# Syntheses, Immunosuppressive Activity, and Structure–Activity Relationships of Myriocin Analogs, 2-*epi*-Myriocin, 14-Deoxomyriocin, *Z*-14-Deoxomyriocin, and Nor-deoxomyriocins

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**Nine myriocin analogs, 2-*epi*-myriocin, 14-deoxomyriocin, *Z*-14-deoxomyriocin, and nor-deoxomyriocins, were synthesized from 2-deoxy-D-glucose *via* common intermediates used in previous myriocin and *Z*-myriocin syntheses. Immunosuppressive activities of those myriocin analogs on mouse allogeneic mixed lymphocyte reaction were examined, and *Z*-14-deoxomyriocin was found to show the most potent activity among them. The structure–activity relationships are discussed.**

**Key words** myriocin; 2-*epi*-myriocin; *Z*-14-deoxomyriocin; nor-deoxomyriocin; immunosuppressive activity; structure–activity relationship

Myriocin (**1**) was isolated as an antifungal principle from the fermentation broth of thermophilic fungi, *Myriococcus albomyces*[1] and *Mycelia sterilia*,[2] and was recently isolated as a potent immunosuppressant from the culture broth of *Isalia sinclairii*.[3] Myriocin (**1**) was reported to show almost two orders of magnitude more effective immunosuppressive activity than cyclosporin A and a myriocin derivative, 14-deoxomyriocin (**15**), has been found to show 5- to 10-fold more potent activity than **1**.[4]

During the course of our chemical transformation studies on the effective utilization of natural carbohydrate as an optically pure starting material, we have so far found versatile methods for the syntheses of aminoglycoside antibiotics, carba-sugar, and carba-nucleoside.[5] As an extension of our synthetic studies of biologically active compounds from carbohydrate, we have developed an effective method for stereoselective formation of chiral α,α-disubstituted amino acids from six-membered cyclic ketones by using a modified Darzen reaction,[6] and have synthesized a novel immunosuppressant myriocin (**1**) and its analog, *Z*-myriocin (**2**), by applying this method to isopropylidene ketone, which was derived from 2-deoxy-D-glucose (**3**).[7]

As part of our continuing synthetic studies to develop new immunosuppressants, we have synthesized new myriocin analogs from 2-deoxy-D-glucose *via* common synthetic intermediates used in previous myriocin (**1**) and *Z*-myriocin (**2**) syntheses,[7] and have examined the immunosuppressive activities of those myriocin analogs together with myriocin (**1**), *Z*-myriocin (**2**), and the known derivative 14-deoxomyriocin (**15**)[4] on the mouse allogeneic mixed lymphocyte reaction. In this paper, we present a full account of the syntheses and immunosuppressive activity of eight new myriocin analogs, 2-*epi*-myriocin (**11**), *Z*-14-deoxomyriocin (**19**), and nor-deoxomyriocins (**16**—**18**, **20**—**22**), and a known myriocin derivative, 14-deoxomyriocin (**15**). Some structure–activity relationships of myriocin have been reported.[8]

**Synthesis of 2-*epi*-Myriocin (11)** 2-*epi*-Myriocin (**11**) was synthesized *via* the azido-aldehyde (**4**) which was the common synthetic intermediate in previous myriocin (**1**) and *Z*-myriocin (**2**) syntheses from 2-deoxy-D-glucose (**3**).[7] Oxidation of the 7-aldehyde group in **4** with sodium chlorite ($NaClO_2$) and sulfamic acid ($NH_4SO_3H$) in dioxane–$H_2O$ followed by selective removal of the 1,3-*p*-methoxybenzylidene group with *p*-toluenesulfonic acid monohydrate (*p*-TsOH·$H_2O$) gave the 7,3-lactone (**5**) in 87% yield. Reduction of **5** with 10% palladium carbon in ethanol under a hydrogen atmosphere and successive benzoylation with benzoyl chloride in pyridine afforded **6** in 98% yield. The IR spectrum of **6** showed absorption bands due to lactone carbonyl (1781 $cm^{-1}$), ester carbonyl (1719 $cm^{-1}$), and amide groups (1653 $cm^{-1}$). The $^1$H-NMR of **6** showed the signals attributable to ten aromatic protons [$\delta$ 7.39—8.06 (10H, m, benzoyl × 2)] and methylene protons on carbon bearing a benzoyl group [$\delta$ 4.44—4.61 (2H, m, 1-$H_2$)], which were shifted to lower field than those ($\delta$ 3.82) of **5**. Deprotection of the benzoyl group at the C-1 position of **6** with 1% sodium methoxide in methanol followed by oxidation with pyridinium chlorochromate (PCC) in dichloromethane ($CH_2Cl_2$) afforded the lactone aldehyde (**7**) in 86% yield. The IR spectrum of **7** showed absorption bands due to lactone carbonyl (1781 $cm^{-1}$), formyl (1723 $cm^{-1}$), and amide groups (1657 $cm^{-1}$). In the FAB-MS of **7**, the quasi-molecular ion peak was observed at *m/z* 334 $(M+H)^+$, and the $^1$H-NMR of **7** showed the signal due to a formyl group at $\delta$ 9.81 (1H, br s). Treatment of **7** with the phosphonium salt (**8**), which was prepared by a literature procedure,[9] in the presence of *n*-BuLi in *tert*-BuOH–THF afforded the condensation product (**9**) (a geometric mixture of *E*-(**9a**) and *Z*-(**9b**) isomers in a *ca.* 1:6 ratio, 97%).[10] The geometric mixture **9** was partly purified by HPLC [column: chromatorex-octadecyl silica (ODS), methanol–$H_2O$ (9:1)] to furnish **9a** and **9b**. In the $^1$H-NMR spectra of **9a** and **9b**, the coupling constants ($J_{(6,7)}$) of olefinic protons were $J$ = 15.2 and 10.9 Hz, which indicated *Z*- and *E*-form structures of **9a** and **9b**, respectively. The photochemical isomerization[11] of the geometric mixture (**9**) with a high-pressure mercury lamp (300 W) in the presence of diphenyl disulfide by using a Pyrex vessel occurred with deprotection of the 2,2-

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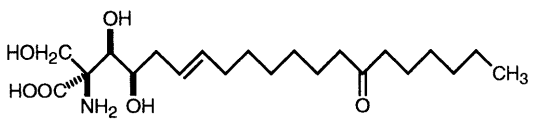
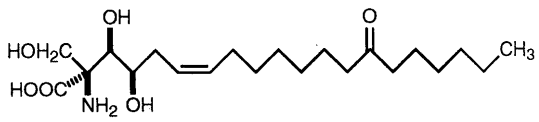
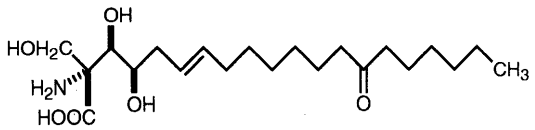


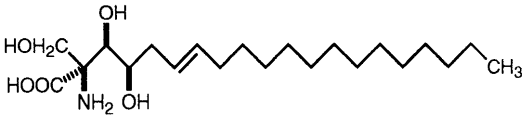
myriocin (**1**)



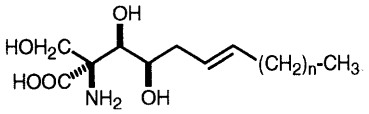
Z-myriocin (**2**)



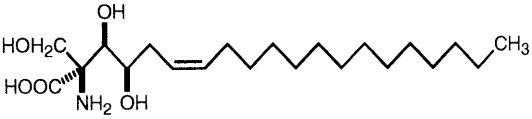
2-*epi*-myriocin (**11**)



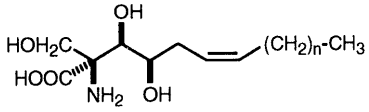
14-deoxomyriocin (**15**)



nor-deoxomyriocin
**16**: n=9 **17**: n=6 **18**: n=3



Z-14-deoxomyriocin (**19**)



nor-Z-deoxomyriocin
**20**: n=9 **21**: n=6 **22**: n=3

Chart 1

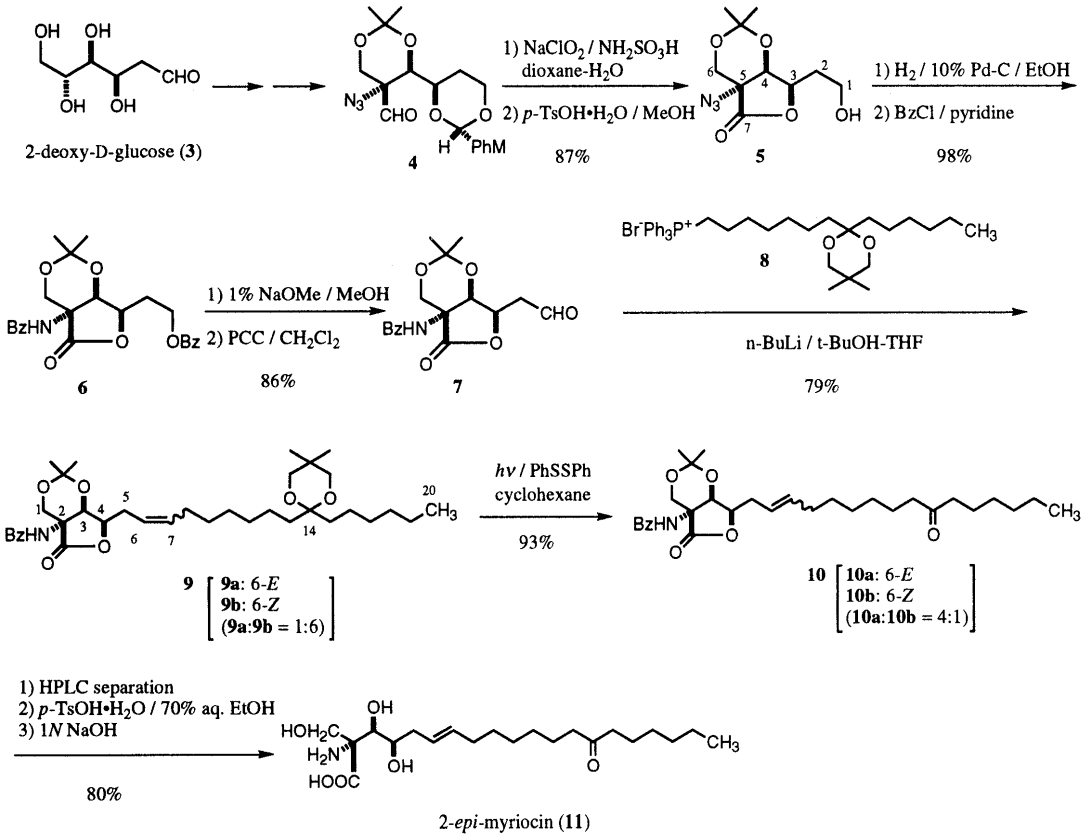



Chart 2

dimethyl-1,3-dioxane group at the 14 position to provide a geometric mixture (**10**) (*E*-(**10a**) and *Z*-(**10b**) isomers in a *ca.* 4 : 1 ratio), which was separated by using HPLC to furnish **10a** and **10b** in 71% and 16% yields, respectively. Treatment of **10a** with *p*-TsOH·$H_2O$ in 70% aqueous ethanol to remove the isopropylidene group, and sub-

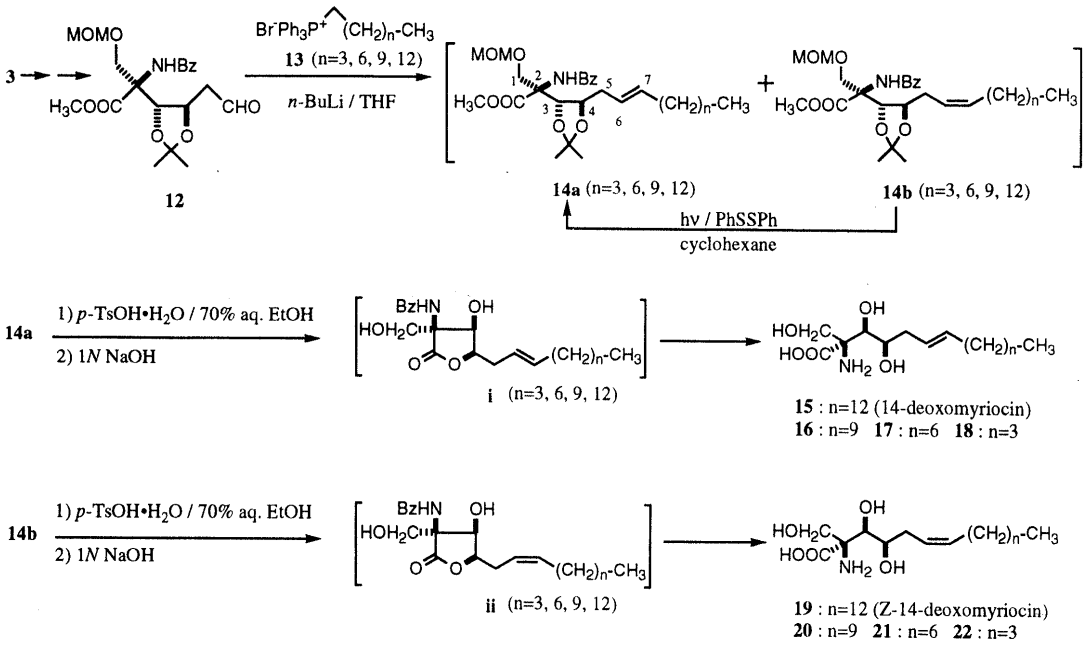



Chart 3

sequent debenzoylation and cleavage of the lactone ring with 1 N sodium hydroxide (NaOH) afforded 2-*epi*-myriocin (**11**) in 11.0% overall yield from 2-deoxy-D-glucose (**3**). 2-*epi*-Myriocin (**11**) was obtained as colorless fine crystals of mp 182—184 °C and the molecular formula of **11** was identical with that of myriocin (**1**). The spectroscopic data of **11** were similar to those of **1** and showed the presence of the same functional groups as those of **1**. However, in the $^1$H-NMR spectrum of **11**, signals due to 1-$H_2$ ($\delta$ 3.78, 3.91) and 3-H ($\delta$ 4.00) were observed at different chemical shifts from those (1-$H_2$: $\delta$ 3.83, 3.97; 3-H: $\delta$ 3.76) of **1**. Based on those findings and the above-mentioned synthetic evidence, the structure of 2-*epi*-myriocin (**11**) was characterized.

**Syntheses of 14-Deoxomyriocins (15, 19) and Nor-deoxomyriocins (16—18, 20—22)** 14-Deoxomyriocin (**15**), *Z*-14-deoxomyriocin (**19**), and nor-deoxomyriocins (**16—18, 20—22**) were synthesized *via* the $\alpha,\alpha$-disubstituted amino acid derivative (**12**), which was also the synthetic intermediate of myriocin (**1**) and *Z*-myriocin (**2**).[7] Namely, treatment of **12** with the phosphonium salt (**13**, $n=12$) in the presence of *n*-BuLi in *tert*-BuOH–THF afforded a geometric mixture (**14**, $n=12$) (*E*-(**14a**) and *Z*-(**14b**) isomers in a *ca.* 1 : 7 ratio), which was subjected to HPLC separation to yield **14a** ($n=12$) and **14b** ($n=12$) in 10.7% and 74.9% yields, respectively. Treatment of **14b** ($n=12$) with *p*-TsOH·$H_2O$ in 70% aqueous ethanol afforded the lactone (ii, $n=12$) in 77.4% yield, and this was subjected to deprotection and cleavage of the lactone ring with 1 N NaOH to furnish *Z*-14-deoxomyriocin (**19**) in 60.1% yield. On the other hand, the photochemical isomerization of the geometric mixture **14** and subsequent HPLC separation gave the *E*-isomer (**14a**, 84.8%) as a major product and the *Z*-isomer (**14b**, 8.4%). Treatment of **14a** with *p*-TsOH·$H_2O$ in 70% aqueous ethanol afforded the lactone (i, $n=12$) in 58.3% yield, and this was subjected to treatment with 1 N NaOH to furnish 14-deoxomyriocin (**15**) in 74.2% yield. Similarly, nor-deoxomyriocins (6*E*-form: **16—18**; 6*Z*-form: **20—22**) were synthesized from **12** and the phosphonium salts (**13**, $n=9, 6, 3$) *via* the lactones (i, ii, $n=9, 6, 3$).

Table 1. Suppressive Effects of Myriocin (**1**) and Its Analogs (**2**, **11**, **15—22**) on Mouse Allogeneic Mixed Lymphocyte Reaction

| Compound | $IC_{50}$ ($\mu$M) |
|---|---|
| Myriocin (**1**) | 0.00929 |
| *Z*-Myriocin (**2**) | 0.00323 |
| 2-*epi*-Myriocin (**11**) | 0.00939 |
| 14-Deoxomyriocin (**15**) | 0.000662 |
| *Z*-14-Deoxomyriocin (**19**) | 0.000457 |
| *E*-Trinor-deoxoxmyriocin (**16**) | 0.00592 |
| *E*-Hexanor-deoxomyriocin (**17**) | 4.38 |
| *E*-Nonanor-deoxomyriocin (**18**) | 57.85 |
| *Z*-Trinor-deoxomyriocin (**20**) | 0.00907 |
| *Z*-Hexanor-deoxomyriocin (**21**) | 10.18 |
| *Z*-Nonanor-deoxomyriocin (**22**) | 238.18 |

## Biological Results and Discussion

Synthetic myriocin analogs (**11**, **16—22**) and *Z*-myriocin (**2**) were evaluated for immunosuppressive activity on the mouse allogeneic mixed lymphocyte reaction (MLR) in comparison with myriocin (**1**)[4] and 14-deoxomyriocin (**15**). Their $IC_{50}$ values ($\mu$M) are recorded in Table 1. *Z*-14-Deoxomyriocin (**19**) showed the most potent suppressive activity on mouse allogeneic MLR, as reported,[4] and the following relationships between structure and immunosuppressive activity were found.

1) The stereostructure at the 2-position of the amino acid moiety in myriocin (**1**) does not affect the activity, since 2-*epi*-myriocin (**11**) shows almost as potent immunosuppressive activity as **1**.

2) Trinor-deoxomyriocins (**16, 20**) exhibit potent activity, like myriocin (**1**) and *Z*-myriocin (**2**), but their activities were less than those of 14-deoxomyriocin (**15**) and *Z*-14-deoxomyriocin (**19**), respectively, while hexanor

and nonanor-deoxomyriocins (**17**, **18**, **21**, **22**) show little activity. Based on those findings, a long carbon chain ($n>9$) bonded to the amino acid moiety is essential to the activity.

3) When the activities of myriocin analogs with twenty carbon chains were compared, 6*Z*-isomers showed more potent activity than 6*E*-ones.

4) The 6*E*-nor-deoxomyriocins (**16**—**18**) were more active than the corresponding 6*Z*-nor-deoxomyriocins (**20**—**22**).

Thus, by comparing the immunosuppressive activities of nine myriocin analogs synthesized from 2-deoxy-D-glucose with those of myriocins (**1**, **2**), some interesting structure–activity relationships have been found. In our synthetic pathway, various epimeric myriocin analogs including α,α-disubstituted amino acid moiety can be prepared by using different sugars as starting materials. We are currently exploring this approach for the synthesis of myriocin analogs in order to characterize further the structure–activity relationships.

## Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and recorded as read. The optical rotations were measured with a Horiba high-sensitivity SEPA-300 digital polarimeter in a 0.5 dm path-length cell. The low- and high-resolution FAB-MS were taken on a JEOL JMS-SX 102 spectrometer. The IR spectra were obtained by using a Shimadzu FT-IR DR-8000 or JASCO IR-810 spectrometer. The $^1$H-NMR spectra were measured with a JEOL EX-270 (270 MHz) spectrometer with $(CH_3)_4Si$ as the internal standard. For HPLC, a Shimadzu LC-10A HPLC system was used. The following experimental conditions were used for chromatography: column chromatography, silica gel BW-200 (Fuji-Davidson Chemical); analytical and preparative thin-layer chromatography (TLC), precoated Silica gel 60 $F_{254}$ plates (Merck, 0.25 and 0.5 mm layer thickness).

**Conversion from 4 to 5** A solution of **4**[7] (20 mg, 0.053 mmol) in dioxane–$H_2O$ (3 : 1, 1 ml) was treated with sodium chlorite (16 mg, 0.21 mmol) and sulfamic acid (9 mg, 0.11 mmol) in an ice-cooling bath and the reaction mixture was stirred at room temperature (25 °C) for 10 min. The reaction mixture was poured into brine and the whole was extracted with $CH_2Cl_2$. The $CH_2Cl_2$ extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product (20 mg, quant.). A solution of the product (485 mg, 1.24 mmol) in MeOH (4 ml) was treated with *p*-TsOH·$H_2O$ (20 mg) and stirred at room temperature (25 °C) for 10 min. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and the whole was extracted with AcOEt. The AcOEt extract was washed with brine and then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 16 g, *n*-hexane–AcOEt (3 : 2)] to furnish **5** (276 mg, 87%).

**5**: A colorless oil, $[\alpha]_D^{24}$ +84.0° ($c=1.35$, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{10}H_{16}N_3O_5$ $(M+H)^+$: 258.1080. Found: 258.1068. IR (film): 3453, 2112, 1781, 1381, 1200 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) δ: 1.38, 1.47 (3H each, both s, isopropylidene), 1.95 (1H, dddd, $J=3.0$, 5.3, 6.3, 11.5 Hz, 2-H), 2.13 (1H, dddd, $J=3.0$, 5.6, 6.3, 11.5 Hz, 2-H), 3.82 (2H, dd, $J=5.3$, 5.6 Hz, 1-$H_2$), 4.06, 4.28 (2H, ABq, $J=11.9$ Hz, 6-$H_2$), 4.12 (1H, d, $J=3.0$ Hz, 4-H), 4.85 (1H, ddd, $J=3.0$, 5.3, 6.3 Hz, 3-H). Positive FAB-MS *m/z* (%): 258 [$(M+H)^+$, 100].

**Hydrogenation of 5 Followed by Benzoylation** A solution of **5** (240 mg, 0.93 mmol) in EtOH (12 ml) was hydrogenated in the presence of 10% Pd–C (60 mg) at room temperature (25 °C) for 4 h. The catalyst was filtered off, and the solvent of the filtrate was evaporated under reduced pressure to give a product (215 mg, quant.). A solution of the product (200 mg, 0.87 mmol) in pyridine (3 ml) was treated with benzoyl chloride (0.40 ml, 1.74 mmol) and the mixture was stirred at room temperature (25 °C) for 10 min. It was poured into ice-water and the whole was extracted with AcOEt. The AcOEt extract was successively washed with 5% aqueous HCl, saturated aqueous $NaHCO_3$ and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by column chromatography [$SiO_2$ 20 g, *n*-hexane–AcOEt (3 : 1→2 : 1)] to furnish **6** (375 mg, 98%).

**6**: A colorless oil, $[\alpha]_D^{24}$ +90.6° ($c=0.65$, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{24}H_{26}NO_7$ $(M+H)^+$: 440.1709. Found: 440.1707. IR (film): 1781, 1719, 1653, 1603, 1277, 712 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) δ: 1.39, 1.47 (3H each, both s, isopropylidene), 2.25—2.42 (2H, m, 2-$H_2$), 4.03 (2H, s, 6-$H_2$), 4.44—4.61 (2H, m, 1-$H_2$), 4.74 (1H, d, $J=5.0$ Hz, 4-H), 5.26 (1H, ddd, $J=5.0$, 5.9, 8.3 Hz, 3-H), 6.83 (1H, br s, NHBz), 7.39—8.06 (10H, m, Bz × 2). Positive FAB-MS *m/z* (%): 440 [$(M+H)^+$, 19], 382 (100).

**Conversion from 6 to 7** A solution of **6** (353 mg, 0.80 mmol) in 1% NaOMe–MeOH (3 ml) was stirred at room temperature (25 °C) for 2 h. The reaction mixture was neutralized with Dowex HCR-W2 and the resin was filtered off. Removal of the solvent from the filtrate under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 9 g, *n*-hexane–AcOEt (1 : 1)] to furnish the alcohol (257 mg, 95%). A solution of the alcohol (57 mg, 0.17 mmol) in $CH_2Cl_2$ (5 ml) was treated with pyridinium chlorochromate (110 mg, 0.51 mmol) and Molecular sieves-3A (powder, 170 mg), and the mixture was stirred at room temperature (25 °C) for 30 min. After removal of the desiccant from the reaction mixture by filtration, the filtrate was poured into saturated aqueous $NaHCO_3$ and the whole was extracted with AcOEt. The AcOEt extract was washed with saturated aqueous $NaHCO_3$, and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 3 g, *n*-hexane–AcOEt (3 : 2)] to furnish **7** (52 mg, 91%).

**7**: A colorless oil, $[\alpha]_D^{24}$ +57.6° ($c=0.21$, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{17}H_{20}NO_6$ $(M+H)^+$: 334.1290. Found: 334.1294. IR (film): 1781, 1723, 1657, 1534, 1225 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) δ: 1.37, 1.44 (3H each, both s, isopropylidene), 3.04—3.09 (2H, m, 2-$H_2$), 3.96, 4.01 (2H, ABq, $J=12.2$ Hz, 6-$H_2$), 4.71 (1H, d, $J=5.3$ Hz, 4-H), 5.55 (1H, ddd, $J=5.3$, 6.6, 6.9 Hz, 3-H), 6.80 (1H, br s, NHBz), 7.44—7.83 (5H, m, Bz), 9.81 (1H, br s, CHO). Positive FAB-MS *m/z* (%): 334 [$(M+H)^+$, 28], 276 (100).

**Wittig Reaction of 7** *n*-Butyl lithium (1.6 M solution in *n*-hexane, 0.51 ml, 0.81 mmol) was added to a stirred solution of phosphonium salt[9] (**8**, 524 mg, 0.81 mmol) in THF (0.85 ml). The reaction mixture was stirred at room temperature (25 °C) for 10 min, then cooled to −78 °C. A solution of **7** (87 mg, 0.27 mmol) in THF (1.05 ml) was added and the whole was stirred at −78 °C for 10 min. *tert*-BuOH (0.12 ml, 1.22 mmol) was added, and the reaction mixture was warmed to room temperature, then stirred for 20 min. It was poured into saturated aqueous $NH_4Cl$ and the whole was extracted with AcOEt. The AcOEt extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 14 g, $CH_2Cl_2$–*n*-hexane–AcOEt (2 : 3 : 1)] to yield **9** [a mixture of **9a** and **9b** (1 : 6), 127 mg, 79%]. The geometric mixture **9** was partly purified by HPLC [column: Chromatorex-ODS, MeOH–$H_2O$ (9 : 1)] to furnish **9a** and **9b**.

**9a**: A colorless oil, $^1$H-NMR ($CDCl_3$) δ: 0.88 (3H, t, $J=7.0$ Hz, 20-$H_3$), 0.95 (6H, s, $C(CH_3)_2$ in dioxane ring), 1.20—1.73 (20H, $CH_2$ × 10), 1.41, 1.51 (3H each, both s, isopropylidene), 1.92—2.10 (2H, m, 8-$H_2$), 2.55 (2H, dd, $J=7.3$, 7.3 Hz, 5-$H_2$), 3.47 (4H, s, $CH_2$ × 2 in dioxane ring), 4.02 (2H, s, 1-$H_2$), 4.66 (1H, d, $J=4.3$ Hz, 3-H), 4.99 (1H, ddd, $J=4.3$, 7.3, 7.3 Hz, 4-H), 5.40 (1H, dt, $J=7.3$, 15.2 Hz, 6-H), 5.60 (1H, dt, $J=7.3$, 15.2 Hz, 7-H), 6.67 (1H, br s, NHBz), 7.43—7.80 (5H, m, Bz).

**9b**: A colorless oil, $[\alpha]_D^{24}$ +50.4° ($c=0.50$, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{36}H_{56}NO_7$ $(M+H)^+$: 614.4057. Found: 614.4045. IR (film): 1781, 1663, 1603, 1534, 1206, 1102 cm$^{-1}$. $^1$H-NMR ($CDCl_3$) δ: 0.89 (3H, t, $J=6.9$ Hz, 20-$H_3$), 0.94, 0.95 (3H each, both s, $C(CH_3)_2$ in dioxane ring), 1.25—1.72 (20H, $CH_2$ × 10), 1.41, 1.52 (3H each, both s, isopropylidene), 2.00—2.15 (2H, m, 8-$H_2$), 2.63 (2H, dd, $J=7.3$, 7.3 Hz, 5-$H_2$), 3.47 (4H, s, $CH_2$ × 2 in dioxane ring), 4.04 (2H, s, 1-$H_2$), 4.69 (1H, d, $J=4.3$ Hz, 3-H), 4.96 (1H, ddd, $J=4.3$, 7.3, 7.3 Hz, 4-H), 5.35 (1H, dt, $J=7.3$, 10.9 Hz, 6-H), 5.56 (1H, dt, $J=7.3$, 10.9 Hz, 7-H), 6.68 (1H, br s, NHBz), 7.43—7.80 (5H, m, Bz). Positive FAB-MS *m/z* (%): 614 [$(M+H)^+$, 11], 470 (100).

**Photoisomerization of 9** A cyclohexane solution (5 ml) of the geometric mixture **9** (27 mg, 0.046 mmol) and diphenyl disulfide (20 mg, 0.092 mmol) was irradiated with a 300 W high-pressure mercury lamp at room temperature (25 °C) for 15 h in a Pyrex vessel. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and the whole was extracted with AcOEt. The AcOEt extract was washed with brine and then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 1.5 g,

$CH_2Cl_2$–*n*-hexane–AcOEt (3:4:1)] to yield **10** [a mixture of **10a** and **10b** (4:1), 23 mg]. The geometric mixture **10** was purified by HPLC [column: Chromatorex-ODS, MeOH–$H_2O$ (17:3)] to furnish **10a** (17 mg, 71%) and **10b** (4 mg, 16%).

**10a**: A colorless oil, $[\alpha]_D^{24}$ +55.5° ($c$=0.60, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{31}H_{46}NO_6$ $(M+H)^+$: 528.3325. Found: 528.3342. IR (film): 1782, 1711, 1665, 1603, 1533, 1204 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.9 Hz, 20-$H_3$), 1.20—1.62 (16H, $CH_2$ ×8), 1.41, 1.51 (3H each, both s, isopropylidene), 1.93—2.02 (2H, m, 8-$H_2$), 2.37 (4H, t-like, 13, 15-$H_2$), 2.50—2.62 (2H, dd, $J$=7.3, 7.3 Hz, 5-$H_2$), 4.03 (2H, s, 1-$H_2$), 4.67 (1H, d, $J$=4.6 Hz, 3-H), 4.98 (1H, ddd, $J$=4.6, 7.3, 7.3 Hz, 4-H), 5.40 (1H, dt, $J$=6.9, 15.2 Hz, 6-H), 5.58 (1H, dt, $J$=6.6, 15.2 Hz, 7-H), 6.76 (1H, br s, NHBz), 7.42—7.81 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 528 $[(M+H)^+$, 22], 470 (100).

**10b**: A colorless oil, $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.9 Hz, 20-$H_3$), 1.21—1.62 (16H, $CH_2$ ×8), 1.41, 1.52 (3H each, both s, isopropylidene), 1.98—2.17 (2H, m, 8-$H_2$), 2.38 (4H, t-like, 13, 15-$H_2$), 2.62 (2H, dd, $J$=7.3 7.3 Hz, 5-$H_2$), 4.04 (2H, s, 1-$H_2$), 4.69 (1H, d, $J$=4.3 Hz, 3-H), 4.96 (1H, ddd, $J$=4.3, 7.3, 7.3 Hz, 4-H), 5.36 (1H, dt, $J$=7.3, 10.9 Hz, 6-H), 5.51 (1H, dt, $J$=7.3, 10.9 Hz, 7-H), 6.70 (1H, br s, NHBz), 7.43—7.82 (5H, m, Bz).

**Conversion of 10a to 2-*epi*-Myriocin (11)** A solution of **10a** (12 mg, 0.023 mmol) in 70% aqueous EtOH (1.5 ml) was treated with *p*-TsOH·$H_2O$ (38 mg) and the mixture was heated under reflux for 30 min. It was neutralized with Amberlite IRA-93ZU and the resin was filtered off. Removal of the solvent from the filtrate under reduced pressure gave a product (11 mg, quant.). A solution of the product (9 mg, 0.018 mmol) in 1 N NaOH (1.5 ml) was heated under reflux for 2 h. The reaction mixture was neutralized with Amberlite IRC-76 and the resin was filtered off. Removal of the solvent from the filtrate under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 2 g, $CH_2Cl_2$–MeOH–$H_2O$ (10:3:1, lower phase)] to furnish 2-*epi*-myriocin (**11**, 6 mg, 81%). 2-*epi*-Myriocin (**11**): Colorless fine crystals, mp 182—184 °C, $[\alpha]_D^{24}$ +107° ($c$=0.04, MeOH). High-resolution FAB-MS: Calcd for $C_{21}H_{40}NO_6$ $(M+H)^+$: 402.2856. Found: 402.2830. IR (KBr): 3197, 1711, 1671, 1032, 972 $cm^{-1}$. $^1$H-NMR ($CD_3OD$) $\delta$: 0.90 (3H, t, $J$=6.6 Hz, 20-$H_3$), 1.22—1.59 (16H, $CH_2$ ×8), 1.98—2.10 (2H, m, 8-$H_2$), 2.29 (2H, dd, $J$=6.9, 6.9 Hz, 5-$H_2$), 2.44 (4H, t-like, 13, 15-$H_2$), 3.78, 3.91 (2H, ABq, $J$=11.2 Hz, 1-$H_2$), 3.80 (1H, t, $J$=6.9 Hz, 4-H), 4.00 (1H, s, 3-H), 5.40 (1H, dt, $J$=6.9, 16.1 Hz, 6-H), 5.54 (1H, dt, $J$=6.9, 16.1 Hz, 7-H). Positive FAB-MS $m/z$ (%): 402 $[(M+H)^+$, 29], 154 (100).

**General Method for the Preparation of 14** **14** ($n$=12): *n*-Butyl lithium (1.6 M solution in *n*-hexane, 0.69 ml, 1.11 mM) was added to a stirred solution of phosphonium salt (**13**, $n$=12, 598 mg, 1.11 mmol) in THF (6 ml). The reaction mixture was stirred at room temperature (25 °C) for 10 min, then was cooled to −78 °C. A solution of **12** (150 mg, 0.37 mmol) in THF (4 ml) was added and the whole was stirred at −78 °C for 10 min. It was warmed to room temperature, stirred for 10 min, and poured into saturated aqueous $NH_4Cl$. The whole was extracted with AcOEt. The AcOEt extract was washed with brine and then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 10 g, $CHCl_3$–AcOEt (20:1)] to yield **14** ($n$=12) [a mixture of **14a** and **14b** (1:7), 195.6 mg]. The geometric mixture **14** was purified by HPLC [column: YMC Pack R & D, $CH_3CN$–$H_2O$ (49:1)] to furnish **14a** (10.7%) and **14b** (74.9%).

**14a** ($n$=12): A white powder, $[\alpha]_D^{28}$ +25.3° ($c$=0.94, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{34}H_{56}NO_7$: 590.4057. Found: 590.4033. IR (KBr): 1750, 1671, 1509, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.9 Hz, 20-$H_3$), 1.25 (22H, $CH_2$ ×11), 1.35, 1.39 (3H each, both s, isopropylidene), 2.02 (2H, m, 8-$H_2$), 2.32, 2.38 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.46 (2H, ABq, $J$=9.9 Hz, 1-$H_2$), 4.33 (1H, m, 4-H), 4.54 (1H, d, $J$=7.9 Hz, 3-H), 4.59, 4.62 (2H, d, $J$=8.6, OMOM), 5.52 (2H, m, 6,7-H), 7.20 (1H, br s, NHBz), 7.41—7.83 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 590 $[(M+H)^+$, 8.9].

**14b** ($n$=12): A white powder, $[\alpha]_D^{28}$ +29.1° ($c$=1.1, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{34}H_{56}NO_7$ $(M+H)^+$: 590.4057. Found: 590.4034. IR (KBr): 1752, 1671, 1516, 1487, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.6 Hz, 20-$H_3$), 1.26 (22H, $CH_2$ ×11), 1.39, 1.63 (3H each, both s, isopropylidene), 2.04 (2H, m, 8-$H_2$), 2.41 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.48 (2H, ABq, $J$=9.6 Hz, 1-$H_2$), 4.35 (1H, m, 4-H), 4.56 (1H, d, $J$=7.6 Hz, 3-H), 4.59 (2H, d, $J$=8.6 Hz, OMOM), 5.52 (2H, m, 6,7-H), 7.21 (1H, br s, NHBz), 7.41—7.84 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 590 $[(M+H)^+$, 4.5].

**14a** and **14b** ($n$=9, 6, 3) were prepared by the same procedure from the phosphonium salts **13** ($n$=9, 6, 3).

**14a** ($n$=9, 8.8%): A white powder, $[\alpha]_D^{28}$ +27.6° ($c$=1.6, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{31}H_{50}NO_7$ $(M+H)^+$: 548.3587. Found: 548.3597. IR (KBr): 1750, 1671, 1516, 1487, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.9 Hz, 17-$H_3$), 1.26 (16H, $CH_2$ ×8), 1.35, 1.38 (3H each, both s, isopropylidene), 2.01 (2H, m, 8-$H_2$), 2.31, 2.38 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.46 (2H, ABq, $J$=9.6 Hz, 1-$H_2$), 4.33 (1H, m, 4-H), 4.53 (1H, d, $J$=7.6 Hz, 3-H), 4.59, 4.62 (1H each, both d, $J$=8.6 Hz, OMOM), 5.54 (2H, m, 6, 7-H), 7.20 (1H, br s, NHBz), 7.41—7.83 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 548 $[(M+H)^+$, 23.1].

**14b** ($n$=9, 66.5%): A white powder, $[\alpha]_D^{28}$ +54.9° ($c$=1.1, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{31}H_{50}NO_7$ $(M+H)^+$: 548.3587. Found: 548.3572. IR (KBr): 1752, 1670, 1518, 1487, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.9 Hz, 17-$H_3$), 1.26 (16H, $CH_2$ ×8), 1.35, 1.39 (3H each, both s, isopropylidene), 2.05 (2H, m, 8-$H_2$), 2.41 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.48 (2H, ABq, $J$=9.6 Hz, 1-$H_2$), 4.35 (1H, m, 4-H), 4.57 (1H, d, $J$=7.6 Hz, 3-H), 4.59, 4.61 (1H each, both d, $J$=8.6 Hz, OMOM), 5.54 (2H, m, 6, 7-H), 7.21 (1H, br s, NHBz), 7.41—7.90 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 548 $[(M+H)^+$, 7.9].

**14a** ($n$=6, 6.4%): A white powder, $[\alpha]_D^{28}$ +35.2° ($c$=0.72, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{28}H_{44}NO_7$ $(M+H)^+$: 506.3117. Found: 506.3131. IR (KBr): 1750, 1671, 1526, 1487, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.9 Hz, 14-$H_3$), 1.26 (10H, $CH_2$ ×5), 1.35, 1.38 (3H each, both s, isopropylidene), 2.02 (2H, m, 8-$H_2$), 2.31, 2.38 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.46 (2H, ABq, $J$=9.6 Hz, 1-$H_2$), 4.32 (1H, m, 4-H), 4.54 (1H, d, $J$=7.6 Hz, 3-H), 4.59, 4.61 (1H each, both d, $J$=8.3 Hz, OMOM), 5.53 (2H, m, 6, 7-H), 7.20 (1H, br s, NHBz), 7.42—7.83 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 506 $[(M+H)^+$, 4.5].

**14b** ($n$=6, 61.5%): A white powder, $[\alpha]_D^{28}$ +34.6° ($c$=1.0, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{28}H_{44}NO_7$ $(M+H)^+$: 506.3117. Found: 506.3125. IR (KBr): 1750, 1669, 1517, 1487, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.9 Hz, 14-$H_3$), 1.27 (10H, $CH_2$ ×5), 1.35, 1.39 (3H each, both s, isopropylidene), 2.05 (2H, m, 8-$H_2$), 2.39 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.48 (2H, ABq, $J$=9.6 Hz, 1-$H_2$), 4.34 (1H, m, 4-H), 4.57 (1H, d, $J$=7.6 Hz, 3-H), 4.59, 4.61 (1H each, both d, $J$=8.6 Hz, OMOM), 5.52 (2H, m, 6, 7-H), 7.22 (1H, br s, NHBz), 7.41—7.83 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 506 $[(M+H)^+$, 29.9].

**14a** ($n$=3, 9.4%): A white powder, $[\alpha]_D^{28}$ +17.7° ($c$=2.3, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{25}H_{38}NO_7$ $(M+H)^+$: 464.2648. Found: 464.2627. IR (KBr): 1750, 1669, 1516, 1487, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.89 (3H, t, $J$=6.6 Hz, 11-$H_3$), 1.35 (4H, $CH_2$ ×2), 1.35, 1.38 (3H each, both s, isopropylidene), 2.04 (2H, m, 8-$H_2$), 2.32, 2.38 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.46 (2H, ABq, $J$=9.6 Hz, 1-$H_2$), 4.33 (1H, m, 4-H), 4.54 (1H, d, $J$=7.6 Hz, 3-H), 4.61 (2H, br s, OMOM), 5.53 (2H, m, 6, 7-H), 7.20 (1H, br s, NHBz), 7.44—7.83 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 464 $[(M+H)^+$, 51.3].

**14b** ($n$=3, 67.3%): A white powder, $[\alpha]_D^{27}$ +73.5° ($c$=1.1, $CHCl_3$). High-resolution FAB-MS: Calcd for $C_{25}H_{38}NO_7$ $(M+H)^+$: 464.2648. Found: 464.2641. IR (KBr): 1750, 1669, 1520, 1487, 1244, 1046 $cm^{-1}$. $^1$H-NMR ($CDCl_3$) $\delta$: 0.90 (3H, t, $J$=6.9 Hz, 11-$H_3$), 1.35 (4H, $CH_2$ ×2), 1.35, 1.39 (3H each, both s, isopropylidene), 2.07 (2H, m, 8-$H_2$), 2.41 (2H, m, 5-$H_2$), 3.29 (3H, s, OMOM), 3.84 (3H, s, $COOCH_3$), 4.05, 4.48 (2H, ABq, $J$=9.9 Hz, 1-$H_2$), 5.54 (2H, m, 6, 7-H), 7.22 (2H, br s, NHBz), 7.42—7.84 (5H, m, Bz). Positive FAB-MS $m/z$ (%): 464 $[(M+H)^+$, 35.5].

**General Method for the Preparation of 19—22** *Z*-14-Deoxomyriocin (**19**): A solution of **14b** ($n$=12, 19.4 mg, 0.033 mmol) in 70% aqueous EtOH (2 ml) was treated with *p*-TsOH·$H_2O$ (50 mg) and the mixture was heated under reflux for 2 h. It was neutralized with Amberlite IRA-93ZU and the resin was filtered off. Removal of the solvent from the filtrate under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 2 g, *n*-hexane–AcOEt (3:1)] to furnish the lactone ii ($n$=12, 15.5 mg, 77.4%). The lactone ii ($n$=12): $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6.6 Hz, 20-$H_3$), 1.26 (22H, $CH_2$ ×11), 2.09 (2H, m, 8-$H_2$), 2.66 (2H, m, 5-$H_2$), 3.94, 4.03 (2H, ABq, $J$=11.9 Hz, 1-$H_2$), 4.66 (1H, ddd, $J$=3.6, 3.6, 7.3 Hz, 4-H), 4.82 (1H, d, $J$=3.6 Hz, 3-H), 5.40 (1H, m, 6-H), 5.59 (1H, m, 7-H), 7.00 (1H, br s, NHBz),

7.42—7.81 (5H, m, Bz). A solution of the lactone ii ($n=12$, 12.0 mg, 0.025 mmol) in 1 N NaOH (2 ml) was heated under reflux for 20 min, then neutralized with Amberlite IRC-76 and the resin was filtered off. Removal of the solvent from the filtrate under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 1.5 g, $CHCl_3$–MeOH–$H_2O$ (10 : 3 : 1, lower phase)] to furnish *Z*-14-deoxomyriocin (**19**, 5.9 mg, 60.1%).

**19**: A white powder, $[\alpha]_D^{27}$ −14.9° ($c=0.11$, MeOH). High-resolution FAB-MS: Calcd for $C_{21}H_{40}NO_5$ $(M-H)^-$: 386.2907. Found: 386.2933. IR (KBr): 3431, 1632 $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) $\delta$: 0.85 (3H, t, $J=5.9$ Hz, 20-$H_3$), 1.24 (22H, $CH_2\times11$), 1.99 (2H, m, 8-$H_2$), 2.19 (2H, m, 5-$H_2$), 3.55 (1H, t-like, 4-H), 3.56, 3.68 (2H, ABq, $J=10.8$ Hz, 1-$H_2$), 3.60 (1H, br s, 3-H), 5.36 (2H, m, 6, 7-H). Negative FAB-MS *m/z* (%): 386 [$(M-H)^-$, 46].

The *Z*-types (**20**—**22**) of nor-deoxomyriocin were prepared by the same procedure as used for **19**, from **14b** ($n=9$, 6, 3). The lactone ii ($n=9$, 72.5%): $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J=6.6$ Hz, 17-$H_3$), 1.26 (16H, $CH_2\times8$), 2.09 (2H, m, 8-$H_2$), 2.67 (2H, m, 5-$H_2$), 3.94, 4.03 (2H, ABq, $J=11.9$ Hz, 1-$H_2$), 4.67 (1H, ddd, $J=3.6$, 3.9, 7.3 Hz, 4-H), 4.84 (1H, d, $J=3.6$ Hz, 3-H), 5.42 (1H, m, 6-H), 5.59 (1H, m, 7-H), 7.00 (1H, br s, NHBz), 7.43—7.82 (5H, m, Bz). The lactone ii ($n=6$, 66.3%): $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J=6.6$ Hz, 14-$H_3$), 1.27 (10H, $CH_2\times5$), 2.08 (2H, m, 8-$H_2$), 2.64 (2H, m, 5-$H_2$), 3.93, 4.00 (2H, ABq, $J=11.9$ Hz, 1-$H_2$), 4.64 (1H, ddd, $J=3.6$, 3.9, 7.3 Hz, 4-H), 4.78 (1H, d, $J=3.6$ Hz, 3-H), 5.40 (1H, m, 6-H), 5.58 (1H, m, 7-H), 7.03 (1H, br s, NHBz), 7.39—7.79 (5H, m, Bz). The lactone ii ($n=3$, 73.2%): $^1$H-NMR ($CDCl_3$) $\delta$: 0.90 (3H, t, $J=6.9$ Hz, 11-$H_3$), 1.35 (4H, $CH_2\times2$), 2.10 (2H, m, 8-$H_2$), 2.66 (2H, m, 5-$H_2$), 3.93, 4.02 (2H, ABq, $J=11.9$ Hz, 1-$H_2$), 4.66 (1H, ddd, $J=3.6$, 3.6, 7.3 Hz, 4-H), 4.81 (1H, d, $J=3.6$ Hz, 3-H), 5.42 (1H, m, 6-H), 5.59 (1H, m, 7-H), 7.01 (1H, br s, NHBz), 7.42—7.81 (5H, m, Bz).

**20** (84.5%): A white powder, $[\alpha]_D^{27}$ +13.2° ($c=0.20$, MeOH). High-resolution FAB-MS: Calcd for $C_{18}H_{34}NO_5$ $(M-H)^-$: 344.2437. Found: 344.2459. IR (KBr): 3453, 1638 $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) $\delta$: 0.86 (3H, t, $J=6.3$ Hz, 17-$H_3$), 1.25 (16H, $CH_2\times8$), 1.99 (2H, m, 8-$H_2$), 2.19 (2H, m, 5-$H_2$), 3.58, 3.69 (2H, ABq, $J=10.2$ Hz, 1-$H_2$), 3.60 (1H, br s, 3-H), 3.65 (1H, t-like, 4-H), 5.37 (2H, m, 6, 7-H). Negative FAB-MS *m/z* (%): 344 [$(M-H)^-$, 30].

**21** (52.4%): A white powder, $[\alpha]_D^{30}$ +7.5° ($c=0.14$, MeOH). High-resolution FAB-MS: Calcd for $C_{15}H_{28}NO_5$ $(M-H)^-$: 302.1967. Found: 302.1942. IR (KBr): 3432, 1638 $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) $\delta$: 0.86 (3H, t, $J=6.3$ Hz, 14-$H_3$), 1.26 (10H, $CH_2\times5$), 2.00 (2H, m, 8-$H_2$), 2.18 (2H, m, 5-$H_2$), 3.59, 3.70 (2H, ABq, $J=10.2$ Hz, 1-$H_2$), 3.60 (1H, br s, 3-H), 3.66 (1H, t-like, 4-H), 5.35 (2H, m, 6, 7-H). Negative FAB-MS *m/z* (%): 302 [$(M-H)^-$, 54].

**22** (86.4%): A white powder, $[\alpha]_D^{28}$ −8.4° ($c=0.17$, MeOH). High-resolution FAB-MS: Calcd for $C_{12}H_{22}NO_5$ $(M-H)^-$: 260.1498. Found: 260.1508. IR (KBr): 3453, 1638 $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) $\delta$: 0.87 (3H, t, $J=6.9$ Hz, 11-$H_3$), 1.29 (4H, $CH_2\times2$), 2.00 (2H, m, 8-$H_2$), 2.18 (2H, m, 5-$H_2$), 3.59, 3.70 (2H, ABq, $J=10.6$ Hz, 1-$H_2$), 3.60 (1H, br s, 3-H), 3.66 (1H, t-like, 4-H), 5.37 (2H, m, 6, 7-H). Negative FAB-MS *m/z* (%): 260 [$(M-H)^-$, 100].

**Photoisomerization of 14** A cyclohexane solution (6 ml) of the geometric mixture **14** ($n=12$, 28.1 mg, 0.048 mmol) and diphenyl disulfide (21 mg, 0.096 mmol) was irradiated with a 300 W high-pressure lamp at room temperature (25 °C) for 4 h in a Pyrex vessel. The reaction mixture was poured into saturated aqueous $NaHCO_3$ and the whole was extracted with AcOEt. The AcOEt extract was washed with brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product which was purified by column chromatography [$SiO_2$ 5 g, $CHCl_3$–AcOEt (20 : 1)] and subsequent HPLC [column: Develosil 100-5, $CH_2Cl_2$–*n*-hexane–AcOEt (4 : 6 : 1)] to furnish **14a** (19.7 mg, 84.8%) and **14b** (1.9 mg, 8.4%). Photoisomerization of **14** ($n=9$, 6, 3) was carried out by the same procedure. **14a** and **14b** ($n=9$), (59.2%: 7.3%); **14a** and **14b** ($n=6$), (72.2%: 6.8%); **14a** and **14b** ($n=3$), (85.7%: 6.5%).

**General Method for the Preparation of 15—18** 14-Deoxomyriocin (**15**): A solution of **14a** ($n=12$, 18 mg, 0.031 mmol) in 70% aqueous EtOH (2 ml) was treated with *p*-TsOH·$H_2O$ (50 mg) and the mixture was heated under reflux for 2 h. It was neutralized with Amberlite IRA-93ZU and the resin was filtered off. Removal of the solvent from the filtrate under reduced pressure gave a product which was purified by column chromatography [$SiO_2$ 2 g, *n*-hexane–AcOEt (1 : 1)] to furnish the lactone i ($n=12$, 8.4 mg, 58.3%). i ($n=12$): $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J=6.6$ Hz, 20-$H_3$), 1.26 (22H, $CH_2\times11$), 2.01 (2H, m, 8-$H_2$), 2.60 (2H, m, 5-$H_2$), 3.94, 4.03 (2H, ABq, $J=11.9$ Hz, 1-$H_2$), 4.66 (1H, ddd, $J=3.6$, 3.6, 7.3 Hz, 4-H), 4.82 (1H, d, $J=3.6$ Hz, 3-H), 5.45 (1H, dt, $J=15.2$, 6.9 Hz, 6-H), 5.66 (1H, dt, $J=15.2$, 6.6 Hz, 7-H), 7.00 (1H, br s, NHBz), 7.43—7.82 (5H, m, Bz). A solution of the lactone i ($n=12$, 8.4 mg, 0.018 mmol) in 1 N NaOH (2 ml) was heated under reflux for 20 min, then neutralized with Amberlite IRC-76, and the resin was filtered off. Removal of the solvent from the filtrate under reduced pressure gave a product, which was purified by column chromatography [$SiO_2$ 1.5 g, $CHCl_3$–MeOH–$H_2O$ (10 : 3 : 1, lower phase)] to furnish 14-deoxomyriocin (**15**, 5.1 mg, 74.2%), which was identified by comparing the IR, $^1$H-NMR, and high-resolution FAB-MS data with reported values.[4]

14-Deoxomyriocin (**15**): A white powder, $[\alpha]_D^{27}$ −4.6° ($c=0.066$, MeOH). $^1$H-NMR ($C_5D_5N$) $\delta$: 0.89 (3H, t, $J=6.9$ Hz, 20-$H_3$), 1.26 (22H, $CH_2\times11$), 1.95 (2H, m, 8-$H_2$), 2.77, 2.88 (1H each, both m, 5-$H_2$), 4.63, 4.87 (2H, ABq, $J=10.8$ Hz, 1-$H_2$), 4.78 (1H, br s, 3-H), 4.82 (1H, t-like, 4-H), 5.60 (2H, m, 6, 7-H). The $[\alpha]_D$ value and $^1$H-NMR spectrum (recorded in $C_5D_5N$) were not previously reported.

The *E*-types (**16**—**18**) of nor-deoxomyriocin were prepared by the same procedure as used for **15**, from **14a** ($n=9$, 6, 3). The lactone i ($n=9$, 80.0%): $^1$H-NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J=6.9$ Hz, 17-$H_3$), 1.27 (16H, $CH_2\times8$), 2.02 (2H, m, 8-$H_2$), 2.60 (2H, m, 5-$H_2$), 3.94, 4.03 (2H, ABq, $J=11.9$ Hz, 1-$H_2$), 4.66 (1H, ddd, $J=3.6$, 3.6, 7.3 Hz, 4-H), 4.83 (1H, br s, 3-H), 5.45 (1H, dt, $J=15.5$, 6.9 Hz, 6-H), 5.66 (1H, dt, $J=15.5$, 6.6 Hz, 7-H), 6.99 (1H, br s, NHBz), 7.42—7.83 (5H, m, Bz). The lactone i ($n=6$, 65.4%): $^1$H-NMR ($CDCl_3$) $\delta$: 0.89 (3H, t, $J=6.9$ Hz, 14-$H_3$), 1.28 (10 H, $CH_2\times5$), 2.02 (2H, m, 8-$H_2$), 2.59 (2H, m, 5-$H_2$), 3.93, 4.02 (2H, ABq, $J=11.9$ Hz, 1-$H_2$), 4.66 (1H, ddd, $J=3.6$, 3.6, 7.3 Hz, 4-H), 4.82 (1H, br s, 3-H), 5.46 (1H, dt, $J=15.5$, 6.9 Hz, 6-H), 5.66 (1H, dt, $J=15.5$, 6.6 Hz, 7-H), 7.00 (1H, br s, NHBz), 7.42—7.82 (5H, m, Bz); The lactone i ($n=3$, 70.5%): $^1$H-NMR ($CDCl_3$) $\delta$: 0.90 (3H, t, $J=6.9$ Hz, 11-$H_3$), 1.34 (4H, $CH_2\times2$), 2.03 (2H, m, 8-$H_2$), 2.59 (2H, m, 5-$H_2$), 3.93, 4.02 (2H, ABq, $J=11.9$ Hz, 1-$H_2$), 4.65 (1H, ddd, $J=3.9$, 3.9, 7.3 Hz, 4-H), 4.81 (1H, br s, 3-H), 5.45 (1H, dt, $J=15.2$, 6.9 Hz, 6-H), 5.66 (1H, dt, $J=15.2$, 6.6 Hz, 7-H), 7.01 (1H, br s, NHBz), 7.42—7.81 (5H, m, Bz).

**16** (92.3%): A white powder, $[\alpha]_D^{27}$ −20.6° ($c=0.073$, MeOH). High-resolution FAB-MS: Calcd for $C_{18}H_{34}NO_5$ $(M-H)^-$: 344.2437. Found: 344.2474. IR (KBr): 3422, 1630 $cm^{-1}$. $^1$H-NMR ($C_5D_5N/D_2O$) $\delta$: 0.87 (3H, t, $J=6.6$ Hz, 17-$H_3$), 1.22 (16H, $CH_2\times8$), 1.93 (2H, m, 8-$H_2$), 2.74, 2.87 (1H each, both m, 5-$H_2$), 4.63, 4.85 (2H, ABq, $J=10.8$ Hz, 1-$H_2$), 4.79 (1H, br s, 3-H), 4.83 (1H, t-like, 4-H), 5.59 (2H, m, 6, 7-H). Negative FAB-MS *m/z* (%): 344 [$(M-H)^-$, 100].

**17** (89.9%): A white powder, $[\alpha]_D^{27}$ +8.7° ($c=0.046$, MeOH). High-resolution FAB-MS: Calcd for $C_{15}H_{28}NO_5$ $(M-H)^-$: 302.1967. Found: 302.1942. IR (KBr): 3432, 1637 $cm^{-1}$. $^1$H-NMR ($C_5D_5N/D_2O$) $\delta$: 0.85 (3H, t, $J=6.6$ Hz, 14-$H_3$), 1.20 (10H, $CH_2\times5$), 1.92 (2H, m, 8-$H_2$), 2.73, 2.86 (1H each, both m, 5-$H_2$), 4.65, 4.83 (2H, ABq, $J=10.9$ Hz, 1-$H_2$), 4.72 (1H, br s, 3-H), 4.77 (1H, t-like, 4-H), 5.55 (2H, m, 6, 7-H). Negative FAB-MS *m/z* (%): 302 [$(M-H)^-$, 100].

**18** (73.4%): A white powder, $[\alpha]_D^{27}$ −2.8° ($c=0.35$, MeOH). High-resolution FAB-MS: Calcd for $C_{12}H_{22}NO_5$ $(M-H)^-$: 260.1498. Found: 260.1532. IR (KBr): 3432, 1632 $cm^{-1}$. $^1$H-NMR ($C_5D_5N/D_2O$) $\delta$: 0.78 (3H, t, $J=6.9$ Hz, 11-$H_3$), 1.18 (4H, $CH_2\times2$), 1.88 (2H, m, 8-$H_2$), 2.72, 2.83 (1H each, both m, 5-$H_2$), 4.64, 4.82 (2H, ABq, $J=10.9$ Hz, 1-$H_2$), 4.72 (1H, br s, 3-H), 4.77 (1H, t-like, 4-H), 5.53 (2H, m, 6, 7-H). Negative FAB-MS *m/z* (%): 260 [$(M-H)^-$, 100].

**MLR** This assay was carried out according to the literature method.[4] Namely, mouse allogeneic MLR was carried out by culturing BALB/c mouse spleen cells ($5\times10^5$ cells, responder, H-$2^d$) and an equal number of C57BL/b mouse spleen cells treated with mitomycin C at 50 $\mu$g/ml for 30 min at 37 °C (stimulator, H-$2^b$) in 200 $\mu$l of RPMI 1640 medium containing 30 $\mu$M 2-mercaptoethanol, 10% fetal bovine serum and a test compound. The RPMI 1640 was supplemented with 2 mM L-glutamine, 100 U/ml penicillin G sodium, 100 $\mu$g/ml streptomycin sulfate, 0.25 $\mu$g/ml amphotericin B and 25 mM HEPES buffer. The fetal bovine serum was heat-inactivated at 56 °C for 45 min before use. The cells were placed in a 96-well flat-bottomed microtest plate and cultured at 37 °C in an atmosphere of 5% $CO_2$. After 54 h, the cells in each well were pulsed for 18 h at 37 °C with $^3$H-thymidine at 18.5 kBq/well and harvested by using a multiple cell harvester. The radioactivity incorporated into the cells was measured with a liquid scintillation counter. Activities of the test compounds were expressed as $IC_{50}$ values.

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