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Formal Total Synthesis of (–)-Raphidecursinol B[‡]

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An efficient enantioselective formal total synthesis of antimalarial natural product (–)-raphidecursinol B along with its all stereoisomers is described from commercially available 3,4,5-trimethoxybenzaldehyde using the Sharpless asymmetric dihydroxylation, regioselective α-tosylation, epoxide opening and Mitsunobu reaction as the key reaction steps.

Introduction

Optically active 3-arylpropane-1,2-diols are often found as parts of various natural products[1] and serve as important building blocks for different pharmaceuticals and fine chemicals.[2] They are also found in 8,4′-oxyneolignan series, having a wide range of biological effects, viz. anticercaria penetration, inhibition of the growth of silkworm larvae, antileukemic, antifungal, antileishmanial etc.[3,4] This kind of neolignan is structurally comparable to the major interunit linkage of lignin, out of which about 40% of the arylpropane units are 8-*O*-4′-linked.[5] Diverse naturally occurring members of the subgroup 8,4′-oxyneolignan, such as raphidecursinol B (**1**),[6] polysphorin (**2**),[6b] virolin (**3**),[7] surinamensin (**4**),[4,7] were isolated from Myristicaceae and other primitive plant families in neotropical regions and display interesting and varied biological properties[4,6b,8–12] (Figure 1).

The antimalarial properties of these compounds are of prime importance. In continuation of our on going research programme in developing new antimalarial therapeutic agents,[13,14] the present manuscript describes a formal total synthesis of antimalarial natural product (–)-raphidecursinol B, (–)-**1**.

(–)-Raphidecursinol B belongs to the subgroup 8,4′-oxyneolignan and was first isolated from the leaves and stems extracts of *Rhaphidophora decursiva* Schott (Araceae), a perennial, evergreen, semisucculent epiphytic vine found in the Cuc Phuong National Park (Nho quan District, Ninh Binh Province, Vietnam)[1b] and was found to be active against *Plasmodium falciparum*,[1b,15] the parasite responsible for the most severe form of malaria,[16] with no apparent toxicity.[1b] The structural investigation of this newly isolated oxyneolignan reveals that it is composed of a propanediol backbone equipped with highly substituted aryl and aryloxy components.[17]

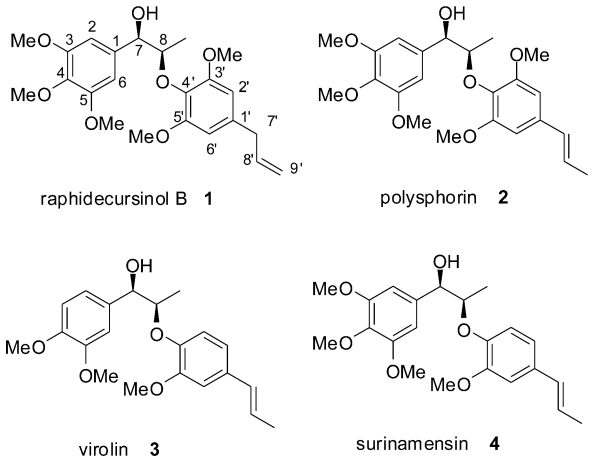

Figure 1. Representative members of the 8,4′-oxyneolignan family.

Results and Discussion

Although there are several reports in the literature describing the racemic synthesis of both *syn*- and *anti*-8,4′-oxyneolignan natural products,[3,4,7,11a,18,19] less attention has been payed to their stereoselective sythesis. In 2003, Lee et al. developed a general route to synthesize both enantiomers of polysphorin using polymer-supported reagents and scavengers.[15] Recently, Curti et al. described enantioselective synthesis of (–)-raphidecursinol B [(–)-**1**], along with (–)-polysphorine (**2**), (–)-viroline (**3**) and some related variant using (*S*)- or (*R*)-methyl lactate as the source of chirality.[17] Herein, we describe enantioselective syntheses of important advanced intermediates **15**, **19**, **28** and **30** which could allow the complete synthesis of all the setereisomers of raphidecursinol B.

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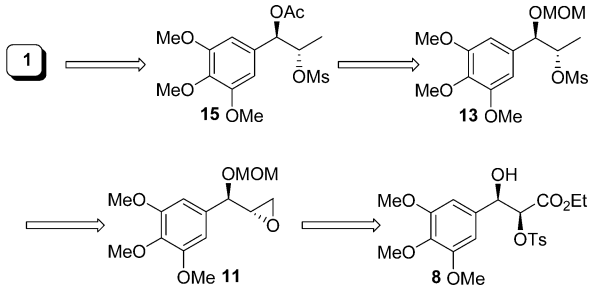
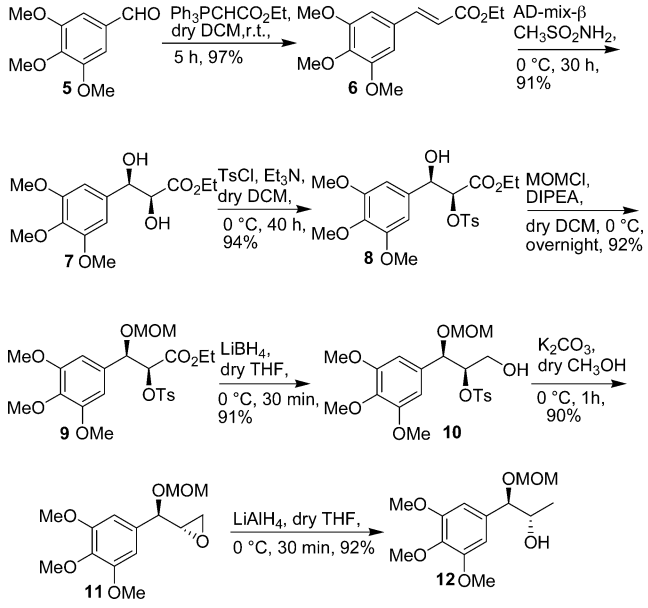
Retrosynthetic analysis suggests that advanced intermediate **15** required for the synthesis of natural product **1** (Scheme 1) could be accessed from **13** which, in turn, could be synthesizeded from epoxide **11**. Epoxide **11** was made from the β-hydroxy-α-tosyloxy ester **8**.



Scheme 1. Retrosynthetic analysis of **1**.

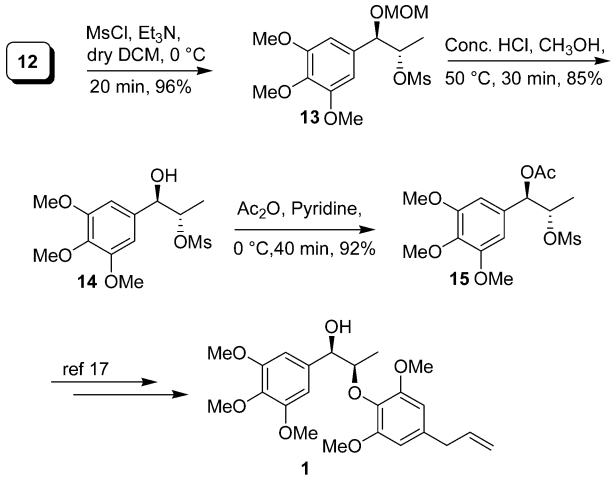
Our synthesis started with commercially available 3,4,5-trimethoxybenzaldehyde **5**, which was first converted into *trans*-cinnamate ester **6** by Wittig olefination with (ethoxycarbonylmethylene)triphenylphosphorane in dry CH_2Cl_2 at room temperature in 97% yield. **6** was then subjected to Sharpless asymmetric dihydroxylation reaction with AD-mix-β in *t*BuOH/H_2O (1:1) at 0 °C for 30 h giving enantiopure dihydroxy derivative **7** in excellent yield (91%) and with high enantiomeric excess (*ee* >99%, as determined by chiral HPLC measurements). In the next step, conversion of dihydroxy ester **7** into β-hydroxy-α-tosyloxy ester **8** was achieved by the regioselective α-tosylation[20] in presence of TsCl/Et_3N in dry CH_2Cl_2 at 0 °C for 40 h (94%) (Scheme 2). Free secondary alcohol **8** was then protected as MOM ether under standard conditions with MOMCl/DIPEA at 0 °C to furnish **9** in 92% yield. At this stage, $LiAlH_4$-mediated one-pot conversion of compound **9** into monoprotected alcohol **12** employing Huang's method[21] was not successful and gave rise to inseparable complex



Scheme 2. Synthesis of monoprotected alcohol **12**.

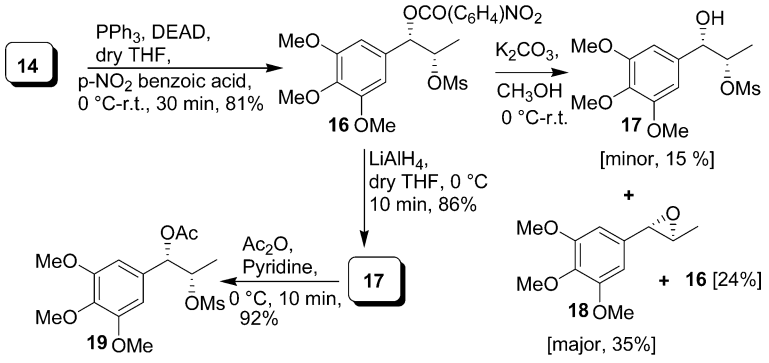
product mixture only. Also, conversion of compound **9** into MOM-protected epoxide **11** using Yadav's $NaBH_4$-meadiated one-pot ester reduction–epoxide formation method[22] was attempted which resulted in recovery of majority of starting material together with trace amount of the corresponding ester-reduced product. We were pleased to observe that treatment of **9** with $LiBH_4$ in dry THF at 0 °C provided the corresponding ester-reduced product **10** which, was treated in the next step with K_2CO_3 in dry methanol to furnish epoxide **11**. The last two steps were very efficient which accounted for high two-step overall yield (82%) and subsequent regioselective epoxide opening of **11** by $LiAlH_4$ at 0 °C afforded **12** in 92% yield.

In the next step, the secondary alcohol **12** was converted into mesyl derivative **13** in presence of MsCl/Et_3N at 0 °C (96%) and MOM ether was cleaved with concd. HCl in methanol at 50 °C in 30 min to furnish free alcohol **14** in 85% yield, which was then acylated using Ac_2O/Py to provide **15** (92%) (Scheme 3). Compound **15** was fully characterised by incisive analysis and analytical/spectroscopic data which were comparable to that reported in the literature by Curti et al.[17] {($[\alpha]_D^{22}$ = –40.5 (*c* = 0.8, $CHCl_3$); lit. $[\alpha]_D^{25}$ = –41.6 (*c* = 0.8, $CHCl_3$)}. Thus, starting from a commercially available material, a formal total synthesis of (–)-**1** was achieved in excellent overall yield (43%) for the nine-step sequence.



Scheme 3. Synthesis of compound **1**.

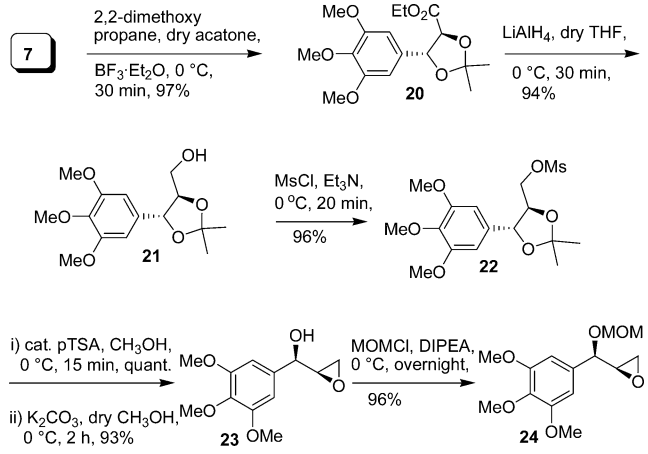
After completion of synthesis of advanced intermediate **15**, we investigated to synthesize the C-3 epimer of compound **15** and to perform that synthesis, the remaining task was to invert the stereochemistry at C-3 centre followed by acetylation of the alcohol with opposite stereochemistry. The stereoinversion at C-3 centre was examined by the Mitsunobu reaction (PPh_3, DEAD and *p*-nitro benzoic acid) followed by saponification (K_2CO_3/CH_3OH). In this two step sequences, the first step went very well but the base-catalyzed conventional hydrolysis in the second step was found to be problematic. When the hydrolysis was carried out by using 5 equiv. K_2CO_3 in dry CH_3OH in 10 min (when starting material was completely consumed), we were not able to isolate the desired product **17**, instead the prod-



Scheme 4. Synthesis of C-3 epimer **19** of compound **15**.

uct isolated was the epoxide **18** (undesired product, 72%). When the same reaction was carried out with only 1 equiv. of K_2CO_3 and the reaction time was reduced to 5 min, the desired product **17** was isolated in very poor yield (15%) along with undesired epoxide **18** (35%) and also unreacted starting material **16** (24%). The epoxide **18** was formed due to intramolecular nucleophilic substitution reaction by the alkoxide nucleophile generated in situ in presence of K_2CO_3 in the reaction medium. Next, we performed the same reaction in mild condition using $LiOH·H_2O$ as base. But the result was same as in the earlier case. Then we thought to apply the Schotten–Baumann reaction condition (biphasic solvent system) using K_2CO_3 as base in a combined solvent system (water/CH_2Cl_2, 1:1) so that once the product (**17**) formed would come into organic solvent and the base (K_2CO_3) should remain in water and thus preventing further epoxidation but in the present case reaction did not proceed at all and starting material was recovered as such. Subsequently, the troublesome ester hydrolysis was circumvented by switching to reductive cleavage of the ester linkage by means of $LiAlH_4$. Gratifyingly, $LiAlH_4$-mediated (1.0 equiv.) reductive cleavage of the ester linkage in dry THF within 10 min provided exclusively the desired product **17** in very good yield (86%) and finally, the so formed secondary alcohol was acetylated using Ac_2O/pyridine providing the desired product **19** (92%) in 10 min in good overall yield (30%) from compound **6** after 11 steps (Scheme 4).

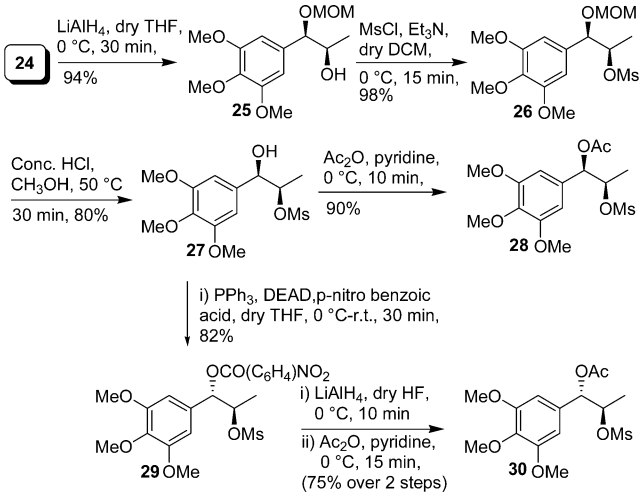
Now, to synthesize the C-2 epimer of compound **15**, from which C-8 epimer of (–)-raphidecursinol B could be achieved, we first protected the *syn* dihydroxy ester **7** as acetonide **20** in almost quantitative yield (97%) in the presence of 2,2-dimethoxypropane in dry acetone and $BF_3·Et_2O$ as catalyst at 0 °C in 30 min. In the next step, this acetonide-protected ester **20** was subjected to $LiAlH_4$-mediated reduction in dry THF at 0 °C to furnish alcohol **21** in very good yield (94%), which was then activated as the corresponding mesylate **22** as colourless solid in 96% yield by treating with MsCl/Et_3N in dry CH_2Cl_2 at 0 °C. With the activated mesylate **22** in our hand, to obtain the chiral epoxy alcohol **23**, we first cleaved the acetonide protecting group quantitatively by using catalytic amounts of *p*TSA/CH_3OH at 0 °C in 15 min and then the resulting diol was stirred vigorously in dry methanol in presence of K_2CO_3 for 2 h affording the requisite epoxy alcohol **23** as the sole product with excellent yield (93%). After achieving this epoxy alcohol **23**, it was again protected as MOM ether to furnish the MOM-protected epoxide **24** in chirally pure form under standard condition using MOMCl/Hünig's base in dry CH_2Cl_2 at 0 °C to room temperature for overnight under innert atmosphere with excellent yield (96%) (Scheme 5).



Scheme 5. Synthesis of chiral epoxide **24**.

With the epoxide **24** in our hand, we opened the epoxide ring regioselectively by $LiAlH_4$ at 0 °C as described earlier for **12** to afford secondary alcohol **25** in very good yield (94%) and derived alcohol **25** was then activated as mesylate **26** by using MsCl/Et_3N in dry CH_2Cl_2 at 0 °C in almost quantitative yield (98%). In the next step, concd. HCl/CH_3OH-mediated MOM cleavage transformed **26** into secondary alcohol **27** (80%) and subsequent acetylation of the free alcohol **27** was carried out with Ac_2O/Py at 0 °C providing the desired C-2 epimer **28** of compound **15** in 90% yield as white solid and 54% over all yield from **7** after 10 steps (Scheme 6).

Finally, to accomplish the synthesis of the fourth stereoisomer (enantiomer) of **15**, the remaining task was to invert the stereochemistry at C-3 centre of **27** through a intermediate **29** (Mitsunobu product) followed by acetylation of the alcohol intermediate. Inverted stereochemistry of the corresponding chiral centre (C-3) was installed by a combination



Scheme 6. Synthesis of compound **28** and **30**.

of Mitsunobu reaction/reductive cleavage of the ester linkage as described earlier in the case of **17** and thus providing the required stereoisomer **30** in good overall yield (37%) from 7 after 11 steps (Scheme 6).

Conclusions

In summary, we have disclosed a concise, efficient, enantioselective formal total synthesis of (–)-raphidecursinol B along with all other stereoisomers of compound **15** in enantiomerically pure form using Sharpless asymmetric dihydroxylation as the source of chirality from commercially available 3,4,5-trimethoxybenzaldehyde. Furthermore, regioselective α-tosylation of **7**, regioselective epoxide opening and a combination of Mitsunobu reaction/reductive cleavage have been employed very efficiently providing the corresponding advanced intermediates in respective cases. Our synthetic strategy provides not only all stereoisomers of (–)-raphidecursinol B, but may furnish related natural products, viz. polysphorin (**2**),[6b] virolin (**3**),[7] surinamensin (**4**),[4,7] as well.

Experimental Section

General Methods: Organic solvents were dried by standard methods. All the products were characterized by ^{1}H, ^{13}C, IR, ESI-MS, and EI-HRMS (C, H, O). Analytical TLC was performed with 2.5 × 5 cm plates coated with silica gel (60F-254, 0.25 mm thickness), visualization was accomplished with iodine and under UV light and with $CeSO_4$ (1% in 2.0 N H_2SO_4) and subsequent charring on a hot plate. Column chromatography was performed using silica gel (100–200 mesh). NMR spectra were recorded on Bruker Avance 300 MHz. Spectrometer at 300 MHz (^{1}H) and 75 MHz (^{13}C). Experiments were recorded in $CDCl_3$ at 25 °C. Chemical shifts are given on the δ scale and are referenced to the TMS signal at δ = 0.00 ppm for proton and 0.00 ppm for carbon NMR. For ^{13}C NMR reference the $CDCl_3$ signal at δ = 77.00 ppm was used. IR spectra were recorded on Perkin–Elmer 881 and FTIR-8210 PC Shimadzu Spectrophotometers. Mass spectra were recorded on a JEOL JMS-600H high resolution spectrometer using EI mode at 70 eV. Optical rotations were determined on an Autopol III polarimeter using a 1-dm cell at 22 °C in methanol as the solvent; concentrations are given in g/100 mL units.

Dihydroxy Ester 7: To a stirred solution of *tert*-butyl alcohol (110 mL) and water (110 mL) were added AD-mix-β (31.5 g), and methanesulfonamide (2.14 g, 22.5 mmol) at room temperature. The mixture was vigorously stirred at room temperature until both phases were clear and then cooled to 0 °C. A solution of cinnamate ester **6** (6.0 g, 22.5 mmol) in *tert*-butyl alcohol (10 mL) was added at 0 °C. The reaction mixture was stirred at the same temperature for 30 h. The reaction was quenched at 0 °C by the addition of sodium sulfite (33.7 g, 267 mmol), warmed to room temperature, and further stirred for 1 h. The reaction mixture was extracted with EtOAc (3 × 100 mL). The combined organic layer was washed with aqueous 2 N KOH solution (100 mL), water (100 mL), and brine (100 mL). The organic layer was dried with anhydrous Na_2SO_4, filtered, and then concentrated in vacuo. Purification of the crude product by silica gel column chromatography (2% $CH_3OH/CHCl_3$) afforded **7** (6.2 g, 91%) as colourless liquid. $[\alpha]_D^{22}$ = –13.1 (*c* = 1.44, CH_3OH). R_f = 0.40 (4% $CH_3OH/CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.47 (s, 2 H, ArH), 4.73 (br. s, 1 H), 4.15–4.08 (m, 3 H), 3.73 (s, 6 H), 3.69 (s, 3 H), 3.57 (d, *J* = 6.15 Hz, 1 H), 2.36 (br. s, 1 H), 1.17 (t, *J* = 7.14 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 172.5, 152.9, 137.3, 135.8, 103.4, 96.1, 74.9, 74.6, 61.6, 60.5, 55.8, 14 ppm. IR (neat): $\tilde{\nu}$ = 3451, 3020, 2362, 1732, 1217, 762, 670 cm^{-1}. ESI-MS: *m*/*z* (%) = 300.2 (100) $[M]^+$. $C_{14}H_{20}O_7$ (300.31): calcd. C 55.99, H 6.71; found C 55.87, H 6.77.

Tosylate 8: To an ice-cooled solution of compound **7** (3.4 gm, 11.0 mmol) in dry CH_2Cl_2 (30 mL), Et_3N (2.7 mL, 19.8 mmol) was added at 0 °C followed by addition of TsCl (2.4 g, 12.4 mmol). Then the reaction mixture was kept in freeze for 30 h. After completion of the reaction, water was added, the organic layerwas separated, and the aqueous phase was extracted thrice with CH_2Cl_2 (3 × 100 mL). The combined organic layer was washed with brine, dried with anhydrous Na_2SO_4, filtered and then concentrated under reduced pressure to obtain yellow crude product. The crude product was purified over silica gel column chromatography to furnish **8** (4.8 g, 94%) as colourless solid, m.p. 122 °C. $[\alpha]_D^{22}$ = –83.8 (*c* = 0.55, CH_3OH). R_f = 0.42 (60% EtOAc/hexane). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.45 (d, *J* = 8.2 Hz, 2 H, ArH), 7.13 (d, *J* = 8.1 Hz, 2 H, ArH), 6.35 (s, 2 H, ArH), 4.98 (t, *J* = 5.0 Hz, 1 H), 4.79 (d, *J* = 4.0 Hz, 1 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 3.73 (s, 3 H), 3.69 (s, 6 H), 2.34 (s, 3 H), 1.09 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 166.9, 153.0, 145.2, 137.8, 133.0, 132.4, 129.5, 127.7, 103.0, 81.1, 73.6, 62.1, 60.7, 55.9, 21.5, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 3452, 2947, 2363, 1761, 1593, 1367, 1198, 1101, 1037, 917, 844, 660, 547 cm^{-1}. ESI-MS: *m*/*z* (%) = 477.0 (30) $[M + Na]^+$, 436.9 (100) $[M – H_2O]^+$. $C_{21}H_{26}O_9S$ (454.49): calcd. C 55.50, H 5.77; found C 55.55, H 5.85.

Compound 9: To an ice-cooled solution of compound **8** (1.0 g, 2.2 mmol) in dry CH_2Cl_2 (10 mL), DIPEA (1.9 mL, 11.0 mmol) was added at 0 °C under N_2 atmosphere. After 2 min MOMCl (0.4 mL, 5.5 mmol) was added and the reaction mixture was allowed to stir at room temperature for 10 min, and then at 50 °C for 1 h. After completion of the reaction, water was added, organic layer was separated and aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was washed with brine (50 mL), dried with anhydrous Na_2SO_4, filtered and then concentrated under reduced pressure to obtain reddish crude product. This crude product was purified over silica gel column chromatography by 30% EtOAc/hexane as an eluent to furnish the pure compound **9** (1.0 g, 92%) as colourless solid, m.p. 224–225 °C. $[\alpha]_D^{22}$ =

–101.2 (c = 0.74, CH_3OH). R_f = 0.50 (60% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.50 (d, J = 8.2 Hz, 2 H, ArH), 7.18 (d, J = 8.0 Hz, 2 H, ArH), 6.42 (s, 2 H, ArH), 5.05 (d, J = 3.8 Hz, 1 H), 4.91 (d, J = 3.9 Hz, 1 H), 4.56–4.50 (m, 2 H), 4.14 (q, J = 7.1 Hz, 2 H), 3.82 (s, 3 H), 3.75 (s, 6 H), 3.30 (s, 3 H), 1.20 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 166.7, 152.9, 144.9, 137.7, 132.5, 130.3, 129.3, 127.5, 103.9, 93.9, 80.7, 76.2, 62.0, 60.5, 55.7, 21.4, 13.7 ppm. IR (neat): $\tilde{\nu}$ = 2941, 2363, 1771, 1596, 1368, 1192, 1124, 1036, 841, 553 cm^{-1}. ESI-MS: m/z (%) = 499.6 (100) $[M + H]^+$. $C_{23}H_{30}O_{10}S$ (498.54): calcd. C 55.41, H 6.07; found C 55.32, H 6.17.

Alcohol 10: To an ice-cooled solution of compound **9** (1.0 g, 2.0 mmol) in dry THF (20 mL) in a 100 mL round-bottomed flask fitted with a $CaCl_2$ guard tube, 2 M $LiBH_4$ in THF (1.5 mL, 3.0 mmol) was added. The reaction mixture was allowed to stir at the same temperature for 30 min. After completion of the reaction, water was added to it, organic phase was separated and the aqueous phase was extracted thrice with EtOAc (3 × 100 mL). The combined organic layer was washed with brine (50 mL), dried with anhydrous Na_2SO_4, filtered and concentrated under vacuo to afford white crude product. This crude product was chromatographed over silca gel, 50% EtOAc/hexane as an eluent, to furnish the alcohol **10** (0.85 g, 91%) as colourless oil. $[\alpha]_D^{29}$ = –81.2 (c = 1.24, CH_3OH). R_f = 0.31 (60% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.64 (d, J = 8.1 Hz, 2 H, ArH), 7.25 (d, J = 8.1 Hz, 2 H, ArH), 6.43 (s, 2 H, ArH), 4.88–4.45 (m, 5 H), 3.83 (s, 3 H), 3.78 (s, 6 H), 3.73–3.64 (m, 1 H), 3.42–3.34 (m, 1 H), 3.27 (s, 3 H), 2.43 (s, 3 H) ppm. IR (neat): $\tilde{\nu}$ = 3661, 3633, 3449, 2926, 2361, 1679, 1208, 1107, 760, 671 cm^{-1}. ESI-MS: m/z (%) = 457.6 (100) $[M + H]^+$. $C_{21}H_{28}O_9S$ (456.51): calcd. C 55.25, H 6.18; found C 55.39, H 6.02.

Epoxide 11: To an ice-cooled solution of the previously prepared alcohol **10** (1.0 g, 2.1 mmol) in dry methanol (30 mL) in a 100 mL round-bottomed flask fitted with a $CaCl_2$-guard tube, anhydrous K_2CO_3 (580.1 mg, 4.2 mmol) was added and allowed to stir at room temperature for 2 h. After completion of the reaction, methanol was removed under reduced pressure, water was added and aqueous part was extracted thrice with EtOAc (3 × 100 mL). The combined organic layer was washed with brine (50 mL), dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to a colourless residue. The crude product was purified over silica gel column chromatography (30% EtOAc/hexane) to furnish **11** (0.56 g, 90%) as colourless oil. $[\alpha]_D^{29}$ = –44.5 (c = 0.88, CH_3OH). R_f = 0.50 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.60 (s, 2 H, ArH), 4.63 (dd, J_1 = 12.2, J_2 = 6.6 Hz, 2 H), 3.87 (s, 6 H), 3.84 (s, 3 H), 3.38 (s, 3 H), 3.17 (dd, J_1 = 6.45, J_2 = 3.8 Hz, 1 H), 2.83–2.77 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.3, 137.8, 133.7, 104.2, 94.5, 76.6, 60.8, 56.1, 55.5, 54.1, 45.2 ppm. IR (neat): $\tilde{\nu}$ = 3661, 3633, 3019, 2930, 2361, 1679, 1214, 1104, 760, 671 cm^{-1}. ESI-MS: m/z (%) = 285.3 (100) $[M]^+$. $C_{14}H_{20}O_6$ (284.31): calcd. C 59.14, H 7.09; found C 59.21, H 7.02.

Alcohol 12: To an ice-cooled solution of compound **11** (0.5 g, 1.7 mmol) in dry THF (10 mL), LAH (83.6 mg, 2.2 mmol) was added and allowed to stir at room temperature for 30 min. After completion of the reaction, it was quenched with drop by drop addition of cold NH_4Cl solution and then the organic layer was extracted with EtOAc (3 × 50 mL). The combined organic layer was washed with brine, dried with anhydrous Na_2SO_4, filtered and then concentrated under reduced pressure to obtain colourless crude oil. This crude product was purified by column chromatography (40% ethyl acetate/hexane) to furnish **12** (463.5 mg, 92%) as colourless oil. $[\alpha]_D^{29}$ = –91.8 (c = 0.12, CH_3OH). R_f = 0.35 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.57 (s, 2 H, ArH), 4.60 (s, 2 H), 4.40 (d, J = 5.4 Hz, 1 H), 3.94 (s, 1 H), 3.86 (s, 6 H), 3.84 (s, 3 H), 3.41 (s, 3 H), 2.05 (s, 1 H), 1.21 (d, J = 6.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.1, 137.4, 133.7, 104.4, 94.5, 82.3, 70.6, 60.7, 56.0, 55.7, 18.4 ppm. IR (neat): $\tilde{\nu}$ = 3444, 1637, 1128, 770 cm^{-1}. ESI-MS: m/z (%) = 287.2 (46) $[M + H]^+$, 268.3 (100) $[M – H_2O]^+$. $C_{14}H_{22}O_6$ (286.32): calcd. C 58.73, H 7.74; found C 58.81, H 7.64.

Mesylate 13: To an ice-cooled solution of compound **12** (0.2 g, 0.7 mmol) in dry CH_2Cl_2 (5 mL), Et_3N (0.3 mL, 2.1 mmol) was added followed by methanesulfonyl chloride (0.08 mL, 1.0 mmol) and the reaction mixture was stirred at 0 °C for 1.5 h. After completion of the reaction, water was added, organic layer was separated and the aqueous layer was extracted thrice with CH_2Cl_2 (3 × 25 mL). The combined organic layer was washed with brine (25 mL), dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to a yellow coloured crude product. This crude product was purified over silica gel column (25% EtOAc/hexane) to furnish **13** (0.24 mg, 95%) as colourless oil. $[\alpha]_D^{22}$ = –46.4 (c = 0.87, CH_3OH). R_f = 0.35 (40% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.58 (s, 2 H), 4.87–4.83 (m, 1 H), 4.67 (d, J = 4.9 Hz, 1 H), 4.61 (s, 2 H), 3.86 (s, 6 H), 3.83 (s, 3 H), 3.41 (s, 3 H), 2.74 (s, 3 H), 1.44 (d, J = 5.9 4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.2, 138.0, 132.6, 104.6, 94.3, 81.4, 78.8, 60.7, 56.1, 55.8, 38.0, 16.9 ppm. IR (neat): $\tilde{\nu}$ = 2369, 1636, 1461, 1349, 1126, 770 cm^{-1}. ESI-MS: m/z (%) = 365.2 (100) $[M + H]^+$. $C_{15}H_{24}O_8S$ (364.41): calcd. C 49.44, H 6.64; found C 49.54, H 6.58.

Alcohol 14: To an ice-cooled solution of compound **13** (100.0 mg, 0.2 mmol) in CH_3OH (2 mL), concd. HCl (0.5 mL) was added drop by drop. The reaction mixture was heated at 50 °C for 30 min and then it was neutralized by saturated $NaHCO_3$ solution. The organic layer was extracted thrice with EtOAc (3 × 10 mL), dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was then purified (30% EtOAc/hexane) over silica gel column to furnish **14** (74.0 mg, 85%) as colourless oil. $[\alpha]_D^{22}$ = –8.8 (c = 0.56, CH_3OH). R_f = 0.35 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.60 (s, 2 H), 4.92–4.88 (m, 2 H), 3.86 (s, 6 H), 3.83 (s, 3 H), 2.90 (s, 3 H), 2.33 (br., 1 H), 1.35 (d, J = 6.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.2, 137.7, 134.6, 103.5, 83.3, 75.4, 60.8, 56.1, 38.4, 15.3 ppm. IR (neat): $\tilde{\nu}$ = 3434, 2360, 1218, 1127, 769 cm^{-1}. ESI-MS: m/z. (%) = 321.1 (100) $[M + H]^+$. $C_{13}H_{20}O_7S$ (320.36): calcd. C 48.74, H 6.29; found C 48.69, H 6.35.

Acylate 15: To an ice-cooled solution of compound **14** (100.0 mg, 0.3 mmol) in dry pyridine (1.0 mL), acetic anhydride (0.03 mL) was added and the reaction mixture was stirred for 10 min. After completion of the reaction was neutralized by cold 5 M HCl solution and the aqueous phase was extracted thrice with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified over silica gel column (35% EtOAc/hexane) to furnish **15** (80.0 mg, 92%) as colourless oil. $[\alpha]_D^{22}$ = –40.5 (c = 0.8, $CHCl_3$). R_f = 0.40 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.52 (s, 2 H), 5.72 (d, J = 4.5 Hz, 1 H), 4.94 (qd, J_1 = 6.3, J_2 = 4.6 Hz, 1 H), 3.80 (s, 6 H), 3.76 (s, 3 H), 2.77 (s, 3 H), 2.09 (s, 3 H), 1.31 (d, J = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 169.6, 153.2, 138.1, 130.8, 104.4, 79.3, 76.0, 60.8, 56.1, 38.4, 21.0, 16.8 ppm. IR (neat): $\tilde{\nu}$ = 2936, 2364, 1743, 1461, 1351, 1235, 1175, 1126, 927 cm^{-1}. ESI-MS: m/z (%) = 363.3 (100) $[M + H]^+$. $C_{15}H_{22}O_8S$ (362.39): calcd. C 49.71, H 6.12; found C 49.77, H 6.09.

Ester 16: To an ice-cooled solution of PPh_3 (122.7 mg, 0.4 mmol) in dry THF (7.0 mL) under N_2 atmosphere, DEAD (0.07 mL, 0.4 mmol) was added, followed by compound **14** (50.0 mg, 0.15 mmol) and *p*-nitrobenzoic acid (31.2 mg, 0.18 mmol). The mixture was stirred at room temperature for 30 min. The solvent was removed under vacuo and residue was directly purified by column chromatography (40% EtOAc/hexane) on silica gel to afford **16** (59 mg, 81%) as a light yellow oil. $[\alpha]_D^{29}$ = –22.5 (*c* = 0.46, CH_3OH). R_f = 0.55 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.25–8.24 (m, 4 H), 6.62–6.57 (m, 2 H), 5.95–5.80 (m, 1 H), 5.18–5.14 (m, 1 H), 3.80 (s, 6 H), 3.77 (s, 3 H), 2.86 (s, 3 H), 1.21 (d, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 163.5, 153.7, 153.3, 150.7, 134.9, 130.9, 129.8, 123.7, 104.9, 104.5, 60.8, 56.2, 38.9, 18.0 ppm. IR (neat): $\tilde{\nu}$ = 1648, 1527, 1346, 1269, 1225, 1125, 771 cm^{-1}. ESI-MS: *m*/*z* (%) = 470.5 (100) $[M + H]^+$. $C_{20}H_{23}NO_{10}S$ (469.46): calcd. C 51.17, H 4.94, N 2.98; found C 51.12, H 4.99, N 3.00.

Alcohol 17: To an ice-cooled solution of compound **16** (100.0 mg, 0.21 mmol) in dry THF (3 mL), LAH (8.0 mg, 0.21 mmol) was added and the reaction mixture was stirred for 10 min at 0 °C. After completion of the reaction was quenched by cold NH_4Cl solution, organic layer was separated and the aqueus phase was extracted thrice with EtOAc (3 × 20 mL). The combined organic layer was dried with anhydrous Na_2SO_4, filtered and then concentrated under reduced pressure. The crude product was purified over silica gel column (30% EtOAc/hexane) to furnish **17** (74.2 mg, 86%) as colourless oil. $[\alpha]_D^{29}$ = –29.4 (*c* = 0.46, CH_3OH). R_f = 0.42 (60% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.54 (s, 2 H), 4.87–4.76 (m, 2 H), 3.79 (s, 6 H), 3.76 (s, 3 H), 2.83 (s, 3 H), 1.60 (br., 1 H), 1.28 (d, *J* = 6.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.3, 137.9, 134.5, 103.5, 82.3, 75.5, 60.8, 56.2, 38.4, 15.3 ppm. IR (neat): $\tilde{\nu}$ = 3436, 2356, 1215, 1133, 769 cm^{-1}. ESI-MS: *m*/*z* (%) = 321.2 (100) $[M + H]^+$. $C_{13}H_{20}O_7S$ (320.36): calcd. C 48.74, H 6.29; found C 48.66, H 6.38.

Compound 18: To an ice-cooled solution of compound **16** (100.0 mg, 0.21 mmol) in dry CH_3OH (3 mL), K_2CO_3 (29 mg, 0.21 mmol) was added and the reaction mixture was stirred for 5 min. After complete consumption of the starting material, the reaction was quenched by the addition of water. The aqueous layer was extracted with EtOAc (3 × 25 mL), combined organic layer was washed with brine (25 mL), dried with anhydrous Na_2SO_4, filtered and then concentrated under reduced pressure to obtain an oily residue. Purification of the crude product provide compound **17** (15%) as colourless oil and the epoxide **18** (48%) as colourless oil. The analytical and spectroscopic data of **18** are as follows. $[\alpha]_D^{29}$ = –42.5 (*c* = 0.84, CH_3OH). R_f = 0.80 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.52 (s, 2 H), 3.86 (s, 6 H), 3.84 (s, 3 H), 3.34–3.28 (m, 1 H), 3.01–2.96 (s, 1 H), 1.12 (d, *J* = 5.4 Hz, 3 H) ppm. IR (neat): $\tilde{\nu}$ = 2938, 2362, 1460, 1351, 1233, 1180, 1125, 931 cm^{-1}. ESI-MS: *m*/*z* (%) = 225.3 (100) $[M + H]^+$. $C_{12}H_{16}O_4$ (224.26): calcd. C 64.27, H 7.19; found C 64.41, H 7.09.

Compound 19 (C-3 Epimer of 15): To an ice-cooled solution of compound **17** (100.0 mg, 0.3 mmol) in dry pyridine (1 mL), acetic anhydride (0.03 mL) was added and the reaction mixture was stirred for 10 min. After completion of the reaction was neutralized by 5 M HCl and the aqueous phase was extracted thrice with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried with anhydrous Na_2SO_4, filtered and then concentrated under reduced pressure. The crude product was purified over silica gel column (30% EtOAc/hexane) to furnish **19** (80.0 mg, 92%) as colourless oil. $[\alpha]_D^{29}$ = +44.5 (*c* = 0.31, CH_3OH). R_f = 0.50 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.56 (s, 2 H), 5.70 (d, *J* = 7.53 Hz, 1 H), 5.03–4.94 (m, 1 H), 3.88 (s, 6 H), 3.83 (s, 3 H), 2.93 (s, 3 H), 2.14 (s, 3 H), 1.29 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 169.7, 153.2, 138.1, 130.9, 104.5, 79.3, 76.1, 60.8, 56.1, 38.5, 21.1, 16.9 ppm. IR (neat): $\tilde{\nu}$ = 2940, 2362, 1743, 1460, 1355, 1233, 1177, 1130, 927 cm^{-1}. ESI-MS: *m*/*z* (%) = 363.2 (100) $[M + H]^+$. $C_{15}H_{22}O_8S$ (362.39): calcd. C 49.71, H 6.12; found C 49.75, H 6.01.

Ester 20: To an ice-cooled solution of compound **7** (2.0 g, 6.6 mmol) in dry acetone (15 mL), 2,2-dimethoxypropane(8 mL) was added. Under ice-cooled condition catalytic amount of $BF_3{\cdot}OEt_2$ (0.1 mL) was added and allowed to stir for 30 min under the same reaction condition. The reaction mixture was quenched by addition of few drops of triethylamine until it became colourless and then the solvent was evaporated under reduced pressure. To this, water was added and extracted with ethyl acetate (3 × 100 mL) and the organic layer was washed with brine (100 mL). The organic layer was dried with anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (20% EtOAc/hexane) to furnish pure **20** (2.2 g, 97%) as a white solid, m.p. 57–59 °C. $[\alpha]_D^{22}$ = 42.3 (*c* = 0.34, CH_3OH). R_f = 0.41 (40% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.53 (s, 2 H, ArH), 5.00 (d, *J* = 7.35 Hz, 1 H), 4.21–4.14 (m, 3 H), 3.78 (s, 6 H), 3.73 (s, 3 H), 1.51 (s, 3 H), 1.45 (s, 3 H), 1.24 (t, *J* = 7.14 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 170.0, 153.2, 137.9, 133.4, 111.2, 103.1, 96.0, 81.0, 80.3, 61.0, 60.4, 55.8, 26.9, 25.6, 14.2 ppm. IR (neat): $\tilde{\nu}$ = 2990, 1753, 1595, 1462, 1381, 1235, 1132, 1000, 834 cm^{-1}. ESI-MS: *m*/*z* (%) = 357 (100) $[M + NH_3]^+$. $C_{17}H_{24}O_7$ (340.37): calcd. C 59.99, H 7.11; found C 60.08, H 7.19.

Alcohol, 21: To an ice-cooled solution of previously obtained intermediate **20** (2.0 gm, 5.8 mmol) in dry THF (40 mL) in a 250 mL RB flask fitted with a guard tube, calculated amount of LAH (222.2 mg, 5.8 mmol) was added and stirred the reaction mixture at the same temperature for 30 min, after which time the reaction was quenched with cold NH_4Cl and extracted thrice with EtOAc (3 × 100 mL). The combined organic layer was washed with brine (100 mL) and dried with anhydrous Na_2SO_4. The organic layer was concentrated under reduced pressure to a colourless crude product. The crude product was purified over silica gel column chromatography (30% EtOAc/hexane) to furnish **21** (1.65 g, 94%) as colourless solid. $[\alpha]_D^{22}$ = –37.0 (*c* = 0.82, CH_3OH). R_f = 0.35 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.49 (s, 2 H, ArH), 4.73 (d, *J* = 8.4 Hz, 1 H), 3.78 (s, 6 H), 3.72–3.67 (m, 4 H), 3.52 (d, *J* = 9.6 Hz, 1 H), 2.45 (br. s, 1 H), 1.47 (s, 3 H), 1.42 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.3, 138.0, 133.3, 108.8, 103.3, 96.0, 83.4, 78.4, 60.4, 60.1, 55.9, 27.1, 27.0 ppm. IR (neat): $\tilde{\nu}$ = 3422, 3019, 2362, 1595, 1461, 1217, 1128, 763, 670 cm^{-1}. ESI-MS: *m*/*z* (%) = 298.2 (100) $[M]^+$. $C_{15}H_{22}O_6$ (298.34): calcd. C 60.39, H 7.43; found C 60.48, H 7.37.

Mesylate 22: To an ice-cooled solution of compound **21** (2.0 gm, 6.7 mmol) in dry CH_2Cl_2 (30 mL), Et_3N (2.3 mL, 16.7 mmol) was added followed by methanesulfonyl chloride (0.5 mL, 7.3 mmol) and then the reaction mixture was stirred for 20 min at the same temperature. To this water was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layer was dried with anhydrous Na_2SO_4, filtered and then concentrated under reduced pressure to yellow coloured crude oil. The crude product was purified over silica gel column chromatography (20% EtOAc/hexane) to furnish **22** (2.4 g, 96%) as colourless solid, m.p. 42 °C. $[\alpha]_D^{22}$ = –8.4 (*c* = 0.67, CH_3OH). R_f = 0.40 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.56 (s, 2 H, ArH), 4.76 (d, *J* = 8.6 Hz, 1 H), 4.39–4.34 (m, 1 H), 4.28–4.23 (m,

1 H), 3.94–3.89 (m, 1 H), 3.80 (s, 6 H), 3.76 (s, 3 H), 3.01 (s, 3 H), 1.52 (s, 3 H), 1.45 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.5, 138.1, 132.1, 109.9, 103.3, 80.5, 78.9, 66.9, 60.7, 56.1, 37.7, 27.0, 26.7 ppm. IR (neat): $\tilde{\nu}$ = 3019, 2361, 1631, 1218, 1127, 762, 670 cm^{-1}. ESI-MS: *m*/*z* (%) = 393.9 (100) $[M + NH_3]^+$. $C_{16}H_{24}O_8S$ (376.42): calcd. C 51.05, H 6.43; found C 51.00, H 6.32.

Epoxide 24: To an ice-cooled methanolic solution of compound **22** (1.0 g, 2.65 mmol) catalytic amount of *p*-toluenesulfonic acid (50.0 mg, 0.26 mmol) was added and stirred for 15 min. After completion of the reaction water was added and neutralized with saturated $NaHCO_3$ solution. Aqueous phase was extracted thrice with EtOAc (3 × 50 mL), the combined organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to obtain colourless oil (0.9 g) which was used in the next step without characterization due to instability of the intermediate.

To an ice-cooled solution of previously obtained intermediate (0.9 g, 2.67 mmol) in dry methanol (20 mL), anhydrous K_2CO_3 (0.72 g, 5.34 mmol) was added and the reaction mixture was stirred for 2 h at room temperature. After completion of the reaction methanol was removed under reduced pressure, water was added to it and extracted with EtOAc (3 × 100 mL). The combined organic layer was dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by simple filtration through silica gel to provide **23** (0.6 g, 93%) and was used in the next step without further characterization.

To an ice-cooled solution of compound **23** (1.0 gm, 4.1 mmol) in dry CH_2Cl_2 (8 mL) under N_2 atmosphere, DIPEA (3.6 mL, 20.8 mmol) was added and stirred the solution. After 2 min, methoxymethyl chloride (0.8 mL, 10.2 mmol) was added and allowed to stir at room temperature for overnight. After completion of the reaction, water was added and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was washed with brine (100 mL), dried with anhydrous Na_2SO_4, filtered and then the organic layer was concentrated under reduced pressure to the brown coloured crude product. The crude product was chromatographed (30% EtOAc/hexane) over silica gel to furnish **24** (1.2 g, 96%) as colourless oil. $[\alpha]_D^{22}$ = –65.5 (*c* = 0.30, CH_3OH). R_f = 0.55 (55% EtOAc/hexane). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.59 (s, 2 H, ArH), 4.73–4.63 (m, 2 H), 4.28 (d, *J* = 6.3 Hz, 1 H), 3.87 (s, 6 H), 3.84 (s, 3 H), 3.41 (s, 3 H), 3.24–3.20 (m, 1 H), 2.78 (t, *J* = 4.3 Hz, 1 H), 2.69–2.66 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.3, 137.9, 133.4, 104.0, 94.0, 78.6, 60.7, 56.1, 55.5, 55.0, 44.5 ppm. IR (neat): $\tilde{\nu}$ = 3761, 3633, 3026, 2930, 2361, 1677, 1209, 1102, 760, 672 cm^{-1}. ESI-MS: *m*/*z* (%) = 299.5 (100) $[M]^+$. $C_{15}H_{23}O_6$ (299.34): calcd. C 60.19, H 7.74; found C 60.11, H 7.63.

Alcohol 25: To an ice-cooled solution of compound **24** (1.0 g, 3.5 mmol) in dry THF (30 mL), LAH (167.2 mg, 4.4 mmol) was added and allowed to stir at room temperature for 30 min. After completion of the reaction, it was quenched with drop by drop addition of cold water and the organic layer was extracted with EtOAc (3 × 100 mL). The combined organic layer was washed with brine (100 mL), dried with anhydrous Na_2SO_4, filtered and then the organic layer was concentrated under reduced pressure to a colourless crude product. This crude product was chromatographed (40% EtOAc/hexane) over silica gel column to furnish **25** (947.6 mg, 94%) as colourless oil. $[\alpha]_D^{22}$ = –111.3 (*c* = 0.64, CH_3OH). R_f = 0.31(50% EtOAc/hexane). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.44 (s, 2 H, ArH), 4.54–4.48 (m, 2 H,), 4.16 (d, *J* = 4.5 Hz, 1 H), 3.78 (s, 6 H), 3.77 (s, 3 H), 3.33 (s, 3 H), 2.82 (s, 1 H), 1.18 (s, 1 H), 0.96 (d, *J* = 6.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.2, 137.7, 133.9, 104.4, 94.2, 83.6, 71.0, 60.7, 56.0, 55.8, 18.3 ppm. IR (neat): $\tilde{\nu}$ = 3452, 3019, 2363, 1593, 1461, 1217, 1129, 1031, 762, 670 cm^{-1}. ESI-MS: *m*/*z* (%) = 287.3 (100) $[M + H]^+$. $C_{14}H_{22}O_6$ (286.32): calcd. C 58.73, H 7.74; found C 58.66, H 7.79.

Mesylate 26: To an ice-cooled solution of compound **25** (0.5 g, 1.7 mmol) in dry CH_2Cl_2 (10 mL), Et_3N (0.6 mL, 4.3 mmol) was added followed by methanesulfonyl chloride (0.16 mL, 2.0 mmol) and the reaction mixture was stirred at 0 °C for 15 min. After completion of the reaction, water was added and the organic layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layer was washed with brine (50 mL), dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to a yellow coloured crude product. This crude product was purified over silica gel column (25% EtOAc/hexane) to furnish **26** (623.0 mg, 98%) as colourless oil. $[\alpha]_D^{22}$ = –44.2 (*c* = 0.55, CH_3OH). R_f = 0.50 (30% EtOAc/hexane). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.58 (s, 2 H, ArH), 4.89–4.81 (m, 1 H), 4.67 (d, *J* = 5.1 Hz, 1 H), 4.61 (s, 2 H), 3.86 (s, 6 H), 3.84 (s, 3 H), 3.41 (s, 3 H), 2.74 (s, 3 H), 1.44 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.3, 137.9, 132.7, 104.5, 94.3, 81.5, 78.8, 60.8, 56.2, 55.9, 38.0, 17.0 ppm. IR (neat): $\tilde{\nu}$ = 2934, 2369, 1652, 1515, 1463, 1347, 1119, 907, 772 cm^{-1}. ESI-MS: *m*/*z* (%) = 364.4 (100) $[M]^+$. $C_{15}H_{24}O_8S$ (364.41): calcd. C 49.44, H 6.64; found C 49.32, H 6.67.

Alcohol 27: Starting from 100 mg (0.2 mmol) of **26**, the title compound was prepared in the same manner as that described for **14**. Purification of the crude product by silica gel column chromatography (30% EtOAc/hexane) afforded **27** (70.2 mg, 80%) as a colourless gum. $[\alpha]_D^{29}$ = –27.9 (*c* = 1.02, CH_3OH). R_f = 0.55 (50% EtOAc/hexane). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.55 (s, 2 H), 4.85–4.76 (m, 1 H), 4.55 (d, *J* = 7.3 Hz, 1 H), 3.84 (s, 6 H), 3.80 (s, 3 H), 3.01 (s, 3 H), 2.81 (br., 1 H), 1.23 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 153.3, 137.9, 134.8, 103.8, 83.2, 76.8, 60.7, 56.0, 38.3, 18.0 ppm. IR (neat): $\tilde{\nu}$ = 3458, 1637, 1526, 770 cm^{-1}. ESI-MS: *m*/*z* (%) = 320.5 (100) $[M]^+$. $C_{13}H_{20}O_7S$ (320.36): calcd. C 48.74, H 6.29; found C 48.79, H 6.22.

Compound 28 (C-2 epimer of 15): The title compound was prepared starting from **27** (100.0 mg, 0.3 mmol) following the same procedure as described earlier for **15**. Purification of the crude product by silica gel column chromatography provided **28** (101.8 mg, 90%) as white solid, m.p. 118 °C. $[\alpha]_D^{22}$ = –49.9 (*c* = 0.35, CH_3OH). R_f = 0.45 (50% EtOAc/hexane). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.55 (m, 2 H), 5.68 (d, *J* = 7.5 Hz, 1 H), 5.01–4.92 (m, 1 H), 3.86 (s, 6 H), 3.82 (s, 3 H), 2.91 (s, 3 H), 2.13 (s, 3 H), 1.27 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 169.6, 153.5, 138.4, 131.3, 104.4, 79.7, 76.5, 60.7, 56.2, 38.5, 20.9, 18.1 ppm. IR (neat): $\tilde{\nu}$ = 3014, 2948, 2846, 2368, 1749, 1596, 1510, 1462, 1338, 1233, 1178, 1125, 1043, 926, 827 cm^{-1}. ESI-MS: *m*/*z* (%) = 363.2 (100) $[M]^+$. $C_{15}H_{22}O_8S$ (362.39): calcd. C 49.71, H 6.12; found C 49.77, H 6.07.

Ester 29: To synthesize the title compound, **27** (50.0 mg, 0.15 mmol) was first converted into corresponding ester by Mitsunobu reaction as described earlier for **16**. Purification of the crude product by silica gel column chromatography provided the pure ester (60.0 mg, 82%) as light yellow oil. $[\alpha]_D^{22}$ = –34.5 (*c* = 0.56, CH_3OH). R_f = 0.52 (50% EtOAc/hexane). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.33–8.32 (m, 4 H), 6.70–6.65 (m, 2 H), 5.91 (d, *J* = 8.0 Hz, 1 H), 5.27–5.22 (m, 1 H), 3.88 (s, 6 H), 3.85 (s, 3 H), 2.94 (s, 3 H), 1.36 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 163.5, 153.7, 153.3, 134.9, 130.9, 129.8, 123.7, 105.0, 104.5, 60.8, 56.3, 38.9, 16.9 ppm. ESI-MS: *m*/*z* (%) = 470.3 (100) $[M]^+$. $C_{20}H_{23}NO_{10}S$ (469.46): calcd. C 51.17, H 4.94, N 2.98; found C 51.23, H 4.88, N 3.01.

Compound 30 (enantiomer of 15): To prepare the title compound **30**, ester **29** (50.0 mg, 0.15 mmol) was converted into the corresponding alcohol in the same manner as described earlier for **17**. Purification of the crude product by silica gel column chromatography provided alcohol (36.5 mg, 85%) as colourless oil. The compound was not stable and hence was used in the next step without further characterization.

The title compound was prepared starting from previously obtained intermediate (20.0 mg, 0.06 mmol) following the same procedure as described earlier for **15**. Purification of the crude product by silica gel column chromatography provided **30** (20.5 mg, 90%) as colourless oil. $[a]_D^{22}$ = +38.2 (c = 0.62, $CHCl_3$). R_f = 0.48 (50% EtOAc/hexane). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.52 (s, 2 H, ArH), 5.72 (d, J = 4.5 Hz, ArH), 4.99–4.89 (m, 1 H), 3.80 (s, 6 H), 3.76 (s, 3 H), 2.77 (s, 3 H), 2.09 (s, 3 H), 1.31 (d, J = 6.5 Hz, 3 H) ppm. IR (neat): $\tilde{\nu}$ = 2928, 2361, 1739, 1472, 1355, 1235, 1178, 1126, 930 cm^{-1}. ESI-MS: m/z (%) = 363.3 (100) $[M + H]^+$. $C_{15}H_{22}O_8S$ (362.39): calcd. C 49.71, H 6.12; found C 49.82, H 5.99.

Supporting Information (see also the footnote on the first page of this article): ^1H and ^{13}C NMR spectra of all new compounds.

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