General Routes to 4-Methyl-2-substituted-furans: a Total Synthesis of Pleraplysillin-2, a Metabolite of the Sponge, *Pleraplysilla spinifera*

By David W. Knight* + and David C. Rustidge, Chemistry Department, University College, P.O. Box 78, Cardiff, Wales CF1 1XL

A general approach to 4-methyl-2-substituted-furans is described in which 4-methyl-2-furyl-lithium is the key intermediate. Using this method, pleraplysillin-2, a sesquiterpenoid ester from the sponge *Pleraplysilla spinifera*, has been synthesised. An alternative, less efficient, route to this type of furan, *via* acyclic keto-epoxides, is also discussed.

THE 4-methyl-2-furyl group occurs in a small number of natural terpenoids such as the lasiospermans 1 [e.g. (1) and (2)] and solanofuran (3).² It is also to be found in



the sponge metabolite pleraplysillin-2 $(4)^3$ and the recently isolated hydroquinone $(5).^4$ We wish to report two approaches to this class of compound, one of which we have employed in a total synthesis of pleraplysillin-2 (4).

RESULTS AND DISCUSSION

Our initial efforts were directed towards a construction of the 4-methyl-2-furyl unit from an appropriate acyclic keto-epoxide. This type of approach was used some years ago by Cornforth ⁵ to prepare 3-methylfuran (7) from the epoxide acetal (6) by treatment of the latter with dilute acid. We reasoned that 4-methyl-2-substituted-furans (8) could be prepared from the ketoepoxides (9) which could in turn be obtained from condensations between chloro-epoxide (10) and 1,3-dithian anions (11).⁶ As our target molecules were all terpenoids we chose to test this route using 2-geranyl-1,3-

† Present address: Chemistry Department, University Park, Nottingham NG7 2RD.

dithian (12),⁷ obtained by condensation of geranyl bromide with 2-lithio-1,3-dithian.⁶

Reaction between the anion derived from (12) and 1chloro-2-methyl-2,3-epoxypropane (10)⁸ proceeded as expected ⁶ to give the epoxy-dithian (13) in good yield. Removal of the dithian group proved to be more troublesome. As the final step of the sequence $[(9) \rightarrow (8)]$ could hopefully be effected using aqueous acid, we first examined deprotection methods which involved the generation of acidic conditions as the reaction proceeded (*e.g.* CuCl₂, HgCl₂, CuO in wet acetone,⁹ or MeI in wet acetone or acetonitrile ¹⁰), hoping that (13) would yield



the desired furan (8; R = geranyl) directly; in our hands, these methods were, however, singularly unsuccessful. The most suitable method for the unmasking of the ketone group was found to be *brief* treatment of (13) with *N*-chlorosuccinimide and silver nitrate in wet acetonitrile containing 2,4,6-trimethylpyridine,¹¹ which gave the keto-epoxide (9; R = geranyl) in reasonable yield.



The epoxyketone (9; R = geranyl) gave no more than traces of furan (8; R = geranyl) when treated with mineral acids under a variety of conditions. Eventually, we found that prolonged exposure of the keto-epoxide to Amberlite 1R-120(H) resin¹² did give the desired furan but only in moderate yield. Undoubtedly this was in part due to the instability of the furan itself to acidic conditions; attempts to shorten the reaction time or to find alternative reagents met with little success. Pyrolysis of epoxide acetals related to (6) is also known to yield, the corresponding furans.¹³ We observed that simple vacuum distillation of (9; R = geranyl) at 120 °C (0.6 mmHg) did indeed produce the desired furan but again the yield was only moderate (*ca.* 20%). Further work ¹⁴ with simpler 2-alkyl-1,3-dithians as starting materials led us to the conclusion that these approaches are probably only of use for the efficient preparation of simple, volatile furans which can be rapidly removed from the acidic or pyrolytic conditions used in their generation from keto-epoxides (9).

We therefore considered an alternative approach involving a pre-formed furan ring. As the preparation and use in synthesis of furyl-lithium species is well established,¹⁵ it seemed that a route involving 4-methyl-2-furyl-lithium (14) could be most expedient. The obvious precursor to (14) was 2-bromo-4-methylfuran



(15), which surprisingly is not mentioned in *Chemical* Abstracts. However, its preparation proved to be relatively straightforward by sequential bromination, saponification,¹⁶ and decarboxylation of readily-available methyl 3-methyl-2-furoate (16).¹³ Treatment of (15) with n-butyl-lithium in tetrahydrofuran at -78 °C produced an orange solution of the anion (14), which condensed rapidly and cleanly with acctone or benzaldehyde to give (17a) and (17b), respectively, in 60-65%



yield, as the sole isolated products. Alkylations of (14) were rather sluggish and resulted in somewhat lower yields of the desired products; this was partly due to competitive reaction with the n-butyl bromide formed in the initial metal-halogen exchange reaction used to generate (14). Thus, reaction between (14) and 1-iodopent-4-ene gave, after purification by preparative-scale gas-liquid chromatography, the furan (18) in *ca.* 50% yield, together with *ca.* 5% of 2-butyl-4-methylfuran. Significantly, reaction of (14) with geranyl bromide gave the original model compound (8; R = geranyl) in 65% isolated yield.

We then further exemplified the usefulness of this method by a total synthesis of pleraplysillin-2 (4), a metabolite of the sponge *Pleraplysilla spinifera.*³ Coupling of (14) with the bromo-geraniol derivative (19)¹⁷ led to furan (20a) in *ca.* 55% yield which, on subsequent

deprotection, gave alcohol (20b). This was separated by silica-gel chromatography from the major contaminant, a C_{20} diol arising from self-condensation of (19) presumably *via* metal-halogen exchange with



(14). Due to the considerable instability of most of the intermediates (20a--e) and of the final product (4), the remaining steps were carried out rapidly. The alcohol (20b) was oxidised to ester (20d) by sequential treatment with manganese dioxide [to give (20c)] and MnO_{2} -NaCN.¹⁸ Saponification with aqueous alcoholic potassium hydroxide afforded acid (20e), which was esterified with 3-furylmethanol in the presence of NN'-dicyclohexylcarbodi-imide and 4-dimethylaminopyridine ¹⁹ to give pleraplysillin-2 (4), which exhibited spectral data (u.v., i.r., ¹H n.m.r., m.s.) identical to that reported ³ for the natural product.

EXPERIMENTAL

M.p.s are corrected. ¹H N.m.r. spectra were determined with a Perkin-Elmer R32 spectrometer in CDCl₃, with tetramethylsilane as internal standard unless otherwise stated. Coupling constants (J) are in Hz. Mass spectra and molecular weights were determined using a Varian CH5 double-focusing mass spectrometer linked to a Varian 620i data system. All solvents for chromatography were redistilled; petrol refers to light petroleum, b.p. 41–45 °C. Preparative-scale gas–liquid chromatography was carried out on a Pye 105 instrument with a 15-ft $\times \frac{3}{8}$ -in glass column packed with 3% OV 225 on 60–80 mesh Gas-Chrom Q using nitrogen as carrier gas at a flow rate of 85 ml min⁻¹. All organic solutions were dried over anhydrous magnesium sulphate.

2-[(2E)-3,7-Dimethylocta-2,6-dienyl]-2-(2,3-epoxy-2-

methylpropyl)-1,3-dithian (13).-A solution of n-butyllithium (18 ml, 1.6M in hexane) was added dropwise to a stirred solution of 2-[(2E)-3,7-dimethylocta-2,6-dienyl]-1,3dithian (12) (6.4 g, 25 mmol) 7 in dry tetrahydrofuran (50 ml) at -30 °C under nitrogen. The resulting solution was stirred at this temperature for 2 h, then cooled to -78 °C and treated with 1-chloro-2,3-epoxy-2-methylpropane (10) (3.2 g, 30 mmol).⁸ The mixture was stirred for a further 1 h at --78 °C, warmed to 0 °C during 2 h. and left at this temperature overnight; it was then diluted with water (150 ml) and extracted with ether (3 \times 50 ml). The combined organic extracts were washed with water and saturated aqueous sodium chloride, then dried and evaporated. Chromatography of the residue over silica gel using petrolether (4:1) gave the epoxy-dithian (13) (7.02 g, 86%) as a pale yellow oil, $R_{\rm F}$ 0.57; $\nu_{\rm max.}$ (film) 1 660, 1 645, 1 274, and 909 cm⁻¹; τ 4.71 [t, \int 7, CH=C(Me)CH₂], 4.88 (br, CH= CMe_2), 7.00–7.31 (m, 2 × SCH₂), 7.20 (OCH₂), 7.38–7.76 (m, SCH₂CH₂), 7.84–8.10 (m, $4 \times$ CH₂), 8.34 (=CMe), 8.38 (=CMe), 8.41 (=CMe), and 8.50 [CH₂C(*Me*)O] (Found: *M*⁺, 326.173 1; C₁₈H₃₀OS₂ requires *M*, 326.173 8. Found: C, 66.9; H, 9.6. C₁₈H₃₀OS₂ requires C, 66.2; H, 9.3%).

(6E)-1,2-Epoxy-2,7,11-trimethyldodeca-6,10-dien-4-one.

A solution of the foregoing dithian (13) (0.97 g, 3 mmol) in acetonitrile (1 ml) was added in one portion to a stirred mixture of N-chlorosuccinimide (1.62 g, 12 mmol), silver nitrate (2.31 g, 13.5 mmol), and 2,4,6-trimethylpyridine (4.5 ml) in 80% aqueous acetonitrile (50 ml). After 10 min, the reaction mixture was worked up as previously described ¹¹ to give the *keto-epoxide* (0.54 g, 77%) as a yellow oil; v_{max} (film) 1 710, 1 625, and 1 297 cm⁻¹; τ 4.70 [t, J 7, CH=C(Me)CH₂], 4.81—4.98 (m, CH=CMe₂), 6.84 (d, J 7, O=CCH₂CH=), 7.26—7.51 (m, 4 H), 7.80—7.98 (m, 4 H), 8.33 (Me), 8.39 (Me), 8.41 (Me), and 8.65 [MeC(O)], which was used without further purification.

2-[(2E)-3,7-Dimethylocta-2,6-dienyl]-4-methylfuran (8; R =geranyl).—(a) The crude keto-epoxide (0.54 g) and Amberlite 1R-120(H) resin (10 g, washed before use with dry methanol and dry ether) were stirred together for 44 h in dry ether (50 ml) at room temperature. The resin was removed by filtration and the filtrate dried and evaporated. Chromatography of the residue over silica gel eluted with petrol-0.5% ether gave the geranyl-furan (0.11 g, 22%) as a colourless oil, $R_{\rm F}$ 0.63; $v_{\rm max}$ (film) 1 625, 1 565, 1 570, 1 139, 1 080, 892, and 765 cm⁻¹; τ 2.93 (q, J ca. 1, furyl 5-H), 4.14 (furyl 3-H), 4.67 [br t, J 7, CH=C(Me)CH₂], 4.79—4.93 (br, CH=CMe₂), 6.70 [d, J 7, =C(O)CH₂], 7.80—7.98 (m, 4 H), 8.05 (d, J ca. 1, furyl 4-Me), 8.38 (2 × Me), and 8.43 (Me) (Found: M^+ , 218.167 2. $C_{15}H_{22}$ O requires M, 218.167 1).

(b) The keto-epoxide (0.5 g) was distilled in a short-path apparatus at 120 °C and 0.6 mmHg. Chromatography of the distillate as above gave the desired furan (0.09 g), with identical spectral data to that mentioned above.

2-Bromo-4-methylfuran (15).-Methyl 3-methyl-2-furoate $(10 \text{ g})^{13}$ was treated with bromine (5.8 ml) as previously described ¹⁶ to give methyl 5-bromo-3-methyl-2-furoate [τ 3.72 (furyl 4-H), 6.18 (CO₂Me) and 7.73 (3-Me)] contaminated with ca. 10% of the corresponding 4,5-dibromofuran (¹H n.m.r. integration and m.s. data). The crude mixture was added to an ice-cold solution of potassium hydroxide (10 g) in methanol (190 ml) and water (10 ml), and the resulting dark red solution stirred overnight at room temperature, then diluted with water (500 ml) and washed with ether (2 imes 150 ml). The aqueous solution was acidified with concentrated hydrochloric acid and ether-extracted $(3 \times 100 \text{ ml})$. The combined extracts were washed with water and brine, then dried and evaporated. Crystallisation of the residue from aqueous methanol gave 5-bromo-3-methyl-2-furoic acid (9.5 g) as prisms, m.p. 160-163 °C (decomp.) (lit., ¹⁶ m.p. 160–162 °C); τ [CDCl₃-(CD₃)₂SO] 0.76 (br, CO₂H), 3.68 (furyl 4-H), and 7.71 (3-Me) (Found: C, 34.7; H, 2.2. Calc. for C₆H₅BrO₃: C, 35.1; H, 2.4%). A mixture of the acid (9.4 g), and copper powder (1.65 g) in freshly distilled quinoline (17 ml) was heated at 260 °C (pre-heated oil bath) under an atmosphere of nitrogen in a small distillation apparatus, and the fraction boiling between 120 and 160 °C was collected during 1.5 h in an ice-cooled receiver. The crude distillate was dried and re-distilled to give 2-bromo-4-methylfuran (2.5 g, 22% from methyl 3methyl-2-furoate) as a colourless liquid, b.p. 138-144 °C; ν_{max.} (film) 1 592, 1 495, 1 387, 1 355, 1 255, 1 197, 1 103, 1077, 925, 815, and 760 cm⁻¹; τ 2.80 (q, J ca. 1, 5-H), 3.82 (3-H), and 8.02 (d, J ca. 1, 4-Me). A small amount of the product was subjected to bulb-to-bulb distillation (oven temperature 135 °C) to give an analytical sample (Found; C, 37.2; H, 2.8. C_5H_5BrO requires C, 37.3; H, 3.1%).

2-(1-Hydroxy-1-methylethyl)-4-methylfuran (17a).—n-Butyl-lithium (1.9 ml of a 1.6M solution in hexane, 3 mmol) was added dropwise to a stirred solution of 2-bromo-4methylfuran (0.48 g, 3 mmol) in dry THF (8 ml) maintained at -78 °C under nitrogen. The resulting clear, orange solution of the 2-lithio-derivative was stirred at -78 °C for 5 min, then treated with dry acetone (0.22 ml, 3 mmol); the solution was rapidly decolourised. After a further 0.5 h at -78 °C, the reaction mixture was poured into water (20 ml) containing a few drops of concentrated hydrochloric acid, and ether-extracted $(3 \times 5 \text{ ml})$. The combined extracts were washed with water and brine, then dried and evaporated to leave a pale yellow oil (0.33 g), a sample (43 mg) of which was purified by preparative-scale g.l.c. at 125 °C to give the *alcohol* (36 mg) as a colourless oil, R_t 3.8 min; v_{max} . (film) 3 450, 1 620, 1 550, 1 470, 920, 855, 815, and 735 cm⁻¹; τ 2.88 (q, J ca. 1, furyl 5-H), 3.93 (furyl 3-H), 8.03 (d, J ca. 1, furyl 4-Me + OH), and 8.48 (2 \times Me) (Found: M^+ , 140.083 5. $C_8H_{12}O_2$ requires *M*, 140.083 7).

2-(α -Hydroxybenzyl)-4-methylfuran (17b).—Freshly distilled benzaldehyde (0.3 ml) was added to a solution of 2-lithio-4-methylfuran (3 mmol) prepared as described above. Reaction appeared to take place instantaneously; the solution was stirred at -78 °C for 0.5 h, then worked up exactly as described above. Chromatography of the product over silica gel, eluting with petrol-ether (4 : 1) gave the alcohol (0.37 g) as a pale yellow oil, $R_{\rm F}$ 0.34, b.p. 85 °C (oven temperature) at 0.1 mmHg on bulb-to-bulb distillation; $\nu_{\rm max}$ (CHCl₃) 3 600, 1 520, and 1 480 cm⁻¹, τ 2.50—2.75 (m, Ph), 2.87 (q, J ca. 1, furyl 5-H), 4.06 (furyl 3-H), 4.28 [CH(OH)Ph], 7.29 (OH), and 8.08 (d, J ca. 1, furyl 4-Me) (Found: M^+ , 188.083 6. $C_{12}H_{13}O_2$ requires M, 188.083 7).

4-Methyl-2-(pent-4-enyl)furan (18).—1-Iodopent-4-ene (0.59 g, 3 mmol) was added to a solution of 2-lithio-4-methylfuran (3 mmol), prepared as described above. The resulting orange solution was stirred at -78 °C for 1 h, then warmed to 0 °C during 2 h, and left at this temperature overnight, to give a red solution which was diluted with water (10 ml) and ether-extracted $(3 \times 5 \text{ ml})$. The combined extracts were washed with water and brine, then dried and evaporated (temperature < 30 °C) to give a yellow oil (0.4 g), which was purified by preparative-scale g.l.c. at 115 °C to give: (i) 2-n-butyl-4-methylfuran (24 mg), R_t 2.8 min; τ 2.94 (q, J ca. 1, furyl 5-H), 4.14 (furyl 3-H), 7.45 [t, J 8, $=C(O)CH_2$], 8.04 (d, J ca. 1, furyl 4-Me), 8.4-8.7 (m, $2 \times CH_2$, and 9.09 (t, J 8, CH_2Me): (ii) 1-iodopent-4-ene (80 mg), Rt 3.8 min: and (iii) 4-methyl-2-(pent-4-enyl) furan (236 mg) as a colourless oil, R_t 5.6 min; v_{max} (film) 1 650, 1 630, 1 560, 930, 820, and 755 cm⁻¹; τ 2.95 (q, J ca. 1, furyl 5-H), 3.94-4.40 (m, CH=CH₂), 4.15 (furyl 3-H), 4.85—5.11 (m, CH= CH_2), 7.44 [t, J 8, =C(O)C H_2], 7.8–8.1 (m, CH₂CH=), 8.06 (d, J ca. 1, furyl 4-Me), and 8.18-8.53 (m, CH₂CH₂CH₂) (Found: M⁺, 150.104 5. C₁₀H₁₄O requires M, 150.104 5).

2-[(2E)-3,7-Dimethylocta-2,6-dienyl]-4-methylfuran (8; R = geranyl).—Geranyl bromide (0.65 g, 3 mmol) was added to a solution of 2-lithio-4-methylfuran (3 mmol), prepared as described above, and the mixture stirred at -78 °C for 1 h, then for 4 h with the cooling bath removed. The resulting pale yellow solution was worked up as described above for (18), to give a pale yellow oil which was rapidly chromatographed over silica gel, eluting with petrol-0.5% ether to give the *geranyl-furan* (0.41 g), which exhibited identical spectral properties to those described above.

(E,E)-1-Bromo-2,6-dimethyl-8-(tetrahydropyran-2-yloxy)octa-2,6-diene (19).—Geranyl tetrahydropyranyl ether (34.7 g) was refluxed with selenium dioxide (16.6 g) in dry ethanol (250 ml) containing dry pyridine (24 ml) for 17 h.²⁰ The cooled solution was filtered and evaporated and the residue taken up in ether (250 ml), washed with water (4 \times 50 ml) and brine (50 ml), then dried and evaporated. The resulting oil was dissolved in ethanol (250 ml), and sodium borohydride (3 g) added in small portions during 0.25 h; the solution was then stirred at room temperature for 3 h, then diluted with water (500 ml), carefully acidified with hydrochloric acid, and quickly extracted with ether $(3 \times 100 \text{ ml})$. The combined extracts were washed with water $(2 \times 50 \text{ ml})$ and brine (50 ml), then dried and evaporated. The residue was purified by preparative-scale high-pressure liquid chromatography using LiChoprep eluted with cyclohexaneether (3:2) to give starting ether (5.5 g) and (E,E)-2,6dimethyl-8-(tetrahydropyran-2-yloxy)octa-2,6-dien-1-ol (8.3 g).²⁰

Dimethyl sulphide (0.37 ml, 5 mM) was added dropwise to a stirred solution of N-bromosuccinimide (0.73 g, 4.1 mmol) in dry dichloromethane (15 ml) at 0 °C under nitrogen, followed by the foregoing alcohol (0.69 g, 2.7 mmol), and the resulting mixture stirred at room temperature for 3.75 h.²¹ Pentane (30 ml) and cold water (20 ml) were then added and the organic layer separated, washed with brine, and filtered through a plug of silica gel; subsequent evaporation yielded the *bromide* (0.53 g) as a pale yellow oil; τ 4.47 (br t, J 7, =CHCH₂O), 4.65 (br t, J 7, =CH[CH₂]₂), 5.40 [br, OCH(O)-CH₂], 5.75—6.65 (m, 4 H), 6.07 (CH₂Br), 7.80—8.00 (m, $2 \times CH_2$), 8.39 (Me), 8.45 (Me), and 8.2—8.53 (m, 6 H), which was used promptly in the next step, without further purification.¹⁷

2-[(E,E)-2,6-Dimethyl-8-hydroxyocta-2,6-dienyl]-4-methylfuran (20b).—The foregoing bromide (0.53 g) was added to a solution of 2-lithio-4-methylfuran (2 mmol) prepared as described above. The mixture was kept below -- 60 °C for 6 h, then warmed to room temperature during 2 h, poured into water, and ether-extracted $(3 \times 5 \text{ ml})$. The combined extracts were washed with water and brine, then dried and evaporated to leave a pale yellow oil (0.51 g), containing ca. 55% of the desired product (¹H n.m.r. analysis), which was immediately dissolved in methanol (20 ml) containing toluene-p-sulphonic acid (20 mg). The resulting solution was stirred at room temperature for 16 h, diluted with water (60 ml), and ether-extracted $(3 \times 20$ ml). The combined extracts were washed with saturated aqueous sodium carbonate (10 ml), water (2 imes 10 ml), and finally brine (10 ml), then dried and evaporated. Chromatography of the residue over silica gel eluting with petrolether (3:1) gave the *alcohol* (0.12 g) as a colourless oil; v_{max} (film) 3 390, 1 676, 1 570, 828, and 765 cm⁻¹; τ 2.96 (q, ca. 1, furyl 5-H), 4.16 (furyl 3-H), 4.48-4.76 (m, 2 H), 5.88 (d, J 7, CH_2OH), 6.80 [=C(O)CH₂], 7.85-8.02 (m, 4 H), 8.06 (d, J ca. 1, furyl 4-Me), 8.38 (Me), and 8.42 (Me) (Found: M^+ , 234.161 2. $C_{15}H_{22}O_2$ requires M, 234.162 0).

Methyl (E,E)-3,7-Dimethyl-8-(4-methyl-2-furyl)octa-2,6dienoate (20d).—The foregoing alcohol (0.11 g) was vigorously stirred with manganese dioxide (1.8 g) in hexane (25 ml) at room temperature for 3 h, then filtered through a bed of silica gel. The filter cake was washed thoroughly with ether, and the combined filtrates evaporated to give the

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aldehyde (20c) (0.10 g) as a yellow oil; v_{max} (film) 1 687 cm⁻¹; τ 0.02 (d, J 9, CHO), 2.96 (q; J ca. 1, furyl 5-H), 4.13 (br d, J 9, =CHCHO), 4.16 (furyl 3-H), 4.78-4.93 (m, 1 H), 6.79 [=C(O)CH₂], 7.70-7.92 (m, 4 H), 7.86 (Me), 8.05 (d, J ca. 1, furyl 4-Me), and 8.40 (Me). This was immediately added to a solution of sodium cyanide (0.17 g) and glacial acetic acid (0.06 g) in methanol (25 ml) containing manganese dioxide (1.15 g), and the resulting mixture stirred for 16 h at room temperature.¹⁸ Filtration of the mixture through a small plug of silica gel and evaporation of the filtrate gave a yellow oil, which was partitioned between ether (20 ml) and water (10 ml). Evaporation of the dried ether solution followed by chromatography over silica gel eluting with petrol-ether (95:5) gave the ester (0.075 g) as a colourless oil; λ_{max} (MeOH) 224 nm; v_{max} (film) 1 730, 1 660, 1 246, 1 170, 833, and 770 cm⁻¹, τ 2.94 (q, *J ca.* 1, furyl 5-H), 4.13 (furyl 3-H), 4.32 (br s, =CHCO₂Me), 4.73-4.85 (m, 1 H), 6.33 (OMe), 6.80 [= $C(O)CH_2$], 7.77–7.94 (m, 4 H), 7.87 (Me), 8.06 (d, J ca. 1, furyl 4-Me), and 8.42 (Me) (Found: M^+ , 262.156 6. $C_{16}H_{22}O_3$ requires M, 262.156 9).

(E,E)-3,7-Dimethyl-8-(4-methyl-2-furyl)octa-2,6-dienoic Acid (20e).—A solution of the methyl ester (20d) (0.07 g) in methanol (5 ml) containing potassium hydroxide (0.2 g) and water (0.25 ml) was stirred at 50 °C for 3 h, then poured into ice-cold water and extracted with ether (2 × 10 ml) to give recovered ester (20d) (0.015 g). The aqueous layer was carefully acidified with concentrated hydrochloric acid, then saturated with sodium chloride and ether-extracted (3 × 5 ml). The combined extracts were washed with brine, dried, and evaporated to give the acid (0.045 g) as a colourless oil; $\lambda_{\rm max}$ (MeOH) 221 nm; $v_{\rm max}$, 1 715, 1 656, 834, and 766 cm⁻¹; $\tau 2.95$ (q, J ca. 1, furyl 5-H), 4.16 (furyl 3-H), 4.31 (br s, =CHCO₂H), 4.73—4.83 (m, 1 H), 6.80 [=C(O)CH₂], 7.78— 7.96 (m, 4 H), 7.88 (Me), 8.06 (d, J ca. 1, furyl 4-Me), and 8.42 (Me) (Found: M^+ , 248.141 1. C₁₅H₂₀O₃ requires M, 248.141 2).

3-Furylmethyl (E,E)-3,7-dimethyl-8-(4-methyl-2-furyl)octa-2,6-dienoate (Pleraplysillin-2) (4).—The foregoing acid (20e) (0.04 g) dissolved in dry dichloromethane (1 ml) at 0 °C was treated sequentially with 4-dimethylaminopyridine (4 mg), 3-furylmethanol (0.028 g), and NN'-dicyclohexylcarbodiimide (0.03 g), and the solution stirred without cooling for 3 h.19 A drop of glacial acetic acid was then added followed by n-pentane (6 ml). The precipitated urea was filtered off and the filtrate washed with 0.5M hydrochloric acid (2 imes 2 ml) and saturated aqueous sodium hydrogencarbonate $(2 \times 2 \text{ ml})$, then dried and evaporated. Chromatography of the residue over silica gel eluted with petrol-ether (95:5) gave pure pleraplysillin-2 (0.025 g) as an unstable, colourless oil, $R_{\rm F}$ 0.47; $\lambda_{\rm max.}$ (MeOH) 221 nm; $\nu_{\rm max.}$ (film) 1 715, 1 655, 1 047, 902, and 763 cm⁻¹; τ 2.54 (br s, furyl 2''-H), 2.63 (apparent d, *J ca.* 1, furyl 5''-H), 2.97 (q, *J ca.* 1, furyl 5''-H), 3.59 (bs, furyl 3''-H), 4.16 (furyl 3'-H), 4.32 (bs, $=CHCO_2$), 4.73-4.81 (m, $=CHCH_2$), 5.00 (OCH₂), 6.80 [=C(O)CH₂], 7.80-7.94 (m, 4 H), 7.96 (Me), 8.06 (d, J ca. 1, furyl 4'-Me), and 8.42 (Me); m/e 328 (20%), 247 (35), 231 (15), 149 (69), and 95 (100) (Found: M^+ , 328.1673. $C_{20}H_{24}O_4$ requires M, 328.167 5).

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