New hennoxazoles from a sponge Polyfibrospongia sp.

New hennoxazoles from a sponge *Polyfibrospongia* sp.

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Abstract

A series of hennoxazoles (**1**, **4-6**, **9-11**) and miyakolide (**8**) were isolated from two specimens of the sponge *Polyfibrospongia* sp. Structures of hennoxazole E (**5**), hennoxazole A 4-acetate (**6**), hennoxazole E 4-acetate (**10**), and 3-dehydrohennoxazole D (**11**) will be discussed. In addition, the spectral data for hennoxazole F (**6**) and a diacetate of hennoxazole G (**7**) are reported in this note.

Introduction

In 1991, Ichiba and coworkers reported a series of antiviral bisoxazole alkaloids named hennoxazoles A-D (**1-4**) isolated from an Okinawan sponge *Polyfibrospongia* sp. (Figure 1).[1] Due to the structural novelty and antiviral activity, several synthesis papers have been published on hennoxazole A (**1**) and the absolute stereochemistry of **1** was determined.[2,3] Additional hennoxazoles E-G (**5-7**) were isolated by the initial authors from the original specimen.

A second specimen was collected in 1990, resulting in the isolation of a bryostatin-like macrolide miyakolide (**8**)[4] and hennoxazole A 4-acetate (**9**) in addition to **1** and **4-6**. At the 19th International Symposium on the Chemistry of Natural Products held at Karachi, Pakistan in 1994, one of us (TH) presented the structures of **5-9** and a brief summary was published in a proceeding,[5] but experimental details on new analogs **5-7** and **9** were not reported.

Later, two new members, namely hennoxazole E 4-acetate (**10**) and 3-dehydrohennoxazole D (**11**), were isolated in addition to previous members **1**, **4-6** and **8** from the third specimen collected in 1997. In this note, the structures of **5** and **9-11** are discussed in addition to depositing spectral data for hennoxazole F (**6**) and a diacetate of hennoxazole G (**7**).

Results and Discussion

From the third specimen, hennoxazole E (**5**) was isolated as a dominant member and its structure was reexamined as described below.

NMR spectra of **5** in acetone-d_6 as for previous hennoxazoles look like a mixture of two components in a ratio of 3:1, but the signal ratio changed to 6:1 when the measurement temperature was lowered from 25°C to -30°C, suggesting that hennoxazole E (**5**) exists as a conformational mixture. With the help of 2D NMR, NMR signals of the major conformer were assigned. As two characteristic oxazole signals appeared at δ 7.93 and 8.42, it was identified as a member of hennoxazoles.

The molecular formula of **5** was found to be $C_{28}H_{40}N_2O_6$ by ESIMS corresponding to 14 mass units smaller than that of hennoxazole A (**1**). The

presence of a sole methoxy signal at δ 3.23 suggests that **5** has a hydroxyl group (3391 cm^{-1}) for one of two methoxy groups in **1**. When chemical shifts of **1** and **5** were compared, $\Delta\delta_{1\text{-}5}$ values were almost the same for most part of the molecules except for those at the six membered ring as follows: -6.5 (C-1), +2.9 (C-2), -0.10 (H-1), and +0.34 (H-6) indicating the presence of a hydroxyl group at C-2. Since the interpreted coupling constants are almost identical between **1** and **5**, the chiral centers and double bond geometries in **5** are the same as in hennoxazole A (**1**). Finally, the relation was confirmed by treating **5** with CSA in MeOH to give **1**.

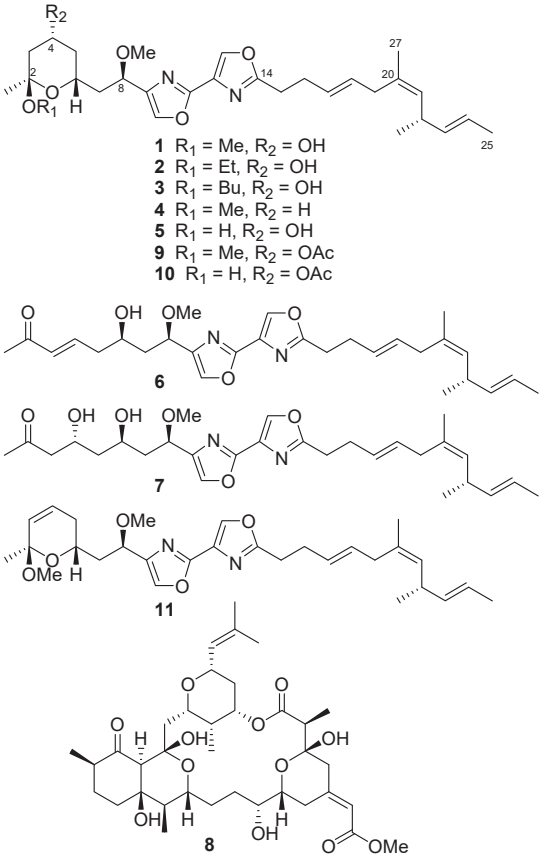

Figure 1. Structures of hennoxazoles (**1**-**7**, **9**-**11**) and miyakolide (**8**)

Since hennoxazole F (**6**) was obtained in a small quantity as an unstable material and hennoxazole G (**7**) was not found from the second and third specimens, their data together with **5** analyzed by the original authors from the first specimen are deposited.[6-8]

Compound **9** was shown to have a molecular formula as $C_{31}H_{44}N_2O_7$, indicating 42 mass or C_2H_2O units larger than hennoxazole A (**1**). In the NMR, signals of an acetate, δ 1.96 (3H, s), δ 21.0 q, 170.2 s, were observed suggesting that **9** is hennoxazole A 4-acetate, which was confirmed by acetylation of **1**.

Compound **10** was found to have a molecular formula as $C_{30}H_{42}N_2O_7$, 14 mass uints or CH_2 less than that of hennoxazole A 4-acetate (**9**). ^1H NMR spectrum of **10** contained the following functionalities: one methoxy at δ 3.23 s, two oxazole signals at δ 7.93 s and 8.41 s, two vinyl methyls at δ 1.58 (overlapping), a doublet methyl at δ 0.96, an acetate at δ 1.96 s, and a singlet methyl at δ 1.39. This was verified by comparing ^{13}C NMR data of **10** with those of **5** or **9**. Larger $\Delta\delta_{5\text{-}10}$ values were observed at +4.3 (C-3), -3.4 (C-4) and +4.2 (C-5), while $\Delta\delta_{9\text{-}10}$ values were at -7.0 (C-1) and +3.0 (C-2). Finally, **10** was prepared by acetylation of **5**. Therefore, compound **10** is hennoxazole E 4-acetate.

Compound **11** was analyzed to have a molecular formula $C_{29}H_{40}N_2O_5$ corresponding to 18 mass units less than that of hennoxazole A (**1**). Therefore, it was expected to be a dehydrated analog, which was supported by the absence of a hydroxyl group in IR and additional double bond signals at δ 5.63 and 5.80 and at δ 126.3 d and 131.6 d. All the signals in **11** were assigned with precise 2D NMR

analysis, and the whole structure was elucidated as 3-dehydrohennoxazole D.

As it is rare to encounter ethyl or butyl ethers as natural products, it was suspected that hennoxazoles B (**2**) and C (**3**) may be artifacts arising during isolation. In fact, we could isolate neither **2** nor **3** from the second and third specimens. Consequently, MeOH or other alcohol was avoided for the third specimen except for two steps of purification with Sephadex LH20 gel filtration and reversed phase HPLC. This resulted in the yield of hennoxazole E (**5**) being much higher than that of hennoxazole A (**1**) suggesting even **1** might also be an artifact. Additionally, when **5** was treated with CSA in EtOH, hennoxazole B (**2**) was formed easily as for **1**.

As mentioned, hennoxazoles E-G (**5**-**7**) were reported without the experimental details.[5] When TH retired in 2005, he left a summary of their spectral data. Therefore, this is an opportunity to publicize the original data here.[6-8]

Experimental

General experimental conditions. Most NMR data were obtained on a Jeol Alpha 500 or a Bruker Avance III 500 instrument. Multiplicities of ^{13}C NMR signals were determined by DEPT and expressed as follows: s for C, d for CH, t for CH_2, and q for CH_3. EIMS or ESIMS spectra were obtained on a Jeol D-300 or a Jeol T100LP instrument. FTIR spectrum was obtained on a Jasco FTIR-300 spectrophotometer. Solvents used were reagent grade without distillation.

Extraction and Isolation. The second specimen (8.4 kg, wet) was collected at 30 m depth near Higashihenna Cape, Miyako Island, July 1990, from where the original sponge material was collected.[1,4] The specimen was cut and extracted three times with acetone (16 L). The EtOAc extract (30 g) was subjected to vacuum flash chromatography on silica gel to give 10 fractions. Of them, fractions 5 and 6 were combined (3.98 g) and the whole was separated successively with Sephadex LH20, Lobar Si60 column (hexane-EtOAc) and HPLC (C-8, MeOH-H_2O, 5-1) followed by further separation on HPLC. As results, hennoxazole D (**4**, 55.4 mg), miyakolide (**8**, 97.1 mg) and hennoxazole A acetate (**9**, 65.0 mg) were obtained. From the 7th fraction (3.51 g) from vacuum flash chromatography, similar separation as above afforded hennoxazole A (**1**, 430 mg), E (**5**, 69.0 mg) and hennoxazole F (**6**, 3.0 mg).

The third specimen (1.6 kg, wet) was collected at 35 m depth of a reef off Irabu Island, June 1997. The material was cut and extracted with acetone (2 L) for three times. After removal of acetone under vacuum, the EtOAc soluble portion (8.76 g) was obtained. Most of the extract was subjected to flash chromatography on silica gel to give 13 fractions. Of these, the sixth fraction (0.47 g) was passed through a Sephadex LH20 column (MeOH-CH_2Cl_2, 1-1) to give four fractions. The second fraction of these (398 mg) was further separated on a silica gel column to afford six subfractions. These subfractions were finally purified on HPLC (ODS, MeOH-H_2O, 10-1) to give hennoxazole E 4-acetate (**10**, 25.7 mg) and 3-dehydrohennoxazole D (**11**, 9.3 mg) in addition to miyakolide (**8**, 46.1 mg) and hennoxazole D (**4**, 27.3 mg). From other fractions, hennoxazole A (**1**, 137.6 mg), E (**5**, 442.0 mg) and F (**6**, 5.0 mg) were obtained.

Hennoxazole E (5). glass; $[\alpha]_D$ -13 (*c* 0.667,

$CHCl_3$); IR (neat) 3391, 2931, 1109 cm^{-1}; ^1H NMR (acetone-d_6, major conformer, at 25°C): δ 0.92 (3H, d, *J* = 6.7 Hz, H-26), 1.12 (1H, q, *J* = 11.6 Hz, H-5α), 1.24 (1H, t, *J* = 11.6 Hz, H-3α), 1.33 (3H, s, H-1), 1.60 (6H, brs, H-25, 27), 1.90 (1H, m, H-5β), 1.94 (1H, m, H-7a), 2.02 (1H, m, H-3β), 2.06 (1H, m, H-7b), 2.51 (1H, q, *J* = 7.0 Hz, H-16), 2.70 (1H, m, H-19), 2.90 (1H, t, *J* = 7.3 Hz, H-15), 3.03 (1H, m, H-22), 3.23 (3H, s, H-28), 3.85 (1H, m, H-6), 3.97 (1H, m, H-4), 4.44 (1H, dd, *J* = 6.4, 7.9 Hz, H-8), 4.98 (1H, d, *J* = 9.1 Hz, H-21), 5.35 (2H, m, H-23, 24), 5.44 (1H, dt, *J* = 15.3, 6.7 Hz, H-17), 5.46 (1H, dt, *J* = 15.3, 6.7Hz, H-18), 7.93 (1H, s, H-10), 8.42 (1H, s, H-13); ^{13}C NMR (acetone-d_6, major conformer): δ 18.0 (C-25), 21.8 (C-26), 23.5 (C-27), 28.6 (C-15), 30.3 (C-16), 30.4 (C-1), 35.8 (C-22), 35.9 (C-19), 41.5 (C-7), 41.9 (C-5), 45.7 (C-3), 56.3 (C-28), 64.8 (C-4), 65.8 (C-6), 73.5 (C-8), 97.0 (C-2), 123.0 (C-24), 129.7 (C-17), 130.1 (C-18), 131.0 (C-21), 132.7 (C-12, 20), 137.0 (C-23), 137.6 (C-10), 139.5 (C-13), 142.4 (C-11), 156.4 (C-9), 166.1 (C-14),; ESIMS *m/z* 523.27940 $[M+Na]^+$ (calcd for $C_{28}H_{40}N_2NaO_6$ 523.27841).

Hennoxazole A acetate (9). glass, ^1H NMR (acetone-d_6): δ 0.96 (3H, d, *J* = 7.0 Hz), 1.22 (1H, m), 1.28 (3H, s), 1.38 (1H, t, *J* = 12 Hz), 1.60 (6H, brs), 1.96 (3H, s), 2.02 (1H, m), 2.06 (2H, m), 2.09 (1H, m), 2.51 (2H, q, *J* = 7.0, Hz), 2.70 (2H, m), 2.90 (2H, t, *J* = 7.3 Hz), 3.07 (3H, s), 3.24 (3H, s), 3.61 (1H, m), 4.48 (1H, dd, *J* = 6.3, 7.6 Hz), 4.98 (1H, d, *J* = 9.3 Hz), 5.04 (1H, m), 5.35 (2H, m), 5.52 (2H, m), 8.01 (1H, s), 8.42 (1H, s); ^{13}C NMR (acetone-d_6): δ 18.0 q, 21.1 q, 21.8 q, 23.4 q, 23.7 q, 28.6 t, 30.3 t, 35.7 t, 35.8 d, 37.4 t, 41.1 t, 41.8 t, 47.9 q, 56.2 q, 66.1 d, 68.1 d, 73.1 d, 100.0 s, 122.9 d, 129.6 d, 130.1 d, 131.0 s, 131.3 s, 132.6 s, 136.9 d, 137.7 d, 139.5 d, 142.1 s, 156.3 s, 166.0 s, 170.2 s; ESIMS: *m/z* 579.30425 $[M+Na]^+$ (calcd for $C_{31}H_{44}N_2NaO_7$ 579.30462).

Hennoxazole E acetate (10). glass, $[\alpha]_D$: -21 (*c* 0.76, $CHCl_3$); IR (neat): 3415, 3131, 1741 cm^{-1}; ^1H NMR (acetone-d_6): δ 0.96 (3H, d, *J* = 6.7 Hz, H-26), 1.22 (1H, q, *J* = 11.6 Hz, H-5a), 1.36 (1H, t, *J* = 11.6 Hz, H-3a), 1.39 (3H, s, H-1), 1.60 (6H, brs, H-25, 27), 1.96 (1H, m, H-7a), 1.96 (3H, s, Ac), 2.00 (1H, m, H-5b), 2.05 (1H, m, H-3b), 2.06 (1H, m, H-7b), 2.51 (2H, q, *J* = 7.0 Hz, H-16), 2.71 (2H, m, H-19), 2.90 (2H, t, *J* = 7.0 Hz, H-15), 3.03 (1H, m, H-22), 3.23 (3H, s, H-28), 3.94 (1H, m, H-6), 4.44 (1H, dd, *J* = 7.6, 6.4 Hz, H-8), 4.97 (1H, d, *J* = 9.2 Hz, H-21), 5.10 (1H, tt, *J* = 11.6, 4.6 Hz, H-4), 5.35 (2H, m, H-23, 24), 5.46 (1H, brdt, *J* = 15.4, 6.3 Hz, H-18), 5.54 (1H, brdt, *J* = 15.4, 6.3 Hz, H-17), 7.93 (1H, s, H-10), 8.41 (1H, s, H-13); ^{13}C NMR (acetone-d_6): δ 18.0 q (C-25), 21.1 q (Ac), 21.8 q (C-26), 23.4 q (C-27), 28.6 t (C-15), 30.3 t (C-16), 30.3 q (C-1), 35.8 t (C-19), 35.9 d (C-22), 37.7 t (C-5), 41.3 t (C-7), 41.6 t (C-3), 56.4 q (C-28), 65.6 d (C-6), 68.7 d (C-4), 73.3 d (C-8), 97.0 s (C-2), 123.0 d (C-24), 129.7 d (C-17), 130.1 d (C-18), 131.0 d (C-21), 131.5 s (C-12), 132.7 s (C-20), 137.0 d (C-23), 137.6 d (C-10), 139.6 d (C-13), 142.2 s (C-11), 156.4 s (C-9), 166.1 s (C-14), 170.3 s (Ac); EIMS: *m/z* 542 $[M]^+$; ESIMS: *m/z* 565.29200 $[M+Na]^+$ (calcd for $C_{30}H_{42}N_2NaO_7$ 565.28897).

3-Dehydrohennoxazole D (11). glass; $[\alpha]_D$ -28 (*c* 0.17, $CHCl_3$); IR (neat) 3124, 1106, 970 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 0.96 (d, *J* = 6.7 Hz, H-26), 1.30 (3H, s, H-1), 1.60 (6H, brs, H-25, 27), 1.94 (2H, m, H-4), 2.10 (2H, m, H-7), 2.51 (2H, q, *J* = 7.3 Hz, H-16), 2.71 (2H, m, H-19), 2.90 (2H, t,

J = 7.3 Hz, H-15), 3.03 (1H, m, H-22), 3.16 (3H, s, H-29), 3.25 (3H, s, H-28), 3.82 (1H, m, H-6), 4.49 (1H, dd, *J* = 7.6, 6.4 Hz, H-8), 4.96 (1H, d, *J* = 9.2 Hz), H-21), 5.35 (2H, m, H-23, 24), 5.46 (1H, m, H-18), 5.53 (1H, m, H-17), 5.63 (1H, ddd, *J* = 10.0, 2.4, 1.6 Hz, H-3), 5.80 (1H, ddd, *J* = 10.0, 5.0, 2.7 Hz, H-4), 7.99 (1H, s, H-10), 8.43 (1H, s, H-13); ^{13}C NMR (125 MHz, acetone-d_6) δ 18.0 q (C-25), 21.8 q (C-26), 23.5 q (C-1), 23.5 q (C-27), 28.6 t (C-15), 30.3 t (C-16), 30.9 t (C-5), 35.8 t (C-19), 35.9 d (C-22), 41.0 t (C-7), 48.4 q (C-29), 56.2 q (C-28), 65.3 d (C-6), 73.3 d (C-8), 96.9 s (C-2), 123.0 d (C-24), 126.3 d (C-4), 129.7 d (C-17), 130.2 d (C-18), 131.1 d (C-21), 131.5 s (C-12), 131.6 d (C-3), 132.7 s (C-20), 137.0 d (C-23), 137.7 d (C-10), 139.6 d (C-13), 142.1 s (C-11), 156.4 s (C-9), 166.1 s (C-14); EIMS *m/z* 496 [M^+]; ESIMS *m/z* 519.28751 [M+Na]$^+$ (calcd for $C_{29}H_{40}N_2NaO_5$ 519.28349.

Acetylation of hennoxazole A (1) to give compound 9. A portion (3.9 mg) of hennoxazole A (**1**) was treated with acetic anhydride (50 μL) and pyridine (50 μL) at room temperature for 2 h. After excess reagent was removed by nitrogen flow, the crude product was separated on preparative TLC (CH_2Cl_2-EtOAc, 4-1) to give 3.1 mg of **9**, which showed the following data: $[\alpha]_D$ -55 (*c* 0.26, $CHCl_3$); ^{1}H NMR δ 0.96 (3H, d, *J* = 7 Hz), 1.29 (3H, s), 3.07 (3H, s), 3.24 (3H, s), 8.01 (1H, s), 8.42 (1H, s); EIMS *m/z* 556 (M^+).

Acetylation of hennoxazole E (5) to give compound 10. A mixture of 2.0 mg of hennoxazole E (**5**) in pyridine (100 μL) and acetic anhydride (100 μL) was kept standing at room temperature for two hours. The product was separated on a preparative TLC (silica, CH_2Cl_2-EtOAc, 1-1) to give compound **10** as a sole product, which showed the same ^{1}H NMR spectrum as **10**.

Conversion of hennoxazole E (5) to A (1). To a solution of hennoxazole E (**5**, 3.0 mg) in MeOH (0.5 mL) a catalytic amount of camphor sulfonic acid (CSA) was added. After confirming hennoxazole A (**1**) was formed after 2 hours on TLC, the product was separated to give 0.5 mg of compound **1**.

Conversion of hennoxazole E (5) to B (2). Hennoxazole E (**5**, 3.0 mg) in EtOH (0.5 mL) was treated as above. After standing for two hours, the mixture was separated on preparative TLC (silica, CH_2Cl_2-EtOAc, 1-1) to give 1.1 mg of hennoxazole B (**2**) which showed the following data: $[\alpha]_D$ -43 ($CHCl_3$); ^{1}H NMR (acetone-d_6) δ 0.90 (3H, t, *J* = 7 Hz, H-30), 3.27 (2H, overlapped, H-29), 8.01 (1H, s), 8.43 (1H, s); EIMS *m/z* 528 (M^+); ESIMS *m/z* 551.30996 [M+Na]$^+$ (calcd for $C_{30}H_{44}N_2NaO_6$ 551.30971).

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6) Data for hennoxazole E (**5**) from the initial specimen: light yellow oil; UV (MeOH) 254 nm (logε 4.0); IR (neat) 3380, 3100, 2930, 2900, 1695, 1630, 1620, 1565, 1515, 1430, 1360, 1300, 1215, 1175, 1100, 1090, 1010, 955, 905, 760 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 0.95 (3H, d, J = 6.6 Hz), 1.06 (1H, q, J = 11.6 Hz), 1.20 (1H, dt, J = 11.1, 4.5 Hz), 1.34 (3H, s), 1.59 (6H, m), 1.88 (1H, m), 1.96 (1H, m), 2.04 (2H, m), 2.51 (2H, q, J = 7.2 Hz), 2.69 (2H, m), 2.89 (2H, t, J = 7.5 Hz), 3.02 (1H, m), 3.21 (3H, s), 3.65 (1H, d, J = 5.1 Hz), 3.83 (1H, m), 3.95 (1H, m), 4.26 (1H, d, J = 2.1 Hz), 4.43 (1H, dd, J = 8.0, 6.3 Hz), 4.96 (1H, d, J = 9.1 Hz), 5.34 (2H, m), 5.45 (1H, dt, J = 15.2, 6.0 Hz), 5.54 (1H, dt, J = 15.3, 6.2 Hz), 7.91 (1H, s), 8.40 (1H, s); ^{13}C NMR (acetone-d_6) δ 18.0 q, 21.8 q (2C), 23.5 q, 28.6 t, 30.3 t, 35.7 t, 35.9 d, 41.5 t, 41.9 t, 45.7 t, 56.3 q, 64.8 d, 65.9 d, 73.5 d, 97.0 s, 122.9 d, 129.7 d, 130.1 d, 131.0 d, 131.4 s, 132.7 s, 137.0 d, 137.5 d, 139.5 d, 142.4 s, 156.3 s, 166.1 s,.

7) hennoxazole F (**6**), light yellow oil; UV (MeOH) 210 nm (logε 4.3), 250 nm (4.1); IR (neat) 3400, 3100, 2940, 2900, 1165, 1660, 1620, 1565, 1520, 1430, 1350, 1240, 1095, 960, 905 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 0.91 (3H, d, J = 6.9 Hz), 1.55 (6H, m), 1.94-1.04 (2H, m), 2.13 (3H, s), 2.22-2.50 (2H, m), 2.46 (2H, q, J = 7.0 Hz), 2.66 (2H, m), 2.86 (2H, t, J = 7.5 Hz), 2.98 (1H, m), 3.22 (3H, s), 3.78 (1H, m), 3.99 (1H, d, J = 4.4 Hz), 4.46 (1H, t, J = 6.9 Hz), 4.92 (1H, d, J = 9.2 Hz), 5.30 (2H, m), 5.40 (1H, dt, J = 15.3, 6.0 Hz), 5.49 (1H, dt, J = 15.3, 6.0 Hz), 6.02 (1H, d, J = 15.9 Hz), 6.86 (1H, dt, J = 15.9, 7.2 Hz), 7.90 (1H, s), 8.38 (1H, s); ^{13}C NMR (acetone-d_6) δ 18.0 q, 21.7 q, 23.4 q, 26.7 q, 28.6 t, 30.3 t, 35.7 t, 35.8 d, 41.3 t, 42.5 t, 56.4 q, 68.3 d, 74.7 d, 122.9 d, 129.6 d, 131.0 d, 131.3 s, 132.6 s, 133.7 d, 137.0 d, 137.4 d, 139.6 d, 142.1 s, 145.5 d, 156.2 s, 166.1 s, 197.9 s; EIMS *m/z* 482 (M^+), 464, 449, 432, 389, 355, 337, 328, 308, 270; HREIMS *m/z* 482.2786 M^+ (calcd for $C_{28}H_{38}N_2O_5$ 482.2791).

8) hennoxazole G (**7**) diacetate, A crude sample (11.4 mg) of hennoxazole G (**7**) was treated with acetic anhydride (0.2 mL) and pyridine (0.1 mL) at room temperature for 1 h. After evaporation of the excess reagents, the residue was separated by HPLC (ODS, MeOH-H_2O, 85-15) to give 2.5 mg of its diacetate as an oil which showed the following data: UV (MeOH) 256 nm (logε 4.0), IR (neat) 3100, 2940, 2900, 1730, 1720, 1665, 1620, 1565, 1425, 1360, 1230, 1090, 1010, 955, 905 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 0.95 (3H, d, J = 6.8 Hz), 1.59 (6H, m), 1.75-2.00 (2H, m), 1.91 (3H, s), 1.94 (3H, s), 2.10 (3H, s), 2.17 (1H, dd, J = 14.1,

8.4 Hz), 2.50 (2H, q, J = 7.2 Hz), 2.70 (2H, m), 2.74 (2H, d, J = 6.4 Hz), 2.89 (2H, t, J = 7.5 Hz), 3.01 (1H, m), 3.21 (3H, s), 4.33 (1H, dd, J = 7.3, 6.1 Hz), 4.96 (1H, d, J = 9.6 Hz), 5.02 (1H, m), 5.25 (1H, m), 5.33 (2H, m), 5.44 (1H, dt, J = 15.2, 6.0 Hz), 5.54 (1H, dt, J = 15.4, 5.9 Hz), 7.94 (1H, s), 8.41 (1H, s); ^{13}C NMR (acetone-d_6) δ 18.0 q, 21.1 q, 21.8 q, 23.4 q, 28.6 t, 29.5 q, 30.1 t, 35.8 t, 35.9 d, 39.1 t, 40.0 t, 48.4 t, 56.4 q, 67.3 d, 68.3 d, 73.7 d, 123.0 d, 129.7 d, 130.1 d, 131.1 d, 131.4 s, 132.7 s, 137.0 d,137.4 d, 139.7 d, 142.1 s, 156.9 s, 166.2 s, 170.3 s, 170.5 s, 206.1 s.