Phenyl 2-Deoxy-2-iodo-1-thio-glycosides: New Glycosyl Donors for the Stereoselective Synthesis of 2-Deoxy-oligosaccharides

Xavier Arnés, Yolanda Díaz,* Sergio Castillón*

Departament de Química Analítica i Química Orgànica, Universitat Rovira i Virigili, 43005 Tarragona, Spain
Fax +34(977)559563.; E-mail: ydiaz@quimica.urv.es; E-mail: castillon@quimica.urv.es

Received 29 July 2003

Abstract: Phenyl 2-deoxy-2-iodo-1-thioglycosides, prepared from simple pentoses by olefination and iodine-induced cyclization, have proved to be efficient glycosyl donors for the stereoselective synthesis of 2-deoxy-2-iodo-oligosaccharides, which are precursors of 2-deoxy-oligosaccharides.

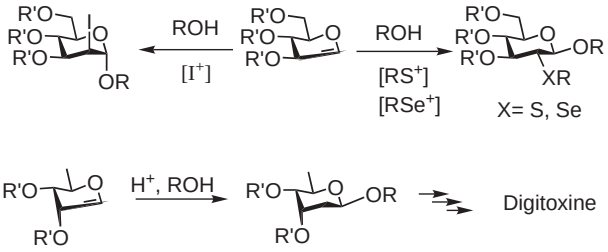
Key words: 2-deoxy-oligosaccharides, glycosylation, stereoselectivity, cyclizations, iodine

The stereocontrolled formation of the glycosidic linkage in 2-deoxy-oligosaccharides has been found to be one of the most challenging tasks in glycosylation reactions,[1] because of the absence of a stereodirecting group at C-2. This problem can be overcome by using electrondonor groups (such as iodo, phenylsulfanyl, and phenylselenenyl) at position 2. Once the corresponding glycosides have been obtained, they are further reductively removed to provide 2-deoxy-glycosides.

Glycosylation can be performed from glycals by activation with iodine,[2] sulfanyl[3] and selenenyl[4] electrophiles through a one-pot procedure to afford mainly *trans*-diaxial (I^+) or *trans*-diequatorial addition (S^+, Se^+) products (Scheme 1). Glycosylation is also performed in a two-step procedure first by isolating a 2-deoxy-2-X-glycosyl donor (X = I, SR, SeR) and subsequent activation in the presence of a glycosyl acceptor.[5] Acid-catalyzed addition of an alcohol to a glycal is also a direct method for synthesising 2-deoxyglycosides, as exemplified in the synthesis of digitoxine, where the starting 6-deoxy-allal is prepared from a non-carbohydrate precursor (Scheme 1).[6]

2-Deoxy-phosphites,[7] -phosphoroimidates[8] and -dithiophosphates[9] have also been used as glycosyl donors to provide mainly the α-derivative. Thio-glycosides[10] are useful glycosyl donors and 2-deoxy-thioglycosides have recently been used as glycosyl donors in a solid-phase-assisted synthesis of 2-deoxyconjugates.[11]

We report here a new procedure for synthesizing phenyl 2-deoxy-2-iodo-1-thio-glycosides of *manno*- and *allo*-configuration and their use as glycosyl donors for the stereocontrolled synthesis of 2-deoxy-2-iodo-α-*manno*- and 2-deoxy-2-iodo-β-*allo*-disaccharides, respectively.



Scheme 1 Synthesis of 2-deoxy-α- and 2-deoxy-β-glycosides from glycals.

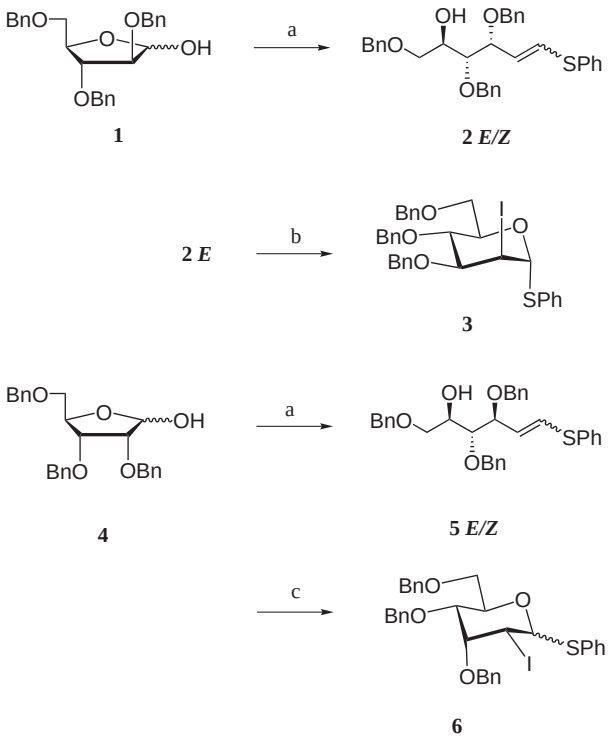
The key step for the synthesis of 2-deoxy-2-iodo-1-thioglycosides is a cyclization of alkenols induced by iodine electrophiles. These alkenols can be prepared starting from different protected pentoses by means of an olefination reaction.

Thus, 2,3,5-tri-*O*-benzyl-arabinose (**1**) was initially submitted to a Peterson olefination reaction by treatment with Me_3SiCH_2SPh to afford compound **2**[12] as an *E*/*Z*-mixture in 65% yield (Scheme 2) (entry 1, Table 1). Compound **2** (*E*-isomer) was then reacted with KH, I_2 in diethyl ether to obtain isomer **3**[13] only (61%) through a regio- and stereoselective 6-*endo*-cyclization. The regioselectivity is governed by the sulfur atom, which stabilizes a positive charge in the neighbouring carbon. The stereoselectivity observed is consistent with that reported for alkenols with an allylic alkoxy group, the iodine atom being *cis* to that group (C-3 alkoxy substituent) in the cyclization product.[14] Moreover, the relative stereochemistry of C-1 and C-2 in thioglycoside **3** depends on the configuration of the starting alkene: thus, from *trans*-alkenylsulfide **2*E*** (Scheme 2), the iodine atom and the phenylsulfanyl group in the cyclization product **3** are in a *trans* arrangement. Isomer *Z*, in turn, did not cyclize in any of the conditions tested.

We then attempted to improve the *E*/*Z*-selectivity by performing a Horner reaction. Both yield and stereoselectivity were higher in these conditions, the *E*-alkene being the major isomer (entry 2, Table 1).[15]

Similarly, 2,3,5-tri-*O*-benzyl-ribose (**4**) was converted into compound **5**[16] (Scheme 2) by reaction with Me_3SiCH_2SPh in basic medium. The yield was 48% and the selectivity was similar to that of entry 1. In this case, small amounts of a second product were also isolated, as a result of epimerization at the allylic position.[17] When pentose **4** was reacted with $PhSCH_2P(O)Ph_2$ in a

SYNLETT 2003, No. 14, pp 2143–2146
Advanced online publication: 07.10.2003
DOI: 10.1055/s-2003-42066; Art ID: G18903ST.pdf



Scheme 2 Synthesis of phenyl 2-deoxy-2-iodo-thioglycosydes from pentoses. *Reagents*: a) See Table 1; b) KH, I_2, Et_2O, –78 ºC, 61%; c) NIS, $NaHCO_3$ in acetonitrile. From **5***E*: 63% yield of **6β**. From **5***E*/**5***Z* = 2:3, 45% yield of **6β**/**α** (2:3).

Horner-type olefination, both the yield and *E*-stereoselectivity improved (entry 4).

Compound **5** (*E*-isomer) rendered 2-deoxy-2-iodo-β-1-thio-*allo*-pyranoside **6β** by treatment with NIS in acetonitrile in a 63% yield.

Starting from a 2:3 *E*/*Z*-mixture, **5** cyclized in the same conditions to give 2-deoxy-2-iodo-1-thio-glycoside **6**[18] as a 2:3 β/α-mixture in a 45% yield. The iodine atom was also *cis* to the neighboring alkoxy chain at C-3, and the β/α-ratio was the same as the *E*/*Z*-ratio in the starting material **5**, thus indicating that the *cis* olefin was also reactive towards cyclization. The less reactive *Z*-alkene, though, required higher temperatures to cyclize and this may well explain the lower yields observed when starting from a *E*/*Z*-mixture of vinylsulfide **5**.

Table 1 Olefination of Pentoses **1**, **4**

Entry	Substrate	Reagent	Product	Yield (%)	*E*/*Z*-ratio[b]
1	**1**	$PhSCH_2SiMe_3$[a]	**2**	65%	38:62
2	**1**	$PhSCH_2P(O)Ph_2$[b]	**2**	80%	87:13
3	**4**	$PhSCH_2SiMe_3$[a]	**5**	48%	38:62
4	**4**	$PhSCH_2P(O)Ph_2$[b]	**5**	72%	80:20

[a] Conditions: BuLi, THF, –78 ºC to r.t.
[b] Conditions: BuLi, THF, –78 ºC to r.t., (**1**), reflux (**4**). Determined by NMR by integration of olefinic protons.

These new glycosyl donors **3** and **6** have proved to be fairly stable and can be stored in the refrigerator for several months without significant decomposition (Scheme 3).

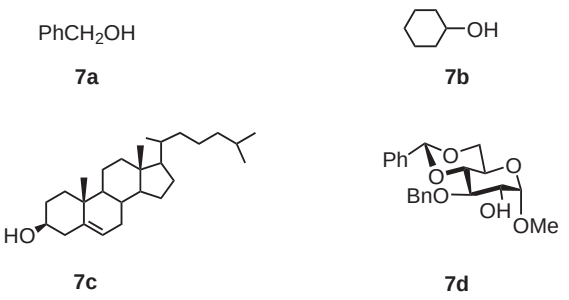
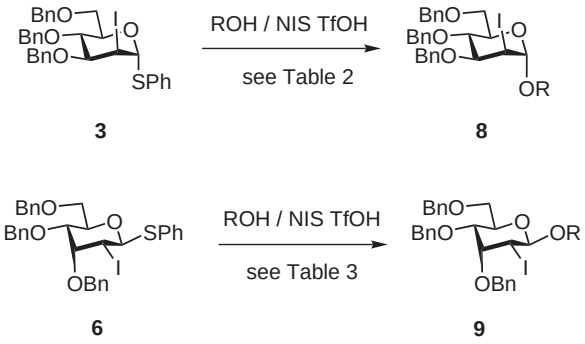


Figure 1



Scheme 3 Glycosylation of **3**, **6**.

We initially tested the benzyl alcohol (**7a**, Figure 1) glycosylation with the 2-deoxy-2-iodo-*manno* derivative **3**. We selected the typical reaction conditions used in glycosylation starting from thioglycosides.[19] Thus, when **3** was treated with benzyl alcohol in the presence of NIS/TfOH,[20] 2-deoxy-2-iodo-α-glycoside (**8a**) was obtained in excellent yield and stereoselectivity (entry 1, Table 2). Cyclohexanol (**7b**), cholesterol (**7c**) and the glucoside **7d** gave **8b**, **8c** and **8d** in α/β-ratios higher than 95:5 with yields of 70% (entries 2, 3, 4, Table 2).

Alcohols **7a**–**d** were also glycosylated with the glycosyl donor **6** in similar conditions (Table 3). The reaction behaved like the reaction with the glycosyl donor **3**, although the stereoselectivities were slightly lower. Thus, the yield was best and the stereoselectivity poorest with the less bulky alcohol **7a** (entry 1, Table 3). For the bulkier alcohols **7b**–**d** glycosylation with **6** provided lower yields than for **7a**, as expected. However, the α/β-stereoselectivity reached values of 10:90.

Furthermore, the conditions for activating thioglycosides are almost the same as those for the cyclization itself. This means that, with an optimun control of the reaction conditions the cyclization and, by consecutive addition of triflic acid and the glycosyl acceptor, the glycosylation can be carried out in a one-pot reaction to afford the 2-deoxy-2-iodo-glycoside.

Table 2 Glycosylation of Alcohols **7a**–**d** with **3**[a]

Entry	Glycosyl donor	Alcohol	Product	Yield (%)	Ratio α/β[b]
1	**3**	**7a**	**8a**	88	94:6
2	**3**	**7b**	**8b**	68	>95:5
3	**3**	**7c**	**8c**	70	>95:5
4	**3**	**7d**	**8d**	70	>95:5

[a] Glycosyl donor (1 mmol), alcohol (2 mmol), NIS (3 mmol), TfOH (0.2 mmol), CH_2Cl_2 (4 mL), –78 to –40 ºC, 2–4 h.
[b] Determined by NMR by integration of anomeric protons.

Table 3 Glycosylation of Alcohols **7a**–**d** with **6**[a]

Entry	Glycosyl donor	Alcohol	Product	Yield (%)	Ratio α/β[b]
1	**6**	**7a**	**9a**	90	14:86
2	**6**	**7b**	**9b**	75	11:89
3	**6**	**7c**	**9c**	72	10:90
4	**6**	**7d**	**9d**	70	10:90

[a] Glycosyl donor (1 mmol), alcohol (2 mmol), NIS (3 mmol), TfOH (0.2 mmol) CH_2Cl_2 (4 mL), –78 to –40 ºC, 2–4 h.
[b] Determined by NMR by integration of anomeric protons.

In this context, the 2-iodo-glycoside (**8c**) was obtained in a 35% yield from **2*E*** in a one-pot reaction by treatment with NIS and then TfOH and cholesterol (**7c**). Additional studies on the refinement and application of this methodology are in progress.

In conclusion, we have developed a procedure for synthesizing phenyl 2-deoxy-2-iodo-1-thio-glycosides. These new glycosyl donors have provided excellent yields and stereoselectivities in the glycosylation of several alcohols. This methodology provides a new access to 2-deoxy-oligosaccarides.

Acknowledgment

Financial support from DGESIC BQU2002-01188 (Ministerio de Ciencia y Tecnología, Spain) is acknowledged. Technical assistance from the Servei de Recursos Cientifics (URV) is acknowledged.

References

(1) (a) Kirschning, A.; Jesberger, M.; Schöning, K.-U. *Synthesis* **2001**, 507. (b) Veyrières, A. In *Carbohydrates in Chemistry and Biology*, Part I, Vol. 1; Ernst, B.; Hart, G. W.; Sinaÿ, P., Eds.; Wiley: Weinheim, **2000**, 367. (c) Marzabadi, H.; Franck, R. W. *Tetrahedron* **2000**, *56*, 8385. (d) Castro-Palomino, J. C.; Schmidt, R. R. *Synlett* **1998**, 501. (e) Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503.

(2) (a) Lemieux, R. U.; Levine, S. *Can. J. Chem.* **1964**, *42*, 1473. (b) Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190. (c) Thiem, J.; Karl, H.; Schwentner, J. *Synthesis* **1978**, 696. (d) Thiem, J.; Klaffke, W. *Top. Curr. Chem.* **1990**, *154*, 285. (e) Danishesky, S.; Bilodeau, M. T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1380.

(3) (a) Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1987**, *28*, 4701. (b) Ramesh, S.; Franck, S. W. *J. Chem. Soc., Chem. Commun.* **1989**, 960. (c) Preuss, R.; Schmidt, R. R. *Synthesis* **1988**, 694. (d) Grewal, G.; Kaila, N.; Franck, R. W. *J. Org. Chem.* **1992**, *57*, 2084.

(4) Perez, M.; Beau, J. M. *Tetrahedron Lett.* **1989**, *30*, 75.

(5) (a) Chong, P. Y.; Roush, W. R. *Org. Lett.* **2002**, *4*, 4523. (b) Kirschning, A.; Jesberger, M.; Schöning, K.-U. *Org. Lett.* **2001**, *53*, 3623. (c) Roush, W. R.; Narayan, S.; Bennett, C. E.; Briner, K. *Org. Lett.* **1999**, *1*, 895. (d) McDonald, F. E.; Reddy, K. S.; Díaz, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4304. (e) Blanchard, N.; Roush, W. R. *Org. Lett.* **1999**, *1*, 895. (f) Kirschning, A. *Eur. J. Org. Chem.* **1998**, *63*, 2267. (g) Roush, W. R.; Sebesta, D. P.; James, R. A. *Tetrahedron* **1997**, *53*, 8837. (h) Roush, W. R.; Sebesta, D. P.; Bennett, C. E. *Tetrahedron* **1997**, *53*, 8825. (i) Roush, W. R.; Bennett, C. E. *J. Am. Chem. Soc.* **1999**, *121*, 3541.

(6) McDonald, F. E.; Reddy, K. S. *Angew. Chem. Int. Ed.* **2001**, *40*, 3653.

(7) Hashimoto, S. I.; Sano, A.; Sakamoto, H.; Nakajima, I.; Yanagiya, Y.; Ikegami, S. *Synlett* **1995**, 1271.

(8) Li, H.; Chan, M.; Zhao, K. *Tetrahedron Lett.* **1997**, *38*, 6143.

(9) Bielawska, H.; Michalska, M. *Tetrahedron Lett.* **1998**, *39*, 9761.

(10) (a) Oscarson, S. In *Carbohydrates in Chemistry and Biology*, Part I, Vol. 1; Ernst, B.; Hart, G. W.; Sinaÿ, P., Eds.; Wiley: Weinheim, **2000**, 93. (b) Garegg, P. J. *Adv. Carbohydr. Chem. Biochem.* **1997**, *52*, 172.

(11) Jaumzens, J.; Hofer, E.; Jesberger, M.; Sourkouni-Argirusi, G.; Kirschning, A. *Angew. Chem. Int. Ed.* **2003**, *42*, 1166.

(12) **Compound 2**: To a solution of 4 mmol of the phosphine oxide in 26 mL of THF at –78 ºC, 4.2 mmol of BuLi were added. The mixture was left to stir at low temperature for 30 min. A solution of 1 mmol of **1** in 2 mL of THF was then added dropwise. The mixture was allowed to warm to r.t. overnight. A sat. solution of NH_4Cl was then added and the olefination product extrated with Et_2O. The combination of ethereal layers was dried with $MgSO_4$ and concentrated. The reaction crude was purified by MPLC (hexane to EtOAc/hexane = 1:3) to render **2** (80% yield) as a mixture of diastereoisomers (*E*/*Z*-ratio = 87:13) as a syrup. Compound **2*E***: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.15 (m, 20 H, aromatics), 6.46 (d, 1 H, $J_{2,1}$ = 15.2 Hz, H-1), 5.87 (dd, 1 H, $J_{1,2}$ = 15.2 Hz, $J_{3,2}$ = 7.6 Hz, H-2), 4.65 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.57 (d, 1 H, *J* = 11.4 Hz, CH_2Ph), 4.52 (d, 1 H, *J* = 11.4 Hz, CH_2Ph), 4.49 (s, 2 H, CH_2Ph), 4.38 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.16 (dd, 1 H, $J_{5,4}$ = 8.0 Hz, $J_{3,4}$ = 3.6 Hz, H-4), 4.00 (m, 1 H, H-5), 3.58 (m, 3 H, H-3, H-6), 2.76 (d, 1 H, *J* = 5.2 Hz, OH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 140.8, 137.7, 137.5, 134.0 (C, aromatics), 130.2–126.0 (CH aromatics, C-1, C-2), 80.4 (C-3), 79.1 (C-4), 74.1, 73.2, 70.7 (CH_2Ph), 70.1 (C-6), 69.9 (C-5). Compound **2*Z***: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.15 (m, 20 H, aromatics), 6.67 (d, 1 H, $J_{2,1}$ = 9.9 Hz, H-1), 6.12 (dd, 1 H, $J_{1,2}$ = 9.9 Hz, $J_{3,2}$ = 9.3 Hz, H-2), 4.88 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.84 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.73 (d, 1 H, *J* = 11.0 Hz, CH_2Ph), 4.68 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.63 (d, 1 H, *J* = 11.5 Hz, CH_2Ph), 4.58 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.21 (m, 1 H, H-5), 3.85 (dd, 1 H, $J_{5,4}$ = 6.9 Hz, $J_{3,4}$ = 3.9 Hz, H-4), 3.77 (m, 3 H, H-3, H-6), 3.12 (d, 1 H, *J* = 5.1 Hz, OH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 140.8, 137.7, 137.5, 134.0 (C, aromatics), 130.2–126.0 (CH aromatics, C-1, C-2), 80.4 (C-3), 79.1 (C-4), 74.1, 73.2, 70.7 (CH_2Ph), 70.1 (C-5), 64.9 (C-6).

(13) **Compound 3**: A 0.175 M suspension of 1.3 mol of KH 30% in dry Et_2O was added dropwise to a 0.085 M solution of **2** (1 mol) in dry Et_2O at 0 ºC, and the resulting mixture was allowed to stir for 30 min until complete formation of the alcoholate. The mixture was cooled to –78 ºC and a 0.43 M solution of iodine (3 mol) in Et_2O was then added. The reaction was allowed to stir at low temperature for 1 h. A solution of $Na_2S_3O_3$ was then added and the reaction product extracted with Et_2O. The combination of the etheral layers was concentrated and the residue purified by radial chromatography to afford **3** (61%) as a yellowish syrup. Compound **3**: $[\alpha]_D^{25}$ +67.8 (*c* 0.0217, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.10 (m, 20 H, aromatics), 5.68 (s, 1 H, H-1), 4.88 (d, 1 H, *J* = 10.4 Hz, CH_2Ph), 4.87 (d, 1 H, $J_{3,2}$ = 3.6 Hz, H-2), 4.72 (d, 1 H, *J* = 11.2 Hz, CH_2Ph), 4.70 (d, 1 H, *J* = 11.6 Hz, CH_2Ph), 4.54 (d, 1 H, *J* = 11.2 Hz, CH_2Ph), 4.52 (d, 1 H, *J* = 10.4 Hz, CH_2Ph), 4.48 (d, 1 H, *J* = 11.6 Hz, CH_2Ph), 4.41 (ddd, 1 H, $J_{4,5}$ = 8.8 Hz, $J_{6a,5}$ = 4.4 Hz, $J_{6b,5}$ = 1.6 Hz, H-5), 3.99 (dd, 1 H, $J_{5,4}$ = 8.8 Hz, $J_{3,4}$ = 8.4 Hz, H-4), 3.85 (dd, 1 H, $J_{6b,6a}$ = 10.8 Hz, $J_{5,6a}$ = 4.4 Hz, H-6a), 3.73 (dd, 1 H, $J_{6a,6b}$ = 10.8 Hz, $J_{5,6b}$ = 1.6 Hz, H-6b), 3.10 (dd, 1 H, $J_{4,3}$ = 8.4 Hz, $J_{2,3}$ = 3.6 Hz, H-3). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 138.0, 137.2, 133.9 (C, aromatics), 132.0–127.4 (CH, aromatics), 89.6 (C-1), 77.5 (C-3), 76.2 (C-4), 75.3 (CH_2Ph), 73.3 (CH_2Ph, C-5), 71.0 (CH_2Ph), 68.7 (C-6), 34.8 (C-2).

(14) (a) Landais, Y.; Panchenault, D. *Synlett* **1995**, 1191.
(b) Bravo, F.; Castillón, S. *Eur. J. Org. Chem.* **2001**, 507.

(15) Suzuki, K.; Mukaiyama, T. *Chem. Lett.* **1982**, 1525.

(16) **Compound 5**: To a solution of 4 mmol of the phosphine oxide in 26 mL of THF at –78 ºC, 4.2 mmol of BuLi were added. The mixture was left to stir at low temperature for 30 min. A solution of 1 mmol of the **4** in 2 mL of THF was then added dropwise. The mixture was allowed to warm to r.t. first and then heated to reflux. A sat. solution of NH_4Cl was then added and the olefination product extrated with Et_2O. The combination of ethereal layers was dried with $MgSO_4$ and concentrated. The reaction crude was purified by MPLC (hexane to EtOAc/hexane = 1:3) to render **5** (72% yield) as a mixture of diastereoisomers (*E*/*Z*-ratio = 80:20) as a syrup. Compound **5*E***: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.25 (m, 20 H, aromatics), 6.54 (d, 1 H, $J_{2,1}$ = 15.1 Hz, H-1), 5.94 (dd, 1 H, $J_{1,2}$ = 15.1 Hz, $J_{3,2}$ = 8.4 Hz, H-2), 4.75 (d, 1 H, *J* = 10.8 Hz, CH_2Ph), 4.67 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.56 (d, 1 H, *J* = 10.8 Hz, CH_2Ph), 4.51 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.48 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.40 (d, 1 H, *J* = 12.0 Hz, CH_2Ph), 4.22 (dd, 1 H, $J_{2,3}$ = 8.4 Hz, $J_{4,3}$ = 4.4 Hz, H-3), 3.82 (m, 1 H, H-5), 3.69 (dd, 1 H, $J_{5,4}$ = 7.6 Hz, $J_{3,4}$ = 4.4 Hz, H-4), 3.61 (m, 2 H, H-6), 2.78 (bs, 1 H, OH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 138.2, 138.1, 137.8, 134.6 (C, aromatics), 129.1–126.9 (CH, aromatics), 128.8 (C-1), 128.4 (C-2), 81.3 (C-3), 80.8 (C-4), 74.2, 73.4 (CH_2Ph), 70.9 (C-6), 70.8 (C-5), 70.5 (CH_2Ph). Compound **5*Z***: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.25 (m, 20 H, aromatics), 6.62 (d, 1 H, J_{21} = 9.6 Hz, H-1), 6.00 (pseudo t, 1 H, J_{12} = J_{32} = 9.6 Hz, H-2), 4.89–4.35 (m, 6 H, CH_2Ph), 3.91 (m, 1 H, H-5), 3.83 (dd, 1 H, J_{54} = 7.6 Hz, J_{34} = 3.4 Hz, H-4), 3.71 (dd, 1 H, J_{23} = 9.6 Hz, J_{43} = 3.4 Hz, H-3), 3.67 (m, 2 H, H-6), 2.85 (bs, 1 H, OH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 138.1, 137.8, 135.5, 134.4 (C, aromatics), 129.8–126.5 (CH, aromatics, C-1, C-2), 80.9 (C-3), 77.1 (C-4), 74.1, 73.3 (CH_2Ph), 71.0, 70.8, 70.5 (C-5, C-6, CH_2Ph).

(17) Freeman, F.; Robarge, K. D. *Carbohydr. Res.* **1986**, *154*, 270.

(18) **Compound 6**: To a 0.5 M solution of **5** (0.084 g, 0.16 mmol) (*E*/*Z* = 2:3) in CH_3CN, $NaHCO_3$ (0.48 mmol) was added. The mixture was cooled to 0 ºC and left to stir at this temperature for 5 min. NIS (0.48 mol) was then added and the reaction mixture was allowed to warm to r.t. and stirred for 8 h. The mixture was diluted with Et_2O and washed with a sat. solution of $Na_2S_3O_3$. The combined aqueous layer was extracted with Et_2O. The combination of ethereal layers was dried with $MgSO_4$ and concentrated. The residue was purified by radial chromatography to afford 0.060 g (58% yield) as a β/α mixture = 2:3. Compound **6β**: $[\alpha]_D^{25}$ +16.0 (*c* 0.7708, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.20 (m, 20 H, aromatics), 5.11 (d, 1 H, $J_{2,1}$ = 10.6 Hz, H-1), 4.92 (d, 1 H, *J* = 10.4 Hz, CH_2Ph), 4.75 (d, 1 H, *J* = 10.4 Hz, CH_2Ph), 4.62 (d, 1 H, *J* = 11.4 Hz, CH_2Ph), 4.60 (d, 1 H, *J* = 12.4 Hz, CH_2Ph), 4.52 (d, 1 H, *J* = 11.4 Hz, CH_2Ph), 4.51 (d, 1 H, *J* = 12.4 Hz, CH_2Ph), 4.18 (m, 1 H, H-3, H-5), 4.02 (dd, 1 H, $J_{1,2}$ = 10.4 Hz, $J_{3,2}$ = 2.4 Hz, H-2), 3.72 (m, 1 H, H-4, H-6a, H-6b). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 138.4, 138.1, 137.6 (C, aromatics), 133.2 (CH, aromatic), 131.7 (C, aromatic), 128.7–127.4 (CH, aromatics), 84.3 (C-1), 78.7 (C-3), 76.1 (C-4), 75.9 (C-5), 75.7, 73.3, 72.2 (CH_2Ph), 69.3 (C-6), 31.8 (C-2). Compound **6α** (spectroscopical data extracted from the α/β-mixture spectrum): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.20 (m, 20 H, aromatics), 5.32 (d, 1 H, $J_{2,1}$ = 5.4 Hz, H-1), 4.91 (d, 1 H, *J* = 11.6 Hz, CH_2Ph), 4.79 (d, 1 H, *J* = 10.8 Hz, CH_2Ph), 4.68 (ddd, 1 H, $J_{4,5}$ = 10.0 Hz, $J_{6a,5}$ = 2.8 Hz, $J_{6b,5}$ = 2.4 Hz, H-5), 4.57 (dd, $J_{1,2}$ = 5.6 Hz, $J_{3,2}$ = 2.4 Hz, H-2), 4.52 (d, 2 H, *J* = 10.4 Hz, CH_2Ph), 4.42 (d, 1 H, *J* = 11.2 Hz, CH_2Ph), 4.40 (d, 1 H, *J* = 12.4 Hz, CH_2Ph), 4.09 (dd, 1 H, $J_{2,3}$ = 2.4 Hz, $J_{4,3}$ = 2.4 Hz, H-3), 3.77 (m, 2 H, H-4, H-6a), 3.62 (dd, 1 H, $J_{6a,6b}$ = 10.8 Hz, $J_{5,6b}$ = 2.4 Hz, H-6b). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 131.4–126.8 (C, CH, aromatics), 90.0 (C-1), 78.1, 76.3, 75.6, 73.5, 72.0, 68.8, 67.7 (C-3, C-4, C-5, C-6, 3 × CH_2Ph), 27.0 (C-2).

(19) **General Procedure of Glycosylation**: A solution of the glycosyl donor (1 mmol) and the glycosyl acceptor (2 mmol) in CH_2Cl_2 (4 mL) were allowed to stir with 4 Å molecular sieves for 2 h. The mixture was then cooled to –78 ºC, and NIS (3 mmol) and TfOH (0.2 mmol) were added. The mixture was allowed to warm to –40 ºC and stirred for 2–4 h. The reaction mixture was then diluted with CH_2Cl_2 and washed with a solution of $Na_2S_3O_3$. The ethereal layer was dried with Na_2SO_4 and concentrated. The residue was then purified by radial chromatography.

(20) Veeneman, G. H.; van Leeuwen, S. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 1331.