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Simple and efficient synthesis of thysanone methyl ether

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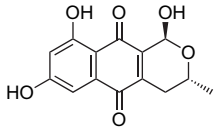
Abstract—The synthesis of thysanone methyl ether is achieved by employing semivioxanthin methyl ether, which in turn is prepared by the tandem Michael addition of an anion of orsellinate to a substituted dihydropyrone.

1. Introduction

Human rhinoviruses (HRVs) are solely responsible for the common cold in humans,[1] and many members of this family of viruses are also human pathogens, e.g., enteroviruses (polioviruses, coxsackieviruses, echoviruses and hepatitis A viruses), aphthoviruses (foot and mouth disease viruses), and cardioviruses (mengo and encephalomyocarditis viruses). They typically infect the upper respiratory tract in humans and target nasal epithelial cells. In common with all these viruses, the positive strand RNA genome of HRVs is translated directly into a large viral polyprotein (200 kDa) precursor, which undergoes a series of controlled proteolytic cleavages to generate functional viral gene products[2] upon entry into the host cell. The replication of many animal and plant viruses is entirely dependent on proteolytic processing. Since processing of the polyprotein is dependent upon two virally encoded proteases (3C-protease and 2A-protease), proteolytic processing of the polyprotein is extremely efficient and does not involve any cellular components. In fact, under normal circumstances, the intact polyprotein does not accumulate in infected cells. The polyprotein is mostly cleaved between glutamine and glycine (Q–G) and tyrosine and glycine (Y–G). The former cleavage is carried out by enzyme 3C-protease and the latter cleavage by 2A-protease.[3] Therefore these enzymes represent an attractive target for the development of antiviral chemotherapeutic agents for the control of HRVs and common cold.



(1*S*, 3*R*) Thysanone 1

(+)-Thysanone **1** was isolated from the fungus *Thysanophora penicilloides* by Singh and co-workers and is one of the few effective inhibitors of human rhinovirus 3C-protease and therefore provides a lead compound for understanding the mechanism of 3C-protease inhibition.[4] The structure and absolute stereochemistry of thysanone, was established by the total synthesis of its antipode by Gill and Donner.[5a] The synthesis of (1*R*,3*S*)-thysanone from (*S*)-propylene oxide established the stereochemistry of the natural product as (1*S*,3*R*). In addition, there are several synthetic analogs of thysanone reported by various groups.[5b]

In our continuing interest to synthesize pyranonaphthoquinone antibiotics,[6] we developed a methodology several years ago for the stereospecific synthesis of (+)-orthosporin and (−)-semivioxanthin methyl ether using the required optically active isomer of ethyl 3-hydroxybutyrate.[7] We also reported a synthetic strategy to prepare racemic semivioxanthin by means of tandem Michael reaction between an orsellinate and a cyclic Michael acceptor.[8] We have extended our methodology for the total synthesis of thysanone methyl ether employing semivioxanthin methyl ether as a starting point and the results are reported herein.

2. Results and discussion

The synthesis began with known methyl orsellinate derivative **2**.[9] It was reacted with dihydropyrone **3**[10] in the presence of lithium diisopropylamide at −78 °C to afford the semivioxanthin methyl ether **4** (Scheme 1).

Keywords: Michael addition; Orsellinate derivative; Semivioxanthin; Human pathogen.
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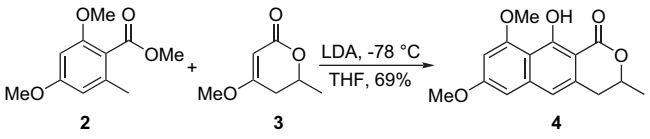


Scheme 1. Synthesis of semivioxanthin methyl ether **4**.

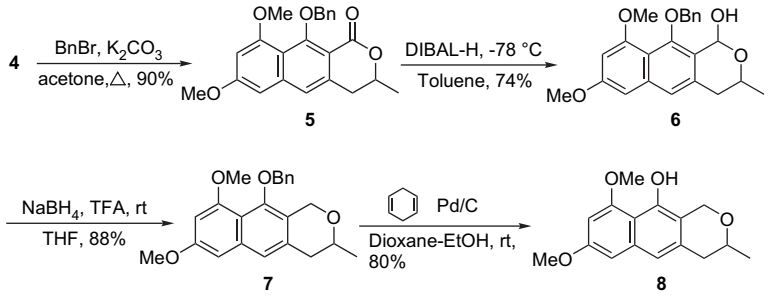
Oxidation of the phenolic functionality in **4** to the corresponding quinone was attempted using several well-known reagents like $K_2Cr_2O_7$ and $Na_2Cr_2O_7$ in aqueous acetic acid,[11] CrO_3,[12] and ceric ammonium nitrate.[13] However, none gave the desired quinone. Probably the lactone functionality could not survive the reaction conditions employed. Therefore, protection of the hydroxyl functionality as benzyl ether **5** and complete reduction of the lactone to a benzopyran were performed to form the stable cyclic ether **7** (Scheme 2).

Accordingly, the benzyl derivative of semivioxanthin methyl ether **5** was prepared using standard conditions. Direct reduction of the lactone to the naphthopyran[14] failed to give the desired product and made us employ a two-step reaction sequence viz. (a) DIBAL reduction of benzyl ether to hemiacetal **6** and (b) reduction of hemiacetal to naphthopyran **7** by stirring with sodium borohydride in the presence of TFA. With the desired naphthopyran in hand, C-10 debenzylation with a 1.0 M solution of BCl_3[15] in dichloromethane furnished the required hydroxynaphthopyran **8** albeit in low yield. Surprisingly mild hydrogenolysis at room temperature using Pd–C and 1,4-cyclohexadiene[16] proved to be the best method for this conversion.

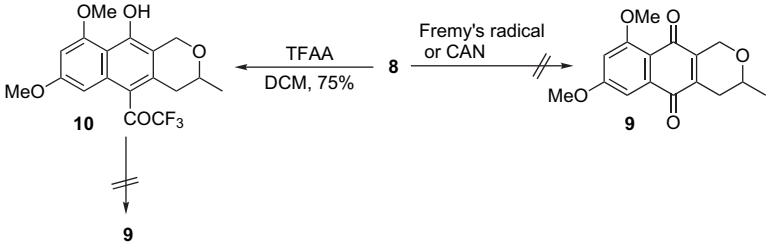
Next the reaction of hydroxynaphthopyran **8** to quinone **9** was explored with selective oxidizing agents like potassium nitrosodisulfonate or Fremy's radical,[17] CAN,[13] and metal nitrates[18] in TFA, none of which gave the required quinone (Scheme 3).

Pavlidis' method[19] employing the *para*-trifluoroacetyl derivative of the corresponding phenol and treating with hydrogen peroxide in aqueous base to afford the desired quinone probably via Bayer–Villiger type oxidation was also unsuccessful.

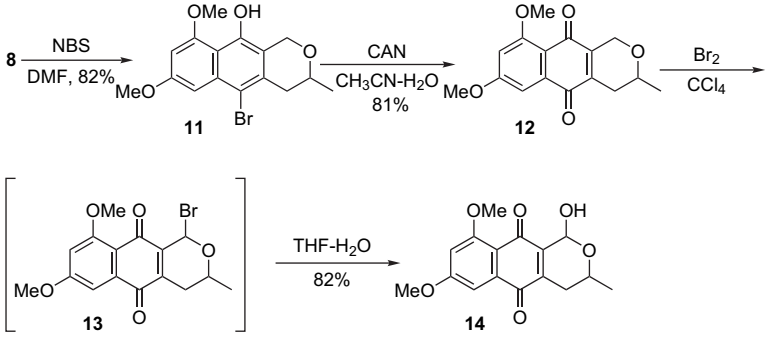
Finally, a method that was analogous to the oxidation of halophenols and halonaphthols reported by Gopinathan and Bhatt[20] using ceric ammonium nitrate yielded the corresponding quinone successfully (Scheme 4).



Scheme 2. Synthesis of hydroxynaphthopyran **8**.



Scheme 3. Attempted synthesis of quinone **9**.



Scheme 4. Synthesis of thysanone methyl ether **14**.

Accordingly, hydroxynaphthopyran **8** was treated with 1 equiv of NBS in DMF[21] at room temperature to effect selective nuclear bromination at the *para* position to give the monobromonaphthol **11**. When bromonaphthol **11** was treated with ceric ammonium nitrate the corresponding quinone **12** was obtained as a yellow solid. Benzylic bromination of quinone **12** was carried out using 1 equiv of bromine followed by treatment of the intermediate bromide **13** with aqueous tetrahydrofuran to give methoxy thysanone **14**.

In conclusion, we have reported a short synthesis of thysanone methyl ether **14** from substituted methyl orsellinate **2**.

3. Experimental

3.1. 3,4-Dihydro-7,9-dimethoxy-10-hydroxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran-1-one (4)

To a stirred solution of LDA [prepared from 1.6 M solution of *n*-BuLi in hexane (6.0 mL) and diisopropylamine (1.35 mL) at 0 °C under argon atmosphere] in THF (15 mL) at −78 °C was injected a solution of methyl 2,4-dimethoxy-6-methyl benzoate (**2**, 1.0 g, 4.7 mmol) in THF (10 mL) and the solution stirred for 15 min. To the resultant orange red solution, a solution of 4-methoxy-6-methyl-5,6-dihydro-2-pyrone (**3**, 0.676 g, 4.7 mmol) in THF (8 mL) was added and the solution stirred further for 30 min at −78 °C. It was then warmed to room temperature by removing dry ice–acetone bath and stirred for 20 min. The reaction mixture was poured slowly into ice-cold dilute hydrochloric acid (50 mL) and extracted with dichloromethane. The organic extracts were washed with brine, dried over sodium sulfate, and concentrated. The residue was chromatographed using 20% acetone in pet. ether as an eluent to afford (**4**) as a crystalline yellow solid (0.945 g, 69%); mp 131 °C (lit.[5b,c] mp 130–132 °C).

IR (Nujol): 1665 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.53 (d, J=6.0 Hz, 3H, $-CH_3$), 2.97 (d, J=6.0 Hz, 2H, $-CH_2$), 3.92 (s, 3H, $-OCH_3$), 3.99 (s, 3H, $-OCH_3$), 4.61–4.82 (m, 1H, $-CH_2-CH-CH_3$), 6.47 (d, J=2 Hz, 1H), 6.58 (d, J=2.0 Hz, 1H), 6.86 (s, 1H), 13.18 (s, 1H, chelated –OH). ^{13}C NMR ($CDCl_3$): δ 20.50 ($-CH_3$), 34.99 ($-CH_2$), 55.20 ($-OCH_3$), 55.97 ($-OCH_3$), 75.42, 98.21, 98.83, 101.16, 110.98, 115.04, 134.16, 141.40, 160.00, 161.88, 164.00, 170.95 (–C=O). MS (*m*/*z*): 288 (M^+, base peak), 244 (18), 226 (18), 181 (3), 145 (3), 121 (4). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.65; H, 8.32. Found: C, 66.52; H, 8.45%.

3.2. 10-Benzyloxy-3,4-dihydro-7,9-dimethoxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran-1-one (5)

A mixture of **4** (0.4 g, 1.3 mmol), potassium carbonate (0.22 g, 1.6 mmol), and benzyl bromide (0.35 g, 1.5 mmol) in acetone (10 mL) was stirred under reflux for 24 h. The acetone was distilled off and to the residue water (20 mL) was added. The product was extracted with ethyl acetate (2×20 mL), washed with water several times followed by brine (10 mL), dried over sodium sulfate, and concentrated on rotary evaporator to provide a crude product, which was chromatographed on silica gel using 10% acetone in pet. ether as an eluent to afford **5** as a white solid (0.472 g, 90%); mp 134.4 °C.

IR ($CHCl_3$): 1713, 1625 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.47 (d, J=7.0 Hz, 3H, $-CH_3$), 2.96 (d, J=8.0 Hz, 2H, $-CH_2$), 3.83 (s, 3H, $-OCH_3$), 3.92 (s, 3H, $-OCH_3$), 4.40–4.62 (m, 1H, $-COOCHCH_3$), 5.04 (d, J=10.0 Hz, 1H), 5.26 (d, J=10.0 Hz, 1H), 6.50 (d, J=2.0 Hz, 1H), 6.60 (d, J=2.0 Hz, 1H), 7.23–7.46 (m, 4H), 7.66 (d, J=8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 20.65, 36.35, 55.35, 55.94, 73.88, 77.39, 98.47, 99.28, 113.87, 116.22, 120.48, 127.62, 128.13, 128.68, 136.62, 137.87, 140.48, 159.19, 159.48, 160.00, 160.66, 162.68. MS (*m*/*z*): 378 (M^+, 78), 360 (12), 345 (10), 287 (98), 269 (90), 242 (53), 185 (35), 141 (38), 115 (70), 91 (100). Anal. Calcd for $C_{23}H_{22}O_5$: C, 72.99; H, 5.81. Found: C, 72.81; H, 5.88%.

3.3. 10-Benzyloxy-3,4-dihydro-7,9-dimethoxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran-1-ol (6)

Benzyl ether **5** (0.611 g, 1.61 mmol) was dissolved in dry toluene (8 mL) under argon atmosphere and cooled to −78 °C in a dry ice–acetone bath. DIBAL-H (2.529 M solution in toluene, 0.286 g, 0.8 mL, 2.0 mmol) was injected through syringe within 5 min and stirring was continued at the same temperature for further 3 h. The reaction mixture was then quenched at the same temperature by adding 0.8 mL methanol and 0.8 mL water and warmed to room temperature. The gelatinous precipitate was filtered through Celite. Concentration of the solution under reduced pressure afforded crude lactol, which was purified by column chromatography using 20% acetone in pet. ether as an eluent to furnish pure lactol **6** as a white solid (0.446 g, 74%); mp 114 °C.

IR (Nujol): 3580 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.39 (d, J=7.0 Hz, 3H, $-CH_3$), 2.69–2.95 (m, 2H, $-CH_2-CH-CH_3$), 3.87 (s, 3H, $-OCH_3$), 3.91 (s, 3H, $-OCH_3$), 4.45–4.65 (m, 1H, $-CH_2-CH-CH_3$), 4.98 (d, J=8.0 Hz, 1H), 5.20 (d, J=8.0 Hz, 1H), 6.48 (d, J=2.0 Hz, 1H), 6.67 (d, J=2.0 Hz, 1H), 7.15–7.68 (m, 6H, aromatic). MS (*m*/*z*): 380 (M^+, 5), 363 (20), 289 (2), 272 (16), 243 (4), 211 (6), 91 (100). Anal. Calcd for $C_{23}H_{24}O_5$: C, 72.61; H, 6.30. Found: C, 72.57; H, 6.37%.

3.4. 10-Benzyloxy-3,4-dihydro-7,9-dimethoxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran (7)

To a mixture of the above lactol **6** (0.150 g, 0.39 mmol) and sodium borohydride (0.014 g, 0.39 mmol) in dry THF (5 mL) under argon atmosphere was added trifluoroacetic acid (0.045 g, 0.030 mL, 0.39 mmol) at 0 °C. The mixture was stirred at the same temperature for 30 min and at room temperature for 30 min. THF was removed by distillation under reduced pressure, to the residue water (20 mL) was added and product was extracted with ethyl acetate (3×20 mL), washed with brine, and concentrated to give crude cyclic ether, which was purified by column chromatography using 5% acetone in pet. ether to afford **7** as a semi-solid (0.125 g, 88%).

^1H NMR ($CDCl_3$): δ 1.41 (d, J=6.0 Hz, 3H, $-CH_3$), 2.85 (d, J=6.0 Hz, 2H, $-CH_2-CH-CH_3$), 3.73–3.87 (m, 1H, $-CH_2-CH-CH_3$), 3.91 (s, 3H, $-OCH_3$), 3.92 (s, 3H, $-OCH_3$), 4.83 (d, J=16.0 Hz, 1H), 4.91 (s, 2H), 5.28 (d, J=16.0 Hz, 1H), 6.52 (d, J=2.0 Hz, 1H), 6.70 (d, J=2.0 Hz, 1H), 7.25–7.57 (m, 6H). ^{13}C NMR ($CDCl_3$): δ 21.48 ($-CH_3$),

35.89 (–CH_2), 55.12 (–OCH_3), 55.73 (–OCH_3), 65.19 (–CH_2), 70.56 (–*C*H–CH_3), 76.02 (–CH_2), 98.33, 98.49, 114.63, 122.23, 123.60, 127.75, 128.33, 134.19, 136.70, 137.98, 150.43, 155.90, 157.69. MS (*m*/*z*): 364 (M^+, 28), 273 (40), 258 (10), 229 (22), 187 (11), 141 (8), 115 (18), 91 (100). Anal. Calcd for $C_{23}H_{24}O_5$: C, 75.80; H, 6.58. Found: C, 75.80; H, 6.50%.

3.5. 3,4-Dihydro-7,9-dimethoxy-10-hydroxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran (8)

Debenzylation by boron trichloride: to a solution of naphthopyran **7** (0.050 g, 0.137 mmol) in dry dichloromethane (4 mL) was added BCl_3 (0.040 g, 0.343 mmol) (1.0 M solution in DCM) at −15 °C under argon atmosphere. It was further stirred at −15 °C for 1 h and quenched with methanol (1.0 mL). DCM was distilled off and water (10 mL) was added to it, extracted with chloroform, washed with brine, dried over sodium sulfate, and concentrated on rotary evaporator to give crude product, which was purified by column chromatography using 10% acetone in pet. ether as an eluent to afford pure hydroxynaphthopyran **8** as a white solid (0.010 g, 27%); mp 133.5 °C.

Debenzylation by hydrogenation in the presence of cyclohexadiene and palladium on carbon: to a solution of naphthopyran **7** (0.106 g, 0.291 mmol) in dry ethanol (5.0 mL) and dry dioxane (5.0 mL), were added 1,4-cyclohexadiene (0.5 mL) and 10% palladium on charcoal (20 mg) and the reaction mixture was stirred for 15 min. The reaction mixture was filtered through Celite and the residue was washed with ethyl acetate. The filtrate along with washings was concentrated to obtain a solid, which was purified by column chromatography using 10% acetone in pet. ether as an eluent to afford pure hydroxynaphthopyran **8** as a white solid (0.063 g, 80%); mp 133.5 °C.

IR ($CHCl_3$): 3412 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.38 (d, J=6.0 Hz, 3H, –CH_3), 2.78 (d, J=6.0 Hz, 2H, –CH_2–CH–CH_3), 3.67–3.85 (m, 1H), 3.87 (s, 3H, –OCH_3), 3.98 (s, 3H, –OCH_3), 4.77 (d, J=16.0 Hz, 1H), 5.13 (d, J=16.0 Hz, 1H), 6.37 (d, J=2.0 Hz, 1H), 6.61 (d, J=2.0 Hz, 1H), 6.94 (s, 1H), 9.20 (s, 1H, –OH). ^{13}C NMR ($CDCl_3$): δ 21.58 (–CH_3), 36.13, 55.24, 56.03, 64.76, 70.41, 97.08, 98.79, 109.05, 115.06, 116.46, 134.99, 135.66, 149.24, 157.14. MS (*m*/*z*): 274 (M^+, 98), 257 (10), 243 (5), 230 (100), 215 (18), 187 (18), 144 (8), 115 (18). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.58. Found: C, 70.09; H, 6.52%.

3.6. 3,4-Dihydro-7,9-dimethoxy-10-hydroxy-3-methyl-5-trifluoroacetyl-1*H*-naphtho[2,3-*c*]pyran (10)

To a solution of hydroxynaphthopyran **8** (0.33 g, 0.12 mmol) in dichloromethane (10 mL) was added trifluoroacetic anhydride (0.025 g, 0.016 mL, 0.12 mmol) at 25 °C with stirring and the reaction mixture was stirred for further 5 min. It was then diluted with water (10 mL) and the organic phase was separated, washed with brine (15 mL), and dried. Evaporation of the solvent afforded the crude product, which was purified by column chromatography on silica gel with dichloromethane as an eluent. The appropriate fractions upon evaporation afforded the pure **10** as a yellow solid (0.033 g, 75%); mp 166.6 °C.

IR ($CHCl_3$): 3404, 1631 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.36 (d, J=6.0 Hz, 3H, –CH_3), 2.73–2.82 (m, 2H, –CH_2–CH–CH_3), 3.70–3.90 (m, 1H, –CH_2–C*H*–CH_3), 3.95 (s, 3H, –OCH_3), 4.10 (s, 3H, –OCH_3), 4.72 (d, J=16.0 Hz, 1H), 5.09 (d, J=16.0 Hz, 1H), 6.43 (s, 1H), 7.04 (s, 1H), 9.14 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 21.50, 36.31, 56.44, 56.45, 64.50, 70.35, 91.00, 108.94, 109.68, 112.84, 116.66, 118.76, 132.28, 138.05, 149.74, 158.71, 161.43. MS (*m*/*z*): 371 (M+1, 100), 353 (5), 326 (60), 302 (70), 257 (85), 241 (20), 213 (10), 170 (12), 128 (22). Anal. Calcd for $C_{18}H_{17}F_3O_5$: C, 58.37; H, 4.59. Found: C, 58.31; H, 4.66%.

3.7. 5-Bromo-3,4-dihydro-7,9-dimethoxy-10-hydroxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran (11)

A solution of NBS (54 mg, 0.30 mmol) in dry DMF (2.5 mL) was added to a solution of hydroxynaphthopyran **8** (84 mg, 0.30 mmol) in dry DMF (2.5 mL) and stirred at room temperature for 16 h. The mixture was poured into water (10 mL) and extracted with dichloromethane (2×20 mL). The extract was washed well with water, dried (Na_2SO_4), and evaporated under reduced pressure to yield crude monobromide, which was purified by chromatography using 10% ethyl acetate in pet. ether to give pure bromonaphthol **11** as a white solid (87 mg, 82%); mp 138.5 °C.

^1H NMR ($CDCl_3$): δ 1.43 (d, J=6.0 Hz, 3H, –CH_3), 2.50–2.75 (m, 1H), 2.88–3.10 (m, 1H), 3.60–3.90 (m, 1H), 3.94 (s, 3H, –OCH_3), 4.03 (s, 3H, –OCH_3), 4.69 (d, J=10.0 Hz, 1H), 5.10 (d, J=10.0 Hz, 1H), 6.47 (d, J=2.0 Hz, 1H), 7.19 (d, J=2.0 Hz, 1H), 9.38 (s, 1H, –OH). ^{13}C NMR ($CDCl_3$): δ 21.61, 29.69, 38.21, 55.39, 56.40, 64.70, 70.68, 97.91, 99.22, 109.99, 112.34, 116.74, 133.83, 135.05, 149.06, 157.30, 158.24. MS (*m*/*z*): 354 (M^+, 100), 352 (M^+, 98), 310 (74), 308 (78), 293 (29), 273 (32), 229 (54), 214 (38), 201 (18), 155 (30), 115 (28). Anal. Calcd for $C_{16}H_{17}BrO_4$: C, 54.40; H, 4.81. Found: C, 54.49; H, 4.75%.

3.8. 3,4-Dihydro-7,9-dimethoxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran-5,10-dione (12)

To a solution of bromonaphthol **11** (0.046 g, 0.130 mmol) in acetonitrile (5.0 mL) was added ceric ammonium nitrate (0.106 g, 0.194 mmol) in water (2.0 mL) at 0 °C and stirred for 15 min at the same temperature. The stirring was further continued for 30 min at room temperature. It was then diluted with water (10 mL) and extracted with chloroform (2× 20 mL), washed with brine, dried over sodium sulfate, and concentrated under reduced pressure to afford crude **12** as a yellow solid, which was purified by column chromatography using 25% ethyl acetate in pet. ether as an eluent to give pure **12** as yellow solid (0.030 g, 81%); mp 211.9 °C.

IR ($CHCl_3$): 1640, 1660 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.37 (d, J=6.0 Hz, 3H), 2.15–2.37 (m, 1H), 2.64 and 2.73 (t, J=2.0 Hz, total 1H), 3.55–3.77 (m, 1H), 3.95 (s, 3H), 3.96 (s, 3H), 4.43 and 4.53 (t, J=2.0 Hz, total 1H), 4.79 and 4.89 (d, J=2.0 Hz, total 1H), 6.71 (d, J=2.0 Hz, 1H), 7.26 (d, J=2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 21.18, 29.21, 55.94, 56.40, 63.75, 69.58, 103.61, 104.13, 114.29, 139.02, 144.45, 162.03, 164.74, 181.80 (quinone C═O), 183.88 (quinone C═O). MS (*m*/*z*): 288 (M^+, 100), 273

(48), 259 (42), 245 (37), 227 (29), 187 (18), 115 (35). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.65; H, 5.54. Found: C, 66.56; H, 5.58%.

3.9. 3,4-Dihydro-7,9-dimethoxy-3-methyl-1*H*-naphtho[2,3-*c*]pyran-1-ol-5,10-dione (14)

To a solution of quinone **12** (0.022 g, 0.076 mmol) in dry CCl_4 (20.0 mL) was added bromine in CCl_4 (0.012 g, 0.076 mmol) at room temperature. It was then exposed to 500 W electric bulb for 30 min with efficient stirring. The reaction mixture was then cooled, THF (10.0 mL) and water (1.0 mL) were added successively and stirring was continued for further 1 h. The mixture of CCl_4 and THF was removed by distillation under reduced pressure, aqueous residue was diluted with water (20.0 mL) and was extracted with ethyl acetate (2×20.0 mL). The ethyl acetate layer was washed with brine, dried over sodium sulfate, and concentrated to give a crude yellow solid, which was purified by column chromatography using 30% acetone in pet. ether to give pure **14** as a yellow solid (0.019 g, 82%); mp 155.5 °C.

IR ($CHCl_3$): 1595, 1656 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.39 and 1.47 (d, J=6.0 Hz, total 3H), 2.14–2.34 (m, 1H), 2.65 and 2.75 (d, J=2.0 Hz, total 1H), 3.95 (s, 3H), 3.97 (s, 3H), 4.20–4.40 (m, 1H), 6.03 and 6.07 (s, total 1H), 6.73 and 6.75 (d, J=2.0 Hz, total 1H), 7.25 and 7.30 (d, J=2.0 Hz, total 1H). ^{13}C NMR ($CDCl_3$): δ 21.18, 29.21, 55.94, 56.40, 63.75, 69.58, 103.61, 104.13, 114.29, 139.02, 144.45, 162.03, 164.74, 181.80 (quinone C=O), 183.88 (quinone C=O). MS (*m*/*z*): 286 (58, M−18), 272 (29), 243 (6), 200 (22), 171 (23), 141 (21), 105 (25), 69 (65), 55 (100). Anal. Calcd for $C_{16}H_{16}O_5$: C, 55.25; H, 5.25. Found: C, 55.24; H, 5.28%.

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References and notes

1. Gwaltney, J. M., Jr. *Viral infection of Man: Epidemiology and Control*, 2nd ed.; Evans, E. A., Ed.; Plenum: New York, NY, 1982; p 491.
2. (a) Palmenberg, A. C. *J. Cell. Biochem.* **1987**, *33*, 191; (b) Krausslich, H. G.; Wimmer, E. *Annu. Rev. Biochem.* **1988**, *57*, 701; (c) Cordingley, M. G.; Register, R. B.; Callahan, P. L.; Garsky, V. M.; Colonno, R. J. *J. Virol.* **1989**, *63*, 5037; (d) Cordingley, M. G.; Callahan, P. L.; Sardana, V. V.; Garsky, V. M.; Colonno, R. J. *J. Biol. Chem.* **1990**, *265*, 9062.
3. Skiles, J. W.; Mcneil, D. *Tetrahedron Lett.* **1990**, *31*, 7277.
4. Singh, S. B.; Cordingley, M. G.; Ball, R. G.; Smith, J. L.; Dombrowski, A. W.; Goetz, M. A. *Tetrahedron Lett.* **1991**, *39*, 5759.
5. (a) Gill, M.; Donner, C. D. *Tetrahedron Lett.* **1999**, *40*, 3921; (b) Donner, C. D.; Gill, M. *J. Chem. Soc., Perkin Trans. 1* **2002**, 938; (c) Brimble, M. A.; Elliott, R. J. R. *Tetrahedron* **2002**, *58*, 183; (d) Singh, S. B.; Graham, P. L.; Reamer, R. A.; Cordingly, M. G. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 3143.
6. Bulbule, V. J.; Koranne, P. S.; Borate, H. B.; Deshpande, V. H. *Synth. Commun.* **2003**, *33*, 587.
7. Deshpande, V. H.; Rai, B.; Khan, R. A. *Tetrahedron Lett.* **1996**, *52*, 7159.
8. Deshpande, V. H.; Khan, R. A.; Rai, B.; Ayyangar, N. R. *Synth. Commun.* **1993**, *23*, 2337.
9. Griffin, D. A.; Leeper, F. J.; Staunton, J. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1035.
10. Meyers, A. I.; Durandedatta, J. L.; Munovu, R. *J. Org. Chem.* **1975**, *40*, 2025.
11. Godfrey, I. M.; Sargent, M. V.; Elix, J. A. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1353.
12. Brokke, M. E.; Christenesen, B. E. *J. Org. Chem.* **1959**, *24*, 523.
13. Sih, C. J.; Massuda, D.; Corey, P.; Gleim, R. D.; Suzuki, F. *Tetrahedron Lett.* **1979**, 1285.
14. (a) Pettit, G. R.; Kasturi, T. R. *J. Org. Chem.* **1960**, *25*, 875; (b) Pettit, G. R.; Ghatak, U. R.; Green, B.; Kasturi, T. R.; Piatak, D. M. *J. Org. Chem.* **1961**, *26*, 1685.
15. Dean, F. M.; Goodchild, J.; Hanghton, L. E.; Martin, J. A.; Morton, R. B.; Parton, B.; Price, A. W.; Sovichien, N. *Tetrahedron Lett.* **1966**, 4153.
16. Tatsuta, K.; Yamazaki, T.; Mase, T.; Yoshimoto, T. *Tetrahedron Lett.* **1998**, *39*, 1771.
17. Zimmer, H.; Lankin, C. D.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 229.
18. Boeckman, R. K.; Cheon, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 4112.
19. Perry, J. P.; Pavlidis, V. H.; Hadfield, J. A.; Coutts, G. C. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1085.
20. Gopinathan, M. B.; Bhatt, V. M. *Indian J. Chem.* **1981**, *20B*, 71.
21. Mitchell, R. H.; Lai, Y. H.; Williams, R. V. *J. Org. Chem.* **1979**, *44*, 4733.