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A Mitsunobu route to C-glycosides

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ABSTRACT

C-Glycosides were successfully prepared via dehydrative alkylation under Mitsunobu conditions, using substituted sulfonyl methanes as nucleophiles. The materials prepared were converted to useful C-glycoside intermediates. An application of this approach toward the synthesis of *C*-glycolipids is presented.

1. Introduction

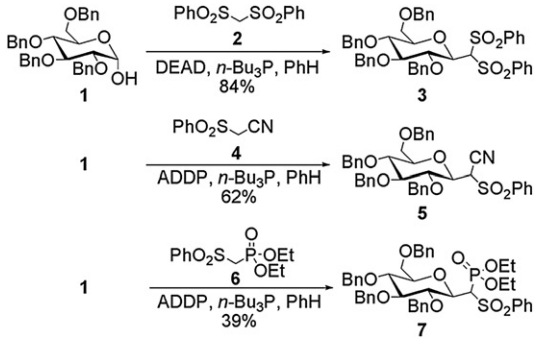
C-Glycosides have attracted much attention as analogs of O-glycosides, in which the hydrolytically labile acetal moiety of the carbohydrate is replaced by a functionality that is resistant to metabolic processing. A variety of C-glycosides, both synthetic and naturally occurring, display interesting pharmaceutical properties. This resulted in an intense effort by the scientific community in developing synthetic strategies to C-glycosides.[1]

Our synthetic approach to C-glycosides involves the use of the Mitsunobu reaction. The classical Mitsunobu reaction is a well-established method to condense an alcohol with a carboxylic acid. The utility of this reaction has been extended to the use of several heteroatom nucleophiles.[2] A dehydrative alkylation of bis-sulfones, mediated by the redox couple triphenylphoshine and DEAD, was described by Falck and co-workers.[3] Similarly, a few other examples of carbon nucleophiles employed in C-alkylation under Mitsunobu conditions have been reported.[4] The chain elongation of primary alcohols of carbohydrates employing bis(2,2,2-trifluoroethyl)-malonate as a nucleophile under Mitsunobu conditions was described.[5] However, when attempts were made to extend the methodology toward reaction at the anomeric position, no formation of C-alkylation product was observed.[6]

We now report our recent discovery that C-glycosides can be efficiently prepared by condensing a partially protected carbohydrate with a C-nucleophile under Mitsunobu conditions.

2. Results and discussion

Inspired by Falck's report,[3] we investigated the use of bis(phenylsulfonyl)methane (**2**) as a possible nucleophile in the synthesis of C-glycosides. Thus reaction of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**) with **2** under Mitsunobu conditions with tributylphosphine provided the β-C-glucoside product **3** in 84% yield, using 1.5 equiv of reagents (Scheme 1). The β-stereochemistry of **3** was easily assigned by ^{1}H NMR, which showed the anomeric proton as a doublet centered at 4.11 ppm with a coupling constant ^3J=9.9 Hz. To extend the utility of this approach to the synthesis of C-glycosides, a screening of potential nucleophiles was investigated. Thus, condensation of nucleophile **4**[7] with **1** provided the β-C-glucoside product **5** as a single diastereomer in 62% yield when 5 equiv of the reagents was employed. The β-stereochemistry of **5** was ascertained also in this case by the coupling constant ^3J=9.7 Hz measured for the signal corresponding to the anomeric proton (a doublet of doublets, which resonated at 3.97 ppm and which presented a smaller coupling ^3J=1.5 Hz with the proton located on the exocyclic carbon). Diethyl(phenylsulfonyl)methylphosphonate (**6**)[8] was found to be another successful nucleophile that gave the C-glucoside **7** as a single diastereomer in 39% yield (using 1.5 equiv of reagents). At this stage the stereochemistry at the anomeric center could not be established due to spectral overlap of diagnostic ^{1}H NMR signals. The β-stereochemistry of **7** was unambiguously confirmed later on when **7** was converted to compound **46**.



Scheme 1.

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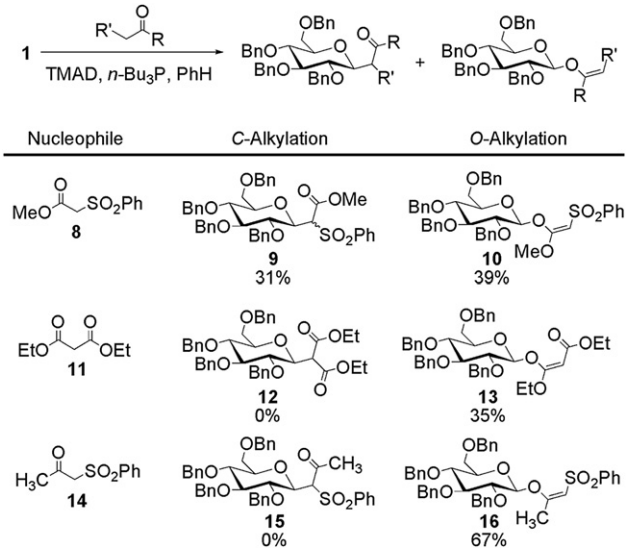
(Phenylsulfonyl)acetonitrile (**4**) was chosen for optimization studies, because of the lower yield obtained compared with the bis(phenylsulfonyl)methane (**2**) and the absence of byproducts (Table 1). Initially, several reaction conditions were explored by screening different solvents and reagents, but maintaining the same concentration (0.18 M starting material **1**) and using 1.5 equiv of the reagents (entries 1–8). The employment of different azo reagents resulted in no dramatic changes in the yields (entries 1–3). The use of tributylphosphine appeared to be crucial: whenever triphenylphosphine was employed the reaction failed[9] (entries 4 and 5). Also, solvents other than benzene were tested, with generally a negative effect in the yield (entries 6–8). Having determined the optimal reagents and solvent (entry 3) the reaction conditions were further investigated, and the reaction's yield improved as the excess of reagents was increased (entries 9 and 10). The use of the sterically less hindered Me_3P did not result in improvement of the yield (entry 11). Entries 12–14 describe the effect on yields that different reagents had on the condensation of **1** with bis(phenylsulfonyl)methane (**2**) under Mitsunobu conditions. As a confirmation of the results obtained for the nucleophile **4**, the yield appeared to be negatively affected by the use of triphenylphosphine (entry 12), while no substantial change in the yield was observed by employing either TMAD or DEAD (entries 13 and 14). Similar optimization studies for the synthesis of **7** did not result in substantial improvement in the yield (entries 15–19).

Ambident nucleophiles were reported to afford competitive alkylation under Mitsunobu reaction.[10] Indeed, when nucleophiles containing carbonyl groups were employed, competition between O- and C-glycosylation was noticed (Scheme 2). The use of methyl (phenylsulfonyl)acetate **8** as nucleophile afforded a 1/1.25 ratio of the C-glucoside **9** versus the O-alkylation product **10**. The β anomer of **10** was largely prevalent over the α, which amounted to 9% of the isolated *O*-glucosylated product. On the contrary, the O-glucoside **13** was the only product observed when diethyl malonate (**11**) was employed with no trace of the C-glycoside **12**, in accordance to what was previously reported for a fluorinated malonate ester.[6] Also phenylsulfonylacetone (**14**) gave the O-glucoside **16** as the sole product. In all cases each epimer of **10** and the products **13** and **16** were observed to be present as single isomers, but the *E* or *Z* configuration could not be established by NMR studies. The O-/C-glycosylation ratio appeared to be unaffected by the solvent used for the preparation of **9** and **10** (benzene, THF, DMF, and methylene chloride were tested).

Table 1
Optimization studies for dehydrative alkylation of **1** under Mitsunobu conditions[a]

Entry	Nucleophile	Product	Reaction conditions[b]	Yield (%)
1	**4** (1.5 equiv)	**5**	TMAD (1.5 equiv), *n*-Bu_3P (1.5 equiv), PhH	26
2	**4** (1.5 equiv)	**5**	DEAD (1.5 equiv), *n*-Bu_3P (1.5 equiv), PhH	27
3	**4** (1.5 equiv)	**5**	ADDP (1.5 equiv), *n*-Bu_3P (1.5 equiv), PhH	35
4	**4** (1.5 equiv)	**5**	ADDP (1.5 equiv), Ph_3P (1.5 equiv), PhH	0
5	**4** (1.5 equiv)	**5**	DEAD (1.5 equiv), Ph_3P (1.5 equiv), PhH	0
6	**4** (1.5 equiv)	**5**	ADDP (1.5 equiv), *n*-Bu_3P (1.5 equiv), CH_2Cl_2	3
7	**4** (1.5 equiv)	**5**	ADDP (1.5 equiv), *n*-Bu_3P (1.5 equiv), DMF	3
8	**4** (1.5 equiv)	**5**	ADDP (1.5 equiv), *n*-Bu_3P (1.5 equiv), THF	15
9	**4** (3 equiv)	**5**	ADDP (3 equiv), *n*-Bu_3P (3 equiv), PhH	50
10	**4** (5 equiv)	**5**	ADDP (5 equiv), *n*-Bu_3P (5 equiv), PhH	*62*
11	**4** (5 equiv)	**5**	ADDP (5 equiv), Me_3P (5 equiv), PhH	56
12	**2** (1.5 equiv)	**3**	DEAD (1.5 equiv), Ph_3P (1.5 equiv), PhH	41
13	**2** (1.5 equiv)	**3**	TMAD (1.5 equiv), *n*-Bu_3P (1.5 equiv), PhH	76
14	**2** (1.5 equiv)	**3**	DEAD (1.5 equiv), *n*-Bu_3P (1.5 equiv), PhH	*84*
15	**6** (1.5 equiv)	**7**	TMAD (1.5 equiv), *n*-Bu_3P (1.5 equiv), PhH	31
16	**6** (1.5 equiv)	**7**	ADDP (1.5 equiv), *n*-Bu_3P (1.5 equiv), PhH	39
17	**6** (3 equiv)	**7**	ADDP (3 equiv), *n*-Bu_3P (3 equiv), PhH	37
18	**6** (5 equiv)	**7**	ADDP (5 equiv), *n*-Bu_3P (5 equiv), PhH	41
19	**6** (5 equiv)	**7**	ADDP (5 equiv), Me_3P (5 equiv), PhH	35

[a] Abbreviations: ADDP: 1,1′-(azodicarbonyl)dipiperidine; DEAD: diethyl azodicarboxylate; TMAD: *N*,*N*,*N*′,*N*′-tetramethylazodicarboxamide.
[b] All reactions were run at room temperature overnight.



Scheme 2.

Interestingly, both the prochiral nucleophiles **4** and **6** provided the C-glucosides **5** and **7**, respectively, as single diastereomers, whose configurations at the carbon α to the sulfone could not be determined by NMR, whereas methyl (phenylsulfonyl)acetate (**8**) gave **9** as a 5/4 mixture of epimers.

In our hands, the success of this reaction was limited to nucleophiles **2**, **4**, **6**, and **8** while the use of nucleophiles **11**, **14**, and **17**–**23** (Fig. 1) resulted in no reaction with recovery of starting materials for **17**–**23** and formation of O-alkylation products in the cases of **11** and **14** (vide supra).

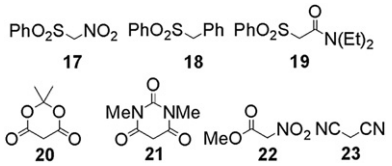
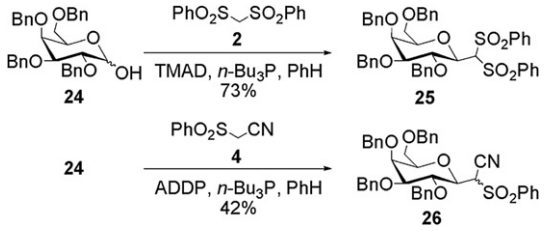


Figure 1. Unreactive nucleophiles.

By analogy with the C-glucosides described so far, the *C*-galactosides **25** and **26** were prepared under the same conditions (Scheme 3). The product **26** resulted to be a 6/1 mixture of epimers that was isolated in 42% yield. Also for the galactose series the β-anomers were the only products isolated. The coupling constant ^3J=10.1 Hz indicated an axial arrangement of the anomeric proton (4.42 ppm) of **25**. The stereochemistry at the anomeric center of **26** was more conveniently assigned later, after the removal of the



Scheme 3.

sulfonyl group, since the mixture of epimers was converted to the single isomer **30**.

The C-glucoside products **3**, **5**, **7**, and **9** were invariably the β-isomers as it would be expected starting from the commercially available 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**). No trace of the α anomer was observed, regardless of the nucleophile used and the reaction conditions. Similarly, complete selectivity toward the β-product was observed when the electrophile in the Mitsunobu step was the 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose (**24**) purchased as a mixture of anomers (α/β∼3/2). We can speculate that the α-phosphonium intermediate **I** would be more accessible to a nucleophilic attack under an S_N2 mechanism (Fig. 2). On the contrary, the antiperiplanar approach of a nucleophile to the β-phosphonium group in **II** would be less favorable because of steric reasons. The discord of the α/β ratio between the reagent and the product may be explained by an equilibrium between the two anomeric forms at some intermediate stage during the reaction.

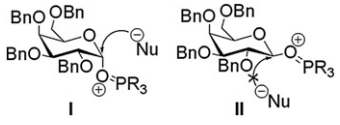
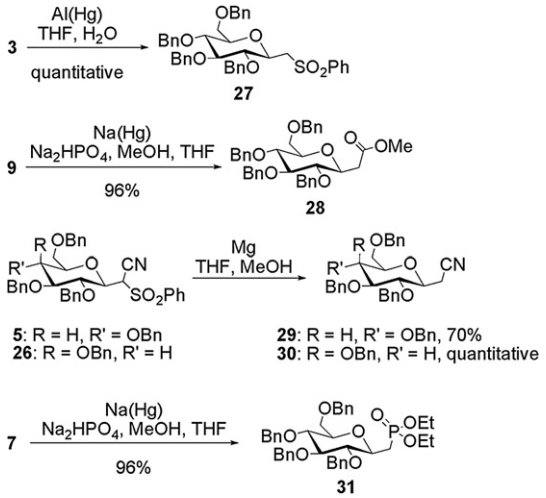


Figure 2. Origin of α/β selectivity.

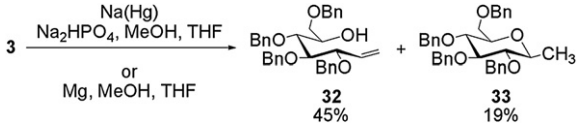
We then decided to investigate the synthetic utility of the materials we had synthesized. Mono-desulfonylation of **3** with aluminum amalgam[11] (Scheme 4) proceeded in quantitative yield, providing the C-glycoside **27** that can be employed in further functionalization by taking advantage of the versatile sulfonyl group.[12] Desulfonylation of compounds **5**, **7**, **9**, and **26** (Scheme 4) could be achieved by treatment with either sodium amalgam[13] or activated magnesium.[14] The ester **28** was isolated in excellent yield, and with spectroscopic data in agreement with those reported.[15] Desulfonylation of **5**, **26**, and **7** proceeded in all cases with good yields as well, providing the C-glycosides **29**,[16] **30**, and **31**,[17]



Scheme 4.

respectively. The coupling constant ^3J=9.3 Hz between the anomeric proton of **30**, centered at 3.46 ppm and the proton on the endocyclic carbon confirmed the β-stereochemistry assigned to the C-galactoside **26**. These materials **28**–**31** represent useful intermediates that can be employed, via further functionalization, in the preparation of more complex C-glycosides.

When the bis-sulfonyl derivative **3** was treated with either sodium amalgam or activated magnesium, the major product was **32**[18] along with the minor β-methyl C-glycoside **33**[19] in a 2.4/1 ratio (Scheme 5). The formation of **32** and **33** probably occurred via a stepwise mechanism that involved a first desulfonylation of **3** to obtain intermediate **27**. A further desulfonylation would convert **27** to a methylene anion intermediate, which would provide either **32** by β-elimination and consequent ring opening[20] or **33** by protonation. Formation of β-elimination products was not observed in the desulfonylation step to obtain compounds **28**–**31**, presumably due to the presence of an electron-withdrawing group α to the sulfone that stabilizes the intermediate carbanion. It may be possible that β-elimination does occur, followed by ring closure via Michael reaction. However, this alternate mechanism would most likely result in the formation of products **28**–**31** as anomeric mixtures.[21]

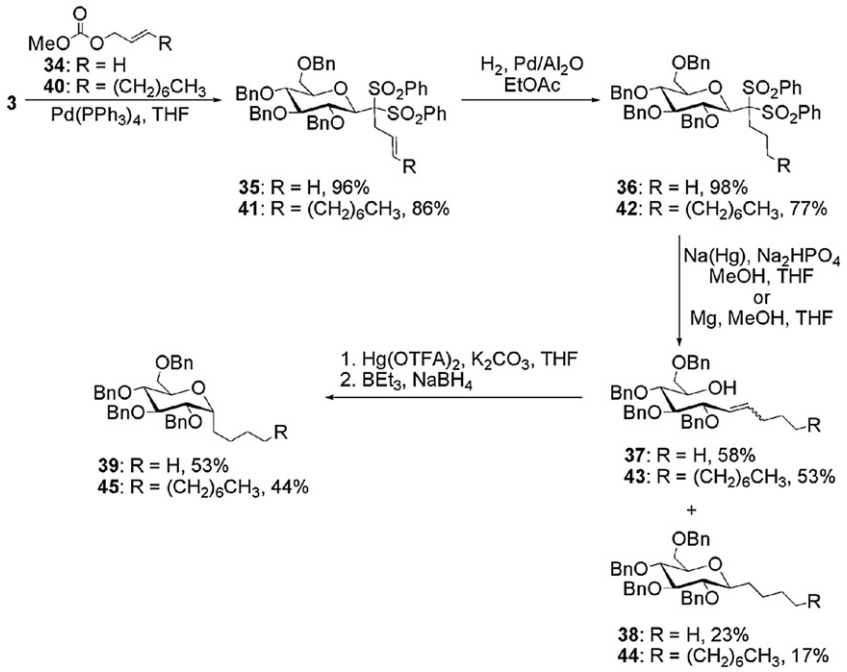


Scheme 5.

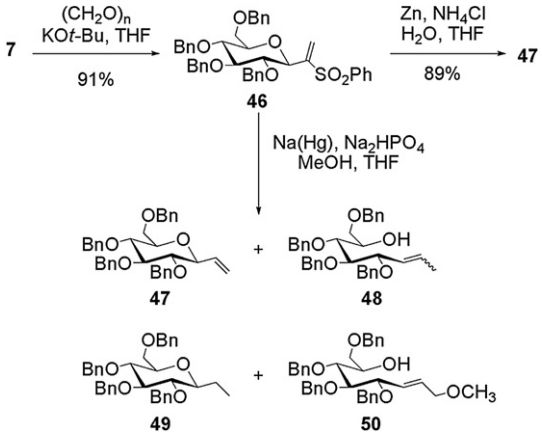
The bis-sulfone **3** was unreactive as a nucleophile in all our efforts at alkylation via deprotonation and treatment with either benzyl, allyl or propargyl bromides. On the contrary, palladium catalyzed allylation[22] of **3** provided in excellent yield the C-glycoside **35**, which was easily hydrogenated to **36** without affecting the benzyl groups by employing palladium on alumina as catalyst (Scheme 6). Desulfonylation with either sodium amalgam[13] or activated Mg[14] afforded invariably a 2.5/1 mixture of **37** (*E*/*Z*=5/1) and **38**.[23] Mercury mediated cyclization of **37**, followed by in situ demercurization,[24] afforded the α-C-glucoside anomer **39**.[23]

C-Glycolipids and their derivatives are important compounds pursued for their interesting antiviral properties against HIV,[25] malaria, and their anticancer activity.[26,27] Our synthetic sequence to the preparation of **39** was easily applied to the synthesis of the *C*-glucolipid **45** (Scheme 6). Thus, the methyl carbonate **40**[28] was prepared from the commercially available *trans*-2-decen-1-ol and coupled with the bis-sulfone **3**. Hydrogenation of **41**, followed by desulfonylation of **42** afforded **43** (*E*/*Z*=2.3/1) and **44** in 3/1 ratio, which were easily separated by column chromatography. Finally, ring closure of **43** gave the α-*C*-glucolipid **45**.

Olefination of **7** under Horner–Wadsworth–Emmons conditions was unsuccessful with propionaldehyde and benzaldehyde, but resulted in high yield of product **46** when paraformaldehyde was employed[29] (Scheme 7). At this stage it was possible to confirm the β-stereochemistry assigned to compound **7** by measuring a coupling constant ^3J=9.7 Hz for the doublet centered at 4.08 ppm and corresponding to the anomeric proton of **46**. The vinyl sulfone **46** could be employed in the preparation of a variety of interesting materials, since it can easily undergo Michael type reactions and cycloadditions.[30,31] Desulfonylation of **46** with sodium amalgam gave a mixture of four easily separable products: the desired olefin **47**[32] (14%) along with the major product **48** (*E*/*Z*=2.7/1, 20%), and small amounts of **49**[23] (9%) and **50** (8%). This last product **50** was likely formed by Michael addition of methanol to the vinyl sulfone **46**, followed by desulfonylation and β-elimination.[20] Mechanistically, products **48** and **49** could arise from reduction of the double bond of **46**, followed either by desulfonylation to obtain **49** or by desulfonylation/elimination to form **48**.



Scheme 6.



Scheme 7.

Complete conversion of **46** to the versatile synthetic intermediate **47** was achieved in excellent yield and with no traces of byproducts by using zinc dust and saturated aqueous NH_4Cl.[33]

3. Conclusions

The dehydrative alkylation of carbohydrates under Mitsunobu conditions is a novel and efficient approach to the synthesis of C-glycosides. This reaction is highly selective toward the β anomer, with no formation of α product ever detected in the glucose and galactose series. The C-glycosides obtained were easily converted into versatile materials that can be employed as intermediates in the synthesis of more complex C-glycosides with pharmacological properties.

In our hands, this strategy proved not to be generally applicable to a wide variety of carbon nucleophiles previously reported successful for the Mitsunobu reaction, but is limited to the four nucleophiles **2**, **4**, **6**, and **8**.

The simple reaction conditions, the accessibility of the starting materials, and the generally good yield obtained make the Mitsunobu reaction an efficient tool for the synthesis of C-glycosides.

4. Experimental section

4.1. General methods

Unless otherwise noted, reagents and solvents were used as received from commercial suppliers. All nonaqueous reactions were carried out under an atmosphere of dry nitrogen. NMR spectra were obtained at 500 MHz for proton and 125 MHz for carbon in deuterated solvents, using tetramethylsilane as an internal standard. The assignment of proton and carbon NMR peaks was supported by routine COSY and HSQC spectra and for some cases by NOESY spectra. Melting points were determined on a Mel-Temp II melting point apparatus and were uncorrected. High resolution mass spectra were obtained on a Q-TOF mass spectrometer using electrospray ionization. Thin layer chromatography analyses were carried out on EMD TLC 60 F_{254} silica gel plates. Flash column chromatography was carried out on ISCO, Inc. Combiflash Companion, using ACS reagent grade solvents.

4.2. General procedure for Mitsunobu reactions

To a stirred solution of the alcohol, phosphine, and nucleophile in benzene at 0 °C, under nitrogen atmosphere, was added the azo reagent. After the reaction mixture was stirred at 0 °C for 30 min, the mixture was allowed to slowly warm to room temperature and then stirred at room temperature overnight. The mixture was then filtered, and the filtrate was concentrated under reduced pressure to give the crude product. The residue was purified by column chromatography.

4.3. General desulfonylation procedure

4.3.1. Method A. A slurry of activated magnesium turnings in MeOH was heated at 50 °C. After a few minutes generation of hydrogen started and the sulfone or bis-sulfone starting material, dissolved in THF, was added. The resulting mixture was stirred at 50 °C and the reaction was monitored by TLC. If necessary, additional Mg was added to drive the reaction to completion. When consumption of all starting material was detected, the reaction

mixture was cooled to room temperature, 1 N HCl was added carefully, and the mixture was extracted with EtOAc. The organic extracts were combined, dried (MgSO4), filtered, and concentrated under reduced pressure to give the crude, which was purified by column chromatography to afford the product(s).

4.3.2. Method B. To a solution of the sulfone or bis-sulfone starting material in THF, MeOH and Na_2HPO_4 were added, followed by sodium amalgam (6 wt %) at room temperature. The mixture was stirred until TLC analysis indicated complete consumption of starting material and then 1 N HCl was added carefully. The mixture was extracted with EtOAc and the organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to obtain a residue that was purified by column chromatography when necessary.

4.4. Experimental procedures

*4.4.1. (2R,3R,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(bis(phenylsulfonyl)methyl)tetrahydro-2H-pyran (**3**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**, 2.0 g, 3.7 mmol), tributylphosphine (1.38 mL, 5.6 mmol), bis(phenylsulfonyl)methane (**2**, 1.7 g, 5.6 mmol), and DEAD (0.98 g, 5.6 mmol) in benzene (20 mL). Purification by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **3** (2.54 g, 84%) as a white solid: mp 55–58 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, J=8.1 Hz, 4H), 7.58 (t, J=6.9 Hz, 2H), 7.47–7.25 (m, 22H), 7.21–7.14 (m, 2H), 5.07 (d, J=11.8 Hz, 1H), 5.01 (s, 1H), 4.94 (d, J=11.1 Hz, 1H), 4.86 (d, J=11.8 Hz, 1H), 4.85 (d, J=11.1 Hz, 1H), 4.79 (d, J=10.7 Hz, 1H), 4.62 (d, J=10.7 Hz, 1H), 4.52 (d, J=12.2 Hz, 1H), 4.40 (t, J=9.4 Hz, 1H), 4.34 (d, J=12.3 Hz, 1H), 4.11 (d, J=9.9 Hz, 1H), 3.77 (t, J=9.4 Hz, 1H), 3.62 (t, J=9.0 Hz, 1H), 3.47 (dd, J=12.1, 3.4 Hz, 1H), 2.98–2.91 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 138.5, 138.3, 138.2, 138.1, 138.0, 134.3, 134.1, 130.2, 129.8, 128.8, 128.7, 128.5, 128.5, 128.4, 128.3, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 127.4, 127.4, 87.6, 82.5, 80.4, 78.0, 77.5, 76.6, 75.5, 75.1, 74.9, 73.4, 67.6; HRMS (ESI), m/z calcd for $[C_{47}H_{46}O_9S_2+NH_4]^+$: 836.2922; found 836.2930.

*4.4.2. 2-(Phenylsulfonyl)-2-((2R,3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)acetonitrile (**5**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**, 100 mg, 0.184 mmol), tributylphosphine (0.23 mL, 0.92 mmol), phenylsulfonyl acetonitrile (**4**, 167 mg, 0.92 mmol), and 1,1′-(azodicarbonyl)dipiperidine (232 mg, 0.92 mmol) in benzene (1 mL). Purification by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **5** (80 mg, 62%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97–7.94 (m, 2H), 7.63–7.57 (m, 1H), 7.49–7.43 (m, 2H), 7.38–7.24 (m, 16H), 7.24–7.21 (m, 2H), 7.21–7.16 (m, 2H), 4.96–4.92 (m, 2H), 4.86 (d, J=11.1 Hz, 1H), 4.77 (d, J=10.8 Hz, 1H), 4.61 (d, J=10.8 Hz, 1H), 4.60 (d, J=11.5 Hz, 1H), 4.38 (d, J=12.2 Hz, 1H), 4.21 (d, J=1.5 Hz, 1H), 4.20 (d, J=12.2 Hz, 1H), 3.97 (dd, J=9.7, 1.5 Hz, 1H), 3.73 (t, J=9.0 Hz, 1H), 3.67–3.60 (m, 2H), 3.44 (dd, J=9.6, 8.9 Hz, 1H), 3.33 (ddd, J=9.7, 3.5, 1.6 Hz, 1H), 3.19 (dd, J=11.8, 1.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3, 138.0, 137.9, 137.0, 137.0, 134.8, 129.9, 129.0, 129.0, 128.5, 128.5, 128.5, 128.3, 128.2, 127.9, 127.9, 127.8, 127.7, 127.5, 127.4, 111.3, 86.4, 79.8, 77.9, 77.5, 75.7, 75.3, 75.1, 75.1, 73.4, 68.0, 59.2; HRMS (ESI), m/z calcd for $[C_{42}H_{41}NO_7S+NH_4]^+$: 721.2942; found 721.2949.

*4.4.3. Diethyl phenylsulfonyl((2R,3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)methylphosphonate (**7**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**, 3.0 g, 5.55 mmol), tributylphosphine (2.1 mL, 8.32 mmol), diethyl (phenylsulfonyl)methylphosphonate (**6**, 2.4 g, 8.32 mmol), and ADDP (2.1 g, 8.32 mmol) in benzene (56 mL). Purification by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **7** (1.74 g, 39%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97–7.94 (m, 2H), 7.61–7.53 (m, 1H), 7.43 (t, J=7.8 Hz, 2H), 7.35–7.21 (m, 18H), 7.20–7.11 (m, 2H), 4.94 (d, J=11.6 Hz, 1H), 4.90 (d, J=11.1 Hz, 1H), 4.86 (d, J=11.2 Hz, 1H), 4.79 (d, J=10.8 Hz, 1H), 4.75 (d, J=11.6 Hz, 1H), 4.56 (d, J=10.8 Hz, 1H), 4.39 (d, J=11.8 Hz, 1H), 4.34 (d, J=11.8 Hz, 1H), 4.19 (t, J=9.2 Hz, 1H), 4.17–4.09 (m, 1H), 4.08–3.89 (m, 5H), 3.73 (t, J=9.5 Hz, 1H), 3.63 (t, J=9.0 Hz, 1H), 3.59 (dd, J=10.7, 3.2 Hz, 1H), 3.25 (dd, J=10.7, 1.1 Hz, 1H), 3.18 (ddd, J=9.6, 2.8, 1.5 Hz, 1H), 1.16 (t, J=7.1 Hz, 3H), 1.10 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.4, 138.5, 138.3, 138.1, 137.9, 133.6, 129.7, 128.5, 128.4, 128.4, 128.4, 127.9, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 87.5, 79.2, 78.4, 77.6, 76.6 (d, J_{C-P}=4.6 Hz), 75.4, 75.1, 74.7, 73.2, 68.4, 64.6 (d, J_{C-P}=136.1 Hz), 63.6 (d, J_{C-P}=5.9 Hz), 62.6 (d, J_{C-P}=6.3 Hz), 16.3 (d, J_{C-P}=6.7 Hz), 16.2 (d, J_{C-P}=7.0 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.1; HRMS (ESI), m/z calcd for $[C_{45}H_{51}O_{10}PS+NH_4]^+$: 832.3279; found 832.3284.

*4.4.4. Methyl 2-(phenylsulfonyl)-2-((2R,3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)acetate (**9**) and (2R,3R,4S,5R)-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-6-(1-methoxy-2-(phenylsulfonyl)vinyloxy)tetrahydro-2H-pyran (**10**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**, 120 mg, 0.22 mmol), tributylphosphine (0.08 mL, 0.33 mmol), methyl (phenylsulfonyl)acetate (**8**, 71 mg, 0.33 mmol), and TMAD (60 mg, 0.34 mmol) in benzene (3 mL). The two products **9** (white foam, 5/4 mixture of epimers, 50 mg, 31%) and **10** (colorless oil, 64 mg, 39%) were separated by column chromatography (silica gel, 0–50% EtOAc/heptane). Compound **9**: ^{1}H NMR (500 MHz, $CDCl_3$, mixture of epimers) δ 8.03–7.99 (m, 4H), 7.59–7.52 (m, 2H), 7.47–7.39 (m, 4H), 7.38–7.12 (m, 40H), 5.00 (d, J=11.1 Hz, 1H), 4.95 (d, J=11.2 Hz, 1H), 4.92 (d, J=10.9 Hz, 1H), 4.85 (d, J=10.9 Hz, 2H), 4.81–4.74 (m, 3H), 4.73 (d, J=11.2 Hz, 1H), 4.62 (d, J=10.8 Hz, 1H), 4.54 (d, J=10.8 Hz, 1H), 4.52–4.45 (m, 3H), 4.44 (d, J=1.0 Hz, 1H), 4.32 (d, J=12.3 Hz, 1H), 4.27 (d, J=9.5 Hz, 1H), 4.19 (d, J=12.3 Hz, 1H), 4.03 (dd, J=9.6, 1.1 Hz, 1H), 3.89 (t, J=9.5 Hz, 1H), 3.73–3.59 (m, 10H), 3.57 (dd, J=11.8, 3.0 Hz, 1H), 3.48 (t, J=9.1 Hz, 1H), 3.35 (dt, J=9.7, 2.9 Hz, 1H), 3.24 (s, 3H), 3.16–3.09 (m, 1H), 3.00 (dd, J=11.8, 1.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, mixture of epimers) δ 163.8, 163.6, 139.2, 138.6, 138.5, 138.1, 138.0, 138.0, 137.9, 137.9, 137.8, 137.7, 133.8, 133.8, 130.1, 129.8, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.5, 127.4, 127.2, 127.2, 86.9, 86.9, 80.5, 79.7, 79.6, 78.2, 78.0, 77.6, 76.4, 76.0, 75.7, 75.6, 75.1, 75.0, 74.9, 74.8, 73.6, 73.5, 73.2, 70.0, 68.4, 67.6, 52.8, 52.6; HRMS (ESI), m/z calcd for $[C_{43}H_{44}O_9S+NH_4]^+$: 754.3044; found 754.3056. Compound **10**: ^{1}H NMR (500 MHz, $CDCl_3$, β anomer) δ 8.03–7.96 (m, 2H), 7.41–7.24 (m, 21H), 7.21–7.15 (m, 2H), 5.33 (d, J=7.5 Hz, 1H), 5.01 (s, 1H), 4.92 (d, J=11.0 Hz, 1H), 4.84 (d, J=10.8 Hz, 1H), 4.83–4.79 (m, 2H), 4.70 (d, J=10.8 Hz, 1H), 4.59 (d, J=10.9 Hz, 1H), 4.50 (d, J=12.0 Hz, 1H), 4.44 (d, J=12.1 Hz, 1H), 3.65 (s, 3H), 3.64–3.54 (m, 5H), 3.46 (ddd, J=9.1, 4.6, 1.8 Hz, 1H); ^{1}H NMR (500 MHz, $CDCl_3$, α anomer) δ 5.88 (d, J=3.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 144.1, 138.3, 138.2, 138.0, 137.9, 132.2, 128.6, 128.5, 128.4, 128.4, 128.5, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.1, 97.4, 84.3, 84.2, 81.2, 77.2, 75.9, 75.7, 75.0, 74.8, 73.3, 68.5, 57.2; HRMS (ESI), m/z calcd for $[C_{43}H_{44}O_9S+NH_4]^+$: 754.3044; found 754.3026.

*4.4.5. Ethyl 3-ethoxy-3-((2S,3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yloxy)acrylate (**13**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**, 50 mg, 0.092 mmol), tributylphosphine (34 μL, 0.14 mmol), diethyl malonate (**11**, 22 mg, 0.14 mmol), and TMAD (24 mg, 0.14 mmol) in benzene (0.5 mL). Purification by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded

13 (22 mg, 35%) as a white solid: mp 69–70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.23 (m, 18H), 7.19–7.13 (m, 2H), 5.37 (d, J=7.8 Hz, 1H), 5.12 (d, J=10.6 Hz, 1H), 4.96 (d, J=11.0 Hz, 1H), 4.86–4.74 (m, 3H), 4.62–4.49 (m, 3H), 4.31 (s, 1H), 4.14–4.09 (m, 2H), 3.93 (q, J=7.0 Hz, 2H), 3.80–3.60 (m, 5H), 3.53 (ddd, J=9.4, 4.9, 1.9 Hz, 1H), 1.29 (t, J=7.0 Hz, 3H), 1.24 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 165.5, 138.5, 138.4, 138.2, 138.1, 128.4, 128.4, 128.3, 128.3, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 97.2, 84.6, 81.4, 77.5, 75.8, 75.6, 75.0, 73.4, 72.2, 68.7, 65.9, 59.1, 14.6, 13.9; HRMS (ESI), m/z calcd for $[C_{41}H_{46}O_9+H]^+$: 683.3215; found 683.3222.

*4.4.6. (2R,3R,4S,5R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(1-(phenylsulfonyl)prop-1-en-2-yloxy)tetrahydro-2H-pyran (**16**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**1**, 200 mg, 0.37 mmol), tributylphosphine (0.14 mL, 0.57 mmol), phenylsulfonylacetone (**14**, 110 mg, 0.55 mmol), and TMAD (96 mg, 0.56 mmol) in benzene (5 mL). Purification by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded the O-glucoside **16** (202 mg, contaminated with 11 wt % of **14**, 67%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01–7.93 (m, 2H), 7.43–7.23 (m, 21H), 7.22–7.16 (m, 2H), 5.67 (s, 1H), 4.99 (d, J=10.8 Hz, 1H), 4.94 (d, J=10.8 Hz, 1H), 4.90 (d, J=7.3 Hz, 1H), 4.84–4.79 (m, 2H), 4.75 (d, J=10.8 Hz, 1H), 4.57 (d, J=10.9 Hz, 1H), 4.47 (d, J=12.0 Hz, 1H), 4.40 (d, J=12.1 Hz, 1H), 3.64 (t, J=8.9 Hz, 1H), 3.60 (dd, J=10.9, 1.6 Hz, 1H), 3.56–3.49 (m, 3H), 3.42 (ddd, J=9.6, 5.2, 1.5 Hz, 1H), 2.01 (s, 3H).

*4.4.7. (2R,3S,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(bis(phenylsulfonyl)methyl)tetrahydro-2H-pyran (**25**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose (**24**, 400 mg, 0.74 mmol), tributylphosphine (0.27 mL, 1.11 mmol), bis(phenylsulfonyl)-methane (**2**, 330 mg, 1.11 mmol), and TMAD (191 mg, 1.11 mmol) in benzene (15 mL). Purification by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **25** (440 mg, 73%) as a white solid: mp 61–63 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J=7.5 Hz, 2H), 7.90 (d, J=7.4 Hz, 2H), 7.59 (t, J=7.5 Hz, 1H), 7.47 (t, J=7.8 Hz, 2H), 7.44–7.20 (m, 21H), 7.01 (t, J=7.9 Hz, 2H), 5.09 (d, J=11.1 Hz, 1H), 5.07 (d, J=10.6 Hz, 1H), 5.01 (d, J=1.0 Hz, 1H), 4.90 (d, J=11.1 Hz, 1H), 4.83–4.75 (m, 2H), 4.69 (d, J=11.6 Hz, 1H), 4.48 (d, J=10.6 Hz, 1H), 4.42 (dd, J=10.1, 1.0 Hz, 1H), 4.33 (d, J=11.7 Hz, 1H), 4.11 (d, J=11.7 Hz, 1H), 3.97 (d, J=1.4 Hz, 1H), 3.60 (dd, J=9.1, 2.4 Hz, 1H), 3.42 (t, J=6.3 Hz, 1H), 3.19 (dd, J=9.4, 7.6 Hz, 1H), 2.88 (dd, J=9.5, 5.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 139.7, 138.7, 138.6, 138.0, 137.9, 134.0, 133.7, 131.6, 129.1, 128.9, 128.5, 128.5, 128.4, 128.4, 128.4, 127.9, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 85.3, 83.6, 78.1, 75.4, 75.3, 74.9, 74.5, 74.1, 73.5, 72.2, 67.7; HRMS (ESI), m/z calcd for $[C_{47}H_{46}O_9S_2+NH_4]^+$: 836.2922; found 836.2939.

*4.4.8. 2-(Phenylsulfonyl)-2-((2R,3R,4S,5S,6R)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)acetonitrile (**26**).* The general Mitsunobu procedure was followed, using 2,3,4,6-tetra-*O*-benzyl-D-galactose (**24**, 100 mg, 0.184 mmol), tributylphosphine (0.14 mL, 0.552 mmol), phenylsulfone acetonitrile (**4**, 100 mg, 0.552 mmol), and ADDP (139 mg, 0.552 mmol) in benzene (1 mL). Purification by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **26** (colorless oil, 6/1 mixture of epimers, 55 mg, 42%): ^{1}H NMR (500 MHz, $CDCl_3$, mixture of epimers) δ 7.93 (d, J=7.8 Hz, 2H, minor epimer), 7.89 (d, J=7.7 Hz, 2H, major epimer), 7.54 (t, J=7.4 Hz, 1H, major epimer), 7.48 (t, J=7.4 Hz, 1H, minor epimer), 7.42–7.20 (m, 22H), 5.09 (d, J=10.7 Hz, 1H, minor epimer), 5.06 (d, J=10.6 Hz, 1H, minor epimer), 4.98 (d, J=11.5 Hz, 1H, major epimer), 4.93 (d, J=10.7 Hz, 1H, minor epimer), 4.88 (t, J=11.1 Hz, 1H, major epimer), 4.73 (d, J=11.7 Hz, 1H, major epimer), 4.63 (d, J=10.3 Hz, 1H, major epimer), 4.61 (d, J=11.2 Hz, 1H, major epimer), 4.55 (d, J=11.8 Hz, 1H, major epimer), 4.38 (d, J=11.9 Hz, 1H, major epimer), 4.32–4.24 (m, 2H), 4.17 (d, J=11.7 Hz, 1H, minor epimer), 3.99–3.94 (m, 2H), 3.87 (t, J=9.4 Hz, 1H, major epimer), 3.69 (dd, J=10.0, 2.1 Hz, 1H, minor epimer), 3.62 (dd, J=9.1, 2.5 Hz, 1H, major epimer), 3.54 (dd, J=9.2, 2.3 Hz, 1H, minor epimer), 3.48 (dd, J=7.9, 5.2 Hz, 1H, major epimer), 3.43–3.38 (m, 1H, minor epimer), 3.28 (t, J=8.5 Hz, 1H, major epimer), 3.18 (dd, J=9.3, 7.6 Hz, 1H, minor epimer), 3.01 (dd, J=9.0, 5.0 Hz, 1H, major epimer), 2.95 (dd, J=9.4, 5.4 Hz, 1H, minor epimer); ^{13}C NMR (125 MHz, $CDCl_3$, major epimer) δ 138.6, 137.7, 137.7, 137.3, 137.0, 134.7, 129.9, 128.9, 128.8, 128.5, 128.5, 128.2, 128.2, 127.9, 127.9, 127.9, 127.6, 127.4, 111.2, 83.9, 77.2, 75.5, 75.4, 74.6, 74.4, 73.3, 72.9, 72.1, 67.2, 59.2; ^{13}C NMR (125 MHz, $CDCl_3$, minor epimer) δ 138.5, 138.1, 134.4, 130.8, 128.6, 128.5, 128.5, 128.3, 128.3, 128.1, 127.6, 113.9, 84.9, 78.0, 77.8, 75.3, 75.1, 73.6, 73.4, 67.7, 58.0; HRMS (ESI), m/z calcd for $[C_{42}H_{41}NO_7S+NH_4]^+$: 721.2942; found 721.2951.

*4.4.9. (2R,3R,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(phenylsulfonylmethyl)tetrahydro-2H-pyran (**27**).* To a solution of **3** (180 mg, 0.22 mmol) in THF (10 mL) was added aluminum foil (250 mg, cut in small squares), followed by $HgCl_2$ (2 wt % in H_2O, 0.5 mL). The mixture was stirred for 20 h at room temperature and then added directly to a short plug of silica gel and eluted with EtOAc. The filtrate was concentrated and the residue purified by column chromatography (silica gel, 0–40% EtOAc/heptane) to afford **27** (144 mg, quantitative yield) as a white solid: mp 110–111 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89–7.86 (m, 2H), 7.57–7.51 (m, 1H), 7.47–7.40 (m, 2H), 7.36–7.20 (m, 18H), 7.16–7.08 (m, 2H), 4.89 (d, J=11.0 Hz, 1H), 4.88 (d, J=11.3 Hz, 1H), 4.84 (d, J=11.0 Hz, 1H), 4.76 (d, J=10.8 Hz, 1H), 4.58 (d, J=11.3 Hz, 1H), 4.52 (d, J=10.8 Hz, 1H), 4.35 (d, J=12.1 Hz, 1H), 4.27 (d, J=12.1 Hz, 1H), 3.72 (td, J=9.6, 1.5 Hz, 1H), 3.65 (t, J=8.9 Hz, 1H), 3.59 (t, J=9.4 Hz, 1H), 3.53 (dd, J=11.1, 3.4 Hz, 1H), 3.42 (dd, J=14.7, 1.5 Hz, 1H), 3.24 (dd, J=9.5, 8.8 Hz, 1H), 3.22–3.14 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.6, 138.2, 138.0, 137.9, 137.4, 133.3, 128.8, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 87.0, 79.3, 78.9, 77.7, 75.6, 75.0, 74.9, 74.5, 73.6, 68.2, 57.8; HRMS (ESI), m/z calcd for $[C_{41}H_{42}O_7S+NH_4]^+$: 696.2989; found 696.3000.

*4.4.10. Methyl 2-((2S,3S,4R,5R,6R)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)acetate (**28**).* The general desulfonylation procedure (method B) was followed, using **9** (27 mg, 0.037 mmol), Na_2HPO_4 (15 mg, 0.11 mmol), and Na(Hg) (6 wt %, 0.6 g) in THF (1 mL) and MeOH (2 mL). The reaction mixture was stirred at room temperature for 1 h. Work up afforded spectroscopically pure **28** (off-white gum, 21 mg, 96%) without the need of further purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.24 (m, 18H), 7.19–7.15 (m, 2H), 4.94–4.90 (m, 2H), 4.87 (d, J=11.0 Hz, 1H), 4.81 (d, J=10.8 Hz, 1H), 4.65–4.55 (m, 3H), 4.54–4.49 (m, 1H), 3.78–3.71 (m, 2H), 3.71–3.68 (m, 2H), 3.65 (t, J=9.3 Hz, 1H), 3.60 (s, 3H), 3.46 (dt, J=9.6, 3.0 Hz, 1H), 3.36 (t, J=9.2 Hz, 1H), 2.73 (dd, J=15.3, 4.0 Hz, 1H), 2.48 (dd, J=15.4, 8.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 138.5, 138.2, 138.1, 138.0, 128.5, 128.4, 128.4, 128.3, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 87.2, 81.3, 79.2, 78.5, 75.9, 75.6, 75.1, 75.0, 73.4, 68.7, 51.7, 37.5; HRMS (ESI), m/z calcd for $[C_{37}H_{40}O_7+NH_4]^+$: 614.3112; found 614.3117.

*4.4.11. 2-((2S,3S,4R,5R,6R)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)acetonitrile (**29**).* The general desulfonylation procedure (method A) was followed, using **5** (80 mg, 0.114 mmol), Mg (80 mg, 3.29) in MeOH (5 mL). The reaction mixture was stirred at 50 °C for 18 h. Work up, followed by column chromatography (silica gel, 0–70% EtOAc/heptane) afforded **29** (45 mg, 70%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.25 (m, 18H), 7.19–7.12 (m, 2H), 4.94 (d, J=11.1 Hz, 2H), 4.93 (d, J=11.1 Hz,

1H), 4.88 (d, J=11.1 Hz, 1H), 4.81 (d, J=10.8 Hz, 1H), 4.67–4.53 (m, 4H), 3.75–3.63 (m, 4H), 3.50–3.45 (m, 2H), 3.45–3.39 (m, 1H), 2.70 (dd, J=16.8, 3.3 Hz, 1H), 2.52 (dd, J=16.8, 6.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.3, 138.0, 137.9, 137.5, 128.7, 128.5, 128.5, 128.4, 128.2, 127.9, 127.9, 127.9, 127.8, 127.7, 127.6, 117.1, 86.8, 80.1, 79.4, 78.1, 75.6, 75.4, 75.1, 74.4, 73.6, 68.6, 21.1; HRMS (ESI), m/z calcd for $[C_{36}H_{37}NO_5+NH_4]^+$: 581.3010; found 581.3012.

*4.4.12. 2-((2S,3S,4R,5S,6R)-3,4,5-Tris(benzyloxy)-6-(benzyloxymethyl) tetrahydro-2H-pyran-2-yl)acetonitrile (**30**).* The general desulfonylation procedure (method A) was followed, using **26** (35 mg, 0.050 mmol), Mg (40 mg×3, added in 2 h intervals) in MeOH (4 mL) and THF (2 mL). The reaction mixture was stirred at 50 °C for 18 h. Work up afforded spectroscopically pure **30** (colorless oil, 28 mg, quantitative) without the need of further purification: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.25 (m, 20H), 4.97 (d, J=11.1 Hz, 1H), 4.93 (d, J=11.6 Hz, 1H), 4.76 (d, J=11.7 Hz, 1H), 4.68–4.58 (m, 3H), 4.49 (d, J=11.8 Hz, 1H), 4.43 (d, J=11.8 Hz, 1H), 4.02 (d, J=2.6 Hz, 1H), 3.75 (t, J=9.3 Hz, 1H), 3.64–3.54 (m, 4H), 3.46 (ddd, J=9.3, 8.0, 3.2 Hz, 1H), 2.70 (dd, J=16.8, 3.2 Hz, 1H), 2.46 (dd, J=16.8, 7.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 137.9, 137.8, 137.8, 128.6, 128.5, 128.5, 128.3, 128.3, 128.1, 128.0, 127.9, 127.9, 127.8, 127.6, 127.6, 117.4, 84.3, 77.4, 77.2, 75.4, 75.1, 74.6, 73.6, 73.5, 72.1, 68.5, 21.3; HRMS (ESI), m/z calcd for $[C_{36}H_{37}NO_5+NH_4]^+$: 581.3010; found 581.3021.

*4.4.13. Diethyl ((2R,3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl)tetrahydro-2H-pyran-2-yl)methylphosphonate (**31**).* The general desulfonylation procedure (method B) was followed, using **7** (230 mg, 0.28 mmol), Na_2HPO_4 (120 mg, 0.85 mmol), and Na(Hg) (6 wt%, 3 g) in THF (5 mL) and MeOH (15 mL). The reaction mixture was stirred at room temperature for 2 h. Work up, followed by column chromatography (silica gel, 0–70% EtOAc/heptane) afforded **31** (182 mg, 96%) as a white solid: mp 87–89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.22 (m, 18H), 7.20–7.13 (m, 2H), 4.91 (d, J=11.4 Hz, 1H), 4.90 (d, J=11.0 Hz, 1H), 4.86 (d, J=11.0 Hz, 1H), 4.82 (d, J=10.8 Hz, 1H), 4.66 (d, J=11.2 Hz, 1H), 4.58 (d, J=11.0 Hz, 1H), 4.55 (d, J=12.0 Hz, 1H), 4.50 (d, J=12.0 Hz, 1H), 4.12–3.98 (m, 4H), 3.76–3.59 (m, 5H), 3.53–3.43 (m, 1H), 3.37–3.33 (m, 1H), 2.27 (ddd, J=19.8, 15.5, 2.3 Hz, 1H), 1.89 (td, J=15.9, 9.6 Hz, 1H), 1.25 (t, J=7.1 Hz, 3H), 1.24 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.1, 138.0, 138.0, 128.5, 128.4, 128.4, 128.4, 127.9, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 87.1 (d, J_{C-P}=2.6 Hz), 81.8 (d, J_{C-P}=13.9 Hz), 78.9, 78.3, 75.5, 75.0, 75.0, 74.8 (d, J_{C-P}=6.5 Hz), 73.5, 68.9, 61.7 (d, J_{C-P}=6.0 Hz), 61.5 (d, J_{C-P}=6.0 Hz), 28.6 (d, J_{C-P}=142.4 Hz), 16.4 (d, J_{C-P}=5.9 Hz), 16.4 (d, J_{C-P}=6.2 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 28.8; HRMS (ESI), m/z calcd for $[C_{39}H_{47}O_8P+H]^+$: 675.3081; found 675.3089.

*4.4.14. (2R,3R,4R,5S)-1,3,4,5-Tetrakis(benzyloxy)hept-6-en-2-ol (**32**) and (2R,3R,4R,5S,6S)-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-6-methyltetrahydro-2H-pyran (**33**).* The general desulfonylation procedure (method B) was followed, using **3** (210 mg, 0.26 mmol), Na_2HPO_4 (120 mg, 0.85 mmol), and Na(Hg) (6 wt%, 3 g) in THF (4 mL) and MeOH (12 mL). The reaction mixture was stirred at room temperature for 2 h. Work up, followed by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **32** (colorless oil, 62 mg, 45%) and **33** (white solid, 26 mg, 19%). Desulfonylation of **3** following method A afforded the products **32** and **33** in the same yields obtained with method B. Compound **32**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.19 (m, 20H), 5.83 (ddd, J=17.9, 10.4, 7.7 Hz, 1H), 5.28 (dd, J=10.4, 1.3 Hz, 1H), 5.24 (ddd, J=17.4, 1.5, 0.8 Hz, 1H), 4.81 (d, J=11.4 Hz, 1H), 4.68 (d, J=11.4 Hz, 1H), 4.61 (d, J=11.7 Hz, 1H), 4.58 (d, J=11.5 Hz, 1H), 4.53 (d, J=11.5 Hz, 1H), 4.50 (d, J=12.0 Hz, 1H), 4.47 (d, J=12.0 Hz, 1H), 4.39 (d, J=11.7 Hz, 1H), 4.20–4.17 (m, 1H), 4.02 (dd, J=9.8, 5.2 Hz, 1H), 3.76 (dd, J=6.1, 3.7 Hz, 1H), 3.73 (dd, J=6.2, 3.7 Hz, 1H), 3.64–3.55 (m, 2H), 2.84 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 138.4, 138.3, 138.1, 135.4, 128.4, 128.4, 128.3, 128.3, 127.9, 127.9, 127.8, 127.7, 127.7, 127.5, 119.1, 81.4, 81.4, 78.4, 74.7, 73.3, 73.2, 71.2, 70.7, 70.4; HRMS (ESI), m/z calcd for $[C_{35}H_{38}O_5+Na]^+$: 561.2611; found 561.2618. Compound **33**: mp 68–69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.22 (m, 18H), 7.18–7.10 (m, 2H), 4.89 (s, 2H), 4.87 (d, J=10.9 Hz, 1H), 4.81 (d, J=10.8 Hz, 1H), 4.66 (d, J=10.9 Hz, 1H), 4.61 (d, J=12.3 Hz, 1H), 4.54 (d, J=12.3 Hz, 1H), 4.53 (d, J=10.8 Hz, 1H), 3.71 (dd, J=10.7, 1.9 Hz, 1H), 3.69–3.63 (m, 2H), 3.59 (t, J=9.4 Hz, 1H), 3.44 (ddd, J=9.5, 4.5, 1.8 Hz, 1H), 3.39 (dq, J=9.1, 6.2 Hz, 1H), 3.21 (t, J=9.1 Hz, 1H), 1.32 (d, J=6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.2, 138.2, 138.1, 128.4, 128.4, 128.4, 128.4, 128.0, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 87.1, 84.0, 78.8, 78.7, 75.6, 75.5, 75.3, 75.0, 73.5, 69.1, 18.2; HRMS (ESI), m/z calcd for $[C_{35}H_{38}O_5+NH_4]^+$: 556.3057; found 556.3063.

*4.4.15. (2R,3R,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(1,1-bis(phenylsulfonyl)but-3-enyl)tetrahydro-2H-pyran (**35**).* Palladium tetrakis triphenyl phosphine (75 mg, 0.06 mmol) was added to a degassed solution of **3** (395 mg, 0.48 mmol) and allyl methyl carbonate (**34**, 220 mg, 1.89 mmol) in THF (6 mL) and the mixture was stirred at 55 °C for 18 h. The mixture was then cooled to room temperature and concentrated under reduced pressure to give a residue that was purified by column chromatography (silica gel, 0–40% EtOAc/heptane) to afford the product **35** (396 mg, 96%) as an off-white solid: mp 64–68 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J=7.7 Hz, 2H), 8.18 (d, J=7.7 Hz, 2H), 7.59 (t, J=7.4 Hz, 1H), 7.45–7.38 (m, 5H), 7.33–7.17 (m, 20H), 5.90 (dddd, J=15.1, 10.2, 7.9, 4.8 Hz, 1H), 5.06 (s, 2H), 5.01 (d, J=10.2 Hz, 1H), 4.89 (d, J=10.8 Hz, 1H), 4.84 (d, J=10.8 Hz, 1H), 4.79 (d, J=11.0 Hz, 1H), 4.64 (d, J=16.8 Hz, 1H), 4.59 (d, J=11.0 Hz, 1H), 4.54 (t, J=9.0 Hz, 1H), 4.27 (d, J=9.9 Hz, 1H), 4.20 (d, J=12.2 Hz, 1H), 4.14 (d, J=12.2 Hz, 1H), 3.68 (t, J=8.6 Hz, 1H), 3.54–3.46 (m, 2H), 3.26–3.20 (m, 2H), 3.01 (dd, J=11.3, 4.8 Hz, 1H), 2.82 (dd, J=16.2, 8.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.2, 138.5, 138.3, 138.1, 138.0, 134.1, 133.6, 132.0, 131.8, 130.2, 128.5, 128.4, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.4, 127.4, 120.2, 96.1, 88.3, 79.7, 78.6, 77.5, 75.8, 74.6, 74.4, 73.1, 68.7, 33.4; HRMS (ESI), m/z calcd for $[C_{50}H_{50}O_9S_2+Na]^+$: 881.2788; found 881.2788.

*4.4.16. (2R,3R,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(1,1-bis(phenylsulfonyl)butyl)tetrahydro-2H-pyran (**36**).* Palladium (5 wt% on alumina, 50 mg) was added to a solution of alkene **35** (120 mg, 0.14 mmol) in EtOAc (12 mL). The mixture was stirred overnight under hydrogen (balloon pressure). The mixture was filtered through Celite® and concentrated to afford **36** (white solid, 118 mg, 98%) that was used in subsequent steps without further purification: mp 73–78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26–8.17 (m, 4H), 7.64 (t, J=7.4 Hz, 1H), 7.53 (t, J=7.8 Hz, 2H), 7.44–7.35 (m, 3H), 7.35–7.13 (m, 20H), 5.15 (d, J=10.8 Hz, 1H), 5.05 (d, J=10.8 Hz, 1H), 4.95 (d, J=10.6 Hz, 1H), 4.92 (d, J=10.6 Hz, 1H), 4.84 (d, J=10.9 Hz, 1H), 4.64 (d, J=11.0 Hz, 1H), 4.52 (t, J=9.2 Hz, 1H), 4.36 (d, J=10.0 Hz, 1H), 4.18 (d, J=12.3 Hz, 1H), 4.08 (d, J=12.3 Hz, 1H), 3.76 (t, J=8.7 Hz, 1H), 3.57 (t, J=9.3 Hz, 1H), 3.38 (ddd, J=9.7, 4.1, 1.7 Hz, 1H), 3.31 (dd, J=11.2, 1.7 Hz, 1H), 3.14 (dd, J=11.2, 4.0 Hz, 1H), 2.64–2.52 (m, 1H), 1.82–1.64 (m, 1H), 1.57–1.50 (m, 1H), 1.45 (t, J=13.1 Hz, 1H), 0.14 (t, J=7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.3, 138.5, 138.3, 138.3, 138.1, 138.1, 134.0, 133.5, 131.9, 131.0, 128.6, 128.4, 128.4, 128.3, 128.2, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 127.3, 97.8, 88.8, 80.0, 79.1, 77.9, 76.6, 76.1, 74.7, 74.7, 73.0, 68.6, 30.5, 17.0, 13.1; HRMS (ESI), m/z calcd for $[C_{50}H_{52}O_9S_2+NH_4]^+$: 878.3391; found 878.3399.

*4.4.17. (2R,3R,4R,5S)-1,3,4,5-Tetrakis(benzyloxy)dec-6-en-2-ol (**37**) and (2R,3R,4R,5S,6S)-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-6-butyltetrahydro-2H-pyran (**38**).* The general desulfonylation procedure (method B) was followed, using **36** (590 mg, 0.69 mmol), Na_2HPO_4 (340 mg, 2.40 mmol), and Na(Hg) (6 wt%, 5 g) in THF

(3 mL) and MeOH (15 mL). The reaction mixture was stirred at room temperature for 2 h. Work up, followed by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **37** (colorless oil, 130 mg, 58%) and **38** (white solid, 51 mg, 23%). Compound **37**: ^{1}H NMR (500 MHz, $CDCl_3$, *E* isomer) δ 7.39–7.17 (m, 20H), 5.60 (dt, *J*=15.5, 6.7 Hz, 1H), 5.41 (dd, *J*=15.5, 8.4 Hz, 1H), 4.83 (d, *J*=11.4 Hz, 1H), 4.69 (d, *J*=11.4 Hz, 1H), 4.63–4.43 (m, 5H), 4.37 (d, *J*=11.7 Hz, 1H), 4.15 (dd, *J*=7.7, 6.2 Hz, 1H), 4.01 (dd, *J*=9.3, 4.9 Hz, 1H), 3.75–3.71 (m, 2H), 3.62–3.55 (m, 2H), 2.01 (q, *J*=7.0 Hz, 2H), 1.42–1.35 (m, 2H), 0.90 (t, *J*=7.4 Hz, 3H); ^{1}H NMR (500 MHz, $CDCl_3$, *Z* isomer, olefinic region) δ 5.67 (dt, *J*=11.2, 7.3 Hz, 1H), 5.49 (dd, *J*=11.0, 9.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.5, 138.5, 138.1, 136.3, 128.5, 128.4, 128.3, 128.3, 127.9, 127.8, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 81.6, 81.2, 78.5, 74.7, 73.3, 73.2, 71.3, 70.4, 70.2, 34.5, 22.3, 13.7; HRMS (ESI), *m*/*z* calcd for $[C_{38}H_{44}O_5+Na]^+$: 603.3081; found 603.3076. Compound **38**: mp 91–92 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.23 (m, 18H), 7.21–7.14 (m, 2H), 4.90 (s, 2H), 4.87 (d, *J*=10.9 Hz, 1H), 4.82 (d, *J*=10.8 Hz, 1H), 4.65 (d, *J*=10.8 Hz, 1H), 4.63 (d, *J*=12.1 Hz, 1H), 4.57 (d, *J*=10.8 Hz, 1H), 4.56 (d, *J*=12.3 Hz, 1H), 3.73 (dd, *J*=10.9, 1.9 Hz, 1H), 3.71–3.65 (m, 2H), 3.60 (t, *J*=9.4 Hz, 1H), 3.39 (ddd, *J*=9.6, 4.4, 1.9 Hz, 1H), 3.27 (t, *J*=9.0 Hz, 1H), 3.23 (td, *J*=8.8, 2.3 Hz, 1H), 1.87–1.76 (m, 1H), 1.58–1.41 (m, 2H), 1.40–1.24 (m, 3H), 0.89 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.4, 138.2, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 87.4, 82.5, 79.3, 79.0, 78.8, 75.5, 75.3, 74.9, 73.4, 69.2, 31.4, 27.7, 22.7, 14.1; HRMS (ESI), *m*/*z* calcd for $[C_{38}H_{44}O_5+NH_4]^+$: 598.3527; found 598.3529.

*4.4.18. (2R,3R,4R,5S,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-butyltetrahydro-2H-pyran (**39**).* Mercuric trifluoroacetate (0.3 M in THF, 1 mL, 0.3 mmol) was added to a solution of alkene **37** (65 mg, 0.11 mmol) and the mixture was stirred for 1 h at room temperature. After this time, K_2CO_3 (30 mg, 0.22 mmol) was added to the mixture and stirred at room temperature for 3 h. The mixture was then cooled to −78 °C and BEt_3 (1 M in THF, 0.2 mL, 0.2 mmol) was added, followed by $NaBH_4$ (15 mg, 0.40 mmol). After stirring at −78 °C for 1 h, the mixture was allowed to warm to room temperature, stirred for 1 h and then quenched with saturated aqueous ammonium chloride, diluted with water, and extracted with EtOAc. The organic extracts were combined, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the crude product. The residue was purified by column chromatography (silica gel, 0–30% EtOAc/heptane) to afford the product **39** (34 mg, 53%) as a white solid: mp 67–68 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.21 (m, 18H), 7.18–7.09 (m, 2H), 4.93 (d, *J*=10.9 Hz, 1H), 4.81 (d, *J*=10.0 Hz, 1H), 4.79 (d, *J*=10.6 Hz, 1H), 4.68 (d, *J*=11.6 Hz, 1H), 4.62 (d, *J*=12.1 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.49 (d, *J*=12.1 Hz, 1H), 4.46 (d, *J*=10.6 Hz, 1H), 4.02 (ddd, *J*=11.2, 5.5, 3.8 Hz, 1H), 3.79 (dd, *J*=9.3, 8.3 Hz, 1H), 3.73 (dd, *J*=9.5, 5.7 Hz, 1H), 3.69 (dd, *J*=10.5, 3.7 Hz, 1H), 3.65 (dd, *J*=10.5, 1.8 Hz, 1H), 3.63–3.53 (m, 2H), 1.78–1.59 (m, 2H), 1.49–1.20 (m, 4H), 0.90 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 138.4, 138.3, 138.1, 128.4, 128.4, 128.3, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 82.7, 80.4, 78.3, 75.5, 75.1, 74.1, 73.5, 73.0, 70.9, 69.2, 27.6, 24.3, 22.5, 14.1; HRMS (ESI), *m*/*z* calcd for $[C_{38}H_{44}O_5+NH_4]^+$: 598.3527; found 598.3532.

*4.4.19. (2R,3R,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-((E)-1,1-bis(phenylsulfonyl)undec-2-enyl)tetrahydro-2H-pyran (**41**).* By following the procedure described for the preparation of **35**, allylation of **3** (1.0 g, 1.2 mmol) using carbonate **40** (0.65 g, 3.1 mmol) and palladium tetrakis triphenyl phosphine (0.141 g, 0.122 mmol) afforded **41** (0.9 g, 77%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J*=7.1 Hz, 2H), 8.16 (d, *J*=7.8 Hz, 2H), 7.58 (t, *J*=7.4 Hz, 1H), 7.49–7.35 (m, 5H), 7.34–7.15 (m, 20H), 5.50–5.37 (m, 1H), 5.07 (br s, 1H), 5.04–4.93 (m, 1H), 4.88 (d, *J*=10.8 Hz, 1H), 4.84 (d, *J*=10.8 Hz, 1H), 4.80 (d, *J*=11.0 Hz, 1H), 4.62–4.50 (m, 2H), 4.24 (d, *J*=9.9 Hz, 1H), 4.21 (d, *J*=12.2 Hz, 1H), 4.12 (d, *J*=12.2 Hz, 1H), 3.69 (t, *J*=8.6 Hz, 1H), 3.46 (t, *J*=9.3 Hz, 1H), 3.31–3.21 (m, 2H), 2.96 (dd, *J*=11.1 Hz, 4.9, 1H), 2.77 (dd, *J*=16.0, 8.3 Hz, 1H), 1.97–1.81 (m, 2H), 1.36–1.15 (m, *J*=26.4, 12.2 Hz, 12H), 0.90 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 138.7, 138.3, 138.1, 138.0, 136.7, 133.9, 133.5, 133.0, 131.9, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.6, 127.4, 127.3, 121.0, 88.4, 79.7, 78.5, 77.6, 76.7, 75.9, 74.6, 74.2, 73.2, 68.9, 32.8, 31.9, 29.3, 29.3, 29.1, 29.0, 22.7, 14.1; HRMS (ESI), *m*/*z* calcd for $[C_{57}H_{64}O_9S_2+NH_4]^+$: 974.4330; found 974.4352.

*4.4.20. (2R,3R,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(1,1-bis(phenylsulfonyl)decyl)tetrahydro-2H-pyran (**42**).* By following the procedure described for the preparation of **36**, hydrogenation of **41** (0.68 g, 0.71 mmol) using palladium (5 wt% on alumina, 136 mg) in EtOAc (14 mL) afforded **42** (0.527 g, 77%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28–8.13 (m, 4H), 7.63 (t, *J*=7.4 Hz, 1H), 7.51 (t, *J*=7.8 Hz, 2H), 7.41–7.35 (m, 3H), 7.34–7.19 (m, 18H), 7.17 (d, *J*=6.9 Hz, 2H), 5.16 (d, *J*=10.9 Hz, 1H), 5.03 (d, *J*=10.6 Hz, 1H), 4.95 (d, *J*=10.6 Hz, 1H), 4.92 (d, *J*=10.6 Hz, 1H), 4.84 (d, *J*=11.0 Hz, 1H), 4.64 (d, *J*=11.0 Hz, 1H), 4.52 (t, *J*=9.2 Hz, 1H), 4.37 (d, *J*=10.0 Hz, 1H), 4.18 (d, *J*=12.4 Hz, 1H), 4.07 (d, *J*=12.4 Hz, 1H), 3.79 (t, *J*=8.7 Hz, 1H), 3.57 (t, *J*=9.3 Hz, 1H), 3.39 (ddd, *J*=9.7, 4.2, 1.9 Hz, 1H), 3.31 (dd, *J*=11.2, 1.8 Hz, 1H), 3.12 (dd, *J*=11.1, 3.9 Hz, 1H), 2.57 (br s, 1H), 1.70–1.57 (m, 1H), 1.52–1.38 (m, 2H), 1.36–1.15 (m, 7H), 1.10 (dt, *J*=14.2, 7.0 Hz, 2H), 1.02–0.93 (m, 2H), 0.93–0.84 (m, 4H), 0.39–0.22 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4, 138.5, 138.4, 138.3, 138.2, 138.1, 133.9, 133.4, 131.9, 131.0, 128.6, 128.4, 128.2, 128.2, 128.0, 127.9, 127.7, 127.7, 127.7, 127.5, 127.4, 127.3, 98.0, 88.8, 80.0, 79.0, 77.9, 76.6, 76.1, 74.6, 73.0, 68.6, 31.9, 29.5, 29.5, 29.5, 29.4, 29.3, 23.7, 22.7, 14.2; HRMS (ESI), *m*/*z* calcd for $[C_{57}H_{66}O_9S_2+NH_4]^+$: 976.4487; found 976.4494.

*4.4.21. (2R,3R,4R,5S)-1,3,4,5-Tetrakis(benzyloxy)heptadec-6-en-2-ol (**43**) and (2R,3R,4R,5S,6S)-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-6-undecyltetrahydro-2H-pyran (**44**).* The general desulfonylation procedure (method A) was followed, using **42** (400 mg, 0.417 mmol), Mg (152 mg, 6.26 mmol) in MeOH (20 mL) and THF (20 mL). The reaction mixture was stirred at 50 °C for 4 h. Work up, followed by column chromatography (silica gel, 0–30% EtOAc/heptane) afforded **43** (colorless oil, 150 mg, 53%) and **44** (colorless oil, 49 mg, 17%). Compound **43**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.13 (m, 20H), 5.67 (dt, *J*=11.0, 7.3 Hz, 1H, *Z* isomer), 5.60 (dt, *J*=15.3, 6.7 Hz, 1H, *E* isomer), 5.47 (dd, *J*=11.0, 9.6 Hz, 1H, *Z* isomer), 5.40 (dd, *J*=15.5, 8.4 Hz, 1H, *E* isomer), 4.83 (d, *J*=11.4 Hz, 1H, *E* isomer), 4.80 (d, *J*=11.4 Hz, 1H, *Z* isomer), 4.70 (d, *J*=11.3 Hz, 1H, *Z* isomer), 4.68 (d, *J*=11.4 Hz, 1H, *E* isomer), 4.65–4.46 (m, 5H), 4.38 (d, *J*=11.7 Hz, 1H, *Z* isomer), 4.37 (d, *J*=11.8 Hz, 1H, *E* isomer), 4.19–4.12 (m, 1H), 4.05–3.98 (m, 1H), 3.77–3.70 (m, 2H), 3.63–3.55 (m, 2H), 2.97 (d, *J*=5.1 Hz, 1H, *Z* isomer), 2.87 (d, *J*=5.5 Hz, 1H, *E* isomer), 2.08–1.98 (m, 2H), 1.39–1.12 (m, 16H), 0.88 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 138.5, 138.5, 138.5, 138.4, 138.2, 138.1, 136.5, 135.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 127.9, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.0, 126.9, 81.9, 81.6, 81.2, 78.6, 78.4, 74.9, 74.7, 73.3, 73.2, 73.2, 71.3, 70.6, 70.5, 70.2, 70.2, 32.4, 31.9, 29.7, 29.7, 29.6, 29.5, 29.4, 29.4, 29.3, 29.1, 28.1, 22.7, 14.1; HRMS (ESI), *m*/*z* calcd for $[C_{45}H_{58}O_5+Na]^+$: 701.4176; found 701.4184. Compound **44**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.22 (m, 18H), 7.20–7.14 (m, 2H), 4.89 (s, 2H), 4.87 (d, *J*=10.9 Hz, 1H), 4.82 (d, *J*=10.8 Hz, 1H), 4.64 (d, *J*=10.8 Hz, 1H), 4.63 (d, *J*=12.2 Hz, 1H), 4.57 (d, *J*=10.8 Hz, 1H), 4.56 (d, *J*=12.3 Hz, 1H), 3.73 (dd, *J*=10.9, 1.9 Hz, 1H), 3.71–3.65 (m, 2H), 3.60 (t, *J*=9.4 Hz, 1H), 3.39 (ddd, *J*=9.6, 4.4, 1.9 Hz, 1H), 3.27 (t, *J*=9.4 Hz, 1H), 3.23 (dt, *J*=9.4, 2.4 Hz, 1H), 1.84–1.76 (m, 1H), 1.54–1.40 (m, 2H), 1.31–1.22 (m, 17H), 0.88 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.4, 138.3, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 87.4, 82.5, 79.3, 79.0, 78.8,

75.5, 75.3, 74.9, 73.4, 69.2, 31.9, 31.8, 29.7, 29.7, 29.7, 29.6, 29.4, 25.5, 22.7, 14.1; HRMS (ESI), *m*/*z* calcd for $[C_{45}H_{58}O_5+Na]^+$: 701.4176; found 701.4177.

*4.4.22. (2R,3R,4R,5S,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-undecyltetrahydro-2H-pyran (**45**).* By following the procedure described for the preparation of **39**, cyclization of **43** (50 mg, 0.074 mmol) using mercuric trifluoroacetate (0.3 M in THF, 0.7 mL, 0.2 mmol), K_2CO_3 (21 mg, 0.150 mmol), BEt_3 (1 M THF, 0.13 mL, 0.132 mmol), and $NaBH_4$ (10 mg, 0.266 mmol) afforded the product **45** (52 mg, 51%) as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88–6.73 (m, 18H), 6.66–6.61 (m, 2H), 4.45 (d, *J*=10.9 Hz, 1H), 4.33 (d, *J*=9.9 Hz, 1H), 4.31 (d, *J*=10.6 Hz, 1H), 4.19 (d, *J*=11.7 Hz, 1H), 4.14 (d, *J*=12.1 Hz, 1H), 4.13 (d, *J*=11.7 Hz, 1H), 4.00 (d, *J*=12.5 Hz, 1H), 3.98 (d, *J*=11.1 Hz, 1H), 3.56–3.50 (m, 1H), 3.33–3.28 (m, 1H), 3.24 (dd, *J*=9.5, 5.7 Hz, 1H), 3.20 (dd, *J*=10.5, 3.7 Hz, 1H), 3.16 (dd, *J*=10.5, 1.8 Hz, 1H), 3.14–3.09 (m, 1H), 3.09–3.04 (m, 1H), 1.26–1.18 (m, 1H), 1.18–1.09 (m, 1H), 1.01–0.90 (m, 1H), 0.87–0.70 (m, 17H), 0.40 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.9, 138.4, 138.3, 138.1, 128.4, 128.4, 128.3, 128.0, 128.0, 127.8, 127.7, 127.7, 127.6, 127.6, 82.7, 80.4, 78.3, 75.5, 75.1, 74.1, 73.5, 73.0, 70.9, 69.2, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 25.4, 24.6, 22.7, 14.1; HRMS (ESI), *m*/*z* calcd for $[C_{45}H_{58}O_5+NH_4]^+$: 696.4623; found 696.4631.

*4.4.23. (2R,3R,4S,5R,6R)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-(1-(phenylsulfonyl)vinyl)tetrahydro-2H-pyran (**46**).* To a stirred solution of **7** (570 mg, 0.70 mmol) in THF (20 mL) at 0 °C, was added KO*t*-Bu. The mixture was stirred at 0 °C for 15 min and then paraformaldehyde (80 mg, 2.67 mmol) was added in one portion. The ice bath was removed and the reaction mixture was allowed to warm to room temperature. Within 30 min, TLC analysis indicated complete consumption of starting material. The mixture was diluted with EtOAc and washed with brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure and the resulting residue was purified by column chromatography (silica gel, 0–30% EtOAc/heptane) to obtain **46** (439 mg, 91%) as a white solid: mp 118–119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95–7.87 (m, 2H), 7.53–7.43 (m, 1H), 7.40–7.16 (m, 20H), 7.16–7.08 (m, 2H), 6.64 (s, 1H), 6.05 (s, 1H), 4.89 (d, *J*=11.1 Hz, 1H), 4.86 (d, *J*=11.1 Hz, 1H), 4.80 (d, *J*=10.8 Hz, 1H), 4.78 (d, *J*=10.6 Hz, 1H), 4.67 (d, *J*=10.7 Hz, 1H), 4.53 (d, *J*=10.8 Hz, 1H), 4.38 (d, *J*=12.1 Hz, 1H), 4.31 (d, *J*=12.1 Hz, 1H), 4.08 (d, *J*=9.7 Hz, 1H), 4.04–3.94 (m, 1H), 3.71–3.59 (m, 2H), 3.46 (dd, *J*=10.7, 4.4 Hz, 1H), 3.34 (dd, *J*=10.7, 1.6 Hz, 1H), 3.25 (ddd, *J*=9.2, 4.2, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.2, 140.7, 138.5, 138.0, 138.0, 137.8, 133.1, 129.4, 128.6, 128.6, 128.4, 128.4, 128.4, 128.2, 127.9, 127.8, 127.8, 127.6, 127.6, 127.5, 86.9, 79.8, 79.3, 78.3, 77.7, 75.6, 75.1, 74.8, 73.2, 68.8; HRMS (ESI), *m*/*z* calcd for $[C_{42}H_{42}O_7S+NH_4]^+$: 708.2989; found 708.2993.

*4.4.24. (2R,3R,4R,5S,6S)-3,4,5-Tris(benzyloxy)-2-(benzyloxymethyl)-6-vinyltetrahydro-2H-pyran (**47**).* To a solution of **46** (58 mg, 0.08 mmol) in THF (1.5 mL) was added Zn dust (400 mg), followed by a saturated solution of NH_4Cl (2 mL). The mixture was stirred at room temperature for 18 h and then diluted with EtOAc, washed with brine, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to obtain spectroscopically pure **47** (white solid, 39 mg, 89%) without the need of further purification: mp 81–82 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.21 (m, 18H), 7.19–7.12 (m, 2H), 5.97 (ddd, *J*=17.1, 10.5, 6.4 Hz, 1H), 5.46 (d, *J*=17.3 Hz, 1H), 5.29 (d, *J*=10.6 Hz, 1H), 4.92 (d, *J*=11.1 Hz, 1H), 4.87 (d, *J*=11.1 Hz, 1H), 4.82 (d, *J*=10.8 Hz, 1H), 4.75 (d, *J*=10.6 Hz, 1H), 4.65 (d, *J*=10.1 Hz, 1H), 4.63 (d, *J*=11.7 Hz, 1H), 4.57 (d, *J*=10.7 Hz, 1H), 4.55 (d, *J*=12.2 Hz, 1H), 3.77 (dd, *J*=9.6, 6.5 Hz, 1H), 3.75–3.68 (m, 3H), 3.65 (t, *J*=9.3 Hz, 1H), 3.48 (ddd, *J*=9.5, 3.7, 2.4 Hz, 1H), 3.34 (t, *J*=9.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.2, 138.2, 138.0, 135.3, 128.4, 128.4, 128.4, 128.1, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 118.3, 86.8, 82.5, 80.2, 78.8, 78.2, 75.6, 75.1, 75.0, 73.5, 69.0; HRMS (ESI), *m*/*z* calcd for $[C_{36}H_{38}O_5+NH_4]^+$: 568.3057; found 568.3068.

*4.4.25. (2R,3R,4R,5S)-1,3,4,5-Tetrakis(benzyloxy)oct-6-en-2-ol (**48**), (2R,3R,4R,5S,6S)-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-6-ethyltetrahydro-2H-pyran (**49**), and (2R,3R,4R,5S,E)-1,3,4,5-tetrakis(benzyloxy)-8-methoxyoct-6-en-2-ol (**50**).* The general desulfonylation procedure (method B) was followed, using **46** (385 mg, 0.56 mmol), Na_2HPO_4 (240 mg, 1.7 mmol), and Na(Hg) (6 wt %, 5 g) in THF (6 mL) and MeOH (20 mL). The reaction mixture was stirred at room temperature for 2 h. Work up, followed by column chromatography (silica gel, 0–50% EtOAc/heptane) afforded **47** (78 mg, 14%) and **48** (colorless oil, 110 mg, 20%), **49** (white solid, 29 mg, 9%), and **50** (colorless oil, 46 mg, 8%). Compound **48**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.15 (m, 20H), 5.83–5.74 (m, 1H, *Z* isomer), 5.60 (dq, *J*=15.1, 6.4 Hz, 1H, *E* isomer), 5.50 (ddd, *J*=11.3, 9.6, 1.8 Hz, 1H, *Z* isomer), 5.42 (ddd, *J*=15.4, 8.3, 1.6 Hz, 1H, *E* isomer), 4.92–4.79 (m, 1H), 4.74–4.66 (m, 1H), 4.63–4.56 (m, 2H), 4.55–4.44 (m, 3H), 4.42–4.31 (m, 1H), 4.13 (dd, *J*=8.2, 5.8 Hz, 1H), 4.06–3.95 (m, 1H), 3.80–3.66 (m, 2H), 3.63–3.48 (m, 2H), 3.45–3.32 (m, 1H, *Z* isomer), 2.91 (d, *J*=5.4 Hz, 1H, *Z* isomer), 2.84 (d, *J*=5.5 Hz, 1H, *E* isomer), 1.70 (dd, *J*=6.4, 1.5 Hz, 3H, *E* isomer), 1.59 (dd, *J*=7.0, 1.8 Hz, 3H, *Z* isomer); ^{13}C NMR (125 MHz, $CDCl_3$, *E* isomer) δ 138.6, 138.5, 138.5, 138.1, 130.8, 128.5, 128.4, 128.3, 128.3, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.4, 81.5, 81.1, 78.5, 74.7, 73.3, 73.2, 71.3, 70.5, 70.2, 17.9; ^{13}C NMR (125 MHz, $CDCl_3$, *Z* isomer) δ 81.7, 78.5, 74.8, 74.7, 73.2, 71.3, 70.2, 13.8; HRMS (ESI), *m*/*z* calcd for $[C_{36}H_{40}O_5+Na]^+$: 575.2768; found 570.2776. Compound **49**: mp 76–77 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.23 (m, 19H), 7.20–7.14 (m, 2H), 4.90 (s, 2H), 4.88 (d, *J*=10.8 Hz, 1H), 4.82 (d, *J*=10.8 Hz, 1H), 4.64 (d, *J*=10.8 Hz, 1H), 4.63 (d, *J*=12.3 Hz, 1H), 4.57 (d, *J*=10.8 Hz, 1H), 4.56 (d, *J*=12.3 Hz, 1H), 3.74 (dd, *J*=10.9, 2.0 Hz, 1H), 3.71–3.66 (m, 2H), 3.61 (t, *J*=9.4 Hz, 1H), 3.40 (ddd, *J*=9.6, 4.4, 2.0 Hz, 1H), 3.29 (t, *J*=9.1 Hz, 1H), 3.18 (dt, *J*=9.0, 2.7 Hz, 1H), 1.90 (dqd, *J*=15.0, 7.5, 2.8 Hz, 1H), 1.55–1.45 (m, 1H), 1.00 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.4, 138.2, 128.4, 128.4, 128.3, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 87.4, 82.2, 80.4, 79.0, 78.8, 75.5, 75.3, 75.0, 73.5, 69.2, 24.7, 9.9; HRMS (ESI), *m*/*z* calcd for $[C_{36}H_{40}O_5+NH_4]^+$: 570.3214; found 570.3219. Compound **50**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.20 (m, 20H), 5.75–5.64 (m, 2H), 4.79 (d, *J*=11.4 Hz, 1H), 4.68 (d, *J*=11.4 Hz, 1H), 4.61 (d, *J*=11.7 Hz, 1H), 4.59 (d, *J*=11.5 Hz, 1H), 4.52 (d, *J*=11.5 Hz, 1H), 4.50 (d, *J*=12.0 Hz, 1H), 4.47 (d, *J*=11.9 Hz, 1H), 4.39 (d, *J*=11.7 Hz, 1H), 4.20 (t, *J*=6.2 Hz, 1H), 4.05–3.97 (m, 1H), 3.87 (d, *J*=4.4 Hz, 2H), 3.76–3.71 (m, 2H), 3.63–3.56 (m, 2H), 3.29 (s, 3H), 2.82 (d, *J*=5.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 138.3, 138.3, 138.1, 131.1, 120.0, 128.5, 128.4, 128.3, 128.3, 127.9, 127.9, 127.7, 127.7, 127.6, 127.5, 81.4, 80.3, 78.3, 74.7, 73.4, 73.2, 72.4, 71.2, 70.8, 70.4, 58.0; HRMS (ESI), *m*/*z* calcd for $[C_{37}H_{42}O_6+H]^+$: 583.3054; found 583.3053.

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Supplementary data

^{1}H and ^{13}C NMR spectra of all compounds prepared. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.08.024.

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