# Total Synthesis of (+)-Dodoneine and Its 6-Epimer

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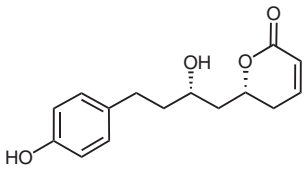
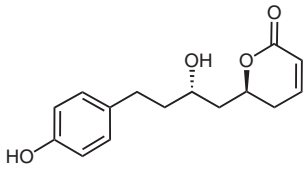
**Abstract:** The total synthesis of dodoneine and its 6-epimer is described, using HKR of epoxide and reduction with $SmI_2$ reactions as key steps, respectively.

**Key words:** dodoneine, epidodoneine, trimethylsulfonium iodide, HKR, $SmI_2$, RCM

Dodoneine (**1**), a dihydropyranone was isolated from a parasitic plant *Tapinanthus dodoneifolius*, which is widely spread in the Sahelian region (West Africa).[1] *T. dodoneifolius* is used as a remedy to treat cholera, diarrhea, stomachache, wounds, and nervous confusion. It is also used for cardiovascular and respiratory diseases. Dodoneine (**1**) was found to exhibit a vasorelaxant effect on preconstricted rat aortic rings (IC = 81.4 ± 0.9 μM).[2] Its structure was assigned on the basis of spectroscopic and X-ray diffraction analyses. In spite of its interesting biological activities, only three syntheses[3] have been reported so far for the natural compound **1**. No synthesis has been reported for its 6-epimer, epidodoneine (**2**). In continuation of our interest on the synthesis of bioactive lactones,[4] we herein report the synthesis of dodoneine (**1**) and its 6-epimer **2** (Figure 1).




dodoneine **1**




epidodoneine **2**

**Figure 1** Dodoneine (**1**) and its 6-epimer **2**

The retrosynthesis reveals that dodoneine (**1**) could be synthesized in two ways from a common intermediate **7**. In route a, the lactone moiety can be constructed through ring-closing metathesis (RCM), whereas in route b, Horner–Wadsworth–Emmons reaction was utilized. Epidodoneine (**2**) could be prepared by $SmI_2$ reduction of alkoxy keto compound **9**, followed by construction of lactone moiety through RCM leading to the target molecule (Scheme 1).

The synthesis began with the known alcohol **7** prepared from MOM protected *p*-iodophenol **10** and the chiral acetylenic alcohol **11** by Cossford protocol followed by some functional group manipulations as described in our earlier communication.[4d] Oxidation of alcohol **7** using IBX yielded the corresponding aldehyde and subsequently treatment with trimethylsulfonium iodide[5] in the presence of NaH in DMSO–THF affords the corresponding racemic epoxide in 60% yield (Scheme 2).

This epoxide was subjected to Jacobsen's hydrolytic kinetic resolution (HKR)[6] by using (*S*,*S*)-Salen-Co-OAc catalyst to give chiral epoxide **4** (43%) in highly enantioenriched form (95% ee). Next, the epoxide **4** was treated with vinylmagnesium bromide in the presence of CuI in THF at –20 °C to give the homoallyl alcohol **12** in 85% yield. The relative stereochemistry of 1,3-diol in **12** was established by their conversion to the corresponding acetonide **13** after removal of MOM group. The *syn* relative configuration of the hydroxy groups was confirmed by the analysis of $^{13}C$ NMR spectrum, which showed signals at δ = 19.8 and 30.0 for the two methyl groups and at δ = 98.8 for the quaternary carbon.[7]

The homoallyl alcohol **12** was esterified with acryloyl chloride in the presence of $Et_3N$ to afford the acryloyl ester **3** in 80% yield. Subsequent ring-closing metathesis of ester **3** with Grubbs' 1st generation catalyst[8] in refluxing $CH_2Cl_2$ for 12 hours afforded the α,β-unsaturated lactone **14** in 68% yield. To complete the synthesis, it was necessary to remove the MOM group in compound **14**. This was achieved under neutral conditions using $CeCl_3 \cdot 7H_2O$ in MeCN–MeOH (1:1)[4j] to afford the target lactone **1** in 79% yield (99.45% ee) (Scheme 2). The spectral data of synthetic compound **1** was comparable with the reported data.

In route b, the alcohol **7** was oxidized using IBX in DMSO–$CH_2Cl_2$ to an aldehyde and chain elongated by treatment with the two carbon stable ylide, (ethoxycarbonylmethylene)triphenylphosphorane, to provide the α,β-unsaturated ester **15** in 81%. MOM ether removal furnished the secondary alcohol **6**. The benzylidene acetal (protected *syn*-1,3-diol) **5** was prepared in 60% yield by base-catalyzed intramolecular conjugate addition using benzaldehyde in the presence of potassium *tert*-butoxide

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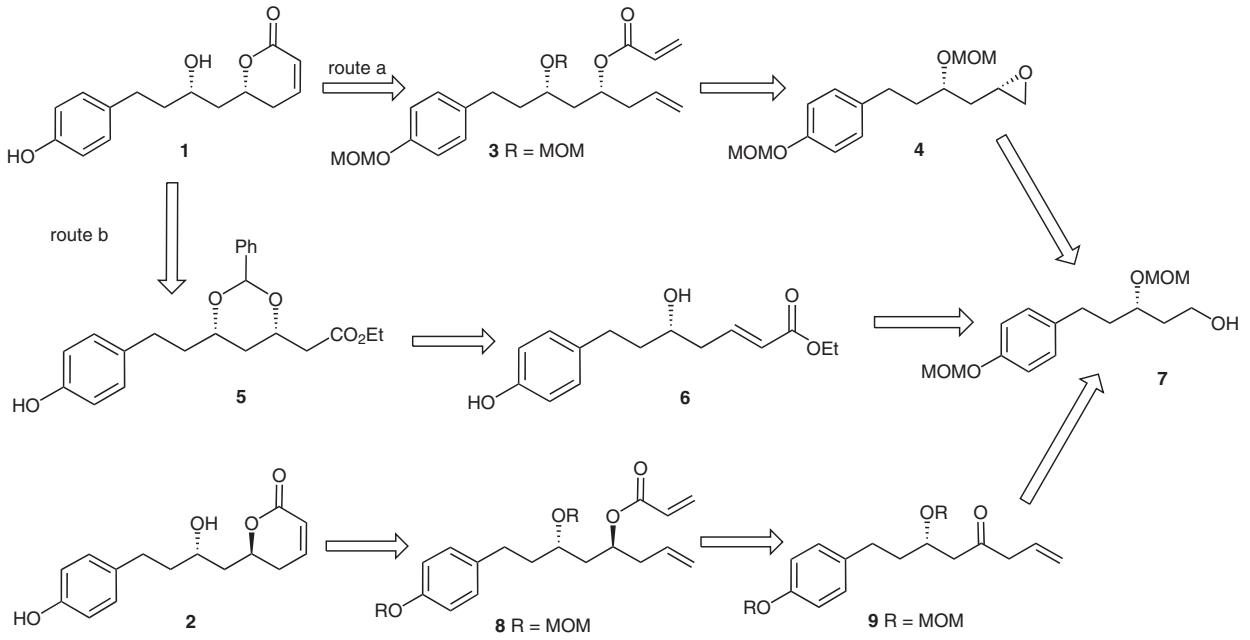
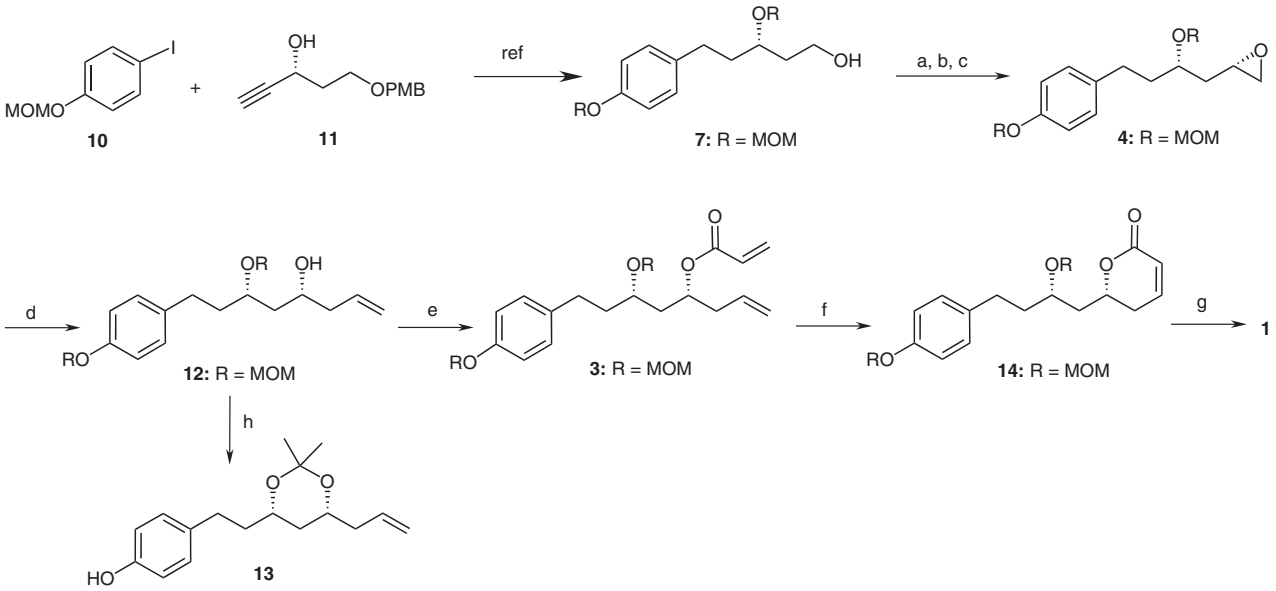


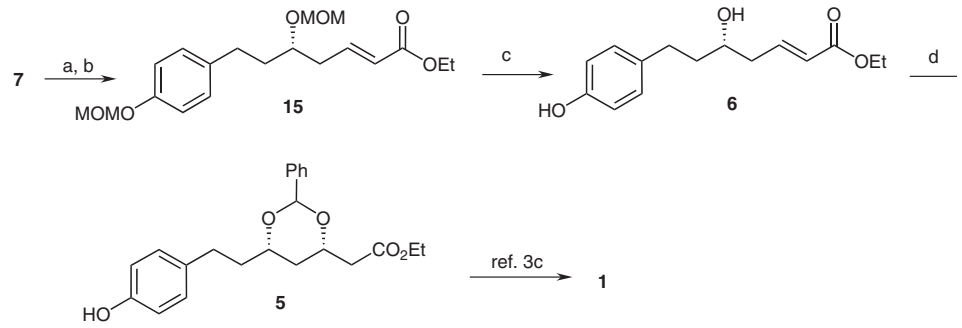

**Scheme 1** Retrosynthetic analysis for the synthesis of dodoneine (**1**) and its 6-epimer **2**



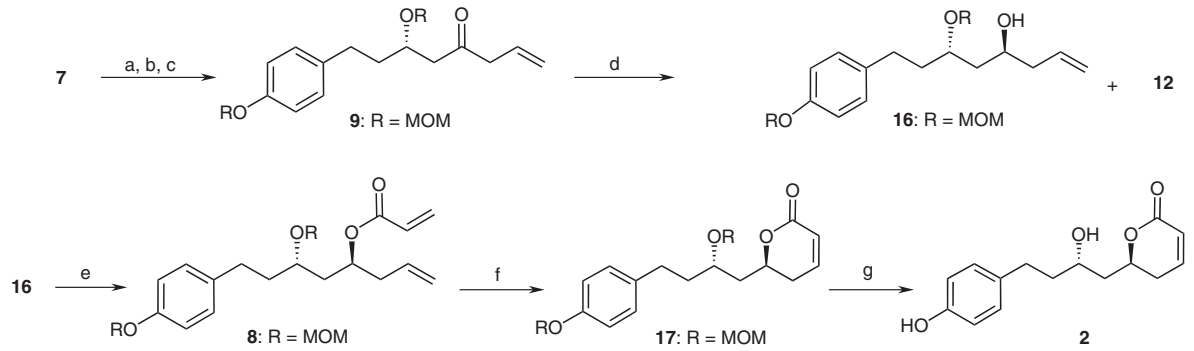

**Scheme 2** *Reagents and conditions*: (a) IBX/DMSO, $CH_2Cl_2$, 0 °C to r.t., 5 h; (b) trimethylsulfonium iodide, DMSO, NaH, THF, 0 °C to r.t., 6 h, 60%; (c) (*S,S*)-Jacobsen catalyst, AcOH, $H_2O$, 12 h, 43%; (d) vinylmagnesium bromide, CuI, THF, 0 °C, 30 min, 85%; (e) acryloyl chloride, anhyd $Et_3N$, $CH_2Cl_2$, 30 min, 80% (f) Grubbs' catalyst I, $CH_2Cl_2$, reflux, 12 h, 68%; (g) $CeCl_3{\cdot}7H_2O$ (20 mol%), MeCN–MeOH (1:1), reflux, 24 h, 79%; (h) i. $CeCl_3{\cdot}7H_2O$ (20 mol%), MeCN–MeOH (1:1), reflux, 24 h, ii. 2,2-DMP, acetone, PPTS, r.t., 2 h, 82%.

in THF at 0 °C for 2 hours and quenching the reaction with pH 7 buffer phosphate solution.[9] Compound **5** was converted into the target molecule **1** (Scheme 3), which has been reported recently in the literature.[3c]

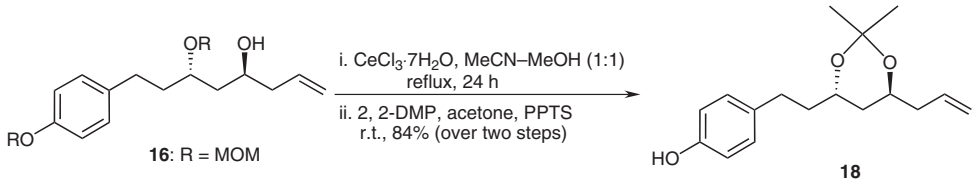
After achieving the synthesis of the natural isomer, dodoneine (**1**), we attempted the synthesis of its 6-epimer **2** as shown in Scheme 4. Thus, the primary alcohol **7** was oxidized using IBX and the ensuing aldehyde was treated with allylzinc bromide at 0 °C, which was preformed from allyl bromide and zinc powder in anhydrous THF[10] to afford diastereomers in 1:1 ratio. Since the 6-epimer **2** has a 1,3-*anti* relationship between two hydroxy centers and in order to increase the diastereoselectivity in favor of the requisite stereocenter (*anti* to the existing one), we resorted to an oxidation-reduction protocol. Hence, the alcohol was oxidized with Dess–Martin periodinane[11] in anhydrous $CH_2Cl_2$ at 0 °C to room temperature for 1 hour to afford **9** in 90% yield (Scheme 4). Our next aim was the selective reduction of ketone **9**. Thus, the stereoselective reduction of keto group was achieved with $SmI_2$ in THF and MeOH[12] as proton source for 12 hours to afford the re-



**Scheme 3** *Reagents and conditions*: (a) IBX/DMSO, $CH_2Cl_2$, 0 °C to r.t., 5 h; (b) $Ph_3P{=}CHCO_2Et$, benzene, 0 °C to r.t., 12 h, 81%; (c) $CeCl_3{\cdot}7H_2O$ (20 mol%), MeCN–MeOH (1:1), reflux, 24 h, 77%; (d) PhCHO/*t*-BuOK, anhyd THF, –10 °C, 2 h, 62%.



**Scheme 4** *Reagents and conditions*: (a) IBX/DMSO, $CH_2Cl_2$, 0 °C to r.t., 5 h (b) allyl bromide, Zn, THF, 0 °C, 30 min, 89% (c) DMP, $NaHCO_3$, $CH_2Cl_2$, 0 °C to r.t., 1 h, 90% (d) $SmI_2$, MeOH–THF, 73% (e) acryloyl chloride, anhyd $Et_3N$, $CH_2Cl_2$, 30 min, 78% (f) Grubb's catalyst I, $CH_2Cl_2$, reflux, 79%, (g) $CeCl_3{\cdot}7H_2O$ (20 mol%), MeCN–MeOH (1:1), reflux, 24 h, 80%.



**Scheme 5**

quired *anti*-1,3-diastereomer as the major product. Another isomer **12** was isolated in very small amount along with **16**. This compound **12** was identical in all respects as that obtained from route a (optical rotation and $^{13}C$ NMR data).

The relative stereochemistry of 1,3-diol in **16** was established by their conversion to the corresponding acetonide **18** after removal of MOM group (Scheme 5). The *anti* relative configuration of the hydroxy groups was confirmed by the analysis of its $^{13}C$ NMR spectrum, which showed signals at 24.9 ppm for the two methyl groups and 100.5 ppm for the quaternary carbon.[7]

The MOM protected homoallyl alcohol **16** was reacted with acryloyl chloride and diisopropylethylamine at 0 °C in $CH_2Cl_2$ to afford ester **8** in 78% yield for ring-closing metathesis. The ring-closing metathesis was achieved with Grubbs' 1st generation catalyst to afford lactone **17** in 79% yield, which was subjected to deprotection of MOM with $CeCl_3{\cdot}7H_2O$ in MeCN–MeOH (1:1) at reflux temperature for 24 hours to produce the epidodoneine (**2**) in 80% yield [99.28% ee, $[\alpha]_D^{25}$ –26.7 (*c* 1.0, $CHCl_3$)] (Scheme 4).

Reactions were conducted under $N_2$ in anhyd solvents such as $CH_2Cl_2$, THF, and EtOAc. All reactions were monitored by TLC (silica-coated plates and visualizing under UV light). Petroleum ether (PE) used refers to the fraction boiling in the range 60–80 °C. Yields refer to chromatographically and spectroscopically ($^1H$ and $^{13}C$ NMR) homogeneous material. Air-sensitive reagents were transferred by syringe or double-ended needle. Evaporation of solvents was performed at reduced pressure on a Büchi rotary evaporator. $^1H$ and $^{13}C$ NMR spectra of samples in $CDCl_3$ were recorded on Varian FT-200 MHz (Gemini) and Bruker UXNMR FT-300 MHz (Avance) spectrometers. Chemical shifts δ are reported relative to TMS (δ = 0.0) as an internal standard. Mass spectra were recorded under ESI conditions at 70 eV on LC-MSD (Agilent technologies) spectrometers. All high-resolution spectra were recorded on QSTAR XL hybrid MS/MS system (Applied Biosystems/MDS sciex, Foster City, CA, USA), equipped with an ESI source (IICT, Hyderabad). Column chromatography was performed on silica gel (60–120 mesh) supplied by Acme Chemical Co., India. TLC was performed on Merck 60 F-254 silica gel plates. Optical ro-

tations were measured with Jasco DIP-370 Polarimeter at 20 °C. The % ee of the products was determined using Chiral HPLC, Dionex (chromeleon, PDA).

**(2*S*)-2-{(2*S*)-2-(Methoxymethoxy)-4-[4-(methoxymethoxy)phenyl]butyl}oxirane (4)**

To an ice-cooled solution of 2-iodoxybenzoic acid (4.33 g, 15.46 mmol) in DMSO (12 mL) was added a solution of **7** (2.2 g, 7.74 mmol) in anhyd $CH_2Cl_2$ (20 mL). The mixture was stirred at r.t. for 5 h, then filtered through a Celite pad (1 g), and washed with $CH_2Cl_2$ (4 × 20 mL). The combined organic filtrates were washed with $H_2O$ (2 × 20 mL) and brine (2 × 20 mL), dried ($Na_2SO_4$), and concentrated in vacuo to afford the crude aldehyde. This was used in the next step without further purification. A solution of NaH (0.46 g, 19.16 mmol) in DMSO (25 mL) was stirred at 70–75 °C for 30 min and cooled to r.t. THF (30 mL) followed by the addition of a suspension of trimethylsulfonium iodide (6.16 g, 30.18 mmol) in DMSO (5 mL) at –5 °C and the reaction mixture was stirred for 5 min. Then, a solution of the above aldehyde in THF (5 mL) was added and the mixture stirred for 4 h at –5 °C, The mixture was quenched with $H_2O$ (20 mL) and extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic layers were washed with $H_2O$ (2 × 20 mL) and brine (2 × 20 mL), and dried ($Na_2SO_4$). The solvent was evaporated and the residue purified by column chromatography (eluent: PE–EtOAc, 7:3) to afford 2-{(2*S*)-2-(methoxymethoxy)-4-[4-(methoxymethoxy)phenyl]butyl}oxirane (racemic) as a gummy liquid; yield: 1.37 g (60%); $R_f$ = 0.3 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ +21.4 (*c* 1.4, $CHCl_3$).

**2-{(2*S*)-2-(Methoxymethoxy)-4-[4-(methoxymethoxy)phenyl]butyl}oxirane**

IR (neat): 2926, 1611, 1510, 1232, 1151, 1079, 1034, 919, 832 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.68–1.92 (m, 4 H), 2.38–2.46 (m, 1 H), 2.51–2.77 (m, 3 H), 2.93–3.02 (m, 1 H), 3.39 (2 s, 6 H), 3.45 (s, 3 H), 3.67–3.82 (m, 1 H), 4.63 (d, *J* = 6.8 Hz, 1 H), 4.66 (d, *J* = 6.8 Hz, 1 H), 5.10 (s, 2 H), 6.90 (d, *J* = 8.3 Hz, 2 H), 7.06 (d, *J* = 8.3 Hz, 2 H).

$^{13}C$ NMR MHz, (75 MHz, $CDCl_3$): δ = 30.7 (2 C), 36.7 (2 C), 37.7 (2 C), 47.1 (2 C), 49.4 (2 C), 55.7, 55.9, 75.2 (2 C), 94.5, 95.7 (2 C), 116.3, 129.2, 135.3, 155.4.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{24}O_5$ + Na ($M^+$ + Na): 319.1521; found: 319.1509.

A mixture of (*S*,*S*)-(+)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminocobalt(II) (12 mg, 0.02 mmol) in toluene (0.04 mL, 0.40 mmol) and AcOH (0.005 mL, 0.08 mmol) was stirred while open to the air for 1 h at r.t. The reaction mixture was concentrated under reduced pressure and the brown residue was dried under vacuum. To the residue was added the above obtained racemic epoxide (1.2 g, 4.05 mmol) in one portion at 0 °C and then $H_2O$ (0.036 mL, 2.0 mmol) was added. The mixture was allowed to warm to r.t. and stirred for 12 h. The residue was purified by column chromatography (eluent: PE–EtOAc, 7:3). (*S*)-Oxirane **4** was eluted first and obtained as a colorless liquid; yield: 510 mg (43%); $R_f$ = 0.3 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ –20.8 (*c* 1.75, $CHCl_3$).

**4**

IR (neat): 2941, 1611, 1511, 1233, 1151, 1080, 1035, 920, 832 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.61–1.73 (m, 2 H), 1.79–1.94 (m, 2 H), 2.5 (dd, *J* = 4.9, 2.6 Hz, 1 H), 2.54–2.75 (m, 2 H), 2.80 (t, *J* = 4.5 Hz, 1 H), 3.01–3.08 (m, 1 H), 3.42 (s, 3 H), 3.47 (s, 3 H), 3.82 (m, 1 H), 4.71 (d, *J* = 7.0 Hz, 1 H), 4.73 (d, *J* = 6.7 Hz, 1 H), 5.15 (s, 2 H), 6.96 (d, *J* = 8.7 Hz, 2 H), 7.11 (d, *J* = 8.5 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 30.6, 36.9, 37.9, 47.4, 49.5, 55.6, 55.8, 75.2, 94.5, 95.8, 116.2, 129.2, 135.3, 155.4.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{24}O_5$ + Na ($M^+$ + Na): 319.1521; found: 319.1531.

The epoxide ring opened diol was eluted next and obtained as a light yellow oil; yield: 611 mg (48%); $R_f$ = 0.2 (PE–EtOAc, 1:1); $[\alpha]_D^{25}$ –48.3 (*c* 0.5, $CHCl_3$).

**Diol**

IR (neat): 3421, 2939, 1610, 1510, 1232, 1151, 1078, 1011, 918, 830, 770 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.50–1.95 (m, 4 H), 2.59 (t, *J* = 8.3 Hz, 2 H), 3.15–3.27 (br s, 1 H), 3.36–3.50 (m, 1 H), 3.40 (s, 3 H), 3.45 (s, 3 H), 3.52–3.67 (br s, 1 H), 3.77–3.89 (m, 2 H), 4.64 (d, *J* = 6.8 Hz, 1 H), 4.70 (d, *J* = 6.8 Hz, 1 H), 5.11 (s, 2 H), 6.90 (d, *J* = 8.3 Hz, 2 H), 7.04 (d, *J* = 9.0 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 30.2, 36.3, 37.6, 55.7, 55.8, 66.4, 70.4, 76.3, 84.4, 95.3, 116.2, 129.0, 135.1, 155.2.

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{26}O_6$ + Na ($M^+$ + Na): 337.1627; found: 337.1627.

**(4*R*,6*S*)-6-(Methoxymethoxy)-8-[4-(methoxymethoxy)phenyl]oct-1-en-4-ol (12)**

To a stirred solution of epoxide **4** (0.4 g, 13.5 mmol) in $CH_2Cl_2$ (60 mL) was added freshly prepared vinylmagnesium bromide (1.35 mL, 2 M) at –10 °C and the reaction mixture was stirred at the same temperature for about 30 min. The reaction was quenched with aq sat. $NH_4Cl$ (10 mL) and the mixture extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (2 × 50 mL), dried ($Na_2SO_4$), and concentrated under reduced pressure. Purification by column chromatography on silica gel (eluent: PE–EtOAc, 7:3) afforded **12** as a thick syrup; yield: 371 mg (85%); $R_f$ = 0.25 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ +39.5 (*c* 1, $CHCl_3$).

IR (neat): 3454, 2932, 1611, 1510, 1443, 1232, 1151, 1079, 1010, 917, 824 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.64–1.70 (m, 2 H), 1.79–1.87 (m, 2 H), 2.21 (t, *J* = 6.2 Hz, 2 H), 2.55–2.62 (m, 2 H), 2.79 (br d, *J* = 2.0 Hz, 1 H, OH), 3.40 (s, 3 H), 3.45 (s, 3 H), 3.73–3.85 (m, 2 H), 4.63 (d, *J* = 6.8 Hz, 1 H), 4.70 (d, *J* = 6.8 Hz, 1 H), 5.11 (s, 2 H), 5.05–5.14 (m, 2 H), 5.72–5.88 (m, 1 H), 6.90 (d, *J* = 8.7 Hz, 2 H), 7.05 (d, *J* = *8*.7 Hz, 2 H).

$^{13}C$ NMR MHz, (100 MHz, $CDCl_3$): δ = 30.2, 36.3, 40.7, 42.1, 55.9 (2 C), 69.9, 77.0, 94.5, 95.2, 116.2, 117.7, 128.1, 129.1 (2 C), 134.7.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{28}O_5$ + Na ($M^+$ + Na): 347.1834; found: 347.1818.

**4-{2-[(4*S*,6*R*)-6-Allyl-2,2-dimethyl-1,3-dioxan-4-yl]ethyl}phenol (13)**

To a stirred solution of compound **12** (0.08 g, 0.25 mmol) in a mixture of MeOH (3 mL) and MeCN (3 mL) was added a catalytic amount of $CeCl_3 \cdot 7H_2O$ (18 mg, 0.05 mmol) under $N_2$. After stirring for 12 h at reflux temperature, the reaction mixture was quenched with solid $NaHCO_3$ (0.05 g) and filtered, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (eluent: PE–EtOAc, 4:6) to afford the pure precursor 1,3-diol; yield: 47 mg (82%); $R_f$ = 0.3 (PE–EtOAc, 4:6); $[\alpha]_D^{25}$ –16.0 (*c* 0.35, $CHCl_3$).

**Precursor 1,3-Diol**

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.46–1.81 (m, 4 H), 2.17–2.28 (m, 2 H), 2.50–2.71 (m, 2 H), 3.55 (br s, 1 H), 3.82–3.95 (m, 2 H), 5.05–5.15 (m, 2 H), 5.68–5.84 (m, 1 H), 6.73 (d, *J* = 8.5 Hz, 2 H), 6.97 (d, *J* = 8.3 Hz, 2 H), 7.12 (br s, 1 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 30.6, 39.5, 41.9, 42.3, 71.9, 72.2, 115.4, 118.3, 129.3, 133.3, 134.0, 154.1.

LCMS: *m*/*z* = 259 ($M^+$ + Na).

To a solution of above obtained 1,3-diol (0.03 g, 0.12 mmol) in anhyd acetone (3 mL) was added 2,2-dimethoxypropane (2,2-DMP, 0.03 mL, 0.25 mmol) and PPTS (10 mol%) were added. The mixture was stirred at r.t. for 2 h, then aq $NaHCO_3$ was added to neutralize PPTS and filtered. Removal of solvent and purification by silica gel column chromatography (eluent: PE–EtOAc, 7:3) afforded the acetonide **13** as a clear liquid; yield: 28 mg (82%); $R_f$ = 0.5 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ –11.0 (*c* 0.55, $CHCl_3$).

**13**

IR (neat): 3371, 2993, 2940, 2865, 1612, 1443, 1381, 1203, 1169, 996, 919, 832, 758 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.35–1.46 (m, 2 H), 1.37 (s, 6 H), 1.52–1.66 (m, 1 H), 1.68–1.81 (m, 1 H), 2.05–2.17 (m, 1 H), 2.20–2.31 (m, 1 H), 2.48–2.70 (m, 2 H), 3.64–3.83 (m, 2 H), 4.49–4.64 (br s, 1 H, OH), 4.97–5.07 (m, 2 H), 5.67–5.82 (m, 1H), 6.67 (d, *J* = 8.5 Hz, 2 H), 6.98 (d, *J* = 8.3 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 19.8, 30.0 (2 C), 36.3, 38.0, 40.6, 67.8, 68.7, 98.8, 115.1, 117.2, 129.4 (2 C), 133.6, 133.9, 153.8.

LCMS: *m*/*z* = 299 ($M^+$ + Na).

**(1*R*)-1-{(2*S*)-2-(Methoxymethoxy)-4-[4-(methoxymethoxy)phenyl]butyl}but-3-enyl Acrylate (3)**

Acryloyl chloride (0.1 mL, 1.10 mmol) was added dropwise under $N_2$ to a solution of compound **12** (0.25 g, 0.77 mmol), $Et_3N$ (0.22 mL, 1.48 mmol), and DMAP (0.05 mmol) in anhyd $CH_2Cl_2$ (10 mL). The mixture was stirred at r.t. for 30 min. After completion of reaction, the mixture was poured into brine (15 mL) and extracted with $CH_2Cl_2$ (2 × 15 mL). The combined organic phases were washed with aq 1 M HCl (6 mL) and brine (2 × 5 mL), dried ($Na_2SO_4$), and evaporated under reducer pressure. The crude product was purified by column chromatography on silica gel (PE–EtOAc, 8:2) to give **3** as a liquid; yield: 232 mg (80%); $R_f$ = 0.5 (PE–EtOAc, 8:2); $[\alpha]_D^{25}$ +8.0 (*c* 0.75, $CHCl_3$).

IR (neat): 2929, 2825, 1722, 1614, 1510, 1406, 1196, 1035, 919, 811 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.66–1.99 (m, 4 H), 2.36 (t, *J* = 6.8 Hz, 2 H), 2.59 (t, *J* = 7.5 Hz, 2 H), 3.38 (s, 3 H), 3.45 (s, 3 H), 3.53–3.63 (m, 1 H), 4.59 (d, *J* = 5.2 Hz, 1 H), 4.62 (d, *J* = 7.5 Hz, 1 H), 5.02–5.18 (m, 3 H), 5.10 (s, 3 H), 5.65–5.85 (m, 1 H), 5.80 (dt, *J* = 10.6, 1.5 Hz, 1 H), 6.08 (dd, *J* = 10.6, 3.8 Hz, 1 H), 6.36 (dt, *J* = 17.4, 2.3 Hz, 1 H), 6.89 (d, *J* = 9.0 Hz, 2 H), 7.04 (d, *J* = 8.3 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 30.5, 36.2, 38.2, 38.8, 55.7, 55.8, 70.7, 74.3, 94.5, 95.6, 116.2, 118.1, 128.6, 129.2, 130.6, 133.2, 135.3, 155.3, 165.6.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{30}O_6$ + Na ($M^+$ + Na): 401.1940; found: 401.1928.

**(6*R*)-6-{(2*S*)-2-(Methoxymethoxy)-4-[4-(methoxymethoxy)phenyl]butyl}5,6-dihydro-2*H*-2-pyranone (14)**

Grubbs's catalyst (30 mg, 0.03 mmol, 10 mol%) was dissolved in $CH_2Cl_2$ (10 mL) and added dropwise to a refluxing solution of the acrylic ester **3** (140 mg, 0.37 mmol) in $CH_2Cl_2$ (100 mL). Refluxing was continued for 12 h by which time all of the starting material was consumed (TLC). The solvent was removed under aspirator vacuum, and the crude product was purified by silica gel column chromatography (PE–EtOAc, 7:3) to obtain of **14** as a colorless liquid; yield: 87 mg (68%); $R_f$ = 0.2 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ +70.4 (*c* 0.6, $CHCl_3$).

IR (neat): 2942, 1722, 1611, 1510, 1388, 1240, 1151, 1080, 1031, 920, 820 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.80–1.92 (m, 2 H), 2.11–2.32 (m, 2 H), 2.30–2.48 (m, 2 H), 2.56–2.74 (m, 2 H), 3.38 (s, 3 H), 3.48 (s, 3 H), 3.75–3.85 (m, 1 H), 4.55–4.73 (m, 1 H), 4.66 (s, 2 H), 5.15 (s, 2 H), 6.03 (dt, *J* = 9.8 Hz, 1 H), 6.84–6.92 (m, 1 H), 6.96 (d, *J* = 8.5 Hz, 2 H), 7.11 (d, *J* = 8.5 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 29.5, 30.6, 36.3, 39.5, 55.8, 55.9, 73.9, 75.1, 94.6, 96.4, 116.3, 121.5, 129.2, 135.2, 145.0, 155.4, 164.2.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{26}O_6$ + Na ($M^+$ + Na): 373.1627; found: 373.1619.

**(+)-Dodoneine (1)**

To a stirred solution of compound **14** (0.06 g, 0.17 mmol) in a mixture of MeOH (10 mL) and MeCN (10 mL) was added a catalytic amount of $CeCl_3 \cdot 7H_2O$ (13 mg, 0.034 mol) under $N_2$. After stirring for 12 h at reflux temperature, the reaction mixture was quenched with solid $NaHCO_3$ (0.1 g) and filtered, the solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (PE–EtOAc, 4:6) to afford compound **1** as a solid; yield: 34 mg (79%); $R_f$ = 0.2 (PE–EtOAc, 4:6); $[\alpha]_D^{25}$ +40.3 (*c* 0.4, $CHCl_3$).

IR (KBr): 3418, 2923, 2854, 1715, 1513, 1221, 1049, 915, 838, 762 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.69–2.05 (m, 5 H), 1.89–2.01, 2.33–2.43 (m, 3 H), 2.60–2.77 (m, 2 H), 3.83–3.93 (m, 1 H), 4.60–4.69 (m, 1 H), 6.04 (dt, *J* = 9.8, 1.7 Hz, 1 H), 6.78 (d, *J* = 8.5 Hz, 2 H), 6.89–6.93 (m, 1 H), 7.05 (d, *J* = 8.3 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 29.6, 30.9, 39.5, 42.2, 68.8, 77.4, 115.5, 121.3, 129.6, 133.6, 145.6, 154.2, 164.5.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{18}O_4$ + Na ($M^+$ + Na): 285.1102; found: 285.1115.

**Ethyl (*E*,5*S*)-5-(Methoxymethoxy)-7-[4-(methoxymethoxy)phenyl]hept-2-enoate (15)**

To an ice-cooled solution of 2-iodoxybenzoic acid (4.33 g, 15.46 mmol) in DMSO (12 mL) was added a solution of **7** (2.2 g 7.74 mmol) in anhyd $CH_2Cl_2$ (20 mL). The mixture was stirred at r.t. for 5 h, then filtered through a Celite pad (1 g) and washed with $CH_2Cl_2$ (4 × 20 mL). The combined organic filtrates were washed with $H_2O$ (2 × 20 mL) and brine (2 × 20 mL), dried ($Na_2SO_4$), and concentrated in vacuo to afford the crude aldehyde. This was used in the next step without further purification. To a solution of the above obtained aldehyde (2.0 g, 4.830 mmol) in $CH_2Cl_2$ (30 mL) was added (methoxycarbonylmethylene)triphenylphosphorane (2.0 g, 5.797 mmol) and the reaction mixture was stirred for 2 h at r.t. The completion of the reaction was monitored by TLC. $CH_2Cl_2$ was removed under reduced pressure, the residue was dissolved in $Et_2O$ (25 mL) and PE (20 mL) was added. The crystallized $Ph_3PO$ was filtered off and the filtrate was concentrated to dryness. The crude product was chromatographed on silica gel (PE–EtOAc, 7:3) to afford the pure ester **15** as a colorless liquid; yield: 2.2 g (81%); $R_f$ = 0.6 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ –21.8 (*c* 0.5, $CHCl_3$).

IR (neat): 2931, 1719, 1654, 1511, 1447, 1233, 1151, 1080, 1035, 920, 828 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.2 Hz, 3 H), 1.67–1.91 (m, 2 H), 2.47 (t, *J* = 7.3 Hz, 2 H), 2.52–2.76 (m, 2 H), 3.39 (s, 3 H), 3.47 (s, 3 H), 3.67–3.77 (m, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 4.89 (d, *J* = 5.8 Hz, 1 H), 4.91 (d, *J* = 5.8 Hz, 1 H), 5.15 (s, 2 H), 5.87 (dt, *J* = 15.7 Hz, 1 H), 6.94 (dd, *J* = 15.5, 7.5 Hz, 1 H), 6.96 (d, *J* = 8.5 Hz, 2 H), 7.10 (d, *J* = 8.7 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 14.2, 29.6, 30.8, 36.5, 55.7, 55.9, 60.2, 75.8, 95.7, 116.3, 123.7, 129.2, 135.1, 144.8, 155.4, 178.0.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{28}O_6$ + Na ($M^+$ + Na): 375.1783; found: 375.1771.

**Ethyl (*E*,5*S*)-5-Hydroxy-7-(4-hydroxyphenyl)hept-2-enoate (6)**

To a stirred solution of compound **15** (0.3 g, 0.59 mmol) in a mixture of MeOH (5 mL) and MeCN (5 mL) was added a catalytic amount of $CeCl_3 \cdot 7H_2O$ under $N_2$. After stirring for 12 h at reflux temperature, the reaction mixture was quenched with solid $NaHCO_3$ (0.5 g) and filtered, the solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (PE–EtOAc, 4:6) to afford compound **6**; yield: 1.15 g (77%); $R_f$ = 0.2 (PE–EtOAc, 4:6); $[\alpha]_D^{25}$ –10.1 (*c* 0.55, $CHCl_3$).

IR (neat): 3387, 2923, 2852, 1696, 1652, 1515, 1450, 1369, 1223, 1042, 980, 828 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.5 Hz, 3 H), 1.74 (q, *J* = 7.5 Hz, 2 H), 2.29–2.42 (m, 2 H), 2.25–2.76 (m, 2 H), 3.67–3.76 (m, 1 H), 4.17 (q, *J* = 6.7 Hz, 2 H), 4.75 (br s, 1 H, OH), 5.85 (d, *J* = 15.10 Hz, 1 H), 6.69 (d, *J* = 8.3 Hz, 2 H), 6.90 (dd, *J* = 15.10, 7.5 Hz, 1 H), 7.0 (d, *J* = 9.0 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 14.2, 31.0, 38.8, 40.3, 60.5, 69.8, 115.3, 124.0, 129.4, 133.4, 145.0, 154.0.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{20}O_4$ + Na ($M^+$ + Na): 287.1259; found: 287.1249.

**Ethyl 2-[(4*S*,6*S*)-6-(4-Hydroxyphenethyl)-2-phenyl-1,3-dioxan-4-yl]acetate (5)**

To a solution of alcohol **6** (700 mg, 2.65 mmol) in anhyd THF (50 mL) at 0 °C was added distilled benzaldehyde (0.29 mL, 2.91 mmol), followed by *t*-BuOK (30 mg, 0.26 mmol). The yellow solution was stirred for 15 min at 0 °C. The addition of benzaldehyde/*t*-BuOK was repeated twice and the mixture was allowed to warm to r.t. after which the reaction was quenched with pH 7 phosphate buffer (25 mL). The layers were separated, and the aqueous layer was extracted with $Et_2O$ (4 × 30 mL). The combined organic layers were washed with brine (2 × 15 mL), dried ($Na_2SO_4$), filtered, and concentrated in vacuo and purified by column chromatography (PE–EtOAc, 7:3) to obtain **5** as a colorless oil; yield: 600 mg (62%); $R_f$ = 0.5 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ –247 (*c* 0.3, $CHCl_3$).

IR (neat): 3419, 2922, 2855, 1714, 1613, 1514, 1218, 1021, 767, 699 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.2 Hz, 3 H), 1.41–1.55 (m, 2 H), 1.69 (dt, *J* = 12.8, 2.45 Hz, 2 H), 1.72–1.83 (m, 2 H), 1.89–2.03 (m, 2 H), 2.50 (dd, *J* = 15.5, 6.0 Hz, 2 H), 2.62–2.82 (m, 2 H), 3.75–3.87 (m, 1 H), 4.17 (q, *J* = 7.2 Hz, 2 H), 4.22–4.34 (m, 1 H), 5.54 (s, 1 H), 6.74 (d, *J* = 8.5 Hz, 2 H), 7.04 (d, *J* = 8.5 Hz, 2 H), 7.31–7.40 (m, 2 H), 7.44–7.53 (m, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 14.17, 30.2, 36.5, 37.5, 41.0, 60.7, 73.2, 75.5, 100.5, 115.2, 126.0, 128.1, 128.6, 129.5, 130.1, 132.7, 138.5, 152.8, 171.0.

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{26}O_5$ + Na ($M^+$ + Na): 393.1677; found: 393.1662.

**(6*S*)-8-(4-Hydroxyphenyl)-6-(methoxymethoxy)oct-1-en-4-one (9)**

To an ice-cooled solution of 2-iodoxybenzoic acid (4.33 g, 15.46 mmol) in DMSO (12 mL) was added a solution of **7** (2.2 g 7.74 mmol) in anhyd $CH_2Cl_2$ (20 mL). The mixture was stirred at r.t. for 5 h, then filtered through a Celite pad (1 g), and washed with $CH_2Cl_2$ (4 × 20 mL). The combined organic filtrates were washed with $H_2O$ (2 × 20 mL) and brine (2 × 20 mL), dried ($Na_2SO_4$), and concentrated in vacuo to afford the crude aldehyde. This was used in the next step without further purification. To the above obtained aldehyde and Zn (1.25 g, 19.23 mmol) in anhyd THF (25 mL) was added allyl bromide (1.0 mL, 11.57 mmol) dropwise at 0 °C and the mixture was allowed to warm to r.t. After 30 min, the mixture was cooled to 0 °C and quenched with aq sat. $NH_4Cl$ (2 × 10 mL). The mixture was filtered through a pad of Celite and washed with EtOAc (2 × 15 mL). Concentration of the filtrate gave a residue, which was purified by silica gel chromatography (PE–EtOAc, 7:3) to give (6*S*)-6-(methoxymethoxy)-8-[4-(methoxymethoxy)phenyl]oct-1-en-4-ol as a pale yellow liquid; yield: 2.22 g (89%); $R_f$ = 0.25 (PE–EtOAc, 7:3).

**(6*S*)-6-(Methoxymethoxy)-8-[4-(methoxymethoxy)phenyl]oct-1-en-4-ol**

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.57–1.94 (m, 3 × $CH_2$), 2.21 (t, *J* = 6.6 Hz, 2 H), 2.52–2.63 (m, 2 H), 3.40 (2 s, 2 × $CH_3$), 3.45 (s, 3 H), 3.74–3.92 (m, 2 H), 5.05–5.12 (m, 2 H), 5.10 (s, 2 H), 5.74–5.87 (m, 1 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 7.04 (d, *J* = 8.8 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 30.2, 30.8, 36.3, 36.8, 40.7, 40.8, 42.0, 42.1, 55.8, 67.1, 69.8, 75.6, 76.9, 94.5 (2 C), 95.2, 96.4, 116.2, 117.5, 117.7, 129.1, 134.6, 134.8, 135.2, 155.3.

To a stirred solution of above obtained racemic compound (2 g, 6.17 mmol) in anhyd $CH_2Cl_2$ (50 mL), Dess–Martin periodinane (3.14 g, 7.4 mmol) was added at 0 °C and stirred for 1 h at r.t. The reaction mixture was quenched with 1:1 ratio of aq sat. $NaHCO_3$ and aq $Na_2S_2O_3$ (5 mL) and allowed to stir for 30 min and extracted with $CH_2Cl_2$ (2 × 50 mL). The combined organic layers were washed with $H_2O$ (2 × 20 mL), dried ($Na_2SO_4$), and concentrated. The crude residue was purified by column chromatography on silica gel (PE–EtOAc, 7:3) to give **9** as a yellow liquid; yield: 1.78 g (90%); $R_f$ = 0.35 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ +5 (*c* 0.45, $CHCl_3$).

**9**

IR (neat): 2926, 2854, 1669, 1629, 1510, 1444, 1233, 1150, 1080, 1014, 919, 830, 771 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.80 (q, *J* = 8.3 Hz, 2 H), 1.91 (d, *J* = 6.8 Hz, 2 H), 2.52–2.72 (m, 3 H), 2.88 (dd, *J* = 15.9, 6.7 Hz, 1 H), 3.34 (s, 3 H), 3.45 (s, 3 H), 4.02–4.11 (m, 1 H), 4.58 (d, *J* = 7.5 Hz, 1 H), 4.65 (d, *J* = 6.8 Hz, 1 H), 5.10 (s, 2 H), 6.10 (dd, *J* = 15.9, 1.5 Hz, 1 H), 6.74–6.86 (m, 2 H), 6.89 (d, *J* = 9.0 Hz, 2 H), 7.05 (d, *J* = 8.3 Hz, 2 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 18.4, 30.8, 37.2, 45.5, 55.6, 55.8, 74.3, 94.5, 96.3, 116.3, 129.2, 132.6, 135.2, 142.6, 155.6, 197.6.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{26}O_5$ + Na ($M^+$ + Na): 345.1677; found: 345.1672.

**(4*S*,6*S*)-8-(4-Hydroxyphenyl)-6-(methoxymethoxy)oct-1-en-4-ol (16)**

To a stirred suspension of **9** (1.5 g, 4.65 mmol) in THF (15 mL) at r.t. was added MeOH (5.6 mL, 139.68 mmol) followed by dropwise addition of $SmI_2$ (6.6 g, 16.33 mmol) in anhyd THF (5 mL). The resulting mixture was stirred for 12 h before the septum was removed and stirring was continued until the color of the solution was changed. The solution was then quenched with aq sat. $Na_2S_2O_3$ (15 mL) and diluted with EtOAc (50 mL). The layers were separated and the organic layer was washed with aq sat. $Na_2S_2O_3$ (2 × 30 mL). The organic layer was then washed with $H_2O$ (2 × 50 mL), dried ($Na_2SO_4$), and concentrated. Purification of this material was accomplished by chromatography on silica gel (eluent: PE–EtOAc, 7:3) to give **16** as a pale yellow liquid; yield: 1.09 g (73%); $R_f$ = 0.25 (PE–EtOAc, 7:3); $[\alpha]_D^{25}$ +16.4 (*c* 0.5, $CHCl_3$).

IR (neat): 3451, 2934, 1612, 1510, 1232, 1151, 1079, 1010, 917, 825 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.62–1.68 (m, 2 H), 1.72–1.98 (m, 2 H), 2.25 (t, *J* = 6.6 Hz, 2 H), 2.51–2.70 (m, 2 H), 2.89 (br s, 1 H, OH), 3.42 (s, 3 H), 3.47 (s, 3 H), 3.81–4.0 (m, 2 H), 4.69 (s, 2 H), 5.07–5.18 (m, 2 H), 5.15 (s, 2 H), 5.77–5.92 (m, 1 H), 6.96 (d, *J* = 8.7 Hz, 2 H), 7.10 (d, *J* = 8.7 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 30.8, 36.9, 40.9, 42.0, 55.9 (2 C), 67.1, 75.7, 94.5, 96.4, 116.3, 117.5, 129.1, 134.9, 135.2, 155.4.

HRMS (ESI): *m*/*z* calcd for $C_{18}H_{28}O_5$ + Na ($M^+$ + Na): 347.1834; found: 347.1836.

**(1*S*)-1-[(2*S*)-4-(4-Hydroxyphenyl)-2-(methoxymethoxy)butyl]but-3-enyl Acrylate (8)**

Compound **8** was prepared from **16** (900 mg, 2.77 mmol) following the procedure described for compound **3** as a colorless liquid; yield: 0.81 g (78%); $R_f$ = 0.5 (PE–EtOAc, 8:2); $[\alpha]_D^{25}$ +28.0 (*c* 0.75, $CHCl_3$).

IR (neat): 2927, 1722, 1613, 1510, 1270, 1195, 1152, 1079, 1012, 919, 812, 771 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.71–1.88 (m, 4 H), 2.36 (t, *J* = 6.7 Hz, 2 H), 2.58 (t, *J* = 8.3 Hz, 2 H), 3.33 (s, 3 H), 3.45 (s, 3 H), 3.57 (q, *J* = 11.3, 5.2 Hz, 1 H), 4.53 (d, *J* = 6.7 Hz, 1 H), 4.61 (d, *J* = 6.7 Hz, 1H), 5.10 (s, 2 H), 5.02–5.17 (m, 3 H), 5.80 (dd, *J* = 10.5, 1.5 Hz, 1 H), 5.67–5.83 (m, 1 H), 6.07 (dd, *J* = 17.4, 10.5 Hz, 1 H), 6.36 (dd, *J* = 17.4, 2.2 Hz, 1 H), 6.89 (d, *J* = 9.0 Hz, 2 H), 7.04 (d, *J* = 9.0 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 30.3, 36.9, 38.7, 39.2, 55.7, 55.9, 70.6, 74.2, 94.6, 96.2, 116.2, 118.0, 128.7, 129.1, 130.5, 133.2, 135.4, 155.4, 165.6.

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{30}O_6$ + Na ($M^+$ + Na): 401.1940; found: 401.1916.

**(6*S*)-6-{(2*S*)-2-(Methoxymethoxy)-4-[4-(methoxymethoxy)phenyl]butyl}5,6-dihydro-2*H*-2-pyranone (17)**

Compound **17** was prepared from **8** (650 mg, 1.71 mmol) following the procedure described for compound **14** as a colorless liquid; yield: 0.470 g (79%); $[\alpha]_D^{25}$ –16.5 (*c* 1, $CHCl_3$).

IR (neat): 2932, 2825, 1721, 1611, 1510, 1387, 1238, 1150, 1079, 1031, 919, 819 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.74–2.07 (m, 4 H), 2.32–2.38 (m, 2 H), 2.62 (t, *J* = 8.3 Hz, 2 H), 3.39 (s, 3 H), 3.48 (s, 3 H), 3.92–4.01 (m, 1 H), 4.62–4.73 (m, 1 H), 4.71 (s, 2 H), 5.15 (s, 2 H), 6.04 (dt, *J* = 9.6, 1.7 Hz, 1 H), 6.86–6.93 (m, 1 H), 6.96 (d, *J* = 8.5 Hz, 2 H), 7.11 (d, *J* = 8.7 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 29.8, 30.1, 37.0, 40.4, 55.6, 55.8, 73.7, 74.6, 94.4, 96.3, 116.2, 121.3, 129.0, 130.2, 145.0, 155.3, 164.1.

HRMS (ESI): *m*/*z* calcd for $C_{19}H_{26}O_6$ + Na ($M^+$ + Na): 373.1627; found: 373.1619.

**(–)-Epidodoneine (2)**

Compound **2** was prepared from **17** (120 mg, 0.034 mmol) following the procedure described for compound **1** as a solid; yield: 71 mg (80%); $R_f$ = 0.2 (PE–EtOAc, 4:6); $[\alpha]_D^{25}$ –26.7 (*c* 1.0, $CHCl_3$).

IR (neat): 3406, 2921, 2855, 1710, 1511, 1395, 1266, 1114, 1058, 831, 704 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.54–1.70 (m, 2 H), 1.77–1.87 (m, 2 H), 2.25–2.45 (m, 1 H), 2.49–2.59 (m, 1 H), 2.60–2.71 (m, 2 H), 3.72–3.84 (m, 1 H), 4.54 (br s, 1 H, OH), 4.65–4.75 (m, 1 H), 5.98 (dt, *J* = 10.3, 2.5 Hz, 1 H), 6.88–7.0 (m, 1 H), 6.65 (d, *J* = 6.9 Hz, 2 H), 6.95 (d, *J* = 7.8 Hz, 2 H).

$^{13}$C NMR MHz, (75 MHz, $CDCl_3$): δ = 29.0, 29.9, 39.5, 41.8, 64.2, 74.0, 114.3, 120.1, 128.1, 131.5, 144.6, 154.3, 163.0.

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{18}O_4$ + Na ($M^+$ + Na): 285.1102; found: 285.1090.

**4-{2-[(4*S*,6*S*)-6-Allyl-2,2-dimethyl-1,3-dioxan-4-yl]ethyl}phenol (18)**

Compound **18** was prepared from **16** (0.07 mg, 0.22 mmol) following the procedure described for compound **13** as a colorless liquid; yield: 49 mg (84%); $[\alpha]_D^{25}$ +16.0 (*c* 0.35, $CHCl_3$).

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 3 H), 1.33 (s, 3 H), 1.50–1.83 (m, 4 H), 2.08–2.31 (m, 2 H), 2.45–2.73 (m, 2 H), 3.63–3.89 (m, 2 H), 4.96–5.11 (m, 2 H), 5.64–5.84 (m, 1 H), 6.67 (d, *J* = 8.5 Hz, 2 H), 6.99 (d, *J* = 8.5 Hz, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 24.8 (2 C), 30.7, 37.6, 38.0, 40.0, 65.9, 66.3, 100.5, 115.2, 116.9, 129.4, 133.8, 134.3, 153.7.

LCMS: *m*/*z* = 299 (($M^+$ + Na).

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