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Furo[2,3-*c*]pyrans from a Vinyl Sulfone Modified Methyl 2,6-*O*-Anhydro-α-D-hexopyranoside: An Experimental and Theoretical Investigation

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Keywords: Chiral pool / Carbohydrates / Enantioselectivity / Nucleophilic substitution / Tautomerism / Density functional calculations /1,3-Dicarbonyl compounds

A vinyl sulfone modified bicyclic sugar molecule undergoes efficient Michael addition of hetero- and carbon nucleophiles to afford single diastereomers. The same molecule consisting of two other masked functional groups, namely an aldehyde and an oxocarbonium ion, turned out to be a unique synthetic intermediate. The adducts generated from this Michael acceptor and a series of β-dicarbonyl compounds and related reagents after acid treatment afforded a new class of furo[2,3-*c*]pyrans, forming up to three new bonds and three stereocenters. In-built chirality centers of the sugar derivative controlled the diastereoselectivity of formation of all new bonds without the requirement for any external reagent for asymmetric induction. DFT calculations revealed the formation of furopyrans as the only possible products, which corroborates the experimentally observed results.

Introduction

Carbohydrates are inexpensive, readily available and versatile building blocks and are easily the most prominent members of the chiral pool.[1] Although a wide range of simple pentoses and hexoses belonging to the carbohydrate chiral pool have been modified as epoxides, ketones and tosylates etc. before further multistep functionalization,[2] synthetic chemists over the decades have also shown great interest in intramolecularly locked bicyclic carbohydrates or anhydro-carbohydrates (non-epoxides) as possible starting materials for synthesis. For example, the locked structural motif of 2,6-anhydro-2-oxopyranosides, known for more than seven decades,[3a,3b] has triggered interest among synthetic chemists as well as led to structural studies of related compounds.[3c–3j] Furthermore, the corresponding 2,6-anhydro-2-thiosugars were found to be useful for the synthesis of erythromycin A, 2,6-dideoxysugars and 1-deoxythiomannojirimycin.[4] An aza heterocycle related to castanospermine was synthesized by using methyl 2,6-benzyloxycarbonylimino-2,6-dideoxy-α-D-altropyranoside as the key intermediate.[5] The concept of connecting C2 and C6 positions of pyranosides was extended further by using $CHCH_2CO_2R$ or $CH(OR)CH(CH_2CO_2Et)$ bridges to afford oxabicyclo[2.2.1] or [2.2.2] systems, respectively; the glycosidic bonds of these bicycle carbohydrates were cleaved to afford densely functionalized cyclopentanes or cyclohexanes, respectively.[6] Different variations of this approach have highlighted further the synthetic utilities of 2,6-bridged bicyclic carbohydrates as a special class of useful intermediates.[7–9] A number of these newly synthesized carbon-bridged bicyclic carbohydrates were also subjected to conformational analysis with relevance to enzymatic hydrolysis of glycosidic bonds.[8]

A perusal of the literature reveals that before the $CHCH_2CO_2R$ or $CH(OR)CH(CH_2CO_2Et)$ bridged bicycle carbohydrates were used as intermediates for generating carbocycles,[6] methyl 3,4-di-*O*-acetyl-2,6-anhydro-α-D-altropyranoside (**A**) was used as an intermediate for generating a mixture of the two diastereomers of (1*R*) and (1*S*) methyl 2,6-anhydro-D-altrose-tetraacetate (**B**) by acetolyzing the glycosidic bonds in the presence of concentrated H_2SO_4 (Scheme 1).[3c,3h] We opined that appropriately functionalized 2,6-*O*-anhydropyranosides would allow easy access to densely functionalized pyrans, which are an important class of compounds in chemistry and biology.[10] However, one of the disadvantages of using bicyclic compounds such as **A** is that only the C3 and C4 positions are available for functionalization. Although a report detailing the order of preference of formation of 2,6-, 3,6- and 4,6-*O*-anhydro compounds was published and several mesylated analogues were reported, the synthetic utilities of these compounds were not explored.[11] An epoxide ring was also created at

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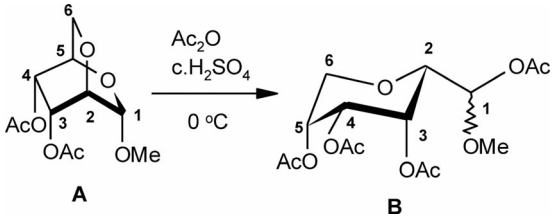
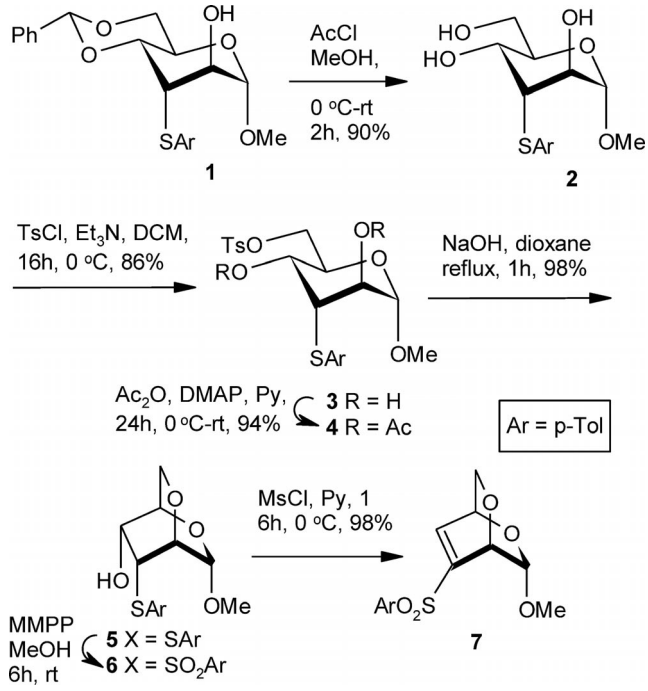
the C3–C4 position of 2,6-*O*-anhydropyranosides but the ring-opening reactions of these synthetically useful epoxides were not effectively pursued.[3g,11,12]



Scheme 1. Acetolysis of a 2,6-*O*-anhydropyranoside.

Result and Discussions

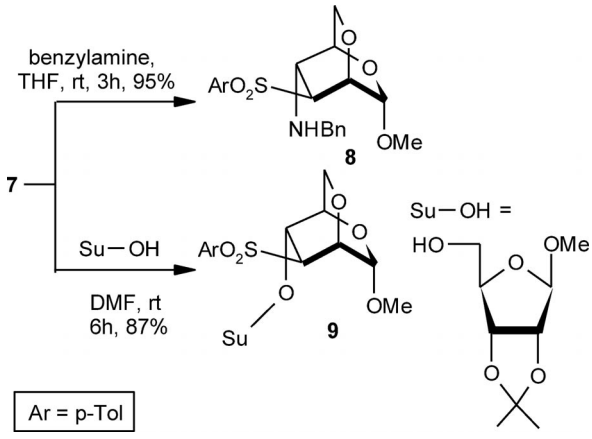
Because the nucleophilic displacement of secondary sufonylates of carbohydrates is sluggish and epoxides cannot be effectively or easily opened by carbon nucleophiles,[2] we have established that the incorporation of a vinyl sulfone group into cyclic carbohydrates broadens the scope of carbohydrate modification, especially in the case of C–C bond formation through Michael addition of a wide range of carbon nucleophiles along with heteronucleophiles.[1c,1e,13] The efficiency of this strategy led us to introduce a vinyl sulfone group at C3–C4 of the 2,6-*O*-anhydropyranosides. Thus, the known thiosugar **1**[9] was debenzylidinated by acetyl chloride in MeOH to obtain triol **2**. The primary hydroxyl group of **2** was selectively tosylated by using tosyl chloride and triethylamine to afford **3**. Direct treatment of **3** with NaOH required harsher reaction conditions for cyclization. Therefore, **3** was acetylated to afford **4**, which, under warm alkaline conditions, underwent deacetylation followed by intramolecular attack of the C2 hydroxyl group at C6 to afford the desired bicyclic compound **5**. The corresponding sulfone derivative **6** was generated in quantitative yield by oxidizing **5** with magnesium bis(monoperoxyphthalate) hexahydrate (MMPP) in MeOH. Compound **6** was sulfonylated by using methanesulfonyl chloride in pyridine at 0–4 °C and the product underwent elimination reaction in a one-pot fashion to afford **7** in 98% yield over two steps (Scheme 2).



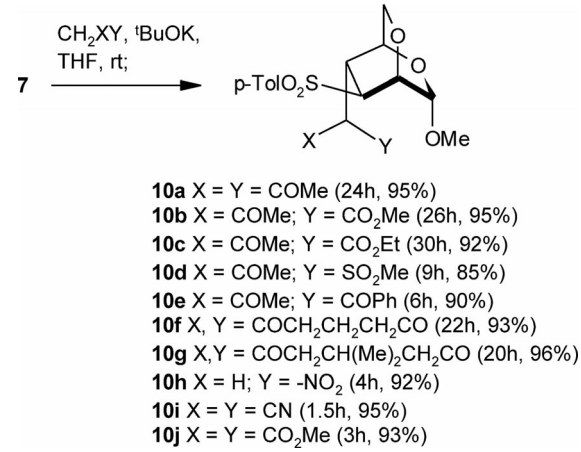
Scheme 2. Synthesis of bicyclic vinyl sulfone **7**.

To test the diastereoselectivity of addition of nucleophiles towards the new Michael acceptor, vinyl sulfone modified 2,6-*O*-anhydropyranoside **7** was treated with benzylamine in tetrahydrofuran (THF) and the oxygen nucleophile derived from a partially protected ribose sugar with NaH/*N*,*N*-dimethylformamide (DMF) at ambient temperature to generate single diastereomers **8** and **9**, respectively, in high yields (Scheme 3). Although the reaction was highly efficient, the acid treatment of **8** and **9** afforded a mixture of inseparable mixtures. We therefore turned our attention to carbon nucleophiles, expecting the adducts to be more stable towards acid treatment. Thus, **7** was treated with the potassium salts of acetylacetone, methyl acetoacetate, ethyl acetoacetate, methylsulfonylacetone, 1-benzoylacetone, 1,3-cyclohexanedione, dimedone, nitromethane, malononitrile and dimethyl malonate to afford the addition products **10a**–**j** (Scheme 4), which are structurally related to **8** and **9**. Compound **7** has one characteristic signal in the region δ = 7.42–7.44 that corresponds to the olefinic proton; this proton is absent in all addition compounds **8**, **9** and **10a**–**j**. Compounds **10b**–**d** are mixtures of inseparable diastereomers and, therefore, it was difficult to extract information from their spectroscopic data. However, in the ^{13}C NMR spectra of **10a**, and both the diastereomers of **10e**, the presence of two carbonyl signals at δ = 202.5/204.1, 195.9/203.3 and 194.2/201.5 ppm, respectively, are clearly evident. Because an OH peak was also absent in the ^{1}H NMR spectra of all three compounds, it was concluded that these molecules tend to exist in their diketo forms. On the other hand, compounds **10f** and **10g** existed preferentially in the enol form, which is indicated by the presence of OH peaks at ca. δ = 9.3 ppm in the ^{1}H NMR spectra, along with a set of *C*=O/(O)CC=*C*(CH$_2$)OH quaternary carbon signals at δ = 196.9/114.1 and 196.9/113.1 ppm, respectively, in the ^{13}C NMR spectra of each of these compounds (see below). However, the configuration of addition products **8** and **10j** were unambiguously confirmed by X-ray diffraction of their single crystals (Figure 1). From the ORTEP diagrams of compounds **8** and **10j**, we presumed that all carbon addition compounds **10a**–**i** also have similar configurations. Due to the presence of an O–CH$_2$ bridge in the bicyclic Michael acceptor **7**, incoming nucleophiles were forced to attack the electron-deficient double bond in an endocyclic fashion. Moreover, the incoming nucleophiles and ArSO$_2$, two sterically bulky groups, positioned themselves in a *trans*-fashion in compounds **8**, **9**, and **10a**–**j**. It is also probable that due to additional stereoelectronic repul-

sions between the anomeric methoxy and $ArSO_2$ groups, the latter moved away as far as possible in the equatorial direction.



Scheme 3. Reactivity of **7** towards oxygen and nitrogen nucleophiles.



Scheme 4. Reactivity of **7** towards carbon nucleophiles.

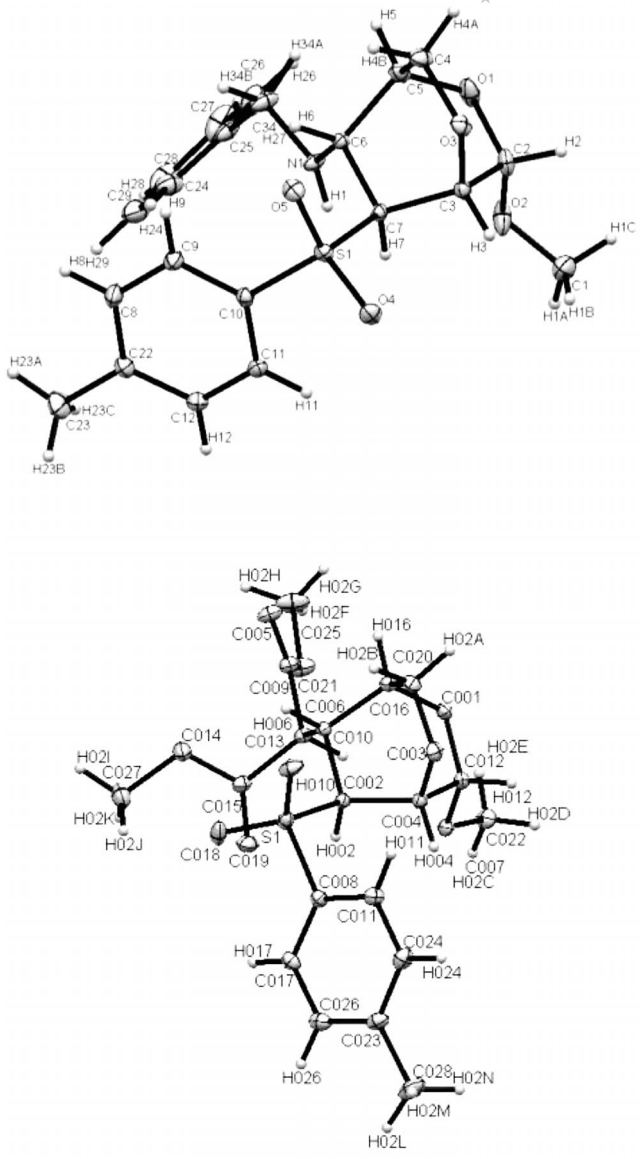
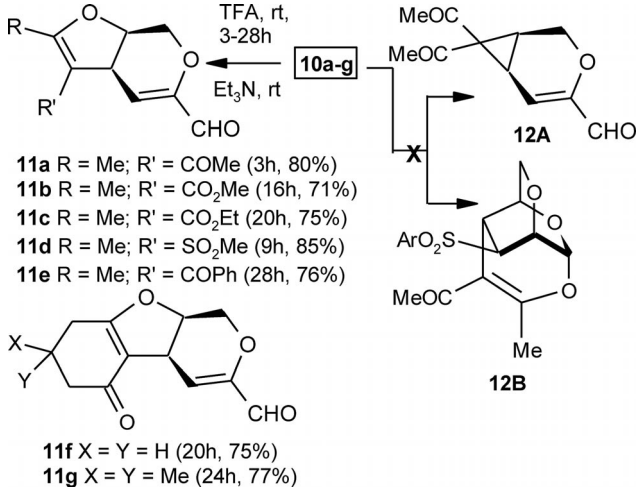


Figure 1. ORTEP diagram of **8** and **10j**.

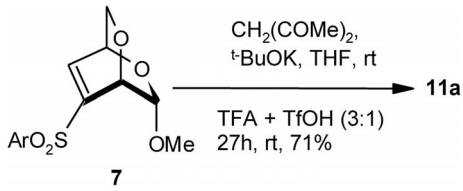
In line with our earlier argument on the probable synthesis of pyrans from 2,6-anhydrosugars (Scheme 1), compounds **10a**–**g** were subjected to acid treatment at ambient temperature, which was followed by triethylamine treatment of the reaction mixture. Surprisingly, the reaction afforded a new class of polycyclic compounds, namely furo[2,3-*c*]pyran derivatives **11a**–**g** (Scheme 5),[14] which are far more complex than the simple pyran structures[10] proposed in Scheme 1. Under similar reaction conditions, compounds **10h**–**j** afforded inseparable mixtures. Although the possibility of formation of compounds **12A** and **12B** was not ruled out in the beginning (see below), the reaction did not afford either of these two compounds.

Importantly, these transformations may also be carried out in a one-pot fashion. Thus, the potassium salt of acetylacetone added to **7** in 24 h (reaction monitored by TLC) in a Michael fashion. A mixture of trifluoroacetic acid (TFA) and TfOH (3:1 ratio, 0.1 mL/mmol) was added to the reac-



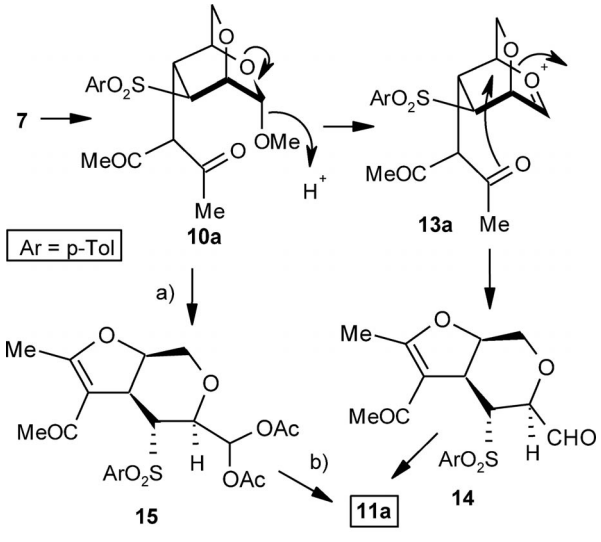
Scheme 5. Synthesis of furopyrans from bicyclic carbohydrates **10a**–**g**.

tion mixture and the solution was stirred for another 3 h. Usual work-up and purification afforded furo[2,3-*c*]pyran derivative **11a** in good overall yield (Scheme 6).



Scheme 6. One-pot synthesis of furopyran **11a** from **7**.

The most plausible pathway of formation of this novel class of furopyrans **11a**–**g** has been elaborated in Scheme 7. Deglycosylation of **10a** generates the oxocarbonium ion intermediate **13a**, which undergoes intramolecular attack by the carbonyl oxygen atom (see below). Interestingly, the C=O$^+$ function, generated in situ, acts as a leaving group and, in stark contrast to the simple ring opening depicted in Scheme 1, the keto oxygen attacks the bridgehead carbon affording the furopyran scaffold; elimination of $ArSO_2H$ from the furopyran intermediate **14** affords **11a**. It is expected that **10b**–**g** would follow the same pathway to afford other analogues **11b**–**g**. The intermediacy of **14** was established by isolating crystalline **15** (Figure 2), which was formed by treating **10a** with acetic anhydride and TfOH. The diacetyl acetal **15** was easily converted into **11a** by mild base treatment (Scheme 7).



Scheme 7. Identification of intermediates in the formation of furopyran derivatives from the Michael adducts of **7**.

Our earlier studies on Michael initiated ring closure on methyl 2,3-dideoxy-5-*O*-mesyl-3-(4-methylphenyl)sulfonyl-α-D-erythro-pent-2-enofuranoside and the corresponding β-

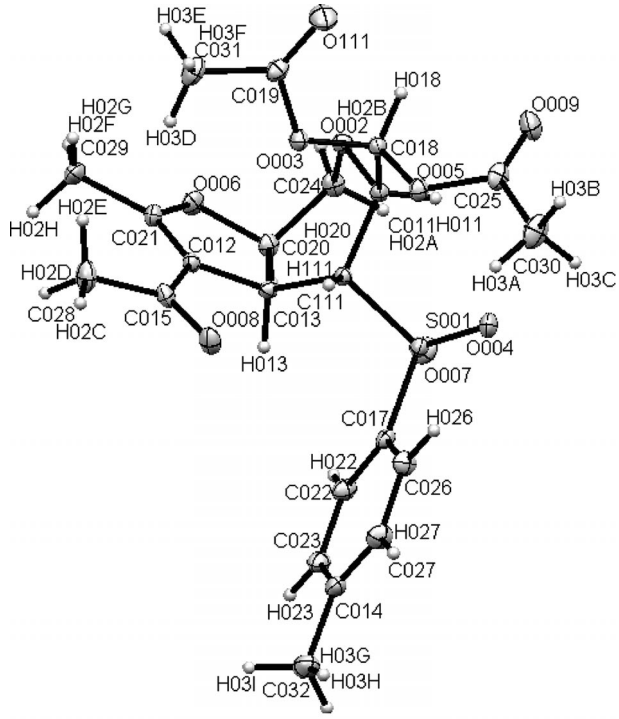
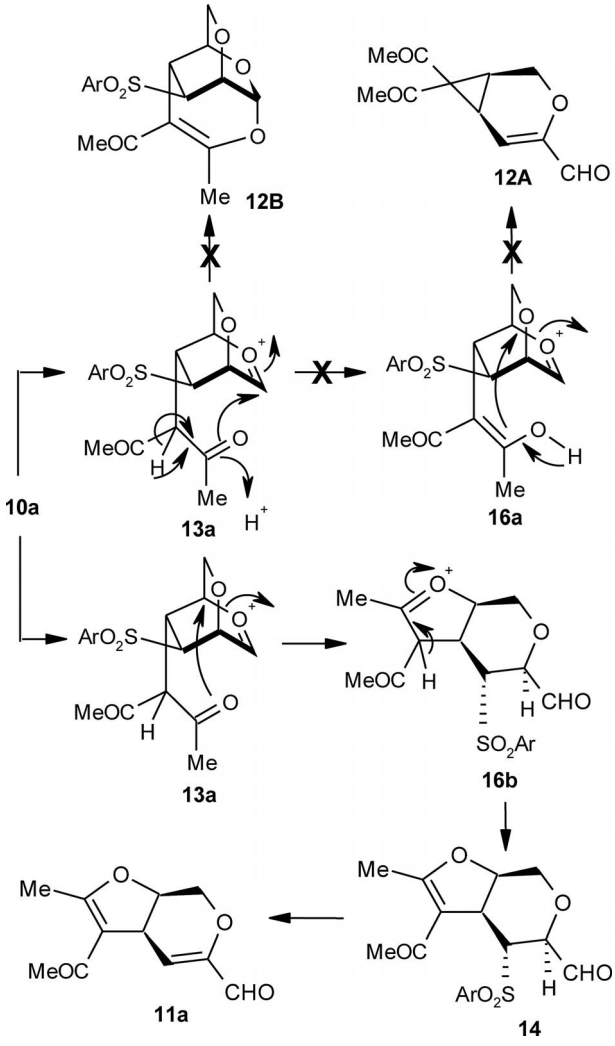


Figure 2. ORTEP diagram of **15**.

analogue established that Michael addition of different nucleophiles to these substrates yielded cyclopropanated carbohydrates by forming a new C–C bond between C3 and C5.[15a] On the other hand, we recently reported the addition of β-dicarbonyl and related reagents to vinyl sulfone modified hex-2-enofuranosyl carbohydrates, and one of the carbonyl groups of the β-dicarbonyl residues of the adduct, on acid treatment, attacked the anomeric carbon in an intramolecular manner under acidic conditions to afford furo[2,3-*b*]furan systems.[15b] We therefore expected that **10a**–**g** would, under similar reaction conditions, either undergo cyclopropanation to afford **12A**, or intramolecular attack of the keto/enol oxygen at the anomeric carbon to yield **12B** via intermediates **16a** and **13a**, respectively (Scheme 8).

To resolve the issue of selective formation of compound **11a** over **12A** or **12B**, it was necessary to understand the involvement of keto/enol forms of the β-dicarbonyl residues in compound **10a**. A computational study was therefore undertaken to examine the formation of furopyran derivative **11a** from **7** at the DFT M06–2X/6-311+G(d)//B3LYP/6-31G(d) level of theory. Full geometrical optimizations and frequency calculations were performed in the gas phase by employing the Becke three-parameter hybrid density functional combined with Lee–Yang–Parr correlation functional (B3LYP) level[16] with a standard 6-31G(d) basis set.[17] The ground-state and transition-state geometries were characterized by vibrational frequency analysis. All single point calculations were performed with the M06-2X method[18] and the 6-311+G(d) basis set[19] with polarizable continuum model (PCM)[20] in TFA medium (ε = 8.22)[21]



Scheme 8. Mechanism of selective formation of **11a** from **10a**.

employing B3LYP/6-31G(d) optimized geometries. All DFT calculations were performed with the Gaussian 09 suite of programs.[22] In these calculations, the SO_2Ar group was modeled with SO_2Me for computational simplicity. The process of enolization of **13a** is shown in Figure 3. The calculated results show that the stable keto form **13a** first attains a sickle-shaped diketo tautomeric[23] intermediate through a rotational transition state, which subsequently leads to a four-membered planar transition state for proton transfer to form **16a**. The computed activation barrier for the rotational transition state is 2.7 kcal/mol (Figure 3). However, the activation barrier computed for the enolization of **13a** to **16a** is 60.5 kcal/mol. Such high energy barriers are also known for other keto-enol tautomerization processes.[24]

Furthermore, the enol form **16a** was calculated to be 18.2 kcal/mol higher in energy than the corresponding keto-form **13a**. These results suggest that the keto-enol process is energetically unfavorable in this case and, hence, it is unlikely that the three-membered pyran derivative **12A** would be formed via intermediate **16a**. The potential energy surface for the formation of product intermediate **16b** is given in Figure 4. Calculations show that the activation barrier for the formation of **16b** through bridgehead ring opening is 28.2 kcal/mol, which is much lower in energy than the keto-enol tautomerization process in **13a**. These results suggest that **13a** would tend to generate **11a**. It is intriguing to note that the other "likely" product **12B** was also not formed from **7** (Scheme 5). We have further undertaken DFT calculations to examine the formation of **12B** from **7**.

The formation of **12B** from **7** would presumably be a multi-step process. Compound **10a** is first formed upon attack of $CH_2(COMe)_2$, followed by formation of keto-oxonium ion **13a**. The orientation of the COMe groups are important for the attack to the bridgehead center or the anomeric carbon center. The COMe group prefers to orient away from the anomeric carbon center in **10a** due to the steric interactions, however, the CO group is in close proximity to the bridgehead center in the calculated geometry (Figure S1). The oxonium ion **13a** formed after the departure of the methoxy group also shows that the COMe group is oriented away from the anomeric carbon atom in the calculated structure. Attack of the C=O oxygen to the anomeric carbon center is only possible by C–C bond rotation (C1–C2) in **13a** (Figure S1). The rotation is hindered due to the electrostatic repulsion between the oxygen atoms of the C=O carbonyl group and the ring oxygen atom (Figure S1). Furthermore, the *endo* hydrogen atom of **13a** leads to steric crowding and rotation of the $CH(COMe)_2$ group towards the anomeric carbon center and would deter the process of rotation. Hence, it is reasonable to conclude that the close proximity of the C=O group to the bridgehead carbon center leads to the formation of **11a**.

It is interesting to note that the relative stability of the acyclic keto oxonium intermediate **13a** compared with the acyclic enol oxonium **16a** is much more favorable (18.2 kcal/mol) (Figure 3), whereas the relative stability of the cyclic keto oxonium **10f**-keto-oxonium compared to the cyclic enol oxonium **10f**-enol-oxonium is only 3.3 kcal/mol (Figure S2). These DFT results suggest that the presence of the enol forms of **10f** and **10g** is possible under similar reaction conditions, which is also supported by the NMR spectroscopic data mentioned above. Therefore, the involvement of the enol form in the cyclization process cannot be ruled out for compounds **10f** and **10g**. However, it can be envisaged that **10f**-enol-oxonium may lead to **17** through attack of the sp^2-carbon center to the bridgehead carbon atom (Scheme 9). The three-membered product intermediate **17** is ca. 4.0 kcal/mol (in TFA) energetically less stable than the observed product intermediate **18**, as calculated at the M06-2X/6-311+G(d)//B3LYP/6-31G(d) level of theory (Figure S3). It should be noted that the enolic oxygen center bears more negative charge (–0.618) than the sp^2-carbon center (–0.003) and, hence, the former center will approach more effectively than the alternative carbon center (Scheme 9). The computed results suggest that the formation of **17**, derived from **10f**, is less likely and, indeed, such products have not been observed.

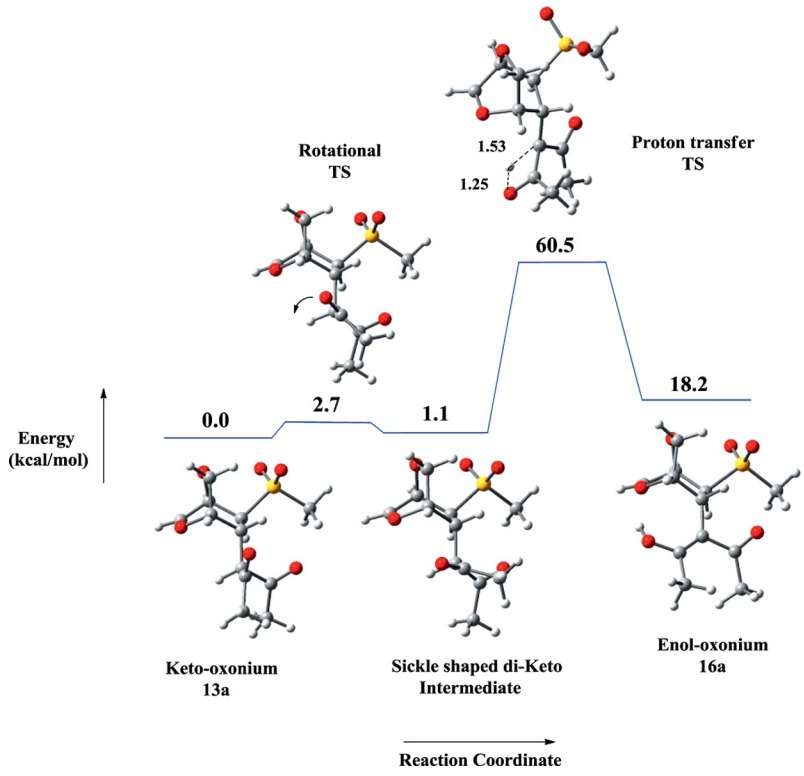


Figure 3. M06–2X/6-311+G(d)//B3LYP/6-31G(d) calculated relative energies of keto to enol transformation of the oxonium ion in TFA. All distances are in Å. Relative energies are given in kcal/mol [gray: carbon; white: hydrogen; red: oxygen; yellow: sulfur].

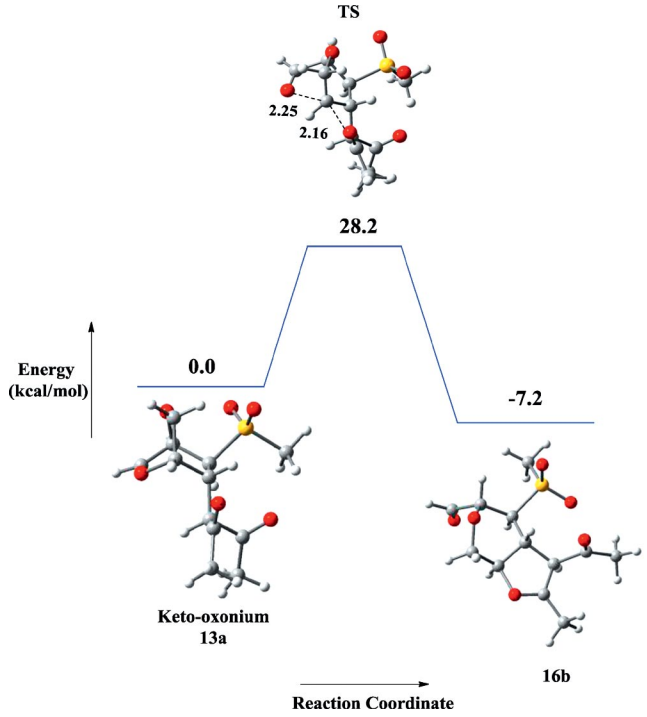
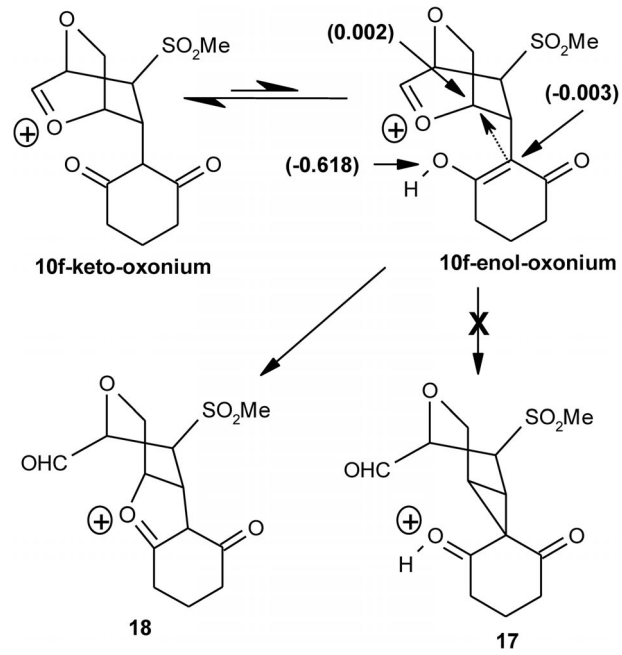


Figure 4. M06–2X/6-311+G(d)//B3LYP/6-31G(d) calculated potential energy surface for the transformation of **13a** into **16b** in TFA. Relative energies are given in kcal/mol. All distances are in Å [gray: carbon; white: hydrogen; red: oxygen; yellow: sulfur].



Scheme 9. Schematic presentation for the formation of **17** and **18** from cyclic **10f**-keto-oxonium. The Mulliken charges in cyclic **10f**-enol-oxonium are in units of electrons [calculated at B3LYP/6-31G(d)].

Conclusions

We have introduced vinyl sulfone modified methyl 2,6-*O*-anhydro α-D-hexopyranoside for the first time as a unique and efficient Michael acceptor. The same molecule consisting of two other masked functionalities, namely an aldehyde and a leaving group in the form of oxocarbonium ion, is capable of reacting with β-dicarbonyl compounds and related reagents in a sequential or one-pot fashion to form a range of enantiomerically pure furo[2,3-*c*]pyrans. These reactions do not require any external reagent for the imposition of asymmetry in the products because the chirality centers of the sugar derivatives controlled the diastereoselectivity of formation of all new bonds. We have also identified the intermediates involved in the reaction processes. DFT calculations revealed that after C–C bond formation, the oxygen nucleophiles of R-C(O)Me moieties of **10a**–**g** attack the bridgehead carbon center and not the anomeric carbon center of intermediates such as **13a** for the cyclization to afford furopyrans. In line with the concept of generating products that are useful as potential substrates for further transformations, the furopyrans reported here are decorated with reactive functional groups, such as R-C=CC(O)-R′, R-C=CSO$_2$R′ and R-C=CCHO, which are capable of combining with other suitably functionalized compounds to generate more complex scaffolds. Work in our laboratory is in progress in this direction.

Experimental Section

General Methods: All reactions were conducted under an N_2 atmosphere. Melting points were determined in open-ended capillary tubes and are uncorrected. Carbohydrates and other fine chemicals were obtained from commercial suppliers and were used without purification. Solvents were dried and distilled by following the standard procedures. TLC was carried out on precoated plates (Merck silica gel 60, f_{254}) and spots were visualized with UV light or by charring the plate dipped in 5% H_2SO_4/MeOH solution. Column chromatography was performed on silica gel (230–400 mesh). ^{1}H and ^{13}C NMR analysis of new compounds were recorded at 200/400 and 50/100 MHz, respectively, by using $CDCl_3$ as solvent unless stated otherwise. DEPT experiments were carried out to identify the methylene and quaternary carbon signals. Optical rotations were recorded at 589 nm. Mass spectroscopy data were obtained from a mass spetrometer consisting of TOF and quadrupole operating in either ESI$^+$ or ESI$^-$ mode.

Compound 2: To a well-stirred, cooled (0 °C) solution of sulfide **1** (4.0 g, 10.31 mmol) in anhyd. MeOH (30 mL) was added AcCl (0.89 mL, 12.37 mmol) at 0 °C and the resulting solution was stirred for 2 h at ambient temperature. After completion of reaction (TLC) pyridine (5 mL) was added and the resulting residue was evaporated to dryness under reduced pressure. The reaction mixture was partitioned between aq. $NaHCO_3$ and EtOAc (3× 20 mL). Organic extracts were pooled together, dried with anhyd. Na_2SO_4, filtered and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel to yield **2** (2.78 g, 90%) as a colorless jelly. $[a]_D^{30}$ = +58.2 (*c* = 1.41, $CHCl_3$). ^{1}H NMR: δ = 2.25 (s, 3 H), 3.32 (s, 3 H), 3.61 (s, 1 H), 3.54 (d, *J* = 9.6 Hz, 2 H), 3.67–3.75 (m, 2 H), 3.85–3.88 (m, 2 H), 4.16 (s, 1 H), 4.22–4.26 (m, 1 H), 4.57 (s, 1 H), 7.02 (d, *J* = 8.0 Hz, 2 H), 7.34 (d, *J* = 7.34 Hz, 2 H) ppm. ^{13}C NMR: δ = 20.9, 55.1, 56.1, 61.3 (CH_2), 62.6, 70.0, 71.8, 100.9, 130.0, 131.0, 133.3 (C), 136.9 (C) ppm. HRMS (ES): calcd. for $C_{14}H_{20}O_5SNa$ [M + Na]$^+$ 323.0914; found: 323.0929.

Compound 3: Compound **2** (2.53 g, 8.43 mmol) in CH_2Cl_2 (30 mL) was added to triethylamine (15 mL, 126.48 mmol) at 0 °C under N_2. After 1 h, TsCl (1.93 g, 10.12 mmol) was added and the reaction mixture was stirred for another 16 h at 0 °C. The reaction mixture was partitioned between aq. $NaHCO_3$ and CH_2Cl_2 (20 mL). Organic extracts were pooled together, dried with anhyd. Na_2SO_4, filtered and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel to yield **3** (3.29 g, 86%) as a colorless jelly. $[a]_D^{30}$ = +19.2 (*c* = 0.51, $CHCl_3$). ^{1}H NMR: δ = 2.30 (s, 3 H), 2.44 (s, 3 H), 3.48 (s, 3 H), 3.57 (t, *J* = 4.4 Hz, 1 H), 3.83–3.87 (m, 1 H), 3.99–4.03 (m, 1 H), 4.16–4.17 (m, 1 H), 4.23–4.27 (m, 1 H), 4.36 (dd, *J* = 1.6, 10.4 Hz, 1 H), 4.58 (s, 1 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 7.34 (t, *J* = 7.6 Hz, 4 H), 7.79 (d, *J* = 8.4 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.0, 21.6, 55.4, 56.7, 63.3, 68.8, 69.5 (CH_2), 71.5, 101.0, 127.9, 129.8, 130.0, 131.3, 132.3 (C), 132.8 (C), 137.5 (C), 144.9 (C) ppm. HRMS (ES): calcd. for $C_{21}H_{26}O_7S_2Na$ [M + Na]$^+$ 477.1029; found 477.1018.

Compound 4: To a cooled (0 °C) solution of **3** (3.01 g, 6.62 mmol) in anhyd. pyridine (40 mL) was added Ac_2O (1.9 mL, 26.52 mmol) in the presence of a catalytic amount of DMAP at 0 °C under N_2 and the mixture was stirred at ambient temperature for 24 h. After completion of reaction (TLC), the reaction mixture was partitioned between aq. $NaHCO_3$ and EtOAc (3× 20 mL). Organic extracts were pooled together, dried with anhyd. Na_2SO_4, filtered, and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel to yield **4** (3.35 g, 94%) as a white solid, m.p. +113 °C; $[a]_D^{30}$ = +69.9 (*c* = 0.84, $CHCl_3$). ^{1}H NMR: δ = 1.50 (s, 3 H), 2.11 (s, 3 H), 2.29 (s, 3 H), 2.43 (s, 3 H), 3.37 (s, 3 H), 3.89–3.91 (m, 1 H), 4.21 (d, *J* = 3.2 Hz, 2 H), 4.38–4.39 (m, 1 H), 4.58 (s, 1 H), 5.09 (dd, *J* = 4.4, 10.0 Hz, 1 H), 5.193 (d, *J* = 1.6 Hz, 1 H), 7.05–7.12 (m, 2 H), 7.28–7.34 (m, 4 H), 7.78 (d, *J* = 8.4 Hz, 2 H) ppm. ^{13}C NMR: δ = 20.0, 21.0 (× 2), 21.6, 48.9, 55.3, 64.9, 66.7, 68.4 (CH_2), 72.6, 98.6, 128.0, 130.0 (× 2), 132.0, 132.5 (C), 132.8 (C), 137.3 (C), 144.8 (C), 169.6 (C), 169.7 (C). HRMS (ES) calcd. for $C_{25}H_{30}O_9S_2Na$ [M + Na]$^+$ 561.1219; found 561.1229.

Compound 5: Compound **4** (2.0 g, 3.72 mmol) in dioxane (35 mL) was added to NaOH (1N, 0.75 g, 18.59 mmol) solution and the resulting solution was heated to reflux for 1 h. After completion of reaction (TLC), the reaction mixture was partitioned between aq. $NaHCO_3$ and EtOAc (3× 20 mL). Organic extracts were pooled together, dried with anhyd. Na_2SO_4, filtered, and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel to yield **5** (1.02 g, 98%) as a colorless jelly. $[a]_D^{30}$ = –66.6 (*c* = 1.33, $CHCl_3$). ^{1}H NMR: δ = 2.29 (s, 3 H), 3.29 (br. s, 1 H), 3.50 (s, 3 H), 3.63–3.67 (m, 2 H), 3.94–3.98 (m, 3 H), 4.09–4.11 (m, 1 H), 4.96 (d, *J* = 3.6 Hz, 1 H), 7.08 (d, *J* = 8 Hz, 2 H), 7.35 (d, *J* = 8 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.0, 50.8, 55.6, 64.1 (CH_2), 66.2, 68.8, 69.5, 100.0, 129.8, 131.6, 132.6 (C), 137.4 (C) ppm. HRMS (ES): calcd. for $C_{14}H_{18}O_4SNa$ [M + Na]$^+$ 305.0807; found 305.0824.

Compound 6: To a solution of **5** (2.19 g, 7.77 mmol) in MeOH (35 mL) was added MMPP (15.37 g, 31.07 mmol) and the mixture was stirred for 6 h at ambient temperature. The mixture was then filtered through Celite and the filtrates were evaporated and dissolved in EtOAc (30 mL). The organic layer was washed with satd. aq. $NaHCO_3$ (3× 30 mL) and separated, dried with anhyd.

Na_2SO_4, filtered, and the filtrate was evaporated under reduced pressure to give pure **6** in quantitative yield as a colorless jelly. $[\alpha]_D^{30}$ = –11.2 (*c* = 0.92, $CHCl_3$). ^1H NMR: δ = 2.42 (s, 3 H), 3.48 (s, 3 H), 3.51 (d, *J* = 10.4 Hz, 1 H), 3.59 (d, *J* = 6.0 Hz, 1 H), 3.94–4. (m, 4 H), 4.46 (s, 1 H), 5.00 (s, 1 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.90 (d, *J* = 8.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.6, 55.6, 63.6 (CH_2), 64.5, 64.6, 65.4, 69.6, 98.4, 128.6, 129.7, 137.3 (C), 144.7 (C) ppm. HRMS (ES): calcd. for $C_{14}H_{18}O_6SNa$ $[M + Na]^+$ 337.0703; found 337.0722.

Compound 7: To a solution of **6** (1.36 g, 4.33 mmol) in anhyd. pyridine (20 mL) was added methanesulfonyl chloride (1.35 mL, 17.33 mmol) in pyridine (5 mL) at 0 °C. The mixture was left overnight at 4 °C, then the reaction mixture was poured into satd. aq. $NaHCO_3$ (70 mL) and filtered through Celite. The filtrate was extracted with CH_2Cl_2 (3× 30 mL) and the organic extracts were collected together. The CH_2Cl_2 solution was dried with anhydrous Na_2SO_4 and filtered. Et_3N (2 mL) was added to the filtrate. The mixture was stirred for 15 min and all volatile matters were evaporated under reduced pressure. The resulting residue was purified on silica gel to afford **7** (1.23 g, 98%) as a white solid; Mp: 90 °C; $[\alpha]_D^{30}$ = +61.8 (*c* = 1.65, $CHCl_3$). ^1H NMR: δ = 2.44 (s, 3 H), 3.06 (s, 3 H), 3.21 (d, *J* = 8.8 Hz, 1 H), 3.97 (dd, *J* = 2.4, 8.8 Hz, 1 H), 4.71 (t, *J* = 2.4 Hz, 1 H), 4.74–4.76 (m, 1 H), 4.96 (d, *J* = 2.8 Hz, 1 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.42–7.44 (m, 1 H), 7.77 (d, *J* = 8.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.7, 54.6, 64.9, 65.7 (CH_2), 65.7, 99.1, 128.6, 129.7, 135.6 (C), 138.4, 143.6 (C), 144.8 (C) ppm. HRMS (ES): calcd. for $C_{14}H_{16}O_5SNa$ $[M + Na]^+$ 319.0620; found 319.0616.

Compound 8: To a solution of **7** (0.50 g, 1.69 mmol) in anhyd. THF (8 mL) was added the benzylamine (0.92 mL, 8.45 mmol) and the solution was stirred at ambient temperature for 3 h. After completion of the reaction (TLC), THF was evaporated under reduced pressure. The residue thus obtained was dissolved in EtOAc (30 mL) and the organic layer was washed with satd. aq. $NaHCO_3$ (3× 30 mL). The organic layer was separated, dried with anhyd. Na_2SO_4, filtered, and the filtrates were evaporated under reduced pressure. The residues were purified over silica gel to give **8** (0.64 g, 95%) as solid crystals, m.p. 131 °C; $[\alpha]_D^{30}$ = +8.8 (*c* = 1.38, $CHCl_3$). ^1H NMR: δ = 2.45 (s, 3 H), 3.31 (s, 1 H), 3.41 (s, 3 H), 3.58 (s, 1 H), 3.66 (d, *J* = 9.6 Hz, 1 H), 3.71 (d, *J* = 13.2 Hz, 1 H), 3.79 (d, *J* = 13.6 Hz, 1 H), 3.91 (dd, *J* = 3.2, 9.2 Hz, 1 H), 4.12–4.13 (m, 2 H), 4.94 (d, *J* = 2.8 Hz, 1 H), 7.22–7.34 (m, 7 H), 7.78 (d, *J* = 8.4 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.6, 50.1 (CH_2), 53.5, 55.4, 64.9, 65.2, 65.5, 68.1, 99.2, 127.0, 128.0, 128.3, 129.0, 129.7, 134.9 (C), 139.5 (C), 144.9 (C) ppm. HRMS (ES): calcd. for $C_{21}H_{25}O_5NSNa$ $[M + Na]^+$ 426.1330; found 426.1351.

Compound 9: To a well-stirred solution of **7** (0.50 g, 1.69 mmol) in DMF was added the sodium salt of (6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methanol (0.65 g, 3.38 mmol), and the mixture was stirred at ambient temperature for 6 h. After completion of the reaction, the mixture was partitioned between aq. $NaHCO_3$ and EtOAc (3× 20 mL), organic extracts were pooled together, dried with anhyd. Na_2SO_4, filtered and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel (EtOAc/petroleum ether) to give **9** (0.72 g, 87%) as a colorless jelly. $[\alpha]_D^{30}$ = –7.0 (c 1.33, $CHCl_3$). ^1H NMR: δ = 1.26 (s, 3 H), 1.43 (s, 3 H), 2.41 (s, 3 H), 3.26 (s, 3 H), 3.37 (s, 3 H), 3.42 (d, *J* = 7.0 Hz, 2 H), 3.64–3.69 (m, 2 H), 3.93 (dd, *J* = 3.2, 9.8 Hz, 1 H), 3.99–4.02 (m, 1 H), 4.06–4.13 (m, 3 H), 4.53 (q, *J* = 6.0, 16.6 Hz, 2 H), 4.89 (s, 1 H), 4.92 (d, *J* = 2.8 Hz, 1 H), 7.33 (d, *J* = 8.2 Hz, 2 H), 7.79 (d, *J* = 8.2 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.6, 24.9, 26.4, 54.8, 54.9, 64.6, 65.0 (CH_2), 65.3, 66.8, 69.3 (CH_2), 73.3, 81.0, 84.7, 85.0, 98.7, 109.4, 112.2 (C), 128.8, 130.0, 134.8 (C), 145.1 (C) ppm. HRMS (ES): calcd. for $C_{23}H_{32}O_{10}SNa$ $[M + Na]^+$ 523.1603; found 523.1614.

General Procedure for the Synthesis of 10a–g from 7: To a suspension of *t*BuOK (1.2 equiv) in anhyd. THF (2 mL) at ambient temperature was added β-dicarbonyl compound (1.6 equiv) and the resulting solution was stirred for 30 min under nitrogen. A solution of sugar derived vinyl sulfone **7** (1 equiv) in anhyd. THF (1 mL) was added dropwise to the reaction mixture and the resulting solution was then stirred for 6–30 h. After completion of the reaction (TLC), the reaction mixture was evaporated under reduced pressure. The crude mass obtained was dissolved in EtOAc and the organic layer was washed with satd. aq. $NaHCO_3$ and separated. The organic layer was dried with anhyd. Na_2SO_4, filtered and the filtrate was evaporated under reduced pressure to give a crude mass. The resulting residue was purified by column chromatography over silica gel (EtOAc/petroleum ether) to give the product. Compound **7** was treated with methanesulfonylacetone in a similar fashion.

Compound 10a: Following the general procedure, acetylacetone (0.22 mL, 2.16 mmol) was treated with **7** (0.40 g, 1.35 mmol) in the presence of *t*BuOK (0.18 g, 1.62 mmol) for 24 h to give **10a** (0.51 g, 95%) as white crystalline solid, m.p. 116 °C; $[\alpha]_D^{30}$ = +148.9 (*c* = 2.16, $CHCl_3$). ^1H NMR: δ = 2.22 (s, 3 H), 2.26 (s, 3 H), 2.41 (s, 3 H), 3.09–3.15 (m, 1 H), 3.39 (s, 3 H), 3.49 (d, *J* = 3.6 Hz, 1 H), 3.62 (d, *J* = 9.6 Hz, 1 H), 3.74 (s, 1 H), 3.79 (dd, *J* = 3.6, 9.6 Hz, 1 H), 3.93 (s, 1 H), 4.13 (d, *J* = 9.6 Hz, 1 H), 4.83 (d, *J* = 2.8 Hz, 1 H), 7.32 (d, *J* = 7.6 Hz, 2 H), 7.77 (d, *J* = 8.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.6, 28.4, 31.8, 35.9, 55.2, 60.6, 65.0, 66.8× 2, 66.9 (CH_2), 69.9, 99.3, 129.4, 129.8, 133.5 (C), 145.3 (C), 202.5 (C), 204.1 (C). HRMS (ES): calcd. for $C_{19}H_{24}O_7SNa$ $[M + Na]^+$ 419.1119; found 419.1140.

Compound 10b: Following the general procedure, methyl acetoacetate (0.15 mL, 1.35 mmol) was treated with **7** (0.25 g, 0.85 mmol) in the presence of *t*BuOK (0.11 g, 1.01 mmol) for 26 h to give a mixture of inseparable diastereomers **10b** (0.33 g, 95%). The mixture was taken directly for the next step.

Compound 10c: Following the general procedure, ethyl acetoacetate (0.10 mL, 1.08 mmol) was treated with **7** (0.20 g, 0.68 mmol) in the presence of *t*BuOK (0.19 g, 0.81 mmol) for 30 h to give a mixture of inseparable diastereomers **10c** (0.27 g, 92%). The mixture was taken directly for the next step.

Compound 10d: Following the general procedure, methylsulfonylacetone (0.22 g, 1.62 mmol) was treated with **7** (0.30 g, 1.01 mmol) in the presence of *t*BuOK (0.14 g, 1.22 mmol) for 9 h to give a colorless solid mixture of inseparable diastereomers **10d** (0.37 g, 85%). The mixture was taken directly for the next step.

Compound 10e: Following the general procedure, 1-benzoylacetone (0.31 g, 1.89 mmol) was treated with **7** (0.35 g, 1.18 mmol) in the presence of *t*BuOK (0.16 g, 1.42 mmol) for 6 h to give a white crystalline solid **10e** (0.53 g, 90%) as a mixture of separable diastereomers with distinct R_f values. The diastereomers were separated. *Faster moving diastereomer*: M.p. 142 °C; $[\alpha]_D^{30}$ = +94.1 (*c* = 1.60, $CHCl_3$). ^1H NMR: δ = 2.19 (s, 3 H), 2.45 (s, 3 H), 3.32 (s, 3 H), 3.39–3.43 (m, 1 H), 3.70–3.77 (m, 3 H), 3.83 (dd, *J* = 3.2, 9.2 Hz, 1 H), 4.03 (s, 1 H), 4.81 (d, *J* = 2.8 Hz, 1 H), 4.98 (d, *J* = 10.0 Hz, 1 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 7.48–7.52 (m, 2 H), 7.60–7.63 (m, 1 H), 7.84 (d, *J* = 8.0 Hz, 2 H), 8.02 (d, *J* = 7.2 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.7,28.1, 36.0, 55.1, 59.9, 64.4, 65.0, 66.9 (CH_2), 67.0, 99.2, 128.6, 129.0, 129.4, 129.8, 133.6 (C), 134.2, 136.6 (C), 145.3 (C), 195.9 (C), 203.3 (C) ppm. HRMS (ES): calcd. for $C_{24}H_{26}O_7SNa$ $[M + Na]^+$ 481.1285; found 481.1297. *Slower moving*

diastereomer: M.p. 139 °C; $[\alpha]_D^{30}$ = +42.93 (*c* = 0.909, $CHCl_3$). ^1H NMR: δ = 2.15 (s, 3 H), 2.40 (s, 3 H), 3.17–3.21 (m, 1 H), 3.53 (s, 1 H), 3.54 (s, 3 H), 3.60 (d, *J* = 9.6 Hz, 1 H), 3.87 (dd, *J* = 3.2, 9.2 Hz, 1 H), 4.19–4.20 (m, 2 H), 5.00 (d, *J* = 2.8 Hz, 1 H), 5.07 (d, *J* = 8.8 Hz, 1 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.46–7.50 (m, 2 H), 7.61–7.66 (m, 3 H), 7.88 (d, *J* = 7.6 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.6, 30.6, 37.9, 55.4, 61.2, 61.5, 67.0 (CH_2), 67.3, 99.6, 128.8, 129.0, 129.5× 2, 134.1, 134.2 (C), 136.6 (C), 144.9 (C), 194.2 (C), 201.5 (C). HRMS (ES): calcd. for $C_{24}H_{26}O_7SNa$ $[M + Na]^+$ 481.1285; found 481.1297.

Compound 10f: Following the general procedure, 1,3-cyclohexanedione (0.15 g, 1.35 mmol) was treated with **7** (0.25 g, 0.85 mmol) in the presence of *t*BuOK (0.11 g,1.01 mmol) for 22 h to give **10f** (0.32 g, 93%) as a white glassy crystalline solid, m.p. 162 °C; $[\alpha]_D^{30}$ = +78.6 (*c* = 1.16, $CHCl_3$). ^1H NMR: δ = 1.75–1.78 (m, 1 H), 2.09–2.35 (m, 4 H), 2.39 (s, 3 H), 3.55 (s, 3 H), 3.65 (d, *J* = 9.2 Hz, 2 H), 3.85–3.88 (m, 2 H), 4.06 (d, *J* = 8.4 Hz, 1 H), 4.52 (s, 1 H), 5.18 (d, *J* = 1.2 Hz, 1 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 7.77 (d, *J* = 8.4 Hz, 2 H), 9.33 (s, 1 H) ppm. ^{13}C NMR: δ = 19.6 (CH_2), 21.6, 29.9 (CH_2), 32.4, 36.0 (CH_2), 57.0, 61.7, 66.3, 68.6 (CH_2), 73.0, 101.4, 114.0 (C), 129.2, 129.7, 134.7 (C), 144.7 (C), 173.6 (C), 196.9 (C) ppm. HRMS (ES): calcd. for $C_{20}H_{24}O_7SNa$ $[M + Na]^+$ 431.1124; found 431.1140.

Compound 10g: Following the general procedure, dimedone (0.30 g, 2.16 mmol) was treated with **7** (0.40 g, 1.35 mmol) in the presence of *t*BuOK (0.18 g, 1.62 mmol) for 20 h to give **10g** (0.21 g, 96%) as a white crystalline solid, m.p. 74 °C; $[\alpha]_D^{30}$ = +24.0 (*c* = 0.95, $CHCl_3$). ^1H NMR: δ = 0.95 (s, 3 H), 1.02 (s, 3 H), 2.17 (d, *J* = 2.4 Hz, 2 H), 2.25 (d, *J* = 17.6 Hz, 1 H), 2.35 (d, *J* = 17.6 Hz, 1 H), 2.41 (s, 3 H), 3.43 (d, *J* = 9.2 Hz, 1 H), 3.57 (s, 3 H), 3.75 (d, *J* = 8.4 Hz, 1 H), 3.82 (d, *J* = 12 Hz, 2 H), 4.03 (d, *J* = 8.4 Hz, 1 H), 4.47 (s, 1 H), 5.16 (d, *J* = 1.6 Hz, 1 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 7.89 (d, *J* = 8.4 Hz, 2 H), 9.35 (s, 1 H) ppm. ^{13}C NMR: δ = 21.6, 26.8, 29.2, 31.0, 32.3, 43.7 (CH_2), 49.9 (CH_2), 57.0, 62.2, 66.8, 68.6 (CH_2), 73.0, 101.5, 113.1 (C), 129.3, 130.2, 134.2 (C), 144.8 (C), 172.0 (C), 196.9 (C) ppm. HRMS (ES): calcd. for $C_{22}H_{29}O_7S$ $[M + H]^+$ 437.1626; found 437.1634.

Compound 10h: Following the general procedure, nitromethane (0.12 mL, 2.16 mmol) was treated with **7** (0.40 g, 1.35 mmol) in the presence of *t*BuOK (0.18 g, 1.62 mmol) for 4 h to give **10h** (0.44 g, 92%) as a white crystalline solid, m.p. 128 °C; $[\alpha]_D^{30}$ = +11.9 (*c* = 1.47, $CHCl_3$). ^1H NMR: δ = 2.45 (s, 3 H), 3.10–3.14 (m, 1 H), 3.28–3.29 (m, 1 H), 3.41 (s, 3 H), 3.58 (d, *J* = 9.6 Hz, 1 H), 3.89 (dd, *J* = 3.2, 9.6 Hz, 1 H), 4.01 (s, 1 H), 4.10 (s, 1 H), 4.25 (dd, *J* = 4.0, 13.6 Hz, 1 H), 4.68–4.74 (m, 1 H), 4.94 (d, *J* = 2.8 Hz, 1 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.83 (d, *J* = 8.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.7, 35.4, 55.4, 59.6, 64.5, 65.9, 66.5 (CH_2), 74.8 (CH_2), 99.0, 129.2, 130.1, 133.6 (C), 145.7 (C) ppm. HRMS (ES): calcd. for $C_{15}H_{19}NO_7SNa$ $[M + Na]^+$ 380.0800; found 380.0780.

Compound 10i: Following the general procedure, malononitrile (0.14 mL, 2.16 mmol) was treated with **7** (0.40 g, 1.35 mmol) in the presence of *t*BuOK (0.18 g, 1.62 mmol) for 1.5 h to give **10i** (0.46 g, 95%) as a white crystalline solid compound, m.p. 135 °C; $[\alpha]_D^{30}$ = +16.9 (*c* = 10.27, $CHCl_3$). ^1H NMR: δ = 2.45 (s, 3 H), 3.02–3.06 (m, 1 H), 3.42 (s, 3 H), 3.52–3.53 (m, 1 H), 3.91 (d, *J* = 9.6 Hz, 1 H), 4.00 (dd, *J* = 3.2, 10.0 Hz, 1 H), 4.09–4.10 (m, 1 H), 4.25 (s, 1 H), 4.40 (d, *J* = 10.0 Hz, 1 H), 4.97 (d, *J* = 2.8 Hz, 1 H), 7.39 (d, *J* = 8.0 Hz, 2 H), 7.85 (d, *J* = 8.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.8, 24.8, 38.2, 56.1, 60.1, 64.3, 65.8 (CH_2), 66.1, 99.3, 110.7 (C), 111.1 (C), 130.0, 130.1, 133.5 (C), 146.2 (C) ppm. HRMS (ES): calcd. for $C_{17}H_{19}N_2O_5S$ $[M + H]^+$ 363.1006; found 363.1014.

Compound 10j: Following the general procedure, dimethyl malonate (0.25 mL, 2.16 mmol) was treated with **7** (0.40 g, 1.35 mmol) in the presence of *t*BuOK (0.18 g, 1.62 mmol) for 3 h to give **10j** (0.54 g, 93%) as a white crystalline solid, m.p. 98 °C; $[\alpha]_D^{30}$ = +25.7 (*c* = 1.23, $CHCl_3$). ^1H NMR: δ = 2.43 (s, 3 H), 2.98–3.06 (m, 1 H), 3.47 (s, 3 H), 3.50 (d, *J* = 9.6 Hz, 1 H), 3.75 (s, 3 H), 3.78 (s, 3 H), 3.80–3.88 (m, 4 H), 4.09–4.11 (m, 1 H), 4.86 (d, *J* = 3.0 Hz, 1 H), 7.39 (d, *J* = 8.0 Hz, 2 H), 7.82 (d, *J* = 8.2 Hz, 2 H) ppm. ^{13}C NMR: δ = 21.7, 36.4, 52.5, 52.7, 53.2, 55.3, 60.0, 65.3, 66.8 (CH_2), 67.2, 99.3, 129.7, 129.8, 133.9 (C), 145.2 (C), 168.0 (C), 168.2 (C) ppm. HRMS (ES): calcd. for $C_{19}H_{24}O_9SNa$ $[M + Na]^+$ 451.1045; found 451.1039.

General Procedure for the Conversion of 10a–g into 11a–g: Compounds **10a**–**g** were treated with TFA (2 equiv) for 3–28 h at ambient temperature. After completion of the reaction (TLC), the reaction mixture was poured into satd. aq. $NaHCO_3$ (30 mL), then partitioned between aq. $NaHCO_3$ and EtOAc (3× 20 mL). Organic extracts were pooled, dried with anhyd. Na_2SO_4 and filtered. The filtrate was stirred for 0.5 h with Et_3N and the mixture was evaporated to dryness under reduced pressure. The resulting residue was purified by column chromatography over silica gel to give the pure product.

Compound 11a: Following the general procedure, in 3 h, **10a** (0.30 g, 0.75 mmol) was converted into **11a** (0.13 g, 80%) as a colorless jelly. $[\alpha]_D^{30}$ = +25.4 (*c* = 1.27, $CHCl_3$). ^1H NMR: δ = 2.24 (s, 3 H), 2.32 (s, 3 H), 3.95–4.00 (m, 2 H), 4.42 (dd, *J* = 2.4, 12.8 Hz, 1 H), 4.88–4.92 (m, 1 H), 6.23 (d, *J* = 3.6 Hz, 1 H), 9.12 (s, 1 H) ppm. ^{13}C NMR: δ = 15.7, 29.2, 38.7 (CH), 65.1 (CH_2), 79.3 (CH), 117.6 (C), 123.3 (CH), 152.2 (C), 168.1 (C), 186.6 (CH), 193.1 (C) ppm. HRMS (ES): calcd. for $C_{11}H_{13}O_4$ $[M + H]^+$ 209.0794; found 209.0814.

Compound 11b: Following the general procedure, in 16 h, compound **10b** (0.16 g, 0.40 mmol) was converted into a **11b** (0.06 g, 71%) as a colorless jelly. $[\alpha]_D^{30}$ = +20.9 (*c* = 0.47, $CHCl_3$). ^1H NMR: δ = 2.19 (s, 3 H), 3.78 (s, 3 H), 3.88–3.90 (m, 1 H), 3.99 (d, *J* = 3.2 Hz, 1 H), 4.39 (dd, *J* = 2.4, 12.8 Hz, 1 H), 4.93–4.95 (m, 1 H), 6.20 (d, *J* = 3.6 Hz, 1 H), 9.17 (s, 1 H) ppm. ^{13}C NMR: δ = 14.3, 38.0, 51.2, 65.1 (CH_2), 79.2, 105.3 (C), 122.8, 152.2 (C), 165.4 (C), 169.4 (C), 186.5 ppm. HRMS (ES): calcd. for $C_{11}H_{13}O_5$ $[M + H]^+$ 225.0770; found 225.0763.

Compound 11c: Following the general procedure, in 20 h, compound **10c** (0.16 g, 0.40 mmol) was converted into **11c** (0.06 g, 75%) as a colorless jelly. $[\alpha]_D^{30}$ = –11.3 (*c* = 2.53, $CHCl_3$). ^1H NMR: δ = 1.16–1.30 (m, 3 H), 2.14 (d, *J* = 1.2 Hz, 3 H), 3.82–3.91 (m, 2 H), 4.08–4.22 (m, 2 H), 4.33 (dd, *J* = 2.8, 12.6 Hz, 1 H), 4.85–4.92 (m, 1 H), 6.15 (dd, *J* = 0.6, 3.8 Hz, 1 H), 9.11 (s, 1 H) ppm. ^{13}C NMR: δ = 14.5× 2, 38.2, 60.1 (CH_2), 65.3 (CH_2), 79.3, 105.7 (C), 122.9, 152.4 (C), 165.2 (C), 169.2 (C), 186.5. HRMS (ES): calcd. for $C_{12}H_{14}O_4Na$ $[M + Na]^+$ 245.0793; found 245.0789.

Compound 11d: Following the general procedure, in 9 h, compound **10d** (0.15 g, 0.35 mmol) was converted into **11d** (0.06 g, 85%) as a colorless jelly. $[\alpha]_D^{30}$ = +18.6 (*c* = 0.64, $CHCl_3$). ^1H NMR: δ = 2.19 (d, *J* = 0.4 Hz, 3 H), 3.02 (s, 3 H), 4.00–4.04 (m, 2 H), 4.41 (dd, *J* = 2.8, 12.8 Hz, 2 H), 5.00–5.03 (m, 1 H), 6.24 (d, *J* = 3.6 Hz, 1 H), 9.21 (s, 1 H) ppm. ^{13}C NMR: δ = 13.5, 38.7, 45.2, 64.8 (CH_2), 79.5, 112.7 (C), 120.5, 152.7 (C), 168.3 (C), 186.1 ppm. HRMS (ES): calcd. for $C_{10}H_{12}O_5SNa$ $[M + Na]^+$ 267.0301; found 267.0303.

Compound 11e: Following the general procedure, in 28 h, compound **10e** (0.24 g, 0.51 mmol) was converted into **11e** (0.11 g, 76%) as a colorless jelly. $[\alpha]_D^{30}$ = +17.5 (*c* = 1.26, $CHCl_3$). ^1H NMR: δ = 1.70 (s, 3 H), 4.05 (d, *J* = 12.4 Hz, 1 H), 4.16 (d, *J* = 8.4 Hz, 1

H), 4.41–4.44 (m, 1 H), 4.99 (d, J = 8.8 Hz, 1 H), 6.41 (d, J = 3.6 Hz, 1 H), 7.42–7.61 (m, 5 H), 9.20 (s, 1 H) ppm. ^{13}C NMR: δ = 15.8, 39.7, 64.9 (CH_2), 78.8, 116.1 (C), 123.3, 127.9, 128.4, 131.5, 140.1 (C), 152.1 (C), 169.0 (C), 186.5, 192.8 (C) ppm. HRMS (ES): calcd. for $C_{16}H_{15}O_4$ $[M + H]^+$ 271.0966; found 271.0970.

Compound 11f: Following the general procedure, in 20 h, compound **10f** (0.24 g, 0.59 mmol) was converted into **11f** (0.09 g, 75%) as a colorless jelly. $[\alpha]_D^{30}$ = +168.4 (c = 0.93, $CHCl_3$). ^{1}H NMR: δ = 1.93–2.06 (m, 2 H), 2.27–2.45 (m, 4 H), 3.89–4.02 (m, 2 H), 4.33–4.42 (m, 1 H), 5.03–5.09 (m, 1 H), 6.22–6.25 (m, 1 H), 9.09 (d, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR: δ = 21.4 (CH_2), 23.8 (CH_2), 35.2, 36.4 (CH_2), 65.4 (CH_2), 87.2, 115.9 (C), 122.9, 152.4 (C), 178.1 (C), 186.3, 195.0 (C) ppm. HRMS (ES): calcd. for $C_{12}H_{13}O_4$ $[M + H]^+$ 221.0803; found 221.0814.

Compound 11g: Following the general procedure, in 24 h, compound **10g** (0.30 g, 0.69 mmol) was converted into **11g** (0.13 g, 77%) as a white solid. $[\alpha]_D^{30}$ = +175.5 (c = 1.02, $CHCl_3$). ^{1}H NMR: δ = 1.05 (s, 3 H), 1.12 (s, 3 H), 2.24 (d, J = 4.2 Hz, 2 H), 2.32 (d, J = 1.2 Hz, 2 H), 3.93–4.07 (m, 2 H), 4.42 (dd, J = 2.8, 12.6 Hz, 1 H), 5.08–5.15 (m, 1 H), 6.29 (d, J = 4.0 Hz, 1 H), 9.14 (s, 1 H) ppm. ^{13}C NMR: δ = 28.1, 28.8, 34.2 (C), 35.2, 37.6 (CH_2), 50.9 (CH_2), 65.4 (CH_2), 82.2, 114.2 (C), 122.6, 152.4 (C), 176.8 (C), 186.2, 194.2 (C) ppm. HRMS (ES): calcd. for $C_{14}H_{17}O_4$ $[M + H]^+$ 249.1131; found 249.1127.

One-Pot Synthesis of 11a: To a suspension of *t*BuOK (0.042 g, 0.37 mmol) in anhyd. THF (0.5 mL) at ambient temperature was added acetylacetone (0.05 mL, 0.473 mmol) and the resulting solution was stirred for 30 min under nitrogen. A solution of **7** (0.10 g, 0.34 mmol) in anhyd. THF (0.5 mL) was added dropwise to the reaction mixture. The resulting solution was then stirred for 24 h at ambient temperature. After completion of the reaction (TLC), a mixture of TFA and TfOH (3:1 ratio, 0.10 mL/mmol) was added and the mixture was stirred for another 3 h. Upon completion of the reaction (TLC), the reaction mixture was poured into satd. aq. $NaHCO_3$ (30 mL), and partitioned between aq. $NaHCO_3$ and EtOAc (3 × 20 mL). Organic extracts were pooled together, dried with anhyd. Na_2SO_4, filtered, and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel (EtOAc/petroleum ether) to obtain **11a** (0.05 g, 71%).

Compound 15: A well-stirred solution of **10a** in Ac_2O (1 mL) was treated with TfOH (0.075 mL, 0.51 mmol) at ambient temperature for 2 h. Upon completion of reaction, satd. aq. $NaHCO_3$ (30 mL) was added carefully and the mixture was partitioned between aq. $NaHCO_3$ and EtOAc (3 × 10 mL). Organic layers were pooled together, dried with anhyd. Na_2SO_4, filtered, and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel to afford **15** (0.06 g, 51%) as a white crystalline solid, m.p. 158 °C; $[\alpha]_D^{30}$ = +45.9 (c = 1.16, $CHCl_3$). ^{1}H NMR: δ = 1.96 (s, 3 H), 2.04 (s, 3 H), 2.21 (s, 3 H), 2.27 (s, 3 H), 2.46 (s, 3 H), 3.94 (d, J = 13.2 Hz, 1 H), 4.03–4.13 (m, 2 H), 4.28 (d, J = 2.4 Hz, 1 H), 4.64–4.66 (m, 1 H), 4.81 (d, J = 11.2 Hz, 1 H), 6.68 (d, J = 5.6 Hz, 1 H), 7.41 (d, J = 8.0 Hz, 1 H), 7.84 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 15.9, 20.5, 20.7, 21.8, 29.5, 37.9, 55.1, 67.0 (CH_2), 70.6, 77.3, 87.7, 113.0 (C), 129.0, 130.0, 134.6 (C), 145.3 (C), 168.2 (C), 168.4 (C), 170.2 (C), 193.1 (C) ppm. HRMS (ES): calcd. for $C_{22}H_{26}O_9SNa$ $[M + Na]^+$ 489.1223; found 489. 1190.

CCDC-936542 (for **8**), -936543 (for **10j**), and -891087 (for **15**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of all new compounds, quantum chemical calculation details, tables of atom coordinates and absolute energies and Figures S1–S3.

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