TOTAL SYNTHESIS OF *(S)*-(+)-MELODORINOL AND *(S)*-(+)-ACETYLMELODORINOL

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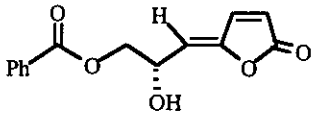
Abstract– *(S)*-(+)-Melodorinol and *(S)*-(+)-acetylmelodorinol have been synthesized by reacting the lithiated butenolide with 2,3-*O*-alkylidene-D-glyceraldehyde followed by successive elimination, hydrolysis, benzoylation and acetylation reactions.

Melodorinol (**1**) and acetylmelodorinol (**2**) have been recently reported to be isolated from *Melodorum fruticosum* Lour. (Annonaceae).[2,3] These compounds have been shown to exhibit significant cytotoxic activities against a panel of human cancer cell lines.[2a,3] The absolute configurations at carbon-7 of melodorinol (**1**) and acetylmelodorinol (**2**) have been determined to be *(S)* by McLaughlin[4] using partial resolution method (Horeau's method[5]). Recently, Shen[6] and Lu[7] have synthesized both compounds in order to confirm their absolute configurations. Despite the preliminary accounts for the syntheses of both natural products by Shen[6] involving the reaction of 5-lithio-2-alkoxyfuran with 2,3-*O*-isopropylidene-D-glyceraldehyde and by Lu[7] using a palladium-catalyzed enyne coupling method, in view of their biological activity, it is still desirable to develop alternative routes to these compounds. In connection with our recent report describing a two-step preparation of γ-arylidenebutenolides, which featured the reaction of lithiated butenolide (**4**) with aromatic aldehydes followed by elimination,[8] we wish to report herein a new route for the synthesis of both **1** and **2**.



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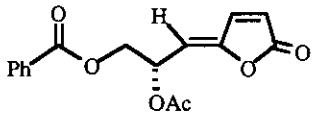
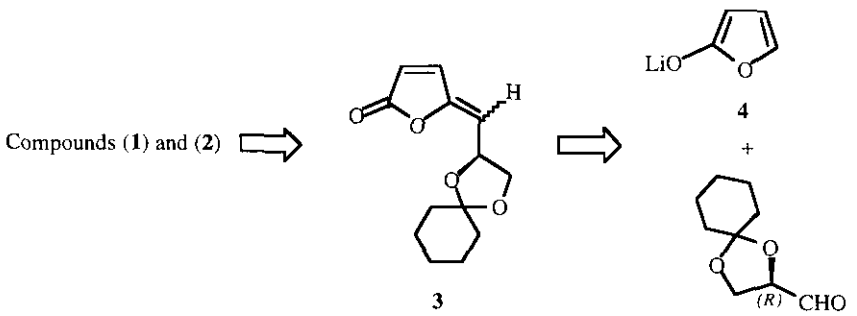


2

Based on our retrosynthetic analysis of compounds (**1**) and (**2**) (Scheme 1), the crucial synthetic step was a synthesis of γ-alkylidenebutenolide (**3**) that would serve as an important intermediate for the preparations of **1** and **2**. It was expected therefore that the key intermediate of type (**3**) could be prepared by taking the advantage of our synthetic sequence for γ-alkylidenebutenolides. Thus, treatment of the lithiated butenolide

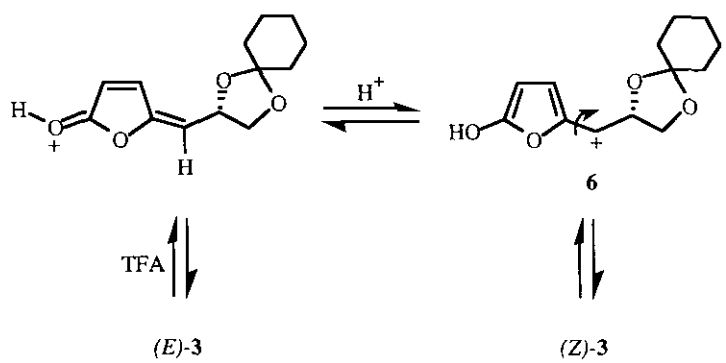
(**4**) with freshly prepared *(R)*-2,3-*O*-cyclohexylidene-D-glyceraldehyde[9] at -78 °C for 1 h gave a crude product containing the desired γ-adduct along with other unidentified products. The crude reaction

Scheme 1



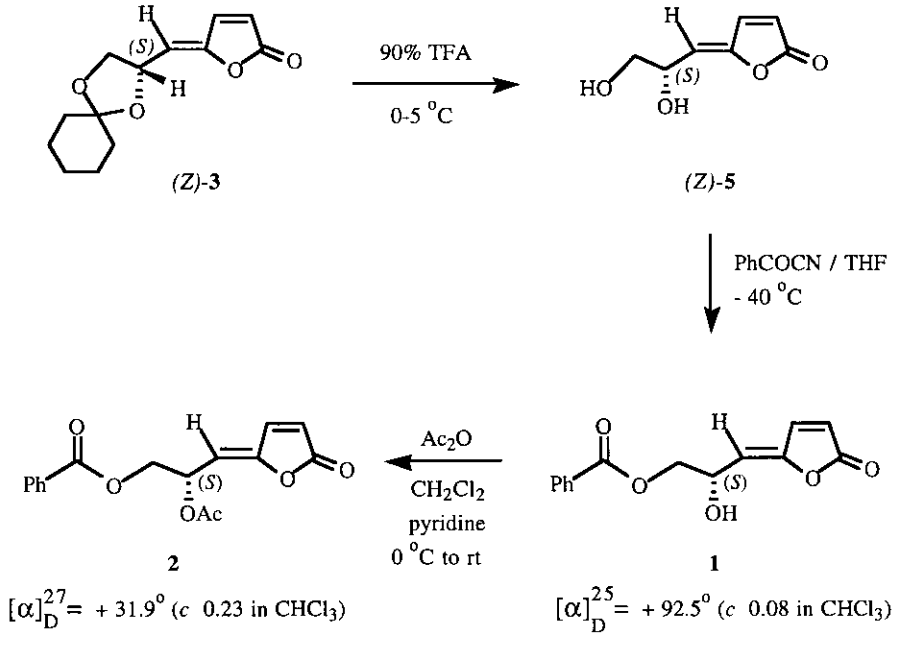
mixture was subjected to elimination without purification by employing methanesulfonyl chloride in pyridine or using methanesulfonyl chloride/triethylamine in dichloromethane followed by treatment with diisopropylamine.[10] The pure *(Z)*-isomer (**3**) could be isolated in 22% yield by MPLC along with 5% yield of pure *(E)*-isomer (**3**) and 4% yield of a 71:29 mixture of the *(Z)*- and *(E)*-isomers. Hydrolysis of *(Z)*-**3** to *(Z)*-diol (**5**) could be accomplished by using 90% aqueous trifluoroacetic acid at 0 °C or 0 °C to room temperature. All attempts led to moderate yield of the desired *(Z)*-diol (**5**) (47-57%) along with the recovered starting material (*(Z)*-**3**) (15-21% yield). The incomplete hydrolysis of *(Z)*-**3** might be due to the fact that the reaction was reversible: cyclohexanone *in situ* generated could presumably react with *(Z)*-diol (**5**) in the presence of trifluoroacetic acid. The structure of *(Z)*-diol (**5**) was established on the basis of interpretation of 300 MHz ^{1}H NMR and NOE spectral data. The ^{1}H NMR data and the sign of the specific rotation of *(Z)*-diol (**5**) were consistent with those reported for the known *(S)*-*(Z)*-5-(2,3-dihydroxypropylidene)-2(5*H*)-furanone.[6] Having succeeded in preparing the *(S)*-*(Z)*-diol (**5**), an attempt was made to hydrolyze the *(E)*-isomer (**3**) by employing the similar conditions for *(Z)*-**3**. It was found that treatment of the pure *(E)*-**3** with 90% aqueous trifluoroacetic acid at 0 °C for 15-16 h provided a 74:26

Scheme 2



mixture of *(E)*- and *(Z)*-diol (**5**) (46 % yield) together with the recovered **3** (26% yield) as a 70:30 mixture of *(E)*- and *(Z)*-isomers. Comparable results were obtained when the reaction was carried out under similar conditions in dichloromethane (23 h): **5** (57% yield; *E*:*Z* = 76:24) and **3** (21% yield; *E*:*Z* = 72:28) could be isolated. The formation of *(E)*- and *(Z)*-isomers of **3** and **5** during the hydrolysis of the pure *(E)*-**3** could presumably arise from acid-catalyzed isomerization *via* an intermediate (**6**) as shown in Scheme 2.

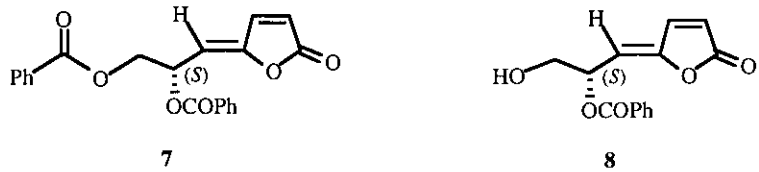
With *(S)*-*(Z)*-diol (**5**) in hand, we next synthesized the desired melodorinol (**1**) and acetylmelodorinol (**2**) by carrying out selective benzoylation followed by acetylation as previously described by Shen[6] and Lu.[7] Thus, the reaction of *(S)*-*(Z)*-diol (**5**) with benzoyl chloride (1.1 equiv.) in dichloromethane in the presence of triethylamine at 0 °C for 22 h afforded 48% yield of the expected melodorinol (**1**) accompanied with 8% yield of dibenzoate (**7**) and a 36:64 mixture of melodorinol (**1**) and compound (**8**) (13% yield) after chromatographic separation. Better result was achieved when the reaction was conducted by employing benzoyl cyanide (3 equiv.)/triethylamine in tetrahydrofuran at - 40 °C for 2 h. The reaction proceeded cleanly to give melodorinol (**1**) in 60% yield along with 18% yield of dibenzoate (**7**). Melodorinol (**1**) was obtained as a pale yellow liquid and its spectral data were in accordance with those of the natural product previously reported by our group,[3] and the synthetic product reported by Shen[6] and Lu.[7] The sign of the



(Z)-**3** *(Z)*-**5**

2 **1**

$[\alpha]_D^{27}$ = + 31.9° (*c* 0.23 in $CHCl_3$) $[\alpha]_D^{25}$ = + 92.5° (*c* 0.08 in $CHCl_3$)



7 **8**

specific rotation of our synthetic melodorinol (**1**) [$[\alpha]_D^{25}$+92.5° (*c* 0.08, $CHCl_3$)] was concordant with *(S)*-(+)-melodorinol as previously synthesized by Shen[6] [$[\alpha]_D^{22}$ +72° (*c* 1.0 $CHCl_3$)] and Lu[7] [$[\alpha]_D^{22}$+86.4° (*c* 0.95, $CHCl_3$)]. *(S)*-(+)-Acetylmelodorinol (**2**) could be finally prepared in 76% yield as a white solid by acetylation of *(S)*-(+)-melodorinol (**1**) with acetic anhydride and pyridine in dichloromethane at 0 °C to room temperature for 14 h. The spectral data including the sign of the specific rotation were found in good agreement with those published in the literature.[6,7]

In summary, we have demonstrated the synthetic utility of the lithiated butenolide as a useful butenolide synthon for the preparation of *(S)*-(+)-melodorinol (**1**) and *(S)*-(+)-acetylmelodorinol (**2**).

EXPERIMENTAL

General: Melting points were determined either by an Electrothermal or a Buechi 510 Melting Point Apparatus and were uncorrected. ^1H NMR spectra were measured with a Bruker DPX300 Spectrometer, using TMS as an internal reference and reported in parts per million (ppm). IR spectra were recorded on a Jasco A-302 or a Perkin Elmer 2000 NIR FT Raman. MS spectra were obtained on a Finnigan MAT INCOS 50 Mass Spectrometer at 70 eV. Elemental analyses were performed by using a Perkin Elmer Elemental Analyzer 2400 CHN. All solvents were dried by using standard methods prior to use.

(S)-(Z)- and *(S)-(E)*-5-(2,3-*O*-Cyclohexylidene-2,3-dihydroxypropylidene)-2(5*H*)-furanone (3).

To a stirred (-78 °C) THF solution of LDA [prepared by reacting diisopropylamine (3.1 mL, 22 mmol) in THF (80 mL) with *n*-BuLi (1.03 M in hexane; 19.5 mL, 22 mmol) at -78 °C for 30 min] was added dropwise a THF (5 mL) solution of 2(5*H*)-furanone (1.68 g, 20 mmol). The resulting mixture was allowed to stir at -78 °C for 1 h. Freshly prepared 2,3-*O*-cyclohexylidene-D-glyceraldehyde (3.74 g, 22 mmol) in THF (5 mL) was added dropwise at -78 °C. The reaction mixture was kept stirring at this temperature for 1.5 h, and quenched with a saturated NH_4Cl solution (20 mL) at -78 °C. After warming up to rt, it was diluted with water (20 mL) and extracted with EtOAc (4 x 50 mL). The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. Filtration and evaporation of the solvent gave a pale yellow viscous liquid of a crude product, which was used without further purification.

The crude product obtained was dissolved in dry pyridine (20 mL) under nitrogen atmosphere at 0 °C and treated with freshly distilled methanesulfonyl chloride (1.8 mL, 23 mmol) at 0 °C. After stirring at 0 °C for 20 min and then at rt for 2 h, the mixture was heated at at 80-90 °C for 10 h. The reaction mixture was diluted with water and extracted with EtOAc (4x50 mL). The combined organic layers were washed with water, brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by MPLC (3.5 x 72 cm column on SiO_2, 0-5% EtOAc in hexane) to give *(Z)*-**3** (1.03 g, 22%), a mixture of *(Z)*- and *(E)*-isomers (**3**) as a viscous liquid (71:29; 0.208 mg, 4%), and *(E)*-**3** (233 mg, 5%).

Elimination employing MsCl/Et$_3$N/CH$_2$Cl$_2$/i-Pr$_2$NH.[10] The crude product obtained from the reaction of the lithiated butenolide (5.0 mmol) and 2,3-*O*-cyclohexylidene-D-glyceraldehyde (1.02 g, 6.0 mmol) was dissolved in CH_2Cl_2 (50 mL), to which was added triethylamine (1.41 mL, 10 mmol) and methanesulfonyl chloride (0.7 mL, 9.0 mmol) at -60 °C. After stirring at the same temperature for 30 min, the resulting mixture was quenched with a saturated NH_4Cl solution (20 mL) and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporation to dryness to give a crude mesylate. This was dissolved in CH_2Cl_2 (50 mL), followed by the addition of diisopropylamine (3.95 mL, 28 mmol). The resulting reaction mixture was stirred at rt for 40 min, then quenched with a saturated NH_4Cl solution (20 mL) and extracted with CH_2Cl_2. The combined extracts were washed with water, brine and dried over anhydrous Na_2SO_4. Filtration and evaporation afforded a crude product (1.41 g), which was purified by MPLC (0-5% ethyl acetate in hexane) to give *(Z)*-**3** (168 mg, 14% yield), *(E)*-**3** (27.7 mg, 2% yield) and a mixture of *(Z)*- and *(E)*-isomers (70:30; 203 mg, 17% yield).

(S)-(-)-*(Z)*-**3**: as a viscous liquid. $[\alpha]_D^{26}$ - 35.6 ° (*c* 0.23, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (d, *J* = 5.4 Hz, 1H, COCH=C*H*-), 6.26 (d, *J* = 5.4 Hz, COC*H*=CH-), 5.37 (d, *J* = 8.4 Hz, 1H, =C*H*CHO-), 5.21-5.12 (m, 1H, =CHC*H*O-), 4.23 (dd, *J* = 8.2, 6.3 Hz, 1H, OCHC*H*HO-), 3.71 (dd, *J* = 8.2, 6.9 Hz, 1H, OCHCH*H*O-), 1.72-1.54 and 1.50-1.35 [each m, 10H, -(C*H*$_2$)$_5$-]. IR (nujol): ν_{max} 1772, 1740, 1676, 1560, 1450, 1370, 1299, 1236, 1166, 1097, 1039, 932, 873, 845 cm^{-1}. MS: m/z (%) relative intensity 236 (M^+, 15), 206 (10), 193 (29), 177 (3), 165 (3), 149 (1), 138 (23), 122(100), 110 (10), 94 (60), 82 (16), 66 (44), 55 (65). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.82. Found: C, 65.68; H; 6.80.

(S)-(-)-*(E)*-**3**: as a pale yellow solid. mp 80-82 °C (ether-hexane); $[\alpha]_D^{25}$ - 13.1° (*c* 0.31, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (d, *J* = 5.6 Hz, 1H, COCH=C*H*-), 6.29 (dd, *J* = 5.6, 1.6 Hz, 1H, COC*H*=CH-), 5.72 (dd, *J* = 7.8, 1.2 Hz, 1H, =C*H*CHO-), 4.92-4.82 (m, 1H, =CHC*H*O-), 4.21 (dd, *J* = 8.2, 6.2 Hz, 1H, OCHC*H*HO-), 3.72 (dd, *J* = 8.2, 7.4 Hz, 1H, OCHCH*H*O-), 1.72-1.56 and 1.50-1.35 [each m, 10H, -(C*H*$_2$)$_5$-]. ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.84, 151.47, 140.35, 121.33, 112.10, 110.84, 71.05, 69.22, 36.14, 35.20, 24.89, 23.80, 23.73. IR (nujol): ν_{max} 1779, 1753, 1670, 1560, 1459, 1450, 1370, 1162, 1119, 1066, 1052, 927, 884, 822 cm^{-1}. MS: m/z (%) relative intensity 236 (M^+, 11), 206 (7), 193 (18), 177 (3), 164 (3), 149 (2), 138 (26), 122 (100), 110 (11), 94 (63), 82 (17), 66 (46), 55 (63). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.82. Found: C, 65.90; H, 6.66.

Preparation of *(S)*-(+)-*(Z)*-5-(2,3-Dihydroxypropylidene)-2(5*H*)-furanone (5).

(S)-(Z)-**3** (0.116 g, 0.5 mmol) was dissolved in 90% trifluoroacetic acid (1 mL) at 0 °C. The solution was kept stirring at 0 °C for 1.5 h. After usual workup and chromatography, the desired *(S)-(Z)*-diol (**5**) (32.3 mg, 42%) as a colorless viscous liquid together with the starting material (*(S)-(Z)*-**3**) (31.2 mg, 27%) was obtained. When the reaction was carried out at 0 °C for 26 h, *(S)-(Z)*-diol (**5**) (44.8 mg, 57%) as a colorless viscous liquid was isolated along with the starting material (*(S)-(Z)*-**3**) (17.4 mg, 15%).

(*Z*)-Diol (**5**): $[\alpha]_D^{29}$+8° (*c* 0.1, MeOH); lit.,[6] $[\alpha]_D^{32}$+12° (*c* 0.5, MeOH), lit.,[7] $[\alpha]_D^{22}$+39° (*c* 0.6, MeOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (d, *J* = 5.5 Hz, 1H, COCH=C*H*-), 6.25 (d, *J* = 5.5 Hz, 1H, COC*H*=CH-), 5.40 (d, *J* = 8.1 Hz, 1H, =C*H*CHO-), 4.88-4.79 (m, 1H, =CHC*H*O-), 3.76 (dd, *J* = 11.4, 3.4 Hz, 1H, -OCHC*H*HO-), 3.59 (dd, *J* = 11.4, 6.9 Hz, 1H, -OCHCH*H*O-), 2.59 (br s, 2H, O*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.58, 149.51, 143.96, 120.47, 114.64, 67.63, 65.46. IR ($CHCl_3$): ν_{max} 3598, 3450, 3029, 3000, 2900, 1780, 1760, 1677, 1561, 1231, 1115, 1066, 941, 836 cm^{-1}. MS: m/z (%) relative intensity 156 (M^+, 2), 139 (1), 125 (94), 109 (2), 97 (100), 82 (19), 79 (16), 69 (49), 65 (3), 61 (6), 54 (37).

Preparation of *(S)*-(+)-*(Z)*-5-(3-Benzoyloxy-2-hydroxypropylidene)-2(5*H*)-furanone (1) (Melodorinol).

Using PhCOCl/Et_3N/CH_2Cl_2 / 0 °C to rt (22 h).

To a cooled (0 °C) solution of *(S)-(Z)*-diol (**5**) (44.8 mg, 0.28 mmol) in dry CH_2Cl_2 (1 mL) were added triethylamine (0.2 mL) and a solution of PhCOCl (44.9 mg, 0.32 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was kept in a refrigerator overnight (22 h), then diluted with water (10 mL) and extracted with EtOAc (4 x 20 mL). The combined extracts were washed with a cold 10% $NaHCO_3$ solution (10 mL), brine and dried over anhydrous Na_2SO_4. Filtration and evaporation of the solvent gave a crude product, which was purified by radial chromatography (SiO_2, 30-100 % EtOAc in hexane) to afford dibenzoate (**7**) (7.8 mg, 8%), melodorinol (**1**) (35.1 mg, 48%) and a mixture of **1** and **8** (36:64; 9.5 mg, 13%) along with the starting material (*(S)-(Z)*-diol **5**) (5.3 mg, 12%).

Using benzoyl cyanide/Et_3N/THF/- 40 °C.

To a cooled (- 40 °C) solution of *(S)-(Z)*-diol (**5**) (77 mg, 0.5 mmol) in THF (30 mL) were added sequentially triethylamine (0.2 mL, 1.5 mmol) and a solution of PhCOCN (0.2191 g, 1.67 mmol) in THF (5 mL). The reaction mixture was stirred at - 40 °C for 2 h and quenched with MeOH (10 mL) in order to destroy the unreacted PhCOCN and allowed to warm to rt gradually. After removal of the solvents under reduced pressure, the residue was taken into EtOAc (100 mL). It was washed with a cold 5% $NaHCO_3$ solution (10 mL), water (10 mL), brine and dried over anhydrous Na_2SO_4. Filtration and evaporation provided a pale yellow viscous liquid, which was purified by radial chromatography (SiO_2) to give dibenzoate (**7**) (32.9 mg, 18%; hexane as an eluent) and melodorinol (**1**) (77.5 mg, 60%; 30-50% EtOAc-hexane elution). $[\alpha]_D^{25}$ +92.5° (*c* 0.08, $CHCl_3$); lit.,[6] $[\alpha]_D^{22}$ +72° (*c* 1, $CHCl_3$), lit.,[7] $[\alpha]_D^{22}$ +86.4°(*c* 0.95, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09-8.02 (m, 2H, Ar*H*), 7.62-7.55 (m, 1H, Ar*H*), 7.50-7.42 (m, 2H, Ar*H*), 7.40 (d, *J* = 5.5 Hz, 1H, COCH=C*H*-), 6.27 (d, *J* = 5.5 Hz, 1H, COC*H*=CH-), 5.40 (d, *J* = 8.0 Hz, 1H, =CHC*H*O-), 5.18 (ddd, *J*= 8.0, 5.9, 4.5 Hz, 1H, OC*H*CH_2O-), 4.50 (dd, *J*= 11.7, 4.5 Hz, 1H, -OCHC*H*HO-), 4.46 (dd, *J* = 11.7, 5.9 Hz, 1H, -OCHCH*H*O-), 1.74 (br s, 1H, O*H*). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.94, 166.69, 150.01, 143.67, 133.35, 129.72, 129.49, 128.46, 121.01, 113.18, 67.48, 65.80. IR ($CHCl_3$): ν_{max} 3472, 3030, 3020, 2940, 1779, 1750, 1721, 1690, 1603, 1562,

1453, 1317, 1273, 1178, 1113, 1067, 1027, 940, 879, 839 cm^{-1}. MS: m/z (%) relative intensity 260 (M^+, 0.3), 243 (2), 230 (6), 215 (0.3), 177 (0.3), 165 (0.3), 154 (0.2), 138 (6), 125 (10), 110 (6), 105 (100), 97 (18), 91 (2), 82 (8), 77 (76), 69 (13), 65 (4), 55 (16), 51 (51).

(Z)-5-(2,3-Dibenzoyloxypropylidene)-2(5*H*)-furanone (7).

$[\alpha]_D^{27}$ -60.8° (*c* 0.34, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 8.17-7.99 (m, 4H, Ar*H*), 7.61-7.54 (m, 2H, Ar*H*), 7.47-7.41 (m, 4H, Ar*H*), 7.40 (d, *J* = 5.4 Hz, 1H, COCH=C*H*), 6.37 (ddd, *J* = 8.1, 5.8, 4.5 Hz, 1H, C*H*OCOPh), 6.30 (d, *J* = 5.4 Hz, COC*H*=CH), 5.45 (d, *J* = 8.1 Hz, 1H, =C*H*CHO-), 4.73 (dd, *J* = 11.8, 5.8 Hz, 1H, -OCHC*H*H-O), 4.68 (dd, *J* = 11.8, 4.5 Hz, 1H, -OCHCH*H*O-). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.41, 166.02, 165.37, 150.84, 143.27, 133.35, 133.25, 129.78, 129.69, 129.52, 129.47, 128.45, 121.65, 108.89, 67.99, 64.61. IR ($CHCl_3$): ν_{max} 3160, 3120, 3100, 3050, 3010, 2970, 2940, 2880, 1786, 1724, 1603, 1562, 1453, 1317, 1280, 1263, 1250, 1178, 1107, 1100, 1069, 1027, 942, 879, 832 cm^{-1}. MS: m/z (%) relative intensity 364 (M^+, 3), 334 (2), 242 (30), 229 (1), 214 (1), 138 (1), 122 (4), 105 (100), 94 (3), 77 (65), 66 (6), 51 (38), 39 (10). Anal. Calcd for $C_{21}H_{16}O_6$: C, 69.22; H, 4.42. Found: C, 68.89; H, 4.38.

Preparation of *(S)*-(+)-*(Z)*-5-(2-Acetoxy-3-benzoyloxypropylidene)-2(5*H*)-furanone (2) (Acetylmelodorinol).

To a cooled (0 °C) solution of melodorinol (**1**) (80 mg, 0.3 mmol) in dry CH_2Cl_2 (20 mL), were added dry pyridine (0.5 mL) and acetic anhydride (0.5 mL, 5.5 mmol). The reaction mixture was stirred at 0 °C and slowly warmed up to rt gradually overnight (14 h). It was diluted with water (5 mL) and EtOAc (100 mL) was added. The resulting mixture was neutralized with a cold 2 *N* HCl solution (10 mL). The organic layer was washed with a saturated $NaHCO_3$ solution (10 mL), water (10 mL), brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give a crude product (77.8 mg) which was purified by radial chromatography (SiO_2, 20% EtOAc in hexane) to afford a white solid of acetylmelodorinol (**2**) (68.9 mg, 76%; mp 78-80 °C from ether-hexane, lit.,[6] mp 78-80 °C from *i*-PrOH-hexane). $[\alpha]_D^{27}$+31.9° (*c* 0.23, $CHCl_3$); lit.,[6] $[\alpha]_D^{22}$+32.5° (*c* 2, $CHCl_3$), lit.,[7] $[\alpha]_D^{22}$+41° (*c* 0.33, $CHCl_3$), lit.,[2] $[\alpha]_D^{23}$ +209° (*c* 1, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 8.07-8.01 (m, 2H, Ar*H*), 7.63-7.55 (m, 1H, Ar*H*), 7.51-7.43 (m, 2H, Ar*H*), 7.38 (d, *J* = 5.4 Hz, 1H, COCH=C*H*), 6.28 (d, *J* = 5.4 Hz, COC*H*=CH), 6.15 (ddd, *J* = 8.1, 5.8, 4.4 Hz, 1H, C*H*OCOCH$_3$), 5.33 (d, *J* = 8.1 Hz, 1H, =C*H*CHO-), 4.58 (dd, *J* = 11.8, 4.4 Hz, 1H, -OCHC*H*HO-), 4.52 (dd, *J* = 11.8, 5.8 Hz, 1H, -OCHCH*H*O-), 2.11 (s, 3H, OCOC*H*$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.74, 168.42, 165.97, 150.66, 143.30, 133.26, 129.66, 129.48, 128.44, 121.55, 108.82, 67.24, 64.57, 20.85. IR ($CHCl_3$): ν_{max} 3029, 2930, 1786, 1755, 1725, 1690, 1603, 1563, 1452, 1373, 1273, 1240, 1178, 1108, 1067, 1028, 945, 877, 833 cm^{-1}. MS: m/z (%) relative intensity 302 (M^+, 2), 272 (1), 258 (0.3), 243 (13), 230 (2), 215 (1), 180 (9), 167 (1), 152 (1), 138 (18), 125 (8), 110 (7), 105 (100), 97 (5), 77 (70), 66 (7), 51 (36), 43 (83).

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REFERENCES

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1. Taken from MSc Thesis of PP, Mahidol University, 1998.
2. (a) J.H. Jung, S. Pummangura, C. Chaichantipyuth, C. Patarapanich, P.E. Fanwick, C.-J. Chang, and J.L. McLaughlin, *Tetrahedron*, 1990, **46,** 5043; (b) J.H. Jung, S. Pummangura, C. Chaichantipyuth, C. Patarapanich, and J.L. McLaughlin, *Phytochemistry*, 1990, **29**, 1667.
3. P. Tuchinda, J. Udchachon, V. Reutrakul, T. Santisuk, W.C. Taylor, N.R. Farnsworth, J.M. Pezzuto, and A.D. Kinghorn, *Phytochemistry*, 1991, **33**, 2685.
4. J.H. Jung, C.-J. Chang, D.L. Smith, and J.L. McLaughlin, *J. Nat. Prod.*, 1991, **54**, 500.
5. A. Horeau, 'Stereochemistry, Fundamental and Methods', Vol. 3, ed. by H.B. Kagan, Georg Thieme Publishers, Stuttgart, 1977, pp. 51-59.
6. C. Shen, S. Chou, and C. Chou, *Tetrahedron: Asymmetry*, 1996, **7**, 3141.
7. X. Lu, G. Chen, L. Xia, and G. Gou, *Tetrahedron: Asymmetry*, 1997, **8**, 3067.
8. M. Pohmakotr, P. Tuchinda, P. Premkaisorn, and V. Reutrakul, *Tetrahedron*, 1998, **54**, 11297.
9. (a) T. Sugiyama, H. Sugawara, M. Watanabe, and K. Yamashita, *Agric. Biol. Chem.*, 1984, **48**, 1841. (b) A. Chattopadhyay, and V.R. Mamdapur, *J. Org. Chem.*, 1995, **60**, 585.
10. T.K.M. Shing, H.-C. Tsui, and Z.-H. Zhou, *J. Org. Chem.*, 1995, **60**, 3121.

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