$CDCl_3$) δ 5.96 (d, J = 2.1 Hz, 1 H), 5.73 (dq, J = 2.1, 1.7 Hz, 1 H), 2.92 (d, J = 14.9 Hz, 1 H), 2.60 (d, J = 14.9 Hz, 1 H), 2.42 (d, J = 13.6 Hz, 1 H), 2.25 (d, J = 13.6 Hz, 1 H), 2.10 (s, 1 H), 1.87 (d, J = 1.7 Hz, 3 H), 1.73 (s, 3 H), 1.56 (s, 3 H), 1.49 (s, 3 H), 1.41 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) 203.3, 184.0, 183.4, 147.5, 145.5, 137.0, 121.3, 111.8, 106.7, 97.4, 84.6, 81.4, 50.4, 41.9, 32.4, 29.4, 29.2, 26.9, 19.8, 6.1 ppm; HRMS m/z (M^+ + H) 327.1608 (calcd for $C_{20}H_{23}O_4$, 327.1596).

(+)-Hydroxyjatrophone A (2). The C(5,6)-cis-olefin **27a** (3.8 mg, 0.012) was semihydrogenated ($Pd/BaSO_4$) and isomerized (KI, HOAc) as described for (+)-hydroxyjatrophone B (3). The crude product was purified by preparative thin-layer chromatography (500 μm; 3 × 20 cm; EtOAc:hexanes; 3:1) to provide (+)-hydroxyjatrophone A (2) as a colorless oil (1.6 mg, 42%): ^1H NMR (500 MHz, $CDCl_3$) δ 6.45 (d, J = 16.2 Hz, 1 H), 6.02 (d, J = 16.2 Hz, 1 H), 5.86 (d, J = 2.0 Hz, 1 H), 5.81 (dq, J = 2.0, 1.7 Hz, 1 H), 2.88 (d, J = 15.1 Hz, 1 H), 2.47 (dd, J = 15.1, 0.6 Hz, 1 H), 2.38 (d, J = 13.8 Hz, 1 H), 2.17 (d, J = 13.8 Hz, 1 H), 1.91 (d, J = 1.7 Hz, 3 H), 1.90 (s, 1 H), 1.74 (d, J = 0.6 Hz, 3 H), 1.46 (s, 3 H), 1.39 (s, 3 H), 1.25 (s, 3 H); HRMS m/z (M^+ + H) 328.1673 (calcd for $C_{20}H_{25}O_4$, 328.1674); $[\alpha]_D$ +277° (c 0.100, $CHCl_3$); TLC R_f 0.30 (Et_2O), 0.35 (EtOAc:hexanes, 3:1), 0.24 ($CHCl_3$:acetone, 4:1), 0.24 (hexanes:acetone, 2:1), 0.36 (CH_2Cl_2:EtOH, 9:1), 0.31 (benzene, EtOH, 19:1).

Synthetic (+)-hydroxyjatrophone A (2) was in all respects (500 MHz ^1H NMR, HRMS, optical rotation and TLC mobility in six solvent systems) identical with an authentic sample of the natural product.[1]

Acknowledgment. Support for this work was provided by the National Institutes of Health (National Cancer Institute) through Grant 22807 and a postdoctoral fellowship to A.T.L. We also thank Drs. G. Furst, J. Dykins, and P. Carroll, Directors of the University of Pennsylvania Spectroscopic Facilities, for aid in obtaining respectively the high-field NMR, high-resolution mass spectral and X-ray crystallographic data.

On the Controlled Oxidative Coupling of Glycals: A New Strategy for the Rapid Assembly of Oligosaccharides

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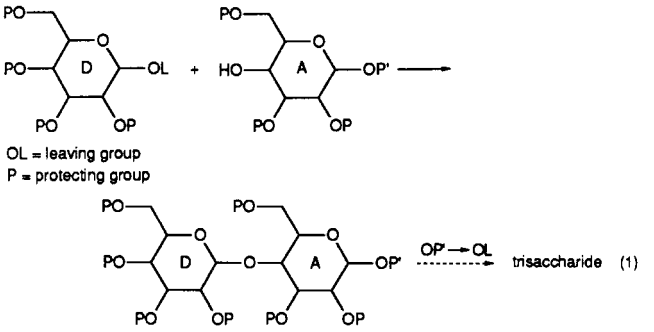
Contribution from the Department of Chemistry, Yale University, New Haven, Connecticut 06511. *Received November 9, 1988. Revised Manuscript Received February 24, 1989*

Abstract: Controlled oxidative coupling of various glucal triethers with glucals containing a single hydroxy group (either at C4 or C3) and acyloxy groups at the other two positions has been demonstrated. The process is readily reiterated. A concise route to α-linked oligosaccharides has been developed.

The ability to couple carbohydrate entities to produce glycosides or higher oligomers is one of the important goals of synthetic organic chemistry.[1] The roles of oligosaccharides as energy storage sources, as structural building blocks, as modifiers of protein folding, as immunological determinants, and as apparent accessories (conjugating agents) to various steroidal hormones and antibiotics are well-known.[2]

Considerable progress has been achieved in the fashioning of the glycosidic bond and in the synthesis of various oligosaccharide patterns.[1] The application of enzymatic techniques at the preparative level has brought with it much progress.[3] The development of more sophisticated blocking and deblocking strategies in glycosyl acceptors, and more efficacious anomeric activating groups for glycosyl donors, have each brought forth improvements in the synthesis of oligosaccharides.[4] While cognizant of these encouraging developments, we have in the course of several synthetic ventures perceived a need for fresh departures in this field, particularly as regards operational conciseness.

Virtually all current glycosylations conserve the oxidation level of both coupling components.[1] Consider the merger of two hexose residues as shown in eq 1. Typically the glycosyl acceptor (A)



enters the reaction with a single free hydroxyl group and four OP appendages (P = protecting groups). The donor D must be equipped with a displaceable group at its anomeric carbon and is presented for coupling with four masked hydroxylic centers. If the AD disaccharide is eventually to function as a glycosyl donor, for elongation to an oligosaccharide, its reducing end must be furnished with glycosyl-donating (i.e., a leaving group) capabilities. Provision for this, in the form of a unique blocking group at the anomeric center of the original A acceptor, was necessary (see unique P′ function in A, which is suitable for conversion to the OL group of AD in eq 1).

The experiments described herein were organized around a new idea involving oxidative coupling of glycals (see eq 2). Manipulations at the anomeric centers are unnecessary since coupling is actuated by attack of the oxidant at the donor[5] glycal. The free hydroxyl function in the acceptor[5] glycal must be differentiated from two (rather than four) other alcohols that must be

(1) For two recent reviews of glycosylation, see: (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. (b) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

(2) For an entry to the biological roles of various carbohydrates, see: Kennedy, J. F.; White, C. A. *Bioactive Carbohydrates in Chemistry, Biochemistry and Biology*; Halsted Press: New York, 1983.

(3) For leading references to enzyme-catalyzed carbohydrate synthesis, see: Wong, C.-H.; Drueckhammer, D. G.; Durrwachter, J. R.; Lacher, B.; Chauvet, C. J.; Wang, Y.-F.; Sweers, H. M.; Smith, G. L.; Yang, L. J.-S.; Hennen, W. J. In "*Trends in Synthetic Carbohydrate Chemistry*", Horton, D., Hawkins, L. D., McGarvey, G. J., Eds.; ACS Symposium *Series 386*; American Chemical Society: Washington, DC, 1989; Chapter 18.

(4) See ref 1, as well as: El Khadem, H. S. *Carbohydrate Chemistry: Monosaccharides and Their Oligomers*; Academic Press: San Diego, CA, 1988, Chapter 7.

(5) In this paper, the donor glycal will be that hexose which supplies what becomes the anomeric carbon of the new glycosidic bond. The acceptor glycal will be that hexose which is incorporated into the new glycoside via its free hydroxyl moiety.

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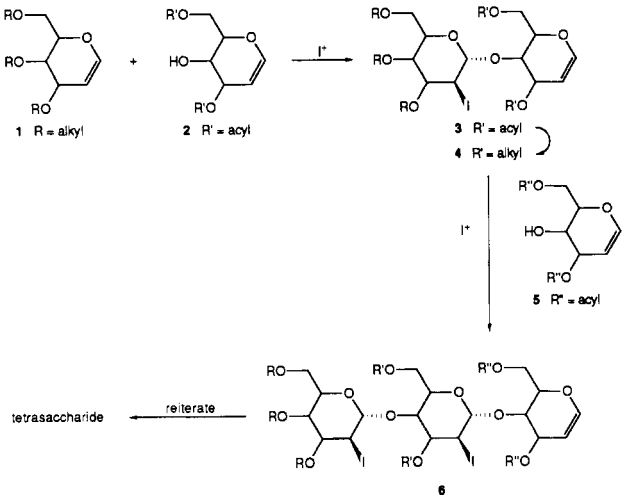
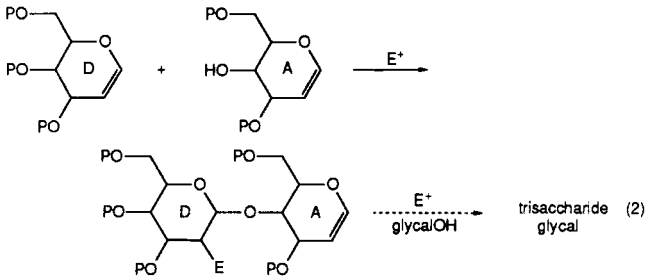
Scheme I



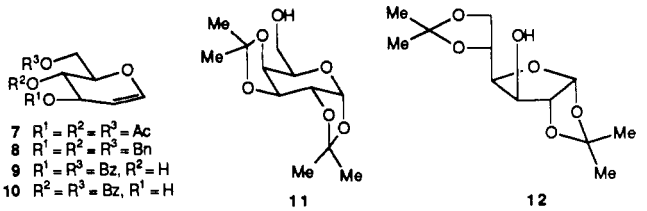
protected. Moreover, the next reiteration is straightforward since the AD disaccharide in eq 2 is itself a glycal, ready for oxidative actuation as before.



For eq 2 to be viable, there must be available a menu of stereospecific oxidative coupling reactions, wherein E is readily translatable to a relevant group (O•, N•, or H). Moreover, if the coupling is to occur via a transient intermediate (some version of an onium species), rather than through an isolable compound, it is crucial that the two glycals assume strictly defined glycosyl donor and acceptor roles. The reaction we first considered for oxidative coupling was haloetherification.[6] The oxidatively triggered addition of alcohols to glycals via presumed 1,2-iodonium ion formation was known.[7] We took up the question whether the nucleophile (i.e., the glycosyl acceptor) could itself be a glycal. It was soon established that the order of presentation of two similar glycals (ca. **7** and **9**) to the oxidizing agent was of no useful consequence. A complex mixture of products was obtained.

Of course only that glycal which bears a free hydroxyl group can be the acceptor (A) component. In principle, however, either glycal can function as a donor. Fortunately, the glycosyl-donating tendencies of the OH-bearing glycal can be suppressed relative to the glycal that lacks a free hydroxyl group. *This is accomplished when the intended acceptor containing the free* OH *group is entered with two acyl protecting groups while the intended donor (no OH groups) is substituted with three ether functions.*[8] When a 1:1 mixture of two such glycals is presented to the oxidizing agent, the disaccharide is assembled with strict regiochemical and stereochemical control (see **1** + **2** → **3c**; Scheme I). To reiterate the scheme, with another glycal, the two ester groups of **3** are cleaved and the hydroxyl groups are reprotected as ethers (see **3** → **4**). The AD glycal **4** is now a glycosyl donor[5] with respect to diacyloxymonohydroxyglycal **5** (see **4** + **5** → **6**). In this way a trisaccharide is readily produced. The coupling reactions, presumably involving a 1,2-iodonium ion intermediate, occur in a clean 1,2-diaxial fashion to afford only the α-glycoside. The process can be reiterated.

Glycals **7**–**10**,[9] readily derivable via D-glucal, were employed in this investigation. As terminating sugars we used diacetone galactose and diacetone glucose derivatives **11** and **12**. Scheme



II delineates the synthesis of triaccharides **14**–**16** and **18**. The exclusive formation of bicyclic glycal **13** from the iodoglycosylation of **8** + **9** is illustrative of the power of the method. No other glycals or stereoisomers of **13** were detected. Oxidative coupling of **13**, this time with "terminating" hexoses **11** and **12** could be achieved in the presence of the benzoyloxy groups. Of course in these cases, **13** can only be a donor and **11** (or **12**) can only be the acceptor. Compounds **14** and **16**, respectively, were obtained in clean stereospecific reactions. For illustrative purposes it was demonstrated that **14** could be doubly deiodinated to provide trisaccharide **15**.

It would be expected that the electron-donating power of a glycal bearing an acyloxy group at the 3-position would be particularly suppressed relative to one in which there is an alkoxy function at this same center. It was important to establish whether the free alcohol of the intended glycosyl acceptor can be situated at the 3-position, i.e., whether acyloxyl substitution at **4** and **6** would suffice to direct the oxidizing agent to the triether glycal. For this purpose glycal **10** proved to be particularly instructive. In the event, iodinative coupling of a mixture of compounds **10** and **8** cleanly provided the "AD glycal" **17**. Again no evidence for the formation of products from an alternative coupling mode, or of stereoisomers of **17**, could be gleaned. As above, reiteration of the scheme with hexose **11** as the terminating group was possible without modification of the benzoyloxy groups. Trisaccharide **18** was produced stereospecifically in 67% yield.

Scheme III describes how this methodology was readily applied to the synthesis of tetrasaccharides. Starting with disaccharide **13**, and following the logic set forth in Scheme I, it was first necessary to convert the diester arrangement in the glycal segment of **13** to a diether. The resultant product could be relied upon to function strictly as a glycosyl donor in the oxidative coupling with respect to a diacyloxymonohydroxyglycal. Accordingly, compound **13** was converted, as shown, to **19**. Glycal **19** was subjected to "I^+"-mediated coupling with glycal **9** to afford **20**. As above (cf. **13** → **14** and **13** → **16**), termination of the sequence with nonglycal **11** occurred smoothly and stereospecifically to provide **21**. By the same logic and protocols, the previously described disaccharide **17** was converted to tetrasaccharide **24** via the agency of bis(ether) **22** and trisaccharide **23**.

Admittedly, the actual accomplishments described here in and of themselves address limited terrain in oligosaccharide synthesis, i.e., the 2-deoxy axially-linked glycoside. To go beyond these findings to more generally encountered problems would require tactics for either (i) displacement of the 2-iodoglycosides or (ii) trans-diaxial introduction of other E^+ electrophiles (see eq 2) that are translatable to C2 oxygen or nitrogen functionalities. Work along these lines is moving forward.

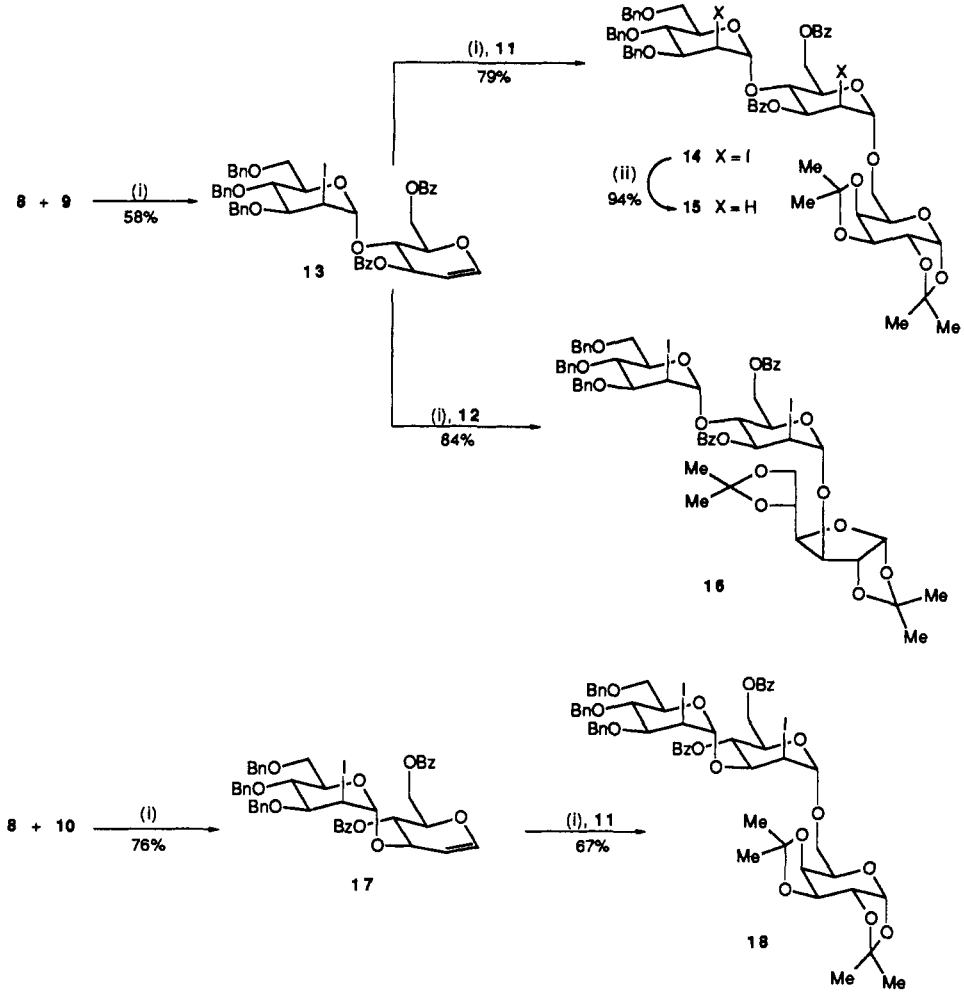
(6) Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190. Lemieux, R. U.; Fraser-Reid, B. *Can. J. Chem.* **1964**, *42*, 532; **1964**, *42*, 539; **1965**, *43*, 1460.

(7) Thiem, J.; Karl, H.; Schwentner, J. *Synthesis* **1978**, 696. This process has been successfully applied to a large variety of glycals and alcohol glycosyl acceptors. For leading references, see: Thiem, J. In ref 3, Chapter 8.

(8) The concept of arranging the nature of the protecting groups to control the susceptibility of *n*-pentenyl glycosides toward electrophilic attack has recently been described. Mootoo, D. R.; Konradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 5583. This methodology has been applied to a very interesting new construction of oligosaccharides.

(9) 3,4,6-Tri-*O*-benzyl-D-glucal (**8**) and 3,6-di-*O*-benzoyl-D-glucal (**9**) were prepared from commercially available 3,4,6-tri-*O*-acetyl-D-glucal (**7**) according to: Blackburne, I. D.; Fredericks, P. M.; Guthrie, R. D. *Aust. J. Chem.* **1976**, *29*, 381. 4,6-Di-*O*-benzoyl-D-glucal (**10**) was prepared from 6-*O*-benzoyl-D-glucal (see reference) by a three-step sequence: (i) (TBS)Cl, imidazole, DMF (87%); (ii) PhCOCl, Et_3N, DMAP, CH_2Cl_2 (99%); (iii) $^nBu_4NF$, THF, 0 °C (86%).

Scheme II[a]



[a] (i) (*sym*-collidine)$_2$I$^+$ClO$_4^-$, CH_2Cl_2, 4A molecular sieves (powdered); (ii) Ph_3SnH, AIBN, PhH.

While mindful of what remains to be accomplished, we nevertheless point out that the oligosaccharide ensembles described here (axially-linked 2-deoxy systems) are in fact encountered in a variety of antibiotics of biological importance.[10]

Also required is a comparable strategy for synthesizing oligosaccharide assemblies with β linkages. Current research in our laboratory is directed to this goal, and considerable progress has already been attained. The possibility of a semiautomated synthesis of oligosaccharides, in the event of a favorable disposition of this research, has not escaped our attention.

Experimental Section

General Procedure for I(*sym*-collidine)$_2$ClO$_4$-Mediated Coupling. To a solution of glycal and alcohol (1.1 equiv) in dry CH_2Cl_2 (0.04 M in glycal) was added powdered 4A molecular sieves (approximately equal weight to that of glycal). The resulting mixture was stirred at room temperature for 30 min and then I(*sym*-collidine)$_2$ClO$_4$[6] was added as a solid. When TLC analysis indicated completion of the reaction (typically 1–2 h), the mixture was filtered, washing with CH_2Cl_2. The resulting filtrate was washed with 10% aqueous $Na_2S_2O_3$, dried (MgSO$_4$), and concentrated. Chromatography of the residual oil on silica gel (hexanes–ethyl acetate, 4:1–5:1 v/v) provided the coupled product.

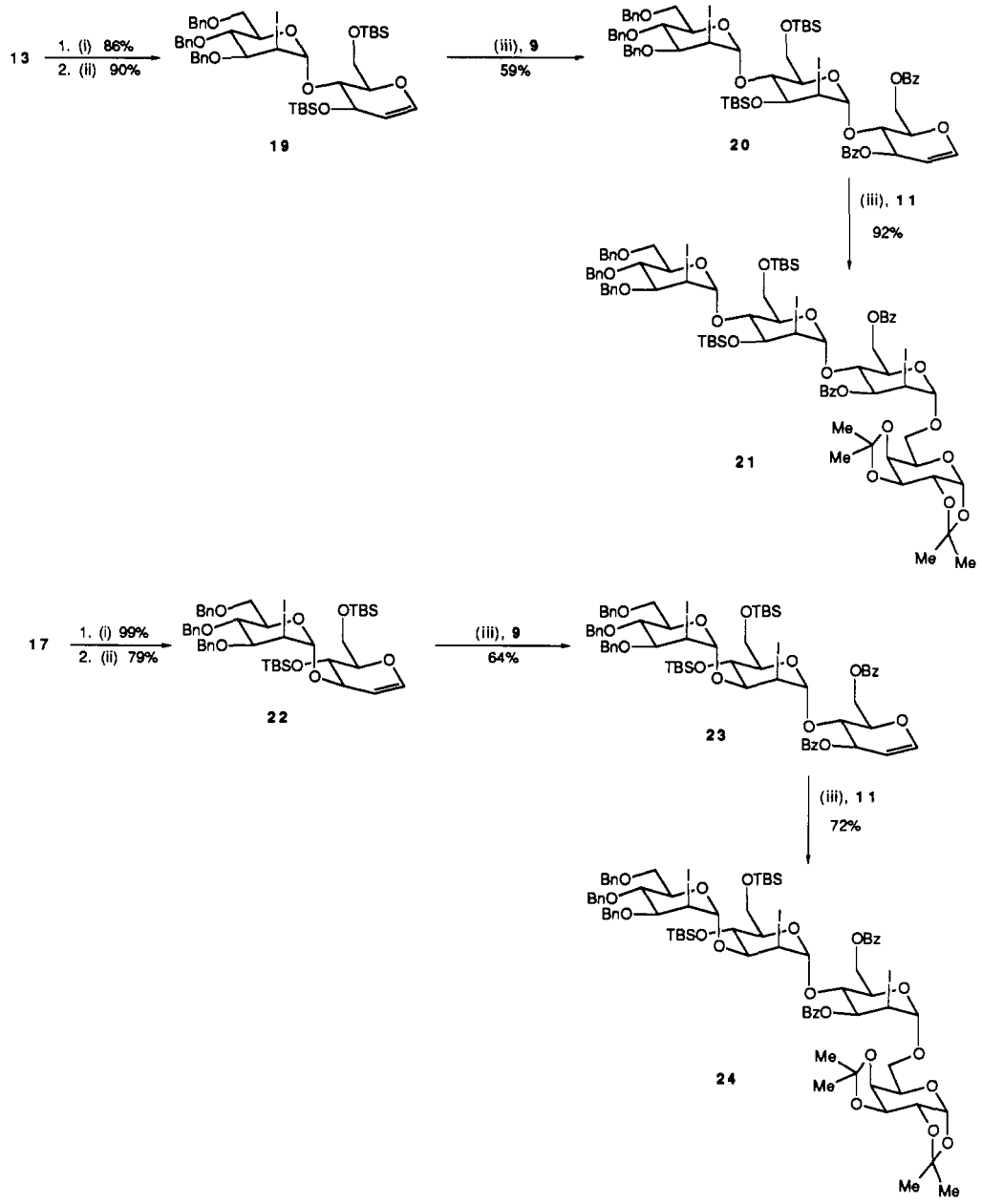
Glycal 13. 3,4,6-Tri-*O*-benzyl-D-glucal (**8**; 563.8 mg) and 3,6-di-*O*-benzoyl-D-glucal (**9**; 527.7 mg) gave 704.1 mg (58%) of **13** as a colorless oil: $[\alpha]^{23}_D$ −18.5° (c = 0.48, $CHCl_3$); IR ($CHCl_3$) 3010, 1717, 1645, 1450, 1270, 1105 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.30 (dd, 1 H, J = 3.6, 8.4 Hz), 3.62 (d, 1 H, J = 10.9 Hz), 3.77 (br d, 1 H, J = 10.9 Hz), 3.96 (m, 2 H), 4.31–4.70 (10 H), 4.82 (d, 1 H, J = 10.7 Hz), 5.00 (dd, 1 H, J = 3.7, 6.4 Hz), 5.53 (t, 1 H, J = 3.7 Hz), 5.65 (d, 1 H, J = 1.4 Hz), 6.53 (dd, 1 H, J = 1.5, 6.4 Hz), 7.14–7.61 (21 H), 8.01–8.06 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 32.7, 62.3, 68.7, 68.8, 71.2, 72.9, 73.4, 74.5, 75.0, 75.8, 76.8, 98.3, 102.6, 127.4, 127.5, 127.6, 127.8, 128.0, 128.2, 128.3, 128.4, 128.6, 129.5, 129.7, 133.0, 133.4, 137.6, 138.2, 138.4, 145.9, 165.9, 166.0; FAB-MS, m/e 895 (M − H)$^+$. Anal. Calcd for $C_{47}H_{45}IO_{10}$: C, 62.95; H, 5.06. Found: C, 63.20; H, 4.87.

Trisaccharide 14. Glycal **13** (149.8 mg) and 1,2,3,4-di-*O*-isopropylidene-D-galactopyranose (**11**; 47.8 mg) gave 169.8 mg (79%) of **14** as a colorless oil: $[\alpha]^{23}_D$ +21.8° (c = 0.74, $CHCl_3$); IR ($CHCl_3$) 3020, 2930, 1720, 1270, 1075 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.30, 1.34, 1.43, 1.55 (s each, 3 H each), 3.15 (dd, 1 H, J = 3.9, 8.0 Hz), 3.54 (d, 1 H, J = 10.0 Hz), 3.71–4.01 (6 H), 4.19–4.76 (15 H), 4.91 (dd, 1 H, J = 4.2, 9.0 Hz), 5.28 (s, 1 H), 5.53 (d, 1 H, J = 5.0 Hz), 5.61 (s, 1 H), 7.08–7.12 (m, 2 H), 7.21–7.34 (12 H), 7.41–7.65 (7 H), 8.12–8.18 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 24.6, 25.0, 26.0, 26.2, 30.4, 32.5, 63.4, 66.3, 67.3, 68.6, 70.2, 70.8, 70.9, 71.1, 72.2, 73.5, 73.7, 74.9, 75.6, 75.7, 76.8, 96.4, 101.3, 104.0, 108.7, 109.6, 127.3, 127.5, 127.6, 127.8, 128.0, 128.2, 128.3, 128.4, 128.8, 129.1, 130.0, 130.1, 130.2, 132.9, 133.8, 137.7, 138.4, 138.6, 165.2, 166.2; FAB-MS, m/e 1283 (M + H)$^+$. Anal. Calcd for $C_{59}H_{64}I_2O_{16}$: C, 55.24; H, 5.03. Found: C, 55.04; H, 5.04.

Trisaccharide 15. A solution of **14** (71.6 mg, 5.6 × 10^{-5} mol), triphenyltin hydride (58.8 mg, 3 equiv), and a catalytic amount of AIBN in benzene (3 mL) was refluxed for 15 min and then concentrated. Chromatography of the residual oil on silica gel (hexanes followed by hexanes–ethyl acetate, 2:1 v/v) provided **15** (54.1 mg, 94%) as a foam: $[\alpha]^{23}_D$ +38.7° (c = 0.63, $CHCl_3$); IR ($CHCl_3$) 3020, 1720, 1275, 1115, 1075 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.37, 1.38, 1.47, 1.60 (s each, 3 H each), 1.5 (1 H buried under Me signals), 1.92 (dt, 1 H, J = 3.6, 12.4 Hz), 2.09 (dd, 1 H, J = 4.8, 12.8 Hz), 2.47 (dd, 1 H, J = 5.2, 12.7 Hz), 3.50–4.75 (20 H), 4.83 (d, 1 H, J = 10.9 Hz), 5.06 (d, 1 H, J = 2.5 Hz), 5.40 (d, 1 H, J = 2.5 Hz), 5.57 (d, 1 H, J = 4.9 Hz), 5.62 (ddd, 1 H, J = 5.1, 8.7, 11.9 Hz), 7.10–7.70 (21 H), 8.13 (m, 4 H); ^{13}C NMR

(10) (a) Crooke, S. T.; Reich, S. D., Eds. *Anthracyclines—Current Status and Development*; Academic Press: New York, 1980. (b) El Khadem, H. S. *Anthracycline Antibiotics*; Academic Press: New York, 1982. (c) Arcamone, F. *Doxorubicin—Anticancer Antibiotics*; Academic Press: New York, 1981. (d) Bieber, L. W.; Da Silva Filho, A. A.; De Mello, J. F.; De Lima, O. G.; Do Nascimento, M. S.; Veith, H. J.; Von der Saal, H. *J. Antibiot.* **1987**, *40*, 1335.

Scheme III[a]



[a] (i) NaOH, MeOH; (ii) (TBS)Cl, imidazole, DMF; (iii) (*sym*-collidine)$_2$I$^+$ClO$_4^-$, CH_2Cl_2, 4A molecular sieves (powdered).

(63 MHz, $CDCl_3$) δ 24.6, 25.0, 26.0, 26.2, 35.1, 64.1, 66.1, 66.2, 68.6, 69.1, 70.8, 71.1, 71.7, 72.2, 72.9, 73.5, 74.6, 76.3, 77.9, 96.4, 97.0, 99.6, 108.6, 109.3, 127.4, 127.6, 127.8, 128.2, 128.4, 128.6, 129.6, 129.8, 130.0, 130.3, 132.8, 133.4, 138.3, 138.6, 165.7, 166.3; FAB-MS, *m/e* 1031 (M + H)$^+$. Anal. Calcd for $C_{59}H_{66}O_{16}$: C, 68.72; H, 6.45. Found: C, 68.61; H, 6.58.

Trisaccharide 16. Glycal **13** (140.0 mg) and 1,2,4,6-di-*O*-isopropylidene-D-glucofuranose (**12**; 44.7 mg) gave 167.9 mg (84%) of **16** as a colorless oil: $[\alpha]^{23}_D$ + 28.8° (*c* = 0.51, $CHCl_3$); IR ($CHCl_3$) 3010, 2920, 1720, 1265, 1095 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.26, 1.36, 1.40, 1.49 (s each, 3 H each), 3.18 (dd, 1 H, *J* = 3.9, 7.7 Hz), 3.62 (d, 1 H, *J* = 10.8 Hz), 3.76 (br d, 1 H, *J* = 10.3 Hz), 3.92–4.77 (21 H), 4.84 (dd, 1 H, *J* = 4.2, 8.9 Hz), 5.54 (s, 1 H), 5.59 (d, 1 H, *J* = 1.6 Hz), 5.95 (d, 1 H, *J* = 3.6 Hz), 7.09–7.14 (m, 2 H), 7.19–7.65 (19 H), 8.12–8.16 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 25.4, 26.2, 26.7, 26.9, 29.1, 32.0, 63.7, 65.8, 68.1, 68.5, 70.9, 71.8, 72.6, 73.5, 73.6, 74.9, 75.6, 75.9, 76.7, 81.6, 81.9, 84.1, 102.4, 104.2, 105.4, 109.5, 112.1, 127.4, 127.7, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 128.8, 128.9, 130.0, 130.1, 133.0, 133.9, 137.6, 138.3, 138.4, 165.2, 166.2. Anal. Calcd for $C_{59}H_{64}I_2O_{16}$: C, 55.24; H, 5.03. Found: C, 55.10; H, 5.05.

Glycal 17. 3,4,6-Tri-*O*-benzyl-D-glucal (**8**; 69.9 mg) and 4,6-di-*O*-benzoyl-D-glucal (**10**; 65.4 mg) gave 114.4 mg (76%) of **17** as a colorless oil: $[\alpha]^{22}_D$ +0.53° (*c* = 0.76, $CHCl_3$); IR ($CHCl_3$) 3020, 1720, 1270, 1115 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.30 (dd, 1 H, *J* = 4.1, 8.5 Hz), 3.73–4.08 (4 H), 4.30–4.72 (10 H), 4.86 (d, 1 H, *J* = 10.7 Hz), 5.01 (dd, 1 H, *J* = 3.8, 6.2 Hz), 5.47–5.52 (m, 2 H), 6.46 (d, 1 H, *J* = 6.2 Hz), 7.17–7.68 (21 H), 8.02–8.10 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 32.9, 61.9, 68.9, 69.1, 70.6, 71.0, 72.8, 73.4, 73.6, 75.1, 75.9, 76.7, 100.3, 102.0, 127.4, 127.5, 127.6, 127.8, 128.0, 128.1, 128.2, 128.3, 128.46, 128.52, 129.2, 129.6, 129.7, 129.8, 133.2, 133.5, 137.6, 138.2, 138.3, 144.6, 165.3, 166.0; FAB-MS, *m/e* 897 (M + H)$^+$. Anal. Calcd for $C_{47}H_{45}IO_{10}$: C, 62.95; H, 5.06. Found: C, 63.10; H, 5.07.

Trisaccharide 18. Glycal **17** (70.0 mg) and 1,2,3,4-di-*O*-isopropylidene-D-galactopyranose (**11**; 22.0 mg) gave 68.5 mg (67%) of **18** as a colorless oil: $[\alpha]^{22}_D$ −6.8° (*c* = 0.47, $CHCl_3$); IR ($CHCl_3$) 3015, 1725, 1210 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.32, 1.34, 1.41, 1.58 (s each, 3 H each), 3.19 (dd, 1 H, *J* = 4.0, 8.3 Hz), 3.65–3.87 (6 H), 3.96 (br t, 1 H, *J* = 6.0 Hz), 4.09–4.80 (12 H), 5.22 (s, 1 H), 5.43 (s, 1 H), 5.51 (d, 1 H, *J* = 5.0 Hz), 5.76 (t, 1 H, *J* = 9.6 Hz), 7.08–7.65 (21 H), 8.00–8.17 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 24.6, 24.9, 26.0, 26.2, 32.3, 32.9, 63.1, 66.4, 67.2, 69.0, 69.6, 70.6, 70.8, 70.9, 71.1, 73.4, 73.8, 74.8, 75.7, 76.0, 76.9, 96.4, 101.4, 104.2, 108.7, 109.6, 127.4, 127.5, 127.6, 127.7, 128.0, 128.3, 128.7, 129.2, 129.8, 129.9, 130.0, 132.9, 133.6, 137.5, 138.3, 138.4, 165.2, 166.2. FAB-MS, *m/e* 1282 M$^+$; Anal. Calcd for $C_{59}H_{64}I_2O_{16}$: C, 55.24; H, 5.03. Found: C, 55.69; H, 5.33.

Glycal 19. To a stirred solution of glycal **13** (134.6 mg, 0.15 mmol) in methanol–ether (10:1, 5 mL) was added 1 mL of a 1% (w/w) solution

of NaOH in methanol. The resulting solution was stirred at room temperature for 1 h and then concentrated. To the residual material were added water (10 mL) and CH_2Cl_2 (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organics were dried (Na_2SO_4) and concentrated. The residual oil was purified by chromatography on silica gel (hexanes–ethyl acetate, 1:1 v/v) to provide 88.7 mg (86%) of the diol which was then dissolved in DMF (1 mL). To this stirred solution were added imidazole (44 mg, 5 equiv) and (TBDMS)Cl (49 mg, 2.5 equiv). After 15 h, water (15 mL) was added and the resulting mixture was extracted with ether (5 × 10 mL). Drying (Na_2SO_4), concentration, and chromatography on silica gel (hexanes–ethyl acetate, 5:1 v/v) provided 105.8 mg (90%) of **19** as a colorless oil: $[\alpha]^{23}_D$ +5.6° (c = 0.46, $CHCl_3$); IR ($CHCl_3$) 3020, 2930, 1650, 915 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.044, 0.046, 0.114, 0.118 (s each, 3 H each), 0.88 and 0.91 (s each, 9 H each), 3.29 (dd, 1 H, J = 4.0, 8.0 Hz), 3.65–4.11 (9 H), 4.47–4.86 (8 H), 5.58 (s, 1 H), 6.30 (d, 1 H, J = 6.2 Hz), 7.12–7.41 (15 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −5.2, −4.5, −4.1, 17.9, 18.4, 25.8, 26.0, 33.9, 62.0, 66.0, 68.7, 71.1, 73.0, 73.5, 74.5, 75.0, 75.9, 76.9, 78.0, 101.1, 101.8, 127.3, 127.5, 127.6, 127.7, 127.9, 128.2, 128.3, 137.8, 138.5, 143.3; FAB-MS, m/e 915 $(M - H)^+$. Anal. Calcd for $C_{45}H_{65}IO_8Si_2$: C, 58.94; H, 7.14. Found: C, 59.40; H, 7.29.

Glycal 22. Glycal **17** (334.1 mg) was converted into the corresponding diol (253.9 mg, 99%) and then into 264.7 mg (79%) of **22** by following the procedure for the preparation of glycal **19**. This colorless oil exhibited the following: $[\alpha]^{22}_D$ −14.9° (c = 0.52, $CHCl_3$); IR ($CHCl_3$) 3010, 1650, 1210, 1120, 840 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.09 and 0.15 (s each, 3 H each), 0.10 (s, 6 H), 0.92 and 0.94 (s each, 9 H each), 3.30 (dd, 1 H, J = 4.2, 8.6 Hz), 3.69–3.94 (8 H), 4.05–4.10 (m, 2 H), 4.48–4.72 (6 H), 4.87 (d, 1 H, J = 10.7 Hz), 4.98 (dd, 1 H, J = 2.7, 6.1 Hz), 5.39 (s, 1 H), 6.21 (d, 1 H, J = 6.1 Hz), 7.17–7.48 (15 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −5.2, −5.0, −4.7, −4.2, 18.1, 18.5, 25.9, 26.0, 33.5, 61.7, 68.1, 69.4, 71.1, 72.7, 73.5, 75.2, 77.2, 79.4, 79.5, 100.8, 103.4, 127.4, 127.5, 127.6, 127.7, 127.8, 128.0, 128.3, 128.4, 137.9, 138.4, 138.5, 144.6; FAB-MS, m/e 917 $(M + H)^+$.

Glycal 20. Glycal **19** (338.0 mg) and 3,6-di-*O*-benzoyl-D-glucal (**9**; 143.6 mg) gave 303.9 mg (59%) of **20** as a colorless glass: $[\alpha]^{23}_D$ +5.5° (c = 1.46, $CHCl_3$); IR ($CHCl_3$) 2950, 2920, 1715, 1650, 1265, 1105, 840 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ −0.02, 0.01, 0.09, 0.15 (s each, 3 H each), 0.84 and 0.94 (s each, 9 H each), 3.23 (dd, 1 H, J = 3.9, 8.7 Hz), 3.43 (m, 1 H), 3.66–3.86 (6 H), 4.02 (t, 1 H, J = 8.3 Hz), 4.07 (t, 1 H, J = 9.2 Hz), 4.17 (t, 1 H, J = 2.8 Hz), 4.29 (t, 1 H, J = 5.9 Hz), 4.46–4.88 (10 H), 5.02 (dd, 1 H, J = 3.5, 6.1 Hz), 5.49 (s, 1 H), 5.53 (t, 1 H, J = 3.8 Hz), 5.66 (br s, 1 H), 6.53 (d, 1 H, J = 6.1 Hz), 7.16–7.62 (21 H), 8.04 (d, 4 H, J = 7.4 Hz); ^{13}C NMR (63 MHz, $CDCl_3$) δ −5.3, −5.0, −4.2, −3.9, 14.0, 18.1, 18.4, 22.6, 25.6, 26.1, 26.2, 31.5, 33.7, 62.6, 69.0, 69.4, 71.2, 72.5, 73.5, 73.6, 74.4, 74.8, 74.9, 75.1, 76.1, 98.6, 101.9, 102.0, 127.2, 127.3, 127.5, 127.6, 127.7, 127.8, 128.1, 128.2, 128.3, 128.4, 128.5, 129.7, 129.8, 133.0, 133.3, 138.0, 138.7, 145.7, 165.8, 166.0. Anal. Calcd for $C_{65}H_{82}I_2O_{14}Si_2$: C, 55.87; H, 5.91. Found: C, 56.19; H, 6.11.

Tetrasaccharide 21. Glycal **20** (212.0 mg) and 1,2,3,4-di-*O*-isopropylidene-D-galactopyranose (**11**; 43.4 mg) gave 248.8 mg (92%) of **21** as a colorless glass: $[\alpha]^{23}_D$ +32.1° (c = 0.90, $CHCl_3$); IR ($CHCl_3$) 2930, 1720, 1265, 1110, 1070, 845 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ −0.12, −0.08, −0.06, 0.05 (s each, 3 H each), 0.81 and 0.84 (s each, 9 H each), 1.34 (s, 6 H), 1.43 and 1.59 (s each, 3 H each), 3.18–3.31 (m, 2 H), 3.55–4.14 (12 H), 4.20–4.90 (16 H), 5.30 (s, 1 H), 5.40 (br s, 1 H), 5.53 (d, 1 H, J = 5.0 Hz), 5.66 (br s, 1 H), 7.15–7.68 (21 H), 8.08–8.18 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −5.4, −4.9, −4.5, −4.1, 18.0, 18.5, 24.5, 25.0, 26.0, 26.07, 26.13, 30.4, 33.8, 61.8, 63.2, 66.3, 67.2, 68.7, 70.0, 70.6, 70.7, 70.9, 71.0, 72.2, 73.2, 73.6, 74.1, 74.2, 74.9, 75.8, 96.3, 101.1, 101.7, 108.6, 109.4, 127.2, 127.3, 127.6, 127.7, 128.0, 128.1, 128.3, 128.4, 128.8, 129.9, 130.0, 133.0, 133.8, 138.0, 138.6, 165.0, 166.0; FAB-MS m/e 1783 $(M + H)^+$. Anal. Calcd for $C_{77}H_{101}I_3O_{20}Si_2$: C, 51.86; H, 5.71. Found: C, 51.97; H, 5.75.

Glycal 23. Glycal **22** (120.7 mg) and 3,6-di-*O*-benzoyl-D-glucal (**9**; 51.3 mg) gave 117.2 mg (64%) of **23** as a colorless glass: $[\alpha]^{23}_D$ −9.2° (c = 0.54, $CHCl_3$); IR ($CHCl_3$) 3020, 2950, 2925, 1720, 1650, 1270 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.01, 0.07, 0.08, 0.13 (s each, 3 H each), 0.91 and 0.92 (s each, 9 H each), 3.20–3.30 (m, 2 H), 3.56–3.84 (5 H), 4.00 (t, 1 H, J = 9.3 Hz), 4.10 (t, 1 H, J = 8.7 Hz), 4.23 (m, 1 H), 4.30 (t, 1 H, J = 5.3 Hz), 4.49–4.78 (10 H), 4.87 (d, 1 H, J = 11.0 Hz), 5.02 (dd, 1 H, J = 3.7, 6.2 Hz), 5.42 (t, 1 H, J = 3.9 Hz), 5.51 (s, 1 H), 5.52 (s, 1 H), 6.53 (d, 1 H, J = 6.2 Hz), 7.18–7.66 (21 H), 8.03–8.08 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −5.5, −4.9, −4.5, −3.9, 18.1, 18.3, 25.7, 25.9, 26.0, 33.5, 61.3, 62.3, 68.5, 68.7, 69.0, 71.2, 71.3, 73.4, 74.3, 74.4, 75.0, 75.9, 76.0, 76.9, 79.0, 98.3, 101.6, 127.4, 127.5, 127.8, 128.0, 128.2, 128.4, 128.5, 129.6, 129.7, 133.2, 137.7, 138.4, 138.5, 145.8, 165.7, 166.0. Anal. Calcd for $C_{65}H_{82}I_2O_{14}Si_2$: C, 55.87; H, 5.91. Found: C, 56.28; H, 6.07.

Tetrasaccharide 24. Glycal **23** (84.3 mg) and 1,2,3,4-di-*O*-isopropylidene-D-galactopyranose (**11**; 17.3 mg) gave 77.8 mg (72%) of **24** as a colorless glass: $[\alpha]^{23}_D$ +2.8° (c = 0.86, $CHCl_3$); IR ($CHCl_3$) 3010, 2930, 1720, 1265, 1075 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ −0.06, −0.05, 0.05, 0.14 (s each, 3 H each), 0.88 and 0.91 (s each, 9 H each), 1.36, 1.38, 1.47, 1.62 (s each, 3 H each), 3.15–3.28 (m, 3 H), 3.49–3.60 (m, 3 H), 3.70–4.90 (24 H), 5.34 (s, 1 H), 5.45 (s, 1 H), 5.52 (s, 1 H), 5.56 (d, 1 H, J = 5.0 Hz), 7.10–7.64 (21 H), 8.04–8.23 (m, 4 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ −5.5, −4.9, −4.6, −4.0, 18.1, 18.3, 24.6, 25.0, 26.0, 26.1, 26.3, 30.4, 33.3, 60.6, 63.3, 66.2, 67.4, 68.1, 69.8, 70.7, 70.9, 71.2, 72.9, 73.3, 74.4, 74.9, 75.8, 76.7, 78.6, 96.3, 101.4, 103.7, 105.2, 108.8, 109.4, 127.3, 127.4, 127.6, 127.7, 127.8, 128.0, 128.1, 128.2, 128.4, 128.8, 129.9, 130.0, 130.1, 133.1, 133.8, 137.8, 138.6, 165.0, 166.1. Anal. Calcd for $C_{77}H_{101}I_3O_{20}Si_2$: C, 51.86; H, 5.71. Found: C, 52.39; H, 5.98.

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