Total Synthesis of a Mevinic Acid Analog

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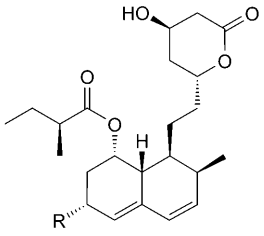
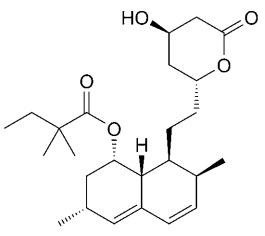
Total synthesis of mevinic acid analog **1** has been achieved efficiently starting from chiral 2,3-*O*-isopropylidene-D-glyceraldehyde (**2**). The synthesis involves *Mitsunobu* reaction and *Evans*' intramolecular oxa-*Michael syn*-addition reactions as key steps.

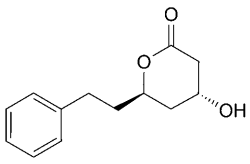
Introduction. – Fungal metabolites such as mevinic acid derivatives mevinoline (**A**), compactin (**B**), and simvastatin (**C**) are potent inhibitors of 3-hydroxy-3-methylglutayl coenzyme A (HMGCo A) reductase [1]. The enzyme reduces cholesterol levels in blood by involving in the rate-limiting step of cholesterol biosynthesis in humans. The simplified structural analog of these inhibitors is β-hydroxy-δ-lactone, which is essential for biological activity [2]. β-Hydroxy-δ-lactone is the common structural feature of all mevinic acids [3]. The lactone moiety, in its (4*R*,6*R*)-configuration, closely resembles the HMG portion of the enzyme and acts as inhibitor by blocking the enzyme [4]. Thus, the synthesis of many analogs of the lactone has been reported in literature [5]. In continuation of our interest in synthesis of biologically active natural products [6], here we report an efficient and practical total synthesis of mevinic acid analogue **1** from commonly available D-mannitol.



A R = Me
B R = H



C



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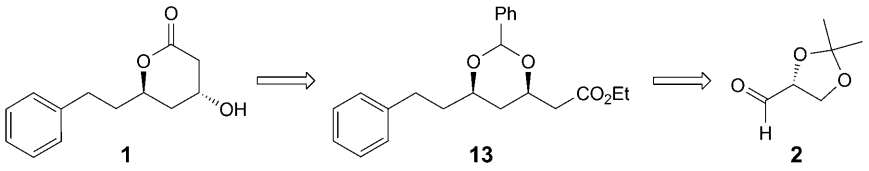
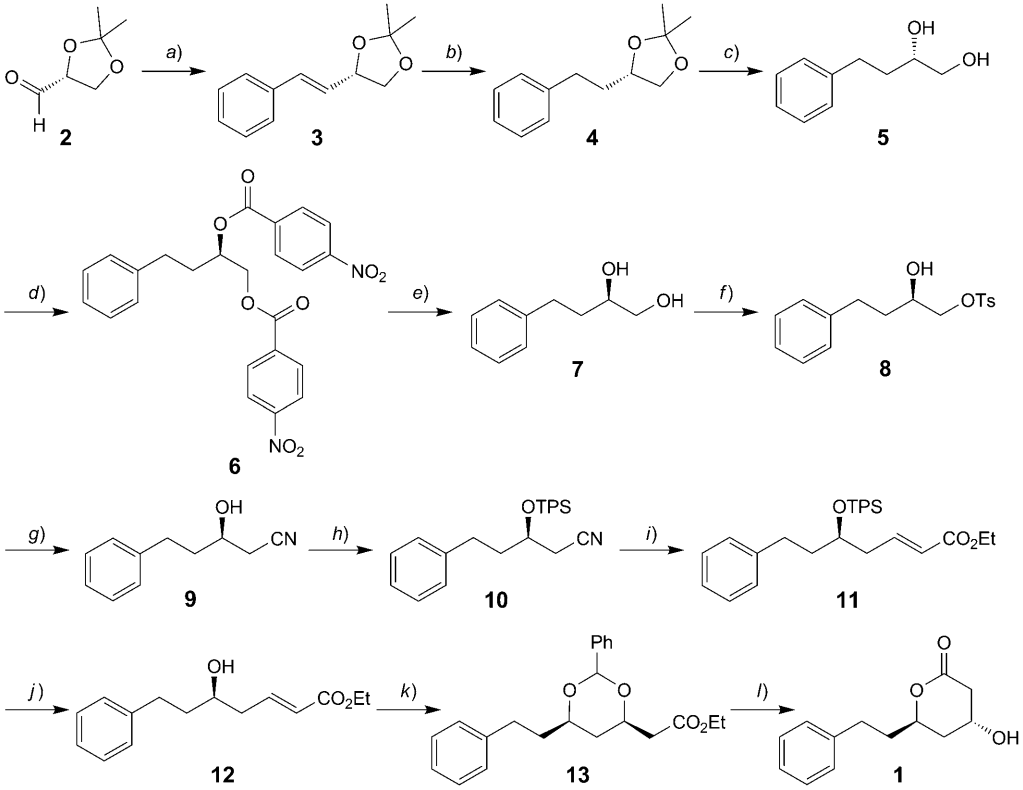
Our planned approach to mevinic acid analogue **1** involved *Mitsunobu* reaction and *Evans*' intramolecular oxa-*Michael syn*-addition reaction as the chirality-transferring steps starting from commonly available D-mannitol (*Scheme 1*).

Results and Discussion. – The synthesis of mevinic acid analogue **1** (*Scheme 2*) was started from the readily available D-mannitol diacetonide, which was oxidized

Scheme 1. *Retrosynthetic Approach to Mevinic Acid Analog*



Scheme 2



a) [Ph_3PCH_2Ph]Br (1 equiv.), BuLi (1 equiv.), THF, 0°, 2 h; 90%. *b*) H_2, 10% Pd/C, MeOH, r.t., 6 h; 98%. *c*) 2M HCl, MeOH, 1 h, r.t.; 95%. *d*) PPh_3 (2 equiv.), Diisopropyl azodicarboxylate (DIAD; 2 equiv.), 4-NO_2–C_6H_4COOH (2 equiv.), THF, r.t., 2 h; 93%. *e*) Cat. Na, MeOH, r.t., 1 h; 94%. *f*) TsCl (1.1 equiv.), Bu_2SnO (0.1 equiv.), Et_3N (2.5 equiv.), 0° to r.t., 4 h; 76%. *g*) KCN (1.5 equiv.), r.t., 12 h; 87%. *h*) (*t*-Bu)Ph_2SiCl (TBDPS-Cl; 1 equiv.), 1*H*-imidazole (2.5 equiv.), dry CH_2Cl_2; 96%. *i*) 1. Diisobutylaluminum hydride (DIBAL-H; 1 equiv.), dry CH_2Cl_2, −78°, 0.5 h; 71%; 2. Ph_3P=CHCOOEt, benzene, reflux, 1 h. *j*) Bu_4NF (TBAF), THF, 30 min; 83%. *k*) PhCHO, *t*-BuOK, THF, pH 7 buffer, 1 h; 51%. *l*) 80% aq. AcOH, 60°, 4 h; TsOH, CH_2Cl_2, 4 h; 61%.

following a known procedure [7], to give (*R*)-2,3-*O*-isopropylidene-D-glyceraldehyde (**2**), which was subjected to a *Wittig* reaction to give compound **3** in 90% yield.

Hydrogenation of compound **3** on 10% Pd/C in MeOH gave acetonide **4**, followed on treating with 2N HCl in MeOH, to afford diol **5** in 95% yield. At this stage, the stereogenic center of the secondary OH group in **5** was inverted by a *Mitsunobu* reaction[1]) [9] to give diol **7** in order to match the configuration at C(6) in compound **1**. The primary OH group in **7** was protected with TsCl using Et_3N and a catalytic amount of Bu_2SnO to give tosylated compound **8** in 76% yield with minor tosylation at the secondary OH group of **7** [10]. *p*-Toluenesulfonate **8** was converted to the corresponding nitrile **9** in 87% yield by reaction with KCN in EtOH/H_2O 3:2 at room temperature. The secondary OH group in **9** was protected with (*t*-Bu)Ph_2SiCl (TBDPS-Cl)/1*H*-imidazole to give TBDPS ether **10** in 96% yield. The CN function was reduced with DIBAL-H in dry CH_2Cl_2 at $-78°$ to afford the aldehyde in 71% yield, which was just subjected to a C_2-*Wittig* reaction using $Ph_3P{=}CHCOOEt$ to afford **11** (*E*/*Z* 95:5) as colorless syrup. The geometrical isomers were separated with a silica-gel column to give the pure (*E*)-form in 76% yield. The TBDPS group in **11** was removed using Bu_4NF (TBAF) to afford homoallylic alcohol **12** in 83% yield. Later, the homoallylic alcohol was subjected to *Evans*' intramolecular oxa-*Michael syn*-addition reaction using PhCHO and *t*-BuOK at 0° in anhydrous THF to furnish benzylidene acetal **13** in 51% yield [11]. Finally, **13** on treatment with 80% aqueous AcOH and TsOH, afforded lactone **1** in 61% yield. The physical ($[\alpha]_D^{25} = +46.8$ ($c = 0.7$, $CHCl_3$)) and spectroscopic data (^{1}H- and ^{13}C-NMR) of **1** were in good agreement with those reported for compound **1** [5].

In conclusion, an efficient and practical total synthesis of a mevinic acid analogue, **1**, has been achieved involving *Mitsunobu* reaction and *Evans*' intramolecular *oxa-Michael syn*-addition reaction as key steps starting from commonly available D-mannitol. The protocol described here has significant potential for the synthesis of a variety of other biologically important substituted β-hydroxy-δ-lactones.

Experimental Part

General. Solvents were dried over standard drying agents and freshly distilled prior to use. The reagents were purchased from *Aldrich* and *Acros*, and were used without further purification unless otherwise stated. All moisture-sensitive reactions were carried out under N_2. Org. solvents were dried over anh. Na_2SO_4 and concentrated *in vacuo* below 40°. All column chromatographic (CC) separations were performed using silica gel (SiO_2; *Acme*'s 60–120 mesh). Optical rotations: *Horiba* high-sensitive polarimeter *SEPA-300* at 25°. IR Spectra: *Perkin-Elmer IR-683* spectrophotometer with NaCl optics. ^{1}H- (300 MHz) and ^{13}C-NMR (75 MHz) spectra: *Bruker-Avance-300* instrument with TMS as internal standard in $CDCl_3$; *J* values are given in Hz. MS: *Agilent Technologies 1100 Series* (*Agilent* Chemistation Software).

*(4*S*)-2,2-Dimethyl-4-[(*E*)-2-phenylethenyl]-1,3-dioxolane* (**3**). To a suspension of $[Ph_3PCH_2Ph]Br$ (9.96 g, 23.03 mmol) in dry THF (100 ml) was added BuLi (1.6M in hexane; 14.16 ml, 22.65 mmol) at 0° and stirred for 15 min. Then, a soln. of ketal **2** (3 g, 23.07 mmol) in THF (20 ml) was added dropwise, and the mixture was stirred for an additional 0.5 h at 0°. After completion, the reaction was quenched with sat. NH_4Cl soln. (30 ml), and the mixture was extracted with Et_2O (3 × 30 ml). The Et_2O soln. was washed with brine and dried (Na_2SO_4). After removal of the solvent, the crude product was purified by flash CC (hexane/AcOEt 98:2) to afford pure **3** (4.24 g, 90%). $[\alpha]_D^{25} = +3.2$ ($c = 1$, $CHCl_3$). IR (neat): 3062, 3024, 2986, 2929, 2860, 1610, 1498, 1296, 1060. ^{1}H-NMR: 7.38–7.23 (*m*, 5 H); 6.67 (*d*, *J* = 11.8, 1 H);

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[1]) For a review on the *Mitsunobu* reaction, see [8].

5.67 (*dd*, *J* = 8.0, 11.8, 1 H); 4.83–4.71 (*m*, 1 H); 3.71 (*t*, *J* = 8.0, 1 H); 3.53 (*t*, *J* = 8.0, 1 H); 1.46 (*s*, 3 H); 1.38 (*s*, 3 H). ^{13}C-NMR: 136.1; 133.2; 128.4; 127.8; 126.3; 126.6; 109.8; 77.0; 69.3; 26.6; 25.7. LC/MS: 227 ($[M+Na]^+$).

*(4*S*)-2,2-Dimethyl-4-(2-phenylethyl)-1,3-dioxolane* (**4**). To a soln. of **3** (4.10 g, 20.09 mmol) in MeOH (30 ml) was added 10% Pd/C (0.33 g) and stirred under H_2 for 6 h at r.t. After completion of the reaction, the catalyst was removed by filtration, the solvent was evaporated, and the crude product was purified by flash CC (hexane/AcOEt 50 : 1) to afford **4** (4.05 g, 98%). Colorless oil. $[\alpha]_D^{25} = -4.6$ ($c = 1.2$, $CHCl_3$). IR (neat): 3059, 3028, 2934, 2860, 1615, 1478, 1216, 1061, 968, 753. ^{1}H-NMR: 7.25–7.12 (*m*, 5 H); 4.08–3.99 (*m*, 1 H); 3.94 (*t*, *J* = 7.5, 1 H); 3.46 (*t*, *J* = 7.5, 1 H); 2.80–2.57 (*m*, 2 H); 1.97–1.71 (*m*, 2 H); 1.39 (*s*, 3 H); 1.32 (*s*, 3 H). ^{13}C-NMR: 141.5; 128.37; 128.32; 125.9; 108.7; 75.3; 69.3; 35.3; 31.9; 26.9; 25.6. LC/MS: 207 ($[M+H]^+$).

*(2*S*)-4-Phenylbutane-1,2-diol* (**5**). To a soln. of **4** (3.9 g, 18.93 mmol) in MeOH (30 ml) was added HCl (2M, 10 ml), and the mixture was stirred for 1 h at r.t. After completion of the reaction, the mixture was neutralized with solid K_2CO_3, MeOH was removed, and the mixture was diluted with H_2O (15 ml) and extracted with AcOEt (3 × 30 ml). The combined org. layer was dried (Na_2SO_4), and the solvent was removed under vacuum to obtain crude **5**, which was purified by flash CC (hexane/AcOEt 1 : 1) to afford **5** (2.98 g, 95%). Colorless oil. $[\alpha]_D^{25} = -31.8$ ($c = 1$, $CHCl_3$). IR (neat): 3425, 3028, 2985, 2930, 1637, 1608, 1486, 1453. ^{1}H-NMR: 7.26–7.14 (*m*, 5 H); 4.02 (br. *s*, 2 H); 3.67–3.56 (*m*, 2 H); 3.43–3.37 (*m*, 1 H); 2.81–2.57 (*m*, 2 H); 1.75–1.64 (*m*, 2 H). ^{13}C-NMR: 141.6; 128.33; 128.31; 125.8; 71.5; 66.5; 34.5; 31.7. LC/MS: 189 ($[M+Na]^+$).

*(2*R*)-4-Phenylbutane-1,2-diyl Bis(4-nitrobenzoate)* (**6**). To a stirred soln. of PPh_3 (8.84 g, 33.73 mmol), **5** (2.8 g, 13.91 mmol), and 4-nitrobenzoic acid (5.63 g, 33.73 mmol) in dry THF (50 ml) was added DIAD (95%, 6.62 ml, 33.73 mmol) dropwise at 0°. The mixture was stirred for 2 h at r.t. After the completion of reaction, the mixture was diluted with H_2O (20 ml) and extracted with AcOEt (3 × 30 ml). The combined org. layer was washed with $NaHCO_3$ and brine solns., and dried (Na_2SO_4). Evaporation of the solvent gave a crude product, which was purified by flash CC (hexane/AcOEt 9 : 1), to afford **6** (7.27 g, 93%). Light yellow viscous liquid. $[\alpha]_D^{25} = -6.3$ ($c = 1$, $CHCl_3$). IR (neat): 3028, 2978, 1734, 1715, 1528, 1336, 1278. ^{1}H-NMR: 8.31–8.24 (*m*, 4 H); 8.20–8.12 (*m*, 4 H); 7.28–7.15 (*m*, 5 H); 5.55 (*m*, 1 H); 4.65 (*dd*, *J* = 3.2, 12.0, 1 H); 4.52 (*dd*, *J* = 6.9, 12.0, 1 H); 2.63 (*t*, *J* = 7.5, 2 H); 1.92–1.76 (*m*, 2 H). ^{13}C-NMR: 164.2; 164.1; 150.5; 141.8; 135.1; 134.8; 130.6; 128.2; 125.7; 123.5; 73.0; 66.2; 32.4; 30.8. LC/MS: 464 (M^+).

*(2*R*)-4-Phenylbutane-1,2-diol* (**7**). To a soln. of **6** (7.1 g, 15.30 mmol) in MeOH (50 ml) was added Na (0.07 g, 3.06 mmol), and the mixture was stirred for 1 h. After completion of the reaction, solid NH_4Cl (0.5 g) was added to the mixture, and MeOH was removed under vacuum, and the mixture was diluted with H_2O (50 ml), extracted with AcOEt (3 × 25 ml), washed with brine, dried (Na_2SO_4), and evaporated. The crude product was purified by flash CC (hexane/AcOEt 1 : 1), to afford **7** (2.18 g, 94%). Colorless oil. Its spectroscopic data were identical to those of **5**, except that the optical rotation value was opposite.

*(2*R*)-2-Hydroxy-4-phenylbutyl 4-Methylbenzenesulfonate* (**8**). To an ice-cold soln. of **7** (2.2 g, 13.2 mmol), cat. amount of Bu_2SnO (0.005 g), and Et_3N (4.5 ml, 33 mmol) in dry CH_2Cl_2 (20 ml) was added dropwise a soln. of TsCl (2.52 g, 13.2 mmol) in CH_2Cl_2 (10 ml), and the mixture was stirred for 4 h at r.t. After completion of reaction, the mixture was diluted with H_2O and extracted with CH_2Cl_2 (3 × 30 ml). The org. layer was washed with brine soln., dried (Na_2SO_4), and concentrated under reduced pressure to yield the crude residue, which was purified by CC (hexane/AcOEt 7 : 3) to afford **8** (3.22 g, 76%). Viscous liquid. IR (neat): 3445, 3063, 2933, 2858, 1636, 1454, 1358, 1212, 1083, 699. ^{1}H-NMR: 7.75 (*d*, *J* = 8.6, 2 H); 7.30 (*d*, *J* = 8.6, 2 H); 7.22–7.08 (*m*, 5 H); 4.02–3.75 (*m*, 3 H); 2.83–2.54 (*m*, 2 H); 2.44 (*s*, 3 H); 1.75–1.63 (*m*, 2 H). ^{13}C-NMR: 145.0; 141.0; 132.5; 129.9; 128.4; 128.3; 127.9; 126.0; 73.8; 68.6; 34.1; 31.3; 21.6. LC/MS: 320 (M^+).

*(3*R*)-3-Hydroxy-5-phenylpentanenitrile* (**9**). To a cooled (0°) soln. of **8** (3.1 g, 9.56 mmol) in 60% aq. EtOH (50 ml) was added KCN (0.94 g, 14.46 mmol). The mixture was stirred at r.t. for 12 h. After completion of the reaction, the solvent was removed under vacuum, and the mixture was diluted with H_2O (20 ml), extracted with AcOEt (3 × 30 ml). The combined org. layer was washed with brine, dried (Na_2SO_4), and the solvent was removed under reduced pressure to obtain crude product, which was

purified by flash CC (hexane/AcOEt 7:3) to afford **9** (1.47 g, 87%). Colorless solid. $[\alpha]_D^{25} = -21.3$ ($c = 1.5$, $CHCl_3$). IR (neat): 3454, 3061, 2954, 2252, 1634, 1492. ^{1}H-NMR: 7.32–7.18 (*m*, 5 H); 3.98–3.90 (*m*, 1 H); 2.86–2.66 (*m*, 2 H); 2.45 (*t*, $J = 4.9$, 2 H); 2.08 (br. *s*, 1 H); 1.95–1.86 (*m*, 2 H). ^{13}C-NMR: 140.6; 128.5; 128.3; 126.2; 117.5; 66.9; 37.8; 31.5; 26.2. LC/MS: 176 ($[M+H]^+$).

*(3*R*)-3-[[(*tert*-Butyl)(diphenyl)silyl]oxy]-5-phenylpentanenitrile* (**10**). To a stirred soln. of **9** (1.3 g, 7.42 mmol) and 1*H*-imidazole (1.51 g, 22.28 mmol) in CH_2Cl_2 (20 ml) at 0° was added (*t*-Bu)Ph_2SiCl (1.92 ml, 7.40 mmol) dropwise. After completion of the reaction, the mixture was diluted with H_2O (10 ml) and extracted with CH_2Cl_2 (3 × 15 ml). The org. layer was washed with brine soln. (10 ml) and dried (Na_2SO_4). The solvent was removed under vacuum to furnish the crude residue, which was purified by flash CC (hexane/AcOEt 9:1) to afford **10** (2.94 g, 96%). Colorless oil. $[\alpha]_D^{25} = +4.2$ ($c = 1$, $CHCl_3$). IR (neat): 3085, 3026, 2925, 2858, 2250, 1635, 1496, 1464, 1255. ^{1}H-NMR: 7.70–7.64 (*m*, 5 H); 7.47–7.35 (*m*, 5 H); 7.23–7.11 (*m*, 5 H); 3.98–3.92 (*m*, 1 H); 2.63–2.53 (*m*, 2 H); 2.39 (*dd*, $J = 5.6$, 8.8, 2 H); 1.98–1.89 (*m*, 2 H); 1.09 (*s*, 9 H). ^{13}C-NMR: 140.7; 135.7; 134.7; 133.1; 130.0; 129.9; 129.4; 128.3; 128.2; 127.8; 127.7; 125.9; 117.2; 68.3; 37.8; 31.0; 26.8; 25.3; 19.1. LC/MS: 436 ($[M+Na]^+$).

*Ethyl (2*E*,5*R*)-5-{[*tert*-Butyl(diphenyl)silyl]oxy}-7-phenylhept-2-enoate* (**11**). To a stirred soln. of **10** (2.8 g, 6.7 mmol) in dry CH_2Cl_2 (30 ml) was added DIBAL-H (1M in toluene; 6.7 ml, 6.7 mmol) slowly for 15 min at −78°, and the mixture was stirred for ½ h at −78°. The reaction was quenched with sat. sodium potassium tartrate soln. (50 ml), and the mixture was stirred vigorously at r.t. for an additional h, and extracted with CH_2Cl_2 (3 × 25 ml). The combined org. layer was washed with brine soln. (20 ml) and dried (Na_2SO_4), and the solvent was removed under vacuum to give a crude product, which was purified by flash CC (hexane/AcOEt 50:2) to afford the aldehyde (2.08 g, 71%) as colorless oil. To a soln. of the aldehyde in benzene (20 ml) was added $Ph_3P{=}CH_2COOEt$ (1.9 g, 5.5 mmol), and the mixture was stirred at reflux for 1 h. After completion of the reaction, the solvent was removed under reduced pressure, and the residue was purified by CC (hexane/AcOEt) to afford **11** as a colorless syrup (mixture of geometrical isomers (*E*)/(*Z*) 95:5), and the geometrical isomers were separated by CC to give **11** (1.77 g, 76%). $[\alpha]_D^{25} = -9.2$ ($c = 1$, $CHCl_3$). IR (neat): 3064, 2953, 1728, 1625, 1495, 1256. ^{1}H-NMR: 7.69–7.54 (*m*, 5 H); 7.41–7.21 (*m*, 5 H); 7.15–6.81 (*m*, 5 H); 6.98–6.84 (*m*, 1 H); 5.88 (*d*, $J = 17.2$, 1 H); 4.25–4.19 (*m*, 1 H); 4.11 (*q*, $J = 7.4$, 2 H); 2.59–2.51 (*m*, 4 H); 1.81–1.75 (*m*, 2 H); 1.29 (*t*, $J = 7.4$, 3 H); 1.05 (*s*, 9 H). ^{13}C-NMR: 164.3; 146.4; 135.8; 134.9; 133.1; 130.2; 129.8; 129.6; 128.4; 128.0; 127.9; 127.8; 127.6; 126.3; 125.8; 73.1; 65.4; 41.0; 36.6; 35.6; 19.1; 14.5. LC/MS: 509 ($[M+Na]^+$).

*Ethyl (2*E*,5*R*)-5-Hydroxy-7-phenylhept-2-enoate* (**12**). To a cooled (0°) soln. of **11** (1.6 g, 3.29 mmol) in dry THF (10 ml) was added Bu_4NF (TBAF; 1.05 ml, 3.62 mmol, 1M soln. in THF) dropwise, and the mixture was stirred for 30 min. After completion of the reaction, H_2O (5 ml) was added to the mixture, and the mixture was extracted with AcOEt (3 × 15 ml). The combined org. extract was washed with brine, dried (Na_2SO_4), and concentrated to give the crude product, which was purified by CC (hexane/AcOEt 4:6) to afford pure **12** (0.67 g, 83%). Liquid. $[\alpha]_D^{25} = -14.2$ ($c = 1$, $CHCl_3$). IR (neat): 3380, 1721, 1639, 1254. ^{1}H-NMR: 7.21–7.09 (*m*, 5 H); 6.91–6.82 (*m*, 1 H); 5.85 (*d*, $J = 17.4$, 1 H); 4.21–4.18 (*m*, 1 H); 4.13 (*q*, $J = 7.5$, 2 H); 2.39–2.07 (*m*, 4 H); 1.76–1.75 (*m* 2 H); 1.29 (*t*, $J = 7.5$, 3 H). ^{13}C-NMR: 164.1; 146.1; 139.3; 129.6; 128.1; 128.0; 126.7; 72.8; 62.1; 40.8; 36.4; 35.7; 14.2. LC/MS: 248 ($[M+H]^+$).

*Ethyl [(4*R*,6*R*)-2-Phenyl-6-(2-phenylethyl)-1,3-dioxan-4-yl]acetate* (**13**). To a cooled (0°) soln. of **12** (0.50 g, 2.0 mmol) in THF (10 ml) was added PhCHO (0.23 g, 2.17 mmol) and *t*-BuOK (0.022 g, 0.20 mmol), and the resulting yellow soln. was stirred for 15 min. This sequence (addition/stirring) was repeated twice, and the reaction was quenched with pH 7 buffer phosphate soln. (20 ml). The layers were separated, and the aq. layer was extracted with AcOEt (3 × 20 ml). The combined org. layer was washed with brine (20 ml), dried (Na_2SO_4), and the solvent was removed under reduced pressure. Crude product was purified by CC (petroleum ether/AcOEt 7:3) to afford **13** (0.36 g, 51%). $[\alpha]_D^{25} = -5.8$ ($c = 1$, $CHCl_3$). IR (neat): 2857, 1735, 1268,1205, 1151. ^{1}H-NMR: 7.64–7.58 (*m*, 2 H); 7.48–7.26 (*m*, 5 H); 7.24–7.18 (*m*, 3 H); 5.58 (*s*, 1 H); 4.31–4.20 (*m*, 1 H); 4.13 (*q*, $J = 6.6$, 2 H); 3.86–3.77 (*m*, 1 H); 2.75 (*t*, $J = 7.5$, 2 H); 2.69 (*dd*, $J = 14.9$, 6.3, 1 H); 2.44 (*dd*, $J = 14.9$, 6.1, 1 H); 1.98–1.48 (*m*, 4 H); 1.23 (*t*, $J = 6.5$, 3 H). ^{13}C-NMR: 170.7; 141.9; 138.7; 128.4; 128.3; 128.1; 128.0; 125.9; 125.5 100.4; 77.1; 74.1; 60.7; 40.5; 37.8; 36.7; 36.1; 14.2. LC/MS: 377 ($[M+Na]^+$).

*(4*R*,6*R*)-Tetrahydro-4-hydroxy-6-(2-phenylethyl)-2*H*-pyran-2-one* (**1**). A soln. of **13** (0.40 g, 1.82 mmol) in 80% aq. AcOH (3 ml) was stirred for 3 h at 60°. After completion of the reaction,

AcOH was removed under reduced pressure, and the mixture was extracted with AcOEt (3×10 ml). The combined org. layer was washed with H_2O and brine soln., dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. The residue obtained was dissolved in CH_2Cl_2 (5 ml), and TsOH (cat.) was added. The mixture was stirred for 4 h. The reaction was quenched with aq. $NaHCO_3$ (2 ml), and the mixture was extracted with CH_2Cl_2 (3×5 ml). The combined org. layer was washed with brine, dried (Na_2SO_4), concentrated *in vacuo*, and purified by CC (hexane/AcOEt 1:1) to afford **1** (0.15 g, 61%). $[\alpha]_D^{25} = +46.8$ ($c = 0.7$, $CHCl_3$). IR (neat): 3442, 2980, 1730, 1650, 1435, 1370, 1135, 1036. ^{1}H-NMR: 7.36–7.18 (*m*, 5 H); 4.74–4.61 (*m*, 1 H); 4.37–4.32 (*m*, 1 H); 2.95–2.52 (*m*, 4 H); 2.07–1.67 (*m*, 4 H); 1.5–1.3 (br. *s*, 1 H). ^{13}C-NMR: 170.5; 141.1; 128.5; 128.3; 126.0; 77.0; 75.0; 38.6; 37.5; 36.0; 32.0. LC/MS: 243 ($[M + Na]^+$).

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