Structure and Synthesis of Pallescensin E Utilising a Modified Wadsworth–Emmons Reaction

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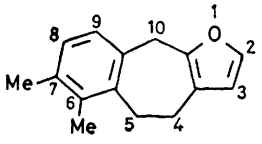
A modified Wadsworth–Emmons reaction using a catalytic amount of 15-crown-5 has been employed in the synthesis of the naturally occurring furosesquiterpene pallescensin E. The structure of this compound has been confirmed by comparison of its spectral data with those of the synthesised isomer, 9,10-dihydro-7,8-dimethyl-4*H*-benzo[4,5]cyclohepta[1,2-*b*]furan.

PALLESCENSIN E (1), a furosesquiterpene containing the monocyclofarnesyl skeleton, has been isolated from the marine sponge *Disidea pallescens*.[1] The structure (1) was proposed on the basis of spectral and chemical data [1] which failed, however, to distinguish structure (1) from its isomer (2),[2] and the decision in favour of the former was made on biogenetic grounds.[1] We report the total synthesis of compounds (1) and (2), and demonstrate that (1) is identical with naturally occurring pallescensin E. Furthermore, in this synthesis we have utilised a modification of the Wadsworth–Emmons procedure for olefin formation involving the addition of a catalytic quantity of crown ether to the reaction mixture.



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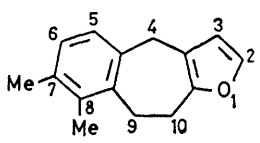

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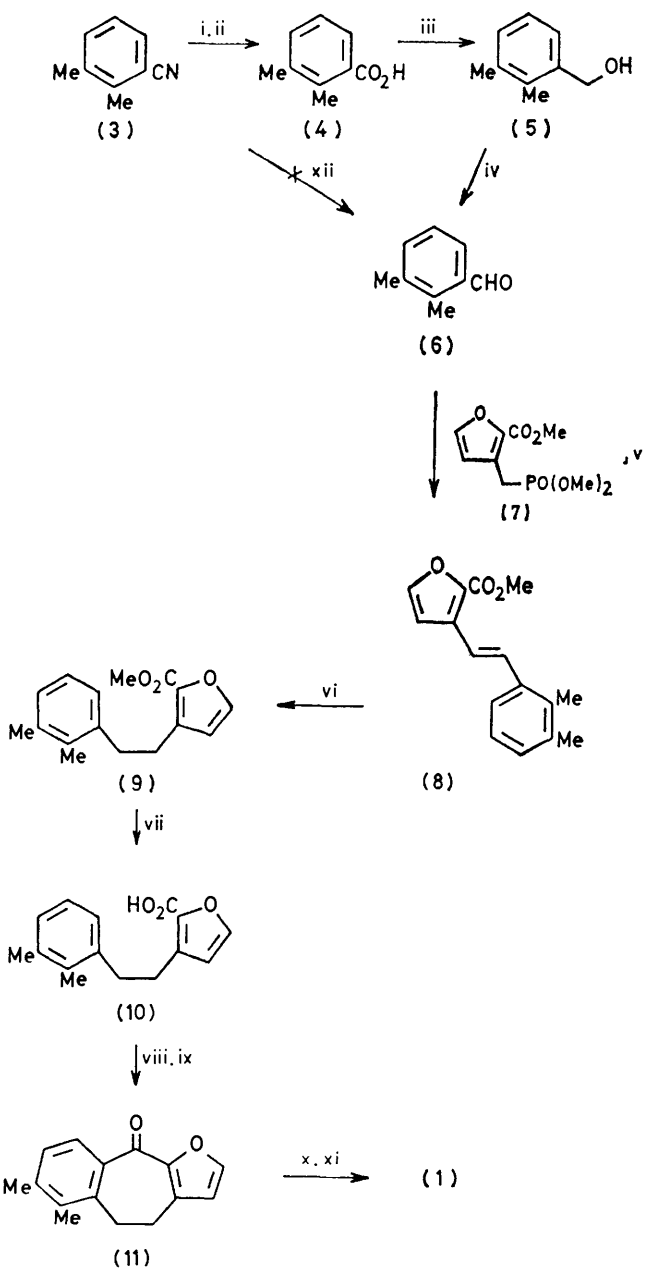
RESULTS AND DISCUSSION

The target compound (1) was synthesised as outlined in Scheme 1. Hydrolysis in basic media of the commercially available nitrile (3) [2] gave 2,3-dimethylbenzoic acid (4), which on reduction with lithium aluminium hydride gave the alcohol (5). Oxidation of the alcohol (5) with pyridinium chlorochromate gave 2,3-dimethylbenzaldehyde (6). This three-step route to (6) was used because direct Stephens reduction [4] of the nitrile (3) did not yield the desired aldehyde (6).

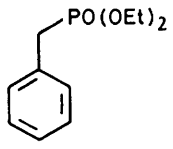
No reaction could be achieved between the phosphonate (7) and the aldehyde (6), either under the conditions of Seus and Wilson [5] or under a number of other literature conditions (*e.g.* NaOMe, 20—110 °C, Me_2-NCHO).[6] A study of the reaction of diethyl benzylphosphonate (12) with a number of aryl and furyl aldehydes and ketones showed that the addition of a catalytic quantity of crown ether greatly facilitated this reaction. Near quantitative yields of olefin products were obtained in short reaction times and at lower temperatures than those conventionally used (0—25 °C instead of 80 °C).[6,7]

In the present study *trans*-stilbene (8) was obtained in 45% yield when a catalytic amount of 15-crown-5 was added to the reaction mixture containing the phos-



SCHEME 1 *Reagents:* i, KOH–H_2O; ii, HCl; iii, $LiAlH_4$-tetrahydrofuran; iv, pyridinium chlorochromate–CH_2Cl_2; v, NaH–$(MeO[CH_2]_2)_2O$–15-crown-5; vi, H_2–$Rh(Ph_3P)_3Cl$; vii, NaOH–H_2O; viii, $SOCl_2$–benzene; ix, $AlCl_3$–$PhNO_2$; x, $TsNHNH_2$–EtOH–TsOH; xi, $NaCNBH_3$–Me_2NCHO; xii, $SnCl_4$–EtOH

phonate (7) and aldehyde (6). Without the addition of crown ether this reaction proceeded in only 10% yield. Hydrogenation of stilbene (8) in the presence of Rh-$(Ph_3P)_3Cl$ [8] gave the ester (9) in 54% yield, which was hydrolysed with aqueous sodium hydroxide to give the acid (10).* Reaction of the acid (10) with thionyl chloride followed by cyclisation of the acid chloride obtained with aluminium chloride gave the ketone (11) in a yield of 78%. Reduction of this ketone by the method of Hutchins [9] gave the desired furosesquiterpene (1).



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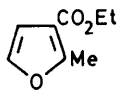

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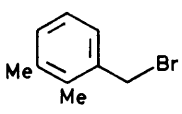

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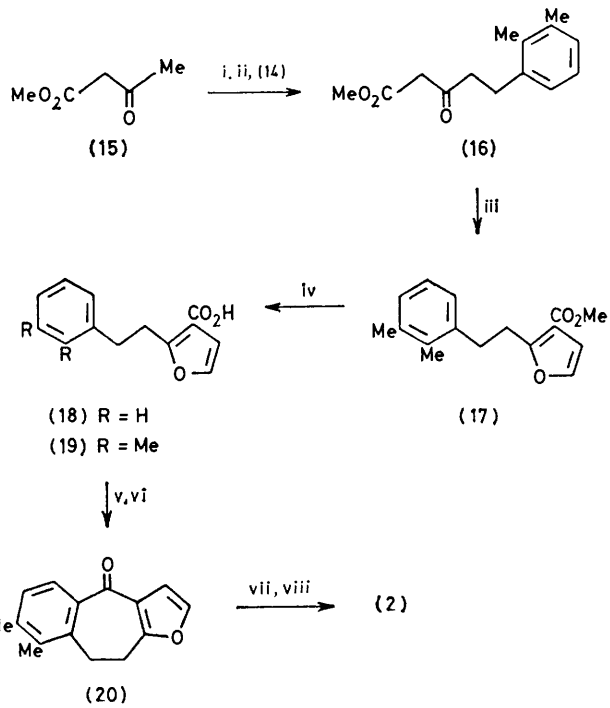
A five-step synthesis has been used by Rivalle to prepare the acid (18) from the furan (13).[10] We found, however, that the furoic acid (19) could be synthesised in three steps from methyl 3-oxobutanoate (15) (Scheme 2). Thus, the target molecule (2) was synthesised as outlined in Scheme 2. Reaction of the dianion of methyl 3-oxobutanoate (15) with 2,3-dimethylbenzyl bromide (14) gave the oxo-ester (16) in 92% yield. Cyclisation of (16) with aqueous chloroacetaldehyde gave the furoic ester (17) in good yield (74%), and this was subsequently hydrolysed to the acid (19). Cyclisation of the acid (19) followed by reduction of the resulting ketone (20) by treatment of its tosylhydrazone with sodium cyanotrihydridoborate gave the furosesquiterpene (2).

The ^1H n.m.r. spectra of compounds (1) and (2) exhibited many similarities but were markedly different in two regions. The spectrum of (2) showed a broad singlet for the two ' dibenzylic ' protons (C-4) at δ 3.57, whereas that of (1) showed a broad singlet for the ' dibenzylic ' protons (C-10) at δ 3.91, in good agreement with the published value of 3.90 for pallascensin E.[1] The spectrum of (2) also showed a single, four-proton multiplet for the ' monobenzylic ' protons (C-9 and C-10) at δ 2.72, whereas the spectrum of (1) showed a pair of two-proton multiplets, at δ 2.82 and 2.42, again in good agreement with the published values of 2.80 and 2.44 for pallescensin E.[1] The remaining spectral data for (1) were in good agreement with the published data.[1]

* A number of alternative hydrogenation conditions (*e.g.* Pt/C, H_2/EtOH; Pd/C, H_2/EtOAc *etc.*) either returned the starting stilbene (8) unchanged or resulted in substantial decomposition.



SCHEME 2 *Reagents:* i, NaH–tetrahydrofuran; ii, BuLi; iii, $ClCH_2CHO$–pyridine–H_2O; iv, KOH–H_2O; v, $SOCl_2$–benzene; vi, $AlCl_3$–$PhNO_2$; vii, $TsNHNH_2$–EtOH–TsOH; viii, NaCN-BH_3–Me_2NCHO

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 157-G spectrometer. N.m.r. spectra were recorded with a Varian Associates XL-100-12 (deuterium lock) spectrometer using tetramethylsilane as internal standard. Routine and high-resolution mass spectra were obtained with a Kratos MS30 instrument fitted with the DS 50S Data System. U.v. spectra were recorded on a Pye–Unicam SP 800 spectrometer. M.p.s were determined using an Electrothermal electrically heated block. ' Flash ' column chromatography refers to the method of Still [11] and was carried out on MN-Kieselgel 60 230—400 mesh silica gel. Elemental analyses were carried out at the micro-analytical laboratory, University College, London.

2,3-*Dimethylbenzyl Alcohol* (5).—2,3-Dimethylbenzonitrile (3) [3] (48 g, 0.36 mol) was hydrolysed in aqueous potassium hydroxide (30%; 300 ml) to give 2,3-dimethylbenzoic acid (4) as a white powder (53.0 g, 96%), m.p. 144—145.5° (lit.,[3] 141.5—144°).

The acid (4) (50.0 g, 0.33 mol) was reduced by lithium aluminium hydride (10 g, 0.33 mol) in tetrahydrofuran (250 ml) to yield 2,3-dimethylbenzyl alcohol (5) as a colourless oil (28 g, 62%), b.p. 128—131° at 13 mmHg (lit.,[12] 128—130° at 12 mmHg), which crystallised; m.p. 63—66° (lit.,[13] 64°).

2,3-*Dimethylbenzaldehyde* (6).—2,3-Dimethylbenzyl alcohol (5) (13.6 g, 0.10 mol) was oxidised by pyridinium chlorochromate [14] (24 g, 0.112 mol) in dichloromethane (40 ml) to give 2,3-dimethylbenzaldehyde (6) as a colourless oil (13.1 g, 98%), b.p. 90° at 13 mmHg (lit.,[3] 86—88° at 10 mmHg).

(E)-*Methyl* 3-(2,3-*Dimethylstyryl*)*furan*-2-*carboxylate* (8).—A solution of dimethyl 2-methoxycarbonyl-3-furylmethylphosphonate (7) [15] (23.1 g, 0.093 mol), 2,3-dimethylbenz-

aldehyde (6) (13.5 g, 0.1 mol), and 15-crown-5 (50 mg, 0.2 mmol) in dry bis-(2-methoxyethyl) ether (50 ml) was added dropwise to a suspension of sodium hydride (50% dispersion in oil; 4.8 g, 0.1 mol) in the same solvent (150 ml) at 80 °C over 0.5 h. After stirring at 80 °C for 1 h, and at room temperature for 1 h, the orange suspension which resulted was poured into saturated aqueous sodium chloride (500 ml) and the mixture extracted with ether (3 × 200 ml). The combined extracts were washed with aqueous sodium hydrogen sulphite (10%; 2 × 50 ml) and saturated aqueous sodium chloride (2 × 100 ml), dried ($MgSO_4$), and evaporated *in vacuo* to give a brown oil which was distilled *in vacuo* to give the *styrylfuran* (8) as a pale yellow oil (11.5 g, 45%), b.p. 158—164° at 0.1 mmHg, which crystallised; m.p. 64—65° (Found: C, 74.9; H, 6.4. $C_{16}H_{16}O_3$ requires C, 75.0; H, 6.3%); $\lambda_{max.}$ (EtOH) 302 (ε 11 900), 246 (10 700), and 213 nm (13 200); $\nu_{max.}$ (CCl_4 soln.) 1 710 cm^{-1}; $\delta_H(CCl_4)$ 2.27 (6 H, s, 2 $ArCH_3$), 3.86 (3 H, s, CO_2CH_3), 6.84 (1 H, d, *J* 2 Hz, furan β-H), 6.98—8.62 (6 H, m, furan α-H, CH=CH, 3 ArH); $\delta_C(C^2HCl_3)$ 15.4, 20.6, 51.7, 109.5, 120.1, 124.3, 126.9, 129.9, 132.2, 132.6, 134.5, 136.1, 136.9, 139.7, 145.5, and 159.8; *m/z* 256 (M^+, 82%), 197 (100), 182 (54), 169 (60), 153 (36), and 105 (36).

Methyl 3-(2,3-*Dimethylphenethyl*)*furan*-2-*carboxylate* (9).—A solution of the styrylfuran (8) (30.5 g, 0.12 mol) and chlorotris(triphenylphosphine)rhodium [8] (1 g) in ethanol–benzene (1 : 1, 800 ml) was degassed with argon and then hydrogenated at 70 °C under 160 atm for 14 days. The solution was evaporated *in vacuo* to give a black oil, which was dissolved in ethanol (200 ml) and filtered through silica gel (Kieselgel GF 254, Type 60). The filtrate was evaporated *in vacuo* to give a mixture as a light brown oil, which was separated by flash column chromatography. Elution with ether–light petroleum (b.p. 40—60 °C) (1 : 4) gave the *phenethylfuran* (9) as colourless microcrystals (16.6 g, 54%), m.p. 34—36° (Found: C, 74.1; H, 7.1. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%), $\lambda_{max.}$ (EtOH) 216 (ε 12 900) and 253 nm (12 600); $\nu_{max.}$ (film) 1 715 cm^{-1}; $\delta_H(C^2HCl_3)$ 2.27 and 2.31 (6 H, 2 s, 2 $ArCH_3$), 2.74—3.17 (4 H, m, 2 CH_2), 3.89 (3 H, s, CO_2CH_3), 6.33 (1 H, d, *J* 2 Hz, furan β-H), 7.10 (3 H, br, s, 3 ArH), and 7.41 (1 H, d, *J* 2 Hz, furan α-H); $\delta_C(C^2HCl_3)$ 14.9, 20.7, 26.8, 34.3, 51.6, 114.0, 125.5, 127.1, 128.0, 134.6, 135.3, 136.9, 139.3, 139.9, 145.0, and 159.8; *m/z* 258 (M^+, 9%), 226 (5), 120 (10), 119 (100), 91 (6), and 77 (4).

3-(2,3-*Dimethylphenethyl*)*furan*-2-*carboxylic Acid* (10).—A solution of the ester (9) (0.80 g, 0.31 mol) in ethanol (10 ml) was treated with aqueous sodium hydroxide solution (10%; 50 ml) and boiled under reflux for 1 h. The mixture was cooled to room temperature, acidified with M-hydrochloric acid, cooled on ice, and filtered to give a white solid, which was crystallised from ethanol–water to yield the *acid* (10) as white microcrystals (0.53 g, 69%), m.p. 174—176° (Found: C, 73.5; H, 6.7. $C_{15}H_{16}O_3$ requires C, 73.8; H, 6.6%); $\lambda_{max.}$ (EtOH) 245 (ε 11 800) and 215 nm (12 800); $\nu_{max.}$ (Nujol) 1 680 cm^{-1}; $\delta_H[(C^2H_3)_2SO]$ 2.23 and 2.26 (6 H, 2 s, $ArCH_3$), 2.64—3.15 (4 H, m, 2 CH_2), 6.56 (1 H, d, *J* 2 Hz, furan β-H), 6.99 (3 H, br, s, 3 ArH), and 7.77 (1 H, d, *J* 2 Hz, furan α-H); $\delta_C[(C^2H_3)_2SO]$ 14.5, 20.4, 26.5, 33.8, 114.0, 125.2, 126.8, 127.7, 134.2, 136.2, 139.3, 140.1, 145.3, and 160.3; *m/z* 244 (M^+, 7%), 120 (8), 119 (100), 91 (6), 77 (3), and 41 (3).

5,10-*Dihydro*-6,7-*dimethyl*-4H-*benzo*[5,6]*cyclohepta*[1,2-b]-*furan*-10-*one* (11).—A suspension of the acid (10) (10.36 g, 0.042 mol) in benzene (300 ml) was treated with thionyl chloride (6.3 ml, 10.3 g, 0.086 mol) and boiled under reflux for 2 h. The solvent was removed *in vacuo* to give an orange solid which was dissolved in nitrobenzene (300 ml). The resulting solution was cooled to 0 °C and aluminium chloride (15 g, 0.11 mol) added. The mixture was stirred at room temperature for 16 h, then at 80 °C for 4 h, poured into water, and extracted with ether (3 × 100 ml). The extracts were washed with aqueous sodium hydroxide (10%; 1 × 50 ml), saturated aqueous sodium hydrogen carbonate (1 × 50 ml), saturated aqueous sodium chloride (2 × 100 ml), and dried ($MgSO_4$). The extracts were evaporated *in vacuo* to leave a black oil which was concentrated to *ca.* 20 ml by distillation at reduced pressure. The residue was dissolved in ether–light petroleum (b.p. 40—60 °C) (1 : 4) and passed down a short silica column (2 in), and the solution was evaporated to give a brown oil (9 g) which crystallized. The solid mixture (3 × 3 g) was separated by flash column chromatography. Elution with ether–light petroleum (b.p. 40—60 °C) (1 : 4) gave the *benzocycloheptafuranone* (11) as colourless microcrystals (7.52 g, 78%), m.p. 143—145° (Found: C, 79.2; H, 6.1. $C_{15}H_{16}O_3$ requires C, 79.6; H, 6.2%); $\lambda_{max.}$ (EtOH) 212 (ε 7 600), 279sh (7 200), 236 (3 600), and 306 nm (10 200); $\nu_{max.}$ ($CHCl_3$ soln.) 1 630 cm^{-1}; $\delta_H(C^2HCl_3)$ 2.33 and 2.36 (6 H, 2 s, 2 $ArCH_3$), 2.70—2.96 (2 H, m, CH_2), 3.04—3.26 (2 H, m, CH_2), 6.46 (1 H, d, *J* 2 Hz, furan β-H), 7.08 (1 H, d, *J* 8 Hz, H-8), 7.50 (1 H, d, *J* 2 Hz, furan α-H), and 7.67 (1 H, d, *J* 8 Hz, H-9); $\delta_C(C^2HCl_3)$ 15.9, 21.7, 25.2, 29.5, 113.4, 127.3, 128.5, 134.0, 136.9, 137.7, 141.8, 146.5, 149.3, and 181.9; *m/z* 226 (M^+, 100%), 225 (31), 211 (25), 197 (21), 183 (21), and 155 (21).

5,10-*Dihydro*-6,7-*dimethyl*-4H-*benzo*[5,6]*cyclohepta*[1,2-b]-*furan* (1).—A mixture of the benzocycloheptafuranone (11) (1.0 g, 4.4 mmol), 4-tolylsulphonylhydrazine (0.82 g, 4.4 mmol) and toluene-4-sulphonic acid (50 mg) in ethanol (2 ml) was heated at 80 °C for 16 h. The solvent was removed from the resulting suspension *in vacuo* to yield a paste, which was dissolved in dimethylformamide (5 ml). To the resulting solution sodium cyanotrihydridoborate (1.0 g, 14.7 mmol) was added, and the mixture heated at 120 °C for 12 h, poured into water (100 ml) and extracted with ether–light petroleum (b.p. 40—60 °C) (1 : 4) (3 × 25 ml). The extracts were dried (K_2CO_3) and evaporated to give a mixture as a red oil (1.1 g) which was separated by flash column chromatography. Elution with light petroleum (b.p. 40—60 °C) gave a two-component mixture as an oil (920 mg) which was separated by flash column chromatography. Elution with light petroleum (b.p. 60—80 °C) gave the *benzocycloheptafuran* [1] (1) as a colourless oil (290 mg, 31%) (Found: M^+, 212.1188. $C_{15}H_{16}O$ requires *M*, 212.1201); $\lambda_{max.}$ (EtOH) 217 nm (ε 12 600); $\delta_H(C_6^2H_6)$ 2.01 (3 H, s, $ArCH_3$), 2.10 (3 H, s, $ArCH_3$), 2.42 (2 H, m, CH_2), 2.82 (2 H, m, CH_2), 3.91 (2 H, br, s, furan CH_2Ar), 5.94 (1 H, d, *J* 2 Hz, furan β-H), 6.77 (2 H, s, 2 ArH), and 7.01 (1 H, d, *J* 2 Hz, furan α-H); *m/z* 213 ($M^+ + 1$, 15%), 212 (M^+, 95), 198 (15), 197 (100), 183 (14), and 167 (27).

Methyl 5-(2,3-*Dimethylphenyl*)-3-*oxopentanoate* (16).—A solution of dry methyl 3-oxobutanoate (15) (8.3 g, 0.07 mol) in anhydrous tetrahydrofuran (20 ml) was added dropwise to a suspension of sodium hydride (50% dispersion in oil; 3.36 g, 0.07 mol) in dry tetrahydrofuran (200 ml) at −5 °C.[16] The mixture was stirred for 15 min at 0 °C and n-butyl-lithium (1.6M-solution in hexane; 43 ml, 0.069 mol) added dropwise; the yellow-orange solution was stirred for 15 min at 0 °C. A solution of 2,3-dimethyl-

benzyl bromide (14) [17] (14.3 g, 0.07 mol) in tetrahydrofuran (30 ml) was added over 5 min. The resulting pale yellow suspension was stirred at 0 °C for 15 min and at room temperature for 5 min. A solution of concentrated hydrochloric acid (14 ml) in water (35 ml) was added, and the suspension stirred for 2 min. The aqueous phase was separated and extracted with ether (2 × 25 ml). The combined extracts were washed with saturated aqueous sodium chloride (2 × 250 ml), dried ($MgSO_4$), and evaporated to give the *oxo-ester* (16) as a pale yellow oil (15.1 g, 92%). Distillation of 1.0 g *in vacuo* gave a colourless oil (0.75 g), b.p. 152° at 0.1 mmHg, which was subjected to flash column chromatography. Eluting with ether–light petroleum (b.p. 40—60 °C) (1 : 4) gave a colourless *oil* (0.52 g) (Found: C, 72.1; H, 7.6. $C_{14}H_{18}O_3$ requires C, 71.8; H, 7.7%); $\lambda_{max.}$ (EtOH) 214 (ε 10 600) and 248 nm (1 550); $\nu_{max.}$ (film) 1 722 and 1 752 cm^{-1}; $\delta_H(C^2HCl_3)$ 2.20 and 2.28 (6 H, 2 s, 2 $ArCH_3$), 2.26—3.10 (4 H, m, 2 CH_2), 2.44 (2 H, s, $CCH_2CO_2CH_3$), 3.72 (3 H, s, CO_2CH_3), and 7.05 (3 H, br, s, 3 ArH); *m/z* 234 (M^+, 0.3%), 216 (29), 142 (47), 133 (32), 119 (100), 118 (48), 117 (23), and 91 (24).

Methyl 2-(2,3-Dimethylphenethyl)furan-3-carboxylate (17).—A mixture of the oxo-ester (16) (14.1 g, 0.06 mol), pyridine (4.8 ml, 4.7 g, 0.06 mol) and chloroacetaldehyde (50—55% solution in water; 9.5 ml) was stirred at room temperature for 16 h. The mixture was poured into saturated aqueous sodium chloride (200 ml) and extracted with ether (3 × 100 ml). The extracts were washed with saturated aqueous sodium chloride (2 × 50 ml), dried ($MgSO_4$), and evaporated to give a pale yellow oil (18.1 g), which was distilled *in vacuo* to yield the furan (17) as a colourless oil (11.5 g, 74%), b.p. 195° at 0.1 mmHg. Crystallisation from di-isopropyl ether gave colourless *microcrystals* m.p. 81—83° (Found: C, 74.1; H, 7.0. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%); $\lambda_{max.}$ (EtOH) 214 (ε 9 700) and 247 nm (6 200); $\nu_{max.}$ (film) 1 712 cm^{-1}; $\delta_H(C^2HCl_3)$ 2.26 and 2.29 (6 H, 2 s, 2 $ArCH_3$), 2.84—3.38 (4 H, m, 2 CH_2), 3.80 (3 H, s, CO_2CH_3), 6.64 (1 H, d, *J* 2 Hz, furan β-H), 7.01 (3 H, s, 3 ArH), and 7.26 (1 H, d, *J* 2 Hz, furan α-H); $\delta_C(C^2HCl_3)$ 164.3, 162.2, 140.7, 138.9, 136.9, 128.2, 127.1, 125.5, 113.3, 110.8, 51.2, 32.6, 28.9, 20.7, and 14.8; *m/z* 259 ($M^+ + 1$, 2%), 258 (M^+, 11%), 226 (10), 139 (5), 120 (10), and 119 (100).

2-(2,3-Dimethylphenethyl)furan-3-carboxylic Acid (19).—Aqueous potassium hydroxide (10%; 50 ml) and ethanol (5 ml) were added to a suspension of the ester (17) (10.5 g, 0.041 mol) in water (20 ml). The mixture was boiled under reflux for 1 h, cooled to room temperature, and set aside for 16 h. The solution was acidified with 2M-hydrochloric acid and filtered to give a yellow powder (8.1 g). The powder was crystallised from ethanol–water to yield the *acid* (19) as a light tan powder (5.5 g, 55%), m.p. 152—154° (decomp.) (Found: C, 73.5; H, 6.8. $C_{15}H_{16}O_3$ requires C, 73.8; H, 6.6%); $\lambda_{max.}$ (EtOH) 215 (ε 14 900), and 202 nm (6 800); $\nu_{max.}$ (Nujol) 1 684 cm^{-1}; $\delta_H(C^2HCl_3)$ 2.27 and 2.29 (6 H, 2 s, 2 Ar CH_3), 3.00 (2 H, m, CH_2), 3.25 (2 H, m, CH_2), 6.70 (1 H, d, *J* 2 Hz, furan β-H), 7.01 (3 H, s, 3 ArH), and 7.30 (1 H, d, *J* 2 Hz, furan α-H); *m/z* 244 (M^+, 7%), 226 (3), 120 (8), 119 (100), and 91 (8).

9,10-Dihydro-7,8-dimethyl-4H-benzo[4,5]cyclohepta[1,2-b]furan-4-one (20).—A suspension of the acid (19) (4.21 g, 0.017 mol) in benzene (50 ml) was treated with thionyl chloride (1.4 ml, 1.63 g, 0.019 mol) and the mixture boiled under reflux for 1.5 h. The solvent was removed *in vacuo* to give an orange-brown paste, which was taken up in nitrobenzene (200 ml); aluminium chloride (4.6 g, 0.034 mol) was added. The resulting mixture was stirred at 95—90 °C for 16 h, poured into water (300 ml), and extracted with ether (3 × 100 ml). The extracts were washed with saturated aqueous sodium hydrogen carbonate (2 × 50 ml) and saturated aqueous sodium chloride (1 × 100 ml). The extracts were dried (K_2CO_3) and evaporated to give a black oil. The oil was dissolved in ether (200 ml) and passed through a silica gel (Kieselgel GF254 Type 60) column (1 in × 4 in diam.); the solution was evaporated to give a brown oil. This oil was concentrated at 0.1 mmHg to *ca.* 5 ml and separated by flash column chromatography. Elution with ether–light petroleum (b.p. 40—60 °C) (1 : 4) gave the *benzocycloheptafuranone* (20) as colourless microcrystals (1.00 g, 26%), m.p. 79—81° (Found: C, 79.6; H, 6.3. $C_{15}H_{14}O_2$ requires C, 79.7; H, 6.2%); $\lambda_{max.}$ (EtOH) 215 (ε 19 400), 226sh (14 500, sh), 267 (9 900), and 395m (7 800); $\nu_{max.}$ (Nujol) 1 638 cm^{-1}; $\delta_H(C^2HCl_3)$ 2.31 and 2.34 (6 H, 2 s, $ArCH_3$), 2.92—3.30 (4 H, m, 2 CH_2), 6.83 (1 H, d, *J* 2 Hz, furan β-H), 7.10 (1 H, d, *J* 8 Hz, H-6), 7.26 (1 H, d, *J* 2 Hz, furan α-H), and 7.54 (1 H, d, *J* 8 Hz, H-5); $\delta_C(C^2HCl_3)$ 15.8, 21.6, 27.2, 110.5, 123.8, 126.8, 128.6, 133.9, 136.4, 138.8, 141.2, 163.4, and 188.7; *m/z* 226 (M^+, 100%), 225 (45), 211 (57), 183 (47), 169 (59), 155 (47), 115 (51), and 91 (41).

9,10-Dihydro-7,8-dimethyl-4H-benzo[4,5]cyclohepta[1,2-b]furan (2).—A mixture of the benzocycloheptafuranone (20) (0.50 g, 2.21 mmol), 4-tolylsulphonylhydrazine (0.41 g, 2.21 mmol), and toluene-4-sulphonic acid (50 mg) was heated at 80 °C for 2.5 h. The solvent was removed from the resulting suspension *in vacuo* to give an orange paste, which was dissolved in dry dimethylformamide (3 ml). Sodium cyanotrihydroborate (0.48 g, 7.6 mmol) and toluene-4-sulphonic acid (20 mg) were added to the solution, and the mixture was heated at 120 °C for 8 h. The solution was left at room temperature for 16 h, poured into water (20 ml) and extracted with ether–light petroleum (b.p. 40—60 °C) (1 : 9) (3 × 10 ml). The extracts were washed with saturated aqueous sodium chloride (2 × 10 ml), dried (K_2CO_3), and evaporated to give a mixture as a pale yellow oil (0.410 mg), which was separated by flash column chromatography. Elution with ether–light petroleum (b.p. 40—60 °C) (1 : 9) gave a mixture as a colourless oil (253 mg) and the benzocycloheptafuranone (20) (30 mg, 6%). The mixture was purified by flash column chromatography; elution with light petroleum (b.p. 40—60 °C) gave the *benzocycloheptafuran* (2) as a colourless oil (211 mg, 45%) (Found: M^+, 212.1080, $C_{15}H_{16}O$ requires *M*, 212.1201); $\delta_H(C_6^2H_6)$ 1.98 (3 H, s, $ArCH_3$), 2.12 (3 H, s, $ArCH_3$), 2.72 (4 H, m, 2 CH_2), 3.57 (2 H, br, s, $ArCH_2$ furan), 6.05 (1 H, d, *J* 2 Hz, furan-β-H), 6.83 (2 H, br, s, 2 ArH), and 7.03 (1 H, d, *J* 2 Hz, furan α-H); *m/z* 212 (M^+, 92%), 197 (100), 169 (33), 149 (27), 91 (42), and 77 (25).

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