Arylbis(arylthio)sulfonium Salts as Reagents for the Synthesis of 2-Deoxy-β-glycosides

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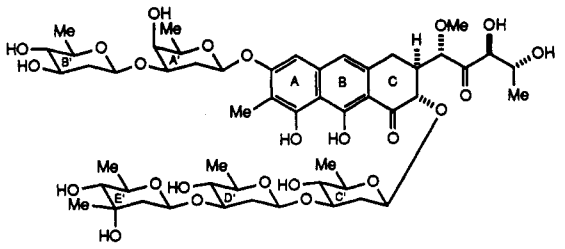
The title sulfonium salts undergo electrophilic addition to glycals in the presence of alcohols to form principally β-glycosides. A substituent effect study has shown that the reagent with a *p*-tolylthio group is the most face-selective. By variation of the alcohol nucleophile, it has been shown that face selectivity is also dependent on the structure of the nucleophile. One instance of double diastereodifferentiation was uncovered when the racemic alcohol **23.5** was used in a reaction with tribenzyl glucal **22.1**. The effect of glycal substitution on the face selectivity has led to the postulation of a heretofore unrecognized and still unexplained stereoelectronic effect.

Introduction

The aureolic acid group of antibiotics, illustrated by the eponymous aureolic acid 1 and also including the chromomycins and olivomycins, have been a subject of study since their isolation in 1953.[1] One of the major problems

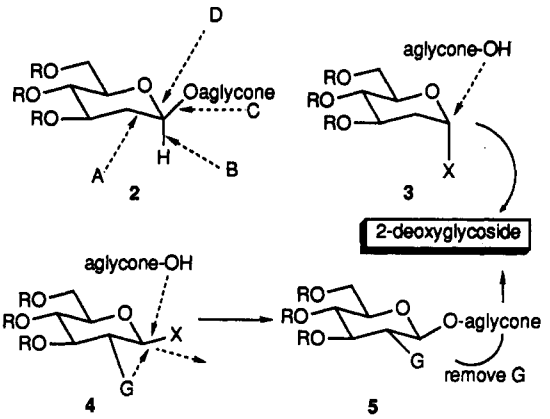


1 AUREOLIC ACID

to be solved in a projected total synthesis of these antibiotics is the forging of the 2-deoxy-β-glycoside linkages between the saccharide chains and the aglycon at positions 2 and 6 and the interglycosidic bonds as well.[2,3] In principle, there are four different bonds one could create in ultimate stereoselective steps to achieve the 2-deoxy-β-glycoside goal as indicated below in generalized structure 2 (Scheme I). In practice, the C–C bond formation gambit A has been reported only once for the synthesis of 4-substituted 1-methoxytetrahydropyrans, not closely related to the problem under discussion.[4] Furthermore, the C–H bond B and endocyclic C–O bond D routes are not common.[5] The vast majority of approaches have involved glycosidations, the C bond pathway, and these can be further categorized. The most direct C bond approach is shown in structure 3 where a simple S_N2 displacement by an aglycon on an α-configured leaving group in a 2-deoxysugar is depicted.

The requirements for success of the S_N2 are either a special leaving group or a special catalyst so that the S_N1-like pathway can be avoided.[6-8] Another version of

Scheme I



the C pathway involves the solvolysis of a leaving group at the anomeric center with participation of an α-configured functional group at C-2 to afford glycoside (outlined in structures 4 and 5) which is then converted to the desired 2-deoxysugar 2 by removal of the C-2 function.[9] An important variation of the C-bond theme is to prepare structures such as 5 via direct addition of an electrophile and aglycon to sugar glycals (Scheme II). To pursue the Scheme II strategy, the solution to the 2-deoxy-β-glycoside problem can be conceptualized as the identification of an electrophile which demonstrates high selectivity for below-plane attack of glycals.

A thorough search of the literature of glycal additions[10] revealed that the below-plane approach is the generally preferred mode for electrophilic reagents, with the exceptions of above-plane attack of iodine[11] and selenium based electrophiles.[12] It should be noted that the ste-

(1) (a) Remers, W. *The Chemistry of Antitumor Antibiotics*: Wiley: New York, 1979; Vol. 1, Chapter 3. (b) Franck, R. W.; Weinreb, S. M. *Studies in Natural Product Chem.* Rahman, A., Ed.; Elsevier: Amsterdam, 1989; p 173.

(2) (a) For the most recent bibliography on the aureolic acid synthesis problem: Roush, W. R.; Lin, X.; Straub, J. A. *J. Org. Chem.* **1991**, *56*, 1649–1655.

(3) For the most recent paper discussing the binding of these drugs to DNA: Patel, D. J.; Gao, X. *Biochemistry* **1990**, *29*, 10940–10956.

(4) (a) Perron, F.; Albizati, K. *J. Org. Chem.* **1987**, *52*, 571–573. (b) Martin, V. A.; Perron, F.; Albizati, K. F. *Tetrahedron Lett.* **1990**, *31*, 301–304. (c) Perron-Siera, F.; Promo, M. A.; Martin, V. A.; Albizati, K. F. *J. Org. Chem.* **1991**, *56*, 6188–6199.

(5) (a) For a recent compilation of references, see our preliminary communication: Ramesh, S.; Kaila, N.; Grewal, G.; Franck, R. W. *J. Org. Chem.* **1990**, *55*, 5–7, ref 8. (b) For a more recent bond D report: Barrett, A. G. M.; Bezuidenhoudt, B. C. B.; Melcher, L. M. *J. Org. Chem.* **1990**, *55*, 5196–5197. (c) For a further B bond paper: Crich, D.; Ritchie, D. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 945–954.

(6) For a recent example of the use of an insoluble silver salt catalyst: Binkley, R. W. *J. Carbohydr. Chem.* **1990**, *9*, 507.

(7) In the special case of an axial substituent at C-3, the β-glycoside is thermodynamically favored; thus, equilibration of a mixture will yield the desired β-isomer. For a recent elegant example in the synthesis of cytovaricin, see: Evans, D. A.; Kaldor, S. W.; Jones, T. K.; Clardy, J.; Stout, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 7001–7031.

(8) Roush, W. R.; Lin, X.-F. *J. Org. Chem.* **1991**, *56*, 5740–5742.

(9) For versions of solvolysis with participation and eventual removal that were omitted from ref 5a above: (a) Gurjar, M. K.; Ghosh, P. K. *Ind. J. Chem.* **1988**, *27B*, 1063. (b) Kiss, L. *Acta Chim. Acad. Sci. Hung.* **1978**, *97*, 345.

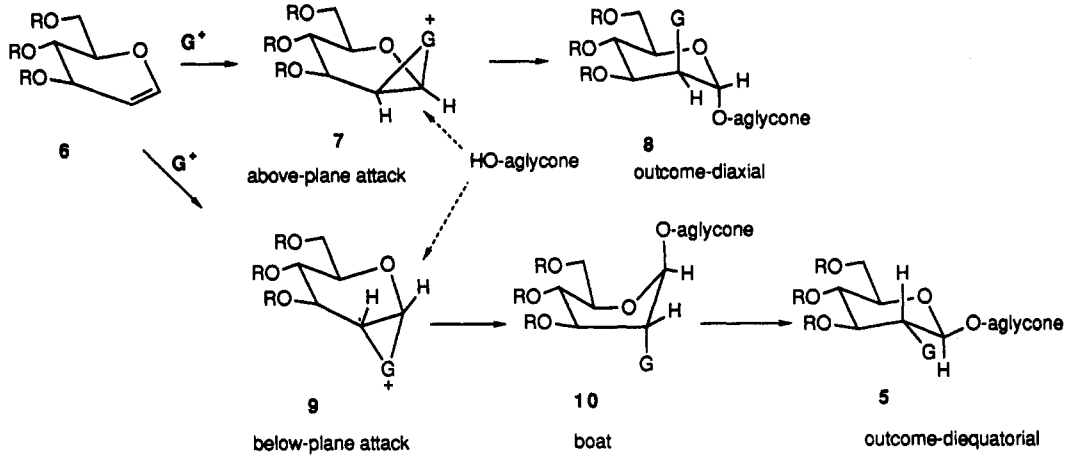
(10) (a) Grewal, G. Doctoral dissertation, CUNY 1991, the literature review chapter will be published in due course. (b) Subsequent to the review in a, an application of the elegant dioxirane method of functionalizing glycals to eventually afford 2-deoxyglycosides has been described: Gervay, J.; Danishefsky, S. J. *J. Org. Chem.* **1991**, *56*, 5448–5451.

(11) Recent examples of studies with iodonium reagents other than from the Thiem group: (a) Horton, D.; Priebe, W.; Sznaidman, M. *Carbohydr. Res.* **1990**, *205*, 71–86. (b) Suzuki, K.; Sulikowski, G. A.; Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1990**, *112*, 8895–8902.

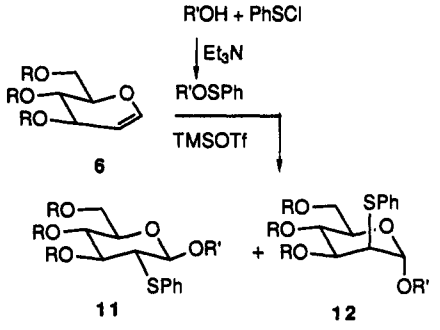
(12) (a) Jaurand, G.; Beau, J.-M.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1981**, 572. (b) Perez, M.; Beau, J. M. *Tetrahedron Lett.* **1989**, *30*, 75. (c) Kaye, A.; Neidle, S.; Reese, C. B. *Tetrahedron Lett.* **1988**, *29*, 2711.

0022-3263/92/1957-2084$03.00/0

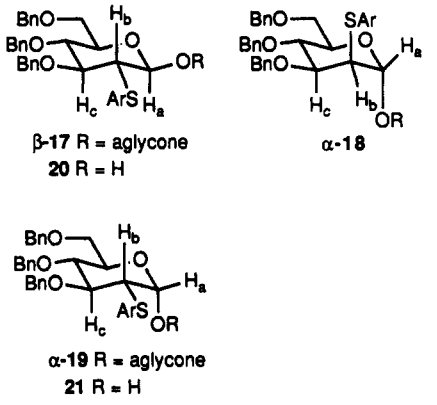
Scheme II



Scheme III



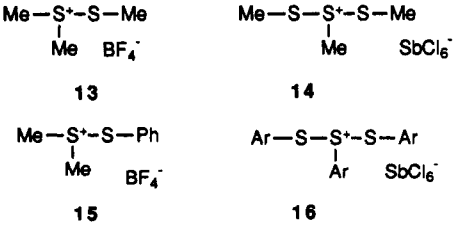
Scheme IV



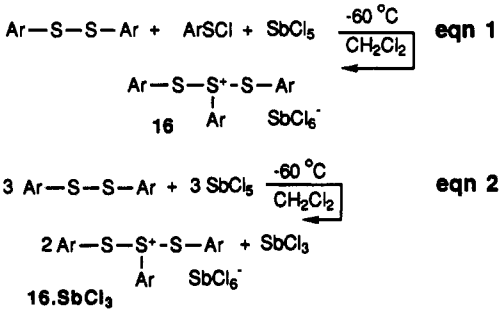
reochemical outcome in the selenium electrophile series is dependent on reaction conditions, since the initial selenonium species can be reversible.[13] From the long list of electrophiles affording the desired below-plane attack, sulfonium species were chosen for examination, since the required 2-deoxy glycosides would be easily accessible via replacement of the sulfur at C-2 by hydrogen. It is the development of a practical reagent that is the subject of this paper.[14]

Results

Reagents and General Procedure. An important lead reference for our work was the paper of Ito and Ogawa where phenylsulfenate esters of the desired aglycon, activated with TMS triflate, in the presence of glycals, afforded largely β-glycosides[15] (Scheme III). Although this method was successful in our hands,[16] the extra step of preparing and purifying the sulfenate ester precursor was onerous and the decision was made to study preformed sulfonium salts which could simply be mixed with the aglycon and the glycal. The methyl reagents **13** and **14**,



although easy to use because of their crystallinity and stability at room temperature,[17] did not give useful diastereofacial selectivity.[18] The phenyl reagent **15** did not give clean results[19] whereas the trisaryl reagent **16** showed the most promise. The reagent **16** can be prepared in two ways as shown in eqs 1 and 2 (the ·$SbCl_3$ signifying the presence of 0.5 equiv of $SbCl_3$ for each equiv of **16**).[20]



The glycosylation reaction could be carried out in two

(13) (a) Reference 12b. (b) Sinay, P. Unpublished results; we thank Prof. Sinay for informing us of these experiments.

(14) A partial report of this investigation was presented by the authors at the American Chemical Society Meeting, April 1990, Boston, ORGN 0363 and CARB 0042.

(15) Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1987**, *28*, 2723.

(16) Ramesh, S.; Franck, R. W. *Chem. Commun.* **1989**, 960.

(17) (a) For a review of reactive sulfonium salts, see: Capozzi, G.; Modena, G. *Organic Sulfur Chemistry: Theoretical and Experimental Advances*; Bernardi, F., Csizmadia, I. G., Mangini, A., Eds.; Elsevier: Amsterdam, 1985. For selected examples of sulfidoetherification using reagents A and B: (b) O'Malley, G. J.; Cava, M. P. *Tetrahedron Lett.* **1985**, *26*, 6159. (c) Capozzi, G.; Lucchini, V.; Marcuzzi, V.; Modena, G. J. *Chem. Soc., Perkin Trans. 1* **1981**, 3106. (d) Capozzi, G.; Lucchini, V.; Modena, G. *Rev. Chem. Intermediates* **1979**, *2*, 347. (e) Trost, B. M.; Shibata, T.; Martin, S. J. *J. Am. Chem. Soc.* **1982**, *104*, 3228–3230.

(18) Reagent 13 plus glycals: ref 5a. For reagent 15 plus glycals: Pasquato, L.; Franck, R. W. Unpublished results, 1991.

(19) Kaila, N. Doctoral dissertation, CUNY, 1991. Kaila, N.; Franck, R. W. Manuscript in preparation.

(20) Gybin, A. S.; Smit, W. A.; Bogdanov, V. S.; Krimer, M. Z.; Kalyan, J. B. *Tetrahedron Lett.* **1980**, *21*, 383.

ways to give essentially equivalent results. Our usual method was to cool an equimolar solution of aglycon and glycal in methylene chloride to −60 °C. Then a −60 °C solution of sulfonium salt was quickly added via syringe technique. Alternately, a −60 °C solution of aglycon and sulfonium salt was first prepared, followed by addition of glycal. In some cases the nucleophilicity of the aglycon hydroxyl group (ROH) was enhanced by prior stannyl ether formation ($ROSnBu_3$) in order to improve yields.[21] The third permutation, preforming a solution of glycal plus sulfonium salt, followed by addition of aglycon, failed to give desired product, but did consume glycal. In every case, the reaction was then processed by addition of aqueous $NaHCO_3$ followed by separation of the organic product which was subjected to chromatography to remove diaryl disulfide byproduct from the glycoside mixture, illustrated for tribenzyl glucal in Scheme IV. The reagent containing a residual 0.5 equiv of $SbCl_3$ (labeled **16·SbCl₃**) caused a little more degradation of isopropylidene blocking groups and more epimerization at C-1 of the desired β-glycoside to afford a *cis*-α-glycoside (α-**19**) where the PhS at C-2 was equatorial. In some of the reactions we observed the α and β anomers of 3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylthio)-D-glucose (**20** and **21**) as the byproducts due to incomplete removal of water from the system.

Structure Assignment. Proton NMR data were used to assign the relative stereochemistry of the isomeric glycosides in most cases. The β-stereochemistry of the glycosidic linkage in glycosides β-**17** was assigned on the basis of the H_b signal. This proton appears at high field compared to the other ring protons since it is attached to the thiophenyl-substituted carbon C-2 and has an axial orientation. It shows a doublet of doublets with two large diaxial couplings (J = 8–12 Hz) to H_a and H_c. The peak for the H_a proton is merged with the ring protons (due to its axial geometry it appears at high field compared to the H_a proton in α glycosides, see below).

The configuration of glycosides α-**18** was characterized by the proton H_a. This proton is at low field compared to the other ring protons because it is anomeric and is equatorial. It appears as a doublet with small diequatorial coupling (J = 0–4 Hz) to H_b. Only in some of the cases does proton H_b appear at sufficiently high field to be resolved from the ring protons. It shows a doublet of a doublet due to two small couplings with H_a (diequatorial) and H_c (equatorial-axial, J = 0–4 Hz). For compounds where the H_b proton is overlapped by other proton signals, the glycoside structure is assigned by a process of elimination or by proton NMR comparison with α glycosides of similar structure. These assignments were further confirmed by 2D homonuclear COSY of one representative example from the β and α series where each ring proton was identified. The *cis*-α-glycosides **19** exhibited a low-field doublet for H_a. This proton is distinct from the other ring protons and shows small equatorial–axial coupling with H_b. In most cases the H_b proton signal is at high field and appears as a doublet of a doublet showing one large diaxial (with H_c) and one small equatorial–axial (with H_a) coupling. The minor products **20** and **21** were assigned on the same basis as β and *cis*-α-glycosides respectively, except that signals for the aglycon protons are absent. The signal for the hydroxy proton at the anomeric center was easily confirmed by D_2O exchange. A homonuclear 2D NMR of one representative case in each series was obtained.

Effect of Aglycon on Diastereoselectivity. Worthy of note is that the face selectivity is highly dependent on the nature of the nucleophile (Table I). The variation is not regular, in that two secondary alcohols (entries 4 and 5) afford the highest β-selectivity while 2-propanol (entry 2) gives the poorest. Note also the variation in selectivity for phenolic aglycons (entries 6–9). It should be added that the "yield" entry for the isolated β- and α-glycosides does not reflect the total below-plane mode for the glucal substrate. In almost every case, the material balance is accounted for by pyranose product where adventitious water is the nucleophile toward an intermediate derived from below-plane attack or by some *cis*-α-**19** material. Therefore, an additional column entry for total below-plane attack is included. Most unusual is a double stereodifferentiation result reported in Table I, entry 5. Thus, the acyloin used was racemic; therefore, two β-diastereomers were expected to be formed in roughly equal amounts, as we had observed earlier in the sulfenate ester series.[14] In the event, the two β isomers were isolated as 10/1 mixture. This enantiomer selection of racemic aglycons in a glycosidation process is a rare event. A similar discrimination in acyloin glycosides has also been noted by Thiem's group[22] though only in 5% yield. In a related experiment, van Boeckel et al. have observed different α/β glycoside ratios when performing Koenigs–Knorr glucosylations of a D- and L-glucofuranoside with the same donor.[23] Enantiomer selection has also been observed during enzymic glycosylation of racemic alcohols by Tanaka's group[24] and also to a moderate extent by Satoh and co-workers.[25] Preliminary application of our method to other racemic alcohols (e.g., tetralol, α-methylbenzyl alcohol) to determine what structural parameters of the racemic alcohols permit one enantiomer to be selected has to date failed to uncover an aglycon with a measurable stereodifferentiation other than the acyloin **23.5**.

Effect of Arylthio Substituents on Face Selectivity. It was found that that the *p*-tolyl reagent gave the best β-selectivity in our test systems using tribenzyl glucal as substrate (Tables II and III). The rather unselective test nucleophiles phenol and methanol were chosen so that any effect of the arylsulfur group would not be obscured by the innate diastereoselectivity of the aglycons. A rough Hammett plot showed that a reasonable correlation would be observed if only the Cl, H, and Me substituents were considered. The *p*-OMe results foiled our attempts at a correlation.[26]

Effect of Glycal Structure on Face Selectivity. To determine what effects the rigidity of the glycal might have on selectivity, the glucals shown in entries 24 and 25 in Table IV and entries 32 and 33 in Table V were tested. These experiments were complicated by the fact that extreme care to avoid traces of acid was necessary to prevent some loss of the acetonide and benzylidene blocking groups of the glucal. The effects of the absence or presence of axial and equatorial oxygen substituents at carbons 3 and 4 of the glycal were tested with the other entries in Tables IV and V. Also worthy of note is that a furanoid glycal **24** can be used with these sulfur reagents. With regard to the compatibility of our glycosylating system with other

(21) Thiem, J.; Klaffke, W. *J. Org. Chem.* **1989**, *54*, 2006. We are indebted to Prof. Thiem for the access to his results prior to publication.

(22) Gerken, M. Doctoral Dissertation, Universität Hamburg, 1983. We are indebted to Prof. Thiem for informing us of these results.

(23) Spijker, N. M.; van Boeckel, C. A. A. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 180–183.

(24) Itano, K.; Yamasaki, K.; Kihara, C.; Tanaka, O. *Carbohydr. Res.* **1980**, *87*, 27.

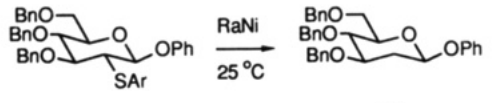
(25) Ooi, Y.; Mitsuo, N.; Satoh, T. *Chem Pharm. Bull.* **1985**, *33*, 5547.

(26) In unpublished work at the University of Padova, *p*-methoxyarylsulfonium species have been observed to undergo electron-transfer to form radical cations. Thus, the reagent may operate by a mechanism different from the others in our series: Modena, G.; Lucchini, V.; Capozzi, G.; De Lucchi, O. Unpublished results.

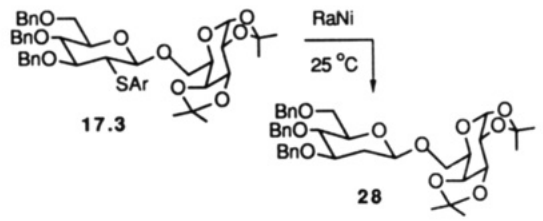
24 25 26

possible alcohol protecting groups, *tert*-butyldiphenylsilyl and SEM groups survive. However, we have not elaborated conditions for using ester-blocked glycals such as triacetyl glucal which undergo Ferrier rearrangement and decomposition with our reagents.[9,19]

The routine completion of the 2-deoxy-β-glycoside synthesis required the removal of the 2-arylthio group. Representative examples, chosen for their potential sensitivity to desulfurization, were desulfurized using Raney nickel with no problem.



17.6 27



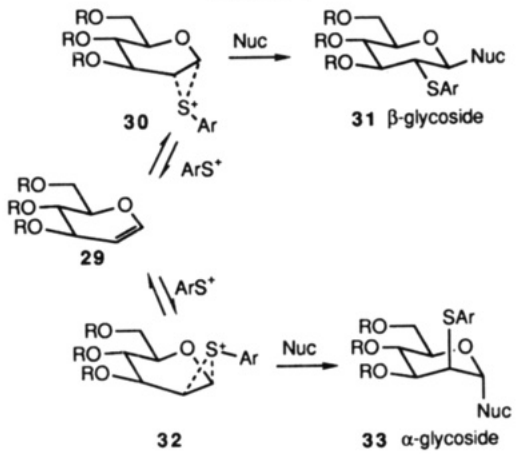
17.3 28

Discussion

Although our stated goal of developing a practical and reasonably general method for 2-deoxy-β-glycosidation has been realized, the results raise some intriguing questions about the detailed mechanism of the reaction and the nature of the intermediate species. The variation of the observed face selectivity with the structure of the nucleophile can be rationalized in two ways. Scheme V illustrates an argument which requires that two stereoisomeric episulfonium ions are formed reversibly whereupon the product-determining steps are governed by the different rates of α and β nucleophilic opening. Hence, each nucleophile would afford its unique product stereochemistry depending on its own α and β proclivity.

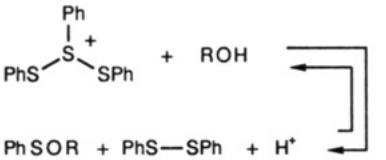
The difficulty with this simple scheme is that even though the required reversibility of episulfonium salt formation has been observed in the cyclooctyl system[27] it has not been seen in glycoside experiments by any of the groups working in the field. As noted above, reversibility of episelenonium species has been detected in glycosidation studies.[28] A second difficulty with Scheme V is that it does not account for the substituent effect on face selectivity produced by the arylthio group. To account for the effect of both the electrophile and the nucleophile on the face selectivity observed, it seems necessary to invoke a species where the electrophile and nucleophile are preassociated. In the Results above, we have already shown that premixing of these species afforded a useful glycosidation

Scheme V



30 31 β-glycoside 29 32 33 α-glycoside

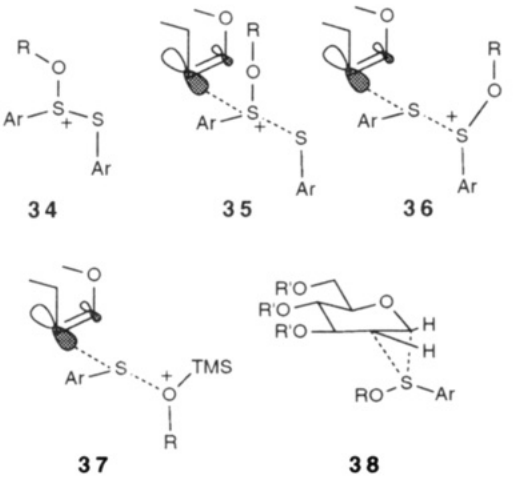
reagent. The simplest preassociation pathway would be to postulate that our method simply preforms the Ogawa sulfenate ester reagent as outlined in eq 3, where in our case the sulfenate ester would be activated by H^+ as opposed to TMS^+ in the Ogawa version. However, the



eqn 3

comparative data for the Ogawa route and our method in Table VI, although showing some similarities, have enough disagreement to convince us that the reagents are, in fact, not identical. Unfortunately, it has not been possible to carry out both methods at the same temperature to control for that variable.

Speculation about the trajectory of attack of the glycal double bond on the positive sulfur species has led us to the tentative conclusion that the reactive species is a dithiosulfenate species **34**. In one postulated transition-state



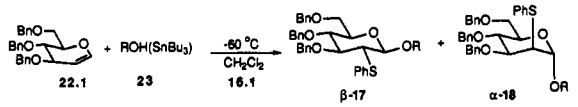
34 35 36 37 38

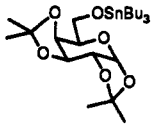
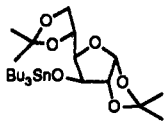
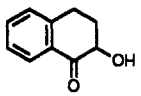
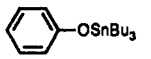
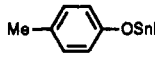
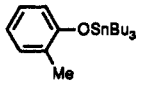
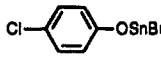
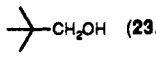
35 for back-side-in-line p-bond nucleophilic attack on the central (sulfinyl) sulfur, it can be seen that the aglycon and the glycal can interact through space as the glycal begins to bond to the sulfur, and a face-differentiating interaction can be envisaged. Similar attack on the sulfenyl sulfur, as shown in **36**, would change the nature of the aglycon–glycal contact. On the other hand, similar back-side attack on the simple TMS-activated sulfenate ester **37** does not seem to require a close interaction of aglycon and glycal. If the reaction proceeded by an addition–elimination

(27) Smit, W. A.; Zefirov, S.; Bodrikov, I. V.; Krimer, M. Z. *Acc. Chem. Res.* **1979**, *12*, 282.

(28) (a) Ito, Y.; Ogawa, T. *Tetrahedron* **1990**, *46*, 89. In two parallel experiments (phenylseleno)- and (phenylthio)sialic acid adducts, were treated with Lewis acid. The phenylseleno adduct reversed and afforded some starting glycal whereas the phenylthio adduct did not. (b) Preuss, R.; Schmidt, R. R. *Synthesis* **1988**, 694. A 2-(phenylthio)-1-imidate adduct, upon Lewis acid treatment, formed glycosides where the 2-phenylthio configuration was maintained.

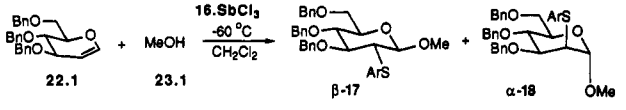
Table I. Glycosyl Transfers Using Reagent[a] 16 (Ar = Ph)

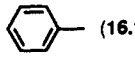
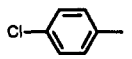
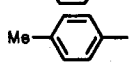
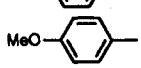
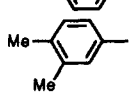
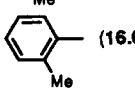
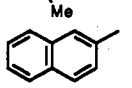


entry	ROH or ROSnBu$_3$ (23)	ratio β-17/α-18	yield (%)	ratio total bp/ap[c,d]
1	MeOH (23.1)	3.7/1 (17.1/18.1)	83 (92)[b]	3.7/1
2	i-PrOH (23.2)	2.7/1 (17.2/18.2)	59	4.4/1 (20.1, 21.1)
3	 (23.3)	5.3/1 (17.3/18.3)	70	6.8/1 (19.3/20.1)
4	 (23.4)	11.5/1 (17.4/18.4)	75	14/1 (19.4, 20.1)
5	 (23.5)	only β-17.5 2 diastereomers β/β′ 10/1	45	only β (20.1)
6	 (23.6)	4.3/1 (17.6/18.6)	64	6.3/1 (20.1, 21.1)
7	 (23.7)	5.3/1 (17.7/18.7)	43	12.2/1 (20.1, 21.1)
8	 (23.8)	3.7/1 (17.8/18.8)	30	10.9/1 (20.1, 21.1)
9	 (23.9)	4.9/1 (17.9/18.9)	53	9.3/1 (20.1, 21.1)
10	 (23.10)	5.7/1 (17.10/18.10)	60	5.7/1

[a] Reagent 16.1 was used for entries 1–6 and 10 and reagent 16.1·SbCl$_3$ for entries 7–9. [b] Reagent 16.1·SbCl$_3$. [c] bp = products from below-plane attack of sulfur reagent including glycosides and pyranoses indicated by their structure numbers in parentheses. ap = product from above-plane attack, only trans α-glycoside. [d] The amount of pyranoses 20 and 21 produced by water trapping was highly dependent on the degree of care used in drying the aglycon nucleophile.

Table II. Glycosyl Transfers to Methanol with Variation of Arylthio Group



entry	Ar–	ratio β-17/α-18	yield (%)
11	 (16.1)	3.7/1 (17.1/18.1)	92
12	 (16.2)	2.5/1 (17.12/18.12)	91.4
13	 (16.3)	4.4/1 (17.13/18.13)	91.7
14	 (16.4)	2.4/1 (17.14/18.14)	82
15	 (16.5)	4.1/1 (17.15/18.15)	90
16	 (16.6)	2.2/1 (17.16/18.16)	86.8
17	 (16.7)	2.6/1 (17.17/18.17)	71.2

mechanism where our postulated structures represented discrete hypervalent sulfur intermediates, the sugar and the aglycon would interact strongly in every possible combination.[29] The logical extension of transition-state 35 is that the first-formed intermediate in the glycosylation process is a sulfurane 38. Sulfuranes of similar structure have been postulated.[23]

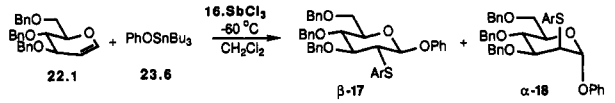
Our experiments are also suggestive as to what structural features of the glycal direct the face selectivity of attack of the sulfur electrophile. With entries 28 and 29 in Table IV, it can be seen that axial alkoxy groups have a powerful effect and direct the electrophile to the opposite face. From the other entries in Tables IV and V, it is clear that equatorial alkoxy groups have a small effect since the 3,4-dideoxy system (entry 27, Table IV) exhibits a below-plane preference. The bicyclic glycals were chosen to test the proposal put forward by both Thiem and Horton in papers on iodination of glycals[30] that below-plane attack might occur on the flipped half-chair conformer of the glycal. The frameworks shown in entries 24 and 25 in Table IV and 32 and 33 in Table V, although flexible enough to assume boat forms, cannot easily flip to alternate half-chair forms, yet still show a preference for below-plane attack. Hence, we discount the Thiem–Horton suggestions, at least for the sulfonium reagents.

A tentative hypothesis for the weak force which destabilizes above-plane attack might be simply the steric effect

(29) Okuyama, T. *The Chemistry of Sulphenic Acids and Their Derivatives*; Patai, S., Ed.; John Wiley and Sons: New York, 1990; Chapter 18. The mechanism of nucleophilic substitution on the sulfur of thiosulfinates is reviewed. There is evidence for attack on both sulfenyl and sulfinyl positions via either S_N2 or addition–elimination pathways.

(30) (a) Reference 11a. (b) Thiem, J.; Ossowski, P. *J. Carbohydr. Chem.* 1984, *3*, 287.

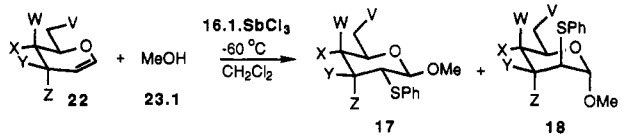
Table III. Glycosyl Transfers to Phenol Using Different Reagents



entry	Ar–	ratio β-17/α-18	yield (%)	ratio total bp/ap[a]
18	(16.1)	4.3/1 (17.6/18.6)	64	6.3/1 (20.1, 21.1)
19	Cl (16.2)	1.7/1 (17.19/18.19)	54	3.1/1 (20.2, 21.2)
20	Me (16.3)	5.7/1 (17.20/18.20)	46	8.3/1 (20.3, 21.3)
21	MeO (16.4)	2.4/1 (17.21/18.21)	61.7	2.9/1 (20.4, 21.4)
22	(16.6) Me	2.6/1 (17.22/18.22)	47	3.6/1 (20.6)

[a] bp = products from below-plane attack of sulfur reagent including glycosides and pyranoses indicated by their structure numbers in parentheses. ap = product from above-plane attack, only trans α-glycoside.

Table IV. Glycosyl Transfers to Methanol Using Different Glycals

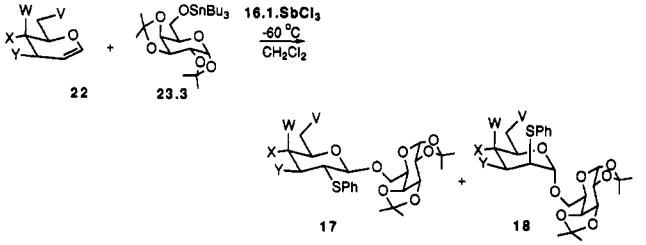


entry	glycal substrate	ratio β-17/α-18	yield (%)
23	(22.1)	3.7/1 (17.1/18.1)	92
24	(22.2)	2.7/1 (17.24/18.24)[a]	86
25	(22.3)	2/1 (17.25/)18.25)[b]	76
26	(22.4)	2/1 (17.26/18.26)[c]	62
27	(22.5)	2/1 (17.27/18.27)	93
28	(22.6)	1/10 (17.28/18.28)	80
29	(22.7)	12/1 (17.29/18.29)	92
30	(24)	2/1 (25/26)	90

[a] The isopropylidene blocking group was lost easily in the product so glycosides **17.24** and **18.24** were characterized as the 4,6-dihydroxy species. [b] Partial loss of the benzylidene occured, thus affording some **17.24** and **18.24**. [c] *cis*-α-**19.26** was formed in 10% yield; hence, ratio of total below-plane/above-plane = 2.5/1.

of the axial proton at C-4. Or, perhaps a stereoelectronic effect induced by the stereogenic group at C-5, which can stabilize the transition-state for below-plane attack could be the key factor. Whatever the cause, with most electrophiles, including the subject thiosulfonium salts, below-plane attack is seen to be favored, if there are no overriding steric effects. It will take more experimentation, perhaps augmented with semiempirical MO calculations of the isomeric transition states, to sort out the factors which control face selectivity in electrophilic attack on glycals. In conclusion, the arylbis(arylthio)sulfonium salt system is a practical and useful electrophile for synthesizing 2-deoxy-β-glycosides from glycals.

Table V. Glycosyl Transfers to Diisopropylidenegalactose Using Different Glycals



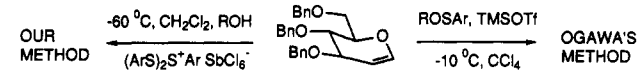
entry	glycal substrate	ratio β-17/α-18	yield (%)
31	(22.1)	5.3/1 (17.31/18.31)	70
32	(22.3)	5.7/1 (17.32/18.32)[a]	79
33	(22.2)	5.7/1 (17.33/18.33)[b]	69
34	(22.4)	3.1/1 (17.34/18.34)	74

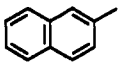
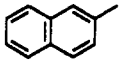
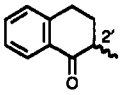
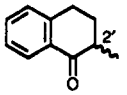
[a] The benzylidene blocking group was lost to some extent so glycoside **18.32** was characterized as the 4,6-dihydroxy species. [b] Partial loss of the isopropylidene occured, thus affording some dihydroxy species. *cis*-α-**19.33** with and without the isopropylidene blocking group were obtained in 10% yield. Hence, the total below-plane/above-plane ratio was 6.7/1.

Experimental Section

General. NMR spectra were recorded on a GE QE 300 instrument with $CDCl_3$ as solvent. Elemental analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Optical rotations were determined using a Rudolph Research AUTOPOL III automatic polarimeter. Thin-layer chromatograms were done on precoated TLC sheets of silica gel 60 F_{254} (E. Merck) and short- and long-wave ultraviolet light was used to visualize the spots. PLC plates were prepared by using Kieselgel 60 PF_{254} (E. Merck), and chromatotron (radial chromatography) plates were prepared by using Kieselgel 60 PF_{254} gipshaltig (E. Merck). Flash chromatography was performed with silica gel (230–400 mesh) purchased from Aldrich Chemical Co. Methanol was distilled from Mg and stored over 3 Å MS. Dry THF was obtained by distillation, under nitrogen, from sodium benzophenone ketyl. Dichloromethane was distilled from P_2O_5. Other solvents were purified and dried by using standard pro-

Table VI. Comparison of $Ar_3S_3^+$ Results with Ogawa's Method



entry	sulfur substituent Ar	substituent on nucleophile R	ratio β/α: our method	ratio β/α: ogawa's method
1		Me	2.6/1	3.5/1
2		i-Pr	2.7/1	3.8/1
3				only β product (1/1 diastereomers at C-2′)
4			only β product (10/1 diastereomers at C-2′, enantiomeric discrimination)	

cedures. Solution of antimony pentachloride in CH_2Cl_2 was bought from Aldrich. All reactions were carried out under an argon atmosphere using standard syringe techniques.

General Procedure for Preparation of Arylbis(arylthio)sulfonium Salt Reagent 16. Method for 16 (eq 1). A solution of diaryl disulfide (1 mmol) and arylsulfenyl chloride (1.1 mmol) in 3.0 mL of dry CH_2Cl_2 is added dropwise to antimony pentachloride (1.0 mL of 1 M solution in CH_2Cl_2) at −60 °C. The mixture is stirred for 30 min at −60 °C to give a 0.25 M solution of **16**.

Method for 16·$SbCl_3$ (eq 2). A solution of diaryl disulfide (1.5 mmol) in 2.5 mL of dry CH_2Cl_2 is added dropwise to antimony pentachloride (1.5 mL of 1 M solution in CH_2Cl_2) at −60 °C. The mixture is stirred for 30 min at −60 °C to give a 0.25 M solution of **16·$SbCl_3$**.

General Procedure for Glycosidation. To a solution of the glucal (0.255 mmol) and the nucleophile alcohol (0.51 mmol) in dry CH_2Cl_2 at −60 °C is added 1.2 mL of the reagent solution (0.30 mmol). After the reaction is complete (about 10 min), saturated aqueous $NaHCO_3$ solution (15 mL) is added and the mixture is stirred for 30 min at rt. The reaction mixture is extracted with CH_2Cl_2 (3×25 mL). The combined organic extracts are dried over anhyd Na_2SO_4. Evaporation of the solvent gives the crude product mixture which is subjected to radial chromatography.

Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylthio)-β-D-glucopyranoside (β-17.6) and Phenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-mannopyranoside (α-18.6). Glycosidation was carried out using phenylbis(phenylthio)sulfonium salt (**16.1·$SbCl_3$**) plus 3,4,6-tri-*O*-benzyl-D-glucal (**22.1**) and phenyl tri-*n*-butyltin ester (**23.6**). Radial chromatography (ethyl acetate–hexane (1:20 to 2:1)) gave 19 mg of α-**18.6** and 82 mg of β-**17.6**; total yield 64%; β/α 4.3/1. In addition, 10 mg (7.3%) of 3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylthio)-β-D-glucose (**20.1**) and 22 mg (16%) of 3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-glucose (**21.1**) were also isolated. A small amount of 4-(phenylthio)phenol was obtained.

Physical Data. First fraction, α-**18.6**: mp 88–89 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.64 (dd, J = 11.0, 1.7 Hz, 1 H, C_6-H), 3.78 (dd, J = 11.0, 4.2 Hz, 1 H, C_6-H), 3.89–3.91 (m, 2 H, C_5-H, C_2-H), 4.00 (dd, J = 9.0, 9.6 Hz, 1 H, C_4-H), 4.42–4.47 (m, 2 H, C_3-H, $^1/_2$×PhCH_2), 4.61–4.71 (m, 3 H, 1.5×PhCH_2), 4.70 (AB q, Δν = 115.0 Hz, J_{AB} = 10.7 Hz, 2 H, PhCH_2), 5.71 (d, J = 1.5 Hz, 1 H, C_1-H), 6.94–7.50 (m, 25 H, Ar-H).

Second fraction, β-**17.6**: mp 92–93 °C; $[\alpha]^{25}_D$ −23.6° (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 3.51 (dd, J = 10.7, 8.6 Hz, 1 H, C_2-H), 3.60–3.82 (m, 5 H, pyran ring protons), 4.55 (AB q, Δν = 21.78 Hz, J_{AB} = 12.0 Hz, 2 H, PhCH_2), 4.85 (AB q, Δν = 10.0 Hz, J_{AB} = 10.0 Hz, 2 H, PhCH_2), 4.86 (AB q, Δν = 145.0 Hz, J_{AB} = 10.6 Hz, 2 H, PhCH_2), 4.98 (d, J = 8.4 Hz, 1 H, C_1-H), 6.90 (d, J = 7.64 Hz, 2 H, Ar-H), 6.99–7.24 (m, 23 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.48 (C_2), 68.74, 73.44, 74.98, 76.29, 79.07, 82.82, 101.83 (C_1), 116.66, 122.42, 126.23, 127.14, 127.52, 127.64, 127.78, 127.84, 128.07, 128.27, 128.35, 128.43, 128.73, 129.31, 132.49, 134.88, 137.86, 138.01, 138.07, 157.24. Anal. Calcd for $C_{39}H_{38}O_5S$: C, 75.70; H, 6.19; S, 5.18. Found: C, 75.61; H, 6.26; S, 5.14.

Third fraction, 4-(phenylthio)phenol: ^1H NMR (300 MHz, $CDCl_3$) δ 5.18 (br s, 1 H, OH), 6.88 (d, J = 8.6 Hz, 2 H, Ar-H), 7.18–7.31 (m, 5 H, Ar-H), 7.41 (d, J = 8.6 Hz, 2 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 116.50, 125.86, 128.31, 129.00, 135.55, 138.45, 155.89 (C_1).

Fourth fraction, **20.1**: ^1H NMR (300 MHz, $CDCl_3$) δ 3.25 (dd, J = 10.7, 8.8 Hz, 1 H, C_2-H), 3.39–3.44 (m, 1 H, pyran ring proton), 3.49 (dd, J = 10.7, 8.6 Hz, 1 H, C_3-H), 3.60–3.73 (m, 3 H, pyran ring protons), 4.42 (d, J = 8.8 Hz, 1 H, C_1-H), 4.49–4.56 (m, 2 H, OH, $^1/_2$×PhCH_2), 4.72 (AB q, Δν = 78.9 Hz, J_{AB} = 12.0 Hz, 2 H, PhCH_2), 4.78 (d, J = 10.8 Hz, 1 H, $^1/_2$×PhCH_2), 4.89 (AB q, Δν = 58.1 Hz, J_{AB} = 10.3 Hz, 2 H, PhCH_2), 7.00–7.47 (m, 20 H, Ar-H).

Fifth fraction, **21.1**: mp 89–90 °C (lit.[10] mp 85.5–86 °C); ^1H NMR (300 MHz, $CDCl_3$) δ 3.25–3.33 (m, 2 H, C_2-H, OH), 3.50–3.63 (m, 3 H, C_4-H, 2×C_6-H), 3.92 (d, J = 11.0, 9.0 Hz, 1 H, C_3-H), 4.02–4.08 (m, 1 H, C_5-H), 4.37–4.53 (m, 3 H, 1.5×PhCH_2), 4.72–4.78 (m, 2 H, PhCH_2), 4.92 (d, J = 10.2 Hz, 1 H, $^1/_2$×PhCH_2), 5.28 (t, J = 3.0 Hz, 1 H, C_1-H), 7.03–7.43 (m, 20 H, Ar-H).

General Procedure for Glycosidation Using a Sugar Alcohol as the Nucleophile. To the sugar alcohol (0.51 mmol) dissolved in 14 mL of dry toluene is added 3.0 g of activated powdered 4-Å MS and bis(tri-*n*-butyl)tin oxide (0.255 mmol). The reaction mixture is refluxed for 12 h, and thereafter toluene is distilled off. To the residue is added a solution of the glucal (0.255 mmol) in dry CH_2Cl_2 (3 mL), and the reaction mixture is cooled to −60 °C. The reagent solution (1.2 mL, 0.30 mmol) is then added. After the reaction is complete (about 10 min), it is quenched with saturated aqueous $NaHCO_3$ solution (15 mL) and the mixture stirred for 30 min at rt. The reaction mixture is filtered through Celite (the Celite is washed with 50 mL of CH_2Cl_2), and the organic layer of the filtrate is dried over anhyd Na_2SO_4. Evaporation of the solvent gives the crude product mixture which is subjected to radial chromatography.

6′-(1′,2′:3′,4′-Diisopropylidenegalactopyranosyl) 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylthio)-β-D-glucopyranoside (β-17.3) and 6′-(1′,2′:3′,4′-Diisopropylidenegalactopyranosyl) 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-mannopyranoside (α-18.3). Glycosidation was carried out using reagent **16.1** plus the glucal **22.1** and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (**23.3**). Radical chromatography (ethyl acetate–hexane (1:20 to 2:1)) gave 4 mg of 6′-(1′,2′:3′,4′-Diisopropylidenegalactopyranosyl) 3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-glucopyranoside (α-**19.3**), 22 mg of α-**18.3**, and 117.8 mg of β-**17.3**, total yield (β-**17.3** + α-**18.3**) 70%; β/α 5.3/1. α-**19.3** was formed in 8% yield. In addition, 28 mg (14%) of **20.1** was also isolated.

Physical Data. First fraction, **20.1**.

Second fraction, α-**19.3**: oil; ^1H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3), 1.61 (s, 6 H, 2×CH_3), 3.41 (d, J = 11.1, 3.1 Hz, 1 H, C_2-H), 3.68–4.07 (m, 8 H, pyran ring protons), 4.33–4.87 (m, 8 H, pyran ring protons, 2.5×PhCH_2), 5.04 (d, J = 10.4 Hz, 1 H, $^1/_2$×PhCH_2), 5.08 (d, J = 3.1 Hz, 1 H, C_1-H), 5.57 (d, J = 5.0 Hz, 1 H, C_1-H), 7.16–7.54 (m, 20 H, Ar-H).

Third fraction, α-**18.3**: oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 6 H, 2×CH_3), 1.45 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.64–4.02 (m, 8 H, pyran ring protons), 4.18–4.40 (m, 3 H, pyran ring protons), 4.50–4.68 (m, 5 H, pyran ring protons, 2×PhCH_2), 4.78 (d, J = 12.6 Hz, 1 H, $^1/_2$×PhCH_2), 4.92 (d, J = 10.7 Hz, 1 H, $^1/_2$×PhCH_2), 5.17 (s, 1 H, C_1-H), 5.55 (d, J = 4.7 Hz, 1 H, C_1-H), 7.18–7.60 (m, 20 H, Ar-H).

Fourth fraction, β-**17.3**: oil; $[\alpha]^{25}_D$ −51.5° (c 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 3.27 (dd, J = 10.8, 8.7 Hz, 1 H, C_2-H), 3.50–3.54 (m, 1 H, pyran ring proton), 3.60 (dd, J = 10.8, 10.6 Hz, 1 H, C_3-H), 3.72–3.80 (m, 4 H, pyran ring protons), 3.98–4.17 (m, 3 H, pyran ring protons), 4.35 (dd, J = 5.0, 2.3 Hz, 1 H, C_2-H), 4.52 (d, J = 8.7 Hz, 1 H, C_1-H), 4.56–4.71 (m, 4 H, pyran ring proton, 1.5×PhCH_2), 4.92 (d, J = 10.0 Hz, 1 H, $^1/_2$×PhCH_2), 5.00 (AB q, Δν = 72.3 Hz, J_{AB} = 10.3 Hz, 2 H, PhCH_2), 5.60 (d, J = 5.0 Hz, 1 H, C_1-H), 7.24–7.67 (m, 20 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.23, 24.98, 25.91, 26.18, 56.61 (C_2), 66.64, 68.55, 68.59, 70.45, 70.55, 70.69, 73.47, 74.74, 74.88, 76.17, 79.09, 83.14, 96.27, 104.19 ($C1$), 108.95, 126.64, 127.55, 127.67, 127.75, 127.83, 128.03, 128.30, 128.39, 128.66, 132.15, 135.90, 138.02, 138.08, 138.24. Anal. Calcd for $C_{45}H_{52}O_{10}S$: C, 68.86; H, 6.68; S, 4.08. Found: C, 68.44; H, 6.87; S, 3.98.

3′-(1′,2′:5′,6′-Diisopropylideneglucofuranosyl) 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylthio)-β-D-glucopyranoside (β-17.4) and 3′-(1′,2′:5′,6′-Diisopropylideneglucofuranosyl) 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-mannopyranoside (α-18.4). Glycosidation was carried out using reagent **16.1** along with the glucal **22.1** and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside (**23.4**). Radial chromatography (ethyl acetate–hexane (1:20 to 2:1)) gave 138 mg of β-**17.4** and 24 mg of a 1:1 mixture (determined by NMR) of 3′-(1′,2′:5′,6′-diisopropylideneglucofuranosyl) 3,4,6-tri-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-glucopyranoside (α-**19.4**) and α-**18.4**, total yield (β-**17.4** + α-**18.4**) 75%; β/α 11.5/1. α-**19.4** was formed in 6% yield. In addition, 12 mg (9%) of **20.1** was also isolated.

Physical Data. First fraction, **20.1**.

Second fraction, α-**19.4** + α-**18.4**: PLC of this mixture gave a faster moving spot, oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 3.63–3.92 (m, 7 H, pyran ring protons), 4.03–4.12 (m, 1 H, pyran ring proton), 4.18–4.34 (m, 3 H, pyran ring protons), 4.50–4.68 (m, 4 H, pyran ring proton, 1.5×PhCH_2), 4.50–4.68 (m, 4 H, pyran ring proton, 1.5×PhCH_2), 4.76 (AB q, Δν = 12 Hz, J_{AB} = 12 Hz, 2 H, PhCH_2), 4.93 (d, J = 10.2 Hz, 1 H, $^1/_2$×PhCH_2), 5.08 (s, 1 H, C_1-H), 6.02 (d, J = 3.7 Hz, 1 H, C_1-H), 7.18–7.55 (m, 20 H, Ar-H); slower moving spot (contaminated with faster moving spot), oil; ^{1}H NMR (300 MHz, $CDCl_3$), characteristic signals δ 1.24 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 5.32 (s, 1 H, C_1-H), 5.85 (d, J = 3.7 Hz, 1 H, C_1-H).

Third fraction, β-**17.4**: oil; $[\alpha]^{25}_D$ −26.7° (c 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 3.24 (dd, J = 10.8, 8.8 Hz, 1 H, C_2-H), 3.48–3.52 (m, 1 H, pyran ring proton), 3.56 (dd, J = 10.8, 8.7 Hz, 1 H, C_3-H), 3.73–3.89 (m, 5 H, pyran ring protons), 4.31–4.40 (m, 3 H, pyran ring protons), 4.54 (d, J = 8.8 Hz, 1 H, C_1-H), 4.53–4.68 (m, 4 H, pyran ring proton, 1.5×PhCH_2), 4.89 (AB q, Δν = 9.7 Hz, J_{AB} = 9.7 Hz, 2 H, PhCH_2), 5.06 (d, J = 10.4 Hz, 1 H, $^1/_2$×PhCH_2), 5.65 (d, J = 3.7 Hz, 1 H, C_1-H), 7.25–7.53 (m, 20 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.31, 26.34, 26.46, 26.85, 56.59 (C_2), 65.55, 68.53, 73.55, 73.60, 75.01, 76.38, 79.02, 80.26, 80.94, 82.56, 82.80, 102.69, 105.19, 108.26, 111.80, 126.94, 127.69, 127.74, 127.80, 127.92, 127.99, 128.03, 128.39, 128.42, 128.51, 128.91, 131.01, 135.65, 137.91, 138.10.

2′(*R*,*S*)-(1′-Oxo-1′,2′,3′,4′-tetrahydronaphthyl) 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(phenylthio)-β-D-glucopyranosides (β-17.5). To a mixture of the glucal **22.1** (106 mg, 0.255 mmol), 2-hydroxytetralone **23.5** (83 mg, 0.51 mmol), and 3.0 g of activated powdered 4-Å MS in dry CH_2Cl_2 at −60 °C was added 1.2 mL of the solution of phenylbis(phenylthio)sulfonium salt, **16.1** (0.30 mmol). After the reaction was complete (about 10 min) it was quenched with saturated aqueous $NaHCO_3$ solution (15 mL) and the mixture stirred for 30 min at rt. The reaction mixture was filtered through Celite (the Celite was washed with 50 mL of CH_2Cl_2), and the organic layer of the filtrate was dried over anhyd Na_2SO_4. Evaporation of the solvent gave the crude product mixture which was subjected to radial chromatography (ethyl acetate–hexane (1:20 to 2:1)) to give 79 mg of β-**17.5**; total yield 45%. The two diastereomeric β glycosides were formed in the ratio 10:1, determined by NMR of the mixture. In addition 40 mg (30%) of **20.1** was also isolated.

Physical Data. First fraction, **20.1**.

Second fraction: minor diastereomer of β-**17.5** (contaminated with major diastereomer): ^{1}H NMR (300 MHz, $CDCl_3$), characteristic signals δ 3.29 (dd, J = 10.3, 8.9 Hz, 1 H, C_2-H), 7.94 (d, J = 7.8 Hz, 1 H, C_8-H).

Third fraction, major diastereomer of β-**17.5**: colorless oil; $[\alpha]^{25}_D$ −20.4° (c 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17–2.32 (m, 2 H, C_3-H), 2.81–2.88 (m, 1 H, C_4-H), 3.08–3.18 (m, 1 H, C_4-H), 3.38 (dd, J = 10.6, 8.9 Hz, 1 H, C_2-H), 3.49–3.78 (m, 5 H, pyran ring protons), 4.38–4.41 (m, 1 H, C_2-H), 4.51 (AB q, Δν = 24.9 Hz, J_{AB} = 12.2 Hz, 2 H, PhCH_2), 4.69 (d, J = 8.9 Hz, 1 H, C_1-H), 4.74 (AB q, Δν = 53.3 Hz, J_{AB} = 10.8 Hz, 2 H, PhCH_2), 4.98 (AB q, Δν = 48.8 Hz, J_{AB} = 10.4 Hz, 2 H, PhCH_2), 7.19–7.62 (m, 23 H, Ar-H), 8.04 (d, J = 7.8 Hz, 1 H, C_8-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.82, 29.01, 56.18 (C_2), 68.70, 73.56, 74.96, 75.09, 76.09, 78.95, 79.66, 83.11, 102.69 (C_1), 126.57, 126.65, 127.47, 127.59, 127.69, 127.80, 127.823, 127.99, 128.05, 128.18, 128.30, 128.33, 128.46, 128.60, 128.66, 131.35, 131.93, 133.35, 138.04, 138.25, 138.32, 143.46, 195.03, 138.20. Anal. Calcd for $C_{43}H_{42}O_6S$: 75.19; H, 6.16; S, 4.67. Found: C, 75.11; H, 6.06.

6′-(1′,2′:3′,4′-Diisopropylidenegalactopyranosyl) 3-*O*-Benzyl-4,6-isopropylidene-2-deoxy-2-(phenylthio)-β-D-glucopyranoside (β-17.33) and 6′-(1′,2′:3′,4′-Diisopropylidenegalactopyranosyl) 3-*O*-Benzyl-4,6-isopropylidene-2-deoxy-2-(phenylthio)-α-D-mannopyranoside (α-18.33). Glycosidation was carried out using reagent **16.1**·$SbCl_5$ with 4,6-*O*-isopropylidene-3-*O*-benzyl-D-glucal (**22.2**) and the galactopyranoside **23.3**. Radial chromatography (ethyl acetate–hexane (1:20 to 2:1)) gave 56 mg of β-**17.33**, 9.0 mg of α-**18.33**, 4.6 mg of 6′-(1′,2′:3′,4′-diisopropylidenegalactopyranosyl) 3-*O*-benzyl-4,6-isopropylidene-2-deoxy-2-(phenylthio)-α-D-glucopyranoside (α-**19.33**), 36 mg of 6′-(1′,2′:3′,4′-diisopropylidenegalactopyranosyl) 3-*O*-benzyl-2-deoxy-2-(phenylthio)-β-D-glucopyranoside (β-**17.33a**), 7 mg of 6′-(1′,2′:3′,4′-diisopropylidenegalactopyranosyl) 3-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-mannopyranoside (α-**18.33a**), and 11 mg of 6′-1′,2′:3′,4′-diisopropylidenegalactopyranosyl) 3-*O*-benzyl-2-deoxy-2-(phenylthio)-α-D-glucopyranoside (α-**19.33a**); total yield (β-**17.33**, β-**17.33a**, α-**18.33** + α-**18.33a**) 69%; β/α 5.7/1. α-**19.33** and α-**19.33a** were formed in 10% yield.

Physical Data. Fraction 1, α-**19.33**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (s, 3 H, CH_3), 1.32 (s, 6 H, 2×CH_3), 1.40 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 3.30 (dd, J = 10.7, 4.6 Hz, 1 H, C_2-H), 3.65–3.87 (m, 7 H), 4.02 (dt, J = 6.9, 2.1 Hz, 1 H), 4.30 (dd, J = 6.0, 3.1 Hz, 1 H), 4.43 (dd, J = 8.4, 2.1 Hz, 1 H), 4.62 (dd, J = 8.4, 3.0 Hz, 1 H), 4.78 (AB q, Δν = 25.6 Hz, J_{AB} = 11.6 Hz, 2 H, PhCH_2), 4.58 (m, 1 H), 4.97 (d, J = 4.6 Hz, 1 H, C_1-H), 5.52 (d, J = 5.6 Hz, 1 H, C_1-H), 7.10–7.50 (m, 10 H, Ar-H).

Fraction 2, α-**18.33**: oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 3.20 (s, 3 H, OCH_3), 3.60 (dd, J = 11.2, 6.5 Hz, 1 H), 3.68–3.87 (m, 4 H), 3.88–3.95 (m, 2 H), 4.00–4.17 (m, 2 H), 4.29 (dd, J = 5.6, 2.4 Hz, 1 H), 4.57 (AB q, Δν = 37.4 Hz, J_{AB} = 12.2 Hz, 2 H, PhCH_2), 5.01 (s, 1 H, C_1-H), 5.50 (d, J = 5.0 Hz, 1 H, C_1-H), 7.10–7.45 (m, 10 H, Ar-H).

Fraction 3, β-**17.33**: Colorless oil; $[\alpha]^{25}_D$ −56.1° (c 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.40 (s, 6 H, 2XCH_3), 1.45 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 3.05 (dd, J = 10.5, 8.9 Hz, 1 H, C_2-H), 3.15–3.25 (m, 1 H), 3.41 (dd, J = 10.4, 8.7 Hz, 1 H), 3.62–3.79 (m, 3 H), 3.86–4.01 (m, 4 H), 4.26 (dd, J = 5.0, 2.3 Hz, 1 H), 4.46–4.50 (m, 2 H), 4.81 (AB q, Δν = 21.0 Hz, J_{AB} = 11.0 Hz, 2 H, PhCH_2), 5.51 (d, J = 5.0 Hz, 1 H, C_1-H), 7.15–7.66 (m, 10 H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.16, 24.29, 25.01, 25.94, 26.21, 29.21, 56.45, 62.20, 66.57, 66.69, 68.90, 70.48, 70.55, 70.71, 75.33, 75.62, 79.74, 96.30, 99.46, 104.63, 108.56, 109.10, 126.97, 127.60, 128.14, 128.20, 128.74, 132.64, 135.39, 138.60.

Fraction 4, α-**19.33a**: oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 6 H, 2XCH_3), 1.43 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 1.95 (br s, 1 H, OH), 2.33 (br s, 1 H, OH), 3.26 (dd, J = 10.2, 4.0 Hz, 1

H, C_2-*H*), 3.52–3.38 (m, 7 H), 4.02 (dt, J = 6.0, 1.5 Hz, 1 H), 4.29 (dd, J = 5.6, 2.5 Hz, 1 H), 4.39 (dd, J = 8.0, 1.5 Hz, 1 H), 4.62 (dd, J = 8.4, 2.5 Hz, 1 H), 4.82 (AB q, $\Delta\nu$ = 83.2 Hz, J_{AB} = 11.6 Hz, 2 H, PhCH_2), 4.96 (d, J = 4.0 Hz, 1 H, C_1-*H*), 5.51 (d, J = 4.6 Hz, 1 H $C_{1'}$-*H*), 7.15–7.50 (m, 10 H, Ar-*H*).

Fraction 5, **α-18.33a**: oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3), 2.10 (br s, 1 H, O*H*), 2.52 (br s, 1 H, O*H*), 3.50–3.95 (m, 8 H), 4.05 (dd, J = 9.4, 4.7 Hz, 1 H), 4.16 (d, J = 9.3 Hz, 1 H), 4.28 (dd, J = 5.6, 2.8 Hz, 1 H), 4.45 (AB q, $\Delta\nu$ = 58.1 Hz, J_{AB} = 11.6 Hz, 2 H, PhCH_2), 4.58 (m, 1 H), 5.06 (s, 1 H, C_1-*H*), 5.50 (d, J = 5.6 Hz, 1 H, $C_{1'}$-*H*), 7.15–7.45 (m, 10 H, Ar-*H*).

Fraction 6, **β-17.33a**: oil; $[\alpha]^{25}_D$ −28.4° (*c* 0.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 3.11 (dd, J = 10.8, 8.8 Hz, 1 H, C_2-*H*), 3.25–3.40 (m, 2 H), 3.55 (t, J = 9.1 Hz, 1 H), 3.62–3.72 (m, 2 H), 3.76–4.00 (m, 4 H), 4.27 (dd, J = 5.0, 2.3 Hz, 1 H), 4.46 (d, J = 8.9 Hz, 1 H, C_1-*H*), 4.49 (dd, J = 8.0, 2.2 Hz, 1 H), 4.91 (AB q, $\Delta\nu$ = 86.9 Hz, J_{AB} = 11.2 Hz, 2 H, PhCH_2), 5.49 (d, J = 5.0 Hz, 1 H, $C_{1'}$-*H*), 7.15–7.58 (m, 10 H, Ar-*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.24, 24.93, 25.87, 26.10, 55.76, 62.54, 66.39, 68.33, 70.45, 70.52, 71.71, 74.74, 75.60, 83.10, 96.32, 104.03, 108.57, 109.13, 126.91, 128.08, 128.65, 128.76, 132.12, 135.19, 138.22.

6′-(1′,2′:3′,4′-Diisopropylidenegalactopyranosyl) 3-*O*-Benzyl-4,6-benzylidene-2-deoxy-2-(phenylthio)-β-D-glucopyranoside (β-17.32). Glycosidation was carried out using reagent **16.1**·$SbCl_5$ plus 4,6-*O*-benzylidene-3-*O*-benzyl-D-glucal (**22.3**) and the galactopyranoside **23.3**. Radial chromatography (ethyl acetate–hexane (1:20 to 2:1)) gave 70 mg of **β-17.32**, 41 mg of **β-17.33a**, and 18 mg of **α-18.33a**; total yield (**β-17.32**, **β-17.33a** + **α-18.33a**) 79%; β/α 5.7/1.

Physical Data. Fraction 1, **β-17.32**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 3.14 (dd, J = 10.3, 8.9 Hz, 1 H, C_2-*H*), 3.39–3.44 (m, 1 H), 3.60 (dd, J = 10.3, 9.0 Hz, 1 H), 3.68–3.80 (m, 3 H), 3.90–4.05 (m, 3 H), 4.25–4.40 (m, 2 H), 4.50 (dd, J = 7.8, 2.2 Hz, 1 H), 4.56 (d, J = 9.2 Hz, 1 H C_1-*H*), 4.89 (AB q, $\Delta\nu$ = 30.2 Hz, J_{AB} = 11.0 Hz, 2 H, PhCH_2), 5.53 (d, J = 5.0 Hz, 1 H, $C_{1'}$-*H*), 5.56 (s, 1 H), 7.17–7.60 (m, 15 H, Ar-*H*); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.28, 24.97, 25.92, 26.18, 56.38, 65.79, 66.58, 68.71, 68.93, 70.47, 70.52, 70.72, 75.58, 79.27, 82.80, 96.27, 101.18, 104.55, 108.53, 109.08, 125.95, 127.02, 127.63, 128.20, 128.74, 128.93, 132.63, 135.00, 137.10, 138.25.

α-18.32: Not isolated.

Fraction 2: **α-18.33a**.

Fraction 3: **β-17.33a**.

General Procedure for Desulfurization of 2-Deoxy-2-(phenylthio)-β-glycosides. A solution of the β-glycoside (0.1 mmol) in dry THF (3.0 mL) is added to a stirred suspension of Raney nickel (WII, ~ 800 mg) in 3.0 mL of THF at rt. The reaction is complete (monitored by TLC) in 30 min. The reaction mixture is then filtered through Celite. Removal of the solvent gives a colorless residue.

Phenyl 3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (27) was obtained via desulfurization of the glycoside **β-17.6**. Purification of the crude desulfurized product by flash chromatography on silica gel (ethyl acetate–petroleum ether (1:9)) gave 36 mg of **27**; yield 70%: mp 51–53 °C; $[\alpha]^{25}_D$ −9.0° (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, CDCl3) δ 1.96 (dt, J = 12.0, 9.8 Hz, 1 H, C_2-H_{ax}), 2.47 (ddd, J = 12.0, 4.9, 1.9 Hz, 1 H, C_2-H_{eq}), 3.57–3.84 (m, 5 H, pyran ring protons), 4.51–4.75 (m, 5 H, 2.5×PhCH_2), 4.93 (d, J = 10.9 Hz, 1 H, $^1/_2$×PhCH_2), 5.08 (dd, J = 9.8, 1.9 Hz, 1 H, C_1-*H*), 6.98–7.45 (m, 15 H, Ar-*H*); ^{13}C NMR (75 MHz, CDCl3) δ 36.47 (C_2), 69.24, 71.50, 73.36, 74.84, 75.41, 76.45, 79.14, 97.62 (C_1), 116.54, 122.18, 127.35, 127.56, 127.61, 127.84, 128.16, 128.24, 128.33, 129.27, 138.25, 157.08. Anal. Calcd for $C_{33}H_{34}O_5$: C, 77.62; H, 6.71. Found: C, 77.28; H, 6.84.

6′-(1′,2′:3′,4′-Diisopropylidenegalactopyranosyl) 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (28) was obtained via desulfurization of the glycoside **β-17.3**. Purification of the crude desulfurized product by flash chromatography on silica gel (ethyl acetate–petroleum ether (2:3)) gave 47 mg of **28** yield 70%: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 1.65–1.76 (m, 1 H, C_2-H_{ax}), 2.51 (ddd, J = 12.5, 4.8, 1.3 Hz, 1 H, C_2-H_{eq}), 3.43–3.46 (m, 1 H, pyran ring proton), 3.58 (dd, J = 9.4, 8.6 Hz, 1 H, pyran ring proton), 3.66–3.85 (m, 3 H, pyran ring protons), 4.04–4.16 (m, 2 H, pyran ring protons), 4.27 (dd, J = 8.0, 1.5 Hz, 1 H, pyran ring proton), 4.36 (dd, J = 4.9, 2.3 Hz, 1 H, C_2-*H*), 4.54–4.74 (m, 8 H, pyran ring protons, 2.5×PhCH_2), 4.95 (d, J = 10.8 Hz, 1 H, $^1/_2$×PhCH_2), 5.60 (d, J = 5.0 Hz, 1 H, $C_{1'}$-*H*), 7.22–7.44 (m, 15 H, Ar-*H*).

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Supplementary Material Available: Experimental procedures for compounds not appearing in Experimental Section and ^{1}H and ^{13}C NMR spectra of all compounds (119 pages). This material is contained in many libraries of microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.