

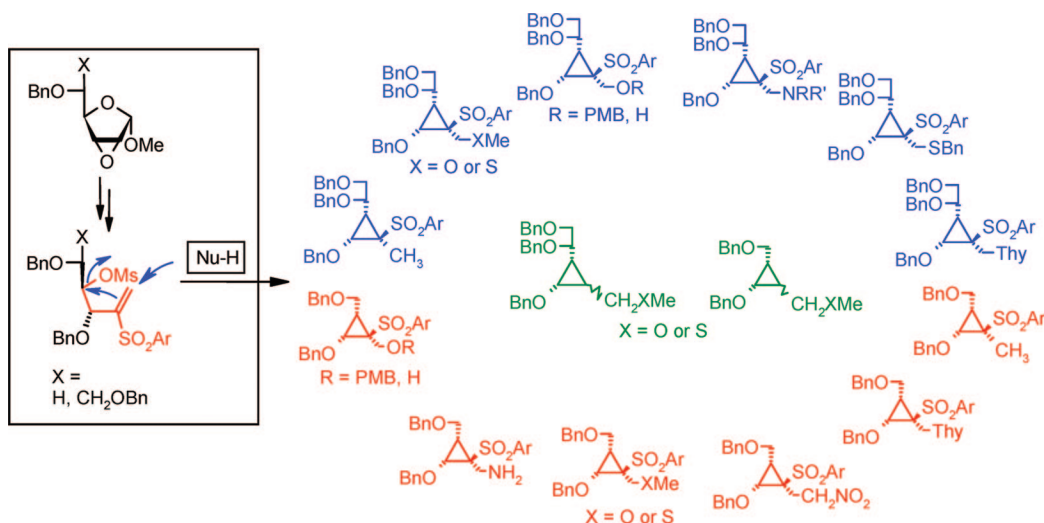
A Diastereoselective Unique Route to Cyclopropanes Functionalized at All Three Ring Carbon Atoms from Acyclic Vinyl Sulfone-Modified Carbohydrates[†]

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In a departure from the current trend of using metal-catalyzed routes to cyclopropanation, pentosyl and hexosyl vinyl sulfone-modified carbohydrates having the terminal double bond and a suitably positioned leaving group are reacted in a stereoselective fashion with a series of nucleophiles to yield a myriad of cyclopropanes substituted at all three ring carbon atoms.

Introduction

Chemists have long been fascinated by the cyclopropane subunit because of its presence in a wide range of natural products as well as the usefulness of this strained cycloalkane in other areas of research.¹ While unactivated cyclopropanes have been directly utilized to a limited extent in chemical synthesis, activated cyclopropanes, such as cyclopropanes substituted with electron withdrawing or electron donating groups, have been used extensively as precursors in several chemical syntheses.^{1c,2} Moreover, cyclopropanes having donor and acceptor groups on vicinal carbons have been identified as

useful synthetic building blocks because of the presence of “push–pull” effects^{1d,2r} imparted by these functional groups. Complex chiral cyclopropanes, especially those having stereo-centers at all three ring carbon atoms, are reported to be of great interest.³

Although transition metal-mediated synthesis of cyclopropanes has emerged as a general and popular route in recent times,⁴ one of the most important advances in cyclopropane chemistry over the past decade has also taken place in the area of integrating cyclopropanes and carbohydrates.^{1c,5} The incorporation of cyclopropanes into a carbohydrate provides an interesting mixture of strained and reactive cyclopropanes combined with the well-defined stereochemistry inherent in carbohydrates.^{1c,5} Although there are several reports on the synthesis of cyclopropane rings on furanosyl⁶ and pyranosyl carbohydrates,⁷ construction of cyclopropanes on acyclic sugars is virtually unknown. In our search for an efficient nonmetal-based route for cyclopropanation, we opined that a suitably

[†] Dedicated to Professor Jyoti Chattopadhyaya on occasion of his 60th birthday.

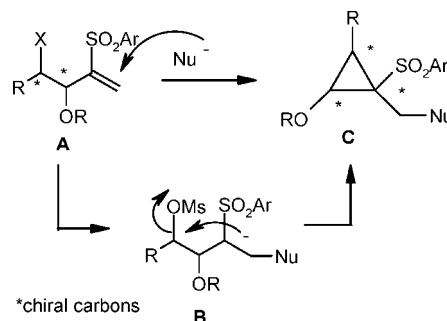
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constructed vinyl sulfone group on an open-chain carbohydrate having a leaving group at the proximity would generate a chirally pure cyclopropane. Although cyclopropanes were synthesized from 3-halo-1-alkenyl sulfones three decades back,^{8d} the strategy stagnated over the years for the nonavailability of straightforward and general methodologies for the synthesis of acyclic vinyl sulfones, especially chirally substituted acyclic vinyl sulfones.^{8a-c} We argued that 1-alkenyl sulfones having leaving groups at the 4-positions, such as **A**, may be derived from carbohydrates. An attack of a nucleophile to such a vinyl sulfone would generate the negative charge on the sulfone to generate **B** and a concomitant attack to the carbon bearing a leaving group would generate the cyclopropane **C** (Scheme 1). The application of this strategy would, however, crucially depend on the availability of appropriate starting materials.

Results and Discussion

There are scant reports on the synthesis of acyclic vinyl sulfone-modified carbohydrates.⁹ In the recent past, several dihydroxylated acyclic vinyl-sulfones, which could be considered as derivatives of pentoses, have been used in the synthesis of diverse groups of heterocyclic and carbocyclic compounds; the synthesis of these vinyl sulfones, however, originated from noncarbohydrate precursors.^{9,10} In an attempt to develop a general strategy for the synthesis of acyclic vinyl sulfone-modified carbohydrates, Suarez and co-workers reacted the derivatives of 3-acetyl-D-glycals with sodium benzenesulfinate in acid medium catalyzed by HgSO₄ to afford diastereoisomeric mixtures of the corresponding 2,3-dideoxy-3-(phenylsulfonyl)-

SCHEME 1. General Strategy for the Synthesis of Cyclopropanes Substituted at All Ring Carbon Atoms



hexopyranoses through a Ferrier rearrangement. The anomeric alkoxy radical fragmentation of these γ -hydroxy sulfones using the system (diacetoxyiodo)benzene and iodine gave vinyl sulfones with structures of 1,2-dideoxy-4-*O*-formyl-2-(phenylsulfonyl)-pent-1-enitol and configurations D-erythro, L-erythro, and D-threo at the two stereogenic centers.¹¹ Although this strategy does provide a route to a new class of acyclic vinyl sulfone-modified carbohydrates, the loss of the one (anomeric) carbon in the process leading to the formation of five-carbon systems from hexoses severely restricts its application. We opined that the best strategy for the synthesis of acyclic vinyl sulfone-modified carbohydrates would be to design a carbohydrate-based route without shortening the chain length.¹¹ This route would provide access to both five-carbon and six-carbon acyclic vinyl sulfone-modified carbohydrates depending on the structure of the starting carbohydrates.

For the synthesis of the starting material, it was necessary to incorporate the thiol group as well as other protecting groups strategically to afford the correct starting material for the cyclopropanation reaction. Thus, our synthesis of the pentose-based acyclic vinyl sulfone-modified carbohydrates started from the easily accessible epoxide **1**,¹² which was regioselectively opened at C2 with thiocresol to provide **2**. The free hydroxyl group of **2** was benzyl protected to afford **3** and the furanosyl ring of **3** was cleaved under acidic conditions. The product thus generated was reduced to the corresponding diol **4**, which was oxidized to the sulfone **5**. Mesylation of **5** and concomitant elimination of methanesulfonic acid under basic conditions afforded the required vinyl sulfone **6** in good overall yield (Scheme 2). For the synthesis of the higher homologue of **6**, the hexofuranosyl epoxide **7**¹² was treated with thiocresol to afford **8** in a regioselective fashion. Compound **8** was converted to the vinyl sulfone **12** via intermediates **9–11** in good overall yield following the route described for **6** (Scheme 2).

Phthalimide reacted with vinyl sulfone **6** in the presence of NaH to afford the cyclopropane **13** (Table 1; entry 1), which was easily deprotected to generate the amino methyl cyclopropane **14** (Table 1; entry 1). The nucleophilic oxygen derived from MeOH/Na and *p*-methoxybenzyl alcohol (PMBOH)/NaH added efficiently to **6** to afford the cyclopropanes **15** (Table 1; entry 2) and **16** (Table 1; entry 3), respectively. Compound **16** was demasked to generate the free alcohol **17** (Table 1; entry 3). NaSMe reacted in a similar fashion to yield the thiomethyl derivative **18** (Table 1; entry 4). The carbon nucleophile generated from CH₃NO₂/NaH also reacted efficiently with **6** to

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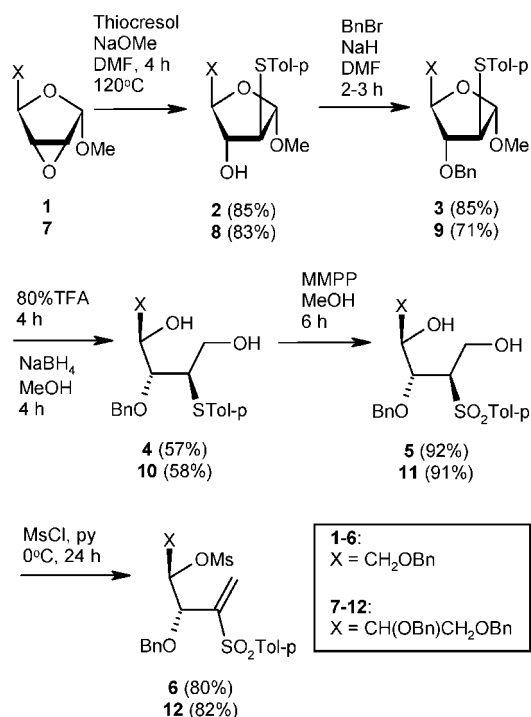
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SCHEME 2. Synthesis of Pentosyl and Hexosyl Acyclic Vinyl Sulfones



generate the nitro cyclopropane **19** (Table 1; entry 5). Interestingly a nucleobase thymine also efficiently added to **6** in a Michael fashion but did not undergo (¹H NMR) concomitant cyclization. Therefore, the intermediate still retaining the mesyl group was treated with NaH to afford the cyclopropane **20** (Table 1; entry 6). On reactions with **6**, NaBH₄ in MeOH generated a mixture of products which were converted to a single compound **21** (Table 1; entry 7) with NaH. The hexosyl vinyl sulfone **12** also reacted with nucleophiles generated from phthalimide, NaOMe, *p*-methoxybenzyl alcohol, NaSMe, BnSH, thymine, and NaBH₄/MeOH to afford cyclopropanes **22–29**, respectively (Table 2; entries 1–6, respectively).

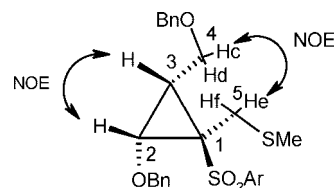
To establish the stereochemistry of the carbon bearing the sulfone group, a representative compound **18** was subjected to NOE experiments. The *cis* relationship between the H-2 and H-3 in compound **18** was deduced from the ¹H NMR parameters. The NOE interactions between H-2/H-3 as well as between H-4/H-5 confirm that H-3 and the sulfonyl group are in a *cis* relationship and the sulfonyl group is in a *trans* relationship with (C₃–C₄) and (C₂–OBn) (Figure 1).¹³ In the ¹H NMR spectra of all cyclopropanes, the H-3 protons appeared within a specific range (δ 2.25–2.50). Possibly the steric interactions between the bulky ArO₂S, R, and OR groups (Scheme 1) determine the diastereoselectivity of ring formation. Compounds **15** and **23** were desulfonylated by using 6% Na–Hg to afford a mixture of isomers **30** and **32**, respectively, in moderate yields (Table 3) whereas **18** and **26** were resistant to desulfonylation under similar reaction conditions. Compounds **18** and **26**, however, were desulfonylated in moderate yields with LAH to afford **31** and **33**, respectively (Table 3).

In conclusion, we have described an alternative and powerful general strategy for the synthesis of a new class of polysubsti-

TABLE 1. Cyclopropanes from Pentosyl Acyclic Vinyl Sulfone **6**

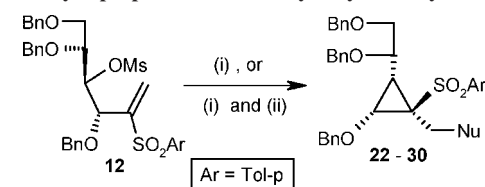
Entry	Products	Conditions
1	13 Y = phthalimido 14 Y = NH ₂	(i) phthalimide, NaH, DMF, 50 °C, 8 h, 58%. (ii) NH ₂ NH ₂ , H ₂ O, EtOH, reflux, 6 h, 70%.
2	15	(i) NaOMe, MeOH, rt, 5–6 h, 57%.
3	16 R ₁ = PMB 17 R ₁ = H	(i) PMBOH, NaH, DMF, rt, 6–8 h, 58%. (iv) DDQ, DCM, H ₂ O, rt, 18 h, 74%.
4	18	(i) NaSMe, DMF, rt, 1 h, 58%.
5	19	(i) CH ₃ NO ₂ , NaH, DMF, rt, 3 h, 47%.
6	20 T = thymynyl	(i) thymine, TMG, DMF, rt, 5 h. (ii) NaH, DMF, rt, 1 h, 48%.
7	21	(i) NaBH ₄ , MeOH, rt, 12 h. (ii) NaH, DMF, rt, 1 h, 50%.

tuted and optically pure cyclopropanes without using metal catalysts. Depending on the nucleophiles used, the end product is a wide range of α -substituted cyclopropanols having functional groups at all three ring carbon atoms. These compounds also belong to a special class of long-sought but difficult-to-obtain cyclopropanes attached to vicinal donor (–OR) and acceptor (–SO₂Ar) groups.¹⁴ It should be noted that during the past decade serious attempts have been made by several groups to synthesize cyclopropanes functionalized with sulfones.^{2r,15} Our expedient and general strategy enriches the arsenal available to synthetic organic chemists interested in this class of compounds. Research is in progress to expand the scope of this

FIGURE 1. NOE interactions of compound **18**.

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TABLE 2. Cyclopropanes from Hexosyl Acyclic Vinyl Sulfone 12



Entry	Products	Conditions
1	22 Y = phthalimido	(i) Phthalimide, NaH, DMF, 50 °C, 8 h, 52%.
2	23	(i) NaOMe, MeOH, rt, 5-6 h, 46%.
3	24 R ₁ = PMB 25 R ₁ = H	(i) PMBOH, NaH, DMF, rt, 6-8 h, 57%. (iv) DDQ, DCM, H ₂ O, rt, 18 h, 71%.
4	26 R ₂ = Me 27 R ₂ = Bn	For 26 (i) NaSMc, DMF, rt, 1 h, 56%. For 27 (i) BnSH, NaH, DMF, rt, 2-3 h, 49%.
5	28 R = thymynyl	(i) thymine, TMG, DMF, rt, 5 h. (ii) NaH, DMF, rt, 1 h, 46%.
6	29	(i) NaBH ₄ , MeOH, rt, 12 h. (ii) NaH, DMF, rt, 1 h, 48%.

methodology by using these donor–acceptor cyclopropanes as novel synthons for further transformations.

Experimental Section

General Methods. See the Supporting Information.

5-Methoxy-2-(benzyloxymethyl)-4-[(4-methylphenyl)sulfanyl]tetrahydrofuran-3-ol, 2. To a well-stirred solution of the epoxide **1** (3.70 g, 15.68 mmol) in DMF (40 mL) was added thiocresol (9.73 g, 78.4 mmol) and NaOMe (2.54 g, 47.04 mmol). The mixture was heated at 90–100 °C with stirring under N₂. After 4–5 h, the reaction mixture was poured into an aq saturated solution

TABLE 3. Desulfonylation of Selected Compounds

Sulfonylated cyclopropanes	Desulfonylated Products	Conditions
15	30	Na-Hg, Na ₂ HPO ₄ , MeOH, rt, 6 h, 56%.
18	31	LAH, THF, rt, 18 h, 58%.
23	32	Na-Hg, Na ₂ HPO ₄ , MeOH, rt, 6 h, 55%.
26	33	LAH, THF, rt, 18 h, 42%.

of NaHCO₃, and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ then filtered, and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel to afford the sulfide **2** (4.69 g, 83%). Yellow oil, [α]_D²⁴ −1.2 (c 0.15, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.33 (s, 3H), 2.55 (d, 1H, *J* = 8 Hz), 3.38 (s, 3H), 3.54–3.55 (m, 1H), 3.63–3.73 (m, 2H), 3.96–4.00 (m, 1H), 4.17–4.21 (m, 1H), 4.61 (q, 2H, *J* = 12 Hz), 4.96 (s, 1H), 7.12 (d, 2H, *J* = 8 Hz), 7.27–7.38 (m, 7H); ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 55.2, 58.2, 70.4 (CH₂), 73.5 (CH₂), 77.7, 84.1, 108.6, 127.7, 127.8, 128.4, 129.9, 130.3, 131.1, 137.3, 137.8; HRMS [ES⁺, (M + Na)⁺] for C₂₀H₂₄O₄Na obsd 383.1275, calcd 383.1293.

3-Benzyloxy-5-methoxy-2-(benzyloxymethyl)-4-[(4-methylphenyl)sulfanyl]tetrahydrofuran, 3. Compound **2** (5.58 g, 15.50 mmol) was stirred at 0 °C with NaH (0.90 g, 18.60 mmol) and BnBr (2.40 mL, 20.15 mmol) in DMF (50 mL). The mixture was stirred at room temperature under N₂. After 5–6 h, the reaction mixture was poured into an aq saturated solution of NH₄Cl and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **3** (5.96 g, 71%). Yellow oil, [α]_D²⁴ +25.9 (c 0.10, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.40 (s, 3H), 3.44 (s, 3H), 3.61–3.69 (m, 2H), 3.71–3.72 (m, 1H), 3.88–3.91 (m, 1H), 4.31–4.35 (m, 1H), 4.42 (d, 1H, *J* = 12 Hz), 4.59–4.66 (m, 3H), 5.0 (s, 1H), 7.17 (d, 2H, *J* = 8 Hz), 7.24–7.26 (m, 2H), 7.33–7.43 (m, 10H); ¹³C NMR (100 MHz, CDCl₃) δ 21.1, 55.2, 56.6, 69.7 (CH₂), 72.1 (CH₂), 73.4 (CH₂), 81.9, 83.7, 109.2, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 129.9, 130.7, 131.2, 137.2, 137.6, 138.0; HRMS [ES⁺, (M + Na)⁺] for C₂₇H₃₀O₄Na obsd 473.1762, calcd 473.1762.

(2R,3R,4R)-3,5-Dibenzoyloxy-2-[(4-methylphenyl)sulfanyl]pentane-1,4-diol, 4. Compound **3** (5 g, 11.11 mmol) was added to 75% aq trifluoroacetic acid and the mixture was stirred at room temperature for 5–6 h. The reaction mixture was partitioned between EtOAc and an aq saturated solution of NaHCO₃. The separated organic layer was washed with water, followed by brine. The combined organic layer was dried over anhyd Na₂SO₄ and concentrated in vacuo. The residue was dissolved in EtOH (40 mL), and sodium borohydride (1.68 g, 44.44 mmol) was added at 0 °C. After being stirred for 3 h at room temperature, the reaction

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mixture was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **4** (2.77 g, 58%). Brown solid, mp 70 °C, $[\alpha]_D^{24} +10.5$ (c 0.10, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.92–2.18 (m, 2H), 2.31 (s, 3H), 3.55–3.58 (m, 1H), 3.66–3.83 (m, 4H), 3.89 (d, 1H, *J* = 8 Hz), 4.18–4.21 (m, 1H), 4.50–4.61 (m, 4H), 7.08 (d, 2H, *J* = 8 Hz), 7.24–7.38 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 54.6, 62.8 (CH₂), 70.7, 70.9 (CH₂), 73.4 (CH₂), 73.9 (CH₂), 78.1, 127.8, 127.9, 128 (2 × C), 128.4, 128.5, 129.8, 131.9, 132.2, 137.1, 137.7, 137.9; HRMS [ES⁺, (M + Na)⁺] for C₂₆H₃₀O₄Na obsd 461.1749, calcd 461.1763.

(2R,3R,4R)-3,5-Dibenzoyloxy-2-[(4-methylphenyl)sulfonyl]pentane-1,4-diol, 5. To a well-stirred solution of sulfide **4** (3.70 g, 8.44 mmol) in dry MeOH (40 mL) was added magnesium monoperoxyphthalate hexahydrate (12.52 g, 25.32 mmol), and the mixture was stirred at room temperature under N₂. After 6 h, MeOH was evaporated to dryness under reduced pressure, and the residue was dissolved in an aq saturated solution of NaHCO₃. The aqueous part was washed with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ and concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford sulfone **5** (3.61 g, 91%). Brown gum, $[\alpha]_D^{24} +81.3$ (c 0.17, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.40 (s, 3H), 2.80–2.97 (m, 2H), 3.58–3.65 (m, 2H), 3.72–3.75 (m, 1H), 3.95 (dd, 1H, *J* = 4.4, 12.4 Hz), 4.08–4.18 (m, 3H), 4.36 (d, 1H, *J* = 11.2 Hz), 4.45 (q, 2H, *J* = 6.4 Hz), 4.53 (d, 1H, *J* = 11.6 Hz), 7.04–7.06 (m, 2H), 7.21 (d, 2H, *J* = 8 Hz), 7.26–7.37 (m, 8H), 7.73 (d, 2H, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 59.1 (CH₂), 68.4, 70.4 (CH₂), 70.7, 73.5 (CH₂), 73.5, 76.5, 127.8, 128.0, 127.9, 128.1, 128.3, 128.5, 128.8, 129.6, 136.7, 137.3, 137.8, 144.7; HRMS [ES⁺, (M + H)⁺] for C₂₆H₃₁O₆S obsd 471.1844, calcd 471.1841.

(2R,3R)-1,3-Dibenzoyloxy-4-[(4-methylphenyl)sulfonyl]pent-2-en-2-yl Methanesulfonate, 6. To a well-stirred solution of sulfone **5** (2.63 g, 5.60 mmol) in pyridine (15 mL) was added methanesulfonyl chloride (1.7 mL, 22.40 mmol) in pyridine (10 mL) dropwise at 0 °C under N₂. After completion of the addition, the reaction mixture was kept at +4 °C. After 24 h (TLC), the reaction mixture was poured into an aq saturated solution of NaHCO₃ and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ and concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford the vinyl sulfone **6** (2.43 g, 82%). Yellow oil, $[\alpha]_D^{24} -43.2$ (c 0.04, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.44 (s, 3H), 2.97 (s, 3H), 3.72–3.81 (m, 2H), 4.05 (d, 1H, *J* = 11.6 Hz), 4.19 (d, 1H, *J* = 11.6 Hz), 4.42–4.54 (m, 3H), 5.19 (br s, 1H), 6.21 (s, 1H), 6.67 (s, 1H), 6.99 (d, 2H, *J* = 5.2 Hz), 7.22–7.36 (m, 10H), 7.77 (d, 2H, *J* = 7.6 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 38.1, 67.3 (CH₂), 71.8 (CH₂), 73.2 (CH₂), 75.2, 81.3, 127.6, 127.7, 127.8, 127.9, 128.2, 128.3, 128.4 (CH₂), 128.7, 129.9, 135.1, 136.3, 137.4, 145.0, 147.5; HRMS [ES⁺, (M + Na)⁺] for C₂₇H₃₀O₇S₂Na obsd 553.1332, calcd 553.1331.

2-[(1,2-Dibenzoyloxyethyl)-5-methoxy-4-[(4-methylphenyl)sulfonyl]tetrahydrofuran-3-ol, 8. Compound **7** (5.70 g, 16.01 mmol) was converted to **8** (6.13 g, 80%) following the procedure described for the preparation of **2**. Yellow oil, $[\alpha]_D^{24} -9.9$ (c 0.12, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.32 (s, 3H), 3.07 (d, 1H, *J* = 4.8 Hz), 3.34 (s, 3H), 3.54–3.55 (m, 1H), 3.63–3.66 (m, 1H), 3.75–3.83 (m, 2H), 4.05 (t, 1H, *J* = 5.6 Hz), 4.21–4.25 (m, 1H), 4.53 (d, 1H, *J* = 12 Hz), 4.61 (d, 1H, *J* = 12 Hz), 4.67–4.74 (m, 2H), 4.89 (d, 1H, *J* = 1.6 Hz), 7.10 (d, 2H, *J* = 8 Hz), 7.27–7.37 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 21.1, 55.2, 57.9, 70.5 (CH₂), 72.9 (CH₂), 73.7 (CH₂), 76.2, 78.1, 84.5, 108.7, 127.6, 127.7, 127.8, 127.9, 128.4, 128.5, 129.9, 130.9, 136.9, 137.7, 138.4; HRMS [ES⁺, (M + Na)⁺] for C₂₈H₃₂O₅SNa obsd 503.1866, calcd 503.1868.

2-[(1,2-Dibenzoyloxyethyl)-5-methoxy-3-benzoyloxy-4-[(4-methylphenyl)sulfonyl]tetrahydrofuran, 9. Compound **8** (6.90 g, 14.38 mmol) was converted to **9** (6.96 g, 85%) following the procedure described for the preparation of **3**. Yellow oil, $[\alpha]_D^{24} +45.9$ (c 0.14,

CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.33 (s, 3H), 3.35 (s, 3H), 3.55–3.59 (m, 1H), 3.64–3.67 (m, 2H), 3.80–3.84 (m, 1H), 4.03–4.05 (m, 1H), 4.27–4.34 (m, 2H), 4.46–4.54 (m, 3H), 4.72 (q, 2H, *J* = 12 Hz), 4.91 (s, 1H), 7.09 (d, 2H, *J* = 8 Hz), 7.15–7.16 (m, 2H), 7.22–7.35 (m, 15H); ¹³C NMR (100 MHz, CDCl₃) δ 21.1, 55.1, 56.6, 70.3 (CH₂), 71.8 (CH₂), 73.1 (CH₂), 73.4 (CH₂), 77.9, 83.5, 83.6, 108.9, 127.4, 127.5 (2 × C), 127.6, 127.8, 127.9, 128.1, 128.2, 128.3, 129.9, 130.9, 131.2, 137.2, 137.8, 138.3, 138.6; HRMS [ES⁺, (M + Na)⁺] for C₃₅H₃₈O₅SNa obsd 593.2339, calcd 593.2338.

(2R,3R,4R)-3,5,6-Tribenzoyloxy-2-[(4-methylphenyl)sulfonyl]hexane-1,4-diol, 10. Compound **9** (3.40 g, 5.97 mmol) was converted to **10** (1.90 g, 57%) following the procedure described for the preparation of **4**. Semisolid, $[\alpha]_D^{24} -32.0$ (c 0.11, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.07–2.19 (m, 1H), 2.31 (s, 3H), 3.12 (d, 1H, *J* = 5.6 Hz), 3.51–3.54 (m, 1H), 3.63–3.67 (m, 1H), 3.77–3.85 (m, 4H), 3.96–3.98 (m, 1H), 4.29–4.33 (m, 1H), 4.48–4.62 (m, 5H), 4.70 (d, 1H, *J* = 11.6 Hz), 7.06 (d, 2H, *J* = 8 Hz), 7.22–7.32 (m, 17H); ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 54.3, 62.9 (CH₂), 69.9 (CH₂), 72.0 (CH₂), 72.9 (CH₂), 73.5 (CH₂), 77.9, 78.3, 127.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 129.8, 131.6, 132.2, 137.2, 137.8, 137.9, 138.2; HRMS [ES⁺, (M + Na)⁺] for C₃₄H₃₈O₅SNa obsd 581.2337, calcd 581.2338.

(2R,3R,4R)-3,5,6-Tribenzoyloxy-2-[(4-methylphenyl)sulfonyl]hexane-1,4-diol, 11. Compound **10** (4.00 g, 7.17 mmol) was converted to **11** (3.89 g, 92%) following the procedure described for the preparation of **5**. Semisolid, $[\alpha]_D^{24} -13.4$ (c 0.10, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.37 (s, 3H), 2.95 (br s, 1H), 3.46 (d, 1H, *J* = 6 Hz), 3.56–3.60 (m, 1H), 3.67–3.73 (m, 2H), 3.78–3.82 (m, 1H), 3.96–3.98 (m, 1H), 4.07–4.10 (m, 1H), 4.11–4.16 (m, 1H), 4.24–4.26 (m, 1H), 4.41–4.59 (m, 5H), 4.66 (d, 1H, *J* = 11.6 Hz), 7.05–7.07 (m, 2H), 7.15 (d, 2H, *J* = 8 Hz), 7.21–7.36 (m, 13H), 7.66 (d, 2H, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.5, 59.0 (CH₂), 68.5, 69.8 (CH₂), 72.2, 72.3 (CH₂), 72.8 (CH₂), 73.5 (CH₂), 77.4, 78.1, 127.5, 127.7, 127.8, 127.9, 128.1, 128.4, 129.5, 136.9, 137.5, 137.8, 138.0, 144.4; HRMS [ES⁺, (M + H)⁺] for C₃₄H₃₉O₇S obsd 591.2416, calcd 591.2417.

(2R,3R,4R)-5-[(4-Methylphenyl)sulfonyl]-1,2,4-tribenzoyloxyhex-5-en-3-yl Methanesulfonate, 12. Compound **11** (3.50 g, 5.93 mmol) was converted to **12** (3.09 g, 80%) following the procedure described for the preparation of **6**. Colorless oil, $[\alpha]_D^{24} -23.8$ (c 0.10, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.40 (s, 3H), 2.94 (s, 3H), 3.56–3.60 (m, 1H), 3.81 (d, 1H, *J* = 10 Hz), 4.02 (d, 2H, *J* = 10.8 Hz), 4.14 (d, 1H, *J* = 11.6 Hz), 4.41–4.51 (m, 3H), 4.64 (q, 2H, *J* = 5.2 Hz), 5.24 (d, 1H, *J* = 5.2 Hz), 6.16 (s, 1H), 6.59 (s, 1H), 6.98 (d, 2H, *J* = 6 Hz), 7.24–7.34 (m, 15H), 7.74 (d, 2H, *J* = 8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 38.6, 69.7 (CH₂), 71.6 (CH₂), 72.2 (CH₂), 73.2 (CH₂), 74.9, 76.4, 81.6, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 128.6, 128.7 (CH₂), 128.9, 129.9, 135.2, 136.4, 137.7, 138.1, 144.9, 148.1; HRMS [ES⁺, (M + Na)⁺] for C₃₅H₃₈O₈S₂Na obsd 673.1909, calcd 673.1906.

2-[(1S,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-(4-methylphenyl)sulfonyl]cyclopropylmethyl]-1H-isoindole-1,3(2H)-dione, 13. To a well-stirred solution of phthalimide (0.39 g, 2.66 mmol) and NaH (0.09 g, 1.90 mmol) in DMF (10 mL) was added **6** (0.20 g, 0.38 mmol) and the mixture was stirred at 50 °C under N₂. After 8 h, the reaction mixture was poured into an aq saturated solution of NH₄Cl and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **13** (0.13 g, 58%). Colorless oil, $[\alpha]_D^{26} +40.8$ (c 0.22, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.21 (s, 3H), 2.59 (q, 1H, *J* = 8, 14.4 Hz), 3.85–3.93 (m, 2H), 4.20–4.24 (m, 1H), 4.32 (d, 1H, *J* = 8 Hz), 4.39 (d, 1H, *J* = 15.2 Hz), 4.61 (q, 2H, *J* = 12, 26.4 Hz), 4.79 (q, 2H, *J* = 11.6, 26.4 Hz), 6.99 (d, 2H, *J* = 8 Hz), 7.27–7.37 (m, 10H), 7.59 (d, 2H, *J* = 8 Hz), 7.63–7.68 (m, 4H); ¹³C NMR (100 MHz, CDCl₃) δ 21.5, 27.8, 32.4 (CH₂), 43.7, 61.1, 63.6 (CH₂), 73.1 (CH₂), 74.0 (CH₂), 123.1, 127.6, 127.8, 127.9, 127.9, 128.1, 128.4, 128.5, 129.5, 131.9, 133.8, 136.4, 136.9, 138.2,

144.1, 167.4; HRMS $[\text{ES}^+, (\text{M} + \text{Na})^+]$ for $\text{C}_{34}\text{H}_{31}\text{NO}_6\text{SNa}$ obsd 604.1768, calcd 604.1770.

1-[(1S,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-[(4-methylphenyl)sulfonyl]cyclopropyl]methanamine, 14. A solution of compound **13** (0.04 g, 0.069 mmol) and hydrazine hydrate (0.15 mL) in EtOH (15 mL) was heated under reflux. After 6 h, EtOH was evaporated to dryness under reduced pressure to afford a residue. The residue was purified over silica gel to afford **14** (0.021 g, 70%). Colorless oil, $[\alpha]_D^{26} + 7.7$ (*c* 0.09, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 2.41 (q, 1H, *J* = 8, 15.2 Hz), 2.44 (s, 3H), 3.01 (d, 1H, *J* = 16 Hz), 3.10 (d, 1H, *J* = 16 Hz), 3.63–3.67 (m, 1H), 3.71–3.76 (m, 1H), 4.12 (d, 1H, *J* = 8 Hz), 4.36–4.43 (m, 2H), 4.44–4.50 (m, 2H), 7.20–7.23 (m, 4H), 7.26–7.34 (m, 8H), 7.76 (d, 2H, *J* = 8 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.6, 26.9, 36.7 (CH_2), 50.0, 62.0, 63.3 (CH_2), 72.8 (CH_2), 73.9 (CH_2), 127.5, 127.7, 127.8, 128.2, 128.3, 128.5, 128.6, 129.9, 135.4, 136.3, 137.6, 144.7; HRMS $[\text{ES}^+, (\text{M} + \text{H})^+]$ for $\text{C}_{26}\text{H}_{30}\text{NO}_4\text{S}$ obsd 452.1891, calcd 452.1896.

(1S,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-[(methoxy)methyl]cyclopropyl 4-Methylphenyl Sulfone, 15. To a well-stirred solution of **6** (0.20 g, 0.38 mmol) in dry MeOH (10 mL) was added NaOMe (0.12 g, 2.28 mmol) and the mixture was stirred at ambient temperature under N_2 . After 5–6 h, MeOH was evaporated to dryness under reduced pressure and the residue was dissolved in an aq saturated solution of NH_4Cl . The product was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. A solution of the residue in DMF (10 mL) was treated with NaH (0.04 g, 0.76 mmol) for 1 h. Then the reaction mixture was poured into an aq saturated solution of NaHCO_3 and the product was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **15** (0.10 g, 57%). Colorless oil, $[\alpha]_D^{24} + 21.2$ (*c* 0.03, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 2.35 (m, 1H), 2.44 (s, 3H), 3.09 (s, 3H), 3.59–3.63 (m, 2H), 3.71–3.75 (m, 1H), 3.85 (d, 1H, *J* = 11.6 Hz), 4.22 (d, 1H, *J* = 7.6 Hz), 4.43–4.58 (m, 4H), 7.26–7.38 (m, 12H), 7.74 (d, 2H, *J* = 8 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 27.8, 48.3, 58.5, 62.1, 63.3 (CH_2), 66.2 (CH_2), 72.6 (CH_2), 73.9 (CH_2), 127.6 (2 \times C), 127.9, 128.1, 128.3, 128.5, 128.8, 129.3, 136.7, 136.8, 138.1, 144.2; HRMS $[\text{ES}^+, (\text{M} + \text{Na})^+]$ for $\text{C}_{27}\text{H}_{30}\text{O}_5\text{SNa}$ obsd 489.1712, calcd 489.1712.

(1S,2R,3S)-2-Benzoyloxy-1-[[4-(methoxybenzyl)oxy]methyl]-3-(benzyloxymethyl)cyclopropyl 4-Methylphenyl Sulfone, 16. To a well-stirred solution of *p*-methoxybenzyl alcohol (0.50 mL, 3.99 mmol) and NaH (0.14 g, 2.85 mmol) in DMF (10 mL) was added **6** (0.30 g, 0.57 mmol) and the mixture was stirred at ambient temperature under N_2 . After 6 h, the reaction mixture was poured into an aq saturated solution of NH_4Cl and the product was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **16** (0.19 g, 58%). Colorless oil, $[\alpha]_D^{26} + 44.8$ (*c* 0.25, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 2.35–2.39 (m, 1H), 2.41 (s, 3H), 3.55–3.60 (m, 1H), 3.66 (d, 1H, *J* = 12 Hz), 3.73–3.77 (m, 1H), 3.80 (s, 3H), 3.94 (d, 1H, *J* = 11.6 Hz), 4.16–4.25 (m, 3H), 4.41–4.58 (m, 4H), 6.75 (d, 2H, *J* = 8.4 Hz), 6.92 (d, 2H, *J* = 8.4 Hz), 7.18–7.38 (m, 12H), 7.70 (d, 2H, *J* = 8 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.6, 27.9, 48.3, 55.3, 62.2, 63.5 (CH_2), 63.6 (CH_2), 72.6 (2 \times CH_2), 73.9 (CH_2), 113.5, 127.6, 127.6, 127.9, 128.1, 128.3, 128.5, 128.8, 129.1, 129.3, 129.5, 136.6, 136.9, 138.2, 144.1, 159.1; HRMS $[\text{ES}^+, (\text{M} + \text{Na})^+]$ for $\text{C}_{34}\text{H}_{36}\text{O}_6\text{SNa}$ obsd 595.2135, calcd 595.2130.

{(1S,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-[(4-ethylphenyl)sulfonyl]cyclopropyl}methanol, 17. Compound **16** (0.09 g, 0.158 mmol) and DDQ (0.04 g, 0.19 mmol) were added to a well-stirred mixture of DCM– H_2O (20:1) and the mixture was stirred at ambient temperature. After 16–18 h, the reaction mixture was

poured into an aq saturated solution of NaHCO_3 and then extracted with DCM (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **17** (0.05 g, 74%). Colorless oil, $[\alpha]_D^{26} + 4.5$ (*c* 0.21, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 2.37 (q, 1H, *J* = 8, 16.0 Hz), 2.43 (s, 3H), 3.01–3.04 (m, 1H), 3.70–3.79 (m, 2H), 3.84–3.89 (m, 1H), 4.14–4.19 (m, 1H), 4.28 (d, 1H, *J* = 7.6 Hz), 4.36–4.42 (m, 2H), 4.51 (s, 2H), 7.09–7.11 (m, 2H), 7.26–7.37 (m, 10H), 7.81 (d, 2H, *J* = 8 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.6, 27.3, 50.0, 56.4 (CH_2), 62.7, 63.2 (CH_2), 72.6 (CH_2), 74.2 (CH_2), 127.4, 127.8, 128.1, 128.2, 128.3, 128.5, 128.9, 129.6, 135.7, 136.1, 137.1, 144.6; HRMS $[\text{ES}^+, (\text{M} + \text{Na})^+]$ for $\text{C}_{26}\text{H}_{28}\text{O}_5\text{SNa}$ obsd 475.1522, calcd 475.1555.

(1R,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-[(methylsulfonyl)methyl]cyclopropyl 4-Methylphenyl Sulfone, 18. To a well-stirred solution of **6** (0.36 g, 0.68 mmol) in dry DMF (10 mL) was added NaMe (0.33 g, 4.76 mmol) and the mixture was stirred at ambient temperature under N_2 . After 1 h, the reaction mixture was poured into an aq saturated solution of NaHCO_3 and the product was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **18** (0.19 g, 58%). Yellow oil, $[\alpha]_D^{26} + 17.4$ (*c* 0.08, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 1.97 (s, 3H), 2.40–2.44 (m, 1H), 2.46 (s, 3H), 2.76 (d, 1H, *J* = 14.4 Hz), 2.97 (d, 1H, *J* = 14.4 Hz), 3.61–3.65 (m, 1H), 3.83–3.87 (m, 1H), 4.24 (d, 1H, *J* = 8 Hz), 4.48–4.56 (m, 2H), 4.63 (s, 2H), 7.26–7.38 (m, 12H), 7.81 (d, 2H, *J* = 8 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 17.8, 21.7, 27.9, 28.8 (CH_2), 47.8, 62.2, 63.4 (CH_2), 72.8 (CH_2), 73.9 (CH_2), 127.5, 127.6, 127.8, 128.1, 128.3, 128.5, 128.9, 129.6, 135.6, 136.6, 137.9, 144.7; HRMS $[\text{ES}^+, (\text{M} + \text{Na})^+]$ for $\text{C}_{27}\text{H}_{30}\text{O}_4\text{S}_2\text{Na}$ obsd 505.1480, calcd 505.1483.

(1R,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-(2-nitroethyl)-cyclopropyl 4-Methylphenyl Sulfone, 19. To a well-stirred solution of nitromethane (0.22 mL, 4.18 mmol) and NaH (0.09 g, 1.90 mmol) in DMF (10 mL) was added **6** (0.20 g, 0.38 mmol) and the mixture was stirred at ambient temperature under N_2 . After 3 h, the reaction mixture was poured into an aq saturated solution of NH_4Cl and the product was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **19** (0.09 g, 47%). Colorless oil, $[\alpha]_D^{24} - 75.0$ (*c* 0.04, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 2.29–2.42 (m, 3H), 2.46 (s, 3H), 3.47 (t, 1H, *J* = 10.4 Hz), 3.67–3.71 (m, 1H), 4.10 (d, 1H, *J* = 7.6 Hz), 4.38–4.48 (m, 4H), 4.71–4.85 (m, 2H), 7.22 (br s, 2H), 7.31–7.36 (m, 10H), 7.73 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 21.7, 27.1, 45.6, 61.4, 63.0 (CH_2), 72.5 (CH_2), 73.1 (CH_2), 74.1 (CH_2), 127.7, 127.9, 128.5, 128.6, 128.7, 130.2, 134.5, 136.0, 137.4, 145.4; HRMS $[\text{ES}^+, (\text{M} + \text{Na})^+]$ for $\text{C}_{27}\text{H}_{29}\text{NO}_6\text{SNa}$ obsd 518.1616, calcd 518.1613.

1-[(1S,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-(4-methylphenylsulfonyl)cyclopropyl]methyl]-5-methylpyrimidine-2,4(1H,3H)-dione, 20. To a well-stirred solution of thymine (0.42 g, 3.36 mmol) and TMG (0.30 mL, 2.40 mmol) in DMF (10 mL) was added **6** (0.25 g, 0.48 mmol) and the mixture was stirred at ambient temperature under N_2 . After 5 h, the reaction mixture was diluted with EtOAc (30 mL) and the undissolved solid was filtered off. The filtrate was washed with an aq saturated solution of NaHCO_3 and the aqueous phase was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 then filtered, and the filtrate was concentrated under reduced pressure. A solution of the crude material in DMF (10 mL) was treated with NaH (0.05 g, 0.96 mmol) for 1 h. Then the reaction mixture was poured into an aq saturated solution of NaHCO_3 and the product was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to afford a residue. The residue was purified over

silica gel to afford **20** (0.126 g, 48%). White gum, $[\alpha]_D^{26} +13.0$ (*c* 0.2, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.67 (s, 3H), 2.40 (s, 3H), 2.46 (q, 1H, *J* = 7.2, 15.0 Hz), 3.56–3.63 (m, 1H), 3.67–3.71 (m, 1H), 3.92 (d, 1H, *J* = 15.6 Hz), 4.35 (d, 1H, *J* = 7.6 Hz), 4.41–4.48 (m, 2H), 4.59–4.65 (m, 3H), 7.21 (d, 2H, *J* = 6.4 Hz), 7.26–7.42 (m, 11H), 7.71 (d, 2H, *J* = 8.4 Hz), 8.57 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 12.3, 21.7, 28.0, 40.2 (CH₂), 45.6, 61.1, 62.6 (CH₂), 73.1 (CH₂), 74.2 (CH₂), 110.4, 127.7, 127.9, 128.1, 128.4, 128.5, 128.6, 128.8, 129.9, 135.4, 135.9, 137.4, 139.6, 145.3, 151.2, 163.7; HRMS [ES⁺, (M + H)⁺] for C₃₁H₃₃N₂O₆S obsd 561.2056, calcd 561.2059.

(1R,2R,3S)-2-Benzoyloxy-3-(benzyloxymethyl)-1-methylcyclopropyl 4-Methylphenyl Sulfone, 21. To a well-stirred solution of **6** (0.10 g, 0.187 mmol) in dry MeOH (10 mL) was added NaBH₄ (0.07 g, 1.87 mmol) and the mixture was stirred at ambient temperature under N₂. After 1 h, MeOH was evaporated to dryness under reduced pressure, and the residue was dissolved in an aq saturated solution of NaHCO₃ and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ and concentrated under reduced pressure to afford a residue. A solution of the crude material in DMF (10 mL) was treated with NaH (0.02 g, 0.37 mmol) for 1 h. Then the reaction mixture was poured into an aq saturated solution of NaHCO₃ and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ and concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **21** (0.04 g, 50%). Colorless oil, $[\alpha]_D^{27} +63.8$ (*c* 0.08, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.31 (s, 3H), 2.28 (q, 1H, *J* = 14 Hz), 2.43 (s, 3H), 3.44–3.54 (m, 1H), 3.62–3.71 (m, 1H), 4.15 (d, 1H, *J* = 16 Hz), 4.34–4.51 (m, 4H), 7.14–7.19 (m, 2H), 7.26–7.36 (m, 10H), 7.75 (d, 2H, *J* = 16.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 7.2, 21.7, 26.2, 43.7, 60.6, 63.4 (CH₂), 72.5 (CH₂), 73.8 (CH₂), 127.4, 127.5, 127.9, 128.1, 128.3, 128.5, 128.7, 129.7, 135.3, 136.7, 138.1, 144.3; HRMS [ES⁺, (M + Na)⁺] for C₂₆H₂₈O₄Na obsd 459.1582, calcd 459.1606.

2-[(1S,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzyloxy-1-(4-methylphenylsulfonyl)cyclopropyl)methyl]-1H-isoidole-1,3(2H)-dione, 22. Compound **12** (0.40 g, 0.61 mmol) was converted to **22** (0.22 g, 52%) following the procedure described for the preparation of **13**. Colorless oil, $[\alpha]_D^{26} +52.3$ (*c* 0.11, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.31 (s, 3H), 2.49 (q, 1H, *J* = 8.8, 10.4 Hz), 3.67–3.71 (m, 1H), 3.82–3.85 (m, 1H), 3.94–4.01 (m, 2H), 4.32 (d, 1H, *J* = 8.8 Hz), 4.43 (d, 1H, *J* = 14.8 Hz), 4.52 (d, 1H, *J* = 11.2 Hz), 4.61 (q, 2H, *J* = 12.4 Hz), 4.72–4.80 (m, 2H), 5.08 (d, 1H, *J* = 11.6 Hz), 7.02 (d, 2H, *J* = 8 Hz), 7.24–7.38 (m, 15H), 7.65–7.67 (m, 4H), 7.70–7.72 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 29.3, 31.4 (CH₂), 42.9, 61.7, 71.2 (CH₂), 71.7 (CH₂), 72.4, 73.4 (CH₂), 74.2 (CH₂), 123.1, 127.4, 127.7, 127.8, 127.9, 127.9, 128.1, 128.2, 128.4, 128.5, 129.5, 132.1, 133.8, 136.1, 137.2, 138.1, 138.2, 144.1, 167.5; HRMS [ES⁺, (M + Na)⁺] for C₄₂H₃₉NO₇Na obsd 724.2348, calcd 724.2345.

(1S,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzyloxy-1-(methoxy-methyl)cyclopropyl 4-Methylphenyl Sulfone, 23. Compound **12** (0.20 g, 0.30 mmol) was converted to **23** (0.08 g, 46%) following the procedure described for the preparation of **15**. Colorless oil, $[\alpha]_D^{24} +48.9$ (*c* 0.21, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.29 (t, 1H, *J* = 9.2 Hz), 2.43 (s, 3H), 3.08 (s, 3H), 3.62–3.72 (m, 3H), 3.75–3.83 (m, 2H), 4.13 (d, 1H, *J* = 8.4 Hz), 4.28 (d, 1H, *J* = 11.2 Hz), 4.47 (d, 1H, *J* = 11.6), 4.54–4.63 (m, 4H), 7.04–7.07 (m, 2H), 7.20–7.38 (m, 15H), 7.77 (d, 2H, *J* = 8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 30.2, 47.9, 58.5, 61.2, 66.1 (CH₂), 71.6 (CH₂), 72.6 (CH₂), 73.4 (CH₂), 73.5, 74.0 (CH₂), 127.2, 127.5, 127.6, 127.8, 127.9, 128.0, 128.3, 128.4, 128.9, 129.2, 136.6, 136.8, 138.2, 138.5, 143.9; HRMS [ES⁺, (M + Na)⁺] for C₃₅H₃₈O₆Na obsd 609.2282, calcd 609.2287.

(1S,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzyloxy-1-[(4-methoxybenzyl)oxy]methyl]cyclopropyl 4-Methylphenyl Sulfone, 24. Compound **12** (0.30 g, 0.46 mmol) was converted to **24** (0.18 g, 57%) following the procedure described for the preparation of **16**.

Colorless oil, $[\alpha]_D^{26} +56.7$ (*c* 0.10, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.33 (m, 1H), 2.38 (s, 3H), 3.66–3.70 (m, 2H), 3.75–3.80 (m, 5H), 3.93 (d, 1H, *J* = 11.6 Hz), 4.14 (d, 1H, *J* = 8.4 Hz), 4.19–4.24 (m, 3H), 4.50–4.59 (m, 5H), 6.69 (d, 2H, *J* = 8.4 Hz), 6.88 (d, 2H, *J* = 8.4 Hz), 6.97 (d, 2H, *J* = 6 Hz), 7.12 (d, 2H, *J* = 8 Hz), 7.16–7.34 (m, 13H), 7.71 (d, 2H, *J* = 8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 30.3, 47.9, 55.2, 61.3, 63.9 (CH₂), 71.6 (CH₂), 72.6 (CH₂), 73.1 (CH₂), 73.5 (CH₂), 73.7, 74.1 (CH₂), 113.5, 127.1, 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.4, 128.5, 128.9, 129.2, 129.3, 129.5, 136.7, 137.1, 138.3, 138.6, 143.8, 159.2; HRMS [ES⁺, (M + Na)⁺] for C₄₂H₄₄O₇Na obsd 715.2705, calcd 715.2693.

{(1S,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzyloxy-1-[(4-methylphenyl)sulfonyl]cyclopropyl}methanol, 25. Compound **24** (0.09 g, 0.13 mmol) was converted to **25** (0.05 g, 71%) following the procedure described for the preparation of **17**. Colorless oil, $[\alpha]_D^{26} +20.5$ (*c* 0.11, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.30 (q, 1H, *J* = 8.8, 10.0 Hz), 2.40 (s, 3H), 3.05 (d, 1H, *J* = 9.2 Hz), 3.62–3.66 (m, 1H), 3.74–3.77 (m, 1H), 3.79–3.84 (m, 1H), 3.91 (d, 1H, *J* = 13.6 Hz), 3.99–4.01 (m, 1H), 4.22 (d, 1H, *J* = 11.2 Hz), 4.28 (d, 1H, *J* = 8.4 Hz), 4.48 (d, 1H, *J* = 11.2 Hz), 4.54–4.61 (m, 3H), 4.66 (d, 1H, *J* = 11.2 Hz), 6.91 (d, 2H, *J* = 6.4 Hz), 7.18–7.37 (m, 15H), 7.79 (d, 2H, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 29.9, 49.3, 56.8 (CH₂), 61.8, 70.5 (CH₂), 71.2 (CH₂), 72.6, 73.3 (CH₂), 74.3 (CH₂), 127.2, 127.5, 127.6, 127.7, 128.0, 128.1 (2 × C), 128.4, 128.5, 128.8, 129.6, 135.5, 136.4, 137.5, 137.9, 144.6; HRMS [ES⁺, (M + Na)⁺] for C₃₄H₃₆O₆Na obsd 595.2102, calcd 595.2130.

(1R,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzyloxy-1-[(methyl-sulfonyl)methyl]cyclopropyl 4-Methylphenyl Sulfone, 26. Compound **12** (0.30 g, 0.46 mmol) was converted to **26** (0.16 g, 56%) following the procedure described for the preparation of **18**. Colorless oil, $[\alpha]_D^{24} +15.3$ (*c* 0.04, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.94 (s, 3H), 2.37 (t, 1H, *J* = 8.8 Hz), 2.46 (s, 3H), 2.75–2.83 (m, 2H), 3.65–3.70 (m, 2H), 3.78–3.81 (m, 1H), 4.21 (d, 1H, *J* = 8.8 Hz), 4.37 (d, 1H, *J* = 11.2 Hz), 4.57–4.65 (m, 4H), 4.80 (d, 1H, *J* = 11.6 Hz), 7.02–7.04 (m, 2H), 7.20–7.37 (m, 15H), 7.85 (d, 2H, *J* = 8.4 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 17.9, 21.7, 29.0 (CH₂), 31.1, 47.3, 61.2, 71.4 (CH₂), 72.1 (CH₂), 73.0, 73.4 (CH₂), 74.4 (CH₂), 127.3, 127.6, 127.7, 128.0, 128.4, 128.5, 128.9, 129.5, 135.7, 136.8, 138.1, 138.4, 144.4; HRMS [ES⁺, (M + Na)⁺] for C₃₅H₃₈O₅S₂Na obsd 625.2031, calcd 625.2058.

(1R,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzyloxy-1-[(benzyl-sulfonyl)methyl]cyclopropyl 4-Methylphenyl Sulfone, 27. To a well-stirred solution of benzylthiol (0.20 mL, 1.53 mmol) and TMG (0.10 mL, 0.918 mmol) in DMF (10 mL) was added **12** (0.10 g, 0.153 mmol) and the mixture was stirred at ambient temperature under N₂. After 3 h, the reaction mixture was poured into an aq saturated solution of NH₄Cl and the product was extracted with EtOAc (3 × 10 mL). The combined organic layer was dried over anhyd Na₂SO₄ then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford **27** (0.05 g, 49%). Colorless oil, $[\alpha]_D^{26} +63.3$ (*c* 0.05, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.29–2.34 (m, 1H), 2.43 (s, 3H), 2.64 (d, 1H, *J* = 13.6 Hz), 2.81 (d, 1H, *J* = 14 Hz), 3.51 (s, 3H), 3.58–3.62 (m, 1H), 3.71 (d, 1H, *J* = 10.4 Hz), 4.15–4.21 (m, 2H), 4.51–4.60 (m, 4H), 4.68 (d, 1H, *J* = 11.6 Hz), 6.94 (d, 2H, *J* = 7.2 Hz), 7.07 (br s, 2H), 7.15–7.33 (m, 18H), 7.76 (d, 2H, *J* = 7.6 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 21.7, 25.9 (CH₂), 31.2, 38.2 (CH₂), 46.8, 61.2, 71.5 (CH₂), 71.9 (CH₂), 73.2, 73.3 (CH₂), 74.3 (CH₂), 126.9, 127.2, 127.4, 127.6, 127.8, 127.9, 128.0, 128.3 (2 × C), 128.4, 128.7, 128.9, 129.4, 135.4, 136.7, 137.7, 138.1, 138.3, 144.2; HRMS [ES⁺, (M + Na)⁺] for C₄₁H₄₂O₅S₂Na obsd 701.2372, calcd 701.2371.

1-[(1S,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzyloxy-1-(4-methylphenyl sulfonyl)cyclopropyl]methyl]-5-methylpyrimidine-2,4(1H, 3H)-dione, 28. Compound **12** (0.25 g, 0.38 mmol) was converted to **28** (0.12 g, 46%) following the procedure described for the preparation of **20**. Colorless oil, $[\alpha]_D^{24} -72.4$ (*c* 0.04, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 1.69 (s, 3H), 2.37 (s, 3H), 2.40–2.42

(m, 1H), 3.69–3.77 (m, 2H), 3.82–3.87 (m, 1H), 4.02 (d, 1H, $J = 16$ Hz), 4.34–4.39 (m, 2H), 4.52–4.66 (m, 6H), 7.02–7.04 (m, 2H), 7.15–7.37 (m, 15H), 7.52 (d, 1H, $J = 0.8$ Hz), 7.73 (d, 2H, $J = 8$ Hz), 8.40 (br s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 12.2, 21.6, 31.1, 40.6 (CH_2), 45.3, 61.5, 70.9 (CH_2), 71.3 (CH_2), 72.3, 73.5 (CH_2), 73.9 (CH_2), 110.2, 127.2, 127.4, 127.8, 127.9 ($2 \times \text{C}$), 128.2, 128.5, 128.6, 128.7, 129.7, 134.9, 135.9, 137.7, 139.7, 144.9, 151.0, 163.6; HRMS [ES^+ , ($\text{M} + \text{Na}$) $^+$] for $\text{C}_{39}\text{H}_{40}\text{N}_2\text{O}_7\text{SNa}$ obsd 703.2452, calcd 703.2454.

(1R,2S,3R)-2-(1,2-Dibenzoyloxyethyl)-3-benzoyloxy-1-methylcyclopropyl 4-Methylphenyl Sulfone, 29. Compound **12** (0.25 g, 0.38 mmol) was converted to **29** (0.10 g, 48%) following the procedure described for the preparation of **21**. Colorless oil, $[\alpha]_{\text{D}}^{27} +63.0$ (c 0.2, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 1.32 (s, 3H), 2.21 (t, 1H, $J = 8.8$ Hz), 2.42 (s, 3H), 3.56–3.61 (m, 1H), 3.64–3.68 (m, 1H), 3.76 (dd, 1H, $J = 2.4, 10.4$ Hz), 4.12 (d, 1H, $J = 8.4$ Hz), 4.23 (d, 1H, $J = 11.6$ Hz), 4.47–4.64 (m, 5H), 6.96–6.98 (m, 2H), 7.18–7.38 (m, 15H), 7.76 (d, 2H, $J = 8$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 7.7, 21.6, 28.9, 43.6, 60.1, 71.2 (CH_2), 72.4 (CH_2), 73.3 (CH_2), 73.4, 73.7 (CH_2), 127.5, 127.6, 127.7, 128.0, 128.3, 128.4, 128.5, 128.7, 129.6, 135.2, 136.5, 138.2, 138.3, 144.2; HRMS [ES^+ , ($\text{M} + \text{Na}$) $^+$] for $\text{C}_{34}\text{H}_{36}\text{O}_5\text{SNa}$ obsd 579.2181, calcd 579.2154.

Compound 30. To a solution of **15** (0.15 g, 0.32 mmol) in dry MeOH (10 mL) were added Na_2HPO_4 (0.272 g, 1.92 mmol) and 6% Na (Hg) (excess) at 0 °C. The mixture was stirred for 6 h at room temperature under N_2 then filtered through a short silica gel column. The filtrate was concentrated and the product was purified over silica gel to afford a mixture of **30** (0.056 g, 56%). Colorless oil, ^1H NMR (400 MHz, CDCl_3) δ 1.19–1.22 (m, 1H), 1.27–1.33 (m, 2H), 1.72 (s, 1H), 1.89 (br s, 1H), 3.27 (d, 1H, $J = 6.4$ Hz), 3.32 (s, 3H), 3.34 (s, 3H), 3.49–3.77 (m, 8H), 4.49–4.69 (m, 8H), 7.26–7.38 (m, 20H).

Compound 31. To a well-stirred solution of **18** (0.09 g, 0.19 mmol) in dry THF (10 mL) was added LAH (0.04 g, 0.95 mmol) at 0 °C under argon, and the mixture was stirred at room temperature

under N_2 . After 12 h, the reaction mixture was poured into an aq saturated solution of NH_4Cl and the product was extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhyd Na_2SO_4 then filtered, and the filtrate was concentrated under reduced pressure to afford a residue. The residue was purified over silica gel to afford a mixture of **31** (0.04 g, 58%). Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 1.11–1.31 (m, 4H), 2.15 (s, 3H), 2.18 (s, 3H), 2.43–2.49 (m, 3H), 2.72–2.73 (m, 1H), 3.32–3.35 (m, 1H), 3.51 (t, 1H, $J = 6.4$ Hz), 3.58–3.79 (m, 4H), 4.55–4.67 (m, 8H), 7.26–7.39 (m, 20H).

Compound 32. Compound **23** (0.06 g, 0.10 mmol) was converted to a mixture of **32** (0.02 g, 55%) following the procedure described for the preparation of **30**. Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 1.03–1.08 (m, 1H), 1.23–1.29 (m, 2H), 1.81 (br s, 1H), 3.07–3.11 (m, 1H), 3.21–3.24 (m, 1H), 3.33 (s, 3H), 3.34 (s, 3H), 3.35–3.45 (m, 2H), 3.60–3.81 (m, 8H), 4.47–4.76 (m, 12H), 7.23–7.41 (m, 30H).

Compound 33. Compound **26** (0.12 g, 0.20 mmol) was converted to a mixture of **33** (0.04 g, 42%) following the procedure described for the preparation of **31**. Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 1.03–1.09 (m, 2H), 1.13–1.22 (m, 2H), 2.15 (s, 3H), 2.18 (s, 3H), 2.21–2.30 (m, 1H), 2.49–2.53 (m, 2H), 2.81–2.85 (m, 1H), 3.14–3.17 (m, 1H), 3.37–3.40 (m, 1H), 3.58–3.80 (m, 6H), 4.48–4.79 (m, 12H), 7.22–7.40 (m, 30H).

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Supporting Information Available: Experimental procedures, full spectroscopic data of all compounds, and NOE data for **18**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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