Crenulacetal C, a Marine Diterpene, and Its Synthetic Mimics Inhibiting *Polydora websterii*, a Harmful Lugworm Damaging Pearl Cultivation

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***Polydora websterii*, a harmful lugworm that has serious adverse effects on pearl oyster cultivation, was inhibited by a marine diterpene, crenulacetal C, isolated from the brown alga *Dictyota dichotoma*. Based on consideration of the activity–structure relationship, several synthetic compounds having an aromatic moiety with a hydroxyalkyl chain were prepared. Bioassay using larvae of *Polydora websterii* as well as pearl oysters (*Pinctada fucata martensii*) suggested that 1-(2-furyl)-1-nonanol was the most promising inhibitor.**

Key words *Polydora websterii*; crenulacetal C; pearl oyster; 1-(2-furyl)-1-nonanol

Since pearl oyster (*Pinctada fucata martensii*) farming was invented in Japan, it has played an economically important role in Japanese aquatic culture.[1] With the increase in the number of pearl oyster cultivation sites, serious problems have arisen.[2] One of them is caused by a tiny marine lugworm, *Polydora websterii*,[3] an invertebrate inflicting heavy damage on pearl oysters as well as scallops.[4] *P. websterii*, a creature 10 mm in size, makes a hole, in which it dwells, in the shell of the pearl oyster (Fig. 1). The shellfish attacked by the *Polydora* are sometimes infected with bacteria, which invade the host through the hole and ultimately cause its death. The total loss of income from pearl oyster culture caused by *Polydora* is assumed to amount to several billion yen annually. Effective measures to protect the pearl oyster from attack by *Polydora* have been long awaited.[5]

During our investigations into the pharmaceutically active components of marine organisms, we have looked for compounds able to kill *Polydora*, primarily because Shikoku Island, where our university is located, is famous for its pearl production. We herein describe the isolation of *Polydora*-killing compounds from the brown alga, *Dictyota dichotoma*, and preparation of the simple synthetic pesticides which effectively inhibit the larvae of *P. websterii*.

Firstly, a bioassay system was established to find marine organisms that contain substances killing or repelling *Polydora*. After several attempts, the following bioassay using larval *P. websterii* (Fig. 2) was found to be effective.

Bioassay Method A constant supply of *P. websterii* is available by keeping the pearl oyster shells, which the adult *P. websterii* inhabits, in sea water: the larvae hatch from the eggs once a month. The larvae are collected on a filter paper, and transferred to a flask containing sea water. Bioassay was performed by applying a substance from a marine organism to three one-week old larvae of 0.5 mm in length in a well of a multidish (Nunclon) containing 1.0 ml filtered (Toyo 5C) sea water. Three replicates were performed for each sample. After incubation, each larva was observed under a microscope (×40) to estimate the

Fig. 1. A Picture of Adult *Polydara websterii* Dwelling in the Hole on the Pearl Oyster Shell

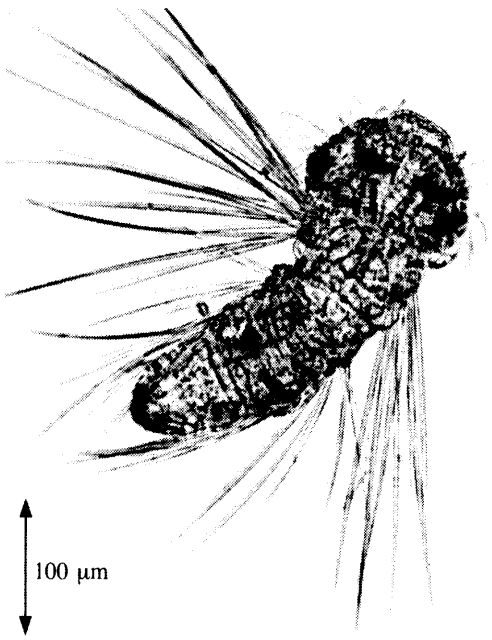

Fig. 2. A Microscopic Picture of a Larval *Polydora websterii*, One Week after Hatching

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effect of the sample. The activity of the sample was represented as the minimum concentration (ppm) to kill 80% of the larvae within 3 h.

Methanol (MeOH) was used for the sample solution. The concentration of MeOH in the assay was set at 25 ppm in sea water (25 μl of a MeOH solution of the test sample added to 1.0 ml sea water), and this concentration of MeOH did not affect the larvae in any way. As a control, MeOH of the same concentration without test sample was incubated in the assay.

Screening of Marine Organisms Twenty-seven marine organisms (eighteen algae, four sponges, and five invertebrates) were collected from beaches around Shikoku Island. The organisms were soaked in MeOH for a week, and the extracts were concentrated. The activity of the crude MeOH extracts was tested in the above assay. Among these organisms, the MeOH extracts of the brown alga, *Dictyota dichotoma* collected at Ehime, showed the strongest activity against larval *P. websterii*: The larvae were killed completely after 3 h in a 300 ppm solution of the extract of *D. dichotoma*, although extracts of other organisms were inactive at the same concentration.

Isolation of Active Compounds The methanol extract of *D. dichotoma* was successively extracted with hexane, dichloromethane, and ethyl acetate. The hexane extract, showing activity at 100 ppm, was fractionated by repeated chromatography on silica-gel and monitoring the activity to yield two active compounds. Comparison of their ^{1}H- and ^{13}C-NMR spectra with literature data confirmed that they were crenulacetal C (**1**)[6] and 10-acetoxy-18-hydroxy-2,7-dollabelladiene (**2**).[7] Crenulacetal C (**1**) was treated with hydrochloric acid to give acetoxycrenulide (**3**).[6] The activity of **1**, **2**, and **3** against the larvae of *P. websterii* was 1.5, 6.5, and 10 ppm, respectively.

Preparation of Simpler Pesticides From a practical point of view, the content of **1** in the algal body was too low (several mg from 10 kg of algae) to be used at the pearl oyster cultivation sites. We noticed that acetoxycrenulide (**3**) had a much weaker activity than **1**, although both compounds have the same carbon skeleton. The difference is only that there is a 2,5-dihydro-2,5-dimethoxyfuran (**4**) moiety in **1** instead of the 5-membered lactone ring in **3**. This suggests that **4** may play an important role in exhibiting the activity against *P. websterii*. Therefore, compounds having the dihydrodimethoxyfuran moiety were prepared (Chart 2). Diacetals **4b** and **5b** were prepared by treating furan and 3-methylfuran, respectively, with bromine in methanol.[8] The homologous compounds, **7d** and **8d**, were synthesized starting from 3-furaldehyde (**6**) through the Grignard reaction (**7a**, **8a**), acetylation (**7b**, **8b**), reductive deacetoxylation (**7c**, **8c**), and then treatment with bromine in methanol.

Both **4b** and **5b** had practically no activity against larval *P. websterii*. The nonyl derivative (**7d**), however, killed all the larvae after 3 h incubation at 1.5 ppm, which is the same potency as the natural compound (**1**). However, **8d** with a nonadecyl group had weaker activity (> 50 ppm) than **7d**, probably due to its low solubility in sea water.

During this synthetic work, we found that the activity of furyl alcohol (**7a**) is almost the same as that of **7d**, which means that the dimethoxydihydrofuran moiety is not necessary for activity against *Polydora*. Therefore, the

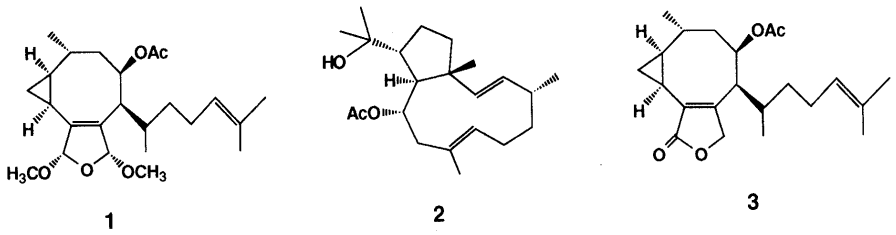
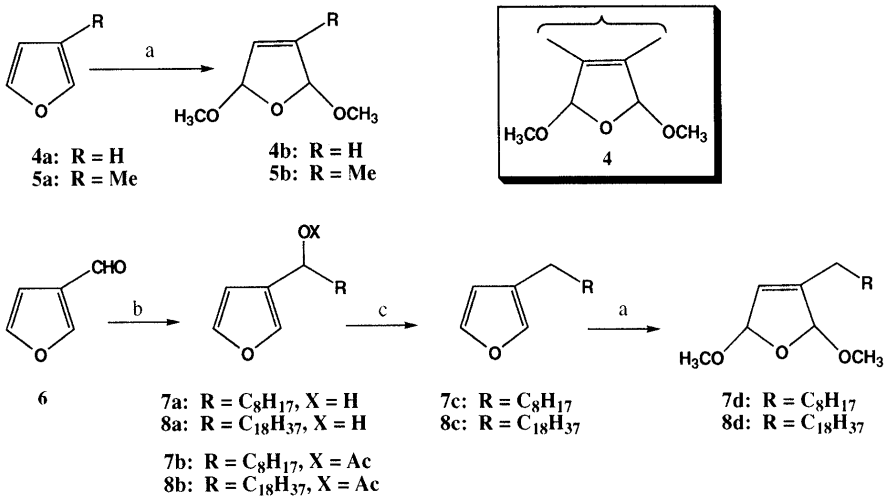
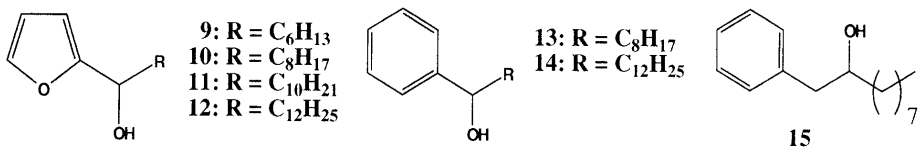


Chart 1



a; Br_2/MeOH/K_2CO_3 b; RMgBr then Ac_2O/Pyr c; Ca/liq. NH_3

Chart 2



16 17

Chart 3

Table 1. Inhibitory Activity (LD_{80}) of the Synthetic Compounds against Larval *Polydora webstrii*

Compound	LD_{80} (ppm)
7d	2.5
8d	>100
9	50.0
Ac-**9**	>100
10	1.0
Ac-**10**	>100
11	2.5
12	5.0
13	5.0
14	10.0
15	2.5
16	>100
17	2.5

Table 2. Toxicity (LD_{80}) of the Synthetic Compounds against *Pinctada fucata martensii*

Compound	LD_{80} (ppm)
10	50.0
11	10.0
15	10.0
17	5.0

alcohols **9**—**14** were prepared from much less expensive precursors, furfural and benzaldehyde, by a Grignard reaction. For comparison, 1-phenyl-2-decanol (**15**) was synthesized. Their IC_{80} (ppm, after 3 h) against larval *P. websterii* is summarized in Table 1, which also includes the results for two surfactants, sodium stearate (**16**) and sodium octadecylbenzenesulfonate (**17**), and the acetates of **9** and **10**. Sodium stearate (**16**) showed no activity at 100 ppm, while the alkylbenzenesulfonate (**17**) is active at 2.5 ppm. The acetates of **9** and **10** were inactive (>100 ppm). Of the furyl alcohols, compound **10** with an octylcarbinol moiety showed the strongest activity (1.0 ppm). The activity of the rest was in the range 5.0—50 ppm. The benzyl alcohol **13** was active at 5.0 ppm, while the activity of **14** was 10 ppm. The alcohol, **15**, having the hydroxyl group next to the benzylic position also showed strong activity (2.5 ppm). These results indicate that **10**, **11**, **15**, or **17** would be a promising pesticide.

In parallel with this assay, the toxicity of these synthetic compounds against the pearl oyster (*Pinctada fucata martensii*) was tested. Twenty three-month old pearl oysters were used. After keeping the pearl oyster in sea water containing various concentrations of the samples for 3 h, it was cultivated in fresh sea water for 96 h, during which time its condition was observed. The approximate activity of the compounds against *P. fucata martensii* is given in Table 2. The data revealed that the most potent compound for field-testing was **10**, because its toxicity against *P. fucata martensii* was relatively weak (50 ppm), while **11**, **15**, and **17** showed stronger toxicity around at 5—10 ppm.

The above findings suggest that compound **10** is the most promising owing to its strong activity against *Polydora* websterii, mild toxicity to *Pinctada fucata martensii*, and ease of synthesis from a less expensive starting material, furfural. Field-tests to confirm its utility in preventing damage to pearl oysters from the lugworm is now in progress.

Experimental

^{1}H-NMR and ^{13}C-NMR spectra were recorded on Hitachi R-90H, JEOL FX-200, JEOL GSX-400, Bruker ARX-400, and Varian 600 spectrometers. Chemical shifts are reported in parts per million (ppm) relative to $CHCl_3$ (δ 7.26), and coupling constants are given in hertz. IR spectra were measured on a Perkin-Elmer 1720 FT-IR spectrophotometer.

Collection of Marine Organisms The following algae were collected at Maruyama and Oishi beaches, Awaji Island, in April, 1993: *Sargassum horneri*, *Sargassum thunbergii*, *Dictyota species*, *Gymnogongrus flabelliformis*, *Gracilaria verrucosa*, *Gracilaria textorii*, *Spatoglossum pacificum*, *Ahnfeltia concinna*, *Valonia aegagropila*, *Schizymenia dubyi*, and *Chondria crassicaulis*. The following organisms were collected at Nagahama beach, Ehime, in June, 1993: *Codium fragile*, *Dictyota dichotoma*, yellow eggs of *Aplysia kurodai*, and three kinds of unidentified algae. The following organisms were collected at Kamaguchi beach, Awaji Island, in June, 1993: *Codium fragile*, pink eggs of *Aplysia kurodai*, *Halichondria okadai*, and one unidentified alga. The following algae were collected at Naruto beach, Tokushima, in August, 1993: *Chondria crassicaulis*, *Halichondria okadai*, and four unidentified algae.

Isolation of Crenulacetal C (1) and 10-Acetoxy-18-hydroxy-2,7-dollabelladiene (2) The MeOH extract (10 g) of *Dictyota dichotoma* was shaken with hexane, CH_2Cl_2, and AcOEt. The hexane extract (2.41 g) was subjected to SiO_2 (Merck, Kieselgel 60) flash column chromatography (FCC) with AcOEt–hexane (0, 10, 20, 40, and 100% of AcOEt) as an eluting solvent. The active fraction (672 mg) eluted with 20% AcOEt was further separated by preparative TLC (SiO_2, 20% AcOEt in hexane). The fraction was finally purified by HPLC (Hibar RT250-25, LiChrosorb Si60) to give compounds **1** (6.3 mg) and **2** (3.8 mg). The compounds were identified as crenulacetal C (**1**)[6] and 10-acetoxy-18-hydroxy-2,7-dollabelladiene (**2**)[7] by comparison of their NMR data with those reported in the literature. Conversion of **1** to acetoxycrenulide (**3**) was performed as described in reference 6.

2,5-Dimethoxyoxacyclopent-3-ene (4b) Furan (**4a**; 14.6 g) was allowed to react with bromine (10.6 ml) in benzene (50 ml), methanol (50 ml) and anhydrous Na_2CO_3 (38 g) at −5 °C. The mixture was stirred for 2 h and filtered. The collected solid was washed with two portions of benzene

(each 10 ml). After drying over $MgSO_4$, the benzene solution was treated with anhydrous K_2CO_3 and concentrated to a brown oil. The crude material was distilled using a short packed column to give 4.1 g (16%) **4b** as a 1 : 1 mixture of *cis* and *trans* isomers: a colorless oil; bp 80 °C (50 Torr); ^{1}H-NMR (90 MHz, $CDCl_3$) *cis* isomer δ: 3.38 (s, 6H, CH_3O), 5.88 (br s, 2H), 6.03 (br s, 2H), *trans* isomer δ: 3.41 (s, 6H, CH_3O), 5.60 (br s, 2H), 6.03 (br s, 2H).

2,5-Dimethoxy-3-methyloxacyclopent-3-ene (5b) 3-Methylfuran (**5a**; 1.0 g) was treated with bromine (0.6 ml) in benzene (2.83 ml), methanol (2.83 ml), and anhydrous Na_2CO_3 (2.1 g) at −5 °C . The mixture was stirred for an additional 2 h and filtered. The work-up described above afforded an oil, which was purified by FCC (**5b**; 0.74 g; 43%). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.80 (s, 3H, CH_3–C=C), 3.32—3.37 (singlets, 6H, CH_3O), 5.37—5.75 (m, 3H, CH_3O–C<u>H</u>, CH=). This material was subjected to bioassay without further purification.

1-(3-Furyl)-1-nonanol (7a) In a three-necked flask, fitted with a stirrer, a dropping funnel, and a reflux condenser to which a drying tube was attached, were placed magnesium turnings (0.76 g) and dry ether (1.0 ml). A small portion of 1-bromooctane (0.2 ml) was added to start the reaction. After adding dry ether (9.0 ml), 1-bromooctane (5.4 ml) was added dropwise with refluxing. The mixture was refluxed for 1.5 h. A solution of 3-furaldehyde (**6**, 1.0 g) in dry ether (4.1 ml) was added dropwise to the Grignard solution. After refluxing for 2.5 h, aqueous saturated NH_4Cl was added to stop the reaction. The reaction mixture was extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated into an oily residue. The residue was purified by FCC on silica-gel (CH_2Cl_2) to give 2.22 g (100%) of **7a**: IR (liquid film) cm^{-1}: 3361, 2927, 2856, 1504, 1466, 1161, 1024, 875, 792, 726, 601. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.87 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.26 (br s, 12H), 1.5—1.9 (m, 2H, CH_2O), 1.85 (br s, 1H, O<u>H</u>CH), 4.61 (br t, 1H, J=5.6 Hz, C<u>H</u>OH), 6.36 (br s, 1H, furan), 7.34 (m, 2H, furan). The compound gave EI-MS *m/z*: 210.1629 (Calcd for $C_{13}H_{22}O_2$; 210.1620).

Acetylation of 1-(3-Furyl)-1-nonanol (7b) Acetic anhydride (1.6 ml) was added to a solution of **7a** (2.07 g) in pyridine (1.0 ml), and the reaction mixture was allowed to stand at room temperature for 13 h. The excess reagent and pyridine were then removed *in vacuo* to yield 2.42 g (97.5%) **7b**, which was judged pure from its TLC and NMR spectra: a pale yellow oil; IR (liquid film) cm^{-1}: 2927, 2857, 1740, 1371, 1239, 1024. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.89 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.26 (br s, 12H), 1.6—2.0 (m, 2H), 2.04 (s, 3H, CH_3CO), 5.74 (t, 1H, J=6.3 Hz, C<u>H</u>(OAc)CH$_2$), 6.36 (br s, 1H, furan), 7.36 (m, 2H, furan). The compound gave EI-MS *m/z*: 252.1725 (Calcd for $C_{15}H_{24}O_3$: 252.1725).

3-Nonylfuran (7c) The acetate **7b** (2.42 g) in dry tetrahydrofuran (4.0 ml) was placed in an uninsulated two-necked flask equipped with a stirrer and a dropping funnel and attached to a short air-condenser, which was plugged at the top with a drying tube. The flask was cooled with a mixture of dry ice and acetone. Ammonia was introduced from the dropping funnel into the flask to give a concentrated liquid (*ca.* 10 ml), and then calcium (1.4 g) was added. The mixture was stirred for 10 min. The excess calcium was destroyed by dropwise addition of brine (5 ml) and the ammonia was allowed to evaporate. After warming to room temperature, the product was taken up in ether and dried over Na_2SO_4. The organic layer was concentrated to give an oily residue (1.8 g). Purification by FCC on silica-gel (hexane) gave 459 mg (24%) of **7c**: A colorless oil; IR (liquid film) cm^{-1}: 2927, 2856, 1503, 1466, 1164, 1027, 874, 776, 600. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.91 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.28 (br s, 12H), 2.42 (t, 2H, J=6.3 Hz, C<u>H</u>$_2$-furan), 6.26 (br s, 1H, furan), 7.19 (br s, 1H, furan), 7.33 (m, 1H, furan). The compound gave EI-MS *m/z*: 194.1670 (Calcd for $C_{13}H_{22}O$: 194.1671).

2,5-Dimethoxy-3-nonyloxacyclopent-3-ene (7d) Nonyl derivative **7b** (100 mg) was treated with bromine (25 μl) in benzene (0.12 ml), methanol (0.12 ml) and anhydrous Na_2CO_3 (90 mg) at −5 °C. The mixture was stirred for an additional 5.5 h, and 10 ml water was added. The product was extracted with benzene and the organic layer was washed with aqueous saturated $Na_2S_2O_3$ solution and then with brine. After concentration, the residue was purified to give 11 mg (8.8%) **7d**: a pale yellow oil; ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.89 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.27 (br s, 14H), 2.0—2.2 (m, 2H), 3.35—3.40 (m, 6H, isomeric CH_3O), 5.61 (m, 1H, CH=C), 5.40—5.78 (m, 2H, isomeric C<u>H</u>OMe). The compound gave FAB-MS *m/z*: 256.2010 (Calcd for $C_{15}H_{28}O_3$: 256.2038).

2,5-Dimethoxy-3-nonadecyloxacyclopent-3-ene (8d) Nonadecyl derivative **8c** (55 mg) was treated with bromine (7 ml) in benzene (1.0 ml), methanol (1.0 ml) and anhydrous Na_2CO_3 (26 mg) at −5 °C. Working-up and purification using SiO_2 chromatography gave 38 mg (57.7%) **8d**: A white powder; ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.91 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.28 (s, 34H), 2.05—2.15 (m, 2H), 3.36—3.41 (m, 6H, CH_3O), 5.63 (m, 1H, CH=C), 5.3—5.8 (m, 2H, C<u>H</u>–OMe). The compound gave EI-MS *m/z*: 396.3582 (Calcd for $C_{25}H_{48}O_3$: 396.3603).

1-(3-Furyl)-1-nonadecanol (8a) The procedure was identical with that used for **7a**. **8a**: a white powder; IR (KBr) cm^{-1}: 3324, 3209, 2952, 2915, 2851, 1475. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.91 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.27 (s, 32H), 1.5—1.7 (m, 2H), 4.66 (m, 1H, C<u>H</u>-furan), 6.4 (s, 1H, furan), 7.37 (d, 2H, J=1.8 Hz). The compound gave EI-MS *m/z*: 350.3160 (Calcd for $C_{23}H_{42}O_2$: 350.3185).

Acetylation of 1-(3-Furyl)-1-nonadecanol (8a) Acetic anhydride (0.5 ml) was added to a solution of **8a** (493 mg) in pyridine (0.6 ml), and the reaction mixture was allowed to stand at room temperature for 5 h. The excess reagent and pyridine were then removed *in vacuo* to yield 522 mg **8b**: ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.91 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.35 (s, 32H), 1.5—1.7 (m, 2H), 2.12 (s, 3H, CH_3CO), 5.75 (t, 1H, J=7.2 Hz, CH–OAc), 6.38 (s, 1H, furan), 7.37 (m, 2H, furan). The compound gave EI-MS *m/z*: 392.3308 (Calcd for $C_{25}H_{44}O_3$: 392.3290).

Conversion of 8b to 3-Nonadecylfuran (8c) The acetate **8b** (522 mg), which was contaminated with a small amount of octadecanol, in dry tetrahydrofuran (2.5 ml), was placed in an uninsulated two-necked flask equipped with a stirrer and a dropping funnel and attached to a short air-condenser, which was plugged at the top with a drying tube. The flask was cooled at −78 °C, and ammonia (20 ml) condensed. Calcium (0.13 g) was added little by little. The mixture was stirred for an additional 14 min. The excess calcium was destroyed by dropwise addition of brine (2 ml) and the ammonia was allowed to evaporate. The product was taken up in ether and dried over Na_2SO_4. The organic layer was concentrated to give an oily residue (565 mg). Purification of the residue by FCC on silica-gel (hexane) gave 143 mg (64%) **8c**: A colorless oil; IR (liquid film) cm^{-1}: 2918, 2851, 1468. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.90 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.28 (br s, 34H), 2.43 (t, 2H, J=7.4 Hz, C<u>H</u>$_2$-furan), 6.26 (br s, 1H, furan), 7.20 (br s, 1H, furan), 7.33 (br s, 1H, furan). The compound gave EI-MS *m/z*: 334.3224 (Calcd for $C_{23}H_{42}O$: 334.3235).

1-(2-Furyl)-1-heptanol (9) Magnesium turnings (3.51 g, 0.15 mol) and dry ether (30 ml) were placed in a three-necked flask, fitted with a stirrer, a dropping funnel, and a reflux condenser to which a drying tube was attached. The reaction started after adding 2.0 ml 1-bromohexane. After dry ether (200 ml) was added, the rest of the 1-bromohexane (22.0 ml) was added dropwise with refluxing. The mixture was then refluxed for 1 h. A solution of furfural (10.0 ml, 0.12 mol) was added dropwise to the Grignard solution. After refluxing for 2.5 h, aqueous saturated NH_4Cl solution was added to stop the reaction. The reaction mixture was extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated into an oily residue. The residue was purified by FCC on silica-gel to give 19.9 g (99%) 1-(2-furyl)-1-heptanol. ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.92 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.65—2.00 (br s, 10H), 4.65 (br t, 1H, J=5.4 Hz, CH–O), 6.27 (m, 1H, furan), 7.36 (m, 2H, furan). The compound gave FAB-MS *m/z*: 182.1308 (Calcd for $C_{11}H_{18}O_2$: 182.1308).

1-(2-Furyl)-1-nonanol (10) ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.87 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.26 (br s, 12H), 1.58 (br s, 2H), 1.82 (br s, 1H, OH), 4.66 (br t, 1H, J=5.4 Hz, CH–O), 6.26 (s, 2H, furan), 7.35 (m, 1H, furan). The compound gave FAB-MS *m/z*: 210.1601 (Calcd for $C_{13}H_{22}O_2$: 210.1620).

1-(2-Furyl)-1-undecanol (11) ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.90 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.27 (br s, 18H), 4.68 (m, 1H, CH–O), 6.27 (s, 2H, furan), 7.35 (m, 1H, furan). The compound gave FAB-MS *m/z*: 238.1922 (Calcd for $C_{15}H_{26}O_2$: 238.1933).

1-(2-Furyl)-1-tridecanol (12) ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.92 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.29 (s, 21H), 1.85 (br s, 2H), 4.70 (m, 1H, C<u>H</u>OH), 6.29 (s, 2H, furan), 7.37 (s, 1H, furan). The compound gave FAB-MS *m/z*: 266.2221 (Calcd for $C_{17}H_{30}O_2$: 266.2246).

1-Phenyl-1-nonanol (13) ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.76 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.24 (br s, 12H), 1.73 (br s, 2H), 4.64 (br s, 1H, C<u>H</u>OH), 7.33 (s, 5H, C_6H_5). The compound gave FAB-MS *m/z*: 220.1833 (Calcd for $C_{15}H_{24}O$: 220.1827).

1-Phenyl-1-tridecanol (14) ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.19 (br t, 3H, J=5.4 Hz, C<u>H</u>$_3$CH$_2$), 1.29 (br s, 22H), 4.69 (m, 1H, C<u>H</u>OH), 7.33 (s, 5H, C_6H_5). The compound gave FAB-MS *m/z*: 276.2448 (Calcd for

$C_{19}H_{32}O$: 276.2453).

1-Phenyl-2-decanol (15) ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 1.20 (br t, 3H, J=5.4 Hz, $C\underline{H}_3CH_2$), 1.58—1.82 (br s, 14H), 3.00 (m, 2H, $C\underline{H}_2C_6H_5$), 3.98 (m, 1H, $C\underline{H}OH$), 7.30 (s, 5H, C_6H_5). The compound gave FAB-MS m/z: 234.1962 (Calcd for $C_{16}H_{26}O$: 234.1984).

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