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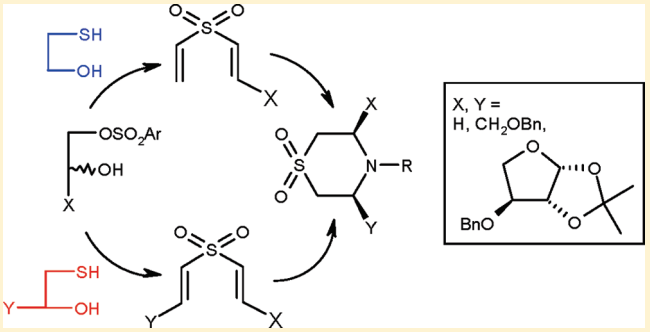
A General Route to Mono- and Disubstituted Divinyl Sulfones: Acyclic Michael Acceptors for the Synthesis of Polyfunctionalized Cyclic Sulfones

Tarun Kumar Pal, Santu Dey, and Tanmaya Pathak*

Department of Chemistry, Indian Institute of Technology Kharagpur, Kharagpur 721 302, India

Supporting Information

ABSTRACT: Nucleophilic C−S bond formation using easily available β-hydroxysulfonate derivatives allowed direct access to new mono- and disubstituted divinyl sulfones. Our strategy uses thioethanol ($HSCH_2CH_2OH$) and its analogues such as $HSCH_2CH(Y)OH$ generated in situ. The strategy also allows the synthesis of modified divinyl sulfones attached to chiral appendages like carbohydrates. Bis-heteronucleophilic Michael addition reactions with 1 equiv of a primary amine afforded new generations of *S*,*S*-dioxothiomorpholine derivatives known for their therapeutic applications. Further synthetic manipulations of some of these cyclic compounds led to the synthesis of novel bicyclic derivatives.



INTRODUCTION

Divinyl sulfone (DVS) or 1,1′-sulfonylbisethene (**1**, Scheme 1) is a unique molecule having diverse applications in chemistry[1,2] and biology.[3] Conjugate addition of carbon nucleophiles[4] and heteronucleophilic addition of primary amines,[5] thiols,[6] selenium,[7] tellurium,[7] and phosphanes[8] to the two vinyl groups of **1** constitute a class of efficient and synthetically useful reactions for the generation of cyclic compounds represented by the general structure **2** (Scheme 1).[1−3] Compound **1** has also been used in the preparation of macrocycles[2,9] and polymeric compounds.[10] DVS **1** is shown to be a component of the Stetter reaction in the synthesis of 1,4-diketo derivatives.[1]

Compound **1** was also studied recently for its inhibitory properties against glyceraldehyde-3-phosphate dehydrogenase,[11a] inducible vascular cell adhesion molecule-1 (VCAM-1) expression,[11b] SrtA, a transpeptidase required for cell wall protein anchoring and virulence in *Staphylococcus aureus*,[11c] cysteine protease of *Plasmodium falciparum*,[11d] etc. Functionalized divinyl sulfones such as **3** were screened as anti-inflammatory[12a] and tumor cell growth inhibitory[12a] agents.[12b−d]

In the quest for new chemical entities with potential biological activities, we recently reported the synthesis of divinyl sulfone-modified pent-2-enofuranosides for the first time; one of these modified divinyl sulfones initiated significant cell death in *Entameaba* species; the most active compound in this series was found to be devoid of any toxicity.[13]

RESULTS AND DISCUSSION

In spite of the reported applications of DVS **1**, the utilization of DVS in chemistry and biology is restricted to a great extent because of the nonavailability of suitable and efficient strategies for the synthesis of functionalized divinyl sulfones **3**, especially the DVS skeleton attached to chiral moieties. Knoevenagel condensation of sulfonyl acetic acids with aldehydes and other reagents,[15] metal-mediated coupling of sulfonyl chlorides and olefins,[15] Friedel−Crafts reactions of olefins,[16] and functionalization of dimethyl sulfone[17] are the most popular methods used so far for the synthesis of substituted divinyl sulfones. More recently, commercially available DVS **1** was converted to (*E*)-alkenylvinyl sulfones and (*E*,*E*)-dialkenyl sulfones by using cross-metathesis strategy; however, this strategy depends crucially on the availability of olefinic compounds required for coupling with DVS and the process also incurs a loss of up to two molecules of C_2H_4 for the synthesis of each molecule of disubstituted divinyl sulfones.[3]

Considering the acute shortage of the synthetic strategies for accessing substituted divinyl sulfones mentioned above, our association with vinyl sulfone chemistry[18] prompted us to opine that one of the easiest ways of forming a C−S bond is to treat a thiolate nucleophile with carbon-bearing leaving groups such as sulfonates derived from the corresponding alcohols. Thus, following this strategy, the thio nucleophile generated from mercaptoethanol ($HSCH_2CH_2OH$) would easily react with a β-hydroxysulfonate derivative **4** to generate the starting material **5** for the synthesis of substituted divinyl sulfones. Moreover, two molecules of **4** may be coupled with a sulfur atom to generate more complex intermediates **6** for accessing densely substituted divinyl sulfones (Scheme 2).

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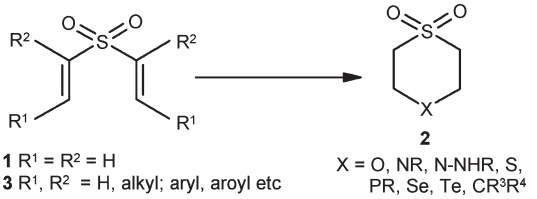
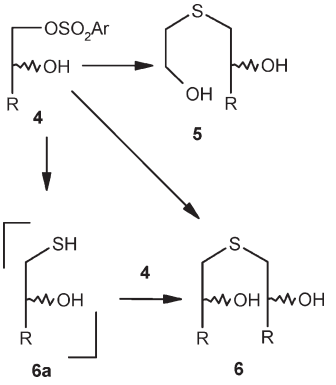
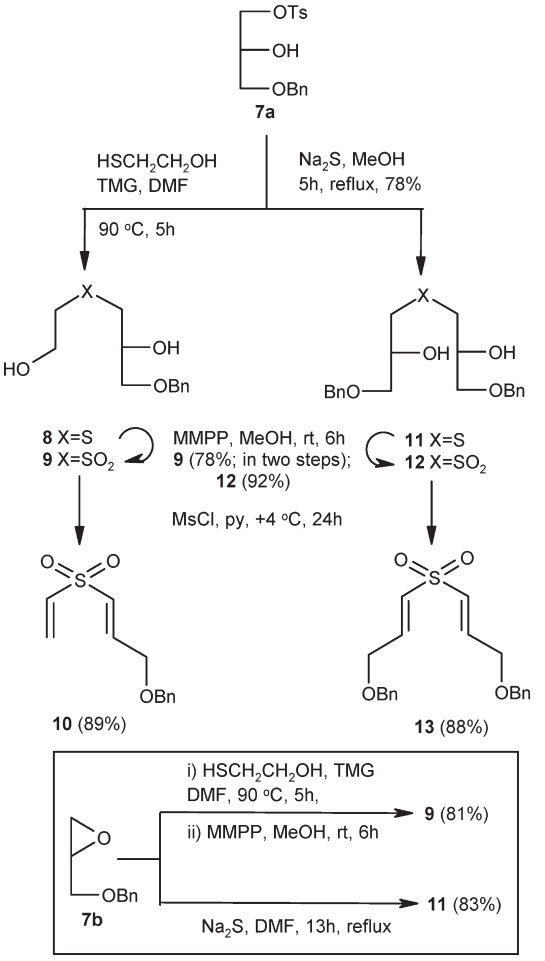
Scheme 1. Reaction Patterns of Divinyl Sulfones



Scheme 2. Strategy for the Synthesis of Intermediates for Accessing Substituted Divinyl Sulfones



Scheme 3. Synthesis of Mono- and Disubstituted Divinyl Sulfones from Glycerol Derivatives



To test the hypothesis, we targeted the synthesis of two triose derived divinyl sulfones **10** and **13** (Scheme 3). Thus the synthesis started from the easily available monotosylated and partially protected glycerol derivative **7a**,[7a,19] which was treated with mercaptoethanol in the presence of tetramethylguanidine (TMG) at an elevated temperature to obtain the sulfide **8** contaminated with inseparable materials. The impure sulfide **8** was therefore oxidized directly with magnesium monoperoxyphthalate hexahydrate (MMPP) to the corresponding sulfone **9**, which was isolated in pure form in 78% overall yield in two steps. Mesylation of the diol and the consequent elimination of mesyl groups generated the monosubstituted divinyl sulfone **10** in 89% yield. On the other hand, when 2 equiv of the same starting material **7a** was treated with 1 equiv of Na_2S, a symmetrical sulfide **11** was obtained in 78% yield. The sulfide **11** was oxidized to sulfone **12** in excellent yield and the latter was converted to disubstituted divinyl sulfone **13** by using mesyl chloride in pyridine (Scheme 3). It is also possible to use epoxide **7b**[7b] as an alternative starting material, which can also react efficiently with sulfur nucleophiles to generate **8** or **11**. Thus, **7b** was treated with mercaptoethanol in the presence of tetramethylguanidine (TMG) to generate **8**. In this case also it was difficult to obtain sulfide **8** in pure form. Therefore the impure sulfide was isolated as sulfone **9** in pure form as above. Reactions of epoxide **7b** with 0.5 equiv of Na_2S in MeOH, however, generated a mixture of products from which **11** could not be separated. Use of DMF instead of MeOH afforded a single product **11** in high yield.

The disappearance of the tosylate methyl signal at δ 2.44 (^{1}H NMR) and the appearance of two extra methylene carbon signals at δ 35.9 and 61.3 confirmed the formation of the product **8** from **7**. Compound **8** generates five methylene carbon signals as indicated by its ^{13}C NMR spectra. Two of these peaks (δ 35.9 and 36.2) shifted downfield (δ 56.2 and 56.8) when **8** was oxidized to **9**. These latter set of methylene carbon signals disappeared in compound **10**. Compound **10** has five olefinic protons in the range δ 6.07−6.96. The vinylic methylene protons at δ 6.07 (J = 9.6 Hz) and δ 6.4 (J = 16.4 Hz) indicate the cis and trans nature, respectively. The peaks at δ 6.96 representing the other vinyl proton possessing a J value of 15.2 Hz indicate the trans configuration of the substituted vinyl group. The two protons α to the SO_2 group overlap in the region δ 6.59−6.61. The vinylic methylene carbon and the other vinylic carbon signals appeared at δ 128.9 and 144.7, respectively. The two carbons connected to the SO_2 group appeared at δ 128.4 ($CH_2CH{=}\mathit{CH}SO_2$) and 137.3 ($CH_2{=}\mathit{CH}SO_2$).

In the ^{1}H NMR spectrum of the product obtained by treating **7a** with Na_2S, the tosylate methyl signal at δ 2.44 disappeared and an extra methylene carbon signal at δ 36.4 confirmed the formation of the product **11** from **7a** and **7b**. However, the ^{13}C NMR spectrum of the product indicated the presence of three methylene carbon signals as opposed to five signals in the spectra of **8**. We therefore concluded that the product in this case was dimeric and assigned the structure **11**. Out of three methylene carbon signals, the signal at δ 36.4 shifted downfield (δ 57.8 and 57.9) when **11** was oxidized to **12**. Dimerization of racemic **7a** or **7b** is expected to produce a mixture of racemates and the meso compound. Therefore, there should have been six methylene signals in the ^{13}C NMR spectra of **11**. We presume that in the

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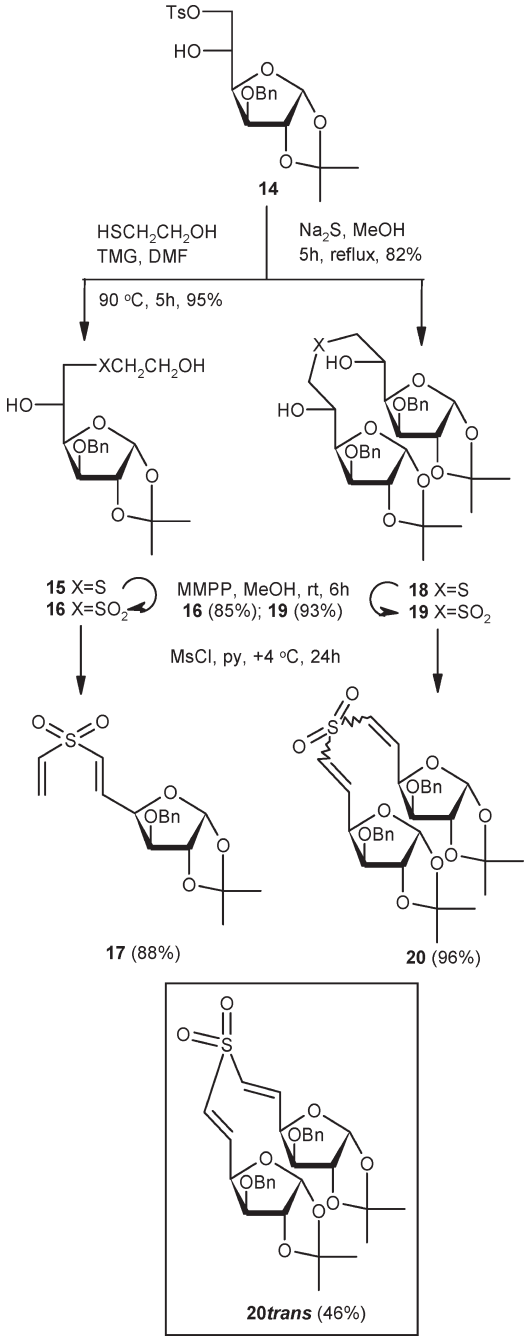
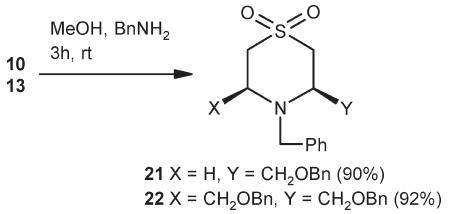
Scheme 4. Synthesis of Mono- and Disubstituted Divinyl Sulfones from a D-Glucose Derivative



case of **11** two sets of chemical shift values overlapped and thus only three methylene carbon signals appeared. However, for the sulfone **12**, the ^{13}C NMR spectrum did indeed show six methylene carbon signals as expected. Two methylene carbon signals of **12** at δ 57.8 and 57.9 disappeared in the spectra of compound **13**. For compound **13** four olefinic protons (δ 6.60 and 6.92) appeared in the ^{1}H NMR spectrum. Both of these proton signals possessed J values of ~15 Hz, which once again indicated trans configurations of both the olefinic bonds of compound **13**.

A more complex system, partially protected monotosylated derivative **14**[20] (Scheme 4) of D-glucose, was selected next to establish the general application of the strategy shown above. Thus, compound **14** was treated with mercaptoethanol and TMG at an elevated temperature to obtain the sulfide **15** in 95% yield. The sulfide was oxidized with MMPP to the corresponding sulfone **16** in 85% yield. Mesylation of the diol generated the monosubstituted divinyl sulfone **17** in one pot fashion in 88% yield. When 2 equiv of the same starting material **14** was treated with 1 equiv of Na_2S, a symmetrical sulfide **18** was obtained in 82% yield. The sulfide **18** was oxidized to sulfone **19** in excellent yield and the latter was converted to disubstituted divinyl sulfone **20** in the usual way. Compound **20** was a mixture of isomers from which the trans−trans isomer **20*trans*** was separated by crystallization (Scheme 4).

Scheme 5. Reactions of Glycerol Derived Divinyl Sulfones with Benzylamine



The disappearance of the tosylate methyl signal at δ 2.44 (^{1}H NMR) and the appearance of two extra methylene carbon signals at δ 35.6 and 60.9 confirmed the formation of the product **15** from **14**. Two (δ 35.6 and 36.9) of the four methylene carbon signals generated from **15** shifted downfield (δ 56.1 and 56.8) when it was oxidized to **16**. As expected, the latter set of methylene carbon signals disappeared when compound **17** was formed. Compound **17** generated five olefinic proton signals at δ 5.98−6.92; three of them possess J values of 16.8, 15.2, and 14.8 Hz indicating the trans configuration of the substituted double bond present in **17**. Compound **18** generated only two methylene carbon signals at δ 37.7 and 72.2, indicating the presence of a dimeric structure in the product. The peak at δ 37.7 shifted downfield to δ 58.4 when **18** was oxidized to **19**. The methylene carbon signal at δ 58.4 generated from **19** disappeared in the ^{13}C spectra of pure **20*trans***. The J values 15.2 and 14.8 Hz of the olefinic proton signals generated by **20*trans*** indicated the presence of trans-configured double bonds. The structure of compound **20*trans*** was unambiguously established on the basis of the X-ray diffraction studies of its single crystal.

Synthetic Applications of Divinyl Sulfones. We subjected these new divinyl sulfones to bis-heteronucleophilic Michael addition reactions with a primary amine because there are numerous references on the use of *S*,*S*-dioxothiomorpholine derivatives (**2**, X = NR, N-NHR) as components of therapeutically relevant compounds.[3,21] Although this class of compounds can be easily obtained by reacting a primary amine or hydrazine with divinyl sulfone **1**, a substituted variety of *S*,*S*-dioxothiomorpholine would be easily accessible from the new substituted divinyl sulfones **10**, **13**, **17**, or **20**. Thus, 1 equiv of benzylamine at room temperature reacted with the monosubstituted divinyl sulfone **10** to afford a cyclic product **21**. The disubstituted divinyl sulfone **13** also underwent bis-heteronucleophilic Michael addition reactions with 1 equiv of benzylamine at room temperature to afford a new thiomorpholine *S*,*S*-dioxide derivative **22** (Scheme 5). The disappearance of olefinic proton signals in the ^{1}H NMR spectra and the appearance of the extra methylene

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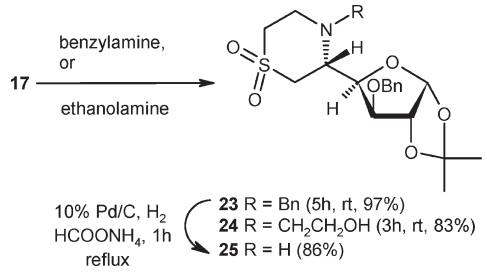
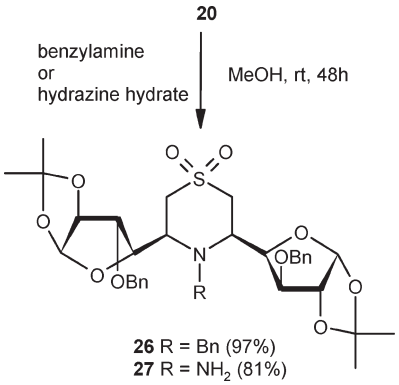
Scheme 6. Reactions of Sugar Substituted Divinyl Sulfone with Primary Amines



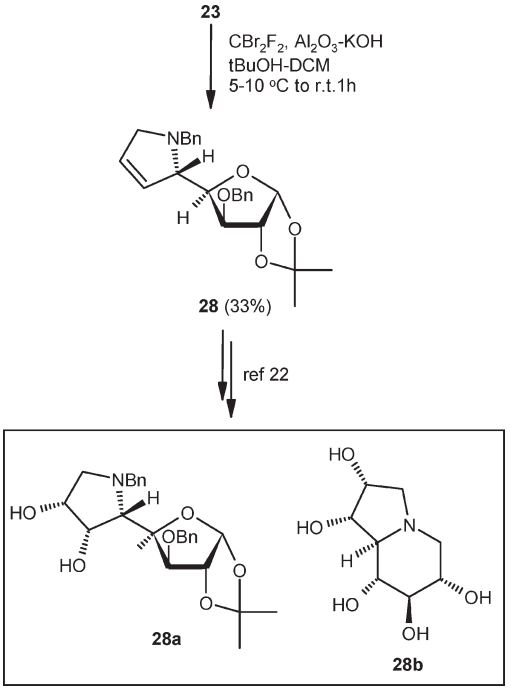
Scheme 7. Reactions of D-Glucose Derived Disubstituted Divinyl Sulfone with Benzylamine and Hydrazine Hydrate



carbon signals at δ 46.9, 49.2, 51.6, and 55.1 of the product obtained from the reactions of **10** and benzylamine clearly indicated the formation of **21**. Similar observations also indicated the transformation of **13** to the cyclic sulfone **22**. The efficiency of transformations of **10** and **13** to **21** and **22** respectively established the highly reactive nature of substituted divinyl sulfones. We presumed that in both cases, the bulky $-OCH_2OBn$ group occupied equatorial position(s) of the six-membered rings of compound **21**, which is racemic, with **22** being a meso-compound. When **21** was treated with 1 equiv of *n*-butylamine in MeOH for 4 h at 40 °C, unreacted starting material was isolated; this reaction established that a compound like **21** did not undergo retro-Michael addition reaction and the process of addition of amines to vinyl sulfone-modified carbohydrates is not reversible.

The easy synthesis of **21** and **22** prompted us to treat monosubstituted divinyl sulfone **17** with 1 equiv of benzylamine and ethanolamine at room temperature; the amines added smoothly to **17** in Michael fashion to afford the thiomorpholine *S*,*S*-dioxide derivatives **23** and **24** in excellent yields (Scheme 6). The absence of signals of olefinic protons in the ^{1}H NMR spectrum of **23** and the appearance of four additional methylene carbon signals at δ 43.4, 49.9, 51.3, and 56.7 clearly indicated the formation of the cyclic product containing benzylamine. Similar change of spectral data also confirmed the formation of **24** from **17**. The structure of compound **23** was unambiguously established on the basis of the X-ray diffraction studies of its single crystal. The mixture of sugar derived disubstituted divinyl sulfones **20** also underwent bis-heteronucleophilic Michael addition reactions with 1 equiv of benzylamine at room temperature to

Scheme 8. SO_2-Extrusion Reaction of a Sugar Derived Thiomorpholine *S*,*S*-Dioxide



afford a single thiomorpholine *S*,*S*-dioxide derivative **26**. Hydrazine hydrate too added smoothly to **20** to afford a single cyclic analogue **27** (Scheme 7). The absence of signals of olefinic protons in the ^{1}H NMR spectrum of **26** and the appearance of the new methylene carbon peaks at δ 48.9 and 51.5 clearly indicated the formation of the product **26**. For the hydrazine derivative **27** the new methylene carbon signals appeared at δ 56.6 and 57.2. In this case also we presumed that the bulky sugar residues occupied equatorial position(s) of the six-membered rings and each of the compounds **26** and **27** is a single diastereomer.

Synthetic manipulations of this new generation of thiomorpholine *S*,*S*- dioxides are expected to afford novel compounds. For example, compound **23** was debenzylated efficiently in the presence of commonly used protecting groups to generate **25** (Scheme 6) having the basic thiomorpholine *S*,*S*-dioxide skeleton with a sugar substitution attached to the ring as well as a reactive secondary amino group; the compound may be used for attaching this new scaffold with other molecules. The sulfur extrusion reaction performed on **23** by using modified Ramberg–Bäcklund conditions afforded an olefinic derivative **28** (Scheme 8) that is reportedly the starting material for the synthesis of sugar substituted dihydroxylated pyrrolidine **28a** and uniflorine A analogue **28b**.[22]

Sugar ring opening of **23** followed by debenzylation of the thiomorpholine group and cyclization of the intermediate **23a** afforded a new generation of octahydropyrido[2,1-*c*][1,4] thiazine 2,2-dioxide derivative **29**, which was isolated as the acetylated compound **30** (Scheme 9). The structuture of the compound was unambiguously identified by the X-ray analysis of its single crystal. Although analogues of octahydropyrido[2,1-*c*]-[1,4]thiazine-7,8,9-triol are known[23] for their modest glycosidase inhibitory activities, virtually nothing is known about the properties of a compound like **30**.

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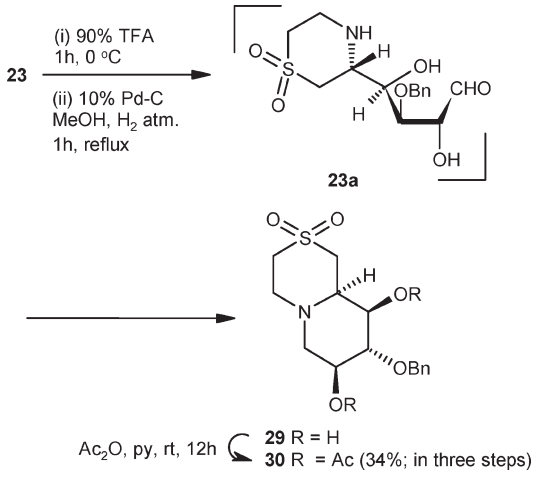
Scheme 9. Synthesis of Octahydropyrido[2,1-*c*][1,4]thiazine 2,2-Dioxide



In conclusion we have designed an efficient and general strategy for the synthesis of mono- and disubstituted divinylsulfones. The advantage of using our synthetic strategy would be that mono- and disubstituted divinyl sulfones can be synthesized from the same starting material by using different reaction procedures. Moreover, DVSs attached to chiral appendages are virtually unknown and none of the methods reported so far[3,14−17] is shown to be capable of attaching DVS to chiral appendages like carbohydrates. Compounds **17** and **20** depicted in Scheme 4 constitute the first generation of chirally modified divinyl sulfones attached to the most easily accessible chiral entities like carbohydrates. We have delineated the synthetic potential of the substituted divinyl sulfones by preparing a series of new *S,S*-dioxide thiomorpholine derivatives which were also shown to be useful synthetic intermediates. We are currently expanding the scope of substituted divinyl sulfones and their derivatives as useful synthetic intermediates.

EXPERIMENTAL SECTION

General Methods. See the Supporting Information.

Compound 7b: A mixture of NaOMe (0.80 g, 14.88 mmol) and **7a** (2.50 g, 7.44 mmol) in dry DMF (15 mL) was stirred at room temperature for 12 h. After completion of the reaction (TLC), the mixture was poured into satd. $NaHCO_3$ solution (20 mL) and the compound was extracted by EtOAc (3 × 15 mL). The organic layer was separated, dried over anhyd. Na_2SO_4, and filtered and the filtrate was evaporated to dryness under reduced pressure to obtain a residue. The residual mass was purified over silica gel column to afford **7b**[7b] (0.98 g, 80%). ^{1}H NMR ($CDCl_3$) δ 2.51−2.55 (m, 1H), 2.71 (t, 1H, J = 4.6 Hz), 3.06−3.14 (m, 1H), 3.30−3.39 (m, 1H), 3.69 (dd, 1H, J = 3 Hz, 11.4 Hz), 4.41−4.60 (m, 2H), 7.14−7.35 (m, 5H). ^{13}C NMR δ 44.2 (CH_2), 50.8, 70.8 (CH_2), 73.3 (CH_2), 127.7, 128.4, 137.9 (C).

Compound 9 from 7a: A mixture of marcaptoethanol (0.85 mL, 11.9 mmol) and TMG (1.5 mL, 11.9 mmol) in DMF (20 mL) was heated at 90 °C for 30 min. The tosylate **7a** (2.0 g, 5.95 mmol) was added to this mixture and the mixture was heated at 90 °C under N_2. After 5 h, the reaction mixture was poured into a satd. solution of $NaHCO_3$ (30 mL) and the product was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhyd. Na_2SO_4 and filtered and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel column to obtain the sulfide **8** contaminated with an inseparable compound. A small amount of compound **8** was obtained in pure form. Eluent: EtOAc:petroleum ether (1:1). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 2.55 (br s, 1H), 2.62−2.67 (m, 1H), 2.74−2.78 (m, 3H), 2.89 (br s, 1H), 3.48−3.57 (m, 2H), 3.74−3.76 (m, 2H), 3.95 (br s, 1H), 4.56 (s, 2H), 7.29−7.38 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 35.9 (CH_2), 36.2 (CH_2), 61.3 (CH_2), 70.1, 73.1 (CH_2), 73.7 (CH_2), 128.0, 128.7, 128.4, 138.0. HRMS [ES^+, $(M + Na)^+$] for $C_{12}H_{18}O_3SNa$ obsd 265.0872, calcd 265.0874. To a well-stirred solution of the impure **8** (1.32 g) in dry MeOH (25 mL) was added MMPP (5.38 g, 11.89 mmol) and the mixture was stirred under N_2. After 6 h, MeOH was evaporated under reduced pressure and the residue thus obtained was dissolved in satd. $NaHCO_3$ solution (30 mL). The solution was washed with EtOAc (3 × 15 mL). Combined organic layers were dried over anhyd. Na_2SO_4 and filtered and the filtrate was concentrated under reduced pressure to obtain a residue. The residue was purified over silica gel to obtain sulfone **9** (1.27 g, 78%). Eluent: EtOAc:petroleum ether (3:2). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 2.99 (br s, 1H), 3.13 (d, J = 14.8 Hz, 1H), 3.21−3.36 (m, 1H), 3.39−3.54 (m, 5H), 4.08 (br s, 2H), 4.43 (br s, 1H), 4.52−4.58 (m, 2H), 7.30−7.46 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 56.2 (CH_2), 56.8 (CH_2), 57.9 (CH_2), 65.7, 72.6 (CH_2), 73.4 (CH_2), 127.8, 128.0, 128.5, 137.3. HRMS [ES^+, $(M + Na)^+$] for $C_{12}H_{18}O_5SNa$ obsd 297.0764, calcd 297.0773.

Compound 9 from 7b: A mixture of marcaptoethanol (2.6 mL, 36.58 mmol) and TMG (4.6 mL, 36.58 mmol) in DMF (20 mL) was heated at 90 °C for 30 min. The epoxide **7b** (3.0 g, 18.29 mmol) was added to this mixture and the mixture was heated at 90 °C under N_2. After 5 h, the reaction mixture was poured into a satd. solution of $NaHCO_3$ (60 mL) and the product was extracted with EtOAc (3 × 30 mL). The combined organic layers were dried over anhyd. Na_2SO_4 and filtered and the filtrate was concentrated under reduced pressure. The residue was purified over silica gel column to obtain the sulfide **8** contaminated with an inseparable compound. To a solution of the sulfide **8** (3.45 g) in dry MeOH (30 mL) was added MMPP (14.11 g, 28.52 mmol). Sulfone **9** was purified and isolated following the procedure described above. Yield: 3.17 g (81%).

Compound 10: To a well-stirred solution of **9** (0.4 g, 1.46 mmol) in pyridine (15 mL) was added a solution of MsCl (1.0 mL, 8.76 mmol) in pyridine (10 mL) dropwise at 0 °C under N_2 and the reaction mixture was kept at +4 °C. After 24 h, the reaction mixture was poured into ice-cold water and the solution was extracted with EtOAc (3 × 10 mL). Combined organic layers were dried over anhyd. Na_2SO_4 and filtered and the filtrate was concentrated under reduced pressure to obtain a residue. A solution of the residue in DCM (15 mL) was treated with triethylamine (0.5 mL, 2.92 mmol). After 15 h volatile matter was evaporated under reduced pressure and the residue was purified over silica gel to obtain compound **10** (0.31 g, 89%). Eluent: EtOAc:petroleum ether (1:4). Colorless liquid. ^{1}H NMR ($CDCl_3$; ^{1}H−^{1}H COSY) δ 4.23−4.24 (CH_2OBn, m, 2H), 4.58 (CH_2Ph, s, 2H), 6.07 (*cis*-CH=$CHSO_2$, d, J = 9.6 Hz, 1H), 6.40 (*trans*-CH=$CHSO_2$, d, J = 16.4 Hz, 1H), 6.59−6.61 ($CHSO_2CH$, m, 2H), 6.96 (CH_2CH=$CHSO_2$, dt, J = 15.2, 3.2 Hz, 1H), 7.30−7.39 (Ph, m, 5H). ^{13}C NMR ($CDCl_3$; ^{1}H−^{13}C HETCOR) δ 67.7 (CH_2OBn), 73.0 (CH_2Ph), 127.7 (Ph), 127.9 (Ph), 128.4 (CH_2CH=$CHSO_2$), 128.5 (Ph), 128.9 (CH_2=$CHSO_2$), 137.2 (4), 137.3 (CH_2=$CHSO_2$), 144.7 (CH_2CH=$CHSO_2$). HRMS [ES^+, $(M + Na)^+$] for $C_{12}H_{14}O_3SNa$ obsd 261.0572, calcd 261.0561.

Compound 11 from 7a: To a well-stirred solution of compound **7a** (2.0 g, 5.95 mmol) in methanol (15 mL) was added Na_2S (0.23 g, 2.97 mmol). The reaction mixture was heated under reflux. After 5 h, the reaction mixture was cooled and volatile matter was removed under reduced pressure. The residue was dissolved in satd. $NaHCO_3$ solution (30 mL) and the solution was washed with EtOAc (3 × 10 mL). Combined organic layers were dried over anhyd. Na_2SO_4 and filtered and the filtrate was concentrated under reduced pressure to obtain a residue. The residue was purified over silica gel to afford compound **11**

(1.68 g, 78%). Eluent: EtOAc:petroleum ether (1:1). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 2.63−2.68 (m, 2H), 2.75−2.80 (m, 2H), 3.01 (br s, 2H), 3.47−3.56 (m, 4H), 3.94 (br s, 2H), 4.55 (s, 4H), 7.28−7.37 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 36.4 (CH_2), 69.6, 69.8, 72.7 (CH_2), 73.4 (CH_2), 127.7, 127.8, 128.4, 137.7. HRMS [ES$^+$, $(M + H)^+$] for $C_{20}H_{27}O_4S$ obsd 363.1615, calcd 363.1630.

Compound 11 from 7b: To a well-stirred solution of compound **7b** (3.2 g, 19.51 mmol) in DMF (10 mL) was added Na_2S (0.76 g, 9.76 mmol). The reaction mixture was heated under reflux. After 13 h, the reaction mixture was cooled and satd. $NaHCO_3$ solution (30 mL) was added. The solution was washed with EtOAc (3 × 10 mL). Combined organic layers were dried over anhyd. Na_2SO_4 and filtered and the filtrate was concentrated under reduced pressure to obtain a residue. The residue was purified over silica gel to afford compound **11** (5.86 g, 83%).

Compound 12: Compound **11** (0.281 g, 0.77 mmol) was converted to **12** (0.28 g, 92%) following the procedure described for the synthesis of compound **9**. Eluent: EtOAc:petroleum ether (3:2). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 3.04−3.15 (m, 2H), 3.29−3.37 (m, 2H), 3.45−3.60 (m, 6H), 4.44 (br m, 2H), 4.56 (m, 4H), 7.30−7.38 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 57.8 (CH_2), 57.9 (CH_2), 65.6, 65.9, 72.4 (CH_2), 72.6 (CH_2), 73.4 (CH_2), 73.4 (CH_2), 127.7, 127.8, 127.9, 128.4, 128.5, 137.4. HRMS [ES$^+$, $(M + Na)^+$] for $C_{20}H_{26}O_6SNa$ obsd 417.1317, calcd 417.1348.

Compound 13: Compound **12** (0.15 g, 0.38 mmol) was converted to **13** (0.12 g, 88%) following the procedure described for the synthesis of compound **10**. Eluent: EtOAc:petroleum ether (1:4). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 4.22−4.23 (m, 4H), 4.58 (s, 4H), 6.60 (dt, J = 14.8, 2 Hz, 2H), 6.92 (dt, J = 15.2, 3.2 Hz, 2H), 7.30−7.39 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 67.6 (CH_2), 73.1 (CH_2), 127.7, 127.8, 128.5, 129.1, 137.2, 143.7. HRMS [ES$^+$, $(M + Na)^+$] for $C_{20}H_{22}O_4NaS$ obsd 381.1116, calcd 381.1137.

Compound 15: Compound **14** (0.5 g, 1.07 mmol) was converted to **15** (0.38 g, 95%) following the procedure described for the synthesis of compound **8**. Eluent: EtOAc:petroleum ether (1:1). Colorless liquid. $[\alpha]^{25.2}_D$ (+) 15.4 (*c* 0.10, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.49 (s, 3H), 2.42 (br s, 1H), 2.66−2.77 (m, 4H), 2.96 (dd, J = 3.2, 14.4 Hz, 1H), 3.73−3.75 (m, 2H), 4.07−4.11 (m, 3H), 4.56 (d, J = 11.6 Hz, 1H), 4.62 (d, J = 3.6 Hz, 1H), 4.73 (d, J = 12 Hz, 1H), 5.91 (d, J = 3.6 Hz, 1H), 7.30−7.39 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 26.2, 26.7, 35.6 (CH_2), 36.9 (CH_2), 60.9 (CH_2), 67.7, 72.2 (CH_2), 81.6, 82.2, 105.0, 111.8, 127.8, 128.1, 128.6, 137.2. HRMS [ES$^+$, $(M + Na)^+$] for $C_{18}H_{26}O_6SNa$ obsd 393.1329, calcd 393.1348.

Compound 16: Compound **15** (0.38 g, 1.02 mmol) was converted to **16** (0.35 g, 85%) following the procedure described for the synthesis of compound **9**. Eluent: EtOAc:petroleum ether (3:2). Semi solid. $[\alpha]^{25.2}_D$ (−)11.5 (*c* 0.79, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.48 (s, 3H), 2.62 (br s, 1H), 3.03 (br s, 1H), 3.23−3.39 (m, 3H), 3.49−3.59 (m, 1H), 4.08−4.09 (m, 4H), 4.52−4.55 (m, 2H), 4.63 (br d, J = 2.8 Hz, 1H), 4.73 (d, J = 12 Hz, 1H), 5.91 (br d, J = 2.8 Hz, 1H), 7.34−7.41 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 26.2, 26.7, 56.1 (CH_2), 56.8 (CH_2), 58.2 (CH_2), 64.5, 72.2 (CH_2), 81.1, 81.5, 82.1, 105.0, 112.0, 127.8, 128.2, 128.7, 137.0. HRMS [ES$^+$, $(M + Na)^+$] for $C_{18}H_{26}O_8SNa$ obsd 425.1227, calcd 425.1246.

Compound 17: Compound **16** (0.35 g, 0.87 mmol) was converted to **17** (0.28 g, 88%) following the procedure described for the synthesis of compound **10**. Eluent: EtOAc:petroleum ether (1:4). Colorless liquid. $[\alpha]^{25.2}_D$ (−)30.8 (*c* 1.94, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3H), 1.48 (s, 3H), 4.04 (s, 1H), 4.46 (d, J = 12 Hz, 1H), 4.61−4.66 (m, 2H), 4.88 (s, 1H), 5.98−6.02 (m, 2H), 6.36 (d, J = 16.8 Hz, 1H), 6.48−6.55 (m, 1H), 6.64 (d, J = 14.8 Hz, 1H), 6.92 (dd, J = 2.8, 15.2 Hz, 1H), 7.26−7.37 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 26.2, 26.8, 72.2 (CH_2), 78.7, 82.3, 82.5, 104.9, 112.2, 127.8, 128.2, 128.6, 128.8, 130.4 (CH_2), 136.7, 137.4, 141.8. HRMS [ES$^+$, $(M + Na)^+$] for $C_{18}H_{22}O_6SNa$ obsd 389.1010, calcd 389.1035.

Compound 18: Compound **14** (3.0 g, 6.46 mmol) was converted to **18** (1.64 g, 82%) following the procedure described for the synthesis of compound **11**. Eluent: EtOAc:petroleum ether (1:1). Colorless liquid. $[\alpha]^{25.2}_D$ (−)27.3 (*c* 4.70, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 6H), 1.48 (s, 6H), 2.68−2.73 (m, 2H), 2.98 (d, J = 13.6 Hz, 2H), 4.08 (s, 6H), 4.56−4.62 (m, 4H), 4.69 (d, J = 12 Hz, 2H), 5.89 (d, J = 3.6 Hz, 2H), 7.30−7.34 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 26.3, 26.8, 37.7 (CH_2), 67.7, 72.2 (CH_2), 81.5, 81.6, 82.3, 105.1, 111.8, 127.9, 128.1, 128.6, 137.2. HRMS [ES$^+$, $(M + H)^+$] for $C_{32}H_{43}O_{10}S$ obsd 619.2566, calcd 619.2577.

Compound 19: Compound **18** (1.43 g, 2.31 mmol) was converted to **19** (1.4 g, 93%) following the procedure described for the synthesis of compound **9**. Eluent: EtOAc:petroleum ether (3:2). Colorless solid. Mp 50 °C. $[\alpha]^{25.2}_D$ (−)25.6 (*c* 0.43, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 6H), 1.47 (s, 6H), 2.95 (d, J = 4.8 Hz, 2H), 3.38−3.48 (m, 4H), 4.04−4.07 (m, 4H), 4.52−4.61 (m, 6H), 4.70 (d, J = 11.6 Hz, 2H), 5.89 (d, J = 3.6 Hz, 2H), 7.30−7.37 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 26.2, 26.8, 58.4 (CH_2), 64.6, 72.2 (CH_2), 80.9, 81.3, 82.2, 105.1, 111.9, 127.9, 128.3, 128.7, 136.9. HRMS [ES$^+$, $(M + Na)^+$] for $C_{32}H_{42}O_{12}SNa$ obsd 673.2283, calcd 673.2295.

Compound 20*trans*: Compound **19** (0.83 g, 1.27 mmol) was converted to **20** (0.75 g, 96%) following the procedure described for the synthesis of compound **10**. The major compound of the mixture **20*trans*** was separated up to 46%. Eluent: EtOAc:petroleum ether (1:2). Crystalline solid. Mp 52 °C. $[\alpha]^{25.2}_D$ (+)21.3 (*c* 0.01, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 6H), 1.48 (s, 6H), 4.00 (d, J = 3.2 Hz, 2H), 4.46 (d, J = 12 Hz, 2H), 4.59−4.64 (m, 4H), 4.81 (br s, 2H), 5.96 (d, J = 3.6 Hz, 2H), 6.61 (dd, J = 1.6, 14.8 Hz, 2H), 6.88 (dd, J = 4, 15.2 Hz, 2H), 7.27−7.38 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 26.3, 26.9, 72.3 (CH_2), 78.8, 82.4, 82.7, 105.0, 112.2, 127.9, 128.2, 128.7, 131.2, 136.9, 140.9. HRMS [ES$^+$, $(M + Na)^+$] for $C_{32}H_{38}O_{10}SNa$ obsd 637.2075, calcd 637.2083.

Compound 21: Benzylamine (0.046 mL, 0.42 mmol) was added to a suspension of **10** (0.1 g, 0.42 mmol) in MeOH (15 mL) and the mixture was stirred at room temperature for 3 h. Volatile matter was removed under reduced pressure. The product was purified over silica gel to afford compound **21** (0.13 g, 90%). Eluent: EtOAc:petroleum ether (1:4). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 2.89−3.04 (m, 3H), 3.09−3.14 (m, 1H), 3.18−3.27 (m, 2H), 3.42−3.48 (m, 1H), 3.67 (d, J = 13.6 Hz, 1H), 3.70−3.74 (m, 1H), 3.77−3.81 (m, 1H), 3.87 (d, J = 13.6 Hz, 1H), 4.49−4.56 (m, 2H), 7.28−7.37 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 46.9 (CH_2), 49.2 (CH_2), 51.6 (CH_2), 55.1 (CH_2), 58.9, 68.9 (CH_2), 73.3 (CH_2), 127.5, 127.8, 127.9, 128.5, 128.5, 128.6, 137.5, 137.9. HRMS [ES$^+$, $(M + H)^+$] for $C_{19}H_{24}NO_3S$ obsd 346.1466, calcd 346.1477.

Compound 22: Compound **13** (0.09 g, 0.25 mmol) was converted to compound **22** (0.108 g, 92%) in 3 h following the procedure described for the synthesis of compound **21**. Eluent: EtOAc:petroleum ether (1:4). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 3.01−3.09 (m, 2H), 3.14−3.21 (m, 2H), 3.41−3.45 (m, 1H), 3.51−3.55 (m, 1H), 3.61 (br s, 1H), 3.67−3.69 (m, 1H), 3.74−3.76 (m, 1H), 3.80−3.84 (m, 1H), 3.89 (s, 1H), 4.04 (d, J = 14.4 Hz, 1H), 4.20 (d, J = 12 Hz, 1H), 4.29 (d, J = 12 Hz, 1H), 4.43−4.52 (m, 2H), 7.14−7.34 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 47.4 (CH_2), 48.9 (CH_2), 50.9 (CH_2), 55.1, 60.4, 69.6 (CH_2), 70.7 (CH_2), 73.1 (CH_2), 73.2 (CH_2), 126.8, 127.1, 127.4, 127.7, 127.8, 128.1, 128.2, 128.3, 128.4, 128.5, 137.6, 138.3, 140.7. HRMS [ES$^+$, $(M + H)^+$] for $C_{27}H_{32}NO_4S$ obsd 466.2031, calcd 466.2052.

Compound 23: Compound **17** (1.0 g, 2.7 mmol) was converted to compound **23** (1.25 g, 97%) in 5 h following the procedure described for the synthesis of compound **21**. Eluent: EtOAc:petroleum ether (1:3). Crystalline solid. Mp 124 °C. $[\alpha]^{25.2}_D$ (+)37.4 (*c* 0.10, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.52 (s, 3H), 2.78−2.81 (m, 1H), 2.94 (br s, 2H), 3.04−3.07 (m, 2H), 3.29−3.34 (m, 1H), 3.80−3.86 (m,

2H), 3.95−4.01 (m, 2H), 4.44 (d, J = 12 Hz, 1H), 4.67 (d, J = 3.2 Hz, 1H), 4.72 (d, J = 12 Hz, 1H), 4.90 (d, J = 9.2 Hz, 1H), 6.00 (s, 1H), 7.26−7.38 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 26.3, 26.9, 43.4 (CH_2), 49.9 (CH_2), 51.3 (CH_2), 56.7 (CH_2), 57.8, 71.4 (CH_2), 76.2, 81.2, 81.9, 105.0, 111.8, 127.3, 128.1, 128.3, 128.4 (2 × C), 128.5, 128.6, 128.7, 136.5, 138.6. HRMS [ES$^+$, $(M + Na)^+$] for $C_{25}H_{32}NO_6S$ obsd 474.1927, calcd 474.1950.

Compound 24: Ethanolamine (0.016 mL, 0.27 mmol) was added to a suspension of **17** (0.1 g, 0.27 mmol) in MeOH (15 mL) and the mixture was stirred at room temperature for 3 h. Volatile matter was removed under reduced pressure. The product was purified over silica gel to afford compound **24** (0.097 g, 83%). Eluent: EtOAc:petroleum ether (4:1). Colorless solid. Hygroscopic material. $[\alpha]^{25.2}_D$ (+)9.37 (c 0.10, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3H), 1.51 (s, 3H), 2.60−2.65 (m, 1H), 2.79−2.88 (m, 3H), 2.95 (br s, 3H), 3.26−3.29 (m, 1H), 3.58 (br s, 3H), 3.70−3.72 (m, 1H), 3.95 (s, 1H), 4.42 (d, J = 11.6 Hz, 1H), 4.64−4.74 (m, 3H), 5.94 (s, 1H), 7.32−7.39 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 26.3, 26.8, 46.1 (CH_2), 47.9 (CH_2), 48.7 (CH_2), 52.4 (CH_2), 57.5, 59.4 (CH_2), 71.5 (CH_2), 76.8, 80.7, 81.5, 104.8, 111.9, 128.2, 128.5, 128.7, 136.3. HRMS [ES$^+$, $(M + Na)^+$] for $C_{20}H_{30}NO_7S$ obsd 428.1747, calcd 428.1743.

Compound 25: To a solution of compound **23** (0.1 g, 0.21 mmol), 10% Pd/C (0.01 g) in MeOH, and ammonium formate (catalytic amount) was refluxed for an hour under H_2 atmosphere. The reaction mixture was cooled to room temperature. The suspension was filtered through a Celite bed and the bed was washed with MeOH. The filtrate was concentrate under vacuuo to give a thick viscous liquid. The residue was dissolved in water and the water layer was washed with $CHCl_3$. The $CHCl_3$ layers were pooled together, dried over anhyd. Na_2SO_4, and filtered and the filtrate was evaporated to dryness. The residue was purified over silica gel to give product **25** (0.07 g, 86%). Eluent: EtOAc:petroleum ether (2:3). Colorless solid. Mp 164 °C. $[\alpha]^{25.2}_D$ (−)16.3 (c 0.11, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.47 (s, 3H), 2.58−2.70 (m, 2H), 2.92−3.07 (m, 2H), 3.22−3.29 (m, 1H), 3.33−3.38 (m, 1H), 3.55−3.60 (m, 1H), 3.84 (d, J = 3.2 Hz, 1H), 3.96−3.99 (m, 1H), 4.41 (d, J = 12 Hz, 1H), 4.67 (d, J = 3.6 Hz, 1H), 4.75 (d, J = 12 Hz, 1H), 5.94 (d, J = 3.6 Hz, 1H), 7.34−7.44 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 26.2, 26.7, 43.6 (CH_2), 52.7 (CH_2), 53.7 (CH_2), 54.2, 71.6 (CH_2), 79.8, 81.1, 81.7, 104.9, 112.1, 128.6, 128.7, 128.9, 136.1. HRMS [ES$^+$, $(M + Na)^+$] for $C_{18}H_{26}NO_6S$ obsd 384.1466, calcd 384.1481.

Compound 26: Compound **20** (0.56 g, 0.91 mmol) was converted to compound **26** (0.64 g, 97%) in 48 h following the procedure described for the synthesis of compound **21**. Eluent: EtOAc:petroleum ether (1:2). Colorless solid. Mp 62 °C. $[\alpha]^{25.2}_D$ (−)52.3 (c 0.17, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 6H), 1.35 (s, 6H), 2.85−2.94 (m, 4H), 3.76 (d, J = 13.6 Hz, 1H), 3.89 (d, J = 2.0 Hz, 2H), 3.98 (br s, 2H), 4.10 (d, J = 14 Hz, 1H), 4.40 (d, J = 12 Hz, 4H), 4.56−4.59 (m, 4H), 5.93 (d, J = 3.6 Hz, 2H), 7.20−7.43 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 26.4, 26.7, 48.9 (CH_2), 51.5 (CH_2), 53.9, 71.2 (CH_2), 77.3, 81.2, 81.6, 104.9, 111.7, 127.2, 127.9, 128.2, 128.3, 128.7, 128.9, 136.7, 138.9. HRMS [ES$^+$, $(M + H)^+$] for $C_{39}H_{48}NO_{10}S$ obsd 722.2967, calcd 722.2999.

Compound 27: Hydrazine hydrate (0.016 mL, 0.32 mmol) was added to a suspension of **20** (0.2 g, 0.32 mmol) in MeOH (25 mL) and the mixture was stirred at room temperature for 6 h. Volatile matter was removed under reduced pressure. The product was purified over silica gel to afford compound **27** (0.17 g, 81%). Eluent: EtOAc:petroleum ether (1:4). Colorless solid. Mp 74 °C. $[\alpha]^{25.2}_D$ (−)17.1 (c 0.70, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.33 (s, 3H), 1.48 (s, 3H), 1.49 (s, 3H), 2.65 (d, J = 13.6 Hz, 1H), 2.77−2.83 (m, 1H), 3.26−3.31 (m, 2H), 3.42−3.46 (m, 1H), 3.52−3.58 (m, 1H), 3.65−3.71 (m, 1H), 3.76 (s, 1H), 3.84 (d, J = 9.2 Hz, 1H), 4.02−4.15 (m, 2H), 4.41 (d, J = 11.6 Hz, 1H), 4.53−4.74 (m, 4H), 5.85 (s, 1H), 5.94 (s, 1H), 7.26−7.43 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 26.0, 26.1, 26.6, 26.7, 50.5, 56.6 (CH_2), 57.2 (CH_2), 57.7, 71.6 (CH_2), 72.4 (CH_2), 79.6, 79.7, 81.3, 81.6, 81.9, 82.0, 104.8, 105.1, 111.5, 112.1, 127.6, 127.9, 128.0, 128.3, 128.4, 128.5, 128.7, 128.9, 135.9, 137.4. HRMS [ES$^+$, $(M + H)^+$] for $C_{32}H_{43}N_2O_{10}S$ obsd 647.2640, calcd 647.2638.

Compound 28: CBr_2F_2 (1 mL) was dropwise added to a vigorously stirred mixture of the sulfone **23** (0.1 g, 0.21 mmol), alumina-supported KOH (2 g), ^{t}BuOH (20 mL), and DCM (10 mL) kept at 5−10 °C. The reaction mixture was stirred at room temperature for an additional 1 h after which the solid catalyst was removed by suction filtration through a Celite bed. The filtrate was evaporated to dryness. The filter cake was washed thoroughly with DCM and the washes were combined with the residue from the first filtrate. The resultant organic solution was washed with brine and water, dried, and evaporated. The residue was purified on silica gel to obtain compound **27** (0.028 g, 33%). Eluent: EtOAc: petroleum ether (1:4). Colorless liquid. ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.51 (s, 3H), 3.20−3.28 (m, 1H), 3.55−3.67 (m, 2H), 3.94 (br s, 1H), 4.12 (br m, 2H), 4.39−4.51 (m, 2H), 4.62−4.75 (m, 2H), 5.39 (d, J = 6.6 Hz, 1H), 5.77 (d, J = 6.3 Hz, 1H), 6.01 (d, J = 3.9 Hz, 1H), 7.21−7.39 (m, 10H). ^{13}C NMR ($CDCl_3$) δ 26.3, 26.7, 59.8, 60.4, 69.7, 71.7, 81.6, 82.8, 85.1, 105.2, 111.4, 126.6, 127.4, 127.9, 128.0, 128.1, 128.5, 128.9, 129.4, 137.3. HRMS [ES$^+$, $(M + H)^+$] for $C_{25}H_{30}NO_4$ obsd 408.2143, calcd 408.2175.

Compound 30: A solution of compound **23** (0.2 g, 0.42 mmol) in 10 mL of aqueous 90% CF_3CO_2H was stirred for an hour at 0 °C. It was allowed to come to room temperature within this time. Then this reaction mixture was coevaporated with toluene to afford a syrupy residue, which was immediately used for the next reaction. A solution of this crude material, 10% Pd/C (0.01 g), and ammonium formate (catalytic amount) in MeOH (15 mL) was heated under reflux for an hour under H_2 atmosphere. The reaction mixture was brought to room temperature, the suspension was filtered through a Celite bed and washed with MeOH, and the filtrate was concentrated to give a thick viscous liquid containing compound **29**. The residue was dissolved in pyridine (10 mL) and acetic anhydride (0.2 mL, 2.1 mmol) was added. After 6 h, the reaction mixture was poured into ice-cold water and an aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhydr. Na_2SO_4 and filtered and the filtrate was concentrated under reduced pressure to obtain a residue. The residue was purified over silica gel to afford the product **30** (0.059 g, 34%). Eluent: EtOAc:petroleum ether (1:4). Crystalline solid. Mp 196 °C. $[\alpha]^{25.2}_D$ (+)32.1 (c 0.12, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ 2.10 (s, 3H), 2.11 (s, 3H), 2.80−2.84 (m, 2H), 2.92−2.98 (m, 3H), 3.12−3.23 (m, 2H), 3.29−3.39 (m, 2H), 3.63−3.65 (m, 1H), 4.68 (s, 2H), 4.88 (br s, 1H), 4.98 (d, J = 2.8 Hz, 1H), 7.26−7.39 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 20.9, 21.3, 49.9 (CH_2), 51.0 (CH_2), 52.1 (CH_2), 52.9 (CH_2), 56.3, 68.4, 70.4, 71.2, 72.9 (CH_2), 127.7, 128.1, 128.6, 137.1, 169.8, 170.2. HRMS [ES$^+$, $(M + Na)^+$] for $C_{19}H_{26}NO_7S$ obsd 412.1407, calcd 412.1430.

■ ASSOCIATED CONTENT

Supporting Information. General methods, full spectroscopic data of all new compounds, and ORTEPs and CIF files of compounds **20*trans***, **23** and **30**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: tpathak@chem.iitkgp.ernet.in.

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