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The cycloaddition way to novel deoxy disaccharide analogs

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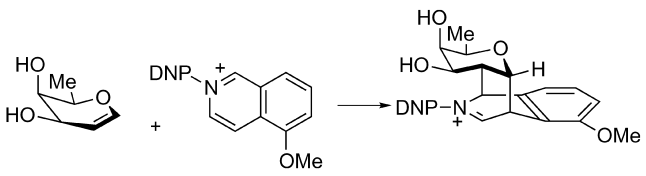
Abstract—A novel heterocycloaddition merges 2-thiono-3-ketolactones with carbohydrate glycals to afford materials which resemble disaccharides with an *O*-glycosidic linkage at the anomeric center and a thioether linking both C-2 and C-2′, thus creating a third heterocyclic ring. Upon desulfurization, these novel cycloadducts afford materials which are models for 2-deoxydisaccharides. Studies with two keto lactones and seven glycals are described.

1. Introduction

The chemistry of glycosyl transfer represents an enormous research endeavor. The most frequently used methodologies for forging the glycosidic linkage involve, generation of a leaving group at the anomeric carbon of the glycosyl donor which is then displaced by a nucleophilic group from the glycosyl acceptor. The art and subtlety of this step are found in a complicated algorithm which includes solvent, leaving group, Lewis acid catalyst, and the influence of the neighboring group at C-2.[1] The extensive methodology developed for solution chemistry is now being adapted for solid supports.[2]

An important niche in the field is the synthesis of 2-deoxyglycosides, a linkage found in antibiotics.[3] For these materials, the glycosyl transfer algorithm must be patched to take account of the absence[4] of a neighboring group at C-2 or more commonly, to have a group at C-2 that can be reductively removed after its control features are no longer needed.[5] The work to be described had its origin in our Bradsher cycloaddition program where a facile, inverse-electron-demand cycloaddition with carbohydrate-derived glycals or with synthetic glycal-like materials to form two new C–C bonds led smoothly to natural product materials (Eq. (1)).[6] We speculated that an analogous heterocycloaddition with a sulfur/oxygen diene could produce glycosidic materials that, upon subsequent desulfurization, would produce 2-deoxy glycosides (Eq. (2)). The two-step sequence would thus be a glycosyl transfer that would be orthogonal to conventional glycosidation chemistry. At about the time that we were developing the all-carbon version of the Bradsher cycloaddition to glycals and planning the hetero version, LeBlanc and Fitzimmons elegantly realized the hetero concept in their synthesis of 2-amino glycosides (Eq. (3)).[7,8] Our own plans were stalled until Capozzi reported a key observation.[9] Thus, decomposition of phthalimidosulfenyl derivative **9** apparently produced thione **10** which acted as a dienophile in reaction with isoprene (Eq. (4)). Our collaborating groups then showed that **10** and related materials could behave as oxothiono dienes in reactions with glycals.[10] The application of this concept to a disaccharide analog synthesis requires that the thionocarbonyl diene be incorporated into a pyran or furan ring. The development of such heterodienes and their cycloaddition behavior is described in this article.[11] A report by the Capozzi group describing a 'true' carbohydrate heterodiene has appeared and is nicely complementary to the research described below.[12]



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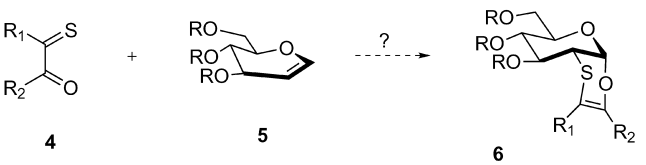

4 **5** **6** (2)

Keywords: desulfurization; tetronic acid; cycloaddition; glycosyl transfer.

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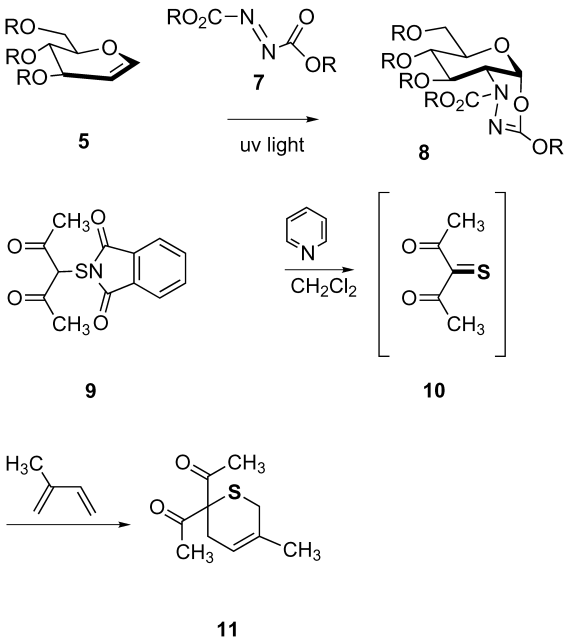
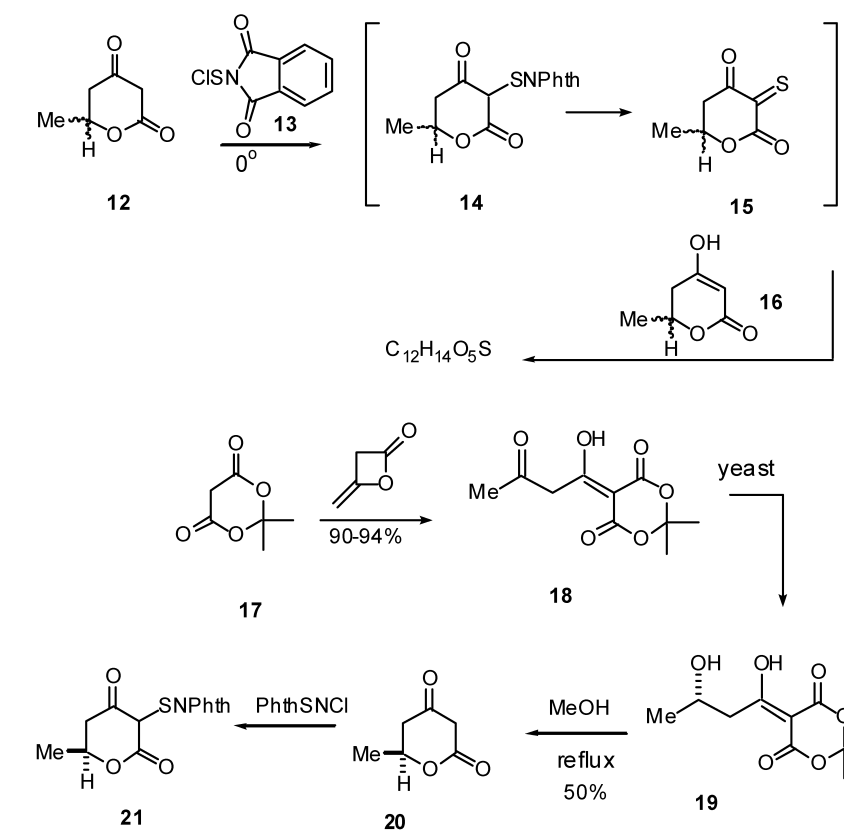


cycloaddition of heterodiene **15** with excess **12** as its enol **16** (Eq. (5)). A similar dimer has been reported by Cava in work with dimedone.[13]

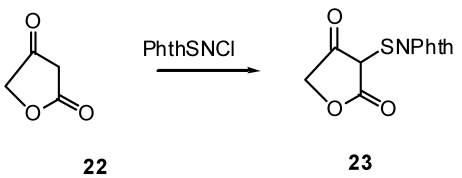
The desired sulfenylated lactone **14** was obtained by an inverse addition procedure where the lactone was added to the sulfenylating agent which was kept at −40°. Although the reaction appears to be quantitative, recrystallization of the desired material **14** reduces the yield to about 40%. In order to obtain a single enantiomer of the heterodiene precursor, a synthesis of **20**, the *S*-enantiomer of racemic lactone **12** was developed using a combination of published methods (Eq. (6)). Hence, Meldrum's acid **17** was reacted with diketene to afford the highly enolic **18** in greater than 90% yield.[14] Then, a reduction with actively fermenting yeast afforded the *S*-alcohol **19** which provided the desired lactone **20** in about 50% yield for the two steps simply by refluxing in MeOH.[15] Using conditions developed for the racemic lactone, **20** was phthalimidosulfenylated to produce **21**. Similar sulfenylation conditions applied to commercially available tetronic acid **22** afforded the phthalimidothiofuranolactone **23** (Eq. (7)).



2. Results and discussion

2.1. Synthesis of heterodiene precursors

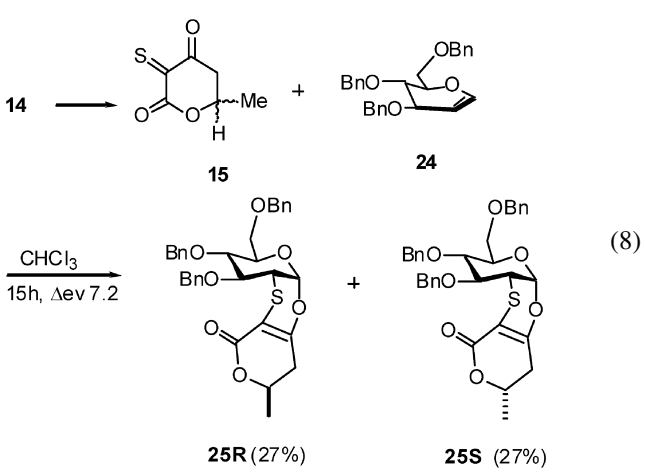
Ketolactone **12** is commercially available in racemic form. Simply reacting it at 0° by addition of phthalimidosulfenyl chloride **13** led to an incompletely characterized dimeric material which might be rationalized as the product of a



2.2. Cycloadditions

The reactions were carried out simply by mixing heterodiene precursor and glycal in solvent along with a limited amount of lutidine and are illustrated in Eqs. (8)–(18). Reaction rates varied over a wide range from hours to days. A rough correlation with the HOMO–LUMO gap can be made with smaller gaps correlating with faster cycloaddition rates. The HOMO–LUMO gaps in ev and approximate rates are displayed in each equation. The MO values were calculated at the semi-empirical AM1 level using either Spartan or Chem3D platforms. Methyl ethers were used in place of benzyl in the calculations. The structures of the products were routinely assigned using proton NMR data. Observed J values were consistent with the carbohydrate literature. X-Ray crystallographic structural data for bottom-face adduct **25** (*R*-diastereomer at the CH_3) obtained from the *R*,*S* mixture formed when racemic diene precursor **14** was used, and X-ray data for top-face material **45** reinforced our confidence in the NMR assignments. For the adducts derived from 2-acetoxyglycal **39**, with no proton at C-2, hence no $J_{1,2}$ or $J_{2,3}$ values, the assignments are less compelling. For example, our assignment of adducts **40** and **41** relies both on their displayed anomeric protons at 6.42 and 6.21, respectively, and the nOe between protons 1 and 3 in top-face isomer **41** (Eq. (14)). In adducts **28** and **29** whose structures are secure, the comparable resonances are 5.71 and 5.39 (Eq. (9)). Thus, the axial anomeric proton of the top-face adduct resonates upfield of the equatorial anomeric proton of the bottom-face adduct; and this behavior is consistent in other similar comparisons. The upfield–downfield anomeric resonance relationship holds in the tetronic acid series as well. Thus for **44** and **45**, the shifts are 5.78 and 5.41 (Eq. (15)). For **46** and **47**, the data are 5.83 and 5.58 (Eq. (16)). Our assignment difficulty arises in the case of the adduct of glycal **39** with tetronic acid **23**, where we have conflicting data. The adduct's anomeric proton resonance is at 6.21, suggesting, by comparison to **40** and **41**, a top-face adduct **50**. However, if we rely on a comparison of its nOe behavior to that of **40** and **41** where the decisive difference is the absence or presence of an interaction between H-1 and H-3, we would reach a different conclusion (Eq. (18)). Thus, the adduct **49** or **50** also exhibits an absence of interaction between its H-1 and H-3, so we should assign it as a bottom-face adduct **49** (although it is recognized that absence of an nOe is not as compelling as presence). We rule out an assignment as the regioisomeric adduct with anomeric sulfur because the expected chemical shift for the anomeric H is between δ 5–6. It should be noted that the dominant stereochemical outcomes are consistent with the literature on face selectivity of attack of glycal double bonds, bottom-face for glucals and galactals and top-face for allals, with one exception. Thus, when the cycloaddition of glucal triacetate and the tetronic acid heterodiene precursor **23** was carried out in DMSO, we observed a predominance of top-face attack producing adduct **47**. A survey of solvent effects was then carried out with the tetronic acid precursor and tribenzyl glucal. No dramatic effects were observed. However, the survey was carried out in the absence of any added lutidine because it was noted that the tetronic acid precursor spontaneously formed heterodiene upon standing in solution at room temperature. Solvent effects were cursorily examined in the hexanolactone series, with an inconclusive result shown in Eq. (9). There is little precedent on face selectivity in 2-acetoxy glycals and our limited data does not permit generalization. Adduct **37** was labile to traces of acid in $CDCl_3$, thus leading to unprotected adduct **38** which was not accessible directly by cycloaddition (Eq. (13)).

There are two features of selectivity, S vs O with C-1 and C-2 and ketone carbonyl vs. lactone carbonyl that were observed and expected. First, the ketone vs lactone distinction: the observed product is an enol of a ketone whereas, if the lactone carbonyl participated in the addition process, the product would have been a ketene acetal, a less stable entity. Second, the coefficient of the p orbital on the ketone oxygen in the LUMO of the diene is much larger than the corresponding coefficient of the lactone. In fact, in one cycloaddition reaction pairing **21** and **27** (Eq. (9)), the NMR analysis of the crude product revealed spectra of two closely related materials. One set of peaks matched those of the isolated and characterized material **28**. The other set of peaks were almost identical and suggested the possibility of an adduct where the lactone carbonyl had participated in competition with the ketone. Although the mixture survived florisil chromatography intact and unseparated, the material, conceivably regioisomeric to **28** did not survive silica gel chromatography of the reaction product mixture. The regioisomeric possibility where sulfur would be attached to C-1 was dismissed because the anomeric proton chemical shift was not significantly shielded. With regard to the sulfur selectivity for C-2 of the glycal, the p-orbital coefficients (and simple 'electron-pushing' considerations) for the sulfur and C-2 of the glycal are the largest and thus would be predicted to begin bonding strongly as the reaction progresses. In one cycloaddition, that of glycal **39** with **21**, an additional cycloadduct was isolated in 13% yield, with its anomeric proton resonance at 5.71, upfield from the that of adducts **40** and **41**. Hence, we tentatively assign it structure **42** (Eq. (14)) where the sulfur is now linked to C-1. This reversal can be rationalized because the glycal double bond now has oxygen substitution on both C-1 and C-2.



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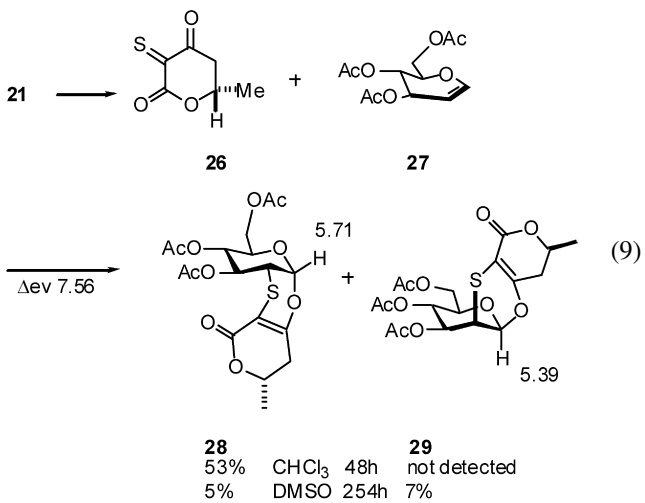

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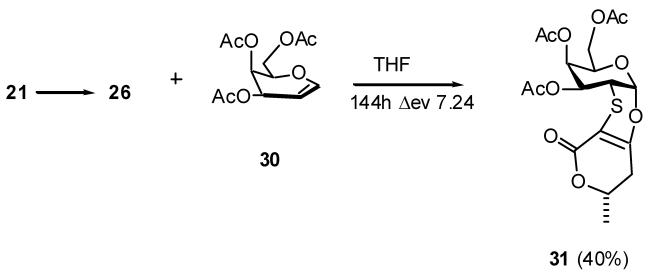

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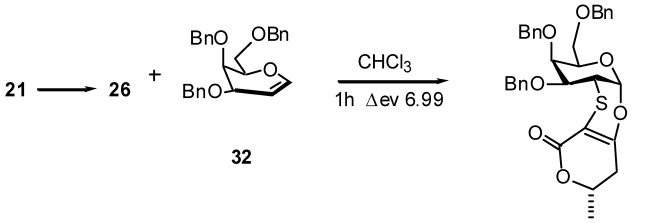

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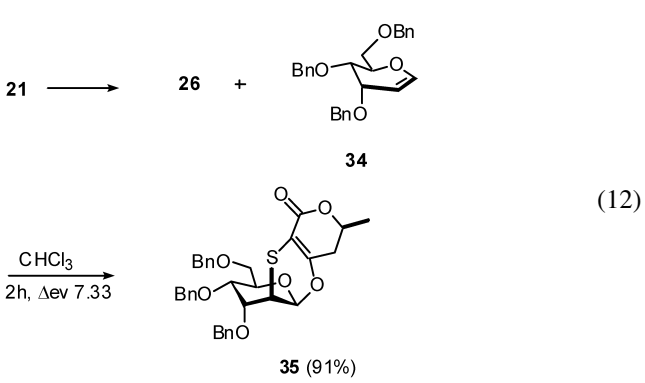

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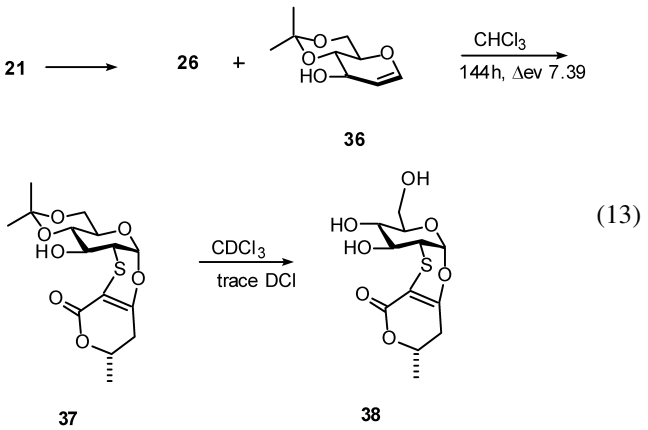

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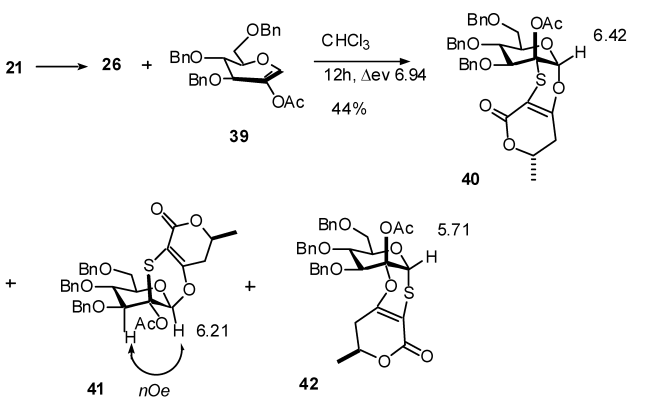

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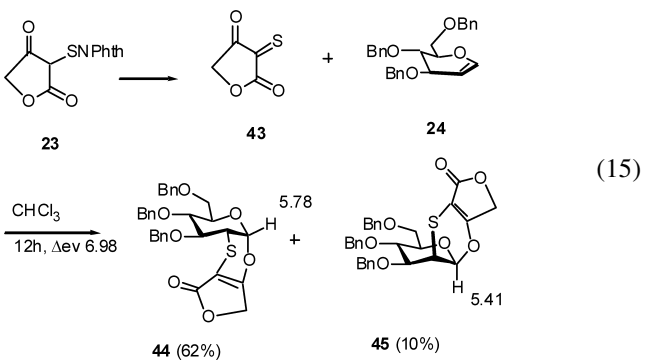

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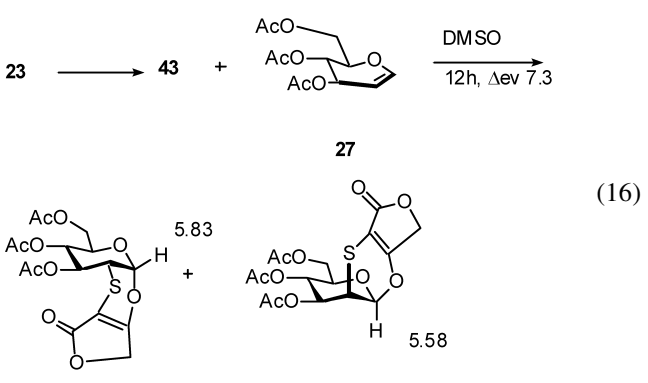

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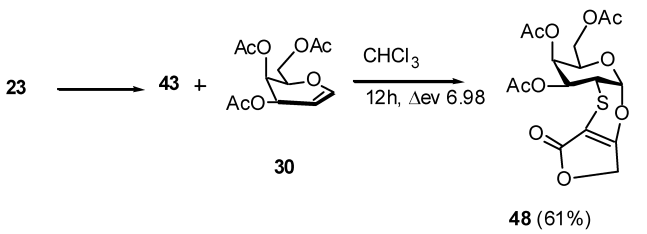

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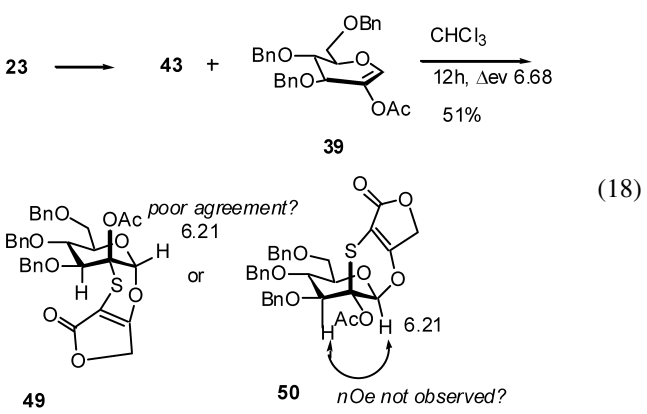

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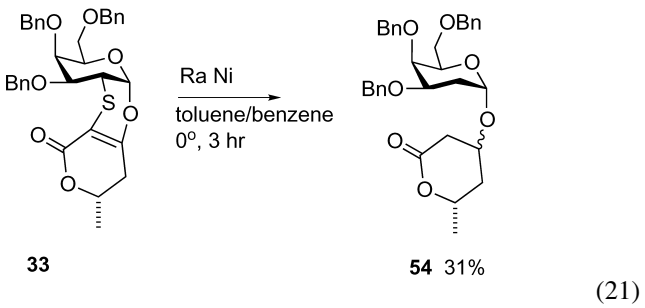

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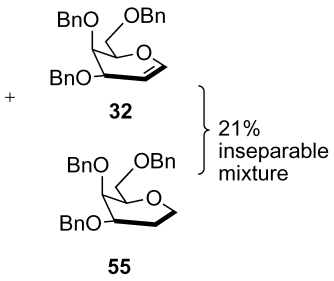

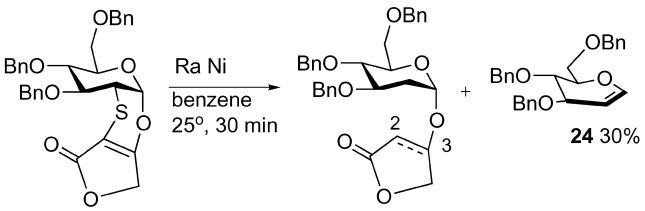

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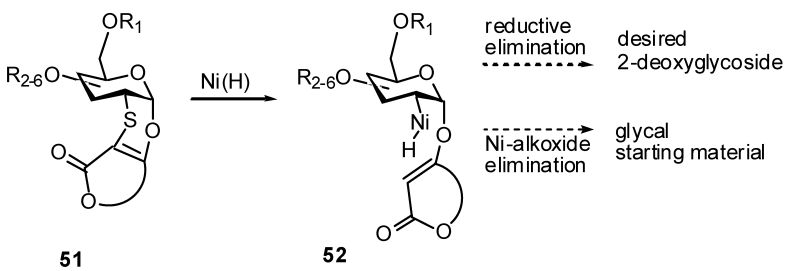

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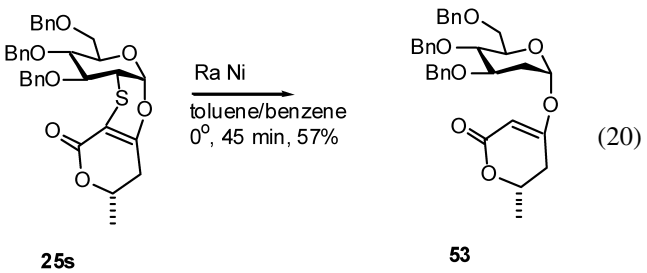

(20)

2.3. Desulfurizations

The removal of sulfur from our adducts is the 'Achilles Heel' of our synthetic method, in this series and also in 2-thio-substituted glycosides described in earlier work from these labs.[16] Raney Nickel has proven to be the only reagent that extrudes sulfur from our heterocycles. In addition to the variability from batch to batch of the nickel catalyst, there is a problem of elimination competing with reduction. Thus, whatever the exact details, there is probably a NiH intermediate depicted as **52** in Eq. (19). To obtain the desired desulfurization, a reductive elimination of nickel occurs. A competing elimination of nickel alkoxide would produce the glycal starting material of our sequence; and this is observed in every desulfurization reaction. Eqs. (20)–(22) summarize three representative examples. In some experiments with adduct **32**, reduced and desulfurized

glycoside **54** was obtained accompanied by starting tribenzyl galactal **27** and its reduced form **55** in 21% combined yield (Eq. (21)). In the tetronic acid example, the by-products included material **57** where the double bond of **56** is reduced (10% yield), starting glycal **24** in 30% yield and reduced glycal (not shown) in 20% yield (Eq. (22)). Other desulfurization reagents examined to no avail were nickelocene/LAH[17] and nickel boride.[18]

3. Conclusion

Novel tricyclic materials derived from glycal hetero-cycloadditions have been prepared. Desulfurization of these materials affords model disaccharide analogs. The two-step sequence of cycloaddition–desulfurization may be viewed as a glycosyl transfer method which is orthogonal to conventional glycosidation chemistry.

4. Experimental

4.1. General information

^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz instrument, in most cases using $CDCl_3$ (99.8%, 0.03 v/v TMS) as solvent. Chemical shifts are reported in δ units with coupling constants reported in Hz. TMS and residual chloroform (δ 7.26 for ^{1}H, δ 77.23 for ^{13}C) were used as internal references. IR spectra were recorded on a Perkin–Elmer Model 1420 infrared spectrophotometer. High resolution mass spectra were performed at University of Illinois Mass Spectrometry Laboratory (Champaign-Urbana) and medium resolution mass spectra were obtained at the Hunter College Mass Spectrometry Laboratory. Optical rotations were measured on a Rudolph Autopol III polarimeter at the reported temperatures and concentrations. Melting points were measured on a Fisher–Johns stage melting point apparatus and are uncorrected. Elemental analyses were performed by Robertson Microlit Laboratories Inc., Madison, NJ and by Schwarzkopf Microanalytical Laboratory, Inc., Woodside, NY.

All reactions were conducted in oven-dried or flame-dried glassware under an atmosphere of dry argon or nitrogen. All solvents were purified before use; THF was distilled from sodium benzophenone ketyl; dichloromethane and chloroform were distilled from P_2O_5; triethylamine, diethylamine, DMF, and pyridine were distilled from CaH_2; and methanol was distilled from magnesium turnings. Other solvents were purified and dried using standard procedures. Phthalimide-*N*-sulfenyl chloride,[19] 3,4,5-tri-*O*-benzyl-D-galactal,[20] tri-*O*-benzyl-D-allal,[21] 4,6-*O*-isopropylidene-D-glucal[22] and 2-acetoxy-3,4,5-tribenzyl-D-glucal[23] were prepared as describe in the literature. 3,4,5-Tri-*O*-acetyl-D-galactal and diketene, were purchased from Aldrich. Analytical TLC was performed with the use of plates coated with a 0.25 mm thickness of silica gel containing PF_{254} indicator (EM Science) and short–long-wave ultraviolet light was used to visualize the spots. Chromatotron Plates (radial chromatography) were prepared by using Kielesgel 60 PF_{254} (EM Science). Flash chromatography was performed as described by Still[24] with Kieselgel 60 (230–400 mesh) purchased from Aldrich and EM Science. All compounds isolated by chromatography were sufficiently pure (>95% by NMR analysis) for use in subsequent preparative reactions.

4.1.1. 3-(1,3-Dioxoisoindolin-2-ylthio)-6-methyl-3,5,6-trihydro-2H-pyran-2,4-dione (*R*/*S*)-(14). A stirred solution of phthalimidosulfenyl chloride (170.8 mg, 0.8 mmol) in THF (8 mL) was cooled at −40°C and the racemic 5,6-dihydro-4-hydroxy-6-methyl-2H-pyran-2-one **12** (50 mg, 0.4 mmol) dissolved in 2 mL of THF was added dropwise in a period of 7 min. After 25 min all of the starting material was consumed. Pentane (10 mL) was added and a white precipitate was formed, the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature without stirring. Filtration of this mixture provided 122 mg of a white crude solid. Recrystallization from CH_2Cl_2:hexane afforded pure compound (*R*/*S*)-(**14**) (55.4 mg, 46%) as colorless crystals: R_f=0.05 (9:1 CH_2Cl_2:MeOH); ^{1}H NMR δ 1.53 (d, J=6.3 Hz, 3H), 2.86 (dd, J=2.36, 16 Hz, 1H), 3.04 (dd, J=11.33, 16 Hz, 1H), 5.02–5.06 (m, 1H), 7.77–7.80 (m, 4Harom); ^{13}C NMR δ 21.1, 44.2, 72.2, 101.4, 124.7, 132.0, 135.3, 165.3, 167.9, 194.7.

4.2. (2*R*,3*R*,4*R*,8*R*)- and (8*S*,2*R*,3*R*,4*R*)-3,4-Bis-(phenylmethoxy)-8-methyl-2-[(phenylmethoxy)methyl]-2,3,4,8,9,4a-hexahydro-10aH,4aH-2H-pyrano[2,3-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-6-one (25, *R*,*S* diastereomers at CH_3–C): general cycloaddition procedure

The racemic sulfino lactone (*R*/*S*)-(**14**). (35.5 mg, 0.116 mmol) and tribenzylglucal **24** (48.4 mg, 0.116 mmol) were dissolved in CH_2Cl_2 (1 mL), and pyridine (55.1 mg, 0.696 mmol) was added, and the solution was stirred at room temperature for 5 days. ^{1}H NMR of an aliquot was taken. The ratio of the anomeric protons of the product and the glucal was H_p:H_g=1:1. The reaction was left stirring 2 more days, but the ratio of glucal to product remained the same. The reaction was worked up by dissolving it in CH_2Cl_2, extracting with saturated aqueous NH_4Cl and back extracting the aqueous layer with CH_2Cl_2. The organic extracts were washed twice with brine, dried (Na_2SO_4), and concentrated in vacuo to give 95.2 mg of a crude brown solid. Purification was done by flash chromatography, eluting with petroleum ether:ethyl acetate (3:1), and finally with pure ethyl acetate in order to remove the product, 35.6 mg (53.5%, 100% based in the recovered glucal), as a 1:1 mixture of diastereomers. This mixture was separated by silica gel P-plate (1000 μm 20×10 cm) eluting first with ethyl acetate then 5 times with petroleum ether:ethyl acetate 3:1. This separation afforded two diastereomers: upper spot 7.3 mg and lower spot 2.8 mg both as white foamy solids.

4.2.1. Compound 25, upper spot, *R* at CH_3. R_f=0.59 (1:3 ethyl acetate:hexane, eluted 5 times); mp 128–130°C; ^{1}H NMR δ 1.47 (d, J=6.3 Hz, 3H), 2.40 (dd, J=3.6, 17.4 Hz, 1H), 2.48 (dd, J=12.3, 17.4 Hz, 1H), 2.37 (dd, J=2.8, 10.6 Hz, 1H), 3.67–3.85 (m, 4H), 4.04 (app d, J=10 Hz, 1H), 4.42–4.50 (m, 1H), 4.57 (d, a part of an AB system, J_{AB}=12 Hz, $\Delta\nu$=34.65 Hz, 1H), 4.59 (d, a part of an AB system, J_{AB}=10.2 Hz, $\Delta\nu$=95.55 Hz, 1H), 4.68 (d, J_{AB}=12.3 Hz, $\Delta\nu$=34.65 Hz, 1H), 4.88 (d, a part of an

AB system, J_{AB}=10.2 Hz, $\Delta\nu$=29.85 Hz, 1H), 4.91 (d, a part of an AB system, J_{AB}=9.3 Hz, $\Delta\nu$=95.55 Hz, 1H), 4.97 (d, a part of an AB system, J_{AB}=10.5 Hz, $\Delta\nu$=29.85 Hz, 1H), 5.69 (d, J=2.7 Hz, 1H), 7.20–7.50 (m, 15Harom); ^{13}C NMR δ 20.5, 35.2, 42.9, 68.1, 72.8, 73.6, 73.8, 75.5, 76.3, 78.6, 94.7, 96.6, 128.1, 128.2, 128.4, 128.6, 128.7, 128.8, 137.6, 137.9, 159.4, 164.6; IR (thin film): 1703 cm^{-1} (ν C=O); ESMS *m/z* 592 (M+18).

4.2.2. Compound 25, lower spot, *S* at CH_3. R_f=0.48 (1:3 ethyl acetate:hexane, eluted 5 times); mp 44–47°C; $[\alpha]_D$=+128.8° (*c*=2.56, $CHCl_3$); ^{1}H NMR δ 1.46 (d, J=6.3 Hz, 3H), 2.48 (dd, J=4.5, 17 Hz, 1H), 2.62 (dd, J=10.8, 17 Hz, 1H), 3.29 (dd, J=3, 10.8 Hz, 1H), 3.55 (dd, J=9, 10.5 Hz, 1H), 3.68–3.82 (m, 3H), 3.96 (app dt, J=3, 10.1 Hz, 1H), 4.52–4.69 (m, 4H), 4.79 (d, J_{AB}=10.2 Hz, a part of an AB system, 1H), 4.98 (d, J=10.2 Hz, a part of an AB system, 1H), 5.72 (d, J=3 Hz, 1H), 7.15–7.44 (m, 15Harom); ^{13}C NMR δ 21.7, 36.0, 43.3, 69.3, 73.2, 74.7, 74.8, 76.5, 78.4, 79.3, 95.1, 98.1, 102.4, 129.0, 129.1, 129.3, 129.6, 138.8, 138.9, 161.3, 164.85; IR (thin film): 1704 cm^{-1} (ν C=O); ESMS *m/z* 592 (M+18). Anal. calcd for $C_{33}H_{34}0_7S$: C, 68.97; H, 5.96; S, 5.58. Found: C, 68.96, H, 5.96; S, 5.70.

4.2.3. 5-((3*S*)-1,3-Dihydroxybutylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione [(*S*)-19]. Dried Fleischman's yeast (75 g), sucrose (37.5 g), and 'tap' water (150 mL) were divided into five portions and placed in 5×500 mL Erlenmeyer flasks and shaken for 24 h, at which time the yeast suspension expanded to entirely fill the flasks. Acetoacetylated Meldrum's acid **18** (1.14 g, 5 mmol), divided in five 0.228 g portions was placed in each flask and shaken for 1 day. Most of the water was evaporated. Celite (10 g) and NaCl (5 g) were placed in each flask and mixed until became a paste. This paste was extracted 6 times with CH_2Cl_2 by vigorous mechanical stirring, followed by decantation, starting with 150 mL of CH_2Cl_2 and the remaining five extractions with 100 mL. The combined organic extracts were dried ($MgSO_4$), and concentrated in vacuo to give 1.42 g (100%) of the crude chiral alcohol (*S*)-**19** as a gold oil: R_f=0.50 (CH_2Cl_2:MeOH); $[\alpha]_D$=+41.80° (*c*=0.55, EtOH), (lit.[43] $[\alpha]_D$=+50.5, *c*=2.05, EtOH); ^{1}H NMR δ 1.3 (d, J=6.3 Hz, 3H), 1.7 (s, 6H), 3.1 (dd, J=3.9, 13.5 Hz, 1H), 3.3 (dd, J=8.4, 13.5 Hz, 1H), 4.3 (m, 1H).

4.2.4. (*S*)-6-Methyl-3,5,6-trihydro-2H-pyran-2,4-dione-(20). The enantiopure alcohol (*S*)-**19**, (1.91 g, 8.29 mmol) was dissolved in dried MeOH (30 mL) and stirred under reflux. After 2.5 h, the starting material was consumed as indicated by TLC, and the reaction mixture was cooled to room temperature and concentrated in vacuo to provide 1.10 g of crude. Purification of this crude by flash column chromatography using florisil and eluting with CH_2Cl_2:MeOH (20:1) afforded 0.600 g (56%) of the enantiopure lactone (*S*)-**19** as a white granular solid: R_f=0.53 (9:1 CH_2Cl_2:MeOH); mp 127–129°C $[\alpha]^{25}$=+150.74° (*c*=2.1, EtOH), lit.[43] $[\alpha]^{29}$=+153.4°, *c*=2.1, EtOH); ^{1}H NMR δ 1.53 (d, J=6.3 Hz, 3H), 2.46 (dd, J=11.1, 18.3 Hz, 1H), 2.73 (dd, J=2.7, 18.3 Hz, 1H), 3.44 (d, a part of an AB system, J_{AB}=18.9 Hz, $\Delta\nu$=38.25 Hz, 1H), 3.57 (d, a part of an AB system, J_{AB}=18.9 Hz, $\Delta\nu$=38.25 Hz, 1H), 4.76–4.84 (m, 1H); ^{13}C NMR (DMSO-d_6) δ 20.3, 34.0, 71.5, 90.6, 167.1, 172.7; IR (KBr): 1675 cm^{-1} (ν C=O).

4.2.5. (6*S*,12*S*,17*S*,18*S*,1*R*,10*R*)-18-Hydroxy-6,15,15-trimethyl-5,9,11,14,16-pentaoxa-2-thiatetracyclo[8.8.0.0-⟨3,8⟩.0⟨12,17⟩]octadec-3(8)-en-4-one (37). Following the general stepwise cycloaddition procedure, the enantiopure sulfino-lactone (*S*)-**21** (0.339 g, 1.11 mmol), and isopropylidene glucal **36** (0.206 g, 1.11 mmol) in $CHCl_3$ (4 mL), were combined with 2,6-lutidine (18.9 mg, 1.11 mmol), and after stirring for 6 days, the reaction was worked up to give 0.352 g of a light brown crude solid. Purification of this crude by radial chromatography, eluting with hexane:ethyl acetate (8:1 to 3:1), afforded 98.6 mg (79% based on the reacted glucal) of compound **37**: R_f=0.12 (1:1 hexane:ethyl acetate); ^{1}H NMR δ 1.44 (s, 3H), 1.50 (d, J=6.3 Hz, 3H), 1.55 (s, 3H), 2.50 (dd, J=4.2, 17 Hz, 1H), 2.73 (dd, 11.1, 17 Hz, 1H), 3.2 (dd, J=3, 10 Hz, 1H), 3.8 (d, J=2.4 Hz, 1H), 3.65–3.93 (m, 5H), 4.11–4.68 (m, 1H), 5.7 (d, J=3 Hz, 1H). Anal. calcd for $C_{15}H_{20}O_7S$: C, 52.32; H, 5.85; S, 9.31. Found: C, 52.15; H, 5.80; S, 9.05.

4.2.6. (3*S*,4*S*,8*S*,2*R*,10a*R*)-3,4-Dihydroxy-2-(hydroxymethyl)-8-methyl-2,3,4,8,9,4a-hexahydro-2H-pyrano[2,3-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-6-one (38). The isopropylidene adduct **37** was left sitting in the refrigerator in $CDCl_3$ inside an NMR tube for 3 days, at which time the original clear solution became cloudy. Filtration of this cloudy solution afforded the trihydroxy adduct, **38**, as a white powder: R_f=0.01 (neat ethyl acetate); mp 212–213°C (decomposed); ^{1}H NMR in DMSO-d_6 δ 0.47 (d, J=6.3 Hz, 3H), 1.64 (t, J=1.8 Hz, 2H), 1.75 (d, J=6.9 Hz, 2H), 2.25–2.83 (m, 4H), 3.76–3.84 (m, 2H), 4.4 (d, J=5.1 Hz, 1H), 4.63 (t, J=2.4 Hz, 1H), 4.83 (d, J=2.7 Hz, 1H); ^{1}H NMR in acetone-d_6: δ 1.40 (d, J=6.3 Hz, 3H), 2.60 (dd, J=4.8, 16.8 Hz, 1H), 2.72 (dd, J=9.6, 16.8 Hz, 1H), 2.84 (br s, 1H), 3.13 (dd, J=2.7, 9.9 Hz, 1H), 3.47–3.58 (m, 2H), 3.60–3.84 (m, 3H), 4.49 (br s, 1H), 4.50–4.69 (m, 1H), 4.79 (br s, 1H), 5.69 (d, J=2.7 Hz, 1H); ^{13}C NMR DMSO-d_6: δ 20.1, 33.7, 42.3, 60.4, 69.1, 70.6, 71.9, 75.5, 92.3, 96.4, 160.5, 163.5; IR (KBr): 1672 (ν C=O); ESMS *m/z* 322 (M+18, 100), HRMS calcd for $C_{12}H_{16}0_7S$ 305.0695 (M+H). Found: 305.0689 (M+H).

4.2.7. ((8*S*,2*R*,3*R*,4*R*)-3-Acetyloxy-2-(acetyloxymethyl)-8-methyl-6-oxo-2,3,4,8,9,4a-hexahydro-10aH,4aH-2H-pyrano[2,3-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-4-yl acetate (28). Following the stepwise cycloaddition procedure, a solution of 0.200 g (0.65 mmol) of thioketolactone **21**, tri-*O*-acetyl glucal **27** (0.177 g, 0.65 mmol) in chloroform (2.5 mL), and 2,6-lutidine (0.65 mmol, 69.7 mg) was stirred for 48 h to provide 0.354 g of a crude solid which after flash chromatography with florisil, eluting with petroleum ether:ethyl acetate (4:1 to 2:1) afforded compound **28** (0.139 g, 53%) contaminated with an unstable material that converted to **28** on silica (and guessed to be an adduct with the lactonic rather than the ketonic oxygen). ^{1}H NMR δ 1.48–1.51 (m, 6H), 2.02–2.1 (m, 18H), 2.54–2.67 (m, 4H), 3.34–3.38 (m, 2H), 4.1–4.31 (m, 6H), 4.6–4.8 (m, 2H), 5.11–5.21 (m, 4H), 5.71 (d, J=2.14 Hz, 1H), 5.79 (d, J=2.52 Hz). Anal. calcd for $C_{18}H_{22}O_{10}S$: C, 50.23; H, 5.15; S, 7.45. Found: C, 50.35; H, 5.19; S, 7.44.

4.2.8. ((8*S*)-3,4-Diacetyloxy-8-methyl-6-oxo-2,3,4,8,9,4a-hexahydro-10aH-2H-pyrano[2,3-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-2-yl)methyl acetate [28 (below face)] and [29 (above face)]. Following the stepwise cycloaddition procedure a solution of 0.879 g (2.88 mmol) of the thioketolactone **21**, tri-*O*-acetyl glucal **27** (0.784 g, 2.88 mmol) in DMSO (12 mL), and 2,6-lutidine (0.309 g, 2.88 mmol) was stirred for 11 days to provide 0.192 g of crude. Flash column chromatography of this crude, eluting with hexane:ethyl acetate (3:1 to 2:1), afforded 63 mg (5%) of the below face adduct, compound **28**: R_f=0.4 (1:1 hexane:ethyl acetate), and 88.2 mg (7%) of the top face adduct, compound **29**: R_f=0.34 (1:1 hexane:ethyl acetate); mp 88–90°C; ^{1}H NMR δ 1.44 (d, J=6.3 Hz, 3H), 2.05 (s, 3H), 2.085 (s, 3H), 2.09 (s, 3H), 2.49 (dd, J=4.5, 17.1 Hz, 1H), 2.61 (dd, J=10.8, 17.1 Hz, 1H), 3.83–3.87 (m, 2H), 4.22–4.23 (m, 2H), 4.24–4.29 (m, 1H), 4.62–4.69 (m, 1H), 5.39 (d, J=1.5 Hz, 1H), 5.48 (dd=t, $J_A \cong J_B$=9.3 Hz, 1H); ^{13}C NMR δ 20.8, 21.0, 22.9, 31.9, 34.7, 41.1, 65.3, 71.9, 72.3, 74.4, 77.4, 92.1, 96.8, 156.9, 163.9, 169.45, 170.08; IR (thin film): 1750 (ν C=O, –OC(O)CH$_3$), 1702 (ν C=O, lactone, cm^{-1}; ESMS m/z 448 (M+18, 100), 431 (M+1, 11). Anal. calcd for $C_{18}H_{22}O_{10}S$: C, 50.23; H, 5.15; S, 7.45. Found: C, 50.22; H, 5.06; S, 7.20.

4.2.9. (3*S*,8*S*,2*R*,4*R*)-3-Acetyloxy-2-(acetyloxymethyl)-8-methyl-6-oxo-2,3,4,8,9,4a-hexahydro-10aH,4aH-2H-pyrano[2,3-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-4-yl acetate (31). Following the general 'one pot' cycloaddition procedure, a solution of sulfenyl chloride (0.253 g, 1.2 mmol) and the (*S*)-lactone **21** (0.101 g, 0.79 mmol) in THF, was combined with tri-*O*-acetyl galactal **30** (0.215 g, 0.79 mmol), and 2,6-lutidine (128.6 mg, 1.2 mmol). After stirring for 6 days, the reaction mixture was worked up to provide 0.452 g of a dark brown crude solid. Purification of this crude by radial chromatography, eluting with hexane: ethyl acetate (5:1 to 3:1) gave 0.136 g (40%) of compound **31** as a clear thick oil: R_f=0.13 (2:1 hexane:ethyl acetate); ^{1}H NMR δ 1.45 (d, J=6.3 Hz, 3H), 2.01 (s, 3H), 2.04 (s, 3H), 2.14 (s, 3H), 2.53 (dd, J=4.8, 17.1 Hz, 1H), 2.64 (dd, J=9.6, 17.1 Hz, 1H), 3.61 (dd, J=2.7, 11.7 Hz, 1H), 4.12 (d, J=6.6 Hz, 2H), 4.38 (t, J=6.6 Hz, 1H), 4.61–4.68 (m, 1H), 4.95 (dd, J=3, 12 Hz, 1H), 5.40 (app d, J=1.8 Hz, 1H), 5.75 (d, J=2.7 Hz, 1H); ^{13}C NMR δ 20.6, 20.7, 20.8, 34.6, 36.4, 61.6, 65.8, 67.2, 69.3, 72.5, 77.4, 96.4, 124.5, 135.1, 158.9, 169.9, 170.0, 170.5; ESMS m/z 448 (M+18, 100), 431 (M+H, 50). Anal. calcd for $C_{18}H_{22}O_{10}S$: C, 50.23; H, 5.15; S, 7.45. Found: C, 50.06; H, 5.25.

4.2.10. (8*S*)-3,4-Bis(phenylmethoxy)-8-methyl-2-[(phenylmethoxy)methyl]-2,3,4,8,9,4a-hexahydro-10aH-2Hpyrano[2,3-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-6-one (33). Following the general cycloaddition procedure, a solution of sulfenyl chloride (668.4 mg, 3.13 mmol), and the (*S*)-lactone **21** (267.5 mg, 2.09 mmol) in $CHCl_3$ was combined with tri-*O*-benzylgalactal **32** (665.6 mg, 1.6 mmol) and 2,6-lutidine (2.09 mmol, 224 mg). The reaction was stirred 17 h to provide upon work up and removal of the phthalimide, 0.658 g of a crude oily residue. Flash column purification of this crude afforded 255 mg (28%) of compound **33** as a single regioisomer: R_f=0.16 (3:1 petroleum ether:ethyl acetate); ^{1}H NMR δ 1.4 (d, J=6.4 Hz, 3H), 2.4 (app d, J=8.1 Hz, 2H), 3.40 (dd, J=2.42, 11.12 Hz, 1H), 3.56 (app d, J=5.6 Hz, 2H), 3.83 (dd, J=2.83, 11.1 Hz, 1H), 3.96 (app d, J=1.20 Hz, 1H), 4.42 (d, a part of an AB system, J_{AB}=11.81 Hz, 1H), 4.45 (d, a part of an AB system, J_{AB}=11.81 Hz, 1H), 4.57–4.62 (m, 2H), 4.74 (s, 2H), 4.95 (d, a part of an AB system, J_{AB}=11.2 Hz, 1H), 5.73 (d, J=2.79 Hz, 1H), 7.27–7.41 (m 15Harom); ^{1}HNMR (Benzene-d_6): δ 0.84 (d, J=6.3 Hz, 3H), 1.57 (dd, J=4.5, 16.65 Hz, 1H), 1.76 (dd, J=10.5, 16.65 Hz, 1H), 3.38 (dd, J=2.7, 11.1 Hz, 1H), 3.63 (dd, J=5.4, 9 Hz, 1H), 3.71–3.79 (m, 3H), 3.94 (app d, J=0.9 Hz, 1H), 4.09 (t, J=6.6 Hz, 1H), 4.24 (AB q, J_{AB}=12 Hz, $\Delta\nu/J$=2.4 Hz, 2H), 4.57 (d, a part of an AB system, J_{AB}=11.1 Hz, $\Delta\nu$=135 Hz, 1H), 4.66 (d, J=12 Hz, 2H), 5.02 (d, a part of an AB system, J_{AB}=11.1 Hz, $\Delta\nu$=135 Hz, 1H), 5.4 (d, J=2.7 Hz, 1H), 7.05–7.45 (m, 15H); ^{13}C NMR δ 20.8, 35.0, 38.6, 68.8, 72.2, 72.6, 73.1, 73.4, 73.7, 73.9, 75.2, 77.4, 77.8, 77.9, 94.2, 97.8, 128.1, 128.2, 128.4, 128.5, 128.6, 128.7, 128.8, 137.8, 138.3, 159.9, 164.0; IR (thin film): 1703 (ν C=O) cm^{-1}; ESMS m/z: 592 (M+1). Anal. calcd for $C_{33}H_{34}O_7S$: C, 68.97; H, 5.96; S, 5.58. Found: C, 69.08; H, 6.01.

4.2.11. (2*S*,5a*S*,6*R*,7*R*,9a*R*)-6,7-Bis(phenylmethoxy)-2-methyl-8-[(phenylmethoxy)methyl]-1,2,3,6,7,8,9,5a,9a-nonahydro-3-oxaphenoxathiin-4-one (35). Following the general stepwise cycloaddition procedure, the sulfino-lactone **21** (155.8 mg, 0.51 mmol), tribenzyl allal **34** (212.16 mg, 0.51 mmol) in $CHCl_3$ (5.0 mL), were combined with 2,6-lutidine (54.7 mg, 0.0.51 mmol), and stirred for 1.5 h, upon which time, more sulfino-lactone (155.8 mg 0.51 mmol) was added. The stirring was continued for an additional 0.5 h. The reaction was worked up, and the phthalimide was removed to provide 275.2 mg of a very pure crude solid. Filtration of this crude through a short pad of silica gel, afforded compound **35** (265.2 mg, 91%) as an off-white solid: R_f=0.56 (3:1 hexane:ethyl acetate); ^{1}H NMR δ 1.39 (d, J=6.3 Hz, 3H), 2.26 (dd, J=4.0, 16.95 Hz, 1H), 2.45 (dd, J=11.7, 16.95 Hz, 1H), 3.45 (dd, J=1.5, 4.95 Hz, 1H), 3.61 (app dd, J=3.6, 4.5 Hz, 2H), 3.74 (dd, 3.0, 4.95 Hz, 1H), 4.02 (dd, J=3.6, 8.4 Hz, 1H), 4.29 (dt, $2J_A$=J_B, J=4.2, 8.4 Hz, 1H), 4.36–4.50 (m, 5H), 4.6 (d, J=12 Hz, 2H), 5.6 (d, J=1.5 Hz, 1H), 7.13–7.34 (m, 15H); ^{13}C NMR δ 20.7, 35.1, 39.7, 69.7, 72.0, 72.3, 73.1, 73.7, 76.6, 77.0, 93.5, 97.6, 127.2, 127.9, 128.2, 128.7, 137.7, 138.2, 157.9, 164.2; IR (thin film): 1701 (ν C=O) cm^{-1}; ESMS m/z 592 (M+18). Anal. calcd for $C_{33}H_{34}O_7S$: C, 66.87; H, 6.12. Found: C, 66.70; H, 6.55.

4.2.12. (8*S*)-3,4-Bis(phenylmethoxy)-8-methyl-6-oxo-2-[(phenylmethoxy)methyl]-2,3,4,8,9,4a-hexahydro-10aH-2H-pyrano[2,3-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-4a-ylacetate (40 and 41) and (2*S*,4*S*,7*S*,3*R*,10a*R*,4a*R*)-3,4-bis(phenylmethoxy)-7-methyl-9-oxo-2-[(phenylmethoxy)-methyl]-2,3,4,6,7,4a-hexahydro-2H-pyrano-[3,2-*b*]2H-pyrano[3,4-*e*]1,4-oxathiin-4a-yl acetate (42). Following the general 'one pot' cycloaddition procedure, sulfenyl chloride (1.41 g, 6.58 mmol) in THF (35.8 mL), was combined with the chiral lactone **21** (0.421 g, 3.29 mmol) in THF (32.9 mL), the glucal **39** (1.56 g, 3.29 mol) in THF (10.9 mL) and 2,6-lutidine (0.762 mL, 6.58 mmol) and after stirring for 10 days at room temperature, the reaction was worked up to give 2.46 g of crude solid. Removal of the phthalimide from this crude

using NaOH gave 1.64 g of dark brown crude syrup which ^{1}H NMR showed three different regioisomers, represented by the anomeric protons at 5.71, 6.21 and 6.41 ppm in a ratio 1.23:1.9:1, respectively. Separation by flash column chromatography using silica gel, eluting with hexane: ethyl acetate (2:1) gave 0.91 g of the three diastereomers (44% combined yield), as a clear oil. This 0.91 g corresponded to 0.389 g of the anomer at 6.21 ppm, 0.149 g of the anomer at 6.42 ppm, 0.187 g of the anomer at 5.71 ppm, and 0.184 g of an inseparable mixture of the three diastereomers.

4.2.13. Compound 42. (H_1 at 5.71 ppm). ^{1}H NMR δ 1.37 (d, J=6.3 Hz, 3H), 1.93 (dd, J=11.7, 17.4 Hz, 1H), 2.15 (s, 3H), 2.3 (dd, J=4.2, 17.4 Hz, 1H), 3.65–3.70 (m, 4H), 3.92 (d, J=8.4 Hz, 1H), 4.40–4.55 (m, 1H), 4.46 (d, J=12 Hz, 1H), 4.51 (d, J=10.8 Hz, 1H), 4.63 (d, J=12 Hz, 1H), 4.46 (d, J=12 Hz, 1H), 4.63 (d, J=12 Hz, 1H), 4.73 (d, J=12 Hz, 1H), 4.99 (d, J=10.5 Hz, 1H), 4.99 (d, J=12.3 Hz, 1H), 5.72 (s, 1H), 7.2–7.36 (m, 15Harom), ^{13}C NMR δ 20.6, 21.2, 30.9, 68.1, 73.4, 73.8, 75.5, 75.9, 85.8, 92.6, 104.7, 127.4, 127.9, 128.0, 128.0, 128.1, 128.3, 128.6, 128.7, 137.8, 138.1, 138.3, 161.5, 169.3; ESMS m/z 650 ($M+NH_4^+$).

4.2.14. Compound 41. (H_1 at 6.21 ppm). White foamy solid; mp 47–49°C; ^{1}H NMR δ 1.45 (d, J=6.3 Hz, 3H), 2.08 (s, 3H), 2.50 (d, J=4.8 Hz, 1H), 2.53 (d, J=10.5 Hz, 1H), 3.72–3.81 (m, 4H), 4.03 (app d, J=6.9 Hz, 1H), 4.50 (d, J=12.3 Hz, 1H), 4.6 (d, J=12 Hz, 1H), 4.6–4.67 (m, 1H), 4.78 (d, J=10.5 Hz, 1H), 4.80 (d, 10.8 Hz, 2H), 5.1 (d, J=10.2 Hz, 1H), 6.20 (s, 1H) 7.15–7.40 (m, 15Harom); ^{13}C NMR δ 20.8, 21.8, 34.7, 68.4, 72.7, 73.6, 74.1, 75.4, 76.0, 80.2, 82.7, 95.0, 98.0, 127.6, 127.9, 128.1, 128.5, 128.5, 128.6, 128.8, 137.6, 137.9, 138.1, 157.3, 163.1, 169.6; ESMS m/z 650 ($M+NH_4$). Anal. calcd for $C_{35}H_{36}O_9S$: C, 66.44; H, 5.73; S, 5.07. Found: C, 66.51; H, 5.87; S, 4.91; IR (thin film): 1760 (ν C=O), 1706 (ν C=O) cm^{-1}.

4.2.15. Compound 40. (H_1 at 6.42 ppm): ^{1}H NMR δ 1.38 (d, J=6.3 Hz, 3H), 2.02 (dd, J=11.7, 17.3 Hz, 1H), 2.13 (s, 3H), 2.31 (dd, J=3.9, 17.4 Hz, 1H), 3.63–3.76 (m, 3H), 3.95 (app dd, J=2.1, 9.9 Hz, 1H), 4.24 (d, J=9.3 Hz, 1H), 4.48 (d, J=12.3 Hz, 1H), 4.53 (d, J=10.8 Hz, 1H), 4.5–4.6 (m, 1H), 4.64 (d, J=12.3 Hz, 1H), 4.76 (d, 12.3 Hz, 1H), 4.80 (d, J=10.8 Hz, 1H), 4.97 (d, J=12 Hz, 1H), 6.42 (s, 1H), 7.13–7.44 (m, 15Harom); ^{13}C NMR δ 20.6, 21.2, 31.1, 68.3, 73.6, 73.9, 74.3, 75.7, 75.8, 77.0, 77.4, 81.6, 93.4, 103.6, 127.4, 127.9, 128.0, 128.2, 128.4, 128.7, 137.9, 138.2, 138.5, 161.9, 169.0; ESMS m/z 650 ($M+NH_4$).

4.2.16. Preparation of phthalimidesulfenyltetronic acid, 23. To a solution of phthalimide-*N*-sulfenyl chloride (1.0 mmol) in THF (5 mL) under a nitrogen atmosphere at −20°C (by internal thermometer), was added over a 15 min period via syringe a solution of tetronic acid **22** (1.0 mmol) in THF (5 mL) also prepared under a nitrogen atmosphere. After 20 min at −20°C the cooling bath was removed and pentane (20 mL) was added. The reaction mixture was warmed to room temperature and the solid material was removed by vacuum filtration and was confirmed to be the desired **23** by NMR. This pure sample was obtained in 22% yield. The filtrate was concentrated to provide additional amounts of **23** of about 80% purity in 67% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ10.4 (bs, 1H), 8.0–7.77 (m, 4H), 4.76 (s, 2H).

4.3. Typical procedure for cycloaddition of glycals with 23 as heterodiene precursor

To a chloroform (3 mL) solution of the glycal (0.25 mmol) was added phthalimide sulfenyltetronic acid **24** (0.50 mmol) and lutidine (29 μL, 0.25 mmol). The reaction mixture was stirred at room temperature until total consumption of the starting glycal was indicated by proton NMR of an aliquot of the reaction mixture. The time for completion of the reaction was usually not more than 24 h. At this time the reaction mixture was quenched with an aqueous solution of ammonium chloride and extracted with dichloromethane (3×10 mL). The combined organic extracts were dried over sodium sulfate and concentrated to give a crude material which was purified by radial chromatography (ethyl acetate:petroleum ether).

4.3.1. 3′,4′,6t-Tri-*O*-benzyl-D-glucosyl-below-face cycloadduct 44. Yield 61.7%, $[\alpha]_D^{25}$=+120.0° ($CDCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 7.35–7.15 (m, 15H), 5.78 (d, J=2.54 Hz, 1H), 4.93–4.51 (m, 10H), 4.03–3.98 (m, 1H), 3.85–3.56 (m, 4H), 3.32 (dd, J=10.91, 2.61 Hz, 1H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 169.3, 166.8, 137.7, 128.7, 128.3, 128.1, 98.8, 93.2, 78.5, 77.3, 75.6, 74.1, 73.8, 68.0, 67.3, 42.0. Anal. calcd for $C_{31}H_{30}0_7S$: C, 68.11; H, 5.53; S, 5.87. Found: C, 68.01; H, 5.29; S, 5.90.

4.3.2. 3′,4′,6′-Tri-*O*-benzyl-D-glucosyl-above-face cycloadduct 45. Yield 10.3%, $[\alpha]_D^{25}$=+76.8° ($CDCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.16 (m, 15H, −OBn), 5.41 (d. J=1.22 Hz, 1H, Cl′–H), 4.84–4.48 (m,8H, $-OCH_2-Ph$, $-OCH_2-$), 4.05 (q, J=8.34, 3.89 Hz, 1H, C3′–H), 3.98–3.91 (m, 2H, C4′–H, C5′–H), 3.81 (dd, J=3.31, 1.12 Hz, 1H, C2′–H), 3.71 (d, J=2.25 Hz, 2H, C6′–H, C6″–H). ^{13}C NMR (300 MHz, $CDCl_3$), δ 169.7, 164.2, 138.0, 137.9, 137.0, 128.8, 128.6, 128.3, 128.0, 97.6, 94.6, 79.9, 78.0, 77.2, 75.4, 73.8, 73.5, 71.4, 69.0, 67.9, 41.3. Anal. calcd for $C_{31}H_{30}0_7S$: C, 68.11; H, 5.53; S, 5.87. Found: C, 67.96; H, 5.39; S, 6.00.

4.3.3. 3′,4′,6′-Tri-*O*-acetyl-D-glucosyl-below-face cycloadduct 46. Yield 9.7%, $[\alpha]_D^{25}$=+186.0° ($CDCl_3$); ^{1}H NMR (300 MHz $CDCl_3$) δ 5.83 (d, J=2.55 Hz, 1H), 5.18–5.14 (m, 2H), 4.79, (dd, J=15.97, 11.28 Hz, 2H), 4.35–4.16 (abq, J=12.23, 4.42 Hz, 2H), 4.27–4.42 (m, 1H), 3.42 (dd, J=2.55 Hz, 1H), 2.12, 2.08, 2.03 (s×3, 9H). ^{13}C NMR (300 MHz, $CDCl_3$) 170.7, 169.9, 169.6, 168.7, 166.1, 134.5, 97.6, 93.5, 71.0, 68.9, 67.8, 61.6, 39.9, 20.9, 20.7. Anal. calcd for $C_{16}H_{18}0_{10}S$: C, 47.76; H,4.47; S, 7.97. Found: C, 47.78; H, 4.61; S, 7.64.

4.3.4. 3′,4′,6′-Tri-*O*-acetyl-gluco-above-face cycloadduct 47. Yield 58.3%, $[\alpha]_D^{25}$=+29.8° ($CDC1_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.58 (d, J=1.22 Hz, 1H), 5.46 (t, J=9.47 Hz, 1H), 5.34 (dd, J=9.28, 4.45 Hz, 1H), 4.78 (s, 2H), 4.24 (d, J=3.95 Hz, 2H), 3.95–3.91 (t, J=3.95 Hz, 1H), 3.88 (dd, J=4.32, 1.06 Hz, 1H), 2.11, 2.08, 2.05 (s ×3, 9H, −OAc). ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.8, 169.9, 169.4, 169.0, 163.9, 95.4, 93.7, 74.8, 71.6, 67.8, 65.0, 62.2,

41.0, 20.9, 20.8, 20.7. Anal. calcd for $C_{16}H_{18}0_{10}S$: C, 47.76; H, 4.47; S, 7.97. Found: C, 47.97; H, 4.27; S, 8.16.

4.3.5. 3′,4′,6′-Tri-*O*-acetyl-D-galactosyl-below-face cycloadduct 48. Yield 61%, ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (d, J=2.46 Hz, 1H), 5.47 (d, J=2.15 Hz, 1H), 5.01 (dd, J=11.85, 1.16 Hz, 1H), 4.78 (d, J=5.34 Hz, 2H), 4.45 (t, J=6.46 Hz, 1H), 4.16 (d, J=6.5 Hz, 2H), 3.70 (dd, J=9.32, 2.52 Hz, 1H), 2.18, 2.08, 2.05 (s×3, 9H, –OAc). Anal. calcd for $C_{16}H_{18}0_{10}S$: C, 47.76; H, 4.47; S, 7.97. Found: C, 47.57; H, 4.46; S, 7.96.

4.3.6. 2′-Acetoxy-3′,4′,6′-tri-*O*-benzyl-D-glucosyl cycloadduct 49 or 50. Yield 51%, $[\alpha]_D^{25}$=+5.45° ($CDCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.16 (m, 15H), 6.21 (s, 1H), 4.99–4.49 (m, 8H), 4.07 (d, J=5.66 Hz, 2H), 3.85–3.82 (m, 1H), 3.77 (dd, J=10.86, 3.09 Hz, 1H), 3.71 (d, J=10.66 Hz, 1H), 2.09 (s, 3H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 168 6, 168.4, 163.9, 138.0–127.8, 96.9, 96.5, 82.6, 79.4, 76.9, 76.8, 75.7, 75.5, 74.5, 68.1, 67.2, 21.8. Anal. calcd for $C_{33}H_{32}0_9S$: C, 65.55; H, 5.33; S, 5.30. Found: C, 65.44; H, 5.31; S, 5.06.

4.3.7. 4-{3,4,6-Tribenzyl-2-deoxy-D-α-glucosyl}-6-[*S*]-methyl-5,6-dihydro-2H-pyran-2-one (53). Desulfurization with W-2 Raney nickel. *General procedure*. A slurry of W-2 RaNi[25] (3 teaspoons, 9.0 g) in absolute ethanol was transferred to a flask provided with a stirring bar and a nitrogen inlet, and rinsed with absolute ethanol, followed by benzene until it became pH neutral. Toluene (2 mL) and benzene (2 mL) were added to this neutralized slurry and this slurry was cooled to 0°C, followed by the addition of compound **25***S* (500 mg, 0.871 mmol) in benzene (6 mL). After stirring this cooled reaction mixture for 45 min, TLC indicated disappearance of all of the starting material. The reaction mixture was filtered through a celite pad, which was rinsed exhaustively with ethyl acetate. The filtrate was concentrated in vacuo to provide 409.6 mg of an oily residue. Radial chromatography of this residue, eluting with hexane:ethyl acetate (4:1 to 1:1) afforded 270.4 mg (57%) of the disaccharide **53** as a clear oil: R_f=0.33 (1:1 hexane:ethyl acetate); ^{1}H NMR δ 1.3 (d, J=6.3 Hz, 3H), 1.79–1.83 (m, 1H), 2.16 (dd, J=2.83, 16.9 Hz, 1H), 2.26–2.36 (m, 2H), 3.52–3.59 (m, 2H), 3.69–3.72 (m, 2H), 3.91–3.93 (m, 1H), 4.36–4.60 (m, 5H), 4.82 (d, J=10.8 Hz, 1H), 7.11–7.33 (m, 15H); ^{13}C NMR δ 20.7, 34 6, 34.7, 68.5, 72.2, 72.4, 72.8, 73.8, 75.3, 76.9, 77.4, 94.4, 96.8, 127.9, 127.9, 128.0, 128.1, 128.6, 138.0, 138.4, 138.4, 167.4, 168.9; IR (thin film): 1710 (ν C=O) cm^{-1}. Anal. calcd for $C_{33}H_{36}0_7$: C, 72.78; H, 6.66. Found: C, 72.60; H, 6.78.

4.3.8. 4-{3,4,6-Tribenzyl-2-deoxy-α-D-galactosyl}-6-[*S*]-methyl-3,4,5,6-tetrahydrohydro-2H-pyran-2-one (54). Following the general desulfurization procedure, compound **33** (50 mg 0.087 mmol), W-2 RaNi (1/2 teaspoon, 1.5 g), in benzene (2 mL), and toluene (1 mL) were stirred for 3 h to provide 56 mg of an oily residue. Purification of this crude by flash column chromatography, eluting with hexane:ethyl acetate (9:1 to 5:1) afforded 14.7 mg (31%) of compound **54**: R_f=0.39 (3:1 petroleum ether:ethyl acetate); ^{1}H NMR δ 1.42 (d, J=6.3 Hz, 3H), 2.09 (dd, J=4.5, 13.2 Hz, 1H), 2.25 (dd, J=3.9, 17.4 Hz, 1H), 2.32–2.42 (m, 1H), 2.44 (ddd, J=1.8, 11.7, 17.4 Hz, 1H), 3.50 (dd, J=5.4, 9.15 Hz, 1H), 3.65 (app t, J=9 Hz, 1H), 3.84 (app t, J=6.3 Hz, 1H), 3.92 (ddd, J=2.1, 4.5, 13.95 Hz, 1H), 3.99 (s, 1H), 4.39 (d, a part of an AB system, J_{AB}=11.4 Hz, $\Delta\nu$=19.8 Hz, 1H), 4.46 (d, a part of an AB system, J_{AB}=11.7 Hz, $\Delta\nu$=19.8 Hz, 1H), 4.46–4.58 (m, 1H), 4.61 (d, a part of an AB system, J_{AB}=11.1 Hz, $\Delta\nu$=97.65 Hz, 1H), 4.66 (s, J_{AB}=0, 2H), 4.93 (d, a part of an AB system, J=11.4 Hz, $\Delta\nu$=97.65 Hz, 1H), 5.49 (d, J=1.8 Hz, 1H), 5.63 (d, J=2.7 Hz, 1H), 7.22–7.38 (m, 15H); ^{13}C NMR δ 20.7, 30.6, 34.7, 69.0, 70.8, 72.1, 72.3, 72.6, 73.8, 74.1, 74.8, 94.4, 97.4, 127.5, 127.9, 129.0, 128.0, 128.4, 128.5, 128.6, 128.7, 138.0, 138.31, 138.7, 167.5, 169.3; IR (thin film): 1706 (ν C=O) cm^{-1}.

4.3.9. 4-(2′-Deoxy-3′,4′,6′-tri-*O*-benzyl-α-D-glucosyl)-*O*-tetronic acid glycoside 56. Yield 40%, $[\alpha]_D^{25}$=+139.8° ($CDCl_3$): ^{1}H NMR (300 MHz, $CDCI_3$) δ 7.35–7.15 (m, 15H), 5.61 (d, J=2.10 Hz, 1H), 5.40 (s, 1H), 4.91–4.45 (m, 8H), 4.02–3.93 (m,1H), 3.81–3.75 (m, 2H), 3.62 (t, J=9.79 Hz, 2H), 2.47–2.41 (dd, J=4.84, 0.95 Hz, 1H), 1.96–1.86 (dd, J=10.96, 3.41 Hz, 1H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 176.0, 173.6, 138.3, 138.3, 137.8, 128.7, 128.6, 128.1, 128.0, 127.8, 99.8, 92.8, 76.6, 75.4, 73.8, 73.2, 72.4, 68.3, 68.0, 34.6. Anal. calcd for $C_{31}H_{32}0_7$: C, 72.08; H, 6.24. Found: C, 71.83; H, 6.31.

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