Asymmetric Synthesis of Anthracyclinones: Synthesis of a New Chiral AB-Synthon, (5*R*,6*R*)-6-Ethyl-5,6-dihydroxy-5,6,7,8-tetrahydro-1,4-naphthoquinone, and Its Application for a Novel Regioselective Synthesis of (−)-γ-Rhodomycinone

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A new chiral AB-synthon, (5*R*,6*R*)-6-ethyl-5,6-dihydroxy-5,6,7,8-tetrahydro-1,4-naphthoquinone (4), for the synthesis of optically active rhodomycinones was prepared stereoselectively from a (−)-α-hydroxy ketone (6). The coupling reactions of 4 with homophthalic anhydride derivatives (9, 12) proceeded in a regioselective manner to give the tetracyclic compounds 10 and 13, respectively. Compound 10 was converted to (−)-γ-rhodomycinone (3) in a two-step sequence. The optical purity (100% ee) of 3 was unambiguously determined by high performance liquid chromatography analysis using a chiral column.

Keywords asymmetric synthesis; (−)-γ-rhodomycinone; rigioselective coupling reaction; chiral AB-synthon; (5*R*, 6*R*)-6-ethyl-5,6-dihydroxy-5,6,7,8-tetrahydro-1,4-naphthoquinone; CD-synthon; homophthalic anhydride derivative

The rhodomycins were discovered early as anthracycline antibiotics.[1] Although they have been long-known and are structurally very similar to daunomycin and adriamycin, the clinically used anticancer anthracyclines, not much attention has been paid to them until quite recently because of their strong toxicity.[2] However, the recent discoveries of new rhodomycins such as betaclamycin A,[3] distrisarubin B[4] and oxaunomycin (**1**),[5] showing promising antitumor activity, have made synthetic studies of the rhodomycinones, β-rhodomycinone (**2**) and α-rhodomycinone (**3**), an attractive area of research. Although many asymmetric syntheses of anthracyclinones have been accomplished,[6] few studies on the asymmetric syntheses of rhodomycinones have been done.[7] Recently, Krohn and Hamann[8] reported the first total synthesis of optically active natural rhodomycinones.

A few years ago we succeeded in an asymmetric synthesis of (−)-7-deoxydaunomycinone, a late-stage precursor of (+)-daunomycinone, the aglycone of daunomycin.[9] Our asymmetric synthesis using nucleophilic addition to the chiral α-keto acetal has the following advantages: (i) direct asymmetric introduction of the appropriate alkyl unit at the C9 position (anthracycline numbering) and ii) the use of acetal as a chiral auxiliary which is a synthetic equivalent to the versatile carbonyl function.

Very recently, we have applied our chiral α-keto acetal method to the synthesis of (−)-γ-rhodomycinone (**3**).[10] Characteristic points of our method are the synthesis of a new chiral AB-synthon, (5*R*,6*R*)-6-ethyl-6-hydroxy-5,6,7,8-tetrahydro-1,4-naphthoquinone (**4**), by using the chiral acetal not only as the chiral auxiliary but also for the introduction of the C10 hydroxy functionality, and a novel regioselective cycloaddition of **4** to 4-acetoxyhomophthalic anhydride derivatives (**9** and **12**). Here we present a full account of this work.

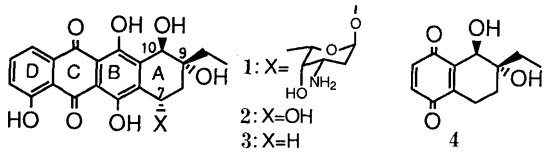


Chart 1

The chiral AB synthon **4** was synthesized as shown in Chart 2. The chiral (2*R*)-2-ethyl-2-hydroxy-5,8-dimethoxy-1-oxotetraline (**6**) was prepared from 5,8-dimethoxy-1,2-dioxotetraline 1-[(2*S*,3*S*)-1,4-dimethoxy-2,3-butylene] acetal (**5**) by alkylation and acid hydrolysis as described before by us.[11] Reduction of benzylic ketone of **6** with potassium borohydride in methanol afforded a mixture of *trans* diol **7** and *cis* diol **7a** in a ratio of 15:2, which was easily separated by column chromatography to give **7** in 82% yield. The stereochemistries of the secondary alcohols of **7** and **7a** were determined as *R* configuration for **7** and as *S* configuration for **7a**, since **7a** afforded the acetonide **8** and **7** was recovered unchanged, in the reactions with 2,2-dimethoxypropane in the presence of a catalytic amount of *p*-toluenesulfonic acid (*p*-TsOH). Oxidation of **7** with ceric ammonium nitrate (CAN) in 50% aqueous acetonitrile afforded **4**.

The coupling reaction of **4** with 4-acetoxy-5-methoxyhomophthalic anhydride (**9**)[12] was achieved as described before. The anhydride **9** was treated with sodium hydride and reacted with **4** to afford the adduct **10** in 55% yield. Treatment of **10** with 66% aqueous trifluoroacetic acid at 50—55 °C caused deacetylation and a shift of the quinone moiety to the C-ring to give **11** in 93% yield. Similarly, the

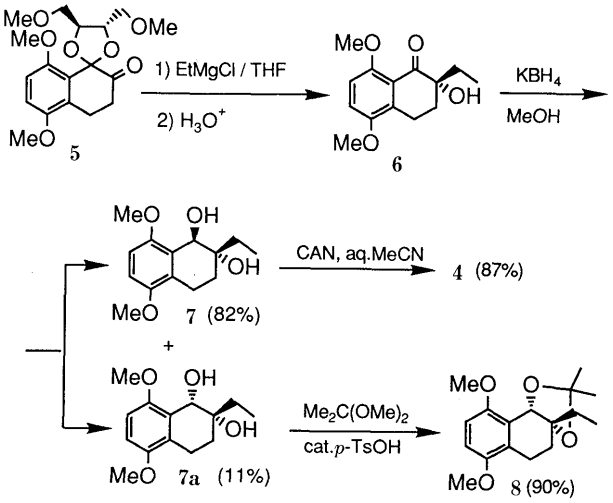


Chart 2

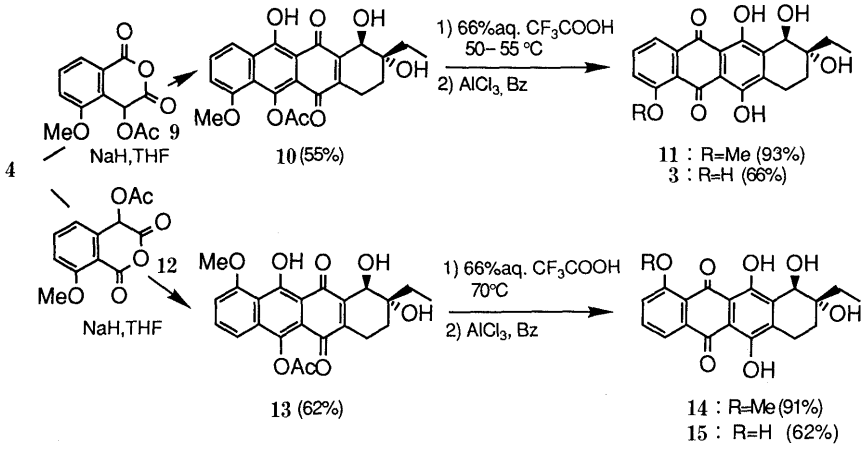
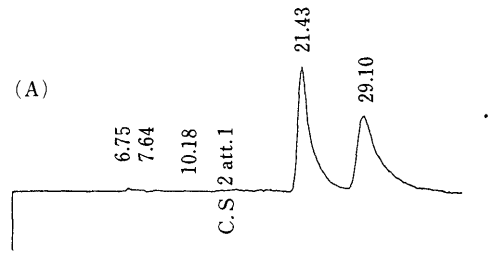


Chart 3



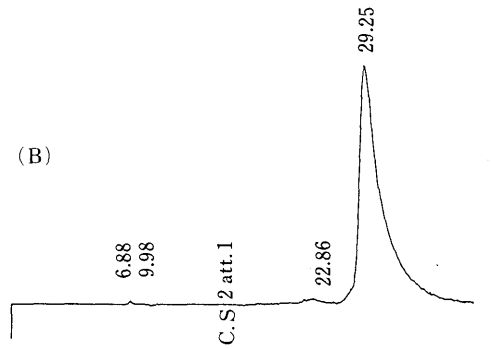


Fig. 1. HPLC Analyses of (±)- and (−)-γ-Rhodomycinone; see Experimental

A, (±)-γ-rhodomycinone; B, (−)-γ-rhodomycinone.

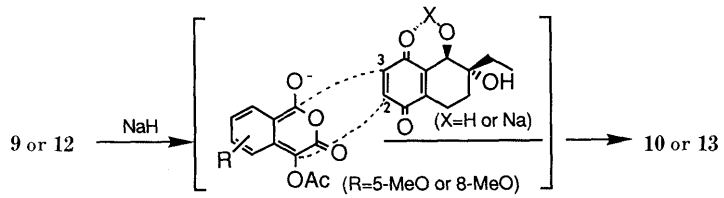


Chart 4

reaction of **4** with 4-acetoxy-8-methoxyhomophthalic anhydride (**12**)[12] afforded the adduct **13** in 62% yield, and this was converted to **14** in 91% yield. Compounds **11** and **14** were easily distinguishable by ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectroscopic analysis and thin layer chromatography (TLC). Thus, the ^{1}H-NMR signals due to two phenolic hydroxy functions were seen as two singlets at δ: 13.68 and 13.73 ppm for **11** and two singlets at δ: 13.34 and 14.09 ppm for **14**, and compounds **11** and **14** showed good separation on TLC (silica gel, $CHCl_3 : Me_2CO = 5 : 1$ or CH_2Cl_2 : ether = 1 : 3). Since crude **11** and crude **14** did not contain regioisomers of each other, it was proved that the cycloadditions of **4** to **9** and of **4** to **12** proceeded regioselectively.

The structures of **10**, **11**, **13**, and **14** were determined by conversion of **11** and **14** to (−)-γ-rhodomycinone (**3**) and 4-dehydroxy-1-hydroxy-γ-rhodomycinone (**15**), respectively. Thus, demethylation of **11** with aluminum chloride in benzene afforded (−)-γ-rhodomycinone (**3**) in 66% yield. In the same manner, **14** afforded **15** in 62% yield. The melting point (mp), ^{1}H-NMR, and infrared (IR) spectra of **3** obtained here were identical with those reported.[13] The optical rotation of **3** showed good agreement with that of the natural product[14] {$[\alpha]_D^{25} -20.7°$ ($c = 0.06$); natural $-20.2°$ ($c = 0.06$)}. The enantiomeric excess (100% ee) of **3** was determine by high performance liquid chromatography (HPLC) analysis using a chiral column (Fig. 1).

As mentioned above, the synthesis of optically pure (−)-γ-rhodomycinone was achieved through a regioselective cycloaddition reaction of a new chiral AB synthon **4** with the homophthalic anhydride (**9**). Although the strong base-induced cycloaddition of homophthalic anhydrides is known to proceed regioselectively in the reactions with haloquinone derivatives,[15] this is the first example of regiocontrolled addition to 2,3-unsubstituted naphthoquinone derivatives. This extremely high regioselectivity might be rationalized as follows. Hydrogen bonding or chelation through the X atom (X = H or Na) between the C5 oxygen atom and C4 quinoid carbonyl of **4** produced an electron-poor (δ^+) center at the C2 position and an electron-rich (δ^-) center at the C3 position, and the cycloaddition reactions proceeded as shown in Chart 4.

The discovery of a strong effect of the benzylic secondary hydroxy function of **4** upon the regioselectivity of the coupling reactions should also be very useful in the regioselective syntheses of other anthracyclinones having the C10 (anthracycline numbering) hydroxy function, such as β-rhodomycinone and feudomycinones.[16]

Experimental

The following instruments were used to obtain physical data: specific rotation, Perkin-Elmer 241 polarimeter; IR spectra, JASCO HPIR-102 spectrometer; ^{1}H-NMR spectra, Hitachi R-22 (90 MHz), JEOL JNM-FX 90Q FT-NMR (90 MHz) or JEOL LNM-GX 500 FT-NMR (500 MHz) spectrometer (with tetramethylsilane as an internal standard); low- and high-resolution mass spectra (MS), JEOL JMS D-300 mass spectrometer

(with a direct inlet system). A JASCO Trirotar-II high-pressure liquid chromatograph (ultraviolet (UV) detector) was used for HPLC analysis. E. Merck silica gel (0.063—0.200 mm, 70—230 mesh ASTM) was used for column chromatography and E. Merck TLC plates pre-coated with Silica gel $60F_{254}$ for preparative TLC (0.5 mm) and TLC detection (0.2 mm). Specific rotation was measured at 25 °C in $CHCl_3$, unless otherwise mentioned. All melting points are uncorrected.

(1*R*,2*R*)-2-Ethyl-1,2-dihydroxy-5,8-dimethoxytetralin (7) A solution of **6** (100 mg, 0.40 mmol) in MeOH (3 ml) was added dropwise to a stirred suspension of KBH_4 (86.0 mg, 1.6 mmol) in MeOH (3 ml) at −78 °C. The resulting mixture was stirred at the same temperature for 30 min and at 0 °C overnight. H_2O (10 ml) was added to the reaction mixture and MeOH was evaporated off. The mixture was acidified (*ca.* pH 1) with 10% aqueous HCl at 0 °C and then extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel using hexane–ether (1 : 2) as an eluent to give **7** (82.7 mg, 82%) and (1*S*,2*R*)-2-ethyl-1,2-dihydroxy-5,8-dimethoxytetralin (**7a**) (11.0 mg, 11%). **7**: colorless oil, $[\alpha]_D$ −42.5° (*c* = 3.14). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 2400, 1600, 1485. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (t, 3H, *J* = 7.3 Hz, $-CH_2CH_3$), 1.30—1.70 (m, 2H, $-CH_2-$), 1.75 (q, 2H, *J* = 7.3 Hz, $-CH_2CH_3$), 2.58—2.74 (m, 2H, $-CH_2-$), 3.74, 3.76 (both s, 3H each, $-OCH_3$ × 2), 4.64 (s, 1H, $-CHOH-$), 6.65 (s, 2H, aromatic protons). Exact MS Calcd for $C_{14}H_{20}O_4$: 252.1359. Found: 252.1356. **7a**: colorless oil, $[\alpha]_D$ −29.4° (*c* = 0.54). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3545, 1560, 1485. ^{1}H-NMR ($CDCl_3$) δ: 1.06 (t, 3H, *J* = 6.8 Hz, $-CH_2CH_3$), 1.40—2.06 (m, total 4H, $-CH_2-$ and $-CH_2CH_3$), 2.59—2.98 (m, 2H, $-CH_2-$), 3.77, 3.98 (both s, 3H each, $-OCH_3$ × 2), 4.67 (s, 1H, $-CHOH-$), 6.70 (s, 2H, aromatic protons). Exact MS Calcd for $C_{14}H_{20}O_4$: 252.1360. Found: 252.1345.

(5*R*,6*R*)-6-Ethyl-5,6-dihydroxy-5,6,7,8-tetrahydro-1,4-naphthoquinone (4) A solution of CAN (350 mg) in H_2O (4 ml) was added dropwise to a stirred solution of **7** (80.0 mg, 0.31 mmol) in MeCN (4 ml) at 0 °C. The resulting mixture was stirred for 1 h at the same temperature, then poured into water, and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to column chromatography on silica gel using hexane–ether (1 : 4) as an eluent to give **4** (61.0 mg, 87%). Yellow prisms (CH_2Cl_2), mp 110—112 °C. $[\alpha]_D$ −32.6° (*c* = 0.96). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 1655, 1300. ^{1}H-NMR ($CDCl_3$) δ: 0.85 (t, 3H, *J* = 7.4 Hz, $-CH_2CH_3$), 1.05—1.76 (m, total 4H, $-CH_2CH_3$ and $-CH_2-$), 2.26—2.41 (m, 2H, $-CH_2-$), 4.30 (s, 1H, $-CHOH-$), 6.02 (s, 2H, olefinic protons), 7.16 (br s, 1H, $-OH$). Exact MS Calcd for $C_{12}H_{18}O_4$: 222.0890. Found: 222.0889.

(1*S*,2*R*)-2-Ethyl-1,2-dihydroxy-1,2-isopropylidene-5,8-dimethoxytetralin (8) 2,2-Dimethoxypropane (0.25 ml) and a catalytic amount of *p*-TsOH were added to a stirred solution of **7a** (25.0 mg, 0.10 mmol) in tetrahydrofuran (THF) (0.5 ml) at room temperature. The mixture was stirred for 2 h, treated with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2 : ether = 4 : 1) to give **8** (26.0 mg, 90%). Colorless needles (CH_2Cl_2), mp 57—59 °C, $[\alpha]_D^{20}$ −81.6° (*c* = 0.62). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1600, 1485, 1260. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (t, 3H, *J* = 7.0 Hz, $-CH_2CH_3$), 1.18—2.20 (m, total 4H, $-CH_2CH_3$ and $-CH_2-$), 1.36, 1.50 (both s, 3H each, $-CH_3$ × 2), 2.60—2.82 (m, 2H, $-CH_2-$), 3.77, 3.83 (both s, 3H each, $-OCH_3$ × 2), 5.08 (s, 1H, $-CHOH-$), 6.73 (s, 2H, aromatic protons). Exact MS Calcd for 292.1672. Found: 292.1672.

(1*R*,2*R*)-6-Acetoxy-2-ethyl-1,2,11-trihydroxy-7-methoxy-1,2,3,4-tetrahydronaphthacene-5,12-dione (10) A solution of **9** (30.0 mg, 0.12 mmol) in dry THF (1 ml) was added dropwise to a stirred suspension of NaH (60% in oil, 5.70 mg) in dry THF (1 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred for 10 min, then a solution of **4** (22.0 mg, 0.10 mmol) in dry THF (2 ml) was added dropwise. The reaction mixture was stirred at 0 °C for 30 min and then the reaction was quenched with saturated aqueous NH_4Cl. The mixture was acidified (*ca.* pH = 1) with 10% aqueous HCl and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by preparative TLC ($CHCl_3$: acetone = 5 : 1) to give **10** (23.4 mg, 55%). Yellow plates (hexane–CH_2Cl_2), mp 115—117 °C, $[\alpha]_D$ −18.9° (*c* = 0.12). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600—3200, 1760, 1670, 1635, 1590. ^{1}H-NMR ($CDCl_3$) δ: 1.08 (t, 3H, *J* = 7.0 Hz, $-CH_2CH_3$), 1.78 (q, 2H, *J* = 7.0 Hz, $-CH_2CH_3$), 1.60—2.10 (m, 2H, $-CH_2-$), 2.48 (s, 3H, $-OCOCH_3$), 2.60—2.90 (m, 2H, $-CH_2-$), 4.00 (s, 3H, $-OCH_3$), 4.79 (s, 1H, $-CHOH-$), 7.30 (d, 1H, *J* = 9.7 Hz, aromatic proton), 7.68 (t, 1H, *J* = 9.7 Hz, aromatic proton), 7.90 (d, 1H, *J* = 9.7 Hz, aromatic proton), 13.54 (s, 1H, $-OH$). Exact MS Calcd for $C_{23}H_{22}O_8$: 426.1315. Found: 426.1318.

(1*R*,2*R*)-6-Acetoxy-2-ethyl-1,2,11-trihydroxy-10-methoxy-1,2,3,4-tetrahydronaphthacene-5,12-dione (13) Compound **13** (26.4 mg, 62%) was prepared from **12** (30.0 mg, 0.12 mmol), NaH (60% in oil, 12.0 mg), and **4** (22.0 mg, 0.10 mmol) in the same manner as in the case of **10**. Orange powder (CCl_4), mp 94—96 °C, $[\alpha]_D$ −12.3° (*c* = 0.11). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3690—3600, 1773, 1665, 1590, 1430. ^{1}H-NMR ($CDCl_3$) δ: 1.07 (t, 3H, *J* = 7.3 Hz, $-CH_2CH_3$), 1.20—2.10 (m, total 4H, $-CH_2CH_3$ and $-CH_2-$), 2.46 (s, 3H, $-COCH_3$), 2.60—3.10 (m, 2H, $-CH_2-$), 4.09 (s, 3H, $-OCH_3$), 4.80 (s, 1H, $-CHOH-$), 7.35 (dd, 1H, *J* = 7.5, 1.8 Hz, aromatic proton), 7.70 (t, 1H, *J* = 7.5 Hz, aromatic proton), 7.85 (dd, 1H, *J* = 7.5, 1.8 Hz, aromatic proton), 14.02 (s, 1H, $-OH$). Exact MS Calcd for $C_{23}H_{22}O_8$: 426.1315. Found: 426.1332.

(7*R*,8*R*)-8-Ethyl-6,7,8,11-tetrahydroxy-1-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (11) A solution of **10** (10.0 mg, 0.023 mmol) in CF_3COOH–H_2O (2 : 1) (2 ml) was stirred at 50—55 °C for 2 h. The resulting mixture was neutralized with 10% aqueous NaOH at 0 °C and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by preparative TLC ($CHCl_3$: acetone = 5 : 1) to give **11** (8.20 mg, 93%). Red powder (CH_2Cl_2), mp 100—102 °C, $[\alpha]_D$ +2.25° (*c* = 0.133). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3675, 3600—3300, 1610, 1595, 1445, 1285. ^{1}H-NMR ($CDCl_3$) δ: 1.09 (t, 3H, *J* = 7.3 Hz, $-CH_2CH_3$), 1.69 (q, 2H, *J* = 7.3 Hz, $-CH_2CH_3$), 1.84—1.99 (m, 2H, $-CH_2-$), 2.80—3.02 (m, 2H, $-CH_2-$), 4.09 (s, 3H, $-OCH_3$), 4.80 (s, 1H, $-CHOH-$), 7.38 (d, 1H, *J* = 7.3 Hz, aromatic proton), 7.77 (t, 1H, *J* = 7.3 Hz, aromatic proton), 8.02 (d, 1H, *J* = 7.3 Hz, aromatic proton), 13.68 (s, 1H, $-OH$), 13.73 (s, 1H, $-OH$). Exact MS Calcd for $C_{21}H_{20}O_7$: 384.1218. Found: 384.1213.

(7*R*,8*R*)-8-Ethyl-6,7,8,11-tetrahydroxy-4-methoxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (14) A solution of **13** (8.0 mg, 0.018 mmol) in CF_3COOH–H_2O (2 : 1) (2 ml) was stirred for 4 h at 70 °C. Usual work-up afforded a crude product, which was purified by preparative TLC ($CHCl_3$: acetone = 5 : 1) to give **14** (6.3 mg, 91%). Red powder (hexane–CH_2Cl_2), mp 237—239 °C, $[\alpha]_D^{15}$ −9.26° (*c* = 0.11). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3690, 3620, 1580, 1520, 1420, 1210. ^{1}H-NMR ($CDCl_3$) δ: 1.11 (t, 3H, *J* = 7.3 Hz, $-CH_2CH_3$), 1.65—1.71 (m, 2H, $-CH_2CH_3$), 1.84—2.00 (m, 2H, $-CH_2-$), 2.80—3.00 (m, 2H, $-CH_2-$), 4.09 (s, 3H, $-OCH_3$), 4.80 (s, 1H, $-CHOH-$), 7.38 (d, 1H, *J* = 8.0 Hz, aromatic proton), 7.77 (t, 1H, *J* = 8.0 Hz, aromatic proton), 8.04 (d, 1H, *J* = 8.0 Hz, aromatic proton), 13.34 (s, 1H, $-OH$), 14.09 (s, 1H, $-OH$). Exact MS Calcd for $C_{21}H_{20}O_7$: 384.1210. Found: 384.1220.

(7*R*,8*R*)-8-Ethyl-1,6,7,8,11-pentahydroxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (3) [=(−)-γ-Rhodomycinone] $AlCl_3$ (50.0 mg) was added to a stirred solution of **11** (5.0 mg, 0.013 mmol) in dry benzene (5 ml) and the resulting mixture was stirred at room temperature for 2.5 h under a nitrogen atmosphere, then the reaction was quenched with 10% aqueous NaOH. The mixture was stirred for 10 min, acidified with concentrated HCl, and extracted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by preparative TLC ($CHCl_3$: acetone = 5 : 1) to give **3** (3.20 mg, 66%). Red powder (hexane–CH_2Cl_2), mp 253—254 °C, $[\alpha]_D$ −20.7° (*c* = 0.06) [natural **3** −20.2° (*c* = 0.06)]. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3675, 3400, 1600, 1445, 1295. ^{1}H-NMR ($CDCl_3$) δ: 1.10 (t, 3H, *J* = 7.4 Hz, $-CH_2CH_3$), 1.63—2.02 (m, 2H, $-CH_2CH_3$), 1.83—1.98 (m, 2H, $-CH_2-$), 2.76—2.92(m, 2H, $-CH_2-$), 4.78 (s, 1H, $-CHOH-$), 7.34 (d, 1H, *J* = 8.3 Hz, aromatic proton), 7.73 (t, 1H, *J* = 8.3 Hz, aromatic proton), 7.91 (d, 1H, *J* = 8.3 Hz, aromatic proton), 12.25 (s, 1H, $-OH$), 12.75 (s, 1H, $-OH$), 13.83 (s, 1H, $-OH$). Exact MS Calcd for $C_{20}H_{18}O_7$: 370.1051. Found: 370.1051. HPLC analysis [Daicel chiral cel OA; eluent, hexane : EtOH : MeOH : AcOH = 170 : 20 : 10 : 1; flow rate, 0.5 ml/min; t_R, 21.43 and 29.10 min for (±)-**3** and t_R, 29.25 min for (−)-**3**].

(7*R*,8*R*)-8-Ethyl-4,6,7,8,11-pentahydroxy-7,8,9,10-tetrahydronaphthacene-5,12-dione (15) Compound **15** (3.20 mg, 62%) was prepared from **14** (5.60 mg, 0.014 mmol) in the same manner as in the case of **3**. Red powder (CH_2Cl_2), mp 231—233, $[\alpha]_D^{15}$ +8.0° (*c* = 0.10). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3690, 3600, 1600, 1440, 1290. ^{1}H-NMR ($CDCl_3$) δ: 1.10 (t, 3H, *J* = 7.4 Hz, $-CH_2CH_3$), 1.69—1.74 (m, 2H, $-CH_2CH_3$), 1.87—1.95 (m, 2H, $-CH_2-$), 2.81—3.02 (m, 2H, $-CH_2-$), 4.78 (s, 1H, $-CHOH-$), 7.31 (d, 1H, *J* = 9.4 Hz, aromatic proton), 7.72 (t, 1H, *J* = 9.4 Hz, aromatic proton), 7.88 (d, 1H, *J* = 9.4 Hz, aromatic proton), 12.21 (s, 1H, $-OH$), 13.01 (s, 1H, $-OH$), 13.51 (s, 1H, $-OH$). Exact MS Calcd for $C_{20}H_{18}O_7$: 370.1050. Found: 370.1032.

Acknowledgement We thank Prof. K. Krohn (Technischen Universitat Braunschweig) for his gift of (±)-γ-rhodomycinone and Prof. Y. Chen

(Sichuan Industrial Institute of Antibiotics) for (−)-γ-rhodomycinone.

References and Notes

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