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A new synthetic route to oxazole and pyrrole 2-deoxy-C-ribosides☆

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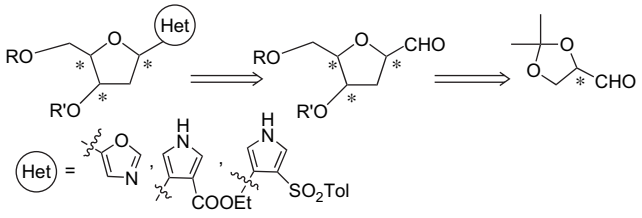
Abstract—The synthesis of oxazole and pyrrole 3-carbethoxy/3-arylsulfonyl D and L-2-deoxyribosides by TosMIC addition/cyclization on D and L-2-deoxyribo-1-carboxaldehyde and unsaturated esters in moderate to good yields is reported.

1. Introduction

In recent years nucleoside mimetics have attracted considerable attention in synthetic chemistry owing to their biological and chemotherapeutic properties.[1] Inspired by the recent upsurge in this area of research, we reported the synthesis of oxazole and pyrrole C-nucleosides by the TosMIC (tosylmethyl isocyanide) anion addition to sugar derivatives and subsequent ring closing reaction.[2] Previously, several groups have synthesized deoxy C-nucleosides by divergent methods such as C–C bond formation between the existing deoxyribose moiety and an appropriate nucleophile,[3] constructing the heteroaryl ring on 2-deoxy ribosyl cyanide,[4] aryl nucleophilic addition to either ribonolactone or 2-deoxyribino lactone followed by deoxygenation of the ensuing hydroxy functionality to afford corresponding deoxy-C-ribosides[5] and a Heck[6] type of coupling between the sugar anomeric carbon and a heterocycle. Interestingly, however, the above cited researchers were limited to using 2-deoxy-D-ribose as the starting material though some recent attempts were directed at the synthesis of 2-deoxy-D-ribo-C-nucleosides.[7] Thus the need to devise alternative yet practical synthetic protocols for deoxy-C-ribosides is warranted. Therefore, we choose to synthesize deoxy-C-ribosides by the key reaction of TosMIC addition and cyclization on 2-deoxy-D- and L-ribo-1-carboxaldehydes, which in turn could be realized by a common strategy from (*R*) and (*S*)-2,3-*O*-isopropylidene glyceraldehydes, respectively, as delineated in Scheme 1.



Scheme 1.

2. Results and discussion

2.1. Synthesis of D-2-deoxy-ribo oxazole and pyrrole C-nucleosides from (*R*)-2,3-*O*-isopropylidene glyceraldehyde

Based on our continued interest in the design and synthesis of modified nucleosides, herein we report the synthesis of D and L-2-deoxy-ribo oxazole and pyrrole C-nucleosides starting from (*R*) and (*S*)-2,3-*O*-isopropylidene glyceraldehydes, respectively. Thus, the known homoallyl alcohol[8] **1** (Scheme 2), obtained from (*R*)-2,3-*O*-isopropylidene glyceraldehyde, was converted to its methyl ether (**2a** and **2b**) by using NaH, MeI in dry THF in good yields (81%). The two diastereomers formed were separated by column chromatography wherein **2a** was obtained in 73% and **2b** in 8% yield. The isopropylidene group of **2a** was deprotected using 60% acetic acid to give diol **3** in 81% yield. Compound **3** was selectively protected (BnBr, K_2CO_3, and acetone) as its primary benzyl ether **4** in 65% yield. Compound **4** on treatment with *m*CPBA afforded a 1:1 diastereomeric mixture of 2-deoxy-D-ribo-1-methanol **5** in 71% yield. The formation of **5** could be rationalized by an epoxidation and subsequent ring opening reaction in one pot to afford the tetrahydrofuran moiety, which is the crucial intermediate

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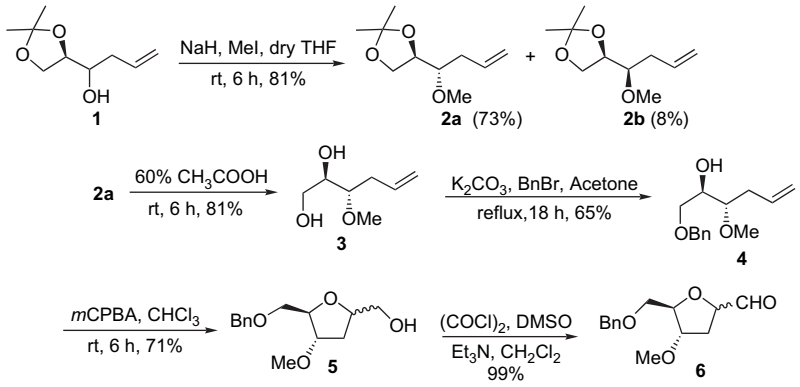


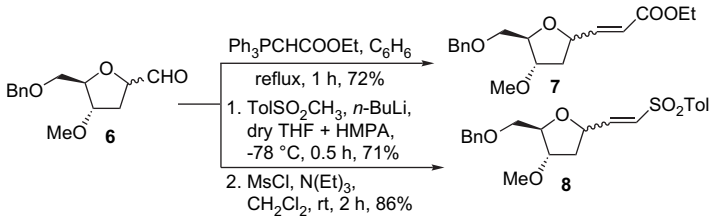
Scheme 2.

in the present study. Further, methanol **5** was oxidized to aldehyde **6** under Swern oxidation conditions in 99% yield.

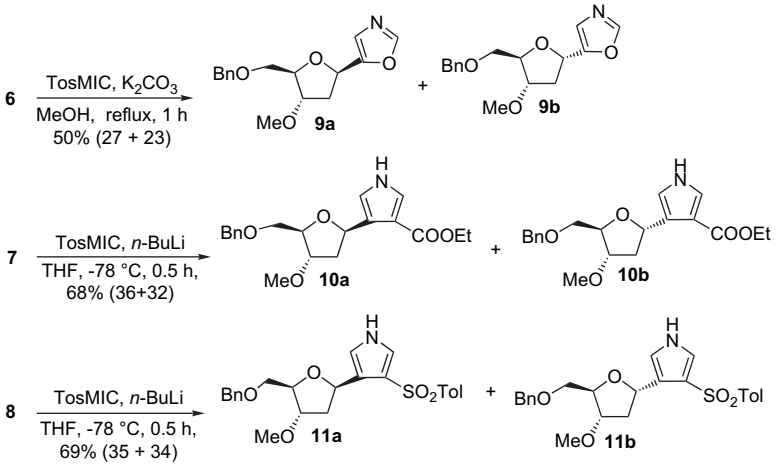
2.2. α,β Unsaturated ester/aryl sulfonyl ester functionality needs to be developed for obtaining a pyrrole ring

Accordingly, aldehyde **6** (Scheme 3) on treatment with (ethoxycarbonylmethylene)triphenylphosphorane in refluxing benzene was converted to α,β unsaturated ester **7** (72%, only *E* isomer). Independently, aldehyde **6** on exposure to the lithium salt of methyl-*p*-toulyl sulfone in a mixture of THF and HMPA (7:3) led to the addition product, which was further converted to α,β unsaturated aryl sulfonyl ester **8** (61%, two steps, only *E* isomer) on dehydration under MsCl, NEt_3, and CH_2Cl_2 conditions.

After successful preparation of **6**, **7**, and **8**, we aimed at the construction of oxazole and pyrrole nucleosides (Scheme 4). Firstly, aldehyde **6** on treatment with potassium salt of TosMIC[2] in methanol resulted in a chromatographically separable α/β anomeric mixture of oxazole-C-ribosides **9a** and **9b** in 50% under our earlier reported reaction conditions.[2] Likewise treatment of **7** and **8** independently with lithium salt of TosMIC[2] afforded the corresponding pyrrole C-nucleosides **10a** (36%), **10b** (32%), **11a** (35%), and **11b** (34%). The α/β anomeric mixtures of all pyrrole *C*-ribonucleosides were resolved into pure entities by column chromatography and thoroughly characterized. The assignment of α,β-nucleosides was made based on Kool's[9] observation for deoxy nucleosides by comparing the multiplicity of H-1 proton. The reported ^{1}H NMR values for β-C-nucleosides revealed



Scheme 3.



Scheme 4.

that H-1 proton resonates as a double doublet (*J* 10.0, 5.0 Hz) while the same proton for α isomer appears as a triplet (*J* 6.0 Hz). In comparison, for β-C-nucleosides **9a**, **10a**, and **11a** the H-1 proton resonated as double doublet (*J* 9–10, 5–6 Hz) and for α-C-nucleosides **9b**, **10b**, and **11b** H-1 proton appeared as a triplet (7-7.5 Hz). The 1-D-NOE studies (Fig. 1) carried out on **10a** and **10b** unequivocally established the assigned stereochemistry at the anomeric carbon for both the isomers was indeed true. The same analogy was extended to other C-nucleosides for their stereochemical evaluation.

2.3. Synthesis of L-2-deoxy-ribo oxazole and pyrrole C-nucleosides from (*S*)-2,3-*O*-isopropylidene glyceraldehyde

Next we focused our attention on the preparation of L-nucleosides. Due to the specificity of enzymes, L-ribose modified oligoribonucleotides become attractive candidates for diagnostic and therapeutic uses because L-RNA ligands remain uncleaved in biological fluids.[10] For these reasons, modified L-nucleosides, especially L-ribose and its derivatives are of interest. So far, several syntheses of L-ribose and L-ribosides from L-arabinose,[11a,b] D-glucose,[12] D-ribose,[11b] L-xylose,[13] and D-galactose[11a] have been reported. Besides, the synthesis of L-nucleosides is complicated by the unavailability of L-sugars as starting materials. Though some syntheses of 2-deoxy L-ribose are already reported,[14] their C-nucleosides are rare. Hence, synthesis of C-nucleosides of 2-deoxy-L-ribosides was considered important.[15] Herein we also report the synthesis of L-ribose-1-methanol from (*S*)-2,3-*O*-isopropylidene glyceraldehyde and its *C*-oxazole and pyrrole derivatives.

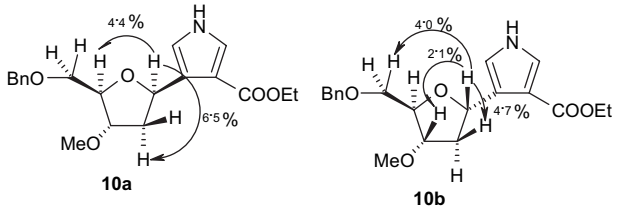
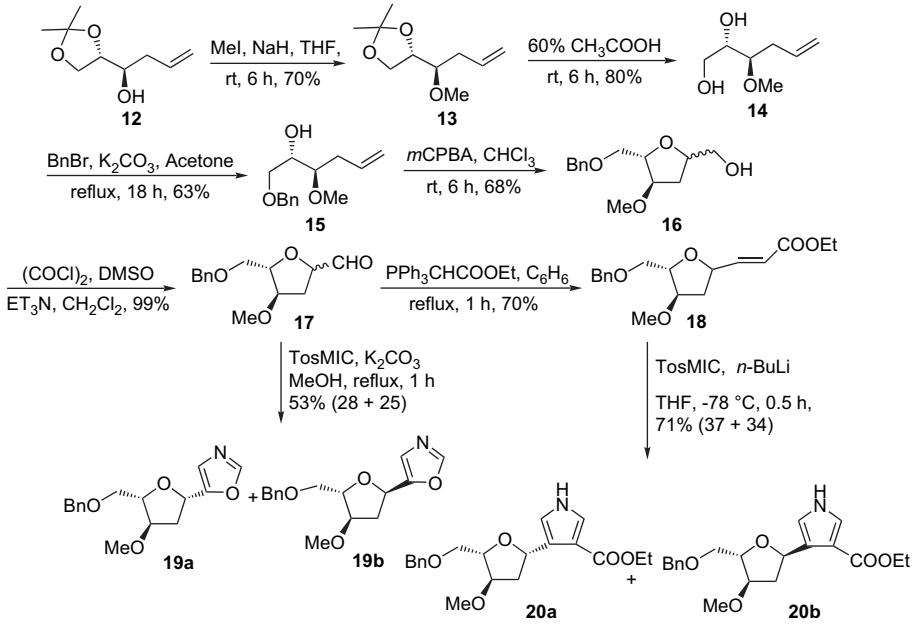


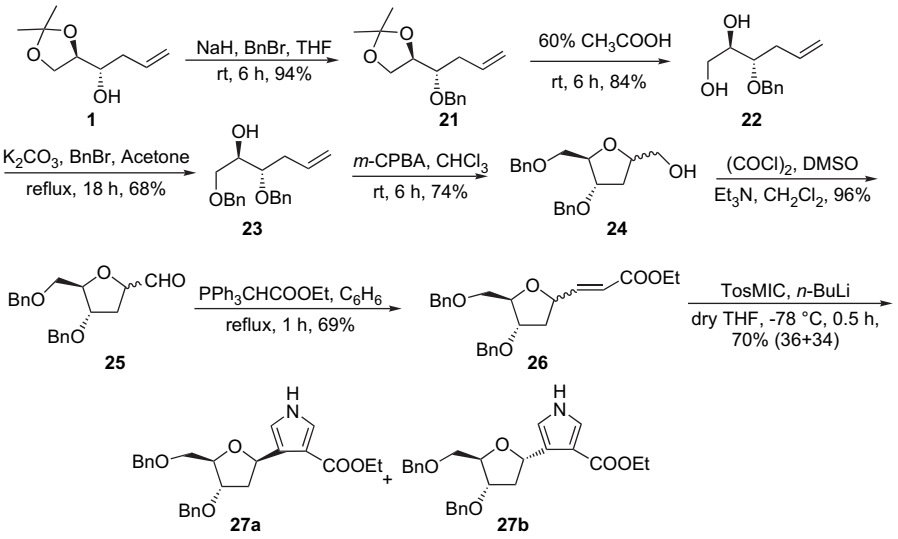
Figure 1.

Consequently, 2-deoxy-L-ribo-1-methanol (**16**, Scheme 5) is identified as an appropriate starting material, which could be obtained by adopting conceptually a related strategy to that devised for **5**. Thus applying the same sequence of reactions on the known[8] homoallyl alcohol **12** resulted in **16** in 24% yield, which was oxidized to aldehyde **17** under Swern's conditions. TosMIC addition reaction (Scheme 5) on **17** and **18** resulted in both oxazole (**19a** and **19b**) and pyrrole (**20a** and **20b**) C-nucleosides, respectively, as 1:1 anomeric mixtures that were easily separated by column chromatography. The stereochemical assignment was made individually for each L-nucleosides and it was found that the ^{1}H NMR spectra displayed the same multiplicity for H-1 as that observed for their corresponding D-ribo-analogs. For instance, in the ^{1}H NMR spectra H-1 of α nucleosides resonated as double doublet and the same proton appeared as a triplet in β-nucleosides. The β-nucleosides were further confirmed by comparing the sign of optical rotation values, which proved to be opposite to that of D-nucleosides [**10a**. $[\alpha]_D$ +51.6 (*c* 0.8, $CHCl_3$), **20a**. $[\alpha]_D$ −46.3 (*c* 0.6, $CHCl_3$) and **10b**. $[\alpha]_D$ −15.4 (*c* 0.8, $CHCl_3$), **20b**. $[\alpha]_D$ +17.1 (*c* 0.35, $CHCl_3$)].

After successfully establishing a synthetic route to deoxy nucleosides, we examined the synthesis of nucleosides with easily removable protecting groups at C-3 and C-5 (Scheme 6) to demonstrate the efficacy of the protocol and their potential use in the synthesis of oligomers. Toward this endeavor, the synthetic sequence was repeated by changing the protecting group from OMe to OBn (**13**). Expectedly, similar observations were made in obtaining the



Scheme 5.



Scheme 6.

α,β-anomeric ratios of C-ribosides as observed earlier (Schemes 1, 2, and 3). The study resulted in pyrrole 2-deoxy D-ribo-C-nucleosides **27a** and **27b**.

3. Conclusion

In conclusion the synthesis of oxazole and substituted pyrrole 2-deoxy-D and -ribo-C-nucleosides is reported for the first time by the TosMIC approach. Novel routes were accomplished for the synthesis of 2-deoxy-D- and L-ribose-1-methanol from readily accessible (*R*)- and (*S*)-2,3-*O*-isopropylidene glyceraldehydes, respectively, in simple steps. Additionally, synthesis of L-ribo-C-nucleosides, a rare class of valuable compounds is also disclosed.

4. Experimental

4.1. General

Solvents were dried over standard drying agents and freshly distilled prior to use. Chemicals were purchased and used without further purification. All column chromatographic separations were performed using silica gel (Acme's, 60–120 mesh). Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40 °C vacuo. ^{1}H NMR (200 MHz, 300 MHz, and 400 MHz) and ^{13}C NMR (50 MHz and 75 MHz) spectra were measured with a Varian Gemini FT-200 MHz spectrometer, Bruker Avance 300 MHz and Unity 400 MHz with tetramethylsilane as internal standard for solutions in deuteriochloroform. *J* values are given in hertz. IR spectra were recorded on Perkin–Elmer IR-683 spectrophotometer with NaCl optics. Optical rotations were measured with JASCO DIP 300 digital polarimeter at 25 °C. Mass spectra were recorded on CEC-21-11013 or Finnigan Mat 1210 double focusing mass spectrometers operating at a direct inlet system.

4.1.1. 1-[2,2-Dimethyl-(4*R*)-1,3-dioxolan-4-yl]-(1*S*)-3-butenyl methyl ether and 1-[2,2-dimethy-L-(4*R*)-1,3-dioxolan-4-yl]-(1*R*)-3-butenyl methyl ether (2a and 2b). To a stirred solution of **1** (8.3 g, 47.1 mmol) in dry THF (80 mL) at 0 °C was added sodium hydride (3.77 g, 94.2 mmol, 60% dispersion in mineral oil) and the mixture was stirred for 20 min. Methyl iodide (10 g, 70.7 mmol) was added and the mixture was stirred for 6 h. The reaction mixture was quenched by the addition of satd NH_4Cl (20 mL) at 0 °C and stirred for 10 min. The organic compound was extracted into EtOAc (2×100 mL). The organic layer was washed with water (1×50 mL), brine (1×50 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:50 EtOAc:hexane) to obtain **2a** (6.5 g, 73%) as a colorless liquid. R_f (10% EtOAc/hexane) 0.32; $[\alpha]_D$ +7.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90–5.76 (m, 1H, –C*H*=CH_2), 5.07–5.10 (m, 2H, –CH=CH_2), 4.00–3.92 (m, 2H, –CH_2O), 3.84–3.79 (m, 1H, –C*H*O), 3.40 (s, 3H, –CHOCH_3), 3.24 (q, *J* 6.0 Hz, 1H, –*CH*OMe), 2.35 (dt, *J* 13.3, 5.9 Hz, 1H, –C*H*CH=CH_2), 2.25 (dt, *J* 13.2, 6.0 Hz, 1H, –C*H*CH=CH_2), 1.38 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.2, 28.1, 57.1, 62.5, 70.1, 100.4, 109.5, 126.1; IR (neat): 3100, 2950, 1620, 1460, 1400 cm^{-1}; FABMS (*m*/*z*, %): 187 (M^++H, 16%), 109 (32), 95 (72), 81 (76). Anal. Calcd for $C_{10}H_{18}O_3$; C 64.49, H 9.74%; found C 64.75, H 9.53%.

The second eluted was **2b** (0.71 g, 8%). R_f (10% EtOAc/hexane) 0.31; $[\alpha]_D$ +2.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90–5.76 (m, 1H, –C*H*=CH_2), 5.10–5.00 (m, 2H, –CH=CH_2), 4.10 (dd, *J* 13.9, 6.4 Hz, 1H, –CH_2O), 3.92 (dd, *J* 7.9, 6.7 Hz, 1H, –CH_2O), 3.61 (t, *J* 7.5 Hz, 1H, –C*H*O), 3.44 (s, 3H, –OCH_3), 3.21 (q, *J* 6.4 Hz, 1H, –C*H*OCH_3), 2.32–2.08 (m, 2H, –CH_2CH=CH_2), 1.38 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.1, 28.1, 57.1, 63.5, 71.5, 100.5, 109.5, 126.1; IR (neat): 3100, 2950, 1620, 1460, 1400 cm^{-1}; FABMS (*m*/*z*, %): 187 (M^++H, 16%), 109 (32), 95 (72), 81 (76). Anal. Calcd for $C_{10}H_{18}O_3$; C 64.49, H 9.74%; found C 64.32, H 9.71%.

4.1.2. 3-Methoxy-(2*R*,3*S*)-5-hexene-1,2-diol (3). The methyl ether **2a** (3 g, 16.1 mmol) was dissolved in 60% aq

acetic acid (30 mL) and stirred for 6 h. The reaction mixture was then neutralized with solid $NaHCO_3$ and the organic compound was extracted with EtOAc (3×100 mL) and sequentially washed with satd $NaHCO_3$ soln (2×100 mL), water (1×100 mL), brine (1×100 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:4 EtOAc:hexane) to give **3** (1.9 g, 81%) as a light yellow liquid. R_f (50% EtOAc/hexane) 0.49; $[\alpha]_D$ +2.75 (*c* 0.81, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.92–5.69 (m, 1H, –C*H*=CH_2), 5.16–5.05 (m, 2H, –CH=CH_2), 3.64–3.55 (m, 3H, –CH_2OH and C*H*OH), 3.40 (s, 3H, –OCH_3), 3.34–3.24 (m, 1H, –C*H*OCH_3), 2.34 (m, 2H, –CH_2CH=CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.0, 57.5, 65.0, 66.5, 72.1, 114.5, 126.0; IR (neat): 3400, 2920, 1630, 1420, 1400 cm^{-1}; FABMS (*m*/*z*, %): 169 (M^++Na, 8), 147 (M^++H, 54), 137 (40), 69 (60), 55 (100). Anal. Calcd for $C_7H_{14}O_3$; C 57.51, H 9.65%; found C 57.78, H 9.59%.

4.1.3. 1-Benzyloxy-3-methoxy-(2*R*,3*S*)-5-hexen-2-ol (4). To a stirred solution of **3** (1.8 g, 12.3 mmol) in acetone (30 mL) were added K_2CO_3 (6.8 g, 36.9 mmol), TBAI (0.02 g), and benzyl bromide (1.6 mL, 13.5 mmol). The mixture was heated to reflux for 18 h. The reaction mixture was then concentrated under reduced pressure, the crude dissolved in water (20 mL) and extracted into EtOAc (3×20 mL). The organic layer was washed with water (1×20 mL), brine (1×20 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:10 EtOAc:hexane) to obtain 1-benzyloxy-3-methoxy-(2*R*,3*S*)-5-hexen-2-ol **4** (1.9 g, 65%) as a yellow syrup. R_f (30% EtOAc/hexane) 0.48; $[\alpha]_D$ +16.5 (*c* 1.6, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30 (br s, 5H, Ar–H), 5.90–5.75 (m, 1H, –C*H*=CH_2), 5.12–5.02 (m, 2H, –CH=CH_2), 4.53 (s, 2H, –OCH_2Ph), 3.78–3.72 (m, 1H, –C*H*OH), 3.61–3.49 (m, 2H, –CH_2OBn), 3.36 (s, 3H, –O*Me*), 3.24 (q, *J* 4.9 Hz, 1H, –C*H*OMe), 2.37–2.30 (m, 2H, –CH_2CH=CH_2), 1.40 (br s, 1H, –O*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.2, 57.8, 65.1, 71.1, 73.4, 81.2, 117.0, 126.9, 127.5, 128.4, 134.6, 138.0; FABMS (*m*/*z*, %): 259 (M^++Na, 18), 237 (M^++H, 8), 137 (40), 69(100). Anal. Calcd for $C_{14}H_{20}O_3$; C 71.16, H 8.53%; found C 71.10, H 8.49%.

4.1.4. 5-Benzyloxymethyl-4-methoxy-(4*S*,5*R*)-tetrahydro-2-furanylmethanol (5). To a stirred solution of **4** (1.1 g, 4.7 mmol) in $CHCl_3$ (5 mL) was added *m*-chloroperbenzoic acid (1.9 g, 5.6 mmol, 50–55% in water) dissolved in $CHCl_3$ (10 mL) and stirred for 6 h. The reaction mixture was diluted with $CHCl_3$ (10 mL), washed with satd $NaHCO_3$ (2×5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:5 EtOAc:hexane) to obtain alcohol **5** (0.82 g, 71%) as a yellow oil. R_f (50% EtOAc/hexane) 0.39; $[\alpha]_D$ +18.7 (*c* 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30 (br s, 5H, Ar–H), 4.50 (s, 2H, –OCH_2Ph), 4.21–4.14 (m, 1H, –C*H*O–), 3.94–3.85 (m, 2H, –CH_2OBn), 3.59–3.35 (m, 3H, –CH_2OH and –C*H*O–), 3.37 (s, 3H, –OCH_3), 3.26 (q, *J* 4.8, 1H, C*H*–OMe), 2.23–2.03 (m, 1H, –CH_2), 1.90–1.76 (m, 1H, –CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.1, 58.2, 65.2, 66.3, 72.5, 74.3, 81.9, 83.0, 127.9, 128.6, 135.0, 137.6; IR (neat): 3540, 2920, 1030, 1100 cm^{-1}; FABMS (*m*/*z*, %): 253 (M^++H, 2), 215 (4), 181 (6), 136(6), 91(100). Anal. Calcd for $C_{14}H_{20}O_4$; C 66.65, H 7.99%; found C 66.55, H 7.86%.

4.1.5. 5-Benzyloxymethyl-4-methoxy-(4*S*,5*R*)-tetrahydro-2-furancarbaldehyde (6). To a stirred solution of oxalyl chloride (0.37 mL, 3.0 mmol) in dry CH_2Cl_2 (5 mL) was added dry DMSO (0.47 mL, 6.1 mmol) drop wise at −78 °C. After 2 min **5** (0.7 g, 2.7 mmol) dissolved in CH_2Cl_2 (5 mL) was added and stirred for 30 min. To this Et_3N (1.6 mL, 16.6 mmol) was added at −78 °C and allowed to stir at room temperature for 20 min. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with water (2×5 mL), brine (1×10 mL), dried (Na_2SO_4), and concentrated under reduced pressure to obtain **6** (0.69 g, 99%) as a light yellow oil. The crude aldehyde was used without further purification or characterization.

4.1.6. Ethyl 3-[5-benzyloxymethyl-4-methoxy-(4*S*,5*R*)-tetrahydro-2-furanyl]-(*E*)-2-propenoate (7). To a stirred solution of **6** (0.6 g, 2.5 mmol) in benzene (6 mL) at reflux was added (ethoxycarbonylmethylene)triphenylphosphorane (1.3 g, 3.75 mmol) and the mixture stirred at reflux for 1 h. The reaction mixture was concentrated under reduced pressure and purified by column chromatography (60–120 Silica gel, 1:5 EtOAc:hexane) to afford **7** (0.55 g, 72%, only *E* isomer) as a colorless oil. R_f (40% EtOAc/hexane) 0.52; $[\alpha]_D$ +11.1 (*c* 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27 (br s, 5H, Ar–H), 6.94–6.85 (m, 1H, –C*H*=CHCOOEt), 5.98 (t, *J* 15.8 Hz, 1H, –CH=C*H*COOEt), 4.69–4.54 (m, 1H, –C*H*CH=CHCOOEt), 4.54 (s, 2H, –OCH_2Ph), 4.23–4.05 (m, 2H, –COOC$H_2$$CH_3$), 3.93–3.83 (m, 1H, –C*H*OMe), 3.50–3.40 (m, 2H, –CH_2OBn), 3.30 (s, 3H, –OCH_3), 2.40–2.07 (m, 1H, –CH_2), 1.85–1.65 (m, 1H, –CH_2), 1.29 (t, *J* 7.2 Hz, 3H, –COOCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 31.2, 56.0, 60.0, 71.3, 72.1, 82.0, 83.1, 89.0, 127.4, 127.9, 128.9, 131.0, 135.1, 145.2, 163.8; IR (neat): 2960, 1660, 1450, 1190, 1010 cm^{-1}; FABMS (*m*/*z*, %): 343 (M^++Na, 2), 321 (M^++H, 13), 215 (27), 138 (62), 73 (100). Anal. Calcd for $C_{18}H_{24}O_5$; C 67.48, H 7.55%; found C 67.40, H 7.49%.

4.1.7. 2-Benzyloxymethyl-3-methoxy-5-[2-(4-methylphenylsulfonyl)-(*E*)-1-ethenyl]-(2*R*,3*S*)-tetrahydrofuran (8). To a stirred solution of methyl *p*-toulenesulfone (0.52 g, 3.0 mmol) in THF:HMPA (7:3, 10 mL) was added *n*-BuLi (2.8 mL, 4.6 mmol, 1.6 M soln in hexanes) at −78 °C and stirred for 20 min. To this **6** (0.7 g, 2.8 mmol) dissolved in dry THF (5 mL) was added and the mixture stirred for 30 min. The reaction mixture was quenched with satd NH_4Cl (5 mL) and the organic compound was extracted into EtOAc (3×10 mL). The organic layer was washed with water (1×10 mL), brine (1×10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:3 EtOAc:hexane) to obtain the sulfone addition product (0.83 g, 71%) as a syrupy liquid.

To the above obtained adduct (0.83 g, 1.9 mmol) in CH_2Cl_2 (10 mL) were added triethylamine (0.82 mL, 5.9 mmol) and methane sulfonylchloride (0.27 mL, 2.3 mmol) and the mixture stirred for 2 h at room temperature. The reaction mixture was diluted with CH_2Cl_2 (10 mL), washed with water (1×10 mL), dried (Na_2SO_4), and concentrated under

reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:9 EtOAc:hexane) to obtain **8** (0.68 g, 86%, only *E* isomer) as a syrupy liquid. R_f (30% EtOAc/hexane) 0.47; $[\alpha]_D$ +24.2 (*c* 1.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.68 (2H, Ar–*H*), 7.28 (m, 7H, Ar–*H*), 6.95–6.88 (m, 1H, –C*H*=CHSO$_2$Tol), 6.54–6.44 (m, 1H, –CH=C*H*SO$_2$Tol), 4.78–4.60 (m, 1H, –C*H*CH=CHSO$_2$Tol), 4.50 (s, 2H, –OCH_2Ph), 4.10–4.02 (m, 1H, –C*H*CH$_2$OBn), 3.90–3.82 (s, 1H, –C*H*OMe), 3.50–3.35 (m, 2H, –CH_2OBn), 3.30 (s, 3H, –OCH_3), 3.20 (s, 2H, CH_2S), 2.42 (s, 3H, Ar–CH_3), 2.20–2.12 (m, 1H, CH_2), 1.90–1.70 (m, 1H, –CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 31.5, 37.1, 56.7, 70.7, 76.3, 82.3, 82.8, 83.8, 127.2, 127.5, 127.6, 128.2, 128.3, 129.7,129.8, 129.8, 130.1, 137.9; FABMS (*m*/*z*, %): 425 (M^++Na, 2), 296 (54), 200 (24), 154 (100), 107 (38), 57 (92). Anal. Calcd for $C_{23}H_{28}SO_5$; C 66.32, H 6.78, S 7.70%; found C 66.29, H 6.71, S 7.65%.

4.1.8. 5-[5-Benzyloxymethyl-4-methoxy-(2*R*,4*S*,5*R*)-tetrahydro-2-furanyl]-1,3-oxazole and 5-[5-benzyloxymethyl-4-methoxy-(2*S*,4*S*,5*R*)-tetrahydro-2-furanyl]-1,3-oxazole (9a and 9b). To a stirred solution of **6** (0.1 g, 0.41 mmol) in methanol (1 mL) were added TosMIC (0.08 g, 0.41 mmol) and potassium carbonate (0.172 g, 1.25 mmol) and the contents stirred at reflux for 1 h. The reaction mixture was concentrated under reduced pressure, the residue dissolved in water (10 mL) and extracted into EtOAc (2×10 mL). The combined organic layers were washed with water (1×10 mL), brine (1×10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:5 EtOAc:hexane) the first eluted was **9a** (0.031 g, 27%) as a thick yellow syrup. R_f (50% EtOAc/hexane) 0.39; $[\alpha]_D$ +0.5 (*c* 0.8, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 7.78 (s, 1H, oxa-*H*), 7.28 (br s, 5H, Ar–*H*), 6.97 (s, 1H, oxa-*H*), 5.07 (dd, *J* 9.8, 6.0 Hz, 1H, –C*H*oxazole), 4.54 (s, 2H, –CH_2Ph), 4.10 (m, 1H, –C*H*CH$_2$OBn), 3.95 (m, 1H, –C*H*OCH$_3$), 3.58 (dd, *J* 10.2, 4.2 Hz, 1H, –CH_2OBn), 3.46 (dd, *J* 10.2, 5.6 Hz, 1H, –CH_2OBn), 3.33 (s, 3H, –OCH_3), 2.14–2.24 (m, 2H, –CH_2); ^{13}C NMR (50 MHz): δ 36.3, 56.7, 70.9, 71.4, 73.5, 83.0, 83.7, 124.0, 127.6, 128.3, 129.6, 130.2, 138.2, 151.1; IR (neat): 2920, 1500, 1450, 1120 cm^{-1}; LCMS; 312 (M^++Na). Anal. Calcd for $C_{16}H_{19}NO_4$: C 66.42, H 6.62, N 4.84%; found C 66.39, H 6.61, N 4.71%.

The second eluted was 5-[5-benzyloxymethyl-4-methoxy-(2*S*,4*S*,5*R*)-tetrahydro-2-furanyl]-1,3-oxazole **9b** (0.027 g, 23%) as a thick syrup. R_f (50% EtOAc/hexane) 0.38; $[\alpha]_D$ +7.4 (*c* 0.35, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 7.80 (s, 1H, oxa-*H*), 7.30 (br s, 5H, Ar–*H*), 7.00 (s, 1H, oxa-*H*), 5.17 (t, *J* 7.3 Hz, 1H, –C*H*oxazole), 4.58 (d, *J* 2.9 Hz, 2H, –CH_2Ph), 4.14–3.98 (m, 2H, –C*H*OCH$_3$ and –C*H*CH$_2$OBn), 3.58 (d, *J* 3.6 Hz, 2H, –CH_2OBn), 3.32 (s, 3H, –OCH_3), 2.53 (m, 1H, –CH_2), 2.19 (m, 1H, –CH_2); ^{13}C NMR (50 MHz): δ 36.2, 56.6, 70.9, 71.5, 73.5, 83.1, 84.0, 124.5, 127.0, 128.5, 129.6, 130.1, 138.5, 152.0; IR (neat): 2920, 1500, 1450, 1120 cm^{-1}; LCMS; 307 $(M+NH_4)^+$. Anal. Calcd for $C_{16}H_{19}NO_4$: C 66.42, H 6.62, N 4.84%; found C 66.35, H 6.59, N 4.69%.

4.1.9. Ethyl 4-[5-benzyloxymethyl-4-methoxy-(2*R*,4*S*,5*R*)-tetrahydro-2-furanyl]-1*H*-3-pyrrolecarboxylate and ethyl 4-[5-benzyloxymethyl-4-methoxy-(2*S*,4*S*,5*R*)-tetrahydro-2-furanyl]-1*H*-3-pyrrolecarboxylate (10a and 10b). To a stirred solution of TosMIC (0.087 g, 0.45 mmol) in dry THF (2 mL) at −78 °C was added *n*-BuLi (0.46 mL, 0.75 mmol, 1.6 M solution in *n*-hexane) and the solution stirred for 15 min. To this **7** (0.120 g, 0.375 mmol) dissolved in dry THF (2 mL) was added and the mixture stirred for 30 min. After completion of the reaction, the mixture was quenched with satd aq NH_4Cl (1 mL), extracted with EtOAc (2×5 mL) and the combined organic layers were washed with water (1×5 mL), brine (1×5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (Silica gel 60–120, 1:5 EtOAc:hexane), first eluted was the **10a** (0.048 g, 36%) as syrup. R_f (30% EtOAc/hexane) 0.38; $[\alpha]_D$ +51.6 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.4 (s, 1H, –NH), 7.28 (br s, 5H, Ar–*H*), 7.21 (s, 1H, pyrrole-*H*), 6.64 (s, 1H, pyrrole-*H*), 5.44 (dd, *J* 9.4, 5.2 Hz, 1H, –C*H*pyrrole), 4.55 (s, 2H, –CH_2Ph), 4.27–4.23 (m, 2H, –COOCH_2CH$_3$), 4.10–4.05 (m, 1H, –C*H*CH$_2$OBn), 3.79–3.84 (m, 1H, –C*H*OCH$_3$), 3.62–3.51 (m, 2H, –CH_2OBn), 3.32 (s, 3H, –OCH_3), 2.47 (ddd, *J* 8.2, 5.6, 1.8 Hz, 1H, –CH_2), 1.78–1.69 (m, 1H, –CH_2), 1.32 (t, *J* 7.1 Hz, 3H, –COOCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 29.9, 39.5, 56.8, 59.5, 60.0, 71.2, 73.3, 83.1, 83.6, 113.6, 116.6, 125.2, 126.9, 127.6, 128.6, 138.3, 164.8; IR (neat): 3260, 2920, 1500, 1450, 1120 cm^{-1}; FABMS (*m*/*z*, %): 360 (M^++H, 4), 327 (4), 207 (6), 147 (12), 91 (54), 69 (64), 55 (100). Anal. Calcd for $C_{20}H_{25}NO_5$; C 66.83, H 7.01, N 3.90%; found C 66.74, H 7.11, N 3.85%.

The second eluted was **10b** (0.042 g, 32%) as syrup. R_f (30% EtOAc/hexane) 0.37; $[\alpha]_D$ −15.4 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.92 (br s, 1H, –N*H*–), 7.28 (br s, 5H, Ar–*H*), 7.21 (s, 1H, pyrrole-*H*), 6.64 (s, 1H, pyrrole-*H*), 5.48 (t, *J* 7.6 Hz, 1H, –C*H*pyrrole), 4.58 (s, 2H, –CH_2Ph), 4.26–4.16 (m, 3H, –C*H*CH$_2$OBn and COOCH_2CH$_3$), 3.96–3.91 (m, 1H, –C*H*OCH$_3$), 3.56 (d, *J* 5.1 Hz, 2H, –CH_2OBn), 3.28 (s, 3H, –OCH_3), 2.82–2.72 (m, 1H, –CH_2), 1.76–1.85 (m, 1H, –CH_2), 1.31 (t, *J* 7.1 Hz, 3H, –COOCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 29.9, 39.5, 56.7, 57.1, 59.5, 60.0, 71.2, 74.1, 83.0, 83.6, 113.6 116.6, 125.2, 126.9, 127.6, 128.6, 138.3, 164.8; IR (neat): 3260, 2920, 1500, 1450, 1120 cm^{-1}; FABMS (*m*/*z*, %): 360 (M^++H, 4), 327 (4), 147 (12), 91(54), 69 (64), 55 (100). Anal. Calcd for $C_{20}H_{25}NO_5$; C 66.83, H 7.01, N 3.90%; found C 66.80, H 7.10, N 3.79%.

4.1.10. 3-[5-Benzyloxymethyl-4-methoxy-(2*R*,4*S*,5*R*)-tetrahydro-2-furanyl]-4-ethylsulfonyl-1*H*-pyrrole and 3-[5-benzyloxymethyl-4-methoxy-(2*S*,4*S*,5*R*)-tetrahydro-2-furanyl]-4-ethylsulfonyl-1*H*-pyrrole (11a and 11b). To a stirred solution of TosMIC (0.058 g, 0.29 mmol) in dry THF (1 mL) was added *n*-BuLi (0.23 mL, 0.37 mmol, 1.6 M soln in *n*-hexane) and the mixture stirred for 15 min. To this **8** (0.1 g, 0.24 mmol) dissolved in dry THF (1 mL) was added and the mixture stirred for 30 min. The mixture was quenched with satd NH_4Cl (1 mL), extracted with EtOAc (2×5 mL) and the combined organic layers were washed with water (1×5 mL), brine (1×5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (Silica gel 60–120, 1:5 EtOAc:hexane) the first eluted was the

11a (0.037 g, 35%) as a yellow oil. R_f (40% EtOAc/hexane) 0.35; $[\alpha]_D$ +69.85 (*c* 1.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 9.15 (s, 1H, –N*H*), 7.70 (2H, Ar–*H*), 7.28–7.13 (9H, Ar–*H*), 6.92 (s, 1H, pyrrole-*H*), 6.59 (s, 1H, pyrrole-*H*), 5.09 (dd, *J* 10.6, 5.9 Hz, 1H, –C*H*pyrrole), 4.50 (s, 2H, $-SO_2CH_2Ar$), 3.99 (m, 1H, –C*H*CH_2OBn), 3.78 (m, 1H, –C*H*OMe), 3.50 (dd, *J* 12.7, 5.9 Hz, 2H, –CH_2OBn), 3.30 (s, 3H, –OCH_3), 2.35 (s, 3H, Ar–CH_3), 2.28 (dd, *J* 9.8, 5.9 Hz, 1H, –CH_2), 1.75–1.68 (m, 1H, –CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.3, 29.5, 57.1, 68.1, 71.4, 73.7, 83.4, 83.5, 116.2, 118.2, 124.6, 125.1, 125.3, 126.2, 126.2, 127.1, 127.3, 127.9, 128.8, 129.8; FABMS (*m*/*z*, %): 464 (M^++Na, 100), 442 (M^++H, 38), 391 (36), 288 (34), 248 (66), 167 (72), 154 (92). Anal. Calcd for $C_{25}H_{29}NO_5S$; C 65.91, H 6.42, N 3.07, S 7.04%; found C 65.79, H 6.40, N 3.00, S 6.95%.

The second eluted was **11b** (0.035 g, 34%) as a yellow oil. R_f (40% EtOAc/hexane) 0.34; $[\alpha]_D$ −22.7 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.99 (s, 1H, –N*H*), 7.71 (2H, Tol-*H*), 7.29–7.09 (m, 9H, Ar–*H*), 6.89 (s, 1H, pyrrole-*H*), 6.66 (s, 1H, pyrrole-*H*), 5.25 (t, *J* 7.4 Hz, 1H, –C*H*pyrrole), 4.54 (s, 2H, –OCH_2Ph), 4.10–4.04 (m, 1H, –C*H*CH_2OBn), 3.93–3.85 (m, 1H, –C*H*OMe), 3.50 (dd, *J* 9.6, 5.8 Hz, 2H, –CH_2OBn), 3.25 (s, 3H, –OCH_3), 2.69–2.52 (m, 1H, –CH_2), 2.33 (s, 3H, Ar–CH_3), 1.88–1.74 (m, 1H, –CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.3, 29.5, 37.9, 57.1, 68.0, 71.4, 73.7, 73.8, 83.4, 84.3, 116.2, 118.2, 124.5, 125.3, 126.2, 126.2, 127.1, 127.3, 127.9, 128.7, 129.8; FABMS (*m*/*z*, %): 464 (M^++Na, 100), 442 (M^++H, 38), 391 (36), 288 (34), 248 (66), 167 (72), 154 (92). Anal. Calcd for $C_{25}H_{29}NO_5S$; C 65.91, H 6.42, N 3.07, S 7.04%; found C 65.90, H 6.39, N 2.99, S 7.00%.

4.1.11. 1-[2,2-Dimethyl-(4*S*)-1,3-dioxolan-4-yl]-(1*R*)-3-butenyl methyl ether (13). To a stirred solution of **12** (2.8 g, 16.2 mmol) in dry THF (30 mL) at 0 °C was added sodium hydride (1.3 g, 32.5 mmol, 60% dispersion in mineral oil) and stirred for 20 min. Methyl iodide (3.46 g, 24.4 mmol) was added and stirred for 6 h. The mixture was quenched with satd NH_4Cl (1 mL), extracted with EtOAc (2×5 mL), and the combined organic layers were washed with water (1×5 mL), brine (1×5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (Silica gel 60–120, 1:5 EtOAc:hexane) to afford **13** (2.1 g, 70%) as a light yellow oil. R_f (10% EtOAc/hexane) 0.32; $[\alpha]_D$ −6.8 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.88–5.76 (m, 1H, –C*H*=CH_2), 5.12–5.07 (m, 2H, –CH=CH_2), 4.00–3.92 (m, 2H, –CH_2O–), 3.84–3.79 (m, 1H, –C*H*O–), 3.40 (s, 3H, –CHOCH_3), 3.23 (q, *J* 10.0, 6.0 Hz, 1H, –*CH*OMe), 2.42–2.32 (m, 1H, –C*H*CH=CH_2), 2.30–2.21 (m, 1H, –C*H*CH=CH_2), 1.38 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.2, 28.1, 57.1, 62.5, 70.1, 100.4, 109.5, 126.1; IR (neat): 3100, 2950, 1620, 1460, 1400 cm^{-1}; FABMS (*m*/*z*, %): 187 (M^++H, 16%), 109 (32), 95 (65), 81 (79). Anal. Calcd for $C_{10}H_{18}O_3$; C 64.19, H 9.74%; found C 63.94, H 9.53%.

4.1.12. 3-Methoxy-(2*S*,3*R*)-5-hexene-1,2-diol (14). The **13** (1.8 g, 9.6 mmol) was dissolved in 60% aq AcOH (15 mL) and stirred for 6 h. The workup and purification as described for compound **3** afforded **14** (1.13 g, 80%) as syrup. R_f (50% EtOAc/hexane) 0.49; $[\alpha]_D$ −2.7 (*c* 1.0, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ 5.92–5.69 (m, 1H, –C*H*=CH_2), 5.15–5.06 (m, 2H, –CH=CH_2), 3.72–3.61 (m, 3H, –CH_2OH and *CH*OH), 3.42 (s, 3H, –OCH_3), 3.34 (q, 1H, –C*H*OCH_3), 2.44–2.23 (m, 2H, –CH_2CH=CH_2), 1.45 (br s, 1H, –O*H*); ^{13}C NMR (50 MHz, $CDCl_3$): δ 34.1, 57.5, 64.9, 66.5, 72.1, 116.7, 126.1; IR (neat): 3400, 2920, 1630, 1420, 1400 cm^{-1}; FABMS (*m*/*z*, %): 169 (M^++Na, 8), 147 (M^++H, 54), 137 (40), 69 (60), 55 (100). Anal. Calcd for $C_7H_{14}NO_3$; C 57.51, H 9.65%; found C 57.50, H 9.59%.

4.1.13. 1-Benzyloxy-3-methoxy-(2*S*,3*R*)-5-hexen-2-ol (15). To a stirred solution of **14** (1.4 g, 9.5 mmol) in acetone were added K_2CO_3 (4.14 g, 30.0 mmol), TBAI 0.02 g), and benzyl bromide (1.3 mL, 10.5 mmol) and the mixture heated for 18 h. The workup and purification as described for **4** afforded **15** (1.42 g, 63%) as a colorless liquid. R_f (30% EtOAc/hexane) 0.48; $[\alpha]_D$ −15.4 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (br s, 5H, Ar–*H*), 5.89–5.75 (m, 1H, –C*H*=CH_2), 5.12–5.02 (m, 2H, –CH=CH_2), 4.53 (s, 2H, –OCH_2Ph), 3.77–3.71 (m, 1H, –C*H*OH), 3.57(dd, *J* 9.0, 6.7 Hz, 1H, –CH_2OBn), 3.51 (dd, *J* 9.0, 6.8 Hz, 1H, –CH_2OBn), 3.35 (s, 3H, –O*Me*), 3.24 (q, 1H, –C*H*OMe), 2.32 (m, 2H, –CH_2CH=CH_2), 1.4 (br s, 1H, –O*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.0, 57.5, 65.0, 66.5, 72.1; IR (neat): 3400, 2920, 1630, 1420, 1400 cm^{-1}; FABMS (*m*/*z*, %): 259 (M^++Na, 11), 237 (M^++H, 21), 69 (100). Anal. Calcd for $C_{14}H_{20}NO_3$; C 71.16, H 8.53%; found C 71.09, H 8.49%.

4.1.14. 5-Benzyloxymethyl-4-methoxy-(4*R*,5*S*)-2*H*,3*H*,4*H*-2-furanylmethanol (16). To a stirred solution of **15** (1 g, 4.2 mmol) in $CHCl_3$ (5 mL) was added *m*-chloroperbenzoic acid (3.8 g, 6.2 mmol, 50–55% in water) dissolved in $CHCl_3$ (5 mL) and stirred for 6 h. The workup and purification as described for compound **5** afforded **16** (0.72 g, 68%) as a colorless liquid. R_f (50% EtOAc/hexane) 0.39; $[\alpha]_D$ +3.2 (*c* 1.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (br s, 5H, Ar–*H*), 4.53 (s, 2H, –OCH_2Ph), 4.25–3.87 (m, 3H, –CH_2OBn, C*H*OMe, and C*H*CH_2OH), 3.62–3.41 (m, 4H, –CH_2OH and CH_2OBn), 3.30 (s, 3H, –OCH_3), 2.28–2.04 (m, 1H, –CH_2), 1.93–1.79 (m, 1H, –CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 39.0, 58.1, 65.3, 66.3, 72.5, 74.2, 81.9, 128.0, 128.6, 135.0, 137.3; IR (neat): 3540, 2920, 1030, 1100 cm^{-1}; FABMS (*m*/*z*, %): 253 (M^++H, 2), 215 (4), 181 (6), 136(6), 91(100). Anal. Calcd for $C_{14}H_{20}O_4$; C 66.65, H 7.99%; found C 66.64, H 7.85%.

4.1.15. 5-Benzyloxymethyl-4-methoxy-(4*R*,5*S*)-tetrahydro-2-furancarbaldehyde (17). To a stirred solution of oxallyl chloride (0.37 mL, 3.0 mmol) in dry CH_2Cl_2 (5 mL) was added dry DMSO (0.47 mL, 6.1 mmol) drop wise at −78 °C, after 2 min **16** (0.35 g, 1.35 mmol) dissolved in CH_2Cl_2 (5 mL) was added and stirred for 30 min. To this Et_3N (0.8 mL, 8.4 mmol) was added at −78 °C and the mixture allowed to stir at room temperature for 20 min. The workup and purification as described for compound **6** afforded **17** (0.69 g, 99%) as a colorless liquid. The crude aldehyde was used without further purification and characterization.

4.1.16. Ethyl 3-[5-benzyloxymethyl-4-methoxy-(4*R*,5*S*)-2*H*,3*H*,4*H*-2-furanyl]-(*E*)-2-propenoate (18). To a stirred

solution of **16** (0.35 g, 1.4 mmol) in benzene (3 mL) at reflux (ethoxycarbonylmethylene)triphenylphosphorane (0.73 g, 2.1 mmol) was added and the mixture allowed to reflux for 1 h. The workup and purification as described for compound **7** afforded **18** (0.31 g, 70% only *E* isomer) as a yellow syrup. R_f (40% EtOAc/hexane) 0.52; $[\alpha]_D$ +9.3 (*c* 0.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.27 (br s, 5H, Ar–*H*), 6.94–6.85 (m, 1H, –C*H*=CHCOOEt), 5.98 (t, *J* 15.8 Hz, 1H, –CH=C*H*COOEt), 4.69–4.54 (m, 1H, –C*H*CH=CHCOOEt), 4.54 (s, 2H, –OCH_2Ph), 4.23–4.05 (m, 3H, –COOCH_2CH$_3$ and –C*H*O–), 3.93–3.83 (m, 1H, –C*H*OMe), 3.55–3.40 (m, 2H, –CH_2OBn), 3.30 (s, 3H, –OCH_3), 2.41–2.07 (m, 1H, –CH_2), 1.85–1.65 (m, 1H, –CH_2), 1.29 (t, *J* 7.2 Hz, 3H, –COOCH$_2$CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 15.0, 31.2, 56.0, 60.1, 71.2, 72.1, 82.1, 83.0, 89.1, 127.4, 127.9, 128.8, 131.1, 135.1, 145.2, 163.8; IR (neat): 2960, 1660, 1450, 1190, 1010 cm^{-1}; FABMS (*m*/*z*, %): 343 (M^++Na, 2), 321 (M^++H, 13), 215 (27), 138 (62), 73 (100). Anal. Calcd for $C_{18}H_{24}O_5$; C 67.48, H 7.55%; found C 67.38, H 7.50%.

4.1.17. 4-Methoxy-2-(1,3-oxazol-5-yl)-(2*S*,4*R*,5*S*)-2*H*,3*H*,4*H*-5-furanylmethoxy-(phenyl)methane and 4-methoxy-2-(1,3-oxazol-5-yl)-(2*R*,4*R*,5*S*)-2*H*,3*H*,4*H*-5-furanylmethoxy (phenyl)methane (19a and 19b). To a stirred solution of aldehyde **17** (0.15 g, 0.6 mmol) in methanol (2 mL) were added TosMIC (0.14 g, 0.72 mmol) and potassium carbonate (0.248 g, 1.8 mmol) and the mixture allowed to reflux for 1 h. The reaction mixture was concentrated under reduced pressure, the residue dissolved in water (10 mL) and extracted into EtOAc (2×10 mL). The combined organic layers were washed with water (1×10 mL), brine (1×10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:5 EtOAc:hexane) the first eluted was **19a** (0.048 g, 28%) as a thick yellow syrup. R_f (50% EtOAc/hexane) 0.39; $[\alpha]_D$ −0.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.78 (s, 1H, oxazole-*H*), 7.28 (br s, 5H, Ar–*H*), 6.96 (s, 1H, oxazole-*H*), 5.08 (dd, *J* 9.8, 6.0 Hz, 1H, –C*H*oxazole), 4.53 (s, 2H, –CH_2Ph), 4.10 (m, 1H, –C*H*CH$_2$OBn), 3.95–3.89 (m, 1H, –C*H*OCH$_3$), 3.57 (dd, *J* 10.5, 5.2 Hz, 1H, –CH_2OBn), 3.46 (dd, *J* 10.5, 5.2 Hz, 1H, –CH_2OBn), 3.33 (s, 3H, –OCH_3), 2.21–2.16 (m, 2H, –CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 36.3, 56.7, 70.8, 71.3, 73.5, 83.0, 83.7, 124.0, 127.5, 128.3, 129.6, 130.1, 138.1, 151.0; LCMS: 307 (M+NH_4)$^+$. Anal. Calcd for $C_{16}H_{19}NO_4$; C 66.42, H 6.62, N 4.84%; found C 66.40, H 6.59, N 4.80%.

The second eluted was **19b** (0.043 g, 25%) as a yellow syrup. R_f (50% EtOAc/hexane) 0.38; $[\alpha]_D$ −8.5 (*c* 10.35, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.78 (s, 1H, Oxazole-*H*), 7.27 (br s, 5H, Ar–*H*), 7.01 (s, 1H, Oxazole-*H*), 5.16 (t, *J* 7.5 Hz, 1H, –C*H*Oxazole), 4.56 (d, *J* 2.9 Hz, 2H, –OCH_2Ph), 4.12–4.08 (m, 1H, –C*H*CH$_2$OBn), 4.03–3.97 (m, 1H, –C*H*OCH$_3$), 3.56 (d, *J* 4.5 Hz, 2H, –CH_2OBn), 3.32 (s, 3H, –OCH_3), 2.56–2.47 (m, 1H, –CH_2), 2.20–2.15 (m, 1H, –CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 36.3, 56.7, 70.8, 71.3, 73.5, 83.0, 83.7, 124.0, 127.5, 128.3, 129.6, 130.1, 138.1, 151.0; LCMS: 312 (M^++Na). Anal. Calcd for $C_{16}H_{19}NO_4$; C 66.42, H 6.62, N 4.84%; found C 66.29, H 6.65, N 4.83%.

4.1.18. Ethyl 4-[5-benzyloxymethyl-4-methoxy-(2*S*,4*R*,5*S*)-2*H*,3*H*,4*H*-2-furanyl]-1*H*-3-pyrrolecarboxylate and ethyl 4-[5-benzyloxymethyl-4-methoxy-(2*R*,4*R*,5*S*)-2*H*,3*H*,4*H*-2-furanyl]-1*H*-3-pyrrolecarboxylate (20a and 20b). To a stirred solution of TosMIC (0.080 g, 0.41 mmol) in dry THF (2 mL) at −78 °C was added *n*-BuLi (1.6 M solution in *n*-hexane, 0.25 mL, 1.2 mmol) and the mixture stirred for 15 min. To this **18** (0.110 g, 0.34 mmol) dissolved in dry THF (2 mL) was added and the mixture stirred for 30 min. After completion of the reaction, the mixture was quenched with satd NH_4Cl (1 mL), extracted with EtOAc (2×5 mL), and the combined organic layers were washed with water (1×5 mL), brine (1×5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (Silica gel 60–120, 1:5 EtOAc:hexane), first eluted was **20a** (0.046 g, 37%) as a light yellow syrup. R_f (30% EtOAc/hexane) 0.38; $[\alpha]_D$ −48.3 (*c* 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.4 (s, 1H, –N*H*–), 7.27 (br s, 5H, Ar–*H*), 7.21 (s, 1H, pyrrole-*H*), 6.64 (s, 1H, pyrrole-*H*), 5.42 (dd, *J* 9.4, 5.2 Hz, 1H, –C*H*pyrrole*)*, 4.54 (s, 2H, –CH_2Ph), 4.22 (m, 2H, –COOCH_2CH$_3$), 4.09–4.05 (m, 1H, –C*H*CH$_2$OBn), 3.84–3.79 (m, 1H, –C*H*OCH$_3$), 3.62–3.51 (m, 2H, –CH_2OBn), 3.32 (s, 3H, –OCH_3), 2.47 (ddd, *J* 8.2, 5.6, 1.8 Hz, 1H, –CH_2–), 1.78–1.69 (m, 1H, –CH_2–), 1.32 (t, *J* 7.1 Hz, 3H, –COOCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 29.9, 39.5, 56.8, 59.5, 60.0, 71.2, 73.3, 83.1, 83.6, 113.6, 116.6, 125.2, 126.9, 127.6, 128.6, 138.3, 164.8; IR (neat): 3260, 2920, 1500, 1450, 1120 cm^{-1}; FABMS (*m*/*z*, %): 360 (M^++H, 9), 327 (14), 207 (3), 147 (19), 91 (59), 69 (74), 55 (100). Anal. Calcd for $C_{20}H_{25}NO_5$: C 66.83, H 7.01, N 3.90%; found C 66.74, H 7.11, N 3.85%.

The second eluted was **20b** (0.042 g, 34%) as a colorless syrup. R_f (30% EtOAc/hexane) 0.37; $[\alpha]_D$ +17.1 (*c* 0.35, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.90 (br s, 1H, –N*H*–), 7.27 (br s, 5H, Ar–*H*), 7.21 (s, 1H, pyrrole-*H*), 6.69 (s, 1H, pyrrole-*H*), 5.47 (t, *J* 7.3 Hz, 1H, –C*H*pyrrole), 4.60 (s, 2H, –CH_2Ph), 4.25–4.18 (m, 3H, –C*H*CH$_2$OBn and –COOCH_2CH$_3$), 3.96–3.90 (m, 1H, –C*H*OCH$_3$), 3.56 (d, *J* 5.2 Hz, 2H, –CH_2OBn), 3.26 (s, 3H, –OCH_3), 2.81–2.72 (m, 1H, –CH_2), 1.85–1.76 (m, 1H, –CH_2), 1.31 (t, *J* 7.1 Hz, 3H, –COOCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 29.8, 39.5, 56.6, 57.2, 59.5, 60.1, 71.1, 74.2, 83.0, 83.6, 113.5, 116.6, 125.1, 126.9, 127.5, 128.6, 138.4, 164.9; IR (neat): 3260, 2920, 1500, 1450, 1120 cm^{-1}; FABMS (*m*/*z*, %): 360 (M^++H, 5), 327 (2), 147 (21), 91(59), 69 (72), 55 (100). Anal. Calcd for $C_{20}H_{25}NO_5$: C 66.83, H 7.01, N 3.90%; found C 66.80, H 7.10, N 3.79%.

4.1.19. (4*S*)-4-[(1*R*)-1-(Benzyloxy)-3-butenyl]-2,2-dimethyl-1,3-dioxolane (21). To a stirred solution of **1** (2.5 g, 14.5 mmol) in dry DMF (8 mL) at 0 °C was added sodium hydride (0.68 g, 29.04 mmol, 60% dispersion in mineral oil) and stirred for 20 min. Benzyl bromide (2.47 g, 14.5 mmol) was added and the reaction stirred for 6 h. The reaction mixture was quenched with satd NH_4Cl (20 mL) at 0 °C and stirred for 10 min. The organic compound was extracted into EtOAc (2×100 mL). The organic layer was washed with water (1×50 mL), brine (2×50 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (60–120 Silica gel, 1:50 EtOAc:hexane) to obtain **21** (2.48 g, 94%) as a colorless liquid. R_f (10% EtOAc/hexane) 0.41; $[\alpha]_D$ +8.1 (*c* 1.25, $CHCl_3$); ^1H NMR

(300 MHz, $CDCl_3$): δ 7.27 (br s, 5H, Ar–*H*), 5.91–5.76 (m, 1H, –C*H*=CH_2), 5.07 (t, *J* 10.3 Hz, 2H, –CH=CH_2), 4.60–4.55 (m, 2H, –OCH_2Ph), 4.01–3.92 (m, 2H, –CH_2O), 3.84–3.74 (m, 1H, –C*H*O), 3.24 (q, *J* 6.0 Hz, 1H, –C*H*OBn), 2.55–2.35 (m, 2H, –CH_2CH=CH_2), 1.38 (s, 3H, –CH_3), 1.30 (s, 3H, –CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 18.1, 28.0, 34.3, 65.8, 66.7, 82.3, 83.1, 100.8, 115.5, 126.1, 127.1, 128.3, 131.4, 135.0; IR (neat): 3100, 2950, 1620, 1460, 1400 cm^{-1}; FABMS (*m*/*z*, %): 263 (M^++H, 16%), 155 (32), 95 (72), 81 (76). Anal. Calcd for $C_{16}H_{22}O_3$: C 73.5, H 8.30%; found C 73.42, H 8.26%.

4.1.20. (2*S*,3*R*)-3-(Benzyloxy)-5-hexene-1,2-diol (22). The methyl ether **21** (3.2 g, 12.3 mmol) was dissolved in 60% aq acetic acid (30 mL) and stirred for 6 h. The reaction mixture was neutralized with solid $NaHCO_3$. The workup and purification as described for compound **3** afforded **22** (2.25 g, 84%) as a colorless oil. R_f (50% EtOAc/hexane) 0.52; $[\alpha]_D$ +4.28 (*c* 0.92, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52 (br s, 5H, Ar–*H*), 5.92–5.72 (m, 1H, –C*H*=H_2), 5.17–5.05 (m, 2H, –CH=CH_2), 4.68–4.46 (m, 2H, –O–CH_2–Ar), 3.65–3.55 (m, 4H, –C*H*OBn, –CH_2OH, and –C*H*OH), 2.55–2.35 (m, 2H, –CH_2CH=CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 33.1, 66.2, 69.8, 71.9, 80.2, 116.5, 126.0, 127.6, 128.9, 133.2, 137.1; IR (neat): 3400, 2920, 1630, 1420, 1400 cm^{-1}; FABMS (*m*/*z*, %): 245 (M^++Na, 8), 223 (M^++H, 54), 137 (40), 69 (60), 55 (100). Anal. Calcd for $C_{13}H_{18}O_3$: C 70.10, H 8.00%; found C 70.09, H 7.95%.

4.1.21. (2*S*,3*R*)-1,3-Di(benzyloxy)-5-hexen-2-ol (23). To a stirred solution of **22** (2.25 g, 10.2 mmol) in acetone were added K_2CO_3 (3.0 g, 30.5 mmol), TBAI (0.02 g), and benzyl bromide (1.3 mL, 11.2 mmol) and the mixture allowed to reflux for 18 h. The workup and purification as described for **4** afforded **23** (2.15 g, 68%) as a light yellow oil. R_f (30% EtOAc/hexane) 0.53; $[\alpha]_D$ +19.5 (*c* 0.69, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$); δ 7.30 (br s, 10H, Ar–*H*), 5.98–5.75 (m, 1H, –C*H*=CH_2), 5.12–5.02 (m, 2H, –CH=CH_2), 4.65–4.45 (m, 4H, –OCH_2Ph), 3.85–3.74 (m, 1H, –C*H*OH), 3.65–3.45 (m, 3H, –CH_2OBn and –C*H*OBn), 2.47–2.37 (m, 2H, –CH_2CH=CH_2), 1.41 (br s, 1H, –O*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.2, 57.8, 65.1, 71.1, 73.9, 81.2, 82.3, 117.0, 126.9, 127.5, 127.7, 128.4, 128.4, 134.6, 138.0; FABMS (*m*/*z*, %): 335 (M^++Na, 18), 313 (M^++H, 8), 137 (40), 69 (100). Anal. Calcd for $C_{20}H_{24}O_3$: C 76.90, H 7.10%; found C 76.87, H 7.11%.

4.1.22. (4*R*,5*R*)-4-(Benzyloxy)-5-[(benzyloxy)methyl]-tetrahydro-2-furanylmethanol (24). To a stirred solution of **23** (0.88 g, 2.8 mmol) in $CHCl_3$ (5 mL) was added *m*-chloroperbenzoic acid (0.73 g, 4.2 mmol, 50–55% in water) dissolved in $CHCl_3$ (5 mL) and stirred for 6 h. The workup and purification as described for compound **5** afforded **24** (0.68 g, 74%) as a light yellow syrup. R_f (50% EtOAc/hexane) 0.43; $[\alpha]_D$ +34.3 (*c* 1.85, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30 (br s, 10H, Ar–*H*), 4.67–4.47 (m, 4H, –OCH_2Ph), 4.35–4.05 (m, 4H, –CH_2OBn, –*CH*–O–, and –C*H*–OBn), 3.67–3.37 (m, 3H, –CH_2OH and –C*H*O), 2.90 (br s, 1H, –O*H*), 2.30–1.85 (m, 2H, –CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 38.7, 65.1, 66.5, 67.2, 72.4, 74.5, 82.4, 83.1, 127.0, 127.6, 127.9, 128.6, 134.5, 135.0, 137.6, 138.1; IR (neat): 3540, 2920, 1030, 1100 cm^{-1}; FABMS (*m*/*z*, %): 329 (M^++H, 2), 245 (4), 181 (6), 136(6), 91(100). Anal. Calcd for $C_{20}H_{24}O_4$: C 73.45, H 7.55%; found C 73.39, H 7.52%.

4.1.23. (4*R*,5*R*)-4-(Benzyloxy)-5-[(benzyloxy)methyl]-tetrahydro-2-furancarbaldehyde (25). To a stirred solution of oxallyl chloride (0.2 mL, 2.27 mmol) in dry CH_2Cl_2 (5 mL) was added dry DMSO (0.32 mL, 4.55 mmol) dropwise at −78 °C, after 2 min. Compound **24** (0.68 g, 2.07 mmol) dissolved in CH_2Cl_2 (5 mL) was added and stirred for 30 min. To this Et_3N (1.74 mL, 9.9 mmol) was added at −78 °C and allowed to stir at room temperature for 20 min. The workup and purification as reported for compound **17** afforded **25** (0.68, 96%) as a colorless liquid. The crude aldehyde was used without further purification and characterization.

4.1.24. Ethyl 3-[5-benzyloxymethyl-4-benzyloxy-(4*R*,5*S*)-2*H*,3*H*,4*H*-2-furanyl]-(*E*)-2-propenoate (26). To a stirred solution of **25** (0.5 g, 1.53 mmol) in benzene (5 mL) at reflux was added (ethoxycarbonylmethylene)triphenylphosphorane (0.8 g, 2.3 mmol) and the reaction was allowed to stir at reflux for 1 h. The workup and purification as described for compound **6** afforded **26** (0.62 g, 69%) as a light yellow liquid. R_f (30% EtOAc/hexane) 0.48; $[\alpha]_D$ −3.5 (*c* 1.85, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.27 (br s, 10H, Ar–*H*), 6.97–6.86 (m, 1H, –C*H*=CHCOOEt), 6.05–5.95 (m, 1H, –CH=*H*COOEt), 4.55–4.49 (m, 5H, –OCH_2Ph and –C*H*–CH=CHCOOEt), 4.24–4.15 (m, 4H, –COOC$H_2$$CH_3$ and –CH_2OBn), 3.57–3.51 (m, 1H, –C*H*O–), 3.46–3.36 (m, 1H, –C*H*OBn), 2.32–2.13 (m, 1H, –CH_2–), 1.95–1.69 (m, 1H, –CH_2–), 1.29 (t, *J* 7.2 Hz, 3H, –COOCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.2, 31.3, 60.2, 71.5, 72.2, 81.9, 82.8, 83.2, 89.2, 127.1, 127.3, 127.4, 127.7, 127.8, 128.9, 129.2, 131.0, 135.3, 145.1, 163.8; IR (neat): 2960, 1660, 1450, 1190, 1010 cm^{-1}; FABMS (*m*/*z*, %): 419 (M^++Na, 2), 397 (M^++H, 13), 215 (27), 138 (62), 73 (100). Anal. Calcd for $C_{24}H_{28}O_5$: C 72.6, H 7.41%; found C 72.58, H 7.43%.

4.1.25. Ethyl 5-(2*R*,4*R*,5*R*)-4-(benzyloxy)-5-[(benzyloxy)-methyl]tetrahydro-2-furanyl-1*H*-3-pyrrolecarboxylate and ethyl 5-(2*S*,4*R*,5*R*)-4-(benzyloxy)-5-[(benzyloxy)-methyl]tetrahydro-2-furanyl-1*H*-3-pyrrolecarboxylate (27a and 27b). To a stirred solution of TosMIC (0.06 g, 0.31 mmol) in dry THF (1 mL) at −78 °C was added *n*-BuLi (1.6 M soln in *n*-hexane, 0.19 mL, 0.41 mmol) followed by **18** (0.1 g, 0.26 mmol) dissolved in dry THF (1 mL) and the reaction was stirred for 30 min. After completion of the reaction mixture, it was quenched with satd NH_4Cl (1 mL), extracted with EtOAc (2×5 mL), and the combined organic layers were washed with water (1×5 mL), brine (1×5 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography (Silica gel 60–120, 1:5 EtOAc:hexane) the first eluted **27a** (0.040 g, 36%) was obtained as a yellow syrup. R_f (30% EtOAc/hexane) 0.41; $[\alpha]_D$ +44.7 (*c* 0.6, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.02 (s, 1H, –N*H*), 7.27 (br s, 11H, Ar–*H*), 6.70 (s, 1H, pyrl-*H*), 5.52 (dd, *J* 9.5, 5.5 Hz, 1H, –C*Hpyrrole*), 4.60–4.42 (m, 4H, –CH_2Ph), 4.40–4.38 (m, 1H, –C*H*O–), 4.30–4.02 (m, 4H, –C*H*OBn, –CHO–, –COOC$H_2$$CH_3$), 3.60–3.35 (m, 2H, –C$H_2$OBn), 2.62 (ddd, *J* 9.2, 4.7, 2.2 Hz, 1H, –CH_2), 1.85–1.71 (m, 1H, –CH_2), 1.27 (t, *J* 6.8 Hz, 3H,

–$COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.5, 31.2, 56.5, 60.2, 61.7, 71.3, 82.9, 83.5, 84.0, 113.1, 115.9, 125.3, 126.1, 126.2, 127.3, 127.5, 127.5, 128.2, 128.2, 128.3, 138.1, 164.7; IR (neat): 3260, 2920, 1500, 1450, 1120 cm $^{-1}$; FABMS (*m/z*, %): 436 (M^++H, 4), 377 (4), 147 (12), 91 (54), 69 (64), 55 (100). Anal. Calcd for $C_{26}H_{29}NO_5$: C 71.90, H 6.5%; found C 71.92, H 6.54%.

The second eluted **27b** (0.038 g, 34%) was obtained as a yellow syrup. R_f (40% EtOAc/hexane) 0.40; $[\alpha]_D$ −18.8 (*c* 0.35, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.74 (br s, 1H, –N*H*–), 7.27 (br s, 11H, Ar–*H*), 6.72 (s, 1H, Ar–*H*), 5.48 (t, *J* 7.3 Hz, 1H, –Ar–*H*), 4.61–4.40 (m, 4H, –OCH_2Ph), 4.38–4.32 (m, 1H, –C*H*O–), 4.30–4.10 (m, 3H, –C*H*O– and –COOCH_2CH_3), 3.73–3.46 (m, 3H, –CH_2OBn and –C*H*OBn), 2.82–2.72 (m, 1H, –CH_2), 1.92–1.80 (m, 1H, –CH_2), 1.27 (t, *J* 6.8 Hz, 3H, –$COOCH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.5, 31.0, 56.3, 60.1, 61.5, 71.9, 83.1, 83.9, 84.5, 113.9, 116.4, 123.0, 126.2, 126.3, 127.3, 127.5, 127.6, 128.1, 128.2, 128.3, 138.2, 164.9; IR (neat): 3260, 2920, 1500, 1450, 1120 cm^{-1}; FABMS (*m/z*, %): 436 (M^++H, 7), 377 (2), 147 (19), 91 (62), 69 (71), 55 (100). Anal. Calcd for $C_{26}H_{29}NO_5$: C 71.90, H 6.5%; found C 71.89, H 6.51%.

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References and notes

1. (a) Simons, C. *Nucleoside Mimetics Their Chemistry and Biological Properties*; Gordon and Breach Science: Amsterdam, 2001; (b) Peasley, K. *Medical Hypotheses* **2000**, *55*, 408.
2. (a) Krishna, P. R.; Reddy, V. V. R.; Sharma, G. V. M. *Synlett* **2003**, 1619–1622; (b) Leusen, D. A.; Leusen, A. M. V. *Org. React.* **2001**, *57*, 417–666.
3. (a) Ren, R.; Chaudhuri, N. C.; Pairs, P. L.; Rumney, P. S.; Kool, E. T. *J. Am. Chem. Soc.* **1996**, *118*, 7671–7678; (b) Pirrung, M. C.; Zhao, X.; Harria, S. V. *J. Org. Chem.* **2001**, *66*, 2067–2071; (c) Beuck, C.; Singh, I.; Bhattachraya, A.; Hecker, W.; Parmer, V. S.; Seitz, O.; Weinhold, E. *Angew. Chem., Int. Ed,* **2003**, *42*, 3958–3960.
4. (a) Adlington, R. M.; Baldwin, J. E.; Pritchard, G. J.; Spencer, K. C. *Tetrahedron Lett.* **2000**, *41*, 575–578; (b) Miller, T. J.; Farquar, H. D.; Sheybani, A.; Tallini, C. E.; Saurage, A. S.; Fronczek, F. R.; Hammer, R. P. *Org. Lett.* **2002**, *4*, 877–880.
5. (a) Reese, C. B.; Wu, Q. *Org. Biomol. Chem.* **2003**, *1*, 3160–3172; (b) Chen, D. W.; Beuscher, A. E., IV; Stevens, R. C.; Wirsching, P.; Learner, R. A.; Janda, K. D. *J. Org. Chem.* **2001**, *66*, 1725–1732; (c) Brotschi, C.; Häberli, A.; Leumann, C. *Angew. Chem., Int. Ed.* **2001**, *40*, 3012–3014; (d) Wichai, U.; Woski, S. A. *Org. Lett.* **1999**, *1*, 1173–1175; (e) Wichai, V.; Woski, S. A. *Bioorg. Med. Chem. Lett.* **1998**, 3465–3468.
6. (a) Hacksell, U.; Daves, G. D. *J. Org. Chem.* **1983**, *48*, 2870–2876; (b) Hsieh, H. P.; Mclaughlin, L. W. *J. Org. Chem.* **1995**, *60*, 5356–5359; (c) Zhang, H. C.; Daves, G. D., Jr. *J. Org. Chem.* **1992**, *57*, 4690–4696; (d) Haberli, A.; Leumann, C. J. *Org. Lett.* **2001**, *3*, 489–492.
7. (a) Calter, M. A.; Zhu, C. *J. Org. Chem.* **1999**, *64*, 1415–1419; (b) Solomon, M. S.; Hopkins, P. B. *Tetrahedron Lett.* **1991**, *32*, 3297–3330; (c) Watterson, M. P.; Edwards, A. A.; Leach, J. A.; Smith, M. D.; Ichihara, O.; Fleet, G. W. *Tetrahedron Lett.* **2003**, *44*, 5853–5857.
8. Chatopadhayay, A. *J. Org. Chem.* **1996**, *61*, 6104–6107.
9. Chaudhuri, N. C.; Ren, R. X.-F.; Kool, E. T. *Synlett* **1997**, 341–347.
10. Nolte, A.; Klubman, S.; Bald, R.; Erdmann, V. A.; Furste, J. P. *Nat. Biotechnol.* **1996**, *14*, 1116–1119.
11. (a) Shi, Z.-D.; Yang, B.-H.; Wu, Y.-L. *Tetrahedron Lett.* **2001**, *42*, 7651–7653; (b) Jung, M. E.; Xu, Y. *Tetrahedron Lett.* **1997**, *38*, 4199–4202.
12. Pitsch, S. *Helv. Chim. Acta* **1997**, *80*, 2286–2314.
13. Moyroud, E.; Strazewski, P. *Tetrahedron* **1999**, *55*, 1277–1284.
14. (a) Jung, M. E.; Nichols, C. *Tetrahedron Lett.* **1998**, *39*, 4615–4618; (b) Stewart, A. J.; Evans, R. M.; Wilson, A. C. W.; Cowley, A. R.; Watkin, D. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2002**, *13*, 2667–2672.
15. Zhu, W.; Gumina, G.; Schinazi, R. F.; Chu, C. K. *Tetrahedron* **2003**, *59*, 6423–6431.