performed on columns of Merck 60H silica packed under vacuum. The crude product was dissolved in CH_2Cl_2 and the equivalent amount of silica added, concentrated, placed on column, and finally covered with acid-rinsed sea sand. Chromatography was hereafter run with the appropriate eluents until product was collected. Microwave experiments were carried out in a Biotage Initiator (Biotage, Sweden). The reaction times are

specified as ramp time and hold time at the final temperature. Temperatures were measured by IR and pressure via the septum. The new compounds described in this paper are all fully characterized. All known compounds have been verified by NMR and ESI-MS.

2,4-Dinitro-6-(methoxycarbonyl)phenyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-D-glucopyranoside (3)

DMAP procedure: To a stirred suspension of 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-D-glucopyranose **1**[8] (75 mg, 0.17 mmol) and Li_2CO_3 (25 mg, 0.33 mmol) in dry DCM (0.5 mL) was added DISAL-F **2** (49 mg, 0.2 mmol). DMAP (5.6 mg, 0.05 mmol) was dissolved in DCM (0.5 mL) and added in five portions over 20 min. Upon addition of DMAP the solution changed from colorless to orange. After 45 min the reaction mixture was purified by VLC (DCM) to give the title compound as a yellow foam (106 mg, 94%, α/β 1:2.7).

DMP procedure: The glucose derivative **1**[8] (100 mg, 0.22 mmol) and Li_2CO_3 (33 mg, 0.45 mmol) was suspended in dry DCM (0.8 mL) in a 10-mL flask. To this suspension was added DISAL-F **2** (65 mg, 0.27 mmol) and DMP (15 μL, 0.11 mmol). After 3(1/2) h a solution of DMAP (7.5 mg, 0.07 mmol) in DCM was added and after another 15 min the reaction mixture was purified by VLC (DCM) to give the title compound as a yellow foam (137 mg, 91%, α/β 1:14.3). ^{1}H NMR **3α** (300 MHz, $CDCl_3$): δ 8.68 (d, 1H, $J = 2.9$ Hz), 8.51 (d, 1H, $J = 2.9$ Hz), 7.52–6.93 (m, 15H, ArH), 5.57 (s, 1H, $PhCHO_2$), 5.43 (d, 1H, $J = 3.5$ Hz, H-1α), 4.96–4.34 (m, 4H, Ph-C*H*), 4.33 (dd, 1H, $J = 9.6$ Hz, $J = 5.0$ Hz, H-6), 4.16 (dd, 1H, $J = 9.6$ Hz, $J = 9.4$ Hz, H-6′), 4.12 (ddd, 1H, $J = 10.1$ Hz, $J = 9.4$ Hz, $J = 5.0$ Hz, H-5), 3.92 (s, 3H, OMe), 3.73 (dd, 1H, $J = 10.1$ Hz, $J = 9.6$ Hz, H-4), 3.67 (dd, 1H, $J = 9.6$ Hz, $J = 9.6$ Hz, H-3), 3.64 (dd, 1H, $J = 9.6$ Hz, $J = 3.5$ Hz, H-2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.6, 154.3, 144.8, 141.4, 138.5, 137.2, 137.0, 129.7, 126.7, (m, Ar), 123.5, 104.3, 101.6 (C-1), 81.2, 80.6, 78.4, 75.6, 75.0, 68.7, 65.7, 53.5 (OMe). ^{1}H NMR **3β** (500 MHz, $CDCl_3$): δ 8.83 (d, 1H, $J = 3.0$ Hz), 8.72 (d, 1H, $J = 3.0$ Hz), 7.48–7.25 (m, 15H, ArH), 5.57 (s, 1H, $PhCHO_2$), 5.31 (d, 1H, $J = 7.7$ Hz, H-1β), 4.97–4.81 (m, 4H, Ph-C*H*), 4.18 (dd, 1H, $J = 10.2$ Hz, $J = 4.9$ Hz, H-6), 3.90 (s, 3H, OMe), 3.86–3.82 (m, 2H, H-2, H-3), 3.77–3.73 (m, 1H, H-4), 3.69 (t, 1H, $J = 10.2$ Hz, H-6′), 3.39 (ddd, 1H, $J = 9.8$ Hz, $J = 9.8$ Hz, $J = 4.9$ Hz, H-5). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.3, 151.3, 146.9, 143.3, 138.4, 138.1, 137.1, 130.0-126.1 (m, Ar), 122.9, 104.7, 101.4 (C-1), 82.0, 80.9, 80.5, 75.5, 75.2, 68.2, 66.6, 53.5 (OMe). ES-HR-MS: m/z calcd for $C_{35}H_{32}N_2O_{12}$ 672.1955; $[M + Na]^+$ 695.1853; found: 695.1731.

Methyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (4α)

The DISAL donor **3β** (20 mg, 0.03 mmol) and MeOH (700 μL) were placed in an Eppendorf tube and heated to 40°C on an Eppendorf Thermomixer 5436. After 20 h the solvent was evaporated and the reaction mixture purified by VLC (toluene-EtOAc 5:1) to give the title compound as white crystals (13 mg, 95%), mp 89–91°C (crystallized from toluene and EtOAc; lit. 93°C[18]). The observed NMR data were identical with literature values.[19]

Methyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside (4β)

The donor **3α** (20 mg, 0.03 mmol) and MeOH (700 μL) were placed in an Eppendorf tube and heated to 40°C on an Eppendorf Thermomixer 5436. After 96 h the solvent was evaporated and the reaction mixture was purified by VLC (toluene-EtOAc 5:1) to give the title compound as white crystals (12.4 mg, 90%, α/β 0:1), mp 116–118°C (crystallized from toluene and EtOAc; lit. 118–120°C[20]). The observed NMR data were identical with literature values.[21]

Cyclohexyl 2,3-di-*O*-Benzyl-4,6-*O*-benzylidene-D-glucopyranoside (5)

The donor **3β** (20 mg, 0.03 mmol, α/β 1:14.3), cyclohexanol (16 μL, 0.15 mmol), and NMP (900 μL) were placed in an Eppendorf tube and heated to 60°C on an Eppendorf Thermomixer 5436. After 24 h EtOAc (30 mL) was added and the reaction mixture was washed with brine (2 × 20 mL), NaOH (0.5 M, 2 × 20 mL), and again with brine (2 × 20 mL). The organic phase was dried with Na_2SO_4, evaporated, and purified by VLC (EtOAc-toluene 1:60 → 1:5) to give the title compound as an off-white powder (10 mg, 63%, α/β 1.9:1). ^{1}H NMR **5α** (500 MHz, $CDCl_3$): δ 7.51–7.27 (m, 15H, ArH), 5.56 (s, 1H, PhC*H*O_2), 4.95–4.68 (m, 4H, Ph-C*H*), 4.93 (d, 1H, $J = 3.8$ Hz, H-1), 4.26 (dd, 1H, $J = 10.3$ Hz, $J = 5.4$ Hz, H-6), 4.07 (t, 1H, $J = 9.4$ Hz, H-3), 3.96 (ddd, 1H, $J = 10.3$ Hz, $J = 9.9$ Hz, $J = 5.4$ Hz, H-5), 3.70–3.67 (m, 1H, H-6′), 3.61 (t, 1H, $J = 9.4$ Hz, H-4), 3.57–3.52 (m, 1H, C*H*-OGlc, cyclohexyl), 3.55 (dd, 1H, $J = 9.4$ Hz, $J = 3.8$ Hz, H-2), 1.2–2.0 (m, 10H, CH_2, cyclohexyl). ^{1}H NMR **5β** (500 MHz, $CDCl_3$): δ 7.51–7.27 (m, 15H, ArH), 5.56 (s, 1H, PhC*H*O_2), 4.95–4.78 (m, 4H, Ph-C*H*), 4.62 (d, 1H, $J = 7.6$ Hz, H-1), 4.34 (dd, 1H, $J = 10.3$ Hz, $J = 4.9$ Hz, H-6), 3.79 (t, 1H, $J = 10.3$ Hz, H-6′), 3.75–3.79 (m, 1H, H-3), 3.70–3.67 (m, 1H, H-4), 3.57–3.52 (m, 1H, C*H*-OGlc, cyclohexyl), 3.46 (t, 1H, $J = 8.2$ Hz, H-2), 3.39 (ddd, 1H, $J = 10.3$ Hz, $J = 9.6$ Hz, $J = 4.9$ Hz, H-5), 1.2–2.0 (m, 10H, CH_2, cyclohexyl). ^{13}C NMR **5α/β**

(126 MHz, $CDCl_3$): δ 139.2, 138.6, 137.7, 129.0–127.6 (m, Ar), 126.2, 101.3, 96.3 (C-1), 82.6, 82.4, 81.7, 81.3, 79.6, 78.9, 76.2, 75.5, 75.4, 73.5, 69.3, 69.1, 66.2, 62.6, 33.9, 33.6, 32.1, 31.7, 25.8, 24.5, 24.3, 24.2.

The donor **3α** (12 mg, 18 μmol), cyclohexanol (9.4 μL, 89 μmol), and NMP (600 μL) were placed in an Eppendorf tube and heated to 60°C on an Eppendorf Thermomixer 5436. After 27 h EtOAc (20 mL) was added, and the reaction mixture was washed with brine (2 × 20 mL), NaOH (0.5 M, 2 × 20 mL), and again with brine (2 × 20 mL). The organic phase was dried with Na_2SO_4, evaporated, and purified by VLC (EtOAc-toluene 1:60 → 1:5) to give the title compound as an off-white powder (5.0 mg, 53%, α/β 1.7:1).

4-Methoxyphenyl 2,3:4,6-Di-*O*-benzylidene-α-D-mannopyranoside (6)

In a 50-mL flask 4-methoxyphenyl mannoside (synthesized from mannose according to[4,22,23]) (230 mg, 0.80 mmol), benzaldehyde dimethylacetal (600 μL, 4.0 mmol) and camphorsulfonic acid (CSA, 19 mg, 0.08 mmol) were dissolved in CH_3CN (20 mL). A part (15 mL) of the reaction mixture was removed by distillation and Et_3N (five drops) were added followed by evaporation. MeOH (10 mL) was added and heated to boiling where a white solid (**6-***exo*) precipitated from the solution and was filtered off. When the mother liquor was left to cool down the corresponding *endo*-isomer precipitated out and was filtered off as a white powder (308 mg, 83%, *endo*/*exo* 1:3.3).

Data of **6-***endo*: mp (*endo*) 131–132°C; $[\alpha]_D = 36.0$ (c 8.83 × 10^{-3} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60–7.34 (m, 10H, ArH), 7.03–7.00 (m, 2H, ArH), 6.88–6.85 (m, 2H, ArH), 6.05 (s, 1H, PhC*H*O_2), 5.82 (s, 1H, H-1), 5.54 (s, 1H, PhC*H*O_2), 4.65 (dd, 1H, J = 7.5 Hz, J = 6.2 Hz, H-3), 4.55 (d, 1H, J = 6.2 Hz, H-2), 4.23 (dd, 1H, J = 10.2 Hz, J = 5.1 Hz, H-6), 4.01 (ddd, 1H, J = 10.2 Hz, J = 9.8 Hz, J = 5.1 Hz, H-5), 3.82 (dd, 1H, J = 9.8 Hz, J = 7.5 Hz, H-4), 3.79 (s, 3H, OMe), 3.72 (t, 1H, J = 10.2 Hz, H-6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.4, 149.9, 137.3, 137.1, 129.6–126.2 (m, benzylidene), 2 × 118.1, 2 × 114.9, 104.4, 102.0, 97.0 (C-1), 80.5, 78.5, 74.3, 68.9, 61.4, 55.8. ES-HR-MS: m/z calcd for $C_{27}H_{26}O_7$ 462.1679; $[M + H]^+$: 463.1757; found: 463.1755.

Data of **6-*exo***: mp (*exo*) 189–192°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57–7.35 (m, 10H, ArH), 7.00–6.97 (m, 2H, ArH), 6.86–6.83 (m, 2H, ArH), 6.35 (s, 1H, PhC*H*O_2), 5.75 (s, 1H, H-1), 5.66 (s, 1H, PhC*H*O_2), 4.81 (dd, 1H, J = 7.7 Hz, J = 5.6 Hz, H-3), 4.39 (d, 1H, J = 5.6 Hz, H-2), 4.29 (dd, 1H, J = 10.4 Hz, J = 4.5 Hz, H-6), 4.04 (ddd, 1H, J = 10.4 Hz, J = 9.7 Hz, J = 4.5 Hz Hz, H-5), 3.97 (dd, 1H, J = 9.7 Hz, J = 7.7 Hz, H-4), 3.81 (t, 1H, J = 10.4 Hz, H-6′), 3.78 (s, 3H, OMe). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.4, 150.0, 138.6, 137.2, 129.6–126.2 (m, benzylidene), 2 × 118.1, 2 × 114.9, 103.3, 102.2, 97.1 (C-1), 77.6, 75.8, 75.6, 68.9, 61.3, 55.8. ES-HR-MS: m/z calcd for $C_{27}H_{26}O_7$: 462.1679;

$[M + H]^+$: 463.1757; found: 463.1805. Anal. Calcd. for $C_{27}H_{26}O_7$: C, 70.12; H, 5.67. Found: C, 70.10; H, 5.64.

2,3:4,6-Di-*O*-benzylidene-D-mannopyranose (7-*exo*)

In a 25-mL flask the mannoside **6**-*exo* (360 mg, 0.78 mmol) was dissolved in CH_3CN (10 mL) and a solution of $Ce(NH_4)_2(NO_3)_6$ (CAN, 1.92 g, 3.5 mol) in H_2O (2.5 mL) was added. The orange solution was stirred for 20 min followed by addition of EtOAc (20 mL), washed with brine (3 × 20 mL), and dried with solid $MgSO_4$. The crude compound was purified by preparative HPLC to give the title compound as an off-white powder (113 mg, 41%, α/β 3.2:1; ratio obtained by integration of the benzylidene peaks around 5.65 ppm). ^{1}H NMR (α-anomer; 300 MHz, $CDCl_3$): δ 7.57–7.35 (m, 10H, ArH), 6.30 (s, 1H, PhC*H*O_2), 5.65 (s, 1H, PhC*H*O_2), 5.54 (s, 1H, H-1), 4.69 (dd, 1H, $J = 8.1$ Hz, $J = 5.5$ Hz, H-3), 4.34 (dd, 1H, $J = 10.4$ Hz, $J = 5.0$ Hz, H-6), 4.20 (d, 1H, $J = 5.5$ Hz, H-2), 4.06 (ddd, 1H, $J = 10.1$ Hz, $J = 9.9$ Hz, $J = 5.0$ Hz, H-5), 3.91 (dd, 1H, $J = 9.9$ Hz, $J = 8.3$ Hz, H-4), 3.81 (dd, 1H, $J = 10.4$ Hz, $J = 10.1$ Hz, H-6′), 2.68 (broad s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.7, 137.2, 129.6–126.2 (m, benzylidene), 103.2, 102.2, 92.9, 77.5, 75.6, 75.5, 69.0, 60.8. ES-HR-MS: m/z calcd for $C_{20}H_{20}O_6$: 356.1260; $[M + H]^+$: 357.1338; found: 357.1539.

2,4-Dinitro-6-(methoxycarbonyl)phenyl 2,3:4,6-Di-*O*-benzylidene-α-D-mannopyranoside (8-*exo*)

In a 10-mL flask the dibenzylidene-protected mannose **7**-*exo* (35 mg, 98 μmol) and Li_2CO_3 (15 mg, 0.20 mmol) were suspended in dry DCM. DISAL-F **2** (29 mg, 0.12 mmol) was added followed by a solution of DMAP (3.5 mg, 31 μmol) dissolved in DCM (0.3 mL) added in five portions over 20 min. The solution gradually changed from colorless to strong orange. After 1 h the reaction mixture was purified by VLC (DCM) to give the title compound as yellow foam (52 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.90 (d, 1H, $J = 3.0$ Hz), 8.72 (d, 1H, $J = 3.0$ Hz), 7.55–7.36 (m, 10H, ArH), 6.30 (s, 1H, PhC*H*O_2), 5.76 (s, 1H, H-1), 5.61 (s, 1H, PhC*H*O_2), 4.81 (dd, 1H, $J = 8.2$ Hz, $J = 5.8$ Hz, H-3), 4.69 (d, 1H, $J = 5.8$ Hz, H-2), 4.27 (dd, 1H, $J = 9.3$ Hz, $J = 4.4$ Hz, H-6), 3.91 (dd, 1H, $J = 9.3$ Hz, $J = 8.2$ Hz, H-4), 3.89 (s, 3H, OMe), 3.76 (ddd, 1H, $J = 9.8$ Hz, $J = 9.3$ Hz, $J = 4.4$ Hz, H-5), 3.68 (dd, 1H, $J = 9.8$ Hz, $J = 9.3$ Hz, H-6′). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.9, 153.0, 146.0, 143.0, 138.2, 136.9, 130.1–123.4 (m, ArH), 104.5, 103.3, 102.0 (C-1), 76.4, 75.4, 75.3, 68.3, 63.8, 53.7. Hetero-nuclear coupling constant $^1J_{C1,H1} = 180.6$ (α). ES-HR-MS: m/z calcd for $C_{28}H_{24}N_2O_{12}$: 580.1329; $[M + H]^+$: 581.1408; found: 581.1420.

4-Methylphenyl 4,6-*O*-Benzylidene-1-thio-α-D-mannopyranoside (10)

4-Methylphenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranoside (**9**)[10] (4.4 g, 9.7 mmol) was dissolved in dry MeOH (35 mL) and treated with NaOMe in dry MeOH (33% w/v, 4.6 mL) for 2.5 h. The solution was neutralized with Dowex 50W-X8 (H^+-form, 200–400 mesh) ion-exchange resin, filtered, and passed through a layer of sand and silica gel, which after evaporation yielded crude 4-methylphenyl 1-thio-α-D-mannopyranoside. The crude 4-methylphenyl 1-thio-α-D-mannopyranoside (1.67 g, 5.8 mmol) was dissolved in DMF (7 mL) and cooled to 0°C. Benzaldehyde dimethylacetal (879 μL, 5.8 mmol) and $HBF_4 \cdot OEt_2$ (54% Et_2O solution, 640 μL, 4.7 mmol) were added at 0°C, and the solution were stirred at rt overnight. Et_3N (1 mL) was added, and the mixture was poured into water (10 mL) and the formed precipitate was filtered, washed with cold Et_2O, and purified by VLC (DCM-MeOH 1:0 → 9:1) to give **10** as fine white crystals (1.44 g, 79%), mp 213–214°C (crystallized from MeOH). $[\alpha]_D = -54.6$ (c 8.08 × 10^{-3} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45–7.13 (m, 10H, ArH), 5.59 (s, 1H, PhC*H*O_2), 5.37 (d, 1H, $J = 5.1$ Hz, H-1), 5.18 (m, 2H, 2 × OH), 4.16 (dd, 1H, $J = 4.6$ Hz, $J = 9.9$ Hz, H-6), 3.95 (m, 1H, H-2), 3.82–3.69 (m, 3H, H-3, H-4, H-6), 3.43 (m, 1H, H-5), 2.27 (s, 3H, Ph-C*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.9, 135.8, 132.2, 129.8-126.2 (m, Ar*C*), 101.0, 87.6 (C-1), 78.1, 72.7, 70.4, 67.8, 20.5. ES-HR-MS: m/z calcd for $C_{20}H_{22}O_5S$: 374.1188; $[M + H]^+$: 375.1266; found: 375.1246.

p-Methylphenyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (11)

NaH (*ca* 60% in mineral oil, 500 mg) in DMF (6 mL) was added to a 0°C cold solution of **10** (1.6 g, 4.3 mmol) in DMF (20 mL) and the mixture was stirred for 30 min. To the mixture was added benzyl bromide (1.4 mL, 11.8 mmol), and the reaction was stirred for 19 h. MeOH (5 mL) was added, and the reaction mixture was concentrated at reduced pressure, poured into H_2O, and extracted with EtOAc. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated at reduced pressure. The residue was purified by column chromatography (EtOAc/hexane = 1/9) to give **11** (1.6 g, 67%) as colorless crystals. mp 153–159°C (crystallized from hexane and EtOAc). $[\alpha]_D = -39.3$ (c 7.83 × 10^{-3} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54–7.11 (m, 20H, ArH), 5.65 (s, 1H, PhC*H*O_2), 5.13–4.73 (m, 4H, Ph-C*H*), 4.81 (d, 1H, $J = 1.1$ Hz, H-1), 4.36–4.29 (m, 2H, H-4, H-6), 4.20 (dd, 1H, $J = 3.0$ Hz, $J = 1.1$ Hz, H-2), 3.96 (dd, 1H, $J = 10.4$ Hz, H-6), 3.75 (dd, 1H, $J = 9.8$ Hz, $J = 3.1$ Hz, H-3), 3.41 (ddd, 1H, $J = 14.4$ Hz, $J = 5.0$ Hz, $J = 5.0$ Hz, H-5), 2.35 (s, 3H, Ph-C*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5–137.0 (m, Ar*C*), 132.3–126.1 (m, Ar*C*), 101.4, 89.6 (C-1),

79.9, 79.0, 78.8, 75.9, 73.2, 71.7, 69.0, 68.5, 21.1. ES-MS: m/z calcd for $C_{34}H_{34}O_5S$: 554.21; $[M+H]^+$: 555.22; found: 555.25. $[M+Na]^+$: 577.20; found: 577.22. Anal. Calcd. for $C_{34}H_{34}O_5$: C, 73.62; H, 6.18. Found: C, 73.24; H, 6.12.

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranose (12)

N-Bromosuccinimide (0.61 g, 3.4 mmol) was added at rt to a stirred solution of **11** (0.5 g, 0.9 mmol) in 9:1 acetone:water (22 mL). Stirring was continued for 20 min after which the solvent was concentrated until turbidity arose. The residue was dissolved in EtOAc (30 mL), washed with a saturated solution of Na_2CO_3 (3 × 10 mL) and water (3 × 10 mL), dried over anhydrous Na_2SO_4, and concentrated to dryness. The residue was purified by column chromatography (EtOAc/hexane = 3:2), yielding **12** (330 mg, 82%) as colorless syrup. ES-HR-MS: m/z calcd for $C_{27}H_{28}O_6$: 448.1886; $[M+H]^+$: 448.1964; found: 448.1989. The observed NMR data were identical with literature values.[13b]

2,4-Dinitro-6-(methoxycarbonyl)phenyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (13)

To a stirred suspension of **12** (300 mg, 0.67 mmol) and Li_2CO_3 (100 mg, 1.35 mmol) in dry DCM (10 mL) was added DISAL-F **2** (197 mg, 0.81 mmol). DMAP (25 mg, 0.2 mmol) was dissolved in DCM (2 mL) and added in five portions over 20 min. Upon addition of DMAP the solution changed from colorless to orange. After 40 min the reaction mixture was purified by VLC (DCM) to give the title compound as yellow foam (417 mg, 93%,). $[\alpha]_D = -11.0$ (c 8.25×10^{-3} $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.84 (d, 1H, $J = 2.7$ Hz), 8.72 (d, 1H, $J = 2.9$ Hz), 7.54–7.28 (m, 15H, ArH), 5.63 (s, 1H, PhC*H*O_2), 5.52 (d, 1H, $J = 1.3$ Hz, H-1α), 4.93–4.66 (m, 4H, Ph-C*H*), 4.42 (dd, 1H, $J = 3.2$ Hz, $J = 1.3$ Hz, H-2), 4.32 (dd, 1H, $J = 9.5$ Hz, H-6), 4.18–4.09 (m, 2H, H-3, H-6′), 3.97 (s, 3H, OMe), 3.82 (m, 2H, H-4, H-5). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.9 153.0, 145.4, 142.4, 138.4, 137.8, 137.3, 129.4–123.1 (m, Ar), 105.5, 101.5 (C-1), 77.6, 76.3, 75.7, 74.1, 73.4, 68.2, 67.3, 53.5 (OMe). ES-MS: m/z calcd for $C_{35}H_{32}N_2O_{12}$: 672.20; $[M+H]^+$: 673.20; found: 673.24. $[M+Na]^+$: 695.19; found: 695.20. Anal. Calcd. for $C_{35}H_{32}N_2O_{12}$: C, 62.50; H, 4.80. Found: C, 61.44; H, 4.61.

Optimization of glycosylation conditions (Table 2)

Conventional heating: The glycosyl donor (0.027 to 0.05 mmol) was dissolved in dry NMP (1 mL) in a micro centrifuge tube (Plasticbrand), and

crushed 3 Å molecular sieves and cyclohexanol (5 eq.) were added. The tube was stirred at 70°C during, and the progress of the reactions was monitored by HPLC and TLC (30% EtOAc in hexane). Evaporation of the solvent was followed by purification by either VLC chromatography (hexane:EtOAc 18:1 → 1:1) or preparative HPLC to give product indicated by Table 2.

Microwave heating: Glycosyl donor (typically 0.05 mmol) was dissolved in either dry methanol or NMP (500 μL), and in the case of NMP, cyclohexanol (0.25 mmol) was added followed by mixing. The reaction mixture was subjected to microwave radiation (reaction time and temperature, see Table 2); a sample (12 μL) was diluted in acetonitrile (0.7 mL) and analyzed by analytical HPLC. From a series of test reactions, the product was purified by preparative HPLC and characterized by NMR and ES-MS.

Methyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (14)

The observed NMR data were identical with literature values.[24]

Cyclohexyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranoside (15)

The observed NMR data were identical with literature values.[3c]

General procedure for the microwave-assisted glycosylation reactions (Tables 3 and 4)

Glycosyl donor (0.075 mmol, 1,5 equiv.); glycosyl acceptor (0.05 mmol, 1 equiv.); activators and additives if required (see Tables); crushed 3 Å molecular sieves; and a magnet were placed in a 5-mL microwave reaction vial and fitted with a septum, which was then pierced with a needle. The closed vial was then evacuated under high vacuum; Ar was let in followed by re-evacuation. This cycle was repeated twice and then left to dry for 1 to 2 h. Ar was let in, the needle was removed, and dry solvent (500 μL) was added under argon. The reaction mixture was subjected to microwave radiation for 5 min at 100°C (unless stated otherwise), transferred to a 15-mL Falcon plastic tube, and centrifuged for 3 min at 4000 rpm, and the supernatant was transferred to a new 15-mL Falcon plastic tube and concentrated to dryness under a stream of air. The residue was loaded onto a preparative HPLC column with 2 mL of CH_3CN and purified, followed by evaporation of appropriate fractions.

1,2;3,4-Di-*O*-isopropylidene-6-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranosyl)-α-D-galactopyranoside (17)

The observed NMR data were identical with literature values.[3c]

2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α/β-D-mannopyranosyl trichloroacetimidate (18)

A solution of **12** (336 mg; 0.75 mmol) and trichloroacetonitrile (1 mL) in dry CH_2Cl_2 (10 mL) was stirred vigorously with anhydrous K_2CO_3 (0.5 g) overnight at rt under Ar atmosphere. The mixture was diluted with dry Et_2O (10 mL) and filtered through a layer of sand and silica gel. The silica gel layer was washed several times with Et_2O and the combined filtrates were evaporated to give the trichloroacetimidate **18** (330 mg, 75%, α/β 5:1) in a chromatographically pure form as colorless syrup. Observed NMR data were identical with literature values.[4]

1,2;5,6-DI-*O*-ISOPROPYLIDENE-3-*O*-(2,3-DI-*O*-BENZYL-4,6-*O*-BENZYLIDENE-α/β-D-MANNOPYRANOSYL)-α-D-GLUCOFURANOSIDE (20)

The observed NMR data were identical with literature values.[3c]

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