butoxide to the isotopomers of [^{16}O,^{17}O,^{18}O]dcAMP by the method of Jarvest et al.[17] Purification by DEAE Sephadex A-25 chromatogrpahy as described gave [^{16}O,^{17}O,^{18}O]dcAMP (10.1 μmol, 20%). After evaporation of the solvent in vacuo and conversion to the potassium-18-crown-6 salt, the product was methylated by using methyl iodide in Me_2SO-d_6 as described. The ^{31}P NMR spectrum and the data thereof are presented in Figure 4.

(R_P,S_P)-2′-Deoxythymidylyl(3′→5′)-2′-deoxyadenosine Methyl Ester (25a/b). Compound **15** (10 μmol) was methylated as described[8] for U_pA to give the methyl esters **25a/b** as a solution in Me_2SO-d_6: ^{31}P NMR (Me_2SO-d_6) δ 0.08 (s) for the S_P diastereomer and 0.01 (s) for the R_P diastereomer; ^{31}P NMR (Me_2SO-d_6/MeOH, 1:1) δ −0.06 (s) for the S_P diastereomer and −0.10 (s) for the R_P diastereomer.

(R_P,S_P)-[^{18}O]-2′-Deoxythymidylyl(3′→5′)-2′-deoxyadenosine Methyl Ester (26a/b). (R_P)-[^{18}O]-2′-Deoxythymidylyl(3′→5′)-2′-deoxyadenosine (**11a**) was methylated as described for the unlabeled dimer **15** to give the methyl esters **26a/b**: ^{31}P NMR (Me_2SO-d_6) δ 0.04 (s) for the S_P diastereomer and 0.00 (s) for the R_P diastereomer. After mixing with an approximately equal amount of unlabeled material the following isotope shifts were recorded: P—[^{18}O]Me, 1.3 Hz; P=[^{18}O], 4.1 Hz; ^{31}P NMR (Me_2SO-d_6/MeOH, 1:1) δ −0.10 (s) for the S_P diastereomer and −0.11 (s) for the R_P diastereomer.

(R_P,S_P)-2′-Deoxycytidylyl(3′→5′)-2-deoxyadenosine Methyl Ester (27a/b). 2′-Deoxycytidylyl(3′→5′)-2′-deoxyadenosine (**23**) (10 μmol) was methylated as described[8] for U_pA to give the methyl esters **27a/b** as a solution in Me_2SO-d_6: ^{31}P NMR (Me_2SO-d_6/MeOH, 1:1) δ −0.06 (s) for the R_P diastereomer and −0.09 (s) for the S_P diastereomer.

(R_P,S_P)-[^{18}O]-2′-Deoxycytidylyl(3′→5′)-2′-deoxyadenosine Methyl Ester (28a/b). (R_P)-[^{18}O]-2′-Deoxycytidylyl(3′→5′)-2′-deoxyadenosine (**19a**) was methylated as described for the unlabeled compound **23** to give the methyl esters **28a/b** as a solution in Me_2SO-d_6: ^{31}P NMR (Me_2SO-d_6/MeOH, 1:1) δ −0.08 (s) for the R_P diastereomer and −0.13 for the S_P diastereomer. After mixing with an approximately twofold amount of unlabeled material, the following isotope shifts were recorded: P—[^{18}O]Me, 1.6 Hz; P=[^{18}O], 4.0 Hz.

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General Synthesis of (1→3)-β-D-Galacto Oligosaccharides and Their Methyl β-Glycosides by a Stepwise or a Blockwise Approach

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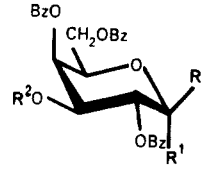
All intermediates for the chemical synthesis of (1→3)-β-D-galacto oligosaccharides or their methyl β-glycosides are prepared from one readily available substance, namely methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranoside (**1**). Debenzylation of **1** gives **2**, the initial nucleophile for the synthesis of methyl β-glycosides of (1→3)-β-D-galacto oligosaccharides. Reaction of **1** with 1,1-dichloromethyl methyl ether affords the key glycosyl donor **3** permitting the extension of the oligosaccharide chain through HO-3. 1,1-Dichloromethyl methyl ether is a suitable reagent also for the conversion of derivatives of higher oligosaccharides into the corresponding glycosyl chlorides, and these are sufficiently reactive under the conditions of silver triflate promoted glycosidation reactions. Reaction of the halide **3** with silver acetate, followed by reductive cleavage of the benzyl group from the formed 1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranose (**4**), gives **5**, the initial nucleophile for the synthesis of free (1→3)-β-D-galacto oligosaccharides. The sequential or blockwise synthesis of higher title oligosaccharides using the above intermediates is demonstrated by the preparation of various (1→3)-β-D-galacto oligosaccharides and their methyl β-glycosides. The per-*O*-benzoate of the methyl β-glycoside of (1→3)-β-D-galactoheptaose (**26**) was obtained in 62% yield by a condensation of a trisaccharide nucleophile with a glycosyl chloride derived from (1→3)-β-D-galactotetraose. The structure of all mono- and disaccharide intermediates was confirmed by 2D NMR carbon–proton correlation experiments, and that of higher oligosaccharides was verified by comparison of their ^{13}C NMR spectra with those of the lower members of the respective series.

The *O*-β-D-galactopyranosyl-(1→3)-D-galactopyranosyl or 3-*O*-substituted β-D-galactopyranosyl sequence occurs widely in nature.[2-7] 3-*O*-β-D-Galactopyranosyl-D-galactose has been synthesized,[4,8,9] but a systematic synthesis of higher members of this series or of their methyl β-glycosides has not been carried out due to the difficulties involved in the preparation of suitable intermediates. We have reported[10] a synthesis of methyl 3-*O*-β-D-galactopyranosyl-β-D-galactopyranoside, a compound previously obtained[11] only in admixture with its α-, 2-*O*-α-, and 2-*O*-β-isomers. Here we describe efficient syntheses of intermediates needed to prepare virtually *any* of the compounds of the above series by either a stepwise or a blockwise synthesis. The use of the present approach is demonstrated by the syntheses of a series of the title methyl β-glycosides up to and including the heptasaccharide.

(1) (a) NIADDK. (b) University of Missouri.
(2) Rodén, L. "Metabolic Conjugation and Metabolic Hydrolysis"; Fishman, W. H., Ed.; Academic Press: New York, 1970; Vol. 2, pp 345–442.
(3) Bailey, R. W. "Oligosaccharides"; Pergamon Press: Oxford, 1965; p 48.
(4) Benzing-Nguyen, L.; Roden, L. *Carbohydr. Res.* **1977**, *53*, 123–128 and references cited therein.
(5) Marcus, D. M. *Mol. Immunol.* **1984**, *21*, 1083–1091.
(6) Roy, N.; Glaudemans, C. P. J. *Carbohydr. Res.* **1978**, *63*, 318–322.
(7) Collins, J. G.; Bradbury, J. H.; Trifonoff, E.; Messer, C. R. *Carbohydr. Res.* **1981**, *92*, 136–140 and references cited therein.
(8) Ball, D. H.; Jones, J. K. N. *J. Chem. Soc.* **1958**, 905–907.
(9) Chacon-Fuertes, M. E.; Martin-Lomas, M. *Carbohydr. Res.* **1975**, *43*, 51–56.
(10) Kováč, P.; P.; Glaudemans, C. P. J.; Taylor, R. B. *Carbohydr. Res.* **1985**, *142*, 158–164.
(11) Gorin, P. *Carbohydr. Res.* **1982**, *101*, 13–20.

Synthesis

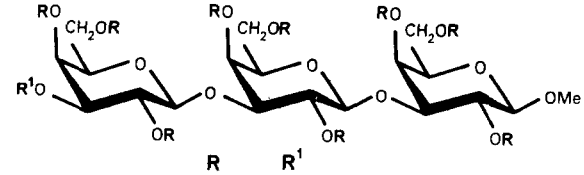
The stepwise construction of a high homooligosaccharide such as, e.g., 24 requires three intermediates: (a) a 2,4,6-tri-*O*-substituted derivative of methyl β-D-galactopyranoside as the initial nucleophile (to become the terminal methyl β-D-galactopyranoside residue), (b) a protected galactosyl halide bearing a blocking group at position 3 which is selectively removable (to form the internal units), and (c) a protected glycosyl halide derived from D-galactose (to form the D-galactopyranosyl end group of the oligosaccharide). The above glycosyl halides must[12] bear a substituent at position O-2 capable of neighboring group participation. In the blockwise synthesis at least one of the intermediates, but often all, is a derivative of a related, lower oligosaccharide. In the present series of (1→3)-β-linked D-galacto oligosaccharides and their methyl β-glycosides all intermediates required by either the stepwise or by the blockwise approach can be prepared from a single starting compound, namely, methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranoside (**1**). This crystalline substance is readily obtainable in high yield.[10] Simple reductive cleavage of the benzyl group in **1** yielded[10] **2**, the compound used in the present approach as the initial nucleophile to synthesize methyl β-glycosides of (1→3)-β-D-galacto oligosaccharides.



	R	R¹	R²
1	OMe	H	Bn
3	H	Cl	Bn
30	H	OBz	Bz
31	H	Br	Bz

By treatment of **1** with 1,1-dichloromethyl methyl ether (DCMME) under controlled conditions[13] the corresponding glycosyl chloride **3** can be obtained in good yield. Since it contains a blocking group at position O-3 which eventually can be selectively removed, compound **3** is suitable to form an internal 3-*O*-glycosylated β-D-galactopyranosyl residue of any oligosaccharide. Glycosyl chlorides are insufficiently reactive for practicable syntheses of oligosaccharides by the classical Koenigs–Knorr reaction but the use of silver perchlorate or silver triflate as promoters of glycosylation reactions makes these halides useful. At present, therefore, reagents for the facile preparation of glycosyl chlorides have acquired new importance. 1,1-Dihalogenomethyl methyl ethers have been convincingly shown[14] to convert a variety of carbohydrate derivatives, including those bearing acid labile groups, into their corresponding glycosyl halides. Use of the commercially available DCMME is very convenient since it is stable and side reactions[15] are less likely to occur with it than with its bromo analogue. Also, the formed glycosyl chlorides are easier to purify and have a longer shelf life than their bromo counterparts. We have previously extended the use of this class of reagents to the conversion into glycosyl halides of carbohydrate derivatives bearing alkyl ether protecting groups.[13,16,17] Others[18] have also been successful in this respect. We here show that DCMME is a convenient reagent to form α-glycosyl chlorides from 1-*O*-acetates of oligosaccharides (Scheme I). Nucleophile **5**, obtained by hydrogenolysis of the corresponding 3-*O*-benzyl derivative **4**, was treated with 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide (**31**) to yield the derivative of galactobiose **6**. Treatment of **6** with DCMME, gave the disaccharide glycosyl chloride **7** in excellent yield. The corresponding glycosyl bromide has been prepared in an unrelated way by Garegg et al.[19] but was never characterized. The halide **7** has now been fully characterized and its structure verified by analysis of its ^1H and ^{13}C NMR spectra (Tables I and II). The crystalline glycosyl halide **9** was obtained by condensation of the nucleophile **5** with the chloride **3** and subsequent treatment of the resulting disaccharide **8** with DCMME. This glycosyl donor contains a selectively removable blocking group at O-3′ and is, therefore, valuable for a blockwise insertion into an oligosaccharide chain allowing further glycosylation at its position O-3′. As an example of the above strategy, reductive cleavage of the benzyl group in **8** readily gave the disaccharide nucleophile **10**, which was condensed with the glycosyl halide **7** to afford the D-galactotetraose **11**. For the conversion of **11** into the corresponding glycosyl halide **12** the amount of the zinc chloride catalyst is critical. Noticeable (TLC) cleavage of the interglycosidic linkages takes place, in addition to that of the anomeric acetyl group, if the amount of zinc chloride catalyst is too high. With the proper amount of the Lewis acid catalyst the halide **12** was formed smoothly and was isolated in 82% yield.

The projected synthesis of methyl β-glycosides of (1→3)-β-D-galacto oligosaccharides (Scheme II) was first conducted by the stepwise approach. Thus, condensation of the glycosyl halide **3** with the nucleophile **2** gave the disaccharide derivative **13**. Upon debenzylation, followed by debenzoylation **13** afforded the disaccharide glycoside **15**, which was identical with the previously described and independently synthesized substance.[10] Compound **13** was partially deprotected to give the disaccharide nucleophile **14**. In one approach, compound **14** was condensed with the halide **3** to yield the fully blocked trisaccharide derivative **16**, which was readily debenzylated to form the nucleophile **17**. Compound **17** was debenzoylated to give the crystalline methyl β-glycoside of β-D-galactotriose **18**. Benzoylation of **17** gave **32**, whose ^{13}C NMR spectrum was used to aid assignment of spectra of related oligosaccharides. In the reversed deblocking sequence, not

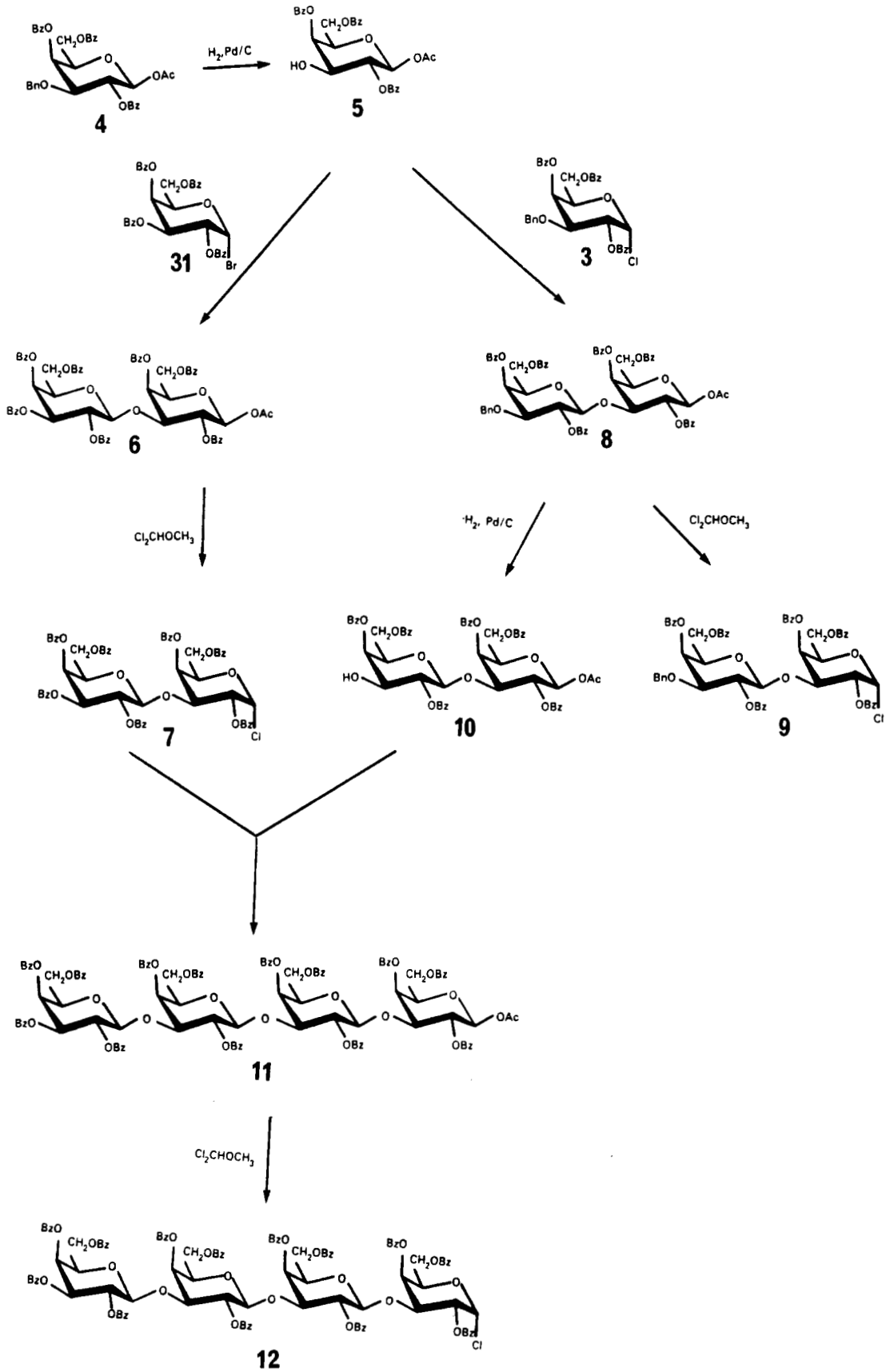


	R	R¹
19	H	Bn
32	Bz	Bz

shown in the Schemes, compound **16** was first debenzoylated to give the glycoside **18** via the crystalline O-3″-benzyl

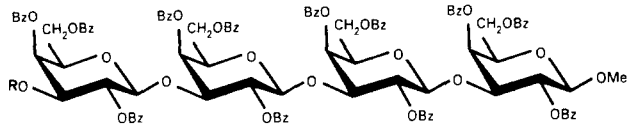
(12) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155–173.
(13) Kováč, P.; Whittaker, N. F.; Glaudemans, C. P. J. *J. Carbohydr. Chem.* **1985**, *4*, 243–254.
(14) Gross, H.; Farkas, I.; Bognár, R. *Z. Chem.* **1978**, *18*, 201–210 and papers cited therein.
(15) Bock, K.; Pedersen, C.; Rasmussen, P. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1456–1461.
(16) Kováč, P.; Palovčík, R *Carbohydr. Res.* **1977**, *56*, 399–403.
(17) Kováč, P.; Farkas, I.; Mihálov, V.; Palovčík, R.; Bognár, R. *J. Carbohydr. Nucleosides Nucleotides* **1976**, *3*, 57–69.
(18) Iversen, T.; Bundle, D. R. *Carbohydr. Res.* **1982**, *103*, 29–40.
(19) Garegg, P. J.; Lindberg, B.; Norberg, T. *Acta. Chem. Scand., Ser. B* **1979**, *33*, 449–452.

Scheme I



derivative **19**. In the second approach, the nucleophile **14** was treated with the disaccharide halide **7** to yield the tetrasaccharide glycoside **20**. Debenzoylation of the latter then gave the crystalline target tetrasaccharide **21**.

To demonstrate the versatility of the described glycosyl halides derived from oligosaccharides as glycosyl donors for the block synthesis of higher members of the series, the tetrasaccharide nucleophile **23** was prepared (not shown in the schemes). The nucleophile **14** was treated with the halide **9** to give the tetrasaccharide derivative **22** from which the temporary blocking group was removed by catalytic hydrogenolysis. The resulting nucleophile **23**,



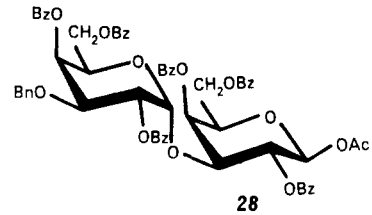
R

22 Bn
23 H

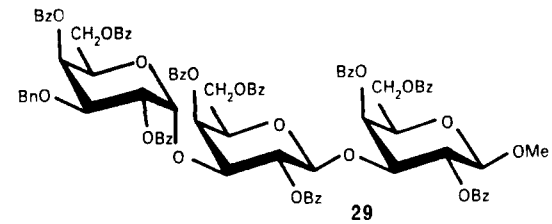
a convenient glycosyl acceptor for synthesizing higher oligosaccharides, was debenzoylated to afford **21**, which was identical with the independently synthesized substance. To prepare the methyl β-glycoside of (1→3)-β-D-galactopentaose (**25**) the nucleophile **17** was condensed with the disaccharide halide **7**, to give the pentasaccharide derivative **24**. Following debenzoylation of **24** gave the target glycoside **25**. The highest oligosaccharide described in this series was obtained by a condensation of the trisaccharide nucleophile **17** with the tetrasaccharide glycosyl chloride **12** to give the heptasaccharide derivative **26** in 62% yield. Subsequently, **26** was debenzoylated to afford the methayl β-glycoside of (1→3)-β-D-galactoheptaose (**27**) in 88% yield.

Notes on the Procedure for Coupling

Due to the varied reactivity of the glycosyl halides and nucleophiles used throughout this work, all coupling reactions could not be performed according to a general procedure (cf. ref 20). Our observations fully confirm that there are no universal conditions for oligosaccharide syntheses.[12] The base-deficient reaction conditions which generally produced best results in this laboratory (cf. ref 10, 21, and 22) could be applied only when the very reactive 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl bromide was used as the glycosyl donor (synthesis of the disaccharide **6**). With less reactive glycosyl chlorides and nucleophiles, particularly those derived from oligosaccharides, the reactions were carried out at temperatures ranging from −5 to +25 °C, rather than at the more commonly used −25 °C, in order to maintain reasonable reaction rates. At these temperatures the reactions were run under only slightly acidic or neutral conditions in order to minimize acid-catalyzed acyl group migration in the nucleophiles and/or partial deblocking (more severe with the derivatives of the 1-*O*-acetate **5** than with those of the methyl glycoside **2**). Consequently, somewhat decreased yields of the desired β-linked oligosaccharides, and the byproducts formed, may have resulted from partial survival under these conditions of the ortho esters which are intermediates in the eventual formation of 1,2-trans end products.[23,24] Acyl migration and unwanted deblocking was less pronounced when reactions were run under less solvolytic conditions in pure toluene rather than the more common toluene–nitromethane mixtures. However, in that case, poorer stereoselectivity[20] resulted in a lower yield of the desired β-linked products. In fact, the α-linked oligosaccharides **28** and **29** were isolated in high yields from coupling reactions carried out under those conditions (see Experimental Section). Although byproducts formed in coupling reactions were



28



29

not always examined, from the TLC patterns we believe that the formation of products analogous to **28** and **29**, i.e., oligosaccharides having an α-linked D-galactosyl group at the site of the newly formed glycosidic linkage, might account for the somewhat decreased yields of the 1,2-trans-linked oligosaccharides. Also, it was observed with some reaction pairs that the order of addition of components, a factor not yet duly explored, affected the outcome of the reactions. Complete optimization of the reaction conditions was not always pursued due to the labor involved in the preparation of certain intermediates.

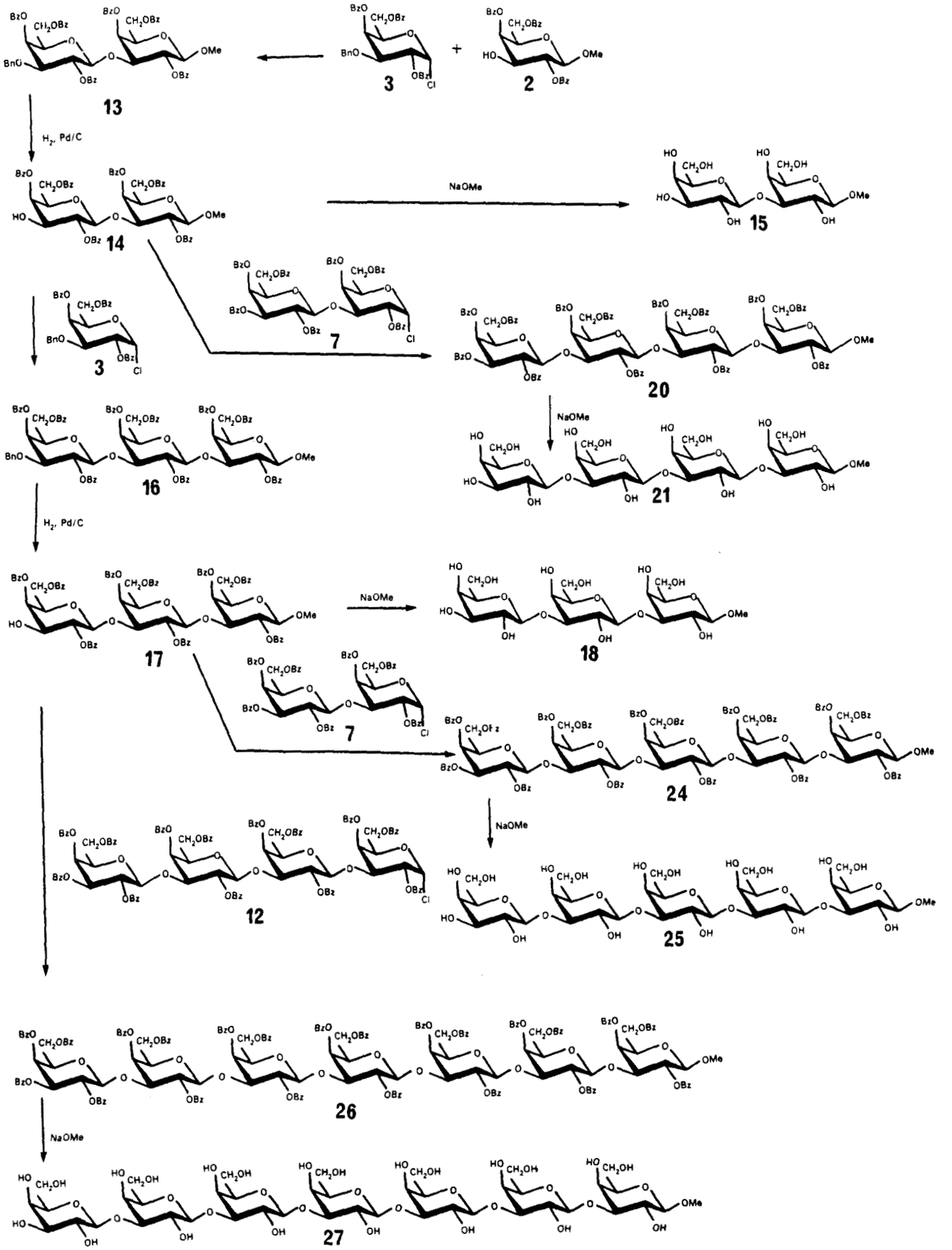
Notes on ^{13}C NMR Assignments

Unambiguous ^{1}H and ^{13}C NMR assignments for all mono- and disaccharide derivatives listed in Tables I and II, as well as for the trisaccharide derivative **29** (see Experimental Section), have been achieved. Each of the monosaccharide derivatives was first characterized by a first-order analysis of its one-dimensional (1D) ^{1}H NMR spectrum which allowed assignments of all protons. ^{13}C NMR assignments were then accomplished by ^{1}H–^{13}C correlation utilizing the recently introduced 1D decoupled selective population transfer (SPT) experiment.[25] ^{1}H and ^{13}C NMR assignments for the oligosaccharide derivatives were accomplished through a combination of two-dimensional (2D) homo- and heteronuclear chemical shift correlation spectroscopy techniques (COSY[26] and CSCM[27]) as previously described.[10] Ambiguities in the previous assignments[28] of the benzoate **30** which were based only on comparisons with spectra of related compounds have now been eliminated. While the halide **31** was previously reported[29] NMR data for this compound was limited to the chemical shift and coupling constant of H-1.

^{13}C NMR assignments for higher oligosaccharides (see Experimental Section) are based on comparison of the observed parameters with those of closely related oligosaccharides. For example, the correct structure of the trisaccharide **19** followed clearly from the comparison of its ^{13}C NMR spectrum with that of methyl 3-*O*-benzyl-β-D-galactopyranoside[10] and the spectrum of the trisaccharide **18**. Assignments in the spectrum of **18** were

(20) Nashed, M. A.; Anderson, L. *J. Am. Chem. Soc.* **1982**, *104*, 7282–7286.
(21) Kováč, P.; Glaudemans, C. P. J.; Guo, W.; Wong, T. C. *Carbohydr. Res.* **1985**, *140*, 299–311.
(22) Ekborg, G.; Vranešić, B.; Bhattacharjee, A. K.; Kováč, P.; Glaudemans, C. P. J. *Carbohydr. Res.* **1985**, *142*, 203–211.
(23) Garegg, P. J.; Norberg, T. *Acta. Chem. Scand., Ser. B.* **1979**, *33*, 116–118.
(24) Banoub, J.; Bundle, D. R. *Can. J. Chem.* **1979**, *51*, 2091–2097.
(25) Sarkar, S. K.; Bax, A. *J. Magn. Reson.* **1985**, *62*, 109–112.
(26) Aue, W. P.; Bartholdi, E.; Ernst, R. K. *J. Am. Chem. Phys.* **1976**, *64*, 2229–2246.
(27) Wong, T. C.; Rutar, V.; Wang, J. S. *J. Am. Chem. Soc.* **1984**, *106*, 7046–7050.
(28) D'Accorso, N. B.; Thiel, I. M. E.; Schuller, M. *Carbohydr. Res.* **1983**, *124*, 177–184.
(29) Lundt, I.; Pedersen, C. *Acta Chem. Scand., Ser. B* **1976**, *30*, 680–684.

Scheme II



made using as an aid the spectrum[10] of the disaccharide **15**. The former spectrum differed from that of **19** mainly in the position of signals for C-2″, C-3″, and C-4″. The observed chemical shifts for these carbons are in agreement with the recognized α- and β-effects of alkoxylation at C-3″ and compare well with the ^{13}C NMR shifts observed[10] for C-2, C-3, and C-4 in the spectrum of the model monosaccharide derivative.

Table I. ^{1}H NMR Chemical Shifts (δ, in $CDCl_3$), Peak Multiplicities,[a] and Coupling Constants (Hz)

	compound												
	3	4	5	6	7	8	9	10	13	14	28	30	31
Proton Signals													
H-1	6.596 d	5.875 d	5.984 d	5.883 d	6.522 d	5.860 d	6.497 d	5.856 d	4.503 d	4.49 m	5.875 d	6.973 d	6.988 d
H-2	5.626 dd	5.676 dd	5.509 dd	5.743 dd	5.634 dd	5.705 dd	5.623 dd	5.733 dd	5.567 dd	5.606 dd	5.80 m	6.046 dd	5.683 dd
H-3	4.306 dd	3.869 dd	4.206 m	4.32 m	4.70 m	4.221 dd	4.568 dd	4.30 m	4.187 dd	4.31 dd	4.285 dd	6.148 dd	6.070 dd
H-4	6.055 br d	5.953 dd	5.797 dd	6.067 dd	6.128 br d	6.027 br d	6.084 d	6.016 d	5.980 dd	5.969 dd	5.78 m	6.211 dd	6.133 dd
H-5	4.746 br t	4.238 td	4.275 td	4.213 td	4.67 m	4.173 td	4.64 m	4.165 t	4.067 td	4.06 t	3.897 td	4.856 td	4.930 br t
H-6a	4.575 dd	4.583 dd	4.541 dd	4.489 d	4.47 m	4.473 br d	4.47 m	4.454 d	4.520 d	4.5 m	4.205 m	4.646 dd	4.647 dd
H-6b	4.456 dd	4.431 dd	4.404 dd	4.489 d	4.47 m	4.473 br d	4.47 m	4.454 d	4.520 d	4.5 m	4.47 m	4.435 dd	4.472 dd
H-1′				5.007 d	5.162 d	4.830 d	4.972 d	4.898 d	4.838 d	4.903 d	5.730 d		
H-2′				5.593 dd	5.598 dd	5.331 dd	5.335 dd	5.153 dd	5.317 dd	5.128 dd	5.508 dd		
H-3′				5.406 dd	5.468 dd	3.653 dd	3.716 dd	3.922 m	3.647 dd	3.893 m	3.743 dd		
H-4				5.87 d	5.929 d	5.805 br d	5.845 d	5.645 d	5.798 dd	5.639 d	5.204 d		
H-5′				4.281 td	4.39 m	4.050 br t	4.149 t	4.087 t	4.030 td	4.06 t	4.25 m		
H-6a′				4.700 dd	4.768 dd	4.331 dd	4.681 dd	4.596 dd	4.315 dd	4.599 dd	4.14 m		
H-6b′				4.32 m	4.42 m	4.606 dd	4.40 m	4.33 m	4.613 dd	4.28 m	4.50 m		
CH_2Ph	4.795 d					4.362 d	4.396 d		4.569 d		4.383 d		
	4.609 d					4.577 d	4.61 m		4.353 d		4.151 d		
CH_3O									3.405 s	3.436 s			
CH_3CO		2.065 s	2.072 s	1.959 s		1.933 s		1.964 s		2.678 d	2.108 s		
OH			2.978 d					2.578 d					
Coupling Constants													
$J_{1,2}$	4.0	8.4	8.3	8.2	4.0	8.2	3.9	8.2	7.7	8.8	8.2	3.6	4.0
$J_{2,3}$	10.2	9.9	8.3	9.7	10.3	9.7	10.3	9.6	9.7	9.8	10.0	10.7	10.4
$J_{3,4}$	3.3	3.3	3.2	3.3	2.7	3.6	3.4	3.0	3.5	3.1	3.1	3.2	3.3
$J_{4,5}$	*b*	*b*	*b*	*b*	*b*	*b*	*b*	*b*	*b*	*b*	*b*	*1.2*	*b*
$J_{5,6a}$	6.8	6.9	6.9	6.2	*d*	6.0	*d*	5.6	5.8	*d*	6.6	6.4	6.8
$J_{5,6b}$	5.6	5.8	5.9	6.2	*d*	6.0	*d*	5.6	6.1	*d*	6.6	7.0	6.0
$J_{6a,6b}$	11.5	11.5	11.4	*c*	*d*	*c*	*d*	*c*	6.1	*d*	*d*	11.3	11.5
$J_{1',2'}$				7.7	7.7	7.8	7.9	7.7	7.8	7.7	3.7		
$J_{2',3'}$				10.5	10.4	10.0	10.0	9.9	10.1	10.0	10.4		
$J_{3',4'}$				3.3	3.3	3.3	3.3	3.1	3.3	2.6	3.3		
$J_{4',5'}$				*b*	*b*	*b*	*b*	*b*	*b*	*b*	*b*		
$J_{5',6a'}$				5.7	5.0	6.0	7.3	6.9	6.2	6.7	*d*		
$J_{5',6b'}$				*d*	*d*	6.9	*d*	*d*	11.4	*d*	*d*		
$J_{6a',6b'}$				10.4	10.0	11.4	11.4	11.4	11.4	11.4	*d*		
J_{CH_2Ph}	12.3					12.9	12.8		12.7		12.3		
$J_{3',OH}$			6.0					6.5		6.4			

[a] Multiplicities: s, singlet; d, doublet; t, triplet; m, multiplet; br, broadened. [b] <1 Hz. [c] H-6a and H-6b are equivalent. [d] Unresolved due to overlapping resonances.

Table II. ^{13}C NMR Chemical Shifts (δ, in $CDCl_3$) of the Monosaccharides and Disaccharides

	compound												
C	3	4	5	6	7	8	9	10	13	14	28	30	31
C-1	92.08	92.21	91.99	92.08	91.92	92.00	92.00	92.17	101.79	102.00	92.10	90.49	88.27
C-2	69.98	69.89	71.84	69.93	70.07	69.78	69.87	70.11	70.68	71.12	64.80	67.54	68.44
C-3	72.48	76.05	71.01	77.18	72.69	77.35	72.93	76.86	77.43	76.67	72.12	68.39	68.78
C-4	67.13	66.30	70.17	69.90	70.41	69.93	70.48	70.00	70.18	70.26	69.30	68.33	67.97
C-5	70.15	72.32	72.16	72.67	70.58	72.60	70.58	72.72	71.53	71.64[a]	72.24	69.30	71.72
C-6	62.15	62.29	62.11	62.63	62.45	62.66	62.52	62.72	62.85	62.88	61.65	61.68	61.54
C-1′				101.39	101.48	101.46	101.54	101.01	101.36	100.83	92.40		
C-2′				69.41	69.58	70.81	71.01	73.23	70.80	73.34	68.93		
C-3′				71.26	71.40	75.70	75.81	71.30	75.73	71.31	72.97		
C-4′				67.48	67.59	65.92	66.01	69.98	65.91	69.99	67.56		
C-5′				71.11	71.33	71.07	71.28	71.30	70.91	71.18[a]	67.60		
C-6′				61.64	61.85	62.14	62.31	62.10	62.04	62.05	62.99		
CH_2Ph	71.49	71.00				70.51	70.65		70.48		71.35		
CH_3O									56.31	56.58			
CH_3CO		20.71	20.48	20.50		20.39		20.63			20.74		

[a] Based on comparison with other compounds; assignment by 2D heteronuclear carbon–proton correlation impossible (cf. Table I, H-5 and H-5′ resonate at the same frequency).

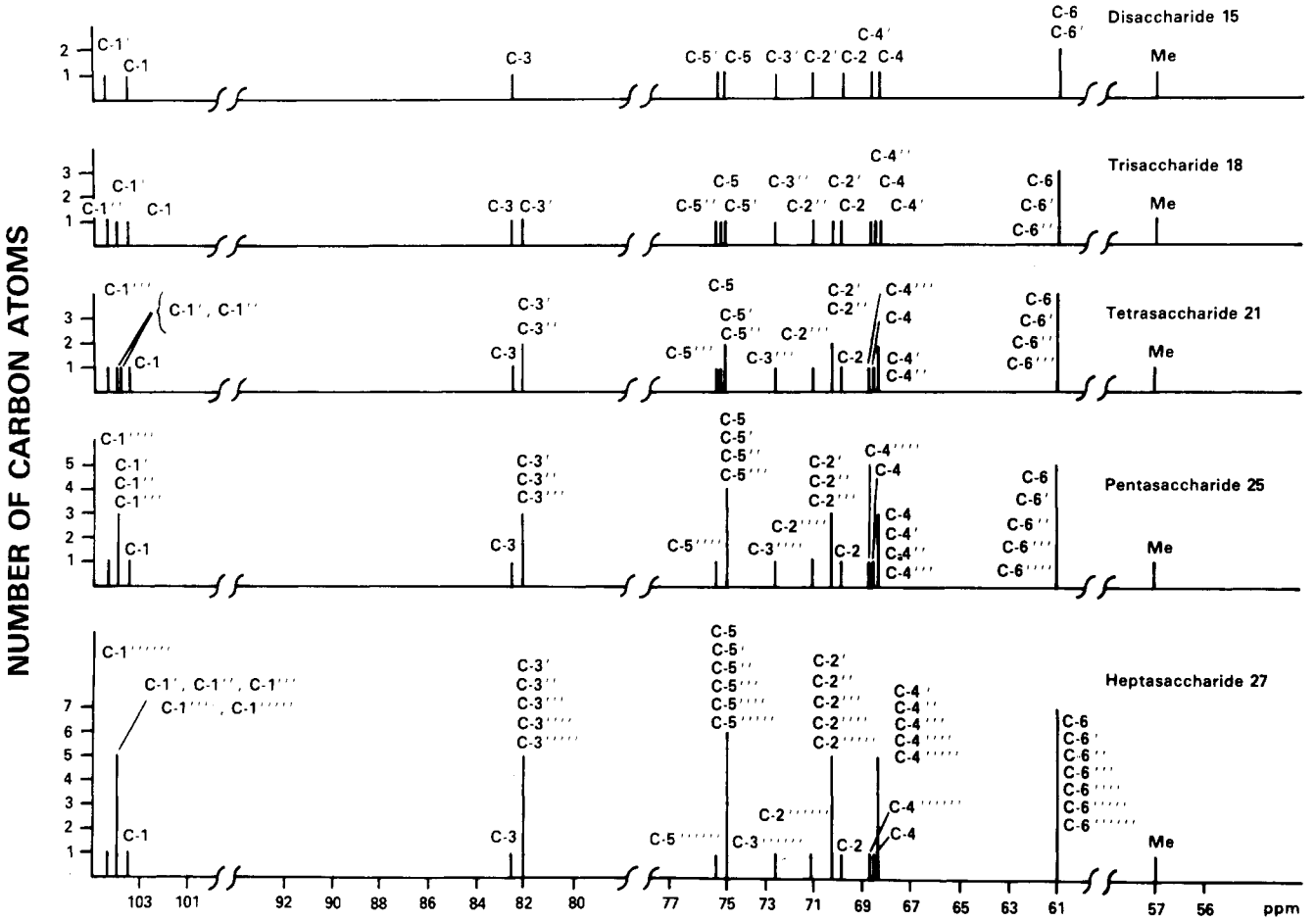


Figure 1. Comparison of ^{13}C NMR spectra of methyl β-glycosides of (1→3)-β-D-galaco oligosaccharides. (Data for the disaccharide taken from ref 10.)

In the case of other oligosaccharides, it was possible to recognize regularities showing that certain substances belonged to the same homologous series (e.g. **13**, **16**, and **22**). However, complete analysis of the ^{13}C NMR spectra of higher, substituted oligosaccharides was not possible because of complexities of which we have little understanding. For example, the α-linked rings of oligosaccharides **28** and **29** should be good models for each other. However, the order of the chemical shifts for C-4′ and C-5′ in the disaccharide derivative **28** were observed to be reversed relative to C-4″ and C-5″ in the trisaccharide derivative **29** (c.f. Table II and ^{13}C NMR data for compound **29** in the Experimental Section). This would lead to misassignment of C-4″ and C-5″ in **29** if they were assigned solely by comparison to the data observed for **28**. The observed irregularities probably result from long-range effects of substituents that are several bonds distant but could also be due to differences in conformation or solvation of the interglycosidic linkages. This is suggested by the fact that the complexities observed in the spectra of substituted oligosaccharides are virtually absent in the ^{13}C NMR spectra of the title methyl glycosides. Here, the carbon-signal assignments (Figure 1) could be readily based on the variation of peak intensities with chain length. This

was in full agreement with the previous observation[30-32] that carbon atoms which occupy similar positions relative to the glycosidic linkage show similar ^{13}C NMR chemical shifts. Thus, the similarity of chemical shifts for equivalent carbon atoms of the internal residues helped to differentiate peaks associated with them from those assigned to the terminal residues.

The ^{13}C NMR spectrum of compound **26** taken at 67.5 MHz did not conclusively reveal that the substance was a heptasaccharide. The diagnostically most important signals for determination of the number of sugar residues in the molecule are the anomeric, glycosylated, and C-6 carbon atoms. A ^{13}C NMR spectrum of an oligosaccharide consisting of n sugar residues should show signals corresponding to n anomeric, n C-6, and $n - 1$ glycosylated carbon atoms. The ^{13}C NMR spectrum of **26** was insufficiently resolved to show the requisite number of individual carbons of each type (see Experimental Section), and although integration of each region indicated that the requisite number of carbon atoms for a heptasaccharide were present, more conclusive evidence was sought. This was found in the form of a 500-MHz ^1H NMR spectrum of compound **26** which contained seven broad doublets in the H-4 region, each of which exhibited a coupling constant $J_{3,4} \sim 3.5$ Hz, as expected.

Discussion and Conclusions

During the past decade considerable progress has been made in the chemical synthesis of oligosaccharides but the preparation of higher oligosaccharides is still a formidable task. Many problems associated with the poor reactivity of certain pairs of reactants have been eliminated by the introduction of powerful promoters such as silver perchloride or silver triflate. In this way, the less reactive glycosyl chlorides, at times unattractive for chemical synthesis of oligosaccharides, have now become important. Each particular project requires its own efficient blocking group strategy to allow systematic coupling of intermediates followed by partial deprotection of the product to obtain the starting materials for the next step. Hence, there exists the trend[12,20] to synthesize "building units" and use "standardized intermediates". Thus, the synthesis of appropriate, specifically protected derivatives is the key to the entire synthetic scheme.

The synthesis of methyl β-glycosides of (1→3)-β-D-galacto oligosaccharides described above uses as such a key intermediate the glycoside **1**. It ideally fulfills the requirements for a convenient starting material for the synthesis of oligosaccharides. It is a readily obtainable crystalline comound and it can be easily converted into *both* the initial nucleophile **2** and the glycosyl donor **3**. Also, simple conversion of **3** by treatment with silver acetate gives **4**, which can be hydrogenolyzed to give crystalline **5**. The latter is the suitable starting material to synthesize *any reducing* oligosaccharide of this series. Thus, **1** is a versatile and pivotal intermediate. The use of the glycosyl donor **3** permits a stepwise chain extension at position O-3 of D-galactose. It can also be used to synthesize a disaccharide such as **8**, which is suitable for further conversion into either the nucleophile **10** or a very useful disaccharide glycosyl donor **9**. The latter two compounds or their longer chain analogues, such as **12**, can be used in a blockwise fashion for the extension of the oligosaccharide chain. (1→3)-β-D-Galacto oligosaccharides **6** and **11** or higher members of this homologous series, prepared from the halide **3** via the acetate **5**, can be used to synthesize glycosyl donors such as **7** or **12**. For this purpose 1,1-dichloromethyl methyl ether was found to be a very convenient reagent, and the resulting oligoglycosyl chlorides are sufficiently reactive in glycosylation reactions promoted with silver triflate. In addition, DCMME can also be used to prepare α-chlorides from α-acetates,[14,16] known to be unreactive[33] under the conditions of trimethylsilyl trifluoromethanesulfonate catalyzed glycosylations.

Glycosyl halides **7** and **12** can be used for an extension of any oligosaccharide by multiplets of β-linked D-galactose residues. By selecting the appropriate combination of nucleophile and glycosyl donor, virtually *any* oligosaccharide or its methyl β-glycoside in the (1→3)-β-D-galacto oligosaccharide series can be prepared from a single intermediate by applying the above described principles. Hitherto, the 3-*O*-β-D-galactopyranosyl building blocks were available[9,19,33,34] only via difficultly accessible derivatives of 1,6-anhydro-β-D-galactopyranose or from synthetic β-D-galactopyranosyl-(1→3)-D-galactopyranose. Our exploratory demonstration of bypassing the necessity to use the latter compounds appeared as a preliminary communication.[35]

Experimental Section

Melting points were determined with a Büchi melting point apparatus. Optical rotations were measured at 25 °C with a Perkin-Elmer automatic polarimeter, Model 241 MC. Preparative chromatography was performed by gradient elution from short columns of slurry packed silica gel 60 (Merck, 15111). Except for the purification of glycosyl halides, the silica gel was deactivated with 3–5% of water. All reactions were monitored by thin-layer chromatography (TLC) on silica gel coated glass slides (Analtech), performed with mixtures of carbon tetrachloride and acetone, toluene and acetone, dichloromethane and acetone, and dichloromethane and methanol. Detection was effected by charring with 5% sulfuric acid in ethanol and, when applicable, UV light.

All 1D and 2D NMR spectra of the compounds listed in Tables I and II, and the spectrum of compound **29** were recorded at 25 °C for solutions in $CDCl_3$ on a Nicolet NT 300 wide-bore spectrometer operating at 300.05 and 75.45 MHz for ^1H and ^{13}C, respectively, equipped with 5-mm probes. The proton spectra were referenced to internal Me_4Si, and chemical shifts were usually accurate to 0.005 ppm. The ^{13}C NMR spectra were referenced to the $CDCl_3$ line at 77.0 ppm. Samples for ^{13}C NMR experiments routinely consisted of 150–250 mg of the compound dissolved in 0.7–1.0 mL of the solvent. For ^1H NMR measurements, the same samples were used after ~20-fold dilution. Data sets of 128 × 2 K and 512 × 512 data points were generated for CSCM[27] and COSY[26] experiments, respectively. The interpretive methodology has been previously described.[10] One-dimensional NMR spectra (^1H and ^{13}C) of all other compounds were routinely recorded on a Varian FX 100, HR 220, or 300 XL or Nicolet NT 270 or NT 500 spectrometer.

2,3,4,6-Tetra-*O*-benzoyl-α-D-galactopyranosyl bromide (**31**) was prepared as described,[29] and the crude product was purified by column chromatography. When kept dry at −15 °C, the amorphous **31** was stable during several months (TLC).

The coupling reactions were performed in an argon atmosphere using common laboratory glassware equipped with rubber septa. Moisture-free conditions were maintained by flusing the reaction system at the outset with dry argon and by handling solvents and reagents with 1000 Series Hamilton gas-tight syringes. When the

(30) Gast, J. C.; Atalla, R. H.; McKelvey, R. D. *Carbohydr. Res.* **1980**, *84*, 137–146.
(31) Kováč, P.; Hirsch, J. *Carbohydr. Res.* **1982**, *100*, 177–193.
(32) Hirsch, J.; Kováč, P.; Petráková, E. *Carbohydr. Res.* **1982**, *106*, 203–216.
(33) Paulsen, H.; Paal, M. *Carbohydr. Res.* **1984**, *135*, 53–69.
(34) Takeo, K.; Kutajuna, M.; Fukatsu, T. *Carbohydr. Res.* **1983**, *112*, 158–164.
(35) Kováč, P.; Glaudemans, C. P. J. *Carbohydr. Res.* **1985**, *138*, C10–C12.

reactions were thought to be complete, the mixtures were neutralized with *sym*-collidine, if necessary, diluted with dichloromethane, and filtered, the filtrate was washed with aqueous sodium thiosulfate solution, dried, and concentrated, and the residue was treated with benzoyl chloride in pyridine. This converted the unchanged nucleophiles, products of hydrolysis of the used glycosyl halides, and other polar byproducts to materials that otherwise would have chromatographic mobilities too close to the desired products.

Silver triflate, purchased from Aldrich Chemical Co., was dried at 100 °C (133 Pa) for 8 h. 1,1-Dichloromethyl methyl ether was purchased from Aldrich Chemical Co. and used as supplied. Chloroform was washed with concentrated sulfuric acid (twice), water, and aqueous sodium hydrogen carbonate, dried with phosphorus pentoxide, and distilled. Hydrogenolyses were performed at ambient temperature and atmospheric pressure using 5% palladium-on-charcoal catalyst (Engelhardt Industries). Unless otherwise stated, solutions in organic solvents were dried with anhydrous sodium sulfate and concentrated at 40 °C (2 kPa).

1-*O*-Acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranose (5). A solution of 1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranose[13] (11.5 g) in 2-methoxyethanol–ethanol (1:5, 300 mL) together with the hydrogenation catalyst was vigorously stirred overnight in a hydrogen atmosphere. The mixture was processed conventionally, and crystallization from ethanol gave **5** (6 g). Chromatography of the material in the mother liquor and crystallization yielded a further 2.2 g of the same material (total yield 90.7%). A portion, when recrysallized from the same solvent, melted at 166–166.5 °C and showed $[\alpha]_D$ +27.7° (*c* 0.72, chloroform). Anal. Calcd for $C_{29}H_{26}O_{10}$ (534.49): C, 65.16; H, 4.90. Found: C, 65.10; H, 5.18.

***O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-1-*O*-acetyl-2,3,6-tri-*O*-benzoyl-β-D-galactopyranose (6).** A solution of 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyrnosyl bromide (3.95 g, 6 mmol), the nucleophile **5** (2.67 g, 5 mmol), and *sym*-collidine (0.54 mL, 4.5 mmol) in toluene (25 mL) was added at −25 °C to a solution of silver triflate (1.8 g, 7 mmol) in the same solvent (20 mL). After 30 min at −20 °C, the mixture was processed as described above and chromatography yielded the major product **6** (3.95 g, 71.8%) as an amorphous solid, $[\alpha]_D$ +104° (*c* 1.2, chloroform). Anal. Calcd for $C_{63}H_{52}O_{19}$ (1113.05): C, 67.99; H, 4.70. Found: C, 67.82; H, 4.65.

***O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-galactopyranosyl Chloride (7).** To a solution of the above acetate **6** (5.6 g) in alcohol-free chloroform (10 mL) was added DCMME (10 mL), followed by freshly fused zinc chloride (50 mg). The mixture was stirred with the exclusion of moisture at 45–50 °C until TLC showed that only traces of the starting material remained (30–40 min). It was concentrated and coevaporated with toluene, and the residue was passed through a column of silica gel (150 g) to give the fastest moving component **7** (5.3 g, 96%) as an amorphous solid, $[\alpha]_D$ +145° (*c* 0.9, chloroform). Anal. Calcd for $C_{61}H_{49}ClO_{17}$ (1089.45): C, 67.24; H, 4.53; Cl, 3.25. Found: C, 67.31; H, 4.84; Cl, 3.16.

***O*-(2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactoyranose (8).** A solution of the nucleophile **5** (1.6 g, 3 mmol) and glycosyl donor **2** (2.16 g, 3.6 mmol) in toluene–nitromethane (1:1, 15 mL) was added at −10 °C to a solution of silver triflate (1 g, 3.9 mmol) and *sym*-collidine (0.436 mL, 3.3 mmol). The mixture was stirred at the same temperature for 1 h, when the solution was slightly acidic to litmus. Workup, as described above, and chromatography yielded pure **8** (amorphous solid, 1.7 g, 56%), $[\alpha]_D$ +87.3° (*c* 0.66, chloroform). Anal. Calcd for $C_{63}H_{54}O_{18}$ (1099.06): C, 68.84; H, 4.95. Found: C, 68.89; H, 5.17.

When the reaction was run under neutral conditions at 0 °C fewer byproducts were formed, but the desired disaccharide **8** was isolated in only 41% yield. From spectral evidence, the major product (having a faster TLC mobility than **8**), isolated as an amorphous solid in 55% yield, was the α-linked product **28**, $[\alpha]_D$ +154° (*c* 1.3, chloroform). Anal. Calcd for $C_{63}H_{54}O_{18}$ (1099.06): C, 68.84; H, 4.95. Found: C, 68.80; H, 5.01.

***O*-(2,4,6-Tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranose (10).** A solution of compound **8** (1.2 g) in 2-methoxyethanol (50 mL) was hydrogenated as described for the preparation of **5**, and the crude product was purified by chromatography to give pure **10** (1 g, 91.5%), $[\alpha]_D$ +43.5° (*c* 0.7, chloroform). Anal. Calcd for $C_{56}H_{48}O_{18}$ (1008.94): C, 66.65; H, 4.79. Found: C, 66.63; H, 4.76.

***O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-1-*O*-acetyl-2,4,6-tri-*O*-benzoyl-β-D-galactopyranose (11).** A solution of the nucleophile **10** (0.95 g, 0.94 mmol), the glycosyl donor **7** (1.23 g, 1.12 mmol), and *sym*-collidine (0.15 mL, 1.12 mmol) in toluene–nitromethane (1:1, 10 mL) was added at 0 °C to a solution of silver triflate (0.36 g, 1.4 mmol) in the same solvent (10 mL). The mixture was stirred overnight without cooling. The major product **11**, moving on TLC only slightly faster than the nucleophile **10**, was isolated as described above as an amorphous solid (1.05 g, 54%): $[\alpha]_D$ +65° (*c* 0.75, chloroform); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.45 (C-1‴), 101.13, 101.02 (C-1′, C-1″), 92.18 (C-1), 76.61 (C-3), 76.32 (C-3′), 76.13 (C-3″), 72.82 (C-5), 71.86, 71.56, 71.37 (2 C), 71.21, 70.95, (C-2′, C-2″, C-3‴, C-5′, C-5″, C-5‴), 70.23 (C-2), 69.85 (3 C, C-4, C-4′, C-4″), 69.32 (C-2‴), 67.45 (C-4‴), 62.77 (C-6), 62.56, 62.35 (C-6′, C-6″), 61.47 (6‴). Anal. Calcd for $C_{117}H_{96}O_{35}$ (2061.93): C, 68.14; H, 4.69. Found: C, 68.08; H, 4.80.

***O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-benzoyl-α-galactopyranosyl Chloride (12).** A solution of the acetate **11** (1.25 g, 0.6 mmol) in chloroform (3 mL) was treated with DCMME (0.55 mL) and freshly fused zinc chloride (2–3 mg), and the mixture was stirred at 40 °C for 10 min. TLC showed that only traces of unchanged starting material were present and that a major, faster moving product was formed. The mixture was concentrated and chromatographed to give pure **12** (1.025 g, 82%): $[\alpha]_D$ +86.5° (*c* 0.6, chloroform); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.53 (C-1‴), 101.31, 101.07 (C-1′, C-1″), 91.99 (C-1), 76.61, 76.34 (C-3′, C-3″), 72.31 (C-3), 72.04, 71.56, 71.45, 71.37, 71.27, 70.97, 70.71, 70.44, 70.20, 69.96, 69.85, (C-2, C-2′, C-2″, C-3‴, C-4, C-4′, C-4″, C-5, C-5′, C-5″, C-5‴), 69.34 (C-2), 67.45 (4‴), 62.75, 62.51, 62.40 (C-6, C-6′, C-6″), 61.49 (C-6‴); definite signals in the ^1H NMR spectrum (300 MHz, $CDCl_3$) were at δ 6.42 (d, $J_{1,2}$ = 3.9 Hz, H-1), 5.97 (br d, $J_{3,4}$ = 3.4 Hz, H-4‴), 5.90, 5.88, 5.80 (3 × br d, $J_{3,4}$ = 3.9, 3.9, 2.9 Hz, H-4, H-4′, H-4″), 5.48 (dd, $J_{1,2}$ = 3.9 Hz, $J_{2,3}$ ~ 10Hz, H-2), 5.42, 5.28, 5.25 (3 × dd, $J_{1,2}$ ~ 8 Hz, $J_{2,3}$ ~ 10 Hz, H-2′, H-2″, H-2‴), 5.18 (dd, $J_{3,4}$ = 3.4 Hz, H-3‴), 4.87, 4.74, 4.71 (3 × d, $J_{1,2}$ ~ 8 Hz, H-1′, H-1″, H-1‴). Anal. Calcd for $C_{115}H_{93}ClO_{33}$ (2038.34): C, 67.75; H, 4.59; Cl, 1.73. Found: C, 67.67; H, 4.82; Cl, 2.05.

***O*-(2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-α-D-galactopyranosyl Chloride (9).** To a solution of the acetate **8** (1.36 g, 1.18 mmol) in chloroform (2 mL) was added DCMME (1.2 mL), followed by freshly fused zinc chloride (10 mg). The mixture was stirred at 50 °C for 20 min and concentrated. The residue was extracted with dichloromethane and the extract washed with ice–water, dried, and concentration, to give a solid residue. Crystallization from dichloromethane–petroleum ether gave material (0.6 g) melting at 195–196 °C. Chromatography of the material that remained in the mother liquor afforded the fastest moving component (0.55 g, total yield, 86.4%). Recrystallization of a portion from the same solvent gave the analytical sample of **9**: mp 196–196.5 °C; $[\alpha]_D$ +132° (*c* 0.4, chloroform). Anal. Calcd for $C_{61}H_{51}ClO_{16}$ (1075.47): C, 68.12; H, 4.78; Cl, 3.29. Found: C, 68.16; H, 4.89; Cl, 3.18.

Methyl *O*-(2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranoside (13). (a) A solution of the nucleophile **2** (0.5 g, 1 mmol), glycosyl donor **3** (0.9 g, 1.5 mmol), and *sym*-collidine (0.12 mL, 0.9 mmol) in toluene (10 mL) was added at 0 °C to a solution of silver triflate (0.46 g, 1.8 mmol) in the same solvent (10 mL). After 30 min, the mixture was neutralized with *sym*-collidine, allowed to come to room temperature, and worked up after an additional 1.5 h. Chromatography yielded pure, amorphous **13** (0.71 g, 66.3%), $[\alpha]_D$ +72° (*c* 0.8, chloroform). Anal. Calcd for $C_{62}H_{54}O_{17}$ (1071.05): C, 69.52; H, 5.08. Found: C, 69.34; H, 5.25.

(b) A mixture of **2** (0.5 g, 1 mmol), **3** (0.9 g, 1 mmol), mercuric cyanide (0.164 g, 0.65 mmol), and mercuric bromide (30 mg) in benzene (10 mL) was stirred at 75 °C until TLC showed that all

glycosyl donor was consumed (~10 days). TLC showed virtually the same pattern as that observed for the reaction a and the product **13** was isolated in 62% yield by chromatography.

Methyl O-(2,4,6-Tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (14). Compound **13** (2 g) in 2-methoxyethanol (70 mL) was treated as described for the preparation of **5**. After processing the crude product was purified by chromatography to give pure **14** (1.5 g, 82%): mp 116–119 °C (sintered 112 °C, from ethanol); $[\alpha]_D$ +31° (*c* 1.5, chloroform). Anal. Calcd for $C_{55}H_{48}O_{17}$ (980.93): C, 67.33; H, 4.93. Found: C, 67.60; H, 5.04.

Methyl O-β-D-Galactopyranosyl-(1→3)-β-D-galactopyranoside (15). A solution of **14** (0.2 g) in methanol (10 mL) was rendered strongly alkaline by addition of methanolic sodium methoxide (1 M) and left at room temperature for 16 h. It was neutralized with Dowex 50 W (H^+ form) resin and concentrated at 70 °C (133 Pa) to remove methyl benzoate, and the solid residue was recrystallized from methanol to give **5** (0.6 g 82%), mp 200–202 °C (lit.[10] mp 200–201 °C).

Methyl O-(2,4,6-tri-O-benzoyl-3-O-benzyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (16). A solution of silver triflate (1.08 g, 4.2 mmol) and *sym*-collidine (0.357 mL, 2.7 mmol) in toluene (30 mL) was added at −5 °C to a stirred solution of the nucleophile **14** (2.94 g, 3 mmol) and the glycosyl donor **3** (2.16 g, 3.6 mmol) in the same solvent (10 mL). The mixture was agitated at 0 °C for 2 h, and TLC then showed that both starting materials were consumed and that two major products had been formed. After conventional processing, chromatography first gave the byproduct, shown to be the α-linked product **29** (1.55 g, 33.5%): $[\alpha]_D$ +96° (*c* 0.8, chloroform); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.83 (C-1), 101.60 (C-1′), 91.94 (C-1″), 78.40 (C-3), 73.14 (C-3″), 71.68 (C-3′), 71.62 (C-5), 71.33 (CH_2 benzylic), 71.01 (C-5′), 70.58 (C-2), 69.80 (2C, C-4, C-2′), 68.69 (C-2″), 67.38 (C-4″), 67.16 (C-5″), 64.32 (C-4′), 62.95 (C-6), 62.43 (C-6″), 61.43 (C-6′), 56.47 (CH_3); ^1H NMR (300 MHz, $CDCl_3$) δ 5.896 (br d, $J_{4,5}$ < 1 Hz, H-4), 5.662 (br d, $J_{4',5'}$ < 1 Hz, H-4′), 5.638 (d, $J_{1'',2''}$ = 3.8 Hz, H-1″), 5.596 (dd, $J_{2,3}$ = 9.7 Hz, H-2), 5.500 (dd, $J_{2',3'}$ = 10.3 Hz, H-2′), 5.402 (dd, $J_{2'',3''}$ = 10.4 Hz, H-2″), 4.976 (br d, $J_{4'',5''}$ < 1 Hz, H-4″), 4.56 (m, $J_{6a',6b'}$ not determined due to overlapping of signals, H-6a′), 4.55 (m, 3 H, $J_{1',2'}$ = 7.8 Hz, $J_{6a,6b}$ not determined due to overlapping of signals, H-1′, H-6a, H-6b), 4.54 (m, $J_{1,2}$ = 7.7 Hz, H-1), 4.22 (m, 3 H, $J_{6a'',6b''}$ and ^2J not determined due to overlapping of signals, H-6a″, H-6b″, CH benzylic), 4.10 (m, $J_{5,6a}$ and $J_{5,6b}$ not determined due to overlapping of signals, H-5), 4.07 (m, $J_{3,4}$ = 3.2 Hz, H-3), 4.03 (m, $J_{3',4'}$ = 2.7 Hz, H-3′), 4.02 (m, $J_{6a',6b'}$ not determined due to overlapping of signals, H-6b′), 3.98 (m, $J_{5'',6a''}$ and $J_{5'',6b''}$ not determined due to overlapping of signals, H-5″), 3.953 (d, ^2J = 12 Hz, CH benzylic), 3.831 (br t, $J_{5',6a'} = J_{5',6b'}$ = 6.6 Hz, H-5′), 3.504 (dd, $J_{3'',4''}$ = 3.3 Hz, H-3″), 3.431 (s, OCH_3). Anal. Calcd for $C_{89}H_{76}O_{25}$ (1545.49): C, 69.16; H, 4.95. Found: C, 69.07; H, 5.05.

Eluted next was pure **16** (2.8 g, 60.6%): $[\alpha]_D$ +58.3° (*c* 0.44, chloroform); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.93 (C-1), 101.30 (C-1″), 101.13 (C-1′), 76.92 (C-3), 76.20 (C-3′), 75.90 (C-3″), 71.75, 71.27, 71.15, 71.08, 71.00 (2 C, 4 × 1 C, C-2, C-2′, C-2″, C-5, C-5′, C-5″), 70.68 (CH_2 benzylic), 70.07 (2 C, C-4, C-4′), 66.00 (C-4″), 63.00 (C-6), 62.62 (C-6′), 62.18 (C-6″), 56.41 (CH_3); definitive signals in the ^1H NMR spectrum (300 MHz, $CDCl_3$, assigned by selective homonuclear decoupling) were at δ 5.89, 5.86 (2 × br d, $J_{3,4}$ = 3.5 Hz, H-4, H-4′), 5.72 (br d, $J_{3'',4''}$ = 3 Hz, H-4″), 5.46 (dd, $J_{2,3}$ = 9.5 Hz, H-2), 5.33 (dd, $J_{2',3'}$ = 10 Hz, H-2′), 5.18 (dd, $J_{2'',3''}$ = 10 Hz, H-2″), 4.82 (d, $J_{1',2'}$ = 8 Hz, H-1′), 4.65 (d, $J_{1'',2''}$ = 8 Hz, H-1″), 4.52 (d, *J* = 12 Hz, CH_2 benzylic), 4.36 (d, $J_{1,2}$ = 8 Hz, H-1), 4.26 (d, *J* = 12 Hz, CH_2 benzylic), 4.16 (dd, $J_{3,4}$ = 3.5 Hz, H-3), 4.04 (dd, $J_{3',4'}$ = 3.5 Hz, H-3′), 3.89 (br t, $J_{5'',6''}$ = 7 Hz, H-5″), 3.51 (dd, $J_{3'',4''}$ = 3 Hz, H-3″), 3.31 (3 H, CH_3). Anal. Calcd for $C_{89}H_{76}O_{25}$ (1545.49): C, 69.16; H, 4.95. Found: C, 69.73, H, 4.72.

Methyl O-(2,4,6-Tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (17). Compound **16** (2 g) in 2-methoxyethanol (100 mL) was hydrogenated as described above for the preparation of **14**. After processing, pure **17** (1.65 g, 87.7%) was obtained as an amorphous solid having $[\alpha]_D$ +26° (*c* 0.9, chloroform): ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.96 (C-1), 101.26 (C-1′), 100.65 (C-1″), 76.45 (C-3), 76.18 (C-3′), 73.40 (C-2″), 71.75, 71.64 (C-5, C-5′), 71.40 (2 C, C-3″, C-5″), 71.13 (2 C, C-2, C-2′), 70.16 (C-4), 70.07 (C-4′), 6.99 (C-4″), 63.01 (C-6), 62.53 (C-6′), 62.05 (C-6″), 56.47 (CH_3); definitive signals in the ^1H NMR spectrum (300 MHz, 3:1 $CDCl_3$–CD_3OD) were at δ 5.84 (m, 2 H, H-4, H-4′), 5.52 (d, $J_{3'',4''}$ = 3.5 Hz, H-4″), 5.43 (dd, $J_{2,3}$ = 10 Hz, H-2), 5.32 (dd, $J_{2',3'}$ = 10 Hz, H-2′), 4.98 (dd, $J_{2'',3''}$ = 10 Hz, H-2″), 4.77 (d, $J_{1',2'}$ = 8 Hz, H-1′), 4.66 (d, $J_{1'',2''}$ = 8 Hz, H-1″), 4.36 (d, $J_{1,2}$ = 8 Hz, H-1), 4.16 (dd, $J_{3,4}$ = 3.5 Hz, H-3), 4.07 (dd, $J_{3',4'}$ = 3.5 Hz, H-3′), 3.95 (2 H, m, H-5, H-5′), 3.88 (br t, $J_{5'',6''}$ = 6.5 Hz, H-5″), 3.70 (dd, $J_{3'',4''}$ = 3.5 Hz, $J_{2'',3''}$ = 10 Hz, H-3″, appears in pure $CDCl_3$ as a multiplet due to coupling to 3″-OH), 3.36 (s, 3 H, CH_3). Anal. Calcd for $C_{82}H_{70}O_{25}$ (1455.38): C, 67.66; H, 4.77. Found: C, 67.45; H, 4.98.

Conventional benzoylation of **17** gave the fully benzoylated derivative **32** (amorphous solid) in a virtually theoretical yield: $[\alpha]_D$ +72° (*c* 0.6, chloroform); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.96 (C-1), 101.23 (2 C, C-1′, C-1″), 76.64 (C-3), 76.32 (C-3′), 71.78 (C-5), 71.69 (C-3″), 71.43, 71.29 (C-2′, C-5′), 71.19 (C-5″), 71.03 (C-2), 69.96, 70.04 (C-4, C-4′), 69.37 (C-2″), 67.50 (C-4″), 63.01 (C-6), 62.51 (C-6′), 61.57 (C-6″), 56.47 (CH_3); definite signals in the ^1H NMR spectrum (220 MHz, $CDCl_3$) were at δ 5.92, 5.88, 5.79 (3 × br d, $J_{3,4}$ = 3.5 Hz, H-4, H-4′, H-4″), 5.53–5.30 (3 H, m, H-2, H-2′, H-2″), 5.22 (dd, $J_{2,3}$ = 10 Hz, $J_{3,4}$ = 3.5 Hz, H-3″), 5.06, 5.03 (2 × d, $J_{1,2}$ = 8 Hz, H-1′, H-1″), 4.39 (d, $J_{1,2}$ = 8 Hz, H-1). Anal. Calcd for $C_{89}H_{74}O_{26}$ (1559.48): C, 68.54; H, 4.78. Found: C, 68.57; H, 4.70.

Methyl O-(3-O-Benzyl-β-D-galactopyranosyl)-(1→3)-O-β-D-galactopyranosyl-(1→3)-β-D-galactopyranoside (19). A solution of **16** (1.55 g) in methanol (50 mL), rendered strongly alkaline by addition of methanolic sodium methoxide (~1 M), was kept at 50 °C overnight. The mixture was cooled to room temperature and treated as described above for the preparation of **15**. The compound solidified on concentration and was chromatographically homogeneous. Crystallization from water–acetone gave pure **19** (0.51 g, 83.8%): mp 161–163 °C; $[\alpha]_D$ +42.5° (*c* 0.4, water); ^{13}C NMR (25 MHz, D_2O) δ 104.4 (C-1), 104.1 (C-1′), 103.6 (C-1″), 82.6 (C-3), 82.2 (C-3′), 79.9 (C-3″), 75.1 (C-5″), 74.8 (2 C, C-5, C-5′), 71.3 (triplet in an "off resonance" spectrum, CH_2 benzylic), 70.3 (2 C, C-2′, C-2″), 70.0 (C-2), 68.6, 68.4 (C-4, C-4′), 65.3 (C-4″), 61.0 (3 C, C-6, C-6′, C-6″), 57.2 (CH_3). Anal. Calcd for $C_{26}H_{40}O_{16}$ (608.58): C, 51.30; H, 6.62. Found: C, 51.16; H, 6.47.

Methyl O-β-D-Galactopyranosyl-O-(1→3)-β-D-galactopyranosyl-(1→3)-β-D-galactopyranoside (18). (a) A solution of **19** (0.3 g) in water was treated with hydrogen as described for the preparation of **14**. The mixture was filtered, concentrated, and an equal amount of ethanol was added. After filtration, more ethanol was added to the clear solution, whereupon the compound readily crystallized at room temperature (0.2 g, 78.4%). After drying at 100 °C for 6 h the glycoside **18** showed mp 233–235 °C and $[\alpha]_D$ +31.4° (*c* 0.7, water): ^{13}C NMR (75 MHz, D_2O) δ 104.40 (C-1″), 104.14 (C-1′), 103.57 (C-1), 82.55 (C-3), 82.15 (C-3′), 75.18 (C-5″), 74.86 (C-5), 74.78 (C-5′), 72.65 (C-3″), 71.18 (C-2″), 70.35 (C-2′), 69.95 (C-2), 68.69 (C-4″), 68.59 (C-4), 68.43 (C-4′), 61.05 (3 C, C-6, C-6′, C-6″), 57.21 (CH_3). Anal. Calcd for $C_{19}H_{36}O_{16}$ (518.46): C, 44.01; H, 6.61. Found: C, 43.79; H, 6.68.

(b) Compound **17** was treated as described for the preparation of **19** and the product, crystallized as described above, was identical (mp, ^{13}C NMR) with the above described substance **18**.

Methyl O-(2,3,4,6-Tetra-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (20). A solution of the nucleophile **14** (0.98 g, 1 mmol), the glycosyl halide **6** (1.3 g, 1.2 mmol), and *sym*-collidine (0.133 mL, 1 mmol) in toluene (10 mL) was added at 0 °C to a solution of silver triflate (0.36 g, 1.4 mmol). The mixture was stirred while it was allowed to come to room temperature. After 4 h, the slightly acidic solution was neutralized and worked up as described above. Chromatography gave the amorphous derivatives **20** (1.25 g, 61.4%), moving on TLC only slightly slower than the nucleophile **4**, $[\alpha]_D$ +57° (*c* 1.4, chloroform): ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.93 (C-1), 101.21 (C-1‴), 101.07 (2 C, C-1′, C-1″), 76.37 (C-3), 76.26 (C-3′), 76.13 (C-3″), 71.78 (2 C, C-5, C-5′), 71.56 (C-3‴), 71.43, 71.16 (2 × 2 C, C-2′, C-2″, C-5″, C-5‴), 70.97 (C-2), 70.01, 69.88 (2 C, 1 C, C-4, C-4′, C-4″), 69.34 (C-2‴), 67.47 (C-4‴), 63.01 (C-6),

62.51, 62.35 (C-6′, C-6″), 61.52 (C-6‴), 56.4 (CH_3). Anal. Calcd for $C_{116}H_{96}O_{34}$ (2033.92): C, 68.49; H, 4.75. Found: C, 68.72; H, 5.07.

Methyl O-(2,4,6-Tri-O-benzoyl-3-O-benzyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (22). A solution of the nucleophile **14** (1.25 g, 1.27 mmol), the glycosyl donor **9** (1.64 g, 1.52 mmol), and *sym*-collidine (0.2 mL, 1.5 mmol) in toluene–nitromethane (1:1, 15 mL) was added at 0 °C to a solution of silver triflate (0.47 g, 1.82 mmol) in the same solvent (10 mL). The mixture was stirred, while it was allowed to warm to room temperature, and stirring was continued overnight. After usual processing and chromatography, the major component of the reaction mixture (**22**) was obtained as an amorphous solid (1.41 g, 55%): $[\alpha]_D$ +46° (*c* 0.9, chloroform); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.93 (C-1), 101.18 (C-1‴), 101.10, 100.97 (C-1′, C-1″), 76.53 (C-3), 76.21, 75.94 (C-3′, C-3″), 75.83 (C-3‴), 71.75, 71.56, 71.48, 71.21, 71.13, 70.97 (2 C, 4 × 1 C, 2C, C-2, C-2′, C-2″, C-2‴, C-5, C-5′, C-5″, C-5‴), 70.68 (CH_2 benzylic), 69.99 (3 C, C-4, C-4′, C-4″), 66.01 (C-4‴), 63.01 (C-6), 62.51, 62.43 (C-6′, C-6″), 62.08 (C-6‴), 56.42 (CH_3). Anal. Calcd for $C_{116}H_{98}O_{33}$ (2019.94): C, 68.97; H, 4.89. Found: C, 68.82; H, 5.06.

Methyl O-(2,4,6-Tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (23). Compound **22** (0.9 g) was treated as described for the preparation of **17** to afford amorphous **23** (0.8 g, 93.5%): $[\alpha]_D$ +22° (*c* 0.8, chloroform); ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.90 (C-1), 101.18, 101.07 (C-1′, C-1″), 100.35 (C-1‴), 76.21 (2 C, C-3, C-3′), 75.62 (C-3‴), 73.56 (C-2‴), 71.72 (2 C, C-5, C-5′), 71.56 (C-3‴), 71.48 (C-5‴), 71.40, 71.16 (2 × 2 C, C-2, C-2′, C-2″, C-5″), 69.99 (3 C, C-4, C-4′, C-4″), 69.83 (C-4‴), 63.01 (C-6), 62.51, 62.29 (C-6′, C-6″), 61.89 (C-6‴), 56.44 (CH_3). Anal. Calcd for $C_{109}H_{92}O_{33}$ (1929.82): C, 67.83; H, 4.80. Found: C, 67.48; H, 4.87.

Methyl O-(β-D-Galactopyranosyl)-(1→3)-O-β-D-galactopyranosyl-(1→3)-O-β-D-galactopyranosyl-(1→3)-β-D-galactopyranoside (21). (a) A solution of **20** (1 g) in methanol (150 mL) was treated as described for the preparation of **19**. Crystals that appeared in the warm solution were separated, washed with methanol, and dissolved in water. The aqueous solution was neutralized with Dowex 50 W (H^+ form) resin and concentrated to a small volume. Compound **21** (0.11 g), which crystallized on addition of methanol, showed mp 215–218 °C and $[\alpha]_D$ +33.3° (*c* 0.8, water): ^{13}C NMR (75 MHz, D_2O) δ 104.41 (C-1‴), 104.11, 104.03 (C-1′, C-1″), 103.55 (C-1), 82.55 (C-3), 82.15 (2 C, C-3′, C-3″), 75.13 (C-5‴), 74.74 (C-5), 74.76 (2 C, C-5′, C-5″), 72.62 (C-3‴), 71.15 (C-2‴), 70.32 (2 C, C-2′, C-2″), 69.92 (C-2), 68.67 (C-4), 68.48 (2 C, C-4′, C-4″), 61.0 (4 C, C-6, C-6′, C-6″, C-6‴), 57.18 (CH_3). Anal. Calcd for $C_{25}H_{44}O_{21}$ (680.60): C, 44.11; H, 6.51. Found: C, 43.95; H, 6.68.

The material in the combined mother liquors was neutralized as described above and freeze-dried to give more **21** (0.19 g, total yield 90%), showing the same spectral characteristics as the crystalline material.

(b) When compound **23** was treated as described above in a, it yielded material indistinguishable from the above described substance.

Methyl O-(2,3,4,6-Tetra-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (24). A solution of the nucleophile **17** (1.45 g, 1 mmol), the glycosyl donor **6** (1.3 g, 1.2 mmol), and *sym*-collidine (0.16 mL, 1.2 mmol) in toluene–nitromethane (1:1, 10 mL) was added at room temperature to a solution of silver triflate (0.36 g, 1.4 mmol) in the same solvent (10 mL), and the mixture was stirred overnight. TLC then showed that almost all of the nucleophile had reacted and that the mixture contained a major component (**24**), moving on TLC slightly faster than **17**. Processing in the usual manner gave **24** (1.35 g, 69%) as an amorphous solid having $[\alpha]_D$ +45° (*c* 0.7, chloroform): ^{13}C NMR (75 MHz, $CDCl_3$) δ 101.90 (C-1), 101.16 (C-1⁗), 101.02, 100.89 (2 C, 1 C, C-1′, C-1″, C-1‴), 76.29 (C-3), 76.10 (2 C, C-3′, C-3″), 75.65 (C-3‴), 71.75, 71.40, 71.13 (2 C, 3 C, 2 C, C-2′, C-2″, C-2‴, C-5, C-5′, C-5″, C-5‴), 71.56 (C-3⁗), 70.92 (C-2), 69.96, 69.83 (2 × 2 C, C-4, C-4′, C-4″, C-4‴), 69.29 (C-2⁗), 67.42 (C-4⁗), 62.99 (C-6), 62.51, 62.24 (1 C, 2 C, C-6′, C-6″, C-6‴), 61.47 (C-6⁗), 56.42 (CH_3). Anal. Calcd for $C_{143}H_{118}O_{42}$ (2508.37): C, 68.46; H, 4.74. Found: C, 68.08; H, 4.97.

Methyl O-β-D-Galactopyranosyl-(1→3)-O-β-D-galactopyranosyl-(1→3)-O-β-D-galactopyranosyl-(1→3)-O-β-D-galacopyranosyl-(1→3)-β-D-galactopyranoside (25). A solution of the above described benzoate **24** (1.3 g) in methanol (200 mL) was treated as described above for the preparation of **19**. The jellylike materials that separated from the warm solution was treated as described above for the preparation of **21** and freeze-dried to give snow white **25** (0.32 g, 74.5%) as an amorphous, hygroscopic solid: $[\alpha]_D$ +34.6° (*c* 0.3, water); ^{13}C NMR (75 MHz, D_2O) δ 104.40 (C-1⁗), 104.10 (3 C, C-1′, C-1″, C-1‴), 103.57 (C-1), 82.53 (C-3), 82.07 (3 C, C-3′, C-3″, C-3‴), 75.16 (C-5⁗), 74.78 (4 C, C-5, C-5′, C-5″, C-5‴), 72.62 (C-3⁗), 71.15 (C-2⁗), 70.32 (3 C, C-2′, C-2″, C-2‴), 69.92 (C-2), 68.67 (C-4⁗), 68.59 (C-4), 68.48 (3 C, C-4′, C-4″, C-4‴), 61.00 (5 C, C-6, C-6′, C-6″, C-6‴, C-6⁗), 57.18 (CH_3).

The remaining solution was processed as described above for the mother liquor after crystallization of **21**, to give another crop of **25** having the same ^{13}C NMR characteristics as the above described substance.

Methyl O-(2,3,4,6-Tetra-O-benzoyl-β-D-galacopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-O-(2,4,6-tri-O-benzoyl-β-D-galactopyranosyl)-(1→3)-2,4,6-tri-O-benzoyl-β-D-galactopyranoside (26). A solution of the nucleophiles **17** (0.363 g, 0.25 mmol), the glycosyl donor **12** (0.63 g, 0.3 mmol), and *sym*-colllidine (0.033 mL, 0.25 mmol) was added at room temperature to a solution of silver triflate (0.103 g, 0.4 mmol). After 2 h when all glycosyl donor was consumed, the slightly acidic solution was processed as described for the preparation of **20**, and chromatography gave pure, amorphous **26** (540 mg, 62%): $[\alpha]_D$ +33.8° (*c* 1, chloroform); diagnostically important lines in the ^{13}C NMR spectrum (67.5 MHz, $CDCl_3$) were at δ 101.95 (C-1), 101.22 (C-1⁗⁗), 101.07, 100.87 (2 or 3 C, 2 or 3 C, C-1′, C1″, C-1‴, C-1⁗, C-1⁗⁗), 76.39 (C-3), 76.16, 76.08, 75.68 (1 C, 1 C, 2 C, C-3′, C-3″, C-3‴, C-3⁗), 75.61 (C-3⁗⁗), 71.61 (C-3⁗⁗), 69.40 (C-2⁗⁗), 67.56 (C-4⁗⁗), 63.07 (C-6), 62.55, 62.36, 62.29 (1 C, 1 C, 3 C, C-6′, C-6″, C-6‴, C-6⁗, C-6⁗⁗), 61.53 (C-6⁗⁗), 56.40 (CH_3). In the ^1H NMR spectrum (500 MHz, $CDCl_3$) seven broad doublets for H-4 through H-4⁗⁗ were present at δ 5.83, 5.82, 5.77, 5.76, 5.71, 5.69, and 5.67 each showing a coupling constant $J_{3,4} \sim 3.5$ Hz. Anal. Calcd for $C_{197}H_{162}O_{58}$ (3457.26): C, 68.43; H, 4.72. Found: H, C, 68.42; H, 4.86.

Methyl O-β-Galactopyranosyl-(1→3)-O-β-D-galactopyranosyl-(1→3)-O-β-D-galactopyranosyl-(1→3)-O-β-D-galactopyranosyl-(1→3)-O-β-D-galacopytranosyl-(1→3)-O-β-D-galacopyranosyl-(1→3)-β-D-galacopyranoside (27). A mixture of **26** (125 mg) in methanol (50 mL) was treated with methanolic sodium methoxide (1 M) until strongly alkaline, stirred at 50 °C until all solids dissolved, and then left overnight. The separated gel was collected, washed with methanol, and dissolved in water. This solution was treated with a little Dowex 50 W (H^+ form) resin and freeze-dried, to give **27** as an amorphous hygroscopic solid (37 mg, 88%): $[\alpha]_D$ +36.2° (*c* 0.4, water); ^{13}C NMR (75 MHz, D_2O) δ 104.40 (C-1⁗⁗), 104.08 (5 C, C-1′, C-1″, C-1‴, C-1⁗, C-1⁗⁗), 103.57 (C-1), 82.53 (C-3), 82.07 (5 C, C-3′, C-3″, C-3‴, C-3⁗, C-3⁗⁗), 75.18 (C-5⁗⁗), 74.81 (6 C, C-5, C-5′, C-5″, C-5‴, C-5⁗, C-5⁗⁗), 72.65 (C-3⁗⁗), 71.15 (C-2⁗⁗), 70.35 (5 C, C-2, C-2′, C-2″, C-2‴, C-2⁗), 69.95 (C-2), 68.67 (C-4⁗⁗), 68.59 (C-4), 68.51 (5 C, C-4′, C-4″, C-4‴, C-4⁗, C-4⁗⁗), 61.03 (7 C, C-6, C-6′, C-6″, C-6‴, C-6⁗, C-6⁗⁗, C-6⁗⁗), 57.21 (CH_3).

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