Enantiopure Trisubstituted Tetrahydrofurans with Appendage Diversity: Vinyl Sulfone- and Vinyl Sulfoxide-Modified Furans Derived from Carbohydrates as Synthons for Diversity Oriented Synthesis

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Abstract: Enantiomerically pure 2-substituted-2,5-dihydro-3-(aryl) sulfonyl/sulfinyl furans have been prepared from the easily accessible carbohydrate derivatives. The orientation of the substituents attached at the C-2 position of furans is sufficient to control the diastereoselectivity of the addition of various nucleophiles to the vinyl sulfone/sulfoxide-modified tetrahydrofurans, irrespective of the size of the group. The orientation of the substituents at the C-2 center also suppresses the influence of sulfoxides on the diastereoselectivity of the addition of various nucleophiles. The strategy leads to the creation of appendage diversity, affording a plethora of enantiomerically pure trisubstituted furanics for the first time.

Keywords: vinyl sulfone; vinyl sulfoxide; modified tetrahydrofuran; Michael addition; diastereoselectivity

1. Introduction

In order to increase the efficiency of a synthetic strategy for creating appendage, stereochemical, and scaffold diversities, explosive growth has taken place in the area of diversity-oriented synthesis (DOS) [1–12]. However, the imposition of stereocontrol in DOS remains a most difficult task. The asymmetric version of multicomponent reactions, considered as the cornerstone of DOS [4,7], has started emerging only recently [13]. It would be logical to use enantiopure substrates for the generation of new appendage or skeletal diversities with defined stereogenic centers in DOS, but in reality only a limited number of enantiopure “chiral pool” substrates such as carbohydrates have been utilized [2,3,7,8,13].

Carbohydrates as the source of chirality carbons are thoroughly underutilized and understudied in DOS [13], although carbohydrates are by far the most abundant organic compounds on earth. Carbohydrates represent the major portion of the annually renewable biomass [14,15], and it is estimated that, in 2025, up to 30% of raw materials for the chemical industry will be produced from renewable sources such as biomass [16]. As a result of continued efforts, 2,5-dimethylfuran (DMF) [17], a molecule with the potential of an alternative fuel, is now generated from the easily available biomass precursor D-fructose via 5-hydroxymethylfurfural (HMF). However, the conversion of biomass is not restricted to use as an alternative fuel alone. Recent research in this area is generating new tetrahydrofuran derivatives (furanics) such as 2,5-dimethyltetrahydrofuran (DMTHF), 2-methylfuran (2-MF), methyltetrahydrofuran (MTHF), 2-methylfurfural alcohol (MFA), 5-methyltetrahydrofurfural alcohol (MTHFA) etc. from DMF (Figure 1) [18].
Figure 1. Selected examples of biomass-derived “petrochemicals”.

Since substituted tetrahydrofuran moiety occurs extensively in natural and synthetic compounds, synthetic approaches to access this class of oxaheterocycles, especially in an enantiopure form, has proliferated during last several decades, and the overall work has been reviewed [19,20]. As part of a program for the generation of enantiomerically pure non-carbohydrate chemicals from easily available carbohydrates, we developed a DOS-based strategy for the construction of enantiopure furofurans from vinyl sulfone-modified mono- as well as bicyclic-carbohydrates [21–23]. In such a synthesis, our tool was to use highly reactive vinyl sulfone [24–29] and vinyl sulfoxide [30–32] functional groups that are known as powerful Michael acceptors and efficient partners in Diels–Alder reactions.

Interestingly, 2,5-dihydro-3-(alkyl/aryl sulfonyl) furans 1 (Figure 2), employed long ago, are the special class of cyclic vinyl sulfone which underwent cycloaddition as well as Michael addition reactions with various nucleophiles [33–35]. 2,5-dihydro-3-(alkyl/aryl sulfinyl) furans 2 (Figure 2) are also important in synthetic chemistry due to their ability to participate in the Michael addition reactions. Since it is well-known that unsaturated sulfoxides have the potential to act as chiral auxiliaries in asymmetric synthesis, Compound 2 has the added advantage of inducing asymmetric induction. [36–40] Although these cyclic Michael acceptors have high potential as synthetic intermediates [33–40], there are scattered publications, few in number, on the synthesis and utility of 2,5-dihydro-3-(alkyl/aryl) sulfonyl/sulfinyl furans (Figure 2) [23,41–47]. To date, these compounds are thoroughly understudied and underutilized, partly because these molecules are difficult to access in reasonably large amount using conventional synthetic strategies.

Figure 2. Representative examples of vinyl sulfone- and vinyl sulfoxide-modified tetrahydrofurans.
2. Result and Discussion

2-benzyloxyethyl-2,5-dihydro-3-(p-tolyl sulfonyl)- and 2-benzyloxyethylene-2,5-dihydro-3-(p-tolyl sulfonyl)-furans 3 and 4 (Figure 2) undergoes nucleophilic attack at C-4 position from the -side of the tetrahydrofuran ring in such a fashion that all substituents attached to the furan ring occupy anti-orientations [23]. In order to broaden the scope of converting carbohydrates to furanics, we examined whether the steric bulk at C-2 position of furans would play the deciding role in determining the diastereoselectivity of the addition of nucleophiles to vinyl sulfones and vinyl sulfoxides structurally close to 3 and 4. Therefore, two vinyl sulfone-modified tetrahydrofurans, one with a “small” methyl group at the C-2 position of the furan ring and another with the “large” -CH₂OTr group at the same position, were prepared and subjected to addition reactions.

Thus, the preparation of vinyl sulfone-modified tetrahydrofuran 10 with a methyl group at C-2 position started from Compound 5 (Scheme 1) [45]. The tosyl compound 5 was heated with p-thiocresol in the presence of NaOMe at 120 °C to afford the sulfide (6). Compound 6 was consecutively treated with trifluoroacetic acid (TFA) and sodium borohydride (NaBH₄) to afford the acyclic compound 7. Selective tosylation of Compound 7 afforded the desired enantiomerically pure cyclic compound 8. Oxidation of 8 with magnesium monoperoxyphthalate hexahydrate (MMPP) afforded the sulfone compound 9. The hydroxyl group of 9 was mesylated, and the subsequent elimination of the mesyl group produced the desired vinyl sulfone 10 (Scheme 1). The vinylic proton of 10 at δ 7.17 (1H-NMR) and the corresponding carbon at δ 138.3 (13C-NMR) confirmed the formation of the vinyl sulfone moiety of Compound 10.

![Scheme 1. Synthesis of vinyl sulfone-modified tetrahydrofuran 10.](image)

The vinyl sulfone-modified tetrahydrofuran 16, having a bulky group like -CH₂OTr group at C-2 position, was obtained as follows. α-Anomeric arabino sulfide 11 [48,49] was treated with 70% TFA in water to afford the acyclic aldehyde 12. The aldehyde was directly treated with trityl chloride in pyridine to selectively protect the primary alcohol; the crude material was reduced with NaBH₄ in ethanol to produce the trityl protected acyclic sulfide 13 in two steps. Selective tosylation of 13 afforded the cyclic compound 14. Oxidation of 14 produced the corresponding sulfone 15, which, after mesylation, produced the desired tritylated vinyl sulfone 16 (Scheme 2). The vinylic proton of 16 at δ 7.00 and the corresponding carbon at δ 140.8 confirmed the formation of the vinyl sulfone moiety of Compound 16.
To synthesize the corresponding vinyl sulfoxides, Compound 8 was oxidized under controlled condition \[31\] using NaIO\(_4\)/MeOH-H\(_2\)O to afford the sulfoxides. Two sulfoxides 17S\(_S\) and 17R\(_S\), formed almost in a 1:1 ratio, were separated. The structure of Sulfoxide 17S\(_S\) was confirmed by X-ray crystallography (Figure 3), which indirectly confirmed the structure of 17R\(_S\). The sulfoxides were separately mesylated to afford 18S\(_S\) and 18R\(_S\), respectively, which were treated with DBU in DCM at room temperature for 3 h to afford desired vinyl sulfoxides 19R\(_S\) and 19S\(_S\), respectively, in excellent yields (Scheme 3). The crystal structure of sulfoxide 17S\(_S\) (Figure 3) also indirectly confirmed the structure of the corresponding vinyl sulfoxide 19R\(_S\).

Scheme 3. Synthesis of vinyl sulfoxide-modified tetrahydrofurans 19R\(_S\)/19S\(_S\).
The absolute configuration at the sulfur of vinyl sulfoxides $19R_S$ and $19S_S$ could also be confirmed by comparing the NMR data of $19$ with those reported for 2-aryl-3-sulfinyl-2,5-dihydrofuran [23,50]. In the reported data, the vinylic proton was used as a tool for assigning the stereochemistry of sulfur atom because of the highly deshielding effect induced by the sulfinyl oxygen on the vinylic hydrogen [50]. The vinylic proton of Compound $19R_S$ appeared at $\delta\ 6.59$ in its $^1H$-NMR spectrum, whereas that for Compound $19S_S$ appeared at $\delta\ 6.52$. Thus, it was clear that the chemical shift value of the vinylic proton of $19R_S$ was much more deshielded than that of $19S_S$. According to the reported data [50], the higher chemical shift value of the vinylic proton is possible if sulfur oxygen is oriented towards the vinylic proton. It was therefore clear that in Compound $19S_S$ the sulfur oxygen was oriented opposite the vinylic proton. The corresponding trityl protected vinyl sulfoxides were synthesized from the cyclic sulfide (14) via sulfoxides (20). These sulfoxides could not be separated at this stage and therefore were directly converted to vinyl sulfoxides (21) in excellent yields, once again as an inseparable mixture (Scheme 4); two vinylic protons appeared at $\delta\ 6.50$ and $\delta\ 6.81$, confirming the formation of the vinyl sulfoxide group.

Vinyl sulfone 10 was reacted with sodium methoxide/methanol, dimethylmalonate/KO$_t$Bu, thymine/TMG, benzylamine, cyclohexylamine, and morpholine at room temperature to afford the Michael-adducts 22–27, respectively (Scheme 5). The spectral data of all these compounds were found to be similar to the spectra of compounds obtained from 4 [23]. However, the structures 24 and 25 were confirmed by X-ray crystallography (Figures 4 and 5). Thus, it was clear that all the addition compounds in Scheme 5 were in “arabino” configuration. The tritylated vinyl sulfone-modified tetrahydrofuran 16 was also reacted with sodium methoxide/MeOH, nitromethane/KO$_t$Bu, dimethylmalonate/KO$_t$Bu, thymine/TMG, benzylamine, cyclohexylamine, and morpholine to afford the single diastereomers 28–34, respectively (Scheme 6). Once again, the spectral data established the similarity between the Michael adducts of 4 and Compounds 22–27.

To identify the asymmetric induction by the sulfoxide group, if any, vinyl sulfoxide-modified tetrahydrofurans were treated with sodium methoxide/MeOH, dimethylmalonate/NaH, benzylamine, and cyclohexylamine. Thus, $19R_S$ afforded single diastereomers $35S_S$–$38S_S$, respectively, and $19S_S$ afforded $35R_S$–$38R_S$, respectively (Scheme 7). All these Michael-adduct pairs, $35S_S$/$35R_S$, $36S_S$/$36R_S$, $37S_S$/$37R_S$, and $38S_S$/$38R_S$ were separately oxidized with MMPP in MeOH to afford
22–26, respectively, (Scheme 7). The oxidation reactions of amino compounds were terminated within 0.5 h to avoid over-oxidation. The tritylated vinyl sulfoxides 21 were also reacted with a selected group of nucleophiles, namely sodium methoxide/MeOH, dimethylmalonate/NaH, and cyclohexylamine. The products, 39–41 were inseparable and therefore those individual mixtures were directly oxidized to the corresponding sulfones 28, 30, and 33 in good overall yields (Scheme 8).

\[ \text{NaOMe, MeOH} \]
\[ \text{or} \]
\[ \text{CH}_2(\text{CO}_2\text{Me})_2/K\text{O}t\text{Bu, THF} \]
\[ \text{or} \]
\[ \text{Thymine, TMG, DMF} \]
\[ \text{or} \]
\[ \text{BnNH}_2, \text{MeOH} \]
\[ \text{or} \]
\[ \text{Cyclohexyl amine, MeOH} \]
\[ \text{or} \]
\[ \text{Morpholine, MeOH} \]

*all reactions were performed at room temperature

\[ \text{Ar = p-Tol} \]

Scheme 5. Synthesis of enantiopure furanics from 10.

Figure 4. Crystal structure of 24.

Figure 5. Crystal structure of 25.
Scheme 6. Synthesis of enantiopure furanics from 16.

Scheme 7. Synthesis of enantiopure furanics from 19RS and 19SS.
NaOMe, MeOH, rt or CH₂(CO₂Me)₂, NaH, DMF, 60 °C or cyclohexylamine (neat), rt

NaHCO₃, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure. The residue was dissolved in EtOH (15 mL), and NaBH₄ (0.55 g, 14.28 mmol) was added at 0 °C. After 4 h at room temperature, the reaction mixture was concentrated under reduced pressure to get a residue. The residue was poured into satd. Aqueous solution of NaHCO₃, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure. The crude material was purified over silica gel to afford the title compound.

3. Experimental Section

General Methods

All reactions were conducted in a N₂ atmosphere. Melting points were determined in open-end capillary tubes and are uncorrected. Carbohydrates and other fine chemicals were obtained from commercial suppliers and are used without purification. Solvents were dried and distilled following the standard procedures. TLC was carried out on pre-coated plates (Merck silica gel 60, Merck, Darmstadt, Germany), and the spots were visualized with UV light or by charring the plate dipped in a 5% H₂SO₄–MeOH solution. Column chromatography was performed on silica gel (230–400 mesh). ¹H- and ¹³C-NMR for new compounds were recorded at 200/400 and 50/100 MHz, respectively, using CDCl₃ as the solvent in Bruker (Massachusetts, MA, USA) NMR instrument DEPT experiments had been carried out to identify the methylene carbons. Optical rotations were recorded at 589 nm. Mass spectroscopy data were obtained from a mass analyzer (Xevo G2 QTof) consisting of TOF and quadrupole in either ESI⁺ or ESI⁻ mode. The electronic information of compounds is available in the Supplementary Materials.

Compound 6: A solution of p-thiocresol (2.83 g, 22.85 mmol) and NaOMe (0.98 g, 18.28 mmol) in anhyd DMF (10 mL) was stirred at room temperature for 0.5 h in a nitrogen atmosphere. A solution of Compound 5 (1.5 g, 4.57 mmol) in anhyd DMF (5 mL) was added, and the final solution was heated at 120 °C. After 5 h (tlc), the reaction mixture was cooled to room temperature, poured into cold satd. aqueous solution of NaHCO₃, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure. The crude material was purified over silica gel to afford the title compound.

Compound 7: A mixture of Compound 6 (1.0 g, 3.57 mmol) and 70% trifluoroacetic acid in water (10 mL) was stirred at room temperature. After 3 h (tlc) the reaction mixture was poured into ice-cold satd. aqueous solution of NaHCO₃, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was dissolved in EtOH (15 mL), and NaBH₄ (0.55 g, 14.28 mmol) was added at 0 °C. After 4 h at room temperature, the reaction mixture was concentrated under reduced pressure to get a residue. The residue was poured into satd. aqueous solution of NaHCO₃, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure.
The residue was purified over silica gel to get 7 (0.42 g, 49%). Eluent: EtOAc: PE (2:3); yellowish gum; \([\alpha]^D_{D,5} = \) (+) 14.6 (c = 1.02, CHCl\(\_3\); \(1^H\)-NMR (400 MHz, CDCl\(\_3\)): \(\delta = 1.35 (d, \(J = 6.4\) Hz, 3H), 2.32 (s, 3H), 2.50 (bs, 1H), 3.17–3.20 (m, 2H), 3.30 (s, 1H), 3.71–3.75 (m, 1H), 3.88–3.90 (m, 2H), 4.16 (t, \(J = 6.0\) Hz, 1H), 7.11 (d, \(J = 7.6\) Hz, 2H), 7.36 (d, \(J = 7.6\) Hz, 2H); \(\text{\(13\)}\)-C-NMR (100 MHz, CDCl\(\_3\)): \(\delta = 21.0, 21.0, 60.6, 64.5\) (CH\(\_2\)), 78.4, 72.9, 130.1, 130.7, 132.2, 137.8; HRMS [ES\(^+\), (M + Na\(^+\))]: for C\(\text{\(12\)}\)H\(\text{\(16\)}\)O\(\text{\(3\)}\)NaS obsd 265.0850, calcd 265.0874.

Compound 8: A solution of toslychloride (0.6 g, 3.09 mmol) in anhyd toluene (5 mL) was dropwise added to a solution of 7 (0.5 g, 2.06 mmol) in a mixture of anhyd pyridine and toluene (1:1; 5 mL) at 0 °C. The solution was stirred for 0.5 h at 0 °C, and the reaction mixture was stored at +4 °C for 96 h. The mixture was filtered through celite, and the filtrate was evaporated to dryness. Residual pyridine was co-evaporated with toluene. The residue was purified over silica gel to afford 8 (0.28 g, 60%). Eluent: EtOAc: PE (1:4); white solid; Mp = 97 °C; \([\alpha]^D_{D,5} = \) (+) 98.6 (c = 1.01, CHCl\(\_3\); \(1^H\)-NMR (400 MHz, CDCl\(\_3\)): \(\delta = 1.38 (d, \(J = 6.4\) Hz, 3H), 2.33 (s, 3H), 3.0 (s, 1H), 3.10 (dd, \(J = 4.8, 10.4\) Hz, 1H), 3.80–3.86 (m, 2H), 4.10 (dd, \(J = 4.4, 10.0, 1H\)), 4.25 (s, 1H), 7.13 (d, \(J = 8.0\) Hz, 2H), 7.34 (d, \(J = 8.0\) Hz, 2H); \(\text{\(13\)}\)-C-NMR (100 MHz, CDCl\(\_3\)): \(\delta = 19.0, 21.0, 61.4, 70.9, 73.7\) (CH\(\_2\)), 76.4, 129.8, 130.1, 131.8, 137.9; HRMS [ES\(^+\), (M + H\(^+\))]: for C\(\text{\(12\)}\)H\(\text{\(17\)}\)O\(\text{\(2\)}\)S obsd 225.0920, calcd 225.0949.

Compound 9: MMPP (3.3 g, 6.69 mmol) was added to a solution of 8 (0.5 g, 2.23 mmol) in MeOH (8 mL), and the mixture was stirred at room temperature. After 6 h (tlc), the mixture was evaporated under reduced pressure. The solid residue was stirred in a mixture of EtOAc and satd. aqueous NaHCO\(\_3\) solution for 1 h. The organic part was separated, dried over anhyd Na\(\text{\(2\)}\)SO\(\_4\), and filtered, and the filtrate was evaporated to dryness. The residue was purified over silica gel to afford 9 (0.51 g, 90%). Eluent: EtOAc: PE (2:3); white solid; Mp = 110 °C; \([\alpha]^D_{D,5} = \) (+) 26.2 (c = 0.98, CHCl\(\_3\); \(1^H\)-NMR (400 MHz, CDCl\(\_3\)): \(\delta = 1.26 (d, \(J = 6.4\) Hz, 3H), 2.44 (s, 3H), 3.23–3.26 (m, 1H), 3.65 (d, \(J = 5.2\) Hz, 1H), 3.75 (dd, \(J = 2.8, 10.0\) Hz, 1H), 3.94 (dd, \(J = 4.4, 10.0\) Hz, 1H), 4.49–4.58 (m, 2H), 7.37 (d, \(J = 8.4\) Hz, 2H), 7.83 (d, \(J = 8.0\) Hz, 2H); \(\text{\(13\)}\)-C-NMR (100 MHz, CDCl\(\_3\)): \(\delta = 19.0, 21.0, 61.4, 70.9, 73.8, 73.9\) (CH\(\_2\)), 128.3, 130.0, 136.3, 145.4; HRMS [ES\(^+\), (M + Na\(^+\))]: for C\(\text{\(12\)}\)H\(\text{\(16\)}\)O\(\text{\(4\)}\)NaS obsd 279.0691, calcd 279.0667.

Compound 10: A solution of mesylchloride (0.5 mL, 5.85 mmol) in anhyd pyridine (3 mL) was added dropwise to a solution of 9 (0.5g, 1.95 mmol) in anhyd pyridine (5 mL). The mixture was stirred for 0.5 h and stored at +4 °C. After 24 h (tlc), the reaction mixture was poured into ice-cold water, and the product was extracted with EtOAc. The organic layer was dried over anhyd Na\(\text{\(2\)}\)SO\(\_4\) and filtered, and the filtrate was evaporated to dryness. The residue was co-evaporated with toluene. The residue was purified over silica gel to afford 10 (0.39 g, 85%). Eluent: EtOAc: PE (1:4); yellowish gum; \([\alpha]^D_{D,5} = \) (+) 98.6 (c = 1.01, CHCl\(\_3\); \(1^H\)-NMR (400 MHz, CDCl\(\_3\)): \(\delta = 1.31 (d, \(J = 6.4\) Hz, 3H), 2.43 (s, 3H), 4.61–4.78 (m, 2H), 4.89–4.93 (m, 1H), 7.17 (s, 1H), 7.34 (d, \(J = 8.4\) Hz, 2H), 7.76 (d, \(J = 8.4\) Hz, 2H); \(\text{\(13\)}\)-C-NMR (100 MHz, CDCl\(\_3\)): \(\delta = 20.9, 21.6, 73.3\) (CH\(\_2\)), 80.5, 127.9, 130.0, 136.6, 138.3, 145.0, 145.3; HRMS [ES\(^+\), (M + H\(^+\))]: for C\(\text{\(12\)}\)H\(\text{\(16\)}\)O\(\text{\(4\)}\)S obsd 239.0729, calcd 239.0742.

Compound 13: A mixture of Compound 11 (1.5 g, 1.11 mmol) and aqueous 70% trifluoroacetic acid (10 mL) was stirred at room temperature. After 24 h (tlc), the reaction mixture was poured into the ice-cold satd. aqueous solution of NaHCO\(\_3\) and the product was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na\(\text{\(2\)}\)SO\(\_4\) and filtered, and the filtrate was concentrated under reduced pressure to get the residue 12. The residue was dissolved in pyridine, and tritylchloride (0.93 g, 3.33 mmol) was added. The mixture was stirred at room temperature in an inert atmosphere. After 48 h (tlc), the reaction mixture was poured into ice-cold satd. aqueous solution of NaHCO\(\_3\) and the product was extracted with EtOAc (3 × 10 mL). Organic layers were pooled, dried over anhyd Na\(\text{\(2\)}\)SO\(\_4\), and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was dissolved in EtOH (40 mL) and NaBH\(\_4\) (0.17 g, 4.44 mmol) was added at 0 °C. After 5 h at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was poured into satd. aqueous solution of NaHCO\(\_3\), and the product...
was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel to afford 13 (1.11 g, 40%). Eluent: EtOAc: PE (3:2); yellowish gum; [α]₂⁰⁵D = (−) 7.6 (c = 1.32, CHCl₃); ¹H-NMR (200 MHz, CDCl₃): δ = 2.29 (s, 3H), 3.28–3.34 (m, 2H), 3.40–3.47 (m, 1H), 3.61–3.68 (m, 1H), 3.80–3.90 (m, 1H), 4.00–4.10 (m, 2H), 7.00 (d, J = 15.6 Hz, 2H), 7.17–7.36 (m, 16H); ¹³C-NMR (50 MHz, CDCl₃): δ = 21.3, 54.8, 64.8 (CH₂), 65.8 (CH₃), 71.9, 72.9, 87.4, 127.4, 128.1, 128.8, 130.1, 131.3, 132.2, 137.5, 143.8 (3 × C); HRMS [ES⁺, (M + Na)⁺]: for C₃₁H₃₂O₄NaS obsd 523.1964, calc 523.1919.

Compound 14: Compound 13 (1.0 g, 2.0 mmol) was converted to 14 (0.73 g, 76%) following the procedure described for the preparation of 8. Eluent: EtOAc: PE (1:4); colorless gum; [α]₂⁰⁵D = (+) 13.8 (c = 1.7, CHCl₃); ¹H-NMR (200 MHz, CDCl₃): δ = 2.29 (s, 3H), 3.10 (dd, J = 3.0, 10.4 Hz, 1H), 3.42 (d, J = 3.8 Hz, 2H), 3.61 (dd, J = 2.6, 10.4 Hz, 1H), 3.89–4.12 (m, 4H), 7.04 (d, J = 7.8, 2H), 7.16–7.46 (m, 18H); ¹³C-NMR (50 MHz, CDCl₃): δ = 21.2, 54.6, 64.8 (CH₂), 74.7 (CH₂), 77.4, 83.2, 87.9, 127.4, 128.1, 128.9, 130.1, 130.7, 131.4, 137.3, 143.5 (3 × C); HRMS [ES⁺, (M + H)⁺]: for C₃₅H₃₄O₆NaS obsd 483.1939, calc 483.1916.

Compound 15: Compound 14 (0.5 g, 1.04 mmol) was converted to 15 (0.45 g, 84%) following the procedure described for the preparation of 9. Eluent: EtOAc: PE (2:3); white solid; [α]₂⁰⁵D = (+) 26.9 (c = 1.06, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3H), 2.75 (dd, J = 8.0, 10.8 Hz, 1H), 3.32 (s, 1H), 3.55–3.64 (m, 2H), 4.02–4.03 (m, 2H), 4.40–4.42 (m, 1H), 4.72 (s, 1H), 7.25–7.39 (m, 18H), 7.62 (d, J = 8.0 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 21.9, 64.4 (CH₂), 72.6, 73.2, 75.5 (CH₂), 77.9, 87.7, 127.5, 128.2, 128.5, 128.8, 130.3, 135.1, 136.5, 143.4 (3 × C), 145.4; HRMS [ES⁺, (M + Na)⁺]: for C₃₉H₃₉O₆NaS obsd 557.1689, calc 557.1712.

Compound 16: Compound 15 (0.5 g, 0.97 mmol) was converted to 16 (0.43 g, 89%) following the procedure described for the preparation of 10. Eluent: EtOAc: PE (1:4); yellowish gum; [α]₂⁰⁵D = (+) 23.5 (c = 1.06, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 2.41 (s, 3H), 3.14–3.18 (m, 1H), 3.41 (d, J = 10.4 Hz, 1H), 4.77–4.96 (m, 2H), 5.28 (s, 1H), 7.0 (s, 1H), 7.18–7.38 (m, 18H), 7.61 (d, J = 8.0 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 21.6, 65.2 (CH₂), 74.6 (CH₂), 84.1, 86.6, 127.0, 127.7, 128.7, 129.9, 136.5, 140.8, 141.9, 143.8 (3 × C), 144.7; HRMS [ES⁺, (M + Na)⁺]: for C₄₃H₄₁O₇NaS obsd 519.1578, calc 519.1606.

Compounds 17S₅ and 17R₅: A solution of NaIO₄ (2.27 g, 10.7 mmol) in water (3 mL) was added to a well-stirred solution of 8 (2.0 g, 8.92 mmol) in MeOH (25 mL), and the mixture was stirred at room temperature. After 5 h, volatile matters were evaporated to dryness under reduced pressure, and the residue was partitioned between satd. aqueous solution of NaHCO₃ and EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was purified over silica gel to afford 17S₅ and 17R₅. Compound 17S₅: Yield (1.13 g, 53%); Eluent: EtOAc: PE (3:2); white solid; Mp = 127 °C; [α]₂⁰⁵D = (−) 80.7 (c = 0.93, CHCl₃); ¹H-NMR (200 MHz, CDCl₃): δ = 0.90 (d, J = 17.2 Hz, 3H), 2.41 (s, 3H), 2.84 (t, J = 7.0 Hz, 1H), 3.71 (dd, J = 4.4, 11.2 Hz, 1H), 3.97 (dd, J = 4.8, 9.6 Hz, 1H), 4.47–4.67 (m, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H); ¹³C-NMR (50 MHz, CDCl₃): δ = 21.4, 21.6, 72.7, 73.1, 73.4, 73.8 (CH₂), 124.5, 130.1, 138.5, 141.7; HRMS [ES⁺, (M + Na)⁺]: for C₁₂H₁₄O₂NaS obsd 263.0688, calc 263.0718. Compound 17R₅: Yield (0.96 g, 45%); Eluent: EtOAc: PE (4:1); white solid; Mp = 98 °C; [α]₂⁰⁵D = (−) 23.1 (c = 1.01, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 0.78 (d, J = 6.0 Hz, 3H), 2.42 (s, 3H), 2.82–2.85 (m, 1H), 3.83 (dd, J = 2.4, 9.6 Hz, 1H), 3.94 (dd, J = 4.4, 10.8 Hz, 1H), 4.16–4.19 (m, 1H), 4.79 (s, 1H), 5.08 (s, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 19.8, 21.7, 73.1, 73.6, 74.3 (CH₂), 74.5, 125.7, 130.5, 138.4, 143.1; HRMS [ES⁺, (M + Na)⁺]: for C₁₂H₁₄O₂NaS obsd 263.0699, calc 263.0718.

Compound 18S₅: Compound 17S₅ (0.5 g, 2.08 mmol) was converted to 18S₅ (0.57 g, 86%) following the procedure described for the preparation of 10. Eluent: EtOAc: PE (1:1); colorless gum; [α]₂⁰⁵D = (+) 130.7 (c = 1.01, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 0.96 (d, J = 6.0 Hz, 3H), 2.43 (s, 3H), 3.00 (t, J = 7.2 Hz,
Compound **18RS**: Compound **17RS** (1.0 g, 4.16 mmol) was converted to **18RS** (1.17 g, 89%) following the procedure described for the preparation of **10**. Eluent: EtOAc: PE (3:2); colorless gum; [α]_{D}^{23.5} = (+) 188.7 (c = 1.07, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 0.48 (d, J = 6.4 Hz, 3H), 2.43 (s, 3H), 3.20–3.23 (m, 1H), 3.27 (s, 3H), 3.99–4.04 (m, 2H), 4.22 (d, J = 11.2 Hz, 1H), 4.45 (bs, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 19.9, 21.8, 38.6, 72.4 (CH₂), 72.9, 75.2, 81.8, 125.8, 130.7, 138.4, 143.9; HRMS [ES⁺, (M + Na)⁺]: for C₁₃H₁₅O₃Na₂S₂ obse 341.0480, calcd 341.0493.

Compound **19RS**: Compound **18SS** (0.5 g, 1.58 mmol) was treated with DBU (0.5 mL, 3.16 mmol) in DCM (5 mL) at ambient temperature for 3 h. Solvent was evaporated under reduced pressure, and the resulting residue was purified over silica gel to afford **18RS** (0.34 g, 95%). Eluent: EtOAc: PE (2:3); colorless gum; [α]_{D}^{20.5} = (+) 137.5 (c = 0.98, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.21 (d, J = 6.4 Hz, 3H), 2.41 (s, 3H), 4.54–4.55 (m, 1H), 4.69 (d, J = 14.4 Hz, 1H), 4.82 (dd, J = 5.6, 14.0 Hz, 1H), 6.59 (s, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 7.6 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 21.2, 21.7, 74.7 (CH₂), 80.6, 125.7, 130.5, 130.5, 138.6, 142.9, 148.8; HRMS [ES⁺, (M + H)⁺]: for C₁₂H₁₅O₂S obse 223.0784, calcd 223.0793.

Compound **19SS**: Compound **18RS** (0.5 g, 1.58 mmol) was converted to **19SS** (0.34 g, 95%) following the procedure described for the preparation of **19RS**. Eluent: EtOAc: PE (2:3); Yellowish gum; [α]_{D}^{23.5} = (+) 55.7 (c = 1.01, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.25 (d, J = 6.0 Hz, 3H), 2.37 (s 3H), 4.56 (d, J = 12.8 Hz, 1H), 4.69–4.77 (m, 2H), 6.52 (s, 1H), 7.28 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 21.4, 21.7, 73.6 (CH₂), 80.4, 124.7, 130.0, 134.4, 138.4, 141.8, 146.9; HRMS [ES⁺, (M + H)⁺]: for C₁₂H₁₅O₂S obse 223.0806, calcd 223.0793.

Compound **20**: A solution of mesyl chloride (0.25 mL, 3.0 mmol) in anhyd pyridine (3 mL) was dropwise added to a stirred solution of **20** (0.5 g, 1.00 mmol) in anhyd pyridine (5 mL) at 0 °C. After 0.5 h, the solution was stored at +4 °C. After 24 h (tlc), the reaction mixture was poured into ice-cold water, and the compound was extracted with EtOAc. The organic layer was separated, dried over anhyd Na₂SO₄, and filtered, and the filtrate was evaporated to dryness. Residual pyridine was co-evaporated with toluene. The residue was treated with DBU (0.4 mL, 2.5 mmol) in DCM (8 mL) at ambient temperature for 2 h. Solvent was evaporated under reduced pressure, and the resulting residue was purified over silica gel to afford the diastereomeric mixture of vinyl sulfones **21** (0.44 g, 92%). Colorless gum; ¹H-NMR (400 MHz, CDCl₃): δ = 2.25, 2.44, 3.03–3.07, 3.17–3.21, 3.33–3.92, 4.50, 4.74–5.04, 6.50, 6.51, 7.24–7.47; HRMS [ES⁺, (M + Na)⁺]: for C₃₁H₃₃O₁₄NaS obse 530.1664, calcd 530.1657.

Compound **22**: Sodium methoxide (0.02 g, 0.36 mmol) was added to an anhyd methanolic solution (5 mL) of vinyl sulfone **10** (0.043 g, 0.18 mmol), and the mixture was stirred at room temperature. After 4 h (tlc), volatile matters were removed under reduced pressure. The solid residue was stirred in a mixture of EtOAc and satd. aqueous NaHCO₃ solution for 1 h. Organic layers were pooled together, dried over anhyd Na₂SO₄, and filtered, and the filtrate was evaporated. The residue thus obtained was purified over silica gel to afford **22** (0.04 g, 89%). Eluent: EtOAc: PE (1:4); White solid;Mp = 89 °C; [α]_{D}^{23.5} = (+) 14.1 (c = 0.42, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.20 (d, J = 6.0 Hz, 3H), 2.50 (s, 3H), 3.20 (s, 3H), 3.21–3.24 (m, 1H), 3.72 (dd, J = 4.4, 10.4 Hz, 1H), 4.01 (d, J = 10.4 Hz, 1H), 4.23–4.32 (m, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 20.4, 21.6,
56.9, 72.5 (CH₂), 75.6, 75.6, 82.9, 128.5, 130.1, 135.2, 145.3; HRMS [ES⁺, (M + H)⁺]: for C₁₃H₁₉O₄S obsd 271.1015, calc 271.1004.

Compound 23: A mixture of dimethylmalonate (0.28 mL, 2.52 mmol) and KO⁻Bu (0.23 g, 2.1 mmol) in THF (5 mL) was stirred at room temperature in a N₂ atmosphere. After 0.5 h, a solution of 10 (0.2 g, 0.84 mmol) in THF (4 mL) was added to the reaction mixture. After stirring for 6 h (tlc), the mixture was evaporated under reduced pressure. The residue was partitioned between a mixture of EtOAc and satd. aqueous NH₄Cl. The organic part was separated, dried over anhyd Na₂SO₄, and filtered, and the filtrate was evaporated to dryness. The residue thus obtained was purified over silica gel column to afford 23 (0.23 g, 78%). Eluent: EtOAc: PE (1:4); Colorless gum; [α]D25 = (+) 45.6 (c = 1.07, CHCl₃); ¹H-NMR (200 MHz, CDCl₃): δ = 1.11 (d, J = 6.0 Hz, 3H), 2.47 (s, 3H), 3.33–3.46 (m, 6H), 3.70 (d, J = 14.0 Hz, 6H), 3.86–3.89 (m, 2H), 4.16–4.22 (m, 1H), 7.40 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H); ¹³C-NMR (50 MHz, CDCl₃): δ = 20.2, 21.8, 42.0, 52.9, 53.9, 70.7 (CH₂), 71.5, 76.3, 128.9, 130.3, 135.1, 145.5, 168.2; HRMS [ES⁺, (M + H)⁺]: for C₁₃H₁₉O₄S obsd 355.1249, calc 355.1215.

Compound 24: A well-stirred solution of thymine (0.16 g, 1.26 mmol) and TMG (0.11 mL, 0.9 mmol) in DMF (10 mL) was added to 10 (0.043 g, 0.18 mmol), and the mixture was stirred at ambient temperature in a nitrogen atmosphere. After 5 h, the reaction mixture was diluted with EtOAc (20 mL), and the precipitated solid was filtered off. The filtrate was washed with an aqueous satd. aqueous solution of NaHCO₃, and the aqueous part was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel to get 24 (0.05 g, 88%). Eluent: EtOAc: PE (1:3); White solid; Mp = 145 °C; [α]D25 = (−) 69.5 (c = 0.99, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.43 (d, J = 6.4 Hz, 3H), 1.86 (s, 3H), 2.43 (s, 3H), 3.55 (dd, J = 4.8, 7.6 Hz, 1H), 3.94–4.03 (m, 2H), 4.35–4.41 (m, 1H), 5.40–5.43 (m, 1H), 7.06 (s, 1H), 7.37 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.0 Hz, 2H), 9.12 (s, 1H); ¹³C-NMR (100 MHz, CDCl₃): δ = 12.5, 20.3, 21.7, 58.8, 71.2 (CH₂), 74.1, 76.1, 112.4, 128.7, 130.1, 134.5, 136.9, 145.8, 149.9, 163.3; HRMS [ES⁺, (M + H)⁺]: for C₁₇H₂₃N₂O₅S obsd 365.1156, calc 365.1171.

Compound 25: Benzylamine (0.2 mL, 1.8 mmol) was added to an anhyd methanolic solution (5 mL) of 10 (0.043 g, 0.18 mmol), and the mixture was stirred at room temperature. After 4 h (tlc), volatile matters were removed under reduced pressure. The residue was partitioned between EtOAc and satd. aqueous NH₄Cl solution. Then, the organic part was dried over anhyd Na₂SO₄ and filtered, and the filtrate was evaporated to dryness. The residue thus obtained was purified over silica gel to afford 25 (0.05 g, 88%). Eluent: EtOAc: PE (1:3); Brown solid; Mp = 139 °C; [α]D25 = (−) 23.1 (c = 0.48, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.22 (d, J = 6.4 Hz, 3H), 2.46 (s, 3H), 3.13–3.16 (m, 1H), 3.72 (q, J = 3.2 Hz, 2H), 3.76–3.85 (m, 3H), 4.22–4.25 (m, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.23–7.35 (m, 6H), 7.71 (d, J = 8.4 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 20.9, 21.6, 51.4 (CH₂), 60.8, 72.6 (CH₂), 75.3, 75.8, 127.1, 128.0, 128.4, 128.5, 130.0, 135.0, 139.1, 145.1; HRMS [ES⁺, (M + H)⁺]: for C₁₉H₂₄NO₅S obsd 346.1447, calc 346.1477.

Compound 26: Cyclohexylamine (1.9 mL, 16.80 mmol) was reacted with 10 (0.2 g, 0.84 mmol) following the procedure described for 25 to afford 26 (0.24 g, 89%). Eluent: EtOAc: PE (1:3); Brownish gum; [α]D25 = (−) 37.6 (c = 1.09, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.02–1.16 (m, 3H), 1.21–1.25 (m, 4H), 1.54–1.60 (m, 7H), 2.12–2.18 (m, 1H), 2.46 (s, 3H), 3.08 (dd, J = 3.2, 7.2 Hz, 1H), 3.72–3.82 (m, 3H), 4.25–4.28 (m, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 21.2, 21.6, 24.6 (CH₂), 24.8 (CH₂), 25.8 (CH₂), 33.3 (2 × CH₂), 54.2, 58.4, 73.7 (CH₂), 75.0, 75.9, 128.5, 130.0, 135.3, 145.1; HRMS [ES⁺, (M + H)⁺]: for C₁₉H₂₈N₂O₅S obsd 338.1771, calc 338.1790.

Compound 27: Morpholine (1.4 mL, 16.80 mmol) was reacted with 10 (0.2 g, 0.84 mmol) following the procedure described for 25 to afford 27 (0.22 g, 86%). Eluent: EtOAc: PE (1:4); Brownish solid; Mp = 121 °C; [α]D25 = (−) 33.6 (c = 1.05, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.00 (d, J = 6.0 Hz, 3H), 2.08–2.11 (m, 2H), 2.41 (s, 3H), 3.25 (d, J = 7.2 Hz, 1H), 3.55–3.59 (m, 4H), 3.66–3.71 (m, 1H), 3.82–3.83 (m, 1H), 4.00 (d, J = 10.4 Hz, 1H), 4.11 (t, J = 6.8 Hz, 1H), 7.34 (d, J = 7.6 Hz, 2H), 7.74
Compound 28: Compound 16 (0.043 g, 0.09 mmol) was converted to 28 (0.04 g, 89%) following the procedure described for the preparation of 22. Eluent: EtOAc: PE (1:4); White solid; Mp = 111 °C; [α] D 25 = (+) 56.3 (c = 0.86, CHCl 3 ); 1 H-NMR (400 MHz, CDCl 3 ): δ = 2.40 (s, 3H), 2.70 (dd, J = 3.8, 10.4 Hz, 1H), 3.26 (dd, J = 3.8, 10.4 Hz, 1H), 3.62 (d, J = 1.9, 9.3 Hz, 2H) 7.27–7.41 (m, 18H), 7.60 (d, J = 7.3 Hz, 6H); 13 C-NMR (100 MHz, CDCl 3 ): δ = 21.8, 56.9, 63.5 (CH 2 ), 69.6, 73.3 (CH 2 ), 78.8, 82.1, 86.4, 126.9, 127.7, 128.3, 128.6, 130.0, 135.0, 143.5 (3 x C), 144.9; HRMS [ES +, (M + Na) +]: for C 32 H 32 O 8 NaS obsd 551.1858, calcd 551.1868.

Compound 29: A mixture of nitromethane (0.03 mL, 0.27 mmol) and KO t Bu (0.02 g, 0.22 mmol) in THF (5 mL) was reacted with Compound 16 (0.043 g, 0.09 mmol) in THF (4 mL) following the procedure described for 23 to afford 29 (0.047 g, 94%). Eluent: EtOAc: PE (1:4); Colorless gum; [α] D 25 = (+) 89.2 (c = 0.95, CHCl 3 ); 1 H-NMR (400 MHz, CDCl 3 ): δ = 2.40 (s, 3H), 2.70 (dd, J = 3.8, 10.4 Hz, 1H), 3.26 (dd, J = 3.8, 10.4 Hz, 1H), 3.62 (d, J = 1.9, 9.3 Hz, 2H) 7.27–7.41 (m, 18H), 7.60 (d, J = 7.3 Hz, 6H); 13 C-NMR (100 MHz, CDCl 3 ): δ = 21.8, 56.9, 63.5 (CH 2 ), 69.6, 73.3 (CH 2 ), 78.8, 82.1, 86.4, 126.9, 127.7, 128.3, 128.6, 130.0, 135.0, 143.5 (3 x C), 144.9; HRMS [ES +, (M + Na) +]: for C 32 H 32 O 8 NaS obsd 551.1858, calcd 551.1868.

Compound 30: A mixture of dimethylmalonate (0.13 mL, 1.21 mmol) and KO t Bu (0.11 g, 1.0 mmol) in THF (5 mL) was reacted with Compound 16 (0.2 g, 0.4 mmol) in THF (4 mL) following the procedure described for 23 to afford 30 (0.24 g, 96%). Eluent: EtOAc: PE (1:4); Colorless gum; [α] D 25 = (+) 73.6 (c = 0.59, CHCl 3 ); 1 H-NMR (400 MHz, CDCl 3 ): δ = 2.40 (s, 3H), 2.70 (dd, J = 3.8, 10.4 Hz, 1H), 3.26 (dd, J = 3.8, 10.4 Hz, 1H), 3.62 (d, J = 1.9, 9.3 Hz, 2H) 7.27–7.41 (m, 18H), 7.60 (d, J = 7.3 Hz, 6H); 13 C-NMR (100 MHz, CDCl 3 ): δ = 21.8, 56.9, 63.5 (CH 2 ), 69.6, 73.3 (CH 2 ), 78.8, 82.1, 86.4, 126.9, 127.7, 128.6, 128.7, 129.9, 134.7, 143.4 (3 x C), 144.9, 167.9, 168.1; HRMS [ES +, (M + Na) +]: for C 36 H 36 O 8 NaS obsd 651.2018, calcd 651.2029.

Compound 31: Compound 16 (0.043 g, 0.09 mmol) was converted to 31 (0.046 g, 88%) following the procedure described under the preparation of 24. Eluent: EtOAc: PE (1:3); White solid; Mp = 110 °C; [α] D 25 = (+) 129.6 (c = 0.91, CHCl 3 ); 1 H-NMR (400 MHz, CDCl 3 ): δ = 1.43 (s, 3H), 2.42 (s, 3H), 3.07 (dd, J = 3.2, 10.8 Hz, 1H), 3.66 (dd, J = 1.6, 10.8 Hz, 1H), 4.05–4.21 (m, 3H), 4.41–4.46 (m, 1H), 5.73–5.77 (m, 1H), 7.27–7.41 (m, 18H), 7.75 (d, J = 8.0 Hz, 2H), 9.31 (s, 1H); 13 C-NMR (100 MHz, CDCl 3 ): δ = 12.3, 21.9, 55.9, 63.5 (CH 2 ), 68.5, 72.4 (CH 2 ), 79.4, 87.6, 112.7, 127.6, 128.1, 128.8, 130.3, 134.5, 136.8, 143.2 (3 x C), 145.8, 150.4, 163.6; HRMS [ES +, (M + Na) +]: for C 36 H 36 O 8 NaS obsd 645.2030, calcd 645.2029.

Compound 32: Compound 16 (0.043 g, 0.09 mmol) was converted to 32 (0.046 g, 88%) following the procedure described for 25. Eluent: EtOAc: PE (1:3); Colorless gum; [α] D 25 = (+) 91.4 (c = 0.69, CHCl 3 ); 1 H-NMR (400 MHz, CDCl 3 ): δ = 2.42 (s, 3H), 2.70 (dd, J = 3.2, 10.4 Hz, 1H), 3.44–3.46 (m, 1H), 3.62 (d, J = 13.6 Hz, 1H), 3.70–3.73 (m, 2H), 3.81–3.82 (m, 1H), 3.95–4.03 (m, 2H), 4.34–4.35 (m, 1H), 7.19–7.29 (m, 16H), 7.37 (d, J = 6.4 Hz, 6H), 7.59 (d, J = 8.0 Hz, 2H); 13 C-NMR (100 MHz, CDCl 3 ): δ = 21.7, 51.2 (CH 2 ), 60.3, 63.8 (CH 2 ), 69.6, 73.8 (CH 2 ), 78.3, 86.9, 127.0, 127.8, 128.0, 128.3, 128.6, 130.0, 134.9, 139.3, 143.4 (3 x C), 144.8; HRMS [ES +, (M + H) +]: for C 38 H 38 NO 4 S obsd 640.2511, calcd 640.2522.

Compound 33: Cyclohexylamine (0.92 mL, 8.06 mmol) was reacted with 16 (0.2 g, 0.40 mmol) following the procedure described for 25 to afford 33 (0.21 g, 89%). Eluent: EtOAc: PE (1:3); Colorless gum; [α] D 25 = (+) 103.6 (c = 1.03, CHCl 3 ); 1 H-NMR (400 MHz, CDCl 3 ): δ = 0.90–1.37 (m, 7H), 1.52–1.66 (m, 7H), 2.22–2.27 (m, 1H), 2.43 (s, 3H), 2.73 (dd, J = 3.2, 10.4 Hz, 1H), 3.45 (dd, J = 2.8, 10.4 Hz, 1H), 3.61–3.65 (m, 1H), 3.88–4.02 (m, 3H), 4.34–4.37 (m, 1H), 7.25–7.42 (m, 18H), 7.66 (d, J = 8.4 Hz, 2H); 13 C-NMR (100 MHz, CDCl 3 ): δ = 21.6, 24.6 (CH 2 ), 24.8 (CH 2 ), 26.0 (CH 2 ), 32.9 (CH 2 ), 33.3 (CH 2 ), 53.9,
77.1, 70.5 (CH$_2$), 76.7, 83.5, 124.2, 130.0, 137.8, 141.9; HRMS [ES$^+$, (M + H)$^+$]: for C$_{13}$H$_9$O$_2$S obsd 255.1071, calc 255.1055.

Compound 22 from 35R$_S$ or 35S$_S$: Compound 35R$_S$ (0.1 g, 0.39 mmol) was converted to 22 (0.09 g, 85%) following the procedure described for the preparation of 9. Compound 35S$_S$ was converted to 22 in a similar fashion.

Compound 36S$_S$: Dimethylmalonate (0.5 mL, 4.05 mmol) was added to a well stirred solution of NaH (0.05 g, 3.37 mmol) in DMF (5 mL), and the mixture was stirred for 0.5 h at ambient temperature in an inert atmosphere. Vinyl sulfoxide 19R$_S$ (0.3 g, 1.35 mmol) was added, and the whole mixture was stirred at 60 °C. After 6 h (tlc), the reaction mixture was partitioned between aqueous satd. solution of NaHCO$_3$ and EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na$_2$SO$_4$ and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The residue was purified over silica gel to get 36S$_S$ (0.045 g, 95%). Eluent: EtOAc: PE (1:3); Colorless gum; [s$^+$]$^D$ = (+) 126.8 (c = 0.99, CHCl$_3$); $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ = 1.22 (d, $J$ = 6.4 Hz, 3H), 2.41 (s, 3H), 2.78 (d, $J$ = 7.6 Hz, 1H), 2.97 (s, 3H), 3.65–3.69 (m, 1H), 3.96–4.02 (m, 2H), 4.23 (s, 1H), 7.34 (d, $J$ = 7.6 Hz, 2H), 7.53 (d, $J$ = 8.0 Hz, 2H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ = 19.7, 21.4, 56.5, 72.8 (CH$_2$), 75.0, 75.6, 80.8, 124.5, 130.0, 138.5, 142.1; HRMS [ES$^+$, (M + Na)$^+$]: for C$_{13}$H$_9$O$_2$NaS obsd 255.1069, calc 255.1055.

Compound 36R$_S$: A mixture of dimethylmalonate (0.5 mL, 4.05 mmol) and NaH (0.05 g, 3.37 mmol) in DMF (5 mL) was reacted with Compound 19S$_S$ (0.3 g, 1.35 mmol) in DMF (4 mL) following the procedure described for 36S$_S$ to afford Compound 36R$_S$ (0.045 g, 95%). Eluent: EtOAc: PE (1:3); Colorless gum compound; [s$^+$]$^D$ = (+) 112.5 (c = 0.98, CHCl$_3$); $^1$H-NMR (400 MHz, CDCl$_3$): $\delta$ = 1.15 (d, $J$ = 6.0 Hz, 3H), 2.41 (s, 3H), 2.94–2.97 (m, 1H), 3.02 (d, $J$ = 6.4 Hz, 1H), 3.27–3.32 (m, 1H), 3.62 (s, 3H), 3.68 (s, 3H), 3.76–3.82 (m, 2H), 3.80 (dd, $J$ = 2.8, 9.6 Hz, 1H), 4.00 (q, $J$ = 6.4 Hz, 1H), 7.33 (d, $J$ = 8.0 Hz, 2H), 7.52 (d, $J$ = 8.0 Hz, 2H); $^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ = 19.5, 21.4, 39.4, 52.6, 53.8, 70.6 (CH$_2$), 71.6, 75.3, 124.5, 130.1, 138.2, 142.1, 161.8, 168.2; HRMS [ES$^+$, (M + Na)$^+$]: for C$_{17}$H$_{22}$O$_6$NaS obsd 377.1058, calc 377.1035.
Compound 26 from 36RS or 36SS: Compound 36RS (0.06 g, 0.16 mmol) was converted to 26 (0.048 g, 77%) following the procedure described for the preparation of 9. Compound 36SS was converted to 26 in a similar fashion.

Compound 37SS: A mixture of vinyl sulfoxide 19RS (0.3 g, 1.35 mmol) and benzylamine (2.9 mL, 27.0 mmol) was stirred at room temperature for 42 h. After completion of reaction, the mixture was partitioned between EtOAc and satd. aqueous NH₄Cl solution. Then, the organic part was separated, dried over anhyd Na₂SO₄, and filtered, and the filtrate was evaporated to dryness. The residue thus obtained was purified over silica gel to afford Compound 37SS (0.41 g, 93%). Eluent: EtOAc: PE (2:3); Brownish gum; [α]D₂⁵ = (−) 103.7 (c = 0.76, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 1.19 (d, J = 6.0 Hz, 3H), 2.42 (s, 3H), 2.68–2.70 (m, 1H), 3.49 (t, J = 15.2 Hz, 2H), 3.79–3.85 (m, 3H), 4.00–4.06 (m, 1H), 7.09 (d, J = 6.8 Hz, 2H), 7.21–7.34 (m, 6H), 7.52 (d, J = 8.0 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 20.0, 21.4, 51.9 (CH₂), 59.0, 73.0 (CH₂), 74.8, 76.0, 124.4, 127.1, 128.0, 128.3, 130.1, 138.6, 142.1; HRMS [ES⁺, (M + H)⁺]: for C₁₉H₂₄NO₂S obsd 330.1563, calcd 330.1528.

Compound 25 from 37RS or 37SS: Compound 37RS (0.1 g, 0.30 mmol) was converted to 25 (0.031 g, 30%) following the procedure described for the preparation of 9. Compound 37SS was converted to 25 in a similar fashion. The oxidation of 37RS/37SS was quenched within 0.5 h to avoid over-oxidation.

Compound 38SS: Cyclohexylamine (3.1 mL, 27.0 mmol) was reacted with 19RS (0.3 g, 1.35 mmol) following the procedure described for 37SS to afford 38SS (0.39 g, 90%). Eluent: EtOAc: PE (2:3); Brownish gum; [α]D₂⁵ = (−) 39.5 (c = 0.86, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 0.94–1.01 (m, 5H), 1.08–1.19 (m, 3H), 1.57–1.74 (m, 7H), 2.28 (t, J = 10.4 Hz, 1H), 2.41 (s, 3H), 2.61–2.63 (m, 1H), 3.62 (d, J = 3.6 Hz, 1H), 3.74 (d, J = 3.2 Hz, 2H), 4.22 (t, J = 6.4 Hz, 1H), 7.33 (d, J = 7.6 Hz, 2H), 7.52 (d, J = 7.6 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 21.4, 21.4, 24.8 (CH₂), 25.8, 33.2 (CH₂), 33.6 (CH₂), 54.7, 58.5, 72.9, 72.9 (CH₂), 74.6, 124.4, 130.0, 138.4, 141.9; HRMS [ES⁺, (M + H)⁺]: for C₁₈H₂₅NO₂S obsd 322.1875, calcld 322.1841.

Compound 38RS: Cyclohexylamine (3.1 mL, 27.0 mmol) was reacted with 19RS (0.3 g, 1.35 mmol) following the procedure described for 37SS to afford 38RS (0.39 g, 90%). Eluent: EtOAc: pet ether (2:3); Brownish gum; [α]D₂⁵ = (−) 120.3 (c = 0.91, CHCl₃); ¹H-NMR (400 MHz, CDCl₃): δ = 0.46–0.58 (m, 2H), 0.95–1.03 (m, 3H), 1.22–1.35 (m, 4H), 1.69–1.75 (m, 4H), 2.44 (s, 3H), 2.92–2.95 (m, 1H), 3.05 (t, J = 5.6 Hz, 1H), 3.30–3.36 (m, 1H), 4.08 (t, J = 8.0 Hz, 1H), 4.39 (t, J = 6.4 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 7.6 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃): δ = 16.5, 21.4, 24.7 (CH₂), 24.8 (CH₂), 25.7 (CH₂), 33.0 (CH₂), 33.8 (CH₂), 55.1, 57.0, 73.7 (CH₂), 75.5, 76.3, 126.3, 130.1, 138.8, 142.9; HRMS [ES⁺, (M + H)⁺]: for C₁₈H₂₅NO₂S obsd 322.1825, calcld 322.1841.

Compound 26 from 38RS or 38SS: Compound 38RS (0.1 g, 0.31 mmol) was converted to 26 (0.029 g, 28%) following the procedure described for the preparation of 9. Compound 38SS was converted to 26 in a similar fashion. The oxidation of 38RS or 38SS was quenched within 0.5 h to avoid over-oxidation.

Compound 28 from 21: Compound 21 (0.3 g, 0.62 mmol) was converted to 39 following the procedure described for the preparation of 22. The inseparable mixture 39 was converted to 28 following the procedure described for the preparation of 9.
Compound 30 from 21: Compound 21 (0.3 g, 0.62 mmol) was converted to 40 following the procedure described under the preparation of 36S. The inseparable mixture 40 was converted to 30 following the procedure described for the preparation of 9.

Compound 33 from 21: Compound 21 (0.3 g, 0.62 mmol) was converted to 41 following the procedure described for the preparation of Compound 37S. The inseparable mixture 41 was converted to 33 following the procedure described for the preparation of 9. The oxidation of 41 was quenched within 0.5 h to avoid over-oxidation.

4. Conclusions

A simple strategy was devised for the synthesis of enantiomerically pure 2-substituted 2,5-dihydro-3-(arylsulfonyl)- and 2-substituted-2,5-dihydro-3-(arylsulfinyl)-furans from easily accessible carbohydrate derivatives. Since appendage diversity is one of the three major components of DOS [9], each of the four pure, and a diastereomeric mixture of, Michael acceptors were reacted with a variety of nucleophiles. The reactions were highly efficient, and each of 10, 16, 19R, and 19S afforded single diastereomers with varied appendages. The mixture of diastereomers 21 also afforded a pair of diastereomers from the Michael addition. Although the varying steric bulk at C-2 in combination with different nucleophiles could not alter the diastereoselectivity of addition, this strategy opens up a novel route for the synthesis of new enantiopure furanics with appendage diversity. In addition to the synthetic utility of this strategy, the other major observation is that the group, attached to a single chirality carbon (i.e., C-2) originating from carbohydrate irrespective of its size, dictated the formation of all products in anti-anti configurations. Moreover, the group at C-2 suppressed the effect of chiral sulfoxides in the case of vinyl sulfoxide-modified tetrahydrofurans. This strategy is now currently pursued to generate different sets of densely functionalized tetrahydrofurans using a DOS strategy.

Supplementary Materials: Supplementary materials can be accessed at: http://www.mdpi.com/1420-3049/21/6/690/s1.

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References

1. Schreiber, S.L. Target-oriented and diversity-oriented organic synthesis in drug discovery. Science 2000, 287, 1964–1969. [PubMed]
2. Burke, M.D.; Schreiber, S.L. A planning strategy for diversity-oriented synthesis. Angew. Chem. Int. Ed. 2004, 43, 46–58. [CrossRef] [PubMed]
3. Arya, P.; Quevillon, S.; Joseph, R.; Wei, C.-Q.; Gan, Z.; Parisien, M.; Sesmilo, E.; Reddy, P.T.; Chen, Z.-X.; Durieux, P.; et al. Toward the library generation of natural product-like polycyclic derivatives by stereocontrolled diversity-oriented synthesis. Pure Appl. Chem. 2005, 77, 163–178. [CrossRef]
4. Tejedor, D.; Gonzalez-Cruz, D.; Santos-Exposito, A.; Marrero-Tellado, J.J.; de Armas, P.; Garcia-Tellado, F. Multicomponent domino processes based on the organocatalytic generation of conjugated acetylides: Efficient synthetic manifolds for diversity-oriented molecular construction. Chem. Eur. J. 2005, 11, 3502–3510. [CrossRef] [PubMed]
5. Ganem, B. Strategies for innovation in multicomponent reaction design. Acc. Chem. Res. 2009, 42, 463–472. [CrossRef] [PubMed]
6. Dandapani, S.; Marcacurelle, L.A. Current strategies for diversity-oriented synthesis. Curr. Opin. Chem. Biol. 2010, 14, 362–370. [CrossRef] [PubMed]
1. Maier, M.E. Design and synthesis of analogues of natural products. *Curr. Opin. Chem. Biol.*, 2010, 14, 371–382. [CrossRef] [PubMed]
2. Scheffelaar, R.; Ruijter, E.; Orru, R.V.A. Multicomponent reaction design strategies: Towards scaffold and stereochemical diversity. *Top. Het. Chem.*, 2010, 25, 95–126.
3. Ruijter, E.; Scheffelaar, R.; Orru, R.V.A. Design and synthesis of analogues of natural products. *Angew. Chem. Int. Ed.*, 2011, 50, 6234–6246. [CrossRef] [PubMed]
4. Eckert, H. Diversity oriented syntheses of conventional heterocycles by smart multi component reactions (MCRs) of the last decade. *Molecules*, 2012, 17, 1074–1102. [CrossRef] [PubMed]
5. O’Connor, C.J.; Beckmann, H.S.G.; Spring, D.R. Diversity oriented syntheses of conventional heterocycles by smart multi component reactions (MCRs) of the last decade. *Molecules*, 2012, 17, 1074–1102. [CrossRef] [PubMed]
6. Maier, M.E. Design and synthesis of analogues of natural products. *Org. Biomol. Chem.*, 2015, 13, 5302–5343. [CrossRef] [PubMed]
7. Lenci, E.; Menchi, G.; Trabocchi, A. Carbohydrates in diversity-oriented synthesis: Challenges and opportunities. *Org. Biomol. Chem.*, 2016, 14, 808–825. [CrossRef] [PubMed]
8. Lichtenhager, F.W. Enantiopure building blocks from sugars: Towards improving the utility of ketoses as organic raw materials. *Carbohydr. Res.*, 1998, 313, 69–89. [CrossRef]
9. Morris, D. The next economy: From dead carbon to living carbon. *Sci. Food Agric.*, 2006, 86, 1743–1746. [CrossRef]
10. Kamm, B. Production of platform chemicals and synthesis gas from biomass. *Angew. Chem. Int. Ed.*, 2007, 46, 5056–5058. [CrossRef] [PubMed]
11. Singh, S.P.; Singh, D. Biodiesel production through the use of different sources and characterization of oils and their esters as the substitute of diesel: A review. *Renew. Sustain. Energy Rev.*, 2010, 14, 200–216. [CrossRef]
12. Saha, B.; Abu-Omar, M.M. Current technologies, economics, and perspectives for 2,5-dimethylfuran production from biomass-derived intermediates. *ChemSusChem*, 2015, 8, 1133–1142. [CrossRef] [PubMed]
13. Wolfe, J.P.; Hay, M.B. Recent advances in the stereoselective synthesis of tetrahydrofurans. *Tetrahedron*, 2015, 63, 261–290. [CrossRef] [PubMed]
14. Rainer, J.D. Synthesis of substituted tetrahydrofurans. *Top. Het. Chem.*, 2014, 35, 1–41.
15. Manna, C.; Pathak, T. Diversity-oriented synthesis of enantiopure furfurans from carbohydrates: An expedient approach with built-in Michael acceptor, masked aldehyde and leaving group in a single sugar derivative. *Eur. J. Org. Chem.*, 2013, 6084–6097. [CrossRef]
16. Manna, C.; Sahu, D.; Ganguly, B.; Pathak, T. Furo[2,3-c]pyrans from a vinyl sulfone modified methyl 2,6-O-anhydro-α-D-hexopyranoside: An experimental and theoretical investigation. *Eur. J. Org. Chem.*, 2013, 36, 8197–8207. [CrossRef]
17. Dey, D.; Bhaumik, A.; Pathak, T. Vinyl sulfone- and vinyl sulfoxide-modified tetrahydrofurans: A preliminary account of the enantiomeric synthesis of and diastereoselectivity of addition to new classes of Michael acceptors. *Tetrahedron*, 2013, 69, 8705–8712. [CrossRef]
18. Wei, W.; Li, J.; Yang, D.; Wen, J.; Jiao, Y.; You, J.; Wang, H. Copper-catalyzed highly selective direct hydrosulfonylation of alkenes with arylsulfinic acids leading to vinyl sulfones. *Org. Biomol. Chem.*, 2014, 12, 1861–1864. [CrossRef] [PubMed]
19. Kawamoto, T.; Uehara, S.; Hirao, H.; Fukuyama, T.; Matsubara, H.; Ryu, I. Borohydride-mediated radical addition reactions of organic iodides to electron-deficient alkenes. *J. Org. Chem.*, 2014, 79, 3999–4007. [CrossRef] [PubMed]
20. Bobinski, T.P.; Fuchs, P.L. Citric acid mediated catalytic osmylation/oxidative cleavage of electron deficient olefins: A vinyl sulfone study. *Tetrahedron Lett.*, 2015, 56, 4151–4154. [CrossRef]
21. Gao, X.; Pan, X.; Gao, J.; Huang, H.; Yuan, G.; Li, Y. Ammonium iodide-induced sulfonylation of alkenes with DMSO and water toward the synthesis of vinyl methyl sulfones. *Chem. Commun.*, 2015, 51, 210–212. [CrossRef] [PubMed]
22. Doherty, W.; Evans, P. Aminooxylation Horner-Wadsworth-Emmons sequence for the synthesis of enantioenriched γ-functionalized vinyl sulfones. *J. Org. Chem.*, 2016, 81, 1416–1424. [CrossRef] [PubMed]
23. Kiemele, E.R.; Wathier, M.; Bichler, P.; Love, J.A. Total synthesis of K777: Successful application of transition-metal-catalyzed alkyne hydrothiolation toward the modular synthesis of a potent cysteine protease inhibitor. *Org. Lett.*, 2016, 18, 492–495. [CrossRef] [PubMed]
30. Opekar, S.; Pohl, R.; Eigner, V.; Beier, P. Conjugate addition of diethyl 1-fluoro-1-phenylsulfonylmethanephosphonate to α,β-unsaturated compounds. J. Org. Chem. 2013, 78, 4573–4579. [CrossRef] [PubMed]

31. Sokolenko, L.V.; Yagupolskii, Y.L.; Vlasenko, Y.G.; Babichenko, L.N.; Lipetskij, V.O.; Anselmi, E.; Magnier, E. Arylation of perfluoroalkyl vinyl sulfoxides via the Heck reaction. Tetrahedron Lett. 2015, 56, 1259–1262. [CrossRef] [PubMed]

32. Coote, S.C.; Poethig, A.; Bach, T. Enantioselective template-directed [2+2] photocycloadditions of isoquinolones: Scope, mechanism and synthetic applications. Chem. Eur. J. 2015, 21, 6906–6912. [CrossRef]

33. Boell, W.; Koenig, H. Vitamin B6: A new synthesis by Diels–Alder reaction. Liebigs Ann. Chem. 1979, 1657–1664. [CrossRef]

34. Boell, W. A new synthesis of vinyl sulfoxides. Liebigs Ann. Chem. 1979, 1665–1674. [CrossRef]

35. Paquette, L.A.; Crouse, G.D. An indirect method for engaging unactivated alkenes as effective dienophiles in regioselective Diels–Alder reactions. J. Org. Chem. 1983, 48, 141–142. [CrossRef]

36. Mikolajczyk, M. Asymmetric cyclopropanation of chiral (1-phosphoryl) vinyl sulfoxides: A new approach to constrained analogs of biologically active compounds. Pure Appl. Chem. 2005, 77, 2091–2098.

37. Rivero, M.R.; Adrio, J.; Carretero, J.C. Pauson-Khand reactions of alkenyl sulfoxides and alkenyl sulfoxides: Applications in asymmetric synthesis. Synlett 2005, 26–41. [CrossRef]

38. Pellissier, H. Use of chiral sulfoxides in asymmetric synthesis. Tetrahedron 2006, 62, 5559–5601.

39. Carmen Carreno, M.; Hernández-Torres, G.; Ribagorda, M.; Urbano, A. Enantiopure sulfoxides: Recent applications in asymmetric synthesis. Chem. Commun. 2009, 6129–6144. [CrossRef]

40. Stingl, K.A.; Tsogoeva, S.B. Recent advances in sulfoxidation reactions: A metal-free approach. Tetrahedron Asymmetry 2010, 21, 1055–1074.

41. Walker, A.J. Asymmetric carbon-carbon bond formation using sulfoxide-stabilized carbanions. Tetrahedron Asymmetry 1992, 3, 961–998. [CrossRef]

42. Li, Y.; Xu, M.-H. Simple sulfur-olefins as new promising chiral ligands for asymmetric catalysis. Chem. Commun. 2014, 50, 3771–3782. [CrossRef] [PubMed]

43. Latypova, L.Z.; Saigitbatalova, E.S.; Chulakova, D.R.; Lodochnikova, O.A.; Kurbangalieva, A.R.; Berdnikov, E.A.; Chmutova, G.A. Sulfides, sulfones, and sulfoxides of the furan-2(5H)-one series. synthesis and structure. Russ. J. Org. Chem. 2014, 50, 521–534. [CrossRef]

44. Trost, B.M.; Rao, M. Development of chiral sulfoxide ligands for asymmetric catalysis. Angew. Chem. Int. Ed. 2015, 54, 5026–5043. [CrossRef] [PubMed]

45. Chen, C.C.; Waser, J. One-pot, three-component arylalkynyl sulfone synthesis. Org. Lett. 2015, 17, 736–739. [CrossRef] [PubMed]

46. Sim, J.; Yoon, I.; Yun, H.; An, H.; Suh, Y.-G. Divergent synthetic route to new cyclopentan[c]pyran iridoids: Synthesis of jatamanin A, F, G and J, gastro lactone and nepetalactone. Org. Biomol. Chem. 2016, 14, 1244–1251. [CrossRef] [PubMed]

47. Fuerstner, A.; Jumbam, D.; Teslic, J.; Weidmann, H. Metal-graphite reagents in carbohydrate chemistry. The scope and limitations of the use of zinc/silver-graphite in the synthesis of carbohydrate-derived substituted hex-5-enals and pent-4-enals. J. Org. Chem. 1991, 56, 2213–2217. [CrossRef]

48. Sanki, A.K.; Pathak, T. Synthesis of anomerically pure vinyl sulfone-modified pent-2-enofuranosides and hex-2-enopyranosides: A group of highly reactive Michael acceptors for accessing carbohydrate-based synthons. Tetrahedron 2003, 59, 7203–7214. [CrossRef]

49. Pathak, T.; Bhattacharya, R. A vinyl sulfone-modified carbohydrate mediated new route to aminosugars and branched-chain sugars. Carbohydr. Res. 2008, 343, 1980–1998. [CrossRef] [PubMed]

50. Diaz Buezo, N.; Alonso, I.; Carretero, J.C. Sulfinyl group as a novel chiral auxiliary in asymmetric Heck reactions. J. Am. Chem. Soc. 1998, 120, 7129–7130. [CrossRef]

Sample Availability: Samples of the compounds are not available.

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